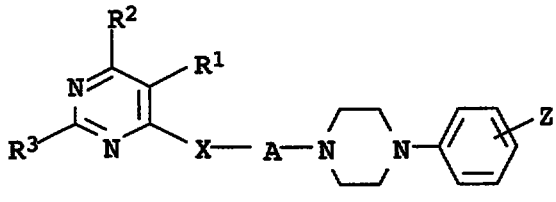
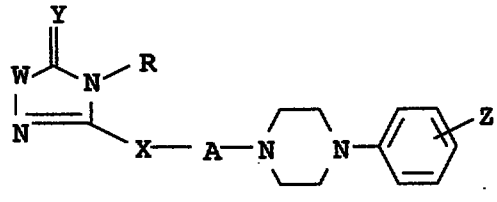
Substituted aza- and diazacycloheptane and -cyclooctane compounds and their use

The invention relates to substituted aza- and diazacycloheptane and -cyclooctane compounds and to the use of such compounds. Said compounds have valuable therapeutic properties and can be used in particular for treating disorders which respond to dopamine D_3 ligands.

Compounds of the type under discussion here and having physiological activity have in some cases been disclosed. Thus, DE 21 39 082 and DE 22 58 561 describe pyrimidine derivatives and pyrimidone derivatives with basic substituents as drugs for lowering blood pressure. These pyrimidine and pyrimidone derivatives have the formulae:



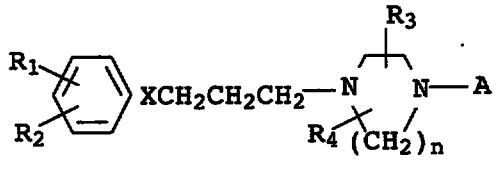
(A)



(B)

where in (A) X is, inter alia, a sulfur atom, A is a C_1-C_6-alkylene group, and R^1, R^2, R^3 and Z are various substituents. In (B), X and Y are an oxygen or sulfur atom, A is a C_2-C_6-alkylene group, W is a vinylene group and R and Z are various substituents.

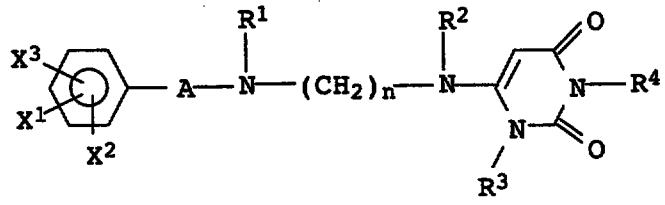
EP-A-361271 describes pyridyl and pyrimidyl derivatives of the formula:



where R_1 is halogen or hydrogen, and R_2 is halogen; X is oxygen, sulfur or methylene; R_3 and R_4, which are identical or different, are hydrogen or lower alkyl; n is 2 or 3; A is a 2-pyrimidyl group or a 2- or 3-pyridyl group, it being possible for these groups to be substituted.

These compounds can be used to treat mental disturbances.

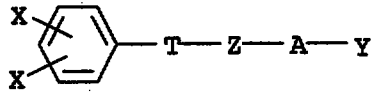
EP-A-454498 describes compounds of the formula



where A is, inter alia, $-(CH_2)_m-$ or $-B-(CH_2)_k-$, where B is O, S, an unsubstituted or substituted amino group, -CONH- or -COO-, R^1 and R^2 can, inter alia, together form an alkylene chain, R^3 and R^4 are a hydrogen atom or a lower alkyl group, and X^1, X^2 and X^3 are various substituents. These compounds can be used to treat cardiac arrhythmias.

EP-A-452107 and EP-A-369627 describe structurally similar compounds which can likewise be used for treating cardiac arrhythmias.

In addition, BE-A-628 766 describes compounds of the formula



where X is a halogen atom or a lower alkyl radical, T is piperazine, methylpiperazine, homopiperazine or methylhomopiperazine; Z is alkylene or alkenylene; A is O or S; and Y is a naphthyl, halonaphthyl or an unsubstituted or mono- to trisubstituted phenyl radical. These compounds can be used to treat schistosomiasis.

Neurones obtain their information inter alia via G-protein-coupled receptors. There are numerous substances which exert their effect via these receptors. One of these is dopamine.

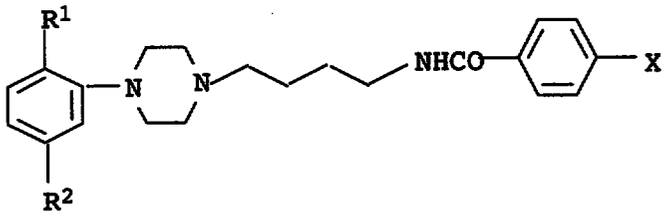
Confirmed information on the presence of dopamine and its physiological function as neurotransmitter is available. Cells responding to dopamine are connected with the etiology of schizophrenia and Parkinson's disease. These and other diseases are treated with drugs which interact with dopamine receptors.

Up to 1990, two subtypes of dopamine receptors had been clearly defined pharmacologically, mainly 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 antipsychotics (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 1992, pages 135-144).

D_3 receptors are mainly expressed in the limbic system. It is therefore assumed that a selective D_3 antagonist is likely to have the antipsychotic properties of the D_2 antagonists but not their 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)).

P.J. Murray et al., Bioorganic & Medicinal Chemistry Letters, Vol. 5, No. 3, 219-222 (1995), have described arylpiperazines of the formula



where R^1 and R^2 are H or CH_3O, and X is Br, 4-acetylphenyl, 4-methylsulfonylphenyl or 4-aminophenyl, with higher affinity and selectivity for the dopamine D_3 receptor.

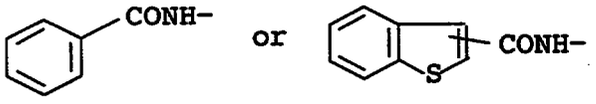
We have now found, surprisingly, that certain aza- and diazacycloheptane and -cyclooctane compounds have a high affinity for the dopamine D_3 receptor and a low affinity for the D_2 receptor. They are thus selective D_3 ligands.

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

$$Ar^1\text{-}A\text{-}B\text{-}Ar^2 \qquad (I)$$

where

Ar^1 is



or a 5- or 6-membered heteroaromatic ring with 1, 2 or 3 heteroatoms which are selected, independently of one another, from O, N and S, where Ar^1 may have 1, 2, 3 or 4 substituents

which are selected, independently of one another, from OR^1, alkyl which is unsubstituted or substituted by OH, OC_1-C_8-alkyl or halogen, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, cycloalkyl, halogen, CN, CO_2R^1, NO_2, NR^1R^2, SR^1, CF_3, CHF_2, phenyl which is unsubstituted or substituted by C_1-C_6-alkyl, OC_1-C_6-alkyl, acyl, phenyl, amino, nitro, cyano or halogen, or phenoxy which is unsubstituted or substituted by C_1-C_6-alkyl, OC_1-C_6-alkyl or halogen, or C_1-C_6-alkanoyl or benzoyl;

R^1 is H, alkyl which is unsubstituted or substituted by OH, OC_1-C_6-alkyl, phenyl or halogen;

R^2 has the meanings stated for R^1 or is COR^1 or CO_2R^1;

A is a C_3-C_{15}-alkylene group when Ar^1 is C_6H_5CONH, or, when Ar^1 is a 5- or 6-membered heteroaromatic ring, is a C_4-C_{15}-alkylene group or a C_3-C_{15}-alkylene group which comprises at least one group Z which is selected from O, S, NR^1, a double and a triple bond, where R^1 is as defined above,

B is a 7- or 8-membered saturated ring with one or two nitrogen heteroatoms, the nitrogen heteroatoms being located in the 1,4 or 1,5 position and the ring being bonded in position 1 to the radical A and in position 4 or 5 to the radical Ar^2, and it additionally being possible for the ring to have a double bond in position 3 or 4 in the monoaza ring and in position 6 in the 1,4-diaza ring;

Ar^2 is phenyl, pyridyl, pyrimidinyl or triazinyl, it being possible for Ar^2 to have 1, 2, 3 or 4 substituents which are selected, independently of one another, from OR^1, alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, alkoxyalkyl, haloalkyl, halogen, CN, CO_2R^1, NO_2, SO_2R^1, NR^1R^2, $SO_2NR^1R^2$, SR^1, a 5- or 6-membered carbocyclic, aromatic or non-aromatic ring and a 5- or 6-membered heterocyclic aromatic or non-aromatic ring with 1 to 3 heteroatoms which are selected from O, S and N, the carbocyclic or heterocyclic ring being unsubstituted or substituted by C_1-C_8-alkyl, phenyl, phenoxy, halogen, OC_1-C_8-alkyl, OH, NO_2 or CF_3, where R^1 and R^2 have the abovementioned meanings, and Ar^2 may also be fused to a carbocyclic ring of the type defined above, and where Ar^2 cannot be a pyrimidinyl radical substituted by 2 hydroxyl groups,
and the salts thereof with physiologically tolerated acids.

The compounds according to the invention are selective dopamine D_3 receptor ligands which intervene regioselectively in the limbic system and, because of their low affinity for the D_2 receptor,

have fewer side effects than classical neuroleptics, which are D_2 receptor antagonists. The compounds can therefore be used to treat disorders which respond to dopamine D_3 receptor antagonists or agonists, eg. for treating disorders of the central nervous system, in particular schizophrenia, depression, neuroses and psychoses.

For the purpose of the present invention, the following terms have the meanings indicated thereafter:

alkyl (also in radicals such as alkoxy, alkylamino etc.) is a straight-chain or branched alkyl group with 1 to 8 carbon atoms, preferably 1 to 6 carbon atoms and, in particular, 1 to 4 carbon atoms. The alkyl group may have one or more substituents which are selected, independently of one another, from OH and OC_1-C_8-alkyl.

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

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

Alkylene is a straight-chain or branched radical with, preferably, 4 to 15 carbon atoms, particularly preferably 4 to 10 carbon atoms, or with 3 to 15, in particular 3 to 10, carbon atoms when the alkylene group comprises one of said groups.

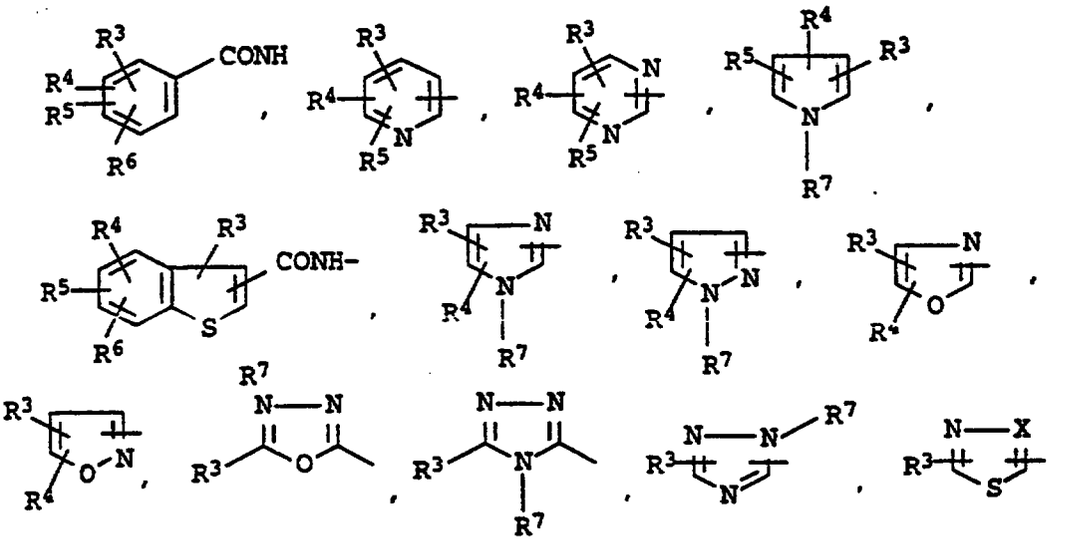
The alkylene groups may comprise at least one of the groups Z indicated above in the definition of A. This may, just like the said double or triple bond, be located anywhere in the alkylene chain or in position 1 or 2 of group A (seen from the Ar^1 radical). A is particularly preferably compounds according to formula I where A is -Z-C_3-C_6-alkylene, in particular -Z-$CH_2CH_2CH_2$-, -Z-$CH_2CH_2CH_2CH_2$-, -Z-CH_2C=$CHCH_2$-, -Z-$CH_2C(CH_3)$=$CHCH_2$-, -Z-$CH_2C(=CH_2)CH_2$-, -Z-$CH_2CH(CH_3)CH_2$- or a linear -Z-C_7-C_{10}-alkylene radical. In this case, A is particularly preferably -Z-C_3-C_6-alkylene when Ar^1 is an unsubstituted or substituted pyrimidine or triazole residue, and a linear -Z-C_7-C_{10}-alkylene radical when Ar^1 is an unsubstituted or substituted thiadiazole residue. In this case, Z can also be CH_2 and is preferably CH_2, O and, in particular, S.

Halogen is F, Cl, Br or I.

Haloalkyl may comprise one or more, in particular 1, 2 or 3, halogen atoms which can be located on one or more carbon atoms, preferably in the α or ω position. CF_3, CHF_2, CF_2Cl or CH_2F is particularly preferred.

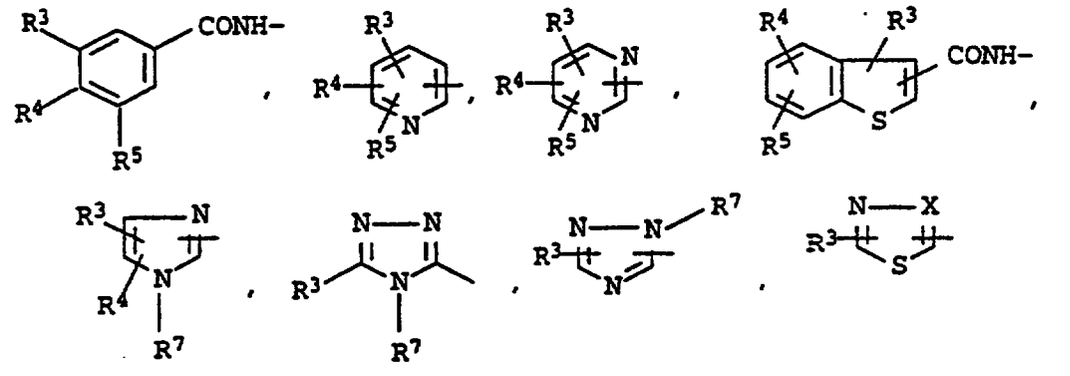
Acyl is preferably HCO or C_1-C_6-alkyl-CO, in particular acetyl. If Ar^1 is substituted, the substituent can also be located on the nitrogen heteroatom.

Ar^1 is preferably

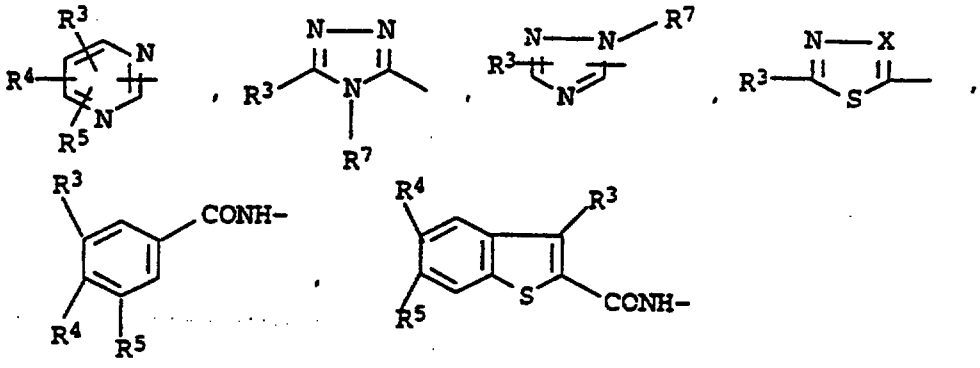


where
R^3 to R^6 are H or one of the abovementioned substituents of the Ar^1 radical,
R^7 has the meanings indicated above for R^2, and
X is N or CH. When the benzamide residue is substituted, the substituents are preferably in the m or p position.

Ar^1 is particularly preferably



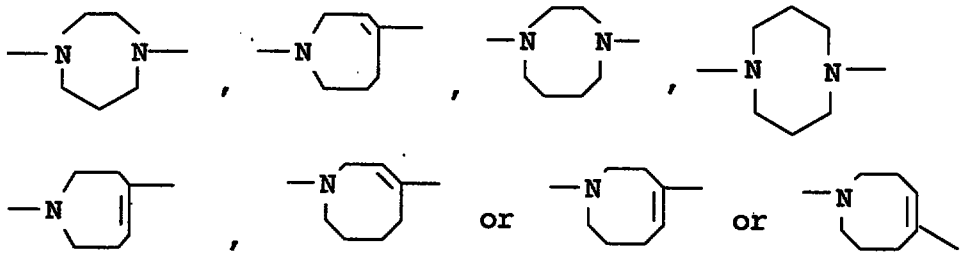
where R^3 to R^5, R^7 and X have the abovementioned meanings, and in particular



where R^3 to R^5, R^7 and X have the abovementioned meanings.

The radicals R^3 to R^6 are preferably H, C_1-C_6-alkyl, OR^1, NR^1R^2, SR^1, phenyl which is unsubstituted or substituted by C_1-C_6-alkyl, acyl or halogen, and halogen, where R^1 and R^2 have the abovementioned meanings.

The radical B is preferably



The radical Ar^2 may have one, two, three or four substituents, preferably one or two substituents, which are located in particular in the m position and/or p position. They are preferably selected, independently of one another, from C_1-C_6-alkyl, haloalkyl, NO_2, halogen, in particular chlorine, phenyl, pyrrolyl, imidazolyl, pyrazolyl, thienyl, cyclopentyl and cyclohexyl. If one of the substituents is C_1-C_8-alkyl, a branched group is preferred, in particular isopropyl or t-butyl.

Ar^2 is preferably unsubstituted or substituted phenyl, 2-, 3- or 4-pyridinyl or 2-, 4(6)- or 5-pyrimidinyl.

If one of the substituents on the radical Ar^2 is a 5- or 6-membered heterocyclic ring, it is, for example, a pyrrolidine, piperidine, morpholine, piperazine, pyridine, 1,4-dihydropyridine, pyrimidine, triazine, pyrrole, thiophene,

thiazole, imidazole, oxazole, isoxazole, pyrazole or thiadiazole residue, with a pyrrole, imidazole, pyrrazole or thienyl radical being preferred.

If one of the substituents on the radical Ar^2 is a carbocyclic radical, it is, in particular, a phenyl, cyclopentyl or cyclohexyl radical.

If Ar^2 is fused to a carbocyclic radical, it is, in particular, a naphthalene, di- or tetrahydronaphthalene residue.

The invention also comprises 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, Volume 10, pages 224 et seq., Birkhäuser Verlag, Basel and Stuttgart, 1966.

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

The process for preparing the compounds (I) comprises

a) reacting a compound of the general formula II

$$Ar^1 - Z - A - Y^1 \quad (II)$$

where Y^1 is a conventional leaving group such as Hal, alkanesulfonyloxy, arylsulfonyloxy etc., and Z has the abovementioned meanings, with a compound of the general formula (III)

$$H - B - Ar^2 \quad (III)$$

or

b) reacting a compound of the general formula (IV)

$$Ar^1 - A^1 - Z^1H \quad (IV)$$

where Z^1 is O, NR^1 or S and A^1 is C_1-C_{15}-alkylene or a bond, with a compound of the general formula V

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

where Y^1 has the abovementioned meaning, and A^2 is C_2-C_{15}-alkylene, where A^1 and A^2 together have 3 to 15 carbon atoms;

or

c) reacting a compound of the general formula (VI)

$$Ar^1 - Y^1 \quad (VI)$$

where Y^1 has the abovementioned meaning, with a compound of the general formula VII

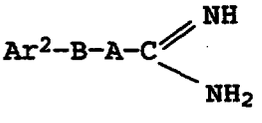
$$H - Z^1 - A - B - Ar^2 \quad (VII)$$

where Z^1 has the abovementioned meanings; or

d) converting a compound of the formula (VIII)

$$NC - A - B - Ar^2 \quad (VIII)$$

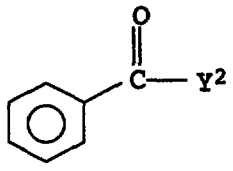
into a compound of the type of (IX)



(IX)

and reacting the latter with a dicarbonyl compound in a conventional way; or

e) to prepare a compound of the formula I where Ar^1 is a benzamide residue:
reacting a compound of the general formula (X)



(X)

where Y^2 is OH, OC_1-C_4-alkyl, Cl or together with CO an activated ester group, with a compound of the formula (XI)

$$Z^2 - A^2 - B - Ar^2 \quad (XI)$$

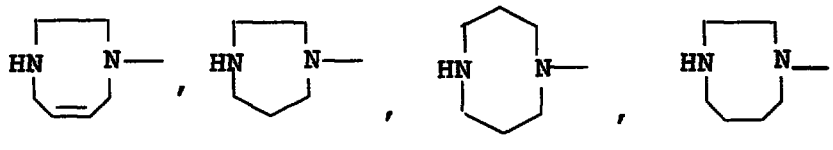
where A^2 has the abovementioned meanings, and Z^2 is OH or NH_2.

The compounds of the formula III are starting compounds for preparing compounds of the formulae V, VII and VIII and are prepared by

a) reacting a compound of the general formula (XII)

$$HB^1 \quad (XII)$$

where B^1 is



with a compound of the general formula (XIII)

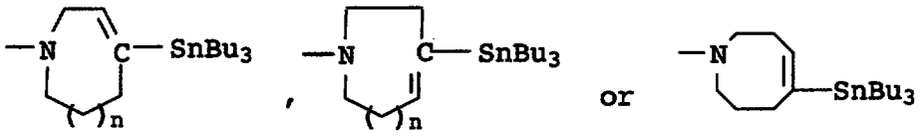
$$Y^1 - Ar^2 \quad (XIII)$$

where Y^1 is one of the abovementioned leaving groups and Ar^2 has the abovementioned meaning, in a conventional way; or

b) reacting a compound of the general formula (XIV)

$$H - B^2$$

where B^2 is

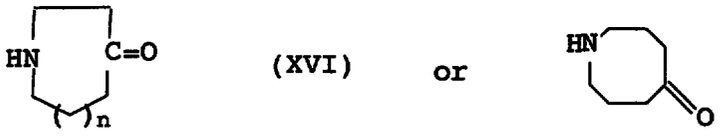


with n = 1 or 2,
with a compound of the general formula (XV)

$$Y^2 - Ar^2$$

where Y^2 is Br, Cl or I, and Ar^2 has the above meanings, by known processes as described, for example, by S.C. Buchwald et al., Angew. Chem. 1995, 107, 1456 or J.F. Hartweg et al., Tetrahedron Lett 1995, 36, 3604 and J.K. Stille et al., Angew. Chem. 1986, 98, 504 or Pereyre M. et al., Tin in Organic Synthesis, Butterworth 1987; or

c) reacting a compound of the general formula (XVI)



where n = 1 or 2,
with a compound M-Ar^2 where M is a metal such as Li or MgY^2. MAr^2 can be obtained from compounds of the formula XV by methods known from the literature.

Compounds of the type of Ar^1 and Ar^2 are either known or can be prepared by known processes as described, for example, in A.R. Katritzky, CW. Rees (ed.) "Comprehensive Heterocyclic Chemistry", Pergamon Press, or "The Chemistry of Heterocyclic Compounds", J. Wiley & Sons Inc. NY and the literature cited therein.

Compounds of type B are either known or can be prepared by processes similar to known ones, for example

1,4- and 1,5-diazacycloalkanes:	L. Börjeson et al. Acta Chem. Scand. 1991, 45, 621 Majahrzah et al Acta Pol. Pharm., 1975, 32, 145
1,4-diazacyclooct-6-enes:	W. Schroth et al. Z. Chem. 1969, 9, 143
1-azacyclooctanones:	N.J. Leonard et al. J. Org. Chem. 1964, 34, 1066

1-azacyclo-heptanones: A. Yokoo et al. Bull Chem. Soc. Jpn. 1956, 29, 631

The novel compounds and the starting materials and intermediates can also be prepared by methods similar to those described in the patent publications mentioned at the outset.

The reactions described above generally take place in a solvent at temperatures between room temperature and the boiling point of the solvent used. Solvents which can be used are, for example, ethyl acetate, tetrahydrofuran, dimethylformamide, dimethyl sulfoxide, dimethoxyethane, toluene, xylene, a ketone such as acetone or methyl ethyl ketone, or an alcohol such as ethanol or butanol.

An acid-binding agent is present if required. Suitable acid-binding agents are inorganic bases such as sodium or potassium carbonate, sodium methoxide, sodium ethoxide, sodium hydride or organometallic compounds such as butyllithium or alkylmagnesium compounds, or organic bases such as triethylamine or pyridine. The latter can also act as solvent.

The reactions take place where appropriate with use of a catalyst such as transition metals or complexes thereof, eg. $Pd(PPh_3)_4$, $Pd(OAc)_2$ or $Pd(P(oTol)_3)_4$, or of a phase-transfer catalyst, eg. tetrabutylammonium chloride or tetrapropylammonium bromide.

The crude product is isolated in a conventional way, for example by filtration, removal of the solvent by distillation, or extraction from the reaction mixture etc. The resulting compounds can be purified in a conventional way, for example by recrystallization from a solvent, chromatography or conversion into an acid addition compound.

The acid addition salts are prepared in a conventional way by mixing the free base with the appropriate 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 t-butyl ether, a ketone such as acetone or methyl ethyl ketone, or an ester such as ethyl acetate.

To treat the abovementioned disorders, the compounds according to the invention are administered orally or parenterally (subcutaneously, intravenously, intramuscularly, intraperitoneally) in a conventional way. Administration can also

take place with vapors or sprays through the nasopharyngeal space.

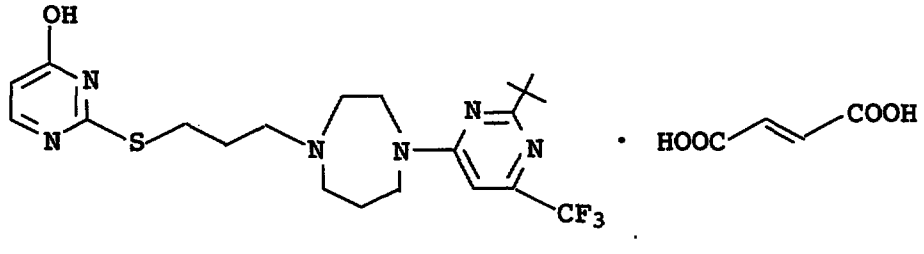
The dosage depends on the age, condition and weight of the patient and on the mode of administration. As a rule, the daily dose of active substance is about 10 to 1000 mg per patient and day on oral administration and about 1 to 500 mg per patient and day on parenteral administration.

The invention also relates to pharmaceutical compositions which comprise the compounds according to the invention. These compositions are in the form of the conventional solid or liquid pharmaceutical presentations, for example as uncoated or (film-)coated tablets, capsules, powders, granules, suppositories, solutions or sprays. The active substances can for this purpose be processed with conventional pharmaceutical aids such as tablet binders, bulking agents, preservatives, tablet disintegrants, flow regulators, plasticizers, wetting agents, dispersants, emulsifiers, solvents, release-slowing agents, antioxidants and/or propellant gases (cf. H. Sucker et al., Pharmazeutische Technologie, Thieme-Verlag, Stuttgart, 1978). The presentations obtained in this way normally contain from 1 to 99% by weight of active substance.

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

Example 1

1-[2-t-Butyl-6-trifluoromethyl-pyrimidin-4-yl]-4-[3-[4-hydroxy-pyrimidin-2-yl)mercaptopropyl]hexahydro-(1H)-1,4-diazepine [sic] fumarate



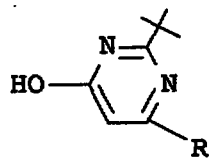
Preparation of the starting materials:

a) 2-t-Butyl-4-hydroxy-6-trifluoromethylpyrimidine.
The above pyridimine was synthesized in a conventional way by condensing 2,2-dimethylpropionamidine with ethyl trifluoroacetoacetate and sodium ethoxide in ethanol, see

Heterocyclic Compounds, Vol. 52, The Pyrimidines, page 189 et seq., D.J. Brown et al. (Eds.) John Wiley and Sons, 1994.

Melting point 187-188°C

The 4-hydroxypyrimidines of the formula

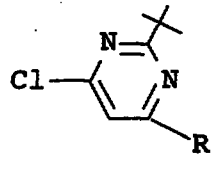


were obtained in a similar way.

R	M.p. [°C]
$t\text{-}C_4H_9$	169
$n\text{-}C_3H_7$	120
CF_2Cl	135-136

b) 2-t-Butyl-4-chloro-6-trifluoromethylpyrimidine
The hydroxypyrimidine from stage a) was converted with phosphorus oxychloride or thionyl chloride in a conventional way into the chlorine compound, see Heterocyclic Compounds, Vol. 52, The Pyrimidines, page 329 et seq., John Wiley and Sons, 1994. The compound is in the form of a yellowish oil.

The 4-chloropyrimidines of the formula



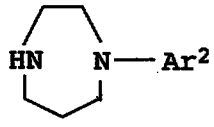
were obtained in a similar way:

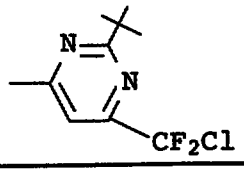
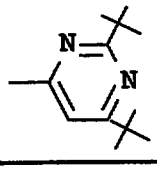
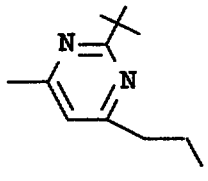
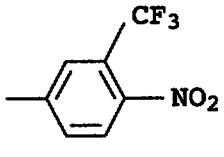
R	M.p. [°C]
$t\text{-}C_4H_9$	oil
$n\text{-}C_3H_7$	oil
CF_2Cl	oil

c) 1-[2-t-Butyl-6-trifluoromethylpyrimidin-4-yl]hexahydro-(1H)-1,4-diazepine
18 g (0.18 mol) of homopiperazine were dissolved in 25 ml of ethanol and, while refluxing, a solution of 7.2 g (0.03 mol) of the chloride obtained in b), dissolved in 10 ml of ethanol, was added dropwise over the course of 1 h. After reacting for a further 30 min, the cooled mixture was worked

up by adding 200 ml of water and extracting several times with a total of 200 ml of methylene chloride. The organic phase was then washed with water, dried with anhydrous sodium sulfate and concentrated. The required compound was obtained as a yellowish oil which was further processed unpurified. Yield: 98% of theory.

The following compounds were obtained in a corresponding way: 1-aryl-1,4-diazepine of the formula:



Ar^2	M.p. [°C]
	Oil
	Oil
	Oil
	74-75

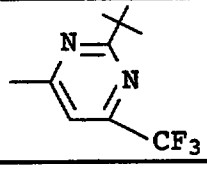
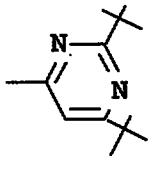
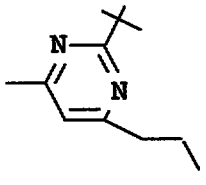
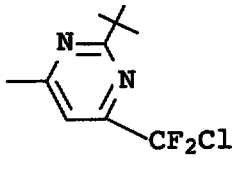
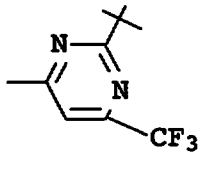
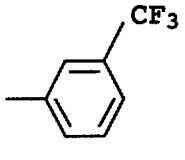
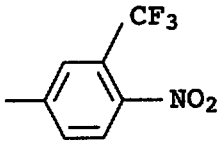
d) 1-[2-t-Butyl-6-trifluoromethylpyrimidin-4-yl]-4-(3-chloropropyl)hexahydro-(1H)-1,4-diazepine

5 g (0.0165 mol) of the compound obtained above under c) were refluxed together with 2.5 g (0.025 mol) of triethylamine and 3.15 g (0.02 mol) of 1-bromo-3-chloropropane in 50 ml of tetrahydrofuran for 10 h. The solvent was then removed by distillation, and the residue was washed with water and extracted with methylene chloride. The residue obtained after drying and concentrating was then purified by flash chromatography (silica gel).

Yield: 4.8 g (77% of theory) of yellow oil

The compounds listed below were obtained in a similar manner:

1-aryl-4-haloalkyl-1,4-diazepines of the formula

Hal	alk	Ar^2	M.p. [°C]
Cl	$-CH_2-CH(CH_3)-CH_2-$		Oil
"	$-CH_2C(=CH_2)-CH_2-$	"	Oil
"	$-(CH_2)_3-$		Oil
"	"		Oil
"	"		Oil
"	$-CH_2-C(CH_3)=CH-CH_2-$		Oil
"	$-(CH_2)_3-$		Oil
"	"		Oil

Preparation of the final product

5 g (0.013 mol) of the product obtained in d) were dissolved in 25 ml of dimethylformamide and added dropwise to a stirred solution at 100°C of 2.03 g (0.016 mol) of 2-thiouracil, 0.38 g (0.016 mol) of lithium hydroxide and 1 g of sodium iodide in 50 ml of dimethylformamide over the course of 1 h. After reaction for 3 hours, the solvent was removed by distillation under reduced pressure, and the residue was mixed with 150 ml of water and extracted twice with ethyl acetate. The residue obtained after washing with water, drying with sodium sulfate and concentrating was purified by chromatography. (Flash chromatography, silica gel, mobile phase methylene chloride with 2.5-5% methanol)

Yield: 4 g of pale oil

NMR: $CDCl_3$. δ 1.3(s,9H); 1.85-2.25(m,4H); 2.6(m,4H); 2.8(m,2H); 3.2(t,2H); 3.5(m,2H); 4.0(m,2H); 6.2(d,1H); 6.5(s,1H); 7.8(d;1H)

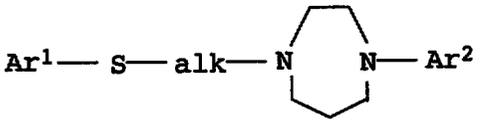
The substance was obtained as fumarate by adding an ethanolic solution with fumaric acid.

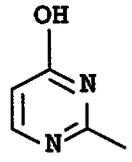
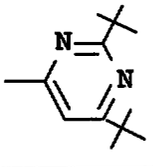
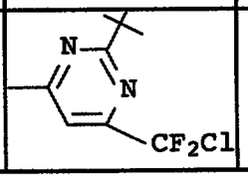
$C_{21}H_{29}F_3N_6OS \cdot C_4H_4O_4$ MW 586.6

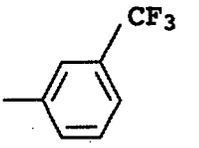
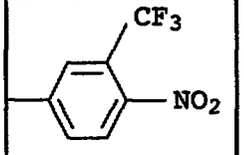
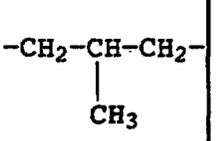
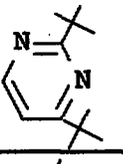
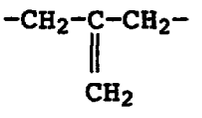
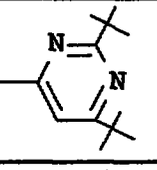
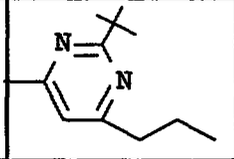
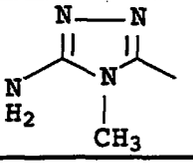
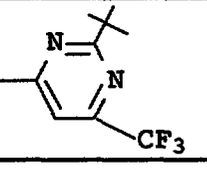
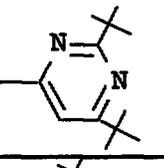
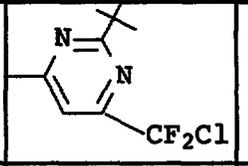
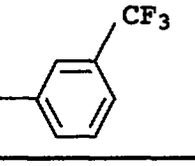
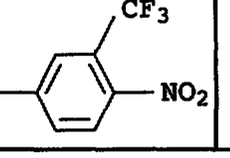
Melting point: 188-189°C

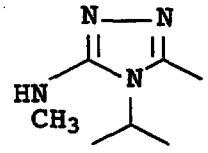
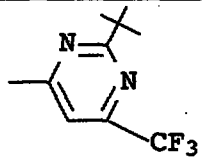
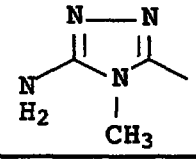
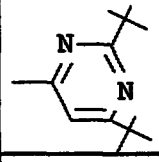
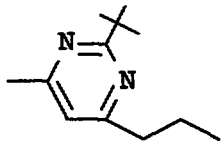
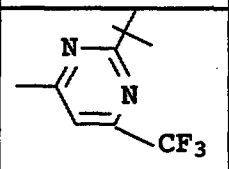
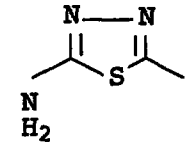
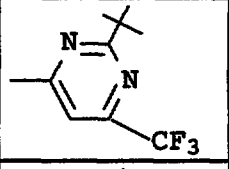
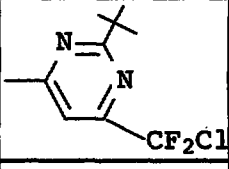
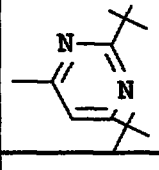
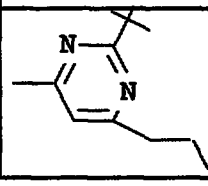
The compounds listed in the following Table 1 were obtained in a similar way using various haloalkyl-1,4-diazepines (eg. 1d) and various mercapto-substituted heterocycles such as thiouracil, 5-amino-2-mercaptotriazoles and 5-amino-2-mercaptothiadiazole:

Table 1



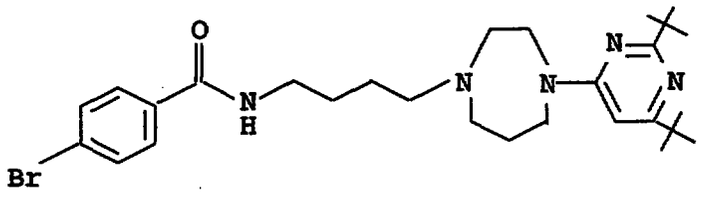
Ex. No.	Ar^1	alk	Ar^2	M.p. [°C]
2		$-(CH_2)_3-$		155-162 Oxalate
3	"	"		83-85 Oxalate

Ex. No.	Ar^1	alk	Ar^2	M.p. [°C]
4	"	"		177-182 Fumarate
5	"	"		72-74
6	"			116-119
7	"			174-180 Oxalate
8	"	"		60-70 Oxalate
9		$-(CH_2)_3-$		166-167 Fumarate
10	"	"		55-60
11	"	"		110-115 Oxalate
12	"	"		136-140 Hydro-chloride
13	"	"		95-98

Ex. No.	Ar^1	alk	Ar^2	M.p. [°C]
14		"		142-144
15		$-CH_2-CH(CH_3)-CH_2-$		125-128
16	"	$-CH_2-C(=CH_2)-CH_2-$		113-119 Oxalate
17	"	"		230-232 Hydro-chloride
18		$-(CH_2)_3-$		Oil
19	"	"		109-110
20	"	"		60-67
21	"	$-CH_2-CH(CH_3)-CH_2-$	"	180-190 Hydro-chloride
22	"	$-CH_2-C(=CH_2)-CH_2-$	"	119-122
23	"	$-CH_2-CH(CH_3)-CH_2-$		92-97 Oxalate

Example 24

4-Bromobenzoic acid-[4-{-4-(2,6-bis-t-butyl-4-pyrimidinyl)}-(hexahydro-(1H)-1,4-diazepin-1-yl-)butyl]amide [sic]

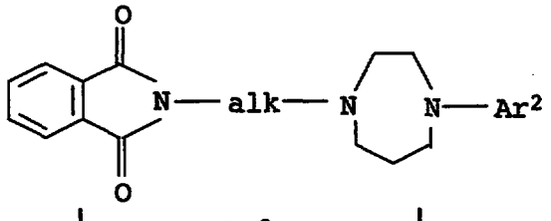


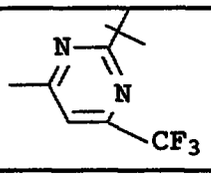
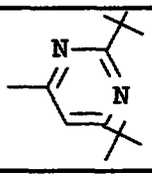
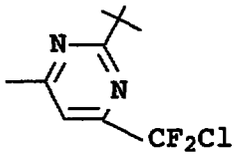
Preparation of the starting materials

a) Hexahydro-1H-1-[2-t-butyl-6-trifluoromethyl-4-pyrimidinyl]-4-(4-phthalimidobutyl)-(1H)-1,4-diazepine [sic]

10 g (0.033 mol) of the diazepine prepared in Example 1c) were refluxed with 9.8 g (0.035 mol) of N-(4-bromobutyl)phthalimide and 9.1 g (0.066 mol) of potassium carbonate in 120 ml of acetonitrile for 8 h. The mixture was filtered and the filtrate was concentrated. The residue was processed further unpurified.
Yield: 16.2 g (98% of theory)
A sample was recrystallized from ethanol.
Melting point 97-99°C

The following were obtained in a similar way:



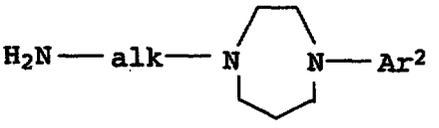
alk	Ar^2	M.p. [°C]
$-(CH_2)_3-$		89-92
$-CH_2-C(CH_3)=CH-CH_2-$	"	130-132
$-(CH_2)_3-$		119-121
$-(CH_2)_4-$	"	207-209
$-(CH_2)_4-$		190-192

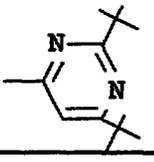
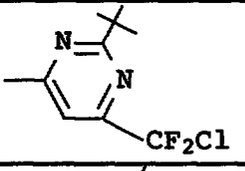
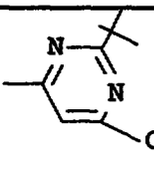
b) Hexahydro-1H-1-[2-t-butyl-6-trifluoromethyl-4-pyrimidinyl]-4-(4-aminobutyl)-1,4-diazepine

15 g (0.03 mol) of the product described above under a) were refluxed with 6 g of hydrazine hydrate in 200 ml of ethanol for 2 h, and then the precipitate was filtered off with suction and the filtrate was evaporated. The residue was taken up in ethyl acetate, filtered again, washed with water, dried and again evaporated.

9.2 g (83% of theory) were obtained as an oil.

The following were obtained in a similar way:



alk	Ar^2	M.p. [°C]
$-(CH_2)_4-$		Oil
$-(CH_2)_3-$	"	Oil
$-(CH_2)_4-$		Oil
$-(CH_2)_3-$		Di-Hydro-chloride: 241-245

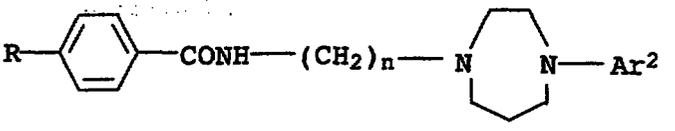
Preparation of the final products:

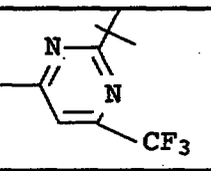
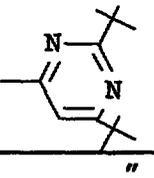
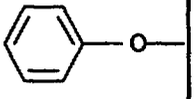
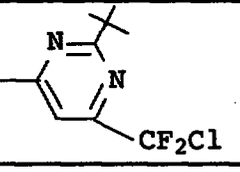
3 g (0.0083 mol) of the product obtained above under b) were dissolved with 0.9 g (0.009 mol) of triethylamine in 60 ml of tetrahydrofuran, and a solution of 2 g (0.009 mol) of 4-bromobenzoyl chloride in 10 ml of tetrahydrofuran was added dropwise at room temperature over the course of 10 min. After 1 h, the solvent was removed by distillation under reduced pressure, and the residue was mixed with water and extracted

twice with methylene chloride. The dried and concentrated solvent phase was purified by flash chromatography (silica gel, mobile phase methylene chloride with 3% methanol).
Yield: 4.2 g (93% of theory)
Melting point 125-127°C (from diisopropyl ether/isopropanol)
$C_{28}H_{42}BrN_5O$ (544.6)

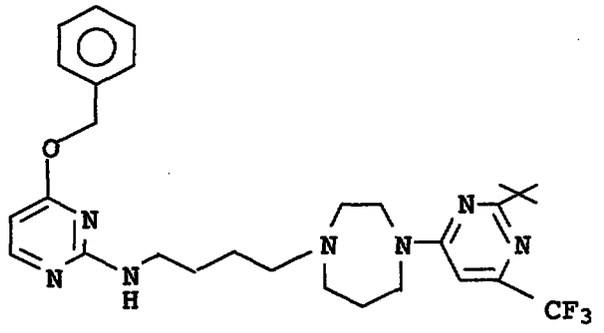
The compounds listed in Table 2 below were obtained using various amino derivatives (similar to 24b) and known benzoyl chlorides.

Table 2



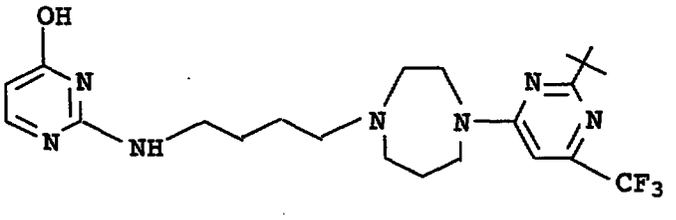
Ex. No.	R	n	Ar^2	M.p. [°C]
25	Br	3	"	169-171
26	"	4		74-76 Oxalate
27	t-Butyl	4		165-167 Oxalate
28		4	"	104-107 Oxalate
29	Br	4		92-94 Oxalate
30	I	4	"	110-115 Oxalate

Example 31
4-[4-{4-Benzyloxy-2-pyrimidinyl}aminobutyl]-1-[2-t-butyl-6-trifluoromethyl-4-pyrimidinyl]hexahydro-1H-1,4-diazepine [sic] oxalate



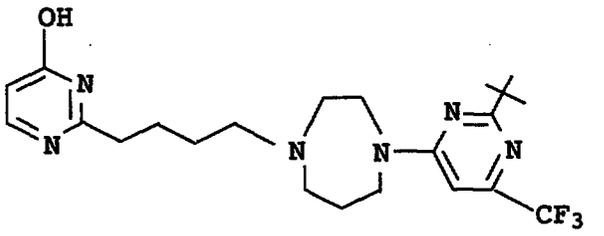
2.7 g (0.007 mol) of the amino compound prepared in Example 24b) were introduced with 0.3 g of sodium hydride (0.009 mol) into 20 ml of dimethylformamide. After reaction for 1 h, 1.6 g (0.006 mol) of 4-benzyloxy-2-methylsulfonylpyrimidine (prepared by oxidizing 4-benzyloxy-2-methylmercaptopyrimidine), dissolved in 10 ml of dimethylformamide, were added, and the mixture was stirred at room temperature for 72 h.
Subsequently, water was added, the mixture was extracted with ethyl acetate, and the solution was dried and concentrated. The residue was purified by column chromatography (silica gel, methylene chloride with 4% methanol)
Pure yield: 1.0 g (30% of theory)
Oxalate: Melting point 145-150°C
$C_{29}H_{38}F_3N_7O \cdot C_2H_2O_4$ (647.7)

Example 32:
1-[2-t-Butyl-6-trifluoromethyl-4-pyrimidinyl]-4-[4-{4-hydroxy-2-pyrimidinyl}aminobutyl]hexahydro-(1H)-1,4-diazepine [sic]



0.7 g (0.001 mol) of the compound described in the previous example was hydrogenated in methanol with palladium on carbon catalyst (10% Pd) under normal conditions.
Yield: 0.6 g (100% of theory)
Melting point 111-115°C
$C_{22}H_{32}F_3N_7O \cdot C_2H_4O_4$ (557.5)

Example 33:
1-[2-t-Butyl-6-trifluoromethyl-4-pyrimidinyl]-4-[4-(4-hydroxy-2-pyrimidinyl)butyl-hexahydro-1H-1,4-diazepine [sic]



a) 1-[2-t-Butyl-6-trifluoromethyl-4-pyrimidinyl]-4-(4-cyanobutyl)hexahydro-1,4-diazepine

9.1 g (0.03 mol) of the diazepine from Example 1c) were dissolved with 3.5 g (0.03 mol) of 5-chlorovaleronitrile and 9.1 g of triethylamine (0.09 mol) in 100 ml of dimethylformamide and heated at 100°C for 24 h. The solvent was then removed by distillation under reduced pressure, water was added, the mixture was extracted with ethyl acetate, and this phase was dried with sodium sulfate and concentrated. The residue was processed further unpurified.

Yield: 9.1 g as brown oil

b) 1-[2-t-Butyl-6-trifluoromethyl-4-pyrimidinyl]-4-(4-amidinobutyl)hexahydro-1,4-diazepine hydrochloride

9.1 g (0.024 mol) of the nitrile described above were dissolved in 2 ml of ethanol and 50 ml of methylene chloride (both anhydrous) and, while cooling to 0-10°C, dry hydrogen chloride gas was passed in to saturation. After stirring overnight, the precipitate was filtered off with suction and the filtrate was concentrated.

Yield: 7.6 g (58% of theory)

Preparation of the final product

4.4 g (0.01 mol) of the amidine described above were stirred with the sodium compound of ethyl formylacetate (preparation J. Org. Chem. 35 (1970), 2515 et seq.) (2.8 g (0.02 mol)) in 50 ml of water and 20 ml of tetrahydrofuran overnight. The reaction mixture was then extracted several times with ethyl acetate, and the organic phase was dried and concentrated. The residue was purified by column chromatography (silica gel, eluent methylene chloride with 4% methanol)

Yield: 1.9 g (42%) of oil

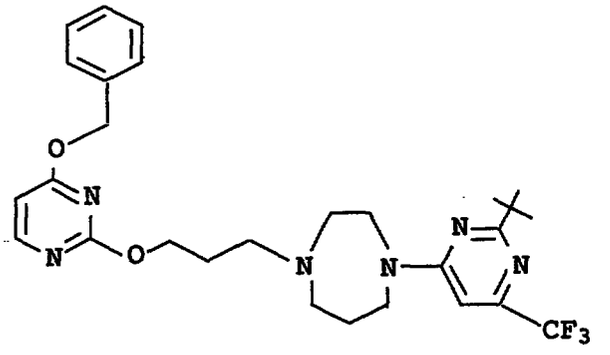
NMR: ($CDCl_3$) δ: 1.3(s,9H); 1.8-2.0(m,4H); 2.0(m,2H); 2.4-2.6(m/br,6H); 2.5(t,2H); 3.5(m,1H); 4.0(m,2H); 6.2(d,1H); 6.5(s,1H); 7.8(d,1H)

$C_{22}H_{31}F_3N_6O$ (425.5)

Oxalate: $C_{22}H_{31}F_3N_6O \cdot C_2H_2O_4$ (542.5)
Melting point 173-177°C (decomposition)

Example 34

1-[2-t-Butyl-6-trifluoromethyl-4-pyrimidinyl]-4-[3-{4-benzyloxy-2-pyrimidinyl}oxypropyl]hexahydro-(1H)-1,4-diazepine [sic]



a) Starting material
8.9 g (64.5 mmol) of 3-bromo-1-propanol were taken up in 50 ml of abs. THF, and 6.52 g (64.5 mmol) of triethylamine, a catalytic amount of sodium iodide and 16.2 g (53.7 mmol) of the azepine prepared in Example 1c) were successively added, and the mixture was refluxed for 16 h. For workup, the precipitate salts were filtered off and the mother liquor was concentrated under reduced pressure. The resulting oil was taken up in dichloromethane, and the organic phase was washed with water, dried over sodium sulfate and then purified by column chromatography (SiO_2, mobile phase CH_2Cl_2:MeOH=98:2) to result in a colorless oil.
Yield: 10.11 g (53%)

b) Final product
0.26 g (8.52 mmol) of sodium hydride (80%) was added in portions to 2.45 g of the product described above, dissolved in 25 ml of abs. DMF, at room temperature under a protective gas atmosphere, and the mixture was stirred for 30 min. Then 1.5 g (5.68 mmol) of 2-methanesulfonyl-4-benzyloxypyrimidine (prepared by methods similar to the literature: W.E. Barnett, R.F. Koebel Tetrahedron Lett. 1971, 20, 2867) dissolved in 15 ml of abs. DMF, were added dropwise. After 7 h, the mixture was worked up by pouring into water and extracting with tert-butyl methyl ether. The organic phase was washed with water, dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting oil was purified by column chromatography (SiO_2, mobile phase CH_2Cl_2:MeOH = 98:2) to afford the substance as an oil.
Yield: 1.6 g (2.9 mmol, 52%)
To form the hydrochloride, the oil was dissolved in ethyl

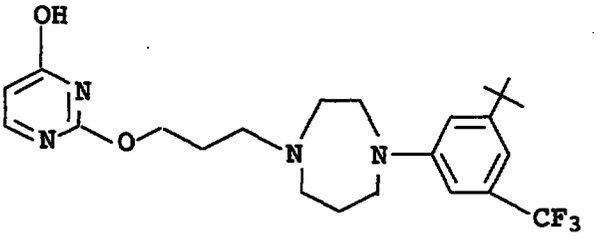
acetate/Et_2O, ethereal hydrochloric acid was added under protective gas, and the resulting salt was filtered off with suction.

Melting point: 110-112°C

$C_{28}H_{36}ClF_3N_6O_2$ (581.1)

Example 35

1-[2-t-Butyl-6-trifluoromethyl-2-pyrimidinyl]-4-[3-(4-hydroxy-2-pyrimidinyl)oxypropyl]hexahydro-(1H)-1,4-diazepine [sic]



1.4 g (2.6 mmol) of the substance from Example 34, dissolved in 40 ml of ethyl acetate, were mixed at room temperature with 0.2 g of Pd/C (10% Pd) and hydrogenated with hydrogen at 40-50°C under atmospheric pressure. After the reaction was complete, the catalyst was filtered off with suction and, after washing with ethyl acetate, the filtrated was concentrated under reduced pressure.

Yield: 1.2 g (100%)

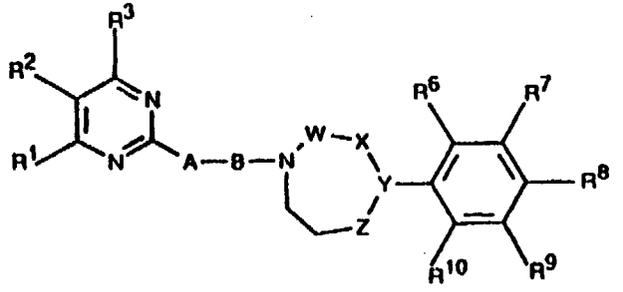
To form the hydrochloride, the oil was dissolved in ethyl acetate/Et_2O, ethereal hydrochloric acid was added under protective gas, and the resulting salt was filtered off with suction.

Melting point: 78-80°C

$C_{21}H_{30}ClF_3N_6O_2$ (491)

The compounds mentioned in the following Tables 3 to 17 are obtained in a similar way.

Table 3



Example No.	R1	R2	R3	R6	R7	R8	R9	R10	W	X-Y-Z	A	B
36	H	H	OH	H	tBut	H	Me	H	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
37	H	H	OH	H	tBut	H	Ph	H	CH_2-CH_2	CH=C-CH_2	S	-$(CH_2)_3$-
38	Me	H	OH	H	tBut	H	1-Pyrrolyl	H	CH_2	CH=C-CH_2	S	-$(CH_2)_3$-
39	H	H	NH_2	H	iProp	H	2-Napht	H	CH_2-CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
40	H	Me	OH	H	Et	H	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
41	H	H	OH	H	CHF_2	H	H	H	CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
42	H	H	NH_2	OMe	CF_3	H	H	H	CH_2	CH=C-CH_2	S	-$(CH_2)_3$-
43	H	H	OH	H	CF_3	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
44	H	H	NHMe	H	iProp	H	H	H	CH_2	CH_2-N-CH_2	O	-$(CH_2)_4$-
45	Me	H	OH	H	H	CN	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
46	H	H	OH	H	H	F	tBut	H	CH_2-CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
47	H	Me	NH_2	H	H	Cl	iProp	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
48	H	H	NHMe	H	tBut	H	H	OMe	CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
49	H	H	OH	H	iProp	H	H	OMe	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_4$-

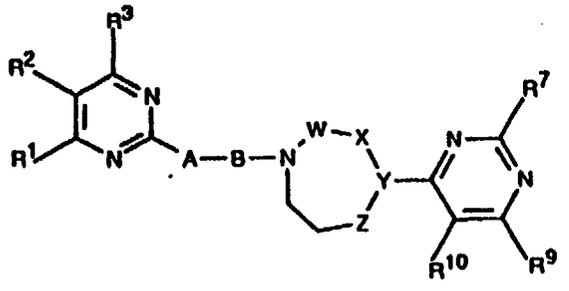
REPLACEMENT SHEET (RULE 26)

50	H	H	OH	H	CHF_2	H	tBut	H	CH_2-CH_2	CH=C-CH_2	S	-$(CH_2)_3$-
51	H	H	OH	OMe	tBut	H	CF_3	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
52	Me	H	OH	H	CF_3	H	tBut	H	CH_2	CH_2-N-CH_2	O	-$(CH_2)_5$-
53	H	H	NH_2	H	nProp	CN	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
54	H	Me	OH	H	CF_3	CN	iProp	H	CH_2	CH=C-CH_2	S	-$(CH_2)_3$-
55	H	H	OH	H	Ph	C≡CH	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
56	H	H	NH_2	H	tBut	CN	H	H	CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
57	H	H	NHMe	H	tBut	CN	CF_3	OMe	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_5$-
58	H	H	OH	OMe	nProp	F	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_4$-
59	H	H	OH	H	Ph	CN	tBut	Me	CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
60	H	H	OH	OMe	tBut	F	H	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
61	H	H	OH	H	tBut	H	Me	H	CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-C(=CH_2)-CH_2-
62	H	H	OH	H	tBut	H	Ph	H	CH_2	CH_2-CH=C	S	-CH_2-C(=CH_2)-CH_2-
63	Me	H	OH	H	tBut	H	1-Pyrrolyl	H	CH_2-CH_2	CH=C-CH_2	S	-CH_2-C(=CH_2)-CH_2-
64	H	H	NH_2	H	iProp	H	2-Napht	H	CH_2-CH_2	CH_2-CH=C	S	-CH_2-C(CH_3)=CH-CH_2-
65	H	Me	OH	H	Et	H	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-CH(CH_3)-CH_2-
66	H	H	OH	H	CHF_2	H	H	H	CH_2-CH_2	CH=C-CH_2	S	-CH_2-C(=CH_2)-CH_2-
67	H	H	NH_2	OMe	CF_3	H	H	H	CH_2	CH_2-CH=C	S	-CH_2-CH(CH_3)-CH_2-
68	H	H	OH	H	CF_3	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-C(=CH_2)-CH_2-
69	H	H	NHMe	H	iProp	H	H	H	CH_2	CH_2-N-CH_2	O	-CH_2-C(=CH_2)-CH_2-
70	Me	H	OH	H	H	CN	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-CH=CH-CH_2-

71	H	H	OH	H	H	F	tBut	H	CH_2-CH_2	CH_2-CH=C	S	-CH_2-C(CH_3)=CH-CH_2-
72	H	Me	NH_2	H	H	Cl	iProp	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-C(=CH_2)-CH_2-
73	H	H	NHMe	H	tBut	H	H	OMe	CH_2	CH_2-CH=C	S	-CH_2-CH(CH_3)-CH_2-
74	H	H	OH	H	iProp	H	H	OMe	CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-CH(CH_3)-CH_2-
75	H	H	OH	H	CHF_2	H	tBut	H	CH_2-CH_2	CH_2-CH=C	S	-CH_2-C(=CH_2)-CH_2-
76	H	H	OH	OMe	tBut	H	CF_3	H	CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-CH=CH-CH_2-
77	Me	H	OH	OMe	CF_3	H	tBut	H	CH_2	CH_2-N-CH_2	O	-CH_2-C(=CH_2)-CH_2-
78	H	H	NH_2	H	nProp	CN	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-C(CH_3)=CH-CH_2-
79	H	Me	OH	H	CF_3	CN	iProp	H	CH_2	CH_2-CH=C	S	-CH_2-CH(CH_3)-CH_2-
80	H	H	OH	H	Ph	C≡CH	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-CH(CH_3)-CH_2-
81	H	H	NH_2	H	tBut	CN	H	H	CH_2	CH_2-CH=C	S	-CH_2-C(CH_3)=CH-CH_2-
82	H	H	NHMe	H	tBut	CN	CF_3	OMe	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-CH=CH-CH_2-
83	H	H	OH	H	nProp	F	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-CH(CH_3)-CH_2-
84	H	H	OH	H	Ph	CN	tBut	Me	CH_2-CH_2	CH_2-CH=C	S	-CH_2-C(CH_3)=CH-CH_2-
85	H	H	OH	H	tBut	F	H	H	CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-C(=CH_2)-CH_2-

REPLACEMENT SHEET (RULE 26)

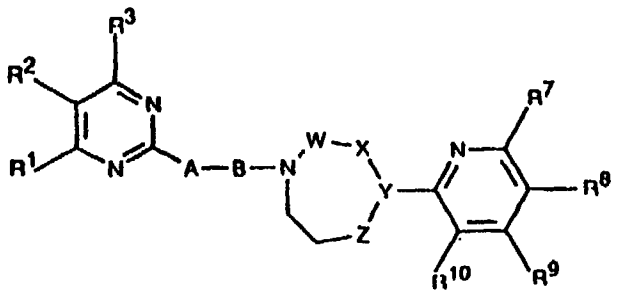
Table 4



Example No.	R1	R2	R3	R7	R9	R10	W	X-Y-Z	A	B
86	H	H	OH	tBut	Ph	H	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
87	H	H	OH	tBut	2-Napht	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
88	Me	H	OH	tBut	1-Pyrrolyl	H	CH_2	CH_2-N-CH_2	S	-CH_2-C(=CH_2)-CH_2-
89	H	H	NH_2	tBut	cHex	H	CH_2-CH_2	CH=C-CH_2	-CH_2-	-CH_2-C(CH_3)=CH-CH_2-
90	H	H	OH	tBut	nHex	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
91	H	H	OH	tBut	H	OMe	CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-CH(CH_3)-CH_2-
92	H	Me	OH	iProp	F	H	CH_2-CH_2	CH_2-N-CH_2	S	-CH_2-CH=CH-CH_2-
93	H	H	NH_2	CH_3	1-Pyrrolyl	H	CH_2	CH_2-C=CH	NH	-$(CH_2)_3$-
94	H	H	OH	OMe	1-Pyrrolyl	H	CH_2	CH_2-N-CH_2	O	-CH_2-CH(CH_3)-CH_2-
95	H	H	OH	tBut	H	CH_3	CH_2-CH_2	CH=C-CH_2	S	-CH_2-CH(CH_3)-CH_2-
96	H	H	OH	tBut	tBut	OMe	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
97	Me	H	OH	tBut	iProp	H	CH_2	CH_2-N-CH_2	S	-CH_2-C(=CH_2)-CH_2-
98	H	H	NH_2	Ph	tBut	Cl	CH_2	CH_2-C=CH	-CH_2-	-CH_2-C(CH_3)=CH-CH_2-
99	H	H	OH	2-Napht	tBut	Me	CH_2-CH_2	CH=C-CH_2	S	-$(CH_2)_3$-
100	H	H	OH	tBut	CF_3	Me	CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-C(=CH_2)-CH_2-

REPLACEMENT SHEET (RULE 26)

Table 5



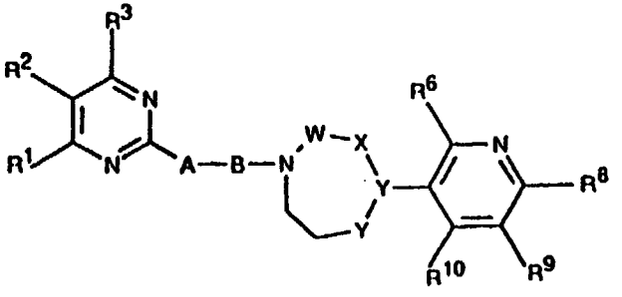
Example No.	R1	R2	R3	R7	R8	R9	R10	W	X-Y-Z	A	B
101	H	H	OH	tBut	H	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
102	H	H	OH	tBut	CN	H	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
103	Me	H	OH	tBut	H	Cl	H	CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
104	H	H	OH	H	CN	tBu	H	CH_2-CH_2	CH_2-CH=C	-CH_2-	-CH_2-CH(CH_3)-CH_2-
105	H	H	NH_2	CF_3	H	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
106	H	H	OH	nProp	H	iProp	H	CH_2-CH_2	CH=C-CH_2	-CH_2-	-CH_2-CH(CH_3)-CH_2-
107	H	Me	OH	H	H	iProp	OMe	CH_2-CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
108	H	H	OH	tBut	H	tBut	H	CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
109	H	H	OH	tBut	CN	H	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_4$-
110	H	H	NH_2	tBut	H	Cl	H	CH_2	CH_2-N-CH_2	O	-$(CH_2)_3$-
111	Me	H	OH	H	CN	tBu	H	CH_2	CH=C-CH_2	S	-CH_2-C(CH_3)=CH-CH_2-
112	H	H	OH	CF_3	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-C(=CH_2)-CH_2-
113	H	H	OH	nProp	H	iProp	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-

REPLACEMENT SHEET (RULE 26)

114	H	H	NHMe	H	H	iProp	OMe	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
115	H	H	OH	nProp	CN	tBut	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_4$-
116	H	H	OH	CF_3	CN	iProp	H	CH_2-CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
117	Me	H	OH	Ph	C≡CH	tBut	H	CH_2	CH_2-N-CH_2	NH	-CH_2-CH(CH_3)-CH_2-
118	H	H	OH	tBut	CN	tBut	H	CH_2-CH_2	CH≡C-CH_2	-CH_2-	-CH_2-CH(CH_3)-CH_2-
119	H	H	NH_2	tBut	H	nProp	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
120	H	H	OH	Ph	H	tBut	OMe	CH_2	CH_2-CH=C	-CH_2-	-$(CH_2)_5$-
121	H	Me	OH	CF_3	H	tBut	F	CH_2-CH_2	CH≡C-CH_2	S	-CH_2-CH(CH_3)-CH_2-
122	H	H	OH	tBut	F	H	Me	CH_2	CH_2-N-CH_2	NH	-CH_2-CH=CH-CH_2-
123	H	H	OH	nProp	CN	tBut	Me	CH_2-CH_2	CH_2-CH=C	S	-CH_2-C(=CH_2)-CH_2-
124	H	H	NH_2	nProp	C≡CH	tBut	H	CH_2	CH≡C-CH_2	-CH_2-	-CH_2-C(CH_3)=CH-CH_2-
125	H	H	OH	tBut	CN	H	Me	CH_2	CH_2-N-CH_2	S	-$(CH_2)_4$-

REPLACEMENT SHEET (RULE 26)

Table 6

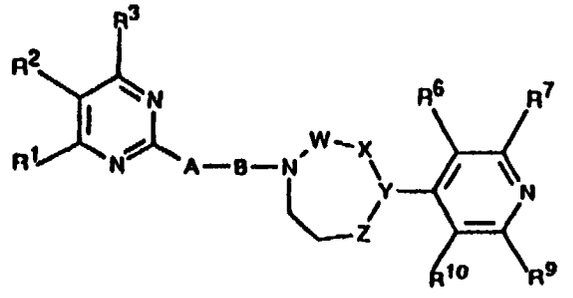


Example No.	R1	R2	R3	R6	R8	R9	R10	W	X-Y-Z	A	B
126	H	H	OH	OMe	H	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
127	H	H	OH	OMe	H	CF_3	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
128	Me	H	OH	OMe	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
129	H	H	OH	H	CN	tBut	H	CH_2	CH=C-CH_2	-CH_2-	-CH_2-C(CH_3)=CH-CH_2-
130	H	H	NH_2	H	F	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
131	H	H	OH	Me	Cl	iProp	H	CH_2	CH_2-CH=C	-CH_2-	-CH_2-C(=CH_2)-CH_2-
132	H	Me	OH	H	H	iProp	H	CH_2-CH_2	CH=C-CH_2	S	-$(CH_2)_3$-
133	H	H	OH	H	H	tBut	OMe	CH_2-CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
134	H	H	OH	CN	H	CF_3	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_4$-
135	H	H	NH_2	H	CN	H	OMe	CH_2	CH_2-N-CH_2	O	-CH_2-CH(CH_3)-CH_2-
136	Me	H	OH	H	H	tBu	F	CH_2	CH_2-CH=C	S	-CH_2-C(CH_3)=CH-CH_2-
137	H	H	OH	H	CN	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
138	H	H	OH	Me	H	iProp	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
139	H	H	NHMe	OMe	H	iProp	H	CH_2-CH_2	CH_2-N-CH_2	S	-CH_2-CH(CH_3)-CH_2-

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140	H	H	OH	OMe	CN	tBut	H	CH_2	$CH{\equiv}C\text{-}CH_2$	S	$-(CH_2)_3-$
141	H	H	OH	OMe	Me	tBut	H	CH_2	$CH_2\text{-}N\text{-}CH_2$	S	$-(CH_2)_3-$
142	Me	H	OH	H	CN	tBut	H	$CH_2\text{-}CH_2$	$CH_2\text{-}N\text{-}CH_2$	NH	$-CH_2\text{-}CH{=}CH\text{-}CH_2-$
143	H	H	OH	Me	H	tBut	H	CH_2	$CH_2\text{-}CH{=}C$	$-CH_2-$	$-CH_2\text{-}C(=CH_2)\text{-}CH_2-$
144	H	H	NH_2	H	Cl	CF_3	Me	$CH_2\text{-}CH_2$	$CH_2\text{-}N\text{-}CH_2$	S	$-(CH_2)_3-$
145	H	H	OH	OMe	CN	tBut	Me	CH_2	$CH{\equiv}C\text{-}CH_2$	$-CH_2-$	$-CH_2\text{-}CH(CH_3)\text{-}CH_2-$
146	H	Me	OH	Me	Me	iProp	Me	CH_2	$CH_2\text{-}CH{=}C$	S	$-(CH_2)_3-$

Table 7

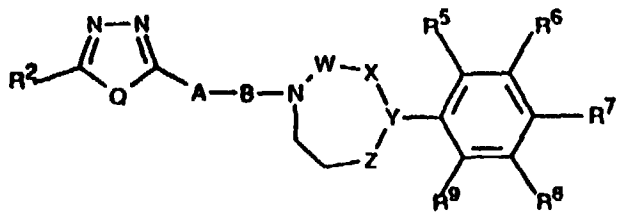


Example No.	R1	R2	R3	R6	R7	R9	R10	W	X-Y-Z	A	B
147	H	H	OH	H	tBut	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
148	H	H	OH	H	tBut	Ph	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
149	Me	H	OH	H	tBut	1-Pyrrolyl	H	CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
150	H	H	OH	H	*n*Propyl	tBut	H	CH_2-CH_2	CH_2-CH=C	-CH_2-	-CH_2-C(CH_3)=CH-CH_2-
151	H	H	NH_2	H	CF_3	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
152	H	H	OH	H	2-Naphl	tBut	H	CH_2-CH_2	CH=C-CH_2	-CH_2-	-CH_2-C(=CH_2)-CH_2-
153	H	Me	OH	OMe	tBut	H	H	CH_2-CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
154	H	H	OH	OMe	iProp	H	H	CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
155	H	H	OH	OMe	H	CF_3	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_4$-
156	H	H	NH_2	H	tBut	H	H	CH_2	CH_2-N-CH_2	O	-CH_2-CH(CH_3)-CH_2-
157	Me	H	OH	H	iProp	H	Me	CH_2	CH=C-CH_2	S	-CH_2-C(CH_3)=CH-CH_2-
158	H	H	OH	CN	tBut	H	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
159	H	H	OH	H	H	CF_3	Me	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
160	H	H	NHMe	H	*n*Prop	tBut	H	CH_2	CH_2-N-CH_2	S	-CH_2-CH(CH_3)-CH_2-

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161	H	H	OH	OMe	tBut	iProp	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
162	H	H	OH	OMe	CF_3	tBut	H	CH_2-CH_2	CH=C-CH_2	NH	-$(CH_2)_3$-
163	Me	H	OH	Me	tBut	nProp	H	CH_2	CH_2-CH=C	-CH_2-	-CH_2-CH=CH-CH_2-
164	H	H	OH	Me	tBut	H	H	CH_2-CH_2	CH_2-N-CH_2	S	-CH_2-C(=CH_2)-CH_2-
165	H	H	NH_2	H	tBut	tBut	H	CH_2	CH=C-CH_2	-CH_2-	-$(CH_2)_3$-
166	H	H	OH	Me	CF_3	tBut	H	CH_2	CH_2-CH=C	S	-CH_2-CH(CH_3)-CH_2-

Table 8



Example No.	Q	R2	R5	R6	R7	R8	R9	W	X-Y-Z	A	B
167	NCH_3	NH_2	H	tBut	H	Me	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
168	S	NH_2	H	tBut	H	Ph	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
169	NCH_3	NH_2	H	tBut	H	1-Pyrrolyl	H	CH_2-CH_2	CH_2-N-CH_2	NH	-$(CH_2)_3$-
170	NCH_3	NH_2	H	iProp	H	2-Naphtl	H	CH_2	CH_2-CH=C	-CH_2-	-$(CH_2)_3$-
171	S	NH_2	H	Et	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
172	S	NH_2	H	CHF_2	H	H	H	CH_2	CH=C-CH_2	-CH_2-	-$(CH_2)_8$-
173	NCH_3	NH_2	H	CHF_2	H	tBut	H	CH_2	CH_2-CH=C	S	-$(CH_2)_{10}$-
174	NCH_3	NH_2	H	CF_3	H	tBut	H	CH_2	CH_2-N-CH_2	NH	-$(CH_2)_3$-
175	NCH_3	NH_2	H	iProp	F	H	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
176	NCH_3	NH_2	H	H	CN	tBut	H	CH_2	CH_2-CH=C	O	-$(CH_2)_3$-
177	S	NH_2	H	H	F	tBut	H	CH_2-CH_2	CH=C-CH_2	S	-$(CH_2)_3$-
178	NCH_3	NH_2	H	H	Cl	iProp	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
179	NCH_3	NH_2	H	tBut	H	H	OMe	CH_2	CH=C-CH_2	S	-$(CH_2)_3$-
180	S	NH_2	H	nProp	CN	tBut	H	CH_2-CH_2	CH_2-CH=C	-CH_2-	-$(CH_2)_3$-
181	NCH_3	NH_2	H	CF_3	CN	iProp	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
182	NCH_3	NH_2	H	Ph	C≡CH	tBut	H	CH_2	CH=C-CH_2	-CH_2-	-$(CH_2)_3$-

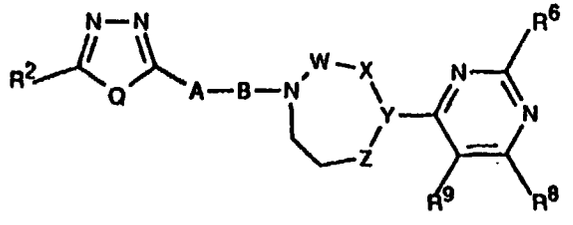
REPLACEMENT SHEET (RULE 26)

183	NCH_3	NH_2	OMe	tBut	CN	H	H	CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
184	S	NH_2	H	tBut	CN	CF_3	OMe	CH_2-CH_2	CH_2-N-CH_2	NH	-$(CH_2)_3$-
185	NCH_3	NH_2	H	Ph	CN	tBut	Me	CH_2-CH_2	CH_2-N-CH_2	O	-$(CH_2)_3$-
186	NCH_3	NH_2	Me	tBut	F	H	H	CH_2-CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
187	S	NH_2	H	iProp	H	H	OMe	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
188	N(iProp)	NH_2	H	tBut	H	Me	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
189	N(iProp)	NH_2	H	tBut	H	Ph	H	CH_2-CH_2	CH_2-N-CH_2	NH	-$(CH_2)_4$-
190	S	NH_2	H	tBut	H	1-Pyrrolyl	H	CH_2	CH=C-CH_2	S	-$(CH_2)_8$-
191	N(iProp)	NH_2	H	iProp	H	2-Napht	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
192	S	NH_2	H	Et	H	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_{10}$-
193	N(iProp)	NH_2	H	CF_3	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_4$-
194	N(iProp)	NH_2	H	H	CN	tBut	H	CH_2-CH_2	CH=C-CH_2	NH	-$(CH_2)_3$-
195	N(iProp)	NH_2	H	H	F	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
196	N(iProp)	NH_2	H	H	Cl	iProp	H	CH_2	CH=C-CH_2	-CH_2-	-$(CH_2)_3$-
197	S	NH_2	H	tBut	H	H	OMe	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_8$-
198	N(iProp)	NH_2	H	nProp	CN	tBut	H	CH_2	CH_2-CH=C	-CH_2-	-$(CH_2)_3$-
199	S	NH_2	H	CF_3	CN	iProp	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_4$-
200	N(iProp)	NH_2	H	Ph	C≡CH	tBut	H	CH_2-CH_2	CH=C-CH_2	-CH_2-	-$(CH_2)_3$-
201	N(iProp)	NH_2	H	tBut	CN	CF_3	OMe	CH_2	CH_2-N-CH_2	NH	-$(CH_2)_3$-
202	N(iProp)	NH_2	H	Ph	CN	tBut	Me	CH_2-CH_2	CH_2-N-CH_2	O	-$(CH_2)_3$-
203	S	NH_2	H	iProp	H	H	OMe	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_8$-
204	N(iProp)	NHMe	H	tBut	H	Me	H	CH_2	CH_2-N-CH_2	S	-CH_2-C(=CH_2)-CH_2-

REPLACEMENT SHEET (RULE 26)

205	N(iProp)	NHMe	H	tBut	H	Ph	H	CH_2	CH_2-CH=C	-CH_2-	-CH_2-C(=CH_2)-CH_2-
206	S	NHMe	H	tBut	H	1-Pyrrolyl	H	CH_2-CH_2	CH=C-CH_2	S	-CH_2-CH=CH-CH_2-
207	N(iProp)	NHMe	H	iProp	H	2-Napht	H	CH_2	CH_2-N-CH_2	NH	-CH_2-CH(CH_3)-CH_2-
208	N(iProp)	NHMe	H	Et	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	S	-CH_2-C(CH_3)=CH-CH_2-
209	N(iProp)	OH	H	tBut	H	Cl	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-CH(CH_3)-CH_2-
210	N(iProp)	OH	H	CF_3	H	Cl	H	CH_2	CH=C-CH_2	NH	-CH_2-CH(CH_3)-CH_2-
211	N(iProp)	OH	H	CF_3	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	S	-CH_2-C(=CH_2)-CH_2-
212	S	OH	H	iProp	CN	F	H	CH_2-CH_2	CH=C-CH_2	-CH_2-	-CH_2-C(=CH_2)-CH_2-
213	N(iProp)	OMe	H	H	CN	tBut	H	CH_2	CH_2-CH=C	-CH_2-	-CH_2-C(=CH_2)-CH_2-
214	N(iProp)	OMe	H	H	F	tBut	H	CH_2	CH_2-CH=C	S	-CH_2-C(CH_3)=CH-CH_2-
215	S	OMe	H	H	Cl	iProp	H	CH_2	CH=C-CH_2	O	-CH_2-CH(CH_3)-CH_2-
216	N(iProp)	OMe	H	tBut	H	H	OMe	CH_2-CH_2	CH=C-CH_2	NH	-CH_2-C(CH_3)=CH-CH_2-
217	N(iProp)	NHMe	H	nProp	CN	tBut	H	CH_2	CH_2-N-CH_2	NH	-CH_2-CH(CH_3)-CH_2-
218	S	NHMe	H	CF_3	CN	iProp	H	CH_2-CH_2	CH_2-N-CH_2	S	-CH_2-CH(CH_3)-CH_2-
219	N(iProp)	OH	H	Ph	C≡CH	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-C(CH_3)=CH-CH_2-
220	N(iProp)	OH	OMe	tBut	CN	H	H	CH_2	CH_2-CH=C	NH	-CH_2-CH(CH_3)-CH_2-
221	N(iProp)	OH	H	tBut	CN	CF_3	OMe	CH_2	CH_2-N-CH_2	S	-CH_2-C(=CH_2)-CH_2-
222	S	OH	H	nProp	F	tBut	H	CH_2-CH_2	CH=C-CH_2	-CH_2-	-CH_2-C(=CH_2)-CH_2-
223	S	OMe	H	Ph	CN	tBut	Me	CH_2	CH_2-CH=C	-CH_2-	-CH_2-C(=CH_2)-CH_2-
224	N(iProp)	OMe	OMe	tBut	F	H	H	CH_2	CH=C-CH_2	S	-CH_2-CH(CH_3)-CH_2-
225	N(iProp)	OMe	H	iProp	H	H	OMe	CH_2	CH_2-CH=C	S	-CH_2-C(CH_3)=CH-CH_2-

Table 9

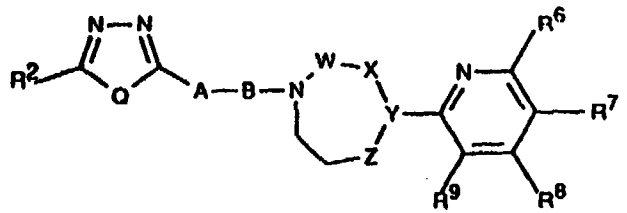


Example No.	Q	R2	R6	R8	R9	W	X-Y-Z	A	B
226	NCH_3	NH_2	tBut	Ph	H	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
227	NCH_3	NH_2	tBut	2-Napht	H	CH_2	CH_2-N-CH_2	S	-CH_2-C(=CH_2)-CH_2-
228	NCH_3	NH_2	tBut	1-Pyrrolyl	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
229	NCH_3	NHMe	tBut	cHex	H	CH_2-CH_2	CH_2-CH=C	-CH_2-	-$(CH_2)_3$-
230	NCH_3	NH_2	tBut	nHex	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_5$-
231	S	NH_2	tBut	Ph	H	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_8$-
232	S	NHMe	iProp	1-Pyrrolyl	H	CH_2	CH_2-N-CH_2	S	-CH_2-CH(CH_3)-CH_2-
233	S	NH_2	CH_3	CH_3	H	CH_2-CH_2	CH_2-CH=C	NH	-$(CH_2)_3$-
234	NCH_3	NH_2	H	CHF_2	H	CH_2	CH_2-N-CH_2	O	-CH_2-C(=CH_2)-CH_2-
235	S	NH_2	tBut	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_{10}$-
236	S	NHMe	tBut	iProp	H	CH_2-CH_2	CH_2-N-CH_2	S	-CH_2-C(CH_3)=CH-CH_2-
237	NCH_3	NH_2	tBut	tBut	H	CH_2	CH_2-N-CH_2	S	-CH_2-C(=CH_2)-CH_2-
238	NCH_3	NH_2	2-Napht	tBut	Me	CH_2-CH_2	CH=C-CH_2	-CH_2-	-CH_2-CH(CH_3)-CH_2-
239	S	NH_2	tBut	CF_3	H	CH_2-CH_2	CH_2-CH=C	S	-$(CH_2)_8$-
240	NCH_3	NH_2	tBut	H	CH_3	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-

REPLACEMENT SHEET (RULE 26)

241	N(iProp)	NH_2	tBut	Ph	H	CH_2-CH_2	CH=C-CH_2	S	-CH_2-C(=CH_2)-CH_2-
242	N(iProp)	NH_2	tBut	2-Napht	H	CH_2	CH_2-CH=C	NH	-$(CH_2)_3$-
243	N(iProp)	NH_2	tBut	1-Pyrrolyl	H	CH_2	CH_2-N-CH_2	O	-CH_2-CH(CH_3)-CH_2-
244	N(iProp)	NH_2	tBut	cHex	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
245	S	NH_2	tBut	tBut	H	CH_2	CH_2-N-CH_2	S	-CH_2-C(=CH_2)-CH_2-
246	S	OH	tBut	F	H	CH_2-CH_2	CH=C-CH_2	S	-$(CH_2)_{10}$-
247	N(nProp)	OMe	iProp	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-CH=CH-CH_2-
248	N(nProp)	OMe	CH_3	1-Pyrrolyl	H	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
249	N(nProp)	NCH_2Ph	H	iProp	H	CH_2-CH_2	CH_2-N-CH_2	S	-CH_2-C(CH_3)=CH-CH_2-
250	N(iProp)	OH	tBut	tBut	H	CH_2	CH=C-CH_2	-CH_2-	-$(CH_2)_4$-
251	N(iProp)	OH	tBut	iProp	F	CH_2-CH_2	CH_2-N-CH_2	S	-CH_2-CH=CH-CH_2-
252	N(iProp)	OMe	Ph	tBut	Cl	CH_2	CH_2-N-CH_2	S	-$(CH_2)_5$-
253	N(nProp)	OMe	2-Napht	tBut	Me	CH_2	CH=C-CH_2	-CH_2-	-$(CH_2)_3$-
254	N(nProp)	NCH_2Ph	tBut	CF_3	OMe	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_4$-
255	N(nProp)	NHMe	tBut	H	CH_3	CH_2	CH=C-CH_2	S	-CH_2-CH(CH_3)-CH_2-

Table 10

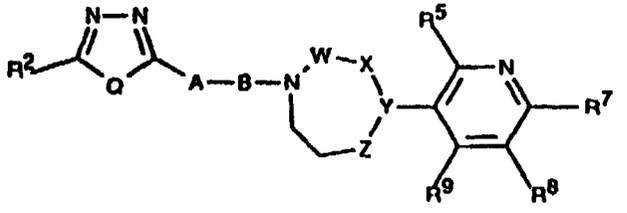


Example No.	Q	R2	R6	R7	R8	R9	W	X-Y-Z	A	B
256	NCH_3	NH_2	tBut	H	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
257	S	OH	tBut	CN	H	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_8$-
258	N(iProp)	NHMe	tBut	H	Cl	H	CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
259	NCH_3	NH_2	H	CN	tBu	H	CH_2	CH_2-CH=C	-CH_2-	-CH_2-CH(CH_3)-CH_2-
260	NCH_3	NHMe	CF_3	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
261	N(cProp)	NH_2	nProp	H	iProp	H	CH_2-CH_2	CH=C-CH_2	-CH_2-	-CH_2-C(=CH_2)-CH_2-
262	S	NHMe	H	H	iProp	H	CH_2	CH_2-CH=C	S	-$(CH_2)_{10}$-
263	NCH_3	NH_2	tBut	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
264	N(iProp)	NH_2	tBut	CN	H	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_4$-
265	NOH	NHMe	tBut	H	H	OMe	CH_2	CH_2-CH=C	O	-$(CH_2)_3$-
266	NCH_3	OH	H	CN	tBu	H	CH_2	CH=C-CH_2	S	-CH_2-CH(CH_3)-CH_2-
267	NEt	NH_2	CF_3	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-	-CH_2-CH(CH_3)-CH_2-
268	S	NH_2	nProp	H	iProp	H	CH_2	CH_2-N-CH_2	S	-CH_2-C(=CH_2)-CH_2-
269	NCH_3	NH_2	nProp	CN	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_4$-
270	NCH_3	OH	CF_3	CN	iProp	H	CH_2-CH_2	CH=C-CH_2	S	-$(CH_2)_3$-

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271	N(iProp)	NHMe	Ph	C≡CH	tBut	H	CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
272	S	NH_2	tBut	CN	tBut	H	CH_2-CH_2	CH_2-CH=C	-CH_2-	-CH_2-CH(CH_3)-CH_2-
273	NCH_3	NHMe	tBut	H	nProp	OMe	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
274	N(cProp)	NH_2	Ph	H	tBut	H	CH_2	CH=C-CH_2	-CH_2-	-$(CH_2)_4$-
275	S	NHMe	CF_3	H	tBut	H	CH_2-CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
276	NCH_3	NH_2	tBut	F	H	Me	CH_2	CH_2-N-CH_2	NH	-CH_2-CH=CH-CH_2-
277	S	NH_2	nProp	CN	tBut	Me	CH_2-CH_2	CH=C-CH_2	S	-CH_2-C(=CH_2)-CH_2-
278	NCH_3	OH	nProp	C≡CH	tBut	OMe	CH_2	CH=C-CH_2	-CH_2-	-CH_2-C(CH_3)=CH-CH_2-
279	N(iProp)	OMe	tBut	CN	H	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_4$-
280	NCH_3	OMe	H	H	iProp	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-

Table 11

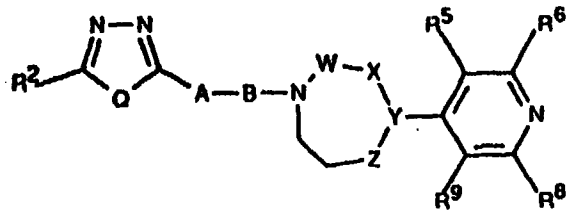


Example No.	Q	R2	R5	R7	R8	R9	W	X-Y-Z	A	B
281	NCH_3	NH_2	H	CN	tBut	H	CH_2	CH=C-CH_2	-CH_2-	-CH_2-C(=CH_2)-CH_2-
282	NCH_3	NHMe	H	F	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
283	N(cProp)	NH_2	Me	Cl	iProp	H	CH_2	CH_2-CH=C	-CH_2-	-$(CH_2)_3$-
284	S	NHMe	H	H	iProp	H	CH_2-CH_2	CH=C-CH_2	S	-$(CH_2)_{10}$-
285	NCH_3	NH_2	H	H	tBut	OMe	CH_2-CH_2	CH_2-N-CH_2	NH	-CH_2-CH(CH_3)-CH_2-
286	N(iProp)	NH_2	CN	H	CF_3	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_4$-
287	S	NHMe	H	CN	tBut	H	CH_2	CH_2-N-CH_2	O	-$(CH_2)_8$-
288	S	OH	H	H	tBu	H	CH_2-CH_2	CH=C-CH_2	S	-CH_2-C(=CH_2)-CH_2-
289	NEt	NH_2	H	CN	CHF_2	H	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
290	NCH_3	NH_2	Me	H	iProp	H	CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
291	N(iProp)	NH_2	F	CN	tBut	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_4$-
292	S	NH_2	OMe	Me	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_{10}$-
293	NCH_3	NHMe	H	CN	tBut	F	CH_2-CH_2	CH_2-N-CH_2	NH	-CH_2-CH(CH_3)-CH_2-
294	NCH_3	NH_2	H	C=CH	tBut	H	CH_2-CH_2	CH=C-CH_2	-CH_2-	-CH_2-C(CH_3)=CH-CH_2-
295	N(iProp)	NH_2	H	Cl	CF_3	Me	CH_2	CH_2-N-CH_2	S	-$(CH_2)_5$-

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296	NEt	H	CN	tBul	Me	CH_2-CH_2	CH_2-CH=C	-CH_2-	-CH_2-C(=CH_2)-CH_2-
297	S	OH	C≡CH	iProp	Me	CH_2	CH_2-CH=C	S	-$(CH_2)_8$-
298	NCH_3	OH	H	iProp	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-

Table 12



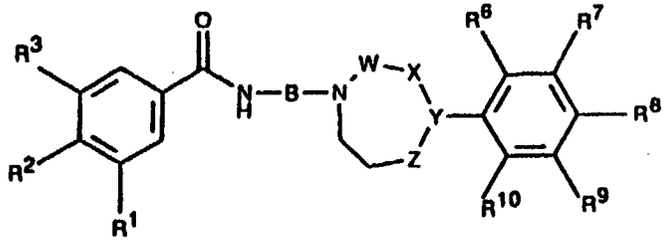
Example No.	Q	R2	R5	R6	R8	R9	W	X-Y-Z	A	B
299	NCH_3	NH_2	H	tBut	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
300	S	OH	H	tBut	Ph	H	CH_2	CH_2-N-CH_2	S	-CH_2-C(=CH_2)-CH_2-
301	N(iProp)	NHMe	H	tBut	1-Pyrrolyl	H	CH_2	CH_2-N-CH_2	NH	-CH_2-CH=CH-CH_2-
302	NCH_3	NH_2	H	nPropyl	tBut	H	CH_2-CH_2	CH=C-CH_2	-CH_2-	-CH_2-CH(CH_3)-CH_2-
303	NCH_3	NHMe	H	CF_3	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
304	N(cProp)	NH_2	H	2-Napht	tBut	H	CH_2-CH_2	CH=C-CH_2	-CH_2-	-$(CH_2)_3$-
305	S	NHMe	H	tBut	H	H	CH_2-CH_2	CH_2-CH=C	S	-$(CH_2)_8$-
306	NCH_3	NH_2	H	iProp	CHF_2	H	CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
307	N(iProp)	NH_2	OMe	H	CF_3	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_4$-
308	NOH	NHMe	H	tBut	H	F	CH_2-CH_2	CH_2-CH=C	O	-$(CH_2)_3$-
309	NCH_3	OH	H	iProp	H	Me	CH_2	CH=C-CH_2	S	-CH_2-C(CH_3)=CH-CH_2-
310	NEt	NH_2	CN	tBut	H	H	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
311	NCH_3	NH_2	H	H	CF_3	Me	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
312	S	NHMe	H	1-Pyrrolyl	H	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_{10}$-
313	NCH_3	OH	H	CF_3	tBut	H	CH_2	CH=C-CH_2	NH	-CH_2-C(=CH_2)-CH_2-

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314	NEt	NH_2	Me	tBut	nProp	H	CH_2-CH_2	CH_2-CH=C	-CH_2-	-CH_2-CH(CH_3)-CH_2-
315	NCH_3	NH_2	Me	tBut	H	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_5$-
316	S	NH_2	H	tBut	tBut	H	CH_2	CH=C-CH_2	-CH_2-	-CH_2-CH(CH_3)-CH_2-
317	N(IProp)	NH_2	Me	CF_3	tBut	H	CH_2-CH_2	CH_2-CH=C	S	-$(CH_2)_4$-
318	NCH_3	OH	H	nProp	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-

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Table 13



Example No.	R1	R2	R3	R6	R7	R8	R9	R10	W	X-Y-Z	B
319	H	Br	H	H	tBut	H	Me	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
320	H	J	H	H	tBut	H	Ph	H	CH_2-CH_2	CH=C-CH_2	-$(CH_2)_4$-
321	H	Ph	H	H	tBut	H	1-Pyrrolyl	H	CH_2	CH=C-CH_2	-$(CH_2)_4$-
322	H	p(iProp)-Ph	H	H	iProp	H	2-Napht	H	CH_2-CH_2	CH_2-CH=C	-$(CH_2)_4$-
323	H	pAcetyl-Ph	H	H	Et	H	tBut	H	CH_2	CH_2-N-CH_2	-$(CH_2)_3$-
324	H	pBr-Ph	H	H	CHF_2	H	H	H	CH_2	CH_2-CH=C	-$(CH_2)_4$-
325	H	pJ-Ph	H	OMe	CF_3	H	H	H	CH_2	CH=C-CH_2	-$(CH_2)_4$-
326	H	iProp	H	H	CF_3	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
327	H	tBut	H	H	iProp	H	H	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
328	H	CN	H	H	H	CN	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_3$-
329	H	COOEt	H	H	H	F	tBut	H	CH_2-CH_2	CH_2-CH=C	-$(CH_2)_4$-
330	H	OPh	H	H	H	Cl	iProp	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
331	Me	Br	H	H	tBut	H	H	OMe	CH_2	CH_2-CH=C	-$(CH_2)_4$-
332	CN	J	H	H	iProp	H	H	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
333	Me	Ph	H	H	CHF_2	H	tBut	H	CH_2-CH_2	CH=C-CH_2	-$(CH_2)_3$-

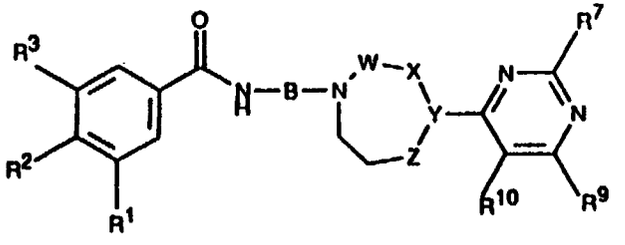
REPLACEMENT SHEET (RULE 26)

334	F	p(iProp)-Ph	H	OMe	tBut	H	CF_3	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
335	Me	pAcetyl-Ph	H	H	CF_3	H	tBut	H	CH_2	CH_2-N-CH_2	-$(CH_2)_5$-
336	H	pBr-Ph	Me	H	nProp	CN	tBut	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
337	H	pJ-Ph	F	H	CF_3	CN	iProp	H	CH_2	CH=C-CH_2	-$(CH_2)_4$-
338	H	iProp	Me	H	Ph	C=CH	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
339	H	tBut	CN	H	tBut	CN	H	H	CH_2	CH_2-CH=C	-$(CH_2)_4$-
340	H	CN	Me	H	tBut	CN	CF_3	OMe	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_5$-
341	H	COOEt	Me	H	nProp	F	tBut	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
342	H	OPh	F	H	Ph	CN	tBut	Me	CH_2	CH_2-CH=C	-$(CH_2)_3$-
343	Cl	F	H	H	tBut	F	H	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
344	H	Br	H	H	tBut	H	Me	H	CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
345	H	J	H	H	tBut	H	Ph	H	CH_2	CH_2-CH=C	-CH_2-C(=CH_2)-CH_2-
346	H	Ph	H	H	tBut	H	1-Pyrrolyl	H	CH_2-CH_2	CH=C-CH_2	-CH_2-C(=CH_2)-CH_2-
347	H	NEt_2	H	H	iProp	H	2-Napht	H	CH_2-CH_2	CH_2-CH=C	-CH_2-C(CH_3)=CH-CH_2-
348	H	pAcetyl-Ph	H	H	Et	H	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-CH(CH_3)-CH_2-
349	H	pBr-Ph	H	H	CHF_2	H	H	H	CH_2-CH_2	CH=C-CH_2	-CH_2-C(=CH_2)-CH_2-
350	H	pJ-Ph	H	F	CF_3	H	H	H	CH_2	CH_2-CH=C	-CH_2-CH(CH_3)-CH_2-
351	H	iProp	H	H	CF_3	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
352	H	tBut	H	H	iProp	H	H	H	CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
353	H	CN	H	H	H	CN	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-CH=CH-CH_2-
354	H	COOEt	H	H	H	F	tBut	H	CH_2-CH_2	CH_2-CH=C	-CH_2-C(CH_3)=CH-CH_2-

REPLACEMENT SHEET (RULE 26)

355	H	OPh	H	H	H	Cl	iProp	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
356	Me	Br	H	H	tBut	H	H	OMe	CH_2	CH_2-CH=C	-CH_2-CH(CH_3)-CH_2-
357	Me	J	H	H	iProp	H	H	OMe	CH_2	CH_2-N-CH_2	-CH_2-CH(CH_3)-CH_2-
358	Cl	Ph	H	H	CHF_2	H	tBut	H	CH_2-CH_2	CH_2-CH=C	-CH_2-C(=CH_2)-CH_2-
359	CN	p(iProp)-Ph	H	OMe	tBut	H	CF_3	H	CH_2	CH_2-N-CH_2	-CH_2-CH=CH-CH_2-
360	F	pAcetyl-Ph	H	OMe	CF_3	H	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
361	Me	pBr-Ph	H	H	nProp	CN	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-C(CH_3)=CH-CH_2-
362	H	pJ-Ph	CN	H	CF_3	CN	iProp	H	CH_2	CH_2-CH=C	-CH_2-CH(CH_3)-CH_2-
363	H	iProp	Cl	H	Ph	C=CH	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-CH(CH_3)-CH_2-
364	H	tBut	F	H	tBut	CN	H	H	CH_2	CH_2-CH=C	-CH_2-C(CH_3)=CH-CH_2-
365	H	CN	Cl	H	tBut	CN	CF_3	OMe	CH_2-CH_2	CH_2-N-CH_2	-CH_2-CH=CH-CH_2-
366	H	COOEt	CN	H	nProp	F	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-CH(CH_3)-CH_2-
367	H	OPh	Cl	H	Ph	CN	tBut	Me	CH_2-CH_2	CH_2-CH=C	-CH_2-C(CH_3)=CH-CH_2-
368	H	F	Me	H	tBut	F	H	H	CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-

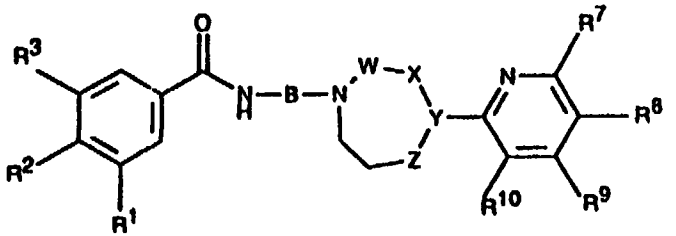
Table 14



Example No.	R1	R2	R3	R7	R9	R10	W	X-Y-Z	B
369	H	Br	H	tBut	Ph	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
370	H	J	H	tBut	2-Napht	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
371	H	Ph	H	tBut	1-Pyrrolyl	H	CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
372	H	p(iProp)-Ph	H	tBut	cHex	H	CH_2-CH_2	CH=C-CH_2	-CH_2-C(CH_3)=CH-CH_2-
373	H	pAcetyl-Ph	H	tBut	nHex	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
374	H	pBr-Ph	H	tBut	H	OMe	CH_2	CH_2-N-CH_2	-CH_2-CH(CH_3)-CH_2-
375	H	pJ-Ph	H	iProp	F	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-CH=CH-CH_2-
376	H	iProp	H	CH_3	1-Pyrrolyl	H	CH_2	CH_2-C=CH	-$(CH_2)_4$-
377	H	tBut	H	OMe	1-Pyrrolyl	H	CH_2	CH_2-N-CH_2	-CH_2-CH(CH_3)-CH_2-
378	H	CN	H	tBut	H	CH_3	CH_2-CH_2	CH=C-CH_2	-CH_2-CH(CH_3)-CH_2-
379	H	COOEt	H	tBut	tBut	OMe	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
380	H	OPh	H	tBut	iProp	H	CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
381	Me	Br	H	Ph	tBut	Cl	CH_2	CH_2-C=CH	-CH_2-C(CH_3)=CH-CH_2-
382	CN	J	H	2-Napht	tBut	Me	CH_2-CH_2	CH=C-CH_2	-$(CH_2)_4$-
383	Me	Ph	H	tBut	CF_3	Me	CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-

REPLACEMENT SHEET (RULE 26)

Table 15



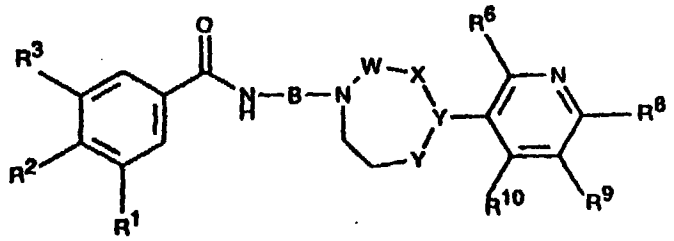
Example No.	R1	R2	R3	R7	R8	R9	R10	W	X-Y-Z	B
384	H	Br	H	tBut	H	tBut	H	CH_2	CH_2-N-CH_2	-(CH_2)4-
385	H	J	H	tBut	CN	H	H	CH_2	CH_2-N-CH_2	-(CH_2)4-
386	H	Ph	H	tBut	H	Cl	H	CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
387	H	p(iProp)-Ph	H	H	CN	tBu	H	CH_2-CH_2	CH_2-CH=C	-CH_2-CH(CH_3)-CH_2-
388	H	pAcetyl-Ph	H	CF_3	H	tBut	H	CH_2	CH_2-N-CH_2	-(CH_2)4-
389	H	pBr-Ph	H	nProp	H	iProp	H	CH_2-CH_2	CH=C-CH_2	-CH_2-CH(CH_3)-CH_2-
390	H	pJ-Ph	H	H	H	iProp	OMe	CH_2-CH_2	CH_2-CH=C	-(CH_2)4-
391	H	iProp	H	tBut	H	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
392	H	tBut	H	tBut	CN	H	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
393	H	CN	H	tBut	H	Cl	H	CH_2	CH_2-N-CH_2	-$(CH_2)_3$-
394	H	COOEt	H	H	CN	tBu	H	CH_2	CH=C-CH_2	-CH_2-C(CH_3)=CH-CH_2-
395	H	OPh	H	CF_3	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
396	Me	Br	H	nProp	H	iProp	H	CH_2	CH_2-N-CH_2	-(CH_2)4-
397	CN	J	H	H	H	iProp	OMe	CH_2	CH_2-N-CH_2	-(CH_2)4-

REPLACEMENT SHEET (RULE 26)

398	Me	Ph	H	nProp	CN	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
399	F	p(iProp)-Ph	H	CF_3	CN	iProp	H	CH_2-CH_2	CH_2-CH=C	-$(CH_2)_4$-
400	Me	pAcetyl-Ph	H	Ph	C≡CH	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-CH(CH_3)-CH_2-
401	H	pBr-Ph	Me	tBut	CN	tBut	H	CH_2-CH_2	CH=C-CH_2	-CH_2-CH(CH_3)-CH_2-
402	H	pJ-Ph	F	tBut	H	nProp	H	CH_2	CH_2-N-CH_2	-$(CH_2)_3$-
403	H	iProp	Me	Ph	H	tBut	OMe	CH_2	CH_2-CH=C	-$(CH_2)_5$-
404	H	tBut	CN	CF_3	H	tBut	F	CH_2-CH_2	CH=C-CH_2	-CH_2-CH(CH_3)-CH_2-
405	H	CN	Me	tBut	F	H	Me	CH_2	CH_2-N-CH_2	-CH_2-CH=CH-CH_2-
406	H	COOEt	Me	nProp	CN	tBut	Me	CH_2-CH_2	CH_2-CH=C	-CH_2-C(=CH_2)-CH_2-
407	H	pAcetyl-Ph	F	nProp	C≡CH	tBut	H	CH_2	CH=C-CH_2	-CH_2-C(CH_3)=CH-CH_2-
408	Cl	F	H	tBut	CN	H	Me	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-

REPLACEMENT SHEET (RULE 26)

Table 16

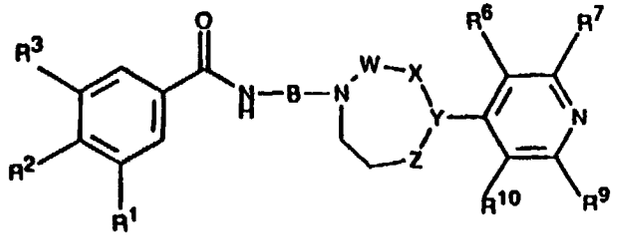


Example No.	R1	R2	R3	R6	R8	R9	R10	W	X-Y-Z	B
409	H	Br	H	OMe	H	tBut	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
410	H	J	H	OMe	H	CF_3	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
411	H	Ph	H	OMe	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
412	H	p(iProp)-Ph	H	H	CN	tBut	H	CH_2	CH=C-CH_2	-CH_2-C(CH_3)=CH-CH_2-
413	H	pAcetyl-Ph	H	H	F	tBut	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
414	H	pBr-Ph	H	Me	Cl	iProp	H	CH_2	CH_2-CH=C	-CH_2-C(=CH_2)-CH_2-
415	H	pJ-Ph	H	H	H	iProp	H	CH_2-CH_2	CH=C-CH_2	-$(CH_2)_4$-
416	H	iProp	H	H	H	tBut	OMe	CH_2-CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
417	H	tBut	H	CN	H	CF_3	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
418	H	CN	H	H	CN	H	OMe	CH_2	CH_2-N-CH_2	-CH_2-CH(CH_3)-CH_2-
419	H	COOEt	H	H	H	tBu	F	CH_2	CH_2-CH=C	-CH_2-C(CH_3)=CH-CH_2-
420	H	OPh	H	H	CN	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_3$-
421	Me	Br	H	Me	H	iProp	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
422	CN	J	H	OMe	H	iProp	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-CH(CH_3)-CH_2-
423	Me	Ph	H	OMe	CN	tBut	H	CH_2	CH=C-CH_2	-$(CH_2)_4$-

REPLACEMENT SHEET (RULE 26)

424	F	p(iProp)-Ph	H	OMe	Me	tBut	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
425	Me	pAcetyl-Ph	H	H	CN	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-CH=CH-CH_2-
426	H	pBr-Ph	Me	Me	H	tBut	H	CH_2	CH_2-CH=C	-CH_2-C(=CH_2)-CH_2-
427	H	pJ-Ph	F	H	Cl	CF_3	Me	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
428	H	iProp	Me	OMe	CN	tBut	Me	CH_2	CH=C-CH_2	-CH_2-CH(CH_3)-CH_2-
429	H	tBut	CN	Me	Me	iProp	Me	CH_2	CH_2-CH=C	-$(CH_2)_4$-

Table 17



Example No.	R1	R2	R3	R6	R7	R9	R10	W	X-Y-Z	B
430	H	Br	H	H	tBut	tBut	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
431	H	J	H	H	tBut	Ph	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
432	H	Ph	H	H	tBut	1-Pyrrolyl	H	CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
433	H	p(iProp)-Ph	H	H	nPropyl	tBut	H	CH_2-CH_2	CH_2-CH=C	-CH_2-C(CH_3)=CH-CH_2-
434	H	pAcetyl-Ph	H	H	CF_3	tBut	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
435	H	pBr-Ph	H	H	2-Napht	tBut	H	CH_2-CH_2	CH=C-CH_2	-CH_2-C(=CH_2)-CH_2-
436	H	pJ-Ph	H	OMe	tBut	H	H	CH_2-CH_2	CH_2-CH=C	-$(CH_2)_4$-
437	H	iProp	H	OMe	iProp	H	H	CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
438	H	tBut	H	OMe	H	CF_3	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
439	H	CN	H	H	tBut	H	H	CH_2	CH_2-N-CH_2	-CH_2-CH(CH_3)-CH_2-
440	H	COOEt	H	H	iProp	H	Me	CH_2	CH=C-CH_2	-CH_2-C(CH_3)=CH-CH_2-
441	H	OPh	H	CN	tBut	H	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_3$-
442	Me	Br	H	H	H	CF_3	Me	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
443	CN	J	H	H	nProp	tBut	H	CH_2	CH_2-N-CH_2	-CH_2-CH(CH_3)-CH_2-
444	Me	Ph	H	OMe	tBut	iProp	H	CH_2-CH_2	CH_2-N-CH_2	-$(CH_2)_4$-

REPLACEMENT SHEET (RULE 26)

445	F	p(iProp)-Ph	H	OMe	CF_3	tBut	H	CH_2-CH_2	$-(CH_2)_4-$
446	Me	pAcetyl-Ph	H	Me	tBut	nProp	H	CH_2	$-CH_2-CH=CH-CH_2-$
447	H	pBr-Ph	Me	Me	tBut	H	H	CH_2-CH_2	$-CH_2-C(=CH_2)-CH_2-$
448	H	pJ-Ph	F	H	tBut	tBut	H	CH_2	$-(CH_2)_3-$
449	H	iProp	Me	Me	CF_3	tBut	H	CH_2	$-CH_2-CH(CH_3)-CH_2-$

Examples of pharmaceutical presentations

A) Tablets

Tablets of the following composition were compressed in a tabletting machine in a conventional way:

40 mg	of substance of Example 1
120 mg	of corn starch
13.5 mg	of gelatin
45 mg	of lactose
2.25 mg	of Aerosil® (chemically pure silica in submicroscopically fine distribution)
6.75 mg	of potato starch (as 6% paste)

B) Coated tablets

20 mg	of substance from Example 4
60 mg	of core composition
70 mg	of sugar-coating composition

The core composition consists of 9 parts of corn starch, 3 parts of lactose and 1 part of vinylpyrrolidone/vinyl acetate 60:40 copolymer. The sugar-coating composition consists of

5 parts of sucrose, 2 parts of corn starch, 2 parts of calcium carbonate and 1 part of talc. The coated tablets produced in this way are subsequently provided with an enteric coating.

Biological investigations - receptor-binding studies

1) D_3 binding assay

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

Cell preparation

The D_3 expressing cells were grown in RPMI-1640 with 10% fetal calf serum (GIBCO No. 041-32400 N); 100 U/ml penicillin and 0.2% streptomycin (GIBCO BRL, Gaithersburg, MD, USA). After 48 h, the cells were washed with PBS and incubated with 0.05% trypsin-containing PBS for 5 min. After neutralization with medium, the cells were collected by centrifugation at 300 g. For cell lysis, the pellet was briefly washed with lysis buffer (5 mM tris-HCl, pH 7.4 with 10% glycerol) and then incubated at a

concentration of 10^7 cells/ml of lysis buffer at 4°C for 30 min. The cells were centrifuged at 200 g for 10 min and the pellet was stored in liquid nitrogen.

Binding assays

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

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

The K_i values were determined by non-linear regression analysis using the LIGAND program.

2) D_2 binding assay

Cell culture

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

The cells were prepared for binding studies by trypsinization (0.05% trypsin solution) at room temperature for 3-5 minutes. The cells were then 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 centrifugation at 250 g for 10 minutes, the residue was stored at -20°C until used.

Receptor binding assays

1) Dopamine D_2 receptor "low affinity state" with ^{125}I-spiperone (81 TBq/mmol, Du Pont de Nemours, Dreieich)

The mixtures (1 ml) consisted of 1×10^5 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 nM ^{125}I-spiperone (total binding) or with the addition of 1 µm [sic] haloperidol (nonspecific binding) or test substance.

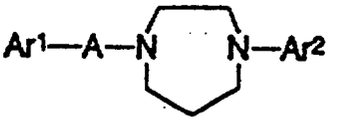
After incubation at 25°C for 60 minutes, the mixtures were filtered through GF/B glass fiber filters (Whatman, England) in a skatron cell collector (Zinsser, Frankfurt), and the filters were washed with ice-cold 50 mM tris-HCl buffer, pH 7.4. The radioactivity collected on the filters was quantified using a Packard 2200 CA liquid scintillation counter.

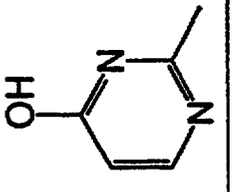
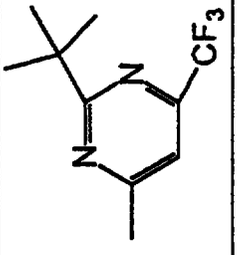
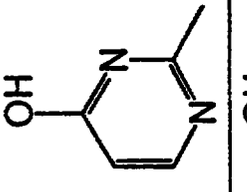
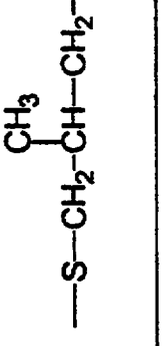
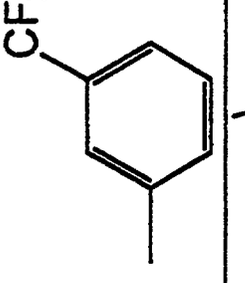
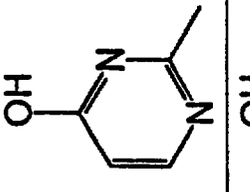
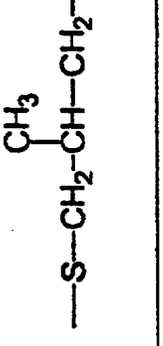
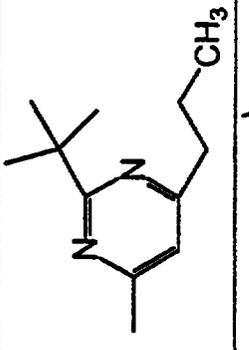
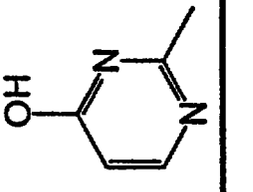
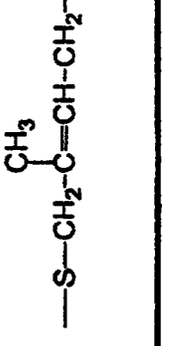
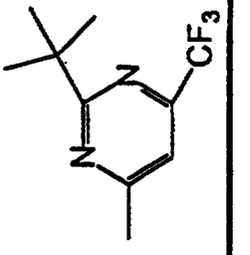
Evaluation took place as under a).

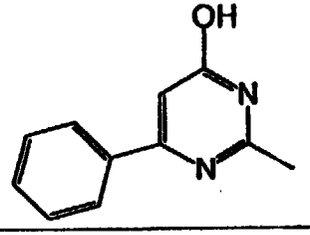
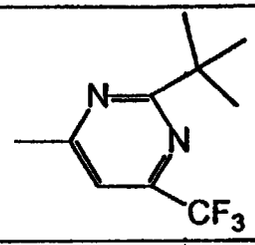
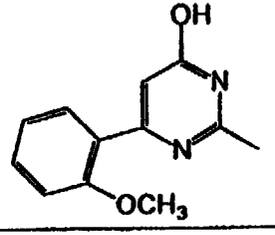
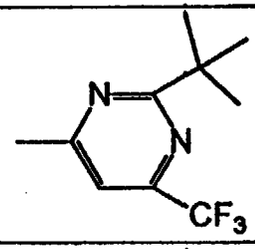
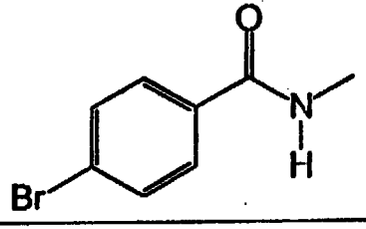
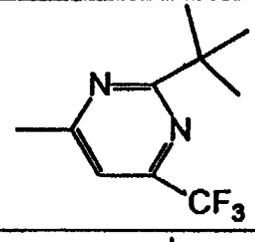
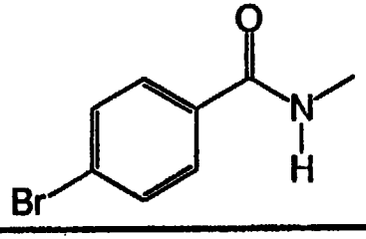
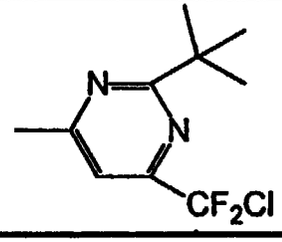
The K_i values were determined by nonlinear regression analysis using the ligand program or by conversion of the IC_{50} values using the formula of Cheng and Prusoff.

In these assays, the compounds according to the invention show very good affinities on the D_3 receptor and high selectivities for the D_3 receptor.

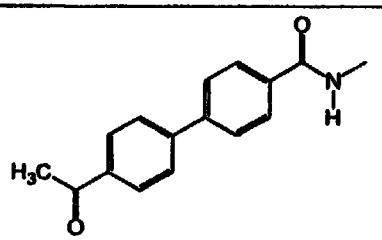
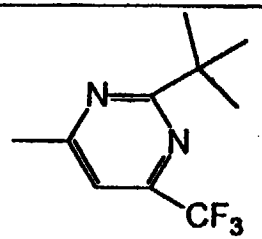
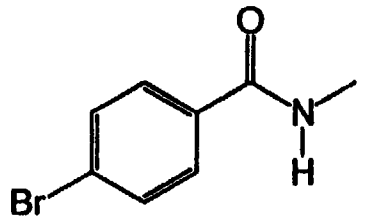
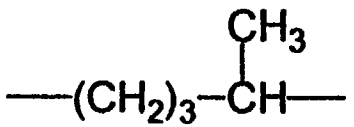
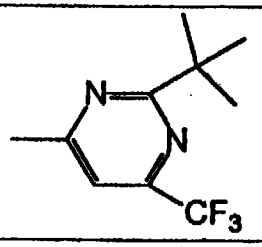
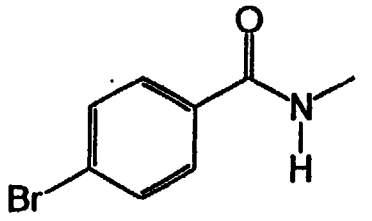
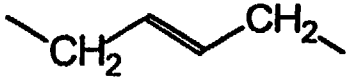
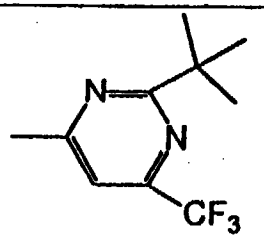
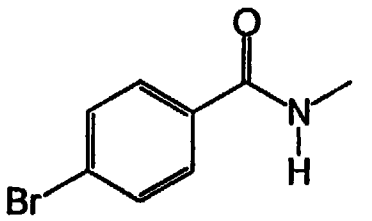
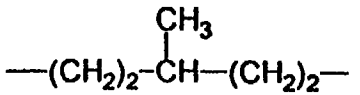
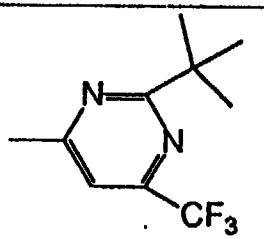
The following compounds were obtained by the processes described above:



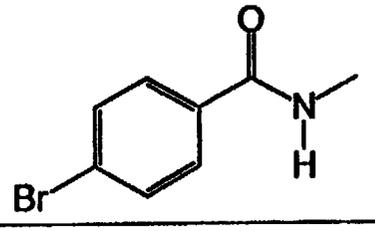
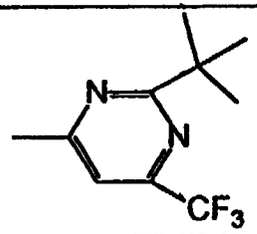
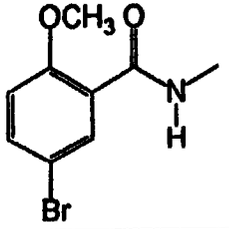
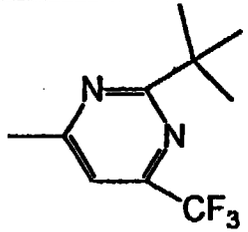
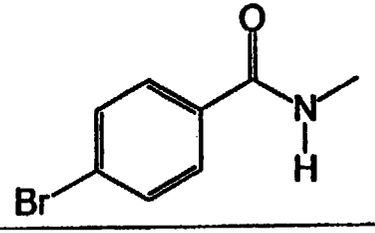
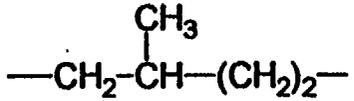
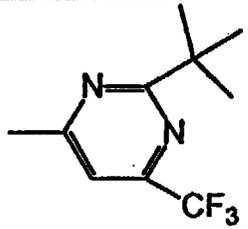
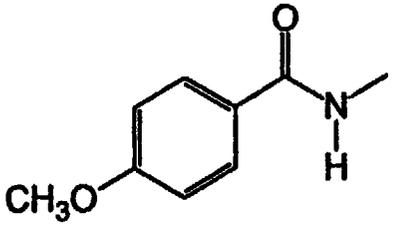
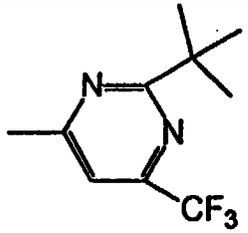
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
450				80 - 90 (Oxalate)
451				110 - 113
452				106 - 108
453				129 -131

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
454		—S—$(CH_2)_3$—		227 - 131 (Hydrochloride)
455		—S—$(CH_2)_3$—		165 - 166 (Hydrochloride)
456		—$(CH_2)_5$—		115 - 118 (Oxalate)
457		—$(CH_2)_4$—		94 - 97 (Hydrochloride)

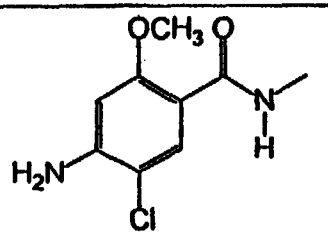
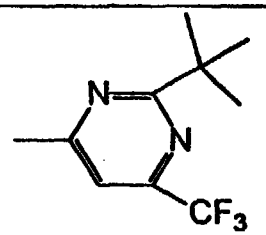
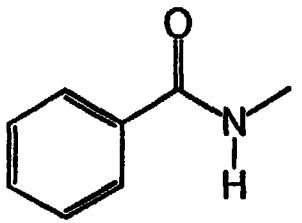
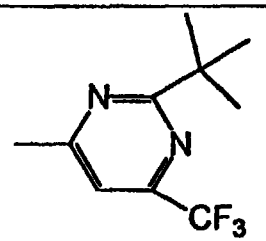
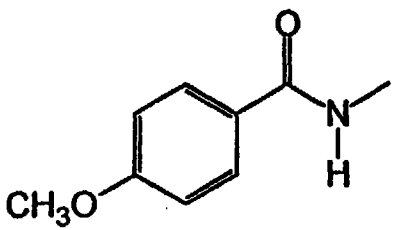
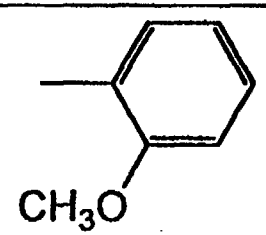
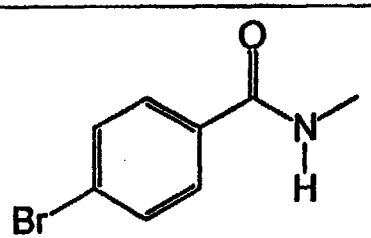
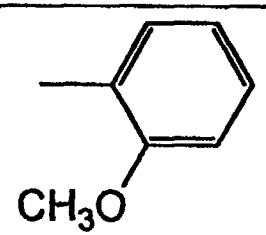
REPLACEMENT SHEET (RULE 26)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
458		$-(CH_2)_4-$		123 - 126 (Fumarate)
459				130 - 133 (Fumarate)
460				118 - 125 (Fumarate)
461				130 - 132 (Oxalate)

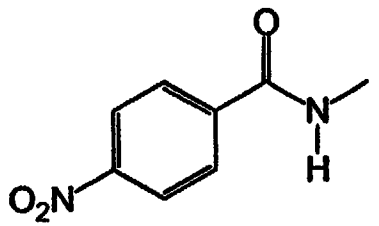
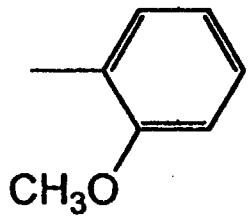
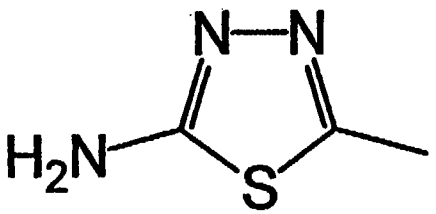
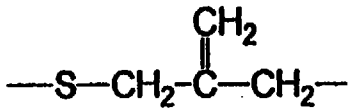
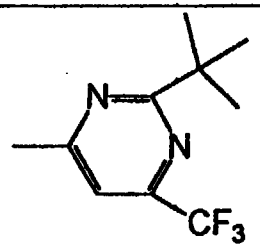
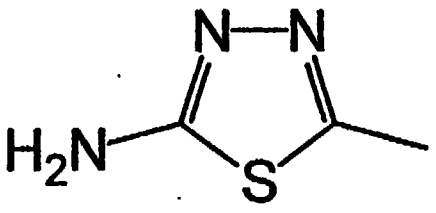
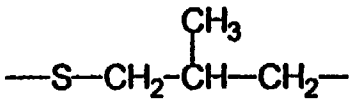
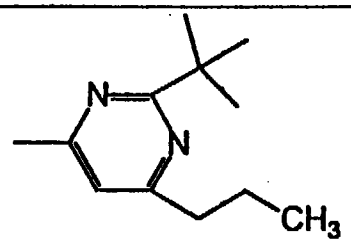
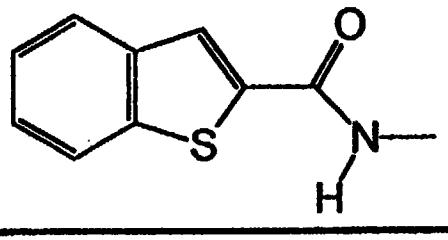
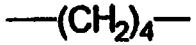
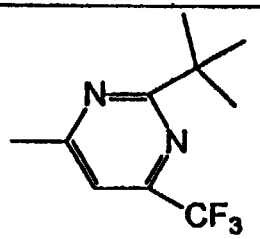
REPLACEMENT SHEET (RULE 26)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
462		$-(CH_2)_6-$		144 - 150 (Fumarate)
463		$-(CH_2)_4-$		148 - 154 (Oxalate)
464				171 - 176 (Fumarate)
465		$-(CH_2)_4-$		122 - 124 (Fumarate)

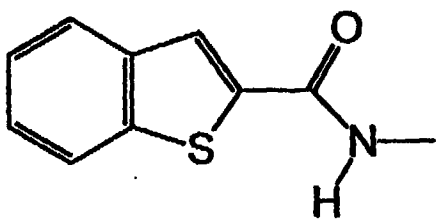
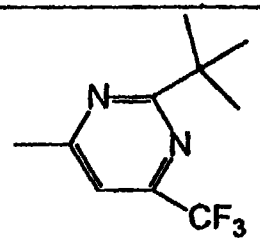
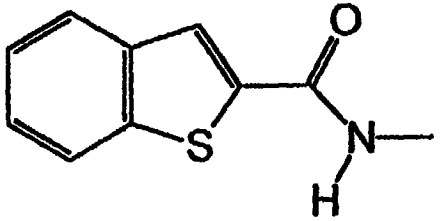
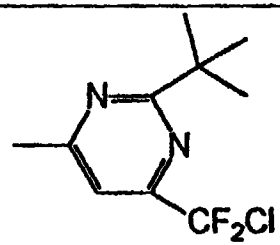
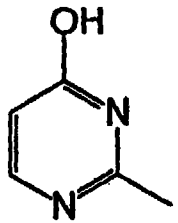
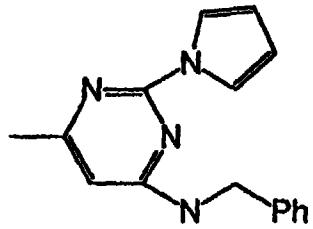
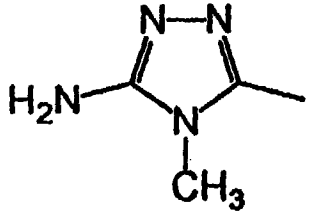
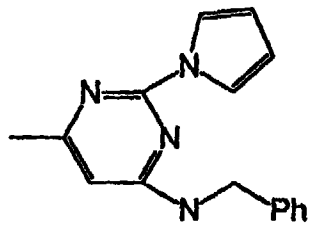
REPLACEMENT SHEET (RULE 26)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
466		$-(CH_2)_4-$		108 - 112 (Oxalate)
467		$-(CH_2)_4-$		140 - 142 (Oxalate)
468		$-(CH_2)_4-$		149 - 152 (Fumarate)
469		$-(CH_2)_4-$		147 - 149 (Hydrochloride)

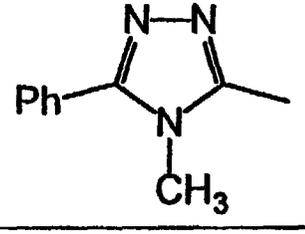
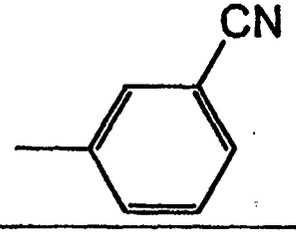
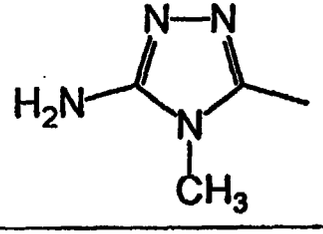
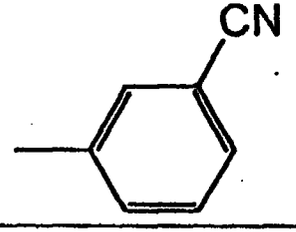
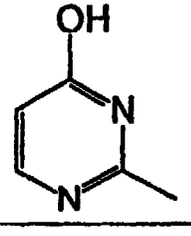
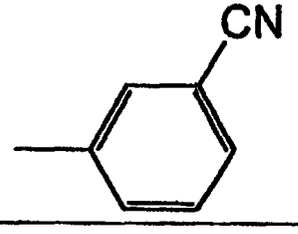
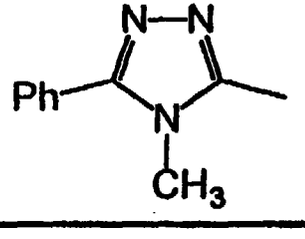
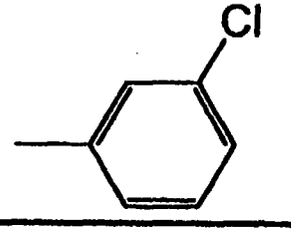
REPLACEMENT SHEET (RULE 26)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
470				235 - 236 (Fumarate)
471				92 - 98
472				87 - 90
473				112 - 115 (Fumarate)

REPLACEMENT SHEET (RULE 26)

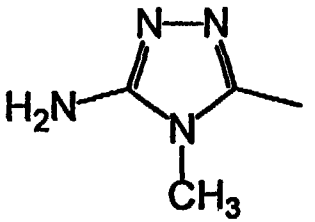
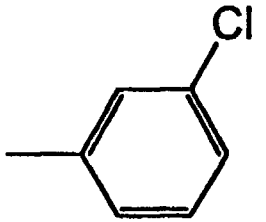
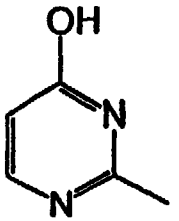
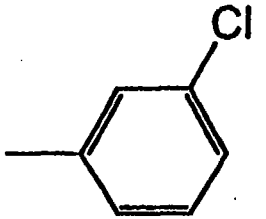
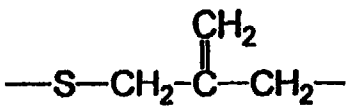
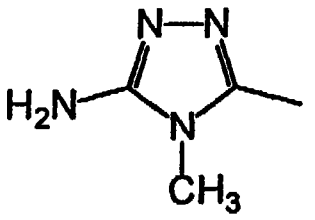
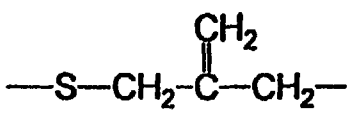
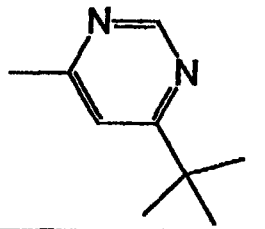
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
474		$-(CH_2)_6-$		101 - 105 (Oxalate)
475		$-(CH_2)_4-$		127 - 129 (Oxalate)
476		$-S-(CH_2)_3-$		
477		$-S-(CH_2)_3-$		

REPLACEMENT SHEET (RULE 26)

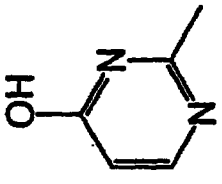
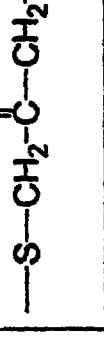
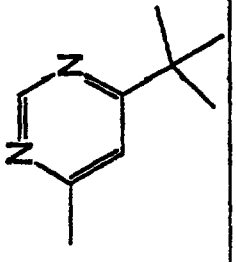
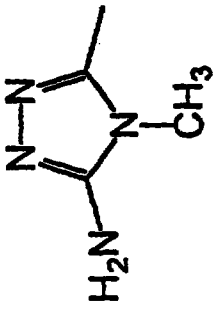
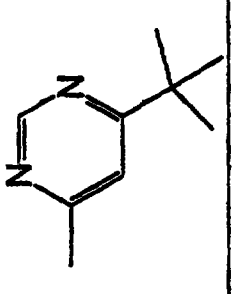
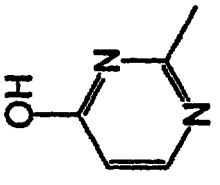
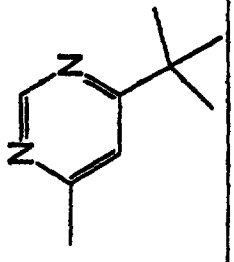
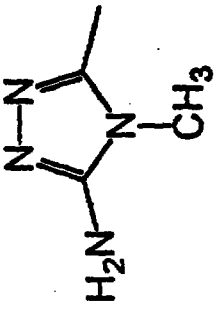
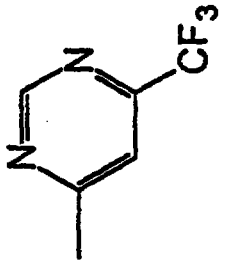
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
478		—S—$(CH_2)_3$—		126 - 128 (Fumarate)
479		—S—$(CH_2)_3$—		150 - 156 (Fumarate)
480		—S—$(CH_2)_3$—		158 - 165 (Fumarate)
481		—S—$(CH_2)_3$—		

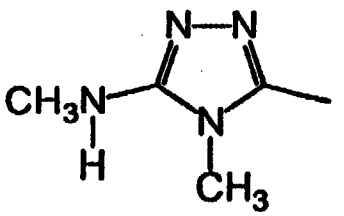
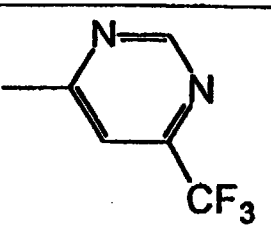
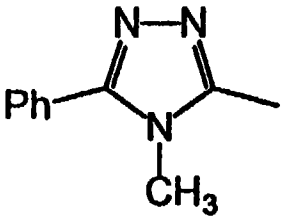
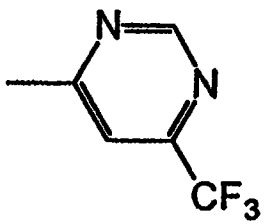
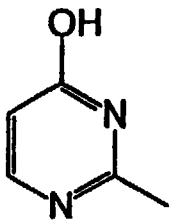
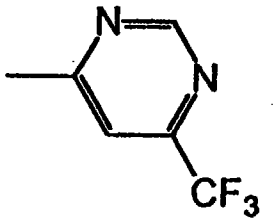
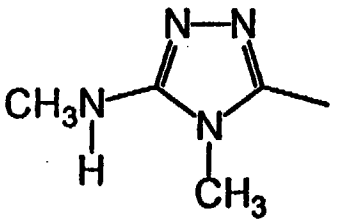
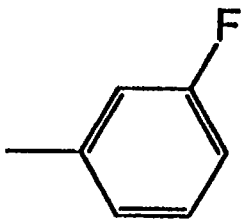
Ph = Phenyl

REPLACEMENT SHEET (RULE 26)

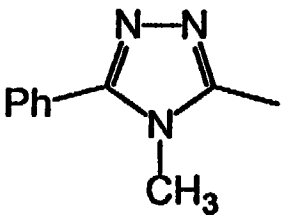
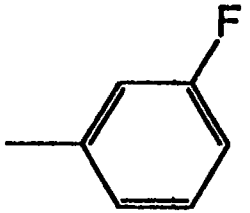
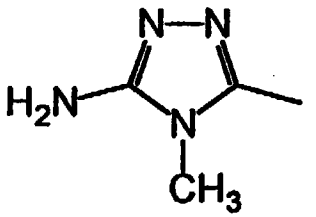
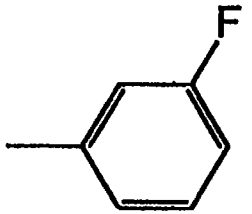
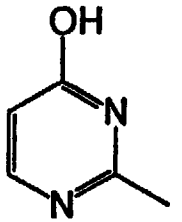
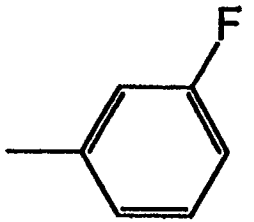
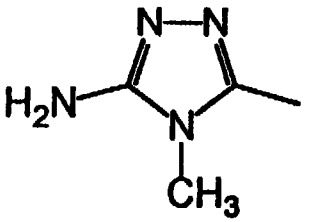
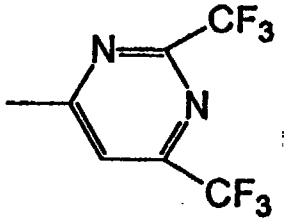
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
482				184 - 188 (Oxalate)
483				185 - 187 (Oxalate)
484				
485				127

REPLACEMENT SHEET (RULE 26)

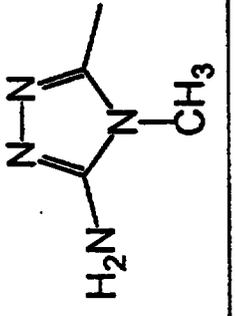
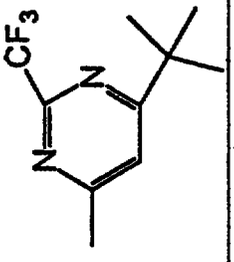
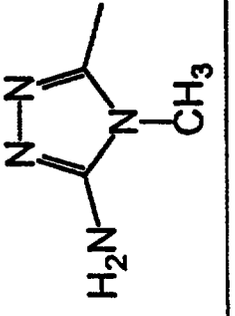
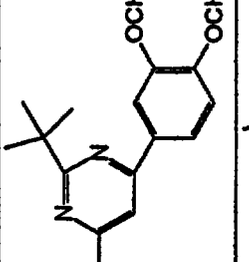
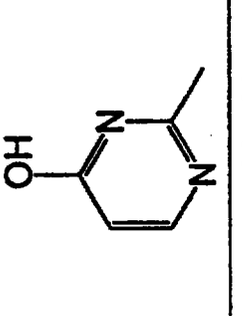
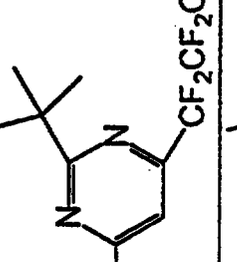
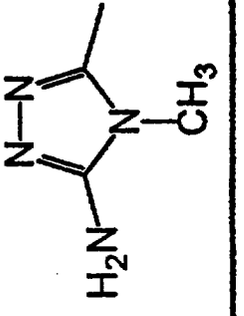
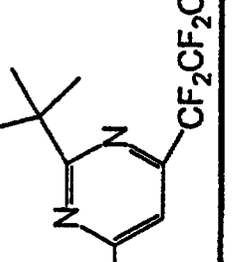
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
486				128
487				123
488				120
489				187 - 191 (Oxalate)

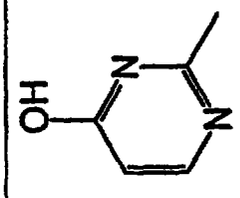
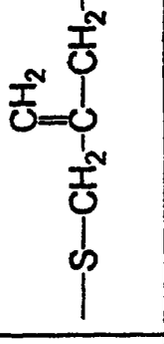
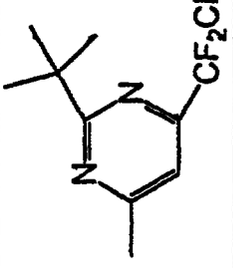
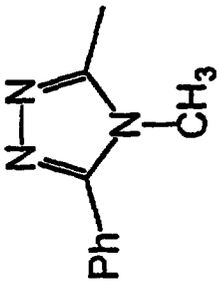
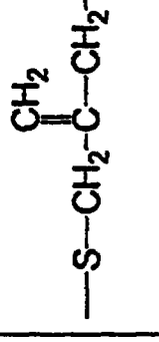
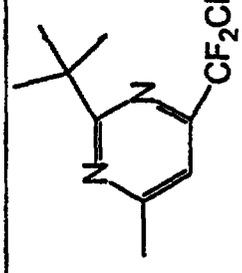
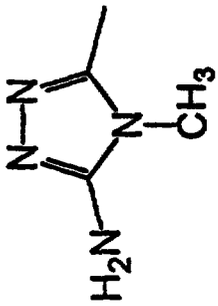
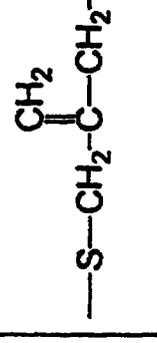
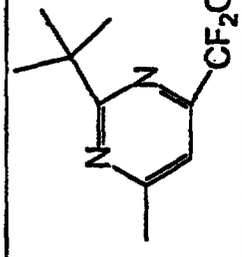
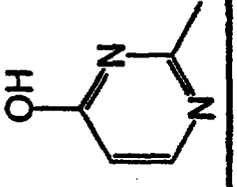
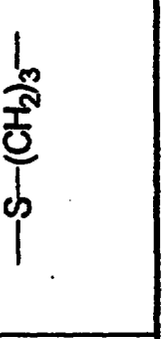
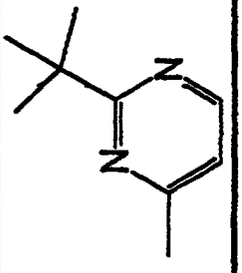
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
490		—S—$(CH_2)_3$—		187 - 191 (Oxalate)
491		—S—$(CH_2)_3$—		
492		—S—$(CH_2)_3$—		
493		—S—$(CH_2)_3$—		

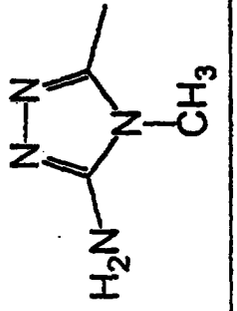
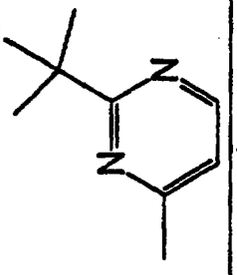
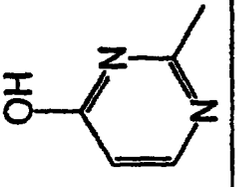
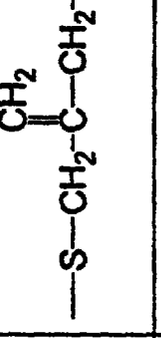
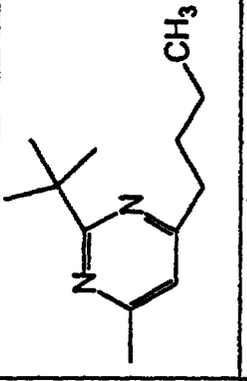
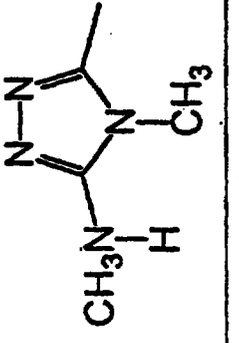
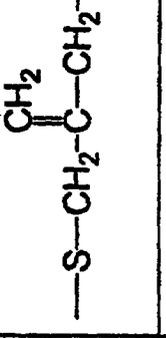
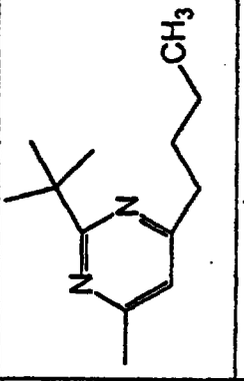
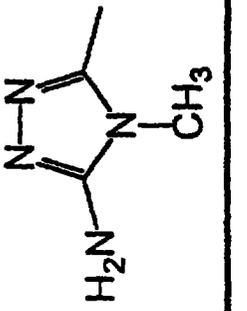
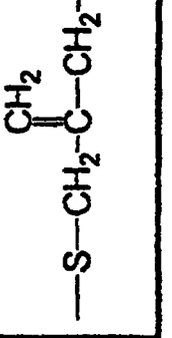
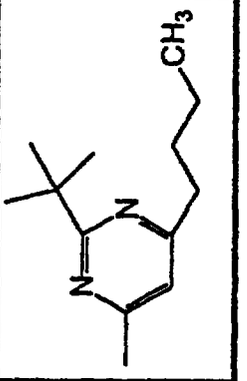
REPLACEMENT SHEET (RULE 26)

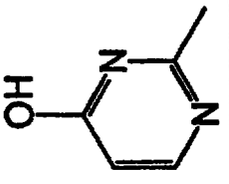
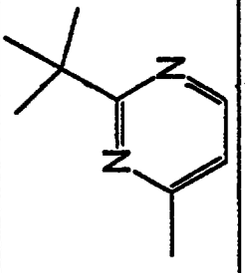
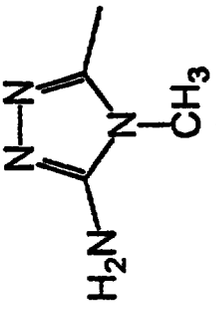
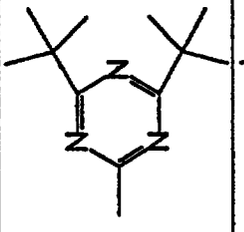
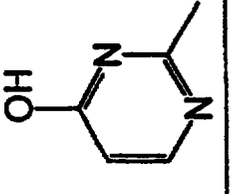
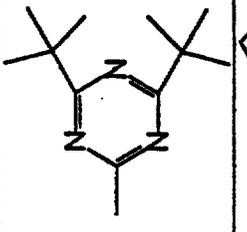
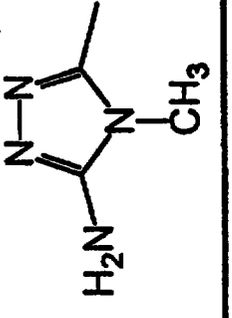
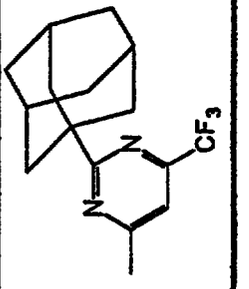
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
494		—S—$(CH_2)_3$—		93 - 94 (Oxalate)
495		—S—$(CH_2)_3$—		
496		—S—$(CH_2)_3$—		168 - 170 (Fumarate)
497		—S—$(CH_2)_3$—		

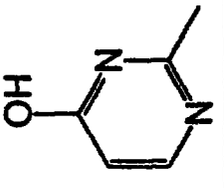
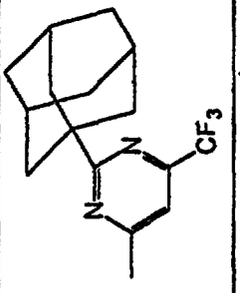
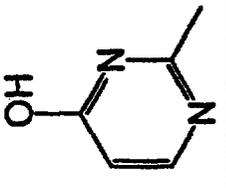
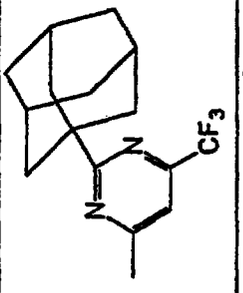
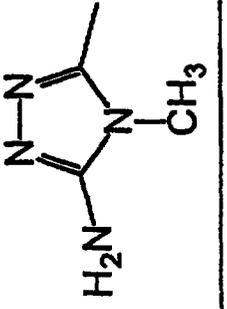
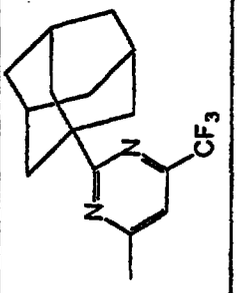
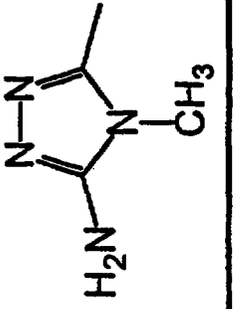
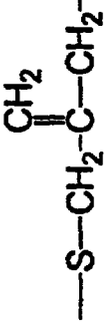
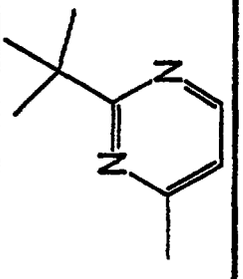
REPLACEMENT SHEET (RULE 26)

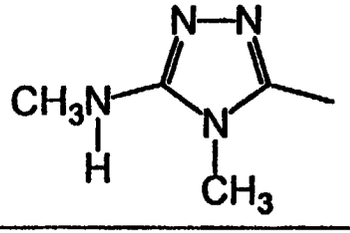
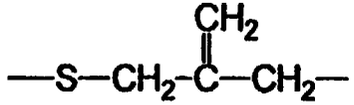
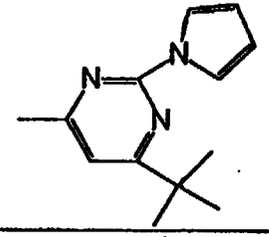
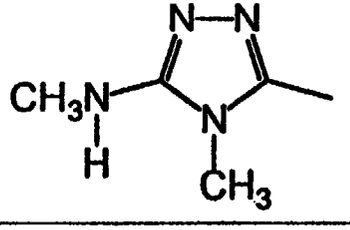
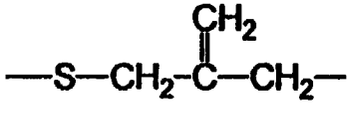
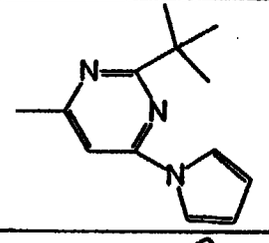
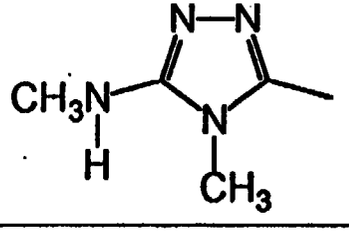
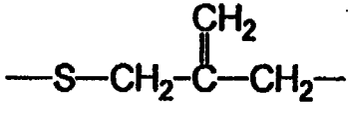
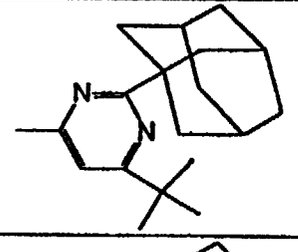
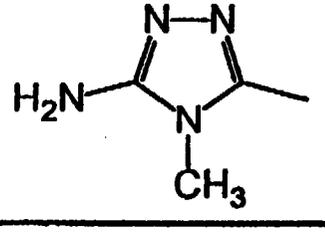
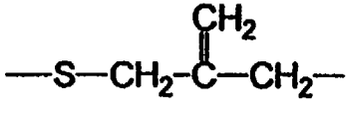
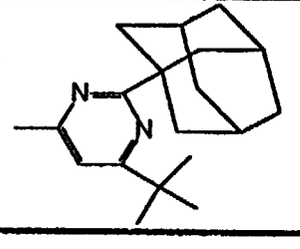
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
498				
499				
500				
501				

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
502				
503				
504				
505				

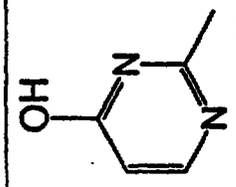
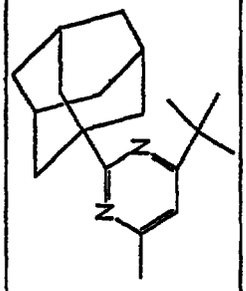
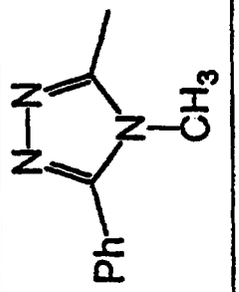
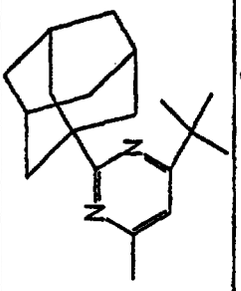
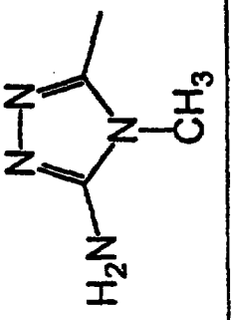
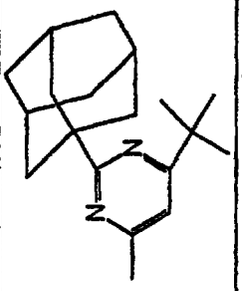
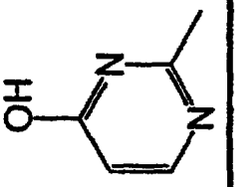
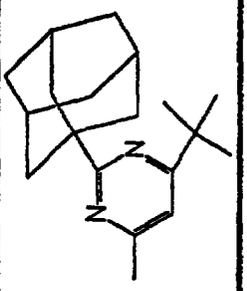
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
506				
507				
508				
509				

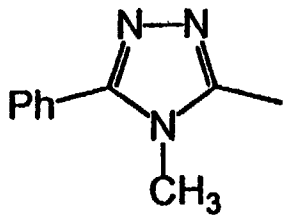
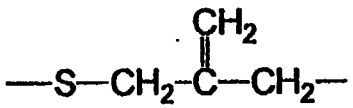
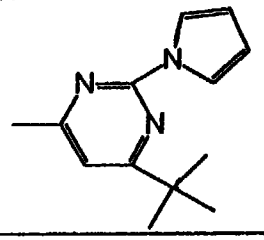
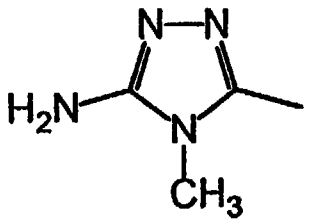
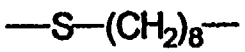
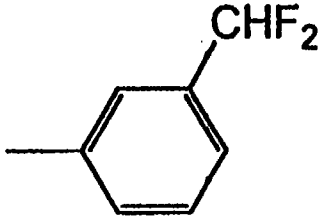
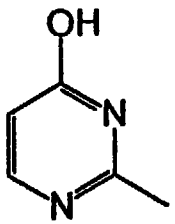
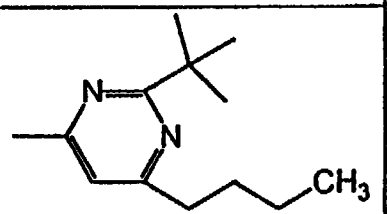
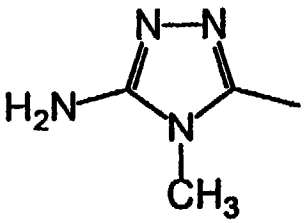
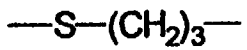
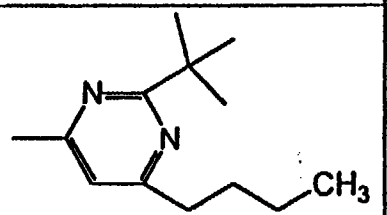
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
510				
511				
512				
513				

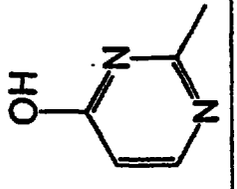
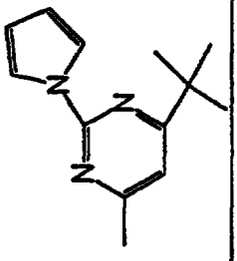
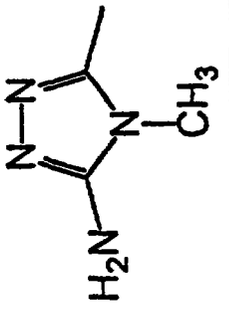
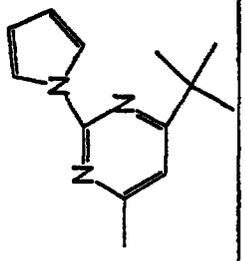
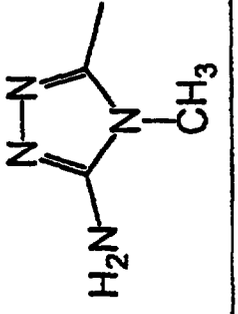
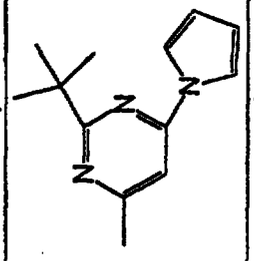
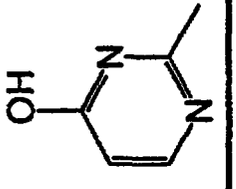
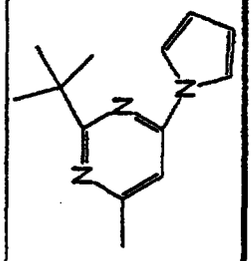
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
514				
515				
516				81 - 85
517				

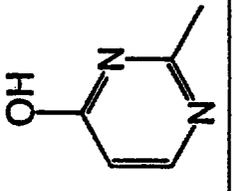
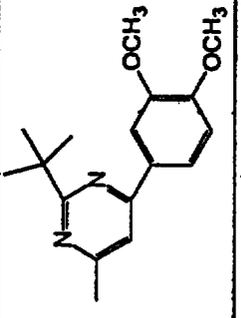
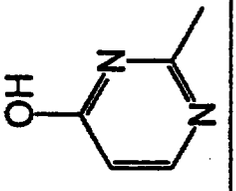
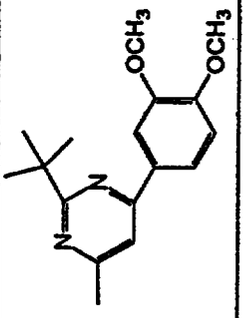
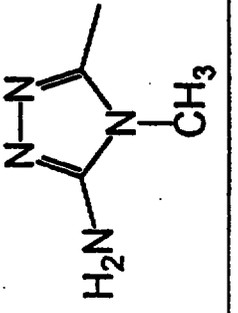
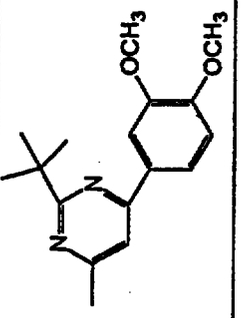
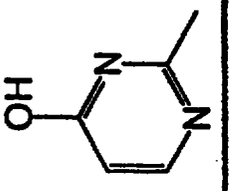
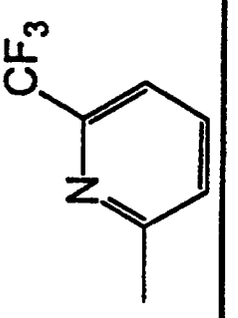
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
518				
519				
520				75 - 80
521				110 - 112 (Hydrochloride)

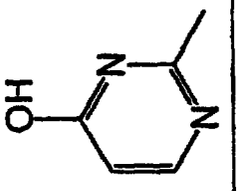
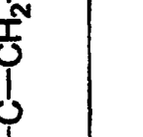
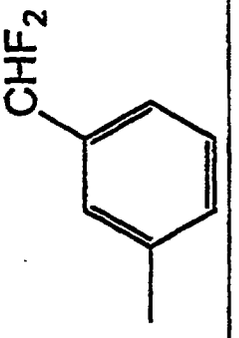
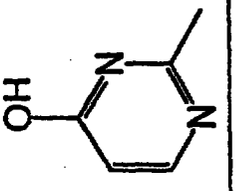
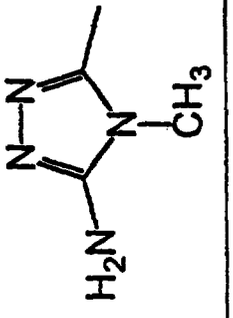
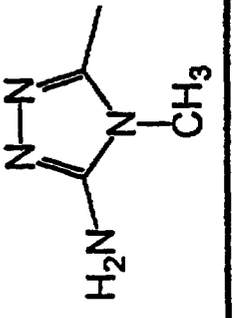
REPLACEMENT SHEET (RULE 26)

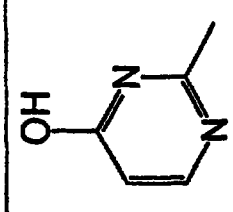
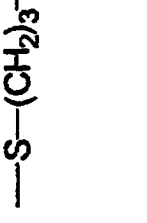
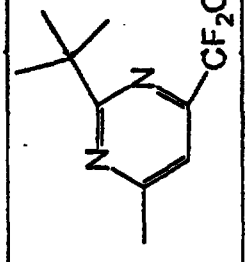
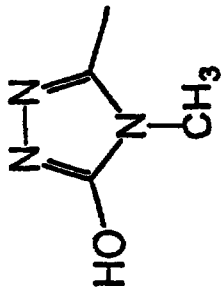
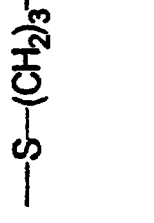
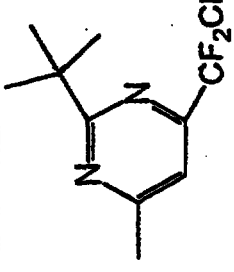
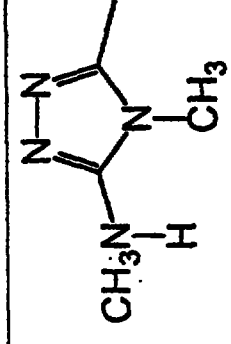
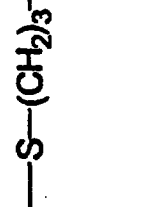
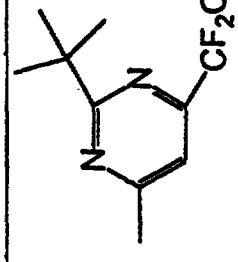
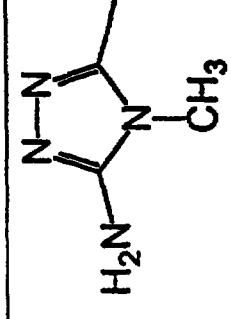
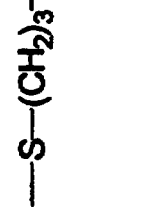
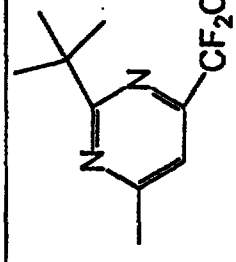
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
522		$-S-(CH_2)_3-$		78 - 80
523		$-S-CH_2-C(=CH_2)-CH_2-$		95 - 97 (Hydrochloride)
524		$-S-CH_2-C(=CH_2)-CH_2-$		142 - 145
525		$-S-CH_2-C(=CH_2)-CH_2-$		80 - 91

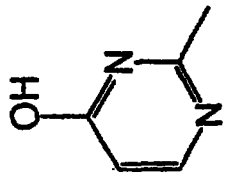
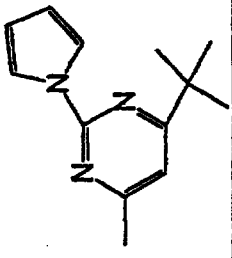
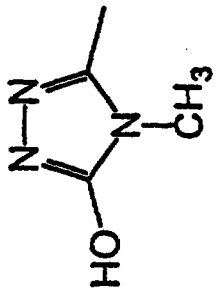
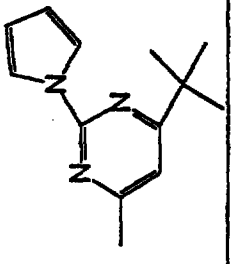
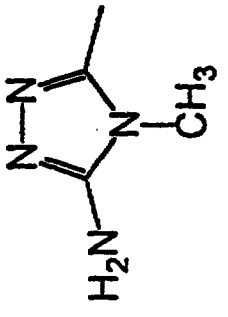
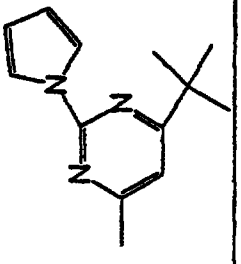
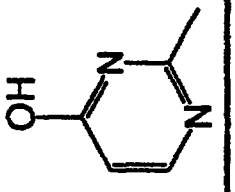
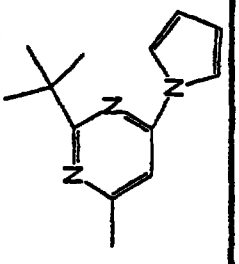
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
526				Oxalate
527				Hydrochloride
528				Oxalate
529				Dihydro-chloride

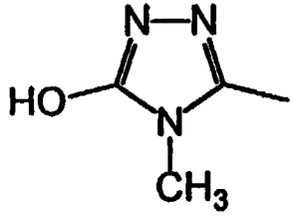
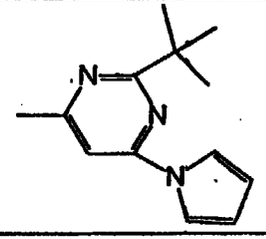
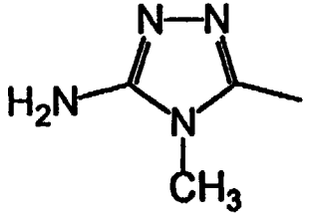
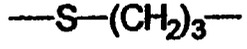
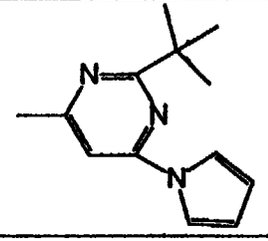
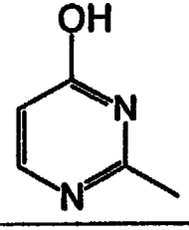
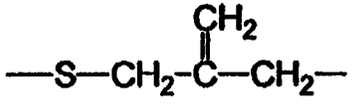
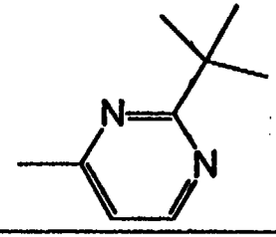
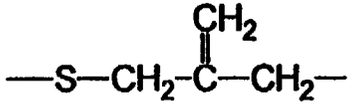
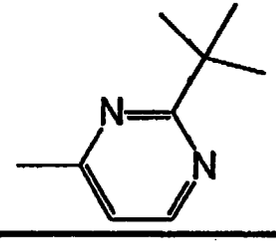
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
530				Oxalate
531				
532				
533				

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
534				95 - 96
535				92
536				90
537				97

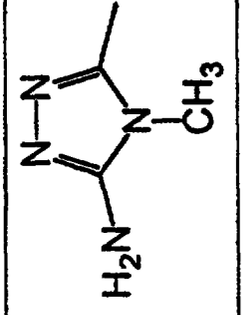
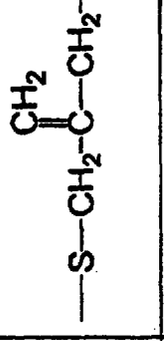
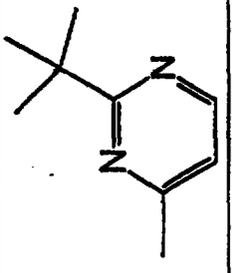
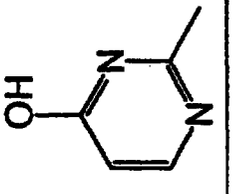
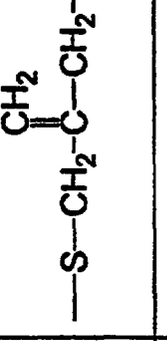
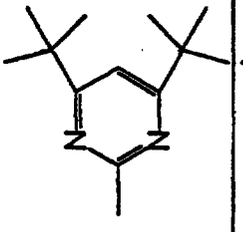
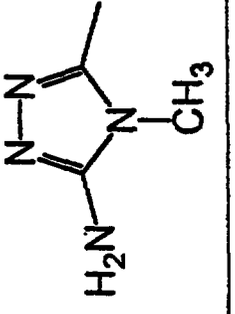
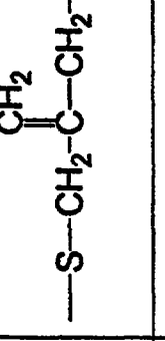
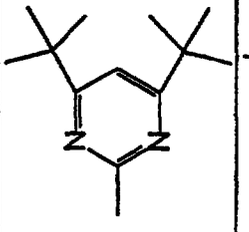
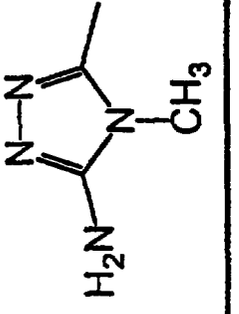
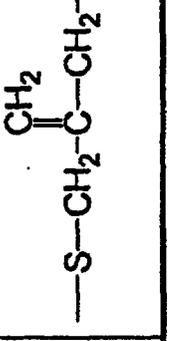
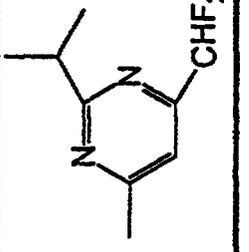
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
538				98 - 100
539				
540				
541				66 - 72

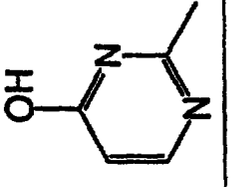
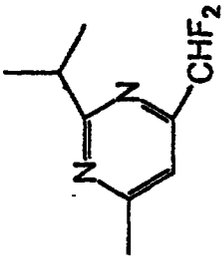
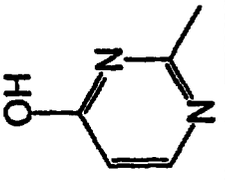
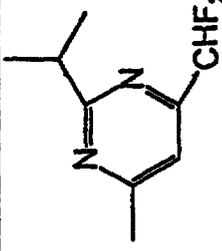
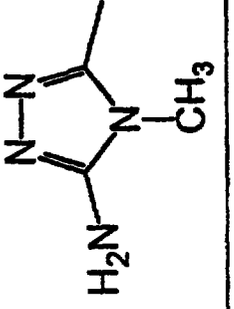
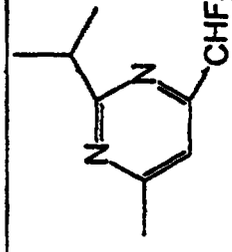
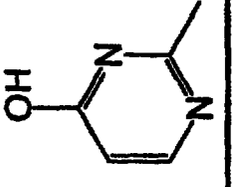
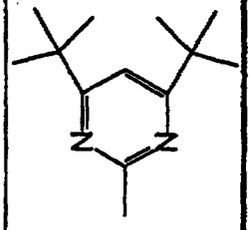
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
542				
543				
544				
545				

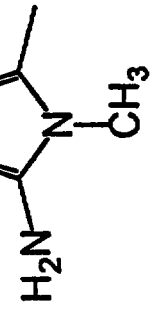
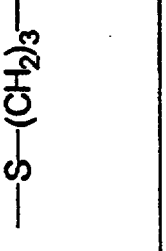
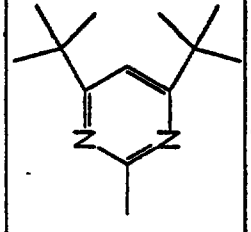
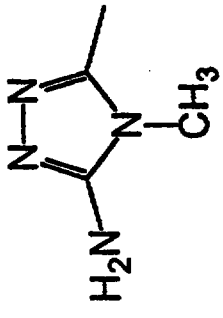
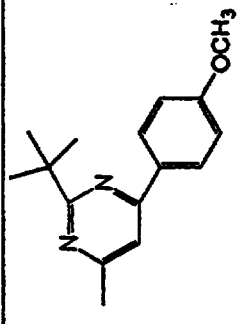
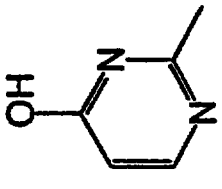
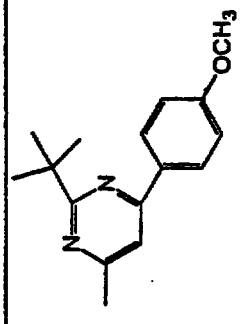
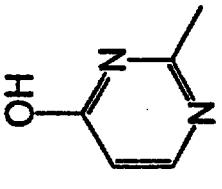
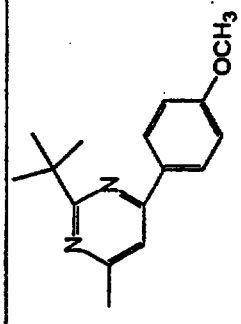
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
546		$-S-(CH_2)_3-$		
547		$-S-(CH_2)_3-$		
548		$-S-(CH_2)_3-$		
549		$-S-(CH_2)_3-$		

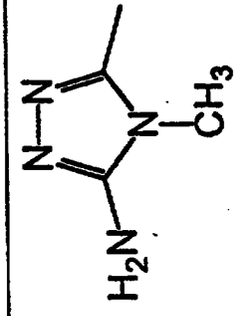
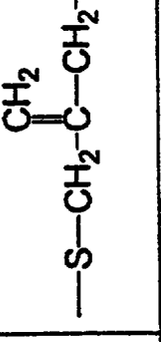
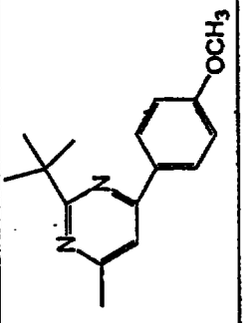
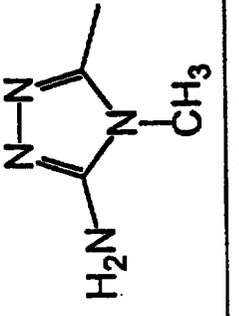
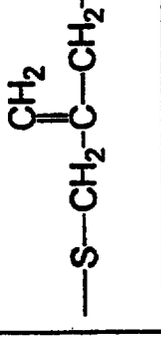
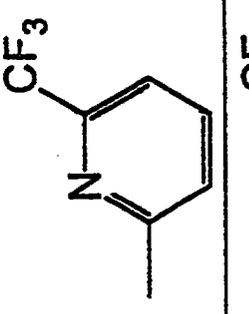
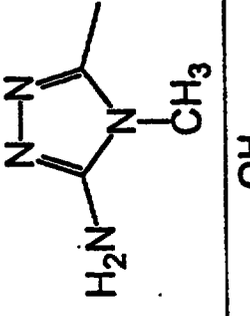
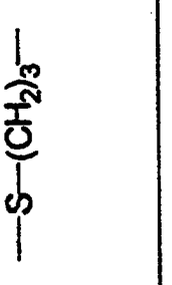
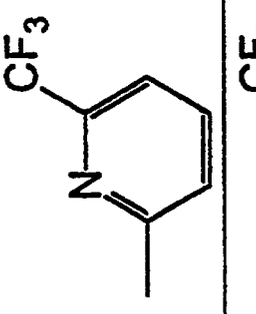
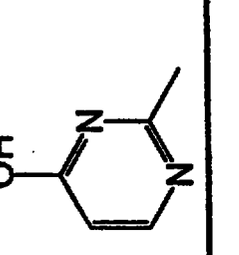
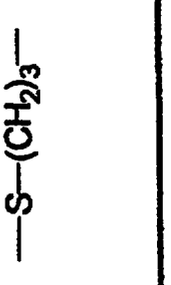
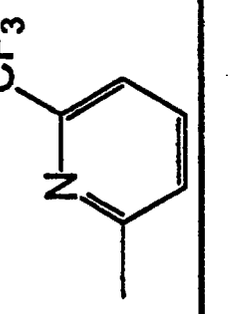
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
550				
551				
552				
553				

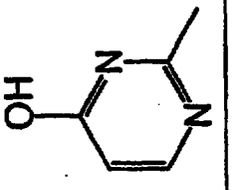
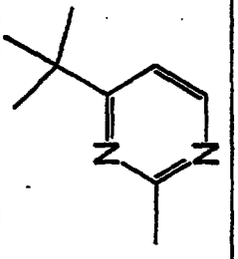
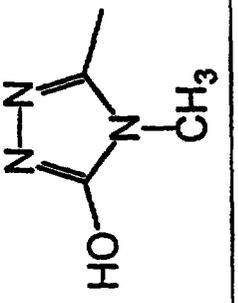
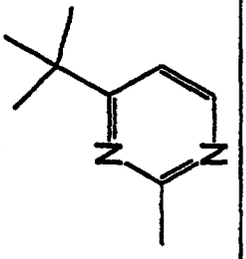
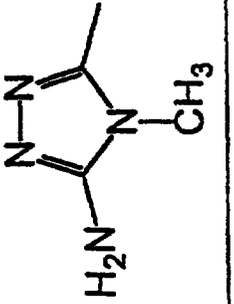
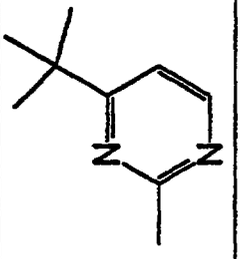
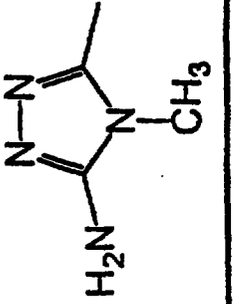
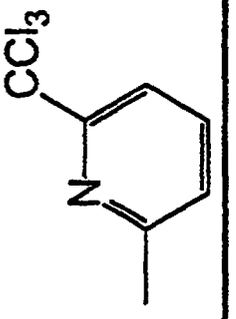
REPLACEMENT SHEET (RULE 26)

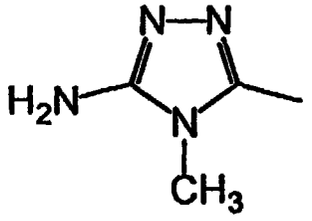
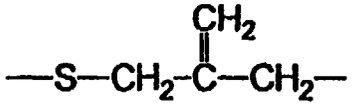
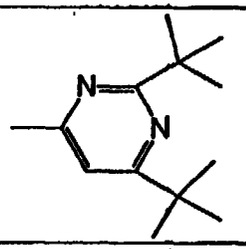
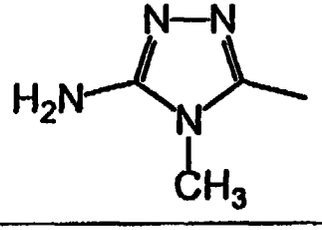
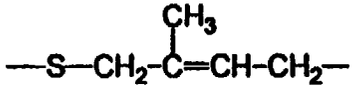
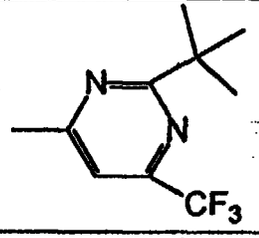
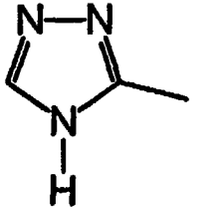
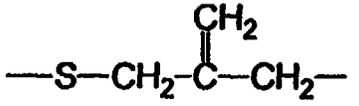
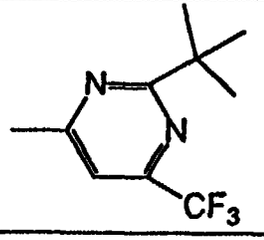
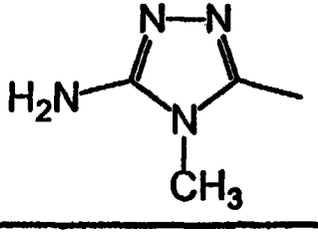
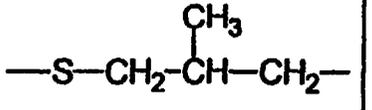
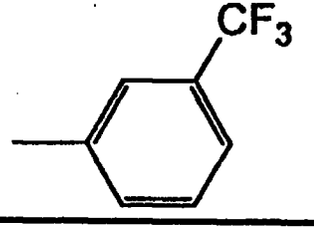
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
554				
555				
556				
557				

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
558				100 - 103
559				
560				109 - 112
561				

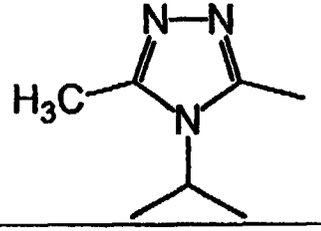
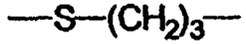
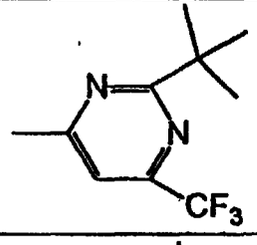
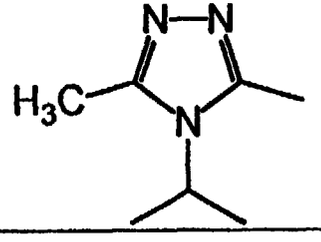
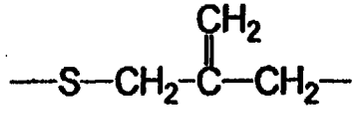
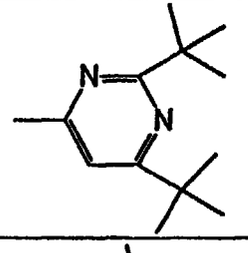
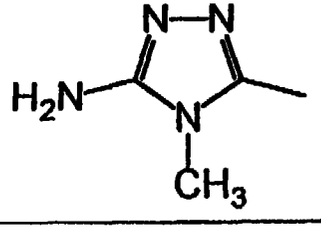
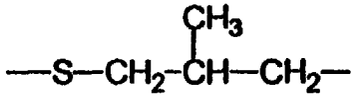
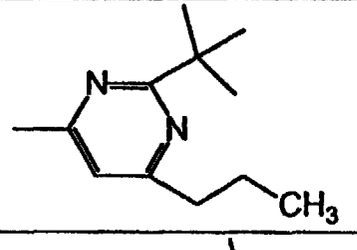
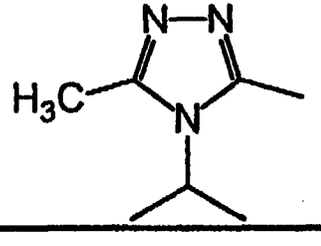
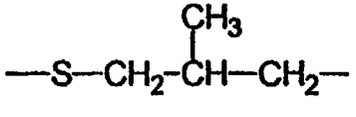
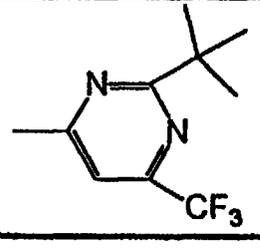
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
562				
563				
564				
565				84 - 85

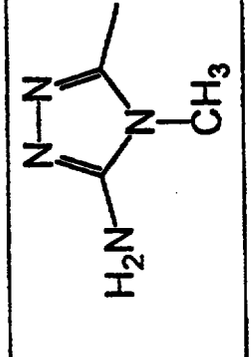
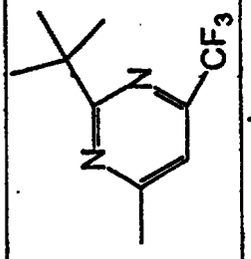
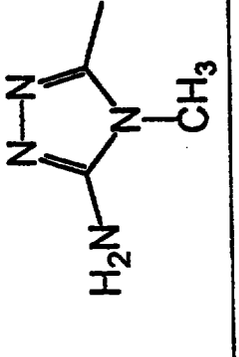
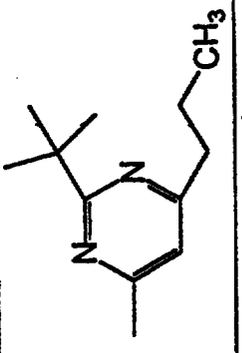
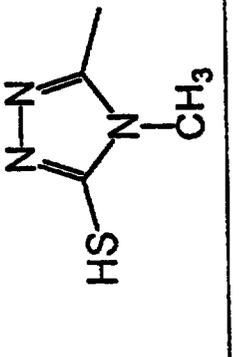
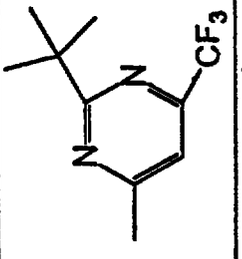
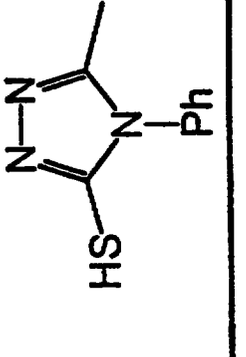
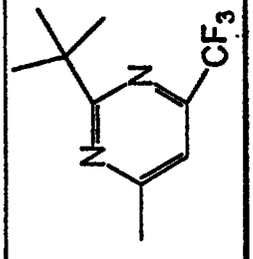
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
566				
567				
568				
569				

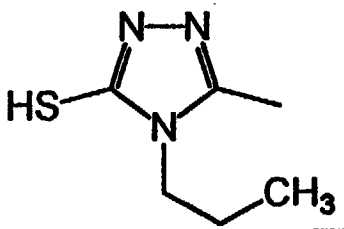
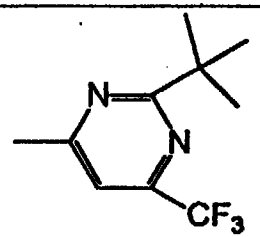
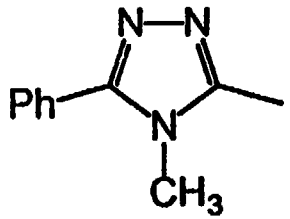
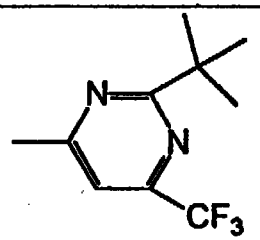
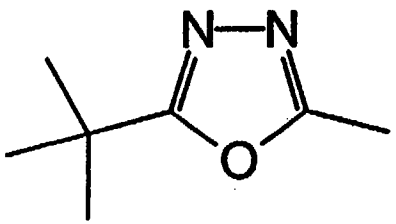
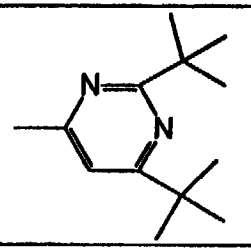
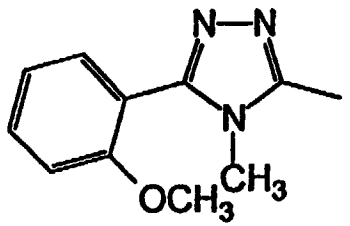
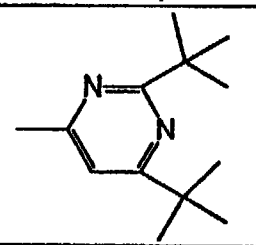
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
570		$-S-(CH_2)_3-$		
571		$-S-(CH_2)_3-$		
572		$-S-(CH_2)_3-$		
573		$-S-(CH_2)_3-$		185 - 190

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
574				145 - 148
575				120 - 122
576				70 - 80 (Oxalate)
577				155 - 160 (Hydrochloride)

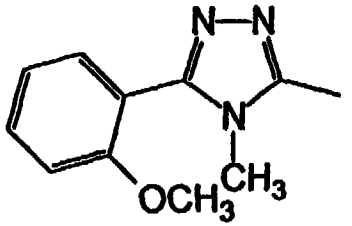
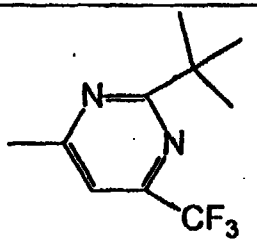
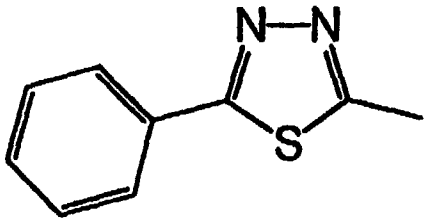
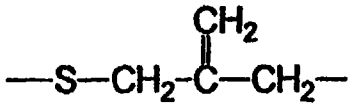
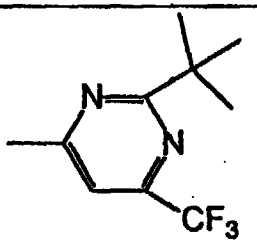
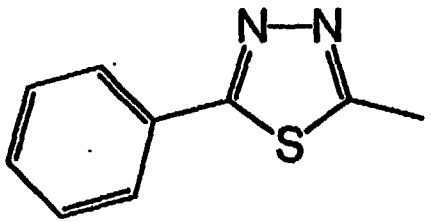
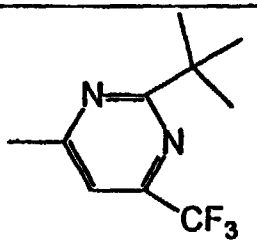
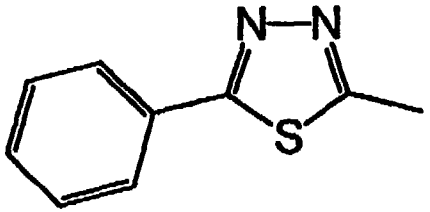
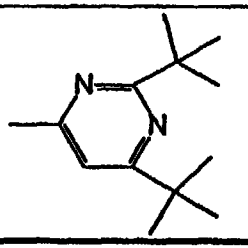
REPLACEMENT SHEET (RULE 26)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
578				97 - 98 (Hydrochloride)
579				141 - 143 (Fumarate)
580				105 - 108 (Hydrochloride)
581				139 - 143 (Hydrochloride)

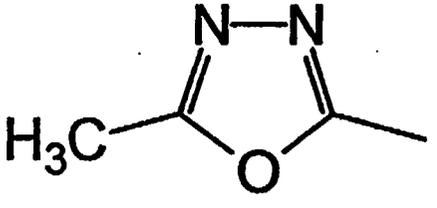
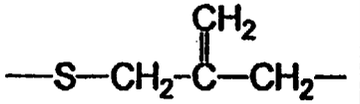
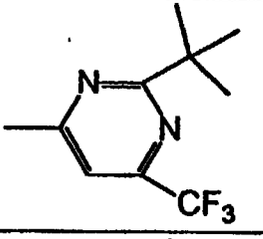
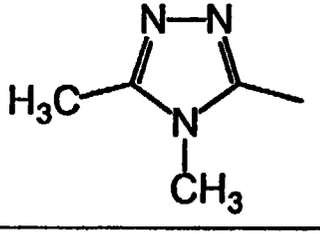
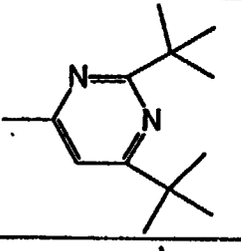
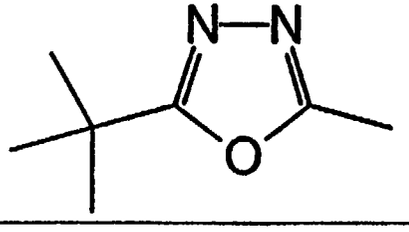
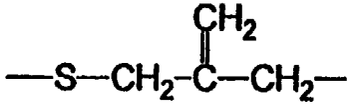
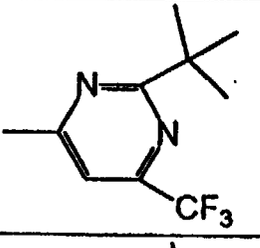
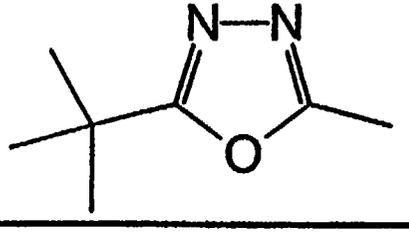
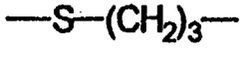
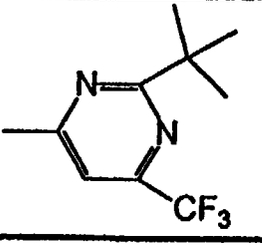
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
582				89 - 95
583				160 - 165 (Oxalate)
584				62 - 64
585				148 - 149

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
586		$-(CH_2)_4-$		38 - 41
587		$-CH=CH-(CH_2)_2-$		Oil
588		$-S-(CH_2)_3-$		90 (Decomposition) (Hydrochloride)
589		$-S-(CH_2)_3-$		90 - 93 (Fumarate)

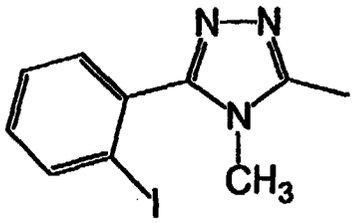
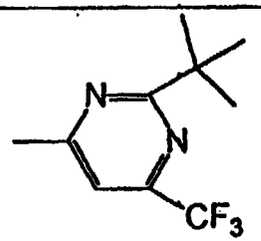
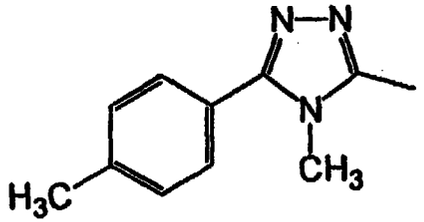
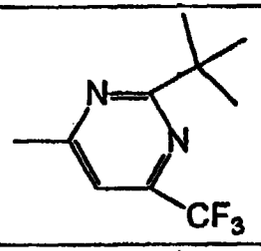
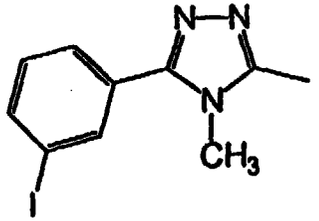
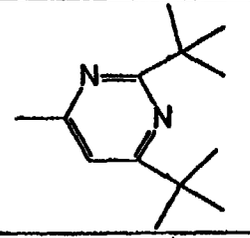
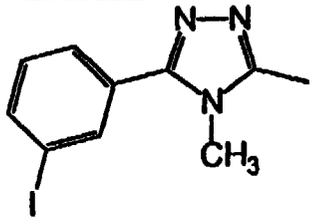
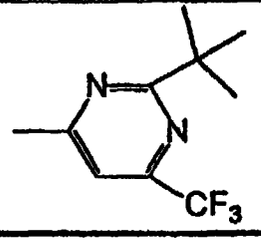
REPLACEMENT SHEET (RULE 26)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
590				75 - 78 (Fumarate)
591				Oil
592				130 - 133 (Hydrochloride) [sic]
593				Oil

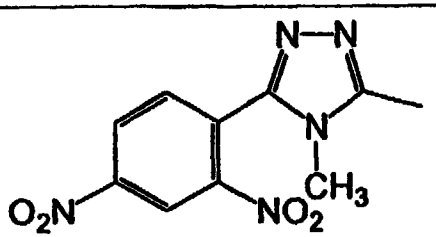
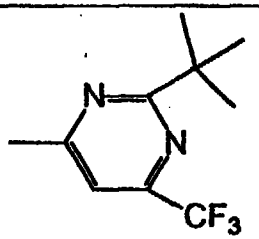
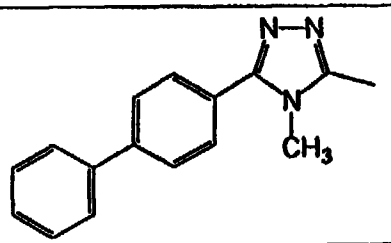
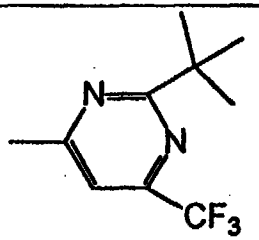
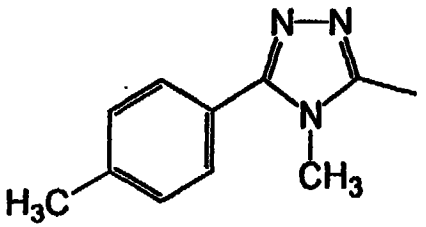
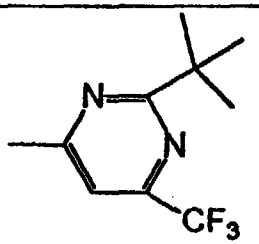
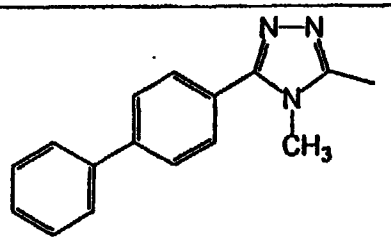
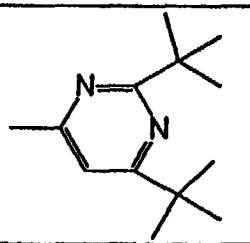
REPLACEMENT SHEET (RULE 26)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
594				126 - 130 (Hydrochloride)
595				90 - 95 (Decomposition) (Hydrochloride)
596				Oil
597				Oil

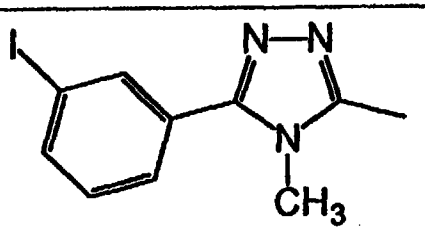
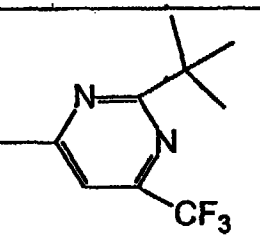
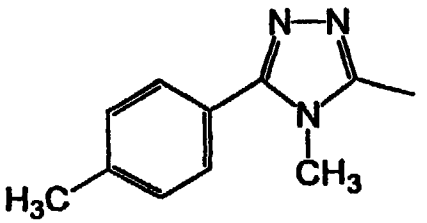
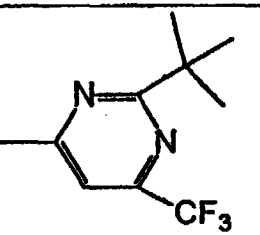
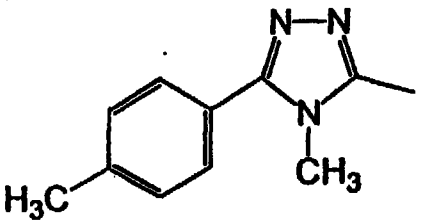
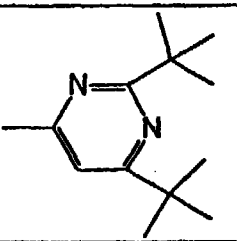
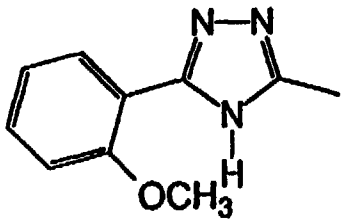
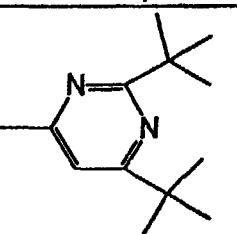
REPLACEMENT SHEET (RULE 26)

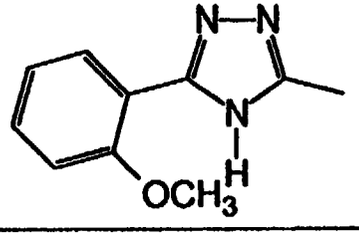
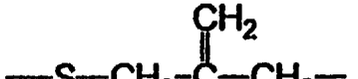
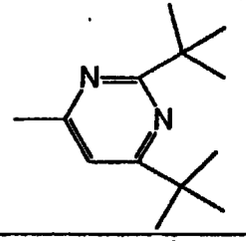
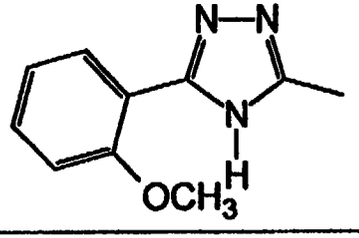
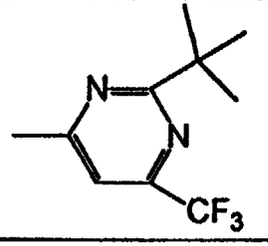
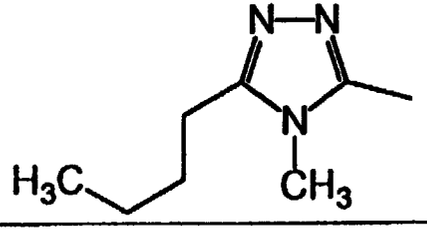
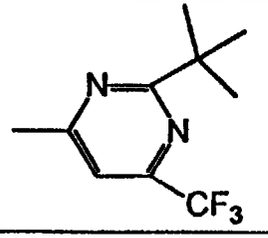
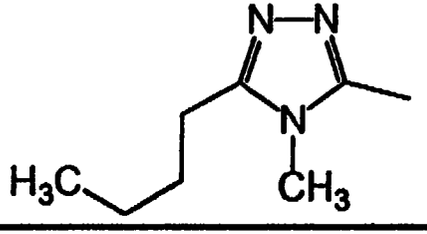
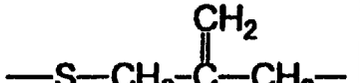
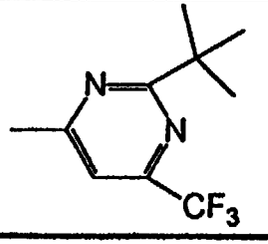
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
598		—S—$(CH_2)_3$—		106 (Hydrochloride)
599		—S—$(CH_2)_3$—		148 (Hydrochloride)
600		—S—$(CH_2)_3$—		137 - 139 (Hydrochloride)
601		—S—CH_2—C(CH_2)—CH_2—		109 - 115 (Hydrochloride)

REPLACEMENT SHEET (RULE 26)

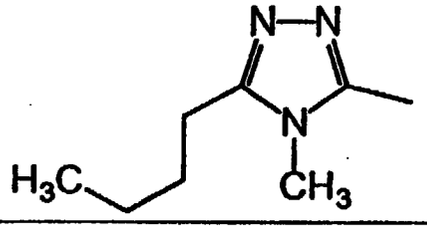
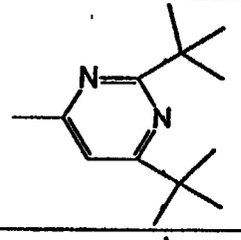
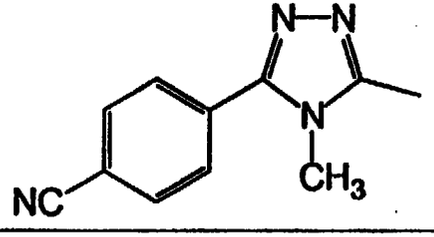
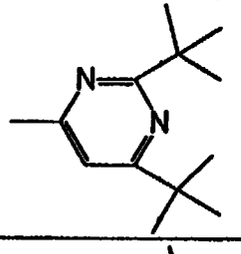
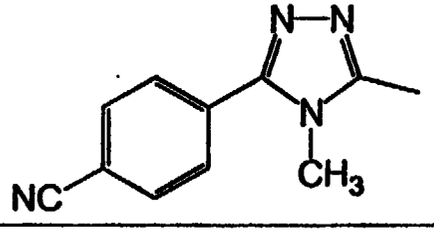
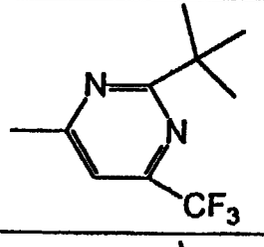
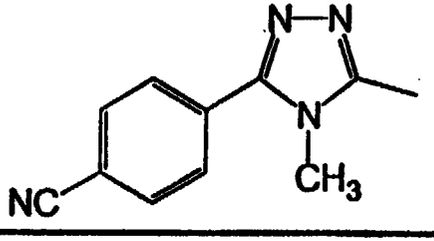
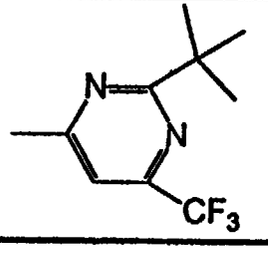
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
602		—S—$(CH_2)_3$—		90 (Decomposition) (Hydrochloride)
603		—S—CH_2—C(=CH_2)—CH_2—		132 (Decomposition) (Hydrochloride)
604		—S—CH_2—C(=CH_2)—CH_2—		103 - 105 (Hydrochloride)
605		—S—$(CH_2)_3$—		142 - 144

REPLACEMENT SHEET (RULE 26)

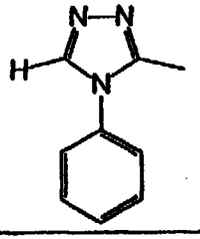
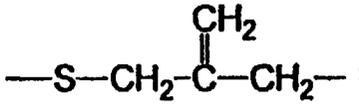
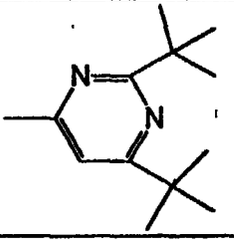
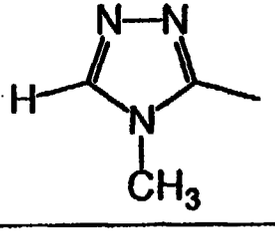
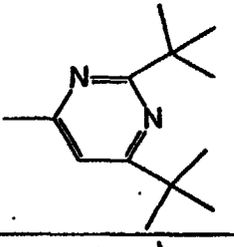
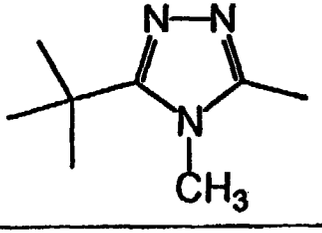
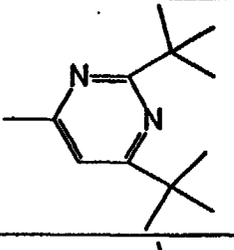
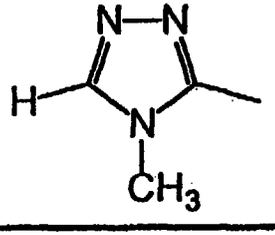
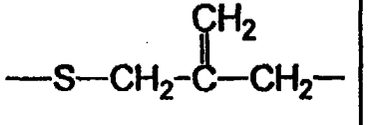
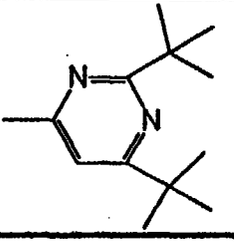
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
606		—S—$(CH_2)_3$—		Oil
607		—S—$(CH_2)_3$—		Oil
608		—S—$(CH_2)_3$—		120 - 123 (Hydrochloride)
609		—S—$(CH_2)_3$—		187 - 189 (Fumarate)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
610				95 - 98 (Fumarate)
611				68 - 72 (Fumarate)
612				240 (Hydrochloride)
613				190 (Hydrochloride)

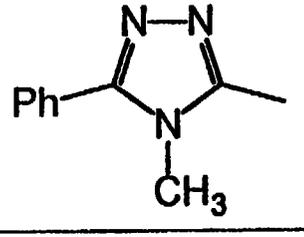
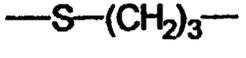
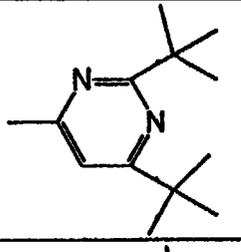
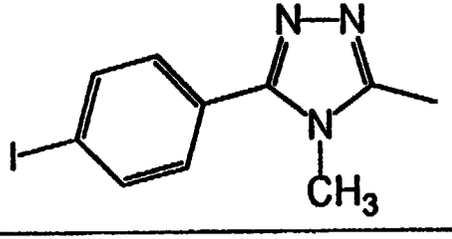
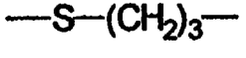
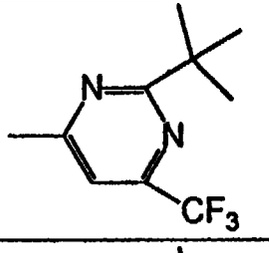
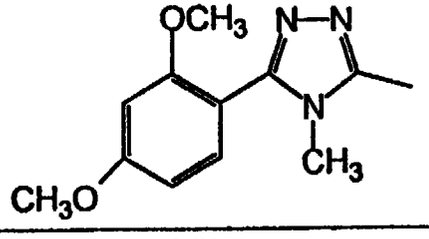
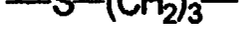
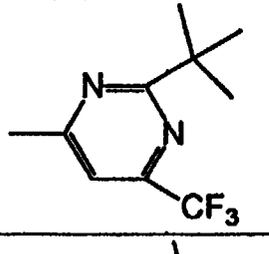
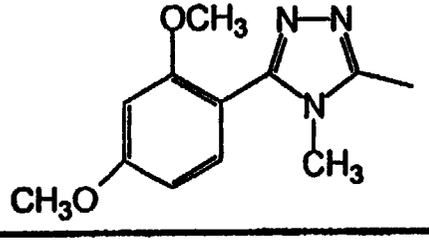
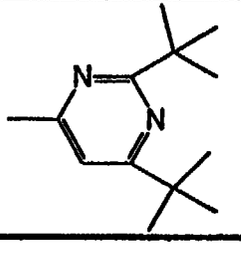
REPLACEMENT SHEET (RULE 26)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
614		—S—$(CH_2)_3$—		243 (Hydrochloride)
615		—S—$(CH_2)_3$—		101 - 104
616		—S—$(CH_2)_3$—		Oil
617		—S—CH_2—C(CH_2)—CH_2—		90 - 94 (Decomposition) (Hydrochloride)

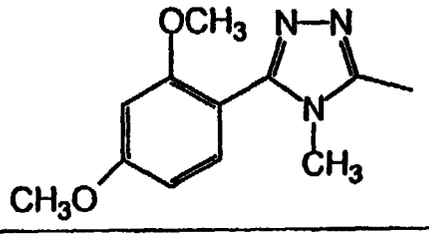
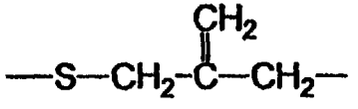
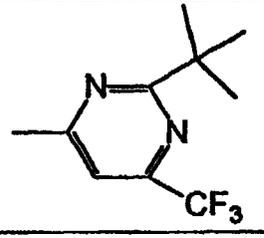
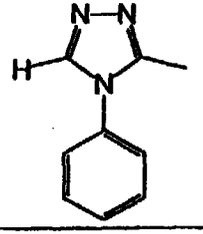
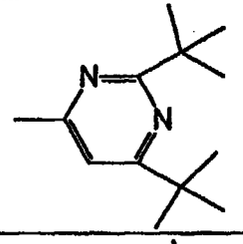
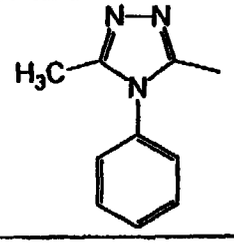
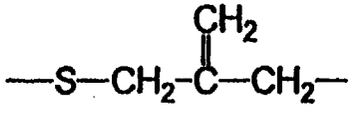
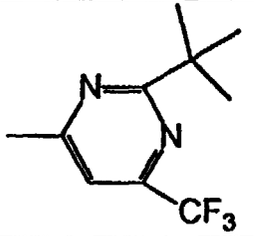
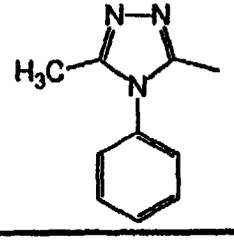
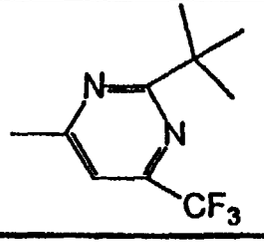
REPLACEMENT SHEET (RULE 26)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
618				152 (Hydrochloride)
619				Oil
620				Oil
621				152 (Hydrochloride)

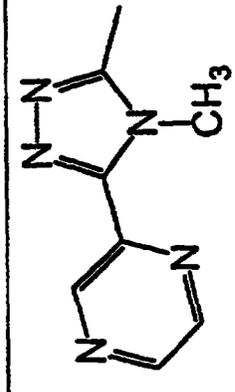
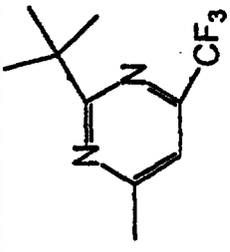
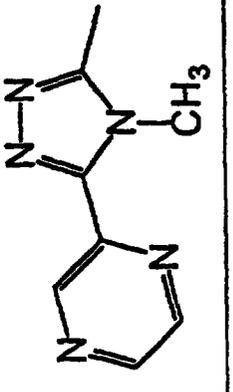
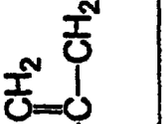
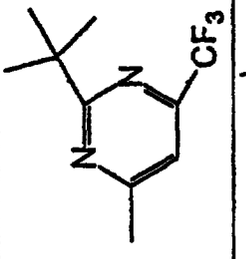
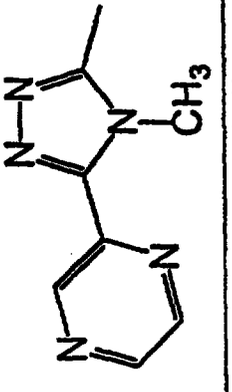
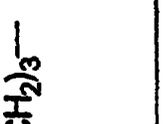
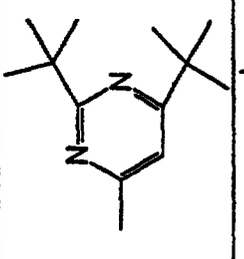
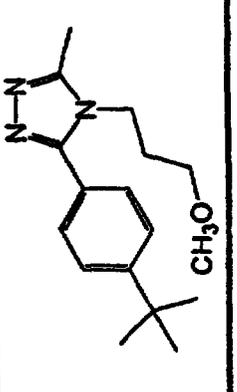
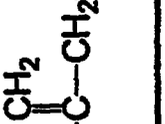
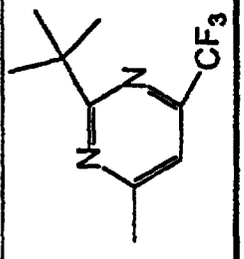
REPLACEMENT SHEET (RULE 26)

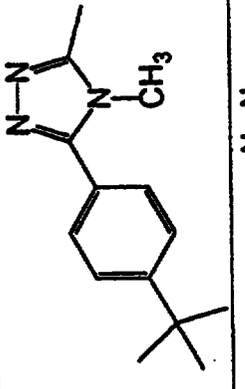
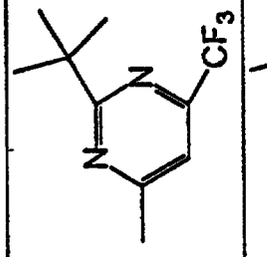
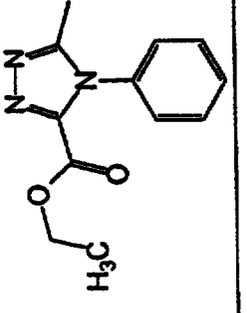
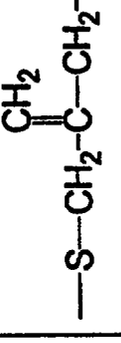
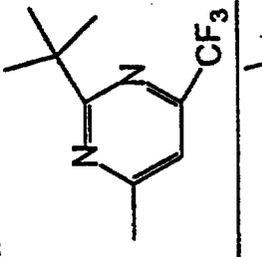
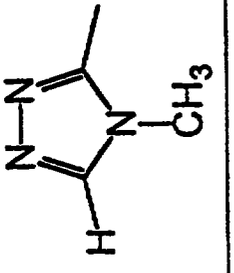
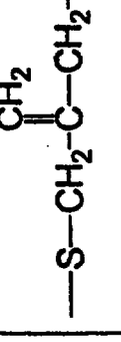
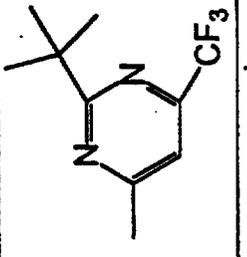
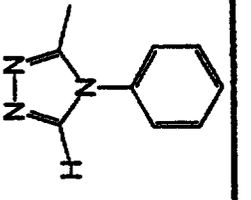
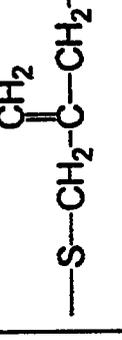
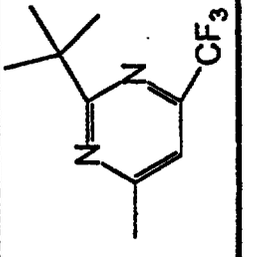
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
622				110 (Hydrochloride)
623				126 - 131 (Hydrochloride)
624				91 (Hydrochloride)
625				116 - 120 (Hydrochloride)

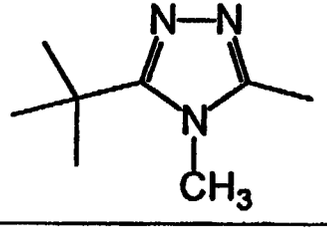
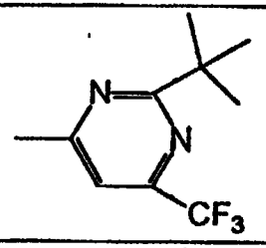
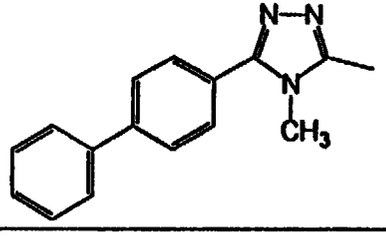
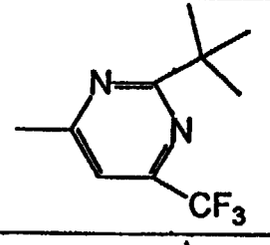
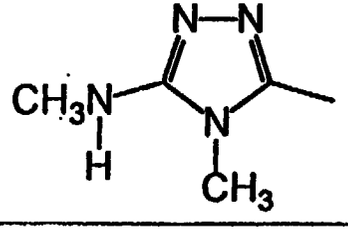
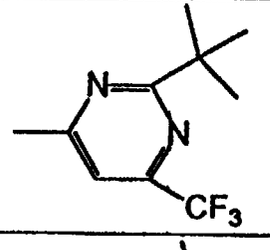
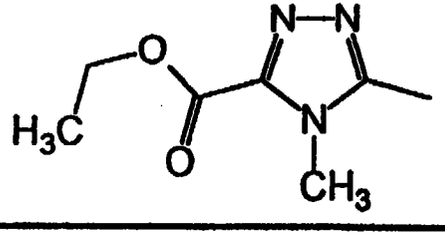
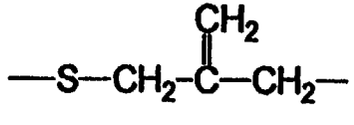
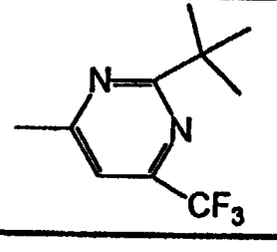
REPLACEMENT SHEET (RULE 26)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
626				103 (Hydrochloride)
627				150 (Hydrochloride)
628				140 (Hydrochloride)
629				130 (Hydrochloride)

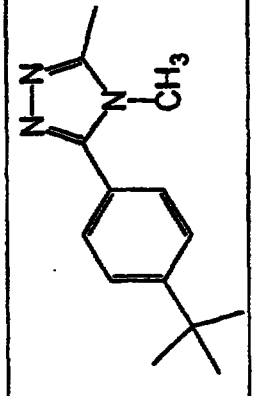
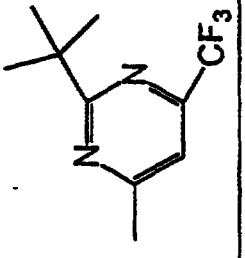
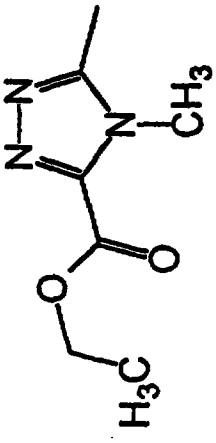
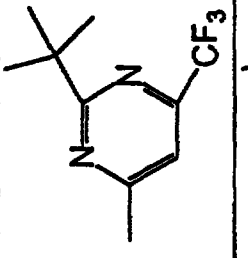
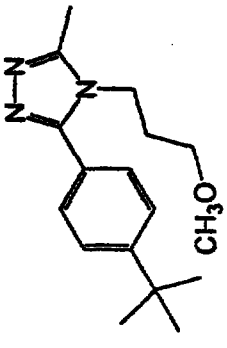
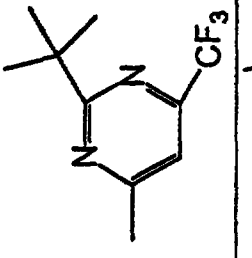
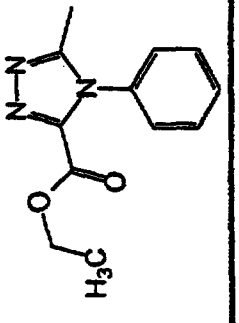
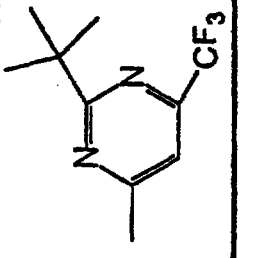
REPLACEMENT SHEET (RULE 26)

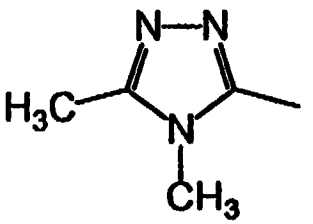
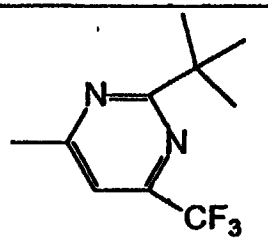
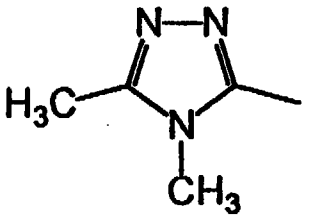
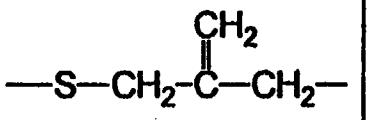
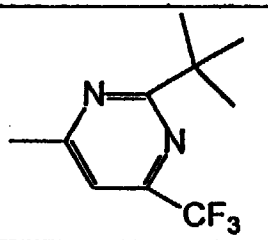
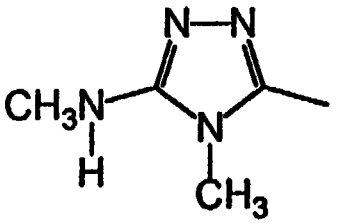
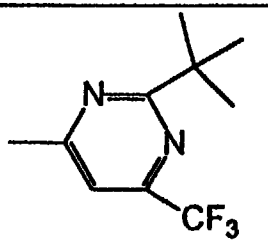
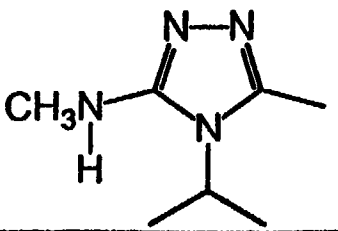
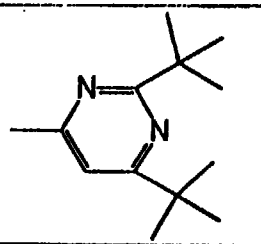
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
630				98 - 104 (Hydrochloride)
631				65 - 68 (Hydrochloride)
632				131 - 136 (Hydrochloride)
633				105 (Hydrochloride)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
634				132 (Hydrochloride)
635				92 (Hydrochloride)
636				95 (Hydrochloride)
637				102 (Hydrochloride)

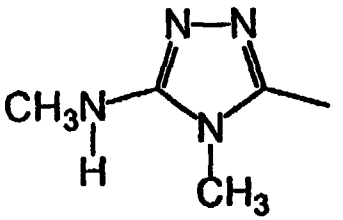
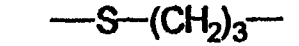
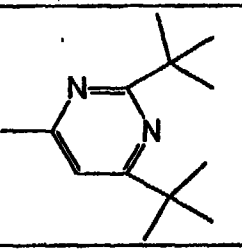
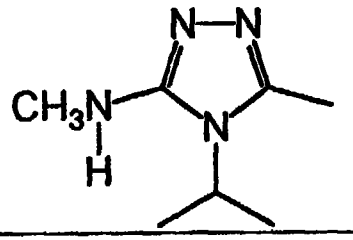
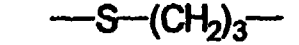
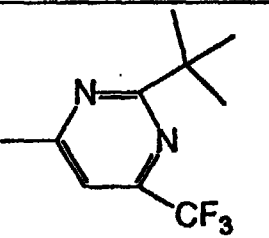
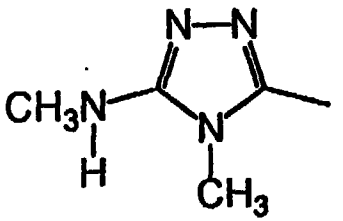
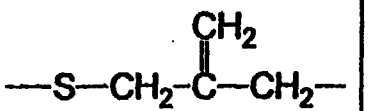
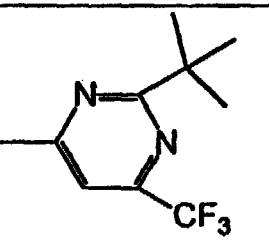
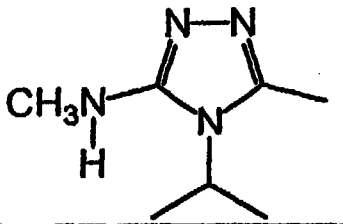
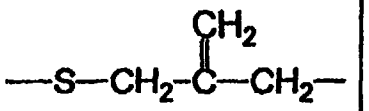
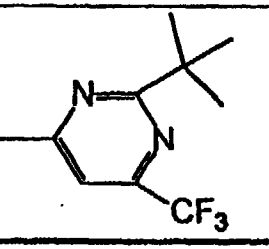
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
638		$-S-(CH_2)_3-$		214 - 216 (Hydrochloride)
639		$-S-(CH_2)_3-$		160 - 162 (Hydrochloride)
640		$-S-(CH_2)_3-$		73 - 75 (Fumarate)
641				178

REPLACEMENT SHEET (RULE 26)

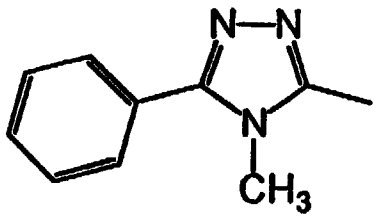
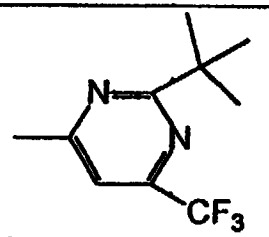
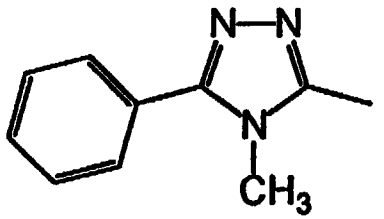
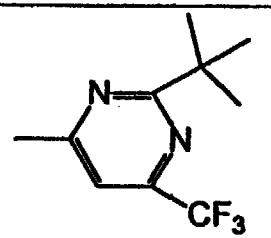
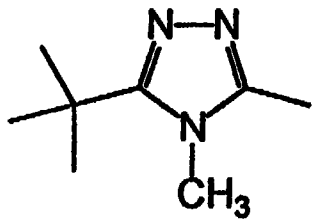
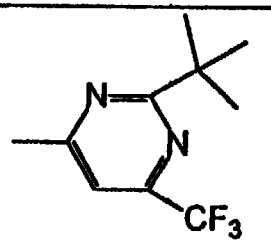
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
642		$-S-(CH_2)_3-$		155
643		$-S-(CH_2)_3-$		125 - 128 (Hydrochloride)
644		$-S-(CH_2)_3-$		102 (Hydrochloride)
645		$-S-(CH_2)_3-$		88 (Hydrochloride)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
646				132 (Hydrochloride)
647				190 (Hydrochloride)
648				134 - 138 (Hydrochloride)
649				170 - 174 (Hydrochloride)

REPLACEMENT SHEET (RULE 26)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
650				115 (Hydrochloride)
651				117 (Hydrochloride)
652				151 - 155
653				158 - 161 (Hydrochloride)

REPLACEMENT SHEET (RULE 26)

Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
654		—S—$(CH_2)_3$—		184 - 185 (Hydrochloride)
655		—S—CH_2—C(CH_2)—CH_2—		194 - 195 (Hydrochloride)
656		—S—CH_2—C(CH_2)—CH_2—		114 (Hydrochloride)

REPLACEMENT SHEET (RULE 26)

The above compounds which are not characterized by the melting point have the following NMR spectra (d_6-DMSO):

Ex. No.		
476		1.8-2.1 (m,4H); 2.6-2.7 (m,4H); 2.8 (t,2H); 3.2 (t,2H); 3.5-3.7 (b,2H); 3.7-3.9 (b,2H); 4.5 (d,2H); 5.1 (t,1H); 5.2 (s,1H); 6.1 (d,1H); 6.2 (m,2H); 7.3 (m,5H); 7.7 (m,2H); 7.8 (d,1H)
477		1.8-1.9 (m,4H); 2.5-2.6 (m,4H); 2.7 (t,2H); 3.0 (t,2H); 3.3 (s,3H); 3.5-3.8 (b,4H); 4.2 (s,2H); 4.5 (d,2H); 5.1 (t,1H); 5.2 (s,1H); 6.2 (m,2H); 7.3-7.4 (m,5H); 7.7 (m,2H)
481	Oxalate	2.1 (b,4H); 3.2-3.4 (m,8H); 3.6 (s,3H); 3.7 (b,2H); 6.6-6.8 (m,3H); 7.2 (t,1H); 7.6 (m,3H); 7.7 (m,2H)
484	Oxalate	2.0 (b,2H); 2.8-3.0 (b,4H); 3.4-3.5 (m,4H); 3.6-3.7 (b,2H); 3.9 (s,2H); 5.3 (d,2H); 6.1 (d,1H); 6.5-6.8 (m,3H); 7.21 (t,1H); 7.9 (d,1H);
491	Oxalate	2.0-2.3 (b,4H); 3.0-3.4 (b,8H); 3.6 (s,3H); 3.9 (b,2H); 4.1 (b,2H); 7.1-7.3 (b,1H); 7.5 (m,3H); 7.6 (m,2H); 8.6 (s,1H);
492		1.7-1.9 (m,4H); 2.6 (b,2H); 2.8 (b,2H); 3.1 (t,2H); 3.6-3.9 (b,4H); 6.1 (d,1H); 7.0 (d,1H); 7.8 (d,1H); 8.5 (s,1H);
493	Oxalate	1.9-2.1 (b,4H); 2.7 (s,3H); 2.8 (t,2H); 3.0-3.3 (b,6H); 3.3 (s,3H); 3.4 (t,2H); 3.7 (b,2H); 6.3 (b,1H); 6.4-6.5 (m,3H); 7.0 (m,1H);

495	Fumarate	1.6-1.8 (b,4H); 2.6 (m,2H); 2.7 (t,2H); 3.2 (s,3H); 3.3-3.5 (m,4H); 5.9 (s,2H); 6.2-6.5 (m,3H); 7.0 (m,1H);
497	Fumarate	1.6-1.8 (m,2H); 1.8-2.0 (b,2H); 2.5-2.7 (b,4H); 2.8-2.9 (m,4H); 3.2 (s,3H); 3.7-3.9 (m,4H); 5.9 (b,2H); 6.5 (s,2H); 7.4 (d,1H);
498	Fumarate	1.3 (s,9H); 1.8-2.1 (b,4H); 2.7-3.0 (b,6H); 3.3 (s,3H); 3.5-3.8 (b,6H); 6.1 (b,2H); 6.6 (s,2H); 6.7 (s,1H);
499	Hydro-chloride	1.3 (s,9H); 1.9 (b2H); 2.2 (s,2H); 2.5 (b,2H); 2.7 (b,2H); 3.1 (s,2H); 3.4 (s,3H); 3.7 (s,2H); 3.8 (s,3H); 3.9 (s,3H); 5.0 (d,2H); 6.5 (s,1H); 6.9 (d,1H); 7.5 (d,1H); 7.7 (s,1H);11.3 (b,1H);
500	Fumarate	1.3 (s,9H); 1.7-1.9 (b,4H); 2.5-2.7 (b,4H); 2.8-2.9 (b,2H); 3.1 (t,2H); 3.6-3.7 (b,2H); 3.8-4.0 (b,2H); 6.1 (d,1H); 6.6 (s,2H); 6.9 (d,1H); 7.8 (d,1H)
501		1.3 (s,9H); 1.8-2.0 (m,4H); 2.6 (m,4H); 2.8 (b,2H); 3.1 (t,2H); 3.4 (s,3H); 3.5 (b,2H); 3.9-4.1 (b,2H); 4.4 (b,2H); 6.5 (s,1H)
502	Fumarate	1.3 (s,9H); 1.8-1.9 (b,2H); 2.5-2.6 (b,2H); 2.7 (b,2H); 3.1 (s,2H); 3.6-3.7 (b,2H); 3.7-4.0 (m,4H); 5.1 (s,1H); 5.2 (s,1H); 6.1 (d,1H); 6.6 (s,2H); 6.9 (d,1H); 7.8 (d,1H)

503	Fumarate	1.3 (s,9H); 1.8-1.9 (b,2H); 2.5-2.6 (b,2H); 2.7-2.8 (b,2H); 3.2 (s,2H); 3.6 (s,3H); 3.6-3.7 (b,2H); 3.7 (s,2H); 3.8-4.0 (b,2H); 5.0 (s,1H); 5.1 (s,1H); 6.6 (s,2H); 6.9 (d,1H); 7.6 (m,3H); 7.7 (m,2H)
504	Fumarate	1.3 (s,9H); 1.8-1.9 (b,2H); 2.5 (b,2H); 2.6-2.7 (b,2H); 3.1 (s,2H); 3.3 (s,3H); 3.4 (s,2H); 3.5-3.7 (b,2H); 3.8-4.0 (b,2H); 4.9 (d,2H); 6.0 (s,2H); 6.6 (s,2H); 6.9 (d,1H)
505	Fumarate	1.3 (s,9H); 1.7-1.9 (b,4H); 2.5-2.7 (b,4H); 2.8 (t,2H); 3.1 (t,2H); 3.4-4.0 (b,4H); 6.1 (d,1H); 6.5 (d,1H); 6.6 (s,2H); 7.8 (d,1H); 8.2 (d,1H)
506		1.4 (s,9H); 1.8 (m,2H); 2.1-2.2 (b,2H); 2.6 (m,4H); 2.7 (t,2H); 3.0 (t,2H); 3.4 (s,3H); 3.5-4.0 (b,4H); 4.6 (b,2H); 6.2 (d,1H); 8.2 (d,1H)
507		0.9 (t,3H); 1.3 (s,9H); 1.4 (m,2H); 1.7 (m,2H); 2.1 (b,2H); 2.6 (t,2H); 2.7 (t,2H); 2.8 (t,2H); 3.3 (s,2H); 3.6-3.7 (b,2H); 3.8 (s,2H); 3.9-4.0 (b,2H); 5.1 (s,1H); 5.2 (s,1H); 6.1 (s,1H); 6.2 (d,1H); 7.8 (d,1H)
508		0.9 (t,3H); 1.3 (s,9H); 1.4 (m,2H); 1.7 (m,2H); 1.9 (m,2H); 2.6 (m,4H); 2.7 (t,2H); 3.1 (d,3H); 3.2 (s,2H); 3.3 (s,3H); 3.6 (m,1H); 3.7 (s,2H); 3.6-3.8 (b,4H); 5.0 (d,2H); 6.0 (s,1H)

509	Dihydro-chloride	0.9 (t,3H); 1.3 (m,2H); 1.4 (s,9H); 1.7 (m,2H); 2.4-2.5 (b,2H); 2.9 (t,2H); 3.2-3.4 (b,4H); 3.5 (s,3H); 3.7-3.8 (b,2H); 3.9 (s,2H); 3.9-4.2 (b,2H); 4.1 (s,2H); 5.4 (s,2H); 6.9 (s,1H);8.5 (s,2H); 11.7 (b,1H); 14.0 (b,1H)
510		1.3 (s,9H); 2.0-2.1 (b,2H); 2.7 (t,2H); 2.8 (t,2H); 3.3 (s,2H); 3.5-3.8 (b,2H); 3.8 (s,2H); 3.8-4.1 (b,2H); 5.1 (s,1H); 5.2 (s,1H); 6.2 (m,2H); 7.8 (d,1H); 8.2 (d,1H)
511		1.3 (s,18H); 1.6-1.9 (b,4H); 2.4 (b,2H); 2.7 (b,2H); 2.8 (t,2H); 3.2 (s,3H); 3.7 (m,4H); 5.8 (s,1H);
512		1.3 (s,18H); 1.7-1.8 (m,4H); 2.5 (b,2H); 2.7 (b,2H); 3.0 (t,2H); 3.7-3.8 (m,4H); 6.0 (d,1H); 7.8 (d,1H);
513		1.6-2.1 (m,17H); 2.7 (s,2H); 3.1 (s,2H); 3.3-3.6 (b,6H); 3.4 (s,3H); 3.8-3.9 (b,2H); 4.8 (b,2H); 6.0 (b,2H); 6.8 (s,1H);
514		1.6-2.0 (m,17H); 2.5 (s,2H); 2.6 (s,2H); 3.0 (s,2H); 3.5-3.9 (b,6H); 5.0 (d,2H); 6.0 (d,1H); 6.8 (d,1H); 7.8 (d,1H);
515		1.7-2.0 (m,19H); 2.5 (b,2H); 2.7 (s,2H); 3.0 (t,2H); 3.5-3.8 (b,4H); 6.0 (d,1H); 6.8 (d,1H); 7.8 (d,1H);

517	Dihydro-chloride	1.4 (s,9H); 2.4-2.5 (b,2H); 3.3-3.6 (b,4H); 3.5 (s,3H); 3.7-3.8 (b,2H); 3.8-3.9 (b,2H); 3.9-4.2 (b,4H); 5.4 (s,2H); 7.1 (d,1H); 8.3 (d,1H); 8.5 (s,2H); 11.7 (b,1H); 14.5 (b,1H)
518		1.3 (s,9H); 1.8-2.0 (b,2H); 2.6 (t,2H); 2.7 (t,2H); 3.0 (d,3H); 3.2 (s,2H); 3.3 (s,3H); 3.6 (s,2H); 3.6-3.9 (b,5H); 5.0 (d,2H); 6.2 (s,1H); 6.3 (m,2H); 7.8 (m,2H)
519		1.4 (s,9H); 1.9 (m,2H); 2.6 (t,2H); 2.7 (t,2H); 3.0 (d,3H); 3.2 (s,2H); 3.3 (s,3H); 3.7 (s,2H); 3.6-3.9 (b,5H); 5.0 (d,2H); 6.1 (s,1H); 6.3 (m,2H); 7.6 (m,2H)
527	Hydro-chloride	1.2-1.5 (b,10H); 1.5-1.8 (b,4H); 3.1 (m,4H); 3.5 (m,4H); 3.8-4.0 (b,4H); 6.8 (t,1H); 6.9 (b,3H); 7.1 (t,1H); 10.5 (b,1H);
526	Oxalate	1.3 (s,9H); 1.9-2.1 (b,2H); 2.7-3.0 (b,4H); 3.4 (b,2H); 3.6 (s,3H); 3.6-3.8 (b,2H); 3.8 (s,2H); 3.9-4.1 (b,2H); 5.2 (d,2H); 6.2 (m,2H); 6.4 (s,1H); 7.6 (m,3H); 7.7 (m,4H)
528	Oxalate	0.9 (t,3H); 1.3 (s,9H); 1.4 (m,2H); 1.6 (m,2H); 1.9-2.2 (b,4H); 2.5 (m,2H); 3.0-3.2 (b,4H); 3.2-3.4 (b,4H); 3.5-3.7 (b,2H); 3.9-4.1 (b,2H); 6.1 (d,1H); 6.4 (s,1H); 7.8 (d,1H)

529	Dihydro-chloride	0.9 (t,3H); 1.3 (m,2H); 1.4 (s,9H); 1.7 (m,2H); 2.2 (b,3H); 3.0 (t,2H); 3.2 (b,5H); 3.5 (s,3H); 3.5-4.2 (b,7H); 4.5-4.7 (b,1H); 7.0 (d,1H); 8.6 (s,2H); 11.7 (b,1H); 14.2 (b,1H)
530	Oxalate	1.3 (s,9H); 1.9-2.1 (b,2H); 2.7-3.0 (b,4H); 2.3-2.4 (b,2H); 2.6-4.1 (b,4H); 3.9 (s,2H); 5.2 (s,1H); 5.3 (s,1H); 6.1 (d,1H); 6.2 (m,2H); 6.4 (s,1H); 7.7 (m,2H); 7.8 (d,1H)
531		1.3 (s,9H); 1.9 (m,2H); 2.6 (t,2H); 2.7 (t,2H); 3.2 (s,2H); 3.3 (s,3H); 3.7 (s,2H); 3.6-3.9 (b,4H); 4.3 (s,2H); 5.0 (d,2H); 6.2 (s,1H); 6.3 (m,2H); 7.8 (m,2H)
533		1.3 (s,9H); 2.1 (m,2H); 2.7 (m,2H); 2.9 (m,2H); 3.3 (s,2H); 3.6-3.8 (b,2H); 3.8 (s,2H); 3.9-4.1 (b,2H); 5.1 (s,1H); 5.2 (s,1H); 6.1 (s,1H); 6.2 (d,1H); 6.3 (m,2H); 7.5 (m,2H); 7.8 (d,1H)
532		1.3 (s,9H); 1.9 (m,2H); 2.6 (t,2H); 2.7 (t,2H); 3.2 (s,2H); 3.3 (s,3H); 3.7 (s,2H); 3.6-3.6 (b,4H); 4.3 (s,2H); 5.0 (s,2H); 6.1 (s,1H); 6.3 (m,2H); 7.6 (m,2H)
539	Hydro-chloride	2.2-2.3 (b,2H); 3.0-3.2 (b,2H); 3.5-4.0 (b,8H), 4.2 (s,2H); 5.5 (d,2H); 6.2 (d,1H); 6.9-7.0 (m,3H); 7.0 (t,1H); 7.4 (m,1H); 7.9 (d,1H); 10.9 (b,1H);
540	Hydro-chloride	2.4 (b,2H); 3.2 (b,4H); 3.4 (s,3H); 3.5 (m,2H); 3.7 (b,4H); 4.0 (s,2H); 5.3 (d,2H); 6.8-7.1 (m,4H); 7.2-7.4 (m,3H);

542		1.3 (s,9H); 1.9 (m,2H); 1.9-2.1 (b,2H); 2.6 (m,4H); 2.8 (b,2H); 3.2 (t,2H); 3.5-3.7 (b,2H); 3.9-4.2 (b,2H); 6.2 (d,1H); 6.5 (s,1H); 6.8 (d,1H)
543		1.3 (s,9H); 1.9 (m,2H); 1.9-2.0 (b,2H); 2.6-2.7 (b,4H); 2.8 (b,2H); 3.1 (t,2H); 3.2 (s,3H); 3.5-3.6 (b,2H); 3.9-4.1 (b,2H); 6.5 (s,1H); 10.8 (b,1H)
544		1.3 (s,9H); 1.8-2.0 (b,4H); 2,6 (m,4H); 2.7-2.8 (b,2H); 3.0 (m,5H); 3.3 (s,3H); 3.5-3.6 (b,2H); 3.9-4.1 (b,3H); 6.5 (s,1H)
545	Hydro-chloride	1.3 (s,9H); 2.1-2.2 (b,3H); 2.5-2.6 (b,1H); 3.1-3.3 (b,6H); 3.4 (s,3H); 3.4-3.8 (b,4H); 4.0-4.1 (b,1H); 4.6-4.7 (b,1H); 7.0 (s,1H); 8.6 (s,2H); 11.3 (b,1H)
546		1.3 (s,9H); 1.9 (m,2H); 2.1 (m,2H); 2.7 (m,4H); 2.9 (m,2H); 3.2 (t,2H); 3.8-3.9 (b,2H); 3.9-4.0 (b,2H); 6.2 (d,2H); 6.3 (m,2H); 7.8 (m,3H)
547		1.3 (s,9H); 1.9 (m,4H); 2.6 (m,4H); 2.8 (t,2H); 3.1 (t,2H); 3.2 (s,3H); 3.6-4.0 (b,4H); 6.2 (s,1H); 6.3 (m,2H); 7.8 (m,2H); 9.2 (s,1H)
548		1.3 (s,9H); 1.9 (m,4H); 2.6 (t,4H); 2.8 (t,2H); 3.1 (t,2H); 3.3 (s,3H); 3.5-3.9 (b,4H); 4.1 (s,2H); 6.2 (s,1H); 6.3 (m,2H); 7.8 (m,2H)

549		1.4 (s,9H); 1.9 (m,2H); 2.0-2.1 (b,2H); 2.7 (m,4H); 2.9 (m,2H); 3.2 (t,2H); 3.6-3.8 (b,2H); 3.8-4.1 (b,2H); 6.1 (s,1H); 6.2 (d,1H); 6.3 (m,2H); 7.6 (m,2H), 7.8 (d,1H)
550		1.4 (s,9H); 1.9 (m,4H); 2.6 (m,4H); 2.8 (b,2H); 3.1 (t,2H); 3.2 (s,3H); 3.6-4,0 (b,4H); 6.1 (s,1H); 6.3 (m,2H); 7.5 (m,2H); 10.0 (b,1H)
551		1.4 (s,9H); 1.9 (m,4H); 2.6 (m,4H); 2.8 (b,2H); 3.1 (t,2H); 3.4 (s,3H); 3.5-4.0 (b,4H); 4.3 (s,2H); 6.1 (s,1H); 6.3 (m,2H); 7.5 (m,2H)
552		1.3 (s,9H); 2.1 (m,2H); 2.8 (m,2H); 2.9 (m,2H); 3.3 (s,2H); 3.8 (s,2H); 3.9 (t,2H); 4.1 (b,2H); 5.1 (s,1H); 5.2 (s,1H); 6.2 (d,1H); 6.5 (d,1H); 7.8 (d,1H); 8.2 (d,1H)
553	Hydro-chloride	1.3 (s,9H); 2.2-2.3 (b,1H); 2.5-2.7 (b,1H); 3.1 (s,3H); 3.0-3.2 (b,2H); 3.5-3.7 (b,3H); 3.8-4.1 (m,6H); 4.4-4.5 (b,1H); 5.4 (d,2H); 6.8 (d,1H); 8.3 (d,1H); 11.2 (b,1H); 11.9 (s,1H)
554		1.3 (s,9H); 1.9 (m,2H); 2.6 (t,2H); 2.7 (t,2H); 3.2 (s,2H); 3.4 (s,3H); 3.7 (s,2H); 3.8 (m,4H); 4.4 (s,2H); 5.0 (s,2H); 6.5 (d,1H); 8.2 (d,1H)
555		1.3 (s,18H); 2.1 (m,2H); 2.8 (t,2H); 3.0 (t,2H); 3.3 (s,2H); 3.8 (s,2H); 3.9 (t,2H); 4.1 (t,2H); 5.1 (s,1H); 5.2 (s,1H); 6.2 (d,1H); 6.5 (s,1H); 7.8 (d,1H)

556		1.3 (s,18H); 1.9 (m,2H); 2.6 (t,2H); 2.7 (t,2H); 3.2 (s,2H); 3.4 (s,3H); 3.6 (s,2H); 3.9 (m,4H); 4.2 (s,2H); 5.0 (s,2H); 6.5 (s,1H)
557	Hydro-chloride	1.3 (d,6H); 2.2 (b,1H); 2.6 (b,1H); 3.0 (b,4H); 3.4 (s,3H); 3.5-3.7 (b,4H); 3.8 (s,2H); 4.1 (s,2H); 5.4 (s,2H); 6.8 (t,1H); 6.9 (s,1H); 8.5 (b,2H); 11.6 (b,1H);
559	Hydro-chloride	1.2 (d,6H); 2.1 (b,4H); 3.0-3.2 (b,8H); 3.5-4.2 (b,4H); 6.1 (d,1H); 6.8 (t,1H); 6.9 (b,1H); 7.8 (d,1H); 11.3 (b,1H);
561		1.3 (s,18H); 1.9 (m,2H); 2.0 (m,2H); 2.7 (t,2H); 2.8 (t,2H); 3.0 (t,2H); 3.2 (t,2H); 3.9 (t,2H); 4.0 (t,2H); 6.1 (d,1H); 6.5 (s,1H); 7.8 (d,1H)
562		1.3 (s,18H); 1.9 (m,4H); 2.6 (m,4H); 2.8 (t,2H); 3.0 (t,2H); 3.4 (s,3H); 3.8 (t,2H); 3.9 (t,2H); 4.3 (s,2H); 6.5 (s,1H)
564	Oxalate	1.3 (s,9H); 2.0 (b,2H); 2.2 (b,2H); 3.1-3.4 (b,8H); 3.3 (b,2H); 3.8 (s,3H); 4.0 (b,2H); 6.1 (d,2H); 6.9 (s,1H); 7.0 (d,1H); 7.8 (d,1H); 8.1 (d,1H);
563	Oxalate	1.3 (s,9H); 1.9 (b,2H); 2.2 (b,2H); 2.9 (t,2H); 3.1 (t,2H); 3.3 (b,4H); 3.4 (s,3H); 3.7 (b,2H); 3.8 (s,3H); 4.0 (b,2H); 5.3 (b,2H); 6.8 (s,1H); 6.9 (d,1H); 8.0 (d,1H);

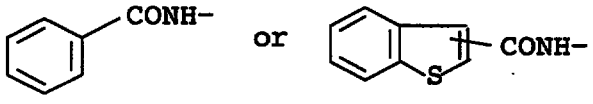
566		1.4 (s,9H); 1.9 (b,2H); 2.5 (b,2H); 2.8 (b,2H); 3.2 (s,2H); 3.3 (s,3H); 3.6 (s,2H); 3.6-3.8 (b,4H); 3.8 (s,3H); 4.8 (b,2H); 5.0 (s,2H); 6.5 (s,1H); 7.0 (d,1H); 8.0 (d,1H);
567	Oxalate	2.0 (b,2H); 2.8 (b,2H); 3.0 (b,2H); 3.3 (s,3H); 3.4 (s,2H); 3.6 (b,4H); 3.8 (b,2H); 5.1 (s,2H); 5.5 (b,2H); 7.0 (m,2H); 7.7 (t,1H);
568	Oxalate	2.0 (b,2H); 2.2 (b,2H); 3.0 (t,2H); 3.1 (m,2H); 3.2 (b,4H); 3.4 (s,3H); 3.6 (m,2H); 3.9 (b,2H); 6.7 (b,2H); 7.0 (t,2H); 7.7 (t,1H);
569	Oxalate	2.0-2.2 (b,4H); 3.0-3.4 (m,8H); 3.5 (m,2H); 3.9 (b,2H); 6.1 (d,1H); 6.5 (b,2H); 7.0 (t,2H); 7.7 (t,1H); 7.8 (d,1H);
570	Hydro-chloride	1.3 (s,9H); 2.0-2.2 (b,3H); 2.3-2.4 (b,1H); 3.2 (m, 6H); 3.4-4.0 (b,5H); 4.3-4.5 (b,1H); 6.2 (d,1H); 6.8 (d,1H); 7.9 (d,1H); 8.3 (d,1H); 10.8 (b,1H)
571	Hydro-chloride	1.3 (s,9H); 2.0-2.2 (b,3H); 2.3-2.4 (b,1H); 3.1 (s,3H); 3.0-3.2 (m,6H); 3.4-4.0 (b,5H); 4.3-4.5 (b,1H); 6.8 (d,1H); 8.3 (d,1H); 10.9 (b,1H); 11.9 (s,1H)
572		1.3 (s,9H); 1.9-2.0 (m,4H); 2.6 (m,4H); 2.8 (t,2H); 3.0 (t,2H); 3.4 (s,3H); 3.8 (t,2H); 3.9 (b,2H); 4.6 (b,2H); 6.5 (d,1H); 8.2 (d,1H)

We claim:

1. A compound of the formula I

$$Ar^1\text{-}A\text{-}B\text{-}Ar^2 \qquad (I)$$

where
Ar^1 is



or a 5- or 6-membered heteroaromatic ring with 1, 2 or 3 heteroatoms which are selected, independently of one another, from O, N and S, where Ar^1 may have 1, 2, 3 or 4 substituents which are selected, independently of one another, from OR^1, alkyl which is unsubstituted or substituted by OH, OC_1-C_8-alkyl or halogen, or C_2-C_6-alkenyl, C_2-C_6-alkynyl, cycloalkyl, halogen, CN, CO_2R^1, NO_2, NR^1R^2, SR^1, CF_3, CHF_2, phenyl which is unsubstituted or substituted by C_1-C_6-alkyl, OC_1-C_6-alkyl, acyl, phenyl, amino, nitro, cyano or halogen, or phenoxy which is unsubstituted or substituted by C_1-C_6-alkyl, OC_1-C_6-alkyl or halogen, or C_1-C_6-alkanoyl or benzoyl;

R^1 is H, alkyl which is unsubstituted or substituted by OH, OC_1-C_6-alkyl, phenyl or halogen;

R^2 has the meanings stated for R^1 or is COR^1 or CO_2R^1;

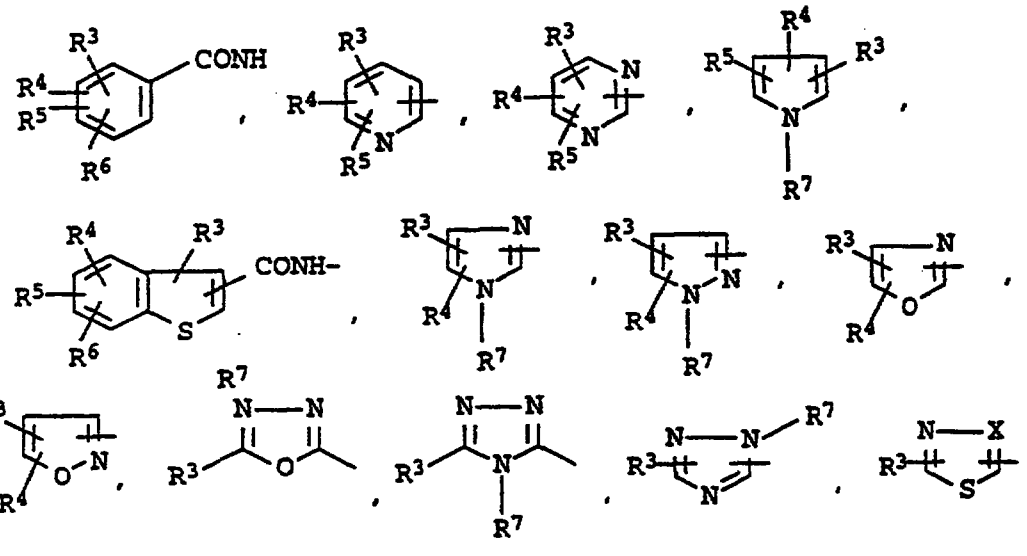
A is a C_3-C_{15}-alkylene group when Ar^1 is C_6H_5CONH, or, when Ar^1 is a 5- or 6-membered heteroaromatic ring, is a C_4-C_{15}-alkylene group or a C_3-C_{15}-alkylene group which comprises at least one group Z which is selected from O, S, NR^1, a double and a triple bond, where R^1 is as defined above,

B is a 7- or 8-membered saturated ring with one or two nitrogen heteroatoms, the nitrogen heteroatoms being located in the 1,4 or 1,5 position and the ring being bonded in position 1 to the radical A and in position 4 or 5 to the radical Ar^2, and it additionally being possible for the ring to have a double bond in position 3 or 4;

Ar^2 is phenyl, pyridyl, pyrimidinyl or triazinyl, it being possible for Ar^2 to have 1, 2, 3 or 4 substituents which are selected, independently of one another, from OR^1, alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, alkoxyalkyl, haloalkyl, halogen, CN, CO_2R^1, NO_2, SO_2R^1, NR^1R^2, $SO_2NR^1R^2$, SR^1, a 5- or 6-membered carbocyclic, aromatic or non-aromatic ring and a 5- or 6-membered heterocyclic aromatic or non-aromatic ring with 1 to 3 heteroatoms which are selected from O, S and N, the carbocyclic or heterocyclic ring being unsubstituted or substituted by C_1-C_8-alkyl, phenyl, halogen, OC_1-C_8-alkyl, OH, NO_2 or CF_3, where Ar^2 may also be fused to a carbocyclic ring of the type defined above, and where Ar^2 cannot be a pyrimidinyl radical substituted by 2 hydroxyl groups,

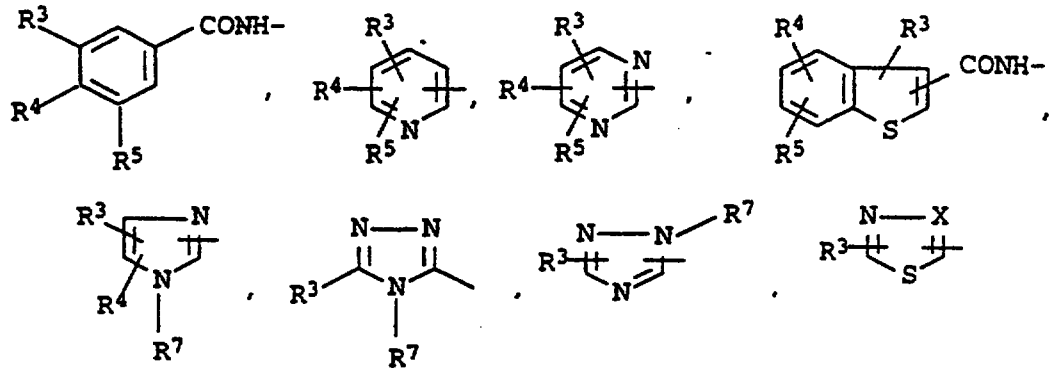
and the salts thereof with physiologically tolerated acids.

2. A compound as claimed in claim 1 of the formula I where Ar^1 is



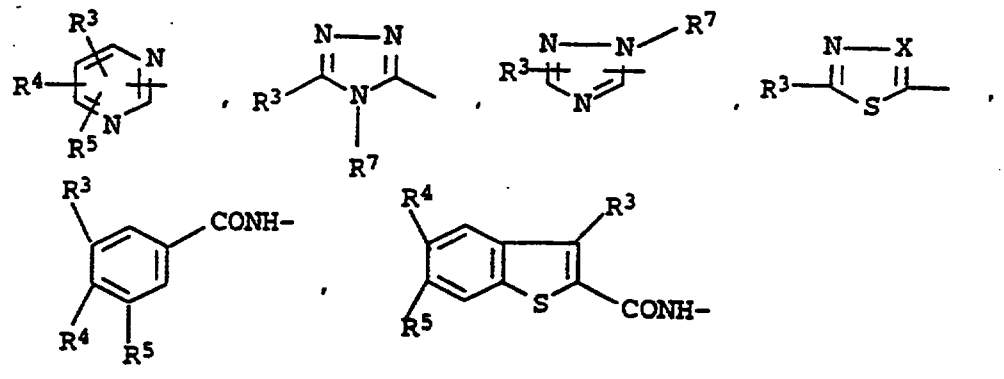
where
R^3 to R^6 are, independently of one another, H or the substituents mentioned in claim 1 for the radical Ar^1,
R^7 has the meanings stated for R^2 in claim 1 or is cycloalkyl, and
X is N or CH.

3. A compound as claimed in claim 1 of the formula I where Ar^1 is



where R^3 to R^5, R^7 and X have the meanings stated in claim 2.

4. A compound as claimed in claim 3 of the formula I where Ar^1 is



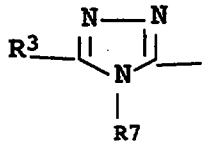
where R^3 to R^5, R^7 and X have the meanings stated in claim 2.

5. A compound as claimed in claim 4 of the formula I where R^3, R^4 and R^5 are, independently of one another, H, OR^1, alkyl, NR^1R^2, halogen, phenoxy, CN, phenyl which is unsubstituted or substituted by C_1-C_6-alkyl, acyl or halogen, or $COOR^1$;
R^1 and R^2 are, independently of one another, H, alkyl or benzyl;
R^7 is H, alkyl or cycloalkyl; and
X is N or CH.

6. A compound as claimed in claim 5, where R^3 to R^6 are selected, independently of one another, from H, C_1-C_6-alkyl, OR^1, NR^1R^2, phenyl which is unsubstituted or substituted by C_1-C_6-alkyl, acyl or halogen, and halogen, where R^1 and R^2 have the abovementioned meanings, R^7 is H or alkyl, and X is N.

7. A compound as claimed in claim 6, where Ar^1 is pyrimidinyl which is unsubstituted or substituted by OH, Oalkyl or Obenzyl.

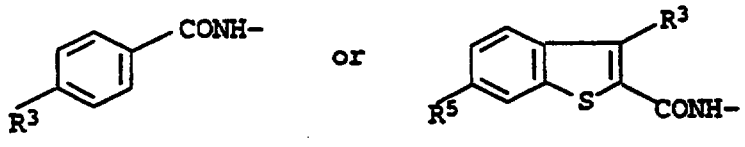
8. A compound as claimed in claim 6, where Ar^1 is



where R^3 is NR^1R^2, where R^1 and R^2 have the meanings stated in claim 5, and R^7 is H or alkyl.

9. A compound as claimed in claim 6, where Ar^1 is thiadiazole which is unsubstituted or substituted by NR^1R^2, where R^1 and R^2 have the meanings stated in claim 5.

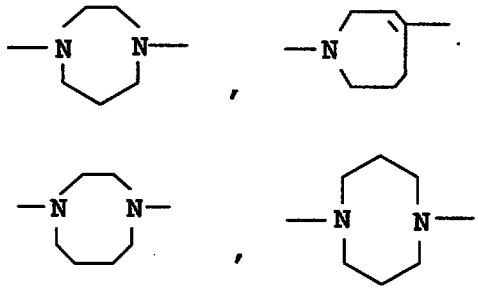
10. A compound as claimed in claim 6, where Ar^1 is



where R^3 and R^5 are, independently of one another, H or halogen, alkyl or phenyl.

11. A compound as claimed in any of the preceding claims of the formula I, where A is $-Z-C_3-C_6$-alkylene, in particular $-Z-CH_2CH_2CH_2-$, $-Z-CH_2CH_2CH_2CH_2-$, $-Z-CH_2CH=CHCH_2-$, $-Z-CH_2C(CH_3)=CHCH_2-$, $-Z-CH_2C(=CH_2)CH_2-$, $-Z-CH_2CH(CH_3)CH_2-$ or a linear $-Z-C_7-C_{10}$-alkylene radical, where Z is bonded to Ar^1 and is CH_2, O or S.

12. A compound as claimed in any of the preceding claims of the formula I, where B is



13. A compound as claimed in any of the preceding claims of the formula I, where Ar^2 is phenyl, pyridinyl or pyrimidinyl, which may have one or two substituents which are selected, independently of one another, from C_1-C_6-alkyl, C_2-C_6-alkynyl, halogen, CN, haloalkyl,Oalkyl, NO_2, phenyl, pyrrolyl, imidazolyl, pyrazolyl, thienyl, cyclopentyl and cyclohexyl.

14. A compound as claimed in claim 13 of the formula I, where the substituent(s) are selected, independently of one another, from C_1-C_6-alkyl, NO_2 and haloalkyl, in particular CF_3, CHF_2 and CF_2Cl.

15. A pharmaceutical composition comprising at least one compound as claimed in any of claims 1 to 15 [sic], with or without physiologically acceptable vehicles and/or ancillary substances.

16. The use of at least one compound as claimed in any of claims 1 to 15 for producing a pharmaceutical composition for the treatment of disorders which respond to dopamine D_3 receptor antagonists or agonists.