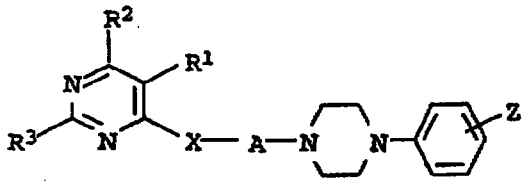
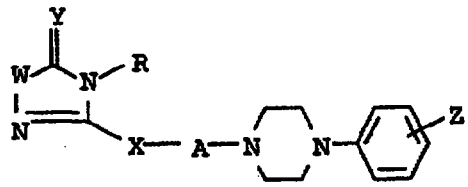
SUBSTITUIERTE AZA- UND DIAZACYCLOHEPTAN- UND -CYCLOOCTANVERBINDUNGEN UND DEREN VERWENDUNG

Die Erfindung betrifft substituierte Aza- und Diazacycloheptan- und -cyclooctanverbindungen und die Verwendung derartiger Verbindungen. Die erwähnten Verbindungen besitzen wertvolle therapeutische Eigenschaften und sind insbesondere zur Behandlung von Erkrankungen brauchbar, die auf Dopamin-D_3-Liganden ansprechen.

Verbindungen der hier in Rede stehenden Art mit physiologischer Aktivität sind bereits teilweise bekannt. So beschreiben DE 21 39 082 und DE 22 58 561 basisch substituierte Pyrimidinderivate bzw. Pyrimidonderivate als Arzneimittel zur Senkung des Blutdrucks. Diese Pyrimidin- bzw. Pyrimidonderivate besitzen die Formeln:



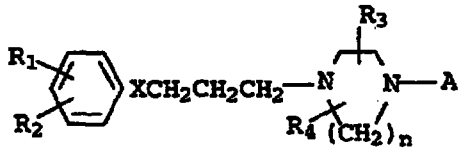
(A)



(B)

worin in (A) X unter anderem ein Schwefelatom bedeutet, A eine C_1-C_6-Alkylengruppe bedeutet und R^1, R^2, R^3 und Z für verschiedene Substituenten stehen. In (B) stehen X und Y für ein Sauerstoff- oder Schwefelatom, A für eine C_2-C_6-Alkylengruppe, W für eine Vinylengruppe und R und Z für verschiedene Substituenten.

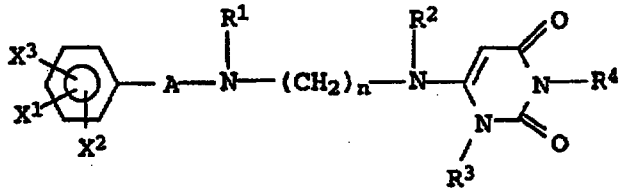
Die EP-A-361271 beschreibt Pyridyl- und Pyrimidylderivate der Formel:



worin R_1 für Halogen oder Wasserstoff steht und R_2 für Halogen steht; X für Sauerstoff, Schwefel oder Methylen steht; R_3 und R_4, die gleich oder verschieden sind, für Wasserstoff oder Niedrigalkyl stehen; n für 2 oder 3 steht; A für eine 2-Pyrimidylgruppe oder eine 2- oder 3-Pyridylgruppe steht, wobei diese Gruppen substituiert sein können.

Diese Verbindungen sind zur Behandlung von mentalen Störungen brauchbar.

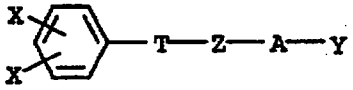
Die EP-A-454498 beschreibt Verbindungen der Formel



worin A unter anderem für $-(CH_2)_m-$ oder $-B-(CH_2)_k-$ steht, wobei B für O, S, eine gegebenenfalls substituierte Aminogruppe, -CONH- oder -COO- steht, R^1 und R^2 unter anderem zusammen eine Alkylenkette bilden können, R^3 und R^4 ein Wasserstoffatom oder eine Niedrigalkylgruppe bedeuten und X^1, X^2 und X^3 verschiedene Substituenten bedeuten. Diese Verbindungen sind zur Behandlung von Herzarrhythmien brauchbar.

Die EP-A-452107 und EP-A-369627 beschreiben strukturell ähnliche Verbindungen, die ebenfalls zur Behandlung von Herzarrhythmien brauchbar sind.

Außerdem beschreibt die BE-A-628 766 Verbindungen der Formel



worin X ein Halogenatom oder einen Niedrigalkylrest bedeutet, T für Piperazin, Methylpiperazin, Homopiperazin oder Methylhomopiperazin steht; Z für Alkylen oder Alkenylen steht; A für O oder S steht; und Y für einen Naphthyl-, Halogennaphthyl oder einen gegebenenfalls mit 1 bis 3 Resten substituierten Phenylrest steht. Diese Verbindungen sind zur Behandlung von Schistosomiasis brauchbar.

Neuronen erhalten ihre Informationen unter anderem über G-Protein-gekoppelte Rezeptoren. Es gibt zahlreiche Substanzen, welche ihre Wirkung über diese Rezeptoren ausüben. Eine davon ist Dopamin.

Es liegen gesicherte Erkenntnisse über die Anwesenheit von Dopamin und dessen physiologische Funktion als Neurotransmitter vor. Auf Dopamin ansprechende Zellen stehen im Zusammenhang mit der

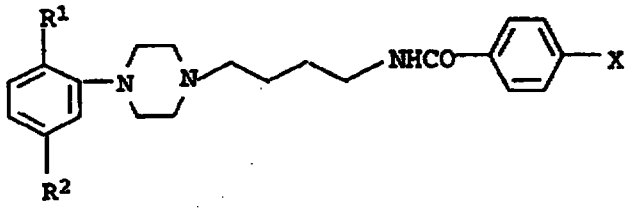
Etiologie von Schizophrenie und der Parkinson'schen Krankheit. Die Behandlung dieser und anderer Erkrankungen erfolgt mit Arzneimitteln, die mit den Dopaminrezeptoren in Wechselwirkung treten.

Bis 1990 waren zwei Subtypen von Dopaminrezeptoren pharmakologisch klar definiert, nämlich die D_1 und D_2-Rezeptoren.

In jüngerer Zeit wurde ein dritter Subtyp gefunden, nämlich der D_3-Rezeptor, der einige Effekte der Antipsychotika zu vermitteln scheint. (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, Seiten 135-144)

D_3-Rezeptoren werden hauptsächlich im limbischen System exprimiert. Es wird daher angenommen, daß ein selektiver D_3-Antagonist wohl die antipsychotischen Eigenschaften der D_2-Antagonisten, nicht aber ihre neurologischen Nebenwirkungen haben sollte. (P. Solokoff et al., Localization and Function of the D_3 Dopamine Receptor, Arzneim. Forsch./Drug Res. 42(1), 224 (1992); P. Solokoff 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), beschreiben bereits Arylpiperazine der Formel



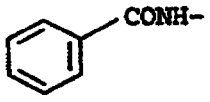
worin R^1 und R^2 für H oder CH_3O stehen und X für Br, 4-Acetylphenyl, 4-Methylsulfonylphenyl oder 4-Aminophenyl steht, mit hoher Affinität und Selektivität gegenüber dem Dopamin D_3-Rezeptor.

Überraschenderweise wurde nun gefunden, daß bestimmte Aza- und Diazacycloheptan- und -cyclooctanverbindungen eine hohe Affinität zum Dopamin-D_3-Rezeptor und eine geringe Affinität zum D_2-Rezeptor aufweisen. Es handelt sich somit um selektive D_3-Liganden.

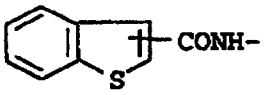
Gegenstand der vorliegenden Erfindung sind daher die Verbindungen der allgemeinen Formel I:

$Ar^1-A-B-Ar^2$ (I)

worin
Ar^1 für



oder



oder einen 5- oder 6-gliedrigen aromatischen Heteromonocyclus mit 1, 2 oder 3 Heteroatomen, die unabhängig voneinander ausgewählt sind unter O, N und S steht, wobei Ar^1 gegebenenfalls 1, 2, 3 oder 4 Substituenten aufweist, die unabhängig voneinander ausgewählt sind unter OR^1, Alkyl, das gegebenenfalls durch OH, OC_1-C_8-Alkyl oder Halogen substituiert ist, C_2-C_6-Alkenyl, C_2-C_6-Alkinyl, Cycloalkyl, Halogen, CN, CO_2R^1, NO_2, NR^1R^2, SR^1, CF_3, CHF_2, Phenyl, das gegebenenfalls durch C_1-C_6-Alkyl, OC_1-C_6-Alkyl, Acyl, Phenyl, Amino, Nitro, Cyano oder Halogen substituiert ist, Phenoxy, das gegebenenfalls durch C_1-C_6-Alkyl, OC_1-C_6-Alkyl oder Halogen substituiert ist, C_1-C_6-Alkanoyl oder Benzoyl;

R^1 für H, Alkyl, das gegebenenfalls durch OH, OC_1-C_6-Alkyl, Phenyl oder Halogen substituiert ist, steht;

R^2 die für R^1 angegebenen Bedeutungen besitzt oder für COR^1 oder CO_2R^1 steht;

A für eine C_3-C_{15}-Alkylengruppe steht, wenn Ar^1 für C_6H_5CONH steht, oder, wenn Ar^1 einen 5- oder 6-gliedrigen aromatischen Heteromonocyclus bedeutet, für eine C_4-C_{15}-Alkylengruppe oder eine C_3-C_{15}-Alkylengruppe steht, die wenigstens eine Gruppe Z umfaßt, die ausgewählt ist unter O, S, NR^1, einer Doppel- und einer Dreifachbindung, wobei R^1 wie oben definiert ist,

B für einen 7- oder 8-gliedrigen gesättigten Ring mit einem oder zwei Stickstoffheteroatomen steht, wobei sich die Stickstoffheteroatome in 1,4- oder 1,5-Position befinden und der Ring in 1-Position an den Rest A und in 4- oder 5-Position an den Rest Ar^2 gebunden ist und wobei der Ring außerdem eine Doppelbindung in 3- oder 4-Position im Monoazacyclus und in 6-Position im 1,4-Diazacyclus aufweisen kann;

Ar^2 für Phenyl, Pyridyl, Pyrimidinyl oder Triazinyl steht, wobei Ar^2 gegebenenfalls 1, 2, 3 oder 4 Substituenten aufweisen kann, die unabhängig voneinander ausgewählt sind unter OR^1, Alkyl, C_2-C_6-Alkenyl, C_2-C_6-Alkinyl, Alkoxyalkyl, Halogenalkyl, Halogen, CN, CO_2R^1, NO_2, SO_2R^1, NR^1R^2, $SO_2NR^1R^2$, SR^1, einem 5- oder 6-gliedrigen carbocyclischen, aromatischen oder nicht-aromatischen Ring und einem 5- oder 6-gliedrigen heterocyclischen aromatischen oder

nicht-aromatischen Ring mit 1 bis 3 Heteroatomen, die ausgewählt sind unter O, S und N, wobei der carbocyclische oder der heterocyclische Ring gegebenenfalls substituiert ist durch C_1-C_8-Alkyl, Phenyl, Phenoxy, Halogen, OC_1-C_8-Alkyl, OH, NO_2 oder CF_3, wobei R^1 und R^2 die oben angegebenen Bedeutungen besitzen und Ar^2 gegebenenfalls auch mit einem carbocyclischen Ring der oben definierten Art kondensiert sein kann und wobei Ar^2 nicht für einen Pyrimidinylrest stehen kann, der mit 2 Hydroxygruppen substituiert ist, und die Salze davon mit physiologisch verträglichen Säuren.

Bei den erfindungsgemäßen Verbindungen handelt es sich um selektive Dopamin-D_3-Rezeptor-Liganden, die regioselektiv im limbischen System angreifen und aufgrund ihrer geringen Affinität zum D_2-Rezeptor nebenwirkungsärmer als die klassischen Neuroleptika sind, bei denen es sich um D_2-Rezeptorantagonisten handelt. Die Verbindungen sind daher zur Behandlung von Erkrankungen brauchbar, die auf Dopamin-D_3-Rezeptorantagonisten bzw. -agonisten ansprechen, z.B. zur Behandlung von Erkrankungen des zentralen Nervensystems insbesondere Schizophrenie, Depressionen, Neurosen und Psychosen.

Im Rahmen der vorliegenden Erfindung besitzen die nachfolgenden Ausdrücke die anschließend angegebenen Bedeutungen:

Alkyl (auch in Resten wie Alkoxy, Alkylamino etc) bedeutet eine geradkettige oder verzweigte Alkylgruppe mit 1 bis 8 Kohlenstoffatomen, vorzugsweise 1 bis 6 Kohlenstoffatomen und insbesondere 1 bis 4 Kohlenstoffatomen. Die Alkylgruppe kann einen oder mehrere Substituenten aufweisen, die unabhängig voneinander ausgewählt sind unter OH und OC_1-C_8-Alkyl.

Beispiele für eine Alkylgruppe sind Methyl, Ethyl, n-Propyl, i-Propyl, n-Butyl, iso-Butyl, t-Butyl, etc.

Cycloalkyl steht insbesondere für C_3-C_6-Cycloalkyl, wie Cyclopropyl, Cyclobutyl, Cyclopentyl und Cyclohexyl.

Alkylen steht für geradkettige oder verzweigte Reste mit vorzugsweise 4 bis 15 Kohlenstoffatomen, besonders bevorzugt 4 bis 10 Kohlenstoffatomen, bzw. mit 3 bis 15, insbesondere 3 bis 10 Kohlenstoffatomen, wenn die Alkylengruppe eine der genannten Gruppen umfaßt.

Die Alkylengruppen können gegebenenfalls wenigstens eine der oben bei der Definition von A angegebenen Gruppen Z umfassen. Diese kann - ebenso wie die erwähnte Doppel- oder Dreifachbindung - in der Alkylenkette an beliebiger Stelle oder in Position 1 oder 2 der Gruppe A (vom Rest Ar^1 her gesehen) angeordnet sein. Besonders

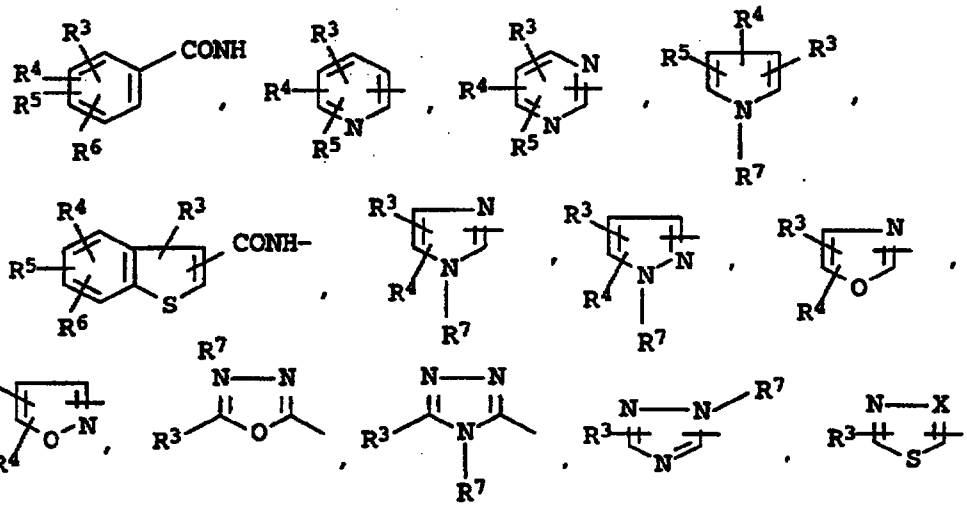
bevorzugt steht A für Verbindungen nach der Formel I, worin A für -Z-C_3-C_6-Alkylen, insbesondere -Z-$CH_2CH_2CH_2$-, -Z-$CH_2CH_2CH_2CH_2$-, -Z-CH_2CH=$CHCH_2$-, -Z-$CH_2C(CH_3)$=$CHCH_2$-, -Z-$CH_2C(=CH_2)CH_2$-, -Z-$CH_2CH(CH_3)CH_2$- oder für einen linearen -Z-C_7-C_{10}-Alkylenrest steht. Dabei steht A besonders bevorzugt für -Z-C_3-C_6-Alkylen, wenn Ar^1 für einen gegebenenfalls substituierten Pyrimidin- oder Triazolrest steht und für einen linearen -Z-C_7-C_{10}-Alkylenrest, wenn Ar^1 für einen gegebenenfalls substituierten Thiadiazolrest steht. Z kann dabei auch CH_2 bedeuten und steht vorzugsweise für CH_2, O und insbesondere S.

Halogen bedeutet F, Cl, Br oder I.

Halogenalkyl kann ein oder mehrere, insbesondere 1, 2 oder 3 Halogenatome umfassen, die sich an einem oder mehreren C-Atomen befinden können, vorzugsweise in α- oder ω-Position. Besonders bevorzugt sind CF_3, CHF_2, CF_2Cl oder CH_2F.

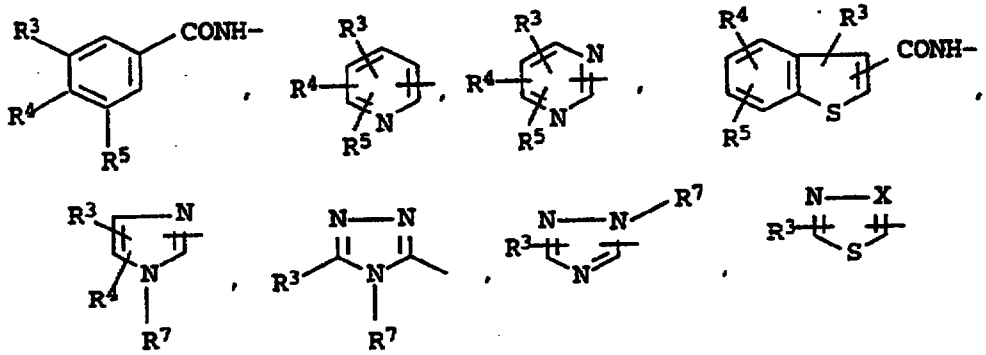
Acyl steht vorzugsweise für HCO oder C_1-C_6-Alkyl-CO, insbesondere Acetyl.
Wenn Ar^1 substituiert ist, kann sich der Substituent auch an dem Stickstoffheteroatom befinden.

Vorzugsweise steht Ar^1 für

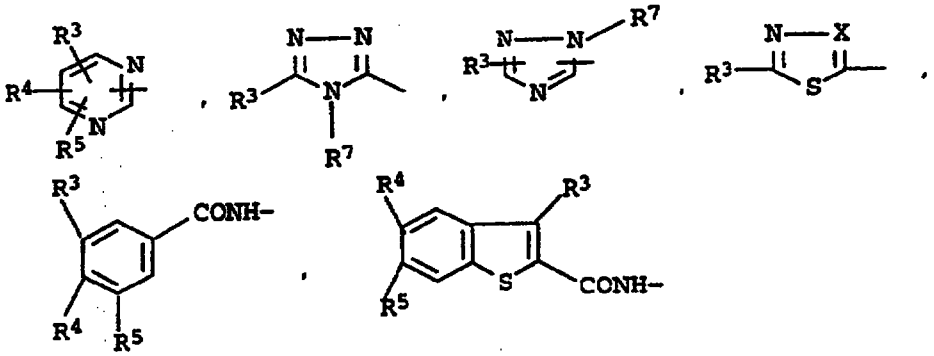


worin
R^3 bis R^6 für H oder die oben genannten Substituenten des Restes Ar^1 stehen,
R^7 die oben für R^2 angegebenen Bedeutungen besitzt und
X für N oder CH steht. Wenn der Benzamidrest substituiert ist, stehen die Substituenten vorzugsweise in m- oder p-Stellung.

Besonders bevorzugt steht Ar^1 für



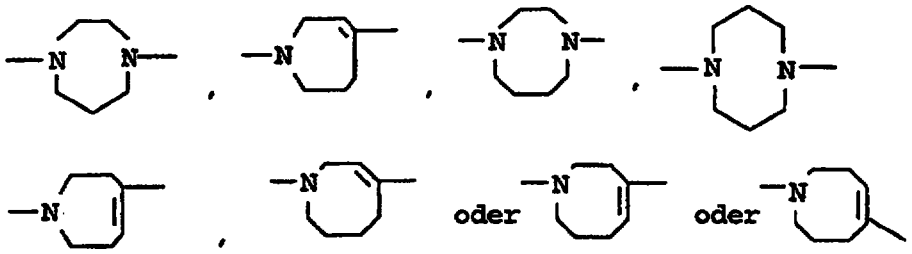
worin R^3 bis R^5, R^7 und X die oben angegebenen Bedeutungen besitzen und insbesondere für



worin R^3 bis R^5, R^7 und X die oben angegebenen Bedeutungen besitzen.

Die Reste R^3 bis R^6 stehen vorzugsweise für H, C_1-C_6-Alkyl, OR^1, NR^1R^2, SR^1, Phenyl, das gegebenenfalls durch C_1-C_6-Alkyl, Acyl oder Halogen substitutiert ist, und Halogen, wobei R^1 und R^2 die oben angegebenen Bedeutungen besitzen.

Der Rest B steht vorzugsweise für



Der Rest Ar^2 kann einen, zwei, drei oder vier Substituenten, vorzugsweise einen oder zwei Substituenten, die sich insbesondere in m-Stellung und/oder p-Stellung befinden, aufweisen. Vorzugsweise sind sie unabhängig voneinander ausgewählt unter C_1-C_6-Alkyl, Halogenalkyl, NO_2, Halogen, insbesondere Chlor, Phenyl, Pyrrolyl, Imidazolyl, Pyrazolyl, Thienyl, Cyclopentyl und Cyclohexyl. Wenn

einer der Substituenten für C_1-C_8-Alkyl steht, ist eine verzweigte Gruppe und insbesondere Isopropyl oder t-Butyl bevorzugt.

Vorzugsweise steht Ar^2 für gegebenenfalls substituiertes Phenyl, 2-, 3- oder 4-Pyridinyl oder 2-, 4(6)- oder 5- Pyrimidinyl.

Wenn einer der Substituenten des Restes Ar^2 für einen 5- oder 6-gliedrigen heterocyclischen Ring steht, so handelt es sich beispielsweise um einen Pyrrolidin-, Piperidin-, Morpholin-, Piperazin-, Pyridin-, 1,4-Dihydropyridin-, Pyrimidin-, Triazin-, Pyrrol-, Thiophen-, Thiazol-, Imidazol-, Oxazol-, Isoxazol-, Pyrazol-, oder Thiadiazolrest, wobei ein Pyrrol-, Imidazol-, Pyrazol- oder Thienylrest bevorzugt ist.

Wenn einer der Substituenten des Restes Ar^2 für einen carbocyclischen Rest steht, handelt es sich insbesondere um einen Phenyl-, Cyclopentyl- oder Cyclohexylrest.

Wenn Ar^2 mit einem carbocyclischen Rest kondensiert ist, handelt es sich insbesondere um einen Naphthalin-, Di- oder Tetrahydronaphthalinrest.

Die Erfindung umfaßt auch die Säureadditionssalze der Verbindungen der Formel I, mit physiologisch verträglichen Säuren. Als physiologisch verträgliche organische und anorganische Säuren kommen beispielsweise Salzsäure, Bromwasserstoffsäure, Phosphorsäure, Schwefelsäure, Oxalsäure, Maleinsäure, Fumarsäure, Milchsäure, Weinsäure, Adipinsäure oder Benzoesäure in Betracht. Weitere brauchbare Säuren sind in Fortschritte der Arzneimittelforschung, Band 10, Seiten 224 ff, Birkhäuser Verlag, Basel und Stuttgart, 1966, beschrieben.

Die Verbindungen der Formel I können ein oder mehrere Asymmetriezentren aufweisen. Zur Erfindung zählen daher nicht nur die Racemate, sondern auch die betreffenden Enantiomere und Diastereomere. Auch die jeweiligen tautomeren Formen zählen zur Erfindung.

Das Verfahren zur Herstellung der Verbindungen (I) besteht darin, daß man

a) eine Verbindung der allgemeinen Formel II

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

worin Y^1 für eine übliche Abgangsgruppe wie beispielsweise Hal, Alkansulfonyloxy, Arylsulfonyloxy etc. steht, und Z die oben genannten Bedeutungen besitzt,
mit einer Verbindung der allgemeinen Formel (III)

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

umsetzt; oder

b) eine Verbindung der allgemeinen Formel (IV)

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

worin Z^1 für O, NR^1 oder S und A^1 für C_1-C_{15}-Alkylen oder eine Bindung steht, mit einer Verbindung der allgemeinen Formel V

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

wobei Y^1 die oben angegebene Bedeutung besitzt und A^2 für C_2-C_{15}-Alkylen steht, wobei A^1 und A^2 zusammen 3 bis 15 C-Atome aufweisen,

umsetzt; oder

c) eine Verbindung der allgemeinen Formel (VI)

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

worin Y^1 die oben angegebene Bedeutung besitzt, mit einer Verbindung der allgemeinen Formel VII

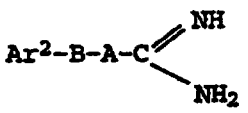
$$H - Z^1 - A - B - Ar^2 \quad (VII)$$

worin Z^1 die oben angegebenen Bedeutungen besitzt, umsetzt; oder

d) eine Verbindung der Formel (VIII)

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

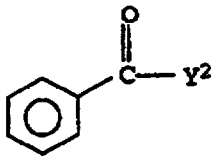
in eine Verbindung des Typs (IX)



(IX)

überführt,
und diese mit einer Dicarbonyl-Verbindung in bekannter Weise umsetzt; oder

e) zur Herstellung einer Verbindung der Formel I, worin Ar^1 für einen Benzamidrest steht:
eine Verbindung der allgemeinen Formel (X)



(X)

worin Y^2 für OH, OC_1-C_4-Alkyl, Cl oder zusammen mit CO für eine aktivierte Estergruppe steht, mit einer Verbindung der Formel (XI)

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

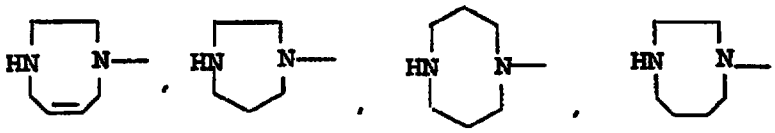
worin A^2 die oben angegebenen Bedeutungen besitzt und Z^2 für OH oder NH_2 steht, umsetzt.

Die Verbindungen der Formel III sind Ausgangsverbindungen zur Herstellung von Verbindungen der Formeln V, VII, VIII und werden hergestellt, indem man

a) eine Verbindung der allgemeinen Formel (XII)

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

worin B^1 für



mit einer Verbindung der allgemeinen Formel (XIII)

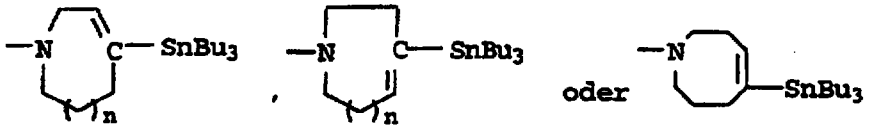
$$Y^1 - Ar^2 \quad (XIII)$$

worin Y^1 für eine der vorstehend erwähnten Abgangsgruppen und Ar^2 die oben angegebenen Bedeutung besitzt,
in bekannter Weise umsetzt; oder

b) eine Verbindung der allgemeinen Formel (XIV)

$$H - B^2$$

worin B^2 für

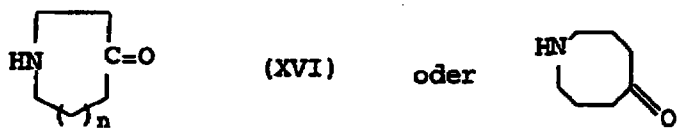


mit n = 1, oder 2 steht,
mit einer Verbindung der allgemeinen Formel (XV)

$$Y^2 - Ar^2$$

worin Y^2 für Br, Cl, I steht und Ar^2 obige Bedeutungen besitzt, nach bekannten Verfahren umsetzt, wie beschrieben z.B. von S.C. Buchwald et al., Angew. Chem. 1995, 107, 1456 oder J.F. Hartweg et al., Tetrahedron Lett 1995, 36, 3604 bzw. J.K. Stille et al., Angew. Chem. 1986, 98, 504 oder Pereyre M. et al., Tin in Organic Synthesis, Butterworth 1987; oder

c) eine Verbindung der allgemeinen Formel (XVI)



(XVI)

wobei n = 1 oder 2,
mit einer Verbindung M-Ar^2, worin M für ein Metall wie z.B. Li, MgY^2 steht, umsetzt. MAr^2 kann erhalten werden aus Verbindungen der Formel XV nach literaturbekannten Methoden.

Verbindungen des Typs Ar^1 sowie Ar^2 sind entweder bekannt oder können nach bekannten Verfahren hergestellt werden wie z.B. beschrieben in A.R. Katritzky, CW. Rees (ed.) "Comprehensive Heterocyclic Chemistry", Pergamon Press, oder "The Chemistry of Heterocyclic Compounds", J. Wiley & Sons Inc. NY und der dort zitierten Literatur.

Verbindungen des Typs B sind entweder bekannt oder sie können analog zu bekannten Verfahren hergestellt werden, wie z.B.

1,4- und 1,5-Diazacycloalkane: L. Börjeson et al. Acta Chem. Scand. 1991, 45, 621

	Majahrzah et al Acta Pol. Pharm., 1975, 32, 145
1,4-Diazacyclooct-6ene:	W. Schroth et al. Z. Chem. 1969, 9, 143
1-Azacyclooctanone:	N.J. Leonard et al. J. Org. Chem. 1964, 34, 1066
1-Azacyclo-heptanone:	A. Yokoo et al. Bull Chem. Soc. Jpn. 1956, 29, 631

Die Herstellung der erfindungsgemäßen Verbindungen und der Ausgangsmaterialien und Zwischenprodukte kann auch analog zu den in den eingangs genannten Patentpublikationen beschriebenen Methoden erfolgen.

Die oben beschriebenen Umsetzungen erfolgen im allgemeinen in einem Lösungsmittel bei Temperaturen zwischen Raumtemperatur und der Siedetemperatur des verwendeten Lösungsmittels. Brauchbare Lösungsmittel sind beispielsweise Ethylacetat, Tetrahydrofuran, Dimethylformamid, Dimethylsulfoxid, Dimethoxyethan, Toluol, Xylol, ein Keton, wie Aceton oder Methylethylketon oder ein Alkohol, wie Ethanol oder Butanol.

Gewünschtenfalls arbeitet man in Gegenwart eines säurebindenden Mittels. Geeignete säurebindende Mittel sind anorganische Basen, wie Natrium- oder Kaliumcarbonat, Natriummethylat, Natriumethylat, Natriumhydrid oder metallorganische Verbindungen wie Butyllithium oder Alkylmagnesium Verbindungen, oder organische Basen, wie Triethylamin oder Pyridin. Letztere können gleichzeitig als Lösungsmittel dienen.

Die Umsetzungen erfolgen gegebenenfalls unter Verwendung eines Katalysators, wie z.B. Übergangsmetalle und deren Komplexe, z.B. $Pd(PPh_3)_4$, $Pd(OAc)_2$ oder $Pd(P(oTol)_3)_4$, oder eines Phasen-Transfer-Katalysators, z.B. Tetrabutylammoniumchlorid oder Tetrapropylammoniumbromid.

Die Isolierung des Rohprodukts erfolgt in üblicher Weise, beispielsweise durch Filtration, Abdestillieren des Lösungsmittels oder Extraktion aus dem Reaktionsgemisch etc. Die Reinigung der erhaltenen Verbindungen kann in üblicher Weise erfolgen, beispielsweise durch Umkristallisieren aus einem Lösungsmittel, Chromatographie oder Überführen in eine Säureadditionsverbindung.

Die Säureadditionssalze werden in üblicher Weise durch Mischen der freien Base mit der entsprechenden Säure, gegebenenfalls in Lösung in einem organischen Lösungsmittel, beispielsweise einem niedrigen Alkohol, wie Methanol, Ethanol oder Propanol, einem

Ether, wie Methyl-t-butylether, einem Keton, wie Aceton oder Methylethylketon oder einem Ester, wie Essigsäureethylester, hergestellt.

Zur Behandlung der oben erwähnten Erkrankungen werden die erfindungsgemäßen Verbindungen in üblicher Weise oral oder parenteral (subkutan, intravenös, intramuskulär, intraperitoneal) verabreicht. Die Applikation kann auch mit Dämpfen oder Sprays durch den Nasen-Rachen-Raum erfolgen.

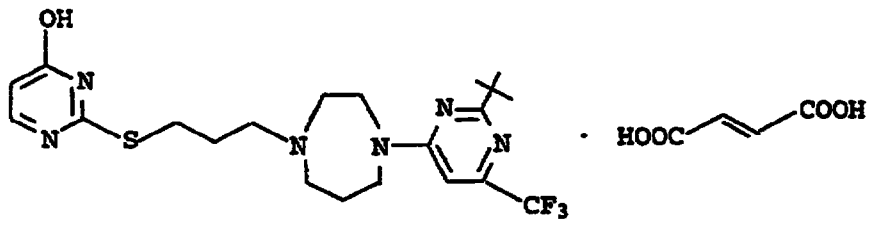
Die Dosierung hängt vom Alter, Zustand und Gewicht des Patienten sowie von der Applikationsart ab. In der Regel beträgt die tägliche Wirkstoffdosis etwa 10 bis 1000 mg pro Patient und Tag bei oraler Gabe und etwa 1 bis 500 mg pro Patient und Tag bei parenteraler Gabe.

Die Erfindung betrifft auch pharmazeutische Mittel, die die erfindungsgemäßen Verbindungen enthalten. Diese Mittel liegen in den üblichen galenischen Applikationsformen in fester oder flüssiger Form vor, beispielsweise als Tabletten, Filmtabletten, Kapseln, Pulver, Granulate, Dragees, Suppositorien, Lösungen oder Sprays. Die Wirkstoffe können dabei mit den üblichen galenischen Hilfsmitteln, wie Tablettenbindemitteln, Füllstoffen, Konservierungsmitteln, Tablettensprengmitteln, Fließregulierungsmitteln, Weichmachern, Netzmitteln, Dispergiermitteln, Emulgatoren, Lösungsmitteln, Retardierungsmitteln, Antioxidantien und/oder Treibgasen verarbeitet werden (vgl. H. Sucker et al., Pharmazeutische Technologie, Thieme-Verlag, Stuttgart, 1978). Die so erhaltenen Applikationsformen enthalten den Wirkstoff normalerweise in einer Menge von 1 bis 99 Gew.-%.

Die nachfolgenden Beispiele dienen zur Erläuterung der Erfindung ohne sie zu begrenzen.

Beispiel 1

1-[2-t-Butyl-6-trifluormethyl-pyrimidin-4-yl]-4-[3-[4-hydroxypyrimidin-2-yl)-mercaptopropyl]-hexahydro-(1H)-1,4-diazepin-fumarat

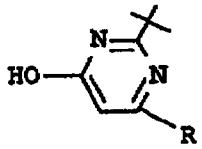


Herstellung der Ausgangsprodukte:

a) 2-t-Butyl-4-hydroxy-6-trifluormethyl-pyrimidin.
Der Aufbau des obigen Pyrimidins erfolgte in an sich bekannter Weise durch Kondensation von 2,2-Dimethylpropion-amidin mit Trifluoracetessigsäureethylester und Natriumethylat in Ethanol, siehe Heterocyclic Compounds, Vol. 52, The Pyrimidines, S. 189 ff., D.J. Brown et al. (Eds.) John Wiley and Sons, 1994.

Fp. 187-188°C

In analoger Weise wurden die 4-Hydroxypyrimidine der Formel

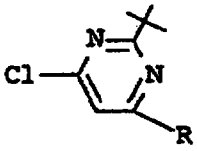


erhalten.

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

b) 2-t-Butyl-4-chlor-6-trifluormethylpyrimidin
Das Hydroxypyrimidin aus Stufe a) wurde mit Phosphoroxychlorid oder Thionylchlorid in an sich bekannter Weise in die Chlorverbindung überführt, siehe Heterocyclic Compounds, Vol. 52, The Pyrimidines, S. 329 ff., John Wiley and Sons, 1994.
Die Verbindung liegt als gelbliches Öl vor.

In analoger Weise wurden die 4-Chlorpyrimidine der Formel



erhalten:

R	Fp [°C]
$t\text{-}C_4H_9$	öl
$n\text{-}C_3H_7$	Öl
CF_2Cl	öl

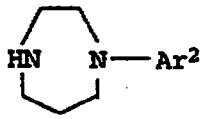
c) 1-[2-t-Butyl-6-trifluormethylpyrimidin-4-yl]-hexahydro-(1H)-1,4-diazepin

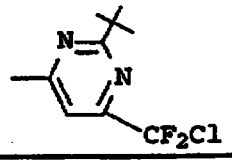
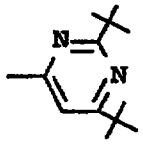
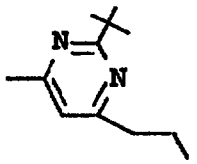
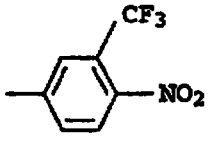
18 g (0,18 Mol) Homopiperazin wurden in 25 ml Ethanol gelöst und bei Rückflußtemperaturen eine Lösung von 7,2 g (0,03 Mol) des nach b) erhaltenen Chlorids, gelöst in 10 ml Ethanol, innerhalb 1 h zugetropft. Nach 30 min. Nachreaktion wurde der erkaltete Ansatz zur Aufarbeitung mit 200 ml Wasser versetzt und mehrfach mit insgesamt 200 ml Methylenchlorid extrahiert. Die organische Phase wurde anschließend mit Wasser gewaschen, mit wasserfreiem Natriumsulfat getrocknet und eingeengt. Man erhielt die gewünschte Verbindung als gelbliches Öl, das roh weiter verarbeitet wurde.

Ausbeute: 98% d.Th.

Die folgenden Verbindungen wurden in entsprechender Weise erhalten:

1-Aryl-1,4-Diazepine der Formel:

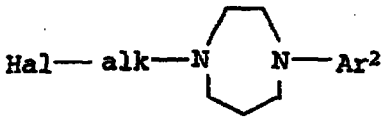


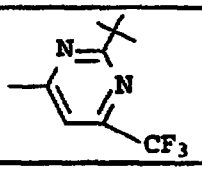
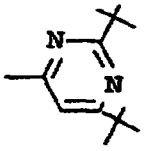
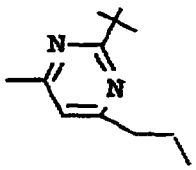
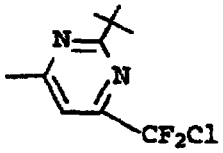
Ar^2	Fp. [°C]
	Öl
	Öl
	Öl
	74-75

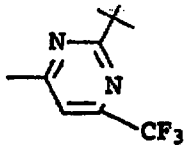
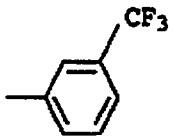
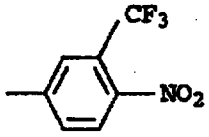
d) 1-[2-t-Butyl-6-trifluormethylpyrimidin-4-yl]-4-(3-chlorpropyl)hexahydro-(1H)-1,4-diazepin
5 g (0,0165 Mol) der vorstehend unter c) erhaltenen Verbindung wurden zusammen mit 2,5 g (0,025 Mol) Triethylamin und 3,15 g (0,02 Mol) 1-Brom-3-chlorpropan in 50 ml Tetrahydrofuran 10 h zum Sieden unter Rückfluß erhitzt. Anschließend wurde das Lösungsmittel abdestilliert, der Rückstand mit Wasser versetzt und mit Methylenchlorid extrahiert. Der nach dem Trocknen und Einengen erhaltene Rückstand wurde anschließend mittels Flash-Chromatographie (Kieselgel) gereinigt.
Ausbeute: 4,8 g (77% d.Th.) gelbes Öl

Die nachfolgend aufgeführten Verbindungen wurden in analoger Weise erhalten:

1-Aryl-4-halogenalkyl-1,4-diazepine der Formel



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

"	$-CH_2-C(CH_3)=CH-CH_2-$		Öl
"	$-(CH_2)_3-$		Öl
"	"		Öl

Herstellung des Endproduktes

5 g (0,013 Mol) des nach d) erhaltenen Produktes wurden in 25 ml Dimethylformamid gelöst und bei 100°C unter Rühren zu einer Lösung von 2,03 g (0,016 Mol) 2-Thio-uracil, 0,38 g (0,016 Mol) Lithiumhydroxid und 1 g Natriumiodid in 50 ml Dimethylformamid innerhalb 1 h zugetropft. Nach 3-stündiger Reaktion wurde das Lösungsmittel im Vakuum abdestilliert, der Rückstand mit 150 ml Wasser versetzt und zweimal mit Essigsäureethylester extrahiert. Der nach Waschen mit Wasser, Trocknen mit Natriumsulfat und Einengen hinterbliebene Rückstand wurde chromatographisch gereinigt. (Flash-Chromatographie, Kieselgel, Laufmittel Methylenchlorid mit 2,5-5% Methanol)

Ausbeute: 4 g helles Öl

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)

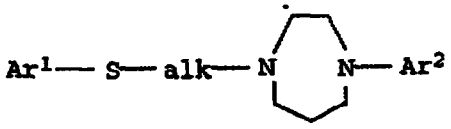
Durch Versetzen einer ethanolischen Lösung mit Fumarsäure wurde die Substanz als Fumarat erhalten.

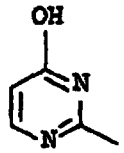
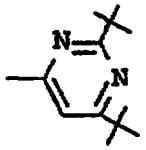
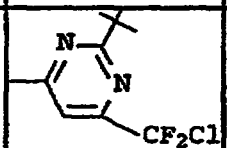
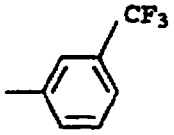
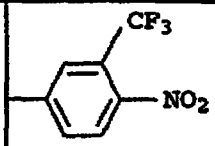
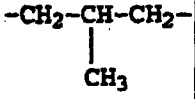
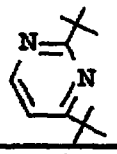
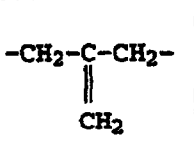
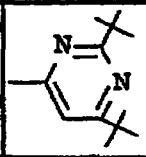
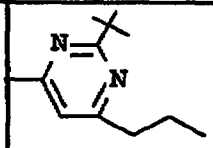
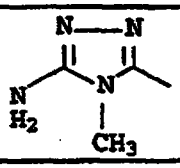
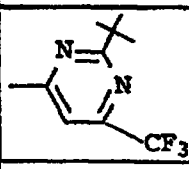
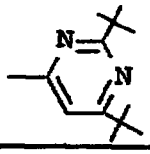
$C_{21}H_{29}F_3N_6OS \cdot C_4H_4O_4$ MG 586,6

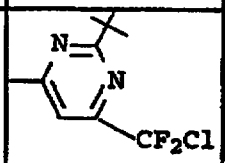
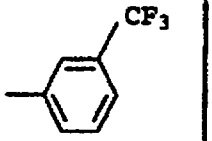
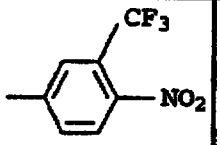
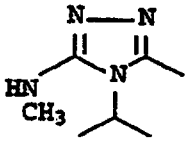
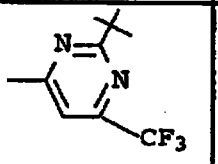
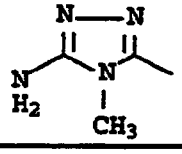
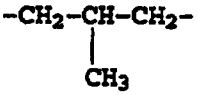
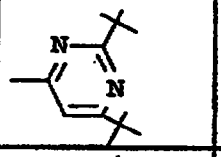
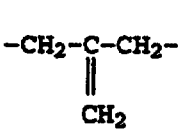
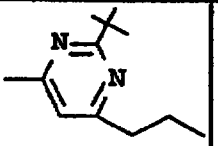
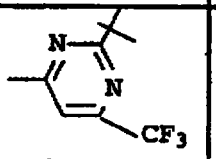
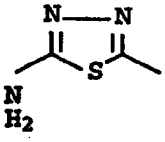
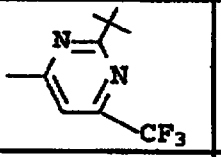
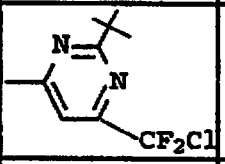
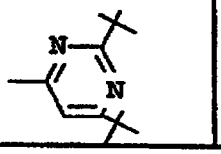
Fp. 188-189°C

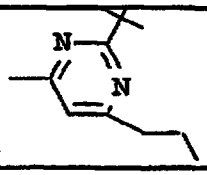
Unter Verwendung verschiedener Halogenalkyl-1,4-Diazepine (wie z.B. 1d) und verschiedener mercaptosubstituierter Heterocyclen wie Thiouracil, 5-Amino-2-mercapto-triazole und 5-Amino-2-mercapto-thiadiazol wurden in analoger Weise die nachfolgend in Tabelle 1 aufgeführten Verbindungen erhalten:

Tabelle 1

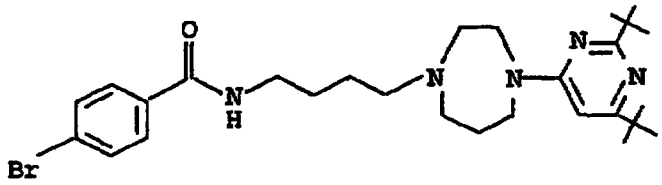


Bsp. Nr.	Ar^1	alk	Ar^2	Fp. [°C]
2		$-(CH_2)_3-$		155-162 Oxalat
3	"	"		83-85 Oxalat
4	"	"		177-182 Fumarat
5	"	"		72-74
6	"			116-119
7	"			174-180 Oxalat
8	"	"		60-70 Oxalat
9		$-(CH_2)_3-$		166-167 Fumarat
10	"	"		55-60

Bsp. Nr.	Ar^1	alk	Ar^2	Fp. [°C]
11	"	"		110-115 Oxalat
12	"	"		136-140 Hydrochlorid
13	"	"		95-98
14		"		142-144
15				125-128
16	"			113-119 Oxalat
17	"	"		230-232 Hydrochlorid
18		$-(CH_2)_3-$		Öl
19	"	"		109-110
20	"	"		60-67

Bsp. Nr.	Ar¹	alk	Ar²	Fp. [°C]
21	"	$-CH_2-CH(CH_3)-CH_2-$	"	180-190 Hydrochlorid
22	"	$-CH_2-C(=CH_2)-CH_2-$	"	119-122
23	"	$-CH_2-CH(CH_3)-CH_2-$		92-97 Oxalat

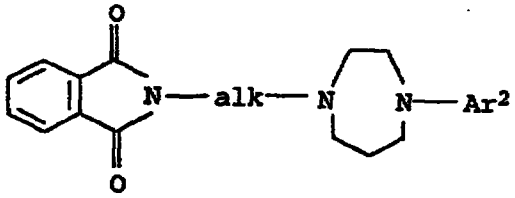
Beispiel 24:
4-Brombenzoesäure-[4-{-4-(2,6-bis-t-butyl-pyrimidin-4-yl)}-(hexahydro-(1H)-1,4-diazepin-1-yl-)butyl]amid

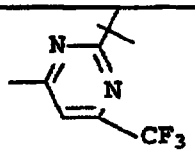
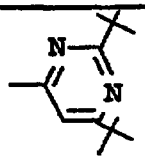
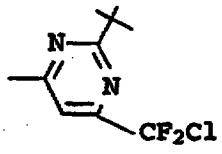


Herstellung der Ausgangsprodukte

a) Hexahydro-1H-1-[2-t-butyl-6-trifluormethyl-pyrimidin-4-yl]-4-(4-phthalimido-butyl)-(1H)-1,4-diazepin

10 g (0,033 Mol) des nach Beispiel 1c) hergestellten Diazepins wurden mit 9,8 g (0,035 Mol) N-(4-Brombutyl)-phthalimid und 9,1 g (0,066 Mol) Kaliumcarbonat in 120 ml Acetonitril 8 h zum Sieden unter Rückfluß erhitzt. Anschließend wurde filtriert und das Filtrat wurde eingeengt. Der Rückstand wurde roh weiterverarbeitet.
Ausbeute: 16,2 g (98% d.Th.)
Eine Probe wurde aus Ethanol umkristallisiert.
Fp. 97-99°C
Auf analoge Weise wurden erhalten:



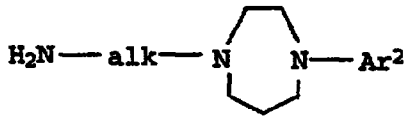
alk	Ar^2	Fp. [°C]
$-(CH_2)_3-$		89-92
$-CH_2-C(CH_3)=CH-CH_2-$	"	130-132
$-(CH_2)_3-$		119-121
$-(CH_2)_4-$	"	207-209
$-(CH_2)_4-$		190-192

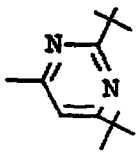
b) Hexahydro-1H-1-[2-t-butyl-6-trifluormethylpyrimidin-4-yl]-4-(4-aminobutyl)-1,4-diazepin

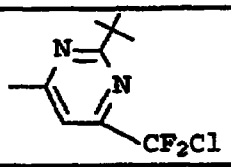
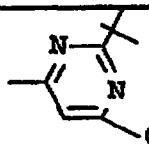
15 g (0,03 Mol) des vorstehend unter a) beschriebenen Produkts wurden mit 6 g Hydrazinhydrat in 200 ml Ethanol 2 h unter Rühren zum Sieden erhitzt; anschließend wurde der Niederschlag abgesaugt und das Filtrat eingedampft. Der Rückstand wurde in Essigsäureethylester aufgenommen, nochmals filtriert, mit Wasser gewaschen, getrocknet und wiederum eingedampft.

Es wurden erhalten:
9,2 g (83% d.Th.) als Öl

Auf analoge Weise wurden erhalten:



alk	Ar^2	Fp. [°C]
$-(CH_2)_4-$		Öl

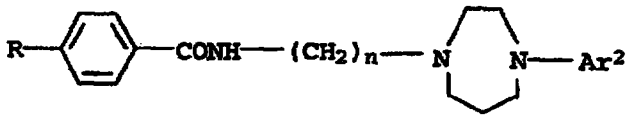
alk	Ar^2	Fp. [°C]
$-(CH_2)_3-$	"	Öl
$-(CH_2)_4-$		Öl
$-(CH_2)_3-$		Di-Hydrochlorid: 241-245

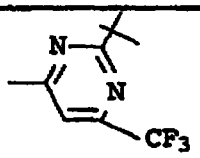
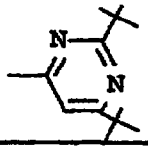
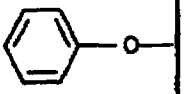
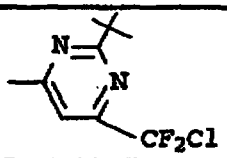
Herstellung der Endprodukte:

3 g (0,0083 Mol) des vorstehend unter b) erhaltenen Produkts wurden mit 0,9 g (0,009 Mol) Triethylamin in 60 ml Tetrahydrofuran gelöst und eine Lösung von 2 g (0,009 Mol) 4-Brombenzoylchlorid in 10 ml Tetrahydrofuran wurde innerhalb 10 min. bei Raumtemperatur zugetropft. Nach 1 h wurde das Lösungsmittel im Vakuum abdestilliert, der Rückstand mit Wasser versetzt und zweimal mit Methylenchlorid extrahiert. Die getrocknete und eingeengte Lösungsmittelphase wurde mittels Flash-Chromatographie (Kieselgel, Laufmittel Methylenchlorid mit 3% Methanol) gereinigt.
Ausbeute: 4,2 g (93% d.Th.)
Fp. 125-127°C (aus Diisopropylether/Isopropanol)
$C_{28}H_{42}BrN_5O$ (544,6)

Unter Verwendung verschiedener Aminoderivate (analog 24b) und bekannter Benzoylchloride wurden die nachstehend in Tabelle 2 aufgeführten Verbindungen erhalten.

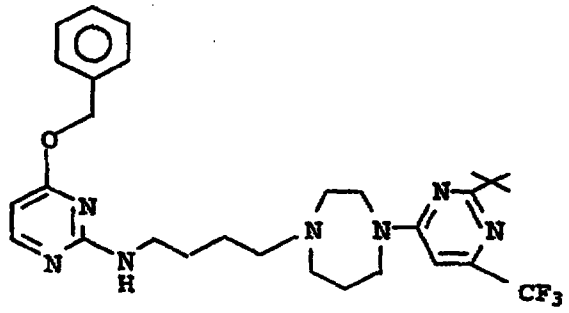
Tabelle 2



Bsp. Nr.	R	n	Ar^{2-}	Fp. [°C]
25	Br	3	"	169-171
26	"	4		74-76 Oxalat
27	t-Butyl	4		165-167 Oxalat
28		4	"	104-107 Oxalat
29	Br	4		92-94 Oxalat
30	I	4	"	110-115 Oxalat

Beispiel 31

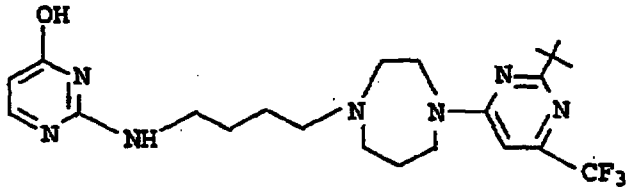
4-[4-(4-Benzyloxy-pyrimidin-2-yl)aminobutyl]-1-[2-t-butyl-6-trifluormethyl-pyrimidin-4-yl]hexahydro-1H-1,4-diazepin-oxalat



2,7 g (0,007 Mol) der nach Beispiel 24b) hergestellten Aminoverbindung wurden mit 0,3 g Natriumhydrid (0,009 Mol) in 20 ml Dimethylformamid vorgelegt. Nach 1 h Reaktionszeit wurden 1,6 g (0,006 Mol) 4-Benzyloxy-2-methylsulfonylpyrimidin (hergestellt durch Oxidation von 4-Benzyloxy-2-methylmercapto-pyrimidin), ge-

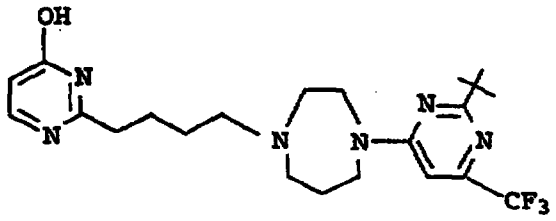
löst in 10 ml Dimethylformamid, zugegeben und 72 h bei Raumtemperatur gerührt.
Anschließend wurde mit Wasser versetzt, mit Essigsäureethylester extrahiert, getrocknet und die Lösung eingeengt. Der Rückstand wurde säulenchromatographisch gereinigt (Kieselgel, Methylenchlorid mit 4% Methanol)
Reinausbeute: 1,0 g (30% d.Th.)
Oxalat: Fp. 145-150°C
$C_{29}H_{38}F_3N_7O \cdot C_2H_2O_4$ (647,7)

Beispiel 32:
1-[2-t-butyl-6-trifluormethyl-pyrimidin-4-yl]-4-[4-(4-hydroxy-pyrimidin-2-yl)aminobutyl]hexahydro-(1H)-1,4-diazepin



0,7 g (0,001 Mol) der im vorstehenden Beispiel beschriebenen Verbindung wurden in Methanol unter Normalbedingungen mit Palladium auf Kohle-Katalysator (10% Pd) hydriert.
Ausbeute: 0,6 g (100% d.Th.)
Fp. 111-115°C
$C_{22}H_{32}F_3N_7O \cdot C_2H_4O_4$ (557,5)

Beispiel 33:
1-[2-t-Butyl-6-trifluormethyl-pyrimidin-4-yl]-4-[4-(4-hydroxypyrimidin-2-yl)butyl-hexahydro-1H-1,4-diazepin



a) 1-[2-t-Butyl-6-trifluormethyl-pyrimidin-4-yl]-4-(4-cyanobutyl)-hexahydro-1,4-diazepin

9,1 g (0,03 Mol) des Diazepins aus Beispiel 1c) wurden mit 3,5 g (0,03 Mol) 5-Chlorvaleronitril, 9,1 g Triethylamin (0,09 Mol) in 100 ml Dimethylformamid gelöst und 24 h auf 100° erwärmt.
Anschließend wurde das Lösungsmittel im Vakuum abdestilliert,

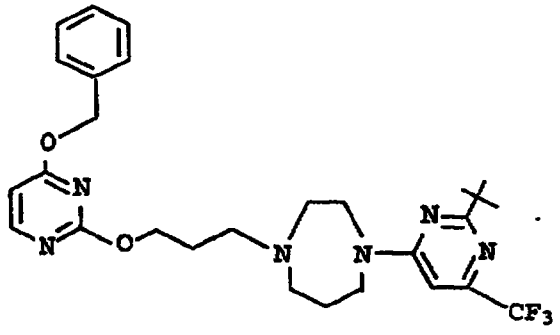
Wasser zugegeben, mit Essigsäureethylester extrahiert, diese Phase mit Natriumsulfat getrocknet und eingeengt. Der Rückstand wurde roh weiterverarbeitet.
Ausbeute: 9,1 g als braunes Öl

b) 1-[2-t-Butyl-6-trifluormethyl-pyrimidin-4-yl]-4-(4-amidinobutyl)-hexahydro-1,4-diazepinhydrochlorid

9,1 g (0,024 Mol) des vorstehend beschriebenen Nitrils wurden in 2 ml Ethanol und 50 ml Methylenchlorid (beides wasserfrei) gelöst und bei 0-10° unter Kühlung wurde trockenes Chlorwasserstoffgas bis zur Sättigung eingeleitet. Nach Rühren über Nacht wurde der Niederschlag abgesaugt und das Filtrat eingeengt.
Ausbeute: 7,6 g (58% d.Th.)

Herstellung des Endprodukts
4,4 g (0,01 Mol) des vorstehend beschriebenen Amidins wurden mit der Natriumverbindung des Formylessigsäureethylesters (Herstellung J. Org. Chem. 35 (1970), 2515 ff) (2,8 g (0,02 Mol)) in 50 ml Wasser und 20 ml Tetrahydrofuran über Nacht gerührt. Der Reaktionsansatz wurde dann mehrfach mit Essigsäureethylester extrahiert, die organische Phase wurde getrocknet und eingeengt. Der Rückstand wurde säulenchromatographisch gereinigt (Kieselgel, Elutionsmittel Methylenchlorid mit 4% Methanol)
Ausbeute: 1,9 g (42%) Öl
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)
Oxalat: $C_{22}H_{31}F_3N_6O \cdot C_2H_2O_4$ (542,5)
Fp. 173-177° (Z)

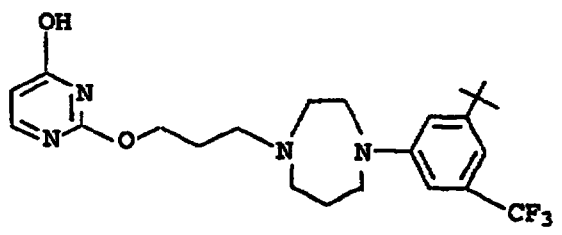
Beispiel 34
1-[2-t-Butyl-6-trifluormethyl-pyrimidin-4-yl]-4-[3-(4-benzyloxypyrimidin-2-yl)oxypropyl]-hexahydro-(1H)-1,4-diazepin



a) Ausgangsprodukt
8,9 g (64,5 mmol) 3-Brom-propanol-1 wurde in 50 ml THF_{abs} aufgenommen und nacheinander mit 6,52 g (64,5 mmol) Triethylamin einer katalytischen Menge Natriumjodid sowie 16,2 g (53,7 mmol) des unter Beispiel 1c) hergestellten Azepins versetzt und 16 h unter Rückfluß erhitzt. Zur Aufarbeitung wurde von den ausgefallenen Salzen abfiltriert und die Mutterlauge i. Vak. eingeengt. Das erhaltene Öl nahm man in Dichlormethan auf, wusch die organische Phase mit Wasser, trocknete über Natriumsulfat und reinigte dann mittels Säulenchromatographie (SiO_2, Laufmittel CH_2Cl_2:MeOH=98:2) und erhielt ein farbloses Öl.
Ausbeute: 10,11 g (53%)

b) Endprodukt
2,45 g des vorstehend beschriebenen Produkts, gelöst in 25 ml DMF_{abs}, wurden bei Raumtemperatur unter Schutzgasatmosphäre mit 0,26 g (8,52 mmol) Natriumhydrid (80%) portionsweise versetzt und 30 min. nachgerührt. Dann tropfte man 1,5 g (5,68 mmol) 2-Methansulfonyl-4-benzyloxy-pyrimidin (wurde analog Literatur hergestellt: W.E. Barnett, R.F. Koebel Tetrahedron Lett. 1971, 20, 2867) gelöst in 15 ml DMF_{abs} zu. Nach 7 h wurde zur Aufarbeitung auf Wasser gegossen, mit tert.-Butyl-methylether extrahiert, die organische Phase mit Wasser gewaschen, über Natriumsulfat getrocknet, filtriert und i.Vak. eingeengt. Aufreinigung des erhaltenen Öls mittels Säulenchromatographie (SiO_2, Laufmittel CH_2Cl_2:MeOH = 98:2) ergab die Substanz als Öl.
Ausbeute: 1,6 g (2,9 mmol, 52%)
Zur Bildung des Hydrochlorids wurde das in Essigester/Et_2O gelöste Öl unter Schutzgas mit etherischer Salzsäure versetzt und das entstandene Salz abgesaugt.
Fp.: 110-112°C
$C_{28}H_{36}ClF_3N_6O_2$ (581,1)

Beispiel 35
1-[2-t-Butyl-6-trifluormethyl-pyrimidin-2-yl]-4-[3-(4-hydroxypyrimidin-2-yl)oxypropyl]hexahydro-(1H)-1,4-diazepin



1,4 g (2,6 mmol) der Substanz des Beispiels 34, gelöst in 40 ml Essigester, wurden bei Raumtemperatur mit 0,2 g Pd/C (10% Pd) versetzt und bei 40-50°C unter Atmosphärendruck mit Wasserstoff hydriert. Nach beendeter Reaktion saugte man den Katalysator ab, wusch mit Essigester nach und engte i. Vak. ein.
Ausbeute: 1,2 g (100%)
Zur Bildung des Hydrochlorids wurde das in Essigester/Et_2O gelöste Öl unter Schutzgas mit etherischer Salzsäure versetzt und das entstandene Salz abgesaugt.
Fp.: 78-80°C
$C_{21}H_{30}ClF_3N_6O_2$ (491)

In analoger Weise erhält man die in den nachfolgenden Tabellen 3 bis 17 genannten Verbindungen.

Tabelle 3

Beispiel Nr.	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-Naphl	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-	-$(CH_2)_4$-

50	H	H	OH	H	CHF_2	H	tBut	H	CH_2-CH_2	$CH{\equiv}C$-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	$CH{\equiv}C$-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	$CH{\equiv}C$-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	$CH{\equiv}C$-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-

Tabelle 4

Beispiel Nr.	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-

Tabelle 5

Beispiel Nr.	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	-$(CH_2)_3$-

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	-$(CH_2)_4$-		

Tabelle 6

Beispiel Nr.	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-

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

Tabelle 7

Beispiel Nr.	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	nPropyl	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-Napht	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	-$(CH_2)_3$-
184	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	nProp	tBut	H	CH_2	CH_2-N-CH_2	S	-CH_2-CH(CH_3)-CH_2-

161	H	H	OH	OMe	tBut	iProp	H	CH_2-CH_2	S
162	H	H	OH	OMe	CF_3	tBut	H	CH_2-CH_2	NH
163	H	Me	OH	Me	tBut	nProp	H	CH_2	$-CH_2-$
164	H	H	OH	Me	tBut	H	H	CH_2-CH_2	S
165	H	H	NH_2	H	tBut	tBut	H	CH_2	$-CH_2-$
166	H	H	OH	Me	CF_3	tBut	H	CH_2	S

161	CH_2-N-CH_2	$-(CH_2)_3-$
162	$CH{\equiv}C$-CH_2	$-(CH_2)_3-$
163	CH_2-$CH{=}C$	$-CH_2$-$CH{=}CH$-CH_2-
164	CH_2-N-CH_2	$-CH_2$-$C(=CH_2)$-CH_2-
165	$CH{\equiv}C$-CH_2	$-(CH_2)_3-$
166	CH_2-$CH{=}C$	$-CH_2$-$CH(CH_3)$-CH_2-

Tabelle 8

Beispiel Nr.	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-	-$(CH_2)_3$-

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-Naphl	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	Cl_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-

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

205	-CH_2-C(=CH_2)-CH_2-
206	-CH_2-CH=CH-CH_2-
207	-CH_2-CH(CH_3)-CH_2-
208	-CH_2-C(CH_3)=CH-CH_2-
209	-CH_2-CH(CH_3)-CH_2-
210	-CH_2-CH(CH_3)-CH_2-
211	-CH_2-C(=CH_2)-CH_2-
212	-CH_2-C(=CH_2)-CH_2-
213	-CH_2-C(=CH_2)-CH_2-
214	-CH_2-C(CH_3)=CH-CH_2-
215	-CH_2-CH(CH_3)-CH_2-
216	-CH_2-C(CH_3)=CH-CH_2-
217	-CH_2-CH(CH_3)-CH_2-
218	-CH_2-CH(CH_3)-CH_2-
219	-CH_2-C(CH_3)=CH-CH_2-
220	-CH_2-CH(CH_3)-CH_2-
221	-CH_2-C(=CH_2)-CH_2-
222	-CH_2-C(=CH_2)-CH_2-
223	-CH_2-C(=CH_2)-CH_2-
224	-CH_2-CH(CH_3)-CH_2-
225	-CH_2-C(CH_3)=CH-CH_2-

Tabelle 9

Beispiel Nr.	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-	-$(CH_2)_6$-
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	-$(CH_2)_6$-
240	NCH_3	NH_2	tBut	H	CH_3	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-

241	N(iProp)	NH_2	tBut	Ph	H	CH_2-CH_2	$CH{\equiv}C$-CH_2	S	-CH_2-C(=CH_2)-CH_2-
242	N(iProp)	NH_2	tBut	2-Naphtl	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	$CH{\equiv}C$-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	$CH{\equiv}C$-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-Naphtl	tBut	Me	CH_2	$CH{\equiv}C$-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	$CH{\equiv}C$-CH_2	S	-CH_2-CH(CH_3)-CH_2-

Tabelle 10

Beispiel Nr.	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	-$(CH_2)_3$-

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	-$(CH_2)_3$-

Tabelle 11

Beispiel Nr.	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	-$(CH_2)_5$-

296	NHMe	H	CN	tBut	Me	CH_2-CH_2	CH_2-CH=C	-CH_2-	-CH_2-C(=CH_2)-CH_2-
297	OH	H	C≡CH	iProp	Me	CH_2	CH_2-CH=C	S	-$(CH_2)_8$-
298	OH	Cl	H	iProp	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-

Tabelle 12

Beispiel Nr.	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-Naphl	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-

314	NEt	NH_2	Me	tBut	H	CH_2-CH_2		CH_2-CH_2	$-CH_2-CH(CH_3)-CH_2-$
315	NCH_3	NH_2	Me	tBut	H	CH_2	CH_2-N-CH_2	S	$-(CH_2)5-$
316	S	NH_2	H	tBut	tBut	CH_2	CH=C-CH_2	$-CH_2-$	$-CH_2-CH(CH_3)-CH_2-$
317	N(iProp)	NH_2	Me	CF_3	tBut	CH_2-CH_2	CH_2-CH=C	S	$-(CH_2)4-$
318	NCH_3	OH	H	nProp	tBut	CH_2	CH_2-N-CH_2	S	$-(CH_2)3-$

Tabelle 13

Beispiel Nr.	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	-$(CH_2)_3$-

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-Naphtl	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-

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

Tabelle 14

Beispiel Nr.	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-

Tabelle 15

Beispiel Nr.	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-

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

Tabelle 16

Beispiel Nr.	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	-$(CH_2)_4$-

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	-$(CH_2)_4$-

Tabelle 17

Beispiel Nr.	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	-$(CH_2)_4$-

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-

Beispiele für galenische Applikationsformen

A) Tabletten

Auf einer Tablettenpresse werden in üblicher Weise Tabletten folgender Zusammensetzung gepreßt:

40 mg	Substanz des Beispiels 1
120 mg	Maisstärke
13,5 mg	Gelatine
45 mg	Milchzucker
2,25 mg	Aerosil® (chemisch reine Kieselsäure in submikroskopisch feiner Verteilung)
6,75 mg	Kartoffelstärke (als 6 %iger Kleister)

B) Dragees

20 mg	Substanz des Beispiels 4
60 mg	Kernmasse
70 mg	Verzuckerungsmasse

Die Kernmasse besteht aus 9 Teilen Maisstärke, 3 Teilen Milchzucker und 1 Teil Vinylpyrrolidon-Vinylacetat-Mischpolymerisat 60:40. Die Verzuckerungsmasse besteht aus

5 Teilen Rohrzucker, 2 Teilen Maisstärke, 2 Teilen Calciumcarbonat und 1 Teil Talk. Die so hergestellten Dragees werden anschließend mit einem magensaftresistenten Überzug versehen.

Biologische Untersuchungen - Rezeptorbindungsstudien

1) D_3-Bindungstest

Für die Bindungsstudien wurden klonierte humane D_3-Rezeptor-exprimierende CCL 1,3 Mäusefibroblasten, erhältlich bei Res. Biochemicals Internat. One Strathmore Rd., Natick, MA 01760-2418 USA, eingesetzt.

Zellpräparation

Die D_3 exprimierenden Zellen wurden in RPMI-1640 mit 10 % fötalem Kälberserum (GIBCO Nr. 041-32400 N); 100 E/ml Penicillin und 0,2 % Streptomycin (GIBCO BRL, Gaithersburg, MD, USA) vermehrt. Nach 48 h wurden die Zellen mit PBS gewaschen und mit 0,05 % trypsinhaltiger PBS 5 min inkubiert. Danach wurde mit Medium neutralisiert und die Zellen durch Zentrifugation bei 300 g gesammelt. Zur Lyse der Zellen wurde kurz das Pellet mit Lysispuffer (5mM Tris-HCl, pH 7,4 mit 10 % Glycerin) gewaschen und danach in einer

Konzentration von 10^7-Zellen /ml Lysispuffer 30 min bei 4°C inkubiert. Die Zellen wurden bei 200 g 10 min zentrifugiert und das Pellet in flüssigem Stickstoff gelagert.

Bindungstests

Für den D_3-Rezeptorbindungstest wurden die Membranen in Inkubationspuffer (50 mM Tris-HCl, pH 7,4 mit 120 mM NaCl, 5 mM KCl, 2 mM $CaCl_2$, 2 mM $MgCl_2$, 10µM Quinolinol, 0,1 % Ascorbinsäure und 0,1 % BSA) in einer Konzentration von ca. 10^6 Zellen/250 µl Testansatz suspendiert und bei 30°C mit 0,1 nM ^{125}Jodsulpirid in Anwesenheit und Abwesenheit von Testsubstanz inkubiert. Die unspezifische Bindung wurde mit 10^{-6}M Spiperon bestimmt.

Nach 60 min wurde der freie und der gebundene Radioligand durch Filtration über GF/B Glasfaserfilter (Whatman, England) an einem Skatron-Zellsammler (Skatron, Lier, Norwegen) getrennt und die Filter mit eiskaltem Tris-HCl-Puffer, pH 7,4 gewaschen. Die auf den Filtern gesammelte Radioaktivität wurde mit einem Packard 2200 CA Flüssigkeitszintillationszähler quantifiziert.

Die Bestimmung der K_i-Werte erfolgte über nichtlineare Regressionsanalyse mit dem Programm LIGAND.

2) D_2-Bindungstest

Zellkultur

HEK-293 Zellen mit stabil exprimierten humanen Dopamin-D2A-Rezeptoren wurden in RPMI 1640 mit Glutamax I™ und 25 mM HEPES mit 10% fötalem Kälberserumalbumin kultiviert. Alle Medien enthielten 100 Einheiten pro ml Penicillin und 100 µg/ml Streptomycin. Die Zellen wurden in feuchter Atmosphäre mit 5% CO_2 bei 37°C gehalten.

Die Zellpräparation für Bindungsstudien erfolgte durch Trypsinisierung (0,05% Trypsinlösung) für 3-5 Minuten bei Raumtemperatur. Danach wurden die Zellen bei 250 g 10 Minuten zentrifugiert und 30 Minuten bei 4°C mit Lysispuffer (5 mM Tris-HCl, 10% Glycerol, pH 7,4) behandelt. Nach Zentrifugation bei 250 g für 10 Minuten wurde der Rückstand bei -20°C bis zum Gebrauch aufbewahrt.

Rezeptorbindungstests

1) Dopamin-D_2-Rezeptor "low affinity state" mit ^{125}I-Spiperon (81 TBq/mmol, Du Pont de Nemours, Dreieich)

Die Ansätze (1 ml) setzten sich zusammen aus 1 x 10^5 Zellen in Inkubationspuffer (50 mM Tris, 120 mM NaCl, 5 mM KCl, 2 mM $MgCl_2$ und 2 mM $CaCl_2$, pH 7,4 mit HCl) und 0,1 nM ^{125}I-Spiperon (totale Bindung) oder zusätzlich 1 µM Haloperidol (unspezifische Bindung) oder Prüfsubstanz.

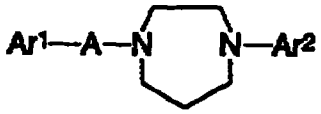
Nach erfolgter Inkubation bei 25°C für 60 Minuten wurden die Ansätze über GF/B Glasfaserfilter (Whatman, England) an einem Skatron-Zellsammler (Fa. Zinsser, Frankfurt) filtriert und die Filter mit eiskaltem 50 mM Tris-HCl-Puffer, pH 7,4 gewaschen. Die auf den Filtern gesammelte Radioaktivität wurde mit einem Packard 2200 CA Flüssigkeitszintillationszähler quantifiziert.

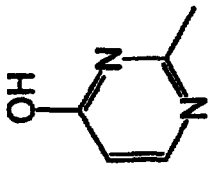
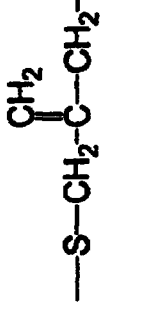
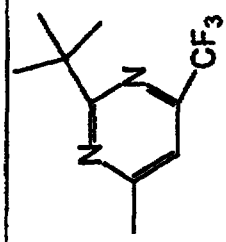
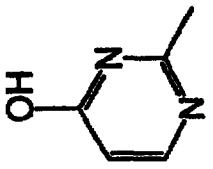
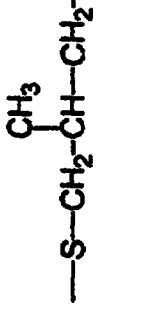
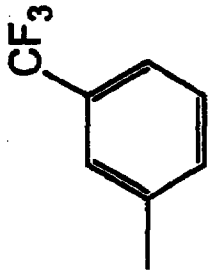
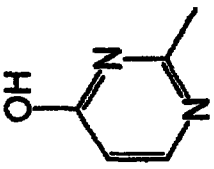
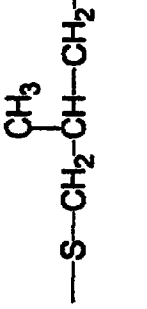
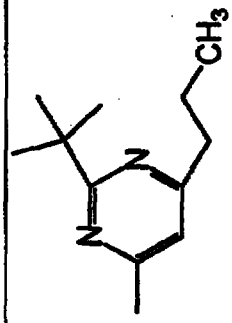
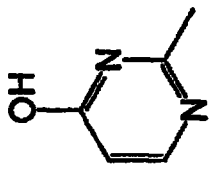
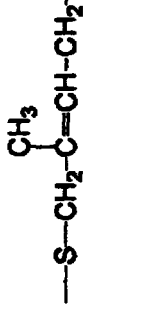
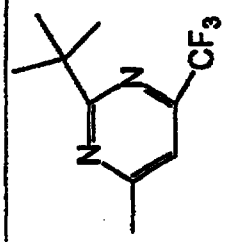
Die Auswertung erfolgte wie unter a).

Die Bestimmung der K_i-Werte erfolgte über nichtlineare Regressionsanalyse mit dem Programm LIGAND oder durch Umrechnung der IC_{50}-werte mit Hilfe der Formel von Cheng und Prusoff.

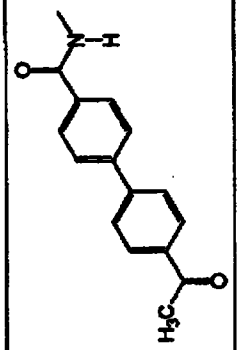
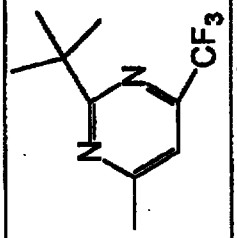
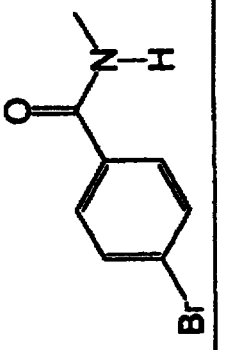
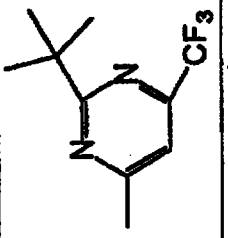
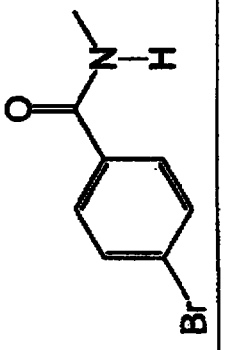
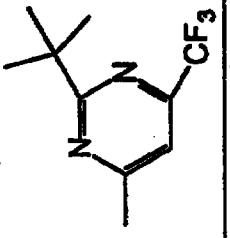
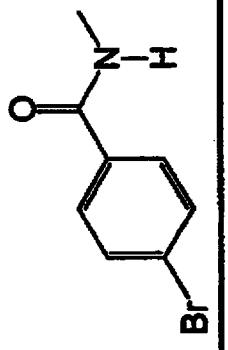
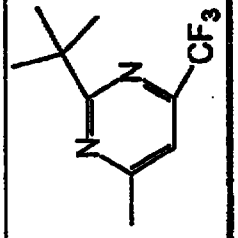
Die erfindungsgemäßen Verbindungen zeigen in diesen Tests sehr gute Affinitäten am D_3-Rezeptor und hohe Selektivitäten gegenüber dem D_3-Rezeptor.

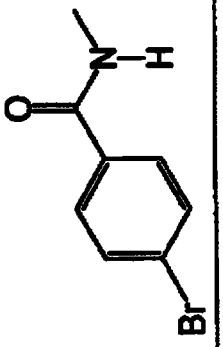
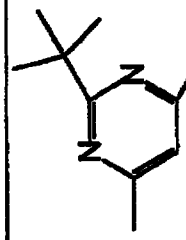
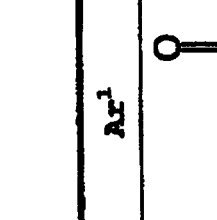
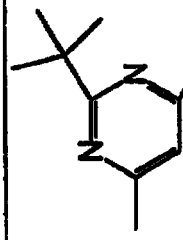
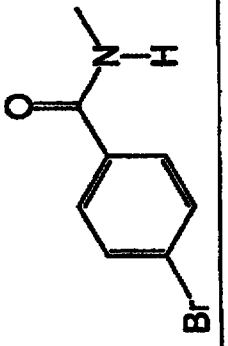
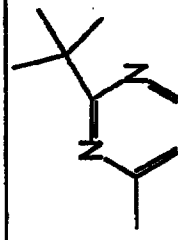
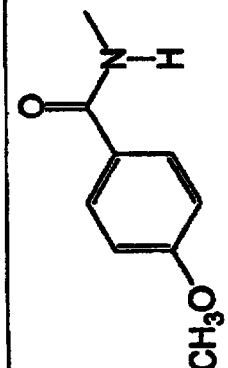
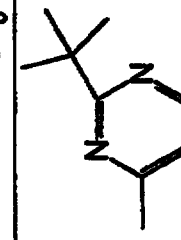
Die folgenden Verbindungen wurden durch die oben beschriebenen Verfahren erhalten:

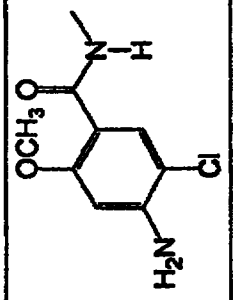
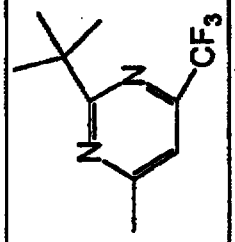
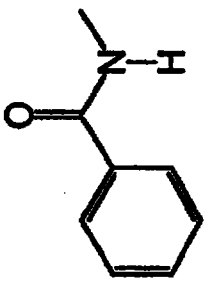
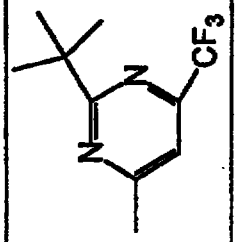
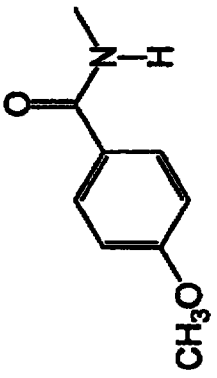
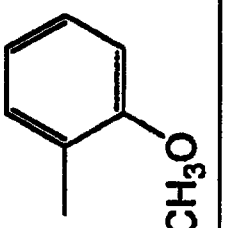
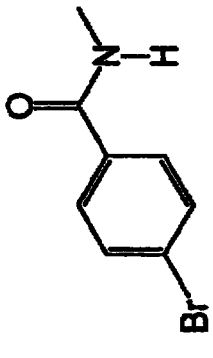
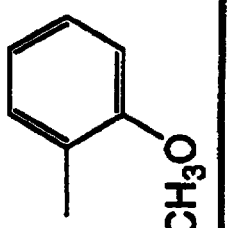


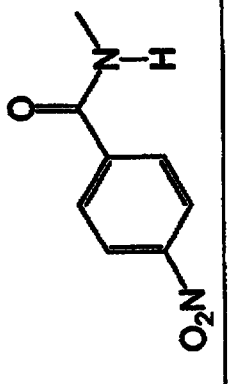
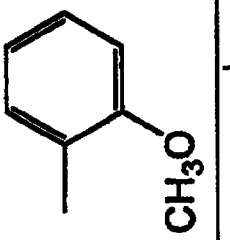
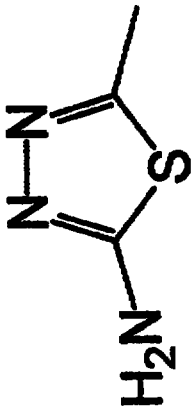
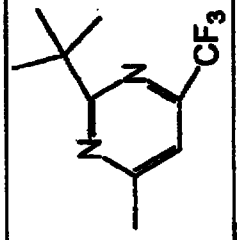
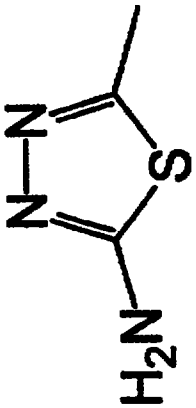
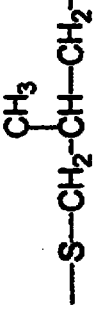
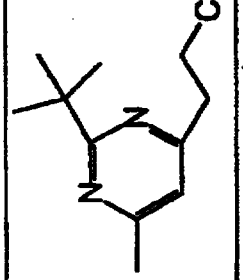
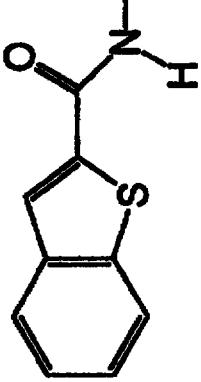
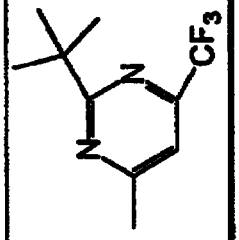
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
450				80 - 90 (Oxalat)
451				110 - 113
452				106 - 108
453				129 -131

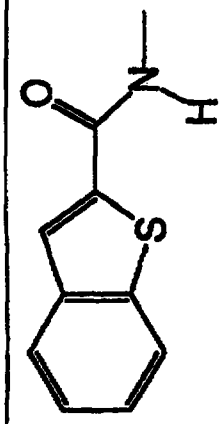
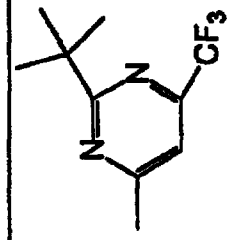
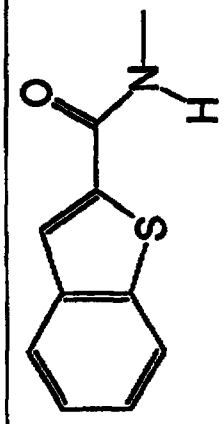
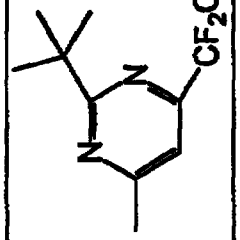
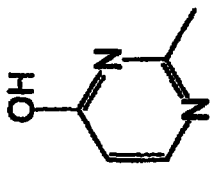
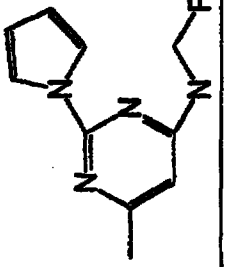
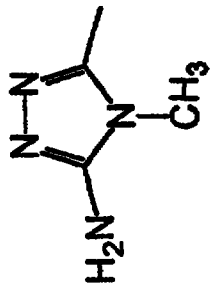
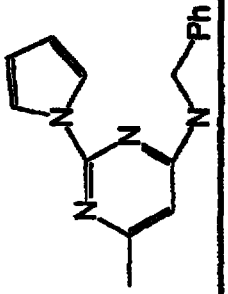
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
454		—S—$(CH_2)_3$—		227 - 131 (Hydrochlorid)
455		—S—$(CH_2)_3$—		165 - 166 (Hydrochlorid)
456		—$(CH_2)_5$—		115 - 118 (Oxalat)
457		—$(CH_2)_4$—		94 - 97 (Hydrochlorid)

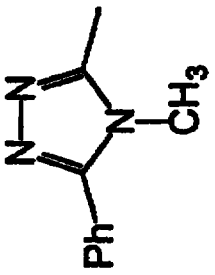
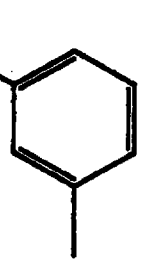
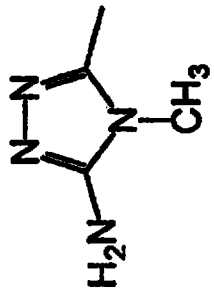
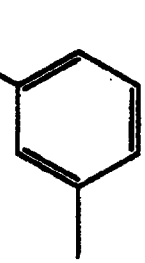
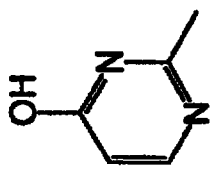
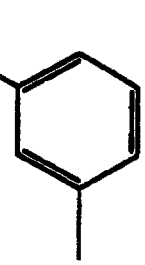
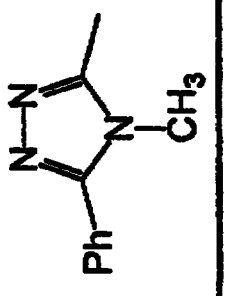
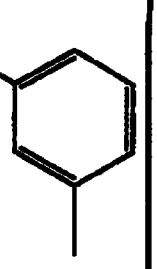
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
458		$-(CH_2)_4-$		123 - 126 (Fumarat)
459		$-(CH_2)_3-CH(CH_3)-$		130 - 133 (Fumarat)
460		$-CH_2-CH=CH-CH_2-$		118 - 125 (Fumarat)
461		$-(CH_2)_2-CH(CH_3)-(CH_2)_2-$		130 - 132 (Oxalat)

Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
462		$-(CH_2)_6-$		144 - 150 (Fumarat)
463		$-(CH_2)_4-$		148 - 154 (Oxalat)
464		$-CH_2-\underset{CH_3}{CH}-(CH_2)_2-$		171 - 176 (Fumarat)
465		$-(CH_2)_4-$		122 - 124 (Fumarat)

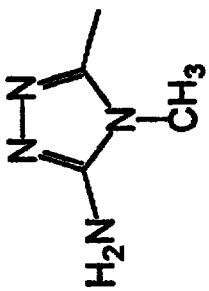
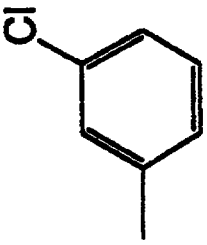
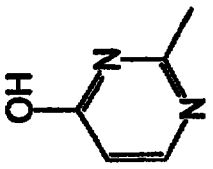
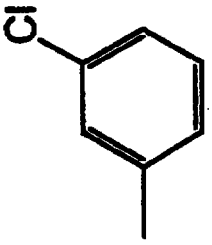
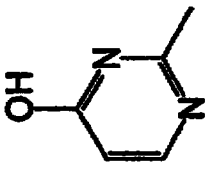
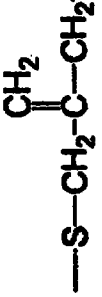
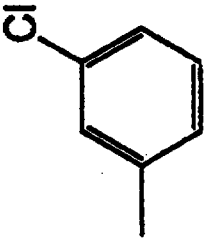
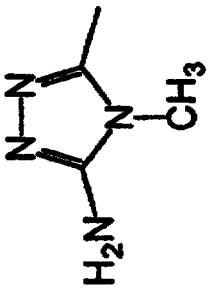
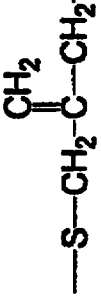
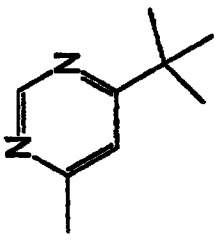
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
466		$-(CH_2)_4-$		108 - 112 (Oxalat)
467		$-(CH_2)_4-$		140 - 142 (Oxalat)
468		$-(CH_2)_4-$		149 - 152 (Fumarat)
469		$-(CH_2)_4-$		147 - 149 (Hydrochlorid)

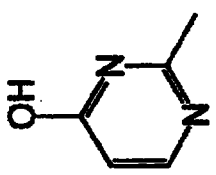
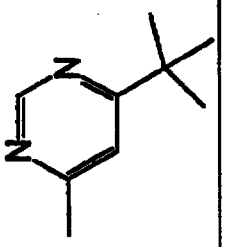
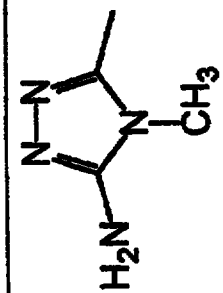
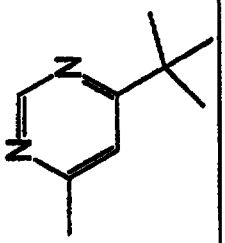
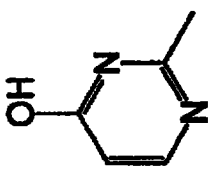
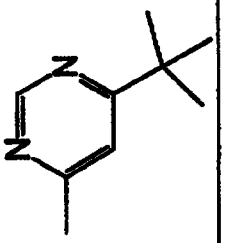
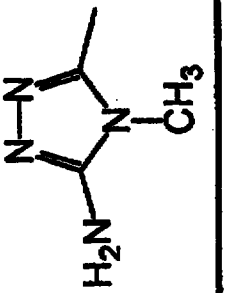
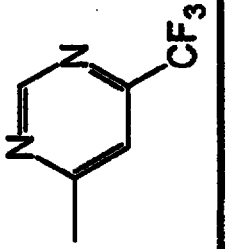
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
470				235 - 236 (Fumarat)
471				92 - 98
472				87 - 90
473				112 - 115 (Fumarat)

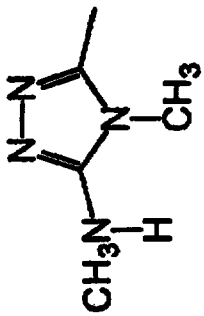
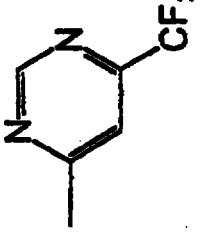
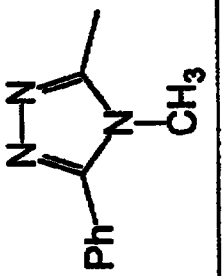
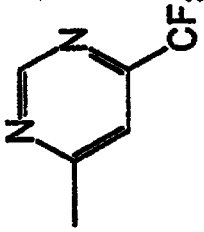
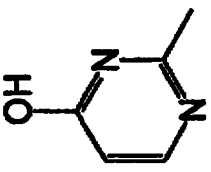
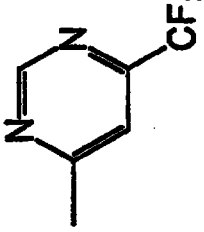
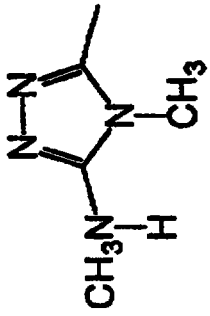
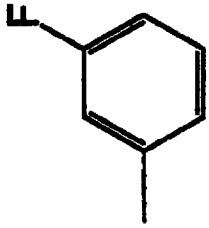
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
474		$-(CH_2)_6-$		101 - 105 (Oxalat)
475		$-(CH_2)_4-$		127 - 129 (Oxalat)
476		$-S-(CH_2)_3-$		
477		$-S-(CH_2)_3-$		

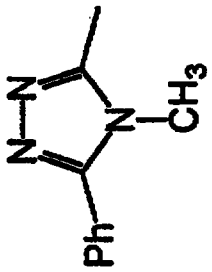
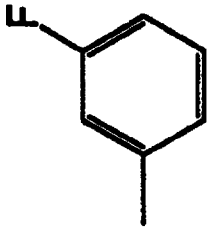
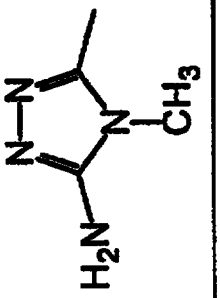
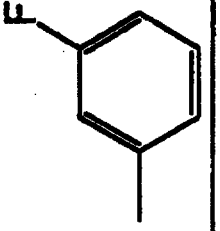
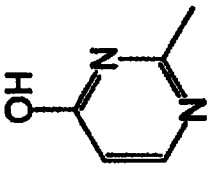
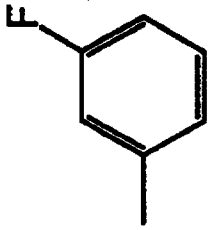
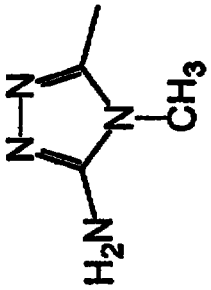
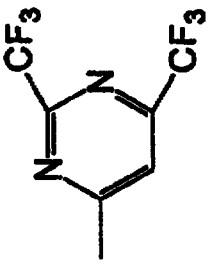
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
478		$-S-(CH_2)_3-$		126 - 128 (Fumarat)
479		$-S-(CH_2)_3-$		150 - 156 (Fumarat)
480		$-S-(CH_2)_3-$		158 - 165 (Fumarat)
481		$-S-(CH_2)_3-$		

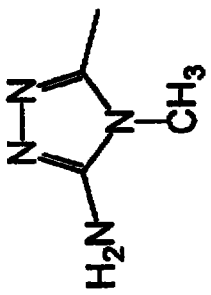
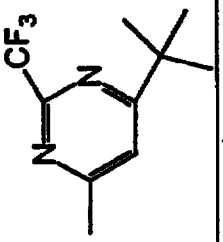
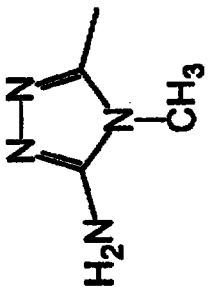
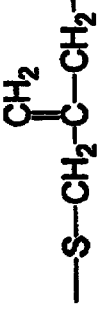
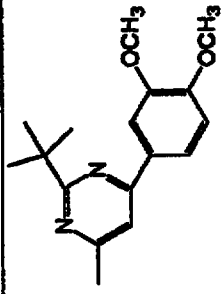
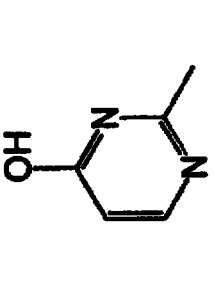
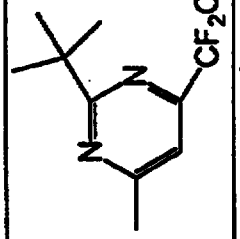
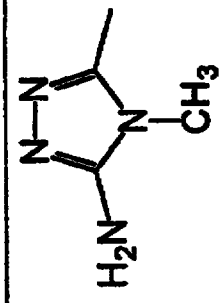
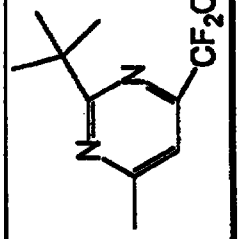
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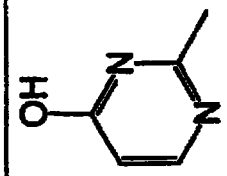
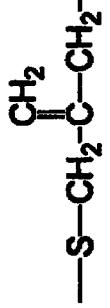
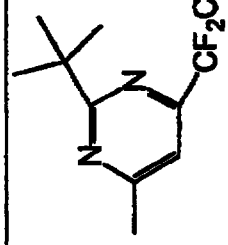
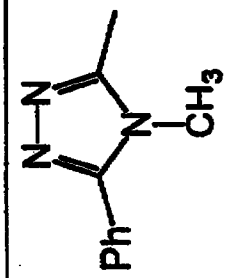
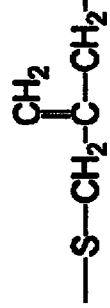
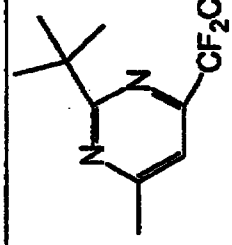
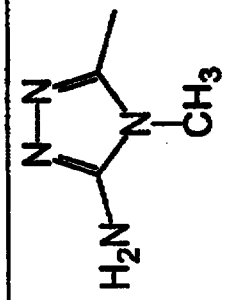
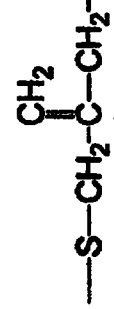
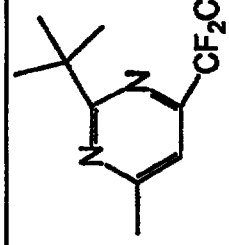
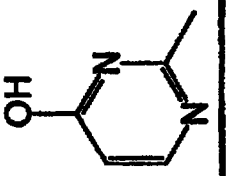
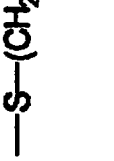
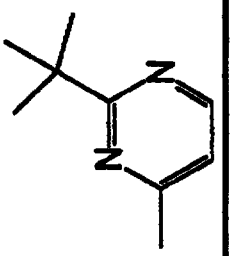
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
482				184 - 188 (Oxalat)
483				185 - 187 (Oxalat)
484				
485				127

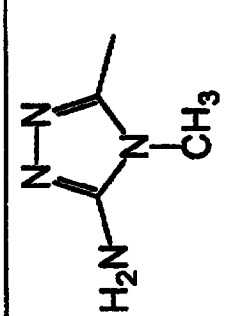
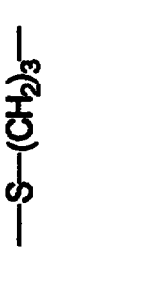
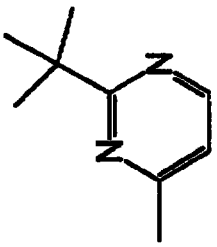
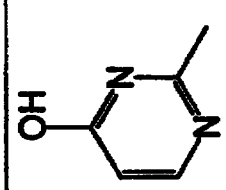
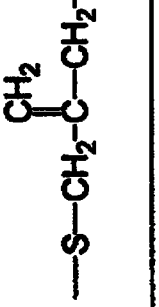
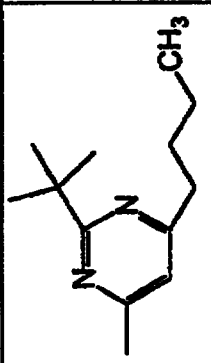
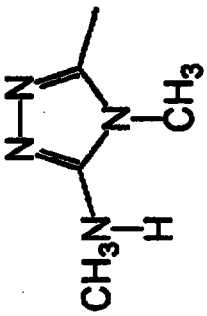
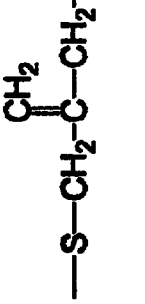
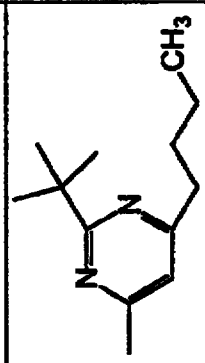
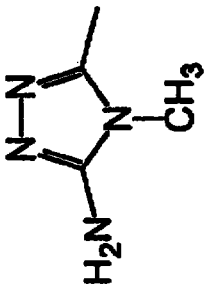
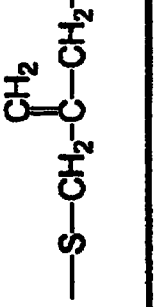
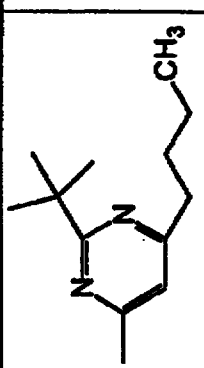
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
486				128
487				123
488				120
489				187 - 191 (Oxalat)

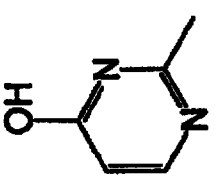
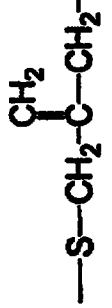
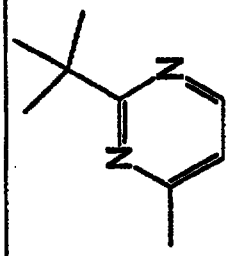
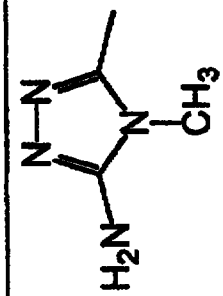
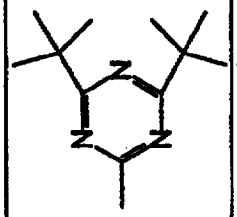
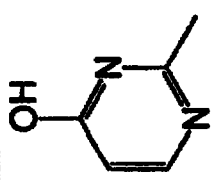
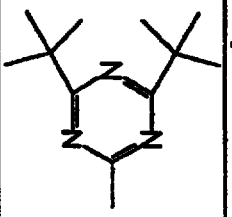
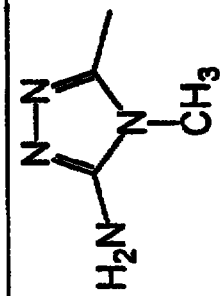
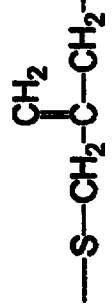
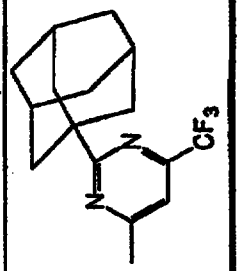
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
490		$-S-(CH_2)_3-$		187 - 191 (Oxalat)
491		$-S-(CH_2)_3-$		
492		$-S-(CH_2)_3-$		
493		$-S-(CH_2)_3-$		

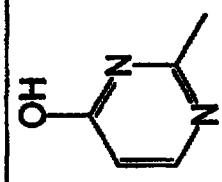
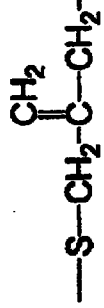
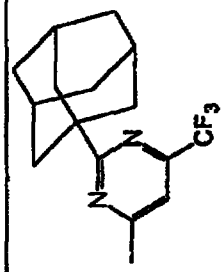
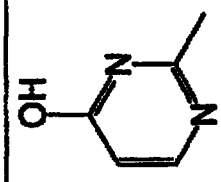
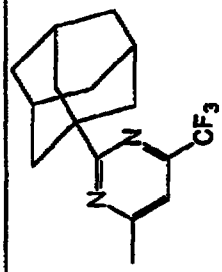
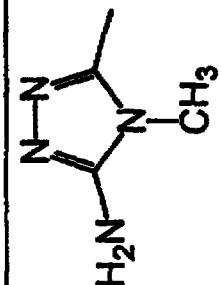
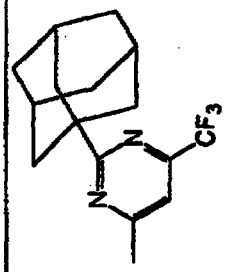
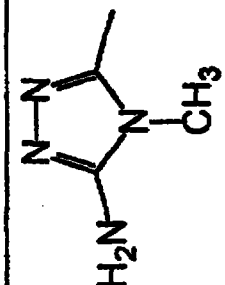
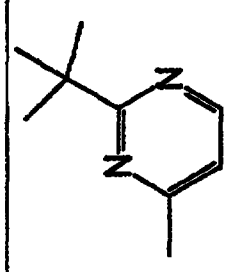
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
494				93 - 94 (Oxalat)
495				
496				168 - 170 (Fumarat)
497				

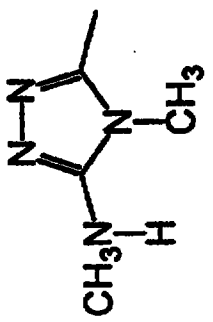
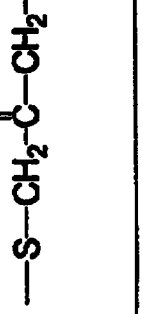
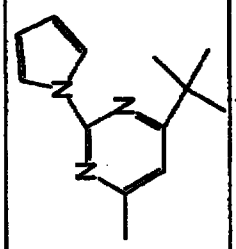
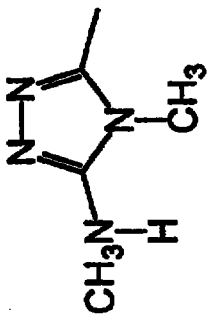
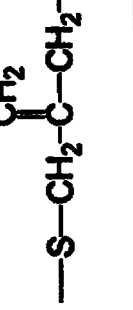
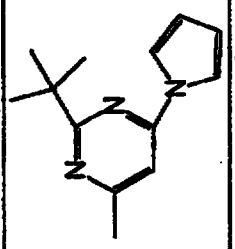
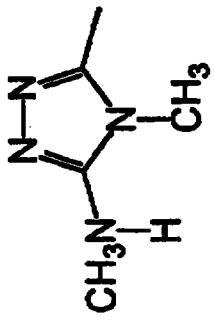
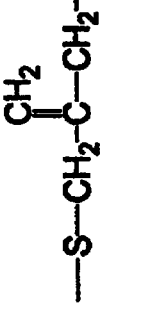
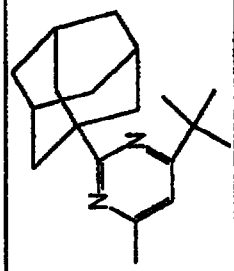
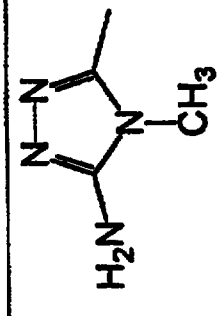
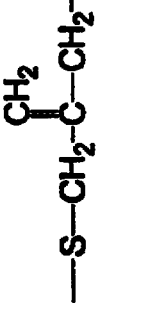
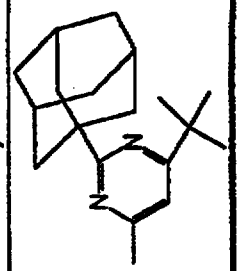
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
498				
499				
500				
501				

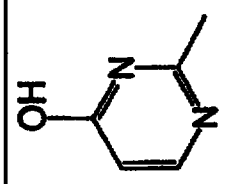
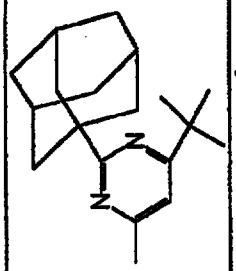
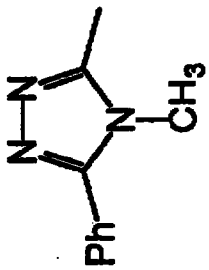
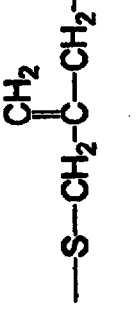
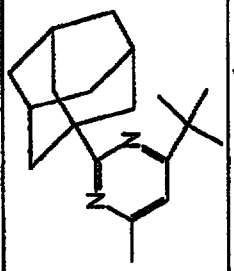
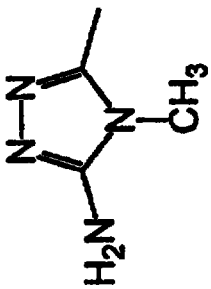
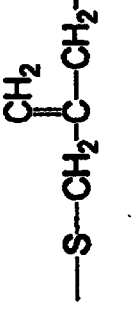
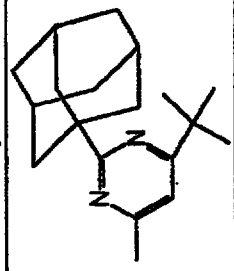
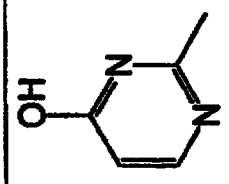
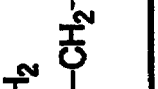
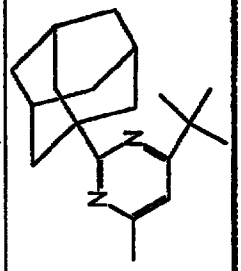
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
502				
503				
504				
505				

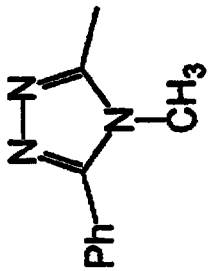
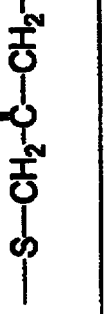
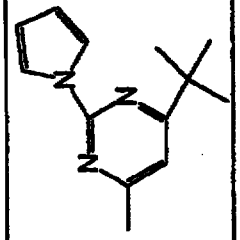
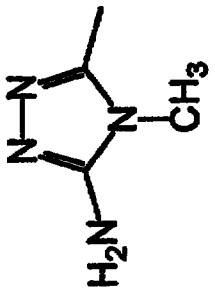
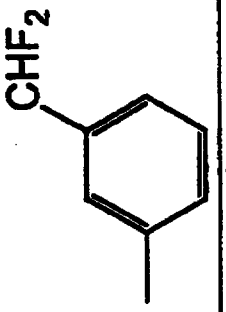
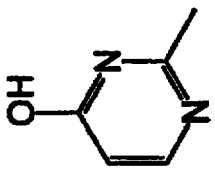
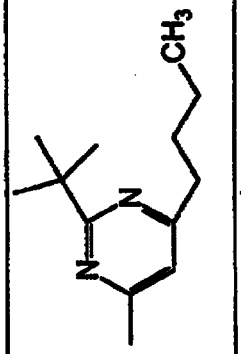
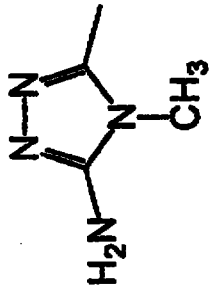
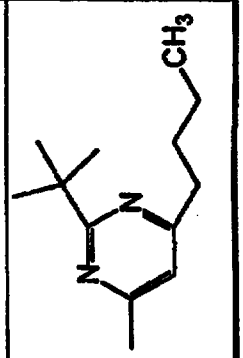
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
506				
507				
508				
509				

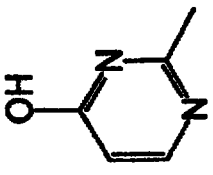
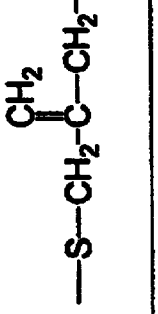
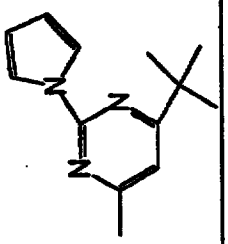
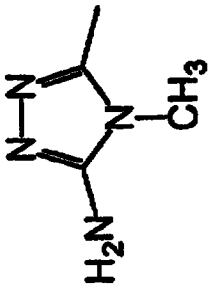
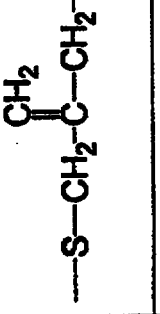
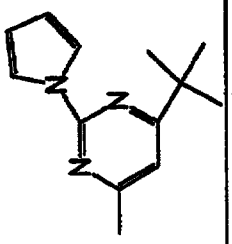
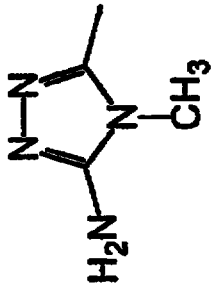
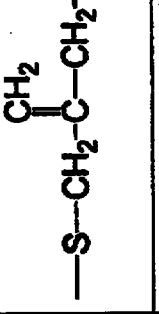
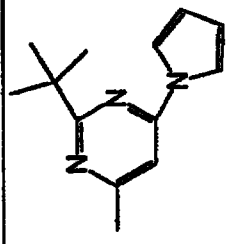
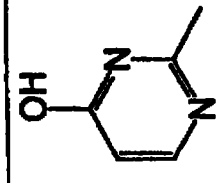
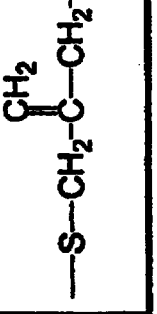
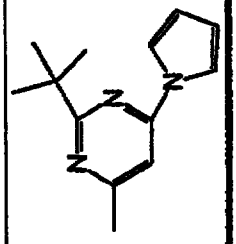
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
510				
511				
512				
513				

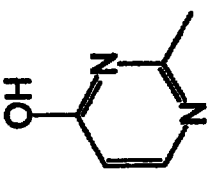
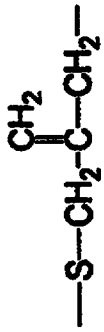
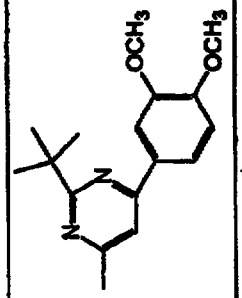
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
514				
515				
516				81 - 85
517				

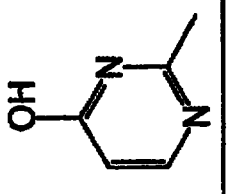
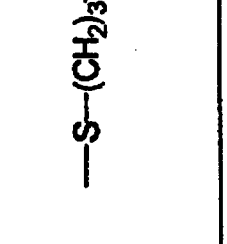
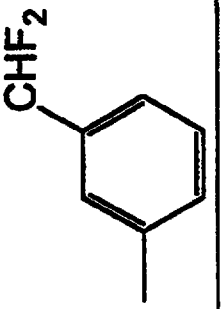
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
518				
519				
520				75 - 80
521				110 - 112 (Hydrochlorid)

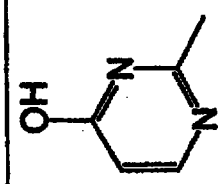
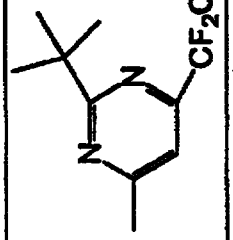
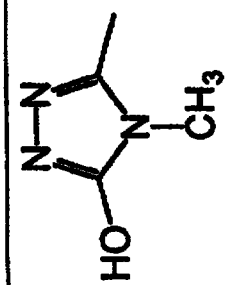
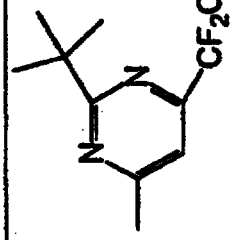
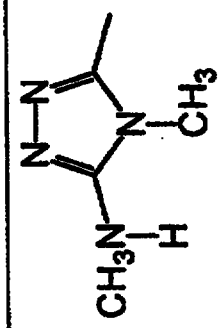
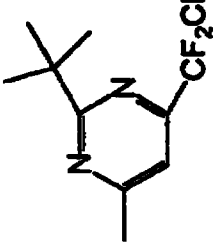
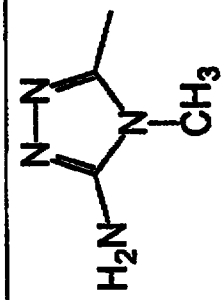
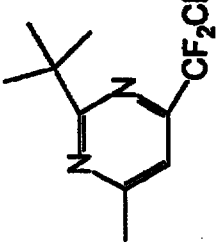
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
522				78 - 80
523				95 - 97 (Hydrochlorid)
524				142 - 145
525				80 - 91

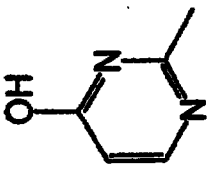
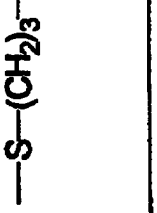
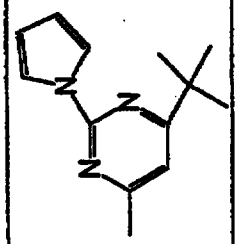
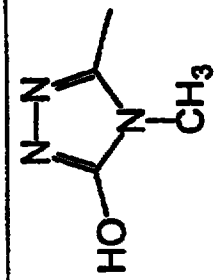
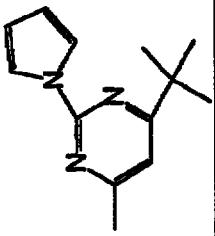
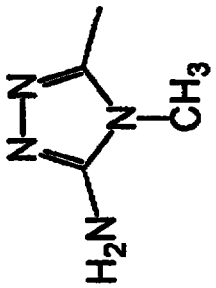
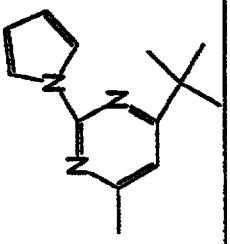
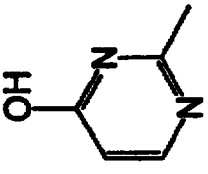
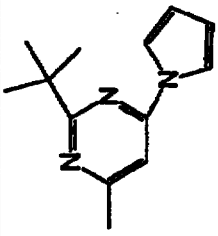
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
526				Oxalat
527		—S—$(CH_2)_8$—		Hydrochlorid
528		—S—$(CH_2)_3$—		Oxalat
529		—S—$(CH_2)_3$—		Dihydrochlorid

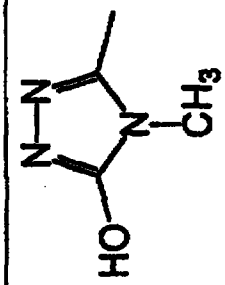
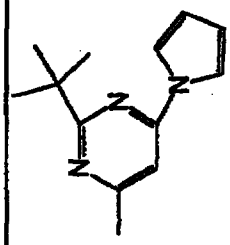
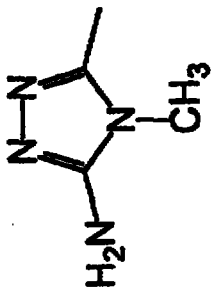
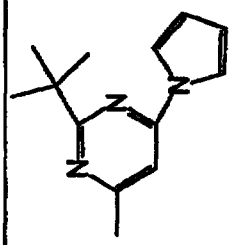
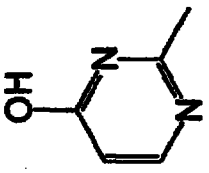
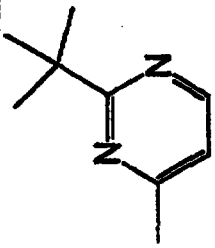
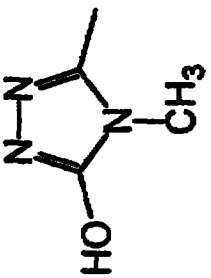
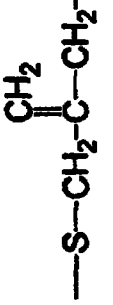
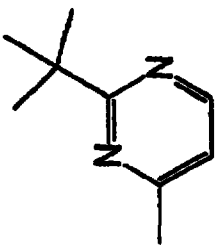
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
530				Oxalat
531				
532				
533				

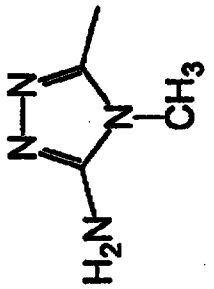
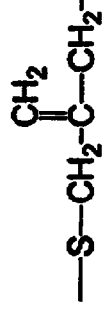
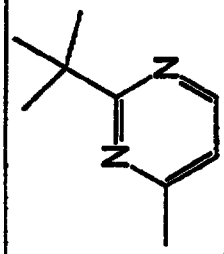
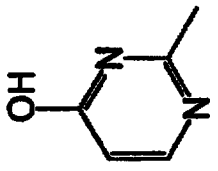
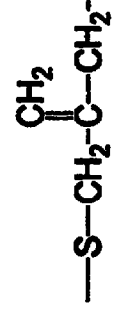
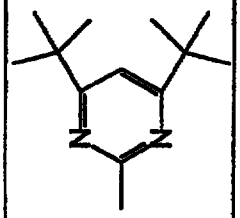
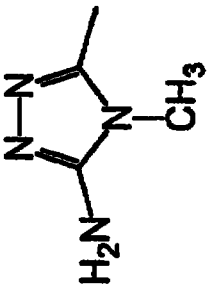
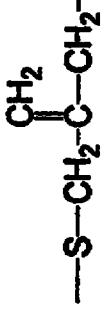
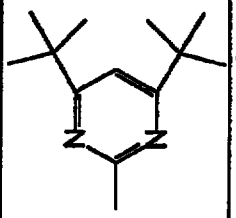
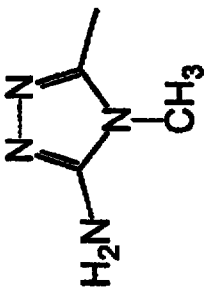
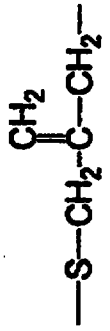
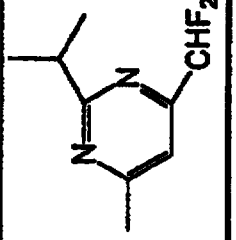
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
534				95 - 96
535				92
536				90
537				97

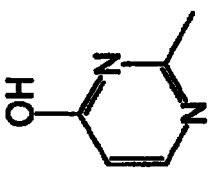
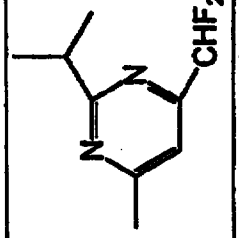
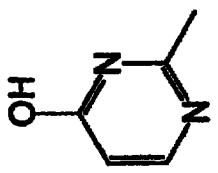
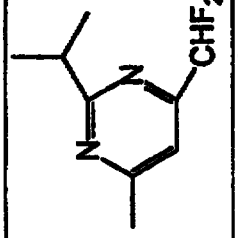
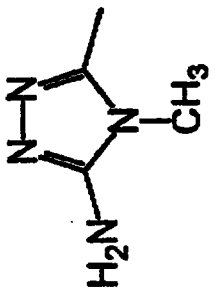
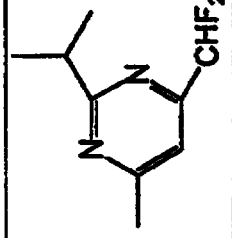
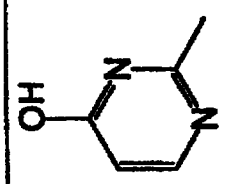
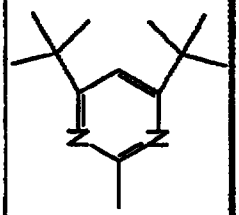
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
538				98 - 100
539				
540				
541				66 - 72

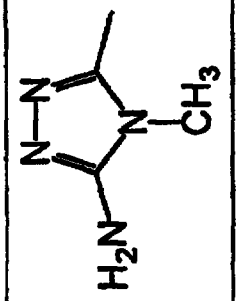
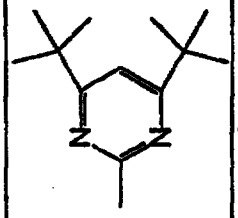
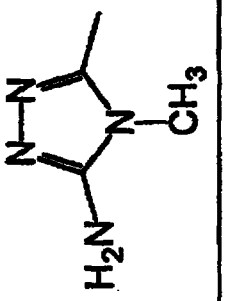
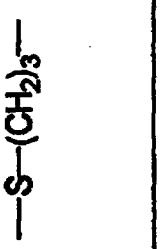
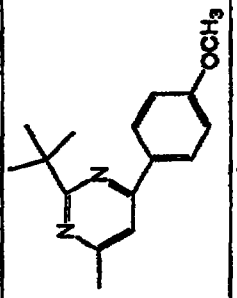
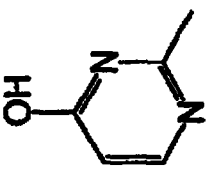
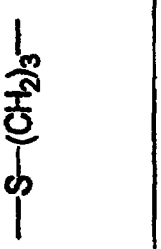
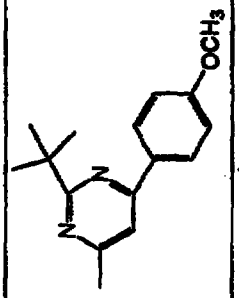
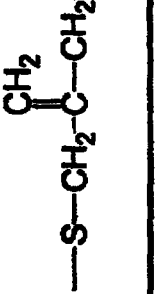
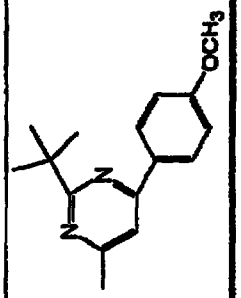
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
542				
543				
544				
545				

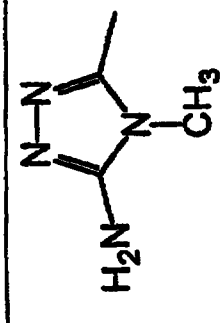
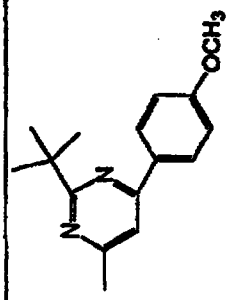
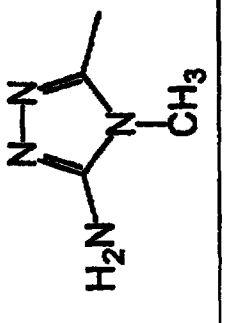
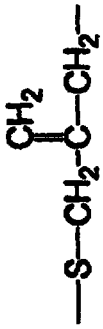
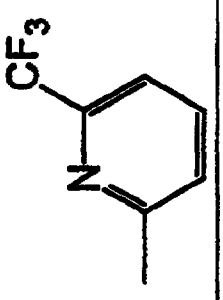
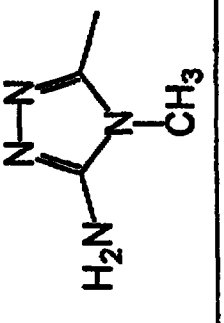
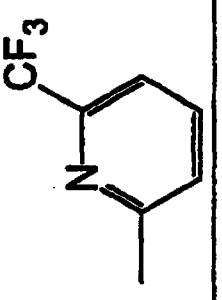
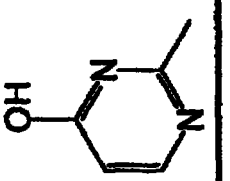
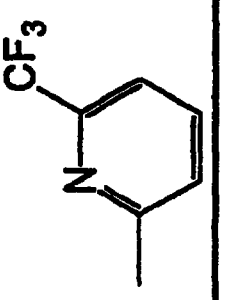
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
546				
547				
548				
549				

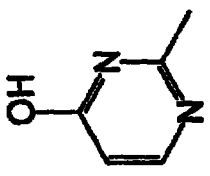
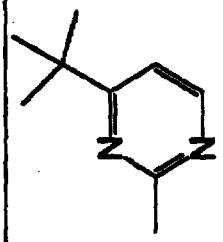
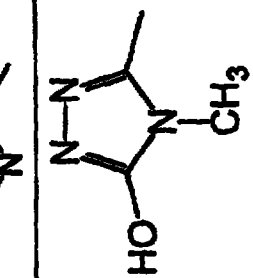
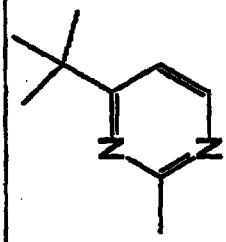
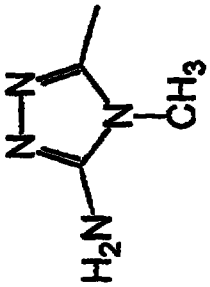
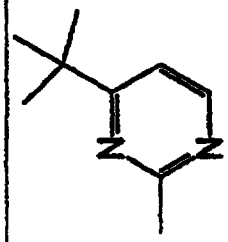
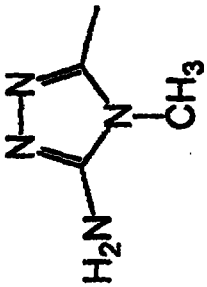
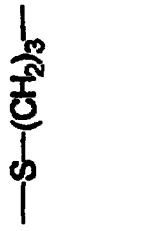
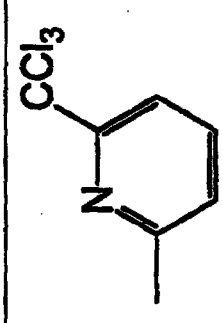
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
550				
551				
552				
553				

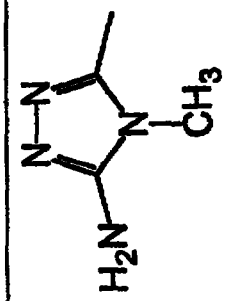
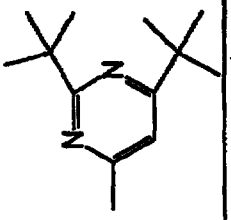
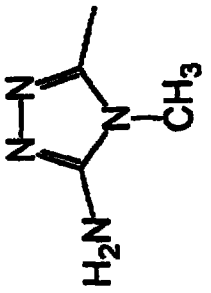
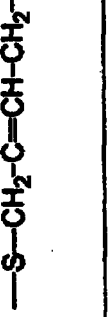
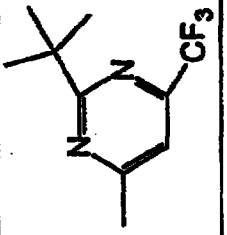
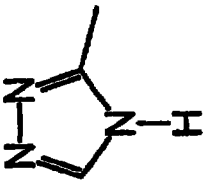
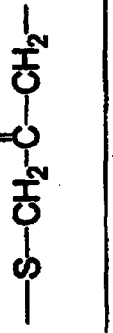
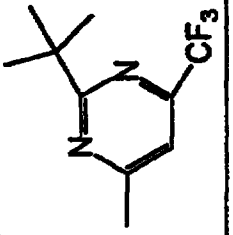
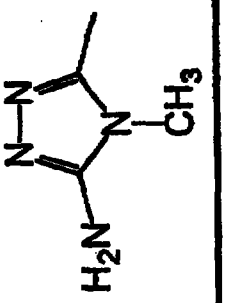
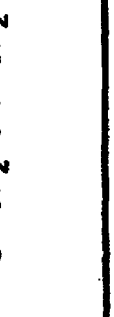
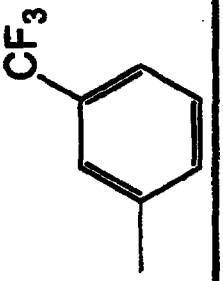
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
554				
555				
556				
557				

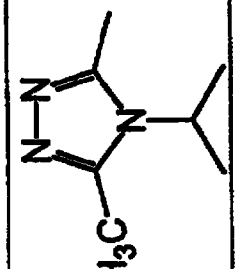
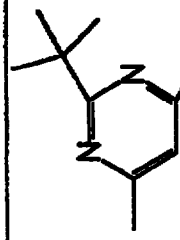
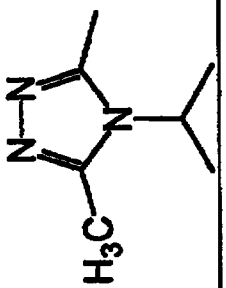
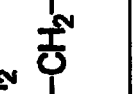
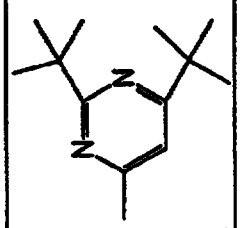
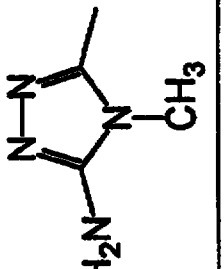
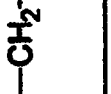
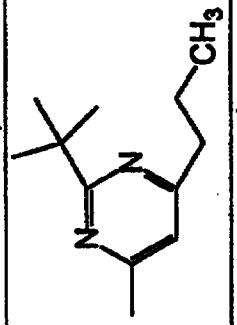
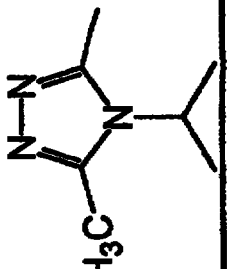
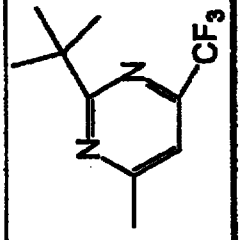
Rsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
558				100 - 103
559				
560				109 - 112
561				

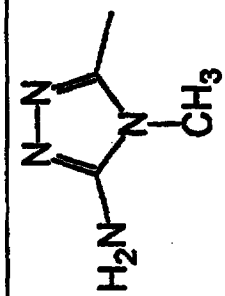
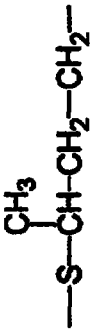
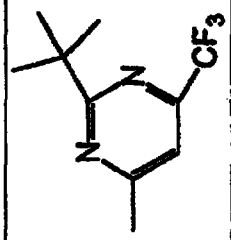
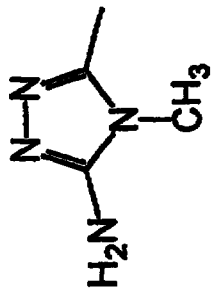
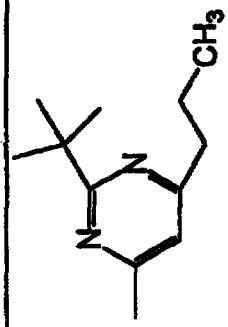
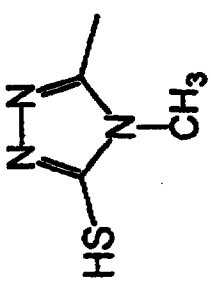
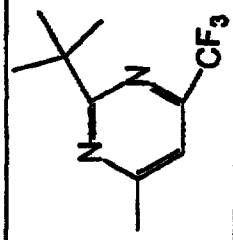
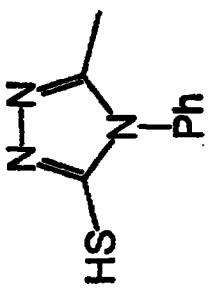
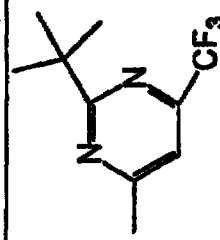
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
562				
563				
564				
565				84 - 85

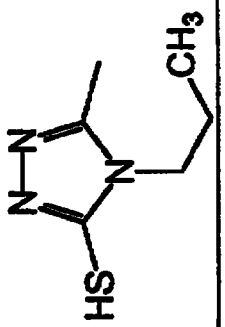
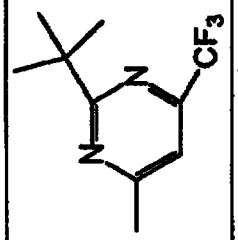
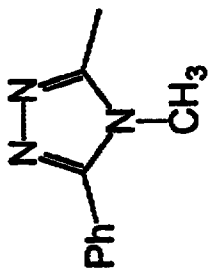
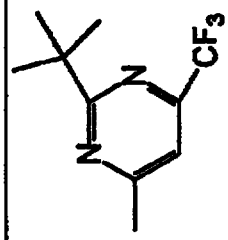
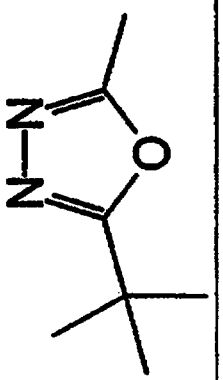
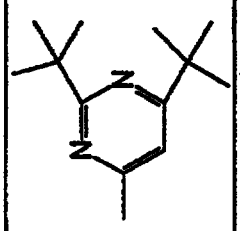
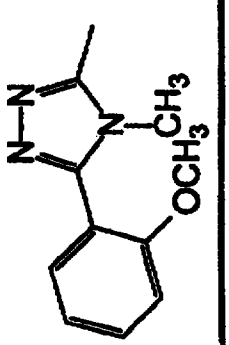
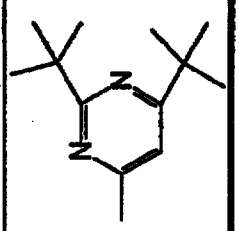
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
566				
567				
568				
569				

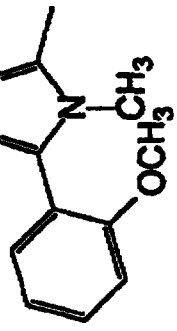
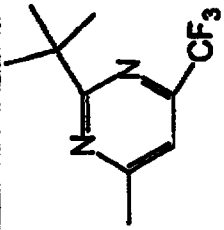
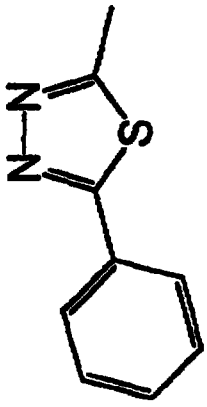
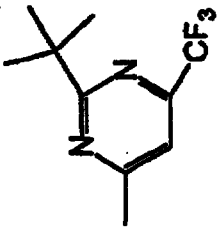
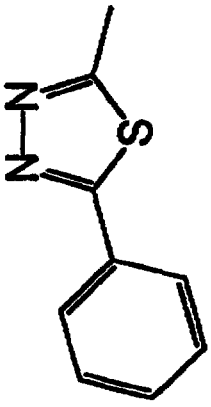
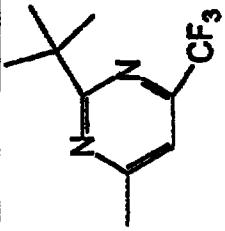
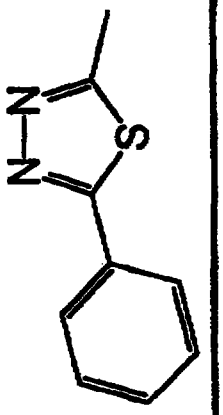
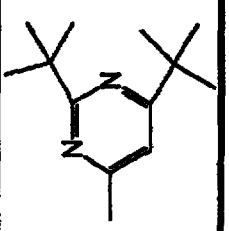
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
570				
571				
572				
573				185 - 190

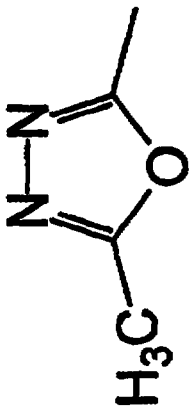
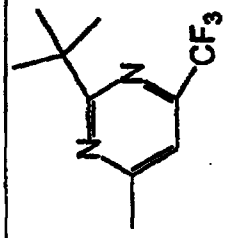
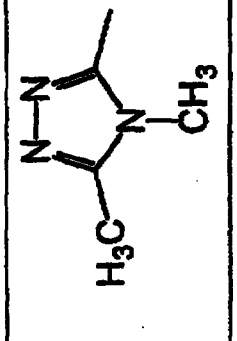
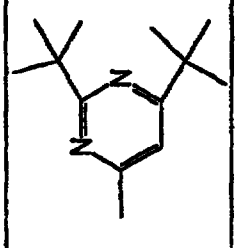
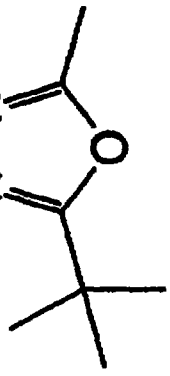
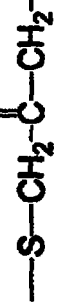
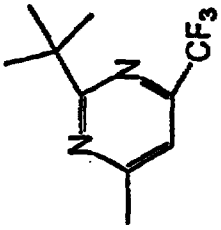
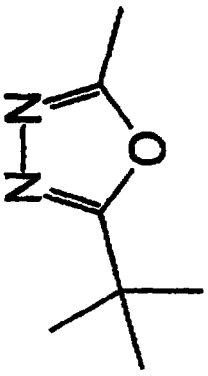
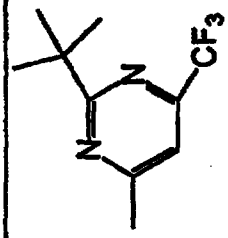
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
574				145 - 148
575				120 - 122
576				70 - 80 (Oxalat)
577				155 - 160 (Hydrochlorid)

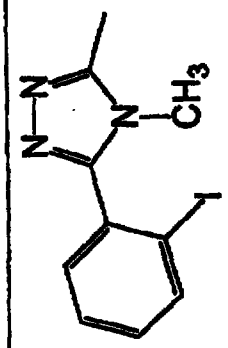
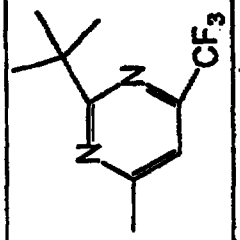
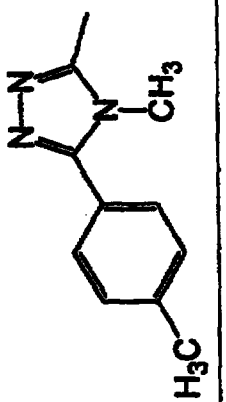
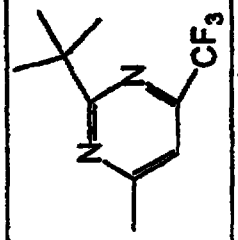
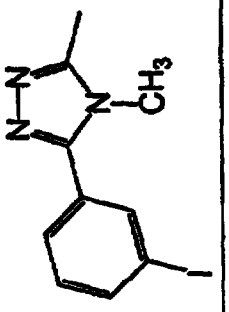
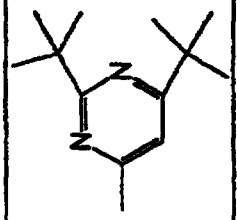
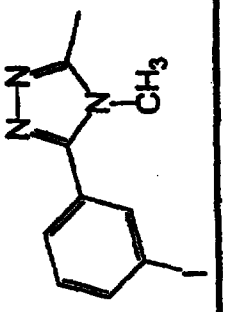
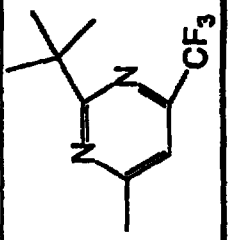
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
578				97 - 98 (Hydrochlorid)
579				141 - 143 (Fumarat)
580				105 - 108 (Hydrochlorid)
581				139 - 143 (Hydrochlorid)

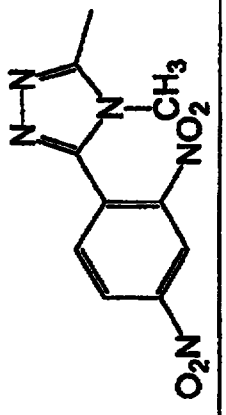
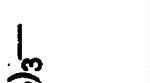
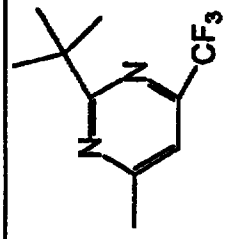
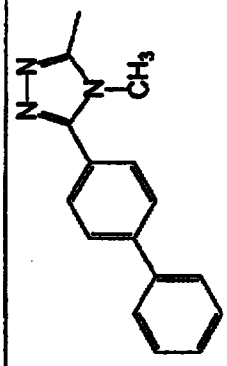
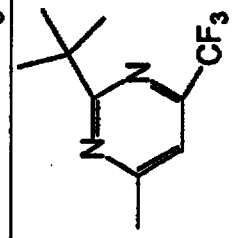
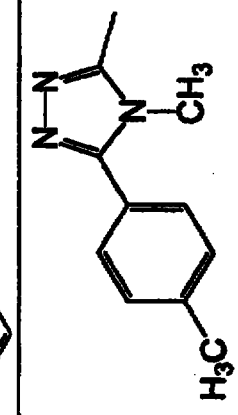
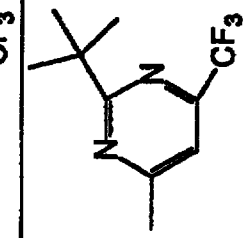
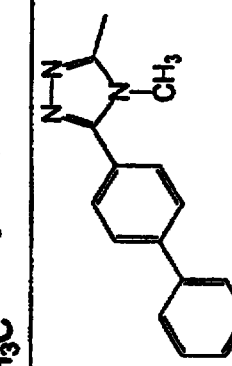
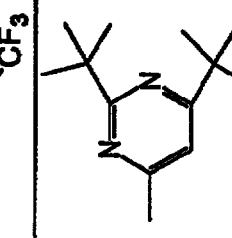
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
582				89 - 95
583				160 - 165 (Oxalat)
584				62 - 64
585				148 - 149

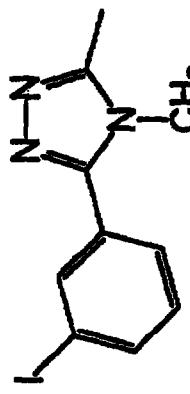
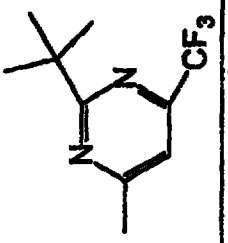
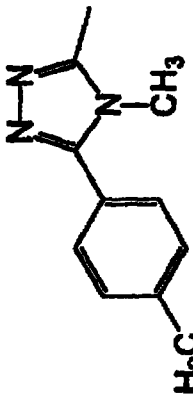
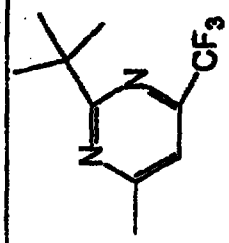
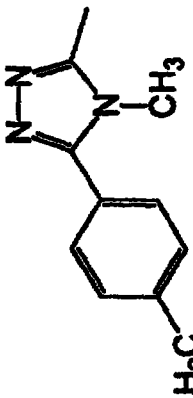
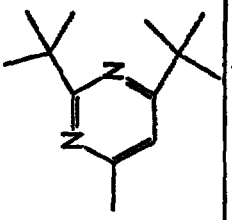
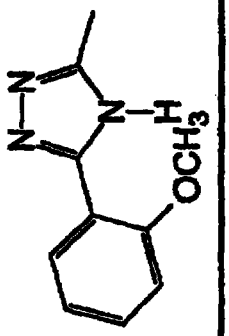
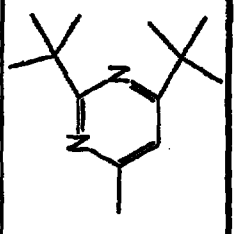
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
586		$-(CH_2)_4-$		38 - 41
587		$-CH=CH-(CH_2)_2-$		Öl
588		$-S-(CH_2)_3-$		90 (Zersetzung) (Hydrochlorid)
589		$-S-(CH_2)_3-$		90 - 93 (Fumarat)

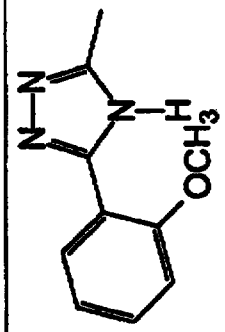
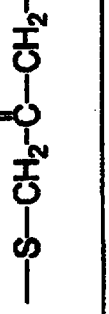
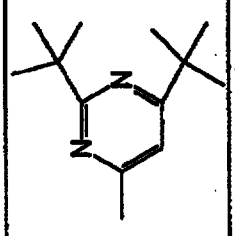
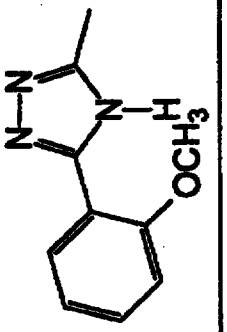
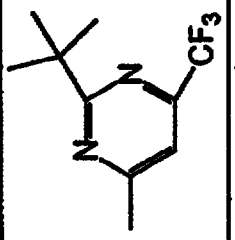
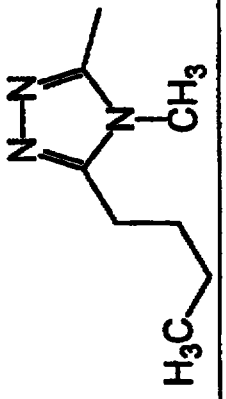
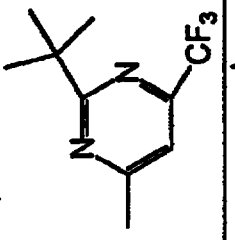
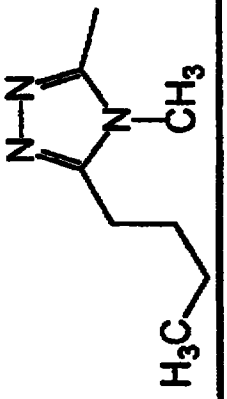
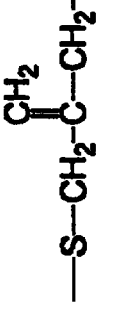
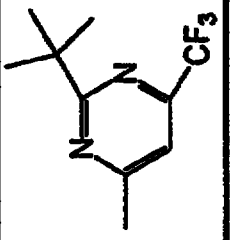
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
590				75 - 78 (Fumarat)
591				Öl
592				130 - 133 (Hyrochlorid)
593				Öl

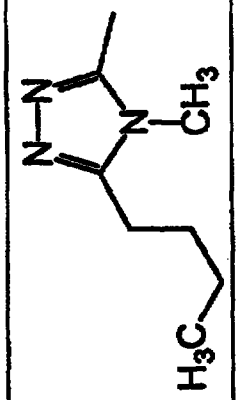
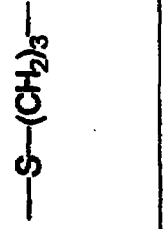
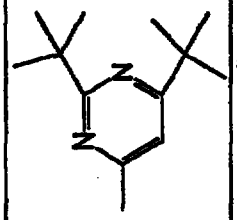
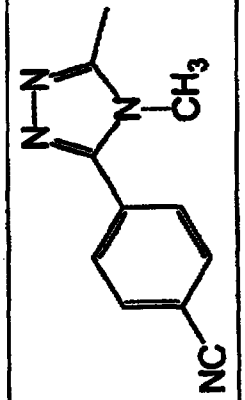
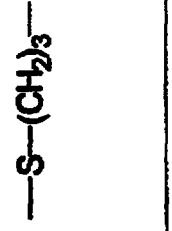
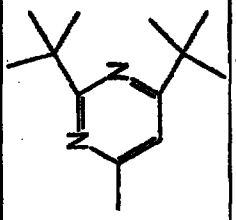
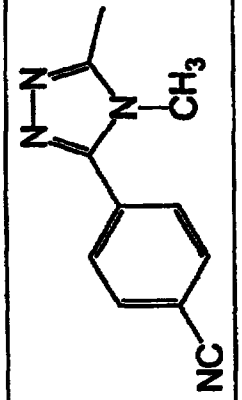
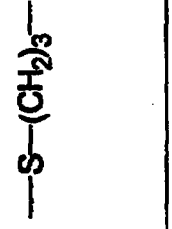
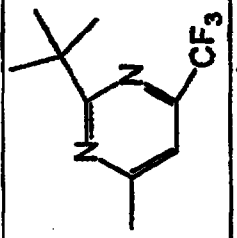
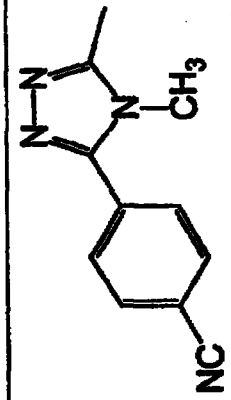
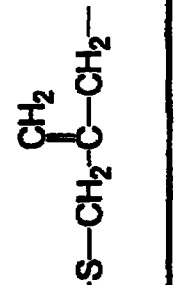
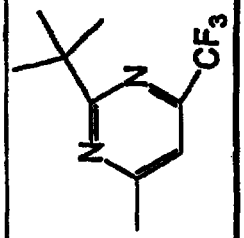
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
594				126 - 130 (Hydrochlorid)
595				90 - 95 (Zersetzung) (Hydrochlorid)
596				Öl
597				Öl

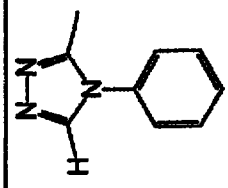
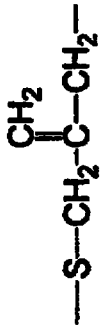
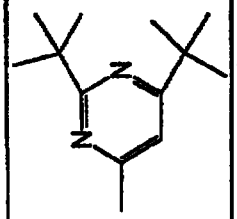
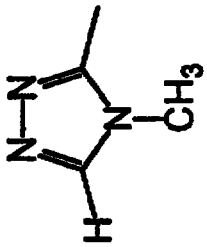
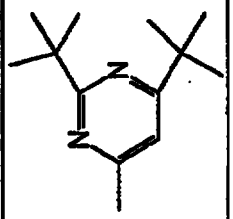
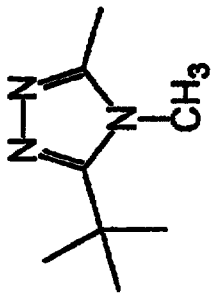
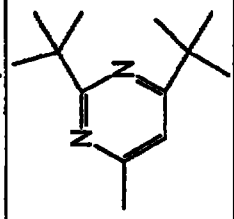
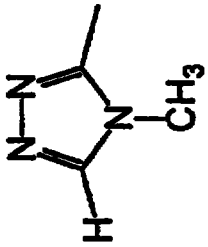
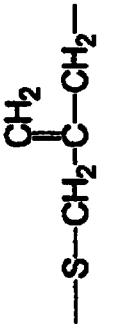
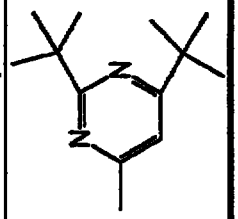
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
598		—S—$(CH_2)_3$—		106 (Hydrochlorid)
599		—S—$(CH_2)_3$—		148 (Hydrochlorid)
600		—S—$(CH_2)_3$—		137 - 139 (Hydrochlorid)
601		—S—CH_2—C(CH_2)—CH_2—		109 - 115 (Hydrochlorid)

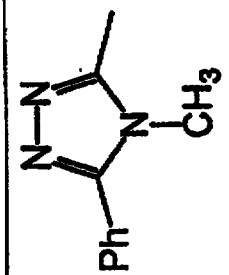
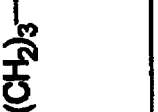
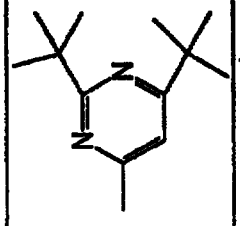
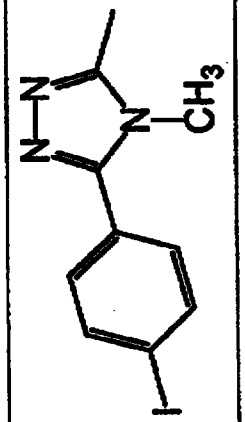
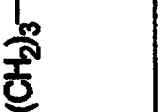
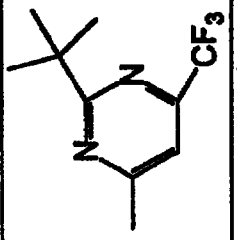
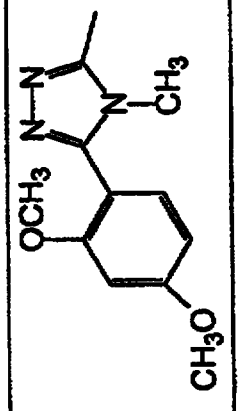
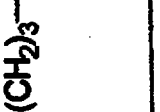
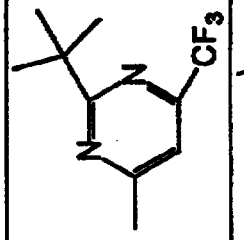
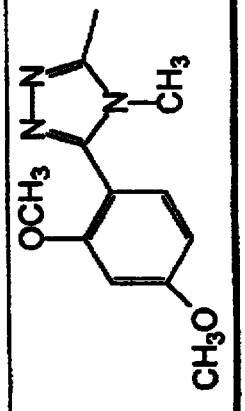
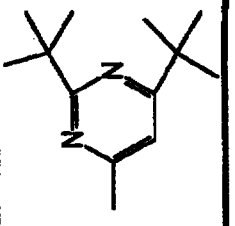
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
602				90 (Zersetzung) (Hydrochlorid)
603				132 (Zersetzung) (Hydrochlorid)
604				103 - 105 (Hydrochlorid)
605				142 - 144

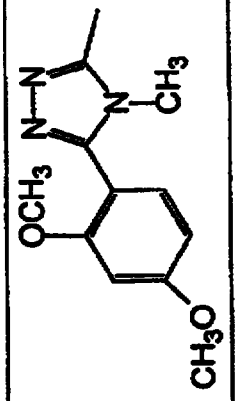
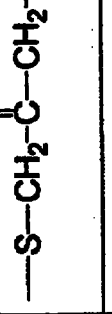
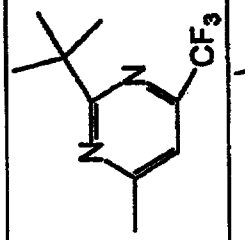
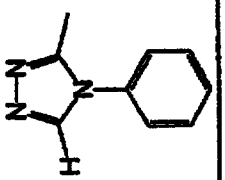
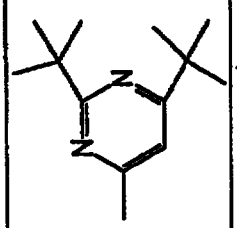
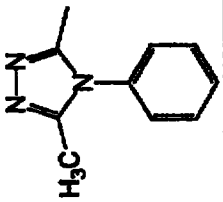
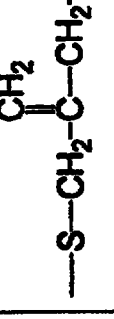
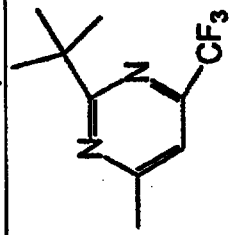
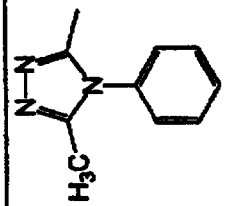
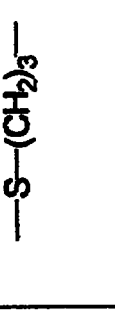
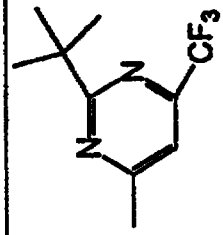
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
606		$-S-(CH_2)_3-$		Öl
607		$-S-(CH_2)_3-$		Öl
608		$-S-(CH_2)_3-$		120 - 123 (Hydrochlorid)
609		$-S-(CH_2)_3-$		187 - 189 (Fumarat)

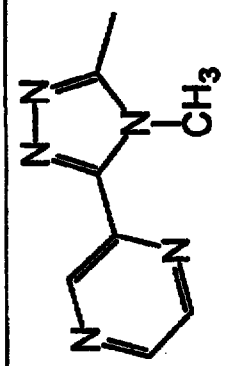
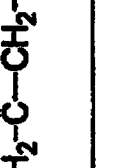
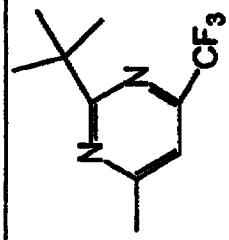
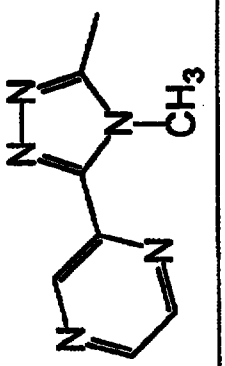
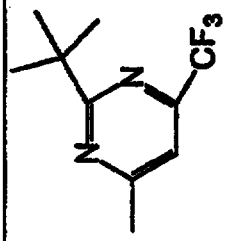
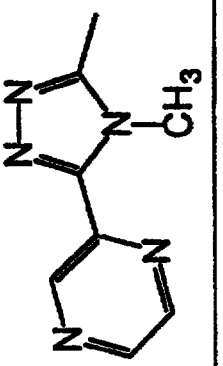
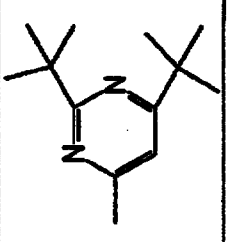
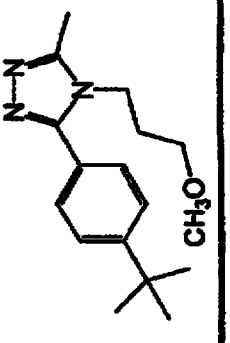
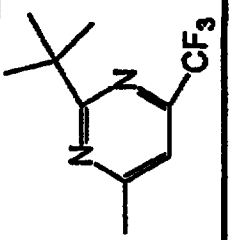
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
610				95 - 98 (Fumarat)
611				68 - 72 (Fumarat)
612				240 (Hydrochlorid)
613				190 (Hydrochlorid)

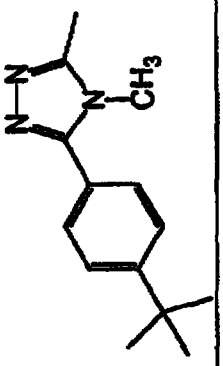
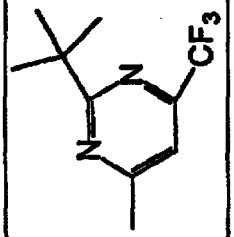
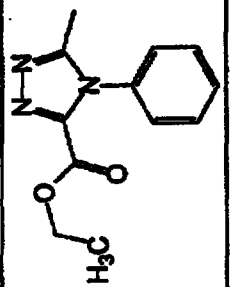
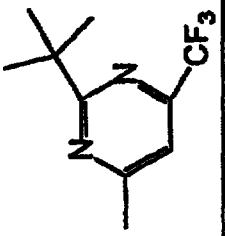
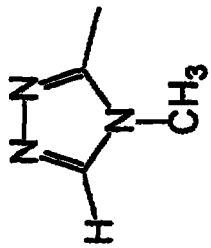
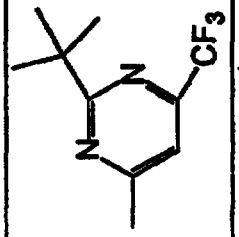
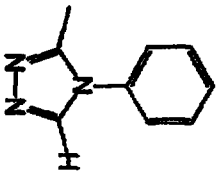
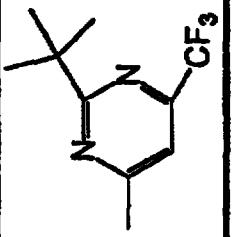
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
614				243 (Hydrochlorid)
615				101 - 104
616				öl
617				90 - 94 (Zersetzung) (Hydrochlorid)

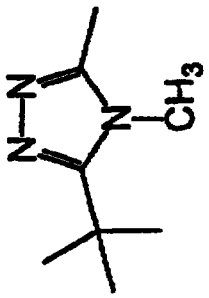
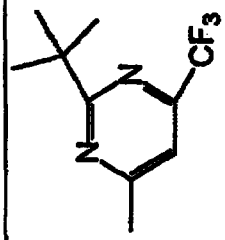
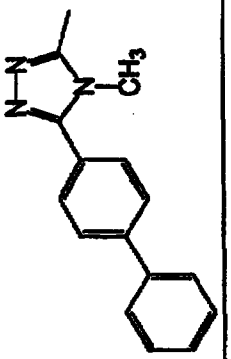
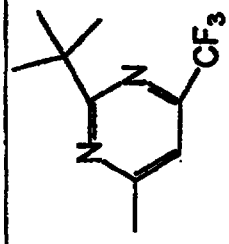
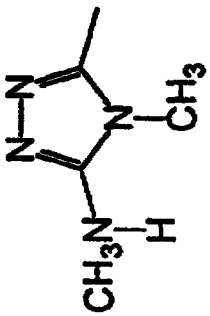
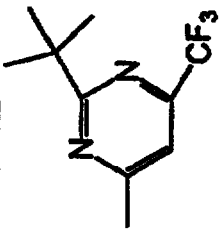
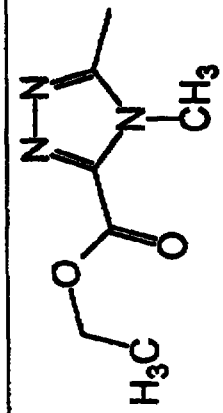
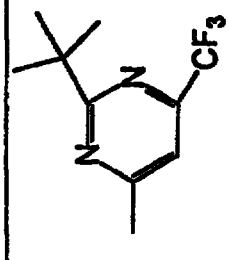
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
618				152 (Hydrochlorid)
619				Öl
620				Öl
621				152 (Hydrochlorid)

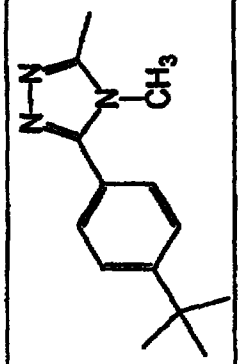
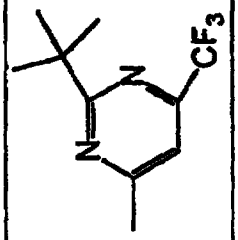
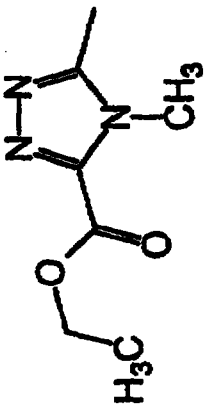
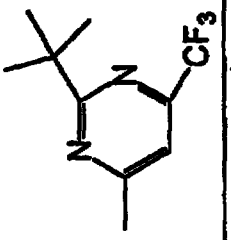
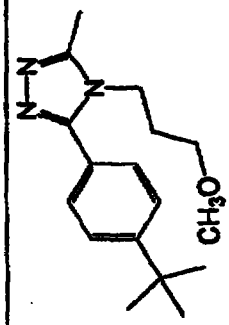
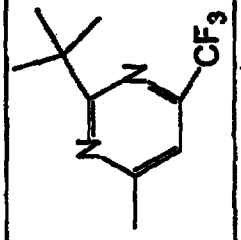
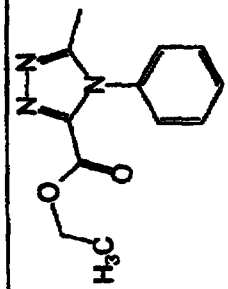
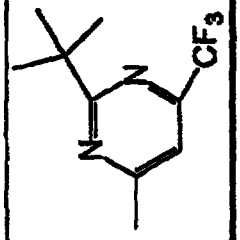
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
622				110 (Hydrochlorid)
623				126 - 131 (Hydrochlorid)
624				91 (Hydrochlorid)
625				116 - 120 (Hydrochlorid)

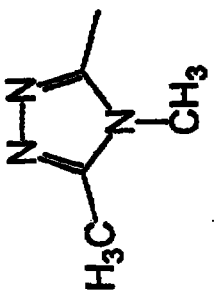
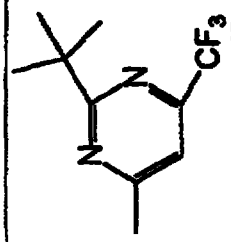
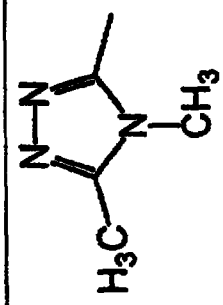
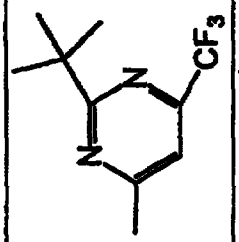
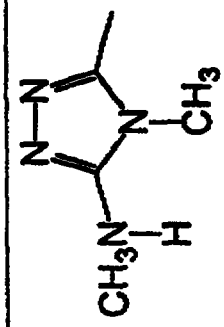
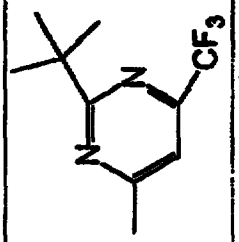
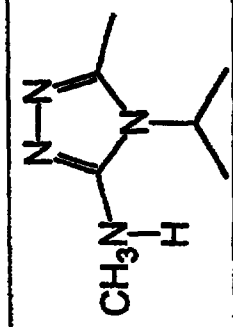
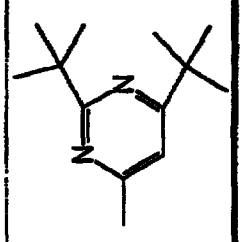
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
626				103 (Hydrochlorid)
627				150 (Hydrochlorid)
628				140 (Hydrochlorid)
629				130 (Hydrochlorid)

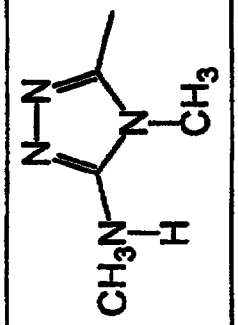
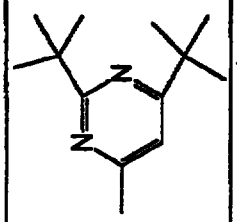
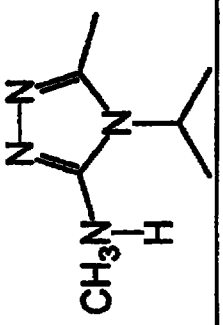
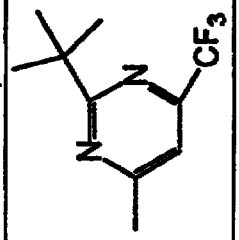
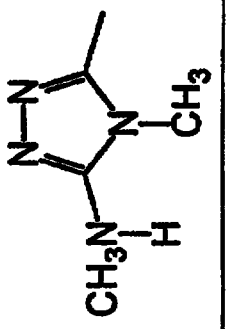
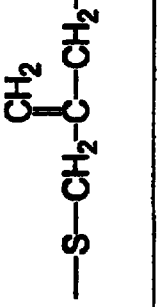
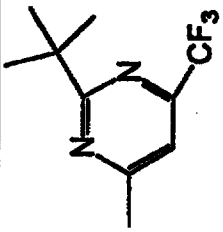
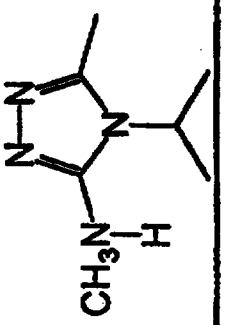
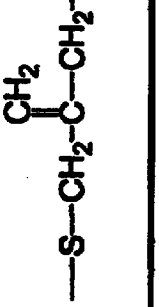
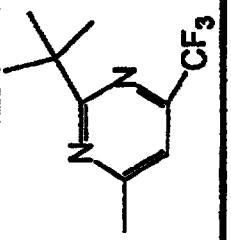
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
630				98 - 104 (Hydrochlorid)
631				65 - 68 (Hydrochlorid)
632				131 - 136 (Hydrochlorid)
633				105 (Hydrochlorid)

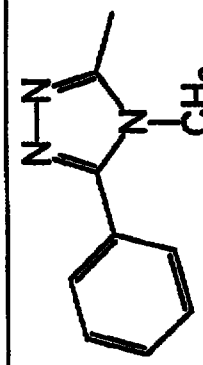
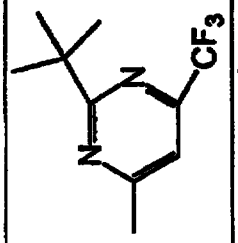
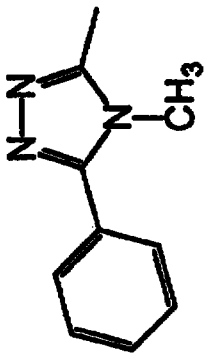
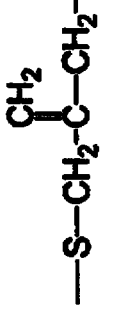
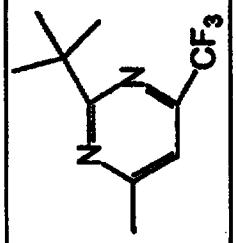
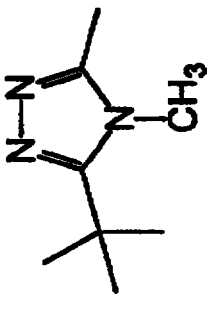
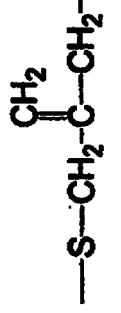
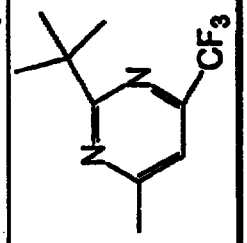
Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
634				132 (Hydrochlorid)
635				92 (Hydrochlorid)
636				95 (Hydrochlorid)
637				102 (Hydrochlorid)

Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
638		$-S-(CH_2)_3-$		214 - 216 (Hydrochlorid)
639		$-S-(CH_2)_3-$		160 - 162 (Hydrochlorid)
640		$-S-(CH_2)_3-$		73 - 75 (Fumarat)
641		$-S-CH_2-C(CH_2)-CH_2-$		178

Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
642		—S—$(CH_2)_3$—		155
643		—S—$(CH_2)_3$—		125 - 128 (Hydrochlorid)
644		—S—$(CH_2)_3$—		102 (Hydrochlorid)
645		—S—$(CH_2)_3$—		88 (Hydrochlorid)

Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
646				132 (Hydrochlorid)
647				190 (Hydrochlorid)
648				134 - 138 (Hydrochlorid)
649				170 - 174 (Hydrochlorid)

Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
650				115 (Hydrochlorid)
651				117 (Hydrochlorid)
652				151 - 155
653				158 - 161 (Hydrochlorid)

Bsp.-Nr.	Ar^1	A	Ar^2	Schmelzpunkt [°C]
654				184 - 185 (Hydrochlorid)
655				194 - 195 (Hydrochlorid)
656				114 (Hydrochlorid)

Die obigen Verbindungen, die nicht durch den Schmelzpunkt charakterisiert sind, besitzen die folgenden NMR-Spektren (d_6-DMSO):

Bsp.-Nr.		
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	Oxalat	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	Oxalat	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	Oxalat	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	Oxalat	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	Fumarat	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	Fumarat	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	Fumarat	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-chlorid	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	Fumarat	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	Fumarat	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	Fumarat	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	Fumarat	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	Fumarat	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-chlorid	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-chlorid	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-chlorid	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	Oxalat	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	Oxalat	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-chlorid	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	Oxalat	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-chlorid	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-chlorid	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-chlorid	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-chlorid	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-chlorid	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-chlorid	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	Oxalat	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	Oxalat	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);

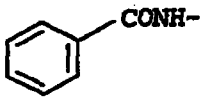
566		1,4 (s,9H); 1,9 (b,2H); 2,5 (b,2H); 2,8 (b,2H); 3,2 (s,2H); 3,3 (s,3H); 3,6 (s,2H); 3,6-3,8 (b,4H); 3,8 (s,3H); 4,8 (b,2H); 5,0 (s,2H); 6,5 (s,1H); 7,0 (d,1H); 8,0 (d,1H);
567	Oxalat	2,0 (b,2H); 2,8 (b,2H); 3,0 (b,2H); 3,3 (s,3H); 3,4 (s,2H); 3,6 (b,4H); 3,8 (b,2H); 5,1 (s,2H); 5,5 (b,2H); 7,0 (m,2H); 7,7 (t,1H);
568	Oxalat	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	Oxalat	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-chlorid	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-chlorid	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)

Patentansprüche

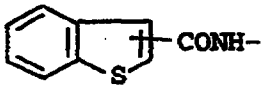
1. Verbindungen der allgemeinen Formel I

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

worin
Ar^1 für



oder



oder einen 5- oder 6-gliedrigen aromatischen Heteromonocyclus mit 1, 2 oder 3 Heteroatomen, die unabhängig voneinander ausgewählt sind unter O, N und S steht, wobei Ar^1 gegebenenfalls 1, 2, 3 oder 4 Substituenten aufweist, die unabhängig voneinander ausgewählt sind unter OR^1, Alkyl, das gegebenenfalls durch OH, OC_1-C_8-Alkyl oder Halogen substituiert ist, C_2-C_6-Alkenyl, C_2-C_6-Alkinyl, Cycloalkyl, Halogen, CN, CO_2R^1, NO_2, NR^1R^2, SR^1, CF_3, CHF_2, Phenyl, das gegebenenfalls durch C_1-C_6-Alkyl, OC_1-C_6-Alkyl, Acyl, Phenyl, Amino, Nitro, Cyano oder Halogen substituiert ist, Phenoxy, das gegebenenfalls durch C_1-C_6-Alkyl, OC_1-C_6-Alkyl oder Halogen substituiert ist, C_1-C_6-Alkanoyl oder Benzoyl;

R^1 für H, Alkyl, das gegebenenfalls durch OH, OC_1-C_6-Alkyl, Phenyl oder Halogen substituiert ist, steht;

R^2 die für R^1 angegebenen Bedeutungen besitzt oder für COR^1 oder CO_2R^1 steht;

A für eine C_3-C_{15}-Alkylengruppe steht, wenn Ar^1 für C_6H_5CONH steht, oder, wenn Ar^1 einen 5- oder 6-gliedrigen aromatischen Heteromonocyclus bedeutet, für eine C_4-C_{15}-Alkylengruppe oder eine C_3-C_{15}-Alkylengruppe steht, die wenigstens eine Gruppe Z umfaßt, die ausgewählt ist unter O, S, NR^1, einer Doppel- und einer Dreifachbindung, wobei R^1 wie oben definiert ist,

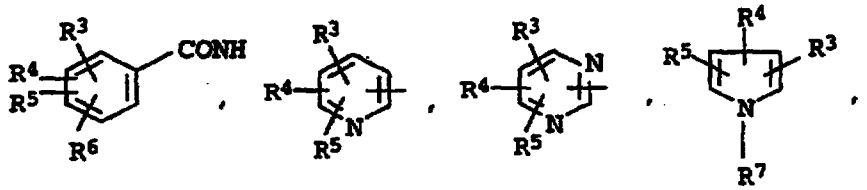
B für einen 7- oder 8-gliedrigen gesättigten Ring mit einem oder zwei Stickstoffheteroatomen steht, wobei sich die Stickstoffheteroatome in 1,4- oder 1,5-Position befinden und der Ring in 1-Position an den Rest A und in 4- oder 5-Position an den Rest Ar^2 gebunden ist und wobei der Ring außerdem eine Doppelbindung in 3- oder 4-Position aufweisen kann;

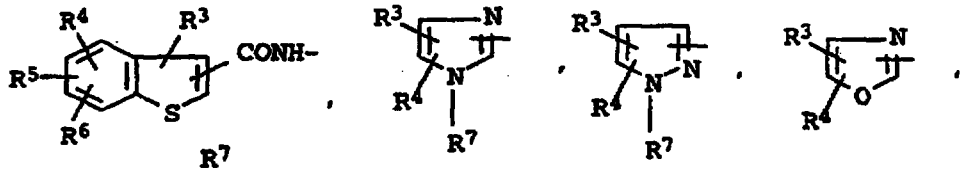
* C L M S *

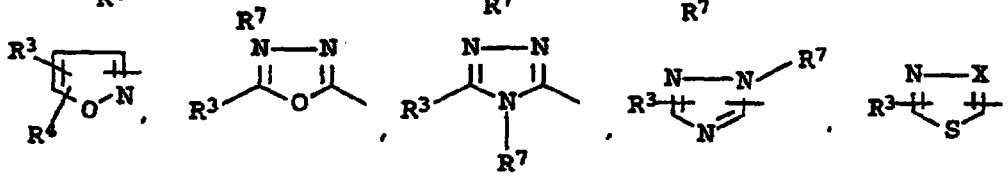
Ar^2 für Phenyl, Pyridyl, Pyrimidinyl oder Triazinyl steht, wobei Ar^2 gegebenenfalls 1, 2, 3 oder 4 Substituenten aufweisen kann, die unabhängig voneinander ausgewählt sind unter OR^1, Alkyl, C_2-C_6-Alkenyl, C_2-C_6-Alkinyl, Alkoxyalkyl, Halogenalkyl, Halogen, CN, CO_2R^1, NO_2, SO_2R^1, NR^1R^2, $SO_2NR^1R^2$, SR^1, einem 5- oder 6-gliedrigen carbocyclischen, aromatischen oder nicht-aromatischen Ring und einem 5- oder 6-gliedrigen heterocyclischen aromatischen oder nicht-aromatischen Ring mit 1 bis 3 Heteroatomen, die ausgewählt sind unter O, S und N, wobei der carbocyclische oder der heterocyclische Ring gegebenenfalls substituiert ist durch C_1-C_8-Alkyl, Phenyl, Halogen, OC_1-C_8-Alkyl, OH, NO_2 oder CF_3, wobei Ar^2 gegebenenfalls mit einem carbocyclischen Ring der oben definierten Art kondensiert sein kann und wobei Ar^2 nicht für einen Pyrimidinylrest stehen kann, der mit 2 Hydroxygruppen substituiert ist,

und die Salze davon mit physiologisch verträglichen Säuren.

2. Verbindungen nach Anspruch 1 der Formel I, worin Ar^1 für

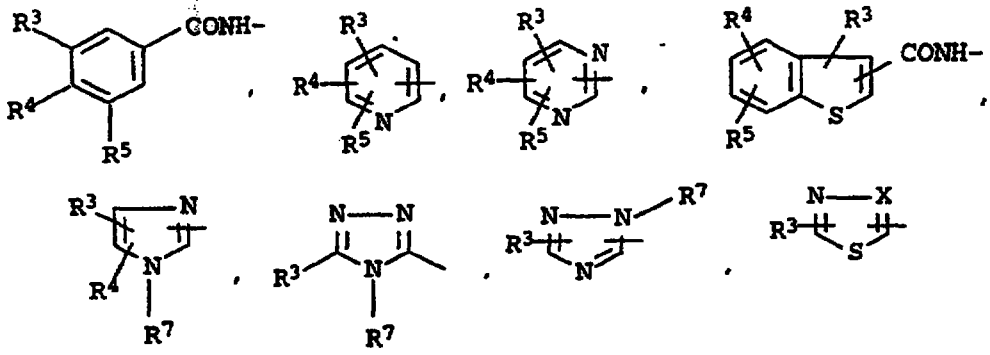






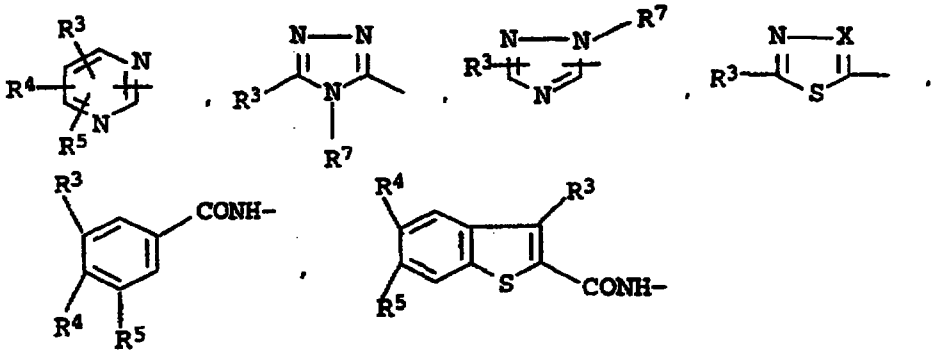
steht, worin
R^3 bis R^6 unabhängig voneinander für H oder die in Anspruch 1 genannten Substituenten des Restes Ar^1 stehen,
R^7 die in Anspruch 1 für R^2 angegebenen Bedeutungen besitzt oder für Cycloalkyl steht und
X für N oder CH steht.

3. Verbindungen nach Anspruch 1 der Formel I, worin Ar^1 für



steht, worin R^3 bis R^5, R^7 und X die in Anspruch 2 angegebenen Bedeutungen besitzen.

4. Verbindungen nach Anspruch 3 der Formel I, worin
Ar^1 für



steht,
worin R^3 bis R^5, R^7 und X die in Anspruch 2 angegebenen Bedeutungen besitzen.

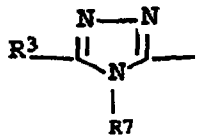
5. Verbindungen nach Anspruch 4 der Formel I, worin R^3, R^4 und R^5 unabhängig voneinander für H, OR^1, Alkyl, NR^1R^2, Halogen, Phenoxy, CN, Phenyl, das gegebenenfalls durch C_1-C_6-Alkyl, Acyl oder Halogen substituiert ist, oder $COOR^1$ steht;
R^1 und R^2 unabhängig voneinander für H, Alkyl oder Benzyl stehen;
R^7 für H, Alkyl oder Cycloalkyl steht; und
X für N oder CH steht.

6. Verbindungen nach Anspruch 5, wobei R^3 bis R^6 unabhängig voneinander ausgewählt sind unter H, C_1-C_6-Alkyl, OR^1, NR^1R^2, Phenyl, das gegebenenfalls durch C_1-C_6-Alkyl, Acyl oder Halogen substituiert ist, und Halogen, wobei R^1 und R^2 die oben angegebenen Bedeutungen besitzen, R^7 für H oder Alkyl steht und X für N steht.

* C L M S *

7. Verbindungen nach Anspruch 6, wobei Ar^1 für Pyrimidinyl steht, das gegebenenfalls durch OH, OAlkyl oder OBenzyl substituiert ist.

8. Verbindungen nach Anspruch 6, wobei Ar^1 für



steht, worin R^3 für NR^1R^2 steht, wobei R^1 und R^2 die in Anspruch 5 angegebenen Bedeutungen besitzen und R^7 für H oder Alkyl steht.

9. Verbindungen nach Anspruch 6, wobei Ar^1 für Thiadiazol steht, das gegebenenfalls durch NR^1R^2 substituiert ist, wobei R^1 und R^2 die in Anspruch 5 angegebenen Bedeutungen besitzen.

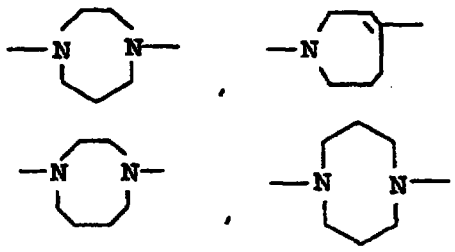
10. Verbindungen nach Anspruch 6, wobei Ar^1 für



steht, worin R^3 und R^5 unabhängig voneinander für H oder Halogen, Alkyl oder Phenyl stehen.

11. Verbindungen nach einem der vorhergehenden Ansprüche der Formel I, worin A für -Z-C_3-C_6-Alkylen, insbesondere -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-$CH_2CH(CH_3)CH_2$- oder für einen linearen -Z-C_7-C_{10}-Alkylenrest steht, wobei Z an Ar^1 gebunden ist und für CH_2, O oder S steht.

12. Verbindungen nach einem der vorhergehenden Ansprüche der Formel I, worin B für



steht.

13. Verbindungen nach einem der vorhergehenden Ansprüche der Formel I, worin Ar^2 für Phenyl, Pyridinyl oder Pyrimidinyl steht, das gegebenenfalls einen oder zwei Substituenten aufweist, die unabhängig voneinander ausgewählt sind unter C_1-C_6-Alkyl, C_2-C_6-Alkinyl, Halogen, CN, Halogenalkyl, OAlkyl, NO_2, Phenyl, Pyrrolyl, Imidazolyl, Pyrazolyl, Thienyl, Cyclopentyl und Cyclohexyl.

14. Verbindungen nach Anspruch 13 der Formel I, worin der und die Substituenten unabhängig voneinander ausgewählt sind unter C_1-C_6-Alkyl, NO_2, und Halogenalkyl, insbesondere CF_3, CHF_2 und CF_2Cl.

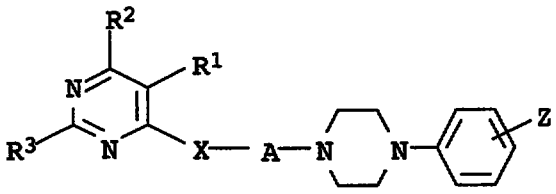
15. Pharmazeutisches Mittel, enthaltend wenigstens eine Verbindung nach einem der Ansprüche 1 bis 15, gegebenenfalls zusammen mit physiologisch akzeptablen Trägern und/oder Hilfsstoffen.

16. Verwendung wenigstens einer Verbindung nach einem der Ansprüche 1 bis 15 zur Herstellung eines pharmazeutischen Mittels zur Behandlung von Erkrankungen, die auf Dopamin-D_3-Rezeptorantagonisten bzw. -agonisten ansprechen.

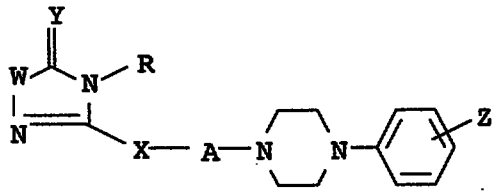
Substituted aza- and diazacycloheptane and -cyclooctane compounds and their use

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:



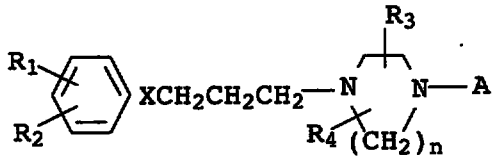
(A)



(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.

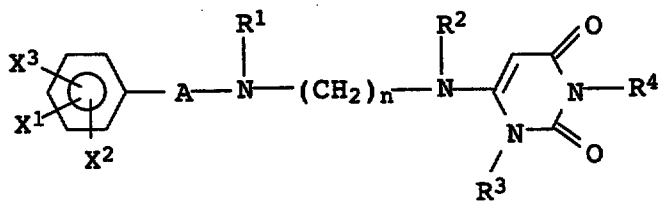
EP-A-361271 describes pyridyl and pyrimidyl derivatives of the formula:



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.

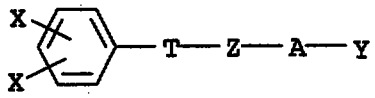
EP-A-454498 describes compounds of the formula



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.

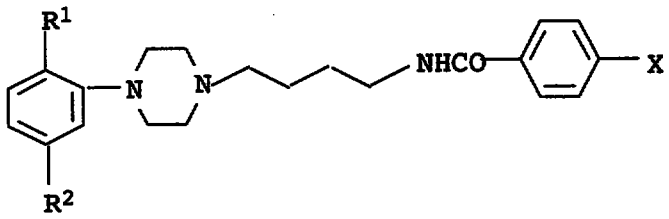
Confirmed information on the presence of dopamine and its physiological function as neurotransmitter is available. Cells responding to dopamine are connected with the etiology of schizophrenia and Parkinson's disease. These and other diseases are treated with drugs which interact with dopamine receptors.

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.

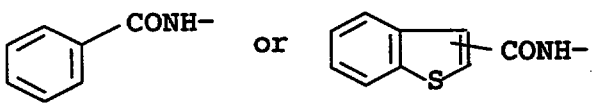
We have now found, surprisingly, that certain aza- and diazacycloheptane and -cyclooctane compounds have a high affinity for the dopamine D_3 receptor and a low affinity for the D_2 receptor. They are thus selective D_3 ligands.

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.

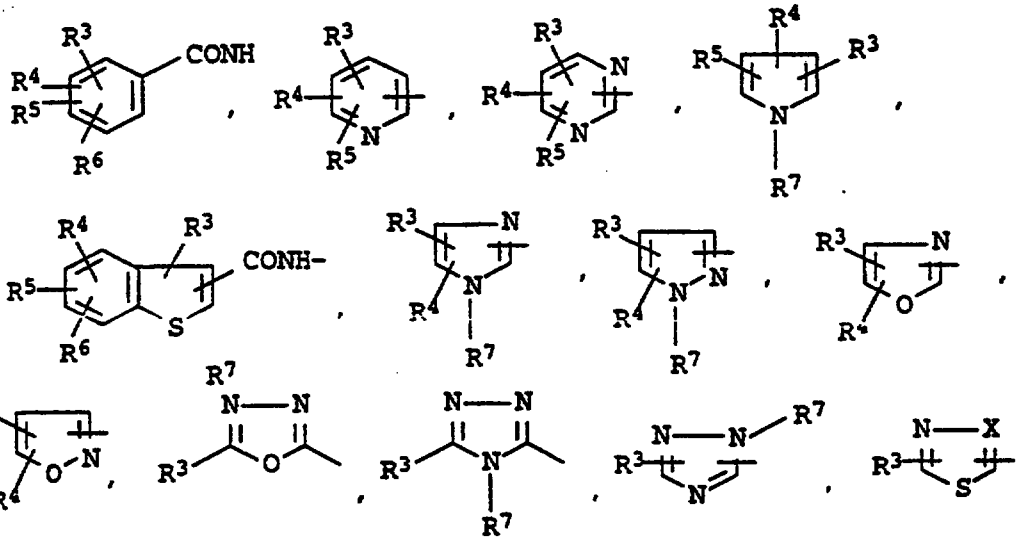
The alkylene groups may comprise at least one of the groups Z indicated above in the definition of A. This may, just like the said double or triple bond, be located anywhere in the alkylene chain or in position 1 or 2 of group A (seen from the Ar^1 radical). A is particularly preferably compounds according 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.

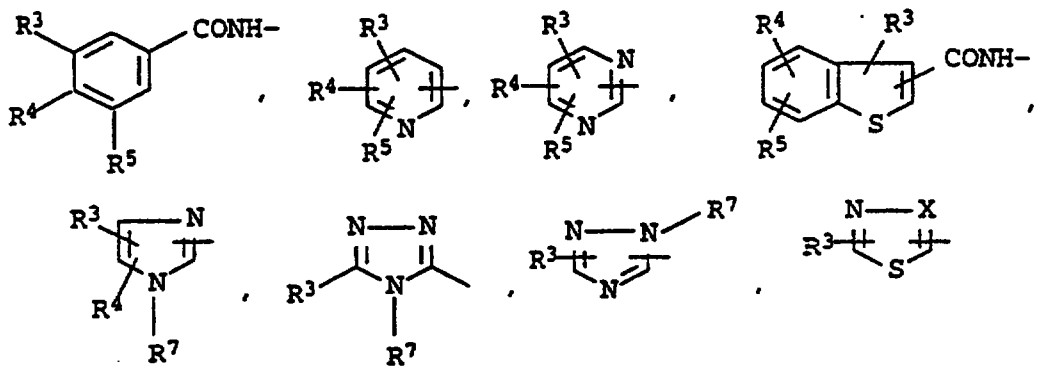
Acyl is preferably HCO or C_1-C_6-alkyl-CO, in particular acetyl. If Ar^1 is substituted, the substituent can also be located on the nitrogen heteroatom.

Ar^1 is preferably

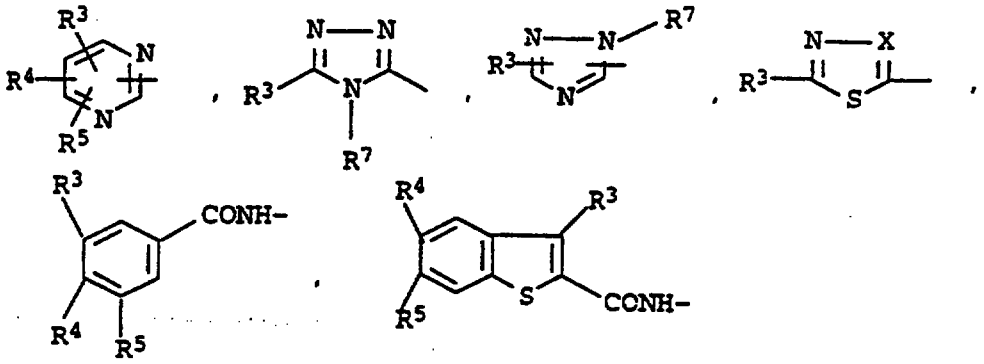


where
R^3 to R^6 are H or one of the abovementioned substituents of the Ar^1 radical,
R^7 has the meanings indicated above for R^2, and
X is N or CH. When the benzamide residue is substituted, the substituents are preferably in the m or p position.

Ar^1 is particularly preferably



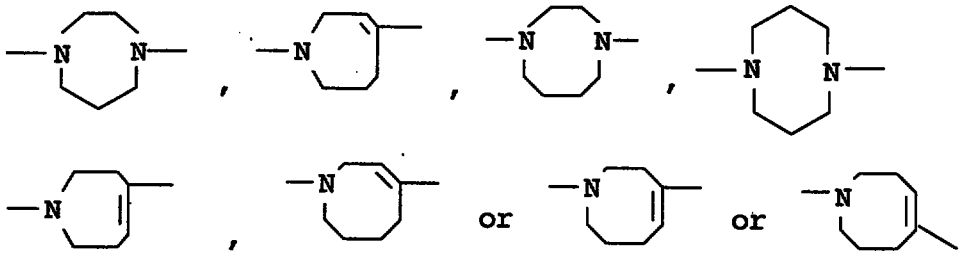
where R^3 to R^5, R^7 and X have the abovementioned meanings, and in particular



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

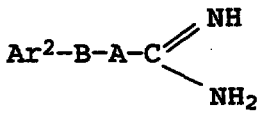
$$H - Z^1 - A - B - Ar^2 \quad (VII)$$

where Z^1 has the abovementioned meanings; or

d) converting a compound of the formula (VIII)

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

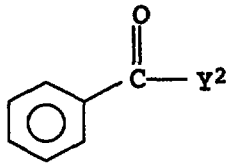
into a compound of the type of (IX)



(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)

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

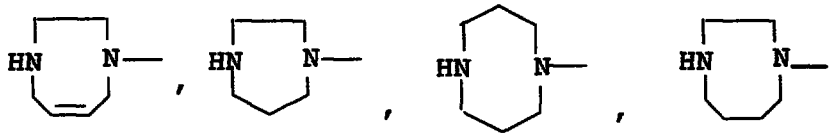
where A^2 has the abovementioned meanings, and Z^2 is OH or NH_2.

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)

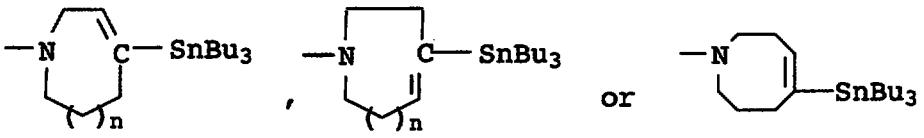
$$Y^1 - Ar^2 \quad (XIII)$$

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

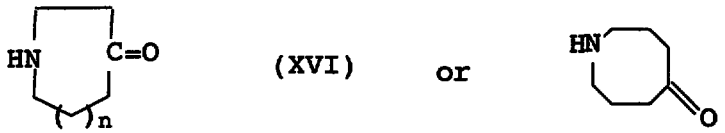


with n = 1 or 2,
with a compound of the general formula (XV)

$$Y^2 - Ar^2$$

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.

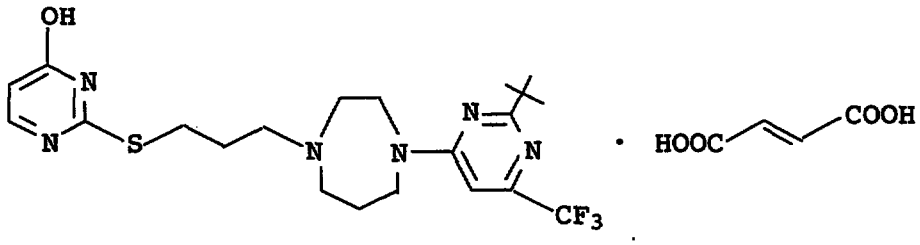
The dosage depends on the age, condition and weight of the patient and on the mode of administration. As a rule, the daily dose of active substance is about 10 to 1000 mg per patient and day on oral administration and about 1 to 500 mg per patient and day on parenteral administration.

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



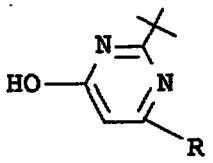
Preparation of the starting materials:

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

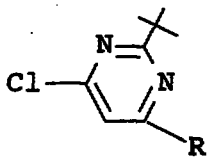


were obtained in a similar way.

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



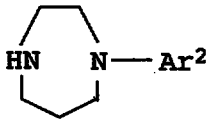
were obtained in a similar way:

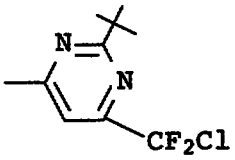
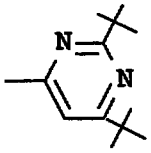
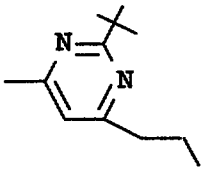
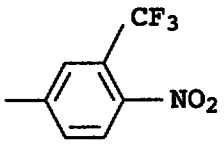
R	M.p. [°C]
$t\text{-}C_4H_9$	oil
$n\text{-}C_3H_7$	oil
CF_2Cl	oil

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

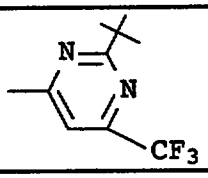
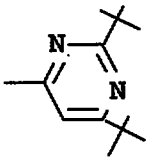
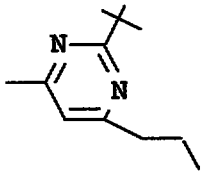
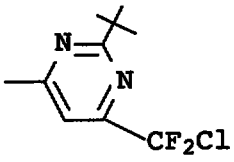
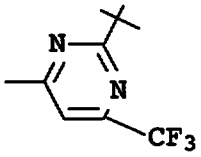
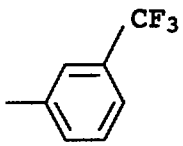
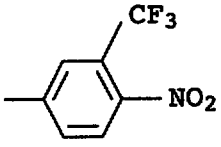
d) 1-[2-t-Butyl-6-trifluoromethylpyrimidin-4-yl]-4-(3-chloropropyl)hexahydro-(1H)-1,4-diazepine

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)

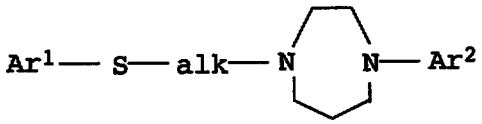
The substance was obtained as fumarate by adding an ethanolic solution with fumaric acid.

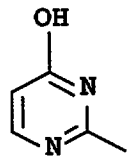
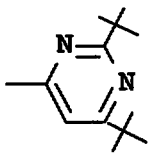
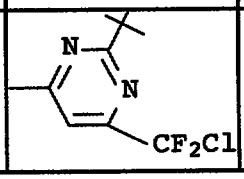
$C_{21}H_{29}F_3N_6OS \cdot C_4H_4O_4$ MW 586.6

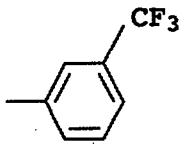
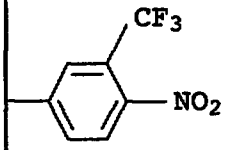
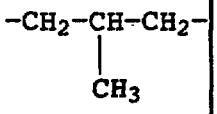
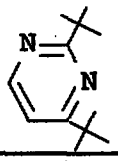
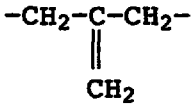
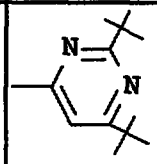
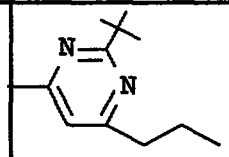
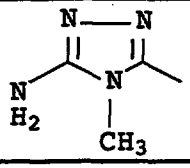
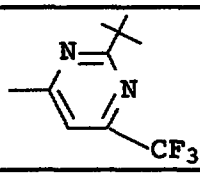
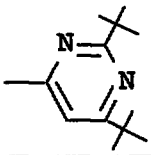
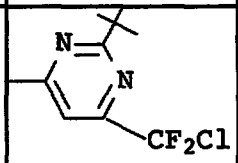
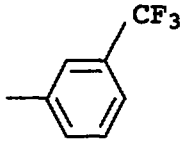
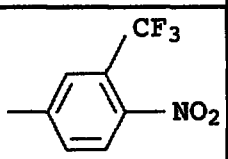
Melting point: 188-189°C

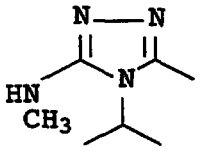
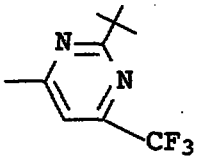
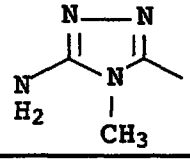
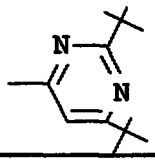
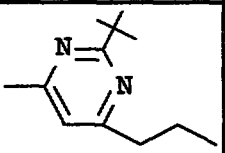
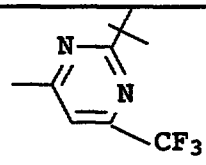
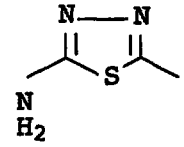
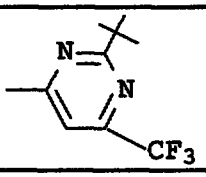
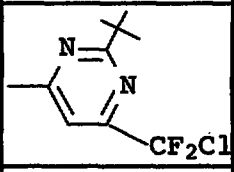
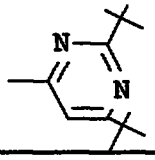
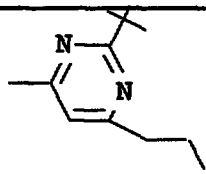
The compounds listed in the following Table 1 were obtained in a similar way using various haloalkyl-1,4-diazepines (eg. 1d) and various mercapto-substituted heterocycles such as thiouracil, 5-amino-2-mercaptotriazoles and 5-amino-2-mercaptothiadiazole:

Table 1



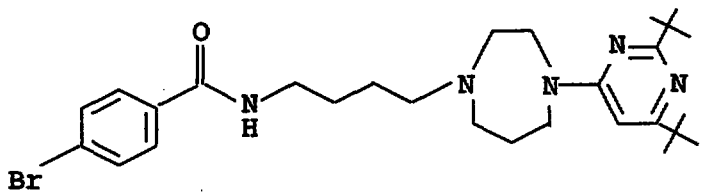
Ex. No.	Ar^1	alk	Ar^2	M.p. [°C]
2		$-(CH_2)_3-$		155-162 Oxalate
3	"	"		83-85 Oxalate

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]

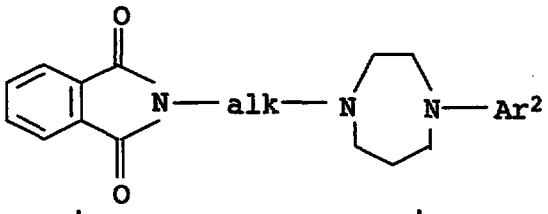


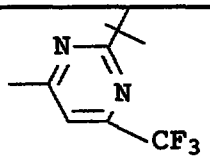
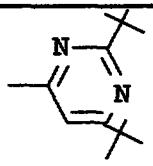
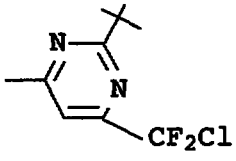
Preparation of the starting materials

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:



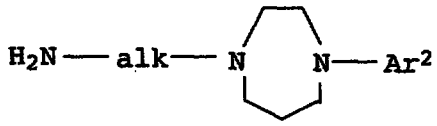
alk	Ar^2	M.p. [°C]
$-(CH_2)_3-$		89-92
$-CH_2-C(CH_3)=CH-CH_2-$	"	130-132
$-(CH_2)_3-$		119-121
$-(CH_2)_4-$	"	207-209
$-(CH_2)_4-$		190-192

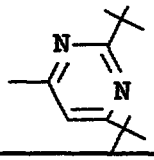
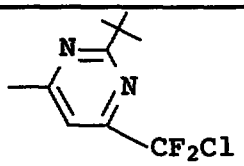
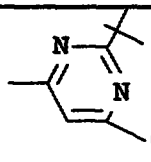
b) Hexahydro-1H-1-[2-t-butyl-6-trifluoromethyl-4-pyrimidinyl]-4-(4-aminobutyl)-1,4-diazepine

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

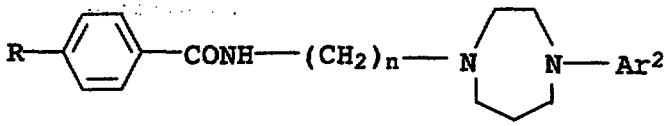
Preparation of the final products:

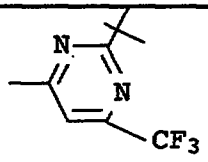
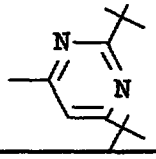
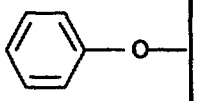
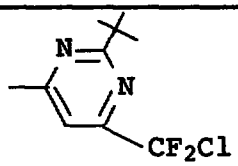
3 g (0.0083 mol) of the product obtained above under b) were dissolved with 0.9 g (0.009 mol) of triethylamine in 60 ml of tetrahydrofuran, and a solution of 2 g (0.009 mol) of 4-bromobenzoyl chloride in 10 ml of tetrahydrofuran was added dropwise at room temperature over the course of 10 min. After 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)

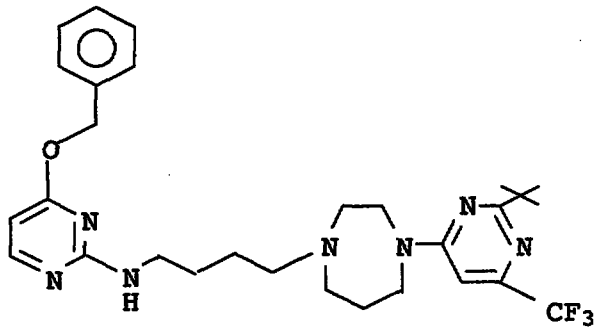
The compounds listed in Table 2 below were obtained using various amino derivatives (similar to 24b) and known benzoyl chlorides.

Table 2



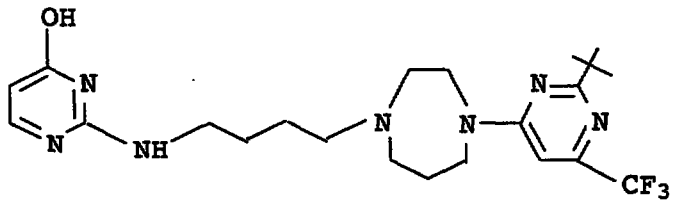
Ex. No.	R	n	Ar^2	M.p. [°C]
25	Br	3	"	169-171
26	"	4		74-76 Oxalate
27	t-Butyl	4		165-167 Oxalate
28		4	"	104-107 Oxalate
29	Br	4		92-94 Oxalate
30	I	4	"	110-115 Oxalate

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



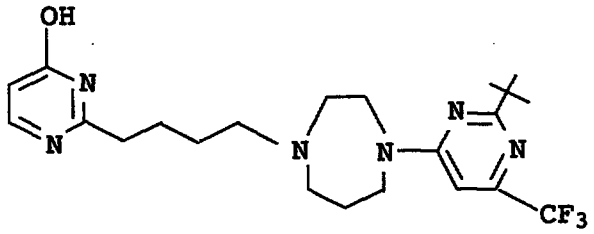
2.7 g (0.007 mol) of the amino compound prepared in Example 24b) were introduced with 0.3 g of sodium hydride (0.009 mol) into 20 ml of dimethylformamide. After reaction for 1 h, 1.6 g (0.006 mol) of 4-benzyloxy-2-methylsulfonylpyrimidine (prepared by oxidizing 4-benzyloxy-2-methylmercaptopyrimidine), 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

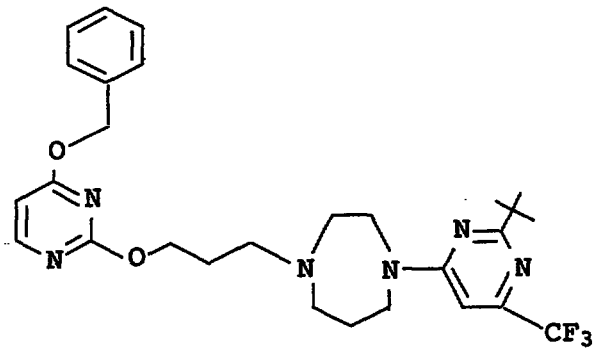
b) 1-[2-t-Butyl-6-trifluoromethyl-4-pyrimidinyl]-4-(4-amidinobutyl)hexahydro-1,4-diazepine hydrochloride

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

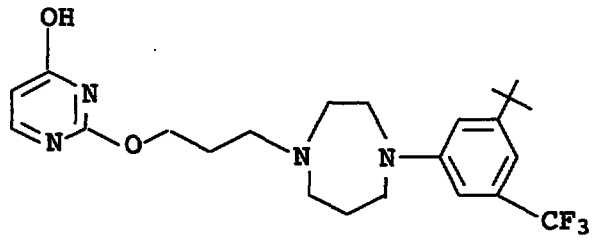
acetate/Et_2O, ethereal hydrochloric acid was added under protective gas, and the resulting salt was filtered off with suction.

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%)

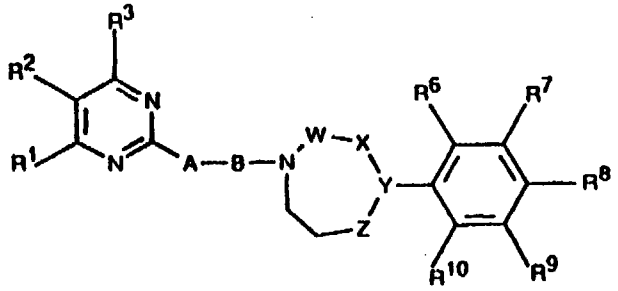
To form the hydrochloride, the oil was dissolved in ethyl acetate/Et_2O, ethereal hydrochloric acid was added under protective gas, and the resulting salt was filtered off with suction.

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



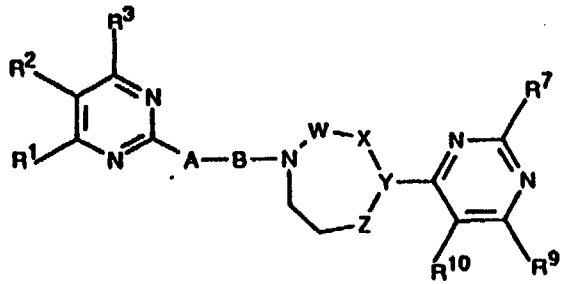
Example No.	R1	R2	R3	R6	R7	R8	R9	R10	W	X-Y-Z	A	B
36	H	H	OH	H	tBut	H	Me	H	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
37	H	H	OH	H	tBut	H	Ph	H	CH_2-CH_2	CH=C-CH_2	S	-$(CH_2)_3$-
38	Me	H	OH	H	tBut	H	1-Pyrrolyl	H	CH_2	CH=C-CH_2	S	-$(CH_2)_3$-
39	H	H	NH_2	H	iProp	H	2-Napht	H	CH_2-CH_2	CH_2-CH=C	S	-$(CH_2)_3$-
40	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_2-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-Naphl	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-

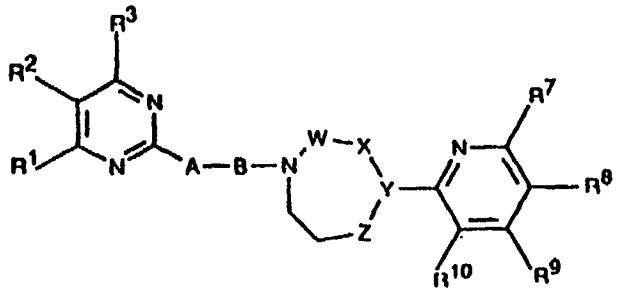
Table 4



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

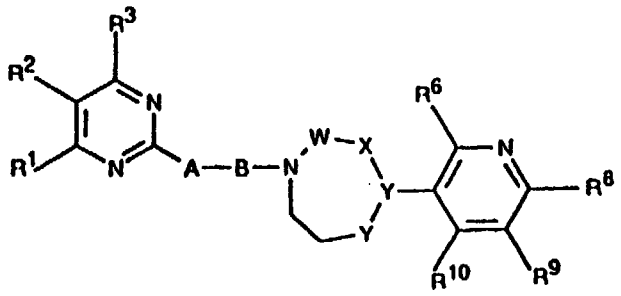


Example No.	R1	R2	R3	R7	R8	R9	R10	W	X-Y-Z	A	B
101	H	H	OH	tBut	H	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
102	H	H	OH	tBut	CN	H	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
103	Me	H	OH	tBut	H	Cl	H	CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
104	H	H	OH	H	CN	tBu	H	CH_2-CH_2	CH_2-CH=C	-CH_2-	-CH_2-CH(CH_3)-CH_2-
105	H	H	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	-$(CH_2)_4$-

Table 6

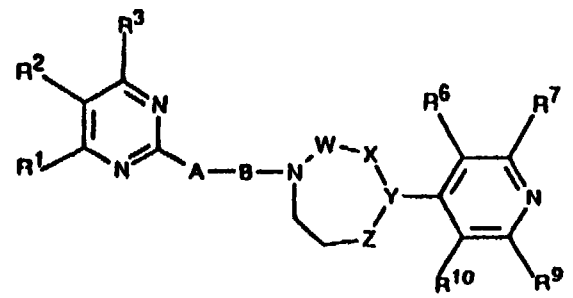


Example No.	R1	R2	R3	R6	R8	R9	R10	W	X-Y-Z	A	B
126	H	H	OH	OMe	H	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
127	H	H	OH	OMe	H	CF_3	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
128	Me	H	OH	OMe	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
129	H	H	OH	H	CN	tBut	H	CH_2	CH=C-CH_2	-CH_2-	-CH_2-C(CH_3)=CH-CH_2-
130	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-

REPLACEMENT SHEET (RULE 26)

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

Table 7

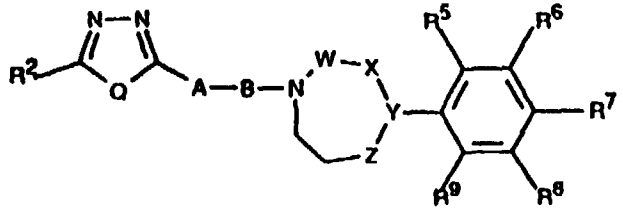


Example No.	R1	R2	R3	R6	R7	R9	R10	W	X-Y-Z	A	B
147	H	H	OH	H	tBut	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
148	H	H	OH	H	tBut	Ph	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
149	Me	H	OH	H	tBut	1-Pyrrolyl	H	CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
150	H	H	OH	H	*nPropyl*	tBut	H	CH_2-CH_2	CH_2-CH=C	-CH_2-	-CH_2-C(CH_3)=CH-CH_2-
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	nProp	tBut	H	CH_2	CH_2-N-CH_2	S	-CH_2-CH(CH_3)-CH_2-

REPLACEMENT SHEET (RULE 26)

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-	-$(CH_2)_3$-

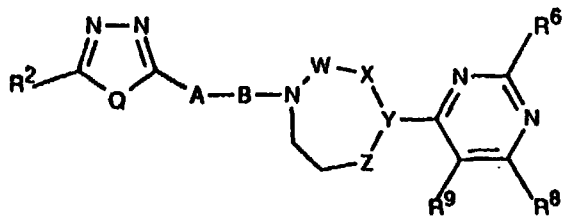
REPLACEMENT SHEET (RULE 26)

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-Naphl	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

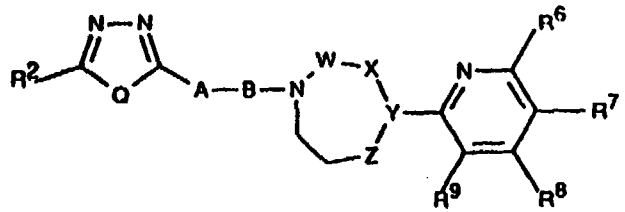


Example No.	Q	R2	R6	R8	R9	W	X-Y-Z	A	B
226	NCH_3	NH_2	tBut	Ph	H	CH_2	CH_2-N-CH_2	-CH_2-	-$(CH_2)_3$-
227	NCH_3	NH_2	tBut	2-Napht	H	CH_2	CH_2-N-CH_2	S	-CH_2-C(=CH_2)-CH_2-
228	NCH_3	NH_2	tBut	1-Pyrrolyl	H	CH_2-CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
229	NCH_3	NHMe	tBut	cHex	H	CH_2-CH_2	CH_2-CH=C	-CH_2-	-$(CH_2)_3$-
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	$CH{\equiv}C$-CH_2	S	-CH_2-C(=CH_2)-CH_2-
242	N(iProp)	NH_2	tBut	2-Napht	H	CH_2	CH_2-$CH{\equiv}C$	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	$CH{\equiv}C$-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	$CH{\equiv}C$-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	$CH{\equiv}C$-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	$CH{\equiv}C$-CH_2	S	-CH_2-$CH(CH_3)$-CH_2-

Table 10

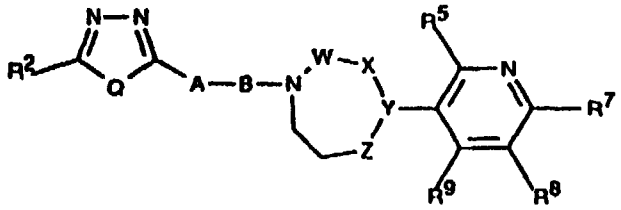


Example No.	Q	R2	R6	R7	R8	R9	W	X-Y-Z	A	B
256	NCH_3	NH_2	tBut	H	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
257	S	OH	tBut	CN	H	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_8$-
258	N(iProp)	NHMe	tBut	H	Cl	H	CH_2	CH_2-N-CH_2	NH	-CH_2-C(=CH_2)-CH_2-
259	NCH_3	NH_2	H	CN	tBu	H	CH_2	CH_2-CH=C	-CH_2-	-CH_2-CH(CH_3)-CH_2-
260	NCH_3	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

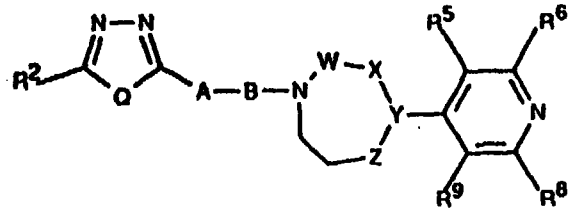


Example No.	Q	R2	R5	R7	R8	R9	W	X-Y-Z	A	B
281	NCH_3	NH_2	H	CN	tBut	H	CH_2	CH=C-CH_2	-CH_2-	-CH_2-C(=CH_2)-CH_2-
282	NCH_3	NHMe	H	F	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
283	N(cProp)	NH_2	Me	Cl	iProp	H	CH_2	CH_2-CH=C	-CH_2-	-$(CH_2)_3$-
284	S	NHMe	H	H	iProp	H	CH_2-CH_2	CH=C-CH_2	S	-$(CH_2)_{10}$-
285	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	-$(CH_2)_5$-

REPLACEMENT SHEET (RULE 26)

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

Table 12

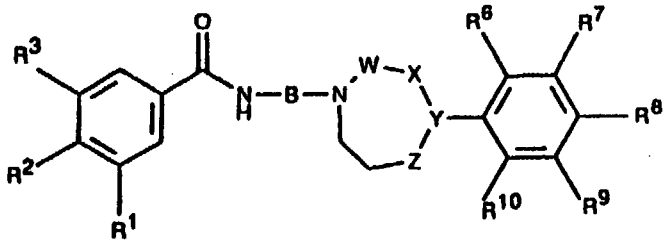


Example No.	Q	R2	R5	R6	R8	R9	W	X-Y-Z	A	B
299	NCH_3	NH_2	H	tBut	tBut	H	CH_2	CH_2-N-CH_2	S	-$(CH_2)_3$-
300	S	OH	H	tBut	Ph	H	CH_2	CH_2-N-CH_2	S	-CH_2-C(=CH_2)-CH_2-
301	N(iProp)	NHMe	H	tBut	1-Pyrrolyl	H	CH_2	CH_2-N-CH_2	NH	-CH_2-CH=CH-CH_2-
302	NCH_3	NH_2	H	nPropyl	tBut	H	CH_2-CH_2	CH=C-CH_2	-CH_2-	-CH_2-CH(CH_3)-CH_2-
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-

REPLACEMENT SHEET (RULE 26)

314	NEt	NH_2	Me	tBut	nProp	H	CH_2-CH_2	CH_2-CH=C	-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 -$(CH_2)_3$-

Table 13



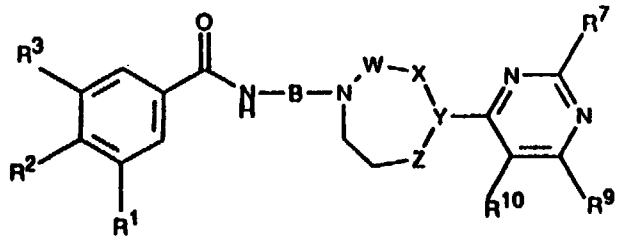
Example No.	R1	R2	R3	R6	R7	R8	R9	R10	W	X-Y-Z	B
319	H	Br	H	H	tBut	H	Me	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
320	H	J	H	H	tBut	H	Ph	H	CH_2-CH_2	CH=C-CH_2	-$(CH_2)_4$-
321	H	Ph	H	H	tBut	H	1-Pyrrolyl	H	CH_2	CH=C-CH_2	-$(CH_2)_4$-
322	H	p(iProp)-Ph	H	H	iProp	H	2-Napht	H	CH_2-CH_2	CH_2-CH=C	-$(CH_2)_4$-
323	H	pAcetyl-Ph	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-Naphtl	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-

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

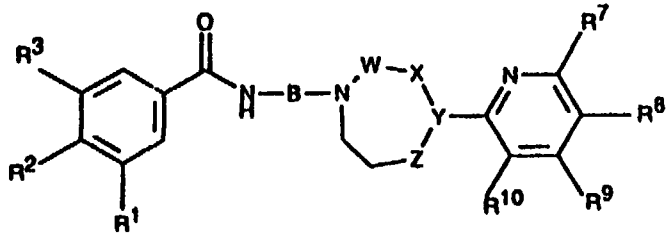
Table 14



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

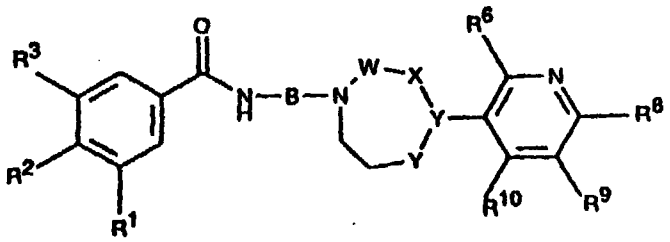


Example No.	R1	R2	R3	R7	R8	R9	R10	W	X-Y-Z	B
384	H	Br	H	tBut	H	tBut	H	CH_2	CH_2-N-CH_2	-(CH_2)4-
385	H	J	H	tBut	CN	H	H	CH_2	CH_2-N-CH_2	-(CH_2)4-
386	H	Ph	H	tBut	H	Cl	H	CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
387	H	p(iProp)-Ph	H	H	CN	tBu	H	CH_2-CH_2	CH_2-CH=C	-CH_2-CH(CH_3)-CH_2-
388	H	pAcetyl-Ph	H	CF_3	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	-$(CH_2)_4$-

Table 16

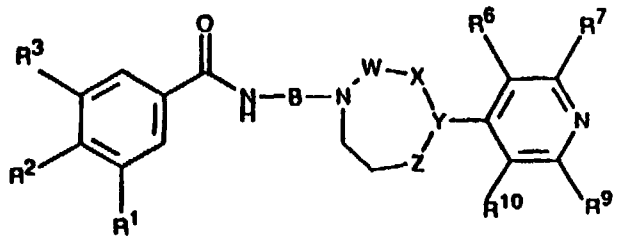


Example No.	R1	R2	R3	R6	R8	R9	R10	W	X-Y-Z	B
409	H	Br	H	OMe	H	tBut	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
410	H	J	H	OMe	H	CF_3	H	CH_2	CH_2-N-CH_2	-$(CH_2)_4$-
411	H	Ph	H	OMe	H	tBut	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
412	H	p(iProp)-Ph	H	H	CN	tBut	H	CH_2	CH=C-CH_2	-CH_2-C(CH_3)=CH-CH_2-
413	H	pAcetyl-Ph	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=C-CH_2	-$(CH_2)_4$-
446	Me	pAcetyl-Ph	H	Me	tBut	nProp	H	CH_2	CH_2-CH=C	-CH_2-CH=CH-CH_2-
447	H	pBr-Ph	Me	Me	tBut	H	H	CH_2-CH_2	CH_2-N-CH_2	-CH_2-C(=CH_2)-CH_2-
448	H	pJ-Ph	F	H	tBut	tBut	H	CH_2	CH=C-CH_2	-$(CH_2)_3$-
449	H	iProp	Me	Me	CF_3	tBut	H	CH_2	CH_2-CH=C	-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 $\times 10^5$ 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.

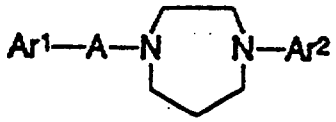
After incubation at 25°C for 60 minutes, the mixtures were filtered through GF/B glass fiber filters (Whatman, England) in a skatron cell collector (Zinsser, Frankfurt), and the filters were washed with ice-cold 50 mM tris-HCl buffer, pH 7.4. The radioactivity collected on the filters was quantified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

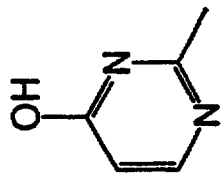
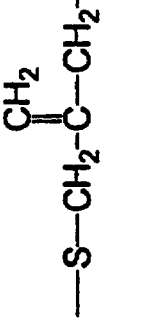
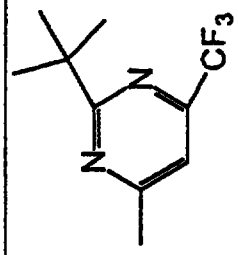
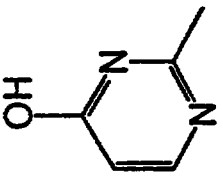
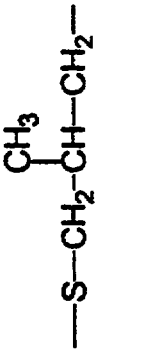
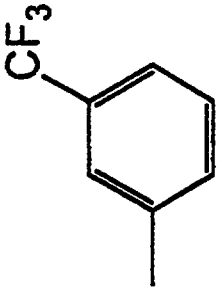
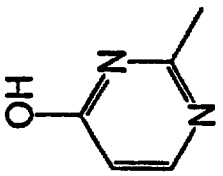
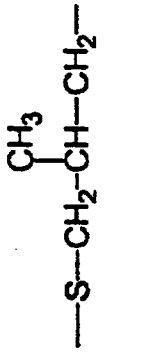
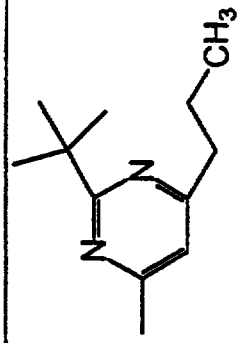
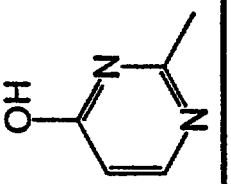
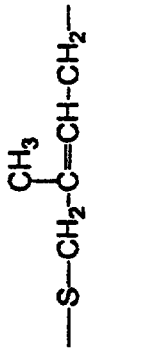
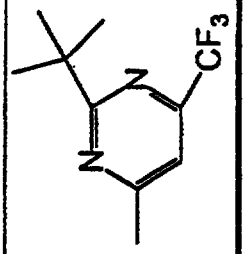
Evaluation took place as under a).

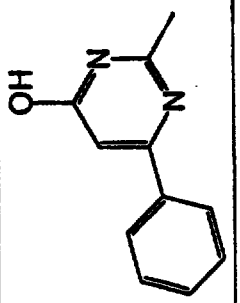
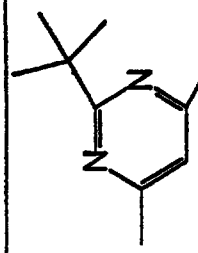
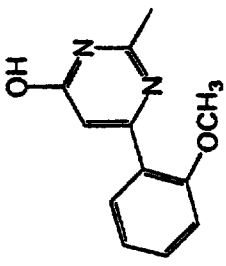
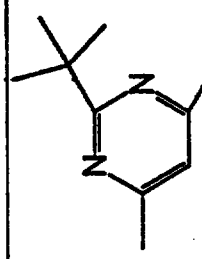
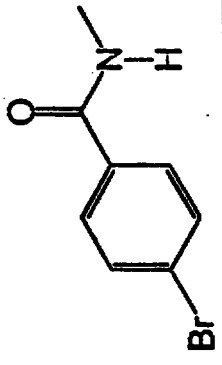
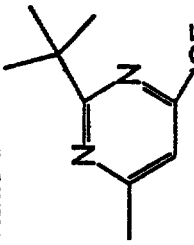
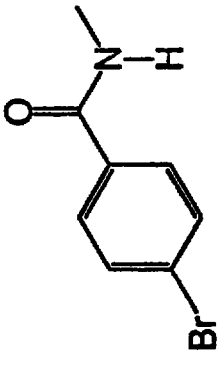
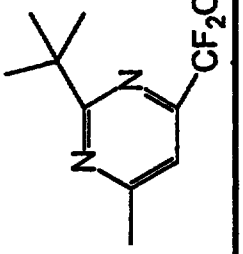
The K_i values were determined by nonlinear regression analysis using the ligand program or by conversion of the IC_{50} values using the formula of Cheng and Prusoff.

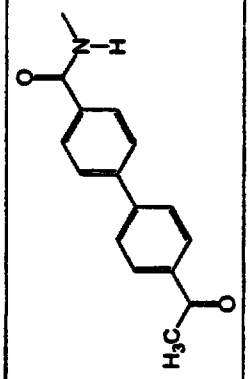
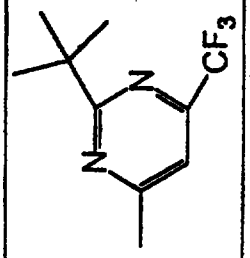
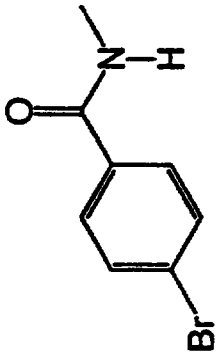
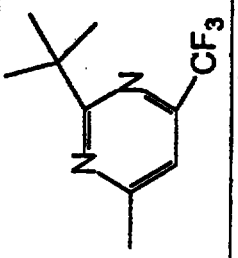
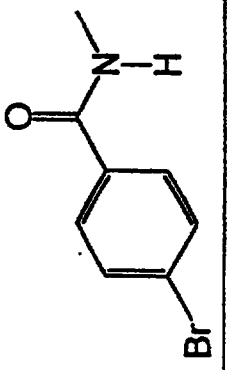
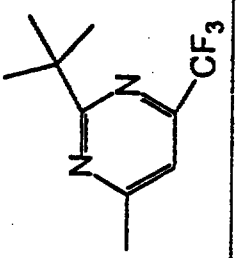
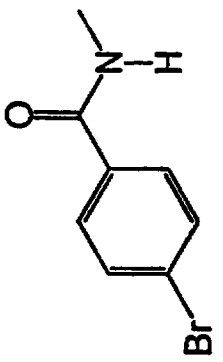
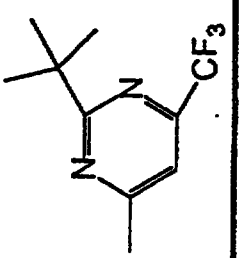
In these assays, the compounds according to the invention show very good affinities on the D_3 receptor and high selectivities for the D_3 receptor.

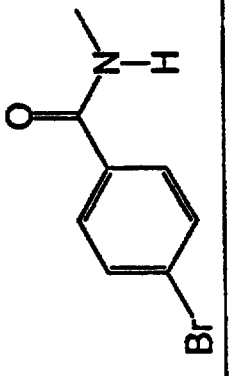
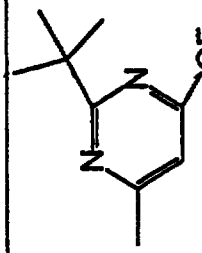
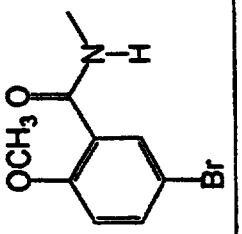
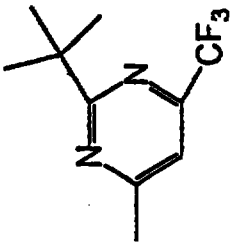
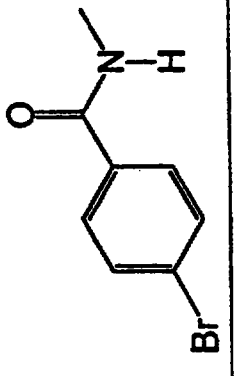
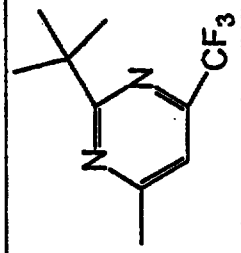
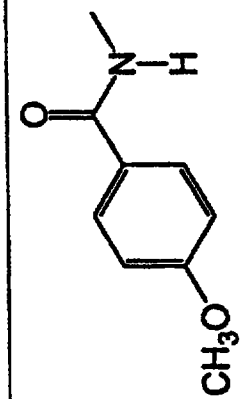
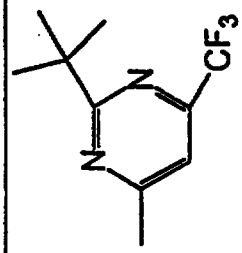
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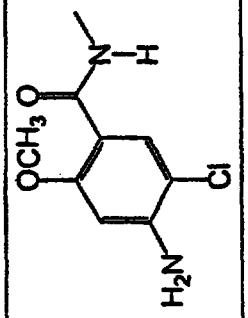
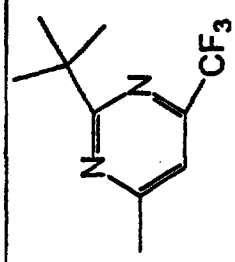
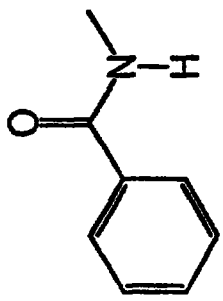
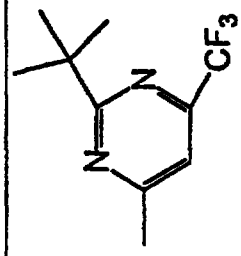
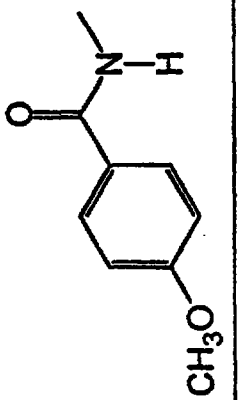
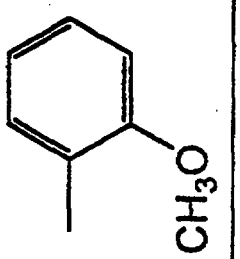
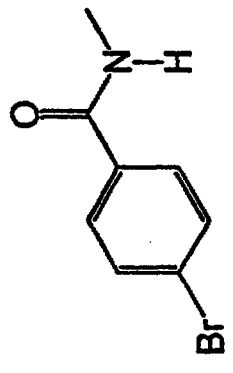
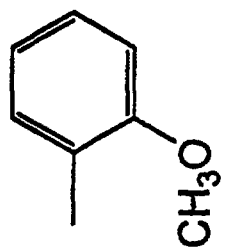


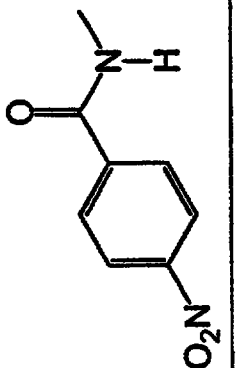
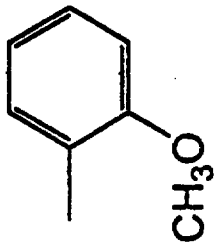
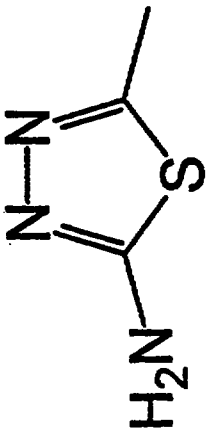
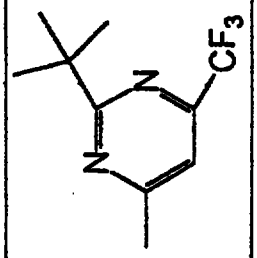
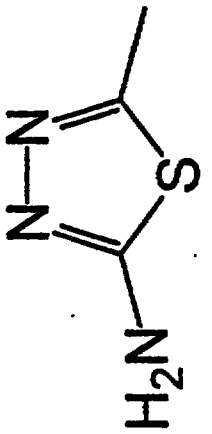
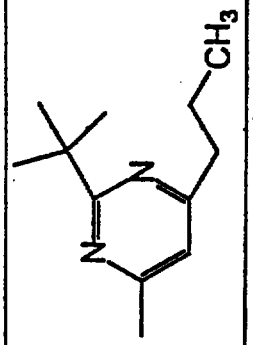
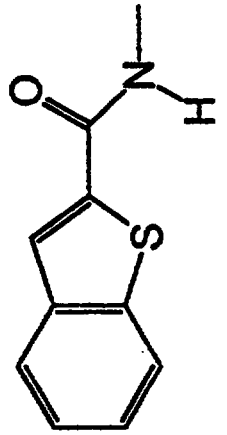
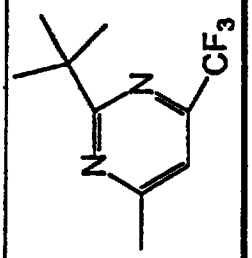
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
450				80 - 90 (Oxalate)
451				110 - 113
452				106 - 108
453				129 -131

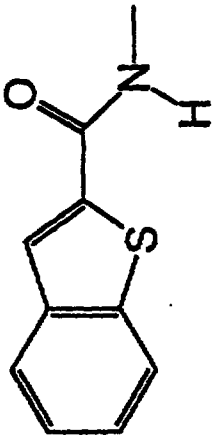
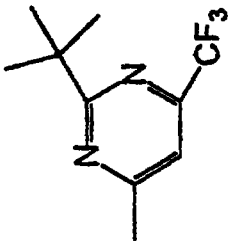
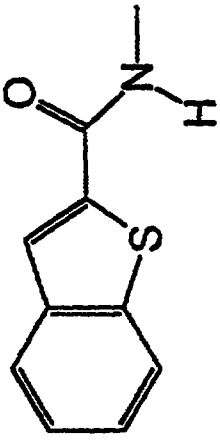
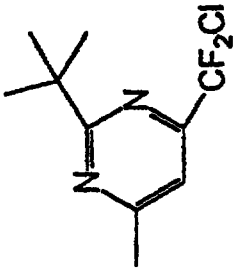
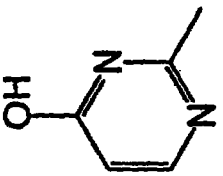
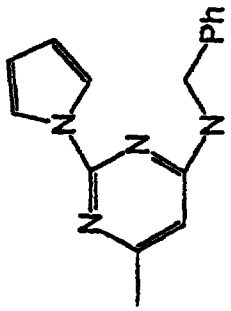
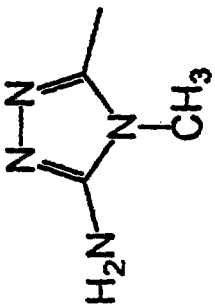
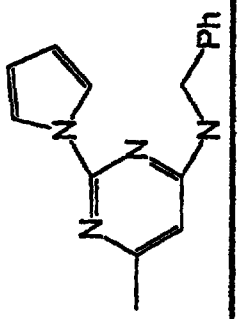
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
454		$-S-(CH_2)_3-$		227 - 131 (Hydrochloride)
455		$-S-(CH_2)_3-$		165 - 166 (Hydrochloride)
456		$-(CH_2)_5-$		115 - 118 (Oxalate)
457		$-(CH_2)_4-$		94 - 97 (Hydrochloride)

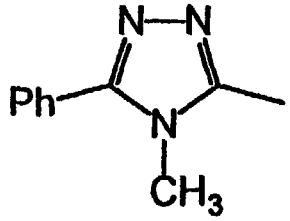
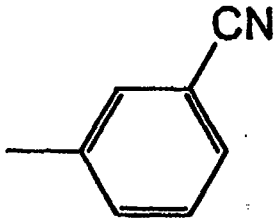
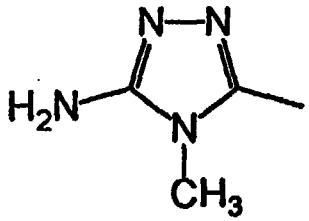
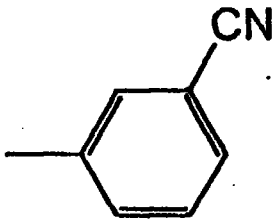
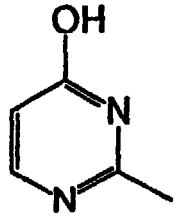
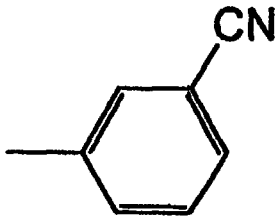
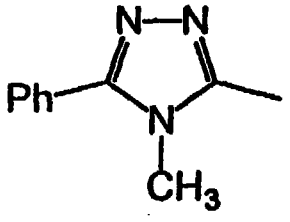
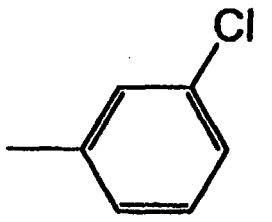
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
458		$-(CH_2)_4-$		123 - 126 (Fumarate)
459		$-(CH_2)_3-CH(CH_3)-$		130 - 133 (Fumarate)
460		$-CH_2-CH=CH-CH_2-$		118 - 125 (Fumarate)
461		$-(CH_2)_2-CH(CH_3)-(CH_2)_2-$		130 - 132 (Oxalate)

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		$-CH_2-\underset{CH_3}{CH}-(CH_2)_2-$		171 - 176 (Fumarate)
465		$-(CH_2)_4-$		122 - 124 (Fumarate)

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)

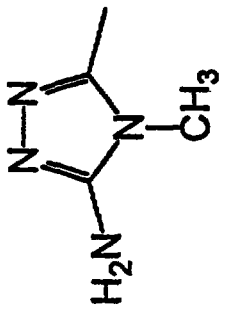
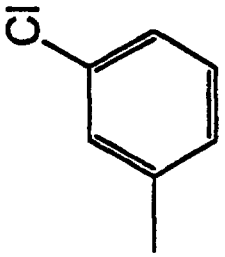
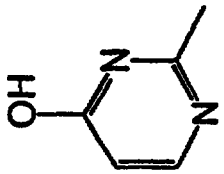
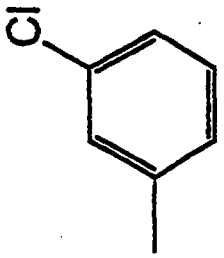
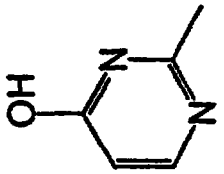
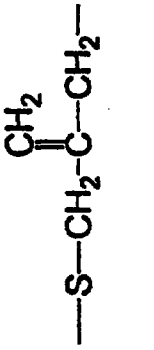
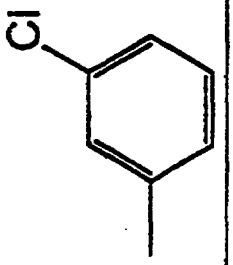
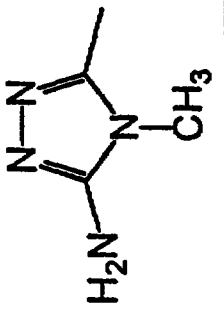
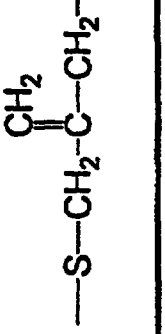
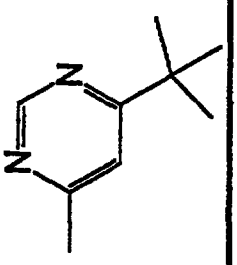
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
470		$-(CH_2)_4-$		235 - 236 (Fumarate)
471				92 - 98
472				87 - 90
473		$-(CH_2)_4-$		112 - 115 (Fumarate)

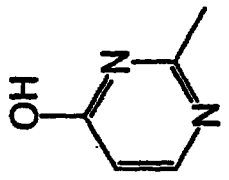
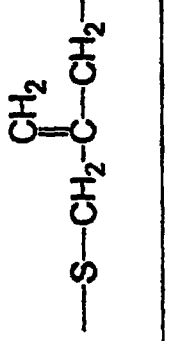
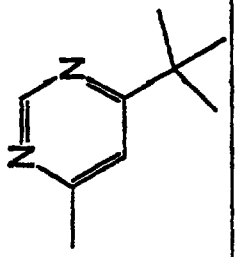
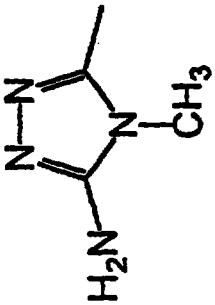
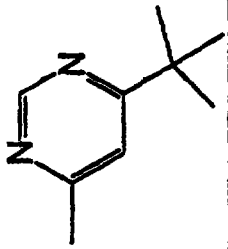
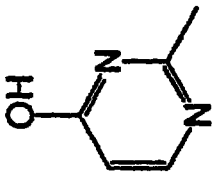
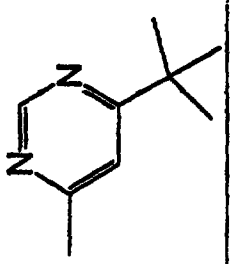
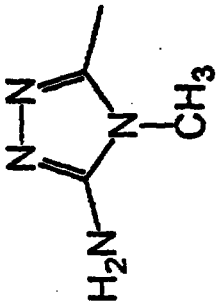
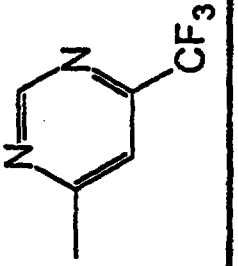
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
474		$-(CH_2)_6-$		101 - 105 (Oxalate)
475		$-(CH_2)_4-$		127 - 129 (Oxalate)
476		$-S-(CH_2)_3-$		
477		$-S-(CH_2)_3-$		

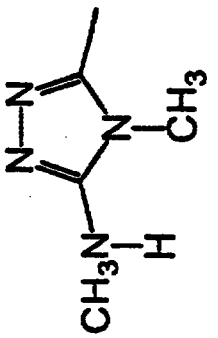
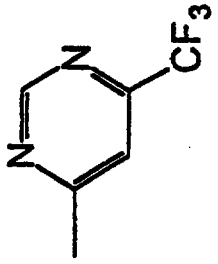
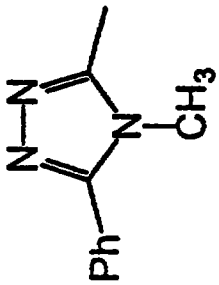
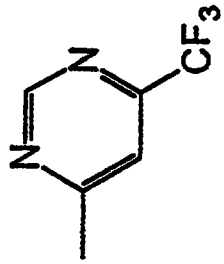
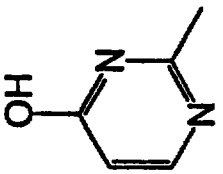
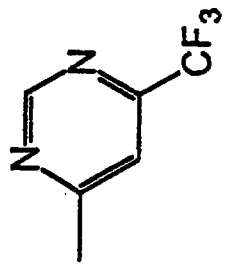
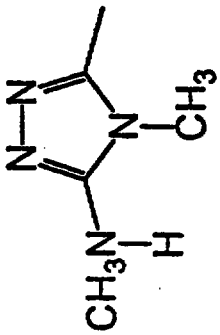
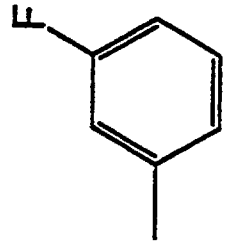
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
478		—S—$(CH_2)_3$—		126 - 128 (Fumarate)
479		—S—$(CH_2)_3$—		150 - 156 (Fumarate)
480		—S—$(CH_2)_3$—		158 - 165 (Fumarate)
481		—S—$(CH_2)_3$—		

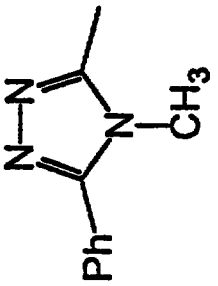
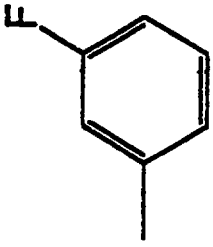
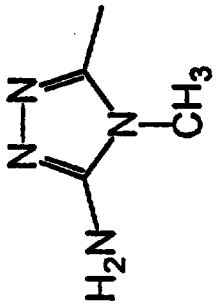
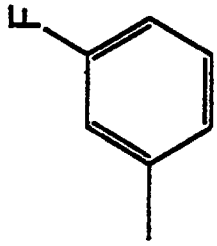
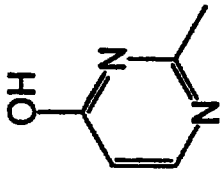
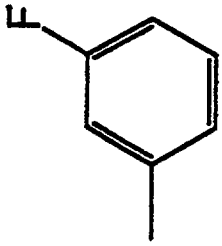
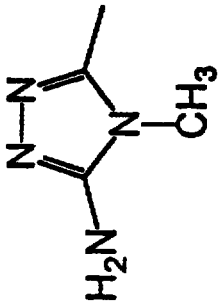
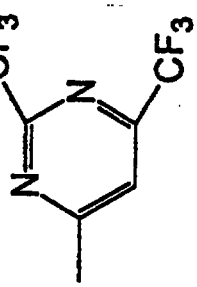
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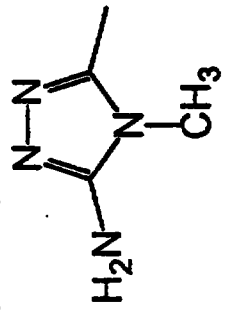
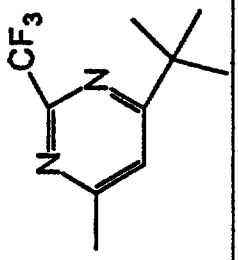
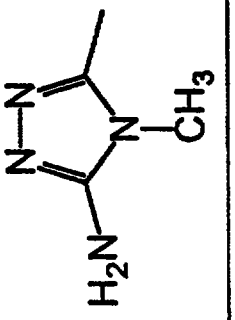
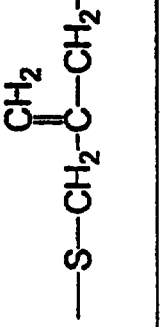
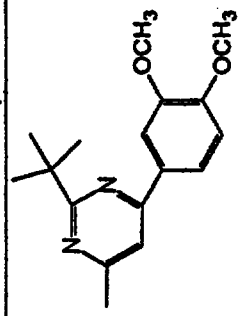
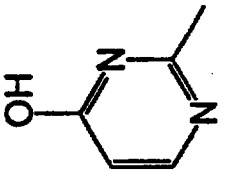
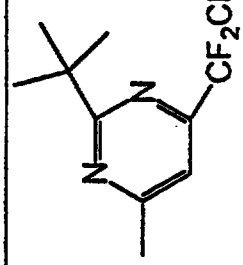
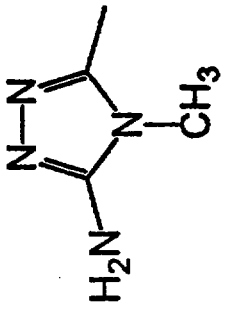
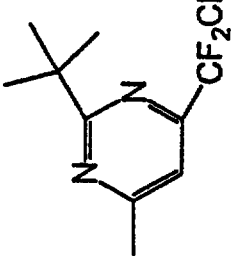
REPLACEMENT SHEET (RULE 26)

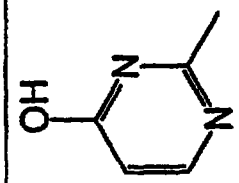
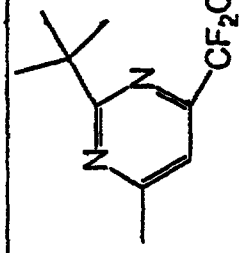
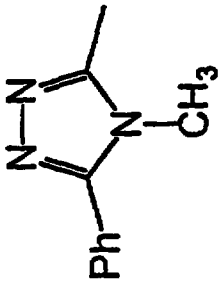
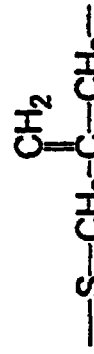
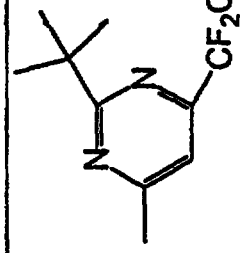
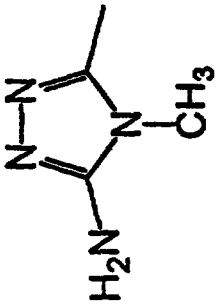
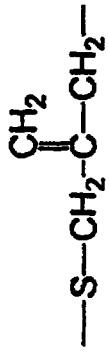
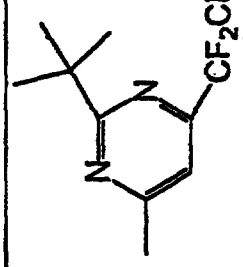
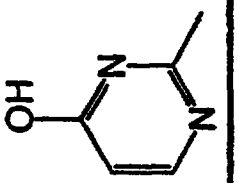
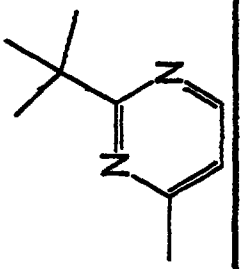
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
482				184 - 188 (Oxalate)
483				185 - 187 (Oxalate)
484				
485				127

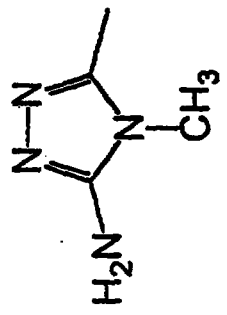
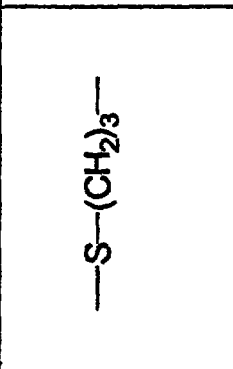
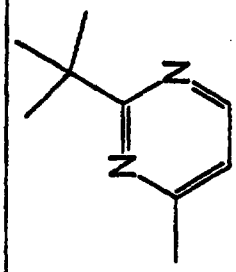
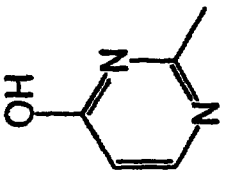
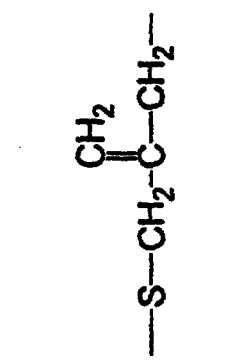
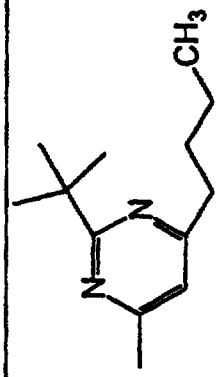
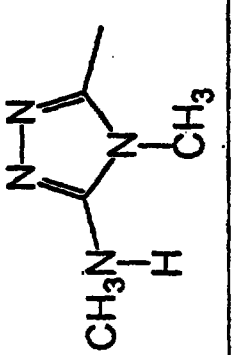
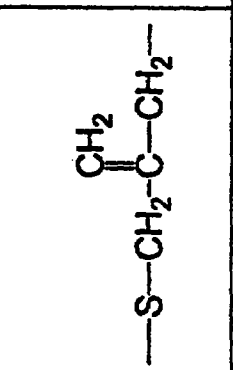
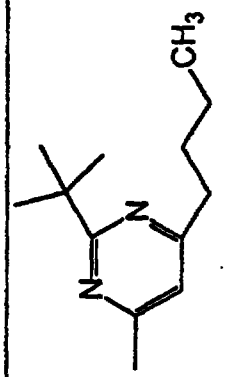
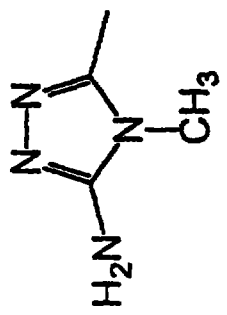
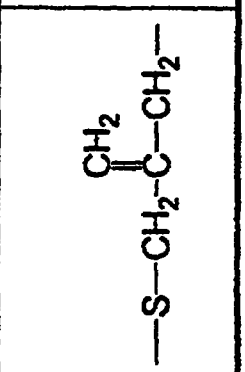
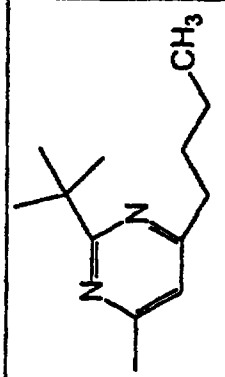
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
486				128
487				123
488				120
489				187 - 191 (Oxalate)

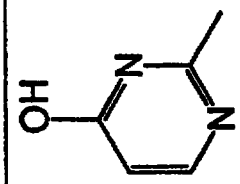
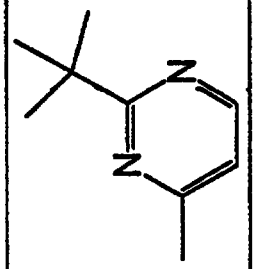
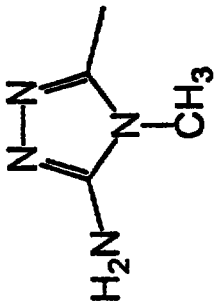
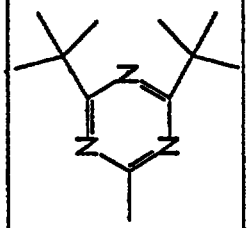
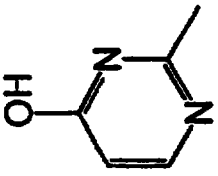
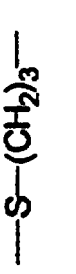
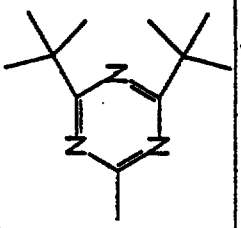
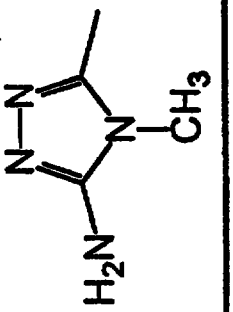
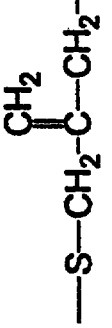
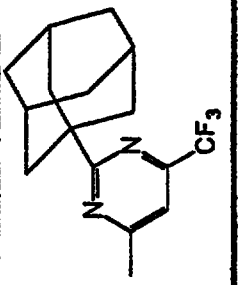
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
490		$-S-(CH_2)_3-$		187 - 191 (Oxalate)
491		$-S-(CH_2)_3-$		
492		$-S-(CH_2)_3-$		
493		$-S-(CH_2)_3-$		

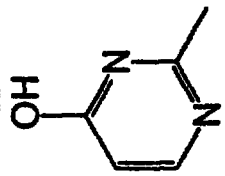
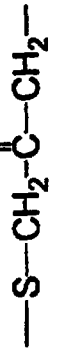
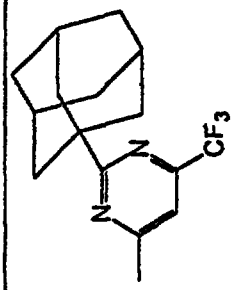
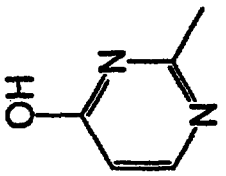
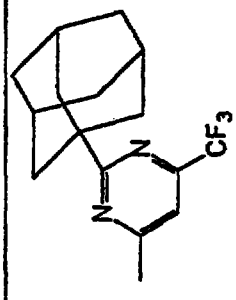
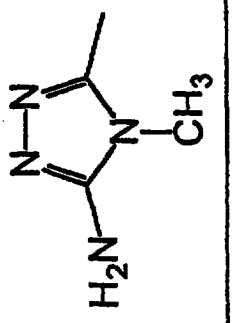
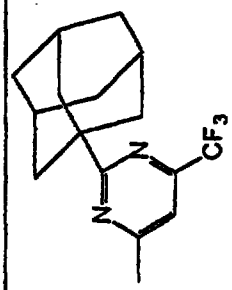
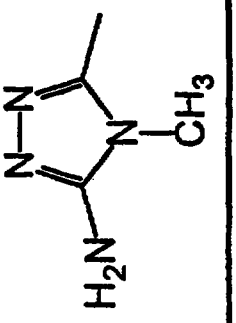
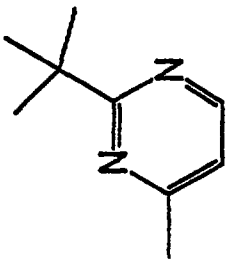
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
494		$-S-(CH_2)_3-$		93 - 94 (Oxalate)
495		$-S-(CH_2)_3-$		
496		$-S-(CH_2)_3-$		168 - 170 (Fumarate)
497		$-S-(CH_2)_3-$		

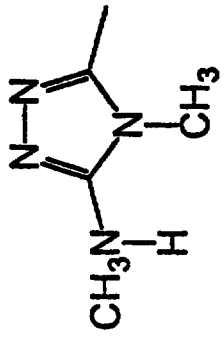
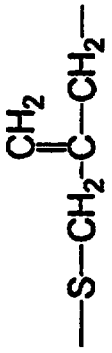
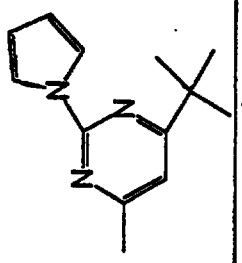
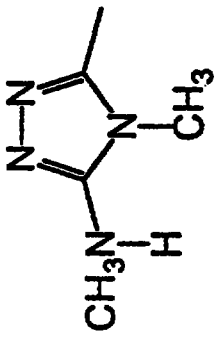
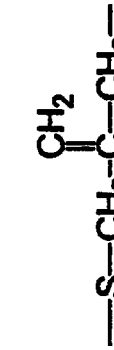
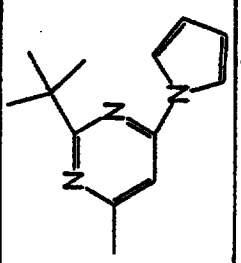
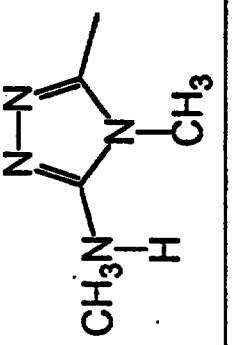
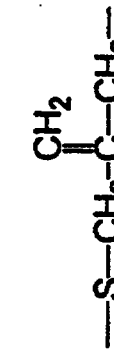
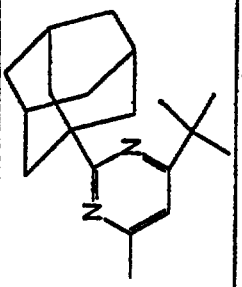
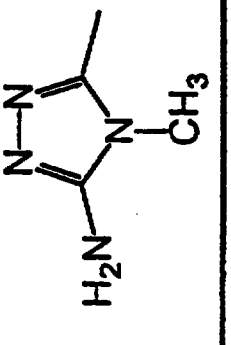
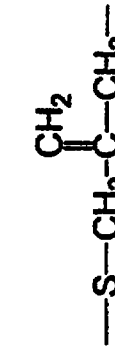
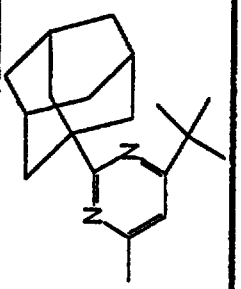
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
498				
499				
500				
501				

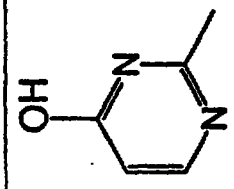
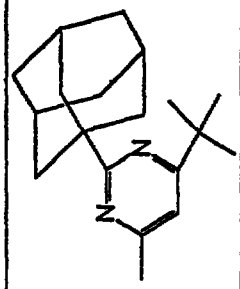
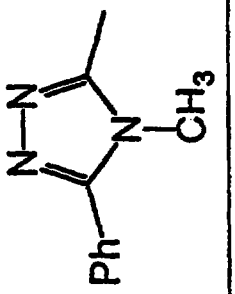
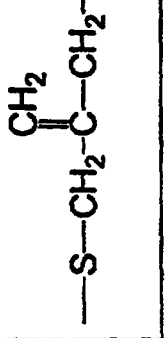
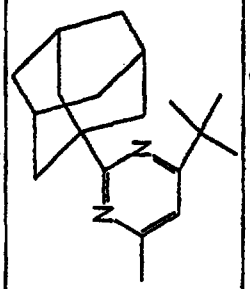
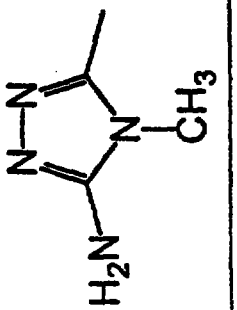
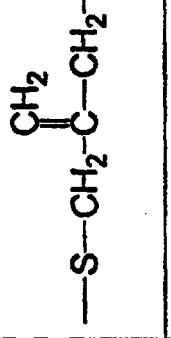
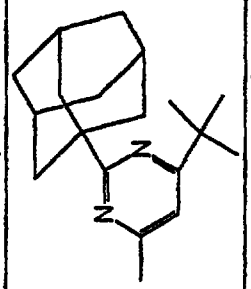
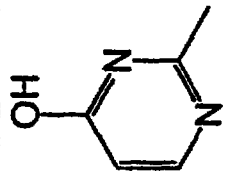
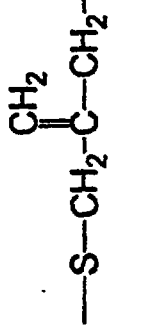
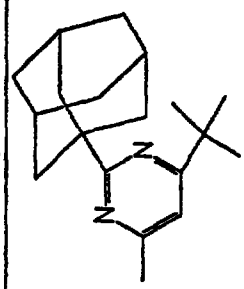
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
502				
503				
504				
505				

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

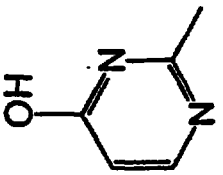
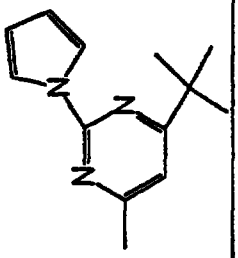
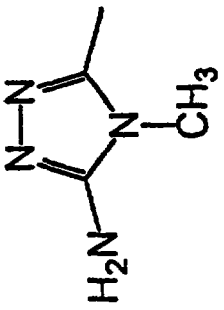
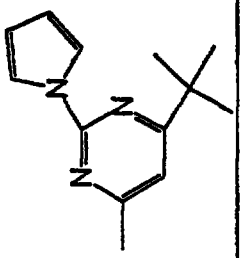
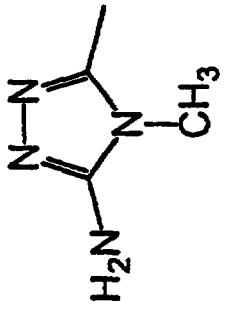
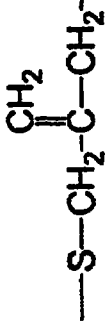
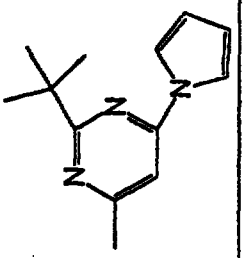
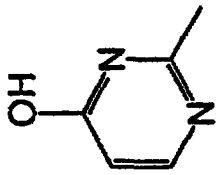
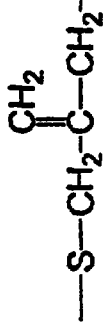
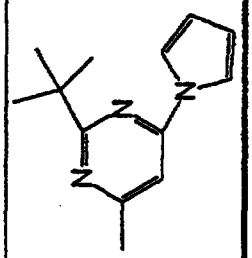
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
510				
511				
512				
513				

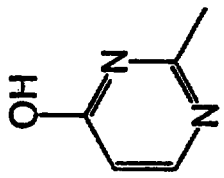
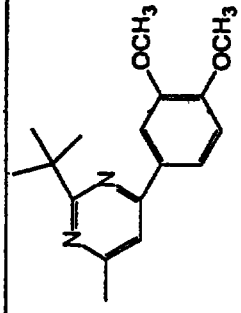
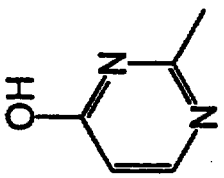
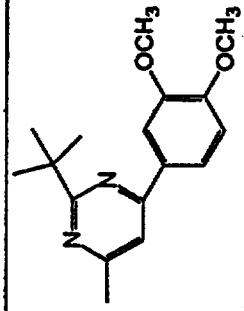
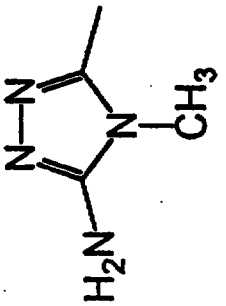
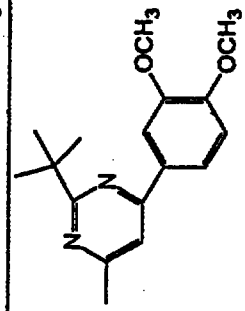
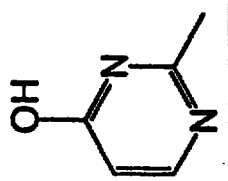
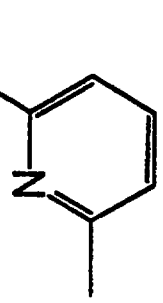
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
514				
515				
516				81 - 85
517				

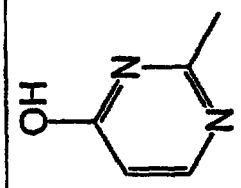
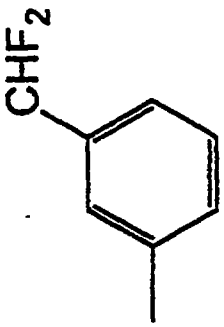
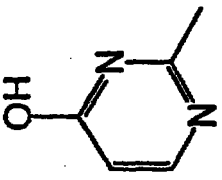
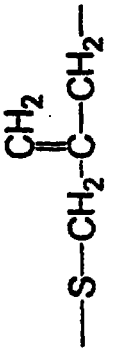
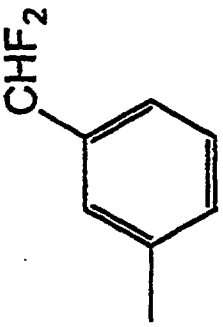
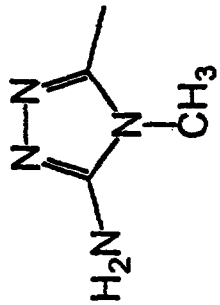
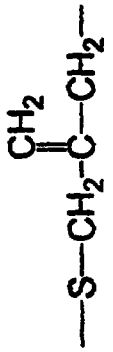
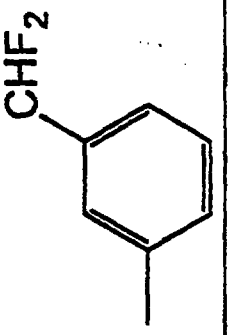
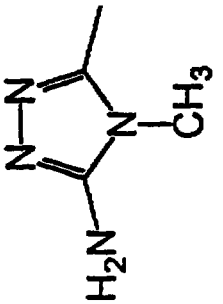
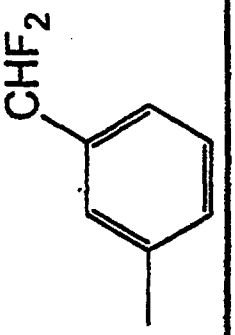
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
518				
519				
520				75 - 80
521				110 - 112 (Hydrochloride)

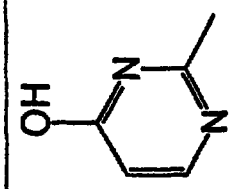
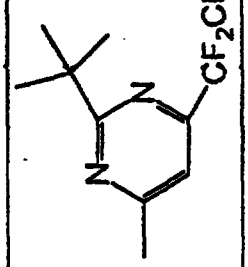
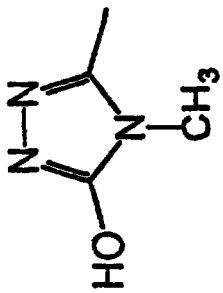
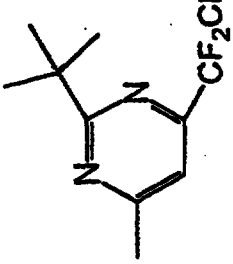
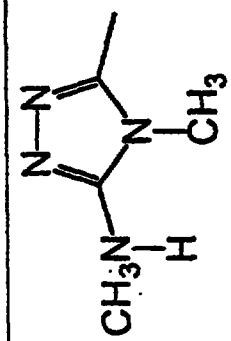
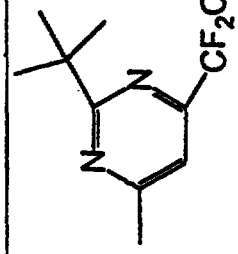
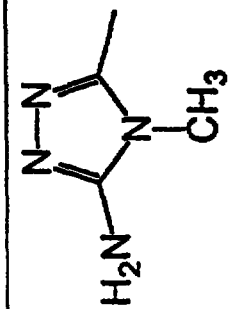
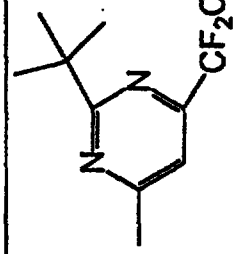
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
522				78 - 80
523				95 - 97 (Hydrochloride)
524				142 - 145
525				80 - 91

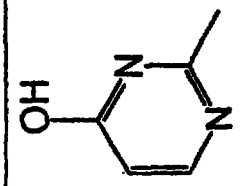
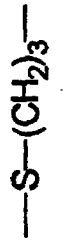
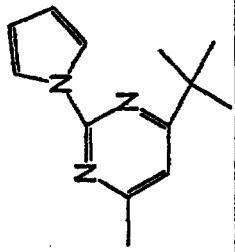
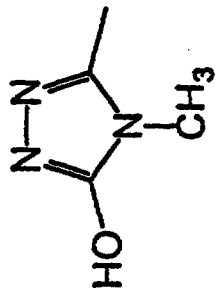
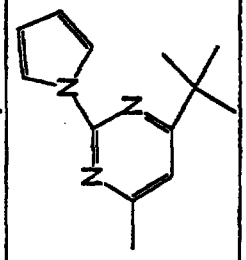
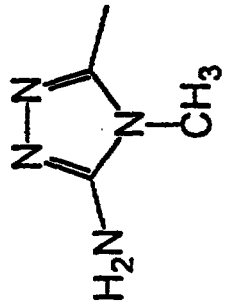
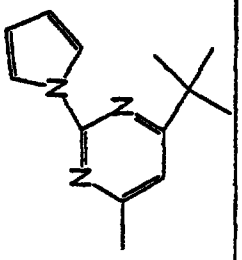
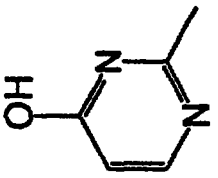
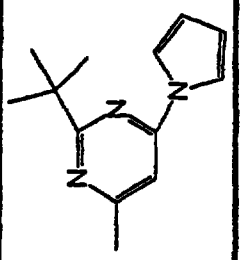
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
526				Oxalate
527				Hydrochloride
528				Oxalate
529				Dihydro-chloride

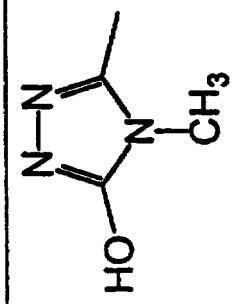
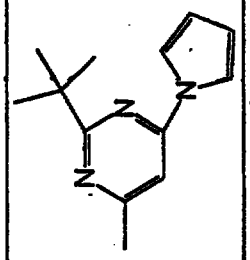
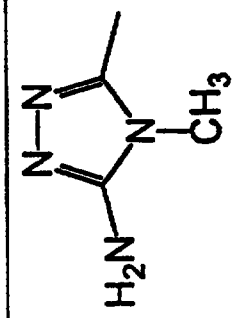
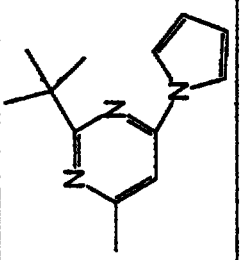
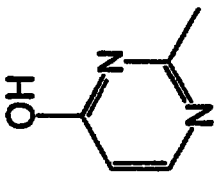
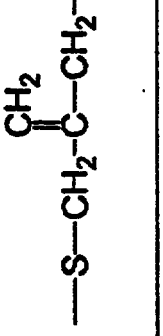
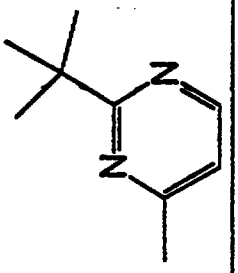
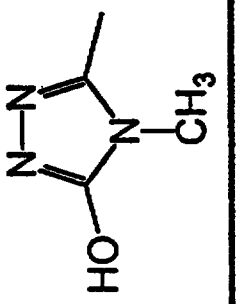
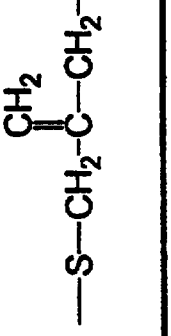
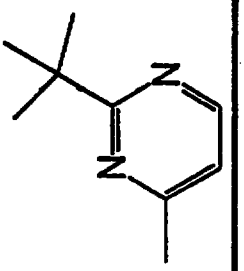
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
530				Oxalate
531				
532				
533				

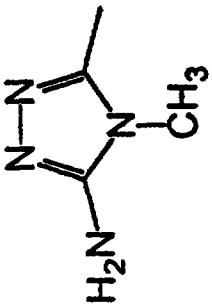
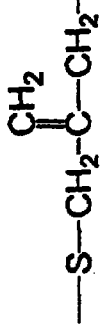
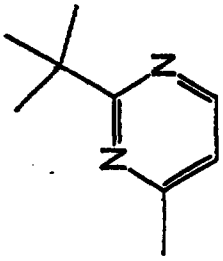
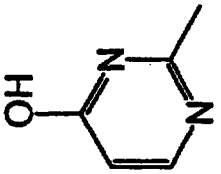
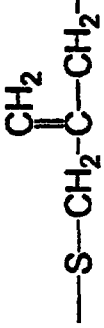
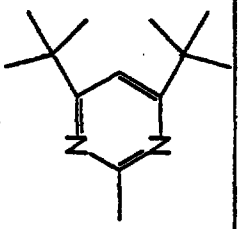
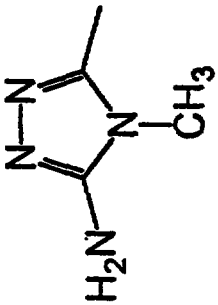
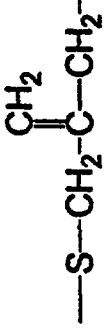
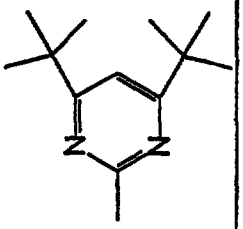
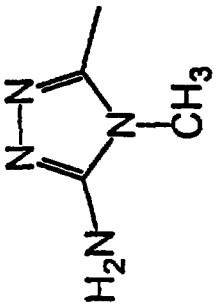
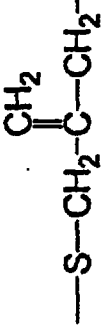
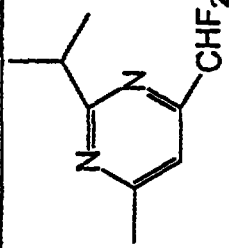
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
534				95 - 96
535				92
536				90
537				97

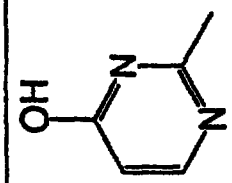
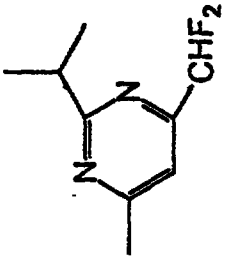
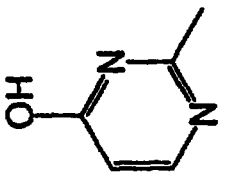
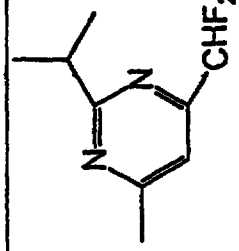
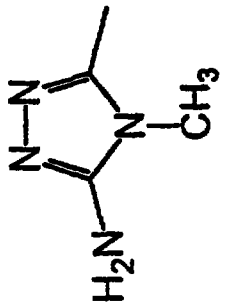
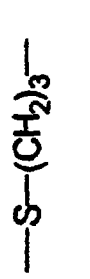
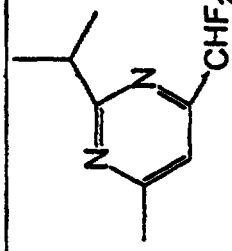
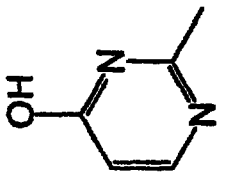
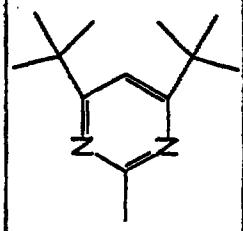
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
538				98 - 100
539				
540				
541				66 - 72

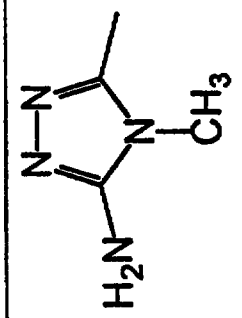
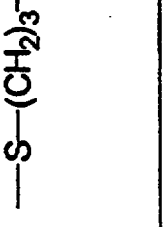
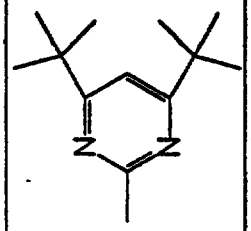
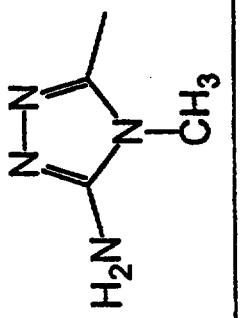
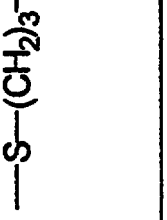
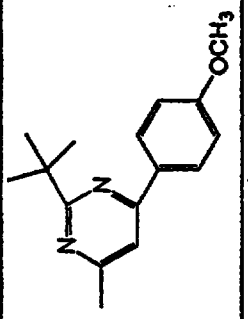
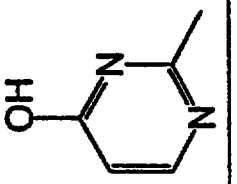
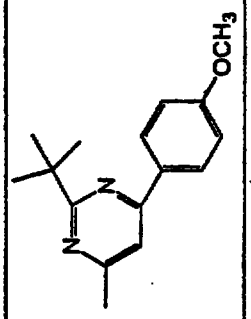
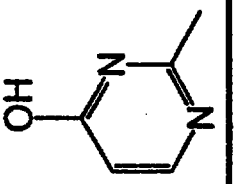
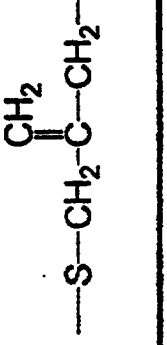
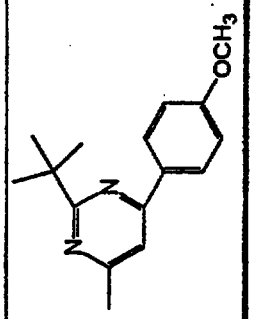
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
542		$-S-(CH_2)_3-$		
543		$-S-(CH_2)_3-$		
544		$-S-(CH_2)_3-$		
545		$-S-(CH_2)_3-$		

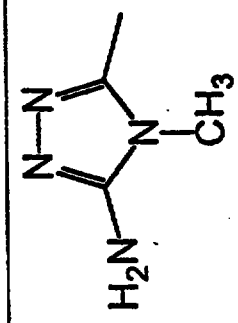
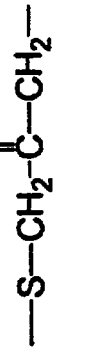
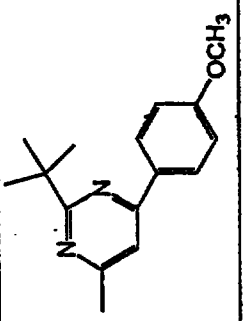
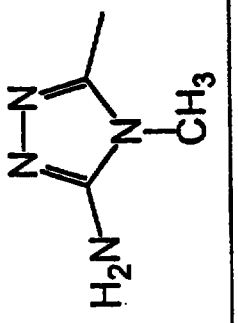
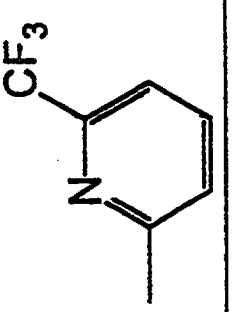
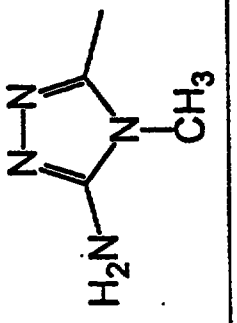
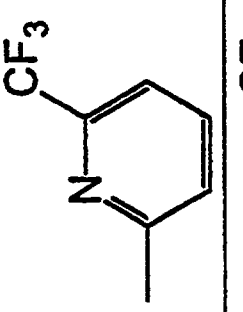
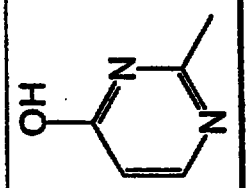
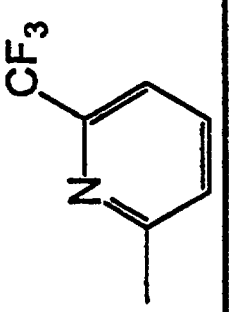
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
546				
547				
548				
549				

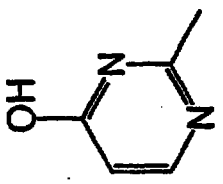
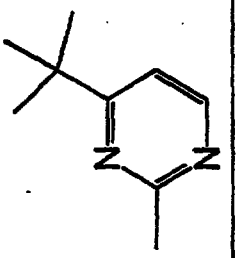
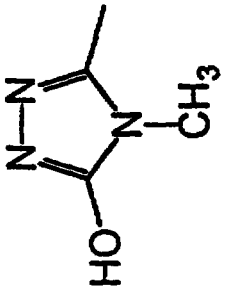
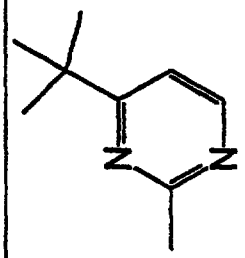
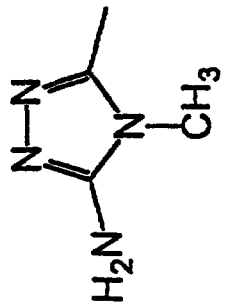
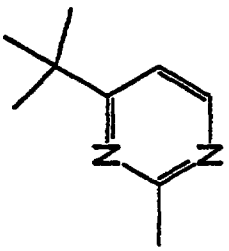
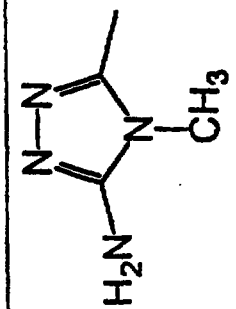
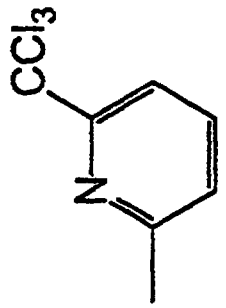
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
550				
551				
552				
553				

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

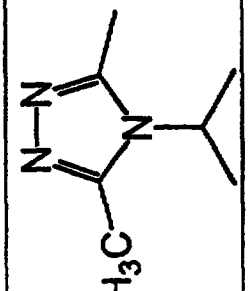
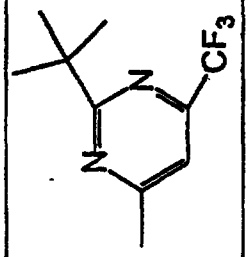
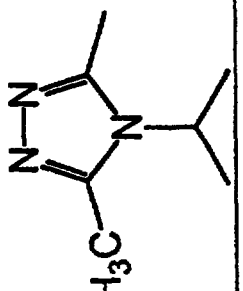
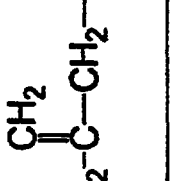
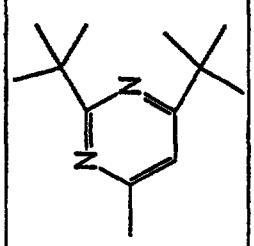
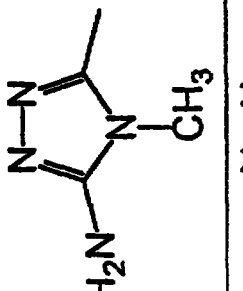
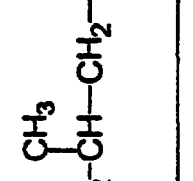
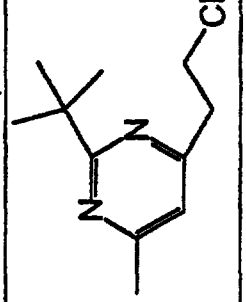
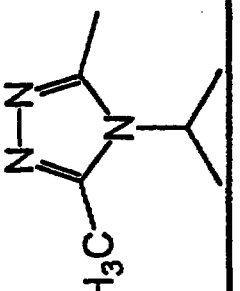
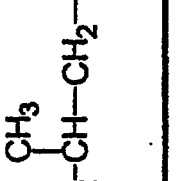
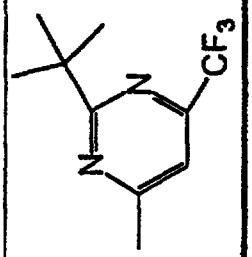
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
558				100 - 103
559				
560				109 - 112
561				

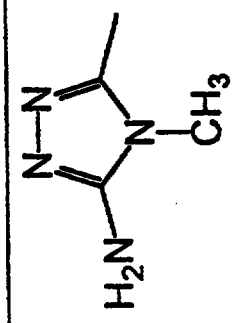
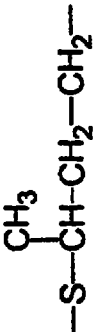
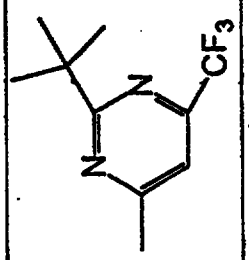
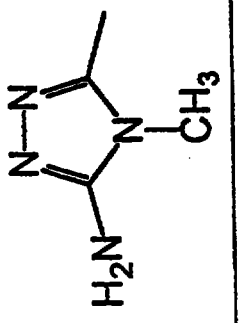
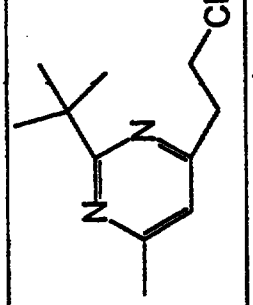
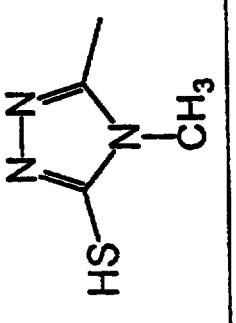
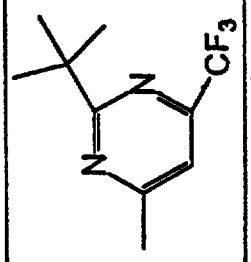
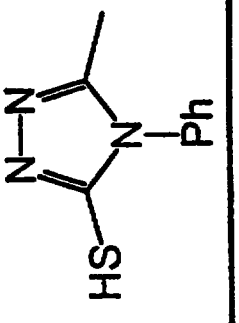
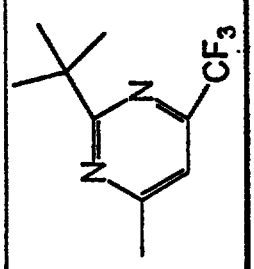
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
562				
563				
564				
565				84 - 85

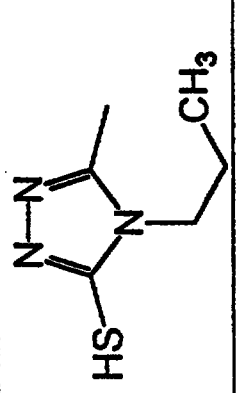
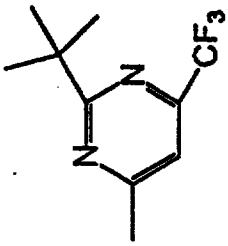
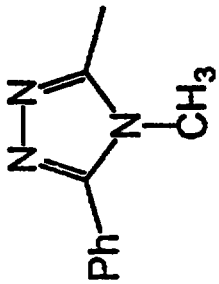
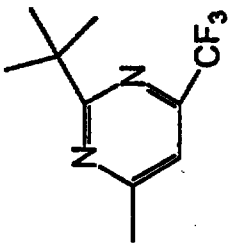
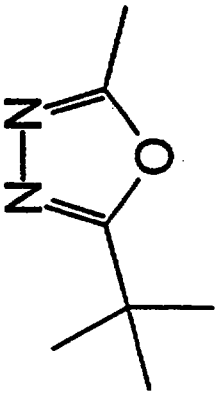
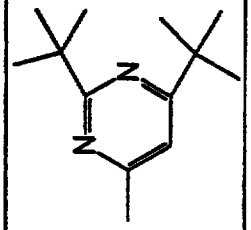
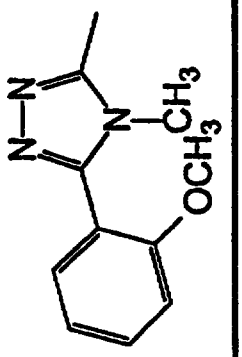
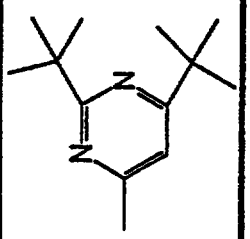
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
566				
567				
568				
569				

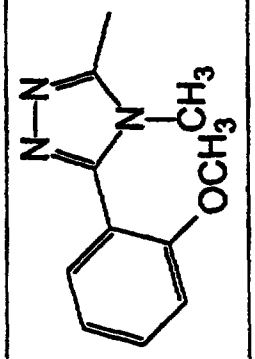
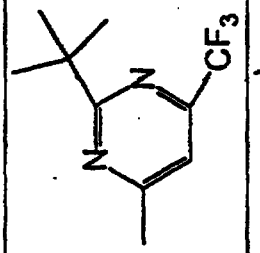
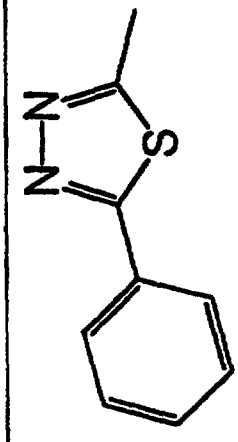
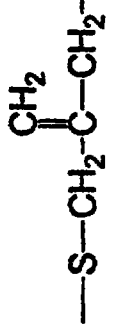
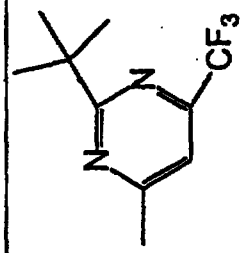
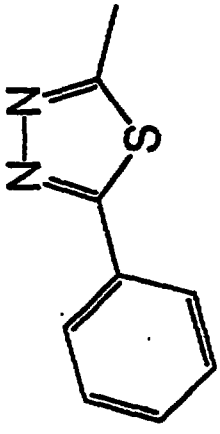
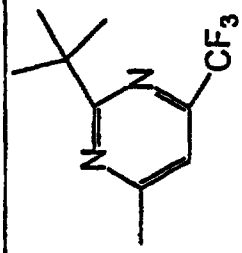
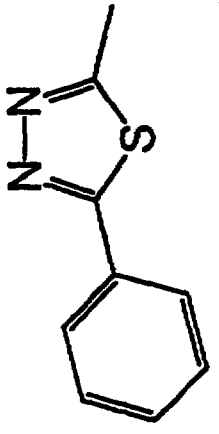
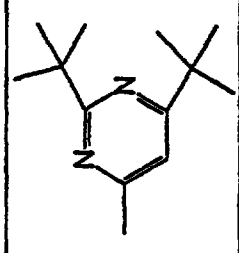
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
570		$-S-(CH_2)_3-$		
571		$-S-(CH_2)_3-$		
572		$-S-(CH_2)_3-$		
573		$-S-(CH_2)_3-$		185 - 190

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

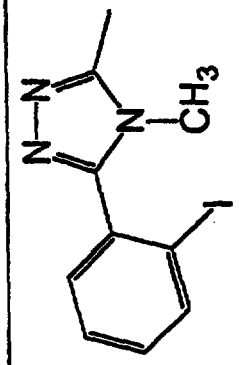
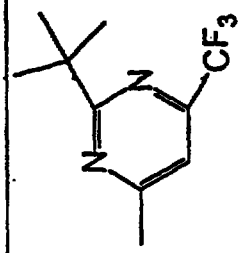
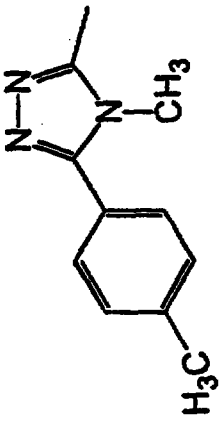
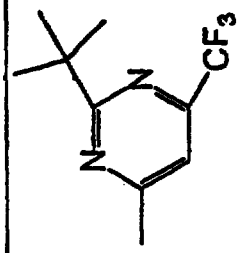
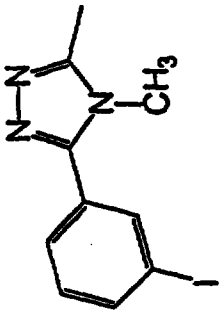
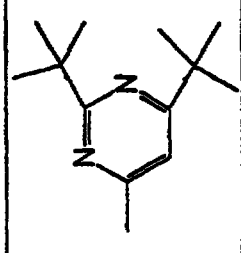
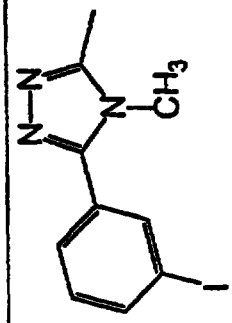
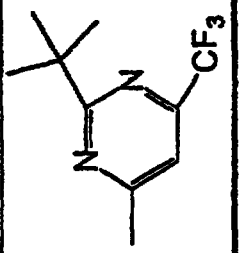
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
578				97 - 98 (Hydrochloride)
579				141 - 143 (Fumarate)
580				105 - 108 (Hydrochloride)
581				139 - 143 (Hydrochloride)

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

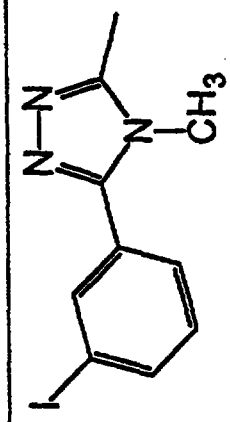
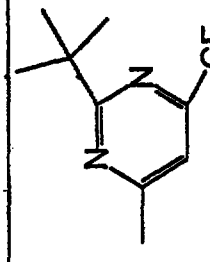
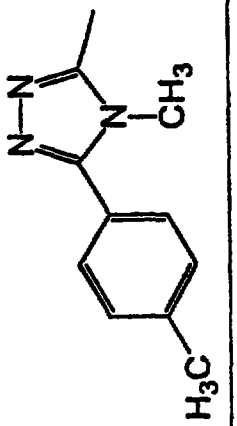
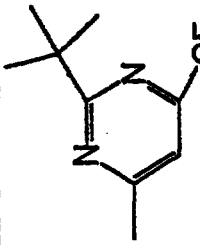
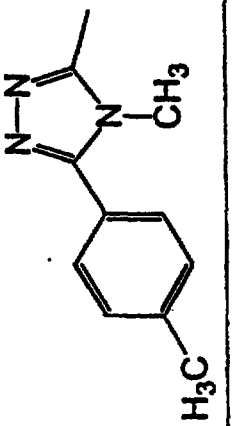
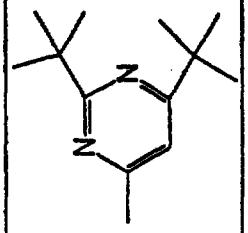
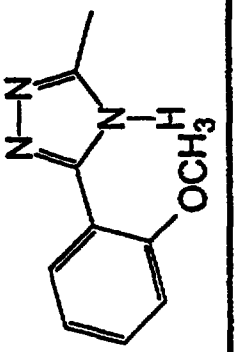
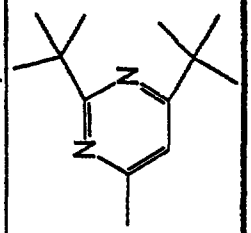
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
586		$-(CH_2)_4-$		38 - 41
587		$-CH=CH-(CH_2)_2-$		oil
588		$-S-(CH_2)_3-$		90 (Decomposition) (Hydrochloride)
589		$-S-(CH_2)_3-$		90 - 93 (Fumarate)

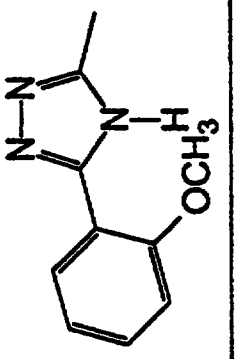
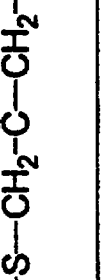
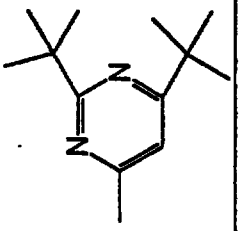
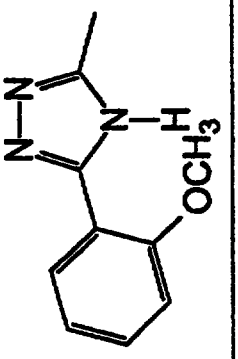
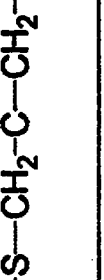
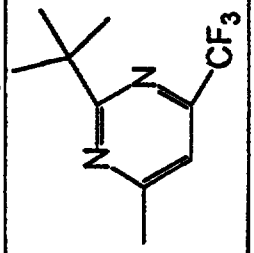
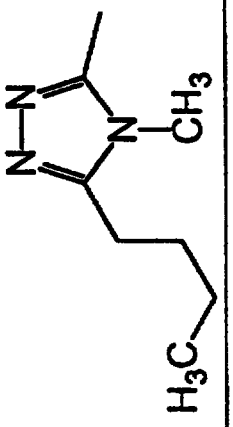
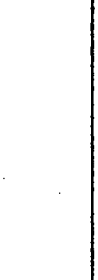
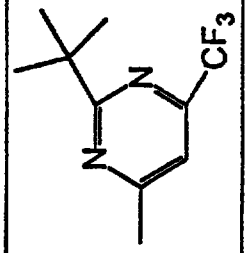
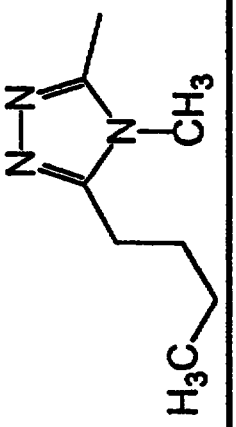
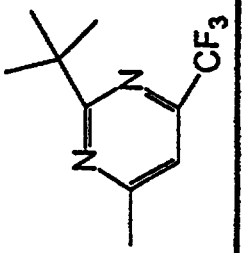
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
590				75 - 78 (Fumarate)
591				Oil
592				130 - 133 (Hydrochloride) [sic]
593				Oil

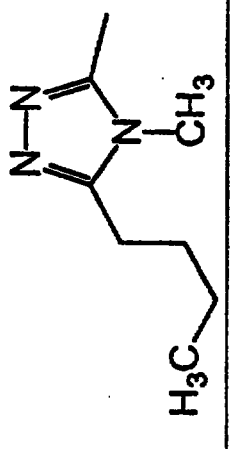
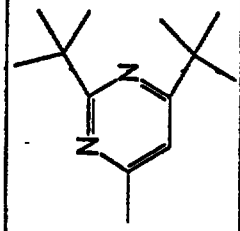
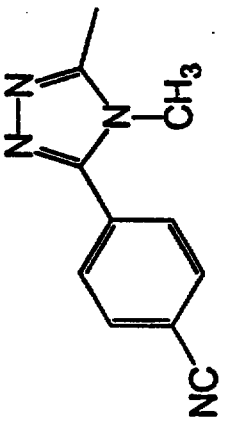
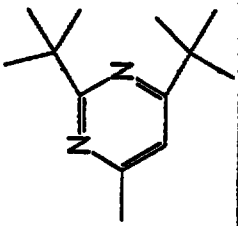
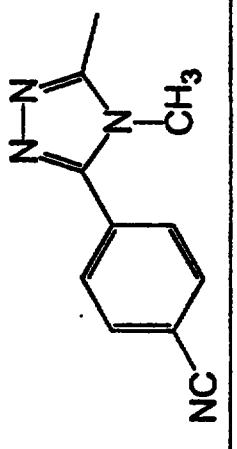
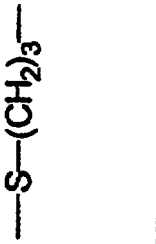
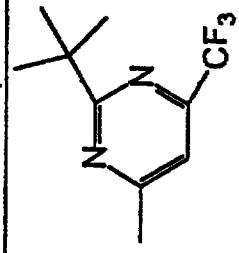
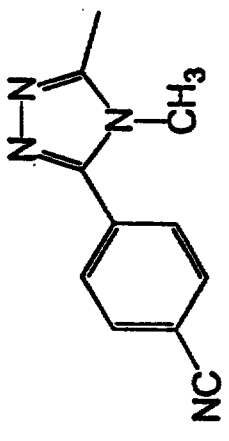
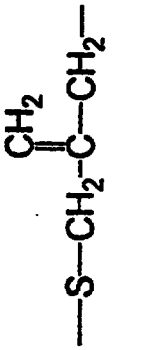
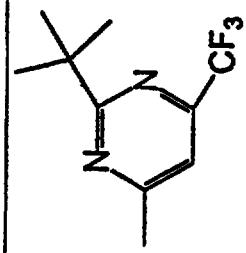
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
594				126 - 130 (Hydrochloride)
595				90 - 95 (Decomposition) (Hydrochloride)
596				Oil
597				Oil

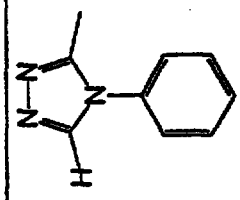
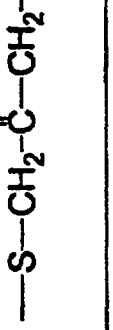
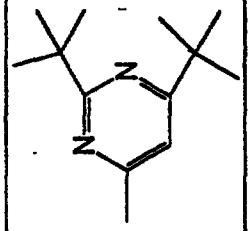
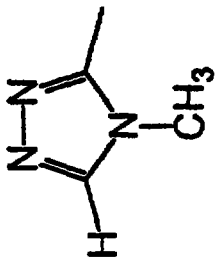
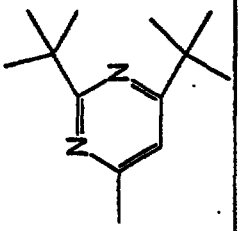
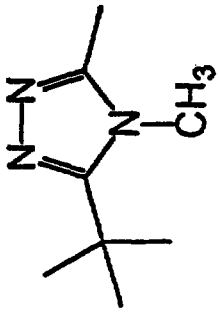
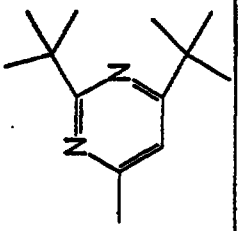
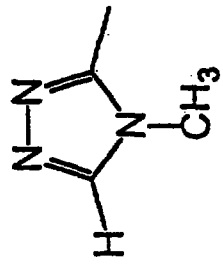
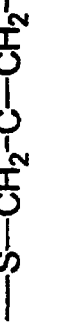
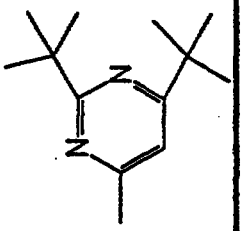
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
598				106 (Hydrochloride)
599				148 (Hydrochloride)
600				137 - 139 (Hydrochloride)
601				109 - 115 (Hydrochloride)

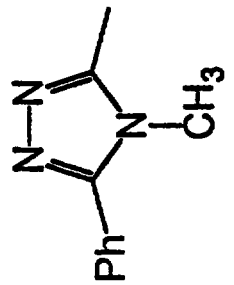
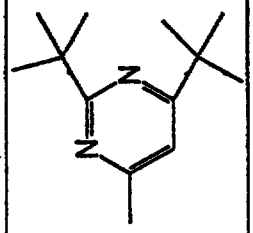
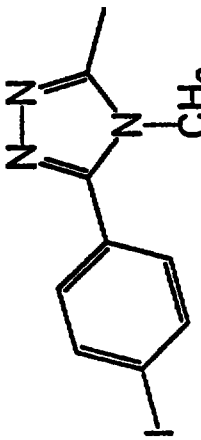
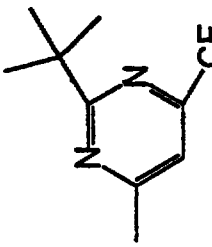
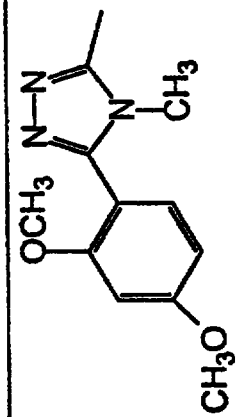
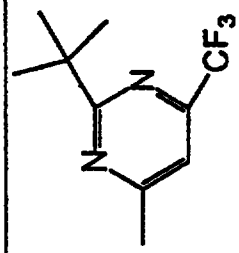
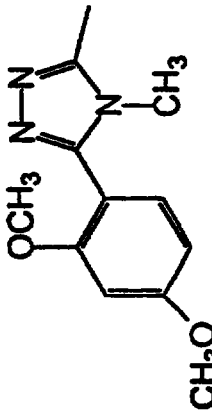
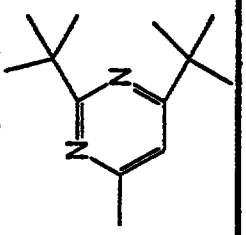
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
602				90 (Decomposition) (Hydrochloride)
603				132 (Decomposition) (Hydrochloride)
604				103 - 105 (Hydrochloride)
605				142 - 144

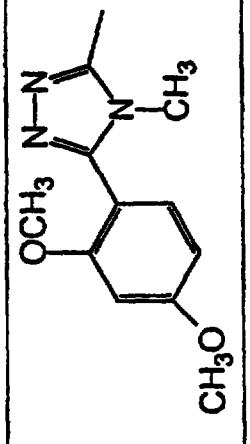
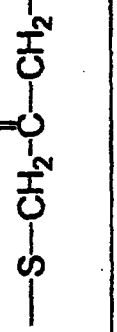
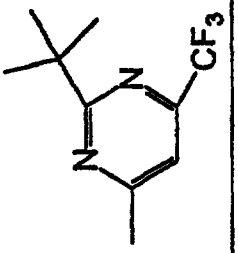
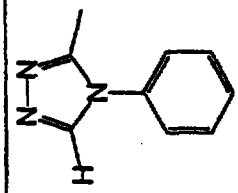
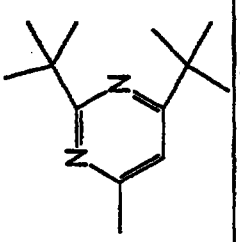
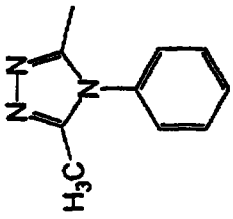
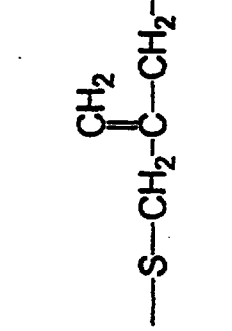
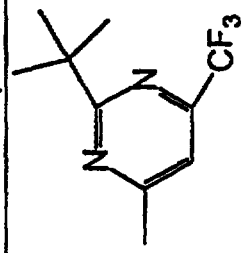
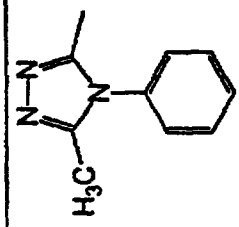
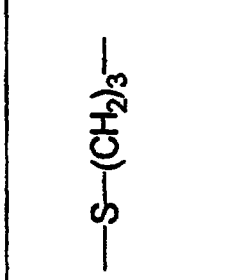
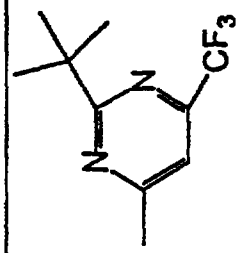
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
606		$-S-(CH_2)_3-$		Oil
607		$-S-(CH_2)_3-$		Oil
608		$-S-(CH_2)_3-$		120 - 123 (Hydrochloride)
609		$-S-(CH_2)_3-$		187 - 189 (Fumarate)

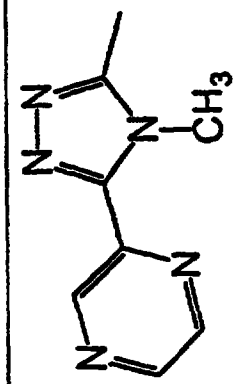
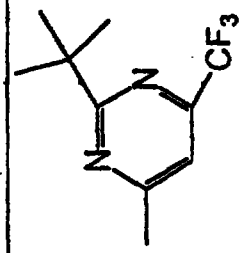
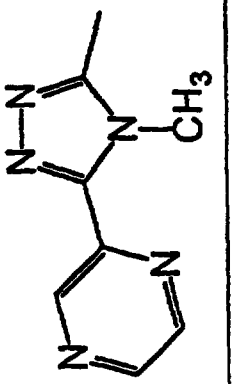
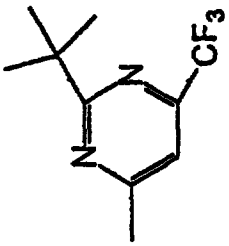
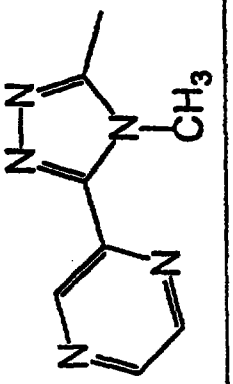
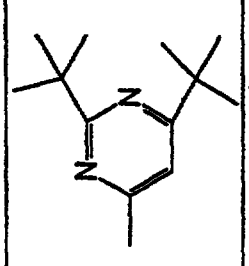
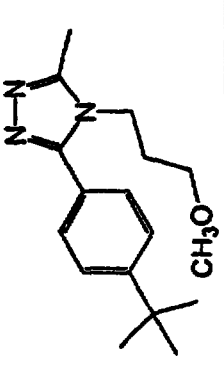
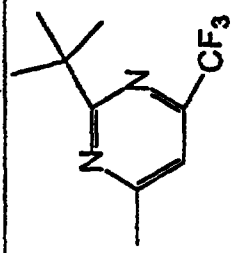
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
610				95 - 98 (Fumarate)
611				68 - 72 (Fumarate)
612				240 (Hydrochloride)
613				190 (Hydrochloride)

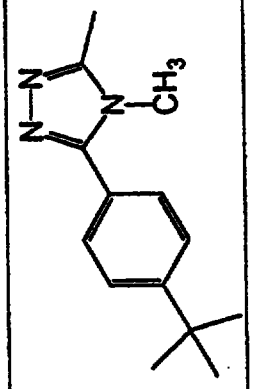
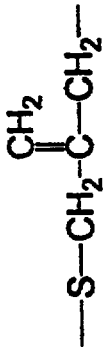
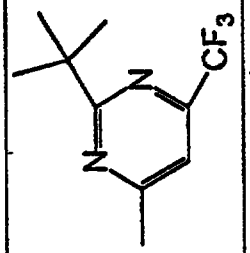
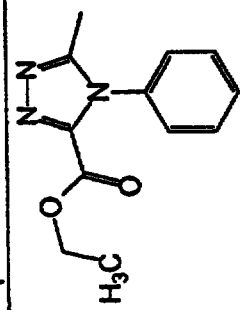
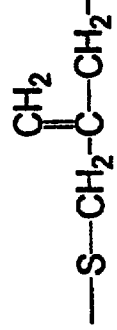
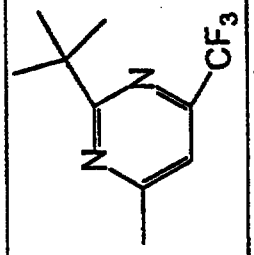
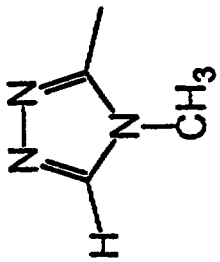
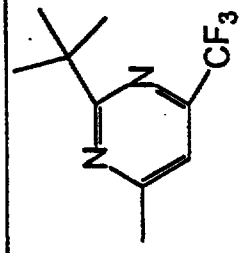
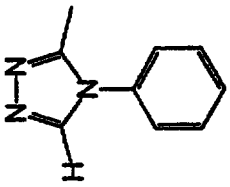
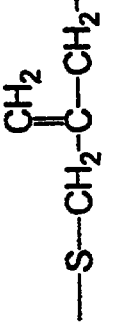
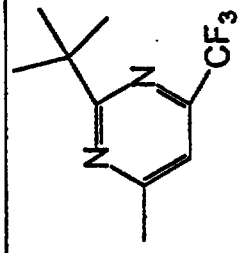
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
614				243 (Hydrochloride)
615				101 - 104
616				Oil
617				90 - 94 (Decomposition) (Hydrochloride)

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

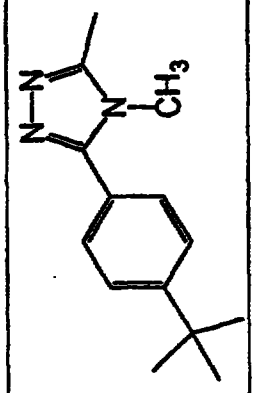
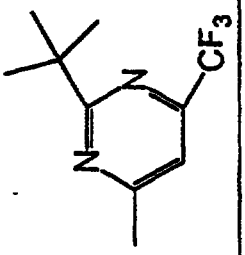
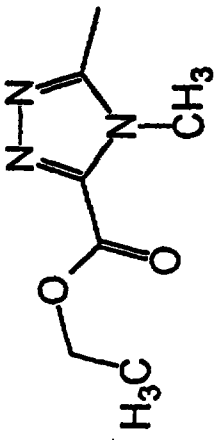
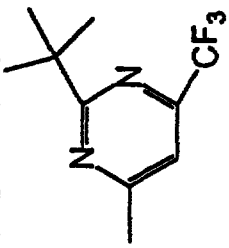
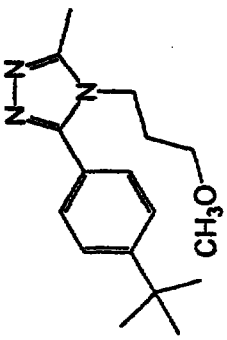
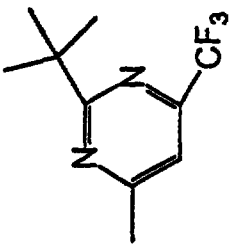
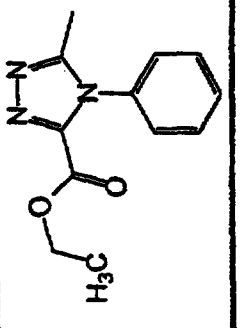
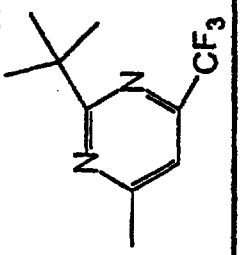
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
622		$-S-(CH_2)_3-$		110 (Hydrochloride)
623		$-S-(CH_2)_3-$		126 - 131 (Hydrochloride)
624		$-S-(CH_2)_3-$		91 (Hydrochloride)
625		$-S-(CH_2)_3-$		116 - 120 (Hydrochloride)

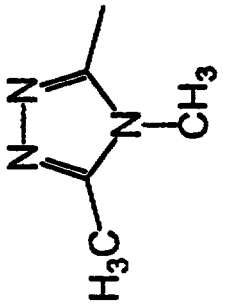
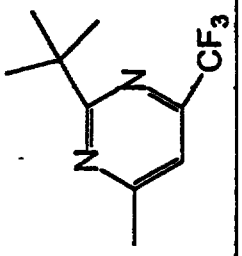
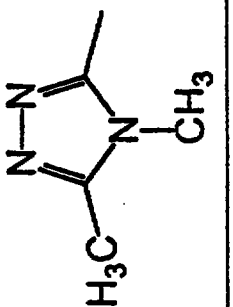
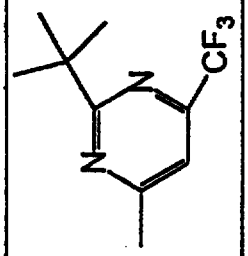
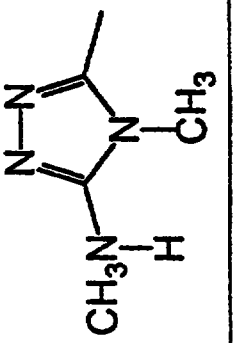
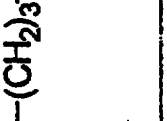
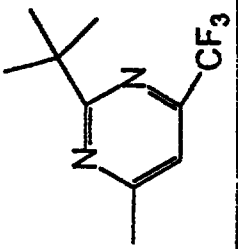
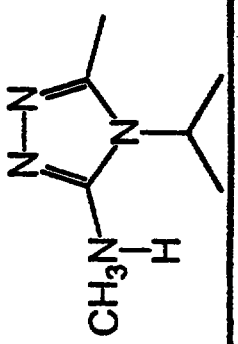
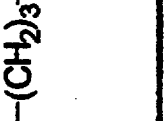
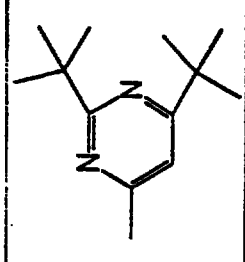
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
626				103 (Hydrochloride)
627				150 (Hydrochloride)
628				140 (Hydrochloride)
629				130 (Hydrochloride)

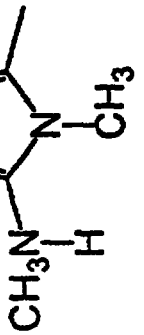
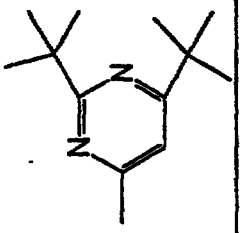
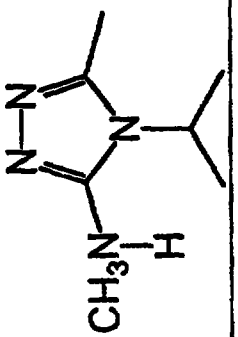
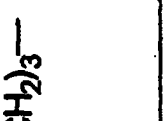
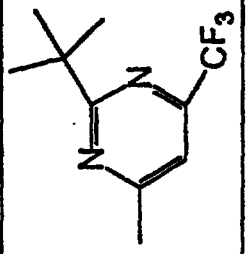
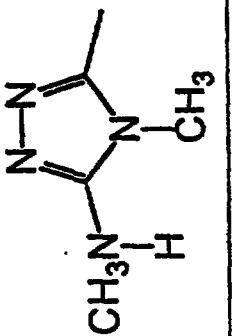
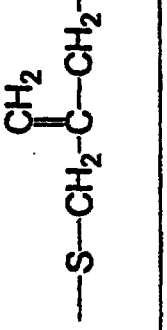
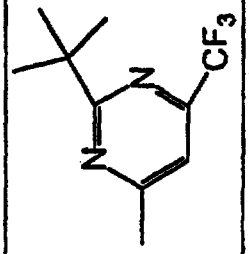
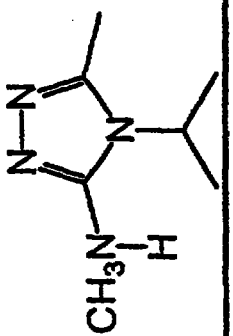
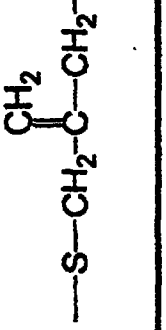
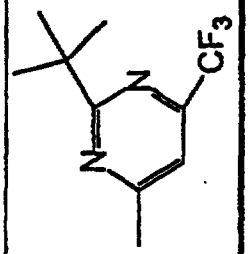
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
630				98 - 104 (Hydrochloride)
631				65 - 68 (Hydrochloride)
632				131 - 136 (Hydrochloride)
633				105 (Hydrochloride)

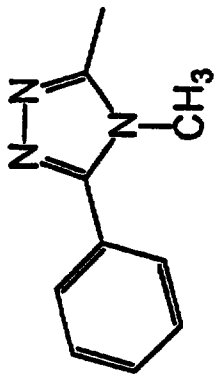
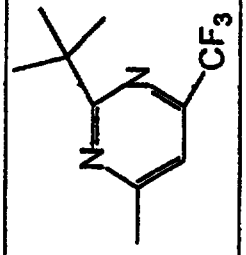
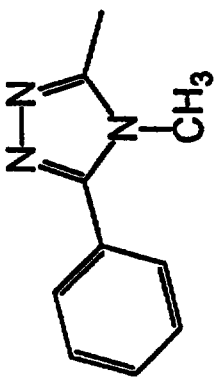
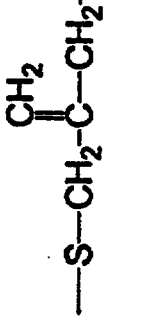
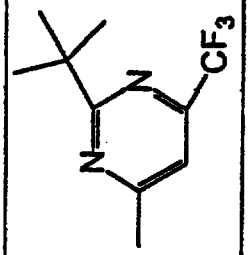
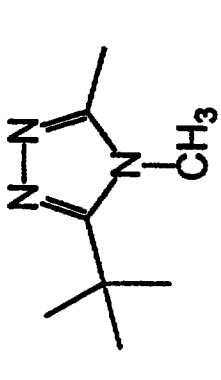
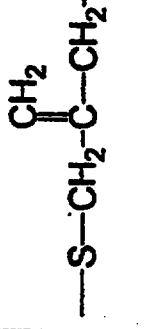
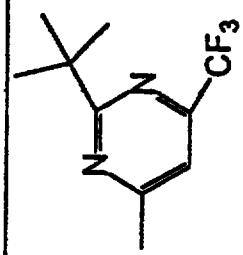
Ex. No.	Ar^1	A	Ar^2	Melting point [°C]
634				132 (Hydrochloride)
635				92 (Hydrochloride)
636				95 (Hydrochloride)
637				102 (Hydrochloride)

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

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)

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

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

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)
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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)
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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)
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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)
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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);

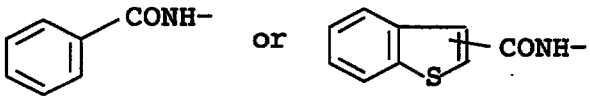
566		1.4 (s,9H); 1.9 (b,2H); 2.5 (b,2H); 2.8 (b,2H); 3.2 (s,2H); 3.3 (s,3H); 3.6 (s,2H); 3.6-3.8 (b,4H); 3.8 (s,3H); 4.8 (b,2H); 5.0 (s,2H); 6.5 (s,1H); 7.0 (d,1H); 8.0 (d,1H);
567	Oxalate	2.0 (b,2H); 2.8 (b,2H); 3.0 (b,2H); 3.3 (s,3H); 3.4 (s,2H); 3.6 (b,4H); 3.8 (b,2H); 5.1 (s,2H); 5.5 (b,2H); 7.0 (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;

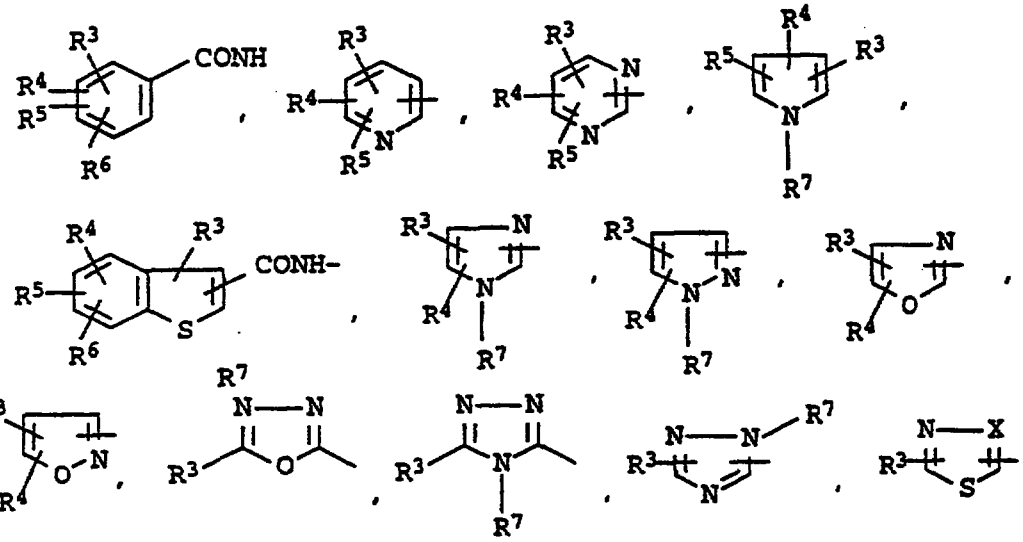
A is a C_3-C_{15}-alkylene group when Ar^1 is C_6H_5CONH, or, when Ar^1 is a 5- or 6-membered heteroaromatic ring, is a C_4-C_{15}-alkylene group or a C_3-C_{15}-alkylene group which comprises at least one group Z which is selected from O, S, NR^1, a double and a triple bond, where R^1 is as defined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

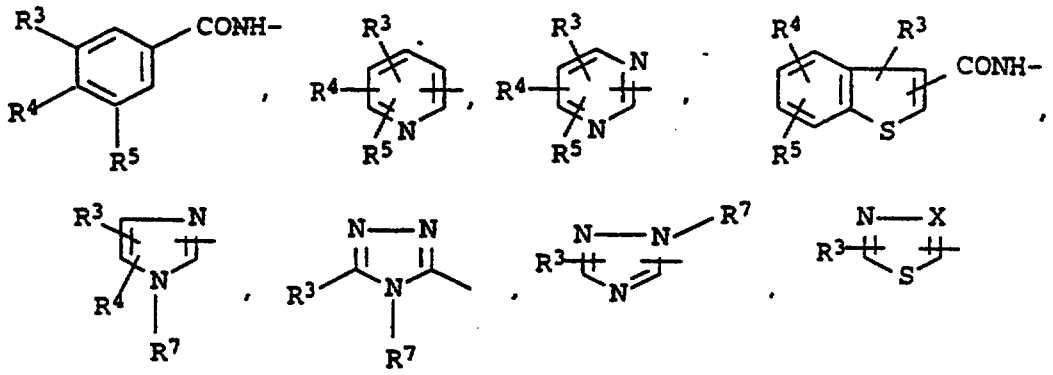
and the salts thereof with physiologically tolerated acids.

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



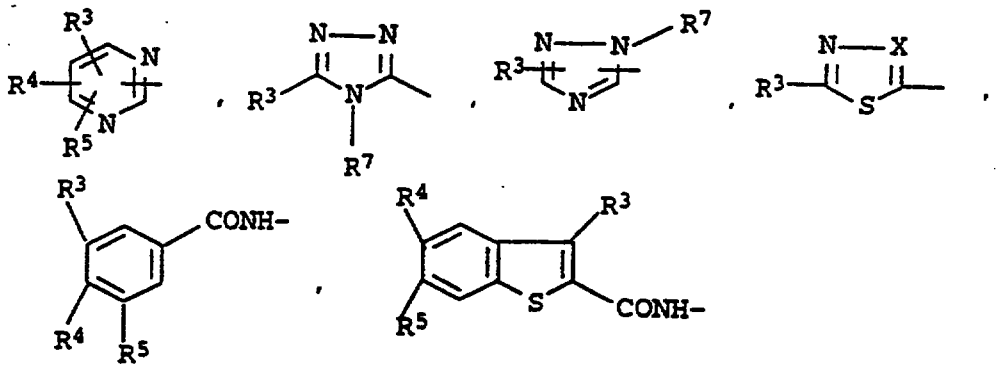
where
R^3 to R^6 are, independently of one another, H or the substituents mentioned in claim 1 for the radical Ar^1,
R^7 has the meanings stated for R^2 in claim 1 or is cycloalkyl, and
X is N or CH.

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



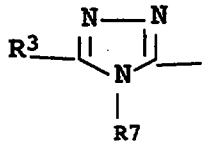
where R^3 to R^5, R^7 and X have the meanings stated in claim 2.

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.

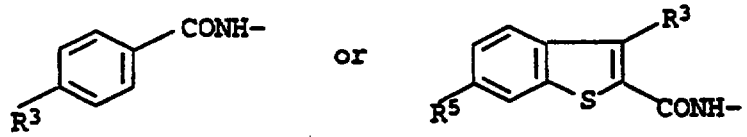
8. A compound as claimed in claim 6, where Ar^1 is



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.

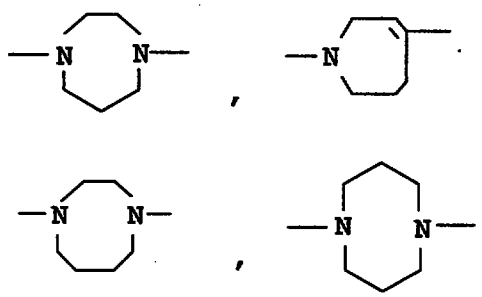
10. A compound as claimed in claim 6, where Ar^1 is



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.

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(54) Bezeichnung: SUBSTITUIERTE AZA- UND DIAZACYCLOHEPTAN- UND -CYCLOOCTANVERBINDUNGEN UND DEREN VERWENDUNG

(57) Abstract

The present invention concerns aza- and diazacycloheptane and cyclooctane compounds from the following formula (I) Ar^1-A-B-Ar^2 wherein Ar^1, A, B, and Ar^2 have the meanings given in the description. The compounds according to the invention possess a high affinity with the dopamine-D_3-receptors and can therefore be used for the treatment of illness, which react to dopamine-D_3-ligands.

(57) Zusammenfassung

Die vorliegende Erfindung betrifft Aza- und Diazacycloheptan- und -cyclooctanverbindungen der folgenden Formel (I) Ar^1-A-B-Ar^2, worin Ar^1, A, B und Ar^2 die in der Beschreibung angegebenen Bedeutungen besitzen. Die erfindungsgemäßen Verbindungen besitzen eine hohe Affinität zum Dopamin-D_3-Rezeptor und sind daher zur Behandlung von Erkrankungen brauchbar, die auf Dopamin-D_3-Liganden ansprechen.