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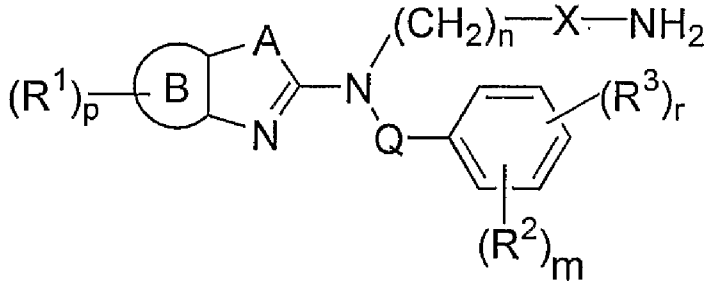
(54) **Title**: FUSED OXAZOLE AND THIAZOLE DERIVATIVES AS TRPMS MODULATORS



(I)

(57) **Abstract**: The present invention provides fused oxazole and thiazole derivatives as TRPM8 (Transient Receptor Potential subfamily M, member 8) modulators. In particular, compounds described herein are useful for treating diseases, disorders, conditions modulated by TRPM8. Also provided herein are processes for preparing compounds described herein, intermediates used in their synthesis, pharmaceutical compositions thereof, and methods for treating or preventing diseases, conditions and/or disorders modulated by TRPM8.

WO 2010/010435 A2

FUSED OXAZOLE AND THIAZOLE DERIVATIVES AS TRPM8 MODULATORS

Related Applications

This application claims the benefit of Indian Patent Application Nos. 1559/MUM/2008 filed on July 22, 2008; 1735/MUM/2008 filed on August 14, 2008; and 2608/MUM/2008 filed on December 15, 2008 and US Provisional Application Nos. 61/087,877 filed on August 11, 2008; 61/095,354 filed on September 09, 2008; and 61/141,102 filed on December 29, 2008, all of which are hereby incorporated by reference.

Technical Field

The present patent application relates to fused oxazole and thiazole derivatives with TRPM8 activity.

Background

Transient receptor potential (TRP) family of ion channels act as sensors of the physical and chemical environment (*Nature* **2003**, *426*, 517-524). These channels are activated by temperature, light and touch etc. They have been classified into seven subfamilies: TRPC (Canonical), TRPV (Vanilloid), TRPM(Melastatin), TRPP(Polycystins), TRPML (Mucolipins), TRPA (ANKTM1, Ankyrin) and TRPN ('*N*OMPC') families. The TRPC family can be divided into 4 subfamilies (TRPC1, TRPC2, TRPC3, 6, 7 and TRPC4, 5) based on sequence functional similarities. Currently the TRPV family has 6 members. TRPV5 and TRPV6 are more closely related to each other than to TRPV1, TRPV2, TRPV3 or TRPV4. TRPA1 is most closely related to TRPV3 and is more closely related to TRPV1 and TRPV2 than to TRPV5 and TRPV6. The TRPM family has 8 members. Constituents include the following: the founding member TRPM1 (Melastatin or LTRPC1), TRPM3 (KIAA1616 or LTRPC3), TRPM7 (TRP-PLIK, ChaK(1), LTRPC7), TRPM6 (ChaK2), TRPM2 (TRPC7 or LTRPC2), TRPM8 (Trp-p8 or CMR1), TRPM5 (Mtr1 or LTRPC5) and TRPM4 (FLJ20041 or LTRPC4). The TRPML family consists of the mucolipins, which include TRPML1 (Mucolipin 1), TRPML2 (Mucolipin 2) and TRPML3 (Mucolipin 3). The TRPP family

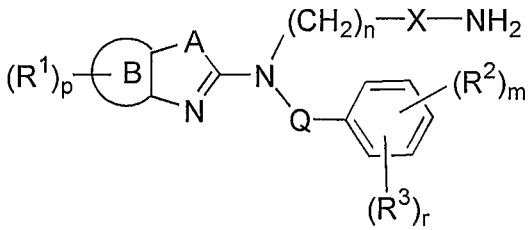
consists of two groups of channels: those predicted to have six transmembrane domains and those that have 11. TRPP2 (PKD2), TRPP3 (PKD2L1), TRPP5 (PKD2L2) are all predicted to have six transmembrane domains. TRPP1 (PKD1, PC1), PKD-REJ and PKD-1L1 are all thought to have 11 transmembrane domains.

Several TRP channels are thermosensitive and together they confer the ability to sense temperature throughout the range from noxious cold to noxious heat. TRPM8 (McKemy DD et al., *Nature,* **2002,** *416(6876)*: 52-58) also called cold-menthol receptor-1(CMR-1) expressed on a subpopulation of somatic sensory nerves on dorsal root ganglion and trigeminal ganglia, which causes sensory nerve excitation. The receptor is known to be stimulated by cool to cold temperatures as well as synthetic cooling compounds such as menthol and icilin, which may be responsible for the therapeutic cooling sensation that these agents evoke.

WO 2006/040136, WO 2007/017092, WO 2007/017093, WO 2007/017094 and WO 2007/080109 describes substituted benzyloxy derivatives as cold menthol receptor-1 (CMR-1) antagonists for the treatment of urological disorders. WO 2007/134107 describes phosphorous bearing compounds as TRPM8 antagonists useful for treating TRPM8 mediated disorders.

Summary

The present patent application relates to compounds of the formula (I):



(I)

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof,

wherein,

A is selected from oxygen or sulfur;

B is selected from fused six membered cycloalkyl ring, aryl ring or heteroaryl ring containing 1, 2 or 3 nitrogen atoms;

X is selected from a bond, -CO, -$CO(CH_2)_n$-, -C=S or -SO_2-;

Q is selected from -$(CH_2)_n$, -CO, -CO-$(CH_2)_n$, -CONH-, -CONHC(R^4R^5)-, -SO_2-, -SO_2CH_2- or -SO_2NR^6-;

at each occurrence of R^1, R^2 and R^3 are independently selected from hydroxyl, halogen, nitro, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted haloalkoxy, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclyl, -COR^7, -$CONR^7$, -$COOR^7$, -NR^4R^5, -$NR^7C(O)R^7$, -$NR^7C(S)R^7$, -OR^8, -$OCOR^7$, -$OC(O)OR^7$or -SR^7;

at each occurrence of R^4, R^5, R^6 and R^7 are independently selected from hydrogen or lower alkyl;

R^8 is selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heteroarylalkyl;

'm' is an integer ranging from 0 to 3, inclusive;

'n' is an integer ranging from 1 to 3, inclusive;

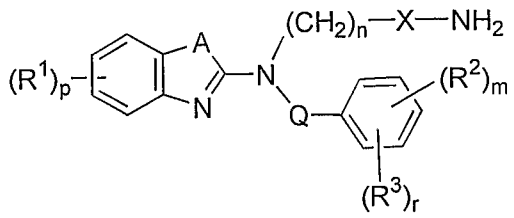
'p' is an integer ranging from 0 to 4, inclusive; and

'r' is an integer ranging from 0 to 2, inclusive.

It should be understood that the formula (I) structurally encompasses all stereo isomer, including enantiomer and diasteriomer, that may be contemplated from the chemical structure of the genus described herein.

The compounds of formula (I) may involve one or more embodiments. It is to be understood that the embodiments below are illustrative of the present invention and are not intended to limit the claims to the specific embodiments exemplified.

According to one embodiment, specifically provided are compounds of the formula (II):



(II)

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof,

wherein,

A is selected from oxygen or sulfur;

X is selected from a bond, -CO, -$CO(CH_2)_n$-, -C=S or -SO_2-;

Q is selected from -$(CH_2)_n$-, -C(O)-, -CO-$(CH_2)_n$-, -CONH-, -$CONHC(R^4R^5)$-, -SO_2-, -SO_2CH_2- or -SO_2NR^6-;

at each occurrence of R^1, R^2 and R^3 are independently selected from hydroxyl, halogen, nitro, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted haloalkoxy, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclyl, -COR^7, -$CONR^7$, -$COOR^7$, -NR^4R^5, -$NR^7C(O)R^7$, -$NR^7C(S)R^7$, -OR^8, -$OCOR^7$, -$OC(O)OR^7$or -SR^7;

at each occurrence of R^4, R^5, R^6 and R^7 are independently selected from hydrogen or lower alkyl;

R^8 is selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heteroarylalkyl;

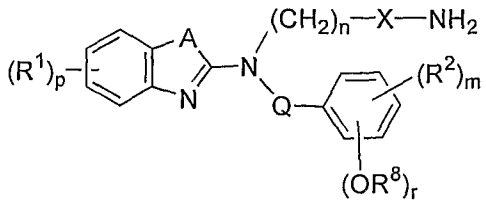
'm' is an integer ranging from 0 to 3, inclusive;

'n' is an integer ranging from 1 to 3, inclusive;

'p' is an integer ranging from 0 to 4, inclusive; and

'r' is an integer ranging from 0 to 2, inclusive.

According to one embodiment, specifically provided are compounds of the formula (IIa):



(IIa)

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof,

wherein,

A is selected from oxygen or sulfur;

X is selected from a bond, -CO, -$CO(CH_2)_n$-, -C=S or -SO_2-;

Q is selected from -$(CH_2)_n$, -CO, -CO-$(CH_2)_n$, -CONH-, -$CONHC(R^4R^5)$-, -SO_2-, -SO_2CH_2- or -SO_2NR^6-;

at each occurrence of R^1 and R^2 are independently selected from hydroxyl, halogen, nitro, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted haloalkoxy, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclyl, -COR^7, -$CONR^7$, -$COOR^7$, -NR^4R^5, -$NR^7C(O)R^7$, -$NR^7C(S)R^7$, -OR^8, -$OCOR^7$, -$OC(O)OR^7$or -SR^7;

at each occurrence of R^4, R^5, R^6 and R^7 are independently selected from hydrogen or lower alkyl;

R^8 is selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heteroarylalkyl;

'm' is an integer ranging from 0 to 3, inclusive;

'n' is an integer ranging from 1 to 3, inclusive;

'p' is an integer ranging from 0 to 4, inclusive; and

'r' is an integer ranging from 0 to 2, inclusive.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which A is oxygen.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which A is sulfur.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which Q is $-(CH_2)-$.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which Q is -CONH-.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which Q is $-CONH-CH(CH_3)-$.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which Q is $-CO-CH_2-CH_2-$.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which Q is $-SO_2-$.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which n is 1 or 2.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which X is bond.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which p, m are 0 and r is 0 or 1.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which R^1 is haloalkyl preferably trifluoromethyl, p is 1.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which R^2 is one or more substituents selected from halogen (e.g., fluorine, chlorine, bromine or iodine), alkyl (e.g., methyl, *tert* butyl), haloalkyl preferably trifluoromethyl or R^8 is alkyl preferably methyl.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which R^8 is alkyl preferably isobutyl, aryl preferably phenyl, arylalkyl preferably benzyl, cycloalkyl preferably cyclopentyl, substituted or unsubstituted heteroaryl preferably pyridyl wherein substituent is selected from cyano or haloalkyl preferably trifluoromethyl.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which R^8 is heteroarylalkyl preferably $-CH_2$-pyridyl.

According to one embodiment, specifically provided are compounds of the formula (IIa) in which R^8 is cycloalkylalkyl (e.g., cyclopropylmethyl, cyclohexylmethyl).

Below are representative compounds, which are illustrative in nature only and are not intended to limit to the scope of the invention:

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(2-fluorobenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-benzothiazol-2-yl)-*N*-(2-fluorobenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(2-chlorobenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(2-bromobenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(3,4-difluorobenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-isobutoxy-3-methoxybenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-cyclopropylmethoxy-3-methoxybenzyl)]ethane -1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-cyclopentyloxy-3-methoxybenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-[cyclohexylmethoxy]-3-methoxybenzyl)] ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(3-methoxy-4-phenoxybenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(3-methoxy-4-{[5-(trifluoromethyl)pyridin-2-yl]oxy} benzyl)]ethane-1,2-diamine hydrochloride;

6-(4-{[(2-Aminoethyl)(1,3-benzoxazol-2-yl)amino]methyl}-2-methoxyphenoxy) nicotinonitrile hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(3-methoxy-4-[pyridin-4-ylmethoxy]benzyl) ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-[pyridin-2-yloxy]benzyl)] propane-1,3-diamine hydrochloride;

1-(2-Aminoethyl)-1-(1,3-benzoxazol-2-yl)-3-(4-*tert*-butylphenyl)urea hydrochloride;

1-(2-Aminoethyl)-1-(1,3-benzoxazol-2-yl)-3-[4-fluoro-2-(trifluoromethyl) phenyl]urea hydrochloride;

1-(2-Aminoethyl)-1-(1,3-benzothiazol-2-yl)-3-[4-fluoro-2-(trifluoromethyl) phenyl]urea hydrochloride;

1-(2-Aminoethyl)-1-(1,3-benzothiazol-2-yl)-3-[(1*S*)-1-phenylethyl]urea hydrochloride;

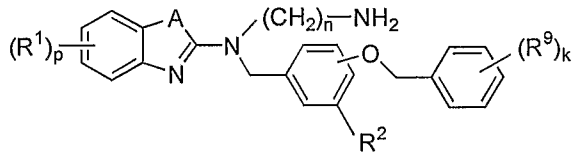
N-(2-Aminoethyl)-*N*-1,3-benzothiazol-2-yl-[3-(2-benzyloxy)phenyl]propanamide hydrochloride;

N-(2-Aminoethyl)-*N*-1,3-benzothiazol-2-yl-4-methylbenzenesulfonamide hydrochloride;

1-[*N*-(2-Aminoethyl)-*N*-(1,3-benzothiazol-2-yl)]-3,4-dichlorobenzenesulfonamide hydrochloride;

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof.

According to one embodiment, specifically provided are compounds of the formula (IIb):



(IIb)

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof,

wherein,

A is selected from oxygen or sulfur;

at each occurrence of R^1 and R^2 are independently selected from hydroxyl, halogen, nitro, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted haloalkoxy, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclyl, $-COR^7$, $-CONR^7$, $-COOR^7$, $-NR^4R^5$, $-NR^7C(O)R^7$, $-NR^7C(S)R^7$, $-OR^8$, $-OCOR^7$, $-OC(O)OR^7$or $-SR^7$;

at each occurrence of R^4, R^5, R^6 and R^7 are hydrogen or lower alkyl;

R^8 is selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heteroarylalkyl;

R^9 is selected from halogen, hydroxyl, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted haloalkyl, substituted or unsubstituted haloalkoxy, nitro, cyano, $-SR^7$, $-NR^4R^5$, $-NR^7C(O)R^7$, $-NR^7C(S)R^7$, $-OCOR^7$, $-OC(O)OR^7$, $-COR^7$, $-COOR^7$ or $-CONR^7$;

'n' is an integer ranging from 1 to 3, inclusive;

'p' is an integer ranging from 0 to 4, inclusive; and

'k' is an integer ranging from 0 to 4, inclusive.

According to one embodiment, specifically provided are compounds of the formula (IIb) in which A is oxygen.

According to one embodiment, specifically provided are compounds of the formula (IIb) in which A is sulfur.

According to one embodiment, specifically provided are compounds of the formula (IIb) in which n is 1 or 2.

According to one embodiment, specifically provided are compounds of the formula (IIb) in which p and k is 0.

According to one embodiment, specifically provided are compounds of the formula (IIb) in which m is 1.

According to one embodiment, specifically provided are compounds of the formula (IIb) in which R^1 is one or more substituents independently selected from halogen (e.g., fluorine, chlorine, bromine or iodine), alkyl (e.g., methyl), haloalkyl preferably trifluoromethyl, haloalkoxy (e.g., $-OCF_3$) or R^8 is alkyl preferably methyl.

According to one embodiment, specifically provided are compounds of the formula (IIb) in which R^2 is halogen (e.g., fluorine, chlorine, bromine or iodine), wherein R^8 is alkyl preferably methyl.

According to one embodiment, specifically provided are compounds of the formula (IIb) in which R^9 is one or more substituents independently selected from halogen (e.g., fluorine, chlorine, bromine or iodine), alkyl (e.g., methyl) or haloalkyl preferably trifluoromethyl.

Below are representative compounds, which are illustrative in nature only and are not intended to limit to the scope of the invention:

N-(1,3-Benzoxazol-2-yl)-*N*-(2-benzyloxybenzyl)ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{2-(4-trifluoromethylbenzoxy)benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)]-*N*-{2-(2-fluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)]-*N*-{2-(2,6-difluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)]-*N*-[{2-(2,4-difluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-[(2-benzyloxy)benzyl]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{2-(2-fluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{2-[(4-trifluoromethyl)benzyloxy]benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{2-(2,4-difluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-{2-(Benzyloxybenzyl)}-*N*-(6-chloro-1,3-benzothiazol-2-yl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(2-Benzyloxybenzyl)-*N*-(5-trifluorormethoxy-1,3-benzothiazol-2-yl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-benxyloxybenzyl)]ethane-1,2-diamine hydro chloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-benzyloxybenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(4-Benzyloxybenzyl)-*N*-(5-trifluromethyl-1,3-benzothiazol-2-yl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{(4-benzyloxy-3-chlorobenzyl}]ethane-1,2-diamine hydrochloride;

1[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-benzyloxy-3-methoxybenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{3-methoxy-[4-(2-methylbenzyloxy)]benzyl}ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-benzyloxy-3-chlorobenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)]-*N*-(4-benzyloxy-3-methoxybenzyl)ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{3-methoxy-[4-(2-methylbenzyloxy)benzyl]} ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)]-*N*-{4-(2-fluorobenzyloxy)-3-methoxybenzyl}] ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{4-(2-trifluromethylbenzyloxy)-3-methoxy benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{4-(3-trifluromethylbenzyloxy)-3-methoxy benzyl}] ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{4-(2,4-difluorobenzyloxy)-3-methoxy benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{[4-(2,6-difluorobenzyloxy)]-3-methoxybenzyl}] ethane-1,2-diamine hydrochloride;

1-[*N*-[(4-Benzyloxy-3-methoxy)benzyl]-*N*-(5-trifluorormethoxy-1,3-benzothiazol-2-yl)]ethane-1,2-diamine hydrochloride;

1-[*N*-[(4-Benzyloxy-3-methoxy)benzyl]-*N*-(6-chloro-1,3-benzothiazol-2-yl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-(5-chloro-1,3-benzothiazol-2-yl)ethane-1,2-diamine hydrochloride;

1-[*N*-[(4-Benzyloxy-3-methoxy)benzyl]-*N*-(5-trifluromethyl-1,3-benzothiazol-2-yl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(5-Fluoro-1,3-benzothiazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxy benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(5,6-Dimethoxy-1,3-benzothiazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxy benzyl}] ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(2-benzyloxybenzyl)]propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{2-(2-fluorobenzyloxy)benzyl}]propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{4-(2,6-difluorobenzyloxy)benzyl}]propane-1,3-diamine hydrochloride;

1-[*N*-(2-Benzyloxybenzyl)-*N*-(5-chloro-1,3-benzoxazol-2-yl)]propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-[2-methylbenzyloxy]benzyl)]propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-benzyloxy-3-methoxybenzyl)]propane-1,3-diamine hydrochloride;

1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-(5-fluoro-1,3-benzoxazol-2-yl)propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxybenzyl}] propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(3-methoxy-[4-(2-methylbenzyloxy)]benzyl)] propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(3-methoxy-[4-(2-trifluoromethylbenzyloxy)] benzyl)ethane-1,2-diamine hydrochloride;

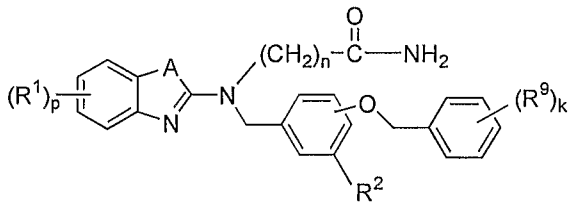
1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{[4-(2,6-diflurobenzyloxy)]-3-methoxybenzyl}] propane-1,3-diamine hydrochloride;

1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-(5-methyl-1,3-benzoxazol-2-yl)propane-1,3-diamine hydrochloride;

1-[*N*-(5-Chloro-1,3-benzoxazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxybenzyl}]propane-1,3-diamine hydrochloride;

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof.

According to another embodiment, specifically provided are compounds of the formula (IIc):



(IIc)

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof,

wherein,

A is selected from oxygen or sulfur;

at each occurrence of R^1 and R^2 are independently selected from hydroxyl, halogen, nitro, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted haloalkoxy, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclyl, $-COR^7$, $-CONR^7$, $-COOR^7$, $-NR^4R^5$, $-NR^7C(O)R^7$, $-NR^7C(S)R^7$, $-OR^8$, $-OCOR^7$, $-OC(O)OR^7$or $-SR^7$;

at each occurrence of R^4, R^5, R^6 and R^7 are independently selected from hydrogen or lower alkyl;

R^8 is selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heteroarylalkyl;

R^9 is hydrogen, halogen, hydroxyl, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted haloalkyl, substituted or unsubstituted haloalkoxy, nitro, cyano, $-SR^7$, $-NR^4R^5$, $-NR^7C(O)R^7$, $-NR^7C(S)R^7$, $-OCOR^7$, $-OC(O)OR^7$, $-COR^7$, $-COOR^7$ or $-CONR^7$;

'n' is an integer ranging from 1 to 3, inclusive;

'p' is an integer ranging from 0 to 4, inclusive; and

'k' is an integer ranging from 0 to 4, inclusive.

According to one embodiment, specifically provided are compounds of the formula (IIc) in which A is oxygen.

According to one embodiment, specifically provided are compounds of the formula (IIc) in which A is sulfur.

According to one embodiment, specifically provided are compounds of the formula (IIc) in which n is 1.

According to one embodiment, specifically provided are compounds of the formula (IIc) in which R^1 and R^9 both are hydrogen.

According to one embodiment, specifically provided are compounds of the formula (IIc) in which R^1 is substituent independently selected from halogen (e.g., fluorine, chlorine, bromine or iodine).

According to one embodiment, specifically provided are compounds of the formula (IIc) in which R^2 is $-OR^8$ wherein R^8 is alkyl preferably methyl.

According to one embodiment, specifically provided are compounds of the formula (IIc) in which R^9 is independently selected from halogen (e.g., fluorine, chlorine, bromine or iodine) or alkyl (e.g., methyl).

Below are representative compounds, which are illustrative in nature only and are not intended to limit to the scope of the invention:

2-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-benzyloxy-3-methoxybenzyl)amino]acetamide;

2-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxybenzyl}amino) acetamide;

2-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-benzyloxy-3-methoxybenzyl)amino]acetamide;

2-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxybenzyl} amino] acetamide ;

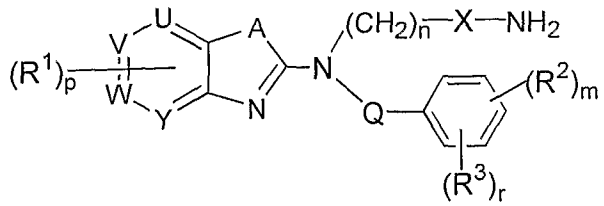
2-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{[4-(2,6-difluorobenzyloxy)]-3-methoxybenzyl} amino] acetamide;

2-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{[3-methoxy-[4-(2-methylbenzyloxy)]benzyl} amino] acetamide;

2-{*N*-[4-(Benzyloxy)-3-methoxybenzyl]-*N*-(5-fluoro-1,3-benzothiazol-2-yl) amino}acetamide;

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof.

According to one embodiment, specifically provided are compounds of the formula (III):



(III)

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof,

wherein,

A is selected from oxygen or sulfur;

U, V, W and Y are independently selected from carbon or nitrogen; with the proviso that atleast one of the U, V, W and Y is nitrogen;

X is selected from a bond, -CO, $-CO(CH_2)_n-$, -C=S or $-SO_2-$;

Q is selected from $-(CH_2)_n$, -CO, $-CO-(CH_2)_n$, -CONH-, $-CONHC(R^4R^5)-$, $-SO_2-$, $-SO_2CH_2-$ or $-SO_2NR^6-$;

at each occurrence of R^1, R^2 and R^3 are independently selected from hydroxyl, halogen, nitro, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted haloalkoxy, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclyl, $-COR^7$, $-CONR^7$, $-COOR^7$, $-NR^4R^5$, $-NR^7C(O)R^7$, $-NR^7C(S)R^7$, $-OR^8$, $-OCOR^7$, $-OC(O)OR^7$or $-SR^7$;

at each occurrence of R^4, R^5, R^6 and R^7 are independently selected from hydrogen or lower alkyl;

R^8 is selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heteroarylalkyl;

'm' is an integer ranging from 0 to 3, inclusive;

'n' is an integer ranging from 1 to 3, inclusive;

'p' is an integer ranging from 0 to 4, inclusive; and

'r' is an integer ranging from 0 to 2, inclusive.

According to one embodiment, specifically provided are compounds of the formula (III) in which U is nitrogen and remaining V, W and Y are carbon.

According to one embodiment, specifically provided are compounds of the formula (III) in which V is nitrogen and remaining U, W and Y are carbon.

According to one embodiment, specifically provided are compounds of the formula (III) in which Y is nitrogen and remaining U, V and W are carbon.

According to one embodiment, specifically provided are compounds of the formula (III) in which A is oxygen.

According to one embodiment, specifically provided are compounds of the formula (III) in which A is sulfur.

According to one embodiment, specifically provided are compounds of the formula (III) in which Q is $-(CH_2)-$.

According to one embodiment, specifically provided are compounds of the formula (III) in which n is 1.

According to one embodiment, specifically provided are compounds of the formula (III) in which X is bond.

According to one embodiment, specifically provided are compounds of the formula (III) in which X is -(CO)-.

According to one embodiment, specifically provided are compounds of the formula (III) in which p, m and k are 0.

According to one embodiment, specifically provided are compounds of the formula (III) in which R^1 is substituent may be at any carbon are independently selected from halogen (e.g., fluorine, chlorine, bromine or iodine) or haloalkyl preferably trifluoromethyl.

According to one embodiment, specifically provided are compounds of the formula (III) in which R^2 is $-OR^8$ wherein R^8 is alkyl preferably methyl.

According to one embodiment, specifically provided are compounds of the formula (III) in which R^3 is $-OR^8$ wherein, R^8 is substituted or unsubstituted arylalkyl preferably benzyl wherein one or more substituents are independently selected from halogen (e.g., fluorine, chlorine, bromine or iodine), alkyl (e.g., methyl).

Below are representative compounds, which are illustrative in nature only and are not intended to limit to the scope of the invention:

1-[*N*-{4-[(2-methylbenzyloxy)]benzyl}-*N*-[1,3]oxazolo[4,5-*b*]pyridin-2-yl]ethane-1,2-diamine hydrochloride;

1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-[1,3]thiazolo[5,4-*b*]pyridin-2-yl]ethane-1,2-diamine hydrochloride;

1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-[1,3]thiazolo[4,5-*b*]pyridin-2-yl]ethane-1,2-diamine hydrochloride;

1-[*N*-{3-Methoxy-4-[(2-methylbenzyloxy)]benzyl}-*N*-[1,3]thiazolo[5,4-*b*]pyridin-2-yl]ethane-1,2-diamine hydrochloride;

1-[*N*-{4-(2-Fluorobenzyloxy)-3-methoxybenzyl}-*N*-[1,3]thiazolo[5,4-*b*]pyridin-2-yl]ethane-1,2-diamine hydrochloride;

1-[*N*-{4-(2-Fluorobenzyloxy)-3-methoxybenzyl}-*N*-[1,3]thiazolo[4,5-*b*]pyridin-2-yl]ethane-1,2-diamine hydrochloride;

1-[*N*-{4-(2,6-Difluorobenzyloxy)-3-methoxybenzyl}-*N*-[1,3]thiazolo[5,4-*b*]pyridin-2-yl]ethane-1,2-diamine hydrochloride;

1-[*N*-(7-Chloro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxybenzyl}]ethane-1,2-diamine hydrochloride;

N-(7-Chloro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-{3-methoxy-4-[(2-methylbenzyl oxy)] benzyl}ethane-1,2-diamine hydrochloride;

1-[*N*-{4-(2-Fluorobenzyloxy)-3-methoxybenzyl}-*N*-[6-(trifluoromethyl)[1,3] thiazolo [4,5-*b*] pyridin-2-yl] ethane-1,2-diamine hydrochloride;

1-[*N*-{4-[(2,6-Difluorobenzyloxy)-3-methoxybenzyl]}-*N*-[1,3]thiazolo[5,4-*c*]pyridin-2-yl]ethane-1,2-diamine hydrochloride;

N-(7-Bromo[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-{3-methoxy-[4-(2-methylbenzyl oxy)] benzyl}ethane-1,2-diamine hydrochloride;

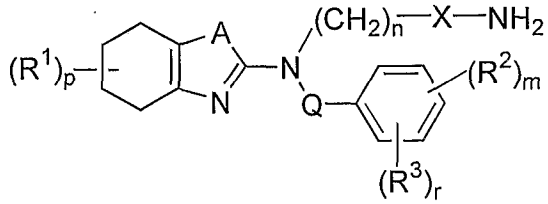
N-(7-Bromo[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-{[4-(2,6-difluorobenzyloxy)]-3-methoxybenzyl} ethane-1,2-diamine hydrochloride;

2-{[4-(Benzyloxy)-3-methoxybenzyl]([1,3]thiazolo[5,4-*b*]pyridin-2-yl)amino} acetamide;

2-{[4-(Benzyloxy)-3-methoxybenzyl]([1,3]thiazolo[4,5-*b*]pyridin-2-yl) amino}acetamide;

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof.

According to one embodiment, specifically provided are compounds of the formula (IV):



(IV)

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof,

wherein,

A is selected from oxygen or sulfur;

X is selected from a bond, -CO, -$CO(CH_2)_n$-, -C=S or -SO_2-;

Q is selected from -$(CH_2)_n$, -CO, -CO-$(CH_2)_n$, -CONH-, -$CONHC(R^4R^5)$-, -SO_2-, -SO_2CH_2- or -SO_2NR^6-;

at each occurrence of R^1, R^2 and R^3 are independently selected from hydroxyl, halogen, nitro, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted haloalkoxy, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclyl, -COR^7, -$CONR^7$, -$COOR^7$, -NR^4R^5, -$NR^7C(O)R^7$, -$NR^7C(S)R^7$, -OR^8, -$OCOR^7$, -$OC(O)OR^7$or -SR^7;

at each occurrence of R^4, R^5, R^6 and R^7 are independently selected from hydrogen or lower alkyl;

R^8 is selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heteroarylalkyl;

'm' is an integer ranging from 0 to 3, inclusive;

'n' is an integer ranging from 1 to 3, inclusive;

'p' is an integer ranging from 0 to 4, inclusive; and

'r' is an integer ranging from 0 to 2, inclusive

Certain compounds of formula (I) are capable of existing in stereoisomeric forms (e.g. diastereomers and enantiomers). The present invention includes these stereoisomeric forms (including diastereomers and enantiomers) and mixtures of them.

According to one embodiment, specifically provided are compounds of the formula (IV) in which A is sulfur.

According to one embodiment, specifically provided are compounds of the formula (IV) in which Q is -(CH_2)-.

According to one embodiment, specifically provided are compounds of the formula (IV) in which n is 1.

According to one embodiment, specifically provided are compounds of the formula (IV) in which X is bond.

According to one embodiment, specifically provided are compounds of the formula (IV) in which m, p and r are 0.

According to one embodiment, specifically provided are compounds of the formula (IV) in which R^2 is $-OR^8$ wherein R^8 is alkyl preferably methyl.

According to one embodiment, specifically provided are compounds of the formula (IV) in which R^3 is halogen (e.g., fluorine, chlorine, bromine or iodine) or $-OR^8$ wherein, R^8 is substituted or unsubstituted arylalkyl preferably benzyl wherein one or more substituents are independently selected from halogen (e.g., fluorine, chlorine, bromine or iodine), alkyl (e.g., methyl, isopropyl, ethyl).

Below are representative compounds, which are illustrative in nature only and are not intended to limit to the scope of the invention:

N-(3,4-Difluorobenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl)ethane-1,2-diamine hydrochloride;

N-(4-[2-Methylbenzyloxy]benzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) ethane-1,2-diamine hydrochloride;

N-(4-Benzyloxy-3-methoxybenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) ethane-1,2-diamine hydrochloride;

N-(3-Methoxy-[4-(2-methylbenzyloxy)]benzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzo thiazol-2-yl) ethane-1,2-diamine hydrochloride;

N-([4-(2-Ethylbenzyloxy)]-3-methoxy]benzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzo thiazol-2-yl) ethane-1,2-diamine hydrochloride;

N-{4-(2-Isopropylbenzyloxy)-3-methoxybenzyl}-N-(4,5,6,7-tetrahydro-1,3-benzo thiazol-2-yl) ethane-1,2-diamine hydrochloride;

N-([4-(2-Fluorobenzyloxy)]-3-methoxybenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzo thiazol-2-yl) ethane-1,2-diamine hydrochloride;

N-(4-[(2,6-Difluorobenzyloxy)]-3-methoxybenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzo thiazol-2-yl) ethane-1,2-diamine hydrochloride;

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof.

The present invention also provides a pharmaceutical composition that includes at least one compound described herein and at least one pharmaceutically acceptable excipient (such as a pharmaceutically acceptable carrier or diluent). Preferably, the pharmaceutical composition comprises a therapeutically effective amount of at least one compound described herein. The compounds described in the present patent application may be associated with a pharmaceutically acceptable excipient (such as a carrier or a diluent) or be diluted by a carrier, or enclosed within a carrier which can be in the form of a capsule, sachet, paper or other container.

The compounds and pharmaceutical compositions of the present invention are useful for modulating TRPM receptors, which modulation is believed to be related to a variety of disease states.

The present patent application further provides a method of inhibiting TRPM8 receptors in a subject in need thereof by administering to the subject one or more compounds described herein in an amount effective to cause inhibition of such receptor.

Detailed Description

Definitions

The terms "halogen" and "halo" include fluorine, chlorine, bromine or iodine.

The term "alkyl" unless otherwise specified refers to an optionally substituted straight or branched saturated hydrocarbon chain having from 1 to 16 carbon atoms, which is attached to the rest of the molecule by a single bond, e.g. methyl, ethyl, n-propyl, 1-methylethyl (isopropyl), n-butyl, n-pentyl and 1,1-dimethylethyl (t-butyl). Alkyl groups are optionally interrupted by atom(s) or group(s) independently selected from oxygen, sulfur, oxidized sulfur or NR^t (wherein R^t is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl or aryl).

The term "alkenyl" unless otherwise specified refers to an optionally substituted aliphatic hydrocarbon group containing atleast one double bond and which may be a straight or branched chain having from 2 to about 20 carbon atoms, with *cis* or *trans*; *E* or *Z* stereochemistry e.g. ethenyl, 1-propenyl, 2-propenyl (allyl), iso-propenyl, 2-methyl-1-propenyl, 1-butenyl and 2-butenyl. Alkenyl groups are optionally interrupted by atom(s)

or group(s) independently selected from oxygen, sulfur, oxidized sulfur or NR^t (wherein R^t is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl or aryl).

The term "alkynyl" unless otherwise specified refers to an optionally substituted straight or branched chain hydrocarbyl radical having at least one carbon-carbon triple bond, and having from 2 to about 20 carbon atoms, e.g. ethynyl, propynyl, and butynyl. It is optionally interrupted by atom(s) or group(s) independently selected from oxygen, sulfur, oxidized sulfur or NR^t (wherein R^t is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl or aryl).

The term "haloalkyl" refers to a group containing at least one halogen and an alkyl portion as define above, that is, a haloalkyl is a substituted alkyl group that is substituted with one or more halogens. Unless otherwise specified, all structural isomers of a given structure, for example, all enantiomers and all diasteriomers, are included within this definition. Exemplary haloalkyl groups include fluoromethyl, chloromethyl, fluoroethyl, chloroethyl, trifluoromethyl and the like. Unless otherwise specified, a haloalkyl group has from 1 to 20 carbon atoms.

The term "haloalkoxy" refers to an alkoxy group with a halo substituent, where alkoxy refers to an alkyl group attached via an oxygen linkage to the rest of the molecule and halo groups are as defined above. Exemplary haloalkoxy groups include fluoromethoxy, chloromethoxy, trifluoromethoxy, trichloroethoxy, fluoroethoxy, chloroethoxy, trifloroethoxy, perfluoroethoxy($-OCF_2CF_3$), trifluoro-*tert*-butoxy, hexafluoro-*tert*-butoxy, perfluoro-*tert*-butoxy($-OC(CF_3)_3$) and the like. Unless otherwise specified, an haloalkoxy group typically has from 1 to 20 carbon atoms.

The term "cycloalkyl" denotes a non-aromatic mono or multicyclic ring system of 3 to about 12 carbon atoms, such as cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. Examples of multicyclic cycloalkyl groups include, but are not limited to, perhydronapththyl, adamantyl and norbornyl groups, bridged cyclic groups or sprirobicyclic groups, e.g., spiro(4,4) non-2-yl.

The term "cycloalkylalkyl" refers to a cyclic ring-containing radical having 3 to about 8 carbon atoms directly attached to an alkyl group. The cycloalkylalkyl group may be attached to the main structure at any carbon atom in the alkyl group that results in the

creation of a stable structure. Non-limiting examples of such groups include cyclopropylmethyl, cyclobutylethyl, and cyclopentylethyl.

The term "aryl" unless otherwise specified refers to an optionally substituted carbocyclic aromatic radical having from 6 to 14 carbon atoms, wherein the ring is mono-, bi- or tricyclic, such as, but not limited to, phenyl, naphthyl, indanyl, and biphenyl.

The term "arylalkyl" refers to an aryl group as defined above directly bonded to an alkyl group as defined above, e.g., $-CH_2C_6H_5$ or $-C_2H_4C_6H_5$.

The term "heteroaryl" refers to an optionally substituted 5–14 membered aromatic heterocyclic ring radical with one or more heteroatoms independently selected from N, O and S. The heteroaryl may be monocyclic, bicyclic or tricyclic ring system. Examples of such heteroaryl ring radicals includes but are not limited to oxazolyl, imidazolyl, pyrrolyl, furanyl, pyridinyl, pyrimidinyl, pyrazinyl, benzofuranyl, indolyl, benzothiazolyl, benzoxazolyl, carbazolyl, quinolyl and isoquinolyl. The heteroaryl ring radical may be attached to the main structure at any heteroatom or carbon atom.

The term "heteroarylalkyl" unless otherwise specified refers to optionally substituted heteroaryl ring radical directly bonded to an alkyl group. The heteroarylalkyl radical may be attached to the main structure at any carbon atom in the alkyl group that results in the creation of a stable structure, wherein the heteroaryl and alkyl are the same as defined earlier.

The term "heterocyclic ring" or "heterocyclyl" unless otherwise specified refers optionally substituted non-aromatic 3 to 15 membered ring radical which consists of carbon atoms and from one to five heteroatoms selected from nitrogen, phosphorus, oxygen and sulfur. The heterocyclic ring radical may be a mono-, bi- or tricyclic ring system, which may include fused, bridged or spiro ring systems and the nitrogen, phosphorus, carbon, oxygen or sulfur atoms in the heterocyclic ring radical may be optionally oxidized to various oxidation states. In addition, the nitrogen atom may be optionally quaternized; also, unless otherwise constrained by the definition the heterocyclic ring or heterocyclyl may optionally contain one or more olefinic bond(s). Examples of such heterocyclic ring radicals include, but are not limited to, azepinyl, azetidinyl, acridinyl, benzodioxolyl, benzodioxanyl, benzofurnyl, carbazolyl, cinnolinyl, dioxolanyl, indolizinyl, thienyl, naphthyridinyl, perhydroazepinyl, phenazinyl,

phenothiazinyl, phenoxazinyl, indolyl, phthalazinyl, pyridyl, pteridinyl, purinyl, quinazolinyl, quinoxalinyl, quinolinyl, isoquinolinyl, tetrazoyl, imidazolyl, tetrahydroisouinolyl, piperidinyl, piperazinyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, 2-oxoazepinyl, pyrrolyl, 4-piperidonyl, pyrrolidinyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazolyl, oxazolinyl, oxasolidinyl, triazolyl, indanyl, isoxazolyl, isoxasolidinyl, morpholinyl, thiazolyl, thiazolinyl, thiazolidinyl, isothiazolyl, quinuclidinyl, isothiazolidinyl, isoindolyl, indolinyl, isoindolinyl, octahydroindolyl, octahydroisoindolyl, quinolyl, isoquinolyl, decahydroisoquinolyl, benzimidazolyl, thiadiazolyl, benzopyranyl, benzothiazolyl, benzoxazolyl, furyl, tetrahydrofuryl, tetrahydropyranyl, benzothienyl, thiamorpholinyl, thiamorpholinyl sulfoxide, thiamorpholinyl sulfone, dioxaphospholanyl, oxadiazolyl, chromanyl and isochromanyl. The heterocyclic ring radical may be attached to the main structure at any heteroatom or carbon atom that results in the creation of a stable structure.

Unless otherwise specified, the term "substituted" as used herein refers to substitution with (fully or partially) any one or any combination of the following substituents: hydroxy, halogen, carboxyl, cyano, nitro, oxo (=O), thio (=S), substituted or unsubstituted alkyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenylalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heterocyclylalkyl ring, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclic ring, substituted or unsubstiuted guanidine, $-COOR^x$, $-C(O)R^x$, $-C(S)R^x$, $-C(O)NR^xR^y$, $-C(O)ONR^xR^y$, $-NR^xCONR^yR^z$, $-N(R^x)SOR^y$, $-N(R^x)SO_2R^y$, $-(=N-N(R^x)R^y)$, $-NR^xC(O)OR^y$, $-NR^xR^y$, $-NR^xC(O)R^y$, $-NR^xC(S)R^y$, $-NR^xC(S)NR^yR^z$, $-SONR^xR^y$, $-SO_2NR^xR^y$, $-OR^x$, $-OR^xC(O)NR^yR^z$, $-OR^xC(O)OR^y$, $-OC(O)R^x$, $-OC(O)NR^xR^y$, $-R^xNR^yC(O)R^z$, $-R^xOR^y$, $-R^xC(O)OR^y$, $-R^xC(O)NR^yR^z$, $-R^xC(O)R^y$, $-R^xOC(O)R^y$, $-SR^x$, $-SOR^x$, $-SO_2R^x$ and $-ONO_2$, wherein R^x, R^y and R^z are independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl,

substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkenyl, substituted or unsubstituted amino, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted heterocyclylalkyl ring, substituted or unsubstituted heteroarylalkyl or substituted or unsubstituted heterocyclic ring. According to one embodiment, the substituents in the aforementioned "substituted" groups cannot be further substituted. For example, when the substituent on "substituted alkyl" is "substituted aryl", the substituent on "substituted aryl" cannot be "substituted alkenyl".

The term "prodrug" means a compound that is transformed in vivo to yield a compound of Formula (I) or a pharmaceutically acceptable salt of the compound. The transformation may occur by various mechanisms, such as through hydrolysis in blood. A discussion of the use of prodrugs is provided by T. Higuchi and W. Stella, "Pro-drugs as Novel Delivery Systems," Vol. 14 of the *A.C.S. Symposium Series, and in Bioreversible Carriers in Drug Design, ed.* Edward B. Roche, *American Pharmaceutical Association and Pergamon Press*, 1987.

The term "treating" or "treatment" of a state, disorder or condition includes: (a) preventing or delaying the appearance of clinical symptoms of the state, disorder or condition developing in a subject that may be afflicted with or predisposed to the state, disorder or condition but does not yet experience or display clinical or subclinical symptoms of the state, disorder or condition; (b) inhibiting the state, disorder or condition, i.e., arresting or reducing the development of the disease or at least one clinical or subclinical symptom thereof; or (c) relieving the disease, i.e., causing regression of the state, disorder or condition or at least one of its clinical or subclinical symptoms.

The term "subject" includes mammals (especially humans) and other animals, such as domestic animals (e.g. household pets including cats and dogs) and non-domestic animals (such as wildlife).

A "therapeutically effective amount" means the amount of a compound that, when administered to a subject for treating a state, disorder or condition, is sufficient to effect such treatment. The "therapeutically effective amount" will vary depending on the compound, the disease and its severity and the age, weight, physical condition and responsiveness of the subject to be treated.

The compounds described in the present patent application may form salts. Non-limiting examples of pharmaceutically acceptable salts forming part of this patent application include salts derived from inorganic bases salts of organic bases, salts of chiral bases, salts of natural amino acids and salts of non-natural amino acids.

Certain compounds of the present invention, including compounds of formula (I), are capable of existing in stereoisomeric forms (e.g. diastereomers and enantiomers). The present invention includes these stereoisomeric forms (including diastereomers and enantiomers) and mixtures of them. The various stereoisomeric forms of the compounds of the present invention may be separated from one another by methods known in the art or a given isomer may be obtained by stereospecific or asymmetric synthesis. Tautomeric forms and mixtures of compounds described herein are also contemplated.

Pharmaceutical Compositions

The pharmaceutical composition provided in the present invention includes at least one compound described herein and at least one pharmaceutically acceptable excipient (such as a pharmaceutically acceptable carrier or diluent). Preferably, the contemplated pharmaceutical compositions include the compound(s) described herein in an amount sufficient to inhibit TRPM8 receptor in a subject.

The subjects contemplated include, for example, a living cell and a mammal, including human mammal. The compound of the present invention may be associated with a pharmaceutically acceptable excipient (such as a carrier or a diluent) or be diluted by a carrier, or enclosed within a carrier which can be in the form of a capsule, sachet, paper or other container.

Examples of suitable carriers include, but are not limited to, water, salt solutions, alcohols, polyethylene glycols, polyhydroxyethoxylated castor oil, peanut oil, olive oil, gelatin, lactose, terra alba, sucrose, dextrin, magnesium carbonate, sugar, cyclodextrin, amylose, magnesium stearate, talc, gelatin, agar, pectin, acacia, stearic acid or lower alkyl ethers of cellulose, silicic acid, fatty acids, fatty acid amines, fatty acid monoglycerides and diglycerides, pentaerythritol fatty acid esters, polyoxyethylene, hydroxymethylcellulose and polyvinylpyrrolidone.

The carrier or diluent may include a sustained release material, such as glyceryl monostearate or glyceryl distearate, alone or mixed with a wax.

The pharmaceutical composition may also include one or more pharmaceutically acceptable auxiliary agents, wetting agents, emulsifying agents, suspending agents, preserving agents, salts for influencing osmotic pressure, buffers, sweetening agents, flavoring agents, colorants, or any combination of the foregoing. The pharmaceutical composition of the invention may be formulated so as to provide quick, sustained, or delayed release of the active ingredient after administration to the subject by employing procedures known in the art.

The pharmaceutical compositions described herein may be prepared by conventional techniques known in the art. For example, the active compound can be mixed with a carrier, or diluted by a carrier, or enclosed within a carrier, which may be in the form of an ampoule, capsule, sachet, paper, or other container. When the carrier serves as a diluent, it may be a solid, semi-solid, or liquid material that acts as a vehicle, excipient, or medium for the active compound. The active compound can be adsorbed on a granular solid container, for example, in a sachet.

The pharmaceutical compositions may be in conventional forms, for example, capsules, tablets, aerosols, solutions, suspensions or products for topical application.

The route of administration may be any route which effectively transports the active compound of the invention to the appropriate or desired site of action. Suitable routes of administration include, but are not limited to, oral, nasal, pulmonary, buccal, subdermal, intradermal, transdermal, parenteral, rectal, depot, subcutaneous, intravenous, intraurethral, intramuscular, intranasal, ophthalmic (such as with an ophthalmic solution) or topical (such as with a topical ointment).

Solid oral formulations include, but are not limited to, tablets, capsules (soft or hard gelatin), dragees (containing the active ingredient in powder or pellet form), troches and lozenges. Tablets, dragees, or capsules having talc and/or a carbohydrate carrier or binder or the like are particularly suitable for oral application. Liquid formulations include, but are not limited to, syrups, emulsions, soft gelatin and sterile injectable

liquids, such as aqueous or non-aqueous liquid suspensions or solutions. For parenteral application, particularly suitable are injectable solutions or suspensions formulation.

Liquid formulations include, but are not limited to, syrups, emulsions, soft gelatin and sterile injectable liquids, such as aqueous or non-aqueous liquid suspensions or solutions.

For parenteral application, particularly suitable are injectable solutions or suspensions, preferably aqueous solutions with the active compound dissolved in polyhydroxylated castor oil.

Suitable doses of the compounds for use in treating the diseases and disorders described herein can be determined by those skilled in the relevant art. Therapeutic doses are generally identified through a dose ranging study in humans based on preliminary evidence derived from the animal studies. Doses must be sufficient to result in a desired therepautic benefit without causing unwanted side effects. For example, the daily dosage of the TRPM8 modulator can range from about 0.1 to about 30.0 mg/kg. Mode of administration, dosage forms, suitable pharmaceutical excipients, diluents or carriers can also be well used and adjusted by those skilled in the art. All changes and modifications are envisioned within the scope of the present invention.

Methods of Treatment

The compounds of the present inventions are useful for treatment of Urological diseases such as detrusor overactivity (overactive bladder), urinary incontinence, neurogenic detrusor overactivity (detrusor hyperflexia), idiopathic detrusor overactivity (detrusor instability), benign prostatic hyperplasia and lower urinary tract symptoms.

The compounds and pharmaceutical compositions of the present invention can be administered to treat any disorder, condition or disease treatable by inhibition of TRPM8.

For instance, the compounds and pharmaceutical compositions of the present invention are suitable for treatment or prophylaxis of the following diseases, conditions, and disorders mediated or associated with the activity of TRPM8 receptors: pain, chronic pain, complex regional pain syndrome, neuropathic pain, postoperative pain, rheumatoid arthritic pain, osteoarthritic pain, back pain, visceral pain, cancer pain, algesia, neuralgia, migraine, neuropathies, diabetic neuropathy, sciatica, HIV-related neuropathy, post-

herpetic neuralgia, fibromyalgia, nerve injury, ischaemia, neurodegeneration, stroke, post stroke pain, multiple sclerosis, respiratory diseases, asthma, cough, COPD, inflammatory disorders, oesophagitis, gastroeosophagal reflux disorder (GERD), irritable bowel syndrome, inflammatory bowel disease, pelvic hypersensitivity, cystitis, burns, psoriasis, eczema, emesis, stomach duodenal ulcer, pruritus, prostate cancer, benign prostatic hyperalgesia, overactive bladder, painful bladder, dental pain and cold hypersensitivity of teeth.

General Methods of Preparation

The compounds described herein, including compounds of general formula (I) and specific examples described herein can be prepared by techniques known to one skilled in the art, for example, through the reaction sequences depicted in Synthetic Schemes 1-9. Furthermore, in the following schemes, where specific acids, bases, reagents, coupling agents, solvents, etc. are mentioned, it is understood that other suitable acids, bases, reagents, coupling agents etc. may be used and are included within the scope of the present invention. Modifications to reaction conditions, for example, temperature, duration of the reaction or combinations thereof are envisioned as part of the present invention. The compounds obtained by using the general reaction scheme may be of insufficient purity. These compounds can be purified by any of the methods for purification of organic compounds known in the art, for example, crystallization or silica gel or alumina column chromatography using different solvents in suitable ratios.

The 2-chlorobenzoxazole and 2-chlorobenzothiazole derivatives used for the synthesis of compounds of the present invention were either commercially available or prepared using reported procedure (Sharpe, C. J.; Palmer, P. J.; Evans, D. E.; Brown, G. R.; King, Gillian; Shadbolt, R. S.; Trigg, R. J.; Ward, R. J. *J. Med. Chem.* **1972**, *15*, 523). 2-Chloropyridothiazoles were prepared using reported procedures as described in WO2006/44775. 2-Aminobenzoxazole and 2-aminobenzothiazole derivatives were prepared using a reported procedure as described in Jimonet, P. et al. *J. Med. Chem.* **1999**, *42*, 2828.

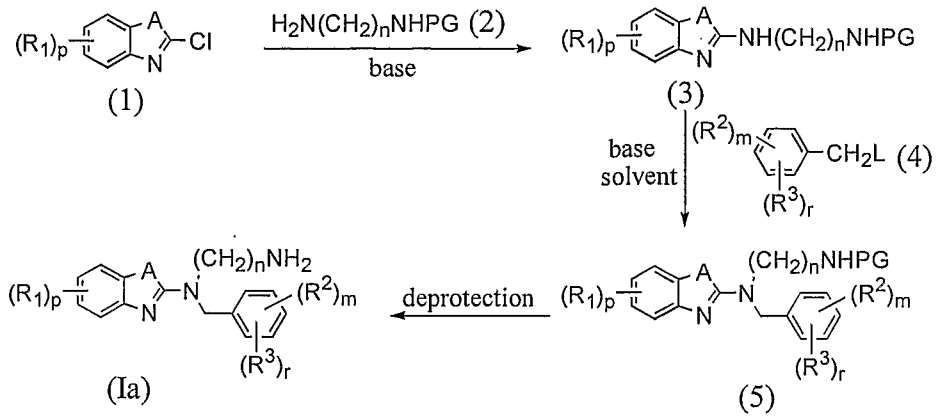
Several of the substituted benzyl bromides used in the present study was purchased from commercial sources. Some of the commercially unavailable derivatives were prepared according to reported procedures [(a) Yang, L-M. et al. *Bioorg. & Med.*

Chem. Lett. **1996**, *6*, 941; (b) Thomas, G. W. et al. *Phytochemistry* **1985**, *24*, 469; (c) Thomas, J. et al. *Phytochemistry* **1998**, *48*, 893; (d) Potter, Barry V. L. et al. *J. Med. Chem.* **2007**, *50*, 3540.] Substituted benzyl methanesulfonates were prepared from the corresponding alcohols according to a reported procedure (Yang, L-M. et al. *Bioorg. & Med. Chem. Lett.* **1996**, *6*, 941). 3-Methoxy-4-phenoxybenzyl bromide used was prepared according to the procedure described in Tomita, M. et al. *Chem. Pharma. Bull.* **1965**, *13*(11), 1341. The corresponding bromomethyl pyridyl ethers were prepared according to the procedure described in Bargar, T. M. et al. *J. Med. Chem.* **1986**, *29*, 427.

The compounds of the present invention represented by the formula (Ia) to (Ih) were prepared using methods described in synthetic schemes 1 to 9.

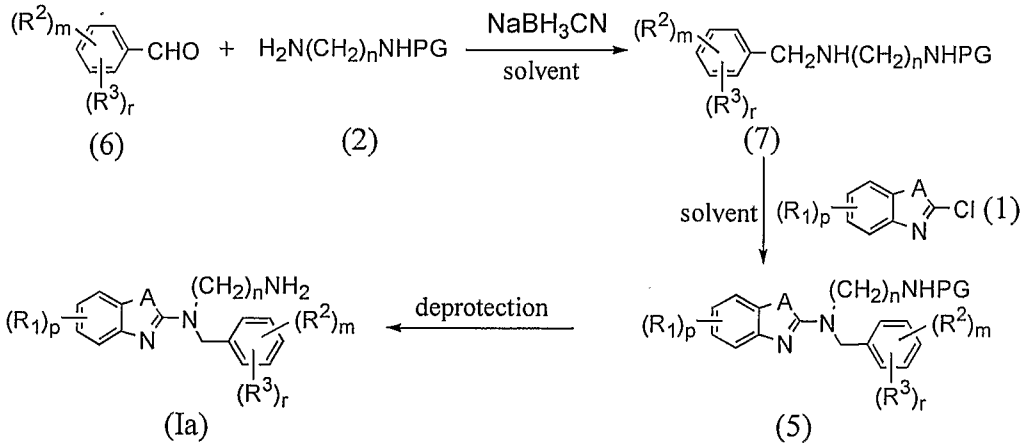
Compounds of the general formula (Ia) where R^1, R^2, R^3, m, n, p, r and 'A' are defined as above and is prepared as shown in synthetic scheme 1. 2-Chlorobenzoxazole or 2-chlorobenzothiazole of the formula (1) is coupled with an aminoalkylcarbamate (where PG represent *tert*-butyloxy carbonyl group) of the formula (2) in the presence of a suitable base gives compounds of the general formula (3). Intermediate of the general formula (3) on coupling with benzyl halide (L is a halogen) of the general formula (4) in the presence of a suitable base gives intermediate of the formula (5). The coupling reaction of (3) is also carried out with intermediate of the formula (4), where L is a methanesulfonate group, preferably in the presence of strong base such as sodium hydride and tetra-butylammonium iodide to give intermediate of the formula (5). The carbamate (PG is *tert*-butyloxycarbonyl) of the formula (5) is converted to compounds of the general formula (Ia) under strong acidic conditions such as hydrochloric acid in ethyl acetate or trifluoroacetic acid to give the free amine represented by the general formula (Ia). Useful approaches for protection of amino group and its deprotection may be found in Greene, T. W. *Protective Groups in Organic Synthesis*, John Wiley and Sons, New York, 1991.

Synthetic Scheme 1



An alternative synthetic approach is described in synthetic scheme 2 for the preparation of compounds of the general formula (Ia). Reductive amination (analogous procedure described in Davioud, C. et. al. *J. Med. Chem.* **2005**, *48*, 22, 7024) of benzaldehyde derivative of formula (6) with aminoalkylcarbamate (PG is *tert*-butyloxycarbonyl) of the formula (2) using sodium cyanoborohydride in a suitable solvent such as dichloroethane gives the substituted *tert*-butyl benzylamino alkyl carbamate derivative of the general formula (7). This intermediate (7) is coupled with 2-halo-benzoxazole or benzothiazole of the formula (1) in the presence of a suitable base such as triethylamine and in a suitable solvent gives compounds of the formula (5). Deprotection of compound (5) affords the free amine of formula (Ia) as described in synthetic scheme 1.

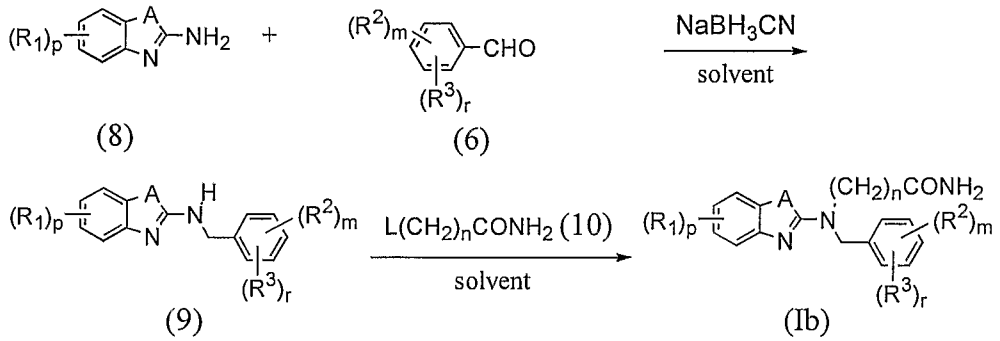
Synthetic Scheme-2



Compounds of the general formula (Ib) where R^1, R^2, R^3, m, n, p, r and 'A' are as defined above, is prepared as shown in synthetic scheme 3. Reductive amination (analogous

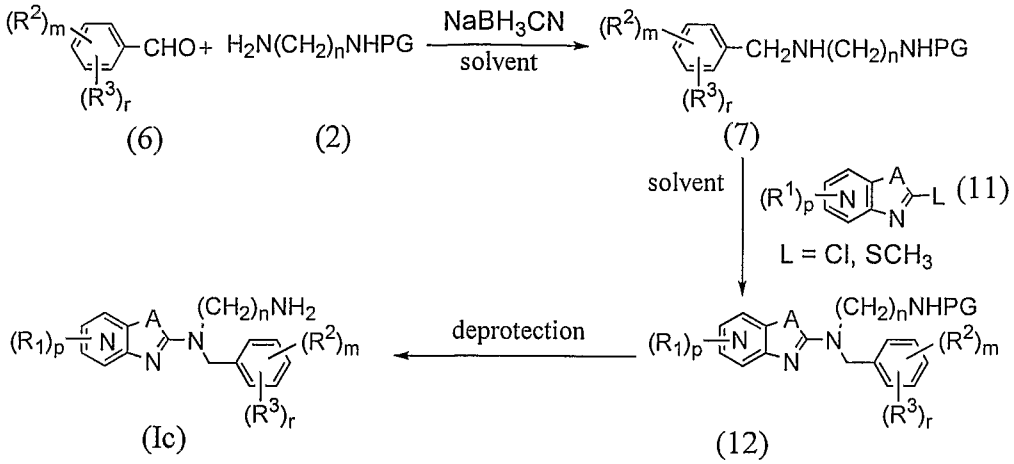
procedure described in Davioud, C. et. al. *J. Med. Chem.* **2005**, *48*, 22, 7024) of benzaldehyde derivative of the formula (6) with intermediate (8) in a solvent such as xylene using sodium cyanoborohydride gives compound of the formula (9). The intermediate of the formula (9) is coupled with an appropriate haloalkyl amide of the formula (10) in the presence of a suitable base such as sodium hydride or cesium carbonate, in a suitable solvent gives compound of general formula (Ib).

Synthetic Scheme 3



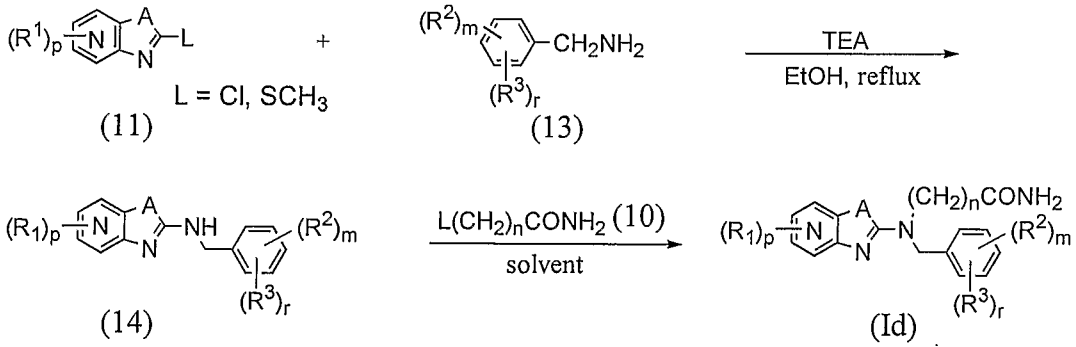
Oxazolopyridine and thiazolopyridine derivatives (N represents a nitrogen atom on the six-membered ring) represented by the general formula (Ic), where R^1, R^2, R^3, m, n, p, r and 'A' are as defined above, is prepared as shown in synthetic scheme 4. Thus, aldehyde of the general formula (6) on reductive amination (analogous procedure described in Davioud, C. et. al. *J. Med. Chem.* **2005**, *48*, 22, 7024) with aminoalkyl carbamate of the formula (2), using sodium cyanoborohydride in a suitable solvent (DCE) gives the substituted *tert*-butyl benzylamino alkyl carbamate derivative of the general formula (7). Intermediate (7) on coupling with 2-chlorothiazolopyridine or 2-methylthio thiazolo pyridine derivatives of the general formula (11) in the presence of a base gives the tertiary amine derivative (12). The carbamate (12) is cleaved to the corresponding amine under strongly acidic conditions to give intermediate of the general formula (Ic).

Synthetic Scheme 4



Various oxazolopyridines and thiazolopyridines derivatives (N represents a nitrogen atom on the six-membered ring) of the general formula (Id), where R^1, R^2, R^3, m, n, p, r and 'A' are as defined above, are prepared as shown in synthetic scheme 5. Thus, coupling reaction of intermediate of the formula (11), where L is chlorine or thioalkyl group, with substituted benzylamine of the formula (13) in the presence of a suitable base such as triethylamine gives thiazolopyridine amine derivative of the formula (14). The intermediate of the formula (14) is coupled with a haloacetamide of the formula (10) in the presence of a suitable base such as sodium hydride or cesium carbonate affords compound represented by the general formula (Id).

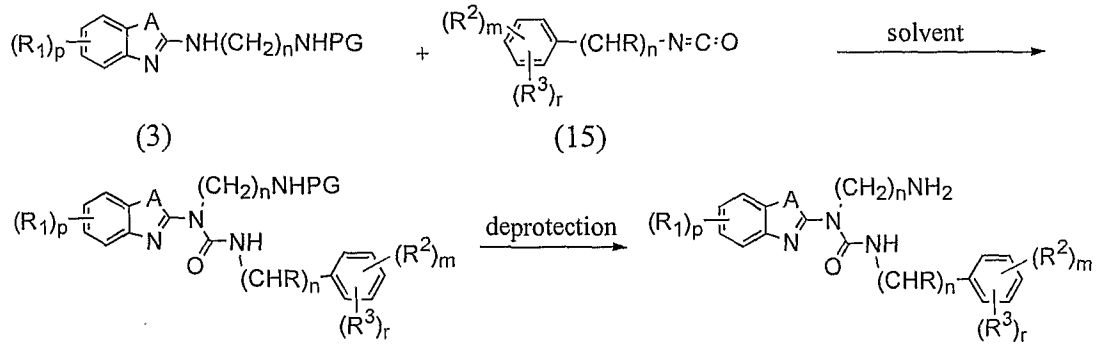
Synthetic Scheme 5



Compounds of the general formula (Ie) where R^1, R^2, R^3, m, n, p, r and 'A' are as defined above, are prepared as shown in synthetic scheme 6. Thus, Intermediate (3) on reaction with substituted phenyl isocynate of the formula (15) in a suitable solvent such as dichloromethane under neutral conditions gives urea derivative of the formula (16).

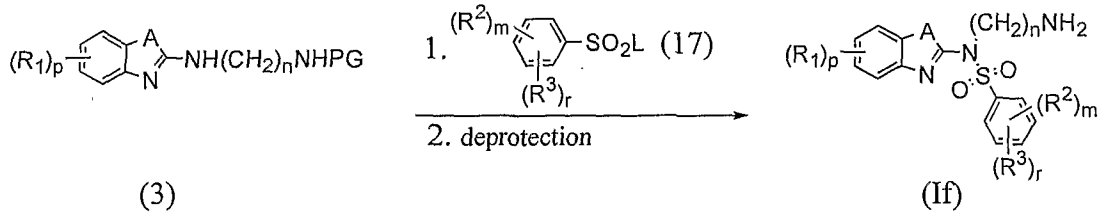
Deprotection of intermediate of the formula (16), where PG represents a *tert*-butyloxycarbonyl group, with strong acids such as hydrochloric acid or trifluoroacetic acid gives compounds of the present invention represented by the formula (Ie).

Synthetic Scheme 6



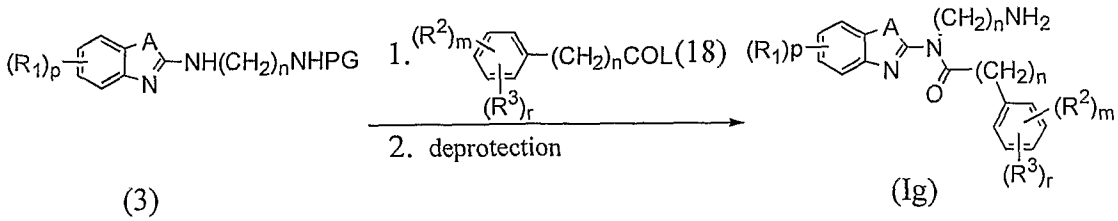
In another embodiment of the present invention, compounds of the general formula (If) where R^1, R^2, R^3, m, n, p, r and 'A' are as defined above, are prepared as shown in synthetic scheme 7. Thus, intermediate (3) is coupled with substituted arylsulfonyl chloride of the general formula (17) in the presence of a suitable base such as triethylamine in a suitable solvent followed by cleavage of the carbamate (PG represents tert-butyloxycarbonyl) under acidic conditions gives compounds of general formula (If)

Synthetic Scheme 7



In another embodiment of the present invention, where R^1, R^2, R^3, m, n, p, r and 'A' are as defined above, is prepared as shown in synthetic scheme (8). Thus, base mediated coupling reaction of intermediate of the formula (3) with a substituted phenyl acetyl chloride of the general formula (18), followed by deprotection of the carbamate group gives amides of the general formula (Ig).

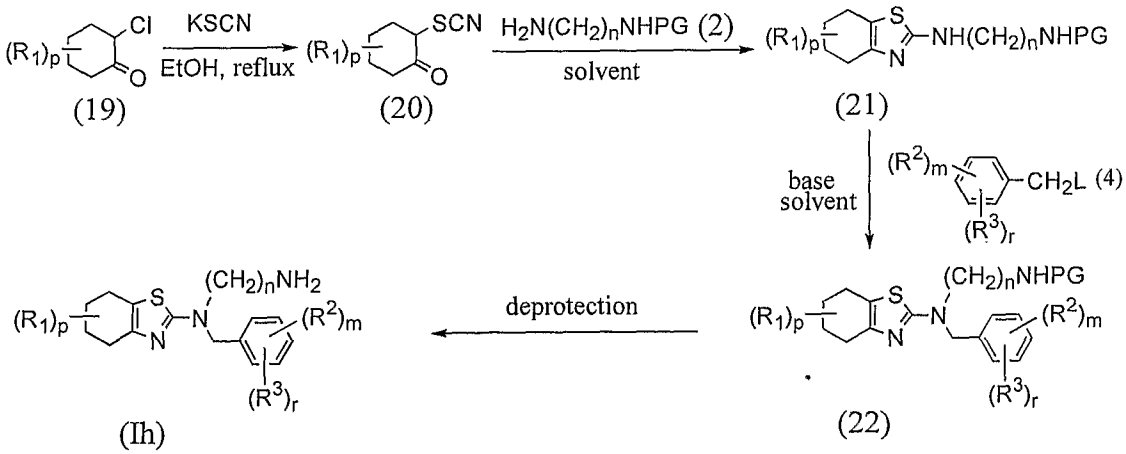
Synthetic Scheme 8



(3) (Ig)

In another embodiment of the present invention, 1,2-3,4-tetrahydrobenzothiazoleamine derivatives of the general formula (Ih) where R^1, R^2, R^3, m, n, p, r and 'A' are as defined above. are prepared as shown in synthetic scheme 9. Thus α-halocyclohexanone of the formula (19) is treated with potassium thiocyanate in the presence of an appropriate solvent such as ethanol gives thiocynate of the formula (20) (Modi, S. K. et al. *Indian J. Chem.* **1972**, *10*, 605-607). The thiocynate (20) on reaction with aminoalkylcarbamate of the formula (2) gives intermediate of the formula (21). Reaction of intermediate (21) with benzyl halide of the general formula (4) followed by deprotection under strongly acidic conditions gives compounds represented by the general formula (Ih).

Synthetic Scheme 9



(19) (20) (21)

(Ih) (22)

All Intermediates and Examples described in the experimental section are prepared using appropriate methods described above. The approaches described in the "General Methods of Preparation" are not intended to limit the scope of methods of preparation. The methods described above are illustrative in nature and the intermediates and compound of

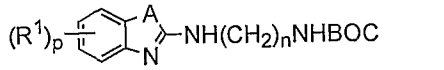
invention can be prepared by alternative approaches known to people skilled in the art and such methods and procedures are within the scope of the present invention.

Experimental Section

Preparation of Intermediates

All the intermediates of the General Formula (3), (7), (9), (14) and (21) given below are prepared using the approaches given in Synthetic Schemes 1 - 9. Experimental procedures for their preparation and structural information of intermediates are given below.

General procedure for the preparation of Intermediates of the General Formula (3)

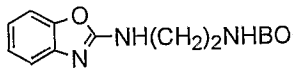
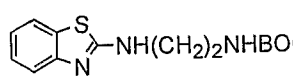


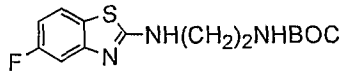
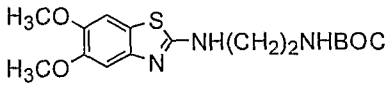
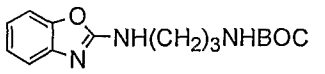
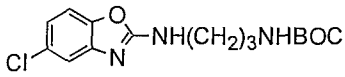
Intermediate (3)

To a stirred solution of aminoalkylcarbamate derivative (1.0 equiv.) in ethanol (10 ml/g) was added appropriate 2-chloroazole derivative (1.0 equiv.) followed by triethylamine (2.0 equiv) at room temperature. The reaction mixture was refluxed overnight. The residue obtained after evaporation of the solvent was purified by silica gel column chromatography using 20-25% ethyl acetate in petroleum ether to furnish the products as white to off-white solid.

The following intermediates were prepared according to the procedure described above. The structure, ^{1}H NMR data and mass spectral data are given in Table 1.

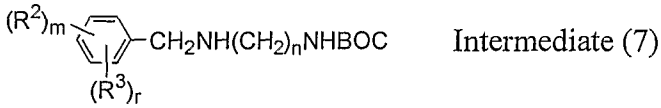
Table 1: Structure and analytical data for Intermediates of the General Formula (3)

No	Structure	^{1}H NMR (300 MHz, $CDCl_3$) δ ppm	MS (m/z)
1.		1.42 (s, 9H), 3.40-3.46 (m, 2H), 3.55-3.62 (m, 2H), 5.00 (br s, 1H), 5.86 (br s, 1H), 7.02 (t, J = 7.8 Hz, 1H), 7.12 (t, J = 7.8 Hz, 1H), 7.21 (d, J = 7.2 Hz, 1H), 7.33 (d, J = 7.2 Hz, 1H)	ESI: 278.12 $(MH)^+$
2.		1.43 (s, 9H), 3.39-3.45 (m, 2H), 3.55-3.67 (m, 2H), 5.06 (br s, 1H), 6.00 (br s, 1H), 7.06 (t, J = 6.6 Hz, 1H), 7.26 (t, J = 7.2 Hz, 1H), 7.52 (t, J = 8.7 Hz, 2H)	APCI: 293.96 $(M)^+$

3.		1.42 (s, 9H), 3.35-3.43 (m, 2H), 3.47-3.59 (m, 2H), 5.06 (br s, 1H), 6.14 (br s, 1H), 6.79 (t, J = 8.7 Hz, 1H), 7.18 (dd, J = 2.7, 7.2 Hz, 1H), 7.39-7.45 (m, 1H).	ESI: 312.31 $(MH)^+$
4.		1.43 (s, 9H), 3.40-3.46 (m, 2H), 3.52-3.60 (m, 2H), 3.88 (s, 6H), 5.16 (br s, 1H), 7.02 (s, 1H), 7.11 (s, 1H)	ESI: 354.23 $(MH)^+$
5.		1.45 (s, 9H), 1.76-1.81 (m, 2H), 3.20-3.28 (m, 2H), 3.48-3.53 (m, 2H), 4.88 (br s, 1H), 5.79 (br s, 1H), 7.00 (t, J = 7.8 Hz, 1H), 7.11 (t, J = 6.3 Hz, 1H), 7.20 (d, J = 7.2 Hz, 1H), 7.32 (d, J = 7.2 Hz, 1H)	ESI: 292.16 $(MH)^+$
6.		1.45 (s, 9H), 1.76-1.82 (m, 2H), 3.21-3.27(m, 2H), 3.48-3.55 (m, 2H), 4.88 (br s, 1H), 6.10 (br s, 1H), 6.97 (d, J = 8.4 Hz, 1H), 7.11 (d, J = 8.4 Hz, 1H), 7.30 (s, 1H)	APCI: 326.39 $(MH)^+$

All the intermediates of the General Formula (7) given in Table 2 are prepared using the general procedure given below. The structure, ^{1}H NMR data and mass spectral data are also given in Table 2.

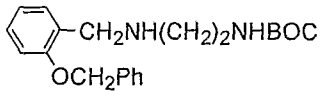
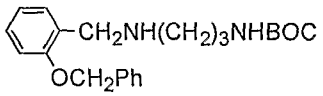
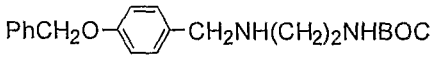
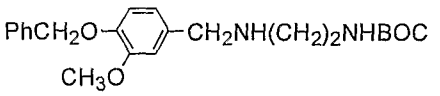
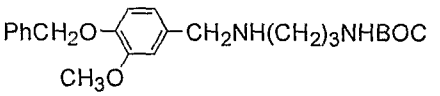
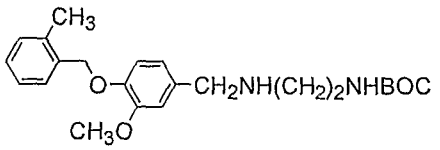
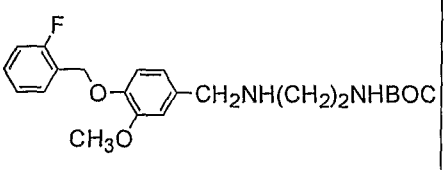
General procedure for the preparation of Intermediates of the General Formula (7)

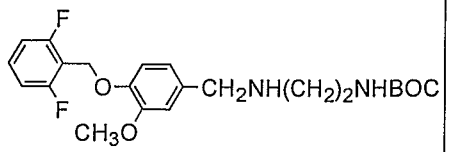
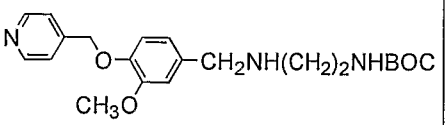
 Intermediate (7)

To a stirred solution of benzaldehyde derivative (1.0 equiv.) in dry methanol (10 ml/g) was added *tert*-butylaminoalkylcarbamate (1.0 equiv.) at room temperature. The reaction mixture was stirred at the same temperature for 5 h. To this mixture was added sodium cyanoborohydride (2 equiv.) over 5 min and further stirred for 18 h. The residue obtained after evaporation of methanol was diluted with water and extracted twice with chloroform. The combined organic layers were washed with water and dried over anhydrous sodium sulfate. The chloroform solution was evaporated and the residue obtained was purified by silica gel column chromatography using 5-10 % ethyl acetate in

chloroform to obtain the products of the general formula (7) as off-white to pale yellow solid.

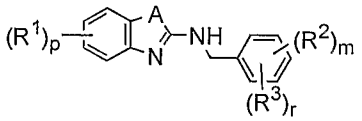
Table 2: Structure and analytical data for Intermediate of the General Formula (7)

No	Structure	^{1}H NMR (300 MHz, δ ppm)	MS (m/z)
1.		$CDCl_3$: 1.49 (s, 9H), 2.67 (t, J = 5.4 Hz, 2H), 3.15-3.23 (m, 2H), 3.81 (s, 2H), 5.01 (br s, 1H), 5.07 (s, 2H), 6.85-6.92 (m, 2H), 7.21 (d, J = 7.8 Hz, 3H), 7.26-7.38 (m, 4H)	ESI: 357.75 $(MH)^+$
2.		$CDCl_3$: 1.35 (s, 9H), 1.59-1.64 (m, 2H), 2.62-2.68 (m, 2H), 2.90-2.96 (m, 2H), 3.87 (s, 2H), 5.13 (s, 2H), 6.86-6.95 (m, 2H), 7.07 (d, J = 8.4 Hz, 1H), 7.23-7.40 (m, 5H), 7.46 (d, J = 7.5 Hz, 1H), 8.30 (br s, 1H)	APCI: 371.41 $(MH)^+$
3.		$CDCl_3$: 1.39 (s, 9H), 3.10-3.16 (m, 2H), 3.65-3.75 (m, 2H), 4.20-4.26 (m, 2H), 5.04 (s, 2H), 6.94 (d, J = 8.4 Hz, 2H), 7.20-7.26 (m, 2H), 7.32-7.39 (m, 5H)	ESI: 357.75 $(MH)^+$
4.		DMSO-d_6: 1.36 (s, 9H), 2.49-2.55 (m, 2H), 3.02 (d, J = 5.4 Hz, 2H), 3.62 (s, 2H), 3.75 (s, 3H), 5.02 (s, 2H), 6.73-6.78 (m, 2H), 6.90-6.96 (m, 2H), 7.31-7.41 (m, 4H)	ESI: 387.61, $(MH)^+$
5.		$CDCl_3$: 1.36 (s, 9H), 1.58-1.66 (m, 2H), 2.64 (t, J = 7.5 Hz, 2H), 2.92-2.99 (m, 2H), 3.76 (s, 3H), 3.81 (s, 2H), 5.02 (br s 1H), 5.05 (s, 2H), 6.83-6.88 (m, 1H), 6.96 (d, J = 8.4 Hz, 1H), 7.09 (s, 1H), 7.27-7.42 (m, 5H)	ESI: 401.05 $(MH)^+$
6.		$CDCl_3$: 1.44 (s, 9H), 2.38 (s, 3H), 2.72-2.78 (m, 2H), 3.21-3.28 (m, 2H), 3.48 (s, 2H), 3.88 (s, 3H), 5.02 (br s, 1H), 5.09 (s, 2H), 6.79 (d, J = 7.8 Hz, 1H), 6.82 (d, J = 7.8 Hz, 1H), 6.90 (br s, 1H), 6.15-6.22 (m, 3H), 7.40 (d, J = 6.9 Hz, 1H)	ESI: 401.57 $(MH)^+$
7.		$CDCl_3$: 1.43 (s, 9H), 2.70-2.76 (m, 2H), 3.20-3.28 (m, 2H), 3.70 (s, 2H), 3.88 (s, 3H), 4.93 (br s, 1H), 5.18 (s, 2H), 6.75 (d, J = 7.8 Hz, 1H), 6.81-6.87 (m, 2H), 7.03 (t, J = 8.7 Hz, 1H), 7.10 (t, J = 7.2 Hz, 1H), 7.20-7.28 (m,	ESI: 405.29 $(MH)^+$

		1H), 7.49 (t, J = 7.2 Hz, 1H)	
8.		$CDCl_3$: 1.44 (s, 9H), 2.70-2.77 (m, 2H), 3.20-3.28 (m, 2H), 3.73 (s, 2H), 3.85 (s, 3H), 4.95 (br s, 1H), 5.15 (s, 2H), 6.81 (d, J = 7.8 Hz, 1H), 6.85-6.92 (m, 2H), 6.95-7.02 (m, 2H), 7.30-7.36 (m, 1H)	APCI: 423.11 $(MH)^+$
9.		$CDCl_3$: 1.43 (s, 9H), 2.70-2.76 (m, 2H), 3.22-3.28 (m, 2H), 3.92 (s, 3H), 5.02 (br s, 1H), 5.14 (s, 2H), 6.70-6.80 (m, 2H), 6.97 (s, 1H), 7.30-7.36 (m, 2H), 8.55-8.62 (m, 2H)	ESI: 388.41 $(MH)^+$

All the intermediates of the General Formula (9) are prepared using the general procedure given below. The structure, ^{1}H NMR and mass spectral data of intermediates prepared by this method are given in Table 3.

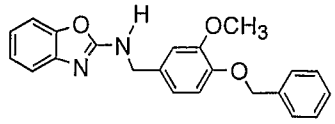
General procedure for the preparation of intermediates of the General Formula (9)

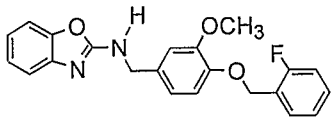
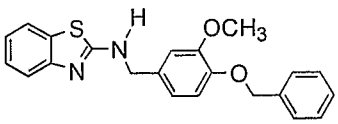
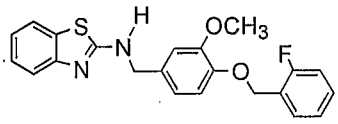
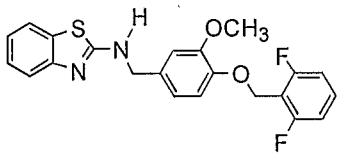
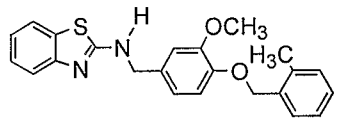
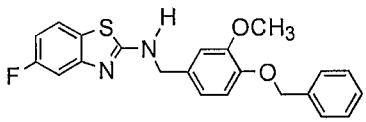


Intermediate (9)

A mixture of benzaldehyde derivative (1.0 equiv.) and 2-aminobenzoxazole or 2-aminobenzothiazole (1.0 equiv.) in *p*-xylene was stirred at reflux temperature for 18 h. The mixture containing the imino derivative was cooled to room temperature and sodium cyanoborohydride (1.2 equiv.) was added over 5 min. The reaction mixture was then further stirred at room temperature for 48 h. The mixture was diluted with ethyl acetate and washed twice with water. The organic layer was dried and evaporated to give a viscous residue, which was purified by silica gel column chromatography to yield the compound of general formula (9) as off-white to yellow solid.

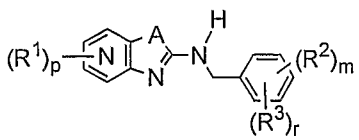
Table 3: Structure and analytical data for Intermediates of General Formula (9)

No	Structure	^{1}H NMR data (300 MHz) δ ppm	MS (m/z)
1.		$CDCl_3$: 3.86 (s, 3H), 4.58 (s, 2H), 5.13 (s, 2H), 6.82 (s, 2H), 6.92 (s, 1H), 7.03 (t, J = 7.8 Hz, 1H), 7.16 (t, J = 7.2 Hz, 1H), 7.29-7.41 (m, 8H)	APCI: 361.21 $(MH)^+$

2.		$CDCl_3$: 3.80 (s, 3H), 4.59 (s, 2H), 5.14 (s, 2H), 5.27 (br s, 1H), 6.82-6.90 (m, 4H), 6.95-7.01 (m, 2H), 7.03 (d, J = 7.5 Hz, 1H), 7.15 (t, J = 7.2 Hz, 1H), 7.21-7.29 (m, 2H), 7.34 (d, J = 7.8 Hz, 1H)	ESI: 379.06 $(MH)^+$
3.		$CDCl_3$: 3.85 (s, 3H), 4.53 (s, 2H), 5.13 (s, 2H), 6.80-6.88 (m, 2H+ NH), 6.91 (s, 1H), 7.08 (t, J = 7.2 Hz, 1H), 7.28-7.39 (m, 6H), 7.49-7.57 (m, 2H)	APCI: 377.17 $(MH)^+$
4.		$CDCl_3$: 3.84 (s, 3H), 4.54 (s, 2H), 5.19 (s, 2H), 5.76 (br s, 1H), 6.85 (s, 2H), 6.92 (s, 1H), 7.01-7.13 (m, 3H), 7.24-7.30 (m, 2H), 7.46-7.51 (m, 2H), 7.55 (d, J = 7.8 Hz, 1H)	ESI: 395.70 $(MH)^+$
5.		$CDCl_3$: 3.80 (s, 3H), 4.55 (s, 2H), 5.14 (s, 2H), 5.62 (br s, 1H), 6.84-6.90 (m, 4H), 6.96 (d, J = 7.8 Hz, 1H), 7.07 (t, J = 7.8 Hz, 1H), 7.20-7.30 (m, 2H), 7.50-7.57 (m, 2H);	ESI: 413.43 $(MH)^+$
6.		$CDCl_3$: 2.37 (s, 3H), 3.83 (s, 3H), 4.55 (s, 2H), 5.09 (s, 2H), 5.92 (br s, 1H), 6.84-6.91 (m, 2H), 6.94 (s, 1H), 7.09 (t, J = 7.8 Hz, 1H), 7.15-7.22 (m, 3H), 7.25-7.31 (m, 1H), 7.39 (d, J = 7.5 Hz, 1H), 7.50 (d, J = 8.1 Hz, 1H), 7.58 (d, J = 7.8 Hz, 1H)	ESI: 391.22 $(MH)^+$
7.		$CDCl_3$: 3.85 (s, 3H), 4.51 (s, 2H), 5.13 (s, 2H), 5.73 (br s, 1H), 6.77-6.82 (m, 3H), 6.89 (s, 1H), 7.17 (dd, J = 2.7, 7.8 Hz, 1H), 7.28-7.46 (m, 6H)	ESI: 396.17 $(MH)^+$

All the intermediates of the General Formula (14) are prepared using the general procedure given below. The structure, ^1H NMR and mass spectral data of intermediates prepared by this method are given in Table 4.

General procedure for the preparation of intermediates of the General Formula (14)

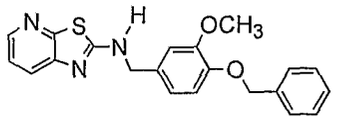
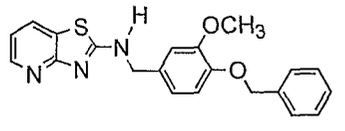


Intermediate (14)

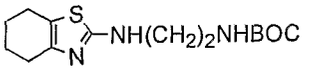
A mixture of benzylamine derivative (1.0 equiv.), 2-chloropyridothiazole (1.0 equiv.) and triethylamine (3.0 equiv.) in ethanol (10 ml/g) was stirred at reflux temperature for 18 h.

The mixture was cooled to room temperature, diluted with ethyl acetate and washed twice with water. The organic layer was dried and evaporated to give crude product, which was purified by silica gel column chromatography to yield the compound of general formula (14) as off-white to yellow solid.

Table 4: Structure and analytical data for Intermediates of General Formula (14)

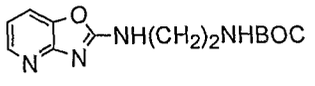
No	Structure	1H NMR data (300 MHz) δ ppm	MS (m/z)
1.		$CDCl_3$: 3.85 (s, 3H), 4.55 (s, 2H), 5.13 (s, 2H), 6.82 (s, 2H), 6.89 (s, 1H), 7.18 (dd, J = 4.8, 8.4 Hz, 1H), 7.28-7.38 (m, 5H), 7.62 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 4.8 Hz, 1H)	ESI: 378.73 $(MH)^+$
2.		$CDCl_3$: 3.80 (s, 3H), 4.57 (s, 2H), 5.15 (s, 2H), 5.71 (br s, 1H), 6.85 (s, 2H), 6.92 (s, 1H), 7.18-7.24 (m, 1H), 7.36 (t, J = 6.9 Hz, 3H), 7.44 (d, J = 7.2 Hz, 2H), 7.69 (d, J = 8.4 Hz, 1H), 8.19 (d, J = 4.2 Hz, 1H)	ESI: 378.70 $(MH)^+$

Preparation of *tert*-Butyl [2-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-ylamino)ethyl] carbamate Intermediate (21)



To a stirred solution of 2-oxocyclohexylthiocyanate (1.0 g, 0.006 mol) in ethanol (10 ml) was added *tert*-butyl (2-aminoethyl) carbamate (1.03 g, 0.006 mol) and the mixture was refluxed overnight. Solvent was evaporated under reduced pressure and the crude mass obtained was purified by silica gel column chromatography using 20% ethyl acetate in petroleum ether to give 500 mg of the title compound as a yellow solid; 1.43 (s, 9H), 1.76-1.86 (m, 4H), 2.50-2.60 (m, 4H), 3.35-3.41 (m, 4H), 5.04 (br s, 1H); ESI- MS (m/z) 298.03 $(MH)^+$.

Preparation of *tert*-Butyl [2-([1,3]oxazolo[4,5-*b*]pyridin-2-ylamino)ethyl]carbamate



A mixture of 2-(methylthio)-[1,3]-thiazolo[4,5-*b*]pyridine (100 mg, 0.602 mmol) and *tert*-butyl (2-aminoethyl)carbamate (193 mg, 1.204 mmol) was heated neat at 85°C for 1

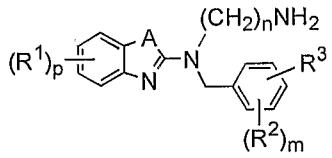
h. The reaction mixture was cooled to room temperature, the residue obtained was purified by silica gel column chromatography using 2% methanol in chloroform as eluent to give the title compound as an off-white solid; 1.40 (s, 9H), 3.45-3.52 (m, 2H), 3.65-3.70 (m, 2H), 6.90-6.96 (m, 1H), 7.45 (d, J = 7.2 Hz, 1H), 8.17-8.23 (m, 1H); ESI- MS (m/z) 279.11 $(MH)^+$.

Preparation of compounds of invention

All the Examples of the general formula (Ia) to (Ih) were prepared from appropriate intermediates of the general formula (3), (7), (9), (14) and (21) given in Table 1 to 4 by using the approaches given in Synthetic Schemes 1 - 9. Experimental procedures for their preparation and structural details of examples are given below.

The examples represented by the general formula (Ia) is prepared by 3 different approaches (Method A, Method B and Method C) and the detailed procedure is given below.

General procedure for the preparation of compounds of the formula (Ia)



Formula (Ia)

Method A:

Step 1: To a stirred solution of aminobenzoxazole or aminobenzothiazole carbamate of the formula (3) (1.0 equiv.) in *N,N*-dimethylformamide (10 ml/g), was added sodium hydride (60 % dispersion in mineral oil, 1.5-2.0 equiv.) or cesium carbonate (1.5-2.0 equiv.) at 0°C. The reaction mixture was stirred at the same temperature for 15-20 min. Then to this reaction mixture was added benzyl bromide derivative (1.0 equiv.) followed by TBAI (1.0 equiv.). The resulting mixture was allowed to warm to room temperature and further stirred overnight. The reaction mixture was diluted with ethyl acetate and water, and the layers were separated. The aqueous layer was extracted twice with ethyl acetate and the combined organic extracts were washed with water and dried over

anhydrous sodium sulfate. The organic extract was concentrated under reduced pressure and the residue obtained was purified by silica gel column chromatography using 20% ethyl acetate in petroleum ether to obtain the product as off-white solid.

Step 2: To a stirred solution of Step 1 intermediate (1.0 equiv.) in ethyl acetate (10 ml/g) was added saturated solution of hydrochloric acid in ethyl acetate (10 ml/g) and the mixture was stirred at 10°C for 30 min to 2.0 h. The solvent and excess hydrochloric acid were distilled under reduced pressure and the residue obtained was crystallized from 1:1 mixture of ethyl acetate-diethyl ether to give the product of the formula (Ia) as a white solid.

Method B:

Step 1: To a stirred and cooled (0°C) solution of aminobenzoxazole or aminobenzothiazole carbamate of the formula (3) (1.0 equiv.) in *N,N*-dimethylformamide (10 ml/g) was added 60 % sodium hydride in mineral oil (1.5-2.0 equiv.) and the mixture was stirred at the same temperature for 15-20 min. Benzyl methane sulphonate (1.0 equiv.) was added and the mixture was further stirred at room temperature for 6 h. Work-up and purification of the reaction as described in Method A afforded the product as an off-white solid.

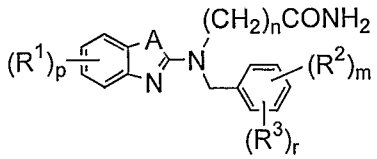
Step 2: The Step 1 intermediate on treatment with hydrochloric acid in ethyl acetate, as described in Method A, gave compounds of the formula (Ia) as a white solid.

Method C:

Step 1: A solution of 2-chlorobenzothiazole or 2-chlorobenzoxazole of the formula (1) (1.0 equiv.), benzylamino alkyl carbamate derivative of the formula (7) (1.0 equiv.) and excess triethylamine or *N,N*-diisopropylethylamine (2.0-2.5 equiv.) in ethanol (1 ml/g) was refluxed overnight under stirring. The solvent was evaporated and the residue obtained was purified by silica gel column chromatography using 20-25% ethyl acetate in petroleum ether to give the product as an off-white solid.

Step 2: The Step 1 intermediate on treatment with hydrochloric acid in ethyl acetate, as described in Method A, gave compounds of the formula (Ia) as a white solid.

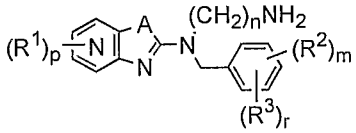
General procedure for the preparation of compounds of the formula (Ib)



Formula (Ib)

To the stirred solution of 2-benzylaminobenzoxazole or 2-benzylaminobenzothiazole of the formula (9) (1.0 equiv.) in acetonitrile was added 2-haloacetamide (1.0 equiv.) and cesium carbonate (1.0 equiv.) and the mixture was refluxed for 18 h under stirring. The reaction mixture was diluted with water and extracted twice with ethyl acetate. The combined organic extracts were dried and evaporated under reduced pressure. The residue obtained was purified by silica gel column chromatography to obtain compound of the general formula (Ib) as white to off-white solid.

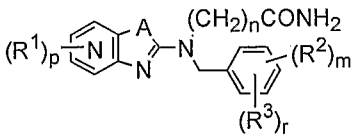
General procedure for the preparation of compounds of the formula (Ic)



Formula (Ic)

Compounds of the general formula (Ic) were prepared in two steps from appropriate 2-chloropyridothiazole (1.0 equiv) of the formula (11) and appropriate benzylamino alkyl carbamate derivative (1.0 equiv) of the formula (7) as described for the synthesis of compounds of the general formula (Ia) by using Method C.

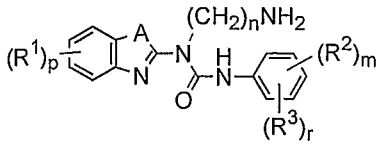
General procedure for the preparation of compounds of the formula (Id)



Formula (Id)

Compounds of the general formula (Id) were prepared by reaction of substituted 2-benzylaminopyridothiazole (1.0 equiv.) of the formula (14) with iodoalkyl amide (1.2 equiv.) of the formula (10) in the presence of cesium carbonate (1.2 equiv.) as described in the preparation of (Ib).

General procedure for the preparation of compounds of the formula (Ie)

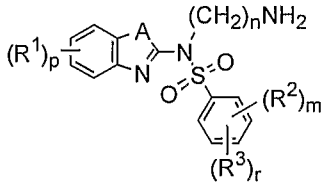


Formula (Ie)

To a stirred and cooled (0 °C) solution of arylamino alkyl carbamate (1.0 equiv.) of the formula (3) in dichloromethane (1.0 ml/g) was added the phenyl isocyanate derivative (1.0 equiv.) of the formula (15) and the mixture is further stirred at room temperature for 6 h. The residue obtained after evaporation of the solvent was purified by silica gel column chromatography using 20-30 % ethyl acetate in petroleum ether to compound of the formula (16) as an off-white solid.

Step 2: The Step 1 intermediate on treatment with hydrochloric acid in ethyl acetate gave compounds of the formula (Ie) as a white solid.

General procedure for the preparation of compounds of the formula (If)

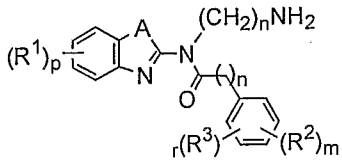


Formula (If)

Step 1: To a stirred and cooled (0 °C) solution of arylamino alkyl carbamate (1.0 equiv.) of the formula (3) in dichloromethane (1.0 ml/g) and arylsulfonyl chloride (1.0 equiv.) of the formula (17) was added triethylamine (2.0 equiv.) and 4-(dimethylamino)pyridine (0.10 equiv.) at room temperature. The reaction mixture was stirred at the same temperature for 18 h. The resulting mixture was diluted with chloroform and washed twice with water and dried over anhydrous sodium sulfate. The solvent was evaporated and the residue obtained was concentrated under reduced pressure. The residue obtained was purified by silica gel column chromatography using 15 - 20% ethyl acetate in petroleum ether to give product as white to off-white solid.

Step 2: The Step 1 intermediate on treatment with hydrochloric acid in ethyl acetate gave compounds of the formula (If) as a white solid.

General procedure for the preparation of compounds of the formula (Ig)

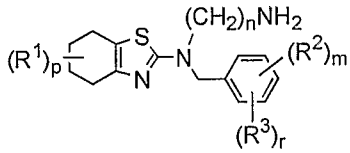


Formula (Ig)

Step 1: To a stirred mixture of arylaminoalkyl carbamate (1.0 equiv.) of the formula (3) and arylalkyl acid (1.0 equiv.) of the formula (18) in dichloromethane (1.0 ml/g) was added EDCI hydrochloride (1.5 equiv.), N-hydroxybenzotriazole (1.5 equiv.) and triethylamine (3.0 equiv.) at room temperature. The reaction mixture was stirred overnight at the same temperature. The mixture was then diluted with chloroform, washed twice with water and dried over anhydrous sodium sulfate. The solvent was evaporated and the residue obtained was purified by silica gel column chromatography using 15 to 20 % ethyl acetate in petroleum ether to obtain the product as a white solid.

Step 2: The Step 1 intermediate on treatment with hydrochloric acid in ethyl acetate gave compounds of the formula (Ig) as a white solid.

General procedure for the preparation of compounds of the formula (Ih)



Formula (Ih)

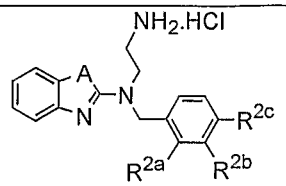
Step 1: To a stirred solution of 4,5,6,7-tetrahydro-1,3-benzothiazol-2-ylamino)alkyl carbamate (1.0 equiv.) of the formula (21) in *N,N*-dimethylformamide (10 ml/g), was added 60 % sodium hydride (1.5 - 2.0 equiv.) at 0°C. After the mixture was stirred at the same temperature for 15 min., benzyl bromide derivative of the formula (4) (1.0 equiv.) and tetrabutyl ammonium iodide (0.1 equiv.) were added. The resulting mixture was allowed to warm to room temperature and further stirred overnight. Usual work-up and purification by silica gel column chromatography using 15 to 20% ethyl acetate in petroleum ether gave the product as a white solid.

Step 2: The Step 1 intermediate on treatment with hydrochloric acid in ethyl acetate gave compounds of the formula (Ih) as a white solid.

Examples 1 to 95 given below represent preferred embodiments of the invention and are intended to be illustrative and not limiting.

Examples 1 to 5 were prepared according to the general procedure (Method A) described for Formula (Ia). Structural information and mass spectral details are given in Table 5.

Table 5: Structural details and mass spectral data of Examples 1 - 5



Example No	A	R^{2a}	R^{2b}	R^{2c}	MS (m/z)
Example 1	O	F	H	H	ESI: 286.51 $(MH)^+$
Example 2	S	F	H	H	APCI: 302.17 $(MH)^+$
Example 3	S	Cl	H	H	ESI: 317.04 $(M)^+$
Example 4	S	Br	H	H	APCI: 362.04 $(MH)^+$.
Example 5	S	H	F	F	APCI: 320.09 $(MH)^+$

Example 1: 1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(2-fluorobenzyl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-*N*-(1,3-benzoxazol-2-yl)aminoethyl] carbamate (200 mg, 0.72 mmol) with 2-fluorobenzyl bromide (136 mg, 0.72 mmol) in the presence of 60 % sodium hydride (34 mg, 1.44 mmol) in *N,N*-dimethylformamide (5 ml) provided 160 mg of *tert*-butyl{2-[*N*-(1,3-benzoxazol-2-yl)-*N*-(2-fluorobenzyl) amino] ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 9H), 3.40-3.46 (m, 2H), 3.60-3.70 (m, 2H), 4.85 (s, 2H), 4.94 (br s, 1H), 6.94-7.08 (m, 3H), 7.15 (t, J = 7.8 Hz, 1H), 7.25-7.30 (m, 2H), 7.33-7.40 (m, 2H); APCI-MS (*m/z*) 386.46 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.17 (br s, 2H), 3.78-3.82 (m, 2H), 4.87 (s, 2H), 7.00-7.06 (m, 1H), 7.17-7.26 (m, 3H), 7.34-7.40 (m, 4H), 8.20 (br s, 3H).

Example 2: 1-[*N*-(1,3-benzothiazol-2-yl)-*N*-(2-fluorobenzyl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-*N*-(1,3-benzothiazol-2-yl) amino ethyl] carbamate (300 mg, 1.021 mmol) with 2-fluorobenzyl bromide (183 mg, 0.97 mmol) in the presence of 60 % sodium hydride (49 mg, 2.042 mmol) in N,N-dimethylformamide (5 ml) provided 315 mg of *tert*-butyl{2-*N*-[(1,3-benzothiazol-2-yl)-*N*-(2-fluorobenzyl) amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (s, 9H), 3.40-3.46 (m, 2H), 3.68-3.74 (m, 2H), 4.82 (s, 2H), 5.10 (br s, 1H), 7.00-7.10 (m, 3H), 7.25-7.33 (m, 3H), 7.52-7.58 (m, 2H); ESI-MS (*m/z*) 402.15 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.14-3.20 (m, 2H), 3.80-3.88 (m, 2H), 4.83 (s, 2H), 7.07 (t, J = 8.1 Hz, 1H), 7.15-7.22 (m, 2H), 7.28-7.38 (m, 3H), 7.47 (d, J = 7.2 Hz, 1H), 7.75 (d, J = 7.2 Hz, 1H), 8.07 (br s, 3H).

Example 3: 1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(2-chlorobenzyl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-*N*-(1,3-benzothiazol-2-yl)amino ethyl] carbamate (200 mg, 0.681 mmol) with 2-chlorobenzyl bromide (140 mg, 0.681 mmol) in the presence of 60 % sodium hydride (16 mg, 0.681 mmol) in N,N-dimethylformamide (5 ml) provided 200 mg of *tert*-butyl{2-(*N*-[(1,3-benzothiazol-2-yl)-*N*-(2-chloro benzyl)] amino)ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.40-3.48 (m, 2H), 3.72-3.78 (m, 2H), 4.85 (s, 2H), 5.18 (br s, 1H), 7.06 (t, J = 7.2 Hz, 2H), 7.20-7.31 (m, 3H), 7.38 (d, J = 7.2 Hz, 1H), 7.54 (d, J = 7.8 Hz, 2H); ESI-MS (*m/z*) 418.12 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.05-3.10 (m, 2H), 4.61 (s, 2H), 5.14 (s, 2H), 6.93-7.07 (m, 3H), 7.15 (d, J = 6.9 Hz, 1H), 7.23-7.38 (m, 2H), 7.42 (d, J = 7.8 Hz, 1H), 7.62 (d, J = 7.8 Hz, 1H), 8.02 (br s, 3H).

Example 4: 1-[*N*-(1,3-benzothiazol-2-yl)-*N*-(2-bromobenzyl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-*N*-(1,3-benzothiazol-2-yl)aminoethyl] carbamate (200 mg, 0.681 mmol) with 1-bromo-2-(bromomethyl)benzene (169 mg, 0.681 mmol) in the presence of 60 % sodium hydride (16 mg, 0.681 mmol) and TBAI (265 mg, 0.681 mmol) in N,N-dimethylformamide (5 ml) provided 190 mg of *tert*-butyl{2-*N*-[(1,3-benzothiazol-2-yl)-*N*-(2-bromobenzyl)amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (s, 9H), 3.40-3.50 (m, 2H), 3.72-3.82 (m, 2H), 4.81 (s, 2H), 5.19 (br s, 1H), 7.06-7.14 (m, 2H), 7.20-7.30 (m, 3H), 7.50-7.60 (m, 3H); ESI-MS (*m/z*) 462.09 $(MH)^+$.

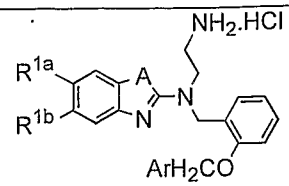
Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.18-3.25 (m, 2H), 3.96-4.05 (m, 2H), 4.82 (s, 2H), 7.08 (t, J = 7.2 Hz, 2H), 7.17 (t, J = 7.5 Hz, 1H), 7.25-7.38 (m, 2H), 7.50 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.75 (d, J = 7.2 Hz, 1H), 8.23 (br s, 3H).

Example 5: 1-[*N*-(1,3-benzothiazol-2-yl)-*N*-(3,4-difluorobenzyl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-*N*-(1,3-benzothiazol-2-yl)aminoethyl] carbamate (200 mg, 0.681 mmol) with 4-(bromomethyl)-1,2-difluorobenzene (141 mg, 0.681 mmol) in the presence of 60 % sodium hydride (24 mg, 1.024 mmol) and TBAI (219 mg, 0.683 mmol) in N,N-dimethylformamide (5 ml) provided 85 mg of *tert*-butyl{2-*N*-[(1,3-benzothiazol-2-yl)-*N*-(3,4-difluorobenzyl)amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.35-3.42 (m, 2H), 3.62-3.68 (m, 2H), 4.72 (s, 2H), 5.02 (br s, 1H), 7.04-7.11 (m, 4H), 7.26-7.31 (m, 1H), 7.54 (t, J = 8.4 Hz, 2H); APCI-MS (*m/z*) 420.50 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.13-3.18 (m, 2H), 3.80-3.88 (m, 2H), 4.79 (s, 2H), 7.09 (t, J = 7.8 Hz, 1H) 7.18-7.25 (m, 1H), 7.26 (d, J = 7.8 Hz, 1H), 7.40-7.50 (m, 3H), 7.77 (d, J = 7.2 Hz, 1H), 8.15 (br s, 3H).

Table 6: Structural details and mass spectral data of Examples 6 - 16



Example No	R^{1a}	R^{1b}	A	Ar	MS (m/z)
Example 6	H	H	O	Ph	APCI: 374.43 $(MH)^+$
Example 7	H	H	O	4-CF_3Ph	APCI: 442.17 $(M)^+$
Example 8	H	H	O	2-FPh	APCI: 392.36$(MH)^+$
Example 9	H	H	O	2,6-F_2Ph	APCI: 410.19 $(MH)^+$
Example 10	H	H	O	2,4-F_2Ph	APCI: 410.32 $(MH)^+$
Example 11	H	H	S	Ph	APCI: 390.17 $(MH)^+$
Example 12	H	H	S	2-F-Ph	APCI: 408.55 $MH)^+$
Example 13	H	H	S	4-CF_3Ph	APCI: 458.28 $(MH)^+$
Example 14	H	H	S	2,4-F_2Ph	ESI: 426.28 $(MH)^+$
Example 15	Cl	H	S	Ph	APCI: 424.55 $(MH)^+$
Example 16	H	OCF_3	S	Ph	APCI: 474.35 $(MH)^+$

Example 6: *N*-(1,3-Benzoxazol-2-yl)-*N*-(2-benzyloxybenzyl)ethane-1,2-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl-{2-[*N*-(2-benzyloxybenzyl)amino]ethyl} carbamate (240 mg, 0.703 mmol) with 2-chloro-1,3-benzoxazole (90 mg, 0.586 mmol) in the presence of triethylamine (162 µl, 1.172 mmol) in ethanol (5 ml) provided 138 mg of *tert*-butyl[2-(1,3-benzoxazol-2-yl-(2-benzyloxybenzyl)amino)ethyl]carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 9H), 3.31-3.40 (m, 2H), 3.60-3.66 (m, 2H), 4.84 (s, 2H), 4.96 (br s, 1H), 5.06 (s, 2H), 6.88-6.94 (m, 3H), 7.11-7.18 (m, 2H), 7.27-7.35 (m, 8H); APCI-MS (*m/z*) 474.43 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.03-3.12 (m, 2H),

3.76-3.87 (m, 2H), 4.80 (s, 2H), 5.13 (s, 2H), 6.91 (t, J = 7.2 Hz, 1H), 7.00 (t, J = 7.2 Hz, 1H), 7.10-7.20 (m, 3H), 7.26-7.32 (m, 6H), 7.38-7.42 (m, 2H), 8.06 (br s, 3H).

Example 7: 1-[*N*-(1,3-benzoxazol-2-yl)-*N*-{2-(4-trifluoromethylbenzoxy) benzyl]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-*N*-(1,3-benzoxazol-2-yl)aminoethyl] carbamate (150 mg, 0.541 mmol) with 1-(bromomethyl)-2-[4-(trifluoromethyl) benzyloxy]benzene (161 mg, 0.541 mmol) in the presence of 60 % sodium hydride (12 mg, 0.541 mmol) and TBAI (200 mg, 0.541 mmol) in N,N-dimethylformamide (5 ml) provided 120 mg of *tert*-butyl{[(1,3-benzoxazol-2-yl){2-(4-trifluoromethyl benzyloxy) benzyl}amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (s, 9H), 3.30-3.36 (m, 2H), 3.60-3.67 (m, 2H), 4.86 (s, 2H), 4.98 (br s, 1H), 5.09 (s, 2H), 6.89-6.99 (m, 3H), 7.10-7.16 (m, 2H), 7.22-7.32 (m, 3H), 7.40-7.50 (m, 4H); APCI-MS (*m/z*) 542.02 $(M)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.16 (m, 2H), 3.70-3.78 (m, 2H), 4.83 (s, 2H), 5.23 (s, 2H), 6.94-7.00 (m, 2H), 7.10-7.17 (m, 2H), 7.25-7.33 (m, 4H), 7.55-7.61 (m, 4H), 8.08 (br s, 3H).

Example 8: 1-[*N*-(1,3-Benzoxazol-2-yl)]-*N*-{2-(2-fluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-*N*-(1,3-benzoxazol-2-yl)amino ethyl] carbamate (150 mg, 0.541 mmol) with 1-{[2-(bromomethyl)phenoxy]methyl}-2-fluoro benzene (170 mg, 0.542 mmol) in the presence of 60 % sodium hydride (19.49 mg,0.812 mmol) and TBAI (196 mg, 0.542 mmol) in N,N-dimethylformamide (5 ml) provided 134 mg of *tert*-butyl{2-[*N*-(1,3-benzoxazol-2-yl){2-(2-fluorobenzyloxy) benzyl}amino] ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 9H), 3.32-3.38 (m, 2H), 3.60-3.68 (m, 2H), 4.83 (s, 2H), 4.97 (br s, 1H), 5.12 (s, 2H), 6.90-7.01 (m, 6H), 7.10-7.17 (m, 3H), 7.32-7.40 (m, 3H); ESI-MS (*m/z*) 492.32 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.18 (m, 2H),

3.68-3.75 (m, 2H), 4.76 (s, 2H), 5.16 (s, 2H), 6.90-6.98 (m, 2H), 7.09-7.16 (m, 5H), 7.24-7.32 (m, 4H), 7.45 (t, J = 7.8 Hz, 1H), 8.04 (br s, 3H).

Example 9: 1-[*N*-(1,3-Benzoxazol-2-yl)]-*N*-{2-(2,6-difluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-*N*-(1,3-benzoxazol-2-yl)amino ethyl] carbamate (200 mg, 0.72 mmol) with 2-{[2-(bromomethyl)phenoxy]methyl}-1,3-difluorobenzene (225 mg, 0.72 mmol) in the presence of 60 % sodium hydride (17 mg, 0.72 mmol) and TBAI (266 mg, 0.72 mmol) in N,N-dimethylformamide (5 ml) provided 185 mg of *tert*-butyl{2-[*N*-(1,3-benzoxazol-2-yl){2-(2,6-difluoro benzyl oxy) benzyl} amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (s, 9H), 3.28-3.34 (m, 2H), 3.55-3.61 (m, 2H), 4.74 (s, 2H), 4.96 (br s 1H), 5.10 (s, 2H), 6.77 (t, J = 7.8 Hz, 2H), 6.93 (t, J = 7.8 Hz, 2H), 7.05-7.16 (m, 4H), 7.20-7.33 (m, 3H); ESI-MS (*m/z*) 510.17 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.03-3.10 (m, 2H), 3.63-3.69 (m, 2H), 4.66 (s, 2H), 5.11 (s, 2H), 6.94-7.00 (m, 4H), 7.08 (t, J = 7.8 Hz, 1H), 7.19-7.25 (m, 4H), 7.29-7.35 (m, 2H), 7.94 (br s, 3H).

Example 10: 1-[*N*-(1,3-Benzoxazol-2-yl)]-*N*-[{2-(2,4-difluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-*N*-(1,3-benzoxazol-2-yl)amino ethyl] carbamate (98 mg, 0.339 mmol) with 1-{[2-(bromomethyl)phenoxy]methyl}-2,4-difluorobenzene (100 mg, 0.339 mmol) in the presence of 60 % sodium hydride (12.20 mg, 0.508 mmol) and TBAI (123 mg, 0.339 mmol) in N,N-dimethylformamide (5 ml) provided 83 mg of *tert*-butyl{2-[*N*-(1,3-benzoxazol-2-yl){2-(2,4-difluoro benzyl oxy) benzyl}amino] ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 9H), 3.30-3.36 (m, 2H), 3.57-3.63 (m, 2H), 4.81 (s, 2H), 4.88 (br s, 1H), 5.03 (s, 2H), 6.64-6.70 (m, 2H), 6.91-6.99 (m, 4H), 7.10-7.16 (m, 2H), 7.26-7.31 (m, 3H); APCI-MS (*m/z*) 510.20 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.03-3.10 (m, 2H), 3.69-3.75 (m, 2H), 4.73 (s, 2H), 5.09 (s, 2H), 6.92-6.98 (m, 4H), 7.12-7.29 (m, 6H), 7.54-7.60 (m, 1H), 8.02 (br s, 3H).

Example 11: 1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-[(2-benzyloxy)benzyl]ethane-1,2-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl{2-[*N*-(2-benzyloxybenzyl) amino]ethyl} carbamate (200 mg, 0.589 mmol) with 2-chloro-1,3-benzothiazole (83 mg, 0.491 mmol) in the presence of triethylamine (99 mg, 0.982 mmol) in ethanol (5 ml) provided 78 mg of *tert*-butyl{2-*N*-[(1,3-benzothiazol-2-yl)-*N*-(2-benzyloxy benzyl) amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 9H), 3.32-3.38 (m, 2H), 3.70-3.76 (m, 2H), 4.75 (s, 2H), 5.07 (s, 2H), 5.25 (br s, 1H), 6.86-6.96 (m, 2H), 7.02 (t, J = 7.5 Hz, 1H), 7.22-7.30 (m, 7H), 7.33-7.40 (m, 2H), 7.49 (t, J = 7.5 Hz, 1H); APCI-MS (*m/z*) 490.28 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.12-3.18 (m, 2H), 3.85-3.92 (m, 2H), 4.74 (s, 2H), 5.17 (s, 2H), 6.90-6.96 (m, 1H), 7.05-7.15 (m, 3H), 7.26-7.32 (m, 5H), 7.42-7.48 (m, 3H), 7.69 (d, J = 8.1 Hz, 1H), 7.95 (br s, 3H).

Example 12: 1-[*N*-(1,3-benzothiazol-2-yl)-*N*-{2-(2-fluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl] carbamate (200 mg, 0.681 mmol) with 1-(bromomethyl)-2-{2-fluorobenzyloxy}benzene (200 mg, 0.681 mmol) in the presence of 60 % sodium hydride (32 mg, 1.362 mmol) in N,N-dimethylformamide (5 ml) provided 60 mg of *tert*-butyl{2-*N*-[(1,3-benzothiazol-2-yl)-*N*-(2-[2-fluorobenzyloxy]benzyl) amino] ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 9H), 3.32-3.40 (m, 2H), 3.68-3.74 (m, 2H), 4.75 (s, 2H), 5.13 (s, 2H), 5.26 (br s, 1H), 6.91 (t, J = 7.2 Hz, 1H), 6.98-7.05 (m, 3H), 7.26-7.37 (m, 5H), 7.42 (t, J = 7.8 Hz, 1H), 7.49 (t, J = 7.2 Hz, 2H); APCI-MS (*m/z*) 508.28 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.09-3.14 (m, 2H), 3.80-3.90 (m, 2H), 4.70 (s, 2H), 5.19 (s, 2H), 6.94 (t, J = 6.6 Hz, 1H), 7.05-7.16 (m, 5H), 7.20-7.30 (m, 3H), 7.40-7.46 (m, 2H), 7.50-7.56 (m, 1H), 8.03 (br s, 3H).

Example 13: 1-[*N*-(1,3-benzothiazol-2-yl)-*N*-{2-[(4-trifluoromethyl)benzyloxy]benzyl}] ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl] carbamate (150 mg, 0.541 mmol) with 1-(bromomethyl)-2-{4-(trifluoromethyl) benzyloxy} benzene (161 mg, 0.541mmol) in the presence of 60 % sodium hydride (12 mg, 0.541 mmol) and TBAI (200 mg, 0.541 mmol) in N,N-dimethylformamide (5 ml) provided 120 mg of *tert*-butyl{2-*N*-[(1,3-benzothiazol-2-yl)-*N*-(2-[4-(trifluoromethyl) benzyloxy]benzyl)amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 9H), 3.32-3.40 (m, 2H), 3.68-3.74 (m, 2H), 4.78 (s, 2H), 5.12 (s, 2H), 5.26 (br s, 1H), 6.91 (d, J = 7.8 Hz, 2H), 7.06 (t, J = 6.9 Hz, 1H), 7.29-7.35 (m, 4H), 7.47-7.62 (m, 5H); APCI-MS (*m/z*) 557.02 $(M)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.12-3.18 (m, 2H), 3.84-4.00 (m, 2H), 4.79 (s, 2H), 5.27 (s, 2H), 6.93 (t, J = 6.9 Hz, 1H), 7.03-7.13 (m, 3H), 7.28 (t, J = 7.2 Hz, 2H), 7.46 (d, J = 7.5 Hz, 1H), 7.58-7.64 (m, 4H), 7.68-7.73 (m, 1H), 8.10 (br s, 3H).

Example 14: 1-[*N*-(1,3-benzothiazol-2-yl)-*N*-{2-(2,4-difluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl] carbamate (200 mg, 0.681 mmol) with 1-{[4-(bromomethyl)phenoxy]methyl}-2,4-difluorobenzene (212 mg, 0.681 mmol) in the presence of 60 % sodium hydride (32 mg, 0.681 mmol) in N,N-dimethylformamide (5 ml) provided 135 mg of *tert*-butyl{2-[*N*-(1,3-benzothiazol-2-yl)-*N*-{2-(2,4-difluorobenzyloxy)benzyl}amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 9H), 3.32-3.38 (m, 2H), 3.67-3.73 (m, 2H), 4.72 (s, 2H), 5.05 (s, 2H), 5.12 (br s, 1H), 6.67-6.76 (m, 2H), 6.90-6.98 (m, 2H),

7.04 (t, J = 7.2 Hz, 1H), 7.20-7.33 (m, 4H), 7.45-7.51 (m, 2H); APCI-MS (*m/z*) 526.23 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.07-3.12 (m, 2H), 3.79-3.83 (m, 2H), 4.67 (s, 2H), 5.13 (s, 2H), 6.96 (app. q, J = 7.2 Hz, 2H), 7.07 (t, J = 7.8 Hz, 1H), 7.12-7.20 (m, 3H), 7.26-7.32 (m, 2H), 7.43 (d, J = 7.8 Hz, 1H), 7.58 (d, J = 8.1 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H), 8.01 (br s, 3H).

Example 15: 1-[*N*-{2-(Benzyloxybenzyl)}-*N*-(6-chloro-1,3-benzothiazol-2-yl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl{2-[*N*-(2-benzyloxybenzyl) amino] ethyl} carbamate (252 mg, 0.739 mmol) with 2,6-dichloro-1,3-benzothiazole (150 mg, 0.739 mmol) in the presence of *N,N*-diisopropylethylamine (286 mg, 2.217 mmol) in ethanol (5 ml) provided 162 mg of *tert*-butyl{2-[*N*-(6-chloro-1,3-benzothiazol-2-yl)-*N*-(2-benzyl oxybenzyl)amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 9H), 3.30-3.36 (m, 2H), 3.65-3.71 (m, 2H), 4.73 (s, 2H), 5.06 (s, 2H), 5.14 (br s, 1H), 6.83-6.96 (m, 2H), 7.19-7.26 (m, 6H), 7.30-7.36 (m, 2H), 7.40-7.50 (m, 2H); APCI-MS (*m/z*) 524.30 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.11-3.17 (m, 2H), 3.86-3.93 (m, 2H), 4.76 (s, 2H), 5.16 (s, 2H), 6.91 (t, J = 7.2 Hz, 1H), 7.07-7.14 (m, 2H), 7.24-7.34 (m, 5H), 7.44 (d, J = 7.8 Hz, 3H), 7.84 (s, 1H), 8.17 (br s, 3H).

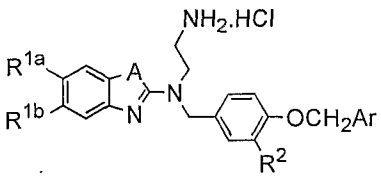
Example 16: 1-[*N*-(2-benzyloxybenzyl)-*N*-(5-trifluorormethoxy-1,3-benzothiazol-2-yl)] ethane -1,2-diamine hydrochloride

Coupling reaction (Method C) of t*ert*-butyl{2-[*N*-(2-benzyloxybenzyl)amino]ethyl} carbamate (296 mg, 0.863 mmol) with 2-chloro-5-(trifluoromethoxy)-1,3-benzothiazole (200 mg, 0.781 mmol) in the presence of triethyl amine (440 mg, 4.356 mmol) in ethanol (5 ml) provided 190 mg of *tert*-butyl{2-*N*-[(2-benzyloxybenzyl)-*N*-(5-trifluoromethoxy-1,3-benzothiazol-2-yl)amino] ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 9H), 3.30-3.36 (m, 2H), 3.65-3.71 (m, 2H), 4.72 (s, 2H), 5.05 (s, 2H),

5.13 (br s, 1H), 6.88-6.97 (m, 3H), 7.08-7.14 (m, 2H), 7.20-7.33 (m, 5H), 7.43 (d, J = 8.1 Hz, 2H); APCI-MS (*m/z*) 574.33 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.15 (br s, 2H), 3.88 (br s, 2H), 4.75 (s, 2H), 5.16 (s, 2H), 6.92 (t, J = 8.1 Hz, 1H), 7.09 (t, J = 8.4 Hz, 2H), 7.25-7.32 (m, 5H), 7.43 (d, J = 6.9 Hz, 2H), 7.50 (d, J = 8.7 Hz, 1H), 7.84 (s, 1H), 8.07 (br s, 3H).

Table 7: Structural details and mass spectral data of Examples 17 to 36



Example No.	R^{1a}	R^{1b}	A	R^2	Ar	MS (m/z)
Example 17	H	H	O	H	Ph	ESI: 374.13 $(MH)^+$
Example 18	H	H	S	H	Ph	ESI: 390.19 $(MH)^+$
Example 19	H	CF_3	S	H	Ph	ESI: 457.14 $(M)^+$
Example 20	H	H	O	Cl	Ph	APCI: 408.45 $(MH)^+$
Example 21	H	H	O	OCH_3	Ph	ESI: 426.62 $(MH)^+$.
Example 22	H	H	O	OCH_3	2-CH_3Ph	APCI: 418.36 $(MH)^+$
Example 23	H	H	S	Cl	Ph	APCI 424.72 $(MH)^+$
Example 24	H	H	S	OCH_3	Ph	ESI- 432.38 $(MH)^+$
Example 25	H	H	S	OCH_3	2-CH_3Ph	APCI: 434.14 $(MH)^+$
Example 26	H	H	S	OCH_3	2-FPh	APCI: 438.33 $(MH)^+$
Example 27	H	H	S	OCH_3	2-CF_3Ph	APCI: 486.63 $(M-H)^-$
Example 28	H	H	S	OCH_3	3-CF_3Ph	APCI: 486.63 $(M-H)^-$
Example 29	H	H	S	OCH_3	2,4-F_2Ph	APCI: 456.07 $(MH)^+$
Example 30	H	H	S	OCH_3	2,6-F_2Ph	ESI: 456.09 $(MH)^+$
Example 31	H	OCF_3	S	OCH_3	Ph	ESI: 504.12 $(MH)^+$
Example 32	Cl	H	S	OCH_3	Ph	APCI: 454.51 $(MH)^+$

Example 33	H	Cl	S	OCH_3	Ph	ESI: 454.49 $(MH)^+$
Example 34	H	CF_3	S	OCH_3	Ph	APCI: 494.03 $(MH)^+$.
Example 35	H	F	S	OCH_3	2-FPh	ESI: 456.68 $(MH)^+$
Example 36	OCH_3	OCH_3	S	OCH_3	2-FPh	ESI: 516.27 $(M+NH_4)^+$

Example 17: 1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-benxyloxybenzyl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl(2-{*N*-[4-(benzyloxybenzyl]amino}ethyl) carbamate (248 mg, 0.703 mmol) with 2-chloro-1,3-benzoxazole (90 mg, 0.586 mmol) in the presence of triethyl amine (119 mg, 1.172 mmol) in ethanol (5 ml) provided 170 mg *tert*-butyl{2-[*N*-(1,3-benzoxazol-2-yl)-*N*-(4-benxyloxybenzyl)amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 9H), 3.34-3.41 (m, 2H), 3.57-3.63 (m, 2H), 4.72 (s, 2H), 4.91 (br s, 1H), 5.03 (s, 2H), 6.92 (d, J = 8.4 Hz, 2H), 7.01 (t, J = 7.8 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 7.21-7.29 (m, 1H), 7.35-7.41 (m, 8H); ESI-MS (*m/z*) 474.38 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.09-3.17 (m, 2H), 3.65-3.73 (m, 2H), 4.70 (s, 2H), 5.06 (s, 2H), 6.96-7.04 (m, 3H), 7.16 (t, J = 8.1 Hz, 1H), 7.24-7.30 (m, 5H), 7.35-7.43 (m, 4H), 8.03 (br s, 3H).

Example 18: 1-[*N*-(1,3-benzothiazol-2-yl)-*N*-(4-benzyloxybenzyl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method B) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl] arbamate (200 mg, 0.683 mmol) with 4-(benzyloxy)benzyl methanesulfonate (198 mg, 0.683 mmol) in the presence of 60 % sodium hydride (24 mg, 1.024 mmol) and TBAI (247 mg, 0.683 mmol) in N,N-dimethylformamide (5 ml) provided 125 mg of *tert*-butyl{2-*N*-[(1,3-benzothiazol-2-yl)-*N*-(4-benzyloxybenzyl)amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.35-3.42 (m, 2H), 3.65-3.71 (m, 2H), 4.68 (s, 2H), 5.02 (s, 2H), 5.12 (br s, 1H), 6.92 (d, J = 8.4 Hz, 2H), 7.05 (d, J = 8.7 Hz, 1H), 7.20-7.38 (m, 8H), 7.54 (d, J = 7.8 Hz, 2H); ESI-MS (*m/z*) 490.36 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.08-3.18 (m, 2H), 3.75-3.82 (m, 2H), 4.67 (s, 2H), 5.06 (s, 2H), 6.98 (d, J = 8.4 Hz, 2H), 7.07 (t, J = 8.7 Hz, 1H), 7.24-7.39 (m, 8H), 7.46 (d, J = 7.8 Hz, 1H), 7.74 (d, J = 7.2 Hz, 1H), 8.03 (br s, 3H).

Example 19: 1-[*N*-(4-Benzyloxybenzyl)-*N*-(5-trifluromethyl-1,3-benzothiazol-2-yl)] ethane -1,2-diamine hydrochloride

Coupling reaction of (Method C) of *tert*-butyl(2-{*N*-[4-(benzyloxybenzyl]-amino}ethyl) carbamate (190 mg, 0.531 mmol) with 2-chloro-5-(trifluoromethyl)-1,3-benzothiazole (126 mg, 0.531 mmol) in the presence of *N,N*-diisopropylethylamine (205 mg, 1.266 mmol) in ethanol (5 ml) provided 58 mg of *tert*-butyl(2-{*N*-(4-benzyloxybenzyl)-*N*-[5-(trifluoromethyl)-1,3-benzothiazol-2-yl]amino}ethyl)carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.35-3.42 (m, 2H), 3.60-3.67 (m, 2H), 4.73 (s, 2H), 4.92 (br s, 1H), 5.20 (s, 2H), 7.05 (d, J = 8.1 Hz, 1H), 7.14 (d, J = 7.8 Hz, 1H), 7.30-7.42 (m, 7H), 7.51 (s, 1H), 7.75-7.82 (m, 2H); APCI-MS (*m/z*) 557.62 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.18 (m, 2H), 3.85-3.92 (m, 2H), 4.76 (s, 2H), 5.16 (s, 2H), 6.90 (t, J = 7.2 Hz, 1H), 7.05-7.13 (m, 2H), 7.24-7.33 (m, 5H), 7.40-7.46 (m, 3H), 7.84 (s, 1H), 8.21 (br s, 3H).

Example 20: 1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{(4-benzyloxy-3-chlorobenzyl}]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-*N*-(1,3-benzoxazol-2-yl)aminoethyl] carbamate (150 mg, 0.541 mmol) with 1-(benzyloxy)-4-(bromomethyl)-2-chlorobenzene (168 mg, 0.541 mmol) in the presence of 60 % sodium hydride (12 mg, 0.541 mmol) and TBAI (200 mg, 0.541 mmol) in N,N-dimethylformamide (5 ml) provided 180 mg of *tert*-butyl{2-[*N*-(1,3-benzoxazol-2-yl)(4-benzyloxy-3-chlorobenzyl)amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 9H), 3.35-3.42 (m, 2H), 3.57-3.63 (m, 2H), 4.69 (s, 2H), 4.88 (br s, 1H), 5.12 (s, 2H), 6.88 (d, J = 8.4 Hz, 1H), 7.01 (t,

J = 8.4 Hz, 1H), 7.14 (q, J = 7.8 Hz, 3H), 7.26-7.43 (m, 7H); ESI-MS (*m/z*) 508.57 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.18 (m, 2H), 3.69-3.73 (m, 2H), 4.71 (s, 2H), 5.18 (s, 2H), 7.05 (t, J = 7.8 Hz, 1H), 7.16-7.22 (m, 2H), 7.30-7.47 (m, 9H), 8.06 (br s, 3H).

Example 21: 1[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-benzyloxy-3-methoxybenzyl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl{2-[(4-benzyloxy-3-methoxybenzyl)amino] ethyl}carbamate (204 mg, 0.547 mmol) with 2-chloro-1,3-benzoxazole (70 mg, 0.456 mmol) in the presence of triethylamine (126 µl, 0.912 mmol) in ethanol (5 ml) provided 72 mg *tert*-butyl{2-[(1,3-benzoxazol-2-yl)-(4-benzyloxy-3-methoxybenzyl)amino] ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 9H), 3.32-3.39 (m, 2H), 3.55-3.62 (m, 2H), 3.83 (s, 3H), 4.71 (s, 2H), 4.89 (br s, 1H), 5.12 (s, 2H), 6.75-6.82 (m, 2H), 6.82 (s, 1H), 7.00 (t, J = 7.8 Hz, 1H), 7.16 (t, J = 7.8 Hz, 2H), 7.35-7.41 (m, 6H); ESI-MS (*m/z*) 526.26 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.09-3.15 (m, 2H), 3.74 (s, 3H), 4.20 (s, 2H), 4.71 (s, 2H), 5.03 (s, 2H), 6.84 (d, J = 7.8 Hz, 1H), 6.97-7.06 (m, 3H), 7.17 (t, J = 6.6 Hz, 1H), 7.30-7.41 (m, 7H), 8.13 (br s, 3H).

Example 22: 1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{3-methoxy-[4-(2-methylbenzyloxy)]benzyl }ethane-1,2-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl [2-({3-methoxy-4-(2-methylbenzyloxy) benzyl}amino)ethyl]carbamate (150 mg, 0.375 mmol) with 2-chloro-1,3-benzoxazole (57 mg, 0.375 mmol) in the presence of triethylamine (199 µl, 1.125 mmol) in ethanol (5 ml) provided 113 mg *tert*-butyl {3-[*N*-(1,3-benzoxazol-2-yl)-*N*-{3-methoxy-[4-(2-methylbenzyloxy)]benzyl}amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 9H), 2.37 (s, 3H), 3.36-3.43 (m, 2H), 3.58-3.64 (m, 2H), 3.83 (s, 3H),

4.74 (s, 2H), 4.91 (br s, 1H), 5.08 (s, 2H), 6.80-6.84 (m, 2H), 6.86-6.92 (m, 1H), 7.03 (t, *J* = 7.8 Hz, 1H), 7.15-7.22 (m, 4H), 7.33-7.42 (m, 3H); APCI-MS (*m/z*) 518.21 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.30 (s, 3H), 3.08-3.15 (m, 2H), 3.65-3.71 (m, 2H), 3.74 (s, 3H), 4.72 (s, 2H), 5.02 (s, 2H), 6.86-6.92 (m, 1H), 7.02-7.09 (m, 3H), 7.15-7.23 (m, 4H), 7.31-7.40 (m, 2H), 7.44 (d, *J* = 7.8 Hz, 1H), 8.10 (br s, 3H).

Example 23: 1-[*N*-(1,3-benzothiazol-2-yl)-*N*-(4-benzyloxy-3-chlorobenzyl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl] carbamate (141 mg, 0.483 mmol) with 1-(benzyloxy)-4-(bromomethyl)-2-chlorobenzene (150 mg, 0.483 mmol) in the presence of 60 % sodium hydride (17 mg, 0.725 mmol) and TBAI (175 mg, 0.483 mmol) in N,N-dimethylformamide (5 ml) provided 69 mg of *tert*-butyl{2-[*N*-(1,3-benzothiazol-2-yl)-*N*-(4-benzyloxy-3-chlorobenzyl)amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.35-3.41 (m, 2H), 3.62-3.68 (m, 2H), 4.66 (s, 2H), 5.06 (br s, 1H), 5.12 (s, 2H), 6.87 (d, *J* = 7.8 Hz, 1H), 7.05-7.12 (m, 2H), 7.28-7.40 (m, 7H), 7.54 (t, *J* = 7.8 Hz, 2H); APCI-MS (*m/z*) 523.99 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.20 (m, 2H), 3.75-3.85 (m, 2H), 4.70 (s, 2H), 5.18 (s, 2H), 7.08 (t, *J* = 7.8 Hz, 1H), 7.22-7.31 (m, 4H), 7.38-7.50 (m, 6H), 7.76 (d, *J* = 7.5 Hz, 1H), 8.04 (br s, 3H).

Example 24: 1-[*N*-(1,3-Benzothiazol-2-yl)]-*N*-(4-benzyloxy-3-methoxybenzyl)ethane-1,2-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl{2-[(4-benzyloxy-3-methoxybenzyl)-amino]ethyl}carbamate (170 mg, 0.497 mmol) with 2-chloro-1,3-benzothiazole (70 mg, 0.473 mmol) in the presence of triethylamine (95 mg, 0.946 mmol) in ethanol and butanol (4:1, 15 mL) for 40 h provided 63 mg *tert*-butyl{2-[1,3-benzothiazol-2-yl(4-benzyloxy-3-methoxybenzyl)amino]ethyl} carbamate as a white solid; ^{1}H NMR (300

MHz, DMSO-d_6) δ 1.38 (s, 9H), 3.36-3.41 (m, 2H), 3.55-3.67 (m, 2H), 3.82 (s, 3H), 4.66 (s, 2H), 5.11 (s, 2H), 6.77-6.85 (m, 3H), 7.05-7.10 (m, 2H), 7.31-7.41 (m, 5H), 7.53 (t, J = 7.8 Hz, 2H); APCI-MS (*m/z*) 520.17 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.11-3.20 (m, 2H), 3.74 (s, 3H), 3.81-3.88 (m, 2H), 4.67 (s, 2H), 5.03 (s, 2H), 6.81 (d, J = 7.8 Hz, 1H), 6.98-7.10 (m, 2H), 7.28-7.49 (m, 6H), 7.75 (d, J = 7.8 Hz, 1H), 8.06 (br s, 3H).

Example 25: 1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{3-methoxy-[4-(2-methylbenzyloxy)benzyl]}ethane-1,2-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl [2-({3-methoxy-4-(2-methylbenzyloxy) benzyl}amino)ethyl]carbamate (355 mg, 0.887 mmol) with 2-chloro-1,3-benzothiazole (150 mg, 0.887 mmol) in the presence of triethylamine (472 µl, 2.661 mmol) in ethanol (10 ml) provided 67 mg of *tert*-butyl {2-[*N*-(1,3-benzothiazol-2-yl)-*N*-{3-methoxy-(4-[2-methylbenzyloxy])benzyl}amino]ethyl}carbamate as an off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 2.37 (s, 3H), 3.39-3.45 (m, 2H), 3.67-3.73 (m, 2H), 3.82 (s, 3H), 4.69 (s, 2H), 5.08 (s, 2H), 5.14 (br s, 1H), 6.78-6.83 (m, 2H), 6.86-6.90 (m, 1H), 7.15-7.28 (m, 3H), 7.31 (d, J = 7.5 Hz, 1H), 7.39 (d, J = 6.9 Hz, 2H), 7.56 (t, J = 6.6 Hz, 2H); APCI-MS (*m/z*) 534.30 $(M+H)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.30 (s, 1H), 3.13-3.19 (m, 2H), 3.75 (s, 3H), 3.82-3.88 (m, 2H), 4.78 (s, 2H), 5.03 (s, 2H), 6.86 (d, J = 7.8 Hz, 1H), 7.02-7.13 (m, 3H), 7.18-7.24 (m, 3H), 7.32 (t, J = 7.8 Hz, 1H), 7.38 (d, J = 6.9 Hz, 1H), 7.51 (d, J = 7.8 Hz, 1H), 7.79 (d, J = 7.8 Hz, 1H), 8.18 (br s, 3H).

Example 26: 1-[*N*-(1,3-Benzothiazol-2-yl)]-*N*-{4-(2-fluorobenzyloxy)-3-methoxy benzyl]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl] carbamate (156 mg, 0.533 mmol) with 4-(bromomethyl)-1-[2-fluorobenzyloxy]-2-methoxybenzene (180 mg, 0.533 mmol) in the presence of 60 % sodium hydride (19 mg, 0.799 mmol) and TBAI (193 mg, 0.533 mmol) in N,N-dimethylformamide (5 ml)

provided 67 mg of *tert*-butyl{2-*N*-[(1,3-benzothiazol-2-yl)-*N*-{4-(2-fluorobenzyloxy)-3-methoxybenzyl}amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.35-3.41 (m, 2H), 3.65-3.71 (m, 2H), 3.83 (s, 3H), 4.68 (s, 2H), 5.01 (br s, 1H), 5.18 (s, 2H), 6.80-6.86 (m, 3H), 7.04-7.14 (m, 3H), 7.25-7.32 (m, 2H), 7.49-7.57 (m, 3H); ESI-MS (*m/z*) 538.06 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure (Method A) gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.17 (m, 2H), 3.73 (s, 3H), 3.80-3.86 (m, 2H), 4.68 (s, 2H), 5.06 (s, 2H), 6.83 (d, J = 7.8 Hz, 1H), 6.99-7.07 (m, 3H), 7.19-7.29 (m, 3H), 7.38-7.51 (m, 3H), 7.75 (d, J = 7.2 Hz, 1H), 8.04 (br s, 3H).

Example 27: 1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{4-(2-trifluromethylbenzyloxy)-3-methoxy benzyl}] ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl] carbamate (110 mg, 0.251 mmol) with 4-(bromomethyl)-2-methoxy-1-{[2-(trifluoro methyl)benzyl]oxy} benzene (61 mg, 0.251 mmol) in the presence of cesium carbonate (83 mg, 0.251 mmol) and TBAI (180 mg, 0.511 mmol) in N,N-dimethylformamide (5 ml) provided 75 mg of *tert*-butyl{2-[*N*-(1,3-benzothiazol-2-yl)-*N*-{4-(2-trifluro methyl benzyloxy)-3-methoxybenzyl}amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.35-3.41 (m, 2H), 3.64-3.74 (m, 2H), 3.85 (s, 3H), 4.67 (s, 2H), 5.10 (br s, 1H), 5.32 (s, 2H), 6.72-6.78 (m, 2H), 6.88 (s, 1H), 7.05-7.11 (m, 1H), 7.25-7.31 (m, 1H), 7.36-7.41 (m, 1H), 7.50-7.56 (m, 3H), 7.64 (d, J = 7.8 Hz, 1H), 7.74 (d, J = 7.8 Hz, 1H); APCI-MS (*m/z*) 588.18 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure (Method A) gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.18 (m, 2H), 3.75 (s, 3H), 3.80-3.86 (m, 2H), 4.68 (s, 2H), 5.17 (s, 2H), 6.80-6.86 (m, 1H), 6.92-6.98 (m, 2H), 7.05-7.11 (m, 1H), 7.25-7.31 (m, 1H), 7.40-7.46 (m, 1H), 7.52-7.58 (m, 1H), 7.70-7.80 (m, 4H), 8.01 (br s, 3H).

Example 28: 1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{4-(3-trifluromethylbenzyloxy)-3-methoxy benzyl}] ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl] carbamate (150 mg, 0.511 mmol) with 4-(bromomethyl)-2-methoxy-1-{[3-(trifluoro methyl)benzyloxy}]benzene(191 mg, 0.511 mmol) in the presence of 60 % sodium hydride (12 mg, 0.511 mmol) and TBAI (180 mg, 0.511 mmol) in *N,N*-dimethylformamide (5 ml) provided 150 mg of *tert*-butyl{2-[*N*-(1,3-benzothiazol-2-yl)-*N*-{4-(3-trifluromethylbenzyloxy)-3-methoxybenzyl}amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.35-3.45 (m, 2H), 3.65-3.72 (m, 2H), 3.83 (s, 3H), 4.68 (s, 2H), 5.10 (br s, 1H), 5.14 (s, 2H), 6.77 (br s, 1H), 6.85-6.91 (m, 2H), 7.04-7.10 (m, 1H), 7.20-7.30 (m, 1H), 7.46-7.54 (m, 5H), 7.65-7.75 (m, 1H); APCI-MS (*m/z*) 588.16 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.16 (m, 2H), 3.76 (s, 3H), 3.80-3.86 (m, 2H), 4.68 (s, 2H), 5.15 (s, 2H), 6.80-6.86 (m, 1H), 7.00-7.07 (m, 3H), 7.25-7.31 (m, 1H), 7.44-7.51 (m, 1H), 7.64-7.77 (m, 5H), 8.09 (br s, 3H).

Example 29: 1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{4-(2,4-difluorobenzyloxy)-3-methoxy benzyl}]ethane-1,2-diamine hydrochloride

Coupling reaction (Method B) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl] carbamate (200 mg, 0.683 mmol) with 4-(2,4-difluorobenzyloxy)-3-methoxybenzyl methanesulfonate (247 mg, 0.683 mmol) in the presence of 60 % sodium hydride (24 mg, 1.024 mmol) and TBAI (247 mg, 0.683 mmol) in *N,N*-dimethylformamide (5 ml) provided 120 mg of *tert*-butyl{2-[*N*-(1,3-benzothiazol-2-yl)-*N*-{4-(2,4-difluorobenzyl oxy)-3-methoxybenzyl}amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.35-3.42 (m, 2H), 3.65-3.71 (m, 2H), 3.81 (s, 3H), 4.67 (s, 2H), 5.10 (s, 2H), 6.77-6.85 (m, 5H), 7.05 (t, J = 7.5 Hz, 1H), 7.28-7.34 (m, 1H), 7.45 (d, J = 7.5 Hz, 1H), 7.53 (t, J = 8.4 Hz, 2H); APCI-MS (*m/z*) 556.20 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.30-3.38 (m, 2H), 3.73 (s, 3H), 3.80-3.86 (m, 2H), 4.69 (s, 2H), 5.03 (s, 2H), 6.83 (d, J = 8.4 Hz, 1H), 7.00-7.11 (m, 4H), 7.25-7.35 (m, 2H), 7.47 (d, J = 8.4 Hz, 1H), 7.57 (d, J = 7.5 Hz, 1H), 7.72-7.80 (m, 1H), 8.09 (br s, 3H).

Example 30:1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{[4-(2,6-difluorobenzyloxy)]-3-methoxy benzyl}] ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl] carbamate (200 mg, 0.683 mmol) with 2-{[4-(bromomethyl)-2-methoxyphenoxy] methyl}-1,3-difluorobenzene (326 mg, 0.683 mmol) in the presence of 60 % sodium hydride (24 mg, 1.024 mmol) and TBAI (247 mg, 0.683 mmol) in *N,N*-dimethylformamide (5 ml) provided 120 mg of *tert*-butyl {3-[*N*-(1,3-Benzothiazol-2-yl)-*N*-([4-(2,6-difluorobenzyloxy)]-3-methoxybenzyl}])amino] ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.35-3.41 (m, 2H), 3.65-3.74 (m, 2H), 3.78 (s, 3H), 4.67 (s, 2H), 5.13 (s, 2H), 6.80-6.95 (m, 4H), 7.05 (t, J = 6.9 Hz, 1H), 7.17 (d, J = 7.2 Hz, 1H), 7.25-7.35 (m, 2H), 7.54 (t, J = 8.7 Hz, 2H). ESI-MS (*m/z*) 556.22 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d6) δ 3.10-3.18 (m, 2H), 3.70 (s, 3H), 3.78-3.85 (m, 2H), 4.68 (s, 2H), 5.03 (s, 2H), 6.84 (d, J = 8.4 Hz, 1H), 6.92-6.98 (m, 1H), 7.06 (d, J = 7.8 Hz, 2H), 7.15 (t, J = 7.8 Hz, 2H), 7.28 (t, J = 8.4 Hz, 1H), 7.45-7.55 (m, 2H), 7.75 (d, J = 7.8 Hz, 1H), 8.04 (br s, 3H).

Example 31: 1-[*N*-[(4-Benzyloxy-3-methoxy)benzyl]-*N*-(5-trifluorormethoxy-1,3-benzo thiazol -2-yl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method C) of t*ert*-butyl{2-[(4-benzyloxy-3-methoxybenzyl)amino] ethyl}carbamate (250 mg, 0.985 mmol) with 2-chloro-5-(trifluoromethoxy)-1,3-benzo thiazole (250 mg, 0.985 mmol) in the presence of *N,N*- diisopropylethylamine (381 mg, 2.957 mmol) in ethanol (5 ml) provided 90 mg of *tert*-butyl{2-*N*-[(4-benzyloxy-3-methoxybenzyl)-*N*-(5-trifluoromethoxy-1,3-benzothiazol-2-yl)amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 9H), 3.35-3.42 (m, 2H), 3.62-3.68 (m, 2H), 3.84 (s, 3H), 4.65 (s, 2H), 5.00 (br s, 1H), 5.12 (s, 2H), 6.76-6.84 (m, 3H), 7.14 (d, J = 7.2 Hz, 1H), 7.24-7.48 (m, 7H); APCI-MS (*m/z*) 604.28 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.16 (m, 2H),

3.75 (s, 3H), 3.80-3.86 (m, 2H), 4.67 (s, 2H), 5.03 (s, 2H), 6.80 (d, J = 8.1 Hz, 1H), 6.98 (s, 1H), 6.99 (d, J = 8.1 Hz, 1H), 7.25-7.39 (m, 6H), 7.50 (d, J = 8.7 Hz, 1H), 7.91 (s, 1H), 8.04 (br s, 3H).

Example 32: 1-[*N*-[(4-Benzyloxy-3-methoxy)benzyl]-*N*-(6-chloro-1,3-benzothiazol-2-yl)] ethane-1,2-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl{2-[(4-benzyloxy-3-methoxybenzyl)amino] ethyl}carbamate (497 mg, 0.985 mmol) with 2,6-dichloro-1,3-benzothiazole (200 mg, 0.985 mmol) in the presence of *N,N*-diisopropylethylamine (381 mg, 2.955 mmol) in ethanol (5 ml) provided 210 mg of *tert*-butyl{2-[*N*-(6-chloro-1,3-benzothiazol-2-yl)-*N*-(4-benzyloxy-3-methoxybenzyl)amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.33 (s, 9H), 3.12-3.20 (m, 2H), 3.49-3.55 (m, 2H), 3.72 (s, 3H), 4.67 (s, 2H), 5.02 (s, 2H), 6.76 (d, J = 8.4 Hz, 1H), 6.94-7.00 (m, 3H), 7.22-7.40 (m, 6H), 7.84 (s, 1H); APCI-MS (*m/z*) 554.50 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.20 (m, 2H), 3.75 (s, 3H), 3.80-3.88 (m, 2H), 4.68 (s, 2H), 5.03 (s, 2H), 6.78-6.85 (m, 1H), 6.95-7.02 (m, 2H), 7.31-7.46 (m, 7H), 7.90 (s, 1H), 8.19 (br s, 3H).

Example 33: 1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-(5-chloro-1,3-benzothiazol-2-yl)ethane-1,2-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl{2-[(4-benzyloxy-3-methoxybenzyl)amino] ethyl}carbamate (200 mg, 0.581 mmol) with 2,5-dichloro-1,3-benzothiazole (117 mg, 0.581 mmol) in the presence of DIEA (224 mg, 1.739 mmol) provided 61 mg of *tert*-butyl {2-*N*-[(5-chloro-1,3-benzothiazol-2-yl)-*N*-(4-benzyloxy-3-methoxybenzyl)amino] ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.37 (d, J = 5.7 Hz, 2H), 3.63-3.68 (m, 2H), 3.83 (s, 3H), 4.65 (s, 2H), 4.98 (br s, 1H), 5.12 (s, 2H), 6.76-6.84 (m, 3H), 7.01 (d, J = 8.4 Hz, 1H), 7.26-7.38 (m, 5H), 7.41-7.49 (m, 2H).

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.18 (m, 2H), 3.74 (s, 3H), 3.77-3.83 (m, 2H), 4.66 (s, 2H), 5.03 (s, 2H), 6.80 (d, J = 8.1 Hz, 1H), 6.97

(s, 1H), 6.99 (d, J = 8.4 Hz, 1H), 7.09 (d, J = 8.7 Hz, 1H), 7.29-7.41 (m, 5H), 7.47 (s, 1H), 7.77 (d, J = 8.4 Hz, 1H), 8.04 (br s, 3H).

Example 34: 1-[*N*-[(4-Benzyloxy-3-methoxy)benzyl]-*N*-(5-trifluromethyl-1,3-benzo thiazol-2-yl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl(2-{[4-(benzyloxy)-3-methoxy benzyl] amino}ethyl)carbamate (426 mg, 0.843 mmol) with 2-chloro-5-(trifluoromethyl)-1,3-benzothiazole (200 mg, 0.843 mmol) in the presence of *N,N*-diisopropylethylamine (326 mg, 2.539 mmol) in ethanol (5 ml) provided 56 mg of *tert*-butyl(2-{*N*-[5-(tri fluoromethyl)-1,3-benzothiazol-2-yl]-*N*-[(4-Benzyloxy-3-methoxy)benzyl] amino}ethyl) carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (s, 9H), 3.30-3.37 (m, 2H), 3.58-3.65 (m, 2H), 3.82 (s, 3H), 4.66 (br s, 2H), 5.07 (s, 2H), 5.23 (br s, 1H), 6.75-6.81 (m, 2H), 7.28-7.37 (m, 3H), 7.47-7.54 (m, 2H), 7.81-7.87 (m, 2H), 8.06 (d, J = 12.0 Hz, 2H); APCI-MS (*m/z*) 594.03 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.18 (m, 2H), 3.74 (s, 3H), 3.80-3.86 (m, 2H), 4.68 (s, 2H), 5.03 (s, 2H), 6.80 (d, J = 8.7 Hz, 1H), 6.98 (d, J = 6.9 Hz, 1H), 7.00 (s, 1H), 7.31-7.46 (m, 7H), 7.90 (s, 1H), 8.21 (br s, 3H).

Example 35: 1-[*N*-(5-Fluoro-1,3-benzothiazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxybenzyl}]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl {2-[(5-fluoro-1,3-benzothiazol-2-yl)amino] ethyl}carbamate (124 mg, 0.398 mmol) with 4-(bromomethyl)-1-[2-fluorobenzyloxy]-2-methoxybenzene (129 mg, 0.398 mmol) in the presence of 60 % sodium hydride (15 mg, 0.611 mmol) in N,N-dimethylformamide (5 ml) provided 120 mg of *tert*-butyl {2-[*N*-(5-fluoro-1,3-benzothiazol-2-yl)-*N*-{4-(2-fluorobenzyloxy)-3-methoxybenzyl}amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.35-3.42 (m, 2H), 3.60-3.66 (m, 2H), 3.82 (s, 3H), 4.65 (s, 2H), 5.02 (br s, 1H), 5.17 (s, 2H), 6.75-6.84 (m, 5H), 7.00-7.13 (m, 2H), 7.25-7.33 (m, 1H), 7.41-7.50 (m, 2H); ESI-MS (*m/z*) 556.34 $(MH)^+$.

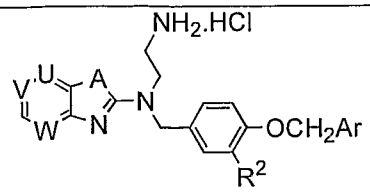
Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.08-3.15 (m, 2H), 3.73 (s, 3H), 3.78-3.85 (m, 2H), 4.67 (s, 2H), 5.06 (s, 2H), 6.81 (d, J = 8.1 Hz, 1H), 6.90-6.97 (m, 2H), 7.03 (d, J = 9.0 Hz, 1H), 7.21-7.27 (m, 3H), 7.36-7.42 (m, 1H), 7.50 (d, J = 7.5 Hz, 1H), 7.74-7.80 (m, 1H), 8.00 (br s, 3H).

Example 36: 1-[*N*-(5,6-Dimethoxy-1,3-benzothiazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxybenzyl}] ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl {2-[(5,6-dimethoxy-1,3-benzothiazol-2-yl)amino]ethyl}carbamate (200 mg, 0.608 mmol) with 4-(bromomethyl)-[1-(2-fluorobenzyloxy)]-2-methoxybenzene (198 mg, 0.608 mmol) in the presence of 60 % sodium hydride (22 mg, 0.912 mmol) and TBAI (220 mg, 0.608 mmol) in *N,N*-dimethylformamide (5 ml) provided 69 mg of *tert*-butyl {2-[*N*-(5,6-dimethoxy-1,3-benzothiazol-2-yl)-*N*-{4-(2-fluorobenzyloxy)-3-methoxybenzyl}amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.45-3.55 (m, 2H), 3.77-3.85 (m, 2H), 3.89 (s, 3H), 3.93 (s, 3H), 3.95 (s, 3H), 4.66 (s, 2H), 5.15 (s, 2H), 6.78-6.85 (m, 3H), 6.90 (t, J = 6.3 Hz, 2H), 6.97 (d, J = 6.0 Hz, 1H), 7.06 (s, 1H), 7.25-7.31 (m, 2H); ESI-MS (*m/z*) 616.27 $(M+NH_4)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.08-3.16 (m, 2H), 3.61-3.80 (m, 2H), 3.70 (s, 3H), 3.73 (s, 3H), 3.76 (s, 3H), 4.64 (s, 2H), 5.03 (s, 2H), 6.82 (d, J = 7.8 Hz, 1H), 6.96 (s, 1H), 7.05-7.18 (m, 4H), 7.39 (s, 1H), 7.50 (t, J = 8.4 Hz, 2H), 8.02 (br s, 3H).

Table 8: Structural details and mass spectral data of Examples 37 to 49



Example No	U	V	W	R^2	A	Ar	Mass (m/z)
Example 37	CH	CH	N	H	O	2-CH_3Ph	APCI: 389.22 $(MH)^+$
Example 38	N	CH	CH	OCH_3	S	Ph	ESI: 421.44 $(MH)^+$
Example 39	CH	CH	N	OCH_3	S	Ph	ESI: 421.74 $(MH)^+$
Example 40	N	CH	CH	OCH_3	S	2-CH_3Ph	APCI: 435.11 $(MH)^+$
Example 41	N	CH	CH	OCH_3	S	2-FPh	ESI: 439.59 $(MH)^+$
Example 42	CH	CH	N	OCH_3	S	2-FPh	ESI: 439.26 $(MH)^+$
Example 43	N	CH	CH	OCH_3	S	2,6-F_2Ph	ESI: 457.01 $(MH)^+$
Example 44	CH	N	CCl	OCH_3	S	2-FPh	APCI: 473.09 $(MH)^+$
Example 45	CH	N	CCl	OCH_3	S	2-CH_3Ph	APCI: 469.12 $(MH)^+$
Example 46	CH	CCF_3	N	OCH_3	S	2-FPh	APCI: 507.30 $(MH)^+$
Example 47	CH	N	CCl	OCH_3	S	2,6-F_2Ph	ESI: 491.11 $(M)^+$
Example 48	CH	N	CBr	OCH_3	S	2-CH_3Ph	APCI: 513.09 $(M)^+$
Example 49	CH	N	CBr	OCH_3	S	2,6-F_2Ph	APCI: 469.12 $(MH)^+$

Example 37: 1-[*N*-{4-[(2-methylbenzyloxy)]benzyl}-*N*-[1,3]oxazolo[4,5-*b*]pyridin-2-yl]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl [2-([1,3]oxazolo[4,5-*b*]pyridin-2-ylamino) ethyl]carbamate (150 mg, 0.539 mmol) with 1-{[4-(bromomethyl)phenoxy]methyl}-2-methylbenzene (157 mg, 0.539 mmol) in the presence of 60 % sodium hydride (28 mg, 0.593 mmol) in N,N-dimethyl formamide (5 ml) afforded 92 mg of *tert*-butyl {2-[(4-[(2-methylbenzyloxy)]benzyl)([1,3]oxazolo[4,5-*b*]pyridin-2-yl)amino]ethyl} carbamate as off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 9H), 2.36 (s, 3H), 3.38-3.45 (m, 2H), 3.62-3.68 (m, 2H), 4.77 (s, 2H), 4.84 (br s, 1H), 5.01 (s, 2H), 6.90-7.00 (m, 4H), 7.20-7.30 (m, 4H), 7.40-7.46 (m, 2H), 8.20-8.26 (m, 1H); ESI-MS (*m/z*) 489.23 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.31 (s, 3H), 3.12-3.20 (m, 2H), 3.75-3.81 (m, 2H), 4.82 (s, 2H), 5.07 (s, 2H), 7.04 (d, J = 7.8 Hz, 2H), 7.16-7.28 (m, 4H), 7.35-7.42 (m, 4H), 7.98-8.06 (m, 1H), 8.23 (br s, 3H).

Example 38: 1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-[1,3]thiazolo[5,4-*b*]pyridin-2-yl] ethane-1,2-diamine hydrochloride

Coupling reaction of *tert*-butyl{2-[(4-benzyloxy-3-methoxybenzyl)amino]ethyl} carbamate (340 mg, 0.882 mmol) with 2-chloro[1,3]thiazolo[5,4-*b*]pyridine (150 mg, 0.882 mmol) in the presence of *N,N*-diisopropylethylamine (341 mg, 2.041 mmol) in ethanol (5 ml) according to the procedure described for Formula (Ic) afforded 167 mg of *tert*-butyl {2-*N*-[(4-benzyloxy-3-methoxybenzyl) ([1,3]thiazolo[5,4-*b*]pyridin-2-yl) amino]ethyl}carbamate as an off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 9H), 3.35-3.42 (m, 2H), 3.62-3.68 (m, 2H), 3.83 (s, 3H), 4.68 (s, 2H), 4.98 (br s, 1H), 5.12 (s, 2H), 6.74-6.84 (m, 3H), 7.18 (dd, J = 4.8, 8.4 Hz, 2H), 7.33 (t, J = 7.8 Hz, 2H), 7.38 (d, J = 7.2 Hz, 2H), 7.68 (d, J = 7.8 Hz, 1H), 8.15 (d, J = 4.5 Hz, 1H); APCI-MS (*m/z*) 521.58 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.08-3.15 (m, 2H), 3.75 (s, 3H), 3.82-3.88 (m, 2H), 4.73 (s, 2H), 5.03 (s, 2H), 6.83 (d, J = 8.1 Hz, 1H), 7.01 (d, J = 8.4 Hz, 1H), 7.02 (s, 1H), 7.29-7.41 (m, 6H), 7.80 (d, J = 7.8 Hz, 1H), 8.17 (dd, J = 1.5, 4.2 Hz, 1H), 8.28 (br s, 3H).

Example 39: 1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-[1,3]thiazolo[4,5-*b*]pyridin-2-yl]ethane-1,2-diamine hydrochloride

Coupling reaction of *tert*-butyl{2-[(4-benzyloxy-3-methoxybenzyl)amino]ethyl} carbamate (454 mg, 1.176 mmol) with 2-chloro[1,3]thiazolo[4,5-*b*]pyridine (200 mg, 1.176 mmol) in the presence of *N,N*-diisopropylethylamine (458 mg, 3.529 mmol) in ethanol (5 ml) according to the procedure described for Formula (Ic) afforded 127 mg of *tert*-butyl {2-[*N*-(4-benzyloxy-3-methoxybenzyl)-*N*-([1,3]thiazolo[4,5-*b*]pyridin-2-yl)-amino]ethyl}carbamate as off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H),

3.35-3.42 (m, 2H), 3.65-3.71 (m, 2H), 3.83 (s, 3H), 4.68 (s, 2H), 4.97 (br s, 1H), 5.12 (s, 2H), 6.78-6.85 (m, 3H), 7.15-7.22 (m, 2H), 7.28-7.41 (m, 4H), 7.66 (dd, J = 4.5, 8.4 Hz, 1H), 8.15 (dd, J = 1.2, 4.8 Hz, 1H); APCI-MS (*m/z*) 521.72 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.08-3.15 (m, 2H), 3.75 (s, 3H), 3.80-3.86 (m, 2H), 4.71 (s, 2H), 5.03 (s, 2H), 6.84 (d, J = 7.8 Hz, 1H), 6.95-7.02 (m, 2H), 7.29-7.41 (m, 6H), 7.77 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 5.1 Hz, 1H), 8.21 (br s, 3H).

Example 40: 1-[*N*-{3-Methoxy-4-[(2-methylbenzyloxy)]benzyl}-*N*-[1,3]thiazolo[5,4-*b*] pyridin-2-yl]ethane-1,2-diamine hydrochloride

Coupling reaction of *tert*-butyl [2-({3-methoxy-4-(2-methylbenzyloxy)benzyl} amino) ethyl]carbamate (80 mg, 0.200 mmol) with 2-chloro[1,3]thiazolo[5,4-*b*]pyridine (34 mg, 0.200 mmol) in the presence of triethylamine (82 µl, 0.600 mmol) in ethanol (5 ml) according to the procedure described for Formula (Ic) afforded 49 mg of *tert*-butyl {2-[*N*-(4-[2-methylbenzyloxy]-3-methoxybenzyl)-*N*-([1,3]thiazolo[5,4-*b*]pyridin-2-yl)amino]ethyl} carbamate as off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 9H), 2.37 (s, 3H), 3.40-3.48 (m, 2H), 3.72-3.78 (m, 2H), 3.84 (s, 3H), 4.73 (s, 2H), 5.09 (br s, 1H), 5.09 (s, 2H), 6.80-6.90 (m, 3H), 7.20-7.30 (m, 4H), 7.39 (d, J = 6.9 Hz, 1H), 7.77-7.83 (m, 1H), 8.20-8.26 (m, 1H); ESI-MS (*m/z*) 535.09 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure (Method A, Step 2) gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.30 (s, 3H), 3.10-3.18 (m, 2H), 3.75 (s, 3H), 3.85-3.88 (m, 2H), 4.74 (s, 2H), 5.03 (s, 2H), 6.88 (d, J = 7.2 Hz, 1H), 7.00-7.10 (m, 2H), 7.18-7.26 (m, 3H), 7.32-7.42 (m, 2H), 7.84 (d, J = 7.8 Hz, 1H), 8.17-8.23 (m, 1H + 3H).

Example 41: 1-[*N*-{4-(2-Fluorobenzyloxy)-3-methoxybenzyl}-*N*-[1,3]thiazolo[5,4-*b*] pyridin -2-yl]ethane-1,2-diamine hydrochloride

Coupling reaction of *tert*-butyl [2-{[4-(2-fluorobenzyloxy)-3-methoxybenzyl]amino} ethyl]carbamate (380 mg, 0.941 mmol) with 2-chloro[1,3]thiazolo[5,4-*b*]pyridine (160 mg, 0.941 mmol) in the presence of *N,N*-diisopropylethylamine (364 mg, 2.823 mmol) in

ethanol (5 ml) according to the procedure described for Formula (Ic) afforded 138 mg of *tert*-butyl{2-[*N*-(4-[2-fluorobenzyloxy]-3-methoxybenzyl)-*N*-([1,3]thiazolo[5,4-*b*] pyridine-2-yl)amino]ethyl}carbamate as off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.35-3.41 (m, 2H), 3.63-3.70 (m, 2H), 3.85 (s, 3H), 4.69 (s, 2H), 4.99 (br s, 1H), 5.17 (s, 2H), 6.73-6.80 (m, 1H), 6.83 (d, J = 8.4 Hz, 2H), 7.00-7.08 (m, 1H), 7.11 (d, J = 7.8 Hz, 1H), 7.17-7.22 (m, 2H), 7.47 (t, J = 7.2 Hz, 1H), 7.66 (dd, J = 1.5, 8.1 Hz, 1H), 8.15 (dd, J = 1.5, 4.8 Hz, 1H); ESI-MS (*m/z*) 561.11 $(M+Na)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.16 (m, 2H), 3.73 (s, 3H), 3.82-3.88 (m, 2H), 4.72 (br s, 2H), 5.06 (s, 2H), 6.85 (d, J = 8.7 Hz, 1H), 7.02 (br s, 1H), 7.04 (d, J = 7.5 Hz, 1H), 7.18-7.24 (m, 2H), 7.32-7.40 (m, 2H), 7.50 (t, J = 7.8 Hz, 1H), 7.80 (d, J = 8.1 Hz, 1H), 8.17 (d, J = 4.8 Hz, 1H), 8.27 (br s, 3H).

Example 42: 1-[*N*-{4-(2-Fluorobenzyloxy)-3-methoxybenzyl}-*N*-[1,3]thiazolo[4,5-*b*] pyridin-2-yl]ethane-1,2-diamine hydrochloride

Coupling reaction of *tert*-butyl [2-{[4-(2-fluorobenzyloxy)-3-methoxybenzyl] amino} ethyl]carbamate (237 mg, 0.588 mmol) with 2-chloro[1,3]thiazolo[4,5-*b*]pyridine (100 mg, 0.588 mmol) in the presence of *N,N*-diisopropylethylamine (227 mg, 1.704 mmol) in ethanol (5 ml) according to the procedure described for Formula (Ic) afforded 138 mg of *tert*-butyl{2-[*N*-(4-[2-fluorobenzyloxy]-3-methoxybenzyl)-*N*-([1,3]thiazolo[4,5-*b*] pyridin-2-yl)-amino]ethyl}carbamate as off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.35-3.43 (m, 2H), 3.65-3.72 (m, 2H), 3.84 (s, 3H), 4.71 (s, 2H), 4.98 (br s, 1H), 5.19 (s, 2H), 6.75-6.82 (m, 1H), 6.86 (d, J = 8.4 Hz, 2H), 7.05 (t, J = 8.7 Hz, 1H), 7.13 (t, J = 7.8 Hz, 1H), 7.16-7.22 (m, 1H), 7.25-7.32 (m, 1H), 7.50 (t, J = 7.5 Hz, 1H), 7.69 (d, J = 8.4 Hz, 1H), 8.15-8.21 (m, 1H); ESI-MS (*m/z*) 538.63 $(M)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.10-3.16 (m, 2H), 3.75 (s, 3H), 3.80-3.86 (m, 2H), 4.74 (s, 2H), 5.08 (s, 2H), 6.89 (d, J = 8.4 Hz, 1H), 7.00-7.08 (m, 2H), 7.20-7.26 (m, 2H), 7.32-7.40 (m, 2H), 7.55 (t, J = 8.1 Hz, 1H), 7.80 (d, J = 7.8 Hz, 1H), 8.15-8.22 (m, 1H + 3H).

Example 43: 1-[*N*-{4-(2,6-Difluorobenzyloxy)-3-methoxybenzyl}-*N*-[1,3]thiazolo[5,4-*b*] pyridin-2-yl]ethane-1,2-diamine hydrochloride

Coupling reaction [described for Formula (Ic)] of *tert*-butyl [2-{[4-(2,4-difluoro benzyl oxy)-3-methoxybenzyl]amino}ethyl]carbamate (309 mg, 0.714 mmol) with 2-chloro[1,3]thiazolo[5,4-*b*]pyridine (130 mg, 0.714 mmol) in the presence of *N,N*-diisopropylethylamine (276 mg, 2.142 mmol) in ethanol (5 ml) according to the procedure described for Formula (Ic) afforded 97 mg of *tert*-butyl {2-[*N*-(4-[2,6-difluorobenzyloxy]-3-methoxybenzyl)-*N*-([1,3] thiazolo[5,4-*b*]pyridin-2-yl)amino]ethyl} carbamate as off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.38-3.46 (m, 2H), 3.65-3.72 (m, 2H), 3.80 (s, 3H), 4.71 (s, 2H), 5.00 (br s, 1H), 5.15 (s, 2H), 6.83-6.98 (m, 5H), 7.20-7.36 (m, 2H), 7.70 (d, J = 7.8 Hz, 1H), 8.18 (d, J = 4.5 Hz, 1H); APCI-MS (*m/z*) 557.06 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.08-3.14 (m, 2H), 3.72 (s, 3H), 3.80-3.90 (m, 2H), 4.75 (s, 2H), 5.05 (s, 2H), 6.89 (d, J = 7.8 Hz, 1H), 7.03 (s, 1H), 7.09 (d, J = 8.1 Hz, 1H), 7.18 (t, J = 7.8 Hz, 2H), 7.30-7.38 (m, 1H), 7.49-7.56 (m, 1H), 7.81 (d, J = 7.2 Hz, 1H), 8.15-8.23 (m, 1H + 3H).

Example 44: 1-[*N*-(7-Chloro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxybenzyl}]ethane-1,2-diamine hydrochloride

Coupling reaction of *tert*-butyl [2-{[4-(2-fluorobenzyloxy)-3-methoxybenzyl]amino} ethyl]carbamate (305 mg, 0.735 mmol) with 2,7-dichloro[1,3]thiazolo[5,4-*c*]pyridine (150 mg, 0.735 mmol) in the presence of *N,N*-diisopropylethylamine (284 mg, 2.205 mmol) in ethanol (5 ml) according to the procedure described for Formula (Ic) afforded 105 mg of *tert*-butyl {2-[*N*-(7-chloro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-(4-[2-fluoro benzyloxy]-3-methoxybenzyl)amino] ethyl}carbamate as an off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.40-3.48 (m, 2H), 3.68-3.75 (m, 2H), 3.85 (s, 3H), 4.73 (br s, 2H), 5.20 (s, 2H), 6.78-6.86 (m, 2H), 6.92-6.98 (m, 1H), 7.02-7.08 (m, 1H), 7.12-7.18 (m, 2H), 7.45-7.52 (m, 1H), 8.42 (s, 1H), 8.59 (s, 1H); APCI-MS (*m/z*, Cl^{35}, Cl^{37}) 573.23 $(MH)^+$ (100 %), 575.14 (35%).

Deprotection of the above intermediate as described in the general procedure afforded the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.18-3.25 (m, 2H), 3.70-3.76 (m, 5H), 4.87 (br s, 2H), 5.09 (s, 2H), 6.90-6.96 (m, 1H), 7.08 (d, J = 8.1 Hz, 2H), 7.20-7.30 (m, 2H), 7.35-7.42 (m, 1H), 7.50-7.56 (m, 1H), 8.32 (br s, 3H), 8.75 (s, 1H), 9.08 (s, 1H).

Example 45: *N*-(7-Chloro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-{3-methoxy-4-[(2-methyl benzyloxy)] benzyl}ethane-1,2-diamine hydrochloride

Coupling reaction of *tert*-butyl{2-[(4-[(2-methylbenzyloxy)-3-methoxybenzyl) amino] ethyl} carbamate (80 mg, 0.196 mmol) with 2-chloro[1,3]thiazolo[5,4-*c*]pyridine (40 mg, 0.196 mmol) in the presence of triethylamine (60 mg, 0.594 mmol) in ethanol (5 ml) according to the procedure described for Formula (Ic) afforded 51 mg of *tert*-butyl {2-[*N*-(7-chloro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-(4-[2-methylbenzyloxy]-3-methoxybenzyl)amino] ethyl}carbamate as an off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 2.37 (s, 3H), 3.40-3.46 (m, 2H), 3.72-3.78 (m, 2H), 3.84 (s, 3H), 4.74 (br s, 2H), 5.09 (s, 2H), 6.80-6.86 (m, 2H), 6.90-6.96 (m, 1H), 7.20-7.28 (m, 3H), 7.35-7.41 (m, 1H), 8.42 (s, 1H), 8.60 (s, 1H); APCI-MS (*m/z*, Cl^{35}, Cl^{37}) 569.12 $(MH)^+$ (100 %), 471.13 (35%).

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.30 (s, 3H), 3.20-3.27 (m, 2H), 3.60-3.68 (m, 2H), 3.76 (s, 3H), 4.86 (s, 2H), 5.04 (s, 2H), 6.92-6.98 (m, 1H), 7.08 (d, J = 7.8 Hz, 2H), 7.19-7.27 (m, 3H), 7.38 (d, J = 6.0 Hz, 1H), 8.28 (br s, 3H), 8.72 (s, 1H), 9.06 (s, 1H).

Example 46: 1-[*N*-{4-(2-Fluorobenzyloxy)-3-methoxybenzyl}-*N*-[6-(trifluoromethyl) [1,3] thiazolo[4,5-*b*]pyridin-2-yl] ethane-1,2-diamine hydrochloride

Coupling reaction of *tert*-butyl [2-{[4-(2-fluorobenzyloxy)-3-methoxybenzyl] amino}ethyl]carbamate (368 mg, 0.884 mmol) with 2-chloro-6-(trifluoromethyl) [1,3]thiazolo[4,5-*b*]pyridine (200 mg, 0.884 mmol) in the presence of *N,N*-diisopropylethylamine (342 mg, 2.654 mmol) in ethanol (5 ml) according to the procedure described for Formula (Ic) afforded 176 mg of *tert*-butyl (2-{*N*-[4-(2-

fluorobenzyloxy)-3-methoxybenzyl]-*N*-[6-(trifluoromethyl)[1,3]thiazolo[4,5-*b*]pyridin-2-yl]amino}ethyl) carbamate; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 9H), 3.40-3.48 (m, 2H), 3.70-3.80 (m, 2H), 3.85 (s, 3H), 4.75 (br s, 2H), 4.85 (br s, 1H), 5.20 (s, 2H), 6.80-6.86 (m, 3H), 7.06 (t, J = 8.7 Hz, 1H), 7.14 (d, J = 7.5 Hz, 1H), 7.20-7.28 (m, 1H), 7.51 (t, J = 7.8 Hz, 1H), 8.05 (s, 1H), 8.66 (s, 1H); APCI-MS (*m/z*) 507.13 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.15-3.21 (m, 2H), 3.75-3.85 (m, 5H), 4.80 (s, 2H), 5.09 (s, 2H), 6.86-6.92 (m, 1H), 7.04-7.10 (m, 2H), 7.20-7.30 (m, 2H), 7.38-7.45 (m, 1H), 7.51-7.58 (m, 1H), 8.29 (br s, 3H), 8.64-8.72 (m, 2H).

Example 47: 1-[*N*-{4-[(2,6-Difluorobenzyloxy)-3-methoxybenzyl]}-*N*-7-chloro [1,3] thiazolo[5,4-*c*] pyridin-2-yl]ethane-1,2-diamine hydrochloride

Coupling reaction of *tert*-butyl [2-{[4-(2,4-difluorobenzyloxy)-3-methoxy benzyl] amino}ethyl]carbamate (200 mg, 0.461 mmol) with 2,7-dichloro[1,3]thiazolo[5,4-*c*]pyridine (94 mg, 0.461 mmol) in the presence of *N,N*-diisopropylethylamine (178 mg, 1.382 mmol) in ethanol (5 ml) according to the procedure described for Formula (Ic) afforded 81 mg of *tert*-butyl {2-[*N*-(7-chloro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-(4-[2,6-difluorobenzyloxy]-3-methoxybenzyl)amino]ethyl}carbamate as off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.40-3.48 (m, 2H), 3.62-3.83 (m, 5H), 4.75 (br s, 2H), 5.16 (s, 2H), 6.84-6.97 (m, 4H), 7.10-7.19 (m, 1H), 7.30-7.40 (m, 1H), 8.42 (s, 1H), 8.61(s, 1H); APCI-MS (*m/z*, Cl^{35}, Cl^{37}) 591.10 $(M)^+$ (100 %), 593.08 (35%).

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.20-3.28 (m, 2H), 3.73 (s, 3H), 4.00-4.06 (m, 2H), 4.88 (br s, 2H), 5.06 (s, 2H), 6.92-6.99 (m, 1H), 7.10-7.21 (m, 4H), 7.53 (t, J = 7.8 Hz, 1H), 8.35 (br s, 3H), 8.77 (s, 1H) 9.10 (s, 1H).

Example 48: *N*-(7-Bromo[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-{3-methoxy-[4-(2-methyl benzyloxy)] benzyl}ethane-1,2-diamine hydrochloride

Coupling reaction of *tert*-butyl{2-[(4-[2-methylbenzyloxy]-3-methoxy benzyl) amino] ethyl}carbamate (102 mg, 0.241 mmol) with 2-chloro-7-bromo[1,3]thiazolo[5,4-*c*]pyridine (60 mg, 0.241 mmol) in the presence of triethylamine (73 mg, 0.725 mmol) in

ethanol (5 ml) according to the procedure described for Formula (Ic) afforded 34 mg of *tert*-butyl {2-[*N*-(7-bromo[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-(3-methoxy-[4-(2-methyl benzyloxy)]benzyl)amino]ethyl}carbamate as an off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (s, 9H), 2.37 (s, 3H), 3.43-3.62 (m, 3H), 3.86 (s, 3H), 3.96-4.02 (m, 1H), 4.65-4.72 (m, 1H), 5.05-5.12 (m, 3H), 6.80-6.89 (m, 3H), 7.15-7.25 (m, 3H), 7.37 (d, J = 7.8 Hz, 1H), 8.53 (s, 1H), 8.82 (s, 1H); APCI-MS (*m/z*, Br^{79}, Br^{81}) 613.09 $(M)^+$ (100 %), 615.05 (100%).

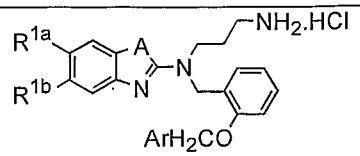
Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.30 (s, 3H), 3.20-3.28 (m, 2H), 3.77 (s, 3H), 3.97-4.04 (m, 2H), 4.85 (s, 2H), 5.04 (s, 2H), 6.92-6.98 (m, 1H), 7.08 (d, J = 8.4 Hz, 2H), 7.19-7.27 (m, 3H), 7.74 (d, J = 6.9 Hz, 1H), 8.32 (br s, 3H), 8.80 (s, 1H), 9.09 (s, 1H).

Example 49: *N*-(7-Bromo[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-{[4-(2,6-difluoro benzyl oxy)] -3 -methoxybenzyl} ethane-1,2-diamine hydrochloride

Coupling reaction of *tert*-butyl{2-[4-(2,6-difluorobenzyloxy)]-3-methoxybenzyl) amino] ethyl} carbamate (250 mg, 0.592 mmol) with 7-bromo-2-chloro[1,3]thiazolo[5,4-*c*] pyridine (146 mg, 0.592 mmol) in the presence of triethylamine (179 mg, 1.777 mmol) in ethanol (5 ml) according to the procedure described for Formula (Ic) afforded 78 mg of *tert*-butyl {2-[(7-bromo[1,3]thiazolo[5,4-*c*]pyridin-2-yl)([4-(2,6-difluorobenzyloxy)]-3-methoxybenzyl)amino]ethyl}carbamate as white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.40-3.49 (m, 2H), 3.62-3.83 (m, 5H), 4.73 (s, 2H), 5.16 (s, 2H), 6.84-6.99 (m, 5H), 7.25-7.32 (m, 1H), 8.53 (s, 1H), 8.61 (s, 1H); APCI-MS (*m/z*, Br^{79}, Br^{81}) 635.11 $(M)^+$ (100 %), 637.09 (100%).

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.16-3.24 (m, 2H), 3.74 (s, 3H), 4.00-4.06 (m, 2H), 4.88 (s, 2H), 5.06 (s, 2H), 6.92-6.99 (m, 1H), 7.10-7.21 (m, 4H), 7.54 (t, J = 7.8 Hz, 1H), 8.37 (br s, 3H), 8.83 (s, 1H) 9.11 (s, 1H).

Table 9: Structural details and mass spectral data of Examples 50 to 53



Example No.	R^{1a}	R^{1b}	A	Ar	MS (m/z)
Example 50	H	H	O	Ph	ESI: 388.20 $(MH)^+$
Example 51	H	H	O	2-FPh	APCI: 406.28 $(M)^+$
Example 52	H	H	O	2,6-F_2Ph	ESI: 424.03 $(MH)^+$
Example 53	H	Cl	O	Ph	APCI: 422.92 $(MH)^+$

Example 50: 1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(2-benzyloxybenzyl)]propane-1,3-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl{2-[*N*-(2-benzyloxybenzyl) amino]ethyl} carbamate (480 mg, 1.311 mmol) with 2-chloro-1,3-benzoxazole (200 mg, 1.311 mmol) in the presence of triethyl amine (260 mg, 2.621 mmol) in ethanol (10 ml) provided 300 mg of *tert*-butyl[3-*N*-(1,3-benzoxazol-2-yl)-*N*-(2-benzyloxybenzyl) amino) propyl] carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43 (s, 9H), 1.70-1.78 (m, 2H), 3.05-3.12 (m, 2H), 3.48-3.58 (m, 2H), 4.79 (s, 2H), 5.05 (s, 2H), 5.44 (br s, 1H), 6.92-7.00 (m, 3H), 7.10-7.17 (m, 2H), 7.21-7.28 (m, 6H), 7.33-7.40 (m, 2H); ESI-MS (*m/z*) 488.43 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.90-1.96 (m, 2H), 2.75-2.81 (m, 2H), 3.55-3.61 (m, 2H), 4.77 (s, 2H), 5.13 (s, 2H), 6.93 (t, J = 6.9 Hz, 1H), 7.02 (t, J = 7.8 Hz, 1H), 7.14-7.25 (m, 7H), 7.30-7.40 (m, 4H), 8.00 (br s, 3H).

Example 51: 1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{2-(2-fluorobenzyloxy)benzyl}]propane-1,3-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[3-*N*-(1,3-benzoxazol-2-ylamino)propyl] carbamate (200 mg, 0.681 mmol) with 1-(bromomethyl)-2-[(2-fluorobenzyl)oxy]benzene (202 mg, 0.681 mmol) in the presence of 60 % sodium hydride (16 mg, 0.681 mmol) and TBAI (250 mg, 0.681 mmol) in dimethyl formamide (10 ml) provided 200 mg of *tert*-butyl{3-[1,3-benzoxazol-2-yl(2-[(2-fluorobenzyl)oxy]benzyl) amino]propyl}carbamate

as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43 (s, 9H), 1.72-1.78 (m,2H), 3.05-3.12 (m, 2H), 3.53-3.59 (m, 2H), 4.78 (s, 2H), 5.11 (s, 2H), 5.48 (br s, 1H), 6.90-7.00 (m, 5H), 7.10-7.20 (m, 3H), 7.26-7.38 (m, 4H); APCI-MS (*m/z*) 506.64 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.85-1.95 (m, 2H), 2.72-2.78 (m, 2H), 3.52-3.60 (m, 2H), 4.73 (s, 2H), 5.16 (s, 2H), 6.97 (t, J = 7.8 Hz, 2H), 7.05-7.11 (m, 3H), 7.16-7.24 (m, 3H), 7.28-7.34 (m, 3H), 7.45-7.52 (m, 1H), 8.00 (br s, 3H).

Example 52: 1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{4-(2,6-difluorobenzyloxy) benzyl}] propane-1,3-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[3-*N*-(1,3-benzoxazol-2-ylamino)propyl] carbamate (200 mg, 0.687 mmol) with 2-{[2-(bromomethyl)phenoxy]methyl}-1,3-di fluorobenzene (214 mg, 0.687 mmol) in the presence of 60 % sodium hydride (16 mg, 0.687 mmol) and TBAI (250 mg, 0.687 mmol) in N,N-dimethylformamide (5 ml) provided 200 mg of *tert*-butyl{2-[*N*-(1,3-benzoxazol-2-yl)-*N*-{4-(2,6-difluorobenzyl oxy) benzyl}amino]propyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43 (s, 9H), 1.65-1.71 (m, 2H), 3.02-3.08 (m, 2H), 3.49-3.56 (m, 2H), 4.69 (s, 2H), 5.11 (s, 2H), 5.24 (br s, 1H), 6.79 (t, J = 7.8 Hz, 2H), 6.90-6.96 (m, 2H), 7.04-7.14 (m, 4H), 7.20-7.31 (m, 3H); ESI-MS (*m/z*) 524.36 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.85-1.95 (m, 2H), 2.72-2.78 (m, 2H), 3.50-3.56 (m, 2H), 4.65 (s, 2H), 5.13 (s, 2H), 6.95-7.05 (m, 4H), 7.12-7.18 (m, 1H), 7.24-7.34 (m, 6H), 7.99 (br s, 3H).

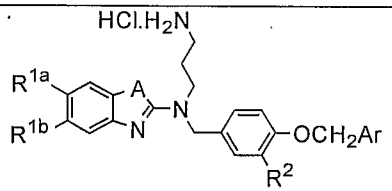
Example 53: 1-[*N*-(2-Benzyloxybenzyl)-*N*-(5-chloro-1,3-benzoxazol-2-yl)]propane-1,3-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl{3-[*N*-(2-benzyloxy benzyl) amino] propyl} carbamate (250 mg, 0.702 mmol) with 2,5-dichloro-1,3-benzothiazole (132 mg, 0.702 mmol), in the presence of DIEA (271 mg, 2.106 mmol) provided 68 mg of *tert*-butyl {3-

[*N*-(2-benzyloxybenzyl)-*N*-(5-chloro-1,3-benzoxazol-2-yl)amino] propyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43 (s, 9H), 1.71 (t, *J* = 6.9 Hz, 2H), 3.00-3.08 (m, 2H), 3.53 (t, *J* = 6.9 Hz, 2H), 4.75 (s, 2H), 5.03 (s, 2H), 6.89-7.03 (m, 4H), 7.25-7.35 (m, 8H); APCI-MS (*m/z*) 522.19 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.86-1.94 (m, 2H), 2.72-2.78 (m, 2H), 3.52-3.58 (m, 2H), 4.74 (s, 2H), 5.12 (s, 2H), 6.92 (t, *J* = 7.5 Hz, 2H), 6.98 (d, *J* = 8.4Hz, 1H), 7.10-7.16 (m, 2H), 7.20-7.29 (m, 4H), 7.34-7.40 (m, 3H), 7.88 (br s, 3H).

Table 10: Structural details and mass spectral data of Examples 54 to 62



Example No.	R^{1a}	R^{1b}	A	R^2	Ar	MS (m/z)
Example 54	H	H	O	H	2-CH_3Ph	ESI: 402.20 $(MH)^+$
Example 55	H	H	O	OCH_3	Ph	ESI: 418.31 $(MH)^+$
Example 56	H	F	O	OCH_3	Ph	APCI: 436.31 $(MH)^+$
Example 57	H	H	O	OCH_3	2-FPh	APCI: 436.34 $(MH)^+$
Example 58	H	H	O	OCH_3	2-CH_3Ph	ESI: 432.17 $(MH)^+$
Example 59	H	H	O	OCH_3	2-CF_3Ph	APCI: 486.26 $(MH)^+$
Example 60	H	H	O	OCH_3	2,6-F_2Ph	APCI: 454.19 $(MH)^+$
Example 61	H	CH_3	O	OCH_3	Ph	APCI: 432.24 $(MH)^+$
Example 62	H	Cl	O	OCH_3	2-FPh	ESI: 470.14 $(MH)^+$

Example 54: 1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-[2-methylbenzyloxy]benzyl)]propane-1,3-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[3-*N*-(1,3-benzoxazol-2-ylamino)propyl] carbamate (200 mg, 0.692 mmol) with 1-{[4-(bromomethyl)phenoxy]methyl}-2-methyl benzene (200 mg, 0.692 mmol) in the presence of 60 % sodium hydride (18 mg, 0.751

mmol) in dimethyl formamide (5 ml) provided 121 mg of *tert*-butyl{3-[*N*-(1,3-benzoxazol-2-yl){4-(2-methylbenzyloxy) benzyl} amino]propyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (s, 9H), 1.75-1.83 (m, 2H), 2.36 (s, 3H), 3.10-3.16 (m, 2H), 3.52-3.58 (m, 2H), 4.69 (s, 2H), 5.01 (s, 2H), 5.38 (br s, 1H), 6.95-7.05 (m, 3H), 7.20-7.30 (m, 8H), 7.30-7.38 (m, 1H); APCI-MS (*m/z*) 502.15 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.92-1.98 (m, 2H), 2.50 (s, 3H), 2.80-2.86 (m, 2H), 3.53-3.59 (m, 2H), 4.69 (s, 2H), 5.06 (s, 2H), 7.02 (d, J = 7.8 Hz, 3H), 7.20-7.32 (m, 7H), 7.35-7.44 (m, 2H), 7.94 (br s, 3H).

Example 55: 1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-benzyloxy-3-methoxybenzyl)]propane-1,3-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl(3-{*N*-[4-benzyloxy-3-methoxybenzyl] amino}propyl) carbamate (500 mg, 1.255 mmol) with 2-chloro-1,3-benzoxazole (160 mg, 1.046 mmol) in the presence of triethyl amine (211 mg, 2.092 mmol) in ethanol (10 ml) provided 110 mg of *tert*-butyl {3-[*N*-(1,3-benzoxazol-2-yl)-*N*-(4-benzyloxy-3-methoxy benzyl)amino]propyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (s, 9H), 1.75-1.81 (m, 2H), 3.10-3.16 (m, 2H), 3.45-3.51 (m, 2H), 3.83 (s, 3H), 4.66 (s, 2H), 5.13 (s, 2H), 5.33 (br s, 1H), 6.75-6.83 (m, 4H), 6.98-7.05 (m, 1H), 7.12-7.20 (m, 1H), 7.30-7.40 (m, 6H); APCI-MS (*m/z*) 519.34 $(M)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.80-1.90 (m, 2H), 2.80-2.90 (m, 2H), 3.55-3.61 (m, 2H), 3.81 (s, 3H), 4.62 (s, 2H), 5.10 (s, 2H), 6.80-6.85 (m, 1H), 6.90-7.00 (m, 3H), 7.15-7.21 (m, 1H), 7.24-7.34 (m, 7H), 8.05 (br s, 3H).

Example 56: 1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-(5-fluoro-1,3-benzoxazol-2-yl) propane-1,3-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl (3-{*N*-[4-benzyloxy-3-methoxy benzyl] amino}propyl) carbamate (500 mg, 1.261 mmol) with 2-chloro-5-fluoro-1,3-benzoxazole (180 mg, 1.049 mmol) in the presence of triethyl amine (215 mg, 2.105 mmol) in ethanol (10 ml) provided 200 mg of *tert*-butyl {3-[*N*-(4-benzyloxy-3-methoxybenzyl)-*N*-(5-

fluoro-1,3-benzoxazol-2-yl)amino]propyl}carbamate as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.38 (s, 9H), 1.70-1.80 (m, 2H), 2.90-3.00 (m, 2H), 3.42-3.48 (m, 2H), 3.78 (s, 3H), 4.67 (s, 2H), 5.02 (s, 2H), 6.86-6.94 (m, 3H), 7.00-7.10 (m, 2H), 7.30-7.50 (m, 6H); APCI-MS (*m/z*) 536.41 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure (Method A) gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.90-1.96 (m, 2H), 2.78-2.85 (m, 2H), 3.54 (t, J = 7.2 Hz, 2H), 3.74 (s, 3H), 4.66 (s, 2H), 5.03 (s, 2H), 6.82 (d, J = 6.9 Hz, 2H), 7.00 (d, J = 6.3 Hz, 2H), 7.13 (d, J = 6.9 Hz, 1H), 7.29-7.42 (m, 6H), 7.92 (br s, 3H).

Example 57: 1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxy benzyl }]propane-1,3-diamine hydrochloride

Coupling reaction (Method B) of *tert*-butyl [3-*N*-(1,3-benzoxazol-2-ylamino)propyl]carbamate (212 mg, 0.728 mmol) with 1-[(2-fluorobenzyl)oxy]-2-methoxy-4-[(methylsulfonyl)methyl] benzene (250 mg, 0.728 mmol) in the presence of 60 % sodium hydride (26.23 mg, 1.093 mmol) and TBAI (263 mg, 0.728 mmol) in dimethyl formamide (10 ml) provided 60 mg of *tert*-butyl{3-[*N*-(1,3-benzoxazol-2-yl){4-(2-flurobenzyloxy)-3-methoxybenzyl}amino]propyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (s, 9H), 1.75-1.81 (m, 2H), 3.10-3.18 (m, 2H), 3.52-3.58 (m, 2H), 3.82 (s, 3H), 4.67 (s, 2H), 5.18 (s, 2H), 5.31 (br s, 1H), 6.70-7.77 (m, 1H), 6.83-6.90 (m, 2H), 6.98-7.03 (m, 2H), 7.10-7.16 (m, 2H), 7.26-7.36 (m, 3H), 7.48 (t, J = 8.4 Hz, 1H); ESI-MS (*m/z*) 536.14 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.92-1.98 (m, 2H), 2.80-2.86 (m, 2H), 3.57-3.63 (m, 2H), 3.72 (s, 3H), 4.68 (s, 2H), 5.06 (s, 2H), 6.84-6.91 (m, 1H), 6.98-7.05 (m, 3H), 7.12-7.21 (m, 3H), 7.28 (d, J = 7.2 Hz, 1H), 7.40 (d, J = 7.2 Hz, 2H), 7.51 (t, J = 8.4 Hz, 1H), 7.95 (br s, 3H).

Example 58: 1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(3-methoxy-[4-(2-methylbenzyl oxy)] benzyl)] propane-1,3-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl [2-({3-methoxy-4-(2-methylbenzyloxy) benzyl}amino)ethyl]carbamate (150 mg, 0.362 mmol) with 2-chloro-1,3-benzoxazole (55 mg, 0.362 mmol) in the presence of triethylamine (192 µl, 1.086 mmol) in ethanol (10 ml) provided 44 mg of *tert*-butyl {3-[*N*-(1,3-benzoxazol-2-yl)-*N*-(3-methoxy-[4-(2-methylbenzyloxy)]benzyl) amino]propyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (s, 9H), 1.80-1.86 (m, 2H), 2.37 (s, 3H), 3.10-3.16 (m, 2H), 3.57 (t, J = 6.6 Hz, 2H), 3.82 (s, 3H), 4.69 (s, 2H), 5.09 (s, 2H), 5.35 (br s, 1H), 6.78 (d, J = 7.8 Hz, 1H), 6.84 (d, J = 7.5 Hz, 2H), 7.03 (t, J = 7.8 Hz, 1H), 7.15-7.21 (m, 2H), 7.24-7.30 (m, 3H), 7.35-7.45 (m, 2H); APCI-MS (*m/z*) 532.22 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure (Method A) gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.90-1.99 (m, 2H), 2.31 (s, 3H), 2.82-2.88 (m, 2H), 3.58-3.64 (m, 2H), 3.75 (s, 3H), 4.72 (s, 2H), 5.03 (s, 2H), 6.89-6.95 (m, 1H), 7.03-7.10 (m, 3H), 7.14-7.24 (m, 4H), 7.31-7.40 (m, 2H), 7.45-7.52 (m, 1H), 8.14 (br s, 3H).

Example 59: 1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(3-methoxy-[4-(2-trifluoromethyl benzyl oxy)]benzyl) ethane-1,2-diamine hydrochloride

Coupling reaction (Method B) of *tert*-butyl[3-*N*-(1,3-benzoxazol-2-yl amino) propyl] carbamate (200 mg, 0.687 mmol) with 2-[{3-methoxy-4-(2-trifluoromethyl benzyl oxy)]benzyl}methanesulfonate (270 mg, 0.691 mmol) in the presence of 60 % sodium hydride (40 mg, 1.666 mmol) and TBAI (250 mg, 0.689 mmol) in *N,N* dimethyl formamide (10 ml) provided 270 mg of *tert*-Butyl {3-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(3-methoxy-[4-(2-trifluoromethylbenzyloxy)]benzyl)amino] propyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (s, 9H), 1.75-1.85 (m, 2H), 3.14-3.20 (m, 2H), 3.56 (t, J = 6.3 Hz, 2H), 3.87 (s, 3H), 4.69 (s, 2H), 5.34 (s, 2H), 6.76 (s, 2H), 6.88 (s, 1H), 6.04 (t, J = 7.2 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 7.24-7.30 (m, 1H), 7.35-7.45 (m, 2H), 7.52 (t, J = 7.2 Hz, 1H), 7.67 (d, J = 7.8 Hz, 1H), 7.76 (d, J = 7.8 Hz, 1H); APCI-MS (*m/z*) 586.25 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.93-1.99 (m, 2H), 2.80-2.88 (m, 2H), 3.55-3.61 (m, 2H), 3.76 (s, 3H), 4.69 (s, 2H), 5.19 (s, 2H), 6.86 (d, J =

8.4 Hz, 1H), 6.97-7.05 (m, 3H), 7.17 (t, J = 8.1 Hz, 1H), 7.31 (d, J = 7.8 Hz, 1H), 7.42 (d, J = 7.8 Hz, 1H), 7.59 (d, J = 6.9 Hz, 1H), 7.71-7.80 (m, 3H), 7.92 (br s, 3H).

Example 60: 1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{[4-(2,6-diflurobenzyloxy)]-3-methoxy benzyl}]propane-1,3-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[3-*N*-(1,3-benzoxazol-2-ylamino) propyl] carbamate (200 mg, 0.687 mmol) with 2-{[4-(bromomethyl)-2-methoxy phenoxy] methyl}-1,3-difluorobenzene (237 mg, 0.687 mmol) in the presence of 60 % sodium hydride (24 mg, 1.031 mmol) and TBAI (249 mg, 0.687 mmol) in *N,N* dimethyl formamide (10 ml) provided 65 mg of tert-butyl{3-[N-(1,3-benzoxazol-2-yl){4-(2,6-diflurobenzyloxy)-3-methoxybenzyl}amino]propyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44 (s, 9H), 1.77 (t, J = 6.3 Hz, 2H), 3.10-3.18 (m, 2H), 3.54 (t, J = 6.6 Hz, 2H), 3.77 (s, 3H), 4.67 (s, 2H), 5.13 (s, 2H), 5.34 (br s, 1H), 6.77-6.95 (m, 5H), 7.00 (t, J = 8.1 Hz, 1H), 7.14 (t, J = 7.8 Hz, 2H), 7.27-7.35 (m, 2H); APCI-MS (m/z) 586.09 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d6) δ 1.90-1.98 (m, 2H), 2.70-2.82 (m, 2H), 3.30-3.40 (m, 2H), 3.69 (s, 3H), 4.67 (s, 2H), 5.03 (s, 2H), 6.85 (d, J = 6.6 Hz, 1H), 6.99-7.04 (m, 4H), 7.15 (t, J = 8.4 Hz, 2H), 7.28 (d, J = 7.2 Hz, 1H), 7.40 (d, J = 7.8 Hz, 1H), 7.45-7.55 (m, 1H), 7.86 (br s, 3H).

Example 61: 1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-(5-methyl-1,3-benzoxazol-2-yl) propane-1,3-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl(3-{*N*-[4-benzyloxy-3-methoxy benzyl] amino}propyl)carbamate (477 mg, 1.189 mmol) with 2-chloro-5-methyl-1,3-benzoxazole (200 mg, 1.189 mmol) in the presence of triethyl amine (241 mg, 2.379 mmol) in ethanol (5 ml) provided 78 mg of *tert*-butyl {3-[*N*-(4-benzyloxy-3-methoxybenzyl)-*N*-(5-methyl-1,3-benzoxazol-2-yl)amino]propyl}carbamate as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.35 (s, 9H), 1.68-1.75 (m, 2H), 2.31 (s, 3H), 2.90-3.00 (m, 2H), 3.40-3.48 (m, 2H), 3.72 (s, 3H), 4.63 (s, 2H), 5.02 (s, 2H), 6.86-6.92 (m, 2H), 6.96-7.01 (m, 1H),

7.06-7.11 (m, 2H), 7.24 (s, 1H), 7.33 (d, J = 7.8 Hz, 1H), 7.38-7.46 (m, 4H); APCI-MS (*m/z*) 532.37 $(MH)^+$.

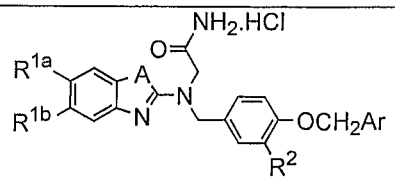
Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.91-1.98 (m, 2H), 2.33 (s, 3H), 2.78-2.84 (m, 2H), 3.52-3.60 (m, 2H), 3.74 (s, 3H), 4.68 (s, 2H), 5.04 (s, 2H), 6.84-6.90 (m, 2H), 7.00-7.06 (m, 1H), 7.13 (s, 1H), 7.30 (s, 1H), 7.35-7.42 (m, 6H), 8.05 (br s, 3H).

Example 62: 1-[*N*-(5-Chloro-1,3-benzoxazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxy benzyl}]propane-1,3-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl {3-[(5-chloro-1,3-benzoxazol-2-yl)amino] propyl}carbamate (200 mg, 0.613 mmol) with 4-(bromomethyl)-1-[(2-fluorobenzyl)oxy]-2-methoxybenzene (200 mg, 0.613 mmol in the presence of 60 % sodium hydride (22 mg, 0.921 mmol) and TBAI (222 mg, 0.613 mmol) in *N,N* dimethyl formamide (10 ml) provided 65 mg of tert-butyl{3-[N-(1,3-benzoxazol-2-yl){4-(2,6-diflurobenzyloxy)-3-methoxybenzyl}amino] propyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 9H), 1.75-1.82 (m,2H), 3.08-3.14 (m, 2H), 3.48-3.55 (m, 2H), 3.82 (s, 3H), 4.65 (s, 2H), 5.18 (s, 2H), 6.76-6.88 (m, 3H), 6.95-7.03 (m, 3H), 7.28-7.34 (m, 2H), 7.45-7.51 (m, 2H); ESI-MS (*m/z*) 570.54 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.88-1.95 (m, 2H), 2.78-2.84 (m, 2H), 3.53-3.60 (m, 2H), 3.72 (s, 3H), 4.66 (s, 2H), 5.06 (s, 2H), 6.83 (d, J = 7.5 Hz, 1H), 7.00-7.06 (m, 3H), 7.20-7.26 (m, 2H), 7.33-7.43 (m, 3H), 7.48 (t, J = 6.3 Hz, 1H), 7.90 (br s, 3H).

Table 11: Structural details and mass spectral data of Examples 63 to 69



Example No	R^{1a}	R^{1b}	A	R^2	Ar	MS (m/z)

Example 63	H	H	O	OCH_3	Ph	ESI: 418.53 $(MH)^+$
Example 64	H	H	O	OCH_3	2-FPh	ESI: 436.21 $(MH)^+$
Example 65	H	H	S	OCH_3	Ph	APCI: 432.57 $(M-H)^-$
Example 66	H	H	S	OCH_3	2-FPh	ESI: 452.40 $(MH)^+$
Example 67	H	H	S	OCH_3	2,6-F_2Ph	ESI: 470.33 $(MH)^+$
Example 68	H	H	S	OCH_3	2-CH_3Ph	ESI: 448.11 $(MH)^+$
Example 69	H	F	S	OCH_3	Ph	ESI: 452.25 $(MH)^+$

Example 63: 2-[*N*-(1,3-benzoxazol-2-yl)-*N*-(4-benzyloxy-3-methoxybenzyl) amino] acetamide

Reaction of *N*-[4-(benzyloxy)-3-methoxybenzyl]-1,3-benzoxazol-2-amine (188 mg, 0.501 mmol) with 2-chloro acetamide (46 mg, 0.501 mmol) in presence of 60 % sodium hydride (24 mg, 0. 501 mmol) and sodium iodide (75 mg, 0.501 mmol) in dimethyl formamide (5 ml) according to the general procedure described for formula (Ib) gave 15 mg of the title compound as off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.84 (s, 3H), 4.10 (s, 2H), 4.76 (s, 2H), 5.12 (s, 2H), 5.36 (br s, 1H), 6.24 (br s, 1H), 6.80 (s, 2H), 6.88 (s, 1H), 7.07 (d, J = 7.5 Hz, 1H), 7.14-7.20 (m, 1H), 7.28-7.38 (m, 7H).

Example 64: 2-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxy benzyl}amino) acetamide

Reaction of *N*-{4-[(2-fluorobenzyl)oxy]-3-methoxybenzyl}-1,3-benzoxazol-2-amine (200 mg, 0.529 mmol) with 2-iodoacetamide (97 mg, 0.529 mmol) in presence of cesium carbonate (345 mg, 1.058 mmol) in acetonoitrile (5 ml) according to the general procedure described for formula (Ib) gave 28 mg of the title compound as off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.87 (s, 3H), 3.89 (s, 2H), 4.60 (s, 2H), 5.20 (s, 2H), 6.76-6.95 (m, 5H), 6.98-7.15 (m, 4H), 7.24-7.30 (m, 1H), 7.47-7.55 (m, 1H).

Example 65: 2-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-benzyloxy-3-methoxy benzyl) amino]acetamide

Reaction of *N*-[4-(benzyloxy)-3-methoxybenzyl]-1,3-benzothiazol-2-amine (100 mg, 0.266 mmol) with 2-chloroacetamide (25 mg, 0.266 mmol) in presence of 60 % sodium

hydride (12 mg, 0.532 mmol) in dimethyl formamide (5 ml) according to the general procedure described for formula (Ib) gave 18 mg of the title compound as off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.84 (s, 3H), 4.19 (s, 2H), 4.66 (s, 2H), 5.12 (s, 2H), 5.36 (br s, 1H), 6.51 (br s, 1H), 6.80 (s, 2H), 6.87 (s, 1H), 7.07-7.13 (m, 1H), 7.30-7.39 (m, 6H), 7.50-7.58 (m, 2H).

Example 66: 2-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxy benzyl}amino]acetamide

Reaction of *N*-{4-[(2-fluorobenzyloxy)]-3-methoxybenzyl}-1,3-benzothiazol-2-amine (125 mg, 0.317 mmol) with 2-iodoacetamide (58 mg, 0.317 mmol) in presence of cesium carbonate(206 mg, 0.634 mmol) in acetonoitrile (5 ml) according to the general procedure described for formula (Ib) gave 32 mg of the title compound as off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.83 (s, 3H), 4.20 (s, 2H), 4.67 (s, 2H), 5.18 (s, 2H), 5.33 (br s, 1H), 6.52 (br s, 1H), 6.83-6.88 (m, 3H), 7.00-7.13 (m, 3H), 7.27-7.33 (m, 2H), 7.47 (t, J = 7.8 Hz, 1H), 7.54-7.60 (m, 2H).

Example 67: 2-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{[4-(2,6-difluorobenzyloxy)]-3-methoxy benzyl}amino] acetamide

Reaction of *N*-{[4-(2,6-difluorobenzyloxy)]-3-methoxybenzyl}-1,3-benzothiazol-2-amine (125 mg, 0.303 mmol) with 2-iodo acetamide (56 mg, 0.303 mmol) in presence of cesium carbonate (98 mg, 0.303 mmol) in acetonoitrile (5 ml) according to the general procedure described for formula (Ib) gave 29 mg of the title compound as off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.79 (s, 3H), 4.20 (s, 2H), 4.68 (s, 2H), 5.13 (s, 2H), 5.28 (br s, 1H), 6.51 (br s, 1H), 6.83-6.96 (m, 5H), 7.10 (t, J = 7.2 Hz, 1H), 7.20-7.33 (m, 2H), 7.54-7.64 (m, 2H).

Example 68: 2-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{[3-methoxy-[4-(2- methylbenzyloxy)] benzyl}amino] acetamide

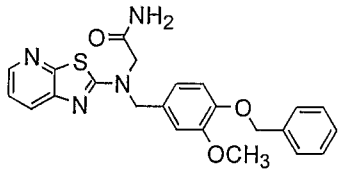
Reaction of *N*-{3-methoxy-[4-(2-methylbenzyloxy)]benzyl}-1,3-benzothiazol-2-amine (101 mg, 0.256 mmol) with 2-iodo acetamide (47 mg, 0.256 mmol) in presence of cesium carbonate (167 mg, 0.512 mmol) in acetonoitrile (10 ml) according to the general

procedure described for formula (Ib) gave 48 mg of the title compound as off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.37 (s, 3H), 3.83 (s, 3H), 4.22 (s, 2H), 4.69 (s, 2H), 5.09 (s, 2H), 5.42 (br s, 1H), 6.58 (br s, 1H), 6.85 (s, 2H), 6.89 (s, 1H), 7.12-7.22 (m, 4H), 7.32-7.40 (m, 2H), 7.56-7.63 (m, 2H).

Example 69: 2-{*N*-[4-(Benzyloxy)-3-methoxybenzyl]-*N*-(5-fluoro-1,3-benzothiazol-2-yl)amino} acetamide

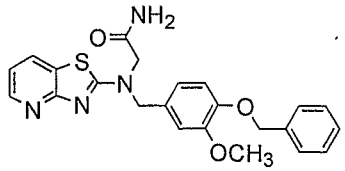
Reaction of *N*-[4-(Benzyloxy)-3-methoxybenzyl]-5-fluoro-1,3-benzothiazol-2-amine (120 mg, 0.303 mmol) with 2-iodo acetamide (95 mg, 0.517 mmol) in presence of cesium carbonate(223 mg, 0.689 mmol) in acetonoitrile (5 ml) according to the general procedure described for formula (Ib) gave 54 mg of the title compound as off-white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.73 (s, 3H), 4.07 (s, 2H), 4.66 (s, 2H), 5.03 (s, 2H), 6.81 (d, J = 8.4 Hz, 1H), 6.89 (t, J = 9.0 Hz, 1H), 6.96-7.02 (m, 3H), 7.11 (br s, 1H), 7.23-7.41 (m, 5H), 7.48 (br s, 1H), 7.70-7.75 (m, 1H).

Example 70: 2-{[4-(Benzyloxy)-3-methoxybenzyl]([1,3]thiazolo[5,4-*b*]pyridin-2-yl) amino}acetamide



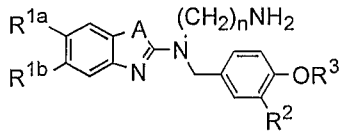
Reaction of *N*-[4-(benzyloxy)-3-methoxybenzyl][1,3]thiazolo[5,4-*b*]pyridin-2-amine (130 mg, 0.344 mmol) with 2-iodo acetamide (95 mg, 0.517 mmol) in presence of cesium carbonate (223 mg, 0.689 mmol) in acetonoitrile (5 ml) according to the general procedure described for formula (Id) gave 54 mg of the title compound as off-white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.73 (s, 3H), 4.09 (s, 2H), 4.68 (s, 2H), 5.03 (s, 2H), 6.81 (d, J = 8.4 Hz, 1H), 6.96-7.05 (m, 2H), 7.26-7.41 (m, 8H), 7.73 (d, J = 7.8 Hz, 1H), 8.12 (d, J = 4.8 Hz, 1H); Mass ESI-MS (*m/z*) ESI: 434.51 $(M)^+$.

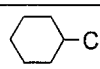
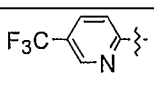
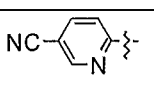
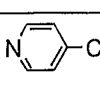
Example 71: 2-{[4-(Benzyloxy)-3-methoxybenzyl]([1,3]thiazolo[4,5-*b*]pyridin-2-yl) amino}acetamide

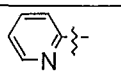


Reaction of *N*-[4-(benzyloxy)-3-methoxybenzyl][1,3]thiazolo[4,5-*b*]pyridin-2-amine (120 mg, 0.319 mmol) with 2-iodo acetamide (88 mg, 0.475 mmol) in presence of cesium carbonate(309 mg, 0.951 mmol) in acetonitrile (5 ml) according to the general procedure described for formula (Id) gave 41 mg of the title compound as off-white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.74 (s, 3H), 4.11 (s, 2H), 4.70 (s, 2H), 5.05 (s, 2H), 6.86 (d, J = 7.8 Hz, 1H), 6.98-7.04 (m, 2H), 7.20 (br s, 1H), 7.30-7.44 (m, 6H), 7.52 (br s, 1H), 7.77 (d, J = 7.8 Hz, 1H), 8.15 (d, J = 4.8 Hz, 1H); ESI-MS (*m/z*): 434.14 $(M)^+$.

Table 12: Structural details and mass spectral data of Examples 72 to 80



Example No.	R^{1a}	R^{1b}	A	R^2	R^3	MS (m/z)
Example 72	H	H	S	OCH_3	$(CH_3)_2CHCH_2$-	APCI: 386.38 $(MH)^+$
Example 73	H	H	S	OCH_3		APCI: 384.83 $(MH)^+$
Example 74	H	H	S	OCH_3		APCI: 398.29 $(MH)^+$
Example 75	H	H	S	OCH_3		ESI: 426.36 $(MH)^+$
Example 76	H	H	S	OCH_3		ESI: 406.17 $(MH)^+$
Example 77	H	H	S	OCH_3		ESI: 475.36 $(MH)^+$
Example 78	H	H	S	OCH_3		APCI: 432.09 $(MH)^+$
Example 79	H	H	S	OCH_3		ESI: 421.25 $(MH)^+$

Example 80	H	H	O	H		ESI: 375.36 $(MH)^+$.

Example 72: 1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-isobutoxy-3-methoxybenzyl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method B) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl] carbamate (150 mg, 0.511 mmol) with 4-isobutoxy-3-methoxybenzyl methanesulfonate (177 mg, 0.614 mmol) in the presence of 60 % sodium hydride (31 mg, 1.291 mmol) and TBAI (185 mg, 0.511 mmol) in N,N-dimethylformamide (5 ml) provided 180 mg of *tert*-butyl{2-[*N*-(1,3-benzothiazol-2-yl)-*N*-(4-isobutoxy-3-methoxybenzyl)amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.94 (d, J = 6.9 Hz, 6H), 1.33 (s, 9H), 1.93-2.02 (m, 1H), 3.14-3.22 (m, 2H), 3.48-3.53 (m, 2H), 3.66 (d, J = 6.3 Hz, 2H), 3.71 (s, 3H), 4.67 (s, 2H), 6.70-6.78 (m, 1H), 6.85-6.93 (m, 1H), 6.98-7.05 (m, 2H), 7.23 (t, J = 7.5 Hz, 1H), 7.41 (d, J = 7.2 Hz, 1H), 7.69 (d, J = 7.2 Hz, 1H); APCI-MS (*m/z*) 486.38 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.95 (d, J = 6.0 Hz, 6H), 1.94-2.02 (m, 1H), 3.09-3.16 (m, 2H), 3.66-3.82 (m, 7H), 4.67 (s, 2H), 6.80-6.86 (m, 1H), 6.89 (d, J = 7.8 Hz, 1H), 6.96 (s, 1H), 7.08 (t, J = 7.8 Hz, 1H), 7.28 (t, J = 7.8 Hz, 1H), 7.47 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 7.8 Hz, 1H), 8.12 (br s, 3H).

Example 73: 1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-cyclopropylmethoxy-3-methoxybenzyl)] ethane-1,2-diamine hydrochloride

Coupling reaction (Method B) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino) ethyl] carbamate (200 mg, 0.682 mmol) with 4-cyclopropylmethoxy-3-methoxybenzyl methane sulfonate (220 mg, 0.768 mmol) in the presence of 60 % sodium hydride (40 mg, 1.666 mmol) and TBAI (247 mg, 0.682 mmol) in N,N-dimethylformamide (5 ml) provided 150 mg of *tert*-butyl{2-[*N*-(1,3-benzothiazol-2-yl)-*N*-(4-cyclopropylmethoxy-3-methoxy benzyl)amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.31-0.36 (m, 2H), 0.60-0.66 (m, 2H), 1.30-1.40 (m, 10H), 3.35-3.41 (m, 2H), 3.65-3.71 (m, 2H),

3.80 (s, 2H), 3.81 (s, 3H), 4.66 (s, 2H), 6.75-6.84 (m, 3H), 7.05 (t, J = 7.8 Hz, 1H), 7.26-7.32 (m, 1H), 7.53 (t, J = 8.1 Hz, 2H); APCI-MS (*m/z*) 484.59 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.26-0.32 (m, 2H), 0.50-0.60 (m, 2H), 1.12-1.20 (m, 1H), 3.08-3.14 (m, 2H), 3.72 (s, 2H), 3.74 (s, 3H), 3.80-3.85 (m, 2H), 4.68 (s, 2H), 6.79-6.87 (m, 2H), 6.96 (s, 1H), 7.08 (t, J = 7.2 Hz, 1H), 7.28 (t, J = 7.8 Hz, 1H), 7.48 (d, J = 7.8 Hz, 1H), 7.76 (d, J = 7.5 Hz, 1H), 8.16 (br s, 3H).

Example 74: 1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-cyclopentyloxy-3-methoxybenzyl)] ethane -1,2-diamine hydrochloride

Analogous to the general procedure described above in method B for (Ia), reaction of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl]carbamate (200 mg, 0.682 mmol) with 4-cyclopentyloxy-3-methoxybenzyl methanesulfonate (204 mg, 0.682 mmol) in the presence of cesium carbonate (444 mg, 1.364 mmol) in acetonitrile (5 ml) provided 110 mg of *tert*-butyl{2-[*N*-(1,3-benzothiazol-2-yl)-*N*-(4-cyclopentyloxy-3-methoxy benzyl) amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 1.85-1.95 (m, 8H), 3.35-3.43 (m, 2H), 3.68-3.73 (m, 2H), 3.79 (s, 3H), 4.68 (s, 2H), 5.15 (br s, 1H), 6.77-6.85 (m, 2H), 7.02-7.12 (m, 1H), 7.24-7.32 (m, 2H), 7.53-7.59 (m, 2H); ESI-MS (*m/z*) 498.54 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.55-1.63 (m, 2H), 1.67-1.80 (m, 4H), 1.89-1.97 (m, 2H), 3.09-3.14 (m, 2H), 3.71 (s, 3H), 3.81-3.90 (m, 2H), 4.74 (s, 2H), 6.89 (d, J = 6.9 Hz, 2H), 7.07 (s, 1H), 7.10 (d, J = 6.0 Hz, 1H), 7.28 (t, J = 6.0 Hz, 1H), 7.50 (d, J = 6.0 Hz, 1H), 7.77 (d, J = 6.0 Hz, 1H), 8.18 (br s, 3H).

Example 75: 1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-[cyclohexylmethoxy]-3-methoxy benzyl)] ethane-1,2-diamine hydrochloride

Coupling reaction (Method B) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl] carbamate (250 mg, 0.853 mmol) with 4-cyclohexylmethoxy-3-methoxybenzyl methane sulfonate (310 mg, 0.945 mmol) in the presence of 60% sodium hydride (50 mg, 2.083 mmol) and TBAI (310 mg, 0.855 mmol) in N,N-dimethylformamide (5 ml) provided 200

mg of *tert*-butyl{2-[*N*-(1,3-benzothiazol-2-yl)-*N*-(4-cyclohexylmethoxy-3-methoxy benzyl)amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98-1.06 (m, 2H), 1.15-1.30 (m, 4H), 1.38 (s, 9H), 1.66-1.72 (m, 3H), 3.35-3.42 (m, 2H), 3.65-3.72 (m, 2H), 3.76 (d, J = 6.0 Hz, 2H), 3.79 (s, 3H), 4.66 (s, 2H), 5.13 (s, 2H), 6.74-6.82 (m, 3H), 7.05 (t, J = 7.2 Hz, 1H), 7.25-7.32 (m, 1H), 7.54 (t, J = 7.5 Hz, 2H); APCI-MS (*m/z*) 526.32 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96-1.05 (m, 2H), 1.18-1.25 (m, 4H), 1.66-1.80 (m, 5H), 2.76-2.81 (m, 2H), 3.43-3.50 (m, 2H), 3.68 (s, 2H), 3.70 (s, 3H), 4.70 (s, 2H), 6.77 (d, J = 7.5 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 6.93 (s, 1H), 7.00 (t, J = 7.8 Hz, 1H), 7.22 (t, J = 8.1 Hz, 1H), 7.40 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 7.8 Hz, 1H), 8.18 (br s, 3H).

Example 76: 1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(3-methoxy-4-phenoxybenzyl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino) ethyl] carbamate (200 mg, 0.682 mmol) with 4-(bromomethyl)-2-methoxy-1-phenoxybenzene (220 mg, 0.750 mmol) in the presence of 60% sodium hydride (41 mg, 1.708 mmol) and TBAI (247 mg, 0.682 mmol) in N,N-dimethylformamide (5 ml) provided 100 mg of *tert*-butyl{2-[*N*-(1,3-benzothiazol-2-yl)-*N*-(3-methoxy-4-phenoxybenzylbenzyl)amino] ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (s, 9H), 3.38-3.45 (m, 2H), 3.68-3.74 (m, 2H), 3.78 (s, 3H), 4.73 (s, 2H), 5.10 (br s, 1H), 6.80-6.95 (m, 5H), 6.99-7.08 (m, 2H), 7.26-7.31 (m, 3H), 7.55 (t, J = 8.4 Hz, 2H); APCI-MS (*m/z*) 506.02 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.20-3.26 (m, 2H), 3.78 (s, 3H), 3.84-3.90 (m, 2H), 4.78 (s, 2H), 7.70-7.78 (m, 2H), 6.80-6.85 (m, 1H), 6.90-6.96 (m, 2H), 7.04-7.18 (m, 2H), 7.22-7.30 (m, 3H), 7.34-7.40 (m, 1H), 7.70-7.80 (m, 1H), 8.18 (br s, 3H).

Example 77: 1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(3-methoxy-4-{[5-(trifluoromethyl) pyridine -2-yl]oxy} benzyl)]ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino) ethyl] carbamate (93 mg, 0.317 mmol) with 2-[4-(bromomethyl)-2-methoxyphenoxy]-5-(trifluoromethyl)pyridine (220 mg, 0.318 mmol) in the presence of 60% sodium hydride (20 mg, 0.833 mmol) and TBAI (115 mg, 0.317 mmol) in N,N-dimethylformamide (5 ml) provided 120 mg of *tert*-butyl{2-[*N*-(1,3-benzothiazol-2-yl)-*N*-(3-methoxy-4-{[5-(trifluoromethyl)pyridin-2-yl]oxy}benzyl)amino] ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (s, 9H), 3.42-3.48 (m, 2H), 3.68-3.74 (m, 5H), 4.78 (s, 2H), 5.10 (br s, 1H), 6.92-7.00 (m, 3H), 7.06-7.12 (m, 2H), 7.20-7.32 (m, 1H), 7.57 (t, J = 9.0 Hz, 1H), 7.87 (d, J = 8.4 Hz, 2H), 8.38 (s, 1H); APCI-MS (*m/z*) 575.63 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.15-3.21 (m, 2H), 3.69 (s, 3H), 3.88-3.93 (m, 2H), 4.82 (s, 2H), 6.93 (d, J = 8.4 Hz, 1H), 7.11-7.22 (m, 5H), 7.32 (t, J = 7.8 Hz, 1H), 7.51 (d, J = 8.4 Hz, 1H), 7.79 (d, J = 7.8 Hz, 1H), 8.18 (br s, 3H), 8.50 (s, 1H).

Example 78: 6-(4-{[(2-aminoethyl)(1,3-benzoxazol-2-yl)amino]methyl}-2-methoxy phenoxy)nicotinonitrile hydrochloride

Coupling reaction (Method A) of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino) ethyl] carbamate (200 mg, 0.682 mmol) with 6-[4-(bromomethyl)-2-methoxy phenoxy] nicotinonitrile (180 mg, 0.682 mmol) in the presence of 60% sodium hydride (40 mg, 1.666 mmol) and TBAI (247 mg, 0.682 mmol) in N,N-dimethylformamide (5 ml) provided 147 mg of *tert*-butyl {2-[*N*-(1,3-benzothiazol-2-yl)-*N*-{4-[(5-cyanopyridin-2-yl)oxy]-3-methoxybenzyl}amino)ethyl]carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.39 (s, 9H), 3.42-3.48 (m, 2H), 3.70 (s, 3H), 3.72-3.78 (m, 2H), 4.79 (s, 2H), 5.10 (br s, 1H), 6.82-7.10 (m, 5H), 7.28-7.34 (m, 1H), 7.54-7.60 (m, 2H), 7.89 (d, J = 8.4 Hz, 1H), 8.41 (s, 1H); APCI-MS (*m/z*) 532.13 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.88-2.95 (m, 2H), 3.58-3.64 (m, 2H), 3.66 (s, 3H), 4.84 (s, 2H), 6.91 (d, J = 8.4 Hz, 1H), 7.05 (t, J = 7.5 Hz, 1H),

7.12-7.18 (m, 2H), 7.22 (d, J = 8.7 Hz, 1H), 7.28 (d, J = 7.2 Hz, 1H), 7.45 (d, J = 8.1 Hz, 1H), 7.75 (d, J = 7.8 Hz, 1H), 8.25-8.32 (m, 1H), 8.58 (s, 1H).

Example 79: 1-[*N*-(1,3-benzothiazol-2-yl)-*N*-(3-methoxy-4-[pyridin-4-ylmethoxy] benzyl) ethane-1,2-diamine hydrochloride

Coupling reaction (Method C) of *tert*-butyl{2-[*N*-(3-methoxy-4-[pyridin-4-ylmethoxy] benzyl)amino]ethyl}carbamate (360 mg, 0.929 mmol) with 2-chloro-1,3-benzothiazole (160 mg, 0.943 mmol) in the presence triethylamine (189 mg, 1.886 mmol) of in ethanol and butanol (4:1, 10 mL) provided 57 mg of *tert*-butyl{2-[*N*-(1,3-benzothiazol-2-yl)-*N*-{3-methoxy-4-[pyridin-4-ylmethoxy] benzyl}amino]propyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 3.38-3.42 (m, 2H), 3.66-3.72 (m, 2H), 3.86 (s, 3H), 4.69 (s, 2H), 5.12-5.18 (m, 3H), 6.73-6.79 (m, 2H), 6.89-6.93 (m, 1H), 7.08 (t, J = 8.4 Hz, 1H), 7.26-7.36 (m, 3H), 7.56 (t, J = 7.8 Hz, 2H), 8.59 (d, J = 4.8 Hz, 2H); APCI- 521.13 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.12-3.18 (m, 2H), 3.50-3.56 (m, 2H), 3.82 (s, 3H), 4.72 (s, 2H), 5.42 (s, 2H), 6.85 (d, J = 8.7 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 7.08-7.12 (m, 2H), 7.31 (t, J = 8.4 Hz, 1H), 7.49 (d, J = 8.1 Hz, 1H), 7.78 (d, J = 7.8 Hz, 1H), 8.08-8.14 (m, 2H), 8.21 (br s, 3H), 8.90 (d, J = 5.4 Hz, 2H).

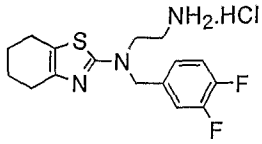
Example 80: 1-[*N*-(1,3-benzoxazol-2-yl)-*N*-(4-[pyridin-2-yloxy]benzyl)] propane-1,3-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl [3-*N*-(1,3-benzoxazol-2-ylamino) propyl] carbamate (200 mg, 0.687 mmol) with 2-[4-(bromo methyl)phenoxy]pyridine (180 mg, 0.687 mmol) in the presence of 60 % sodium hydride (40 mg, 1.666 mmol) and TBAI (250 mg, 0.687 mmol) in N,N-dimethylformamide (5 ml) provided 300 mg of *tert*-butyl{3-[*N*-(1,3-benzoxazol-2-yl)-*N*-{4-(pyridin-2-yloxy)benzyl}amino]propyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (s, 9H), 1.78-1.84 (m, 2H), 3.12-3.18 (m, 2H), 3.60 (d, J = 6.6 Hz, 2H), 4.76 (s, 2H), 5.40 (br s, 1H), 6.91 (d, J = 8.1 Hz, 1H), 6.95-7.05 (m, 2H), 7.13 (d, J = 8.4 Hz, 2H), 7.18 (t, J = 7.2 Hz, 1H), 7.26-

7.38 (m, 4H), 7.69 (d, J = 6.9 Hz, 1H), 8.17 (d, J = 3.6 Hz, 1H). APCI (m/z) 475.10 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.96-2.01 (m, 2H), 2.85-2.91 (m, 2H), 3.60-3.68 (m, 2H), 4.79 (s, 2H), 7.00-7.06 (m, 2H), 7.09-7.14 (m, 3H), 7.20 (t, J = 7.2 Hz, 1H), 7.33 (d, J = 7.5 Hz, 1H), 7.40-7.47 (m, 3H), 7.82-7.88 (m, 1H), 8.03 (br s, 3H), 8.12 (d, J = 3.6 Hz, 1H).

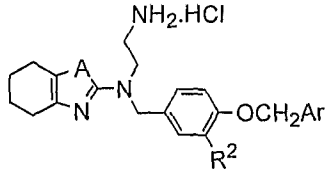
Example 81: *N*-(3,4-Difluorobenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl)ethane-1,2 -diamine hydrochloride



Coupling reaction (Method A) of *tert*-butyl [2-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-ylamino)ethyl]carbamate (100 mg, 0.336 mmol) with 4-(bromomethyl)-1,2-difluoro benzene (69 mg, 0.336 mmol) in the presence of 60 % sodium hydride (8 mg, 336 mmol) in N,N-dimethylformamide (2 ml) provided 75 mg of *tert*-butyl {2-[(3,4-difluoro benzyl) (4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl)amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41 (s, 9H), 1.77-1.85 (m, 4H), 2.52-2.58 (m, 4H), 3.30-3.38 (m, 2H), 3.53-3.58 (m, 2H), 4.57 (s, 2H), 5.19 (br s, 1H,), 6.97-7.03 (m, 1H), 7.07-7.12 (m, 2H); APCI-MS (m/z) 424.18 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure (Method A) gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.70-1.78 (m, 4H), 3.04-3.10 (m, 4H), 3.68-3.74 (m, 2H), 4.64 (s, 2H), 7.11-7.17 (m, 1H), 7.35-7.48 (m, 2H), 7.99 (br s, 3H); APCI-MS (m/z) 324.15 $(MH)^+$.

Table 13: Structural details and mass spectral data of Examples 82 to 88



Example No.	R^2	Ar	MS (m/z)
Example 82	H	(2-methyl)phenyl	ESI: 408.30 $(MH)^+$
Example 83	OCH_3	phenyl	APCI: 424.23 $(MH)^+$
Example 84	OCH_3	(2-methyl)phenyl	ESI: 438.18 $(MH)^+$
Example 85	OCH_3	(2-ethyl)phenyl	ESI: 452.25 $(MH)^+$
Example 86	OCH_3	(2-isopropyl)phenyl	ESI: 466.37 $(MH)^+$
Example 87	OCH_3	2-fluorophenyl	APCI: 442.22 $(M-H)^-$
Example 88	OCH_3	2,6-difluorophenyl	APCI: 400.46 $(M-H)^-$

Example 82: *N*-(4-[2-Methylbenzyloxy]benzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl)ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) *tert*-butyl [2-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-ylamino)ethyl]carbamate (150 mg, 0.505 mmol) with 1-{[4-(bromomethyl) phenoxy] methyl}-2-methylbenzene (139 mg, 0.505 mmol) in the presence of 60 % sodium hydride (12 mg, 0.505 mmol) in N,N-dimethylformamide (5 ml) provided 105 mg of *tert*-butyl {2-[*N*-(4-[2-methylbenzyloxy]benzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41 (s, 9H), 1.76-1.82 (m, 4H), 2.36 (s, 3H), 2.52-2.60 (m, 4H), 3.30-3.36 (m, 2H), 3.54-3.60 (m, 2H), 4.53 (s, 2H), 5.01 (s, 2H), 5.43 (br s, 1H), 6.93 (d, J = 7.8 Hz, 2H), 7.15-7.26 (m, 5H), 735-7.41 (m, 1H); ESI-MS (*m/z*) 508.23 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.70-1.76 (m, 5H), 2.28-2.36 (m, 4H), 3.05-3.10 (m, 4H), 3.75-3.81 (m, 2H), 4.67 (s, 2H), 5.07 (s, 2H), 7.00-7.08 (m, 2H), 7.20-7.30 (m, 5H), 7.35-7.41 (m, 1H), 8.18 (br s, 3H).

Example 83: *N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzo thiazol-2-yl)ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl [2-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-ylamino)ethyl]carbamate (150 mg, 0.505 mmol) with 1-(benzyloxy)-4-(bromomethyl)-2-methoxybenzene (155 mg, 0.505 mmol) in the presence of 60 % sodium hydride (12 mg, 0.505 mmol) in N,N-dimethylformamide (5 ml) provided 125 mg of *tert*-butyl {2-[*N*-(4-

benzyloxy-3-methoxybenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl)amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41 (s, 9H), 1.76-1.84 (m, 4H), 2.52-2.58 (m, 4H), 3.30-3.36 (m, 2H), 3.54-3.60 (m, 2H), 3.85 (s, 3H), 4.50 (s, 2H), 5.13 (s, 2H), 5.39 (br s, 1H), 6.73-6.83 (m, 3H), 7.20-7.30 (m, 5H); APCI-MS (*m/z*) 524.10 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.70-1.78 (m, 4H), 2.48-2.54 (m, 4H), 3.06-3.12 (m, 2H), 3.74-3.85 (m, 5H), 4.66 (s, 2H), 5.06 (s, 2H), 6.81 (d, J = 7.5 Hz, 1H), 6.98-7.05 (m, 2H), 7.30-7.42 (m, 5H), 8.22 (br s, 3H).

Example 84: *N*-(3-Methoxy-[4-(2-methylbenzyloxy)]benzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl [2-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-ylamino)ethyl]carbamate (138 mg, 0.464 mmol) with 4-(bromomethyl)-2-methoxy-1-[(2-methylbenzyl)oxy]benzene (150 mg, 0.464 mmol) in the presence of 60 % sodium hydride (11 mg, 0.458 mmol) in N,N-dimethylformamide (5 ml) provided 110 mg of *tert*-butyl{2-[*N*-(3-methoxy-[4-(2-methylbenzyloxy)]benzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzo thiazol-2-yl)amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40 (s, 9H), 1.77-1.83 (m, 4H), 2.52-2.58 (m, 4H), 3.32-3.38 (m, 2H), 3.60-3.66 (m, 2H), 3.84 (s, 3H), 4.52 (s, 2H), 5.08 (s, 2H), 5.51 (br s, 1H), 6.72-6.78 (m, 1H), 6.80-6.86 (m, 2H), 7.18-7.30 (m, 3H), 7.37-7.43 (m, 1H); APCI-MS (*m/z*) 538.16 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.70-1.78 (m, 4H), 2.31 (s, 3H), 3.04-3.10 (m, 2H), 3.73-3.79 (m, 5H), 3.88-3.94 (m, 4H), 4.63 (s, 2H), 5.04 (s, 2H), 6.82 (d, J = 7.8 Hz, 1H), 6.98 (s, 1H), 7.06 (d, J = 8.1 Hz, 1H), 7.20-7.26 (m, 3H), 7.35-7.41 (m, 1H), 8.14 (br s, 3H).

Example 85: *N*-([4-(2-Ethylbenzyloxy)]-3-methoxy]benzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzo thiazol-2-yl) ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl [2-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-ylamino)ethyl]carbamate (200 mg, 0.673 mmol) with 4-(bromomethyl)-1-[(2-

ethylbenzyl)oxy]-2-methoxybenzene (226 mg, 0.673 mmol) in the presence of 60 % sodium hydride (16 mg, 0.673 mmol) and TBAI (248 mg, 0.673 mmol) in N,N-dimethylformamide (5 ml) provided 210 mg of *tert*-butyl {2-[*N*-(4-(2-ethylbenzyloxy)]-3-methoxy)]benzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl)amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (t, J = 7.2 Hz, 3H), 1.41 (s, 9H), 1.76-1.84 (m, 4H), 2.54-2.60 (m, 4H), 2.70-2.76 (m, 2H), 3.30-3.36 (m, 2H), 3.55-3.61 (m, 2H), 3.83 (s, 3H), 4.52 (s, 2H), 5.11 (s, 2H), 5.41 (br s, 1H), 6.75-6.85 (m, 2H), 7.15-7.24 (m, 4H), 7.38-7.44 (m, 1H); APCI-MS (*m/z*) 552.32 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.14-1.20 (m, 3H), 1.70-1.78 (m, 4H), 2.47-2.53 (m, 4H), 2.63-2.69 (m, 2H), 3.06-3.12 (m, 2H), 3.72-3.80 (m, 5H), 4.67 (s, 2H), 5.05 (s, 2H), 6.80-6.86 (m, 1H), 7.00-7.08 (m, 2H), 7.20-7.30 (m, 4H), 8.25 (br s, 3H).

Example 86: *N*-{4-(2-Isopropylbenzyloxy)-3-methoxybenzyl}-N-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl [2-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-ylamino)ethyl]carbamate (200 mg, 0.673 mmol) with 4-(bromomethyl)-1-[(2-isopropylbenzyl)oxy]-2-methoxybenzene (234 mg, 0.673 mmol) in the presence of 60 % sodium hydride (16 mg, 0.673 mmol) in N,N-dimethylformamide (5 ml) provided 200 mg of *tert*-butyl {2-[*N*-(3-methoxy-[4-(2-isoproyl)benzyloxy)]benzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl)amino]ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (d, J = 6.3 Hz, 6H), 1.41 (s, 9H), 1.77-1.84 (m, 4H), 2.53-2.59 (m, 4H), 3.17-3.23 (m, 1H), 3.30-3.36 (m, 2H), 3.54-3.60 (m, 2H), 3.82 (s, 3H), 4.52 (s, 2H), 5.12 (s, 2H), 5.42 (br s, 1H), 6.78-6.88 (m, 3H), 7.15-7.21 (m, 1H), 7.30-7.40 (m, 3H); APCI-MS (*m/z*) 566.32 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.19 (d, J = 6.3 Hz, 6H), 1.70-1.76 (m, 4H), 3.05-3.16 (m, 3H), 3.72-3.80 (m, 5H), 3.90-3.98 (m, 4H), 4.61 (s, 2H), 5.06 (s, 2H), 6.82 (d, J = 6.9 Hz, 1H), 6.97 (s, 1H), 7.08 (d, J = 8.4 Hz, 1H), 7.18 (t, J = 6.3 Hz, 1H), 7.32-7.40 (m, 3H), 8.10 (br s, 3H).

Example 87: *N*-([4-(2-Fluorobenzyloxy)]-3-methoxybenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl [2-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-ylamino)ethyl]carbamate (100 mg, 0.336 mmol) with 4-(bromomethyl)-1-[(2-fluorobenzyl)oxy]-2-methoxybenzene (109 mg, 0.336 mmol) in the presence of 60 % sodium hydride (80 mg, 0.336 mmol) in N,N-dimethylformamide (5 ml) provided 130 mg of *tert*-butyl {2-[*N*-([4-(2-fluorobenzyloxy)]-3-methoxybenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl)amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41 (s, 9H), 1.76-1.84 (m, 4H), 2.53-2.58 (m, 4H), 3.30-3.36 (m, 2H), 3.53-3.59 (m, 2H), 3.85 (s, 3H), 4.51 (s, 2H), 5.19 (s, 2H), 5.39 (br s, 1H), 6.72-6.78 (m, 1H), 6.83-6.90 (m, 2H), 7.05 (d, J = 9.0 Hz, 1H), 7.14 (t, J = 7.8 Hz, 2H), 7.51 (t, J = 7.2 Hz, 1H).

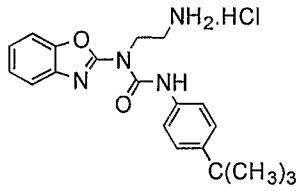
Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.73-1.79 (m, 4H), 2.47-2.53 (m, 4H), 3.05-3.12 (m, 2H), 3.76 (s, 3H), 3.80-3.86 (m, 2H), 4.67 (s, 2H), 5.05 (s, 2H), 6.82 (d, J = 7.5 Hz, 1H), 7.00-7.10 (m, 2H), 7.20-7.30 (m, 2H), 7.40-7.46 (m, 1H), 7.50-7.58 (m, 1H), 8.23 (br s, 3H).

Example 88: *N*-(4-[(2,6-Difluorobenzyloxy)]-3-methoxybenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) ethane-1,2-diamine hydrochloride

Coupling reaction (Method A) of *tert*-butyl [2-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-ylamino)ethyl]carbamate (100 mg, 0.336 mmol) with 4-(bromomethyl)-1-[(2,6-difluorobenzyl)oxy]-2-methoxybenzene (113 mg, 0.336 mmol) in the presence of 60 % sodium hydride (80 mg, 0.336 mmol) in N,N-dimethylformamide (5 ml) provided 135 mg of *tert*-butyl {2-[*N*-(4-[(2,6-difluorobenzyloxy)]-3-methoxybenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl)amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41 (s, 9H), 1.75-1.82 (m, 4H), 2.54-2.60 (m, 4H), 3.30-3.36 (m, 2H), 3.54-3.60 (m, 2H), 3.81 (s, 3H), 4.52 (s, 2H), 5.14 (s, 2H), 5.39 (br s, 1H), 6.77-6.83 (m, 2H), 6.88-6.96 (m, 3H), 7.30-7.35 (m, 1H); ESI-MS (*m/z*) 424.05 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.70-1.78 (m, 4H), 2.48-2.54 (m, 4H), 3.05-3.12 (m, 2H), 3.73 (s, 3H), 3.82-3.88 (m, 2H), 4.68 (s, 2H), 5.06 (s, 2H), 6.86 (d, J = 7.2 Hz, 1H), 7.01 (s, 1H), 7.10 (d, J = 8.4 Hz, 1H), 7.18 (t, J = 7.8 Hz, 2H), 7.54 (t, J = 7.8 Hz, 1H), 8.24 (br s, 3H).

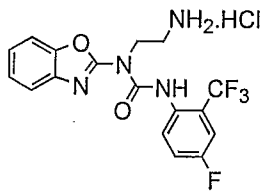
Example 89: 1-(2-Aminoethyl)-1-(1,3-benzoxazol-2-yl)-3-(4-*tert*-butylphenyl)urea hydrochloride



Reaction of *tert*-butyl[2-*N*-(1,3-benzoxazol-2-yl)aminoethyl]carbamate (150 mg, 0.541 mmol) with 1-*tert*-butyl-4-isocyanatobenzene (94 g, 0.541 mmol) in dichloromethane (10 ml) gave 180 mg of *tert*-butyl[2-(1,3-benzoxazol-2-yl{[(4-*tert*-butylylphenyl)amino]-carbonyl}amino)ethyl] carbamate as white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 (s, 9H), 1.42 (s, 9H), 3.42-3.52 (m, 2H), 4.22-4.31 (m, 2H), 5.05 (br s, 1H), 7.12-7.20 (m, 2H), 7.27-7.40 (m, 4H), 7.42-7.52 (m, 2H); APCI-MS (*m/z*) 453.33 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure (Method A) gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.28 (s, 9H), 3.17-3.22 (m, 2H), 4.24-4.30 (m, 2H), 7.29-7.38 (m, 4H), 7.49 (d, J = 8.1 Hz, 2H), 7.64 (t, J = 8.7 Hz, 2H), 8.06 (br s, 3H), 11.47 (s, 1H); ESI-MS (*m/z*) 353.19 $(MH)^+$.

Example 90: 1-(2-Aminoethyl)-1-(1,3-benzoxazol-2-yl)-3-[4-fluoro-2-(trifluoro methyl) phenyl]urea hydrochloride

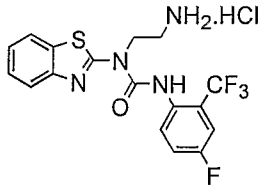


Reaction of *tert*-butyl[2-*N*-(1,3-benzoxazol-2-yl)aminoethyl]carbamate (200 mg, 0.722 mmol) with 4-fluoro-1-isocyanato-2-(trifluoromethyl)benzene (148 mg, 0.722 mmol) in

dichloromethane (10 ml) according to the procedure described in (Ie) gave 350 mg of *tert*-butyl{2-[1,3-benzoxazol-2-yl({[4-fluoro-2-(trifluoromethyl)phenyl] amino}carbonyl) amino]ethyl}carbamate as white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.35 (s, 9H), 3.50-3.56 (m, 2H), 4.28-4.34 (m, 2H), 4.92 (br s, 1H), 7.20-7.32 (m, 3H), 7.34 (d, J = 8.4 Hz, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.50 (d, J = 7.8 Hz, 1H), 8.00-8.07 (m, 1H), 12.15 (br s, 1H); ESI-MS (*m/z*) 483.32 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.17-3.24 (m, 2H), 4.28-4.33 (m, 2H), 7.29-7.39 (m, 2H), 7.54 (d, J = 7.5 Hz, 1H), 7.63-7.71(m, 4H), 8.04-8.14 (m, 3H),o11.93 (s, 1H); APCI-MS (*m/z*) 383.39 $(MH)^+$.

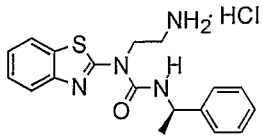
Example 91: 1-(2-Aminoethyl)-1-(1,3-benzothiazol-2-yl)-3-[4-fluoro-2-(trifluoromethyl) phenyl]urea hydrochloride



Reaction of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl]carbamate (200mg, 0.683 mmol) with 4-fluoro-1-isocyanato-2-(trifluoromethyl) benzene (140 mg, 0.683 mmol) in dichloromethane (15 ml) according to the procedure described in (Ie) gave 210 mg of *tert*-butyl{2-[*N*-(1,3-benzothiazol-2-yl)-*N*-({[4-fluoro-2-(trifluoromethyl)phenyl]amino} carbonyl) amino]ethyl}carbamate as white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9H), 1.41 (s, 9H), 3.52-3.58 (m, 2H), 4.12-4.20 (m, 2H), 4.96 (br s, 1H), 7.24-7.30 (m, 2H), 7.38-7.45 (m, 2H), 7.71-7.78 (m, 2H), 8.10-8.18 (m, 1H), 12.63 (br s, 1H); APCI-MS (*m/z*) 499.49 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.25-3.32 (m, 2H), 4.47-4.53 (m, 2H), 7.30 (t, J = 7.8 Hz, 1H), 7.44 (t, J = 7.5 Hz, 1H), 7.63-7.74 (m, 3H), 7.81-7.87 (m, 1H), 7.95 (d, J = 7.5 Hz, 1H), 8.13 (br s, 3H), 10.67 (br s, 1H) ; APCI-MS (*m/z*) 399.13 $(MH)^+$.

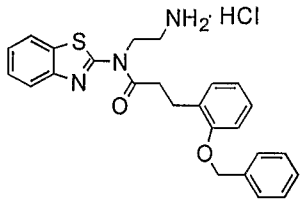
Example 92: 1-(2-Aminoethyl)-1-(1,3-benzothiazol-2-yl)-3-[(1*S*)-1-phenylethyl]urea hydrochloride



Reaction of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl]carbamate (200 mg, 0.683 mmol) with [(*S*)-(-)-α-methylbenzyl isocyanate (100 mg, 0.683 mmol) in dichloromethane (5 ml) according to the procedure described in (Ie) gave105 mg of the *tert*-butyl{2-[1,3-benzothiazol-2-yl({[(1*S*)-1-phenylethyl]amino}carbonyl)amino] ethyl} carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.45 (s, 9H), 1.61 (d, J = 6.9 Hz, 3H), 3.40-3.51 (m, 2H), 4.12-4.19 (m, 2H), 5.04-5.13 (m, 2H), 7.16-7.21 (m, 3H), 7.31-7.41 (m, 4H), 7.66 (dd, J = 7.8, 3.3 Hz, 2H), 9.34 (br s, 1H); ESI-MS (*m/z*) 441.01 $(MH)^+$.

Deprotection of the above intermediate as described in the general procedure gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.56 (d, J = 6.9 Hz, 3H), 3.12-3.19 (m, 2H), 4.48-4.55 (m, 2H), 4.97-5.02 (m, 1H), 7.21-7.31 (m, 2H), 7.31-7.38 (m, 2H), 7.45 (d, J = 7.5 Hz, 2H), 7.66 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 7.8 Hz, 1H), 8.19 (br s, 3H), 8.34 (br s, 1H); APCI-MS (*m/z*) 341.15 $(MH)^+$.

Example 93: *N*-(2-Aminoethyl)-*N*-1,3-benzothiazol-2-yl-[3-(2-benzyloxy) phenyl] propanamide hydrochloride:

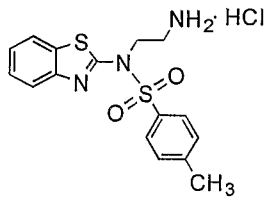


To a stirred mixture of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl]carbamate (200 mg, 0.683 mmol) and 3-[2-(benzyloxy)phenyl]propanoic acid (175 mg, 0.683 mmol) in dichloromethane (10 ml) was added EDCI hydrochloride (195 mg, 1.024 mmol) followed by HOBt (156 mg, 1.024 mmol) and triethylamine (284 µl, 2.048 mmol) at room temperature over 10 min. The reaction mixture was stirred overnight at the same temperature. The reaction mixture was diluted with chloroform (100 ml) and the organic

layer was washed with water (2 x 50 ml), dried (Na_2SO_4) and concentrated to obtain a crude residue which was purified by silica gel column chromatography using 15% ethyl acetate in petroleum ether to obtain 98 mg of the *tert*-butyl{2-[1,3-benzothiazol-2-yl[3-(2-benzyloxy)phenylpropanoyl]amino]ethyl}carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 9H), 2.96-3.01 (m, 2H), 3.10-3.15 (m, 2H), 3.40-3.46 (m, 2H), 4.24 (br s, 2H), 4.95 (br s, 1H), 5.08 (s, 2H), 6.89 (d, J = 7.8 Hz, 2H), 7.14-7.21 (m, 2H), 7.29-7.41 (m, 7H), 7.74-7.78 (m, 2H); ESI-MS (*m/z*) 532.06 $(MH)^+$.

Deprotection of the above intermediate using excess hydrochloric acid in ethyl acetate gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.97-3.04 (m, 2H), 3.07-3.12 (m, 2H), 3.12-3.24 (m, 2H), 4.40-4.45 (m, 2H), 5.14 (s, 2H), 6.81-6.89 (m, 1H), 7.03 (d, J = 7.8 Hz, 1H), 7.17 (t, J = 6.9 Hz, 1H), 7.30-7.37 (m, 5H), 7.46 (d, J = 6.9 Hz, 3H), 7.77 (d, J = 8.4 Hz, 1H), 7.97 (d, J = 7.8 Hz, 1H), 8.17 (br s, 3H); APCI-MS (*m/z*) 432.16 $(MH)^+$.

Example 94: *N*-(2-Aminoethyl)-*N*-1,3-benzothiazol-2-yl-4-methylbenzenesulfonamide hydrochloride

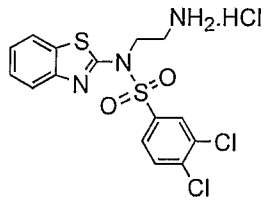


To a stirred solution of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl]carbamate (150 mg, 0.512 mmol) in dichloromethane (5 ml) was added *p*-tolylsulfonyl chloride (97 mg, 0.512 mmol) followed by triethylamine (142 µl,1.024 mmol) and 4-(dimethylamino) pyridine (12 mg, 0.102 mmol) at room temperature. The reaction mixture was stirred at the same temperature for 18 h. The resulting mixture was diluted with chloroform (100 ml) and the organic layer was washed with water (2 x 50 ml), dried (Na_2SO_4) and concentrated to obtain a crude product which was purified by silica gel column chromatography using 20% ethyl acetate in petroleum ether to obtain 171 mg of tert-Butyl(2-{1,3-benzothiazol-2-yl[(4-methylphenyl)sulfonyl]amino}ethyl) carbamate as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.43 (s, 9H), 2.38 (s, 3H), 3.44-3.58 (m, 2H),

4.10-4.18 (m, 2H), 5.11 (br s, 1H), 7.24-7.31 (m, 4H), 7.37 (t, J = 7.8 Hz, 1H), 7.68-7.72 (m, 3H); ESI-MS (*m/z*) 448.65 $(MH)^+$.

Deprotection of *tert*-butyl(2-{1,3-benzothiazol-2-yl[(4-methylphenyl)sulfonyl]amino } ethyl) carbamate using hydrochloric acid in ethyl acetate (Method A) gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.37 (s, 3H), 3.10-3.16 (m, 2H), 4.24 (t, J = 5.7 Hz, 2H), 7.32-7.37 (m, 1H), 7.43-7.48 (m, 3H), 7.71 (d, J = 7.8 Hz, 1H), 7.80 (d, J = 7.8 Hz, 2H), 8.00 (d, J = 7.8 Hz, 1H), 8.11 (br s, 3H); APCI-MS (*m/z*) 548.36 $(MH)^+$.

Example 95: 1-[*N*-(2-Aminoethyl)-*N*-(1,3-benzothiazol-2-yl)]-3,4-dichlorobenzene sulfonamide hydrochloride



Reaction of *tert*-butyl[2-(1,3-benzothiazol-2-ylamino)ethyl]carbamate (200 mg, 0.681 mmol) with 3,4-dichlorobenzenesulfonyl chloride (167 mg, 0.681 mmol) in the presence of triethylamine as described in Example 94 gave 160 mg of the *tert*-butyl (2-*N*-[(1,3-benzothiazol-2-yl)-*N*-[(3,4-dichlorophenyl)sulfonyl] amino}ethyl)carbamate as an off-white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.42 (s, 9H), 3.45-3.51 (m, 2H), 4.18-4.25 (m, 2H), 4.99 (br s, 1H), 7.27-7.39 (m, 1H), 7.39 (t, J = 7.5 Hz, 1H), 7.52-7.59 (m, 1H), 7.67-7.73 (m, 2H), 7.98 (s, 1H), 8.07-8.15 (m, 1H); APCI-MS (*m/z*) 502.13 $(MH)^+$.

Deprotection of the above intermediate using excess hydrochloric acid in ethyl acetate gave the title compound as a white solid; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.15-3.25 (m, 2H), 4.25-4.35 (m, 2H), 7.37-7.46 (m, 2H), 7.75 (d, J = 6.9 Hz, 1H), 7.91 (dd, J = 8.4, 8.1 Hz, 2H), 8.00-8.08 (m, 1H + 3H), 8.15-8.21 (m, 1H); APCI-MS (*m/z*) 400.46 $(M-H)^-$.

Pharmacological activity

The illustrative examples of the present invention are screened for TRPM8 antagonist activity according to a modified procedure described in Tóth, A. *et al. Life Sciences* (2003), 73, 487-498. Other related methods and procedures may be found in

Behrendt, H. J. *et al. Br. J. Pharmacol.* (2004), 141, 737-745; Anderson, D. A. *et al. J. Neuroscience* (2004), 24, 5364-5369.

Screening for TRPM8 antagonist using ^{45}Calcium uptake assay

In this assay, inhibition of TRPM8 receptor activation was followed as inhibition of agonist induced cellular uptake of radioactive calcium using hTRPM8/CHO cells. Test compounds were dissolved in dimethylsulfoxide (DMSO) to prepare 10 mM stock and then diluted using plain medium containing 0.1% bovine serum albumin (BSA) and 1.8 mM $CaCl_2$ to obtain the desired concentration. Final concentration of DMSO in the reaction was 0.5% (v/v). Human TRPM8 expressing CHO cells were grown in F-12 Dulbecco's Modified Eagle *Medium* (DMEM) with 10% fetal bovine serum (FBS), 1% penicillin-streptomycin solution and 400 µg/ml of G-418. Cells were seeded 24 h prior to the assay in 96 well plates so as to get ~50,000 cells per well on the day of experiment. Cells were treated with test compounds for 10 minutes followed by addition of icilin or menthol at a pre-defined concentration and 5 µCi/ml of $^{45}Ca^{+2}$ for 3 minutes. Cells were washed and lysed using buffer containing 1% Triton X-100, 0.1% deoxycholate and 0.1% SDS. Radioactivity in the lysate was measured in Packard Top count after addition of liquid scintillant. Concentration response curves were plotted as a percentage of maximal response obtained in the absence of test antagonist. IC_{50} values were calculated from concentration response curve by nonlinear regression analysis using GraphPad PRISM software.

The IC_{50} (nM) values of the compounds are set forth in Table 14 wherein "A" refers to an IC_{50} value of less than 20 nM, "B" refers to IC_{50} value in range of 20.1 - 100 nM, "C" refers to an IC_{50} value in range of 100.1 - 500 nM and "D" refers to an IC_{50} value of more than 500 nM.

Table 14: In-vitro screening results of compounds of invention

Examples	Percentage Inhibition		IC_{50} (nM)
	1.0 µM	10.0 µM	
Example 1	48.23	99.38	-
Example 2	42.32	99.07	-

Example 3	92.19	99.90	B
Example 4	80.32	100	D
Example 5	70.61	100	-
Example 6	100	100	A
Example 7	92.08	100	C
Example 8	100	98.25	A
Example 9	100	100	A
Example 10	100	99.56	B
Example 11	100	100	B
Example 12	91.77	98.63	C
Example 13	24.45	98.58	-
Example 14	87.40	99.38	C
Example 15	100	100	C
Example 16	98.50	100	B
Example 17	100	100	A
Example 18	99.75	99.01	B
Example 19	12.55	97.03	-
Example 20	100	100	B
Example 21	100	100	A
Example 22	100	100	A
Example 23	72.54	100	C
Example 24	99.00	96	A
Example 25	100	100	A
Example 26	100	100	A
Example 27	98.47	100	C
Example 28	6.88	98.70	-
Example 29	97.53	98.52	B
Example 30	100	100	A
Example 31	59.89	100	D
Example 32	20.37	56.21	-

Example 33	63.1	100	-
Example 34	13.83	54.31	-
Example 35	100	100	B
Example 36	19.86	59.99	-
Example 37	99.03	99.96	A
Example 38	99.74	99.89	C
Example 39	99.87	100	B
Example 40	97.71	100	B
Example 41	100	100	B
Example 42	100	100	B
Example 43	100	100	A
Example 44	94.75	100	B
Example 45	100	100	B
Example 46	32.54	98.78	-
Example 47	97.03	100	B
Example 48	87.37	96.97	C
Example 49	100	100	B
Example 50	77.15	99.29	D
Example 51	77.12	99.84	D
Example 52	91.61	99.45	C
Example 53	55.09	100	-
Example 54	100	100	B
Example 55	99.21	98.5	A
Example 56	100	100	C
Example 57	99.21	100	A
Example 58	100	100	A
Example 59	98.41	100	C
Example 60	100	100	A
Example 61	6.42	97.61	-
Example 62	49.81	100	-

Example 63	100	99.69	A
Example 64	8.18	47.84	-
Example 65	100	100	A
Example 66	100	100	B
Example 67	100	100	A
Example 68	99.02	99.53	A
Example 69	79	97.63	-
Example 70	20.43	51.34	-
Example 71	23.62	78.19	-
Example 72	51.29	100	-
Example 73	60.15	100	-
Example 74	74.80	100	C
Example 75	38.01	97.32	-
Example 76	91.38	100	C
Example 77	22.51	98.91	-
Example 78	44.23	99.28	-
Example 79	44.11	100	-
Example 80	95.46	100	C
Example 81	47.01	99.15	-
Example 82	100	100	B
Example 83	99.67	98.91	A
Example 84	100	100	A
Example 85	100	99.89	A
Example 86	94.66	99.53	C
Example 87	100	100	A
Example 88	100	100	A
Example 89	0.00	38.51	-
Example 90	16.98	84.33	-
Example 91	10.17	89.33	-
Example 92	53.37	100	D

Example 93	51.11	82.53	D
Example 94	14.88	100	-
Example 95	10.44	99.38	-

Estimation of *In Vitro* Metabolic Stability of TRPM8 compounds in various species liver microsomes:

In vitro metabolic stability data of illustrative examples of the present invention was determined using liver microsomes. A 5 mM stock of the test compound was prepared in DMSO from which a working standard of 0.1 mM was prepared in DMSO. A 5 µl aliquot of test item from the working standard and 25 µl of 20 mg/ml of protein (mouse/rat/dog/monkey and pooled human liver microsomes) was spiked into 445 µl of KH_2PO_4 Buffer (pH 7.4) to get a final concentration of 1.0 µM test item and 1.0 mg/ml protein, respectively. Reaction was initiated by the addition of 25 µl of $NADPH^+H^+$ to get a final concentration of 2 mM. The reaction mixture was incubated at 37^0C for 60 min and terminated by the addition of 3.0 ml of TBME. For the 0 hr samples reaction was terminated with 3 ml of TBME prior to the addition of $NADPH^+H^+$. 25 µl of 30.0 µg/ml of the internal standard in diluent (Water: Acetonitrile::20: 80) was spiked in both 0 hr and 60 min samples. The samples were processed by vortex mixing for 5 min and centrifuging at 3000 rpm for 5 min; Clear supernatant was separated and dried under nitrogen. The residue was reconstituted by adding 100 µl of Water: Acetonitrile (20: 80) and 75 µl sample was injected into HPLC system. The area ratios of test item to internal standard in all samples were analyzed by HPLC method. Based on the comparison of area ratios of test item to internal standard in both the 0 hr samples and 60min samples, the percent metabolized and percent remaining of the test compound was estimated.

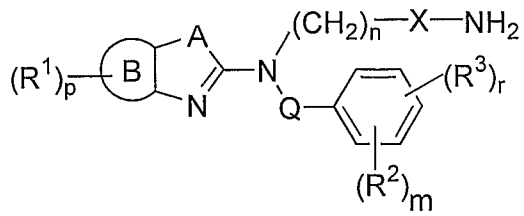
The percentage of compound remaining after metabolism in various species are set forth in Table 15 wherein "A" refers to an percentage 0-25, "B" refers to to an percentage 25-50, "C" refers to to an percentage 50-75 and "D" refers to to an percentage 75-100. These results are presented in Table 15.

Table 15: *In Vitro* Metabolic Stability

Example No.	Percentage of compound remaining after metabolisim in various species of liver microsomes				
	Mouse (CD 1)	Rat (Wistar)	Dog (Beagle)	Monkey (Cyno)	Human
Example 15	C	A	C	A	D
Example 16	D	D	C	C	D
Example 26	B	C	B	A	D
Example 29	A	B	B	A	D
Example 35	D	D	B	D	D
Example 40	C	D	A	A	C
Example 45	B	B	C	A	B
Example 47	A	B	C	A	C
Example 54	B	B	C	A	D
Example 58	A	C	C	A	B

WE CLAIM:

1. A compound of the formula (I):



(I)

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof,

wherein,

A is selected from oxygen or sulfur;

B is selected from fused six membered cycloalkyl ring, aryl ring or heteroaryl ring containing 1, 2 or 3 nitrogen atoms;

X is a bond, -CO, -$CO(CH_2)_n$-, -C=S or -SO_2-;

Q is -$(CH_2)_q$, -CO, -CO-$(CH_2)_q$, -CONH-, -$CONHC(R^4R^5)$-, -SO_2-, -SO_2CH_2- or -SO_2NR^6-;

at each occurrence of R^1, R^2 and R^3 are independently selected from hydrogen, hydroxyl, halogen, nitro, cyano, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted haloalkyl, substituted or unsubstituted haloalkoxy, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylalkyl, substituted or unsubstituted heterocyclyl, -COR^7, -$CONR^7$, -$COOR^7$, -NR^4R^5, -$NR^7C(O)R^7$, -$NR^7C(S)R^7$, -OR^8, -$OCOR^7$, -$OC(O)OR^7$or -SR^7;

at each occurrence of R^4, R^5, R^6 and R^7 are independently selected from hydrogen or lower alkyl;

R^8 is selected from substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted aryl, substituted

or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl or substituted or unsubstituted heteroarylalkyl;

'm' is an integer selected from 1, 2 or 3;

'n' is an integer selected from 1, 2 or 3;

'p' is an integer selected from 1, 2, 3 or 4;

'q' is an integer selected from 1, 2 or 3;

'r' is an integer selected from 0,1 or 2.

2. A compound according to claim 1, wherein ring B is substituted or unsubstituted aryl preferably phenyl.

3. A compound according to claim 1, wherein ring B is substituted or unsubstituted heteroaryl preferably pyridyl.

4. A compound according to claim 1, wherein ring B is substituted or unsubstituted cycloalkyl preferably cyclohexyl.

5. A compound according to claim 1, wherein A is oxygen.

6. A compound according to claim 1, wherein A is sulfur.

7. A compound according to claim 1, wherein Q is $-(CH_2)-$.

8. A compound according to claim 1, wherein Q is -CONH-.

9. A compound according to claim 1, wherein Q is $-CONH-CH-CH_3$.

10. A compound according to claim 1, wherein Q is $-CO-CH_2-CH_2-$.

11. A compound according to claim 1, wherein Q is $-SO_2-$.

12. A compound according to claim 1, wherein n is 1 or 2.

13. A compound according to claim 1, wherein X is bond.

14. A compound according to claim 1, wherein X is -(CO)-.

15. A compound according to claim 1, wherein R^1, R^2 and R^3 are hydrogen where p and m is 1.

16. A compound according to claim 1, wherein R^1 are one or more substituents on ring B are independently selected from halogen, alkyl, haloalkyl, alkoxy or haloalkoxy.

17. A compound according to claim 16, wherein one or more halogen is fluorine, chlorine or bromine.

18. A compound according to claim 16, wherein alkyl is methyl or ethyl.

19. A compound according to claim 16, wherein haloalkyl is trifluoromethyl.

20. A compound according to claim 16, wherein haloalkoxy is trifluoromethoxy.

21. A compound according to claim 16, wherein alkoxy is methoxy.

22. A compound according to claim 1, wherein R^2 is one or more substituents on phenyl ring comprising of halogen, alkyl, haloalkyl or alkoxy.

23. A compound according to claim 22, wherein one or more halogen is fluorine, chlorine or bromine.

24 A compound according to claim 22, wherein alkyl is methyl, *tert.* butyl.

25. A compound according to claim 22, wherein haloalkyl is trifluoromethyl.

26. A compound according to claim 22, wherein alkoxy is methoxy.

27. A compound according to claim 1, wherein R^3 is $-OR^8$; where R^8 is alkyl, cycloalkyl, cycloalkylalkyl, aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl or heteroarylalkyl.

28. A compound according to claim 27, wherein alkyl is $-CH_2CH(CH_3)_2$.

29. A compound according to claim 27, wherein cycloalkyl is cyclopentyl.

30. A compound according to claim 27, wherein cycloalkylalkyl is cyclopropylmethyl, cyclohexylmethyl

31. A compound according to claim 27, wherein aryl is phenyl.

32. A compound according to claim 27, wherein unsubstituted arylalkyl is unsubstituted benzyl.

33. A compound according to claim 27, wherein arylalkyl is mono or disubstituted benzyl.

34. A compound according to claim 27 or 33, wherein one or more substituents comprise of halogen, alkyl or haloalkyl.

35. A compound according to claim 34, wherein one or more halogen is fluorine, chlorine or bromine.

36. A compound according to claim 34, wherein alkyl is methyl, isopropyl, ethyl.

37. A compound according to claim 34, wherein haloalkyl is trifluoromethyl.

38. A compound according to claim 27, wherein substituted heteroaryl is pyridyl.

39. A compound according to claim 38, wherein one or more substituents comprise of cyano or haloalkyl.

40. A compound according to claim 39, wherein haloalkyl is trifluoromethyl.

41. A compound according to claim 27, wherein heteroarylalkyl is $-CH_2$-pyridyl.

42. The compounds according to claim 1, selected from,

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(2-fluorobenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(2-fluorobenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(2-chlorobenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(2-bromobenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(3,4-difluorobenzyl)]ethane-1,2-diamine hydrochloride;

N-(1,3-Benzoxazol-2-yl)-*N*-(2-benzyloxybenzyl)ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{2-(4-trifluoromethylbenzoxy)benzyl}]ethane-1,2-diamine;

1-[*N*-(1,3-Benzoxazol-2-yl)]-*N*-{2-(2-fluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)]-*N*-{2-(2,6-difluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)]-*N*-[{2-(2,4-difluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-[(2-benzyloxy)benzyl]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{2-(2-fluorobenzyloxy)benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{2-[(4-trifluoromethyl)benzyloxy]benzyl}]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{2-(2,4-difluorobenzyloxy)benzyl}]ethane-1,2-diamine Hydrochloride;

1-[*N*-{2-(Benzyloxybenzyl)}-*N*-(6-chloro-1,3-benzothiazol-2-yl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(2-Benzyloxybenzyl)-*N*-(5-trifluorormethoxy-1,3-benzothiazol-2-yl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-benxyloxybenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-benzyloxybenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(4-Benzyloxybenzyl)-*N*-(5-trifluromethyl-1,3-benzothiazol-2-yl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{(4-benzyloxy-3-chlorobenzyl}]ethane-1,2-diamine hydrochloride;

1[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-benzyloxy-3-methoxybenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{3-methoxy-[4-(2-methylbenzyloxy)]benzyl} ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-benzyloxy-3-chlorobenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)]-*N*-(4-benzyloxy-3-methoxybenzyl)ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{4-(2-trifluromethylbenzyloxy)-3-methoxybenzyl}] ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)]-*N*-{4-(2-fluorobenzyloxy)-3-methoxybenzyl}] ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{4-(2-trifluromethylbenzyloxy)-3-methoxybenzyl}] ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{4-(3-triflurомethylbenzyloxy)-3-methoxybenzyl}] ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{4-(2,4-difluorobenzyloxy)-3-methoxybenzyl}] ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{[4-(2,6-difluorobenzyloxy)]-3-methoxybenzyl}] ethane-1,2-diamine hydrochloride;

1-[*N*-[(4-Benzyloxy-3-methoxy)benzyl]-*N*-(5-trifluorormethoxy-1,3-benzothiazol-2-yl)]ethane-1,2-diamine hydrochloride;

1-[*N*-[(4-Benzyloxy-3-methoxy)benzyl]-*N*-(6-chloro-1,3-benzothiazol-2-yl)] ethane-1,2-diamine hydrochloride;

1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-(5-chloro-1,3-benzothiazol-2-yl)ethane-1,2-diamine hydrochloride;

1-[*N*-[(4-Benzyloxy-3-methoxy)benzyl]-*N*-(5-triflurомethyl-1,3-benzothiazol-2-yl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(5-Fluoro-1,3-benzothiazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxybenzyl}] ethane-1,2-diamine hydrochloride;

1-[*N*-(5,6-Dimethoxy-1,3-Benzothiazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxybenzyl}] ethane-1,2-diamine hydrochloride;

1-[*N*-{4-[(2-Methylbenzyloxy)]benzyl}-*N*-[1,3]oxazolo[4,5-*b*]pyridin-2-ylethane-1,2-diamine hydrochloride;

1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-[1,3]thiazolo[5,4-*b*]pyridin-2-yl]ethane-1,2-diamine hydrochloride;

1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-[1,3]thiazolo[4,5-*b*]pyridin-2-yl]ethane-1,2-diamine hydrochloride;

1-[*N*-{4-(2-Fluorobenzyloxy)-3-methoxybenzyl}-*N*-[1,3]thiazolo[5,4-*b*]pyridin-2-yl]ethane-1,2-diamine hydrochloride;

1-[*N*-{4-(2-Fluorobenzyloxy)-3-methoxybenzyl}-*N*-[1,3]thiazolo[4,5-*b*]pyridin-2-yl]ethane-1,2-diamine hydrochloride;

1-[*N*-{4-(2,6-Difluorobenzyloxy)-3-methoxybenzyl}-*N*-[1,3]thiazolo[5,4-*b*] pyridin-2-yl]ethane-1,2-diamine hydrochloride;

1-[*N*-(7-Chloro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxybenzyl}]ethane-1,2-diamine hydrochloride;

N-(7-Chloro[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-{3-methoxy-4-[(2-methylbenzyloxy)] benzyl}ethane-1,2-diamine;

1-[*N*-{4-(2-Fluorobenzyloxy)-3-methoxybenzyl}-*N*-[6-(trifluoromethyl)[1,3] thiazolo[4,5-*b*]pyridin-2-yl] ethane-1,2-diamine hydrochloride;

1-[*N*-{4-[(2,6-Difluorobenzyloxy)-3-methoxybenzyl]}-*N*-[1,3]thiazolo[5,4-*c*]pyridin-2-yl]ethane-1,2-diamine hydrochloride;

N-(7-Bromo[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-{3-methoxy-[4-(2-methylbenzyloxy)] benzyl}ethane-1,2-diamine;

N-(7-Bromo[1,3]thiazolo[5,4-*c*]pyridin-2-yl)-*N*-{[4-(2,6-difluorobenzyloxy)]-3-methoxybenzyl} ethane-1,2-diamine;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(2-benzyloxybenzyl)]propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{2-(2-fluorobenzyloxy)benzyl}]propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{4-(2,6-difluorobenzyloxy)benzyl}]propane-1,3-diamine hydrochloride;

1-[*N*-(2-Benzyloxybenzyl)-*N*-(5-chloro-1,3-benzoxazol-2-yl)]propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-[2-methylbenzyloxy]benzyl)]propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-benzyloxy-3-methoxybenzyl)]propane-1,3-diamine hydrochloride;

1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-(5-fluoro-1,3-benzoxazol-2-yl)propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{[4-(2-flurobenzyloxy)]-3-methoxybenzyl}] propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(3-methoxy-[4-(2-methylbenzyloxy)]benzyl)] propane-1,3-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(3-methoxy-[4-(2-trifluoromethylbenzyloxy)] benzyl) ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{[4-(2,6-diflurobenzyloxy)]-3-methoxybenzyl}] propane-1,3-diamine hydrochloride;

1-[*N*-(4-Benzyloxy-3-methoxybenzyl)-*N*-(5-methyl-1,3-Benzoxazol-2-yl)propane-1,3-diamine hydrochloride;

1-[*N*-(5-Chloro-1,3-benzoxazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxy benzyl}] propane-1,3-diamine hydrochloride;

2-[*N*-(1,3-Benzoxazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxybenzyl} amino) acetamide;

2-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-benzyloxy-3-methoxybenzyl)amino]acetamide;

2-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-benzyloxy-3-methoxybenzyl)amino] acetamide;

2-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{[4-(2-fluorobenzyloxy)]-3-methoxybenzyl} amino] acetamide;

2-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{[3-methoxy-[4-(2-methylbenzyloxy)]benzyl} amino]acetamide;

2-[*N*-(1,3-Benzothiazol-2-yl)-*N*-{[4-(2,6-difluorobenzyloxy)]-3-methoxybenzyl} amino]acetamide;

2-{*N*-[4-(Benzyloxy)-3-methoxybenzyl]-*N*-(5-fluoro-1,3-benzothiazol-2-yl)amino}acetamide;

2-{[4-(Benzyloxy)-3-methoxybenzyl]([1,3]thiazolo[5,4-*b*]pyridin-2-yl)amino} acetamide;

2-{[4-(Benzyloxy)-3-methoxybenzyl]([1,3]thiazolo[4,5-*b*]pyridin-2-yl)amino} acetamide;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-isobutoxy-3-methoxybenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-cyclopropylmethoxy-3-methoxybenzyl)] ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-cyclopentyloxy-3-methoxybenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(4-[cyclohexylmethoxy]-3-methoxybenzyl)] ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(3-methoxy-4-phenoxybenzyl)]ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(3-methoxy-4-{[5-(trifluoromethyl)pyridin-2-yl]oxy} benzyl)]ethane-1,2-diamine hydrochloride;

6-(4-{[(2-Aminoethyl)(1,3-benzoxazol-2-yl)amino]methyl}-2-methoxyphenoxy) nicotinonitrile hydrochloride;

1-[*N*-(1,3-Benzothiazol-2-yl)-*N*-(3-methoxy-4-[pyridin-4-ylmethoxy]benzyl) ethane-1,2-diamine hydrochloride;

1-[*N*-(1,3-Benzoxazol-2-yl)-*N*-(4-[pyridin-2-yloxy]benzyl)] propane-1,3-diamine hydrochloride;

N-(3,4-Difluorobenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl)ethane-1,2-diamine hydrochloride;

N-(4-[2-Methylbenzyloxy]benzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) ethane-1,2-diamine hydrochloride;

N-(4-Benzyloxy-3-methoxybenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) ethane-1,2-diamine hydrochloride;

N-(3-Methoxy-[4-(2-methylbenzyloxy)]benzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) ethane-1,2-diamine hydrochloride;

N-([4-(2-Ethylbenzyloxy)]-3-methoxy]benzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) ethane-1,2-diamine hydrochloride;

N-{4-(2-Isopropylbenzyloxy)-3-methoxybenzyl}-N-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) ethane-1,2-diamine hydrochloride;

N-([4-(2-Fluorobenzyloxy)]-3-methoxybenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) ethane-1,2-diamine hydrochloride;

N-(4-[(2,6-Difluorobenzyloxy)]-3-methoxybenzyl)-*N*-(4,5,6,7-tetrahydro-1,3-benzothiazol-2-yl) ethane-1,2-diamine hydrochloride;

1-(2-Aminoethyl)-1-(1,3-benzoxazol-2-yl)-3-(4-*tert*-butylphenyl)urea hydrochloride;

1-(2-Aminoethyl)-1-(1,3-benzoxazol-2-yl)-3-[4-fluoro-2-(trifluoromethyl)phenyl] urea Hydrochloride;

1-(2-Aminoethyl)-1-(1,3-benzothiazol-2-yl)-3-[4-fluoro-2-(trifluoromethyl)phenyl] urea hydrochloride;

1-(2-Aminoethyl)-1-(1,3-benzothiazol-2-yl)-3-[(1*S*)-1-phenylethyl]urea hydrochloride;

N-(2-Aminoethyl)-*N*-1,3-benzothiazol-2-yl-[3-(2-benzyloxy)phenyl]propanamide hydrochloride;

N-(2-Aminoethyl)-*N*-1,3-benzothiazol-2-yl-4-methylbenzenesulfonamide hydrochloride;

1-[*N*-(2-Aminoethyl)-*N*-(1,3-benzothiazol-2-yl)]-3,4-dichlorobenzenesulfonamide hydrochloride;

or ester thereof, tautomer thereof, stereoisomer thereof, prodrug thereof and pharmaceutically acceptable salt thereof.

43. A pharmaceutical composition comprising a compound according to any one of claim 1 to 42, either as a free base or pharmaceutically acceptable salt and a pharmaceutically acceptable excipient.

44. The pharmaceutical composition according to claim 33, wherein the pharmaceutically acceptable excipient is a carrier or diluent.

45. A method for preventing, ameliorating or treating a disease, disorder or syndrome modulated by TRPM-8 in a subject in need thereof comprising administering to the subject a therapeutically effective amount of a compound according to any one of claims 1 to 42.