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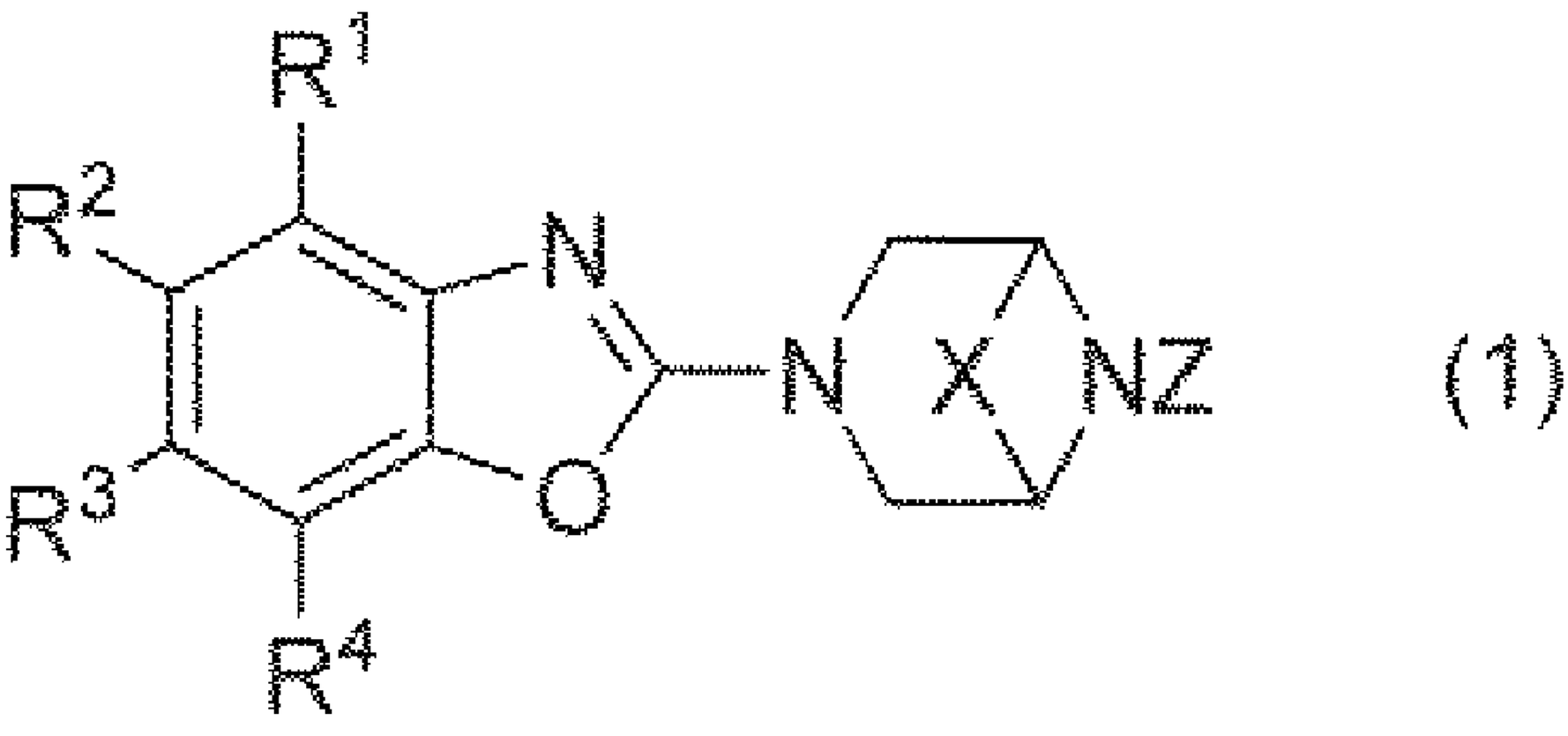
(54) Title: NOVEL COMPOUND AND PHARMACOLOGICALLY ACCEPTABLE SALT



(1)

(57) Abrégé/Abstract:
Provided is a compound represented by general formula (1) or a pharmaceutically-acceptable salt thereof. [In formula (1), R^1 and R^2 may be the same or different from each other, and each represents a hydrogen atom, a halogen atom, a hydroxy group, a carboxy group, a cyano group, or an optionally-substituted C_{1-6} alkyl group or the like; R^3 represents a hydrogen atom; R^4 represents an optionally-substituted 4- to 10-membered monocyclic heterocyclic group containing 1-4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom; X represents a group represented by $-CH_2-$, $-CH_2-CH_2-$, $-CH_2-CH_2-CH_2-$, or $-CH_2-O-CH_2-$; and Z represents a hydrogen atom or a hydroxy group.]

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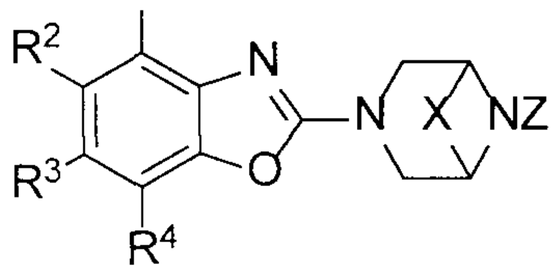
[ABSTRACT]

A compound represented by the general formula (1) below or a pharmacologically acceptable salt thereof :



(1)

[In the formula (1),

R^1 and R^2 may be the same or different and each represents a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group et al.; R^3 represents a hydrogen atom; R^4 represents an optionally substituted 4- to 10-membered monocyclic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom; X represents a group represented by the following formula: $-CH_2-$, $-CH_2-CH_2-$, $-CH_2-CH_2-CH_2-$, or $-CH_2-O-CH_2-$; and Z represents a hydrogen atom or a hydroxyl group.]

DEMANDE OU BREVET VOLUMINEUX

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THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

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NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

[DESCRIPTION]

[TITLE OF THE INVENTION]

NOVEL COMPOUND AND PHARMACOLOGICALLY ACCEPTABLE SALT THEREOF

[TECHNICAL FIELD]

The present invention relates to a novel compound and a pharmacologically acceptable salt thereof, and particularly relates to a novel compound, a pharmacologically acceptable salt thereof, and a PDE4 inhibitor containing the same.

[RELATED BACKGROUND ART]

Phosphodiesterase (PDE) is known as an important enzyme which inactivates cyclic nucleotides (cAMP and cGMP) being second messengers by hydrolyzing one side of phosphodiester bonds present in the cyclic nucleotides. PDEs which break down cAMP are classified into several isoforms. Among these, type IV phosphodiesterase (PDE4) is one of the principal cAMP-breaking enzymes present in many inflammatory cells, immune cells, blood, and organs such as the brain and the lungs (Non-Patent Document 1: International Journal of Chronic Obstructive Pulmonary Disease, 2008, 3(4), pp. 543-561).

A PDE4 inhibitor reduces the production and the release of various inflammatory cytokines such as TNF-α and IL-23, and therefore is known to be effective

for the treatment of various inflammatory diseases involving TNF-α and the like (Non-Patent Document 2: Expert Opinion on Investigational Drugs, 2002, 11(1), pp. 1-13). In addition, the PDE4 inhibitor is reported to have an effect not only on respiratory inflammatory diseases (asthma and chronic obstructive pulmonary disease (COPD)) but also on dermal inflammatory diseases (psoriasis and atopic dermatitis), and moreover is reported to have a potential to produce an effect on mental illnesses such as depressive disorder and dysmnesia (see Non-Patent Document 2). Furthermore, in animal models, the PDE4 inhibitor is also suggested to be effective on interstitial pneumonia such as idiopathic pulmonary fibrosis (Non-Patent Document 3: British Journal of Pharmacology, 2009, 156, pp. 534-544). What is more, the PDE4 inhibitor is suggested to be effective on various fibrosis (Non-Patent Document 4: Journal of Cellular Physiology, 2011, 226, pp. 1970-1980) and on systemic sclerosis being a type of fibrosis (Non-Patent Document 5: Annals of the Rheumatic Diseases 2017, 76, pp. 1133-1141) because the PDE4 is involved in the functions of fibroblasts.

It has been known in recent years that expression levels of the PDE4 are excessively high in cells derived from patients with colorectal cancer,

and its inhibitor has antitumor activity (Non-Patent Document 6: Molecular Cancer, 2012, 11:46). There has been also reported that the PDE4 is involved in the growth of lung cancer and angiogenesis, and its inhibitor has a potential to produce an effect on lung cancer as well (Non-Patent Document 7: Oncogene, 2013, 32, pp. 1121-1134) and is a possible candidate for a promising method for treating brain tumors (Non-Patent Document 8: Trends in Pharmacological Sciences, June 2011, Vol. 32, No. 6, pp. 337-344) and acute lymphocytic leukemia (Non-Patent Document 9: Blood, May 2002, Vol. 99, No. 9, pp .3390-3397), for example. Thus, the PDE4 inhibitor might be effective on various types of cancer.

There has been also reported that the PDE4 inhibitor might be effective on metabolic diseases such as obesity and diabetes (Non-Patent Document 10: Cell 148, February 2012, pp. 421-433) and on cognitive disorders caused by aging, Alzheimer's disease, Parkinson's disease, schizophrenia, and Huntington's disease (Non-Patent Document 11: Expert Opinion on Therapeutic Targets, September 2013, 17(9), pp. 1011-1027).

Theophylline, which is known as a non-selective PDE inhibitor, has conventionally been used for the treatment of asthma (Non-Patent Document 12: British

Journal of Pharmacology, 2008, 155, pp. 308-315). In addition, ibudilast, a non-selective PDE inhibitor, shows a treatment effect on bronchial asthma and cerebrovascular diseases thanks to its anti-inflammatory action and vasodilation action (Non-Patent Document 13: Expert Opinion on Pharmacotherapy, 2009, 10, pp. 2897-2904) and is used for allergic conjunctivitis (eye lotion) (Non-Patent Document 14: Eye Contact Lens, September 2009, Vol. 35, No. 5, pp. 251-254). Ibudilast is also expected to produce an effect on multiple sclerosis and neuropathic pain (Non-Patent Document 15: Expert Opinion on Investigational Drugs, 2016, Vol. 25, No. 10, pp. 1231-1237). Roflumilast, which is a strong oral PDE4 inhibitor, has been approved and used in Europe and the United States, as a drug applied to chronic obstructive pulmonary disease (COPD) (Non-Patent Document 16: British Journal of Pharmacology, 2011, 163, pp. 53-67). In animal models, roflumilast has been also suggested to be effective on interstitial pneumonia such as idiopathic pulmonary fibrosis (see Non-Patent Document 3). Moreover, clinical trials have been carried out for obesity, dementia, and atopic dermatitis (Non-Patent Document 17: Nature Reviews Drug Discovery, April 2014, Vol. 13, pp. 290-314), and alopecia areata (Non-Patent Document 18:

Summer Meeting of the American Academy of Dermatology (AAD) 2016, Abstract 4070). Furthermore, an effect has been reported of lowering blood sugar levels of patients with diabetes (Non-Patent Document 19: The Journal of Clinical Endocrinology & Metabolism, September 2012, 97(9), pp. 1720-1725). In recent years, apremilast, which is an oral PDE4 inhibitor too, has been approved and widely used in Europe and the United States as a medication for the treatment of psoriatic arthritis and psoriasis vulgaris, and its clinical trials have been carried out for acne, ankylosing spondylitis, rheumatism, Behçet's disease, and atopic dermatitis (Non-Patent Document 17 and Non-Patent Document 20: Drugs, 2014, 74, pp. 825-837). Clinical trials of crisaborole, which is a topical PDE4 inhibitor, have been reported in that crisaborole has an effect on atopic dermatitis of children and adults (Non-Patent Document 21: Journal of the American Academy of Dermatology, September 2016, Vol. 75, No. 3, pp. 494-503). Clinical trials of the PDE4 inhibitor have been carried out for various inflammatory diseases (inflammatory bowel disease, Crohn's disease, multiple sclerosis, rheumatism, sarcoidosis, Behçet's disease, and rhinitis) in addition to the above. Also, non-clinical studies have also pointed out a possibility that the PDE4

inhibitor might be effective on systemic lupus erythematosus. Further, many compounds as the PDE4 inhibitors have a central action and have been reported to have an effect on depressive disorder, Parkinson's disease, learning disability, dysmnesia, and Alzheimer's disease (Non-Patent Document 2 and Non-Patent Document 22: BMC Medicine, 2013, 11:96).

As described above, diseases on which the PDE4 inhibitor might produce effects include asthma, COPD, interstitial pneumonia, various fibrosis such as idiopathic pulmonary fibrosis and systemic sclerosis, inflammatory bowel diseases such as Crohn's disease, multiple sclerosis, rheumatism, ankylosing spondylitis, acne, atopic dermatitis, alopecia areata, allergic conjunctivitis, rhinitis, psoriatic arthritis, psoriasis vulgaris, sarcoidosis, Behçet's disease, systemic lupus erythematosus, cerebrovascular disease, neuropathic pain, depressive disorder, cognitive disorders, learning disability, Parkinson's disease, Alzheimer's disease, Huntington's disease, schizophrenia, various types of cancer (such as colorectal cancer, lung cancer, hematologic cancer, and brain tumor), and metabolic diseases (such as diabetes and obesity).

Japanese Patent Application Publication No. Hei 6-345744 (Patent Document 1) and Japanese Patent

Application Publication No. Hei 10-29987 (Patent Document 2) have reported the activity of a benzoxazole derivative on serotonin 5-HT_3. Additionally, International Publication No. Wo 2015/005429 (Patent Document 3) has reported a benzoxazole derivative which has a PDE4 inhibitory activity. However, the substituent at position 2 in each of these benzoxazole derivatives is a monocyclic heterocycle.

[CITATION LIST]

[PATENT LITERATURE]

[PTL 1] Japanese Unexamined Patent Application Publication No. Hei 6-345744

[PTL 2] Japanese Unexamined Patent Application Publication No. Hei 10-29987

[PTL 3] International Publication No. WO2015/005429

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[NPL 2] Dyke H.J. and Montana J.G.,Expert Opinion on Investigational Drugs,2002,11(1),p.1-13

[NPL 3] Cortijo J. et al.,British Journal of Pharmacology,2009,156,p.534-544

[NPL 4] Selige J. et al.,Journal of Cellular Physiology,2011,226,p.1970-1980

[NPL 5] Maier C. et al.,Annals of the Rheumatic Diseases 2017,76,p.1133-1141

[NPL 6] Tsunoda T. et al.,Molecular Cancer,2012,11:46

[NPL 7] Pullamsetti S.S. et al.,Oncogene,2013,32,p.1121-1134

[NPL 8] Sengupta R. et al.,Trends in Pharmacological Sciences,June 2011,Vol.32,No.6,p.337-344

[NPL 9] Ogawa R. et al.,Blood,May 2002,Vol.99,No.9,p.3390-3397

[NPL 10] Park S.-J. et al.,Cell 148,February 2012,p.421-433,2012

[NPL 11] Richter W. et al.,Expert Opinion on Therapeutic Targets,September 2013,17(9),p.1011-1027

[NPL 12] Spina D.,British Journal of Pharmacology,2008,155,p.308-315

[NPL 13] Rolan P. et al.,Expert Opinion on Pharmacotherapy,2009,10,p.2897-2904

[NPL 14] Sakuma K. et al.,Eye Contact Lens,September 2009,Vol.35,No.5,p.251-254

[NPL 15] Goodman A.D. et al.,Expert Opinion on Investigational Drugs,2016,Vol.25,No.10,p.1231-1237

[NPL 16] Rabe K.F.,British Journal of Pharmacology,2011,163,p.53-67

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Discovery,April 2014,Vol.13,p.290-314

[NPL 18] Shrager D.,Summer Meeting of the American Academy of Dermatology(AAD) 2016, Abstract 4070

[NPL 19] Wouters E.F.W. et al., The Journal of Clinical Endocrinology & Metabolism,September 2012,97(9),p.1720-1725

[NPL 20] Poole R.M. et al.,Drugs,2014,74,p.825-837

[NPL 21] Paller A.S. et al.,Journal of the American Academy of Dermatology,September 2016,Vol.75,No.3,p.494-503

[NPL 22] Kumar N. et al.,BMC Medicine,2013,11:96

[Summary of Invention]

[Technical Problem]

A conventional PDE4 inhibitor has been reported to cause dose-dependent side effects such as gastrointestinal disorders like diarrhea, vomiting, and nausea. The efficacy of the PDE4 inhibitory activity at oral administration and topical administration was not sufficient. Additionally, better pharmacokinetics and metabolic stability are required for sufficient efficacy particularly at oral administration.

The present invention has been made in view of the above problem of the related art, and an object thereof is to provide a novel compound and a pharmacologically acceptable salt thereof which have

an excellent PDE4 inhibitory activity and an excellent metabolic stability. Such a compound and a pharmacologically acceptable salt thereof can be an excellent prevention and therapeutic agent for inflammatory diseases (such as respiratory disease, dermatosis, digestive system disease, Musculoskeletal disease, sensory system disease), fibroses, central nervous system diseases, cancerous diseases, and metabolic diseases.

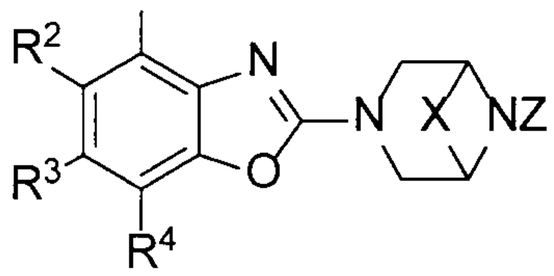
[MEANS FOR SOLVING THE PROBLEMS]

The inventors have conducted extensive research to solve the above problems and found out that a benzoxazole derivative with a bicyclic piperazine ring and a pharmacologically acceptable salt thereof have an excellent PDE4 inhibitory activity and an excellent metabolic stability, thereby completing the present invention.

To be more specific, the present invention is

[1]

a compound represented by the general formula (1) below or a pharmacologically acceptable salt thereof:



(1)

[In the formula (1),

R^1 and R^2 may be the same or different and each represents a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyl group, an optionally substituted C_{6-10} monocyclic or polycyclic aryl group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkyl group, an optionally substituted 4- to 10-membered monocyclic or bicyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic or bicyclic nonaromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted di-C_{1-6} alkyl amino group, an optionally substituted C_{3-7} cycloalkyl amino group, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{2-6} alkenyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted C_{6-10} monocyclic or polycyclic aryloxy group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkyloxy group, an

optionally substituted 4- to 10-membered monocyclic or bicyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic or bicyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group [two C_{1-6} alkyl groups in the di-C_{1-6} alkylsulfamoyl group may form a pyrrolidin-1-yl group or a morpholino group with an adjacent nitrogen atom], a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkylaminocarbonyl group, an optionally substituted C_{1-6} alkyloxycarbonyl group, or an optionally substituted hydroxyaminocarbonyl group,

R^3 represents a hydrogen atom,

R^4 represents an optionally substituted 4- to 10-membered monocyclic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom,

X represents a group represented by the following formula: $-CH_2-$, $-CH_2-CH_2-$, $-CH_2-CH_2-CH_2-$, or $-CH_2-O-CH_2-$, and

Z represents a hydrogen atom or a hydroxyl group.]

[2]

The compound or the pharmacologically acceptable salt thereof according to [1] wherein, in the general formula (1),

R^1 represents a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyl group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} acylamino group, an

optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group [two C_{1-6} alkyl groups in the di-C_{1-6} alkylsulfamoyl group may form a pyrrolidin-1-yl group or a morpholino group with an adjacent nitrogen atom], a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic

aralkylaminocarbonyl group, an optionally substituted C_{1-6} alkyloxycarbonyl group, or an optionally substituted hydroxyaminocarbonyl group, and

R^2 represents a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{2-6} alkenyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an

optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group, a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkylaminocarbonyl group, or an optionally substituted C_{1-6} alkyloxycarbonyl group.

[3]

The compound or the pharmacologically acceptable salt thereof according to [1] wherein, in the general formula (1),

R^1 represents a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyl group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-

membered monocyclic nonaromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group [two C_{1-6} alkyl groups in the di-C_{1-6} alkylsulfamoyl group may form a pyrrolidin-1-yl group or a morpholino group with an adjacent nitrogen atom], a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6}

alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic aralkylaminocarbonyl group, an optionally substituted C_{1-6} alkyloxycarbonyl group, or an optionally substituted hydroxyaminocarbonyl group, and

R^2 represents a hydrogen atom.

[4]

The compound or the pharmacologically acceptable salt thereof according to [1] wherein, in the general formula (1),

R^1 represents a hydrogen atom, and

R^2 represents a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{2-6} alkenyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclyloxy group containing 1 to 4

heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group, a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an aminocarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkylaminocarbonyl group, or an optionally substituted C_{1-6} alkyloxycarbonyl group.

[5]

The compound or the pharmaceuticaly acceptable salt thereof according to [1] wherein, the compound represented by the formula (1) is 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-

(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

7-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(furan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(oxazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(5-fluoropyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-

(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,
7-(5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole,
2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole,
7-(5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,
7-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole,
7-(5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,
2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

N-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)acetamide,

N-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)acetamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole,

N-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide,

N-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide,

N-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-ol,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-isopropoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(oxetan-3-ylmethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)methyl)propane-1,3-diol,

5-(allyloxy)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)acetonitrile,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)acetic acid,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-ol,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-cyclobutoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)acetonitrile,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3-methoxypropan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydrofuran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4,7-di(thiazol-2-yl)benzo[d]oxazole,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)propan-2-ol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)propan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-N,N-dimethyl-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(morpholino)methanone,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(piperidin-1-yl)methanone,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(azetidin-1-yl)methanone,

N-benzyl-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazole-5-carboxamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide,

N-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-N-methylacetamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(morpholinomethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-N,N-dimethylmethanamine,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-one,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-one,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-

yl)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol,

(2-(3,6-diazabicyclo[3.1.1]hepan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-N,N-dimethyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(morpholino)methanone,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(piperidin-1-yl)methanone,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-

yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,
(R)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,
(S)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,
1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,
(R)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,
(S)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,
(R)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,
(S)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,
1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethan-1-ol,
2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-

2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol,

(R)-2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol,

(S)-2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethoxy)-2-methylpropan-2-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethan-1-ol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

1-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-

yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,
(R)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,
(S)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,
1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,
1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethyl acetate,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,
(R)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,
(S)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,
2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-

trifluoroethoxy)ethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)ethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)acetonitrile,

2-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)acetonitrile,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazole,

1-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)propan-2-ol,

1-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

2-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

2-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-

carboxylate,

2-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)propan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(methoxymethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)methanol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)propan-2-ol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)propan-2-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-one,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-

2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-one,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-

yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

2-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)(azetidin-1-yl)methanone,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-N-(2-hydroxyethyl)-N-methyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxamide,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)(3-hydroxy-3-(trifluoromethyl)azetidin-1-yl)methanone,(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)methanol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol,

(R)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol,

(S)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2-methylpropan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(R)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(S)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(R)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(S)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-

(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

(E)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-

(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime,

(Z)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime,

(E)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime,

(Z)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)ethan-1-ol,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetonitrile,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)ethan-1-ol,

2-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetonitrile,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazole,

4-(1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

4-(1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

1-((1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)methyl)cyclopropan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethane-1,1-diol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol,

(R)-2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol,

(S)-2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol,

methyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylic acid,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)propan-2-ol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)propan-2-ol,

1-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(1-

methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-one,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-one,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

(R)-1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

(S)-1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetic acid,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydro-2H-pyran-4-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2-methylpropan-2-ol,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetamide,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-1,1-difluoro-2-methylpropan-2-ol,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2,2-difluoroethan-1-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)propan-2-ol,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)propan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydro-2H-pyran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-2-ol,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-1,1-difluoropropan-2-ol,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-

2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutane-1-carbonitrile,

2-(3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutyl)propan-2-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)cyclopropan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)cyclopropan-1-ol,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1,1-trifluoropropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-2-ol,

3-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2,3-dimethylbutan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxy-2-methylpropoxy)ethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-((1-methoxycyclopropyl)methoxy)ethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxycyclopropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2-methylpropan-2-ol,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutan-1-ol,

1-((1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)methyl)cyclopropan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(pyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(oxazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((tetrahydro-2H-pyran-4-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

4-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-4,4-difluoro-2-methylbutan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)cyclopropan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(R)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(S)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(R)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(S)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

4-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclohexan-1-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(4-methylthiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-4,4,4-trifluoro-2-methylbutan-2-ol,

4-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)tetrahydro-2H-thiopyran 1,1-dioxide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(pyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(pyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(4-methylthiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(5-fluoropyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(oxazol-2-

yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(2H-1,2,3-triazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(((S)-tetrahydrofuran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(((R)-tetrahydrofuran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(oxetan-3-yloxy)-7-(thiazol-2-yl)benzo[d]oxazole,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3,3-difluoro-2-methylpropane-1,2-diol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1,2,4-thiadiazol-5-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1-methyl-1H-pyrazol-3-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(5-fluoropyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-

(pyrimidin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(isothiazol-3-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(5-fluoropyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(3-methyl-1,2,4-thiadiazol-5-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-((trifluoromethyl)sulfonyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carbonitrile,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-((5-(trifluoromethyl)pyridin-2-yl)oxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyridin-2-yloxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyrimidin-2-yloxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyrazin-2-yloxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((6-methyl-4-(trifluoromethyl)pyridazin-3-yl)oxy)-7-(thiazol-2-

yl)benzo[d]oxazole,

(6-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)pyridin-3-yl)methanol,

(6-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-5-(trifluoromethyl)pyridin-3-yl)methanol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-((5-(trifluoromethoxy)pyridin-2-yl)oxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-cyclopropyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)thio)ethan-1-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)sulfinyl)ethan-1-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)sulfonyl)ethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((1,1-difluoroallyl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((5-(methylsulfonyl)pyridin-2-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-hydroxyethyl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-cyclopropyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-ethyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(morpholino)methanone,

(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(pyrrolidin-1-yl)methanone,

N-benzyl-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-3-

methylbutan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(5-chloropyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

(R)-3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3,3-difluoro-2-methylpropane-1,2-diol,

(S)-3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3,3-difluoro-2-methylpropane-1,2-diol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylic acid,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-hydroxy-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-morpholino-7-(thiazol-2-yl)benzo[d]oxazole,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3,3-difluoropropane-1,2-diol,

3-(4-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

(R)-3-(4-(1,1-difluoro-2-hydroxypropoxy)-7-(thiazol-2-

yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

(S)-3-(4-(1,1-difluoro-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

3-(4-(1,1-difluoro-2-hydroxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

3-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

(2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)pyridin-3-yl)methanol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropane-2,2-diol,

(R)-3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

(S)-3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

3-(7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N,N-dimethyl-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-hydroxyethyl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyrrolidin-1-ylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(morpholinosulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1,1-difluoro-2-methoxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1,1-difluoro-2-methoxy-2-methylpropoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1-methyl-1H-pyrazol-3-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluorobutan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)piperidin-4-ol,

4-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)thiomorpholine 1,1-dioxide,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-bromo-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-

(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1,1-difluoropropoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

4-(benzo[d]oxazol-2-yldifluoromethoxy)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((1,1-difluoro-3-(pyridin-3-yl)allyl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-N-(2-hydroxyethyl)-N-methylacetamide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-N,N-dimethylacetamide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-1-morpholinoethan-1-one,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroacetamide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-N-(2-hydroxyethyl)acetamide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-1-(3-hydroxyazetidin-1-yl)ethan-1-one,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-((5-(trifluoromethyl)pyridin-2-yl)oxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-cyclobutyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyrrolidin-1-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

(6-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)pyridin-3-yl)methanol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carbonitrile,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(pyridin-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole, or

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-cyclobutoxy-7-(thiazol-2-yl)benzo[d]oxazole.

[6]

A PDE4 inhibitor comprising at least one selected from the group consisting of the compound and the pharmacologically acceptable salt thereof

according to any one of [1] to [5] as an active ingredient.

[7]

A pharmaceutical composition comprising at least one selected from the group consisting of the compound and the pharmacologically acceptable salt thereof according to any one of [1] to [5] as an active ingredient.

[8]

A method for treating a disease attributed to PDE4, comprising administering to a patient at least one selected from the group consisting of the compound and the pharmacologically acceptable salt thereof according to any one of [1] to [5].

[9]

The compound or the pharmacologically acceptable salt thereof according to any one of [1] to [5], used for treatment of a disease attributed to PDE4.

[10]

A method for inhibiting PDE4, comprising administering to a patient at least one selected from the group consisting of the compound and the pharmacologically acceptable salt thereof according to any one of [1] to [5].

[11]

A therapeutic agent for a disease attributed to

PDE4, comprising at least one selected from the group consisting of the compound and the pharmacologically acceptable salt thereof according to any one of [1] to [5] as an active ingredient.

[12]

The compound or the pharmacologically acceptable salt thereof according to any one of [1] to [5], used to inhibit PDE4.

[13]

Use of the compound or the pharmacologically acceptable salt thereof according to any one of [1] to [5] for manufacturing a PDE4 inhibitor.

[14]

Use of the compound or the pharmacologically acceptable salt thereof according to any one of [1] to [5] for manufacturing a therapeutic agent for a disease attributed to PDE4.

[EFFECTS OF THE INVENTION]

The present invention makes it possible to provide a novel compound and a pharmacologically acceptable salt thereof which have an excellent PDE4 inhibitory activity and an excellent metabolic stability.

The novel compound and the pharmacologically acceptable salt thereof of the present invention are useful in treating and/or preventing various diseases

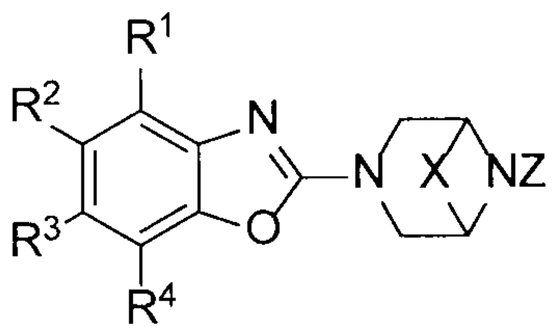
attributed to PDE4 and diseases relating to PDE4 thanks to an excellent PDE4 inhibitory activity. The diseases attributed to PDE4 and diseases relating to PDE4 include, for example, asthma, COPD, interstitial pneumonia, various fibrosis such as idiopathic pulmonary fibrosis and systemic sclerosis, inflammatory bowel diseases such as Crohn's disease, multiple sclerosis, rheumatism, ankylosing spondylitis, acne, atopic dermatitis, alopecia areata, allergic conjunctivitis, rhinitis, psoriatic arthritis, psoriasis vulgaris, sarcoidosis, Behçet's disease, systemic lupus erythematosus, depressive disorder, cognitive disorders, Parkinson's disease, Alzheimer's disease, Huntington's disease, schizophrenia, various types of cancer (such as colorectal cancer, lung cancer, hematologic cancer, and brain tumor), and metabolic diseases (such as diabetes and obesity). Moreover, because of the excellence in metabolic stability and also in pharmacokinetics, the novel compound and the pharmacologically acceptable salt thereof of the present invention make it possible to sufficiently lower the frequency of side effects even in the case of oral administration.

[DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS]

Hereinafter, the present invention is described

in detail based on its preferred embodiments. Note that in the following description, the same or corresponding elements are given the same reference numerals and overlapping explanations thereof are omitted.

In a compound of the present invention or a pharmacologically acceptable salt thereof, the compound of the present invention is represented by the general formula (1) below:



(1)

In the general formula (1), the halogen atom means a fluorine atom, a chlorine atom, a bromine atom, or an iodine atom, or preferably a fluorine atom or a chlorine atom.

In the general formula (1), the C_{1-6} alkyl group means a linear chain or a branched chain alkyl group having 1 to 6 carbon atoms. The C_{1-6} alkyl group is, for example, a methyl group, an ethyl group, an n-propyl group, an isopropyl group, an n-butyl group, an isobutyl group, a tert-butyl group, an n-pentyl group, an isoamyl group, or an n-hexyl group, preferably a linear chain or a branched chain C_{1-4} alkyl group

having 1 to 4 carbon atoms, or more preferably a methyl group, an ethyl group, an n-propyl group, an isopropyl group, or an n-butyl group.

In the general formula (1), the C_{3-7} cycloalkyl group means a cyclic alkyl group having 3 to 7 carbon atoms. The C_{3-7} cycloalkyl group is, for example, a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a cyclohexyl group, or a cycloheptyl group, preferably C_{3-6} cycloalkyl group having 3 to 6 carbon atoms, or more preferably a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, or a cyclohexyl group.

In the general formula (1), the C_{6-10} monocyclic or polycyclic aryl group means a monocyclic aromatic hydrocarbon group or polycyclic aromatic hydrocarbon group having 6 to 10 carbon atoms. The C_{6-10} monocyclic or polycyclic aryl group is, for example, a phenyl group or a naphthyl group, preferably monocyclic, or more preferably a phenyl group.

In the general formula (1), the C_{7-11} monocyclic or polycyclic aralkyl group means a group having 7 to 11 carbon atoms, which is formed by substituting one hydrogen atom of the C_{1-6} alkyl group with a monocyclic aromatic hydrocarbon group or polycyclic aromatic hydrocarbon group (the C_{6-10} monocyclic or polycyclic aryl group) having 6 to 10 carbon atoms. The C_{7-11}

monocyclic or polycyclic aralkyl group is, for example, a benzyl group or a naphthylmethyl group, preferably monocyclic, or more preferably a benzyl group.

In the general formula (1), the 4- to 10-membered monocyclic or bicyclic aromatic heterocyclic group means a 4- to 10-membered monocyclic aromatic heterocycle or bicyclic aromatic heterocycle containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom. The 4- to 10-membered monocyclic or bicyclic aromatic heterocyclic group is, for example, a pyrrolyl group, a furanyl group, a thienyl group, a pyrazolyl group, an oxazolyl group, an isoxazolyl group, an oxadiazolyl group, a thiazolyl group, an isothiazolyl group, a thiadiazolyl group, an imidazolyl group, a triazolyl group, a pyridyl group, a pyrimidinyl group, a pyridazinyl group, a pyradinyl group, a tetrazolyl group, a quinolyl group, or an isoquinolyl group, preferably monocyclic, or more preferably a furanyl group, a thienyl group, a pyrazolyl group, an oxazolyl group, an isoxazolyl group, an oxadiazolyl group, a thiazolyl group, an isothiazolyl group, an imidazolyl group, a triazolyl group, a pyridyl group, or a pyrimidinyl group.

In the general formula (1), the 4- to 10-

membered monocyclic or bicyclic nonaromatic heterocyclic group means a 4- to 10-membered monocyclic nonaromatic heterocycle or bicyclic nonaromatic heterocycle containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom. The 4- to 10-membered monocyclic or bicyclic nonaromatic heterocyclic group is, for example, a tetrahydrofuranyl group, a tetrahydropyranyl, a tetrahydro-2H-thiopyranyl group, an oxetanyl group, a pyrrolidinyl group, a piperidyl group, a piperazinyl group, an oxazolidinyl group, a morpholinyl group, an aziridinyl group, an azetidinyl group, a thiomorpholinyl group, or a tetrahydroquinolyl group, preferably monocyclic, or more preferably a tetrahydrofuranyl group, a tetrahydropyranyl, a tetrahydro-2H-thiopyranyl group, an oxetanyl group, a pyrrolidinyl group, a piperidyl group, a piperazinyl group, a morpholinyl group, or an azetidinyl group.

In the general formula (1), the di-C_{1-6} alkyl amino group means a group which is formed by substituting two hydrogen atoms of the amino group with the C_{1-6} alkyl groups. The di-C_{1-6} alkyl amino group is, for example, a dimethylamino group, a diethylamino group, or a methylethylamino group, preferably a di-C_{1-3} alkyl amino group in which the

alkyl group has 1 to 3 carbon atoms, or more preferably a dimethylamino group or a diethylamino group.

In the general formula (1), the C_{3-7} cycloalkyl amino group means a group which is formed by substituting one or two (one, preferably) hydrogen atoms of the amino group with the C_{3-7} cycloalkyl group(s). The C_{3-7} cycloalkyl amino group is, for example, a cyclobutylamino group, a cyclopentylamino group, or a cyclohexylamino group, preferably a C_{3-6} cycloalkyl amino group in which the cycloalkyl group has 3 to 6 carbon atoms, or more preferably a cyclobutylamino group or a cyclopentylamino group.

In the general formula (1), the C_{1-6} acylamino group means an amide group (group represented by the formula: R-CO-NH-) having one C_{1-6} alkyl group (represented by the formula: R-) described above. The C_{1-6} acylamino group is, for example, an acetamide group, an propionylamino group, a butyrylamino group, an isobutyrylamino group, a valerylamino group, or an isovalerylamino group, preferably a C_{1-3} acylamino group in which the alkyl group has 1 to 3 carbon atoms, or more preferably an acetamide group, an propionylamino group, a butyrylamino group, or an isobutyrylamino group.

In the general formula (1), the C_{1-6} alkyloxy

group means a group which is formed by bonding one C_{1-6} alkyl group described above to an oxygen atom. The C_{1-6} alkyloxy group is, for example, a methoxy group, an ethoxy group, an n-propoxy group, an isopropoxy group, an n-butoxy group, an isobutoxy group, a tert-butoxy group, an n-pentyloxy group, an isopentyloxy group, a tert-pentyloxy group, a neopentyloxy group, a (3-methylbutan-2-yl)oxy group, an n-hexyloxy group, a (4-methylpentyl)oxy group, a 3,3-dimethylbutoxy group, a (2-methylpentan-2-yl)oxy group, a (2,3-dimethylbutan-2-yl)oxy group, or a (3,3-dimethylbutan-2-yl)oxy group, preferably a C_{1-5} alkyloxy group in which the alkyl group has 1 to 5 carbon atoms, or more preferably a methoxy group, an ethoxy group, an n-propoxy group, an isopropoxy group, an n-butoxy group, an isobutoxy group, an n-pentyloxy group, an isopentyloxy group, a tert-pentyloxy group, or a (3-methylbutan-2-yl)oxy group.

In the general formula (1), the C_{2-6} alkenyloxy group means a group which is formed by bonding one unsaturated hydrocarbon group having 2 to 6 carbon atoms to an oxygen atom. The C_{2-6} alkenyloxy group is, for example, a vinyloxy group, an allyloxy group, or an isopropenyloxy group, preferably a C_{2-3} alkenyloxy group in which the unsaturated hydrocarbon group has 2 or 3 carbon atoms, or more preferably an allyloxy

group.

In the general formula (1), the C_{1-6} alkyloxy-C_{1-6} alkyl group means a group which is formed by substituting one or more (one, preferably) hydrogen atoms of the C_{1-6} alkyl group with the C_{1-6} alkyloxy group(s). The C_{1-6} alkyloxy-C_{1-6} alkyl group is, for example, a methoxymethyl group, a methoxyethyl group, an ethoxymethyl group, an ethoxyethyl group, an n-propoxymethyl group, an n-propoxyethyl group, an isopropoxymethyl group, an isopropoxyethyl group, an n-butoxymethyl group, an isobutoxymethyl group, an n-pentyloxymethyl group, or an n-hexyloxymethyl group, preferably a C_{1-5} alkyloxy-C_{1-3} alkyl group in which the alkyl group has 1 to 3 carbon atoms and the alkyloxy group has 1 to 5 carbon atoms, or more preferably a methoxymethyl group, a methoxyethyl group, an ethoxymethyl group, an ethoxyethyl group, an n-propoxymethyl group, an isopropoxymethyl group, an n-butoxymethyl group, or an isobutoxymethyl group.

In the general formula (1), the C_{3-7} cycloalkyloxy group means a group which is formed by bonding one C_{3-7} cycloalkyl group described above to an oxygen atom. The C_{3-7} cycloalkyloxy group is, for example, a cyclopropyloxy group, a cyclobutyloxy group, a cyclopentyloxy group, or a cyclohexyloxy group, preferably a C_{3-6} cycloalkyloxy group in which

the cycloalkyl group has 3 to 6 carbon atoms, or more preferably a cyclopropyloxy group, a cyclobutyloxy group, a cyclopentyloxy group, or a cyclohexyloxy group.

In the general formula (1), the C_{6-10} monocyclic or polycyclic aryloxy group means a group which is formed by bonding one C_{6-10} monocyclic or polycyclic aryl group described above to an oxygen atom. The C_{6-10} monocyclic or polycyclic aryloxy group is, for example, a phenyloxy group or a naphthyloxy group, preferably monocyclic, or more preferably a phenyloxy group.

In the general formula (1), the C_{7-11} monocyclic or polycyclic aralkyloxy group means a group which is formed by bonding one C_{7-11} monocyclic or polycyclic aralkyl group described above to an oxygen atom. The C_{7-11} monocyclic or polycyclic aralkyloxy group is, for example, a benzyloxy group or a naphthylmethyloxy group, preferably monocyclic, or more preferably a benzyloxy group.

In the general formula (1), the 4- to 10-membered monocyclic or bicyclic aromatic heterocyclyloxy group means a group which is formed by bonding one 4- to 10-membered monocyclic or bicyclic aromatic heterocyclic group described above to an oxygen atom. The 4- to 10-membered monocyclic or

bicyclic aromatic heterocyclyloxy group is, for example, a thiazolyloxy group, an oxazolyloxy group, a pyridiloxy group, a pyrimidinyloxy group, a pyrazinyloxy group, or a pyridazinyloxy group, preferably monochyclic, or more preferably a pyridiloxy group, a pyrimidinyloxy group, a pyrazinyloxy group, or a pyridazinyloxy group.

In the general formula (1), the 4- to 10-membered monocyclic or bicyclic nonaromatic heterocyclyloxy group means a group which is formed by bonding one 4- to 10-membered monocyclic or bicyclic nonaromatic heterocyclic group described above to an oxygen atom. The 4- to 10-membered monocyclic or bicyclic nonaromatic heterocyclyloxy group is, for example, an oxetanyloxy group, a tetrahydrofuranyloxy group, a tetrahydropyranyloxy group, or a 1,1-dioxidotetrahydro-2H-thiopyran-4-yloxy group, preferably monocyclic, or more preferably an oxetanyloxy group, a tetrahydrofuranyloxy group, a tetrahydropyranyloxy group, or a 1,1-dioxidotetrahydro-2H-thiopyran-4-yloxy group.

In the general formula (1), the C_{1-6} alkylthio group means a group which is formed by bonding one C_{1-6} alkyl group described above to a sulfur atom. The C_{1-6} alkylthio group is, for example, a methylthio group, an ethylthio group, a propylthio group, or an

isopropylthio group, preferably a C_{1-3} alkylthio group in which the alkyl group has 1 to 3 carbon atoms, or more preferably a methylthio group or an ethylthio group.

In the general formula (1), the C_{1-6} alkylsulfonyl group means a sulfonyl group (group represented by the formula: R-SO_2-) having the C_{1-6} alkyl group (represented by the formula: R-) described above. The C_{1-6} alkylsulfonyl group is, for example, a methylsulfonyl group, an ethylsulfonyl group, or a propylsulfonyl group, preferably a C_{1-3} alkylsulfonyl group in which the alkyl group has 1 to 3 carbon atoms, or more preferably a methylsulfonyl group or an ethylsulfonyl group.

In the general formula (1), the C_{1-6} alkylsulfinyl group means a sulfinyl group (group represented by the formula: R-SO-) having the C_{1-6} alkyl group (represented by the formula: R-) described above. The C_{1-6} alkylsulfinyl group is, for example, a methylsulfinyl group, an ethylsulfinyl group, or a propylsulfinyl group, preferably a C_{1-3} alkylsulfinyl group in which the alkyl group has 1 to 3 carbon atoms, or more preferably a methylsulfinyl group or an ethylsulfinyl group.

In the general formula (1), the mono-C_{1-6} alkylsulfamoyl group means a group (group represented

by the formula: R-NH-SO_2-) which is formed by substituting one hydrogen atom of the sulfamoyl group with the C_{1-6} alkyl group (represented by the formula: R-). The mono-C_{1-6} alkylsulfamoyl group is, for example, a methylsulfamoyl group, an ethylsulfamoyl group, or a propylsulfamoyl group, preferably a mono-C_{1-3} alkylsulfamoyl group in which the alkyl group has 1 to 3 carbon atoms, or more preferably a methylsulfamoyl group.

In the general formula (1), the di-C_{1-6} alkylsulfamoyl group means a group (group represented by the formula: R-NR'-SO_2-) which is formed by substituting two hydrogen atoms of the sulfamoyl group with the C_{1-6} alkyl groups (represented by the formulae: R- and R'-). The di-C_{1-6} alkylsulfamoyl group is, for example, a dimethylsulfamoyl group, a diethylsulfamoyl group, a dipropylsulfamoyl group, or a methylethylsulfamoyl group, preferably a di-C_{1-3} alkylsulfamoyl group in which the alkyl group has 1 to 3 carbon atoms, or preferably a dimethylsulfamoyl group. As the di-C_{1-6} alkylsulfamoyl group of the present invention, two C_{1-6} alkyl groups (R, R') in the di-C_{1-6} alkylsulfamoyl group may form a pyrrolidin-1-yl group or a morpholino group with an adjacent nitrogen atom.

In the general formula (1), the C_{1-6}

alkylcarbonyl group means a group which is formed by bonding one C_{1-6} alkyl group described above to a carbonyl group. The C_{1-6} alkylcarbonyl group is, for example, an acetyl group, an ethylcarbonyl group, a propylcarbonyl group, or a butylcarbonyl group, preferably a C_{1-3} alkylcarbonyl group in which the alkyl group has 1 to 3 carbon atoms, or more preferably an acetyl group.

In the general formula (1), the 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group means a group (represented by the formula: -C (-R) = N-OR') which is formed by substituting the C_{1-6} alkyloxy group (represented by the formula: -OR') for one hydrogen atom bonded to the nitrogen atom of an imino-C_{1-6} alkyl group (represented by the formula: -C (-R) = NH) being an imino group bonded with the C_{1-6} alkyl group (represented by the formula: R-). The 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group is, for example, a 1-(methoxy)iminoethyl group, a 1-(ethoxy)iminoethyl group, or a 1-(methoxy)iminopropyl group, preferably a 1-(C_{1-3} alkyloxy)imino-C_{1-3} alkyl group in which the alkyl group has 1 to 3 carbon atoms, or more preferably a 1-(methoxy)iminoethyl group.

In the general formula (1), the mono-C_{1-6} alkylaminocarbonyl group means a group which is formed by substituting one hydrogen atom of an aminocarbonyl

group with the C_{1-6} alkyl group. The mono-C_{1-6} alkylaminocarbonyl group is, for example, a methylaminocarbonyl group, an ethylaminocarbonyl group, or a propylaminocarbonyl group, preferably a mono-C_{1-3} alkylaminocarbonyl group in which the alkyl group has 1 to 3 carbon atoms, or more preferably a methylaminocarbonyl group or an ethylaminocarbonyl group.

In the general formula (1), the di-C_{1-6} alkylaminocarbonyl group means a group which is formed by substituting two hydrogen atoms of an aminocarbonyl group with the C_{1-6} alkyl groups. The di-C_{1-6} alkylaminocarbonyl group is, for example, a dimethylaminocarbonyl group, a diethylaminocarbonyl group, or a dipropylaminocarbonyl group, preferably a di-C_{1-3} alkylaminocarbonyl group in which the alkyl group has 1 to 3 carbon atoms, or more preferably a dimethylaminocarbonyl group or a diethylaminocarbonyl group.

In the general formula (1), the C_{3-7} cycloalkylaminocarbonyl group means a group which is formed by substituting one or two (one, preferably) hydrogen atoms of an aminocarbonyl group with the C_{3-7} cycloalkyl group(s). The C_{3-7} cycloalkylaminocarbonyl group is, for example, a cyclobutylaminocarbonyl group, a cyclopentylaminocarbonyl group, or a

cyclohexylaminocarbonyl group, preferably a C_{4-6} cycloalkylaminocarbonyl group in which the cycloalkyl group has 4 to 6 carbon atoms, or more preferably a cyclobutylaminocarbonyl group or a cyclohexylaminocarbonyl group.

In the general formula (1), the C_{7-11} monocyclic or polycyclic aralkylaminocarbonyl group means a group which is formed by substituting one or two (one, preferably) hydrogen atoms of an aminocarbonyl group with the C_{7-11} monocyclic or polycyclic aralkyl group(s). The C_{7-11} monocyclic or polycyclic aralkylaminocarbonyl group is preferably monocyclic, for example a benzylaminocarbonyl group.

In the general formula (1), the C_{1-6} alkyloxycarbonyl group means a group which is formed by bonding one C_{1-6} alkyloxy group described above to a carbonyl group. The C_{1-6} alkyloxycarbonyl group is, for example, a methoxycarbonyl group, an ethoxycarbonyl group, or an isopropoxycarbonyl group, preferably a C_{1-3} alkyloxycarbonyl group in which the alkyloxy group has 1 to 3 carbon atoms, or more preferably a methoxycarbonyl group or an ethoxycarbonyl group.

In the general formula (1), the hydroxyaminocarbonyl group means a group which is formed by substituting one or two (one, preferably)

hydrogen atoms of an aminocarbonyl group with hydroxyl group(s).

In the general formula (1), "optionally substituted" means that each group may be further substituted by one or more substituents. The substituent in the case of substitution may be any group which can be substituted for the corresponding group and may be, for example, a halogen atom; a carboxy group; a cyano group; a hydroxyl group; a C_{1-6} alkyl group optionally substituted with one or more halogen atom; a C_{2-6} alkenyl group optionally substituted with 4- to 10-membered monocyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom; a C_{3-6} cycloalkyl group; a hydroxy-C_{1-6} alkyl group; a C_{1-6} alkyloxy group optionally substituted with one or more halogen atom; a carbamoyl group; an aminocarbonyl group; a C_{1-6} alkylcarbonyl group, an oxo group, a nitro group, a mono-C_{1-6} alkyl amino group optionally substituted with one or more hydroxyl group; a di-C_{1-6} alkyl amino group optionally substituted with one or more hydroxyl group; a C_{1-6} alkylthio group; a C_{1-6} alkylsulfonyl group; a C_{6-10} aryl group (monocyclic or polycyclic (monocyclic, preferably)); or a 4- to 10-membered monocyclic or bicyclic heterocyclic group (aromatic or nonaromatic,

optionally substituted with a C_{1-6} alkyl group or hydroxyl group) containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom. Note that the hydroxy-C_{1-6} alkyl group means a group which is formed by substituting one or more (one, preferably) hydrogen atoms of the C_{1-6} alkyl group with hydroxyl group(s), and is, for example, a hydroxymethyl group, a 1-hydroxyethyl group, or a 2-hydroxypropan-2-yl group.

Consider the case where the substituent is a halogen atom. The C_{1-6} alkyl group substituted with fluorine atoms is, for example, a trifluoromethyl group, a trifluoroethyl group, a difluoromethyl group, or a difluoroethyl group. The C_{1-6} alkyloxy group substituted with fluorine atoms is, for example, a trifluoromethoxy group, a difluoromethoxy group, or a trifluoroethoxy group. The C_{1-6} alkyloxy-C_{1-6} alkyl group substituted with fluorine atoms is, for example, a 2,2,2-trifluoro-1-methoxyethyl group, a 1-ethoxy-2,2,2-trifluoroethyl group, or a 2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl group.

Consider the case where the substituent is a hydroxyl group. The C_{1-6} alkyloxy group substituted with a hydroxyl group is, for example, a 2-hydroxy-2-methylpropoxy group or a 2-hydroxypropoxy group. The C_{1-6} alkylthio group substituted with a hydroxyl group

is, for example, a (2-hydroxyethyl)thio group. The C_{1-6} alkylsulfonyl group substituted with a hydroxyl group is, for example, a (2-hydroxyethyl)sulfonyl group.

Consider the case where the substituents are a halogen atom and a hydroxyl group. The C_{1-6} alkyloxy group substituted with a fluorine atom and a hydroxyl group is, for example, a 1,1-difluoro-2-hydroxyethoxy group, a 1,1-difluoro-2-hydroxypropoxy group, a 1,1-difluoro-2-hydroxy-2-methylpropoxy group, or a 1,1-difluoro-3-hydroxypropoxy group. The C_{1-6} alkyl group substituted with a fluorine atom and a hydroxyl group is, for example, a 2,2,2-trifluoro-1-hydroxyethyl group, a 1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 2,2-difluoro-1-hydroxyethyl group, or a 1,1-difluoro-2-hydroxypropan-2-yl group. In addition, the C_{1-6} alkyloxy-C_{1-6} alkyl group substituted with a fluorine atom and a hydroxyl group is, for example, a 2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl group or a 2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl group.

Consider the case where the substituents are a halogen atom and a cyano group. The C_{1-6} alkyloxy-C_{1-6} alkyl group substituted with a halogen atom and a cyano group is, for example, a 1-(cyanomethoxy)-2,2,2-trifluoroethyl group.

Consider the case where the substituent is an oxo group. The tetrahydro-2H-thiopyranyl group substituted with the oxo group is, for example, a 1,1-dioxidotetrahydro-2H-thiopyranyl group.

In the present invention, in the general formula (1), R^1 and R^2 may be the same or different and each represents a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyl group, an optionally substituted C_{6-10} monocyclic or polycyclic aryl group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkyl group, an optionally substituted 4- to 10-membered monocyclic or bicyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic or bicyclic nonaromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted di-C_{1-6} alkyl amino group, an optionally substituted C_{3-7} cycloalkyl amino group, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{2-6} alkenyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an

optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted C_{6-10} monocyclic or polycyclic aryloxy group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkyloxy group, an optionally substituted 4- to 10-membered monocyclic or bicyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic or bicyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group [two C_{1-6} alkyl groups in the di-C_{1-6} alkylsulfamoyl group may form a pyrrolidin-1-yl group or a morpholino group with an adjacent nitrogen atom], a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7} cycloalkylaminocarbonyl

group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkylaminocarbonyl group, an optionally substituted C_{1-6} alkyloxycarbonyl group, or an optionally substituted hydroxyaminocarbonyl group.

In the present invention, the group represented by R^1 in the general formula (1) is preferably a hydrogen atom, a fluorine atom, a chlorine atom, a carboxy group, a cyano group, a methyl group, an ethyl group, an isopropyl group, a trifluoromethyl group, a difluoromethyl group, a hydroxymethyl group, a methoxymethyl group, a 2-hydroxypropan-2-yl group, a morpholinomethyl group, a (dimethylamino)methyl group, a 2,2,2-trifluoro-1-hydroxyethyl group, a 2,2,2-trifluoro-1-methoxyethyl group, a 1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-methoxyethyl group, a 1,1-difluoro-2-hydroxypropan-2-yl group, a 1,1,1-trifluoro-2-methoxypropan-2-yl group, a 1-hydroxyethyl group, a 1-hydroxypropyl group, a 1-hydroxy-2-methylpropyl group, a 1-methoxyethyl group, a 2-methoxypropan-2-yl group, a 1-acetoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl group, a 1-ethoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl group, a 2,2,2-trifluoro-1,1-

dihydroxyethyl group, a 1-(cyanomethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxypropoxy)ethyl group, a 2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxypropan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxy-2-methylpropan-2-yl)oxy)ethyl group, a 1-(1,1-difluoro-2-hydroxypropoxy)-2,2,2-trifluoroethyl group, a 1-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-2,2,2-trifluoroethyl group, a 1-(difluoro(1-hydroxycyclopropyl)methoxy)-2,2,2-trifluoroethyl group, a 1-(carboxymethoxy)-2,2,2-trifluoroethyl group, a 1-(2-amino-2-oxoethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-((methylsulfonyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-(sulfamoylmethoxy)ethyl group, a 1,1,1-trifluoro-3-hydroxypropan-2-yl group, a 1,1,1,4,4,4-hexafluoro-3-hydroxybutan-2-yl group, a 1-((1,3-dihydroxypropan-2-yl)oxy)-2,2,2-trifluoroethyl group, a 1,1,1-trifluoro-3-hydroxybutan-2-yl group, a 1,1,1-trifluoro-3-oxobutan-2-yl group, a 1,1,1,4,4,4-hexafluoro-3-oxobutan-2-yl group, a 1,1,1-trifluoro-3,4-dihydroxybutan-2-yl group, a 1,1,1-trifluoro-4-hydroxy-3-oxobutan-2-yl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl group, a 1-((2H-

tetrazol-5-yl)methoxy)-2,2-difluoroethyl group, a 1-hydroxy-3-(methylsulfonyl)propyl group, a 2,2-difluoro-1-hydroxy-3-(methylsulfonyl)propyl group, a 3-(ethylsulfonyl)-1-hydroxypropyl group, a 3-(ethylsulfonyl)-2,2-difluoro-1-hydroxypropyl group, a 1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2-difluoro-1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2,2-trifluoro-1-(2-morpholino-2-oxoethoxy)ethyl group, a 1-hydroxy-2-morpholinoethyl group, a 2,2-difluoro-1-hydroxy-2-morpholinoethyl group, a 1-carboxy-2,2-difluoro-1-hydroxyethyl group, a 1-carboxy-2,2,2-trifluoro-1-hydroxyethyl group, a 2,2-difluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a 2,2,2-trifluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a 1,1-difluoro-3-hydroxypropan-2-yl group, a 1,1-difluoro-3-hydroxy-3-methylbutan-2-yl group, a 1,1,1-trifluoro-3-hydroxy-3-methylbutan-2-yl group, a 3-cyano-1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 1,3-dihydroxypropyl group, a 1-hydroxy-3-methoxypropyl group, a 4,4,4-trifluoro-1,3-dihydroxybutyl group, a 1,3-dihydroxybutyl group, a 1,3-dihydroxy-3-methylbutyl group, a cyclopropyl (hydroxy)methyl group, a carboxy(hydroxy)methyl group, a hydroxy (2H-tetrazol-5-yl)methyl group, a hydroxy (3-hydroxycyclobutyl)methyl group, a 3-amino-1-hydroxy-3-oxopropyl group, a 1-hydroxy-2-

(methylsulfonamide)ethyl group, a 2-cyanoethyl group, a 1,2-dihydroxyethyl group, a 3,3,3-trifluoro-1,2-dihydroxypropyl group, a 3,3,3-trifluoro-1-hydroxy-2-oxopropyl group, a 3,3,3-trifluoro-1-hydroxypropyl group, a 3,3,3-trifluoro-2-hydroxypropyl group, a 3,3,3-trifluoro-2-oxopropyl group, a 1-hydroxy-3-oxobutyl group, a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a phenyl group, a benzyl group, a thiazol-2-yl group, a 1H-pyrazol-1-yl group, a 5-methylthiazol-2-yl group, a 5-methoxycarbonylthiazol-2-yl group, a 5-hydroxymethylthiazol-2-yl group, a 5-(1-hydroxyethyl)thiazol-2-yl group, a 5-(2-hydroxypropan-2-yl)thiazol-2-yl group, a 5-(N,N-dimethylaminomethyl)thiazol-2-yl group, a 5-methylthiazol-4-yl group, an oxazol-2-yl group, an oxazol-4-yl group, a 5-methyloxazol-4-yl group, a 1H-imidazol-1-yl group, a 2,5-dimethyl-1H-imidazol-1-yl group, a 1H-imidazol-4-yl group, a 1-methyl-1H-imidazol-2-yl group, a 1-methyl-1H-imidazol-4-yl group, a pyridin-2-yl group, a pyridin-3-yl group, a pyridin-4-yl group, a 3,5-dimethylpyridin-4-yl group, a 6-hydroxypyridin-2-yl group, a 5-hydroxypyridin-2-yl group, a 4-hydroxypyridin-2-yl group, a 3-hydroxypyridin-2-yl group, a 6-methoxypyridin-2-yl group, a 5-methoxypyridin-2-yl group, a 4-

methoxypyridin-2-yl group, a 3-methoxypyridin-2-yl group, a pyrimidin-2-yl group, a pyrimidin-4-yl group, a 1,3,5-triazin-2-yl group, a tetrahydrofuran-2-yl group, a tetrahydrofuran-3-yl group, a tetrahydropyran-2-yl group, a tetrahydropyran-3-yl group, a tetrahydropyran-4-yl group, an oxetanyl group, a pyrrolidin-1-yl-1-yl group, a piperidin-1-yl group, a piperazin-1-yl group, a morpholin-4-yl group, an azetidin-1-yl group, a 4-hydroxypiperidin-1-yl group, a 3-hydroxypyrrolidin-1-yl group, a 3-hydroxyazetidin-1-yl group, a dimethylamino group, a diethylamino group, a methylethylamino group, a cyclobutylamino group, a cyclopentylamino group, a cyclohexylamino group, an acetamide group, an N-methylacetamide group, an propionylamino group, a butyrylamino group, an isobutyrylamino group, a valerylamino group, an isovalerylamino group, a methoxy group, an ethoxy group, an n-propoxy group, an isopropoxy group, an n-butoxy group, an isobutoxy group, a trifluoromethoxy group, a difluoromethoxy group, a 2,2,2-trifluoroethoxy group, a cyanomethoxy group, a carboxymethoxy group, a 2-hydroxyethoxy group, a 2-methoxyethoxy group, a 2-hydroxypropoxy group, a 2-hydroxy-2-methylpropoxy group, a (1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxy-2-methylpropoxy group, a difluoro(1-

hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxyethoxy group, a (1,1,1-trifluoro-3-hydroxypropan-2-yl)oxy group, a 3,3,3-trifluoro-2-hydroxypropoxy group, a 2,2-difluoro-2-hydroxyethoxy group, a 2-(trifluoromethoxy)ethoxy group, a (1,3-dihydroxypropan-2-yl)oxy group, a (1-hydroxy-3-(trifluoromethoxy)propan-2-yl)oxy group, a 2-oxopropoxy group, a 1,1-difluoro-2-oxopropoxy group, a (1,1,1-trifluoro-3-oxobutan-2-yl)oxy group, a 3,3,3-trifluoro-2-oxopropoxy group, a 1,1-difluoro-2-hydroxypropoxy group, a (1,1,1-trifluoro-3-hydroxybutan-2-yl)oxy group, an oxetan-3-yl methoxy group, a 3-hydroxy-2-(hydroxymethyl)propoxy group, an allyloxy group, a cyclobutoxy group, a (methylsulfonyl)methoxy group, a (ethylsulfonyl)methoxy group, a (isopropylsulfonyl)methoxy group, a (2H-tetrazol-5-yl)methoxy group, a 2-amino-2-oxoethoxy group, a cyanodifluoromethoxy group, a carboxydifluoromethoxy group, a difluoro(2H-tetrazol-5-yl)methoxy group, a difluoro(methylsulfonyl)methoxy group, a 2-carboxyethoxy group, a 2-cyanoethoxy group, a 2-(methylsulfonyl)ethoxy group, a 2-morpholinoethoxy group, a 3-hydroxycyclobutoxy group, a 3-cyanocyclobutoxy group, a 3-carboxycyclobutoxy group, a 3-(methylsulfonyl)cyclobutoxy group, a 3-(2H-

tetrazol-5-yl)cyclobutoxy group, a (4-hydroxycyclohexyl)oxy group, a 2-hydroxy-3-methoxypropoxy group, a phenyloxy group, a benzyloxy group, a thiazol-5-yloxy group, a thiazol-4-yloxy group, a pyridin-4-yloxy group, a pyridin-3-yl oxy group, a methylthio group, a methylsulfonyl group, a methylsulfinyl group, a methylsulfamoyl group, a dimethylsulfamoyl group, a sulfamoyl group, an acetyl group, a 2,2-difluoroacetyl group, a 1-(methoxyimino)ethyl group, a carbamoyl group, a dimethylcarbamoyl group, a morpholine-4-carbonyl group, a piperidine-1-carbonyl group, an azetidine-1-carbonyl group, a benzylcarbamoyl group, a methylcarbamoyl group, a 3-hydroxy-3-(trifluoromethyl)azetidine-1-carbonyl group, a methoxycarbonyl group, an ethoxycarbonyl group, a (tetrahydro-2H-pyran-4-yl)oxy group, a 1-(1,1-difluoro-2-hydroxyethoxy)-2,2,2-trifluoroethyl group, a tetrahydro-2H-pyran-3-yl)oxy group, a 3-(2-hydroxypropan-2-yl)cyclobutoxy group, a (1-hydroxy-2-methylpropan-2-yl)oxy group, a 2,2,2-trifluoro-1-((3-hydroxy-2,3-dimethylbutan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-methoxycyclopropyl)methoxy)ethyl group, a 1,1-difluoro-3-hydroxy-3-methylbutoxy group, a (1,1-

dioxido tetrahydro-2H-thiopyran-4-yl)oxy) group, an oxetan-3-yl oxy group, a 1,1-difluoro-2,3-dihydroxy-2-methylpropoxy group, a (trifluoromethyl)sulfonyl group, a (5-(trifluoromethyl)pyridin-2-yl)oxy group, a pyridin-2-yloxy group, a pyrimidin-2-yloxy group, a pyrazin-2-yloxy group, a (6-methyl-4-(trifluoromethyl)pyridazin-3-yl)oxy group, a (5-(hydroxymethyl)pyridin-2-yl)oxy group, a (5-(hydroxymethyl)-3-(trifluoromethyl)pyridin-2-yl)oxy group, a (5-(trifluoromethoxy)pyridin-2-yl)oxy group, a (2-hydroxyethyl)thio group, a (2-hydroxyethyl)sulfinyl group, a (2-hydroxyethyl)sulfonyl group, a (1,1-difluoroallyl)oxy group, a (5-(methylsulfonyl)pyridin-2-yl)oxy group, a (2-methoxyethyl)carbamoyl group, a (2-hydroxyethyl)carbamoyl group, a (2-hydroxyethyl)(methyl)carbamoyl group, a cyclopropylcarbamoyl group, an ethylcarbamoyl group, a pyrrolidine-1-carbonyl group, a hydroxy carbamoyl group, a 1,1-difluoro-2,3-dihydroxypropoxy group, a 3-((hydroxymethyl)pyridin-2-yl)oxy group, a 1,1-difluoro-2,2-dihydroxypropoxy group, an N-(2-hydroxyethyl)sulfamoyl group, an N-(2-methoxyethyl)sulfamoyl group, an N-(2-hydroxyethyl)-N-methylsulfamoyl group, a pyrrolidin-1-ylsulfonyl group, a morpholinosulfonyl group, a 1,1-difluoro-2-methoxyethoxy group, a 1,1-difluoro-2-methoxy-2-

methylpropoxy group, a 1,1-difluoro-2-hydroxybutoxy group, a 1,1-dioxidothio morpholino group, a 1,1-difluoropropoxy group, or a 1,1-difluoro-2-hydroxy-3-methylbutoxy group, or more preferably a hydrogen atom, a chlorine atom, a carboxy group, a methyl group, a trifluoromethyl group, a hydroxymethyl group, a 2-hydroxypropan-2-yl group, a 2,2,2-trifluoro-1-hydroxyethyl group, a 2,2,2-trifluoro-1-methoxyethyl group, a 1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-methoxyethyl group, a 1,1-difluoro-2-hydroxypropan-2-yl group, a 1,1,1-trifluoro-2-methoxypropan-2-yl group, a 1-hydroxyethyl group, a 1-methoxyethyl group, a 2-methoxypropan-2-yl group, a 2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl group, a 1-ethoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl group, a 2,2,2-trifluoro-1,1-dihydroxyethyl group, a 1-(cyanomethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxypropoxy)ethyl group, a 2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxypropan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxy-2-methylpropan-2-yl)oxy)ethyl group, a 1-(1,1-difluoro-

2-hydroxypropoxy)-2,2,2-trifluoroethyl group, a 1-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-2,2,2-trifluoroethyl group, a 1-(difluoro(1-hydroxycyclopropyl)methoxy)-2,2,2-trifluoroethyl group, a 1-(carboxymethoxy)-2,2,2-trifluoroethyl group, a 1-(2-amino-2-oxoethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-((methylsulfonyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-(sulfamoylmethoxy)ethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2-difluoroethyl group, a 1-hydroxy-3-(methylsulfonyl)propyl group, a 3-(ethylsulfonyl)-1-hydroxypropyl group, a 1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2,2-trifluoro-1-(2-morpholino-2-oxoethoxy)ethyl group, a 1-carboxy-2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a phenyl group, a thiazol-2-yl group, an acetamide group, a methoxy group, a trifluoromethoxy group, a cyanomethoxy group, a carboxymethoxy group, a 2-hydroxyethoxy group, a 2-methoxyethoxy group, a 2-hydroxypropoxy group, a 2-hydroxy-2-methylpropoxy group, a (1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxy-2-methylpropoxy group, a difluoro(1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxyethoxy group, a 3,3,3-trifluoro-2-

hydroxypropoxy group, a 2,2-difluoro-2-hydroxyethoxy group, a 2-(trifluoromethoxy)ethoxy group, a 1,1-difluoro-2-hydroxypropoxy group, a (1,1,1-trifluoro-3-hydroxybutan-2-yl)oxy group, a cyclobutoxy group, a (methylsulfonyl)methoxy group, a (ethylsulfonyl)methoxy group, a (isopropylsulfonyl)methoxy group, a (2H-tetrazol-5-yl)methoxy group, a 2-amino-2-oxoethoxy group, a carboxydifluoromethoxy group, a 2-carboxyethoxy group, a 2-cyanoethoxy group, a 2-(methylsulfonyl)ethoxy group, a 2-morpholinoethoxy group, a 3-hydroxycyclobutoxy group, a 3-cyanocyclobutoxy group, a 3-carboxycyclobutoxy group, a 3-(methylsulfonyl)cyclobutoxy group, a 3-(2H-tetrazol-5-yl)cyclobutoxy group, a (4-hydroxycyclohexyl)oxy group, a 2-hydroxy-3-methoxypropoxy group, a benzyloxy group, an acetyl group, a carbamoyl group, a dimethylcarbamoyl group, a morpholine-4-carbonyl group, a piperidine-1-carbonyl group, a methoxycarbonyl group, an ethoxycarbonyl group, a (tetrahydro-2H-pyran-4-yl)oxy group, a 1-(1,1-difluoro-2-hydroxyethoxy)-2,2,2-trifluoroethyl group, a tetrahydro-2H-pyran-3-yl)oxy group, a difluoromethoxy group, a 3-(2-hydroxypropan-2-yl)cyclobutoxy group, a (1-hydroxy-2-methylpropan-2-yl)oxy group, a 2,2,2-trifluoro-1-((3-hydroxy-2,3-

dimethylbutan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-methoxycyclopropyl)methoxy)ethyl group, a 1,1-difluoro-3-hydroxy-3-methylbutoxy group, a (1,1-dioxido tetrahydro-2H-thiopyran-4-yl)oxy) group, an oxetan-3-yl oxy group, a 1,1-difluoro-2,3-dihydroxy-2-methylpropoxy group, a (trifluoromethyl)sulfonyl group, a (5-(trifluoromethyl)pyridin-2-yl)oxy group, a pyridin-2-yloxy group, a pyrimidin-2-yloxy group, a pyrazin-2-yloxy group, a (6-methyl-4-(trifluoromethyl)pyridazin-3-yl)oxy group, a (5-(hydroxymethyl)pyridin-2-yl)oxy group, a (5-(hydroxymethyl)-3-(trifluoromethyl)pyridin-2-yl)oxy group, a (5-(trifluoromethoxy)pyridin-2-yl)oxy group, a methylsulfonyl group, a cyclopropyl group, a methylthio group, a methylsulfinyl group, a (2-hydroxyethyl)thio group, a (2-hydroxyethyl)sulfinyl group, a (2-hydroxyethyl)sulfonyl group, a (1,1-difluoroallyl)oxy group, a (5-(methylsulfonyl)pyridin-2-yl)oxy group, a (2-methoxyethyl)carbamoyl group, a (2-hydroxyethyl)carbamoyl group, a (2-hydroxyethyl)(methyl)carbamoyl group, a cyclopropylcarbamoyl group, an ethylcarbamoyl group, a pyrrolidine-1-carbonyl group, a benzylcarbamoyl group, hydroxycarbamoyl group, a 1,1-difluoro-2,3-dihydroxypropoxy group, a 3-

((hydroxymethyl)pyridin-2-yl)oxy group, a 1,1-difluoro-2,2-dihydroxypropoxy group, an N-(2-hydroxyethyl)sulfamoyl group, an N-(2-methoxyethyl)sulfamoyl group, an N-(2-hydroxyethyl)-N-methylsulfamoyl group, a pyrrolidin-1-ylsulfonyl group, a morpholinosulfonyl group, a 1,1-difluoro-2-methoxyethoxy group, a 1,1-difluoro-2-methoxy-2-methylpropoxy group, a 1,1-difluoro-2-hydroxybutoxy group, a 1,1-dioxidothio morpholino group, a 1,1-difluoropropoxy group, or a 1,1-difluoro-2-hydroxy-3-methylbutoxy group.

The group represented by R^2 in the general formula (1) is preferably a hydrogen atom, a fluorine atom, a chlorine atom, a bromine atom, a carboxy group, a cyano group, a methyl group, an ethyl group, an isopropyl group, a trifluoromethyl group, a difluoromethyl group, a hydroxymethyl group, a methoxymethyl group, a 2-hydroxypropan-2-yl group, a morpholinomethyl group, a (dimethylamino)methyl group, a 2,2,2-trifluoro-1-hydroxyethyl group, a 2,2,2-trifluoro-1-methoxyethyl group, a 1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-methoxyethyl group, a 1,1-difluoro-2-hydroxypropan-2-yl group, a 1,1,1-trifluoro-2-methoxypropan-2-yl group, a 1-hydroxyethyl group, a 1-hydroxypropyl group, a 1-

hydroxy-2-methylpropyl group, a 1-methoxyethyl group, a 2-methoxypropan-2-yl group, a 1-acetoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl group, a 1-ethoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl group, a 2,2,2-trifluoro-1,1-dihydroxyethyl group, a 1-(cyanomethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxypropoxy)ethyl group, a 2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxypropan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxy-2-methylpropan-2-yl)oxy)ethyl group, a 1-(1,1-difluoro-2-hydroxypropoxy)-2,2,2-trifluoroethyl group, a 1-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-2,2,2-trifluoroethyl group, a 1-(difluoro(1-hydroxycyclopropyl)methoxy)-2,2,2-trifluoroethyl group, a 1-(carboxymethoxy)-2,2,2-trifluoroethyl group, a 1-(2-amino-2-oxoethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-((methylsulfonyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-(sulfamoylmethoxy)ethyl group, a 1,1,1-trifluoro-3-hydroxypropan-2-yl group, a 1,1,1,4,4,4-hexafluoro-3-hydroxybutan-2-yl group, a 1-((1,3-

dihydroxypropan-2-yl)oxy)-2,2,2-trifluoroethyl group, a 1,1,1-trifluoro-3-hydroxybutan-2-yl group, a 1,1,1-trifluoro-3-oxobutan-2-yl group, a 1,1,1,4,4,4-hexafluoro-3-oxobutan-2-yl group, a 1,1,1-trifluoro-3,4-dihydroxybutan-2-yl group, a 1,1,1-trifluoro-4-hydroxy-3-oxobutan-2-yl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2-difluoroethyl group, a 1-hydroxy-3-(methylsulfonyl)propyl group, a 2,2-difluoro-1-hydroxy-3-(methylsulfonyl)propyl group, a 3-(ethylsulfonyl)-1-hydroxypropyl group, a 3-(ethylsulfonyl)-2,2-difluoro-1-hydroxypropyl group, a 1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2-difluoro-1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2,2-trifluoro-1-(2-morpholino-2-oxoethoxy)ethyl group, a 1-hydroxy-2-morpholinoethyl group, a 2,2-difluoro-1-hydroxy-2-morpholinoethyl group, a 1-carboxy-2,2-difluoro-1-hydroxyethyl group, a 1-carboxy-2,2,2-trifluoro-1-hydroxyethyl group, a 2,2-difluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a 2,2,2-trifluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a 1,1-difluoro-3-hydroxypropan-2-yl group, a 1,1-difluoro-3-hydroxy-3-methylbutan-2-yl group, a 1,1,1-trifluoro-3-hydroxy-3-methylbutan-2-yl group, a 3-cyano-1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 1,3-dihydroxypropyl group, a 1-hydroxy-3-methoxypropyl

group, a 4,4,4-trifluoro-1,3-dihydroxybutyl group, a 1,3-dihydroxybutyl group, a 1,3-dihydroxy-3-methylbutyl group, a cyclopropyl (hydroxy)methyl group, a carboxy(hydroxy)methyl group, a hydroxy (2H-tetrazol-5-yl)methyl group, a hydroxy (3-hydroxycyclobutyl)methyl group, a 3-amino-1-hydroxy-3-oxopropyl group, a 1-hydroxy-2-(methylsulfonamide)ethyl group, a 2-cyanoethyl group, a 1,2-dihydroxyethyl group, a 3,3,3-trifluoro-1,2-dihydroxypropyl group, a 3,3,3-trifluoro-1-hydroxy-2-oxopropyl group, a 3,3,3-trifluoro-1-hydroxypropyl group, a 3,3,3-trifluoro-2-hydroxypropyl group, a 3,3,3-trifluoro-2-oxopropyl group, a 1-hydroxy-3-oxobutyl group, a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a phenyl group, a benzyl group, a thiazol-2-yl group, a 1H-pyrazol-1-yl group, a 5-methylthiazol-2-yl group, a 5-methoxycarbonylthiazol-2-yl group, a 5-hydroxymethylthiazol-2-yl group, a 5-(1-hydroxyethyl)thiazol-2-yl group, a 5-(2-hydroxypropan-2-yl)thiazol-2-yl group, a 5-(N,N-dimethylaminomethyl)thiazol-2-yl group, a 5-methylthiazol-4-yl group, an oxazol-2-yl group, an oxazol-4-yl group, a 5-methyloxazol-4-yl group, a 1H-imidazol-1-yl group, a 2,5-dimethyl-1H-imidazol-1-yl group, a 1H-imidazol-4-yl group, a 1-methyl-1H-

imidazol-2-yl group, a 1-methyl-1H-imidazol-4-yl group, a pyridin-2-yl group, a pyridin-3-yl group, a pyridin-4-yl group, a 3,5-dimethylpyridin-4-yl group, a 6-hydroxypyridin-2-yl group, a 5-hydroxypyridin-2-yl group, a 4-hydroxypyridin-2-yl group, a 3-hydroxypyridin-2-yl group, a 6-methoxypyridin-2-yl group, a 5-methoxypyridin-2-yl group, a 4-methoxypyridin-2-yl group, a 3-methoxypyridin-2-yl group, a pyrimidin-2-yl group, a pyrimidin-4-yl group, a 1,3,5-triazin-2-yl group, a tetrahydrofuran-2-yl group, a tetrahydrofuran-3-yl group, a tetrahydropyran-2-yl group, a tetrahydropyran-3-yl group, a tetrahydropyran-4-yl group, an oxetanyl group, a pyrrolidin-1-yl group, a piperidin-1-yl group, a piperazin-1-yl group, a morpholin-4-yl group, an azetidin-1-yl group, a 4-hydroxypiperidin-1-yl group, a 3-hydroxypyrrolidin-1-yl group, a 3-hydroxyazetidin-1-yl group, a dimethylamino group, a diethylamino group, a methylethylamino group, a cyclobutylamino group, a cyclopentylamino group, a cyclohexylamino group, an acetamide group, an N-methylacetamide group, an propionylamino group, a butyrylamino group, an isobutyrylamino group, a valerylamino group, an isovalerylamino group, a methoxy group, an ethoxy group, an n-propoxy group, an isopropoxy group, an n-butoxy group, an isobutoxy

group, a trifluoromethoxy group, a difluoromethoxy group, a 2,2,2-trifluoroethoxy group, a cyanomethoxy group, a carboxymethoxy group, a 2-hydroxyethoxy group, a 2-methoxyethoxy group, a 2-hydroxypropoxy group, a 2-hydroxy-2-methylpropoxy group, a (1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxy-2-methylpropoxy group, a difluoro(1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxyethoxy group, a (1,1,1-trifluoro-3-hydroxypropan-2-yl)oxy group, a 3,3,3-trifluoro-2-hydroxypropoxy group, a 2,2-difluoro-2-hydroxyethoxy group, a 2-(trifluoromethoxy)ethoxy group, a (1,3-dihydroxypropan-2-yl)oxy group, a (1-hydroxy-3-(trifluoromethoxy)propan-2-yl)oxy group, a 2-oxopropoxy group, a 1,1-difluoro-2-oxopropoxy group, a (1,1,1-trifluoro-3-oxobutan-2-yl)oxy group, a 3,3,3-trifluoro-2-oxopropoxy group, a 1,1-difluoro-2-hydroxypropoxy group, a (1,1,1-trifluoro-3-hydroxybutan-2-yl)oxy group, an oxetan-3-yl methoxy group, a 3-hydroxy-2-(hydroxymethyl)propoxy group, an allyloxy group, a cyclobutoxy group, a (methylsulfonyl)methoxy group, a (ethylsulfonyl)methoxy group, a (isopropylsulfonyl)methoxy group, a (2H-tetrazol-5-yl)methoxy group, a 2-amino-2-oxoethoxy group, a cyanodifluoromethoxy group, a carboxydifluoromethoxy

group, a difluoro(2H-tetrazol-5-yl)methoxy group, a difluoro(methylsulfonyl)methoxy group, a 2-carboxyethoxy group, a 2-cyanoethoxy group, a 2-(methylsulfonyl)ethoxy group, a 2-morpholinoethoxy group, a 3-hydroxycyclobutoxy group, a 3-cyanocyclobutoxy group, a 3-carboxycyclobutoxy group, a 3-(methylsulfonyl)cyclobutoxy group, a 3-(2H-tetrazol-5-yl)cyclobutoxy group, a (4-hydroxycyclohexyl)oxy group, a 2-hydroxy-3-methoxypropoxy group, a phenyloxy group, a benzyloxy group, a thiazol-5-yloxy group, a thiazol-4-yloxy group, a pyridin-4-yloxy group, a pyridin-3-yl oxy group, a methylthio group, a methylsulfonyl group, a methylsulfinyl group, a methylsulfamoyl group, a dimethylsulfamoyl group, a sulfamoyl group, an acetyl group, a 2,2-difluoroacetyl group, a 1-(methoxyimino)ethyl group, a carbamoyl group, a dimethylcarbamoyl group, a morpholine-4-carbonyl group, a piperidine-1-carbonyl group, an azetidine-1-carbonyl group, a benzylcarbamoyl group, a methylcarbamoyl group, a 3-hydroxy-3-(trifluoromethyl)azetidine-1-carbonyl group, a methoxycarbonyl group, an ethoxycarbonyl group, a 1-hydroxycyclopropyl group, or a 1-methoxycyclopropyl group, or more preferably a hydrogen atom, a chlorine atom, a carboxy group, an isopropyl group, a

trifluoromethyl group, a hydroxymethyl group, a methoxymethyl group, a 2-hydroxypropan-2-yl group, a morpholinomethyl group, a (dimethylamino)methyl group, a 2,2,2-trifluoro-1-hydroxyethyl group, a 2,2,2-trifluoro-1-methoxyethyl group, a 1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-methoxyethyl group, a 1,1-difluoro-2-hydroxypropan-2-yl group, a 1,1,1-trifluoro-2-methoxypropan-2-yl group, a 1-hydroxyethyl group, a 1-hydroxypropyl group, a 1-hydroxy-2-methylpropyl group, a 1-methoxyethyl group, a 2-methoxypropan-2-yl group, a 1-acetoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl group, a 1-ethoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl group, a 2,2,2-trifluoro-1,1-dihydroxyethyl group, a 1-(cyanomethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxypropoxy)ethyl group, a 2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxypropan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxy-2-methylpropan-2-yl)oxy)ethyl group, a 1-(1,1-difluoro-2-hydroxypropoxy)-2,2,2-trifluoroethyl group, a 1-

(1,1-difluoro-2-hydroxy-2-methylpropoxy)-2,2,2-trifluoroethyl group, a 1-(difluoro(1-hydroxycyclopropyl)methoxy)-2,2,2-trifluoroethyl group, a 1-(carboxymethoxy)-2,2,2-trifluoroethyl group, a 1-(2-amino-2-oxoethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-((methylsulfonyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-(sulfamoylmethoxy)ethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2-difluoroethyl group, a 1-hydroxy-3-(methylsulfonyl)propyl group, a 3-(ethylsulfonyl)-1-hydroxypropyl group, a 1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2,2-trifluoro-1-(2-morpholino-2-oxoethoxy)ethyl group, a 1-carboxy-2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a 1,3-dihydroxypropyl group, a 1-hydroxy-3-methoxypropyl group, a 4,4,4-trifluoro-1,3-dihydroxybutyl group, a 1,3-dihydroxybutyl group, a 1,3-dihydroxy-3-methylbutyl group, a carboxy(hydroxy)methyl group, a hydroxy (2H-tetrazol-5-yl)methyl group, a hydroxy (3-hydroxycyclobutyl)methyl group, a 1-hydroxy-2-morpholinoethyl group, a 3-amino-1-hydroxy-3-oxopropyl group, a 1-hydroxy-2-(methylsulfonamide)ethyl group, a 2-cyanoethyl group, a 1,2-dihydroxyethyl group, a 3,3,3-trifluoro-1,2-dihydroxypropyl group, a 3,3,3-

trifluoro-1-hydroxy-2-oxopropyl group, a 3,3,3-trifluoro-1-hydroxypropyl group, a 3,3,3-trifluoro-2-hydroxypropyl group, a 3,3,3-trifluoro-2-oxopropyl group, a 1-hydroxy-3-oxobutyl group, an acetamide group, an N-methylacetamide group, a methoxy group, an isopropoxy group, a trifluoromethoxy group, a 2,2,2-trifluoroethoxy group, a cyanomethoxy group, a carboxymethoxy group, a 2-hydroxyethoxy group, a 2-methoxyethoxy group, a 2-hydroxypropoxy group, a 2-hydroxy-2-methylpropoxy group, a (1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxy-2-methylpropoxy group, a difluoro(1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxyethoxy group, a 3,3,3-trifluoro-2-hydroxypropoxy group, a 2,2-difluoro-2-hydroxyethoxy group, a 2-(trifluoromethoxy)ethoxy group, a 1,1-difluoro-2-hydroxypropoxy group, a (1,1,1-trifluoro-3-hydroxybutan-2-yl)oxy group, an oxetan-3-ylmethoxy group, a 3-hydroxy-2-(hydroxymethyl)propoxy group, an allyloxy group, a cyclobutoxy group, a (methylsulfonyl)methoxy group, a (ethylsulfonyl)methoxy group, a (isopropylsulfonyl)methoxy group, a (2H-tetrazol-5-yl)methoxy group, a 2-amino-2-oxoethoxy group, a carboxydifluoromethoxy group, a 2-carboxyethoxy group, a 2-cyanoethoxy group, a 2-(methylsulfonyl)ethoxy

group, a 2-morpholinoethoxy group, a 3-hydroxycyclobutoxy group, a 3-cyanocyclobutoxy group, a 3-carboxycyclobutoxy group, a 3-(methylsulfonyl)cyclobutoxy group, a 3-(2H-tetrazol-5-yl)cyclobutoxy group, a (4-hydroxycyclohexyl)oxy group, a 2-hydroxy-3-methoxypropoxy group, a benzyloxy group, a methylthio group, a methylsulfonyl group, a methylsulfinyl group, a methylsulfamoyl group, a dimethylsulfamoyl group, a sulfamoyl group, an acetyl group, a 1-(methoxyimino)ethyl group, a carbamoyl group, a dimethylcarbamoyl group, a morpholine-4-carbonyl group, a piperidine-1-carbonyl group, an azetidine-1-carbonyl group, a benzylcarbamoyl group, a methylcarbamoyl group, a 3-hydroxy-3-(trifluoromethyl)azetidine-1-carbonyl group, a methoxycarbonyl group, an ethoxycarbonyl group, a 1-hydroxycyclopropyl group, or a 1-methoxycyclopropyl group.

In the present invention, the group represented by R^3 in the general formula (1) is a hydrogen atom.

In the present invention, the group represented by R^4 in the general formula (1) is an optionally substituted 4- to 10-membered monocyclic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, and may be aromatic and nonaromatic. In addition, if R^4 is

to be substituted with the substituent described above, the substitution may take place at any position. The group represented by R^4 in the general formula (1) is preferably an oxazolyl group, an isoxazolyl group, an oxadiazolyl group, a thiazolyl group, a chlorothiazolyl group, a cyanothiazolyl group, a methylthiazolyl group, a hydroxymethylthiazolyl group, a carbamoylthiazolyl group, a nitrothiazolyl group, a fluorothiazolyl group, a difluorothiazolyl group, a deuterated thiazolyl group, an isothiazolyl group, an imidazolyl group, a methylimidazolyl group, a triazolyl group, a pyridyl group, a chloropyridyl group, a fluoropyridyl group, a cyanopyridyl group, a methylpyridyl group, a pyrimidinyl group, a tetrazolyl group, or a furanyl group, more preferably an oxazolyl group, a thiazolyl group, a fluorothiazolyl group, a difluorothiazolyl group, a deuterated thiazolyl group, an isothiazolyl group, a pyridyl group, a fluoropyridyl group, or a furanyl group, or still more preferably a thiazol-2-yl group, a thiazol-4-yl group, a pyridin-2-yl group, an oxazol-2-yl group, a 1H-pyrazol-1-yl group, a 4-methylthiazol-2-yl group, a 5-fluoropyridin-2-yl group, a 2H-1,2,3-triazol-2-yl group, a 1,2,4-thiadiazol-5-yl group, a 1-methyl-1H-pyrazol-3-yl group, a pyrimidin-2-yl group, an isothiazol-3-yl

group, a 3-methyl-1,2,4-thiadiazol-5-yl group, or a 5-chloropyridin-2-yl group.

In the present invention, X in the general formula (1) represents a group represented by the formulae: $-CH_2-$, $-CH_2-CH_2-$, $-CH_2-CH_2-CH_2-$, or $-CH_2-O-CH_2-$.

In the present invention, Z in the general formula (1) represents a hydrogen atom or a hydroxyl group.

Preferred embodiments of the compound of the present invention or the pharmacologically acceptable salt thereof are, for example, embodiments where the compound of the present invention is in the form of compounds (1a) to (1i).

[Compound (1a)]

A compound in which, in the general formula (1),

R^1 represents, among the above, a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyl group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclic group containing 1 to 4 heteroatoms selected from an

oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group [two C_{1-6} alkyl groups in the di-C_{1-6} alkylsulfamoyl group may form a pyrrolidin-1-yl group or a morpholino group with an adjacent nitrogen atom], a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally

substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic aralkylaminocarbonyl group, an optionally substituted C_{1-6} alkyloxycarbonyl group, or an optionally substituted hydroxyaminocarbonyl group, and

R^2 represents, among the above, a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{2-6} alkenyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an

oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group, a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkylaminocarbonyl group, or an optionally substituted C_{1-6} alkyloxycarbonyl group.

[Compound (1b)]

A compound in which, in the general formula (1),

R^1 represents, among the above, a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyl group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4-

to 10-membered monocyclic nonaromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom(s), and a sulfur atom, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group [two C_{1-6} alkyl groups in the di-C_{1-6} alkylsulfamoyl group may form a pyrrolidin-1-yl group or a morpholino group with an adjacent nitrogen atom], a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6}

alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic aralkylaminocarbonyl group,an optionally substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{1-6} alkyloxycarbonyl group, or an optionally substituted hydroxyaminocarbonyl group, and

R^2 represents, among the above, a hydrogen atom.

[Compound (1c)]

A compound in which, in the general formula (1),

R^1 represents, among the above, a hydrogen atom, and

R^2 represents, among the above, a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{2-6} alkenyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an

oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group, a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an aminocarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkylaminocarbonyl group, or an optionally substituted C_{1-6} alkyloxycarbonyl group.

[Compound (1d)]

A compound in which, in the general formula (1), the groups represented by R^1 and R^2 may be the same or different and each of them is, among the above, a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally

substituted C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyl group, an optionally substituted C_{6-10} monocyclic or polycyclic aryl group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkyl group, an optionally substituted 4- to 10-membered monocyclic or bicyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic or bicyclic nonaromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, a di-C_{1-6} alkyl amino group, an optionally substituted C_{3-7} cycloalkyl amino group, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{2-6} alkenyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted C_{6-10} monocyclic or polycyclic aryloxy group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkyloxy group, an optionally substituted 4- to 10-membered monocyclic or bicyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic or bicyclic

nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group, a sulfamoyl group [two C_{1-6} alkyl groups in the di-C_{1-6} alkylsulfamoyl group may form a pyrrolidin-1-yl group or a morpholino group with an adjacent nitrogen atom], a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkylaminocarbonyl group, or an optionally substituted C_{1-6} alkyloxycarbonyl group.

[Compound (1e)]

A compound in which, in the general formula (1), the group represented by R^1 is, among the above, a hydrogen atom; a halogen atom; a hydroxyl group; a carboxy group; a cyano group; a C_{1-3} alkyl group

optionally substituted with one or more substituents selected from a fluorine atom, a hydroxyl group, a methyl group, a methoxy group, an oxo group, and a 4- to 6-membered monocyclic nonaromatic heterocyclic group containing 1 to 3 heteroatoms selected from an oxygen atom and a nitrogen atom; a C_{3-6} cycloalkyl group; a 4- to 6-membered monocyclic aromatic heterocyclic group containing 1 to 3 heteroatoms selected from a nitrogen atom and a sulfur atom; a 4- to 6-membered monocyclic nonaromatic heterocyclic group containing one or two heteroatoms selected from an oxygen atom and a nitrogen atom; a C_{1-3} acylamino group; a C_{1-5} alkyloxy group optionally substituted with one or more substituents selected from a fluorine atom, a hydroxyl group, a methyl group, an ethyl group, a cyano group, and a methoxy group; a C_{1-3} alkyloxy-C_{1-3} alkyl group optionally substituted with one or more substituents selected from a fluorine atom, a hydroxyl group, a cyano group, a carboxy group, a carbamoyl group, a methyl group, a tetrazolyl group, a methoxy group, and a cyclopropyl group; a C_{3-6} cycloalkyloxy group optionally substituted with one or more substituents selected from a C_{1-3} alkyl group optionally substituted with a hydroxyl group, a hydroxyl group, and a cyano group; a 5- or 6-membered monocyclic aromatic heterocyclyloxy group containing 1

to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, which may be optionally substituted with one or more substituents selected from a C_{1-3} alkyl group optionally substituted with a hydroxyl group, a C_{1-3} alkyl group, a trifluoromethyl group, and a C_{1-3} alkylsulfonyl group; a 4- to 6-membered monocyclic nonaromatic heterocyclyloxy group which contains 1 to 3 heteroatoms selected from an oxygen atom and a sulfur atom and which, if containing a sulfur atom, may have one or more oxo groups bonded to the sulfur atom; a C_{1-3} alkylthio group optionally substituted with a hydroxyl group; a C_{1-3} alkylsulfonyl group optionally substituted with one or more substituents selected from a hydroxyl group and a fluorine atom; a C_{1-3} alkylsulfinyl group optionally substituted with one or more substituents selected from a hydroxyl group and a fluorine atom; a sulfamoyl group; a C_{1-3} alkylcarbonyl group; an aminocarbonyl group; a mono-C_{1-3} alkylaminocarbonyl group optionally substituted with one or more substituents selected from a hydroxyl group, a C_{1-3} alkyloxy group, and a phenyl group; a di-C_{1-3} alkylaminocarbonyl group optionally substituted with a hydroxyl group; a C_{3-6} cycloalkyl amino group; a C_{7-9} monocyclic aralkylaminocarbonyl group; or a C_{1-3} alkyloxycarbonyl group,

the group represented by R^2 is, among the above, a hydrogen atom; a halogen atom; a hydroxyl group; a carboxy group; a C_{1-3} alkyl group optionally substituted with one or more substituents selected from a fluorine atom, a hydroxyl group, a methyl group, a methoxy group, an oxo group, a dimethylamino group, and a 4- to 6-membered monocyclic nonaromatic heterocyclic group containing 1 to 3 heteroatoms selected from an oxygen atom and a nitrogen atom; a C_{3-6} cycloalkyl group; a di-C_{1-3} alkyl amino group optionally substituted with an oxo group; a C_{1-3} acylamino group; a C_{1-5} alkyloxy group optionally substituted with one or more substituents selected from a fluorine atom, a hydroxyl group, a methyl group, an ethyl group, a cyano group, a methoxy group, an oxetan-3-yl group, a hydroxymethyl group, a vinyl group, and a carboxy group; a C_{1-3} alkyloxy-C_{1-3} alkyl group optionally substituted with one or more substituents selected from a fluorine atom, a hydroxyl group, a cyano group, a methyl group, an oxo group, and a methoxy group; a C_{3-6} cycloalkyloxy group optionally substituted with one or more substituents selected from a C_{1-3} alkyl group optionally substituted with a hydroxyl group, a hydroxyl group, and a cyano group; a 4- to 6-membered monocyclic nonaromatic heterocyclyloxy group which contains 1 to 3

heteroatoms selected from an oxygen atom and a sulfur atom and which, if containing a sulfur atom, may have one or more oxo groups bonded to the sulfur atom; a C_{1-3} alkylthio group; a C_{1-3} alkylsulfonyl group optionally substituted with one or more substituents selected from a hydroxyl group and a fluorine atom; a C_{1-3} alkylsulfinyl group optionally substituted with one or more substituents selected from a hydroxyl group and a fluorine atom; a sulfamoyl group; a C_{1-3} alkylcarbonyl group; an aminocarbonyl group; a mono-C_{1-3} alkylaminocarbonyl group; a di-C_{1-3} alkylaminocarbonyl group optionally substituted with a hydroxyl group; a C_{3-6} cycloalkyl amino group; a C_{7-9} monocyclic aralkylaminocarbonyl group; or a C_{1-3} alkyloxycarbonyl group, and

the group represented by R^4 is, among the above, an oxazolyl group, a thiazolyl group, a methylthiazolyl group, an isothiazolyl group, a pyrazolyl group, a methylpyrazolyl group, a triazolyl group, a 1,2,4-thiadiazolyl, a methyl-1,2,4-thiadiazolyl, a pyridyl group, a chloropyridyl group, a fluoropyridyl group, a pyrimidinyl group, or a furanyl group, all of which may be optionally substituted at any position.

[Compound (1f)]

A compound in which, in the general formula (1),

the group represented by R^1 is, among the above, a hydrogen atom, a fluorine atom, a chlorine atom, a carboxy group, a cyano group, a methyl group, an ethyl group, an isopropyl group, a trifluoromethyl group, a difluoromethyl group, a hydroxymethyl group, a methoxymethyl group, a 2-hydroxypropan-2-yl group, a morpholinomethyl group, a (dimethylamino)methyl group, a 2,2,2-trifluoro-1-hydroxyethyl group, a 2,2,2-trifluoro-1-methoxyethyl group, a 1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-methoxyethyl group, a 1,1-difluoro-2-hydroxypropan-2-yl group, a 1,1,1-trifluoro-2-methoxypropan-2-yl group, a 1-hydroxyethyl group, a 1-hydroxypropyl group, a 1-hydroxy-2-methylpropyl group, a 1-methoxyethyl group, a 2-methoxypropan-2-yl group, a 1-acetoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl group, a 1-ethoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl group, a 2,2,2-trifluoro-1,1-dihydroxyethyl group, a 1-(cyanomethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxypropoxy)ethyl group, a 2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl

group, a 2,2,2-trifluoro-1-((1-hydroxypropan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxy-2-methylpropan-2-yl)oxy)ethyl group, a 1-(1,1-difluoro-2-hydroxypropoxy)-2,2,2-trifluoroethyl group, a 1-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-2,2,2-trifluoroethyl group, a 1-(difluoro(1-hydroxycyclopropyl)methoxy)-2,2,2-trifluoroethyl group, a 1-(carboxymethoxy)-2,2,2-trifluoroethyl group, a 1-(2-amino-2-oxoethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-((methylsulfonyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-(sulfamoylmethoxy)ethyl group, a 1,1,1-trifluoro-3-hydroxypropan-2-yl group, a 1,1,1,4,4,4-hexafluoro-3-hydroxybutan-2-yl group, a 1-((1,3-dihydroxypropan-2-yl)oxy)-2,2,2-trifluoroethyl group, a 1,1,1-trifluoro-3-hydroxybutan-2-yl group, a 1,1,1-trifluoro-3-oxobutan-2-yl group, a 1,1,1,4,4,4-hexafluoro-3-oxobutan-2-yl group, a 1,1,1-trifluoro-3,4-dihydroxybutan-2-yl group, a 1,1,1-trifluoro-4-hydroxy-3-oxobutan-2-yl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2-difluoroethyl group, a 1-hydroxy-3-(methylsulfonyl)propyl group, a 2,2-difluoro-1-hydroxy-3-(methylsulfonyl)propyl group, a 3-(ethylsulfonyl)-1-hydroxypropyl group, a 3-(ethylsulfonyl)-2,2-difluoro-1-hydroxypropyl group, a

1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2-difluoro-1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2,2-trifluoro-1-(2-morpholino-2-oxoethoxy)ethyl group, a 1-hydroxy-2-morpholinoethyl group, a 2,2-difluoro-1-hydroxy-2-morpholinoethyl group, a 1-carboxy-2,2-difluoro-1-hydroxyethyl group, a 1-carboxy-2,2,2-trifluoro-1-hydroxyethyl group, a 2,2-difluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a 2,2,2-trifluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a 1,1-difluoro-3-hydroxypropan-2-yl group, a 1,1-difluoro-3-hydroxy-3-methylbutan-2-yl group, a 1,1,1-trifluoro-3-hydroxy-3-methylbutan-2-yl group, a 3-cyano-1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 1,3-dihydroxypropyl group, a 1-hydroxy-3-methoxypropyl group, a 4,4,4-trifluoro-1,3-dihydroxybutyl group, a 1,3-dihydroxybutyl group, a 1,3-dihydroxy-3-methylbutyl group, a cyclopropyl (hydroxy)methyl group, a carboxy(hydroxy)methyl group, a hydroxy (2H-tetrazol-5-yl)methyl group, a hydroxy (3-hydroxycyclobutyl)methyl group, a 3-amino-1-hydroxy-3-oxopropyl group, a 1-hydroxy-2-(methylsulfonamide)ethyl group, a 2-cyanoethyl group, a 1,2-dihydroxyethyl group, a 3,3,3-trifluoro-1,2-dihydroxypropyl group, a 3,3,3-trifluoro-1-hydroxy-2-oxopropyl group, a 3,3,3-trifluoro-1-hydroxypropyl group, a 3,3,3-trifluoro-2-hydroxypropyl group, a

3,3,3-trifluoro-2-oxopropyl group, a 1-hydroxy-3-oxobutyl group, a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a phenyl group, a benzyl group, a thiazol-2-yl group, a 1H-pyrazol-1-yl group, a 5-methylthiazol-2-yl group, a 5-methoxycarbonylthiazol-2-yl group, a 5-hydroxymethylthiazol-2-yl group, a 5-(1-hydroxyethyl)thiazol-2-yl group, a 5-(2-hydroxypropan-2-yl)thiazol-2-yl group, a 5-(N,N-dimethylaminomethyl)thiazol-2-yl group, a 5-methylthiazol-4-yl group, an oxazol-2-yl group, an oxazol-4-yl group, a 5-methyloxazol-4-yl group, a 1H-imidazol-1-yl group, a 2,5-dimethyl-1H-imidazol-1-yl group, a 1H-imidazol-4-yl group, a 1-methyl-1H-imidazol-2-yl group, a 1-methyl-1H-imidazol-4-yl group, a pyridin-2-yl group, a pyridin-3-yl group, a pyridin-4-yl group, a 3,5-dimethylpyridin-4-yl group, a 6-hydroxypyridin-2-yl group, a 5-hydroxypyridin-2-yl group, a 4-hydroxypyridin-2-yl group, a 3-hydroxypyridin-2-yl group, a 6-methoxypyridin-2-yl group, a 5-methoxypyridin-2-yl group, a 4-methoxypyridin-2-yl group, a 3-methoxypyridin-2-yl group, a pyrimidin-2-yl group, a pyrimidin-4-yl group, a 1,3,5-triazin-2-yl group, a tetrahydrofuran-2-yl group, a tetrahydrofuran-3-yl group, a tetrahydropyran-2-yl group, a tetrahydropyran-3-yl

group, a tetrahydropyran-4-yl group, an oxetanyl group, a pyrrolidin-1-yl group, a piperidin-1-yl group, a piperazin-1-yl group, a morpholin-4-yl group, an azetidin-1-yl group, a 4-hydroxypiperidin-1-yl group, a 3-hydroxypyrrolidin-1-yl group, a 3-hydroxyazetidin-1-yl group, a dimethylamino group, a diethylamino group, a methylethylamino group, a cyclobutylamino group, a cyclopentylamino group, a cyclohexylamino group, an acetamide group, an N-methylacetamide group, an propionylamino group, a butyrylamino group, an isobutyrylamino group, a valerylamino group, an isovalerylamino group, a methoxy group, an ethoxy group, an n-propoxy group, an isopropoxy group, an n-butoxy group, an isobutoxy group, a trifluoromethoxy group, a difluoromethoxy group, a 2,2,2-trifluoroethoxy group, a cyanomethoxy group, a carboxymethoxy group, a 2-hydroxyethoxy group, a 2-methoxyethoxy group, a 2-hydroxypropoxy group, a 2-hydroxy-2-methylpropoxy group, a (1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxy-2-methylpropoxy group, a difluoro(1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxyethoxy group, a (1,1,1-trifluoro-3-hydroxypropan-2-yl)oxy group, a 3,3,3-trifluoro-2-hydroxypropoxy group, a 2,2-difluoro-2-hydroxyethoxy group, a 2-(trifluoromethoxy)ethoxy group, a (1,3-

dihydroxypropan-2-yl)oxy group, a (1-hydroxy-3-(trifluoromethoxy)propan-2-yl)oxy group, a 2-oxopropoxy group, a 1,1-difluoro-2-oxopropoxy group, a (1,1,1-trifluoro-3-oxobutan-2-yl)oxy group, a 3,3,3-trifluoro-2-oxopropoxy group, a 1,1-difluoro-2-hydroxypropoxy group, a (1,1,1-trifluoro-3-hydroxybutan-2-yl)oxy group, an oxetan-3-ylmethoxy group, a 3-hydroxy-2-(hydroxymethyl)propoxy group, an allyloxy group, a cyclobutoxy group, a (methylsulfonyl)methoxy group, a (ethylsulfonyl)methoxy group, a (isopropylsulfonyl)methoxy group, a (2H-tetrazol-5-yl)methoxy group, a 2-amino-2-oxoethoxy group, a cyanodifluoromethoxy group, a carboxydifluoromethoxy group, a difluoro(2H-tetrazol-5-yl)methoxy group, a difluoro(methylsulfonyl)methoxy group, a 2-carboxyethoxy group, a 2-cyanoethoxy group, a 2-(methylsulfonyl)ethoxy group, a 2-morpholinoethoxy group, a 3-hydroxycyclobutoxy group, a 3-cyanocyclobutoxy group, a 3-carboxycyclobutoxy group, a 3-(methylsulfonyl)cyclobutoxy group, a 3-(2H-tetrazol-5-yl)cyclobutoxy group, a (4-hydroxycyclohexyl)oxy group, a 2-hydroxy-3-methoxypropoxy group, a phenyloxy group, a benzyloxy group, a thiazol-5-yloxy group, a thiazol-4-yloxy group, a pyridin-4-yloxy group, a pyridin-3-yloxy

group, a methylthio group, a methylsulfonyl group, a methylsulfinyl group, a methylsulfamoyl group, a dimethylsulfamoyl group, a sulfamoyl group, an acetyl group, a 2,2-difluoroacetyl group, a 1-(methoxyimino)ethyl group, a carbamoyl group, a dimethylcarbamoyl group, a morpholine-4-carbonyl group, a piperidine-1-carbonyl group, an azetidine-1-carbonyl group, a benzylcarbamoyl group, a methylcarbamoyl group, a 3-hydroxy-3-(trifluoromethyl)azetidine-1-carbonyl group, a methoxycarbonyl group, an ethoxycarbonyl group, a (tetrahydro-2H-pyran-4-yl)oxy group, a 1-(1,1-difluoro-2-hydroxyethoxy)-2,2,2-trifluoroethyl group, a (tetrahydro-2H-pyran-3-yl)oxy group, a difluoromethoxy group, a 3-(2-hydroxypropan-2-yl)cyclobutoxy group, a (1-hydroxy-2-methylpropan-2-yl)oxy group, a 2,2,2-trifluoro-1-((3-hydroxy-2,3-dimethylbutan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-methoxycyclopropyl)methoxy)ethyl group, a 1,1-difluoro-3-hydroxy-3-methylbutoxy group, a (1,1-dioxido tetrahydro-2H-thiopyran-4-yl)oxy) group, an oxetan-3-yloxy group, a 1,1-difluoro-2,3-dihydroxy-2-methylpropoxy group, a (trifluoromethyl)sulfonyl group, a (5-(trifluoromethyl)pyridin-2-yl)oxy group, a pyridin-2-

yloxy group, a pyrimidin-2-yloxy group, a pyrazin-2-yloxy group, a (6-methyl-4-(trifluoromethyl)pyridazin-3-yl)oxy group, a (5-(hydroxymethyl)pyridin-2-yl)oxy group, a (5-(hydroxymethyl)-3-(trifluoromethyl)pyridin-2-yl)oxy group, a (5-(trifluoromethoxy)pyridin-2-yl)oxy group, a (2-hydroxyethyl)thio group, a (2-hydroxyethyl)sulfinyl group, a (2-hydroxyethyl)sulfonyl group, a (1,1-difluoroallyl)oxy group, a (5-(methylsulfonyl)pyridin-2-yl)oxy group, a (2-methoxyethyl)carbamoyl group, a (2-hydroxyethyl)carbamoyl group, a (2-hydroxyethyl)(methyl)carbamoyl group, a cyclopropylcarbamoyl group, an ethylcarbamoyl group, a pyrrolidine-1-carbonyl group, hydroxy carbamoyl group, a 1,1-difluoro-2,3-dihydroxypropoxy group, a 3-((hydroxymethyl)pyridin-2-yl)oxy group, a 1,1-difluoro-2,2-dihydroxypropoxy group, an N-(2-hydroxyethyl)sulfamoyl group, an N-(2-methoxyethyl)sulfamoyl group, an N-(2-hydroxyethyl)-N-methylsulfamoyl group, a pyrrolidin-1-ylsulfonyl group, a morpholinosulfonyl group, a 1,1-difluoro-2-methoxyethoxy group, a 1,1-difluoro-2-methoxy-2-methylpropoxy group, a 1,1-difluoro-2-hydroxybutoxy group, a 1,1-dioxidothio morpholino group, a 1,1-difluoropropoxy group, a 1,1-difluoro-2-hydroxy-3-methylbutoxy group, a benzo[d]oxazol-2-yldifluoromethoxy group, a (1,1-difluoro-3-(pyridin-3-

yl)aryl)oxy group, a 1,1-difluoro-2-((hydroxyethyl)(methyl)amino)-2-oxoethoxy group, a 2-(dimethylamino)-1,1-difluoro-2-oxoethoxy group, a 1,1-difluoro-2-morpholino-2-oxoethoxy group, a 2-amino-1,1-difluoro-2-oxoethoxy group, a 1,1-difluoro-2-((2-hydroxyethyl)amino)-2-oxoethoxy group, a 1,1-difluoro-2-(3-hydroxyazetidin-1-yl)-2-oxoethoxy group, or cyclobutyl group,

the group represented by R^2 is, among the above, a hydrogen atom, a fluorine atom, a chlorine atom, a bromine atom, a carboxy group, a cyano group, a methyl group, an ethyl group, an isopropyl group, a trifluoromethyl group, a difluoromethyl group, a hydroxymethyl group, a methoxymethyl group, a 2-hydroxypropan-2-yl group, a morpholinomethyl group, a (dimethylamino)methyl group, a 2,2,2-trifluoro-1-hydroxyethyl group, a 2,2,2-trifluoro-1-methoxyethyl group, a 1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-methoxyethyl group, a 1,1-difluoro-2-hydroxypropan-2-yl group, a 1,1,1-trifluoro-2-methoxypropan-2-yl group, a 1-hydroxyethyl group, a 1-hydroxypropyl group, a 1-hydroxy-2-methylpropyl group, a 1-methoxyethyl group, a 2-methoxypropan-2-yl group, a 1-acetoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl group, a 2,2,2-

trifluoro-1-(2-methoxyethoxy)ethyl group, a 1-ethoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl group, a 2,2,2-trifluoro-1,1-dihydroxyethyl group, a 1-(cyanomethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxypropoxy)ethyl group, a 2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxypropan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxy-2-methylpropan-2-yl)oxy)ethyl group, a 1-(1,1-difluoro-2-hydroxypropoxy)-2,2,2-trifluoroethyl group, a 1-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-2,2,2-trifluoroethyl group, a 1-(difluoro(1-hydroxycyclopropyl)methoxy)-2,2,2-trifluoroethyl group, a 1-(carboxymethoxy)-2,2,2-trifluoroethyl group, a 1-(2-amino-2-oxoethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-((methylsulfonyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-(sulfamoylmethoxy)ethyl group, a 1,1,1-trifluoro-3-hydroxypropan-2-yl group, a 1,1,1,4,4,4-hexafluoro-3-hydroxybutan-2-yl group, a 1-((1,3-dihydroxypropan-2-yl)oxy)-2,2,2-trifluoroethyl group, a 1,1,1-trifluoro-3-hydroxybutan-2-yl group, a 1,1,1-trifluoro-3-oxobutan-2-yl group, a 1,1,1,4,4,4-hexafluoro-3-oxobutan-2-yl group, a 1,1,1-trifluoro-

3,4-dihydroxybutan-2-yl group, a 1,1,1-trifluoro-4-hydroxy-3-oxobutan-2-yl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2-difluoroethyl group, a 1-hydroxy-3-(methylsulfonyl)propyl group, a 2,2-difluoro-1-hydroxy-3-(methylsulfonyl)propyl group, a 3-(ethylsulfonyl)-1-hydroxypropyl group, a 3-(ethylsulfonyl)-2,2-difluoro-1-hydroxypropyl group, a 1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2-difluoro-1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2,2-trifluoro-1-(2-morpholino-2-oxoethoxy)ethyl group, a 1-hydroxy-2-morpholinoethyl group, a 2,2-difluoro-1-hydroxy-2-morpholinoethyl group, a 1-carboxy-2,2-difluoro-1-hydroxyethyl group, a 1-carboxy-2,2,2-trifluoro-1-hydroxyethyl group, a 2,2-difluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a 2,2,2-trifluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a 1,1-difluoro-3-hydroxypropan-2-yl group, a 1,1-difluoro-3-hydroxy-3-methylbutan-2-yl group, a 1,1,1-trifluoro-3-hydroxy-3-methylbutan-2-yl group, a 3-cyano-1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 1,3-dihydroxypropyl group, a 1-hydroxy-3-methoxypropyl group, a 4,4,4-trifluoro-1,3-dihydroxybutyl group, a 1,3-dihydroxybutyl group, a 1,3-dihydroxy-3-methylbutyl group, a cyclopropyl (hydroxy)methyl group, a carboxy(hydroxy)methyl group, a hydroxy (2H-

tetrazol-5-yl)methyl group, a hydroxy (3-hydroxycyclobutyl)methyl group, a 3-amino-1-hydroxy-3-oxopropyl group, a 1-hydroxy-2-(methylsulfonamide)ethyl group, a 2-cyanoethyl group, a 1,2-dihydroxyethyl group, a 3,3,3-trifluoro-1,2-dihydroxypropyl group, a 1-hydroxycyclopropyl group, a 1-methoxycyclopropyl group, a 3,3,3-trifluoro-1-hydroxy-2-oxopropyl group, a 3,3,3-trifluoro-1-hydroxypropyl group, a 3,3,3-trifluoro-2-hydroxypropyl group, a 3,3,3-trifluoro-2-oxopropyl group, a 1-hydroxy-3-oxobutyl group, a cyclopropyl group, a cyclobutyl group, a cyclopentyl group, a phenyl group, a benzyl group, a thiazol-2-yl group, a 1H-pyrazol-1-yl group, a 5-methylthiazol-2-yl group, a 5-methoxycarbonylthiazol-2-yl group, a 5-hydroxymethylthiazol-2-yl group, a 5-(1-hydroxyethyl)thiazol-2-yl group, a 5-(2-hydroxypropan-2-yl)thiazol-2-yl group, a 5-(N,N-dimethylaminomethyl)thiazol-2-yl group, a 5-methylthiazol-4-yl group, an oxazol-2-yl group, an oxazol-4-yl group, a 5-methyloxazol-4-yl group, a 1H-imidazol-1-yl group, a 2,5-dimethyl-1H-imidazol-1-yl group, a 1H-imidazol-4-yl group, a 1-methyl-1H-imidazol-2-yl group, a 1-methyl-1H-imidazol-4-yl group, a pyridin-2-yl group, a pyridin-3-yl group, a pyridin-4-yl group, a 3,5-dimethylpyridin-4-yl group,

a 6-hydroxypyridin-2-yl group, a 5-hydroxypyridin-2-yl group, a 4-hydroxypyridin-2-yl group, a 3-hydroxypyridin-2-yl group, a 6-methoxypyridin-2-yl group, a 5-methoxypyridin-2-yl group, a 4-methoxypyridin-2-yl group, a 3-methoxypyridin-2-yl group, a pyrimidin-2-yl group, a pyrimidin-4-yl group, a 1,3,5-triazin-2-yl group, a tetrahydrofuran-2-yl group, a tetrahydrofuran-3-yl group, a tetrahydropyran-2-yl group, a tetrahydropyran-3-yl group, a tetrahydropyran-4-yl group, an oxetanyl group, a pyrrolidin-1-yl group, a piperidin-1-yl group, a piperazin-1-yl group, a morpholin-4-yl group, an azetidin-1-yl group, a 4-hydroxypiperidin-1-yl group, a 3-hydroxypyrrolidin-1-yl group, a 3-hydroxyazetidin-1-yl group, a dimethylamino group, a diethylamino group, a methylethylamino group, a cyclobutylamino group, a cyclopentylamino group, a cyclohexylamino group, an acetamide group, an N-methylacetamide group, an propionylamino group, a butyrylamino group, an isobutyrylamino group, a valerylamino group, an isovalerylamino group, a methoxy group, an ethoxy group, an n-propoxy group, an isopropoxy group, an n-butoxy group, an isobutoxy group, a trifluoromethoxy group, a difluoromethoxy group, a 2,2,2-trifluoroethoxy group, a cyanomethoxy group, a carboxymethoxy group, a 2-hydroxyethoxy

group, a 2-methoxyethoxy group, a 2-hydroxypropoxy group, a 2-hydroxy-2-methylpropoxy group, a (1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxy-2-methylpropoxy group, a difluoro(1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxyethoxy group, a (1,1,1-trifluoro-3-hydroxypropan-2-yl)oxy group, a 3,3,3-trifluoro-2-hydroxypropoxy group, a 2,2-difluoro-2-hydroxyethoxy group, a 2-(trifluoromethoxy)ethoxy group, a (1,3-dihydroxypropan-2-yl)oxy group, a (1-hydroxy-3-(trifluoromethoxy)propan-2-yl)oxy group, a 2-oxopropoxy group, a 1,1-difluoro-2-oxopropoxy group, a (1,1,1-trifluoro-3-oxobutan-2-yl)oxy group, a 3,3,3-trifluoro-2-oxopropoxy group, a 1,1-difluoro-2-hydroxypropoxy group, a (1,1,1-trifluoro-3-hydroxybutan-2-yl)oxy group, an oxetan-3-ylmethoxy group, a 3-hydroxy-2-(hydroxymethyl)propoxy group, an allyloxy group, a cyclobutoxy group, a (methylsulfonyl)methoxy group, a (ethylsulfonyl)methoxy group, a (isopropylsulfonyl)methoxy group, a (2H-tetrazol-5-yl)methoxy group, a 2-amino-2-oxoethoxy group, a cyanodifluoromethoxy group, a carboxydifluoromethoxy group, a difluoro(2H-tetrazol-5-yl)methoxy group, a difluoro(methylsulfonyl)methoxy group, a 2-carboxyethoxy group, a 2-cyanoethoxy group, a 2-

(methylsulfonyl)ethoxy group, a 2-morpholinoethoxy group, a 3-hydroxycyclobutoxy group, a 3-cyanocyclobutoxy group, a 3-carboxycyclobutoxy group, a 3-(methylsulfonyl)cyclobutoxy group, a 3-(2H-tetrazol-5-yl)cyclobutoxy group, a (4-hydroxycyclohexyl)oxy group, a 2-hydroxy-3-methoxypropoxy group, a phenyloxy group, a benzyloxy group, a thiazol-5-yloxy group, a thiazol-4-yloxy group, a pyridin-4-yloxy group, a pyridin-3-yloxy group, a methylthio group, a methylsulfonyl group, a methylsulfinyl group, a methylsulfamoyl group, a dimethylsulfamoyl group, a sulfamoyl group, an acetyl group, a 2,2-difluoroacetyl group, a 1-(methoxyimino)ethyl group, a carbamoyl group, a dimethylcarbamoyl group, a morpholine-4-carbonyl group, a piperidine-1-carbonyl group, an azetidine-1-carbonyl group, a benzylcarbamoyl group, a methylcarbamoyl group, a 3-hydroxy-3-(trifluoromethyl)azetidine-1-carbonyl group, a methoxycarbonyl group, an ethoxycarbonyl group, a (5-(trifluoromethyl)pyridin-2-yl)oxy group, or a (5-(hydroxymethyl)pyridin-2-yl)oxy group, and

the group represented by R^4 is, among the above, an oxazolyl group, an isoxazolyl group, an oxadiazolyl group, a thiazolyl group, a chlorothiazolyl group, a cyanothiazolyl group, a methylthiazolyl group, a

hydroxymethylthiazolyl group, a carbamoylthiazolyl group, a nitrothiazolyl group, a fluorothiazolyl group, a difluorothiazolyl group, a deuterated thiazolyl group, an isothiazolyl group, an imidazolyl group, a methylimidazolyl group, a triazolyl group, a pyridyl group, a chloropyridyl group, a fluoropyridyl group, a cyanopyridyl group, a methylpyridyl group, a pyrimidinyl group, a tetrazolyl group, or a furanyl group.

[Compound (1g)]

A compound in which, in the general formula (1), the group represented by R^1 is, among the above, a hydrogen atom, a chlorine atom, a cyano group, a carboxy group, a methyl group, a trifluoromethyl group, a hydroxymethyl group, a 2-hydroxypropan-2-yl group, a 2,2,2-trifluoro-1-hydroxyethyl group, a 2,2,2-trifluoro-1-methoxyethyl group, a 1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-methoxyethyl group, a 1,1-difluoro-2-hydroxypropan-2-yl group, a 1,1,1-trifluoro-2-methoxypropan-2-yl group, a 1-hydroxyethyl group, a 1-methoxyethyl group, a 2-methoxypropan-2-yl group, a 2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl group, a 1-ethoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-

hydroxyethoxy)ethyl group, a 2,2,2-trifluoro-1,1-dihydroxyethyl group, a 1-(cyanomethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxypropoxy)ethyl group, a 2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxypropan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxy-2-methylpropan-2-yl)oxy)ethyl group, a 1-(1,1-difluoro-2-hydroxypropoxy)-2,2,2-trifluoroethyl group, a 1-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-2,2,2-trifluoroethyl group, a 1-(difluoro(1-hydroxycyclopropyl)methoxy)-2,2,2-trifluoroethyl group, a 1-(carboxymethoxy)-2,2,2-trifluoroethyl group, a 1-(2-amino-2-oxoethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-((methylsulfonyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-(sulfamoylmethoxy)ethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2-difluoroethyl group, a 1-hydroxy-3-(methylsulfonyl)propyl group, a 3-(ethylsulfonyl)-1-hydroxypropyl group, a 1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2,2-trifluoro-1-(2-morpholino-2-oxoethoxy)ethyl group, a 1-carboxy-2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a phenyl

group, a thiazol-2-yl group, an acetamide group, a methoxy group, a trifluoromethoxy group, a cyanomethoxy group, a carboxymethoxy group, a 2-hydroxyethoxy group, a 2-methoxyethoxy group, a 2-hydroxypropoxy group, a 2-hydroxy-2-methylpropoxy group, a (1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxy-2-methylpropoxy group, a difluoro(1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxyethoxy group, a 3,3,3-trifluoro-2-hydroxypropoxy group, a 2,2-difluoro-2-hydroxyethoxy group, a 2-(trifluoromethoxy)ethoxy group, a 1,1-difluoro-2-hydroxypropoxy group, a (1,1,1-trifluoro-3-hydroxybutan-2-yl)oxy group, a cyclobutoxy group, a (methylsulfonyl)methoxy group, a (ethylsulfonyl)methoxy group, a (isopropylsulfonyl)methoxy group, a (2H-tetrazol-5-yl)methoxy group, a 2-amino-2-oxoethoxy group, a carboxydifluoromethoxy group, a 2-carboxyethoxy group, a 2-cyanoethoxy group, a 2-(methylsulfonyl)ethoxy group, a 2-morpholinoethoxy group, a 3-hydroxycyclobutoxy group, a 3-cyanocyclobutoxy group, a 3-carboxycyclobutoxy group, a 3-(methylsulfonyl)cyclobutoxy group, a 3-(2H-tetrazol-5-yl)cyclobutoxy group, a (4-hydroxycyclohexyl)oxy group, a 2-hydroxy-3-methoxypropoxy group, a benzyloxy group, an acetyl group, a carbamoyl group, a

dimethylcarbamoyl group, a morpholine-4-carbonyl group, a piperidine-1-carbonyl group, a methoxycarbonyl group, an ethoxycarbonyl group, a (tetrahydro-2H-pyran-4-yl)oxy group, a 1-(1,1-difluoro-2-hydroxyethoxy)-2,2,2-trifluoroethyl group, a tetrahydro-2H-pyran-3-yl)oxy group, a difluoromethoxy group, a 3-(2-hydroxypropan-2-yl)cyclobutoxy group, a (1-hydroxy-2-methylpropan-2-yl)oxy group, a 2,2,2-trifluoro-1-((3-hydroxy-2,3-dimethylbutan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-methoxycyclopropyl)methoxy)ethyl group, a 1,1-difluoro-3-hydroxy-3-methylbutoxy group, a (1,1-dioxido tetrahydro-2H-thiopyran-4-yl)oxy) group, an oxetan-3-yloxy group, a 1,1-difluoro-2,3-dihydroxy-2-methylpropoxy group, a (trifluoromethyl)sulfonyl group, a (5-(trifluoromethyl)pyridin-2-yl)oxy group, a pyridin-2-yloxy group, a pyrimidin-2-yloxy group, a pyrazin-2-yloxy group, a (6-methyl-4-(trifluoromethyl)pyridazin-3-yl)oxy group, a (5-(hydroxymethyl)pyridin-2-yl)oxy group, a (5-(hydroxymethyl)-3-(trifluoromethyl)pyridin-2-yl)oxy group, a (5-(trifluoromethoxy)pyridin-2-yl)oxy group, a methylsulfonyl group, a cyclopropyl group, a methylthio group, a methylsulfinyl group, a (2-

hydroxyethyl)thio group, a (2-hydroxyethyl)sulfinyl group, a (2-hydroxyethyl)sulfonyl group, a (1,1-difluoroallyl)oxy group, a (5-(methylsulfonyl)pyridin-2-yl)oxy group, a (2-methoxyethyl)carbamoyl group, a (2-hydroxyethyl)carbamoyl group, a (2-hydroxyethyl)(methyl)carbamoyl group, a cyclopropylcarbamoyl group, an ethylcarbamoyl group, a pyrrolidine-1-carbonyl group, a benzylcarbamoyl group, hydroxy carbamoyl group, a 1,1-difluoro-2,3-dihydroxypropoxy group, a 3-((hydroxymethyl)pyridin-2-yl)oxy group, a 1,1-difluoro-2,2-dihydroxypropoxy group, an N-(2-hydroxyethyl)sulfamoyl group, an N-(2-methoxyethyl)sulfamoyl group, an N-(2-hydroxyethyl)-N-methylsulfamoyl group, a pyrrolidin-1-ylsulfonyl group, a morpholinosulfonyl group, a 1,1-difluoro-2-methoxyethoxy group, a 1,1-difluoro-2-methoxy-2-methylpropoxy group, a 1,1-difluoro-2-hydroxybutoxy group, a 1,1-dioxidothio morpholino group, a 1,1-difluoropropoxy group, a 1,1-difluoro-2-hydroxy-3-methylbutoxy group, a benzo[d]oxazol-2-yldifluoromethoxy group, a (1,1-difluoro-3-(pyridin-3-yl)aryl)oxy group, a 1,1-difluoro-2-((hydroxyethyl)(methyl)amino)-2-oxoethoxy group, a 2-(dimethylamino)-1,1-difluoro-2-oxoethoxy group, a 1,1-difluoro-2-morpholino-2-oxoethoxy group, a 2-amino-1,1-difluoro-2-oxoethoxy group, a 1,1-difluoro-2-((2-

hydroxyethyl)amino)-2-oxoethoxy group, a 1,1-difluoro-2-(3-hydroxyazetidin-1-yl)-2-oxoethoxy group, or cyclobutyl group,

the group represented by R^2 is, among the above, a hydrogen atom, a chlorine atom, a bromine atom, a carboxy group, an isopropyl group, a trifluoromethyl group, a hydroxymethyl group, a methoxymethyl group, a 2-hydroxypropan-2-yl group, a morpholinomethyl group, a (dimethylamino)methyl group, a 2,2,2-trifluoro-1-hydroxyethyl group, a 2,2,2-trifluoro-1-methoxyethyl group, a 1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-methoxyethyl group, a 1,1-difluoro-2-hydroxypropan-2-yl group, a 1,1,1-trifluoro-2-methoxypropan-2-yl group, a 1-hydroxyethyl group, a 1-hydroxypropyl group, a 1-hydroxy-2-methylpropyl group, a 1-methoxyethyl group, a 2-methoxypropan-2-yl group, a 1-acetoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl group, a 1-ethoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl group, a 2,2,2-trifluoro-1,1-dihydroxyethyl group, a 1-(cyanomethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxypropoxy)ethyl group, a 2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl group, a 2,2,2-

trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxypropan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxy-2-methylpropan-2-yl)oxy)ethyl group, a 1-(1,1-difluoro-2-hydroxypropoxy)-2,2,2-trifluoroethyl group, a 1-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-2,2,2-trifluoroethyl group, a 1-(difluoro(1-hydroxycyclopropyl)methoxy)-2,2,2-trifluoroethyl group, a 1-(carboxymethoxy)-2,2,2-trifluoroethyl group, a 1-(2-amino-2-oxoethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-((methylsulfonyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-(sulfamoylmethoxy)ethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2-difluoroethyl group, a 1-hydroxy-3-(methylsulfonyl)propyl group, a 3-(ethylsulfonyl)-1-hydroxypropyl group, a 1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2,2-trifluoro-1-(2-morpholino-2-oxoethoxy)ethyl group, a 1-carboxy-2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a 1,3-dihydroxypropyl group, a 1-hydroxy-3-methoxypropyl group, a 4,4,4-trifluoro-1,3-dihydroxybutyl group, a 1,3-dihydroxybutyl group, a 1,3-dihydroxy-3-methylbutyl group, a carboxy(hydroxy)methyl group, a hydroxy (2H-tetrazol-5-yl)methyl group, a hydroxy (3-

hydroxycyclobutyl)methyl group, a 1-hydroxy-2-morpholinoethyl group, a 3-amino-1-hydroxy-3-oxopropyl group, a 1-hydroxy-2-(methylsulfonamide)ethyl group, a 2-cyanoethyl group, a 1,2-dihydroxyethyl group, a 3,3,3-trifluoro-1,2-dihydroxypropyl group, a 1-hydroxycyclopropyl group, 1-methoxycyclopropyl group, a 3,3,3-trifluoro-1-hydroxy-2-oxopropyl group, a 3,3,3-trifluoro-1-hydroxypropyl group, a 3,3,3-trifluoro-2-hydroxypropyl group, a 3,3,3-trifluoro-2-oxopropyl group, a 1-hydroxy-3-oxobutyl group, an acetamide group, an N-methylacetamide group, a methoxy group, an isopropoxy group, a trifluoromethoxy group, a 2,2,2-trifluoroethoxy group, a cyanomethoxy group, a carboxymethoxy group, a 2-hydroxyethoxy group, a 2-methoxyethoxy group, a 2-hydroxypropoxy group, a (1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxy-2-methylpropoxy group, a difluoro(1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxyethoxy group, a 3,3,3-trifluoro-2-hydroxypropoxy group, a 2,2-difluoro-2-hydroxyethoxy group, a 2-(trifluoromethoxy)ethoxy group, a 1,1-difluoro-2-hydroxypropoxy group, a (1,1,1-trifluoro-3-hydroxybutan-2-yl)oxy group, an oxetan-3-ylmethoxy group, a 3-hydroxy-2-(hydroxymethyl)propoxy group, an allyloxy group, a cyclobutoxy group, a (methylsulfonyl)methoxy group, a

(ethylsulfonyl)methoxy group, a (isopropylsulfonyl)methoxy group, a (2H-tetrazol-5-yl)methoxy group, a 2-amino-2-oxoethoxy group, a carboxydifluoromethoxy group, a 2-carboxyethoxy group, a 2-cyanoethoxy group, a 2-(methylsulfonyl)ethoxy group, a 2-morpholinoethoxy group, a 3-hydroxycyclobutoxy group, a 3-cyanocyclobutoxy group, a 3-carboxycyclobutoxy group, a 3-(methylsulfonyl)cyclobutoxy group, a 3-(2H-tetrazol-5-yl)cyclobutoxy group, a (4-hydroxycyclohexyl)oxy group, a 2-hydroxy-3-methoxypropoxy group, a benzyloxy group, a methylthio group, a methylsulfonyl group, a methylsulfinyl group, a methylsulfamoyl group, a dimethylsulfamoyl group, a sulfamoyl group, an acetyl group, a 1-(methoxyimino)ethyl group, a carbamoyl group, a dimethylcarbamoyl group, a morpholine-4-carbonyl group, a piperidine-1-carbonyl group, an azetidine-1-carbonyl group, a benzylcarbamoyl group, a methylcarbamoyl group, a 3-hydroxy-3-(trifluoromethyl)azetidine-1-carbonyl group, a methoxycarbonyl group, an ethoxycarbonyl group, a (5-(trifluoromethyl)pyridin-2-yl)oxy group, or a (5-(hydroxymethyl)pyridin-2-yl)oxy group, and

the group represented by R^4 is, among the above, a thiazol-2-yl group, a thiazol-4-yl group, a pyridin-2-yl group, an oxazol-2-yl group, a 1H-pyrazol-1-yl

group, a 4-methylthiazol-2-yl group, a 5-fluoropyridin-2-yl group, a 2H-1,2,3-triazol-2-yl group, a 1,2,4-thiadiazol-5-yl group, a 1-methyl-1H-pyrazol-3-yl group, a pyrimidin-2-yl group, an isothiazol-3-yl group, a 3-methyl-1,2,4-thiadiazol-5-yl group, or a 5-chloropyridin-2-yl group.

[Compound (1h)]

A compound in which, in the general formula (1), the group represented by R^1 is, among the above, a hydrogen atom, a chlorine atom, a cyano group, a carboxy group, a methyl group, a trifluoromethyl group, a hydroxymethyl group, a 2-hydroxypropan-2-yl group, a 2,2,2-trifluoro-1-hydroxyethyl group, a 2,2,2-trifluoro-1-methoxyethyl group, a 1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-methoxyethyl group, a 1,1-difluoro-2-hydroxypropan-2-yl group, a 1,1,1-trifluoro-2-methoxypropan-2-yl group, a 1-hydroxyethyl group, a 1-methoxyethyl group, a 2-methoxypropan-2-yl group, a 2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl group, a 1-ethoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl group, a 2,2,2-trifluoro-1,1-dihydroxyethyl group, a 1-(cyanomethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-

hydroxypropoxy)ethyl group, a 2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxypropan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxy-2-methylpropan-2-yl)oxy)ethyl group, a 1-(1,1-difluoro-2-hydroxypropoxy)-2,2,2-trifluoroethyl group, a 1-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-2,2,2-trifluoroethyl group, a 1-(difluoro(1-hydroxycyclopropyl)methoxy)-2,2,2-trifluoroethyl group, a 1-(carboxymethoxy)-2,2,2-trifluoroethyl group, a 1-(2-amino-2-oxoethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-((methylsulfonyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-(sulfamoylmethoxy)ethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2-difluoroethyl group, a 1-hydroxy-3-(methylsulfonyl)propyl group, a 3-(ethylsulfonyl)-1-hydroxypropyl group, a 1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2,2-trifluoro-1-(2-morpholino-2-oxoethoxy)ethyl group, a 1-carboxy-2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a phenyl group, a thiazol-2-yl group, an acetamide group, a methoxy group, a trifluoromethoxy group, a cyanomethoxy group, a carboxymethoxy group, a 2-

hydroxyethoxy group, a 2-methoxyethoxy group, a 2-hydroxypropoxy group, a 2-hydroxy-2-methylpropoxy group, a (1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxy-2-methylpropoxy group, a difluoro(1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxyethoxy group, a 3,3,3-trifluoro-2-hydroxypropoxy group, a 2,2-difluoro-2-hydroxyethoxy group, a 2-(trifluoromethoxy)ethoxy group, a 1,1-difluoro-2-hydroxypropoxy group, a (1,1,1-trifluoro-3-hydroxybutan-2-yl)oxy group, a cyclobutoxy group, a (methylsulfonyl)methoxy group, a (ethylsulfonyl)methoxy group, a (isopropylsulfonyl)methoxy group, a (2H-tetrazol-5-yl)methoxy group, a 2-amino-2-oxoethoxy group, a carboxydifluoromethoxy group, a 2-carboxyethoxy group, a 2-cyanoethoxy group, a 2-(methylsulfonyl)ethoxy group, a 2-morpholinoethoxy group, a 3-hydroxycyclobutoxy group, a 3-cyanocyclobutoxy group, a 3-carboxycyclobutoxy group, a 3-(methylsulfonyl)cyclobutoxy group, a 3-(2H-tetrazol-5-yl)cyclobutoxy group, a (4-hydroxycyclohexyl)oxy group, a 2-hydroxy-3-methoxypropoxy group, a benzyloxy group, an acetyl group, a carbamoyl group, a dimethylcarbamoyl group, a morpholine-4-carbonyl group, a piperidine-1-carbonyl group, a methoxycarbonyl group, an ethoxycarbonyl group, a

(tetrahydro-2H-pyran-4-yl)oxy group, a 1-(1,1-difluoro-2-hydroxyethoxy)-2,2,2-trifluoroethyl group, a tetrahydro-2H-pyran-3-yl)oxy group, a difluoromethoxy group, a 3-(2-hydroxypropan-2-yl)cyclobutoxy group, a (1-hydroxy-2-methylpropan-2-yl)oxy group, a 2,2,2-trifluoro-1-((3-hydroxy-2,3-dimethylbutan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-methoxycyclopropyl)methoxy)ethyl group, a 1,1-difluoro-3-hydroxy-3-methylbutoxy group, a (1,1-dioxidotetrahydro-2H-thiopyran-4-yl)oxy) group, an oxetan-3-yloxy group, a 1,1-difluoro-2,3-dihydroxy-2-methylpropoxy group, a (trifluoromethyl)sulfonyl group, a (5-(trifluoromethyl)pyridin-2-yl)oxy group, a pyridin-2-yloxy group, a pyrimidin-2-yloxy group, a pyrazin-2-yloxy group, a (6-methyl-4-(trifluoromethyl)pyridazin-3-yl)oxy group, a (5-(hydroxymethyl)pyridin-2-yl)oxy group, a (5-(hydroxymethyl)-3-(trifluoromethyl)pyridin-2-yl)oxy group, a (5-(trifluoromethoxy)pyridin-2-yl)oxy group, a methylsulfonyl group, a cyclopropyl group, a methylthio group, a methylsulfinyl group, a (2-hydroxyethyl)thio group, a (2-hydroxyethyl)sulfinyl group, a (2-hydroxyethyl)sulfonyl group, a (1,1-difluoroallyl)oxy group, a (5-(methylsulfonyl)pyridin-2-yl)oxy group, a (2-methoxyethyl)carbamoyl group, a

(2-hydroxyethyl)carbamoyl group, a (2-hydroxyethyl)(methyl)carbamoyl group, a cyclopropylcarbamoyl group, an ethylcarbamoyl group, a pyrrolidine-1-carbonyl group, a benzylcarbamoyl group, hydroxy carbamoyl group, a 1,1-difluoro-2,3-dihydroxypropoxy group, a 3-((hydroxymethyl)pyridin-2-yl)oxy group, a 1,1-difluoro-2,2-dihydroxypropoxy group, an N-(2-hydroxyethyl)sulfamoyl group, an N-(2-methoxyethyl)sulfamoyl group, an N-(2-hydroxyethyl)-N-methylsulfamoyl group, a pyrrolidin-1-ylsulfonyl group, a morpholinosulfonyl group, a 1,1-difluoro-2-methoxyethoxy group, a 1,1-difluoro-2-methoxy-2-methylpropoxy group, a 1,1-difluoro-2-hydroxybutoxy group, a 1,1-dioxidothio morpholino group, a 1,1-difluoropropoxy group, a 1,1-difluoro-2-hydroxy-3-methylbutoxy group, a benzo[d]oxazol-2-yldifluoromethoxy group, a (1,1-difluoro-3-(pyridin-3-yl)aryl)oxy group, a 1,1-difluoro-2-((hydroxyethyl)(methyl)amino)-2-oxoethoxy group, a 2-(dimethylamino)-1,1-difluoro-2-oxoethoxy group, a 1,1-difluoro-2-morpholino-2-oxoethoxy group, a 2-amino-1,1-difluoro-2-oxoethoxy group, a 1,1-difluoro-2-((2-hydroxyethyl)amino)-2-oxoethoxy group, a 1,1-difluoro-2-(3-hydroxyazetidin-1-yl)-2-oxoethoxy group, or cyclobutyl group,

the group represented by R^2 is, among the above,

a hydrogen atom, and

the group represented by R^4 is, among the above, a thiazol-2-yl group, a thiazol-4-yl group, a pyridin-2-yl group, an oxazol-2-yl group, a 1H-pyrazol-1-yl group, a 4-methylthiazol-2-yl group, a 5-fluoropyridin-2-yl group, a 2H-1,2,3-triazol-2-yl group, a 1,2,4-thiadiazol-5-yl group, a 1-methyl-1H-pyrazol-3-yl group, a pyrimidin-2-yl group, an isothiazol-3-yl group, a 3-methyl-1,2,4-thiadiazol-5-yl group, or a 5-chloropyridin-2-yl group.

[Compound (1i)]

A compound in which, in the general formula (1),

the group represented by R^1 is, among the above, a hydrogen atom,

the group represented by R^2 is, among the above, a chlorine atom, a carboxy group, an isopropyl group, a trifluoromethyl group, a hydroxymethyl group, a methoxymethyl group, a 2-hydroxypropan-2-yl group, a morpholinomethyl group, a (dimethylamino)methyl group, a 2,2,2-trifluoro-1-hydroxyethyl group, a 2,2,2-trifluoro-1-methoxyethyl group, a 1,1,1-trifluoro-2-hydroxypropan-2-yl group, a 2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-methoxyethyl group, a 1,1-difluoro-2-hydroxypropan-2-yl group, a 1,1,1-trifluoro-2-methoxypropan-2-yl group, a 1-hydroxyethyl group, a 1-hydroxypropyl group, a 1-

hydroxy-2-methylpropyl group, a 1-methoxyethyl group, a 2-methoxypropan-2-yl group, a 1-acetoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl group, a 2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl group, a 1-ethoxy-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl group, a 2,2,2-trifluoro-1,1-dihydroxyethyl group, a 1-(cyanomethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-(2-hydroxypropoxy)ethyl group, a 2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxypropan-2-yl)oxy)ethyl group, a 2,2,2-trifluoro-1-((1-hydroxy-2-methylpropan-2-yl)oxy)ethyl group, a 1-(1,1-difluoro-2-hydroxypropoxy)-2,2,2-trifluoroethyl group, a 1-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-2,2,2-trifluoroethyl group, a 1-(difluoro(1-hydroxycyclopropyl)methoxy)-2,2,2-trifluoroethyl group, a 1-(carboxymethoxy)-2,2,2-trifluoroethyl group, a 1-(2-amino-2-oxoethoxy)-2,2,2-trifluoroethyl group, a 2,2,2-trifluoro-1-((methylsulfonyl)methoxy)ethyl group, a 2,2,2-trifluoro-1-(sulfamoylmethoxy)ethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl group, a 1-((2H-tetrazol-5-yl)methoxy)-2,2-difluoroethyl group,

a 1-hydroxy-3-(methylsulfonyl)propyl group, a 3-(ethylsulfonyl)-1-hydroxypropyl group, a 1-hydroxy-3-(isopropylsulfonyl)propyl group, a 2,2,2-trifluoro-1-(2-morpholino-2-oxoethoxy)ethyl group, a 1-carboxy-2,2-difluoro-1-hydroxyethyl group, a 2,2-difluoro-1-hydroxy-1-(2H-tetrazol-5-yl)ethyl group, a 1,3-dihydroxypropyl group, a 1-hydroxy-3-methoxypropyl group, a 4,4,4-trifluoro-1,3-dihydroxybutyl group, a 1,3-dihydroxybutyl group, a 1,3-dihydroxy-3-methylbutyl group, a carboxy(hydroxy)methyl group, a hydroxy (2H-tetrazol-5-yl)methyl group, a hydroxy (3-hydroxycyclobutyl)methyl group, a 1-hydroxy-2-morpholinoethyl group, a 3-amino-1-hydroxy-3-oxopropyl group, a 1-hydroxy-2-(methylsulfonamide)ethyl group, a 2-cyanoethyl group, a 1,2-dihydroxyethyl group, a 3,3,3-trifluoro-1,2-dihydroxypropyl group, a 1-hydroxycyclopropyl group, a 1-methoxycyclopropyl group, a 3,3,3-trifluoro-1-hydroxy-2-oxopropyl group, a 3,3,3-trifluoro-1-hydroxypropyl group, a 3,3,3-trifluoro-2-hydroxypropyl group, a 3,3,3-trifluoro-2-oxopropyl group, a 1-hydroxy-3-oxobutyl group, an acetamide group, an N-methylacetamide group, a methoxy group, an isopropoxy group, a trifluoromethoxy group, a 2,2,2-trifluoroethoxy group, a cyanomethoxy group, a carboxymethoxy group, a 2-hydroxyethoxy group, a 2-methoxyethoxy group, a 2-hydroxypropoxy group, a (1-

hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxy-2-methylpropoxy group, a difluoro(1-hydroxycyclopropyl)methoxy group, a 1,1-difluoro-2-hydroxyethoxy group, a 3,3,3-trifluoro-2-hydroxypropoxy group, a 2,2-difluoro-2-hydroxyethoxy group, a 2-(trifluoromethoxy)ethoxy group, a 1,1-difluoro-2-hydroxypropoxy group, a (1,1,1-trifluoro-3-hydroxybutan-2-yl)oxy group, an oxetan-3-ylmethoxy group, a 3-hydroxy-2-(hydroxymethyl)propoxy group, an allyloxy group, a cyclobutoxy group, a (methylsulfonyl)methoxy group, a (ethylsulfonyl)methoxy group, a (isopropylsulfonyl)methoxy group, a (2H-tetrazol-5-yl)methoxy group, a 2-amino-2-oxoethoxy group, a carboxydifluoromethoxy group, a 2-carboxyethoxy group, a 2-cyanoethoxy group, a 2-(methylsulfonyl)ethoxy group, a 2-morpholinoethoxy group, a 3-hydroxycyclobutoxy group, a 3-cyanocyclobutoxy group, a 3-carboxycyclobutoxy group, a 3-(methylsulfonyl)cyclobutoxy group, a 3-(2H-tetrazol-5-yl)cyclobutoxy group, a (4-hydroxycyclohexyl)oxy group, a 2-hydroxy-3-methoxypropoxy group, a benzyloxy group, a methylthio group, a methylsulfonyl group, a methylsulfinyl group, a methylsulfamoyl group, a dimethylsulfamoyl group, a sulfamoyl group, an acetyl group, a 1-(methoxyimino)ethyl group, a carbamoyl

group, a dimethylcarbamoyl group, a morpholine-4-carbonyl group, a piperidine-1-carbonyl group, an azetidine-1-carbonyl group, a benzylcarbamoyl group, a methylcarbamoyl group, a 3-hydroxy-3-(trifluoromethyl)azetidine-1-carbonyl group, a methoxycarbonyl group, an ethoxycarbonyl group, a (5-(trifluoromethyl)pyridin-2-yl)oxy group, or a (5-(hydroxymethyl)pyridin-2-yl)oxy group, and

the group represented by R^4 is, among the above, a thiazol-2-yl group or a 1H-pyrazol-1-yl group.

A specific embodiment of the compound of the present invention or the pharmacologically acceptable salt thereof is, for example, an embodiment where the compound of the present invention is in the form of the compound described below. However, the present invention is not limited to the aforementioned particular examples.

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

7-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethoxy)benzo[d]oxazole,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(furan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(oxazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(5-fluoropyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,
2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,
7-(5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole,
2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole,

7-(5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,

7-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole,

7-(5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

N-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)acetamide,

N-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)acetamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole,

N-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide,

N-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide,

N-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-ol,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-isopropoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(oxetan-3-ylmethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)methyl)propane-1,3-diol,

5-(allyloxy)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)acetonitrile,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)acetic acid,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-ol,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-cyclobutoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)acetonitrile,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3-methoxypropan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydrofuran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4,7-di(thiazol-2-yl)benzo[d]oxazole,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(1H-

pyrazol-1-yl)benzo[d]oxazole-5-carboxylate,
2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)propan-2-ol,
2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)propan-2-ol,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazole,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazole,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-N,N-dimethyl-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide,
(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(morpholino)methanone,
(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(piperidin-1-yl)methanone,
(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(azetidin-1-yl)methanone,
N-benzyl-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide,
N-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-N-methylacetamide,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-

(morpholinomethyl)-7-(thiazol-2-yl)benzo[d]oxazole,
1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-N,N-dimethylmethanamine,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole,
1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-one,
1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-one,
1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,
1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-ol,
1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-ol,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,
(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-

yl)benzo[d]oxazol-4-yl)methanol,

(2-(3,6-diazabicyclo[3.1.1]hepan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-N,N-dimethyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(morpholino)methanone,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(piperidin-1-yl)methanone,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,

(R)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,

(S)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-

2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,
(R)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,
(S)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,
(R)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,
(S)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,
1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethan-1-ol,
2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol,
(R)-2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol,
(S)-2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol,
1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethoxy)-2-methylpropan-2-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethan-1-ol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

1-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

(R)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

(S)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1H-

pyrazol-1-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethyl acetate,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

(R)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

(S)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-

trifluoroethoxy)ethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)acetonitrile,

2-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)acetonitrile,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazole,

1-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)propan-2-ol,

1-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-

diol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

2-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

2-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate,

2-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)propan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(methoxymethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-

yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)methanol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)propan-2-ol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)propan-2-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-one,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-one,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)-2,2-

difluoroethan-1-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-

yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

2-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)(azetidin-1-yl)methanone,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-N-(2-hydroxyethyl)-N-methyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxamide,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)(3-hydroxy-3-(trifluoromethyl)azetidin-1-yl)methanone,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)methanol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol,

(R)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol,

(S)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2-methylpropan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(R)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(S)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(R)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(S)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-

one,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

(E)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime,

(Z)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime,

(E)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime,

(Z)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-

(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)ethan-1-ol,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetonitrile,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)ethan-1-ol,

2-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetonitrile,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazole,

4-(1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

4-(1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

1-((1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)methyl)cyclopropan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethane-1,1-diol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol,

(R)-2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol,

(S)-2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol, methyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate, 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylic acid, 2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)propan-2-ol, 2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)propan-2-ol, 1-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol, 1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol, 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole, 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole, 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole, 1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-one, 1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-one, 1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-

methylpropan-2-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

(R)-1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

(S)-1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetic acid,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydro-2H-pyran-4-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2-methylpropan-2-ol,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetamide,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-1,1-difluoro-2-methylpropan-2-ol,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2,2-difluoroethan-1-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)propan-2-ol,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)propan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydro-2H-pyran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-2-ol,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-1,1-difluoropropan-2-ol,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutane-1-carbonitrile,

2-(3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutyl)propan-2-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-

yl)cyclopropan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)cyclopropan-1-ol,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1,1-trifluoropropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-2-ol,

3-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2,3-dimethylbutan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxy-2-methylpropoxy)ethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-((1-methoxycyclopropyl)methoxy)ethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxycyclopropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2-methylpropan-2-ol,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutan-1-ol,

1-((1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)methyl)cyclopropan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(pyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(oxazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((tetrahydro-2H-pyran-4-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

4-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-4,4-difluoro-2-methylbutan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-

methoxypropan-2-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)cyclopropan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(R)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(S)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(R)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(S)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

4-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclohexan-1-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(4-methylthiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-4,4,4-trifluoro-2-methylbutan-2-ol,

4-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)tetrahydro-2H-thiopyran 1,1-dioxide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(pyridin-

2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,
1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,
1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(pyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,
1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(4-methylthiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,
2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(5-fluoropyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,
2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,
1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(oxazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,
1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(2H-1,2,3-triazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(((S)-tetrahydrofuran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(((R)-

tetrahydrofuran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(oxetan-3-yloxy)-7-(thiazol-2-yl)benzo[d]oxazole,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3,3-difluoro-2-methylpropane-1,2-diol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1,2,4-thiadiazol-5-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1-methyl-1H-pyrazol-3-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(5-fluoropyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(pyrimidin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(isothiazol-3-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(5-fluoropyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(3-methyl-

1,2,4-thiadiazol-5-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-((trifluoromethyl)sulfonyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carbonitrile,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-((5-(trifluoromethyl)pyridin-2-yl)oxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyridin-2-yloxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyrimidin-2-yloxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyrazin-2-yloxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((6-methyl-4-(trifluoromethyl)pyridazin-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

(6-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)pyridin-3-yl)methanol,

(6-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-5-(trifluoromethyl)pyridin-3-yl)methanol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-((5-(trifluoromethoxy)pyridin-2-

yl)oxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-cyclopropyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)thio)ethan-1-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)sulfinyl)ethan-1-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)sulfonyl)ethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((1,1-difluoroallyl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((5-(methylsulfonyl)pyridin-2-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-

hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-hydroxyethyl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-cyclopropyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-ethyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(morpholino)methanone,

(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(pyrrolidin-1-yl)methanone,

N-benzyl-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-3-methylbutan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(5-chloropyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

(R)-3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3,3-difluoro-2-methylpropane-1,2-diol,

(S)-3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3,3-difluoro-2-

methylpropane-1,2-diol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylic acid,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-hydroxy-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-morpholino-7-(thiazol-2-yl)benzo[d]oxazole,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3,3-difluoropropane-1,2-diol,

3-(4-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

(R)-3-(4-(1,1-difluoro-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

(S)-3-(4-(1,1-difluoro-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

3-(4-(1,1-difluoro-2-hydroxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

3-(5-chloro-7-(thiazol-2-yl)-4-

(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

(2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)pyridin-3-yl)methanol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropane-2,2-diol,

(R)-3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

(S)-3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

3-(7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-

(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N,N-dimethyl-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-hydroxyethyl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyrrolidin-1-ylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(morpholinosulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1,1-difluoro-2-methoxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1,1-difluoro-2-methoxy-2-methylpropoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1-

methyl-1H-pyrazol-3-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluorobutan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)piperidin-4-ol,

4-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)thiomorpholine 1,1-dioxide,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-bromo-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1,1-difluoropropoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

4-(benzo[d]oxazol-2-yldifluoromethoxy)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((1,1-difluoro-3-(pyridin-3-yl)allyl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-N-(2-hydroxyethyl)-N-methylacetamide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-N,N-dimethylacetamide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-1-morpholinoethan-1-one,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroacetamide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-N-(2-hydroxyethyl)acetamide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-1-(3-hydroxyazetidin-1-yl)ethan-1-one,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-((5-(trifluoromethyl)pyridin-2-yl)oxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-cyclobutyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyrrolidin-1-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

(6-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)pyridin-3-yl)methanol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carbonitrile,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(pyridin-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-cyclobutoxy-7-(thiazol-2-yl)benzo[d]oxazole.

In the present invention, the compound of the present invention represented by the general formula (1) may be in the form of a free base (educt) and may also be a pharmacologically acceptable salt thereof. The pharmacologically acceptable salt is preferably in the form of an acid addition salt. The acid of the acid addition salt is, for example, a salt of hydrohalic acid such as hydrofluoric acid, hydrochloric acid, hydrobromic acid, or hydroiodic acid; a salt of inorganic acid such as sulfuric acid, nitric acid, phosphoric acid, hydrogen peroxide acid, or carbonic acid; a salt of organic carboxylic acid such as acetic acid, trichloroacetic acid,

trifluoroacetic acid, hydroxyacetic acid, lactic acid, citric acid, tartaric acid, oxalic acid, benzoic acid, mandelic acid, butyric acid, maleic acid, propionic acid, formic acid, or malic acid; acidic amino acid such as aspartic acid or glutamic acid; alkyl sulfonic acid such as methanesulfonic acid; or aryl sulfonic acid such as p-toluenesulfonic acid.

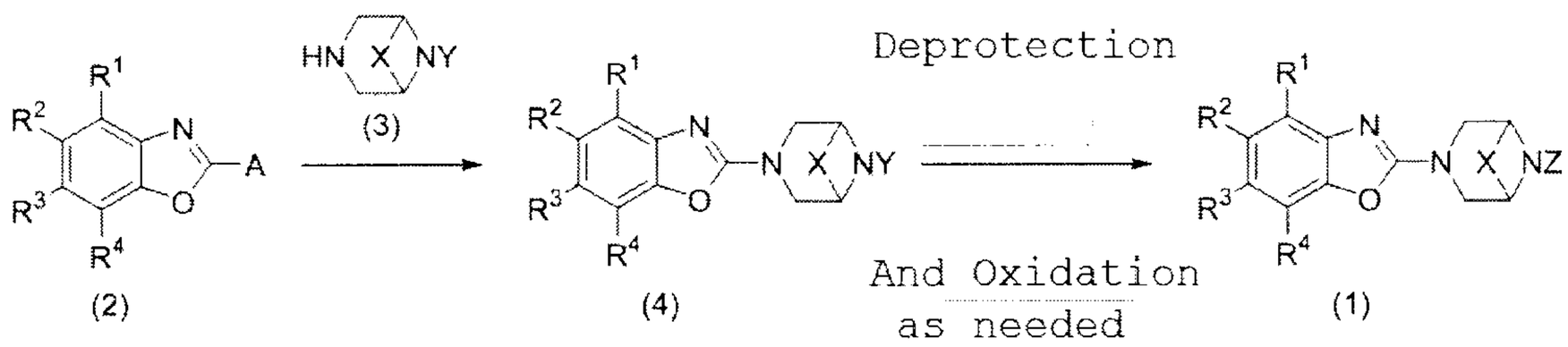
Besides, although there is a case where the compound represented by the general formula (1) or the pharmacologically acceptable salt thereof of the present invention has one or more asymmetric carbon atoms depending on the type of substituent, the scope of the present invention encompasses, e.g., optically active substances based on one or more asymmetric carbon atoms, diastereomers, geometrical isomers, tautomers, any mixture thereof, and racemates. In addition, the compound represented by the general formula (1) or the pharmacologically acceptable salt thereof of the present invention includes corresponding hydrates and solvates. The solvates include, for example, 2-propanol solvate.

Furthermore, the compound represented by the general formula (1) or the pharmacologically acceptable salt thereof of the present invention includes corresponding radioisotopes and labeled compounds with nonradioisotope; and hydrates, and

solvates thereof.

In the present description, when the compound has isometric(s) or isotope(s) and there is not a reference about it in particular in their name, the name of compound means isometric(s), isotope(s) or mixture thereof, or racemate(s).

The method for manufacturing the compounds of the present invention and the pharmacologically acceptable salt thereof is not particularly limited. With starting materials, precursors, reagents, and solvents which are commercially available or synthesizable by a method known to those skilled in the art, it is possible to manufacture compounds of the present invention and the pharmacologically acceptable salt thereof by a combination of e.g. methods such as a wide variety of synthesizing methods known to those skilled in the art and methods which are, if necessary, an improved version of those methods. For example, it is possible to manufacture them by representative methods indicated as follows.



In the above general formulae (2) to (4), R^1, R^2, R^3, R^4, and X have the same meanings as those of R^1, R^2, R^3, R^4, and X in the general formula (1), including preferred embodiments. In the above general formula (2), A represents a leaving group such as a halogen atom, a thiol group, a p-toluenesulfonyloxy group, a trifluoromethanesulfonyloxy group, or a phenoxy group. In the above general formula (3), Y represents a protecting group of amino group. In the above general formula (4), Y represents the same group as Y in the general formula (3). As the protecting group of amino group, it is possible to use, for example, a tert-butoxycarbonyl group and a benzyloxycarbonyl group described in "Protective Groups in Organic Synthesis (John Wiley and Sons, 1991)," written by T. W. Greene.

First, in a solvent, the compound represented by the general formula (4) was obtained from the compound represented by the general formula (2) with the treatment of 1 to 50 equivalents of the bicyclic diamine represented by the general formula (3) with respect to the number of moles of the compound represented by the general formula (2). Next, it is possible to obtain the compound represented by the general formula (1) by removing the protecting group Y (deprotection) and subsequently performing oxidation when necessary. In the present manufacture method, in

the compound represented by the general formula (4) obtained in the above reaction, deprotection of the protecting group Y affords a compound in which Z in the general formula (1) is a hydrogen atom, and subsequent oxidation affords a compound in which Z in the general formula (1) is a hydroxyl group.

The solvent used for the above reaction is, for example, dichloromethane, chloroform, benzene, toluene, xylene, tetrahydrofuran, diethylether, dimethoxyethane, N,N-dimethylformamide, or dimethyl sulfoxide. In the above reaction, the reaction temperature is selected from a range of -78 to 200°C, preferably of -78 to 150°C, and the reaction time is in a range of 5 minutes to 48 hours, preferably 30 minutes to 20 hours. Additionally, for the purpose of promoting the above reaction or performing reaction under milder conditions, appropriate additives (for example, triethylamine or N,N-diisopropylethylamine) can be added to the above reaction.

Moreover, in the present manufacture method, in the compound represented by the general formula (4) obtained by the above reaction, it is possible to perform transformation of functional group on each of the substituents (R^1, R^2, R^3, and R^4) and convert it to another compound within the scope of the present invention. For example, functional groups are

introduced by various coupling reactions with metal catalysts (for example, the Kumada-Tamao-Corriu coupling, the Migita-Kosugi-Stille coupling, the Suzuki-Miyaura coupling, the Negishi coupling, and the Buchwald-Hartwig coupling), oxidation reaction, reduction reaction, amidation reaction, hydrolysis reaction, nucleophilic reaction on a carbonyl compound, alkylation reaction, and dealkylation reaction.

The compound of the present invention or the pharmacologically acceptable salt thereof can be used to treat diseases attributed to PDE4 and to inhibit PDE4. The pharmaceutical composition of the present invention contains as an active ingredient the compound of the present invention or the pharmacologically acceptable salt thereof and can be used as a PDE4 inhibitor and as a therapeutic agent for diseases attributed to PDE4. The pharmaceutical composition of the present invention may be administered in any of an oral administration route and a nonoral administration route, and can be administered to humans and animals other than humans. Thus, the pharmaceutical composition of the present invention can be a preparation of appropriate dosage form depending on the administration route.

To be more specific, the preparation is, for

example, an oral preparation such as a tablet, a pill, a capsule, a granule, a powder, an elixir, a suspension, an emulsion, or a syrup, or a nonoral preparation such as an injection, an inhalant, a preparation for rectal administration, a suppository, a lotion, a spray, an ointment, a cream, a patch, or a preparation for sustained release.

These types of preparations can be manufactured in a usual manner by use of e.g. excipients, disintegrators, binders, lubricants, and colorants usually used as appropriate in the pharmaceutical field.

In the pharmaceutical composition of the present invention, the content of the compound of the present invention or the pharmacologically acceptable salt thereof (the content of the compound represented by the general formula (1), the content of the pharmacologically acceptable salt thereof, or, in the case of a mixture thereof, the total content of the mixture) cannot be generally specified because it is adjusted as appropriate depending on the administration purpose and the dosage form of the preparation. Nonetheless, the content is usually, in terms of educt, 0.01 to 70% by mass, preferably 0.05 to 50% by mass with respect to the total mass of the pharmaceutical composition.

The amount of the compound of the present invention or the pharmacologically acceptable salt thereof administered (the amount of the compound represented by the general formula (1) administered, the amount of the pharmacologically acceptable salt thereof administered, or, in the case of a mixture thereof, the total amount of the mixture administered) cannot be generally specified because it is determined as appropriate case by case in consideration of e.g. the ages, weights, sexes, and the difference in symptom of the patients. Nonetheless, the amount administered to an adult is usually, in terms of educt, 0.01 to 1000 mg, preferably 0.1 to 300 mg per day, and it is possible to administer the compound of the present invention or the pharmacologically acceptable salt thereof in one or several times per a day.

[Examples]

The present invention is hereinafter described in further detail using Examples. Note that the present invention is not limited to these examples. Also, methods of manufacturing a raw compound used in Examples are described as reference examples. Note that these are also examples for specific explanation of the embodiments of the present invention. These examples do not limit the scope of the present

invention, and it is apparent that various applications, variations, modifications, etc. can be made within a scope not departing from the scope of the present invention.

In the following description, the abbreviations in Examples and Reference Examples mean as listed below:

M: mol/L

DMSO: dimethyl sulfoxide

DMPU: N,N'-dimethylpropyleneurea

ESI: electrospray ionization

ee: enantiomeric excess

HPLC: high performance liquid chromatography

mCPBA: meta-chloroperoxybenzoic acid

MS: mass spectrum

n: normal

sec: secondary

tert: tertiary

TLC: thin-layer chromatography

UV: ultraviolet

LC-MS: liquid chromatography-mass spectrometry

(Reference Example 1)

7-Bromo-5-isopropylbenzo[d]oxazole-2-thiol

(a) 2-Bromo-4-isopropyl-6-nitrophenol

2.5 g of 2-bromo-4-isopropylphenol was dissolved in dichloromethane (50 mL), then concentrated sulfuric

acid (0.8 mL, 1.3 equivalents) was added dropwise thereto at 0°C over 5 minutes, and thereafter 70% nitric acid (0.7 mL, 1.0 equivalent) was added thereto over 5 minutes, followed by stirring at room temperature for 2 hours. The formation of the product was confirmed by TLC, and then solid sodium hydrogen carbonate was added to adjust the pH to 7. The reaction mixture was filtered and the filtrate was extracted using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining as a crude product 2.8 g of the title compound obtained by vacuum concentration of the filtrate.

MS (ESI) m/z: 260 $(M-H)^-$

(b) 2-Amino-6-bromo-4-isopropylphenol

Sodium dithionite (9.4 g, 5 equivalents) was dissolved in distilled water (32 mL) at 0°C, and ethanol (12 mL) solution of 2.8 g of 2-bromo-4-isopropyl-6-nitrophenol obtained in Reference Example 1(a) was added dropwise thereto over 10 minutes. Stirring was performed after the temperature rose to room temperature, and the formation of the product was confirmed by TLC. The reaction mixture was filtered and the solid was washed by ethanol. 20 mL of distilled water was added to the residue obtained by vacuum concentration of the filtrate, followed by

stirring at 0°C for 15 minutes. The obtained solid was filtered and washed by distilled water, followed by vacuum drying, thus obtaining 1.9 g of the title compound.

MS (ESI) m/z: 228 $(M-H)^-$

(c) 7-Bromo-5-isopropylbenzo[d]oxazole-2-thiol

1.9 g of the 2-amino-6-bromo-4-isopropylphenol obtained in Reference Example 1(b) was dissolved in ethanol (14 mL), and then 0.5 M potassium hydroxide solution in ethanol(7.4 mL) and carbon disulfide (2.3 mL, 5 equivalents) were added thereto, followed by heating at 50°C for 4 hours. The formation of the product was confirmed by TLC, and then distilled water (4 mL) and 6 M hydrochloric acid (4 mL) were added thereto at room temperature. The obtained solid was filtered, followed by vacuum drying, thus obtaining 1.5 g of the title compound.

(Reference Example 2)

7-Bromo-4-methylbenzo[d]oxazole-2-thiol

(a) 6-Bromo-3-methyl-2-nitrophenol

1.5 g of the title compound was obtained from 2.5 g of 2-bromo-5-methylphenol using a similar method to Reference Example 1(a) except that the crude product was refined by silica gel column chromatography (hexane:ethyl acetate = 95:5).

MS (ESI) m/z: 230 $(M-H)^-$

(b) 2-Amino-6-bromo-3-methylphenol

610 mg of the title compound was obtained from 1.5 g of 6-bromo-3-methyl-2-nitrophenol obtained in Reference Example 2(a), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 200 $(M-H)^-$

(c) 7-Bromo-4-methylbenzo[d]oxazole-2-thiol

360 mg of the title compound was obtained from 610 mg of 2-amino-6-bromo-3-methylphenol obtained in Reference Example 2(b), using a similar method to Reference Example 1(c).

(Reference Example 3)

7-Bromo-4-(trifluoromethoxy)benzo[d]oxazole-2-thiol

(a) 6-Bromo-2-nitro-3-(trifluoromethoxy)phenol

36 g of the title compound was obtained as a crude product from 30 g of 2-bromo-5-(trifluoromethoxy)phenol using a similar method to Reference Example 1(a).

MS (ESI) m/z: 300 $(M-H)^-$

(b) 2-Amino-6-bromo-3-(trifluoromethoxy)phenol

18 g of the title compound was obtained from 36 g of 6-bromo-2-nitro-3-(trifluoromethoxy)phenol obtained in Reference Example 3(a), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 272 $(M+H)^+$

(c) 7-Bromo-4-(trifluoromethoxy)benzo[d]oxazole-2-

thiol

9.5 g of the title compound was obtained from 21 g of 2-amino-6-bromo-3-(trifluoromethoxy)phenol obtained in Reference Example 3(b), using a similar method to Reference Example 1(c).

(Reference Example 4)

7-Bromo-4-(trifluoromethyl)benzo[d]oxazole-2-thiol

(a) 6-Bromo-2-nitro-3-(trifluoromethyl)phenol

5.2 g of the title compound was obtained as a crude product from 5 g of 2-bromo-5-(trifluoromethyl)phenol using a similar method to Reference Example 1(a).

MS (ESI) m/z: 284 $(M-H)^-$

(b) 2-Amino-6-bromo-3-(trifluoromethyl)phenol

1.7 g of the title compound was obtained from 5.2 g of 6-bromo-2-nitro-3-(trifluoromethyl)phenol obtained in Reference Example 4(a), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 256 $(M+H)^+$

(c) 7-Bromo-4-(trifluoromethyl)benzo[d]oxazole-2-thiol

400 mg g of the title compound was obtained from 1.7 g of 2-amino-6-bromo-3-(trifluoromethyl)phenol obtained in Reference Example 4(b), using a similar method to Reference Example 1(c).

(Reference Example 5)

N-(7-bromo-2-mercaptobenzo[d]oxazol-4-yl)acetamide

(a) N-(4-bromo-3-hydroxyphenyl)acetamide

10 g of N-(3-hydroxyphenyl)acetamide was dissolved in acetic acid (80 mL), and then acetic acid solution (4.1 mL, 1.2 equivalents) of bromine was added thereto, followed by stirring at room temperature for 16 hours. The formation of the product was confirmed by TLC, then the reaction mixture was poured into distilled water under ice-cooling, followed by filtration, and thus obtaining 4 g of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane:ethyl acetate = 3:2).

MS (ESI) m/z: 230 $(M+H)^+$

(b) N-(4-bromo-3-hydroxy-2-nitrophenyl)acetamide

6.1 g of N-(4-bromo-3-hydroxyphenyl)acetamide obtained in Reference Example 5(a) was dissolved in concentrated sulfuric acid (140 mL), and then a liquid mixture of concentrated sulfuric acid (71 mL) and 70% nitric acid (1.4 mL, 1.2 equivalents) was added thereto at 0°C over 25 minutes, followed by stirring at room temperature for 2 hours. The formation of the product was confirmed by TLC, and then the reaction mixture was poured into distilled water under ice-cooling, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous

magnesium sulfate, followed by filtration, and thus obtaining 6.9 g of the title compound as a crude product obtained by vacuum concentration of the filtrate.

MS (ESI) m/z: 273 $(M-H)^-$

(c) N-(2-amino-4-bromo-3-hydroxyphenyl)acetamide

5 g of the title compound was obtained from 6.9 g of N-(4-bromo-3-hydroxy-2-nitrophenyl)acetamide obtained in Reference Example 5(b), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 245 $(M+H)^+$

(d) N-(7-bromo-2-mercaptobenzo[d]oxazol-4-yl)acetamide

2.5 g of the title compound was obtained from 5 g of N-(2-amino-4-bromo-3-hydroxyphenyl)acetamide obtained in Reference Example 5(c), using a similar method to Reference Example 1(c).

(Reference Example 6)

7-Bromo-4-chlorobenzo[d]oxazole-2-thiol

(a) 6-Bromo-3-chloro-2-nitrophenol

3.1 g of the title compound was obtained as a crude product from 2.5 g of 2-bromo-5-chlorophenol using a similar method to Reference Example 1(a).

MS (ESI) m/z: 252 $(M+H)^+$

(b) 2-Amino-6-bromo-3-chlorophenol

3.3 g of the title compound was obtained from 3.1 g of 6-bromo-3-chloro-2-nitrophenol obtained in

Reference Example 6(a), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 222 $(M+H)^+$

(c) 7-Bromo-4-chlorobenzo[d]oxazole-2-thiol

1.8 g of the title compound was obtained from 3.3 g of 2-amino-6-bromo-3-chlorophenol obtained in Reference Example 6(b), using a similar method to Reference Example 1(c).

(Reference Example 7)

7-Bromo-5-(methylthio)benzo[d]oxazole-2-thiol

(a) 2-Bromo-4-(methylthio)phenol

2.5 g of 4-(methylthio)phenol was dissolved in dichloromethane (50 mL), then 47% hydrobromic acid (7.8 mL, 8 equivalents) was added thereto, followed by heating to 45°C, and 30% hydrogen peroxide solution (0.84 mL, 2 equivalents) was added dropwise thereto, followed by stirring at that temperature for 6 hours. The formation of the product was confirmed by TLC, and then the reaction mixture was poured into distilled water under ice-cooling, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous sodium sulfate, followed by filtration, and thus obtaining 3.5 g of the title compound as a crude product obtained by vacuum concentration of the filtrate.

MS (ESI) m/z: 219 $(M+H)^+$

(b) 2-Bromo-4-(methylthio)-6-nitrophenol

1.5 g of the title compound was obtained as a crude product from 3.5 g of 2-bromo-4-(methylthio)phenol obtained in Reference Example 7(a), using a similar method to Reference Example 1(a).

MS (ESI) m/z: 264 $(M+H)^+$

(c) 2-Amino-6-bromo-4-(methylthio)phenol

3.2 g of the title compound was obtained from 3.8 g of 2-bromo-4-(methylthio)-6-nitrophenol obtained in Reference Example 7(b), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 234 $(M+H)^+$

(d) 7-Bromo-5-(methylthio)benzo[d]oxazole-2-thiol

2.4 g of the title compound was obtained from 3.2 g of 2-amino-6-bromo-4-(methylthio)phenol obtained in Reference Example 7(c), using a similar method to Reference Example 1(c).

(Reference Example 8)

7-Bromo-5-(methylsulfinyl)benzo[d]oxazole-2-thiol

(a) 2-Bromo-4-(methylsulfinyl)phenol

300 mg of the title compound was obtained from 1 g of 4-(methylsulfinyl)phenol using a similar method to Reference Example 9(a) except that the crude product was refined by silica gel column chromatography.

MS (ESI) m/z: 235 $(M+H)^+$

(b) 2-Bromo-4-(methylsulfinyl)-6-nitrophenol

2 g of the title compound was obtained as a crude product from 3.5 g of 2-bromo-4-(methylsulfinyl)phenol obtained in Reference Example 8(a), using a similar method to Reference Example 1(a).

MS (ESI) m/z: 281 $(M+2H)^+$

(c) 2-Amino-6-bromo-4-(methylsulfinyl)phenol

3.2 g of the title compound was obtained from 3.8 g of 2-bromo-4-(methylsulfinyl)-6-nitrophenol obtained in Reference Example 8(b), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 250 $(M+H)^+$

(d) 7-Bromo-5-(methylsulfinyl)benzo[d]oxazole-2-thiol

2.5 g of the title compound was obtained from 3.2 g of 2-amino-6-bromo-4-(methylsulfinyl)phenol obtained in Reference Example 8(c), using a similar method to Reference Example 1(c).

(Reference Example 9)

N-(7-bromo-2-mercaptobenzo[d]oxazol-5-yl)acetamide

(a) N-(3-bromo-4-hydroxyphenyl)acetamide

1 g of N-(4-hydroxyphenyl)acetamide and chlorotrimethylsilane (0.16 mL, 0.2 equivalent) were dissolved in acetonitrile (20 mL), and then N-bromosuccinimide (1.29 g, 1.1 equivalents) was added thereto at 0°C, followed by stirring at room

temperature for 14 hours. The formation of the product was confirmed by TLC, and then the reaction mixture was poured into distilled water under ice-cooling, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 1 g of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane:ethyl acetate = 3:2).

MS (ESI) m/z: 230 $(M+H)^+$

(b) N-(3-bromo-4-hydroxy-5-nitrophenyl)acetamide

2 g of the title compound was obtained as a crude product from 1.6 g of N-(3-bromo-4-hydroxyphenyl)acetamide obtained in Reference Example 9(a), using a similar method to Reference Example 1(a).

MS (ESI) m/z: 275 $(M+H)^+$

(c) N-(3-amino-5-bromo-4-hydroxyphenyl)acetamide

1.2 g of the title compound was obtained from 2 g of N-(3-bromo-4-hydroxy-5-nitrophenyl)acetamide obtained in Reference Example 9(b), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 245 $(M+H)^+$

(d) N-(7-bromo-2-mercaptobenzo[d]oxazol-5-yl)acetamide

650 mg of the title compound was obtained from

1.2 g of N-(3-amino-5-bromo-4-hydroxyphenyl)acetamide obtained in Reference Example 9(c), using a similar method to Reference Example 1(c).

(Reference Example 10)

7-Bromo-5-(trifluoromethoxy)benzo[d]oxazole-2-thiol

(a) 2-Bromo-6-nitro-4-(trifluoromethoxy)phenol

5.8 g of the title compound was obtained as a crude product from 5.2 g of 2-bromo-4-(trifluoromethoxy)phenol using a similar method to Reference Example 1(a).

MS (ESI) m/z: 300 $(M-H)^-$

(b) 2-Amino-6-bromo-4-(trifluoromethoxy)phenol

4.4 g of the title compound was obtained from 5.8 g of 2-bromo-6-nitro-4-(trifluoromethoxy)phenol obtained in Reference Example 10(a), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 272 $(M+H)^+$

(c) 7-Bromo-5-(trifluoromethoxy)benzo[d]oxazole-2-thiol

5.0 g of the title compound was obtained from 4.4 g of 2-amino-6-bromo-4-(trifluoromethoxy)phenol obtained in Reference Example 10(b), using a similar method to Reference Example 1(c).

(Reference Example 11)

7-Bromo-2-mercaptobenzo[d]oxazole-5-sulfonamide

(a) 3-Bromo-4-methoxybenzenesulfonyl chloride

10 g of 1-bromo-2-methoxybenzene was dissolved in chloroform (56 mL), and then chlorosulfuric acid (11 mL, 3 equivalents) was added thereto at -10°C, followed by stirring at room temperature for 1 hour. The formation of the product was confirmed by TLC, and then the reaction mixture was poured into distilled water under ice-cooling, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining as a crude product 14 g of the title compound by vacuum concentration of the filtrate.

MS (ESI) m/z: 285 $(M+H)^+$

(b) 3-Bromo-4-methoxybenzenesulfonamide

14 g of 3-bromo-4-methoxybenzenesulfonyl chloride obtained in Reference Example 11(a) was dissolved in dichloromethane (1000 mL), and then 0.5 M ammonia solution in 1,4-dioxane (518 mL) and triethylamine (26 mL) were added thereto at 0°C, followed by stirring at room temperature for 2 hours. The formation of the product was confirmed by TLC, and 5% aqueous solution of citric acid was added to stop the reaction, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 11.4 g of the title compound as a

crude product by vacuum concentration of the filtrate.

MS (ESI) m/z: 266 $(M+H)^+$

(c) 3-Bromo-4-hydroxybenzenesulfonamide

5 g of 3-bromo-4-methoxybenzenesulfonamide obtained in Reference Example 11(b) was dissolved in dichloromethane (1000 mL), and then 1 M boron tribromide solution in dichloromethane (56 mL, 3 equivalents) was added thereto at -78°C, followed by stirring at room temperature for 36 hours. The formation of the product was confirmed by TLC, and then distilled water was added to stop the reaction. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining as a crude product 4 g of the title compound by vacuum concentration of the filtrate.

MS (ESI) m/z: 252 $(M+H)^+$

(d) 3-Bromo-4-hydroxy-5-nitrobenzenesulfonamide

2.4 g of the title compound was obtained as a crude product from 2.5 g of 3-bromo-4-hydroxybenzenesulfonamide obtained in Reference Example 11(c), using a similar method to Reference Example 5(b).

MS (ESI) m/z: 297 $(M+H)^+$

(e) 3-Amino-5-bromo-4-hydroxybenzenesulfonamide

1.5 g of the title compound was obtained as a crude product from 5.6 g of 3-bromo-4-hydroxy-5-

nitrobenzenesulfonamide obtained in Reference Example 11(d), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 267 $(M+H)^+$

(f) 7-Bromo-2-mercaptobenzo[d]oxazole-5-sulfonamide

600 mg of the title compound was obtained from 1.5 g of 3-amino-5-bromo-4-hydroxybenzenesulfonamide obtained in Reference Example 11(e), using a similar method to Reference Example 1(c).

(Reference Example 12)

7-Bromo-5-methoxybenzo[d]oxazole-2-thiol

(a) 2-Bromo-4-methoxy-6-nitrophenol

2.5 g of 2-bromo-4-methoxyphenol was dissolved in ethyl acetate (125 mL), and then 70% nitric acid (0.8 mL, 1.0 equivalent) was added thereto at 0°C over 10 minutes, followed by stirring at room temperature for 10 hours. The formation of the product was confirmed by TLC, and then solid sodium hydrogen carbonate was added to adjust the pH to 7. The reaction mixture was filtered and the filtrate was extracted using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining as a crude product 2.8 g of the title compound obtained by vacuum concentration of the filtrate.

MS (ESI) m/z: 248 $(M+H)^+$

(b) 2-Amino-6-bromo-4-methoxyphenol

1 g of the title compound was obtained from 1.2 g of 2-bromo-4-methoxy-6-nitrophenol obtained in Reference Example 12(a), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 218 $(M+H)^+$

(c) 7-Bromo-5-methoxybenzo[d]oxazole-2-thiol

600 mg of the title compound was obtained from 1 g of 2-amino-6-bromo-4-methoxyphenol obtained in Reference Example 12(b), using a similar method to Reference Example 1(c).

(Reference Example 13)

7-Bromo-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole-2-thiol

(a) 1-(Benzyloxy)-4-(2,2,2-trifluoroethoxy) benzene

5 g of 4-(benzyloxy)phenol was dissolved in N,N-dimethylformamide (40 mL), and then potassium carbonate (10.3 g, 3 equivalents) and 2,2,2-trifluoroethyl p-toluenesulfonate (6.3 g, 2 equivalents) were added thereto, followed by stirring at 110°C for 22 hours. The formation of the product was confirmed by TLC, and then distilled water was added to stop the reaction, followed by extraction using ethyl acetate. The organic phase was washed by distilled water and then dried over anhydrous magnesium sulfate, followed by filtration, and thus

obtaining 4 g of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane:ethyl acetate = 98:2).

MS (ESI) m/z: 283 $(M+H)^+$

(b) 4-(2,2,2-Trifluoroethoxy)phenol

500 mg of 1-(benzyloxy)-4-(2,2,2-trifluoroethoxy) benzene obtained in Reference Example 13(a) was dissolved in ethanol (10 mL), and then 10% Pd/C (300 mg) was added thereto under argon atmosphere. The reaction mixture was stirred under a hydrogen atmosphere (1 atm) at room temperature for 17 hours. The formation of the product was confirmed by TLC, and the reaction mixture was filtered through Celite®, thus obtaining the title compound as a crude product by vacuum concentration of the filtrate.

MS (ESI) m/z: 191 $(M-H)^-$

(c) 2-Bromo-4-(2,2,2-trifluoroethoxy)phenol

1.9 g of the title compound was obtained as a crude product from 1.2 g of 4-(2,2,2-trifluoroethoxy)phenol obtained in Reference Example 13(b), using a similar method to Reference Example 9(a).

MS (ESI) m/z: 271 $(M+H)^+$

(d) 2-Bromo-6-nitro-4-(2,2,2-trifluoroethoxy)phenol

5.2 g of the title compound was obtained as a

crude product from 5.1 g of 2-bromo-4-(2,2,2-trifluoroethoxy)phenol obtained in Reference Example 13(c), using a similar method to Reference Example 1(a).

MS (ESI) m/z: 314 $(M-H)^-$

(e) 2-Amino-6-bromo-4-(2,2,2-trifluoroethoxy)phenol

400 mg of the title compound was obtained from 634 mg of 2-bromo-6-nitro-4-(2,2,2-trifluoroethoxy)phenol obtained in Reference Example 13(d), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 286 $(M+H)^+$

(f) 7-Bromo-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole-2-thiol

2.1 g of the title compound was obtained from 4 g of 2-amino-6-bromo-4-(2,2,2-trifluoroethoxy)phenol obtained in Reference Example 13(e), using a similar method to Reference Example 1(c).

(Reference Example 14)

7-Bromo-4-methoxybenzo[d]oxazole-2-thiol

(a) 3-Methoxy-2-nitrophenol

5 g of 2-nitrobenzene-1,3-diol was dissolved in N,N-dimethylformamide (75 mL), and then potassium carbonate (1.3 g, 0.3 equivalent) and methyl iodide (2.23 mL, 1.1 equivalents) were added thereto at 0°C, followed by stirring at room temperature for 30

minutes. The formation of the product was confirmed by TLC, and then distilled water was added to stop the reaction, followed by extraction using ethyl acetate. The organic phase was washed by 2 M hydrochloric acid (20 mL) and then dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 1.6 g of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane:ethyl acetate = 85:15).

MS (ESI) m/z: 168 $(M-H)^-$

(b) 6-Bromo-3-methoxy-2-nitrophenol

166 mg of the title compound was obtained from 250 mg of 3-methoxy-2-nitrophenol obtained in Reference Example 14(a), using a similar method to Reference Example 9(a).

MS (ESI) m/z: 248 $(M+H)^+$

(c) 2-Amino-6-bromo-3-methoxyphenol

1 g of the title compound was obtained from 6.7 g of 6-bromo-3-methoxy-2-nitrophenol obtained in Reference Example 14(b), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 218 $(M+H)^+$

(d) 7-Bromo-4-methoxybenzo[d]oxazole-2-thiol

635 mg of the title compound was obtained from 1 g of 2-amino-6-bromo-3-methoxyphenol obtained in

Reference Example 14(c), using a similar method to Reference Example 1(c).

(Reference Example 15)

Ethyl 7-bromo-2-mercaptobenzo[d]oxazole-5-carboxylate

(a) Ethyl 3-bromo-4-hydroxybenzoate

5 g of 3-bromo-4-hydroxybenzoic acid was dissolved in ethanol (60 mL), and then concentrated sulfuric acid (7.3 mL, 6 equivalents) was added thereto at 0°C, followed by stirring at 90°C for 24 hours. The formation of the product was confirmed by TLC, and the reaction mixture was subjected to vacuum concentration. The obtained residue was dissolved in ethyl acetate, and then saturated sodium hydrogen carbonate aqueous solution was added thereto. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 5.4 g of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane:ethyl acetate = 70:30).

MS (ESI) m/z: 245 $(M+H)^+$

(b) Ethyl 3-bromo-4-hydroxy-5-nitrobenzoate

6.0 g of the title compound was obtained as a crude product from 5.4 g of ethyl 3-bromo-4-hydroxybenzoate obtained in Reference Example 15(a), using a similar method to Reference Example 1(a).

MS (ESI) m/z: 290 $(M+H)^+$

(c) Ethyl 3-amino-5-bromo-4-hydroxybenzoate

4.0 g of the title compound was obtained from 6.0 g of ethyl 3-bromo-4-hydroxy-5-nitrobenzoate obtained in Reference Example 15(b), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 260 $(M+H)^+$

(d) Ethyl 7-bromo-2-mercaptobenzo[d]oxazole-5-carboxylate

4.1 g of the title compound was obtained from 4.0 g of ethyl 3-amino-5-bromo-4-hydroxybenzoate obtained in Reference Example 15(c), using a similar method to Reference Example 1(c).

(Reference Example 16)

Ethyl 7-bromo-2-mercaptobenzo[d]oxazole-4-carboxylate

(a) 4-Bromo-3-hydroxy-2-nitrobenzoic acid

2.7 g of the title compound was obtained as a crude product from 2.5 g of 4-bromo-3-hydroxybenzoic acid using a similar method to Reference Example 5(b).

MS (ESI) m/z: 262 $(M+H)^+$

(b) Ethyl 4-bromo-3-hydroxy-2-nitrobenzoate

1.3 g of the title compound was obtained as a crude product from 2.7 g of 4-bromo-3-hydroxy-2-nitrobenzoic acid obtained in Reference Example 16(a), using a similar method to Reference Example 15(a).

MS (ESI) m/z: 288 $(M-H)^-$

(c) Ethyl 2-amino-4-bromo-3-hydroxybenzoate

580 mg of the title compound was obtained from 1.3 g of ethyl 4-bromo-3-hydroxy-2-nitrobenzoate obtained in Reference Example 16(b), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 260 $(M+H)^+$

(d) Ethyl 7-bromo-2-mercaptobenzo[d]oxazole-4-carboxylate

245 mg of the title compound was obtained from 580 mg of ethyl 2-amino-4-bromo-3-hydroxybenzoate obtained in Reference Example 16(c), using a similar method to Reference Example 1(c).

(Reference Example 17)

(7-Bromo-2-mercaptobenzo[d]oxazol-4-yl)methanol

500 mg of ethyl 7-bromo-2-mercaptobenzo[d]oxazole-4-carboxylate obtained in Reference Example 16 was dissolved in 10 mL of tetrahydrofuran, and then 1.0 M solution of lithium aluminum hydride in tetrahydrofuran (2.4 mL, 1.5 equivalents) was added thereto at 0°C, followed by stirring at room temperature for 2 hours. The formation of the product was confirmed by TLC, and saturated aqueous solution of sodium sulfate was added to stop the reaction, followed by extraction using ethyl acetate. The aqueous layer was rendered acidic using 1 M aqueous solution of hydrochloric acid,

followed by extraction using ethyl acetate. Thereafter, the obtained organic phase was mixed, washed by distilled water, and dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 240 mg of the title compound as a crude product by vacuum concentration of the filtrate.

(Reference Example 18)

1-(7-Bromo-2-mercaptobenzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol

(a) 1-(3-Bromo-4-methoxyphenyl)-2,2,2-trifluoroethanone

1 g of 2,2,2-trifluoro-1-(4-methoxyphenyl)ethan-1-one was dissolved in carbon tetrachloride (9.5 mL), and then silver oxide(II) (72 mg, 0.12 equivalent), concentrated sulfuric acid (0.47 mL), and bromine (0.26 mL, 1.03 equivalents) were added thereto, followed by stirring at 65°C for 17 hours. The formation of the product was confirmed by TLC, and then the reaction mixture was poured into distilled water under ice-cooling, followed by extraction using dichloromethane. Thereafter, the organic phase was dried over anhydrous sodium sulfate, followed by filtration, and thus obtaining 1.3 g of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane:ethyl acetate =

95:5).

MS (ESI) m/z: 283 $(M+H)^+$

(b) 1-(3-Bromo-4-hydroxyphenyl)-2,2,2-trifluoroethanone

1.3 g of 1-(3-bromo-4-methoxyphenyl)-2,2,2-trifluoroethanone obtained in Reference Example 18(a) was dissolved in N,N-dimethylformamide (13 mL), and then lithium chloride (701 mg, 3.6 equivalents) was added thereto, followed by stirring at 140°C for 2 hours. The formation of the product was confirmed by TLC, and the reaction mixture was subjected to vacuum concentration. The obtained residue was dissolved in methanol, and then the pH was adjusted to 3 using methanol solution of hydrochloric acid. The liquid mixture was subjected to vacuum concentration again, thus obtaining 1.1 g of the title compound by purification of the obtained residue through silica gel column chromatography (hexane:ethyl acetate = 4:1).

MS (ESI) m/z: 269 $(M+H)^+$

(c) 1-(3-Bromo-4-hydroxy-5-nitrophenyl)-2,2,2-trifluoroethanone

1.0 g of the title compound was obtained as a crude product from 1.1 g of 1-(3-bromo-4-hydroxyphenyl)-2,2,2-trifluoroethanone obtained in Reference Example 18(b), using a similar method to

Reference Example 1(a).

MS (ESI) m/z: 312 $(M-H)^-$

(d) 2-Bromo-6-nitro-4-(2,2,2-trifluoro-1-hydroxyethyl)phenol

1.0 g of 1-(3-bromo-4-hydroxy-5-nitrophenyl)-2,2,2-trifluoroethanone obtained in Reference Example 18(c) was dissolved in methanol (10 mL), and then sodium borohydride (129 mg, 1.1 equivalents) was added thereto at 0°C, followed by stirring at that temperature for 1 hour. The formation of the product was confirmed by TLC, and then distilled water under ice-cooling was added to stop the reaction, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining as a crude product 900 mg of the title compound by vacuum concentration of the filtrate.

MS (ESI) m/z: 314 $(M-H)^-$

(e) 2-Amino-6-bromo-4-(2,2,2-trifluoro-1-hydroxyethyl)phenol

650 mg of the title compound was obtained from 900 mg of 2-bromo-6-nitro-4-(2,2,2-trifluoro-1-hydroxyethyl)phenol obtained in Reference Example 18(d), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 284 $(M+H)^+$

(f) 1-(7-Bromo-2-mercaptobenzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol

700 mg of the title compound was obtained from 925 mg of 2-amino-6-bromo-4-(2,2,2-trifluoro-1-hydroxyethyl)phenol obtained in Reference Example 18(e), using a similar method to Reference Example 1(c).

(Reference Example 19)

Ethyl 7-bromo-2-mercapto-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate

(a) 5-Bromo-4-hydroxy-2-(trifluoromethyl)benzoic acid

3.8 g of the title compound was obtained as a crude product from 5.0 g of 4-hydroxy-2-(trifluoromethyl)benzoic acid using a similar method to Reference Example 7(a).

MS (ESI) m/z: 283 $(M-H)^-$

(b) Ethyl 5-bromo-4-hydroxy-2-(trifluoromethyl)benzoate

3.8 g of the title compound was obtained as a crude product from 3.8 g of 5-bromo-4-hydroxy-2-(trifluoromethyl)benzoic acid obtained in Reference Example 19(a), using a similar method to Reference Example 15(a) except that the prification by silica gel column chromatography was not performed.

(c) Ethyl 5-bromo-4-hydroxy-3-nitro-2-(trifluoromethyl)benzoate

3.8 g of the title compound was obtained as a crude product from 3.8 g of ethyl 5-bromo-4-hydroxy-2-(trifluoromethyl)benzoate obtained in Reference Example 19(b), using a similar method to Reference Example 1(a).

MS (ESI) m/z: 359 $(M+2H)^+$

(d) Ethyl 3-amino-5-bromo-4-hydroxy-2-(trifluoromethyl)benzoate

2.7 g of the title compound was obtained from 3.8 g of ethyl 5-bromo-4-hydroxy-3-nitro-2-(trifluoromethyl)benzoate obtained in Reference Example 19(c), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 328 $(M+H)^+$

(e) Ethyl 7-bromo-2-mercapto-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate

1.6 g of the title compound was obtained from 2.7 g of ethyl 3-amino-5-bromo-4-hydroxy-2-(trifluoromethyl)benzoate obtained in Reference Example 19(d), using a similar method to Reference Example 1(c).

(Reference Example 20)

Ethyl 7-bromo-2-mercapto-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

(a) Triisopropyl (3-(trifluoromethoxy)phenoxy)silane

5 g of 3-(trifluoromethoxy)phenol and imidazole

(5.7 g, 3 equivalents) were dissolved in N,N-dimethylformamide (13 mL), and then chlorotriisopropylsilane (12 mL, 2 equivalents) was added thereto, followed by stirring at room temperature for 4 hours. The formation of the product was confirmed by TLC, and then ice-cooled distilled water was added to stop the reaction, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 8.1 g of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane).

(b) 2-(Trifluoromethoxy)-4-((triisopropylsilyl)oxy)benzoic acid

8.1 g of triisopropyl (3-(trifluoromethoxy)phenoxy)silane obtained in Reference Example 20(a) and N,N,N',N'-tetramethylethylenediamine (3.6 mL, 1 equivalent) were dissolved in tetrahydrofuran (162 mL), and then 1.5 M solution of sec-butyllithium in cyclohexane (24 mL, 1.5 equivalents) was added dropwise thereto at -78°C over 20 minutes. Stirring was performed at that temperature for 2 hours, followed by further stirring at -40°C for 1 hour. The reaction mixture was cooled

to -78°C, and carbon dioxide gas was added thereto over 2 hours. After the temperature was raised to 0°C, the formation of the product was confirmed by TLC. Thereafter, saturated aqueous solution of ammonium chloride was added to stop the reaction, and the pH was adjusted to 2 using 6 M hydrochloric acid. The reaction mixture was extracted using ethyl acetate, and the organic phase was washed by distilled water and dried over anhydrous magnesium sulfate, followed by filtration, thus obtaining 9 g of the title compound as a crude product by vacuum concentration of the filtrate.

MS (ESI) m/z: 377 $(M-H)^-$

(c) Ethyl 4-hydroxy-2-(trifluoromethoxy)benzoate

2.3 g of the title compound was obtained from 9 g of 2-(trifluoromethoxy)-4-((triisopropylsilyl)oxy)benzoic acid obtained in Reference Example 20(b), using a similar method to Reference Example 15(a).

MS (ESI) m/z: 248 $(M-2H)^-$

(d) Ethyl 5-bromo-4-hydroxy-2-(trifluoromethoxy)benzoate

3.1 g of the title compound was obtained from 3.6 g of ethyl 4-hydroxy-2-(trifluoromethoxy)benzoate obtained in Reference Example 20(c), using a similar method to Reference Example 9(a).

MS (ESI) m/z: 326 $(M-2H)^-$

(e) Ethyl 5-bromo-4-hydroxy-3-nitro-2-(trifluoromethoxy)benzoate

2.4 g of the title compound was obtained as a crude product from 1.4 g of ethyl 5-bromo-4-hydroxy-2-(trifluoromethoxy)benzoate obtained in Reference Example 20(d), using a similar method to Reference Example 1(a).

MS (ESI) m/z: 372 $(M-H)^-$

(f) Ethyl 3-amino-5-bromo-4-hydroxy-2-(trifluoromethoxy)benzoate

1.5 g of the title compound was obtained from 2.4 g of ethyl 5-bromo-4-hydroxy-3-nitro-2-(trifluoromethoxy)benzoate obtained in Reference Example 20(e), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 344 $(M+H)^+$

(g) Ethyl 7-bromo-2-mercapto-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

980 mg of the title compound was obtained from 1.5 g of ethyl 3-amino-5-bromo-4-hydroxy-2-(trifluoromethoxy)benzoate obtained in Reference Example 20(f), using a similar method to Reference Example 1(c).

(Reference Example 21)

1-(7-Bromo-2-mercaptobenzo[d]oxazol-4-yl)-2,2,2-

trifluoroethan-1-ol

(a) Methyl 4-bromo-3-hydroxybenzoate

52 g of the title compound was obtained from 50 g of 4-bromo-3-hydroxybenzoic acid using a similar method to Reference Example 15(a) except that methanol was used instead of ethanol.

MS (ESI) m/z: 231 $(M+H)^+$

(b) 2-Bromo-5-(hydroxymethyl)phenol

26.8 g of methyl 4-bromo-3-hydroxybenzoate obtained in Reference Example 21(a) was dissolved in tetrahydrofuran (537 mL), and then lithium aluminum hydride (6.6 g, 1.5 equivalents) was added thereto at 0°C over 15 minutes, followed by stirring at room temperature for 17 hours. After the formation of the product was confirmed by TLC, saturated aqueous solution of sodium sulfate was added at 0°C to stop the reaction, and the pH was adjusted to 2 using 6 M hydrochloric acid. The reaction mixture was extracted using ethyl acetate, and the organic phase was washed by distilled water and dried over anhydrous magnesium sulfate, followed by filtration, thus obtaining 20 g of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane:ethyl acetate = 7:3).

MS (ESI) m/z: 201 $(M-H)^-$

(c) 4-Bromo-3-hydroxybenzaldehyde

40 g of 2-bromo-5-(hydroxymethyl)phenol obtained in Reference Example 21(b) was dissolved in dichloromethane (4000 mL), and then Celite® (150 g) and pyridinium chlorochromate (106 g, 2.5 equivalents) were added thereto at 0°C over 45 minutes, followed by stirring at room temperature for 2 hours. The formation of the product was confirmed by TLC, and then the reaction mixture was filtered and washed by dichloromethane, thus obtaining 28 g of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane:ethyl acetate = 7:3).

MS (ESI) m/z: 201 $(M+H)^+$

(d) 2-Bromo-5-(2,2,2-trifluoro-1-hydroxyethyl)phenol

15 g of 4-bromo-3-hydroxybenzaldehyde obtained in Reference Example 21(c) was dissolved in N,N-dimethylformamide (300 mL), and then trifluoromethyltrimethylsilane (33 mL, 3 equivalents) and potassium carbonate (3.1 g, 0.3 equivalent) were added thereto at 0°C, followed by stirring at room temperature for 2.5 hours. The formation of the product was confirmed by TLC, and then distilled water was added thereto at 0°C, followed by stirring at room temperature for 15 hours. After the reaction mixture

was extracted using ethyl acetate, the organic phase was washed by distilled water and dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 16 g of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane:ethyl acetate = 7:3).

MS (ESI) m/z: 271 $(M+H)^+$

(e) 6-Bromo-2-nitro-3-(2,2,2-trifluoro-1-hydroxyethyl)phenol

18 g of the title compound was obtained as a crude product from 25 g of 2-bromo-5-(2,2,2-trifluoro-1-hydroxyethyl)phenol obtained in Reference Example 21(d), using a similar method to Reference Example 1(a).

MS (ESI) m/z: 316 $(M+H)^+$

(f) 2-Amino-6-bromo-3-(2,2,2-trifluoro-1-hydroxyethyl)phenol

11.6 g of the title compound was obtained from 18 g of 6-bromo-2-nitro-3-(2,2,2-trifluoro-1-hydroxyethyl)phenol obtained in Reference Example 21(e), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 286 $(M+H)^+$

(g) 1-(7-Bromo-2-mercaptobenzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol

6.3 g of the title compound was obtained from 11.6 g of 2-amino-6-bromo-3-(2,2,2-trifluoro-1-hydroxyethyl)phenol obtained in Reference Example 21(f), using a similar method to Reference Example 1(c).

(Reference Example 22)

Methyl 7-bromo-2-mercaptobenzo[d]oxazole-4-carboxylate

(a) Methyl 4-bromo-3-hydroxy-2-nitrobenzoate

12.7 g of the title compound was obtained as a crude product from 13 g of 4-bromo-3-hydroxy-2-nitrobenzoic acid obtained in Reference Example 16(a), using a similar method to Reference Example 15(a) except that methanol was used instead of ethanol.

MS (ESI) m/z: 276 $(M+H)^+$

(b) Methyl 2-amino-4-bromo-3-hydroxybenzoate

5.4 g of the title compound was obtained from 12.7 g of methyl 4-bromo-3-hydroxy-2-nitrobenzoate obtained in Reference Example 22(a), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 246 $(M+H)^+$

(c) Methyl 7-bromo-2-mercaptobenzo[d]oxazole-4-carboxylate

2.5 g of the title compound was obtained from 5.4 g of methyl 2-amino-4-bromo-3-hydroxybenzoate obtained in Reference Example 22(b), using a similar method to Reference Example 1(c).

(Reference Example 23)

4-(Benzyloxy)-7-bromobenzo[d]oxazole-2-thiol

(a) (((2-Nitro-1,3-phenylene)bis(oxy))bis(methylene))dibenzene

5 g of 2-nitroresorcinol was dissolved in N,N-dimethylformamide (88 mL), and then benzylbromide (8.4 mL, 2.2 equivalents) and caesium carbonate (25 g, 2.4 equivalents) were added thereto, followed by stirring at room temperature for 12 hours. The formation of the product was confirmed by TLC, and then ethyl acetate was added thereto. The organic phase was washed by 1% aqueous solution of hydrochloric acid and then washed again by distilled water. The organic phase was dried over anhydrous magnesium sulfate, followed by filtration. Hexane was added to the residue obtained by vacuum concentration of the filtrate and the precipitated solid was collected by filtration, thus obtaining 10 g of the title compound.

MS (ESI) m/z: 336 $(M+H)^+$

(b) 3-(Benzyloxy)-2-nitrophenol

10 g of (((2-nitro-1,3-phenylene)bis(oxy))bis(methylene))dibenzene obtained in Reference Example 23(a) was dissolved in dichloromethane (270 mL), and then 1.0 M solution of boron trichloride in heptane (45 mL, 1.5 equivalents) was added thereto at -78°C, followed by stirring at -

78°C for 1 hour. After the formation of the product was confirmed by TLC, methanol was added thereto over 10 minutes, the temperature was raised to room temperature, and distilled water was added thereto. This mixture was extracted twice using dichloromethane and the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 4.7 g of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane:ethyl acetate = 9.5:0.5).

MS (ESI) m/z: 244 $(M-H)^-$

(c) 3-(Benzyloxy)-6-bromo-2-nitrophenol

22 g of the title compound was obtained from 20 g of 3-(benzyloxy)-2-nitrophenol obtained in Reference Example 23(b), using a similar method to Reference Example 9(a).

MS (ESI) m/z: 322 $(M-H)^-$

(d) 2-Amino-3-(benzyloxy)-6-bromophenol

28 g of the title compound was obtained from 22 g of 3-(benzyloxy)-6-bromo-2-nitrophenol obtained in Reference Example 23(c), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 292 $(M-H)^-$

(e) 4-(Benzyloxy)-7-bromobenzo[d]oxazole-2-thiol

28 g of the title compound was obtained from 25

g of 2-amino-3-(benzyloxy)-6-bromophenol obtained in Reference Example 23(d), using a similar method to Reference Example 1(c).

(Reference Example 24)

7-Bromo-4-((tert-butyldimethylsilyl)oxy)benzo[d]oxazole-2-thiol

(a) 3-((tert-Butyldimethylsilyl)oxy)-2-nitrophenol

5.0 g of 2-nitroresorcinol and imidazole (2.7 g, 1.2 equivalents) were dissolved in tetrahydrofuran (160 mL), and then tert-butyldimethylchlorosilane (4.9 g, 1.0 equivalent) was added thereto at 0°C, followed by stirring at room temperature for 30 minutes and thereafter by stirring at 65°C for 3 hours. The formation of the product was confirmed by TLC, and then distilled water was added over 10 minutes to stop the reaction, followed by extraction using ethyl acetate three times. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 4.0 g of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane:ethyl acetate = 9:1).

MS (ESI) m/z: 268 $(M-H)^-$

(b) 6-Bromo-3-((tert-butyldimethylsilyl)oxy)-2-nitrophenol

3.6 g of the title compound was obtained from 4.0 g of 3-((tert-butyldimethylsilyl)oxy)-2-nitrophenol obtained in Reference Example 24(a), using a similar method to Reference Example 9(a).

MS (ESI) m/z: 346 $(M-H)^-$

(c) 2-Amino-6-bromo-3-((tert-butyldimethylsilyl)oxy)phenol

3.0 g of the title compound was obtained from 3.6 g of 6-bromo-3-((tert-butyldimethylsilyl)oxy)-2-nitrophenol obtained in Reference Example 24(b), using a similar method to Reference Example 1(b).

MS (ESI) m/z: 318 $(M+H)^+$

(d) 7-Bromo-4-((tert-butyldimethylsilyl)oxy)benzo[d]oxazole-2-thiol

2.5 g of the title compound was obtained from 3.0 g of 2-amino-6-bromo-3-((tert-butyldimethylsilyl)oxy)phenol obtained in Reference Example 24(c), using a similar method to Reference Example 1(c).

(Example 1)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

700 mg of 7-bromo-5-chloro-4-

(trifluoromethoxy)benzo[d]oxazole-2-thiol (the compound of Reference Example 12 in International Publication No. Wo 2015/005429) and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate (512 mg, 1.2 equivalents) were dissolved in m-xylene (5 mL), followed by stirring overnight in an oil bath at 120°C. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then 1 M aqueous solution of sodium hydroxide was added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 967 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane; then hexane:ethyl acetate = 4:1).

(b) tert-Butyl 3-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

500 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 1(a) was dissolved in toluene (3.2 mL), and 0.5 M solution of 2-thiazolylzinc bromide in tetrahydrofuran (3.8 mL, 2 equivalents) and [1,1'-bis(diphenylphosphino)ferrocene]palladium(II)

dichloride·dichloromethane complex (155 mg, 0.2 equivalent) were added thereto, followed by stirring for 6 hours in an oil bath at 90°C under an argon atmosphere. Saturated sodium hydrogen carbonate aqueous solution was added to the reaction mixture, and the mixture was filtered throuth Celite®. After the filtrate was extracted using ethyl acetate, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 424 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane; then hexane:ethyl acetate = 4:1).

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

420 mg of tert-butyl 3-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 1(b) was dissolved in chloroform (7.9 mL) and trifluoroacetic acid (3 mL), followed by stirring at room temperature for 3 hours. Saturated sodium hydrogen carbonate aqueous solution was added to the reaction mixture, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 340 mg of the title compound by

purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (chloroform; then chloroform:methanol:aqueous solution of ammonia = 4:1:0.1).

(Example 2)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

280 mg of the title compound was obtained from 250 mg of 7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazole-2-thiol using a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

150 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 2(a), bis(triphenylphosphine)palladium(II) dichloride (19 mg, 0.1 equivalent), and 2-

(tributylstannyl)thiazole (0.12 mL, 2.0 equivalents) were dissolved in 1,4-dioxane, followed by stirring for 29 hours in an oil bath at 130°C under an argon atmosphere. The reaction mixture was fitered through Celite®, thus obtaining 100 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane:ethyl acetate = 93:7).

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

100 mg of the title compound was obtained from 200 mg of tert-butyl 3-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 2(b), using a similar method to Example 1(c).

(Example 3)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

347 mg of the title compound was obtained from 300 mg of 7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazole-2-thiol using a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used

instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

275 mg of the title compound was obtained from 347 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 3(a), using a similar method to Example 1(b).

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

157 mg of the title compound was obtained from 275 mg of tert-butyl 3-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 3(b), using a similar method to Example 1(c).

(Example 4)

7-(5-Chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane

(a) tert-Butyl 7-(7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate

280 mg of the title compound was obtained from 250 mg of 7-bromo-5-chloro-4-

(trifluoromethoxy)benzo[d]oxazole-2-thiol using a similar method to Example 1(a) except that tert-butyl 3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 7-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate

100 mg of the title compound was obtained from 200 mg of tert-butyl 7-(7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 4(a), using a similar method to Example 2(b).

(c) 7-(5-Chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane

80 mg of the title compound was obtained from 150 mg of tert-butyl 7-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 4(b), using a similar method to Example 1(c).

(Example 5)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-

diazabicyclo[3.2.1]octane-8-carboxylate

55 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 1(a), 1H-pyrazole (14 mg, 2 equivalents), tris(dibenzylideneacetone)dipalladium(0) (9.5 mg, 0.1 equivalent), 2-di-tert-butylphosphino-3,4,5,6-tetramethyl-2',4',6'-triisopropylbiphenyl (12.5 mg, 0.25 equivalent), and potassium phosphate (44 mg, 2 equivalents) were dissolved in toluene (1.0 mL), followed by stirring for 25 hours in an oil bath at 90°C. Distilled water was added to the reaction mixture, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 10 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane; then hexane:ethyl acetate = 4:1).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethoxy)benzo[d]oxazole

3.8 mg of the title compound was obtained from 10 mg of tert-butyl 3-(5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 5(a), using a similar method to Example 1(c).

(Example 6)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(furan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-chloro-7-(furan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

53 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 1(a), 2-(tributylstannyl)furan (47.2 μL, 1.5 equivalents), and tetrakis(triphenylphosphine)palladium(0) (11.6 mg, 0.1 equivalent) were dissolved in N,N-dimethylformamide (0.5 mL), followed by stirring using a microwave reactor (manufactured by Biotage, conditions: 100°C, 1 hour). Distilled water was added to the reaction mixture, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 56 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane; then hexane:ethyl acetate = 4:1).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(furan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

35 mg of the title compound was obtained from 56

mg of tert-butyl 3-(5-chloro-7-(furan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 6(a), using a similar method to Example 1(c).

(Example 7)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-chloro-7-(pyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

46 mg of the title compound was obtained from 53 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 1(a), using a similar method to Example 6(a) except that 2-(tributylstannyl)pyridine was used instead of 2-(tributylstannyl)furan.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

31 mg of the title compound was obtained from 46 mg of tert-butyl 3-(5-chloro-7-(pyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 7(a), using a similar method to Example 1(c).

(Example 8)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-

(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-chloro-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

60 mg of the title compound was obtained from 53 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 1(a), using a similar method to Example 6(a) except that 4-(tributylstannyl)thiazole was used instead of 2-(tributylstannyl)furan.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole

40 mg of the title compound was obtained from 60 mg of tert-butyl 3-(5-chloro-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 8(a), using a similar method to Example 1(c).

(Example 9)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(oxazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-chloro-7-(oxazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

55 mg of the title compound was obtained from 53 mg of tert-butyl 3-(7-bromo-5-chloro-4-

(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 1(a), using a similar method to Example 6(a) except that 2-(tributylstannyl) oxazole was used instead of 2-(tributylstannyl)furan.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(oxazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

38 mg of the title compound was obtained from 55 mg of tert-butyl 3-(5-chloro-7-(oxazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 9(a), using a similar method to Example 1(c).

(Example 10)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(5-fluoropyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-chloro-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

263 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 1(a), bis(pinacolato)diboron (190 mg, 1.5 equivalents), potassium acetate (147 mg, 3 equivalents), and [1,1'-

bis(diphenylphosphino)ferrocene]palladium(II) dichloride·dichloromethane complex (41 mg, 0.1 equivalent) were dissolved in 1,4-dioxane (2.5 mL), followed by stirring for 5 hours in an oil bath at 90°C under an argon atmosphere. Distilled water was added to the reaction mixture, followed by Celite® filtration. After the filtrate was extracted using ethyl acetate, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 234 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane; hexane:ethyl acetate = 4:1; then hexane:ethyl acetate:methanol = 4:1:0.5).

(b) tert-Butyl 3-(5-chloro-7-(5-fluoropyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

57 mg of tert-butyl 3-(5-chloro-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 10(a), tetrakis(triphenylphosphine)palladium(0) (11.6 mg, 0.1 equivalent), potassium carbonate (55 mg, 4 equivalents), and 2-bromo-5-fluoropyridine (35 mg, 2 equivalents) were dissolved in a mixture solvent of

1,4-dioxane (0.4 mL) and distilled water (0.1 mL), followed by stirring for 4 hours in an oil bath at 100°C under an argon atmosphere. Distilled water was added to the reaction mixture, followed by Celite® filtration. After the filtrate was extracted using ethyl acetate, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 47 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane; then hexane:ethyl acetate = 4:1).

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(5-fluoropyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

33 mg of the title compound was obtained from 47 mg of tert-butyl 3-(5-chloro-7-(5-fluoropyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 10(b), using a similar method to Example 1(c).

(Example 11)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

345 mg of the title compound was obtained from 250 mg of 7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazole-2-thiol (the compound of Reference Example 10 in International Publication No. Wo 2015/005429) and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate using a similar method to Example 1(a).

(b) tert-Butyl 3-(5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

340 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 11(a), 2-(tributylstannyl)pyridine (0.32 mL, 1.5 equivalents), and bis(triphenylphosphine)palladium(II) dichloride (46 mg, 0.1 equivalent) were dissolved in 1,4-dioxane (7 mL), followed by stirring for 4 hours in an oil bath at 110°C. The reaction mixture was subjected to Celite® filtration, thus obtaining 400 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane:ethyl acetate = 93:7).

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

154 mg of the title compound was obtained from 400 mg of tert-butyl 3-(5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 11(b), using a similar method to Example 1(c).

(Example 12)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

860 mg of the title compound was obtained from 600 mg of 7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazole-2-thiol using a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

333 mg of the title compound was obtained as a crude product from 300 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 12(a), using a similar method to Example

11(b).

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

150 mg of the title compound was obtained from 330 mg of tert-butyl 3-(5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 12(b), using a similar method to Example 1(c).

(Example 13)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

700 mg of the title compound was obtained from 650 mg of 7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazole-2-thiol using a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

340 mg of the title compound was obtained as a crude product from 300 mg of tert-butyl 3-(7-bromo-5-

chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 13(a), using a similar method to Example 11(b).

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

160 mg of the title compound was obtained from 340 mg of tert-butyl 3-(5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 13(b), using a similar method to Example 1(c).

(Example 14)

7-(5-Chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane

(a) tert-Butyl 7-(7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate

914 mg of the title compound was obtained from 650 mg of 7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazole-2-thiol using a similar method to Example 1(a) except that tert-butyl 3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 7-(5-chloro-7-(pyridin-2-yl)-4-

(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate

214 mg of the title compound was obtained from 300 mg of tert-butyl 7-(7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 14(a), using a similar method to Example 11(b).

(c) 7-(5-Chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane

150 mg of the title compound was obtained from 214 mg of tert-butyl 7-(5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 14(b), using a similar method to Example 1(c).

(Example 15)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

570 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 11(a), 1H-pyrazole (91 mg, 1.2 equivalents),

copper(I) iodide (21 mg, 0.1 equivalent), trans-N,N'-dimethylcyclohexane-1,2-diamine (31 mg, 0.2 equivalent), and potassium phosphate (498 mg, 2.1 equivalents) were dissolved in toluene (18 mL), followed by stirring at 130°C for 24 hours. Saturated sodium hydrogen carbonate aqueous solution was added to the reaction mixture, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 140 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane; then hexane:ethyl acetate = 94:6).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole

98 mg of the title compound was obtained from 140 mg of tert-butyl 3-(5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 15(a), using a similar method to Example 1(c).

(Example 16)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-

diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 190 mg from 375 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 12(a) by a similar method to Example 15(a).

(b) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of 140 mg from 190 mg of tert-butyl 3-(5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 16(a) by a similar method to Example 1(c).

(Example 17)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane -6-carboxylate

The title compound was obtained in an amount of 240 mg from 400 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 13(a) by a similar method to Example 15(a).

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of 176 mg from 240 mg of tert-butyl 3-(5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane -6-carboxylate obtained in Example 17(a) by a similar method to Example 1(c).

(Example 18)

7-(5-Chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane

(a) tert-Butyl 7-(5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 170 mg from 270 mg of tert-butyl 7-(7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 14(a) by a similar method to Example 15(a).

(b) 7-(5-Chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane

The title compound was obtained in an amount of 120 mg from 170 mg of tert-butyl 7-(5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 18(a) by a similar method to Example 1(c).

(Example 19)

7-(5-Chloro-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane

(a) tert-Butyl 7-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 62 mg from 135 mg of tert-butyl 7-(7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 14(a) by a similar method to Example 1(b).

(b) 7-(5-Chloro-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane

The title compound was obtained in an amount of 41 mg from 62 mg of tert-butyl 7-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 19(a) by a similar method to Example 1(c).

(Example 20)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 202 mg from 300 mg of tert-butyl 3-(7-bromo-5-chloro-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 11(a) by a similar method to Example 1(b).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of 94 mg from 202 mg of tert-butyl 3-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 20(a) by a similar method to Example 1(c).

(Example 21)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-isopropylbenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 140 mg from 100 mg of 7-bromo-5-isopropylbenzo[d]oxazole-2-thiol obtained in Reference Example 1 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-

8-carboxylate

The title compound was obtained as a crude product in an amount of 350 mg from 240 mg of tert-butyl 3-(7-bromo-5-isopropylbenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 21(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 200 mg from 350 mg of tert-butyl 3-(5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 21(b) by a similar method to Example 1(c).

(Example 22)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-isopropylbenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 290 mg from 200 mg of 7-bromo-5-isopropylbenzo[d]oxazole-2-thiol obtained in Reference Example 1 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 409 mg from 240 mg of tert-butyl 3-(7-bromo-5-isopropylbenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 22(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 160 mg from 409 mg of tert-butyl 3-(5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 22(b) by a similar method to Example 1(c).

(Example 23)

7-(5-Isopropyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane

(a) tert-Butyl 7-(7-bromo-5-isopropylbenzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 260 mg from 200 mg of 7-bromo-5-isopropylbenzo[d]oxazole-2-thiol obtained in Reference Example 1 by a similar method to Example 1(a) except

that tert-butyl 3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 7-(5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained as a crude product in an amount of 380 mg from 260 mg of tert-butyl 7-(7-bromo-5-isopropylbenzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 23(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) 7-(5-Isopropyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane

The title compound was obtained in an amount of 155 mg from 380 mg of tert-butyl 7-(5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 23(b) by a similar method to Example 1(c).

(Example 24)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-isopropylbenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of

320 mg from 200 mg of 7-bromo-5-isopropylbenzo[d]oxazole-2-thiol obtained in Reference Example 1 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained as a crude product in an amount of 340 mg from 260 mg of tert-butyl 3-(7-bromo-5-isopropylbenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 24(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 160 mg from 340 mg of tert-butyl 3-(5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 24(b) by a similar method to Example 1(c).

(Example 25)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-methylbenzo[d]oxazol-2-

yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 210 mg from 150 mg of 7-bromo-4-methylbenzo[d]oxazole-2-thiol obtained in Reference Example 2 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(4-methyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 178 mg from 210 mg of tert-butyl 3-(7-bromo-4-methylbenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 25(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 120 mg from 175 mg of tert-butyl 3-(4-methyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 25(b) by a similar method to Example 1(c).

(Example 26)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-methylbenzo[d]oxazol-2-

yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 205 mg from 150 mg of 7-bromo-4-methylbenzo[d]oxazole-2-thiol obtained in Reference Example 2 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(4-methyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 250 mg from 205 mg of tert-butyl 3-(7-bromo-4-methylbenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 26(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 140 mg from 250 mg of tert-butyl 3-(4-methyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 26(b) by a similar method to Example 1(c).

(Example 27)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-4-methyl-7-

(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-methylbenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 220 mg from 150 mg of 7-bromo-4-methylbenzo[d]oxazole-2-thiol obtained in Reference Example 2 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(4-methyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained as a crude product in an amount of 235 mg from 210 mg of tert-butyl 3-(7-bromo-4-methylbenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 27(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 119 mg from 235 mg of tert-butyl 3-(4-methyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 27(b) by a similar method to Example 1(c).

(Example 28)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 140 mg from 100 mg of 7-bromo-4-(trifluoromethoxy)benzo[d]oxazole-2-thiol obtained in Reference Example 3 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 120 mg from 140 mg of tert-butyl 3-(7-bromo-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 28(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 90 mg from 120 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-

diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 28(b) by a similar method to Example 1(c).

(Example 29)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 200 mg from 150 mg of 7-bromo-4-(trifluoromethoxy)benzo[d]oxazole-2-thiol obtained in Reference Example 3 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 250 mg from 200 mg of tert-butyl 3-(7-bromo-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 29(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 140 mg from 250 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 29(b) by a similar method to Example 1(c).

(Example 30)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 220 mg from 150 mg of 7-bromo-4-(trifluoromethoxy)benzo[d]oxazole-2-thiol obtained in Reference Example 3 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained as a crude product in an amount of 300 mg from 220 mg of tert-

butyl 3-(7-bromo-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 30(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 140 mg from 300 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 30(b) by a similar method to Example 1(c).

(Example 31)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 200 mg from 150 mg of 7-bromo-4-(trifluoromethyl)benzo[d]oxazole-2-thiol obtained in Reference Example 4 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-

diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 130 mg from 130 mg of tert-butyl 3-(7-bromo-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 31(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of 100 mg from 130 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 31(b) by a similar method to Example 1(c).

(Example 32)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 190 mg from 150 mg of 7-bromo-4-

(trifluoromethyl)benzo[d]oxazole-2-thiol obtained in Reference Example 4 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 170 mg from 130 mg of tert-butyl 3-(7-bromo-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 32(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of 98 mg from 170 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 32(b) by a similar method to Example 1(c).

(Example 33)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 210 mg from 150 mg of 7-bromo-4-(trifluoromethyl)benzo[d]oxazole-2-thiol obtained in Reference Example 4 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained as a crude product in an amount of 100 mg from 100 mg of tert-butyl 3-(7-bromo-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 33(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II)

dichloride.

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of 50 mg from 100 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 33(b) by a similar method to Example 1(c).

(Example 34)

N-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)acetamide

(a) tert-Butyl 3-(4-acetamido-7-bromobenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 28 mg from 250 mg of N-(7-bromo-2-mercaptobenzo[d]oxazol-4-yl)acetamide obtained in Reference Example 5 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(4-acetamido-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 19 mg from tert-butyl 3-(4-acetamido-7-

bromobenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 34(a) by a similar method to Example 1(b) except that a solution of 6 equivalents of 0.5M solution of 2-thiazolylzinc bromide in tetrahydrofuran was used instead of the 2 equivalents of 0.5M solution of 2-thiazolylzinc bromide in tetrahydrofuran.

(c) N-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)acetamide

The title compound was obtained in an amount of 8.3 mg from 19 mg of tert-butyl 3-(4-acetamido-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 34(b) by a similar method to Example 1(c).

(Example 35)

N-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)acetamide

(a) tert-Butyl 3-(4-acetamido-7-bromobenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 33 mg from 250 mg of N-(7-bromo-2-mercaptobenzo[d]oxazol-4-yl)acetamide obtained in Reference Example 5 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-

carboxylate.

(b) tert-Butyl 3-(4-acetamido-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 21 mg from tert-butyl 3-(4-acetamido-7-bromobenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 35(a) by a similar method to Example 1(b) except that 6 equivalents of 0.5M solution of 2-thiazolylzinc bromide in tetrahydrofuran was used instead of the 2 equivalents of 0.5M solution of 2-thiazolylzinc bromide in tetrahydrofuran.

(c) N-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)acetamide

The title compound was obtained in an amount of 14 mg from 21 mg of tert-butyl 3-(4-acetamido-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 35(b) by a similar method to Example 1(c).

(Example 36)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-chlorobenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of

150 mg from 100 mg of 7-bromo-4-chlorobenzo[d]oxazole-2-thiol obtained in Reference Example 6 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(4-chloro-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 130 mg from 130 mg of tert-butyl 3-(7-bromo-4-chlorobenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 36(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 85 mg from 130 mg of tert-butyl 3-(4-chloro-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 36(b) by a similar method to Example 1(c).

(Example 37)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-chlorobenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 135 mg from 100 mg of 7-bromo-4-chlorobenzo[d]oxazole-2-thiol obtained in Reference Example 6 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(4-chloro-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 200 mg from 130 mg of tert-butyl 3-(7-bromo-4-chlorobenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 37(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 90 mg from 200 mg of tert-butyl 3-(4-chloro-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-

diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 37(b) by a similar method to Example 1(c).

(Example 38)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-chlorobenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 160 mg from 100 mg of 7-bromo-4-chlorobenzo[d]oxazole-2-thiol obtained in Reference Example 6 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(4-chloro-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained as a crude product in an amount of 180 mg from 130 mg of tert-butyl 3-(7-bromo-4-chlorobenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 38(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 90 mg from 180 mg of tert-butyl 3-(4-chloro-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 38(b) by a similar method to Example 1(c).

(Example 39)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(methylthio)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 153 mg from 100 mg of 7-bromo-5-(methylthio)benzo[d]oxazole-2-thiol obtained in Reference Example 7 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(5-(methiylthio)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 300 mg from 150 mg of tert-butyl 3-(7-bromo-5-(methylthio)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained

in Example 39(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 58 mg from 300 mg of tert-butyl 3-(5-(methiylthio)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 39(b) by a similar method to Example 1(c).

(Example 40)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(methylthio)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 120 mg from 100 mg of 7-bromo-5-(methylthio)benzo[d]oxazole-2-thiol obtained in Reference Example 7 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 106 mg from 110 mg of tert-butyl 3-(7-bromo-5-(methylthio)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 40(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 65 mg from 103 mg of tert-butyl 3-(5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 40(b) by a similar method to Example 1(c).

(Example 41)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(methylthio)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of

100 mg from 100 mg of 7-bromo-5-(methylthio)benzo[d]oxazole-2-thiol obtained in Reference Example 7 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 70 mg from 80 mg of tert-butyl 3-(7-bromo-5-(methylthio)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 41(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 40 mg from 65 mg of tert-butyl 3-(5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 41(b) by a similar method to Example 1(c).

(Example 42)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(methylsulfinyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 200 mg from 150 mg of 7-bromo-5-(methylsulfinyl)benzo[d]oxazole-2-thiol obtained in Reference Example 8 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 220 mg from 200 mg of tert-butyl 3-(7-bromo-5-(methylsulfinyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 42(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-

(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 45 mg from 90 mg of tert-butyl 3-(5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 42(b) by a similar method to Example 1(c).

(Example 43)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(methylsulfinyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 200 mg from 150 mg of 7-bromo-5-(methylsulfinyl)benzo[d]oxazole-2-thiol obtained in Reference Example 8 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 200 mg from 200 mg of tert-butyl 3-(7-bromo-5-(methylsulfinyl)benzo[d]oxazol-2-yl)-3,6-

diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 43(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 42 mg from 80 mg of tert-butyl 3-(5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 43(b) by a similar method to Example 1(c).

(Example 44)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(methylsulfinyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 100 mg from 100 mg of 7-bromo-5-(methylsulfinyl)benzo[d]oxazole-2-thiol obtained in Reference Example 8 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-

carboxylate.

(b) tert-Butyl 3-(5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained as in an amount of 150 mg from 165 mg of tert-butyl 3-(7-bromo-5-(methylsulfinyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 44(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 39 mg from 80 mg of tert-butyl 3-(5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 44(b) by a similar method to Example 1(c).

(Example 45)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

120 mg of tert-butyl 3-(5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 42(b) and mCPBA (174 mg, 4 equivalents) were dissolved in dichloromethane (50 mL), followed by reaction at room temperature for 1 hour. The formation of the product was confirmed by TLC, and then saturated sodium hydrogen carbonate aqueous solution was added thereto, followed by extraction using dichloromethane. Thereafter, the organic phase was washed by distilled water and dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining as a crude product 130 mg of the title compound by vacuum concentration of the filtrate.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 40 mg from 80 mg of tert-butyl 3-(5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 45(a) by a similar method to Example 1(c).

(Example 46)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-

diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 90 mg from 115 mg of tert-butyl 3-(5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 43(b) by a similar method to Example 45(a).

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 49 mg from 80 mg of tert-butyl 3-(5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 46(a) by a similar method to Example 1(c).

(Example 47)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 80 mg from 85 mg of tert-butyl 3-(5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 44(b)by a similar method to Example 45(a).

(b) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 48 mg from 80 mg of tert-butyl 3-(5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 47(a) by a similar method to Example 1(c).

(Example 48)

N-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide

(a) tert-Butyl 3-(5-acetamido-7-bromobenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 362 mg from 300 mg of N-(7-bromo-2-mercaptobenzo[d]oxazol-5-yl)acetamide obtained in Reference Example 9 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-acetamido-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 89 mg from 100 mg of tert-butyl 3-(5-acetamido-7-bromobenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 48(a) by a similar method to Example 1(b)

except that a solution of 5 equivalents of 0.5M solution of 2-thiazolylzinc bromide in tetrahydrofuran and 0.3 equivalent of 1,1'-Bis(diphenylphosphino)ferrocene palladium(II) dichloride dichloromethane complex were used.

(c) N-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide

The title compound was obtained in an amount of 45 mg from 88 mg of tert-butyl 3-(5-acetamido-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 48(b) by a similar method to Example 1(c).

(Example 49)

N-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide

(a) tert-Butyl 3-(5-acetamido-7-bromobenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 136 mg from 200 mg of N-(7-bromo-2-mercaptobenzo[d]oxazol-5-yl)acetamide obtained in Reference Example 9 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-acetamido-7-(thiazol-2-

yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 100 mg from 100mg of tert-butyl 3-(5-acetamido-7-bromobenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 49(a) by a similar method to Example 1(b) except that a solution of 5 equivalents of 0.5M solution of 2-thiazolylzinc bromide in tetrahydrofuran and 0.3 equivalent of 1,1'-bis(diphenylphosphino)ferrocene palladium(II) dichloride·dichloromethane complex were used.

(c) N-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide

The title compound was obtained in an amount of 27 mg from 100 mg of tert-butyl 3-(5-acetamido-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 49(b) by a similar method to Example 1(c).

(Example 50)

N-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide

(a) tert-Butyl 3-(5-acetamido-7-bromobenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 107 mg from 120 mg of N-(7-bromo-2-

mercaptobenzo[d]oxazol-5-yl)acetamide obtained in Reference Example 9 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(5-acetamido-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 54 mg from 60 mg of tert-butyl 3-(5-acetamido-7-bromobenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 50(a) by a similar method to Example 1(b) except that 6 equivalents of 0.5M solution of 2-thiazolylzinc bromide in tetrahydrofuran was used instead of 2 equivalents of 0.5M solution of 2-thiazolylzinc bromide in tetrahydrofuran.

(c) N-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide

The title compound was obtained in an amount of 18 mg from 54 mg of tert-butyl 3-(5-acetamido-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 50(b) by a similar method to Example 1(c).

(Example 51)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 109 mg by a similar method to Example 1(a) except that 101 mg of 7-bromo-5-(trifluoromethyl)benzo[d]oxazole-2-thiol (a compound disclosed in International Publication No. WO2015/005429) was used.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 65 mg from 132mg of tert-butyl 3-(7-bromo-5-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 51(a) by a similar method to Example 1(b) except that 3.5 equivalents of 0.5M solution of 2-thiazolylzinc bromide in tetrahydrofuran and 0.3 equivalent of 1,1'-bis(diphenylphosphino)ferrocene palladium(II) dichloride·dichloromethane complex were used.

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of 43 mg from 65 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-

diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 51(b) by a similar method to Example 1(c).

(Example 52)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 134 mg from 150 mg of 7-bromo-5-(trifluoromethyl)benzo[d]oxazole-2-thiol by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 77 mg from 134 mg of tert-butyl 3-(7-bromo-5-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 52(a) by a similar method to Example 1(b).

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of

26 mg from 77 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 52(b) by a similar method to Example 1(c).

(Example 53)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 139 mg from 150 mg of 7-bromo-5-(trifluoromethyl)benzo[d]oxazole-2-thiol by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 95.4 mg from 139 mg of tert-butyl 3-(7-bromo-5-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 53(a) by a similar method to Example 1(b).

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-

2-yl)-5-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of 49.8 mg from 95.4 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 53(b) by a similar method to Example 1(c).

(Example 54)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 192 mg from 150 mg of 7-bromo-5-(trifluoromethoxy)benzo[d]oxazole-2-thiol obtained in Reference Example 10 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 77 mg from 192 mg of tert-butyl 3-(7-bromo-5-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 54(a) by a similar method to Example 1(b)

except that a microwave reactor(by Biotage, 100°C, 20min) was used.

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 49 mg from 74 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 54(b) by a similar method to Example 1(c).

(Example 55)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 195 mg from 150 mg of 7-bromo-5-(trifluoromethoxy)benzo[d]oxazole-2-thiol obtained in Reference Example 10 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 158 mg from 195 mg of tert-butyl 3-(7-bromo-5-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 55(a) by a similar method to Example 1(b) except that the microwave reactor(by Biotage, 100°C, 20min) was used.

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 114 mg from 158 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 55(b) by a similar method to Example 1(c).

(Example 56)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 196 mg from 150 mg of 7-bromo-5-(trifluoromethoxy)benzo[d]oxazole-2-thiol obtained in Reference Example 10 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used

instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate and the microwave reactor(by Biotage, 120°C, 40min) was used.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 133 mg from 194 mg of tert-butyl 3-(7-bromo-5-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 56(a) by a similar method to Example 1(b) except that the microwave reactor(by Biotage, 100°C, 80min) and 2-thiazolylzinc bromide (1.62mL, 4 equivalents) was used.

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 103 mg from 133 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 56(b) by a similar method to Example 1(c).

(Example 57)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide

(a) tert-Butyl 3-(7-bromo-5-sulfamoylbenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 45 mg from 51 mg of 7-bromo-2-mercaptobenzo[d]oxazole-5-sulfonamide obtained in Reference Example 11 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(5-sulfamoyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 12 mg from 45 mg of tert-butyl 3-(7-bromo-5-sulfamoylbenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 57(a) by a similar method to Example 1(b) except that 6.0 equivalents of 0.5M solution of 2-thiazolylzinc bromide in tetrahydrofuran and 0.4 equivalent of 1,1'-bis(diphenylphosphino)ferrocene palladium(II) dichloride·dichloromethane complex were used.

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide

The title compound was obtained in an amount of 4.8 mg from 11 mg of tert-butyl 3-(5-sulfamoyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 57(b) by a similar method to Example 1(c).

(Example 58)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide

(a) tert-Butyl 3-(7-bromo-5-sulfamoylbenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 170 mg from 200 mg of 7-bromo-2-mercaptobenzo[d]oxazole-5-sulfonamide obtained in Reference Example 11 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-sulfamoyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 32 mg from 100 mg of tert-butyl 3-(7-bromo-5-sulfamoylbenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 58(a) by a similar method to Example 1(b) except that 9 equivalents of 0.5M solution of 2-thiazolylzinc bromide in tetrahydrofuran and 0.6 equivalent of 1,1'-bis(diphenylphosphino)ferrocene palladium(II) dichloride·dichloromethane complex were used.

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide

The title compound was obtained in an amount of 12 mg from 32 mg of tert-butyl 3-(5-sulfamoyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 58(b) by a similar method to Example 1(c).

(Example 59)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide

(a) tert-Butyl 3-(7-bromo-5-sulfamoylbenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 56 mg from 202 mg of 7-bromo-2-mercaptobenzo[d]oxazole-5-sulfonamide obtained in Reference Example 11 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-sulfamoyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 30 mg from 56 mg of tert-butyl 3-(7-bromo-5-sulfamoylbenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in

Example 59(a) by a similar method to Example 1(b) except that 6 equivalents of 0.5M solution of 2-thiazolylzinc bromide in tetrahydrofuran and 0.4 equivalent of 1,1'-bis(diphenylphosphino)ferrocene palladium(II) dichloride·dichloromethane complex were used.

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide

The title compound was obtained in an amount of 10 mg from 30 mg of tert-butyl 3-(5-sulfamoyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 59(b) by a similar method to Example 1(c).

(Example 60)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-methoxybenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 70 mg from 50 mg of 7-bromo-5-methoxybenzo[d]oxazole-2-thiol obtained in Reference Example 12 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(5-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 125 mg from 70 mg of tert-butyl 3-(7-bromo-5-methoxybenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 60(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 30 mg from 120 mg of tert-butyl 3-(5-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 60(b) by a similar method to Example 1(c).

(Example 61)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-methoxybenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 230 mg from 175 mg of 7-bromo-5-methoxybenzo[d]oxazole-2-thiol obtained in Reference Example 12 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-methoxy-7-(thiazol-2-

yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 245 mg from 225 mg of tert-butyl 3-(7-bromo-5-methoxybenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 61(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 140 mg from 245 mg of tert-butyl 3-(5-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 61(b) by a similar method to Example 1(c).

(Example 62)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-methoxybenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 150 mg from 100 mg of 7-bromo-5-methoxybenzo[d]oxazole-2-thiol obtained in Reference Example 12 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-

diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(5-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained as a crude product in an amount of 173 mg from 150 mg of tert-butyl 3-(7-bromo-5-methoxybenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 62(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 240 mg from 450 mg of tert-butyl 3-(5-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 62(b) by a similar method to Example 1(c).

(Example 63)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-ol

130 mg of tert-butyl 3-(5-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 60(b) was dissolved in dichloromethane (10 mL), and then 1.0 M solution of boron tribromide in dichloromethane (2.1 mL, 7.5 equivalents) was added thereto at -78°C, followed by

stirring at room temperature for 18 hours. The formation of the product was confirmed by TLC, and then distilled water was added to stop the reaction. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 65 mg of the title compound by vacuum concentration of the filtrate.

(Example 64)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-ol

The title compound was obtained in an amount of 65 mg from 140 mg of tert-butyl 3-(5-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 61(b) by a similar method to Example 63.

(Example 65)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-ol

The title compound was obtained in an amount of 40 mg from 340 mg of tert-butyl 3-(5-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 62(b) by a similar method to Example 63.

(Example 66)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(2,2,2-trifluoroethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 131 mg from 131 mg of 7-bromo-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole-2-thiol obtained in Reference Example 13 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 39 mg from 47 mg of tert-butyl 3-(7-bromo-5-(2,2,2-trifluoroethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 66(a) by a similar method to Example 2(b).

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 33 mg from 39 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 66(b) by a similar method to Example 1(c).

(Example 67)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-

yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-5-(2,2,2-trifluoroethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 168 mg from 164 mg of 7-bromo-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole-2-thiol obtained in Reference Example 13 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 29 mg from 89 mg of tert-butyl 3-(7-bromo-5-(2,2,2-trifluoroethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 67(a) by a similar method to Example 2(b).

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 21 mg from 29 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazol-2-yl)-3,6-

diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 67(b) by a similar method to Example 1(c).

(Example 68)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-isopropoxy-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

332 mg of tert-butyl 3-(5-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 60(b) was dissolved in N,N-dimethylformamide (3.3 mL), and then sodium tert-butoxide (505 mg, 7 equivalents) and 2-(dimethylamino)ethane-1-thiol hydrochloride (319 mg, 3 equivalents) were added thereto, followed by stirring using a microwave reactor (manufactured by Biotage) for 15 minutes at 160°C under an argon atmosphere. 1 M hydrochloric acid was added to the reaction mixture, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous sodium sulfate, followed by filtration, and thus obtaining 134 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane, hexane:ethyl acetate = 1:2).

(b) tert-Butyl 3-(5-isopropoxy-7-(thiazol-2-

yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

Triphenylphosphine (18 mg, 1.5 equivalents), 2.2 M toluene solution (32 mL, 1.5 equivalents) of diethyl azodicarboxylate, and 2-propanol (5.4 µL, 1.5 equivalents) were dissolved in toluene (0.5 mL), and then 20 mg of tert-butyl 3-(5-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 68(a) was added thereto, followed by stirring at room temperature for 17 hours under an argon atmosphere, and thus obtaining 17 mg of the title compound by preparative TLC (eluent, hexane:ethyl acetate = 1:1).

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-isopropoxy-7-(thiazol-2-yl)benzo[d]oxazole

12 mg of the title compound was obtained from 17 mg of tert-butyl 3-(5-isopropoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 68(b), using a similar method to Example 1(c).

(Example 69)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(2-methoxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 90 mg from 20 mg of tert-butyl 3-(5-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 68(a) by a similar method to Example 68(b) except that 2-methoxyethanol (42µL, 11.5 equivalents), triphenylphosphine (144mg, 11.5 equivalents), and a 2.2M solution of diethyl azodicarboxylate in toluene (244µL, 11.5 equivalents) were used instead of 2-propanol.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 6.4 mg from 90 mg of the crude product of tert-butyl 3-(5-(2-methoxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 69(a) by a similar method to Example 1(c).

(Example 70)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(oxetan-3-ylmethoxy)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(oxetan-3-ylmethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

20 mg of tert-butyl 3-(5-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-

8-carboxylate obtained in Example 68(a), 3-(iodomethyl)oxetane (20 mg, 2.1 equivalents) and sodium hydride (6.1 mg, 3 equivalents) were dissolved in a mixed solvent consisting of N,N-dimethylformamide (0.5mL)-tetrahydrofuran (0.5 mL), followed by stirring at 90 °C for 10 hours. The formation of the product was confirmed by TLC, and then saturated ammonium chloride aqueous solution was added and the organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 19 mg of the title compound by purification of the residue by preparative TLC (eluent, hexane:ethyl acetate = 1:1).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(oxetan-3-ylmethoxy)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 6.0 mg from 12 mg of tert-butyl 3-(5-(oxetan-3-ylmethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 70(a) by a similar method to Example 1(c).

(Example 71)

2-(((2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)methyl)propane-1,3-diol

The title compound was obtained in an amount of 4.0 mg from 12 mg of tert-butyl 3-(5-(oxetan-3-

ylmethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 70(a) by a similar method to Example 1(c).

(Example 72)

5-(Allyloxy)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(allyloxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 7.4 mg from 20 mg of tert-butyl 3-(5-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 68(a) by a similar method to Example 70(a) except that cyclopropyl bromide was used instead of 3-(iodomethyl)oxetane.

(b) 5-(Allyloxy)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 5.4 mg from 6.9 mg of tert-butyl 3-(5-(allyloxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 72(a) by a similar method to Example 1(c).

(Example 73)

2-((2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)acetonitrile

(a) tert-Butyl 3-(5-(cyanomethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

10 mg of tert-butyl 3-(5-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 68(a) was dissolved in N,N-dimethylformamide (230μL), and then potassium carbonate (8 mg, 2.4 equivalents) and bromoacetonitrile (4 μL, 2.4 equivalents) were added thereto at room temperature, followed by stirring overnight. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and the organic phase was extracted using water and ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 5.4 mg of the title compound by purification of the residue by preparative TLC (eluent, hexane:ethyl acetate = 1:1).

(b) 2-((2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)acetonitrile

9 mg of tert-butyl 3-(5-(cyanomethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 73(a) was dissolved in chloroform (0.2mL) and trifluoroacetic acid (63μL). A reaction mixture was

obtained by stirring thereof for 3 hours at room temperature. A precipitate was obtained by adding diethyl ether to a residue obtained by vacuum concentration of the reaction mixture. A trifuluoroacetic acid salt of the title compound was obtained in an amount of 3 mg by filtration of the precipitate.

(Example 74)

2-((2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)acetic acid

(a) tert-Butyl 3-(5-(2-(tert-butoxy)-2-oxoethoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 9 mg from 10 mg of tert-butyl 3-(5-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 68(a) by a similar method to Example 73(a) except that tert-butyl 2-bromoacetate was used instead of bromoacetonitrile.

(b) 2-((2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)acetic acid

A trifluoroacetic acid salt of the title compound was obtained in an amount of 7 mg from 9 mg of tert-butyl 3-(5-(2-(tert-butoxy)-2-oxoethoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-

diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 74(a) by a similar method to Example 73(b).

(Example 75)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-methoxybenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 300 mg from 200 mg of 7-bromo-4-methoxybenzo[d]oxazole-2-thiol obtained in Reference Example 14 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(4-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 300 mg from 250 mg of tert-butyl 3-(7-bromo-4-methoxybenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 75(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of Bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-methoxy-

7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 150 mg from 300 mg of tert-butyl 3-(4-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 75(b) by a similar method to Example 1(c).

(Example 76)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-methoxybenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 289 mg from 200 mg of 7-bromo-4-methoxybenzo[d]oxazole-2-thiol obtained in Reference Example 14 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(4-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 300 mg from 280 mg of tert-butyl 3-(7-bromo-4-methoxybenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 76(a) by a similar method to Example 2(b)

except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of Bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 178 mg from 300 mg of tert-butyl 3-(4-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 76(b) by a similar method to Example 1(c).

(Example 77)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-bromo-4-methoxybenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 320 mg from 200 mg of 7-bromo-4-methoxybenzo[d]oxazole-2-thiol obtained in Reference Example 14 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(4-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 180 mg from 279 mg of tert-butyl 3-(7-bromo-4-methoxybenzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 77(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of Bis(triphenylphosphine)palladium(II) dichloride.

(c) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 40 mg from 180 mg of tert-butyl 3-(4-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 77(b) by a similar method to Example 1(c).

(Example 78)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-ol

100 mg of tert-butyl 3-(4-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 75(b) was dissolved in dichloromethane (10 mL), and then 1.0 M solution of boron tribromide in dichloromethane (2.9 mL, 10 equivalents) was added thereto at -78°C, followed by stirring at room temperature for 16 hours. The

formation of the product was confirmed by TLC, and then distilled water was added to stop the reaction. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 40 mg of the title compound by vacuum concentration of the filtrate.

(Example 79)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-ol

The title compound was obtained in an amount of 24 mg from 189 mg of tert-butyl 3-(4-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 76(b) by a similar method to Example 78.

(Example 80)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-ol

The title compound was obtained in an amount of 25 mg from 200 mg of tert-butyl 3-(4-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 77(b) by a similar method to Example 78.

(Example 81)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-cyclobutoxy-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(4-hydroxy-7-(thiazol-2-

yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

400 mg of tert-butyl 3-(4-methoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 75(b) was dissolved in N,N-dimethylformamide (4.0 mL), and then sodium tert-butoxide (608 mg, 7 equivalents) and 2-(dimethylamino)ethane-1-thiol hydrochloride (384 mg, 3 equivalents) were added thereto, followed by stirring using a microwave reactor (manufactured by Biotage) for 15 minutes at 160°C under an argon atmosphere. 1 M hydrochloric acid was added to the reaction mixture, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous sodium sulfate, followed by filtration, and thus obtaining 280 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane, hexane:ethyl acetate = 1:2).

(b) tert-Butyl 3-(4-cyclobutoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 11 mg from 20 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in

Example 81(a) by a similar method to Example 68(b) except that triphenylphosphine (74mg, 6.0 equivalents), diethyl azodicarboxylate(44μL, 6.0 equivalents), cyclobutanol (22μL, 6.0 equivalents) and toluene (0.5mL)- tetrahydrofuran (1.0mL) were used.

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-cyclobutoxy-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 8.9 mg from 11 mg of tert-butyl 3-(4-cyclobutoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 81(b) by a similar method to Example 1(c).

(Example 82)

2-((2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)acetonitrile

(a) tert-Butyl 3-(4-cyanomethoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 22 mg from 20 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 81(a) by a similar method to Example 70(a) except that bromoacetonitrile was used instead of 3-(iodomethyl)oxetane.

(b) 2-((2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)acetonitrile

The title compound was obtained in an amount of 17 mg from 22 mg of tert-butyl 3-(4-cyanomethoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 82(a) by a similar method to Example 1(c).

(Example 83)

1-((2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3-methoxypropan-2-ol

(a) tert-Butyl 3-(4-oxiran-2-ylmethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 17 mg from 20 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 81(a) by a similar method to Example 70(a) except that oxetan-3-yltrifluoromethanesulfonate was used instead of 3-(iodomethyl)oxetane and reacted at room temperature.

(b) tert-Butyl 3-(4-(2-hydroxy-3-methoxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

17 mg of tert-butyl 3-(4-oxiran-2-ylmethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in

Example 83(a) was dissolved in methanol(0.5mL) , then 4.1M solution of sodium methoxide(17 μL, 2 equivalents) in methanol was added thereto, followed by heat refluxing for 30 min under an argon atmosphere. Sodium hydrogen carbonate aqueous solution was added to the reaction mixture, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous sodium sulfate, followed by filtration, and thus obtaining 13 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate by preparative TLC (eluent, hexane:ethyl acetate = 1:2).

(c) 1-((2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3-methoxypropan-2-ol

The title compound was obtained in an amount of 10 mg from 13 mg of tert-butyl 3-(4-(2-hydroxy-3-methoxypropoxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 83(b) by a similar method to Example 1(c).

(Example 84)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydrofuran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(4-((tetrahydrofuran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-

diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 10 mg from 20 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 81(a) by a similar method to Example 70(a) except that tetrahydrofuran-3-yl trifluoromethanesulfonate was used instead of 3-(iodomethyl)oxetane and reacted at room temperature.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydrofuran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 5.5 mg from 10 mg of tert-butyl 3-(4-((tetrahydrofuran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 84(a) by a similar method to Example 1(c).

(Example 85)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4,7-di(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(((trifluoromethyl)sulfonyl)oxy) benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

20 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-

8-carboxylate obtained in Example 81(a) was dissolved in dichloromethane (0.47 mL), and then diisopropylethylamine (12 μL, 1.5 equivalents) and trifluoromethanesulfonic anhydride were sequentially added thereto, followed by stirring at -30°C for 30 minutes under an argon atmosphere. After that, the temperature was caused to rise to 0°C, followed by stirring for 1 hour. Saturated sodium hydrogen carbonate aqueous solution was added to the reaction mixture, followed by extraction using chloroform. Thereafter, the organic phase was dried over anhydrous sodium sulfate, followed by filtration, and thus obtaining 24 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate by preparative TLC (eluent, hexane:ethyl acetate = 1:1).

(b) tert-Butyl 3-(4,7-di(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

23 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(((trifluoromethyl)sulfonyl)oxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 85(a) was dissolved in toluene (0.14 mL), and then tetrahydrofuran solution (409 μL, 5 equivalents) of 0.5 M 2-thiazolylzinc bromide and [1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride·dichloromethane complex (6.7 mg, 0.2

equivalent) were added thereto, followed by stirring using a microwave reactor (manufactured by Biotage) for 20 minutes at 100°C under an argon atmosphere. Saturated sodium hydrogen carbonate aqueous solution was added to the reaction mixture, followed by Celite® filtration. After the filtrate was extracted using ethyl acetate, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 9.0 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate by preparative TLC (eluent, hexane:ethyl acetate = 1:1).

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4,7-di(thiazol-2-yl)benzo[d]oxazole

4.7 mg of the title compound was obtained from 9.0 mg of tert-butyl 3-(4,7-di(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 85(b), using a similar method to Example 1(c).

(Example 86)

Ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate

(a) Ethyl 7-bromo-2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of

145 mg from 100 mg of ethyl 7-bromo-2-methoxybenzo[d]oxazole-5-carboxylate obtained in Reference Example 15 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) Ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained as a crude product in an amount of 350 mg from 240 mg of ethyl 7-bromo-2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)benzo[d]oxazole-5-carboxylate obtained in Example 86(a) by a similar method to Example 2(b).

(c) Ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 105 mg from 350 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate obtained in Example 86(b) by a similar method to Example 1(c).

(Example 87)

Ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate

(a) Ethyl 7-bromo-2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)benzo[d]oxazole-5-

carboxylate

The title compound was obtained in an amount of 140 mg from 100 mg of ethyl 7-bromo-2-mercaptobenzo[d]oxazole-5-carboxylate obtained in Reference Example 15 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) Ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 26 mg from 140 mg of ethyl 7-bromo-2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)benzo[d]oxazole-5-carboxylate obtained in Example 87(a) by a similar method to Example 2(b).

(c) Ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 120 mg from 295 mg of ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate obtained in Example 87(b) by a similar method to Example 1(c).

(Example 88)

Ethyl 2-(3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)-7-

(thiazol-2-yl)benzo[d]oxazole-5-carboxylate

(a) tert-Butyl 7-(7-bromo-5-(ethoxycarbonyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 440 mg from 300 mg of ethyl 7-bromo-2-mercaptobenzo[d]oxazole-5-carboxylate obtained in Reference Example 15 by a similar method to Example 1(a) except that tert-butyl 3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 7-(5-(ethoxycarbonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 300 mg from 400 mg of tert-butyl 7-(7-bromo-5-(ethoxycarbonyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 88(a) by a similar method to Example 2(b).

(c) Ethyl 2-(3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 200 mg from 300 mg of tert-butyl 7-(5-(ethoxycarbonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate

obtained in Example 88(b) by a similar method to Example 1(c).

(Example 89)

Ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate

(a) Ethyl 7-bromo-2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 310 mg from 200 mg of ethyl 7-bromo-2-mercaptobenzo[d]oxazole-5-carboxylate obtained in Reference Example 15 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) Ethyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained as a crude product in an amount of 280 mg from 400 mg of ethyl 7-bromo-2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)benzo[d]oxazole-5-carboxylate obtained in Example 89(a) by a similar method to Example 2(b).

(c) Ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 130 mg from 360 mg of ethyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate obtained in Example 89(b) by a similar method to Example 1(c).

(Example 90)

Ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate

(a) Ethyl 2-(8-(tert-butoxycarbonyl) -3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 140 mg from 300 mg of ethyl 7-bromo-2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)benzo[d]oxazole-5-carboxylate obtained in Example 86(a) by a similar method to Example 15(a).

(b) Ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl) benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 90 mg from 140 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate obtained in Example 90(a) by a similar method to Example 1(c).

(Example 91)

Ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1H-

pyrazol-1-yl)benzo[d]oxazole-5-carboxylate

(a) Ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 160 mg from 300 mg of ethyl 7-bromo-2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)benzo[d]oxazole-5-carboxylate obtained in Example 87(a) by a similar method to Example 15(a).

(b) Ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 110 mg from 160 mg of ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate obtained in Example 91(a) by a similar method to Example 1(c).

(Example 92)

Ethyl 2-(3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate

(a) tert-Butyl 7-(5-(ethoxycarbonyl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 170 mg from 210 mg of tert-butyl 7-(7-bromo-5-(ethoxycarbonyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-

diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 88(a) by a similar method to Example 15(a).

(b) Ethyl 2-(3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 144 mg from 220 mg of tert-butyl 7-(5-(ethoxycarbonyl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 92(a) by a similar method to Example 1(c).

(Example 93)

Ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate

(a) Ethyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 160 mg from 300 mg of ethyl 7-bromo-2-(9-(tert-butoxycarbonyl)-3,9- diazabicyclo[3.3.1]nonan-3-yl)benzo[d]oxazole-5-carboxylate obtained in Example 89(a) by a similar method to Example 15(a).

(b) Ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 100 mg from 160 mg of ethyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-

(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate obtained in Example 93(a) by a similar method to Example 1(c).

(Example 94)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-N,N-dimethyl-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide

(a) 2-(8-(tert-Butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylic acid

250 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate obtained in Example 86(b) was dissolved in tetrahydrofuran : methanol :water = 3:6:1 (2.0 mL), and then 1M sodium hydroxide aqueous solution (1 mL, 2 equivalents)was added thereto, followed by stirring for 7 days at room temperature. 1M hydrochloric acid (1 mL) was added to the reaction mixture, followed by extraction using chloroform : methanol = 10:1. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 220 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (chloroform-chloroform:methanol = 10:1).

(b) tert-Butyl 3-(5-(dimethylcarbamoyl)-7-(thiazol-2-

yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

13 mg of 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylic acid obtained in Example 94(a) was dissolved in N,N-dimethylformamide (0.5mL), and then 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride n-Hydrate (content 82.2%, 16 mg, 2 equivalents) and 2M solution of dimethylamine (28 μL, 2 equivalents) in methanol were added, followed by stirring at room temperature for 19 hours. 10 mg of the title compound was obtained by vacuum concentration of the reaction mixture and purification by preparative TLC (eluent, chloroform:methanol = 10:1).

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-N,N-dimethyl-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide

The title compound was obtained in an amount of 7.4 mg from 10 mg of tert-butyl 3-(5-(dimethylcarbamoyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 94(b) by a similar method to Example 1(c).

(Example 95)

(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(morpholino)methanone

(a) tert-Butyl 3-(5-(morpholine-4-carbonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 28 mg from 24 mg of 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylic acid obtained in Example 94(a) by a similar method to Example 94(b) except that morpholine (9µL, 2 equivalents)was used instead of 2M dimethylamine solution in methanol.

(b) (2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(morpholino)methanone

The title compound was obtained in an amount of 20 mg from 28 mg of tert-butyl 3-(5-(morpholine-4-carbonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 95(a) by a similar method to Example 1(c).

(Example 96)

(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(piperidin-1-yl)methanone

(a) tert-Butyl 3-(5-(piperidine-1-carbonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 27 mg from 24 mg of 2-(8-(tert-butoxycarbonyl)-3,8-

diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylic acid obtained in Example 94(a) by a similar method to Example 94(b) except that piperidine (10μL, 2 equivalents)was used instead of 2M dimethylamine solution in methanol.

(b) (2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(piperidin-1-yl)methanone

The title compound was obtained in an amount of 18 mg from 28 mg of tert-butyl 3-(5-(piperidine-1-carbonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 96(a) by a similar method to Example 1(c).

(Example 97)

(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(azetidin-1-yl)methanone

(a) tert-Butyl 3-(5-(azetidine-1-carbonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 9.8 mg from 25 mg of 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylic acid obtained in Example 94(a) by a similar method to Example 94(b) except that azetidine hydrochloride (10μL, 2 equivalents) and diisopropylethylamine (19μL, 2

equivalents) were used instead of 2M dimethylamine solution in methanol.

(b) (2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(azetidin-1-yl)methanone

The title compound was obtained in an amount of 7.0 mg from 9.8 mg of tert-butyl 3-(5-(azetidine -1-carbonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 97(a) by a similar method to Example 1(c).

(Example 98)

N-benzyl-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide

(a) tert-Butyl 3-(5-(benzylcarbamoyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 39 mg from 25 mg of 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylic acid obtained in Example 94(a) by a similar method to Example 94(b) except that benzylamine (12μL, 2 equivalents) was used instead of 2M dimethylamine solution in methanol.

(b) N-benzyl-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide

The title compound was obtained in an amount of 24 mg from 39 mg of tert-butyl 3-(5-(benzylcarbamoyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 98(a) by a similar method to Example 1(c).

(Example 99)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide

(a) tert-Butyl 3-(5-carbamoyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 28 mg from 25 mg of 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylic acid obtained in Example 94(a) by a similar method to Example 94(b) except that 28% ammonia water (0.1mL, 30 equivalents) was used instead of 2M dimethylamine solution in methanol.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide

The title compound was obtained in an amount of 15 mg from 28 mg of tert-butyl 3-(5-carbamoyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 99(a) by a similar method to Example 1(c).

(Example 100)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide

(a) tert-Butyl 3-(5-(methylcarbamoyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 29 mg from 25 mg of 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylic acid obtained in Example 94(a) by a similar method to Example 94(b) except that 2M methylamine in tetrahydrofuran (55µL, 2 equivalents) was used instead of 2M dimethylamine solution in methanol.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide

The title compound was obtained in an amount of 19 mg from 29 mg of tert-butyl 3-(5-(methylcarbamoyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 100(a) by a similar method to Example 1(c).

(Example 101)

N-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-N-methylacetamide

(a) tert-Butyl 3-(5-(N-methylacetamide)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-

8-carboxylate

The title compound was obtained in an amount of 22 mg from 30 mg of tert-butyl 3-(5-acetamido-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 50(b) by a similar method to Example 70(a) except that methyl iodide was used instead of 3-(iodomethyl)oxetane and only N,N-dimethylformamide was used as the solvent.

(b) N-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-N-methylacetamide

The title compound was obtained in an amount of 13 mg from 22 mg of tert-butyl 3-(5-(N-methylacetamido)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 101(a) by a similar method to Example 1(c).

(Example 102)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

498 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate obtained in Example

86(b) was dissolved in toluene (10 mL), and then 1.0 M toluene solution (5.2 mL, 5 equivalents) of diisobutylaluminum hydride was added thereto at -78°C, followed by stirring for 30 minutes. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated aqueous solution of ammonium chloride was added thereto, followed by Celite® filtration. Thereafter, the organic phase extracted with ethyl acetate was washed by distilled water and dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining a crude product by vacuum concentration of the filtrate. The obtained crude product and Dess-Martin periodinane (864 mg, 2 equivalents) were dissolved in chloroform (10 mL), followed by stirring at 0°C for 90 minutes. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated sodium hydrogen carbonate aqueous solution and saturated aqueous solution of sodium thiosulfate were added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 372 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane, hexane:ethyl acetate =

6:4).

(b) tert-Butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

150 mg of tert-butyl 3-(5-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 102(a) was dissolved in tetrahydrofuran (3.4 mL), and then 0.92 M tetrahydrofuran solution (0.8 mL, 2 equivalents) of methylmagnesium bromide was added thereto at -78°C, followed by stirring at 0°C for 2 hours. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated aqueous solution of ammonium chloride was added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 146 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane, hexane:ethyl acetate = 3:7).

(c) tert-Butyl 3-(5-acetyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

146 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-

diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 102(b) and Dess-Martin periodinane (274 mg, 2 equivalents) were dissolved in chloroform (3.2 mL), followed by stirring at 0°C for 1 hour. The temperature was caused to rise to room temperature, followed by further stirring for 1 hour. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated sodium hydrogen carbonate aqueous solution and saturated aqueous solution of sodium thiosulfate were added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 109 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane, hexane:ethyl acetate = 5:5).

(d) tert-Butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

70 mg of tert-butyl 3-(5-acetyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 102(c), trifluoromethyltrimethylsilane (138 µL, 6 equivalents), and caesium carbonate (2.6 mg, 0.1 equivalent) were dissolved in tetrahydrofuran (3.2

mL), followed by stirring at 0°C for 2 hours. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated sodium hydrogen carbonate aqueous solution was added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining a crude product by vacuum concentration of the filtrate. The obtained crude product was dissolved in tetrahydrofuran (1.5 mL), and then 1.0 M tetrabutylammonium fluoride solution in tetrahydrofuran (308 µL, 2 equivalents) was added thereto, followed by stirring at 0°C for 1 hour. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated aqueous solution of ammonium chloride was added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 76 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane, hexane:ethyl acetate = 6:4).

(e) tert-Butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

41 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 102(d), methyl iodide (20 μL, 4 equivalents), and sodium hydride (15.9 mg, 4.4 equivalents) were dissolved in tetrahydrofuran (780 μL), followed by stirring at room temperature for 10 hours. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated aqueous solution of ammonium chloride was added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 29 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate by preparative TLC (eluent, hexane:ethyl acetate = 1:1).

(f) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole

18 mg of the title compound was obtained from 29 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 102(e), using a similar method to Example 1(c).

(Example 103)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(methoxy(methyl)carbamoyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

91 mg of ethyl 7-bromo-2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)benzo[d]oxazole-5-carboxylate obtained in Example 87(a) and N,O-dimethylhydroxylamine hydrochloride (59 mg, 3 equivalents) were dissolved in tetrahydrofuran (965 µL), and then 2.0 M solution of isopropylmagnesium chloride in tetrahydrofuran (580 µL, 6 equivalents) was added thereto at 0°C, followed by stirring for 30 min. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated aqueous solution of ammonium chloride was added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 82 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (hexane, hexane:ethyl acetate = 1:9).

(b) tert-Butyl 3-(5-acetyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

67 mg of tert-butyl 3-(5-(methoxy(methyl)carbamoyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 103(a) was dissolved in tetrahydrofuran (0.7 mL), and then 0.92 M solution of methylmagnesium bromide in tetrahydrofuran (1.5 mL, 10 equivalents) was added thereto at 0°C, followed by stirring for 30 min at room temperature. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:4), and then saturated aqueous solution of ammonium chloride was added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 61 mg of the title compound as a crude product by vacuum concentration of the residue.

(c) tert-Butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 70 mg from 61 mg of tert-butyl 3-(5-acetyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-

diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 103(b) by a similar method to Example 102(d) except that the purification by the Silica gel column chromatography was not carried out.

(d) tert-Butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro- 2-methoxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 17 mg from 35 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6- carboxylate obtained in Example 103(c) by a similar method to Example 102(e) except that the purification by the Silica gel column chromatography was not carried out.

(e) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 11 mg from 17 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 103(d) by a similar method to Example 1(c).

(Example 104)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-

yl)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol

(a) tert-Butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

44 mg of tert-butyl 3-(5-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 102(a), (difluoromethyl)trimethylsilane (54μL, 4 equivalents), and caesium fluoride (63 mg, 4 equivalents) were dissolved in N,N-dimethylformamide (1.0 mL), and stirred them for 20 hours at room temperature. Saturated aqueous sodium bicarbonate solution was added and organic phase was extracted by ethyl acetate. A filtrate was obtained by drying the extracted organic phase by anhydrous magnesium sulfate and filtering them. The title compound was obtained in an amount of 21 mg by silica gel column chromatography purification (amino silica, hexane-hexane: ethyl acetate = 1:4) of residue obtained by vacuum concentration of the filtrate.

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol

The title compound was obtained in an amount of 4.8 mg from 6.6 mg of tert-butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-

3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 104(a) by a similar method to Example 1(c).

(Example 105)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 9.0 mg from 10 mg of tert-butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 104(a) by a similar method to Example 102(a).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 6.9 mg from 9.0 mg of tert-butyl 3-(5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 105(a) by a similar method to Example 1(c).

(Example 106)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-ol

The title compound was obtained in an amount of

17 mg from 41 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 102(b) by a similar method to Example 1(c)

(Example 107)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-ol

(a) tert-Butyl 3-(5-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

150 mg of ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate obtained in Example 87(b) was dissolved in dichloromethane (3.8 mL), and then 1.0 M solution of diisobutylaluminum hydride in toluene (1.5 mL, 4 equivalents) was added thereto at -78°C, followed by stirring for 1 hour. Saturated aqueous solution of ammonium chloride was added thereto to stop the reaction. Thereafter, the organic phase extracted using ethyl acetate was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining a crude product of the title compound by vacuum concentration of the filtrate.

(b) tert-Butyl 3-(5-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

Curude tert-butyl 3-(5-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 107(a) and Dess-Martin Periodinane (322 mg, 2 equivalents) were dissolved in chloroform (3.8 mL), and stirred them for 1 hour at room temperature. After confirming a reaction product by TLC (eluent, hexane:ethyl acetate = 1:1), saturated aqueous sodium bicarbonate and saturated aqueous sodium thiosulfate were added and organic phase was extracted by ethyl acetate. A filtrate was obtained by drying the extracted organic phase by anhydrous magnesium sulfate and filtering them. The title compound was obtained in an amount of 108 mg by preparative TLC (hexane: ethyl acetate = 1:3) of residue obtained by vacuum concentration of the filtrate.

(c) tert-Butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 55 mg from 108 mg of tert-butyl 3-(5-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 107(b) by a similar method to Example 102(d).

(d) 1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-ol

The title compound was obtained in an amount of 21 mg from 28 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 107(c) by a similar method to Example 1(c).

(Example 108)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-one

The title compound was obtained in an amount of 9.0 mg from 17.2 mg of tert-butyl 3-(5-acetyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 102(c) by a similar method to Example 1(c).

(Example 109)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-one

The title compound was obtained in an amount of 7.6 mg from 46 mg of tert-butyl 3-(5-acetyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 103(b) by a similar method to Example 1(c).

(Example 110)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-

8-carboxylate

The title compound was obtained in an amount of 15 mg from 25 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 102(b) by a similar method to Example 102(e).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 10 mg from 15 mg of tert-butyl 3-(5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 110(a) by a similar method to Example 1(c).

(Example 111)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 25 mg from 28 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 107(c) by a similar method to Example 102(e).

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 21 mg from 25 mg of tert-butyl 3-(5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 111(a) by a similar method to Example 1(c).

(Example 112)

Ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate

(a) Ethyl 7-bromo-2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)benzo[d]oxazole-4-carboxylate

The title compound was obtained in an amount of 195 mg from 150 mg of ethyl 7-bromo-2-mercaptobenzo[d]oxazole-4-carboxylate obtained in Reference Example 16 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) Ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate

The title compound was obtained as a crude product in an amount of 250 mg from 195 mg of ethyl 7-bromo-2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)benzo[d]oxazole-4-carboxylate obtained in Example 112(a) by a similar method to Example 2(b) except that toluene was used

instead of 1,4-dioxane.

(c) Ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate

The title compound was obtained in an amount of 125 mg from 250 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate obtained in Example 112(b) by a similar method to Example 1(c).

(Example 113)

Ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate

(a) Ethyl 7-bromo-2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)benzo[d]oxazole-4-carboxylate

The title compound was obtained in an amount of 164 mg from 150 mg of ethyl 7-bromo-2-mercaptobenzo[d]oxazole-4-carboxylate obtained in Reference Example 16 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) Ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate

The title compound was obtained as a crude

product in an amount of 270 mg from 160 mg of ethyl 7-bromo-2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)benzo[d]oxazole-4-carboxylate obtained in Example 113(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) Ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate

The title compound was obtained in an amount of 98 mg from 270 mg of ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate obtained in Example 113(b) by a similar method to Example 1(c).

(Example 114)

Ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate

(a) Ethyl 7-bromo-2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)benzo[d]oxazole-4-carboxylate

The title compound was obtained in an amount of 186 mg from 150 mg of ethyl 7-bromo-2-mercaptobenzo[d]oxazole-4-carboxylate obtained in Reference example 16 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-

carboxylate.

(b) Ethyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate

The title compound was obtained as a crude product in an amount of 300 mg from 180 mg of ethyl 7-bromo-2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)benzo[d]oxazole-4-carboxylate obtained in Example 114(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) Ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate

The title compound was obtained in an amount of 100 mg from 300 mg of ethyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate obtained in Example 114(b) by a similar method to Example 1(c).

(Example 115)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-N,N-dimethyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide

(a) 2-(8-(tert-Butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylic acid

The title compound was obtained in an amount of 45 mg from 48 mg of ethyl 2-(8-(tert-butoxycarbonyl)-

3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate obtained in Example 112(b) by a similar method to Example 94(a).

(b) tert-Butyl 3-(4-(dimethylcarbamoyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 13 mg from 13 mg of 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylic acid obtained in Example 115(a) by a similar method to Example 94(b).

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-N,N-dimethyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide

The title compound was obtained in an amount of 10 mg from 13 mg of tert-butyl 3-(4-(dimethylcarbamoyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 115(b) by a similar method to Example 1(c).

(Example 116)

(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(morpholino)methanone

(a) tert-Butyl 3-(4-(morpholine-4-carbonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of

20 mg from 17 mg of 2-(8-tert-butoxycarbonyl-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-carboxylic acid obtained in Example 115(a) by a similar method to Example 94(b) except that morpholine (64μL, 2 equivalents) was used instead of 2M dimethylamine solution in methanol.

(b) (2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(morpholino)methanone

The title compound was obtained in an amount of 16 mg from 20 mg of tert-butyl 3-(4-(morpholine-4-carbonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 116(a) by a similar method to Example 1(c).

(Example 117)

(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(piperidin-1-yl)methanone

(a) tert-Butyl 3-(4-(piperidine-1-carbonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 18 mg from 15 mg of 2-(8-tert-butoxycarbonyl-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-carboxylic acid obtained in Example 115(a) by a similar method to Example 94(b) except that piperidine (6.6μL, 2 equivalents) was used

instead of 2M dimethylamine solution in methanol.

(b) (2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(piperidin-1-yl)methanone

The title compound was obtained in an amount of 14 mg from 18 mg of tert-butyl 3-(4-(piperidine-1-carbonyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 117(a) by a similar method to Example 1(c).

(Example 118)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol (optically active)

(a) tert-Butyl 3-(4-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 130 mg from 169 mg of ethyl 2-(8-tert-butoxycarbonyl-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-carboxylate obtained in Example 112(b) by a similar method to Example 102(a).

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (racemic)

38 mg of tert-butyl 3-(4-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-

8-carboxylate obtained in Example 118(a), trifluoromethyltrimethylsilane (51μL, 4 equivalents), and 1.0M tetrabutylammonium fluoride solution in tetrahydrofuran (17.2μL, 0.2 equivalent) were dissolved in tetrahydrofuran (860μL), and stirred them for 2 hours at 0°C. After confirming a reaction product by TLC (eluent, hexane:ethyl acetate = 1:1), 2M methanolic hydrochloric acid was added and stirred them for 30 min at room temperature. After stirring, saturated aqueous sodium bicarbonate solution was added and organic phase was extracted by ethyl acetate. A filtrate was obtained by drying the extracted organic phase by anhydrous magnesium sulfate and filtering them. The title compound was obtained in an amount of 21 mg by silica gel column chromatography purification (hexane-hexane: ethyl acetate = 1:1) of residue obtained by vacuum concentration of the filtrate.

(c) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active)

157 mg of racemic tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 118(b) was purified by a

preparative HPLC (Gilson, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol = 95:5-80:20, flow rate:15mL/min, detection:UV254nm) and the title compound was obtained in an amount of 72 mg by concentrating fractions with the shorter retention time peak. 96% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter: 0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol = 90:10, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:11.7min).

(d) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol (optically active)

The title compound was obtained in an amount of 49 mg from 72 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active) obtained in Example 118(b) by a similar method to Example 1(c). 95% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK ID (particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol:diethylamine = 80:20:0.1, flow rate:1mL/min, detection:UV254nm, temperature:25° C, retention

time:12.0min).

(Example 119)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol (optically active, enantiomer of Example 118)

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active, enantiomer of Example 118(c))

157 mg of racemic tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 118(b) was purified by a preparative HPLC (Gilson, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol = 95:5-80:20, flow rate:15mL/min, detection:UV254nm) and the title compound was obtained in an amount of 70 mg by concentrating fractions with the longer retention time peak. 98% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol = 90:10, flow rate:1mL/min, detection:UV254nm, temperature:25° C, retention time:15.5min).

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol (optically active, enantiomer of Example 118)

The title compound was obtained in an amount of 50 mg from 70 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active, enantiomer of Example 118) obtained in Example 119(a) by a similar method to Example 1(c). 98% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol:diethylamine = 80:20:0.1, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:13.8min).

(Example 120)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol (optically active)

(a) tert-Butyl 3-(4-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 323 mg from 440 mg of ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl) -7-(thiazol-2-yl)benzo[d]oxazol-4-carboxylate obtained

in Example 113(b) by a similar method to Example 102(a).

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (racemic)

100 mg of tert-butyl 3-(4-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 120(a), (trifluoromethyl)trimethylsilane (140μL, 4 equivalents), and caesium fluoride (3.6mg, 0.1 equivalent) were dissolved in tetrahydrofuran (2.3mL), and stirred them for 30min at 0°C. After confirming a reaction product by TLC (eluent, hexane:ethyl acetate = 1:1), 2M methanolic hydrochloric acid was added and stirred them for 2 hours at room temperature. After stirring, saturated aqueous sodium bicarbonate solution was added and organic phase was extracted by ethyl acetate. A filtrate was obtained by drying the extracted organic phase by anhydrous magnesium sulfate and filtering them. The title compound was obtained in an amount of 70 mg by silica gel column chromatography purification (hexane-hexane: ethyl acetate = 7:3) of residue obtained by vacuum concentration of the filtrate.

(c) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-

diazabicyclo[3.1.1]heptane-6-carboxylate (optically active)

145 mg of racemic tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 120(b) was purified by a preparative HPLC (Gilson, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol = 95:5-80:20, flow rate:15mL/min, detection:UV254nm) and the title compound was obtained in an amount of 63 mg by concentrating fractions with the shorter retention time peak. 98% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol = 90:10, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:23.1min).

(d) 1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol (optically active)

The title compound was obtained in an amount of 28 mg from 40 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active) obtained in Example 120(c) by a

similar method to Example 1(c). 99% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IC (particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol:diethylamine = 70:30:0.1, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:19.0min).

(Example 121)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol (optically active, enantiomer of Example 120)

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active, enantiomer of Example 120(c))

145 mg of racemic tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 120(b) was purified by a preparative HPLC (Gilson, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol = 95:5-80:20, flow rate:15mL/min, detection:UV254nm) and the title compound was obtained in an amount of 64 mg by concentrating fractions with the longer retention time peak. 98% ee. Analysis conditions: HPLC (HITACHI,

column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol = 90:10, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:28.6min).

(b) 1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol (optically active, enantiomer of Example 120)

The title compound was obtained in an amount of 27 mg from 40 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active, enantiomer of Example 120(c)) obtained in Example 121(a) by a similar method to Example 1(c). 97% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IC (particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol:diethylamine = 70:30:0.1, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:23.8min).

(Example 122)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole (optically active)

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active)

The title compound was obtained in an amount of 16 mg from 19 mg of optically active tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 120(c) by a similar method to Example 102(e).

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole (optically active)

The title compound was obtained in an amount of 12 mg from 16 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active) obtained in Example 122(a) by a similar method to Example 1(c). 99% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK ID (particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol:diethylamine = 70:30:0.1, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:9.6min).

(Example 123)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole (optically active, enantiomer of Example 122)

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active, enantiomer of Example 122(a))

The title compound was obtained in an amount of 17 mg from 19 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active, enantiomer of Example 120(c)) obtained in Example 121(a) by a similar method to Example 102(e).

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole (optically active, enantiomer of Example 122)

The title compound was obtained in an amount of 13 mg from 17 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active, enantiomer of Example 122(a)) obtained in Example 123(a) by a similar method to Example 1(c). 98% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK ID (particle

diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol:diethylamine = 70:30:0.1, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:11.6min).

(Example 124)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol

41 mg of tert-butyl 3-(4-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 118(a) was dissolved in tetrahydrofuran (924μL). 0.92M Methylmagnesium bromide solution in tetrahydrofuran (0.2mL, 2 equivalents) was added at -78°C and stirred for 2 hours. After confirming a reaction product by TLC (eluent, hexane:ethyl acetate = 1:1), saturated aqueous sodium bicarbonate solution was added and organic phase was extracted by ethyl acetate. A crude product was obtained by drying the extracted organic phase by anhydrous magnesium sulfate and filtering them. The title compound was obtained in an amount of 20 mg from the crude product by a similar method to Example 1(c).

(Example 125)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethan-1-ol

(a) tert-Butyl 3-(4-(2,2-difluoro-1-hyroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude probuct from 10 mg of tert-butyl 3-(4-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 120(a) by a similar method to Example 104(a) except that tetrahydrofuran was used instead of N,N-dimethylformamide and potassium tert-butoxide was used instead of caesium fluoride.

(b) 1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethan-1-ol

The title compound was obtained in an amount of 1.4 mg from tert-butyl 3-(4-(2,2-difluoro-1-hyroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 125(a) by a similar method to Example 1(c).

(Example 126)

2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol

(a) tert-Butyl 3-(4-(2,2-difluoroacetyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

48 mg of tert-butyl 3-(4-(2,2 -difluoro-1-

hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 125(a) and Dess-Martin Periodinane (127mg, 3 equivalents) were dissolved in dichloromethane (1.0mL), and stirred them for 1 hour at 0°C. After confirming a reaction product by TLC (eluent, hexane:ethyl acetate = 1:1), saturated aqueous sodium bicarbonate solution and saturated aqueous sodium thiosulfate were added and organic phase was extracted by ethyl acetate. A filtrate was obtained by drying the extracted organic phase by anhydrous magnesium sulfate and filtering them. The title compound was obtained in an amount of 32 mg by silica gel column chromatography purification (hexane-hexane: ethyl acetate = 4:6) of residue obtained by vacuum concentration of the filtrate.

(b) tert-Butyl 3-(4-(1,1 -difluoro-2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

32 mg of tert-butyl 3-(4-(2,2 -difluoroacetyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 126(a) was dissolved in tetrahydrofuran (700μL). 0.98M Methylmagnesium bromide solution in tetrahydrofuran (0.68 mL, 10 equivalents) was added at -78°C and stirred them for 1 hour at room temperature.

After confirming a reaction product by TLC, saturated ammonium chloride aqueous solution was added and organic phase was extracted by ethyl acetate. A filtrate was obtained by drying the extracted organic phase by anhydrous magnesium sulfate and filtering them. The title compound was obtained in an amount of 22 mg by preparative TLC(hexane-hexane: ethyl acetate = 1:1) of residue obtained by vacuum concentration of the filtrate.

(c) 2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol

The title compound was obtained in an amount of 22 mg from 25 mg of tert-butyl 3-(4-(1,1 -difluoro-2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 126(b) by a similar method to Example 1(c).

(Example 127)

1-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethoxy)-2-methylpropan-2-ol

(a) tert-Butyl 3-(4-(1-(2-(tert-butoxy)-2-oxoethoxy)-2,2-difluoroethyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

9.6 mg of tert-butyl 3-(4-(2,2 -difluoro-1-

hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 125(a), tetrabutylammonium chloride (0.6 mg, 0.1 equivalent), 35% sodium hydroxide aquious solution (75μL), and tert-butyl bromoacetate (4.4μL, 1.5 equivalents) were dissolved in dichloromethane (70μL), and stirred them for 15 hours at room temperature. After confirming a reaction product by TLC, saturated ammonium chloride aqueous solution was added and organic phase was extracted by ethyl acetate. A filtrate was obtained by drying the extracted organic phase by anhydrous magnesium sulfate and filtering them. The title compound was obtained in an amount of 11 mg by preparative TLC (eluent, hexane: ethyl acetate = 1:1) of residue obtained by vacuum concentration of the filtrate.

(b) tert-Butyl 3-(4-(2,2-difluoro-1-(2-hydroxy-2-methylpropoxy)ethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

10 mg of tert-butyl 3-(4-(1-(2-(tert-butoxy)-2-oxoethoxy)-2,2-difluoroethyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 127(a) was dissolved in tetrahydrofuran (170μL). 0.98M Methylmagnesium bromide solution in tetrahydrofuran (17.3μL, 10 equivalents) was added at

0°C and stirred them for 2 hours at room temperature. After confirming a reaction product by TLC, saturated ammonium chloride aqueous solution was added and organic phase was extracted by ethyl acetate. A filtrate was obtained by drying the extracted organic phase by anhydrous magnesium sulfate and filtering them. The title compound was obtained in an amount of 8 mg by preparative TLC(eluent, hexane: ethyl acetate = 1:2) of residue obtained by vacuum concentration of the filtrate.

(c) 1-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethoxy)-2-methylpropan-2-ol

The title compound was obtained in an amount of 5 mg from 8 mg of tert-butyl 3-(4-(2,2-difluoro-1-(2-hydroxy-2-methylpropoxy)ethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 127(b) by a similar method to Example 1(c).

(Example 128)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethan-1-ol

(a) tert- Butyl 3-(4-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of

15 mg from 44 mg of tert-butyl 3-(4-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 118(a) by a similar method to Example 104(a) except that 0.2 equivalent of caesium fluoride was used.

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethan-1-ol

The title compound was obtained in an amount of 3.4 mg from 7 mg of tert- butyl 3-(4-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 128(a) by a similar method to Example 1(c).

(Example 129)

2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol

(a) tert-Butyl 3-(4-(2,2-difluoroacetyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 59 mg from 49 mg tert-butyl 3-(4-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 128(a) by a similar method to Example 126(a).

(b) tert-Butyl 3-(4-(1,1-difluoro-2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 44 mg from 58 mg of tert-butyl 3-(4-(2,2-difluoroacetyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 129(a) by a similar method to Example 126(b).

(c) 2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol

The title compound was obtained in an amount of 29 mg from 43 mg of tert-butyl 3-(4-(1,1-difluoro-2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 129(b) by a similar method to Example 1(c).

(Example 130)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert- Butyl 3-(4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude

product from 7.5 mg of tert-butyl 3-(4-(2,2-difluoro-1-hyroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 125(a) by a similar method to Example 102(e).

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 2.9 mg from the crude product of tert-butyl 3-(4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 130(a) by a similar method to Example 1(c).

(Example 131)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 5.2 mg from 7 mg of tert-butyl 3-(4-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 128(a) by a similar method to Example 102(e).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 3.9 mg from tert- butyl 3-(4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 131(a) by a similar method to Example 1(c).

(Example 132)

(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol

(a) tert-Butyl 3-(7-bromo-4-(hydroxymethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 100 mg from 100mg of (7-bromo-2-mercaptobenzo[d]oxazol-4-yl)methanol obtained in Reference Example 17 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(4-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 60 mg from 120 mg of tert-butyl 3-(7-bromo-4-(hydroxymethyl)benzo[d]oxazol-2-

yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 132(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) (2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol

The title compound was obtained in an amount of 30 mg from 78 mg of tert-butyl 3-(4-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 132(b) by a similar method to Example 1(c).

(Example 133)

(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol

(a) tert-Butyl 3-(7-bromo-4-(hydroxymethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 50 mg from 50 mg of (7-bromo-2-mercaptobenzo[d]oxazol-4-yl)methanol obtained in Reference Example 17 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-

carboxylate.

(b) tert-Butyl 3-(4-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 60 mg from 90 mg of tert-butyl 3-(7-bromo-4-(hydroxymethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 133(a) by a similar method to Example 2(b) except that tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) (2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol

The title compound was obtained in an amount of 20 mg from 60 mg of tert-butyl 3-(4-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 133(b) by a similar method to Example 1(c).

(Example 134)

(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol

(a) tert-Butyl 3-(7-bromo-4-(hydroxymethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of

80 mg from 80 mg of (7-bromo-2-mercaptobenzo[d]oxazol-4-yl)methanol obtained in Reference Example 17 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(4-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 100 mg from 110 mg of tert-butyl 3-(7-bromo-4-(hydroxymethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 134(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) (2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol

The title compound was obtained in an amount of 45 mg from 100 mg of tert-butyl 3-(4-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 134(b) by a similar method to Example 1(c).

(Example 135)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol

(a) tert-Butyl 3-(7-bromo-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 504 mg from 400 mg of 1-(7-Bromo-2-mercaptobenzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol obtained in Reference Example 18 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 144 mg from 300 mg of tert-butyl 3-(7-bromo-5-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 135(a) by a similar method to Example 1(b).

(c) 1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol

The title compound was obtained in an amount of 50 mg from 190 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-

(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 135(b) by a similar method to Example 1(c).

(Example 136)

1-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol

(a) tert-Butyl 3-(7-bromo-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 608 mg from 400 mg of 1-(7-bromo-2-mercaptobenzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol obtained in Reference Example 18 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 244 mg from 300 mg of tert-butyl 3-(7-bromo-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 136(a) by a similar method to Example 1(b).

(c) 1-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol

The title compound was obtained in an amount of 60 mg from 130 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 136(b) by a similar method to Example 1(c).

(Example 137)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol (racemic)

(a) tert-Butyl 3-(7-bromo-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 359 mg from 300 mg of 1-(7-Bromo-2-mercaptobenzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol obtained in Reference Example 18 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (racemic)

The title compound was obtained in an amount of 329 mg from 358 mg of tert-butyl 3-(7-bromo-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-

diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(a) by a similar method to Example 2(b).

(c) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol (racemic)

The title compound was obtained in an amount of 220 mg from 329 mg of racemic tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(b) by a similar method to Example 1(c).

(Example 138)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol (optically active)

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active)

30 mg of racemic tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(b) was purified by a preparative HPLC (Gilson, column: DAICEL CHIRALPAK IC (particle diameter:5μm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol = 90:10

to 80:20, flow rate:15mL/min, detection:UV254nm) and the title compound was obtained in an amount of 14 mg by concentrating fractions with the shorter retention time peak. 98% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IC (particle diameter:5μm, column diameter:0.46 cm, column length:25cm), eluent, hexane:isopropyl alcohol = 90:10, flow rate:1 mL/min, detection:UV254 nm, temperature:25°C, retention time:18.5 min).

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol (optically active)

The title compound was obtained in an amount of 8.1 mg from 14 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active) obtained in Example 138(a) by a similar method to Example 1(c).

(Example 139)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol (optically active, enantiomer of Example 138)

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active, enantiomer of Example 138(a))

30 mg of racemic tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(b) was purified by a preparative HPLC (Gilson, column: DAICEL CHIRALPAK IC (particle diameter:5μm, column diameter:2 cm, column length:25cm), eluent, hexane:isopropyl alcohol = 90:10 to 80:20, flow rate:15mL/min, detection:UV254 nm) and the title compound was obtained in an amount of 13 mg by concentrating fractions with the longer retention time peak. 99.7% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IC (particle diameter:5μm, column diameter:0.46 cm, column length:25 cm), eluent, hexane:isopropyl alcohol = 90:10, flow rate:1 mL/min, detection:UV254 nm, temperature:25°C, retention time:20.0 min).

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol (optically active, enantiomer of Example 138)

The title compound was obtained in an amount of 7.8 mg from 13 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active) obtained in Example 139(a) by a similar method to Example 1(c).

(Example 140)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol

(a) tert-Butyl 3-(7-(1H-pyrazol-1-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 18 mg from 100 mg of tert-butyl 3-(7-bromo-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(a) by a similar method to Example 5(a).

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol

The title compound was obtained in an amount of 12 mg from 18 mg of tert-butyl 3-(7-(1H-pyrazol-1-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 140(a) by a similar method to Example 1(c).

(Example 141)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethyl acetate

(a) tert-Butyl 3-(5-(1-acetoxy-2,2,2-trifluoroethyl-7-bromobenzo[d]oxazol-2-yl)-3,8-

diazabicyclo[3.2.1]octane-8-carboxylate

165 mg of tert-butyl 3-(7-bromo-5-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(a) was dissolved in dichloromethane (20mL). 4-dimethylaminopyridine (8mg, 0.2 equivalent), triethylamine (0.1mL, 3 equivalents), and acetyl chloride (0.1mL, 4 equivalents) were added at 0°C and stirred for 1 hour at room temperature. After confirming a reaction product by TLC, saturated aqueous sodium bicarbonate solution was added at 0°C to stop the reaction and organic phase was extracted by dichloromethane. A filtrate was obtained by drying the extracted organic phase by anhydrous magnesium sulfate and filtering them. The title compound was obtained as a crude product in an amount of 160 mg from the crude residue obtained by vacuum concentration of the filtrate.

(b) tert-Butyl 3-(5-(1-acetoxy-2,2,2-trifluoroethyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 80 mg from 160 mg of tert-butyl 3-(5-(1-acetoxy-2,2,2-trifluoroethyl-7-bromobenzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 141(a) by a similar method to Example 2(b).

(c) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethyl acetate

The title compound was obtained in an amount of 50 mg from 70 mg of tert-butyl 3-(5-(1-acetoxy-2,2,2-trifluoroethyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 141(b) by a similar method to Example 1(c).

(Example 142)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole (optically active)

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (racemic)

The title compound was obtained in an amount of 46 mg from 81 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(b) by a similar method to Example 102(e).

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active)

194 mg of racemic tert-butyl 3-(7-(thiazol-2-

yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 142(a) was purified by a preparative HPLC (Gilson, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol = 95:5-80:20, flow rate:15mL/min, detection:UV254nm) and the title compound was obtained in an amount of 79 mg by concentrating fractions with the shorter retention time peak. 98% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol = 90:10, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:7.8min).

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole (optically active)

The title compound was obtained in an amount of 64 mg from 79 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active) obtained in Example 142(b) by a similar method to Example 1(c). 98% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK ID (particle diameter:5μm, column diameter:0.46cm, column

length:25cm), eluent, hexane:isopropyl alcohol: dimethylamine = 70:30:0.1, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:13min).

(Example 143)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole (optically active, enantiomer of Example 142)

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active, enantiomer of Example 142(b))

194 mg of racemic tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 142(a) was purified by a preparative HPLC (Gilson, column: DAICEL CHIRALPAK IA (particle diameter:5µm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol = 95:5-80:20, flow rate:15mL/min, detection:UV254nm) and the title compound was obtained in an amount of 80 mg by concentrating fractions with the longer retention time peak. 99.5% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IA (particle diameter:5µm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol = 90:10, flow rate:1mL/min,

detection:UV254nm, temperature:25°C, retention time:8.9min).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole (optically active, enantiomer of Example 142)

The title compound was obtained in an amount of 66 mg from 80 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active) obtained in Example 143(a) by a similar method to Example 1(c). 99.4% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK ID (particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol: dimethylamine = 70:30:0.1, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:16min).

(Example 144)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 51 mg from 50 mg of tert-butyl

3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 135(b) by a similar method to Example 102(e) except that the product was not purified by preparative TLC.

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole

The title compound was obtained in an amount of 38 mg from 51 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 144(a) by a similar method to Example 1(c).

(Example 145)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained as a crude product in an amount of 51 mg from 50 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 136(b) by a similar method to Example 102(e)

except that the product was not purified by preparative TLC.

(b) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole

The title compound was obtained in an amount of 30 mg from 51 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 145(a) by a similar method to Example 1(c).

(Example 146)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 23 mg from 41 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(b) by a similar method to Example 102(e) except that 2,2,2-trifluoroethyl trifluoromethanesulfonate was used instead of methyl iodide.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole

The title compound was obtained in an amount of 11 mg from 23 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 146(a) by a similar method to Example 1(c).

(Example 147)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 16 mg from 36 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(b) by a similar method to Example 102(e) except that 2-bromoethyl methyl ether was used instead of methyl iodide.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazole

The title compound was obtained in an amount of 11 mg from 16 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 147(a) by a similar method to Example 1(c).

(Example 148)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(1-ethoxy-2,2,2-trifluoroethyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 19 mg from 20 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(b) by a similar method to Example 102(e) except that ethyl iodide was used instead of methyl iodide.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 12 mg from 30 mg of tert-butyl 3-(5-(1-ethoxy-2,2,2-trifluoroethyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained

in Example 148(a) by a similar method to Example 1(c).

(Example 149)

2-(1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)ethan-1-ol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

60 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(b), (2-bromorthoxy)-tert-butyldimethylsilane (930μL, 36 equivalents), and sodium hydride (57.0 mg, 19.8 equivalents) were dissolved in tetrahydrofuran (1.2mL), and stirred for 10 hours at room temperature. After confirming a reaction product by TLC (eluent, hexane:ethyl acetate = 1:1), saturated ammonium chloride aqueous solution was added and organic phase was extracted by ethyl acetate. A filtrate was obtained by drying the extracted organic phase by anhydrous magnesium sulfate and filtering them. The title compound was obtained as a crude product in an amount of 116 mg from the residue obtained by vacuum concentration of the filtrate.

(b)

2-(1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)ethan-1-ol

The title compound was obtained in an amount of 14 mg from 116 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 149(a) by a similar method to Example 1(c).

(Example 150)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(1-ethoxy-2,2,2-trifluoroethyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 35 mg from 40 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 135(b) by a similar method to Example 102(e) except that ethyl iodide was used instead of methyl iodide.

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of

16 mg from 35 mg of tert-butyl 3-(5-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 150(a) by a similar method to Example 1(c).

(Example 151)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 23 mg from 50 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 135(b) by a similar method to Example 102(e) except that 2,2,2-trifluoroethyl trifluoromethanesulfonate was used instead of methyl iodide.

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole

The title compound was obtained in an amount of 7.5 mg from 23 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-

trifluoroethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 151(a) by a similar method to Example 1(c).

(Example 152)

2-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)acetonitrile

(a) tert-Butyl 3-(5-(1-(cyanomethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 42 mg from 60 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 135(b) by a similar method to Example 102(e) except that bromoacetonitrile was used instead of methyl iodide.

(b) 2-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)acetonitrile

The title compound was obtained in an amount of 9.3 mg from 21 mg of tert-butyl 3-(5-(1-cyanomethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 152(a) by a similar method to Example 1(c).

(Example 153)

2-(1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)acetonitrile

(a) tert-Butyl 3-(5-(1-cyanomethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 46 mg from 61 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(b) by a similar method to Example 102(e) except that bromoacetonitrile was used instead of methyl iodide.

(b) 2-(1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)acetonitrile

The title compound was obtained in an amount of 13 mg from 23 mg of tert-butyl 3-(5-(1-cyanomethoxy)-(2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 153(a) by a similar method to Example 1(c).

(Example 154)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-

methoxyethoxy)ethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 30 mg from 40 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 135(b) by a similar method to Example 102(e) except that 2-bromoethyl methyl ether was used instead of methyl iodide.

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazole

The title compound was obtained in an amount of 18 mg from 30 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 154(a) by a similar method to Example 1(c).

(Example 155)

1-(1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)propan-2-ol

(a) tert-Butyl 3-(5-(1-(cyanomethoxy)-2,2,2-

trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 230 mg from 184 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(b) by a similar method to Example 102(e) except that bromoacetonitrile was used instead of methyl iodide.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-oxopropoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

230 mg of tert-butyl 3-(5-(1-(cyanomethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 155(a) was dissolved in diethyl ether (2.1mL), and then 0.92 M solution of methylmagnesium bromide in tetrahydrofuran (2.9 mL, 6.5 equivalents) was added thereto at 0°C, followed by stirring at 0°C for 5 hours. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then 1M hydrochloric acid was added thereto, followed by extraction using ethyl acetate. Thereafter, extracted organic phase was separated by using saturated aqueous sodium bicarbonate solution and the organic phase was dried

over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 68 mg of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (eluent, hexane:ethyl acetate = 1:1).

(c) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-hydroxypropoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

27 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-oxopropoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 155(b) and sodium borohydride (3.6mg, 2 equivalents) were dissolved in ethanol (480μL) and stirred at 0°C for 2 hours. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated ammonium chloride aqueous solution was added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining the title compound as a crude product by vacuum concentration of the filtrate.

(d) 1-(1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)propan-2-ol

The title compound was obtained in an amount of 15 mg from tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-hydroxypropoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 155(c) by a similar method to Example 1(c).

(Example 156)

1-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1,1-dihydroxyethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

13 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 136(b) and Dess-Martin Periodinane (42mg, 4 equivalents) were dissolved in chloroform (250μL), followed by stirring at room temperature for 1 hour. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated aqueous sodium bicarbonate and saturated aqueous sodium thiosulfate were added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 13 mg of the title compound as a crude

product by vacuum concentration of the filtrate.

(b) 1-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol

The title compound was obtained in an amount of 4.7 mg from 13 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1,1-dihydroxyethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 156(a) by a similar method to Example 1(c).

(Example 157)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1,1-dihydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 110 mg from 100 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 137(b) by a similar method to Example 156(a).

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol

The title compound was obtained in an amount of

3.7 mg from 30 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1,1-dihydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 157(a) by a similar method to Example 1(c).

(Example 158)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1,1-dihydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 89 mg from 84 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro -1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 135(b) by a similar method to Example 156(a).

(b) 1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol

The title compound was obtained in an amount of 16 mg from 30 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1,1-dihydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 158(a) by a similar method to

Example 1(c).

(Example 159)

2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

53 mg of the crude product of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1,1-dihydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 157(a) was dissolved in tetrahydrofuran (3.4 mL), then 0.6M solution of Lanthanum(III) chloride bis-lithium chloride complex in tetrahydrofuran (0.59 mL, 3 equivalents) and 0.92M solution of methylmagnesium bromide in tetrahydrofuran (0.32 mL, 3 equivalents) were added thereto at 0°C, followed by stirring at 0°C for 3 hours. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated ammonium chloride aqueous solution was added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 38 mg of the title compound by purification of the

residue by preparative TLC (eluent, hexane:ethyl acetate = 1:1).

(b) 2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol

The title compound was obtained in an amount of 28 mg from 38 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 159(a) by a similar method to Example 1(c).

(Example 160)

2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 54 mg from 59 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1,1-dihydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 158(a) by a similar method to Example 159(a).

(b) 2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol

The title compound was obtained in an amount of 5 mg from 53 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 160 (a) by a similar method to Example 1(c).

(Example 161)

2-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 56 mg from 72 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1,1-dihydroxyethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 156(a) by a similar method to Example 159(a).

(b) 2-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol

The title compound was obtained in an amount of 19 mg from 26 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 161 (a) by a similar method to

Example 1(c).

(Example 162)

2-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 19 mg from 30 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 161(a) by a similar method to Example 102(e).

(b) 2-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 16 mg from 19 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 162 (a) by a similar method to Example 1(c).

(Example 163)

Ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-

carboxylate

(a) Ethyl 7-bromo-2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 200 mg from 150mg of ethyl 7-bromo-2-mercapto-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate obtained in Reference Example 19 and tert-butyl-3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) Ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate

The title compound was obtained as a crude product in an amount of 250 mg from 200 mg of ethyl 7-bromo-2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate obtained in Example 163(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) Ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-

carboxylate

The title compound was obtained in an amount of 150 mg from 250 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate obtained in Example 163(b) by a similar method to Example 1(c).

(Example 164)

Ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate

(a) Ethyl 7-bromo-2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 200 mg from 150 mg of ethyl 7-bromo-2-mercapto-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate obtained in Reference Example 19 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) Ethyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate

The title compound was obtained as a crude

product in an amount of 350 mg from 200 mg of ethyl 7-bromo-2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate obtained in Example 164(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane.

(c) Ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 150 mg from 350 mg of ethyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate obtained in Example 164(b) by a similar method to Example 1(c).

(Example 165)

Ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate

(a) Ethyl 7-bromo-2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 200 mg from 150 mg of ethyl 7-bromo-2-mercapto-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate

obtained in Reference Example 19 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) Ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 250 mg from 200 mg of ethyl 7-bromo-2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate obtained in Example 165(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) Ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 70 mg from 200 mg of ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate obtained in Example 165(b) by a similar method to

Example 1(c).

(Example 166)

2-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)propan-2-ol

(a) tert-Butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 6.1 mg from 26 mg of ethyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate obtained in Example 164(b) by a similar method to Example 159(a) except that 4 equivalents of 0.6M solution of Lanthanum(III) chloride bis-lithium chloride complex solution in tetrahydrofuran and 8 equivalents of 0.92M solution of methylmagnesium bromide in tetrahydrofuran were used.

(b) 2-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)propan-2-ol

The title compound was obtained in an amount of 3.7 mg from 6.1 mg of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 166(a) by a similar method to Example 1(c).

(Example 167)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(methoxymethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(hydroxymethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

16 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate obtained in Example 163(b) was dissolved in toluene (290µL), then 1.0M solution of diisobutylaluminium hydride complex in toluene (123 µL, 4.2 equivalents) was added thereto at -78°C, followed by stirring for 2 hours. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and the reaction mixture was subjected to Celite® filtration. Thereafter, the organic phase extracted by ethyl acetate was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 13 mg of the title compound by purification of the residue by preparative TLC (eluent, hexane:ethyl acetate = 1:1).

(b) tert-Butyl 3-(5-(methoxymethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 23 mg from 35 mg of tert-butyl 3-(5-(hydroxymethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 167(a) by a similar method to Example 102(e).

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(methoxymethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of 18 mg from 23 mg of tert-butyl 3-(5-(methoxymethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 167(b) by a similar method to Example 1(c).

(Example 168)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(morpholinomethyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 141 mg from 267 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate obtained in Example 86(b) by a similar method to Example

167(a).

(b) tert-Butyl 3-(5-(morpholinomethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

20 mg of tert-butyl 3-(5-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 168(a) was dissolved in dichloromethane (0.5mL), then diisopropylethylamine (23.6 μL, 3 equivalents) and methanesulfonyl chloride (10.5 μL, 3 equivalents) were added thereto, followed by stirring at room temperature for 1 hour. Thereafter, the reacted solution was concentrated and dissolved in N,N-dimethylformamide (0.5mL), and then morpholine (19.7 μL, 5 equivalents) was added thereto, followed by stirring at room temperature for 16 hours, and saturated aqueous sodium bicarbonate was added. Organic phase extracted by ethyl acetate was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 23 mg of the title compound by purification of the residue by preparative TLC (eluent, chloroform:methanol = 10:1).

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(morpholinomethyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of

16 mg from 23 mg of tert-butyl 3-(5-(morpholinomethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 168(b) by a similar method to Example 1(c).

(Example 169)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-N,N-dimethylmethanamine

(a) tert-Butyl 3-(5-(dimethylamino)methyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 10 mg from 20 mg of tert-butyl 3-(5-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 168(a) by a similar method to Example 168(b) except that 2M dimethylamine solution (0.46 mL, 20 equivalents) in methanol was used instead of morpholine.

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-N,N-dimethylmethanamine

The title compound was obtained in an amount of 7.5 mg from 10 mg of tert-butyl 3-(5-(dimethylamino)methyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

obtained in Example 169(a) by a similar method to Example 1(c).

(Example 170)

(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)methanol

30 mg of ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate obtained in Example 163(c) was dissolved in tetrahydrofuran (330µL), then lithium aluminium hydride (10 mg, 4 equivalents) was added thereto at room temperature, followed by stirring for 10 min. The formation of the product was confirmed by TLC (eluent, chloroform:methanol:ammonia water = 3:1:0.1), sodium sulfate 10-hydrate, hexane, Celite® and magnesium sulfate were added, and the mixture was subjected to Celite® filtration. After vacuum concentration of the filtrate, and thus obtaining 19 mg of the title compound by purification of the residue by preparative TLC (eluent, chloroform:methanol:ammonia water = 3:1:0.1).

(Example 171)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(5-formyl-7-(thiazol-2-yl)-4-

(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 172 mg from 200 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate obtained in Example 163(b) by a similar method to Example 102(a).

(b) tert-Butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 165 mg from 215 mg of tert-butyl 3-(5-formyl-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 171(a) by a similar method to Example 102(b).

(c) tert-Butyl 3-(5-acethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 89 mg from 102 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 171(b) by a similar method to Example 102(c).

(d) tert-Butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

89 mg of tert-butyl 3-(5-acethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 171(c) was dissolved in tetrahydrofuran (1.1mL), then 0.6M solution of Lanthanum(III) chloride bis-lithium chloride complex in tetrahydrofuran (2.7 mL, 8 equivalents) and 0.92M solution of methylmagnesium bromide in tetrahydrofuran (1.5 mL, 8 equivalents) was added thereto at -78°C, followed by stirring at -78°C for 30 min. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated ammonium chloride aqueous solution were added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 91 mg of the title compound by purification of the residue by preparative TLC (eluent, hexane:ethyl acetate = 1:1).

(e) tert-Butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 16 mg from 15 mg of the crude product of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 171(d) by a similar method to Example 102(e) except that 25 equivalents of methyl iodide and 20 equivalents of sodium hydride were used.

(f) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of 10 mg from 16 mg of tert-butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 171(e) by a similar method to Example 1(c).

(Example 172)

2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)propan-2-ol

(a) tert-Butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 41 mg from 52 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-

yl)benzo[d]oxazole-5-carboxylate obtained in Example 86(b) by a similar method to Example 171(d).

(b) 2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)propan-2-ol

The title compound was obtained in an amount of 8.9 mg from 11 mg of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 172(a) by a similar method to Example 1(c).

(Example 173)

2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)propan-2-ol

(a) tert-Butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 43 mg from 50 mg of ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate obtained in Example 87(b) by a similar method to Example 171(d).

(b) 2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)propan-2-ol

The title compound was obtained in an amount of 26 mg from 43 mg of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in

Example 173(a) by a similar method to Example 1(c).

(Example 174)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 29 mg from 29 mg of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 173(a) by a similar method to Example 102(e).

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 16 mg from 29 mg of tert-butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 174(a) by a similar method to Example 1(c).

(Example 175)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of

22 mg from 23 mg of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 172(a) by a similar method to Example 102(e).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 15 mg from 23 mg of tert-butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 175(a) by a similar method to Example 1(c).

(Example 176)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(5-formyl-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 166 mg from 228 mg of ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate obtained in Example 165(b) by a similar method to Example 102(a).

(b) tert-Butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-

diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 167 mg from 166 mg of tert-butyl 3-(5-formyl-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 176(a) by a similar method to Example 102(b) except that the product was not purified by silica gel column chromatography.

(c) tert-Butyl 3-(5-acetyl-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 100 mg from 112 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 176(b) by a similar method to Example 102(c).

(d) tert-Butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 77 mg from 74 mg of tert-butyl 3-(5-acetyl-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in

Example 176(c) by a similar method to Example 171(d) except that the temperature of reaction mixture was raised from -78°C to 0°C after stirring and further stirred for 30min.

(e) tert-Butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 29 mg from 29 mg of the crude product of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 176(d) by a similar method to Example 102(e) except that the product was not purified by preparative TLC.

(f) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of 14 mg from 29 mg of tert-butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 176(e) by a similar method to Example 1(c).

(Example 177)

2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-

yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)propan-2-ol

The title compound was obtained in an amount of 9.2 mg from 16 mg of tert-butyl 3-(5-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 171(d) by a similar method to Example 1(c).

(Example 178)

2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)propan-2-ol

The title compound was obtained in an amount of 25 mg from 50 mg of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 176(d) by a similar method to Example 1(c).

(Example 179)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-one

The title compound was obtained in an amount of 18 mg from 31 mg of tert-butyl 3-(5-acethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 171(c) by a similar method to Example 1(c).

(Example 180)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-one

The title compound was obtained in an amount of 17 mg from 25 mg of tert-butyl 3-(5-acetyl-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 176(c) by a similar method to Example 1(c).

(Example 181)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-ol

The title compound was obtained in an amount of 7.0 mg from 12 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 171(b) by a similar method to Example 1(c).

(Example 182)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-ol

The title compound was obtained in an amount of 14 mg from 28 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

obtained in Example 176(b) by a similar method to Example 1(c).

(Example 183)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol

(a) tert-Butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

10 mg of tert-butyl 3-(5-formyl-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 171(a), triphenylphosphine (10.5 mg, 2 equivalents) and (bromodifluoromethyl)trimethylsilane (6.2 µL, 2 equivalents) were dissolved in DMPU (100 µL), followed by stirring at room temperature for 18 hours. 1M potassium hydroxide (0.4mL) was added and stirred at room temperature for 1 hour. Thereafter, the organic phase extracted by ethyl acetate was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 6.4 mg of the title compound by purification of the residue by preparative TLC (eluent, hexane:ethyl acetate = 1:1).

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-

yl)-2,2-difluoroethan-1-ol

The title compound was obtained in an amount of 2.9 mg from 6.4 mg of tert-butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 183(a) by a similar method to Example 1(c).

(Example 184)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 16 mg from 15 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 171(b) by a similar method to Example 102(e) except that the product was not purified by preparative TLC.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of

12 mg from 16 mg of tert-butyl 3-(5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 184(a) by a similar method to Example 1(c).

(Example 185)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

(a) tert-Butyl 3-(5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 22 mg from 21 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 176(b) by a similar method to Example 102(e) except that the product was not purified by preparative TLC.

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole

The title compound was obtained in an amount of 14 mg from 22 mg of tert-butyl 3-(5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-

yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 185(a) by a similar method to Example 1(c).

(Example 186)

Ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

(a) Ethyl 7-bromo-2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 129 mg from 10 mg of ethyl 7-Bromo-2-mercapto-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Reference Example 20 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) Ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

The title compound was obtained as a crude product in an amount of 600 mg from 378 mg of ethyl 7-bromo-2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 186(a) by a similar method to Example 2(b) except that toluene was used instead of

1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) Ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 115 mg from 400 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 186(b) by a similar method to Example 1(c).

(Example 187)

Ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

(a) Ethyl 7-bromo-2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 110 mg from 120 mg of ethyl 7-bromo-2-mercapto-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Reference Example 20 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used

instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) Ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

The title compound was obtained as a crude product in an amount of 170 mg from 110 mg of ethyl 7-bromo-2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 187(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) Ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 75 mg from 170 mg of ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 187(b) by a similar method to Example 1(c).

(Example 188)

Ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

(a) Ethyl 7-bromo-2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 170 mg from 120 mg of ethyl 7-bromo-2-mercapto-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Reference Example 20 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) Ethyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

The title compound was obtained as a crude product in an amount of 180 mg from 170 mg of ethyl 7-bromo-2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 188(a) by a similar method to Example 2(b) except that toluene was used instead of 1,4-dioxane and tetrakis(triphenylphosphine)palladium(0) was used

instead of bis(triphenylphosphine)palladium(II) dichloride.

(c) Ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

The title compound was obtained in an amount of 110 mg from 180 mg of ethyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 188(b) by a similar method to Example 1(c).

(Example 189)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid

54 mg of ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 186(c) was dissolved in tetrahydrofuran (3.2 mL), ethanol (3.2 mL) and distilled water (3.2 mL), and then lithium hydroxide (9 mg, 2 equivalents) was added, followed by stirring at 80°C for 4 hours. After the formation of the product was confirmed by TLC, the pH of residue obtained by vacuum concentration of the reaction mixture was adjusted to 2 by addition of citric acid.

A solid substance formed was filtered and dried under reduced pressure to afford 40 mg of the title compound.

(Example 190)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid

The title compound was obtained in an amount of 25 mg from 39 mg of ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 187(c) by a similar method to Example 189.

(Example 191)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid

The title compound was obtained in an amount of 40 mg from 62 mg of ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 188(c) by a similar method to Example 189.

(Example 192)

(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)(azetidin-

1-yl)methanone

(a) tert-Butyl 3-(5-(azetidine-1-carbonyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 26 mg from 30 mg of 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid obtained in Example 189 by a similar method to Example 94(b) except that azetidine hydrochloride (21 mg, 4 equivalents) and 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride n-hydrate (content 82.2%, 74.7 mg, 4 equivalents) were used instead of 2M solution of dimethylamine in methanol.

(b) (2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)(azetidin-1-yl)methanone

The title compound was obtained in an amount of 21 mg from 26 mg of tert-butyl 3-(5-(azetidine-1-carbonyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 192(a) by a similar method to Example 1(c).

(Example 193)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-N-(2-hydroxyethyl)-N-methyl-7-(thiazol-2-yl)-4-

(trifluoromethoxy)benzo[d]oxazole-5-carboxamide

(a) tert-Butyl 3-(5-((2-hydroxyethyl)(methyl)carbamoyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 16 mg from 16 mg of 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid obtained in Example 189 by a similar method to Example 94(b) except that 2-(methylamino)ethan-1-ol (9.6 µL, 4 equivalents) and 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride n-hydrate (content 82.2%, 40 mg, 4 equivalents) were used instead of 2M solution of dimethylamine in methanol.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-N-(2-hydroxyethyl)-N-methyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxamide

The title compound was obtained in an amount of 13 mg from 16 mg of tert-butyl 3-(5-((2-hydroxyethyl)(methyl)carbamoyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 193(a) by a similar method to Example 1(c).

(Example 194)

(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-

yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)(3-hydroxy-3-(trifluoromethyl)azetidin-1-yl)methanone

(a) tert-Butyl 3-(5-(3-hydroxy-3-(trifluoromethyl)azetidine-1-carbonyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 39 mg from 29 mg of 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid obtained in Example 189 by a similar method to Example 94(b) except that 3-(trifluoromethyl)azetidin-3-ol hydrochloride (38 mg, 4 equivalents) and 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride n-hydrate (content 82.2%, 71 mg, 4 equivalents) were used instead of 2M solution of dimethylamine in methanol.

(b) (2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)(3-hydroxy-3-(trifluoromethyl)azetidin-1-yl)methanone

The title compound was obtained in an amount of 15 mg from 39 mg of tert-butyl 3-(5-(3-hydroxy-3-(trifluoromethyl)azetidine-1-carbonyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in

Example 194(a) by a similar method to Example 1(c).

(Example 195)

2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol

(a) tert-Butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 49 mg from 50 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 186(b) by a similar method to Example 171(d)

(b) 2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol

The title compound was obtained in an amount of 30 mg from 49 mg of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 195(a) by a similar method to Example 1(c).

(Example 196)

2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-

2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol

(a) tert-Butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 26 mg from 49 mg of ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 187(b) by a similar method to Example 171(d) except that the crude product was purified by silica gel column chromatography.

(b) 2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol

The title compound was obtained in an amount of 11 mg from 26 mg of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 196(a) by a similar method to Example 1(c).

(Example 197)

2-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol

(a) tert-Butyl 3-(5-(2-hydroxypropan-2-yl)-7-

(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 59 mg from 86 mg of ethyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 188(b) by a similar method to Example 171(d) except that the crude product was purified by silica gel column chromatography.

(b) 2-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol

The title compound was obtained in an amount of 15 mg from 26 mg of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 197(a) by a similar method to Example 1(c).

(Example 198)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of

18 mg from 30mg of the crude product of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 195(a) by a similar method to Example 102(e).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 11 mg from 18 mg of tert-butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 198(a) by a similar method to Example 1(c).

(Example 199)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 38 mg from 71 mg of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in

Example 196(a) by a similar method to Example 102(e).

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 20 mg from 38 mg of tert-butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 199(a) by a similar method to Example 1(c).

(Example 200)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 23 mg from 32 mg of tert-butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 197(a) by a similar method to Example 102(e).

(b) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 13 mg from 23 mg of tert-butyl 3-(5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 200(a) by a similar method to Example 1(c).

(Example 201)

(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)methanol

(a) tert-Butyl 3-(5-(hydroxymethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

21 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 186(b) was dissolved in toluene (370μL), then 1.0M solution (0.19 mL, 5 equivalents) of diisobutylaluminium hydride in toluene was added thereto at -78°C, followed by stirring for 1 hour. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated ammonium chloride aqueous solution was added thereto, and the reaction mixture was subjected to Celite® filtration. Thereafter, the organic phase extracted by ethyl acetate was washed and dried over anhydrous magnesium sulfate, followed by filtration,

and thus obtaining 20 mg of the title compound as a crude product by vacuum concentration of the filtrate.

(b) (2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)methanol

The title compound was obtained in an amount of 6.3 mg from 15 mg of tert-butyl 3-(5-(hydroxymethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 201(a) by a similar method to Example 1(c).

(Example 202)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol

(a) tert-Butyl 3-(5-formyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

20 mg of tert-butyl 3-(5-(hydroxymethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 201(a) and Dess-Martin Periodinane (31 mg, 2 equivalents) were dissolved in chloroform (370μL), followed by stirring at 0°C for 3 hours. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and then saturated aqueous sodium bicarbonate and saturated aqueous

sodium thiosulfate solution were added thereto, followed by extraction using ethyl acetate. Thereafter, the organic phase was dried over anhydrous magnesium sulfate, followed by filtration, and thus obtaining 19 mg of the title compound as a crude product by vacuum concentration of the filtrate.

(b) tert-Butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 20 mg from 19 mg of the crude product of tert-butyl 3-(5-formyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 202(a) by a similar method to Example 102(b) except that the product was not purified by silica gel column chromatography.

(c) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol

The title compound was obtained in an amount of 12 mg from 20 mg of the crude product of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 202(b) by a similar method to Example 1(c).

(Example 203)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol

(a) tert-Butyl 3-(5-formyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 56 mg from 111 mg of ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 187(b) by a similar method to Example 102(a).

(b) tert-Butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 35 mg from 54 mg of tert-butyl 3-(5-formyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 203(a) by a similar method to Example 102(b).

(c) 1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol

The title compound was obtained in an amount of 18 mg from 26 mg of tert-butyl 3-(5-(1-hydroxyethyl)-

7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 203(b) by a similar method to Example 1(c).

(Example 204)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-1-ol

(a) tert-Butyl 3-(5-(1-hydroxypropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 10 mg from 20 mg of tert-butyl 3-(5-formyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 202(a) by a similar method to Example 102(b) except that 0.96 ethylmagnesium bromide solution in tetrahydrofuran (397μL, 10 equivalents) was used instead of 0.92M methylmagnesium bromide solution in tetrahydrofuran.

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-1-ol

The title compound was obtained in an amount of 8.4 mg from 10 mg of tert-butyl 3-(5-(1-hydroxypropyl)-7-(thiazol-2-yl)-4-

(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 204(a) by a similar method to Example 1(c).

(Example 205)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2-methylpropan-1-ol

(a) tert-Butyl 3-(5-(1-hydroxy-2-methylpropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 3.6 mg from 20 mg of tert-butyl 3-(5-formyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 202(a) by a similar method to Example 102(b) except that 0.74 M solution of isopropylmagnesium bromide in tetrahydrofuran (0.31 mL, 5.9 equivalents) was used instead of 0.92 M sclution of methylmagnesium bromide in tetrahydrofuran.

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2-methylpropan-1-ol

The title compound was obtained in an amount of 2.0 mg from 3.6 mg of tert-butyl 3-(5-(1-hydroxy-2-methylpropyl)-7-(thiazol-2-yl)-4-

(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 205(a) by a similar method to Example 1(c).

(Example 206)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol

(a) tert-Butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 15 mg from 15 mg of tert-butyl 3-(5-formyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 202(a) by a similar method to Example 183(a).

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol

The title compound was obtained in an amount of 6.9 mg from 15 mg of tert-butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 206(a) by a similar method to Example 1(c).

(Example 207)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-

2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol

(a) tert-Butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 40 mg from 40 mg of tert-butyl 3-(5-formyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 203(a) by a similar method to Example 183(a).

(b) 1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol

The title compound was obtained in an amount of 24 mg from 40 mg of tert-butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 207(a) by a similar method to Example 1(c).

(Example 208)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 20 mg from 27 mg of tert-butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 207(a) by a similar method to Example 102(e).

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 15 mg from 19 mg of tert-butyl 3-(5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 208(a) by a similar method to Example 1(c).

(Example 209)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 25 mg from 29 mg of tert-butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-

diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 206(a) by a similar method to Example 102(e).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 18 mg from 24 mg of tert-butyl 3-(5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 209(a) by a similar method to Example 1(c).

(Example 210)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 45 mg from 57 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 202(b) by a similar method to Example 102(e).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-

(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 36 mg from 45 mg of tert-butyl 3-(5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 210(a) by a similar method to Example 1(c).

(Example 211)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 31 mg from 30 mg of the crude product of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 203(b) by a similar method to Example 102(e) except that the product was not purified by preparative TLC.

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of

18 mg from 31 mg of tert-butyl 3-(5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 211(a) by a similar method to Example 1(c).

(Example 212)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one

(a) tert-Butyl 3-(5-acetyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 100 mg from 108 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 203(b) by a similar method to Example 102(c).

(b) 1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one

The title compound was obtained in an amount of 10 mg from 19 mg of tert-butyl 3-(5-acetyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 212(a) by a similar method to Example 1(c).

(Example 213)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one

(a) tert-Butyl 3-(5-acetyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 70 mg from 88 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 202(b) by a similar method to Example 102(c).

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one

The title compound was obtained in an amount of 12 mg from 15 mg of tert-butyl 3-(5-acetyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 213(a) by a similar method to Example 1(c).

(Example 214)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-

trifluoro-2-hydroxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

23 mg of tert-butyl 3-(5-acetyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 212(a), (trifluoromethyl)trimethylsilane (40 μL, 6 equivalents) and caesium fluoride (1.0 mg, 0.2 equivalent) were dissolved in tetrahydrofuran (440 μL), followed by stirring at 0°C for 6 hours. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and 2M hydrochloric acid / isopropyl alcohol was added , followed by stirring at room temperature for 30 min. 1M sodium hydroxide was added into the reaction mixture, and then the organic phase was extracted by ethyl acetate. The organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 14 mg of the title compound by purification of the residue by preparative TLC (eluent, hexane:ethyl acetate = 1:1).

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 7.2 mg from 14 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 214(a) by a similar method to Example 102(e).

(c) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 5.1 mg from 7.2 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 214(b) by a similar method to Example 1(c).

(Example 215)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 33 mg from 38 mg of tert-butyl 3-(5-acetyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-

diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 213(a) by a similar method to Example 102(d) except that 4 equivalents of trifluoromethyltrimethylsilane was used.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl) -3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 15 mg from 15 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 215(a) by a similar method to Example 102(e).

(c) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

The title compound was obtained in an amount of 12 mg from 15 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl) -3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 215(b) by a similar method to Example 1(c).

(Example 216)

2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-1,1,1-

trifluoropropan-2-ol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-((trimethylsilyl)oxy)propan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

21 mg of tert-butyl 3-(5-acetyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 212(a), (trifluoromethyl)trimethylsilane (35 μL, 6 equivalents) and caesium fluoride (1.2 mg, 0.2 equivalent) were dissolved in tetrahydrofuran (400 μL), followed by stirring at 0°C for 3 hours. The formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1), and saturated aqueous sodium bicarbonate solution was added, and then the organic phase was extracted by ethyl acetate. The organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 22 mg of the title compound by purification of the residue by preparative TLC (eluent, hexane:ethyl acetate = 1:1).

(b) 2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol

The title compound was obtained in an amount of

6.9 mg from 22 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-((trimethylsilyl)oxy)propan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 216(b) by a similar method to Example 1(c).

(Example 217)

2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol

The title compound was obtained in an amount of 13 mg from 18 mg of tert-butyl 3-(7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-hydroxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 215(a) by a similar method to Example 1(c).

(Example 218)

(E)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime and

(Z)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime

(a) tert-Butyl (E)-3-(5-(1-(methoxyimino)ethyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate and tert-butyl (Z)-3-(5-(1-(methoxyimino)ethyl-7-(thiazol-

2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

17 mg of tert-butyl 3-(5-acetyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 213(a) was dissolved in N,N-dimethylformamide (0.2 mL), then potassium carbonate (26 mg, 6 equivalents) and O-methylhydroxylamine hydrochloride (8 mg, 3 equivalents) were added thereto at room temperature followed by stirring overnight. After adding O-methylhydroxylamine hydrochloride (4 mg, 1.5 equivalents) and N,N-dimethylformamide (0.2 mL) and stirring at 60°C for 5 hours, the formation of the product was confirmed by TLC (eluent, hexane:ethyl acetate = 1:1) followed by filtration. Thereafter, 8.2 mg of the title compound was obtained by purification of the filtrate by silica gel column chromatography (eluent, hexane:ethyl acetate = 1:1).

(b) (E)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime and (Z)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime

The title compound was obtained in an amount of 8.0 mg from 5.8 mg of tert-butyl (E)-3-(5-(1-

(methoxyimino)ethyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate and tert-butyl (Z)-3-(5-(1-(methoxyimino)ethyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 218(a) by a similar method to Example 1(c).

(Example 219)

(E)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime and (Z)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime

(a) tert-Butyl (E)-3-(5-(1-(methoxyimino)ethyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate and (Z)-3-(5-(1-(methoxyimino)ethyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 10 mg from 15 mg of tert-butyl 3-(5-acetyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 212(a) by a similar method to Example 218(a).

(b) (E)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-

(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime and (Z)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime

The title compound was obtained in an amount of 6.7 mg from 10 mg of tert-butyl (E)-3-(5-(1-(methoxyimino)ethyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate and tert-butyl (Z)-3-(5-(1-(methoxyimino)ethyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 219(a) by a similar method to Example 1(c).

(Example 220)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(4-(1-(ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 17 mg from 26 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 118(b) by a similar method to Example 102(e) except that ethyl iodide was used instead of

methyl iodide.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 24 mg from 35 mg of tert-butyl 3-(4-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 220(a) by a similar method to Example 1(c).

(Example 221)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 14 mg from 51 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 118(b) by a similar method to Example 102(e) except that 2,2,2-trifluoroethyl trifluoromethanesulfonate was used instead of methyl iodide.

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-

2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole

The title compound was obtained in an amount of 10 mg from 14 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 221(a) by a similar method to Example 1(c).

(Example 222)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 48 mg from 51 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 118(b) by a similar method to Example 102(e).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole

The title compound was obtained in an amount of 30 mg from 48 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazol-2-yl)-

3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 222(a) by a similar method to Example 1(c).

(Example 223)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 58 mg from 60 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 120(b) by a similar method to Example 102(e) except that 36 equivalents of 2,2,2-trifluoroethyl trifluoromethanesulfonate was used instead of methyl iodide.

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole

The title compound was obtained in an amount of 35 mg from 58 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-

diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 223(a) by a similar method to Example 1(c).

(Example 224)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(4-(1-ethoxy-2,2,2-trifluoroethyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 24 mg from 50 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 120(b) by a similar method to Example 102(e) except that 36 equivalents of ethyl iodide and 19.8 equivalents of sodium hydride were used instead of methyl iodide.

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 12 mg from 24 mg of tert-butyl 3-(4-(1-ethoxy-2,2,2-trifluoroethyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 224(a) by a similar method to Example 1(c).

(Example 225)

2-(1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)ethan-1-ol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained as a crude product in an amount of 105 mg from 60 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 118(b) by a similar method to Example 149(a).

(b) 2-(1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)ethan-1-ol

The title compound was obtained in an amount of 4.2 mg from 105 mg of the crude product of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 225(a) by a similar method to Example 1(c).

(Example 226)

2-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetonitrile

(a) tert-Butyl 3-(4-(1-(cyanomethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-

3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 54 mg from 60 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 120(b) by a similar method to Example 102(e) except that bromoacetonitrile was used instead of methyl iodide.

(b) 2-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetonitrile

The title compound was obtained in an amount of 15 mg from 26 mg of tert-butyl 3-(4-(1-(cyanomethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 226(a) by a similar method to Example 1(c).

(Example 227)

2-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)ethan-1-ol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 19 mg from 60 mg of tert-butyl

3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 120(b) by a similar method to Example 149(a).

(b) 2-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)ethan-1-ol

The title compound was obtained in an amount of 1.6 mg from 19 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 227(a) by a similar method to Example 1(c).

(Example 228)

2-(1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetonitrile

(a) tert-Butyl 3-(4-(1-(cyanomethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 55 mg from 61 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 118(b) by a similar method to Example 102(e) except that bromoacetonitrile was used instead

of methyl iodide.

(b) 2-(1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetonitrile

The title compound was obtained in an amount of 12 mg from 27 mg of tert-butyl 3-(4-(1-(cyanomethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 228(a) by a similar method to Example 1(c).

(Example 229)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-mthoxyethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 30 mg from 50 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 120(b) by a similar method to Example 102(e) except that 2-bromoethyl methyl ether was used instead of methyl iodide.

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-

methoxyethoxy)ethyl)benzo[d]oxazole

The title compound was obtained in an amount of 19 mg from 30 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-mthoxyethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 229(a) by a similar method to Example 1(c).

(Example 230)

4-(1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(4-1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-(7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

30 mg of tert-butyl 3-(4-(1-(cyanomethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 228(a), sodium azide (11 mg, 3 equivalents), and ammonium chloride (8.8 mg, 3 equivalents) were dissolved in N,N-dimethylformamide (0.68 mL), followed by stirring using a microwave reactor (manufactured by Biotage, conditions: 100°C, 4 hours). The formation of the product was confirmed by TLC (eluent, chloroform:methanol:aqueous solution of ammonia = 4:1:0.1), and then distilled water was added thereto, and then the organic phase was extracted by

ethyl acetate. Thereafter, extracted organic phase was separated by using saturated aqueous sodium bicarbonate solution and the organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 29 mg of the title compound by purification of the residue through silica gel column chromatography (chloroform:methanol:aqueous solution of ammonium = 4:1:0.1).

(b) 4-(1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 16 mg from 29 mg of tert-butyl 3-(4-1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-(7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 230(a) by a similar method to Example 1(c).

(Example 231)

4-(1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(4-(1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of

55 mg from 61 mg of tert-butyl 3-(4-(1-(cyanomethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 226(a) by a similar method to Example 230(a).

(b) 4-(1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 6.4 mg from 55 mg of tert-butyl 3-(4-(1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 231(a) by a similar method to Example 1(c).

(Example 232)

1-((1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)methyl)cyclopropan-1-ol

(a) tert-Butyl 3-(4-(1-(2-(tert-butoxy)-2-oxoethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

250 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 120(b), tetrabutylammonium chloride (13.9 mg, 0.1 equivalent), 35% aqueous sodium hydroxide

solution and tert-butyl bromoacetate (10 μL, 1.5 equivalents) were dissolved in dichloromethane (2.0 mL), followed by stirring at room temperature for 19 hours. The formation of the product was confirmed by TLC, and then saturated ammonium chloride aqueous solution was added thereto, and then the organic phase was extracted by ethyl acetate. The organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 319 mg of the title compound by purification of the residue through silica gel column chromatography (hexane-hexane:ethyl acetate = 1:1).

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

10 mg of tert-butyl 3-(4-(1-(2-(tert-butoxy)-2-oxoethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 232(a) was dissolved in tetrahydrofuran (160 μL), then titanium isopropoxide (9.7 μL, 2 equivalents) and 0.97M ethylmagnesium bromide solution in tetrahydrofuran (102 μL, 6 equivalents) were added, followed by stirring at room temperature for 48 hours. Saturated ammonium chloride aqueous solution was added

into the reaction mixture, and then the organic phase was extracted by ethyl acetate. The organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 1.6 mg of the title compound by purification of the residue by preparative TLC (eluent, hexane:ethyl acetate = 1:1).

(c) 1-((1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)methyl)cyclopropan-1-ol

The title compound was obtained in an amount of 2.6 mg from 2.0 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 232(a) by a similar method to Example 1(c).

(Example 233)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethane-1,1-diol

(a) tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoroacetyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 10 mg from 10 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained

in Example 118(b) by a similar method to Example 102(c).

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethane-1,1-diol

The title compound was obtained in an amount of 5.7 mg from 10 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoroacetyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 233(a) by a similar method to Example 1(c).

(Example 234)

2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol

(a) tert-Butyl 3-(7-bromo-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 574 mg from 500 mg of 1-(7-bromo-2-mercaptobenzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol obtained in Reference Example 21 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-

diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 493 mg from 574 mg of tert-butyl 3-(7-bromo-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 234(a) by a similar method to Example 1(b).

(c) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1,1-dihydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 26 mg from 25 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 234(b) by a similar method to Example 156(a).

(d) tert-Butyl 3-(7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

26 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1,1-dihydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 234(c) was dissolved in tetrahydrofuran (0.5 mL), then 0.92M methylmagnesium bromide solution in tetrahydrofuran (0.54 mL, 10 equivalents) was added at 0°C and stirred for 1 hour, followed by stirring at

room temperature for 90 min. The formation of the product was confirmed by TLC(eluent, hexane:ethyl acetate = 1:1), and then saturated ammonium chloride aqueous solution was added thereto, and then the organic phase was extracted by ethyl acetate. The organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 14 mg of the title compound by purification of the residue through silica gel column chromatography (aminosilica, hexane:ethyl acetate = 1:4).

(e) 2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol

The title compound was obtained in an amount of 4.3 mg from 14 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 234(d) by a similar method to Example 1(c).

(Example 235)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazol-2-yl)-

3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 11 mg from 14 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 234(d) by a similar method to Example 102(e).

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 7.2 mg from 11 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 235(a) by a similar method to Example 1(c).

(Example 236)

2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 4.2 mg from 41 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoroacetyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in

Example 233(a) by a similar method to Example 102(b).

(b) 2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol

The title compound was obtained in an amount of 5.2 mg from 10 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 236(a) by a similar method to Example 1(c).

(Example 237)

Methyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate

(a) Methyl 7-bromo-2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)benzo[d]oxazol-4-carboxylate

The title compound was obtained in an amount of 268 mg from 200 mg of methyl 7-bromo-2-mercaptobenzo[d]oxazole-4-carboxylate obtained in Reference Example 22 and tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate by a similar method to Example 1(a).

(b) Methyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-carboxylate

The title compound was obtained in an amount of

82 mg from 221 mg of methyl 7-bromo-2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)benzo[d]oxazol-4-carboxylate obtained in Example 237(a) by a similar method to Example 1(b).

(c) Methyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate

The title compound was obtained in an amount of 12 mg from 19 mg of methyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-carboxylate obtained in Example 237(b) by a similar method to Example 1(c).

(Example 238)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylic acid

The title compound was obtained in an amount of 6.8 mg from 12 mg of methyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate obtained in Example 237(c) by a similar method to Example 94(a).

(Example 239)

1-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol

(a) Methyl 7-bromo-2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)benzo[d]oxazol-4-carboxylate

The title compound was obtained in an amount of

566 mg from 500 mg of methyl 7-bromo-2-mercaptobenzo[d]oxazole-4-carboxylate obtained in Reference Example 22 by a similar method to Example 1(a) except that tert-butyl 3,9-diazabicyclo[3.3.1]nonane-9-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) Methyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-carboxylate

The title compound was obtained in an amount of 312 mg from 566 mg of methyl 7-bromo-2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)benzo[d]oxazol-4-carboxylate obtained in Example 239(a) by a similar method to Example 1(b).

(c) tert-Butyl 3-(4-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-Diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained as a crude product from 250 mg of methyl 2-(9-(tert-butoxycarbonyl)-3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-carboxylate obtained in Example 239(b) by a similar method to Example 201(a).

(d) tert-Butyl 3-(4-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 120 mg from the crude product of tert-butyl 3-(4-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 239(c) by a similar method to Example 202(a).

(e) tert-Butyl 3-(4-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 68 mg from 120 mg of tert-butyl 3-(4-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 239(d) by a similar method to Example 102(b).

(f) 1-(2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol

The title compound was obtained in an amount of 10 mg from 14 mg of tert-butyl 3-(4-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 239(e) by a similar method to Example 1(c).

(Example 240)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol

(a) Methyl 7-bromo-2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)benzo[d]oxazol-4-

carboxylate

The title compound was obtained in an amount of 501 mg from 500 mg of methyl 7-bromo-2-mercaptobenzo[d]oxazole-4-carboxylate obtained in Reference Example 22 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) Methyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-carboxylate

The title compound was obtained in an amount of 298 mg from 508 mg of methyl 7-bromo-2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)benzo[d]oxazol-4-carboxylate obtained in Example 240(a) by a similar method to Example 1(b).

(c) tert-Butyl 3-(4-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product in an amount of 168 mg from 280 mg of methyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-carboxylate obtained in Example 240(b) by a similar method to Example 201(a) except

that dichloromethane was used instead of toluene.

(d) tert-Butyl 3-(4-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 163 mg from 168 mg of the crude product of tert-butyl 3-(4-(hydroxymethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 240(c) by a similar method to Example 202(a).

(e) tert-Butyl 3-(4-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 117 mg from 175 mg of tert-butyl 3-(4-formyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 240(d) by a similar method to Example 102(b).

(f) 1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol

The title compound was obtained in an amount of 6.8 mg from 13 mg of tert-butyl 3-(4-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 240(e) by a similar method to Example 1(c).

(Example 241)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 11 mg from 18 mg of tert-butyl 3-(4-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 240(e) by a similar method to Example 102(e).

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 14 mg from 22 mg of tert-butyl 3-(4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 241(a) by a similar method to Example 1(c).

(Example 242)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 18 mg from 18 mg of the crude product of tert-butyl 3-(4-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-

yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 124 by a similar method to Example 102(e).

(b) 2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 12 mg from 18 mg of tert-butyl 3-(4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 242(a) by a similar method to Example 1(c).

(Example 243)

2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate

The title compound was obtained in an amount of 13 mg from 14 mg of tert-butyl 3-(4-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 239(e) by a similar method to Example 102(e).

(b) 2-(3,9-Diazabicyclo[3.3.1]nonan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of 8.7 mg from 13 mg of tert-butyl 3-(4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,9-

diazabicyclo[3.3.1]nonane-9-carboxylate obtained in Example 243(a) by a similar method to Example 1(c).

(Example 244)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-one

(a) tert-Butyl 3-(4-acetyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 71 mg from 105 mg of tert-butyl 3-(4-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 240(e) by a similar method to Example 102(c).

(b) 1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-one

The title compound was obtained in an amount of 4.0 mg from 13 mg of tert-butyl 3-(4-acetyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 244(a) by a similar method to Example 1(c).

(Example 245)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-one

(a) tert-Butyl 3-(4-acetyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 64 mg from 72 mg of the crude roduct of tert-butyl 3-(4-(1-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 124 by a similar method to Example 102(c).

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-one

The title compound was obtained in an amount of 4.2 mg from 14 mg of tert-butyl 3-(4-acetyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 245(a) by a similar method to Example 1(c).

(Example 246)

2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)propan-2-ol

(a) tert-Butyl 3-(4-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 37 mg from 67 mg of tert-butyl 3-(4-acetyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 244(a) by a similar method to Example 171(d).

(b) 2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)propan-2-ol

The title compound was obtained in an amount of 4.0 mg from 13 mg of tert-butyl 3-(4-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 246(a) by a similar method to Example 1(c).

(Example 247)

2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)propan-2-ol

(a) tert-Butyl 3-(4-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

The title compound was obtained in an amount of 27 mg from 51 mg of tert-butyl 3-(4-acetyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 245(a) by a similar method to Example 171(d).

(b) 2-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)propan-2-ol

The title compound was obtained in an amount of 3.3 mg from 10 mg of tert-butyl 3-(4-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 247(a) by a similar method to Example 1(c).

(Example 248)

1-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-

methylpropan-2-ol

(a) tert-Butyl 3-(4-(benzyloxyl)-7-bromobenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 2.9 g from 2.3 g of 4-(benzyloxy)-7-bromobenzo[d]oxazole-2-thiol obtained in Reference Example 23 by a similar method to Example 1(a) except that tert-butyl 3,6-diazabicyclo[3.1.1]heptane-6-carboxylate was used instead of tert-butyl 3,8-diazabicyclo[3.2.1]octane-8-carboxylate.

(b) tert-Butyl 3-(4-(benzyloxyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 2.5 g from 2.9 g of tert-butyl 3-(4-(benzyloxyl)-7-bromobenzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(a) by a similar method to Example 1(b).

(c) tert-Butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

1.5 g of tert-butyl 3-(4-(benzyloxyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(b) was dissolved in tetrahydrofuran (60

mL), then 20% palladium hydroxide / carbon (content of water:50%,2.5 g) was added under an argon atmosphere, fcllowed by filling up with hydrogen and stirring at 50°C for 4.5 hours. After Celite® filtration of the reaction solution, 1.0 g of the title compound by purification of the residue obtained by vacuum concentration of the filtrate through silica gel column chromatography (chloroform- chloroform:methanol = 94:6).

(d) tert-Butyl 3-(4-(2-ethoxy-1,1-difluoro-2-oxoethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

1.0 g of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(c) was dissolved in acetonitrile (24 mL), then 1,8-diazabicyclo[5.4.0]undec-7-ene (3.6 mL, 10 equivalents) and ethyl 2-bromo-2,2-difluoroacetate(3.1 mL, 10 equivalents) were added, followed by stirring at room temperature for 2 hours. The formation of the product was confirmed by TLC, and then saturated ammonium chloride aqueous solution was added thereto to stop the reaction, and then the organic phase was extracted by ethyl acetate 3 times. The organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the

filtrate, and thus obtaining 1.0 g of the title compound by purification of the residue through silica gel column chromatography (hexane-hexane:ethyl acetate = 5:5).

(e) tert-Butyl 3-(4-(1,1-difluoro-2-hydroxy)-2-methylpropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

92 mg of tert-butyl 3-(4-(2-ethoxy-1,1-difluoro-2-oxoethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(d) was dissolved in tetrahydrofuran (1.7 mL), then 0.95M methylmagnesium bromide solution in tetrahydrofuran (0.85mL, 5 equivalents) was added at 0°C, followed by stirring at room temperature for 1 hour. Saturated ammonium chloride aqueous solution was added thereto to stop the reaction, and then the organic phase was extracted by ethyl acetate 3 times. The organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 82 mg of the title compound by purification of the residue through silica gel column chromatography (hexane-hexane:ethyl acetate-ethyl acetate).

(f) 1-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol

The title compound was obtained in an amount of 39 mg from 58 mg of tert-butyl 3-(4-(1,1-difluoro-2-hydroxy)-2-methylpropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(e) by a similar method to Example 1(c).

(Example 249)

2-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol

(a) tert-Butyl 3-(4-(1,1-difluoro-2-hydroxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

21 mg of tert-butyl 3-(4-(2-ethoxy-1,1-difluoro-2-oxoethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(d) was dissolved in tetrahydrofuran (390 μL) and methanol (390 μL), then sodium borohydride (18 mg, 12 equivalents) was added at room temperature, followed by stirring for 4 hours. Saturated ammonium chloride aqueous solution was added thereto to stop the reaction, and then the organic phase was extracted by ethyl acetate 3 times. The organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 15 mg of the title compound by purification of the residue by preparative TLC

(hexane:ethyl acetate = 1:2).

(b) 2-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol

The title compound was obtained in an amount of 11 mg from 15 mg of tert-butyl 3-(4-(1,1-difluoro-2-hydroxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 249(a) by a similar method to Example 1(c).

(Example 250)

1-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol (racemic)

(a) tert-Butyl 3-(4-(1,1-difluoro-2-(methoxy(methyl)amino)-2-oxoethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

200 mg of tert-butyl 3-(4-(2-ethoxy-1,1-difluoro-2-oxoethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(d) and N,O-dimethylhydroxylamine hydrochloride (110 mg, 3 equivalents) were dissolved in tetrahydrofuran (3.7 mL), and then 2M solution of isopropylmagnesium bromide in tetrahydrofuran (1.1 mL, 6 equivalents) was dropped thereto at 0°C over 40 min, followed by

stirring at 0°C for 20 min. Saturated ammonium chloride aqueous solution was added thereto to stop the reaction, which was extracted by ethyl acetate 2 times. The organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, thus obtaining 210 mg of the title compound as a crude product.

(b) tert-Butyl 3-(4-(1,1-difluoro-2,2-dihydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

210 mg of the crude product of tert-butyl 3-(4-(1,1-difluoro-2-(methoxy(methyl)amino)-2-oxoethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 250(a) was dissolved in tetrahydrofuran (3.8 mL), and then 0.95M methylmagnesium bromide solution in tetrahydrofuran (0.81 mL, 2 equivalents) was added thereto at 0°C, followed by stirring for 30 min. Saturated ammonium chloride aqueous solution was added thereto to stop the reaction, which was extracted by ethyl acetate 2 times. The organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 200 mg of the title compound as a crude product.

(c) tert-Butyl 3-(4-(1,1-difluoro-2-hydroxypropoxy)-

7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (racemic)

195 mg of tert-butyl 3-(4-(1,1-difluoro-2,2-dihydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 250(b) was dissolved in tetrahydrofuran (3.7 mL) and methanol (3.7 mL), and then sodium borohydride (113 mg, 8 equivalents) was added thereto at 0°C, followed by stirring for 30 min at room temperature. Saturated ammonium chloride aqueous solution was added thereto to stop the reaction, which was extracted by ethyl acetate 2 times. The organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate

. Ethyl acetate (1mL) was added to the residue and the formed precipitate was collected by filteration to give 150 mg of the title compound.

(d) 1-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol (racemic)

The title compound was obtained in an amount of 31 mg from 41 mg of tert-butyl 3-(4-(1,1-difluoro-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 250(c) by a similar method to Example 1(c).

(Example 251)

1-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol (optically active)

(a) tert-Butyl 3-(4-(1,1-difluoro-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active)

1.4 g of racemic tert-butyl 3-(4-(1,1-difluoro-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 250(c) was purified by a Multiple preparative HPLC (YMC, LC-forte/R, column: DAICEL CHIRALPAK IC (particle diameter:5μm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol = 70:30, flow rate:19.8mL/min, detection:UV254nm) and the title compound was obtained in an amount of 687 mg by concentrating fractions with the shorter retention time peak. 99.9% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IC(particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol = 70:30, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:9.84min).

(b) 1-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol (optically active)

The title compound was obtained in an amount of 474 mg from 687 mg of tert-butyl 3-(4-(1,1-difluoro-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active) obtained in Example 251(a) by a similar method to Example 1(c). 99.9% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IC(particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol:diethylamine = 70:30:0.1, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:16.8min).

(Example 252)

1-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol (optically active, enantiomer of Example 251)

(a) tert-Butyl 3-(4-(1,1-difluoro-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active, enantiomer of Example 251(a))

1.4 g of racemic tert-butyl 3-(4-(1,1-difluoro-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 250(c) was purified by a Multiple

preparative HPLC (YMC, LC-forte/R, column: DAICEL CHIRALPAK IC (particle diameter:5μm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol = 70:30, flow rate:19.8mL/min, detection:UV254nm) and the title compound was obtained in an amount of 688 mg by concentrating fractions with the longer retention time peak. 99.0% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IC(particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol = 70:30, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:12.3min).

(b) 1-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol (optically active, enantiomer of Example 251)

The title compound was obtained in an amount of 447 mg from 627 mg of tert-butyl 3-(4-(1,1-difluoro-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active, enantiomer of Example 251(a)) obtained in Example 252(a) by a similar method to Example 1(c). 99.0% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IC(particle diameter:5μm, column diameter:0.46cm, column

length:25cm), eluent, hexane:isopropyl alcohol: diethylamine = 70:30:0.1, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:14.6min).

(Example 253)

2-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetic acid

The title compound was obtained as a crude product from 30 mg of tert-butyl 3-(4-(1-(2-(tert-butoxy)-2-oxoethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 232(a) by a similar method to Example 1(c). The crude product was purified by a preparative HPLC (Gilson, column: Sepax GP-C18 (particle diameter:5μm, cclumn diameter:2.12cm, column length:10cm), eluent, 0.1% formic acid in water: 0.1% formic acid in acetonitrile = 90:10-10:90, flow rate:15mL/min, detection:UV254nm) and the title compound was obtained in an amount of 21 mg by freeze drying of the purified product.

(Example 254)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydro-2H-pyran-4-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole

The title compound was obtained in an amount of

5.5 mg from 20.0 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 81(a) by a similar method to Example 102(e) except that tetrahydro-2H-pyran-4-yl trifluoromethanesulfonate (0.10 mg, 9.1 equivalents) was used instead of methyl iodide.

(Example 255)

1-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-(2,2,2-trifluoroethoxy)-2-methylpropan-2-ol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 33 mg from 40 mg of tert-butyl 3-(4-(1-(2-(tert-butoxy)-2-oxoethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 232(a) by a similar method to Example 248(e).

(b) 1-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-(2,2,2-trifluoroethoxy)-2-methylpropan-2-ol

The title compound was obtained in an amount of 7.9 mg from 33 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-

(2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 255(a) by a similar method to Example 1(C).

(Example 256)

2-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetamide

(a) Methyl 2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetate

To 44 mg of tert-butyl 3-(4-(1-(2-(tert-butoxy)-2-oxoethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 232(a) was added 2M methanolic hydrochloric acid (2.0 mL), followed by stirring at room temperature for 4 days. The formation of the product was confirmed by TLC. The residue obtained by vacuum concentration of the reaction mixture was dissolved in ethyl acetate, then saturated aqueous sodium bicarbonate was added. The organic phase was dried over anhydrous sodium sulfate, followed by filtration and vacuum concentration of the filtrate thus obtaining the title compound as a crude product.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-

trifluoro-1-(2-methoxy-2-oxoethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained in an amount of 16.8 mg from the crude product of methyl 2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetate obtained in Example 256(a) by a similar method to Example 85(a) except that di-tert-butyl dicarbonate was used instead of trifluoromethanesulfonic anhydride.

(c) 2-(1-(2-(6-(tert-Butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetic acid

The title compound was obtained as a crude product from 16.8 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxy-2-oxoethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 256(b) by a similar method to Example 94(a).

(d) tert-Butyl 3-(4-(1-(2-amino-2-oxoethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (11.5 mg, 2 equivalents), 1-

hydroxybenzotriazole monohydrate (8.1 mg, 2 equivalents), N,N-dimethylformamide (0.5 mL) and 7M solution (71 µL, 17 equivalents) of ammonia in methanol were added to 2-(1-(2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetic acid obtained in Example 256(c), followed by stirring at room temperature for 3 days. 7M solution (100 µL, 33 equivalents) of ammonia in methanol was added thereto again, followed by stirring at room temperature for 2.5 hours. The fcrmation of the product was confirmed by TLC and ethyl acetate and water were added to the reaction mixture. Thereafter, the organic phase was dried over anhydrous sodium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 10.7 mg of the title compound by purification of the residue by amino silica gel column chromatography (hexane-ethyl acetate-methanol: ethyl acetate = 1:4).

(e) 2-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetamide

8.9 mg of the title compound was obtained from 10.7 mg of tert-butyl 3-(4-(1-(2-amino-2-oxoethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-

2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 256(d), by a similar method to Example 1(c).

(Example 257)

1-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-1,1-difluoro-2-methylpropan-2-ol

(a) tert-Butyl 3-(4-(1-(2-ethoxy-1,1-difluoro-2-oxoethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

100 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 120(b) was dissolved in N,N-dimethylformamide (1.0 mL), 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (143 µL, 5 equivalents) and ethyl 2-bromo-2,2-difluoroacetate (51 µL, 2 equivalents) were added thereto, followed by stirring at 50°C for 1 hour. 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (143 µL, 5 equivalents) and ethyl 2-bromo-2,2-difluoroacetate (102 µL, 4 equivalents) were added thereto again, followed by stirring at 50°C for an additional 1 hour. Saturated aqueous sodium bicarbonate and ethyl acetate were added to the reaction mixture. Thereafter, the

organic phase was dried over anhydrous sodium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 19 mg of the title compound by purification of the residue through preparative TLC (ethyl acetate: chloroform = 1:6).

(b) tert-Butyl 3-(4-(1-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

16.4 mg of the title compound was obtained from 23 mg of tert-butyl 3-(4-(1-(2-ethoxy-1,1-difluoro-2-oxoethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 257(a) by a similar method to Example 248(d).

(c) 1-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-1,1-difluoro-2-methylpropan-2-ol

11.2 mg of the title compound was obtained from 16.4 mg of tert-butyl 3-(4-(1-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 257(b) by a similar method to Example 1(c).

(Example 258)

2-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2,2-difluoroethan-1-ol

(a) tert-Butyl 3-(4-(1-(1,1-difluoro-2-hydroxyethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

6.1 mg of the title compound was obtained from 10 mg of tert-butyl 3-(4-(1-(2-ethoxy-1,1-difluoro-2-oxoethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 257(a) by a similar method to Example 250(c).

(b) 2-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2,2-difluoroethan-1-ol

16.9 mg of the title compound was obtained from 24 mg of tert-butyl 3-(4-(1-(1,1-difluoro-2-hydroxyethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 258(a) by a similar method to Example 1(c).

(Example 259)

(2R)-1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)propan-2-ol

(a) tert-Butyl 3-(4-((R)-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

26 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(c) was dissolved in N,N-dimethylformamide (0.6 mL), then 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (9.1 μL, 1 equivalent) and (R)-propylene oxide (17.6 μL, 4 equivalents) were added thereto, followed by stirring using a microwave reactor (manufactured by Biotage, conditions: 150°C, 2 hours). Distilled water, saturated ammonium chloride aqueous solution and ethyl acetate were added to the reaction mixture. Thereafter, the organic phase was dried over anhydrous sodium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 22 mg of the title compound by purification of the residue by preparative TLC (methanol: chloroform = 8:92).

(b) <u>(2R)-1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)propan-2-ol (optically active)</u>

13.4 mg of the title compound was obtained from 22mg of tert-butyl 3-(4-((R)-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 259(a) by a similar method to Example 1(c).

(Example 260)

(2S)-1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)propan-2-ol

(a) tert-Butyl 3-(4-((S)-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

21 mg of the title compound was obtained from 25 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(c) by a similar method to Example 259(a) except that (S)-propylene oxide was used instead of (R)-propylene oxide.

(b) (2S)-1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)propan-2-ol

11.6 mg of the title compound was obtained from 21 mg of tert-butyl 3-(4-((S)-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 260(a) by a similar method to Example 1(c).

(Example 261)

1-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)propan-2-ol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-oxoethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

31 mg of the title compound was obtained from 97 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-hydroxyethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 227(a) by a similar method to Example 102(c).

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-hydroxypropoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

9.6 mg of the title compound was obtained from 31 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-oxoethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 261(a) by a similar method to Example 102(b).

(c) 1-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)propan-2-ol

5.1 mg of the title compound was obtained from 9.6 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-hydroxypropoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 261(b) by a similar method to Example 1(c).

(Example 262)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydro-

2H-pyran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(4-((tetrahydro-2H-pyran-3-yl)oxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

9.3 mg of the title compound was obtained from 20.0 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 81(a) by a similar method to Reference Example 23(a) except that tetrahydro-2H-pyran-3-yl 4-methylbenzenesulfonate (3 equivalents) was used instead of benzyl bromide and stirred at 90°C for 5 hours using 3.5 equivalents of caesium carbonate.

(b)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydro-2H-pyran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole

1.0 mg of the title compound was obtained from 9.3 mg of tert-butyl 3-(4-((tetrahydro-2H-pyran-3-yl)oxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 262(a) by a similar method to Example 1(c).

(Example 263)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-

8-carboxylate

11.8 mg of the title compound was obtained from 20.0 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 81(a) by a similar method to Example 262(a) except that ethyl 2-bromo-2,2-difluoroacetate (47.4 mg, 5 equivalents) was used instead of tetrahydro-2H-pyran-3-yl 4-methylbenzenesulfonate.

(b)

2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazole

8.6 mg of the title compound was obtained from 11.8 mg of tert-butyl 3-(4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 263(a) by a similar method to Example 1(c).

(Example 264)

1-((2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-2-ol

(a) tert-Butyl 3-(4-(2-methoxy-2-oxoethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

21.5 mg of the title compound was obtained from 20.0 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-

8-carboxylate obtained in Example 81(a) by a similar method to Example 262(a) except that methyl 2-bromoacetate was used instead of tetrahydro-2H-pyran-3-yl 4-methylbenzenesulfonate.

(b) tert-Butyl 3-(4-(2-hydroxy-2-methylpropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

16.1 mg of the title compound was obtained from 21.5 mg of tert-butyl 3-(4-(2-methoxy-2-oxoethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 264(a) by a similar method to Example 248(e).

(c) 1-((2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-2-ol

12.0 mg of the title compound was obtained from 16.1 mg of tert-butyl 3-(4-(2-hydroxy-2-methylpropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 264(b) by a similar method to Example 1(c).

(Example 265)

1-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-1,1-difluoropropan-2-ol

(a) tert-Butyl 3-(4-(1-(1,1-difluoro-2-(methoxy(methyl)amino)-2-oxoethoxy)-2,2,2-

trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

7.4 mg of the title compound was obtained from 30 mg of tert-butyl 3-(4-(1-(2-ethoxy-1,1-difluoro-2-oxoethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 257(a) by a similar method to Example 250(a).

(b) tert-Butyl 3-(4-(1-(1,1-difluoro-2-oxopropoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as a crude product from 7.4 mg of tert-butyl 3-(4-(1-(1,1-difluoro-2-(methoxy(methyl)amino)-2-oxoethoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 265(a) by a similar method to Example 250(b).

(c) tert-Butyl 3-(4-(1-(1,1-difluoro-2-hydroxypropoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

6.5 mg of the title compound was obtained from the crude product of tert-butyl 3-(4-(1-(1,1-difluoro-2-oxopropoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-

diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 265(b) by a similar method to Example 250(c).

(d) 1-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-1,1-difluoropropan-2-ol

3.4 mg of the title compound was obtained from 6.5 mg of tert-butyl 3-(4-(1-(1,1-difluoro-2-hydroxypropoxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 265(c) by a similar method to Example 1(c).

(Example 266)

3-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutane-1-carbonitrile

(a) tert-Butyl 3-(4-(3-cyanocyclobutoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

33 mg of the title compound was obtained as a crude product from 20 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(c) by a similar method to Reference Example 23(a) except that 3-cyanocyclobutyl 4-methylbenzenesulfonate was used instead of benzyl bromide and stirred at 60°C.

(b) 3-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutane-1-carbonitrile

7.4 mg of the title compound was obtained from 15 mg of tert-butyl 3-(4-(3-cyanocyclobutoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 266(a) by a similar method to Example 1(c).

(Example 267)

2-(3-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutyl)propan-2-ol

(a) tert-Butyl 3-(4-(3-(ethoxycarbonyl)cyclobutoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

52 mg of the title compound was obtained from 45 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(c) by a similar method to Reference Example 23(a) except that 3-(tosyloxy)cyclobutane-1-carboxylate was used instead of benzyl bromide and stirred at 60°C.

(b) tert-Butyl 3-(4-(3-(2-hydroxypropan-2-yl)cyclobutoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-

3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

The title compound was obtained as crude product from 52 mg of tert-butyl 3-(4-(3-(ethoxycarbonyl)cyclobutoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 267(a) by a similar method to Example 248(e).

(c) 2-(3-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutyl)propan-2-ol

7.2 mg of the title compound was obtained from tert-butyl 3-(4-(3-(2-hydroxypropan-2-yl)cyclobutoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 267(b) by a similar method to Example 1(c).

(Example 268) 2-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-1-ol

(a) tert-Butyl 3-(4-((1-ethoxy-2-methyl-1-oxopropan-2-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

1.0 g of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(c) was dissolved in acetonitrile (2.4 mL),

then potassium carbonate (66 mg, 2 equivalents) and ethyl 2-bromo-2-methylpropanoate(71 µL, 2 equivalents) were added, followed by stirring at 80°C for 17 hours. The formation of the product was confirmed by TLC, and then saturated aqueous sodium bicarbonate was added thereto to stop the reaction, which was extracted by ethyl acetate 3 times. The organic phase was dried over anhydrous magnesium sulfate, followed by filtration and vacuum concentration of the filtrate, and thus obtaining 109 mg of the title compound by purification of the residue by preparative TLC (hexane:ethyl acetate = 1:1).

(b) tert-Butyl 3-(4-((1-hydroxy-2-methylpropan-2-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

16 mg of the title compound was obtained from 20 mg of tert-butyl 3-(4-((1-ethoxy-2-methyl-1-oxopropan-2-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 268(a) by a similar method to Example 250(c) except that 31 equivalents of sodium borohydride was used.

(c)

2-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-1-ol

11 mg of the title compound was obtained from 16

mg of tert-butyl 3-(4-((1-hydroxy-2-methylpropan-2-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 268(b) by a similar method to Example 1(c).

(Example 269)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)cyclopropan-1-ol

(a) tert-Butyl 3-(5-(1-hydroxycyclopropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

13.4 mg of the title compound was obtained from 55 mg of ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 187(b) by a similar method to Example 232(b) except that 0.98M methylmagnesium bromide solution in tetrahydrofuran (4 equivalents) and 0.97M ethylmagnesium bromide solution in tetrahydrofuran (6 equivalents) were used instead of 0.97M ethylmagnesium bromide solution in tetrahydrofuran (6 equivalents) and stirred at room temperature for 40 min.

(b)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-

yl)cyclopropan-1-ol

6.5 mg of the title compound was obtained from 13 mg of tert-butyl 3-(5-(1-hydroxycyclopropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 269(a) by a similar method to Example 1(c).

(Example 270)

2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol (optically active)

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active)

72 mg of racemic tert-butyl 3-(7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 234(d) was purified by a preparative HPLC (Gilson, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol = 95:5-80:20, flow rate:15mL/min, detection:UV254nm) and the title compound was obtained in an amount of 28 mg by concentrating fractions with the shorter retention

time peak. 99.9% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IA(particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol = 90:10, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:12.7min).

(b) 2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol (optically active)

The title compound was obtained in an amount of 19 mg from 28 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active) obtained in Example 270(a) by a similar method to Example 1(c).

(Example 271)

2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol (optically active, enantiomer of Example 270)

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active, enantiomer of Example 270(a))

The title compound was obtained in an amount of 31 mg by concentrating fractions with the longer retention time peak obtained in Example 270(a). 99.0%

ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IA(particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol = 90:10, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:16.8min).

(b) 2-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol (optically active, enantiomer of Example 270)

The title compound was obtained in an amount of 20 mg from 31 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-hydroxypropan-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active, enantiomer of Example 270(a)) obtained in Example 271(a) by a similar method to Example 1(c).

(Example 272)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol (optically active)

(a) tert-Butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active)

84.9 mg of racemic tert-butyl 3-(5-(1-

hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 203(b) was purified by a preparative HPLC (Gilson, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol = 80:20, flow rate:15mL/min, detection:UV254nm) and the title compound was obtained in an amount of 32.7 mg by concentrating fractions with the shorter retention time peak.

(b) 1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol (optically active)

The title compound was obtained in an amount of 19.3 mg from 32.7 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active) obtained in Example 272(a) by a similar method to Example 1(c). >99.5% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IA(particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol:diethylamine = 70:30:0.1, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention

time:11.6min).

(Example 273)

1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol (optically active, enantiomer of Example 272)

(a) tert-Butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active, enantiomer of Example 272(a))

The title compound was obtained in an amount of 35.4 mg by concentrating fractions with the longer retention time peak obtained in Example 272(a).

(b) 1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol (optically active, enantiomer of Example 272)

The title compound was obtained in an amount of 19.7 mg from 35.4 mg of tert-butyl 3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate (optically active, enantiomer of Example 272(a)) obtained in Example 273(a) by a similar method to Example 1(c). 89.7% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent,

hexane:isopropyl alcohol:diethylamine = 70:30:0.1, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:15.4min).

(Example 274)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)cyclopropan-1-ol

(a) tert-Butyl 3-(5-(1-hydroxycyclopropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate

10.6 mg of the title compound was obtained from 57 mg of ethyl 2-(8-(tert-butoxycarbonyl)-3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 186(b) by a similar method to Example 232(b) except that 0.98M methylmagnesium bromide solution in tetrahydrofuran (4 equivalents) and 0.97M ethylmagnesium bromide solution in tetrahydrofuran (6 equivalents) were used instead of 0.97M ethylmagnesium bromide solution in tetrahydrofuran (6 equivalents) and stirred at room temperature for 1 hour.

(b)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)cyclopropan-1-ol

10.8 mg of the title compound was obtained from 10 mg of tert-butyl 3-(5-(1-hydroxycyclopropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 274(a) by a similar method to Example 1(c).

(Example 275)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol (optically active)

(a) tert-Butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active)

21 mg of racemic tert-butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate obtained in Example 206(a) was purified by a preparative HPLC (Gilson, column: DAICEL CHIRALPAK IA (particle diameter:5μm, column diameter:2cm, column length:25cm), eluent, hexane:isopropyl alcohol = 90:10-70:30, flow rate:15mL/min, detection:UV254nm) and the title compound was obtained in an amount of 9.9 mg by concentrating fractions with the shorter retention time peak. >99.5% ee. Analysis conditions:

HPLC (HITACHI, column: DAICEL CHIRALPAK IA(particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol = 80:20, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:5.8min).

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol (optically active)

The title compound was obtained in an amount of 5.3 mg from 8.0 mg of tert-butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active) obtained in Example 275(a) by a similar method to Example 1(c).

(Example 276)

1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol (enantiomer of Example 275)

(a) tert-Butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active, enantiomer of Example 275(a))

The title compound was obtained in an amount of 10.9 mg by concentrating fractions with the longer retention time peak obtained in Example 275(a).

>99.5% ee. Analysis conditions: HPLC (HITACHI, column: DAICEL CHIRALPAK IA(particle diameter:5μm, column diameter:0.46cm, column length:25cm), eluent, hexane:isopropyl alcohol = 80:20, flow rate:1mL/min, detection:UV254nm, temperature:25°C, retention time:11.6min).

(b) 1-(2-(3,8-Diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol (enantiomer of Example 275)

The title compound was obtained in an amount of 5.7 mg from 9.5 mg of tert-butyl 3-(5-(2,2-difluoro-1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octane-8-carboxylate (optically active, enantiomer of Example 275(a)) obtained in Example 276(a) by a similar method to Example 1(c).

(Example 277)

3-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1,1-trifluoropropan-2-ol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(3,3,3-trifluoro-2-hydroxypropoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

3.5 mg of the title compound was obtained from 20.0 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-

diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(c) by a similar method to Example 262(a) except that 3-bromo-1,1,1-trifluoropropan-2-ol was used instead of tetrahydro-2H-pyran-3-yl 4-methylbenzenesulfonate.

(b)

3-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1,1-trifluoropropan-2-ol

2.8 mg of the title compound was obtained from 3.5 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(3,3,3-trifluoro-2-hydroxypropoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 277(a) by a similar method to Example 1(c).

(Example 278)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazole

(a) tert-Butyl 3-(4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

12.0 mg of the title compound was obtained from 20.0 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(c) by a similar method to Example 262(a) except that ethyl 2-bromo-2,2-difluoroacetate was used

instead of tetrahydro-2H-pyran-3-yl 4-methylbenzenesulfonate.

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazole

9.1 mg of the title compound was obtained from 12.0 mg of tert-butyl 3-(4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 278(a) by a similar method to Example 1(c).

(Example 279)

1-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-2-ol

(a) tert-Butyl 3-(4-(2-methoxy-2-oxoethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

20.4 mg of the title compound was obtained from 20.0 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(c) by a similar method to Example 262(a) except that methyl 2-bromoacetate was used instead of tetrahydro-2H-pyran-3-yl 4-methylbenzenesulfonate.

(b) tert-Butyl 3-(4-(2-hydroxy-2-methylpropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

20.0 mg of the title compound was obtained from 20.4 mg of tert-butyl 3-(4-(2-methoxy-2-oxoethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 279(a) by a similar method to Example 248(e).

(c) 1-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-2-ol

15.3 mg of the title compound was obtained from 20.0 mg of tert-butyl 3-(4-(2-hydroxy-2-methylpropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 279(b) by a similar method to Example 1(c).

(Example 280)

3-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2,3-dimethylbutan-2-ol

(a) tert-Butyl 3-(4-(1-((1-ethoxy-2-methyl-1-oxopropan-2-yl)oxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

33 mg of the title compound was obtained from 40 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 120(b) by a similar method to Example 271(a)

except that 9 equivalents of potassium carbonate and 9 equivalents of ethyl 2-bromo-2-methylpropanoate were used.

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-((3-hydroxy-2,3-dimethylbutan-2-yl)oxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

15 mg of the title compound was obtained from 33 mg of tert-butyl 3-(4-(1-((1-ethoxy-2-methyl-1-oxopropan-2-yl)oxy)-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 280(a) by a similar method to Example 248(e).

(c) 3-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2,3-dimethylbutan-2-ol

11 mg of the title compound was obtained from 15 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-((3-hydroxy-2,3-dimethylbutan-2-yl)oxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 280(b) by a similar method to Example 1(c).

(Example 281)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxy-2-

methylpropoxy)ethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxy-2-methylpropoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

25 mg of the title compound was obtained from 42 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 255(a) by a similar method to Example 102(e).

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxy-2-methylpropoxy)ethyl)benzo[d]oxazole

16 mg of the title compound was obtained from 25 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxy-2-methylpropoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 281(a) by a similar method to Example 1(c).

(Example 282) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-((1-methoxycyclopropyl)methoxy)ethyl)benzo[d]oxazole

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-((1-methoxycyclopropyl)methoxy)ethyl)benzo[d]oxazol-

2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

30 mg of the title compound was obtained from 36 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 232(b) by a similar method to Example 102(e).

(b) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-((1-methoxycyclopropyl)methoxy)ethyl)benzo[d]oxazole

12 mg of the title compound was obtained from 30 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-((1-methoxycyclopropyl)methoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 282(a) by a similar method to Example 1(c).

(Example 283) 2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxycyclopropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) tert-Butyl 3-(5-(1-methoxycyclopropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

10.8 mg of the title compound was obtained from

15 mg of tert-butyl 3-(5-(1-hydroxycyclopropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 269(a) by a similar method to Example 102(e) except that 6 equivalents of sodium hydride was used.

(b)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxycyclopropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole

8.6 mg of the title compound was obtained from 10.8 mg of tert-butyl 3-(5-(1-methoxycyclopropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 283(a) by a similar method to Example 1(c).

(Example 284)

1-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2-methylpropan-2-ol

(a) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

10.8 mg of the title compound was obtained from 15 mg of tert-butyl 3-(5-(1-hydroxycyclopropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-

yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 269(a) by a similar method to Example 8(a).

(b) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxy-2-oxoethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

136 mg of the title compound was obtained from 182 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 284(a) by a similar method to Example 73(a) except that methyl bromoacetate was used instead of bromoacetonitrile and stirred at 50°C.

(c) tert-Butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

46 mg of the title compound was obtained from 67 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxy-2-oxoethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 284(b) by a similar method to Example 248(e).

(d)

1-(1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2-methylpropan-2-ol

33 mg of the title compound was obtained from 45 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-hydroxy-2-methylpropoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 284(c) by a similar method to Example 1(c).

(Example 285)

3-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutan-1-ol

(a) tert-Butyl 3-(4-(3-benzyloxy)cyclobutoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

83 mg of the title compound was obtained from 100 mg of tert-butyl 3-(4-hydroxy-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 248(c) by a similar method to Reference Example 23(a) except that 3-(benzyloxy)cyclobutyl 4-methylbenzenesulfonate was used instead of benzyl bromide and stirred at 60°C.

(b) tert-Butyl 3-(4-(3-hydroxycyclobutoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

24 mg of the title compound was obtained from 83 mg of tert-butyl 3-(4-(3-benzyloxy)cyclobutoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-

diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 285(a) by a similar method to Example 248(c).

(c) 3-((2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutan-1-ol

11 mg of the title compound was obtained from 24 mg of tert-butyl 3-(4-(3-hydroxycyclobutoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 285(b) by a similar method to Example 1(c).

(Example 286)

1-((1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)methyl)cyclopropan-1-ol

(a) tert-Butyl 3-(7-(thiazol-4-yl)-4-(2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

34 mg of the title compound was obtained from 63 mg of tert-butyl 3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxy-2-oxoethoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 284(b) by a similar method to Example 232(b).

(b) 1-((1-(2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)methyl)cyclopropan-1-ol

18 mg of the title compound was obtained from 34

mg of tert-butyl 3-(7-(thiazol-4-yl)-4-(2,2,2-trifluoro-1-((1-hydroxycyclopropyl)methoxy)ethyl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate obtained in Example 286(a) by a similar method to Example 1(c).

(Example 287)

2-(3,6-Diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole

(a) Ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate

250 mg of the title compound was obtained from 275 mg of ethyl 7-bromo-2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 187(a) by a similar method to Example 8(a).

(b) tert-Butyl 3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptane-6-carboxylate

120 mg of the title compound was obtained from 97 mg of ethyl 2-(6-(tert-butoxycarbonyl)-3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate obtained in Example 287(a) by a similar method to

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CECI EST LE TOME 1 DE 2
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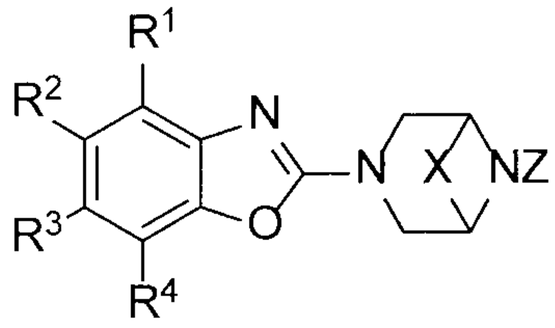
[CLAIMS]

[Claim 1]

A compound represented by the general formula (1) below or a pharmacologically acceptable salt thereof:



(1)

[In the formula (1),

R^1 and R^2 may be the same or different and each represents a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyl group, an optionally substituted C_{6-10} monocyclic or polycyclic aryl group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkyl group, an optionally substituted 4- to 10-membered monocyclic or bicyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic or bicyclic nonaromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted di-C_{1-6} alkyl amino group, an optionally

substituted C_{3-7} cycloalkyl amino group, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{2-6} alkenyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted C_{6-10} monocyclic or polycyclic aryloxy group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkyloxy group, an optionally substituted 4- to 10-membered monocyclic or bicyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic or bicyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group [two C_{1-6} alkyl groups in the di-C_{1-6} alkylsulfamoyl group may form a pyrrolidin-1-yl group or a morpholino group with an adjacent nitrogen atom], a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an optionally

substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkylaminocarbonyl group, an optionally substituted C_{1-6} alkyloxycarbonyl group, or an optionally substituted hydroxyaminocarbonyl group,

R^3 represents a hydrogen atom,

R^4 represents an optionally substituted 4- to 10-membered monocyclic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom,

X represents a group represented by the following formula: $-CH_2-$, $-CH_2-CH_2-$, $-CH_2-CH_2-CH_2-$, or $-CH_2-O-CH_2-$, and

Z represents a hydrogen atom or a hydroxyl group.]

[Claim 2]

The compound or the pharmacologically acceptable salt thereof according to Claim 1 wherein, in the general formula (1),

R^1 represents a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally

substituted C_{3-7} cycloalkyl group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group [two C_{1-6} alkyl groups in the di-C_{1-6} alkylsulfamoyl group may form a pyrrolidin-1-yl group or a morpholino

group with an adjacent nitrogen atom], a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic aralkylaminocarbonyl group, an optionally substituted C_{1-6} alkyloxycarbonyl group, or an optionally substituted hydroxyaminocarbonyl group, and

R^2 represents a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{2-6} alkenyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group,

an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group, a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkylaminocarbonyl group, or an optionally substituted C_{1-6} alkyloxycarbonyl group.

[Claim 3]

The compound or the pharmacologically acceptable salt thereof according to Claim 1 wherein, in the

general formula (1),

R^1 represents a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyl group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an

optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group [two C_{1-6} alkyl groups in the di-C_{1-6} alkylsulfamoyl group may form a pyrrolidin-1-yl group or a morpholino group with an adjacent nitrogen atom], a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7} cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic aralkylaminocarbonyl group, an optionally substituted C_{1-6} alkyloxycarbonyl group, or an optionally substituted hydroxyaminocarbonyl group, and

R^2 represents a hydrogen atom.

[Claim 4]

The compound or the pharmacologically acceptable salt thereof according to Claim 1 wherein, in the general formula (1),

R^1 represents a hydrogen atom, and

R^2 represents a hydrogen atom, a halogen atom, a hydroxyl group, a carboxy group, a cyano group, an optionally substituted C_{1-6} alkyl group, an optionally substituted 4- to 10-membered monocyclic aromatic

heterocyclic group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} acylamino group, an optionally substituted C_{1-6} alkyloxy group, an optionally substituted C_{2-6} alkenyloxy group, an optionally substituted C_{1-6} alkyloxy-C_{1-6} alkyl group, an optionally substituted C_{3-7} cycloalkyloxy group, an optionally substituted 4- to 10-membered monocyclic aromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted 4- to 10-membered monocyclic nonaromatic heterocyclyloxy group containing 1 to 4 heteroatoms selected from an oxygen atom, a nitrogen atom, and a sulfur atom, an optionally substituted C_{1-6} alkylthio group, an optionally substituted C_{1-6} alkylsulfonyl group, an optionally substituted C_{1-6} alkylsulfinyl group, an optionally substituted mono-C_{1-6} alkylsulfamoyl group, an optionally substituted di-C_{1-6} alkylsulfamoyl group, a sulfamoyl group, an optionally substituted C_{1-6} alkylcarbonyl group, an aminocarbonyl group, an optionally substituted 1-(C_{1-6} alkyloxy)imino-C_{1-6} alkyl group, an aminocarbonyl group, an optionally substituted mono-C_{1-6} alkylaminocarbonyl group, an optionally substituted di-C_{1-6} alkylaminocarbonyl group, an optionally substituted C_{3-7}

cycloalkylaminocarbonyl group, an optionally substituted C_{7-11} monocyclic or polycyclic aralkylaminocarbonyl group, or an optionally substituted C_{1-6} alkyloxycarbonyl group.

[Claim 5]

The compound or the pharmaceuticaly acceptable salt thereof according to Claim 1 wherein, the compound represented by the formula (1) is

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

7-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(furan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-

(oxazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(5-fluoropyridin-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,
2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,
7-(5-chloro-7-(pyridin-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole,
2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazole,
7-(5-chloro-7-(1H-pyrazol-1-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,
7-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,
2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-chloro-7-

(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole,

7-(5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3-oxa-7,9-diazabicyclo[3.3.1]nonane,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-isopropyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-methyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-

yl)-4-(trifluoromethyl)benzo[d]oxazole,

N-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)acetamide,

N-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)acetamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-chloro-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-

(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole,

N-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide,

N-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide,

N-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)acetamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-sulfonamide,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-

yl)benzo[d]oxazole-5-sulfonamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-ol,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoroethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-isopropoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(oxetan-3-ylmethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)methyl)propane-1,3-diol,

5-(allyloxy)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazole,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)acetonitrile,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)acetic acid,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-methoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-ol,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-cyclobutoxy-7-(thiazol-2-yl)benzo[d]oxazole,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)acetonitrile,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3-methoxypropan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydrofuran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4,7-di(thiazol-2-yl)benzo[d]oxazole,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3-oxa-7,9-diazabicyclo[3.3.1]nonan-7-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazole-5-carboxylate,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)propan-2-ol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)propan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-N,N-dimethyl-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(morpholino)methanone,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(piperidin-1-yl)methanone,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)(azetidin-1-yl)methanone,

N-benzyl-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-5-carboxamide,

N-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-N-methylacetamide,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(morpholinomethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-N,N-dimethylmethanamine,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-one,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-one,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)ethan-1-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol,

(2-(3,6-diazabicyclo[3.1.1]hepan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)methanol,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-N,N-dimethyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(morpholino)methanone,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(piperidin-1-yl)methanone,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,

(R)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,

(S)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,

(R)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,

(S)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

(R)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

(S)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethan-1-ol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol,

(R)-2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol,

(S)-2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethoxy)-2-methylpropan-2-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2-difluoroethan-1-ol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1-difluoropropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

1-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

(R)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

(S)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethyl acetate,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

(R)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

(S)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)ethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)acetonitrile,

2-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)acetonitrile,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazole,

1-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethoxy)propan-2-ol,

1-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-2,2,2-trifluoroethane-1,1-diol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

2-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

2-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-

yl)benzo[d]oxazole,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole-5-carboxylate,

2-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)propan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(methoxymethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)methanol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)propan-2-

ol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)propan-2-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-one,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-one,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazole,

ethyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-

carboxylate,

ethyl 2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate,

ethyl 2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylate,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxylic acid,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

2-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-

methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)(azetidin-1-yl)methanone,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-N-(2-hydroxyethyl)-N-methyl-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole-5-carboxamide,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)(3-hydroxy-3-(trifluoromethyl)azetidin-1-yl)methanone,

(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)methanol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol,

(R)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-

(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol,

(S)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2-methylpropan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(R)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(S)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(R)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(S)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2,2-difluoro-1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-5-(1,1,1-trifluoro-2-methoxypropan-2-yl)-4-

(trifluoromethoxy)benzo[d]oxazole,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-1,1,1-trifluoropropan-2-ol,

(E)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime,

(Z)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime,

(E)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime,

(Z)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)ethan-1-one O-methyloxime,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-methoxyethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2,2,2-trifluoroethoxy)ethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1-ethoxy-2,2,2-trifluoroethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)ethan-1-ol,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetonitrile,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)ethan-1-ol,

2-(1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetonitrile,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxyethoxy)ethyl)benzo[d]oxazole,

4-(1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

4-(1-((1H-tetrazol-5-yl)methoxy)-2,2,2-trifluoroethyl)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

1-((1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)methyl)cyclopropan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethane-1,1-diol,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol,

(R)-2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol,

(S)-2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(1,1,1-trifluoro-2-methoxypropan-2-yl)benzo[d]oxazole,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-1,1,1-trifluoropropan-2-ol,

methyl 2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylate,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylic acid,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)propan-2-ol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-

yl)benzo[d]oxazol-4-yl)propan-2-ol,

1-(2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,9-diazabicyclo[3.3.1]nonan-3-yl)-4-(1-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-one,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)ethan-1-one,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

(R)-1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

(S)-1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-

(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetic acid,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydro-2H-pyran-4-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2-methylpropan-2-ol,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)acetamide,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-1,1-difluoro-2-methylpropan-2-ol,

2-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2,2-difluoroethan-1-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)propan-2-ol,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)propan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-((tetrahydro-2H-pyran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-2-ol,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-1,1-difluoropropan-2-ol,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutane-1-carbonitrile,

2-(3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutyl)propan-2-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)cyclopropan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)cyclopropan-1-ol,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1,1-trifluoropropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(difluoromethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2-methylpropan-2-ol,

3-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2,3-dimethylbutan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-(2-methoxy-2-methylpropoxy)ethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-((1-methoxycyclopropyl)methoxy)ethyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(1-methoxycyclopropyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

1-(1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)-2-methylpropan-2-ol,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclobutan-1-ol,

1-((1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)-2,2,2-trifluoroethoxy)methyl)cyclopropan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

2-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-

4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(pyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(oxazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)propan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((tetrahydro-2H-pyran-4-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

4-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-4,4-difluoro-2-methylbutan-2-ol,

2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-5-(2-methoxypropan-2-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazole,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)cyclopropan-1-ol,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(R)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-

(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(S)-1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(R)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

(S)-1-(2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)-4-(trifluoromethoxy)benzo[d]oxazol-5-yl)-2,2-difluoroethan-1-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

4-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)cyclohexan-1-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(4-methylthiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-

4-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropan-2-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-4-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-4,4,4-trifluoro-2-methylbutan-2-ol,

4-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)tetrahydro-2H-thiopyran 1,1-dioxide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(pyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(pyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(4-methylthiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-

difluoro-2-methylpropan-2-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(5-fluoropyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1H-pyrazol-1-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(oxazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(2H-1,2,3-triazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(((S)-tetrahydrofuran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(((R)-tetrahydrofuran-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(oxetan-3-yloxy)-7-(thiazol-2-yl)benzo[d]oxazole,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3,3-difluoro-2-methylpropane-1,2-diol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1,2,4-thiadiazol-5-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-

2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(1-methyl-1H-pyrazol-3-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(5-fluoropyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(pyrimidin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(isothiazol-3-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(5-fluoropyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(3-methyl-1,2,4-thiadiazol-5-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-((trifluoromethyl)sulfonyl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carbonitrile,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-((5-(trifluoromethyl)pyridin-2-yl)oxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyridin-2-yloxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyrimidin-2-yloxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyrazin-2-yloxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((6-methyl-4-(trifluoromethyl)pyridazin-3-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

(6-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)pyridin-3-yl)methanol,

(6-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-5-(trifluoromethyl)pyridin-3-yl)methanol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-4-((5-(trifluoromethoxy)pyridin-2-yl)oxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-cyclopropyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(methylthio)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(methylsulfinyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(methylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)thio)ethan-1-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)sulfinyl)ethan-1-ol,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)sulfonyl)ethan-1-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((1,1-difluoroallyl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((5-(methylsulfonyl)pyridin-2-yl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-hydroxyethyl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-cyclopropyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-ethyl-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(morpholino)methanone,

(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)(pyrrolidin-1-yl)methanone,

N-benzyl-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-3-methylbutan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(5-chloropyridin-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

(R)-3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3,3-difluoro-2-methylpropane-1,2-diol,

(S)-3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3,3-difluoro-2-methylpropane-1,2-diol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxylic acid,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-hydroxy-7-(thiazol-2-yl)benzo[d]oxazole-4-carboxamide,

3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-morpholino-7-

(thiazol-2-yl)benzo[d]oxazole,

3-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-3,3-difluoropropane-1,2-diol,

3-(4-(1,1-difluoro-2-hydroxy-2-methylpropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

(R)-3-(4-(1,1-difluoro-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

(S)-3-(4-(1,1-difluoro-2-hydroxypropoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

3-(4-(1,1-difluoro-2-hydroxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

3-(5-chloro-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

(2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)pyridin-3-yl)methanol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoropropane-2,2-diol,

(R)-3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-

hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

(S)-3-(7-(thiazol-2-yl)-4-(2,2,2-trifluoro-1-hydroxyethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

3-(7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,6-diazabicyclo[3.1.1]heptan-6-ol,

3-(5-(2-hydroxypropan-2-yl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethoxy)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

3-(5-(1-hydroxyethyl)-7-(thiazol-2-yl)-4-(trifluoromethyl)benzo[d]oxazol-2-yl)-3,8-diazabicyclo[3.2.1]octan-8-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-hydroxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-methoxyethyl)-7-(thiazol-2-yl)benzo[d]oxazole-4-

sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N,N-dimethyl-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-N-(2-hydroxyethyl)-N-methyl-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyrrolidin-1-ylsulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(morpholinosulfonyl)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1,1-difluoro-2-methoxyethoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1,1-difluoro-2-methoxy-2-methylpropoxy)-7-(thiazol-2-yl)benzo[d]oxazole,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(1-methyl-1H-pyrazol-3-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,

1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluorobutan-2-ol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-4-sulfonamide,

1-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)piperidin-4-ol,

4-(2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-

2-yl)benzo[d]oxazol-4-yl)thiomorpholine 1,1-dioxide,
1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-bromo-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,
1-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,
2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-chloro-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(1,1-difluoropropoxy)-7-(thiazol-2-yl)benzo[d]oxazole,
4-(benzo[d]oxazol-2-yldifluoromethoxy)-2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole,
2-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroethan-1-ol,
1-((2-(3,8-diazabicyclo[3.2.1]octan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-1,1-difluoro-2-methylpropan-2-ol,
2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-((1,1-difluoro-3-(pyridin-3-yl)allyl)oxy)-7-(thiazol-2-yl)benzo[d]oxazole,
2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-N-(2-hydroxyethyl)-N-methylacetamide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-N,N-dimethylacetamide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-1-morpholinoethan-1-one,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoroacetamide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-N-(2-hydroxyethyl)acetamide,

2-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-4-yl)oxy)-2,2-difluoro-1-(3-hydroxyazetidin-1-yl)ethan-1-one,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)-5-((5-(trifluoromethyl)pyridin-2-yl)oxy)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-cyclobutyl-7-(thiazol-2-yl)benzo[d]oxazole,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-4-(pyrrolidin-1-yl)-7-(thiazol-2-yl)benzo[d]oxazole,

(6-((2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazol-5-yl)oxy)pyridin-3-yl)methanol,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole-5-carbonitrile,

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-(pyridin-3-yl)-7-(thiazol-2-yl)benzo[d]oxazole, or

2-(3,6-diazabicyclo[3.1.1]heptan-3-yl)-5-cyclobutoxy-7-(thiazol-2-yl)benzo[d]oxazole.

[Claim 6]

A PDE4 inhibitor comprising at least one selected from the group consisting of the compound and the pharmacologically acceptable salt thereof according to any one of Claims 1 to 5 as an active ingredient.

[Claim 7]

A pharmaceutical composition comprising at least one selected from the group consisting of the compound and the pharmacologically acceptable salt thereof according to any one of Claims 1 to 5 as an active ingredient.

(1)