

TRIAZOLE COMPOUNDS AS T-TYPE CALCIUM CHANNEL BLOCKERS

The present invention relates to novel triazole 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 $\alpha 1$ subunits: Cav3.1 ($\alpha 1$ G), Cav3.2 ($\alpha 1$ H) and Cav3.3 ($\alpha 1$ 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., *Pflügers 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 upregulated 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 (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; Bhawe, 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.;

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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).

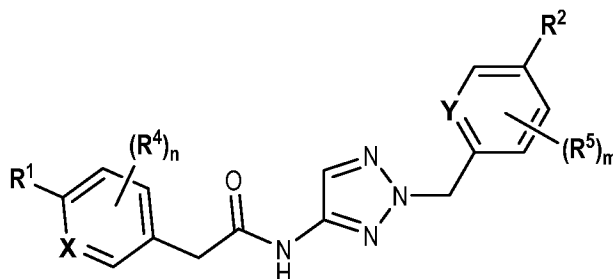
It has been shown that T-type calcium (Ca) channels in the CNS are closely associated with repetitive burst discharges or neuronal oscillations (Llinas, R.; Yarom, Y., *J Physiol* **1986**, 376, 163-82; Gutnick, M. J.; Yarom, Y., *J Neurosci Methods* **1989**, 28 (1-2), 93-9; Iftinca, M. C.; Zamponi, 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-anatomical 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 firing 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).

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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;

• **R¹** represents

- (C₂₋₆)alkyl [in particular isopropyl, *tert*.-butyl, or isobutyl];
- (C₂₋₄)alkyl mono-substituted with cyano, or (C₁₋₃)alkoxy (especially methoxy); [in particular such group is 1-methoxy-ethyl, or 1-cyano-1-methyl-ethyl];
- (C₁₋₄)fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
- (C₁₋₃)fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
- pentafluoro-sulfanyl;
- (C₃₋₆)cycloalkyl-**L¹**- wherein
 - said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)cycloalkyl is unsubstituted; or mono-substituted with fluoro, (C₁₋₃)alkyl (especially methyl), (C₁₋₃)alkoxy (especially methoxy), hydroxy, cyano, or (C₁₋₃)fluoroalkyl (especially trifluoromethyl); or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a (C₁₋₃)alkyl (especially methyl) substituent; and
 - the linker **L¹** represents a direct bond, (C₁₋₂)alkylene, oxygen, or (C₁₋₂)alkylene-oxy (which is attached to the rest of the molecule through the oxygen atom); [in particular such group (C₃₋₆)cycloalkyl-**L¹**- is cyclopropyl, oxetan-3-yl, 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, 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];

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- 5- or 6-membered heteroaryl, independently optionally mono-substituted with (C₁₋₃)alkyl (especially methyl);
 - -NR¹¹R¹², wherein
 - R¹¹ and R¹² independently represent hydrogen, (C₁₋₃)alkyl, (C₂₋₃)fluoroalkyl, (C₃₋₆)cycloalkyl, (C₃₋₆)cycloalkyl mono- or di-substituted with fluoro, (C₃₋₆)cycloalkyl-(C₁₋₃)alkyl, (C₁₋₃)alkoxy-(C₂₋₃)alkyl [in particular such group -NR¹¹R¹² is dimethylamino, ethyl-methyl-amino, diethylamino, cyclopropyl-methyl-amino, (2-methoxyethyl)-methyl-amino, (cyclopropylmethyl)-methyl-amino, or (2,2-difluoro-ethyl)-methyl-amino];
 - or R¹¹ and R¹², together with the nitrogen atom to which they are attached to, form a 4- to 6 membered ring which is optionally mono- or di-substituted with fluoro; a 2-oxo-pyrrolidinyl group; or a morpholinyl group [in particular such group -NR¹¹R¹² is azetidiny, 3-fluoro-azetidiny, 3,3-difluoro-azetidiny, pyrrolidinyl, 3-fluoro-pyrrolidinyl, 3,3-difluoro-pyrrolidinyl, or 2-oxo-pyrrolidinyl];
- and (R⁴)_n represents one or two optional substituents (i.e. n represents the integer 0, 1, or 2) independently selected from (C₁₋₄)alkyl (especially methyl), (C₁₋₄)alkoxy (especially methoxy), (C₁₋₃)fluoroalkyl (especially trifluoromethyl), (C₁₋₃)fluoroalkoxy (especially trifluoromethoxy), halogen (especially fluoro), and cyano [especially (R⁴)_n is absent (i.e. n = 0); or (R⁴)_n represents one halogen or methyl substituent];
- or R¹ together with (R⁴)_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 (C₁₋₃)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 R¹ together with (R⁴)_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 nitrogen atoms, wherein said fused 5- or 6-membered aromatic ring independently is optionally further mono- or di-substituted wherein the substituents are independently selected from (C₁₋₄)alkyl (notably (C₁₋₃)alkyl, especially methyl, propyl, isopropyl, butyl), (C₃₋₆)cycloalkyl (especially cyclopropyl, cyclobutyl), (C₁)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-pyrazolo[3,4-

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b]pyridin-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-propyl-1H-indazol-5-yl, 1-isopropyl-1H-indazol-5-yl, 1-butyl-1H-indazol-5-yl, 3-butyl-1H-indazol-5-yl, 3-trifluoromethyl-1H-indazol-5-yl, 3-cyclopropyl-1H-indazol-5-yl, 3-cyclopropyl-1-methyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 2-methyl-1H-indol-5-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-benzimidazol-6-yl, 1-methyl-1H-benzimidazol-5-yl, 1-methyl-1H-benzimidazol-6-yl, or quinolin-7-yl];

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

R² represents (C₁₋₄)alkyl (especially methyl, ethyl, isopropyl, isobutyl, *tert.*-butyl); (C₃₋₆)cycloalkyl (especially cyclopropyl); (C₁₋₄)alkoxy (especially methoxy, ethoxy, isopropoxy); (C₃₋₆)cycloalkyl-oxy (especially cyclopropyl-oxy); (C₁₋₃)fluoroalkyl (especially trifluoromethyl); (C₁₋₃)fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy, 2,2,2-trifluoroethoxy); (C₁₋₃)alkoxy-(C₂₋₃)alkoxy (especially 2-methoxy-ethoxy); halogen; cyano; or -NR²¹R²², wherein R²¹ and R²² independently represent hydrogen, or (C₁₋₃)alkyl, or R²¹ and R²², 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

(**R⁵**)_m represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from (C₁₋₄)alkyl (especially methyl, ethyl, isobutyl); (C₃₋₆)cycloalkyl (especially cyclopropyl); (C₁₋₄)alkoxy (especially methoxy, isopropoxy); halogen; cyano; (C₁₋₃)fluoroalkyl (especially trifluoromethyl); and (C₁₋₃)fluoroalkoxy (especially trifluoromethoxy, 2,2,2-trifluoroethoxy); [especially (**R⁵**)_m is absent (i.e. m = 0), or (**R⁵**)_m represents one halogen substituent; preferably (**R⁵**)_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-

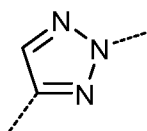
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benzoimidazol-2-yl is understood to signify the same group as 7-methyl-1H-benzoimidazol-2-yl and 4-methyl-3H-benzoimidazol-2-yl and 7-methyl-3H-benzoimidazol-2-yl.

The present invention also includes isotopically labelled, especially ^2H (deuterium) labelled compounds of formula (I) according to embodiments 1) to 18), 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 ^2H (deuterium) labelled compounds of formula (I) and salts thereof are within the scope of the present invention. Substitution of hydrogen with the heavier isotope ^2H (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. $(\text{R}^4)_n$ and $(\text{R}^5)_m$). 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 2H-triazol-2,4-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 19) 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 18), 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
5 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.

10 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
15 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 (C₁₋₆)alkyl group contains from one to six carbon atoms. Examples of (C₁₋₆)alkyl groups are the (C₁₋₄)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 **R**¹ preferred examples
20 of (C₂₋₆)alkyl are isopropyl, *tert*.-butyl, and isobutyl; especially *tert*.-butyl.

Examples of (C₂₋₄)alkyl groups which are mono-substituted with cyano, or (C₁₋₃)alkoxy as used for **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
25 group containing x to y carbon atoms. Examples of alkoxy groups are the (C₁₋₄)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.
30 For example a (C₁₋₃)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 (C₂₋₃)fluoroalkyl groups include 2-fluoroethyl and 2,2,2-trifluoroethyl. In the specific case of (C₁₋₄)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 (C₁₋₄)fluoroalkyl groups as used for **R**¹ include trifluoromethyl,

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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 (C₁₋₃)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 **R**¹ include trifluoromethoxy, difluoromethoxy, 2-fluoroethoxy, 2,2-difluoroethoxy and 2,2,2-trifluoroethoxy; especially 2,2,2-trifluoroethoxy.

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 (C₃₋₆)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 "(C₃₋₆)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 **R**¹, 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 "(C₃₋₆)cycloalkyl-(C₁₋₃)alkyl" refers to a (C₃₋₆)cycloalkyl group as explicitly defined which group is linked to the rest of the molecule through a (C₁₋₃)alkylene group as defined before. For the substituent **R**¹, the (C₁₋₂)alkylene group part of (C₃₋₆)cycloalkyl-(C₁₋₂)alkyl is in particular a methylene group.

The term "(C₃₋₆)cycloalkyl-oxy" refers to a (C₃₋₆)cycloalkyl group as explicitly defined which is linked to the rest of the molecule through an oxygen atom.

The term "(C₃₋₆)cycloalkyl-(C₁₋₂)alkylene-oxy" refers to a (C₃₋₆)cycloalkyl group as explicitly defined which is linked to the rest of the molecule through a -(CH₂)₁₋₂-O- group. For the substituent **R**¹, the -(C₁₋₂)alkylene-oxy group part of (C₃₋₆)cycloalkyl-(C₁₋₂)alkylene-oxy is in particular a -CH₂-O- group.

The term "(C₁₋₃)alkoxy-(C₂₋₃)alkoxy" refers to a (C₁₋₃)alkoxy-group as defined before which is attached to the rest of the molecule through a (C₂₋₃)alkoxy group as defined before. An example is 2-methoxy-ethoxy.

The term "(C₁₋₃)alkoxy-(C₂₋₃)alkyl" means a (C₁₋₃)alkoxy-group as defined before which is attached to the rest of the molecule through a (C₂₋₃)alkylene group as defined before. An example is 2-methoxy-ethyl.

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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. 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, pyrazolo[3,4-b]pyridinyl, indolyl, indazolyl, quinoxalinyl, benzoimidazolyl, and quinolinyl; especially pyrazolo[3,4-b]pyridinyl, indolyl, and indazolyl. 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; especially 2,3-dihydro-1H-indolyl. 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; preferred examples are dimethylamino, diethylamino, cyclopropyl-methyl-amino, and (cyclopropylmethyl)-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 R^1 are especially the four and five-membered rings azetidiny, 3-fluoro-

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azetidiny, 3,3-difluoro-azetidiny, pyrrolidiny (preferred), 3-fluoro-pyrrolidiny, 3,3-difluoro-pyrrolidiny (preferred).

Further embodiments of the invention are presented hereinafter:

2) A second embodiment relates to compounds according to embodiment 1), wherein

5 **X** represents a ring carbon atom.

3) A second embodiment relates to compounds according to embodiment 1), wherein

X represents a ring nitrogen atom.

4) Another embodiment relates to compounds according to any one of embodiments 1) to 3), wherein

• **R¹** represents

- 10 ➤ (C₂₋₆)alkyl [in particular isopropyl, *tert*.-butyl, or isobutyl];
- (C₂₋₄)alkyl mono-substituted with cyano, or (C₁₋₃)alkoxy (especially methoxy); [in particular such group is 1-methoxy-ethyl, or 1-cyano-1-methyl-ethyl];
- (C₁₋₄)fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
- (C₁₋₃)fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
- 15 ➤ pentafluoro-sulfanyl;
- (C₃₋₆)cycloalkyl-**L¹**- wherein
 - said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C₁₋₃)alkyl (especially methyl), (C₁₋₃)alkoxy (especially methoxy), hydroxy, cyano, or (C₁₋₃)fluoroalkyl (especially trifluoromethyl), or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a (C₁₋₃)alkyl (especially methyl) substituent; and
 - 20 ▪ the linker **L¹** represents a direct bond, (C₁₋₂)alkylene, oxygen, or (C₁₋₂)alkylene-oxy (which is attached to the rest of the molecule through the oxygen atom); [in particular such group (C₃₋₆)cycloalkyl-**L¹**- is cyclopropyl, oxetan-3-yl, 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, 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];
 - 25 ➤ -NR¹¹R¹², wherein
 - R¹¹ and R¹² independently represent hydrogen, (C₁₋₃)alkyl, (C₂₋₃)fluoroalkyl, (C₃₋₆)cycloalkyl, (C₃₋₆)cycloalkyl mono- or di-substituted with fluoro, (C₃₋₆)cycloalkyl-(C₁₋₃)alkyl [in particular such group -NR¹¹R¹² is dimethylamino, ethyl-methyl-amino,
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diethylamino, cyclopropyl-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 azetidiny or a pyrrolidiny ring, both independently optionally mono- or di-substituted with fluoro; [in particular such group $-NR^{11}R^{12}$ is azetidiny, 3-fluoro-azetidiny, 3,3-difluoro-azetidiny, pyrrolidiny, 3-fluoro-pyrrolidiny, or 3,3-difluoro-pyrrolidiny];

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 3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl, or 1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-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 to form a bicyclic aromatic ring system selected from pyrazolo[3,4-b]pyridinyl, 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, propyl, isopropyl, butyl), (C_{3-6}) cycloalkyl (especially cyclopropyl, 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-pyrazolo[3,4-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-propyl-1H-indazol-5-yl, 1-isopropyl-1H-indazol-5-yl, 1-butyl-1H-indazol-5-yl, 3-butyl-1H-indazol-5-yl, 3-trifluoromethyl-1H-indazol-5-yl, 3-cyclopropyl-1H-indazol-5-yl, 3-cyclopropyl-1-methyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 2-methyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-5-yl, or 1,3-dimethyl-1H-indol-6-yl].

5) Another embodiment relates to compounds according to any one of embodiments 1) to 3), wherein

- R^1 represents
 - (C_{2-6}) alkyl [in particular isopropyl, or *tert.*-butyl];
 - (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];

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- (C₁₋₄)fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
 - (C₁₋₃)fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
 - pentafluoro-sulfanyl;
 - (C₃₋₆)cycloalkyl-L¹- wherein
 - 5 ▪ said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C₁₋₃)alkyl (especially methyl), (C₁₋₃)alkoxy (especially methoxy), cyano, or (C₁₋₃)fluoroalkyl (especially trifluoromethyl), or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a (C₁₋₃)alkyl (especially methyl) substituent; and
 - 10 ▪ the linker L¹ represents a direct bond, (C₁₋₂)alkylene, oxygen, or (C₁₋₂)alkylene-oxy (which is attached to the rest of the molecule through the oxygen atom);
[in particular such group (C₃₋₆)cycloalkyl-L¹- is cyclopropyl, oxetan-3-yl, 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, or 1-cyano-cyclopropyl; or it is cyclopropyl-oxy, oxetan-3-yl-oxy, cyclobutyl-oxy, or 3,3-difluoro-cyclobutyl-oxy; or it is
 - 15 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];
 - -NR¹¹R¹², wherein
 - 20 ▪ R¹¹ and R¹² independently represent (C₁₋₃)alkyl, (C₂₋₃)fluoroalkyl, (C₃₋₆)cycloalkyl, (C₃₋₆)cycloalkyl mono- or di-substituted with fluoro, or (C₃₋₆)cycloalkyl-(C₁₋₃)alkyl [in particular such group -NR¹¹R¹² is dimethylamino, diethylamino, cyclopropyl-methyl-amino, or (cyclopropylmethyl)-methyl-amino];
 - 25 ▪ or R¹¹ and R¹², together with the nitrogen atom to which they are attached to, form an azetidiny or a pyrrolidiny ring, both independently optionally mono- or di-substituted with fluoro; [in particular such group -NR¹¹R¹² is azetidiny, 3-fluoro-azetidiny, 3,3-difluoro-azetidiny, pyrrolidiny, 3-fluoro-pyrrolidiny, or 3,3-difluoro-pyrrolidiny];
- and (R⁴)_n represents one optional substituent (i.e. n represents the integer 0, or 1) selected from (C₁₋₄)alkyl (especially methyl), (C₁₋₄)alkoxy (especially methoxy), (C₁₋₃)fluoroalkyl (especially trifluoromethyl), (C₁₋₃)fluoroalkoxy (especially trifluoromethoxy), halogen (especially fluoro), and cyano [especially (R⁴)_n is
- 30 absent (i.e. n = 0); or (R⁴)_n represents one halogen or methyl substituent];
- or R¹ together with (R⁴)_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 pyrazolo[3,4-b]pyridiny, indolyl, and indazolyl (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
 - 35 are independently selected from (C₁₋₃)alkyl (especially methyl, propyl, isopropyl, butyl), (C₃₋₆)cycloalkyl (especially cyclopropyl), or (C₁)fluoroalkyl (especially trifluoromethyl), [in particular such aromatic part of

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said aromatic bicyclic ring system is a group selected from 1-methyl-1H-pyrazolo[3,4-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-propyl-1H-indazol-5-yl, 1-isopropyl-1H-indazol-5-yl, 1-butyl-1H-indazol-5-yl, 3-butyl-1H-indazol-5-yl, 3-trifluoromethyl-1H-indazol-5-yl, 3-cyclopropyl-1H-indazol-5-yl, 3-cyclopropyl-1-methyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 2-methyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-5-yl, or 1,3-dimethyl-1H-indol-6-yl].

6) Another embodiment relates to compounds according to any one of embodiments 1) to 3), wherein

R¹ represents

- (C₂₋₆)alkyl [in particular isopropyl, or *tert.*-butyl];
 - (C₁₋₄)fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
 - (C₁₋₃)fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
 - (C₃₋₆)cycloalkyl-**L¹**- wherein
 - said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C₁₋₃)alkyl (especially methyl), (C₁₋₃)alkoxy (especially methoxy), cyano, or (C₁₋₃)fluoroalkyl (especially trifluoromethyl), or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a (C₁₋₃)alkyl (especially methyl) substituent; and
 - the linker **L¹** represents a direct bond, (C₁₋₂)alkylene, oxygen, or (C₁₋₂)alkylene-oxy (which is attached to the rest of the molecule through the oxygen atom);
 - [in particular such group (C₃₋₆)cycloalkyl-**L¹**- is cyclopropyl, oxetan-3-yl, 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, or 1-cyano-cyclopropyl; 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];
 - -NR¹¹R¹², wherein
 - R¹¹ and R¹² independently represent (C₁₋₃)alkyl, (C₃₋₆)cycloalkyl, or (C₃₋₆)cycloalkyl-(C₁₋₃)alkyl [in particular such group -NR¹¹R¹² is dimethylamino, diethylamino, cyclopropyl-methyl-amino, or (cyclopropylmethyl)-methyl-amino];
 - or R¹¹ and R¹², together with the nitrogen atom to which they are attached to, form an azetidiny or a pyrrolidiny ring (especially a pyrrolidiny ring), both independently optionally mono- or di-substituted with fluoro; [in particular such group -NR¹¹R¹² is azetidiny, 3-fluoro-azetidiny, 3,3-difluoro-azetidiny, pyrrolidiny, 3-fluoro-pyrrolidiny, or 3,3-difluoro-pyrrolidiny];
- and (**R⁴**)_n represents one optional substituent (i.e. n represents the integer 0, or 1) selected from (C₁₋₄)alkyl (especially methyl), (C₁₋₄)alkoxy (especially methoxy), (C₁₋₃)fluoroalkyl (especially trifluoromethyl), (C₁₋

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₃fluoroalkoxy (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 3), wherein

- **R**¹ represents

- 5 ➤ (C₂₋₆)alkyl [in particular isopropyl, or *tert*.-butyl];
- (C₁₋₄)fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
- (C₁₋₃)fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
- (C₃₋₆)cycloalkyl wherein
 - 10 ▪ said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C₁₋₃)alkyl (especially methyl), (C₁₋₃)alkoxy (especially methoxy), cyano, or (C₁₋₃)fluoroalkyl (especially trifluoromethyl), or di-substituted with fluoro; [in particular cyclopropyl, oxetan-3-yl, 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, or 1-cyano-cyclopropyl];
- 15 ➤ (C₃₋₆)cycloalkyl-oxy- wherein
 - said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)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];
- (C₃₋₆)cycloalkyl-(C₁₋₂)alkylene-oxy- wherein
 - 20 ▪ said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)cycloalkyl is unsubstituted, or mono-substituted with fluoro, or (C₁₋₃)alkyl (especially methyl), or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a (C₁₋₃)alkyl (especially methyl) substituent; [in particular 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];
 - 25 ▪ -NR¹¹R¹², wherein
 - R¹¹ and R¹², together with the nitrogen atom to which they are attached to, form a pyrrolidinyl ring optionally di-substituted with fluoro [in particular pyrrolidinyl, 3,3-difluoro-pyrrolidinyl];
- 30 and (**R**⁴)_n represents one optional substituent (i.e. n represents the integer 0, or 1) selected from (C₁₋₄)alkyl (especially methyl), (C₁₋₄)alkoxy (especially methoxy), (C₁₋₃)fluoroalkyl (especially trifluoromethyl), (C₁₋₃)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
 - 35 ring to form a bicyclic aromatic ring system selected from pyrazolo[3,4-b]pyridinyl, indolyl, and indazolyl

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(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 (C₁₋₃)alkyl (especially methyl, propyl, isopropyl, butyl), (C₃₋₆)cycloalkyl (especially cyclopropyl), or (C₁)fluoroalkyl (especially trifluoromethyl), [in particular such aromatic part of

5 said aromatic bicyclic ring system is a group selected from 1-methyl-1H-pyrazolo[3,4-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-propyl-1H-indazol-5-yl, 1-isopropyl-1H-indazol-5-yl, 1-butyl-1H-indazol-5-yl, 3-butyl-1H-indazol-5-yl, 3-trifluoromethyl-1H-indazol-5-yl, 3-cyclopropyl-1H-indazol-5-yl, 3-cyclopropyl-1-methyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 2-

10 methyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-5-yl, or 1,3-dimethyl-1H-indol-6-yl].

8) Another embodiment relates to compounds according to any one of embodiments 1) to 3), wherein **R¹** represents

- (C₂₋₆)alkyl [in particular isopropyl, or *tert.*-butyl];
- (C₁₋₄)fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
- 15 ➤ (C₁₋₃)fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
- (C₃₋₆)cycloalkyl wherein
 - said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)cycloalkyl is unsubstituted, or mono-substituted with fluoro, (C₁₋₃)alkyl (especially methyl), (C₁₋₃)alkoxy (especially methoxy), cyano, or (C₁₋₃)fluoroalkyl (especially
 - 20 trifluoromethyl), or di-substituted with fluoro; [in particular cyclopropyl, oxetan-3-yl, 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, or 1-cyano-cyclopropyl];
- (C₃₋₆)cycloalkyl-oxy- wherein
 - said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said
 - 25 (C₃₋₆)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];
- (C₃₋₆)cycloalkyl-(C₁₋₂)alkylene-oxy- wherein
 - said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said
 - 30 (C₃₋₆)cycloalkyl is unsubstituted, or mono-substituted with fluoro, or (C₁₋₃)alkyl (especially methyl), or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a (C₁₋₃)alkyl (especially methyl) substituent; [in particular 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];
- -NR¹¹R¹², wherein

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- R¹¹ and R¹², together with the nitrogen atom to which they are attached to, form a pyrrolidinyl ring optionally di-substituted with fluoro [in particular pyrrolidinyl, 3,3-difluoro-pyrrolidinyl];

and (R⁴)_n represents one optional substituent (i.e. n represents the integer 0, or 1) selected from (C₁₋₄)alkyl (especially methyl), (C₁₋₄)alkoxy (especially methoxy), (C₁₋₃)fluoroalkyl (especially trifluoromethyl),
 5 (C₁₋₃)fluoroalkoxy (especially trifluoromethoxy), halogen (especially fluoro), and cyano [especially (R⁴)_n is absent (i.e. n = 0); or (R⁴)_n represents one halogen or methyl substituent].

9) Another embodiment relates to compounds according to any one of embodiments 1) to 3), wherein R¹ represents

- 10
- (C₂₋₆)alkyl [in particular isopropyl, or *tert*.-butyl, preferably *tert*.-butyl];
 - (C₁₋₄)fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl; preferably 2,2,2-trifluoro-1,1-dimethyl-ethyl];
 - (C₁₋₃)fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
 - (C₃₋₆)cycloalkyl wherein
- 15
- said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)cycloalkyl is mono-substituted with fluoro or (C₁₋₃)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
- 20
- (C₃₋₆)cycloalkyl-oxy- wherein
 - said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)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];
- 25

and (R⁴)_n represents one optional substituent (i.e. n represents the integer 0, or 1) selected from (C₁₋₄)alkyl (especially methyl), or halogen (especially fluoro) [especially (R⁴)_n is absent (i.e. n = 0); or (R⁴)_n represents one halogen or methyl substituent].

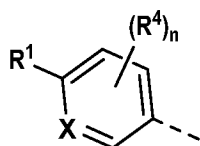
10) Another embodiment relates to compounds according to any one of embodiments 1) to 3), wherein

- 30
- R¹ together with (R⁴)_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
- 35
- and the remaining are (C₁₋₃)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];

- 5 • 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 pyrazolo[3,4-b]pyridinyl, 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, propyl, isopropyl, butyl), (C_{3-6}) cycloalkyl (especially cyclopropyl, 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-pyrazolo[3,4-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-propyl-1H-indazol-5-yl, 1-isopropyl-1H-indazol-5-yl, 1-butyl-1H-indazol-5-yl, 3-butyl-1H-indazol-5-yl, 3-trifluoromethyl-1H-indazol-5-yl, 3-cyclopropyl-1H-indazol-5-yl, 3-cyclopropyl-1-methyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 1-methyl-1H-indol-6-yl, 2-methyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-5-yl, or 1,3-dimethyl-1H-indol-6-yl].

- 11) Another embodiment relates to compounds according to any one of embodiments 1) to 3), wherein the fragment



- represents 4-isopropyl-phenyl, 4-dimethylamino-phenyl, 4-trifluoromethyl-phenyl, 4-*tert*-butyl-phenyl, 4-(1-methoxy-ethyl)-phenyl, 4-(cyclopropyl-oxy)-phenyl, 4-(oxetan-3-yl)-phenyl, 4-(3-fluoro-oxetan-3-yl)-phenyl, 4-(cyclobutyl-oxy)-phenyl, 4-(3-methyl-oxetan-3-yl)-phenyl, 4-(1-cyano-cyclopropyl)-phenyl, 4-(1-cyano-1-methyl-ethyl)-phenyl, 4-(pentafluoro-sulfanyl)-phenyl, 3-methyl-4-(2,2,2-trifluoroethoxy)-phenyl, 4-(3-methoxy-oxetan-3-yl)-phenyl, 4-(oxetan-3-yl-methoxy)-phenyl, 4-(2-trifluoromethyl-cyclopropyl)-phenyl, 4-(1-trifluoromethyl-cyclopropyl)-phenyl, 4-((3-fluoro-oxetan-3-yl)-methoxy)-phenyl, 4-((3-methyl-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-(pyrrolidin-1-yl)-pyridin-5-yl, 2-(cyclopropyl(methyl)amino)-pyridin-5-yl, 2-(diethylamino)-pyridin-5-yl, 3-fluoro-2-(pyrrolidin-1-yl)-pyridin-5-yl, 2-((cyclopropylmethyl)-methyl-amino)-pyridin-5-yl, 2-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-5-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, 1-methyl-1H-pyrazolo[3,4-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-

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ethyl-1H-indazol-5-yl, 1,3-dimethyl-1H-indazol-5-yl, 1-propyl-1H-indazol-5-yl, 1-isopropyl-1H-indazol-5-yl, 1-butyl-1H-indazol-5-yl, 3-butyl-1H-indazol-5-yl, 3-trifluoromethyl-1H-indazol-5-yl, 3-cyclopropyl-1H-indazol-5-yl, 3-cyclopropyl-1-methyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 2-methyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-5-yl, or 1,3-dimethyl-1H-indol-6-yl.

5 12) Another embodiment relates to compounds according to any one of embodiments 1) to 11), wherein

- Y represents a ring carbon or a ring nitrogen atom;
- R² represents (C₁₋₄)alkyl (especially methyl, ethyl, isopropyl, isobutyl, *tert.*-butyl); (C₁₋₄)alkoxy (especially methoxy, ethoxy); (C₁₋₃)fluoroalkyl (especially trifluoromethyl); (C₁₋₃)fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy); (C₁₋₃)alkoxy-(C₂₋₃)alkoxy (especially 2-methoxy-ethoxy); halogen (especially fluoro); or cyano; and
- 10 • (R⁵)_m represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from (C₁₋₄)alkyl (especially methyl); (C₁₋₄)alkoxy (especially methoxy); halogen (especially fluoro); cyano; (C₁₋₃)fluoroalkyl (especially trifluoromethyl); and (C₁₋₃)fluoroalkoxy (especially trifluoromethoxy); [especially (R⁵)_m is absent (i.e. m = 0), or (R⁵)_m represents one halogen
- 15 (especially fluoro) substituent; preferably (R⁵)_m is absent].

13) Another embodiment relates to compounds according to any one of embodiments 1) to 11), wherein

- Y represents a ring nitrogen atom; and
 - R² represents (C₁₋₄)alkyl (especially methyl); (C₁₋₄)alkoxy (especially methoxy); (C₁₋₃)fluoroalkyl (especially trifluoromethyl); (C₁₋₃)fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy);
 - 20 halogen (especially fluoro); or cyano; and
 - (R⁵)_m represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from (C₁₋₄)alkyl (especially methyl); (C₁₋₄)alkoxy (especially methoxy); halogen (especially fluoro); cyano; (C₁₋₃)fluoroalkyl (especially trifluoromethyl); and (C₁₋₃)fluoroalkoxy (especially trifluoromethoxy); [especially (R⁵)_m is absent (i.e. m = 0), or (R⁵)_m
 - 25 represents one halogen (especially fluoro) substituent; preferably (R⁵)_m is absent]; or
- Y represents a ring carbon atom; and
 - R² represents (C₁₋₄)alkyl (especially methyl); (C₁₋₄)alkoxy (especially methoxy, ethoxy); (C₁₋₃)fluoroalkyl (especially trifluoromethyl); (C₁₋₃)fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy); (C₁₋₃)alkoxy-(C₂₋₃)alkoxy (especially 2-methoxy-ethoxy); halogen (especially
 - 30 fluoro); or cyano; and
 - (R⁵)_m represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from (C₁₋₄)alkyl (especially methyl); (C₁₋₄)alkoxy (especially methoxy); halogen (especially fluoro); cyano; (C₁₋₃)fluoroalkyl (especially trifluoromethyl); and (C₁₋₃)fluoroalkoxy (especially trifluoromethoxy); [especially (R⁵)_m is absent (i.e. m = 0), or (R⁵)_m
 - 35 represents one halogen (especially fluoro) substituent; preferably (R⁵)_m is absent].

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14) Another embodiment relates to compounds according to any one of embodiments 1) to 11), wherein

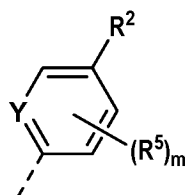
- Y represents a ring nitrogen atom; and
 - R² represents cyano; and
 - (R⁵)_m is absent (i.e. n = 0); or

5 • Y represents a ring carbon atom; and

- R² represents (C₁₋₄)alkyl (especially methyl); (C₁₋₄)alkoxy (especially methoxy, ethoxy); (C₁₋₃)fluoroalkoxy (especially difluoromethoxy, trifluoromethoxy); (C₁₋₃)alkoxy-(C₂₋₃)alkoxy (especially 2-methoxy-ethoxy); halogen (especially fluoro); or cyano; and
- (R⁵)_m represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from (C₁₋₄)alkyl (especially methyl); (C₁₋₄)alkoxy (especially methoxy); halogen; and cyano; [especially (R⁵)_m is absent (i.e. m = 0), or (R⁵)_m represents one halogen substituent; preferably (R⁵)_m is absent].

10

15) Another embodiment relates to compounds according to any one of embodiments 1) to 11), wherein the fragment



15

represents 4-fluorophenyl, 4-methylphenyl, 4-fluoro-3-cyano-phenyl, 3,4-difluorophenyl, 3,5-difluoro-4-methoxy-phenyl, 3-fluoro-4-methoxy-phenyl, 4-cyano-3-fluoro-phenyl, 4-cyano-3-methyl-phenyl, 3-cyano-4-methyl-phenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 3,4-dimethoxyphenyl, 4-fluoro-3-methoxy-phenyl; 3,4-difluoro-5-methoxy-phenyl, 3-cyano-4-methoxy-phenyl, 4-cyano-3-methoxy-phenyl, 4-cyano-3-fluoro-5-methoxy-phenyl, 4-cyanophenyl, 4-(2-methoxy-ethoxy)-phenyl, 4-difluoromethoxy-phenyl, 4-trifluoromethoxy-phenyl, 3-fluoro-4-difluoromethoxy-phenyl; 3-fluoro-4-trifluoromethoxy-phenyl; or 5-cyano-pyridin-2-yl,.

20

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

- X represents a ring carbon or a ring nitrogen atom; and R¹ represents
 - (C₂₋₆)alkyl [in particular isopropyl, or *tert.*-butyl];
 - (C₂₋₄)alkyl mono-substituted with cyano, or (C₁₋₃)alkoxy (especially methoxy); [in particular such group is 1-methoxy-ethyl, or 1-cyano-1-methyl-ethyl];
 - (C₁₋₄)fluoroalkyl [in particular trifluoromethyl, 2,2,2-trifluoro-1,1-dimethyl-ethyl];
 - (C₁₋₃)fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
 - pentafluoro-sulfanyl;
 - (C₃₋₆)cycloalkyl-L¹- wherein

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- 5 ▪ said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)cycloalkyl is unsubstituted; or mono-substituted with fluoro, (C₁₋₃)alkyl (especially methyl), (C₁₋₃)alkoxy (especially methoxy), cyano, or (C₁₋₃)fluoroalkyl (especially trifluoromethyl); or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a (C₁₋₃)alkyl (especially methyl) substituent; and

10 ▪ the linker L¹ represents a direct bond, oxygen, or (C₁₋₂)alkylene-oxy (which is attached to the rest of the molecule through the oxygen atom);

 [in particular such group (C₃₋₆)cycloalkyl-L¹- is oxetan-3-yl, 3-fluoro-oxetan-3-yl, 3-methoxy-oxetan-3-yl, 3-methyl-oxetan-3-yl, 1-trifluoromethyl-cyclopropyl, 2-trifluoromethyl-cyclopropyl, or 1-cyano-cyclopropyl; or it is cyclopropyl-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];

 ➤ -NR¹¹R¹², wherein

15 ▪ R¹¹ and R¹² independently represent (C₁₋₃)alkyl, (C₃₋₆)cycloalkyl, or (C₃₋₆)cycloalkyl-(C₁₋₃)alkyl [in particular such group -NR¹¹R¹² is dimethylamino, diethylamino, cyclopropyl-methyl-amino, or (cyclopropylmethyl)-methyl-amino];

 ▪ or R¹¹ and R¹², together with the nitrogen atom to which they are attached to, form a 4-to-6 membered ring which is optionally mono- or di-substituted with fluoro [in particular

20 such group -NR¹¹R¹² is pyrrolidinyl, or 3,3-difluoro-pyrrolidinyl];

and (R⁴)_n represents one optional substituent (i.e. n represents the integer 0, or 1) selected from (C₁₋₄)alkyl (especially methyl), and halogen (especially fluoro) [especially (R⁴)_n is absent (i.e. n = 0); or (R⁴)_n represents one halogen or methyl substituent];

 - 25 • or X represents a ring carbon atom; and R¹ together with (R⁴)_n forms a non-aromatic 5-membered ring which is fused to the phenyl ring; wherein said 5-membered ring contains one nitrogen atom; wherein said fused 5-membered non-aromatic ring independently is di-, tri-, or tetra-substituted wherein one substituent is oxo and the remaining are (C₁₋₃)alkyl (especially methyl); [in particular such non-aromatic 5-membered ring fused to the phenyl ring forms, together with the phenyl ring, a group selected from 3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl, or 1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl];

30 • or X represents a ring carbon or a ring nitrogen atom; and R¹ together with (R⁴)_n forms an aromatic 5-membered ring which is fused to the phenyl / pyridine ring; wherein said 5-membered ring contains one or two nitrogen atoms, wherein said fused 5-membered aromatic ring independently is optionally further mono- or di-substituted wherein the substituents are independently selected from (C₁₋₄)alkyl (especially methyl, ethyl, propyl, isopropyl, butyl), (C₃₋₆)cycloalkyl (especially cyclopropyl), or (C₁)fluoroalkyl (especially trifluoromethyl) [in particular such aromatic 5-membered ring fused to the phenyl / pyridine

35 ring forms, together with the phenyl / pyridine ring, a group selected from 1-methyl-1H-pyrazolo[3,4-

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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-propyl-1H-indazol-5-yl, 1-isopropyl-1H-indazol-5-yl, 1-butyl-1H-indazol-5-yl, 3-butyl-1H-indazol-5-yl, 3-trifluoromethyl-1H-indazol-5-yl, 3-cyclopropyl-1H-indazol-5-yl, 3-cyclopropyl-1-methyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 2-methyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-5-yl, or 1,3-dimethyl-1H-indol-6-yl];

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

R² represents (C₁₋₄)alkyl (especially methyl); (C₁₋₄)alkoxy (especially methoxy, or ethoxy); (C₁₋₃)fluoroalkoxy (especially difluoromethoxy, or trifluoromethoxy); (C₁₋₃)alkoxy-(C₂₋₃)alkoxy (especially 2-methoxy-ethoxy); halogen (especially fluoro); or cyano; and

10 (R⁵)_m represents one or two optional substituents (i.e. m represents the integer 0, 1, or 2) independently selected from (C₁₋₄)alkyl (especially methyl); (C₁₋₄)alkoxy (especially methoxy); halogen (especially fluoro); or cyano; [especially (R⁵)_m is absent (i.e. m = 0), or (R⁵)_m represents one halogen substituent; preferably (R⁵)_m is absent].

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

- 15 • X represents a ring carbon or a ring nitrogen atom; and R¹ represents
- (C₂₋₆)alkyl [in particular isopropyl, or *tert*-butyl];
 - (C₂₋₄)alkyl mono-substituted with cyano, or (C₁₋₃)alkoxy (especially methoxy); [in particular such group is 1-methoxy-ethyl, or 1-cyano-1-methyl-ethyl];
 - (C₁₋₃)fluoroalkoxy [in particular 2,2,2-trifluoroethoxy];
 - 20 ➤ (C₃₋₆)cycloalkyl-L¹- wherein
 - said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)cycloalkyl is unsubstituted; or mono-substituted with fluoro, (C₁₋₃)alkyl (especially methyl), (C₁₋₃)alkoxy (especially methoxy), cyano, or (C₁₋₃)fluoroalkyl (especially trifluoromethyl); or di-substituted with fluoro; and
 - 25 ▪ the linker L¹ represents a direct bond, oxygen, or methylenoxy (which is attached to the rest of the molecule through the oxygen atom);
- [in particular such group (C₃₋₆)cycloalkyl-L¹- is oxetan-3-yl, 3-fluoro-oxetan-3-yl, 3-methoxy-oxetan-3-yl, 3-methyl-oxetan-3-yl, 1-trifluoromethyl-cyclopropyl, 2-trifluoromethyl-cyclopropyl, or 1-cyano-cyclopropyl; or it is cyclopropyl-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, or (3-methyl-oxetan-3-yl)-methoxy];
- 30 ➤ -NR¹¹R¹², wherein
- R¹¹ and R¹² independently represent (C₁₋₃)alkyl, (C₃₋₆)cycloalkyl, or (C₃₋₆)cycloalkyl-(C₁₋₃)alkyl [in particular such group -NR¹¹R¹² is dimethylamino, diethylamino, cyclopropyl-methyl-amino, or (cyclopropylmethyl)-methyl-amino];
- 35

- 24 -

- or R^{11} and R^{12} , together with the nitrogen atom to which they are attached to, form a 4-to-6 membered ring which is optionally mono- or di-substituted with fluoro [in particular such group $-NR^{11}R^{12}$ is 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), and halogen (especially fluoro) [especially $(R^4)_n$ is absent (i.e. n = 0); or $(R^4)_n$ represents one halogen or methyl substituent];

- or **X** represents a ring carbon atom; and R^1 together with $(R^4)_n$ forms an aromatic 5-membered ring which is fused to the phenyl ring; wherein said 5-membered ring contains one or two nitrogen atoms, wherein said fused 5-membered aromatic ring independently is optionally further mono- or di-substituted wherein the substituents are independently selected from (C_{1-4}) alkyl (especially methyl, ethyl, propyl, isopropyl, butyl), (C_{3-6}) cycloalkyl (especially cyclopropyl), or (C_1) fluoroalkyl (especially trifluoromethyl) [in particular such aromatic 5-membered ring fused to the phenyl ring forms, together with the phenyl 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-propyl-1H-indazol-5-yl, 1-isopropyl-1H-indazol-5-yl, 1-butyl-1H-indazol-5-yl, 3-butyl-1H-indazol-5-yl, 3-trifluoromethyl-1H-indazol-5-yl, 3-cyclopropyl-1H-indazol-5-yl, 3-cyclopropyl-1-methyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 2-methyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-5-yl, or 1,3-dimethyl-1H-indol-6-yl];

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

R^2 represents (C_{1-4}) alkyl (especially methyl); (C_{1-4}) alkoxy (especially methoxy, or ethoxy); (C_{1-3}) fluoroalkoxy (especially difluoromethoxy, or 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 (C_{1-4}) alkyl (especially methyl); (C_{1-4}) alkoxy (especially methoxy); halogen (especially fluoro); or cyano; [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) 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 15), 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, 4+1, 4+2+1, 4+3+1, 5+1, 5+2+1, 5+3+1, 6+1, 6+2+1, 6+3+1, 7+1, 7+2+1, 7+3+1, 8+1, 8+2+1, 8+3+1, 9+1, 9+2+1, 9+3+1, 10+1, 10+2+1, 10+3+1, 11+1, 11+2+1, 11+3+1, 12+1, 12+2+1, 12+3+1, 12+4+1, 12+4+2+1, 12+4+3+1, 12+5+1, 12+5+2+1, 12+5+3+1, 12+6+1, 12+6+2+1, 12+6+3+1, 12+7+1, 12+7+2+1, 12+7+3+1, 12+8+1, 12+8+2+1, 12+8+3+1, 12+9+1, 12+9+2+1, 12+9+3+1, 12+10+1, 12+10+2+1,

- 12+10+3+1, 12+11+1, 12+11+2+1, 12+11+3+1, 13+1, 13+2+1, 13+3+1, 13+4+1, 13+4+2+1, 13+4+3+1, 13+5+1, 13+5+2+1, 13+5+3+1, 13+6+1, 13+6+2+1, 13+6+3+1, 13+7+1, 13+7+2+1, 13+7+3+1, 13+8+1, 13+8+2+1, 13+8+3+1, 13+9+1, 13+9+2+1, 13+9+3+1, 13+10+1, 13+10+2+1, 13+10+3+1, 13+11+1, 13+11+2+1, 13+11+3+1, 14+1, 14+2+1, 14+3+1, 14+4+1, 14+4+2+1, 14+4+3+1, 14+5+1, 14+5+2+1, 14+5+3+1, 14+6+1, 14+6+2+1, 14+6+3+1, 14+7+1, 14+7+2+1, 14+7+3+1, 14+8+1, 14+8+2+1, 14+8+3+1, 14+9+1, 14+9+2+1, 14+9+3+1, 14+10+1, 14+10+2+1, 14+10+3+1, 14+11+1, 14+11+2+1, 14+11+3+1, 15+1, 15+2+1, 15+3+1, 15+4+1, 15+4+2+1, 15+4+3+1, 15+5+1, 15+5+2+1, 15+5+3+1, 15+6+1, 15+6+2+1, 15+6+3+1, 15+7+1, 15+7+2+1, 15+7+3+1, 15+8+1, 15+8+2+1, 15+8+3+1, 15+9+1, 15+9+2+1, 15+9+3+1, 15+10+1, 15+10+2+1, 15+10+3+1, 15+11+1, 15+11+2+1, 15+11+3+1, 16+1, 17+1;
- 10 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).
- 15 19) A further embodiment relates to compounds of formula (I) which are selected from:
 N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
 2-(4-Dimethylamino-phenyl)-N-[2-(4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
- 20 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1H-indol-6-yl)-acetamide;
 2-(4-Cyclobutoxy-phenyl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
 2-(4-Cyclopropoxy-phenyl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- 25 2-[6-(Cyclopropyl(methyl)amino)-pyridin-3-yl]-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
 2-[6-(Cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide;
 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
- 30 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1H-indol-5-yl)-acetamide;
 2-(6-Diethylamino-pyridin-3-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide;
- 35 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;

- N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-oxetan-3-yl-phenyl)-acetamide;
2-(4-Isopropyl-phenyl)-N-[2-(4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
5 2-(4-Isopropyl-phenyl)-N-[2-(4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide;
2-(3-Cyclopropyl-1H-indazol-5-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
10 2-(1-Butyl-1H-indazol-5-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(2-methyl-1H-indol-5-yl)-acetamide;
2-(3-Butyl-1H-indazol-5-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-isopropyl-1H-indazol-5-yl)-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-propyl-1H-indazol-5-yl)-acetamide;
15 2-(3-Cyclopropyl-1-methyl-1H-indazol-5-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(3-trifluoromethyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
20 N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
25 2-(6-Diethylamino-pyridin-3-yl)-N-[2-(3,4-dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(3,4-dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(3,4-dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3,4-Dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(3,4-Dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
30 N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
35 N-[2-(4-Methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
2-(6-Diethylamino-pyridin-3-yl)-N-[2-(4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;

- 2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
5 N-[2-(4-Methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
10 N-[2-(4-Methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
15 2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
20 N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(3,5-difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
25 2-(4-tert-Butyl-phenyl)-N-[2-(4-(2-methoxy-ethoxy)-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-(2-Methoxy-ethoxy)-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-difluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Difluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
30 2-(1-Methyl-1H-indol-5-yl)-N-[2-(4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(1-Methyl-1H-indazol-5-yl)-N-[2-(4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-[4-(3-Methyl-oxetan-3-yl)-phenyl]-N-[2-(4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(6-Diethylamino-pyridin-3-yl)-N-[2-(4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
35 2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;

- N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
5 N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-propyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide;
10 N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
2-[4-(3,3-Difluoro-cyclobutylmethoxy)-phenyl]-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-
acetamide;
15 N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-
acetamide;
N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-
acetamide;
2-[4-(3,3-Difluoro-cyclobutoxy)-phenyl]-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
20 2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-
acetamide;
N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
2-(1-Ethyl-1H-indazol-5-yl)-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(1,3-Dimethyl-1H-indol-5-yl)-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
25 2-(4-tert-Butyl-phenyl)-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-
30 acetamide;
N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-
acetamide;
2-[4-(3,3-Difluoro-cyclobutoxy)-phenyl]-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-
35 acetamide;
N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;

- 2-(1-Ethyl-1H-indazol-5-yl)-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(1,3-Dimethyl-1H-indol-5-yl)-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide;
5 N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
10 N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide;
15 N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-
acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-
20 acetamide;
2-[4-(3,3-Difluoro-cyclobutoxy)-phenyl]-N-[2-(3,5-difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-
acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
25 N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
30 N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
2-[4-(Cyano-dimethyl-methyl)-phenyl]-N-[2-(4-cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-3-fluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
35 N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-trifluoromethyl-phenyl)-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(5-fluoro-6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;

- 2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
5 N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-
acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide;
10 N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(3-cyano-4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3-Cyano-4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(3-Cyano-4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
15 N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-
acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
20 N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-
acetamide;
N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-
25 acetamide;
N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(3-fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
30 N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-
acetamide;
2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(3-fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-
acetamide;
35 2-(1-Ethyl-1H-indazol-5-yl)-N-[2-(3-fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(1,3-Dimethyl-1H-indazol-5-yl)-N-[2-(3-fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;

- N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
5 N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
10 N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(3-cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
15 N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
20 N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide;
N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
25 N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
30 2-(4-tert-Butyl-phenyl)-N-[2-(3-cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(3,4-difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;
35 N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;

- N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
5 N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-
acetamide;
N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-
acetamide;
10 2-[4-(3,3-Difluoro-cyclobutoxy)-phenyl]-N-[2-(3,4-difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-[4-(1-Cyano-cyclopropyl)-phenyl]-N-[2-(4-cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-cyano-3-fluorobenzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-(pentafluorosulfanyl)phenyl)acetamide;
N-[2-(4-Cyano-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-
acetamide;
15 N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
20 2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-
acetamide;
25 N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(5-cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-
acetamide;
N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
30 N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-(5-fluoro-6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenyl]-
acetamide; and
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-((1S*,2S*)-2-trifluoromethyl-cyclopropyl)-phenyl]-
acetamide.

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The compounds of formula (I) according to embodiments 1) to 19) 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).

5 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
10 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 19).

15 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.

20 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.

25 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.

30 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 19) 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:

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- 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.

- 15 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.

- 20 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.

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

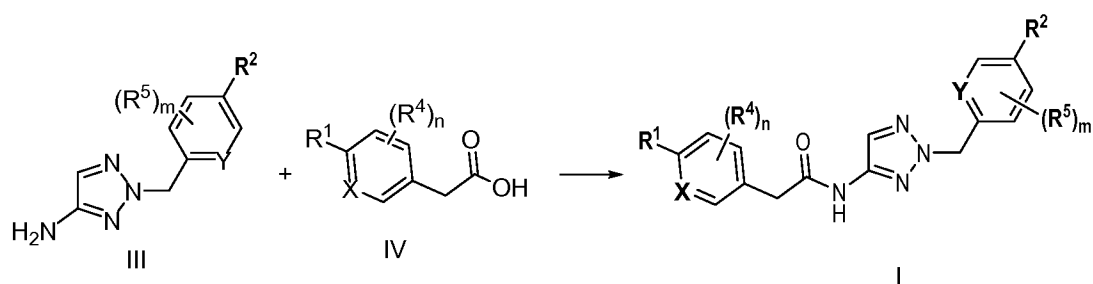
The compounds of formula (I) as defined in embodiments 1) to 19) are also useful in a method of reducing the concentration of calcium in a neuronal cell, and wherein said reduction in calcium is achieved by blocking the calcium T-channel present in such neuronal cell; said method comprising the administration of a compound of formula (I) as defined in embodiments 1) to 19).

- 30 The compounds of formula (I) as defined in embodiments 1) to 19) 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 19).

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, R¹, R², (R⁴)_n, and (R⁵)_m are as defined for the compounds of formula (I). In some instances the generic groups R¹, R², (R⁴)_n, and (R⁵)_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 formula (I) 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.

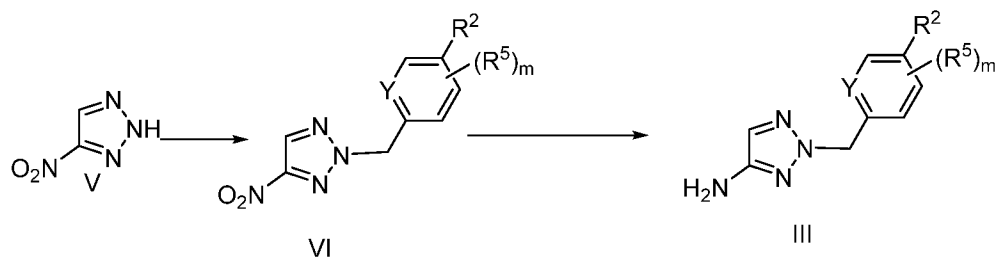
Scheme 1



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

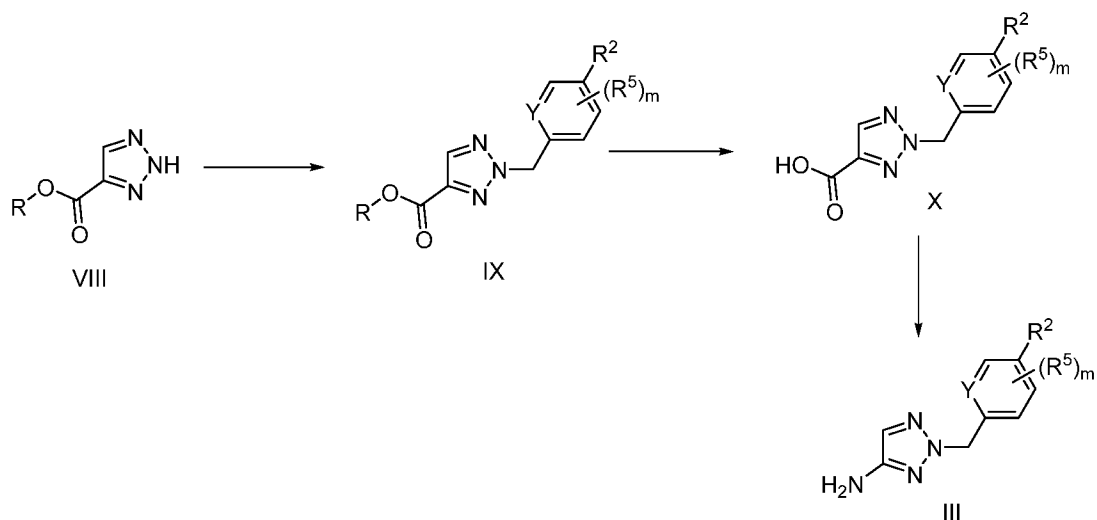
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Scheme 2



Aminotriazoles of type (III) can be prepared via a Curtius rearrangement as well (Scheme 3). A suitable ester from the triazole-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

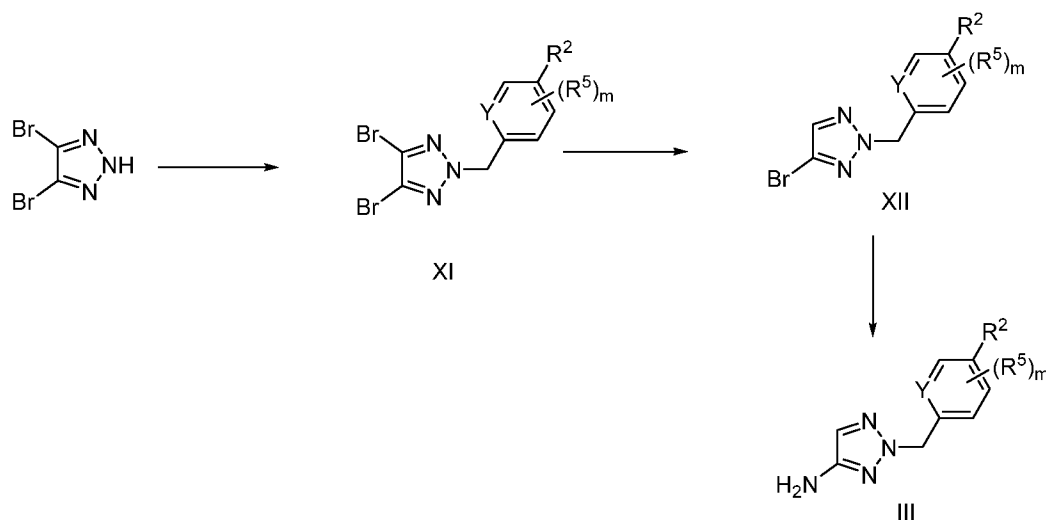


The corresponding benzyl chlorides, benzyl bromides, or benzyl mesylates necessary for the alkylation steps described in Schemes 2 (V $\rightarrow$ VI) and 3 (VIII $\rightarrow$ IX) can be prepared according to standard literature procedures or as described in the examples here below.

A third possibility to prepare a compound of type III starts from 4,5-dibromo-2H-1,2,3-triazole (Scheme 4). An N-alkylation leads to a compound of type (XI). The selective reduction of a bromide with, for instance, $^i\text{PrMgCl}$ (P. Wipf et al., Org. Lett. 2010, 12(20), 4632-4635) leads to a compound of type (XII), and an Ullman amination leads to a compound of type (III).

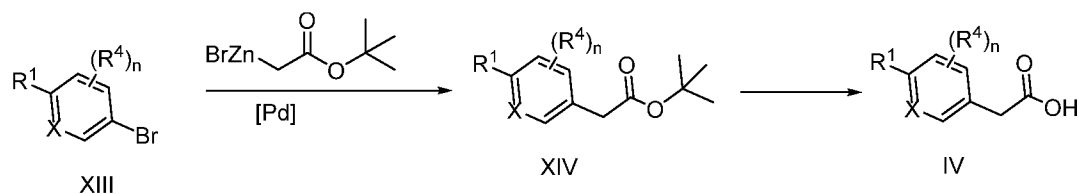
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Scheme 4



The carboxylic acids of type (IV) can be prepared according to known procedures. In particular, a Negishi coupling (Scheme 5), or a similar carbon-carbon coupling between an (hetero)aryl bromide of type (XIII) and (2-(tert-butoxy)-2-oxoethyl)zinc(II) bromide leads to the ester of type (XIV): Hydrolysis, generally under acidic conditions, leads to the acid of type (IV). Bromide of type (XIII) is either commercially available, or can be prepared according to known procedures (see experimental part).

Scheme 5

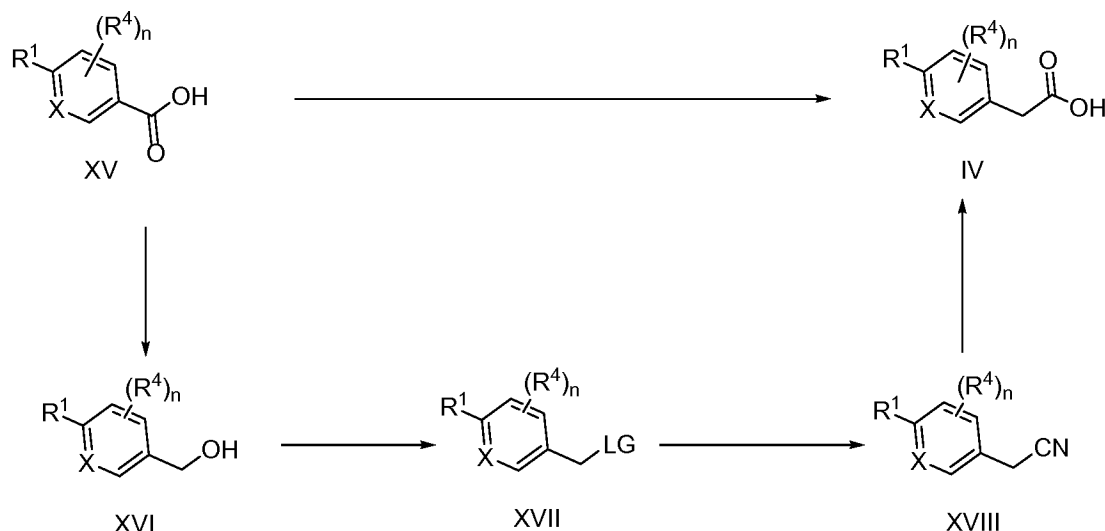


Alternatively, a benzoic acid of type (XV) can be transformed into an acid of type (IV) via a Wolff rearrangement (Scheme 6). The acid of type (XV) can be reduced to an alcohol of type (XVI). This alcohol can then be activated to a compound of type (XVII), wherein LG represents a leaving group such as chloride, bromide, mesylate or tosylate, and homologated to nitrile of type (XVIII): Hydrolysis would then lead to the acid of type (IV).

15

20

Scheme 6



- 5 Whenever required, the substituents R^1 , R^2 , R^4 and / or R^5 can be present as precursors in the starting material, and can be transformed by additional routine transformations during the synthetic pathways presented herein.

- 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 μ m) column, a Daicel ChiralCel OD-H (5-10 μ m) column, or a Daicel ChiralPak IA (10 μ m), IC (5 μ m) or AD-H (5 μ m) 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.

15 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 |
| 20 Bn | Benzyl |
| Bu | Butyl |
| CAS | Chemical abstract system |
| comb. | Combined |

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	conc.	Concentrated
	dba	Dibenzylideneacetone
	DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
	DIBAL	Diisobutylaluminium hydride
5	DIPEA	Diisopropylethylamine
	DMA	Dimethylacetamide
	DMEM	Dulbecco's modified eagle's medium
	DMF	N,N-Dimethylformamide
	DMSO	Dimethylsulfoxide
10	DPPF	1,1'-Bis(diphenylphosphino)ferrocene
	EDTA	Ethylenediaminetetraacetic acid
	eq.	Equivalent
	Et	Ethyl
	Et ₂ O	Diethylether
15	EtOAc	Ethyl acetate
	EtOH	Ethanol
	FC	Flash chromatography
	h	Hour
	HATU	1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid
20		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
25	LC	Liquid chromatography
	Me	Methyl
	MeOH	Methanol
	mesyl	Methanesulfonyl
	MH ⁺	Mass of the protonated molecule
30	min	Minute
	MS	Mass spectroscopy
	NMR	Nuclear magnetic resonance
	org.	Organic
	PBS	Phosphate Buffered Saline
35	Ph	Phenyl
	Q-Phos	1,2,3,4,5-Pentaphenyl-1'-(di-tert-butylphosphino)ferrocene (CAS 312959-24-3)

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	rt	Room temperature
	sat.	saturated
	sol.	solution
	TBDMS	tert-Butyldimethylsilyl
5	tBu	tert-Butyl
	TEA	Triethylamine
	TFA	Trifluoroacetic acid
	THF	tetrahydrofuran
	TLC	Thin layer chromatography
10	t _R	Retention time
	X-Phos	2-Dicyclohexylphosphino-2',4',6'-triisopropylbiphenyl (CAS 564483-18-7)

Preparation of Examples

General procedures

- 15 *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

- 20 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% CH₃CN / 95% H₂O with 0.05% NH₄OH → 95% CH₃CN over 2.0 min, 1.4 mL/min.
 Conditions 2: Waters Atlantis T3 column, C18, 5 µm, 4.6 x 30 mm, 5% CH₃CN / 95% H₂O with 0.04% TFA → 100% CH₃CN over 1.0 min, 4.5 mL/min.
- 25 Conditions 3: Zorbax SB-Aq column, 3.5 µm, 4.6 x 50 mm, 5% CH₃CN / 95% H₂O with 0.04% TFA → 100% CH₃CN over 1.0 min, 4.5 mL/min.
 Conditions 4: Waters XBridge C18, 2.5 µm, 4.6 x 30 mm, 5% CH₃CN / 95% H₂O with 0.04% TFA → 100% CH₃CN over 1.0 min, 4.5 mL/min.
 Conditions 5: Column Acquity UPLC CSH C18 1.7 µm 2.1x50 mm from Waters, thermostated in the Acquity
- 30 UPLC Column Manager at 60°C. Eluents: A1: H₂O + 0.05% HCOOH; B1: CH₃CN + 0.045% HCOOH. Method: Gradient: 2% B 98% B over 2.0 min. Flow: 1.0 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.

Preparations

4-Cyano-3,5-difluorobenzyl methanesulfonate. A mixture of 2,6-difluoro-4-(hydroxymethyl)benzonitrile (WO 2003101423, 1.20 g, 7.10 mmol) in CH₂Cl₂ (40 mL) is cooled to 0 °C. TEA (1.48 mL, 10.6 mmol) and mesyl chloride (0.61 mL, 7.8 mmol) are added. The mixture is stirred at 0 °C for 30 min, and aq. sat. NaHCO₃ is added. The phases are separated, and the aq. layer is extracted with CH₂Cl₂ (3x). The combined org. layers are washed with brine (1x), dried over MgSO₄, filtered, and the solvents are removed under reduced pressure to yield the crude title product.

4-(Hydroxymethyl)-2-methylbenzonitrile. To a sol. of 4-bromo-3-methylbenzyl alcohol (1047 mg, 5 mmol) in DMF (10 mL) are added Zn(CN)₂ (330 mg, 2.75 mmol), Pd₂(dba)₃ (100 mg, 0.109 mmol), DPPF (75 mg, 0.135 mmol) and poly(methylhydrosiloxane) (0.11 mL). The resulting mixture is stirred at 150 °C in a microwave for 40 min. The reaction is repeated twice using the same conditions and quantities. The combined 3 reaction mixtures are filtered over Celite, and the cake is rinsed with EtOAc. The filtrate is concentrated in vacuo. The residue is purified by automated FC (FlashMaster, EtOAc / heptane 0:100 → 60:40) to yield the title product. LC-MS: t_R = 0.62 min., conditions 3.

4-Cyano-3-methylbenzyl methanesulfonate. At 0 °C, TEA (2.55 mL, 18.3 mmol) and methanesulfonyl chloride (1.04 mL, 13.4 mmol) are added to a sol. of 4-(hydroxymethyl)-2-methylbenzonitrile (1900 mg, 12.2 mmol) in CH₂Cl₂ (31.5 mL). The mixture is stirred at 0 °C for 2 h. The mixture is quenched by the addition of aq. sat. NaHCO₃ and the mixture is extracted with CH₂Cl₂ (3x). The comb. org. layers are washed with brine, dried over MgSO₄, filtered, and concentrated in vacuo to yield the crude title product.

2-Fluoro-5-(hydroxymethyl)benzonitrile. To a sol. of 3-bromo-4-fluorobenzyl alcohol (0.609 mL, 5.00 mmol) in DMA (10 mL) is added Zn(CN)₂ (323 mg, 2.75 mmol), Pd₂(dba)₃ (100 mg, 0.109 mmol), DPPF (77.3 mg, 0.135 mmol) and poly(methylhydrosiloxane) (0.11 mL). The resulting mixture is stirred at 150 °C in a microwave for 40 min. The reaction is repeated twice using the same conditions and quantities. The combined 3 reaction mixtures are filtered over Celite, the cake is rinsed with EtOAc, and the filtrate is concentrated in vacuo. Purification of the crude by FC (Combiflash, column 40 g, flow 40 mL/min, EtOAc / heptane 5:95 → 60:40) yields the title product. LC-MS: t_R = 0.59 min., conditions 3.

3-Cyano-4-fluorobenzyl methanesulfonate. At 0 °C TEA (3.13 mL, 22.5 mmol) and methanesulfonyl chloride (1.28 mL, 16.5 mmol) are added to a sol. of 2-fluoro-5-(hydroxymethyl)benzonitrile (2.27 g, 15.0 mmol) in CH₂Cl₂ (39.3 mL). The mixture is stirred at 0 °C for 30 min. The mixture is quenched by the addition of aq. sat.

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NaHCO₃, and is extracted with CH₂Cl₂ (3x). The combined org. layers are washed with brine, dried over MgSO₄, filtered and concentrated in vacuo to give the crude title product.

(4-(Difluoromethoxy)-3-fluorophenyl)methanol. A sol. of 3-fluoro-4-difluoromethoxybenzaldehyde (5.00 g, 26.3 mmol) in MeOH (70.0 mL) is cooled to 0 °C. NaBH₄ (1.49 g, 39.4 mmol) is added portionwise. After addition, the mixture was stirred for 3 days while warming up to rt. Water (10 mL) is added. The mixture is extracted with CH₂Cl₂ (3x50 mL). The combined org. extracts are dried over MgSO₄, filtered, and concentrated under reduced pressure to yield the crude title product. LC-MS: t_R = 0.69 min., conditions 3.

4-(Bromomethyl)-1-(difluoromethoxy)-2-fluorobenzene. To a sol. of (4-(difluoromethoxy)-3-fluorophenyl)methanol (2.00 g, 10.4 mmol) in THF (80 mL) at 0 °C are added PPh₃ (3.00 g, 11.5 mmol) and CBr₄ (4.32 g, 13.0 mmol). The mixture is stirred overnight while warming up to rt. The mixture is filtered, and the filtrate is partitioned between EtOAc and aq. sat. NH₄Cl. The org. layer is dried over MgSO₄, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Büchi, silicagel, EtOAc / heptane 1:99 → 85:15) yields the title product. LC-MS: t_R = 0.89 min., conditions 3.

(3-Fluoro-4-(trifluoromethoxy)phenyl)methanol. NaBH₄ (1.36 g, 36.0 mmol) is added in portions to a sol. of 3-fluoro-4-(trifluoromethoxy)benzaldehyde (5.00 g, 24.0 mmol) in MeOH (80 mL) at 0 °C. The mixture is stirred for 3 h while warming up to rt. Water is added carefully and the solvents are partially removed under reduced pressure. The residue is extracted with CH₂Cl₂ (2x). The combined org. layers are dried over MgSO₄, 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-(Bromomethyl)-2-fluoro-1-(trifluoromethoxy)benzene. To a sol. of (3-fluoro-4-(trifluoromethoxy)phenyl)methanol (4.50 g, 21.4 mmol) in THF (80 mL) at 0 °C are added PPh₃ (6.18 g, 23.6 mmol) and CBr₄ (8.88 g, 26.8 mmol). The mixture is stirred for 4 h while warming up to rt. The mixture is filtered, and the filtrate is partitioned between EtOAc and aq. sat. NH₄Cl. The org. layer is dried over MgSO₄, filtered, and the solvents are removed under reduced pressure. Purification of the crude by automated FC (Büchi, silicagel, EtOAc / heptane 1:99 → 85:15) yields the title product. LC-MS: t_R = 0.94 min., conditions 3.

5-(Hydroxymethyl)-2-methylbenzonitrile. To a sol. of (3-bromo-4-methylphenyl)methanol (3.02 g, 15.0 mmol) in DMA (30 mL) are added Zn(CN)₂ (989 mg, 8.25 mmol), Pd₂(dba)₃ (300 mg, 0.328 mmol), DPPF (225 mg, 0.406 mmol) and poly(methylhydrosiloxane) (0.33 mL). The resulting mixture is stirred at 150 °C overnight. The mixture is allowed to cool to rt, filtered over Celite, and the cake is rinsed with EtOAc. The filtrate is concentrated in vacuo. The residue is purified by automated FC (FlashMaster, 100 g silicagel, 45 mL/min, EtOAc / heptane 0:100 → 60:40) to yield the title product. LC-MS: t_R = 0.62 min., conditions 3.

3-Cyano-4-methylbenzyl methanesulfonate. At 0 °C, TEA (2.1 mL, 15.1 mmol) and methanesulfonyl chloride (0.858 mL, 11.1 mmol) are added to a sol. of 5-(hydroxymethyl)-2-methylbenzonitrile (1.48 g, 10.1 mmol) in CH₂Cl₂ (26 mL). The mixture is stirred at 0 °C for 90 min. The mixture is quenched by the addition of aq. sat.

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NaHCO₃, and is extracted with CH₂Cl₂ (3x). The comb. org. layers are washed with brine, dried over MgSO₄, filtered, and concentrated in vacuo to yield the crude title product.

3-Cyano-4-methoxybenzyl methanesulfonate. At 0 °C, TEA (1.81 mL, 13.0 mmol) and methanesulfonyl chloride (0.741 mL, 9.55 mmol) are added to a sol. of 5-(hydroxymethyl)-2-methoxybenzonitrile (1.50 g, 8.68 mmol) in THF (22 mL). The mixture is stirred overnight while warming up to rt. The mixture is cooled to 0 °C and TEA (1.81 mL, 13.0 mmol) and methanesulfonyl chloride (0.741 mL, 9.55 mmol) are added again. The mixture is stirred at 0 °C for 1 h then at rt for 3 h. The mixture is heated up to 40 °C, and stirred at that temperature overnight. The mixture is quenched by the addition of sat. aq. NaHCO₃ sol., and is extracted with CH₂Cl₂ (3x). The comb. org. layers are washed with brine, dried over MgSO₄, filtered, and concentrated in vacuo to give the crude title product.

(3,4-Difluoro-5-methoxyphenyl)methanol. Borane-THF complex (1M in THF, 53.2 mL, 53.2 mmol) is added dropwise to a sol. of 3,4-difluoro-5-methoxybenzoic acid (5.00 g, 26.6 mmol) in THF (136 mL) at rt. The resulting mixture is stirred at rt overnight. The mixture is diluted with EtOAc (180 mL) and brine (25 mL) is added. The layers are separated and the org. phase is dried over MgSO₄, filtered and concentrated in vacuo to give the crude title product. LC-MS: t_R = 0.66 min., conditions 3.

3,4-Difluoro-5-methoxybenzyl methanesulfonate. At 0 °C, TEA (5.16 mL, 37 mmol) and methanesulfonyl chloride (2.11 mL, 27.2 mmol) are added to a sol. of (3,4-difluoro-5-methoxyphenyl)methanol (4.37 g, 24.7 mmol) in CH₂Cl₂ (64 mL). The mixture is stirred at 0 °C for 2 h. The mixture is cooled down again to 0 °C and TEA (5.16 mL, 37 mmol) followed by mesyl chloride (2.11 mL, 27.2 mmol) are added. The mixture is stirred at 0 °C for 90 min, then at rt overnight. The reaction mixture is quenched by the addition of aq. sat. NaHCO₃ and is extracted with CH₂Cl₂ (3x). The comb. org. layers are washed with brine, dried over MgSO₄, filtered, and concentrated in vacuo. The residue is purified by automated FC (100 g silicagel, flow : 45 mL/min, EtOAc / heptane 0:100 → 30:70) to yield the crude title product.

4-(Hydroxymethyl)-2-methoxybenzonitrile. To a sol. of 2-bromo-5-hydroxymethyl-anisole (0.74 mL, 5 mmol, 1 eq) in DMA (10 mL) are added Zn(CN)₂ (330 mg, 2.75 mmol) Pd₂(dba)₃ (100 mg, 0.109 mmol), DPPF (75 mg, 0.135 mmol) and poly(methylhydrosiloxane) (0.11 mL). The resulting mixture is stirred at 150 °C in a microwave oven for 40 min. The reaction is repeated twice using the same conditions and quantities. The reaction mixture is filtered over Celite, the cake is rinsed with EtOAc and the filtrate is concentrated in vacuo. The residue is purified by automated FC (Combiflash, 24 g silicagel, flow : 35 mL/min, EtOAc / heptane 0:100 → 50:50) to yield the title product. LC-MS: t_R = 0.60 min., conditions 3.

4-Cyano-3-methoxybenzyl methanesulfonate. At 0 °C, TEA (3.07 mL, 22.1 mmol) and methanesulfonyl chloride (1.26 mL, 16.2 mmol) are added to a sol. of 4-(hydroxymethyl)-2-methoxybenzonitrile (2.40 g, 14.7 mmol) in CH₂Cl₂ (40 mL). The mixture is stirred at 0 °C for 30 min. The mixture is quenched by the addition

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of aq. sat. NaHCO_3 , and is extracted with CH_2Cl_2 (3x). The comb. org. layers are washed with brine, dried over MgSO_4 , filtered, and concentrated in vacuo to yield the crude title product.

General procedure for the preparation of aminotriazole from 4,5-dibromo-2H-1,2,3-triazole. K_2CO_3 (2 eq.) is added to a sol. of 4,5-dibromo-2H-1,2,3-triazole (1 eq) in DMF (0.1 M – 0.5 M) at rt. The desired benzyl bromide, benzyl chloride, or benzyl methanesulfonate (1 eq) is added slowly, and the mixture is stirred until completion of the reaction (1 h – overnight). The solvents are partially removed under reduced pressure, and the residue is partitioned between water and EtOAc. The aq. layer is extracted with EtOAc (4x). 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 2-benzyl-4,5-dibromo-2H-1,2,3-triazole. The product is optionally purified by automated FC (silicagel, EtOAc / heptane mixture of solvents).

A sol. of 2-benzyl-4,5-dibromo-2H-1,2,3-triazole (1 eq.) in THF (0.20 – 0.25 M) is cooled to $-5\text{ }^\circ\text{C}$ to $-25\text{ }^\circ\text{C}$ (sometimes $-78\text{ }^\circ\text{C}$). $i\text{PrMgBr}$ (2M in THF, 2.1 eq) is added, and the reaction is allowed to warm up to $-10\text{ }^\circ\text{C}$ – rt. After disappearance of the starting material (0.33 h – 6 h), aq. sat. NH_4Cl is added. The mixture is diluted with Et_2O , and the phases are separated. The aq. layer is washed with Et_2O (2x). 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 (silicagel, EtOAc / heptane mixture of solvents) yields the desired 2-benzyl-4-bromo-2H-1,2,3-triazole.

A mixture of 2-benzyl-4-bromo-2H-1,2,3-triazole (1 eq.) and Cu (0.08 eq.) in aq. 25% NH_4OH (10 eq.) is stirred at $90\text{--}110\text{ }^\circ\text{C}$ until the reaction is complete (18 h – 6 days). The mixture is allowed to cool to rt, and EtOAc is added. The phases are separated, and the aq. layer is extracted with EtOAc (2x). The combined org. layers are dried over MgSO_4 , filtered, and the solvents are removed under reduced pressure to yield the crude desired 2-benzyl-2H-1,2,3-triazol-4-amine.

Following this procedure, the following compounds have been prepared:

Product name	LC-MS 2-benzyl-4,5-dibromo- 2H-1,2,3-triazole t_R (min.), MH^+ , conditions	LC-MS 2-benzyl-4-bromo-2H- 1,2,3-triazole t_R (min.), MH^+ , conditions	LC-MS final product t_R (min.), MH^+ , conditions
2-(4-fluorobenzyl)-2H-1,2,3-triazol-4-amine	0.94, -, cond. 3	0.86, -, cond. 3	0.62, 193.25, cond. 3
2-(3,4-difluorobenzyl)-2H-1,2,3-triazol-4-amine	0.95, -, cond. 3	0.88, -, cond. 3	0.66, 211.15, cond. 3
2-(4-methylbenzyl)-2H-1,2,3-triazol-4-amine	-	0.90, -, cond. 3	0.67, 189.30, cond. 3
2-(4-methoxybenzyl)-2H-1,2,3-triazol-4-amine	0.94, -, cond. 3	0.86, -, cond. 3	0.62, 205.24, cond. 3
4-((4-amino-2H-1,2,3-triazol-2-yl)methyl)benzonitrile	0.90, -, cond.3	0.83, -, cond. 3	-

2-(4-ethoxybenzyl)-2H-1,2,3-triazol-4-amine	0.97, -, cond. 3	0.90, -, cond. 3	0.68, 219.11, cond. 3
2-(3,4-dimethoxybenzyl)-2H-1,2,3-triazol-4-amine	0.90, -, cond. 3	0.81, -, cond. 3	0.58, 235.12, cond. 3
2-(3,5-difluoro-4-methoxybenzyl)-2H-1,2,3-triazol-4-amine	0.95, -, cond. 3	0.89, -, cond. 3	0.69, 241.15, cond. 3
2-(4-(2-methoxyethoxy)benzyl)-2H-1,2,3-triazol-4-amine	0.92, -, cond. 3	0.85, -, cond. 3	0.62, 249.16, cond. 3
2-(4-(difluoromethoxy)benzyl)-2H-1,2,3-triazol-4-amine	0.96, -, cond. 3	0.90, -, cond. 3	0.70, 241.11, cond. 3
2-(4-(trifluoromethoxy)benzyl)-2H-1,2,3-triazol-4-amine	1.00, -, cond. 3	0.94, -, cond. 3	0.77, 259.07, cond. 3
2-(4-fluoro-3-methoxybenzyl)-2H-1,2,3-triazol-4-amine	0.93, -, cond. 3	0.86, -, cond. 3	0.64, 223.19, cond. 3
2-(3-fluoro-4-methoxybenzyl)-2H-1,2,3-triazol-4-amine	0.93, -, cond. 3	0.86, -, cond. 3	0.64, 223.13, cond. 3
2-(4-(difluoromethoxy)-3-fluorobenzyl)-2H-1,2,3-triazol-4-amine	0.93, -, cond. 3	0.90, -, cond. 3	0.72, 300.08, cond. 3
2-(3-fluoro-4-(trifluoromethoxy)benzyl)-2H-1,2,3-triazol-4-amine	0.99, -, cond. 3	0.94, -, cond. 3	0.78, 277.16, cond. 3

General procedure for the preparation of aminotriazole from 4-nitro-2H-1,2,3-triazole. A sol. 4-nitro-1,2,3-triazole (9.6% in DMF, 1 eq.) is diluted in DMF to around 0.25 M. DIPEA (2 eq.) is added. After 45 min., the desired benzyl bromide, benzyl chloride, or benzyl mesylate (1.1 eq) is added. The mixture is stirred at 50 °C until reaction is complete (24 h). The mixture is allowed to cool to rt, and is partitioned between EtOAc and water. The org. layer is dried over MgSO₄, filtered, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (silicagel, EtOAc / heptane) yields the desired 2-benzyl-4-nitro-2H-1,2,3-triazole derivative.

A mixture of the starting 2-benzyl-4-nitro-2H-1,2,3-triazole derivative (1 eq), Fe (powder, 325 mesh, 3 eq), and NH₄Cl (5 eq) in a 1:2 mixture of water and EtOH (0.2 M) is warmed to 80 °C and stirred at this temperature until reaction is complete (1 h). The mixture is allowed to cool to rt, filtered through Celite, and the solvents are partially removed under reduced pressure. The residue is partitioned between CH₂Cl₂ and water. The aq. layer is extracted with CH₂Cl₂ (4x). The combined org. layers are dried over MgSO₄, filtered, and the solvents are removed under reduced pressure to yield the desired 2-benzyl-2H-1,2,3-triazol-4-amine derivative.

Following this procedure, the following compounds have been prepared:

Product name	LC-MS 2-benzyl-4-nitro-2H-1,2,3-triazole t _R (min.), MH ⁺ , conditions	LC-MS final product t _R (min.), MH ⁺ , conditions
4-((4-amino-2H-1,2,3-triazol-2-yl)methyl)-2-fluorobenzonitrile	-	0.64, 218.10, cond. 3

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General procedure for the preparation of aminotriazole from methyl or ethyl 2H-1,2,3-triazole-4-carboxylate. A sol. of methyl 2H-1,2,3-triazole-4-carboxylate (1 eq.) in DMF (0.1 – 0.2 M) is cooled to 0 °C. NaH (55% suspension in oil, about 1.15 eq) is added, and the mixture is stirred at 0 °C for 15 – 45 min. The desired
 5 benzyl bromide, benzyl chloride, or benzyl mesylate (1.1 eq) is added. The mixture is stirred until consumption of the starting material (6 - 24 h) while warming up to rt. If necessary, the mixture can be heated up to 60 °C. The mixture is partitioned between aq. sat. NaHCO₃ and EtOAc. The aq. layer is extracted with EtOAc (3x). The combined org. layers are washed with brine (1x), dried over MgSO₄, filtered, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (silicagel, EtOAc / heptane) or
 10 reversed phase HPLC (CH₃CN / water) yields the desired methyl or ethyl 2-benzyl-2H-1,2,3-triazole-4-carboxylate derivative.

Aq. 1M LiOH (4 – 5 eq.) is added to a sol. of the desired methyl or ethyl 2-benzyl-2H-1,2,3-triazole-4-carboxylate derivative (1 eq.) in a 5:1-mixture of THF and MeOH (0.05 M). The mixture is stirred at rt after consumption of the starting material (1 h – overnight). The solvents are partially removed under reduced
 15 pressure, and the residue is acidified to pH 4 with aq. 2M HCl. Continuous extraction with CH₂Cl₂ leads to an org. layer that is dried over MgSO₄, and filtered. Removal of the solvents under reduced pressure yields the desired 2-benzyl-2H-1,2,3-triazole-4-carboxylic acid derivative. Alternative saponification conditions, as for instance aq. NaOH / EtOH + THF, can be used as well.

TEA (2 eq.) and (PhO)₂P(O)N₃ (1.2 eq.) are added to a sol. of the desired 2-benzyl-2H-1,2,3-triazole-4-carboxylic acid derivative (1 eq.) in toluene (0.05 – 0.1 M) at rt. The mixture is heated to 80 °C under stirring,
 20 and Me₃Si(CH₂)₂OH (1.5 eq.) is added. The mixture is stirred at 90 - 100 °C until consumption of the starting materials (2 - 4 h). The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Purification of the residue by automated FC (silicagel, EtOAc / heptane) yields the desired 2-(trimethylsilyl)ethyl (2-benzyl-2H-1,2,3-triazol-4-yl)carbamate derivative.

TBAF (1.5 eq.) is added slowly to a sol. of the desired 2-(trimethylsilyl)ethyl (2-benzyl-2H-1,2,3-triazol-4-yl)carbamate derivative (1 eq.) in THF (0.25 – 0.5 M) at 0 °C. The mixture is stirred until consumption of the
 25 starting material (1 h – 24 h) while warming up to rt. The mixture was partitioned between EtOAc and aq. 10% Na₂CO₃. The org. layer is washed with aq. 10% Na₂CO₃ (4x), dried over MgSO₄, filtered, and the solvents are removed under reduced pressure to yield the desired 2-benzyl-2H-1,2,3-triazol-4-amine.

30 Following this procedure, the following compounds have been prepared:

Product name	LC-MS methyl 2-benzyl-2H-1,2,3-triazole-4-carboxylate t _R (min.), MH ⁺ , conditions	LC-MS 2-benzyl-2H-1,2,3-triazole-4-carboxylic acid t _R (min.), MH ⁺ , conditions	LC-2-(trimethylsilyl)ethyl (2-benzyl-2H-1,2,3-triazol-4-yl)carbamate t _R (min.), MH ⁺ ,	LC-MS final product t _R (min.), MH ⁺ , conditions
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			conditions	
4-((4-amino-2H-1,2,3-triazol-2-yl)methyl)-2-fluoro-6-methoxy-benzonitrile ¹⁾	-	0.70, -, cond. 3	0.96, -, cond. 3	0.68, -, cond. 3
4-((4-amino-2H-1,2,3-triazol-2-yl)methyl)-2-methylbenzonitrile	0.69, -, cond. 4	0.68, 242.33, cond. 3	0.96, -, cond. 3	0.92, 214.07, cond. 2
5-((4-amino-2H-1,2,3-triazol-2-yl)methyl)-2-fluorobenzonitrile	0.72, 275.07, cond. 4	0.66, -, cond. 3	0.95, -, cond. 3	0.62, 218.13, cond. 3
5-((4-amino-2H-1,2,3-triazol-2-yl)methyl)-2-methylbenzonitrile	0.69, 257.18, cond. 4	0.68, 242.30, cond. 3	0.96, -, cond. 3	1.26, 255.28, cond. 3
5-((4-amino-2H-1,2,3-triazol-2-yl)methyl)-2-methoxy-benzonitrile	0.65, 273.14, cond. 4	0.66, 259.14, cond. 3	0.94, -, cond. 3	0.86, 230.20, cond. 3
2-(3,4-difluoro-5-methoxy-benzyl)-2H-1,2,3-triazol-4-amine	0.74, 284.15, cond. 4	0.72, -, cond. 3	0.98, -, cond. 3	1.05, 241.21, cond. 3
4-((4-amino-2H-1,2,3-triazol-2-yl)methyl)-2-methoxy-benzonitrile	-	0.67, 300.18, cond. 3	0.95, -, cond. 3	0.63, 230.23, cond. 3
5-((4-amino-2H-1,2,3-triazol-2-yl)methyl)picolinonitrile	0.65, 244.17, cond. 3	0.52, 230.16, cond. 3 ²⁾	0.89, 345.12, cond. 3	0.47, 201.21, cond. 3

1) From 4-cyano-3,5-difluorobenzyl methanesulfonate, with displacement of a fluorine with MeOH during saponification.

2) Conditions: To a sol. of the ester (2460 mg, 10.1 mmol) in THF (50 mL) is added aq. 1M HCl (150 mL). The sol. is heated at 75°C for 28 h. The mixture is partially evaporated under reduced pressure.

5 The residue is diluted with aq. 2M HCl, and is extracted with CH₂Cl₂ (6x). The comb. org. layers are washed with brine, dried over MgSO₄, filtered, and concentrated in vacuo to yield the crude desired product.

10 *Methyl 2-(4-cyclobutoxyphenyl)acetate*. Bromocyclobutane (500 mg, 3.70 mmol) and K₂CO₃ (1.25 g, 9.03 mmol) are added to a sol. of methyl 4-hydroxyphenylacetate (500 mg, 3.01 mmol) in DMF (5 mL). The mixture is stirred at 100 °C for 4 h, and is allowed to cool to rt. The solvents are partially removed under reduced pressure, and the residue is purified by automated FC (silicagel, EtOAc / heptane) to yield the title product. LC-MS: t_R = 0.89 min, conditions 3.

15 *Methyl 2-(4-(vinylloxy)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 Na₂CO₃ (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 MgSO₄, 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).

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Methyl 2-(4-cyclopropoxyphenyl)acetate. At -5 °C Et₂Zn (1.0 M in hexanes, 4.8 mL, 4.8 mmol) is added to a sol. of methyl 2-(4-(vinylloxy)phenyl)acetate (384 mg, 2.00 mmol) and CH₂ClI (0.525 mL, 7.20 mmol) in CH₂Cl₂ (15.2 mL). The mixture is stirred between -5 °C and 0 °C for 4 h, and is quenched with aq. sat. NH₄Cl. The mixture is extracted with EtOAc. The combined org. layers are washed with brine, dried over MgSO₄, 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).

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.

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).

(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 CH₂Cl₂, and is dried over MgSO₄. 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.

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).

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

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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).

5 *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).

10 *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).

20 *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).

25 *3-((4-Bromophenoxy)methyl)-3-oxetane*. A mixture of oxetan-3-ylmethyl 4-methylbenzenesulfonate (300 mg, 1.24 mmol), 4-bromophenol (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).

30 *(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-bromophenol (156 mg, 0.904 mmol), KI (59 mg, 0.35 mmol)

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and K₂CO₃ (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 Na₂SO₄, 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).

(3-Methyloxetan-3-yl)methyl 4-methylbenzenesulfonate. p-Toluenesulfonyl chloride (2.17 g, 11.4 mmol) is dissolved in CH₂Cl₂ (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 CH₂Cl₂ and washed with aq. 0.1M HCl and with aq. sat. NaHCO₃. The org. layer is dried over Na₂SO₄, 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-bromophenol (371 mg, 2.15 mmol), KI (139 mg, 0.839 mmol) and K₂CO₃ (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 Na₂SO₄, 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).

1-Bromo-4-(3,3-difluorocyclobutoxy)benzene. PPh₃ (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).

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. NaHCO₃ (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. NaHCO₃ (2 x 200 mL), and brine (1 x 100 mL), are dried over MgSO₄, 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).

(3-Fluorooxetan-3-yl)methyl 4-methylbenzenesulfonate. p-Toluenesulfonyl chloride (216 mg, 1.13 mmol) is dissolved in CH₂Cl₂ (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

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CH₂Cl₂, and washed with aq. 0.1M HCl and with aq. sat. NaHCO₃. The org. layer is dried over Na₂SO₄, 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-bromophenol (101 mg, 0.583 mmol), KI (38 mg, 0.23 mmol) and K₂CO₃ (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 Na₂SO₄, 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).

(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. NaHCO₃. The org. layer is dried over Na₂SO₄, 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-bromophenol (152 mg, 0.879 mmol), KI (57 mg, 0.34 mmol) and K₂CO₃ (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 Na₂SO₄, 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).

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 Cs₂CO₃ (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 MgSO₄, 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

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mixture is extracted with CH₂Cl₂ (3 x). The comb. org. layers are dried over MgSO₄, filtered and the solvents are removed under reduced pressure to yield the crude title product. LC-MS: t_R = 0.80 min (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). PPh₃ (5.07 g, 19.3 mmol) is added and the mixture is cooled to 0 °C.

- 5 CBr₄ (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. NH₄Cl. 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 silicagel, 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).

- 10 *2,6-Difluoro-4-((3-nitro-1H-pyrazol-1-yl)methyl)benzonitrile*. Prepared according to *general procedure 4* from K₂CO₃ (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 Bu₄NBr (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).

- 15 *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 NH₄Cl (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).

- 20 *General procedure 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 Et₂O, 1.2 eq.), Pd₂(dba)₃ (0.05 eq.) and Q-Phos or X-Phos (0.1 eq.) in dioxane or THF (0.5M) is stirred between rt and 90 °C until the starting materials are consumed (0.33 - 48 h). The mixture is allowed to cool to rt, and the solvents are removed under reduced pressure. Chromatographic purification yields the tert-butyl arylacetate.

- 25 A sol. of the tert-butyl arylacetate in an acid (HCl/dioxane, or HCOOH) with optionally CH₂Cl₂ 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 this procedure, 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-methyl-1H-indazol-5-yl)acetic acid	0.88, 247.14, cond. 3	0.60, -, cond. 3	4M HCl / dioxane
2-(1-methyl-1H-indol-5-yl)acetic acid	0.94, 246.28, cond. 3	0.69, -, cond. 3	See conditions below

2-(4-cyclobutoxyphenyl)acetic acid	0.89, -, cond.3 (methyl ester, see above)	0.77, -, cond. 3	See conditions below
2-(4-cyclopropoxyphenyl)acetic acid	0.84, -, cond.3 (methyl ester, see above)	0.71, -, cond. 3	See conditions below
2-(6-(cyclopropyl(methyl)amino)pyridin-3-yl)acetic acid	-	-	4M HCl / dioxane
2-(6-((cyclopropylmethyl)(methyl)amino)pyridin-3-yl)acetic acid	-	-	4M HCl / dioxane
(rac)-2-(4-(1-methoxyethyl)phenyl)acetic acid	0.93, -, cond. 3	0.65, -, cond. 3	4M HCl / dioxane
2-(4-(3-fluorooxetan-3-yl)phenyl)acetic acid	0.90, -, cond. 3	0.63, -, cond. 3	HCOOH
2-(1H-indol-5-yl)acetic acid	0.89, 232.19, cond. 3	0.69, -, cond. 3	See conditions below
2-(6-(diethylamino)pyridin-3-yl)acetic acid	0.66, 265.17, cond. 3	-	4M HCl / dioxane
2-(6-(3,3-difluoropyrrolidin-1-yl)pyridin-3-yl)acetic acid	0.65, 299.17, cond. 3	0.42, 242.90, cond. 3	4M HCl / dioxane
2-(6-(pyrrolidin-1-yl)pyridin-3-yl)acetic acid	0.63, 263.14, cond. 3	0.42, 207.22, cond. 3	4M HCl / dioxane
2-(1,3,3-trimethyl-2-oxoindolin-5-yl)acetic acid	0.89, 290.01, cond. 3	0.63, 275.23, cond. 3	4M HCl / dioxane
2-(4-(3-methoxyoxetan-3-yl)phenyl)acetic acid	0.87, -, cond. 3	0.59, -, cond. 3	HCOOH
2-(3,3-dimethyl-2-oxoindolin-5-yl)acetic acid	0.83, 276.28, cond. 3	-	4M HCl / dioxane
2-(4-(3-methyloxetan-3-yl)phenyl)acetic acid	0.91, -, cond. 3	0.64, -, cond. 3	HCOOH
2-(4-(oxetan-3-yl)phenyl)acetic acid	-	-	HCOOH
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-(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
2-(4-(oxetan-3-ylmethoxy)phenyl)acetic acid	0.89, -, cond. 3	0.61, -, cond. 3	HCOOH
2-(4-((3,3-difluorocyclobutyl)methoxy)phenyl)acetic acid	1.00, -, cond. 3	0.80, -, cond. 3	HCOOH
2-(4-((3-methyloxetan-3-yl)methoxy)phenyl)acetic acid	0.93, -, cond. 3	0.68, -, cond. 3	HCOOH
2-(4-(1-(trifluoromethyl)cyclopropyl)phenyl)acetic acid	1.02, -, cond. 3	0.82, 244.21, cond. 3	HCOOH
2-(4-(3,3-difluorocyclobutoxy)phenyl)acetic acid	0.98, -, cond. 3	0.77, -, cond. 3	HCOOH
2-(4-(2-cyanopropan-2-yl)phenyl)acetic acid	0.94, 260.28, cond. 3	0.70, -, cond. 3	4M HCl / dioxane
2-(5-fluoro-6-(pyrrolidin-1-yl)pyridin-3-yl)acetic acid	0.66, 281.22, cond. 3	0.44, 225.16, cond. 3	4M HCl / dioxane
2-(1-methyl-1H-indazol-6-yl)acetic acid	0.88, 247.14, cond. 3	0.60, -, cond. 3	4M HCl / dioxane
2-(4-(3-fluorooxetan-3-yl)methoxy)phenyl)acetic acid	0.91, -, cond. 3	0.65, -, cond. 3	HCOOH
2-(4-((3,3-difluoro-1-methylcyclobutyl)methoxy)phenyl)acetic acid	1.04, -, cond. 3	0.85, -, cond. 3	HCOOH
2-(4-(1-cyanocyclopropyl)phenyl)acetic acid	0.92, 258.14, cond. 3	0.68, -, cond. 3	TFA
2-(4-(pentafluoro- λ 6-sulfanyl)phenyl)acetic acid	0.89, -, cond. 3	0.66, 281.22, cond. 3	HCOOH
2-(4-(1,1,1-trifluoro-2-methylpropan-2-yl)phenyl)acetic acid	1.02, -, cond. 3	0.82, -, cond. 3	TFA
rac-2-(4-((1R*,2R*)-2-(trifluoromethyl)cyclopropyl)phenyl)acetic acid	1.01, -, cond. 3	0.82, -, cond. 3	TFA

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 CH₂Cl₂, and aq. 1M HCl is added to pH 2-3. The phases are separated, and the org. layer is dried over MgSO₄, and filtered. The solvents are removed under reduced pressure to yield the crude title compound. LC-MS: t_R = 0.69 min (conditions 3).

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2-(4-Cyclobutoxyphenyl)acetic acid. A sol. of methyl 2-(4-cyclobutoxyphenyl)acetate (440 mg, 2.00 mmol) and aq. 2.5M NaOH (3 mL) in MeOH (6 mL) is stirred at rt for 1 h. The solvents are partially removed under reduced pressure, and the residue is covered with CH₂Cl₂. Aq. 1M HCl is added to reach a pH = 3, and the phases are separated in a Separator®. The org. layer is dried over MgSO₄, filtered, and the solvents are removed under reduced pressure to yield the crude title product.

2-(4-Cyclopropoxyphenyl)acetic acid. A sol. of methyl 2-(4-cyclopropoxyphenyl)acetate (364 mg, 1.76 mmol) and LiOH·H₂O (111 mg, 2.65 mmol) in THF / MeOH / H₂O (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 MgSO₄, and filtered. Removing the solvents under reduced pressure yields the crude title compound.

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 CH₂Cl₂, and aq. 1M HCl is added to pH 2-3. The phases are separated, and the org. layer is dried over MgSO₄, and filtered. The solvents are removed under reduced pressure to yield the crude title compound.

General procedure for an amide coupling. Unless indicated otherwise, a mixture of the desired carboxylic acid (1 eq.), the desired amine (1 eq), N-methylmorpholine or DIPEA (5 eq.) and HATU or HBTU (1 eq.) in DMF (0.1 – 0.2 M) is stirred until the reaction is complete (1 h - overnight). 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.

Following this procedure, the following examples have been prepared:

Example number	Product name	LC-MS t _R (min.), MH ⁺ , conditions
1	N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	0.95, 353.26, cond. 3
2	2-(4-Dimethylamino-phenyl)-N-[2-(4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.57, 354.23, cond. 2
5	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	0.96, 371.28, cond. 3
6	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.85, 383.29, cond. 3
7	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.90, 382.29, cond. 3
8	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1H-indol-6-yl)-acetamide	0.86, 368.29, cond. 3

9	2-(4-Cyclobutoxy-phenyl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.94, 399.31, cond. 3
10	2-(4-Cyclopropoxy-phenyl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.92, 385.19, cond. 3
11	2-[6-(Cyclopropyl(methyl)amino)-pyridin-3-yl]-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.67, 399.32, cond. 3
12	2-[6-(Cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.70, 413.32, cond. 3
13	rac-N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide	0.88, 387.32, cond. 3
14	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	0.86, 403.03, cond. 3
15	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1H-indol-5-yl)-acetamide	0.85, 368.25, cond. 3
16	2-(6-Diethylamino-pyridin-3-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.69, 401.21, cond. 3
17	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.69, 435.25, cond. 3
18	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.67, 399.33, cond. 3
19	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide	0.85, 426.31, cond. 3
20	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide	0.84, 415.31, cond. 3
21	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide	0.80, 453.22 ⁽¹⁾ , cond. 3
22	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide	0.87, 399.13, cond. 3
23	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-oxetan-3-yl-phenyl)-acetamide	0.84, 385.06, cond. 3
24	2-(4-Isopropyl-phenyl)-N-[2-(4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.97, 349.37, cond. 3
25	2-(4-Isopropyl-phenyl)-N-[2-(4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.94, 365.35, cond. 3
26	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	0.93, 360.34, cond. 3
27	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide	1.33, 397.08, cond. 1
28	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide	1.29, 397.08, cond. 1
29	2-(3-Cyclopropyl-1H-indazol-5-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.29, 409.12, cond. 1

30	2-(1-Butyl-1H-indazol-5-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.53, 425.13, cond. 1
31	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(2-methyl-1H-indol-5-yl)-acetamide	1.39, 382.09, cond. 1
32	2-(3-Butyl-1H-indazol-5-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.42, 425.05, cond. 1
33	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-isopropyl-1H-indazol-5-yl)-acetamide	1.42, 411.05, cond. 1
34	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-propyl-1H-indazol-5-yl)-acetamide	1.42, 411.13, cond. 1
35	2-(3-Cyclopropyl-1-methyl-1H-indazol-5-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.41, 422.99, cond. 1
38	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-acetamide	1.14, 384.04, cond. 1
39	N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(3-trifluoromethyl-1H-indazol-5-yl)-acetamide	0.88, 437.13, cond. 3
40	N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.91, 390.25, cond. 3
41	2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.70, 443.24, cond. 3
42	N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide	0.88, 407.32, cond. 3
43	2-(4-tert-Butyl-phenyl)-N-[2-(4-ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.99, 393.32, cond. 3
44	N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	0.97, 379.31, cond. 3
45	N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.68, 407.03, cond. 3
46	N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.86, 391.27, cond. 3
47	2-(6-Diethylamino-pyridin-3-yl)-N-[2-(3,4-dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.64, 425.27, cond. 3
48	2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(3,4-dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.64, 459.23, cond. 3
49	2-(4-tert-Butyl-phenyl)-N-[2-(3,4-dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.94, 409.29, cond. 3
50	N-[2-(3,4-Dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	0.92, 395.30, cond. 3
51	N-[2-(3,4-Dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.62, 423.39, cond. 3
52	N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.88, 364.25, cond. 3

53	N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide	0.85, 381.29, cond. 3
54	2-(4-tert-Butyl-phenyl)-N-[2-(4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.97, 367.31, cond. 3
55	N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.65, 381.28, cond. 3
56	N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.83, 365.29, cond. 3
57	N-[2-(4-Methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.88, 376.27, cond. 3
58	2-(6-Diethylamino-pyridin-3-yl)-N-[2-(4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.67, 395.25, cond. 3
59	2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.67, 429.25, cond. 3
60	N-[2-(4-Methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide	0.84, 393.29, cond. 3
61	2-(4-tert-Butyl-phenyl)-N-[2-(4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.97, 379.31, cond. 3
62	N-[2-(4-Methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.65, 393.32, cond. 3
63	N-[2-(4-Methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.82, 377.28, cond. 3
64	N-[2-(4-Methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.90, 360.04, cond. 3
65	2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.69, 413.03, cond. 3
66	2-(4-tert-Butyl-phenyl)-N-[2-(4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.99, 363.08, cond. 3
67	N-[2-(4-Methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide	0.87, 377.02, cond. 3
68	N-[2-(4-Methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.68, 377.04, cond. 3
69	N-[2-(4-Methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.85, 361.02, cond. 3
70	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.87, 388.99, cond. 3
71	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.67, 441.96, cond. 3
72	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide	0.84, 405.99, cond. 3
73	2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.95, 392.03, cond. 3

74	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	0.93, 378.03, cond. 3
75	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.65, 406.01, cond. 3
76	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.82, 389.98, cond. 3
77	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.90, 411.99, cond. 3
78	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide	0.87, 428.99, cond. 3
79	2-(4-tert-Butyl-phenyl)-N-[2-(3,5-difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.98, 415.04, cond. 3
80	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	0.96, 400.99, cond. 3
81	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.68, 429.01, cond. 3
82	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.85, 413.00, cond. 3
83	2-(4-tert-Butyl-phenyl)-N-[2-(4-cyclopropylmethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.01, 419.05, cond. 3
84	N-[2-(4-Cyclopropylmethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.93, 416.94, cond. 3
85	N-[2-(4-Cyclopropylmethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.89, 417.00, cond. 3
86	2-(4-tert-Butyl-phenyl)-N-[2-[4-(2-methoxy-ethoxy)-benzyl]-2H-[1,2,3]triazol-4-yl]-acetamide	0.95, 423.06, cond. 3
87	N-[2-[4-(2-Methoxy-ethoxy)-benzyl]-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.86, 420.02, cond. 3
88	2-(4-tert-Butyl-phenyl)-N-[2-(4-difluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.98, 415.03, cond. 3
89	N-[2-(4-Difluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	0.90, 412.02, cond. 3
90	2-(4-tert-Butyl-phenyl)-N-[2-(4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.01, 432.96, cond. 3
91	2-(1-Methyl-1H-indol-5-yl)-N-[2-(4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.94, 429.94, cond. 3
92	2-(1-Methyl-1H-indazol-5-yl)-N-[2-(4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.90, 430.97, cond. 3
93	2-[4-(3-Methyl-oxetan-3-yl)-phenyl]-N-[2-(4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.92, 446.95, cond. 3
94	2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.67, 417.20, cond. 3

95	2-(6-Diethylamino-pyridin-3-yl)-N-[2-(4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.67, 383.20, cond. 3
96	2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.55, 374.03, cond. 1
97	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	1.21, 423.97, cond. 1
98	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	1.18, 388.05, cond. 1
99	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide	1.26, 371.04, cond. 1
100	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide	1.37, 385.05, cond. 1
101	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	1.07, 372.04, cond. 1
102	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide	1.11, 386.04, cond. 1
103	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide	1.15, 386.03, cond. 1
104	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-propyl-1H-indazol-5-yl)-acetamide	1.24, 400.11, cond. 1
105	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide	0.91, 403.12, cond. 3
106	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide	0.89, 385.11, cond. 3
108	N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide	1.24, 427.13, cond. 1
109	N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	1.20, 395.09, cond. 1
110	N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide	1.21, 427.15, cond. 1
111	2-[4-(3,3-Difluoro-cyclobutylmethoxy)-phenyl]-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.55, 461.13, cond. 1
112	N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide	1.33, 441.16, cond. 1
113	N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.61, 449.09, cond. 1
114	2-[4-(3,3-Difluoro-cyclobutoxy)-phenyl]-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.51, 447.13, cond. 1
115	2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.32, 447.13, cond. 1
116	N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	1.30, 415.08, cond. 1

117	2-(1-Ethyl-1H-indazol-5-yl)-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.27, 409.12, cond. 1
118	2-(1,3-Dimethyl-1H-indol-5-yl)-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.47, 408.12, cond. 1
119	2-(4-tert-Butyl-phenyl)-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.66, 397.14, cond. 1
120	N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide	1.22, 427.12, cond. 1
121	N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	1.19, 395.12, cond. 1
122	N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide	1.20, 427.14, cond. 1
123	N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide	1.32, 441.10, cond. 1
124	N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.60, 449.11, cond. 1
125	2-[4-(3,3-Difluoro-cyclobutoxy)-phenyl]-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.50, 447.15, cond. 1
126	2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.31, 447.15, cond. 1
127	N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	1.27, 415.11, cond. 1
128	2-(1-Ethyl-1H-indazol-5-yl)-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.25, 409.11, cond. 1
129	2-(1,3-Dimethyl-1H-indol-5-yl)-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.47, 408.12, cond. 1
130	2-(4-tert-Butyl-phenyl)-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.65, 397.16, cond. 1
131	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide	1.19, 421.88, cond. 1
132	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	1.16, 389.70, cond. 1
133	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide	1.17, 439.0 ⁽²⁾ , cond. 1
134	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide	1.52, 473.1 ⁽²⁾ , cond. 1
135	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide	1.29, 453.13 ⁽²⁾ , cond. 1
136	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.57, 461.1 ⁽²⁾ , cond. 1
137	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide	1.47, 461.4 ⁽²⁾ , cond. 1

138	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	1.24, 427.1 ⁽²⁾ , cond. 1
139	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide	1.23, 404.09, cond. 1
140	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide	1.44, 403.10, cond. 1
141	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide	1.29, 445.13, cond. 1
142	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	1.26, 413.11, cond. 1
143	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide	1.28, 445.12, cond. 1
144	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide	1.40, 459.13, cond. 1
145	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.66, 467.09, cond. 1
146	2-[4-(3,3-Difluoro-cyclobutoxy)-phenyl]-N-[2-(3,5-difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.56, 465.08, cond. 1
147	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	1.38, 465.11, cond. 1
148	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	1.35, 433.12, cond. 1
149	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide	1.33, 427.12, cond. 1
150	N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide	1.54, 426.10, cond. 1
151	N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	1.18, 395.10, cond. 1
152	N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	1.17, 395.12, cond. 1
153	N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	1.59, 383.08, cond. 1
154	N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	1.58, 383.12, cond. 1
155	N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	1.29, 411.13, cond. 1
156	N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	1.28, 411.14, cond. 1
157	2-[4-(Cyano-dimethyl-methyl)-phenyl]-N-[2-(4-cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.87, 403.16, cond. 3
158	2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-3-fluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	0.96, 422.20, cond. 3

159	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-trifluoromethyl-phenyl)-acetamide	0.90, 404.11, cond. 3
160	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3-methoxy-azetidin-1-yl)-pyridin-3-yl]-acetamide	0.62, 422.15, cond. 3
161	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(5-fluoro-6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.68, 424.18, cond. 3
162	2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.65, 388.12, cond. 1
163	N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	1.20, 386.06, cond. 1
164	N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	1.20, 386.10, cond. 1
165	N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	1.58, 373.82, cond. 1
166	N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide	1.51, 437.80, cond. 1
167	N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	1.22, 437.82, cond. 1
168	N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide	1.27, 400.15, cond. 1
169	N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide	1.23, 400.12, cond. 1
170	N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.89, 402.17, cond. 1
171	N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide	1.47, 399.15, cond. 1
172	2-(4-tert-Butyl-phenyl)-N-[2-(3-cyano-4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.63, 409.15 ⁽²⁾ , cond. 1
173	N-[2-(3-Cyano-4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	1.16, 389.77, cond. 1
174	N-[2-(3-Cyano-4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	1.57, 378.03. cond. 1
175	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide	1.28, 440.08, cond. 1
176	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide	1.63, 487.1 ⁽²⁾ , cond. 1
177	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide	1.20, 404.08, cond. 1
178	2-(4-tert-Butyl-phenyl)-N-[2-(4-difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.72, 433.15, cond. 1
179	N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	1.29, 431.06, cond. 1

180	N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	1.67, 419.13, cond. 1
181	N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.69, 484.93, cond. 1
182	N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	1.35, 483.09, cond. 1
183	N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	1.01, 447.19, cond. 1
184	2-(4-tert-Butyl-phenyl)-N-[2-(3-fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.86, 451.13, cond. 1
185	N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	1.45, 449.10, cond. 1
186	N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	1.43, 449.10, cond. 1
187	N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	1.80, 437.13, cond. 1
188	N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.80, 502.98, cond. 1
189	2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(3-fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.50, 501.02, cond. 1
190	2-(1-Ethyl-1H-indazol-5-yl)-N-[2-(3-fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.62, 463.14, cond. 1
191	2-(1,3-Dimethyl-1H-indazol-5-yl)-N-[2-(3-fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.47, 463.10, cond. 1
192	N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	1.13, 465.13, cond. 1
193	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide	1.26, 435.2 ⁽²⁾ , cond. 1
194	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide	1.22, 421.88, cond. 1
195	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.55, 426.04, cond. 1
196	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide	1.44, 424.26, cond. 1
197	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide	1.59, 452.23, cond. 1
198	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	1.21, 392.15, cond. 1
199	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	0.93, 448.07, cond. 3
200	N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide	1.03, 436.3, cond. 5

201	N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	1.02, 406.3, cond. 5
202	2-(4-tert-Butyl-phenyl)-N-[2-(3-cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.23, 404.3, cond. 5
203	N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.19, 456.3, cond. 5
204	N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.96, 386.3, cond. 5
205	N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	1.18, 390.3, cond. 5
206	N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide	0.98, 418.3, cond. 5
207	N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.71, 454.3, cond. 5
208	N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.92, 402.3, cond. 5
209	N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide	1.16, 438.3, cond. 5
210	N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide	1.05, 427.3, cond. 5
211	N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.76, 438.3, cond. 5
212	N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	1.03, 413.3, cond. 5
213	N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.61, 402.3, cond. 5
214	N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	0.98, 422.3, cond. 5
215	N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	0.97, 386.3, cond. 5
216	N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	1.23, 374.3, cond. 5
217	2-(4-tert-Butyl-phenyl)-N-[2-(3-cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.60, 388.0, cond. 1
218	2-(4-tert-Butyl-phenyl)-N-[2-(3,4-difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.32, 415.3, cond. 5
219	N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide	0.82, 465.3, cond. 5
220	N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide	1.30, 427.2, cond. 1
221	N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.65, 429.3, cond. 5

222	N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide	1.28, 401.3, cond. 5
223	N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide	1.12, 454.3, cond. 5
224	N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	1.07, 433.3, cond. 5
225	N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide	1.03, 413.3, cond. 5
226	N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.56, 440.1, cond. 1
227	N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.27, 467.3, cond. 5
228	N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide	1.04, 445.3, cond. 3
229	N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide	1.08, 463.3, cond. 5
230	2-[4-(3,3-Difluoro-cyclobutoxy)-phenyl]-N-[2-(3,4-difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.20, 465.3, cond. 5
231	2-[4-(1-Cyano-cyclopropyl)-phenyl]-N-[2-(4-cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.03, 401.3, cond. 5
232	N-(2-(4-cyano-3-fluorobenzyl)-2H-1,2,3-triazol-4-yl)-2-(4-(pentafluoro- λ 6-sulfanyl)phenyl)acetamide	1.19, 462.2, cond. 5
233	N-[2-(4-Cyano-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.56, 473.1 ⁽²⁾ , cond. 1
234	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide	0.90, 372.3, cond. 5
235	N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide	1.01, 406.3, cond. 5
236	N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.58, 418.3, cond. 5
237	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide	1.07, 404.0, cond. 1
238	N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide	1.15, 438.3, cond. 5
239	2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.29, 404.3, cond. 5
240	N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide	1.20, 426.3, cond. 5
241	N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.55, 457.2 ⁽²⁾ , cond. 1
242	N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide	1.08, 431.3, cond. 5

243	N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide	1.02, 386.3, cond. 5
244	2-(4-tert-Butyl-phenyl)-N-[2-(5-cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-acetamide	1.15, 375.3, cond. 5
245	N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.11, 427.3, cond. 5
246	N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide	1.03, 425.3, cond. 5
247	N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-(5-fluoro-6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide	0.70, 407.3, cond. 5
249	N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenyl]-acetamide	1.22, 446.3, cond. 5
250	rac-N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-((1S*,2S*)-2-trifluoromethyl-cyclopropyl)-phenyl]-acetamide	1.21, 444.3, cond. 5

(1) CH₃CN-adduct; (2) NH₃-adduct

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 penicillin (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 µg/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.

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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 μ M 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. IC₅₀ 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 (IC₅₀ values) of all exemplified compounds have been measured for the Cav3.1- and the Cav3.3-channel. Antagonistic activities (IC₅₀ values) of all exemplified compounds are in the range of 1.7 to 970 nM with respect to Cav3.1; and in the range of 1.1 to 620 nM with respect to Cav3.3.

In the following table, IC₅₀-values generated for the Cav3.2-channel are presented.

Example	IC50 (nM)	Example	IC50 (nM)	Example	IC50 (nM)
1	21	88	56	170	50
2	17	89	20	171	22
5	30	90	200	172	33
6	9.5	91	7.4	173	150
7	6.4	92	9.9	174	28
8	37	93	15	175	100
9	22	94	10	176	64
10	23	95	46	177	33
11	32	96	44	178	49
12	31	97	36	179	22
13	27	98	83	180	43
14	17	99	19	181	86
15	40	100	22	182	13
16	15	101	480	183	26
17	7.3	102	160	184	83
18	15	103	74	185	17
19	9.7	104	70	186	8.8
20	89	105	20	187	65

21	180	106	36	188	96
22	15	108	300	189	17
23	46	109	190	190	14
24	37	110	140	191	11
25	33	111	57	192	23
26	19	112	190	193	110
27	9.8	113	230	194	340
28	22	114	73	195	63
29	120	115	45	196	41
30	17	116	140	197	52
31	11	117	80	198	130
32	74	118	63	199	17
33	24	119	62	200	410
34	18	120	550	201	310
35	29	121	290	202	320
38	580	122	360	203	220
39	280	123	870	204	280
40	35	124	250	205	160
41	18	125	180	206	900
42	31	126	47	207	130
43	45	127	110	208	600
44	40	128	150	209	180
45	32	129	48	210	260
46	63	130	62	211	82
47	560	131	210	212	230
48	530	132	180	213	120
49	170	133	130	214	250
50	160	134	110	215	650
51	600	135	120	216	74
52	12	136	79	217	160
53	35	137	37	218	590
54	26	138	78	219	120
55	50	139	69	220	190
56	38	140	14	221	160

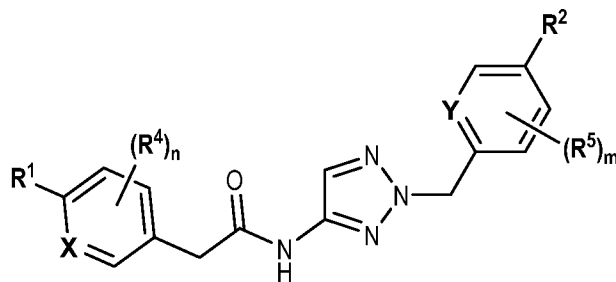
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57	38	141	86	222	300
58	160	142	88	223	120
59	60	143	76	224	190
60	120	144	56	225	560
61	44	145	120	226	250
62	120	146	810	227	770
63	160	147	13	228	300
64	30	148	35	229	130
65	23	149	29	230	350
66	70	150	16	231	36
67	66	151	73	232	110
68	45	152	91	233	110
69	20	153	70	234	76
70	18	154	44	235	92
71	75	155	140	236	160
72	74	156	70	237	200
73	37	157	31	238	24
74	45	158	240	239	210
75	87	159	61	240	180
76	120	161	25	241	110
77	13	162	36	242	54
78	49	163	330	243	110
79	46	164	110	244	34
80	29	165	18	245	190
81	28	166	33	246	680
82	23	167	22	247	690
86	130	168	40	249	91
87	460	169	96	250	29

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Claims

1. A compound of formula (I)



Formula (I)

5 wherein

X represents a ring carbon or a ring nitrogen atom;

• R¹ represents

- (C₂₋₆)alkyl;
- (C₂₋₄)alkyl mono-substituted with cyano, or (C₁₋₃)alkoxy;
- (C₁₋₄)fluoroalkyl;
- (C₁₋₃)fluoroalkoxy;
- pentafluoro-sulfanyl;
- (C₃₋₆)cycloalkyl-L¹, wherein
 - said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)cycloalkyl is unsubstituted; or mono-substituted with fluoro, (C₁₋₃)alkyl, (C₁₋₃)alkoxy, hydroxy, cyano, or (C₁₋₃)fluoroalkyl; or di-substituted with fluoro, or tri-substituted with two fluoro substituents and a (C₁₋₃)alkyl substituent; and
 - the linker L¹ represents a direct bond, (C₁₋₂)alkylene, oxygen, or (C₁₋₂)alkylene-oxy;
- 5- or 6-membered heteroaryl, independently optionally mono-substituted with (C₁₋₃)alkyl;
- -NR¹¹R¹², wherein
 - R¹¹ and R¹² independently represent hydrogen, (C₁₋₃)alkyl, (C₂₋₃)fluoroalkyl, (C₃₋₆)cycloalkyl, (C₃₋₆)cycloalkyl mono- or di-substituted with fluoro, (C₃₋₆)cycloalkyl-(C₁₋₃)alkyl, (C₁₋₃)alkoxy-(C₂₋₃)alkyl;
 - or R¹¹ and R¹², together with the nitrogen atom to which they are attached to, form a 4- to 6 membered ring which is optionally mono- or di-substituted with fluoro; a 2-oxo-pyrrolidinyl group; or a morpholinyl group;

and (R⁴)_n represents one or two optional substituents independently selected from (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, halogen, and cyano;

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- 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 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 nitrogen atoms, 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_{1-4}) alkyl, (C_{3-6}) cycloalkyl, (C_1) fluoroalkyl, or cyano;
- 10 **Y** represents a ring carbon or a ring nitrogen atom; and
- R²** 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;
- 15 and
- (R⁵)_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;
- 20 or a salt of such a compound.
3. A compound according to claim 1 or 2, wherein
- **R¹** represents

 - (C_{2-6}) alkyl;
 - (C_{2-4}) alkyl mono-substituted with cyano, or (C_{1-3}) alkoxy;
 - 25 ➤ (C_{1-4}) fluoroalkyl;
 - (C_{1-3}) fluoroalkoxy;
 - 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, (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 **L¹** represents a direct bond, (C_{1-2}) alkylene, oxygen, or (C_{1-2}) alkylene-oxy;
- 30

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➤ -NR¹¹R¹², wherein

- R¹¹ and R¹² independently represent hydrogen, (C₁₋₃)alkyl, (C₂₋₃)fluoroalkyl, (C₃₋₆)cycloalkyl, (C₃₋₆)cycloalkyl mono- or di-substituted with fluoro, (C₃₋₆)cycloalkyl-(C₁₋₃)alkyl;
- or R¹¹ and R¹², together with the nitrogen atom to which they are attached to, form an azetidiny or a pyrrolidiny ring, both independently optionally mono- or di-substituted with fluoro;

and (R⁴)_n represents one optional substituent selected from (C₁₋₄)alkyl, (C₁₋₄)alkoxy, (C₁₋₃)fluoroalkyl, (C₁₋₃)fluoroalkoxy, halogen, and cyano;

- or R¹ together with (R⁴)_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 (C₁₋₃)alkyl;
- or R¹ together with (R⁴)_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 pyrazolo[3,4-b]pyridinyl, 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 (C₁₋₃)alkyl, (C₃₋₆)cycloalkyl, (C₁)fluoroalkyl, or cyano;

or a salt of such a compound.

4. A compound according to claims 1 or 2, wherein

- R¹ represents

- (C₂₋₆)alkyl;
- (C₁₋₄)fluoroalkyl;
- (C₁₋₃)fluoroalkoxy;
- (C₃₋₆)cycloalkyl wherein

- said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)cycloalkyl is mono-substituted with fluoro or (C₁₋₃)fluoroalkyl, or di-substituted with fluoro; or

- (C₃₋₆)cycloalkyl-oxy- wherein

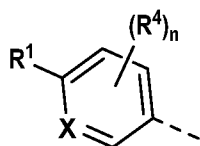
- said (C₃₋₆)cycloalkyl optionally contains one ring oxygen atom; wherein said (C₃₋₆)cycloalkyl is unsubstituted, or di-substituted with fluoro;

and (R⁴)_n represents one optional substituent selected from (C₁₋₄)alkyl, or halogen;

or a salt of such a compound.

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



represents 4-isopropyl-phenyl, 4-dimethylamino-phenyl, 4-trifluoromethyl-phenyl, 4-*tert*-butyl-phenyl, 4-(1-methoxy-ethyl)-phenyl, 4-(cyclopropyl-oxy)-phenyl, 4-(oxetan-3-yl)-phenyl, 4-(3-fluoro-oxetan-3-yl)-phenyl, 4-(cyclobutyl-oxy)-phenyl, 4-(3-methyl-oxetan-3-yl)-phenyl, 4-(1-cyano-cyclopropyl)-phenyl, 4-(1-cyano-1-methyl-ethyl)-phenyl, 4-(pentafluoro-sulfanyl)-phenyl, 3-methyl-4-(2,2,2-trifluoroethoxy)-phenyl, 4-(3-methoxy-oxetan-3-yl)-phenyl, 4-(oxetan-3-yl-methoxy)-phenyl, 4-(2-trifluoromethyl-cyclopropyl)-phenyl, 4-(1-trifluoromethyl-cyclopropyl)-phenyl, 4-((3-fluoro-oxetan-3-yl)-methoxy)-phenyl, 4-((3-methyl-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-(pyrrolidin-1-yl)-pyridin-5-yl, 2-(cyclopropyl(methyl)amino)-pyridin-5-yl, 2-(diethylamino)-pyridin-5-yl, 3-fluoro-2-(pyrrolidin-1-yl)-pyridin-5-yl, 2-((cyclopropylmethyl)-methyl-amino)-pyridin-5-yl, 2-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-5-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, 1-methyl-1H-pyrazolo[3,4-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-propyl-1H-indazol-5-yl, 1-isopropyl-1H-indazol-5-yl, 1-butyl-1H-indazol-5-yl, 3-butyl-1H-indazol-5-yl, 3-trifluoromethyl-1H-indazol-5-yl, 3-cyclopropyl-1H-indazol-5-yl, 3-cyclopropyl-1-methyl-1H-indazol-5-yl, 1-methyl-1H-indol-5-yl, 2-methyl-1H-indol-5-yl, 1,3-dimethyl-1H-indol-5-yl, or 1,3-dimethyl-1H-indol-6-yl;

or a salt of such a compound.

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

- Y represents a ring carbon or a nitrogen atom;
 - R² represents (C₁₋₄)alkyl; (C₁₋₄)alkoxy; (C₁₋₃)fluoroalkyl; (C₁₋₃)fluoroalkoxy; (C₁₋₃)alkoxy-(C₂₋₃)alkoxy; halogen; or cyano; and
 - (R⁵)_m represents one or two optional substituents independently selected from (C₁₋₄)alkyl; (C₁₋₄)alkoxy; halogen; cyano; (C₁₋₃)fluoroalkyl; and (C₁₋₃)fluoroalkoxy;
- or a salt of such a compound.

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

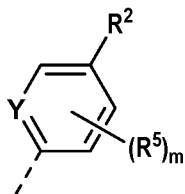
- Y represents a ring nitrogen atom; and
 - R² represents cyano; and
 - (R⁵)_m is absent; or
- Y represents a ring carbon atom; and

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- R^2 represents (C_{1-4}) alkyl; (C_{1-4}) alkoxy; (C_{1-3}) fluoroalkoxy; (C_{1-3}) alkoxy- (C_{2-3}) alkoxy; halogen; or cyano; and
- $(R^5)_m$ represents one or two optional substituents independently selected from (C_{1-4}) alkyl; (C_{1-4}) alkoxy; halogen; and cyano;

5 or a salt of such a compound.

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



represents 4-fluorophenyl, 4-methylphenyl, 4-fluoro-3-cyano-phenyl, 3,4-difluorophenyl, 3,5-difluoro-4-methoxy-phenyl, 3-fluoro-4-methoxy-phenyl, 4-cyano-3-fluoro-phenyl, 4-cyano-3-methyl-phenyl, 3-cyano-4-methyl-phenyl, 4-methoxyphenyl, 4-ethoxyphenyl, 3,4-dimethoxyphenyl, 4-fluoro-3-methoxy-phenyl; 3,4-difluoro-5-methoxy-phenyl, 3-cyano-4-methoxy-phenyl, 4-cyano-3-methoxy-phenyl, 4-cyano-3-fluoro-5-methoxy-phenyl, 4-cyanophenyl, 4-(2-methoxy-ethoxy)-phenyl, 4-difluoromethoxy-phenyl, 4-trifluoromethoxy-phenyl, 3-fluoro-4-difluoromethoxy-phenyl; 3-fluoro-4-trifluoromethoxy-phenyl; or 5-cyano-pyridin-2-yl; or a salt of such a compound.

9. A compound according to claim 1 selected from the group consisting of
- N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
 - 2-(4-Dimethylamino-phenyl)-N-[2-(4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
 - N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
 - N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
 - 20 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
 - N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1H-indol-6-yl)-acetamide;
 - 2-(4-Cyclobutoxy-phenyl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
 - 2-(4-Cyclopropoxy-phenyl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
 - 2-[6-(Cyclopropyl(methyl)amino)-pyridin-3-yl]-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
 - 25 2-[6-(Cyclopropylmethyl-methyl-amino)-pyridin-3-yl]-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
 - N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-methoxy-ethyl)-phenyl]-acetamide;
 - N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
 - N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1H-indol-5-yl)-acetamide;
 - 30 2-(6-Diethylamino-pyridin-3-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
 - N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
 - N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;

- N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3,3-trimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(3,3-dimethyl-2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
5 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-oxetan-3-yl-phenyl)-acetamide;
2-(4-Isopropyl-phenyl)-N-[2-(4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(4-Isopropyl-phenyl)-N-[2-(4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;
10 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide;
2-(3-Cyclopropyl-1H-indazol-5-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(1-Butyl-1H-indazol-5-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(2-methyl-1H-indol-5-yl)-acetamide;
2-(3-Butyl-1H-indazol-5-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
15 N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-isopropyl-1H-indazol-5-yl)-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-propyl-1H-indazol-5-yl)-acetamide;
2-(3-Cyclopropyl-1-methyl-1H-indazol-5-yl)-N-[2-(3,4-difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-pyrazolo[3,4-b]pyridin-5-yl)-acetamide;
N-[2-(3,4-Difluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(3-trifluoromethyl-1H-indazol-5-yl)-acetamide;
20 N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
25 N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Ethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
2-(6-Diethylamino-pyridin-3-yl)-N-[2-(3,4-dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(3,4-dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(3,4-dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
30 N-[2-(3,4-Dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(3,4-Dimethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
35 N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;

- N-[2-(4-Methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
2-(6-Diethylamino-pyridin-3-yl)-N-[2-(4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
5 2-(4-tert-Butyl-phenyl)-N-[2-(4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
10 2-(4-tert-Butyl-phenyl)-N-[2-(4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(4-Methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
15 N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
20 N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-yl)-phenyl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(3,5-difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
25 N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-(2-methoxy-ethoxy)-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-(2-Methoxy-ethoxy)-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-difluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
30 N-[2-(4-Difluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(1-Methyl-1H-indol-5-yl)-N-[2-(4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(1-Methyl-1H-indazol-5-yl)-N-[2-(4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-[4-(3-Methyl-oxetan-3-yl)-phenyl]-N-[2-(4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
35 2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(6-Diethylamino-pyridin-3-yl)-N-[2-(4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;

- 2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indol-5-yl)-acetamide;
5 N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-propyl-1H-indazol-5-yl)-acetamide;
10 N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide;
N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-6-yl)-acetamide;
N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
15 2-[4-(3,3-Difluoro-cyclobutylmethoxy)-phenyl]-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-
acetamide;
N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-
acetamide;
N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-
20 acetamide;
2-[4-(3,3-Difluoro-cyclobutoxy)-phenyl]-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-
acetamide;
N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
25 2-(1-Ethyl-1H-indazol-5-yl)-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(1,3-Dimethyl-1H-indol-5-yl)-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
30 N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-
acetamide;
N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-
acetamide;
35 2-[4-(3,3-Difluoro-cyclobutoxy)-phenyl]-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;

- 2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
- 2-(1-Ethyl-1H-indazol-5-yl)-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- 5 2-(1,3-Dimethyl-1H-indol-5-yl)-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- 2-(4-tert-Butyl-phenyl)-N-[2-(3-fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide;
- N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
- N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
- 10 N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
- N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide;
- N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
- N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
- N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
- 15 N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;
- N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
- N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(oxetan-3-ylmethoxy)-phenyl]-acetamide;
- N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
- N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
- 20 N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide;
- N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
- 2-[4-(3,3-Difluoro-cyclobutoxy)-phenyl]-N-[2-(3,5-difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- 25 N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
- N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
- N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;
- N-[2-(3,5-Difluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
- 30 N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
- N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
- N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
- N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
- N-[2-(4-Fluoro-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
- 35 N-[2-(3-Fluoro-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
- 2-[4-(Cyano-dimethyl-methyl)-phenyl]-N-[2-(4-cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;

- 2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-3-fluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-trifluoromethyl-phenyl)-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(5-fluoro-6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
5 N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-
10 acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
15 2-(4-tert-Butyl-phenyl)-N-[2-(3-cyano-4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3-Cyano-4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(3-Cyano-4-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-
20 acetamide;
N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide;
2-(4-tert-Butyl-phenyl)-N-[2-(4-difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
25 N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-
acetamide;
N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-
acetamide;
N-[2-(4-Difluoromethoxy-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
30 2-(4-tert-Butyl-phenyl)-N-[2-(3-fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-
35 acetamide;

- 2-[6-(3,3-Difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-N-[2-(3-fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- 2-(1-Ethyl-1H-indazol-5-yl)-N-[2-(3-fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- 2-(1,3-Dimethyl-1H-indazol-5-yl)-N-[2-(3-fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- 5 N-[2-(3-Fluoro-4-trifluoromethoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
- N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methyl-oxetan-3-ylmethoxy)-phenyl]-acetamide;
- N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide;
- N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
- N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
- 10 N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-1-methyl-cyclobutylmethoxy)-phenyl]-acetamide;
- N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
- N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
- N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide;
- 15 N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
- 2-(4-tert-Butyl-phenyl)-N-[2-(3-cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
- N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
- 20 N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
- N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
- N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
- N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
- 25 N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
- N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indazol-5-yl)-acetamide;
- N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
- N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
- 30 N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
- N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
- N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
- N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
- 2-(4-tert-Butyl-phenyl)-N-[2-(3-cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- 35 2-(4-tert-Butyl-phenyl)-N-[2-(3,4-difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;

- N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[6-(3,3-difluoro-pyrrolidin-1-yl)-pyridin-3-yl]-acetamide;
- N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-ethyl-1H-indazol-5-yl)-acetamide;
- N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
- 5 N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(4-isopropyl-phenyl)-acetamide;
- N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
- N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
- N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-6-yl)-acetamide;
- N-[2-(3-Cyano-4-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
- 10 N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
- N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
- N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-ylmethoxy)-phenyl]-acetamide;
- 15 2-[4-(3,3-Difluoro-cyclobutoxy)-phenyl]-N-[2-(3,4-difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- 2-[4-(1-Cyano-cyclopropyl)-phenyl]-N-[2-(4-cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- N-[2-(4-cyano-3-fluorobenzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(pentafluorosulfanyl)phenyl]acetamide;
- N-[2-(4-Cyano-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
- 20 N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1-methyl-1H-indazol-5-yl)-acetamide;
- N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-fluoro-oxetan-3-yl)-phenyl]-acetamide;
- N-[2-(3-Cyano-4-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;
- N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3-methoxy-oxetan-3-yl)-phenyl]-acetamide;
- N-[2-(4-Cyano-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutylmethoxy)-phenyl]-acetamide;
- 25 2-(4-tert-Butyl-phenyl)-N-[2-(4-cyano-3-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- N-[2-(3,4-Difluoro-5-methoxy-benzyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
- N-[2-(4-Cyano-3-methyl-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
- N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-[3-methyl-4-(2,2,2-trifluoro-ethoxy)-phenyl]-acetamide;
- 30 N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-(1,3-dimethyl-1H-indol-5-yl)-acetamide;
- 2-(4-tert-Butyl-phenyl)-N-[2-(5-cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-acetamide;
- N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(1-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;
- N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(3,3-difluoro-cyclobutoxy)-phenyl]-acetamide;
- 35 N-[2-(5-Cyano-pyridin-2-ylmethyl)-2H-[1,2,3]triazol-4-yl]-2-(5-fluoro-6-pyrrolidin-1-yl-pyridin-3-yl)-acetamide;

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N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenyl]-acetamide; and

N-[2-(4-Cyano-3-fluoro-benzyl)-2H-[1,2,3]triazol-4-yl]-2-[4-((1S*,2S*)-2-trifluoromethyl-cyclopropyl)-phenyl]-acetamide;

5 or a salt of such a compound.

10. A pharmaceutical composition containing, as active principle, a compound of formula (I) according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, and at least one therapeutically inert excipient.

11. A compound of formula (I) according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, for use as a medicament.
10

12. A compound of formula (I) according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, for use in the treatment or prevention of epilepsy; sleep disorders; sleep disturbances; pain; neurological disorders; cardiovascular disorders; cancer; diabetes; diabetic neuropathy; infertility; and sexual dysfunction.

15 13. Use of a compound of formula (I) according to any one of claims 1 to 9, 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.