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TRIAZOLE COMPOUNDS WITH DOPAMINE-D3-RECEPTOR AFFINITY

The invention relates to triazole compounds and to the use of these compounds. These compounds possess valuable therapeutic properties and can be used for treating diseases which respond to the influence of dopamine D_3 receptor ligands.

Compounds of the type which is under discussion here and which possess physiological activity are already known. Thus, WO 94/25013; 96/02520; 97/43262; 97/47602; 98/06699; 98/49145; 98/50363; 98/50364 and 98/51671 describe compounds which act on the dopamine receptors. DE 44 25 144 A, WO 96/30333 and WO 97/25324, WO 97/40015, WO 97/47602, WO 97/17326, EP 887 350, EP 779 284 A and Bioorg. & Med. Chem. Letters 9 (1999) 2059-2064 disclose further compounds which possess activity as domaine D_3 receptor ligands. US 4,338,453; 4,408,049 and 4,577,020 disclose triazole compounds which possess antiallergic or antipsychotic activity. WO 93/08799 and WO 94/25013 describe compounds of the type which is under discussion here and which constitute endothelin receptor antagonists. Additional triazole compounds, which inhibit blood platelet aggregation and which have a hypotensive effect are described in *Pharmazie* 46 (1991), 109-112. EP 691 342, EP 556 119, WO 97/10210, WO 98/24791, WO 96/31512 and WO 92/20655 disclose further triazole compounds which possess physiological activity.

Neurons obtain their information by way of G protein-coupled receptors, inter alia. There are a large number of substances which exert their effect by way of these receptors. One of them is dopamine.

A number of facts about the presence of dopamine, and its physiological function as a neuron transmitter, are known with certainty. Disturbances of the dopaminergic transmitter system result in diseases such as schizophrenia, depression and Parkinson's disease. These, and other, diseases are treated with drugs which interact with the dopamine receptors.

By 1990, two subtypes of dopamine receptor had been clearly defined pharmacologically, namely the D_1 and D_2 receptors.

More recently, a third subtype has been found, namely the D_3 receptor, which appears to mediate some of the effects of the antipsychotic and anti-Parkinson agents (J.C. Schwartz et al., The Dopamine D_3 Receptor as a Target for Antipsychotics, in Novel Antipsychotic Drugs, H.Y. Meltzer, Ed. Raven Press, New York

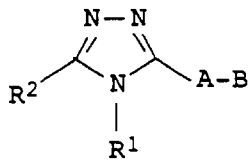
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1992, Seiten 135-144; M. Dooley et al., Drugs and Aging 1998, 12, 495-514).

Since D_3 receptors are chiefly expressed in the limbic system, it is assumed that while a selective D_3 ligand would probably have the properties of known antipsychotic agents, it would not have their dopamine D_3 receptor-mediated neurological side-effects (P. Sokoloff et al., Localization and Function of the D_3 Dopamine Receptor, Arzneim. Forsch./Drug Res. 42(1), 224 (1992); P. Sokoloff et al. Molecular Cloning and Characterization of a Novel Dopamine Receptor (D_3) as a Target for Neuroleptics, Nature, 347, 146 (1990)).

Surprisingly, it has now been found that certain triazole compounds exhibit a high affinity for the dopamine D_3 receptor and a low affinity for the D_2 receptor. These compounds are consequently selective D_3 ligands.

The present invention relates, therefore, to the compounds of the formula I:



(I)

where

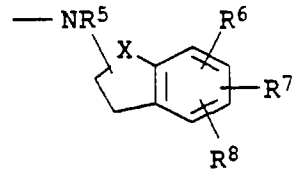
R^1 is H, C_1-C_6-alkyl, which may be substituted by OH, OC_1-C_6-alkyl, halogen or phenyl, C_3-C_6-cycloalkyl or phenyl;

R^2 is H, C_1-C_6-alkyl, which may be substituted by OH, $0C_1$-C_6-alkyl, halogen or phenyl, C_1-C_6-alkoxy, C_1-C_6-alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, halogen, CN, $COOR^3$, $CONR^3R^4$, NR^3R^4, SO_2R^3, $SO_2NR^3R^4$,or an aromatic radical which is selected from phenyl, naphthyl and a 5- or 6-membered heterocyclic radical having 1, 2, 3 or 4 heteroatoms which are selected, independently of each other, from O, N and S, with it being possible for the aromatic radical to have one or two substituents which are selected, independently of each other, from C_1-C_6-alkyl, which may be substituted by OH, OC_1-C_6-alkyl, halogen or phenyl, C_1-C_6-alkoxy, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, halogen, CN, COR^3, NR^3R^4, NO_2, SO_2R^3, $SO_2NR^3R^4$ and phenyl which may be substituted by one or two radicals which are selected, independently of each other, from C_1-C_6-alkyl, C_1-C_6-alkoxy, NR^3R^4, CN, CF_3, CHF_2 or halogen;

R^3 and R^4 are, independently of each other, H, C_1-C_6-alkyl, which may be substituted by OH, OC_1-C_6-alkyl, halogen or phenyl, or phenyl;

A is C_4-C_{10}-alkylene or C_3-C_{10}-alkylene which comprises at least one group Z which is selected from O, S, $CONR^3$, COO, CO, C_3-C_6-cycloalkyl and a double or triple bond;

B is a radical of the following formula:



where

X is CH_2 or CH_2CH_2;

R^5 is H, C_1-C_6-alkyl, which may be substituted by OH, OC_1-C_6-alkyl, halogen or phenyl, C_3-C_6-cycloalkyl, C_2-C_6-alkenyl, which may be substituted by halogen (1 or 2 halogen atoms), or C_2-C_6-alkynyl;

R^6, R^7 and R^8 are, independently of each other, selected from H, C_1-C_6-alkyl, which may be substituted by OH, OC_1-C_6-alkyl, C_1-C_6-alkylthio, halogen or phenyl, OH, C_1-C_6-alkoxy, SH, C_1-C_6-alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, halogen, CN, NO_2, SO_2R^3, $SO_2NR^3R^4$, $CONR^3R^4$, $NHSO_2R^3$ and NR^3R^4;

and the salts thereof with physiologically tolerated acids.

The compounds according to the invention are selective dopamine D_3 receptor ligands which act in the limbic system in a regioselective manner and which, as a result of their low affinity for the D_2 receptor, have fewer side-effects than do the classic neuroleptic agents, which are D_2 receptor antagonists. The compounds can therefore be used for treating diseases which respond to dopamine D_3 ligands, i.e. they are effective for treating those diseases in which affecting (modulating) the dopamine D_3 receptors leads to an improvement in the clinical picture or to the disease being cured. Examples of such diseases are diseases of the cardiovascular system and the kidneys, diseases of the central nervous system, in particular schizophrenia, affective disturbances, neurotic stress and somatoform disturbances, psychoses, Parkinson's, attention disturbances (attention deficit disorder), hyperactivity in children, epilepsy, amnestic and cognitive disturbances, such as learning and memory impairment (impaired cognitive function), anxiety states, dementia, delerium, personality disturbances,

sleep disturbances (e.g. restless legs syndrome), disturbances in sex life (male impotence), eating disturbances and addiction disorders. In addition, they are suitable for treating stroke.

Addiction disorders include the psychic disturbances and behavioral disturbances which are caused by the abuse of psychotropic substances, such as pharmaceutical or drugs, and also other addition disorders such as gambling addiction (impulse control disorders not elsewhere classified). Examples of addiction-producing substances are: opioids (e.g. morphine, heroin and codeine); cocaine; nicotine; alcohol; substances which interact with the BAGA-chloride channel complex, sedatives, hypnotics and tranquilizers, for example benzodiazepines; LSD; cannabinoids; psychomotor stimulants, such as 3,4-methylenedioxy-N-methylamphetamine (ecstasy); amphetamine and amphetamine-like substances, such as methylphenidate or other stimulants including caffeine. Opioids, cocaine, amphetamine or amphetamine-like substances, nicotine and alcohol come into consideration, in particular, as addiction-producing substances.

The compounds according to the invention are preferably employed for treated affective disturbances; neurotic, stress and somatoform disturbances and psychoses, e.g. schizophrenia.

Within the context of the present invention, the following expressions have the meanings given in conjunction with them:

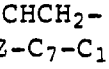
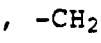
Alkyl (also in radicals such as alkoxy, alkylthio, alkylamino etc.) is a straight-chain or branched alkyl group having from 1 to 6 carbon atoms and, in particular from 1 to 4 carbon atoms. The alkyl group can have one or more substituents which are selected, independently of each other, from OH, OC_1-C_6-alkyl, halogen or phenyl. In the case of a halogen substituent, the alkyl group can, in particular, encompass, 1, 2, 3 or 4 halogen atoms which can be located on one or more C atoms, preferably in the a or ẅ position. CF_3, CHF_2, CF_2Cl or CH_2F are particularly preferred.

Examples of an alkyl group are methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, t-butyl, etc.

Cycloalkyl is, in particular, C_3-C_6-cycloalkyl, such as cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl.

Alkylene radicals are straight-chain or branched. If A does not have a group Z, A then comprises from 4 to 10 carbon atoms, preferably from 4 to 8 carbon atoms. The chain between the

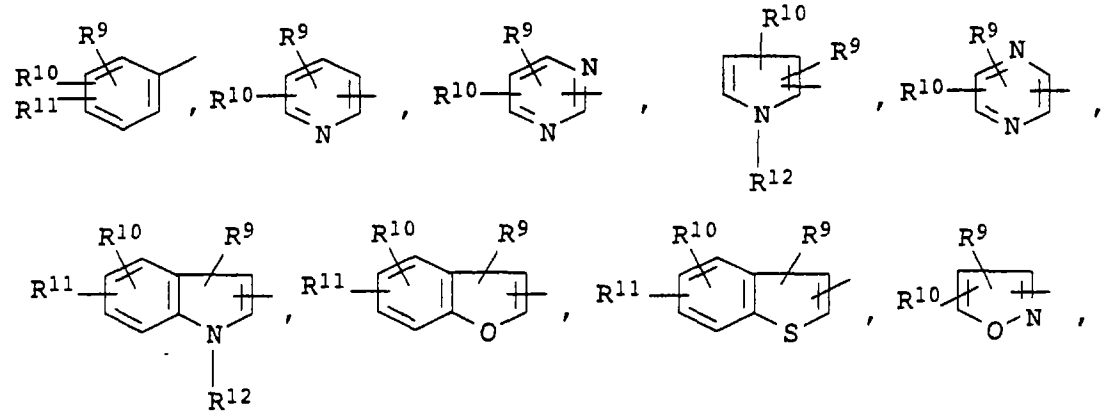
triazole nucleus and group B then has at least four carbon atoms. If A has at least one of said Z groups, A then comprises from 3 to 10 carbon atoms, preferably from 3 to 8 carbon atoms.

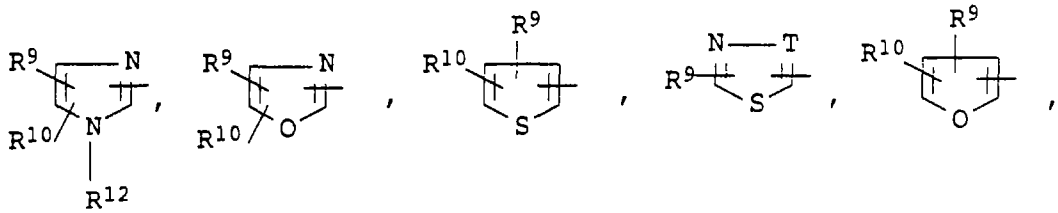
If the alkylene groups comprise at least one of the Z groups, this or these groups can then be arranged in the alkylene chain at an arbitrary site or in position 1 or 2 of the A group (seen from the triazole radical). The radicals $CONR^2$ and COO are preferably arranged such that the carbonyl group is in each case facing the triazole ring. Particular preference is given to the compounds of the formula I in which A is -Z-C_3-C_6-alkylene, in particular -Z-$CH_2CH_2CH_2$-, -Z-$CH_2CH_2CH_2CH_2$-, -Z-CH_2CH=$CHCH_2$-, -Z-$CH_2C(CH_3)$=$CHCH_2$-, —Z—CH_2——CH_2— , -Z-$CH_2CH(CH_3)CH_2$- or a linear -Z-C_7-C_{10}-alkylene radical, with Z being bonded to the triazole ring. Z is preferably CH_2, O and, in particular, S. Preference is additionally given to A being -$(CH_2)_4$-, -$(CH_2)_5$-, -CH_2CH_2CH=$CHCH_2$-, —CH_2——CH_2—, -$CH_2CH_2C(CH_3)$=$CHCH_2$- or -$CH_2CH_2CH(CH_3)CH_2$-.

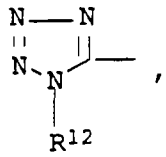
Halogen is F, Cl, Br or I, preferably F or Cl.

R^1 is preferably H, C_1-C_6-alkyl or C_3-C_6-cycloalkyl.

If R^2 is an aromatic radical, this radical is then preferably one of the following radicals:





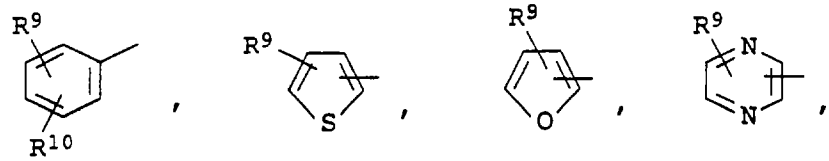


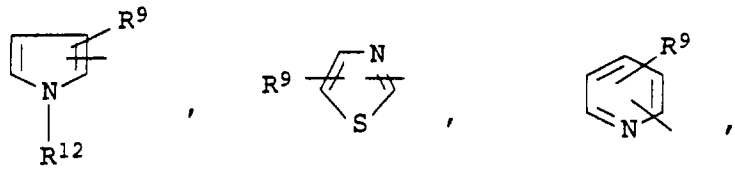
where

R^9 to R^{11} are H or the abovementioned substituents of the aromactic radical,
R^{12} is H, C_1-C_6-alkyl or phenyl, and
T is N or CH.

If the phenyl radical is substituted, the substituents are preferably in the m position or the p position.

The aromatic radical is particularly preferably a group of the formula:





where R^9, R^{10} and R^{12} have the abovementioned meanings. The indicated phenyl, pyridinyl, thiazolyl and pyrrole radicals are particularly preferred.

The radicals R^9 to R^{11} are preferably H, C_1-C_6-alkyl, OR^3, CN, phenyl, which may be substituted by C_1-C_6-alkyl, C_1-C_6-alkoxy or halogen, CF_3 and halogen, and are, in particular, H, C_1-C_6-alkyl, OR^3 and halogen. In this context, R^3 has the abovementioned meanings.

Particularly preferably, R^2 is H, C_1-C_6-alkyl, NR^3R^4 (R^3 and R^4 are, independently of each other, H or C_1-C_6-alkyl), phenyl or a 5-membered aromatic heterocyclic radical which has 1 or 2 heteroatoms which are independently selected from N, S and O. The heterocyclic radical is preferably a pyrrole radical or a pyridine radical.

In the radical B, X is preferably CH_2CH_2.

Preferably, at least one of the radicals R^6, R^7 and R^8 is H.

The radicals R^6, R^7 and R^8 are preferably, and independently of each other, selected from H, C_1-C_6-alkyl, halosubstituted C_1-C_6-alkyl, OH, C_1-C_6-alkoxy, C_1-C_6-alkylthio-C_1-C_6-alkyl, halogen, NO_2, CN, SO_2R^3, $SO_2NR^3R^4$ and $CONR^3R^4$. Particularly preferably, the fused phenyl group has one or two substituents, i.e. one or two of the radicals R^6, R^7 and R^8 is/are C_1-C_6-alkyl, halogen, CN, $SO_2NR^3R^4$, NO_2 or CF_3.

Particular preference is given to the compounds of formula I where

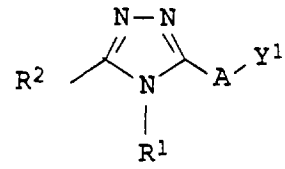
R^1 is H, C_1-C_6-alkyl or phenyl,
R^2 is H, C_1-C_6-alkyl, phenyl, thienyl, furanyl, pyridyl, pyrrolyl, thiazolyl or pyrazinyl,
A is -SC_3-C_{10}-alkylene which can comprise a double bond or C_3-C_6-cycloalkyl, and
R^6, R^7 and R^8 selected from H, C_1-C_6-alkyl, C_1-C_6-alkoxy, halogen, $SO_2NR^3R^4$, CN, NO_2 or CF_3.

The invention also encompasses the acid addition salts of the compounds of the formula I with physiologically tolerated acids. Examples of suitable physiologically tolerated organic and inorganic acids are hydrochloric acid, hydrobromic acid, phosphoric acid, sulfuric acid, oxalic acid, maleic acid, fumaric acid, lactic acid, tartaric acid, adipic acid or benzoic acid. Other acids which can be used are described in Fortschritte der Arzneimittelforschung [Advances in pharmaceutical research], Volume 10, pages 224 ff., Birkhäuser Verlag, Basle and Stuttgart, 1966.

The compounds of the formula I can exhibit one or more centers of asymmetry. The invention therefore includes not only the racemates but also the relevant enantiomers and diastereomers. The respective tautomeric forms are also included in the invention.

The process for preparing the compounds of the formula I consist in

a) reacting a compound of the formula (II)



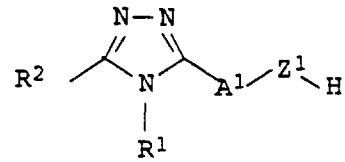
(II)

where Y^1 is a customary leaving group, such as Hal, alkylsulfonyloxy, arylsulfonyloxy, etc., with a compound of the formula (III)

$$HB \qquad (III);$$

or

b) reacting a compound of the formula (IV)



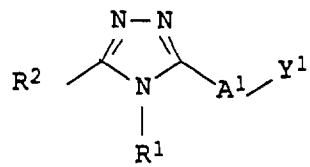
(IV)

where Z^1 is O or S, and A^1 is C_1-C_{10}-alkylene or a bond, with a compound of the formula (V)

$$Y^1 - A^2 - B \qquad (V)$$

where Y^1 has the abovementioned meaning and A^2 is C_2-C_{10}-alkylene, with A^1 and A^2 together having from 3 to 10 C atoms and A^1 and/or A^2 where appropriate comprising at least one group Z; or

c) reacting a compound of the formula (VI)



(VI)

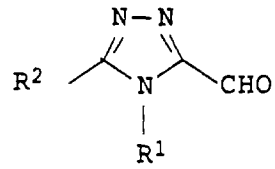
where Y^1 and A^1 have the abovementioned meanings, with a compound of the formula (VII)

$$H - Z^1 - A - B \qquad (VII)$$

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where Z^1 has the abovementioned meanings; or

d) reversing the polarity of a compound of the formula (VIII)

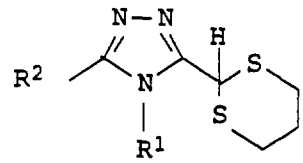


(VIII)

using reagents which are known from the literature, such as 1,3-propanedithiol, KCN/water, TMSCN (trimethylsilyl cyanide) or KCN/morpholine, as described, for example, in

Albright *Tetrahedron*, **1983**, 39, 3207 or
D. Seebach *Synthesis* **1969**, 17 und **1979**, 19 or
H. Stetter *Angew. Chem. Int. Ed.* **1976**, 15, 639 or
van Niel et al. *Tetrahedron* **1989**, 45, 7643
Martin et al. *Synthesis* **1979**, 633,

to give the products (VIIIa) (using 1,3-propanedithiol by way of example)



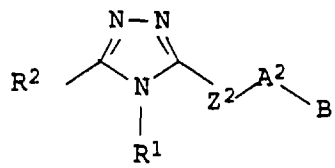
(VIIIa)

and then chain-elongating with compounds of the formula (IX)

$$Y^1 - A^3 - B \qquad \text{(IX)}$$

where Y^1 has the abovementioned meaning and A^3 is C_3-C_9-alkylene which can contain a group Z,

with compounds of the formula (Ia)



(Ia)

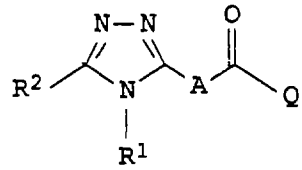
where Z^2 is CO or a methylene group, and Z^2 and A^2 have together from 4 to 10 C atoms, being obtained after deprotecting or reducing, or

e) reacting a compound of the formula (VIII) with a compound of the formula (X)

$$Y^2 - A - B \qquad (X)$$

where Y^2 is a phosphorane or a phosphonic ester, in analogy with customary methods, as described, for example, in Houben Weyl *"Handbuch der Organischen Chemie"* [Textbook of Organic Chemistry], 4th Edition, Thieme Verlag Stuttgart, Volume V/1b p. 383 ff, or Vol. V/1c p. 575 ff, or

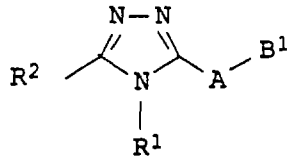
f) reacting a compound of the formula (XI)



(XI)

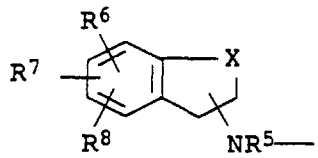
where Q is H or OH, with a compound of the formula III under reductive conditions in analogy with methods known from the literature, for example as described in *J. Org. Chem.* **1986**, 50, 1927; or WO 92/20655, or

g) in order to prepare a compound of the formula (Ib)



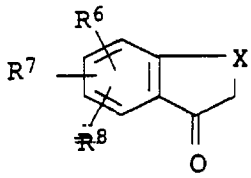
(Ib)

where B^1 is a radical of the formula (XII)

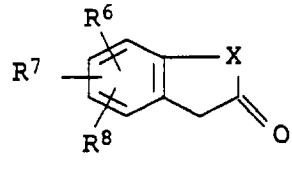


(XII),

reacting compounds of the formula (XIII) or (XIV),

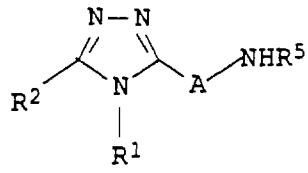


(XIII),



(XIV)

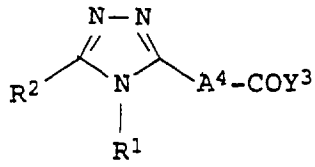
with a compound of the formula (XV)



(XV)

under reductive conditions.

The process for preparing a compound of the formula I where A comprises the groups COO or $CONR^3$ consists in reacting a compound of the formula (XVI)



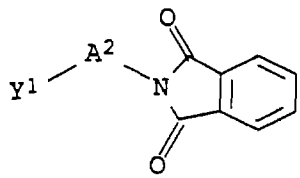
(XVI)

where Y^3 is OH, OC_1-C_4-alkyl, Cl or, together with CO, an activated carboxyl group, and A^4 is C_0-C_9-alkylene, with a compound of the formula (XVII)

$$B - A - Z^3 \qquad \text{(XVII)}$$

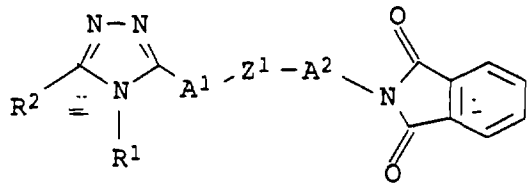
where Z^3 is OH or NHR^3.

Compounds of the type (XV) can be synthesized by alkylating compounds of the formula (IV) with compounds of the formula (XVIII),



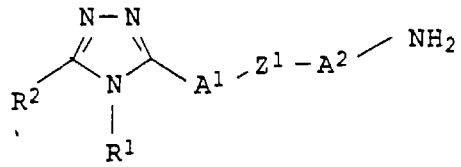
(XVIII)

to give compounds of the formula (XIX),



(XIX)

subsequently carrying out hydrazinolysis to give compounds of the type (XX)



(XX)

and then introducing the radical R^5, by, for example, effecting a reductive amination (as described, for example, in *J. Org. Chem.* **1986**, 50, 1927) using the corresponding aldehyde or by means of alkylation in the presence of a base.

Compounds of the formula XX can also be obtained by reacting compounds of the formula II with azides, such as sodium azide, and then reducing, as described, for example, in H. Staudinger, *Helv. Chim. Acta* ***1919***, 2, 635 or R. Carrie, *Bull. Chem. Soc. Fr.* **1985**, 815.

Compounds of the formula XIII and XIV are known from the literature or can be prepared using known methods, as described, for example, in

A. van Vliet et al. *J. Med. Chem.* **1996**, 39, 4233
M. Langlois *Bioorg. Med. Chem. Lett.* **1993**, 3, 2035
U. Hacksell *J. Med. Chem.* **1993**, 36, 4221
or in WO 93/08799 or WO 95/04713.

The compounds of the formula (IV) type are either known or can be prepared using known methods, as described, for example, in A.R. Katrizky, C.W. Rees (ed.) "Comprehensive Heterocyclic Chemistry", Pergamon Press, or "The Chemistry of Heterocyclic Compounds" J. Wiley & Sons Inc. NY and the literature which is cited therein, or in S. Kubota et al. *Chem. Pharm. Bull.* **1975**, 23, 955 or Vosilevskii et al. Izv. Akad. Nauk. SSSR Ser. Khim. **1975**, 23, 955.

In the above formulae, R^1, R^2, R^5, R^6, R^7, R^8, A, B and X have the meanings given in connection with formula I.

The compounds according to the invention, and the starting materials and the intermediates, can also be prepared in analogy with the methods which are described in the patent publications which were mentioned at the outset.

The above-described reactions are generally effected in a solvent at temperatures of between room temperature and the boiling temperature of the solvent employed. Examples of solvents which can be used are esters, such as ethyl acetate, ethers, such as diethyl ether or tetrahydrofuran, dimethylformamide, dimethyl sulfoxide, dimethoxyethane, toluene, xylene, acetonitrile, ketones, such as acetone or methyl ethyl ketone, or alcohols, such as ethanol or butanol.

If desired, the reactions can be carried out in the presence of an acid-binding agent. Suitable acid-binding agents are inorganic bases, such as sodium carbonate or potassium carbonate, or sodium hydrogencarbonate or potassium hydrogencarbonate, sodium methoxide, sodium ethoxide, sodium hydride, or organometallic compounds, such as butyl lithium or alkyl magnesium compounds, or organic bases, such as triethylamine or pyridine. The latter can also simultaneously serve as the solvent.

Processes (f) and (g) are effected under reducing conditions, e.g. using sodium borohydride, sodium cyanoborohydride or triacetoxy borohydride, where appropriate in an acid medium or in the presence of a Lewis acid, such as zinc chloride, or by way of catalytic hydrogenation.

The crude product is isolated in a customary manner, for example by means of filtering, distilling off the solvent or extracting from the reaction mixture, etc. The resulting compounds can be purified in a customary manner, for example by recrystallization from a solvent, by chromatography or by converting into an acid addition compound.

The acid addition salts are prepared in a customary manner by mixing the free base with the corresponding acid, where appropriate in solution in an organic solvent, for example a lower alcohol, such as methanol, ethanol or propanol, an ether, such as methyl tert-butyl ether, a ketone, such as acetone or methyl ethyl ketone, or an ester, such as ethyl acetate.

For treating the abovementioned diseases, the compounds according to the invention are administered orally or parenterally (subcutaneously, intravenously, intramuscularly or intraperitoneally) in a customary manner. The administration can also be effected through the nasopharyngeal space using vapors or sprays.

The dosage depends on the age, condition and weight of the patient and on the type of administration. As a rule, the daily

dose of active compound is from about 10 to 1000 mg per patient and day when administered orally and from about 1 to above 500 mg per patient and day when administered parenterally.

The invention also relates to pharmaceuticals which comprise the compounds according to the invention. In the customary pharmacological administration forms, these pharmaceuticals are present in solid or liquid form, for example as tablets, film tablets, capsules, powders, granules, sugar-coated tablets, suppositories, solutions or sprays. In this context, the active compounds can be worked up together with the customary pharmacological auxiliary substances, such as tablet binders, fillers, preservatives, tablet disintegrants, flow-regulating agents, plasticizers, wetting agents, dispersants, emulsifiers, solvents, retarding agents, antioxidants and/or propellent gases (cf. H. Sucker et al., Pharmazeutische Technologie, Thieme-Verlag, Stuttgart, 1978). The resulting administration forms normally comprise the active compound in a quantity of from 1 to 99% by weight.

The following examples serve to explain the invention without limiting it.

Examples

Example 1
3-[3-(N-(Indan-2-yl)propylamino)propylmercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole fumarate

1A Preparation of the starting compounds
1A1 2-N-Propylaminoindan
18.8 g (300 mmol) of sodium cyanoborohydride were added to a mixture of 20 g (150 mmol) of 2-aminoindan, 40.9 g (300 mmol) of zinc dichloride and 10.4 g (180 mmol) of propionaldehyde in 550 ml of methanol, and the whole was heated to boiling for 3.5 hours. For the working up, 460 ml of 1M sodium hydroxide solution was added to the mixture and this new mixture was extracted several times with ethyl acetate. The combined organic phases were washed with a saturated solution of sodium chloride and dried, and the solvent was removed under reduced pressure. Chromatographic purification of the crude product (silica gel, methylene chloride/methanol = 9/1) yielded 7.8 g of a pale brown oil.
Yield: 7.8 g (30% of theory)
^{1}H-NMR (DMSO-D_6): 0.9 (t,3H); 1.4 (m, 2H); 2.5-2.7 (m,4H); 3.0-3.1 (m, 2H); 3.3 (sbr, NH); 3.5 (m, 1H).

1A2 2-(N-(3-Chloropropyl)propylamino)indan

7.6 g (44 mmol) of 2-N-propylaminoindan were heated to boiling in 100 ml of acetonitrile, for 4 hours under reflux, together with 17.1 g (109 mmol) of 1-bromo-3-chloropropane, 9.0 g (138 mmol) of potassium carbonate and 3.3 g (150 mmol) of sodium iodide. The mixture was then filtered with suction through Celite, after which the solvent was evaporated under reduced pressure; the crude product was then used for the subsequent reaction.

1B Preparation of the end product

6.1 g (26 mmol) of 3-mercapto-4-methyl-5-phenyl-1,2,4(4H)-triazole (prepared by the method of Kubota et al., Chem. Pharm. Bull 1975, 23, 955) and 9.6 g (38 mmol) of the crude product obtained in 1A2 were heated, together with 2.8 g (19 mmol) of lithium hydroxide, at 80°C for 2.5 hours, and with stirring, in 100 ml of DMF (dimethylformamide). The solvent was subsequently distilled off under reduced pressure and 500 ml of a saturated solution of sodium hydrogen carbonate were added to the residue; this mixture was then extracted several times with methyl tert-butyl ether and ethyl acetate. After drying and evaporating, 9.5 g of an oil remained, with this oil being purified by column chromatography (methylene chloride containing 0-3% methanol).

$C_{24}H_{30}ON_4S$ (406) MS (m/z): 407 $[M+H]^+$

0.71 g of substance was isolated as the fumarate after precipitating in isopropanol/methyl *tert*-butyl ether.
^{1}H-NMR ($CDCl_3$): 0.9 (t, 3H); 1.5 (m, 2H); 1.9 (q, 2H); 2.6-3.2 (m, 10H); 3.5 (s, 3H); 3.6 (m, 1H); 6.6 (s, 2H); 7.2 (m, 4H); 7.5(m, 3H); 7.7 (m, 2H).

Example 2:

3-[3-(N-(6-Methoxyindan-1-yl)propylamino)propylmercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole

6-Methoxy-1-propylaminoindan was obtained by the reductive amination of 6-methoxyindan-1-one with n-propylamine in the presence of zinc dichloride and sodium cyanoborohydride in methanol, as described in 1A1. After conversion into the chloropropyl compound, as described in 1A2, this latter was reacted with 3-mercapto-4-methyl-5-phenyl-1,2,4(4H)-triazole, in analogy with 1B, with the compound of Example 2 being obtained.

$C_{25}H_{32}N_4OS$ (436) MS (m/z): 436 $[M+H^+]^+$

^{1}H-NMR ($CDCl_3$): 0.8 (t, 3H); 1.5 (m, 2H); 1.9 (m, 3H); 2.0 (m, 1H); 2.45-2.9 (m, 6H); 3.2 (m, 1H), 3.3 (m, 1H); 3.6 (s, 3H); 3.7 (s, 3H); 4.6 (t, 1H); 6.8 (dd, 1H); 6.9 (d, 1H); 7.1 (d, 1H); 7.6 (m, 3H); 7.75 (m, 2H).

Example 3

3-[3-(6-Methylmercaptomethyl-1,2,3,4-tetrahydronaphth-2-ylamino)-propylmercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole

3A Preparation of the starting compound

3-(3-Aminopropylmercapto)-4-methyl-5-phenyl-1,2,4(4H)-triazole

3-Mercapto-4-methyl-5-phenyl-1,2,4(4H)-triazole (11.8 g, 50 mmol) was heated, together with 13.8 g (50 mmol) of N-(3-bromopropyl)phthalimide and 1.2 g (50 mmol) of lithium hydroxide, at 100°C for 3.5 hours, in 150 ml of DMF. After the mixture had cooled down, 1 l of water was added and this new mixture was extracted several times with methylene chloride; the organic phase was then dried and evaporated. 14.5 g (75% of theory) of 3-[4-methyl-5-phenyl-3-phthalimidopropylmercapto]-1,2,4(4H)-triazole were obtained.

14.5 g (38 mmol) of the above-described compound were reacted with 2.3 ml (46 mmol) of hydrazine hydrate in ethanol, and 9.7 g (39 mmol) of 3-(3-aminopropylmercapto-4-methyl-5-phenyl-1,2,4(4H)-triazole were isolated.

Yield: 9.7 (quantitative)

^{1}H-NMR ($CDCl_3$): 1.6 sbr, 2H); 2.0 (q, 2H); 2.9 (t, 2H); 3.4 (t, 2H); 3.6 (s, 3H); 7.5 (m, 3H); 7.7 (m, 2H).

3B Preparation of the end product

1.0 g (4 mmol) of the compound described in 3A was initially introduced in 15 ml of methanol; 6-methyl-mercaptomethyltetral-2-one (prepared in accordance with EP 96/01238) (1.0 g, 4.7 mmol), dissolved in 10 ml of methanol, was added, and 0.5 g of sodium cyanoborohydride was introduced in portions. The mixture was heated to boiling for 6 hours. After it had cooled down, 25 ml of 1M sodium hydroxide solution were added and the whole was extracted several times with ethyl acetate. After washing with water, drying and evaporating, the residue was purified by column chromatography on silica gel (eluent: methylene chlorie/methanol = 9/1).

Yield: 0.56 g (32% of theory)

$C_{24}H_{30}N_4S_2$ (438) MS (m/z): 439 $[M+H]^+$

The compounds below were prepared in an analogous manner using the cyclic ketones mentioned:

Example 4
3-[3-(6-Methyl-1,2,3,4-tetrahydronaphth-2-ylamino)propyl-mercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole,
obtained by the analogous reaction of 6-methyltetral-2-one with 3-(3-aminopropylmercapto)4-methyl-5-phenyl-1,2,4(4H)-triazole.
^{1}H-NMR ($CDCl_3$): 1.5-1.6 (mbr, 3H); 2.0 (m, 3H); 2.3 (m, 1H); 2.7-3.0 (m, 7H); 3.4 (t, 3H); 3.6 (s, 3H); 6.8-7.0 (m, 3H); 7.5 (m, 3H); 7.7 (m, 2H).

$C_{23}H_{28}N_4S$ (392)
m.p.: 69-73°C

Example 5
3-[3-(6-Bromo-1,2,3,4-tetrahydronaphth-2-ylamino)propyl-mercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole,
obtained by the analogous reaction of 6-bromotetral-2-one with 3-(3-aminopropylmercapto)-4-methyl-5-phenyl-1,2,4(4H)-triazole.
^{1}H-NMR ($CDCl_3$): 2.1 (m, 1H); 2.5-2.9 (m, 5H); 3.2 (m, 1H); 3.3-3.7 (m,9H); 6.8 (m, 1H); 7.2 (m, 2H); 7.5 (m, 3H); 7.6 (m, 2H).

$C_{22}H_{25}BrN_4S$ (457) MS (m/z): 458 $[M+H]^+$

Example 6
3-[3-(1,2,3,4-Tetrahydronaphth-1-ylamino)propylmercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole hydrochloride

$C_{22}H_{26}N_4S$ (378.5) MS (m/z): 379 $[M+H]^+$

In order to precipitate the hydrochloride, the compound was dissolved in ether/isopropanol, and ethereal hydrochloride acid was then added to the solution while cooling in ice.

$C_{22}H_{26}N_4S$ x HCl
m.p.: 125°C (decomp.)

Example 7
3-[3-(7-Methoxy-1,2,3,4-tetrahydronaphth-2-ylamino)propyl-mercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole,
obtained by the analogous reaction of 7-methoxytetral-2-one with 3-(3-aminopropylmercapto)-4-methyl-5-phenyl-1,2,4(4H)-triazole.
^{1}H-NMR ($CDCl_3$): 1.5 (m, 1H); 2.0 (m, 3H); 2.5 (m,1H); 2.8-3.0 (m, 7H); 3.3 (t, 2H); 3.6 (s, 3H); 3.8 (s, 3H); 6.6 (d, 1H); 6.7 (dd, 1H); 7.0 (d, 1H); 7.5 (m,3H); 7.7 (m,2H).

$C_{23}H_{28}N_4OS$ (408) - MS (m/z) = 408 $[M]^+$ -

Example 8
3-[3-(6-Methoxyindan-1-ylamino)propylmercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole
obtained in analogy with Example 1, starting from 6-methoxyindan-1-one.

$C_{22}H_{26}N_4OS$ (394) MS (m/z): 395 $[M+H]^+$
^{1}H-NMR (DMSO-d_6): 2.1 (m, 3H); 2.4 (m, 1H); 2.75 (m, 1H); 3.0 (m, 3H); 3.3 (t, 2H); 3.6 (s, 3H); 3.8 (s, 3H); 4.7 (t, 1H); 6.5 (s,2H); 6.9 (dd, 1H); 7.2 (d, 1H); 7.25 (d, 1H); 7.5 (m, 3H); 7.7 (m, 2H).

Example 9
3-[3-(5,6-Dimethoxyindan-1-ylamino)propylmercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole hydrochloride,
obtained by the reaction of 5,6-dimethoxyindan-1-one with 3-(3-aminopropylmercapto)-4-methyl-5-phenyl-1,2,4(4H)-triazole in analogy with 3B, and subsequent precipitation of the salt with ethereal HCl.

$C_{23}H_{28}N_4O_2S$ x HCl (461.1)
m.p: 201-202°C
^{1}H-NMR ($CDCl_3$): 2.2-2.5 (m, 4H); 2.8 (m, 1H); 3.2-3.3 (m, 2H); 3.4 (t, 2H); 3.6 (s, 3H); 3.8 (s, 3H); 3.9 (s, 3H); 4.6 (m, 1H); 6.7 (s,1H); 7.0 (br, 2H); 7.4 (s, 1H); 7.6 (m, 5H).

Example 10
5-Amino-3-[3-(1,2,3,4-tetrahydronaphth-1-ylamino)propylmercapto]-4-methyl-1,2,4(4H)-triazole hydrochloride

10A Preparation of the starting compound
N-(3-Chloropropyl)-1,2,3,4-tetrahydronaphthyl-1-amine
5.0 g (34 mmol) of 1,2,3,4-tetrahydronaphth-1-ylamine were dissolved, together with 6.4 g (40 mmol) of 1-bromo-3-chloro-propane and 5.2 g (50 mmol) of triethylamine, in 50 ml of THF and the solution was heated to boiling for 16 h. The solvent was then distilled off and the residue was dissolved in methylene chloride; this solution was washed twice with water, dried and concentrated. The crude product was purified by chromatography on silica gel (eluent: methylene chloride/methanol = 97/3), and 3.4 g of a yellowish oil were isolated.
Yield: 3.4 g (44% of theory)
^{1}H-NMR ($CDCl_3$): 1.1 (sbr, NH); 1.7-2.0 (m, 6H); 2.6-3.0 (m, 4H); 3.6-3.8 (m, 3H); 7.0-7.4 (m, 4H).

$C_{13}H_{18}ClN$ (223.8)

10B Preparation of the end product

670 mg (3 mmol) of the above-described chlorine compound were dissolved, together with 390 mg (3 mmol) of 5-amino-3-mercapto-4-methyl-1,2,4(4H)-triazole and 72 mg (3 mmol) of lithium hydroxide, in 9 ml of DMF and the solution was stirred at 100°C for four hours. Water was added and the whole was extracted three times with methyl *tert*-butyl ether. After the combined organic phases had been dried over sodium sulfate and concentrated, the resulting crude product was purified by chromatography on silica gel (eluent: methylene chloride containing 3-5% methanol).

Yield: 460 mg (48% of theory)

$C_{16}H_{23}N_5S$ (317.5)

Precipitation of the hydrochloride in ethereal hydrochloric acid yielded the title compound as a white solid.

$C_{16}H_{23}N_5S \times HCl$ (352.9)

m.p: 140°C (decomp.)

Example 11

5-Amino-3-({2-[(1,2,3,4-tetrahydronaphth-1-ylamino)-2-methyl]-prop-2-enyl}mercapto)-4-methyl-1,2,4(4H)-triazole hydrochloride

11A Preparation of the starting compound

1-(3-Chloro-2-methylenepropyl)-1,2,3,4-tetrahydronaphthyl-1-amine

5.0 g (34 mmol) of 1,2,3,4-tetrahydronaphth-1-ylamine were dissolved, together with 5.1 g (41 mmol) of 1,3-dichloro-2-methylenepropane and 5.2 g (51 mmol) of triethylamine, in 50 ml of THF and the solution was heated to boiling for 24 h. The solvent was then distilled off and the residue was dissolved in methylene chloride; this solution was washed twice with water, dried and concentrated. The crude product was purified by chromatography on silica gel (eluent: methylene chloride/methanol = 97/3), and 2.6 g of a yellowish oil were isolated.

Yield: 2.6 g (33% of theory)

^{1}H-NMR ($CDCl_3$): 1.3 (m, 1H); 1.7-2.0 (m, 4H); 2.6-2.9 (m, 2H); 3.4 (m, 2H); 3.7 (m, 1H); 4.2 (m, 2H); 5.2 (m, 2H); 7.2 (m, 3H); 7.4 (m, 1H).

11B Preparation of the end product

0.6 g (2.6 mmol) of the above-described chlorine compound was dissolved, together with 0.6 g (2.6 mmol) of 5-amino-3-mercapto-4-methyl-1,2,4(4H)-triazole and 63 mg (2.6 mmol) of lithium hydroxide, in 8 ml of DMF, and the solution was stirred at 100°C for two hours. Water was then added and the whole was extracted three times with methyl *tert*-butyl ether. After the combined organic phases had been dried over sodium

sulfate and concentrated, the resulting crude product was purified by chromatography on silica gel (eluent: methylene chloride containing 3% methanol).
Yield: 0.55 g (53% of theory) of a colorless oil

$C_{17}H_{23}N_5S$ (329.5) MS (m/z) = 331 $[M+H]^+$

The salt was precipitated with ethereal hydrochloric acid at 0°C.

$C_{17}H_{23}N_5S$ x HCl
m.p.: 125°C

Example 12
3-({2-[(1,2,3,4-Tetrahydronaphth-1-ylamino)methyl]prop-2-enyl}-mercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole hydrochloride
The compound was obtained by reacting the precursor 11A from Example 11 with 3-mercapto-4-methyl-5-phenyl-1,2,4(4H)-triazole.
Yield: 53% of theory.

$C_{23}H_{26}N_4S$ x HCl
m.p.: 100°C (decomp.)

Example 13
3-[3-(6-Bromo-1,2,3,4-tetrahydronaphth-2-ylmethylamino)propyl-mercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole hydrochloride
The above substance was obtained by methylating the substance from Example 5 with methyl iodide in a manner known per se.

$C_{23}H_{27}BrN_4S$ (471.5) MS (m/z): 470 $[M-H]^+$
$C_{23}H_{27}BrN_4S$ x HCl
m.p.: 88°C (decomp.)

Example 14
3-[3-(6-Methyl-1,2,3,4-tetrahydronaphth-2-ylmethylamino)propyl-mercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole
The above substance was obtained by methylating 3-[3-(6-methyl-1,2,3,4-tetrahydronaphth-2-ylamino)propyl-mercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole (Example 4) with methyl iodide in a manner known per se.
^{1}H-NMR ($CDCl_3$): 1.9 (m, 2H); 2.3 (s, 3H); 2.5 (mbr, 3H); 2.9 (m, 4H); 3.2 (m, 1H); 3.3-3.5 (m, 4H); 3.6-3.8 (m, 5H); 6.8-7.0 (m, 3H); 7.5 (m, 3H); 7.7 (m, 2H).

$C_{24}H_{30}N_4S$ (406.6)

Example 15
3-[3-(N-(6-Fluoroindan-1-yl)propylamino)propylmercapto]-4-methyl-5-(2-pyrrolyl)-1,2,4(4H)-triazole hydrochloride

15A Preparation of the starting compounds

15A1 6-Fluoro-1-propylaminoindan

3.27 g (55 mmol) of n-propylamine were initially introduced in 100 ml of methanol, and 15 g (110 mmol) of zinc dichloride were added. 10 g (66 mmol) of 6-fluoro-1-indanone, dissolved in 100 ml of methanol, were then added dropwise. After that, 6.94 g (110 mmol) of sodium cyanoborohydride were added in portions and the reaction mixture was heated to boiling for 3 hours while stirring. After the mixture had cooled down, 200 ml of 1M NaOH were added and the precipitated salts were filtered off; the filtrate was then extracted with ethyl acetate. After drying and evaporating, the combined organic phases yielded 10.4 g of an oil which was purified by column chromatography on silica gel (eluent: methylene chloride containing 2-5% methanol).
Yield: 4.0 g (31% of theory)
^{1}H-NMR ($CDCl_3$): 0.9 (t, 3H); 1.3 (sbr, NH); 1.5 (m, 2H); 1.8 (m,1H); 2.6 (t, 2H); 2.8 (m, 1H); 3.0 (m, 1H); 4.2 (t, 1H); 6.9 (m, 2H); 7.3 (m, 1H).

$C_{12}H_{16}FN$ (193.3) MS (m/z): 193 [M^+]

15A2 6-Fluoro-1-(3-chloropropyl)-1-propylaminoindan
The above-described product was subsequently reacted as described under 1A.
^{1}H-NMR ($CDCl_3$): [illegible] 3H); 1.5 (m, 2H); 1.8-2.1 (m, 4H); 2.3 (t, 2H); 2.5 (m, 2H); [illegible] (m, 2H); 3.6 (m, 2H); 4.4 (t, 1H); 6.9 (m, 2H); 7.3 (m, 1H).
$C_{15}H_{21}ClFN$ (269.8)

15A3 3-Mercapto-4-methyl-5-(pyrrol-2-yl)-1,2,4(4H)-triazole
The triazole was prepared by reacting pyrrole-2-carbonyl chloride with N-methylthiosemicarbazide in pyridine and then cyclizing in an aqueous solution of sodium hydrogen carbonate (in analogy with S. Kubota et al., Chem. Pharm. Bull. **1975**,*23*,955).
^{1}H-NMR (DMSO-d_6): 3.7 (s, 3H); 6.2(m, 1H); 6.8 (m, 1H); 7.0 (m, 1H); 11.8 (s, 1H); 14.0 (s, 1H).
$C_7H_8N_4S$ (180)
m.p.: 200-201°C

15B Preparation of the end product
The substance 15 was obtained by reacting 3-mercapto-4-methyl-5-(pyrrol-2-yl)-1,2,4(4H)-triazole with the chlorine base prepared in 15A2, in analogy with Example 1B.

Yield: 73% of theory

$C_{22}H_{28}FN_5S$ (413.6)
^{1}H-NMR ($CDCl_3$): 0.9 (t, 3H); 1.5 (m, 2H); 1.8-2.0 (m, 3H); 2.1 (m, 1H); 2.3 (t, 2H); 2.5 (m, 2H); 2.7-2.9 (m, 2H); 3.15 (m, 1H); 3.3 (m, 1H); 3.7 (s, 3H); 4.4 (t, 1H); 6.3 (s, 1H); 6.5 (s,1H); 6.8 (m, 2H); 7.1 (s, 1H); 7.2 (m, 1H); 12.0 (s, 1H).
Precipitation with isopropanolic hydrochloric acid yielded the title compound as a white solid.

$C_{22}H_{28}FN_5S$ x HCl (450.1)
m.p.: 120°C (decomp.)

Example 16
3-[3-(N-(6-Fluoroindan-1-yl)propylamino)propylmercapto]-4-methyl-5-(4-methylthiazol-5-yl)-1,2,4(4H)-triazole hydrochloride

16A Preparation of the starting compounds
4-Methyl-3-mercapto-5-(4-methylthiazol-5-yl)-1,2,4(4H)-triazole
The triazole was prepared by reacting 4-methylthiazole-5-carbonyl chloride with N-methylthiosemicarbazide in pyridine and then cyclizing in an aqueous solution of sodium hydrogencarbonate.
^{1}H-NMR (DMSO-d_6): 2.4 (s, 3H); 3.4 (s, 3H); 9.2 (s, 1H); 14.1 (s, 1H).

16B Preparation of the end product
The preparation was effected, in analogy with Example 15, by reacting substance 15A with
3-mercapto-4-methyl-5-(4-methylthiazol-5-yl)-1,2,4(4H)-triazole.
Yield: (70% of theory)

$C_{22}H_{28}FN_5S_2$ (445.6) MS (m/z): 447 $[M+H]^+$

^{1}H-NMR ($CDCl_3$): 0.9 (t, 3H); 1.5 (m, 2H); 2.0 (m,3H); 2.15 (m, 1H); 2.4 (t, 2H); 2.6 (m, 5H); 2.8 (m, 1H); 2.9 (m, 1H); 3.3 (m, 1H); 3.4-3.5 (m, 4H); 4.5 (t, 1H); 6.8 (m, 2H); 7.2 (t, 1H); 9.1 (s, 1H).

$C_{22}H_{28}FN_5S_2$ x HCl (482.1)
m.p.: 123°C

The compounds of Examples 17 to 19 were prepared in an analogous manner:

Example 17
5-Amino-3-[3-(N-(8-chloro-1,2,3,4-terahydronaphth-2-yl)propyl-amino)propylmercapto]-4-methyl-1,2,4(4H)-triazole

Example 18
3-[3-(N-(7-Methoxy-1,2,3,4-tetrahydronaphth-2-yl)propylamino)-propylmercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole

$C_{26}H_{34}N_4OS$ x HCl (487.1)
m.p.: 92-95°C

Example 19
3-[3-(Indan-2-yl-amino)propylmercapto]4-methyl-5-phenyl-1,2,4-(4H)-triazole
^{1}H-NMR ($CDCl_3$): 2.0 (m, 2H); 2.2 (sbr, NH), 2.7-2.85 (m, 4H); 3.1 (dd, 2H); 3.3 (t, 2H); 3.5 (s, 3H); 3.7 (t, 1H); 7.1-7.2 (m, 4H); 7.5 (m, 3H); 7.7 (m, 2H).

$C_{21}H_{24}N_4S$ (364.5) MS (m/z): 365 $[M]^+$

Example 20
3-[3-N-(5-Methoxy-1,2,3,4-tetrahydronaphth-2-yl)amino)propyl-mercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole
$C_{23}H_{28}N_4OS$ (409) MS (m/z): 409 $[M]^+$

Example 21
3-[3-(N-5-Methoxy-1,2,3,4-tetrahydronaphth-2-yl)propylamino) propylmercapto]-4-methyl-5-phenyl-1,2,4(4H)-triazole
^{1}H-NMR ($CDCl_3$): δ = 0.9 (t, 3H); 1.5 (m, 2H); 1.6 (m, 1H); 1.9 (q, 2H); 2.0 (m, 1H); 2.5 (m, 3H); 2.6 (t, 2H); 2.7-3.0 (m, 4H); 3.3 (t, 2H); 3.6 (s, 3H); 3.8 (s, 3H), 6.6 (d, 1H); 6.7 (d, 1H); 7.0 (t, 1H); 7.5 (m, 3H); 7.7 (m, 2H).
$C_{26}H_{34}N_4OS$ (450.7)

Example 22
3-[3-(N-(7-Methoxy-1,2,3,4-tetrahydronaphth-2-yl)propylamino) propylmercapto]-5-tert-butyl-4-methyl-1,2,4(4H)-triazole
$C_{24}H_{38}N_4OS$ (430) MS (m/z): 431 $[M+H]^+$

Example 23
3-[3-(N-(7-Methoxy-1,2,3,4-tetrahydronaphth-2-yl)propylamino) propylmercapto]-5-methylamino-4-methyl-1,2,4(4H)-triazole
$C_{21}H_{33}N_5OS$ (403.6) MS (m/z): 404.3 $[M+H]^+$

Example 24
3-({2-[(1,2,3,4-Tetrahydronaphth-1-ylamino)-2-methyl]prop-2-enyl}-mercapto)-4-methyl-5-phenyl-1,2,4(4H)-triazole

$C_{12}H_{25}N_5S$ (391.5)

Example 25

Ethyl 5-{[3-(indan-2-ylamino)propyl]mercapto}-4-methyl-1,2,4(4H)-triazole-3-carboxylate

$C_{18}H_{24}N_4O_2S$ (360)

The hydrochloride was obtained by treating with ethereal hydrochloric acid.

$C_{18}H_{24}N_4O_2S$ x HCl (396.9)

m.p.: 135-139°C

Example 26

3-[3-(N-(7-Methoxy-1,2,3,4-tetrahydronaphth-2-yl)propylamino) propylmercapto]-4-methyl-5-(4-methyl-1,3-thiazol-5-yl)-1,2,4(4H)-triazole

^{1}H-NMR ($CDCl_3$): δ = 0.9 (t, 3H); 1.5 (m, 2H); 1.6 (m, 1H); 2.0 (m, 3H); 2.5 (t, 2H); 2.6 (s, 3H); 2.7-3.0 (m, 7H); 3.4 (t, 2H); 3.5 (s, 3H); 3.8 (s, 3H), 6.6 (s, 1H); 6.7 (d, 1H); 6.9 (d, 1H); 8.9 (s, 1H).

$C_{24}H_{33}N_5OS_2$ (472)

Example 27

3-[3-(N-(5-Methoxy-1,2,3,4-tetrahydronaphth-2-yl)propylamino) butyl]-4-methyl-5-phenyl-1,2,4(4H)-triazole

^{1}H-NMR ($CDCl_3$): δ = 0.9 (t, 3H); 1.5 (m, 3H); 2.0 (m, 2H); 2.2 (m, 1H); 2.5 (m, 3H); 2.7 (t, 2H); 2.9 (m, 4H); 3.0 (m, 2H); 3.6 (s, 3H); 3.8 (s, 3H), 6.6 (d, 1H); 6.7 (d, 1H); 7.0 (t, 1H); 7.5 (m, 3H); 7.7 (m, 2H).

$C_{27}H_{36}N_4O$ (432.6)

Example 28

3-[3-(N-(7-Methoxy-1,2,3,4-tetrahydronaphth-2-yl)propylamino) butyl]-4-methyl-5-phenyl-1,2,4(4H)-triazole

^{1}H-NMR ($CDCl_3$): δ = 0.9 (t, 3H); 1.5 (m, 2H); 1.7 (m, 1H); 1.9 (q, 2H); 2.1 (m, 1H); 2.5 (t, 2H); 2.6 (t, 2H); 2.65-2.8 (m, 8H); 3.1 (s, 1H); 3.5 (s, 3H); 3.8 (s, 3H), 6.5 (s, 1H); 6.6 (dd, 1H); 6.9 (d, 1H); 7.5 (m, 3H); 7.7 (m, 2H).

$C_{27}H_{36}N_4O$ (432.6)

In principle, the following can be prepared in an analogous manner:

Example 29

3-[3-(N-(Indan-2-yl)propylamino)propylmercapto]-4-methyl-5-(pyridin-3-yl)-1,2,4(4H)-triazole

Example 30
3-[3-(N-(5-Mercaptomethylindan-2-yl)propylamino)propylmercapto]-4-methyl-5-thien-3-yl-1,2,4(4H)-triazole

Example 31
4-Cyclopropyl-3-[3-N-(7-methoxy-(1,2,3,4-tetrahydronaphthalen-2-yl)propylamino)propylmercapto]-5-(4-methyl-1,3-thiazol-5-yl)-1,2,4-(4H)-triazole

Example 32
3-[3-(N-(7-Cyano-1,2,3,4-tetrahydronaphth-2-yl)methylamino)propylmercapto]-4-isopropyl-5-(1,3-thiazol-4-yl)-1,2,4(4H)-triazole hydrochloride

Example 33
3-[3-(N-(7-Bromo-1,2,3,4-tetrahydronaphth-2-yl)propylamino)propylmercapto]-4-ethyl-5-(1-methyl-1H-pyrrol-2-yl)-1,2,4(4H)-triazole

Example 34
N-{4-[(5-Methoxy-7-methyl)-1,2,3,4-tetrahydronaphthalen-2-yl](but-2-enyl)amino]propylmercapto}-4-methyl-5-(3-cyanophenyl)-1,2,4(4H)-triazole

Example 35
3-[7-(N-(5-Fluoroindan-2-yl)methylamino)heptylmercapto]-4-propyl-5-(1,3-thiazol-4-yl)-1,2,4(4H)-triazole

Example 36
3-[3-(N-(Indan-2-yl)propylamino)butyl]-4-methyl-5-phenyl-1,2,4(4H)-triazole

Example 37
3-[3-(N-(5-Methoxyindan-2-yl)propylamino)propoxy]-4-methyl-5-phenyl-1,2,4(4H)-triazole

Example 38
N-{4-[(6,7-Dimethoxy-1,2,3,4-tetrahydronaphthalen-2-yl)(propyl)amino]butyl}-4-methyl-5-phenyl-1,2,4(4H)-triazole-3-carboxamide

In principle, the following compounds can be prepared in an analogous manner:

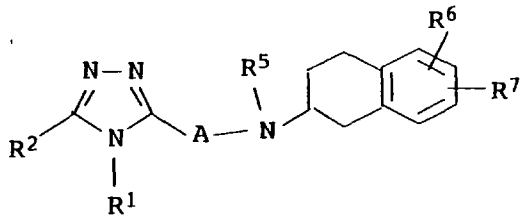


Table 1:

Exp	R^1	R^2	A	R^5	R^6	R^7
39	Me	6-chlorobiphenyl-2-	S-$(CH_2)_3$-	n-propyl	6-chloro	
40	Me	pyridin-4-yl-	S-$(CH_2)_3$-	n-propyl	6-chloro	
41	ethyl	N-methyl-2-pyrrolyl-	CO-CH_2-C(=CH2)-CH_2	n-propyl	7-methoxy	
42	Me	phenyl	S-$(CH_2)_3$-	but-2-enyl	6-iodo	
43	Me	4-methylthiazol-5-yl	S-$(CH_2)_7$-	n-propyl	6-methyl	7-cyano
44	Me	pyridin-4-yl-	S-$(CH_2)_3$-	n-propyl	H	
45	Me	amino	S-$(CH_2)_3$-	n-propyl	6-chloro	
46	Me	4-methylthiazol-5-yl	O-$(CH_2)_3$-	n-propyl	7-trifluoro-methoxy	
47	Me	3-iodophenyl	S-$(CH_2)_3$-	n-propyl	6-methyl	
48	Me	5-methylimidazol-4-yl-	S-$(CH_2)_3$-	n-propyl	6-bromo	
49	Me	4-methoxyphenyl	$(CH_2)_4$-	n-propyl	5-cyano	

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Exp	R^1	R^2	A	R^5	R^6	R^7
50	Me	N-methyl-2-pyrrolyl-	S-$(CH_2)_3$-	n-propyl	6-bromo	
51	Me	methylamino	S-$(CH_2)_3$-	n-propyl	5-cyano	
52	Me	phenyl	CONH-$(CH_2)_5$-	methyl	6-fluoro	
53	Me	4-methylthiazol-5-yl	S-$(CH_2)_3$-	n-propyl	6-methyl	
54	Me	3-Br-pyridin-5-yl-	S-$(CH_2)_3$-	n-propyl	5-cyano	
55	Me	amino	S-$(CH_2)_3$-	n-propyl	5-methanesulfonyl-oxy	
56	Me	3-cyanophenyl	CONH-$(CH_2)_5$-	n-propyl	5-fluoro	
57	Me	pyridin-4-yl-	S-$(CH_2)_3$-	n-propyl	7-methoxy	
58	Me	2,5-dimethylfuranyl-3-	S-$(CH_2)_3$-	n-propyl	6-chloro	
59	Me	oxadiazol-2-yl	S-$(CH_2)_3$-	n-propyl	6-bromo	
60	Me	2-methyl-4-oxazolyl-	S-$(CH_2)_3$-	n-propyl	6-chloro	
61	Me	6-chlorobiphenyl-2-	S-$(CH_2)_3$-	n-propyl	6-methyl	
62	Me	3-iodophenyl	S-CH_2-cyclopropyl-CH_2-	but-2-enyl	5-cyano	
63	Me	3-cyanophenyl	S-$(CH_2)_3$-	n-propyl	6-bromo	
64	Me	oxadiazol-2-yl	S-$(CH_2)_3$-	n-propyl	6-chloro	7-chloro
65	ethyl	phenyl	CO-$(CH_2)_3$-	but-2-enyl	5-cyano	
66	Me	2-Aminothiazol-4-yl-	S-$(CH_2)_3$-	n-propyl	6-bromo	
67	Me	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	6-methyl	
68	Me	2-pyrazinyl-	S-CH_2-cyclopropyl-CH_2-	methyl	5-nitro	
69	ethyl	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	7-methoxy	

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Exp	R^1	R^2	A	R^5	R^6	R^7
70	Me	4-methoxyphenyl	O-$(CH_2)_3$-	n-propyl	5-cyano	
71	Me	3-cyanophenyl	O-$(CH_2)_3$-	n-propyl	5-fluoro	
72	Me	2-thienyl	S-$(CH_2)_3$-	methyl	5-cyano	
73	Me	3-benzothienyl-	S-$(CH_2)_3$-	n-propyl	5-cyano	
74	Me	4-methylthiazol-5-yl	S-$(CH_2)_3$-	n-propyl	6-bromo	
75	Me	cyclohexyl-	S-$(CH_2)_3$-	n-propyl	6-methyl	
76	propyl	phenyl	S-CH_2-CH=CH-CH_2-	methyl	6-fluoro	
77	Me	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	n-propyl	6-methyl	
78	Me	phenyl	O-$(CH_2)_3$-	but-2-enyl	5-cyano	
79	cycprop	6-chlorobiphenyl-2-	S-$(CH_2)_3$-	n-propyl	7-methoxy	
80	butyl	phenyl	O-$(CH_2)_3$-	prop-2-enyl	6-thiomethyl	
81	Me	carboxyethyl	S-$(CH_2)_3$-	methyl	5-cyano	
82	Me	N-methyl-2-pyrrolyl-	S-$(CH_2)_3$-	n-propyl	H	
83	butyl	3-cyanophenyl	O-$(CH_2)_3$-	n-propyl	5-fluoro	
84	Me	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	n-propyl	7-methoxy	
85	Me	methylamino	S-$(CH_2)_3$-	n-propyl	7-methoxy	
86	Me	4-methylthiazol-5-yl	CONH-$(CH_2)_4$-	n-propyl	7-trifluoromethoxy	
87	Me	4-imidazolyl-	S-$(CH_2)_3$-	n-propyl	H	
88	Me	oxadiazol-2-yl	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
89	Me	phenyl	S-$(CH_2)_3$-	n-propyl	6-methyl	

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Exp	R^1	R^2	A	R^5	R^6	R^7
90	Me	cyclohexyl-	S-$(CH_2)_3$-	n-propyl	6-bromo	
91	Me	phenyl	O-$(CH_2)_3$-	prop-2-enyl	6-thiomethyl	
92	Me	phenyl	O-$(CH_2)_3$-	methyl	6-fluoro	
93	Me	phenyl	S-CH_2-cycHex-CH_2-CH_2-	methyl	6-fluoro	
94	Me	phenyl	$(CH_2)_4$-	n-propyl	6-methoxy	
95	ethyl	phenyl	S-$(CH_2)_7$-	methyl	6-fluoro	
96	Me	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	6-chloro	
97	Me	2-methyl-4-oxazolyl-	S-$(CH_2)_3$-	n-propyl	6-methyl	7-cyano
98	Me	oxadiazol-2-yl	S-$(CH_2)_3$-	n-propyl	7-methoxy	
99	propyl	pyridin-3-yl-	S-CH_2-CH=CH-CH_2-	n-propyl	6-bromo	7-bromo
100	Me	4-imidazolyl-	S-$(CH_2)_3$-	n-propyl	7-methoxy	
101	Me	2-aminothiazol-4-yl-	S-$(CH_2)_3$-	n-propyl	7-methoxy	
102	Me	phenyl	O-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
103	Me	phenyl	S-$(CH_2)_3$-	n-propyl	6-bromo	
104	Me	amino	S-$(CH_2)_3$-	n-propyl	6-methyl	
105	Me	3-thienyl	S-$(CH_2)_3$-	n-propyl	7-methoxy	
106	Me	N-methyl-2-pyrrolyl-	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
107	Me	tetrazolyl-	S-$(CH_2)_3$-	n-propyl	7-methoxy	
108	iprop	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	

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Exp	R^1	R^2	A	R^5	R^6	R^7
109	Me	tetrazolyl-	S-$(CH_2)_3$-	n-propyl	H	
110	ethyl	phenyl	SCH_2-$C(CH_3)$=CH-CH_2-	but-2-enyl	5-cyano	
111	Me	2,5-dimethyl-furanyl-3-	S-$(CH_2)_3$-	n-propyl	H	
112	Me	tert-butyl	S-$(CH_2)_3$-	methyl	5-cyano	
113	Me	4-iodophenyl	S-$(CH_2)_3$-	n-propyl	7-methoxy	
114	Me	3-cyanophenyl	S-$(CH_2)_3$-	n-propyl	5-cyano	
115	Me	4-methoxyphenyl	S-CH_2-cyclopropyl-$(CH_2)_2$-	prop-2-enyl	6-thiomethyl	
116	Me	phenyl	S-CH_2-CH=CH-CH_2-	n-propyl	7-methanesulfonyl-oxy	
117	Me	2-aminothiazol-4-yl-	S-$(CH_2)_3$-	n-propyl	5-cyano	
118	cycprop	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	prop-2-enyl	7-methanesulfonyl-oxy	
119	Me	2-methyl-4-oxazolyl-	S-$(CH_2)_3$-	prop-2-enyl	7-methanesulfonyl-oxy	
120	n-hexyl	4-methoxyphenyl	S-$(CH_2)_3$-	n-propyl	6-chloro	
121	Me	2-thienyl	S-$(CH_2)_3$-	n-propyl	H	
122	Me	phenyl	COO-$(CH_2)_4$-	n-propyl	7-methanesulfonyl-oxy	
123	Me	cyclopropyl	S-$(CH_2)_3$-	methyl	5-cyano	
124	Me	4-imidazolyl-	S-$(CH_2)_3$-	n-propyl	5-methanesulfonyl-oxy	
125	Me	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	5-cyano	

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Exp	R^1	R^2	A	R^5	R^6	R^7
126	butyl	4-methylthiazol-5-yl	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
127	iprop	cyclohexyl-	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
128	Me	tetrazolyl-	S-$(CH_2)_3$-	n-propyl	6-bromo	
129	propyl	methylamino	S-$(CH_2)_3$-	methyl	5-cyano	
130	Me	amino	S-$(CH_2)_3$-	n-propyl	6-bromo	
131	Me	3-iodophenyl	S-$(CH_2)_3$-	methyl	5-cyano	
132	Me	2-thienyl	S-$(CH_2)_3$-	n-propyl	6-chloro	
133	Me	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	6-bromo	
134	Me	2-thienyl	S-$(CH_2)_3$-	n-propyl	5-cyano	
135	ethyl	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	n-propyl	7-methoxy	
136	Me	2-pyrazinyl-	$(CH_2)_2$-$CH(CH_3)$-CH_2-CH_2-	n-propyl	6-methyl	
137	Me	3-cyanophenyl	S-$(CH_2)_3$-	n-propyl	6-methyl	
138	Me	N-propyltetrazolyl-	S-$(CH_2)_3$-	n-propyl	H	
139	Me	4-imidazolyl-	S-$(CH_2)_3$-	n-propyl	6-methyl	
140	Me	2-pyrazinyl-	O-$(CH_2)_3$-	n-propyl	6-methyl	
141	Me	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	6-bromo	
142	ethyl	phenyl	CO-$(CH_2)_3$-	prop-2-enyl	6-chloro	7-chloro
143	Me	pyridin-4-yl-	S-$(CH_2)_3$-	n-propyl	5-methanesulfonyl-oxy	
144	Me	4-methylthiazol-5-yl	S-$(CH_2)_3$-	n-propyl	6-chloro	

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Exp	R^1	R^2	A	R^5	R^6	R^7
145	Me	3-iodophenyl	$(CH_2)_2$-CH(CH_3)-CH_2-CH_2-	n-propyl	5-cyano	
146	Me	3-benzothienyl-	S-$(CH_2)_3$-	n-propyl	5-methanesulfonyl-oxy	
147	phenyl	phenyl	S-$(CH_2)_3$-	n-propyl	6-methoxy	
148	Me	2-aminothiazol-4-yl-	S-$(CH_2)_3$-	n-propyl	6-methyl	
149	Me	pyridin-3-yl-	S-$(CH_2)_3$-	n-propyl	7-methoxy	
150	Me	3-Br-pyridin-5-yl-	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
151	Me	4-methoxyphenyl	COO-$(CH_2)_3$-	n-propyl	5-cyano	
152	Me	4-imidazolyl-	S-$(CH_2)_3$-	n-propyl	5-cyano	
153	Me	2-methyl-4-oxazolyl-	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
154	Me	4-imidazolyl-	S-$(CH_2)_3$-	n-propyl	6-chloro	
155	Me	trifluoromethyl	S-$(CH_2)_3$-	methyl	5-cyano	
156	Me	tetrazolyl-	S-$(CH_2)_3$-	n-propyl	5-cyano	
157	Me	pyridin-3-yl-	CONH-$(CH_2)_4$-	n-propyl	6-bromo	
158	Me	pyridin-3-yl-	O-$(CH_2)_3$-	n-propyl	6-bromo	
159	Me	pyridin-4-yl-	S-$(CH_2)_3$-	n-propyl	5-cyano	
160	Me	N-propyltetrazolyl-	S-$(CH_2)_3$-	n-propyl	5-cyano	
161	Me	methylamino	S-$(CH_2)_3$-	n-propyl	6-bromo	
162	Me	N-propyltetrazolyl-	S-$(CH_2)_3$-	n-propyl	6-bromo	
163	Me	phenyl	S-CH_2-cycHex-CH_2-	n-propyl	7-trifluoromethoxy	

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Exp	R^1	R^2	A	R^5	R^6	R^7
164	phenyl	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	6-ethyl	
165	Me	2-thienyl	S-$(CH_2)_3$-	n-propyl	6-methyl	
166	Me	2-methyl-4-oxazolyl-	S-$(CH_2)_3$-	n-propyl	7-methoxy	
167	Me	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	n-propyl	H	
168	Me	4-methoxyphenyl	S-CH_2-C(=CH_2)-CH_2	n-propyl	5-cyano	
169	Me	2-thienyl	S-$(CH_2)_3$-	n-ethyl	6-methxoxy	7-methoxy
170	Me	3-Br-pyridin-5-yl-	S-$(CH_2)_3$-	n-propyl	6-bromo	
171	Me	2-thienyl	O-$(CH_2)_3$-	n-propyl	6-chloro	
172	Me	2-pyrazinyl-	S-$(CH_2)3$-	n-propyl	6-methyl	
173	Me	4-methoxyphenyl	S-$(CH_2)_3$-	n-propyl	7-methoxy	
174	cycprop	2-pyrazinyl-	S-$(CH_2)_3$-	prop-2-enyl	6-carboxamide	
175	Me	amino	S-$(CH_2)_3$-	n-propyl	7-methoxy	
176	Me	3-cyanophenyl	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
177	Me	3-Br-pyridin-5-yl-	S-$(CH_2)_3$-	n-propyl	H	
178	Me	2-thienyl	S-CH_2-C(=CH_2)-CH_2	n-propyl	6-chloro	
179	Me	phenyl	COO-$(CH_2)_4$-	n-propyl	6-methoxy	
180	butyl	tetrazolyl-	S-$(CH_2)_3$-	methyl	5-cyano	
181	Me	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	6-chloro	
182	Me	4-methylthiazol-5-yl	S-$(CH_2)_3$-	n-propyl	H	
183	Me	2,5-dimethylfuranyl-3-	S-$(CH_2)_3$-	n-propyl	5-cyano	

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Exp	R^1	R^2	A	R^5	R^6	R^7
184	Me	N-methyl-2-pyrrolyl-	O-$(CH_2)_3$-	n-propyl	7-methoxy	
185	iprop	3-Br-pyridin-5-yl-	S-$(CH_2)_3$-	n-propyl	6-chloro	7-chloro
186	Me	3-Br-pyridin-5-yl-	S-$(CH_2)_3$-	n-propyl	6-methyl	
187	Me	cyclohexyl-	S-$(CH_2)_7$-	n-propyl	6-chloro	7-chloro
188	Me	N-methyl-2-pyrrolyl-	S-$(CH_2)_3$-	n-propyl	7-methoxy	
189	Me	3-iodophenyl	COO-$(CH_2)_4$-	n-propyl	5-cyano	
190	Me	4-methylthiazol-5-yl	S-$(CH_2)_3$-	n-propyl	5-cyano	
191	Me	2-pyrazinyl-	S-CH_2-CH=CH-CH_2-	n-propyl	6-methyl	
192	Me	3-iodophenyl	S-$(CH_2)_3$-	n-propyl	6-chloro	
193	Me	cyclohexyl-	S-$(CH_2)_3$-	n-propyl	5-cyano	
194	Me	3-cyanophenyl	S-$(CH_2)_3$-	n-propyl	H	
195	Me	pyridin-3-yl-	S-$(CH_2)_3$-	n-propyl	5-cyano	
196	Me	N-propyltetrazolyl-	S-$(CH_2)_3$-	n-propyl	6-chloro	
197	ethyl	3-iodophenyl	S-$(CH_2)_3$-	H	6-chloro	7-chloro
198	Me	3-iodophenyl	O-$(CH_2)3$-	n-propyl	5-cyano	
199	butyl	phenyl	O-$(CH_2)_3$-	methyl	6-fluoro	
200	Me	methylamino	S-$(CH_2)_3$-	n-propyl	H	
201	Me	methylamino	S-$(CH_2)_3$-	n-propyl	6-chloro	
202	Me	phenyl	S-CH_2-cychex-CH_2-CH_2-	n-propyl	5-fluoro	
203	Me	3-iodophenyl	S-CH_2-C(=CH_2)-CH_2	n-propyl	5-cyano	
204	Me	3-benzothienyl-	S-$(CH_2)3$-	n-propyl	6-methyl	

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Exp	R^1	R^2	A	R^5	R^6	R^7
205	Me	pyridin-4-yl-	S-$(CH_2)_3$-	n-propyl	6-methyl	
206	Me	amino	S-$(CH_2)_3$-	n-propyl	5-cyano	
207	Me	N-methyl-2-pyrrolyl-	S-$(CH_2)_3$-	n-propyl	6-chloro	
208	Me	2-thienyl	COO-$(CH_2)_4$-	n-propyl	6-chloro	
209	Me	3-benzothienyl-	S-$(CH_2)_3$-	n-propyl	6-bromo	
210	Me	N-methyl-2-pyrrolyl-	S-$(CH_2)_3$-	n-propyl	6-methyl	
211	Me	phenyl	S-CH_2-cyclopropyl-CH_2-	H	6-bromo	
212	Me	N-propyltetrazolyl-	S-$(CH_2)_3$-	n-propyl	5-methanesulfonyl-oxy	
213	Me	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	7-methoxy	
214	Me	3-benzothienyl-	S-$(CH_2)_3$-	n-propyl	6-chloro	
215	Me	oxadiazol-2-yl	S-$(CH_2)_3$-	n-propyl	6-methyl	
216	Me	methyl	S-$(CH_2)_3$-	prop-2-enyl	7-methanesulfonyl-oxy	
217	Me	tetrazolyl-	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
218	Me	6-chlorobiphenyl-2-	S-$(CH_2)_3$-	methyl	5-cyano	
219	Me	4-methylthiazol-5-yl	S-$(CH_2)_3$-	methyl	5-cyano	
220	Me	2-thienyl	S-CH_2-C(=CH_2)-CH_2	n-propyl	6-chloro	
221	Me	3-benzothienyl-	S-$(CH_2)_3$-	methyl	7-methoxy	
222	Me	4-methoxyphenyl	S-$(CH_2)_3$-	n-propyl	5-cyano	

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Exp	R^1	R^2	A	R^5	R^6	R^7
223	butyl	2-thienyl	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
224	Me	methylamino	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
225	Me	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	7-methoxy	
226	Me	phenyl	S-$(CH_2)_3$-	n-propyl	H	
227	Me	pyridin-3-yl-	S-$(CH_2)_3$-	n-propyl	6-methyl	
228	Me	phenyl	S-$(CH_2)_3$-	prop-2-enyl	7-methanesulfonyl-oxy	
229	ethyl	phenyl	S-CH_2-C(CH_3)=CH-CH_2-	prop-2-enyl	6-chloro	7-chloro
230	Me	N-propyltetrazolyl-	S-$(CH_2)_3$-	n-propyl	6-methyl	
231	Me	dimethylamino	S-$(CH_2)_3$-	methyl	5-cyano	
232	Me	2-aminothiazol-4-yl-	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
233	Me	2,5-dimethylfuranyl-3-	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
234	Me	2-methyl-4-oxazolyl-	S-$(CH_2)_3$-	methyl	5-cyano	
235	Me	4-methoxyphenyl	S-CH_2-cyclopropyl-$(CH_2)_2$-	but-2-enyl	5-methoxy	
236	Me	6-chlorobiphenyl-2-	S-$(CH_2)_3$-	n-propyl	5-cyano	
237	Me	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	H	
238	Me	4-methoxyphenyl	S-$(CH_2)_3$-	n-propyl	5-methanesulfonyl-oxy	

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Exp	R^1	R^2	A	R^5	R^6	R^7
239	n-hexyl	2-pyrazinyl-	S-$(CH_2)_3$-	prop-2-enyl	7-methanesulfonyl-oxy	
240	Me	3-iodophenyl	S-$(CH_2)_3$-	n-propyl	6-bromo	
241	Me	pyridin-3-yl-	S-$(CH_2)_3$-	methyl	5-cyano	
242	Me	N-propyltetrazolyl-	S-$(CH_2)_3$-	n-propyl	7-methoxy	
243	Me	3-Br-pyridin-5-yl-	S-$(CH_2)_3$-	n-propyl	7-methoxy	
244	Me	oxadiazol-2-yl	S-$(CH_2)_3$-	n-propyl	5-cyano	
245	Me	phenyl	O-$(CH_2)_3$-	prop-2-enyl	6-thiomethyl	
246	Me	2-methyl-4-oxazolyl-	S-$(CH_2)_3$-	n-propyl	5-cyano	
247	ethyl	phenyl	S-$(CH_2)_6$-	n-propyl	6-methoxy	
248	Me	pyridin-4-yl-	S-$(CH_2)_3$-	n-propyl	6-bromo	
249	cycprop	3-pyrrolyl	S-$(CH_2)_3$-	prop-2-enyl	7-methanesulfonyl-oxy	
250	Me	benzyl	S-$(CH_2)_3$-	methyl	5-cyano	
251	propyl	4-methylthiazol-5-yl	S-CH_2-CH=CH-CH_2-	n-propyl	7-trifluoromethoxy	
252	Me	phenyl	O-$(CH_2)_3$-	but-2-enyl	5-cyano	
253	Me	6-chlorobiphenyl-2-	S-$(CH_2)_3$-	n-propyl	6-bromo	
254	Me	3-iodophenyl	S-$(CH_2)_3$-	n-propyl	5-cyano	
255	Me	phenyl	O-$(CH_2)_3$-	prop-2-enyl	6-chloro	
256	Me	3-cyanophenyl	S-$(CH_2)_3$-	n-propyl	7-methoxy	
257	Me	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	H	
258	Me	cyano	S-$(CH_2)_3$-	methyl	5-cyano	

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Exp	R^1	R^2	A	R^5	R^6	R^7
259	Me	4-methoxyphenyl	S-(CH_2)3-	n-propyl	6-bromo	
260	ethyl	phenyl	S-CH_2-C(CH_3)=CH-CH_2-	prop-2-enyl	6-thiomethyl	
261	ethyl	phenyl	S-$(CH_2)_6$-	but-2-enyl	5-cyano	
262	Me	2-thienyl	S-$(CH_2)_3$-	prop-2-enyl	5-methanesulfonyl-oxy	
263	Me	3-benzothienyl-	S-$(CH_2)_3$-	n-propyl	H	
264	Me	pyridin-3-yl-	S-$(CH_2)_3$-	n-propyl	6-bromo	
265	Me	cyclohexyl-	S-$(CH_2)_3$-	n-propyl	H	
266	cycprop	cyclohexyl-	S-$(CH_2)_3$-	prop-2-enyl	7-methanesulfonyl-oxy	
267	ethyl	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	7-methoxy	
268	Me	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	5-cyano	
269	Me	phenyl	O-$(CH_2)_3$-	but-2-enyl	5-cyano	
270	Me	2,5-dimethylfuranyl-3-	S-(CH_2)3-	n-propyl	7-methoxy	H
271	cycprop	oxadiazol-2-yl	S-$(CH_2)_3$-	n-propyl	7-methoxy	
272	Me	phenyl	S-(CH_2)3-	n-propyl	6-chloro	
273	Me	methylamino	S-$(CH_2)_3$-	n-propyl	6-methyl	
274	Me	phenyl	S-$(CH_2)_3$-	n-propyl	5-methanesulfonyl-oxy	
275	Me	2-aminothiazol-4-yl-	S-$(CH_2)_3$-	n-propyl	H	
276	Me	N-methyl-2-pyrrolyl-	S-(CH_2)3-	n-propyl	5-cyano	
277	Me	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	n-propyl	6-chloro	

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Exp	R^1	R^2	A	R^5	R^6	R^7
278	Me	6-chlorobiphenyl-2-	S-(CH_2)3-	n-propyl	7-methoxy	
279	n-hexyl	3-cyanophenyl	S-$(CH_2)_3$-	prop-2enyl	6-chloro	
280	Me	oxadiazol-2-yl	S-$(CH_2)_3$-	n-propyl	6-chloro	
281	Me	3-iodophenyl	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
282	Me	3-iodophenyl	S-$(CH_2)_3$-	n-propyl	H	
283	Me	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	H	7-methanesulfonyl-oxy	
284	Me	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	n-propyl	6-trifluoromethoxy	
285	Me	cyclohexyl-	S-$(CH_2)_3$-	n-propyl	6-chloro	
286	Me	2-pyrazinyl-	S-$(CH_2)_7$-	but-2-enyl	7-iodo	8-chloro
287	Me	2-methyl-4-oxazolyl-	S-$(CH_2)_3$-	n-propyl	H	
288	ethyl	phenyl	S-$(CH_2)_7$-	prop-2-enyl	6-thiomethyl	
289	Me	cyclohexyl-	S-(CH_2)3-	n-propyl	7-methoxy	
290	Me	N-methyl-2-pyrrolyl-	CONH-(CH_2)4-	n-propyl	7-methoxy	
291	ethyl	phenyl	$(CH_2)_4$-	but-2-enyl	5-cyano	
292	Me	2,5-dimethylfuranyl-3-	S-$(CH_2)_3$-	n-propyl	6-bromo	
293	Me	pyridin-3-yl-	S-$(CH_2)_3$-	n-propyl	6-chloro	
294	ethyl	2,5-dimethylfuranyl-3-	S-$(CH_2)_3$-	methyl	5-cyano	
295	Me	cyclohexyl-	S-$(CH_2)_3$-	methyl	5-cyano	
296	Me	6-chlorobiphenyl-2-	S-$(CH_2)_3$-	n-propyl	6-methyl	7-methyl
297	Me	4-methoxyphenyl	S-(CH_2)3-	n-propyl	H	

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Exp	R^1	R^2	A	R^5	R^6	R^7
298	Me	tetrazolyl-	S-$(CH_2)_3$-	n-propyl	6-methyl	
299	Me	tetrazolyl-	S-(CH_2)3-	n-propyl	6-chloro	
300	Me	phenyl	$(CH_2)_2$-$CH(CH_3)$-CH_2-CH_2-	n-propyl	7-methanesulfonyl-oxy	
301	Me	Amino	S-$(CH_2)_3$-	n-propyl	H	
302	Me	2-thienyl	S-$(CH_2)_3$-	n-propyl	6-bromo	
303	Me	6-chlorobiphenyl-2-	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
304	Me	oxadiazol-2-yl	S-$(CH_2)_3$-	n-propyl	H	
305	Me	2-methyl-4-oxazolyl-	S-$(CH_2)_3$-	n-propyl	6-methyl	
306	Me	pyridin-3-yl-	S-$(CH_2)_3$-	n-propyl	H	
307	Me	4-methylthiazol-5-yl	S-$(CH_2)_3$-	prop-2-enyl	7-methanesulfonyl-oxy	
308	Me	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	n-propyl	5-cyano	
309	Me	2,5-dimethylfuranyl-3-	S-$(CH_2)_3$-	n-propyl	6-methyl	
310	propyl	3-cyanophenyl	S-CH_2-$C(CH_3)$=CH-CH_2-	n-propyl	5-fluoro	
311	Me	4-methoxyphenyl	S-$(CH_2)_3$-	n-propyl	6-methyl	
312	ethyl	3-cyanophenyl	S-$(CH_2)_8$-	n-propyl	5-fluoro	
313	Me	2-pyrazinyl-	COO-$(CH_2)_4$-	n-propyl	6-methyl	
314	Me	phenyl	S-$(CH_2)_3$-	n-propyl	5-cyano	
315	Me	pyridin-3-yl-	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	

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Exp	R^1	R^2	A	R^5	R^6	R^7
316	Me	4-imidazolyl-	S-$(CH_2)_3$-	n-propyl	6-bromo	
317	iso-propyl	2-aminothiazol-4-yl-	S-$(CH_2)_3$-	n-propyl	6-chloro	
318	n-hexyl	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	7-methanesulfonyl-oxy	
319	Me	2-methyl-4-oxazolyl-	S-$(CH_2)_3$-	n-propyl	6-bromo	
320	cycprop	3-Br-pyridin-5-yl-	S-(CH_2)3-	prop-2-enyl	7-methanesulfonyl-oxy	
321	Me	6-chlorobiphenyl-2-	S-(CH_2)3-	n-propyl	H	
322	Me	oxadiazol-2-yl	S-(CH_2)3-	methyl	5-cyano	

Provided no other meaning is given, R^7 is hydrogen

The following meanings apply here and in the subsequent tables:
cycprop = cyclopropyl
iprop = isopropyl
Me = methyl

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In principle, the following compounds can be prepared in an analogous manner:

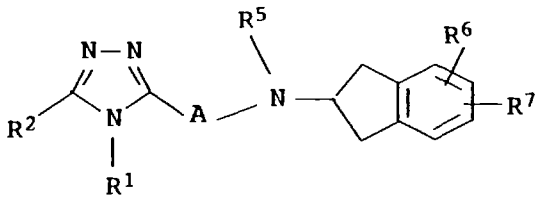


Table 2:

Exp	R^1	R^2	A	R^5	R^6	R^7
323	ethyl	2,5-dimethylfuranyl-3-	S-$(CH_2)_3$-	n-propyl	5-bromo	
324	Me	4-methylthiazol-5-yl	S-$(CH_2)_7$-	n-propyl	5-methyl	7-chloro
325	ethyl	N-methyl-2-pyrrolyl-	S-$(CH_2)_3$-	n-propenyl	5-bromo	
326	Me	N-methyl-2-pyrrolyl-	S-$(CH_2)_3$-	n-propyl	6-methoxy	
327	Me	3-benzothienyl-	S-$(CH_2)_3$-	methyl	6-methoxy	
328	cycprop	cyclohexyl-	S-$(CH_2)_6$-	prop-2-enyl	6-methanesulfonyl-oxy	
329	ethyl	4-methylthiazol-5-yl	S-$(CH_2)_3$-	n-propyl	5-bromo	
330	ethyl	3-benzothienyl-	S-$(CH_2)_3$-	n-propyl	5-bromo	
331	ethyl	2,5-dimethylfuranyl-3-	S-$(CH_2)_3$-	methyl	4-cyano	
332	Me	phenyl	$(CH_2)_2$-$CH(CH_3)$-CH_2-CH_2-	n-propyl	6-methanesulfonyl-oxy	

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Exp	R^1	R^2	A	R^5	R^6	R^7
333	Me	3-cyanophenyl	S-$(CH_2)_3$-	n-propyl	6-methanesulfonyl-oxy	
334	Me	pyridin-4-yl-	S-$(CH_2)_3$-	n-propyl	4-cyano	
335	Me	2,5-dimethylfuranyl-3-	S-$(CH_2)_3$-	n-propyl	6-methanesulfonyl-oxy	
336	Me	2-pyrazinyl-	$(CH_2)_2$-CH(CH_3)-CH_2-CH_2-	n-propyl	5-methyl	
337	Me	methylamino	S-$(CH_2)_3$-	n-propyl	6-methoxy	
338	Me	phenyl	O-$(CH_2)_3$-	but-2-enyl	4-cyano	
339	Me	3-cyanophenyl	S-$(CH_2)_3$-	methyl	6-methoxy	
340	Me	3-iodophenyl	COO-$(CH_2)_4$-	n-propyl	4-cyano	
341	propyl	3-cyanophenyl	S-CH_2-C(CH_3)=CH-CH2-	n-propyl	4-fluoro	
342	Me	2-Me-4-oxazolyl-	S-(CH_2)3-	n-propyl	6-methoxy	
343	Me	N-methyl-2-pyrrolyl-	S-$(CH_2)_3$-	n-propyl	H	
344	Me	4-imidazolyl-	S-$(CH_2)_3$-	n-propyl	5-methyl	
345	ethyl	phenyl	S-CH_2-C(CH_3)=CH-CH_2-	prop-2-enyl	5-thiomethyl	
346	Me	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	4-cyano	
347	Me	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	5-chloro	
348	Me	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	5-methyl	
349	Me	2-pyrazinyl-	S-$(CH_2)_7$-	but-2-enyl	6-iodo	
350	Me	2-pyrazinyl-	COO-$(CH_2)_4$-	n-propyl	5-methyl	
351	Me	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	n-propyl	5-chloro	

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Exp	R^1	R^2	A	R^5	R^6	R^7
352	Me	pyridin-4-yl-	S-$(CH_2)_3$-	n-propyl	H	
353	Me	pyridin-3-yl-	S-(CH_2)3-	n-propyl	5-chloro	
354	Me	N-methyl-2-pyrrolyl-	S-$(CH_2)_3$-	n-propyl	6-methanesulfonyl-oxy	
355	Me	2-thienyl	S-$(CH_2)_3$-	methyl	4-cyano	
356	Me	phenyl	O-$(CH_2)_3$-	prop-2-enyl	5-chloro	
357	Me	tetrazolyl-	S-$(CH_2)_3$-	n-propyl	4-cyano	
358	Me	phenyl	S-$(CH_2)_3$-	n-propyl	5-chloro	
359	Me	pyridin-3-yl-	S-$(CH_2)_3$-	n-propenyl	5-methyl	
360	Me	3-thienyl	S-$(CH_2)_3$-	n-propyl	6-methoxy	
361	Me	phenyl	S-CH_2-cychex-CH_2-	n-propyl	6-trifluoromethoxy	
362	ethyl	phenyl	CO-$(CH_2)_3$-	but-2-enyl	4-cyano	
363	Me	3-Br-pyridin-5-yl-	S-$(CH_2)_3$-	n-propyl	6-methanesulfonyl-oxy	
364	Me	tetrazolyl-	S-$(CH_2)_3$-	n-propyl	H	
365	Me	2-thienyl	S-$(CH_2)_3$-	n-propyl	4-cyano	
366	Me	4-methoxyphenyl	$(CH_2)_4$-	n-propyl	4-cyano	
367	Me	phenyl	O-$(CH_2)_3$-	n-propyl	6-methanesulfonyl-oxy	
368	ethyl	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	6-methoxy	6-chloro
369	Me	phenyl	S-$(CH_2)_3$-	prop-2-enyl	H	

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Exp	R^1	R^2	A	R^5	R^6	R^7
370	butyl	4-methylthiazol-5-yl	S-$(CH_2)_3$-	n-propyl	6-methanesulfonyl-oxy	
371	Me	pyridin-3-yl-	O-$(CH_2)_3$-	n-propyl	5-bromo	
372	Me	4-methylthiazol-5-yl	S-$(CH_2)_3$-	methyl	4-cyano	
373	Me	2-pyrazinyl-	S-CH_2-cycprop-CH_2-	methyl	4-nitro	
374	Me	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	5-methyl	6-methyl
375	Me	amino	S-$(CH_2)_3$-	n-propyl	H	
376	Me	methylamino	S-$(CH_2)_3$-	n-propyl	H	
377	butyl	2-thienyl	S-$(CH_2)_3$-	n-propyl	6-methanesulfonyl-oxy	
378	ethyl	amino	S-$(CH_2)_3$-	n-propyl	5-bromo	
379	Me	4-Methoxyphenyl	S-CH_2-cycprop-$(CH_2)_2$-	but-2-enyl	4-methoxy	
380	iprop	Cyclohexyl-	S-$(CH_2)_3$-	n-propyl	6-methanesulfonyl-oxy	
381	Me	4-methoxyphenyl	S-$(CH_2)_3$-	n-propyl	4-cyano	
382	Me	N-propyl-tetrazolyl-	S-$(CH_2)_3$-	n-propyl	H	
383	Me	2-thienyl	COO-$(CH_2)_4$-	n-propyl	5-chloro	
384	Me	2-thienyl	S-$(CH_2)_3$-	n-ethyl	5-methxoxy	
385	ethyl	2-thienyl	S-$(CH_2)_3$-	n-propyl	5-bromo	
386	cycprop	3-Br-pyridin-5-yl-	S-$(CH_2)_6$-	prop-2-enyl	6-methanesulfonyl-oxy	
387	propyl	methylamino	S-$(CH_2)_3$-	methyl	4-cyano	

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Exp	R^1	R^2	A	R^5	R^6	R^7
388	Me	oxadiazol-2-yl	S-$(CH_2)_3$-	n-propyl	6-methanesulfonyl-oxy	
389	ethyl	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	6-methoxy	
390	Me	pyridin-3-yl-	S-$(CH_2)_3$-	n-propyl	6-methoxy	
391	ethyl	4-imidazolyl-	S-$(CH_2)_3$-	n-propyl	5-bromo	
392	Me	phenyl	O-$(CH_2)_3$-	but-2-enyl	4-cyano	
393	Me	phenyl	S-$(CH_2)_3$-	n-propyl	H	
394	Me	3-iodophenyl	S-$(CH_2)_3$-	H	4-cyano	
395	n-hexyl	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	6-methanesulfonyl-oxy	
396	Me	phenyl	CONH-$(CH_2)_5$-	methyl	5-fluoro	
397	ethyl	phenyl	$(CH_2)_4$-	but-2-enyl	4-cyano	
398	Me	amino	S-$(CH_2)_3$-	n-propyl	5-chloro	
399	cycprop	3-pyrrolyl	S-$(CH_2)_6$-	prop-2-enyl	6-methanesulfonyl-oxy	6-chloro
400	ethyl	phenyl	S-$(CH_2)_7$-	methyl	5-fluoro	
401	Me	phenyl	S-$(CH_2)_3$-	n-propyl	5-methyl	
402	Me	4-methoxyphenyl	S-CH_2-cycprop-$(CH_2)_2$-	prop-2-enyl	5-thiomethyl	
403	ethyl	3-iodophenyl	S-$(CH_2)_3$-	H	5-chloro	6-chloro
404	ethyl	N-methyl-2-pyrrolyl-	CO-CH_2-C(=CH_2)-CH_2	n-propyl	6-methoxy	
405	Me	4-methoxyphenyl	O-$(CH_2)_3$-	n-propyl	4-cyano	
406	ethyl	oxadiazol-2-yl	S-$(CH_2)_3$-	n-propenyl	5-bromo	

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Exp	R^1	R^2	A	R^5	R^6	R^7
407	Me	3-iodophenyl	$(CH_2)_2$-CH(CH_3)-CH_2-CH_2-	n-propyl	4-cyano	
408	Me	phenyl	O-$(CH_2)_3$-	prop-2-enyl	5-thiomethyl	
409	Me	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	4-cyano	
410	Me	3-iodophenyl	S-$(CH_2)_3$-	n-propyl	H	
411	Me	N-methyl-2-pyrrolyl-	CONH-$(CH_2)_4$-	n-propyl	6-methoxy	
412	Me	3-iodophenyl	S-$(CH_2)_3$-	n-propenyl	5-methyl	
413	Me	N-methyl-2-pyrrolyl-	S-$(CH_2)_3$-	n-propyl	4-cyano	
414	Me	phenyl	S-$(CH_2)_3$-	n-propyl	4-cyano	
415	ethyl	phenyl	S-$(CH_2)_6$-	n-propyl	5-methoxy	6-chloro
416	ethyl	phenyl	S-$(CH_2)_6$-	but-2-enyl	4-cyano	
417	Me	cyclohexyl-	S-$(CH_2)_7$-	n-propyl	5-chloro	6-chloro
418	Me	phenyl	O-$(CH_2)_3$-	prop-2-enyl	5-thiomethyl	
419	Me	3-cyanophenyl	S-$(CH_2)_3$-	n-propyl	H	
420	Me	N-propyltetrazolyl-	S-$(CH_2)_3$-	n-propyl	5-methyl	
421	Me	oxadiazol-2-yl	S-$(CH_2)_3$-	methyl	4-cyano	
422	Me	cyclohexyl-	S-(CH_2)3-	n-propyl	4-cyano	
423	Me	2-Me-4-oxazolyl-	S-$(CH_2)_3$-	n-propyl	4-cyano	
424	Me	methylamino	S-$(CH_2)_3$-	n-propyl	5-chloro	
425	Me	2-pyrazinyl-	S-CH_2-CH=CH-CH_2-	n-propyl	5-methyl	
426	cycprop	6-chlorobiphenyl-2-	S-$(CH_2)_3$-	n-propyl	6-methoxy	
427	ethyl	3-cyanophenyl	S-$(CH_2)_8$-	n-propyl	4-fluoro	6-chloro

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Exp	R^1	R^2	A	R^5	R^6	R^7
428	ethyl	phenyl	S-$(CH_2)_3$-	n-propyl	5-bromo	
429	butyl	phenyl	O-$(CH_2)_3$-	methyl	5-fluoro	
430	Me	4-imidazolyl-	S-$(CH_2)_3$-	methyl	6-methoxy	
431	ethyl	phenyl	S-CH_2-C(CH_3)=CH-CH_2-	but-2-enyl	4-cyano	
432	Me	phenyl	COO-$(CH_2)_4$-	n-propyl	6-methanesulfonyl-oxy	
433	Me	3-iodophenyl	S-$(CH_2)_3$-	methyl	4-cyano	
434	Me	2,5-dimethyl-furanyl-3-	S-$(CH_2)_3$-	n-propyl	4-cyano	
435	Me	4-methoxyphenyl	S-$(CH_2)_3$-	n-propyl	5-methyl	
436	Me	tetrazolyl-	S-$(CH_2)_3$-	n-propyl	6-methoxy	
437	Me	3-Br-pyridin-5-yl-	S-$(CH_2)_3$-	n-propyl	4-cyano	
438	Me	tetrazolyl-	S-$(CH_2)_3$-	n-propenyl	5-methyl	
439	Me	pyridin-3-yl-	S-$(CH_2)3$-	n-propyl	4-cyano	
440	Me	3-Br-pyridin-5-yl-	S-$(CH_2)_3$-	n-propyl	5-methyl	
441	Me	4-methoxyphenyl	S-$(CH_2)_3$-	n-propyl	4-methanesulfonyl-oxy	
442	Me	3-benzothienyl-	S-$(CH_2)3$-	n-propyl	5-methyl	
443	Me	pyridin-4-yl-	S-$(CH_2)_3$-	methyl	6-methoxy	
444	Me	3-iodophenyl	S-CH_2-cycprop-CH2-	but-2-enyl	4-cyano	
445	Me	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	H	
446	Me	phenyl	S-CH_2-cycprop-CH2-	H	5-bromo	

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Exp	R^1	R^2	A	R^5	R^6	R^7
447	Me	phenyl	O-$(CH_2)_3$-	methyl	5-fluoro	
448	cycprop	2-pyrazinyl-	S-$(CH_2)_3$-	prop-2-enyl	5-iodo	
449	Me	3-cyanophenyl	CONH-$(CH_2)_5$-	n-propyl	4-fluoro	
450	n-hexyl	2-pyrazinyl-	S-$(CH_2)_3$-	prop-2-enyl	6-methanesulfonyl-oxy	
451	Me	phenyl	S-CH_2-CH=CH-CH_2-	n-propyl	6-methanesulfonyl-oxy	
452	iprop	3-Br-pyridin-5-yl-	S-$(CH_2)_3$-	n-propyl	5-chloro	
453	Me	phenyl	O-$(CH_2)_3$-	but-2-enyl	4-cyano	
454	Me	2-thienyl	S-CH_2-C(=CH_2)-CH_2	n-propyl	5-chloro	
455	Me	pyridin-3-yl-	S-$(CH_2)_3$-	n-propyl	6-methanesulfonyl-oxy	
456	Et	phenyl	S-$(CH_2)_3$-	n-propyl	5-methoxy	6-methoxy
457	propyl	pyridin-3-yl-	S-CH_2-CH=CH-CH_2-	n-propyl	5-bromo	
458	butyl	tetrazolyl-	S-$(CH_2)_3$-	methyl	4-cyano	
459	Me	3-Br-pyridin-5-yl-	S-$(CH_2)_3$-	n-propyl	6-methoxy	
460	Me	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	5-methyl	
461	Me	pyridin-3-yl-	S-$(CH_2)_3$-	n-propyl	H	
462	Me	3-benzothienyl-	S-$(CH_2)_3$-	n-propyl	5-chloro	
463	Me	phenyl	S-CH_2-cychex-CH_2-CH_2-	n-propyl	4-fluoro	
464	butyl	3-cyanophenyl	O-$(CH_2)_3$-	n-propyl	4-fluoro	

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Exp	R^1	R^2	A	R^5	R^6	R^7
465	Me	6-chlorobiphenyl-2-	S-$(CH_2)_3$-	n-propyl	5-fluoro	
466	ethyl	3-iodophenyl	S-$(CH_2)_3$-	n-propenyl	5-bromo	
467	ethyl	2-me-4-oxazolyl-	S-$(CH_2)_3$-	n-propenyl	5-bromo	
468	Me	oxadiazol-2-yl	S-$(CH_2)_3$-	n-propyl	5-chloro	
469	propyl	phenyl	S-CH_2-CH=CH-CH_2-	methyl	5-fluoro	
470	Me	3-iodophenyl	S-$(CH_2)_3$-	n-propyl	6-methanesulfonyl-oxy	
471	butyl	phenyl	O-$(CH_2)_3$-	prop-2-enyl	5-thiomethyl	
472	n-hexyl	3-cyanophenyl	S-CH_2-CH=CH-CH_2-	prop-2-enyl	5-chloro	
473	Me	5-methyl imida-zol-4-yl-	S-$(CH_2)_3$-	n-propyl	4-cyano	
474	Me	2-me-4-oxazolyl-	S-$(CH_2)_3$-	n-propyl	5-chloro	
475	Me	4-methoxyphenyl	S-$(CH_2)_3$-	n-propyl	H	
476	n-hexyl	4-methoxyphenyl	S-$(CH_2)_3$-	n-propyl	5-chloro	
477	Me	2-pyrazinyl-	S-$(CH_2)_3$-	n-propyl	6-methoxy	
478	Me	3-iodophenyl	S-CH_2-C(=CH_2)-CH_2	n-propyl	4-cyano	
479	Me	4-imidazolyl-	S-$(CH_2)_3$-	H	4-cyano	
480	ethyl	5-methyl imida-zol-4-yl-	S-$(CH_2)_3$-	n-propyl	6-methoxy	
481	Me	phenyl	COO-$(CH_2)_4$-	n-propyl	5-methoxy	
482	Me	4-methylthiazol-5-yl	CONH-$(CH_2)_4$-	n-propyl	6-trifluoromethoxy	
483	Me	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	6-methoxy	

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Exp	R^1	R^2	A	R^5	R^6	R^7
484	Me	4-imidazolyl-	S-$(CH_2)_3$-	n-propyl	H	
485	Me	2-thienyl	O-$(CH_2)_3$-	n-propyl	5-chloro	
486	Me	2-thienyl	S-$(CH_2)_3$-	n-propyl	5-chloro	
487	ethyl	phenyl	S-CH_2-C(CH_3)=CH-CH_2-	prop-2-enyl	5-chloro	
488	Me	4-methylthiazol-5-yl	S-$(CH_2)_3$-	n-propyl	5-chloro	
489	Me	pyridin-4-yl-	S-$(CH_2)_3$-	n-propyl	5-fluoro	
490	Me	N-propyl-tetrazolyl-	S-$(CH_2)_3$-	methyl	6-methoxy	
491	ethyl	phenyl	S-$(CH_2)_7$-	prop-2-enyl	5-thiomethyl	
492	cycprop	oxadiazol-2-yl	S-$(CH_2)_3$-	n-propyl	6-methoxy	
493	Me	4-imidazolyl-	S-(CH_2)3-	n-propyl	5-chloro	
494	Me	4-methylthiazol-5-yl	S-$(CH_2)_3$-	n-propyl	H	
495	Me	N-methyl-2-pyrrolyl-	S-$(CH_2)_3$-	prop-2-enyl	5-methyl	
496	Me	phenyl	S-CH_2-cychex-CH_2-CH_2-	methyl	5-fluoro	
497	Me	pyridin-3-yl-	CONH-$(CH_2)_4$-	n-propyl	5-bromo	
498	iprop	2-aminothiazol-4-yl-	S-$(CH_2)_4$-	n-propyl	5-chloro	6-bromo
499	Me	4-methylthiazol-5-yl	S-(CH_2)3-	n-propyl	4-cyano	
500	Me	2-aminothiazol-4-yl-	S-$(CH_2)_3$-	n-propyl	6-methoxy	
501	Me	4-methoxyphenyl	COO-$(CH_2)_3$-	n-propyl	4-cyano	
502	Me	N-methyl-2-pyrrolyl-	S-$(CH_2)_3$-	n-propyl	5-chloro	
503	iprop	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	n-propyl	6-methanesulfonyl-oxy	

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Exp	R^1	R^2	A	R^5	R^6	R^7
504	Me	cyclohexyl-	S-$(CH_2)_3$-	n-propyl	5-chloro	
505	Me	3-pyrrolyl	S-$(CH_2)_3$-	n-propyl	5-chloro	
506	ethyl	6-chlorobiphenyl-2-	S-$(CH_2)_3$-	prop-2-enyl	5-bromo	
507	Me	2-thienyl	S-$(CH_2)_3$-	n-propyl	H	
508	ethyl	pyridin-3-yl-	S-$(CH_2)_3$-	prop-2-enyl	5-bromo	
509	cycprop	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	prop-2-enyl	6-methanesulfonyl-oxy	
510	Me	pyridin-3-yl-	S-$(CH_2)_3$-	methyl	4-cyano	
511	propyl	4-methylthiazol-5-yl	S-CH_2-CH=CH-CH_2-	n-propyl	6-trifluoromethoxy	
512	ethyl	phenyl	CO-$(CH_2)_3$-	prop-2-enyl	5-chloro	
513	Me	2,5-dimethylfuranyl-3-	S-$(CH_2)_3$-	n-propyl	6-methoxy	H
514	Me	2-thienyl	S-CH_2-C(=CH_2)-CH_2	n-propyl	5-chloro	
515	Me	5-methyl imidazol-4-yl-	S-$(CH_2)_3$-	prop-2-enyl	6-cyano	/-methyl
516	Me	phenyl	$(CH_2)_4$-	n-propyl	5-methoxy	
517	Me	4-methoxyphenyl	S-CH_2-C(=CH_2)-CH_2	n-propyl	4-cyano	
518	Me	pyridin-4-yl-	S-$(CH_2)_3$-	n-propyl	5-methyl	
519	Me	4-iodophenyl	S-$(CH_2)_3$-	n-propyl	6-methoxy	
520	Me	3-cyanophenyl	S-$(CH_2)_3$-	n-propyl	5-methyl	

Provided no other meaning is given, R^7 is hydrogen.

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Examples of pharmaceutical administration forms

A) Tablets

Tablets of the following composition were pressed on a tablet pelleting machine in the cusomary manner

40 mg of the substance from Example 1
120 mg of corn starch
13.5 mg of gelatin
45 mg of lactose
2.25 mg of Aerosil® (chemically pure silicic acid in a submicroscopically fine dispersion)
6.75 mg of potato starch (as a 6% paste)

B) Sugar-coated tablets

20 mg of the substance from Example 4
60 mg of core mass
70 mg of saccharification mass

The core mass consists of 9 parts of corn starch, 3 parts of lactose and 1 part of vinylpyrrolidone-vinyl acetate 60:40 mixed polymer. The saccharification mass consists of

5 parts of cane sugar, 2 parts of corn starch, 2 parts of calcium carbonate and 1 part of talc. The sugar-coated tablets which have been prepared in this way are then provided with a gastric juice-resistant film.

Biological investigations - receptor binding studies

1) D_3 binding test

Cloned human D_3-receptor-expressing CCL 1,3 mouse fibroblasts, obtainable from Res. Biochemicals Internat. One Strathmore Rd., Natick, MA 01760-2418 USA, were used for the binding studies.

Cell preparation

The D_3-expressing cells were multiplied in RPMI-1640 containing 10% fetal calf serum (GIBCO No. 041-32400 N); 100 U of penicillin/ml and 0.2% streptomycin (GIBO BRL, Gaithersburg, MD, USA). After 48 h, the cells were washed with PBS and incubated for 5 min with 0.05% trypsin-containing PBS. After that, the solution was

neutralized with medium and the cells were collected by centrifuging at 300 g. In order to lyse the cells, the pellet was washed briefly with lysis buffer (5 mM Tris-HCl, pH 7.4, containing 10% glycerol) and after that incubated, at 4°C for 30 min, at a concentration of 10^7 cells/ml of lysis buffer. The cells were centrifuged at 200 g for 10 min and the pellet was stored in liquid nitrogen.

Binding tests

For the D_3-receptor binding test, the membranes were suspended in incubation buffer (50 mM Tris-HCl, pH 7.4, containing 120 mM NaCl, 5 mM KCl, 2 mM $CaCl_2$, 2 mM $MgCl_2$, 10 mM quinolinol, 0.1% ascorbic acid and 0.1% BSA), at a concentration of approx. 10^6 cells/250 ml of test mixture, and incubated at 30°C for 0.1 nM ^{125}iodine sulpiride in the presence and absence of the test substance. The nonspecific binding was determined using 10^{-6} M spiperone.

After 60 min, the free radioligand and the bound radioligand were separated by filtering through GF/B glass fiber filters (Whatman, England) on a Skatron cell collector (Skatron, Lier, Norway), and the filteres were washed with ice-cold Tris-HCl buffer, pH 7.4. The radioactivity which had collected on the filters was quantified using a Packard 2200 CA liquid scintillation counter.

The K_i values were determined by means of nonlinear regression analysis using the LIGAND program.

2) D_2 binding test

Cell culture

HEK-293 cells possessing stably expressed human dopamine D2A receptors were cultured in RPMI 1640 containing Glutamix I™ and 25 mM HEPES containing 10% fetal calf serum albumin. All the media contained 100 units of penicillin per mol and 100 mg/ml of streptomycin/ml. The cells were maintained at 37°C in a moist atmosphere containing 5% CO_2.

The cells were prepared for the binding studies by trypsinizing them (0.05% solution of trypsin) at room temperature for 3-5 minutes. After that, the cells were centrifuged at 250 g for 10 minutes and treated with lysis buffer (5 mM Tris-HCl, 10% glycerol, pH 7.4) at 4°C for

30 minutes. After centrifuging at 250 g for 10 minutes, the residue was stored at -20°C until used.

Receptor binding tests

Low affinity state dopamine D_2 receptor using ^{125}I-spiperone (81 TBq/mmol, Du Pont de Nemours, Dreieich)

The test mixtures (1 ml) consisted of 1 x 10^5 cells in incubation buffer (50 mM Tris, 120 mM NaCl, 5 mM KCl, 2 mM $MgCl_2$ and 2 mM $CaCl_2$, pH 7.4 with HCl) and 0.1 mM ^{125}I-spiperone (total binding) or additionally 1 mM haloperidol (nonspecific binding) or test substance.

After the test mixtures had been incubated at 25°C for 60 minutes, they were filtered through GM/B glass filters (Whatman, England) on a Skatron cell collector (from Zinsser, Frankfurt), and the filters were washed with ice-cold 50 mM Tris-HCl buffer, pH 7.4. The radioactivity which had collected on the filters was quantified using a Packard 2200 CA liquid scintillation counter.

The results were evaluated as described in a).

The K_i values were determined by way of nonlinear regression analysis using the LIGAND program or by converting the IC_{50} values using the Cheng and Prusoff formula.

In these tests, the compounds according to the invention exhibit very good affinities for the D_3 receptor (< 1 mmolar, in particular < 200 nmolar) and bind selectively to the D_3 receptor.

Table 3 gives the pK_i-D_3 values and the selectivity values ($K_i(D_2)/K_i(D_3)$) for the compounds of Examples 1, 14 and 26.

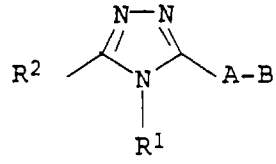
Table 3:

Example	$pK_i(D_3)$*	Selectivity
1	9.05	71
14	7.82	46
26	8.06	157

* negative decadic logarithm of $K_i(D_3)$ [M]

We claim:

1. A triazole compound of the formula I



(I)

where

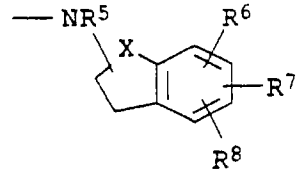
R^1 is H, C_1-C_6-alkyl, which may be substituted by OH, OC_1-C_6-alkyl, halogen or phenyl, C_3-C_6-cycloalkyl or phenyl;

R^2 is H, C_1-C_6-alkyl, which may be substituted by OH, OC_1-C_6-alkyl, halogen or phenyl, C_1-C_6-alkoxy, C_1-C_6-alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, halogen, CN, $COOR^3$, $CONR^3R^4$, NR^3R^4, SO_2R^3, $SO_2NR^3R^4$ or an aromatic radical which is selected from phenyl, naphthyl and a 5- or 6-membered heterocyclic radical having 1, 2, 3 or 4 heteroatoms which are selected, independently of each other, from O, N and S, with it being possible for the aromatic radical to have one or two substituents which are selected, independently of each other, from C_1-C_6-alkyl, which may be substituted by OH, OC_1-C_6-alkyl, halogen or phenyl, C_1-C_6-alkoxy, C_2-C_6-alkenyl, C_2-C_6-alkynyl, C_3-C_6-cycloalkyl, halogen, CN, COR^3, NR^3R^4, NO_2, SO_2R^3, $SO_2NR^3R^4$ and phenyl which may be substituted by one or two radicals which are selected, independently of each other, from C_1-C_6-alkyl, C_1-C_6-alkoxy, NR^3R^4, CN, CF_3, CHF_2 or halogen;

R^3 and R^4 are, independently of each other, H, C_1-C_6-alkyl, which may be substituted by OH, OC_1-C_6-alkyl, halogen or phenyl, or phenyl;

A is C_4-C_{10}-alkylene or C_3-C_{10}-alkylene which comprises at least one group Z which is selected from O, S, $CONR^3$, COO, CO, C_3-C_6-cycloalkyl and a double or triple bond;

B is a radical of the following formula:



where

X is CH_2 or CH_2CH_2;

R^5 is H, C_1-C_6-alkyl, which may be substituted by OH, OC_1-C_6-alkyl, halogen or phenyl, C_3-C_6-cycloalkyl, C_2-C_6-alkenyl, which may be substituted by halogen, or C_2-C_6-alkynyl;

R^6, R^7 and R^8 are, independently of each other, selected from H, C_1-C_6-alkyl, which may be substituted by OH, OC_1-C_6-alkyl, C_1-C_6-alkylthio, halogen or phenyl, OH, C_1-C_6-alkoxy, SH, C_1-C_6-alkylthio, C_2-C_6-alkenyl, C_2-C_6-alkynyl, halogen, CN, NO_2, SO_2R^3, $SO_2NR^3R^4$, $NHSO_2R^3$ and NR^3R^4;

and the salts thereof with physiologically tolerated acids.

2. A compound as claimed in claim 1 of the formula I, where X is CH_2CH_2.

3. A compound as claimed in one of the preceding claims of the formula I, where A is C_4-C_{10}-alkylene of C_3-C_{10}-alkylene which comprises at least one group Z which is selected from O, S; a double bond or triple bond and C_3-C_6-cycloalkyl.

4. A compound as claimed in one of the preceding claims of the formula I, where R^2 is an aromatic radical which is unsubstituted or has one or two substituents which are selected, independently of each other, from C_1-C_6-alkyl, OH, C_1-C_6-alkoxy, phenyl, CN and halogen.

5. A compound as claimed in one of the preceding claims of the formula I, where R^2 is H, C_1-C_6-alkyl, phenyl, thienyl, furanyl, pyridyl, pyrrolyl, thiazolyl or pyrazinyl.

6. A compound as claimed in one of the preceding claims of the formula I, where R^1 is H, C_1-C_6-alkyl or C_3-C_6-cycloalkyl.

7. A compound as claimed in one of the preceding claims of the formula I, where R^6, R^7 and R^8 are selected, independently of each other, from H, C_1-C_6-alkyl, halosubstituted C_1-C_6-alkyl, OH, C_1-C_6-alkoxy, C_1-C_6-akylthio-C_1-C_6-alkyl, halogen, CN, SO_2R^3, $SO_2NR^3R^4$, $CONR^3R^4$ and NO_2.

8. A compound as claimed in claim 1 of the formula I, where

R^1 is H, C_1-C_6-alkyl or phenyl,
R^2 is H, C_1-C_6-alkyl, phenyl, thienyl, furanyl, pyridyl, pyrrolyl, thiazolyl or pyrazinyl,
A is -SC_3-C_{10}-alkylene which may comprise a double bond or C_3-C_6-cycloalkyl, and
R^6, R^7 and R^8 are selected from H, C_1-C_6-alkyl, C_1-C_6-alkoxy, halogen and C_1-C_6-alkylthio-C_1-C_6-alkyl.

9. A pharmaceutical which comprises at least one compound as claimed in one of claims 1 to 8, where appropriate together with physiologically acceptable excipients and/or adjuvants.

10. The use of at least one compound as claimed in one of claims 1 to 8 for preparing a pharmaceutical for treating diseases which respond to the influence of dopamine D_3 receptor antagonists or agonists.