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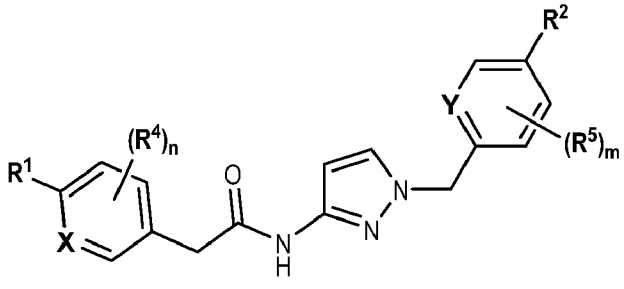

Formula (I)

(57) Abstract: The invention relates to compounds of formula (I) Formula (I) wherein X, Y, R^1, R^2, $(R^4)_n$, and $(R^5)_m$ are as defined in the description, and to pharmaceutically acceptable salts of such compounds. These compounds are useful as calcium T-channel blockers.

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PYRAZOLE COMPOUNDS AND THEIR USE AS T-TYPE CALCIUM CHANNEL BLOCKERS

Pyrazole Compounds

The present invention relates to novel pyrazole compounds and their use as T-type calcium channel blockers in the treatment or prevention of various diseases or disorders where calcium T channels are involved, to pharmaceutical compositions containing these derivatives, and to processes for their preparation.

Intracellular calcium concentrations control important life processes such as signal transduction pathways, hormones and neurotransmitter release, muscular contraction, gene expression and cell division. Control of calcium influx across the cellular membrane is in part regulated by a family of transmembrane proteins termed voltage-gated calcium channels (VOCs). They are activated by changes in electrical potential difference across the membrane and have been further classified into different subtypes based on biophysical and pharmacological considerations: Cav1.x (L-type for Long-lasting), Cav2.x (N-, P/Q- and R-types; N for Neuronal, P for Purkinje cells, Q (after P) and R for Remaining or Resistant) and Cav3.x (T-type for Transient). The L, N, P and Q-type channels activate at more positive potentials (high voltage activated) and display diverse kinetics and voltage-dependent properties. The T-type class (or "low voltage-activated") is characterized by fast inactivation (transient) and small conductance (tiny) and is composed of three members due to the different main pore-forming α1 subunits: Cav3.1 (α1 G), Cav3.2 (α1 H) and Cav3.3 (α1 I).

Nearly all "excitable" cells, such as neurons of the central nervous system (CNS), peripheral nerve cells and muscle cells, including those of skeletal muscles, cardiac muscles, and venous and arterial smooth muscles, have voltage-dependent calcium channels. In consequence, calcium T channels have been linked to various human diseases and disorders, such as especially epilepsy, pain, neuropathic pain, sleep disorders, sleep disturbances, schizophrenia, essential tremors, Parkinson's disease, neurodegenerative disorders, depression, anxiety, psychosis, autism, drug addiction, hypertension, cardiac arrhythmias, heart block, cancer, diabetes, infertility and sexual dysfunction (Bourinet, E.; Alloui, A.; Monteil, A.; Barrere, C.; Couette, B.; Poirot, O.; Pages, A.; McRory, J.; Snutch, T. P.; Eschalier, A.; Nargeot, J., *EMBO J* **2005,** *24* (2), 315-324; Flatters, S.J.L., Drugs Fut. **2005**, 30(6), 573-580 ; Giordanetto, F.; Knerr, L.; Wallberg, A., *Expert Opin Ther Pat* **2011,** *21* (1), 85-101; Huguenard, J. R.; Prince, D. A., *J Neurosci* **1994,** *14* (9), 5485-502; Lory, P.; Mezghrani, A., *IDrugs* **2010,** *13* (7), 467-71; McGivern, J. G., *Drug Discov Today* **2006,** *11* (5-6), 245-53; Uslaner, J. M.; Vardigan, J. D.; Drott, J. M.; Uebele, V. N.; Renger, J. J.; Lee, A.; Li, Z.; Le, A. D.; Hutson, P. H., *Biol Psychiatry* **2010,** *68* (8), 712-8; Wildburger, N. C.; Lin-Ye, A.; Baird, M. A.; Lei, D.; Bao, J., Mol Neurodegener **2009**, 4, 44).

In the brain, T-type calcium channels are essential for regulating neuronal excitability and burst firing, both in the central and peripheral nervous system (Lambert, R. C.; Bessaih, T.; Crunelli, V.; Leresche, N., *Pflugers Arch* **2014,** *466* (3), 415-23.). They are linked to diseases or disorders where abnormal oscillatory activity occurs in the brain, as well as diseases or disorders where there is abnormal coupling of activity, particular

through the thalamus. They are particularly linked to an increasing number of neurological disorders such as the epilepsy disorders and neuropathic pain.

T-type calcium channels play a role in regulating neuronal firing patterns under normal physiological conditions, such as during sleep rhythms (Anderson, M. P.; Mochizuki, T.; Xie, J.; Fischler, W.; Manger, J. P.; Talley, E. M.; Scammell, T. E.; Tonegawa, S., *Proc Natl Acad Sci U S A* **2005**, *102* (5), 1743-8; Destexhe, A.; Contreras, D.; Sejnowski, T. J.; Steriade, M., *J Neurophysiol* **1994**, *72* (2), 803-18; Lee, J.; Kim, D.; Shin, H. S., *Proc Natl Acad Sci U S A* **2004**, *101* (52), 18195-9; Steriade, M., *Trends Neurosci* **2005**, *28* (6), 317-24.). However, T-type calcium channels are also involved in pathophysiological conditions such as epilepsy, autism, hypertension, atrial fibrillation, congenital heart failure, pain, psychoses and cancer (for review, see Iftinca, M. C., *J Med Life* **2011**, *4* (2), 126-38).

T-type calcium channels are critical players in the development of idiopathic generalized seizures in humans and animals (Cheong, E.; Shin, H. S., Pflugers Arch **2014**, 466 (4), 719-34; Khosravani, H.; Zamponi, G. W., *Physiol Rev* **2006**, *86* (3), 941-66; Zamponi, G. W.; Lory, P.; Perez-Reyes, E., *Pflugers Arch* **2010**, *460* (2), 395-403). In animals, knockout of Cav3.1 calcium channels protects mice from absence seizures (Kim, D.; Song, I.; Keum, S.; Lee, T.; Jeong, M. J.; Kim, S. S.; McEnery, M. W.; Shin, H. S., *Neuron* **2001**, *31* (1), 35-45; Song, I.; Kim, D.; Choi, S.; Sun, M.; Kim, Y.; Shin, H. S., *J Neurosci* **2004**, *24* (22), 5249-57). In rat models of absence epilepsy (GAERS or WAG/Rij), a gain of function mutation of the Cav3.2 gene has been reported (Powell, K. L.; Cain, S. M.; Ng, C.; Sirdesai, S.; David, L. S.; Kyi, M.; Garcia, E.; Tyson, J. R.; Reid, C. A.; Bahlo, M.; Foote, S. J.; Snutch, T. P.; O'Brien, T. J., *J Neurosci* **2009**, *29* (2), 371-80), as well as elevated levels of Cav3.1 and Cav3.2 mRNA and an increase in the amplitude of the T-type calcium current in comparison to normal rat strain (Broicher, T.; Kanyshkova, T.; Meuth, P.; Pape, H. C.; Budde, T., *Mol Cell Neurosci* **2008**, *39* (3), 384-99; Talley, E. M.; Solorzano, G.; Depaulis, A.; Perez-Reyes, E.; Bayliss, D. A., *Brain Res Mol Brain Res* **2000**, *75* (1), 159-65; Tsakiridou, E.; Bertollini, L.; de Curtis, M.; Avanzini, G.; Pape, H. C., *J Neurosci* **1995**, *15* (4), 3110-7; Powell, K. L.; Cain, S. M.; Ng, C.; Sirdesai, S.; David, L. S.; Kyi, M.; Garcia, E.; Tyson, J. R.; Reid, C. A.; Bahlo, M.; Foote, S. J.; Snutch, T. P.; O'Brien, T. J., *J Neurosci* **2009**, *29* (2), 371-80). In human, number of mutations have been described in Cav3.2 channels in patients with childhood absence and other forms of idiopathic generalized epilepsies (Heron, S. E.; Khosravani, H.; Varela, D.; Bladen, C.; Williams, T. C.; Newman, M. R.; Scheffer, I. E.; Berkovic, S. F.; Mulley, J. C.; Zamponi, G. W., *Ann Neurol* **2007**, *62* (6), 560-8; Khosravani, H.; Zamponi, G. W., *Physiol Rev* **2006**, *86* (3), 941-66; Zamponi, G. W.; Lory, P.; Perez-Reyes, E., *Pflugers Arch* **2010**, *460* (2), 395-403). Those mutations are predicted to cause a gain of function with increase in calcium current, or can trigger an alteration of the balance between excitatory and inhibitory neuronal elements. As direct consequence, it may result in an increased spiking behavior in neurons that exhibit this rebound bursting, thereby contributing to the generation of epileptiform discharges.

In another type of epilepsy, i.e. the temporal lobe epilepsy, it has been shown in the pilocarpine rodent model that T-type calcium currents were uppregulated after status epilepticus and suggest a role of this channel in long-lasting modification of neuronal firing mode (regular to burst firing) and potential contribution to the development and expression of an epileptic condition after SE (Yaari, Y.; Yue, C.; Su, H., *J Physiol* **2007**, *580* (Pt. 2), 435-50; Becker, A. J.; Pitsch, J.; Sochivko, D.; Opitz, T.; Staniek, M.; Chen, C. C.; Campbell, K. P.; Schoch, S.; Yaari, Y.; Beck, H., *J Neurosci* **2008**, *28* (49), 13341-53; Graef, J. D.; Nordskog, B. K.; Wiggins, W. F.; Godwin, D. W., *J Neurosci* **2009**, *29* (14), 4430-41; Su, H.; Sochivko, D.; Becker, A.; Chen, J.; Jiang, Y.; Yaari, Y.; Beck, H., *J Neurosci* **2002**, *22* (9), 3645-55).

Increased activity of T-type calcium channel has been associated to neuropathic and inflammatory pain states (for review, see Todorovic, S. M.; Jevtovic-Todorovic, V., *Br J Pharmacol* **2011**, *163* (3), 484-95). When nociceptors are in an increased state of responsiveness, they often respond to normal sensory stimuli as if painful (allodynia) and to mildly painful stimuli as though they were acutely painful (hyperalgesia). The electrophysiological answer of these altered pain responses, include lower thresholds of activation, increased frequency of firing in response to suprathreshold stimuli and spontaneous firing (Coderre, T. J.; Katz, J.; Vaccarino, A. L.; Melzack, R., *Pain* **1993**, *52* (3), 259-85; Bhave, G.; Gereau, R. W. t., *J Neurobiol* **2004**, *61* (1), 88-106). T-type calcium channel are abundantly expressed in nociceptors, spinal dorsal horn and thalamic neurons (Talley, E. M.; Cribbs, L. L.; Lee, J. H.; Daud, A.; Perez-Reyes, E.; Bayliss, D. A., *J Neurosci* **1999**, *19* (6), 1895-911) and increased T-type channel activity has been linked to neuropathic and inflammatory pain states in animals and humans (Jagodic, M. M.; Pathirathna, S.; Nelson, M. T.; Mancuso, S.; Joksovic, P. M.; Rosenberg, E. R.; Bayliss, D. A.; Jevtovic-Todorovic, V.; Todorovic, S. M., *J Neurosci* **2007**, *27* (12), 3305-16; Todorovic, S. M.; Jevtovic-Todorovic, V., *Channels (Austin)* **2007**, *1* (4), 238-45; Jagodic, M. M.; Pathirathna, S.; Joksovic, P. M.; Lee, W.; Nelson, M. T.; Naik, A. K.; Su, P.; Jevtovic-Todorovic, V.; Todorovic, S. M., *J Neurophysiol* **2008**, *99* (6), 3151-6). T-channels may play a role in the decrease of the threshold for action potential firing in dorsal root ganglia (DRG) cells that express T-channels (Nelson, M. T.; Todorovic, S. M.; Perez-Reyes, E., *Curr Pharm Des* **2006**, *12* (18), 2189-97; Jagodic, M. M.; Pathirathna, S.; Nelson, M. T.; Mancuso, S.; Joksovic, P. M.; Rosenberg, E. R.; Bayliss, D. A.; Jevtovic-Todorovic, V.; Todorovic, S. M., *J Neurosci* **2007**, *27* (12), 3305-16). T-type calcium channels would play a role of amplifiers of peripheral pain signals. Pharmacological and molecular downregulation of the function of these channels in DRG neurons supports the notion that T-channels contribute to the chronic pain associated with peripheral axonal injury (Bourinet, E.; Alloui, A.; Monteil, A.; Barrere, C.; Couette, B.; Poirot, O.; Pages, A.; McRory, J.; Snutch, T. P.; Eschalier, A.; Nargeot, J., *EMBO J* **2005**, *24* (2), 315-24; Wen, X. J.; Li, Z. J.; Chen, Z. X.; Fang, Z. Y.; Yang, C. X.; Li, H.; Zeng, Y. M., *Acta Pharmacol Sin* **2006**, *27* (12), 1547-52) (or for review, see (Jevtovic-Todorovic, V.; Todorovic, S. M., *Cell Calcium* **2006**, *40* (2), 197-203)).

In addition, T-type calcium channel activity is upregulated during diabetic neuropathy (Hall, K. E.; Sima, A. A.; Wiley, J. W., *J Physiol* **1995**, *486 (2)*, 313-22; Jagodic, M. M.; Pathirathna, S.; Nelson, M. T.; Mancuso, S.;

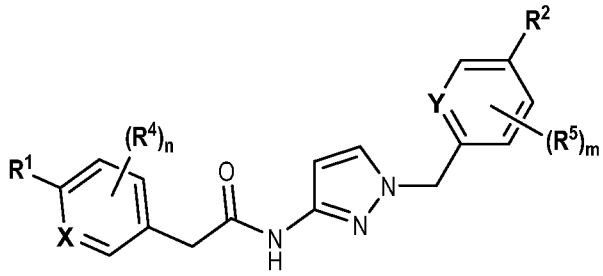
Joksovic, P. M.; Rosenberg, E. R.; Bayliss, D. A.; Jevtovic-Todorovic, V.; Todorovic, S. M., *J Neurosci* **2007**, *27* (12), 3305-16). Selective knock-down of DRG Cav3.2 currents *in vivo* has effectively reversed mechanical and thermal hyperalgesia in STZ-induced diabetic neuropathy in rats (Messinger, R. B.; Naik, A. K.; Jagodic, M. M.; Nelson, M. T.; Lee, W. Y.; Choe, W. J.; Orestes, P.; Latham, J. R.; Todorovic, S. M.; Jevtovic-Todorovic, V., *Pain* **2009**, *145* (1-2), 184-95). Furthermore, significant up-regulation of Cav3.2 T-channel mRNA in DRG tissue homogenates and concomitant up-regulation of Cav3.2 T-currents in nociceptive DRG cells has been reported in another model of painful diabetic neuropathy, leptin-deficient ob/ob mice (Latham, J. R.; Pathirathna, S.; Jagodic, M. M.; Choe, W. J.; Levin, M. E.; Nelson, M. T.; Lee, W. Y.; Krishnan, K.; Covey, D. F.; Todorovic, S. M.; Jevtovic-Todorovic, V., *Diabetes* **2009**, *58* (11), 2656-65). In humans, extracellular recordings from the medial thalamus of patients with neurogenic pain have shown abnormalities of LTS-mediated bursts that could at least contribute to persistent pain (Jeanmonod, D.; Magnin, M.; Morel, A., *Brain* **1996**, *119 (2)*, 363-75).

It has been shown that T-type calcium (Ca) channels in the CNS are closely associated with repetitive burst discharges or neuronal oscillations (Llinas, R.; Yarom, Y., *J Physiol* **1986**, *376*, 163-82; Gutnick, M. J.; Yarom, Y., *J Neurosci Methods* **1989**, *28* (1-2), 93-9; Iftinca, M. C.; Zamponi, G. W., *Trends Pharmacol Sci* **2009**, *30* (1), 32-40). Tremor is a common encountered involuntary movements, and it is associated with various neurological diseases or pathological conditions such as essential tremor (ET) and Parkinson's disease (PD) and its related disorders. As tremor-related neuronal activities may be closely related to repetitive or oscillatory activities in the CNS, controlling T-type Ca channels may have therapeutic effects. This hypothesis is supported by neuro-anotomical and functional expression of expression of T-type calcium channels in area involved pathophysiological mechanisms underlying harmaline-induced tremor, a pharmacological model of ET in rodents (Llinas, R.; Yarom, Y., *J Physiol* **1986**, *376*, 163-82; Cavelier, P.; Lohof, A. M.; Lonchamp, E.; Beekenkamp, H.; Mariani, J.; Bossu, J. L., *Neuroreport* **2008**, *19* (3), 299-303). Moreover, animal data involving selective knockdown of the Cav3.1 gene or mice lacking the Cav3.1 gene showed that Cav3.1 channels play a specific role in ET (Park, Y. G.; Park, H. Y.; Lee, C. J.; Choi, S.; Jo, S.; Choi, H.; Kim, Y. H.; Shin, H. S.; Llinas, R. R.; Kim, D., *Proc Natl Acad Sci U S A* **2010**, *107* (23), 10731-6). On the other hand, the role of the other isoform of the T-type calcium channels (Cav3.2 and Cav 3.3) in this pathology is not known but cannot be excluded (Miwa, H.; Kondo, T., *Cerebellum* **2011**, *10* (3), 563-9).

In Parkinson's disease (PD) patients, deep brain stimulation of the subthalamic nucleus has been shown to be an effective treatment for parkinsonian symptoms indicating a pivotal role of this area in the pathogenesis of PD: In patients, as well as in animal models of PD, this area seems to have an abnormal pattern of firing with an increase of the burst firing mode. And this burst firig mode has been shown to involve the T-type Ca^{2+} channels (for review, see Yang, Y. C.; Tai, C. H.; Pan, M. K.; Kuo, C. C., Pflugers Arch **2014**, 466 (4), 747-55).

The compounds of the present invention are potent calcium T channel blockers and therefore useful for the prevention or treatment of diseases or disorders where calcium T channels are involved.

1) A first aspect of the invention relates to novel compounds of the formula (I)



Formula (I)

wherein

X represents a ring carbon or a ring nitrogen atom;

- R^1 represents
  - (C_{2-6})alkyl [in particular isopropyl, *tert.*-butyl, or isobutyl];
  - (C_{2-4})alkyl mono-substituted with cyano, or (C_{1-3})alkoxy (especially methoxy); [in particular such group is 1-methoxy-ethyl, or 1-cyano-1-methyl-ethyl];
  - (C_{1-4})fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
  - (C_{1-3})fluoroalkoxy [in particular trifluoromethoxy, 2,2,2-trifluoroethoxy, 3,3,3-trifluoropropoxy];
  - pentafluoro-sulfanyl;
  - (C_{3-6})cycloalkyl-L^1- wherein
    - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C_{1-3})alkyl (especially methyl), (C_{1-3})alkoxy (especially methoxy), hydroxy, cyano, or (C_{1-3})fluoroalkyl (especially trifluoromethyl), or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a substituent selected from (C_{1-3})alkyl (especially methyl) and cyano; and
    - the linker L^1 represents a direct bond, (C_{1-2})alkylene, oxygen, or (C_{1-2})alkylene-oxy (which is attached to the rest of the molecule through the oxygen atom);

      [in particular such group (C_{3-6})cycloalkyl-L^1- is cyclopropyl, 3-fluoro-oxetan-3-yl, 3-methoxy-oxetan-3-yl, 3-methyl-oxetan-3-yl, 3,3-difluoro-cyclobutyl, 1-cyano-3,3-difluoro-cyclobutyl, 1-trifluoromethyl-cyclopropyl, 2-trifluoromethyl-cyclopropyl, 1-methyl-cyclopropyl, 1-cyano-cyclopropyl, 1-hydroxy-cyclopropyl, 1-methoxy-cyclopropyl, or 3-hydroxy-oxetan-3-yl; or it is cyclopropyl-methyl; or it is cyclopropyl-oxy, oxetan-3-yl-oxy, cyclobutyl-oxy, or 3,3-difluoro-cyclobutyl-oxy; or it is cyclopropyl-methoxy, oxetan-3-yl-methoxy, (3-fluoro-oxetan-3-yl)-methoxy, (3,3-difluoro-cyclobutyl)-

methoxy, (3-methyl-oxetan-3-yl)-methoxy, or (3,3-difluoro-1-methyl-cyclobutyl)-methoxy];

- 5- or 6-membered heteroaryl, independently optionally mono-substituted with (C_{1-3})alkyl (especially methyl); [in particular oxadiazolyl, pyrazinyl, pyrimidinyl, or pyridinyl];
- $-NR^{11}R^{12}$, wherein
  - R^{11} and R^{12} independently represent hydrogen, (C_{1-3})alkyl, (C_{2-3})fluoroalkyl, (C_{3-6})cycloalkyl, (C_{3-6})cycloalkyl mono- or di-substituted with fluoro, (C_{3-6})cycloalkyl-(C_{1-3})alkyl, (C_{1-3})alkoxy-(C_{2-3})alkyl [in particular such group $-NR^{11}R^{12}$ is dimethylamino, ethyl-methyl-amino, diethylamino, cyclopropyl-methyl-amino, (2-methoxyethyl)-methyl-amino, (cyclopropylmethyl)-methyl-amino, or (2,2-difluoro-ethyl)-methyl-amino];
  - or R^{11} and R^{12}, together with the nitrogen atom to which they are attached to, form a 4- to- 6 membered ring optionally mono- or di-substituted with fluoro; a 2-oxo-pyrrolidinyl group; or a morpholinyl group [in particular such group $-NR^{11}R^{12}$ is azetidinyl, 3-fluoro-azetidinyl, 3,3-difluoro-azetidinyl, pyrrolidinyl, 3-fluoro-pyrrolidinyl, 3,3-difluoro-pyrrolidinyl, or 2-oxo-pyrrolidinyl];

and $(R^4)_n$ represents one or two optional substituents (i.e. n represents the integer 0, 1, or 2) independently selected from (C_{1-4})alkyl (especially methyl, ethyl), (C_{3-6})cycloalkyl (especially cyclopropyl), (C_{1-4})alkoxy (especially methoxy), (C_{1-3})fluoroalkyl (especially trifluoromethyl), (C_{1-3})fluoroalkoxy (especially trifluoromethoxy), halogen (especially fluoro), and cyano [especially $(R^4)_n$ is absent (i.e. n = 0); or $(R^4)_n$ represents one halogen or methyl substituent];

- or R^1 together with $(R^4)_n$ forms a non-aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring; wherein said 5- or 6-membered ring optionally contains one or two heteroatoms independently selected from oxygen and nitrogen; wherein said fused 5- or 6-membered non-aromatic ring independently is optionally further mono-substituted with oxo or (C_{1-3})alkyl (especially methyl); di-substituted with (C_{1-3})alkyl (especially methyl); or di-, tri-, or tetra-substituted wherein one substituent is oxo and the remaining are (C_{1-3})alkyl (especially methyl); [in particular such non-aromatic 5- or 6-membered ring fused to the phenyl / pyridine ring forms, together with the phenyl / pyridine ring, a group selected from 2-oxo-2,3-dihydro-benzooxazol-6-yl, 3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl, 4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl, 3-methyl-2-oxo-2,3-dihydro-benzooxazol-6-yl, 3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl, 1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl, 2,2-dimethyl-2,3-dihydro-benzofuran-6-yl, 2,2-dimethyl-2,3-dihydro-benzofuran-5-yl, 3,3-dimethyl-2,3-dihydro-benzofuran-5-yl, 3,3-dimethyl-2,3-dihydro-benzofuran-6-yl, or 3-methylchroman-7-yl];

- or R^1 together with $(R^4)_n$ forms an aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring; wherein said 5- or 6-membered ring optionally contains one or two heteroatoms selected from nitrogen, wherein said fused 5- or 6-membered aromatic ring independently is optionally further mono- or di-substituted wherein the substituents are independently selected from (C_{1-3})alkyl (especially methyl,

ethyl, isopropyl), (C_{3-6})cycloalkyl (especially cyclobutyl), (C_1)fluoroalkyl (especially trifluoromethyl), or cyano [in particular such aromatic 5- or 6-membered ring fused to the phenyl / pyridine ring forms, together with the phenyl / pyridine ring, a group selected from 1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl, 1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl, 1H-indol-5-yl, 1H-indol-6-yl, 1-methyl-1H-indazol-5-yl, 1-methyl-1H-indazol-6-yl, 1-ethyl-1H-indazol-5-yl, 1-ethyl-1H-indazol-6-yl, 1,3-dimethyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 1,3-dimethyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-6-yl, 3-cyano-1-methyl-1H-indol-5-yl, 3-isopropyl-1-methyl-1H-indol-5-yl, 3-cyclobutyl-1-methyl-1H-indol-5-yl, 1-methyl-3-trifluoromethyl-1H-indol-5-yl, quinoxalin-6-yl, 2-methyl-1H-benzoimidazol-6-yl, 1-methyl-1H-benzoimidazol-5-yl, 1-methyl-1H-benzoimidazol-6-yl, or quinolin-7-yl];

- or **R^1** represents methyl, or halogen (especially fluoro); and **$(R^4)_n$** represents one substituent selected from (C_{1-3})fluoroalkoxy (especially 2,2,2-trifluoroethoxy) which is attached to the phenyl / pyridinyl ring in *ortho* or *meta*-position to the point of attachment of the –CH_2-CO-NH- group;

Y represents a ring carbon or a ring nitrogen atom; and

R^2 represents (C_{1-4})alkyl (especially methyl, ethyl, isopropyl, isobutyl, *tert.*-butyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); (C_{3-6})cycloalkyl-oxy (especially cyclopropyl-oxy); (C_{1-3})fluoroalkyl (especially trifluoromethyl); (C_{1-3})fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy); (C_{1-3})alkoxy-(C_{2-3})alkoxy (especially 2-methoxy-ethoxy); halogen; cyano; or -$NR^{21}R^{22}$, wherein R^{21} and R^{22} independently represent hydrogen, or (C_{1-3})alkyl (especially dimethylamino), or R^{21} and R^{22}, together with the nitrogen atom to which they are attached to, form a 4- to- 6 membered ring optionally mono- or di-substituted with fluoro, or a morpholinyl group (especially azetidinyl, pyrrolidinyl, 3-fluoro-pyrrolidinyl);

and

$(R^5)_m$ represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from (C_{1-4})alkyl (especially methyl, ethyl, isobutyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); halogen; cyano; (C_{1-3})fluoroalkyl (especially difluoromethyl, trifluoromethyl); and (C_{1-3})fluoroalkoxy (especially trifluoromethoxy, 2,2,2-trifluoroethoxy); [especially **$(R^5)_m$** is absent (i.e. m = 0), or **$(R^5)_m$** represents one halogen substituent; preferably **$(R^5)_m$** is absent].

The compounds of formula (I) may contain one or more stereogenic or asymmetric centers, such as one or more asymmetric carbon atoms. The compounds of formula (I) may thus be present as mixtures of stereoisomers or preferably as pure stereoisomers. Mixtures of stereoisomers may be separated in a manner known to a person skilled in the art.

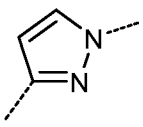
Furthermore, in some instances, the compounds of the present invention may be present in tautomeric forms. Any such tautomeric form is encompassed. For example, it is well understood that, in case a benzimidazole moiety is unsubstituted on the ring nitrogen having a free valency such benzimidazole moiety represents

tautomeric forms. Thus, further substituents of the benzimidazole moiety may be attached in the position(s) *ortho* to the bridgehead atoms (i.e. attached in position(s) 4 and/or 7), and/or in the position(s) *meta* to the bridgehead atoms, (i.e. attached in position(s) 5 and/or 6). It is understood that the two *ortho*, and, respectively, the two *meta* positions are considered equivalent. For example, the group 4-methyl-1H-benzoimidazol-2-yl is understood to signify the same group as 7-methyl-1H-benzoimidazol-2-yl and 4-methyl-3H-benzoimidazol-2-yl and 7-methyl-3H-benzoimidazol-2-yl.

The present invention also includes isotopically labelled, especially ^{2}H (deuterium) labelled compounds of formula (I) according to embodiments 1) to 29), which compounds are identical to the compounds of formula (I) except that one or more atoms have each been replaced by an atom having the same atomic number but an atomic mass different from the atomic mass usually found in nature. Isotopically labelled, especially ^{2}H (deuterium) labelled compounds of formula (I) and salts thereof are within the scope of the present invention. Substitution of hydrogen with the heavier isotope ^{2}H (deuterium) may lead to greater metabolic stability, resulting e.g. in increased *in-vivo* half-life or reduced dosage requirements, or may lead to reduced inhibition of cytochrome P450 enzymes, resulting e.g. in an improved safety profile. In one embodiment of the invention, the compounds of formula (I) are not isotopically labelled, or they are labelled only with one or more deuterium atoms. In a sub-embodiment, the compounds of formula (I) are not isotopically labelled at all. Isotopically labelled compounds of formula (I) may be prepared in analogy to the methods described hereinafter, but using the appropriate isotopic variation of suitable reagents or starting materials.

In this patent application, variably attached bonds may be used for substituents or groups (e.g. $(R^4)_n$ and $(R^5)_m$). In such case it is meant that any such substituent or group may be attached to any carbon atom of the ring system to which the variable attached bond is drawn into, provided that said carbon atom is not already substituted.

In this patent application, a bond drawn as a dotted line shows the point of attachment of the radical drawn. For example, the radical drawn below



is a 1*H*-pyrazol-1,3-diyl group.

Where the plural form is used for compounds, salts, pharmaceutical compositions, diseases and the like, this is intended to mean also a single compound, salt, pharmaceutical composition, disease or the like.

Any reference to compounds of formula (I) according to embodiments 1) to 31) is to be understood as referring also to the salts (and especially the pharmaceutically acceptable salts) of such compounds, as appropriate and expedient.

The term "pharmaceutically acceptable salts" refers to salts that retain the desired biological activity of the subject compound and exhibit minimal undesired toxicological effects. Such salts include inorganic or organic acid and/or base addition salts depending on the presence of basic and/or acidic groups in the subject compound. For reference see for example "Handbook of Pharmaceutical Salts. Properties, Selection and Use.", P. Heinrich Stahl, Camille G. Wermuth (Eds.), Wiley-VCH, 2008; and "Pharmaceutical Salts and Co-crystals", Johan Wouters and Luc Quéré (Eds.), RSC Publishing, 2012.

Definitions provided herein are intended to apply uniformly to the compounds of formula (I), as defined in any one of embodiments 1) to 29), and, *mutatis mutandis*, throughout the description and the claims unless an otherwise expressly set out definition provides a broader or narrower definition. It is well understood that a definition or preferred definition of a term defines and may replace the respective term independently of (and in combination with) any definition or preferred definition of any or all other terms as defined herein.

The term "halogen" means fluorine, chlorine, bromine, or iodine, preferably fluorine or chlorine, especially fluorine.

The term "cyano" refers to a group -CN.

The term "alkyl", used alone or in combination, refers to a saturated straight or branched chain hydrocarbon group containing one to six (especially one to four) carbon atoms. The term "(C_{x-y})alkyl" (x and y each being an integer), refers to an alkyl group as defined before, containing x to y carbon atoms. In case a (C_{1-y})alkyl group (or, in general, a (C_{x-y})alkyl group) is used in combination with another substituent, the term means that said substituent is linked through a (C_{1-y})alkyl group (or a (C_{x-y})alkyl group, respectively) to the rest of the molecule. In some instances such group is also referred to as (C_{1-y})alkylene. For example a (C_{1-6})alkyl group contains from one to six carbon atoms. Examples of (C_{1-6})alkyl groups are the (C_{1-4})alkyl groups methyl, ethyl, n-propyl, isopropyl, n-butyl, sec.-butyl, tert.-butyl, and isobutyl, as well as n-pentyl, and isopentyl. Preferred are methyl, ethyl, n-propyl, and isopropyl. Most preferred is methyl. For the substituent $\mathbf{R^1}$ preferred examples of (C_{2-6})alkyl are isopropyl, *tert.*-butyl, and isobutyl; especially *tert.*-butyl.

Examples of (C_{2-4})alkyl groups which are mono-substituted with cyano, or (C_{1-3})alkoxy as used for $\mathbf{R^1}$ are 1-methoxy-ethyl, and 1-cyano-1-methyl-ethyl.

The term "alkoxy" means a group of the formula alkyl-O- in which the term alkyl has the previously given significance. The term "(C_{x-y})alkoxy" (x and y being an integer) refers to a straight or branched chain alkoxy group containing x to y carbon atoms. Examples of alkoxy groups are the (C_{1-4})alkoxy groups methoxy, ethoxy, *n*-propoxy, isopropoxy, *n*-butoxy, isobutoxy, *sec*-butoxy and tert.-butoxy. Preferred is methoxy.

The term "fluoroalkyl" refers to an alkyl group as defined before containing one to three carbon atoms in which one or more (and possibly all) hydrogen atoms have been replaced with fluorine. The term "(C_{x-y})fluoroalkyl" (x and y each being an integer) refers to a fluoroalkyl group as defined before containing x to y carbon atoms. For example a (C_{1-3})fluoroalkyl group contains from one to three carbon atoms in which one to seven

hydrogen atoms have been replaced with fluorine. A preferred example is trifluoromethyl. Examples of (C_{2-3})fluoroalkyl groups include 2-fluoroethyl, 2,2-difluoroethyl and 2,2,2-trifluoroethyl (especially 2-fluoroethyl and 2,2,2-trifluoroethyl). In the specific case of (C_{1-4})fluoroalkyl groups, the fluoroalkyl group contains from one to four carbon atoms in which one to nine hydrogen atoms have been replaced with fluorine. Examples of (C_{1-4})fluoroalkyl groups as used for **R¹** include trifluoromethyl, 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, and 2,2,2-trifluoro-1,1-dimethyl-ethyl; especially trifluoromethyl, and 2,2,2-trifluoro-1,1-dimethyl-ethyl.

The term "fluoroalkoxy" refers to an alkoxy group as defined before containing one to three carbon atoms in which one or more (and possibly all) hydrogen atoms have been replaced with fluorine. The term "(C_{x-y})fluoroalkoxy" (x and y each being an integer) refers to a fluoroalkoxy group as defined before containing x to y carbon atoms. For example a (C_{1-3})fluoroalkoxy group contains from one to three carbon atoms in which one to seven hydrogen atoms have been replaced with fluorine. Preferred examples are trifluoromethoxy, difluoromethoxy and 2,2,2-trifluoroethoxy. Representative examples of fluoroalkoxy groups as used for **R¹** include trifluoromethoxy, difluoromethoxy, 2-fluoroethoxy, 2,2-difluoroethoxy and 2,2,2-trifluoroethoxy; especially 2,2,2-trifluoroethoxy. An additional example of (C_{1-3})fluoroalkoxy groups as used for **R¹** is 3,3,3-trifluoropropoxy.

The term "cycloalkyl" refers to a saturated mono- or bicyclic carbocyclic ring containing three to eight carbon atoms. The term "(C_{x-y})cycloalkyl" (x and y each being an integer), refers to a cycloalkyl group as defined before containing x to y carbon atoms. For example a (C_{3-6})cycloalkyl group refers to a saturated monocyclic carbocyclic ring containing three to six carbon atoms. Examples of cycloalkyl groups are cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl. Preferred is cyclopropyl.

The term "(C_{3-6})cycloalkyl, wherein the cycloalkyl may optionally contain a ring oxygen atom", refers to a monocyclic cycloalkyl group as defined before. In addition, one ring carbon atom of said cycloalkyl may be replaced by an oxygen atom. For the substituent **R¹**, examples of such groups are especially cyclopropyl, cyclobutyl, and, in addition, oxetan-3-yl. Said groups are unsubstituted or substituted as explicitly defined.

The term "(C_{3-6})cycloalkyl-(C_{1-3})alkyl" refers to a (C_{3-6})cycloalkyl group as explicitly defined which group is linked to the rest of the molecule through a (C_{1-3})alkylene group as defined before. For the substituent **R¹**, the (C_{1-2})alkylene group part of (C_{3-6})cycloalkyl-(C_{1-2})alkyl is in particular a methylene group.

The term "(C_{3-6})cycloalkyl-oxy" refers to a (C_{3-6})cycloalkyl group as explicitly defined which is linked to the rest of the molecule through an oxygen atom.

The term "(C_{3-6})cycloalkyl-(C_{1-2})alkylene-oxy" refers to a (C_{3-6})cycloalkyl group as explicitly defined which is linked to the rest of the molecule through a $-(CH_2)_{1-2}$-O- group. For the substituent **R¹**, the -(C_{1-2})alkylene-oxy group part of (C_{3-6})cycloalkyl-(C_{1-2})alkylene-oxy is in particular a $-CH_2$-O- group.

The term "(C_{1-3})alkoxy-(C_{2-3})alkoxy" refers to a (C_{1-3})alkoxy-group as defined before which is attached to the rest of the molecule through a (C_{2-3})alkoxy group as defined before. An example is 2-methoxy-ethoxy.

The term "(C_{1-3})alkoxy-(C_{2-3})alkyl" means a (C_{1-3})alkoxy-group as defined before which is attached to the rest of the molecule through a (C_{2-3})alkylene group as defined before. An example is 2-methoxy-ethyl.

The term "aryl", used alone or in combination, means phenyl or naphthyl, preferably phenyl. Likewise, an arylene group is an aryl group as defined before having two points of attachment to the respective rests of the molecule. The above-mentioned aryl / arylene groups are unsubstituted or substituted as explicitly defined.

The term "heteroaryl", used alone or in combination, means a 5- to 10-membered monocyclic or bicyclic aromatic ring containing one to a maximum of four heteroatoms, each independently selected from oxygen, nitrogen and sulfur. Examples of such heteroaryl groups are 5-membered heteroaryl such as furanyl, oxazolyl, isoxazolyl, oxadiazolyl, thiophenyl, thiazolyl, isothiazolyl, thiadiazolyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl; 6-membered heteroaryl such as pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl; and bicyclic heteroaryl such as indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzothiophenyl, indazolyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzoisothiazolyl, benzotriazolyl, benzoxadiazolyl, benzothiadiazolyl, quinolinyl, isoquinolinyl, naphthyridinyl, cinnolinyl, quinazolinyl, quinoxalinyl, phthalazinyl, pyrrolopyridinyl, pyrazolopyridinyl, pyrazolopyrimidinyl, pyrrolopyrazinyl, imidazopyridinyl, imidazopyridazinyl, and imidazothiazolyl. Examples of heteroaryl groups as used for **R^1** are especially oxadiazolyl, pyrazinyl, pyrimidinyl, and pyridinyl. The above-mentioned heteroaryl groups are unsubstituted or substituted as explicitly defined.

In case two substituents form an aromatic 5- or 6-membered ring optionally containing one or two nitrogen atoms which ring is fused to a phenyl / pyridine ring, examples of such thus formed bicyclic heteroaryl rings are pyrrolo[2,3-b]pyridinyl, indolyl, indazolyl, quinoxalinyl, benzoimidazolyl, and quinolinyl. The above-mentioned groups do not carry further substituents on the phenyl / pyridine part of the ring, whereas said aromatic 5- or 6-membered ring may be unsubstituted or substituted as explicitly defined.

In case two substituents form a non-aromatic 5- or 6-membered ring optionally containing one or two heteroatoms, which ring is fused to a phenyl / pyridine ring, examples of such thus formed bicyclic partially aromatic rings are 2,3-dihydro-benzooxazolyl, 3,4-dihydro-2H-benzo[1,4]oxazinyl, 2,3-dihydro-1H-indolyl, and 2,3-dihydro-benzofuranyl. A further example is chromanyl. The above-mentioned groups do not carry further substituents on the phenyl / pyridine part of the ring, whereas said non-aromatic 5- or 6-membered ring may be unsubstituted or substituted as explicitly defined.

Examples of -$NR^{11}R^{12}$ groups as used for **R^1** are especially disubstituted amino groups wherein one substituent is methyl or ethyl, and the other is (C_{1-3})alkyl, (C_{2-3})fluoroalkyl, (C_{3-6})cycloalkyl, (C_{3-6})cycloalkyl mono- or di-substituted with fluoro, (C_{3-6})cycloalkyl-(C_{1-3})alkyl, (C_{1-3})alkoxy-(C_{2-3})alkyl. Examples are dimethylamino, ethyl-methyl-amino, diethylamino, cyclopropyl-methyl-amino, (2-methoxyethyl)-methyl-amino, (cyclopropylmethyl)-methyl-amino, and (2,2-difluoro-ethyl)-methyl-amino. Examples of –$NR^{11}R^{12}$ groups wherein R^{11} and R^{12}, together with the nitrogen atom to which they are attached to, form a 4- to- 6 membered

ring as used for **R1** are especially the four and five-membered rings azetidinyl, 3-fluoro-azetidinyl, 3,3-difluoro-azetidinyl, pyrrolidinyl, 3-fluoro-pyrrolidinyl, 3,3-difluoro-pyrrolidinyl.

An example of -$NR^{21}R^{22}$ groups as used for **R2** is dimethylamino. An example of –$NR^{21}R^{22}$ groups wherein R^{21} and R^{22}, together with the nitrogen atom to which they are attached to, form a 4- to- 6 membered ring as used for **R2** is 3-fluoro-pyrrolidinyl. Further examples are azetidinyl and pyrrolidinyl.

Further embodiments of the invention are presented hereinafter:

2) A second embodiment relates to compounds according to embodiment 1), wherein
X represents a ring carbon or a ring nitrogen atom;

- **R1** represents
  - (C_{2-6})alkyl [in particular isopropyl, *tert.*-butyl, or isobutyl];
  - (C_{2-4})alkyl mono-substituted with cyano, or (C_{1-3})alkoxy (especially methoxy); [in particular such group is 1-methoxy-ethyl, or 1-cyano-1-methyl-ethyl];
  - (C_{1-4})fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
  - (C_{1-3})fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
  - pentafluoro-sulfanyl;
  - (C_{3-6})cycloalkyl-**L1**- wherein
    - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C_{1-3})alkyl (especially methyl), (C_{1-3})alkoxy (especially methoxy), hydroxy, cyano, or (C_{1-3})fluoroalkyl (especially trifluoromethyl), or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a (C_{1-3})alkyl (especially methyl) substituent; and
    - the linker **L1** represents a direct bond, (C_{1-2})alkylene, oxygen, or (C_{1-2})alkylene-oxy (which is attached to the rest of the molecule through the oxygen atom);
      [in particular such group (C_{3-6})cycloalkyl-**L1**- is cyclopropyl, 3-fluoro-oxetan-3-yl, 3-methoxy-oxetan-3-yl, 3-methyl-oxetan-3-yl, 3,3-difluoro-cyclobutyl, 1-trifluoromethyl-cyclopropyl, 2-trifluoromethyl-cyclopropyl, 1-methyl-cyclopropyl, 1-cyano-cyclopropyl, 1-hydroxy-cyclopropyl, 1-cyano-cyclopropyl, or 3-hydroxy-oxetan-3-yl; or it is cyclopropyl-methyl; or it is cyclopropyl-oxy, oxetan-3-yl-oxy, cyclobutyl-oxy, or 3,3-difluoro-cyclobutyl-oxy; or it is oxetan-3-yl-methoxy, (3-fluoro-oxetan-3-yl)-methoxy, (3,3-difluoro-cyclobutyl)-methoxy, (3-methyl-oxetan-3-yl)-methoxy, or (3,3-difluoro-1-methyl-cyclobutyl)-methoxy];
  - 5- or 6-membered heteroaryl, independently optionally mono-substituted with (C_{1-3})alkyl (especially methyl); [in particular oxadiazolyl, pyrazinyl, pyrimidinyl, or pyridinyl];
  - -$NR^{11}R^{12}$, wherein

- R^{11} and R^{12} independently represent hydrogen, (C_{1-3})alkyl, (C_{2-3})fluoroalkyl, (C_{3-6})cycloalkyl, (C_{3-6})cycloalkyl mono- or di-substituted with fluoro, (C_{3-6})cycloalkyl-(C_{1-3})alkyl, (C_{1-3})alkoxy-(C_{2-3})alkyl [in particular such group $-NR^{11}R^{12}$ is dimethylamino, ethyl-methyl-amino, diethylamino, cyclopropyl-methyl-amino, (2-methoxyethyl)-methyl-amino, (cyclopropylmethyl)-methyl-amino, or (2,2-difluoro-ethyl)-methyl-amino];
- or R^{11} and R^{12}, together with the nitrogen atom to which they are attached to, form a 4- to- 6 membered ring optionally mono- or di-substituted with fluoro; a 2-oxo-pyrrolidinyl group; or a morpholinyl group [in particular such group $-NR^{11}R^{12}$ is azetidinyl, 3-fluoro-azetidinyl, 3,3-difluoro-azetidinyl, pyrrolidinyl, 3-fluoro-pyrrolidinyl, 3,3-difluoro-pyrrolidinyl, or 2-oxo-pyrrolidinyl];

and $\mathbf{(R^4)_n}$ represents one or two optional substituents (i.e. n represents the integer 0, 1, or 2) independently selected from (C_{1-4})alkyl (especially methyl), (C_{1-4})alkoxy (especially methoxy), (C_{1-3})fluoroalkyl (especially trifluoromethyl), (C_{1-3})fluoroalkoxy (especially trifluoromethoxy), halogen (especially fluoro), and cyano [especially $\mathbf{(R^4)_n}$ is absent (i.e. n = 0); or $\mathbf{(R^4)_n}$ represents one halogen or methyl substituent];

- or $\mathbf{R^1}$ together with $\mathbf{(R^4)_n}$ forms a non-aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring; wherein said 5- or 6-membered ring optionally contains one or two heteroatoms independently selected from oxygen and nitrogen; wherein said fused 5- or 6-membered non-aromatic ring independently is optionally further mono-substituted with oxo; or di-, tri-, or tetra-substituted wherein one substituent is oxo and the remaining are (C_{1-3})alkyl (especially methyl); [in particular such non-aromatic 5- or 6-membered ring fused to the phenyl / pyridine ring forms, together with the phenyl / pyridine ring, a group selected from 2-oxo-2,3-dihydro-benzooxazol-6-yl, 3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl, 4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl, 3-methyl-2-oxo-2,3-dihydro-benzooxazol-6-yl, 3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl, 1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl, 2,2-dimethyl-2,3-dihydro-benzofuran-6-yl, 2,2-dimethyl-2,3-dihydro-benzofuran-5-yl, or 3,3-dimethyl-2,3-dihydro-benzofuran-5-yl];

- or $\mathbf{R^1}$ together with $\mathbf{(R^4)_n}$ forms an aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring; wherein said 5- or 6-membered ring optionally contains one or two heteroatoms selected from nitrogen, wherein said fused 5- or 6-membered aromatic ring independently is optionally further mono- or di-substituted wherein the substituents are independently selected from (C_{1-3})alkyl (especially methyl, isopropyl), (C_{3-6})cycloalkyl (especially cyclobutyl), (C_1)fluoroalkyl (especially trifluoromethyl), or cyano [in particular such aromatic 5- or 6-membered ring fused to the phenyl / pyridine ring forms, together with the phenyl / pyridine ring, a group selected from 1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl, 1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl, 1H-indol-5-yl, 1H-indol-6-yl, 1-methyl-1H-indazol-5-yl, 1-methyl-1H-indazol-6-yl, 1-ethyl-1H-indazol-5-yl, 1-ethyl-1H-indazol-6-yl, 1,3-dimethyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 1,3-dimethyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-6-yl, 3-cyano-1-methyl-1H-indol-5-

yl, 3-isopropyl-1-methyl-1H-indol-5-yl, 3-cyclobutyl-1-methyl-1H-indol-5-yl, 1-methyl-3-trifluoromethyl-1H-indol-5-yl, quinoxalin-6-yl, 2-methyl-1H-benzoimidazol-6-yl, 1-methyl-1H-benzoimidazol-5-yl, 1-methyl-1H-benzoimidazol-6-yl, or quinolin-7-yl];

- or **R**^{1} represents methyl, or halogen (especially fluoro); and **(R**^{4}**)**$_{n}$ represents one substituent selected from (C_{1-3})fluoroalkoxy (especially 2,2,2-trifluoroethoxy) which is attached to the phenyl / pyridinyl ring in *ortho* or *meta*-position to the point of attachment of the –CH_2-CO-NH- group;

Y represents a ring carbon or a ring nitrogen atom; and

R^{2} represents (C_{1-4})alkyl (especially methyl, ethyl, isopropyl, isobutyl, *tert.*-butyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); (C_{3-6})cycloalkyl-oxy (especially cyclopropyl-oxy); (C_{1-3})fluoroalkyl (especially trifluoromethyl); (C_{1-3})fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy); (C_{1-3})alkoxy-(C_{2-3})alkoxy (especially 2-methoxy-ethoxy); halogen; cyano; or -$NR^{21}R^{22}$, wherein R^{21} and R^{22} independently represent hydrogen, or (C_{1-3})alkyl (especially dimethylamino), or R^{21} and R^{22}, together with the nitrogen atom to which they are attached to, form a 4- to- 6 membered ring optionally mono- or di-substituted with fluoro, or a morpholinyl group (especially 3-fluoro-pyrrolidinyl);

and

(R^{5}**)**$_{m}$ represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from (C_{1-4})alkyl (especially methyl, ethyl, isobutyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); halogen; cyano; (C_{1-3})fluoroalkyl (especially trifluoromethyl); and (C_{1-3})fluoroalkoxy (especially trifluoromethoxy, 2,2,2-trifluoroethoxy); [especially **(R**^{5}**)**$_{m}$ is absent (i.e. m = 0), or **(R**^{5}**)**$_{m}$ represents one halogen substituent; preferably **(R**^{5}**)**$_{m}$ is absent].

3) Another embodiment relates to compounds according to any one of embodiments 1) or 2), wherein
X represents a ring carbon atom.

4) Another embodiment relates to compounds according to any one of embodiments 1) or 2), wherein
X represents a ring nitrogen atom.

5) Another embodiment relates to compounds according to any one of embodiments 1) to 4), wherein **R**^{1} represents

- (C_{2-6})alkyl [in particular isopropyl, *tert.*-butyl, or isobutyl];
- (C_{2-4})alkyl mono-substituted with cyano, or (C_{1-3})alkoxy (especially methoxy); [in particular such group is 1-methoxy-ethyl, or 1-cyano-1-methyl-ethyl];
- (C_{1-4})fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
- (C_{1-3})fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
- pentafluoro-sulfanyl;
- (C_{3-6})cycloalkyl-**L**^{1}- wherein

- said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C_{1-3})alkyl (especially methyl), (C_{1-3})alkoxy (especially methoxy), hydroxy, cyano, or (C_{1-3})fluoroalkyl (especially trifluoromethyl), or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a (C_{1-3})alkyl (especially methyl) substituent; and
- the linker **L**^{1} represents a direct bond, (C_{1-2})alkylene, oxygen, or (C_{1-2})alkylene-oxy (which is attached to the rest of the molecule through the oxygen atom);
  [in particular such group (C_{3-6})cycloalkyl-**L**^{1}- is cyclopropyl, 3-fluoro-oxetan-3-yl, 3-methoxy-oxetan-3-yl, 3-methyl-oxetan-3-yl, 3,3-difluoro-cyclobutyl, 1-trifluoromethyl-cyclopropyl, 2-trifluoromethyl-cyclopropyl, 1-methyl-cyclopropyl, 1-hydroxy-cyclopropyl, 1-cyano-cyclopropyl, or 3-hydroxy-oxetan-3-yl; or it is cyclopropyl-methyl; or it is cyclopropyl-oxy, oxetan-3-yl-oxy, cyclobutyl-oxy, or 3,3-difluoro-cyclobutyl-oxy; or it is oxetan-3-yl-methoxy, (3-fluoro-oxetan-3-yl)-methoxy, (3,3-difluoro-cyclobutyl)-methoxy, (3-methyl-oxetan-3-yl)-methoxy, or (3,3-difluoro-1-methyl-cyclobutyl)-methoxy];

➢ 5- or 6-membered heteroaryl selected from oxadiazolyl, pyrazinyl, pyrimidinyl, and pyridinyl; wherein said heteroaryl independently is optionally mono-substituted with (C_{1-3})alkyl (especially methyl); or

➢ -$NR^{11}R^{12}$, wherein

- R^{11} and R^{12} independently represent hydrogen, (C_{1-3})alkyl, (C_{2-3})fluoroalkyl, (C_{3-6})cycloalkyl, (C_{3-6})cycloalkyl mono- or di-substituted with fluoro, (C_{3-6})cycloalkyl-(C_{1-3})alkyl, (C_{1-3})alkoxy-(C_{2-3})alkyl [in particular such group -$NR^{11}R^{12}$ is dimethylamino, ethyl-methyl-amino, diethylamino, cyclopropyl-methyl-amino, (2-methoxyethyl)-methyl-amino, (cyclopropylmethyl)-methyl-amino, or (2,2-difluoro-ethyl)-methyl-amino];
- or R^{11} and R^{12}, together with the nitrogen atom to which they are attached to, form an azetidinyl or a pyrrolidinyl ring, both independently optionally mono- or di-substituted with fluoro; or a 2-oxo-pyrrolidinyl group;[in particular such group -$NR^{11}R^{12}$ is azetidinyl, 3-fluoro-azetidinyl, 3,3-difluoro-azetidinyl, pyrrolidinyl, 3-fluoro-pyrrolidinyl, 3,3-difluoro-pyrrolidinyl, or 2-oxo-pyrrolidinyl];

and **(R**^{4}**)**$_n$ represents one optional substituent (i.e. n represents the integer 0, or 1) selected from (C_{1-4})alkyl (especially methyl), (C_{1-4})alkoxy (especially methoxy), (C_{1-3})fluoroalkyl (especially trifluoromethyl), (C_{1-3})fluoroalkoxy (especially trifluoromethoxy), halogen (especially fluoro), and cyano [especially **(R**^{4}**)**$_n$ is absent (i.e. n = 0); or **(R**^{4}**)**$_n$ represents one halogen or methyl substituent];

- or **R**^{1} together with **(R**^{4}**)**$_n$ forms a non-aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring to form a bicyclic ring system; wherein said bicyclic ring system is selected from 2,3-dihydro-benzooxazolyl, 3,4-dihydro-2H-benzo[1,4]oxazinyl, 2,3-dihydro-1H-indolyl, and 2,3-dihydro-benzofuranyl; wherein said non-aromatic 5- or 6-membered ring part of said bicyclic ring system independently is

optionally further mono-substituted with oxo; or di-, tri-, or tetra-substituted wherein one substituent is oxo and the remaining are (C_{1-3})alkyl (especially methyl); [in particular such bicyclic ring system is a group selected from 2-oxo-2,3-dihydro-benzooxazol-6-yl, 3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl, 4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl, 3-methyl-2-oxo-2,3-dihydro-benzooxazol-6-yl, 3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl, 1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl, or 2,2-dimethyl-2,3-dihydro-benzofuran-6-yl, 2,2-dimethyl-2,3-dihydro-benzofuran-5-yl, or 3,3-dimethyl-2,3-dihydro-benzofuran-5-yl];

- or **R¹** together with **$(R^4)_n$** forms an aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring to form a bicyclic aromatic ring system selected from pyrrolo[2,3-b]pyridinyl, indolyl, indazolyl, quinoxalinyl, benzoimidazolyl, and quinolinyl (especially indolyl or indazolyl); wherein said fused 5- or 6-membered aromatic ring part of said aromatic bicyclic ring system independently is optionally further mono- or di-substituted wherein the substituents are independently selected from (C_{1-3})alkyl (especially methyl, isopropyl), (C_{3-6})cycloalkyl (especially cyclobutyl), (C_1)fluoroalkyl (especially trifluoromethyl), or cyano [in particular such aromatic part of said aromatic bicyclic ring system is a group selected from 1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl, 1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl, 1H-indol-5-yl, 1H-indol-6-yl, 1-methyl-1H-indazol-5-yl, 1-methyl-1H-indazol-6-yl, 1-ethyl-1H-indazol-5-yl, 1-ethyl-1H-indazol-6-yl, 1,3-dimethyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 1,3-dimethyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-6-yl, 3-cyano-1-methyl-1H-indol-5-yl, 3-isopropyl-1-methyl-1H-indol-5-yl, 3-cyclobutyl-1-methyl-1H-indol-5-yl, 1-methyl-3-trifluoromethyl-1H-indol-5-yl, quinoxalin-6-yl, 2-methyl-1H-benzoimidazol-6-yl, 1-methyl-1H-benzoimidazol-5-yl, 1-methyl-1H-benzoimidazol-6-yl, or quinolin-7-yl];

- or **R¹** represents methyl, or halogen (especially fluoro); and **$(R^4)_n$** represents one substituent selected from (C_{1-3})fluoroalkoxy (especially 2,2,2-trifluoroethoxy) which is attached to the phenyl / pyridinyl ring in *ortho* or *meta*-position to the point of attachment of the –CH_2-CO-NH- group.

6) Another embodiment relates to compounds according to any one of embodiments 1) to 4), wherein **R¹** represents

- (C_{2-6})alkyl [in particular isopropyl, *tert.*-butyl, or isobutyl];
- (C_{2-4})alkyl mono-substituted with cyano, or (C_{1-3})alkoxy (especially methoxy); [in particular such group is 1-methoxy-ethyl, or 1-cyano-1-methyl-ethyl];
- (C_{1-4})fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
- (C_{1-3})fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
- pentafluoro-sulfanyl;
- (C_{3-6})cycloalkyl-**L^1**- wherein
  - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C_{1-3})alkyl (especially methyl), (C_{1-3})alkoxy (especially methoxy), hydroxy, cyano, or (C_{1-3})fluoroalkyl

(especially trifluoromethyl), or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a (C_{1-3})alkyl (especially methyl) substituent; and

- the linker **L^1** represents a direct bond, (C_{1-2})alkylene, oxygen, or (C_{1-2})alkylene-oxy (which is attached to the rest of the molecule through the oxygen atom);

  [in particular such group (C_{3-6})cycloalkyl-**L^1**- is cyclopropyl, 3-fluoro-oxetan-3-yl, 3-methoxy-oxetan-3-yl, 3-methyl-oxetan-3-yl, 3,3-difluoro-cyclobutyl, 1-trifluoromethyl-cyclopropyl, 2-trifluoromethyl-cyclopropyl, 1-methyl-cyclopropyl, 1-hydroxy-cyclopropyl, 1-cyano-cyclopropyl, or 3-hydroxy-oxetan-3-yl; or it is cyclopropyl-methyl; or it is cyclopropyl-oxy, oxetan-3-yl-oxy, cyclobutyl-oxy, or 3,3-difluoro-cyclobutyl-oxy; or it is oxetan-3-yl-methoxy, (3-fluoro-oxetan-3-yl)-methoxy, (3,3-difluoro-cyclobutyl)-methoxy, (3-methyl-oxetan-3-yl)-methoxy, or (3,3-difluoro-1-methyl-cyclobutyl)-methoxy];

- 5- or 6-membered heteroaryl selected from oxadiazolyl, pyrazinyl, pyrimidinyl, and pyridinyl; wherein said heteroaryl independently is optionally mono-substituted with (C_{1-3})alkyl (especially methyl); or
- -$NR^{11}R^{12}$, wherein
  - R^{11} and R^{12} independently represent (C_{1-3})alkyl, (C_{2-3})fluoroalkyl, (C_{3-6})cycloalkyl, (C_{3-6})cycloalkyl mono- or di-substituted with fluoro, (C_{3-6})cycloalkyl-(C_{1-3})alkyl, (C_{1-3})alkoxy-(C_{2-3})alkyl [in particular such group -$NR^{11}R^{12}$ is dimethylamino, ethyl-methyl-amino, diethylamino, cyclopropyl-methyl-amino, (2-methoxyethyl)-methyl-amino, (cyclopropylmethyl)-methyl-amino, or (2,2-difluoro-ethyl)-methyl-amino];
  - or R^{11} and R^{12}, together with the nitrogen atom to which they are attached to, form an azetidinyl or a pyrrolidinyl ring, both independently optionally mono- or di-substituted with fluoro; [in particular such group -$NR^{11}R^{12}$ is azetidinyl, 3-fluoro-azetidinyl, 3,3-difluoro-azetidinyl, pyrrolidinyl, 3-fluoro-pyrrolidinyl, or 3,3-difluoro-pyrrolidinyl];

and **$(R^4)_n$** represents one optional substituent (i.e. n represents the integer 0, or 1) selected from (C_{1-4})alkyl (especially methyl), (C_{1-4})alkoxy (especially methoxy), (C_{1-3})fluoroalkyl (especially trifluoromethyl), (C_{1-3})fluoroalkoxy (especially trifluoromethoxy), halogen (especially fluoro), and cyano [especially **$(R^4)_n$** is absent (i.e. n = 0); or **$(R^4)_n$** represents one halogen or methyl substituent].

7) Another embodiment relates to compounds according to any one of embodiments 1) to 4), wherein **R^1** represents

- (C_{2-6})alkyl [in particular isopropyl, *tert.*-butyl, or isobutyl];
- (C_{1-4})fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
- (C_{1-3})fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
- (C_{3-6})cycloalkyl-**L^1**- wherein
  - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C_{1-3})alkyl (especially

methyl), (C_{1-3})alkoxy (especially methoxy), hydroxy, cyano, or (C_{1-3})fluoroalkyl (especially trifluoromethyl), or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a (C_{1-3})alkyl (especially methyl) substituent; and

- the linker **L**[1] represents a direct bond, (C_{1-2})alkylene, oxygen, or (C_{1-2})alkylene-oxy (which is attached to the rest of the molecule through the oxygen atom);
  [in particular such group (C_{3-6})cycloalkyl-**L**[1]- is cyclopropyl, 3-fluoro-oxetan-3-yl, 3-methoxy-oxetan-3-yl, 3-methyl-oxetan-3-yl, 3,3-difluoro-cyclobutyl, 1-trifluoromethyl-cyclopropyl, 2-trifluoromethyl-cyclopropyl, 1-methyl-cyclopropyl, 1-hydroxy-cyclopropyl, 1-cyano-cyclopropyl, or 3-hydroxy-oxetan-3-yl; or it is cyclopropyl-methyl; or it is cyclopropyl-oxy, oxetan-3-yl-oxy, cyclobutyl-oxy, or 3,3-difluoro-cyclobutyl-oxy; or it is oxetan-3-yl-methoxy, (3-fluoro-oxetan-3-yl)-methoxy, (3,3-difluoro-cyclobutyl)-methoxy, (3-methyl-oxetan-3-yl)-methoxy, or (3,3-difluoro-1-methyl-cyclobutyl)-methoxy];

- 5- or 6-membered heteroaryl selected from oxadiazolyl, pyrazinyl, pyrimidinyl, and pyridinyl (especially oxadiazolyl, pyridinyl); wherein said heteroaryl independently is optionally mono-substituted with (C_{1-3})alkyl (especially methyl); or
- -$NR^{11}R^{12}$, wherein
  - R^{11} and R^{12}, together with the nitrogen atom to which they are attached to, form an azetidinyl or a pyrrolidinyl ring, both independently optionally mono- or di-substituted with fluoro; [in particular azetidinyl, 3-fluoro-azetidinyl, 3,3-difluoro-azetidinyl, pyrrolidinyl, 3-fluoro-pyrrolidinyl, or 3,3-difluoro-pyrrolidinyl];

and $(\mathbf{R^4})_n$ represents one optional substituent (i.e. n represents the integer 0, or 1) selected from (C_{1-4})alkyl (especially methyl), (C_{1-4})alkoxy (especially methoxy), (C_{1-3})fluoroalkyl (especially trifluoromethyl), (C_{1-3})fluoroalkoxy (especially trifluoromethoxy), halogen (especially fluoro), and cyano [especially $(\mathbf{R^4})_n$ is absent (i.e. n = 0); or $(\mathbf{R^4})_n$ represents one halogen or methyl substituent].

8) Another embodiment relates to compounds according to any one of embodiments 1) to 4), wherein **R**[1] represents

- (C_{2-6})alkyl [in particular isopropyl, *tert.*-butyl, or isobutyl];
- (C_{1-4})fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
- (C_{1-3})fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
- (C_{3-6})cycloalkyl wherein
  - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C_{1-3})alkyl (especially methyl), (C_{1-3})alkoxy (especially methoxy), hydroxy, cyano, or (C_{1-3})fluoroalkyl (especially trifluoromethyl), or di-substituted with fluoro; [in particular cyclopropyl, 3-fluoro-oxetan-3-yl, 3-methoxy-oxetan-3-yl, 3-methyl-oxetan-3-yl, 3,3-difluoro-cyclobutyl,

1-trifluoromethyl-cyclopropyl, 2-trifluoromethyl-cyclopropyl, 1-methyl-cyclopropyl, 1-hydroxy-cyclopropyl, 1-cyano-cyclopropyl, or 3-hydroxy-oxetan-3-yl];

- (C_{3-6})cycloalkyl-(C_{1-2})alkylene- [in particular cyclopropyl-methyl];
- (C_{3-6})cycloalkyl-oxy- wherein
  - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono- or di-substituted with fluoro; [in particular cyclopropyl-oxy, oxetan-3-yl-oxy, cyclobutyl-oxy, or 3,3-difluoro-cyclobutyl-oxy];
- (C_{3-6})cycloalkyl-(C_{1-2})alkylene-oxy- wherein
  - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono-substituted with fluoro, or (C_{1-3})alkyl (especially methyl), or di-substituted with fluoro; [in particular oxetan-3-yl-methoxy, (3-fluoro-oxetan-3-yl)-methoxy, (3,3-difluoro-cyclobutyl)-methoxy, or (3-methyl-oxetan-3-yl)-methoxy];
- 5- or 6-membered heteroaryl selected from oxadiazolyl, pyrazinyl, pyrimidinyl, and pyridinyl (especially oxadiazolyl, pyridinyl); wherein said heteroaryl independently is optionally mono-substituted with (C_{1-3})alkyl (especially methyl); or
- $-NR^{11}R^{12}$, wherein
  - R^{11} and R^{12}, together with the nitrogen atom to which they are attached to, form a pyrrolidinyl ring optionally mono- or di-substituted with fluoro [in particular pyrrolidinyl, 3-fluoro-pyrrolidinyl, 3,3-difluoro-pyrrolidinyl];

and $\mathbf{(R^4)_n}$ represents one optional substituent (i.e. n represents the integer 0, or 1) selected from (C_{1-4})alkyl (especially methyl), (C_{1-4})alkoxy (especially methoxy), (C_{1-3})fluoroalkyl (especially trifluoromethyl), (C_{1-3})fluoroalkoxy (especially trifluoromethoxy), halogen (especially fluoro), and cyano [especially $\mathbf{(R^4)_n}$ is absent (i.e. n = 0); or $\mathbf{(R^4)_n}$ represents one halogen or methyl substituent].

9) Another embodiment relates to compounds according to any one of embodiments 1) to 4), wherein $\mathbf{R^1}$ represents

- (C_{2-6})alkyl [in particular isopropyl, *tert.*-butyl, or isobutyl, preferably *tert.*-butyl];
- (C_{1-4})fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl; preferably 2,2,2-trifluoro-1,1-dimethyl-ethyl];
- (C_{1-3})fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
- (C_{3-6})cycloalkyl wherein
  - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is mono-substituted with fluoro or (C_{1-3})fluoroalkyl (especially trifluoromethyl), or di-substituted with fluoro; [in particular 3-fluoro-oxetan-3-yl, 3,3-difluoro-cyclobutyl, 1-trifluoromethyl-cyclopropyl, or 2-trifluoromethyl-cyclopropyl,;

especially 3-fluoro-oxetan-3-yl, 3,3-difluoro-cyclobutyl, or 1-trifluoromethyl-cyclopropyl; preferably 1-trifluoromethyl-cyclopropyl]; or

- (C_{3-6})cycloalkyl-oxy- wherein
  - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or di-substituted with fluoro; [in particular cyclopropyl-oxy, oxetan-3-yl-oxy, cyclobutyl-oxy, or 3,3-difluoro-cyclobutyl-oxy, especially 3,3-difluoro-cyclobutyl-oxy];

and $(R^4)_n$ represents one optional substituent (i.e. n represents the integer 0, or 1) selected from (C_{1-4})alkyl (especially methyl), or halogen (especially fluoro) [especially $(R^4)_n$ is absent (i.e. n = 0); or $(R^4)_n$ represents one halogen or methyl substituent].

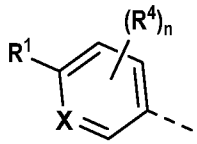
10) Another embodiment relates to compounds according to any one of embodiments 1) to 4), wherein

- R^1 together with $(R^4)_n$ forms a non-aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring to form a bicyclic ring system; wherein said bicyclic ring system is selected from 2,3-dihydro-benzooxazolyl, 3,4-dihydro-2H-benzo[1,4]oxazinyl, 2,3-dihydro-1H-indolyl, and 2,3-dihydro-benzofuranyl; wherein said non-aromatic 5- or 6-membered ring part of said bicyclic ring system independently is optionally further mono-substituted with oxo; or di-, tri-, or tetra-substituted wherein one substituent is oxo and the remaining are (C_{1-3})alkyl (especially methyl); [in particular such bicyclic ring system is a group selected from 2-oxo-2,3-dihydro-benzooxazol-6-yl, 3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl, 4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl, 3-methyl-2-oxo-2,3-dihydro-benzooxazol-6-yl, 3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl, 1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl, 2,2-dimethyl-2,3-dihydro-benzofuran-6-yl, 2,2-dimethyl-2,3-dihydro-benzofuran-5-yl, or 3,3-dimethyl-2,3-dihydro-benzofuran-5-yl];

- or (notably) R^1 together with $(R^4)_n$ forms an aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring to form a bicyclic aromatic ring system selected from pyrrolo[2,3-b]pyridinyl, indolyl, indazolyl, quinoxalinyl, benzoimidazolyl, and quinolinyl; wherein said fused 5- or 6-membered aromatic ring part of said aromatic bicyclic ring system independently is optionally further mono- or di-substituted wherein the substituents are independently selected from (C_{1-3})alkyl (especially methyl, isopropyl), (C_{3-6})cycloalkyl (especially cyclobutyl), (C_1)fluoroalkyl (especially trifluoromethyl), or cyano [especially such aromatic bicyclic ring system is indolyl or indazolyl, both mono-substituted with methyl; in particular such aromatic bicyclic ring system is a group selected from 1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl, 1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl, 1H-indol-5-yl, 1H-indol-6-yl, 1-methyl-1H-indazol-5-yl, 1-methyl-1H-indazol-6-yl, 1-ethyl-1H-indazol-5-yl, 1-ethyl-1H-indazol-6-yl, 1,3-dimethyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 1,3-dimethyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-6-yl, 3-cyano-1-methyl-1H-indol-5-yl, 3-isopropyl-1-methyl-1H-indol-5-yl, 3-cyclobutyl-1-methyl-1H-indol-5-yl, 1-methyl-3-trifluoromethyl-1H-indol-5-yl, quinoxalin-6-yl, 2-methyl-1H-benzoimidazol-6-yl, 1-methyl-1H-benzoimidazol-5-yl, 1-methyl-1H-benzoimidazol-6-yl, or quinolin-7-yl].

11) Another embodiment relates to compounds according to any one of embodiments 1) to 4), wherein **R^1** represents methyl, or halogen (especially fluoro); and **$(R^4)_n$** represents one substituent selected from (C_{1-3})fluoroalkoxy (especially 2,2,2-trifluoroethoxy) which is attached to the phenyl / pyridinyl ring in *ortho* or *meta*-position to the point of attachment of the –CH_2-CO-NH- group.

12) Another embodiment relates to compounds according to any one of embodiments 1) to 4), wherein the fragment



represents 4-cyclopropyl-phenyl, 4-isopropyl-phenyl, 4- dimethylamino -phenyl, 4- trifluoromethyl -phenyl, 4-*tert.*-butyl -phenyl, 4- isobutyl -phenyl, 4-(1-methoxy-ethyl)-phenyl, 4-(1-methyl-cyclopropyl)-phenyl, 4-(cyclopropyl-methyl)-phenyl, 4-(1-hydroxy-cyclopropyl)-phenyl, 4-(cyclopropyl-oxy)-phenyl, 4-(azetidin-1-yl)-phenyl, 4-(oxetan-3-yl-oxy)-phenyl, 4-(3-hydroxy-oxetan-3-yl)-phenyl, 4-(3-fluoro-oxetan-3-yl)-phenyl, 4-(cyclobutyl-oxy)-phenyl, 4-(3-methyl-oxetan-3-yl)-phenyl, 4-([1,2,4]oxadiazol-3-yl)-phenyl, 4-(5-methyl-[1,2,4]oxadiazol-3-yl)-phenyl, 4-(3-fluoro-azetidin-1-yl)-phenyl, 4-(1-cyano-cyclopropyl)-phenyl, 4-(1-cyano-1-methyl-ethyl)-phenyl, 4-(diethylamino)-phenyl, 4-(pentafluoro-sulfanyl)-phenyl, 4-(2,2,2-trifluoroethoxy)-phenyl, 3-methyl-4-(2,2,2-trifluoroethoxy)-phenyl, 3-fluoro-4-(2,2,2-trifluoroethoxy)-phenyl, 4-((2-methoxyethyl)-methyl-amino)-phenyl, 4-(3,3-difluoro-cyclobutyl)-phenyl, 4-(3-methoxy-oxetan-3-yl)-phenyl, 4-(oxetan-3-yl-methoxy)-phenyl, 4-(pyrazin-2-yl)-phenyl, 4-(3-methyl-pyrazin-2-yl)-phenyl, 4-(pyrimidin-4-yl)-phenyl, 4-(5-methyl-pyrimidin-4-yl)-phenyl, 4-(pyrimidin-2-yl)-phenyl, 4-(pyrimidin-5-yl)-phenyl, 4-(pyridin-4-yl)-phenyl, 4-(pyridin-3-yl)-phenyl, 4-(pyridin-2-yl)-phenyl, 4-(3-fluoro-pyrrolidin-1-yl)-phenyl, 4-(3,3-difluoro-azetidin-1-yl)-phenyl, 4-(2-oxo-pyrrolidin-1-yl)-phenyl, 4-(2-trifluoromethyl-cyclopropyl)-phenyl, 4-(1-trifluoromethyl-cyclopropyl)-phenyl, 4-((3-fluoro-oxetan-3-yl)-methoxy)-phenyl, 4-(3,3-difluoro-cyclobutyl-oxy)-phenyl, 4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenyl, 4-((3,3-difluoro-cyclobutyl)-methoxy)-phenyl, 4-((3,3-difluoro-1-methyl-cyclobutyl)-methoxy)-phenyl; 2-cyclopropyl-pyridin-5-yl, 2-dimethylamino-pyridin-5-yl, 2-isopropyl-pyridin-5-yl, 2-(ethyl-methyl-amino)-pyridin-5-yl, 2-(3-fluoro-azetidin-1-yl)-pyridin-5-yl, 2-(pyrrolidin-1-yl)-pyridin-5-yl, 2-(cyclopropyl-methyl-amino)-pyridin-5-yl, 2-(3-fluoro-oxetan-3-yl)-pyridin-5-yl, 2-(diethylamino)-pyridin-5-yl, 2-((2,2-difluoro-ethyl)-methyl-amino)-pyridin-5-yl, 2-((2-methoxyethyl)-methyl-amino)-pyridin-5-yl, 2-(2,2,2-trifluoroethoxy)-pyridin-5-yl, 3-fluoro-2-(2,2,2-trifluoroethoxy)-pyridin-5-yl, 3-fluoro-2-(pyrrolidin-1-yl)-pyridin-5-yl, 2-(3-fluoro-pyrrolidin-1-yl)-pyridin-5-yl, 2-((cyclopropylmethyl)-methyl-amino)-pyridin-5-yl, 2-(3,3-difluoro-azetidin-1-yl)-pyridin-5-yl, 2-(3-methoxy-oxetan-3-yl)-pyridin-5-yl, 2-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-5-yl; 2-oxo-2,3-dihydro-benzooxazol-6-yl, 3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl, 4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl, 3-methyl-2-oxo-2,3-dihydro-benzooxazol-6-yl, 3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl, 1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl, 2,2-dimethyl-2,3-dihydro-benzofuran-6-yl, 2,2-dimethyl-2,3-dihydro-benzofuran-5-yl, 3,3-dimethyl-2,3-dihydro-benzofuran-5-yl; 1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl,

1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl, 1H-indol-5-yl, 1H-indol-6-yl, 1-methyl-1H-indazol-5-yl, 1-methyl-1H-indazol-6-yl, 1-ethyl-1H-indazol-5-yl, 1-ethyl-1H-indazol-6-yl, 1,3-dimethyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 1,3-dimethyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-6-yl, 3-cyano-1-methyl-1H-indol-5-yl, 3-isopropyl-1-methyl-1H-indol-5-yl, 3-cyclobutyl-1-methyl-1H-indol-5-yl, 1-methyl-3-trifluoromethyl-1H-indol-5-yl, quinoxalin-6-yl, 2-methyl-1H-benzoimidazol-6-yl, 1-methyl-1H-benzoimidazol-5-yl, 1-methyl-1H-benzoimidazol-6-yl, quinolin-7-yl; 4-methyl-3-(2,2,2-trifluoroethoxy)-phenyl; or 4-fluoro-2-(2,2,2-trifluoroethoxy)-phenyl.

13) Another embodiment relates to compounds according to any one of embodiments 1) to 12), wherein

- **Y** represents a ring nitrogen atom; and
  - **R^2** represents (C_{1-4})alkyl (especially methyl, ethyl, isopropyl, isobutyl, *tert.*-butyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); (C_{3-6})cycloalkyl-oxy (especially cyclopropyl-oxy); (C_{1-3})fluoroalkyl (especially trifluoromethyl); (C_{1-3})fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy); (C_{1-3})alkoxy-(C_{2-3})alkoxy (especially 2-methoxy-ethoxy); halogen (especially fluoro); cyano; or -$NR^{21}R^{22}$, wherein R^{21} and R^{22} independently represent (C_{1-3})alkyl (especially dimethylamino), or R^{21} and R^{22}, together with the nitrogen atom to which they are attached to, form a ring selected from azetidinyl optionally mono- or di-substituted with fluoro, pyrrolidinyl optionally mono- or di-substituted with fluoro, or piperidinyl optionally mono- or di-substituted with fluoro; and
  - **$(R^5)_m$** represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from the group consisting of (C_{1-4})alkyl (especially methyl, ethyl, isobutyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); halogen (especially fluoro); cyano; (C_{1-3})fluoroalkyl (especially trifluoromethyl); and (C_{1-3})fluoroalkoxy (especially trifluoromethoxy, 2,2,2-trifluoroethoxy); [especially **$(R^5)_m$** is absent (i.e. m = 0), or **$(R^5)_m$** represents one halogen substituent, preferably **$(R^5)_m$** is absent]; or
- **Y** represents a ring carbon atom; and
  - **R^2** represents (C_{1-4})alkyl (especially methyl, ethyl, isopropyl, *tert.*-butyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy); (C_{3-6})cycloalkyl-oxy (especially cyclopropyl-oxy); (C_{1-3})fluoroalkyl (especially trifluoromethyl); (C_{1-3})fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy); halogen (especially fluoro); or cyano; and
  - **$(R^5)_m$** represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from the group consisting of (C_{1-4})alkyl (especially methyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy); halogen (especially fluoro); cyano; (C_{1-3})fluoroalkyl (especially trifluoromethyl); and (C_{1-3})fluoroalkoxy (especially trifluoromethoxy); [especially **$(R^5)_m$** is absent (i.e. m = 0), or **$(R^5)_m$** represents one halogen substituent, preferably **$(R^5)_m$** is absent].

14) Another embodiment relates to compounds according to any one of embodiments 1) to 12), wherein

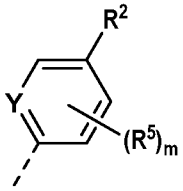
- **Y** represents a ring nitrogen atom; and
  - R^2 represents (C_{1-4})alkyl (especially methyl, ethyl, isobutyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); (C_{1-3})fluoroalkyl (especially trifluoromethyl); (C_{1-3})fluoroalkoxy (especially 2,2,2-trifluoroethoxy); (C_{1-3})alkoxy-(C_{2-3})alkoxy (especially 2-methoxy-ethoxy); halogen (especially fluoro); or cyano; [in particular R^2 represents fluoro or cyano]; and
  - $(R^5)_m$ represents one optional substituent (i.e. m represents the integer 0, or 1) independently selected from the group consisting of (C_{1-4})alkyl (especially methyl, ethyl, isobutyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); halogen (especially fluoro); cyano; (C_{1-3})fluoroalkyl (especially difluoromethyl, trifluoromethyl); and (C_{1-3})fluoroalkoxy (especially trifluoromethoxy, 2,2,2-trifluoroethoxy); [especially $(R^5)_m$ is absent (i.e. m = 0), or $(R^5)_m$ represents one halogen substituent, preferably $(R^5)_m$ is absent]; or
- **Y** represents a ring carbon atom; and
  - R^2 represents (C_{1-4})alkyl (especially methyl, ethyl, isopropyl, *tert.*-butyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy); (C_{3-6})cycloalkyl-oxy (especially cyclopropyl-oxy); (C_{1-3})fluoroalkyl (especially trifluoromethyl); (C_{1-3})fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy); halogen (especially fluoro); or cyano; and
  - $(R^5)_m$ represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from the group consisting of (C_{1-4})alkyl (especially methyl); (C_{1-4})alkoxy (especially methoxy); halogen (especially fluoro); cyano; (C_{1-3})fluoroalkyl (especially trifluoromethyl), and (C_{1-3})fluoroalkoxy (especially trifluoromethoxy) [especially $(R^5)_m$ is absent (i.e. m = 0), or $(R^5)_m$ represents one halogen substituent, preferably $(R^5)_m$ is absent].

15) Another embodiment relates to compounds according to any one of embodiments 1) to 12), wherein

- **Y** represents a ring nitrogen atom; and
  - R^2 represents (C_{1-4})alkyl (especially methyl, ethyl, isopropyl, isobutyl, *tert.*-butyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); (C_{1-3})fluoroalkyl (especially trifluoromethyl); (C_{1-3})fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy); (C_{1-3})alkoxy-(C_{2-3})alkoxy (especially 2-methoxy-ethoxy); halogen (especially fluoro); or (preferably) cyano; [in particular R^2 represents fluoro or cyano]; and
  - $(R^5)_m$ represents one optional substituent (i.e. m represents the integer 0, or 1) independently selected from the group consisting of (C_{1-4})alkyl (especially methyl, ethyl, isobutyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); halogen (especially fluoro); cyano; (C_{1-3})fluoroalkyl (especially difluoromethyl, trifluoromethyl), and (C_{1-}

$_3$)fluoroalkoxy (especially trifluoromethoxy, 2,2,2-trifluoroethoxy) [especially $(R^5)_m$ is absent (i.e. m = 0), or $(R^5)_m$ represents one halogen substituent, preferably $(R^5)_m$ is absent].

16) Another embodiment relates to compounds according to any one of embodiments 1) to 12), wherein the fragment



represents 4-fluorophenyl, 4-chlorophenyl, 4-bromophenyl, 4-methylphenyl, 4-ethylphenyl, 3-fluoro-4-methyl-phenyl, 4-fluoro-3-methyl-phenyl, 4-fluoro-3-cyano-phenyl, 4-fluoro-3,5-dimethylphenyl, 4-chloro-3-fluorophenyl, 3-chloro-4-fluorophenyl, 3,4-difluorophenyl, 3,5-difluoro-4-methoxy-phenyl, 4-cyano-3,5-difluoro-phenyl, 4-methoxyphenyl, 4-cyanophenyl, 4-cyclopropyl-phenyl, 3,4,5-trifluorophenyl, 4-*tert.*-butyl-phenyl, 4-isopropyl-phenyl, 4-(cyclopropyl-oxy)-phenyl, 4-chloro-3-trifluoromethyl-phenyl, 4-fluoro-3-trifluoromethyl-phenyl, 4-methoxy-3-trifluoromethyl-phenyl, 4-difluoromethoxy-phenyl, 4-trifluoromethoxy-phenyl, 4-chloro-3-trifluoromethoxy-phenyl, 4-fluoro-3-trifluoromethoxy-phenyl; 5-fluoro-pyridin-2-yl, 5-bromo-pyridin-2-yl, 5-cyano-pyridin-2-yl, 5-methyl-pyridin-2-yl, 5-ethyl-pyridin-2-yl, 5-methoxy-pyridin-2-yl, 6-chloro-5-fluoro-pyridin-2-yl, 5-cyclopropyl-pyridin-2-yl, 6-cyano-5-fluoro-pyridin-2-yl, 5-cyano-6-fluoro-pyridin-2-yl, 6-chloro-5-cyano-pyridin-2-yl, 5-chloro-6-cyano-pyridin-2-yl, 5-cyano-6-methyl-pyridin-2-yl, 5-cyano-4-methyl-pyridin-2-yl, 6-cyano-5-methyl-pyridin-2-yl, 5-cyano-6-isobutyl-pyridin-2-yl, 5-cyano-6-methoxy-pyridin-2-yl, 5-cyano-6-isopropoxy-pyridin-2-yl, 5-trifluoromethyl-pyridin-2-yl, 5-(2,2,2-trifluoroethoxy)-pyridin-2-yl, 5-cyano-6-(2,2,2-trifluoroethoxy)-pyridin-2-yl, 5-isobutyl-pyridin-2-yl, 5-isopropoxy-pyridin-2-yl, 5-dimethylamino-pyridine-2-yl, 4-cyclopropyl-5-cyano-pyridin-2-yl, 5-(2-methoxy-ethoxy)-pyridin-2-yl, or 5-(3-fluoropyrrolidin-1-yl)-pyridin-2-yl.

17) Another embodiment relates to compounds according to embodiment 1), wherein

X represents a ring carbon or a ring nitrogen atom;

- R^1 represents
  - (C_{2-6})alkyl [in particular isopropyl, *tert.*-butyl, or isobutyl];
  - (C_{2-4})alkyl mono-substituted with cyano or (C_{1-3})alkoxy (especially methoxy); [in particular such group is 1-methoxy-ethyl, or 1-cyano-1-methyl-ethyl];
  - (C_{1-4})fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
  - (C_{1-3})fluoroalkoxy [in particular trifluoromethoxy, 2,2,2-trifluoroethoxy, 3,3,3-trifluoropropoxy];
  - (C_{3-6})cycloalkyl-L^1- wherein
    - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C_{1-3})alkyl (especially methyl), (C_{1-3})alkoxy (especially methoxy), hydroxy, cyano, or (C_{1-3})fluoroalkyl (especially trifluoromethyl), or di-substituted with fluoro; and

- the linker **L**[1] represents a direct bond, (C_{1-2})alkylene, or oxygen;
  [in particular such group (C_{3-6})cycloalkyl-**L**[1]- is cyclopropyl, 3-fluoro-oxetan-3-yl, 3-methoxy-oxetan-3-yl, 3-methyl-oxetan-3-yl, 3,3-difluoro-cyclobutyl, 1-trifluoromethyl-cyclopropyl, 2-trifluoromethyl-cyclopropyl, 1-methyl-cyclopropyl, 1-cyano-cyclopropyl, 1-hydroxy-cyclopropyl, 1-methoxy-cyclopropyl, or 3-hydroxy-oxetan-3-yl; or it is cyclopropyl-methyl; or it is cyclopropyl-oxy, oxetan-3-yl-oxy, cyclobutyl-oxy, or 3,3-difluoro-cyclobutyl-oxy];

➢ 5- or 6-membered heteroaryl, independently optionally mono-substituted with (C_{1-3})alkyl (especially methyl); [in particular oxadiazolyl, pyrazinyl, pyrimidinyl, or pyridinyl];

➢ -$NR^{11}R^{12}$, wherein

- R^{11} and R^{12} independently represent hydrogen, (C_{1-3})alkyl, (C_{3-6})cycloalkyl, (C_{3-6})cycloalkyl-(C_{1-3})alkyl, (C_{1-3})alkoxy-(C_{2-3})alkyl [in particular such group -$NR^{11}R^{12}$ is dimethylamino, ethyl-methyl-amino, diethylamino, cyclopropyl-methyl-amino, (2-methoxyethyl)-methyl-amino, or (cyclopropylmethyl)-methyl-amino];
- or R^{11} and R^{12}, together with the nitrogen atom to which they are attached to, form a 4- to- 6 membered ring optionally mono- or di-substituted with fluoro; [in particular such group -$NR^{11}R^{12}$ is azetidinyl, 3-fluoro-azetidinyl, 3,3-difluoro-azetidinyl, pyrrolidinyl, 3-fluoro-pyrrolidinyl, or 3,3-difluoro-pyrrolidinyl];

and **(R^4)$_n$** represents one or two optional substituents (i.e. n represents the integer 0, 1, or 2) independently selected from (C_{1-4})alkyl (especially methyl, ethyl), (C_{3-6})cycloalkyl (especially cyclopropyl), (C_{1-3})fluoroalkyl (especially trifluoromethyl), (C_{1-3})fluoroalkoxy (especially trifluoromethoxy), halogen (especially fluoro), and cyano [especially **(R^4)$_n$** is absent (i.e. n = 0); or **(R^4)$_n$** represents one halogen or methyl substituent];

- or **R^1** together with **(R^4)$_n$** forms an aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring; wherein said 5- or 6-membered ring contains one or two heteroatoms selected from nitrogen, wherein said fused 5- or 6-membered aromatic ring independently is optionally further mono- or di-substituted wherein the substituents are independently selected from (C_{1-3})alkyl (especially methyl, ethyl, isopropyl), (C_{3-6})cycloalkyl (especially cyclobutyl), (C_1)fluoroalkyl (especially trifluoromethyl), or cyano [in particular such aromatic 5- or 6-membered ring fused to the phenyl / pyridine ring forms, together with the phenyl / pyridine ring, a group selected from 1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl, 1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl, 1H-indol-5-yl, 1H-indol-6-yl, 1-methyl-1H-indazol-5-yl, 1-methyl-1H-indazol-6-yl, 1-ethyl-1H-indazol-5-yl, 1,3-dimethyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 1,3-dimethyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-6-yl, 3-cyano-1-methyl-1H-indol-5-yl, 3-isopropyl-1-methyl-1H-indol-5-yl, 3-cyclobutyl-1-methyl-1H-indol-5-yl, 1-methyl-3-trifluoromethyl-1H-indol-5-yl, quinoxalin-6-yl, 2-methyl-1H-benzoimidazol-6-yl, 1-methyl-1H-benzoimidazol-5-yl, 1-methyl-1H-benzoimidazol-6-yl, or quinolin-7-yl];

Y represents a ring carbon or a ring nitrogen atom; and

R^2 represents (C_{1-4})alkyl (especially methyl, ethyl, isopropyl, isobutyl, *tert.*-butyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); (C_{3-6})cycloalkyl-oxy (especially cyclopropyl-oxy); (C_{1-3})fluoroalkyl (especially trifluoromethyl); (C_{1-3})fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy); halogen; or cyano;

and

$(R^5)_m$ represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from (C_{1-4})alkyl (especially methyl, ethyl, isobutyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); halogen; cyano; (C_{1-3})fluoroalkyl (especially difluoromethyl, trifluoromethyl); and (C_{1-3})fluoroalkoxy (especially trifluoromethoxy, 2,2,2-trifluoroethoxy); [especially **$(R^5)_m$** is absent (i.e. m = 0), or **$(R^5)_m$** represents one halogen substituent; preferably **$(R^5)_m$** is absent].

18) Another embodiment relates to compounds according to embodiment 1), wherein

X represents a ring carbon or a ring nitrogen atom;

- **R^1** represents
  - (C_{2-6})alkyl [in particular isopropyl, *tert.*-butyl, or isobutyl];
  - (C_{2-4})alkyl mono-substituted with cyano; [in particular such group is 1-cyano-1-methyl-ethyl];
  - (C_{1-4})fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
  - (C_{3-6})cycloalkyl-**L^1**- wherein
    - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C_{1-3})alkyl (especially methyl), (C_{1-3})alkoxy (especially methoxy), hydroxy, cyano, or (C_{1-3})fluoroalkyl (especially trifluoromethyl), or di-substituted with fluoro; and
    - the linker **L^1** represents a direct bond, or (C_{1-2})alkylene;

      [in particular such group (C_{3-6})cycloalkyl-**L^1**- is cyclopropyl, 3-fluoro-oxetan-3-yl, 3-methoxy-oxetan-3-yl, 3-methyl-oxetan-3-yl, 3,3-difluoro-cyclobutyl, 1-trifluoromethyl-cyclopropyl, 2-trifluoromethyl-cyclopropyl, 1-methyl-cyclopropyl, 1-cyano-cyclopropyl, 1-hydroxy-cyclopropyl, 1-methoxy-cyclopropyl, or 3-hydroxy-oxetan-3-yl; or it is cyclopropyl-methyl];
  - 5- or 6-membered heteroaryl, independently optionally mono-substituted with (C_{1-3})alkyl (especially methyl); [in particular oxadiazolyl, pyrazinyl, pyrimidinyl, or pyridinyl];

  and **$(R^4)_n$** represents one or two optional substituents (i.e. n represents the integer 0, 1, or 2) independently selected from (C_{1-4})alkyl (especially methyl, ethyl), (C_{3-6})cycloalkyl (especially cyclopropyl), (C_{1-3})fluoroalkyl (especially trifluoromethyl), halogen (especially fluoro), and cyano [especially **$(R^4)_n$** is absent (i.e. n = 0); or **$(R^4)_n$** represents one halogen or methyl substituent];

- or **R¹** together with **$(R^4)_n$** forms an aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring to form a bicyclic aromatic ring system selected from indolyl, indazolyl and quinolinyl; wherein said fused 5- or 6-membered aromatic ring part of said aromatic bicyclic ring system independently is optionally further mono- or di-substituted wherein the substituents are independently selected from (C_{1-3})alkyl (especially methyl, ethyl, isopropyl), (C_{3-6})cycloalkyl (especially cyclobutyl), (C_1)fluoroalkyl (especially trifluoromethyl), or cyano [in particular such aromatic 5- or 6-membered ring fused to the phenyl / pyridine ring forms, together with the phenyl / pyridine ring, a group selected from 1H-indol-5-yl, 1H-indol-6-yl, 1-methyl-1H-indazol-5-yl, 1-methyl-1H-indazol-6-yl, 1-ethyl-1H-indazol-5-yl, 1,3-dimethyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 1,3-dimethyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-6-yl, 3-cyano-1-methyl-1H-indol-5-yl, 3-isopropyl-1-methyl-1H-indol-5-yl, 3-cyclobutyl-1-methyl-1H-indol-5-yl, 1-methyl-3-trifluoromethyl-1H-indol-5-yl, or quinolin-7-yl];

Y represents a ring carbon or a ring nitrogen atom; and

R² represents (C_{1-4})alkyl (especially methyl, ethyl, isopropyl, isobutyl, *tert.*-butyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); (C_{3-6})cycloalkyl-oxy (especially cyclopropyl-oxy); (C_{1-3})fluoroalkyl (especially trifluoromethyl); (C_{1-3})fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy); halogen; or cyano;

and

$(R^5)_m$ represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from (C_{1-4})alkyl (especially methyl, ethyl, isobutyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); halogen; cyano; (C_{1-3})fluoroalkyl (especially difluoromethyl, trifluoromethyl); and (C_{1-3})fluoroalkoxy (especially trifluoromethoxy, 2,2,2-trifluoroethoxy); [especially **$(R^5)_m$** is absent (i.e. m = 0), or **$(R^5)_m$** represents one halogen substituent; preferably **$(R^5)_m$** is absent].

19) Another embodiment relates to compounds according to any one of embodiments 17) or 18), wherein **X** represents a ring carbon atom.

20) Another embodiment relates to compounds according to any one of embodiments 17) or 18), wherein **X** represents a ring nitrogen atom.

21) Another embodiment relates to compounds according to any one of embodiments 1) to 4), 13) to 17), 19) or 20) , wherein

R¹ represents (C_{3-6})cycloalkyl-**L¹**- wherein said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C_{1-3})alkyl (especially methyl), (C_{1-3})alkoxy (especially methoxy), hydroxy, cyano, or (C_{1-3})fluoroalkyl (especially trifluoromethyl), or di-substituted with fluoro; and the linker **L¹** represents a direct bond, (C_{1-2})alkylene, or oxygen;

[in particular such group (C_{3-6})cycloalkyl-**L¹**- is cyclopropyl, 3-fluoro-oxetan-3-yl, 3-methoxy-oxetan-3-yl, 3-methyl-oxetan-3-yl, 3,3-difluoro-cyclobutyl, 1-trifluoromethyl-cyclopropyl, 2-trifluoromethyl-cyclopropyl, 1-

methyl-cyclopropyl, 1-cyano-cyclopropyl, 1-hydroxy-cyclopropyl, 1-methoxy-cyclopropyl, or 3-hydroxy-oxetan-3-yl; or it is cyclopropyl-methyl; or it is cyclopropyl-oxy, oxetan-3-yl-oxy, cyclobutyl-oxy, or 3,3-difluoro-cyclobutyl-oxy].

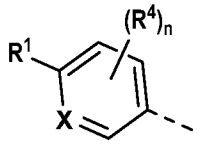
22) Another embodiment relates to compounds according to any one of embodiments 1) to 4) or 13) to 20), wherein

R^1 represents cyclopropyl wherein said cyclopropyl is unsubstituted, or mono-substituted with (C_{1-3})alkyl (especially methyl), (C_{1-3})alkoxy (especially methoxy), cyano, or (C_{1-3})fluoroalkyl (especially trifluoromethyl); [in particular cyclopropyl, 1-trifluoromethyl-cyclopropyl, 2-trifluoromethyl-cyclopropyl, 1-methyl-cyclopropyl, 1-cyano-cyclopropyl, or 1-methoxy-cyclopropyl].

23) Another embodiment relates to compounds according to any one of embodiments 1) to 4) or 13) to 20), wherein

R^1 together with **(R^4)$_n$** forms an aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring to form a bicyclic aromatic ring system selected from indolyl, indazolyl and quinolinyl; wherein said fused 5- or 6-membered aromatic ring part of said aromatic bicyclic ring system independently is optionally further mono- or di-substituted wherein the substituents are independently selected from (C_{1-3})alkyl (especially methyl, ethyl, isopropyl), (C_{3-6})cycloalkyl (especially cyclobutyl), (C_1)fluoroalkyl (especially trifluoromethyl), or cyano [in particular such aromatic 5- or 6-membered ring fused to the phenyl / pyridine ring forms, together with the phenyl / pyridine ring, a group selected from 1H-indol-5-yl, 1H-indol-6-yl, 1-methyl-1H-indazol-5-yl, 1-methyl-1H-indazol-6-yl, 1-ethyl-1H-indazol-5-yl, 1,3-dimethyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 1,3-dimethyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-6-yl, 3-cyano-1-methyl-1H-indol-5-yl, 3-isopropyl-1-methyl-1H-indol-5-yl, 3-cyclobutyl-1-methyl-1H-indol-5-yl, 1-methyl-3-trifluoromethyl-1H-indol-5-yl, or quinolin-7-yl].

24) Another embodiment relates to compounds according to any one of embodiments 1), 3), 4) or 13) to 16), wherein the fragment



represents 4-(1-methoxy-cyclopropyl)-phenyl, 4-(1-cyano-cyclopropyl)-3-trifluoromethyl-phenyl, 4-(1-cyano-3,3-difluoro-cyclobutyl)-phenyl, 4-cyclopropylmethoxy-3-trifluoromethoxy-phenyl, 3-cyano-4-*iso*-butyl-phenyl, 3-methyl-4-trifluoromethoxy-phenyl, 3,5-dimethyl-4-(2,2,2-trifluoroethoxy)-phenyl, 3-ethyl-4-(2,2,2-trifluoroethoxy)-phenyl, 3-methyl-4-(3,3,3-trifluoropropoxy)-phenyl, 3-cyclopropyl-4-(2,2,2-trifluoroethoxy)-phenyl, 5-methyl-6-(2,2,2-trifluoroethoxy)-pyridin-3-yl, 3,3-dimethyl-2,3-dihydro-benzofuran-6-yl, or 3-methylchroman-7-yl.

25) Another embodiment relates to compounds according to any one of embodiments 1) to 12) or 17) to 24), wherein

Y represents a ring nitrogen atom;

R^2 represents (C_{1-4})alkyl (especially methyl, ethyl, isopropyl, isobutyl, *tert.*-butyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); (C_{1-3})fluoroalkyl (especially trifluoromethyl); (C_{1-3})fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy); halogen (especially fluoro); or cyano; and

$(R^5)_m$ represents one optional substituent (i.e. m represents the integer 0, or 1) selected from the group consisting of (C_{1-4})alkyl (especially methyl, ethyl, isobutyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy, isopropoxy); halogen (especially fluoro); cyano; (C_{1-3})fluoroalkyl (especially difluoromethyl); and (C_{1-3})fluoroalkoxy (especially trifluoromethoxy, 2,2,2-trifluoroethoxy); [especially **$(R^5)_m$** is absent (i.e. m = 0), or **$(R^5)_m$** represents one halogen substituent, preferably **$(R^5)_m$** is absent].

26) Another embodiment relates to compounds according to any one of embodiments 1) to 12) or 17) to 24), wherein

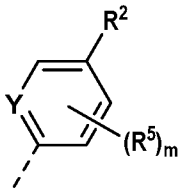
Y represents a ring carbon atom;

R^2 represents (C_{1-4})alkyl (especially methyl, ethyl, isopropyl, *tert.*-butyl); (C_{3-6})cycloalkyl (especially cyclopropyl); (C_{1-4})alkoxy (especially methoxy); (C_{3-6})cycloalkyl-oxy (especially cyclopropyl-oxy); (C_{1-3})fluoroalkyl (especially trifluoromethyl); (C_{1-3})fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy); halogen (especially fluoro); or cyano; and

$(R^5)_m$ represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from the group consisting of (C_{1-4})alkyl (especially methyl); halogen (especially fluoro); cyano; (C_{1-3})fluoroalkyl (especially trifluoromethyl); and (C_{1-3})fluoroalkoxy (especially trifluoromethoxy); [especially **$(R^5)_m$** is absent (i.e. m = 0), or **$(R^5)_m$** represents one halogen substituent, preferably **$(R^5)_m$** is absent].

27) Another embodiment relates to compounds according to any one of embodiments 1) to 15) or 17) to 26), wherein **$(R^5)_m$** is absent (i.e. m = 0).

28) Another embodiment relates to compounds according to any one of embodiments 1) to 12) or 21) to 24), wherein the fragment



represents 5-cyano-3-fluoro-pyridin-2-yl, 4-cyano-5-fluoro-pyridin-2-yl, 5-cyano-6-difluoromethyl-pyridin-2-yl, 5-cyano-4-difluoromethyl-pyridin-2-yl, 5-(azetidin-1-yl)-pyridin-2-yl, 5-(pyrrolidin-1-yl)-pyridin-2-yl, or 5-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-2-yl.

29) The invention, thus, relates to compounds of the formula (I) as defined in embodiment 1), or to such compounds further limited by the characteristics of any one of embodiments 2) to 28), under consideration of their respective dependencies; to pharmaceutically acceptable salts thereof; and to the use of such compounds as medicaments especially in the treatment of diseases or disorders where calcium T channels are involved as described herein below. For avoidance of any doubt, especially the following embodiments relating to the compounds of formula (I) are thus possible and intended and herewith specifically disclosed in individualized form:

1, 2+1, 3+1, 3+2+1, 4+1, 4+2+1, 5+2+1, 5+3+2+1, 5+4+2+1, 6+2+1, 6+3+2+1, 6+4+2+1, 7+2+1, 7+3+2+1, 7+4+2+1, 8+2+1, 8+3+2+1, 8+4+2+1, 9+2+1, 9+3+2+1, 9+4+2+1, 10+2+1, 10+3+2+1, 10+4+2+1, 11+2+1, 11+3+2+1, 11+4+2+1, 12+2+1, 12+3+2+1, 12+4+2+1, 13+1, 13+2+1, 13+3+1, 13+3+2+1, 13+4+1, 13+4+2+1, 13+5+2+1, 13+5+3+2+1, 13+5+4+2+1, 13+6+2+1, 13+6+3+2+1, 13+6+4+2+1, 13+7+2+1, 13+7+3+2+1, 13+7+4+2+1, 13+8+2+1, 13+8+3+2+1, 13+8+4+2+1, 13+9+2+1, 13+9+3+2+1, 13+9+4+2+1, 13+10+2+1, 13+10+3+2+1, 13+10+4+2+1, 13+11+2+1, 13+11+3+2+1, 13+11+4+2+1, 13+12+2+1, 13+12+3+2+1, 13+12+4+2+1, 14+1, 14+2+1, 14+3+1, 14+3+2+1, 14+4+1, 14+4+2+1, 14+5+2+1, 14+5+3+2+1, 14+5+4+2+1, 14+6+2+1, 14+6+3+2+1, 14+6+4+2+1, 14+7+2+1, 14+7+3+2+1, 14+7+4+2+1, 14+8+2+1, 14+8+3+2+1, 14+8+4+2+1, 14+9+2+1, 14+9+3+2+1, 14+9+4+2+1, 14+10+2+1, 14+10+3+2+1, 14+10+4+2+1, 14+11+2+1, 14+11+3+2+1, 14+11+4+2+1, 14+12+2+1, 14+12+3+2+1, 14+12+4+2+1, 15+1, 15+2+1, 15+3+1, 15+3+2+1, 15+4+1, 15+4+2+1, 15+5+2+1, 15+5+3+2+1, 15+5+4+2+1, 15+6+2+1, 15+6+3+2+1, 15+6+4+2+1, 15+7+2+1, 15+7+3+2+1, 15+7+4+2+1, 15+8+2+1, 15+8+3+2+1, 15+8+4+2+1, 15+9+2+1, 15+9+3+2+1, 15+9+4+2+1, 15+10+2+1, 15+10+3+2+1, 15+10+4+2+1, 15+11+2+1, 15+11+3+2+1, 15+11+4+2+1, 15+12+2+1, 15+12+3+2+1, 15+12+4+2+1, 16+1, 16+2+1, 16+3+1, 16+3+2+1, 16+4+1, 16+4+2+1, 16+5+2+1, 16+5+3+2+1, 16+5+4+2+1, 16+6+2+1, 16+6+3+2+1, 16+6+4+2+1, 16+7+2+1, 16+7+3+2+1, 16+7+4+2+1, 16+8+2+1, 16+8+3+2+1, 16+8+4+2+1, 16+9+2+1, 16+9+3+2+1, 16+9+4+2+1, 16+10+2+1, 16+10+3+2+1, 16+10+4+2+1, 16+11+2+1, 16+11+3+2+1, 16+11+4+2+1, 16+12+2+1, 16+12+3+2+1, 16+12+4+2+1, 17+1, 18+1, 19+17+1, 19+18+1, 20+17+1, 20+18+1, 21+1, 21+17+1, 21+19+17+1, 21+20+17+1, 22+1, 22+17+1, 22+18+1, 22+19+17+1, 22+19+18+1, 22+20+17+1, 22+20+18+1, 23+1, 23+17+1, 23+18+1, 23+19+17+1, 23+19+18+1, 23+20+17+1, 23+20+18+1, 24+1, 25+1, 25+17+1, 25+18+1, 25+19+17+1, 25+19+18+1, 25+20+17+1, 25+20+18+1, 25+21+1, 25+21+17+1, 25+21+19+17+1, 25+21+20+17+1, 25+22+1, 25+22+17+1, 25+22+18+1, 25+22+19+17+1, 25+22+19+18+1, 25+22+20+17+1, 25+22+20+18+1, 25+23+1, 25+23+17+1, 25+23+18+1, 25+23+19+17+1, 25+23+19+18+1, 25+23+20+17+1, 25+23+20+18+1, 25+24+1, 26+1, 26+17+1, 26+18+1, 26+19+17+1, 26+19+18+1, 26+20+17+1, 26+20+18+1, 26+21+1, 26+21+17+1, 26+21+19+17+1, 26+21+20+17+1, 26+22+1, 26+22+17+1, 26+22+18+1, 26+22+19+17+1, 26+22+19+18+1, 26+22+20+17+1, 26+22+20+18+1, 26+23+1, 26+23+17+1, 26+23+18+1, 26+23+19+17+1, 26+23+19+18+1, 26+23+20+17+1, 26+23+20+18+1, 26+24+1, 27+1, 27+17+1, 27+18+1, 27+19+17+1, 27+19+18+1, 27+20+17+1, 27+20+18+1, 27+21+1, 27+21+17+1, 27+21+19+17+1, 27+21+20+17+1, 27+22+1, 27+22+17+1, 27+22+18+1, 27+22+19+17+1, 27+22+19+18+1,

27+22+20+17+1, 27+22+20+18+1, 27+23+1, 27+23+17+1, 27+23+18+1, 27+23+19+17+1, 27+23+19+18+1, 27+23+20+17+1, 27+23+20+18+1, 27+24+1, 27+25+1, 27+25+17+1, 27+25+18+1, 27+25+19+17+1, 27+25+19+18+1, 27+25+20+17+1, 27+25+20+18+1, 27+25+21+1, 27+25+21+17+1, 27+25+21+19+17+1, 27+25+21+19+18+1, 27+25+21+20+17+1, 27+25+21+20+18+1, 27+25+22+1, 27+25+22+17+1, 27+25+22+18+1, 27+25+22+19+17+1, 27+25+22+19+18+1, 27+25+22+20+17+1, 27+25+22+20+18+1, 27+25+23+1, 27+25+23+17+1, 27+25+23+18+1, 27+25+23+19+17+1, 27+25+23+19+18+1, 27+25+23+20+17+1, 27+25+23+20+18+1, 27+25+24+1, 27+26+1, 27+26+17+1, 27+26+18+1, 27+26+19+17+1, 27+26+19+18+1, 27+26+20+17+1, 27+26+20+18+1, 27+26+21+1, 27+26+21+17+1, 27+26+21+19+17+1, 27+26+21+20+17+1, 27+26+22+1, 27+26+22+17+1, 27+26+22+18+1, 27+26+22+19+17+1, 27+26+22+19+18+1, 27+26+22+20+17+1, 27+26+22+20+18+1, 27+26+23+1, 27+26+23+17+1, 27+26+23+18+1, 27+26+23+19+17+1, 27+26+23+19+18+1, 27+26+23+20+17+1, 27+26+23+20+18+1, 27+26+24+1, 28+1, 28+21+1, 28+22+1, 28+23+1, 28+24+1; in the list above the numbers refer to the embodiments according to their numbering provided hereinabove whereas "+" indicates the dependency from another embodiment. The different individualized embodiments are separated by commas. In other words, "15+11+2+1" for example refers to embodiment 15) depending on embodiment 11), depending on embodiment 2), depending on embodiment 1), i.e. embodiment "15+11+2+1" corresponds to the compounds of formula (I) according to embodiment 1) further limited by all the features of the embodiments 2), 11), and 15).

30) A further embodiment relates to compounds of formula (I) which are selected from:

N-[1-(4-Chloro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;

N-[1-(4-Chloro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;

2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;

N-[1-(4-Chloro-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide;

N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;

2-(4-Isopropyl-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;

2-(4-Dimethylamino-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;

2-(4-Isopropyl-phenyl)-N-[1-(4-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide;

2-(4-Dimethylamino-phenyl)-N-[1-(4-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide;

N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;

N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;

2-(4-Dimethylamino-phenyl)-N-[1-(4-ethyl-benzyl)-1H-pyrazol-3-yl]-acetamide;

2-(4-Dimethylamino-phenyl)-N-[1-(4-isopropyl-benzyl)-1H-pyrazol-3-yl]-acetamide;

N-[1-(4-tert-Butyl-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;

N-[1-(4-Difluoromethoxy-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;

2-(4-Dimethylamino-phenyl)-N-[1-(4-trifluoromethoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;

N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;

2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-3-trifluoromethoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-3-trifluoromethyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(3,4,5-trifluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-3,5-dimethyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Chloro-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
N-[1-(4-Chloro-3-trifluoromethyl-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
N-[1-(3,5-Difluoro-4-methoxy-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-methoxy-3-trifluoromethyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-3-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3-Chloro-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(3-fluoro-4-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(4-ethyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(4-trifluoromethoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(3-fluoro-4-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(4-fluoro-3-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3-Chloro-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide;
2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(3,4,5-trifluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Chloro-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide;
N-[1-(4-Methoxy-benzyl)-1H-pyrazol-3-yl]-2-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
2-[4-(3,3-Difluoro-azetidin-1-yl)-phenyl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-azetidin-1-yl)-phenyl]-acetamide;
2-[4-(3,3-Difluoro-azetidin-1-yl)-phenyl]-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-[4-(3,3-Difluoro-azetidin-1-yl)-phenyl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Azetidin-1-yl-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Azetidin-1-yl-phenyl)-N-[1-(4-cyano-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Azetidin-1-yl-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
2-(4-Azetidin-1-yl-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((S)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-azetidin-1-yl)-phenyl]-acetamide;
2-(4-Cyclopropoxy-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Cyclopropoxy-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Cyclopropoxy-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;

N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((R)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-((R)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((R)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-azetidin-1-yl)-phenyl]-acetamide;
2-[4-(3-Fluoro-azetidin-1-yl)-phenyl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-((S)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((S)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
2-[4-(3,3-Difluoro-pyrrolidin-1-yl)-phenyl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-pyridin-2-yl-phenyl)-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-pyridin-3-yl-phenyl)-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-pyridin-4-yl-phenyl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-((R)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(5-methyl-pyrimidin-4-yl)-phenyl]-acetamide;
2-(4-Isopropyl-phenyl)-N-{1-[5-(2,2,2-trifluoro-ethoxy)-pyridin-2-ylmethyl]-1H-pyrazol-3-yl}-acetamide;
N-[1-(5-Bromo-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(5-Cyclopropyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(4-Isopropyl-phenyl)-N-[1-(5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(5-Isobutyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(6-Azetidin-1-yl-pyridin-3-yl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(5-Ethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(5-Isopropoxy-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(5-Fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(4-Isopropyl-phenyl)-N-[1-(5-trifluoromethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(6-Chloro-5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(4-Diethylamino-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Diethylamino-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(4-diethylamino-phenyl)-acetamide;
N-[1-(5-Cyano-6-ethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(6-Diethylamino-pyridin-3-yl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;

N-[1-(4-Methoxy-benzyl)-1H-pyrazol-3-yl]-2-{4-[(2-methoxy-ethyl)-methyl-amino]-phenyl}-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-{4-[(2-methoxy-ethyl)-methyl-amino]-phenyl}-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-{4-[(2-methoxy-ethyl)-methyl-amino]-phenyl}-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-{4-[(2-methoxy-ethyl)-methyl-amino]-phenyl}-acetamide;
N-[1-(5-Cyano-6-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-((R)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-((R)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
2-[6-(3,3-Difluoro-azetidin-1-yl)-pyridin-3-yl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-[6-(3,3-Difluoro-azetidin-1-yl)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isobutyl-phenyl)-acetamide;
N-[1-(5-Cyano-6-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-((S)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-((S)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(4-Chloro-5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(4-Cyclopropylmethyl-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3-fluoro-azetidin-1-yl)-pyridin-3-yl]-acetamide;
2-[6-(3-Fluoro-azetidin-1-yl)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-[6-(Cyclopropyl(methyl)amino)-pyridin-3-yl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-[6-(Cyclopropyl(methyl)amino)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(ethyl-methyl-amino)-pyridin-3-yl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-{6-[(2-methoxy-ethyl)-methyl-amino]-pyridin-3-yl}-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-{6-[(2-methoxy-ethyl)-methyl-amino]-pyridin-3-yl}-acetamide;
2-[6-(Cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[6-(cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-acetamide;
2-[6-(Cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-[6-(Cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(6-Diethylamino-pyridin-3-yl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3-Chloro-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-cyclopropyl-pyridin-3-yl)-acetamide;
N-[1-(4-Cyclopropoxy-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(4-cyclobutoxy-phenyl)-acetamide;
2-(4-Cyclobutoxy-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Cyclobutoxy-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Cyclobutoxy-phenyl)-N-[1-(5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;

N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-quinolin-7-yl-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1H-indol-6-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl)-acetamide;
N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(6-Chloro-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(3-methyl-2-oxo-2,3-dihydro-benzooxazol-6-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1H-indol-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-hydroxy-oxetan-3-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((R)-1-methoxy-ethyl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((S)-1-methoxy-ethyl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(5-methyl-[1,2,4]oxadiazol-3-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-[1,2,4]oxadiazol-3-yl-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-yloxy)-phenyl]-acetamide;
N-[1-(4-Bromo-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide;

N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[1-(4-cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[1-(4-cyano-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[1-(3-cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide;

N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-cyclobutyl-1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-isopropyl-1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1-methyl-3-trifluoromethyl-1H-indol-5-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(3-cyclobutyl-1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(3-isopropyl-1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide;
N-(1-(3-cyano-4-fluorobenzyl)-1H-pyrazol-3-yl)-2-(4-(pentafluoro-λ^6-sulfanyl)phenyl)acetamide ;
2-[4-(Cyano-dimethyl-methyl)-phenyl]-N-[1-(3-cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-(1-((5-cyanopyridin-2-yl)methyl)-1H-pyrazol-3-yl)-2-(4-(pentafluoro-λ^6-sulfanyl)phenyl)acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-trifluoromethyl-phenyl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(5-fluoro-6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(5-fluoro-6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-trifluoromethyl-phenyl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[1-(4-cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-[4-(1-Cyano-cyclopropyl)-phenyl]-N-[1-(3-cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;

N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[1-(6-cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-methyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenyl]-acetamide;
N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-methyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-methyl-3-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
and
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-((1S*,2S*)-2-trifluoromethyl-cyclopropyl)-phenyl]-acetamide.

31) A further embodiment relates to compounds of formula (I) which are selected from:
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-cyclopropyl)-phenyl]-acetamide;
N-[1-(5-Cyano-6-difluoromethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(5-cyano-4-difluoromethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3,3-dimethyl-2,3-dihydro-benzofuran-6-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-methyl-chroman-7-yl)-acetamide;
N-[1-(5-Cyano-3-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
2-[4-(1-Cyano-3,3-difluoro-cyclobutyl)-phenyl]-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
2-(3-Cyano-4-isobutyl-phenyl)-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
2-(3-Cyano-4-isobutyl-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(5-Azetidin-1-yl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(4-Isopropyl-phenyl)-N-[1-(5-pyrrolidin-1-yl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-{1-[5-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-2-ylmethyl]-1H-pyrazol-3-yl}-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-cyclopropylmethoxy-3-trifluoromethoxy-phenyl)-acetamide;
2-(4-Cyclopropylmethoxy-3-trifluoromethoxy-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;

N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;

2-(4-tert-Butyl-phenyl)-N-[1-(4-cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;

N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;

N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;

2-[4-(1-Cyano-cyclopropyl)-3-trifluoromethyl-phenyl]-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;

2-[4-(1-Cyano-cyclopropyl)-3-trifluoromethyl-phenyl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;

N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(3,3,3-trifluoro-propoxy)-phenyl]-acetamide;

N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-cyclopropyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;

N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-methyl-4-trifluoromethoxy-phenyl)-acetamide;

N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-cyclopropyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;

N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-cyclopropyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;

N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-methyl-4-trifluoromethoxy-phenyl)-acetamide;

N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-ethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;

N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-ethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;

N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-ethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;

N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3,5-dimethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;

N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3,5-dimethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;

N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3,5-dimethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;

N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[5-methyl-6-(2,2,2-trifluoro-ethoxy)-pyridin-3-yl]-acetamide;

N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[5-methyl-6-(2,2,2-trifluoro-ethoxy)-pyridin-3-yl]-acetamide;

N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(3,3,3-trifluoro-propoxy)-phenyl]-acetamide; and

N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(3,3,3-trifluoro-propoxy)-phenyl]-acetamide.

It is to be understood, that a stereogenic center in a compound disclosed above, which stereogenic center is not specifically assigned, may be in absolute (*R*)- or absolute (*S*)-configuration; for example a compound listed as N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-methyl-chroman-7-yl)-acetamide may be N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-((R)-3-methyl-chroman-7-yl)-acetamide, N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-((S)-3-methyl-chroman-7-yl)-acetamide or any mixture thereof.

The compounds of formula (I) according to embodiments 1) to 31) and their pharmaceutically acceptable salts can be used as medicaments, e.g. in the form of pharmaceutical compositions for enteral (such especially oral) or parenteral administration (including topical application or inhalation).

The production of the pharmaceutical compositions can be effected in a manner which will be familiar to any person skilled in the art (see for example Remington, *The Science and Practice of Pharmacy*, 21st Edition (2005), Part 5, "Pharmaceutical Manufacturing" [published by Lippincott Williams & Wilkins]) by bringing the described compounds of formula (I), or their pharmaceutically acceptable salts, optionally in combination with other therapeutically valuable substances, into a galenical administration form together with suitable, non-toxic, inert, therapeutically compatible solid or liquid carrier materials and, if desired, usual pharmaceutical adjuvants.

The present invention also relates to a method for the prevention or treatment of a disease or disorder mentioned herein comprising administering to a subject a pharmaceutically active amount of a compound of formula (I) as defined in any one of embodiments 1) to 31).

In a preferred embodiment of the invention, the administered amount is comprised between 1 mg and 1000 mg per day, particularly between 5 mg and 500 mg per day, more particularly between 25 mg and 400 mg per day, especially between 50 mg and 200 mg per day.

Whenever the word "between" is used to describe a numerical range, it is to be understood that the end points of the indicated range are explicitly included in the range. For example: if a temperature range is described to be between 40 °C and 80 °C, this means that the end points 40 °C and 80 °C are included in the range; or if a variable is defined as being an integer between 1 and 4, this means that the variable is the integer 1, 2, 3, or 4.

Unless used regarding temperatures, the term "about" (or alternatively the term "around") placed before a numerical value "X" refers in the current application to an interval extending from X minus 10% of X to X plus 10% of X, and preferably to an interval extending from X minus 5% of X to X plus 5% of X. In the particular case of temperatures, the term "about" placed before a temperature "Y" refers in the current application to an interval extending from the temperature Y minus 10 °C to Y plus 10 °C, and preferably to an interval extending from Y minus 5 °C to Y plus 5 °C.

For avoidance of any doubt, if compounds are described as useful for the prevention or treatment of certain diseases, such compounds are likewise suitable for use in the preparation of a medicament for the prevention or treatment of said diseases.

The compounds of formula (I) as defined in any one of embodiments 1) to 31) are useful for the prevention or treatment of diseases or disorders where calcium T channels are involved.

Such diseases or disorders where calcium T channels are involved may be defined as including especially:

- epilepsy (notably absence epilepsy, childhood absence and other forms of idiopathic generalized epilepsies, temporal lobe epilepsy);
- sleep disorders and sleep disturbances;
- pain (notably inflammatory pain, neuropathic pain, peripheral pain, chronic pain associated with peripheral axonal injury);
- neurological diseases and disorders (notably essential tremors, Parkinson's disease, schizophrenia, depression, anxiety, psychosis, neurodegenerative disorders, autism, drug addiction);
- cardiovascular diseases and disorders (notably hypertension, cardiac arrhythmias, atrial fibrillation, congenital heart failure, heart block);
- cancer;
- diabetes and diabetic neuropathy; and
- infertility and sexual dysfunction.

Notably such diseases or disorders where calcium T channels are involved refer to epilepsy, neurological disorders, and pain. Preferably such diseases or disorders refer to epilepsy and pain.

The term "epilepsy" describes recurrent unprovoked seizures wherein the term "seizure" refers to an excessive and/or hypersynchronous electrical neuronal activity. Different types of "epilepsy" are disclosed for example in [Berg et al., Epilepsia. **2010**; 51(4): 676-685], which reference is herewith incorporated by reference. The term "epilepsy" as used herein preferably refers to absence epilepsy, childhood absence and other forms of idiopathic generalized epilepsies, temporal lobe epilepsy.

The term "pain" preferably refers to inflammatory pain, neuropathic pain, peripheral pain, and chronic pain associated with peripheral axonal injury.

The term " neurological diseases and disorders " preferably refers to essential tremors, Parkinson's disease, schizophrenia, depression, anxiety, psychosis, neurodegenerative disorders, autism, drug addiction.

The term " cardiovascular diseases and disorders " preferably refers to hypertension, cardiac arrhythmias, atrial fibrillation, congenital heart failure, heart block.

The compounds of formula (I) as defined in embodiments 1) to 31) are also useful in a method of reducing the concentration of calcium in a neuronal cell, and wherein said reduction in calcium is achieved by blocking the

calcium T-channel present in such neuronal cell; said method comprising the administration of a compound of formula (I) as defined in embodiments 1) to 31).

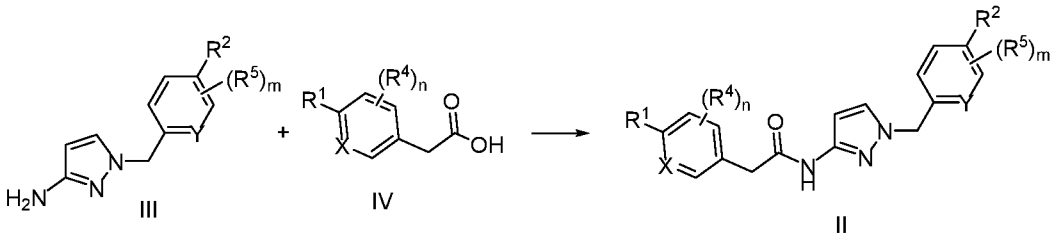
The compounds of formula (I) as defined in embodiments 1) to 31) are also useful in a method of decreasing burst firing discharges in a neuronal cell and wherein said decrease of burst firing is achieved by blocking the calcium T-channel; said method comprising the administration of a compound of formula (I) as defined in embodiments 1) to 31).

Preparation of compounds of formula (I):

The compounds of formula (I) can be prepared by the methods given below, by the methods given in the experimental part below or by analogous methods. Optimum reaction conditions may vary with the particular reactants or solvents used, but such conditions can be determined by a person skilled in the art by routine optimisation procedures. In the schemes below, the generic groups X, Y, R^1, R^2, $(R^4)_n$, and $(R^5)_m$ are as defined for the compounds of formula (I). In some instances the generic groups R^1, R^2, $(R^4)_n$, and $(R^5)_m$ may be incompatible with the assembly illustrated in the schemes and so will require the use of protecting groups (PG). The use of protecting groups is well known in the art (see for example "Protective Groups in Organic Synthesis", T.W. Greene, P.G.M. Wuts, Wiley-Interscience, 1999). For the purposes of this discussion, it will be assumed that such protecting groups as necessary are in place. In some cases the final product may be further modified, for example, by manipulation of substituents to give a new final product. These manipulations may include, but are not limited to, reduction, oxidation, alkylation, acylation, and hydrolysis reactions which are commonly known to those skilled in the art. The compounds obtained may also be converted into salts, especially pharmaceutically acceptable salts in a manner known *per se*.

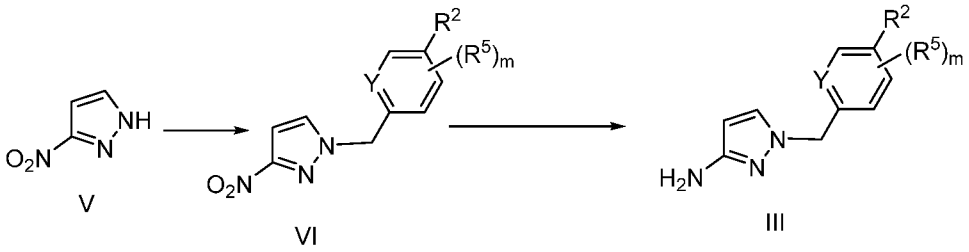
Compounds of general formula (II) can be prepared via an amide coupling as final step (Scheme 1). Generally, the corresponding carboxylic acid (IV) can be activated to the corresponding acid chloride, typically with oxalyl chloride. Alternatively, the carboxylic acid (IV) can be directly coupled to the amine (III) using a coupling reagent, typically HATU or HBTU. In certain instances two coupling products can be formed and are separated by preparative HPLC.

Scheme 1



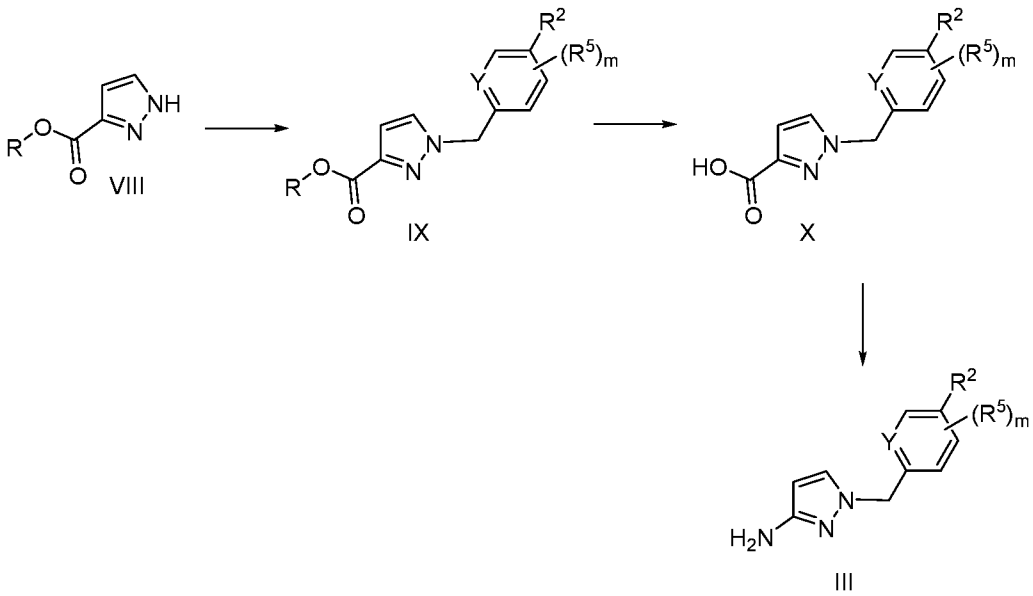
The desired primary aminopyrazole (III) can be prepared from nitropyrazole (V) through an alkylation (compound of type (VI)) and a reduction step. For the reduction step, zinc, iron or palladium are preferentially used.

Scheme 2



Aminopyrazoles of type (III) can be prepared via a Curtius rearrangement as well (Scheme 3). A suitable ester from the pyrazole-3-carboxylic acid (VIII) can be alkylated to compound (IX). Saponification leads to carboxylic acid (X), and subsequent Curtius rearrangement leads to the aminopyrazole (III).

Scheme 3

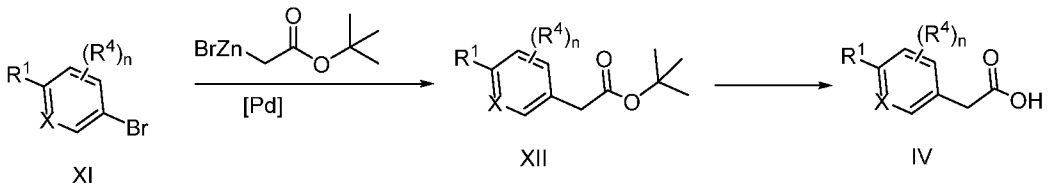


The corresponding benzyl chlorides, benzyl bromides, or benzyl mesylates necessary for the alkylation steps described in Schemes 2 (V → VI) and 3 (VIII → IX) can be prepared according to standard literature procedures or as described in the examples below.

The carboxylic acids of type (IV) can be prepared according to known procedures. In particular, a Negishi coupling (Scheme 4), or a similar carbon-carbon coupling between an (hetero)aryl bromide of type (XI) and (2-(tert-butoxy)-2-oxoethyl)zinc(II) bromide leads to the ester of type (XII): Hydrolysis, generally under acidic

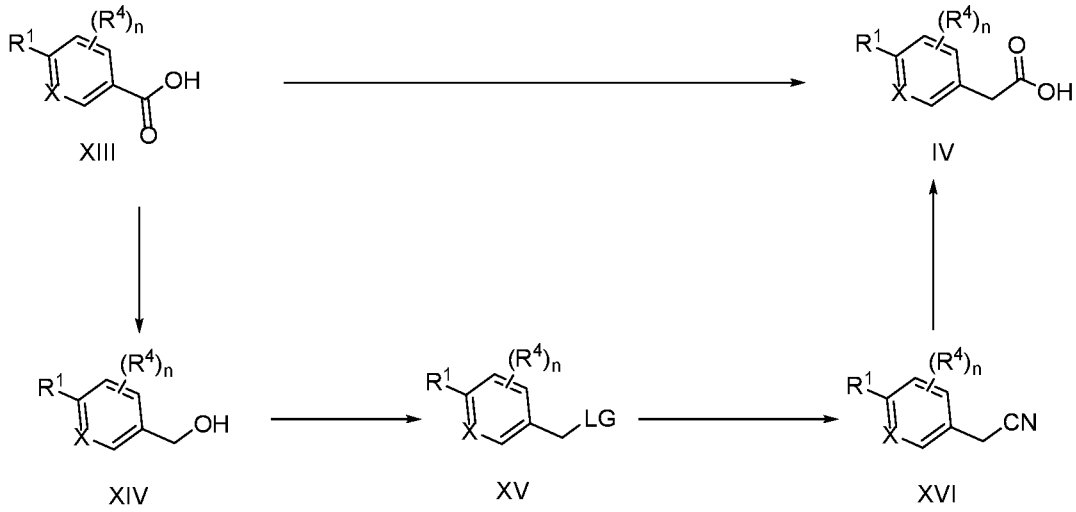
conditions, leads to the acid of type (IV). Bromide of type (XI) is either commercially available, or can be prepared according to known procedures (see experimental part).

Scheme 4



Alternatively, a benzoic acid of type (XIII) can be transformed into an acid of type (IV) via a Wolff rearrangement (Scheme 5). The acid of type (XIII) can be reduced to an alcohol of type (XIV). This alcohol can then be activated to a compound of type (XV), wherein LG represents a leaving group such as chloride, bromide, mesylate or tosylate, and homologated to nitrile of type (XVI): Hydrolysis would then lead to an acid of type (IV).

Scheme 5



Whenever the compounds of formula (I) are obtained in the form of mixtures of enantiomers, the enantiomers can be separated using methods known to one skilled in the art: e.g. by formation and separation of diastereomeric salts or by HPLC over a chiral stationary phase such as a Regis Whelk-O1(R,R) (10 μm) column, a Daicel ChiralCel OD-H (5-10 μm) column, or a Daicel ChiralPak IA (10 μm), IC (5 μm) or AD-H (5 μm) column. Typical conditions of chiral HPLC are an isocratic mixture of eluent A (EtOH, in presence or absence of an amine such as triethylamine or diethylamine) and eluent B (heptane), at a flow rate of 0.8 to 150 mL/min.

EXPERIMENTAL PART

The following examples illustrate the invention but do not at all limit the scope thereof.

Abbreviations: (as used herein and in the description above)

Ac	Acetyl
aq.	Aqueous
Bn	Benzyl
Bu	Butyl
CAS	Chemical abstract system
comb.	Combined
conc.	Concentrated
DavePhos	2-Dicyclohexylphosphino-2'-(N,N-dimethylamino)biphenyl (CAS 213697-53-1)
dba	Dibenzylideneacetone
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DIBAL	Diisobutylaluminium hydride
DIPEA	Diisopropylethylamine
Di-tBuXPhos	2-Di-tert-butylphosphino-2',4',6'-triisopropylbiphenyl (CAS 564483-19-8)
DMEM	Dulbecco's modified eagle's medium
DMF	N,N-Dimethylformamide
DMSO	Dimethylsulfoxide
EDTA	Ethylenediaminetetraacetic acid
eq.	Equivalent
Et	Ethyl
FC	Flash chromatography
h	Hour
HATU	1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate (CAS 148893-10-1)
HBTU	O-Benzotriazole-N,N,N',N'-tetramethyl-uronium-hexafluoro-phosphate (CAS 94790-37-1)
HPLC	High performance liquid chromatography
^{i}Bu	iso-butyl
^{i}Pr	iso-propyl
LC	Liquid chromatography
Me	Methyl
MH+	Mass of the protonated molecule
min	Minute
MS	Mass spectroscopy

NMR	Nuclear magnetic resonance
org.	Organic
PBS	Phosphate Buffered Saline
PEPPSI-IPr	1,3-Bis(2,6-diisopropylphenyl)imidazolidene)-(3-chloropyridyl)palladium(II)dichloride (CAS 905459-27-0)
Ph	Phenyl
Q-Phos	1,2,3,4,5-Pentaphenyl-1'-(di-tert-butylphosphino)ferrocene (CAS 312959-24-3)
rt	Room temperature
RuPhos	2-Dicyclohexylphosphino-2',6'-diisopropoxybiphenyl (CAS 787618-22-8)
sat.	saturated
sol	Solution
TBDMS	tert-Butyldimethylsilyl
tBu	tert-Butyl
TEA	Triethylamine
TFA	Trifluoroacetic acid
THF	tetrahydrofuran
TLC	Thin layer chromatography
t_R	Retention time
Xantphos	4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene (CAS 161265-03-8)
X-Phos	2-Dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (CAS 564483-18-7)

Preparation of Examples

General procedures

General procedure 1 for the preparation of acid chlorides. The desired carboxylic acid (1 eq.) is dissolved in toluene (5 mL/mmol). DMF (about 1 drop/mmol) and oxalyl chloride (1.5 eq.) are added, and the mixture is stirred at rt for 2 h. The solvents are removed under reduced pressure. The excess oxalyl chloride is removed azeotropically with toluene several times under reduced pressure. The residue is dried under high vacuum to yield the desired crude acid chloride.

General procedure 2 for an amide coupling. To a sol. of the desired amine (1 eq.) in dioxane (5 mL/mmol) is added the acid chloride (crude, 1.1 eq.) The mixture is heated to 60 °C to 90 °C for 1 h (or longer if the reaction is not complete). The mixture is allowed to cool to rt and the solvents are removed under reduced pressure. The residue is directly purified by automated FC, or by HPLC, to yield the desired product. Alternatively, the product can be isolated by crystallization.

General procedure 3 for an amide coupling. Unless indicated otherwise, a mixture of the desired carboxylic acid (1 eq.), the desired amine (1.5 eq), N-methylmorpholine (4 eq.) and HBTU (2 eq.) in DMF (around 20 mL / eq.) is stirred until the reaction is complete (a few hours to overnight). Other bases, coupling reagents and / or solvents can be used as well, see experimental details. The solvents are removed under reduced pressure. An aq. work-up (basic and / or acidic) is optionally realized. The residue is purified by automated FC, or by HPLC, to yield the desired product. Alternatively, the product can be isolated by crystallization.

General procedure 4 for the N-alkylation of 5-nitro-1H-pyrazole. K_2CO_3 or NaH is added to a sol. of 5-nitro-1H-pyrazole in acetone or DMF or THF. The mixture is stirred for 15-30 min. The desired electrophile and Bu_4NBr are added. The mixture is stirred efficiently at rt until the reaction is complete. The mixture is optionally filtered (if K_2CO_3 is used) or quenched with water (if NaH is used), and the filtrate is evaporated under reduced pressure. The residue is partitioned between water and EtOAc. The org. layer is dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC or by HPLC yields the desired product.

General procedure 5 for the reduction of a nitro group. Fe or Zn is added to a sol. of the starting material in EtOH or acetone with aq. sat. NH_4Cl. The mixture is heated to 75 °C and stirred at this temperature until the reaction is complete (about 1 h). The mixture is allowed to cool to rt and filtered through Celite®. The solvents were removed under reduced pressure to yield the desired crude product.

General procedure 6 for a Negishi coupling. A sol. of bromoaryl / bromoheteroaryl, (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O), palladium catalyst, and optionally a ligand in THF is stirred between rt and 90 °C until the starting materials are consumed. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Chromatographic purification yields the desired compound.

General procedure 7 for the hydrolysis of a tert-butyl ester. A sol. of the ester and an acid with optionally CH_2Cl_2 is prepared at 0 °C. This mixture is stirred between at 0 °C, optionally warming up to rt, until consumption of the starting material. The solvents are removed under reduced pressure to yield the crude desired compound.

General procedure 9 for the N-alkylation of a pyridine. A mixture of 2,5-dibromopyridine, an amine, and DBU in DMSO is stirred at 80 °C until the reaction is complete. The amine and DBU may have to be added several times. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Purification of the crude by FC yields the desired product.

Analytical conditions for LC-MS

Unless notified otherwise, the following conditions were used for analytical LC-MS data:

Conditions 1: Ascentis Express C18 2.7μm 2.1 x 30mm, 5% CH_3CN / 95% H_2O with 0.05% NH_4OH → 95% CH_3CN over 2.0 min, 1.4 mL/min.

Conditions 2: Waters Atlantis T3 column, C18, 5 μm, 4.6 x 30 mm, 5% CH_3CN / 95% H_2O with 0.04% TFA → 100% CH_3CN over 1.0 min, 4.5 mL/min.

Conditions 3: Zorbax SB-Aq column, 3.5 μm, 4.6 x 50 mm, 5% CH_3CN / 95% H_2O with 0.04% TFA → 100% CH_3CN over 1.0 min, 4.5 mL/min.

Conditions 4: Waters XBridge C18, 2.5 μm, 4.6 x 30 mm, 5% CH_3CN / 95% H_2O with 0.04% TFA → 100% CH_3CN over 1.0 min, 4.5 mL/min.

Preparative HPLC

Reaction mixture can often be separated by preparative HPLC. A person skilled in the art will find suitable conditions for each separation.

Automated FC

Classical flash chromatography is often replaced by automated systems. This does not change the separation process *per se*. A person skilled in the art will be able to replace a classical FC process by an automated one, and *vice versa*. Typical automated systems can be used, as they are provided by Büchi, Isco (Combiflash), or Biotage for instance.

tert-Butyl 2-(6-(dimethylamino)pyridin-3-yl)acetate. According to *general procedure* 6, with 5-bromo-2-(dimethylamino)pyridine (600 mg, 3.00 mmol), 2-*tert*-butoxy-2-oxoethylzinc chloride (0.5M in Et_2O, 9.0 mL, 4.5 mmol), $Pd_2(dba)_3$ (275 mg, 0.300 mmol), and Q-Phos (215 mg, 0.30 mmol) in THF (6.00 mL). The reaction is complete after 4 h at 70 °C. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.51 min, MH^+ = 237.09 (conditions 2).

2-(6-(Dimethylamino)pyridin-3-yl)acetic acid. According to *general procedure 7* with *tert*-butyl 2-(6-(dimethylamino)pyridin-3-yl)acetate (570 mg, 2.41 mmol), HCl (4M in dioxane, 10 mL) and CH_2Cl_2 (10 mL) at 0 °C. The mixture is stirred for 30 min at 0 °C, and for 9 h at rt. Removal of the solvents under reduced pressure yields the crude title compound. LC-MS: t_R = 0.27 min, MH^+ = 181.17 (conditions 2).

1-(4-Methoxybenzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* from K_2CO_3 (2.07 g, 15.0 mmol), 1-(chloromethyl)-4-methoxybenzene (0.405 mL, 3.00 mmol), 5-nitro-1H-pyrazole (339 mg, 3.00 mmol), and Bu_4NBr (197 mg, 0.60 mmol) in acetone (15 mL). The reaction is complete after 3.5 h. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title product. LC-MS: t_R = 0.81 min (conditions 3).

1-(4-Methoxybenzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* from Fe (powder, 592 mg, 10.7 mmol), 1-(3-methoxybenzyl)-3-nitro-1H-pyrazole (250 mg, 1.07 mmol), EtOH (10 mL), and aq. sat. NH_4Cl (1 mL). The reaction is complete after 4 h. This yields the crude title compound. LC-MS: t_R = 0.53 min, MH^+ = 204.47 (conditions 3).

1-(4-Methylbenzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* from K_2CO_3 (2.07 g, 15.0 mmol), 1-(chloromethyl)-4-methylbenzene (0.398 mL, 3.00 mmol), 5-nitro-1H-pyrazole (339 mg, 3.00 mmol), and Bu_4NBr (197 mg, 0.600 mmol) in acetone (15 mL). The reaction is complete after 3.5 h. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title product. LC-MS: t_R = 0.85 min (conditions 3).

1-(4-Methylbenzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* from Fe (powder, 592 mg, 10.7 mmol), 1-(4-methylbenzyl)-3-nitro-1H-pyrazole (233 mg, 1.07 mmol), EtOH (10 mL), and aq. sat. NH_4Cl (1 mL). The reaction is complete after 1 h. This yields the title compound. LC-MS: t_R = 0.57 min, MH^+ = 188.48 (conditions 3).

4-((3-Nitro-1H-pyrazol-1-yl)methyl)benzonitrile. Prepared according to *general procedure 4* from K_2CO_3 (2.07 g, 15.0 mmol), 4-(bromomethyl)benzonitrile (588 mg, 3.00 mmol), 5-nitro-1H-pyrazole (339 mg, 3.00 mmol), and Bu_4NBr (197 mg, 0.60 mmol) in acetone (15 mL). The reaction is complete after 3.5 h. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title product. LC-MS: t_R = 0.77 min (conditions 3).

4-((3-Amino-1H-pyrazol-1-yl)methyl)benzonitrile. Prepared according to *general procedure 5* from Fe (powder, 592 mg, 10.7 mmol), 4-((3-nitro-1H-pyrazol-1-yl)methyl)benzonitrile (245 mg, 1.07 mmol), EtOH (10 mL), and aq. sat. NH_4Cl (1 mL). The reaction is complete after 2.5 h. This yields the title compound. LC-MS: t_R = 0.51 min, MH^+ = 199.46 (conditions 3).

1-(4-Ethylbenzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (4.47 g, 32.3 mmol), 4-ethylbenzyl chloride (0.962 mL, 6.47 mmol), 5-nitro-1H-pyrazole (731 mg, 6.47 mmol), and Bu_4NBr (425 mg, 1.29 mmol) in acetone (45 mL). The reaction is complete after 24 h. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.89 min (conditions 3).

1-(4-Ethylbenzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (2.56 g, 46.3 mmol) and 1-(4-ethylbenzyl)-3-nitro-1H-pyrazole (1.07 g, 4.63 mmol) in EtOH (30 mL), and aq. sat. NH_4Cl (4 mL). The reaction is complete after 20 h and yields the crude title compound. LC-MS: t_R = 0.63 min, MH^+ = 202.29 (conditions 3).

1-(4-Isopropylbenzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (4.47 g, 32.3 mmol), 4-isopropylbenzyl chloride (0.718 mL, 6.47 mmol), 5-nitro-1H-pyrazole (731 mg, 6.47 mmol), and Bu_4NBr (425 mg, 1.29 mmol) in acetone (45 mL). The reaction is complete after 24 h. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.92 min (conditions 3).

1-(4-Isopropylbenzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (1.83 g, 33.0 mmol) and 1-(4-isopropylbenzyl)-3-nitro-1H-pyrazole (810 mg, 3.30 mmol) in EtOH (30 mL), and aq. sat.

NH_4Cl (4 mL). The reaction is complete after 20 h and yields the crude title compound. LC-MS: t_R = 0.67 min, MH^+ = 216.28 (conditions 3).

1-(4-(tert-Butyl)benzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (4.47 g, 32.3 mmol), 4-tert-butylbenzyl chloride (1.25 mL, 6.47 mmol), 5-nitro-1H-pyrazole (731 mg, 6.47 mmol), and Bu_4NBr (425 mg, 1.29 mmol) in acetone (45 mL). The reaction is complete after 24 h. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.95 min (conditions 3).

1-(4-(tert-Butyl)benzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (2.67 g, 48.2 mmol) and 1-(4-(tert-butyl)benzyl)-3-nitro-1H-pyrazole (1.25 g, 4.82 mmol) in EtOH (40 mL), and aq. sat. NH_4Cl (5 mL). The reaction is complete after 20 h and yields the crude title compound. LC-MS: t_R = 0.71 min, MH^+ = 230.21 (conditions 3).

1-(4-(Difluoromethoxy)benzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (4.47 g, 32.3 mmol), 4-difluoromethoxybenzyl chloride (1.25 mL, 6.47 mmol), 5-nitro-1H-pyrazole (731 mg, 6.47 mmol), and Bu_4NBr (425 mg, 1.29 mmol) in acetone (45 mL). The reaction is complete after 5 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.85 min (conditions 3).

1-(4-(Difluoromethoxy)benzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (2.77 g, 50.1 mmol) and 1-(4-(difluoromethoxy)benzyl)-3-nitro-1H-pyrazole (1.35 g, 5.01 mmol) in EtOH (40 mL), and aq. sat. NH_4Cl (5 mL). The reaction is complete after 45 min and yields the crude title compound. LC-MS: t_R = 0.60 min, MH^+ = 240.09 (conditions 3).

3-Nitro-1-(4-(trifluoromethoxy)benzyl)-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (4.47 g, 32.3 mmol), 4-trifluoromethoxylbenzyl chloride (1.36 g, 6.47 mmol), 5-nitro-1H-pyrazole (731 mg, 6.47 mmol), and Bu_4NBr (425 mg, 1.29 mmol) in acetone (45 mL). The reaction is complete after 24 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.90 min (conditions 3).

1-(4-(Trifluoromethoxy)benzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (2.25 g, 40.7 mmol) and 3-nitro-1-(4-(trifluoromethoxy)benzyl)-1H-pyrazole (1.17 g, 4.07 mmol) in EtOH (40 mL), and aq. sat. NH_4Cl (5 mL). The reaction is complete after 20 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.67 min, MH^+ = 257.94 (conditions 3).

1-(3,4-Difluorobenzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (4.47 g, 32.3 mmol), 4-(chloromethyl)-1,2-difluorobenzene (1.05 g, 6.47 mmol), 5-nitro-1H-pyrazole (731 mg, 6.47 mmol), and Bu_4NBr (425 mg, 1.29 mmol) in acetone (45 mL). The reaction is complete after 3 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.83 min (conditions 3).

1-(3,4-Difluorobenzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (2.73 g, 49.3 mmol) and 1-(3,4-difluorobenzyl)-3-nitro-1H-pyrazole (1.18 g, 4.93 mmol) in EtOH (40 mL), and aq. sat. NH_4Cl (4 mL). The reaction is complete after 5 days at 75 °C and yields the crude title compound. LC-MS: t_R = 0.56 min, MH^+ = 210.23 (conditions 3).

1-(3-Fluoro-4-(trifluoromethoxy)benzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (2.53 g, 18.3 mmol), 4-(bromomethyl)-2-fluoro-1-(trifluoromethoxy)benzene (1.00 g, 3.66 mmol), 5-nitro-1H-pyrazole (414 mg, 3.66 mmol), and Bu_4NBr (241 mg, 0.733 mmol) in acetone (45 mL). The reaction is complete after 5 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.90 min (conditions 3).

1-(3-Fluoro-4-(trifluoromethoxy)benzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (1.70 g, 30.8 mmol) and 1-(3-fluoro-4-(trifluoromethoxy)benzyl)-3-nitro-1H-pyrazole (940 mg, 3.08 mmol) in EtOH (40 mL), and aq. sat. NH_4Cl (4 mL). The reaction is complete after 4 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.69 min, MH^+ = 276.13 (conditions 3).

1-(3-Fluoro-4-(trifluoromethyl)benzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (4.47 g, 32.4 mmol), 4-(chloromethyl)-2-fluoro-1-(trifluoromethyl)benzene (1.38 g, 6.47 mmol), 5-nitro-1H-pyrazole (732 mg, 6.47 mmol), and Bu_4NBr (426 mg, 1.29 mmol) in acetone (45 mL). The reaction is complete after 24 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.89 min (conditions 3).

1-(3-Fluoro-4-(trifluoromethyl)benzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (2.33 g, 42.2 mmol) and 1-(3-fluoro-4-(trifluoromethyl)benzyl)-3-nitro-1H-pyrazole (1.22 g, 4.22 mmol) in EtOH (40 mL), and aq. sat. NH_4Cl (4 mL). The reaction is complete after 6 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.67 min, MH^+ = 260.11 (conditions 3).

3-Nitro-1-(3,4,5-trifluorobenzyl)-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (4.47 g, 32.4 mmol), 3,4,5-trifluorobenzyl chloride (1.17 g, 6.47 mmol), 5-nitro-1H-pyrazole (732 mg, 6.47 mmol), and Bu_4NBr (426 mg, 1.29 mmol) in acetone (45 mL). The reaction is complete after 24 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.85 min (conditions 3).

1-(3,4,5-Trifluorobenzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (2.45 g, 44.3 mmol) and 3-nitro-1-(3,4,5-trifluorobenzyl)-1H-pyrazole (1.14 g, 4.43 mmol) in EtOH (40 mL), and aq. sat. NH_4Cl (4 mL). The reaction is complete after 6 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.60 min, MH^+ = 228.16 (conditions 3).

1-(4-Fluoro-3,5-dimethylbenzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (3.18 g, 23.0 mmol), 4-fluoro-3,5-dimethylbenzyl bromide (1.00 g, 4.61 mmol), 5-nitro-1H-pyrazole (521 mg, 4.61 mmol), and Bu_4NBr (303 mg, 0.921 mmol) in acetone (45 mL). The reaction is complete after 30 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.90 min (conditions 3).

1-(4-Fluoro-3,5-dimethylbenzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (2.44 g, 44.1 mmol) and 1-(4-fluoro-3,5-dimethylbenzyl)-3-nitro-1H-pyrazole (1.10 g, 4.41 mmol) in EtOH (40 mL), and aq. sat. NH_4Cl (4 mL). The reaction is complete after 30 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.64 min, MH^+ = 220.24 (conditions 3).

1-(4-Chloro-3-fluorobenzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (1.55 g, 11.2 mmol), 4-chloro-3-fluorobenzyl bromide (500 mg, 2.24 mmol), 5-nitro-1H-pyrazole (253 mg, 2.24 mmol), and Bu_4NBr (147 mg, 0.447 mmol) in acetone (11 mL). The reaction is complete after 4 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.86 min (conditions 2).

1-(4-Chloro-3-fluorobenzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (876 mg, 15.8 mmol) and 1-(4-chloro-3-fluorobenzyl)-3-nitro-1H-pyrazole (405 mg, 1.58 mmol) in EtOH (30 mL), and aq. sat. NH_4Cl (4 mL). The reaction is complete after 18 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.61 min, MH^+ = 226.13 (conditions 3).

1-(4-Chloro-3-(trifluoromethoxy)benzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (1.55 g, 11.2 mmol), 4-chloro-3-trifluoromethoxybenzyl bromide (648 mg, 2.24 mmol), 5-nitro-1H-pyrazole (253 mg, 2.24 mmol), and Bu_4NBr (147 mg, 0.447 mmol) in acetone (11 mL). The reaction is complete after 4 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.95 min (conditions 2).

1-(4-Chloro-3-(trifluoromethoxy)benzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (1.01 g, 18.3 mmol) and 1-(4-chloro-3-(trifluoromethoxy)benzyl)-3-nitro-1H-pyrazole (587 mg, 1.83 mmol) in EtOH (30 mL), and aq. sat. NH_4Cl (4 mL). The reaction is complete after 18 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.73 min, MH^+ = 292.16 (conditions 3).

1-(4-Chloro-3-(trifluoromethyl)benzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (1.55 g, 11.2 mmol), 4-chloro-3-trifluoromethylbenzyl bromide (612 mg, 2.24 mmol), 5-nitro-1H-pyrazole (253 mg, 2.24 mmol), and Bu_4NBr (147 mg, 0.447 mmol) in acetone (11 mL). The reaction is complete after 4 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.92 min (conditions 2).

1-(4-Chloro-3-(trifluoromethyl)benzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (1.24 g, 22.4 mmol) and 1-(4-chloro-3-(trifluoromethyl)benzyl)-3-nitro-1H-pyrazole (684 mg, 2.24 mmol) in EtOH (30 mL), and aq. sat. NH_4Cl (4 mL). The reaction is complete after 18 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.71 min, MH^+ = 276.12 (conditions 3).

1-(3,5-Difluoro-4-methoxybenzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (1.55 g, 11.2 mmol), 3,5-difluoro-4-methoxybenzyl bromide (530 mg, 2.24 mmol), 5-nitro-1H-pyrazole (253 mg, 2.24 mmol), and Bu_4NBr (147 mg, 0.447 mmol) in acetone (11 mL). The reaction is complete after 4 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.83 min (conditions 2).

1-(3,5-Difluoro-4-methoxybenzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (980 mg, 17.7 mmol) and 1-(3,5-difluoro-4-methoxybenzyl)-3-nitro-1H-pyrazole (477 mg, 1.77 mmol) in EtOH (30 mL), and aq. sat. NH_4Cl (4 mL). The reaction is complete after 4 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.59 min, MH^+ = 240.11 (conditions 3).

1-(4-Methoxy-3-(trifluoromethyl)benzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (1.55 g, 11.2 mmol), 4-methoxy-3-trifluorobenzyl bromide (530 mg, 2.24 mmol), 5-nitro-1H-pyrazole (253 mg, 2.24 mmol), and Bu_4NBr (147 mg, 0.447 mmol) in acetone (11 mL). The reaction is complete after 17 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.87 min (conditions 2).

1-(4-Methoxy-3-(trifluoromethyl)benzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (947 mg, 17.1 mmol) and 1-(4-methoxy-3-(trifluoromethyl)benzyl)-3-nitro-1H-pyrazole (516 mg, 1.71 mmol) in EtOH (30 mL), and aq. sat. NH_4Cl (4 mL). The reaction is complete after 1 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.66 min, MH^+ = 272.16 (conditions 3).

1-(4-Fluoro-3-methylbenzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (3.51 g, 25.4 mmol), 4-fluoro-3-methylbenzyl bromide (1.03 g, 5.08 mmol), 5-nitro-1H-pyrazole (574 mg, 5.08 mmol), and Bu_4NBr (334 mg, 1.02 mmol) in acetone (45 mL). The reaction is complete after 8 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.86 min (conditions 3).

1-(4-Fluoro-3-methylbenzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (2.45 g, 44.2 mmol) and 1-(4-fluoro-3-methylbenzyl)-3-nitro-1H-pyrazole (1.04 g, 4.42 mmol) in EtOH (40 mL), and aq. sat. NH_4Cl (4 mL). The reaction is complete after 20 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.59 min, MH^+ = 206.27 (conditions 3).

1-(3-Chloro-4-fluorobenzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (3.51 g, 25.4 mmol), 3-chloro-4-fluorobenzyl chloride (909 mg, 5.08 mmol), 5-nitro-1H-pyrazole (574 mg, 5.08 mmol), and Bu_4NBr (334 mg, 1.02 mmol) in acetone (45 mL). The reaction is complete after 8 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.86 min (conditions 3).

1-(3-Chloro-4-fluorobenzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (433 mg, 7.82 mmol) and 1-(3-chloro-4-fluorobenzyl)-3-nitro-1H-pyrazole (200 mg, 0.782 mmol) in EtOH (20 mL), and aq. sat. NH_4Cl (2 mL). The reaction is complete after 20 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.61 min, MH^+ = 226.12 (conditions 3).

1-(3-Fluoro-4-methylbenzyl)-3-nitro-1H-pyrazole. Prepared according to *general procedure 4* with K_2CO_3 (3.51 g, 25.4 mmol), 3-fluoro-4-methylbenzyl chloride (805 mg, 5.08 mmol), 5-nitro-1H-pyrazole (574 mg, 5.08 mmol), and Bu_4NBr (334 mg, 1.02 mmol) in acetone (45 mL). The reaction is complete after 3 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.86 min (conditions 3).

1-(3-Fluoro-4-methylbenzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (2.21 g, 40.0 mmol) and 1-(3-fluoro-4-methylbenzyl)-3-nitro-1H-pyrazole (940 mg, 4.00 mmol) in EtOH (40 mL), and aq. sat. NH_4Cl (4 mL). The reaction is complete after 2 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.59 min, MH^+ = 206.26 (conditions 3).

6-((3-Nitro-1H-pyrazol-1-yl)methyl)nicotinonitrile. Prepared according to *general procedure 4* with K_2CO_3 (3.51 g, 25.4 mmol), 6-(bromomethyl)nicotinonitrile (1000 mg, 5.08 mmol), 5-nitro-1H-pyrazole (574 mg, 5.08 mmol), and Bu_4NBr (334 mg, 1.02 mmol) in acetone (45 mL). The reaction is complete after 3 days at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.67 min (conditions 3).

6-((3-Amino-1H-pyrazol-1-yl)methyl)nicotinonitrile. Prepared according to *general procedure 5* with Fe (1.05 g, 18.5 mmol) and 6-((3-nitro-1H-pyrazol-1-yl)methyl)nicotinonitrile (425 mg, 1.85 mmol) in EtOH (30 mL), and aq. sat. NH_4Cl (3 mL). The reaction is complete after 1 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.40 min, MH^+ = 200.28 (conditions 3).

5-Methoxy-2-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine. Prepared according to *general procedure 4* with K_2CO_3 (4.39 g, 31.7 mmol), 2-(chloromethyl)-5-methoxypyridine (1000 mg, 6.35 mmol), 5-nitro-1H-pyrazole (717 mg, 6.35 mmol), and Bu_4NBr (417 mg, 1.27 mmol) in acetone (45 mL). The reaction is complete after 3 days at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.66 min (conditions 3).

1-((5-Methoxypyridin-2-yl)methyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (1.36 g, 24.6 mmol) and 5-methoxy-2-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine (575 mg, 2.46 mmol) in EtOH

(20 mL), and aq. sat. NH_4Cl (3 mL). The reaction is complete after 18 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.38 min, MH^+ = 205.28 (conditions 3).

The following examples were prepared according to general procedures 1 and 2, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
1	N-[1-(4-Chloro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide	1.42 min; 368.16; conditions 1
2	N-[1-(4-Chloro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide	1.22 min; 369.15; conditions 1
3	2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	1.13 min; 353.18; conditions 1
4	2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.53 min; 354.18; conditions 2
5	N-[1-(4-Chloro-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide	0.57 min; 370.11; conditions 2
6	N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide	1.33 min; 352.18; conditions 1
7	2-(4-Isopropyl-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.92 min; 364.30; conditions 3
8	2-(4-Dimethylamino-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.62 min; 365.25; conditions 3
9	2-(4-Isopropyl-phenyl)-N-[1-(4-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide	0.95 min; 348.30; conditions 3
10	2-(4-Dimethylamino-phenyl)-N-[1-(4-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide	0.65 min; 349.30; conditions 3
11	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide	0.90 min; 359.26; conditions 3
12	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide	0.59 min; 360.31; conditions 3

13	2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(4-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide	0.64 min; 350.26; conditions 3
14	2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.61 min; 366.32; conditions 3
15	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide	0.59 min; 361.28; conditions 3
16	2-(4-Dimethylamino-phenyl)-N-[1-(4-ethyl-benzyl)-1H-pyrazol-3-yl]-acetamide	0.69 min; 363.19; conditions 3
17	2-(4-Dimethylamino-phenyl)-N-[1-(4-isopropyl-benzyl)-1H-pyrazol-3-yl]-acetamide	0.72 min; 377.16; conditions 3
18	N-[1-(4-tert-Butyl-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide	0.75 min; 391.21; conditions 3
19	N-[1-(4-Difluoromethoxy-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide	0.67 min; 401.07; conditions 3
20	2-(4-Dimethylamino-phenyl)-N-[1-(4-trifluoromethoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.71 min; 419.18; conditions 3
21	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide	0.64 min; 371.12; conditions 3
22	2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-3-trifluoromethoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.72 min; 437.17; conditions 3
23	2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-3-trifluoromethyl-benzyl)-1H-pyrazol-3-yl]-acetamide	0.70 min; 421.17; conditions 3
24	2-(4-Dimethylamino-phenyl)-N-[1-(3,4,5-trifluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.66 min; 389.10; conditions 3
25	2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-3,5-dimethyl-benzyl)-1H-pyrazol-3-yl]-acetamide	0.70 min; 381.15; conditions 3
26	N-[1-(4-Chloro-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide	0.67 min; 387.04; conditions 3
27	N-[1-(4-Chloro-3-trifluoromethyl-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide	0.72 min; 437.18; conditions 3

28	N-[1-(3,5-Difluoro-4-methoxy-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide	0.65 min; 401.08; conditions 3
29	2-(4-Dimethylamino-phenyl)-N-[1-(4-methoxy-3-trifluoromethyl-benzyl)-1H-pyrazol-3-yl]-acetamide	0.70 min; 433.16; conditions 3
30	2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-3-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide	0.66 min; 367.1; conditions 3
31	N-[1-(3-Chloro-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide	0.67 min; 387.11; conditions 3
32	2-(4-Dimethylamino-phenyl)-N-[1-(3-fluoro-4-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide	0.66 min; 367.13; conditions 3
33	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide	0.53 min; 361.07; conditions 3
34	N-[1-(4-Chloro-3-trifluoromethoxy-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide	0.74 min; 453.17; conditions 3
35	2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(4-ethyl-benzyl)-1H-pyrazol-3-yl]-acetamide	0.68 min; 364.18; conditions 3
36	N-[1-(4-Difluoromethoxy-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide	0.66 min; 401.95; conditions 3
37	2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(4-trifluoromethoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.70 min; 420.16; conditions 3
38	2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(3-fluoro-4-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide	0.66 min; 368.13; conditions 3
39	2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(4-fluoro-3-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide	0.65 min; 368.13; conditions 3
40	N-[1-(3-Chloro-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide	0.66 min; 388.08; conditions 3
41	2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(3,4,5-trifluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.65 min; 390.09; conditions 3
42	N-[1-(4-Chloro-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide	0.66 min; 388.06; conditions 3

43	N-[1-(3,5-Difluoro-4-methoxy-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide	0.65 min; 401.91; conditions 3
44	2-(4-Dimethylamino-phenyl)-N-[1-(5-methoxy-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.51 min; 366.12; conditions 3
45	N-[1-(4-Methoxy-benzyl)-1H-pyrazol-3-yl]-2-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.90 min; 420.16; conditions 3
46	N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.90 min; 408.10; conditions 3
47	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.88 min; 415.15; conditions 3

2-(6-Bromopyridin-3-yl)acetic acid. 2-(6-Bromopyridin-3-yl)acetonitrile (370 mg, 1.88 mmol) is diluted in conc. aq. HCl (2.8 mL), and the mixture was stirred at 100 °C for 90 min. The mixture is allowed to cool to rt and was thoroughly evaporated under reduced pressure. Water is added. The mixture is filtered to isolate the crude title product. LC-MS: t_R = 0.54 min, MH^+ = 214.96 (conditions 3).

2-(6-Bromopyridin-3-yl)-N-(1-(4-fluorobenzyl)-1H-pyrazol-3-yl)acetamide was prepared according to *general procedure 3*, starting from 2-(6-bromopyridin-3-yl)acetic acid (286 mg, 1.32 mmol) and 1-(4-fluorobenzyl)-1H-pyrazol-3-amine (253 mg, 1.32 mmol). LC-MS: t_R = 0.80 min, MH^+ = 388.96 (conditions 3).

Example 48, 2-[6-(Ethyl-methyl-amino)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide. 2-(6-Bromopyridin-3-yl)-N-(1-(4-fluorobenzyl)-1H-pyrazol-3-yl)acetamide (50 mg, 0.13 mmol) is dissolved in toluene (3.0 mL), and the sol. is heated to 100 °C. $Pd_2(dba)_3$ (2.4 mg, 0.0026 mmol), chloro(2-dicyclohexylphosphino-2',6'-di-i-propoxy-1,1'-biphenyl)[2-(2-aminoethylphenyl)]palladium(II), methyl-t-butylether adduct (CAS 1028206-60-1, 37 mg, 0.051 mmol), NaO^tBu (19 mg, 0.19 mmol) and a sol. of ethylmethylamine (9.1 mg, 0.15 mmol) in toluene (1.0 mL) are added. The mixture is stirred at 100 °C for 1.5 h, and is allowed to cool to rt. The solvents are removed under reduced pressure, and the residue is mixed with CH_3CN (1.0 mL), water (2 drops) and Et_3N (2 drops). The mixture is filtered, and the filtrate is purified by HPLC to yield Example 48. LC-MS: t_R = 0.64 min, MH^+ = 368.01 (conditions 3).

Ethyl 2-(4-(3,3-difluoroazetidin-1-yl)phenyl)acetate. Xantphos (24 mg, 0.041 mmol), $Pd(OAc)_2$ (7 mg, 0.03 mmol) and Cs_2CO_3 (670 mg, 2.06 mmol) are added to a sol. of ethyl 4-bromophenylacetate (250 mg, 1.03 mmol) in toluene (8 mL). The mixture is heated rapidly to 100 °C, and 3,3-difluoroazetidine hydrochloride (266 mg, 2.06 mmol) is added. The mixture is stirred for 18 h at 100 °C, and is allowed to cool to rt. The mixture is filtered through Celite®, and the solvents are removed under reduced pressure. Purification of the crude by

automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.89 min, MH^+ = 297.22 (conditions 3).

2-(4-(3,3-Difluoroazetidin-1-yl)phenyl)acetic acid. A sol. of ethyl 2-(4-(3,3-difluoroazetidin-1-yl)phenyl)acetate (115 mg, 0.451 mmol) in EtOH (2 mL) and aq. 2.5M NaOH (2 mL) is stirred at rt for 18 h. The solvents are partially removed under reduced pressure, and the residue is suspended in CH_2Cl_2 (50 mL). This mixture is washed with aq. 1M HCl, and the phases are separated. The org. layer is dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude, title compound. LC-MS: t_R = 0.72 min, MH^+ = 269.16 (conditions 3).

Ethyl 2-(4-(azetidin-1-yl)phenyl)acetate. Xantphos (48 mg, 0.082 mmol), $Pd(OAc)_2$ (14 mg, 0.062 mmol) and Cs_2CO_3 (1.34 g, 4.11 mmol) are added to a sol. of ethyl 4-bromophenylacetate (500 mg, 2.06 mmol) in toluene (8 mL). The mixture is heated rapidly to 100 °C, and azetidine hydrochloride (0.28 mL, 4.11 mmol) is added. The mixture is stirred for 4 h at 100 °C, and is allowed to cool to rt. The mixture is filtered through Celite®, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.60 min, MH^+ = 220.26 (conditions 3).

2-(4-(Azetidin-1-yl)phenyl)acetic acid. A sol. of ethyl 2-(4-(azetidin-1-yl)phenyl)acetate (150 mg, 0.684 mmol) in EtOH (1 mL) and aq. 2.5M NaOH (1 mL) is stirred at rt for 18 h. The solvents are partially removed under reduced pressure, and the residue is suspended in CH_2Cl_2 (50 mL). This mixture is washed with aq. 1M HCl, and the phases are separated. The org. layer is dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude, title compound. LC-MS: t_R = 0.40 min (conditions 3).

2-Fluoro-4-((3-nitro-1H-pyrazol-1-yl)methyl)benzonitrile. Prepared according to *general procedure 4* with K_2CO_3 (3.23 g, 23.4 mmol), 4-cyano-3-fluorobenzylbromide (1000 mg, 4.67 mmol), 5-nitro-1H-pyrazole (528 mg, 4.67 mmol), and Bu_4NBr (301 mg, 0.934 mmol) in acetone (40 mL). The reaction is complete after 20 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 5:95 → 10:90 → 15:85 → 25:75 → 35:65, 20 g silicagel, flow 20 mL/min) yields the title compound. LC-MS: t_R = 0.79 min (conditions 3).

4-((3-Amino-1H-pyrazol-1-yl)methyl)-2-fluorobenzonitrile. Prepared according to *general procedure 5* with Fe (2.00 g, 36.1 mmol) and 2-fluoro-4-((3-nitro-1H-pyrazol-1-yl)methyl)benzonitrile (890 mg, 3.61 mmol) in EtOH (40 mL), and aq. sat. NH_4Cl (8 mL). The reaction is complete after 1 h at 75 °C and yields the crude title compound. LC-MS: t_R = 0.55 min, MH^+ = 217.24 (conditions 3).

2-(6-(2,2,2-Trifluoroethoxy)pyridin-3-yl)acetic acid. 2-Chloropyridine-5-acetic acid (343 mg, 2.00 mmol) is added to a solution of NaH (65% in oil, 400 mg, about 10 mmol) in trifluoroethanol (4 mL). The mixture is stirred in a microwave oven at 160 °C for 7 h, and is allowed to cool to rt. The mixture is diluted with water

and the pH is adjusted to 3. Removing the solvents under reduced pressure and drying the residue under high vacuum yields the crude title product. LC-MS: t_R = 0.62 min, MH^+ = 236.18 (conditions 2).

(S)-Ethyl 2-(4-(3-fluoropyrrolidin-1-yl)phenyl)acetate. Xantphos (29 mg, 0.049 mmol), $Pd(OAc)_2$ (9 mg, 0.04 mmol) and Cs_2CO_3 (1.20 g, 3.7 mmol) are added to a sol. of ethyl 4-bromophenylacetate (300 mg, 1.23 mmol) in toluene (10 mL) at rt. The mixture is rapidly heated to 100 °C, and (S)-3-fluoropyrrolidine (310 mg, 2.47 mmol) is added. The mixture is stirred for 3 h at 100 °C, and is allowed to cool to rt. The mixture is filtered through Celite®, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 20 g silicagel, flow 16 mL/min) yields the title compound. LC-MS: t_R = 0.88 min, MH^+ = 252.14 (conditions 3).

(S)-2-(4-(3-Fluoropyrrolidin-1-yl)phenyl)acetic acid. A mixture of (S)-ethyl 2-(4-(3-fluoropyrrolidin-1-yl)phenyl)acetate (76 mg, 0.302 mmol) in EtOH (2.0 mL) and aq. 1M NaOH (1.0 mL) is stirred at rt for 2 h. The solvents are removed under reduced pressure, and the residue is diluted with CH_2Cl_2. The mixture is cooled to 0 °C, and aq. 1M HCl is added to pH3. The phases are separated in a Separator® (Biotage) to yield the crude title product. LC-MS: t_R = 0.70 min, MH^+ = 224.22 (conditions 3).

Ethyl 2-(4-(3-fluoroazetidin-1-yl)phenyl)acetate. Xantphos (29 mg, 0.049 mmol), $Pd(OAc)_2$ (9 mg, 0.04 mmol) and Cs_2CO_3 (1.20 g, 3.70 mmol) are added to a sol. of ethyl 4-bromophenylacetate (300 mg, 1.23 mmol) in toluene (10 mL) at rt. The mixture is rapidly heated to 100 °C, and 3-fluoroazetidine hydrochloride (275 mg, 2.47 mmol) is added. The mixture is stirred for 24 h at 100 °C, and is allowed to cool to rt. The mixture is filtered through Celite, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 20 g silicagel, flow 16 mL/min) yields the title compound. LC-MS: t_R = 0.84 min, MH^+ = 238.14 (conditions 3).

2-(4-(3-Fluoroazetidin-1-yl)phenyl)acetic acid. A mixture of ethyl 2-(4-(3-fluoroazetidin-1-yl)phenyl)acetate (130 mg, 0.548 mmol) in EtOH (2.0 mL) and aq. 1M NaOH (1.0 mL) is stirred at rt for 2 h. The solvents are removed under reduced pressure, and the residue is diluted with CH_2Cl_2. The mixture is cooled to 0 °C, and aq. 1M HCl is added to pH3. The phases are separated in a Separator® (Biotage) to yield the crude title product. LC-MS: t_R = 0.64 min, MH^+ = 210.32 (conditions 3).

Methyl 2-(4-(vinyloxy)phenyl)acetate. A mixture of methyl-4-hydroxyphenylacetate (1.66 g, 10 mmol), vinyl acetate (1.84 mL, 20.0 mmol), chloro(1,5-cyclooctadiene)iridium(I) dimer (133 mg, 0.20 mmol), and Na_2CO_3 (636 mg, 6.00 mmol) in toluene (10 mL) is stirred at 100 °C for 2.5 h. Subsequently, water is added, and the mixture is extracted with EtOAc. The combined org. layers are washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by automated FC (Biotage, 50 g silicagel, EtOAc / heptane 1:9 → 4:6, 50 mL/min) yields the title compound. LC-MS: t_R = 0.83 min (conditions 3).

Methyl 2-(4-cyclopropoxyphenyl)acetate. At -5°C Et_2Zn (1.0 M in hexanes, 4.8 mL, 4.8 mmol) is added to a sol. of methyl 2-(4-(vinyloxy)phenyl)acetate (384 mg, 2.00 mmol) and CH_2ClI (0.525 mL, 7.20 mmol) in CH_2Cl_2

(15.2 mL). The mixture is stirred between -5 °C and 0 °C for 4 h, and is quenched with aq. sat. NH_4Cl. The mixture is extracted with EtOAc. The combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Biotage, 25 g silicagel, EtOAc / heptane 1:19 → 4:6, 25 mL/min) yields the title compound. LC-MS: t_R = 0.84 min (conditions 3).

2-(4-Cyclopropoxyphenyl)acetic acid. A sol. of methyl 2-(4-cyclopropoxyphenyl)acetate (364 mg, 1.76 mmol) and $LiOH \cdot H_2O$ (111 mg, 2.65 mmol) in THF / MeOH / H_2O (3:1:1) (10 ml) is stirred at 0 °C for 3 h. The mixture is acidified with aq. 1 M HCl to pH 3 and extracted with EtOAc. The combined org. layers are washed with brine, dried over $MgSO_4$, and filtered. Removing the solvents under reduced pressure yields the crude title compound. LC-MS: t_R = 0.71 min (conditions 3).

Ethyl 2-(4-(3,3-difluoropyrrolidin-1-yl)phenyl)acetate. Xantphos (29 mg, 0.049 mmol), $Pd(OAc)_2$ (9 mg, 0.04 mmol) and Cs_2CO_3 (1.20 g, 3.70 mmol) are added to a sol. of ethyl 4-bromophenylacetate (300 mg, 1.23 mmol) in toluene (10 mL) at rt. The mixture is rapidly heated to 100 °C, and 3,3-difluoropyrrolidine (354 mg, 2.47 mmol) is added. The mixture is stirred for 48 h at 100 °C, and is allowed to cool to rt. The mixture is filtered through Celite®, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 20 g silicagel, flow 16 mL/min) yields the title compound. LC-MS: t_R = 0.92 min, MH^+ = 270.20 (conditions 3).

2-(4-(3,3-Difluoropyrrolidin-1-yl)phenyl)acetic acid. A mixture of ethyl 2-(4-(3,3-difluoropyrrolidin-1-yl)phenyl)acetate (68 mg, 0.25 mmol) in EtOH (2.0 mL) and aq. 1M NaOH (1.0 mL) is stirred at rt for 1 h. The solvents are removed under reduced pressure, and the residue is diluted with CH_2Cl_2. The mixture is cooled to 0 °C, and aq. 1M HCl is added to pH3. The phases are separated in a Separator® (Biotage) to yield the crude title product. LC-MS: t_R = 0.77 min, MH^+ = 241.92 (conditions 3).

(R)-Ethyl 2-(4-(3-fluoropyrrolidin-1-yl)phenyl)acetate. Xantphos (29 mg, 0.049 mmol), $Pd(OAc)_2$ (9 mg, 0.04 mmol) and Cs_2CO_3 (1.20 g, 3.70 mmol) are added to a sol. of ethyl 4-bromophenylacetate (300 mg, 1.23 mmol) in toluene (10 mL) at rt. The mixture is rapidly heated to 100 °C, and (R)-3-fluoropyrrolidine (310 mg, 2.47 mmol) is added. The mixture is stirred for 18 h at 100 °C, and is allowed to cool to rt. The mixture is filtered through Celite®, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 20 g silicagel, flow 16 mL/min) yields the title compound. LC-MS: t_R = 0.88 min, MH^+ = 252.18 (conditions 3).

(R)-2-(4-(3-Fluoropyrrolidin-1-yl)phenyl)acetic acid. A mixture of (R)-ethyl 2-(4-(3-fluoropyrrolidin-1-yl)phenyl)acetate (250 mg, 1.00 mmol) in EtOH (2.0 mL) and aq. 1M NaOH (1.0 mL) is stirred at rt for 2 h. The solvents are removed under reduced pressure, and the residue is diluted with CH_2Cl_2. The mixture is cooled to 0 °C, and aq. 1M HCl is added to pH3. The phases are separated in a Separator® (Biotage) to yield the crude title product. LC-MS: t_R = 0.70 min, MH^+ = 224.25 (conditions 3).

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
49	2-[4-(3,3-Difluoro-azetidin-1-yl)-phenyl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.88 min; 401.05; conditions 3
50	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-azetidin-1-yl)-phenyl]-acetamide	0.86 min; 408.16; conditions 3
51	2-[4-(3,3-Difluoro-azetidin-1-yl)-phenyl]-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.88 min; 413.18; conditions 3
52	2-[4-(3,3-Difluoro-azetidin-1-yl)-phenyl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.90 min; 419.17; conditions 3
53	2-(4-Azetidin-1-yl-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.67 min; 365.15; conditions 3
54	2-(4-Azetidin-1-yl-phenyl)-N-[1-(4-cyano-benzyl)-1H-pyrazol-3-yl]-acetamide	0.64 min; 372.12; conditions 3
55	2-(4-Azetidin-1-yl-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.67 min; 377.05; conditions 3
56	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide	0.63 min; 372.09; conditions 3
57	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide	0.62 min; 378.11; conditions 3
58	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide	0.61 min; 379.07; conditions 3
59	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(2,2,2-trifluoro-ethoxy)-pyridin-3-yl]-acetamide	0.81 min; 427.09; conditions 2
60	2-(4-Azetidin-1-yl-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.69 min; 383.07; conditions 3
61	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((S)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide	0.89 min; 415.16; conditions 3

62	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-azetidin-1-yl)-phenyl]-acetamide	0.86 min; 401.03; conditions 3
63	2-(4-Cyclopropoxy-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.79 min; 366.31; conditions 2
64	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(4-cyclopropoxy-phenyl)-acetamide	0.75 min; 373.34; conditions 2
65	2-(4-Cyclopropoxy-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.78 min; 378.35; conditions 2
66	2-(4-Cyclopropoxy-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.81 min; 384.32; conditions 2
67	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-pyrrolidin-1-yl)-phenyl]-acetamide	0.92 min; 433.06; conditions 3
68	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((R)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide	0.89 min; 415.16; conditions 3
69	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-((R)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide	0.85 min; 404.16; conditions 3
70	N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((R)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide	0.88 min; 397.12; conditions 3
71	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide	0.83 min; 360.04; conditions 2
72	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-azetidin-1-yl)-phenyl]-acetamide	0.82 min; 389.86; conditions 3
73	2-[4-(3-Fluoro-azetidin-1-yl)-phenyl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.85 min; 383.13; conditions 3
74	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-((S)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide	0.86 min; 403.98; conditions 3
75	N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((S)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide	0.88 min; 397.26; conditions 3
76	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-pyrrolidin-1-yl)-phenyl]-acetamide	0.89 min; 421.99; conditions 3

77	2-[4-(3,3-Difluoro-pyrrolidin-1-yl)-phenyl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.91 min; 414.84; conditions 3

2-(4-Cyclopropylphenyl)acetyl chloride. Prepared according to *general procedure 1* from 2-(4-cyclopropylphenyl)acetic acid (Reger, T. S.; Yang, Z.-Q.; Schlegel, K.-A. S.; Shu, Y.; Mattern, C.; Cube, R.; Rittle, K. E.; McGaughey, G. B.; Hartman, G. D.; T., Cuyue; et al., *Bioorg. Med. Chem. Lett.*, **2011**, 21, 1692; 260 mg, 1.48 mmol) and oxalyl chloride (0.192 mL, 2.21 mmol) to yield to the crude, title compound.

Example 78: N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-cyclopropyl-phenyl)-acetamide. Prepared according to *general procedure 2* from 2-(4-cyclopropylphenyl)acetyl chloride (41 mg, 0.21 mmol) and 6-((3-amino-1H-pyrazol-1-yl)methyl)nicotinonitrile (35 mg, 0.18 mmol). The reaction is complete after 17 h. Purification by HPLC yields example 78. LC-MS: t_R = 0.79 min, MH^+ = 358.07 (conditions 3).

2-(6-Chloropyridin-3-yl)-N-(1-(3,4-difluorobenzyl)-1H-pyrazol-3-yl)acetamide. Prepared according to *general procedure 3* from 2-(6-chloropyridin-3-yl)acetic acid (257 mg, 1.50 mmol), 1-(3,4-difluorobenzyl)-1H-pyrazol-3-amine (314 mg, 1.50 mmol), HATU (856 mg, 2.25 mmol), and DIPEA (1.28 mL, 7.50 mmol) in DMF (5 mL). The reaction is complete after 1 h. The mixture is partitioned between EtOAc and aq. sat. $NaHCO_3$. The combined org. layers are washed with brine, dried over $MgSO_4$, filtered and evaporated. The crude is purified by automated FC (Biotage, CH_2Cl_2/0.5% Et_3N in MeOH, 50g silicagel). Another purification by HPLC yields the title compound. LC-MS: t_R = 0.70 min, MH^+ = 363.07 (conditions 4).

Example 79: 2-(6-Cyclopropyl-pyridin-3-yl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide. A mixture of 2-(6-chloropyridin-3-yl)-N-(1-(3,4-difluorobenzyl)-1H-pyrazol-3-yl)acetamide (100 mg, 0.273 mmol), cyclopropylboronic acid (117 mg, 1.36 mmol), PEPPSI-IPr (27.9 mg, 0.0409 mmol) and K_3PO_4 (290 mg, 1.36 mmol) is prepared in toluene (3.4 ml). The mixture is purged and filled with Ar 3x. Then the mixture is stirred at 100°C overnight. The mixture is filtered and evaporated. The residue is directly purified by HPLC to yield example 79. LC-MS: t_R = 0.54 min, MH^+ = 369.07 (conditions 4).

N-(1-(4-fluorobenzyl)-1H-pyrazol-3-yl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetamide. 1-(4-Fluoro-benzyl)-1H-pyrazol-3-ylamine (300 mg, 1.57 mmol) is dissolved in DMF (3.00 mL). 2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetic acid (411 mg, 1.57 mmol), EDC·HCl (361 mg, 1.88 mmol), HOBt (256 mg, 1.88 mmol) and DIPEA (1.05 ml, 6.12 mmol) are successively added. The mixture is stirred for 3 h at rt, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Combiflash RF200, column 20 g silicagel, flow rate 35 mL/min, EtOAc / heptane 0:100 → 5:95 → 10:90) yields the title product. LC-MS: t_R = 0.94 min, MH^+ = 436.18 (conditions 2).

Example 80: N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-pyrazin-2-yl)-phenyl]-acetamide. N-(1-(4-Fluorobenzyl)-1H-pyrazol-3-yl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetamide (90 mg, 0.207 mmol) is dissolved in dioxane (0.55 mL). 2-Chloro-3-methylpyrazine (31.9 mg, 0.248 mmol),

tricyclohexylphosphine (1.45 mg, 0.00517 mmol), $Pd_2(dba)_3$ (1.89 mg, 0.00207 mmol) and aq.1.7M potassium phosphate (0.28 ml, 0.48 mmol) are added. The resulting mixture is degassed for 10 min, and is heated in a microwave oven at 150 °C for 30 min. The mixture is allowed to cool to rt. EtOAc is added, and the mixture is washed with brine. The org. layer is dried over $MgSO_4$, filtered, the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 80. LC-MS: t_R = 0.74 min, MH^+ = 401.97 (conditions 2).

Example 81: N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-pyrazin-2-yl-phenyl)-acetamide. N-(1-(4-Fluorobenzyl)-1H-pyrazol-3-yl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetamide (90 mg, 0.207 mmol) is dissolved in dioxane (0.55 mL). 2-Chloropyrazine (23.7 mg, 0.248 mmol), tricyclohexylphosphine (1.45 mg, 0.00517 mmol), $Pd_2(dba)_3$ (1.89 mg, 0.00207 mmol) and aq.1.7M potassium phosphate (0.28 ml, 0.48 mmol) are added. The resulting mixture is degassed for 10 min, and is heated in a microwave oven at 150 °C for 30 min. The mixture is allowed to cool to rt. EtOAc is added, and the mixture is washed with brine. The org. layer is dried over $MgSO_4$, filtered, the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 81. LC-MS: t_R = 0.76 min, MH^+ = 387.87 (conditions 2).

Example 82: N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-pyridin-2-yl-phenyl)-acetamide. N-(1-(4-Fluorobenzyl)-1H-pyrazol-3-yl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetamide (90 mg, 0.207 mmol) is dissolved in dioxane (0.55 mL). 2-Chloropyridine (23.5 mg, 0.248 mmol), tricyclohexylphosphine (1.45 mg, 0.00517 mmol), $Pd_2(dba)_3$ (1.89 mg, 0.00207 mmol) and aq.1.7M potassium phosphate (0.28 ml, 0.48 mmol) are added. The resulting mixture is degassed for 10 min, and is heated in a microwave oven at 150 °C for 30 min. The mixture is allowed to cool to rt. EtOAc is added, and the mixture is washed with brine. The org. layer is dried over $MgSO_4$, filtered, the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 82. LC-MS: t_R = 0.60 min, MH^+ = 386.86 (conditions 2).

Example 83: N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-pyridin-3-yl-phenyl)-acetamide. N-(1-(4-Fluorobenzyl)-1H-pyrazol-3-yl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetamide (90 mg, 0.207 mmol) is dissolved in dioxane (0.55 mL). 3-Chloropyridine (23.5 mg, 0.248 mmol), tricyclohexylphosphine (1.45 mg, 0.00517 mmol), $Pd_2(dba)_3$ (1.89 mg, 0.00207 mmol) and aq.1.7M potassium phosphate (0.28 ml, 0.48 mmol) are added. The resulting mixture is degassed for 10 min, and is heated in a microwave oven at 150 °C for 30 min. The mixture is allowed to cool to rt. EtOAc is added, and the mixture is washed with brine. The org. layer is dried over $MgSO_4$, filtered, the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 83. LC-MS: t_R = 0.58 min, MH^+ = 386.92 (conditions 2).

Example 84: N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-pyridin-4-yl-phenyl)-acetamide. N-(1-(4-Fluorobenzyl)-1H-pyrazol-3-yl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetamide (90 mg,

0.207 mmol) is dissolved in dioxane (0.55 mL). 4-Chloropyridine (23.5 mg, 0.248 mmol), tricyclohexylphosphine (1.45 mg, 0.00517 mmol), $Pd_2(dba)_3$ (1.89 mg, 0.00207 mmol) and aq.1.7M potassium phosphate (0.28 ml, 0.48 mmol) are added. The resulting mixture is degassed for 10 min, and is heated in a microwave oven at 150 °C for 30 min. The mixture is allowed to cool to rt. EtOAc is added, and the mixture is washed with brine. The org. layer is dried over $MgSO_4$, filtered, the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 84. LC-MS: t_R = 0.57 min, MH^+ = 386.92 (conditions 2).

Example 85: N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-pyrimidin-2-yl-phenyl)-acetamide. N-(1-(4-Fluorobenzyl)-1H-pyrazol-3-yl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetamide (90 mg, 0.207 mmol) is dissolved in dioxane (0.55 mL). 2-Chloropyrimidine (23.7 mg, 0.248 mmol), tricyclohexylphosphine (1.45 mg, 0.00517 mmol), $Pd_2(dba)_3$ (1.89 mg, 0.00207 mmol) and aq.1.7M potassium phosphate (0.28 ml, 0.48 mmol) are added. The resulting mixture is degassed for 10 min, and is heated in a microwave oven at 150 °C for 30 min. The mixture is allowed to cool to rt. EtOAc is added, and the mixture is washed with brine. The org. layer is dried over $MgSO_4$, filtered, the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 85. LC-MS: t_R = 0.71 min, MH^+ = 387.87 (conditions 2).

Example 86: N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-pyrimidin-5-yl-phenyl)-acetamide. N-(1-(4-Fluorobenzyl)-1H-pyrazol-3-yl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetamide (90 mg, 0.207 mmol) is dissolved in dioxane (0.55 mL). 5-Bromopyrimidine (32.9 mg, 0.248 mmol), tricyclohexylphosphine (1.45 mg, 0.00517 mmol), $Pd_2(dba)_3$ (1.89 mg, 0.00207 mmol) and aq.1.7M potassium phosphate (0.28 ml, 0.48 mmol) are added. The resulting mixture is degassed for 10 min, and is heated in a microwave oven at 150 °C for 30 min. The mixture is allowed to cool to rt. EtOAc is added, and the mixture is washed with brine. The org. layer is dried over $MgSO_4$, filtered, the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 86. LC-MS: t_R = 0.71 min, MH^+ = 387.94 (conditions 2).

Example 87: N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-pyrimidin-4-yl-phenyl)-acetamide. N-(1-(4-Fluorobenzyl)-1H-pyrazol-3-yl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetamide (90 mg, 0.207 mmol) is dissolved in dioxane (0.55 mL). 4-Chloropyrimidine (23.7 mg, 0.248 mmol), tricyclohexylphosphine (1.45 mg, 0.00517 mmol), $Pd_2(dba)_3$ (1.89 mg, 0.00207 mmol) and aq.1.7M potassium phosphate (0.28 ml, 0.48 mmol) are added. The resulting mixture is degassed for 10 min, and is heated in a microwave oven at 150 °C for 30 min. The mixture is allowed to cool to rt. EtOAc is added, and the mixture is washed with brine. The org. layer is dried over $MgSO_4$, filtered, the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 87. LC-MS: t_R = 0.72 min, MH^+ = 387.96 (conditions 2).

Example 88: N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-isopropyl-pyridin-3-yl)-acetamide. A mixture of 2-(6-chloropyridin-3-yl)-N-(1-(3,4-difluorobenzyl)-1H-pyrazol-3-yl)acetamide (95.6 mg, 0.261 mmol), iron(III) acetylacetonate (5 mg, 0.0142 mmol), 1-methyl-2-pyrrolidone (0.174 mL) in toluene (0.9 mL) and THF (0.9 mL) is stirred for 5 min under Ar. ^{i}PrMgCl (2M in THF, 0.52 ml, 1.04 mmol) is added dropwise at rt. The mixture is stirred for further 1 h. ^{i}PrMgCl (2M in THF, 0.26 ml, 0.52 mmol) is added again, and the mixture is stirred for 40 min. ^{i}PrMgCl (2M in THF, 0.26 ml, 0.52 mmol) is added again, and the mixture is stirred overnight. The mixture is quenched with aq. 1M HCl, and the pH is adjusted to 8. The aq. layer is extracted with EtOAc (3x). The combined org. layers are washed with brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the crude by HPLC yields the title compound. LC-MS: t_R = 0.56 min, MH^+ = 371.13; conditions 4.

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
89	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-((R)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide	0.80 min; 404.92; conditions 3
90	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-((S)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide	0.80 min; 404.92; conditions 3
91	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-pyrrolidin-1-yl)-phenyl]-acetamide	0.84 min; 422.91; conditions 3

Example 92: N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(5-methyl-pyrimidin-4-yl)-phenyl]-acetamide. N-(1-(4-Fluorobenzyl)-1H-pyrazol-3-yl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetamide (90 mg, 0.207 mmol) is dissolved in dioxane (0.55 mL). 4-Chloro-5-methylpyrimidine (31.7 mg, 0.248 mmol), tricyclohexylphosphine (1.45 mg, 0.00517 mmol), $Pd_2(dba)_3$ (1.89 mg, 0.00207 mmol) and aq.1.7M potassium phosphate (0.28 ml, 0.48 mmol) are added. The resulting mixture is degassed for 10 min, and is heated in a microwave oven at 150 °C for 30 min. The mixture is allowed to cool to rt. EtOAc is added, and the mixture is washed with brine. The org. layer is dried over $MgSO_4$, filtered, the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 92. LC-MS: t_R = 0.79 min, MH^+ = 401.98 (conditions 2).

Methyl 5-((tert-butyldimethylsilyl)oxy)picolinate. At 0 °C, tert-butyldimethylsilyl chloride (2.71 g, 18.0 mmol) is added to a sol. of methyl 5-hydroxypyridine-2-carboxylate (2.30 g, 15.0 mmol) and imidazole (1.53 g, 22.5 mmol) in DMF (30 mL). The mixture is allowed to warm to rt, and is stirred overnight. More imidazole (11.3 mmol) and TBDMS-Cl (9.00 mmol) are added, and the mixture is stirred at rt for 2 h. The mixture is quenched

with aq. sat. $NaHCO_3$, and is extracted with EtOAc. The comb. org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by FC (EtOAc/heptane 10:90 → 60:40) yields the title compound. LC-MS: t_R = 0.96 min, MH^+ = 268.34 (conditions 3).

(5-((tert-Butyldimethylsilyl)oxy)pyridin-2-yl)methanol. At 0 °C, DIBAL (20 wt% solution in toluene, 1.2 M, 28.6 mL, 34.1 mmol) is slowly added to a sol. of methyl 5-((tert-butyldimethylsilyl)oxy)picolinate (3.65 g, 13.6 mmol) in CH_2Cl_2 (68 mL). The mixture is stirred at 0 °C for 2 h. More DIBAL (11.4 mL) is added and the mixture is stirred at 0°C for an additional hour. More DIBAL (5.7 mL) is added and the mixture is stirred at 0 °C for an additional hour. Water (2.24 mL), followed by aq. 15% NaOH (2.24 mL) and water (5.6 mL) are added, along some THF, and the mixture is stirred at rt for 30 min. $MgSO_4$ was added, the mixture is stirred for 20 min, filtrated, and the filtrate is concentrated under reduced pressure to yield the crude title product. LC-MS: t_R = 0.68 min, MH^+ = 240.35 (conditions 3).

(5-((tert-Butyldimethylsilyl)oxy)pyridin-2-yl)methyl methanesulfonate. At 0°C, Et_3N (0.835 mL, 6.00 mmol) and methansulfonyl chloride (0.341 mL, 4.40 mmol) are added to a sol. of (5-((tert-butyldimethylsilyl)oxy)pyridin-2-yl)methanol (958 mg, 4.00 mmol) in CH_2Cl_2 (20 mL). The mixture is stirred at 0 °C for 20 min. Aq. sat. $NaHCO_3$ is added, and the mixture is extracted with EtOAc. The comb. org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude title compound.

5-((tert-Butyldimethylsilyl)oxy)-2-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine. Prepared according to *general procedure 4* with NaH (60% in oil, 76.5 mg, 3.19 mmol), (5-((tert-butyldimethylsilyl)oxy)pyridin-2-yl)methyl methanesulfonate (1.06 g, 3.34 mmol), and 5-nitro-1H-pyrazole (343 mg, 3.03 mmol) in DMF (15 mL). The reaction is complete after 3 h at rt. Purification of the crude by FC (EtOAc / heptane 20:80 → 80:20) yields the title compound. LC-MS: t_R = 0.97 min, MH^+ = 337.24 (conditions 3).

1-((5-((tert-Butyldimethylsilyl)oxy)pyridin-2-yl)methyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Zn (163 mg, 2.50 mmol) and 5-((tert-butyldimethylsilyl)oxy)-2-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine (83.6 mg, 0.25 mmol) in acetone (2.5 mL) and aq. sat. NH_4Cl (0.5 mL). The reaction is complete after 20 min at rt and yields the crude title compound. LC-MS: t_R = 0.75 min, MH^+ = 305.24 (conditions 3).

N-(1-((5-((tert-Butyldimethylsilyl)oxy)pyridin-2-yl)methyl)-1H-pyrazol-3-yl)-2-(4-isopropylphenyl)acetamide. Prepared according to *general procedure 3*, starting from 2-(4-isopropylphenyl)acetic acid (234 mg, 1.31 mmol) and 1-((5-((tert-butyldimethylsilyl)oxy)pyridin-2-yl)methyl)-1H-pyrazol-3-amine (400 mg, 1.31 mmol). LC-MS: t_R = 1.02 min, MH^+ = 465.25 (conditions 3).

N-(1-((5-Hydroxypyridin-2-yl)methyl)-1H-pyrazol-3-yl)-2-(4-isopropylphenyl)acetamide. At 0°C, a sol. of TBAF (1 M in THF, 0.545 mL, 0.545 mmol) is added to a sol. of N-(1-((5-((tert-butyldimethylsilyl)oxy)pyridin-2-

yl)methyl)-1H-pyrazol-3-yl)-2-(4-isopropylphenyl)acetamide (211 mg, 0.454 mmol) in THF (4.5 mL). The mixture is stirred at 0°C for 20 min, quenched with aq. sat. $NaHCO_3$ and extracted with EtOAc. The combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by FC (MeOH / CH_2Cl_2 2:98 → 5:95) yields the title compound. LC-MS: t_R = 0.71 min, MH^+ = 351.32 (conditions 3).

Example 93: *2-(4-Isopropyl-phenyl)-N-{1-[5-(2,2,2-trifluoro-ethoxy)-pyridin-2-ylmethyl]-1H-pyrazol-3-yl}-acetamide*. A mixture of N-(1-((5-hydroxypyridin-2-yl)methyl)-1H-pyrazol-3-yl)-2-(4-isopropylphenyl)acetamide (28 mg, 0.08 mmol), Cs_2CO_3 (39.1 mg, 0.12 mmol) and 1,1,1-trifluoro-2-iodoethane (0.00946 mL, 0.096 mmol) in CH_3CN (1 mL) is stirred at 70 °C, and for 20 min at 100 °C in a microwave oven. The solvents are removed under reduced pressure. Purification of the residue by HPLC yields example 93. LC-MS: t_R = 0.91 min, MH^+ = 333.20 (conditions 3).

(5-Bromopyridin-2-yl)methyl methanesulfonate. To a sol. of 5-bromo-2-(hydroxymethyl)pyridine (2.50 g, 13.3 mmol) and Et_3N (2.78 mL, 19.9 mmol) in CH_2Cl_2 (67 mL) is added at 0°C methansulfonyl chloride (1.14 mL, 14.6 mmol). The mixture is stirred at 0 °C for 15 min. Aq. sat. $NaHCO_3$ is added, and the phases are separated. The org. layer is washed with brine, dried over Na_2SO_4, filtered, and the solvents are evaporated under reduced pressure. Purification of the crude was purified by automated FC (Biotage, 100g KP column, EtOAc / heptane 0 → 30%) yields the title product. LC-MS: t_R = 0.57 min, MH^+ = 268.15 (conditions 4).

5-Bromo-2-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine. Prepared according to *general procedure 4* with NaH (60% in oil, 378 mg, 9.45 mmol), (5-bromopyridin-2-yl)methyl methanesulfonate (2.90 g, 10.8 mmol), and 5-nitro-1H-pyrazole (1.07 g, 9.00 mmol) in DMF (25 mL). The reaction is complete after 2 h at rt. Purification of the crude by FC (EtOAc / heptane 0:100 → 50:50) yields the title compound. LC-MS: t_R = 0.66 min, MH^+ = 285.02 (conditions 4).

1-((5-Bromopyridin-2-yl)methyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (2.42 g, 43.8 mmol) and 5-bromo-2-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine (1.24 g, 4.38 mmol) in EtOH (50 mL), and aq. sat. NH_4Cl (6.0 mL). The reaction is complete overnight at 70 °C, and yields the crude title compound. LC-MS: t_R = 0.39 min, MH^+ = 253.09 (conditions 4).

Example 94: *N-[1-(5-Bromo-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide*. Prepared according to *general procedure 3*, starting from 2-(4-isopropylphenyl)acetic acid (232 mg, 1.30 mmol) and 1-((5-bromopyridin-2-yl)methyl)-1H-pyrazol-3-amine (329 mg, 1.30 mmol). LC-MS: t_R = 0.83 min, MH^+ = 413.08 (conditions 4).

tert-Butyl 2-(5,6-difluoropyridin-3-yl)acetate. According to *general procedure 6*, from 5-bromo-2,3-difluoropyridine (1.16 g, 6.00 mmol), 2-tert-butoxy-2-oxoethylzinc chloride (0.5M in Et_2O, 14.4 mL, 7.20 mmol), Q-Phos (432 mg, 0.60 mmol), and $Pd_2(dba)_3$ (173 mg, 0.30 mmol) in THF (18 mL). Purification of the crude by

automated FC(Biotage, EtOAc / heptane 20:80 → 40:60), and subsequent purification by HPLC, yields the title product. LC-MS: t_R = 0.81 min (conditions 4).

2-(5-Fluoro-6-(2,2,2-trifluoroethoxy)pyridin-3-yl)acetic acid. NaH (60% in oil, 69.1 mg, 1.73 mmol) is added to 2,2,2-trifluoroethanol (8 mL) at 0 °C, and the mixture is stirred for 15min at rt. tert-Butyl 2-(5,6-difluoropyridin-3-yl)acetate (200 mg, 0.864 mmol) is added, and the mixture is stirred at 120 °C for 3 h, and at 140 °C (microwave) for 1h. The mixture was allowed to cool to rt, and $LiOH \cdot H_2O$ (18.1 mg, 0.432 mmol) and water (2 mL) were added. The mixture is stirred at rt for 1 h, and water is added. The mixture is washed with CH_2Cl_2. The water layer is adjust to pH 1-3 with aq. HCl, and is extracted 3x with CH_2Cl_2. The combined org. layers are dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. The crude is purified by prep. HPLC, and the combined product-containing fractions are partitioned between water and CH_2Cl_2. The combined org. layers are dried over Na_2SO_4, filtered and evaporated under reduced pressure to yield the title compound. LC-MS: t_R = 0.67 min, MH^+ = 254.08 (conditions 3).

Example 95: *N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[5-fluoro-6-(2,2,2-trifluoro-ethoxy)-pyridin-3-yl]-acetamide*. Prepared according to *general procedure 3*, starting from 2-(5,6-difluoropyridin-3-yl)acetic acid (50.6 mg, 0.20 mmol) and 1-(3,4-difluorobenzyl)-1H-pyrazol-3-amine (41.8 mg, 0.20 mmol). LC-MS: t_R = 0.84 min, MH^+ = 445.11 (conditions 4).

Example 96: N-[1-(5-Cyclopropyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. A mixture of example 94 (104 mg, 0.25 mmol), cyclopropylboronic acid (64.4 mg, 0.75 mmol), K_2CO_3 (51.8 mg, 0.375 mmol) and $Pd(PPh_3)_4$ (28.9 mg, 0.025 mmol) in dioxane (1 mL) is degased and is stirred in a closed vial at 110 °C overnight. The mixture is allowed to cool to rt, and is diluted with water and extracted with EtOAc. The org. layer is washed with brine, dried over $MgSO_4$, filtered, and the solvents are evaporated under reduced pressure. The crude was purified by prep. HPLC to yield example 96. LC-MS: t_R = 0.72 min, MH^+ = 375.18 (conditions 4).

Example 97: 2-(4-Isopropyl-phenyl)-N-[1-(5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide. A mixture of example 94 (104 mg, 0.25 mmol), trimethylboroxine (31.4 mg, 0.25 mmol), K_2CO_3 (51.8 mg, 0.375 mmol) and $Pd(PPh_3)_4$ (28.9 mg, 0.025 mmol) in dioxane (1 mL) is degased and is stirred in a closed vial at 110 °C overnight. The mixture is allowed to cool to rt, and is diluted with water and extracted with EtOAc. The org. layer is washed with brine, dried over $MgSO_4$, filtered, and the solvents are evaporated under reduced pressure. The crude was purified by prep. HPLC to yield example 97. LC-MS: t_R = 0.67 min, MH^+ = 349.15 (conditions 4).

Example 98: N-[1-(5-Isobutyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. A mixture of example 94 (60 mg, 0.144 mmol), (2-methylpropyl)boronic acid (44 mg, 0.431 mmol), K_2CO_3 (30 mg, 0.22 mmol) and $Pd(PPh_3)_4$ (16.6 mg, 0.0144 mmol) in dioxane (0.8 mL) is degased and is stirred in a closed vial at 110 °C overnight. The mixture is allowed to cool to rt, and is diluted with water and extracted with EtOAc. The

org. layer is washed with brine, dried over $MgSO_4$, filtered, and the solvents are evaporated under reduced pressure. The crude was purified by prep. HPLC to yield example 98. LC-MS: t_R = 0.80 min, MH^+ = 391.38 (conditions 4).

tert-Butyl 2-(6-(azetidin-1-yl)pyridin-3-yl)acetate. According to *general procedure 6*, from 2-(azetidin-1-yl)-5-bromopyridine (WO 2010139731, 545 mg, 1.56 mmol), 2-tert-butoxy-2-oxoethylzinc chloride (0.5M in diethyl ether, 5.62 ml, 2.81 mmol), $Pd_2(dba)_3$ (117 mg, 0.13 mmol) and Q-PHOS (182 mg, 0.26 mmol) in THF (10.0 mL). The reaction is complete after 1 h at 80 °C. Purification of the crude by automated FC (Combiflash, column 20 g, flow rate 35 mL/min, EtOAc / heptane 0 / 100 → 10:90 → 30 → 70) yields the title product. LC-MS: t_R = 0.60 min, MH^+ = 249.10 (conditions 3).

2-(6-(Azetidin-1-yl)pyridin-3-yl)acetic acid. According to *general procedure 7*, from tert-butyl 2-(6-(azetidin-1-yl)pyridin-3-yl)acetate (480 mg, 1.93 mmol) and HCl (4M in dioxane, 15 mL) in CH_2Cl_2 (10 mL). The reaction is complete after 2 days at rt to yield the crude title product.

Example 99: 2-(6-Azetidin-1-yl-pyridin-3-yl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide. Prepared according to *general procedure 3*, starting from 2-(6-(azetidin-1-yl)pyridin-3-yl)acetic acid (371 mg, 1.93 mmol) and 1-(3,4-difluorobenzyl)-1H-pyrazol-3-amine (474 mg, 2.03 mmol). LC-MS: t_R = 0.64 min, MH^+ = 383.95 (conditions 3).

Example 100: N-[1-(5-Ethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. A mixture of example 94 (60 mg, 0.144 mmol), ethylboronic acid (31.9 mg, 0.431 mmol), K_2CO_3 (30 mg, 0.22 mmol) and $Pd(PPh_3)_4$ (16.6 mg, 0.0144 mmol) in dioxane (0.8 mL) is degased and is stirred in a closed vial at 110 °C overnight. Ethylboronic acid (31.9 mg, 0.431 mmol), K_2CO_3 (29.8 mg, 0.216 mmol) and $Pd(PPh_3)_4$ (16.6 mg, 0.0144 mmol) are added again, and the mixture is stirred at 110°C for 7 h. The mixture is allowed to cool to rt, and is diluted with water and extracted with EtOAc. The org. layer is washed with brine, dried over $MgSO_4$, filtered, and the solvents are evaporated under reduced pressure. The crude was purified by prep. HPLC to yield example 100. LC-MS: t_R = 0.71 min, MH^+ = 363.35 (conditions 4).

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
101	2-(6-Azetidin-1-yl-pyridin-3-yl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.61 min; 377.85; conditions 3
102	2-(6-Azetidin-1-yl-pyridin-3-yl)-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.53 min; 373.99; conditions 3

103	2-(6-Azetidin-1-yl-pyridin-3-yl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.62 min; 365.98; conditions 3

Example 104: 2-(4-Isopropyl-phenyl)-N-{1-[5-(2-methoxy-ethoxy)-pyridin-2-ylmethyl]-1H-pyrazol-3-yl}-acetamide. A mixture of N-(1-((5-hydroxypyridin-2-yl)methyl)-1H-pyrazol-3-yl)-2-(4-isopropylphenyl)acetamide (35 mg, 0.10 mmol), 2-methoxyethanol (0.0118 mL, 0.15 mmol), and PPh_3 (39.3 mg, 0.15 mmol) in THF (2 mL) at 0 °C is treated with diisopropyl azodicarboxylate (0.0295 mL, 0.15 mmol). The mixture is allowed to warm to rt and is stirred overnight. The mixture is conc. and purified by prep. HPLC to yield example 104. LC-MS: t_R = 0.72 min, MH^+ = 409.34 (conditions 4).

Example 105: N-[1-(5-Isopropoxy-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. A mixture of N-(1-((5-hydroxypyridin-2-yl)methyl)-1H-pyrazol-3-yl)-2-(4-isopropylphenyl)acetamide (35 mg, 0.10 mmol), 2-propanol (0.0115 mL, 0.15 mmol), and PPh_3 (39.3 mg, 0.15 mmol) in THF (2 mL) at 0 °C is treated with diisopropyl azodicarboxylate (0.0295 mL, 0.15 mmol). The mixture is allowed to warm to rt and is stirred overnight. The mixture is conc. and purified by prep. HPLC to yield example 105. LC-MS: t_R = 0.79 min, MH^+ = 393.36 (conditions 4).

(5-Fluoropyridin-2-yl)methyl methanesulfonate. To a sol. of (5-fluoropyridin-2-yl)methanol (339 mg, 2.64 mmol) and Et_3N (0.551 mL, 3.96 mmol) in CH_2Cl_2 (13 mL) is added at 0 °C methansulfonyl chloride (225µl, 2.9 mmol). The mixture is stirred at 0 °C for 10 min. Aq. sat. $NaHCO_3$ is added, and the phases are separated. The aq. layer is extracted with CH_2Cl_2 several times. The combined org. layers are washed with brine, dried over Na_2SO_4, filtered and evaporated under reduced pressure to yield the example 106. LC-MS: t_R = 0.45 min, MH^+ = 206.22 (conditions 4).

5-Fluoro-2-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine. Prepared according to *general procedure 4* with NaH (60% in oil, 100 mg, 2.51 mmol), (5-fluoropyridin-2-yl)methyl methanesulfonate (589 mg, 2.87 mmol), and 5-nitro-1H-pyrazole (285 mg, 2.39 mmol) in DMF (6.4 mL). The reaction is complete after 2 h. Purification of the crude by automated FC (Biotage, EtOAc / heptane 0:100 → 50:50, 100 g silicagel) yields the title compound. LC-MS: t_R = 0.56 min, MH^+ = 223.20 (conditions 4).

1-((5-Fluoropyridin-2-yl)methyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (1.32 g, 23.9 mmol) and 5-fluoro-2-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine (531 mg, 2.39 mmol) in EtOH (27 mL), and aq. sat. NH_4Cl (3.3 mL). The reaction is complete after 5 h at 75 °C, and yields the crude title compound. LC-MS: t_R = 0.29 min, MH^+ = 193.32 (conditions 4).

Example 106: N-[1-(5-Fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. Prepared according to general procedures 1 and 2, starting from 2-(4-isopropylphenyl)acetic acid (154 mg, 0.84 mmol) and 1-((5-fluoropyridin-2-yl)methyl)-1H-pyrazol-3-amine (145 mg, 0.747 mmol). LC-MS: t_R = 0.86 min, MH^+ = 353.02 (conditions 3).

Example 107: N-[1-(5-Dimethylamino-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. To a degased mixture of Example 94 (62.6 mg, 0.15 mmol), $Pd_2(dba)_3$ (6.87 mg, 0.0075 mmol), RuPhos (7 mg, 0.015 mmol), ^{t}BuONa (28.8 mg, 0.3 mmol), and molecular sieve (4Å powder, a spatula) in toluene (2 mL) is added Me_2NH (2M in THF, 0.375 ml, 0.75 mmol). The mixture is stirred in a closed vial at 110°C overnight. The mixture is cooled to rt. The mixture is partitioned between EtOAc and aq. sat. $NaHCO_3$, and the org. layer is washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 107. LC-MS: t_R = 0.65 min, MH^+ = 378.20 (conditions 4).

Example 108: N-{1-[5-((S)-3-Fluoro-pyrrolidin-1-yl)-pyridin-2-ylmethyl]-1H-pyrazol-3-yl}-2-(4-isopropyl-phenyl)-acetamide. To a degased mixture of Example 94 (62.6 mg, 0.15 mmol), $Pd_2(dba)_3$ (6.87 mg, 0.0075 mmol), RuPhos (7 mg, 0.015 mmol), ^{t}BuONa (28.8 mg, 0.3 mmol), and molecular sieve (4Å powder, a spatula) in toluene (2 mL) is added (S)-3-fluoropyrrolidine (48.5 mg, 0.375 mmol). The mixture is stirred in a closed vial at 110°C overnight. The mixture is cooled to rt. The mixture is partitioned between EtOAc and aq. sat. $NaHCO_3$, and the org. layer is washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 108. LC-MS: t_R = 0.68 min, MH^+ = 422.22 (conditions 4).

(5-(Trifluoromethyl)pyridin-2-yl)methyl methanesulfonate. To a sol. of (5-(trifluoromethyl)pyridin-2-yl)methanol (480 mg, 2.71 mmol) and Et_3N (0.566 mL, 4.06 mmol) in CH_2Cl_2 (13 mL) is added at 0 °C methansulfonyl chloride (231 µL, 2.98 mmol). The mixture is stirred at 0 °C for 10 min. Aq. sat. $NaHCO_3$ is added, and the phases are separated. The aq. layer is extracted with CH_2Cl_2 several times. The combined org. layers are washed with brine, dried over Na_2SO_4, filtered and evaporated under reduced pressure to yield the title crude product. LC-MS: t_R = 0.63 min, MH^+ = 256.08 (conditions 4).

2-((3-Nitro-1H-pyrazol-1-yl)methyl)-5-(trifluoromethyl)pyridine. Prepared according to *general procedure 4* with NaH (60% in oil, 94.6 mg, 2.36 mmol), (5-(trifluoromethyl)pyridin-2-yl)methyl methanesulfonate (690 mg, 2.70 mmol), and 5-nitro-1H-pyrazole (268 mg, 2.25 mmol) in DMF (6.0 mL). The reaction is complete after 2 h. Purification of the crude by automated FC (Biotage, EtOAc / heptane 0:100 → 50:50, 100 g silicagel) yields the title compound. LC-MS: t_R = 0.70 min, MH^+ = 273.10 (conditions 4).

1-((5-(Trifluoromethyl)pyridin-2-yl)methyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* with Fe (1.10 g, 20.0 mmol) and 2-((3-nitro-1H-pyrazol-1-yl)methyl)-5-(trifluoromethyl)pyridine (544 mg, 2.00 mmol) in EtOH (23 mL), and aq. sat. NH_4Cl (2.8 mL). The reaction is complete overnight at 75 °C, and yields the crude title compound. LC-MS: t_R = 0.44 min, MH^+ = 243.12 (conditions 4).

Example 109: 2-(4-Isopropyl-phenyl)-N-[1-(5-trifluoromethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide. Prepared according to *general procedures 1 and 2*, starting from 2-(4-isopropylphenyl)acetic acid (35.6 mg, 0.20 mmol) and 1-((5-(trifluoromethyl)pyridin-2-yl)methyl)-1H-pyrazol-3-amine (48.4 mg, 0.20 mmol). LC-MS: t_R = 0.86 min, MH^+ = 403.14 (conditions 4).

2-Chloro-6-(hydroxymethyl)nicotinonitrile. Conc. H_2SO_4 (3 drops) is added to a sol. of 2-chloro-3-cyano-6-methylpyridine 1-oxide (Kiss, L. E.; Ferreira, H. S.; Torrao, L.; Bonifacio, M. J.; Palma, P. N.; Soares-da-Silva, P.; Learmonth, D. A., *J. Med. Chem.*, **2010**, *53*, 3396, 512 g, 30.4 mmol) in Ac_2O (59.7 mL, 626 mmol) at rt. The mixture is stirred at 110 °C for 1h and is allowed to cool to rt. The mixture is poured slowly on ice water and stirred with aq. sat. $NaHCO_3$ for 15min. The aq. layer is extracted with EtOAc (3x), and the combined org. layers are washed with brine, dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. The crude is taken up in MeOH (75 mL), water (38 mL), and K_2CO_3 (13.8 g, 100 mmol) is added. The mixture is stirred at rt for 30 min. The solvents are removed under reduced pressure. The residue is diluted with CH_2Cl_2 (400mL) and dried over Na_2SO_4 under stirring for 60min. The mixture is filtered, washed with MeOH, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Biotage, 100g KP column, MeOH / CH_2Cl_2 1:99 → 3:97) yields the title product. . LC-MS: t_R = 0.42 min, MH^+ = 199.00 (conditions 4).

(6-Chloro-5-cyanopyridin-2-yl)methyl methanesulfonate. To a sol. of 2-chloro-6-(hydroxymethyl)nicotinonitrile (1.95 g, 11.5 mmol) and Et_3N (2.41 mL, 17.3 mmol) in CH_2Cl_2 (60 mL) is added at 0 °C methansulfonyl chloride (0.986 mL, 12.7 mmol). The mixture is stirred at 0 °C for 10 min. Aq. sat. $NaHCO_3$ is added, and the phases are separated. The aq. layer is extracted with CH_2Cl_2 several times. The combined org. layers are washed with brine, dried over Na_2SO_4, filtered and evaporated under reduced pressure to yield the title crude product. LC-MS: t_R = 0.58 min (conditions 4).

2-Chloro-6-((3-nitro-1H-pyrazol-1-yl)methyl)nicotinonitrile. Prepared according to *general procedure 4* with NaH (60% in oil, 402 mg, 10.1 mmol), (6-chloro-5-cyanopyridin-2-yl)methyl methanesulfonate (2.84 g, 11.5 mmol), and 5-nitro-1H-pyrazole (1.08 g, 9.58 mmol) in DMF (25 mL). The reaction is complete after 2 h. Purification of the crude by automated FC (Biotage, EtOAc / heptane 5:95 → 80:20, 100 g silicagel) yields the title compound. LC-MS: t_R = 0.66 min (conditions 4).

6-((3-Amino-1H-pyrazol-1-yl)methyl)-2-chloronicotinonitrile. Prepared according to *general procedure 5* with Fe (3.96 g, 71.6 mmol) and 2-chloro-6-((3-nitro-1H-pyrazol-1-yl)methyl)nicotinonitrile (1.89 g, 7.16 mmol) in EtOH (82 mL), and aq. sat. NH_4Cl (10 mL). The reaction is complete overnight at 75 °C, and yields the crude title compound. LC-MS: t_R = 0.41 min, MH^+ = 234.16 (conditions 4).

Example 110: N-[1-(6-Chloro-5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. Prepared according to general procedures 1 and 2, starting from 2-(4-isopropylphenyl)acetic acid (831 mg, 4.66 mmol) and 6-((3-amino-1H-pyrazol-1-yl)methyl)-2-chloronicotinonitrile (1.09 g, 4.66 mmol). LC-MS: t_R = 0.83 min, MH^+ = 394.08 (conditions 3).

Ethyl 2-(4-(diethylamino)phenyl)acetate. A mixture of ethyl 4-bromophenylacetate (500 mg, 2.06 mmol) Et_2NH (181 mg, 2.47 mmol), DavePhos (64.8 mg, 0.165 mmol), K_3PO_4 (611 mg, 2.88 mmol) and $Pd_2(dba)_3$ (94.2 mg, 0.103 mmol) in 1,2-dimethoxyethane (3 mL) is heated to 120 °C for 20 min in a microwave oven. The mixture

is allowed to cool to rt, and Et_2NH (181 mg, 2.47 mmol), DavePhos (64.8 mg, 0.165 mmol), K_3PO_4 (611 mg, 2.88 mmol) and $Pd_2(dba)_3$ (94.2 mg, 0.103 mmol) are added again. The mixture is stirred at 120 °C for 54 h, and is allowed to cool to rt. The suspension is filtered through Celite®, and the precipitate is washed with CH_2Cl_2. The solvents are removed under reduced pressure. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.54 min, MH^+ = 236.34 (conditions 3).

2-(4-(Diethylamino)phenyl)acetic acid. Aq. 2.5M NaOH (0.5 mL) is added to a sol. of ethyl 2-(4-(diethylamino)phenyl)acetate (73 mg, 0.31 mmol) in EtOH (1 mL). The mixture is stirred for 1 h at rt, and the solvents are partially removed under reduced pressure. The residue is diluted in CH_2Cl_2, and aq. 1M HCl is added to adjust the pH to 3. Separation of the phases with a Separator® (Biotage), and removing the solvents under reduced pressure yields to title product. LC-MS: t_R = 0.42 min, MH^+ = 208.15 (conditions 3).

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
111	2-(6-Azetidin-1-yl-pyridin-3-yl)-N-[1-(4-cyano-benzyl)-1H-pyrazol-3-yl]-acetamide	0.60 min; 373.01; conditions 3
112	2-(4-Diethylamino-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.64 min; 392.89; conditions 3
113	2-(4-Diethylamino-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.66 min; 398.98; conditions 3
114	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(4-diethylamino-phenyl)-acetamide	0.62 min; 388.00; conditions 3

Example 115: N-[1-(5-Cyano-6-ethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. Example 110 (80 mg, 0.203 mmol) is mixed with ethylboronic acid (45 mg, 0.61 mmol), K_2CO_3 (42.1 mg, 0.305 mmol) and $Pd(PPh_3)_4$ (23.5 mg, 0.0203 mmol) in dioxane (1 mL), and the mixture is degased. The mixture is stirred in a closed vial at 110 °C overnight, and is allowed to cool to rt. The mixture is diluted with water and extracted with EtOAc. The org. layer is washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. The crude is mixed again with ethylboronic acid (45 mg, 0.609 mmol), K_2CO_3 (42.1 mg, 0.305 mmol), and $Pd(PPh_3)_4$ (23.5 mg, 0.0203 mmol) in dioxane (1 mL), and the mixture is degased. The mixture is stirred in a closed vial at 110 °C overnight, and is allowed to cool to rt. The mixture is diluted with water and extracted with EtOAc. The org. layer is washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 115. LC-MS: t_R = 0.85 min, MH^+ = 388.13 (conditions 4).

Example 116: N-[1-(5-Cyano-6-methoxy-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. To a suspension of NaH (60% in oil, 11.6 mg, 0.289 mmol) in MeOH (1.5 mL) at 0 °C is added Example 110 (80 mg, 0.19 mmol). The mixture is stirred for 3 h at 0 °C, and is warmed to 50 °C. The mixture is stirred at 50 °C overnight. The mixture is partitioned between water and EtOAc, and the org. layer is washed with brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the crude by HPLC yields example 116. LC-MS: t_R = 0.84 min, MH^+ = 390.13 (conditions 4).

Example 117: N-{1-[5-Cyano-6-(2,2,2-trifluoro-ethoxy)-pyridin-2-ylmethyl]-1H-pyrazol-3-yl}-2-(4-isopropyl-phenyl)-acetamide. To a suspension of NaH (60% in oil, 11.6 mg, 0.289 mmol) in CF_3CH_2OH (1.5 mL) at 0 °C is added Example 110 (80 mg, 0.193 mmol). The mixture is stirred for 3 h at 0 °C, and is warmed to 50 °C. The mixture is stirred at 50 °C overnight. The mixture is partitioned between water and EtOAc, and the org. layer is washed with brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the crude by HPLC yields example 117. LC-MS: t_R = 0.89 min, MH^+ = 458.13 (conditions 4).

Example 118: N-[1-(5-Cyano-6-isopropoxy-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. To a suspension of NaH (60% in oil, 11.6 mg, 0.289 mmol) in ^iPrOH (1.5 mL) at 0 °C is added Example 110 (80 mg, 0.193 mmol). The mixture is stirred for 3 h at 0 °C, and is warmed to 50 °C. The mixture is stirred at 50 °C overnight. The mixture is partitioned between water and EtOAc, and the org. layer is washed with brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. Purification of the crude by HPLC yields example 118. LC-MS: t_R = 0.90 min, MH^+ = 417.93 (conditions 4).

5-Bromo-2-(3,3-difluoropyrrolidin-1-yl)pyridine. A mixture of 2,5-dibromopyridine (1.00 g, 4.22 mmol), 3,3-difluoropyrrolidine hydrochloride (1.33 g, 9.04 mmol) and DBU (2.70 mL, 18.1 mmol) in DMSO (30 mL) is stirred at 80 °C for 72 h. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Büchi, 20 g silicagel, EtOAc / heptane 2:98 → 3:97 → 5:95 → 10:90 → 15:85) yields the title product. LC-MS: t_R = 0.78 min, MH^+ = 264.91 (conditions 3).

tert-Butyl 2-(6-(3,3-difluoropyrrolidin-1-yl)pyridin-3-yl)acetate. According to *general procedure 6*, from 5-bromo-2-(3,3-difluoropyrrolidin-1-yl)pyridine (300 mg, 1.14 mmol), 2-tert-butoxy-2-oxoethylzinc chloride (0.5M in diethyl ether, 3.1 mL, 1.25 mmol), $Pd_2(dba)_3$ (52.2 mg, 0.057 mmol) and Q-PHOS (81 mg, 0.114 mmol) in THF (3 mL). The reaction is complete after 3 h at 90 °C. Purification of the crude by automated FC (Büchi, 10 g silicagel, flow 10 mL/min, EtOAc / heptane 2:98 → 5:95 → 10:90) yields the title product. LC-MS: t_R = 0.65 min, MH^+ = 299.17 (conditions 3).

2-(6-(3,3-Difluoropyrrolidin-1-yl)pyridin-3-yl)acetic acid. According to *general procedure 7*, tert-butyl 2-(6-(3,3-difluoropyrrolidin-1-yl)pyridin-3-yl)acetate (50 mg, 0.168 mmol) and HCl (4M in dioxane, 1 mL) in CH_2Cl_2 (1 mL). The reaction is complete after 50 h at rt. Removing the solvents under reduced pressure leads to the title crude product. LC-MS: t_R = 0.42 min, MH^+ = 242.90 (conditions 3).

5-Bromo-N,N-diethylpyridin-2-amine. A mixture of 2,5-dibromopyridine (1.00 g, 4.22 mmol), diethylamine (0.469 mL, 4.52 mmol) and DBU (0.674 mL, 4.52 mmol) in DMSO (30 mL) is stirred at 80 °C for 2 weeks, whereas diethylamine (0.469 mL, 4.52 mmol) and DBU (0.674 mL, 4.52 mmol) are added every 2 days. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Büchi, 20 g silicagel, EtOAc / heptane 2:98 → 3:97 → 5:95 → 10:90 → 15:85 → 20:80) yields the title product. LC-MS: t_R = 0.53 min, MH^+ = 231.00 (conditions 3).

tert-Butyl 2-(6-(diethylamino)pyridin-3-yl)acetate. According to *general procedure 6* from 5-bromo-N,N-diethylpyridin-2-amine (178 mg, 0.726 mmol), 2-tert-butoxy-2-oxoethylzinc chloride (0.5M in diethyl ether, 3.1 mL, 1.25 mmol), $Pd_2(dba)_3$ (33.2 mg, 0.0363 mmol) and Q-PHOS (51.6 mg, 0.726 mmol) in THF (3 mL). The reaction is complete after 90 min at 75 °C. Purification of the crude by automated FC (Büchi, 10 g silicagel, flow 10 mL/min, EtOAc / heptane 2:98 → 5:95 → 10:90 → 20:80) yields the title product. LC-MS: t_R = 0.66 min, MH^+ = 265.17 (conditions 3).

2-(6-(Diethylamino)pyridin-3-yl)acetic acid. According to *general procedure 7*, from tert-butyl 2-(6-(diethylamino)pyridin-3-yl)acetate (53.3 mg, 0.179 mmol) and HCl (4M in dioxane, 3 mL) in CH_2Cl_2 (2 mL). The reaction is complete after 40 h at rt. Removing the solvents under reduced pressure leads to the title crude product.

Ethyl 2-(4-((2-methoxyethyl)(methyl)amino)phenyl)acetate. A mixture of ethyl-4-bromophenylacetate (500 mg, 2.06 mmol), N-(2-methoxyethyl)methylamine (0.45 mL, 4.11 mmol) and K_3PO_4 (1.75 g, 8.23 mmol) in 1,2-dimethoxyethane (4 mL) is degased with nitrogen. DavePhos (130 mg, 0.329 mmol) and $Pd_2(dba)_3$ (188 mg, 0.206 mmol) are added, and the mixture is heated to 120 °C. The mixture is stirred at 120 °C for 48 h, and is allowed to cool to rt. The mixture is filtered through Celite®, and the filtrate is evaporated under reduced pressure. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.57 min, MH^+ = 252.07 (conditions 3).

2-(4-((2-Methoxyethyl)(methyl)amino)phenyl)acetic acid. A mixture of ethyl 2-(4-((2-methoxyethyl)(methyl)amino)phenyl)acetate (215 mg, 0.855 mmol) in EtOH (1 ml) and aq. 2.5M NaOH (0.5 mL) is stirred at rt for 1 h. The solvents are removed under reduced pressure and the residue is diluted with CH_2Cl_2. Aq. 1M HCl is added to adjust pH to 3, and phases are separated in a Separator® (Biotage). The org. layer is dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.41 min, MH^+ = 242.76 (conditions 3).

Ethyl 2-(4-(ethyl(methyl)amino)phenyl)acetate. A mixture of ethyl 4-bromophenylacetate (500 mg, 2.06 mmol), methylethylamine (0.358 mL, 4.11 mmol), 2-dicyclohexylphosphino-2'-(N,N-dimethylamino)biphenyl (130 mg, 0.33 mmol) K_3PO_4 (1.75 g, 8.23 mmol) and $Pd_2(dba)_3$ (188 mg, 0.206 mmol) in 1,2-dimethoxyethane (4 mL) is heated at 120 °C for 2 days, and is allowed to cool to rt. The mixture is filtered through Celite®, and

the cake is washed with CH_2Cl_2. The filtrate is evaporated under reduced pressure. Purification of the crude by HPLC yields the title compound. LC-MS: t_R = 0.53 min, MH^+ = 222.22 (conditions 3).

2-(4-(Ethyl(methyl)amino)phenyl)acetic acid. A mixture of ethyl 2-(6-(ethyl(methyl)amino)pyridin-3-yl)acetate (49 mg, 0.22 mmol) in EtOH (1 mL) and aq. 2.5M NaOH (0.5 mL) is stirred at rt for 1 h. The solvents are partially removed under reduced pressure, and the residue is cooled to 0 °C. CH_2Cl_2 is added, and the mixture is acidified to pH 3 with aq. 1M HCl. The phases are separated in a Separator® (Biotage) to yield the crude title product. LC-MS: t_R = 0.39 min, MH^+ = 194.12 (conditions 3).

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
119	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.57 min; 423.97; conditions 3
120	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.68 min; 433.71; conditions 3
121	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.64 min; 422.94; conditions 3
122	2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.66 min; 416.22; conditions 3
123	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(6-diethylamino-pyridin-3-yl)-acetamide	0.58 min; 390.02; conditions 3
124	2-(6-Diethylamino-pyridin-3-yl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.68 min; 400.07; conditions 3
125	N-[1-(4-Methoxy-benzyl)-1H-pyrazol-3-yl]-2-{4-[(2-methoxy-ethyl)-methyl-amino]-phenyl}-acetamide	0.65 min; 409.05; conditions 3
126	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-{4-[(2-methoxy-ethyl)-methyl-amino]-phenyl}-acetamide	0.68 min; 415.00; conditions 3
127	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-{4-[(2-methoxy-ethyl)-methyl-amino]-phenyl}-acetamide	0.63 min; 403.96; conditions 3

128	N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-{4-[(2-methoxy-ethyl)-methyl-amino]-phenyl}-acetamide	0.66 min; 397.04; conditions 3
129	2-[4-(Ethyl-methyl-amino)-phenyl]-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.62 min; 379.02; conditions 3
130	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(ethyl-methyl-amino)-phenyl]-acetamide	0.64 min; 384.92; conditions 3
131	2-(4-Isopropyl-phenyl)-N-[1-(5-methoxy-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.72 min; 365.09; conditions 4

Example 132: N-[1-(5-Cyano-6-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. A mixture of Example 110 (100 mg, 0.254 mmol), trimethylboroxine (32 mg, 0.25 mmol), K_2CO_3 (53 mg, 0.38 mmol), and $Pd(PPh_3)_4$ (29 mg, 0.025 mmol) in dioxane (1 mL) is stirred at 110 °C overnight. The mixture is allowed to cool to rt, and is diluted with water. The phases are separated, and the aq. layer is extracted with EtOAc. The combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 132. LC-MS: t_R = 0.80 min, MH^+ = 374.12 (conditions 4).

Example 133: N-[1-(5-Cyano-6-cyclopropyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. A mixture of Example 110 (80 mg, 0.20 mmol), cyclopropylboronic acid (52 mg, 0.60 mmol), K_2CO_3 (42 mg, 0.30 mmol), and $Pd(PPh_3)_4$ (24 mg, 0.020 mmol) in dioxane (1 mL) is stirred at 110 °C overnight. The mixture is allowed to cool to rt, and is diluted with water. The phases are separated, and the aq. layer is extracted with EtOAc. The combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 133. LC-MS: t_R = 0.89 min, MH^+ = 400.16 (conditions 4).

Example 134: N-[1-(5-Cyano-6-isobutyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. A mixture of Example 110 (80 mg, 0.20 mmol), 2-methylpropyl boronic acid (62 mg, 0.60 mmol), K_2CO_3 (42 mg, 0.30 mmol), and $Pd(PPh_3)_4$ (24 mg, 0.020 mmol) in dioxane (1 mL) is stirred at 110 °C overnight. The mixture is allowed to cool to rt, and is diluted with water. The phases are separated, and the aq. layer is extracted with EtOAc. The combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 134. LC-MS: t_R = 0.91 min, MH^+ = 416.18 (conditions 4).

(R)-5-Bromo-2-(3-fluoropyrrolidin-1-yl)pyridine. Prepared according to *general procedure 9* from 2,5-dibromopyridine (350 mg, 1.48 mmol), (R)-3-fluoropyrrolidine hydrochloride (199 mg, 1.58 mmol), and DBU (0.472 mL, 3.16 mmol) in DMSO (20 mL). After the same amounts of (R)-3-fluoropyrrolidine hydrochloride and

DBU are added again, and the reaction is complete after 72 h. Purification of the crude by automated FC (Büchi, EtOAc / heptane 2:98 → 3:97 → 5:95 → 10:90 → 15:85, 20 g silicagel, flow 13 mL/min) yields the title product. LC-MS: t_R = 0.52 min, MH^+ = 244.96 (conditions 3).

(R)-tert-Butyl 2-(6-(3-fluoropyrrolidin-1-yl)pyridin-3-yl)acetate. Prepared according to *general procedure 6* from (R)-5-bromo-2-(3-fluoropyrrolidin-1-yl)pyridine (110 mg, 0.449 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.00 mL, 0.50 mmol), $Pd_2(dba)_3$ (21 mg, 0.024 mmol) and Q-Phos (32 mg, 0.045 mmol) in THF (3 mL). The reaction is complete overnight. Purification of the crude by automated FC (Büchi, EtOAc / heptane 2:98 → 5:95 → 10:90, 10 g silicagel, flow 10 mL/min) yields the title product. LC-MS: t_R = 0.61 min, MH^+ = 281.16 (conditions 3).

(R)-2-(6-(3-Fluoropyrrolidin-1-yl)pyridin-3-yl)acetic acid. Prepared according to *general procedure 7* from (R)-tert-butyl 2-(6-(3-fluoropyrrolidin-1-yl)pyridin-3-yl)acetate (54 mg, 0.193 mmol) and HCl (4M in dioxane, 3 mL) in CH_2Cl_2 (2 mL). The reaction is complete after 2 days. Removing the solvents under reduced pressure yields the crude title product.

5-Bromo-2-(3,3-difluoroazetidin-1-yl)pyridine. Prepared according to *general procedure 9* from 2,5-dibromopyridine (1.00 g, 4.22 mmol), 3,3-difluoroazetidine hydrochloride (485 mg, 4.52 mmol), and DBU (1.35 mL, 9.03 mmol) in DMSO (30 mL). The same amounts of 3,3-difluoroazetidine hydrochloride, and DBU are added again each day, and the reaction is complete after 3 days. Purification of the crude by automated FC (Büchi, EtOAc / heptane 2:98 → 3:97 → 5:95 → 10:90 → 15:85, 20 g silicagel, flow 13 mL/min) yields the title product. LC-MS: t_R = 0.78 min, MH^+ = 250.88 (conditions 3).

tert-Butyl 2-(6-(3,3-difluoroazetidin-1-yl)pyridin-3-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-2-(3,3-difluoroazetidin-1-yl)pyridine (473 mg, 1.90 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 4.20 mL, 2.10 mmol), $Pd_2(dba)_3$ (87 mg, 0.095 mmol) and Q-Phos (135 mg, 0.190 mmol) in THF (3 mL). The reaction is complete after 2 h. Purification of the crude by automated FC (Büchi, EtOAc / heptane 2:98 → 5:95 → 10:90, 10 g silicagel, flow 10 mL/min) yields the title product. LC-MS: t_R = 0.64 min, MH^+ = 285.18 (conditions 3).

2-(6-(3,3-Difluoroazetidin-1-yl)pyridin-3-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(6-(3,3-difluoroazetidin-1-yl)pyridin-3-yl)acetate (300 mg, 1.06 mmol) and HCl (4M in dioxane, 12 mL) in CH_2Cl_2 (10 mL). The reaction is complete overnight. Removing the solvents under reduced pressure yields the crude title product.

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
135	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(2-methyl-3H-benzoimidazol-5-yl)-acetamide	0.62 min; 381.99; conditions 3
136	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(2-methyl-3H-benzoimidazol-5-yl)-acetamide	0.58 min; 370.77; conditions 3
137	N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(2-methyl-3H-benzoimidazol-5-yl)-acetamide	0.61 min; 363.93; conditions 3
138	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[6-((R)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.60 min; 406.00; conditions 3
139	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-((R)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.65 min; 416.04; conditions 3
140	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[6-((R)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.61 min; 405.01; conditions 3
141	N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-((R)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.64 min; 397.90; conditions 3
142	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-azetidin-1-yl)-pyridin-3-yl]-acetamide	0.56 min; 409.99; conditions 3
143	2-[6-(3,3-Difluoro-azetidin-1-yl)-pyridin-3-yl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.68 min; 420.01; conditions 3
144	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-azetidin-1-yl)-pyridin-3-yl]-acetamide	0.63 min; 409.03; conditions 3
145	2-[6-(3,3-Difluoro-azetidin-1-yl)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.66 min; 401.69; conditions 3
146	2-[6-(3,3-Difluoro-azetidin-1-yl)-pyridin-3-yl]-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.65 min; 414.04; conditions 3

2-(4-Bromophenyl)-N-(1-(4-fluorobenzyl)-1H-pyrazol-3-yl)acetamide. Prepared according to *general procedure 3* from 2-(4-bromophenyl)acetic acid (1.20 g, 5.58 mmol), 1-(4-fluorobenzyl)-1H-pyrazol-3-amine (1.07 g, 5.58 mmol), HATU (3.18 g, 8.37 mmol), and DIPEA (4.78 mL, 27.9 mmol) in DMF (15 mL). The

reaction is complete overnight. The mixture is partitioned between aq. sat. $NaHCO_3$ and EtOAc. The org. layer is washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Biotage, 50 g silicagel, EtOAc / heptane 0:100 → 90:10) yields the title product. LC-MS: t_R = 0.81 min, MH^+ = 387.98 (conditions 4).

Example 147. N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isobutyl-phenyl)-acetamide. A mixture of 2-(4-bromophenyl)-N-(1-(4-fluorobenzyl)-1H-pyrazol-3-yl)acetamide (60 mg, 0.15 mmol), (2-methylpropyl)boronic acid (47 mg, 0.46 mmol), K_2CO_3 (32 mg, 0.23 mmol) and $Pd(PPh_3)_4$ (18 mg, 0.016 mmol) in dioxane (1.0 mL) is stirred in a closed vial at 110 °C overnight. The mixture is allowed to cool to rt, and is diluted with water and extracted with EtOAc. The org. layer is washed with brine, dried over $MgSO_4$, filtered, and the solvents are evaporated under reduced pressure. Purification of the crude by HPLC yields example 147. LC-MS: t_R = 0.92 min, MH^+ = 366.09 (conditions 4).

Example 148: N-[1-(5-Cyano-6-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. A mixture of Example 110 (30 mg, 0.075 mmol), KF (13 mg, 0.23 mmol), and 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]-hexacosane (42 mg, 0.11 mmol) in DMSO (1 mL) is stirred at 60 °C for 2 h. The mixture is diluted with H_2O, and is extracted with EtOAc. The comb. org. layers are dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 148. LC-MS: t_R = 0.82 min, MH^+ = 378.31 (conditions 4).

5-Bromo-N-(2,2-difluoroethyl)-N-methylpyridin-2-amine. Prepared according to *general procedure 9* from 2,5-dibromopyridine (1.00 g, 4.22 mmol), (2,2-difluoroethyl)(methyl)amine hydrochloride (2.78 g, 21.1 mmol), and DBU (6.30 mL, 42.2 mmol) in DMSO (30 mL). The reaction is complete after 6 days. Purification of the crude by automated FC (Büchi, EtOAc / heptane 2:98 → 3:97 → 5:95 → 10:90 → 15:85, 20 g silicagel, flow 13 mL/min) yields the title product. LC-MS: t_R = 0.38 min (conditions 3).

tert-Butyl 2-(6-((2,2-difluoroethyl)(methyl)amino)pyridin-3-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-N-(2,2-difluoroethyl)-N-methylpyridin-2-amine (255 mg, 1.02 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 2.24 mL, 1.12 mmol), $Pd_2(dba)_3$ (47 mg, 0.051 mmol) and Q-Phos (72 mg, 0.102 mmol) in THF (3 mL). The reaction is complete after 7 days. Purification of the crude by automated FC (Büchi, EtOAc / heptane 2:98 → 5:95 → 10:90, 10 g silicagel, flow 10 mL/min) yields the title product. LC-MS: t_R = 0.64 min, MH^+ = 287.06 (conditions 3).

2-(6-((2,2-Difluoroethyl)(methyl)amino)pyridin-3-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(6-((2,2-difluoroethyl)(methyl)amino)pyridin-3-yl)acetate (40 mg, 0.14 mmol) and HCl (4M in dioxane, 3 mL) in CH_2Cl_2 (3 mL). The reaction is complete overnight. Removing the solvents under reduced pressure yields the crude title product.

(S)-5-Bromo-2-(3-fluoropyrrolidin-1-yl)pyridine. Prepared according to *general procedure 9* from 2,5-dibromopyridine (1.00 g, 4.22 mmol), (S)-3-fluoropyrrolidine hydrochloride (567 mg, 4.52 mmol), and DBU

(1.35 mL, 9.03 mmol) in DMSO (30 mL). The same amounts of (S)-3-fluoropyrrolidine hydrochloride, and DBU are added again after 24 h, and the reaction is complete after 6 days. Purification of the crude by automated FC (Büchi, EtOAc / heptane 2:98 → 3:97 → 5:95 → 10:90 → 15:85, 20 g silicagel, flow 13 mL/min) yields the title product. LC-MS: t_R = 0.52 min, MH^+ = 244.96 (conditions 3).

(S)-tert-Butyl 2-(6-(3-fluoropyrrolidin-1-yl)pyridin-3-yl)acetate. Prepared according to *general procedure 6* from (S)-5-bromo-2-(3-fluoropyrrolidin-1-yl)pyridine (110 mg, 0.449 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.00 mL, 0.50 mmol), $Pd_2(dba)_3$ (21 mg, 0.024 mmol) and Q-Phos (32 mg, 0.045 mmol) in THF (3 mL). The reaction is complete overnight h. Purification of the crude by automated FC (Büchi, EtOAc / heptane 2:98 → 5:95 → 10:90, 10 g silicagel, flow 10 mL/min) yields the title product. LC-MS: t_R = 0.61 min, MH^+ = 281.16 (conditions 3).

(S)-2-(6-(3-Fluoropyrrolidin-1-yl)pyridin-3-yl)acetic acid. Prepared according to *general procedure 7* from (R)-tert-butyl 2-(6-(3-fluoropyrrolidin-1-yl)pyridin-3-yl)acetate (54 mg, 0.193 mmol) and HCl (4M in dioxane, 3 mL) in CH_2Cl_2 (2 mL). The reaction is complete after 2 days. Removing the solvents under reduced pressure yields the crude title product.

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
149	2-(4-Dimethylamino-phenyl)-N-[1-(5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.42 min; 353.84; conditions 3
150	2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.41 min; 355.03; conditions 3
151	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-{6-[(2,2-difluoro-ethyl)-methyl-amino]-pyridin-3-yl}-acetamide	0.56 min; 412.07; conditions 3
152	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[6-((S)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.60 min; 406.00; conditions 3
153	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-((S)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.65 min; 416.04; conditions 3
154	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[6-((S)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.61 min; 405.01; conditions 3
155	N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-((S)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.64 min; 397.90; conditions 3

156	2-[6-((S)-3-Fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.64 min; 409.99; conditions 3

4-Chloro-6-methylnicotinonitrile. A suspension of 4-chloro-6-methylnicotinamide (29.7 g, 195 mmol) in $POCl_3$ (80.2 mL, 860 mmol) is heated at 110 °C for 15 min (gas development). The mixture is allowed to cool to rt, and is treated with PCl_5 (57.0 g, 274 mmol) over 20 min. The mixture is heated again at 110 °C for 1 h. The mixture is allowed to cool to rt, and is evaporated under reduced pressure. The residue is diluted with EtOAc, and cooled to 0 °C. Aq. 10% Na_2CO_3 is added. The mixture is extracted with EtOAc (3x). The combined org. layers are washed with brine, dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Biotage, EtOAc / heptane 2:98 → 30:70) yields the title compound. LC-MS: t_R = 0.55 min, MH^+ = 194.15 (conditions 4).

4-Chloro-5-cyano-2-methylpyridine 1-oxide. To a sol. of 4-chloro-6-methylnicotinonitrile (10.0 g, 65.5 mmol) and $H_2O_2 \cdot H_2NCONH_2$ (18.5 g, 197 mmol) in CH_2Cl_2 (80 mL) at 0 °C is added trifluoroacetic acid anhydride (27.9 mL, 197 mmol) dropwise. The mixture is stirred at rt for 3.5 h. Aq. 10% KI (800mL) is carefully added. The phases are separated, and the aq. Layer is extracted with CH_2Cl_2. The combined org. layers are washed with aq. sat. $Na_2S_2O_3$ and brine. The org. layer is dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure to yield the crude title compound. LC-MS: t_R = 0.34 min, MH^+ = 210.22 (conditions 4).

4-Chloro-6-(hydroxymethyl)nicotinonitrile. 4-Chloro-5-cyano-2-methylpyridine 1-oxide (11.3 g, 66.9 mmol) is dissolved in Ac_2O (132 mL), and conc. H_2SO_4 (3 drops) is added at rt. The mixture is heated to 110 °C and stirred at this temperature for 1 h. The mixture is poured slowly onto ice/water, and aq. sat. $NaHCO_3$ is added. The resulting mixture is stirred for 15min. The phases are separated, and the aq. layer is extracted with EtOAc (2x). The combined org. layers are washed with brine, dried over Na_2SO_4, filtered , and the solvents are removed under reduced pressure. The crude is diluted with MeOH (162 mL). Water (82 mL) and K_2CO_3 (30.5 g, 221 mmol) are added. The mixture is stirred at rt for 30 min. The solvents are partially removed under reduced pressure. Purification of the residue by automated FC (Biotage, MeOH / CH_2Cl_2 1:99 → 3:97, 340 g silicagel, then a second time with EtOAc / heptane 1:99 → 45:55, 100 g silicagel) yields the title product. LC-MS: t_R = 0.41 min, MH^+ = 168.95 (conditions 4).

(4-Chloro-5-cyanopyridin-2-yl)methyl methanesulfonate. Methansulfonyl chloride (0.527 mL, 6.79 mmol) is added to a solution of 4-chloro-6-(hydroxymethyl)nicotinonitrile (1.10 g, 6.17 mmol) and Et_3N (1.29 mL, 9.26 mmol) in CH_2Cl_2 (32 mL) at 0°C, and the mixture is stirred for 15 min. Aq. sat. $NaHCO_3$ is added, and the phases are separated. The org. layer is extracted with CH_2Cl_2, and the combined org. layers are washed with brine, dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure to yield the crude title compound. LC-MS: t_R = 0.56 min, MH^+ = 247.19 (conditions 4).

4-Chloro-6-((3-nitro-1H-pyrazol-1-yl)methyl)nicotinonitrile. Prepared according to *general procedure 4* with NaH (55% suspension in oil, 215 mg, about 5.37 mmol), (4-chloro-5-cyanopyridin-2-yl)methyl methanesulfonate (1.52 g, 6.14 mmol), 5-methyl-3-nitro-1H-pyrazole (609 mg, 5.12 mmol) in DMF (15 mL). The reaction is complete after 2 h at rt. Purification of the crude by automated FC (Biotage, EtOAc / heptane 5:95 → 20:80, 50 g silicagel) yields the title compound. LC-MS: t_R = 0.63 min (conditions 4).

6-((3-Amino-1H-pyrazol-1-yl)methyl)-4-chloronicotinonitrile. Prepared according to *general procedure 5* with Fe (2.32 g, 42.1 mmol) and 4-chloro-6-((3-nitro-1H-pyrazol-1-yl)methyl)nicotinonitrile (1.11 g, 4.21 mmol) in EtOH (48 mL), and aq. sat. NH_4Cl (7 mL). The reaction is complete after 2 days at 75 °C and yields the crude title compound. LC-MS: t_R = 0.38 min, MH^+ = 234.14 (conditions 4).

N-(1-((4-((3H-[1,2,3]Triazolo[4,5-b]pyridin-3-yl)oxy)-5-cyanopyridin-2-yl)methyl)-1H-pyrazol-3-yl)-2-(4-isopropylphenyl)acetamide. Prepared according to *general procedure 3* from 2-(4-isopropylphenyl)acetic acid (407 mg, 2.29 mmol), 6-((3-amino-1H-pyrazol-1-yl)methyl)-4-chloronicotinonitrile (534 mg, 2.29 mmol), HATU (1.30 g, 3.43 mmol), and DIPEA (1.96 mL, 11.4 mmol) in DMF (5 mL). The reaction is complete overnight. Purification by HPLC yields the title compound. LC-MS: t_R = 0.82 min, MH^+ = 494.18 (conditions 4).

Example 157. N-[1-(4-Chloro-5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. A solution of N-(1-((4-((3H-[1,2,3]triazolo[4,5-b]pyridin-3-yl)oxy)-5-cyanopyridin-2-yl)methyl)-1H-pyrazol-3-yl)-2-(4-isopropylphenyl)acetamide (162 mg, 0.328 mmol) in $POCl_3$ (0.65 mL) is stirred at rt for 10 min. The mixture is quenched with aq. sat. $NaHCO_3$, the phases are separated, and the org. layer is extracted with EtOAc. The comb. org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 157. LC-MS: t_R = 0.90 min, MH^+ = 394.26 (conditions 4).

2-(4-Allylphenyl)-N-(1-(4-fluorobenzyl)-1H-pyrazol-3-yl)acetamide. A mixture of 2-(4-bromophenyl)-N-(1-(4-fluorobenzyl)-1H-pyrazol-3-yl)acetamide (252 mg, 0.65 mmol), allylboronic acid pinacol ester (0.366 mL, 1.95 mmol), K_2CO_3 (135 mg, 0.975 mmol) and $Pd(PPh_3)_4$ (75.1 mg, 0.065 mmol) in dioxane (6.5 mL) is stirred at 110 °C for 4 h. The mixture is stirred further at rt overnight. The mixture is filtrated, and the filtrate is diluted with EtOAc and washed with brine. The org. layer is dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Biotage, 25 g silicagel, EtOAc / heptane 30:70 → 100:0) yields the title product. LC-MS: t_R = 0.91 min, MH^+ = 350.26 (conditions 3).

Example 158: 2-(4-Cyclopropylmethyl-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide. A solution of 2-(4-allylphenyl)-N-(1-(4-fluorobenzyl)-1H-pyrazol-3-yl)acetamide (63 mg, 0.18 mmol) and CH_2ClI (0.0472 mL, 0.648 mmol) in CH_2Cl_2 (1.8 mL) is treated at 0 °C with Et_2Zn (1.0 M in hexanes, 0.43 mL, 0.432 mmol). The mixture is stirred at 0 °C for 1 h, and is allowed to warm to rt, and stirred for 2 h. The mixture is again cooled to 0 °C, and CH_2ClI (0.0944 mL, 1.296 mmol), followed by Et_2Zn (1.0 M in hexanes, 0.86 mL, 0.864 mmol) are added. The mixture is stirred at 0 °C for 30 min. Aq. sat. NH_4Cl is added, and the mixture was extracted with

EtOAc. The combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Biotage, 10 g silicagel, EtOAc / heptane 20:80 → 65:35) and subsequently by HPLC yields example 158. LC-MS: t_R = 0.94 min, MH^+ = 364.30 (conditions 3).

5-Bromo-2-(3-fluoroazetidin-1-yl)pyridine. Prepared according to *general procedure 9* from 2,5-dibromopyridine (1.00 g, 4.22 mmol), 3-fluoroazetidine hydrochloride (504 mg, 4.52 mmol), and DBU (1.35 mL, 9.03 mmol) in DMSO (30 mL). The same amounts of 3-fluoroazetidine hydrochloride, and DBU are added again after 24 h, and the reaction is complete after 4 days. Purification of the crude by automated FC (Büchi, EtOAc / heptane 2:98 → 3:97 → 5:95 → 10:90 → 15:85, 20 g silicagel, flow 13 mL/min) yields the title product.

tert-Butyl 2-(6-(3-fluoroazetidin-1-yl)pyridin-3-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-2-(3-fluoroazetidin-1-yl)pyridine (546 mg, 2.36 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 5.20 mL, 2.60 mmol), $Pd_2(dba)_3$ (108 mg, 0.118 mmol) and Q-Phos (168 mg, 0.236 mmol) in THF (3 mL). The reaction is complete after 3 h. Purification of the crude by automated FC (Büchi, EtOAc / heptane 2:98 → 5:95 → 10:90, 20 g silicagel, flow 18 mL/min) yields the title product. LC-MS: t_R = 0.59 min, MH^+ = 267.08 (conditions 3).

2-(6-(3-Fluoroazetidin-1-yl)pyridin-3-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(6-(3-fluoroazetidin-1-yl)pyridin-3-yl)acetate (370 mg, 1.39 mmol) and HCl (4M in dioxane, 12 mL) in CH_2Cl_2 (12 mL). The reaction is complete after 20 h. Removing the solvents under reduced pressure yields the crude title product.

5-Bromo-N-cyclopropyl-N-methylpyridin-2-amine. Prepared according to *general procedure 9* from 2,5-dibromopyridine (1.00 g, 4.22 mmol), N-cyclopropyl methylamine hydrochloride (486 mg, 4.52 mmol), and DBU (1.35 mL, 9.03 mmol) in DMSO (30 mL). The same amounts of N-cyclopropyl methylamine hydrochloride, and DBU are added again after 24 h, and the reaction is complete after 7 days. Purification of the crude by automated FC (Büchi, EtOAc / heptane 2:98 → 3:97 → 5:95 → 10:90 → 15:85, 20 g silicagel, flow 13 mL/min) yields the title product.

tert-Butyl 2-(6-(cyclopropyl(methyl)amino)pyridin-3-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-N-cyclopropyl-N-methylpyridin-2-amine (148 mg, 0.652 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.24 mL, 0.62 mmol), $Pd_2(dba)_3$ (30 mg, 0.033 mmol) and Q-Phos (46 mg, 0.065 mmol) in THF (3 mL). The reaction is complete after 20 h. Purification of the crude by automated FC (Büchi, EtOAc / heptane 2:98 → 5:95 → 10:90, 10 g silicagel, flow 10 mL/min) yields the title product.

2-(6-(Cyclopropyl(methyl)amino)pyridin-3-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(6-(cyclopropyl(methyl)amino)pyridin-3-yl)acetate (459 mg, 1.55 mmol) and HCl (4M in dioxane, 15

mL) in CH_2Cl_2 (15 mL). The reaction is complete after 20 h. Removing the solvents under reduced pressure yields the crude title product.

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
159	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[6-(3-fluoro-azetidin-1-yl)-pyridin-3-yl]-acetamide	0.53 min; 392.30; conditions 3
160	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3-fluoro-azetidin-1-yl)-pyridin-3-yl]-acetamide	0.59 min; 401.73; conditions 3
161	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[6-(3-fluoro-azetidin-1-yl)-pyridin-3-yl]-acetamide	0.59 min; 391.18; conditions 3
162	2-[6-(3-Fluoro-azetidin-1-yl)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.62 min; 383.79; conditions 3
163	2-[6-(3-Fluoro-azetidin-1-yl)-pyridin-3-yl]-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.62 min; 396.01; conditions 3
164	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[6-(cyclopropyl(methyl)amino)-pyridin-3-yl]-acetamide	0.56 min; 387.75; conditions 3
165	2-[6-(Cyclopropyl(methyl)amino)-pyridin-3-yl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.66 min; 397.99; conditions 3
166	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[6-(cyclopropyl(methyl)amino)-pyridin-3-yl]-acetamide	0.62 min; 386.84; conditions 3
167	2-[6-(Cyclopropyl(methyl)amino)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.64 min; 380.02; conditions 3
168	2-[6-(Cyclopropyl(methyl)amino)-pyridin-3-yl]-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.64 min; 392.02; conditions 3

Example 169. N-[1-(5-Cyano-4-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. A mixture of Example 157 (30 mg, 0.0762 mmol), trimethylboroxine (9.56 mg, 0.0762 mmol), K_2CO_3 (15.8 mg, 0.114 mmol) and $Pd(PPh_3)_4$ (8.8 mg, 0.00762 mmol) in dioxane (0.5 mL) is degased, and is stirred in a closed vial at 110°C overnight. The mixture is allowed to cool to rt, is diluted with water, and is extracted with EtOAc. The org. layer is washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced

pressure. Purification of the crude by HPLC yields example 169. LC-MS: t_R = 0.79 min, MH^+ = 374.31 (conditions 4).

Example 170. N-[1-(5-Cyano-4-cyclopropyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. A mixture of Example 157 (30 mg, 0.0762 mmol), cyclopropylboronic acid (19.6 mg, 0.228 mmol), K_2CO_3 (15.8 mg, 0.114 mmol) and $Pd(PPh_3)_4$ (8.8 mg, 0.00762 mmol) in dioxane (0.5 mL) is degased, and is stirred in a closed vial at 110°C overnight. The mixture is allowed to cool to rt, is diluted with water, and is extracted with EtOAc. The org. layer is washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 170. LC-MS: t_R = 0.83 min, MH^+ = 400.32 (conditions 4).

5-Bromo-2-(pyrrolidin-1-yl)pyridine. A mixture of 2,5-dibromopyridine (2.00 g, 8.44 mmol), pyrrolidine (0.698 mL, 8.44 mmol) and DBU (1.35 mL, 9.03 mmol) in DMSO (30 mL) is stirred at 80 °C for 4 days. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Büchi, 20 g silicagel, EtOAc / heptane 2:98 → 3:97 → 5:95 → 10:90 → 15:85) yields the title product. LC-MS: t_R = 0.48 min, MH^+ = 229.01 (conditions 3).

tert-Butyl 2-(6-(pyrrolidin-1-yl)pyridin-3-yl)acetate. According to *general procedure 6*, from 5-bromo-2-(pyrrolidin-1-yl)pyridine (1.63 g, 7.18 mmol), 2-tert-butoxy-2-oxoethylzinc chloride (0.5M in diethyl ether, 15.8 mL, 7.90 mmol), $Pd_2(dba)_3$ (329 mg, 0.359 mmol) and Q-PHOS (510 mg, 0.718 mmol) in THF (3 mL). After 3 h at 90 °C the reaction is complete. Purification of the crude by automated FC (Büchi, 10 g silicagel, flow 10 mL/min, EtOAc / heptane 2:98 → 5:95 → 10:90) yields the title product. LC-MS: t_R = 0.63 min, MH^+ = 263.14 (conditions 3).

2-(6-(Pyrrolidin-1-yl)pyridin-3-yl)acetic acid. According to *general procedure 7*, from tert-butyl 2-(6-(pyrrolidin-1-yl)pyridin-3-yl)acetate (410 mg, 1.56 mmol) and HCl (4M in dioxane, 15 mL) in CH_2Cl_2 (15 mL). After 21 h at rt the reaction is complete. Removing the solvents under reduced pressure leads to the title crude product. LC-MS: t_R = 0.42 min, MH^+ = 207.22 (conditions 3).

5-Bromo-N-(2-methoxyethyl)-N-methylpyridin-2-amine. A mixture of 2,5-dibromopyridine (2.00 g, 8.44 mmol), N-(2-methoxyethyl)methylamine (0.97 mL, 9.03 mmol) and DBU (1.35 mL, 9.03 mmol) in DMSO (30 mL) is stirred at 80 °C for 5 days. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Büchi, 20 g silicagel, EtOAc / heptane 2:98 → 3:97 → 5:95 → 10:90 → 15:85) yields the title product. LC-MS: t_R = 0.50 min, MH^+ = 244.95 (conditions 3).

tert-Butyl 2-(6-((2-methoxyethyl)(methyl)amino)pyridin-3-yl)acetate. According to *general procedure 6*, from 5-bromo-N-(2-methoxyethyl)-N-methylpyridin-2-amine (1.47 g, 6.00 mmol), 2-tert-butoxy-2-oxoethylzinc chloride (0.5M in diethyl ether, 13.2 mL, 6.60 mmol), $Pd_2(dba)_3$ (275 mg, 0.300 mmol) and Q-PHOS (426 mg, 0.600 mmol) in THF (3 mL). The reaction is complete after 4 days at 90 °C. Purification of the crude by automated

FC (Büchi, 10 g silicagel, flow 10 mL/min, EtOAc / heptane 2:98 → 5:95 → 10:90) yields the title product. LC-MS: t_R = 0.60 min, MH^+ = 281.14 (conditions 3).

2-(6-((2-Methoxyethyl)(methyl)amino)pyridin-3-yl)acetic acid. According to *general procedure 7*, from tert-butyl 2-(6-((2-methoxyethyl)(methyl)amino)pyridin-3-yl)acetate (197 mg, 0.703 mmol) and HCl (4M in dioxane, 7 mL) in CH_2Cl_2 (7 mL). The reaction is complete overnight at rt. Removing the solvents under reduced pressure leads to the title crude product. LC-MS: t_R = 0.39 min, MH^+ = 225.13 (conditions 3).

5-Bromo-N-(cyclopropylmethyl)-N-methylpyridin-2-amine. A mixture of 2,5-dibromopyridine (2.00 g, 8.44 mmol), (cyclopropylmethyl)methylamine hydrochloride (1.10, 9.03 mmol) and DBU (2.70 mL, 18.1 mmol) in DMSO (30 mL) is stirred at 80 °C for 2 days. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Büchi, 20 g silicagel, EtOAc / heptane 2:98 → 3:97 → 5:95 → 10:90 → 15:85) yields the title product. LC-MS: t_R = 0.59 min, MH^+ = 240.96 (conditions 3).

tert-Butyl 2-(6-((cyclopropylmethyl)(methyl)amino)pyridin-3-yl)acetate. A mixture of 5-bromo-N-(cyclopropylmethyl)-N-methylpyridin-2-amine (1.50 g, 6.20 mmol), $Pd_2(dba)_3$ (284 mg, 0.31 mmol) and Q-PHOS (440 mg, 0.620 mmol) in THF (3 mL) is heated to 90 °C, and 2-tert-butoxy-2-oxoethylzinc chloride (0.5M in diethyl ether, 13.6 mL, 6.80 mmol) is added. The mixture is stirred at 90 °C for 5 days. $Pd_2(dba)_3$ (284 mg, 0.31 mmol), Q-PHOS (440 mg, 0.620 mmol) and 2-tert-butoxy-2-oxoethylzinc chloride (0.5M in diethyl ether, 13.6 mL, 6.80 mmol) are added again, and the mixture is stirred for 6 days at 80 °C. The mixture is allowed to cool to rt. The mixture is filtered, and the filtrate is evaporated under reduced pressure. Purification of the crude by automated FC (Büchi, 10 g silicagel, flow 10 mL/min, EtOAc / heptane 2:98 → 5:95 → 10:90 → 15:85 → 20:80 → 25:75) yields the title product.

2-(6-((Cyclopropylmethyl)(methyl)amino)pyridin-3-yl)acetic acid. According to *general procedure 7*, from tert-butyl 2-(6-((cyclopropylmethyl)(methyl)amino)pyridin-3-yl)acetate (115 mg, 0.416 mmol) and HCl (4M in dioxane, 6 mL) in CH_2Cl_2 (6 mL). The reaction is complete overnight at rt. Removing the solvents under reduced pressure leads to the title crude product.

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
171	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[6-(ethyl-methyl-amino)-pyridin-3-yl]-acetamide	0.55 min; 375.97; conditions 3
172	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(ethyl-methyl-amino)-pyridin-3-yl]-acetamide	0.65 min; 386.01; conditions 3

173	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[6-(ethyl-methyl-amino)-pyridin-3-yl]-acetamide	0.61 min; 375.04; conditions 3
174	2-[6-(Ethyl-methyl-amino)-pyridin-3-yl]-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.63 min; 380.02; conditions 3
175	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.66 min; 398.00; conditions 3
176	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.62 min; 387.00; conditions 3
177	N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.65 min; 380.02; conditions 3
178	N-[1-(4-Methoxy-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.64 min; 392.01; conditions 3
179	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-{6-[(2-methoxy-ethyl)-methyl-amino]-pyridin-3-yl}-acetamide	0.54 min; 405.99; conditions 3
180	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-{6-[(2-methoxy-ethyl)-methyl-amino]-pyridin-3-yl}-acetamide	0.65 min; 415.98; conditions 3
181	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-{6-[(2-methoxy-ethyl)-methyl-amino]-pyridin-3-yl}-acetamide	0.61 min; 404.98; conditions 3
182	N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-{6-[(2-methoxy-ethyl)-methyl-amino]-pyridin-3-yl}-acetamide	0.64 min; 398.01; conditions 3
183	N-[1-(4-Methoxy-benzyl)-1H-pyrazol-3-yl]-2-{6-[(2-methoxy-ethyl)-methyl-amino]-pyridin-3-yl}-acetamide	0.63 min; 410.00; conditions 3
184	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[6-(cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-acetamide	0.60 min; 402.02; conditions 3
185	2-[6-(Cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.70 min; 412.00; conditions 3
186	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[6-(cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-acetamide	0.66 min; 401.01; conditions 3
187	2-[6-(Cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.68 min; 394.01; conditions 3

188	2-[6-(Cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.68 min; 406.00; conditions 3
189	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(6-diethylamino-pyridin-3-yl)-acetamide	0.64 min; 388.94; conditions 3
190	2-(6-Diethylamino-pyridin-3-yl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.66 min; 382.00; conditions 3
191	2-(6-Diethylamino-pyridin-3-yl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.66 min; 394.00; conditions 3

N-(1-(4-Bromobenzyl)-1H-pyrazol-3-yl)-2-(4-isopropylphenyl)acetamide. According to general procedure 3, from 1-(4-bromobenzyl)-1H-pyrazol-3-amine and 2-(4-isopropylphenyl)acetic acid. LC-MS: t_R = 0.92 min, MH^+ = 412.21 (conditions 4).

Example 192: N-[1-(4-Cyclopropyl-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. A mixture of N-(1-(4-bromobenzyl)-1H-pyrazol-3-yl)-2-(4-isopropylphenyl)acetamide (109 mg, 0.25 mmol), cyclopropylboronic acid (64.4 mg, 0.75 mmol), K_2CO_3 (51.8 mg, 0.375 mmol) and $Pd(Ph_3)_4$ (28.9 mg, 0.025 mmol) in dioxane (1 ml) is degased, and is stirred in a closed vial at 110°C overnight. The mixture is diluted with water and extracted with EtOAc. The org. layer is washed with brine, dried over $MgSO_4$, filtered and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 192. LC-MS: t_R = 0.94 min, MH^+ = 374.35 (conditions 4).

tert-Butyl 2-(6-chloropyridin-3-yl)acetate. $BF_3{\cdot}OEt_2$ (0.2 mL) is added to a mixture of 2-chloropyridine-5-acetic acid (1.72 g, 10 mmol) and tert-butyl 2,2,2-trichloroacetimidate (3.58 mL, 20 mmol) in THF (20 mL), and the mixture is stirred overnight. The mixture is quenched with aq. sat. $NaHCO_3$ and extracted with EtOAc. The comb. org. layers are washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification of the crude by FC (EtOAc / heptane 5:95 → 40:60) yields the title product. LC-MS: t_R = 0.85 min, MH^+ = 228.29 (conditions 3).

tert-Butyl 2-(6-cyclopropylpyridin-3-yl)acetate. A mixture of tert-butyl 2-(6-chloropyridin-3-yl)acetate (250 mg, 1.1 mmol), cyclopropylboronic acid (283 mg, 3.29 mmol), K_2CO_3 (228 mg, 1.65 mmol) and $Pd(PPh_3)_4$ (127 mg, 0.11 mmol) in dioxane (11 mL) is degased. The mixture is stirred in a closed vial at 110 °C overnight. The mixture is extracted between EtOAc and brine, and the org. layer is dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Biotage, 50g silicagel, EtOAc / heptane 2:98 → 90:10) yields the title product. LC-MS: t_R = 0.50 min, MH^+ = 234.37 (conditions 4).

2-(6-Cyclopropylpyridin-3-yl)acetic acid. A mixture of tert-butyl 2-(6-cyclopropylpyridin-3-yl)acetate (148 mg, 0.634 mmol) in HCl (4M in dioxane, 10 mL) is stirred at rt for 7 h. The solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.22 min, MH^+ = 178.44 (conditions 4).

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
193	N-[1-(4-Chloro-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-cyclopropyl-pyridin-3-yl)-acetamide	0.59 min; 385.00; conditions 4
194	N-[1-(3-Chloro-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-cyclopropyl-pyridin-3-yl)-acetamide	0.59 min; 385.17; conditions 4

1-(4-Bromobenzyl)-3-nitro-1H-pyrazole. According to *general procedure 4* from K_2CO_3 (3.46 g, 25.0 mmol), 4-bromobenzyl bromide (2.50 g, 10.0 mmol), 5-nitro-1H-pyrazole (1.13 g, 10.0 mmol), and Bu_4NBr (658 mg 2.00 mmol) in acetone (50 mL). The reaction is complete overnight. Purification of the crude by automated FC (Biotage, 100 g silicagel, EtOAc / heptane 20:80 → 80:20) yields the desired product. LC-MS: t_R = 0.86 min, (conditions 3).

4-((3-Nitro-1H-pyrazol-1-yl)methyl)phenol. A degassed mixture of 1-(4-bromobenzyl)-3-nitro-1H-pyrazole (564 mg, 2 mmol), $Pd_2(dba)_3$ (91.6 mg, 0.1 mmol), tetramethyl di-tBuXPhos (96.2 mg, 0.2 mmol) and KOH (673 mg, 12 mmol) in dioxane (2 mL) and H_2O (4 mL) is stirred at 100 °C for 1 h. The mixture is quenched with aq. 1 M HCl and extracted with EtOAc. The combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification by automated FC (Biotage, 50 g silicagel, MeOH /CH_2Cl_2 2:998 → 15:985), followed by HPLC yields the title product. LC-MS: t_R = 0.69 min, (conditions 3).

3-Nitro-1-(4-(vinyloxy)benzyl)-1H-pyrazole. A mixture of 4-((3-nitro-1H-pyrazol-1-yl)methyl)phenol (304 mg, 1.39 mmol), vinyl acetate (0.256 mL, 2.77 mmol), chloro(1,5-cyclooctadiene)iridium(I) dimer (18.5 mg, 0.0277 mmol) and Na_2CO_3 (88.2 mg, 0.832 mmol) in toluene (2 mL) is stirred at 105 °C for 4 h. The mixture is allowed to cool to rt, and is diluted with H_2O. The mixture is extracted with EtOAc. The combined org. layers is washed with brine, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Biotage, 25 g silicagel, EtOAc / heptane 2:8 → 8:2) yields the title compound. LC-MS: t_R = 0.86 min, (conditions 3).

1-(4-(Vinyloxy)benzyl)-1H-pyrazol-3-amine. Prepared according to *general procedure 5* from Zn (powder, 140 mg, 2.14 mmol), 3-nitro-1-(4-(vinyloxy)benzyl)-1H-pyrazole (105 mg, 0.428 mmol) in acetone (4 mL), and aq. sat. NH_4Cl (1 mL). The title product is obtained. LC-MS: t_R = 0.60 min, MH^+ = 316.31 (conditions 3).

2-(4-Isopropylphenyl)-N-(1-(4-(vinyloxy)benzyl)-1H-pyrazol-3-yl)acetamide. Prepared according to *general procedure 3* from 2-(4-isopropylphenyl)acetic acid (79 mg, 0.44 mmol), 1-(4-(vinyloxy)benzyl)-1H-pyrazol-3-amine (95 mg, 0.44 mmol), HATU (252 mg, 0.662 mmol), and DIPEA (0.227 mL, 1.32 mmol) in DMF (4 mL). The reaction is complete after 1 h. Purification by HPLC yields the title compound. LC-MS: t_R = 0.96 min, MH^+ = 376.33 (conditions 4).

Example 195. N-[1-(4-Cyclopropoxy-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. A soln. of 2-(4-isopropylphenyl)-N-(1-(4-(vinyloxy)benzyl)-1H-pyrazol-3-yl)acetamide (65 mg, 0.173 mmol) in CH_2Cl_2 (1.7 mL) is treated at 0 °C with CH_2ClI (0.0454 mL, 0.623 mmol) and Et_2Zn (1.0 M in hexanes, 0.415 mL, 0.415 mmol). The mixture is stirred at 0 °C for 1 h. Then, more CH_2ClI (0.0908 mL, 1.246 mmol) and Et_2Zn (1.0 M in hexanes, 0.830 mL, 0.830 mmol,4.8 eq) are added. The mixture is allowed to warm to RT and stirred for 30 min. Aq. sat. NH_4Cl is added, and the mixture is extracted with EtOAc. The combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification by HPLC yields example 195. LC-MS: t_R = 0.97 min, MH^+ = 390.33 (conditions 4).

(rac.)-1-Bromo-4-(1-methoxyethyl)benzene. NaH (55% in oil, 197 mg, about 4.51 mmol) is added to a sol. of (rac.)-1-(4-bromophenyl)ethanol (605 mg, 3.01 mmol) in THF (10 mL) at 0 °C. The mixture is stirred for 30 min at 0 °C, and MeI (0.94 mL, 15 mmol) is added. The mixture is allowed to warm up to rt, and is stirred for 4 h. A little water is added, and the solvents are removed under reduced pressure. The residue is diluted with CH_2Cl_2, and is dried over $MgSO_4$. The mixture is filtered, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92, 20 g silicagel, flow 18 mL/min) yields the title product.

(rac.)-tert-butyl 2-(4-(1-methoxyethyl)phenyl)acetate. According to *general procedure 6*, from (rac.)-1-bromo-4-(1-methoxyethyl)benzene (470 mg, 2.19 mmol), 2-tert-butoxy-2-oxoethylzinc chloride (0.5M in Et_2O, 5.0 mL, 2.5 mmol), $Pd_2(dba)_3$ (100 mg, 0.109 mmol), and Q-Phos (158 mg, 0.219 mmol) in THF (5 mL). The reaction is complete after 30 min at 90 °C. Purification of the residue by automated FC (Büchi, EtOAc / heptane 2:98 → 4:96 → 10:90, 20 g silicagel, flow 18 mL/min) yields the title product. LC-MS: t_R = 0.93 min, (conditions 3).

(rac.)-2-(4-(1-Methoxyethyl)phenyl)acetic acid. According to *general procedure 7*, from (rac.)-tert-butyl 2-(4-(1-methoxyethyl)phenyl)acetate (240 mg, 0.959 mmol) and HCl (4M in dioxane, 5 mL) in CH_2Cl_2 (10 mL). The reaction is complete overnight at rt. The solvents are removed under reduced pressure to yield the crude title compound that is used without further purification. LC-MS: t_R = 0.65 min (conditions 3).

Methyl 2-(4-methyl-3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl)acetate. NaH (55% in oil, 12 mg, 0.27 mmol) in added to a sol. of methyl (3,4-dihydro-3-oxo-2H-1,4-benzoxazin-6-yl)acetate (50 mg, 0.22 mmol) in THF (2 mL) at 0 °C. The mixture is stirred for 15 min, and MeI (0.030 mL, 0.34 mmol) is added. The mixture is stirred for 30 min at 0 °C, and the solvents are removed under reduced pressure. Purification by HPLC yields the title product. LC-MS: t_R = 0.71 min, MH^+ = 277.12 (conditions 3).

2-(4-Methyl-3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl)acetic acid. A mixture of methyl 2-(4-methyl-3-oxo-3,4-dihydro-2H-benzo[b][1,4]oxazin-6-yl)acetate (7.0 mg, 0.030 mmol) in aq. 2.5 M NaOH (0.5 mL) and MeOH (1.5 mL) is stirred at rt for 30 min. The solvents are partially removed under reduced pressure, and the pH is adjusted to 3 with aq. 1M HCl. The mixture is extracted with CH_2Cl_2. The combined org. layers are dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the title crude product. LC-MS: t_R = 0.59 min, MH^+ = 263.00 (conditions 3).

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
196[1]	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-cyclobutoxy-phenyl)-acetamide	0.84 min; 387.73; conditions 3
197[1]	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(4-cyclobutoxy-phenyl)-acetamide	0.89 min; 386.71; conditions 3
198[1]	2-(4-Cyclobutoxy-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.92 min; 380.01; conditions 3
199[1]	2-(4-Cyclobutoxy-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide	0.91 min; 392.04; conditions 3
200[1]	2-(4-Cyclobutoxy-phenyl)-N-[1-(5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.84 min; 380.87; conditions 3
201	rac-N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide	0.85 min; 368.02; conditions 3
202	rac-N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide	0.87 min; 385.87; conditions 3
203	rac-N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide	0.76 min; 376.03; conditions 3
204	N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(2-oxo-pyrrolidin-1-yl)-phenyl]-acetamide	0.78 min; 392.99; conditions 3
205	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-quinoxalin-6-yl-acetamide	0.80 min; 379.95; conditions 3

206	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-quinolin-7-yl-acetamide	0.64 min; 378.95; conditions 3
207	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1H-indol-6-yl)-acetamide	0.84 min; 367.25; conditions 3
208	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl)-acetamide	0.76 min; 398.97; conditions 3
209	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl)-acetamide	0.81 min; 412.99; conditions 3

[1] For the preparation of the carboxylic acid, see: Page, D.; Balaux, E.; Boisvert, L.; Liu, Z.; Milburn, C.; Tremblay, M.; Wei, Zhongyong; W., Simon; L., Xuehong; Cheng, Y; et al., Bioorg. Med. Chem. Lett., 2008, 18, 3695.

5-Fluoro-2-((3-(2-(4-isopropylphenyl)acetamido)-1H-pyrazol-1-yl)methyl)pyridine 1-oxide. To a solution of Example 106 (350 mg, 0.993 mmol,) in CH_2Cl_2 (3.5 mL) is added 3-chloroperbenzoic acid (343 mg, 1.99 mmol). The mixture is stirred overnight at rt. The mixture is diluted with EtOAc, and the org. layer is washed with aq. sat. $Na_2S_2O_3$, aq. sat. $NaHCO_3$, and brine. The org. layer is dried over $MgSO_4$, filtered and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Biotage, 50 g silicagel, MeOH / CH_2Cl_2 0:1000 → 15:985) yields the title product. LC-MS: t_R = 0.70 min, MH^+ = 369.21 (conditions 4).

Example 210: N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. To a sol. of 5-fluoro-2-((3-(2-(4-isopropylphenyl)acetamido)-1H-pyrazol-1-yl)methyl)pyridine 1-oxide (175 mg, 0.475 mmol) in CH_3CN (10 mL) is added Me_3SiCN (0.119 ml, 0.95 mmol) at rt. The mixture is stirred for 5 min, and diethylcarbamyl chloride (0.0903 ml, 0.713 mmol) is added dropwise. The mixture is stirred at 85 °C overnight. The mixture is partitioned between aq. sat. $NaHCO_3$ and EtOAc. The combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields example 210. LC-MS: t_R = 0.82 min, MH^+ = 378.31 (conditions 4).

Example 211: N-[1-(6-Chloro-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. 5-Fluoro-2-((3-(2-(4-isopropylphenyl)acetamido)-1H-pyrazol-1-yl)methyl)pyridine 1-oxide (37.7 mg, 0.102 mmol) is added to $POCl_3$ (1 mL) at 0 °C, and the mixture is stirred for 10 min at 0 °C, and then for 2.5 h at rt. The mixture is heated to 60 °C, and stirred at this temperature for 2 h. The mixture is dropped slowly on aq. sat. $NaHCO_3$ at 0 °C. The mixture is extracted with EtOAc, and the combined org. layers are washed with brine, dried over $MgSO_4$, filtered and the solvents are removed under reduced pressure. Purification by HPLC yields example 211. LC-MS: t_R = 0.86 min, MH^+ = 387.26 (conditions 4).

5-Bromo-1-methyl-1H-pyrrolo[2,3-b]pyridine. NaH (55% suspension in oil, 95 mg, about 213 mmol) is added to a sol. of 5-bromo-1H-pyrrolo[2,3-b]pyridine (350 mg, 1.78 mmol) in THF (2 mL) at 0 °C. The mixture is stirred for 15 min, and MeI (0.17 mL, 2.7 mmol) is added. The mixture is stirred for 30 min at 0 °C, and little water was added. The solvents were removed under reduced pressure. Purification of the residue by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92, 20 g silicagel, flow 18 mL/min) yields the title product. LC-MS: t_R = 0.81 min, MH^+ = 211.02 (conditions 3).

tert-Butyl 2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-1-methyl-1H-pyrrolo[2,3-b]pyridine (100 mg, 0.474 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.90 mL, 0.95 mmol), $Pd_2(dba)_3$ (22 mg, 0.024 mmol) and Q-Phos (34 mg, 0.048 mmol) in THF (1 mL). The reaction is complete after 90 min. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92, 20 g silicagel, flow 16 mL/min) yields the title product. LC-MS: t_R = 0.78 min, MH^+ = 247.15 (conditions 3).

2-(1-Methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)acetate (235 mg, 0.954 mmol) and HCl (4M in dioxane, 10 mL) in CH_2Cl_2 (10 mL). The reaction is complete overnight. Removing the solvents under reduced pressure yields the crude title product.

tert-Butyl 2-(3-methyl-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)acetate. Prepared according to *general procedure 6* from 6-bromo-3-methylbenzo[d]oxazol-2(3H)-one (230 mg, 1.01 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 4.00 mL, 2.00 mmol), $Pd_2(dba)_3$ (46 mg, 0.051 mmol) and Q-Phos (73 mg, 0.10 mmol) in dioxane (5 mL). The reaction is complete after 1 h at 90 °C. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 10 g silicagel, flow 10 mL/min) yields the title product. LC-MS: t_R = 0.85 min, MH^+ = 305.12 (conditions 3).

2-(3-Methyl-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(3-methyl-2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)acetate (198 mg, 0.752 mmol) and HCl (4M in dioxane, 4 mL) in CH_2Cl_2 (4 mL). The reaction is complete overnight. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.57 min (conditions 3).

tert-Butyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)acetate. Prepared according to *general procedure 6* from 6-bromobenzo[d]oxazol-2(3H)-one (216 mg, 1.01 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 4.00 mL, 2.00 mmol), $Pd_2(dba)_3$ (46 mg, 0.051 mmol) and Q-Phos (73 mg, 0.10 mmol) in dioxane (5 mL). The reaction is complete after 1 h at 90 °C. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 10 g silicagel, flow 10 mL/min) yields the title product. LC-MS: t_R = 0.78 min, MH^+ = 291.18 (conditions 3).

2-(2-Oxo-2,3-dihydrobenzo[d]oxazol-6-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(2-oxo-2,3-dihydrobenzo[d]oxazol-6-yl)acetate (100 mg, 0.401 mmol) and HCl (4M in dioxane, 3 mL) in

CH_2Cl_2 (3 mL). The reaction is complete overnight. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.50 min (conditions 3).

tert-Butyl 2-(1H-indol-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromoindole (300 mg, 1.53 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 6.00 mL, 3.00 mmol), $Pd_2(dba)_3$ (70 mg, 0.077 mmol) and Q-Phos (110 mg, 0.15 mmol) in dioxane (5 mL). The reaction is complete after 1 h at 90 °C. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 10 g silicagel, flow 10 mL/min) yields the title product. LC-MS: t_R = 0.89 min, MH^+ = 232.19 (conditions 3).

2-(1H-Indol-5-yl)acetic acid. A mixture of tert-butyl 2-(1H-indol-5-yl)acetate (50 mg, 0.22 mmol) and NaOH (11 mg, 0.26 mmol) in MeOH (4 mL) is heated to 55 °C and stirred at this temperature for 2 h. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. The residue is diluted with CH_2Cl_2, and aq. 1M HCl is added to pH 2-3. The phases are separated, and the org. layer is dried over $MgSO_4$, and filtered. The solvents are removed under reduced pressure to yield the crude title compound. LC-MS: t_R = 0.89 min (conditions 3).

tert-Butyl 2-(1-methyl-1H-indol-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-1-methylindole (321 mg, 1.53 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 6.00 mL, 3.00 mmol), $Pd_2(dba)_3$ (70 mg, 0.077 mmol) and Q-Phos (110 mg, 0.15 mmol) in dioxane (5 mL). The reaction is complete after 1 h at 90 °C. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 10 g silicagel, flow 10 mL/min) yields the title product. LC-MS: t_R = 0.94 min, MH^+ = 246.28 (conditions 3).

2-(1-Methyl-1H-indol-5-yl)acetic acid. A mixture of tert-butyl 2-(1H-indol-5-yl)acetate (53 mg, 0.22 mmol) and NaOH (11 mg, 0.26 mmol) in MeOH (4 mL) is heated to 55 °C and stirred at this temperature for 2 h. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. The residue is diluted with CH_2Cl_2, and aq. 1M HCl is added to pH 2-3. The phases are separated, and the org. layer is dried over $MgSO_4$, and filtered. The solvents are removed under reduced pressure to yield the crude title compound. LC-MS: t_R = 0.69 min (conditions 3).

tert-Butyl 2-(1-methyl-1H-indol-6-yl)acetate. Prepared according to *general procedure 6* from 6-bromo-1-methylindole (321 mg, 1.53 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 6.00 mL, 3.00 mmol), $Pd_2(dba)_3$ (70 mg, 0.077 mmol) and Q-Phos (110 mg, 0.15 mmol) in dioxane (5 mL). The reaction is complete after 1 h at 90 °C. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 10 g silicagel, flow 10 mL/min) yields the title product. LC-MS: t_R = 0.95 min, MH^+ = 246.25 (conditions 3).

2-(1-Methyl-1H-indol-6-yl)acetic acid. A mixture of tert-butyl 2-(1H-indol-6-yl)acetate (53 mg, 0.22 mmol) and NaOH (11 mg, 0.26 mmol) in MeOH (4 mL) is heated to 55 °C and stirred at this temperature for 2 h. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. The residue is diluted

with CH_2Cl_2, and aq. 1M HCl is added to pH 2-3. The phases are separated, and the org. layer is dried over $MgSO_4$, and filtered. The solvents are removed under reduced pressure to yield the crude title compound. LC-MS: t_R = 0.69 min (conditions 3).

tert-Butyl 2-(1-methyl-1H-benzo[d]imidazol-6-yl)acetate. Prepared according to *general procedure 6* from 6-bromo-1-methyl-1H-benzo[d]imidazole (490 mg, 2.32 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 5.10 mL, 2.55 mmol), $Pd_2(dba)_3$ (106 mg, 0.116 mmol) and Q-Phos (167 mg, 0.232 mmol) in dioxane (4 mL). The reaction is complete after 1 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 10 g silicagel, flow 10 mL/min) yields the title product. LC-MS: t_R = 0.59 min, MH^+ = 247.11 (conditions 3).

2-(1-Methyl-1H-benzo[d]imidazol-6-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(1-methyl-1H-benzo[d]imidazol-6-yl)acetate (50 mg, 0.203 mmol) and HCl (4M in dioxane, 2 mL) in CH_2Cl_2 (4 mL). The reaction is complete after 90 min. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.36 min (conditions 3).

tert-Butyl 2-(1-methyl-1H-indazol-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-1-methyl-1H-indazole (490 mg, 2.32 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 5.10 mL, 2.55 mmol), $Pd_2(dba)_3$ (106 mg, 0.116 mmol) and Q-Phos (167 mg, 0.232 mmol) in dioxane (4 mL). The reaction is complete after 1 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 10 g silicagel, flow 10 mL/min) yields the title product. LC-MS: t_R = 0.88 min, MH^+ = 247.14 (conditions 3).

2-(1-Methyl-1H-indazol-5-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(1-methyl-1H-indazol-5-yl)acetate (50 mg, 0.20 mmol) and HCl (4M in dioxane, 2 mL) in CH_2Cl_2 (4 mL). The reaction is complete after 4.5 h. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.60 min (conditions 3).

tert-Butyl 2-(1-methyl-1H-indazol-6-yl)acetate. Prepared according to *general procedure 6* from 6-bromo-1-methyl-1H-indazole (490 mg, 2.32 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 5.10 mL, 2.55 mmol), $Pd_2(dba)_3$ (106 mg, 0.116 mmol) and Q-Phos (167 mg, 0.232 mmol) in dioxane (4 mL). The reaction is complete after 1 h at rt. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 8:92 → 15:85, 10 g silicagel, flow 10 mL/min) yields the title product. LC-MS: t_R = 0.88 min, MH^+ = 247.14 (conditions 3).

2-(1-Methyl-1H-indazol-6-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(1-methyl-1H-indazol-6-yl)acetate (50 mg, 0.20 mmol) and HCl (4M in dioxane, 2 mL) in CH_2Cl_2 (4 mL). The reaction is complete after 6.5 h. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.60 min (conditions 3).

tert-Butyl 2-(4-(3-fluorooxetan-3-yl)phenyl)acetate. Prepared according to *general procedure 6* from 3-(4-bromophenyl)-3-fluorooxetane (WO2008156726, 150 mg, 0.649 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.43 mL, 0.714 mmol), $Pd_2(dba)_3$ (29.7 mg, 0.033 mmol) and Q-Phos (46 mg, 0.065 mmol) in THF (4 mL). The reaction is complete after 2 h at 85 °C. Purification of the crude by automated FC (Büchi, EtOAc / heptane 10:90 → 30:70 → 50:50 → 75:25) yields the title product. LC-MS: t_R = 0.90 min (conditions 3).

2-(4-(3-Fluorooxetan-3-yl)phenyl)acetic acid. A mixture of tert-butyl 2-(4-(3-fluorooxetan-3-yl)phenyl)acetate (10 mg, 0.038 mmol) in HCOOH (1 mL) is stirred at rt for 1 h. The solvents are removed under reduced pressure. The residue is dissolved in CH_2Cl_2, and the mixture is washed with aq. 0.01M HCl. After partitioning the layers in a Separator® (Biotage), the org. layer is concentrated under reduced pressure to yield the crude title product. LC-MS: t_R = 0.63 min (conditions 3).

tert-Butyl 2-(4-(3-hydroxyoxetan-3-yl)phenyl)acetate. Prepared according to *general procedure 6* from 3-(4-bromophenyl)oxetan-3-ol (WO2008156726, 200 mg, 0.873 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 3.66 mL, 1.83 mmol), $Pd_2(dba)_3$ (40 mg, 0.044 mmol) and Q-Phos (62 mg, 0.087 mmol) in THF (4 mL). The reaction is complete after 2 h at 85 °C. Purification of the crude by automated FC (Büchi, EtOAc / heptane 10:90 → 30:70 → 50:50 → 75:25) yields the title product. LC-MS: t_R = 0.76 min (conditions 3).

2-(4-(3-Hydroxyoxetan-3-yl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(3-hydroxyoxetan-3-yl)phenyl)acetate (20 mg, 0.076 mmol) in HCOOH (1 mL). The reaction is complete after 1 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.48 min (conditions 3).

tert-butyl 2-(4-(3-Methyloxetan-3-yl)phenyl)acetate. Prepared according to *general procedure 6* from 3-(4-bromophenyl)-3-methyloxetane (105 mg, 0.462 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.02 mL, 0.509 mmol), $Pd_2(dba)_3$ (21 mg, 0.023 mmol) and Q-Phos (33 mg, 0.046 mmol) in THF (2.5 mL). The reaction is complete after 1.5 h at 85 °C. Purification of the crude by automated FC (Büchi, EtOAc / heptane 10:90 → 30:70 → 50:50 → 75:25) yields the title product. LC-MS: t_R = 0.91 min (conditions 3).

2-(4-(3-Methyloxetan-3-yl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(3-methyloxetan-3-yl)phenyl)acetate (25 mg, 0.095 mmol) in HCOOH (1 mL). The reaction is complete after 1 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.64 min (conditions 3).

tert-Butyl 2-(3,3-dimethyl-2-oxoindolin-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-3,3-dimethylindolin-2-one (367 mg, 1.53 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 6.0 mL, 3.0 mmol), $Pd_2(dba)_3$ (70 mg, 0.077 mmol) and Q-Phos (110 mg, 0.153 mmol) in dioxane (5 mL). The reaction is complete after 1.5 h at 90 °C. Purification of the crude by automated FC (Büchi, EtOAc / heptane

1:99 → 3:97 → 5:95 → 10:90 → 25:75 → 50:50) yields the title product. LC-MS: t_R = 0.83 min, MH^+ = 276.28 (conditions 3).

2-(3,3-Dimethyl-2-oxoindolin-5-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(3,3-dimethyl-2-oxoindolin-5-yl)acetate (56 mg, 0.20 mmol) in HCl (4M in dioxane, 2 mL) and CH_2Cl_2 (4 mL). The reaction is complete overnight at rt. Removing the solvents under reduced pressure yields the crude title product.

tert-Butyl 2-(1,3,3-trimethyl-2-oxoindolin-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-1,3,3-trimethylindolin-2-one (170 mg, 0.669 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 2.6 mL, 1.3 mmol), $Pd_2(dba)_3$ (31 mg, 0.033 mmol) and Q-Phos (48 mg, 0.077 mmol) in dioxane (4 mL). The reaction is complete after 20 min at 90 °C. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 10:90 → 25:75 → 50:50) yields the title product. LC-MS: t_R = 0.89 min, MH^+ = 290.01 (conditions 3).

2-(1,3,3-Trimethyl-2-oxoindolin-5-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(1,3,3-trimethyl-2-oxoindolin-5-yl)acetate (90 mg, 0.31 mmol) in HCl (4M in dioxane, 2 mL) and CH_2Cl_2 (4 mL). The reaction is complete overnight at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.63 min, MH^+ = 275.23 (conditions 3).

tert-Butyl 2-(1-methyl-1H-benzo[d]imidazol-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-1-methyl-1H-benzo[d]imidazole (490 mg, 2.32 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 5.1 mL, 2.55 mmol), $Pd_2(dba)_3$ (106 mg, 0.116 mmol) and Q-Phos (167 mg, 0.232 mmol) in dioxane (4 mL). The reaction is complete after 2 h at 90 °C. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 10:90 → 25:75 → 50:50) yields the title product. LC-MS: t_R = 0.60 min, MH^+ = 246.99 (conditions 3).

2-(1-Methyl-1H-benzo[d]imidazol-5-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(1-methyl-1H-benzo[d]imidazol-5-yl)acetate (44 mg, 0.17 mmol) in HCl (4M in dioxane, 2 mL) and CH_2Cl_2 (4 mL). The reaction is complete after 3 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.37 min, MH^+ = 191.16 (conditions 3).

3-(4-Bromophenyl)-3-methoxyoxetane. 3-(4-Bromophenyl)oxetan-3-ol (WO2008156726, 150 mg, 0.65 mmol) is dissolved in DMF (2.00 mL). The mixture is cooled to 0 °C, and NaH (29 mg, 0.72 mmol) is added. The mixture is stirred for 1 h at 0 °C, and MeI (0.05 ml, 0.79 mmol) is added. The mixture is stirred at rt over 3 days. Water is added. The mixture is extracted with ether. The combined org. extracts are dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure under reduced pressure. Purification of the crude by automated FC (Combiflash, column 24 g, flow rate 35 mL/min, EtOAc / heptane 0:100 → 10:90 → 30:70) yields the title product. LC-MS: t_R = 0.80 min, MH^+ = 205.30 (conditions 3).

tert-Butyl 2-(4-(3-methoxyoxetan-3-yl)phenyl)acetate. Prepared according to *general procedure 6* from 3-(4-bromophenyl)-3-methoxyoxetane (100 mg, 0.41 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 0.9 mL, 0.45 mmol), $Pd_2(dba)_3$ (19 mg, 0.021 mmol) and Q-Phos (29 mg, 0.041 mmol) in dioxane (3 mL). The reaction is complete after 2 h at 90 °C. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 3:97 → 5:95 → 10:90 → 25:75 → 50:50) yields the title product. LC-MS: t_R = 0.87 min, (conditions 3).

2-(4-(3-Methoxyoxetan-3-yl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(3-methoxyoxetan-3-yl)phenyl)acetate (40 mg, 0.14 mmol) in HCOOH (1 mL). The reaction is complete after 1 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.59 min (conditions 3).

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
212	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-acetamide	0.75 min; 382.26; conditions 3
213	N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-acetamide	0.73 min; 364.22; conditions 3
214	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-acetamide	0.70 min; 371.25; conditions 3
215	N-[1-(4-Methoxy-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-acetamide	0.73 min; 376.29; conditions 3
216	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-cyclopropyl-pyridin-3-yl)-acetamide	0.51 min; 376.33; conditions 4
217	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(3-methyl-2-oxo-2,3-dihydro-benzooxazol-6-yl)-acetamide	0.80 min; 399.25; conditions 3
218	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(2-oxo-2,3-dihydro-benzooxazol-6-yl)-acetamide	0.75 min; 385.18; conditions 3
219	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1H-indol-5-yl)-acetamide	0.83 min; 367.23; conditions 3

220	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.88 min; 381.29; conditions 3
221	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide	0.88 min; 381.27; conditions 3
222	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(3-methyl-3H-benzoimidazol-5-yl)-acetamide	0.62 min; 382.29; conditions 3
223	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.83 min; 382.30; conditions 3
224	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	0.83 min; 382.28; conditions 3
225	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	0.85 min; 402.82; conditions 3
226	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-hydroxy-oxetan-3-yl)-phenyl]-acetamide	0.73 min; 400.11; conditions 3
227	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide	0.85 min; 398.02; conditions 3
228	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide	0.78 min; 411.29; conditions 3
229	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide	0.83 min; 425.27; conditions 3
230	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-benzoimidazol-5-yl)-acetamide	0.62 min; 382.29; conditions 3
231	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide	0.82 min; 414.28; conditions 3

Examples 232 and 233: N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((R)-1-methoxy-ethyl)-phenyl]-acetamide and N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((S)-1-methoxy-ethyl)-phenyl]-acetamide

Separation of the enantiomers from Example 202 by chiral HPLC yields examples 232 and 233. Absolute configuration of each enantiomer was attributed arbitrarily.

4-Cyanophenethyl acetate. Pyridine (1.1 mL, 13.6 mmol) and Ac_2O (0.51 mL, 5.44 mmol) are added to a sol. of 4-(2-hydroxyethyl)benzonitrile (200 mg, 1.36 mmol) in CH_2Cl_2 (3 mL). The mixture is stirred at rt overnight. The solvents are removed under reduced pressure, and the residue is partitioned between Et_2O and aq. 1M HCl. The org. layer is washed with aq. 1M HCl, aq. 10% Na_2CO_3, and brine. The org. layer is dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.77 min (conditions 3).

4-(N-Hydroxycarbamimidoyl)phenethyl acetate. $H_2NOH{\cdot}HCl$ (97.2 mg, 1.4 mmol) is added to a sol. of 4-cyanophenethyl acetate (241 mg, 1.27 mmol) in MeOH (4.2 mL). The sol. is stirred at 45 °C for 45 h, and is allowed to cool to rt. The solvents are removed under reduced pressure. Purification of the crude by automated FC (Combiflash, 24 g silicagel, MeOH / CH_2Cl_2 0:100 → 5:95) yields the title product. LC-MS: t_R = 0.45 min, MH^+ = 223.08 (conditions 3).

4-(5-Methyl-1,2,4-oxadiazol-3-yl)phenethyl acetate. A mixture of 4-(N-hydroxycarbamimidoyl)phenethyl acetate (50 mg, 0.225 mmol) in Ac_2O (0.225 mL) is stirred at 100 °C for 2 h. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. The residue is dried in a Kugelrohr oven. Purification of the crude by automated FC (Combiflash, 4 g silicagel, MeOH / CH2Cl2 0:100 → 0.5:99.5) yields the title product. LC-MS: t_R = 0.81 min, MH^+ = 247.22 (conditions 3).

2-(4-(5-Methyl-1,2,4-oxadiazol-3-yl)phenyl)ethan-1-ol. A mixture of 4-(5-methyl-1,2,4-oxadiazol-3-yl)phenethyl acetate (38.5 mg, 0.156 mmol), K_2CO_3 (216 mg, 1.56 mmol), in MeOH (1.35 mL) and water (0.15 mL) is stirred at rt overnight. The mixture is taken up in EtOAc and washed twice with water. The org. layer is dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. LC-MS: t_R = 0.65 min (conditions 3).

2-(4-(5-Methyl-1,2,4-oxadiazol-3-yl)phenyl)acetic acid. CrO_3 2M in H_2SO_4, 0.288 mL, 0.575 mmol) is added at rt to a sol. of 2-(4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)ethan-1-ol (23.5 mg, 0.115 mmol) in acetone (1.5 mL). The resulting mixture is stirred at rt for 6 min, and water is added. The mixture is extracted with CH_2Cl_2 (5x). The combined org. layers are dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. LC-MS: t_R = 0.65 min, MH^+ = 260.23 (conditions 3).

4-(1,2,4-Oxadiazol-3-yl)phenethyl acetate. A mixture of 4-(N-hydroxycarbamimidoyl)phenethyl acetate (50 mg, 0.225 mmol) in $HC(OEt)_3$ (0.225 mL) is stirred at 100 °C for 5 h. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. The residue is dried in a Kugelrohr oven to yield the crude title product. LC-MS: t_R = 0.80 min (conditions 3).

2-(4-(1,2,4-Oxadiazol-3-yl)phenyl)ethan-1-ol. A mixture of 4-(1,2,4-oxadiazol-3-yl)phenethyl acetate (52.2 mg, 0.225 mmol), K_2CO_3 (311 mg, 2.25 mmol), in MeOH (1.94 mL) and water (0.22 mL) is stirred at rt overnight. The mixture is taken up in EtOAc and washed twice with water. The org. layer is dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. LC-MS: t_R = 0.59 min (conditions 3).

2-(4-(1,2,4-Oxadiazol-3-yl)phenyl)acetic acid. CrO_3 2M in H_2SO_4, 0.585 mL, 1.17 mmol) is added at rt to a sol. of 2-(4-(1,2,4-oxadiazol-3-yl)phenyl)ethan-1-ol (44.5 mg, 0.234 mmol) in acetone (3 mL). The resulting mixture is stirred at rt for 20 min, and water is added. The mixture is extracted with CH_2Cl_2 (5x). The combined org. layers are dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. LC-MS: t_R = 0.62 min (conditions 3).

tert-Butyl 2-(4-(3,3-difluorocyclobutyl)phenyl)acetate. Prepared according to *general procedure 6* from 1-bromo-4-(3,3-difluorocyclobutyl)benzene (US 20100197591, 22 mg, 0.089 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 0.2 mL, 0.1 mmol), $Pd_2(dba)_3$ (4.1 mg, 0.045 mmol) and Q-Phos (6.3 mg, 0.089 mmol) in dioxane (1 mL). The reaction is complete after 3 h at 60 °C. Purification of the crude by automated FC (Combiflash, EtOAc / heptane 0:100 80:20) yields the title product. LC-MS: t_R = 1.00 min, (conditions 3).

2-(4-(3,3-Difluorocyclobutyl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(3,3-difluorocyclobutyl)phenyl)acetate (12 mg, 0.050 mmol) in HCOOH (0.55 mL). The reaction is complete after 2 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.78 min (conditions 3).

tert-Butyl 2-(4-(oxetan-3-yloxy)phenyl)acetate. Prepared according to *general procedure 6* from 3-(4-bromophenoxy)oxetane (WO 2012120397, 68 mg, 0.30 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 0.70 mL, 0.35 mmol), $Pd_2(dba)_3$ (14 mg, 0.015 mmol) and X-Phos (7.1 mg, 0.015 mmol) in THF (1.85 mL). The reaction is complete overnight at 50 °C. Purification of the crude by automated FC (Combiflash, MeOH / CH_2Cl_2 0:100 2:98) yields the title product. LC-MS: t_R = 0.88 min, (conditions 3).

2-(4-(Oxetan-3-yloxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(oxetan-3-yloxy)phenyl)acetate (40 mg, 0.15 mmol) in HCOOH (1.5 mL). The reaction is complete after 2.5 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.60 min (conditions 3).

1-Bromo-4-(3,3-difluorocyclobutoxy)benzene. PPh_3 (267 mg, 1.02 mmol) is dissolved in dry toluene (2 mL) and cooled to 0 °C. Dropwise, diethyl azodicarboxylate (0.165 mL, 1.02 mmol) is added and the light yellow sol. is stirred at 0 °C for 10 min. A sol. of 3,3-difluorocyclobutanol (100 mg, 0.925 mmol) in toluene (0.8 ml) is added. After stirring for another 10 min at rt, 4-bromophenol (160 mg, 0.925 mmol) is added, and the sol. is stirred at 100°C overnight. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Combiflash, 40 g silicagel, EtOAc / heptane 0:100 → 5:95) yields the title product. LC-MS: t_R = 0.94 min (conditions 3).

tert-Butyl 2-(4-(3,3-difluorocyclobutoxy)phenyl)acetate. Prepared according to *general procedure 6* from 1-bromo-4-(3,3-difluorocyclobutoxy)benzene (78 mg, 0.30 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 0.74 mL, 0.37 mmol), $Pd_2(dba)_3$ (14 mg, 0.015 mmol) and X-Phos (7.1 mg, 0.015 mmol) in THF

(1.85 mL). The reaction is complete overnight at 50 °C. Purification of the crude by automated FC (Combiflash, MeOH / CH_2Cl_2 0:100 2:98) yields the title product. LC-MS: t_R = 0.98 min, (conditions 3).

2-(4-(3,3-Difluorocyclobutoxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(3,3-difluorocyclobutoxy)phenyl)acetate (66 mg, 0.22 mmol) in HCOOH (2.2 mL). The reaction is complete after 40 min at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.77 min (conditions 3).

(3-Methyloxetan-3-yl)methyl 4-methylbenzenesulfonate. p-Toluenesulfonyl chloride (2.17 g, 11.4 mmol) is dissolved in CH_2Cl_2 (9.5 mL) at rt. Pyridine (1.53 mL, 19 mmol) is added, followed by 3-methyl-3-oxetanemethanol (0.977 mL, 9.5 mmol). The sol. is stirred at rt for 4 h. The sol. is diluted with CH_2Cl_2 and washed with aq. 0.1M HCl and with aq. sat. $NaHCO_3$. The org. layer is dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Combiflash, EtOAc/heptane 0:100 → 60:40) yields the title product. LC-MS: t_R = 0.80 min, MH^+ = 257.17 (conditions 3).

3-((4-Bromophenoxy)methyl)-3-methyloxetane. A mixture of (3-methyloxetan-3-yl)methyl 4-methylbenzenesulfonate (500 mg, 1.95 mmol), 4-bromphenol (371 mg, 2.15 mmol), KI (139 mg, 0.839 mmol) and K_2CO_3 (539 mg, 3.9 mmol) in DMF (2.8 mL) is stirred at 130 °C for 1.5 h. The mixture is allowed to cool to rt, and is partitioned between EtOAc and water. The org. layer is washed with water (3x), dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. Purification of the crude by FC (Combiflash, 12 g cartridge, EtOAc / heptane 0:100 → 30:70) yields the title product. LC-MS: t_R = 0.87 min (conditions 3).

tert-Butyl 2-(4-((3-methyloxetan-3-yl)methoxy)phenyl)acetate. Prepared according to *general procedure 6* from 3-((4-bromophenoxy)methyl)-3-methyloxetane (200 mg, 0.778 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 2.34 mL, 1.17 mmol), $Pd_2(dba)_3$ (36 mg, 0.039 mmol) and X-Phos (19 mg, 0.039 mmol) in THF (4.9 mL). The reaction is complete after 1.5 h at rt. Purification of the crude by automated FC (Combiflash, MeOH / CH_2Cl_2 0:100 2:98) yields the title product. LC-MS: t_R = 0.93 min, (conditions 3).

2-(4-((3-methyloxetan-3-yl)methoxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-((3-methyloxetan-3-yl)methoxy)phenyl)acetate (105 mg, 0.36 mmol) in HCOOH (3.4 mL). The reaction is complete after 1.5 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.68 min (conditions 3).

Oxetan-3-ylmethyl 4-methylbenzenesulfonate. p-Toluenesulfonyl chloride (370 mg, 1.94 mmol) is dissolved in pyridine (1.62 mL, 20 mmol). 3-Oxetanemethanol (150 mg, 1.62 mmol) is added. The sol. is stirred at rt for 3 h. The sol. is diluted with EtOAc, and washed with aq. 0.1M HCl and with aq. sat. $NaHCO_3$. The org. layer is dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Combiflash, EtOAc/heptane 0:100 → 50:50) yields the title product. LC-MS: t_R = 0.75 min, MH^+ = 243.12 (conditions 3).

3-((4-Bromophenoxy)methyl)-3-oxetane. A mixture of oxetan-3-ylmethyl 4-methylbenzenesulfonate (300 mg, 1.24 mmol), 4-bromphenol (236 mg, 1.36 mmol), KI (88 mg, 0.43 mmol) and K_2CO_3 (342 mg, 2.48 mmol) in DMF (1.8 mL) is stirred at 130 °C for 1.5 h. The mixture is allowed to cool to rt, and is partitioned between EtOAc and water. The org. layer is washed with water (3x), dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. Purification of the crude by FC (Combiflash, 12 g silicagel, EtOAc / heptane 0:100 → 30:70) yields the title product. LC-MS: t_R = 0.82 min (conditions 3).

tert-Butyl 2-(4-(oxetan-3-ylmethoxy)phenyl)acetate. Prepared according to *general procedure 6* from 3-((4-bromophenoxy)methyl)-3-oxetane (182 mg, 0.749 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 2.2 mL, 1.1 mmol), $Pd_2(dba)_3$ (34 mg, 0.037 mmol) and X-Phos (18 mg, 0.037 mmol) in THF (4.7 mL). The reaction is complete after 2.5 h at rt. Purification of the crude by automated FC (Combiflash, MeOH / CH_2Cl_2 0:100 2:98) yields the title product. LC-MS: t_R = 0.89 min, (conditions 3).

2-(4-(Oxetan-3-ylmethoxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(oxetan-3-ylmethoxy)phenyl)acetate (95 mg, 0.34 mmol) in HCOOH (1.3 mL). The reaction is complete after 2 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.62 min (conditions 3).

(3,3-Difluoro-1-methylcyclobutyl)methyl 4-methylbenzenesulfonate. p-Toluenesulfonyl chloride (252 mg, 1.32 mmol) is dissolved in pyridine (1.1 mL). (3,3-Difluoro-1-methyl-cyclobutyl)methanol (150 mg, 1.10 mmol) is added. The sol. is stirred at rt overnight. The sol. is diluted with EtOAc, and washed with aq. 0.1M HCl and with aq. sat. $NaHCO_3$. The org. layer is dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.93 min, MH^+ = 243.12 (conditions 3).

1-Bromo-4-((3,3-difluoro-1-methylcyclobutyl)methoxy)benzene. A mixture of (3,3-difluoro-1-methylcyclobutyl)methyl 4-methylbenzenesulfonate (232 mg, 0.799 mmol), 4-bromphenol (152 mg, 0.879 mmol), KI (57 mg, 0.34 mmol) and K_2CO_3 (221 mg, 1.60 mmol) in DMF (1.2 mL) is stirred at 130 °C for 2.5 h. The mixture is allowed to cool to rt, and is partitioned between EtOAc and water. The org. layer is washed with water (3x), dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. Purification of the crude by FC (Combiflash, 12 g silicagel, EtOAc / heptane 0:100 → 30:70) yields the title product. LC-MS: t_R = 1.01 min (conditions 3).

tert-Butyl 2-(4-((3,3-difluoro-1-methylcyclobutyl)methoxy)phenyl)acetate. Prepared according to *general procedure 6* from 1-bromo-4-((3,3-difluoro-1-methylcyclobutyl)methoxy)benzene (152 mg, 0.522 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.57 mL, 0.78 mmol), $Pd_2(dba)_3$ (24 mg, 0.026 mmol) and X-Phos (12.4 mg, 0.026 mmol) in THF (3.3 mL). The reaction is complete after 2.5 h at rt. Purification of the crude by automated FC (Combiflash, MeOH / CH_2Cl_2 0:100 2:98) yields the title product. LC-MS: t_R = 1.04 min, (conditions 3).

2-(4-((3,3-Difluoro-1-methylcyclobutyl)methoxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-((3,3-difluoro-1-methylcyclobutyl)methoxy)phenyl)acetate (100 mg, 0.306 mmol) in HCOOH (1.2 mL). The reaction is complete after 2 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.85 min (conditions 3).

(3,3-Difluorocyclobutyl)methyl 4-methylbenzenesulfonate. p-Toluenesulfonyl chloride (281 mg, 1.47 mmol) is dissolved in pyridine (1.23 mL). (3,3-Difluorocyclobutyl)methanol (150 mg, 1.23 mmol) is added. The sol. is stirred at rt overnight. The sol. is diluted with EtOAc, and washed with aq. 0.1M HCl and with aq. sat. $NaHCO_3$. The org. layer is dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.90 min (conditions 3).

1-Bromo-4-((3,3-difluorocyclobutyl)methoxy)benzene. A mixture of (3,3-difluorocyclobutyl)methyl 4-methylbenzenesulfonate (227 mg, 0.822 mmol), 4-bromphenol (156 mg, 0.904 mmol), KI (59 mg, 0.35 mmol) and K_2CO_3 (227 mg, 1.64 mmol) in DMF (1.2 mL) is stirred at 130 °C for 2.5 h. The mixture is allowed to cool to rt, and is partitioned between EtOAc and water. The org. layer is washed with water (3x), dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. Purification of the crude by FC (Combiflash, 12 g silicagel, EtOAc / heptane 0:100 → 30:70) yields the title product. LC-MS: t_R = 0.97 min (conditions 3).

tert-butyl 2-(4-((3,3-difluorocyclobutyl)methoxy)phenyl)acetate. Prepared according to *general procedure 6* from 1-bromo-4-((3,3-difluorocyclobutyl)methoxy)benzene (102 mg, 0.368 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.52 mL, 0.76 mmol), $Pd_2(dba)_3$ (17 mg, 0.018 mmol) and X-Phos (8.8 mg, 0.018 mmol) in THF (2.3 mL). The reaction is complete after 2.5 h at rt. Purification of the crude by automated FC (Combiflash, EtOAc / heptane 0:100 10:90) yields the title product. LC-MS: t_R = 1.00 min, (conditions 3).

2-(4-((3,3-Difluorocyclobutyl)methoxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-((3,3-difluorocyclobutyl)methoxy)phenyl)acetate (72 mg, 0.231 mmol) in HCOOH (0.87 mL). The reaction is complete after 2 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.80 min (conditions 3).

(3-Fluorooxetan-3-yl)methyl 4-methylbenzenesulfonate. p-Toluenesulfonyl chloride (216 mg, 1.13 mmol) is dissolved in CH_2Cl_2 (0.95 mL). Pyridine (0.152 mL, 1.89 mmol) and (3-fluorooxetan-3-yl)methanol (WO 2011084402, 100 mg, 0.943 mmol) is added. The sol. is stirred at rt for 6 h. The sol. is diluted with CH_2Cl_2, and washed with aq. 0.1M HCl and with aq. sat. $NaHCO_3$. The org. layer is dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.80 min, MH^+ = 261.13 (conditions 3).

3-((4-Bromophenoxy)methyl)-3-fluorooxetane. A mixture of (3-fluorooxetan-3-yl)methyl 4-methylbenzenesulfonate (138 mg, 0.530 mmol), 4-bromphenol (101 mg, 0.583 mmol), KI (38 mg, 0.23 mmol)

and K_2CO_3 (147 mg, 1.06 mmol) in DMF (0.75 mL) is stirred at 130 °C for 1.5 h. The mixture is allowed to cool to rt, and is partitioned between EtOAc and water. The org. layer is washed with water (3x), dried over Na_2SO_4, filtered, and the solvents are removed under reduced pressure. Purification of the crude by FC (Combiflash, 12 g silicagel, EtOAc / heptane 0:100 → 30:70) yields the title product. LC-MS: t_R = 0.84 min (conditions 3).

tert-Butyl 2-(4-((3-fluorooxetan-3-yl)methoxy)phenyl)acetate. Prepared according to *general procedure 6* from 3-((4-bromophenoxy)methyl)-3-fluorooxetane (84 mg, 0.32 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.28 mL, 0.64 mmol), $Pd_2(dba)_3$ (15 mg, 0.016 mmol) and X-Phos (7.6 mg, 0.016 mmol) in THF (2.0 mL). The reaction is complete after 3 h at rt. Purification of the crude by automated FC (Combiflash, MeOH / CH_2Cl_2 0:100 → 2:98) yields the title product. LC-MS: t_R = 0.91 min, (conditions 3).

2-(4-((3-Fluorooxetan-3-yl)methoxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-((3-fluorooxetan-3-yl)methoxy)phenyl)acetate (63 mg, 0.21 mmol) in HCOOH (0.80 mL). The reaction is complete after 3 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.65 min (conditions 3).

5-Bromo-2-(3-methoxyoxetan-3-yl)pyridine. To an ice-cooled solution of 3-(5-bromopyridin-2-yl)oxetan-3-ol (US 14/018,993, 1.34 g, 5.82 mmol) in DMF (30 mL), NaH (60% in oil, 303 mg, 7.57 mmol) is added, and the mixture is stirred at 0 °C for 30 min. MeI (0.44 mL, 6.99 mmol) is added, and the mixture is stirred at rt overnight. The mixture is diluted with water (100 mL) and EtOAc (100 mL). The layers are separated. The aq. phase is extracted with EtOAc (2x 50 mL). The combined org. layers are washed with water and brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Flash master, column 100 g, flow : 45 mL/min, EtOAc / heptane 0:100 → 50:50) yields the title product. LC-MS: t_R = 0.66 min, MH^+ = 244.06 (conditions 3).

tert-Butyl 2-(6-(3-methoxyoxetan-3-yl)pyridin-3-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-2-(3-methoxyoxetan-3-yl)pyridine (366 mg, 1.50 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 6.0 mL, 3.0 mmol), $Pd_2(dba)_3$ (69 mg, 0.075 mmol) and X-Phos (37 mg, 0.075 mmol) in THF (20 mL). The reaction is complete overnight at 45 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.71 min, MH^+ = 280.29 (conditions 3).

2-(6-(3-Methoxyoxetan-3-yl)pyridin-3-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(6-(3-methoxyoxetan-3-yl)pyridin-3-yl)acetate (50 mg, 0.18 mmol) in HCOOH (2.0 mL). The reaction is complete overnight at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.40 min, MH^+ = 224.20 (conditions 3).

6-Bromo-1,3-dimethyl-1H-indole. To an ice-cooled solution of 6-bromo-3-methylindole (1.00 g, 4.76 mmol) in DMF (20 mL), NaH (60% in oil, 381 mg, 9.52 mmol) is added, and the mixture is stirred at 0 °C for 30 min. MeI (0.449 mL, 7.14 mmol) is added, and the mixture is stirred at rt for 2 h. The mixture is diluted with water

(100 mL) and EtOAc (100 mL). The layers are separated. The aq. phase is extracted with EtOAc (2x 50 mL). The comb. org. layers are washed with water and brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.95 min (conditions 3).

tert-Butyl 2-(1,3-dimethyl-1H-indol-6-yl)acetate. Prepared according to *general procedure 6* from 6-bromo-1,3-dimethyl-1H-indole (300 mg, 1.34 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 5.4 mL, 2.7 mmol), $Pd_2(dba)_3$ (61 mg, 0.067 mmol) and X-Phos (33 mg, 0.067 mmol) in THF (20 mL). The reaction is complete overnight at 45 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.98 min, MH^+ = 260.29 (conditions 3).

2-(1,3-Dimethyl-1H-indol-6-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(1,3-dimethyl-1H-indol-6-yl)acetate (50 mg, 0.19 mmol) in HCOOH (2.0 mL). The reaction is complete after 3 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.75 min, MH^+ = 204.28 (conditions 3).

tert-Butyl 2-(1,3-dimethyl-1H-indol-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-1,3-dimethyl-1H-indole (Repka, L. M.; Ni, J.; Reisman, S. E. J. Am. Chem. Soc., 2010, 132, 14418, 300 mg, 1.34 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 5.4 mL, 2.7 mmol), $Pd_2(dba)_3$ (61 mg, 0.067 mmol) and X-Phos (33 mg, 0.067 mmol) in THF (20 mL). The reaction is complete overnight at 45 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.98 min, MH^+ = 260.30 (conditions 3).

2-(1,3-Dimethyl-1H-indol-5-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(1,3-dimethyl-1H-indol-5-yl)acetate (50 mg, 0.19 mmol) in HCOOH (2.0 mL). The reaction is complete after 3 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.75 min, MH^+ = 204.30 (conditions 3).

tert-Butyl 2-(4-(1-(trifluoromethyl)cyclopropyl)phenyl)acetate. Prepared according to *general procedure 6* from 1-bromo-4-(1-(trifluoromethyl)cyclopropyl)benzene (1.00 g, 3.77 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 10.6 mL, 5.3 mmol), $Pd_2(dba)_3$ (69 mg, 0.076 mmol) and X-Phos (37 mg, 0.076 mmol) in THF (20 mL). The reaction is complete overnight at rt. Purification of the crude by automated FC (Combiflash, EtOAc / heptane 0:100 to 45:55) yields the title product. LC-MS: t_R = 1.02 min, (conditions 3).

2-(4-(1-(Trifluoromethyl)cyclopropyl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(1-(trifluoromethyl)cyclopropyl)phenyl)acetate (100 mg, 0.33 mmol) in HCOOH (2.3 mL). The reaction is complete after 2.5 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.82 min (conditions 3).

5-Bromo-2-(3-fluorooxetan-3-yl)pyridine. To a sol. of 3-(5-bromopyridin-2-yl)oxetan-3-ol (2.50 g, 10.9 mmol) in CH_2Cl_2 (60 mL) cooled at -78 °C is added (diethylamino)sulfur trifluoride (1.72 mL, 13 mmol) dropwise. The resulting mixture is stirred at -78 °C for 90 min, further at 0 °C for 20 min. The mixture is carefully quenched with aq. sat. $NaHCO_3$ (100 mL). The layers are separated and the aq. phase is extracted with CH_2Cl_2 (2x 100

mL). The comb. org. layers are washed with brine (1 x 100 mL), dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (Flash master, column 100 g, flow 45 mL/min, EtOAc/heptane 0:100 → 25:75) yields the title product. LC-MS: t_R = 0.72 min, MH^+ = 232.04 (conditions 3).

tert-Butyl 2-(6-(3-fluorooxetan-3-yl)pyridin-3-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-2-(3-fluorooxetan-3-yl)pyridine (600 mg, 2.59 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 10.4 mL, 5.2 mmol), $Pd_2(dba)_3$ (118 mg, 0.129 mmol) and X-Phos (64 mg, 0.129 mmol) in THF (20 mL). The reaction is complete overnight at 45 °C. Purification of the crude by automated FC (Combiflash, EtOAc / heptane 0:100 20:80) yields the title product. LC-MS: t_R = 0.80 min, MH^+ = 268.20 (conditions 3).

2-(6-(3-Fluorooxetan-3-yl)pyridin-3-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(6-(3-fluorooxetan-3-yl)pyridin-3-yl)acetate (200 mg, 0.748 mmol) in HCOOH (5.0 mL). The reaction is complete overnight at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.50 min, MH^+ = 212.12 (conditions 3).

5-Bromo-1,3-dimethyl-1H-pyrrolo[2,3-b]pyridine. NaH (60 in oil, 284 mg, 7.11 mmol) is added to an ice-cooled sol. of 5-bromo-3-methyl-7-azaindole (1.0 g, 4.74 mmol) in THF (12 mL). The mixture is stirred at rt for 15 min, then cooled again to 0 °C. MeI (1.19 mL, 19 mmol) is added, and the resulting mixture is stirred at 0 °C for 10 min, then at rt overnight. Water is slowly added, followed by $MgSO_4$. The mixture is filtered, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (Combiflash, column 40 g, flow 40 mL/min, EtOAc / heptane 0:100 →20:80) yields the title product. LC-MS: t_R = 0.87 min, MH^+ = 226.94 (conditions 3).

tert-Butyl 2-(1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-1,3-dimethyl-1H-pyrrolo[2,3-b]pyridine (450 mg, 1.98 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 8.00 mL,4.00 mmol), $Pd_2(dba)_3$ (91 mg, 0.099 mmol) and X-Phos (49 mg, 0.099 mmol) in THF (30 mL). The reaction is complete overnight at 75 °C. Purification of the crude by automated FC (Combiflash, EtOAc / heptane 0:100 30:70) yields the title product. LC-MS: t_R = 0.76 min, MH^+ = 261.16 (conditions 3).

2-(1,3-Dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)acetate (375 mg, 1.41 mmol) in HCOOH (9.3 mL). The reaction is complete overnight at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.50 min, MH^+ = 205.18 (conditions 3).

5-Bromo-3-cyclobutyl-1H-indole. To a sol. of Et_3SiH (2.45 mL, 15 mmol) and trichloroacetic acid (0.75 mL, 7.36 mmol) in toluene (5 mL), is added dropwise at 70 °C a sol. of 5-bromoindole (990 mg, 5 mmol) and cyclobutanone (0.374 mL, 5 mmol) in toluene (2.5 mL). The resulting mixture is stirred at that temperature overnight. The mixture is allowed to cool to rt, and aq. 10% Na_2CO_3 is added. Et_2O is added, and the layers

are separated. The aq. layer is extracted with Et_2O (2x) and the combined org. layers are dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Combiflash, column 24 g, flow 35 mL/min, EtOAc / heptane 0:100 → 20:80) yields the title product. LC-MS: t_R = 0.96 min, MH^+ = 250.07 (conditions 3).

5-Bromo-3-cyclobutyl-1-methyl-1H-indole. NaH (60% in oil, 175 mg, 4.38 mmol) is added to an ice-cooled sol. of 5-bromo-3-cyclobutyl-1H-indole (820 mg, 2.92 mmol) in THF (7.1 mL). The reaction mixture is stirred at rt for 15 min, and is cooled again to 0°C. MeI (0.734 mL, 11.7 mmol) is added, and the resulting mixture is stirred at 0 °C for 10 min, then at rt overnight. Water is slowly added, followed by EtOAc. The layers are separated, and the aq. layer is extracted with EtOAc (2x). The combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the residue by FC (Combiflash, column 24 g, flow 35 mL/min, EtOAc / heptane 0:100 → 15:85) yields the title product. LC-MS: t_R = 1.02 min, MH^+ = 264.08 (conditions 3).

tert-Butyl 2-(3-cyclobutyl-1-methyl-1H-indol-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-3-cyclobutyl-1-methyl-1H-indole (790 mg, 2.39 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 9.7 mL,4.85 mmol), $Pd_2(dba)_3$ (94 mg, 0.102 mmol) and X-Phos (59 mg, 0.119 mmol) in THF (36 mL). The reaction is complete overnight at 45 °C. Purification of the crude by automated FC (Combiflash, EtOAc / heptane 0:100 15:85) yields the title product. LC-MS: t_R = 1.04 min, MH^+ = 300.14 (conditions 3).

2-(3-cyclobutyl-1-methyl-1H-indol-5-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(3-cyclobutyl-1-methyl-1H-indol-5-yl)acetate (538 mg, 1.41 mmol) in HCOOH (9.3 mL). The reaction is complete after 3 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.84 min, MH^+ = 244.21 (conditions 3).

5-Bromo-3-isopropyl-1H-indole. To a sol. of Et_3SiH (2.45 mL, 15 mmol) and trichloroacetic acid (0.75 mL, 7.36 mmol) in toluene (5 mL), is added dropwise at 70 °C a sol. of 5-bromoindole (990 mg, 5 mmol) and acetone (0.532 mL, 7.25 mmol) in toluene (2.5 mL). The resulting mixture is stirred at that temperature overnight. The mixture is allowed to cool to rt, and aq. 10% Na_2CO_3 is added. Et_2O is added, and the layers are separated. The aq. layer is extracted with Et_2O (2x) and the combined org. layers are dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Combiflash, column 24 g, flow 35 mL/min, EtOAc / heptane 0:100 → 35:65) yields the title product. LC-MS: t_R = 0.94 min, MH^+ = 238.11 (conditions 3).

5-Bromo-3-isopropyl-1-methyl-1H-indole. NaH (60% in oil, 782 mg, 7.06 mmol) is added to an ice-cooled sol. of 5-bromo-3-isopropyl-1H-indole (1.12 g, 4.70 mmol) in THF (11.5 mL). The reaction mixture is stirred at rt for 15 min, and is cooled again to 0°C. MeI (1.18 mL, 18.8 mmol) is added, and the resulting mixture is stirred at 0 °C for 10 min, then at rt overnight. Water is slowly added, followed by EtOAc. The layers are separated, and the aq. layer is extracted with EtOAc (2x). The combined org. layers are washed with brine, dried over

$MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the residue by FC (Combiflash, column 24 g, flow 35 mL/min, EtOAc / heptane 0:100 → 30:70) yields the title product. LC-MS: t_R = 1.00 min, MH^+ = 252.14 (conditions 3).

tert-Butyl 2-(3-isopropyl-1-methyl-1H-indol-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-3-isopropyl-1-methyl-1H-indole (570 mg, 2.05 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 8.3 mL,4.15 mmol), $Pd_2(dba)_3$ (94 mg, 0.102 mmol) and X-Phos (59 mg, 0.119 mmol) in THF (31 mL). The reaction is complete overnight at 45 °C. Purification of the crude by automated FC (Combiflash, EtOAc / heptane 0:100 to 20:80) yields the title product. LC-MS: t_R = 1.02 min, MH^+ = 288.20 (conditions 3).

2-(3-Isopropyl-1-methyl-1H-indol-5-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(3-isopropyl-1-methyl-1H-indol-5-yl)acetate (423 mg, 1.41 mmol) in HCOOH (9.3 mL). The reaction is complete after 3 h at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.82 min, MH^+ = 232.23 (conditions 3).

5-Bromo-1-methyl-1H-indole-3-carbonitrile. NaH (60% in oil, 600 mg, 15 mmol) is added to an ice-cooled sol. of 5-bromo-1H-indole-3-carbonitrile (2.26 g, 10.0 mmol) in THF (24 mL). The reaction mixture is stirred at rt for 15 min, and is cooled again to 0°C. MeI (2.52 mL, 40.0 mmol) is added, and the resulting mixture is stirred at 0 °C for 10 min, then at rt overnight. Water is slowly added, followed by EtOAc. The layers are separated, and the aq. layer is extracted with EtOAc (2x). The combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the residue by FC (Combiflash, column 24 g, flow 35 mL/min, EtOAc / heptane 0:100 → 40:60) yields the title product. LC-MS: t_R = 0.86 min, MH^+ = 276.06 (conditions 3).

tert-Butyl 2-(3-cyano-1-methyl-1H-indol-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-1-methyl-1H-indole-3-carbonitrile (2.13 g, 8.87 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 36 mL, 18 mmol), $Pd_2(dba)_3$ (218 mg, 0.443 mmol) and X-Phos (406 mg, 0.443 mmol) in THF (104 mL). The reaction is complete overnight at 45 °C. Purification of the crude by automated FC (Combiflash, EtOAc / heptane 0:100 35:65) yields the title product. LC-MS: t_R = 0.91 min, MH^+ = 271.19 (conditions 3).

2-(3-Cyano-1-methyl-1H-indol-5-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(3-cyano-1-methyl-1H-indol-5-yl)acetate (200 mg, 0.654 mmol) in TFA (0.75 mL) and CH_2Cl_2 (0.77 mL). The reaction is complete after 1 h at rt. Purification by HPLC yields title product. LC-MS: t_R = 0.67 min, MH^+ = 215.19 (conditions 3).

(rac.)-5-Bromo-3-hydroxy-1-methyl-3-(trifluoromethyl)indolin-2-one. To a sol. of 5-bromo-1-methyl-1H-indole-2,3-dione (3.60 g, 15.0 mmol) in THF (100 mL) are added sequentially at rt trifluoromethyl)trimethylsilane (4.43 mL, 30.0 mmol) and CsF (91.1 mg, 0.60 mmol). The resulting sol. is stirred at rt overnight. The mixture is quenched with cold water (100 mL). The mixture is extracted with EtOAc (3 x 100 mL). The comb. org.

layers are washed with brine (100 mL), dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (Combiflash, column 80 g, flow 60 mL/min, EtOAc / heptane 0:100 → 20:80) yields the trimethylsilyl-protected product. To a sol. of this isolated compound in MeOH (50 mL) is added aq. 2M HCl (40 mL). The resulting sol. is stirred at rt for 2 h. The reaction is diluted with CH_2Cl_2 (100 mL). The layers are separated and the aq. phase is extracted with CH_2Cl_2 (2x 50 mL). The comb. org. layers are washed with brine (1 x 50 mL), dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.79 min (conditions 3).

(rac.)-5-Bromo-1-methyl-3-(trifluoromethyl)indolin-3-ol. To an ice-cooled sol. of (rac.)-5-bromo-3-hydroxy-1-methyl-3-(trifluoromethyl)indolin-2-one (2.42 g, 7.80 mmol) in THF (100 mL) is added dropwise BH_3 (1M in THF, 24 mL, 24 mmol). The sol. is allowed to warm to rt overnight. Aq. 2M HCl (40 mL) is carefully added dropwise at 0°C. The biphasic system is stirred at t. for 5 min. Aq. 2M NaOH (40 mL) is added dropwise at 0°C. The resulting mixture is diluted with EtOAc (100 mL). The layers are separated, and the aq. layer is extracted with EtOAc (2x 50 mL). The comb. org. layers are washed with aq. sat. NaHCO3 (1 x 100 mL), brine (1 x 100 mL), dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.85 min (conditions 3).

5-Bromo-1-methyl-3-(trifluoromethyl)-1H-indole. To an ice-cooled solution of (rac.)-5-bromo-1-methyl-3-(trifluoromethyl)indolin-3-ol (3.32 g, 11.2 mmol) in pyridine (40 mL) is added dropwise $SOCl_2$ (1.22 mL, 16.8 mmol, 1.5 eq). The sol. is allowed to warm up to rt overnight. Aq. 2M HCl (40 mL) is carefully added at 0°C. The biphasic system is stirred at rt for 5 min. The resulting mixture is diluted with EtOAc (100 mL). The layers are separated, and the aq. layer is extracted with EtOAc (2x 50 mL). The comb. org. layers are washed with aq. sat. $NaHCO_3$ (1 x 100 mL), brine (1 x 100 mL), dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (Combiflash, column 80 g, flow 60 mL/min, EtOAc / heptane 0:100 → 20:80) yields the title product. LC-MS: t_R = 0.96 min (conditions 3).

tert-Butyl 2-(1-methyl-3-(trifluoromethyl)-1H-indol-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-1-methyl-3-(trifluoromethyl)-1H-indole (850 mg, 3.06 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 6.0 mL, 3.0 mmol), $Pd_2(dba)_3$ (140 mg, 0.153 mmol) and X-Phos (75.1 mg, 0.153 mmol) in THF (50 mL). The reaction is complete overnight at 45 °C. Purification of the crude by automated FC (Combiflash, EtOAc / heptane 0:100 to 25:75) yields the title product. LC-MS: t_R = 0.99 min (conditions 3).

2-(1-Methyl-3-(trifluoromethyl)-1H-indol-5-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(1-methyl-3-(trifluoromethyl)-1H-indol-5-yl)acetate (200 mg, 0.638 mmol) in HCl (4M in dioxane, 5 mL). The reaction is complete overnight at rt. Purification by HPLC yields title product. LC-MS: t_R = 0.79 min (conditions 3).

tert-Butyl 2-(4-fluoro-2-(2,2,2-trifluoroethoxy)phenyl)acetate. Prepared according to *general procedure 6* from 1-bromo-4-fluoro-2-(2,2,2-trifluoroethoxy)benzene (2.40 g, 8.79 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 35.2 mL, 17.6 mmol), $Pd_2(dba)_3$ (402 mg, 0.44 mmol) and X-Phos (216 mg, 0.44 mmol) in THF (110 mL). The reaction is complete overnight at 45 °C. Purification of the crude by automated FC (Combiflash, EtOAc / heptane 0:100 to 25:75) yields the title product. LC-MS: t_R = 0.98 min (conditions 3).

2-(4-fluoro-2-(2,2,2-trifluoroethoxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-fluoro-2-(2,2,2-trifluoroethoxy)phenyl)acetate (2.60 g, 8.43 mmol) in HCl (4M in dioxane, 15 mL). The reaction is complete overnight at rt. Purification by HPLC yields title product. LC-MS: t_R = 0.76 min (conditions 3).

tert-Butyl 2-(4-(pentafluoro-λ⁶-sulfanyl)phenyl)acetate. Prepared according to *general procedure 6* from pentafluoro(4-iodophenyl)-λ⁶-sulfane (660 mg, 2.00 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 8.0 mL, 4.0 mmol), $Pd_2(dba)_3$ (92 mg, 0.10 mmol) and X-Phos (49 mg, 0.10 mmol) in THF (30 mL). The reaction is complete overnight at 45 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.89 min (conditions 3).

2-(4-(Pentafluoro-λ⁶-sulfanyl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(pentafluoro-λ⁶-sulfanyl)phenyl)acetate (103 mg, 0.30 mmol) in HCOOH (3.0 mL). The reaction is complete after 30 min at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.79 min (conditions 3).

tert-Butyl 2-(4-(2-cyanopropan-2-yl)phenyl)acetate. Prepared according to *general procedure 6* from 2-(4-bromophenyl)-2-methylpropanenitrile (462 mg, 2.00 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 8.0 mL, 4.0 mmol), $Pd_2(dba)_3$ (92 mg, 0.10 mmol) and X-Phos (49 mg, 0.10 mmol) in THF (30 mL). The reaction is complete overnight at 45 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.94 min, MH^+ = 260.25 (conditions 3).

2-(4-(2-Cyanopropan-2-yl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(2-cyanopropan-2-yl)phenyl)acetate (77.8 mg, 0.30 mmol) in TFA (0.34 mL) and CH_2Cl_2 (0.35 mL). The reaction is complete overnight at rt. Removing the solvents under reduced pressure yields the crude title product. LC-MS: t_R = 0.70 min (conditions 3).

Methyl 2-(3-methyl-4-(2,2,2-trifluoroethoxy)phenyl)acetate. To an ice-cooled sol. of methyl 4-hydroxy-3-methylphenylacetate (0.33 mL, 2 mmol) and Cs_2CO_3 (1.30 g, 4.00 mmol) in DMF (5.3 mL), is added dropwise 2,2,2-trifluoroethyl trifluoromethanesulfonate (0.46 mL, 3.0 mmol). The mixture is stirred at rt over 3 days while warming up to rt. The mixture is partitioned between water (10 mL) and EtOAc (10 mL). The layers are separated. The aq. layer is extracted with EtOAc (2 x 5 mL). The comb. org. layers are washed with water (2 x 10 mL) and with brine (1x 10 mL), dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.90 min (conditions 3).

2-(3-Methyl-4-(2,2,2-trifluoroethoxy)phenyl)acetic acid. To a sol. of methyl 2-(3-methyl-4-(2,2,2-trifluoroethoxy)phenyl)acetate (710 mg, 2.59 mmol) in THF (8.2 mL) and MeOH (2 mL), is added aq. 1M NaOH (2.8 mL). The sol. is stirred at rt for 1 h. The solvents are removed under reduced pressure. The residue is diluted with water and washed with EtOAc (1 x). The aq. phase is acidified with aq. 1M HCl. The mixture is extracted with CH_2Cl_2 (3 x). The comb. org. layers are dried over $MgSO_4$, filtered and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.80 min (conditions 3).

5-Bromo-3-fluoro-2-(pyrrolidin-1-yl)pyridine. To a sol. of 5-bromo-2,3-difluoropyridine (680 mg, 3.51 mmol) in DMSO (20 mL), are added pyrrolidine (0.307 mL, 3.68 mmol) and then DBU (1.10 mL, 7.36 mmol). The mixture is heated to 80 °C and stirred at this temperature for one day. The mixture is allowed to cool down to rt. The mixture is diluted with aq. sat. $NaHCO_3$ (200 mL) and EtOAc (200 mL). The layers are separated, and the aq. layer is extracted with EtOAc (1x 100 mL). The comb. org. layers are washed with aq. sat. $NaHCO_3$ (2 x 200 mL), and brine (1 x 100 mL), are dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.85 min, MH^+ = 245.09 (conditions 3).

tert-Butyl 2-(5-fluoro-6-(pyrrolidin-1-yl)pyridin-3-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-3-fluoro-2-(pyrrolidin-1-yl)pyridine (504 mg, 2.06 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 8.22 mL, 4.11 mmol), $Pd_2(dba)_3$ (94 mg, 0.10 mmol) and X-Phos (50 mg, 0.10 mmol) in THF (20 mL). The reaction is complete after 1h at 50 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.66 min, MH^+ = 281.22 (conditions 3).

2-(5-Fluoro-6-(pyrrolidin-1-yl)pyridin-3-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(5-fluoro-6-(pyrrolidin-1-yl)pyridin-3-yl)acetate (200 mg, 0.713 mmol) in HCl (4M in dioxane, 10 mL). The reaction is complete overnight at rt. Purification by HPLC yields title product. LC-MS: t_R = 0.44 min, MH^+ = 225.16 (conditions 3).

4-Bromomethyl-2,6-difluorobenzonitrile. 2,6-Difluoro-4-(hydroxymethyl)benzonitrile (WO 2003101423, 2.97 g, 17.6 mmol) is dissolved in THF (80 mL). PPh_3 (5.07 g, 19.3 mmol) is added and the mixture is cooled to 0 °C. CBr_4 (7.28 g, 22.0 mmol) is added in portions. The mixture is stirred for 20 h while warming up to rt. The mixture is filtered, and the filtrate is partitioned between EtOAc and aq. sat. NH_4Cl. The org. layer is dried over MgSO4, filtered, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (Büchi, 50 g slilcagel, flow 26 mL/min, EtOAc / heptane 1:99 → 3:97 → 8:92 → 15:85) yields the title product. LC-MS: t_R = 0.85 min (conditions 3).

2,6-Difluoro-4-((3-nitro-1H-pyrazol-1-yl)methyl)benzonitrile. Prepared according to *general procedure 4* from K_2CO_3 (2.13 g, 15.4 mmol), 4-bromomethyl-2,6-difluorobenzonitrile (716 mg, 3.09 mmol), 5-nitro-1H-pyrazole (349 mg, 3.09 mmol), and Bu_4NBr (114 mg, 0.309 mmol) in acetone (7 mL). The reaction is complete after 1 h. Purification of the crude by automated FC (Büchi, EtOAc / heptane 1:99 → 10:90 → 20:80 → 50:50 →

80:20, 24 g silicagel, flow 35 mL/min) yields the title product. LC-MS: t_R = 0.81 min, MH^+ = 242.22 (conditions 3).

4-((3-Amino-1H-pyrazol-1-yl)methyl)-2,6-difluorobenzonitrile. Prepared according to *general procedure 5* from Fe (powder, 358 mg, 6.42 mmol), 2,6-difluoro-4-((3-nitro-1H-pyrazol-1-yl)methyl)benzonitrile (565 mg, 2.14 mmol) and NH_4Cl (572 mg, 10.7 mmol) in a 2:1-mixture of EtOH and water (21 mL). The reaction is complete after 45 min at 85 °C. This yields the crude title compound. LC-MS: t_R = 0.60 min, MH^+ = 276.16 (conditions 3).

tert-Butyl 2-(4-(1-cyanocyclopropyl)phenyl)acetate. Prepared according to *general procedure 6* from 1-(4-bromophenyl)cyclopropane-1-carbonitrile (227 mg, 1.00 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 4.00 mL, 2.00 mmol), $Pd_2(dba)_3$ (46 mg, 0.05 mmol) and X-Phos (25 mg, 0.05 mmol) in THF (15 mL). The reaction is complete after 2 days at 45 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.92 min, MH^+ = 258.14 (conditions 3).

2-(4-(1-Cyanocyclopropyl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(1-cyanocyclopropyl)phenyl)acetate (77.4 mg, 0.030 mmol) in TFA (0.34 mL) and CH_2Cl_2 (0.35 mL). The reaction is complete after 2.5 h at 0 °C. Purification by HPLC yields title product. LC-MS: t_R = 0.68 min (conditions 3).

tert-Butyl 2-(4-(1-((tert-butyldimethylsilyl)oxy)cyclopropyl)phenyl)acetate. Prepared according to *general procedure 6* from (1-(4-bromophenyl)cyclopropoxy)(tert-butyl)dimethylsilane (Isabel, E.; Bateman, K. P.; Chauret, N.; Cromlish, W.; Desmarais, S.; Duong, Le T.; Falgueyret, J.-P.; Gauthier, J. Y.; Lamontagne, S.; Lau, C. K.; et al., *Bioorg. Med. Chem. Lett.*, **2010**, *20*, 887, 200 mg, 0.601 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 2.40 mL, 1.20 mmol), $Pd_2(dba)_3$ (28 mg, 0.030 mmol) and X-Phos (15 mg, 0.030 mmol) in THF (15 mL). The reaction is complete after 2 days at 45 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 1.13 min, (conditions 3).

tert-Butyl 2-(4-(1-hydroxycyclopropyl)phenyl)acetate. To an ice-cooled sol. of tert-butyl 2-(4-(1-((tert-butyldimethylsilyl)oxy)cyclopropyl)phenyl)acetate (200 mg, 0.534 mmol) in THF (12 mL) is added tetrabutylammonium fluoride (1.0 M in THF, 1.7 mL, 1.7 mmol). The resulting sol. is stirred at 0 °C for 30 min. The sol. is diluted with EtOAc (10 mL), and aq. sat. NH4Cl (25 mL) is added. The mixture is extracted with EtOAc (3 x 30 mL). The comb. org. layers are dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (Flash Master, 25 g silicagel, flow 30 mL/min, EtOAc/heptane 0:100 → 20:80) yields the title product. LC-MS: t_R = 0.83 min, (conditions 3).

2-(4-(1-Hydroxycyclopropyl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(1-hydroxycyclopropyl)phenyl)acetate (75 mg, 0.030 mmol) in TFA (0.34 mL) and CH_2Cl_2 (0.35 mL). The reaction is complete after 2.5 h at 0 °C. Purification by HPLC yields title product. LC-MS: t_R = 0.55 min (conditions 3).

(6-Cyano-5-methylpyridin-2-yl)methyl acetate. To Ac_2O (8.08 mL, 84.7 mmol) at 120°C is added 2-cyano-3,6-dimethylpyridine 1-oxide (WO 2006066968, 2.27 g, 14.9 mmol). The resulting sol. is stirred at 120 °C for 5 min, and is heated to reflux for 1 h. The mixture is allowed to cool to rt, and is poured into ice (63 g). The mixture is then neutralized with $NaHCO_3$. Et_2O (70 mL) is added, and the layers are separated. The aq. phase is extracted with Et_2O (2 x 35 mL), and the combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the residue by automated FC by (Flash Master, column 100 g, flow 45 mL/min, EtOAc/heptane 0:100 → 40:60) yields the title product. . LC-MS: t_R = 0.69 min, MH^+ = 191.95 (conditions 3).

6-(Hydroxymethyl)-3-methylpicolinonitrile. K_2CO_3 (41.7 mg, 0.302 mmol) is added to a sol. of (6-cyano-5-methylpyridin-2-yl)methyl acetate (1.79 g, 9.37 mmol) in MeOH (12.6 mL). The resulting mixture is stirred at rt overnight. Water (25 mL) is added, and the mixture is neutralized with aq. 5% AcOH. CH_2Cl_2 is added, and the phases are separated. The aq. layer is extracted with CH_2Cl_2 (2 x). The combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield to crude title compound. LC-MS: t_R = 0.51 min, MH^+ = 149.18 (conditions 3).

6-(Chloromethyl)-3-methylpicolinonitrile. A sol. of 6-(hydroxymethyl)-3-methylpicolinonitrile (1.49 g, 9.35 mmol) and $SOCl_2$ (1.61 mL, 9.35 mmol) in CH_2Cl_2 (35.2 mL) is stirred at rt for 6 h. The solvents are removed under reduced pressure. Toluene (20 mL) is added, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.74 min, MH^+ = 167.09 (conditions 3).

3-Methyl-6-((3-nitro-1H-pyrazol-1-yl)methyl)picolinonitrile. Prepared according to *general procedure 4* from K_2CO_3 (1.26 g, 9.13 mmol), 6-(chloromethyl)-3-methylpicolinonitrile (1.64 g, 9.19 mmol), 5-nitro-1H-pyrazole (859 mg, 7.60 mmol) in DMF (6 mL). The reaction is complete overnight. Purification of the crude by automated FC (Combiflash, EtOAc / heptane 0:100 → 40:60, 40 g silicagel, flow 40 mL/min) yields the title product. LC-MS: t_R = 0.75 min, MH^+ = 244.18 (conditions 3).

6-((3-Amino-1H-pyrazol-1-yl)methyl)-3-methylpicolinonitrile. Prepared according to *general procedure 5* from Fe (powder, 1.03 g, 18.3 mmol), 3-methyl-6-((3-nitro-1H-pyrazol-1-yl)methyl)picolinonitrile (1.90 g, 6.09 mmol) and NH_4Cl (1.23 g, 30.4 mmol) in a 2:1-mixture of EtOH and water (43 mL). The reaction is complete overnight at 100 °C. This yields the crude title compound.

tert-Butyl 2-(4-(1-methylcyclopropyl)phenyl)acetate. Prepared according to *general procedure 6* from 1-bromo-4-(1-methylcyclopropyl)benzene (500 mg, 2.37 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 9.50 mL, 4.75 mmol), $Pd_2(dba)_3$ (108 mg, 0.118 mmol) and X-Phos (58 mg, 0.12 mmol) in THF (20 mL). The reaction is complete after 2 h at 50 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 1.01 (conditions 3).

2-(4-(1-Methylcyclopropyl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(1-methylcyclopropyl)phenyl)acetate (500 mg, 2.03 mmol) in HCOOH (17 mL). The reaction is complete after 2.5 h at 0 °C. Purification by HPLC yields title product. LC-MS: t_R = 0.79 min (conditions 3).

tert-Butyl 2-(4-(1,1,1-trifluoro-2-methylpropan-2-yl)phenyl)acetate. Prepared according to *general procedure 6* from 1-bromo-4-(1,1,1-trifluoro-2-methylpropan-2-yl)benzene (WO 2013011033, 575 mg, 2.11 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 8.40 mL, 4.20 mmol), $Pd_2(dba)_3$ (97 mg, 0.105 mmol) and X-Phos (52 mg, 0.105 mmol) in THF (32 mL). The reaction is complete overnight at 45 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 1.02 (conditions 3).

2-(4-(1,1,1-Trifluoro-2-methylpropan-2-yl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(1,1,1-trifluoro-2-methylpropan-2-yl)phenyl)acetate (63 mg, 0.20 mmol) in TFA (0.23 mL) and CH_2Cl_2 (0.23 mL). The reaction is complete after 2.5 h at 0 °C. Purification by HPLC yields title product. LC-MS: t_R = 0.82 min (conditions 3).

tert-Butyl 2-(2,2-dimethyl-2,3-dihydrobenzofuran-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-2,2-dimethyl-2,3-dihydrobenzofuran (468 mg, 2.06 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 8.24 mL, 4.12 mmol), $Pd_2(dba)_3$ (94 mg, 0.103 mmol) and X-Phos (51 mg, 0.103 mmol) in THF (20 mL). The reaction is complete overnight at 50 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.96, MH^+ = 263.28 (conditions 3).

2-(2,2-Dimethyl-2,3-dihydrobenzofuran-5-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(2,2-dimethyl-2,3-dihydrobenzofuran-5-yl)acetate (300 mg, 1.14 mmol) in HCl (4M in dioxane, 5.0 mL). The reaction is complete overnight at rt. Purification by HPLC yields title product. LC-MS: t_R = 0.71 min, MH^+ = 207.20 (conditions 3).

tert-Butyl 2-(3,3-dimethyl-2,3-dihydrobenzofuran-5-yl)acetate. Prepared according to *general procedure 6* from 5-bromo-3,3-dimethyl-2,3-dihydrobenzofuran (468 mg, 2.06 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 8.24 mL, 4.12 mmol), $Pd_2(dba)_3$ (94 mg, 0.103 mmol) and X-Phos (51 mg, 0.103 mmol) in THF (20 mL). The reaction is complete overnight at 50 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.96 (conditions 3).

2-(3,3-Dimethyl-2,3-dihydrobenzofuran-5-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(3,3-dimethyl-2,3-dihydrobenzofuran-5-yl)acetate (300 mg, 1.14 mmol) in HCl (4M in dioxane, 5.0 mL). The reaction is complete overnight at rt. Purification by HPLC yields title product. LC-MS: t_R = 0.72 min, MH^+ = 207.20 (conditions 3).

tert-Butyl 2-(2,2-dimethyl-2,3-dihydrobenzofuran-6-yl)acetate. Prepared according to *general procedure 6* from 6-bromo-2,2-dimethyl-2,3-dihydrobenzofuran (Wang, X.; Lu, Y.; Dai, H.-X.; Yu, J.-Q., *J. Am. Chem. Soc.*, **2010**, 132, 12203, 480 mg, 2.11 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 8.46 mL, 4.23 mmol), $Pd_2(dba)_3$ (97 mg, 0.106 mmol) and X-Phos (52 mg, 0.106 mmol) in THF (30 mL). The reaction is

complete after 2 h at 50 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.96 (conditions 3).

2-(2,2-Dimethyl-2,3-dihydrobenzofuran-6-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(2,2-dimethyl-2,3-dihydrobenzofuran-6-yl)acetate (300 mg, 1.14 mmol) in HCl (4M in dioxane, 5.0 mL). The reaction is complete overnight at rt. Purification by HPLC yields title product. LC-MS: t_R = 0.72 min, MH^+ = 207.19 (conditions 3).

4-Bromo-1-methyl-2-(2,2,2-trifluoroethoxy)benzene. To an ice-cooled sol. of 5-bromo-2-methylphenol (1.87 g, 10 mmol) and Cs_2CO_3 (4.23 g, 13 mmol) in DMF (20 mL) is added dropwise 2,2,2-trifluoroethyl trifluoromethanesulfonate (1.67 mL, 11 mmol). The mixture is stirred overnight while warming up to rt. The mixture is partitioned between water (100 mL) and EtOAc (100 mL). The layers are separated. The aq. phase is extracted with EtOAc (2 x 50 mL). The comb. org. layers are washed with water (3 x 100 mL) and brine (1x 100 mL), dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.96 min (conditions 3).

tert-Butyl 2-(4-methyl-3-(2,2,2-trifluoroethoxy)phenyl)acetate. Prepared according to *general procedure 6* from 4-bromo-1-methyl-2-(2,2,2-trifluoroethoxy)benzene (800 mg, 2.97 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 12.0 mL, 6.00 mmol), $Pd_2(dba)_3$ (136 mg, 0.150 mmol) and X-Phos (73 mg, 0.150 mmol) in THF (20 mL). The reaction is complete after 2 h at 50 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 1.00 (conditions 3).

2-(4-methyl-3-(2,2,2-trifluoroethoxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-methyl-3-(2,2,2-trifluoroethoxy)phenyl)acetate (300 mg, 0.986 mmol) in HCl (4M in dioxane, 5.0 mL). The reaction is complete overnight at rt. LC-MS: t_R = 0.81 min (conditions 3).

Ethyl 2-(3-fluoro-4-(2,2,2-trifluoroethoxy)phenyl)acetate. To an ice-cooled sol. of ethyl 2-(3-fluoro-4-hydroxyphenyl)acetate (Cho, Y.; Kim, M. S.; Kim, Ho S.; Ann, J.; Lee, J.; Pearce, L. V.; Pavlyukovets, V. A.; Morgan, M. A.; Blumberg, P. M.; Lee, J., *Bioorg. Med. Chem. Lett.*, **2012**, 22, 5227, 2.87 g, 14.5 mmol) and Cs_2CO_3 (6.13 g, 18.8 mmol) in DMF (20 mL) is added dropwise 2,2,2-trifluoroethyl trifluoromethanesulfonate (2.42 mL, 15.9 mmol). The mixture is stirred overnight while warming up to rt. The mixture is partitioned between water (100 mL) and EtOAc (100 mL). The layers are separated. The aq. phase is extracted with EtOAc (2 x 50 mL). The comb. org. layers are washed with water (3 x 100 mL) and brine (1x 100 mL), dried over $MgSO_4$, filtered, the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.91 min (conditions 3).

2-(3-Fluoro-4-(2,2,2-trifluoroethoxy)phenyl)acetic acid. To a sol. of ethyl 2-(3-fluoro-4-(2,2,2-trifluoroethoxy)phenyl)acetate (2.00 g, 7.14 mmol) in THF (50 mL) and MeOH (10 mL) is added aq. 1M NaOH (10 mL). The sol. is stirred at rt for 1 h. The solvents are removed under reduced pressure. The residue is diluted with water and washed with EtOAc (1x). The aq. phase is acidified with aq. 2M HCl. The mixture is

extracted with CH_2Cl_2 (3 x). The comb. org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.77 min (conditions 3).

rac-tert-Butyl 2-(4-((1R,2R*)-2-(trifluoromethyl)cyclopropyl)phenyl)acetate*. Prepared according to general procedure 6 from rac-1-bromo-4-((1R*,2R*)-2-(trifluoromethyl)cyclopropyl)benzene (0.156 mL, 0.896 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et2O, 3.20 mL, 1.60 mmol), and bis(tri-tert-butylphosphine)palladium(0) (45.8 mg, 0.0896 mmol) in dioxane (7.7 mL). The reaction is complete overnight at rt. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 1.01 (conditions 3).

rac-2-(4-((1R,2R*)-2-(trifluoromethyl)cyclopropyl)phenyl)acetic acid.* Prepared according to *general procedure 7* from rac-tert-butyl 2-(4-((1R*,2R*)-2-(trifluoromethyl)cyclopropyl)phenyl)acetate (61 mg, 0.20 mmol) in TFA (0.23 mL) and CH_2Cl_2 (0.23 mL) The reaction is complete after 3 h at 0 °C. LC-MS: t_R = 0.82 min (conditions 3).

General procedure 10 for the preparation of arylacetic acid derivatives. A sol. of bromoaryl / bromoheteroaryl (1 eq.), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.2 eq.)), $Pd_2(dba)_3$ (0.05 eq.) and Q-Phos or X-Phos (0.1 eq.) in dioxane (0.5M) is stirred between rt and 90 °C until the starting materials are consumed (0.33 - 18 h). The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Chromatographic purification yields the tert-butyl arylacetate.

A sol. of the tert-butyl arylacetate in an acid (HCl/dioxane, or HCOOH) with optionally CH_2Cl_2 is prepared at 0 °C. This mixture is stirred at 0 °C, optionally warming up to rt, until consumption of the starting material. The solvents are removed under reduced pressure to yield the crude desired arylacetic acid derivative.

Following *general procedure 10*, the following examples have been prepared

Product name	LC-MS tert-butyl arylacetate t_R (min.), MH^+, conditions	LC-MS final product t_R (min.), MH^+, conditions	Acid used for ester hydrolysis
2-(1-ethyl-1H-indazol-5-yl)acetic acid	0.90, -, cond. 3	0.64, 205.21, cond. 3	4M HCl / dioxane
2-(1,3-dimethyl-1H-indazol-5-yl)acetic acid	0.90, 261.23, cond. 3	0.63, 205.20, cond. 3	4M HCl / dioxane
2-(3-cyclopropyl-1H-indazol-5-yl)acetic acid	0.87, 273.32, cond. 3	0.64, 217.13, cond. 1	4M HCl / dioxane
2-(1-butyl-1H-indazol-5-yl)acetic acid	0.89, 289.26, cond. 3	0.82, 233.15, cond. 1	4M HCl / dioxane
2-(2-methyl-1H-indol-5-yl)acetic acid	0.91, 246.19, cond. 3	-	4M HCl / dioxane
2-(3-butyl-1H-indazol-5-yl)acetic acid	0.93, 289.26, cond. 3	-	4M HCl / dioxane
2-(1-isopropyl-1H-indazol-5-yl)acetic acid	0.94, 275.30, cond. 3	-	4M HCl / dioxane

2-(1-propyl-1H-indazol-5-yl)acetic acid	0.94, 275.14, cond. 3	-	4M HCl / dioxane
2-(3-cyclopropyl-1-methyl-1H-indazol-5-yl)acetic acid	0.93, 287.18, cond. 3	-	4M HCl / dioxane
2-(benzofuran-5-yl)acetic acid	0.94, -, cond. 3	-	4M HCl / dioxane
2-(benzo[b]thiophen-5-yl)acetic acid	0.97, -, cond. 3	-	4M HCl / dioxane
2-(1-methyl-1H-pyrazolo[3,4-b]pyridin-5-yl)acetic acid	0.83, 248.28, cond. 3	-	4M HCl / dioxane
2-(3-(trifluoromethyl)-1H-indazol-5-yl)acetic acid	-	-	4M HCl / dioxane

tert-Butyl 2-(4-(1-methoxycyclopropyl)phenyl)acetate. Prepared according to general procedure 6 from 1-bromo-4-(1-methoxycyclopropyl)benzene (790 mg, 2.92 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 11.7 mL, 5.80 mmol), $Pd_2(dba)_3$ (133 mg, 0.146 mmol), and X-Phos (72 mg, 0.15 mmol) in THF (44 mL). The reaction is complete after 2.5 h at 45 °C. Purification of the crude by automated FC (Combiflash, acetone / heptane 0:100 → 85:15, 40 g silicagel, flow 40 mL/min) yields the title product. LC-MS: t_R = 0.94 min, MH^+ = 263.25 (conditions 3).

2-(4-(1-Methoxycyclopropyl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(1-methoxycyclopropyl)phenyl)acetate (84 mg, 0.30 mmol) in TFA (0.34 mL) and CH_2Cl_2 (0.35 mL). The reaction is complete after 2.5 h at 0 °C. LC-MS: t_R = 0.70 min (conditions 3).

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
234	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide	0.94 min; 370.33; conditions 3
235	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(5-methyl-[1,2,4]oxadiazol-3-yl)-phenyl]-acetamide	0.85 min; 410.21; conditions 3
236	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-[1,2,4]oxadiazol-3-yl-phenyl)-acetamide	0.83 min; 396.09; conditions 3
237	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide	0.93 min; 418.00; conditions 3
238	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-yloxy)-phenyl]-acetamide	0.82 min; 400.18; conditions 3

239	N-[1-(4-Bromo-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide	0.66 min; 413.11; conditions 3
240	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide	0.92 min; 434.05; conditions 3
241	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide	0.86 min; 428.16; conditions 3
242	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide	0.83 min; 414.18; conditions 3
243	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide	0.97 min; 462.08; conditions 3
244	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide	0.94 min; 448.01; conditions 3
245	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide	0.85 min; 432.07; conditions 3
246	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	0.74 min; 392.14; conditions 3
247	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-yloxy)-phenyl]-acetamide	0.71 min; 390.07; conditions 3
248	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide	0.75 min; 422.16; conditions 3
249	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.71 min; 372.22; conditions 3
250	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	0.80 min; 391.18; conditions 3
251	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-yloxy)-phenyl]-acetamide	0.78 min; 389.19; conditions 3
252	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.78 min; 371.11; conditions 3
253	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	0.82 min; 409.16; conditions 3

254	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-yloxy)-phenyl]-acetamide	0.80 min; 407.13; conditions 3
255	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.80 min; 389.16; conditions 3
256	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide	0.81 min; 421.17; conditions 3
257	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide	0.83 min; 439.12; conditions 3
258	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3-methoxy-oxetan-3-yl)-pyridin-3-yl]-acetamide	0.70 min; 415.10; conditions 3
259	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide	0.91 min; 395.10; conditions 3
260	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide	0.91 min; 395.11; conditions 3
261	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide	0.90 min; 441.05; conditions 3
262	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide	0.80 min; 421.07; conditions 3
263	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide	0.84 min; 435.03; conditions 3
264	2-(4-tert-Butyl-phenyl)-N-[1-(4-cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.94 min; 391.14; conditions 3
265	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	0.93 min; 443.05; conditions 3
266	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide	0.91 min; 377.09; conditions 3
267	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide	0.82 min; 439.07; conditions 4
268	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.78 min; 388.49; conditions 4

269	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-yloxy)-phenyl]-acetamide	0.80 min; 406.92; conditions 4
270	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	0.82 min; 408.48; conditions 4
271	2-(4-tert-Butyl-phenyl)-N-[1-(4-cyano-benzyl)-1H-pyrazol-3-yl]-acetamide	0.92 min; 373.15; conditions 3
272	2-(4-tert-Butyl-phenyl)-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.87 min; 374.20; conditions 3
273	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide	0.88 min; 423.00; conditions 3
274	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide	0.83 min; 424.10; conditions 3
275	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.64 min; 405.12; conditions 3
276	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.56 min; 388.12; conditions 3
277	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	0.92 min; 425.10; conditions 3
278	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	0.87 min; 426.14; conditions 3
279	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide	0.80 min; 421.10; conditions 3
280	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide	0.84 min; 435.09; conditions 3
281	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide	0.90 min; 441.06; conditions 3
282	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide	0.91 min; 377.17; conditions 3
283	2-(4-tert-Butyl-phenyl)-N-[1-(3-cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.94 min; 391.14; conditions 3

284	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide	0.76 min; 418.00; conditions 3
285	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide	0.82 min; 417.07; conditions 3
286	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide	0.78 min; 403.07; conditions 3
287	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide	0.72 min; 404.10; conditions 3
288	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide	0.91 min; 425.11; conditions 3
289	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide	0.92 min; 455.02; conditions 3
290	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide	0.95 min; 468.76; conditions 3
291	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	0.80 min; 389.06; conditions 3
292	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.85 min; 387.99; conditions 3
293	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide	0.86 min; 388.02; conditions 3
294	N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.66 min; 441.07; conditions 3
295	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	0.78 min; 371.11; conditions 3
296	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.83 min; 370.11; conditions 3
297	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide	0.84 min; 369.98; conditions 3
298	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide	0.94 min; 451.06; conditions 3

299	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide	0.90 min; 437.07; conditions 3
300	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide	0.89 min; 406.97; conditions 3
301	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.78 min; 371.07; conditions 3
302	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide	0.77 min; 371.08; conditions 3
303	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide	0.89 min; 452.06; conditions 3
304	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide	0.86 min; 438.07; conditions 3
305	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide	0.85 min; 408.13; conditions 3
306	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.66 min; 441.06; conditions 3
307	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.64 min; 405.14; conditions 3
308	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	0.80 min; 389.09; conditions 3
309	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide	0.85 min; 388.09; conditions 3
310	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.85 min; 388.07; conditions 3
311	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide	0.95 min; 468.93; conditions 3
312	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide	0.91 min; 425.10; conditions 3
313	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide	0.92 min; 455.02; conditions 3

314	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	0.93 min; 443.05; conditions 3
315	N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3-fluoro-oxetan-3-yl)-pyridin-3-yl]-acetamide	0.77 min; 403.05; conditions 3
316	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide	0.82 min; 405.12; conditions 3
317	N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide	0.80 min; 387.15; conditions 3
318	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide	0.73 min; 388.15; conditions 3
319	rac-N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide	0.83 min; 393.14; conditions 3
320	rac-N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide	0.82 min; 375.16; conditions 3
321	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-acetamide	0.72 min; 403.12; conditions 3
322	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-acetamide	0.63 min; 386.05; conditions 3
323	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-cyclobutyl-1-methyl-1H-indol-5-yl)-acetamide	0.89 min; 425.19; conditions 3
324	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-isopropyl-1-methyl-1H-indol-5-yl)-acetamide	0.88 min; 413.19; conditions 3
325	2-(3-Cyano-1-methyl-1H-indol-5-yl)-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.75 min; 396.14; conditions 3
326	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1-methyl-3-trifluoromethyl-1H-indol-5-yl)-acetamide	0.85 min; 439.09; conditions 3
327	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(3-cyclobutyl-1-methyl-1H-indol-5-yl)-acetamide	0.95 min; 442.11; conditions 3
328	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(3-isopropyl-1-methyl-1H-indol-5-yl)-acetamide	0.94 min; 430.14; conditions 3

329	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(3-cyano-1-methyl-1H-indol-5-yl)-acetamide	0.83 min; 413.15; conditions 3
330	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide	0.89 min; 402.05; conditions 3
331	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide	0.82 min; 385.09; conditions 3
332	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-fluoro-2-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.89 min; 451.04; conditions 3
333	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-fluoro-2-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.82 min; 433.94; conditions 3
334	N-(1-(3-cyano-4-fluorobenzyl)-1H-pyrazol-3-yl)-2-(4-(pentafluoro-λ^6-sulfanyl)phenyl)acetamide	0.91 min; 460.87; conditions 3
335	2-[4-(Cyano-dimethyl-methyl)-phenyl]-N-[1-(3-cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.86 min; 402.05; conditions 3
336	N-(1-((5-cyanopyridin-2-yl)methyl)-1H-pyrazol-3-yl)-2-(4-(pentafluoro-λ^6-sulfanyl)phenyl)acetamide	0.85 min; 444.02; conditions 3
337	2-[4-(Cyano-dimethyl-methyl)-phenyl]-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.78 min; 385.09; conditions 3
338	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-trifluoromethyl-phenyl)-acetamide	0.82 min; 386.01; conditions 3
339	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.86 min; 430.11; conditions 3
340	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(5-fluoro-6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.67 min; 423.17; conditions 3
341	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(5-fluoro-6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.58 min; 406.18; conditions 3
342	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-trifluoromethyl-phenyl)-acetamide	0.89 min; 403.01; conditions 3

343	N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.91 min; 447.08; conditions 3
344	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.82 min; 407.15; conditions 3
345	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide	0.91 min; 449.04; conditions 3
346	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	0.82 min; 407.14; conditions 3
347	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	0.83 min; 427.11; conditions 3
348	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide	0.83 min; 421.15; conditions 3
349	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.67 min; 459.03; conditions 3
350	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	0.94 min; 461.03; conditions 3
351	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.66 min; 423.16; conditions 3
352	2-(4-tert-Butyl-phenyl)-N-[1-(4-cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.95 min; 409.18; conditions 3
353	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide	0.93 min; 395.18; conditions 3
354	2-[4-(1-Cyano-cyclopropyl)-phenyl]-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.77 min; 383.17; conditions 3
355	2-[4-(1-Cyano-cyclopropyl)-phenyl]-N-[1-(3-cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.84 min; 400.17; conditions 3
356	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-hydroxy-cyclopropyl)-phenyl]-acetamide	0.55 min; 374.19; conditions 3
357	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide	0.84 min; 421.14; conditions 3

358	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide	0.90 min; 420.14; conditions 3
359	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide	0.81 min; 439.10; conditions 3
360	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide	0.82 min; 439.10; conditions 3
361	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide	0.84 min; 457.04; conditions 3
362	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide	0.86 min; 453.07; conditions 3
363	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide	0.93 min; 473.10; conditions 3
364	N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide	0.96 min; 487.01; conditions 3
365	N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	0.91 min; 444.08; conditions 3
366	N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.63 min; 438.14; conditions 3
367	N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	1.40 min; 444.07; conditions 1
368	N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide	1.03 min; 400.13; conditions 1
369	N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide	1.28 min; 399.09; conditions 1
370	N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide	1.07 min; 400.01; conditions 1
371	2-(4-tert-Butyl-phenyl)-N-[1-(6-cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	1.47 min; 388.16; conditions 1
372	N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.44 min; 440.01; conditions 1

373	N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	1.10 min; 402.14; conditions 1
374	N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide	1.33 min; 438.05; conditions 1
375	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-methyl-cyclopropyl)-phenyl]-acetamide	0.85 min; 472.20; conditions 3
376	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenyl]-acetamide	0.87 min; 428.17; conditions 3
377	N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-methyl-cyclopropyl)-phenyl]-acetamide	0.89 min; 386.12; conditions 3
378	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(2,2-dimethyl-2,3-dihydro-benzofuran-5-yl)-acetamide	0.80 min; 388.18; conditions 3
379	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3,3-dimethyl-2,3-dihydro-benzofuran-5-yl)-acetamide	0.80 min; 388.19; conditions 3
380	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(2,2-dimethyl-2,3-dihydro-benzofuran-6-yl)-acetamide	0.80 min; 388.19; conditions 3
381	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-methyl-3-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.86 min; 430.13; conditions 3
382	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-fluoro-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.83 min; 433.98; conditions 3
383	rac-N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-((1R*,2R*)-2-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	0.87 min; 426.17; conditions 3
384	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-cyclopropyl)-phenyl]-acetamide	0.78 min; 388.19; conditions 3

Example 385: N-[1-(5-Cyano-6-difluoromethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide and Example 386: N-[1-(5-cyano-4-difluoromethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. To a sol. of Example 71 (205 mg, 0.57 mmol) and zinc difluoromethanesulfinate (355 mg, 1.14 mmol) in DMSO (3.2 mL), is added trifluoroacetic acid (0.0446 mL, 0.57 mmol) at rt. Luperox® TBH70X (tert-butyl hydroperoxide; 70% weight sol. in water, 0.23 mL, 1.71 mmol) is added slowly with vigorous stirring. The mixture is stirred at rt overnight. Zinc difluoromethanesulfinate (355 mg, 1.14 mmol) and

Luperox® TBH70X are added again. The mixture was stirred at r.t over 4 nights. The reaction mixture was partitioned between CH_2Cl_2 (5 mL) and aq. sat. $NaHCO_3$ (5 mL). The layers are separated, and the aq. phase is extracted with CH_2Cl_2 (3 x 5 mL). The combined org. layers are dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure. Purification of the residue by prep. HPLC (column: Waters XBridge, 30x75 mm, 10 um, UV/MS, basic conditions) yields the title products. LC-MS: t_R = 0.90 min, MH^+ = 410.18 and t_R = 0.89 min, MH^+ = 410.19 respectively (conditions 3).

2-(1λ4-Diazenylidene)-1-(3,3-dimethyl-2,3-dihydrobenzofuran-6-yl)ethan-1-one and (rac.)-*2-(1λ4-diazenylidene)-1-(3-methylchroman-7-yl)ethan-1-one*. To a mixture of 3,3-dimethyl-2,3-dihydrobenzofuran-6-carboxylic acid (710 mg, 3.69 mmol) in CH_2Cl_2 (20 mL) at -5 °C, are added oxalyl chloride, (0.474 mL, 5.54 mmol) and 4 drops of DMF. The mixture is allowed to warm up to rt over 2 h. The mixture is concentrated *in vacuo* (backfilled with N2). The resulting oil is dissolved in THF (20 mL) and cooled to -5 °C. (Trimethylsilyl)diazomethane (2.0 M in hexanes, 4.15 mL, 8.31 mmol) is added and the mixture is allowed to warm to rt overnight. The solvents are removed under reduced pressure. Purification of the reisdue by automated FC (Combiflash, heptane → EtOAc/heptane 1:3, column : 80 g, flow : 60 mL/min,) yields a mixture of the two title products. LC-MS: t_R = 0.80 min, MH^+ = 217.20 for the mixture (conditions 3).

Ethyl 2-(3,3-dimethyl-2,3-dihydrobenzofuran-6-yl)acetate and (rac.)-*ethyl 2-(3-methylchroman-7-yl)acetate*. To a sol. of the previous mixture (280 mg, 1.29 mmol) in EtOH (30 mL), a sol. of silver benzoate (178 mg, 0.777 mmol) in Et_3N (5.0 mL) is added dropwise. The resulting black sol. is stirred at rt for 19 h. The black suspension is filtered through *Celite*. The pad is rinsed with EtOAc. The filtrate is concentrated *in vacuo*. Purification of the crude by HPLC yielded the two separated title products. LC-MS: t_R = 0.90 min, MH^+ = 235.22 and t_R = 0.90 min, respectively (conditions 3).

(rac.)-2-(3-Methylchroman-7-yl)acetic acid. To a sol. of (rac.)-ethyl 2-(3-methylchroman-7-yl)acetate (38 mg, 0.162 mmol) in DMF (1.00 mL) is added aq. NaOH (1M, 0.5 mL). The resulting sol. is stirred at rt for 4 h. The sol. is neutralized with formic acid (0.5 mL), filtered and then purified by prep. HPLC to yield the crude title product. LC-MS: t_R = 0.74 min (conditions 3).

5-Bromo-3-fluoro-2-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine. Prepared according to *general procedure 4* with K_2CO_3 (1.87 g, 13.6 mmol), 5-bromo-2-(bromomethyl)-3-fluoropyridine (760 mg, 2.71 mmol), and 5-nitro-1H-pyrazole (313 mg, 2.71 mmol) in acetone (25 mL). The reaction is complete after 2 h. The crude is not purified. LC-MS: t_R = 0.78 min, MH^+ = 302.98 (conditions 3).

5-Fluoro-6-((3-nitro-1H-pyrazol-1-yl)methyl)nicotinonitrile. To a sol. of 5-bromo-3-fluoro-2-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine (1.02 g, 3.04 mmol) in N,N-dimethylacetamide (6.2 mL), are added in sequence $Zn(CN)_2$ (196 mg, 1.67 mmol), $Pd_2(dba)_3$ (60.7 mg, 0.066 mmol), 1,1'-bis-(diphenylphosphino)-ferrocene (45.5 mg, 0.082 mmol) and poly(methylhydrosiloxane) (PMHS) (0.067 mL). The resulting mixture is stirred at 150°C in a microwave during 40 min. The mixture is allowed to cool to rt, filtered over *Celite*, and the filtrate is

concentrated in vacuo. Purification of the reisude by automated FC (Combiflash, EtOAc / heptane 0:100 → 40:60, column 24 g, flow 35 mL/min) yields the title product. LC-MS: t_R = 0.70 min, MH^+ = 248.17 (conditions 3).

6-((3-Amino-1H-pyrazol-1-yl)methyl)-5-fluoronicotinonitrile. To a sol. of 5-fluoro-6-((3-nitro-1H-pyrazol-1-yl)methyl)nicotinonitrile (260 mg, 0.899 mmol) in EtOAc (9.22 mL) under N_2, is added Pd (10 wt. % on activated charcoal, 52 mg, 0.489 mmol). The flask is carefully evacuated and backfilled with H_2 (3x). The black suspension was stirred at rt under an H_2 atmosphere for 30 h. The black suspension is filtered through *Celite*, and the *Celite* is rinsed with EtOAc. The filtrate is concentrated in vacuo. To a sol. of the previous residue in THF (9.22 mL) under N_2, Pd (10 wt. % on activated charcoal, 52 mg, 0.49 mmol) is added. The flask is carefully evacuated and backfilled with H_2 (3x). The black suspension is stirred at rt under an H_2 atmosphere overnight. Purification of the residue by HPLC yields the title product. LC-MS: t_R = 0.40 min, MH^+ = 218.16 (conditions 3).

tert-Butyl 2-(4-(1-cyano-3,3-difluorocyclobutyl)phenyl)acetate. Prepared according to general procedure 6 from 1-(4-bromophenyl)-3,3-difluorocyclobutane-1-carbonitrile (WO2012027322, 92.7 mg, 0.337 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.4 mL, 0.70 mmol), $Pd_2(dba)_3$ (15.4 mg, 0.017 mmol), and X-Phos (8.3 mg, 0.017 mmol) in THF (2.9 mL). The reaction is complete overnight at 45 °C. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.95 min, MH^+ = 308.13 (conditions 3).

2-(4-(1-Cyano-3,3-difluorocyclobutyl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-Butyl 2-(4-(1-cyano-3,3-difluorocyclobutyl)phenyl)acetate (42 mg, 0.13 mmol) in TFA (0.15 mL) and CH_2Cl_2 (0.15 mL) The reaction is complete after 3 h at 0 °C. LC-MS: t_R = 0.74 min (conditions 3).

2-Bromo-3-fluoro-6-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine. Prepared according to *general procedure 4* with K_2CO_3 (2.01 g, 14.6 mmol), 2-bromo-6-(bromomethyl)-3-fluoropyridine (799 mg, 2.91 mmol), and 5-nitro-1H-pyrazole (336 mg, 2.91 mmol) in acetone (26 mL). The reaction is complete after 2 h. The crude is not purified. LC-MS: t_R = 0.80 (conditions 3).

3-Fluoro-6-((3-nitro-1H-pyrazol-1-yl)methyl)picolinonitrile. To a sol. of 2-bromo-3-fluoro-6-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine (1.13 g, 3.51 mmol) in N,N-Dimethylacetamide (7.2 mL), are added in sequence $Zn(CN)_2$ (226 mg, 1.93 mmol), $Pd_2(dba)_3$ (70.1 mg, 0.0766 mmol), 1,1'-bis-(diphenylphosphino)-ferrocene (52.6 mg, 0.0948 mmol), and poly(methylhydrosiloxane) (PMHS) (0.077 mL). The mixture is stirred at 150°C in a microwave for 40 min. The mixture is filtered over *Celite*, and the *Celite* is rinced with EtOAc. The filtrate is concentrated in vacuo. Purification of the residue by automated FC (Combiflash, EtOAc/heptane 0:100 → 30:70, column 24 g, flow 35 mL/min) yields the title product. LC-MS: t_R = 0.74, MH^+ = 248.20 (conditions 3).

6-((3-Amino-1H-pyrazol-1-yl)methyl)-3-fluoropicolinonitrile. To a sol. of 3-fluoro-6-((3-nitro-1H-pyrazol-1-yl)methyl)picolinonitrile (320 mg, 1.08 mmol) in EtOAc (11.1 mL) under N_2, is added Pd (10 wt. % on activated charcoal, 64 mg, 0.56 mmol). The flask is carefully evacuated and backfilled with H_2 (3x). The black

suspension was stirred at rt under an H_2 atmosphere overnight. The black suspension is filtered through *Celite*, and the *Celite* is rinsed with EtOAc. The filtrate is concentrated in vacuo. Purification of the residue by HPLC yields the title product. LC-MS: t_R = 0.48 min, MH^+ = 218.18 (conditions 3).

tert-Butyl 2-(3-cyano-4-isobutylphenyl)acetate. Prepared according to general procedure 6 from 5-bromo-2-isobutylbenzonitrile (136 mg, 0.57 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.24 mL, 0.62 mmol), $Pd_2(dba)_3$ (26.2 mg, 0.0286 mmol), and Q-Phos (41.1 mg, 0.0571 mmol) in dioxane (1.5 mL). The reaction is complete after 30 min at 85 °C. Purification by automated FC (Combiflash, EtOAc/heptane 0:100 → 60:40) yields the title product. LC-MS: t_R = 1.00 min, MH^+ = 273.97 (conditions 4).

2-(3-Cyano-4-isobutylphenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(3-cyano-4-isobutylphenyl)acetate (33 mg, 0.12 mmol) in HCl (4M in dioxane, 7 mL) and CH_2Cl_2 (1.4 mL) The reaction is complete overnight at rt. LC-MS: t_R = 0.73 min (conditions 3).

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
387	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3,3-dimethyl-2,3-dihydro-benzofuran-6-yl)-acetamide	0.81 min; 388.19; conditions 3
388	rac-N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-methyl-chroman-7-yl)-acetamide	0.81 min; 388.17; conditions 3
389	N-[1-(5-Cyano-3-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	0.89 min; 444.07; conditions 3
390	2-[4-(1-Cyano-3,3-difluoro-cyclobutyl)-phenyl]-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.81 min; 433.01; conditions 3
391	N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.89 min; 448.08; conditions 3
392	2-(3-Cyano-4-isobutyl-phenyl)-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.86 min; 399.17; conditions 3
393	2-(3-Cyano-4-isobutyl-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.94 min; 409.16; conditions 3

Example 394: N-[1-(5-Azetidin-1-yl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide. To a degased mixture of Example 94 (80 mg, 0.192 mmol), $Pd_2(dba)_3$ (17.5 mg, 0.02 mmol), RuPhos (17.9 mg, 0.04 mmol), NaOtBu (37 mg, 0.38 mmol), and molecular sieve (4A powder, 100 mg) in toluene (2.00 mL) is added azetidine (0.04 mL, 0.57 mmol). The reaction is stirred in a closed vial at 95 °C for 17 h. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.74 min, MH^+ = 390.20 (conditions 3).

Example 395: 2-(4-Isopropyl-phenyl)-N-[1-(5-pyrrolidin-1-yl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide. To a degased mixture of Example 94 (80 mg, 0.192 mmol), $Pd_2(dba)_3$ (17.5 mg, 0.02 mmol), RuPhos (17.9 mg, 0.04 mmol), NaOtBu (37 mg, 0.38 mmol), and molecular sieve (4A powder, 100 mg) in toluene (2.00 mL) is added pyrrolidine (0.05 mL, 0.57 mmol). The reaction is stirred in a closed vial at 110 °C for 17 h. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.75 min, MH^+ = 404.23 (conditions 3).

Example 396: N-{1-[5-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-2-ylmethyl]-1H-pyrazol-3-yl}-2-(4-isopropyl-phenyl)-acetamide. To a degased mixture of Example 94 (80 mg, 0.192 mmol), $Pd_2(dba)_3$ (17.5 mg, 0.02 mmol), RuPhos (17.9 mg, 0.04 mmol), NaOtBu (37 mg, 0.38 mmol), and molecular sieve (4A powder, 100 mg) in toluene (2.00 mL) is added 3,3-difluoropyrrolidine hydrochloride (57.6 mg, 0.57 mmol). The reaction is stirred in a closed vial at 110 °C for 17 h. The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Purification of the crude by HPLC yields the title product. LC-MS: t_R = 0.78 min, MH^+ = 440.17 (conditions 3).

tert-Butyl 2-(4-(cyclopropylmethoxy)-3-(trifluoromethoxy)phenyl)acetate. Prepared according to general procedure 6 from 4-bromo-1-(cyclopropylmethoxy)-2-(trifluoromethoxy)benzene (146 mg, 0.47 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.04 mL, 0.52 mmol), $Pd_2(dba)_3$ (22 mg, 0.020 mmol), and Q-Phos (34 mg, 0.050 mmol) in dioxane (1.5 mL). The reaction is complete after 1 h at 85 °C. Purification by automated FC (Combiflash, EtOAc/heptane 0:100 → 60:40) yields the title product. LC-MS: t_R = 1.04 min, MH^+ = 223.23 (conditions 4).

2-(4-(Cyclopropylmethoxy)-3-(trifluoromethoxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(cyclopropylmethoxy)-3-(trifluoromethoxy)phenyl)acetate (30 mg, 0.087 mmol) in HCOOH (0.60 mL) The reaction is complete after 2 h at rt.

4-Bromo-5-fluoro-2-methylpyridine 1-oxide. To a stirred solution of acetyl bromide (10.7 mL, 143 mmol) in AcOH (22.3 mL), is added portionwise 5-fluoro-2-methyl-4-nitropyridine 1-Oxide (2500 mg, 14.5 mmol). The mixture is stirred at for 2.5 h at rt. The mixture is carefully poured onto ice, and solid K_2CO_3 is carefully added in portions. The aq. layer is extracted with EtOAc (95 mL) and the org. layer is washed with brine (20 mL). The combined aq. layers are saturated with NaCl, and CH_2Cl_2 / iPrOH 3/1 (100 mL) is added. The mixture is stirred at rt for 2h. The layers are separated, and the aq. phase is extracted with CH_2Cl_2 / iPrOH 3/1 (2 x 100

mL) and CH_2Cl_2 (1 x 200 mL). The combined org. layers are dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.51 min, MH^+ = 206.06 (conditions 3).

(4-Bromo-5-fluoropyridin-2-yl)methyl acetate. To Ac_2O (7.39 mL, 77.5 mmol) at 120°C is added 4-bromo-5-fluoro-2-methylpyridine 1-oxide (2.98 g, 13.6 mmol). The resulting sol. is stirred at 120 °C for 5 min, and at reflux for 30 min. The mixture is allowed to cool down to rt, and is poured onto ice (57 g). The mixture is neutralized with $NaHCO_3$. Et_2O (60 mL) is added, and the layers are separated. The aq. phase is extracted with Et_2O (2 x 30 mL), and the combined org. layers are washed with brine, dried over $MgSO_4$, filtered and the solvents are removed under reduced pressure. Purification by automated FC (Combiflash, EtOAc / heptane 0:100 → 30:70, column 80 g, flow 60 mL/min) yields the title product. LC-MS: t_R = 0.73 min, MH^+ = 248.08 (conditions 3).

(4-Bromo-5-fluoropyridin-2-yl)methanol. K_2CO_3 (25.9 mg, 0.187 mmol) is added to a sol. of (4-bromo-5-fluoropyridin-2-yl)methyl acetate (1680 mg, 5.82 mmol) in MeOH (7.8 mL). The resulting mixture is stirred overnight at rt. K_2CO_3 (1674 mg, 12.1 mmol, 2.082 eq) is added again, and the mixture is stirred at rt for 1h. Water (16 mL) is added, and the mixture is neutralized with aq. 5% AcOH. CH_2Cl_2 is added, and the layers are separated. The aq. phase is extracted with CH_2Cl_2 (2x), and the combined org. layers are washed with brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude titel product. LC-MS: t_R = 0.55 min, MH^+ = 206.06 (conditions 3).

4-Bromo-2-(bromomethyl)-5-fluoropyridine. To a warmed (50°C) mixture of (4-bromo-5-fluoropyridin-2-yl)methanol (810 mg, 3.76 mmol) in DMF (4.8 mL) is added PBr_3 (0.389 mL, 4.14 mmol). The mixture is stirred at 50°C for 1.5 h. The mixture is allowed to cool down to rt, is diluted with water (240 mL) and is basified with aq. sat. $NaHCO_3$. EtOAc is added, and the layers are separated. The aq. layer is extracted with EtOAc (2x), and the combined org. layers are washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give the crude title product. LC-MS: t_R = 0.78 min, MH^+ = 269.97 (conditions 3).

4-Bromo-5-fluoro-2-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine. Prepared according to *general procedure 4* with K_2CO_3 (2.38 g, 17.3 mmol), 4-bromo-2-(bromomethyl)-5-fluoropyridine (952 mg, 3.45 mmol), and 5-nitro-1H-pyrazole (399 mg, 3.45 mmol) in acetone (31 mL). The reaction is complete after 3 h. The crude is not purified. LC-MS: t_R = 0.78, MH^+ = 301.02 (conditions 3).

5-Fluoro-2-((3-nitro-1H-pyrazol-1-yl)methyl)isonicotinonitrile. To a sol. of 4-bromo-5-fluoro-2-((3-nitro-1H-pyrazol-1-yl)methyl)pyridine (1.38 g, 4.15 mmol) in N,N-Dimethylacetamide (8.5 mL), are added in sequence $Zn(CN)_2$ (268 mg, 2.28 mmol), $Pd_2(dba)_3$ (83 mg, 0.091 mmol), 1,1'-bis-(diphenylphosphino)-ferrocene (62.3 mg, 0.112 mmol) and poly(methylhydrosiloxane) (0.091 mL). The mixture is stirred at 150°C in a microwave for 40 min. The mixture is filtered over *Celite*, and the Celite is rinsed with EtOAc. The filtrate is concentrated

in vacuo. Purification of the residue by automated FC (Combiflash, EtOAc / heptane 0:100 → 70:30, column 24 g, flow 35 mL/min) yields the title product. LC-MS: t_R = 0.72 (conditions 3).

2-((3-Amino-1H-pyrazol-1-yl)methyl)-5-fluoroisonicotinonitrile. To a sol. of *5*-fluoro-2-((3-nitro-1H-pyrazol-1-yl)methyl)isonicotinonitrile (815 mg, 2.35 mmol) in EtOAc (24 mL) is added Pd on charcoal (10 wt. %, 163 mg, 1.53 mmol). The flask is carefully evacuated and backfilled with H_2 (3x). The black suspension is stirred at rt under an H_2 atmosphere overnight. The black suspension is filtered through *Celite*. The *Celite* is rinsed with EtOAc. The filtrate is concentrated in vacuo. Ca. 300 mg of the residue is purified by HPLC. The resulting fractions are combined and CH_2Cl_2 is added. The layers are separated, and the aq. phase is extracted with CH_2Cl_2 (2x). The combined org. layers are dried over $MgSO_4$, filtered, and the solvents are concentrated in vacuo to give the crude title product. LC-MS: t_R = 0.45, MH^+ = 218.18 (conditions 3).

tert-Butyl 2-(4-(1-cyanocyclopropyl)-3-(trifluoromethyl)phenyl)acetate. Prepared according to general procedure 6 from 1-(4-bromo-2-(trifluoromethyl)phenyl)cyclopropane-1-carbonitrile (WO2006018725, 170 mg, 0.59 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.28 mL, 0.64 mmol), $Pd_2(dba)_3$ (27 mg, 0.029 mmol), and Q-Phos (42 mg, 0.059 mmol) in dioxane (1.5 mL). The reaction is complete after 1 h at 85 °C. Purification by automated FC (Combiflash, EtOAc/heptane 0:100 → 50:50) yields the title product. LC-MS: t_R = 0.91 min, MH^+ = 326.04 (conditions 4).

2-(4-(1-Cyanocyclopropyl)-3-(trifluoromethyl)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(4-(1-cyanocyclopropyl)-3-(trifluoromethyl)phenyl)acetate (36 mg, 0.11 mmol) in TFA (0.36 mL) and CH_2Cl_2 (0.35 mL). The reaction is complete after 2.5 h at 0 °C. LC-MS: t_R = 0.65 (conditions 4).

Methyl 2-(3-methyl-4-(3,3,3-trifluoropropoxy)phenyl)acetate. To a sol. of 2-(4-hydroxy-3-methylphenyl)acetic acid methyl ester (200 mg, 1.11 mmol) in DMF (3 mL) is added Cs_2CO_3 (470 mg, 1.44 mmol). The mixture is cooled to 0 °C, and 3,3,3-trifluoropropyl methanesulfonate (853 mg, 4.44 mmol) is added dropwise. The mixture is stirred overnight while warming up to rt. Cs_2CO_3 (1.88 g, 5.76 mmol) and 3,3,3-trifluoropropyl methanesulfonate (853 mg, 4.44 mmol) are added again. The mixture is stirred overnight. Water is added, and the mixture is extracted with EtOAc (2 x). The solvents are removed under reduced pressure. Purification of the residue by FC (EtOAc / heptane 10:90 → 20:80 → 25:75 → 50:50 → 75:25 → 100:0) yields the title product.

2-(3-Methyl-4-(3,3,3-trifluoropropoxy)phenyl)acetic acid. To a sol. of methyl 2-(3-methyl-4-(3,3,3-trifluoropropoxy)phenyl)acetate (50.0 mg, 0.18 mmol) in THF (1.00 mL) and MeOH (0.15 mL), is added 1M aq. NaOH (0.23 mL). The mixture is stirred overnight at rt, and the organic volatiles are removed in vacuo. The residue is diluted with water and washed with EtOAc (1x). The aq. layer is acidified with aq. 1M HCl. The mixture is extracted with CH_2Cl_2 (3x). The comb. org. layers are dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude title product.

4-Bromo-2-cyclopropyl-1-(2,2,2-trifluoroethoxy)benzene. To a sol. of 4-bromo-2-cyclopropylphenol (240 mg, 1.13 mmol) in DMF (5 mL) are added Cs_2CO_3 (550 mg, 1.69 mmol) and 1,1,1-trifluoro-2-iodoethane (0.555 mL, 5.63 mmol). The mixture is stirred for 2 h at 90 °C, and is allowed to cool to rt. Water is added, and the mixture is extracted with EtOAc (3 x). The combined org. layers are washed with water and with brine, are dried over MgSO4, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Combiflash, EtOAc / heptane 1:1) yields the title product.

tert-Butyl 2-(3-cyclopropyl-4-(2,2,2-trifluoroethoxy)phenyl)acetate. Prepared according to general procedure 6 from 4-bromo-2-cyclopropyl-1-(2,2,2-trifluoroethoxy)benzene (144 mg, 0.488 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 2.20 mL, 1.10 mmol), $Pd_2(dba)_3$ (22 mg, 0.024 mmol), and Q-Phos (23 mg, 0.049 mmol) in dioxane (3.0 mL). The reaction is complete overnight at 85 °C. Purification by automated FC (Combiflash, EtOAc/heptane 0:100 → 50:50) yields the title product.

2-(3-Cyclopropyl-4-(2,2,2-trifluoroethoxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(3-cyclopropyl-4-(2,2,2-trifluoroethoxy)phenyl)acetate (30 mg, 0.091 mmol) in HCOOH (0.80 mL). The reaction is complete after 2.5 h at rt. LC-MS: t_R = 0.77 (conditions 4).

tert-Butyl 2-(3-methyl-4-(trifluoromethoxy)phenyl)acetate. Prepared according to general procedure 6 from 4-bromo-2-methyl-1-(trifluoromethoxy)benzene (300 mg, 1.18 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 3.40 mL, 1.70 mmol), $Pd_2(dba)_3$ (54 mg, 0.059 mmol), and Q-Phos (56 mg, 0.118 mmol) in dioxane (3.0 mL). The reaction is complete overnight at 85 °C. Purification by automated FC (Combiflash, EtOAc/heptane 0:100 → 100:0) yields the title product. LC-MS: t_R = 1.02 (conditions 4).

2-(3-Methyl-4-(trifluoromethoxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(3-methyl-4-(trifluoromethoxy)phenyl)acetate (32 mg, 0.11 mmol) in HCOOH (0.80 mL). The reaction is complete after 2.5 h at rt. LC-MS: t_R = 0.77 (conditions 4) .

4-Bromo-2-ethyl-1-(2,2,2-trifluoroethoxy)benzene. To a sol. of 4-bromo-2-ethylphenol (300 mg, 1.49 mmol) in DMF (3 mL) is added Cs_2CO_3 (632 mg, 1.94 mmol). The mixture is cooled to 0 °C, and 2,2,2-trifluoroethyl trifluoromethanesulfonate (0.215 mL, 1.49 mmol) is added. The imixture is stirred for 90 min while warming up to rt. Water is added,and the mixture is extracted with EtOAc (3 x). The combined org. layers are washed with water and brine, dried over $MgSO_4$, filtered, and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.99 (conditions 3).

tert-Butyl 2-(3-ethyl-4-(2,2,2-trifluoroethoxy)phenyl)acetate. Prepared according to general procedure 6 from 4-bromo-2-ethyl-1-(2,2,2-trifluoroethoxy)benzene (100 mg, 0.353 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.40 mL, 0.70 mmol), $Pd_2(dba)_3$ (16 mg, 0.018 mmol), and X-Phos (17 mg, 0.035 mmol) in dioxane (3.0 mL). The reaction is complete overnight at 85 °C. Purification by automated FC (Combiflash, EtOAc/heptane 0:100 → 80:20) yields the title product. LC-MS: t_R = 1.02 (conditions 4).

2-(3-Ethyl-4-(2,2,2-trifluoroethoxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(3-ethyl-4-(trifluoromethoxy)phenyl)acetate (86 mg, 0.27 mmol) in HCOOH (2.0 mL). The reaction is complete after 2.5 h at rt. LC-MS: t_R = 0.77 (conditions 4) .

5-Bromo-1,3-dimethyl-2-(2,2,2-trifluoroethoxy)benzene. To a sol. of 4-bromo-2,6-xylenol (300 mg, 1.49 mmol, 1 eq) in DMF (3 mL) is added Cs_2CO_3 (632 mg, 1.94 mmol). The mixture is cooled to 0 °C, and 2,2,2-trifluoroethyl trifluoromethanesulfonate (0.215 mL, 1.49 mmol) is added. The mixture is stirred overnight while warming up to rt. Water is added, and the mixture is extracted with EtOAc (3 x). The combined org. layers are washed with water and brine, dried over MgSO4, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Combiflash, EtOAc / heptane 0:100 → 100:0) yields the title product.

tert-Butyl 2-(3,5-dimethyl-4-(2,2,2-trifluoroethoxy)phenyl)acetate. Prepared according to general procedure 6 from 5-bromo-1,3-dimethyl-2-(2,2,2-trifluoroethoxy)benzene (100 mg, 0.353 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 1.40 mL, 0.70 mmol), $Pd_2(dba)_3$ (16 mg, 0.018 mmol), and X-Phos (17 mg, 0.035 mmol) in dioxane (3.0 mL). The reaction is complete overnight at 85 °C. Purification by automated FC (Combiflash, EtOAc/heptane 0:100 → 80:20) yields the title product. LC-MS: t_R = 1.01 (conditions 4).

2-(3,5-Dimethyl-4-(2,2,2-trifluoroethoxy)phenyl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(3,5-dimethyl-4-(2,2,2-trifluoroethoxy)phenyl)acetate (96 mg, 0.30 mmol) in HCOOH (2.2 mL). The reaction is complete after 2.5 h at rt. LC-MS: t_R = 0.76 (conditions 4) .

tert-Butyl 2-(5-methyl-6-(2,2,2-trifluoroethoxy)pyridin-3-yl)acetate. Prepared according to general procedure 6 from 5-bromo-3-methyl-2-(2,2,2-trifluoroethoxy)pyridine (334 mg, 1.17 mmol), (2-(tert-butoxy)-2-oxoethyl)zinc(II) chloride (0.5M in Et_2O, 3.40 mL, 1.70 mmol), $Pd_2(dba)_3$ (54 mg, 0.058 mmol), and X-Phos (56 mg, 0.117 mmol) in dioxane (3.0 mL). The reaction is complete overnight at 85 °C. Purification by automated FC (Combiflash, EtOAc/heptane 0:100 → 80:20) yields the title product. LC-MS: t_R = 0.97 (conditions 4).

2-(5-Methyl-6-(2,2,2-trifluoroethoxy)pyridin-3-yl)acetic acid. Prepared according to *general procedure 7* from tert-butyl 2-(5-methyl-6-(2,2,2-trifluoroethoxy)pyridin-3-yl)acetate (92 mg, 0.30 mmol) in HCOOH (2.2 mL). The reaction is complete after 2.5 h at rt. LC-MS: t_R = 0.70 (conditions 4) .

The following examples were prepared according to general procedure 3, from the appropriate carboxylic acids and aminopyrazoles:

Example No	Name	LC-MS (t_R; MH^+; conditions)
397	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-cyclopropylmethoxy-3-trifluoromethoxy-phenyl)-acetamide	0.90 min; 472.01; conditions 3

398	2-(4-Cyclopropylmethoxy-3-trifluoromethoxy-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.97 min; 481.76; conditions 3
399	N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.88 min; 448.06; conditions 3
400	2-(4-tert-Butyl-phenyl)-N-[1-(4-cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.90 min; 392.18; conditions 3
401	N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide	0.88 min; 378.16; conditions 3
402	N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	0.90 min; 444.07; conditions 3
403	2-[4-(1-Cyano-cyclopropyl)-3-trifluoromethyl-phenyl]-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide	0.71 min; 451.04; conditions 4
404	2-[4-(1-Cyano-cyclopropyl)-3-trifluoromethyl-phenyl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide	0.82 min; 460.99; conditions 4
405	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(3,3,3-trifluoro-propoxy)-phenyl]-acetamide	0.78 min; 444.10; conditions 4
406	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-cyclopropyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.80 min; 456.01; conditions 4
407	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-methyl-4-trifluoromethoxy-phenyl)-acetamide	0.78 min; 416.10; conditions 4
408	N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-cyclopropyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.84 min; 473.76; conditions 4
409	N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-cyclopropyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.83 min; 473.89; conditions 4
410	N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-methyl-4-trifluoromethoxy-phenyl)-acetamide	0.83 min; 433.94; conditions 4
411	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-ethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.80 min; 444.07; conditions 4
412	N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-ethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.85 min; 462.03; conditions 4

413	N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-ethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.84 min; 461.97; conditions 4
414	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3,5-dimethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.79 min; 444.05; conditions 4
415	N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3,5-dimethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.84 min; 462.05; conditions 4
416	N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3,5-dimethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.82 min; 461.94; conditions 4
417	N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[5-methyl-6-(2,2,2-trifluoro-ethoxy)-pyridin-3-yl]-acetamide	0.75 min; 431.04; conditions 4
418	N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[5-methyl-6-(2,2,2-trifluoro-ethoxy)-pyridin-3-yl]-acetamide	0.80 min; 448.93; conditions 4
419	N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[5-methyl-6-(2,2,2-trifluoro-ethoxy)-pyridin-3-yl]-acetamide	0.79 min; 449.01; conditions 4
420	N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(3,3,3-trifluoro-propoxy)-phenyl]-acetamide	0.82 min; 461.98; conditions 4
421	N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(3,3,3-trifluoro-propoxy)-phenyl]-acetamide	0.81 min; 462.03; conditions 4

In vitro Methods – Measurement of calcium channel flux by means of FLIPR assays.

HEK293 cells recombinantly expressing either voltage-dependent T-type calcium channel subunit alpha-1G (Cav3.2) or voltage-dependent L-type calcium channel subunit alpha-1C (Cav1.2) are assayed for calcium flux using the calcium indicator dye Fluo-4-AM (Molecular Devices) and FLIPR technology (Fluorometric Imaging Plate Reader, Molecular Devices) (Xie X, Van Deusen AL, Vitko I, Babu DA, Davies LA, Huynh N, Cheng H, Yang N, Barrett PQ, Perez-Reyes E. Validation of high throughput screening assays against three subtypes of Ca(v)3 T-type channels using molecular and pharmacologic approaches. Assay and Drug Development Technologies 2007, 5(2), 191-203). The HEK293 cells recombinantly expressing Cav3.2 are maintained in DMEM growth medium (Life Technologies) supplemented with 10 % Fetal Bovine Serum (FBS), 100 U/ml penicilin (Life Technologies), 100 µg/ml streptomycin (Life Technologies) and 1 mg/ml G418 (Life Technologies). HEK293 cells recombinantly expressing Cav1.2 are maintained in DMEM growth medium (Life technologies) supplemented with 10 % FBS, 0.1 mg/ml G418 (Life Technologies), 0.1 mg/ml hygromycin (Life Technologies) and 40 ug/ml zeocin (Life Technologies).

Cells are washed once with PBS, then dissociated in 0.25 % trypsin/EDTA (Life Technologies) and seeded into poly-D-lysine coated 384-well black, clear bottom plates (BD Biosciences) at a density of 30,000 cells/well. The seeded plates are incubated overnight at 37°C.

Immediately prior to performing the assay, medium is removed and cells are treated for 1 hour at 37˚C with loading buffer containing HBSS 1X (137 mM NaCl; 5.4 mM KCl; 0.25 mM Na2HPO4; 1.3 mM CaCl2; 0.4 mM MgSO4; 0.5 mM MgCl2; 0.4 mM KH2PO4, pH 7.4), 0.375 g/L NaHCO3, 20 mM Hepes, supplemented with 3 µM Fluo-4-AM and 0.15 % Pluronic (Life Technologies). The cells are then washed three times with assay buffer (HBSS 1X; 0.375 g/L NaHCO3; 20 mM Hepes; 1 % FBS; pH 7.4) and allowed to rest in 50 µl of wash buffer for 30 minutes.

Stock solutions of test compounds are prepared to a concentration of 10 mM in DMSO. For the Cav3.2 assay, serial dilutions of the compounds are prepared in TEAC buffer (100 mM tetraethylammonium chloride; 20 mM Hepes; 2.5 mM CaCl2; 5 mM KCl; 1 mM MgCl2; 1 % FBS; pH 7.2), for the Cav1.2 assay serial dilutions are prepared in assay buffer. Test compounds are added to the cells to give a 3-fold dilution range from 10 µM to 0.05 nM. The compounds are incubated with the cells for 3 minutes and Ca2+ entry is stimulated by adding either CaCl2 to a final concentration of 10 mM (Cav3.2 assay) or by adding KCl to a final concentration of 20 mM (Cav1.2 assay). The kinetics of fluorescence increase are recorded for every well and the area under the fluorescence trace for every compound concentration is used to generate inhibition curves using non-linear regression sigmoidal concentration-response curve analysis with in-house software. IC_{50} values are calculated and represent the compound concentration required to inhibit 50% of the signal that is obtained in the presence of vehicle instead of test compound. In analogy, antagonistic activities (IC_{50} values) of all exemplified compounds have been measured for the for the Cav3.1- and the Cav3.3-channel. Antagonistic activities (IC_{50} values) of all exemplified compounds are in the range of 0.3 to 1210 nM with respect to Cav3.1; and in the range of 0.8 to 1280 nM with respect to Cav3.3.

In the following table, IC_{50}-values generated for the Cav3.2-channel are presented.

Example	IC50 (nM)	Example	IC50 (nM)	Example	IC50 (nM)	Example	IC50 (nM)
1	14	**107**	338	**213**	31	**319**	66
2	4.1	**108**	322	**214**	164	**320**	99
3	12	**109**	22	**215**	599	**321**	91
4	82	**110**	14	**216**	269	**322**	856
5	20	**111**	1330	**217**	15	**323**	36
6	6.6	**112**	21	**218**	79	**324**	31
7	7.9	**113**	4.8	**219**	14	**325**	893
8	47	**114**	14	**220**	3.1	**326**	33
9	12	**115**	57	**221**	5.0	**327**	37

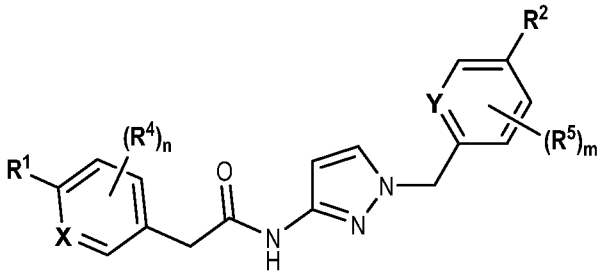
10	10	**116**	75	**222**	117	**328**	33
11	5.4	**117**	332	**223**	8.4	**329**	80
12	20	**118**	97	**224**	21	**330**	4.8
13	133	**119**	137	**225**	13	**331**	9.6
14	650	**120**	6.7	**226**	25	**332**	600
15	374	**121**	68	**227**	4.3	**333**	2790
16	10	**122**	19	**228**	44	**334**	21
17	12	**123**	1270	**229**	3.8	**335**	20
18	25	**124**	9.9	**230**	255	**336**	34
19	10	**125**	64	**231**	21	**337**	168
20	5.1	**126**	3.4	**232**	5.8	**338**	61
21	3.4	**127**	27	**233**	8.1	**339**	7.0
22	5.0	**128**	9.7	**234**	6	**340**	8.5
23	6.4	**129**	128	**235**	42	**341**	64
24	13	**130**	293	**236**	18	**342**	40
25	64	**131**	88	**237**	6.1	**343**	4.5
26	5.4	**132**	51	**238**	32	**344**	52
27	61	**133**	191	**239**	2.4	**345**	34
28	8.0	**134**	428	**240**	11	**346**	159
29	25	**135**	247	**241**	34	**347**	85
30	8.6	**136**	1570	**242**	39	**348**	29
31	4.0	**137**	313	**243**	37	**349**	23
32	7.6	**138**	756	**244**	33	**350**	69
33	101	**139**	36	**245**	30	**351**	65
34	91	**140**	176	**246**	705	**352**	22
35	43	**141**	35	**247**	2590	**353**	30
36	160	**142**	185	**248**	1810	**354**	248
37	29	**143**	19	**249**	295	**355**	26
38	39	**144**	160	**250**	127	**356**	327
39	49	**145**	44	**251**	303	**357**	34
40	16	**146**	136	**252**	56	**358**	20
41	38	**147**	13	**253**	57	**359**	212
42	19	**148**	7.6	**254**	100	**360**	360
43	82	**149**	85	**255**	52	**361**	80

44	372	**150**	682	**256**	251	**362**	117
45	33	**151**	649	**257**	76	**363**	51
46	26	**152**	1160	**258**	934	**364**	62
47	37	**153**	21	**259**	4.1	**365**	18
48	138	**154**	78	**260**	3.1	**366**	147
49	9.2	**155**	70	**261**	15	**367**	10
50	11	**156**	179	**262**	155	**368**	301
51	16	**157**	34	**263**	97	**369**	64
52	2.6	**158**	11	**264**	5.4	**370**	578
53	6.7	**159**	1180	**265**	15	**371**	13
54	28	**160**	29	**266**	6.6	**372**	38
55	33	**161**	258	**267**	90	**373**	349
56	46	**162**	64	**268**	35	**374**	107
57	14	**163**	345	**269**	162	**375**	9.9
58	285	**164**	568	**270**	51	**376**	20
59	136	**165**	13	**271**	3.4	**377**	25
60	4.7	**166**	86	**272**	7.5	**378**	249
61	3.4	**167**	21	**273**	35	**379**	658
62	3.8	**168**	113	**274**	133	**380**	214
63	38	**169**	104	**275**	14	**381**	54
64	80	**170**	191	**276**	188	**382**	114
65	74	**171**	980	**277**	15	**383**	36
66	19	**172**	15	**278**	18	**384**	128
67	3.4	**173**	188	**279**	275	**385**	44
68	4.8	**174**	319	**280**	138	**386**	69
69	16	**175**	17	**281**	21	**387**	122
70	11	**176**	67	**282**	12	**388**	30
71	60	**177**	18	**283**	9.5	**389**	506
72	46	**178**	99	**284**	3070	**390**	47
73	7.9	**179**	2500	**285**	208	**391**	2.1
74	14	**180**	33	**286**	393	**392**	101
75	5.2	**181**	272	**287**	9480	**393**	51
76	6.1	**182**	65	**288**	4.7	**394**	126
77	9.1	**183**	530	**289**	23	**395**	315

78	275	**184**	490	**290**	39	**396**	369
79	218	**185**	7.7	**291**	80	**397**	44
80	92	**186**	41	**292**	6.5	**398**	39
81	131	**187**	15	**293**	6.6	**399**	60
82	33	**188**	60	**294**	22	**400**	49
83	26	**189**	88	**295**	308	**401**	126
84	18	**190**	21	**296**	17	**402**	106
85	301	**191**	93	**297**	20	**403**	97
86	140	**192**	133	**298**	43	**404**	14
87	157	**193**	78	**299**	37	**405**	18
88	109	**194**	61	**300**	7.5	**406**	15
89	61	**195**	47	**301**	71	**407**	25
90	75	**196**	176	**302**	39	**408**	8.5
91	23	**197**	54	**303**	51	**409**	43
92	48	**198**	16	**304**	118	**410**	17
93	39	**199**	74	**305**	29	**411**	7.8
94	8.3	**200**	67	**306**	17	**412**	5.3
95	99	**201**	30	**307**	42	**413**	30
96	53	**202**	16	**308**	263	**414**	6.4
97	31	**203**	1260	**309**	27	**415**	4.9
98	38	**204**	79	**310**	13	**416**	17
99	48	**205**	288	**311**	81	**417**	37
100	60	**206**	50	**312**	10	**418**	94
101	925	**207**	5.3	**313**	45	**419**	9430
102	7050	**208**	88	**314**	32	**420**	8.7
103	145	**209**	53	**315**	240	**421**	41
104	4520	**210**	8.0	**316**	36		
105	31	**211**	3.1	**317**	56		
106	15	**212**	35	**318**	378		

Claims

1. A compound of formula (I)



Formula (I)

wherein

X represents a ring carbon or a ring nitrogen atom;

- R^1 represents
  - (C_{2-6})alkyl;
  - (C_{2-4})alkyl mono-substituted with cyano, or (C_{1-3})alkoxy;
  - (C_{1-4})fluoroalkyl;
  - (C_{1-3})fluoroalkoxy;
  - pentafluoro-sulfanyl;
  - (C_{3-6})cycloalkyl-L^1- wherein
    - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C_{1-3})alkyl, (C_{1-3})alkoxy, hydroxy, cyano, or (C_{1-3})fluoroalkyl, or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a substituent selected from (C_{1-3})alkyl and cyano; and
    - the linker L^1 represents a direct bond, (C_{1-2})alkylene, oxygen, or (C_{1-2})alkylene-oxy;
  - 5- or 6-membered heteroaryl, independently optionally mono-substituted with (C_{1-3})alkyl;
  - $-NR^{11}R^{12}$, wherein
    - R^{11} and R^{12} independently represent hydrogen, (C_{1-3})alkyl, (C_{2-3})fluoroalkyl, (C_{3-6})cycloalkyl, (C_{3-6})cycloalkyl mono- or di-substituted with fluoro, (C_{3-6})cycloalkyl-(C_{1-3})alkyl, (C_{1-3})alkoxy-(C_{2-3})alkyl;
    - or R^{11} and R^{12}, together with the nitrogen atom to which they are attached to, form a 4- to- 6 membered ring optionally mono- or di-substituted with fluoro; a 2-oxo-pyrrolidinyl group; or a morpholinyl group;

and $(R^4)_n$ represents one or two optional substituents independently selected from (C_{1-4})alkyl, (C_{3-6})cycloalkyl, (C_{1-4})alkoxy, (C_{1-3})fluoroalkyl, (C_{1-3})fluoroalkoxy, halogen, and cyano;

- or **R**^{1} together with **(R**^{4}**)**$_{n}$ forms a non-aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring; wherein said 5- or 6-membered ring optionally contains one or two heteroatoms independently selected from oxygen and nitrogen; wherein said fused 5- or 6-membered non-aromatic ring independently is optionally further mono-substituted with oxo or (C_{1-3})alkyl; di-substituted with (C_{1-3})alkyl; or di-, tri-, or tetra-substituted wherein one substituent is oxo and the remaining are (C_{1-3})alkyl;
- or **R**^{1} together with **(R**^{4}**)**$_{n}$ forms an aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring; wherein said 5- or 6-membered ring optionally contains one or two heteroatoms selected from nitrogen, wherein said fused 5- or 6-membered aromatic ring independently is optionally further mono- or di-substituted wherein the substituents are independently selected from (C_{1-3})alkyl, (C_{3-6})cycloalkyl, (C_{1})fluoroalkyl, or cyano;
- or **R**^{1} represents methyl, or halogen; and **(R**^{4}**)**$_{n}$ represents one substituent selected from (C_{1-3})fluoroalkoxy which is attached to the phenyl / pyridinyl ring in *ortho* or *meta*-position to the point of attachment of the –CH_2-CO-NH- group;

Y represents a ring carbon or a ring nitrogen atom; and

R^{2} represents (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; (C_{3-6})cycloalkyl-oxy; (C_{1-3})fluoroalkyl; (C_{1-3})fluoroalkoxy; (C_{1-3})alkoxy-(C_{2-3})alkoxy; halogen; cyano; or -$NR^{21}R^{22}$, wherein R^{21} and R^{22} independently represent hydrogen, or (C_{1-3})alkyl, or R^{21} and R^{22}, together with the nitrogen atom to which they are attached to, form a 4- to- 6 membered ring optionally mono- or di-substituted with fluoro, or a morpholinyl group;
and

(R^{5}**)**$_{m}$ represents one or two optional substituents independently selected from (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; halogen; cyano; (C_{1-3})fluoroalkyl; and (C_{1-3})fluoroalkoxy;
or a salt of such a compound.

2. A compound according to claim 1, wherein **X** represents a ring carbon atom;
or a salt of such a compound.

3. A compound according to claim 1 or 2, wherein **R**^{1} represents
   - (C_{2-6})alkyl;
   - (C_{2-4})alkyl mono-substituted with cyano, or (C_{1-3})alkoxy;
   - (C_{1-4})fluoroalkyl;
   - (C_{1-3})fluoroalkoxy;
   - pentafluoro-sulfanyl;
   - (C_{3-6})cycloalkyl-**L**^{1}- wherein
     - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C_{1-3})alkyl,

(C_{1-3})alkoxy, hydroxy, cyano, or (C_{1-3})fluoroalkyl, or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a (C_{1-3})alkyl substituent; and

- the linker **L^1** represents a direct bond, (C_{1-2})alkylene, oxygen, or (C_{1-2})alkylene-oxy;

- 5- or 6-membered heteroaryl selected from oxadiazolyl, pyrazinyl, pyrimidinyl, and pyridinyl; wherein said heteroaryl independently is optionally mono-substituted with (C_{1-3})alkyl; or
- -$NR^{11}R^{12}$, wherein
  - R^{11} and R^{12} independently represent hydrogen, (C_{1-3})alkyl, (C_{2-3})fluoroalkyl, (C_{3-6})cycloalkyl, (C_{3-6})cycloalkyl mono- or di-substituted with fluoro, (C_{3-6})cycloalkyl-(C_{1-3})alkyl, (C_{1-3})alkoxy-(C_{2-3})alkyl;
  - or R^{11} and R^{12}, together with the nitrogen atom to which they are attached to, form an azetidinyl or a pyrrolidinyl ring, both independently optionally mono- or di-substituted with fluoro; or a 2-oxo-pyrrolidinyl group;

and **$(R^4)_n$** represents one optional substituent selected from (C_{1-4})alkyl, (C_{1-4})alkoxy, (C_{1-3})fluoroalkyl, (C_{1-3})fluoroalkoxy, halogen, and cyano;

- or **R^1** together with **$(R^4)_n$** forms a non-aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring to form a bicyclic ring system; wherein said bicyclic ring system is selected from 2,3-dihydro-benzooxazolyl, 3,4-dihydro-2H-benzo[1,4]oxazinyl, 2,3-dihydro-1H-indolyl, and 2,3-dihydro-benzofuranyl; wherein said non-aromatic 5- or 6-membered ring part of said bicyclic ring system independently is optionally further mono-substituted with oxo; or di-, tri-, or tetra-substituted wherein one substituent is oxo and the remaining are (C_{1-3})alkyl;

- or **R^1** together with **$(R^4)_n$** forms an aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring to form a bicyclic aromatic ring system selected from pyrrolo[2,3-b]pyridinyl, indolyl, indazolyl, quinoxalinyl, benzoimidazolyl, and quinolinyl; wherein said fused 5- or 6-membered aromatic ring part of said aromatic bicyclic ring system independently is optionally further mono- or di-substituted wherein the substituents are independently selected from (C_{1-3})alkyl, (C_{3-6})cycloalkyl, (C_1)fluoroalkyl, or cyano;

- or **R^1** represents methyl, or halogen; and **$(R^4)_n$** represents one substituent selected from (C_{1-3})fluoroalkoxy which is attached to the phenyl / pyridinyl ring in *ortho* or *meta*-position to the point of attachment of the -CH_2-CO-NH- group;

or a salt of such a compound.

4. A compound according to claims 1 or 2, wherein **R^1** represents

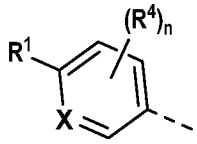
- (C_{2-6})alkyl;
- (C_{1-4})fluoroalkyl;
- (C_{1-3})fluoroalkoxy;

- (C_{3-6})cycloalkyl wherein said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is mono-substituted with fluoro or (C_{1-3})fluoroalkyl, or di-substituted with fluoro; or
- (C_{3-6})cycloalkyl-oxy- wherein said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or di-substituted with fluoro;

and $(R^4)_n$ represents one optional substituent selected from (C_{1-4})alkyl, or halogen;

or a salt of such a compound.

5. A compound according to claims 1 or 2, wherein the fragment



represents 4-cyclopropyl-phenyl, 4-isopropyl-phenyl, 4- dimethylamino -phenyl, 4- trifluoromethyl -phenyl, 4-*tert.*-butyl -phenyl, 4- isobutyl -phenyl, 4-(1-methoxy-ethyl)-phenyl, 4-(1-methyl-cyclopropyl)-phenyl, 4-(cyclopropyl-methyl)-phenyl, 4-(1-hydroxy-cyclopropyl)-phenyl, 4-(cyclopropyl-oxy)-phenyl, 4-(azetidin-1-yl)-phenyl, 4-(oxetan-3-yl-oxy)-phenyl, 4-(3-hydroxy-oxetan-3-yl)-phenyl, 4-(3-fluoro-oxetan-3-yl)-phenyl, 4-(cyclobutyl-oxy)-phenyl, 4-(3-methyl-oxetan-3-yl)-phenyl, 4-([1,2,4]oxadiazol-3-yl)-phenyl, 4-(5-methyl-[1,2,4]oxadiazol-3-yl)-phenyl, 4-(3-fluoro-azetidin-1-yl)-phenyl, 4-(1-cyano-cyclopropyl)-phenyl, 4-(1-cyano-1-methyl-ethyl)-phenyl, 4-(diethylamino)-phenyl, 4-(pentafluoro-sulfanyl)-phenyl, 4-(2,2,2-trifluoroethoxy)-phenyl, 3-methyl-4-(2,2,2-trifluoroethoxy)-phenyl, 3-fluoro-4-(2,2,2-trifluoroethoxy)-phenyl, 4-((2-methoxyethyl)-methyl-amino)-phenyl, 4-(3,3-difluoro-cyclobutyl)-phenyl, 4-(3-methoxy-oxetan-3-yl)-phenyl, 4-(oxetan-3-yl-methoxy)-phenyl, 4-(pyrazin-2-yl)-phenyl, 4-(3-methyl-pyrazin-2-yl)-phenyl, 4-(pyrimidin-4-yl)-phenyl, 4-(5-methyl-pyrimidin-4-yl)-phenyl, 4-(pyrimidin-2-yl)-phenyl, 4-(pyrimidin-5-yl)-phenyl, 4-(pyridin-4-yl)-phenyl, 4-(pyridin-3-yl)-phenyl, 4-(pyridin-2-yl)-phenyl, 4-(3-fluoro-pyrrolidin-1-yl)-phenyl, 4-(3,3-difluoro-azetidin-1-yl)-phenyl, 4-(2-oxo-pyrrolidin-1-yl)-phenyl, 4-(2-trifluoromethyl-cyclopropyl)-phenyl, 4-(1-trifluoromethyl-cyclopropyl)-phenyl, 4-((3-fluoro-oxetan-3-yl)-methoxy)-phenyl, 4-(3,3-difluoro-cyclobutyl-oxy)-phenyl, 4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenyl, 4-((3,3-difluoro-cyclobutyl)-methoxy)-phenyl, 4-((3,3-difluoro-1-methyl-cyclobutyl)-methoxy)-phenyl; 2-cyclopropyl-pyridin-5-yl, 2-dimethylamino-pyridin-5-yl, 2-isopropyl-pyridin-5-yl, 2-(ethyl-methyl-amino)-pyridin-5-yl, 2-(3-fluoro-azetidin-1-yl)-pyridin-5-yl, 2-(pyrrolidin-1-yl)-pyridin-5-yl, 2-(cyclopropyl-methyl-amino)-pyridin-5-yl, 2-(3-fluoro-oxetan-3-yl)-pyridin-5-yl, 2-(diethylamino)-pyridin-5-yl, 2-((2,2-difluoro-ethyl)-methyl-amino)-pyridin-5-yl, 2-((2-methoxyethyl)-methyl-amino)-pyridin-5-yl, 2-(2,2,2-trifluoroethoxy)-pyridin-5-yl, 3-fluoro-2-(2,2,2-trifluoroethoxy)-pyridin-5-yl, 3-fluoro-2-(pyrrolidin-1-yl)-pyridin-5-yl, 2-(3-fluoro-pyrrolidin-1-yl)-pyridin-5-yl, 2-((cyclopropylmethyl)-methyl-amino)-pyridin-5-yl, 2-(3,3-difluoro-azetidin-1-yl)-pyridin-5-yl, 2-(3-methoxy-oxetan-3-yl)-pyridin-5-yl, 2-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-5-yl; 2-oxo-2,3-dihydro-benzooxazol-6-yl, 3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl, 4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl, 3-methyl-2-oxo-2,3-dihydro-benzooxazol-6-yl, 3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-

5-yl, 1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl, 2,2-dimethyl-2,3-dihydro-benzofuran-6-yl, 2,2-dimethyl-2,3-dihydro-benzofuran-5-yl, 3,3-dimethyl-2,3-dihydro-benzofuran-5-yl; 1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl, 1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl, 1H-indol-5-yl, 1H-indol-6-yl, 1-methyl-1H-indazol-5-yl, 1-methyl-1H-indazol-6-yl, 1-ethyl-1H-indazol-5-yl, 1-ethyl-1H-indazol-6-yl, 1,3-dimethyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 1,3-dimethyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-6-yl, 3-cyano-1-methyl-1H-indol-5-yl, 3-isopropyl-1-methyl-1H-indol-5-yl, 3-cyclobutyl-1-methyl-1H-indol-5-yl, 1-methyl-3-trifluoromethyl-1H-indol-5-yl, quinoxalin-6-yl, 2-methyl-1H-benzoimidazol-6-yl, 1-methyl-1H-benzoimidazol-5-yl, 1-methyl-1H-benzoimidazol-6-yl, quinolin-7-yl; 4-methyl-3-(2,2,2-trifluoroethoxy)-phenyl; or 4-fluoro-2-(2,2,2-trifluoroethoxy)-phenyl;

or a salt of such a compound.

6. A compound according to any one of claims 1 to 5, wherein

- **Y** represents a ring nitrogen atom; and
  - $\mathbf{R^2}$ represents (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; (C_{1-3})fluoroalkyl; (C_{1-3})fluoroalkoxy; (C_{1-3})alkoxy-(C_{2-3})alkoxy; halogen; or cyano; and
  - $\mathbf{(R^5)_m}$ represents one optional substituent independently selected from the group consisting of (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; halogen; cyano; (C_{1-3})fluoroalkyl; and (C_{1-3})fluoroalkoxy;

or

- **Y** represents a ring carbon atom; and
  - $\mathbf{R^2}$ represents (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; (C_{3-6})cycloalkyl-oxy; (C_{1-3})fluoroalkyl; (C_{1-3})fluoroalkoxy; halogen; or cyano; and
  - $\mathbf{(R^5)_m}$ represents one or two optional substituents independently selected from the group consisting of (C_{1-4})alkyl; (C_{1-4})alkoxy; halogen; cyano; (C_{1-3})fluoroalkyl, and (C_{1-3})fluoroalkoxy;

or a salt of such a compound.

7. A compound according to any one of claims 1 to 5, wherein

- **Y** represents a ring nitrogen atom; and
  - $\mathbf{R^2}$ represents (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; (C_{1-3})fluoroalkyl; (C_{1-3})fluoroalkoxy; (C_{1-3})alkoxy-(C_{2-3})alkoxy; halogen; or cyano; and
  - $\mathbf{(R^5)_m}$ represents one optional substituent independently selected from the group consisting of (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; halogen; cyano; (C_{1-3})fluoroalkyl, and (C_{1-3})fluoroalkoxy;

or a salt of such a compound.

8. A compound according to claim 1, wherein

X represents a ring carbon or a ring nitrogen atom;

- $\mathbf{R^1}$ represents
  - (C_{2-6})alkyl;

- (C_{2-4})alkyl mono-substituted with cyano;
- (C_{1-4})fluoroalkyl;
- (C_{3-6})cycloalkyl-L^1- wherein
  - said (C_{3-6})cycloalkyl optionally contains one ring oxygen atom; wherein said (C_{3-6})cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C_{1-3})alkyl, (C_{1-3})alkoxy, hydroxy, cyano, or (C_{1-3})fluoroalkyl, or di-substituted with fluoro; and
  - the linker L^1 represents a direct bond, or (C_{1-2})alkylene; or
- 5- or 6-membered heteroaryl, independently optionally mono-substituted with (C_{1-3})alkyl;

and $(R^4)_n$ represents one or two optional substituents independently selected from (C_{1-4})alkyl, (C_{3-6})cycloalkyl, (C_{1-3})fluoroalkyl, halogen, and cyano;

- or R^1 together with $(R^4)_n$ forms an aromatic 5- or 6-membered ring which is fused to the phenyl / pyridine ring to form a bicyclic aromatic ring system selected from indolyl, indazolyl and quinolinyl; wherein said fused 5- or 6-membered aromatic ring part of said aromatic bicyclic ring system independently is optionally further mono- or di-substituted wherein the substituents are independently selected from (C_{1-3})alkyl, (C_{3-6})cycloalkyl, (C_1)fluoroalkyl, or cyano;

Y represents a ring carbon or a ring nitrogen atom; and

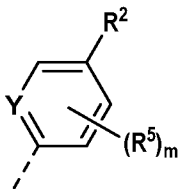
R^2 represents (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; (C_{3-6})cycloalkyl-oxy; (C_{1-3})fluoroalkyl; (C_{1-3})fluoroalkoxy; halogen; or cyano;

and

$(R^5)_m$ represents one or two optional substituents independently selected from (C_{1-4})alkyl; (C_{3-6})cycloalkyl; (C_{1-4})alkoxy; halogen; cyano; (C_{1-3})fluoroalkyl; and (C_{1-3})fluoroalkoxy;

or a salt of such a compound.

9. A compound according to any one of claims 1 to 5, wherein the fragment



represents 4-fluorophenyl, 4-chlorophenyl, 4-bromophenyl, 4-methylphenyl, 4-ethylphenyl, 3-fluoro-4-methyl-phenyl, 4-fluoro-3-methyl-phenyl, 4-fluoro-3-cyano-phenyl, 4-fluoro-3,5-dimethylphenyl, 4-chloro-3-fluorophenyl, 3-chloro-4-fluorophenyl, 3,4-difluorophenyl, 3,5-difluoro-4-methoxy-phenyl, 4-cyano-3,5-difluoro-phenyl, 4-methoxyphenyl, 4-cyanophenyl, 4-cyclopropyl-phenyl, 3,4,5-trifluorophenyl, 4-*tert*.-butyl-phenyl, 4-isopropyl-phenyl, 4-(cyclopropyl-oxy)-phenyl, 4-chloro-3-trifluoromethyl-phenyl, 4-fluoro-3-trifluoromethyl-phenyl, 4-methoxy-3-trifluoromethyl-phenyl, 4-difluoromethoxy-phenyl, 4-trifluoromethoxy-phenyl, 4-chloro-3-trifluoromethoxy-phenyl, 4-fluoro-3-trifluoromethoxy-phenyl; 5-fluoro-pyridin-2-yl, 5-bromo-pyridin-2-yl, 5-

cyano-pyridin-2-yl, 5-methyl-pyridin-2-yl, 5-ethyl-pyridin-2-yl, 5-methoxy-pyridin-2-yl, 6-chloro-5-fluoro-pyridin-2-yl, 5-cyclopropyl-pyridin-2-yl, 6-cyano-5-fluoro-pyridin-2-yl, 5-cyano-6-fluoro-pyridin-2-yl, 6-chloro-5-cyano-pyridin-2-yl, 5-chloro-6-cyano-pyridin-2-yl, 5-cyano-6-methyl-pyridin-2-yl, 5-cyano-4-methyl-pyridin-2-yl, 6-cyano-5-methyl-pyridin-2-yl, 5-cyano-6-isobutyl-pyridin-2-yl, 5-cyano-6-methoxy-pyridin-2-yl, 5-cyano-6-isopropoxy-pyridin-2-yl, 5-trifluoromethyl-pyridin-2-yl, 5-(2,2,2-trifluoroethoxy)-pyridin-2-yl, 5-cyano-6-(2,2,2-trifluoroethoxy)-pyridin-2-yl, 5-isobutyl-pyridin-2-yl, 5-isopropoxy-pyridin-2-yl, 5-dimethylamino-pyridine-2-yl, 4-cyclopropyl-5-cyano-pyridin-2-yl, 5-(2-methoxy-ethoxy)-pyridin-2-yl, or 5-(3-fluoropyrrolidin-1-yl)-pyridin-2-yl;

or a salt of such a compound.

10. A compound according to claim 1 selected from the group consisting of

N-[1-(4-Chloro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(4-Chloro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Chloro-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(4-Isopropyl-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Isopropyl-phenyl)-N-[1-(4-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-ethyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-isopropyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-tert-Butyl-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
N-[1-(4-Difluoromethoxy-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-trifluoromethoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-3-trifluoromethoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-3-trifluoromethyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(3,4,5-trifluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-3,5-dimethyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Chloro-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
N-[1-(4-Chloro-3-trifluoromethyl-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
N-[1-(3,5-Difluoro-4-methoxy-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-methoxy-3-trifluoromethyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(4-fluoro-3-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide;

N-[1-(3-Chloro-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
2-(4-Dimethylamino-phenyl)-N-[1-(3-fluoro-4-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(4-ethyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(4-trifluoromethoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(3-fluoro-4-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(4-fluoro-3-methyl-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3-Chloro-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide;
2-(6-Dimethylamino-pyridin-3-yl)-N-[1-(3,4,5-trifluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Chloro-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide;
N-[1-(4-Methoxy-benzyl)-1H-pyrazol-3-yl]-2-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
2-[4-(3,3-Difluoro-azetidin-1-yl)-phenyl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-azetidin-1-yl)-phenyl]-acetamide;
2-[4-(3,3-Difluoro-azetidin-1-yl)-phenyl]-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-[4-(3,3-Difluoro-azetidin-1-yl)-phenyl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Azetidin-1-yl-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Azetidin-1-yl-phenyl)-N-[1-(4-cyano-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Azetidin-1-yl-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-dimethylamino-pyridin-3-yl)-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
2-(4-Azetidin-1-yl-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((S)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-azetidin-1-yl)-phenyl]-acetamide;
2-(4-Cyclopropoxy-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Cyclopropoxy-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Cyclopropoxy-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((R)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-((R)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((R)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-azetidin-1-yl)-phenyl]-acetamide;
2-[4-(3-Fluoro-azetidin-1-yl)-phenyl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-((S)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((S)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;

N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
2-[4-(3,3-Difluoro-pyrrolidin-1-yl)-phenyl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-pyridin-2-yl-phenyl)-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-pyridin-3-yl-phenyl)-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-pyridin-4-yl-phenyl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-((R)-3-fluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-pyrrolidin-1-yl)-phenyl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(5-methyl-pyrimidin-4-yl)-phenyl]-acetamide;
2-(4-Isopropyl-phenyl)-N-{1-[5-(2,2,2-trifluoro-ethoxy)-pyridin-2-ylmethyl]-1H-pyrazol-3-yl}-acetamide;
N-[1-(5-Bromo-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(5-Cyclopropyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(4-Isopropyl-phenyl)-N-[1-(5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(5-Isobutyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(6-Azetidin-1-yl-pyridin-3-yl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(5-Ethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(5-Isopropoxy-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(5-Fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(4-Isopropyl-phenyl)-N-[1-(5-trifluoromethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(6-Chloro-5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(4-Diethylamino-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Diethylamino-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(4-diethylamino-phenyl)-acetamide;
N-[1-(5-Cyano-6-ethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(6-Diethylamino-pyridin-3-yl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Methoxy-benzyl)-1H-pyrazol-3-yl]-2-{4-[(2-methoxy-ethyl)-methyl-amino]-phenyl}-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-{4-[(2-methoxy-ethyl)-methyl-amino]-phenyl}-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-{4-[(2-methoxy-ethyl)-methyl-amino]-phenyl}-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-{4-[(2-methoxy-ethyl)-methyl-amino]-phenyl}-acetamide;
N-[1-(5-Cyano-6-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-((R)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-((R)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
2-[6-(3,3-Difluoro-azetidin-1-yl)-pyridin-3-yl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-[6-(3,3-Difluoro-azetidin-1-yl)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;

N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isobutyl-phenyl)-acetamide;
N-[1-(5-Cyano-6-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-((S)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-((S)-3-fluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(4-Chloro-5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(4-Cyclopropylmethyl-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3-fluoro-azetidin-1-yl)-pyridin-3-yl]-acetamide;
2-[6-(3-Fluoro-azetidin-1-yl)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-[6-(Cyclopropyl(methyl)amino)-pyridin-3-yl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-[6-(Cyclopropyl(methyl)amino)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(ethyl-methyl-amino)-pyridin-3-yl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-{6-[(2-methoxy-ethyl)-methyl-amino]-pyridin-3-yl}-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-{6-[(2-methoxy-ethyl)-methyl-amino]-pyridin-3-yl}-acetamide;
2-[6-(Cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[6-(cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-acetamide;
2-[6-(Cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-[6-(Cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(6-Diethylamino-pyridin-3-yl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(3-Chloro-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-cyclopropyl-pyridin-3-yl)-acetamide;
N-[1-(4-Cyclopropoxy-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(4-cyclobutoxy-phenyl)-acetamide;
2-(4-Cyclobutoxy-phenyl)-N-[1-(4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Cyclobutoxy-phenyl)-N-[1-(4-methoxy-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-Cyclobutoxy-phenyl)-N-[1-(5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-quinolin-7-yl-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1H-indol-6-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-methyl-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl)-acetamide;
N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(6-Chloro-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-acetamide;

N-[1-(4-Fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(3-methyl-2-oxo-2,3-dihydro-benzooxazol-6-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1H-indol-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-hydroxy-oxetan-3-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((R)-1-methoxy-ethyl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-((S)-1-methoxy-ethyl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(5-methyl-[1,2,4]oxadiazol-3-yl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-[1,2,4]oxadiazol-3-yl-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-yloxy)-phenyl]-acetamide;
N-[1-(4-Bromo-benzyl)-1H-pyrazol-3-yl]-2-(4-dimethylamino-phenyl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide;
N-[1-(3,4-Difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[1-(4-cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;

N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[1-(4-cyano-benzyl)-1H-pyrazol-3-yl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[1-(3-cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide;
N-[1-(4-Cyano-3-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-6-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutyl)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;

N-[1-(4-Cyano-benzyl)-1H-pyrazol-3-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-pyrrolo[2,3-b]pyridin-5-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-cyclobutyl-1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-isopropyl-1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1-methyl-3-trifluoromethyl-1H-indol-5-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(3-cyclobutyl-1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(3-isopropyl-1-methyl-1H-indol-5-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide;
N-(1-(3-cyano-4-fluorobenzyl)-1H-pyrazol-3-yl)-2-(4-(pentafluoro-λ^6-sulfanyl)phenyl)acetamide ;
2-[4-(Cyano-dimethyl-methyl)-phenyl]-N-[1-(3-cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-(1-((5-cyanopyridin-2-yl)methyl)-1H-pyrazol-3-yl)-2-(4-(pentafluoro-λ^6-sulfanyl)phenyl)acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-trifluoromethyl-phenyl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(5-fluoro-6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(5-fluoro-6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-trifluoromethyl-phenyl)-acetamide;
N-[1-(3-Cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[1-(4-cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-[4-(1-Cyano-cyclopropyl)-phenyl]-N-[1-(3-cyano-4-fluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
N-[1-(4-Cyano-3,5-difluoro-benzyl)-1H-pyrazol-3-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[1-(6-cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;

N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-methyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenyl]-acetamide;
N-[1-(6-Cyano-5-methyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-methyl-cyclopropyl)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-methyl-3-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
and
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-((1S*,2S*)-2-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
or a salt of such a compound.

11. A compound according to claim 1 selected from the group consisting of:
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-methoxy-cyclopropyl)-phenyl]-acetamide;
N-[1-(5-Cyano-6-difluoromethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(5-cyano-4-difluoromethyl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3,3-dimethyl-2,3-dihydro-benzofuran-6-yl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-methyl-chroman-7-yl)-acetamide;
N-[1-(5-Cyano-3-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
2-[4-(1-Cyano-3,3-difluoro-cyclobutyl)-phenyl]-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
2-(3-Cyano-4-isobutyl-phenyl)-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
2-(3-Cyano-4-isobutyl-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(5-Azetidin-1-yl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
2-(4-Isopropyl-phenyl)-N-[1-(5-pyrrolidin-1-yl-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-{1-[5-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-2-ylmethyl]-1H-pyrazol-3-yl}-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-cyclopropylmethoxy-3-trifluoromethoxy-phenyl)-acetamide;
2-(4-Cyclopropylmethoxy-3-trifluoromethoxy-phenyl)-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[1-(4-cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
2-[4-(1-Cyano-cyclopropyl)-3-trifluoromethyl-phenyl]-N-[1-(5-cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-acetamide;
2-[4-(1-Cyano-cyclopropyl)-3-trifluoromethyl-phenyl]-N-[1-(3,4-difluoro-benzyl)-1H-pyrazol-3-yl]-acetamide;

N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(3,3,3-trifluoro-propoxy)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-cyclopropyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-methyl-4-trifluoromethoxy-phenyl)-acetamide;
N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-cyclopropyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-cyclopropyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-(3-methyl-4-trifluoromethoxy-phenyl)-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-ethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-ethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-ethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3,5-dimethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3,5-dimethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3,5-dimethyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
N-[1-(5-Cyano-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[5-methyl-6-(2,2,2-trifluoro-ethoxy)-pyridin-3-yl]-acetamide;
N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[5-methyl-6-(2,2,2-trifluoro-ethoxy)-pyridin-3-yl]-acetamide;
N-[1-(6-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(3,3,3-trifluoro-propoxy)-phenyl]-acetamide; and
N-[1-(4-Cyano-5-fluoro-pyridin-2-ylmethyl)-1H-pyrazol-3-yl]-2-[3-methyl-4-(3,3,3-trifluoro-propoxy)-phenyl]-acetamide;
or a salt of such a compound.

12. A pharmaceutical composition containing, as active principle, a compound of formula (I) according to any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, and at least one therapeutically inert excipient.

13. A compound of formula (I) according to any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, for use as a medicament.

14. A compound of formula (I) according to any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, for the treatment or prevention of epilepsy; sleep disorders; sleep disturbances; pain; neurological disorders; cardiovascular disorders; cancer; diabetes; diabetic neuropathy; infertility; and sexual dysfunction.

15. Use of a compound of formula (I) according to any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment or prevention of epilepsy; sleep disorders; sleep disturbances; pain; neurological disorders; cardiovascular disorders; cancer; diabetes; diabetic neuropathy; infertility; and sexual dysfunction.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2015/054164

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D403/12 C07D401/14 C07D405/14 C07D231/40 C07D401/06
C07D401/12 C07D405/12 C07D413/12 C07D471/04 A61K31/415
A61K31/4155 A61K31/4439 A61P3/10 A61P9/00 A61P15/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, CHEM ABS Data, WPI Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2007/120729 A2 (MERCK & CO INC [US]; BARROW JAMES C [US]; BIEBER KELLY-ANN S [US]; CUB) 25 October 2007 (2007-10-25) the whole document -----	1-15

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

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"E" earlier application or patent but published on or after the international filing date

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 July 2015	03/08/2015

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Fink, Dieter

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2015/054164

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