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(71) Demandeur/Applicant:
SCHERING AKTIENGESELLSCHAFT, DE

(72) Inventeurs/Inventors:
BRUMBY, THOMAS, DE;
JAUTELAT, ROLF, DE;
PRIEN, OLAF, DE;
SCHAEFER, MARTINA, DE;

...

(74) Agent: MARKS & CLERK

(54) Titre : PYRIMIDINE INHIBITRICE DE LA CDK, SA PRODUCTION ET SON UTILISATION COMME MEDICAMENT

(54) Title: CDK INHIBITING PYRIMIDINES, PRODUCTION THEREOF AND THEIR USE AS MEDICAMENTS

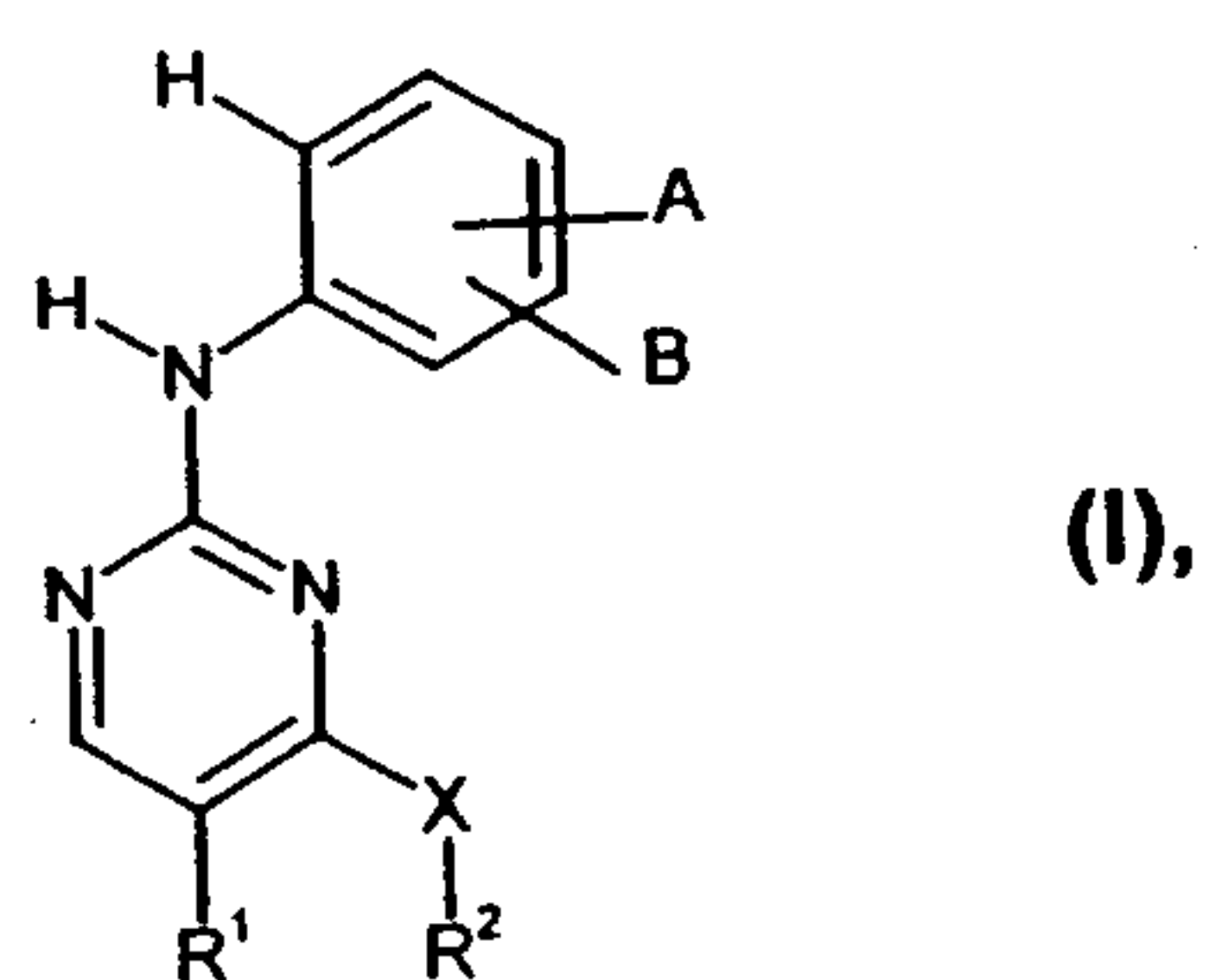
(57) **Abrégé/Abstract:**

The invention relates to the pyrimidine derivatives of general formula (1), wherein R¹, R², X, A and B are defined as in the description, for use as inhibitors of the cyclin-dependent kinase. The invention further relates to the production thereof as well as to their use as medicament in the treatment of various diseases.

(72) **Inventeurs(suite)/Inventors(continued)**: SIEMEISTER, GERHARD, DE; LUECKING, ULRICH, DE;
HUWE, CHRISTOPH, DE

Abstract

This invention relates to pyrimidine derivatives of general formula I



in which R¹, R², X, A and B have the meanings that are contained in the description, as inhibitors of the cyclin-dependent kinases, their production as well as their use as medications for treating various diseases.

CDK-Inhibitory Pyrimidines, Their Production and Use as Pharmaceutical Agents

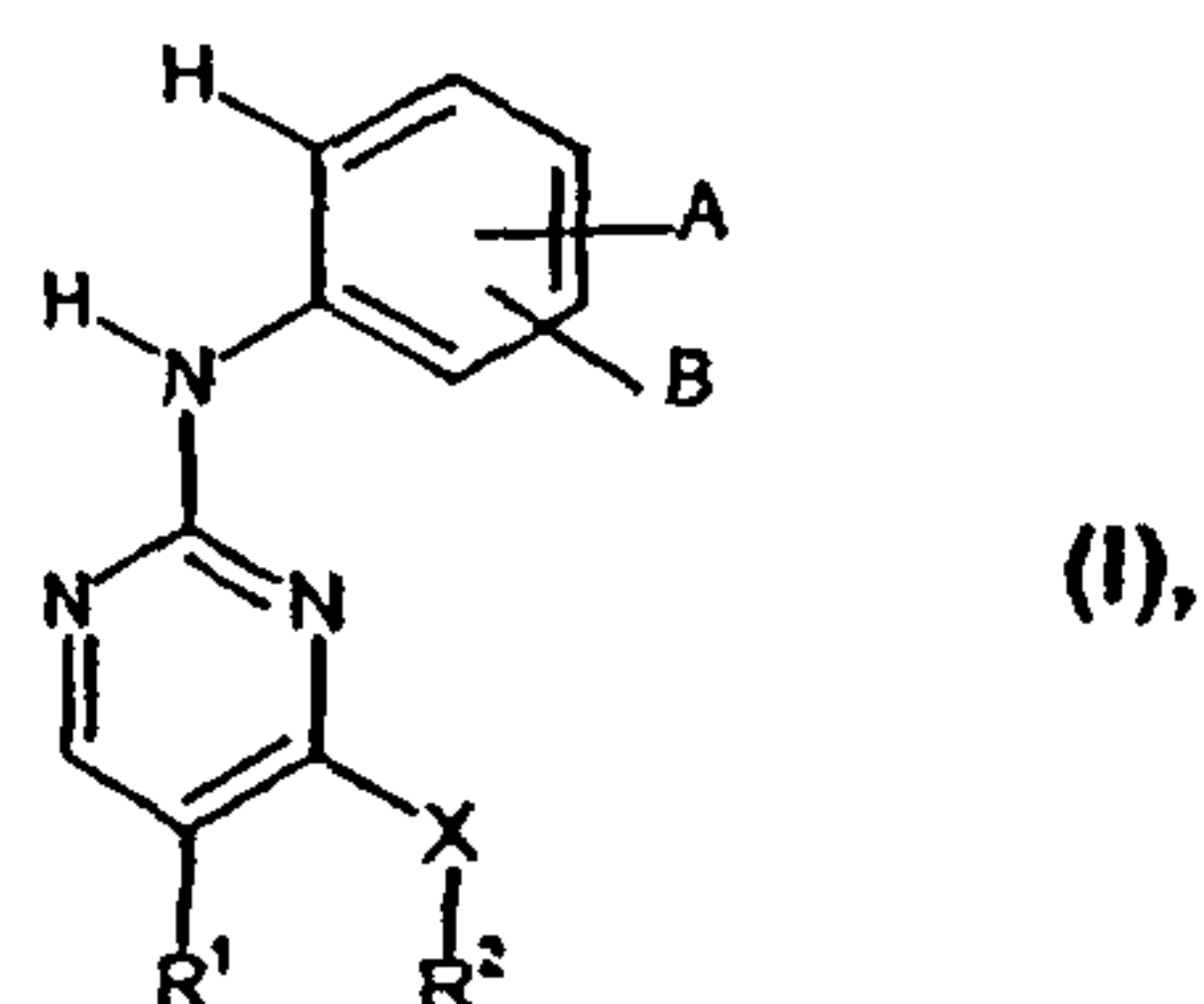
This invention relates to pyrimidine derivatives, their production as well as their use as medications for treating various diseases.

The CDKs (cyclin-dependent kinase) is an enzyme family that plays an important role in the regulation of the cell cycle and thus is an especially advantageous target for the development of small inhibitory molecules. Selective inhibitors of the CDKs can be used for treating cancer or other diseases that cause disruptions of cell proliferation.

Pyrimidines and analogs are already described as active ingredients, such as, for example, the 2-anilino-pyrimidines as fungicides (DE 4029650) or substituted pyrimidine derivatives for treating neurological or neurodegenerative diseases (WO 99/19305). As CDK-inhibitors, the most varied pyrimidine derivatives are described, for example bis(anilino)-pyrimidine derivatives (WO 00/12486), 2-amino-4-substituted pyrimidines (WO 01/14375), purines (WO 99/02162), 5-cyano-pyrimidines (WO 02/04429), anilinopyrimidines (WO 00/12486) and 2-hydroxy-3-N,N-dimethylaminopropoxy-pyrimidines (WO 00/39101).

The object of this invention is to provide compounds that have better properties than the inhibitors that are already known. The substances that are described here are more effective, since they already inhibit in the nanomolar range and can be distinguished from other already known CDK-inhibitors such as, e.g., olomoucine and roscovitine.

It has now been found that compounds of general formula I

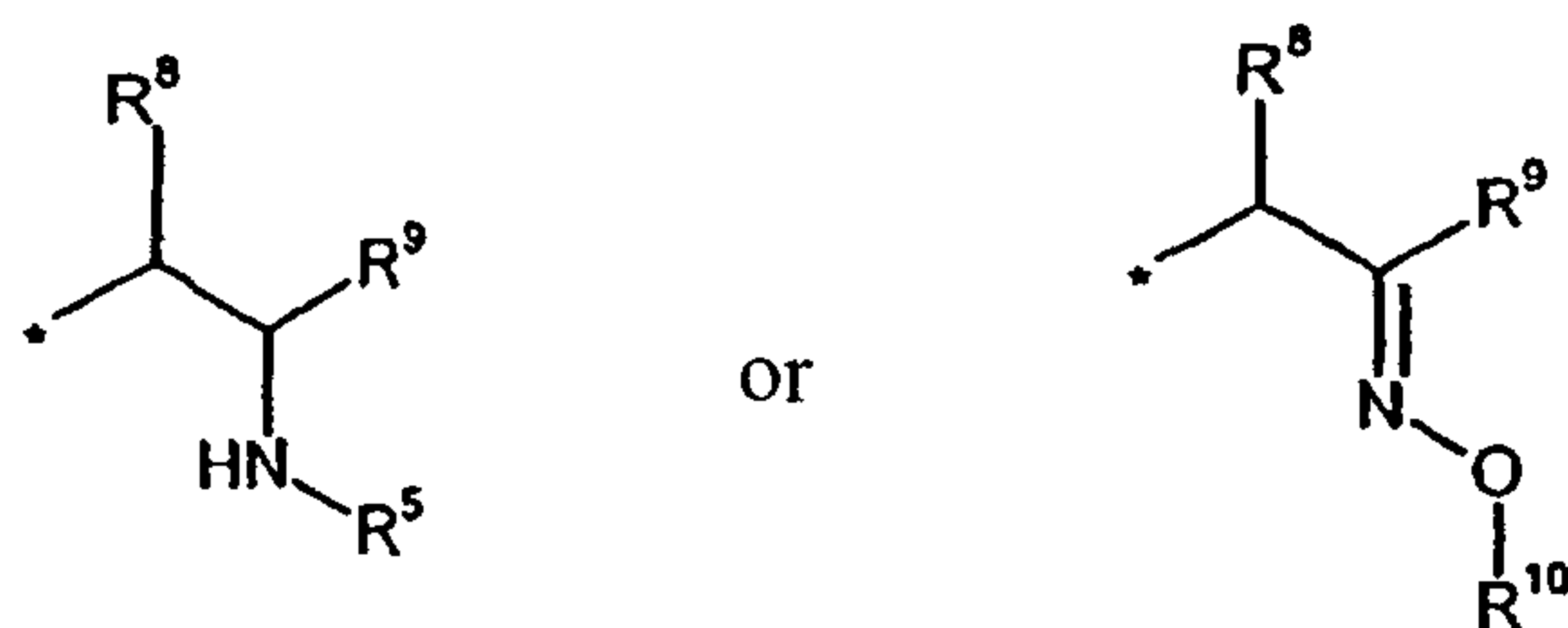


in which

- R^1 stands for hydrogen, halogen, C_1 - C_6 -alkyl, nitro, or for the group $-COR^5$, $-OCF_3$, $-(CH_2)_nR^5$, $-S-CF_3$ or $-SO_2CF_3$,
- R^2 stands for C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl, C_2 - C_{10} -alkinyl, or C_3 - C_{10} -cycloalkyl or for C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl, C_2 - C_{10} -alkinyl, or C_3 - C_{10} -cycloalkyl that is substituted in one or more places in the same way or differently with hydroxy, halogen, C_1 - C_6 -alkoxy, C_1 - C_6 -alkylthio, amino, cyano, C_1 - C_6 -alkyl, $-NH-(CH_2)_n-C_3$ - C_{10} -cycloalkyl, C_3 - C_{10} -cycloalkyl, C_1 - C_6 -hydroxyalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkinyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, $-NHC_1$ - C_6 -alkyl, $-N(C_1$ - C_6 -alkyl) $_2$, $-SO(C_1$ - C_6 -alkyl), $-SO_2(C_1$ - C_6 -alkyl), C_1 - C_6 -alkanoyl, $-CONR^3R^4$, $-COR^5$, C_1 - C_6 -alkylOAc, carboxy, aryl, heteroaryl, $-(CH_2)_n$ -aryl, $-(CH_2)_n$ -heteroaryl, phenyl- $(CH_2)_n$ - R^5 , $-(CH_2)_nPO_3(R^5)_2$ or with the group $-R^6$ or $-NR^3R^4$, and the phenyl, C_3 - C_{10} -cycloalkyl, aryl, heteroaryl, $-(CH_2)_n$ -aryl and $-(CH_2)_n$ -heteroaryl itself optionally can be substituted in one or more places in the same way

or differently with halogen, hydroxy, C_1-C_6 -alkyl, C_1-C_6 -alkoxy, heteroaryl, benzoxy or with the group $-CF_3$ or $-OCF_3$, and the ring of the C_3-C_{10} -cycloalkyl and the C_1-C_{10} -alkyl optionally can be interrupted by one or more nitrogen, oxygen and/or sulfur atoms and/or can be interrupted by one or more $=C=O$ groups in the ring and/or optionally one or more possible double bonds can be contained in the ring, or

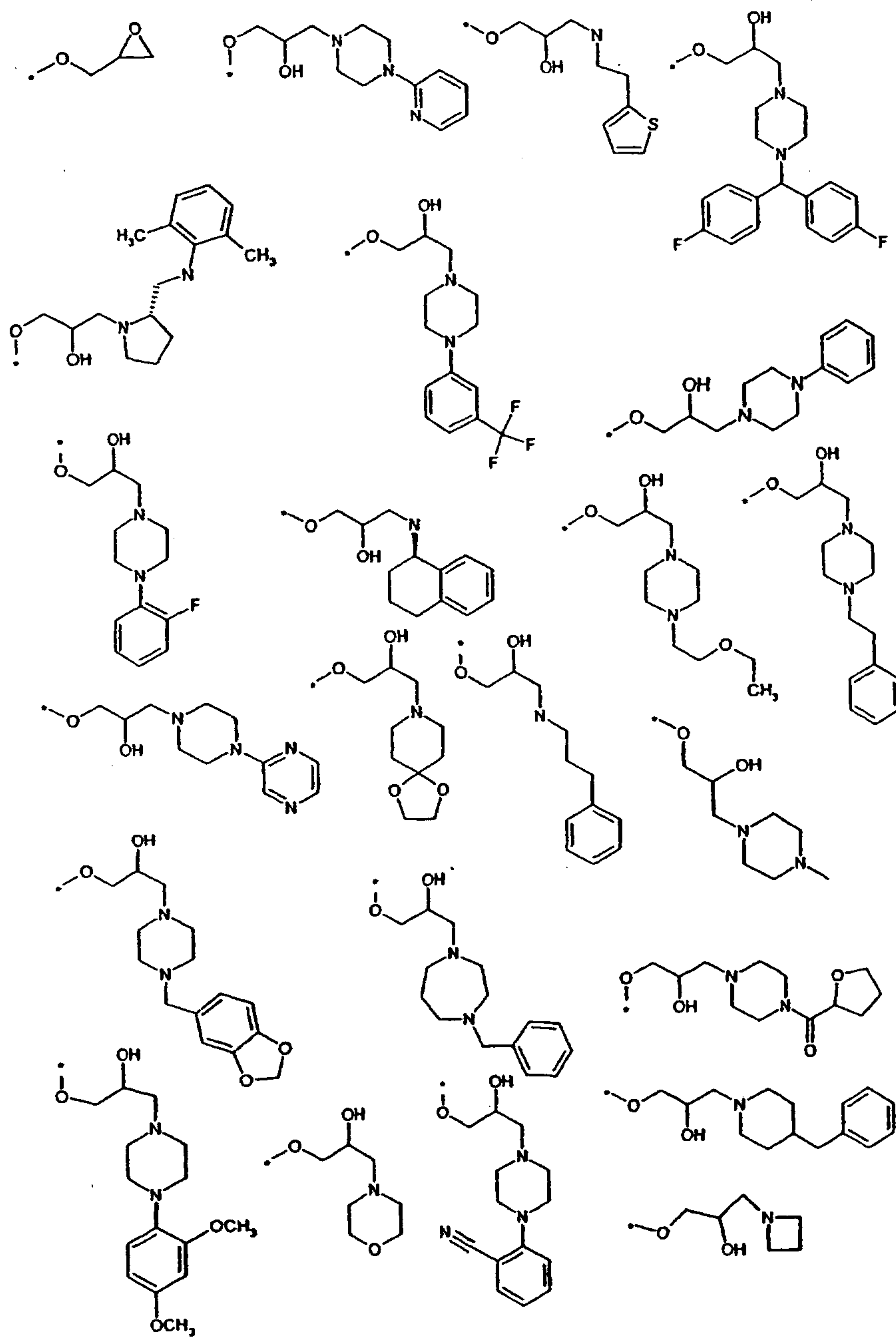
R^2 stands for the group



X stands for oxygen or for the group $-NH-$, $-N(C_1-C_3\text{-alkyl})$ or for $-OC_3-C_{10}$ -cycloalkyl, which can be substituted in one or more places in the same way or differently with a heteroaromatic compound, or

X and R^2 together form a C_3-C_{10} -cycloalkyl ring, which optionally can contain one or more heteroatoms and optionally can be substituted in one or more places with hydroxy, C_1-C_6 -alkyl, C_1-C_6 -alkoxy or halogen,

A and B, in each case independently of one another, stand for hydrogen, hydroxy, C_1-C_3 -alkyl, C_1-C_6 -alkoxy or for the group $-SR^7$, $-S(O)R^7$, $-SO_2R^7$, $-NHSO_2R^7$, $-CH(OH)R^7$, $-CR^7(OH)-R^7$, C_1-C_6 -alkyl $P(O)OR^3OR^4$ or $-COR^7$, or for



or

A and B together form a C₃-C₁₀-cycloalkyl ring that optionally can be interrupted by one or more nitrogen, oxygen and/or sulfur atoms and/or can be interrupted by one or more =C=O or =SO₂ groups in the ring and/or optionally one or more possible double bonds can be contained in the ring, and the C₃-C₁₀-cycloalkyl ring optionally can be substituted in one or more places in the same way or differently with hydroxy, halogen, C₁-C₆-alkoxy, C₁-C₆-alkylthio, amino, cyano, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₃-C₁₀-cycloalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, -NHC₁-C₆-alkyl, -N(C₁-C₆-alkyl)₂, -SO(C₁-C₆-alkyl), -SO₂R⁷, C₁-C₆-alkanoyl, -CONR³R⁴, -COR⁵, C₁-C₆-alkoxyOAc, phenyl or with the group R⁶, whereby the phenyl itself optionally can be substituted in one or more places in the same way or differently with halogen, hydroxy, C₁-C₆-alkyl, C₁-C₆-alkoxy or with the group -CF₃ or -OCF₃,

R³ and R⁴, in each case independently of one another, stand for hydrogen, phenyl, benzyloxy, C₁-C₁₂-alkyl, C₁-C₆-alkoxy, C₂-C₄-alkenyloxy, C₃-C₆-cycloalkyl, hydroxy, hydroxy-C₁-C₆-alkyl, dihydroxy-C₁-C₆-alkyl, heteroaryl, heterocyclo-C₃-C₁₀-alkyl, heteroaryl-C₁-C₃-alkyl, C₃-C₆-cycloalkyl-C₁-C₃-alkyl that is optionally substituted with cyano, or for C₁-C₆-alkyl that is optionally substituted in one or more places in the same way or differently with phenyl, pyridyl, phenyloxy, C₃-C₆-cycloalkyl, C₁-C₆-alkyl or C₁-C₆-alkoxy,

whereby the phenyl itself can be substituted in one or more places in the same way or differently with halogen, C₁-C₆-alkyl, C₁-C₆-alkoxy or with the group -SO₂NR³R⁴,
 or for the group -(CH₂)_nNR³R⁴, -CNHNH₂ or -NR³R⁴,
 or

R³ and R⁴ together form a C₃-C₁₀-cycloalkyl ring that optionally can be interrupted by one or more nitrogen, oxygen and/or sulfur atoms and/or can be interrupted by one or more =C=O groups in the ring and/or optionally one or more possible double bonds can be contained in the ring,
 R⁵ stands for hydroxy, phenyl, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, benzoxy, C₁-C₆-alkylthio or C₁-C₆-alkoxy,
 R⁶ stands for a heteroaryl or C₃-C₁₀-cycloalkyl ring, whereby the ring has the above-indicated meaning,
 R⁷ stands for halogen, hydroxy, phenyl, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkinyl, C₃-C₁₀-cycloalkyl, with the above-indicated meaning, or for the group -NR³R⁴, or for a C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl, C₂-C₁₀-alkinyl or C₃-C₇-cycloalkyl that is substituted in one or more places in the same way or differently with hydroxy, C₁-C₆-alkoxy, halogen, phenyl, -NR³R⁴ or phenyl, which itself can be substituted in one or more places in the same way or differently with halogen, hydroxy, C₁-C₆-alkyl, C₁-C₆-alkoxy, halo-C₁-C₆-alkyl, halo-C₁-C₆-alkoxy, or R⁷ stands for phenyl, which itself can be substituted in one or more places in the same way or differently

with halogen, hydroxy, C₁-C₆-alkyl or C₁-C₆-alkoxy, halo-C₁-C₆-alkyl, or halo-C₁-C₆-alkoxy,

R⁸, R⁹ and

R¹⁰, in each case independently of one another, stand for hydrogen, hydroxy, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl, C₂-C₁₀-alkinyl, C₃-C₁₀-cycloalkyl, aryl, heteroaryl or for C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl, C₂-C₁₀-alkinyl or C₃-C₁₀-cycloalkyl that is optionally substituted in one or more places in the same way or differently with hydroxy, halogen, C₁-C₆-alkoxy, C₁-C₆-alkylthio, amino, cyano, C₁-C₆-alkyl, -NH-(CH₂)_n-C₃-C₁₀-cycloalkyl, C₃-C₁₀-cycloalkyl, C₁-C₆-hydroxyalkyl, C₂-C₆-alkenyl, C₂-C₆-alkinyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkoxy-C₁-C₆-alkyl, -NHC₁-C₆-alkyl, -N(C₁-C₆-alkyl)₂, -SO(C₁-C₆-alkyl), -SO₂(C₁-C₆-alkyl), C₁-C₆-alkanoyl, -CONR³R⁴, -COR⁵, C₁-C₆-alkylOAc, carboxy, aryl, heteroaryl, -(CH₂)_n-aryl, -(CH₂)_n-heteroaryl, phenyl-(CH₂)_n-R⁵, -(CH₂)_nPO₃(R⁵)₂ or with the group -R⁶ or -NR³R⁴, and the phenyl, C₃-C₁₀-cycloalkyl, aryl, heteroaryl, -(CH₂)_n-aryl and -(CH₂)_n-heteroaryl itself optionally can be substituted in one or more places in the same way or differently with halogen, hydroxy, C₁-C₆-alkyl, C₁-C₆-alkoxy or with the group -CF₃ or -OCF₃, and the ring of C₃-C₁₀-cycloalkyl and the C₁-C₁₀-alkyl optionally can be interrupted by one or more nitrogen, oxygen and/or sulfur atoms and/or can be interrupted by one or more =C=O groups in the ring and/or optionally one or more possible double bonds can be contained in the ring, and

n stands for 0-6,

as well as isomers, diastereomers, enantiomers and salts thereof that overcome known drawbacks.

Alkyl is defined in each case as a straight-chain or branched alkyl radical, such as, for example, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, pentyl, isopentyl, hexyl, heptyl, octyl, nonyl and decyl.

Alkoxy is defined in each case as a straight-chain or branched alkoxy radical, such as, for example, methyloxy, ethyloxy, propyloxy, isopropyloxy, butyloxy, isobutyloxy, sec-butyloxy, tert-butyloxy, pentyloxy, isopentyloxy, or hexyloxy.

Alkylthio is defined in each case as a straight-chain or branched alkylthio radical, such as, for example, methylthio, ethylthio, propylthio, isopropylthio, butylthio, isobutylthio, sec-butylthio, tert-butylthio, pentythio, isopentythio or hexylthio.

Cycloalkyl is defined in general as monocyclic alkyl rings, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl or cyclodecyl, but also bicyclic rings or tricyclic rings such as, for example, norbornyl, adamantanyl, etc.

The ring systems, in which optionally one or more possible double bonds can be contained in the ring, are defined as, for example, cycloalkenyls, such as cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclohexenyl, or cycloheptenyl, whereby the linkage can be carried out both to the double bond and to the single bonds.

If A and B, R^3 and R^4 , X and R^2 , in each case independently of one another, together form a C_3 - C_{10} -cycloalkyl ring, which optionally can be interrupted by one or more heteroatoms, such as nitrogen atoms, oxygen atoms and/or sulfur atoms, and/or can

be interrupted by one or more $=C=O$ groups in the ring and/or optionally one or more possible double bonds can be contained in the ring, however, the above-mentioned definitions are also intended to include heteroaryl radical or heterocycloalkyl and heterocycloalkenyl.

Halogen is defined in each case as fluorine, chlorine, bromine or iodine.

The alkenyl substituents in each case are straight-chain or branched, whereby, for example, the following radicals are meant: vinyl, propen-1-yl, propen-2-yl, but-1-en-1-yl, but-1-en-2-yl, but-2-en-1-yl, but-2-en-2-yl, 2-methyl-prop-2-en-1-yl, 2-methyl-prop-1-en-1-yl, but-1-en-3-yl, ethinyl, prop-1-in-1-yl, but-1-in-1-yl, but-2-in-1-yl, but-3-en-1-yl, and allyl.

Alkynyl is defined in each case as a straight-chain or branched alkynyl radical that contains 2-6, preferably 2-4 C atoms. For example, the following radicals can be mentioned: acetylene, propin-1-yl, propin-3-yl, but-1-in-1-yl, but-1-in-4-yl, but-2-in-1-yl, but-1-in-3-yl, etc.

The aryl radical in each case comprises 3-12 carbon atoms and in each case can be benzocondensed.

For example, there can be mentioned: cyclopropenyl, cyclopentadienyl, phenyl, troyl, cyclooctadienyl, indenyl, naphthyl, azulenyl, biphenyl, fluorenyl, anthracenyl, etc.

The heteroaryl radical in each case comprises 3-16 ring atoms, and instead of the carbon can contain one or more heteroatoms that are the same or different, such as oxygen, nitrogen or sulfur, in the ring, and can be monocyclic, bicyclic, or tricyclic and in addition in each case can be benzocondensed.

For example, there can be mentioned:

Thienyl, furanyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl, etc. and benzo derivatives thereof, such as, e.g., benzofuranyl, benzothienyl, benzoxazolyl, benzimidazolyl, indazolyl, indolyl, isoindolyl, etc.; or pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, etc. and benzo derivatives thereof, such as, e.g., quinolyl, isoquinolyl, etc., or azocinyl, indolizinyl, purinyl, etc. and benzo derivatives thereof; or quinolinyl, isoquinolinyl, cinnolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, naphthyridinyl, pteridinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, phenoxazinyl, xanthenyl, oxepinyl, etc.

Heterocycloalkyl stands for an alkyl ring that comprises 3-12 carbon atoms, which instead of the carbon contains one or more heteroatoms that are the same or different, such as, e.g., oxygen, sulfur or nitrogen.

As heterocycloalkyls, there can be mentioned, e.g.: oxiranyl, oxethanyl, aziridinyl, azetidiny, tetrahydrofuranyl, pyrrolidinyl, dioxolanyl, imidazolidinyl, pyrazolidinyl, dioxanyl, piperidinyl, morpholinyl, dithianyl, thiomorpholinyl, piperazinyl, trithianyl, quinuclidinyl, etc.

Heterocycloalkenyl stands for an alkyl ring that comprises 3-12 carbon atoms, which instead of the carbon contains one or more heteroatoms that are the same or different such as, e.g., oxygen, sulfur or nitrogen, and which is partially saturated.

As heterocycloalkenyls, there can be mentioned, e.g.: pyran, thiin, dihydroacet, etc.

If an acid group is included, the physiologically compatible salts of organic and inorganic bases are suitable as salts, such as, for example, the readily soluble alkali and alkaline-earth salts, as well as N-methyl-glucamine, dimethyl-glucamine, ethyl-

glucamine, lysine, 1,6-hexadamine, ethanolamine, glucosamine, sarcosine, serinol, tris-hydroxy-methyl-amino-methane, aminopropane diol, Sovak base, and 1-amino-2,3,4-butanetriol.

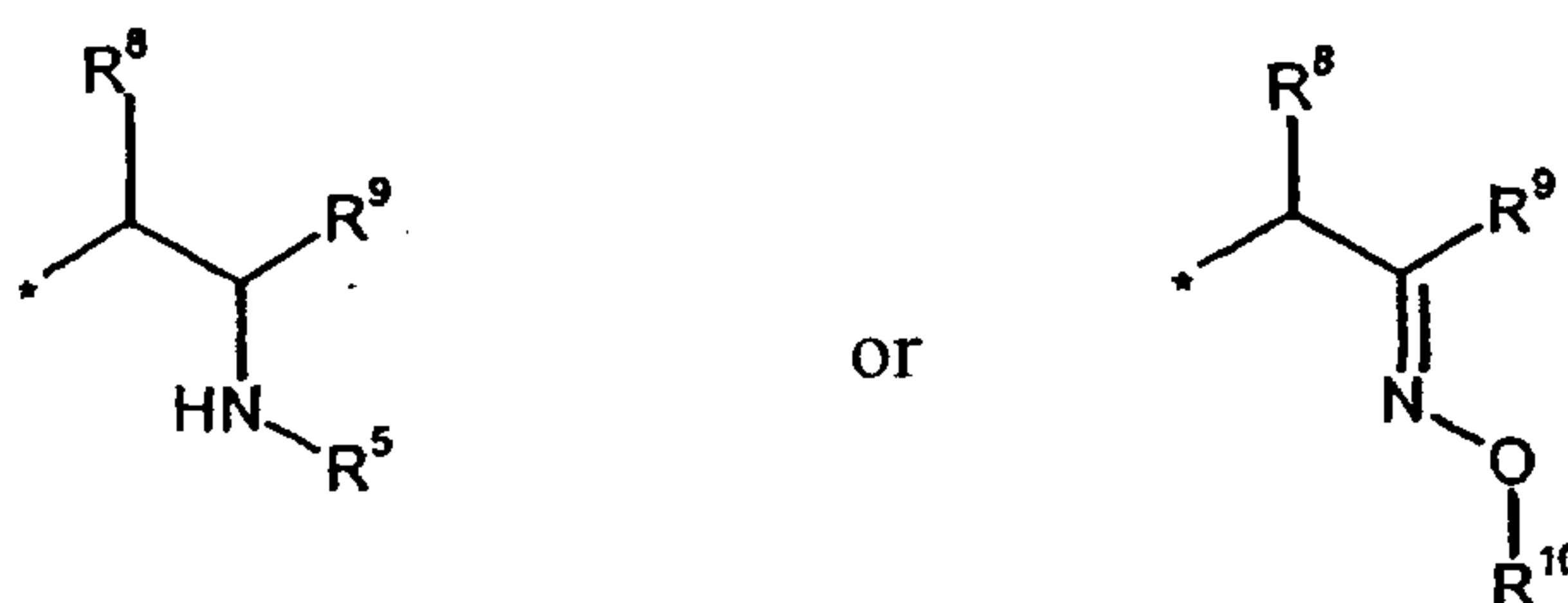
If a basic group is included, the physiologically compatible salts of organic and inorganic acids are suitable, such as hydrochloric acid, sulfuric acid, phosphoric acid, citric acid, tartaric acid, i.a.

Those compounds of general formula (I) in which

- R^1 stands for hydrogen, halogen, C_1 - C_6 -alkyl, nitro, or for the group $-COR^5$, $-OCF_3$, $-(CH_2)_nR^5$, $-S-CF_3$ or $-SO_2CF_3$,
- R^2 stands for C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl, C_2 - C_{10} -alkinyl, or C_3 - C_{10} -cycloalkyl or for C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl, C_2 - C_{10} -alkinyl, or C_3 - C_{10} -cycloalkyl that is substituted in one or more places in the same way or differently with hydroxy, halogen, C_1 - C_6 -alkoxy, C_1 - C_6 -alkylthio, amino, cyano, C_1 - C_6 -alkyl, $-NH-(CH_2)_n-C_3$ - C_{10} -cycloalkyl, C_3 - C_{10} -cycloalkyl, C_1 - C_6 -hydroxyalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkinyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, $-NHC_1$ - C_6 -alkyl, $-N(C_1$ - C_6 -alkyl) $_2$, $-SO(C_1$ - C_6 -alkyl), $-SO_2(C_1$ - C_6 -alkyl), C_1 - C_6 -alkanoyl, $-CONR^3R^4$, $-COR^5$, C_1 - C_6 -alkylOAc, carboxy, aryl, heteroaryl, $-(CH_2)_n$ -aryl, $-(CH_2)_n$ -heteroaryl, phenyl- $(CH_2)_n$ - R^5 , $-(CH_2)_nPO_3(R^5)_2$ or with the group $-R^6$ or $-NR^3R^4$, and the phenyl, C_3 - C_{10} -cycloalkyl, aryl, heteroaryl, $-(CH_2)_n$ -aryl and $-(CH_2)_n$ -heteroaryl itself optionally can be substituted in one or more places in the same way or differently with halogen, hydroxy, C_1 - C_6 -alkyl, C_1 - C_6 alkoxy,

heteroaryl, benzoxy or with the group $-\text{CF}_3$ or $-\text{OCF}_3$, and the ring of the C_3-C_{10} -cycloalkyl and the C_1-C_{10} -alkyl optionally can be interrupted by one or more nitrogen, oxygen and/or sulfur atoms and/or can be interrupted by one or more $=\text{C}=\text{O}$ groups in the ring and/or optionally one or more possible double bonds can be contained in the ring, or

R^2 stands for the group

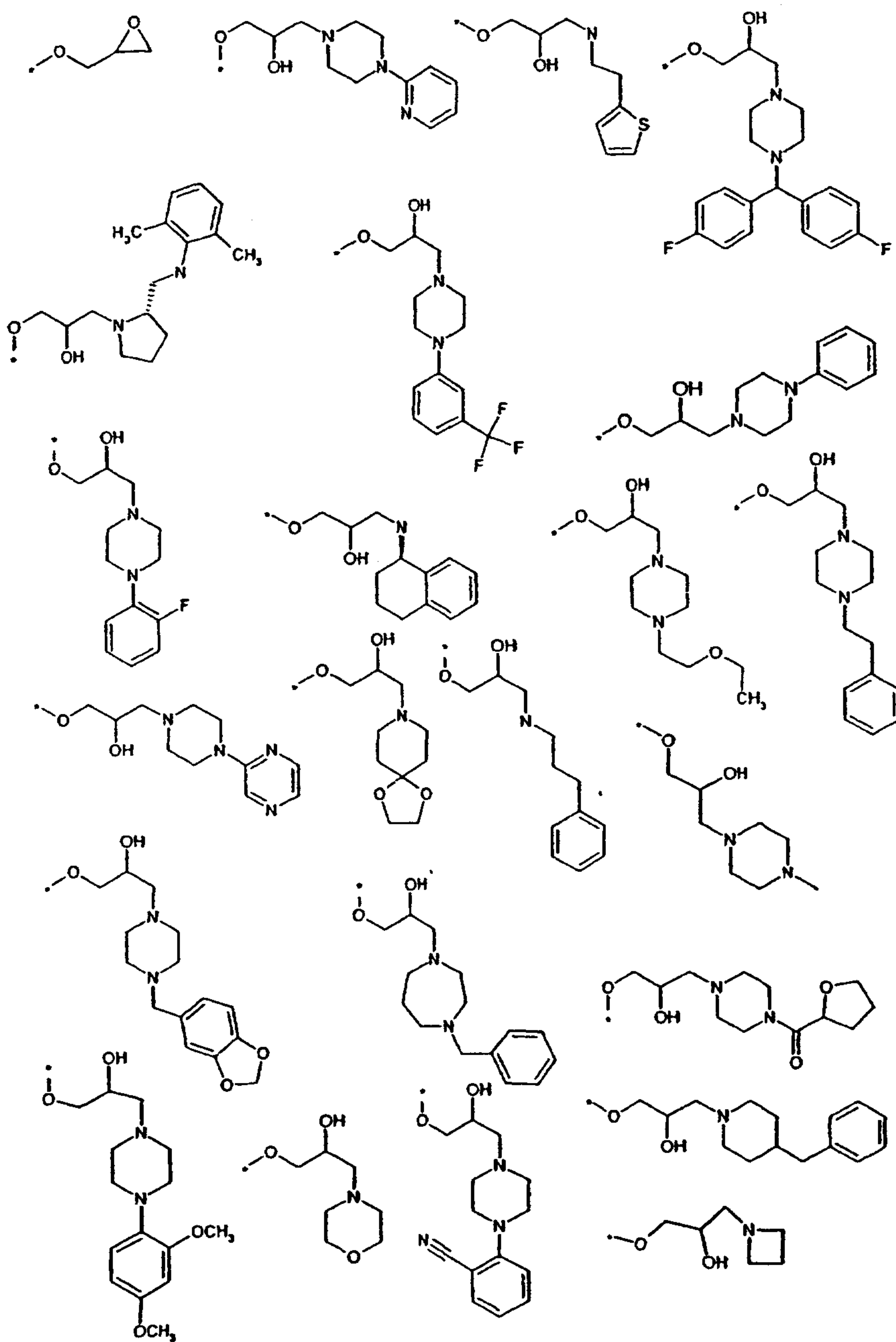


X stands for oxygen or for the group $-\text{NH}-$, $-\text{N}(\text{C}_1-\text{C}_3\text{-alkyl})$ or for $-\text{OC}_3-\text{C}_{10}\text{-cycloalkyl}$, which can be substituted in one or more places in the same way or differently with a heteroaromatic compound,

or

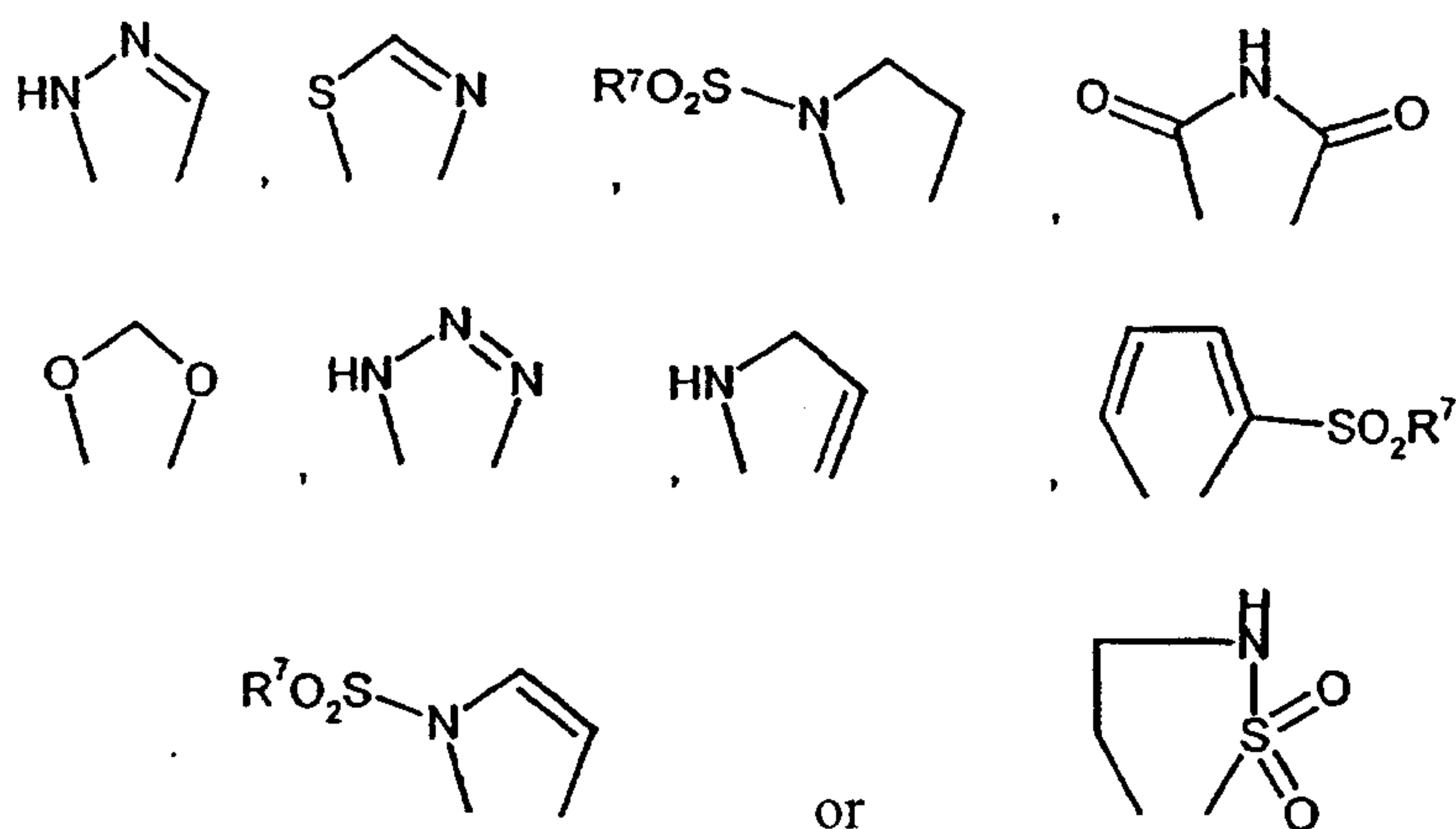
X and R^2 together form a C_3-C_{10} -cycloalkyl ring, which optionally can contain one or more heteroatoms and optionally can be substituted in one or more places with hydroxy, C_1-C_6 -alkyl, C_1-C_6 -alkoxy or halogen,

A and B, in each case independently of one another, stand for hydrogen, hydroxy, C_1-C_3 -alkyl, C_1-C_6 -alkoxy or for the group $-\text{S}-\text{CH}_3$, $-\text{SO}_2-\text{C}_2\text{H}_4-\text{OH}$, $-\text{CO}-\text{CH}_3$, $-\text{S}-\text{CHF}_2$, $-\text{S}-(\text{CH}_2)_n\text{CH}(\text{OH})\text{CH}_2\text{N}-\text{R}^3\text{R}^4$, $-\text{CH}_2\text{P}(\text{O})\text{OR}^3\text{OR}^4$, $-\text{S}-\text{CF}_3$, $-\text{SO}-\text{CH}_3$, $-\text{SO}_2\text{CF}_3$, $-\text{SO}_2-(\text{CH}_2)_n-\text{N}-\text{R}^3\text{R}^4$, $-\text{SO}_2-\text{NR}^3\text{R}^4$, $-\text{SO}_2\text{R}^7$, $-\text{CH}(\text{OH})-\text{CH}_3$ or for



OF

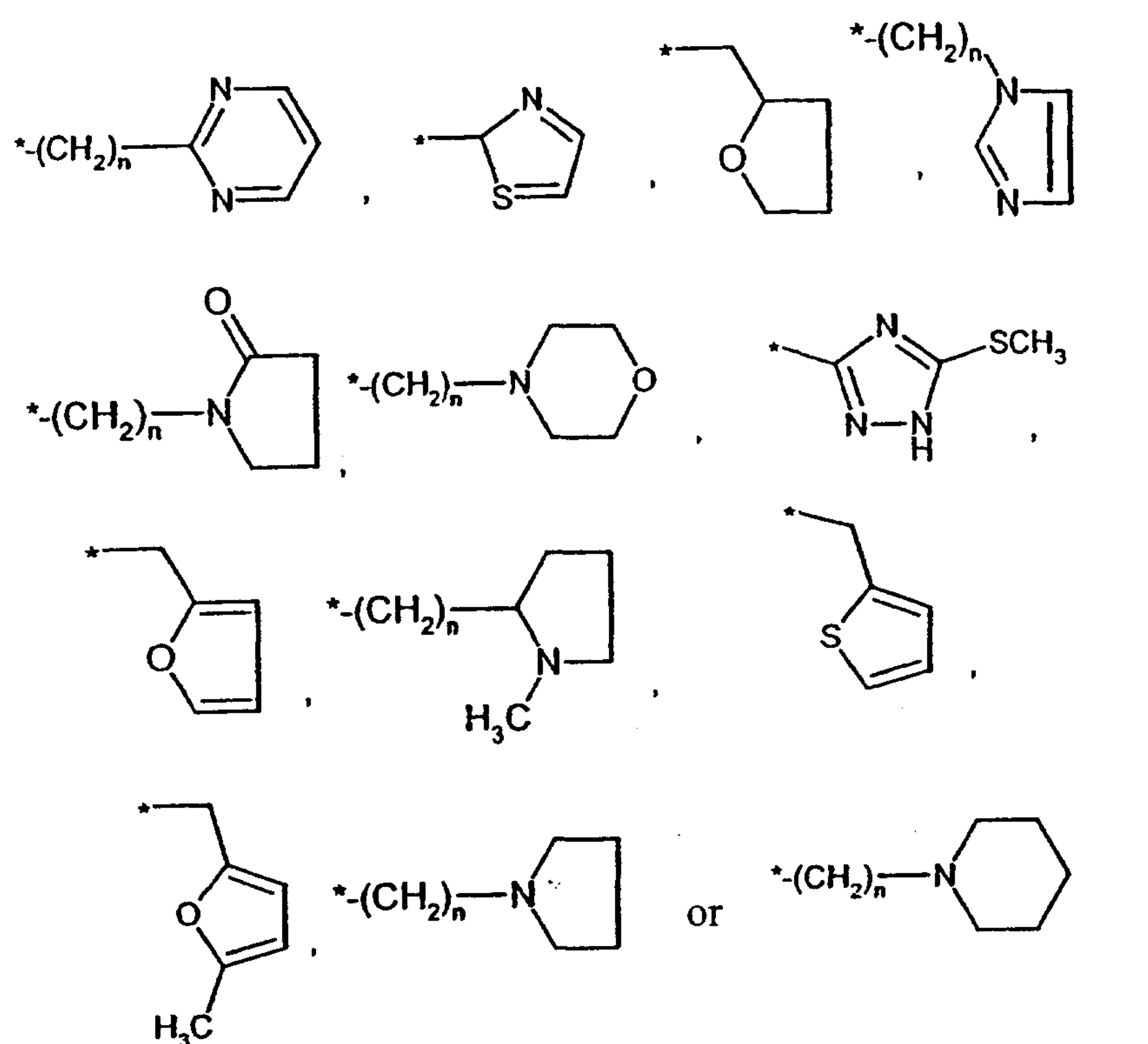
A and B together can form a group



R^3 and R^4 , in each case independently of one another, stand for hydrogen, phenyl, benzyloxy, C_1 - C_{12} -alkyl, C_1 - C_6 -alkoxy, C_2 - C_4 -alkenyloxy, C_3 - C_6 -cycloalkyl, hydroxy, hydroxy- C_1 - C_6 -alkyl, dihydroxy- C_1 - C_6 -alkyl, heteroaryl, heterocyclo- C_3 - C_{10} -alkyl, heteroaryl- C_1 - C_3 -alkyl, C_3 - C_6 -cycloalkyl- C_1 - C_3 -alkyl optionally substituted with cyano, or for C_1 - C_6 -alkyl that is optionally substituted in one or more places in the same way or differently with phenyl, pyridyl, phenyloxy, C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkyl or C_1 - C_6 -alkoxy, whereby the phenyl itself can be substituted in one or more places in the same way or differently with halogen, trifluoromethyl, C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy or with the group $-SO_2NR^3R^4$,

or for the group $-(CH_2)_nNR^3R^4$, $-CNHNH_2$ or $-NR^3R^4$

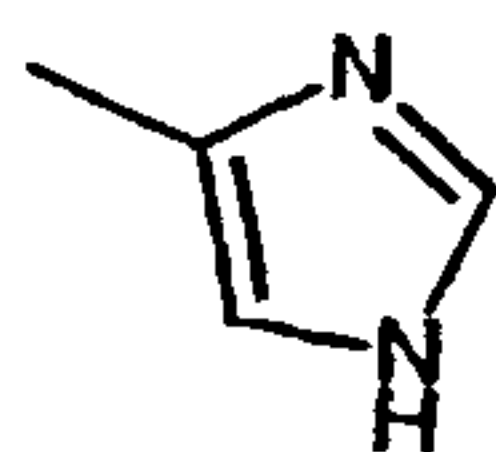
or for



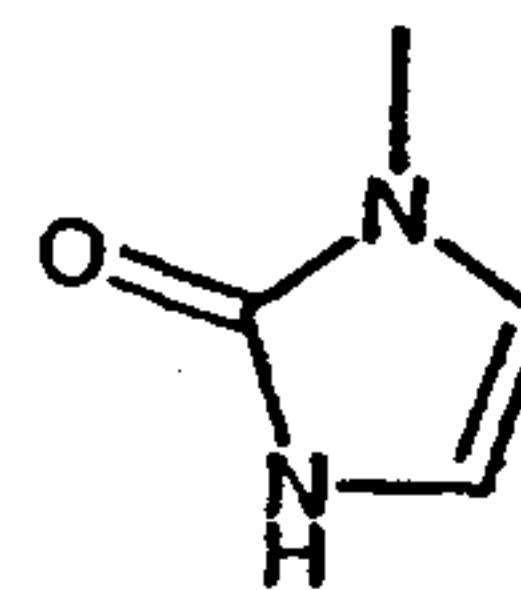
which optionally can be substituted with C_1 - C_6 -alkyl,

R^5 stands for hydroxy, phenyl, C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, benzoxy, C_1 - C_6 -alkylthio or C_1 - C_6 -alkoxy,

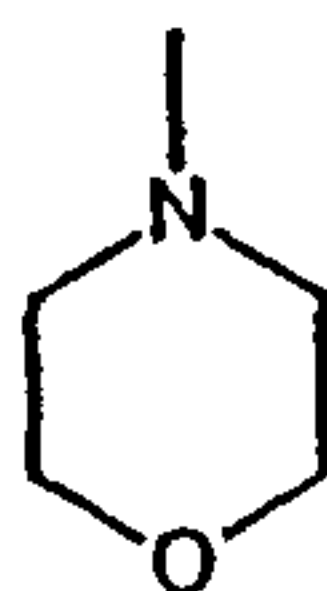
R^6 stands for the group



or

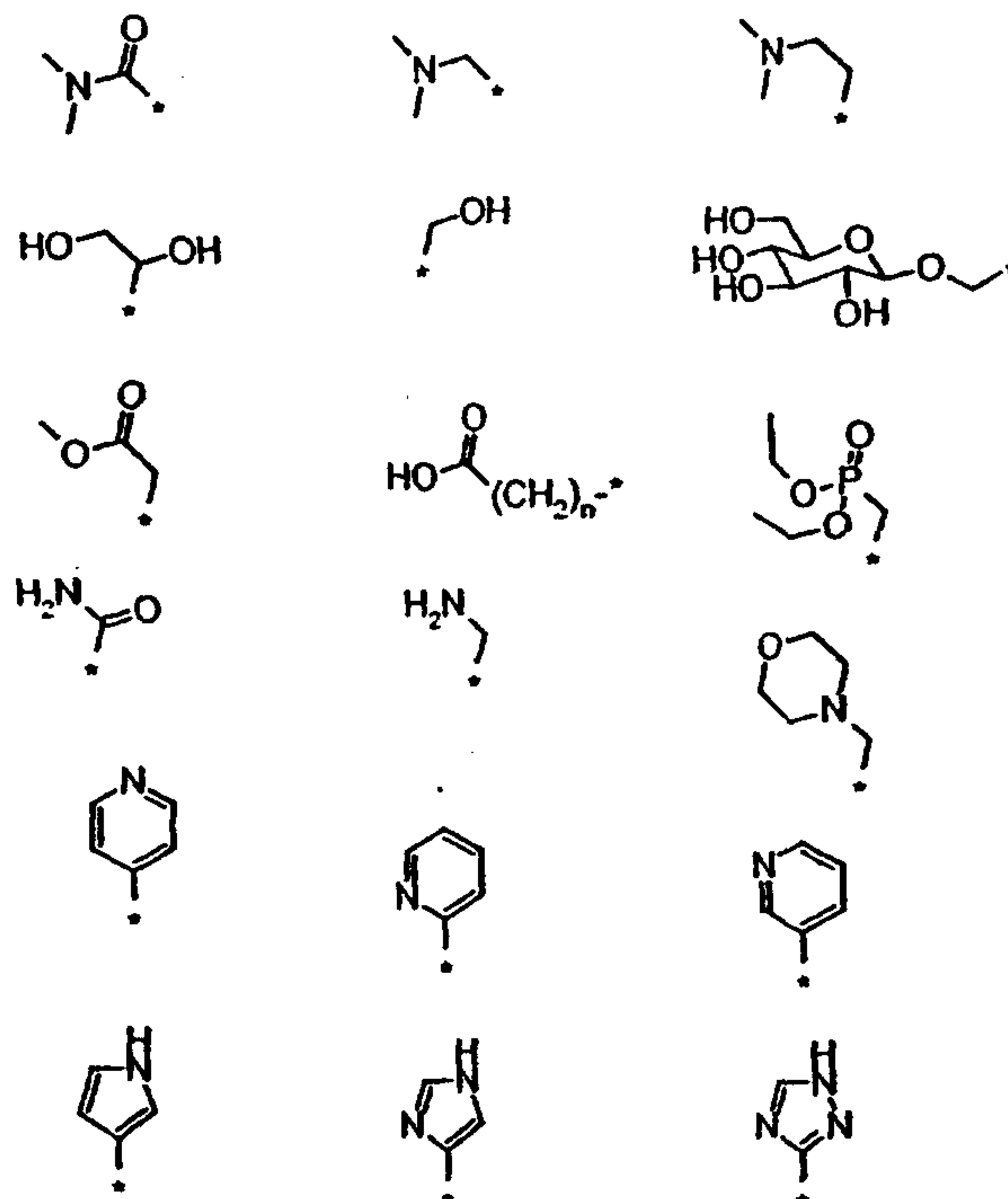


R^7 stands for halogen, hydroxy, phenyl, C_1 - C_6 -alkyl, $-C_2H_4OH$, $-NR^3R^4$, or the group



R^8 , R^9 and

R^{10} , in each case independently of one another, stand for hydrogen, hydroxy, C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl or for the group



and

n stands for 0-6,

as well as isomers, enantiomers, diastereomers, and salts thereof, are especially effective.

Those compounds of general formula I in which

R¹ stands for hydrogen, halogen, C₁-C₃-alkyl, or for the group

-(CH₂)_nR⁵,

R² stands for -CH(CH₃)-(CH₂)_n-R⁵, -CH-(CH₂OH)₂, -(CH₂)_nR⁷, -CH(C₃H₇)-(CH₂)_n-R⁵, -CH(C₂H₅)-(CH₂)_n-R⁵, -CH₂-CN, -CH(CH₃)COCH₃, -CH(CH₃)-C(OH)(CH₃)₂, -CH(CH(OH)CH₃)OCH₃, -CH(C₂H₅)CO-R⁵, C₂-C₄-alkinyl, -(CH₂)_n-COR⁵, -(CH₂)_n-CO-C₁-C₆-alkyl, -(CH₂)_n-C(OH)(CH₃)-phenyl, -CH(CH₃)-C(CH₃)-R⁵, -CH(CH₃)-C(CH₃)(C₂H₅)-R⁵, -CH(OCH₃)-CH₂-R⁵, -CH₂-CH(OH)-R⁵, -CH(OCH₃)-CHR⁵-CH₃, -CH(CH₃)-CH(OH)-CH₂-CH=CH₂, -CH(C₂H₅)-CH(OH)-(CH₂)_n-CH₃, -CH(CH₃)-CH(OH)-(CH₂)_n-CH₃, -CH(CH₃)-CH(OH)-CH(CH₃)₂, (CH₂OAC)₂, -(CH₂)_n-R⁶, -(CH₂)_n-(CF₂)_n-CF₃, -CH(CH₂)_n-R⁵)₂, -CH(CH₃)-CO-NH₂, -CH(CH₂OH)-phenyl, -CH(CH₂OH)-CH(OH)-(CH₂)_nR⁵, -CH(CH₂OH)-CH(OH)-phenyl, -CH(CH₂OH)-C₂H₄-R⁵, -(CH₂)_n-C≡C(CH₃)=CH-COR⁵, -CH(Ph)-(CH₂)_n-R⁵, -(CH₂)_n-COR⁵, -(CH₂)_nPO₃(R⁵)₂, -(CH₂)_n-COR⁵, -CH((CH₂)_nOR⁵)CO-R⁵, -(CH₂)_nCONHCH((CH₂)_nR⁵)₂, -(CH₂)_nNH-COR⁵, -CH(CH₂)_nR⁵-(CH₂)_nC₃-C₁₀-cycloalkyl, -(CH₂)_n-C₃-C₁₀-cycloalkyl, C₃-C₁₀-cycloalkyl; C₁-C₆-alkyl, C₃-C₁₀-cycloalkyl, -(CH₂)_n-O-(CH₂)_n-R⁵, -(CH₂)_n-NR³R⁴ that is optionally substituted in one or more places in the same way or

differently with hydroxy, C₁-C₆-alkyl or the group -COONH(CH₂)_nCH₃ or -NR³R⁴,

-CH(C₃H₇)-(CH₂)_n-OC(O)-(CH₂)_n-CH₃, -(CH₂)_n-R⁵,

-C(CH₃)₂-(CH₂)_n-R⁵, -C(CH₂)_n(CH₃)-(CH₂)_nR⁵,

-C(CH₂)_n-(CH₂)_nR⁵, -CH(t-butyl)-(CH₂)_n-R⁵,

-CCH₃(C₃H₇)-(CH₂)_nR⁵, -CH(C₃H₇)-(CH₂)_n-R⁵,

-CH(C₃H₇)-COR⁵, -CH(C₃H₇)-(CH₂)_n-OC(O)-NH-Ph,

-CH((CH₂)_n(C₃H₇))-(CH₂)_nR⁵,

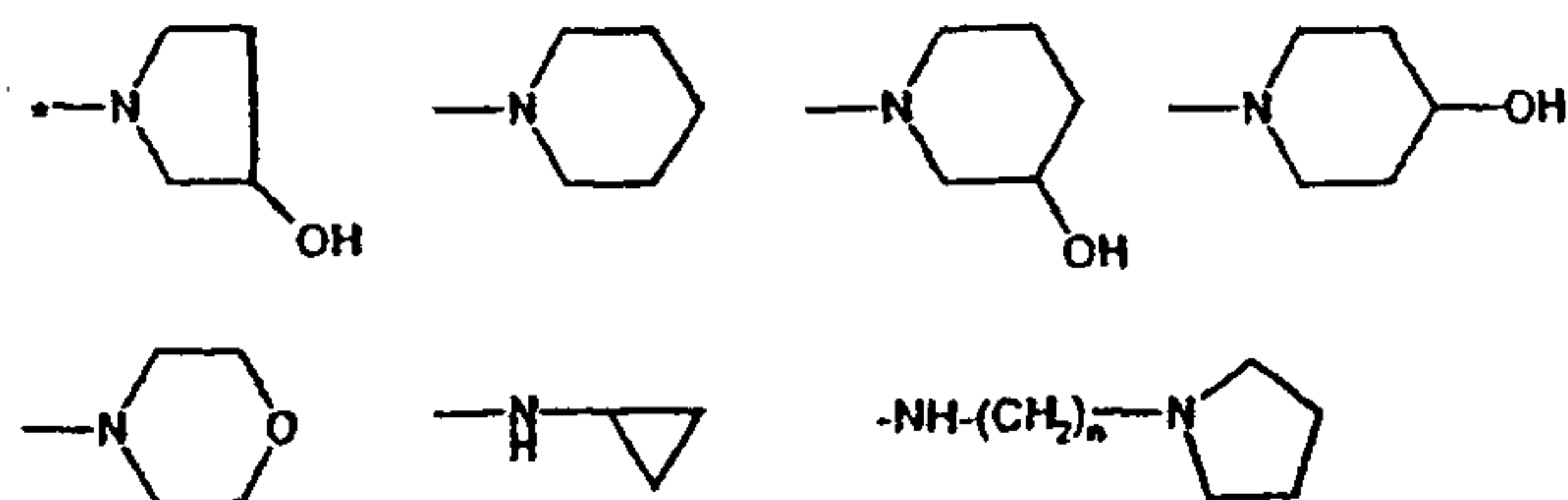
-CH(C₃H₇)-(CH₂)_n-OC(O)-NH-Ph(OR⁵)₃, -NR³R⁴,

-NH-(CH₂)_n-NR³R⁴, R⁵-(CH₂)_n-C^{*}H-CH(R⁵)-(CH₂)_n-R⁵,

-(CH₂)_n-CO-NH-(CH₂)_n-CO-R⁵, -OC(O)NH-C₁-C₆-alkyl or

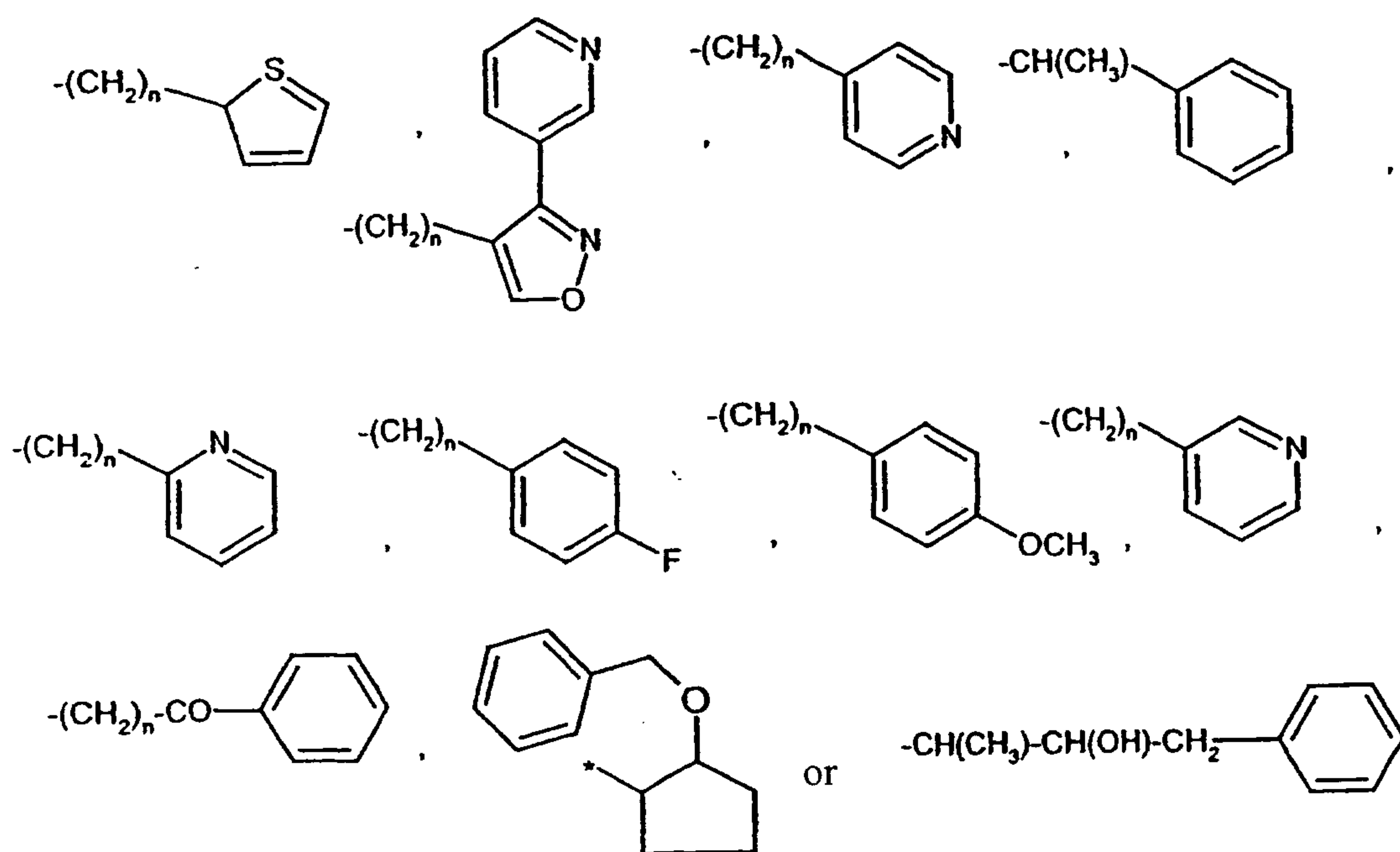
-(CH₂)_n-CO-NH-(CH₂)_n-CH-((CH₂)_nR⁵)₂,

or for C₃-C₁₀-cycloalkyl, which is substituted with the group

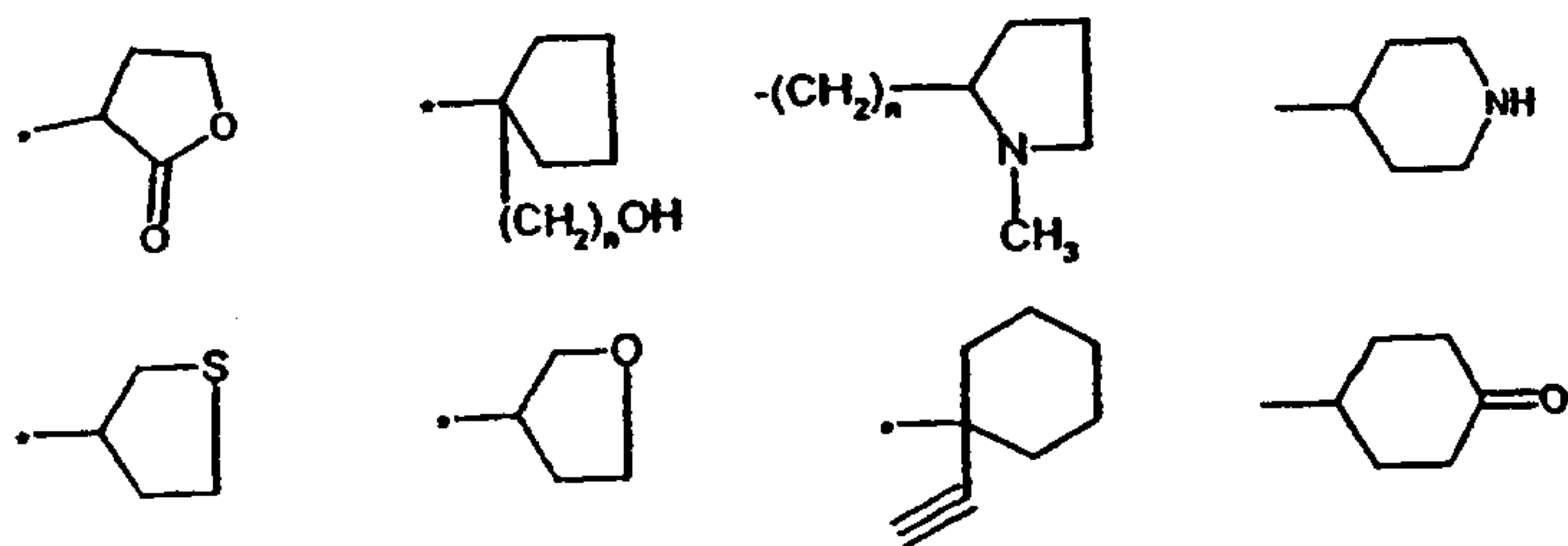


or for the group

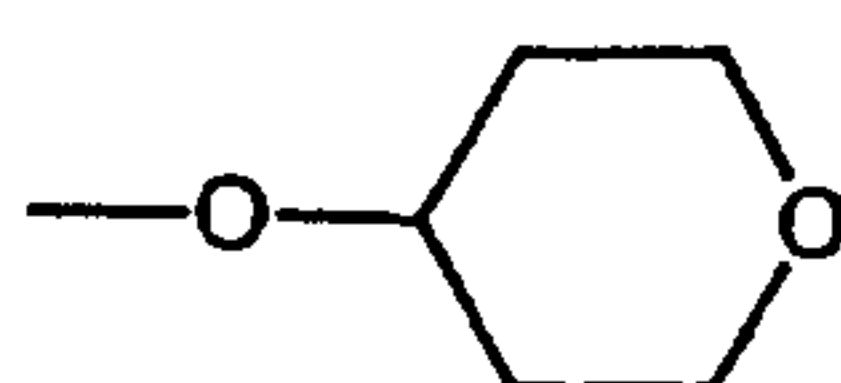
19



or for

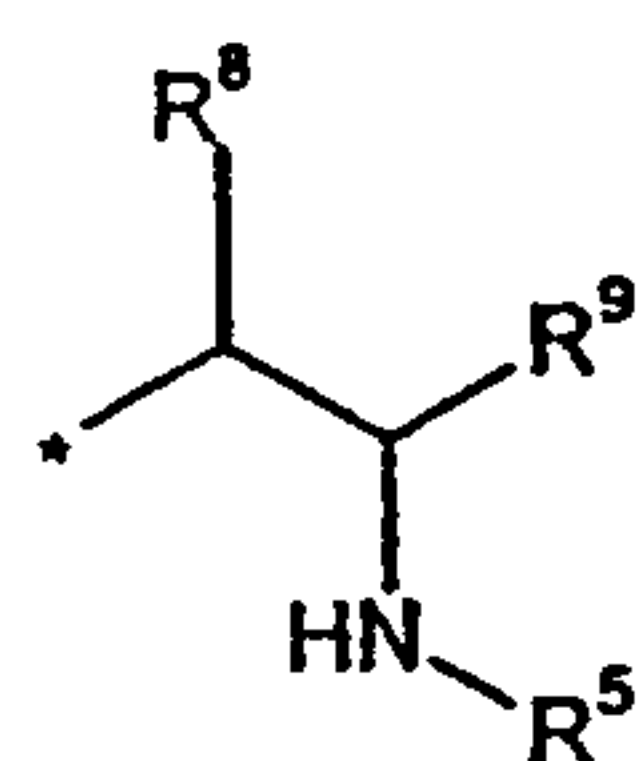


X stands for oxygen or for the group $-NH-$, $-N(C_1-C_3\text{-alkyl})$ or

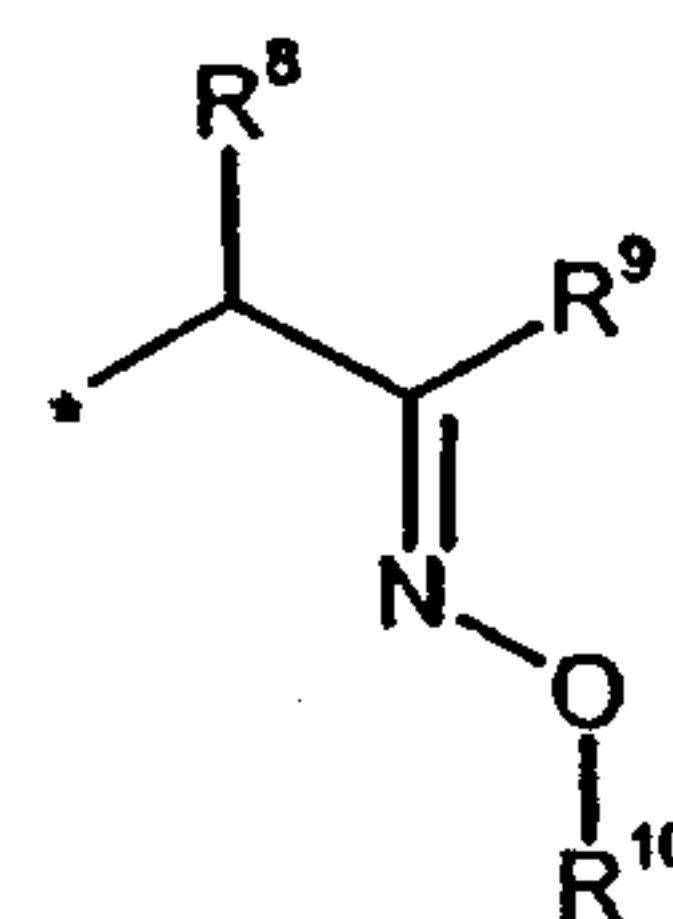


or

R^2 stands for the group

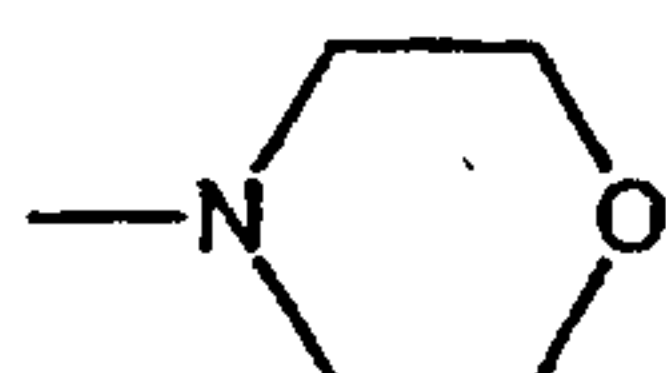


or

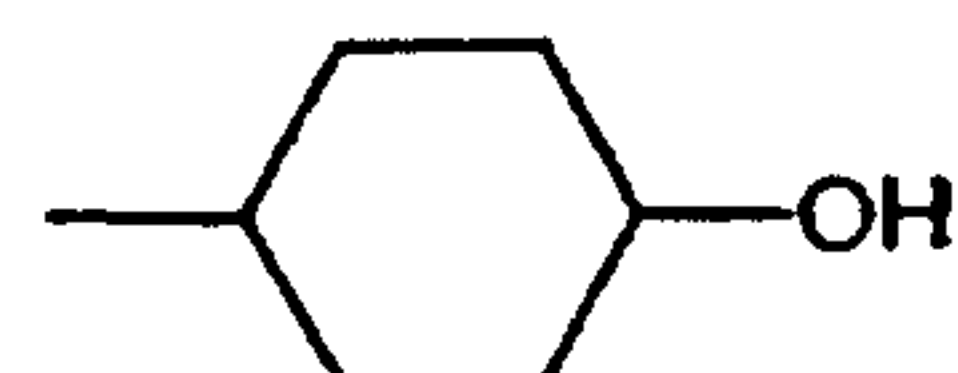


or

X and R^2 together form a group

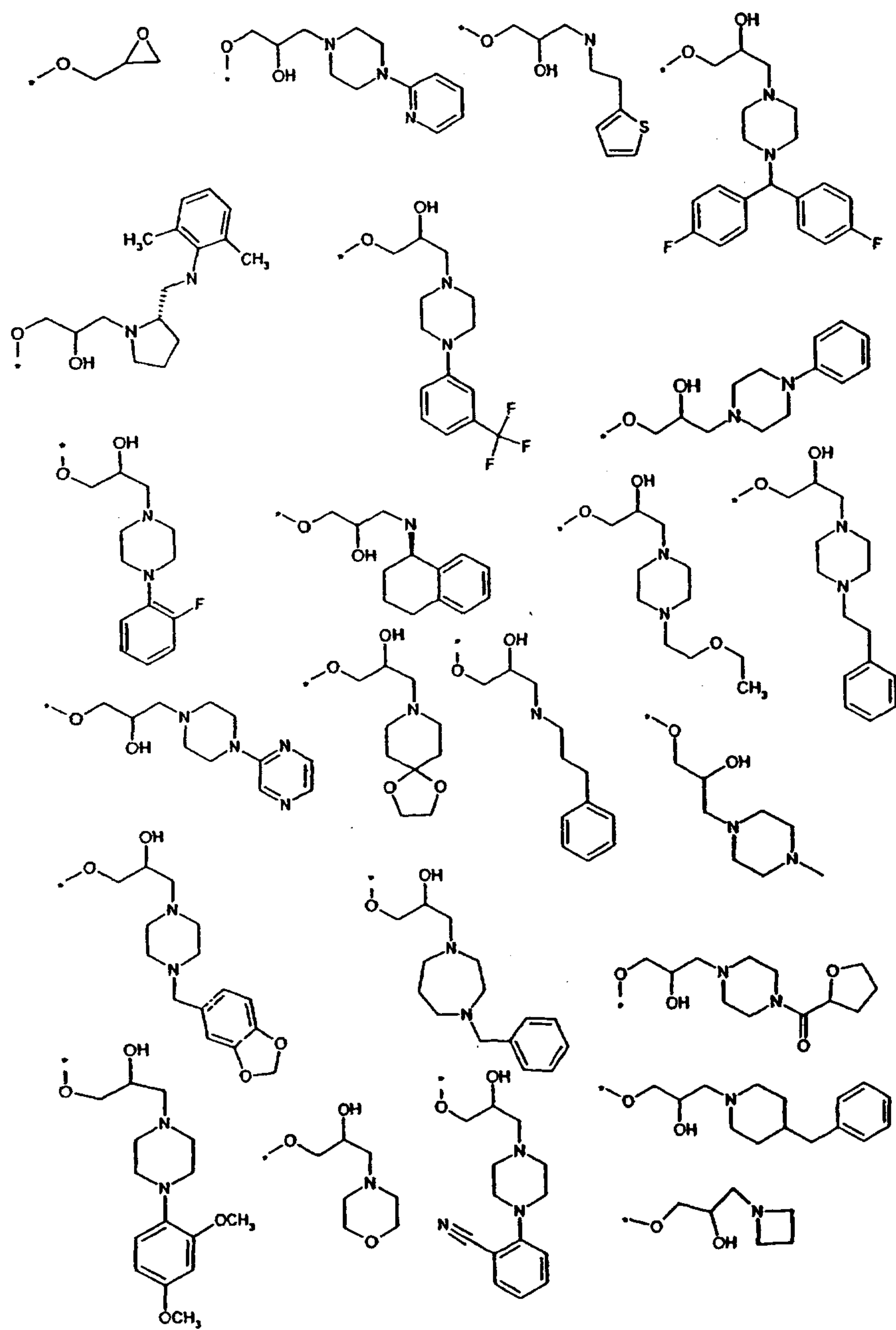


or



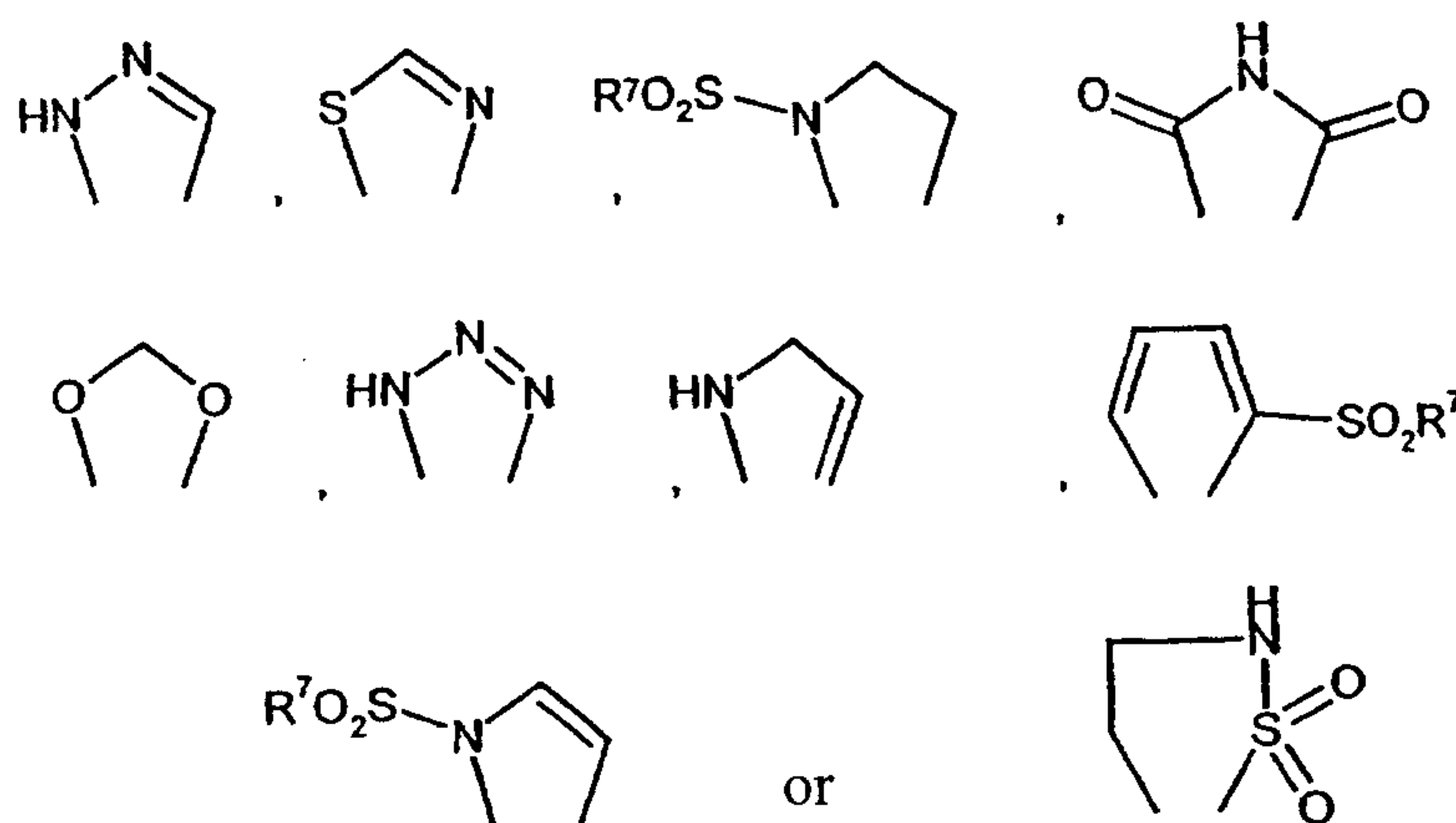
A and B, in each case independently of one another, stand for hydrogen,

hydroxy, C_1 - C_3 -alkyl, C_1 - C_6 -alkoxy or for the group $-S-CH_3$, $-SO_2-C_2H_4-$, $-OH$, $-CO-CH_3$, $-S-CHF_2$, $-S(CH_2)_nCH(OH)CH_2N-R^3R^4$, $-CH_2PO(OC_2H_5)_2$, $-S-CF_3$, $-SO-CH_3$, $-SO_2CF_3$, $-SO_2-(CH_2)_n-N-R^3R^4$, $-SO_2-NR^3R^4$, $-SO_2R^7$, $-CH(OH)-CH_3$, $-COOH$, $-CH((CH_2)_nR^5)_2$, $-(CH_2)_nR^5$, $-COO-C_1-C_6$ -alkyl, $-CONR^3R^4$ or for



or

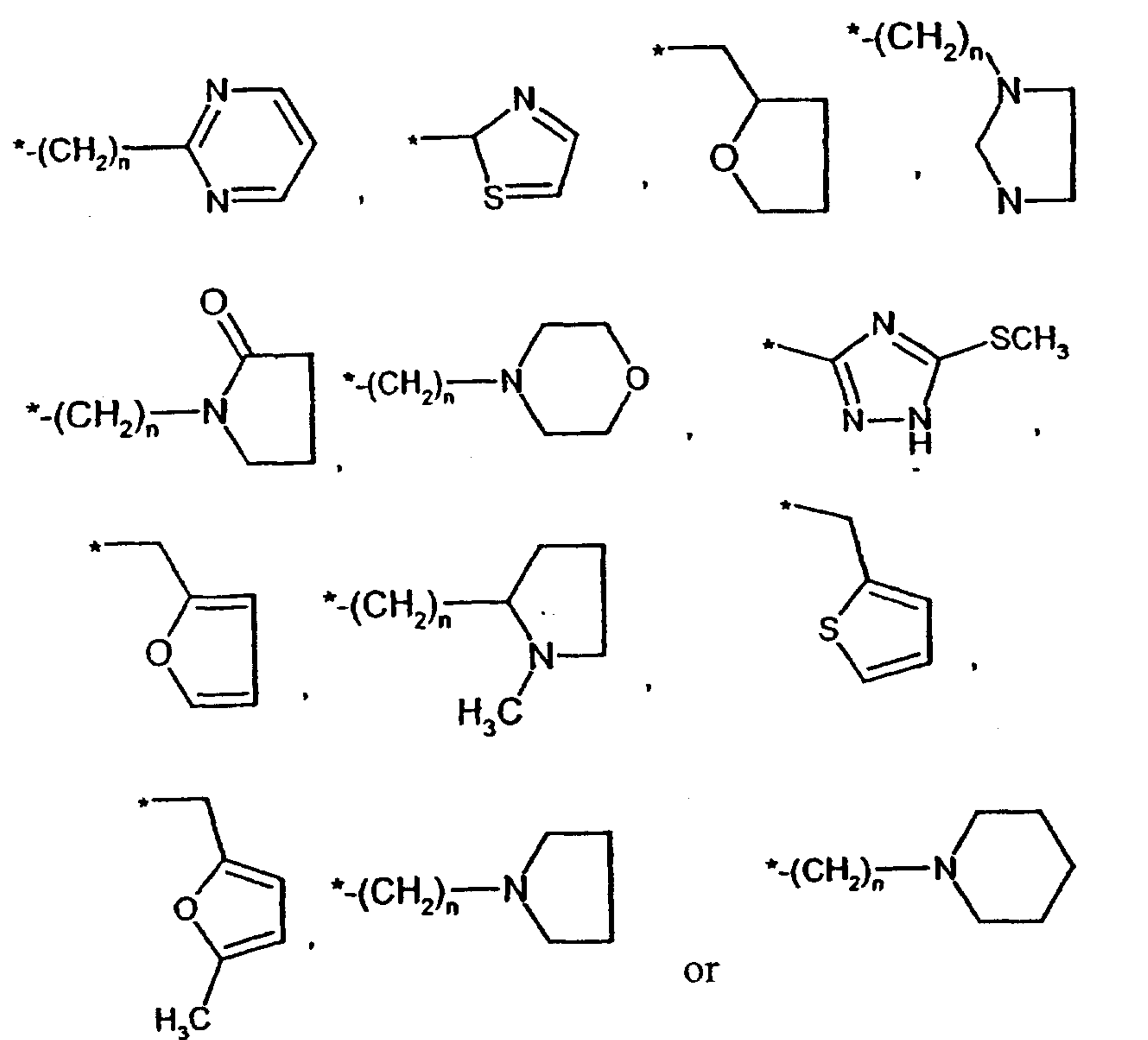
A and B together can form a group



R^3 and R^4 , in each case independently of one another, stand for hydrogen, phenyl, benzyloxy, C_1 - C_{12} -alkyl, C_1 - C_6 -alkoxy, C_2 - C_4 -alkenyloxy, C_3 - C_6 -cycloalkyl, hydroxy, hydroxy- C_1 - C_6 -alkyl, dihydroxy- C_1 - C_6 -alkyl, heteroaryl, heterocyclo- C_3 - C_{10} -alkyl, heteroaryl- C_1 - C_3 -alkyl, C_3 - C_6 -cycloalkyl- C_1 - C_3 -alkyl that is optionally substituted with cyano, or for C_1 - C_6 -alkyl that is optionally substituted in one or more places in the same way or differently with phenyl, pyridyl, phenyloxy, C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkyl or C_1 - C_6 -alkoxy, whereby the phenyl itself can be substituted in one or more places in the same way or differently with halogen, trifluoromethyl, C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy or with the group

$-\text{SO}_2\text{NR}^3\text{R}^4$,

or for the group $-(\text{CH}_2)_n\text{NR}^3\text{R}^4$, $-\text{CNHNH}_2$ or $-\text{NR}^3\text{R}^4$ or for

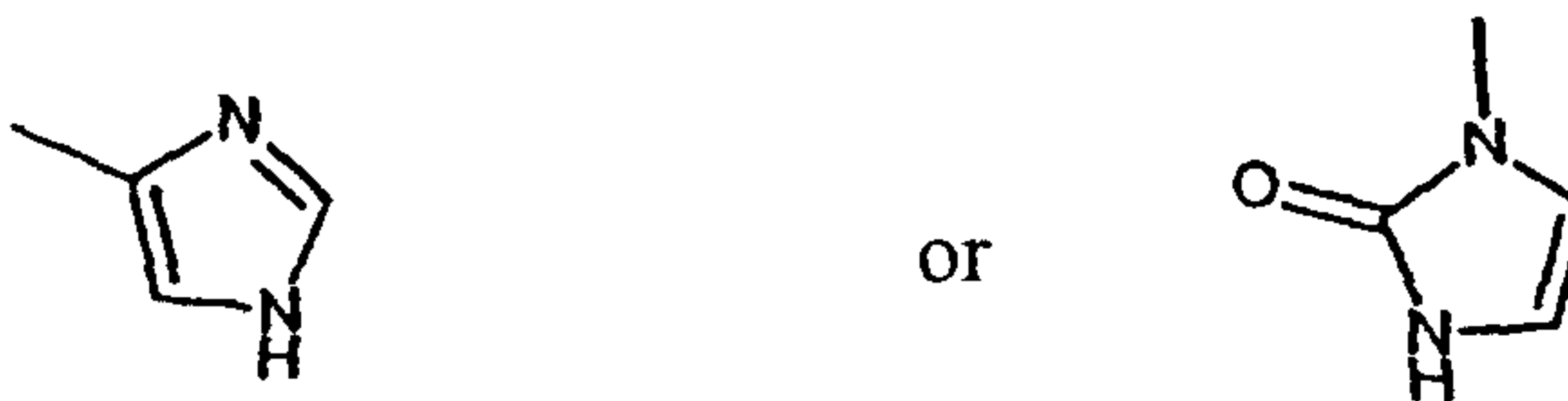


which optionally can be substituted with C_1 - C_6 -alkyl,

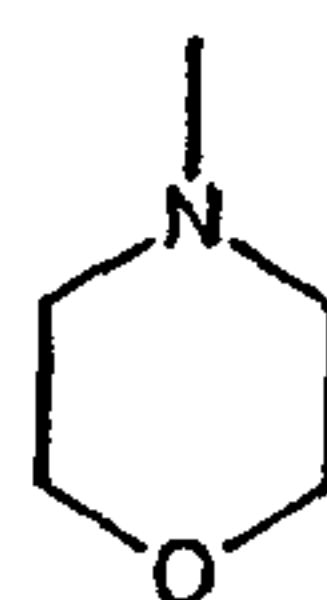
R^5 stands for hydroxy, phenyl, C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, benzoxy,

C_1 - C_6 -alkylthio or C_1 - C_6 -alkoxy,

R^6 stands for the group



R^7 stands for halogen, hydroxy, phenyl, C_1 - C_6 -alkyl, $-(CH_2)_nOH$, $-NR^3R^4$ or the group



R^8 , R^9 and

R^{10} stand for hydrogen, hydroxy, C_1 - C_6 -alkyl or for the group $-(CH_2)_nCOOH$, and

n stands for 0-6,

as well as isomers, diastereomers, enantiomers and salts thereof, have proven quite especially effective.

The compounds according to the invention essentially inhibit cyclin-dependent kinases, upon which is based their action, for example, against cancer, such as solid tumors and leukemia; auto-immune diseases such as psoriasis, alopecia, and multiple sclerosis, chemotherapy-induced alopecia and mucositis; cardiovascular diseases such as stenoses, arterioscleroses and restenoses; infectious diseases, such as, e.g., by unicellular parasites, such as trypanosoma, toxoplasma or plasmodium, or produced by fungi; nephrological diseases, such as, e.g., glomerulonephritis, chronic neurodegenerative diseases, such as Huntington's disease, amyotrophic lateral sclerosis, Parkinson's disease,

AIDS dementia and Alzheimer's disease; acute neurodegenerative diseases, such as ischemias of the brain and neurotraumas; viral infections, such as, e.g., cytomegalic infections, herpes, Hepatitis B and C, and HIV diseases.

The eukaryotic cell division ensures the duplication of the genome and its distribution to the daughter cells by passing through a coordinated and regulated sequence of events. The cell cycle is divided into four successive phases: the G1 phase represents the time before the DNA replication, in which the cell grows and is sensitive to external stimuli. In the S phase, the cell replicates its DNA, and in the G2 phase, preparations are made for entry into mitosis. In mitosis (M phase), the replicated DNA separates, and cell division is completed.

The cyclin-dependent kinases (CDKs), a family of serine/threonine kinases, whose members require the binding of a cyclin (Cyc) as a regulatory subunit in order for them to activate, drive the cell through the cell cycle. Different CDK/Cyc pairs are active in the various phases of the cell cycle. CDK/Cyc pairs that are important to the basic function of the cell cycle are, for example, CDK4(6)/CycD, CDK2/CycE, CDK2/CycA, CDK1/CycA and CDK1/CycB. Some members of the CDK enzyme family have a regulatory function by influencing the activity of the above-mentioned cell cycle CDKs, while no specific function could be associated with other members of the CDK enzyme family. One of the latter, CDK5, is distinguished in that it has an atypical regulatory subunit (p35) that deviates from the cyclins, and its activity is highest in the brain.

The entry into the cell cycle and the passage through the "restriction points," which marks the independence of a cell from further growth signals for the completion of the cell division that has begun, are controlled by the activity of the CDK4(6)/CycD and

CDK2/CycE complexes. The essential substrate of these CDK complexes is the retinoblastoma protein (Rb), the product of the retinoblastoma tumor suppressor gene. Rb is a transcriptional co-repressor protein. In addition to other, still largely little understood mechanisms, Rb binds and inactivates transcription factors of the E2F type and forms transcriptional repressor complexes with histone-deacetylases (HDAC) (Zhang, H. S. *et al.* (2000). Exit from G1 and S Phase of the Cell Cycle is Regulated by Repressor Complexes Containing HDAC-Rb-hSWI/SNF and Rb-hSWI/SNF. *Cell* 101, 79-89). By the phosphorylation of Rb by CDKs, bonded E2F transcription factors are released and result in transcriptional activation of genes, whose products are required for the DNA synthesis and the progression through the S-phase. In addition, the Rb-phosphorylation brings about the breakdown of the Rb-HDAC complexes, by which additional genes are activated. The phosphorylation of Rb by CDK's is to be treated as equivalent to exceeding the "restriction points." For the progression through the S-phase and its completion, the activity of the CDK2/CycE and CDK2/CycA complexes is necessary, e.g., the activity of the transcription factors of the E2F type is turned off by means of phosphorylation by CDK2/CycA as soon as the cells are entered into the S-phase. After replication of DNA is complete, the CDK1 in the complex with CycA or CycB controls the entry into and the passage through phases G2 and M (Fig. 1).

According to the extraordinary importance of the cell-division cycle, the passage through the cycle is strictly regulated and controlled. The enzymes that are necessary for the progression through the cycle must be activated at the correct time and are also turned off again as soon as the corresponding phase is passed. Corresponding control points

("checkpoints") stop the progression through the cell cycle if DNA damage is detected, or the DNA replication or the creation of the spindle device is not yet completed.

The activity of the CDKs is controlled directly by various mechanisms, such as synthesis and degradation of cyclins, complexing of the CDKs with the corresponding cyclins, phosphorylation and dephosphorylation of regulatory threonine and tyrosine radicals, and the binding of natural inhibitory proteins. While the amount of protein of the CDKs in a proliferating cell is relatively constant, the amount of the individual cyclins oscillates with the passage through the cycle. Thus, for example, the expression of CycD during the early G1 phase is stimulated by growth factors, and the expression of CycE is induced after the "restriction points" are exceeded by the activation of the transcription factors of the E2F type. The cyclins themselves are degraded by the ubiquitin-mediated proteolysis. Activating and inactivating phosphorylations regulate the activities of the CDKs, for example phosphorylate CDK-activating kinases (CAKs) Thr160/161 of the CDK1, while, by contrast, the families of Wee1/Myt1 inactivate kinases CDK1 by phosphorylation of Thr14 and Tyr15. These inactivating phosphorylations can be destroyed in turn by cdc25 phosphatases. The regulation of the activity of the CDK/Cyc complexes by two families of natural CDK inhibitor proteins (CKIs), the protein products of the p21 gene family (p21, p27, p57) and the p16 gene family (p15, p16, p18, p19) is very significant. Members of the p21 family bind to cyclin complexes of CDKs 1,2,4,6, but inhibit only the complexes that contain CDK1 or CDK2. Members of the p16 family are specific inhibitors of the CDK4- and CDK6 complexes.

The plane of control point regulation lies above this complex direct regulation of the activity of the CDKs. Control points allow the cell to track the orderly sequence of

the individual phases during the cell cycle. The most important control points lie at the transition from G1 to S and from G2 to M. The G1 control point ensures that the cell does not initiate any DNA synthesis unless it has proper nutrition, interacts correctly with other cells or the substrate, and its DNA is intact. The G2/M control point ensures the complete replication of DNA and the creation of the mitotic spindle before the cell enters into mitosis. The G1 control point is activated by the gene product of the p53 tumor suppressor gene. p53 is activated after detection of changes in metabolism or the genomic integrity of the cell and can trigger either a stopping of the cell cycle progression or apoptosis. In this case, the transcriptional activation of the expression of the CDK inhibitor protein p21 by p53 plays a decisive role. A second branch of the G1 control point comprises the activation of the ATM and Chk1 kinases after DNA damage by UV light or ionizing radiation and finally the phosphorylation and the subsequent proteolytic degradation of the cdc25A phosphatase (Mailand, N. *et al.* (2000). Rapid Destruction of Human cdc25A in Response to DNA Damage. *Science* 288, 1425-1429). A shutdown of the cell cycle results from this, since the inhibitory phosphorylation of the CDKs is not removed. After the G2/M control point is activated by damage of the DNA, both mechanisms are involved in a similar way in stopping the progression through the cell cycle.

The loss of the regulation of the cell cycle and the loss of function of the control points are characteristics of tumor cells. The CDK-Rb signal path is affected by mutations in over 90% of human tumor cells. These mutations, which finally result in inactivating phosphorylation of the RB, include the over-expression of D- and E-cyclins by gene amplification or chromosomal translocations, inactivating mutations or deletions

of CDK inhibitors of the p16 type, as well as increased (p27) or reduced (CycD) protein degradation. The second group of genes, which are affected by mutations in tumor cells, codes for components of the control points. Thus p53, which is essential for the G1 and G2/M control points, is the most frequently mutated gene in human tumors (about 50%). In tumor cells that express p53 without mutation, it is often inactivated because of a greatly increased protein degradation. In a similar way, the genes of other proteins that are necessary for the function of the control points are affected by mutations, for example ATM (inactivating mutations) or cdc25 phosphatases (over-expression).

Convincing experimental data indicate that CDK2/Cyc complexes occupy a decisive position during the cell cycle progression: (1) Both dominant-negative forms of CDK2, such as the transcriptional repression of the CDK2 expression by anti-sense oligonucleotides, produce a stopping of the cell cycle progression. (2) The inactivation of the CycA gene in mice is lethal. (3) The disruption of the function of the CDK2/CycA complex in cells by means of cell-permeable peptides resulted in tumor cell-selective apoptosis (Chen, Y. N. P. *et al.* (1999). Selective Killing of Transformed Cells by Cyclin/Cyclin-Dependent Kinase 2 Antagonists. *Proc. Natl. Acad. Sci. USA* 96, 4325-4329).

Changes of the cell cycle control play a role not only in carcinoses. The cell cycle is activated by a number of viruses, both by transforming viruses as well as by non-transforming viruses, to make possible the replication of viruses in the host cell. The false entry into the cell cycle of normally post-mitotic cells is associated with various neurodegenerative diseases. The mechanisms of the cell cycle regulation, their changes in diseases and a number of approaches to develop inhibitors of the cell cycle progression

and especially the CDKs were already described in a detailed summary in several publications (Sielecki, T. M. *et al.* (2000). Cyclin-Dependent Kinase Inhibitors: Useful Targets in Cell Cycle Regulation. *J. Med. Chem.* 43, 1-18; Fry, D. W. & Garrett, M. D. (2000). Inhibitors of Cyclin-Dependent Kinases as Therapeutic Agents for the Treatment of Cancer. *Curr. Opin. Oncol. Endo. Metab. Invest. Drugs* 2, 40-59; Rosiania, G. R. & Chang, Y. T. (2000). Targeting Hyperproliferative Disorders with Cyclin-Dependent Kinase Inhibitors. *Exp. Opin. Ther. Patents* 10, 215-230; Meijer L. *et al.* (1999). Properties and Potential Applications of Chemical Inhibitors of Cyclin-Dependent Kinases. *Pharmacol. Ther.* 82, 279-284; Senderowicz, A. M. & Sausville, E. A. (2000). Preclinical and Clinical Development of Cyclin-Dependent Kinase Modulators. *J. Natl. Cancer Inst.* 92, 376-387).

To use the compounds according to the invention as pharmaceutical agents, the latter are brought into the form of a pharmaceutical preparation, which in addition to the active ingredient for enteral or parenteral administration contains suitable pharmaceutical, organic or inorganic inert carrier materials, such as, for example, water, gelatin, gum arabic, lactose, starch, magnesium stearate, talc, vegetable oils, polyalkylene glycols, etc. The pharmaceutical preparations can be present in solid form, for example as tablets, coated tablets, suppositories, or capsules, or in liquid form, for example as solutions, suspensions, or emulsions. Moreover, they optionally contain adjuvants, such as preservatives, stabilizers, wetting agents or emulsifiers; salts for changing the osmotic pressure or buffers. These pharmaceutical preparations are also subjects of this invention.

For parenteral administration, especially injection solutions or suspensions, especially aqueous solutions of active compounds in polyhydroxyethoxylated castor oil, are suitable.

As carrier systems, surface-active adjuvants such as salts of bile acids or animal or plant phospholipids, but also mixtures thereof, as well as liposomes or their components can also be used.

For oral administration, especially tablets, coated tablets or capsules with talc and/or hydrocarbon vehicles or binders, such as, for example, lactose, corn or potato starch, are suitable. The administration can also be carried out in liquid form, such as, for example, as a juice, to which optionally a sweetener is added.

Enteral, parenteral and oral administrations are also subjects of this invention.

The dosage of the active ingredients can vary depending on the method of administration, age and weight of the patient, type and severity of the disease to be treated and similar factors. The daily dose is 0.5-1000 mg, preferably 50-200 mg, whereby the dose can be given as a single dose to be administered once or divided into two or more daily doses.

Subjects of this invention also include the use of compounds of general formula I for the production of a pharmaceutical agent for treating cancer, auto-immune diseases, cardiovascular diseases, chemotherapy agent-induced alopecia and mucositis, infectious diseases, nephrological diseases, chronic and acute neurodegenerative diseases and viral infections, whereby cancer is defined as solid tumors and leukemia; auto-immune diseases are defined as psoriasis, alopecia and multiple sclerosis; cardiovascular diseases are defined as stenoses, arterioscleroses and restenoses; infectious diseases are defined as

diseases that are caused by unicellular parasites; nephrological diseases are defined as glomerulonephritis; chronic neurodegenerative diseases are defined as Huntington's disease, amyotrophic lateral sclerosis, Parkinson's disease, AIDS dementia and Alzheimer's disease; acute neurodegenerative diseases are defined as ischemias of the brain and neurotraumas; and viral infections are defined as cytomegalic infections, herpes, hepatitis B or C, and HIV diseases.

Subjects of this invention also include pharmaceutical agents for treating the above-cited diseases, which contain at least one compound according to general formula I, as well as pharmaceutical agents with suitable formulation substances and vehicles.

The compounds of general formula I according to the invention are, i.a., excellent inhibitors of the cyclin-dependent kinases, such as CDK1, CDK2, CDK3, CDK4, CDK5, CDK6, CDK7, CDK8 and CDK9, as well as the glycogen-synthase-kinase (GSK-3 β).

If the production of the starting compounds is not described, these compounds are known or can be produced analogously to known compounds or to processes that are described here. It is also possible to perform all reactions that are described here in parallel reactors or by means of combinatory operating procedures.

The isomer mixtures can be separated into the enantiomers or E/Z isomers according to commonly used methods, such as, for example, crystallization, chromatography or salt formation.

The production of the salts is carried out in the usual way by a solution of the compound of formula I being mixed with the equivalent amount of or excess base or acid, which optionally is in solution, and the precipitate being separated or the solution being worked up in the usual way.

Production of the Compounds According to the Invention

The following examples explain the production of the compounds according to the invention, without the scope of the claimed compounds being limited to these examples.

The compounds of general formula I according to the invention can be produced according to the following general diagrams of the process:

Diagram 1

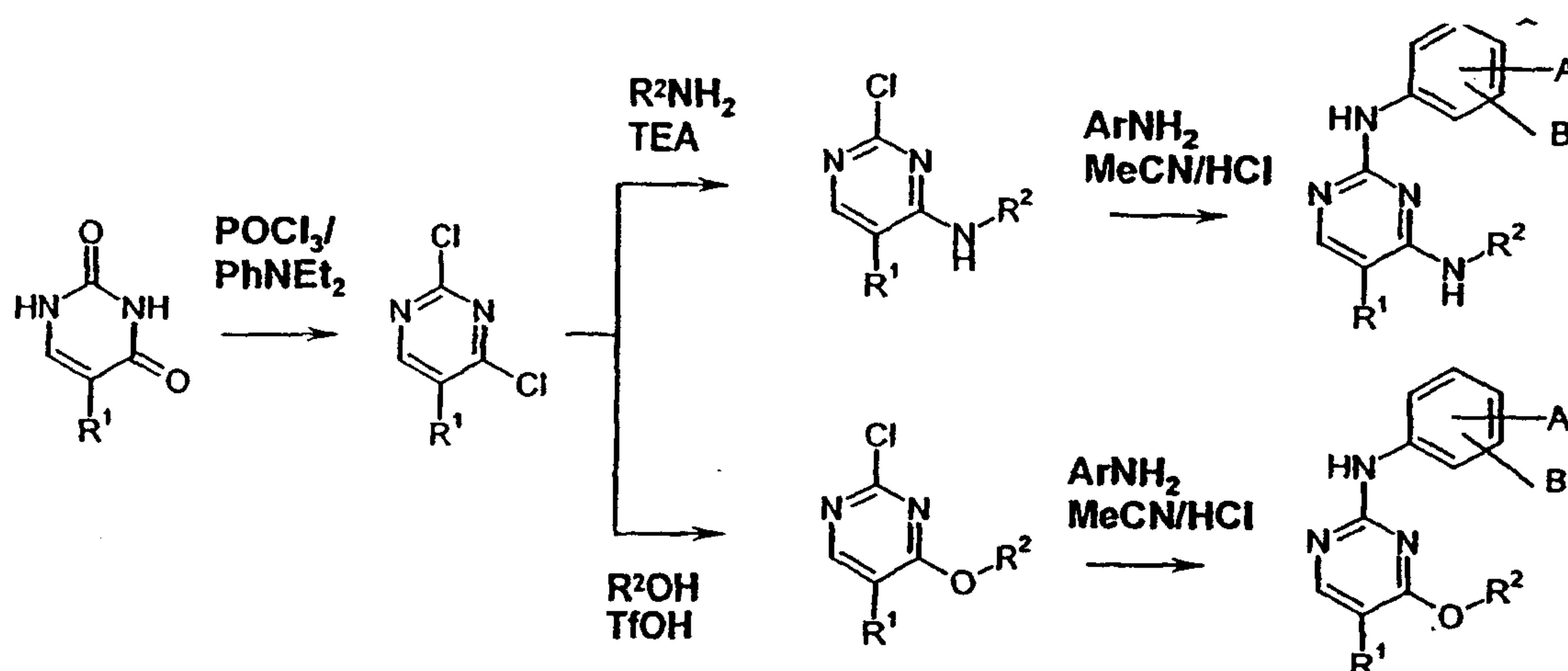
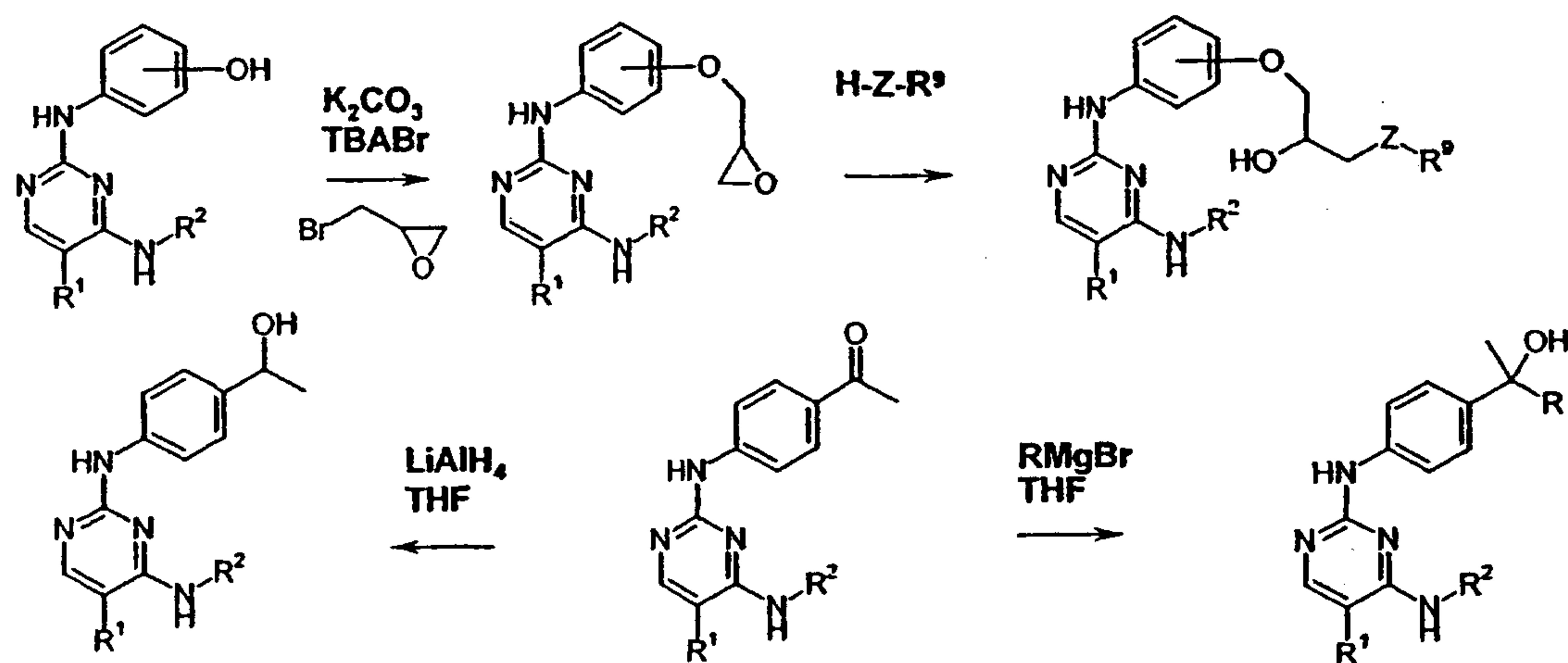
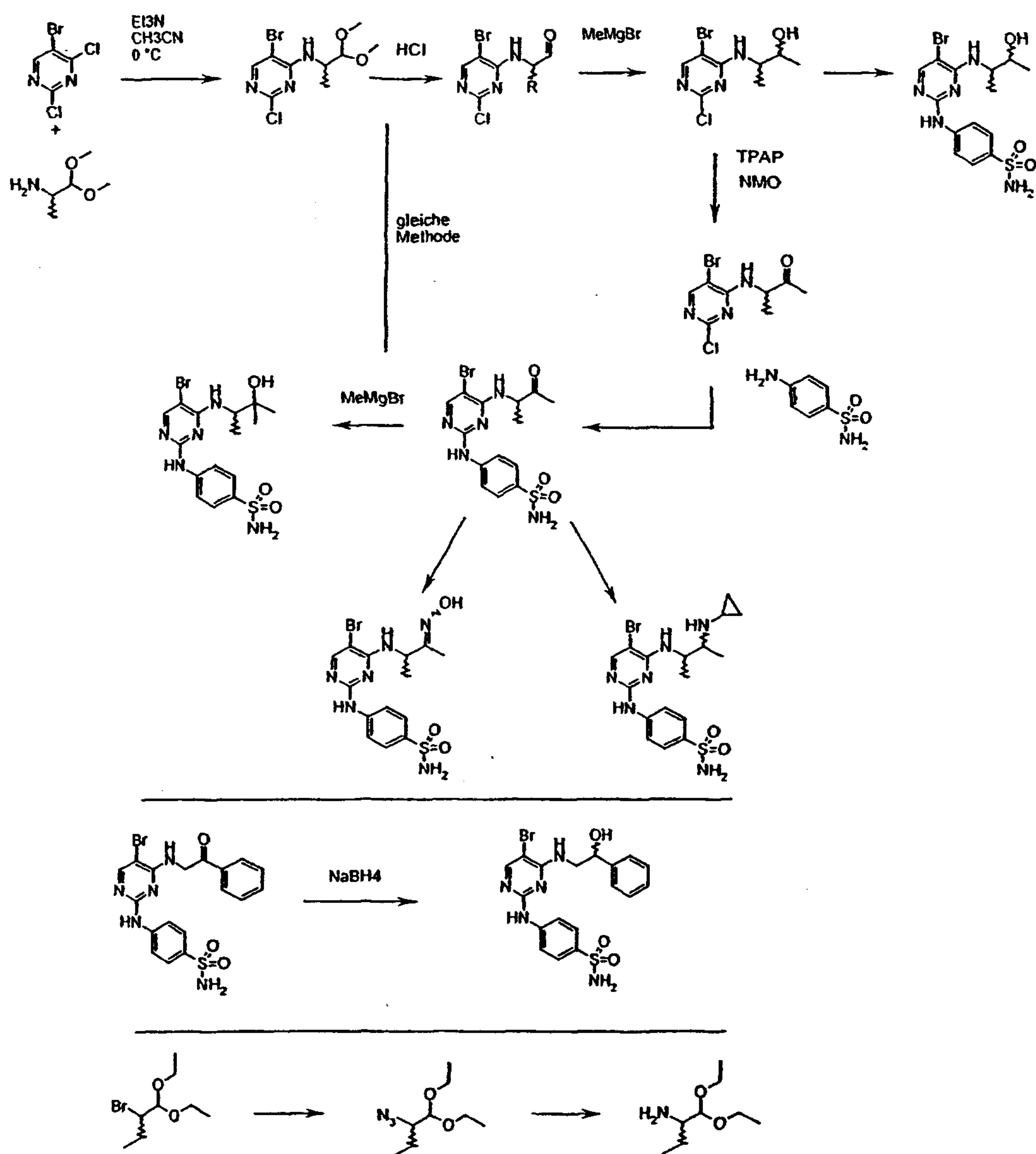


Diagram 2



$Z = O$ or NH

Diagram 3

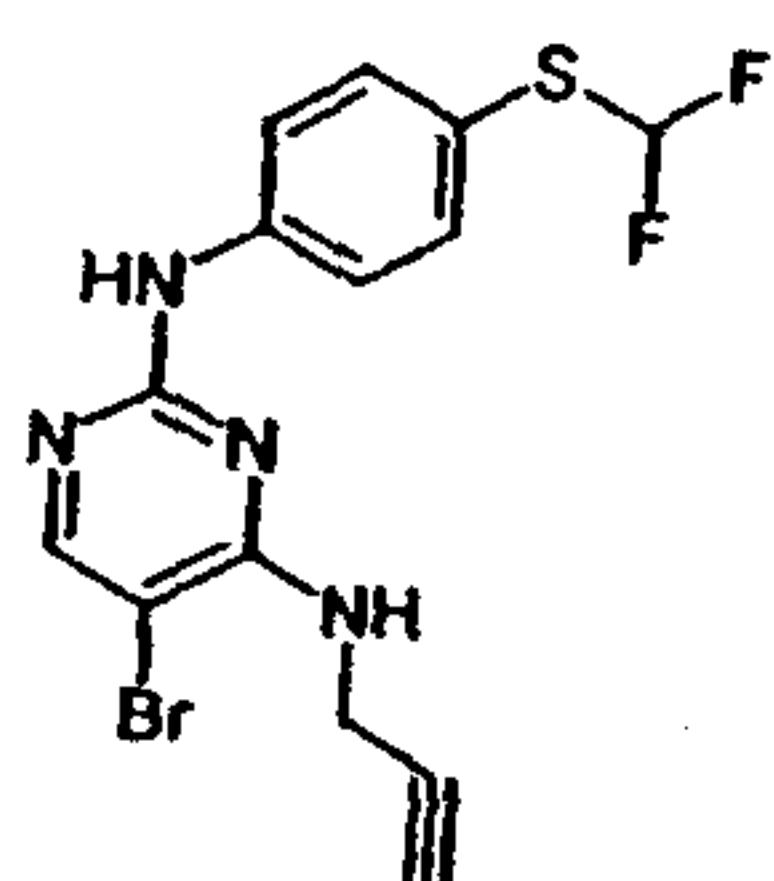


[Key:] gleiche Methode = same method

Example 1

Production of 5-Bromo-N2-(4-difluoromethylthiophenyl)-N4-2-propynyl-2,4-pyrimidine diamine (carried out according to process diagram 1) (compound 23).

245 mg (1 mmol) of 2-chloro-4-2-propynylaminopyrimidine is dissolved in 2 ml of acetonitrile, and a suspension of 4-(difluoromethylthio)-aniline hydrochloride [produced from 352 mg (2 mmol) of 4-(difluoromethylthio)-aniline, 1 ml of acetonitrile and 0.5 ml of aqueous HCl (4M in dioxane)] is added at room temperature. Then, the reaction mixture is refluxed overnight under N₂ atmosphere. After cooling, the mixture is filtered, the remaining solid phase is washed with H₂O and dried. A yield of 328 mg (85%) of the product can be expected

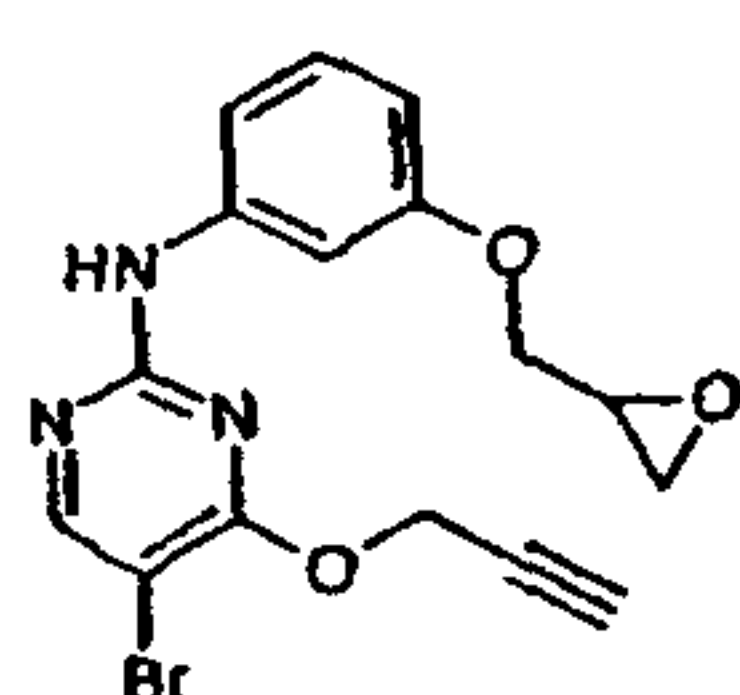


6H	8.25 (s, 1H)	Yield:
2C	7.86 (d, 2H)	85%
H	7.51 (d, 2H)	
	7.38	
	(t, 56.8Hz, 1H)	Melting point:
		> 235°C
4C	4.18 (m, 2H)	
H	3.16 (sb, 1H)	
	10.24 (sb, 1H)	
NH	8.17 (sb, 1H)	

Example 2

Production of 5-bromo-N-(3-(oxiranylmethoxy)phenyl)-2-(2-propynyloxy)-pyrimidinamine (compound 51) and carried out according to process diagram 2.

1.55 g (4.9 mmol) of compound 20 is dissolved in 5.5 ml of epibromohydrin, and 1.38 g of K_2CO_3 and 65 mg of tetrabutylammonium bromide are added to it. The reaction mixture is stirred under nitrogen atmosphere at 100°C for 1 hour. After ethyl acetate is added, the resulting precipitate is collected and recrystallized from ethanol. The product yield is 1.15 g (62%) as a white powder.



6H 8.45 (s, 1H)

2CH 7.47 (s, 1H)

7.32 (d, 1H)

Yield: 62%

7.20 (t, 1H)

6.40 (d, 1H)

Melting point: 173°C

4.32 (dd, 1H)

3.82 (dd, 1H)

3.3-3.4 (m, 1H)

2.87 (t, 1H)

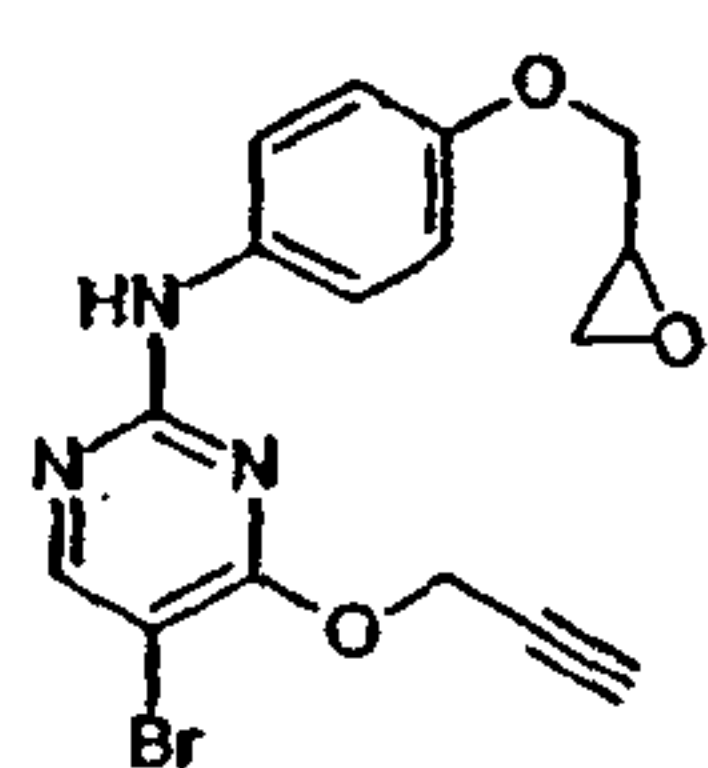
2.72 (dd, 1H)

4CH 5.13 (d, 2H)

3.67 (t, 1H)

NH 9.84 (sb, 1H)

Substance 40 is produced analogously to Example 2.



6-H 8.36 (s, 1H)

Chromatography:

2CH 7.60 (d, 1H)

H/EA 1:3 0.5% TEA

6.91 (d, 1H)

4.28 (dd, 1H)

3.79 (dd, 1H)

Yield: 38%

3.31 (m, 1H)

2.84 (dd, 1H)

Melting point: 140-141°C

2.70 (dd, 1H)

4CH 5.07 (d, 12H)

3.65 (t, 1H)

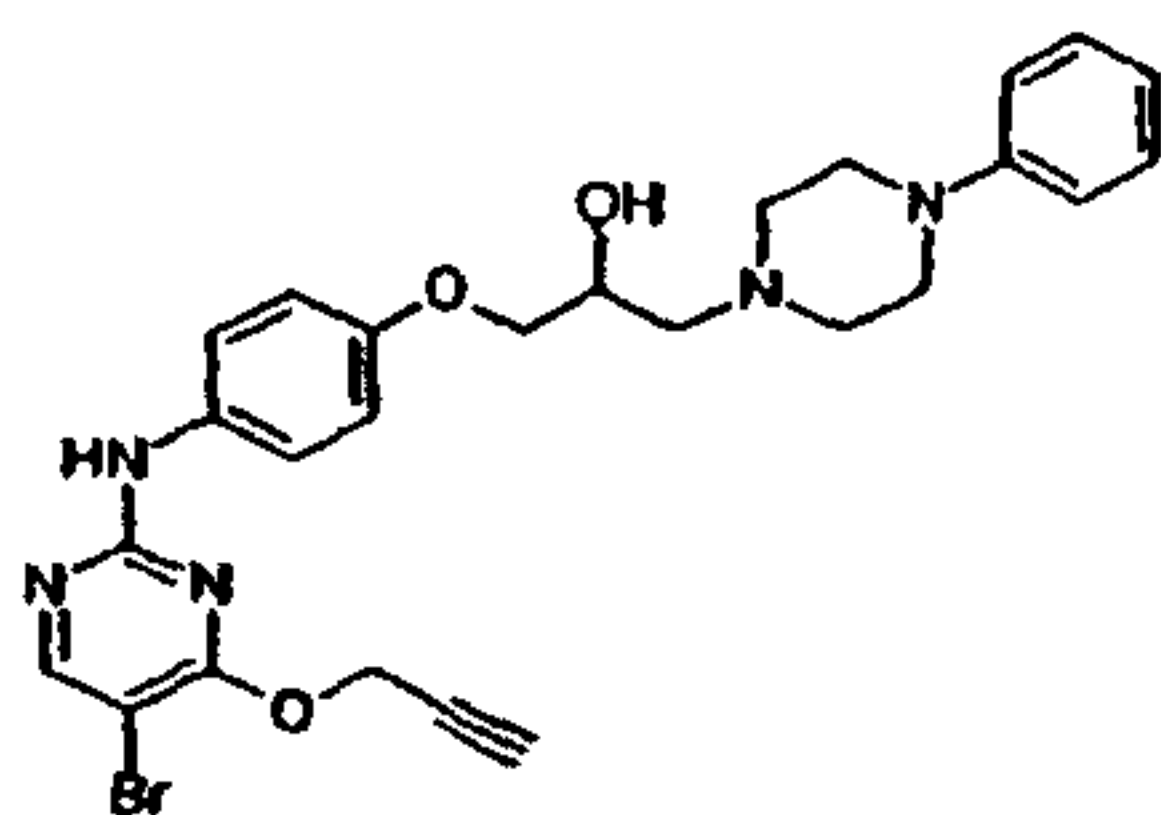
NH 9.65 (sb, 1H)

OH

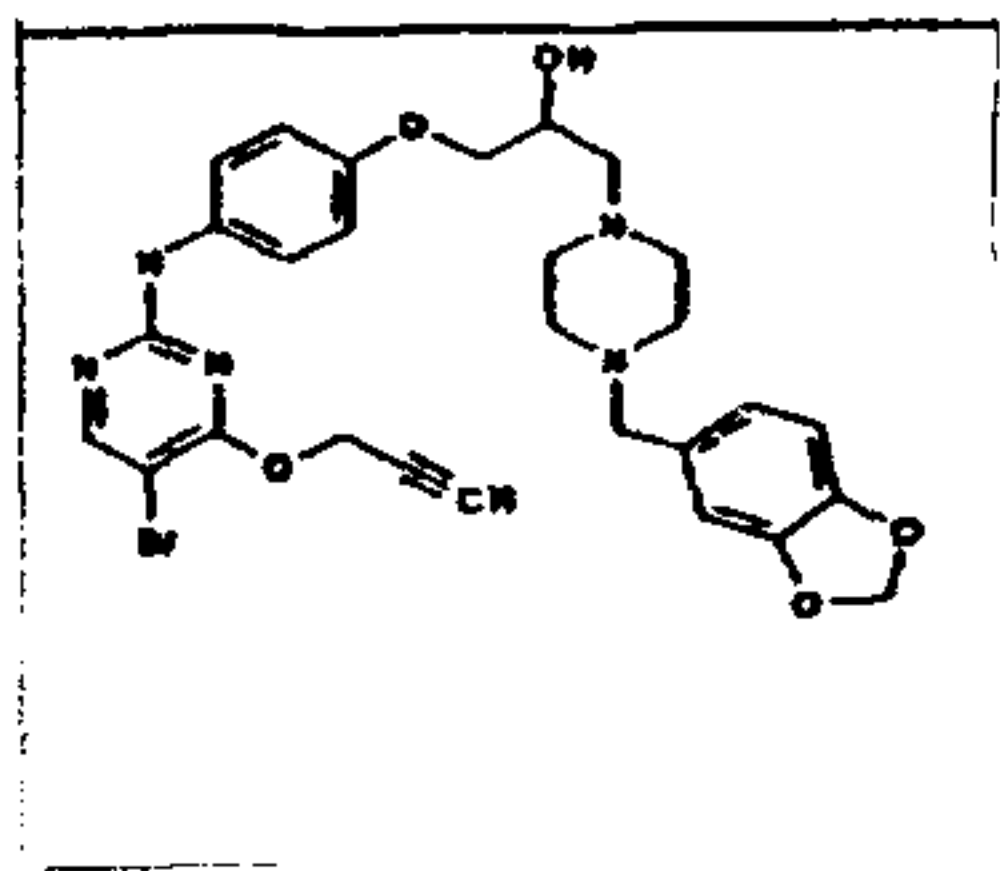
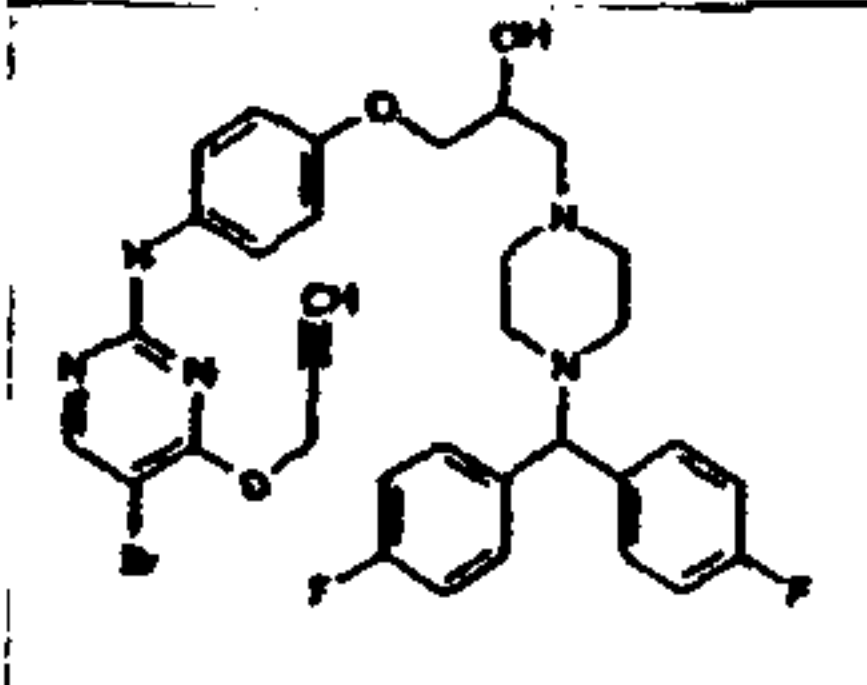
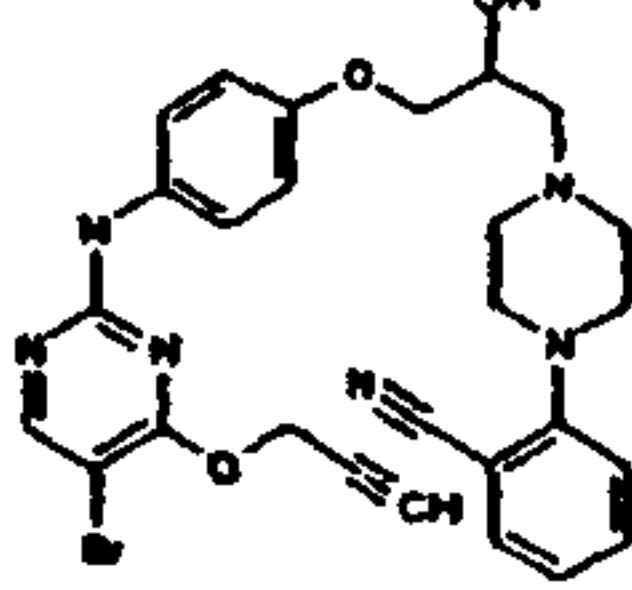
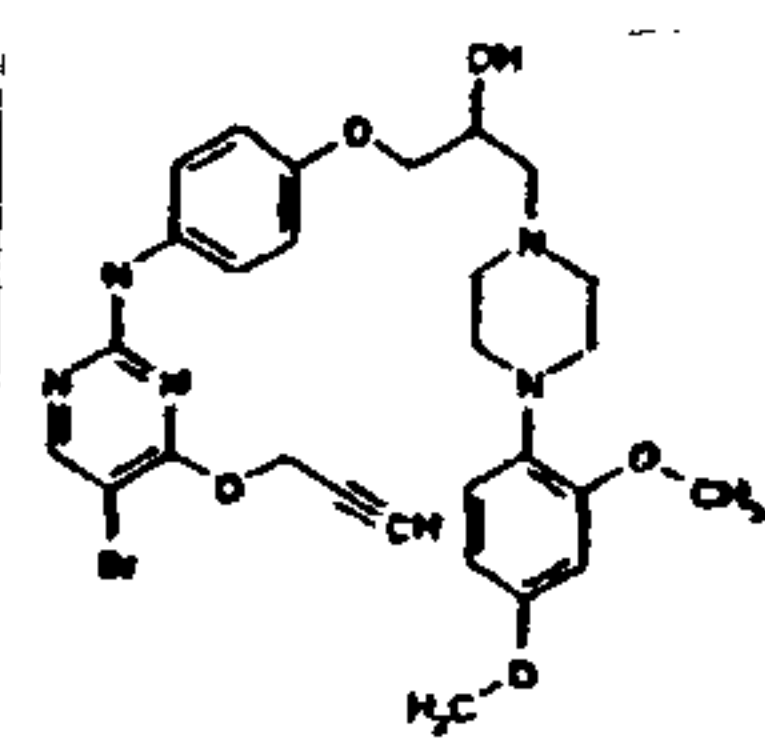
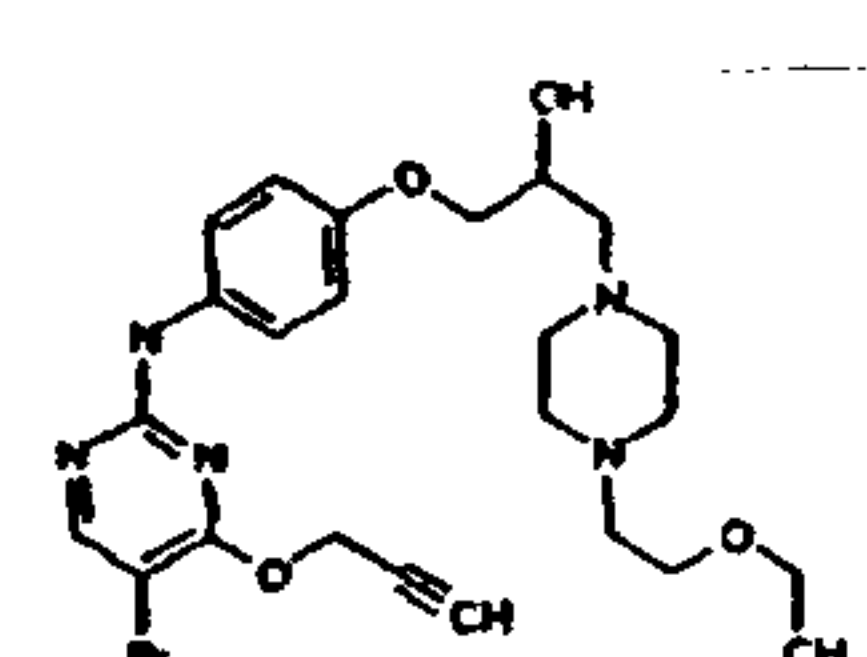
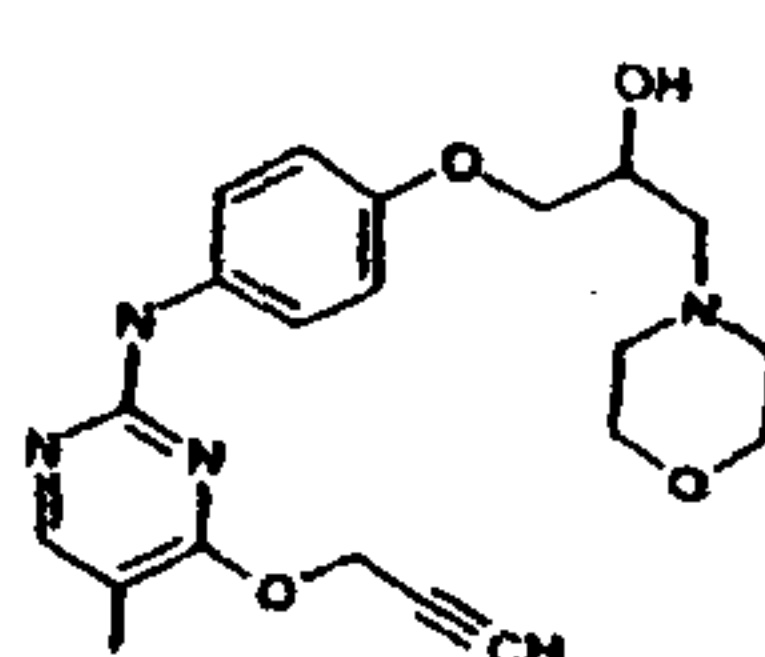
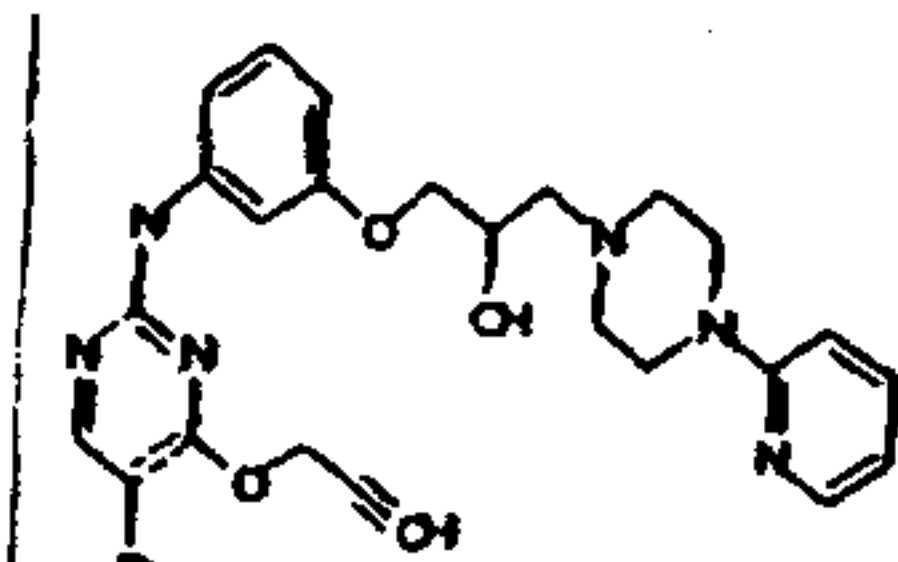
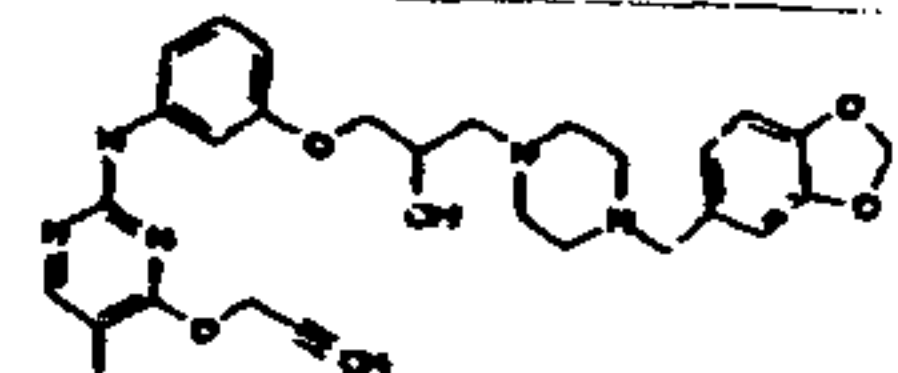
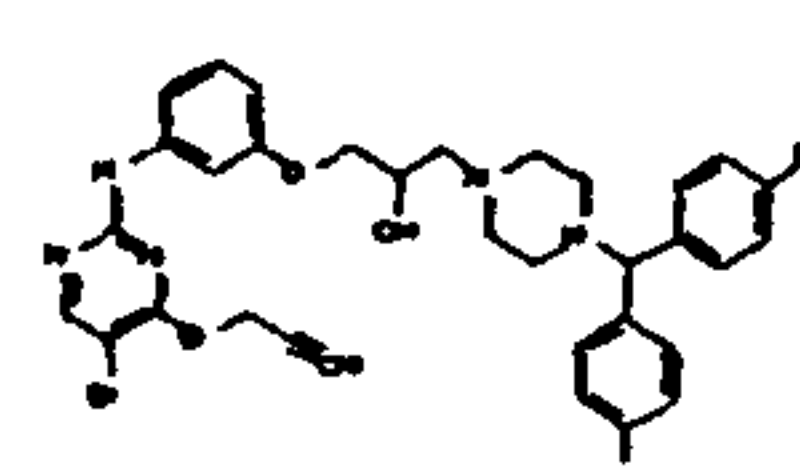
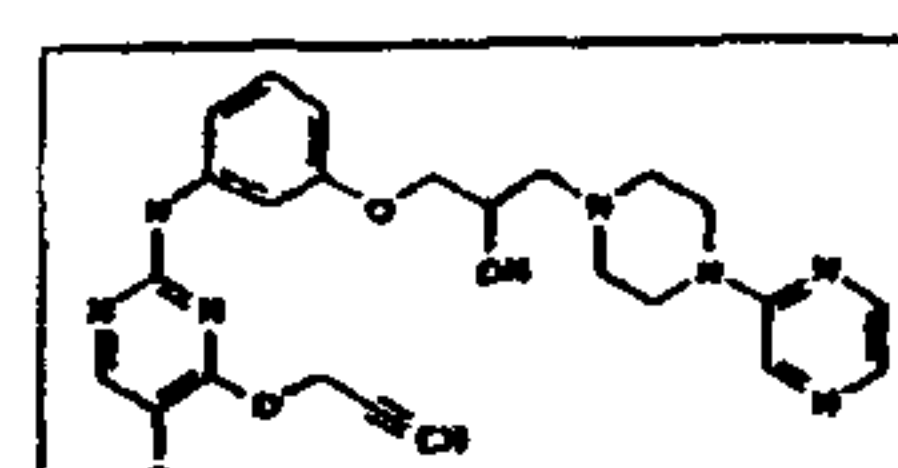
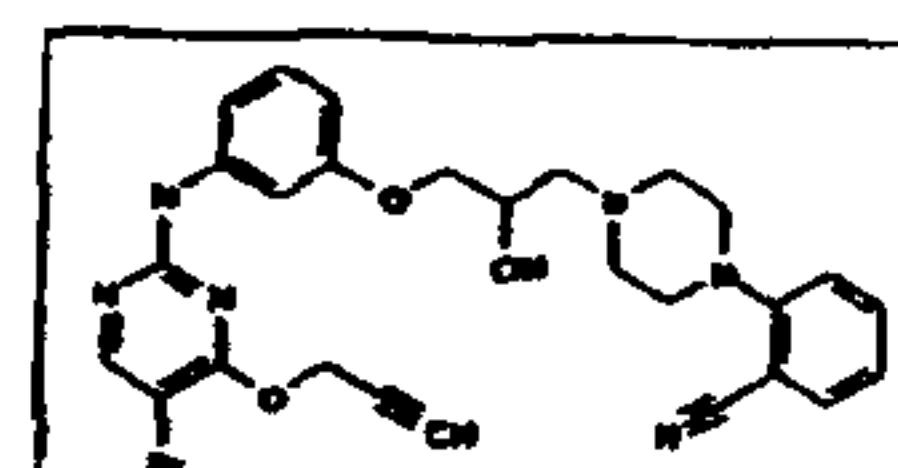
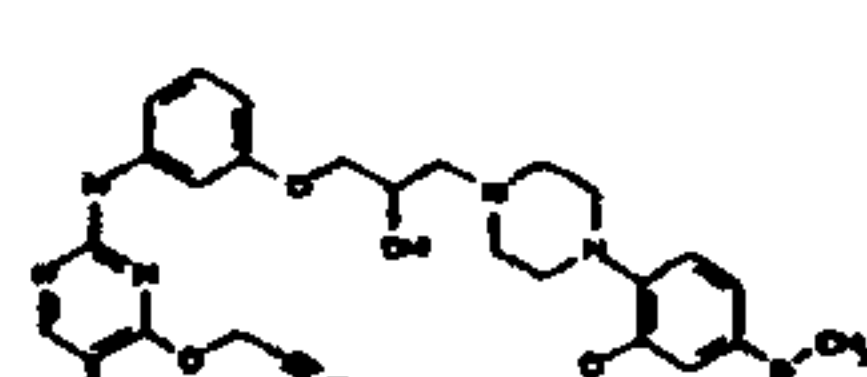
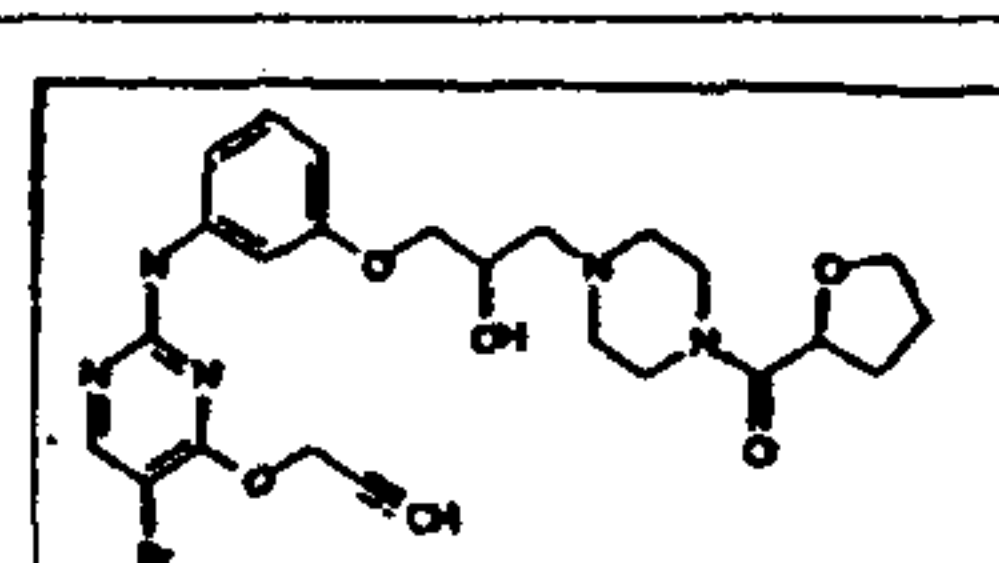
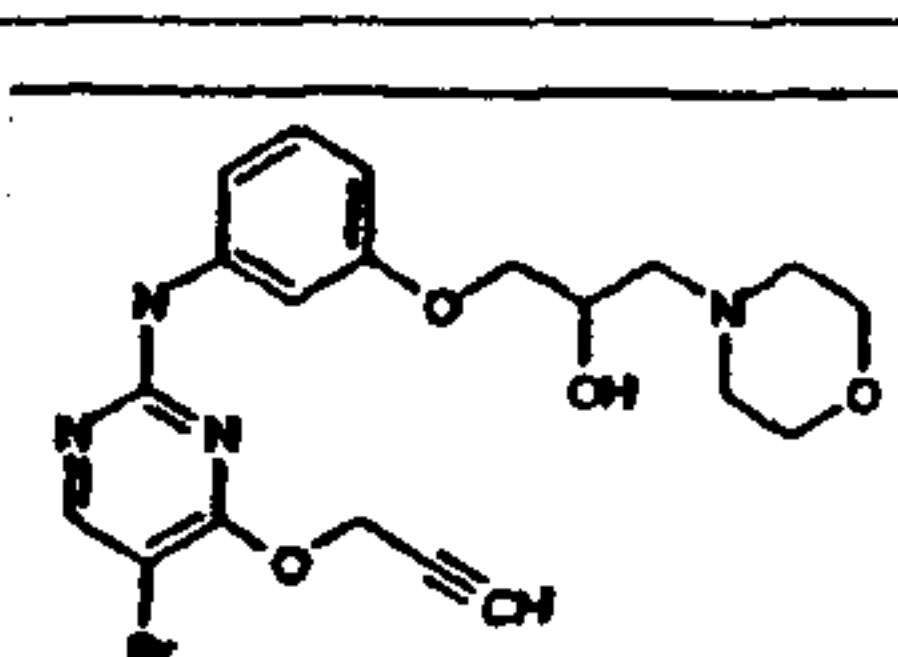
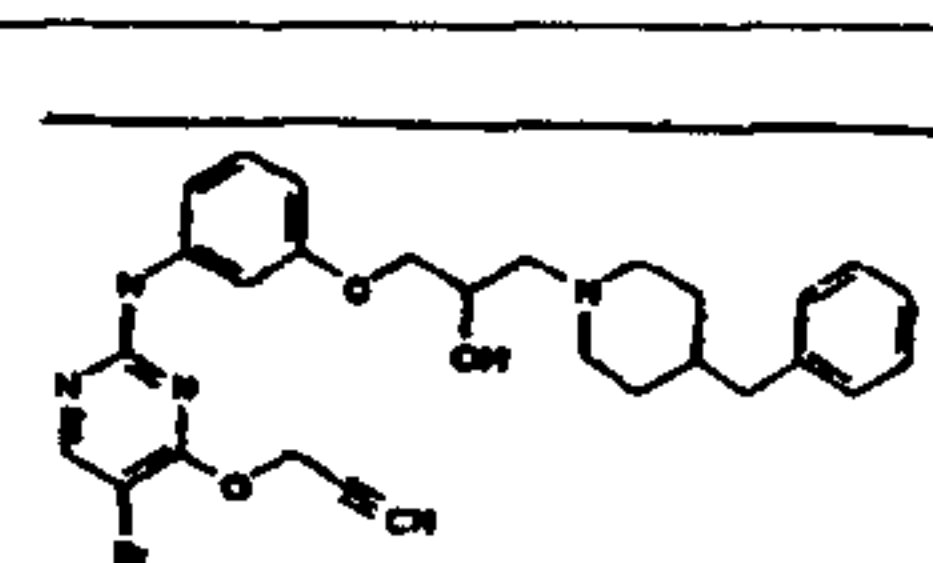
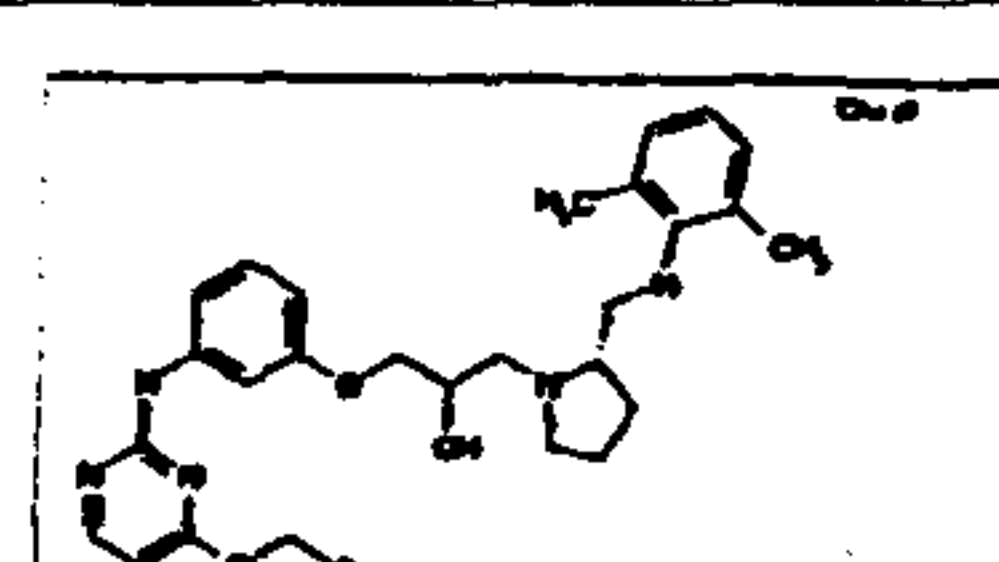
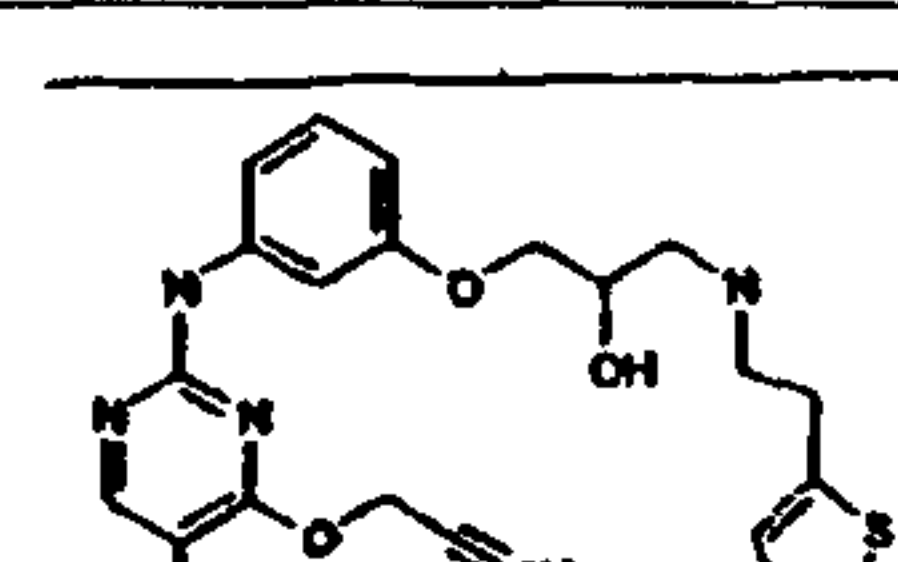
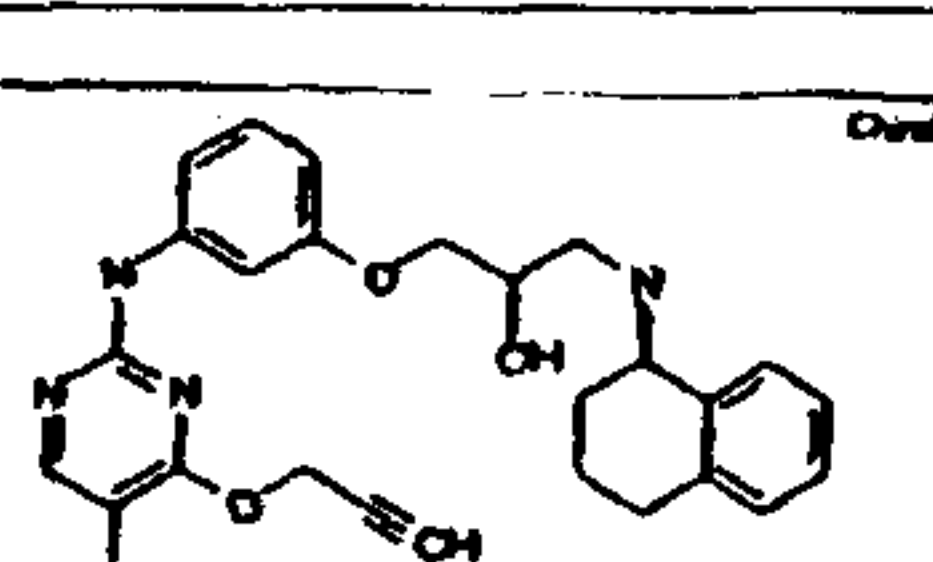
Example 3

Production of 1-(4-((5-bromo-4-(2-propynyloxy)-pyrimidin-2-yl)-amino)phenoxy)-3-(4-phenylpiperazin-1-yl)-2-propanol (compound 41).

0.2 ml of a 0.5 M 4-phenylpiperazine solution in DMPU is added to a solution of 19 mg (0.05 mmol) of substance 51 in N,N'-dimethylpropylurea (DMPU). The reaction mixture is kept for 18 hours at a temperature of 80°C. After cooling, 3.5 ml of tertiary butyl methyl ether is added, and the organic phase is extracted 5 times with 1.5 ml of H₂O and then evaporated in a vacuum. The remaining residue is chromatographed on 1.7 g (15 µM) of Lichrosphere Si60 (gradient: dichloromethane/hexane 1:1 to DCM and then dichloromethane/methanol 99:1 to 93:7). A product yield of 17 mg (64%) is achieved.

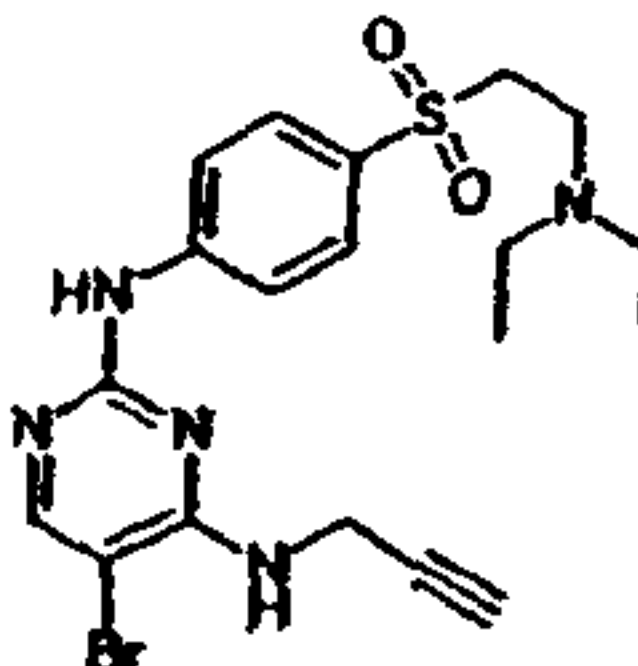
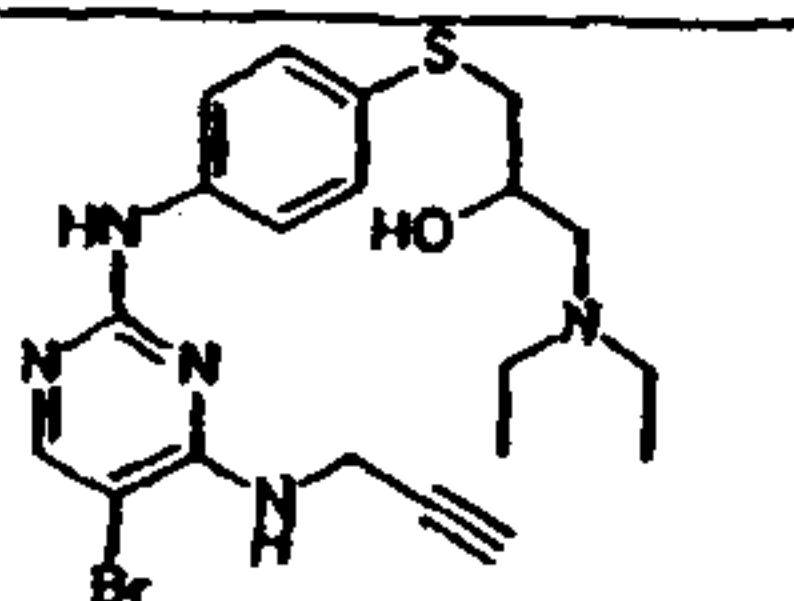
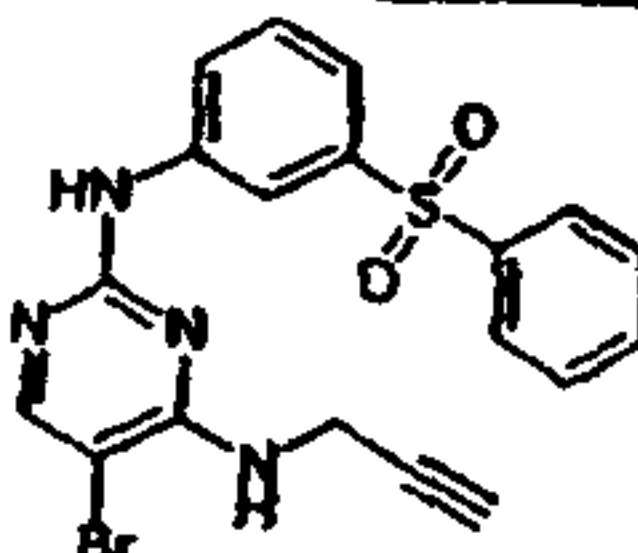


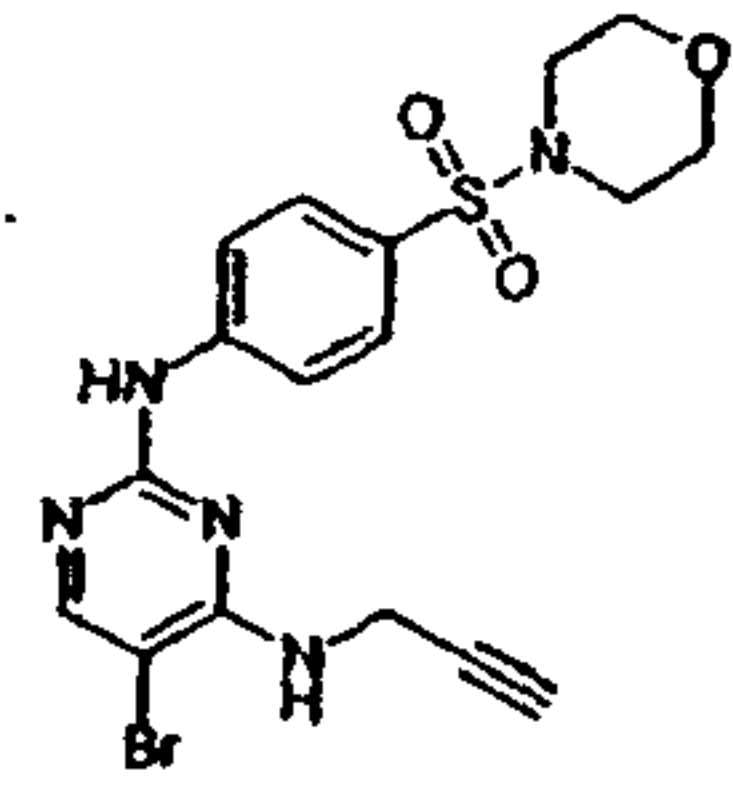
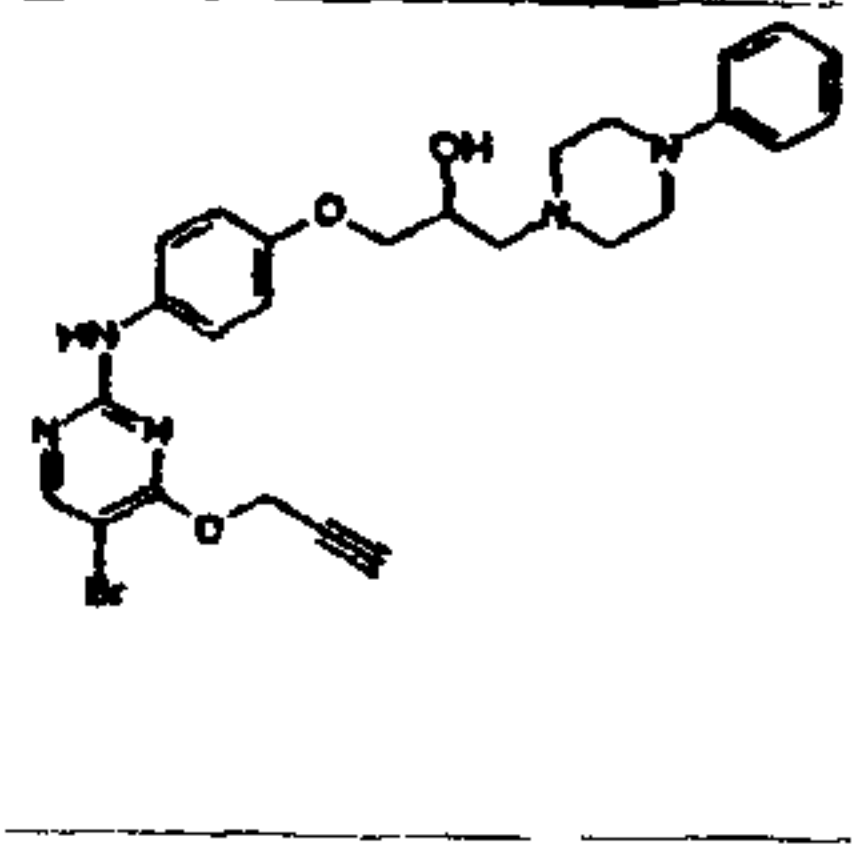
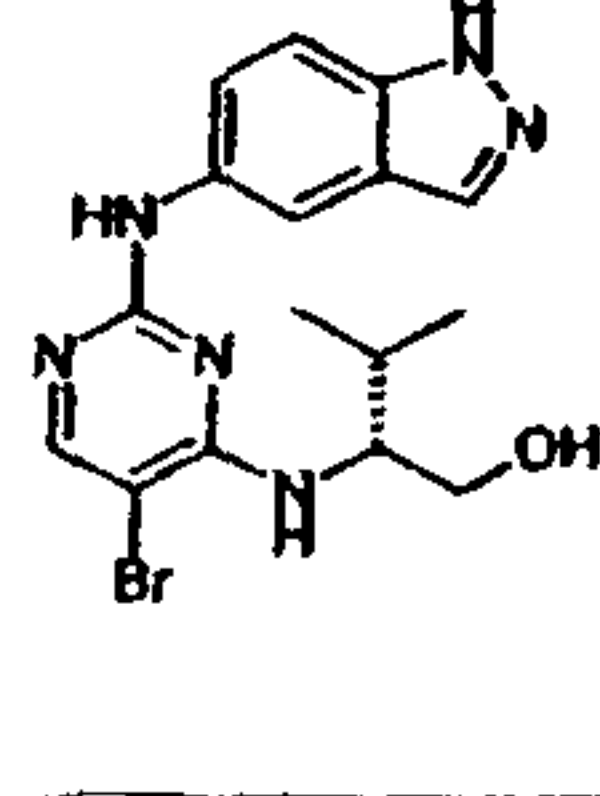
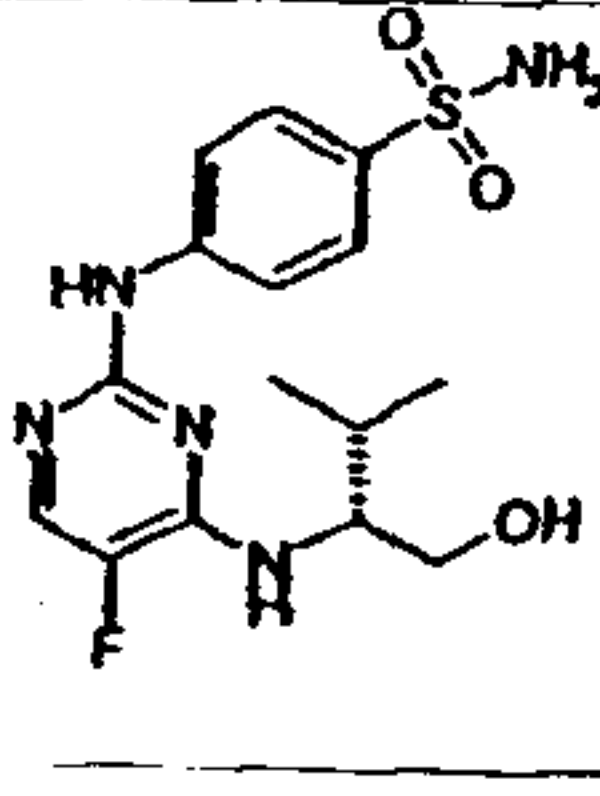
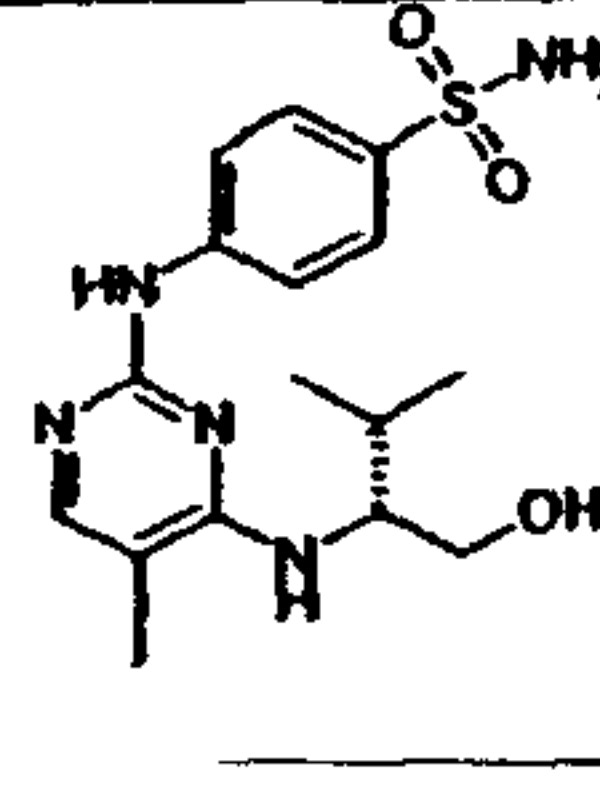
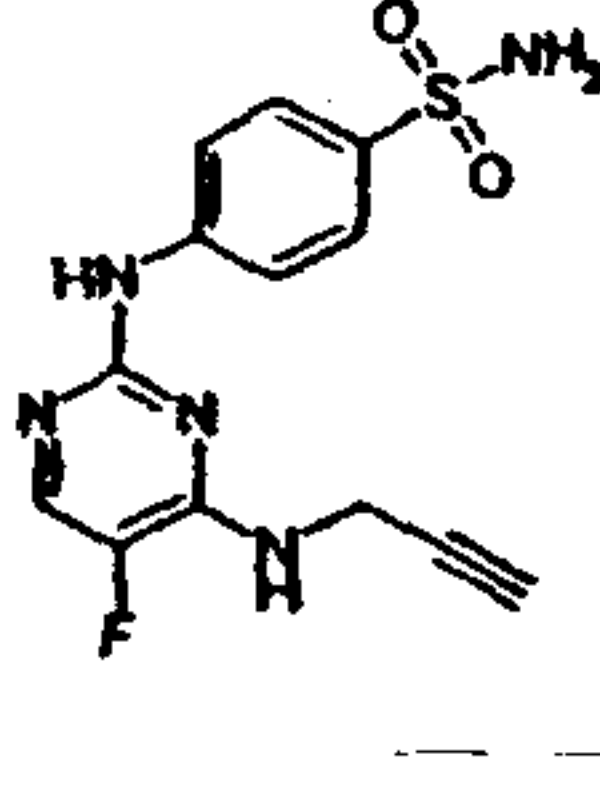
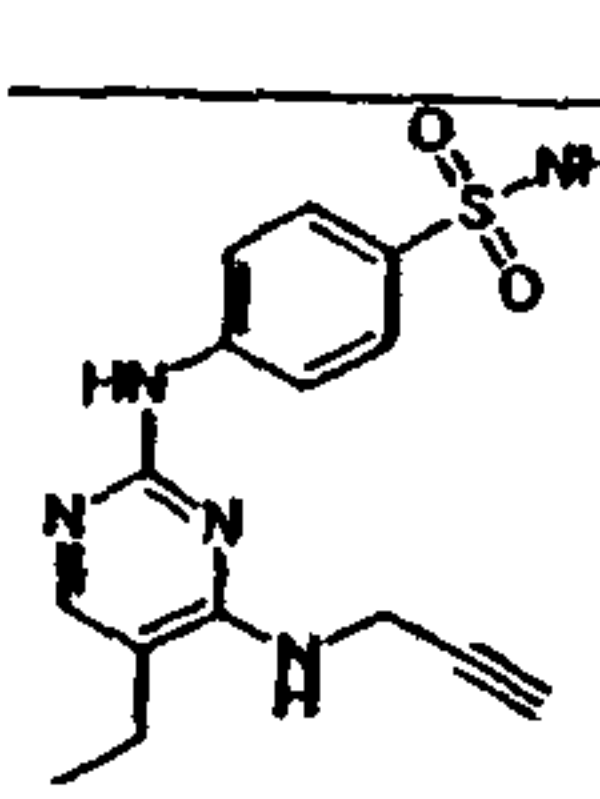
Similarly produced are also the following compounds:

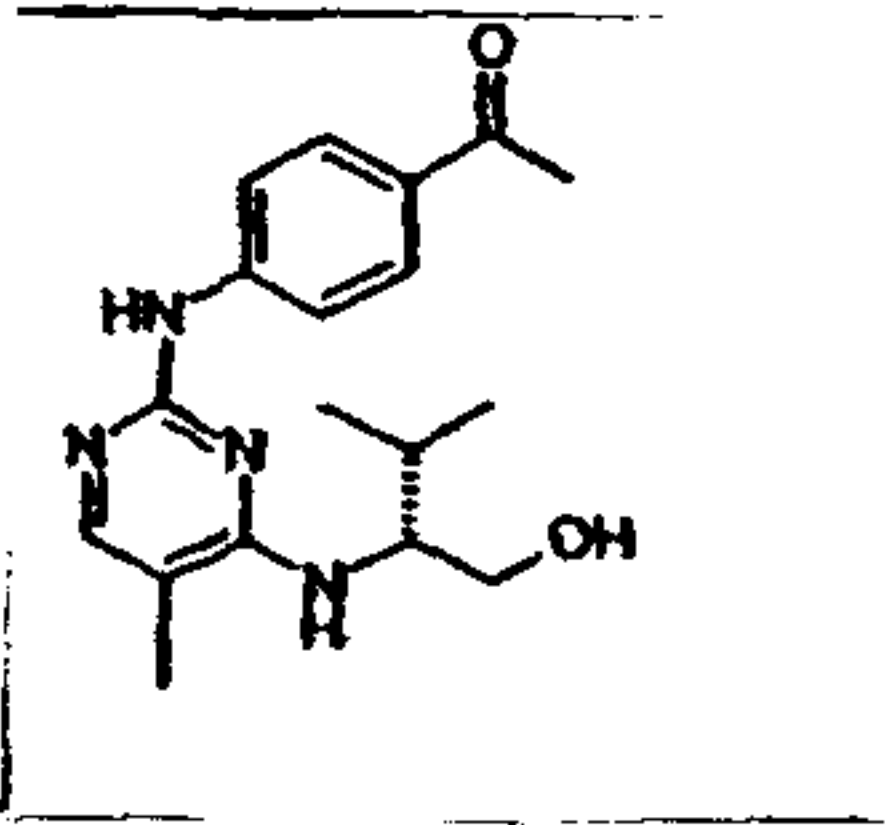
No.	Structure	No.	Structure	No.	Structure
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99		100		101	
102		103		104	
105		106		107	
108		109		110	
111		112		113	

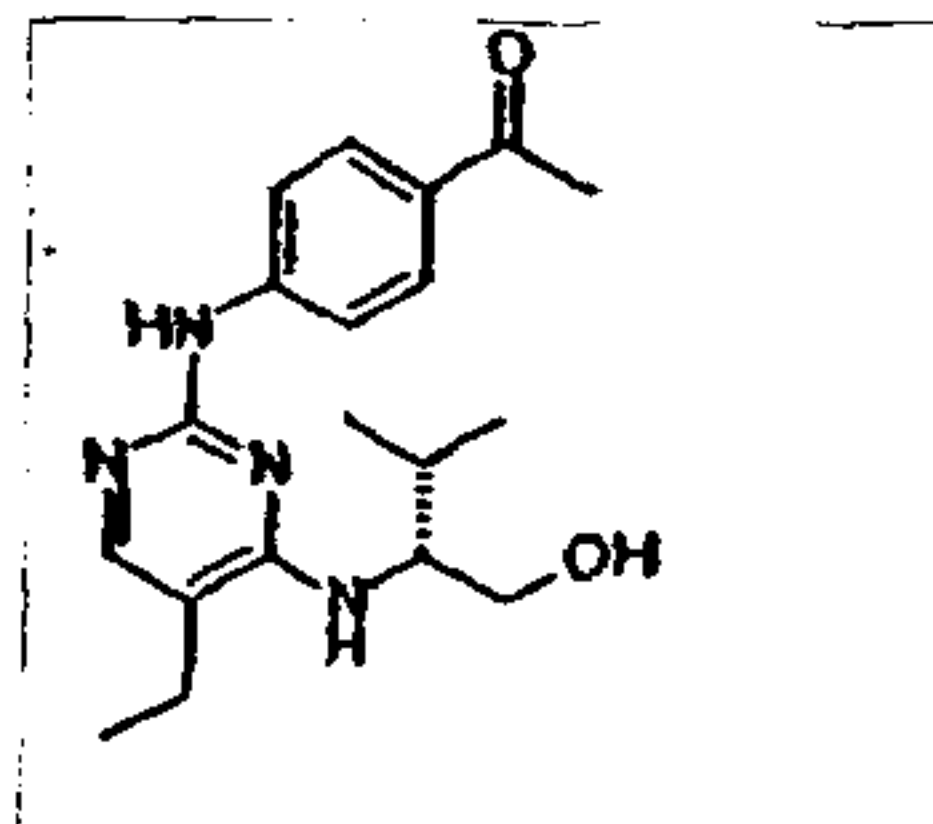
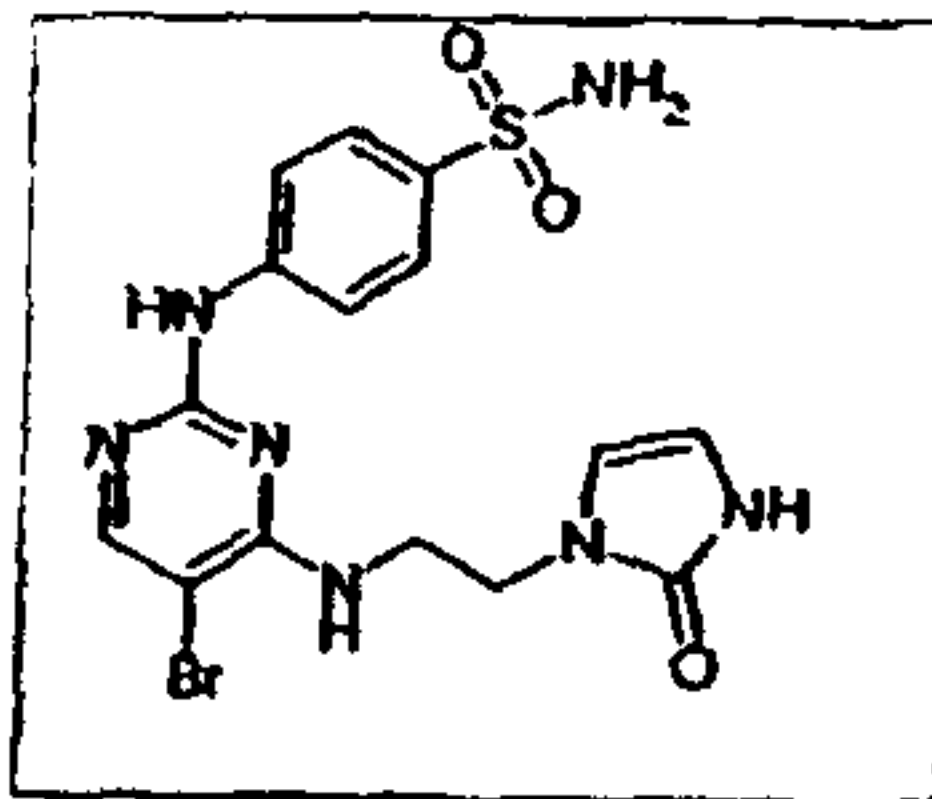
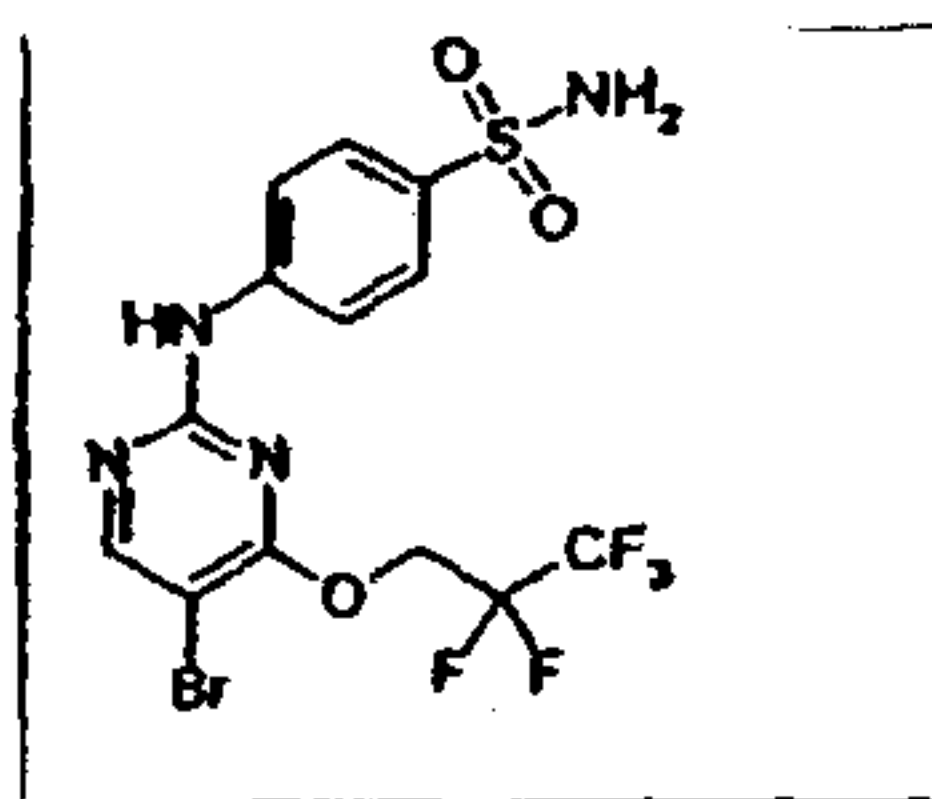
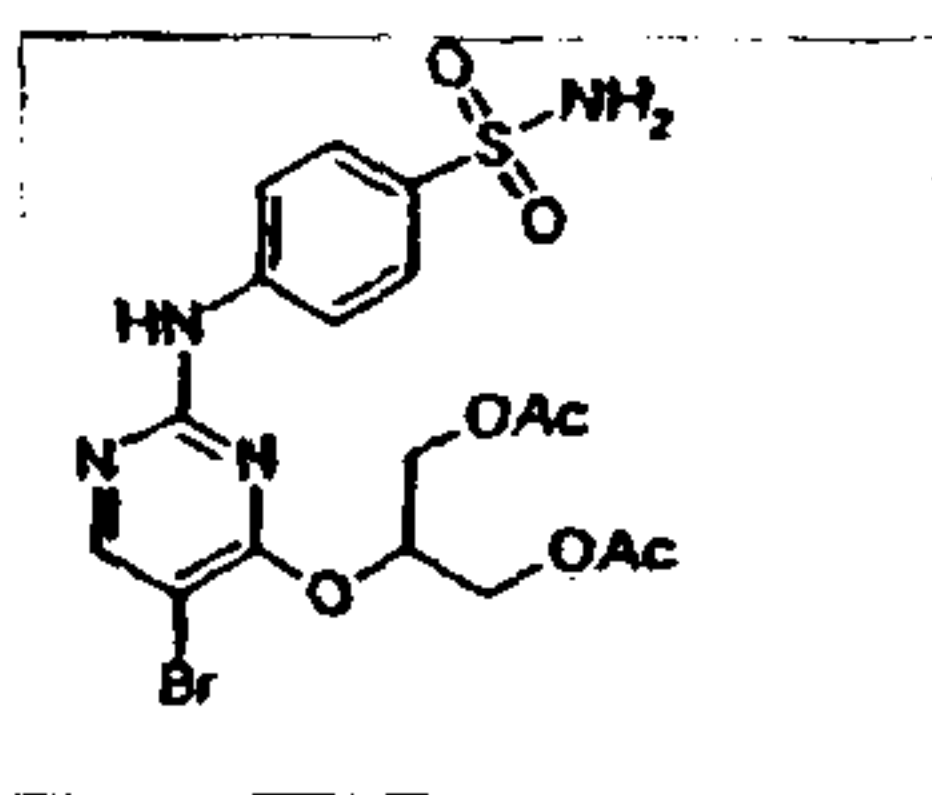
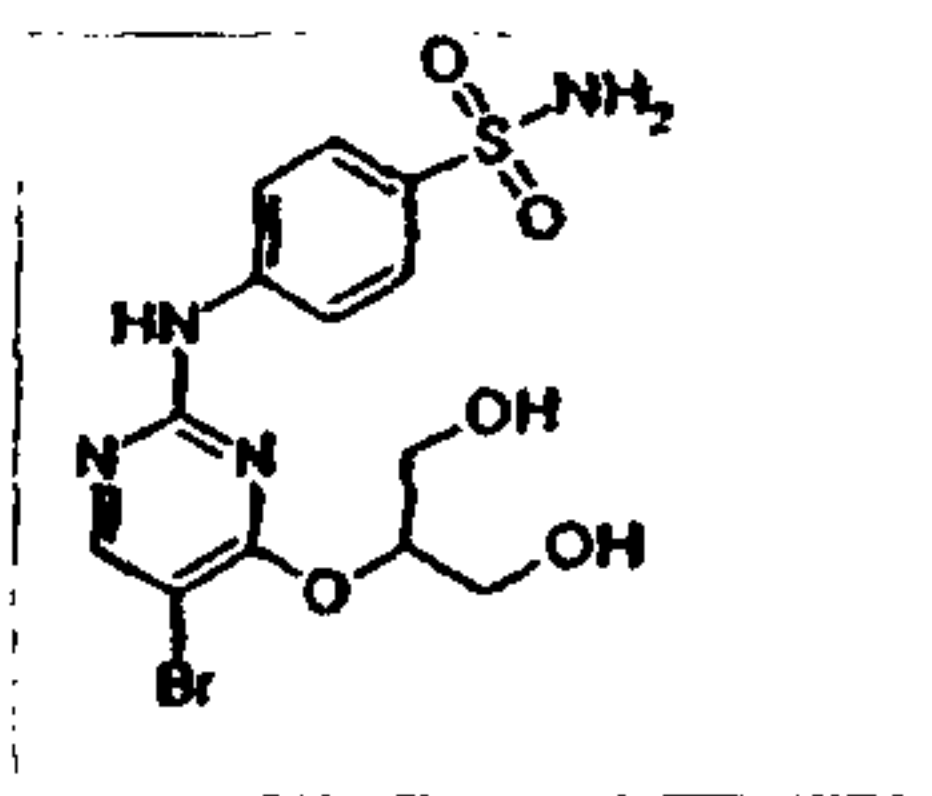
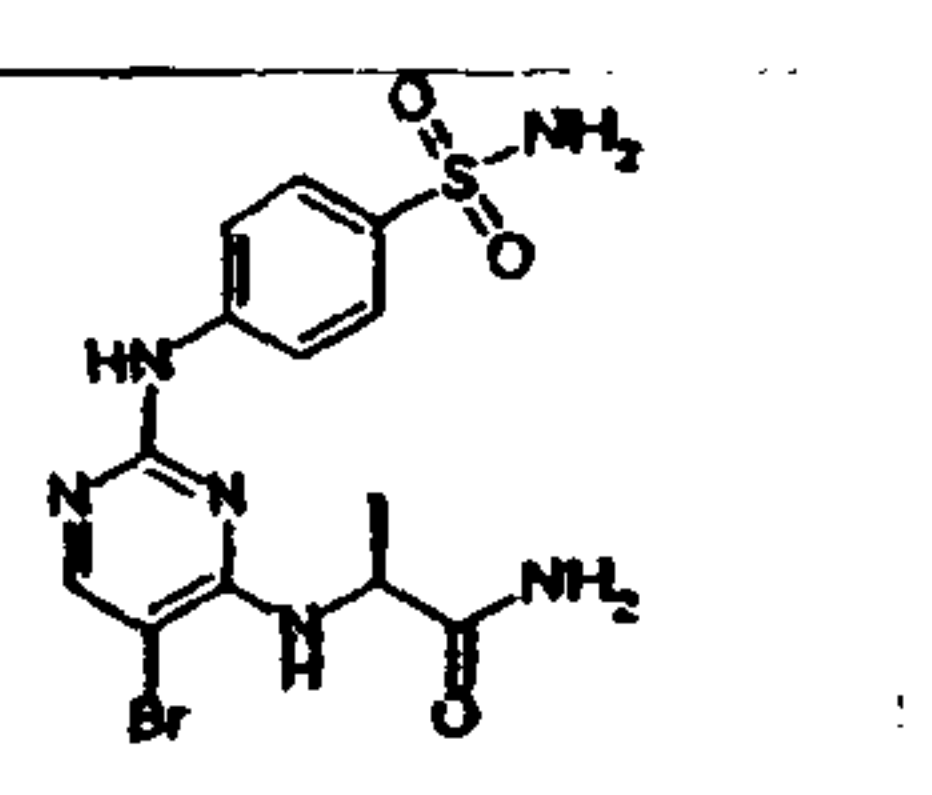
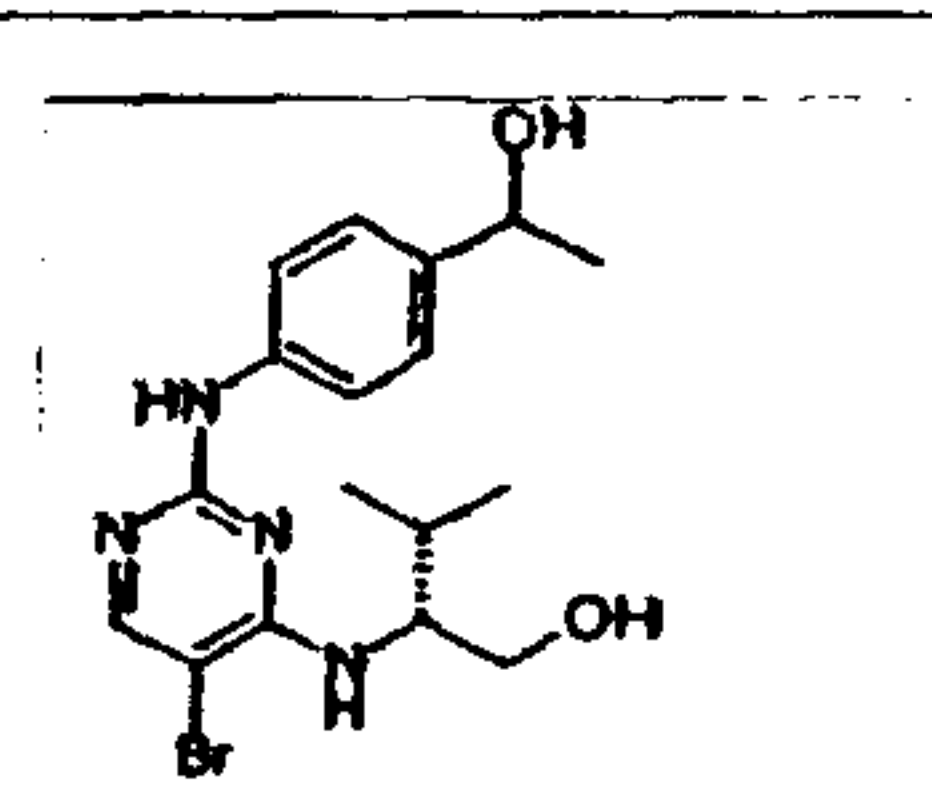
No.	Structure	No.	Structure	No.	Structure
114		115		116	
117		118		119	

The following compounds were similarly produced in the described examples.

No.	Structure	Name
28		5-Bromo-N2-(4-(2-diethylaminoethylsulfonyl)phenyl)- N4-2-propynyl-2,4-pyrimidine diamine
30		1-(4-[5-Bromo-4-(2-propynylamino)-2- pyrimidinyl]amino-phenylthio)-3-(diethylamino)-2- propanol
32		5-Bromo-N2-(3-phenylsulfonylphenyl)-N4-2-propynyl- 2,4-pyrimidine diamine

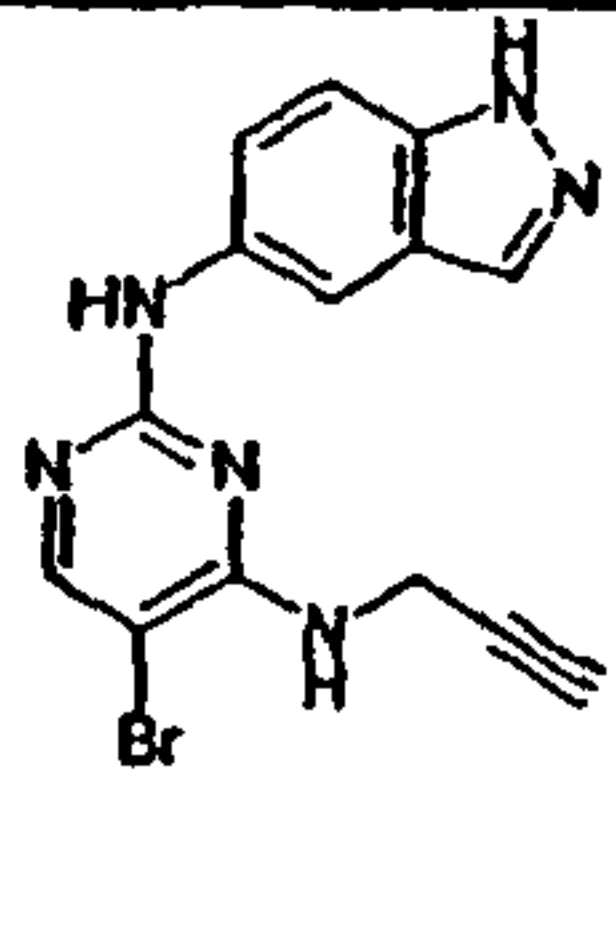
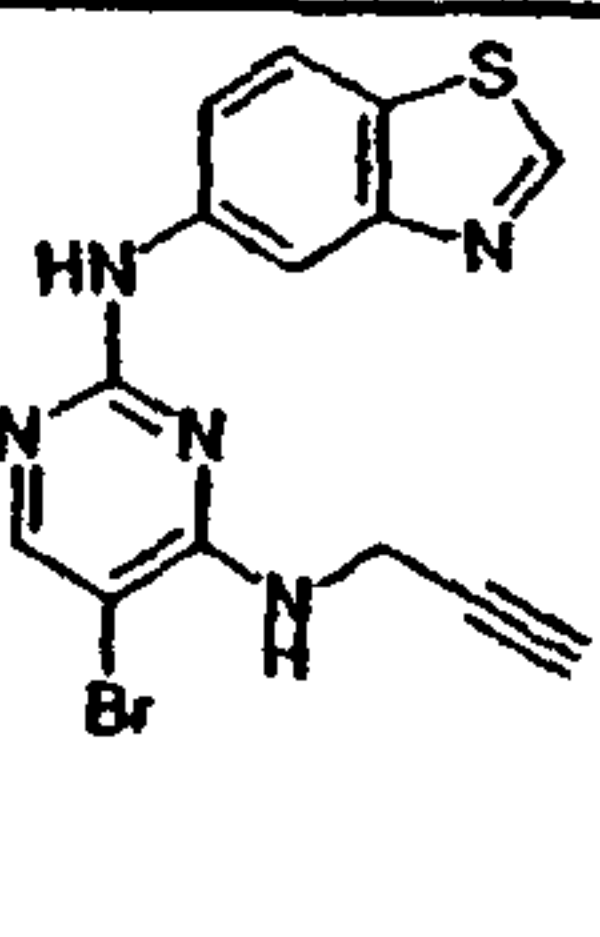
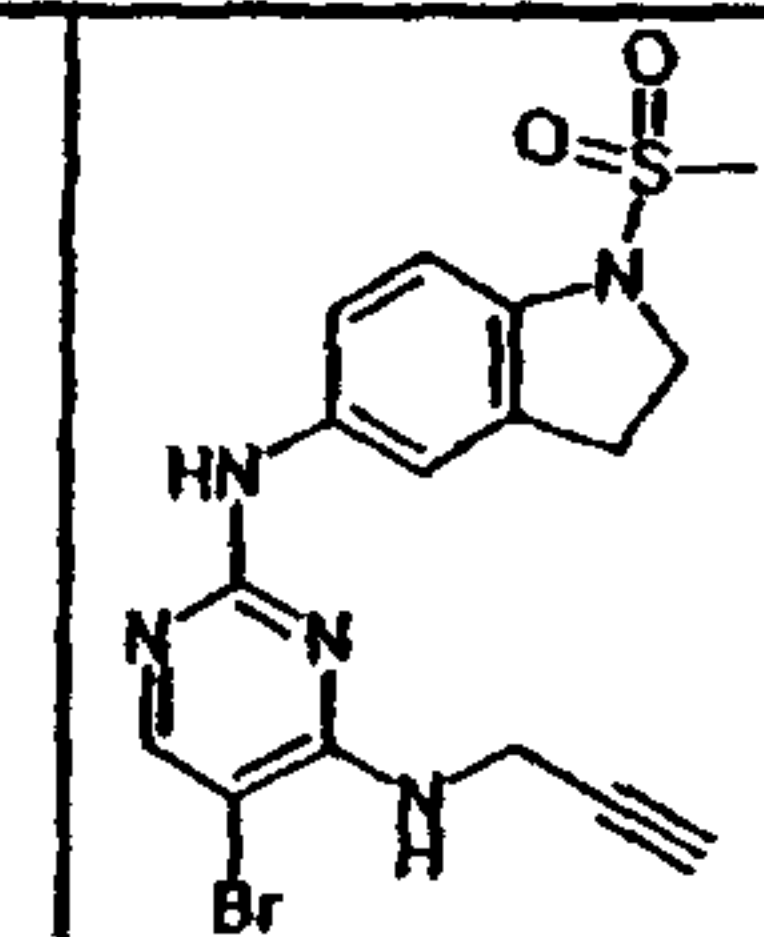
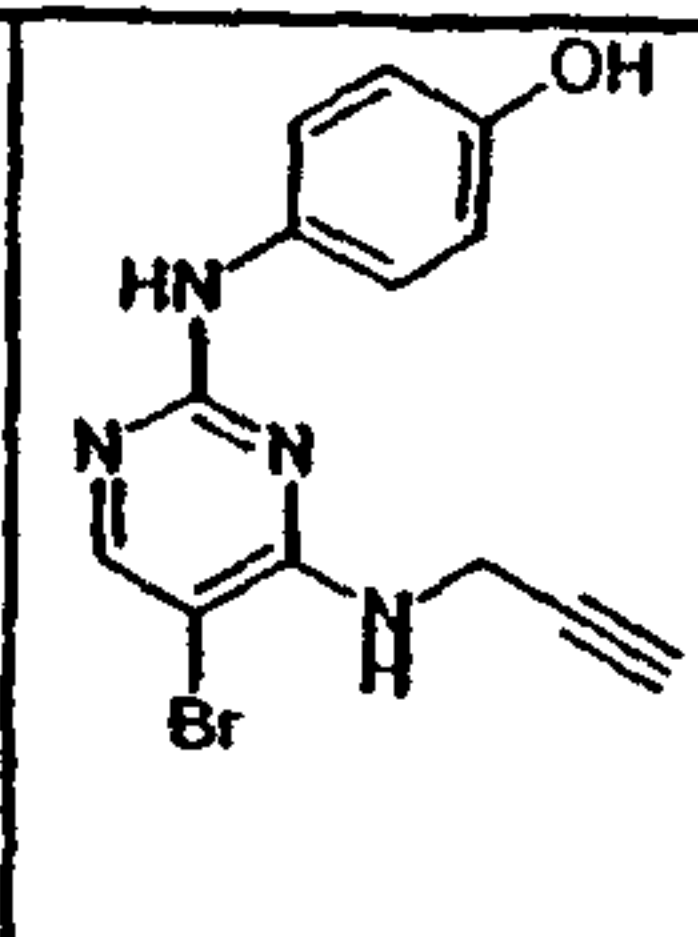
No.	Structure	Name
33		N-[4-[[5-Bromo-4-(2-propynylamino)-2-pyrimidinyl]amino]-benzenesulfonyl]morpholine
41		1-(4-((5-Bromo-4-(2-propynyloxy)-pyrimidin-2-yl)-amino)phenoxy)-3-(4-phenylpiperazin-1-yl)-2-propanol
57		N-[5-Bromo-4-((2R)-1-hydroxy-4-methyl-2-butylamino)-2-pyrimidinyl]-indazol-5-amine
58		4-[[5-Fluoro-4-((2R)-1-hydroxy-3-methyl-2-butylamino)-2-pyrimidinyl]amino]-benzenesulfonamide
59		4-[[5-Iodo-4-((2R)-1-hydroxy-3-methyl-2-butylamino)-2-pyrimidinyl]amino]-benzenesulfonamide
62		4-[[5-Fluoro-4-(2-propynylamino)-2-pyrimidinyl]amino]-benzenesulfonamide
65		4-[[5-Ethyl-4-(2-propynylamino)-2-pyrimidinyl]amino]-benzenesulfonamide

66	 The chemical structure shows a pyrimidine ring with a methyl group at position 6 and an amino group at position 2. This amino group is linked to a 4-iodophenyl ring, which is further substituted with an acetyl group at the para position. The pyrimidine ring also has a (2R)-1-hydroxy-3-methyl-2-butylamino group at position 4.	1-[4-[(5-Iodo-4-((2R)-1-hydroxy-3-methyl-2-butylamino)-2-pyrimidinyl)amino]phenyl]-ethanone
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No.	Structure	Name
68		1-[4-[(5-Ethyl-4-((2R)-1-hydroxy-3-methyl-2-butylamino)-2-pyrimidinyl)amino]phenyl]-ethanone
72		4-[[5-Bromo-4-(2-(2-oxo-imidazolin-1-yl)ethylamine)-2-pyrimidinyl]amino]-benzenesulfonamide
73		4-[[5-Bromo-4-(2,2,3,3,3-pentafluoropropoxy)-2-pyrimidinyl]amino]-benzenesulfonamide
75		4-[[5-Bromo-4-(1,3-bisacetoxy-2-propyloxy)-2-pyrimidinyl]amino]-benzenesulfonamide
76		4-[[5-Bromo-4-(1,3-dihydroxy-2-propyloxy)-2-pyrimidinyl]amino]-benzenesulfonamide
79		N-[(5-Bromo-2-(4-sulfamoylphenyl)amino-pyrimidin-4-yl)-L-alanine amide
83		1-[4-[(5-Bromo-4-(2-propynylamino)-2-pyrimidinyl)amino]phenyl]-ethanol

The following compounds were produced analogously to the described synthesis processes according to Diagram 1 or 2:

All NMR spectra are measured in the indicated solvent or in DMSO.

				
Bsp.-Nr.	37	38	39	5
6-H	8.34 (s,1H)	8.39 (s,1H)	8.30 (s,1H)	8.00 (s,1H)
2CH	12.88 (sb,1H)	9.28 (s,1H)	7.74 (s,1H)	7.52 (d,2H)
	8.07 (s,1H)	8.79 (s,1H)	7.44 (d,1H)	6.65 (d,2H)
	7.93 (s,1H)	7.70 (d,1H)	7.22 (d,1H)	
	7.41 (d,1H)	8.04 (d,1H)	3.98 (t,2H)	
	7.56		3.13 (t,2H)	
4CH	(dd,1H)	4.19 (d,2H)	2.99 (s,3H)	
		3.22 (sb,1H)	4.16 (d,2H)	4.09 (d,2H)
NH	4.15	10.43(sb,1H)	3.28 (sb,1H)	3.09 (s,1H)
	(dd,2H)	8.45 (sb,1H)	10.6(1H)	9.00 (s,1H)
	3.18 (t,1H)		8.75 (1H)	8.96 (s,1H)
	9.30			7.31 (t,1H)
	(sb,1H)			
	7.39			
	(tb,1H)			
Chro- mato- graphie	EA + 0.5% TEA 10%	- 36%	Kristallisiert MeOH 73%	- 20%
Aus- beute				
Schmp.	231°C	>235°C	237°C	157°C

[Key to the following tables and diagrams:]

Bsp.-Nr. [Beispiel Nr.] = Example No.

Chromatographie Ausbeute = Chromatography yield

Schmp. = Melting point

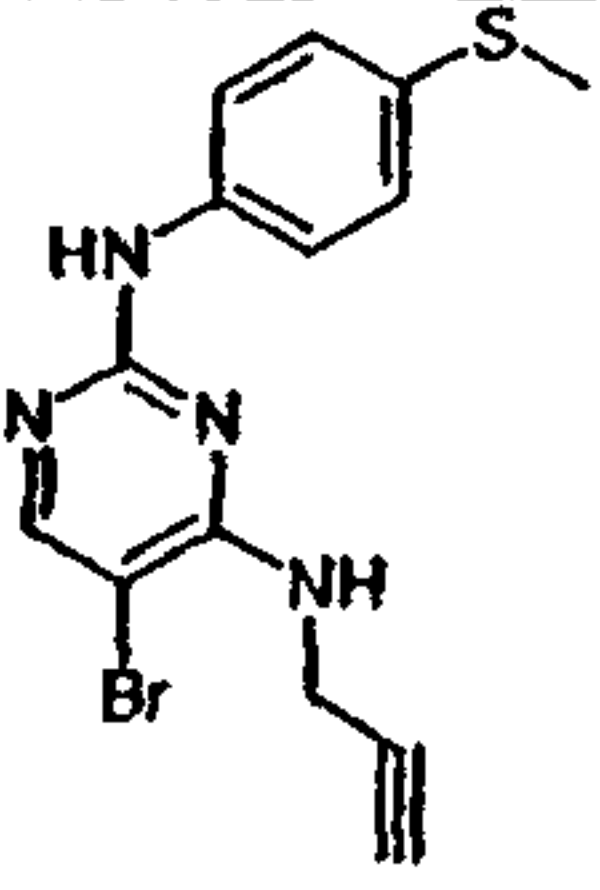
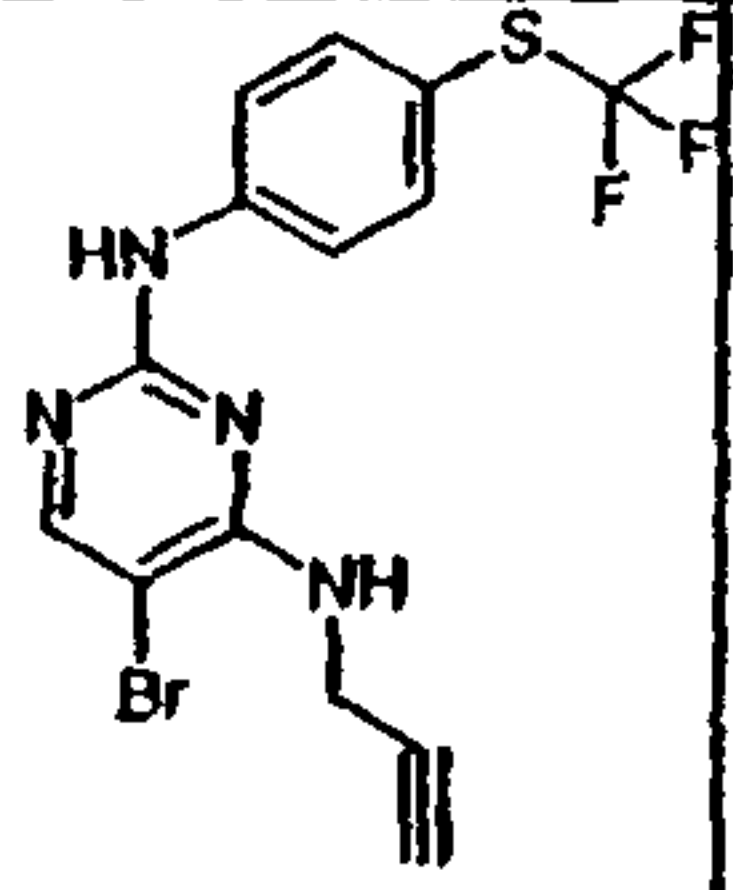
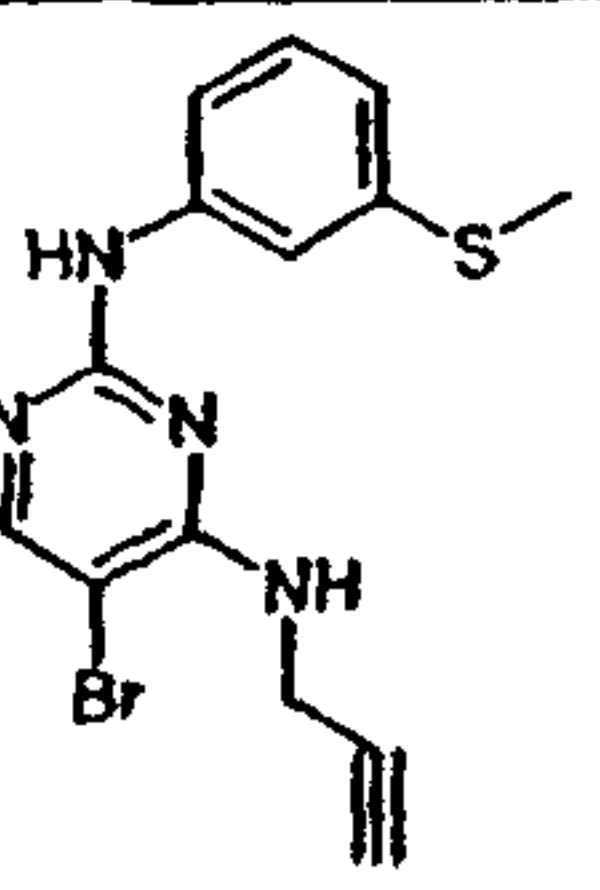
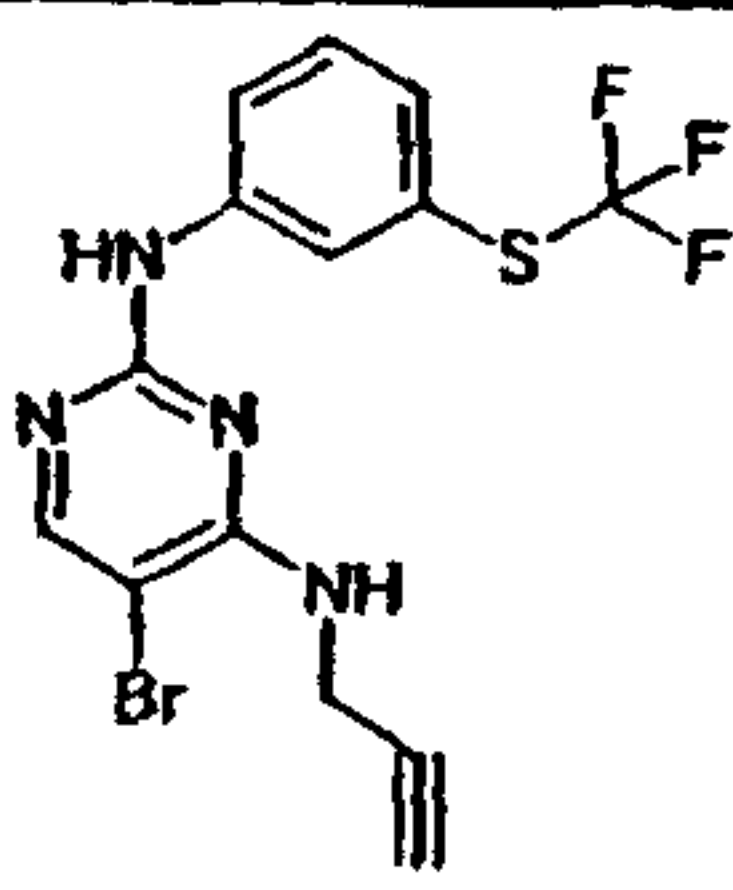
Kristallisiert = Crystallized

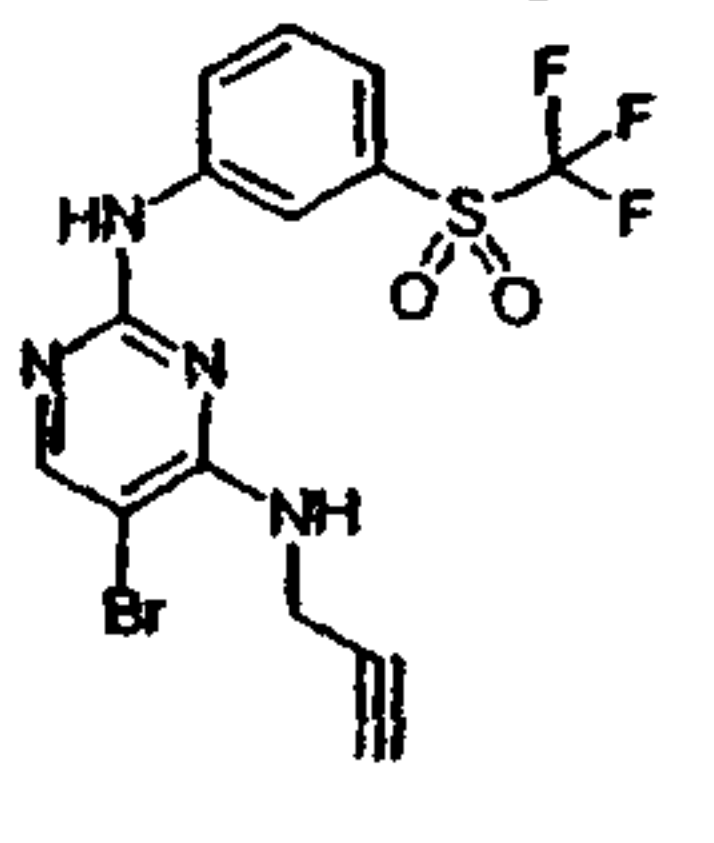
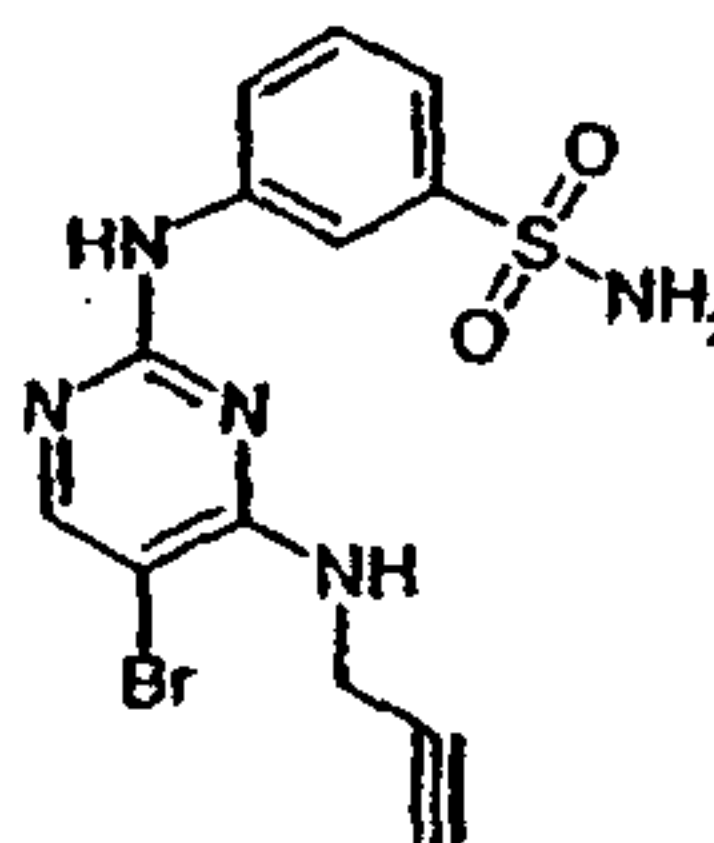
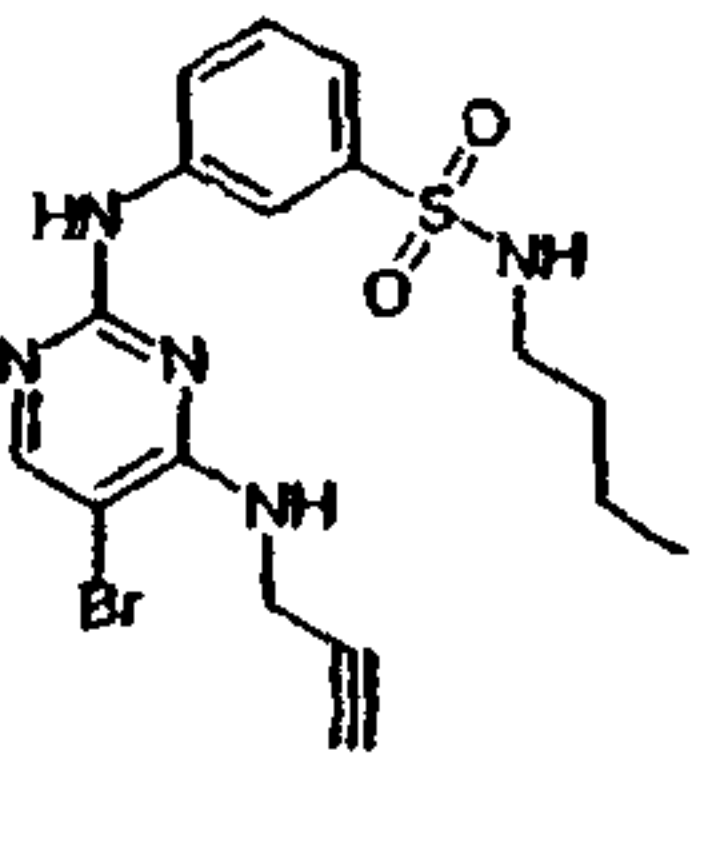
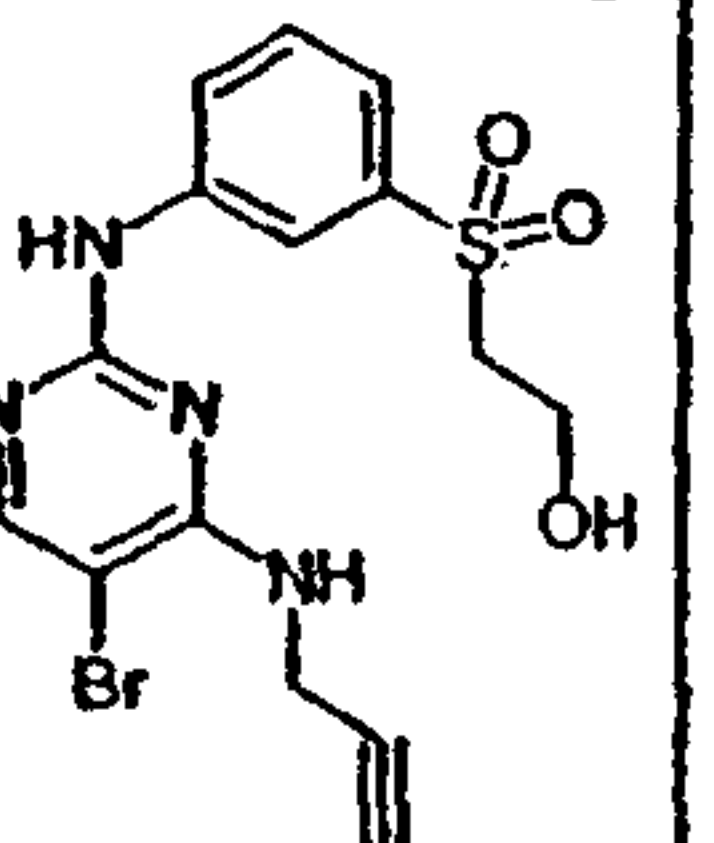
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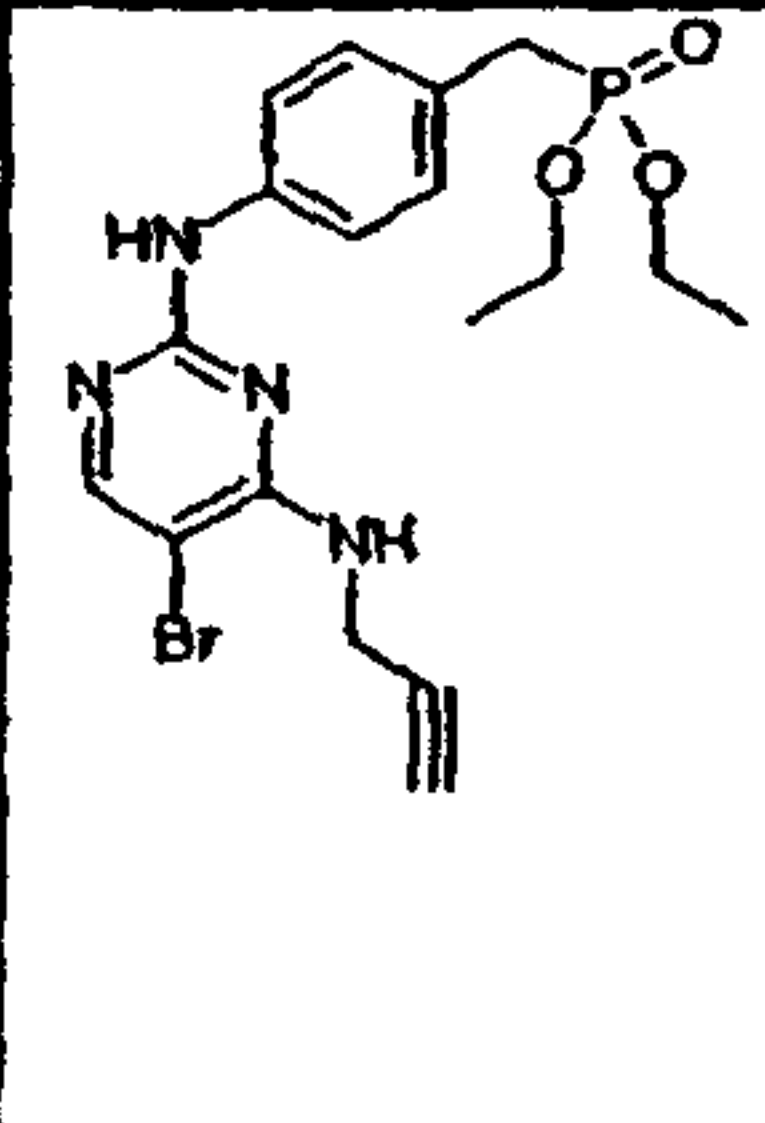
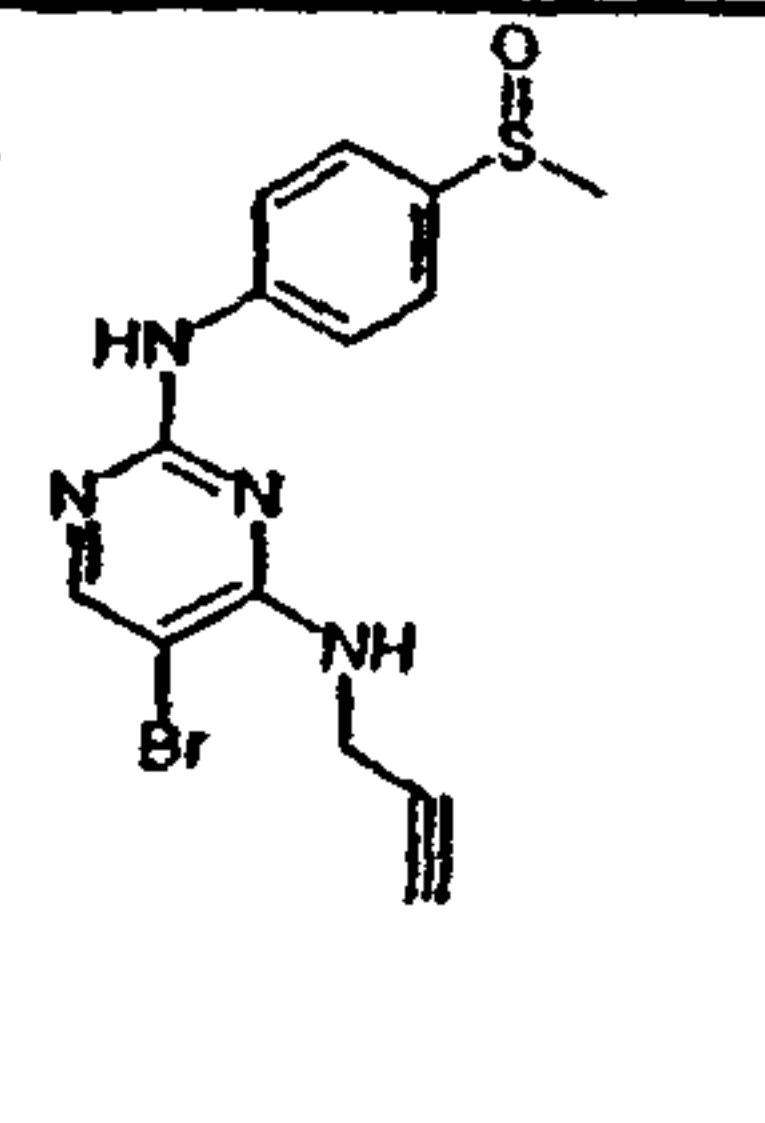
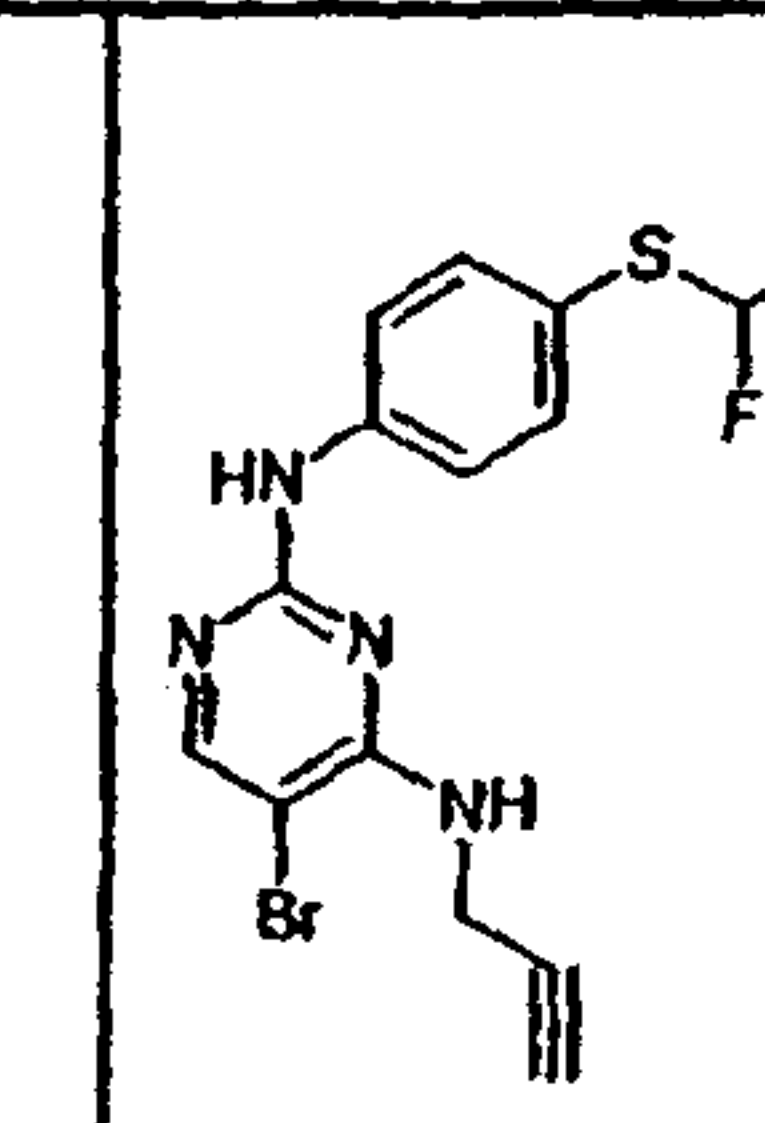
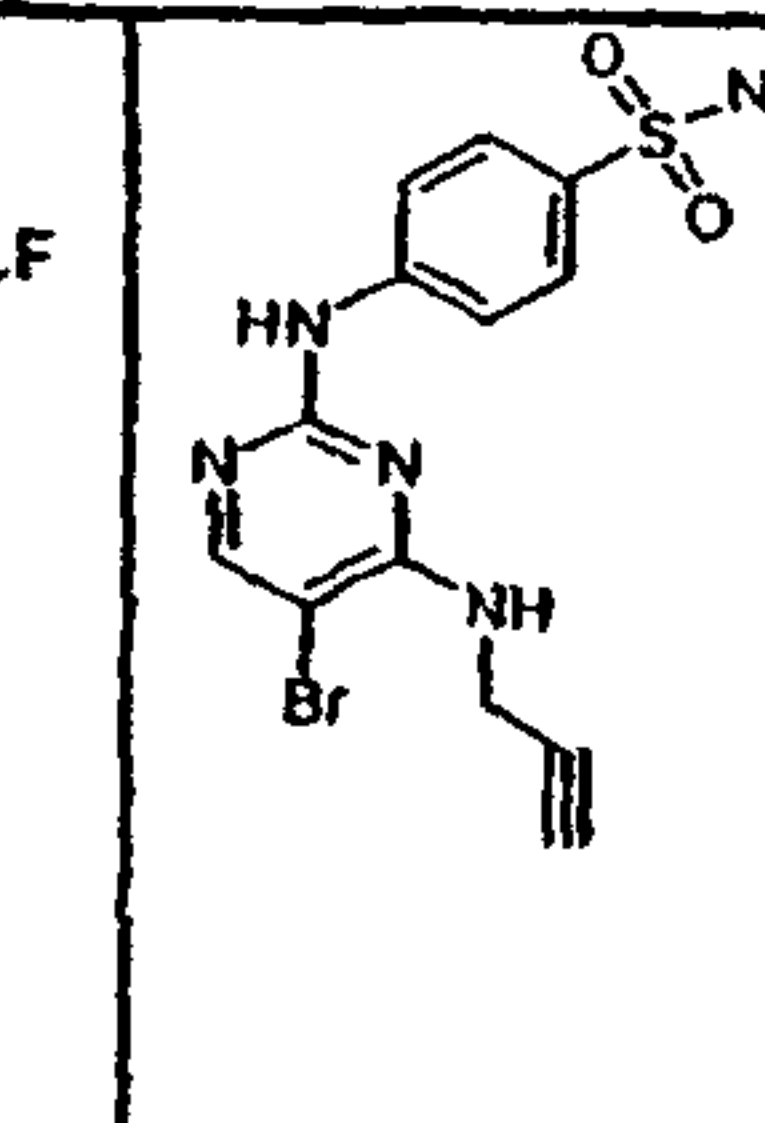
krist. Wasser = Crystallized water

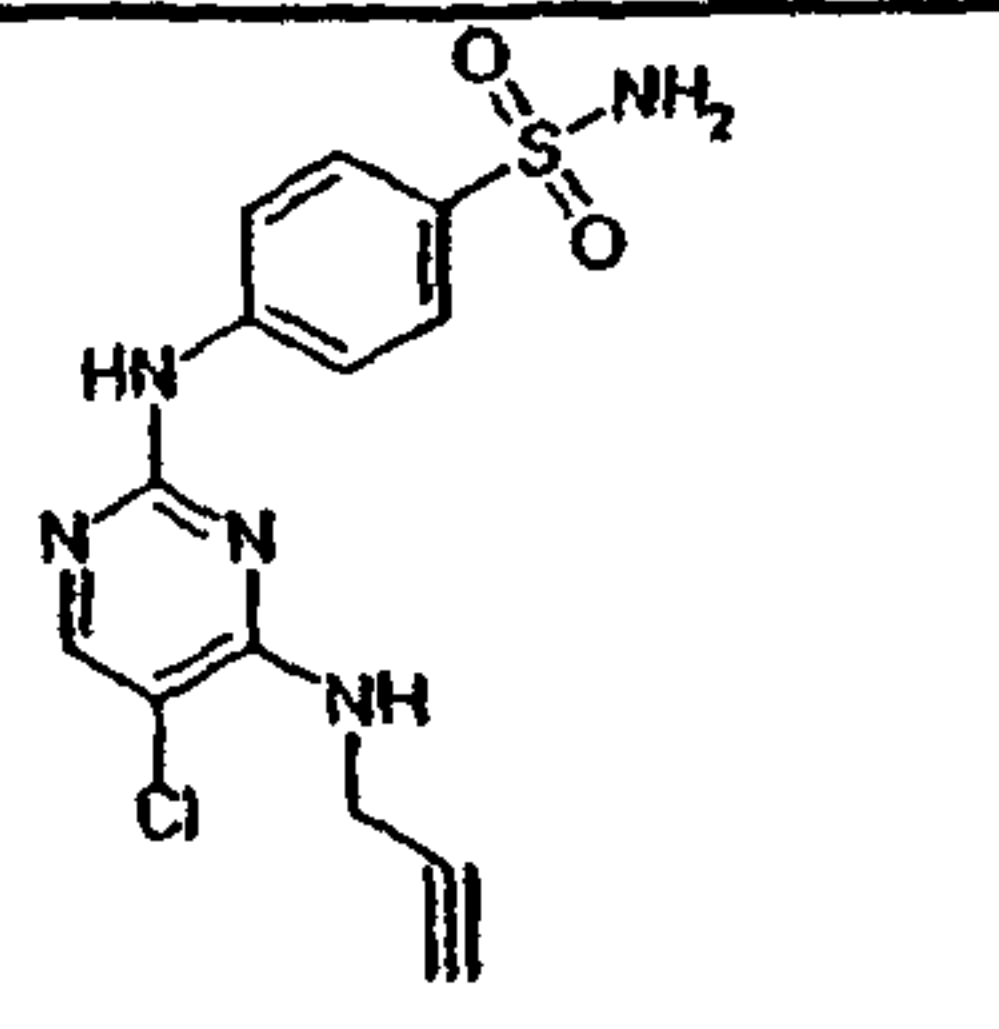
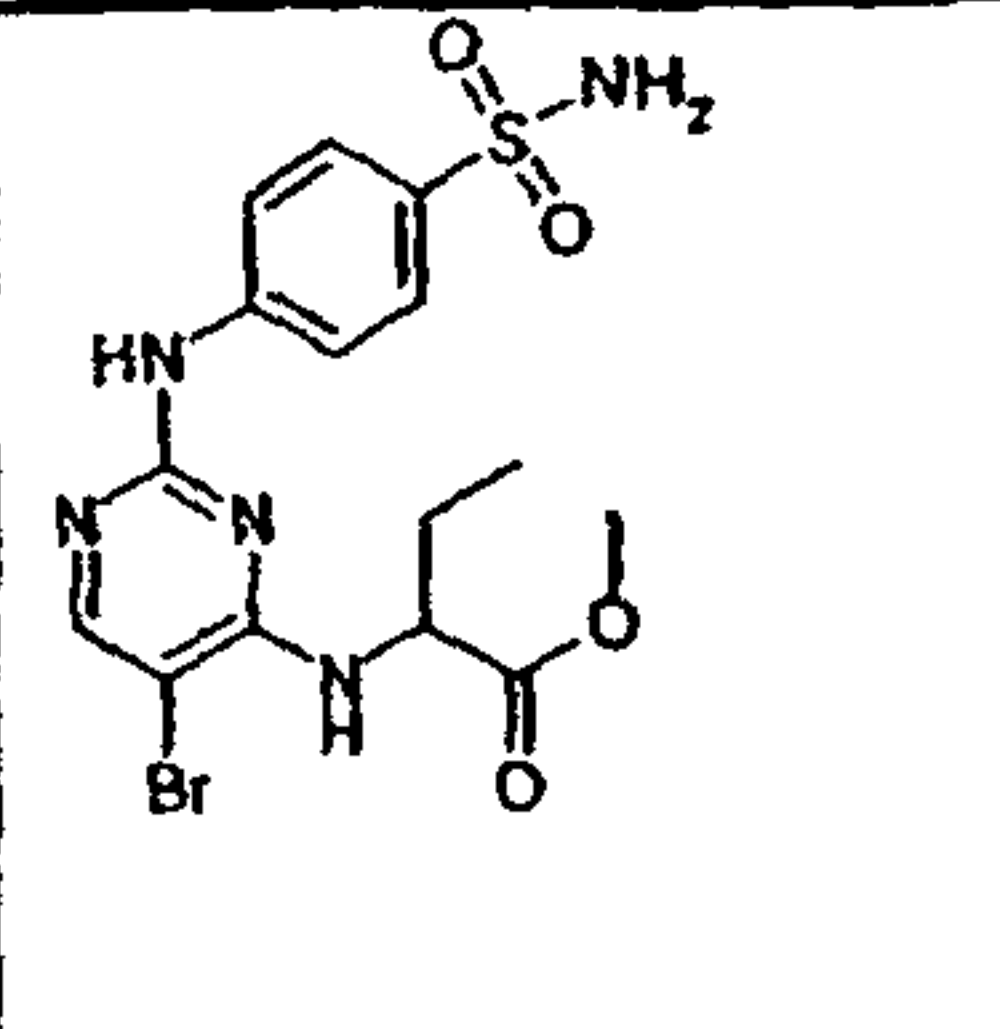
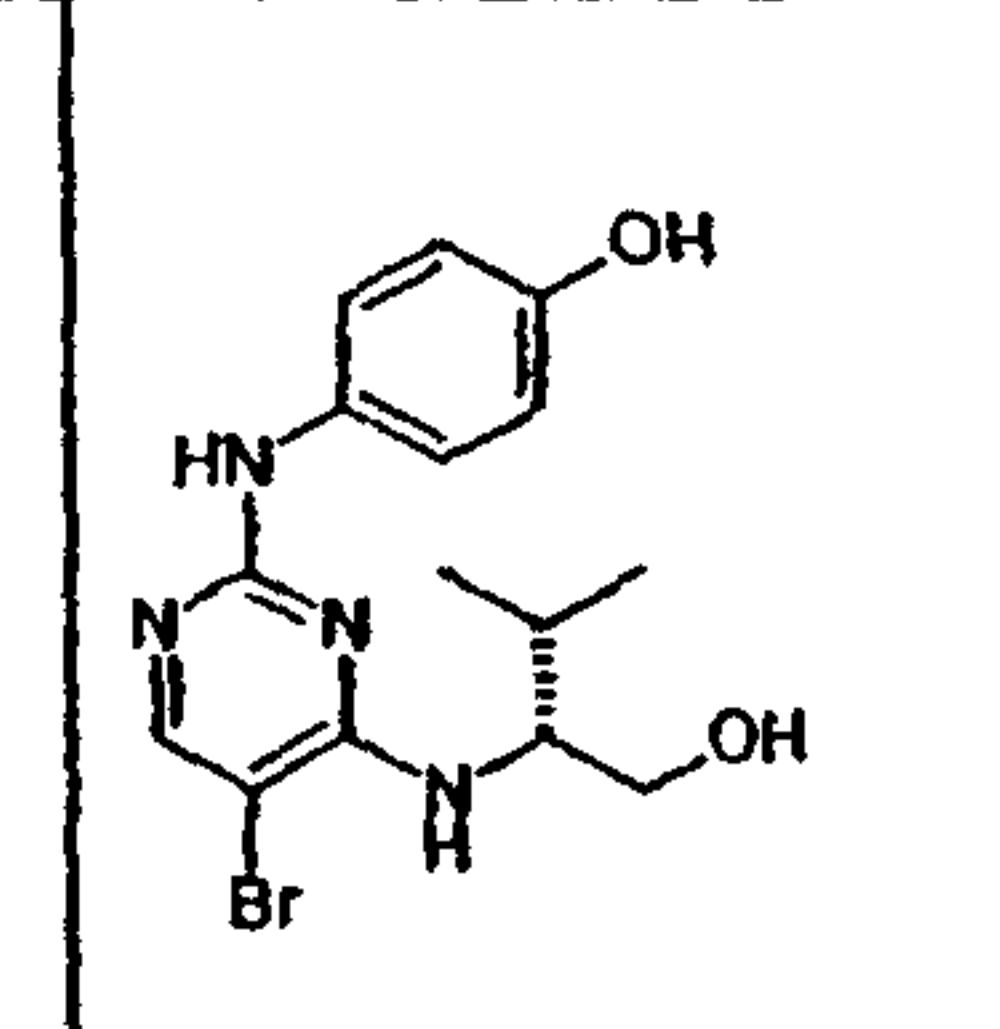
Verbindung = Compound

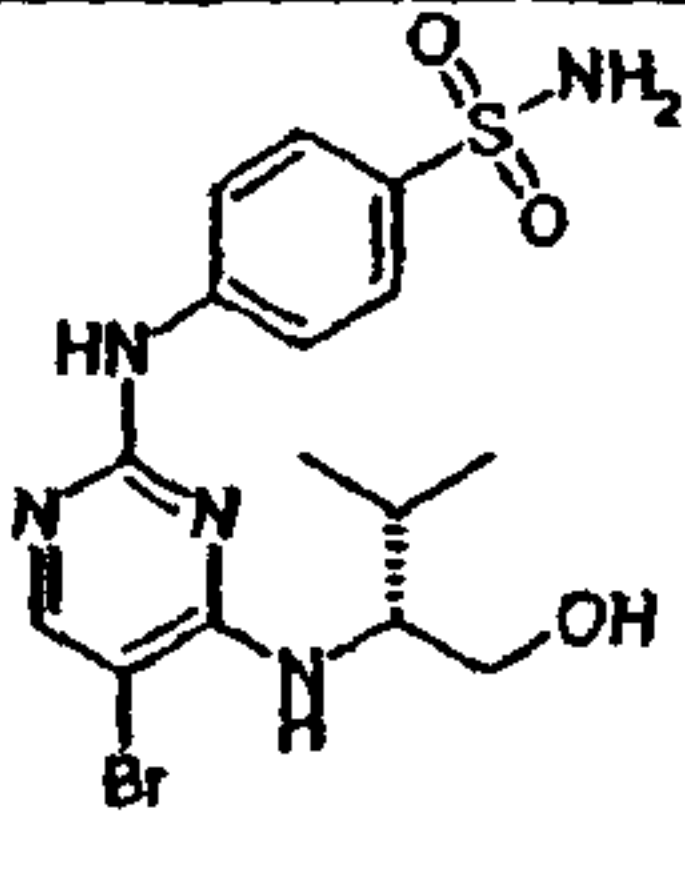
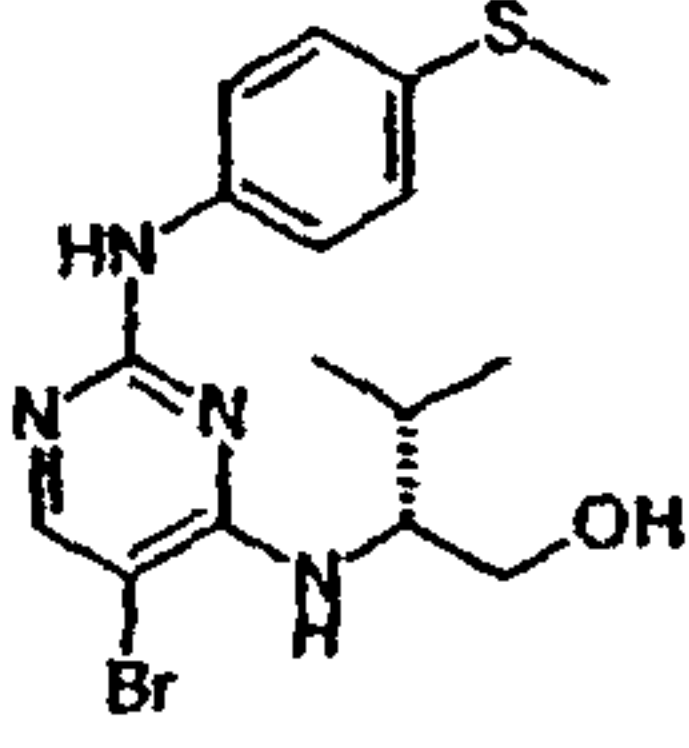
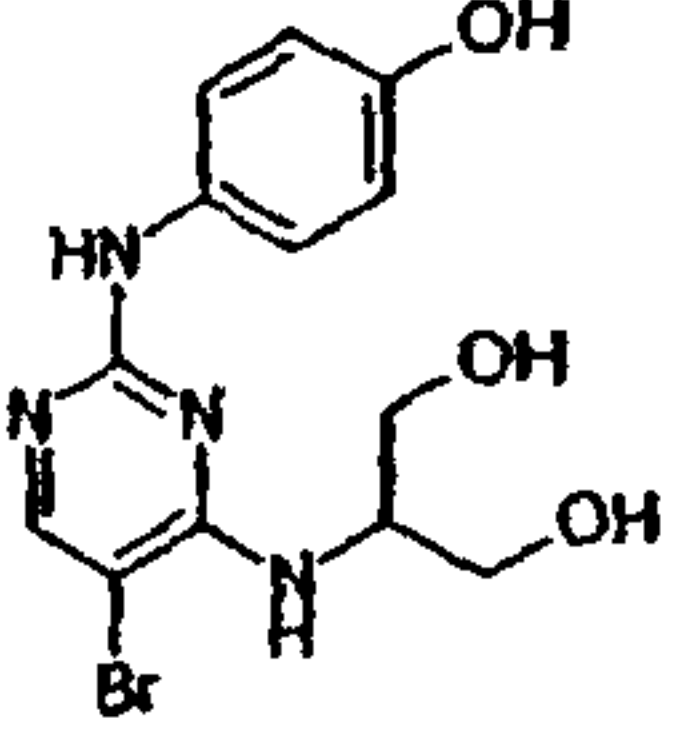
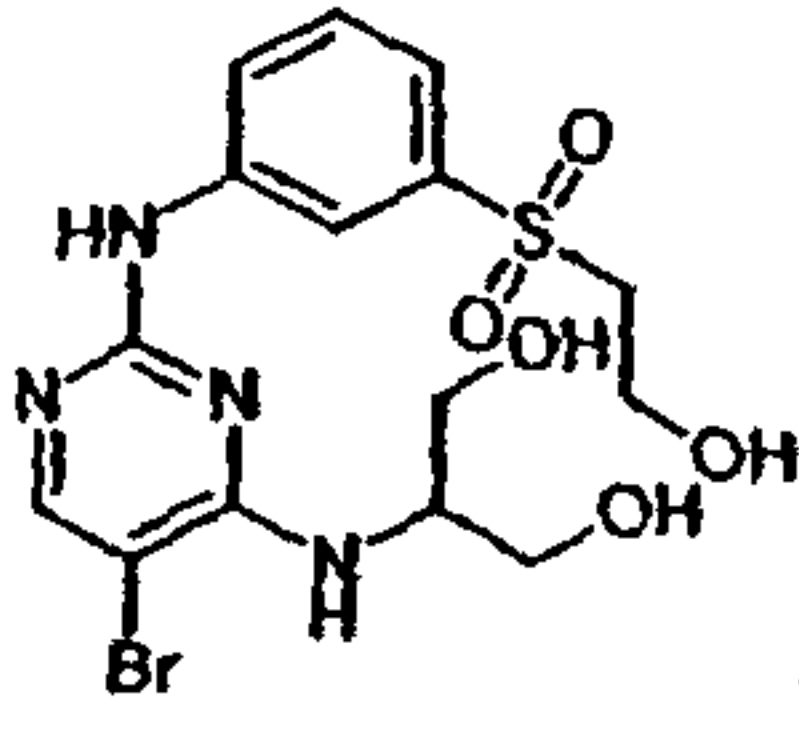
Hitze = Heat

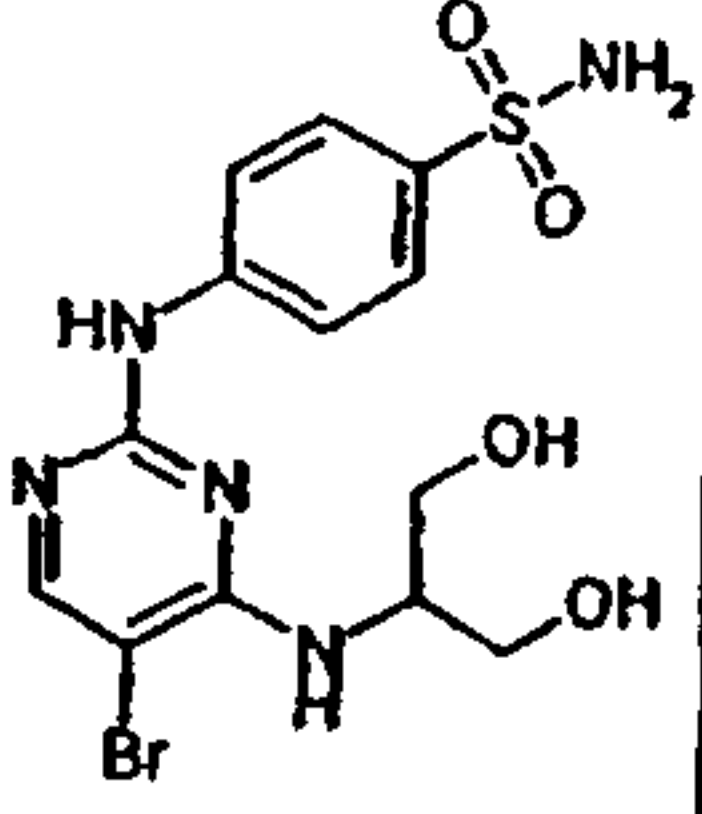
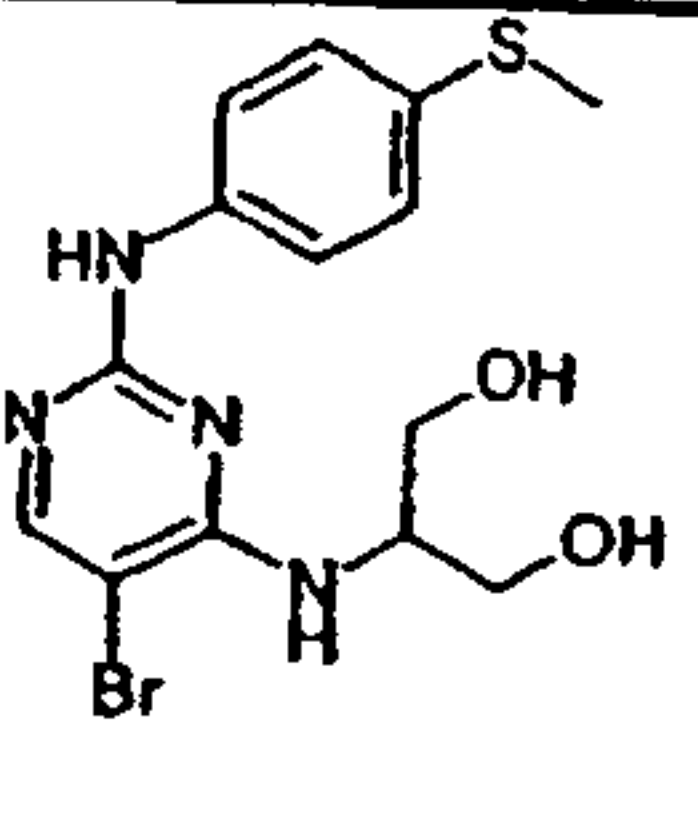
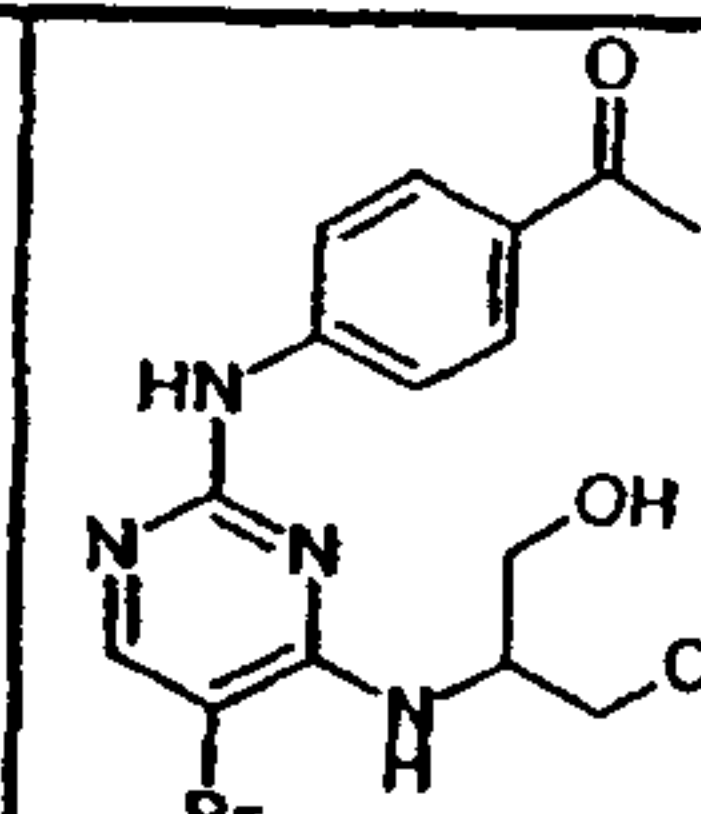
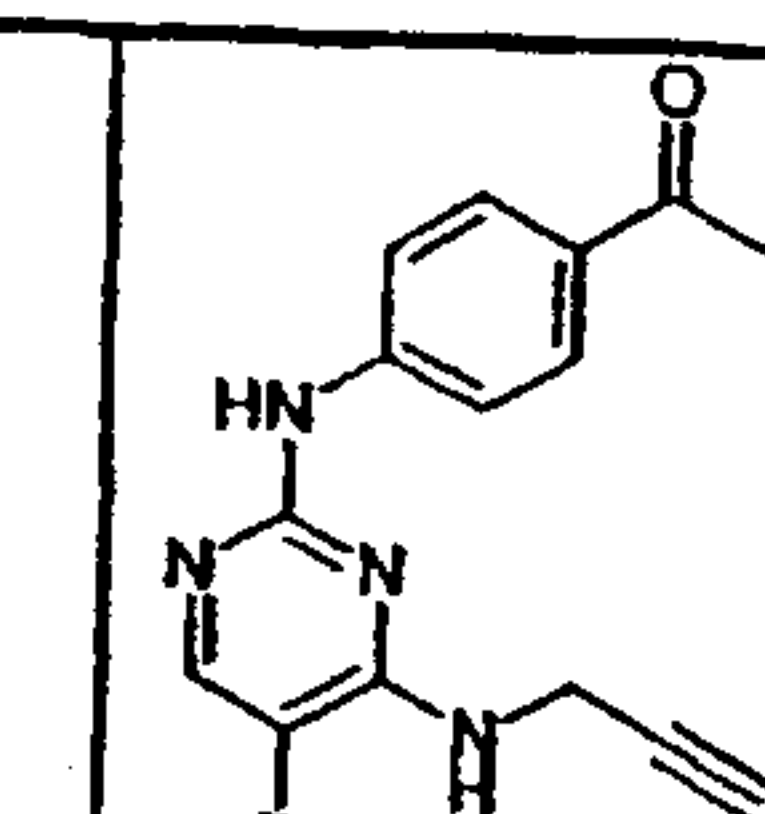
				
Beispiel Nr.	16	24	26	35
6-H	8.80 (s,1H)	8.30 (s,1H)	8.18 (s,1H)	8.14 (s,1H)
2CH	7.67 (d,2H)	7.94 (d,2H)	7.67 (s,1H)	8.28 (s,1H)
	7.27 (d,2H)	7.63 (d,2H)	7.54 (d,1H)	7.98 (d,1H)
	2.47 (s,3H)		7.24 (t,1H)	7.41 (t,1H)
4CH	4.17 (dd,2H)	4.17 (dd,2H)	6.92 (d,1H)	7.25 (d,1H)
	3.75 (t,1H)	3.18 (t,1H)	4.20 (dd,2H)	4.14 (dd,2H)
NH	10.55	10.45	3.12 (sb,1H)	3.04 (sb,1H)
	(sb,1H)	(sb,1H)	9.78 (sb,1H)	9.58 (sb,1H)
	8.68 (sb,1H)	8.22 (sb,1H)	7.95 (sb,1H)	7.46 (sb,1H)
Chrom.	-	-	-	-
Aus- beute	94%	86%	73%	69%
Schmp.	232-234°C	160°C	194°C	143°C

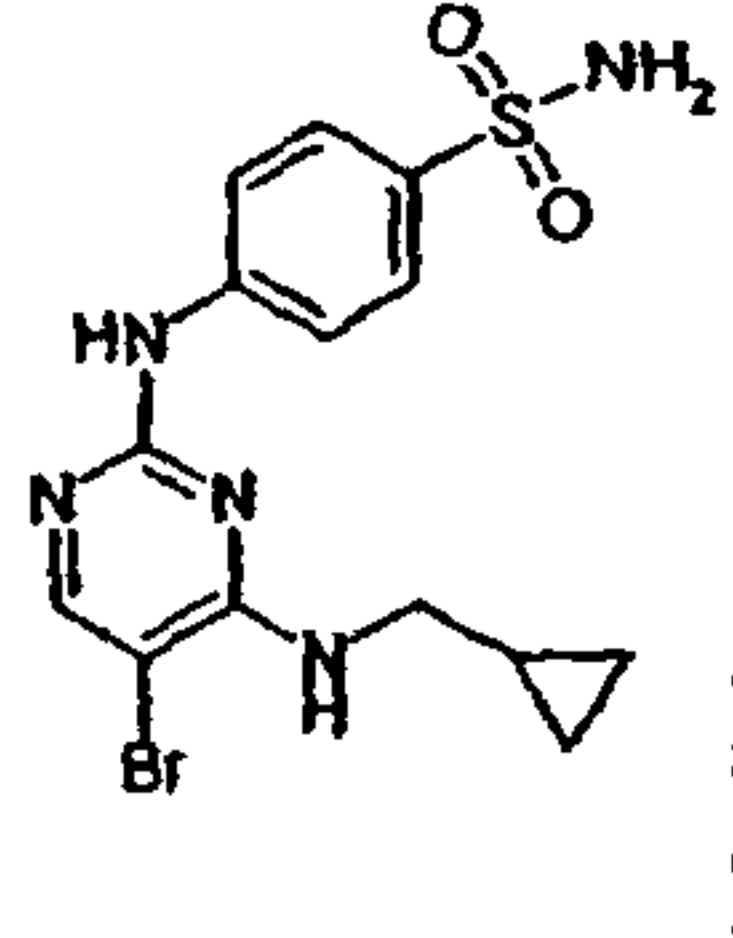
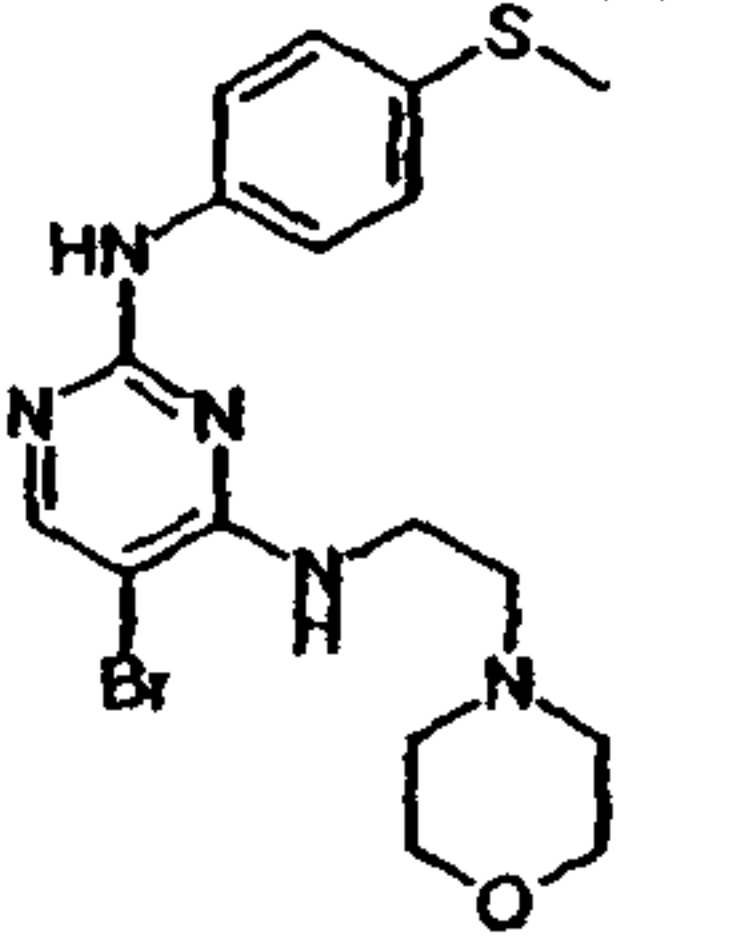
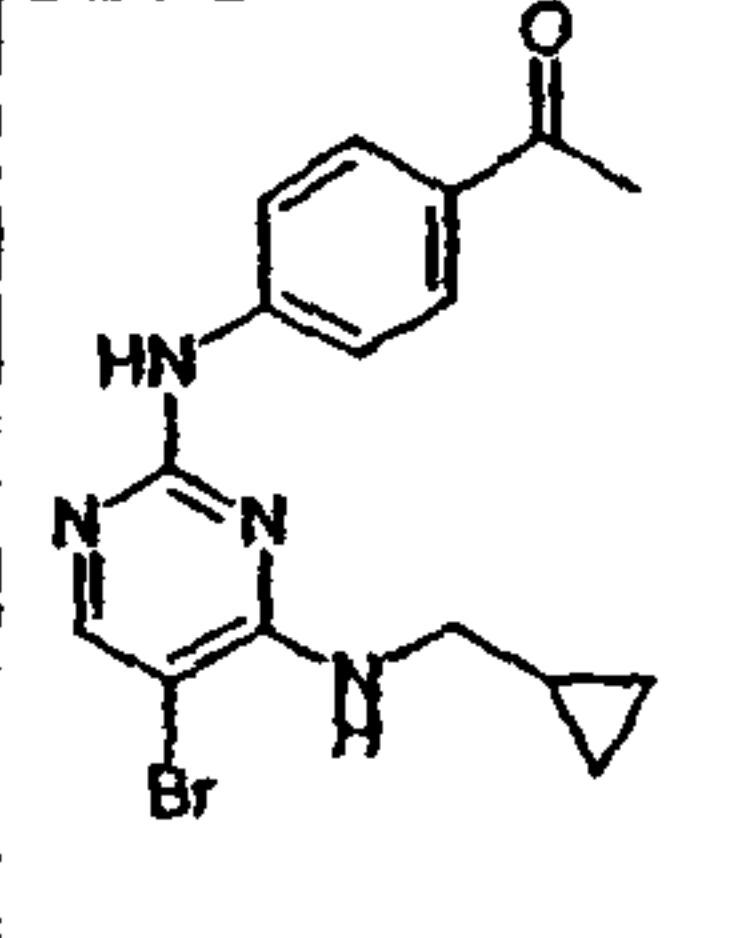
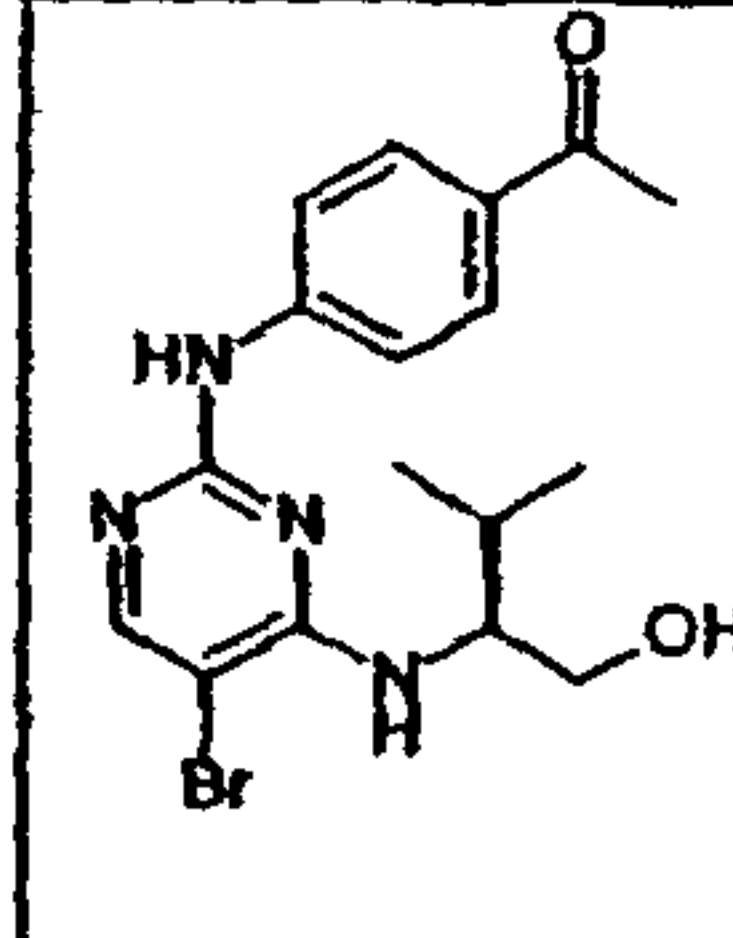
				
Beispiel Nr.	27	36	34	21
6-H 2CH	8.18 (s,1H) 8.73 (s,1H) 7.62 (d,1H) 7.72 (t,1H) 8.31 (d,1H)	8.26 (s,1H) 8.12 (s,1H) 7.35- 7.55(m,3H) 8.06 (d,1H)	8.25 (s,1H) 8.16 (s,1H) 7.43 (d,1H) 7.52 (t,1H) 8.01 (d,1H) 2.78 (m,2H) 1.35 (mc,2H) 1.24 (mc,2H) 0.80 (t,3H)	8.17 (s,1H) 8.74 (s,1H) 7.43 (d,1H) 7.52 (t,1H) 8.08 (d,1H) 3.43 (t,2H) 3.70 (t,2H)
4CH	4.18 (dd,2H) 3.06 (t,1H)	4.21 (d,2H)	4.21 (d,2H) 3.09 (sb,1H)	4.20 (dd,2H) 3.08 (t,1H)
NH	10.02 (s,1H) 7.49 (sb,1H)	3.09 (sb,1H) 9.68 (sb,1H)	10.3 (sb,1H) 8.13 (sb,1H)	9.79 (s,1H) 7.55 (tb,1H)
OH		7.30 (sb,2H)		4.90 (sb,1H)
Chrom.	-	krist.EtOH	-	-
Aus- beute	69%	64%	87%	59%
Schmp.	144°C	219°C	220°C	192.5- 193.5°C

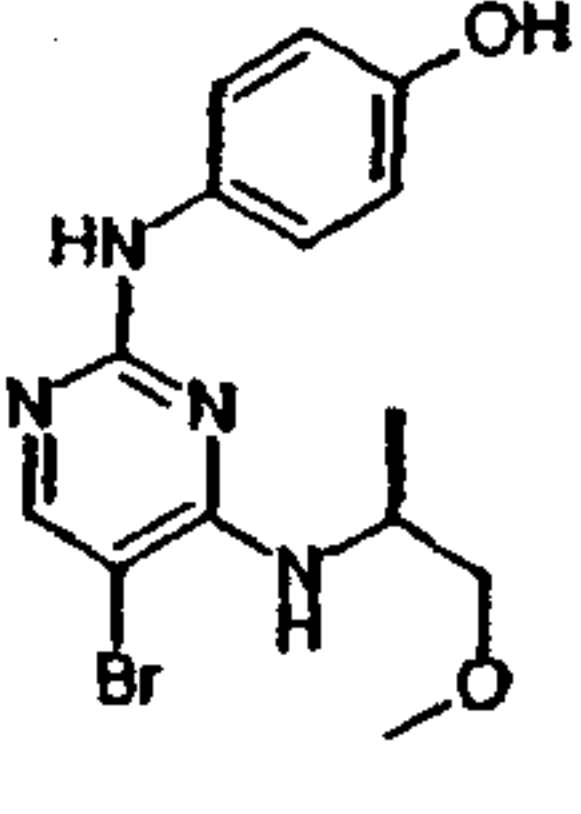
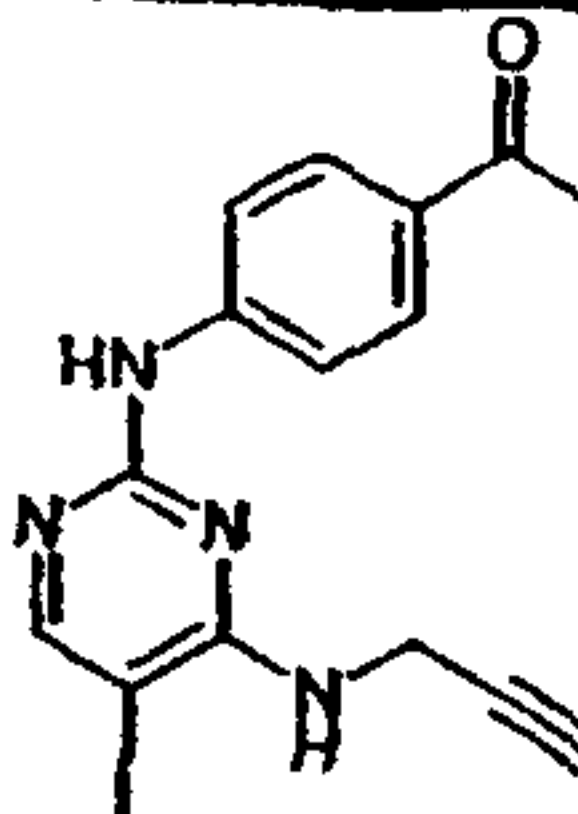
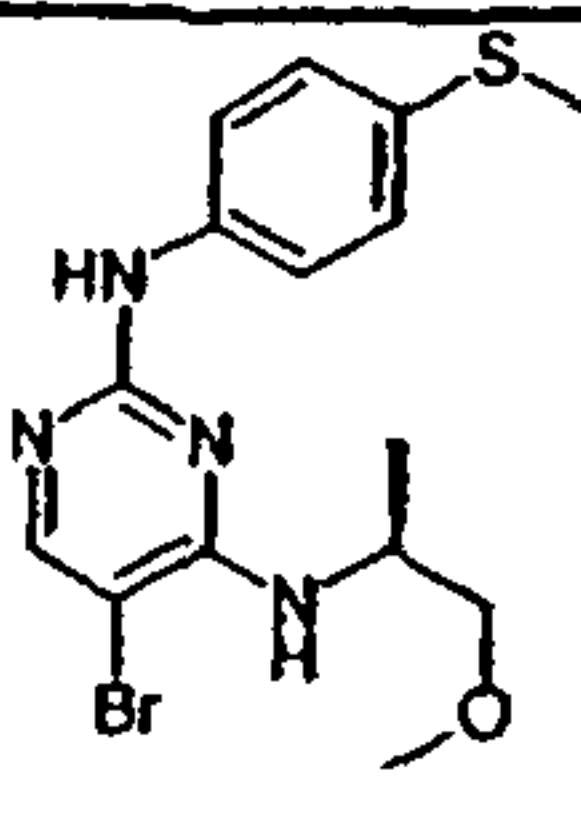
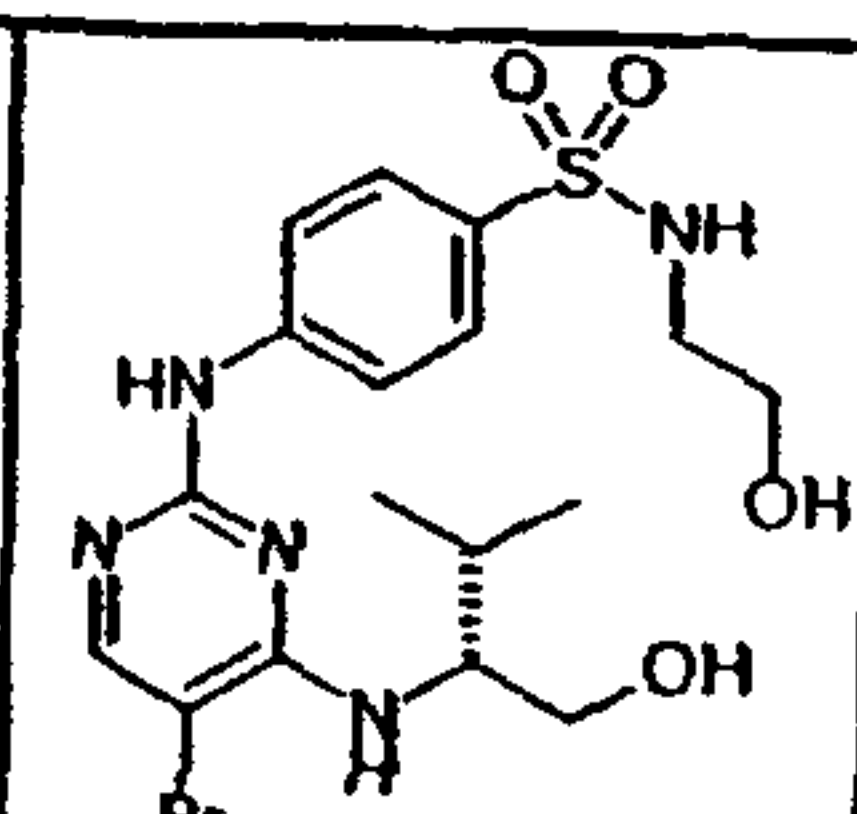
				
Beispiel Nr.	31	25	23	11
6-H	8.25 (s,1H)	8.14 (s,1H)	8.25 (s,1H)	8.29 (s,1H)
2CH	7.65 (d,2H)	8.01 (d,2H)	7.86 (d,2H)	7.95 (d,2H)
	7.24 (d,2H)	7.56 (d,2H)	7.51 (d,2H)	7.78 (d,2H)
	3.19	2.70 (s,3H)	7.38	
	(d,21.3Hz,2 H)		(t,56.8Hz,1H)	
4CH	3.95	4.15 (dd,2H)	4.18 (m,2H)	4.19 (d,2H)
	(mc,4H)	3.14 (t,1H)	3.16 (sb,1H)	3.18 (sb,1H)
NH	1.20 (t,6H)	9.69 (sb,1H)	10.24 (sb,1H)	10.40
	4.17 (sb,2H)	7.55 (tb,1H)	8.17 (sb,1H)	(sb,1H)
	3.15 (sb,1H)			8.24 (sb,1H)
	10.19			7.15 (sb,2H)
	(sb,1H)			
	8.34(sb,1H)			
Chrom.	EA krist.	DCM/MeOH	-	krist.
Aus- beute	H/DIPE 23%	95:5 25%	85%	DIPE/EtOH 17%
Schmp.	198°C	217-218°C	>235°C	>235°C

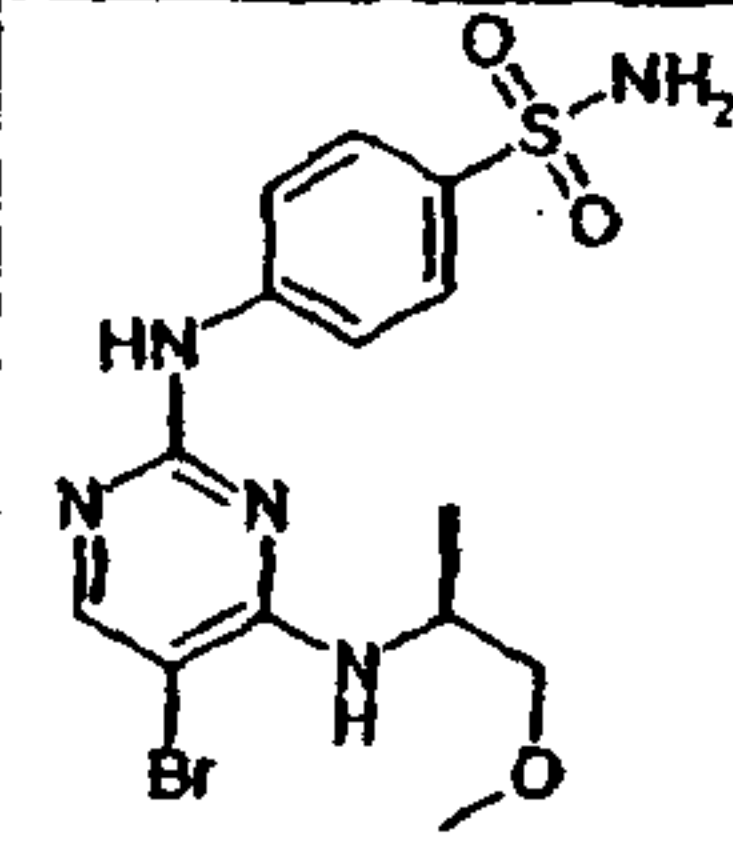
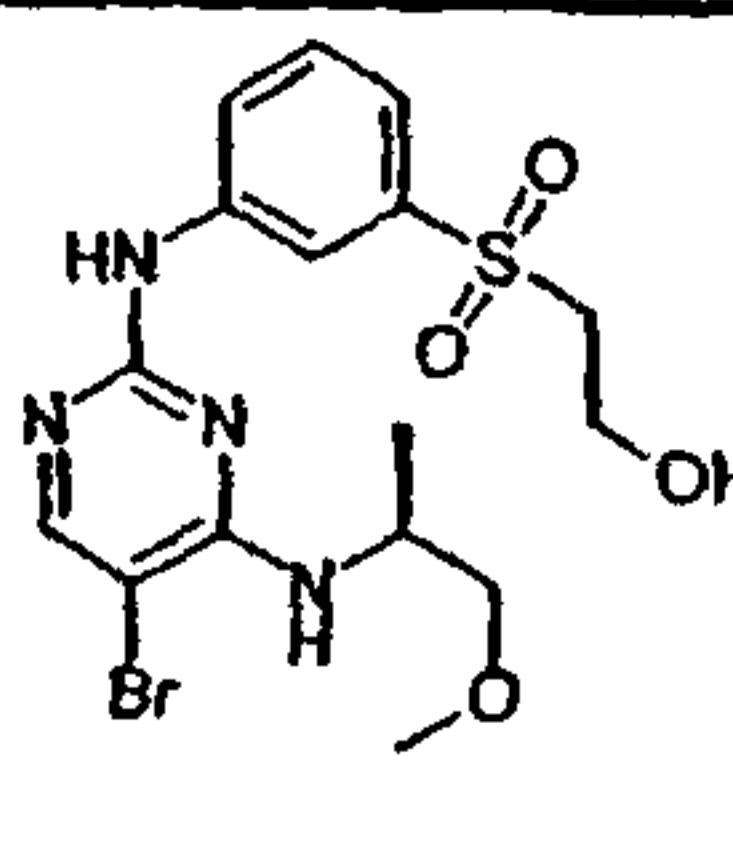
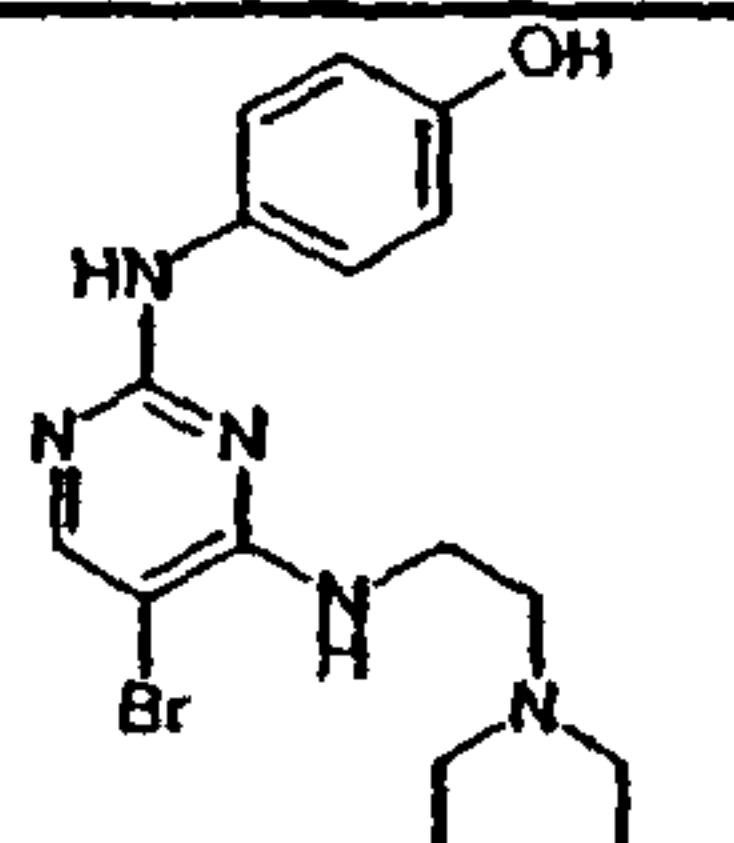
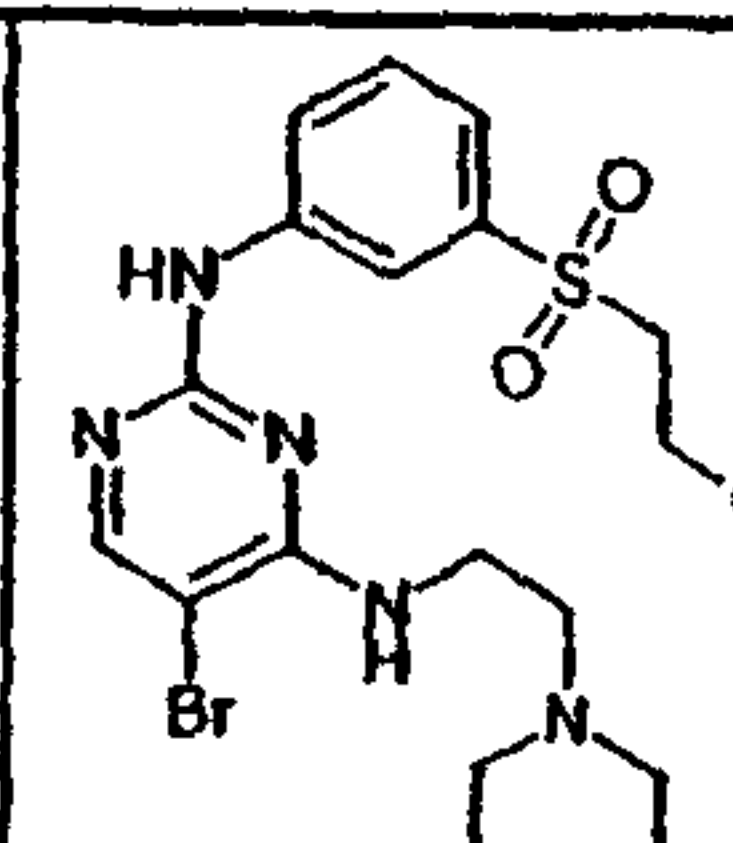
			
Beispiel Nr.	44	45	4
6-H 2CH	8.34 (s,1H) 7.93 (d,2H) 7.79 (d,2H)	8.34 (s,1H) 7.74 (mc,4H)	8.23 n(sb,1H) 7.39 (d,2H) 6.79 (d,2H)
4CH	4.20 (sb,2H) 3.31 (sb,1H)	4.55 (q,1H) 1.98 (dq,2H) 0.94 (t,3H)	3.52-3.71 (2H) 3.97 (mc,1H) 1.96 (mc,1H)
NH	11.03 (sb,1H) 9.04 (sb,1H) 7.34 (sb,2H)	3.61 (s,3H) 10.60 (s,1H) 7.97 (d,1H) 7.31 (db,2H)	0.91 (d,3H) 0.85 (d,3H) 10.35 (sb,1H) 7.76 (sb,1H)
Chrom. Aus- beute	krist. EtOH 27%	krist. EtOH 48%	- 52%
Schmp.	252°C	235°C	242-243°C

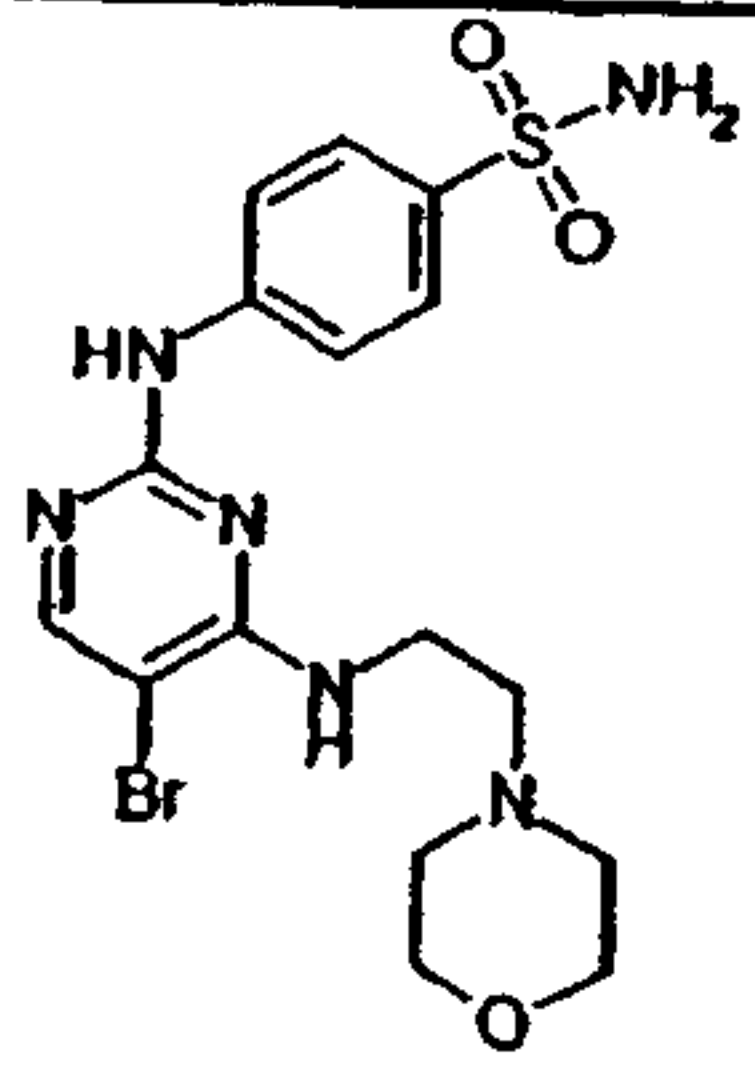
				
Beispiel Nr.	10	15	3	19
6-H 2H	8.27 (s, 1H) 7.80 (mc, 4H)	8.17 (s, 1H) 7.60 (d, 2H) 7.24 (d, 2H) 2.44 (s, 3H)	7.97 (s, 1H) 7.44 (d, 2H) 6.67 (d, 2H)	8.20-8.35 (2H) 7.90 (sb, 1H) 7.50-7.64 (2H) 3.46 (t, 2H) 3.70 (t, 2H)
4H	3.66 (mc, 2H) n. obs. 2.04	3.5-3.7 (2H) 40.1 (mc, 1H) 1.98 (mc, 1H) 0.94 (d, 3H) 0.90 (d, 3H)	3.50-3.65 (4H) 4.12 (mc, 1H)	3.56-3.66 (4H) 4.28 (mc, 1H)
NH OH	(mc, 1H) 0.97 (d, 3H) 0.94 (d, 3H) 10.40 (sb, 1H) 7.18 (sb, 2H) n. obs.	9.95 (sb, 1H) 6.96 (sb, 1H) ca. 4, sehr breit	8.98 (sb, 1H) 5.97 (db, 1H) 8.90 (sb, 1H) 4.80 (tb, 2H)	NH and OH sind sehr breit
Chrom.	-	-	-	Kristallisiert Wasser
Aus- beute	43%	27%	76%	52%
Schmp.	252-253°C	192-193°C	257-258°C	209-210°C

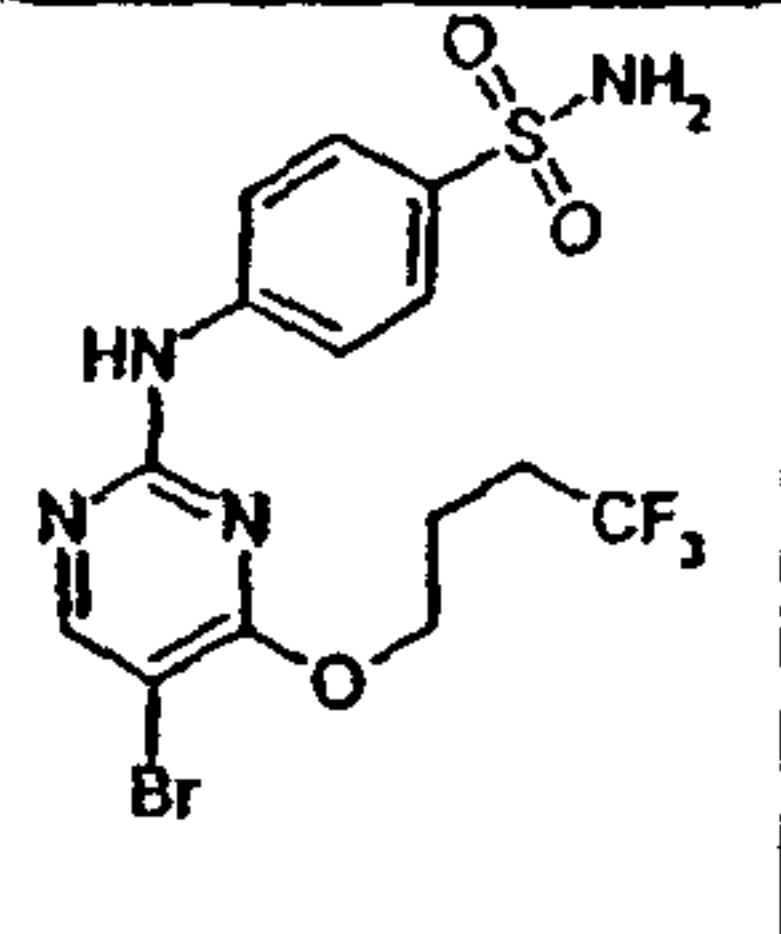
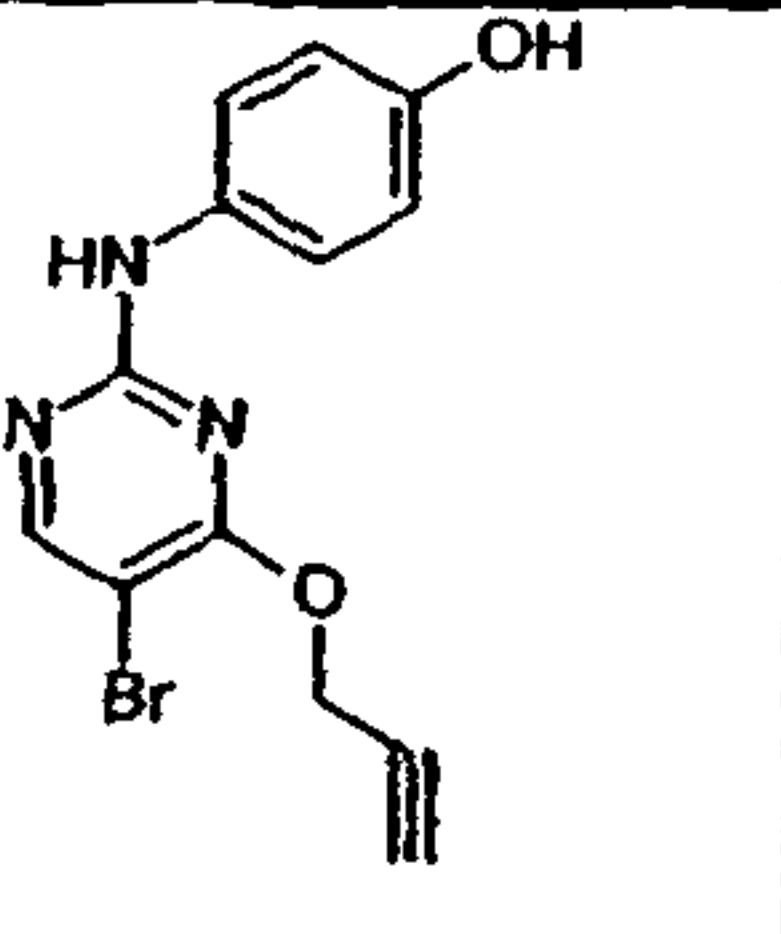
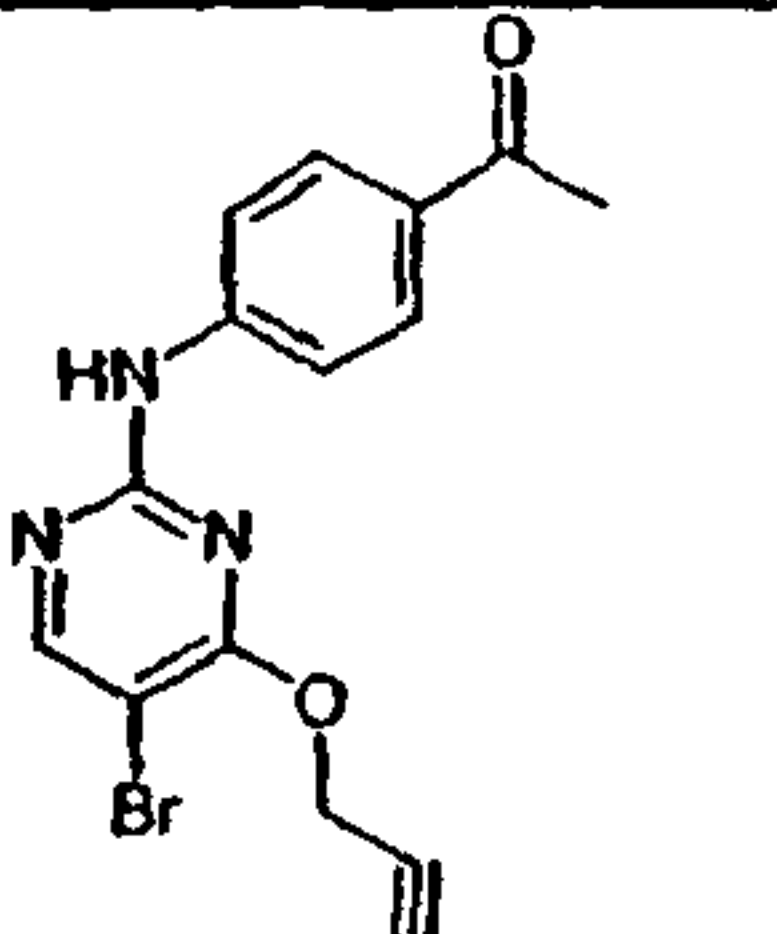
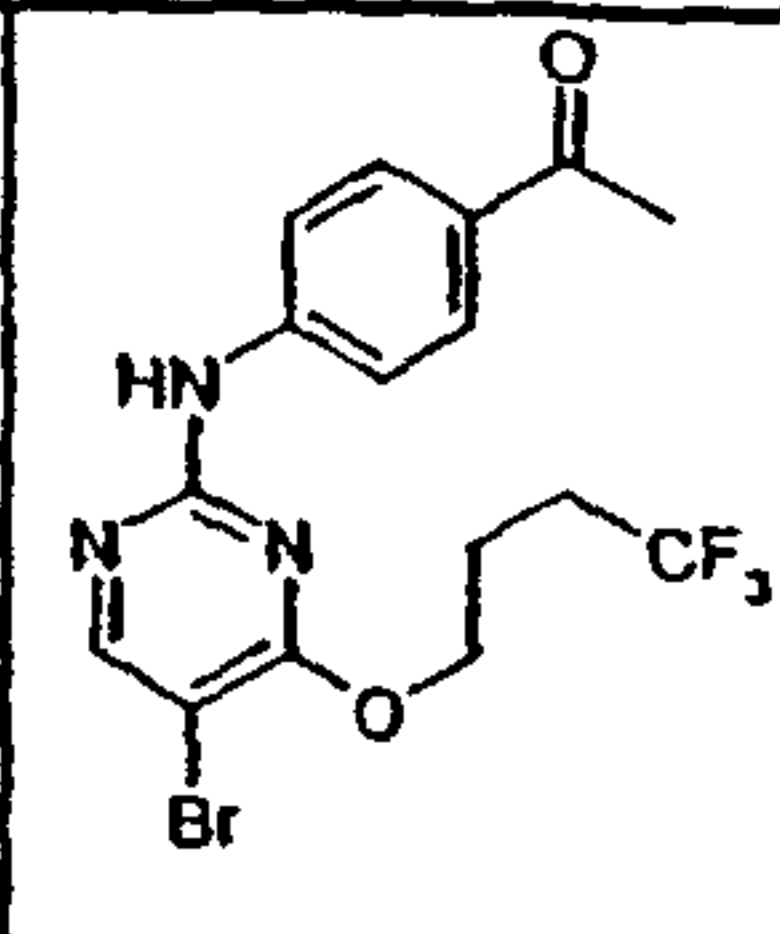
				
Beispiel Nr.	9	14	55	50
6-H 2H	8.30 (s, 1H) 7.82 (mc, 4H)	8.30 (s, 1H) 7.55 (d, 2H) 7.30 (d, 2H) 2.48 (s, 3H)	8.11 (s, 1H) 7.87 (s, 4H) 2.50 (s)	8.17 (s, 1H) 7.95 (d, 2H) 7.86 (d, 2H) 2.50 (s)
4H	3.63 (mc, 4H)	3.54-3.68 (4H) 4.24 (mc, 1H)	4.19 (mc, 1H) 3.61 (mc, 4H)	4.17 (dd, 2H) 3.13 (t, 1H)
NH OH	4.24 (mc, 1H) 10.59 (b, 1H) 7.2 (sb) 6.1 (sb)	10.63 (sb, 1H) 7.60 (sb, 1H) 4.4 (b)	9.73 (s, 1H) 6.20 (s, 1H) 4.88 (t, 2H)	9.81 (s, 1H) 7.58 (t, 1H)
Chrom. Aus- beute	Kristallisiert MeOH 24%	91%	Kristallisiert MeOH/DIPE 27%	- 56%
Schmp.	247-248°C	233-234°C	228-229°C	241°C

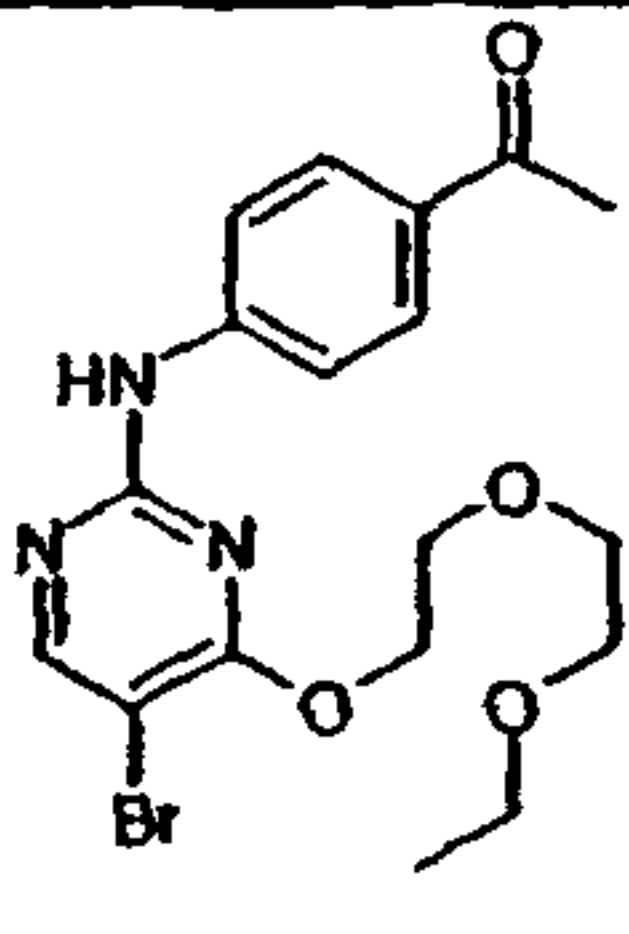
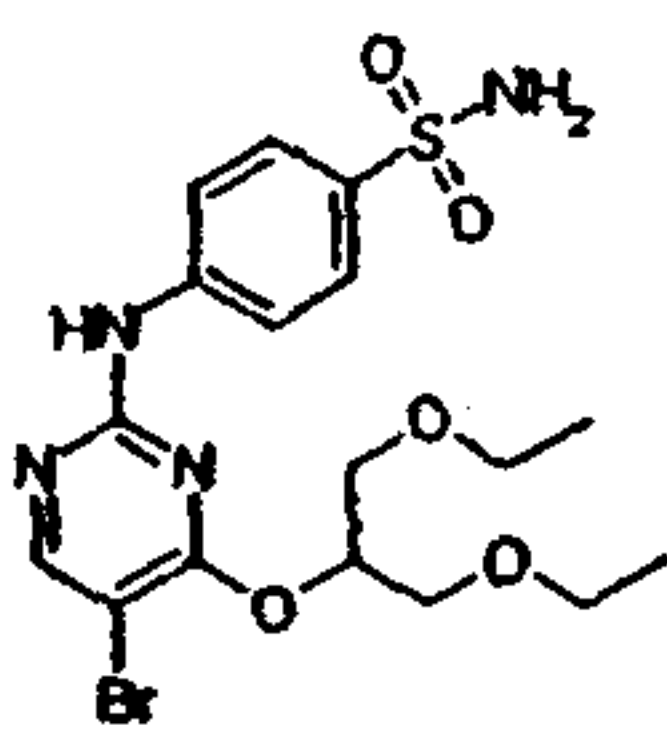
				
Beispiel Nr.	46	13	52	53
6-H 2H	8.07s,1H) 7.91 (d,2H) 7.69 (d,2H)	8.00 (s,1H) 7.68 (d,2H) 7.18 (d,2H)	8.09 (s,1H) 7.88 (s,4H)	8.11 (s,1H) 7.86 (s,4H) not obs.
4H	3.30 (t,2H) n.obs.(mc, 1 H) 0.45 (mc,2H)	3.54 (q,2H) 2.53 (t,2H) 2.40-2.45 (4H) 3.58 (t,4H)	3.32 (t,2H) 1.20 (mc,1H) 0.44 (mc,2H) 0.30 (mc,2H)	3.62 (mc,2H) 4.06 (mc,1H) 2.02 (mc,1H) 0.97 (d,3H) 0.92 (d,3H)
NH	0.30		9.70 (s,1H)	9.70 (s,1H)
OH	(mc,2H) 9.94 (s,1H) 7.21 (t,1H) 7.18 (s,2H)	9.20 (sb,1H) 6.81 (fb,1H)	7.21 (t,1H)	6.24 (d,1H) 4.80 (sb,1H)
Chrom.	H/EA 1:2	-	-	H/EA 1:2
Aus- beute	20%	28%	53%	9%
Schmp.	256°C	185-186°C	183°C	170°C

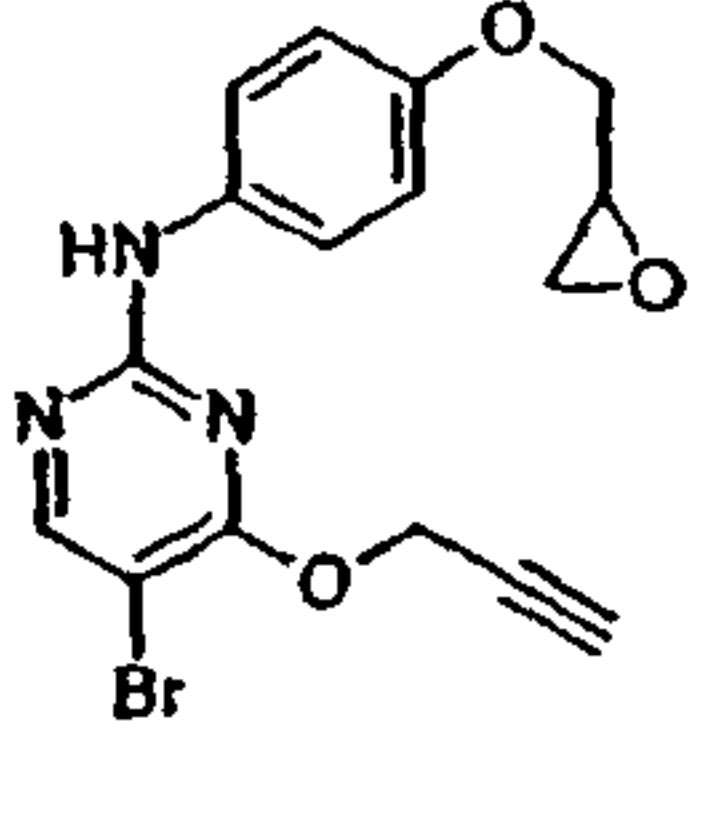
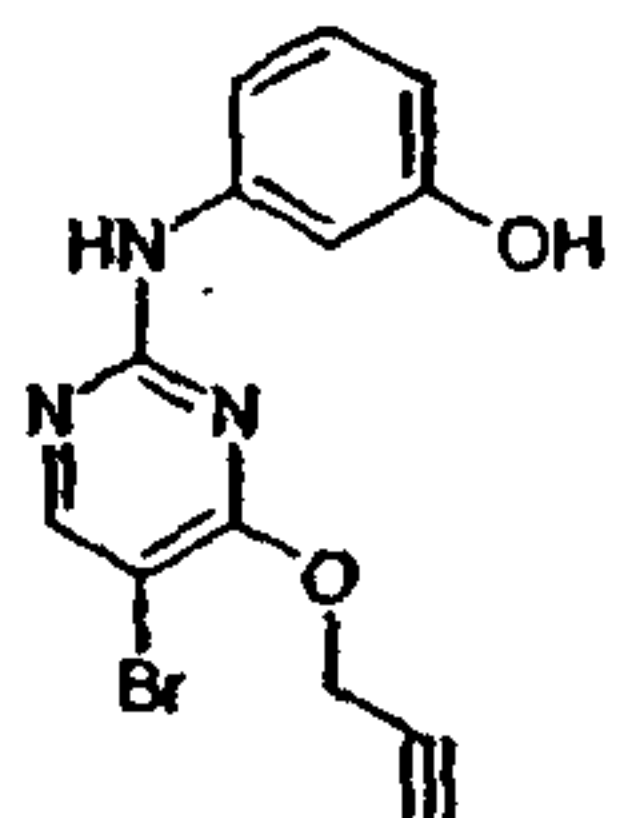
				
Beispiel Nr.	1	54	12	60
6-H 2H	7.96 (s, 1H) 7.43 (d, 2H) 6.67 (d, 2H)	8.22 (s, 1H) 7.93 (d, 2H) 7.85 (d, 2H)	8.03 (s, 1H) 7.68 (d, 2H) 7.19 (d, 2H) 2.43 (s, 3H)	8.10 (s, 1H) 7.92 (d, 2H) 7.66 (d, 2H) not. obs. 2.74 (t, 2H)
4H	1.20 (d, 3H) 4.38 (mc, 1H) 3.37 (dd, 1H) 3.48 (dd, 1H)	4.26 (d, 2H) 3.12 (sb, 1H)	1.20 (d, 3H) 4.42 (mc, 1H) 3.37 (dd, 1H) 3.50 (dd, 1H)	3.61 (mc, 2H) 4.04 (mc, 1H) 2.01 (mc, 1H) 0.94 (d, 3H)
NH	3.28 (s, 3H) 8.92 (sb, 1H) 8.81 (sb, 1H)	9.78 (s, 1H)	3.34 (s, 3H) 9.26 (s, 1H)	0.91 (d, 3H) 9.72 (s, 1H) 7.65 (s, 1H)
OH	6.20 (tb, 1H)	7.21 (t, 1H)	6.42 (d, 1H)	6.27 (d, 1H) 4.80 (sb, 1H) 4.70 (sb, 1H)
Chrom. Aus- beute	Kristallisiert EA 64%	Kristallisiert DIPE/MeOH 52%	Kristallisiert. EA 36%	
Schmp.	165.5- 166°C	210°C	91°C	150-151°C

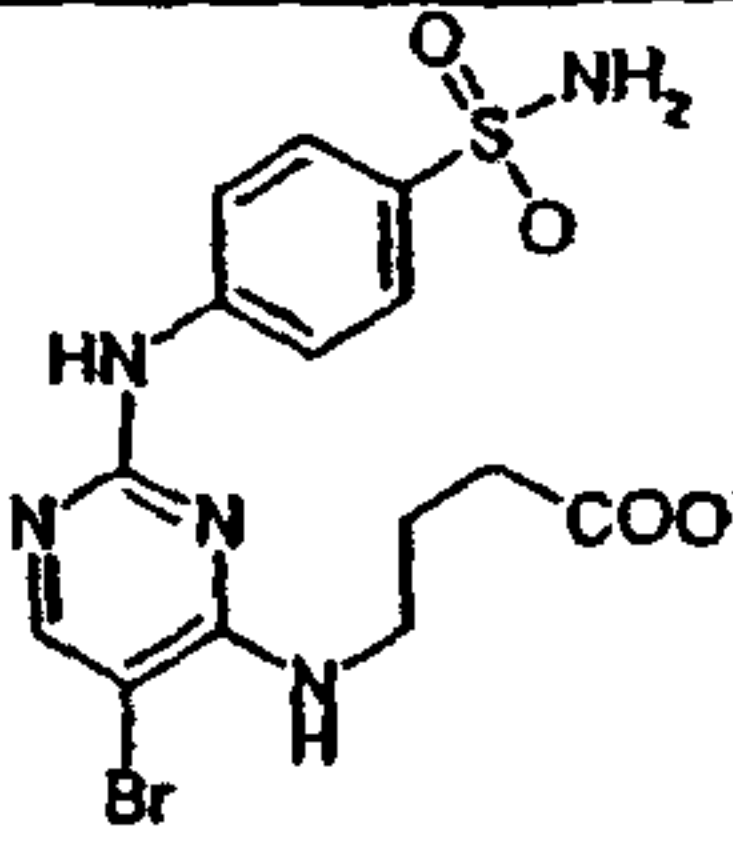
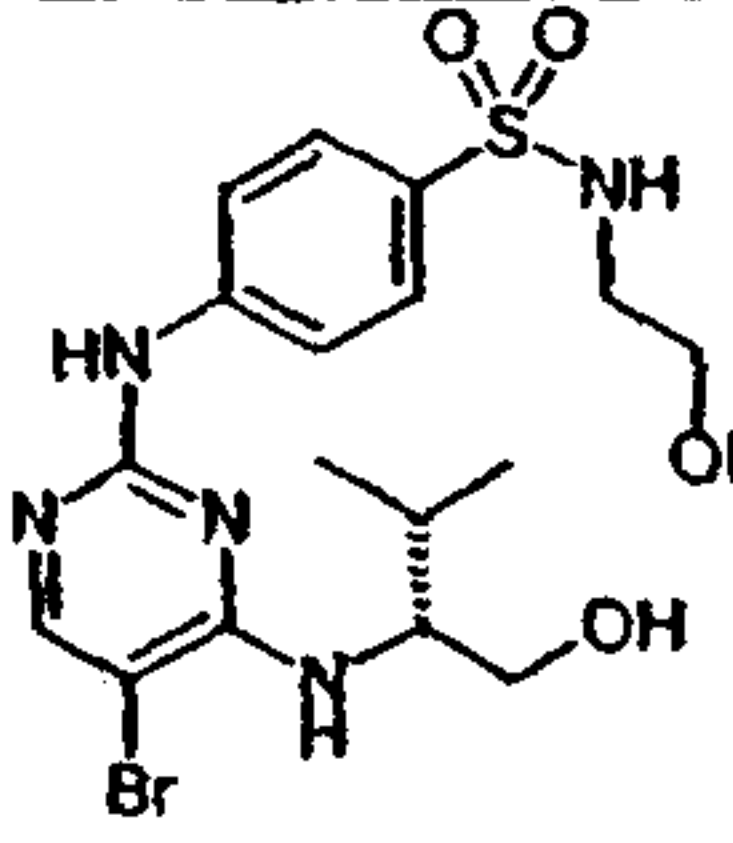
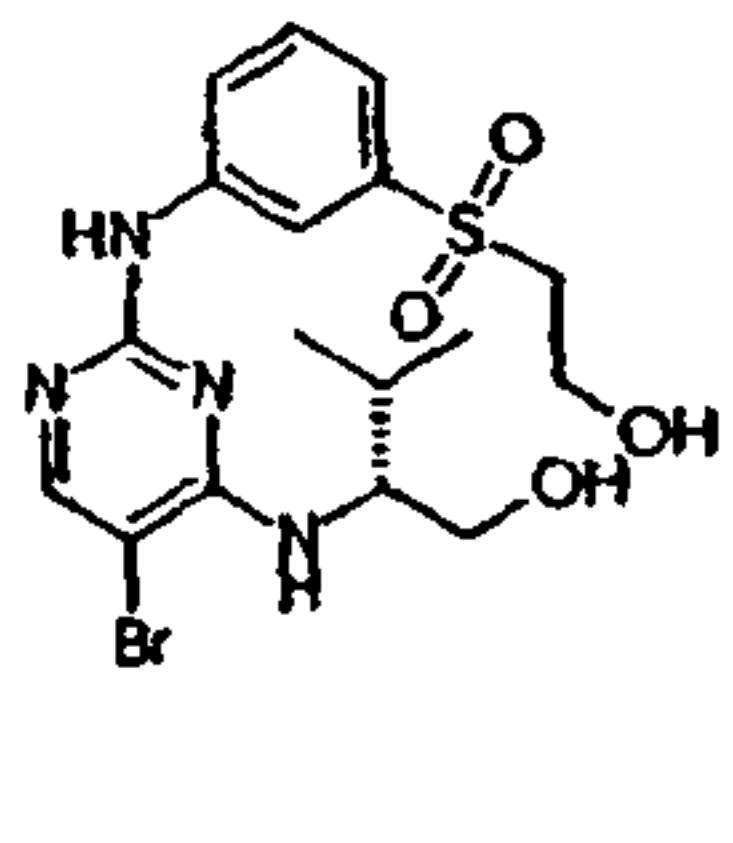
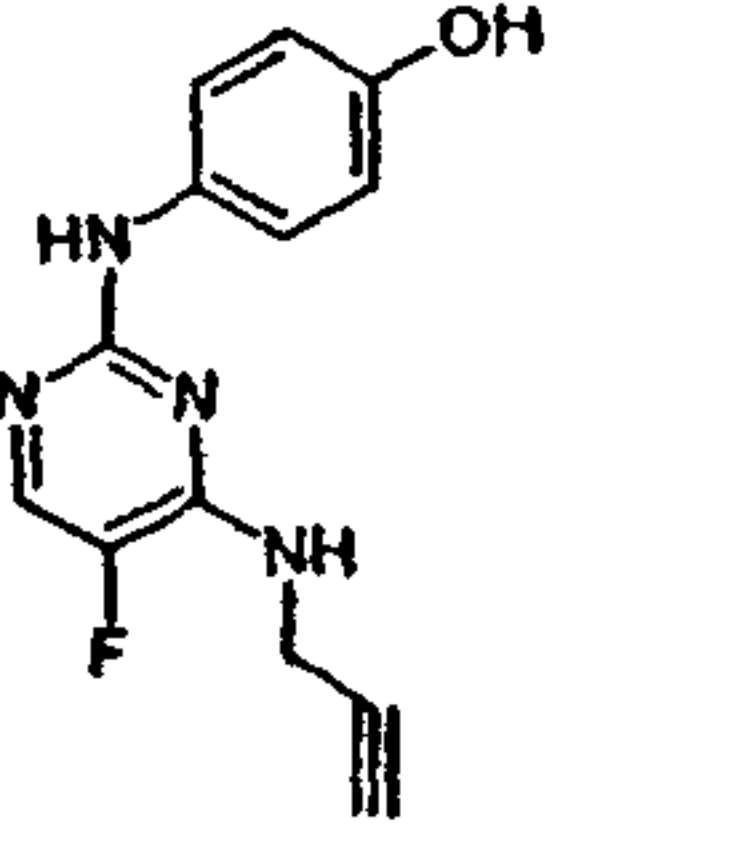
				
Beispiel Nr.	7	17	2	18
6-H	8.32 (s, 1H)	8.08 (s, 1H)	7.95 (s, 1H)	8.32 (s, 1H)
4CH	1.22 (d, 3H)	1.21 (d, 3H)	3.50 (q, 2H)	3.10 (m, 2H)
	4.46	4.53 (mc, 1H)	2.50 (t, 2H)	3.52 (m, 4H)
	(mc, 1H)	3.41 (dd, 1H)	2.40 (t, 4H)	3.77-3.97
	3.40 (dd, 1H)	3.51 (dd, 1H)	3.59 (t, 4H)	(6H)
	3.57 (dd, 1H)	3.27 (s, 3H)		
2CH	3.28 (s, 3H)	8.53 (s, 1H)	7.45 (d, 2H)	
	7.80 (s, 4H)	7.40 (d, 1H)	6.66 (d, 2H)	8.40 (s, 1H)
		7.50 (t, 1H)		7.55-7.70
		7.86 (d, 1H)		(2H)
		3.40 (t, 2H)		7.85 (d, 1H)
		3.68 (t, 2H)		3.48 (m, 2H)
NH		9.65 (sb, 1H)	8.94 (sb, 1H)	3.70 (m, 2H)
	10.79	6.47 (db, 1H)	8.79 (sb, 1H)	
OH	(sb, 1H)	4.84 (tb, 1H)	6.70 (tb, 1H)	11.16 (sb, 1H)
	7.84 (db, 1H)			10.60 (sb, 1H)
	7.31 (sb, 2H)			8.20 (sb, 1H)
Chrom.		-	-	kristall.
Aus- beute	25%	10%	62%	MeOH 50%
Schmp.	247°C Zers.	201-202°C	227.5- 228.5°C	245°C Zers.

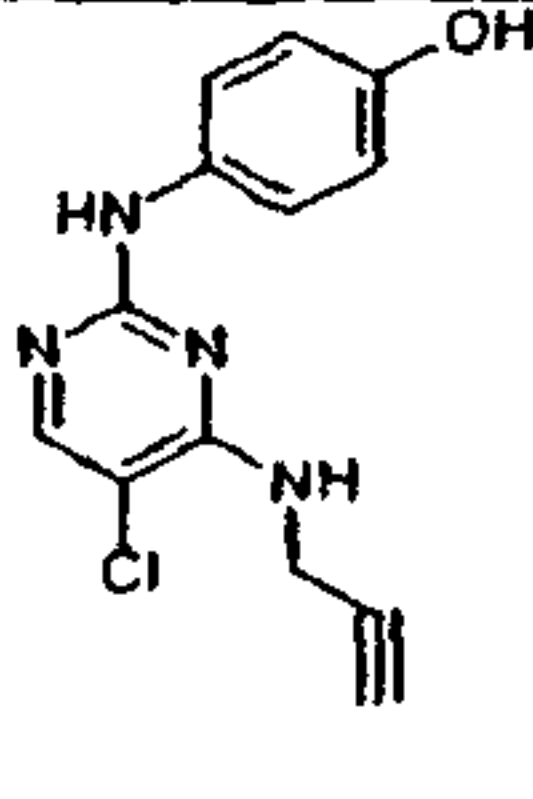
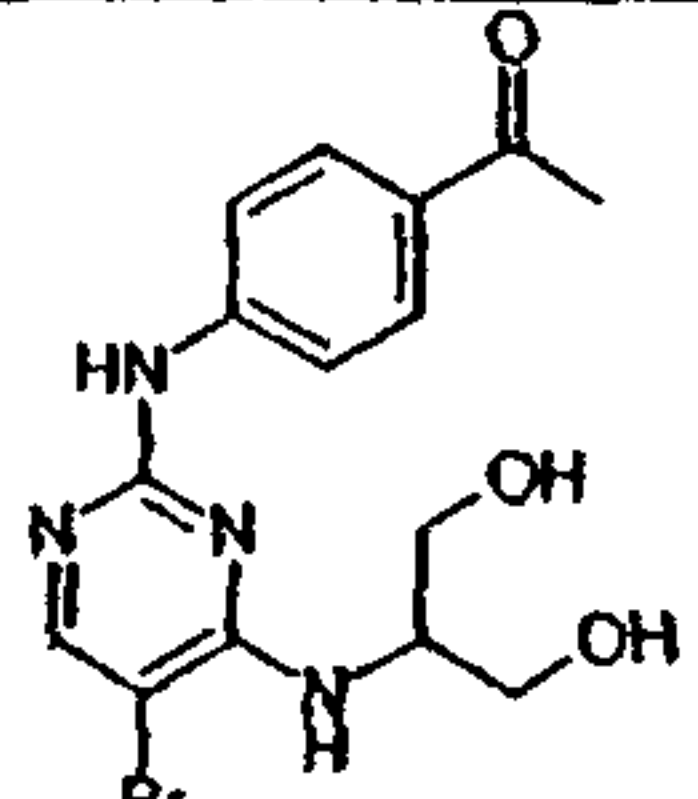
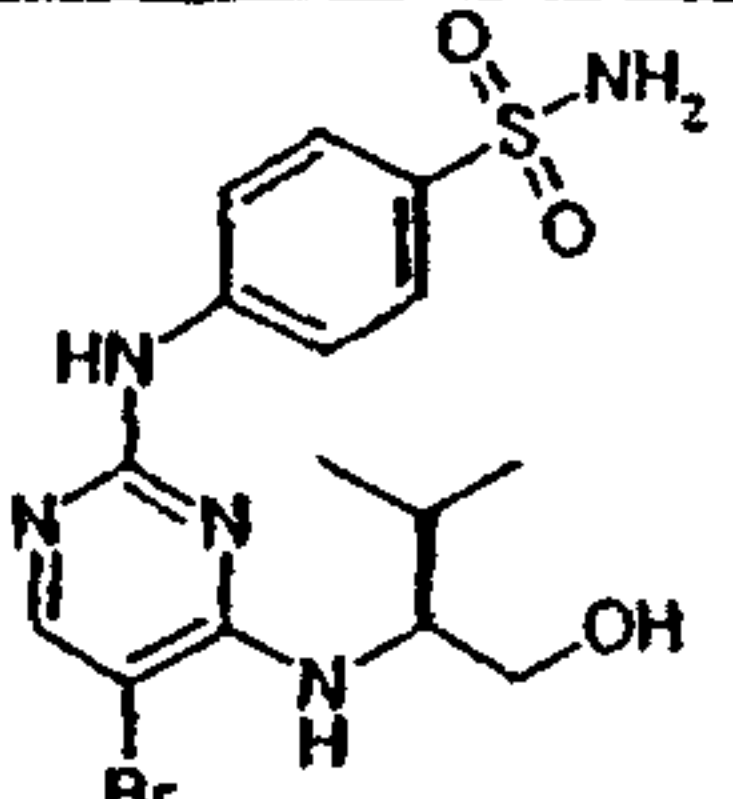
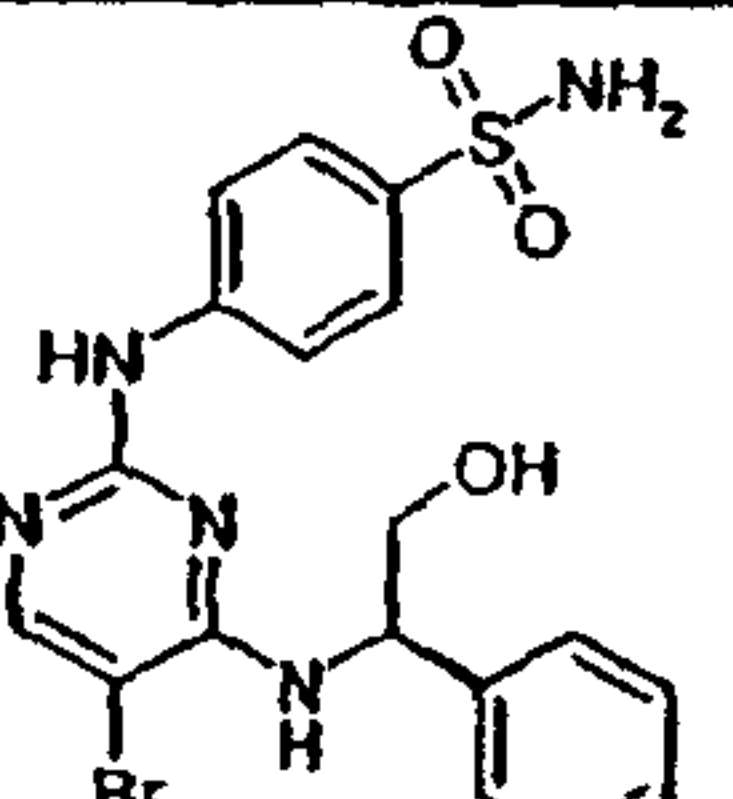
	
Beispiel Nr.	8 (D ₂ O)
6-H 4CH 2CH NH OH	8.14 (s,1H) 3.06 (sb,2H) 3.39 (t,4H) 3.71 (sb,2H) 3.85 (sb,2H) 3.94 (t,2H) 8.00 (d,2H) 7.72 (d,2H)
Chrom. Aus- beute	krist. Wasser 25%
Schmp.	>275°C

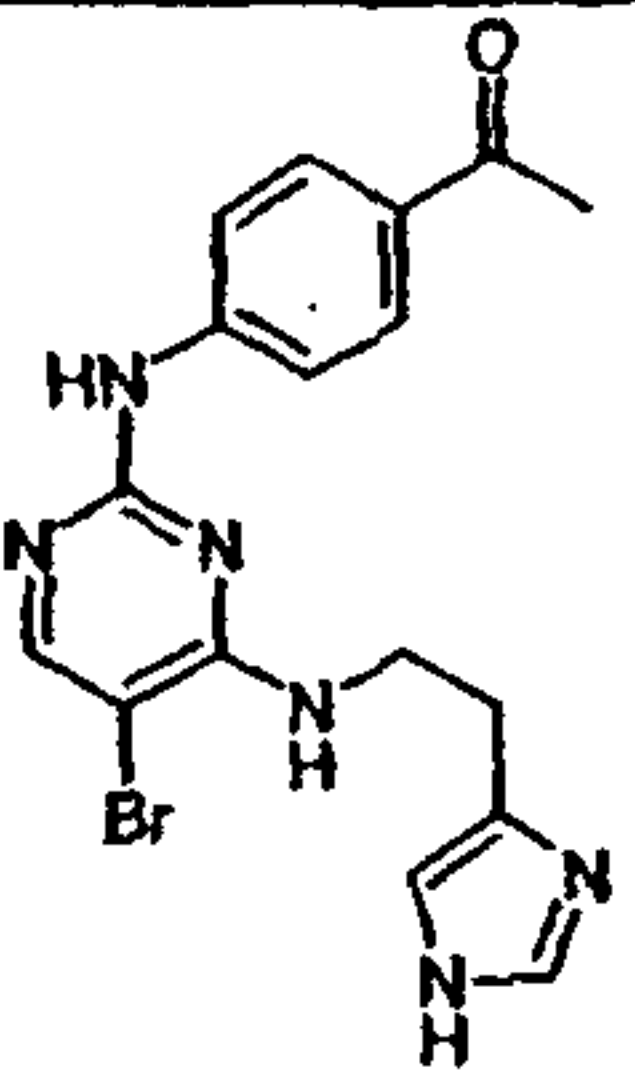
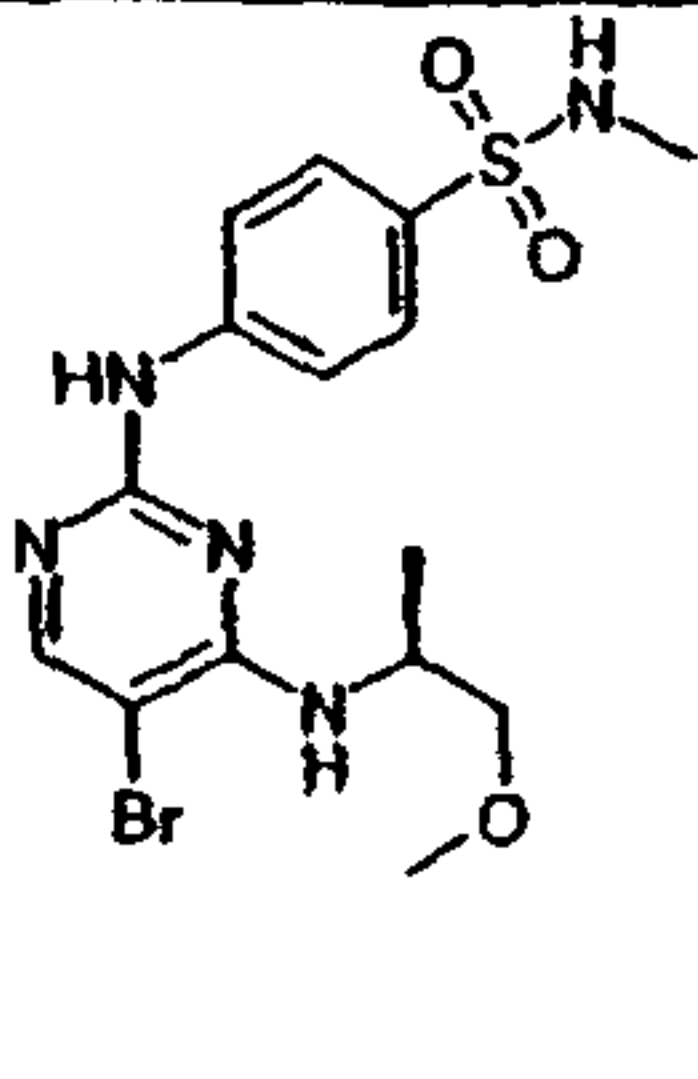
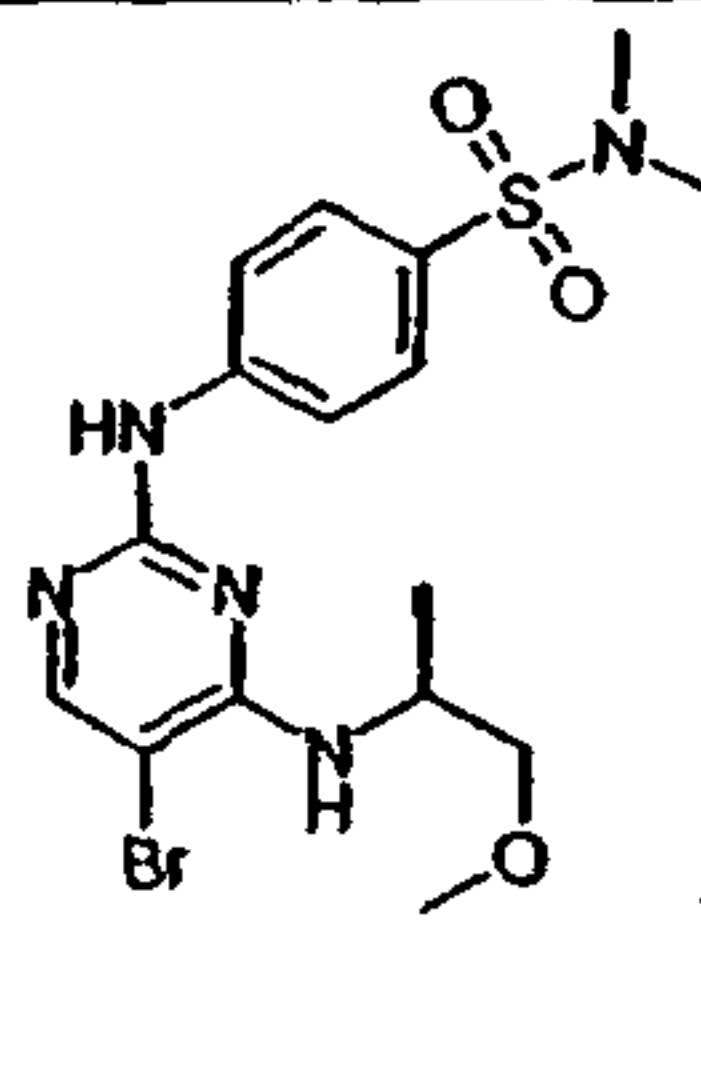
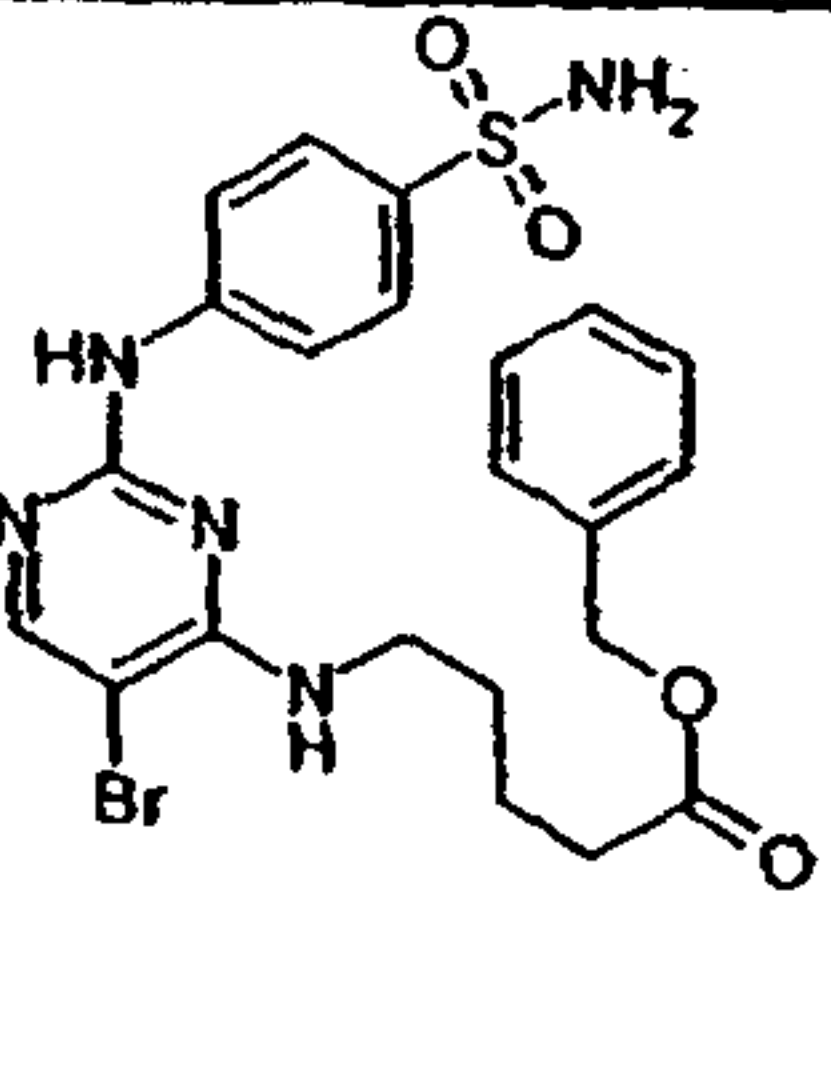
				
Beispiel Nr.	47	6	22	84
5-H 2CH	8.74 (s,1H) 7.87 (d,2H) 7.74 (d,2H)	8.31 (s,1H) 7.47 (d,2H) 6.71 (d,2H)	8.31 (s,1H) 7.76 (d,2H) 7.72 (d,2H) 2.58 (s,3H)	8.47 (s,1H) 4.48 (t,2H) 2.01 (mc,2H) 2.44 (mc,2H)
4CH	4.50 (t,2H) 2.03 (mc,2H) 2.44 (mc,2H)	5.04 (d,2H) 3.59 (t,1H)	5.05 (d,2H) 2.57 (t,1H)	7.91 (d,2H)
2NH	10.14 (s,1H) 7.21 (s,2H)	9.02 (sb,1H) 9.40 (sb,1H)	7.47 (sb,1H)	7.85 (d,2H) 2.50 (s) 10.19 (s,1H)
Chrom. Aus- beute	MeOH/DCM 1:9 4%	66%	- 8%	- 11%
Schmp.	186-187°C	146°C	165-166°C	152°C

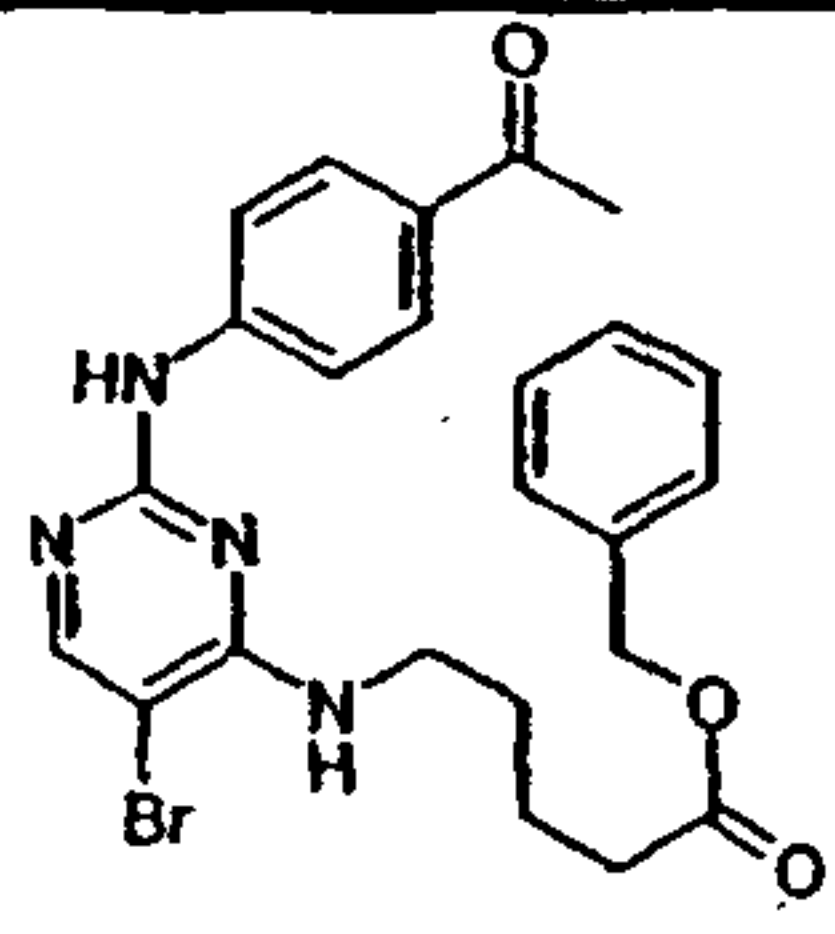
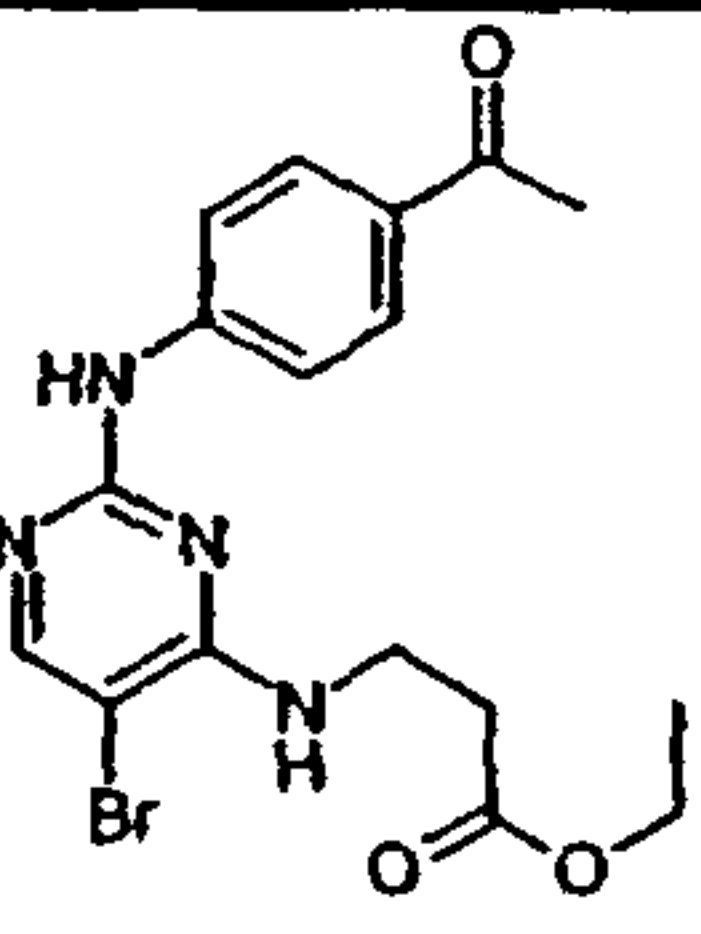
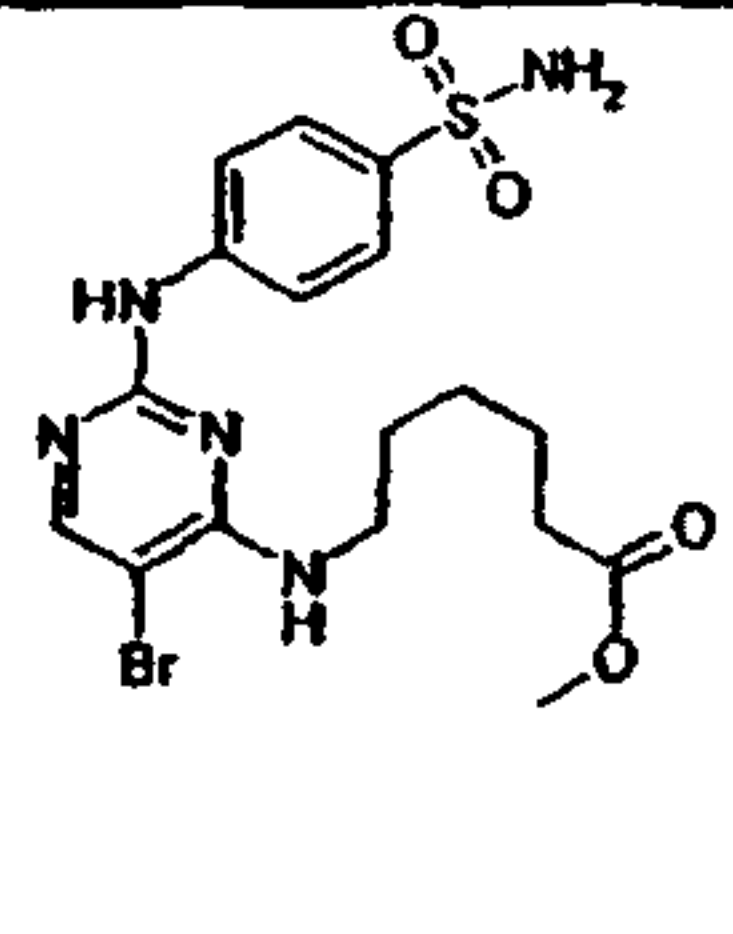
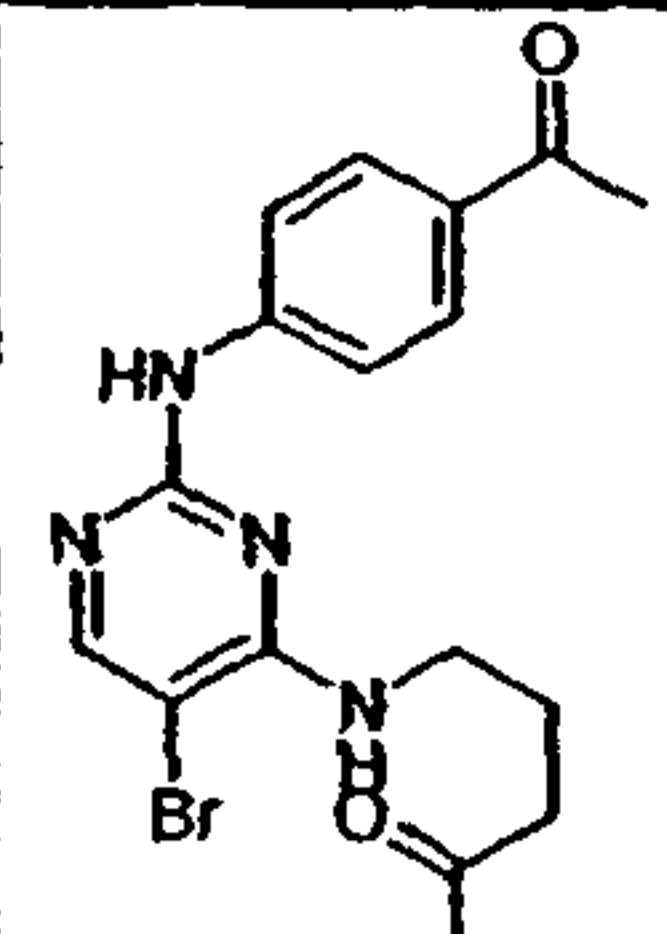
		
Beispiel Nr.	86	77
5-H 2CH	8.47 (s,1H) 4.07 (mc,2H) 3.81 (mc,2H) 3.60 (mc,2H)	8.48 (s,1H) 5.52 (m,1H) 3.68 (d,4H) 3.48 (mc,4H)
4CH	3.48 (mc,2H) 3.41 (t,2H) 1.07 (t,3H)	1.09 (t,6H) 7.84 (d,2H)
2NH	7.84 (d,2H) 7.91 (d,2H) 10.18 (s,1H)	7.74 (d,2H) 8.05 (vb) 3.40 (vb)
Chrom. Aus- beute	- 2%	- 74%
Schmp.	85°C	132°C

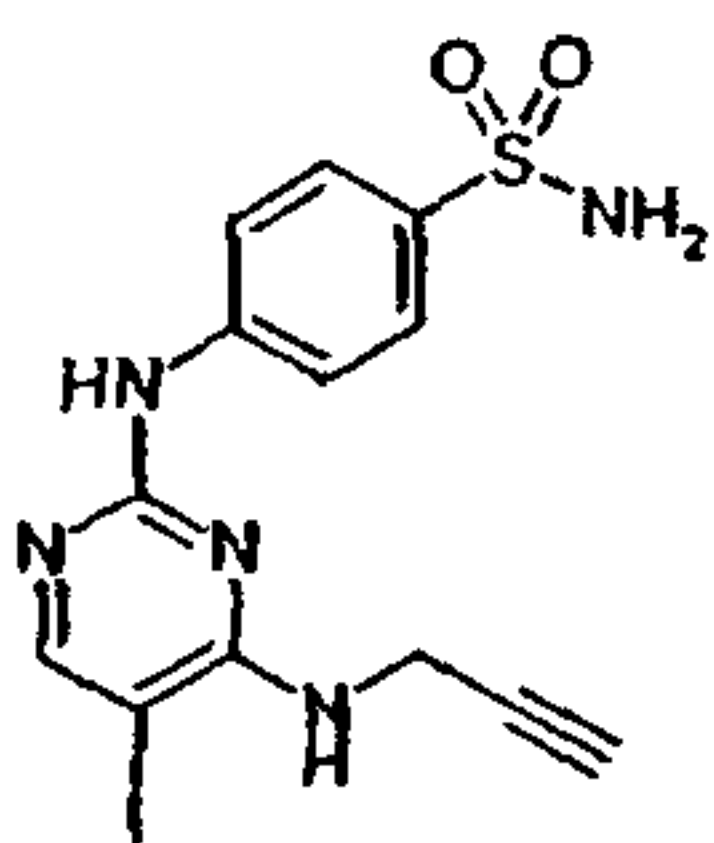
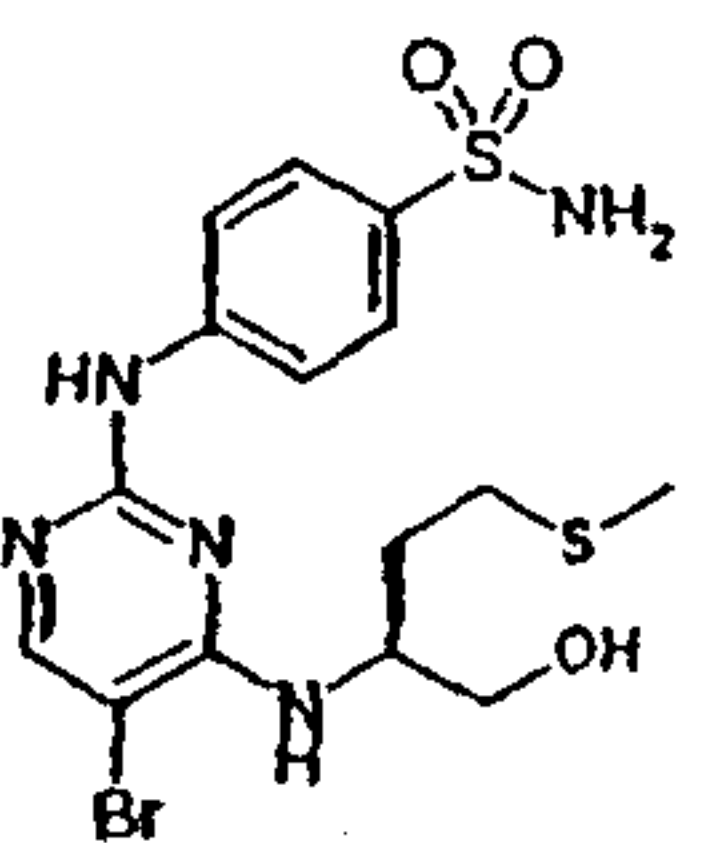
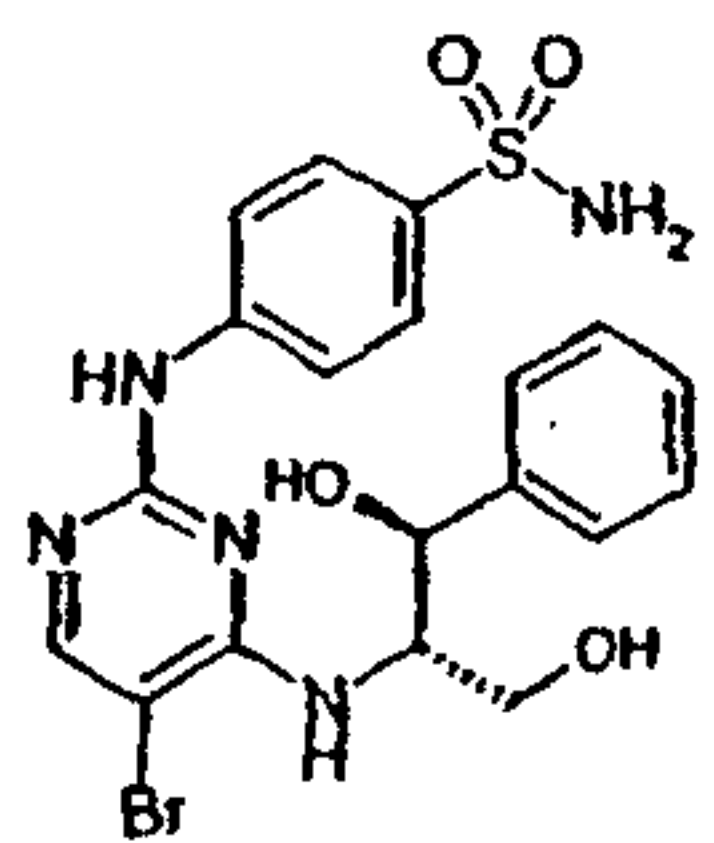
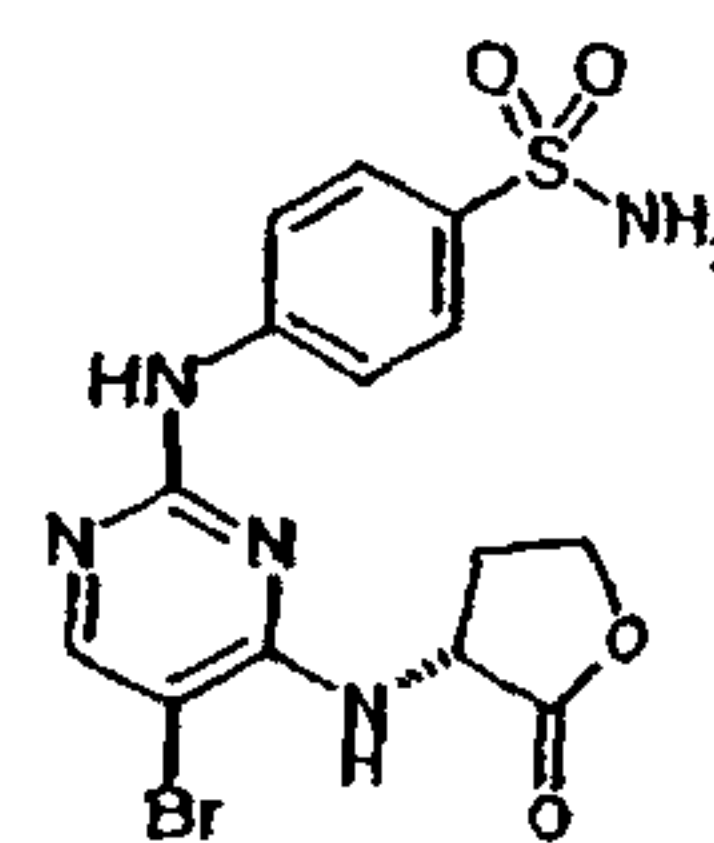
		
Beispiel Nr.	40	20
6-H 2CH	8.36 (s,1H) 7.60 (d,1H) 6.91 (d,1H) 4.28 (dd,1H) 3.79 (dd,1H) 3.31 (m,1H) 2.84 (dd,1H) 2.70 (dd,1H)	8.40 (s,1H) 7.23 (s,1H) 6.42 (d,1H) 7.06 (t,1H) 7.18 (d,1H)
4CH	5.07 (d,12H) 3.65 (t,1H)	5.12 (d,2H) 3.60 (sb,1H)
NH	9.65 (sb,1H)	9.60 (sb,1H)
OH		9.21 (sb,1H)
Chrom.	H/EA 1:3	krist. DIPE
Aus- beute	0.5%TEA 38%	35%
Schmp.	140-141°C	174°C

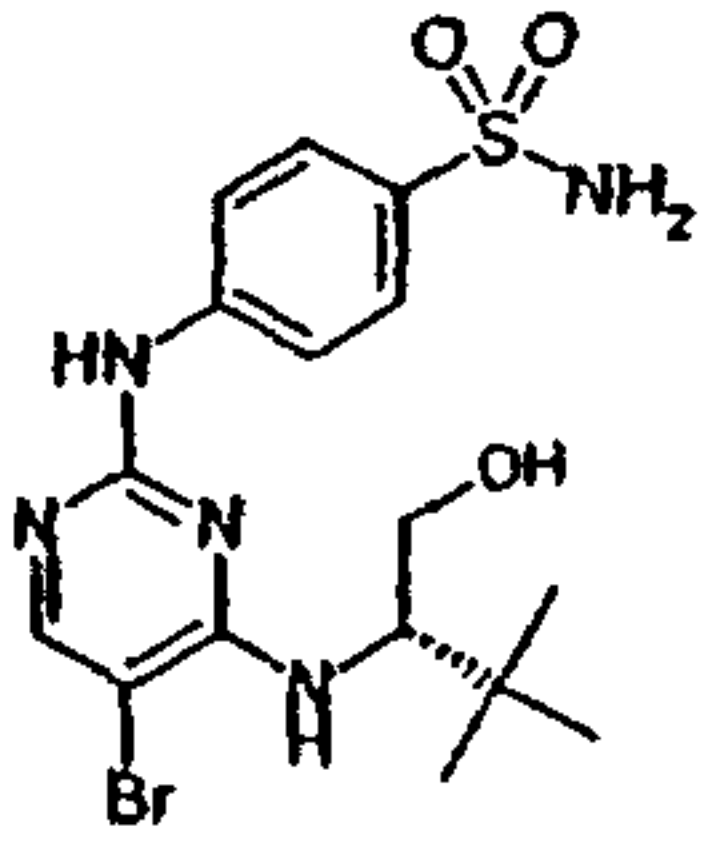
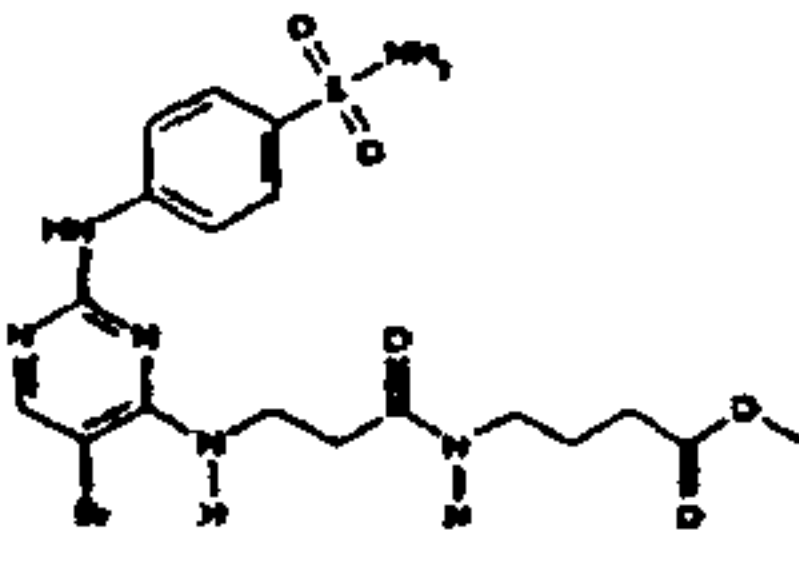
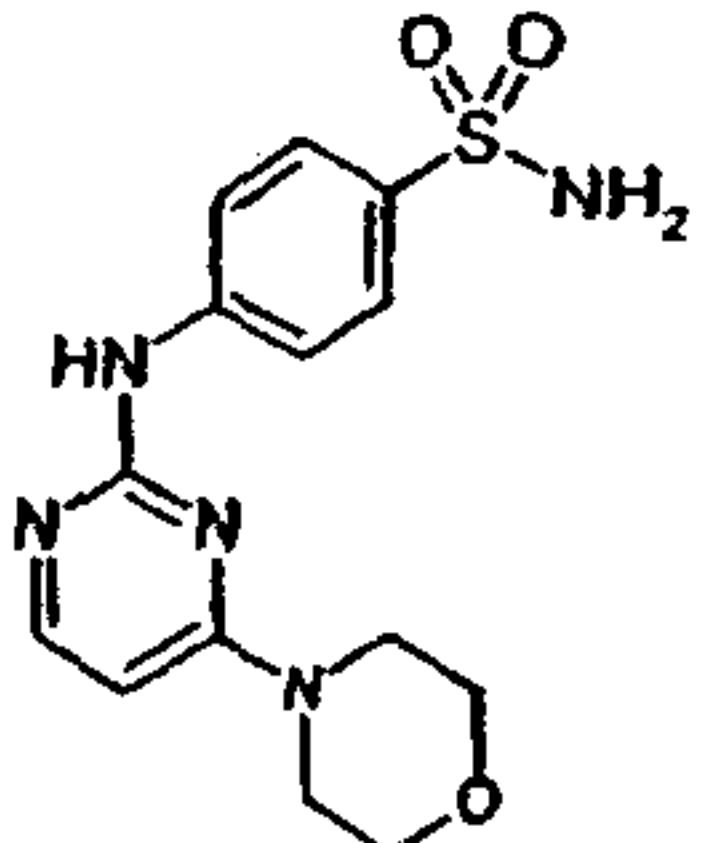
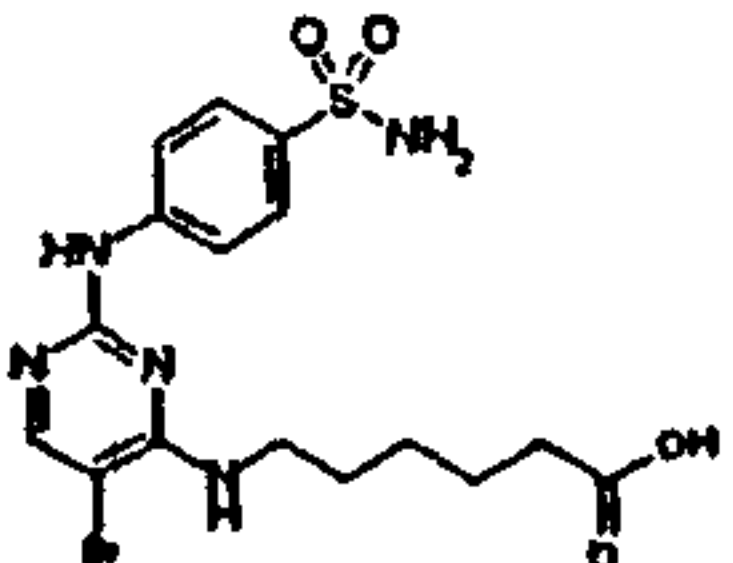
				
Beispiel Nr.	49	48	29	42
6-H 2H	8.14 (s,1H) 7.88 (d,2H) 7.69 (d,2H)	8.10 (s,1H) 7.92 (d,2H) 7.66 (d,2H)	8.09 (s,1H) 8.50 (s,1H) 7.86 (d,1H)	7.87 (d,3.4,1H) 7.51 (d,2H) 6.66 (d,2H)
4H	3.41 (q,2H) 2.20 (t,2H) 1.81 (q,2H)	not. obs. 2.74 (t,2H) 3.61 (mc,2H) 4.04 (mc,1H) 2.01 (mc,1H) 0.94 (d,3H) 0.91 (d,3H)	7.50 (t,1H) 7.40 (d,1H) 3.40 (t,2H) 3.52-3.73 (4H) 4.09 (mc,1H) 1.98 (mc,1H) 0.97 (d,3H)	
NH	9.64 (s,1H) 7.64 (t,1H)	9.72 (s,1H) 7.65 (s,1H)	0.89 (d,3H) 9.68 (s,1H)	8.76 (s,1H) 7.74 (lb,1H)
OH	3.5 (vb)	6.27 (d,1H) 4.80 (sb,1H) 4.70 (sb,1H)	6.17 (d,1H) 4.74 (t,1H) 4.93 (t,1H)	8.88 (s,1H)
Chrom.	-	krist.MeOH/DI	DCM/EA 2:1	H/EA 1:2
Aus- beute	9%	PE 16%	26%	29%
Schmp.	262°C	150-151°C		163°C

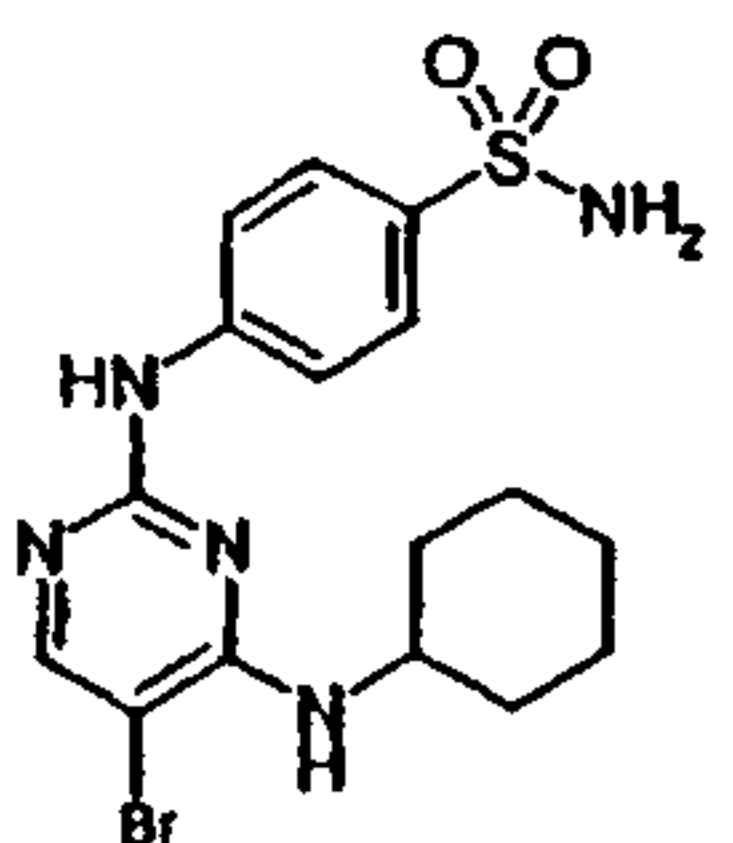
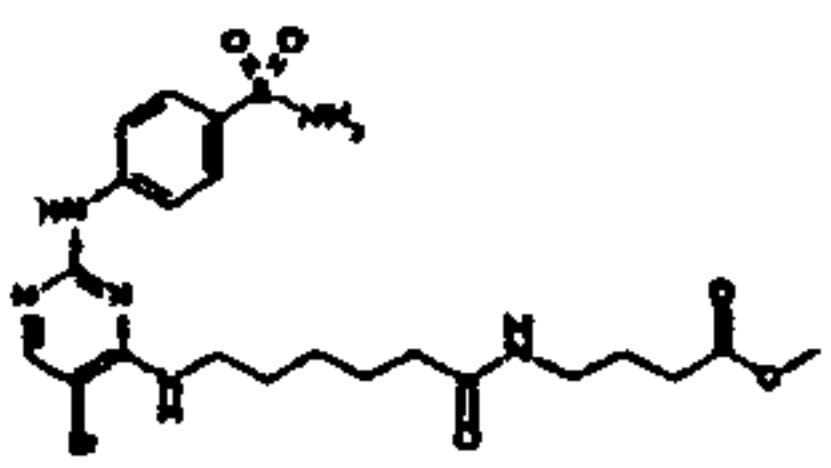
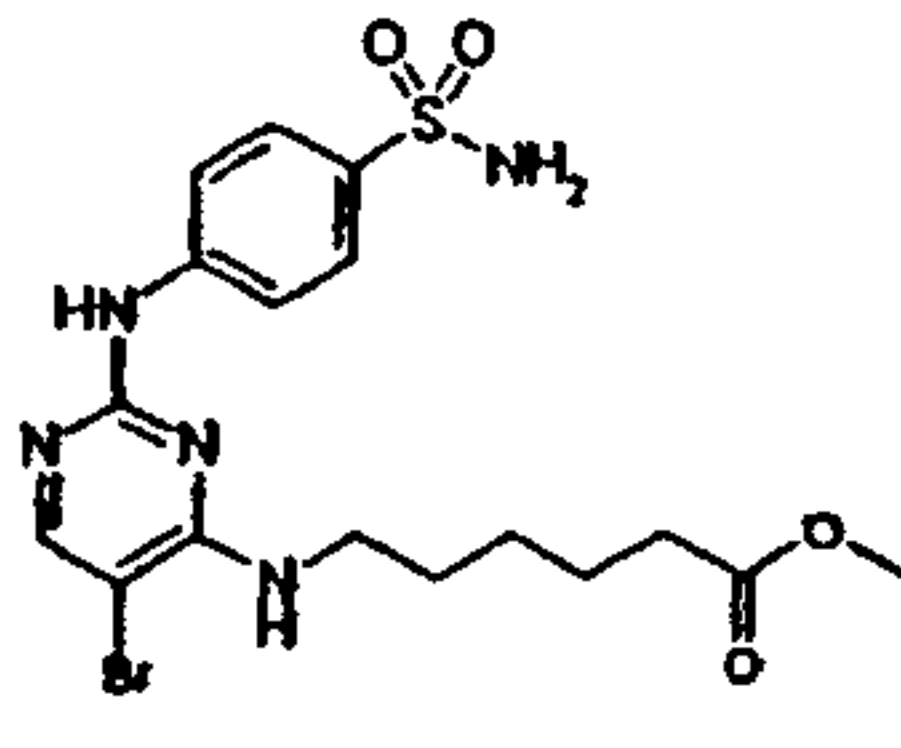
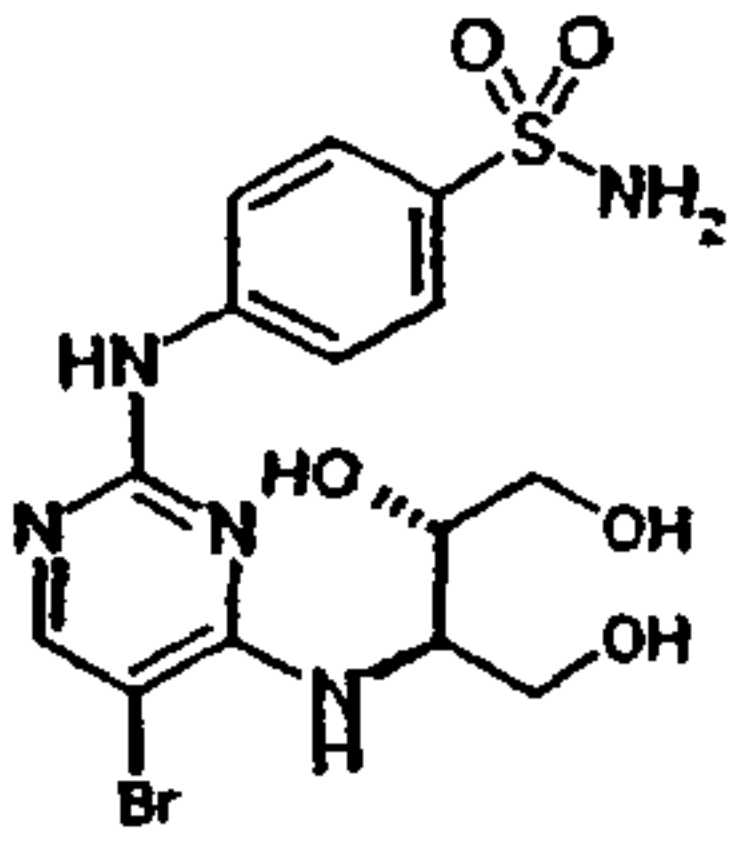
				
Beispiel Nr.	43	55	89	88
6-H 2H	7.93 (s, 1H) 7.52 (d, 2H) 6.68 (d, 2H)	8.11 (s, 1H) 7.87 (s, 4H) 2.50 (s)	8.36 (s, 1H) 7.7-7.8 (5H)	8.29 (s, 1H) 7.73 (d, 2H) 7.57 (d, 2H)
4H	3.09 (s, 1H) 4.14 (d, 2H)	4.19 (mc, 1H) 3.61 (mc, 4H)	3.66 (mc, 2H) 4.04 (m, 1H) 1.99 (mc, 1H) 0.94 (d, 3H) 0.89 (d, 3H)	3.7-3.9 (2H) 5.19 (m, 1H) 7.2-7.4 (5H)
NH	8.98 (sb, 2H) 7.50 (s, 1H)	9.73 (s, 1H) 6.20 (s, 1H)	11.11 (sb, 1H)	10.50 (s, 1H)
OH		4.88 (t, 2H)	7.34 (sb, 2H) n. obs.	5.029 (vb)
Chrom. Aus- beute	H/EA 1:2 35%	krist. MeOH/ DIPE 27%	- 74%	- 27%
Schmp.	168°C	228°C	248°C Zers.	159°C Zers.

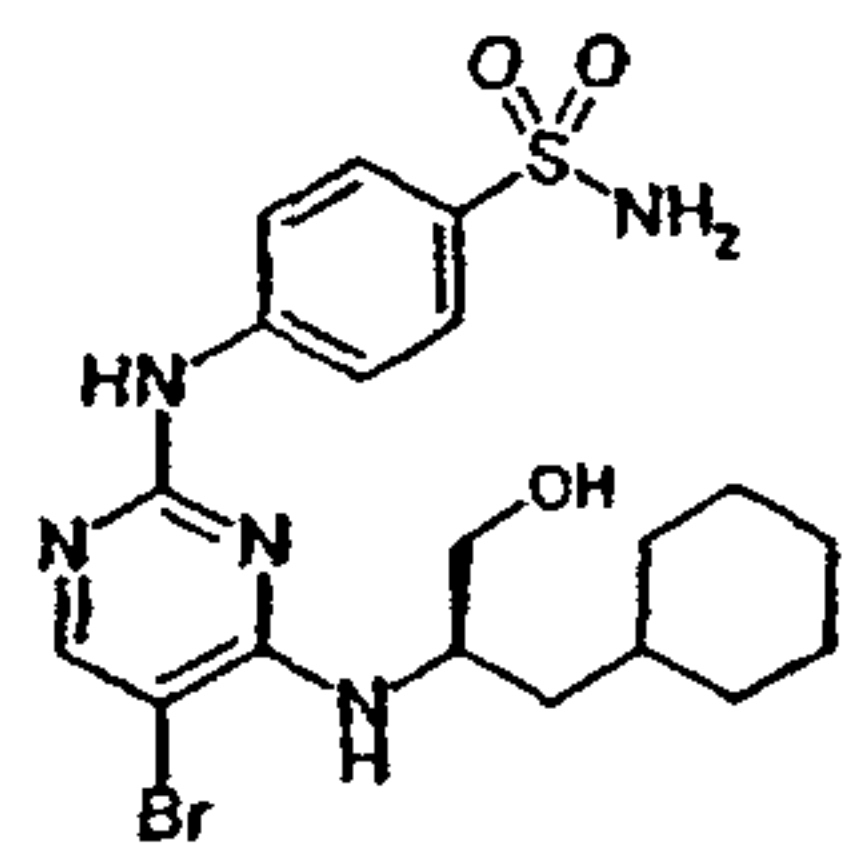
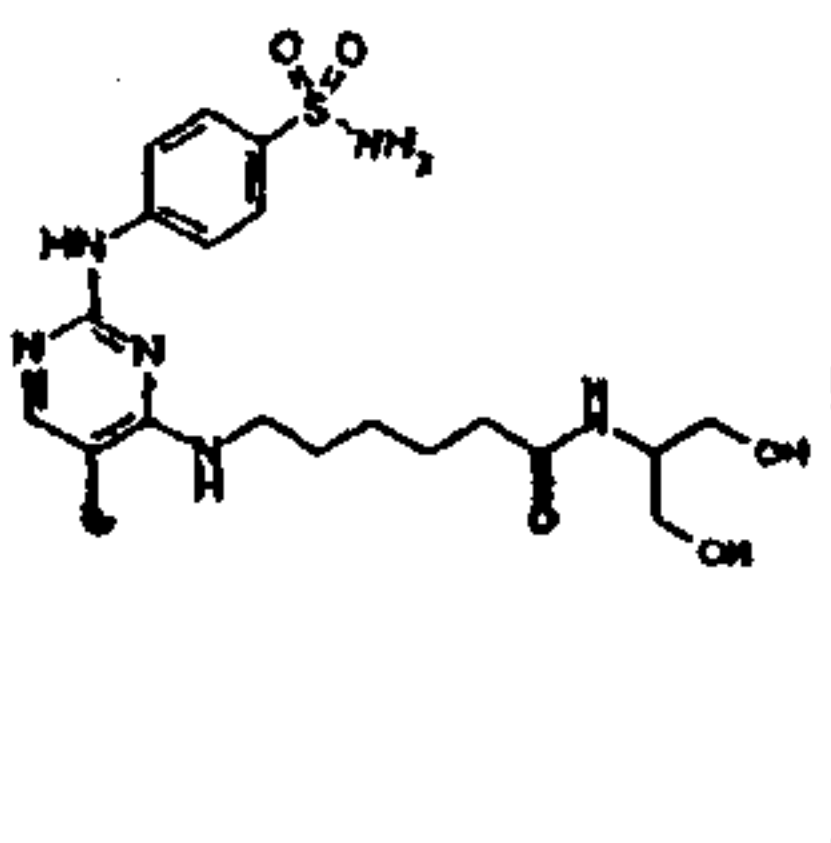
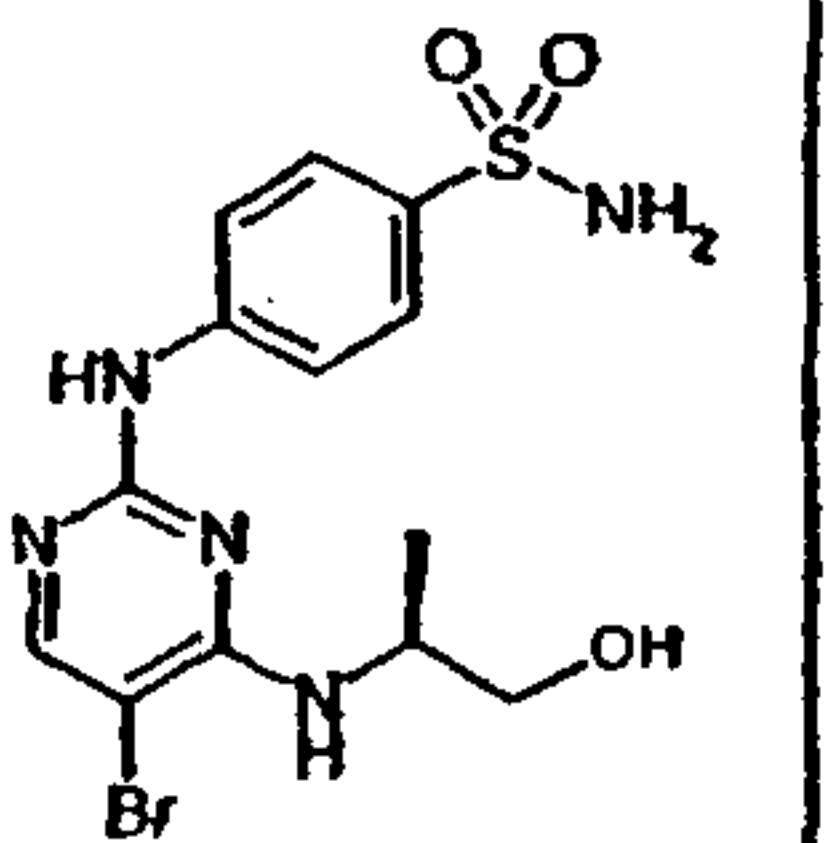
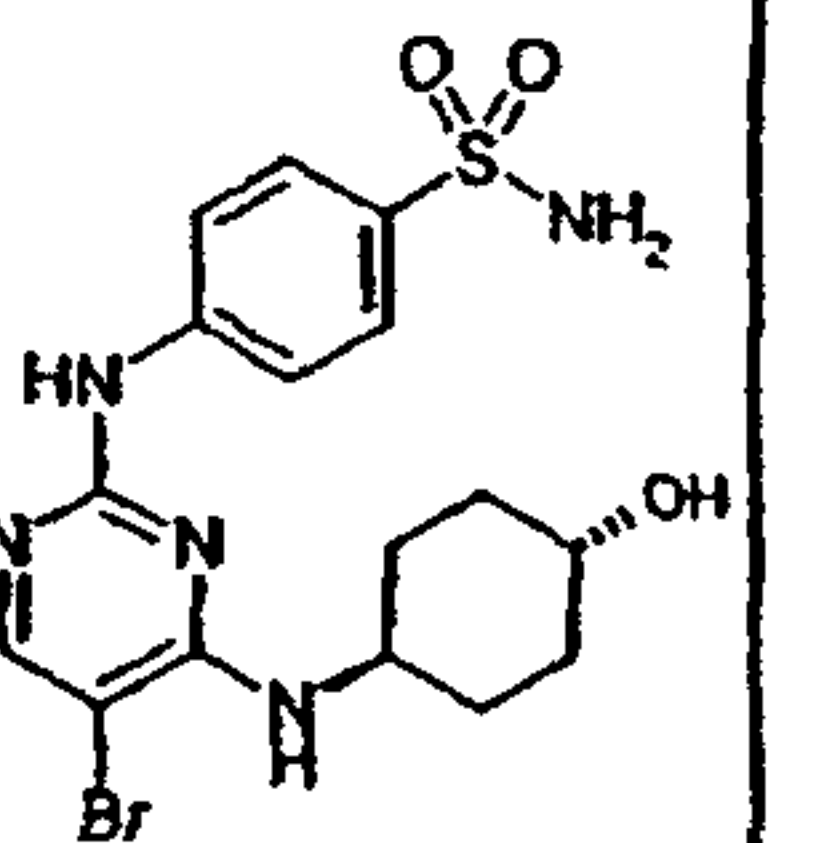
				
Beispiel Nr.	87	92	91	96
6-H 2H	8.09 (s,1H) 7.90 (d,2H) 7.82 (d,2H)	8.10 (s,1H) 7.91 (d,2H) 7.63 (d,2H)	8.09 (s,1H) 7.98 (d,2H) 7.61 (d,2H)	8.06 (s,1H) 7.88 (d,2H) 7.69 (d,2H)
4H	not. obs 3.69 (td,2H) 2.84 (t,2H) 7.60 (s,1H) 6.86 (s,1H)	2.39 (d,3H) 1.21 (d,3H) 4.45 (mc,1H) 3.38 (dd,1H) 3.51 (dd,1H)	2.54 (s,6H) 1.20 (d,3H) 4.46 (mc,1H) 3.47 (dd,1H) 3.51 (dd,1H) 3.38 (s,3H)	
NH	7.34 (tb,1H) 9.72 (s,1H)	9.73 (sb,1H) 7.20 (q,1H)	9.81 (sb,1H) 6.58 (db,1H)	7.32 (s,5H) 9.64 (s,1H) 7.16 (sb,2H)
OH	11.91 (sb,1H)	6.57 (d,1H)		
Chrom.	-	H bis H/EA 1:1	H bis H/EA	-
Aus- beute	16%	21%	1:1 7%	33%
Schmp.	210 °C	167-168°C	105°C	202°C

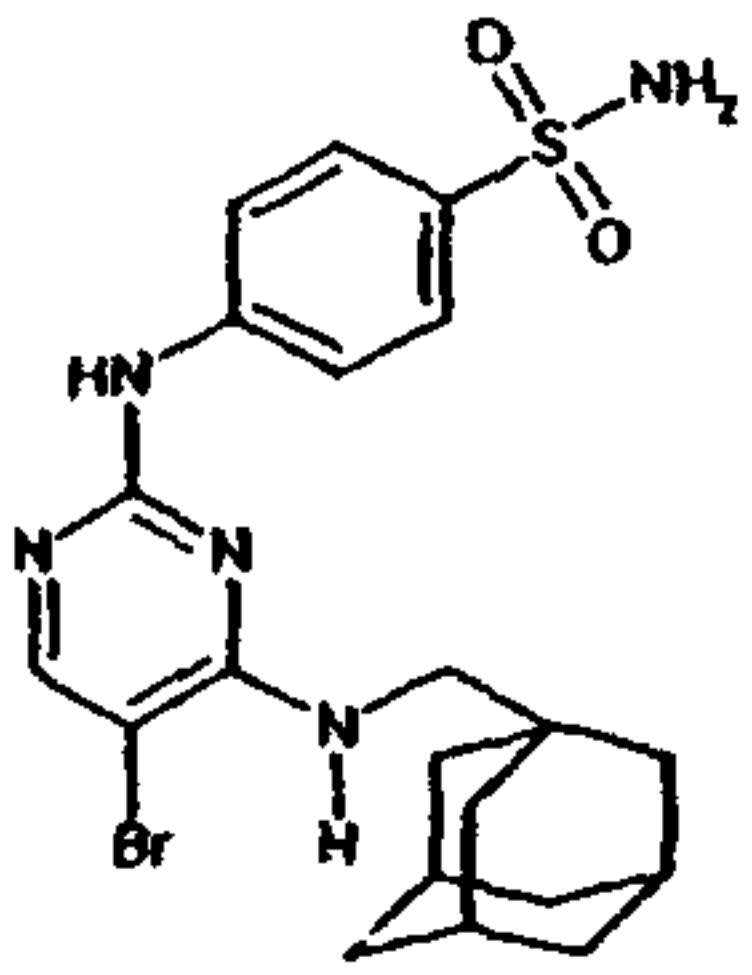
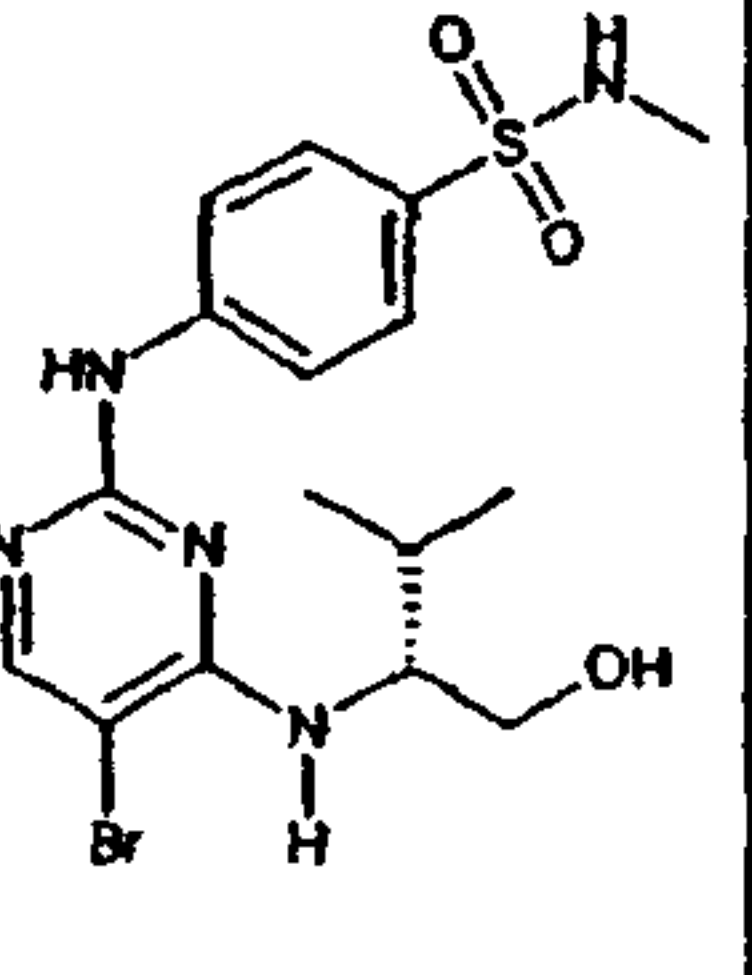
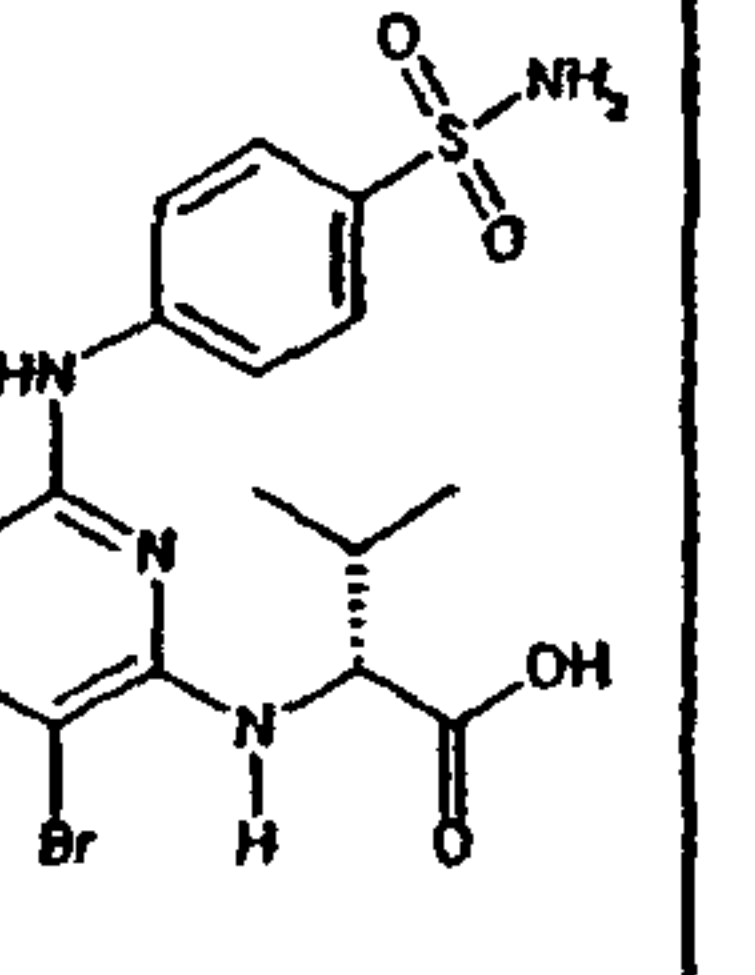
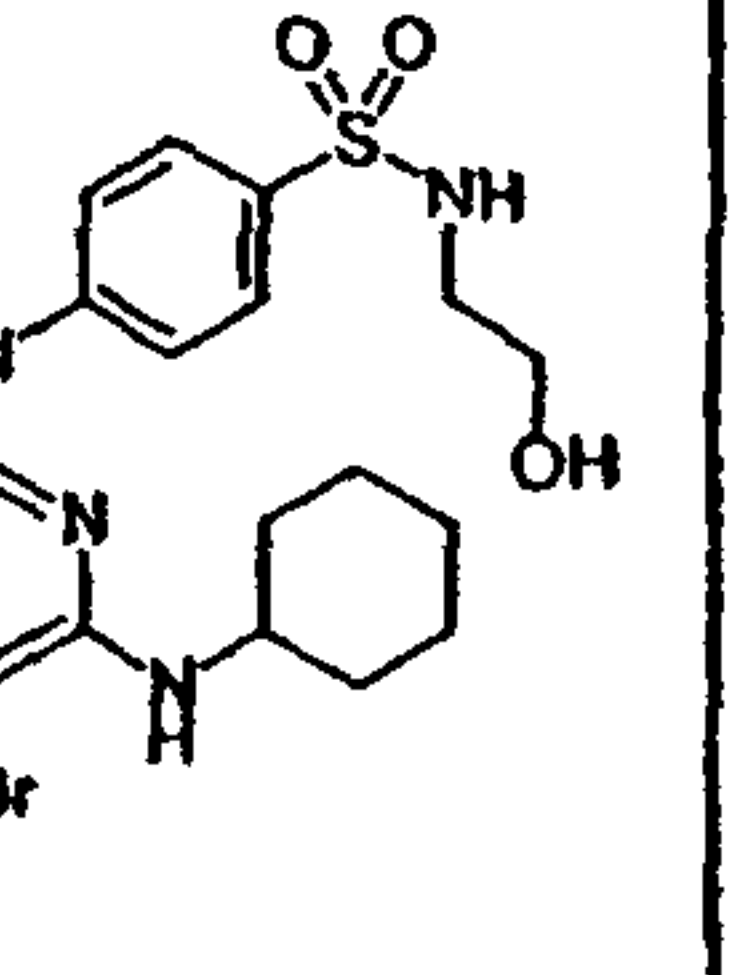
				
Beispiel Nr.	97	98	90	85
6-H 2H	8.07 (s,1H) 7.87 (s,4H) 2.50 (s,3H)	8.10 (s,1H) 7.86 (mc,4H) n. obs.		8.30 (s,1H) 7.95 (d,2H) 7.69 (d,2H)
4H	3.41 (m,2H) 1.61 (m,4H) 2.41 (m,2H) 5.07 (s,2H)	3.68 (t,2H) 2.68 (t,2H) 4.08 (q,2H) 1.17 (t,3H)		2.48 (s,3H) 3.50 (q,2H) 1.87 (m,2H) 2.38 (t,2H) 4.03 (q,2H)
NH	7.32 (s,5H) 9.70 (s,1H) 7.19 (t,1H)	9.74 (s,1H) 7.18 (t,1H)		1.13 (t,3H) 10.86 (s,1H) 8.28 (sb,2H)
Chrom. Aus- beute	- 23%	- 32%		- 53%
Schmp.	152°C	172		184°C

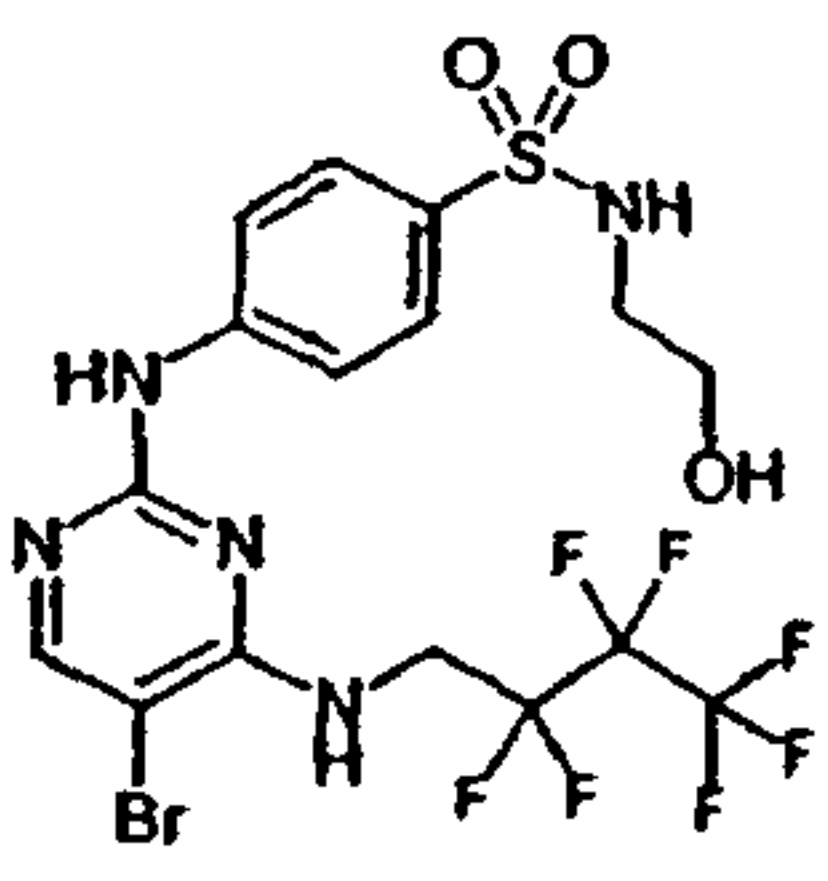
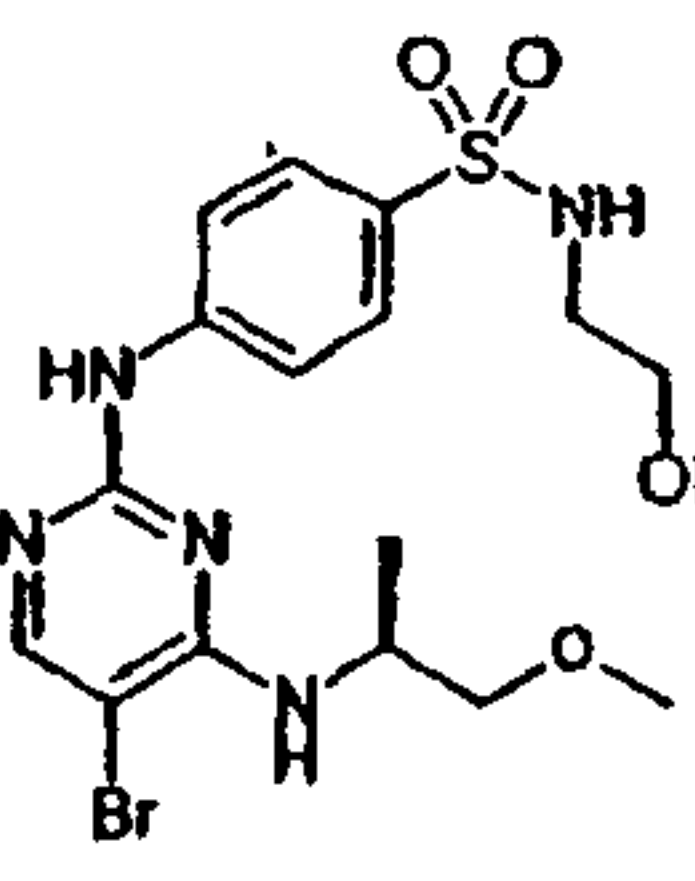
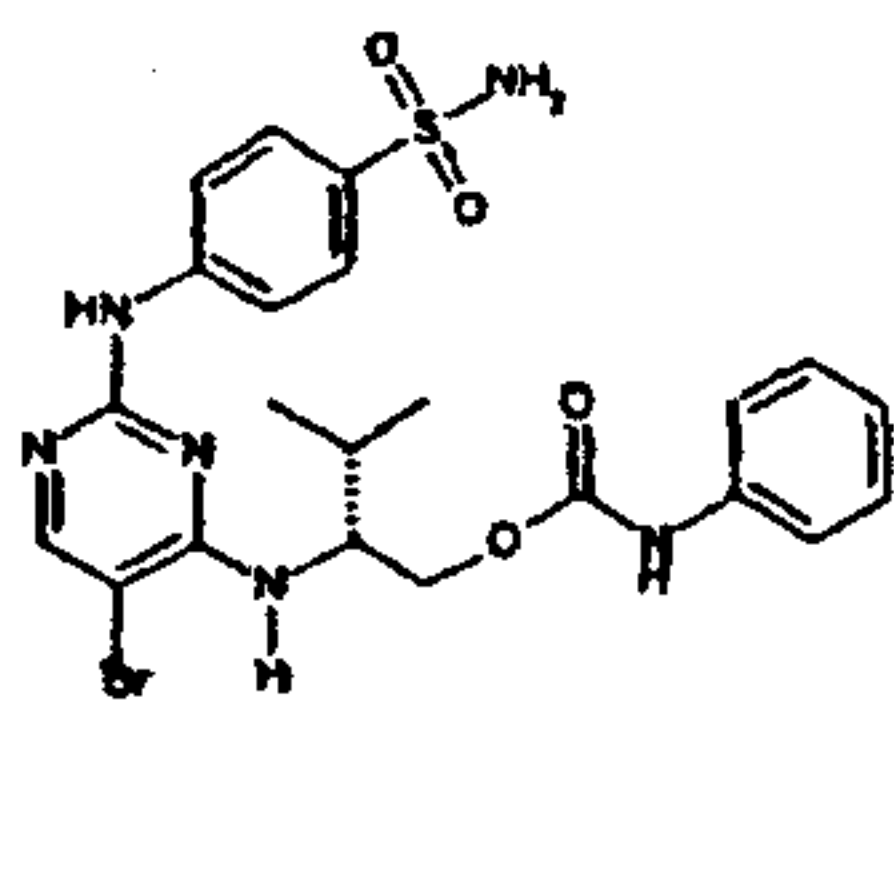
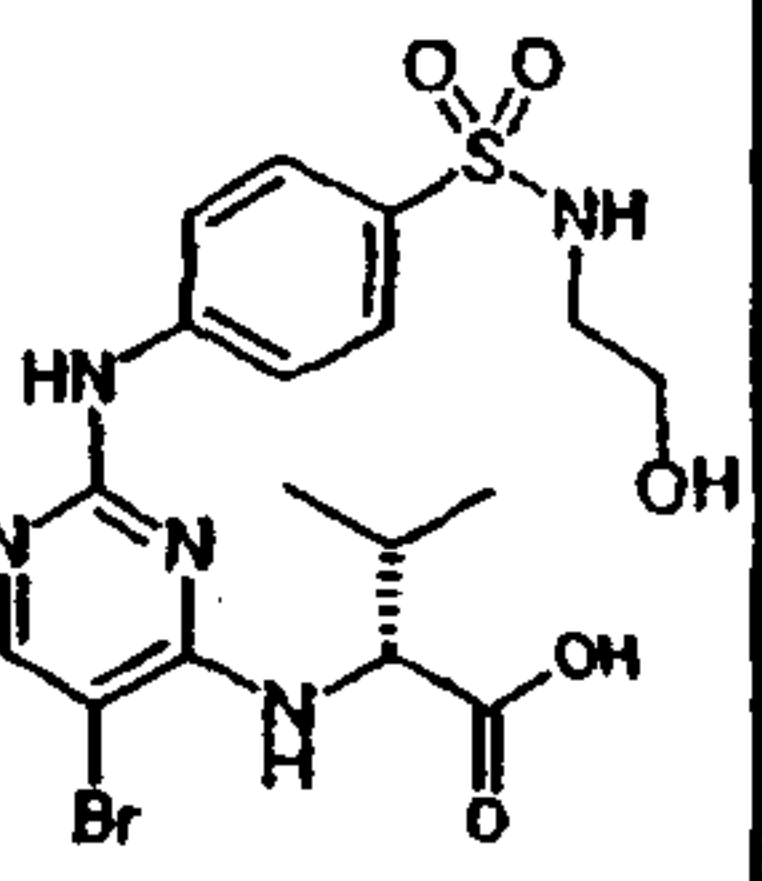
				
Beispiel Nr.	63	94	93	80
	9.73 (s,1H) 8.25 (s,1H) 7.95 (d,2H) 7.67 (d,2H) 7.21 (s,3H) 4.12 (s,2H) 3.12 (s,1H)	10.91 (s,1H) 8.34 (s,1H) 7.80 (s,4H) 7.30 (s,2H) 4.35 (m,1H) 3.58 (m,2H) 2.47 (m,2H) 2.03 (s,3H) 1.91 (m,2H)	10.80 (s,1H) 8.30 (s,1H) 7.81 (d,2H) 7.65 (d,2H) 7.30 (m,8H) 4.95 (d,1H) 4.38 (m,1H) 3.59 (d,1H)	10.88 (s,1H) 8.40 (s,1H) 8.29 (m,1H) 7.79 (s,4H) 7.31 (s,2H) 4.75 (dd,1H) 3.65 (m,1H) 3.49 (m,1H) 2.10 (m,2H)
Aus- beute	61%	24%	70%	51%
Schmp.	220	168	243	
Masse	428 (EI)	462 (ES)	494 (ES)	427 (EI)

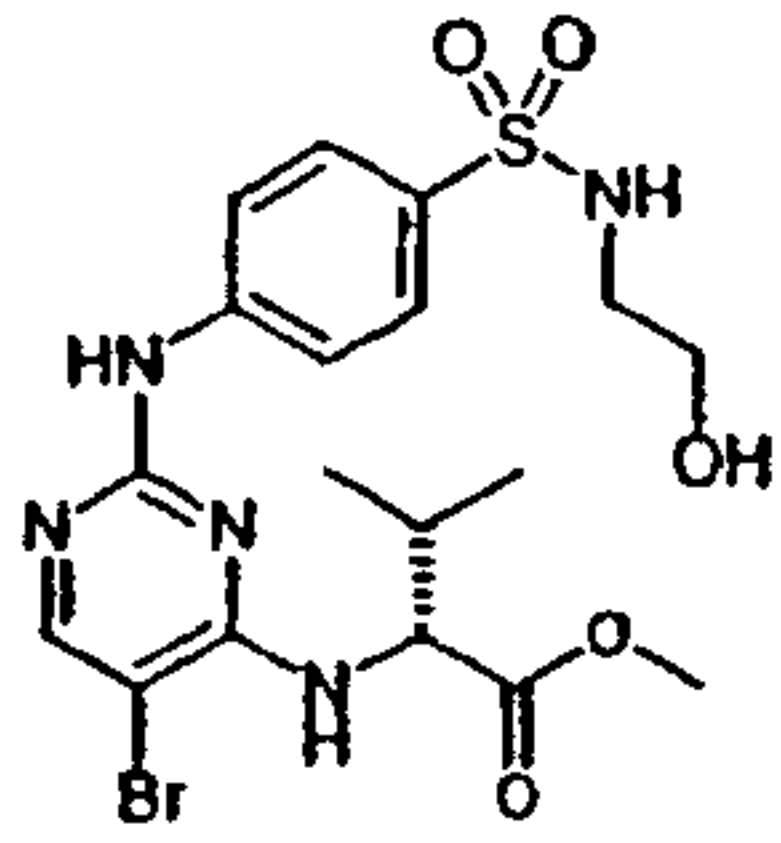
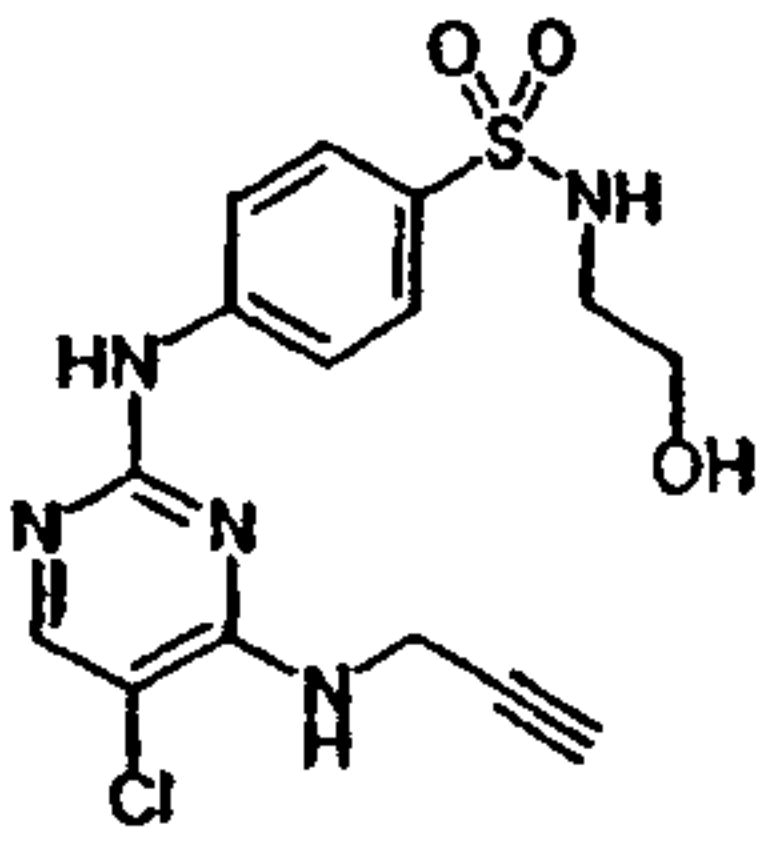
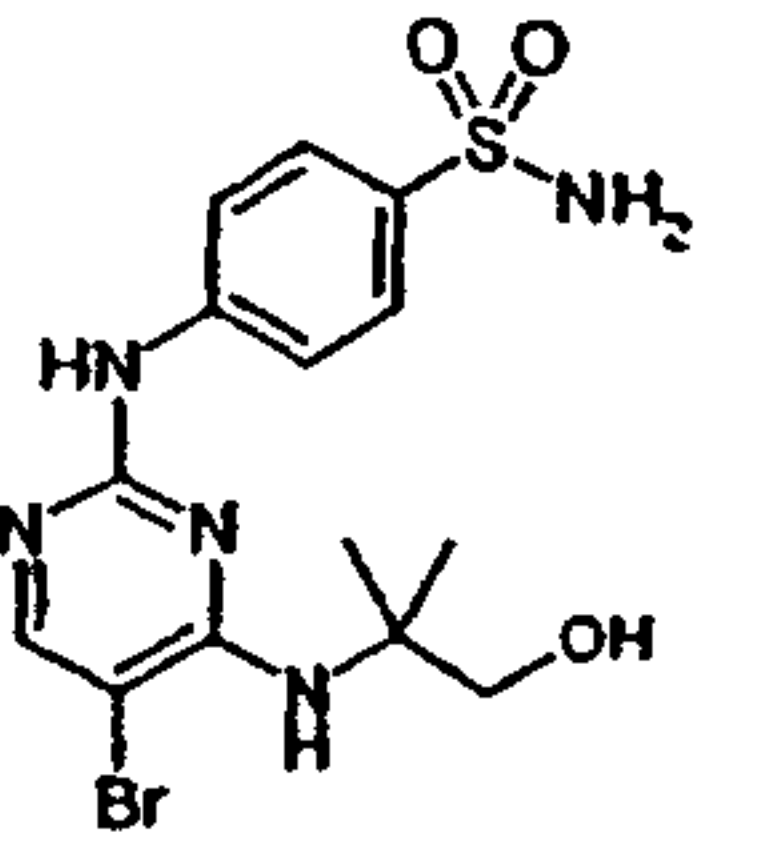
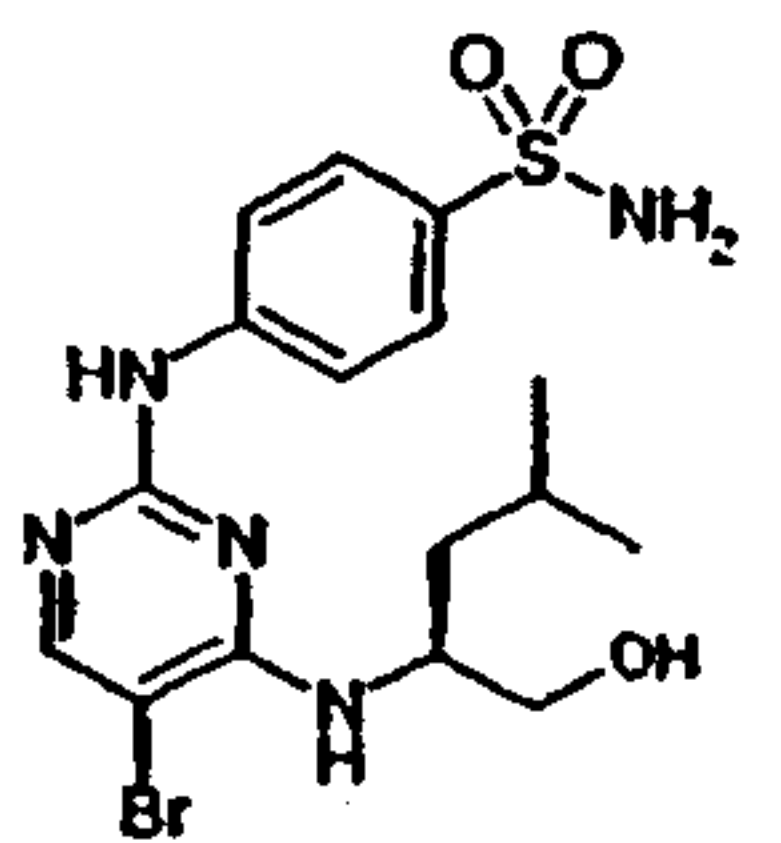
				
Beispiel Nr.	120	121	122	123
	9.65 (s,1H) 8.12 (s,1H) 7.89 (d,2H) 7.65 (d,2H) 7.15 (s,2H) 6.06 (d,1H) 4.71 (t,1H) 4.18 (m,1H) 3.67 (t,1H) 0.95 (s,9H)	9.68 (s,1H) 8.11 (s,1H) 7.93 (t,1H) 7.90 (d,2H) 7.65 (d,2H) 7.15 (s,2H) 7.07 (t,1H) 3.65 (m,2H) 3.56 (s,3H) 3.07 (q,2H) 2.45 (t,2H) 2.30 (t,2H) 1.65 (p,2H)	11.30 (s,1H) 8.11 (d,1H) 7.85 (d,2H) 7.72 (d,2H) 7.31 (s,2H) 6.71 (d,1H) 3.85 (m,8H)	10.79 (s,1H) 8.35 (s,1H) 8.25 (s,1H) 7.80 (s,4H) 7.30 (s,2H) 3.41 (m,2H) 2.22 (t,2H) 1.60 (m,4H) 1.30 (m,2H)
Aus- beute	49%	24%	80%	73%
Schmp.				252
Masse	445 (EI)	516 (EI)	334 (EI)	459 (EI)

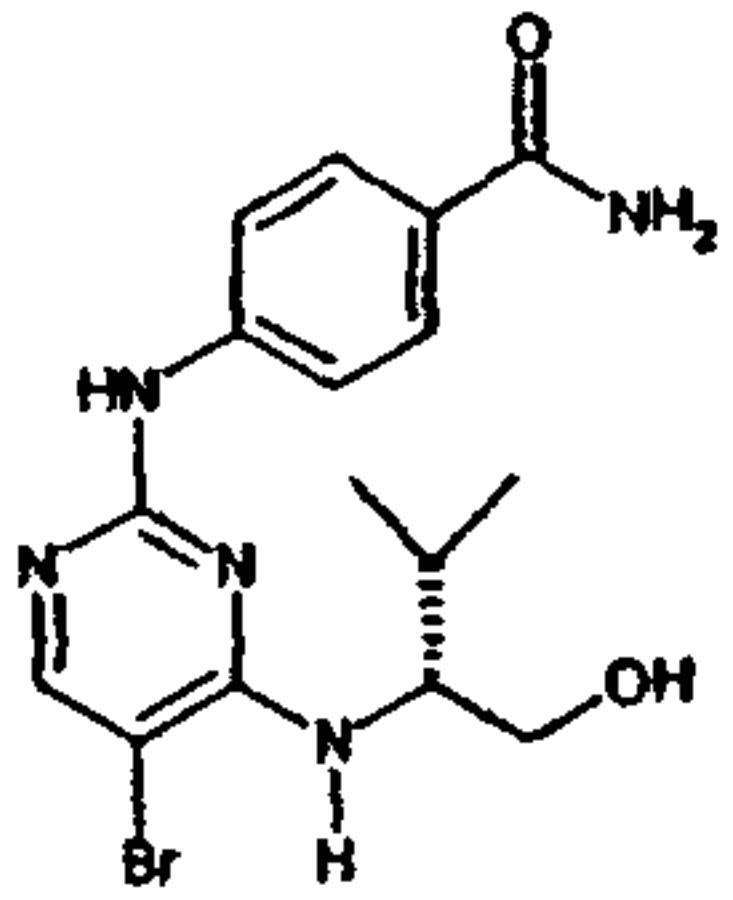
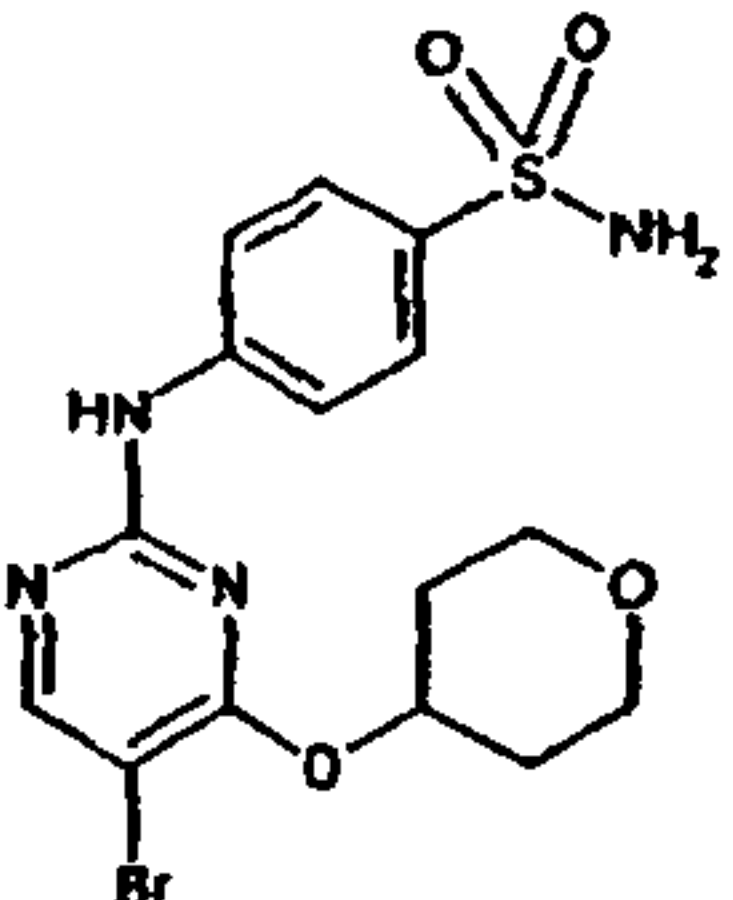
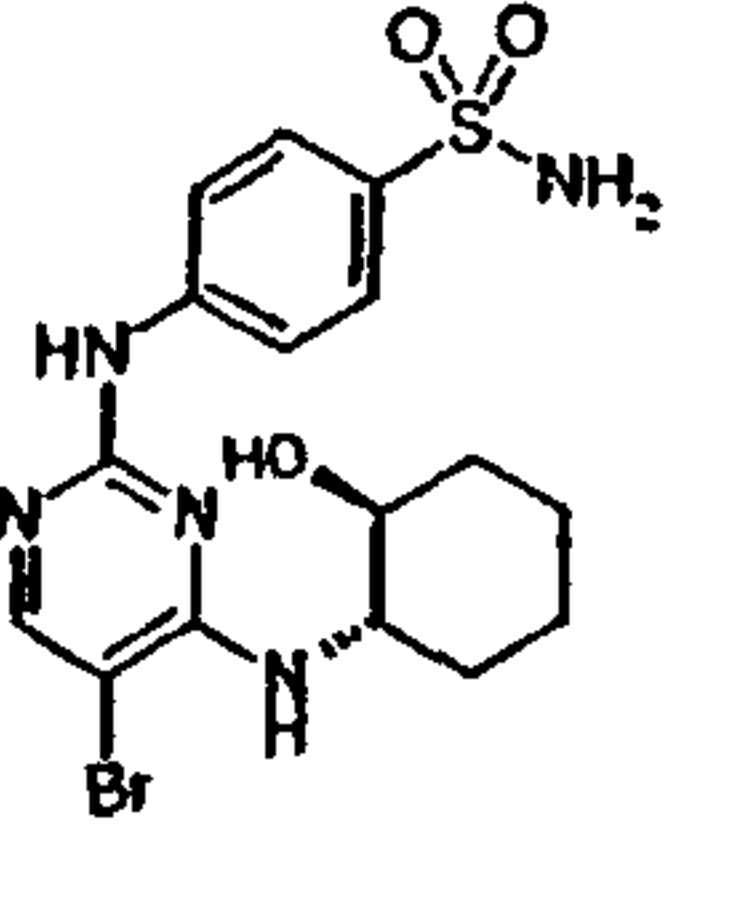
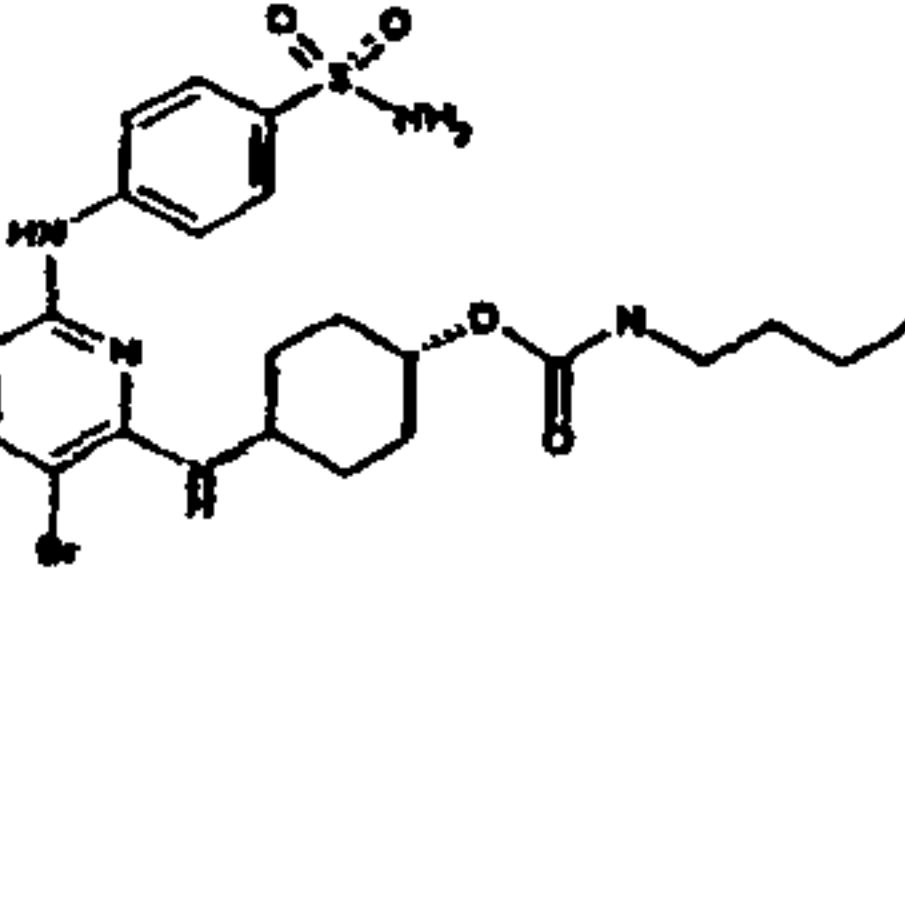
				
Beispiel Nr.	95	124	125	126
	11.19 (s, 1H) 8.37 (s, 1H) 8.11 (d, 1H) 7.80 (s, 4H) 7.31 (s, 2H) 3.91 (m, 1H) 1.89 (m, 4H) 1.67 (m, 1H) 1.55 (m, 2H) 1.34 (m, 2H) 1.15 (m, 1H)	9.62 (s, 1H) 8.04 (s, 1H) 7.88 (m, 3H) 7.66 (d, 2H) 7.13 (s, 3H) 3.58 (s, 3H) 3.40 (m, 2H) 3.05 (m, 2H) 2.25 (m, 2H) 2.05 (m, 2H) 1.60 (m, 5H) 1.32 (m, 3H)	9.62 (s, 1H) 8.04 (s, 1H) 7.86 (d, 2H) 7.66 (d, 2H) 7.12 (s, 3H) 3.58 (s, 3H) 3.40 (m, 2H) 2.30 (t, 2H) 1.60 (m, 4H) 1.32 (m, 2H)	10.91 (s, 1H) 8.38 (s, 1H) 7.83 (d, 2H) 7.77 (d, 2H) 7.28 (s, 2H) 7.04 (d, 1H) 6.40 (br, 3H) 4.35 (m, 1H) 3.87 (m, 1H) 3.60 (d, 2H) 3.41 (dd, 1H) 3.28 (dd, 1H)
Aus- beute	29%	25%	27%	46%
Schmp.	255		218	
Masse	425 (EI)	557 (ES)	471 (EI)	449 (EI)

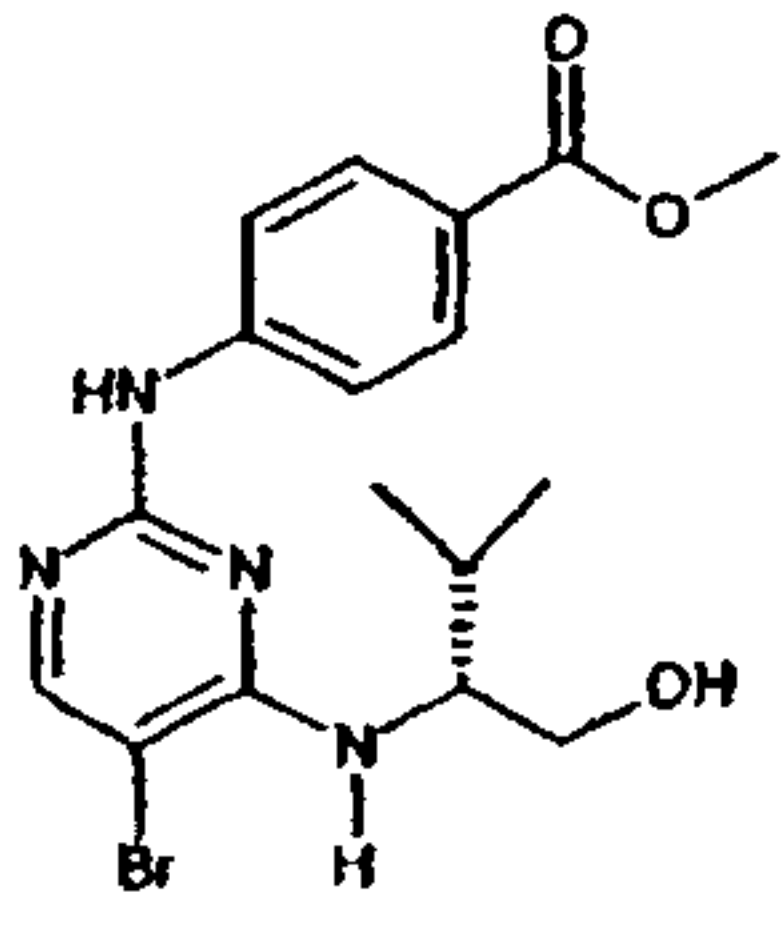
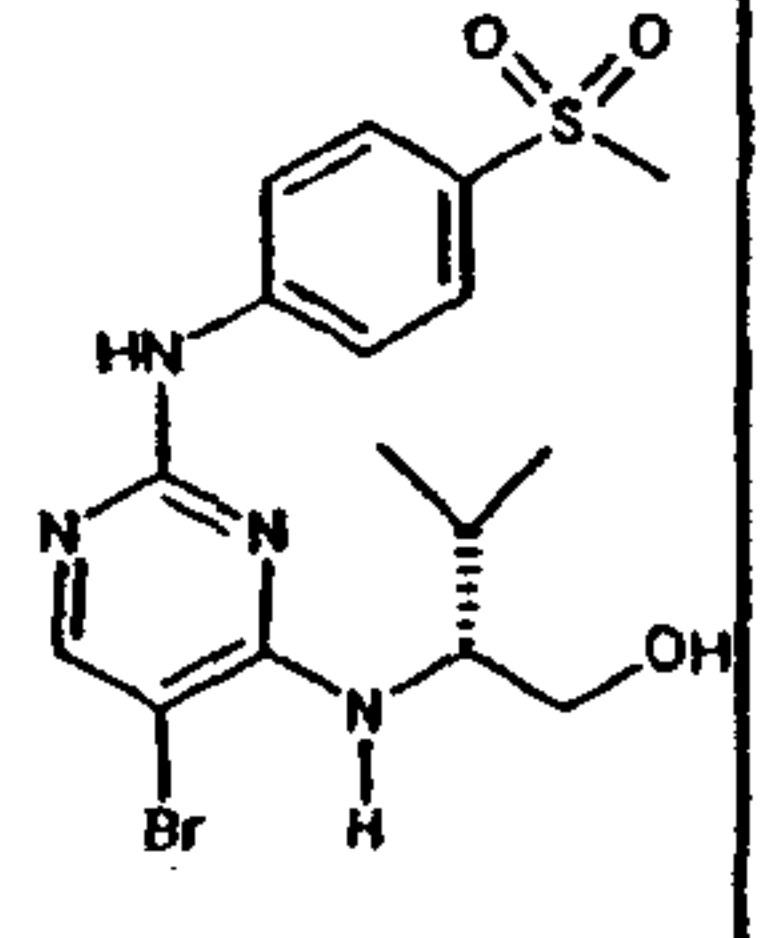
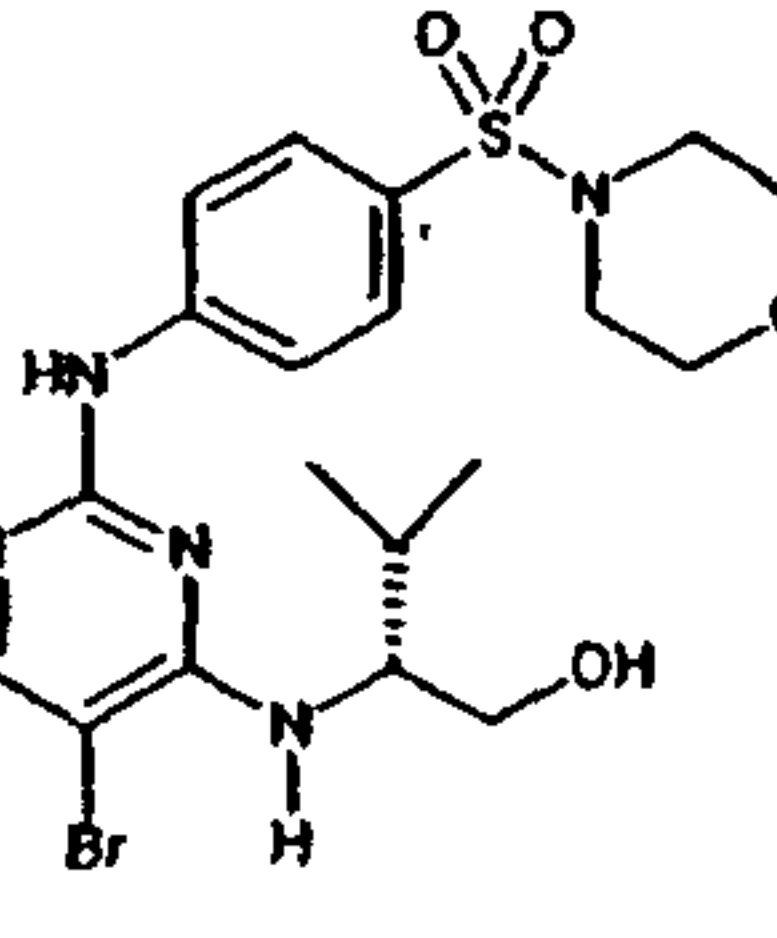
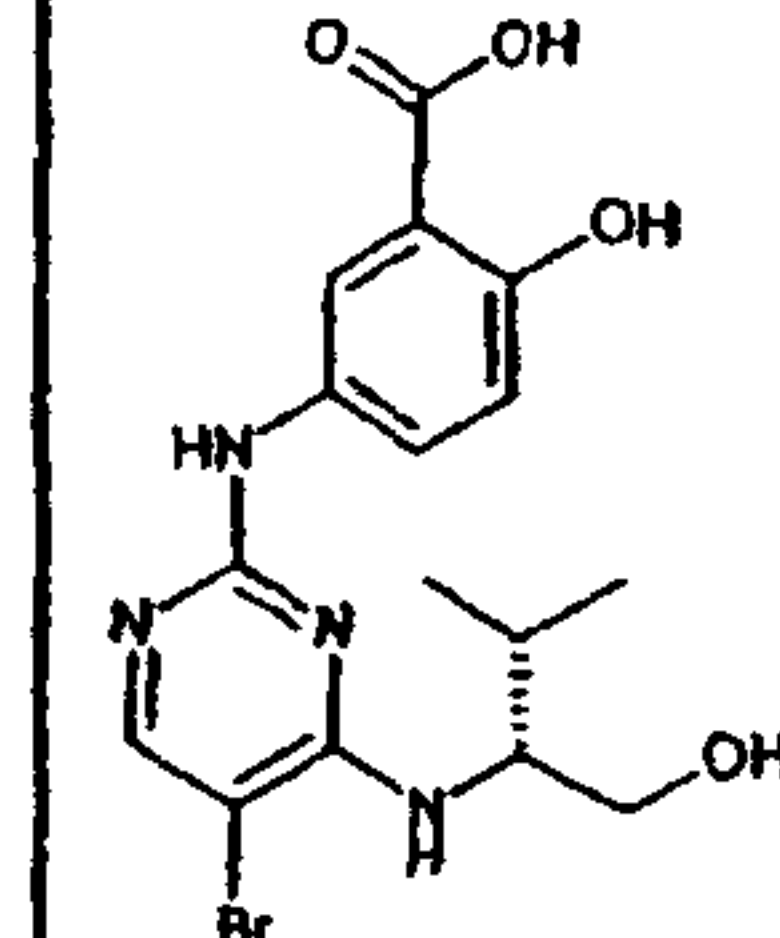
				
Beispiel Nr.	127	128	129	130
	9.96 (s,1H) 8.12 (s,1H) 7.85 (d,2H) 7.69 (d,2H) 7.20 (s,2H) 6.78 (d,1H) 4.35 (m,1H) 3.48 (m,2H) 1.65 (m,7H) 1.10 (m,6H)	9.60 (s,1H) 8.05 (s,1H) 7.90 (d,2H) 7.69 (d,2H) 7.42 (d,1H) 7.16 (m,3H) 4.57 (t,2H) 3.70 (m,1H) 3.4 (m,5H) 2.10 (t,2H) 1.55 (m,4H) 1.30 (m,2H)	9.67 (s,1H) 8.07 (s,1H) 7.87 (d,2H) 7.75 (d,2H) 7.13 (s,2H) 6.40 (d,1H) 4.91 (br,1H) 4.23 (m,1H) 3.52 (m,2H) 1.21 (d,3H)	9.65 (s,1H) 8.08 (s,1H) 7.87 (d,2H) 7.64 (d,2H) 7.14 (s,2H) 6.53 (d,1H) 4.62 (d,1H) 3.90 (br,1H) 3.40 (br,1H) 1.88 (m,4H) 1.50 (m,2H) 1.30 (m,2H)
Aus- beute	18%	94%	61%	58%
Schmp.	220		259	262
Masse	485 (EI)	531 (ES)	403 (EI)	443 (EI)

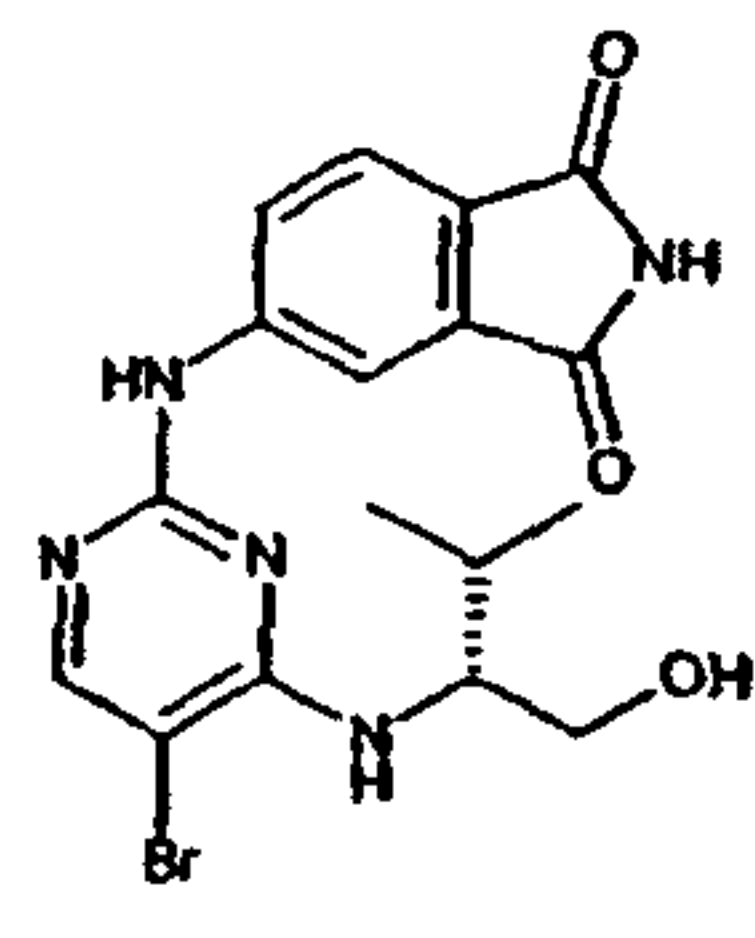
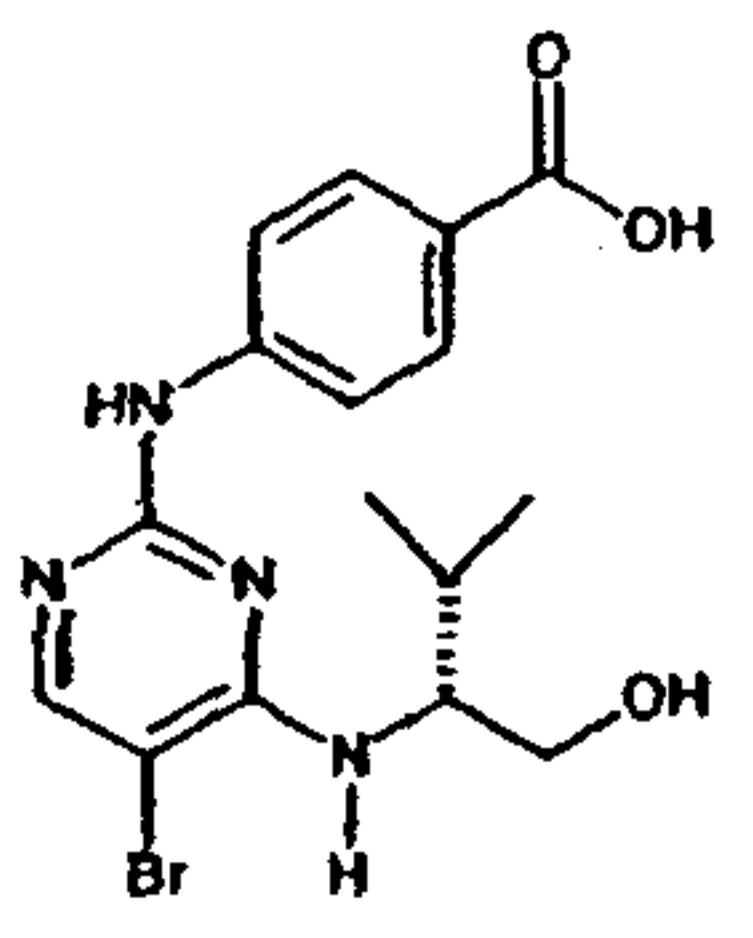
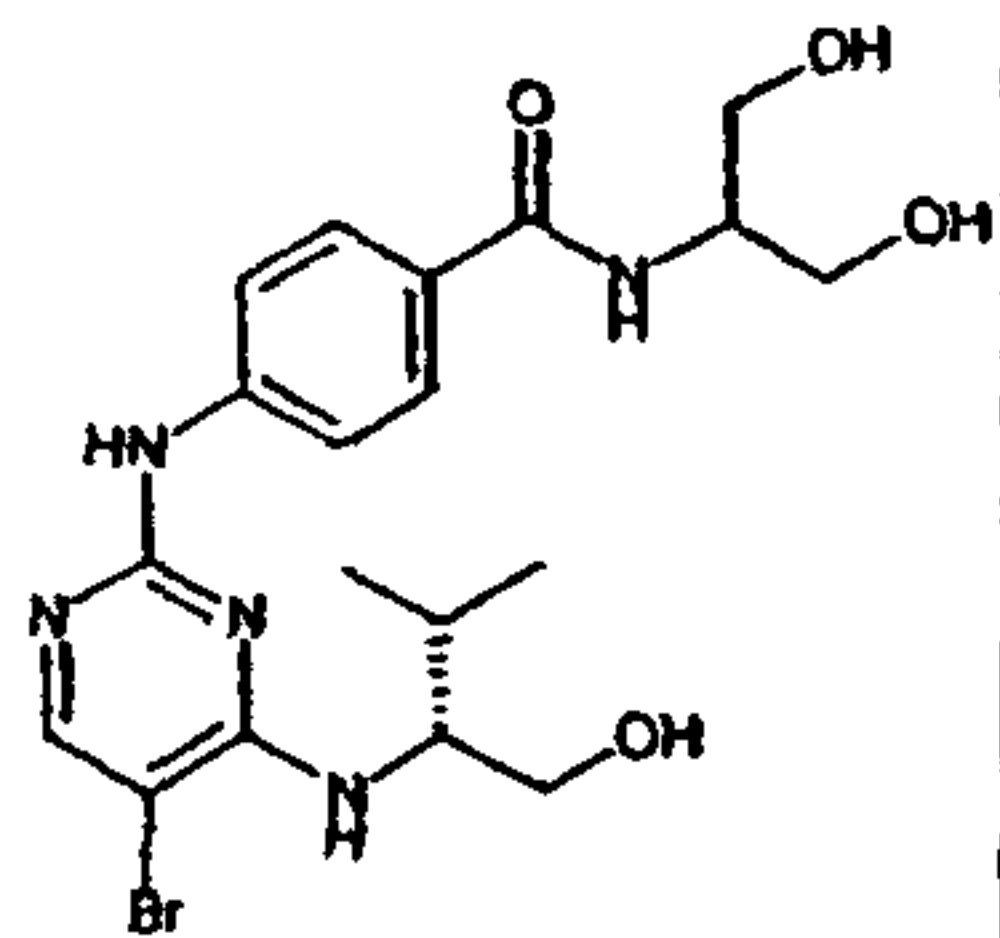
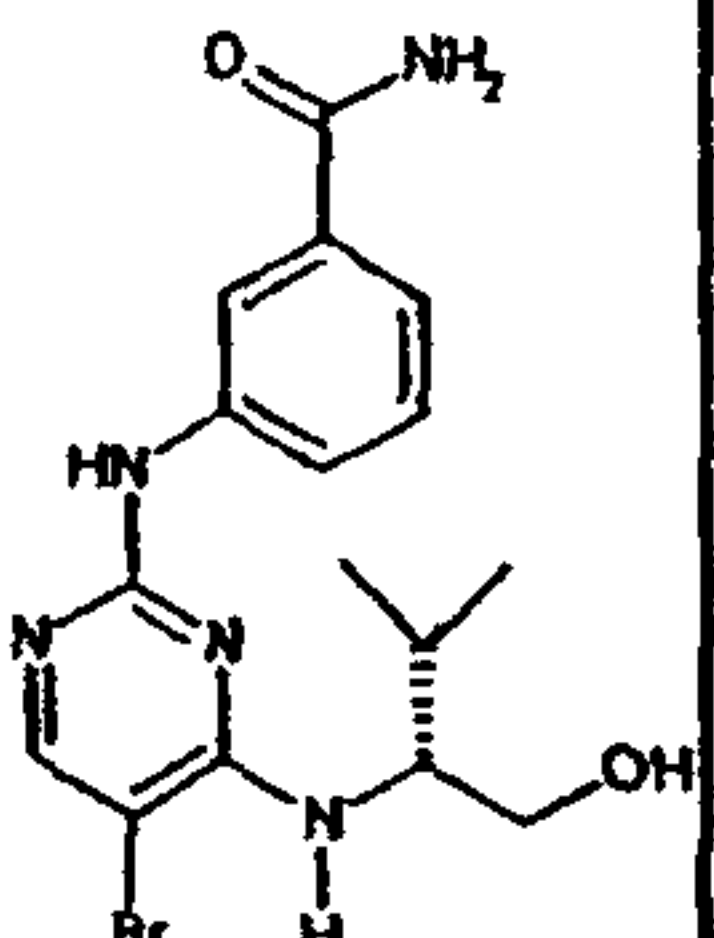
				
Beispiel Nr.	131	132	133	134
	9.62 (s,1H) 8.08 (s,1H) 7.92 (d,2H) 7.67 (d,2H) 7.23 (s,2H) 6.75 (t,1H) 3.22 (d,2H) 1.95 (s,3H) 1.60 (m,12H)	9.70 (s,1H) 8.11 (s,1H) 7.90 (d,2H) 7.60 (d,2H) 7.21 (q,1H) 5.25 (d,1H) 4.77 (t,1H) 4.02 (m,1H) 3.60 (m,2H) 2.39 (d,3H) 2.02 (m,1H) 0.95 (dd,6H)	9.69 (s,1H) 8.11 (s,1H) 7.88 (d,2H) 7.66 (d,2H) 7.15 (s,2H) 6.52 (d,1H) 4.35 (dd,1H) 2.29 (m,1H) 1.07 (d,3H) 0.91 (d,3H)	10.85 (s,1H) 8.31 (s,1H) 7.90 (d,1H) 7.85 (d,2H) 7.75 (d,2H) 7.54 (s,1H) 3.90 (m,1H) 3.38 (t,2H) 2.78 (br,2H) 1.50 (m,11H)
Aus- beute	9%	42%	25%	64%
Schmp.	229	141		
Masse	491 (EI)	443 (EI)	444 (FAB)	

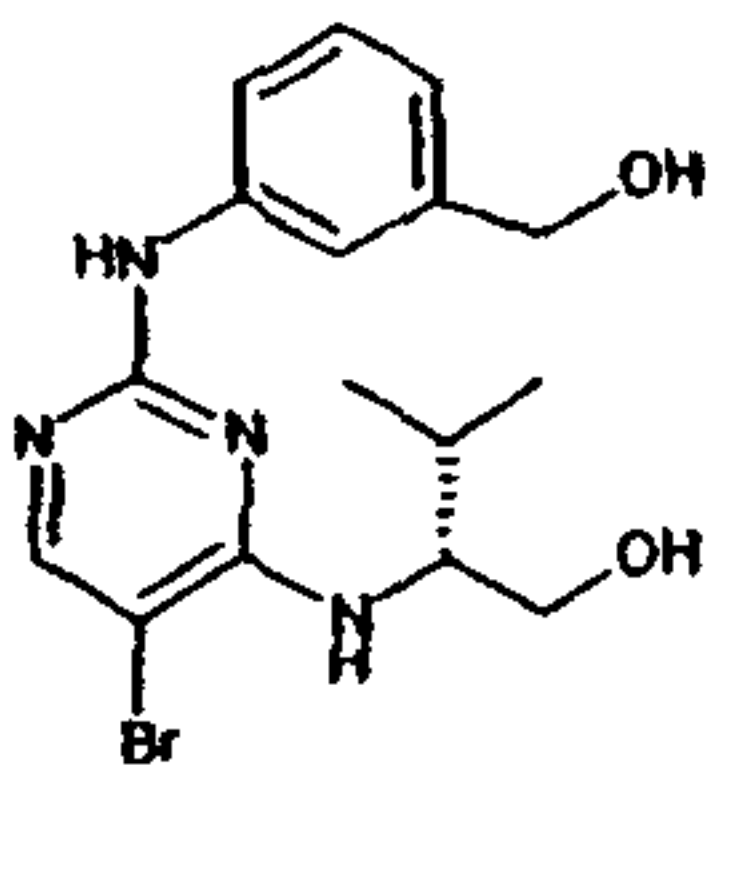
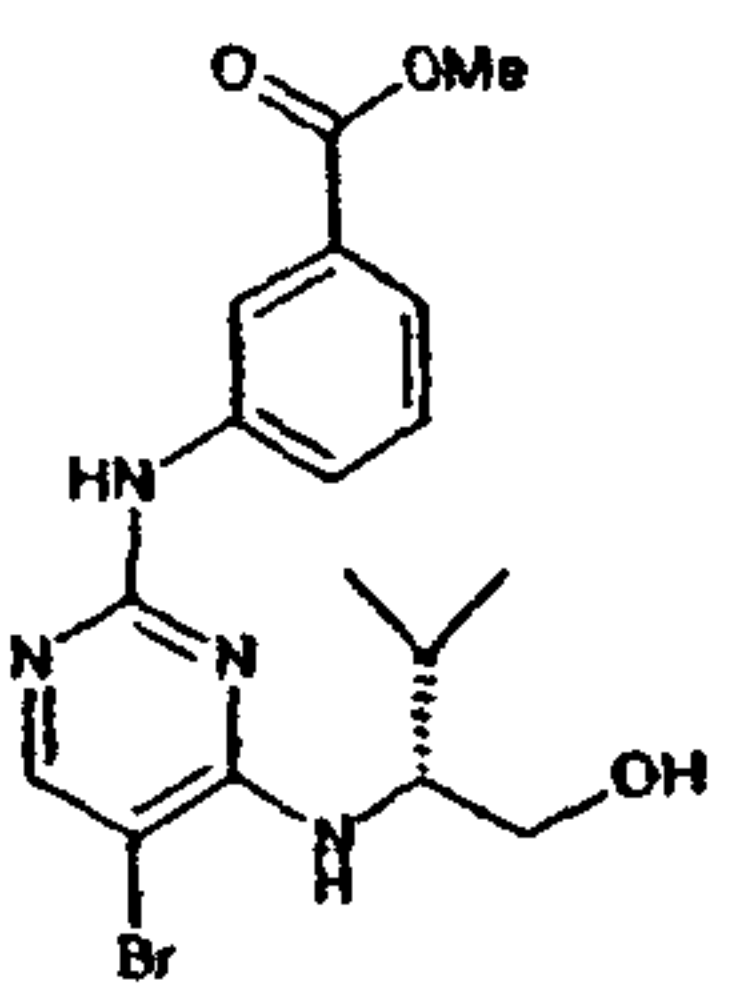
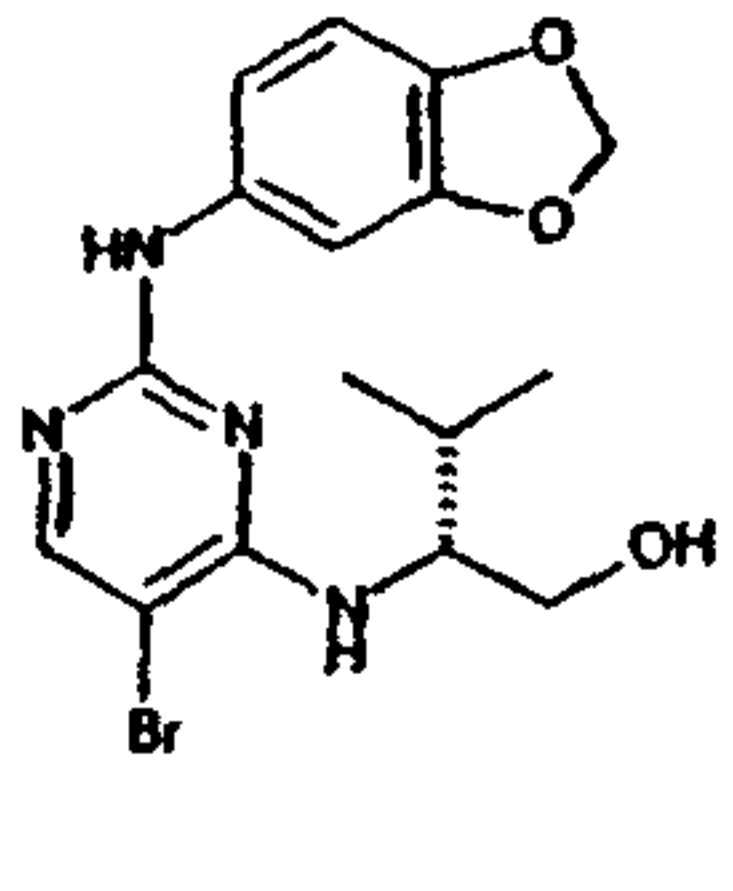
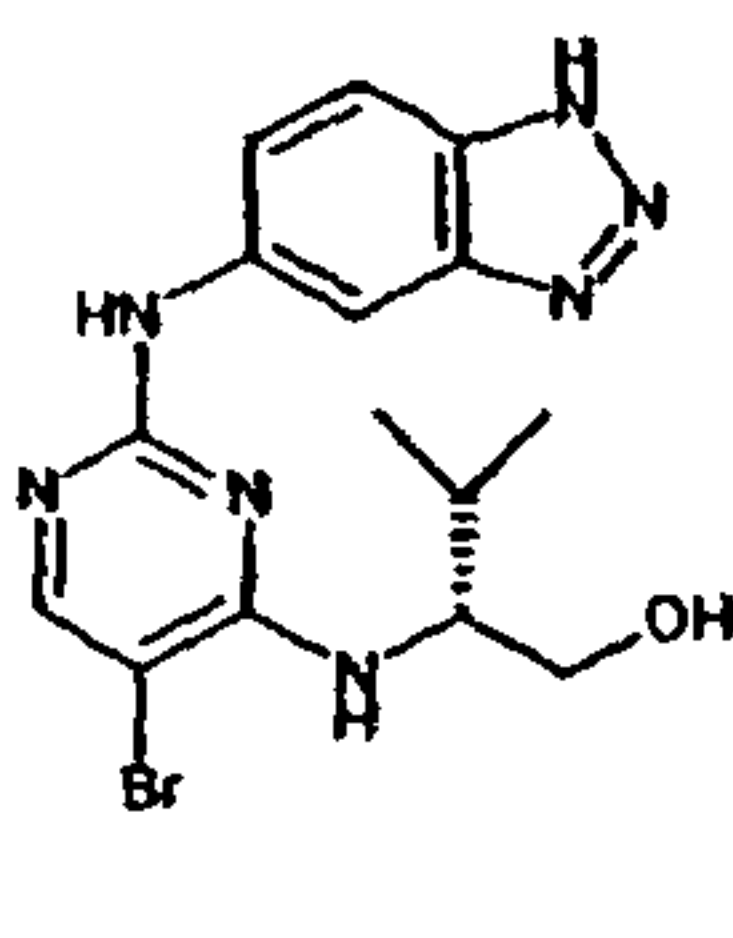
				
Beispiel Nr.	135	136	137	138
	10.01 (s,1H) 8.28 (s,1H) 7.81 (d,2H) 7.71 (t,1H) 7.63 (d,2H) 7.45 (br,1H) 4.34 (dt,2H) 3.32 (t,2H) 2.71 (br,2H)	9.70 (s,1H) 8.11 (s,1H) 7.90 (d,2H) 7.64 (d,2H) 7.35 (t,1H) 6.55 (d,1H) 4.65 (t,1H) 4.45 (m,1H) 3.53 (m,1H) 3.44 (m,6H) 2.75 (q,2H) 1.20 (d,3H)	9.65 (s,1H) 9.58 (s,1H) 8.10 (s,1H) 7.85 (d,2H) 7.68 (d,2H) 7.40 (m,2H) 7.18 (m,4H) 6.94 (t,1H) 6.75 (d,1H) 4.40 (m,3H) 2.05 (m,1H) 0.96 (dd,6H)	9.70 (s,1H) 8.10 (s,1H) 7.89 (d,2H) 7.63 (d,2H) 7.39 (t,1H) 6.68 (d,1H) 4.34 (dd,1H) 3.36 (m,3H) 2.25 (q,2H) 2.29 (m,1H) 1.05 (dd,6H)
Aus- beute	34%	53%	59%	57%
Schmp.				
Masse	570 (ES)	460 (ES)	549 (ES)	488 (ES)

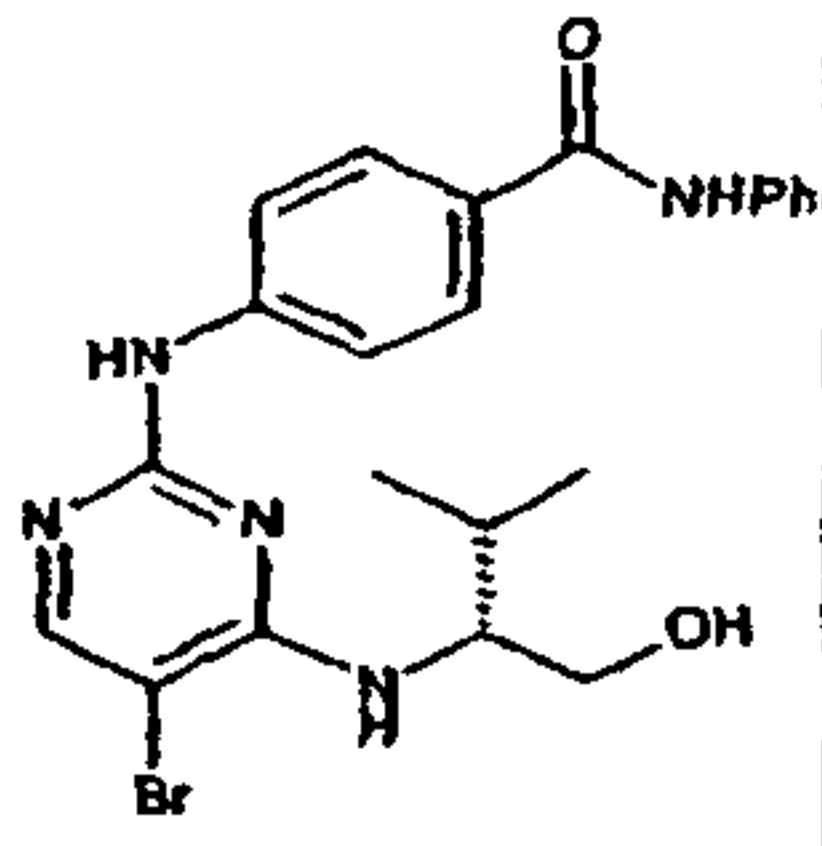
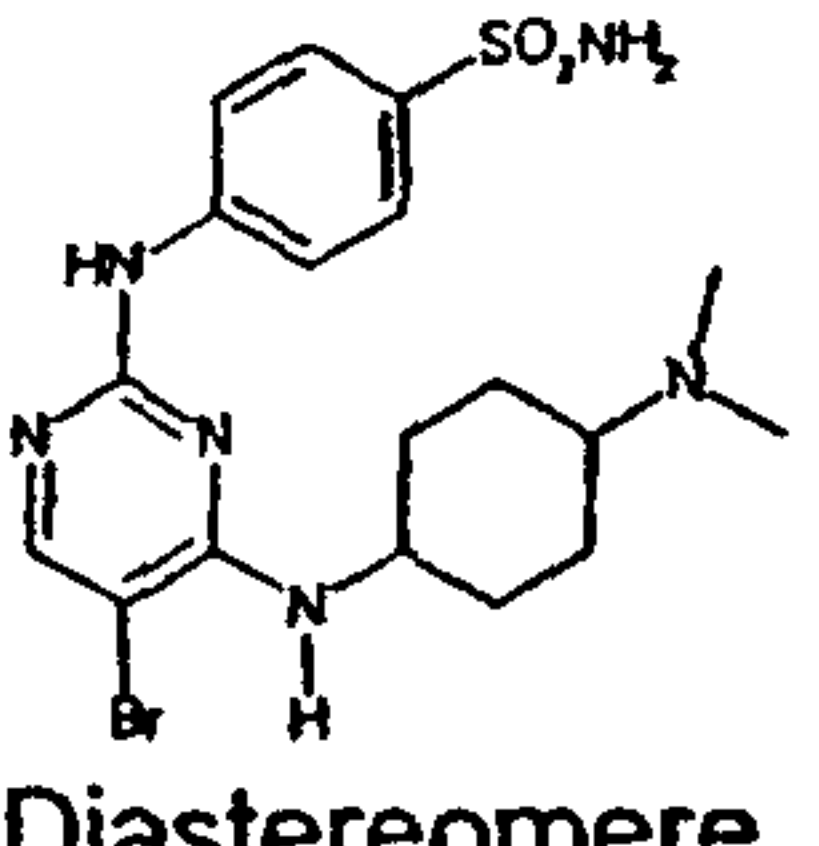
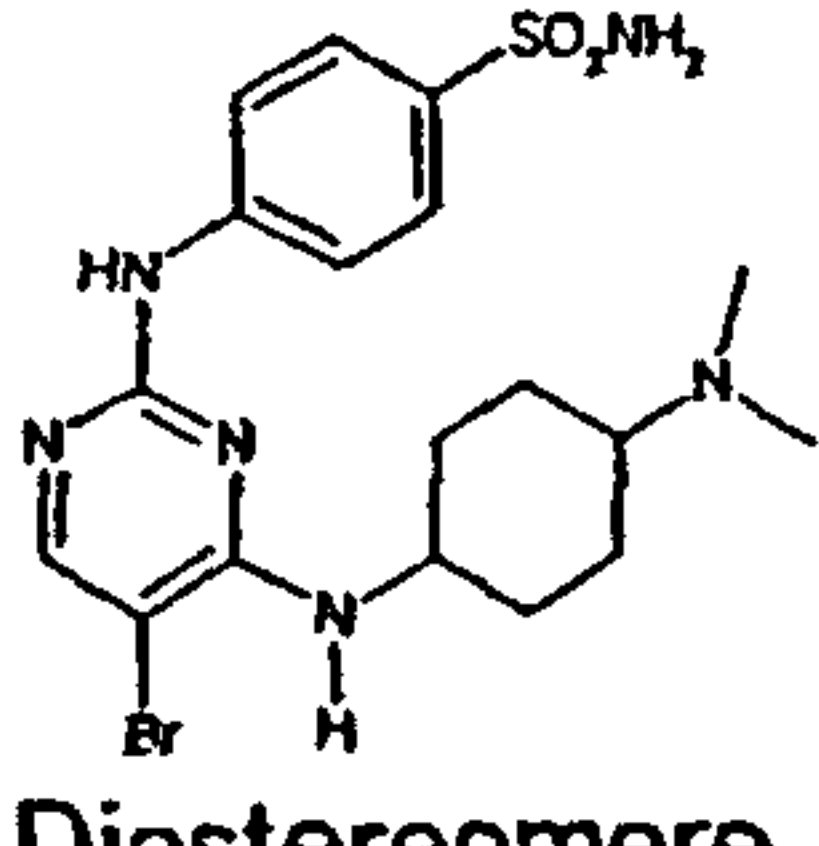
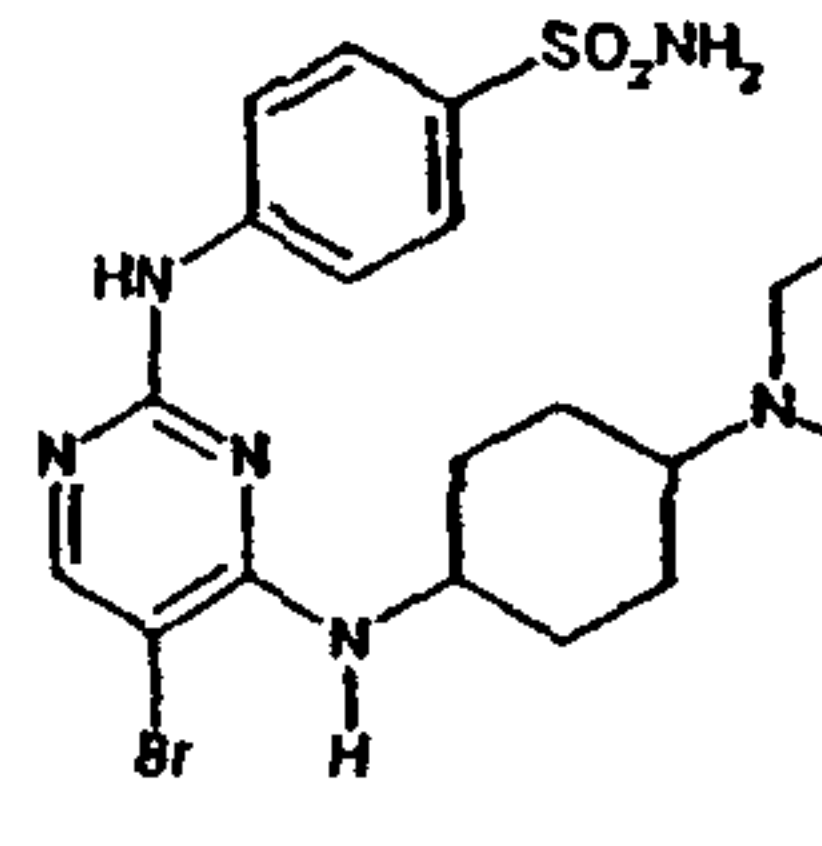
				
Beispiel Nr.	139	140	141	142
	9.82 (s,1H) 8.15 (s,1H) 7.82 (d,2H) 7.64 (d,2H) 7.39 (t,1H) 6.55 (d,1H) 4.64 (t,1H) 4.50 (t,1H) 3.65 (s,3H) 3.4 (m,2H) 2.75 (m,2H) 2.35 (m,1H) 1.00 (dd,6H)	9.82 (s,1H) 8.08 (s,1H) 7.96 (d,2H) 7.75 (t,1H) 7.62 (d,2H) 7.30 (t,1H) 4.64 (t,1H) 4.14 (m,2H) 3.35 (m,2H) 3.16 (m,1H) 2.75 (q,2H)	9.58 (s,1H) 8.12 (s,1H) 7.83 (d,2H) 7.68 (d,2H) 7.15 (s,2H) 5.92 (s,1H) 5.28 (t,1H) 3.50 (d,2H) 1.42 (s,6H)	9.62 (s,1H) 8.07 (s,1H) 7.87 (d,2H) 7.67 (d,2H) 7.14 (s,2H) 6.36 (d,1H) 4.81 (t,1H) 4.32 (m,1H) 3.47 (m,2H) 1.52 (m,3H) 0.90 (d,3H) 0.86 (d,3H)
Aus- beute	20%	63%	23%	8%
Schmp.				
Masse	502 (ES)	382 (ES)	415 (EI)	443 (EI)

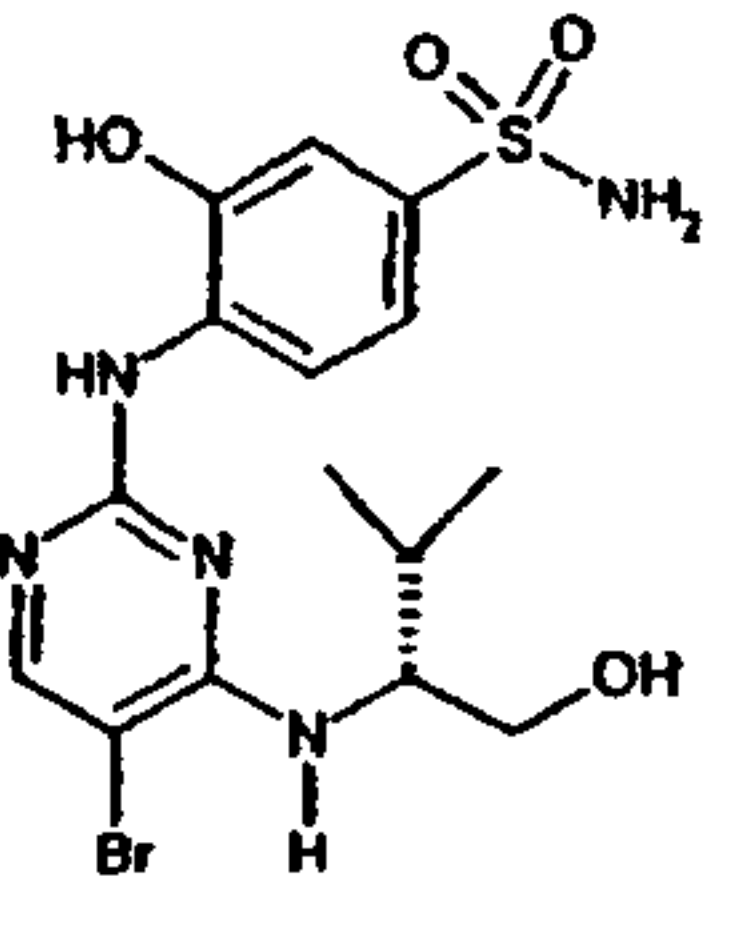
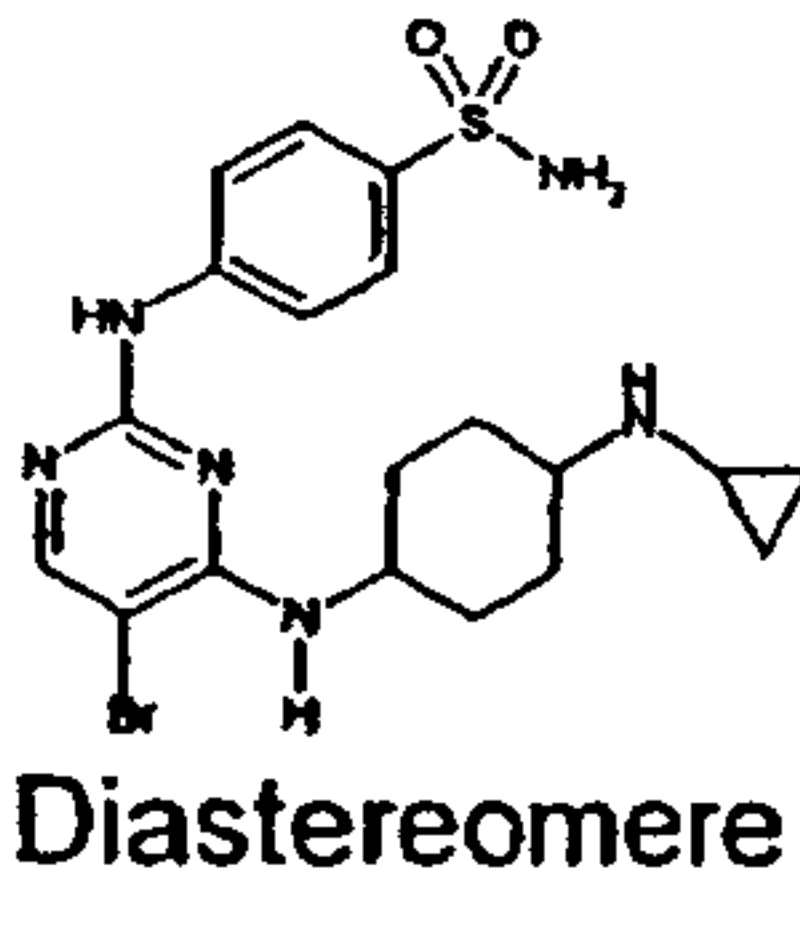
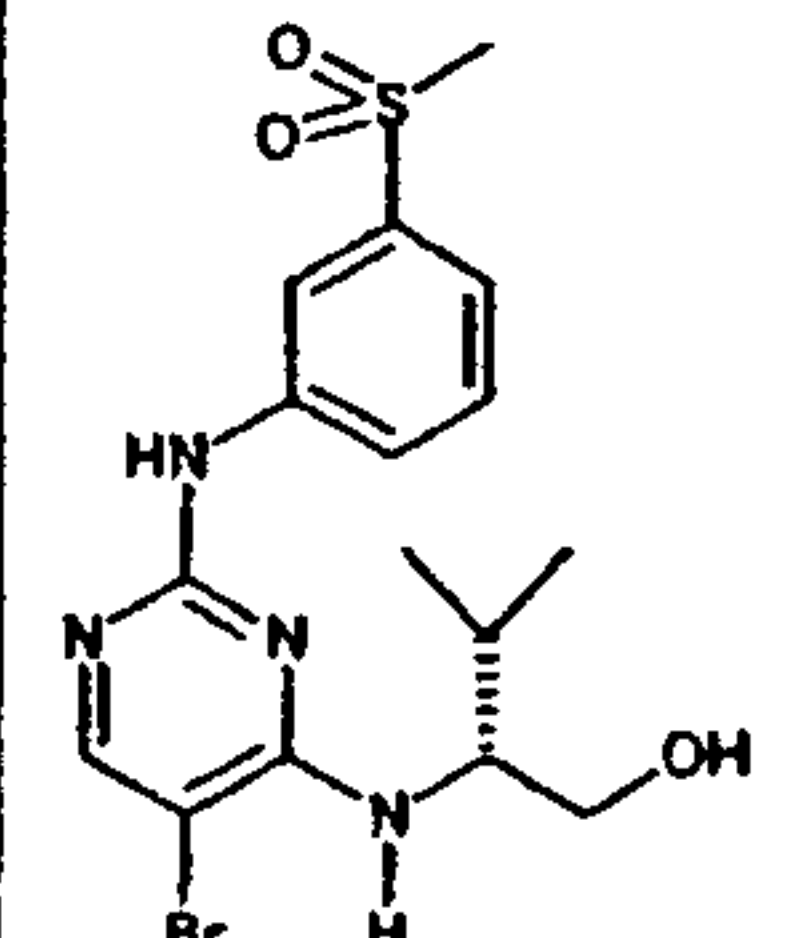
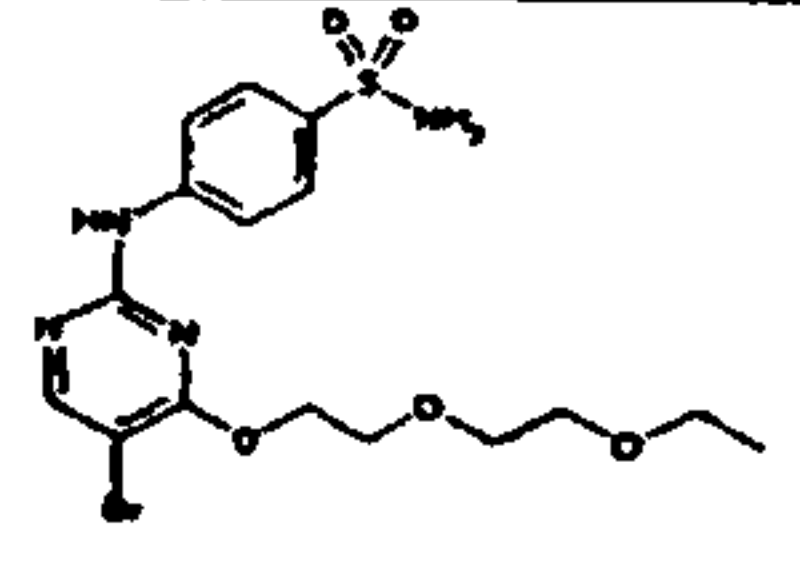
				
Beispiel Nr.	143	144	145	78
	10.6 (s,1H) 8.28 (s,1H) 8.30 (m,5H) 7.48 (d,1H) 7.20 (s,1H) 4.05 (br,1H) 3.60 (br,2H) 2.01 (m,1H) 0.90 (m,6H)	10.11 (s,1H) 8.45 (s,1H) 7.86 (d,2H) 7.78 (d,2H) 7.15 (br,2H) 5.32 (m,1H) 3.91 (m,2H) 3.53 (m,2H) 2.05 (m,2H) 1.70 (m,2H)	11.05 (s,1H) 8.32 (s,1H) 8.08 (d,1H) 7.80 (m,4H) 7.30 (br,2H) 3.88 (m,1H) 3.65 (m,1H) 1.95 (m,2H) 1.69 (m,2H) 1.35 (m,4H)	9.69 (s,1H) 8.06 (s,1H) 7.88 (d,2H) 7.63 (d,2H) 7.18 (s,2H) 7.10 (t,1H) 6.65 (d,1H) 4.47 (m,1H) 3.97 (m,1H) 2.98 (m,2H) 2.00 (m,4H) 1.40 (m,8H) 0.85 (t,3H)
Aus- beute	13%	47%	42%	20%
Schmp.				
Masse	392 (EI)	428 (EI)	441 (EI)	541 (ES)

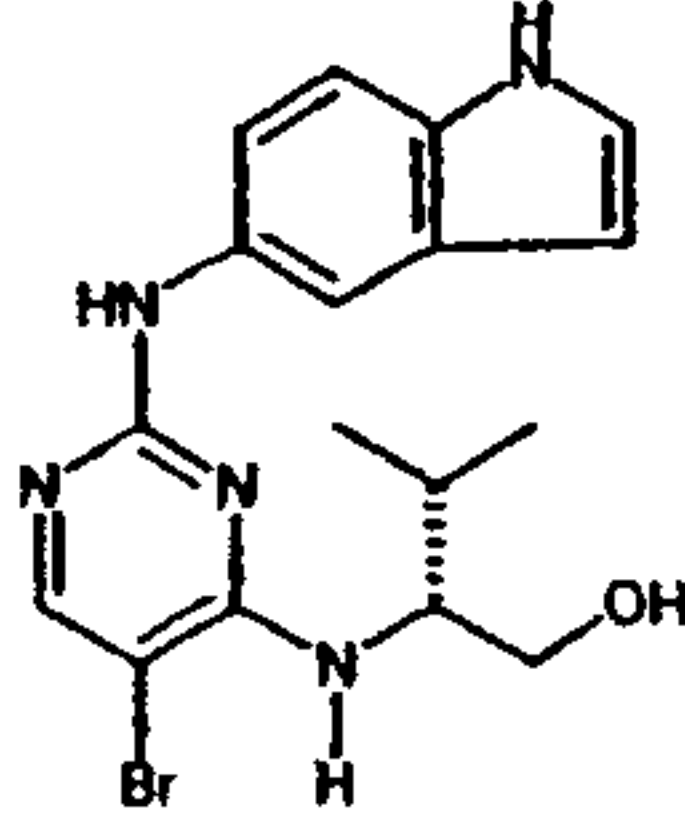
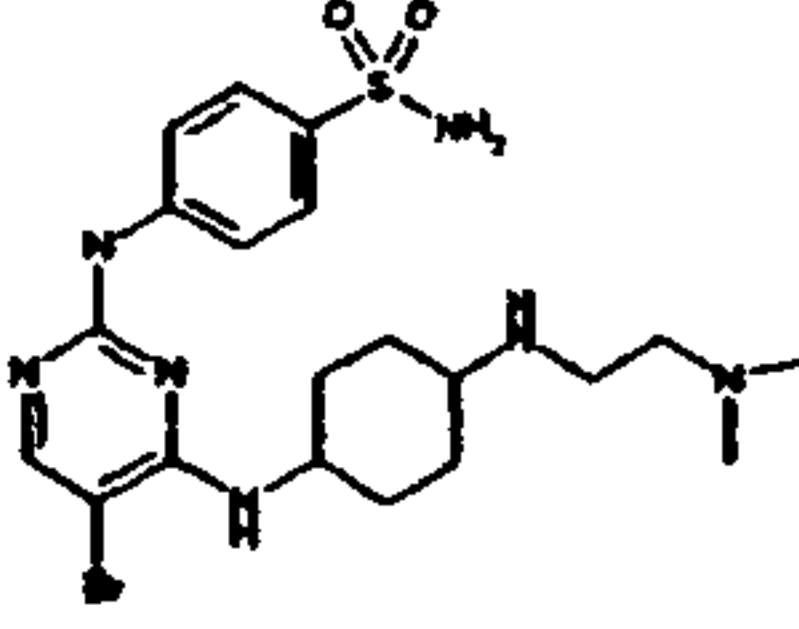
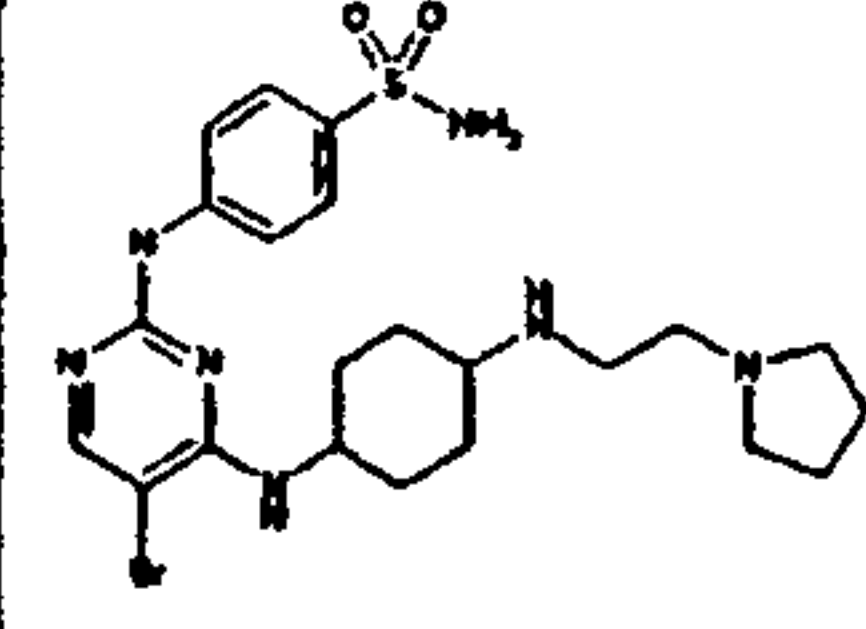
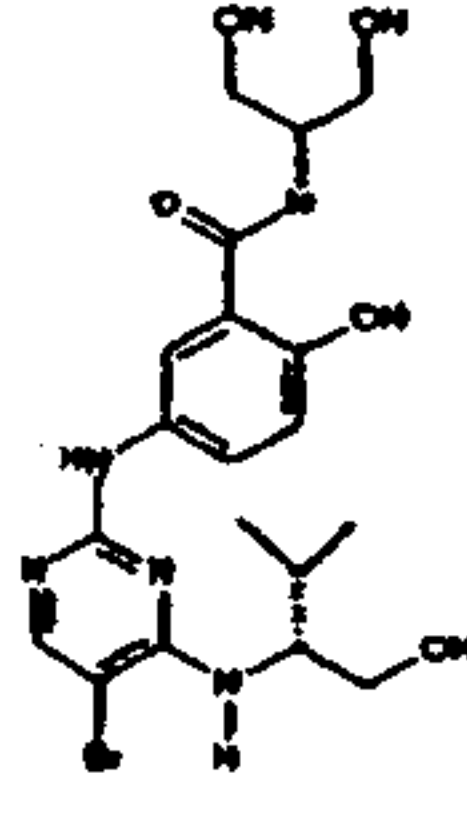
				
Beispiel Nr.	146	147	148	149
	11.13 (s,1H) 8.38 (s,1H) 7.92 (d,2H) 7.75 (m,3H) 4.04 (m,1H) 3.80 (s,3H) 3.65 (m,2H) 2.00 (m,1H) 0.96 (d,3H) 0.89 (d,3H)	11.18 (s,1H) 8.35 (s,1H) 7.90 (s,4H) 7.62 (d,1H) 4.02 (m,1H) 3.62 (m,2H) 3.02 (s,3H) 2.00 (m,1H) 0.95 (d,3H) 0.89 (d,3H)	11.15 (s,1H) 8.35 (s,1H) 7.90 (d,2H) 7.65 (m,3H) 4.01 (m,1H) 3.60 (m,6H) 2.85 (m,4H) 2.00 (m,1H) 0.95 (d,3H) 0.85 (d,3H)	9.19 (s,1H) 8.30 (s,1H) 8.02 (s,1H) 7.62 (m,1H) 6.85 (d,1H) 6.05 (d,1H) 4.03 (m,1H) 3.56 (m,2H) 1.96 (m,1H) 0.97 (d,3H) 0.90 (d,3H)
Aus- beute	86%	33%	79%	42%
Schmp.	225	211	232	241
Masse	408 (EI)	428 (EI)	501 (EI)	411 (ES)

				
Beispiel Nr.	150	151	152	153
	11.19 (s,1H) 10.80 (s,1H) 8.30 (m,2H) 7.85 (d,1H) 7.72 (d,1H) 7.20 (d,1H) 4.02 (m,1H) 3.60 (m,2H) 2.00 (m,1H) 1.01 (d,3H) 0.90 (d,3H)	10.96 (s,1H) 8.35 (s,1H) 7.95 (m,2H) 7.65 (m,3H) 4.04 (m,1H) 3.62 (m,2H) 2.00 (m,1H) 0.90 (M,6H)	9.50 (s,1H) 8.08 (s,1H) 7.75 (m,5H) 6.17 (d,1H) 4.80 (br,1H) 4.64 (br,2H) 4.05 (m,1H) 3.94 (m,1H) 3.52 (m,6H) 2.01 (m,1H) 0.93 (dd,6H)	12.90 (s,1H) 9.45 (s,1H) 8.52 (s,1H) 8.05 (s,1H) 7.82 (d,1H) 7.50 (d,1H) 7.32 (t,1H) 6.11 (d,1H) 4.72 (s,1H) 4.10 (s,1H) 3.60 (m,2H) 2.01 (m,1H) 0.99 (d,3H) 0.92 (d,3H)
Aus- beute	27%	65%	85%	9%
Schmp.				231
Masse	420 (ES)	395 (ES)	468 (ES)	395 (ES)

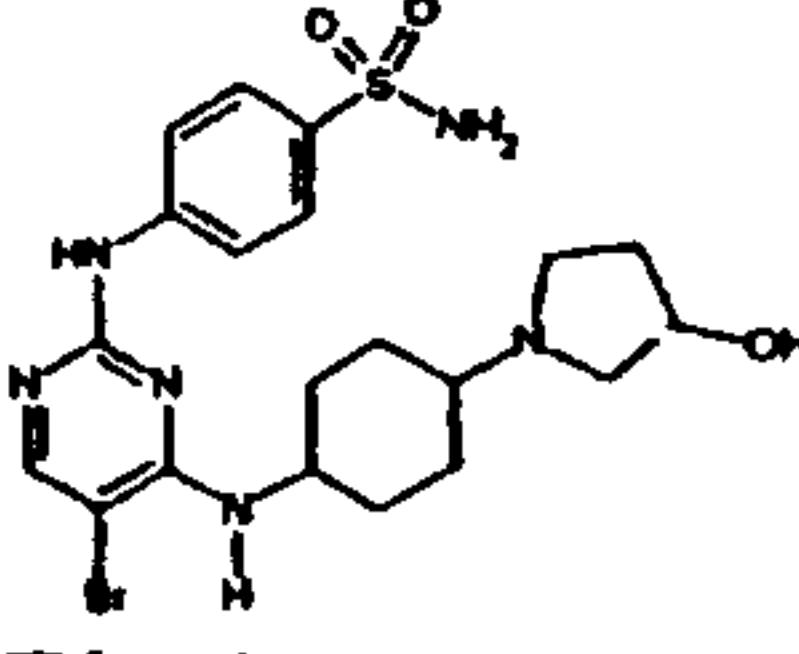
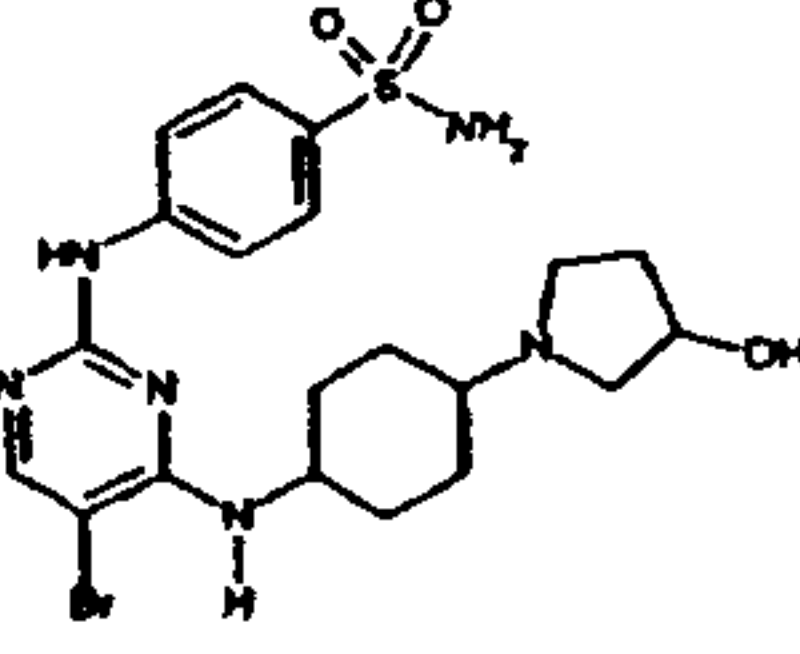
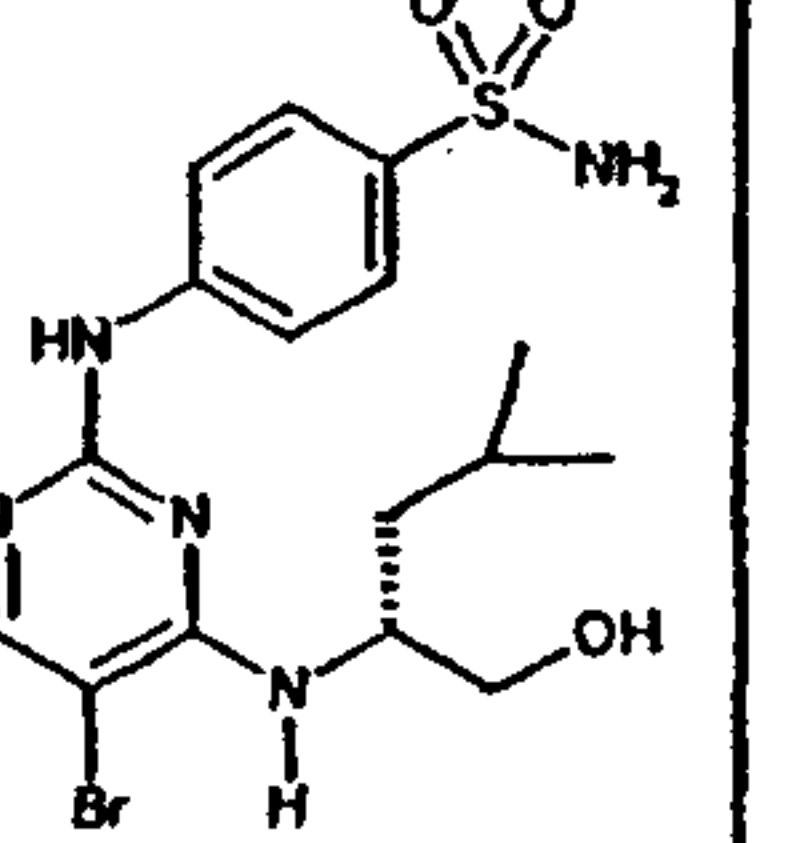
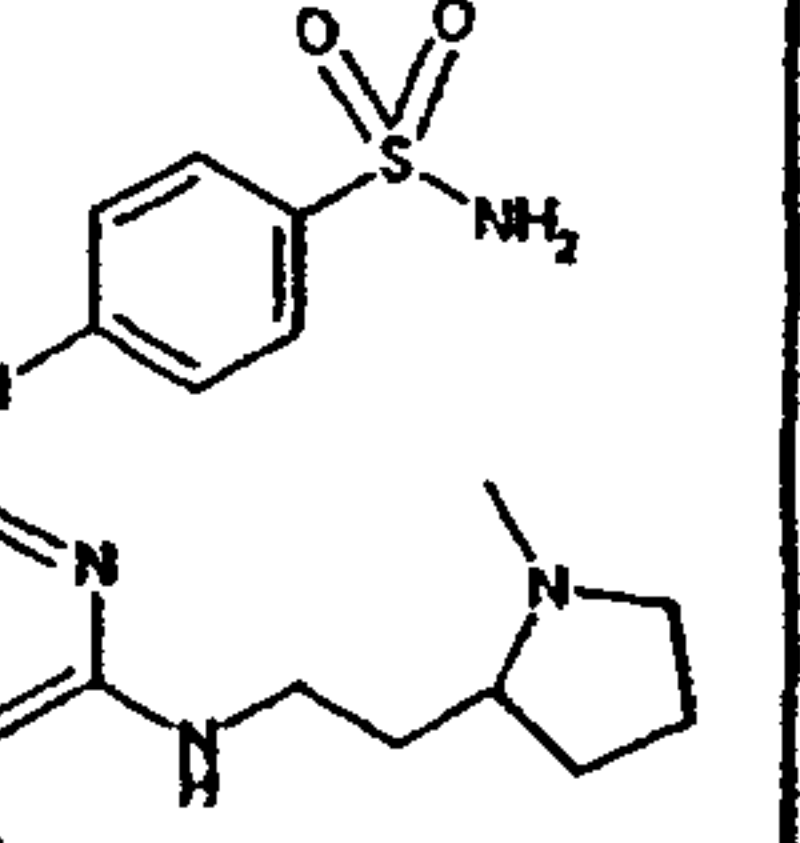
				
Beispiel Nr.	154	155	156	157
	10.91 (s,1H) 8.38 (s,1H) 7.90 (d,1H) 7.80 (m,4H) 7.05 (d,1H) 4.50 (s,2H) 4.04 (m,1H) 3.62 (m,2H) 1.96 (m,1H) 0.93 (d,3H) 0.85 (d,3H)	11.05 (s,1H) 8.34 (m,2H) 7.75 (m,3H) 7.52 (t,1H) 4.04 (m,1H) 3.85 (s,3H) 3.65 (m,2H) 2.00 (m,1H) 0.94 (d,3H) 0.85 (d,3H)	10.51 (s,1H) 8.22 (s,1H) 7.71 (d,1H) 7.27 (m,1H) 6.86 (m,2H) 6.06 (s,2H) 3.96 (m,1H) 3.62 (m,2H) 1.99 (m,1H) 0.90 (m,6H)	15.50 (s,1H) 9.50 (s,1H) 8.40 (s,1H) 8.11 (s,1H) 7.80 (d,1H) 7.53 (d,1H) 6.16 (d,1H) 4.78 (br,1H) 4.03 (m,1H) 3.60 (m,2H) 2.01 (m,1H) 0.91 (dd,6H)
Aus- beute	90%	48%	77%	21%
Schmp.	170	181	177	196
Masse	381 (ES)	409 (ES)	394 (EI)	391 (EI)

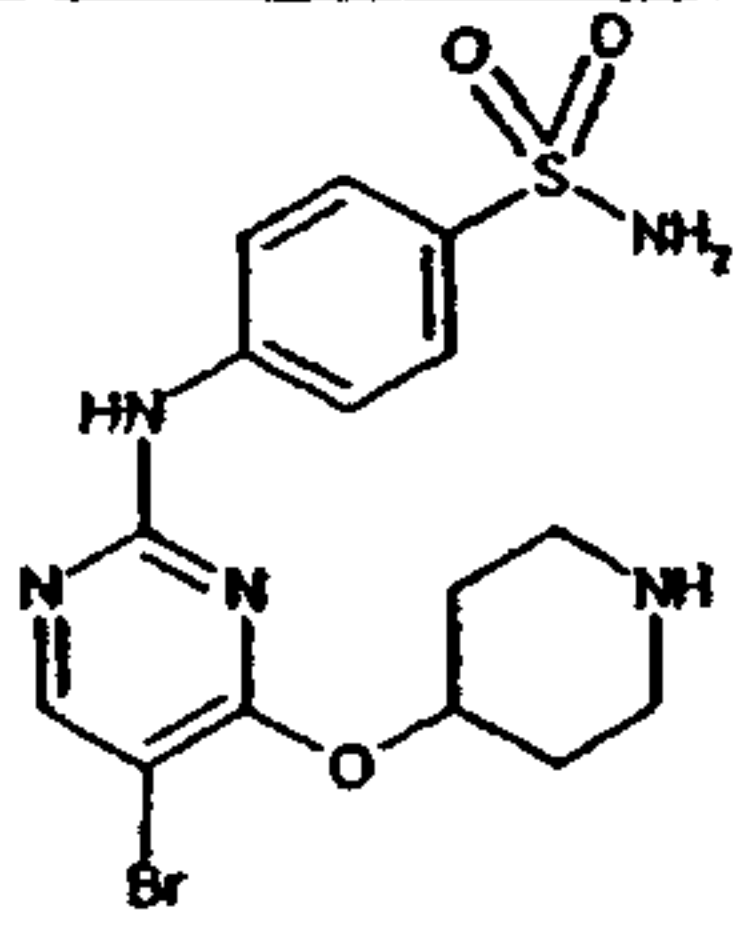
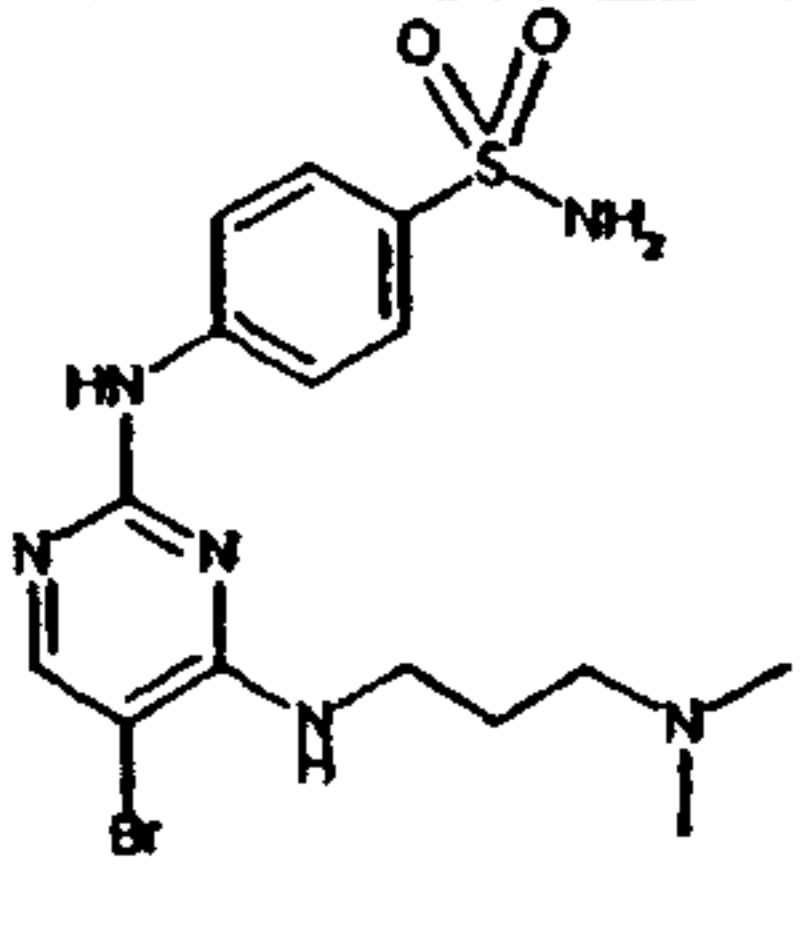
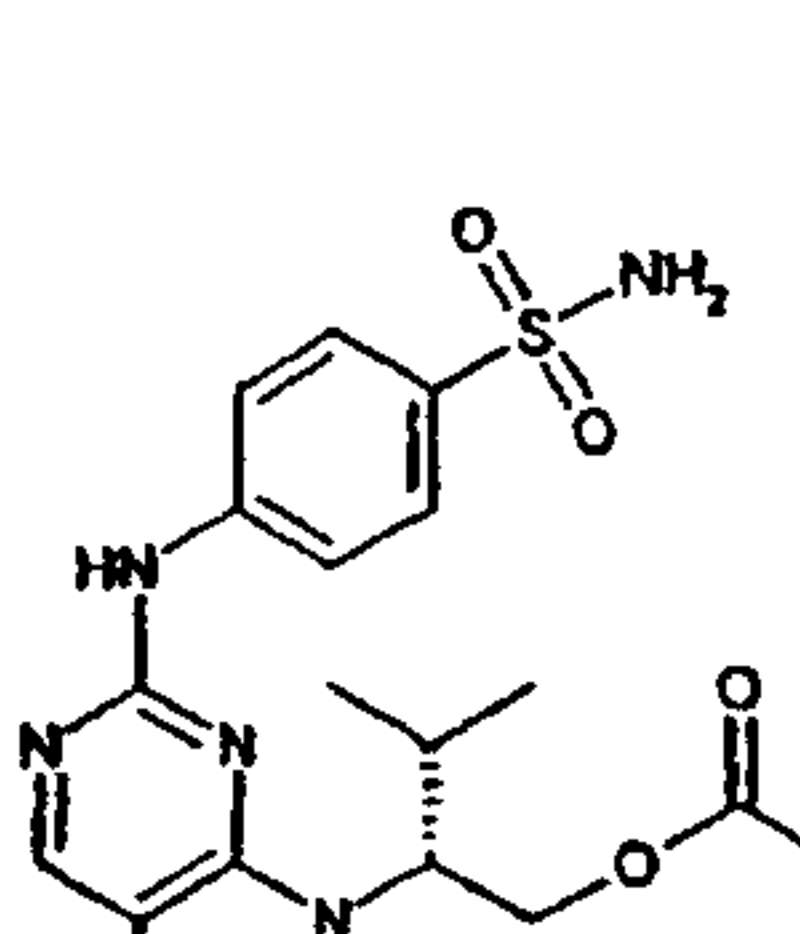
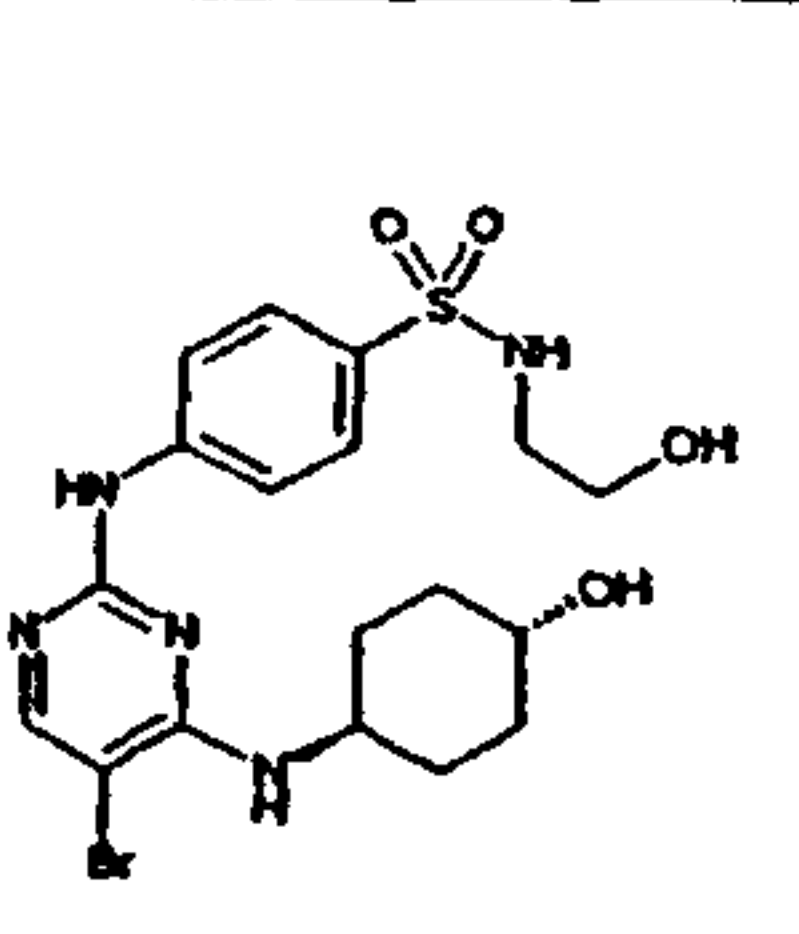
				
		Diastereomere 1/2 (ca. 1:3)	Diastereomere 1/2 (ca. 6:1)	
Beispiel Nr.	158	159 *	160 *	161 *
	10.80 (s,1H) 8.31 (s,1H) 7.97 (d,2H) 7.88 (m,3H) 7.52 (m,5H) 4.01 (m,1H) 3.62 (m,2H) 2.00 (m,1H) 0.91 (m,6H)	9.65 (s,1H,1+2) 8.08 (s,1H,1+2) 7.88 (d,2H,1+2) 7.65 (d,2H,1+2) 7.15 (s,1H,1+2) 6.62 (d,1H,2) 6.40 (d,1H,1) 4.05 (m,1H,1) 3.89 (m,1H,2) 2.30-1.20 (m,15H,1+2)	9.65 (s,1H,1+2) 8.08 (s,1H,1+2) 7.88 (d,2H,1+2) 7.65 (d,2H,1+2) 7.15 (s,1H,1+2) 6.62 (d,1H,2) 6.40 (d,1H,1) 4.05 (m,1H,1) 3.89 (m,1H,2) 2.30-1.20 (m,15H,1+2)	7.92 (s,1H) 7.84 (d,2H) 7.58 (d,2H) 3.72 (m,1H) 3.35 (m,2H) 3.10 (m,1H) 2.91 (m,2H) 2.00 (m,2H) 1.89 (m,2H) 1.66 (m,4H) 1.39 (m,5H)
Aus- beute	37%	21%	14%	8%
Schmp.			199	> 300
Masse	469 (EI)	468 (EI)	468 (EI)	508 (EI)

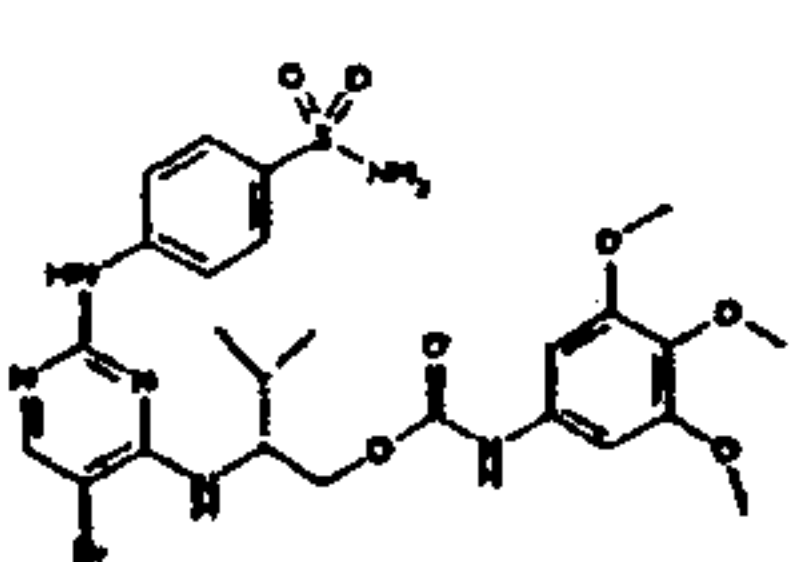
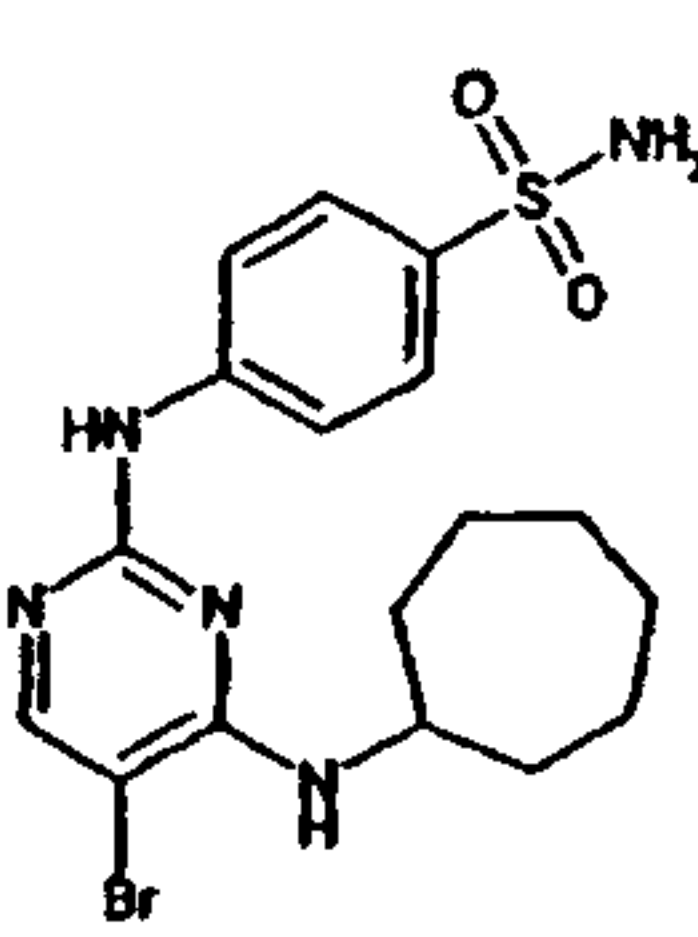
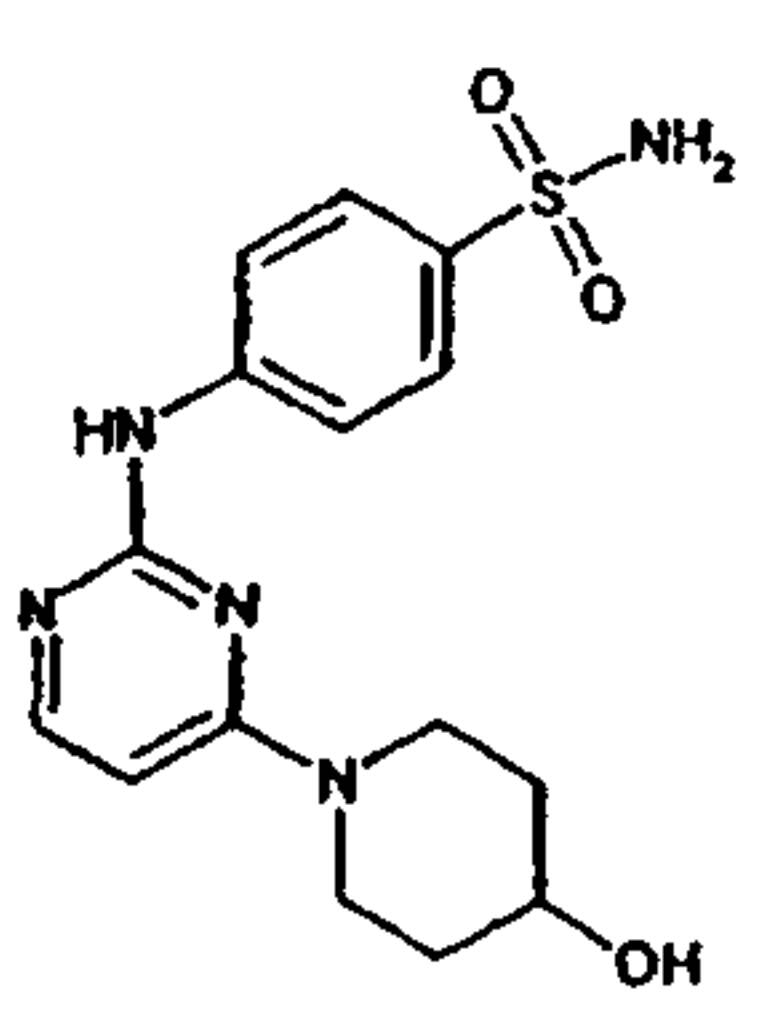
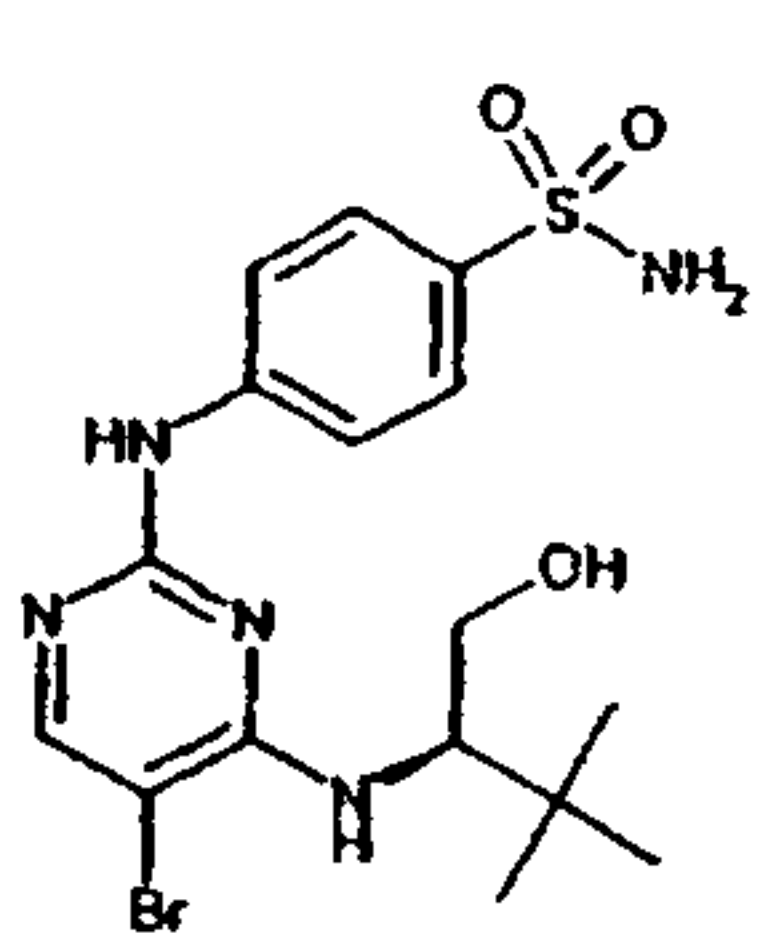
		 Diastereomere 1/2 (ca. 1:1)		
Bsp.-Nr.	162	163 *	164	165
	11.25 (s,1H) 9.40 (s,1H) 8.47 (s,1H) 8.29 (s,1H) 7.63 (s,1H) 7.43 (d,1H) 7.07 (m,3H) 4.06 (m,1H) 3.63 (m,2H) 1.98 (m,1H) 0.95 (d,3H) 0.85 (d,3H)	10.95 (s,1H) 10.72 (s,1H) 9.47 (br,2H) 9.30 (br,2H) 8.32 (2xs,2H) 8.08 (d,1H) 7.88 (d,2H) 7.75 (m,6H) 7.30 (br,4H) 6.95 (d,1H) 4.12 (m,1H) 3.98 (m,1H) 3.30 (m,1H) 3.10 (m,1H) 2.69 (m,2H) 2.25 (m,2H) 1.80 (m,18H) 1.01 (m,4H) 0.72 (m,4H)	9.65 (s,1H) 8.54 (s,1H) 8.10 (s,1H) 7.82 (d,1H) 7.45 (m,2H) 6.20 (d,1H) 4.70 (t,1H) 4.10 (m,1H) 3.60 (m,2H) 3.15 (s,3H) 2.00 (m,1H) 0.96 (d,3H) 0.89 (d,3H)	
Aus- beute	16%	33%	14%	51%
Schmp.	195			162-164
Masse	446 (ES)	480 (EI)	429 (ES)	462 (EI)

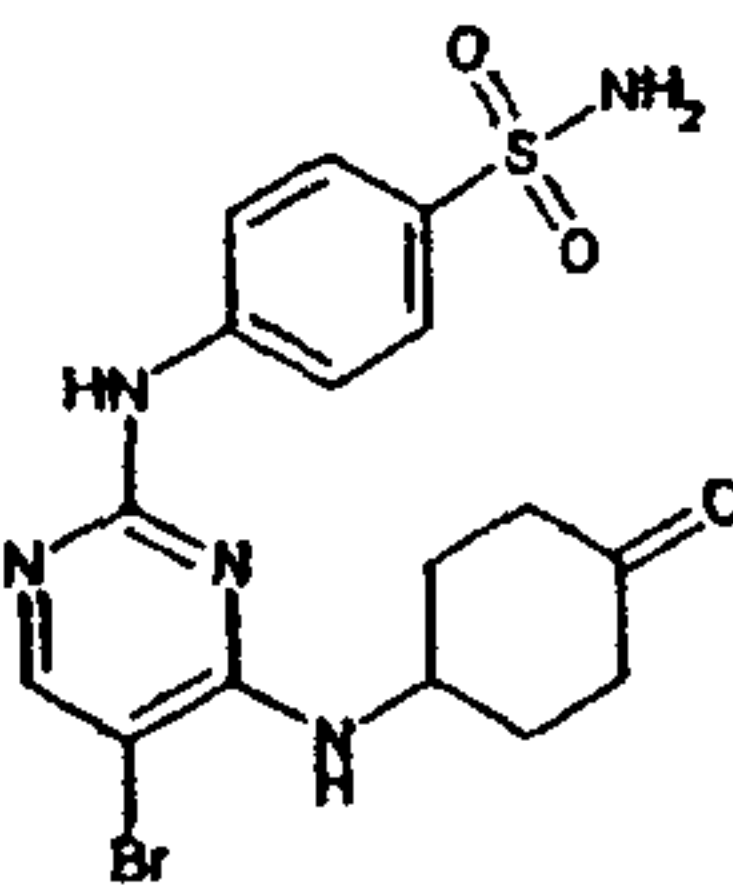
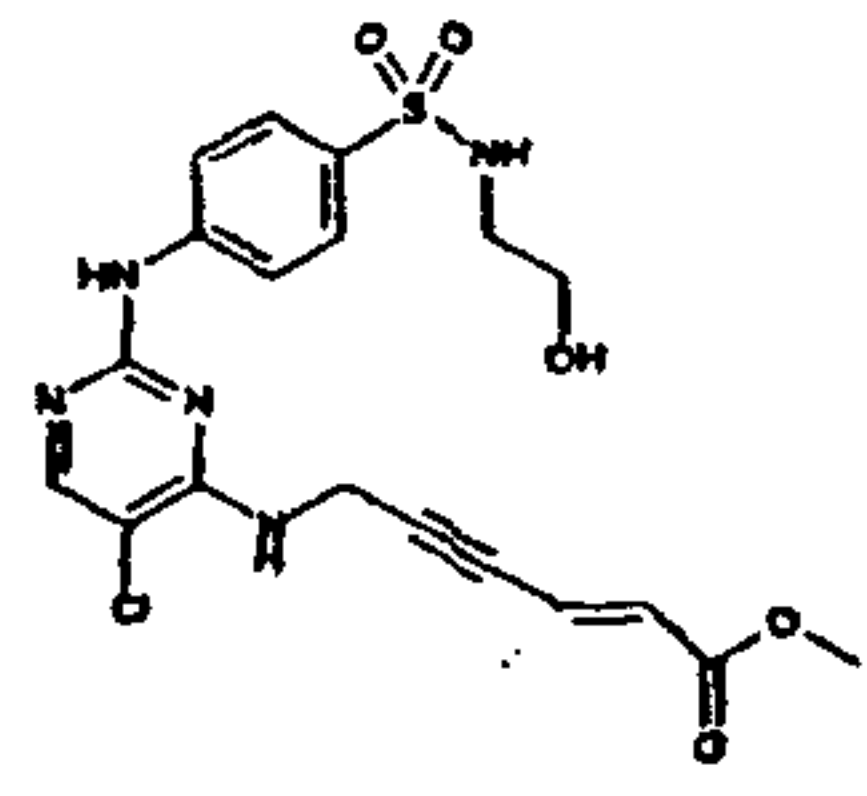
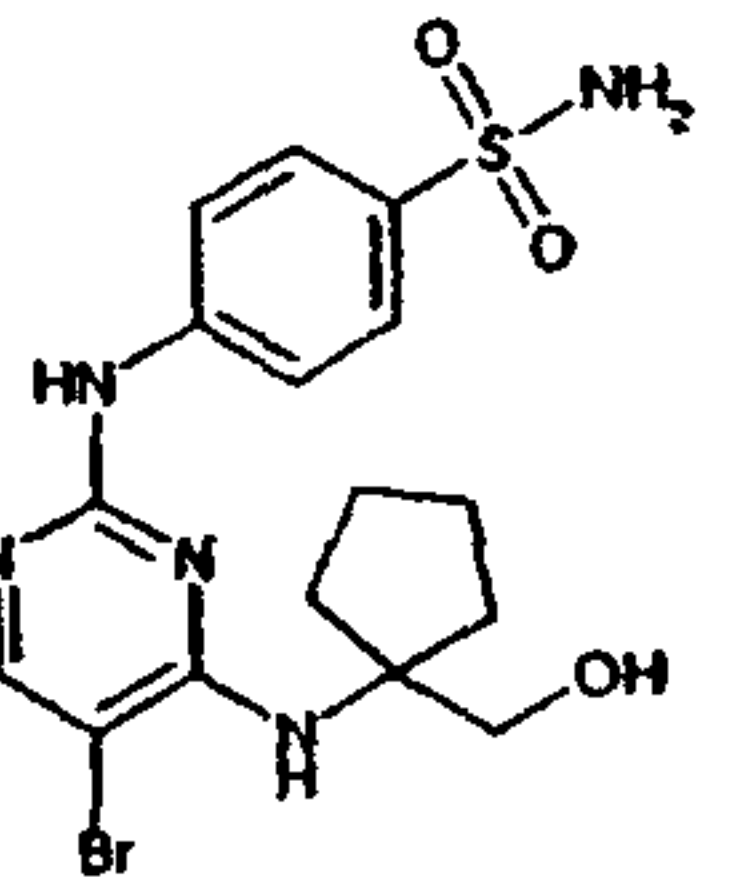
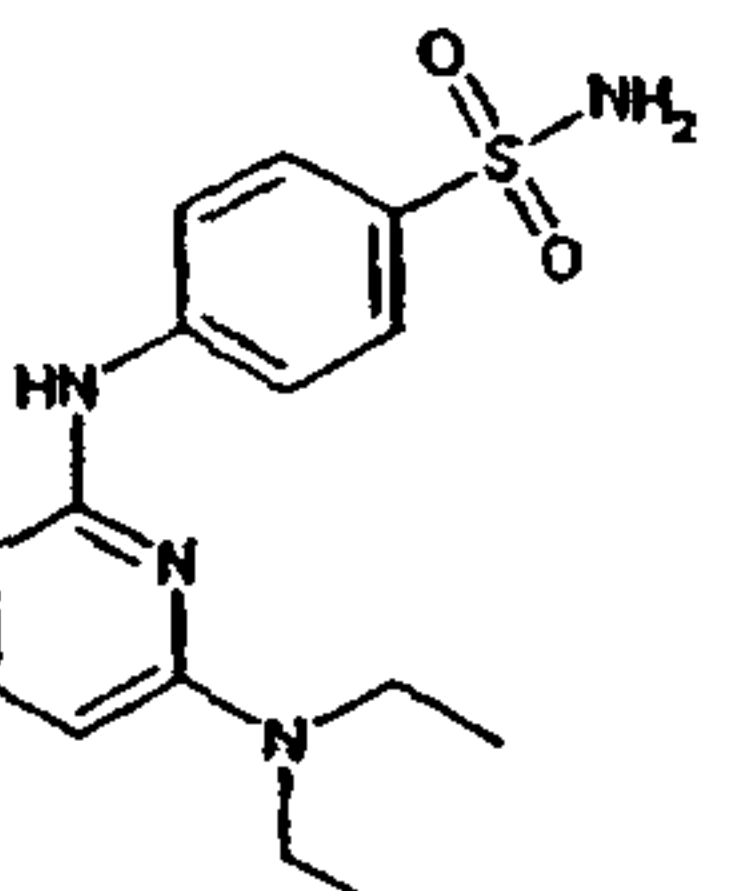
			 Diastereomere 1/2 (ca.1:1)	
Beispiel Nr.	166	167 *	168 *	169
	10.90 (s,1H) 8.95 (s,1H) 7.93 (m,2H) 7.25 (m,3H) 6.30 (s,1H) 6.00 (d,1H) 4.75 (tr,1H) 4.05 (m,1H) 3.60 (m,2H) 2.00 (m,1H) 1.00 (m,6H)	11.15 (br,1H) 10.90 (s,1H) 9.75 (br,2H) 8.35 (s,1H) 7.78 (m,4H) 7.30 (br,2H) 4.15 (m,1H) 3.50 (m,5H) 2.85 (s,6H) 1.90 (m,8H)	11.30 (br,2H) 11.08 (s,1H) 10.92 (s,1H) 9.90 (s,1H) 9.70 (s,1H) 8.36 (2xs,2H) 8.20 (d,1H) 7.93 (d,2H) 7.75 (m,6H) 7.35 (br,4H) 7.10 (d,1H) 4.15 (m,1H) 3.98 (m,1H) 3.64 (m,8H) 3.40 (m,5H) 3.10 (m,5H) 1.95 (m,26H)	9.05 (br,1H) 8.85 (s,1H) 8.11 (d,1H) 7.97 (s,1H) 7.47 (dd,1H) 6.80 (d,1H) 5.95 (d,1H) 4.80 (br,2H) 3.90 (m,2H) 3.45 (m,6H) 2.00 (m,1H) 0.90 (m,6H)
Aus- beute	6%	16%	58%	60%
Schmp.		256	261	
Masse	390 (ES)	512 (ES)	538 (ES)	484 (ES)

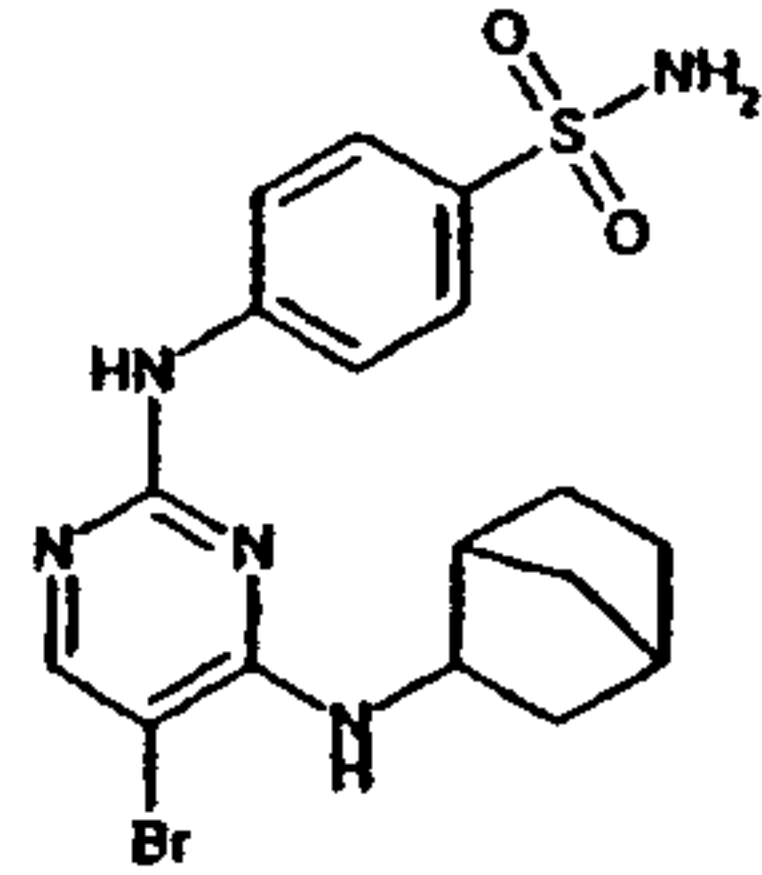
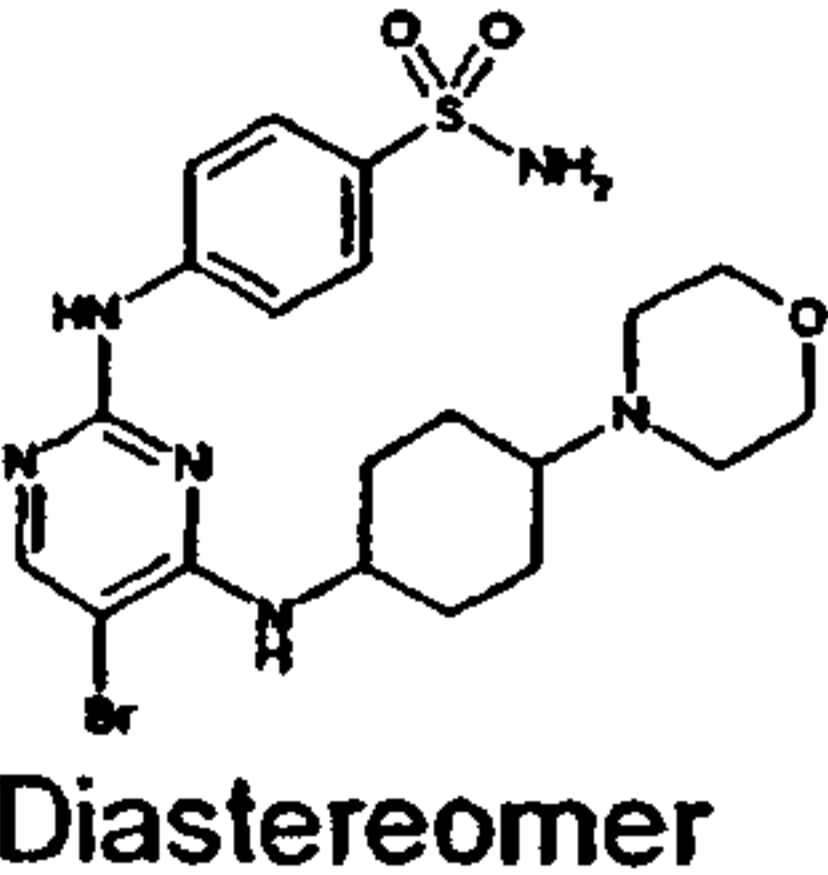
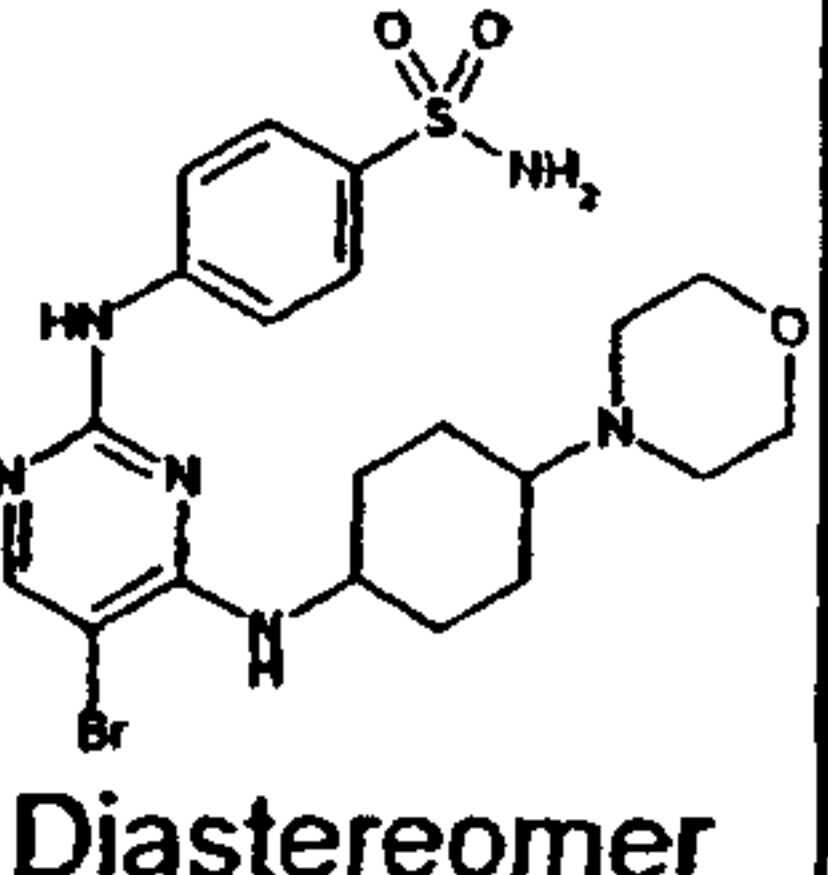
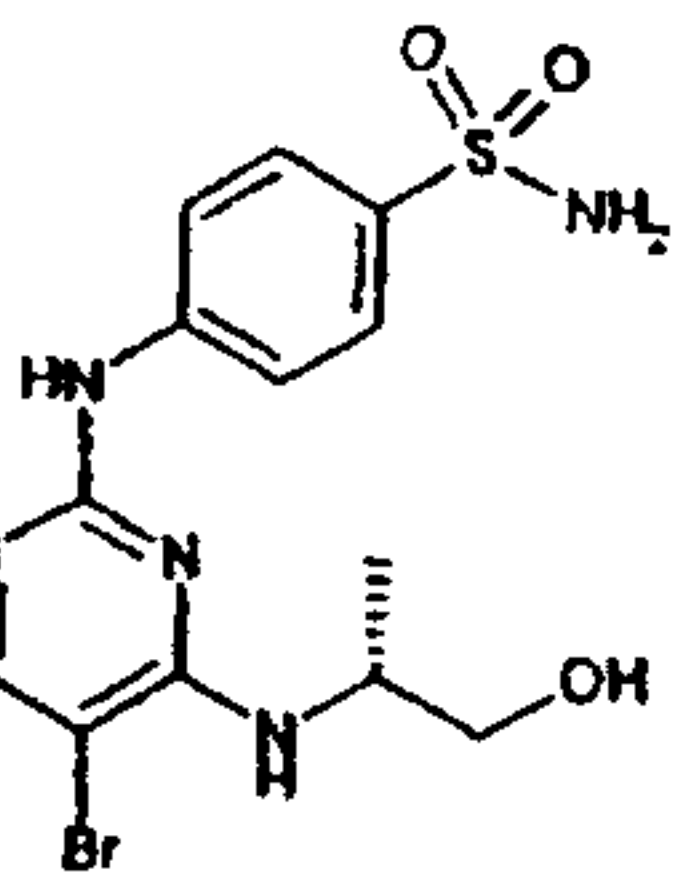
	Diastereomere 1/2 (ca. 1:1)			
Beispiel Nr.	170 *	171	172	173
	11.05 (s,1H) 10.90 (s,1H) 10.6 (br,2H) 8.35 (2xs,2H) 8.15 (d,1H) 7.80 (m,8H) 7.30 (br,4H) 7.05 (m,1H) 4.25 (m,1H) 3.95 (m,2H) 3.65 (m,1H) 3.20 (m,10H) 1.90 (m,24H)	10.45 (s,1H) 8.25 (s,1H) 8.00 (br,1H) 7.85 (d,2H) 7.75 (d,2H) 7.45 (br,1H) 3.60 (m,5H) 3.35 (m,2H) 2.80 (m,2H) 2.41 (t,2H) 1.90 (m,2H)	11.05 (s,1H) 8.35 (m,2H) 7.82 (d,1H) 7.65 (d,2H) 7.50 (t,1H) 4.05 (m,1H) 3.62 (m,2H) 2.00 (m,1H) 0.96 (d,3H) 0.85 (d,3H)	8.90 (s,1H) 8.72 (s,1H) 7.95 (s,1H) 7.18 (m,1H) 7.05 (dd,1H) 6.75 (d,1H) 5.99 (d,1H) 4.74 (t,1H) 4.03 (m,1H) 3.70 (s,3H) 3.60 (m,2H) 2.00 (m,1H) 0.90 (m,6H)
Aus- beute	64%	7%	65%	40%
Schmp.	226	164	206	144
Masse	525 (ES)	488 (ES)	395 (ES)	397 (ES)

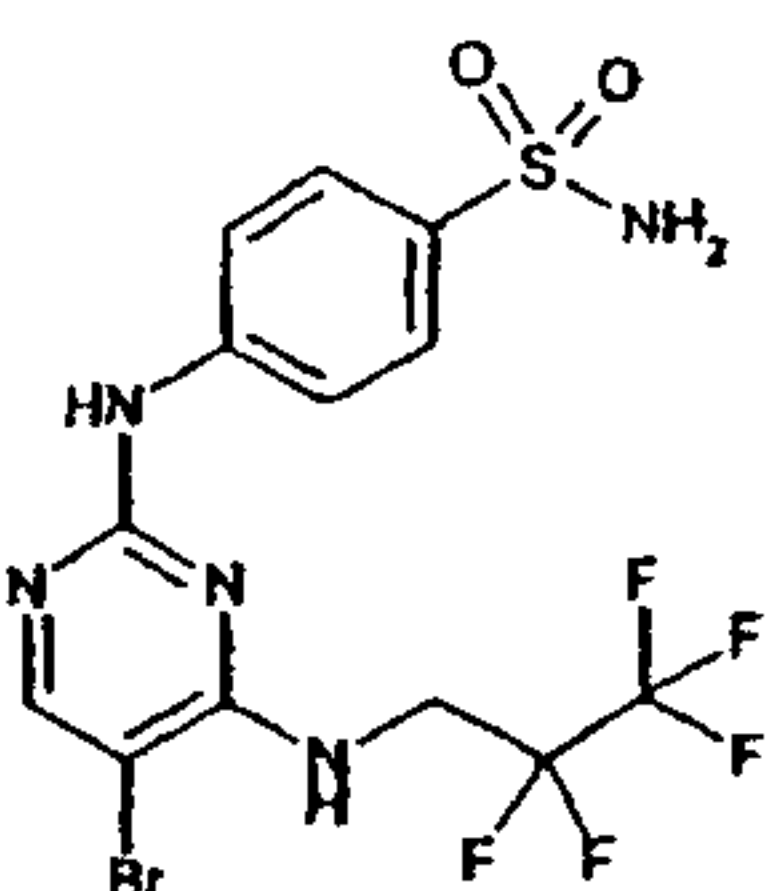
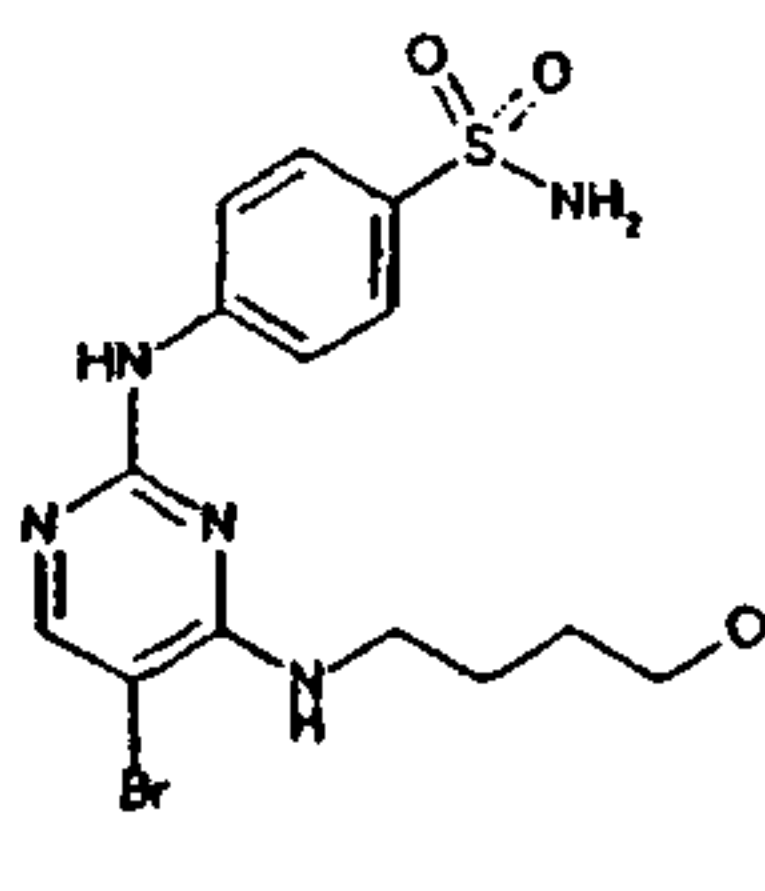
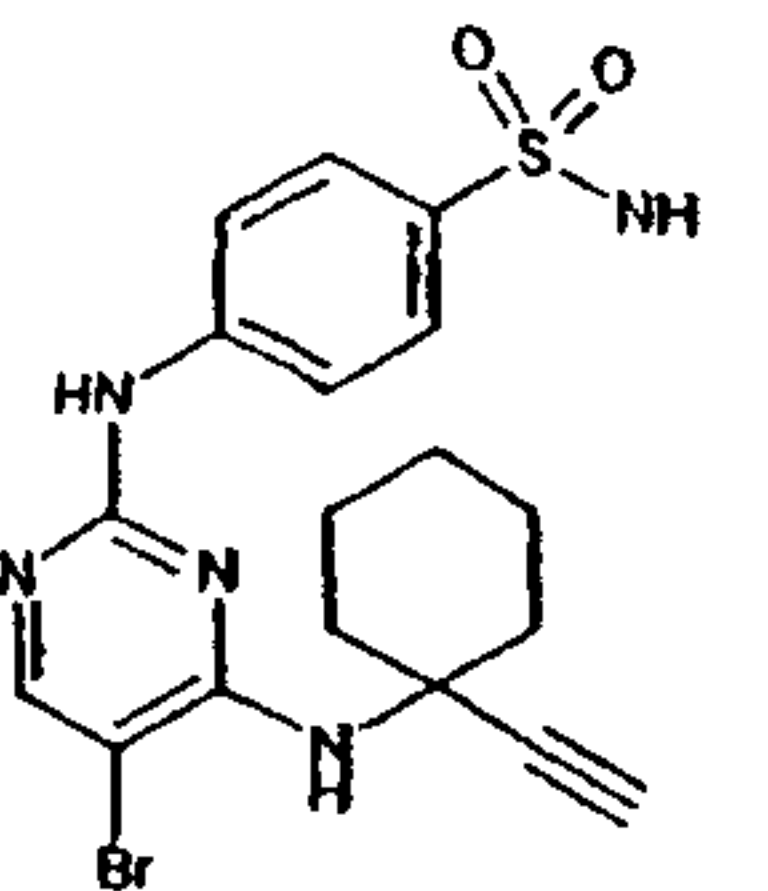
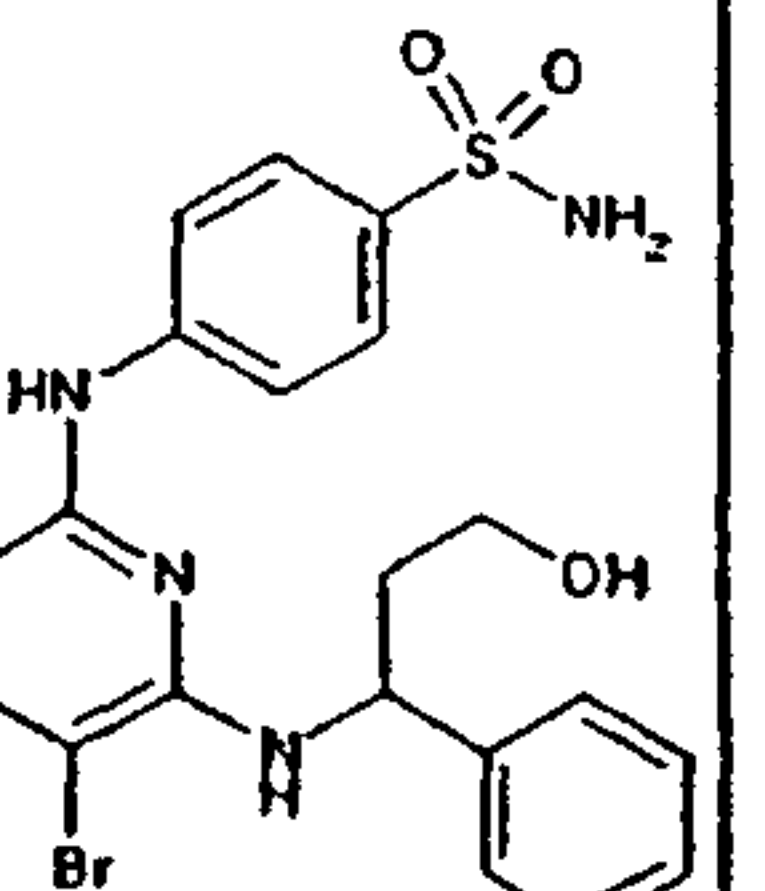
	 Diastereomere 1/2 (ca. 1:1)	 Diastereomere 3/4 (ca. 1:1)		
Beispiel Nr.	174 *	175 *	176	177
	11.05 (m,3H) 10.48 (s,1H) 8.38 (s,2H) 7.80 (m,8H) 7.80 (br,4H) 7.10 (s,1H) 6.95 (s,1H) 4.42 (m,2H) 4.18 (m,2H) 3.70-2.90 (m,10H) 2.40-1.60 (m,20H)	11.15 (br,1H) 11.05 (s,2H) 10.65 (br,1H) 8.30 (s,2H) 8.13 (m,2H) 7.88 (m,8H) 7.30 (br,4H) 4.40 (m,2H) 4.00 (br,2H) 3.70-2.90 (m,10H) 2.40-1.40 (m,20H)	8.00 (s,1H) 7.80 (m,4H) 4.48 (m,1H) 3.65 (d,2H) 1.75 (m,1H) 1.59 (m,2H) 1.01 (d,3H) 0.92 (d,3H)	9.65 (s,1H) 8.08 (s,1H) 7.85 (d,2H) 7.65 (d,2H) 7.40 (br,1H) 7.15 (s,2H) 3.55 (m,2H) 2.55 (m,2H) 2.15 (m,2H) 1.80 (m,3H) 1.65 (m,1H)
Aus- beute	95%	51%	3%	8%
Schmp.				
Masse	511 (ES)	511 (ES)	443 (EI)	456 (EI)

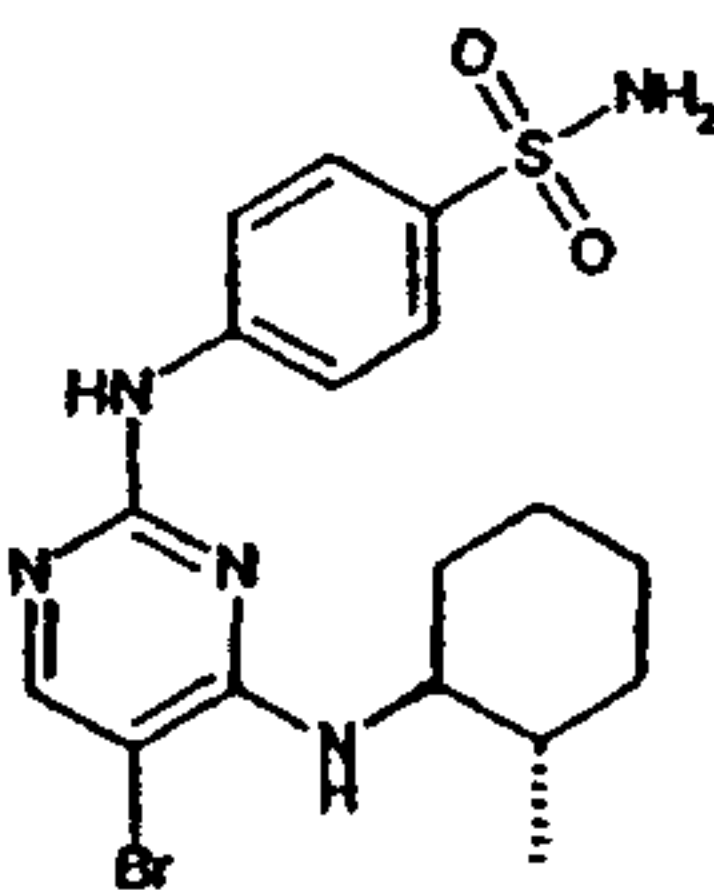
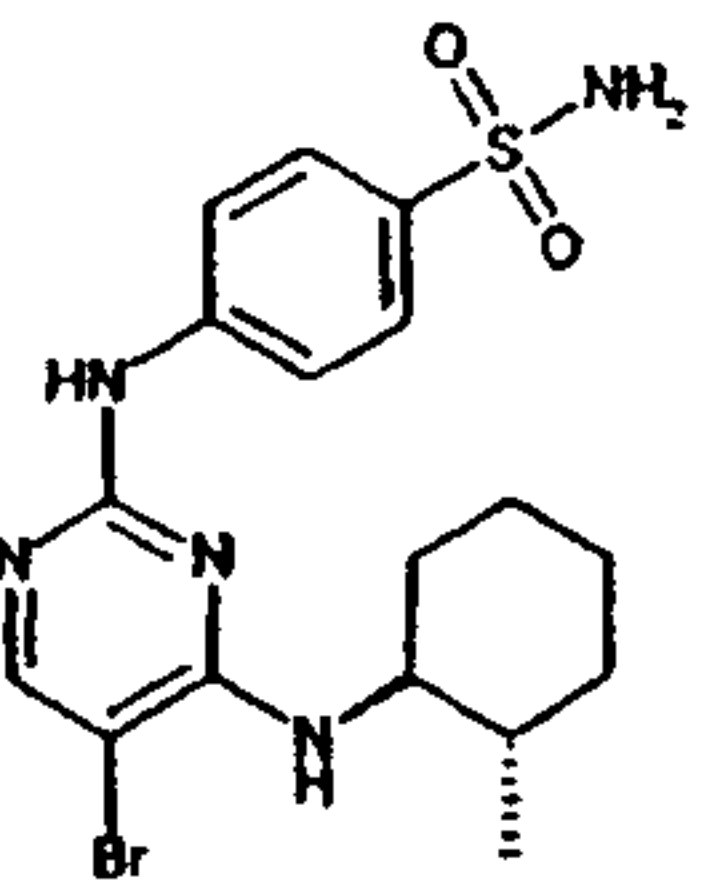
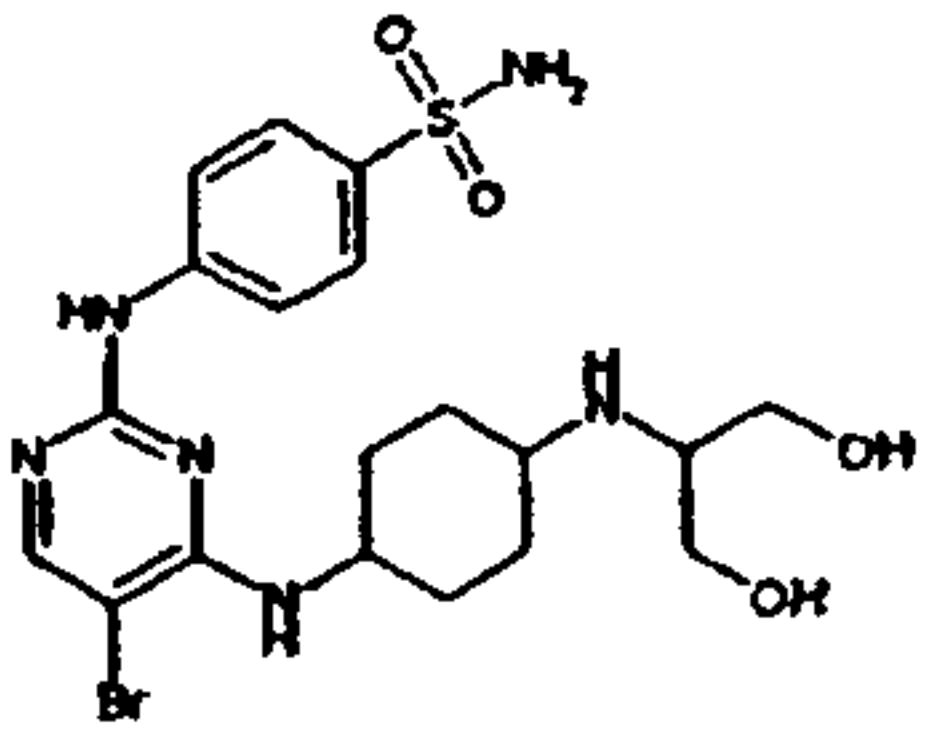
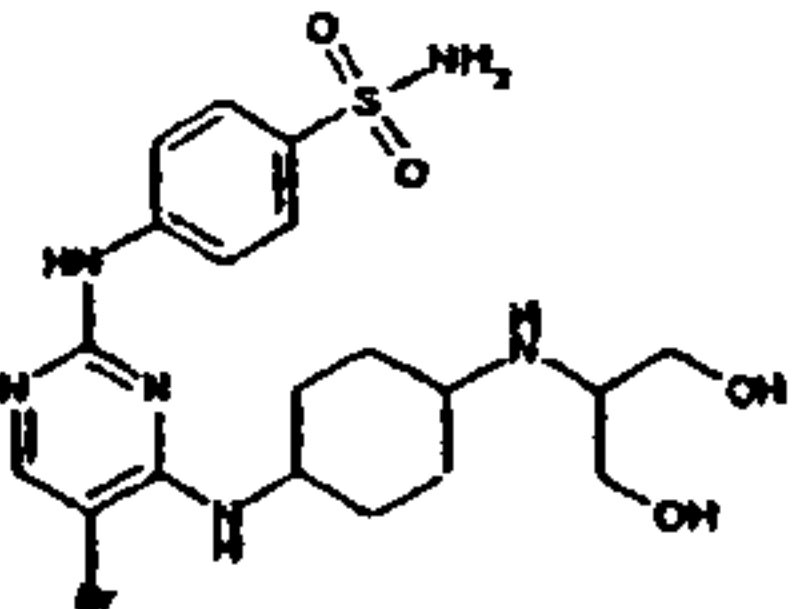
				
Beispiel Nr.	178	179	180	181
	9.49 (s,1H) 8.25 (s,1H) 7.80 (m,4H) 7.32 (br,2H) 4.03 (m,2H) 3.75 (m,1H) 3.35 (m,2H) 1.80 (m,2H) 1.40 (m,2H)	9.61 (s,1H) 8.08 (s,1H) 7.88 (d,2H) 7.65 (d,2H) 7.60 (t,1H) 7.15 (s,2H) 3.45 (m,2H) 2.40 (t,2H) 2.20 (s,6H) 1.75 (t,2H)	9.65 (s,1H) 8.11 (s,1H) 7.81 (s,2H) 7.63 (d,2H) 7.15 (s,2H) 6.64 (d,1H) 4.28 (m,3H) 2.00 (m,1H) 1.98 (s,3H) 0.98 (d,3H) 0.93 (d,3H)	9.71 (s,1H) 8.06 (s,1H) 7.90 (d,2H) 7.61 (d,2H) 7.37 (t,1H) 6.56 (d,1H) 4.66 (m,2H) 3.90 (m,1H) 3.39 (m,3H) 2.78 (q,2H) 1.96 (m,4H) 1.56 (m,2H) 1.29 (m,2H)
Aus- beute	17%	9%	27%	24%
Schmp.				
Masse	427 (EI)	428 (EI)	472 (ES)	486 (ES)

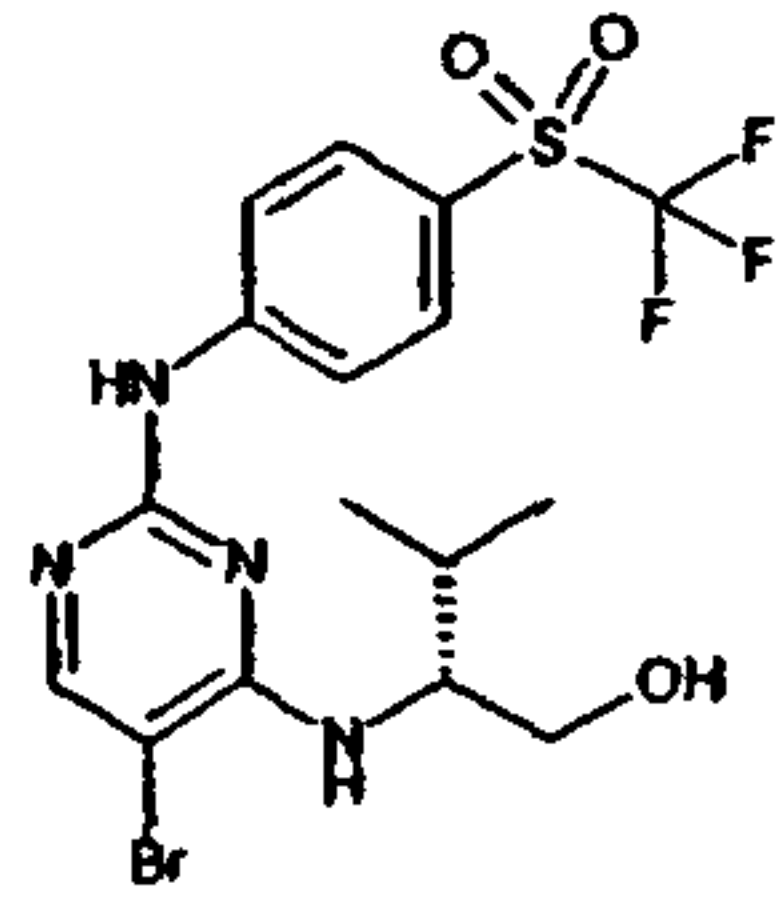
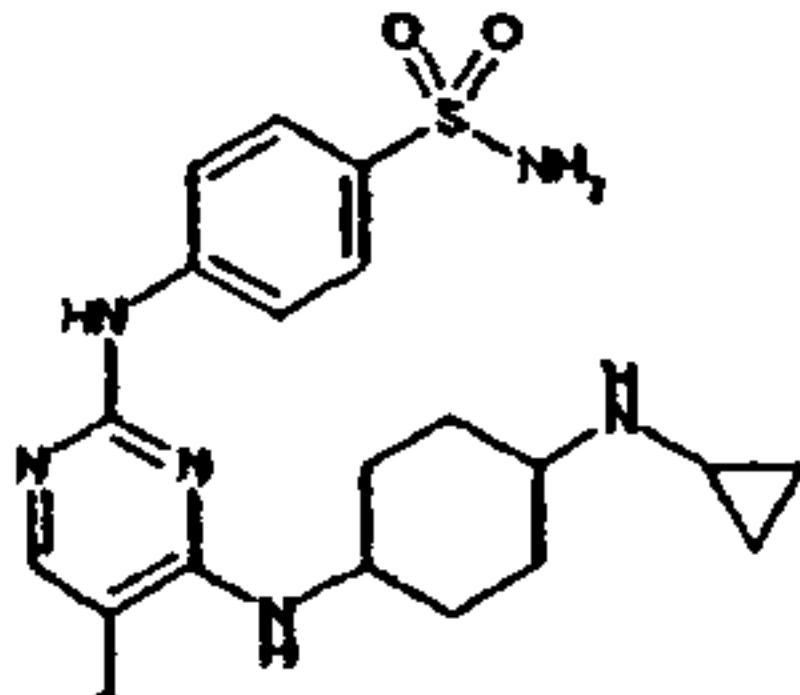
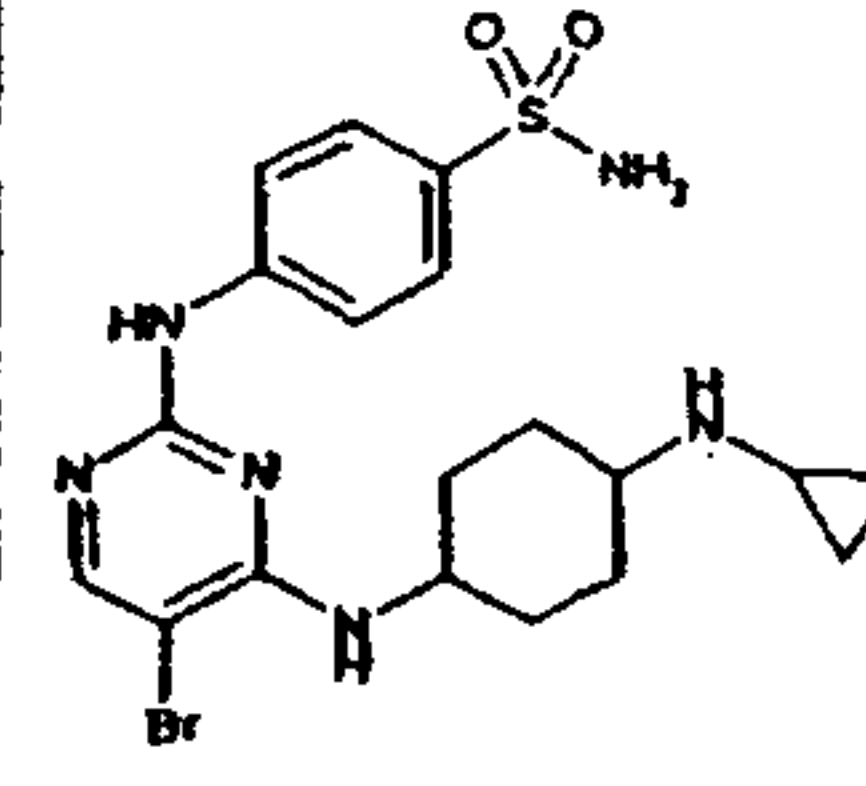
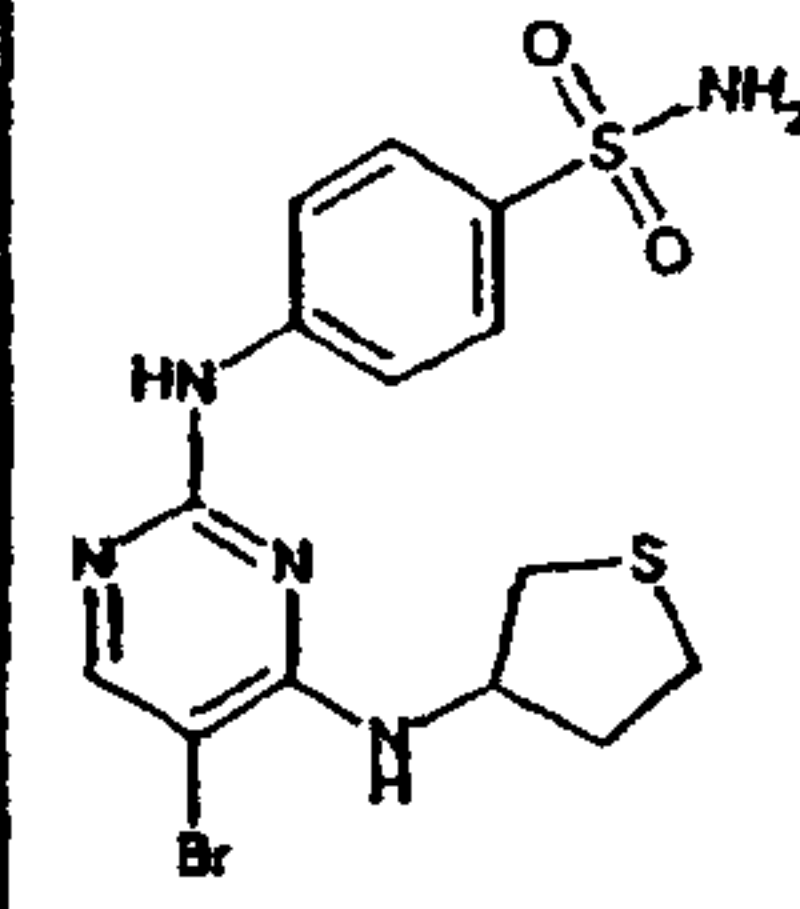
				
Beispiel Nr.	182	183	184	185
	9.68 (s,1H) 9.47 (s,1H) 8.10 (s,1H) 7.81 (d,2H) 7.67 (d,2H) 7.14 (s,2H) 6.76 (m,3H) 4.47 (m,2H) 4.30 (m,1H) 3.65 (s,6H) 3.54 (s,3H) 1.99 (m,1H) 0.98 (d,3H) 0.92 (d,3H)	10.97 (s,1H) 8.30 (s,1H) 8.02 (d,1H) 7.81 (m,4H) 7.30 (s,2H) 4.14 (m,1H) 1.80 (m,12H)	11.06 (s,1H) 8.04 (m,1H) 7.82 (m,2H) 7.70 (m,2H) 7.30 (s,2H) 6.72 (m,1H) 3.75 (m,5H) 1.88 (m,2H) 1.48 (m,2H)	11.01 (s,1H) 8.38 (s,1H) 7.82 (s,4H) 7.40 (d,1H) 7.32 (s,2H) 4.20 (m,1H) 3.70 (m,2H) 0.97 (s,9H)
Aus- beute	57%	78%	26%	76%
Schmp.				
Masse	639 (ES)	439 (EI)	348 (EI)	445 (EI)

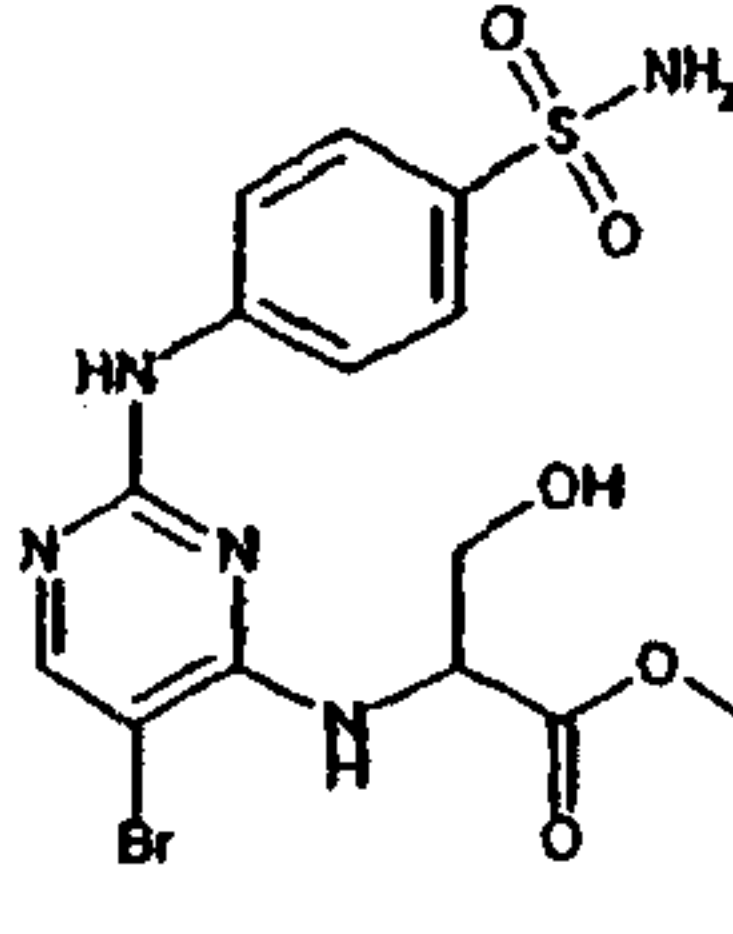
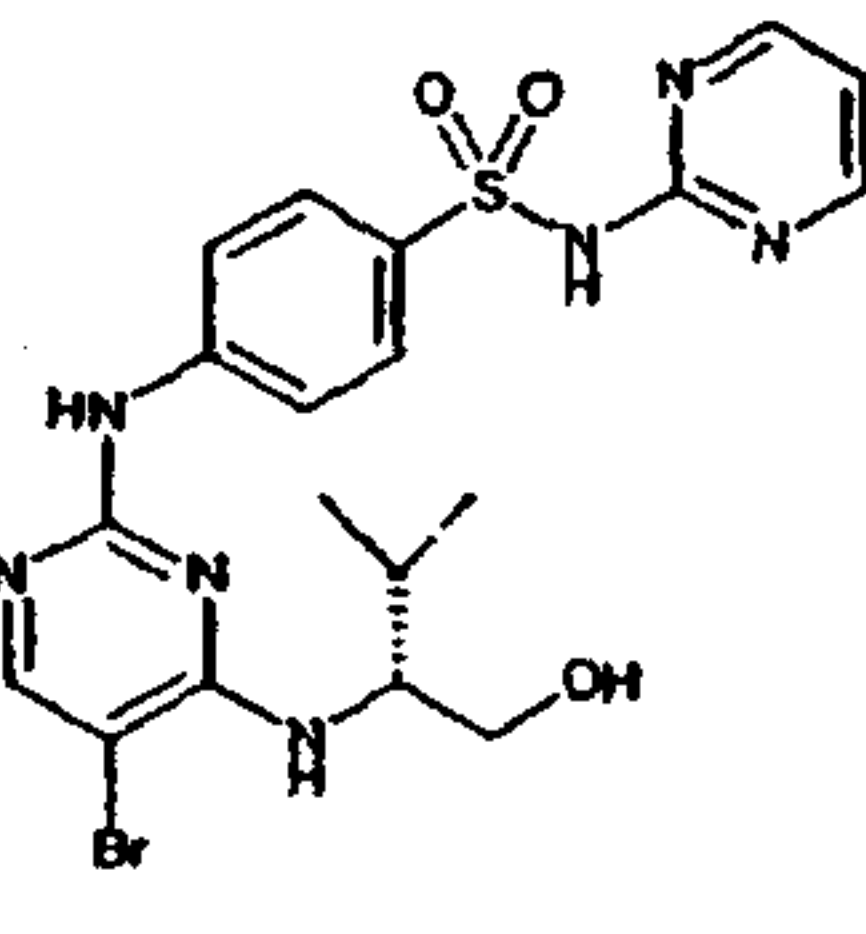
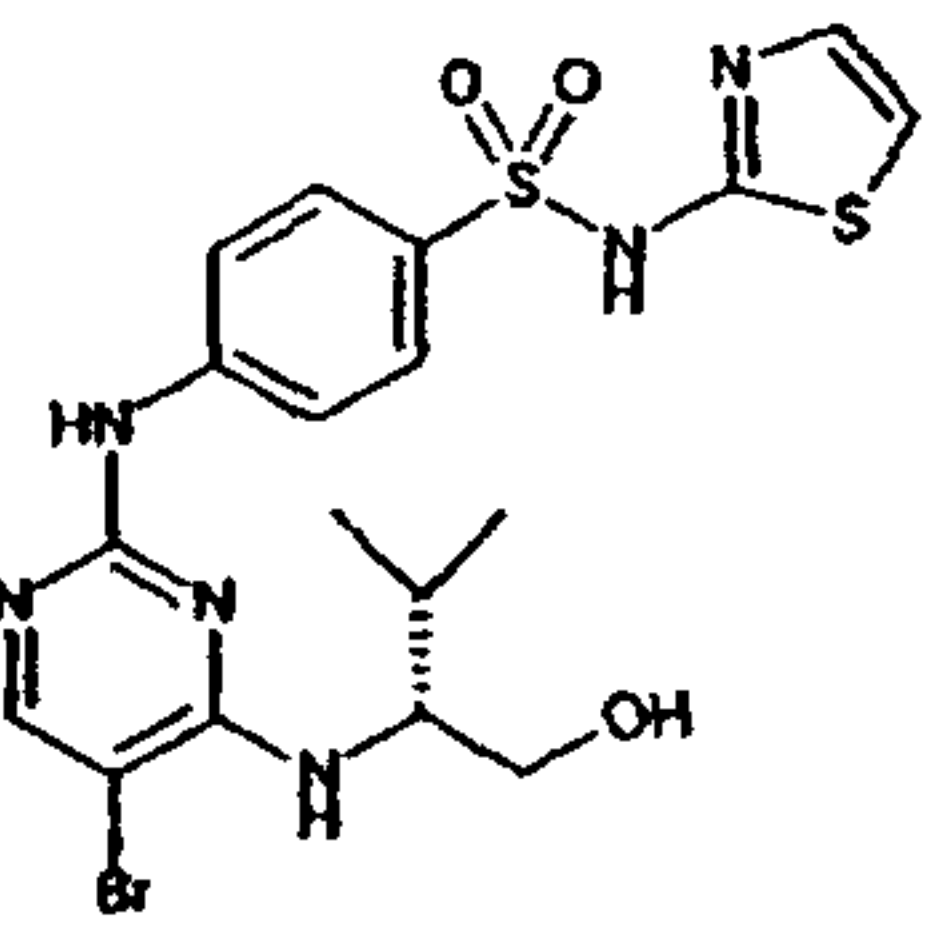
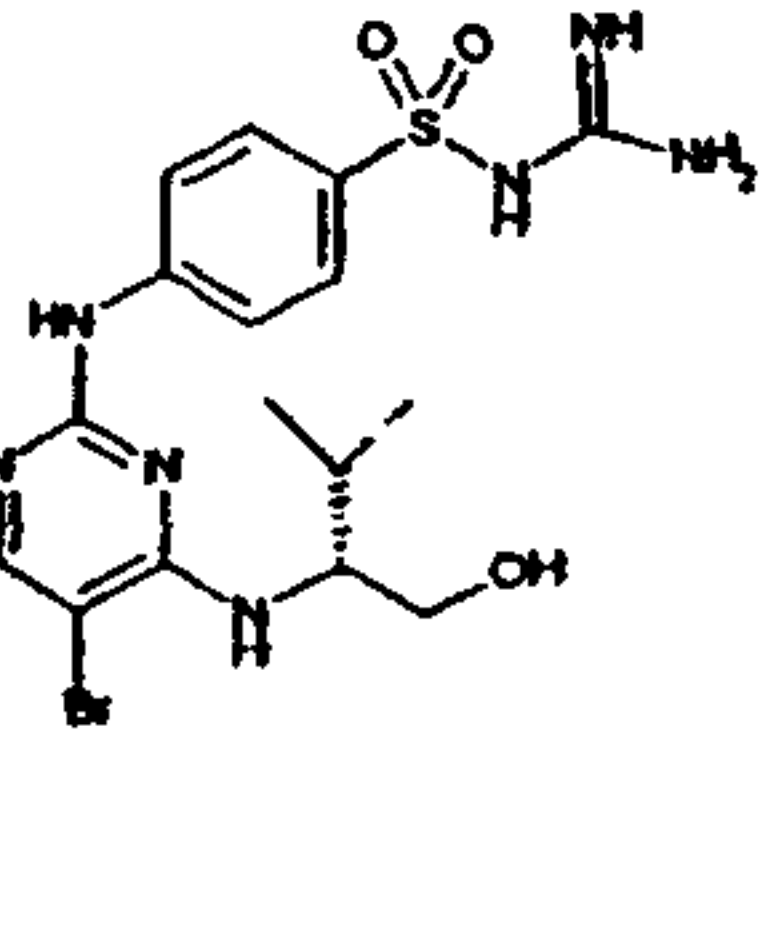
				
Beispiel Nr.	186	187	188	189
	9.71 (s,1H) 8.11 (s,1H) 7.90 (d,2H) 7.70 (d,2H) 7.12 (s,2H) 6.75 (d,1H) 4.45 (m,1H) 2.25 (m,6H) 1.90 (m,2H)	7.75 (s,1H) 7.65 (d,2H) 7.58 (d,2H) 5.82 (s,1H) 4.25 (s,2H) 3.40 (t,2H) 2.82 (t,2H) 2.06 (s,3H)	10.60 (s,1H) 8.29 (s,1H) 7.79 (d,2H) 7.71 (d,2H) 7.28 (s,2H) 6.60 (s,1H) 3.58 (s,2H) 2.10 (m,2H) 1.78 (m,2H) 1.55 (m,4H)	11.19 (s,1H) 8.03 (d,1H) 7.88 (d,2H) 7.78 (d,2H) 7.31 (s,2H) 6.58 (d,1H) 3.60 (m,4H) 1.20 (m,6H)
Aus- beute	16%	7%	61%	35%
Schmp.				
Masse	440 (ES)	480 (ES)	443 (EI)	321 (EI)

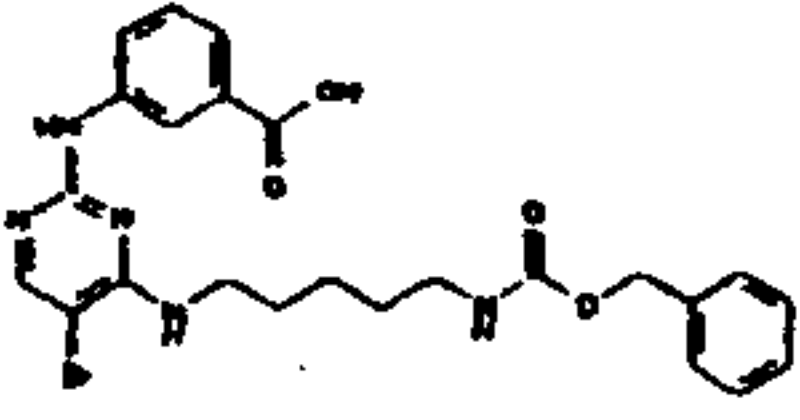
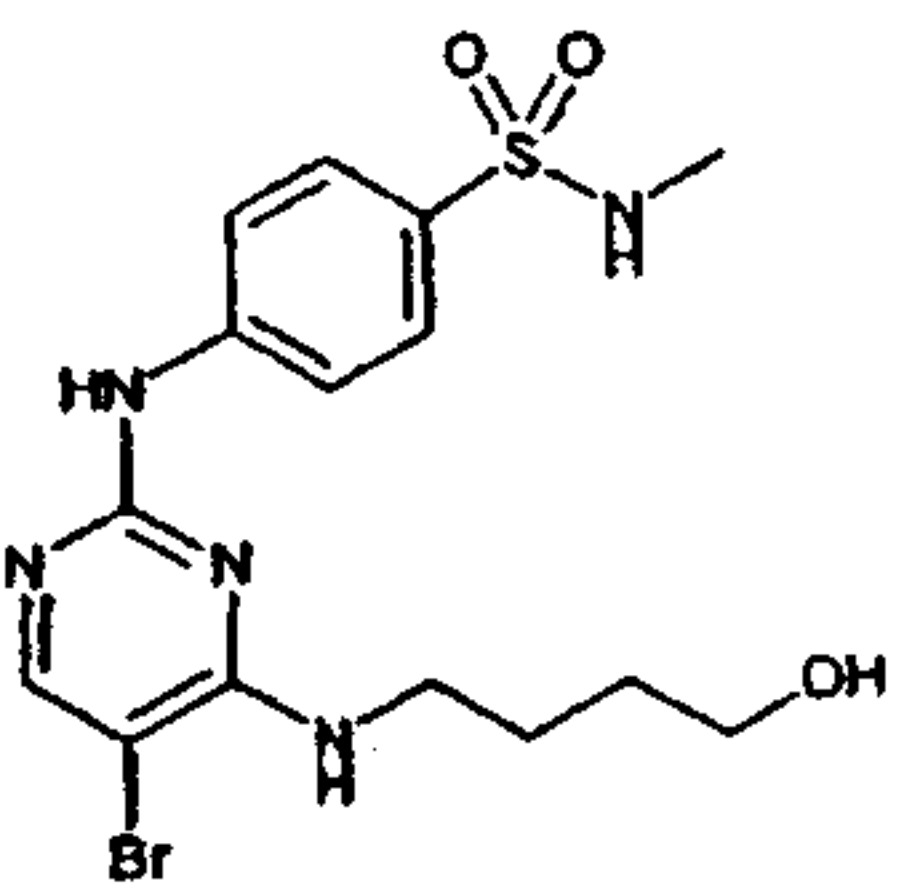
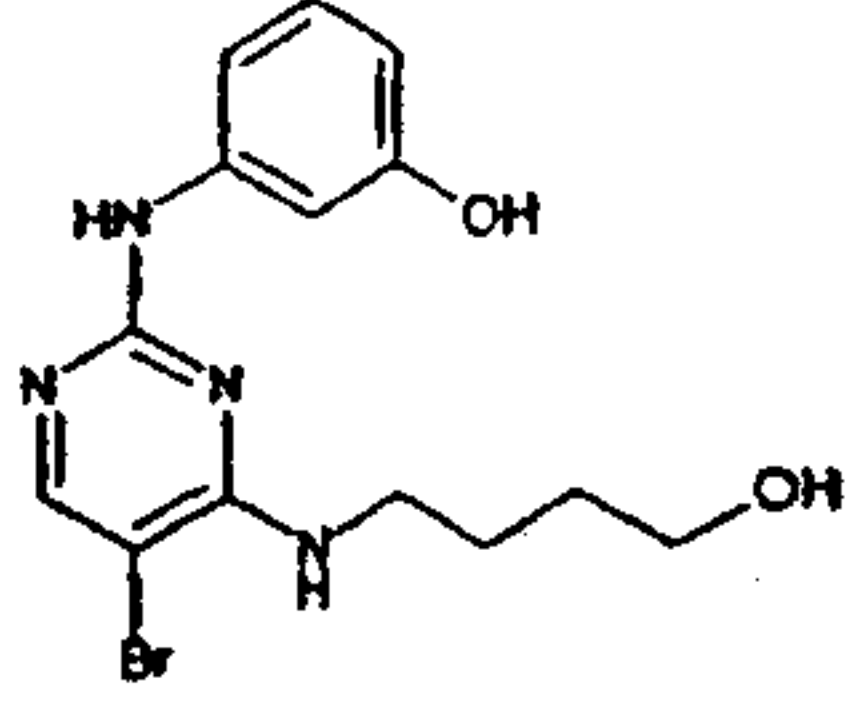
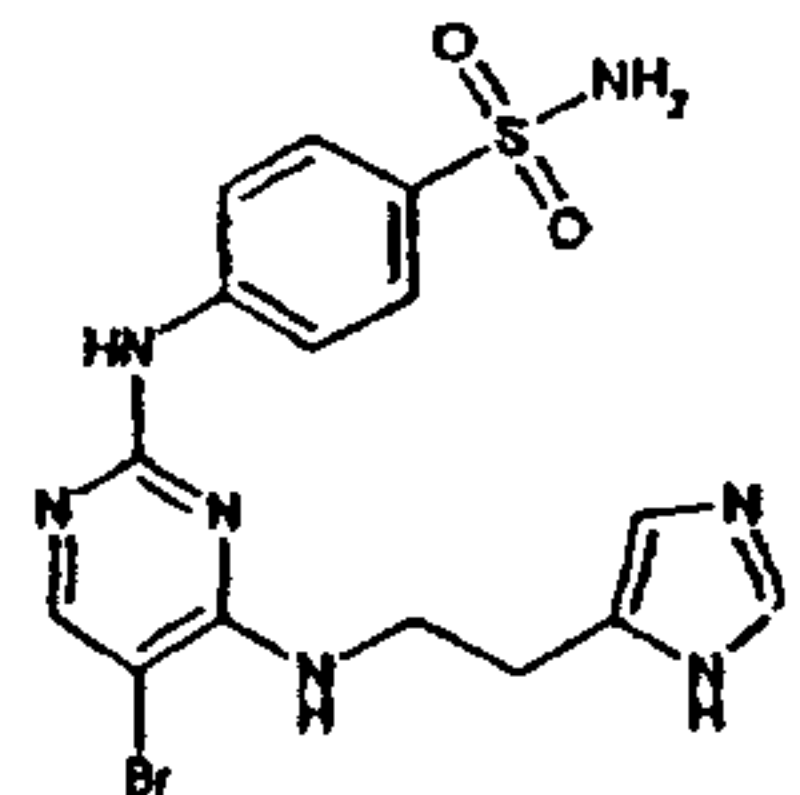
				
Beispiel Nr.	190	191 *	192 *	193
	10.61 (s,1H) 8.28 (s,1H) 7.82 (d,2H) 7.73 (d,2H) 7.53 (br,1H) 7.25 (s,2H) 4.25 (m,1H) 2.59 (br,1H) 2.21 (br,1H) 1.94 (m,1H) 1.40 (m,7H)	9.67 (s,1H) 8.08 (s,1H) 7.88 (d,2H) 7.65 (d,2H) 7.11 (s,2H) 6.35 (d,1H) 4.10 (m,1H) 3.62 (m,4H) 2.45 (m,4H) 2.19 (m,1H) 1.88 (m,4H) 1.65 (m,4H)	9.63 (s,1H) 8.06 (s,1H) 7.85 (d,2H) 7.65 (d,2H) 7.15 (s,2H) 6.55 (d,1H) 3.95 (m,1H) 3.58 (m,4H) 2.50 (m,4H) 1.96 (m,1H) 1.50 (m,4H) 1.30 (m,4H)	10.61 (s,1H) 8.28 (s,1H) 7.78 (m,4H) 7.45 (d,1H) 7.20 (s,2H) 4.30 (br,2H) 3.53 (m,2H) 1.21 (d,3H)
Aus- beute	63%	15%	17%	57%
Schmp.				
Masse	437 (EI)	511 (ES)	511 (EI)	403 (EI)

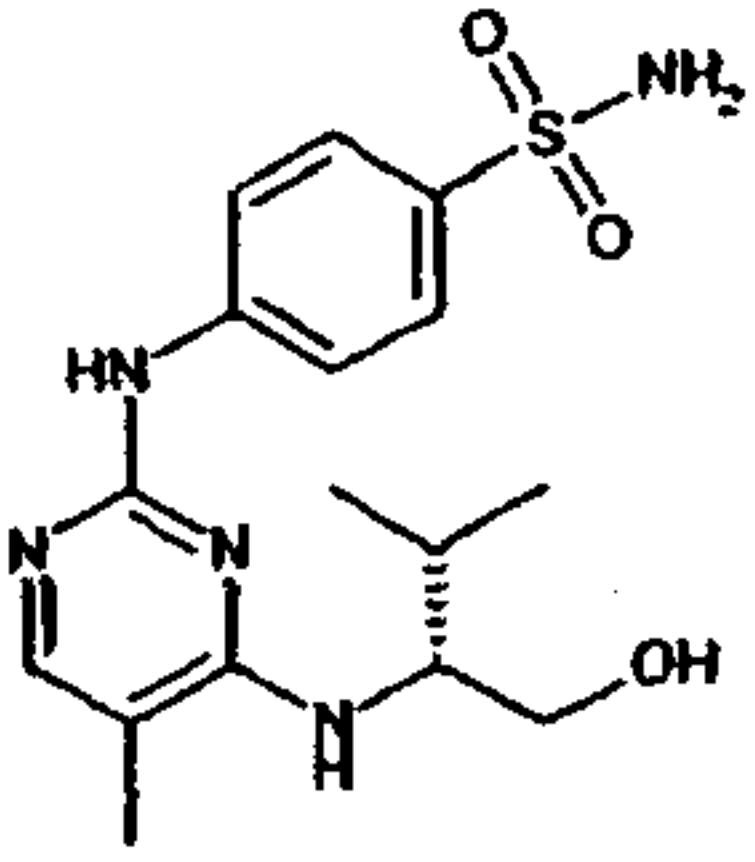
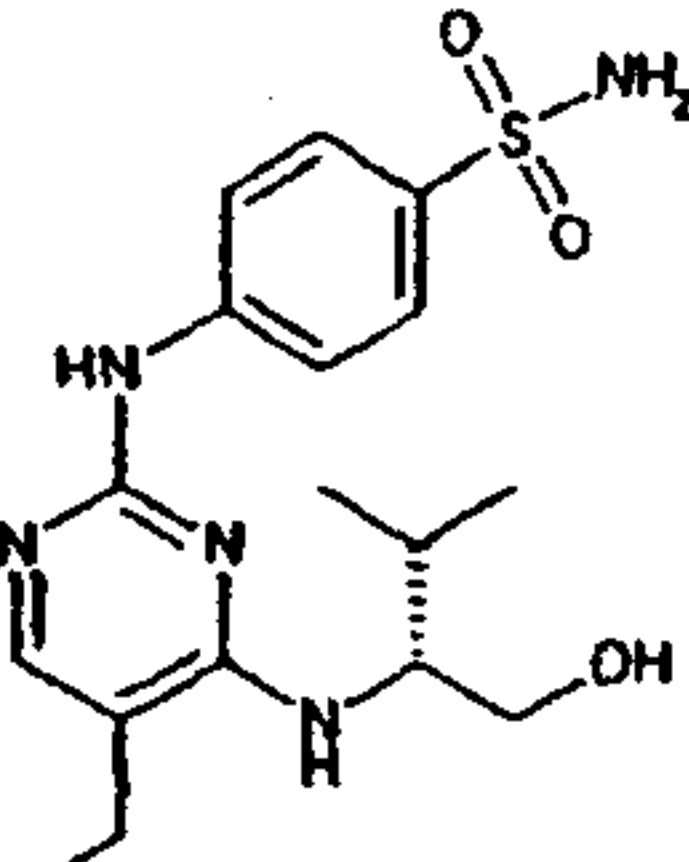
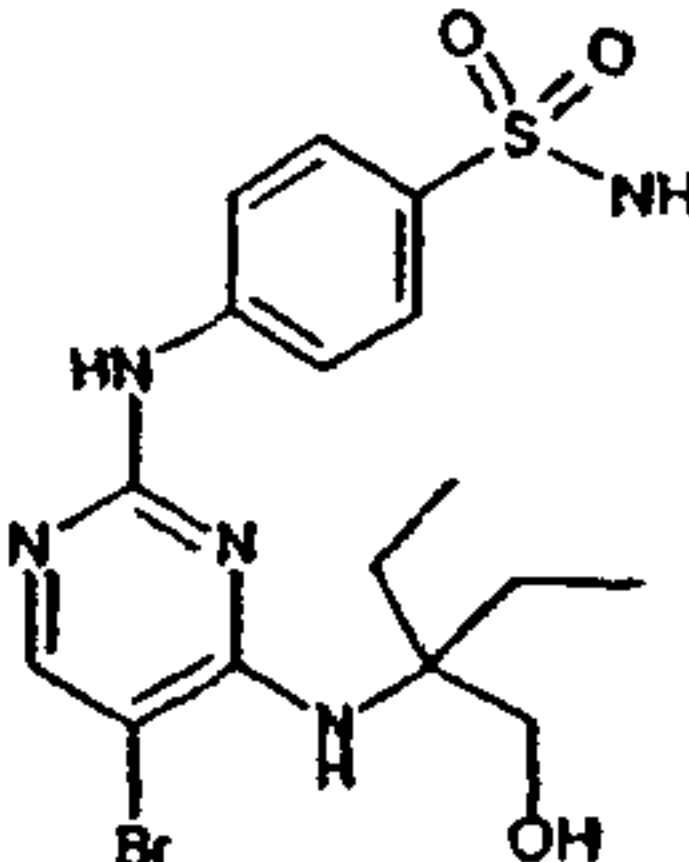
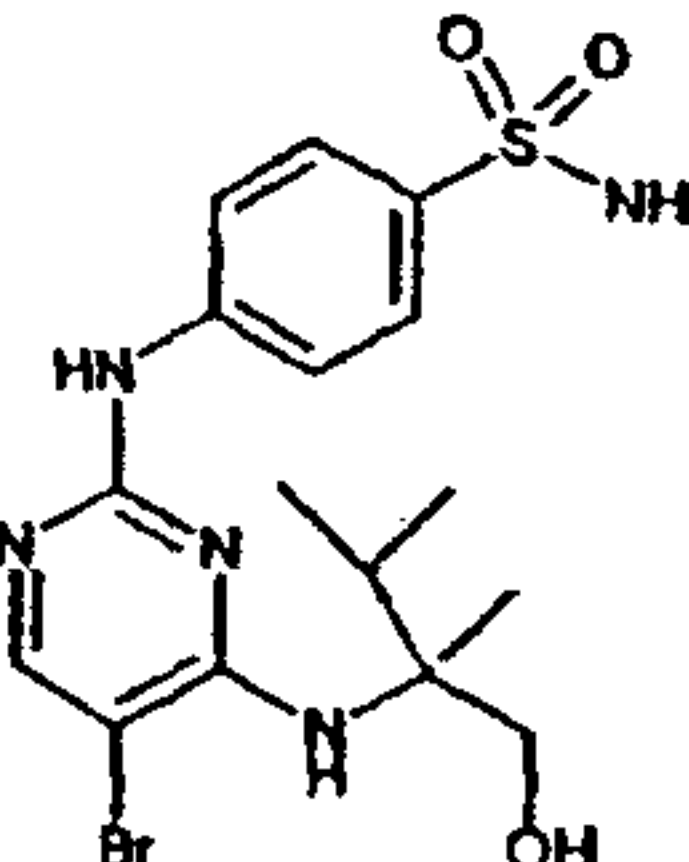
				
Beispiel Nr.	194	195	196	197
	9.89 (s,1H) 8.21 (s,1H) 7.82 (d,2H) 7.65 (m,3H) 7.17 (br,2H) 4.30 (m,2H)	10.98 (s,1H) 8.51 (br,1H) 8.29 (s,1H) 7.81 (m,4H) 7.29 (br,2H) 3.45 (m,4H) 1.68 (m,2H) 1.45 (m,2H)	10.39 (s,1H) 8.30 (s,1H) 8.04 (d,2H) 7.70 (d,2H) 7.21 (br,2H) 6.55 (s,1H) 3.49 (s,1H) 2.32 (m,2H) 1.85 (m,2H) 1.60 (m,5H) 1.29 (m,1H)	10.85 (s,1H) 8.71 (d,1H) 8.31 (s,1H) 7.72 (d,2H) 7.55 (d,2H) 7.30 (m,6H) 5.41 (m,1H) 3.49 (m,2H) 2.11 (m,2H)
Aus- beute	26%	56%	12%	61%
Schmp.				
Masse	476 (EI)	417 (EI)	450 (EI)	479 (EI)

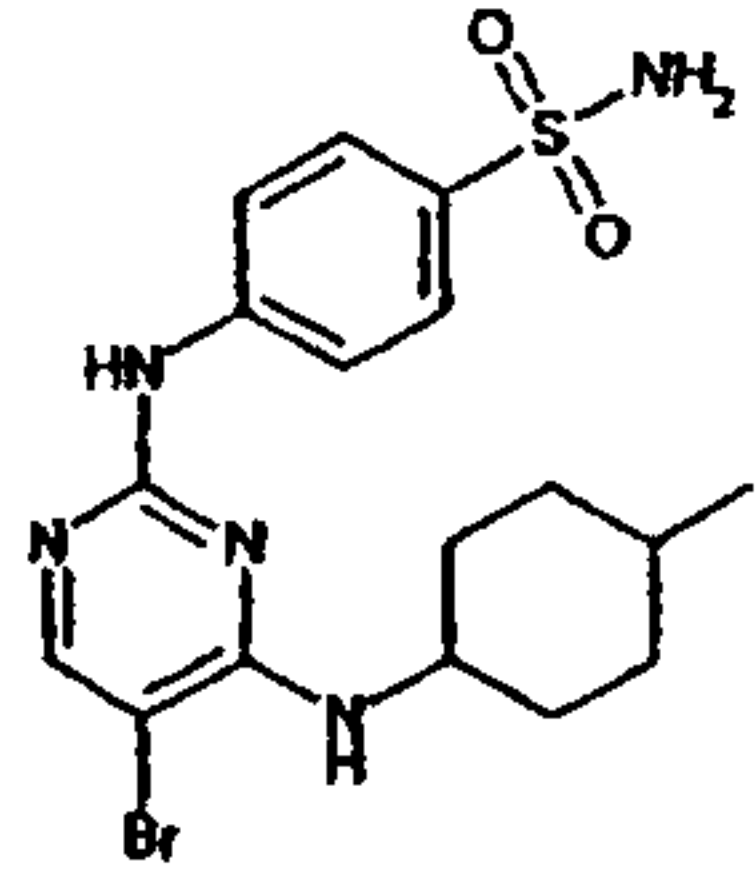
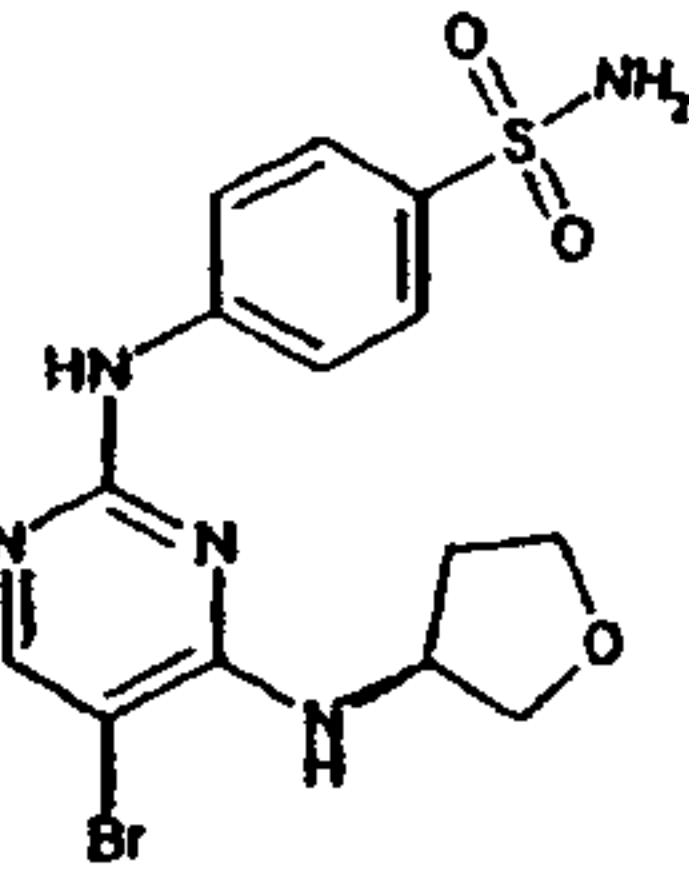
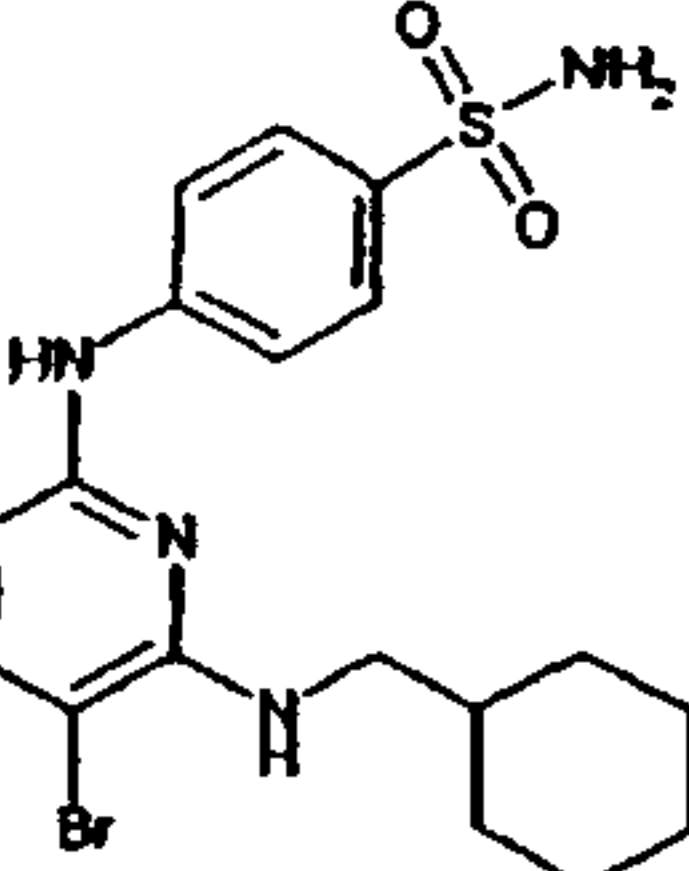
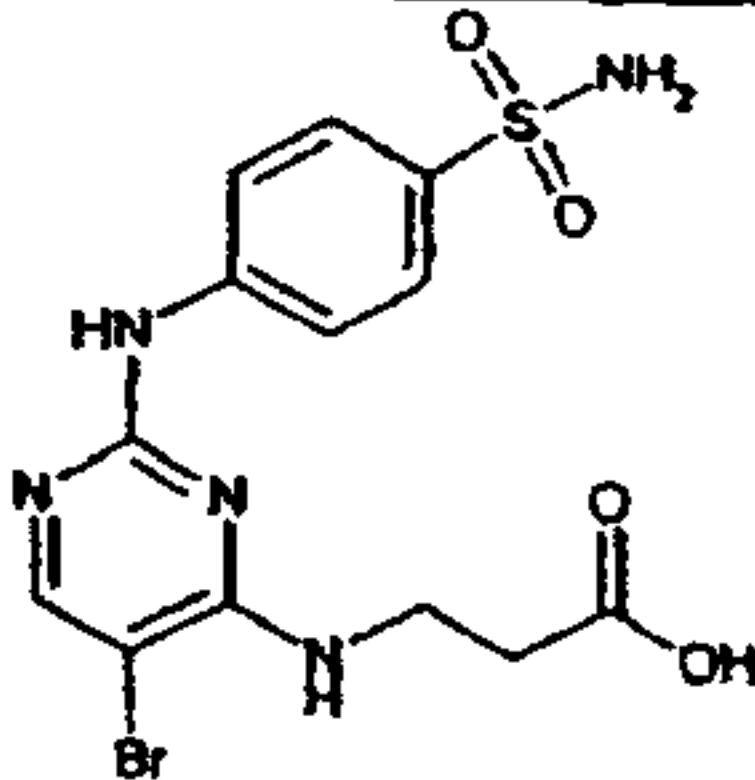
	 (+)- Enantiomer	 (-)- Enantiomer	 Diastereomer 1	 Diastereomer 2
Beispiel Nr.	198	199	200	201
	11.01 (s,1H) 8.32 (s,1H) 8.10 (d,1H) 7.80 (m,4H) 7.30 (br,2H) 3.70 (m,1H) 1.80 (m,5H) 1.48 (m,1H) 1.29 (m,2H) 1.07 (m,1H) 0.83 (d,3H)	11.01 (s,1H) 8.32 (s,1H) 8.10 (d,1H) 7.80 (m,4H) 7.30 (br,2H) 3.70 (m,1H) 1.80 (m,5H) 1.48 (m,1H) 1.29 (m,2H) 1.07 (m,1H) 0.83 (d,3H)		9.16 (s,1H) 8.07 (s,1H) 7.89 (d,2H) 7.67 (d,2H) 7.15 (s,2H) 6.45 (d,1H) 4.35 (s,2H) 3.97 (m,1H) 3.40 (m,4H) 2.85 (m,1H) 2.55 (m,1H) 1.82 (m,2H) 1.61 (m,6H)
Aus- beute	4%	4%	7%	2%
Schmp.				
Masse	439 (EI)	439 (EI)	515 (ES)	515 (ES)

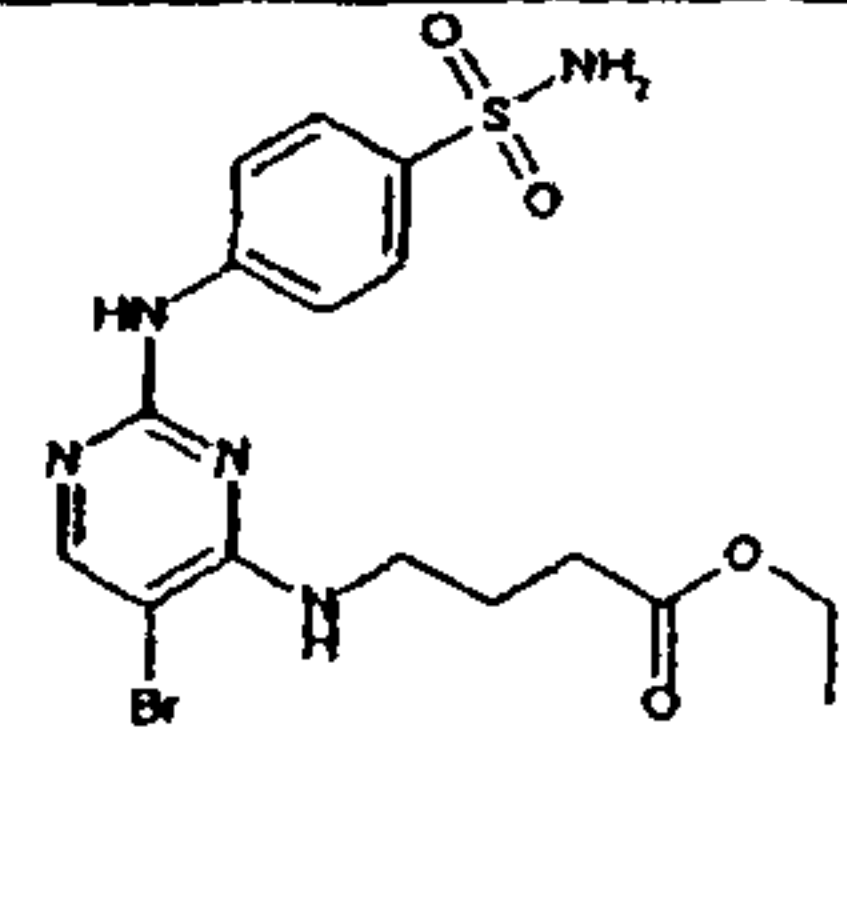
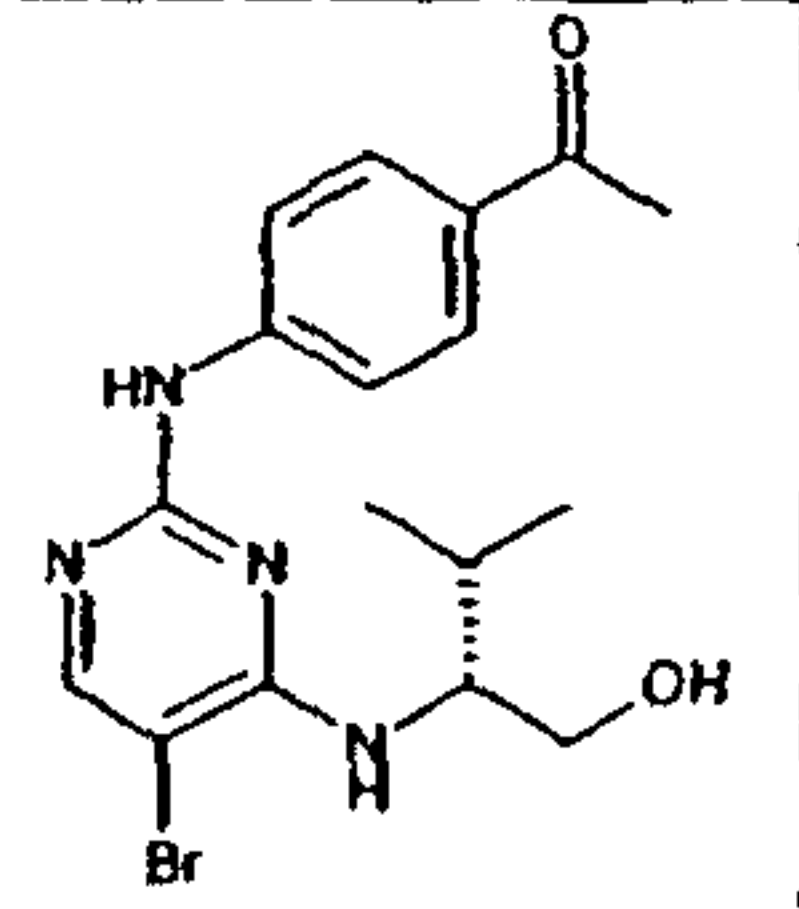
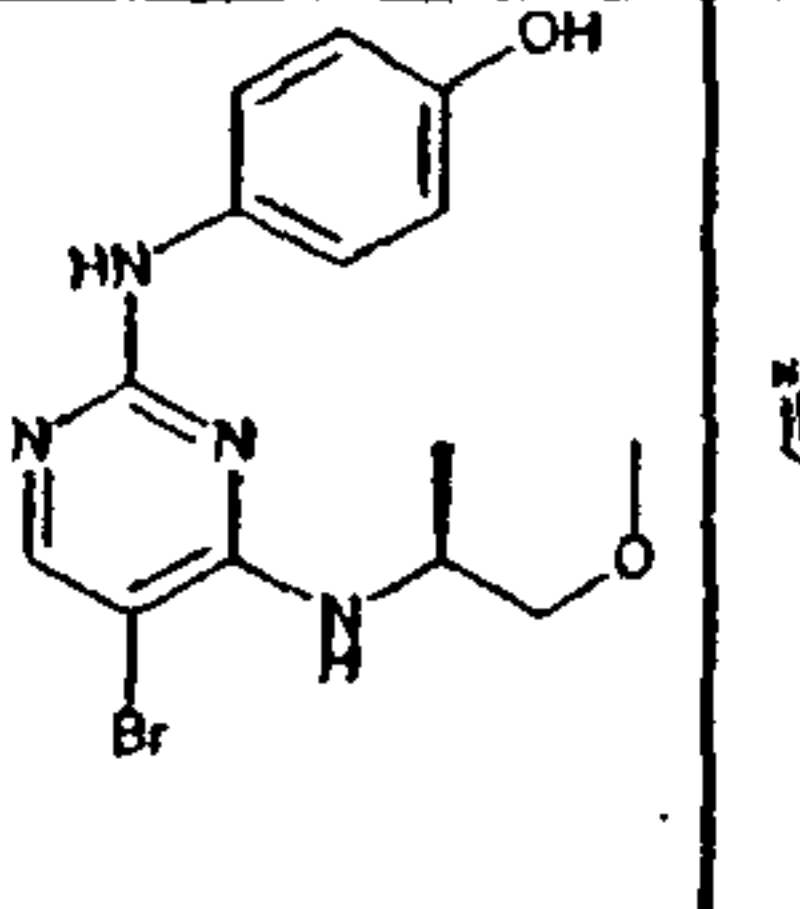
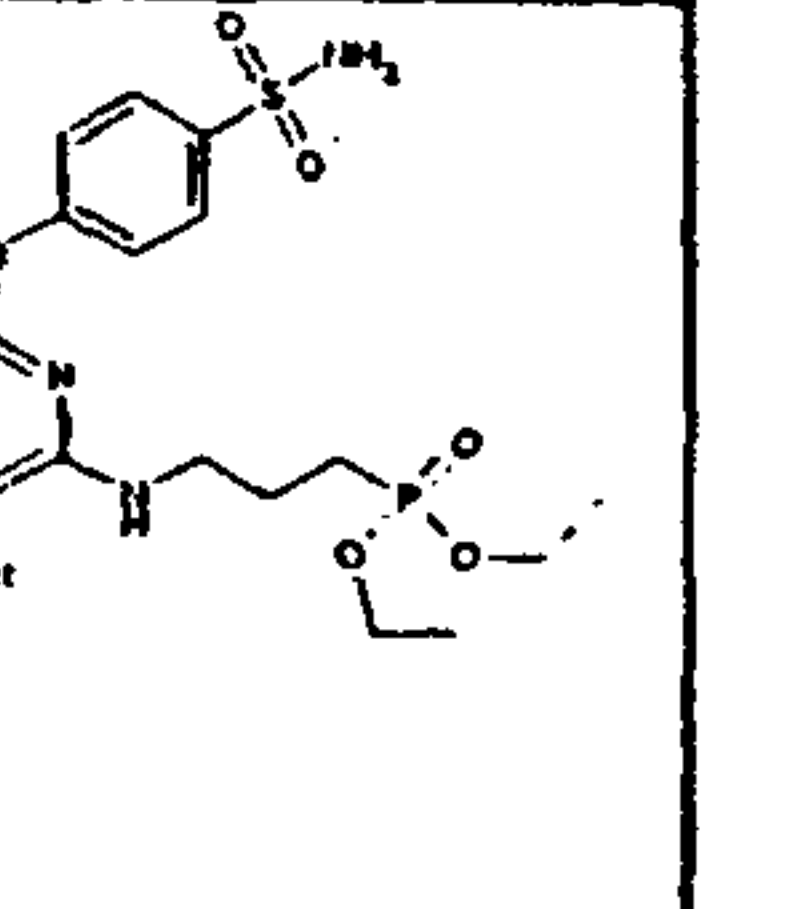
		 Diastereomer 1	 Diastereomer 2	
Beispiel Nr.	202	203 *	204 *	205
	10.21 (s,1H) 8.18 (s,1H) 8.10 (d,2H) 7.92 (d,2H) 6.39 (d,1H) 4.80 (br,1H) 4.05 (m,1H) 3.62 (m,2H) 2.00 (m,1H) 0.99 (d,3H) 0.92 (d,3H)		9.66 (s,1H) 8.08 (s,1H) 7.90 (d,2H) 7.69 (d,2H) 7.15 (s,2H) 6.53 (d,1H) 3.93 (m,1H) 2.05 (m,5H) 1.51 (m,2H) 1.15 (m,2H) 0.42 (m,2H) 0.25 (m,2H)	9.73 (s,1H) 8.11 (s,1H) 7.82 (d,2H) 7.65 (d,2H) 7.12 (s,2H) 6.80 (d,1H) 4.67 (m,1H) 3.13 (m,1H) 2.86 (m,3H) 2.18 (m,2H)
Aus- beute	10%	2%	2%	16%
Schmp.				
Masse	483 (ES)	480 (EI)	480 (EI)	430 (ES)

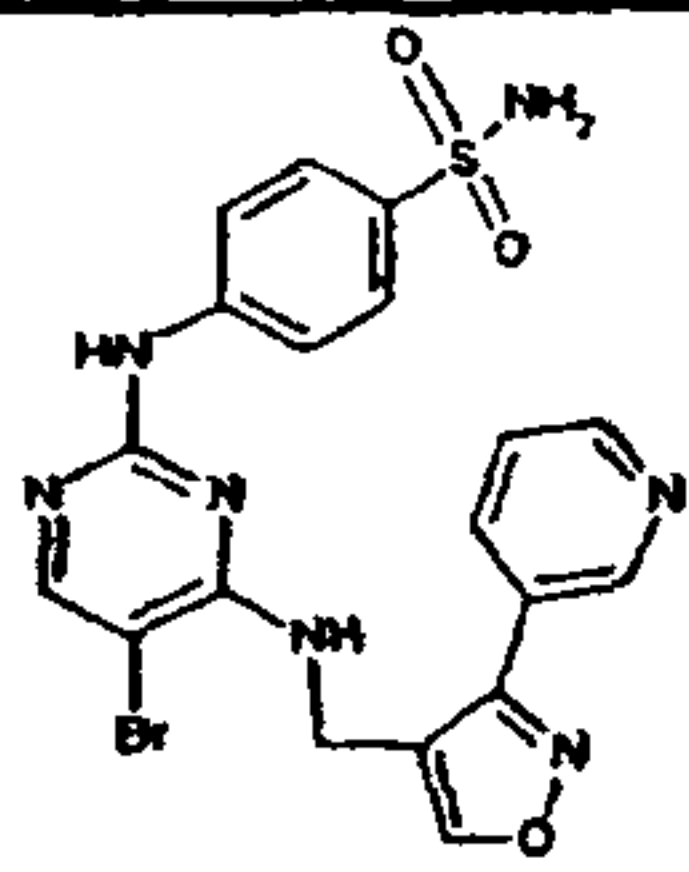
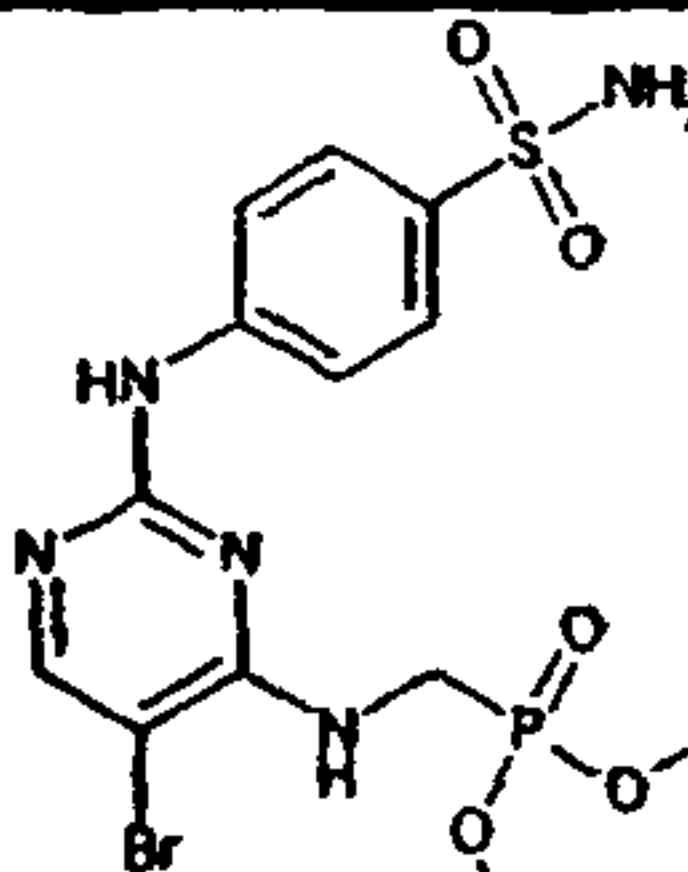
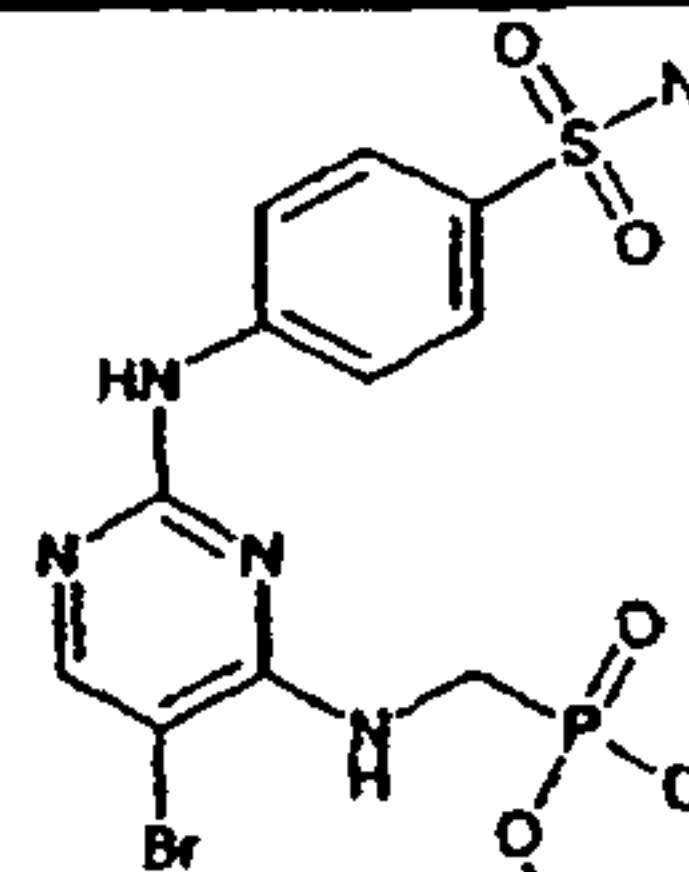
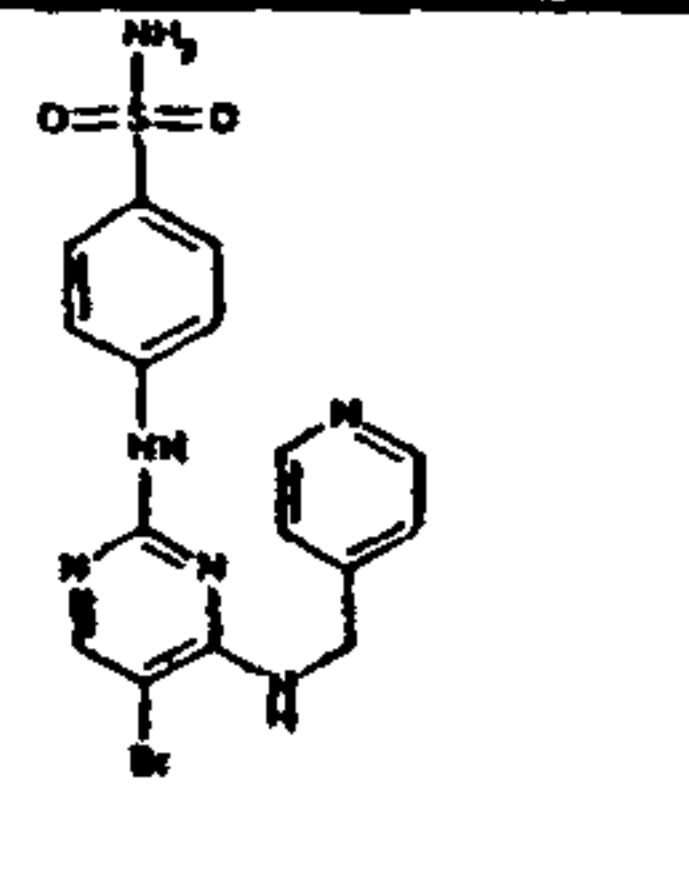
				
Beispiel Nr.	206	207	208	209
	9.75 (s, 1H) 8.19 (s, 1H) 7.75 (d, 2H) 7.18 (d, 2H) 7.17 (s, 2H) 6.68 (d, 1H) 5.35 (t, 1H) 4.71 (m, 1H) 3.91 (m, 2H) 3.65 (s, 3H)	10.98 (s, 1H) 8.50 (d, 2H) 8.31 (s, 1H) 7.97 (d, 2H) 7.78 (d, 2H) 7.57 (d, 1H) 7.00 (t, 1H) 4.01 (m, 1H) 3.62 (m, 2H) 1.97 (m, 1H) 0.98 (d, 3H) 0.92 (d, 3H)	11.00 (s, 1H) 8.31 (s, 1H) 7.74 (m, 5H) 7.21 (d, 1H) 6.80 (d, 1H) 4.00 (m, 1H) 3.62 (m, 2H) 1.95 (m, 1H) 0.98 (d, 3H) 0.90 (d, 3H)	9.55 (s, 1H) 8.08 (s, 1H) 7.80 (d, 2H) 7.60 (d, 2H) 6.58 (br, 4H) 6.20 (d, 1H) 4.80 (br, 1H) 4.04 (m, 1H) 3.60 (m, 2H) 2.00 (m, 1H) 0.99 (d, 3H) 0.92 (d, 3H)
Aus- beute	5%	55%	44%	77%
Schmp.	223	248	228	231
Masse	446 (ES)	507 (EI)	514 (EI)	

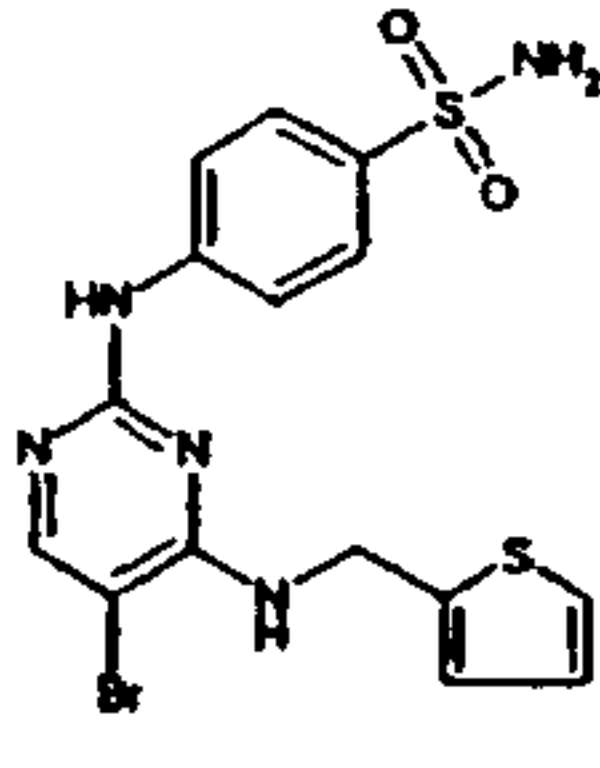
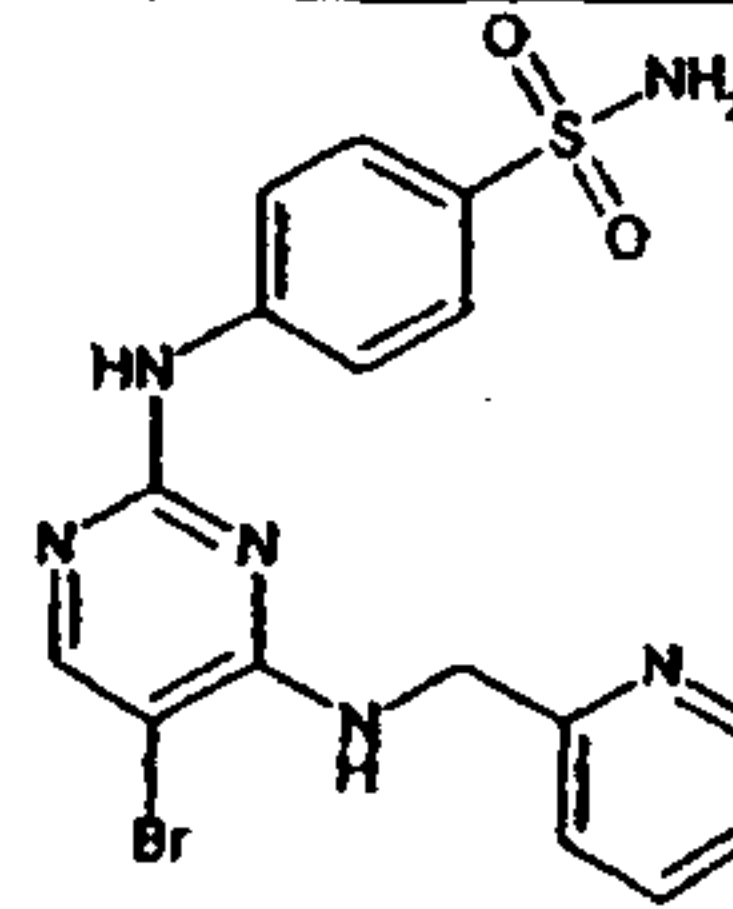
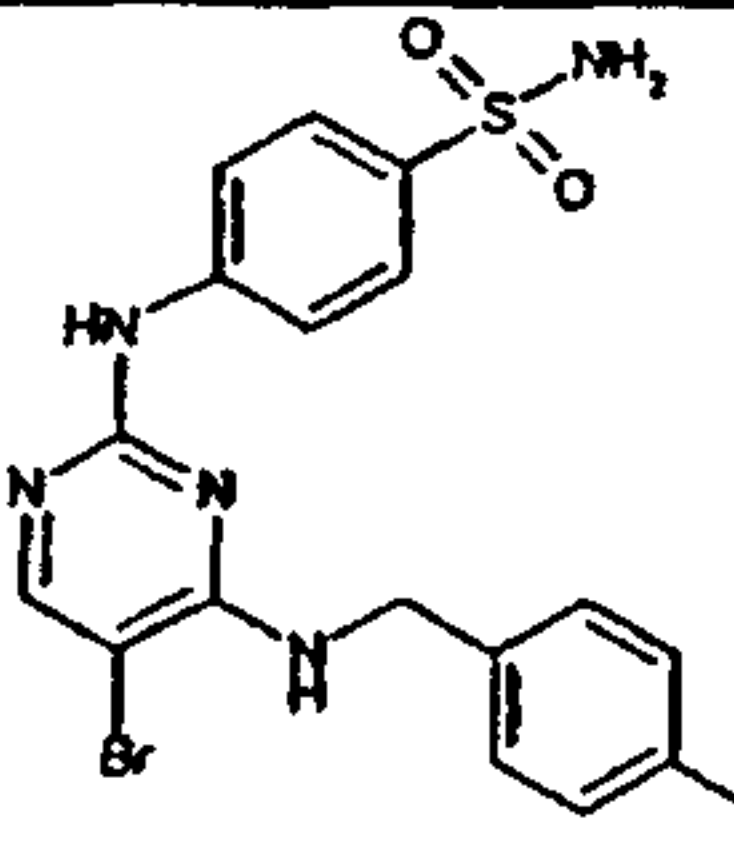
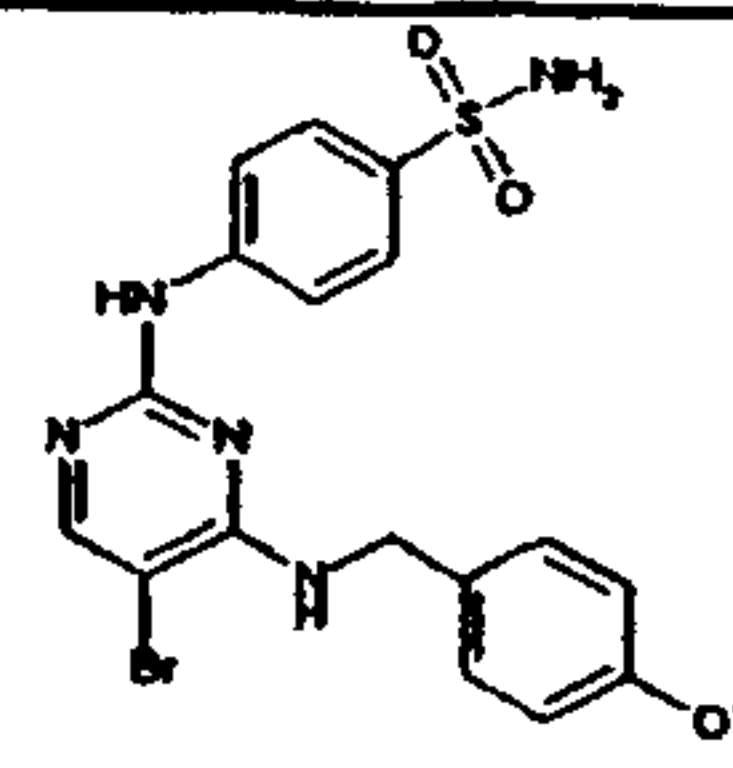
				
Beispiel Nr.	210	211	212	71
	10.03 (s, 1H) 8.38 (s, 1H) 8.14 (s, 1H) 7.81 (d, 2H) 7.60 (d, 1H) 7.30 (m, 7H) 4.99 (s, 2H) 3.42 (m, 2H) 2.97 (m, 2H) 1.58 (m, 2H) 1.30 (m, 4H)	10.90 (s, 1H) 8.40 (m, 1H) 8.30 (s, 1H) 7.88 (d, 2H) 7.73 (d, 2H) 7.38 (br, 1H) 3.45 (m, 4H) 2.38 (s, 3H) 1.62 (m, 2H) 1.45 (m, 2H)	9.18 (s, 1H) 9.05 (s, 1H) 7.98 (s, 1H) 7.18 (m, 2H) 6.98 (m, 2H) 6.31 (m, 1H) 4.45 (t, 1H) 3.47 (m, 4H) 1.63 (m, 2H) 1.48 (m, 2H)	9.66 (s, 1H) 8.08 (s, 1H) 7.88 (d, 2H) 7.63 (m, 3H) 7.28 (t, 1H) 7.11 (s, 2H) 6.88 (s, 1H) 3.65 (m, 2H) 2.88 (t, 2H)
Aus- beute	86%	22%	41%	77%
Schmp.				
Masse	528 (CI)	429 (EI)	352 (EI)	437 (EI)

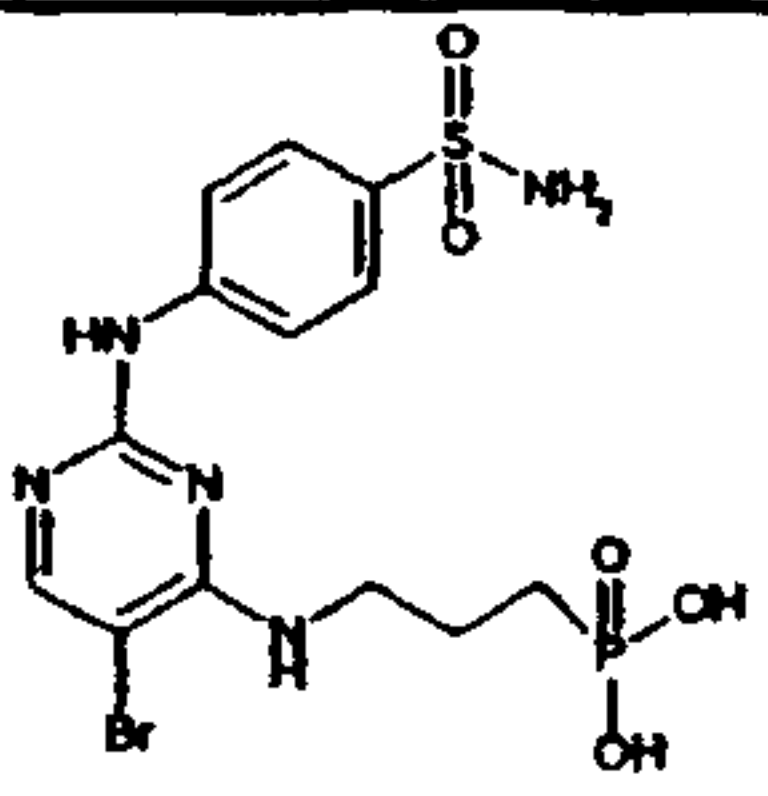
				
Beispiel Nr.	213	61	214	215
	12.40 (br, 1H) 11.10 (s, 1H) 8.08 (d, 2H) 7.79 (m, 4H) 7.30 (s, 2H) 4.04 (m, 1H) 3.60 (m, 2H) 2.07 (s, 3H) 2.00 (m, 1H) 0.97 (d, 3H) 0.90 (d, 3H)	12.41 (br, 1H) 11.11 (s, 1H) 8.10 (d, 1H) 7.80 (m, 5H) 7.30 (s, 2H) 4.08 (m, 1H) 3.63 (m, 2H) 2.50 (m, 2H) 2.01 (m, 1H) 1.15 (t, 3H) 0.99 (d, 3H) 0.92 (d, 3H)	8.03 (s, 1H) 7.76 (m, 4H) 3.70 (s, 2H) 1.92 (m, 4H) 0.92 (m, 6H) (in MeOD)	9.55 (s, 1H) 8.10 (s, 1H) 7.80 (d, 2H) 7.68 (d, 2H) 7.15 (s, 2H) 5.82 (s, 1H) 3.74 (d, 1H) 3.52 (d, 1H) 2.72 (m, 1H) 1.35 (s, 3H) 0.97 (d, 3H) 0.91 (d, 3H)
Aus- beute	49%	25%	2%	9%
Schmp.				
Masse	365 (EI)	379 (EI)	443 (ES)	444 (ES)

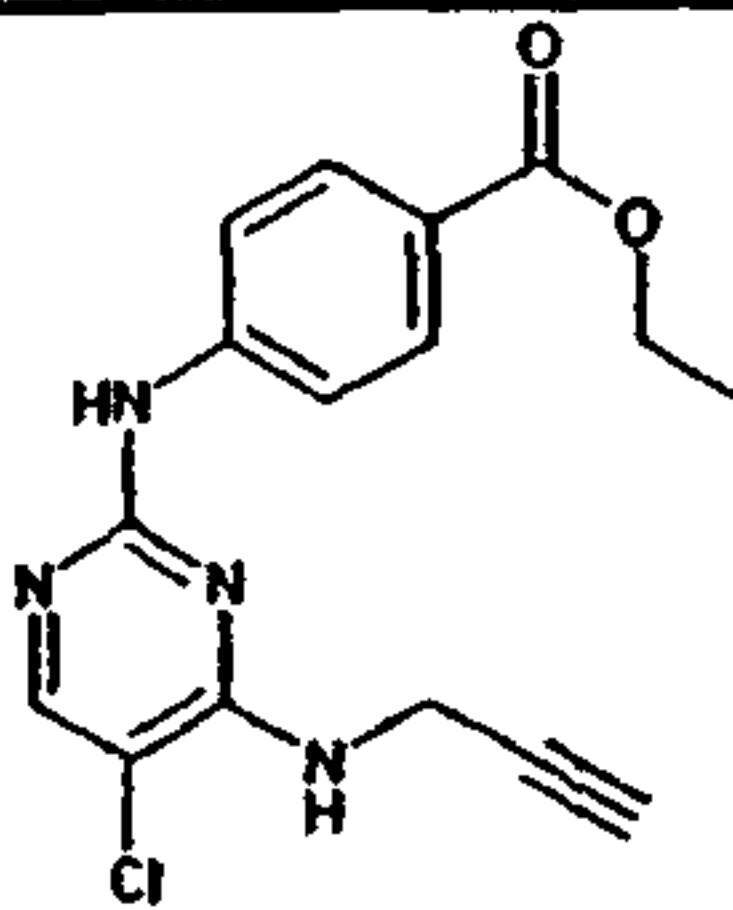
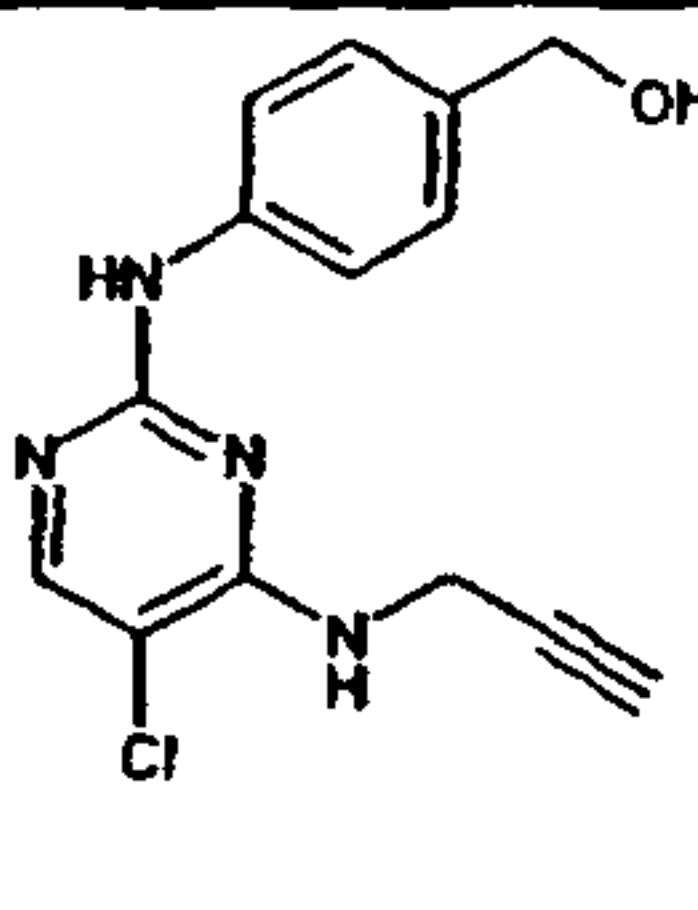
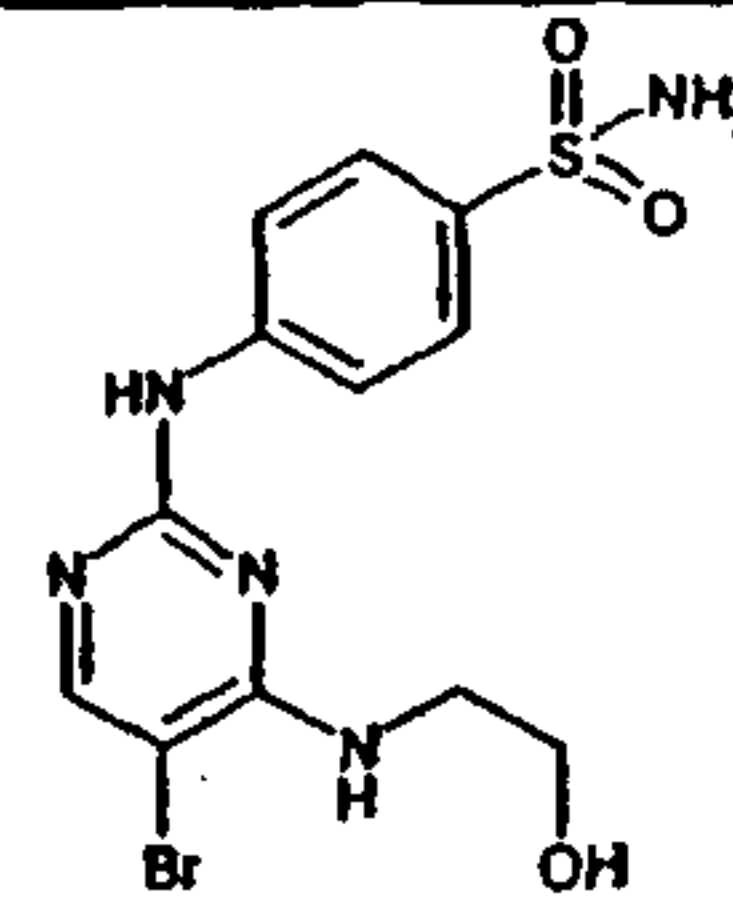
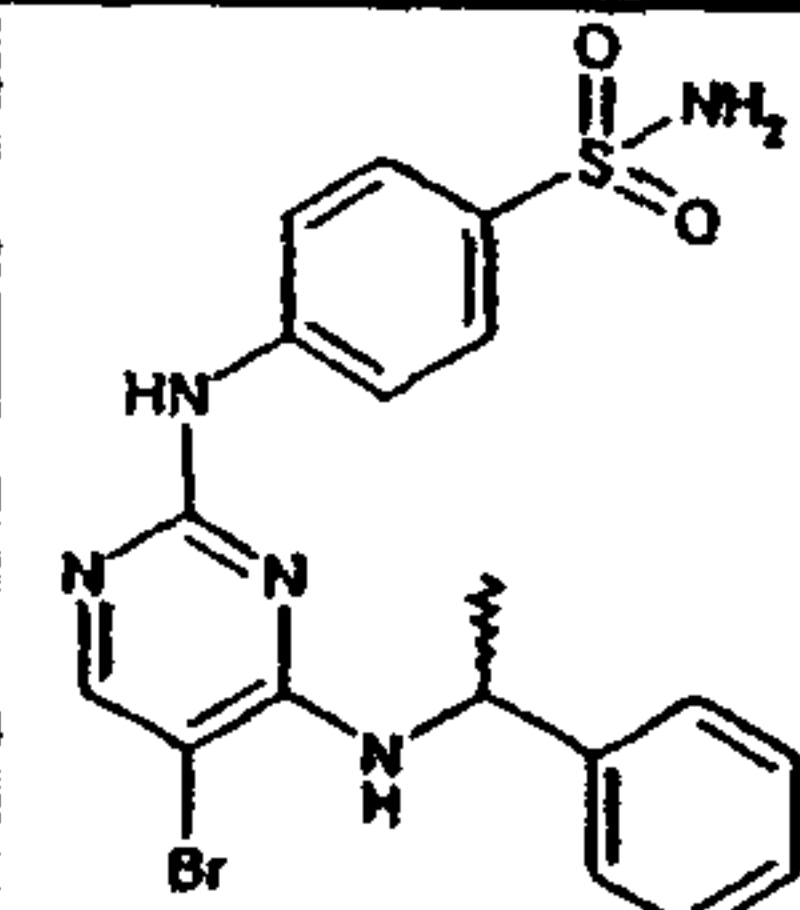
				
Beispiel Nr.	216	217	218	219
	10.88 (s,1H) 8.36 (s,1H) 8.03 (d,1H) 7.79 (m,4H) 7.28 (br,2H) 4.65 (m,1H) 3.89 (m,2H)	10.88 (s,1H) 8.36 (s,1H) 8.03 (d,1H) 7.79 (m,4H) 7.28 (br,2H) 4.65 (m,1H) 3.89 (m,2H) 3.71 (m,2H) 2.19 (m,2H)	11.01 (s,1H) 8.52 (br,1H) 8.29 (s,1H) 7.78 (m,4H) 7.32 (s,2H) 3.39 (m,2H) 1.70 (m,6H) 1.15 (m,3H) 0.96 (m,2H)	11.11 (s,1H) 8.53 (m,1H) 8.36 (s,1H) 7.80 (m,4H) 7.31 (s,2H) 3.71 (m,2H) 2.65 (m,2H)
Aus- beute	65%	34%	58%	88%
Schmp.	239	239	238	280
Masse	439 (EI)	413 (EI)	439 (EI)	416 (EI)

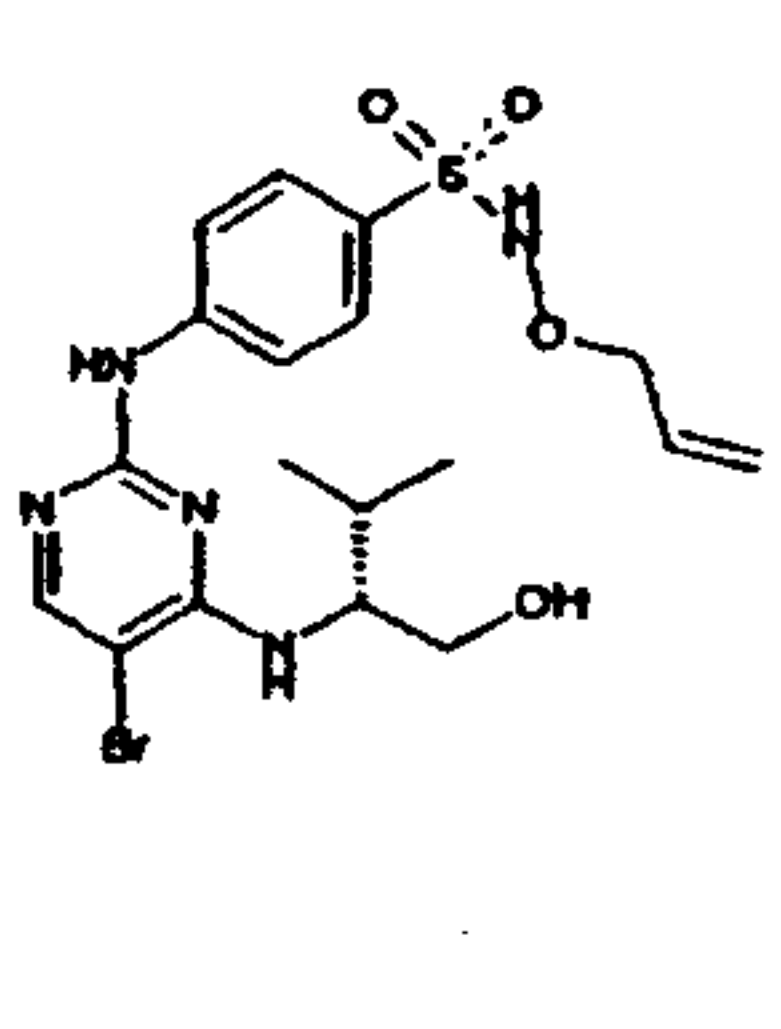
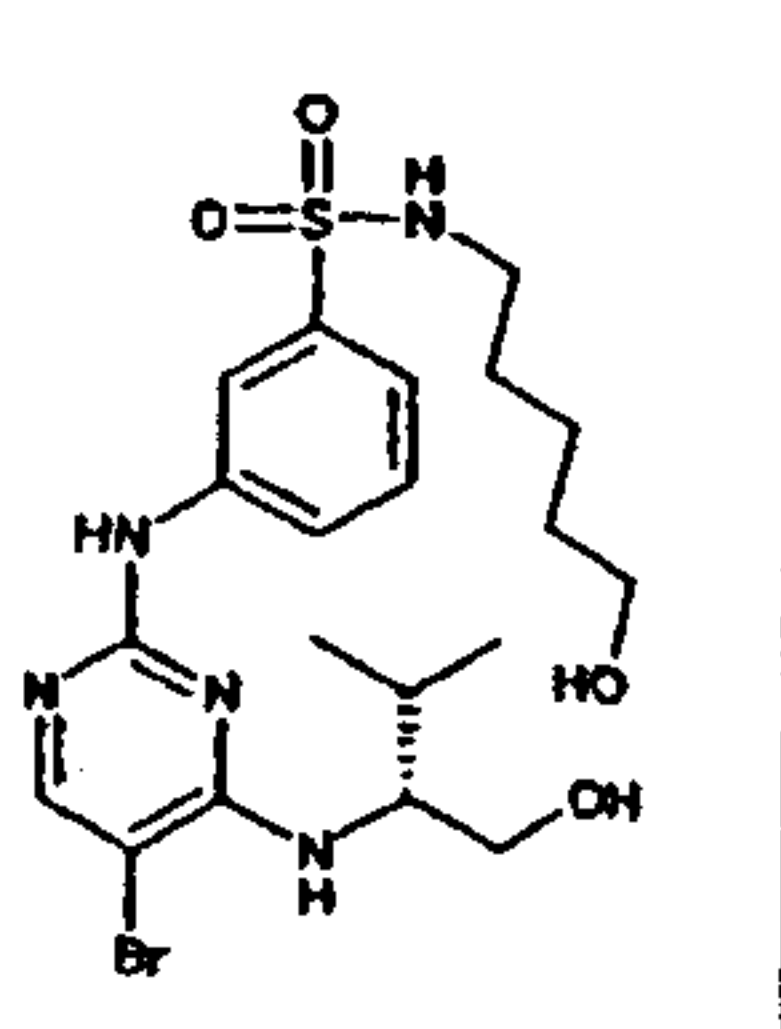
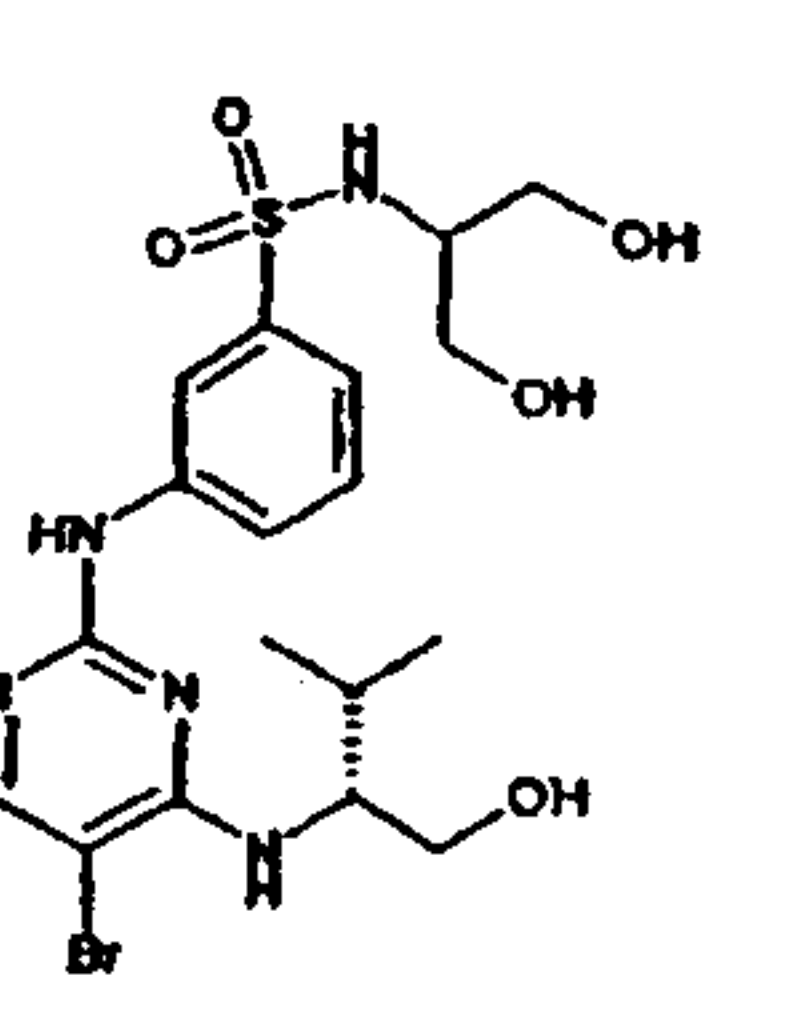
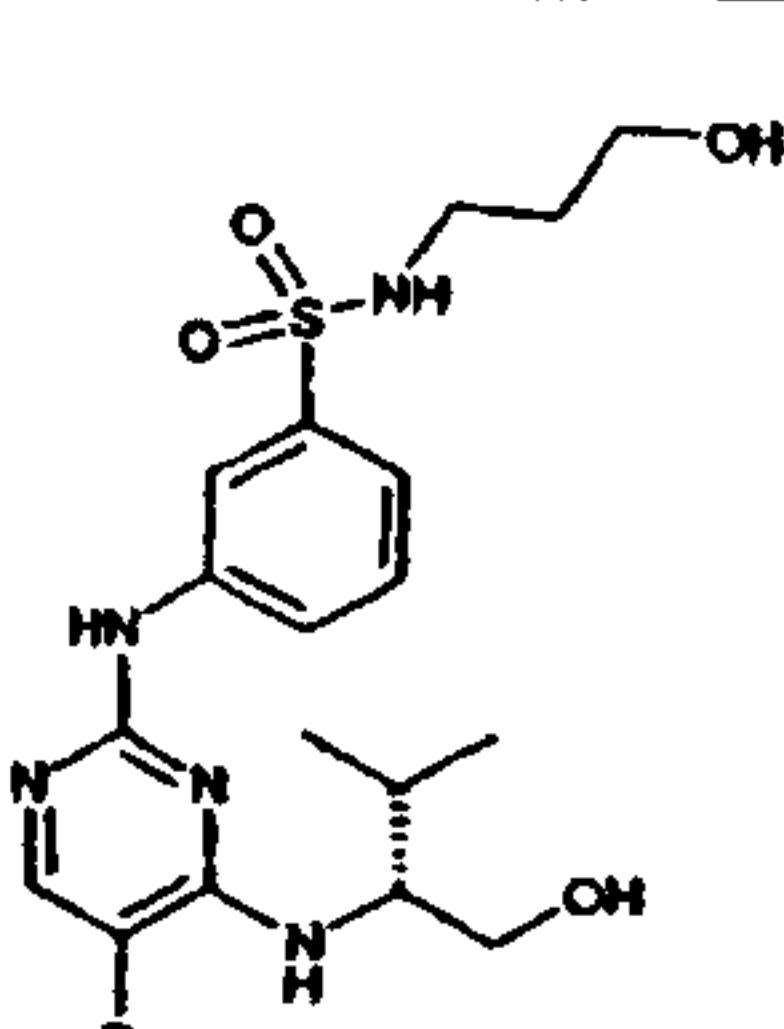
				
Beispiel Nr.	74	56	220	221
	9.67 (s, 1H)	9.70 (s, 1H) 8.11 (s, 1H) 7.88 (m, 4H) 6.25 (d, 1H) 4.81 (m, 1H) 4.05 (m, 1H) 3.61 (m, 2H) 2.01 (m, 1H) 0.97 (d, 3H) 0.92 (d, 3H)	8.92 (m, 1H) 8.81 (m, 1H) 7.96 (s, 1H) 7.43 (d, 2H) 6.67 (d, 2H) 6.20 (m, 1H) 4.38 (m, 1H) 3.48 (m, 1H) 3.37 (m, 1H) 1.20 (d, 3H)	9.66 (s, 1H) 8.08 (s, 1H) 7.83 (d, 2H) 7.68 (d, 2H) 7.22 (t, 1H) 7.11 (s, 2H) 3.95 (m, 4H) 3.48 (m, 2H) 1.79 (m, 4H) 1.18 (t, 6H)
Aus- beute	7%	17%	65%	19%
Schmp.	285	158	166	
Masse	457 (EI)	392 (EI)	354 (EI)	522 (ES)

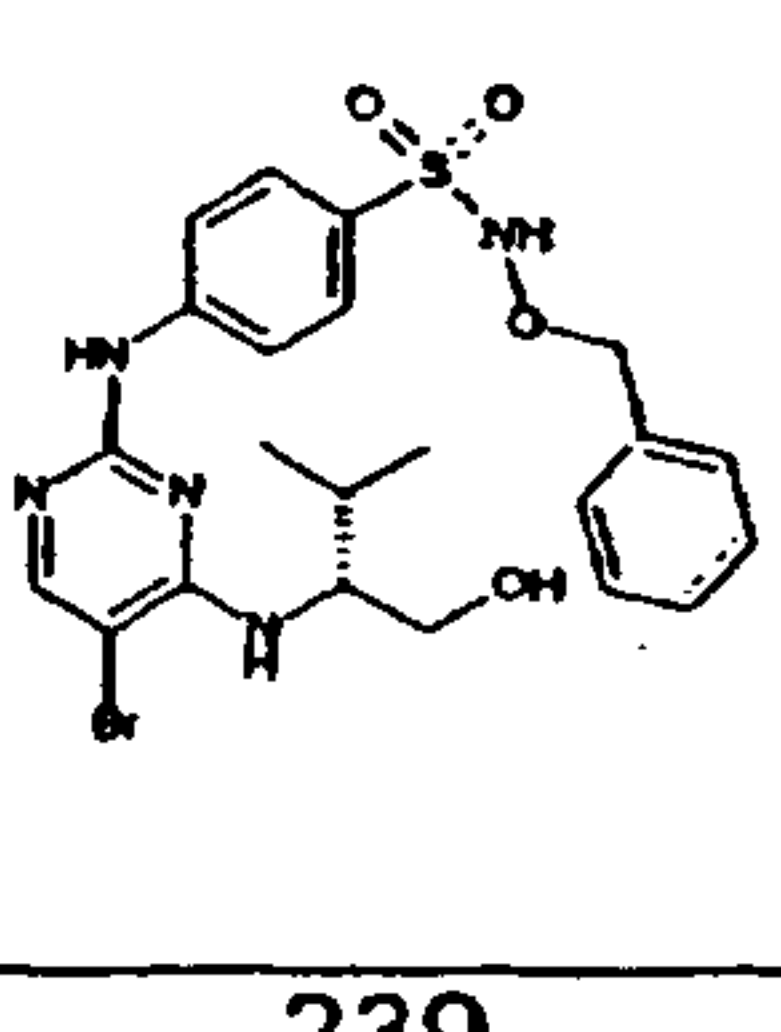
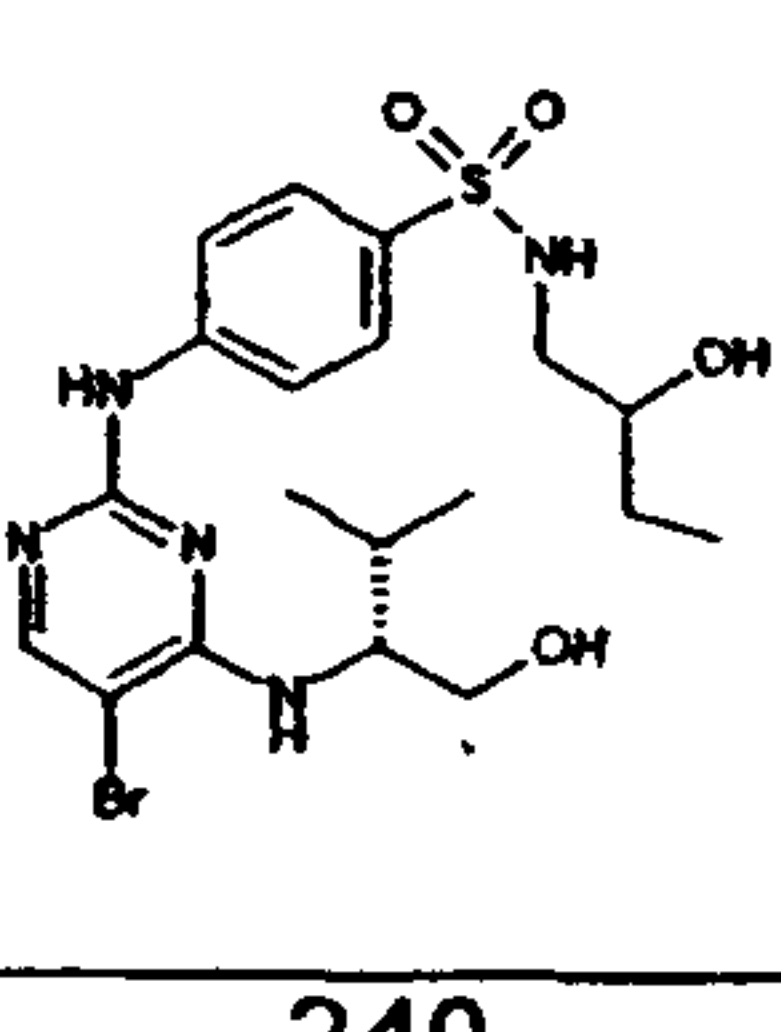
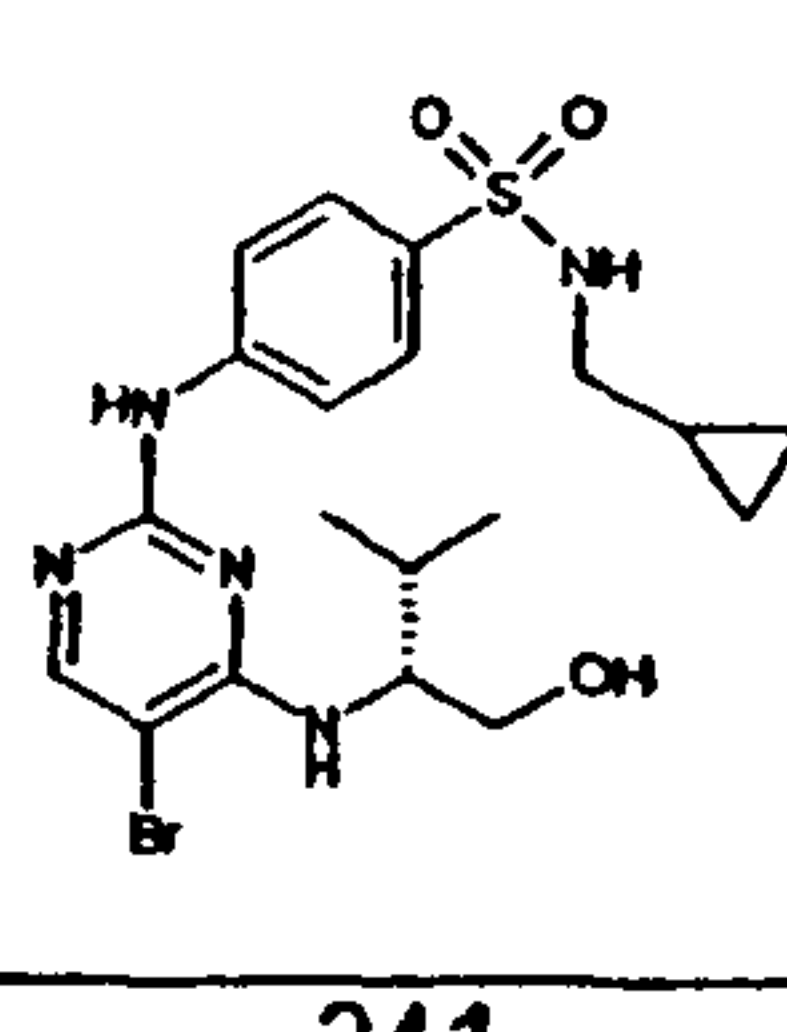
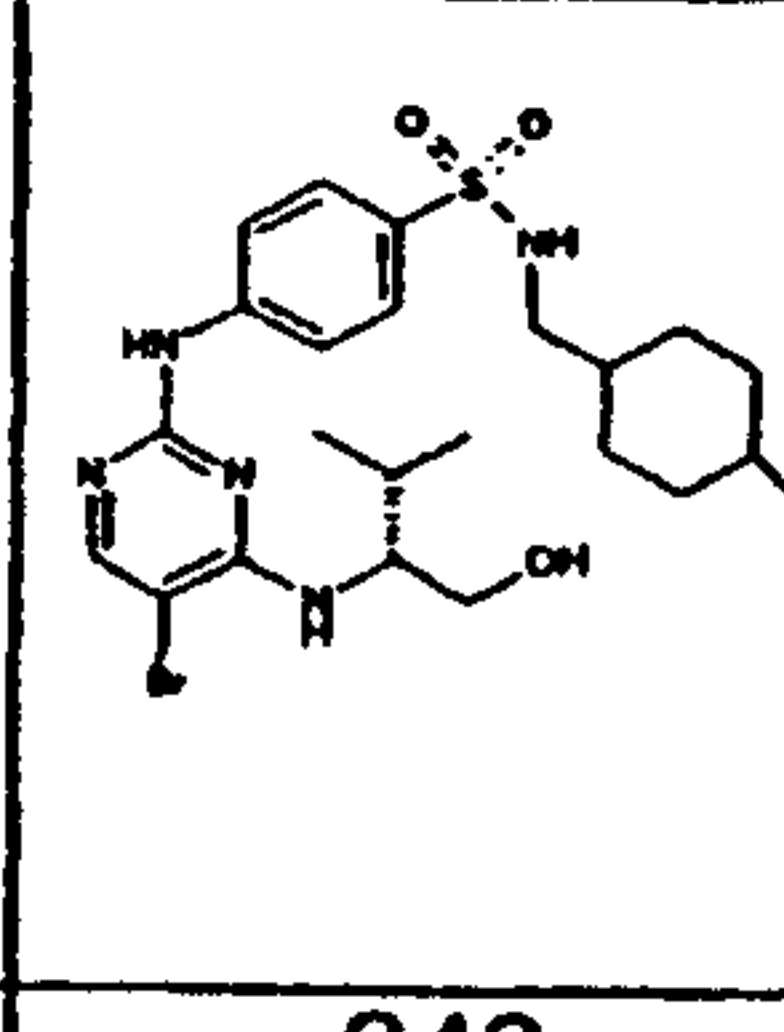
				
Beispiel Nr.	222	223	224	225
	9.81 (s,1H) 9.08 (s,1H) 8.68 (s,1H) 8,35 (m,1H) 8.20 (s,1H) 8.02 (t,1H) 7.63 (m,5H) 7.17 (s,2H) 7.03 (s,1H) 4.82 (d,2H)	9.71 (s,1H) 8.13 (s,1H) 7.89 (d,2H) 7.66 (d,2H) 7.31 (t,1H) 7.14 (s,2H) 3.98 (m,2H) 3.69 (s,3H) 3.64 (s,3H)	9.70 (s,1H) 8.08 (s,1H) 7.88 (d,2H) 7.65 (d,2H) 7.25 (m,3H) 6.11 (m,1H) 3.40 (m,5H)	10.29 (s,1H) 8.83 (m,2H) 8.51 (m,1H) 8.26 (s,1H) 7.93 (d,2H) 7.60 (d,2H) 7.51 (d,2H) 7.25 (br,2H) 4.90 (d,2H)
Aus- beute	54%	23%	7%	43
Schmp.	300	300		243
Masse	501 (EI)	465 (EI)		434 (EI)

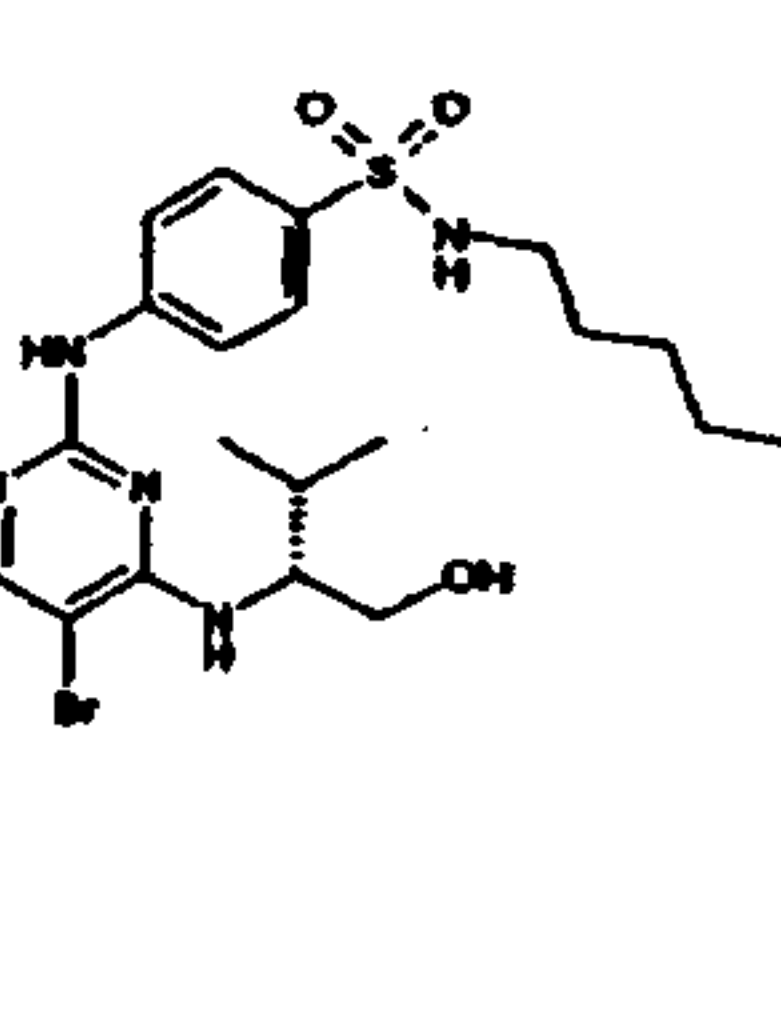
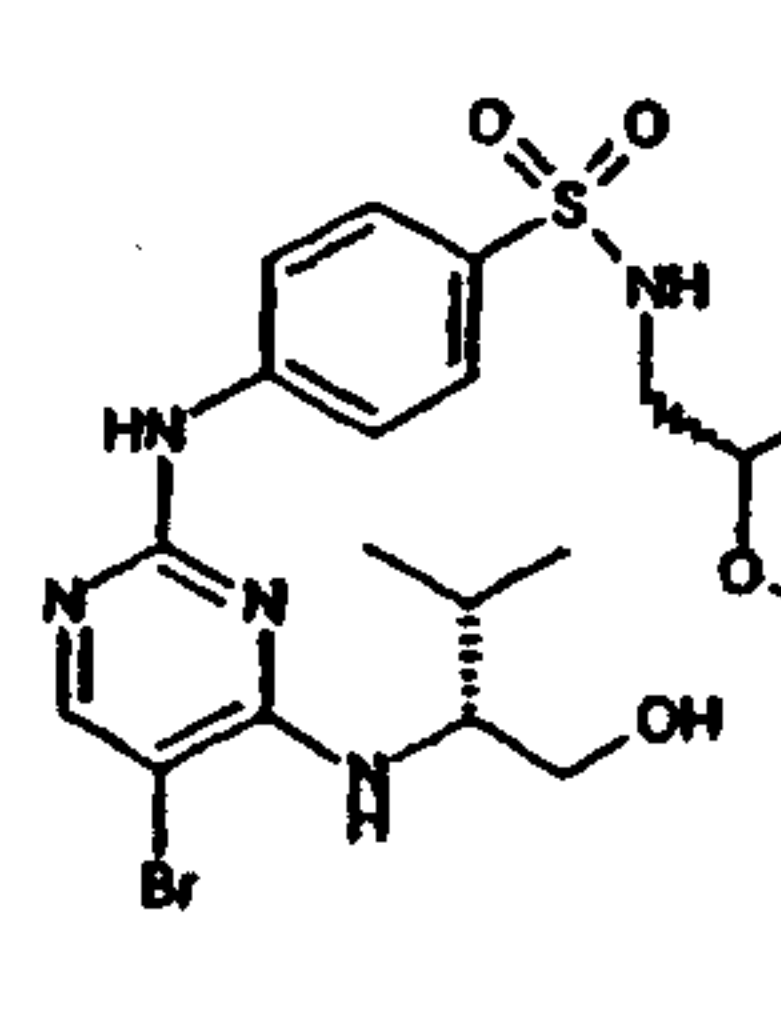
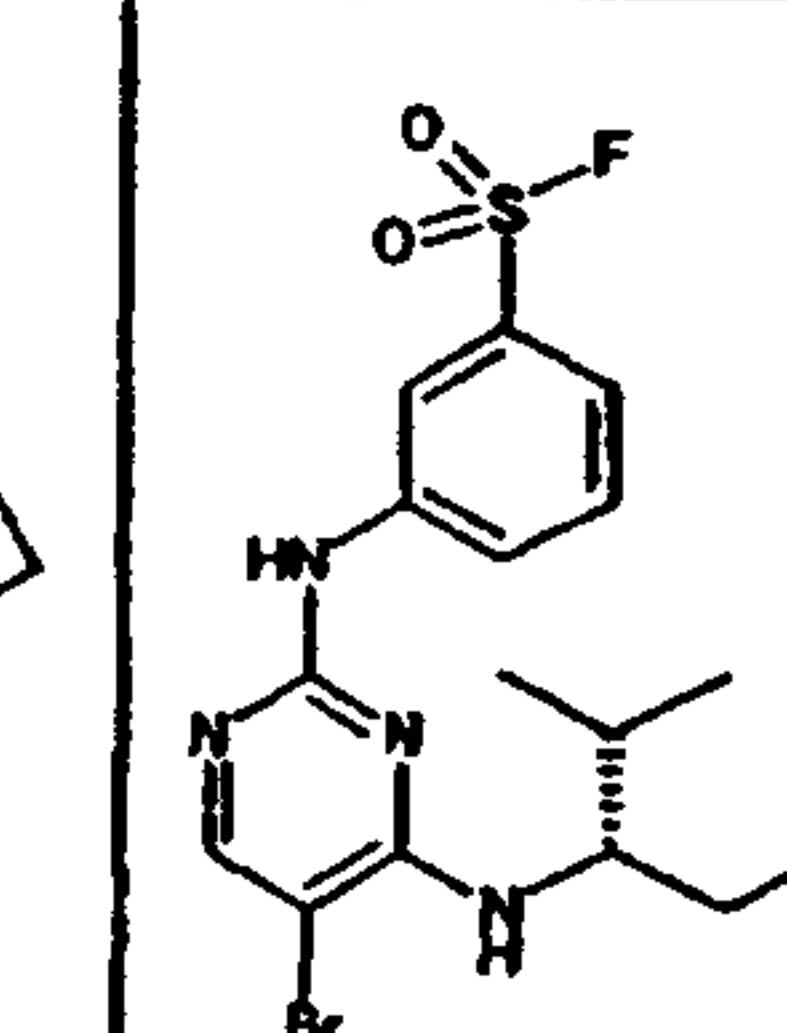
				
Beispiel Nr.	226	227	228	229
	10.38 (s, 1H) 8.52 (br, 1H) 8.23 (s, 1H) 7.72 (m, 4H) 7.36 (m, 1H) 7.22 (s, 2H) 7.03 (m, 1H) 6.95 (m, 1H) 4.80 (d, 2H)	10.30 (s, 1H) 8.78 (m, 1H) 8.36 (m, 3H) 7.81 (m, 2H) 7.60 (m, 4H) 7.22 (br, 2H) 4.94 (d, 2H)	10.52 (s, 1H) 8.66 (m, 1H) 8.28 (s, 1H) 7.63 (m, 4H) 7.26 (m, 6H) 4.63 (d, 2H)	10.88 (s, 1H) 8.92 (m, 1H) 8.33 (s, 1H) 7.72 (d, 2H) 7.62 (d, 2H) 7.30 (m, 4H) 6.89 (d, 2H) 4.62 (d, 2H) 3.70 (s, 3H)
Aus- beute	47%	41%	88%	89%
Schmp.	229	287	259	233
Masse	440 (CI)	434 (EI)	451 (EI)	463 (EI)

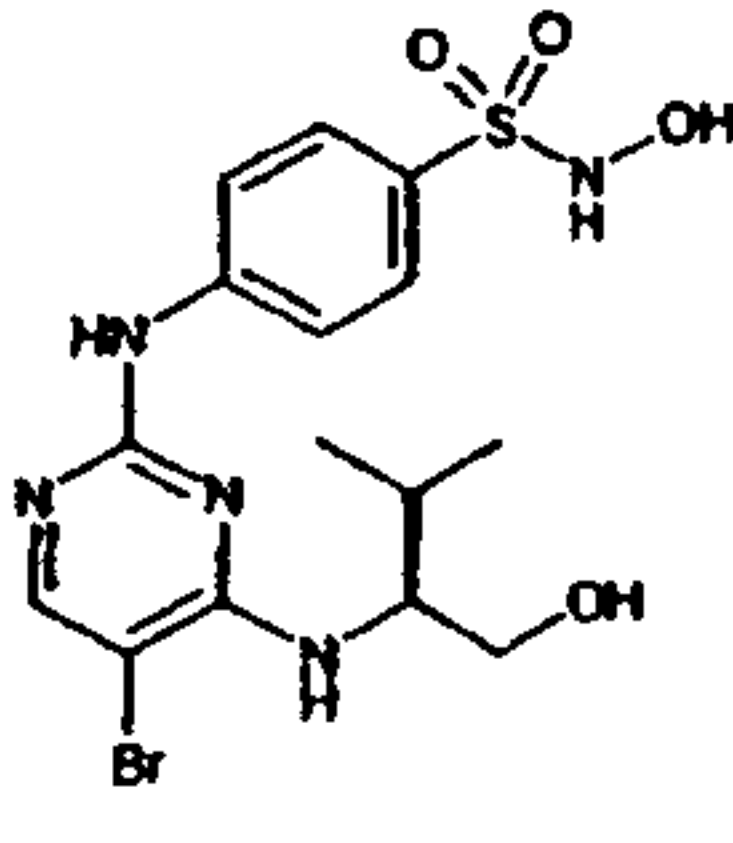
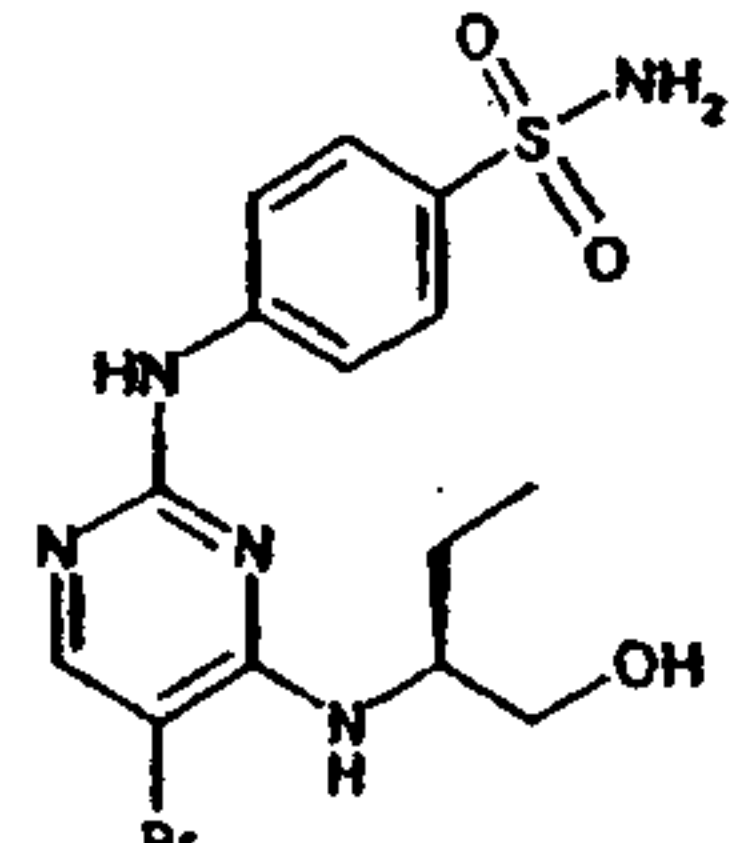
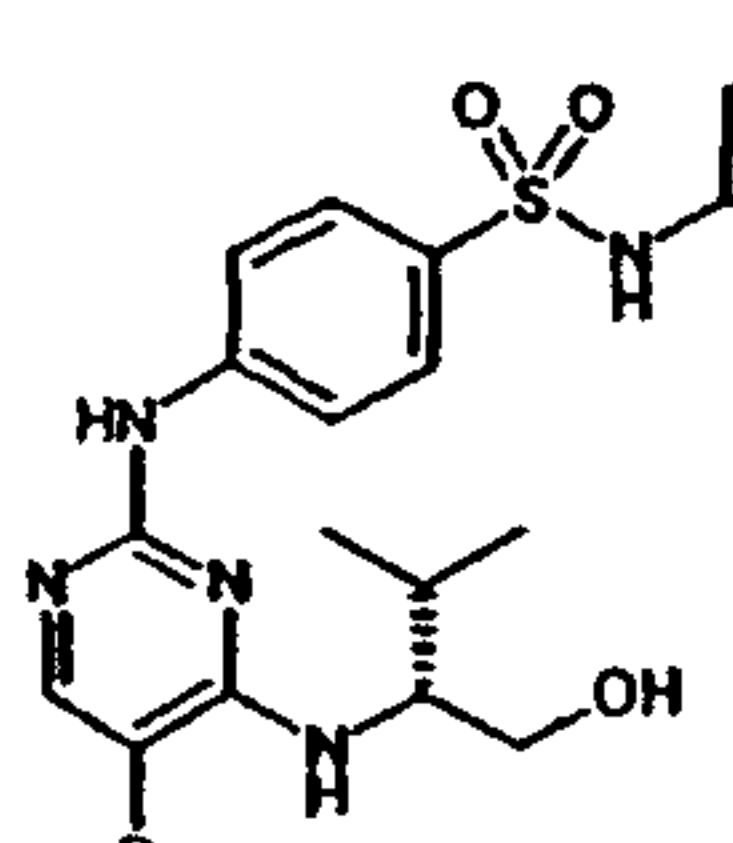
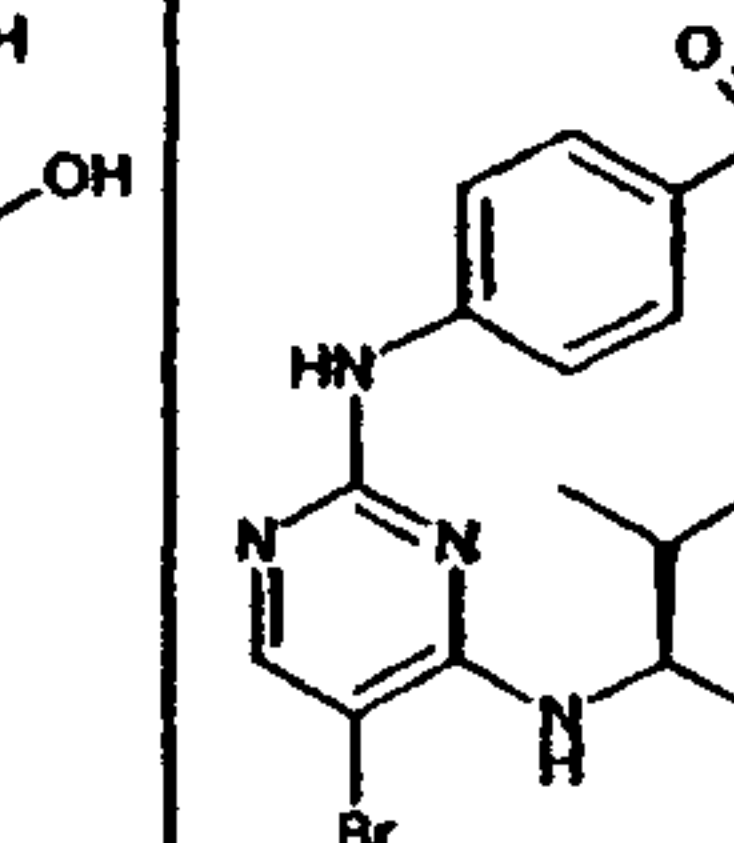
	
BeispielNr.	230
	10.45 (s,1H) 8.20 (s,1H) 8.05 (m,1H) 7.79 (m,4H) 7.21 (s,2H) 3.50 (m,2H) 1.83 (m,2H) 1.56 (m,2H)
Ausbeute	58%
Schmp.	>300
Masse	466 (ES)

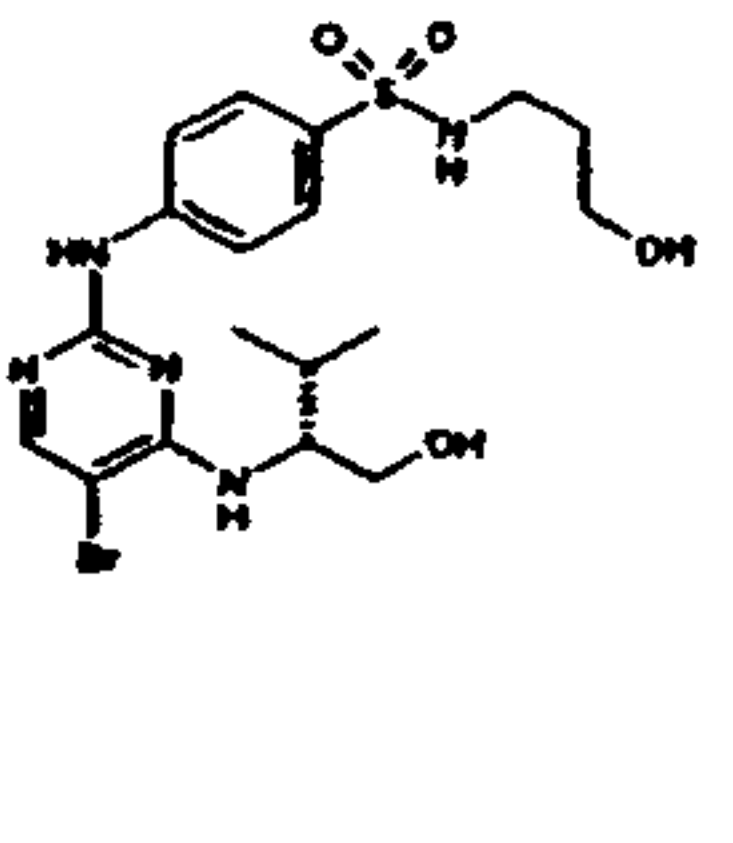
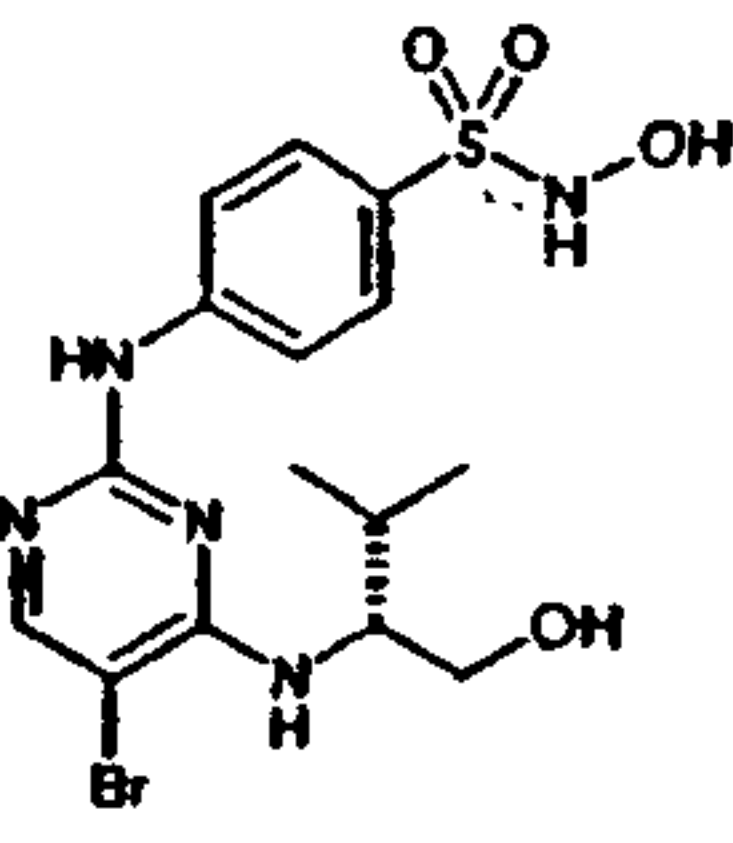
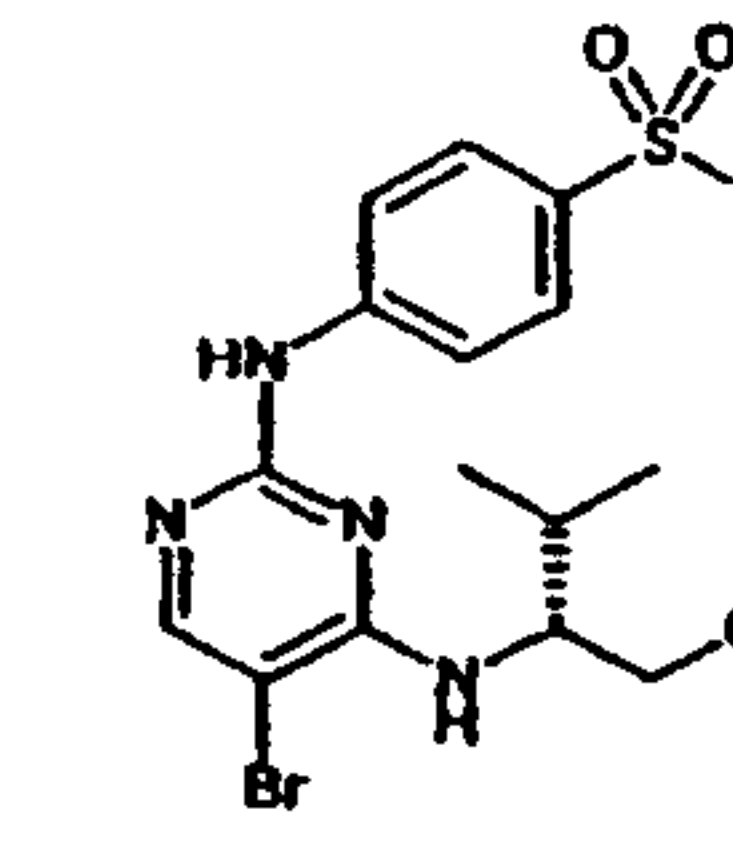
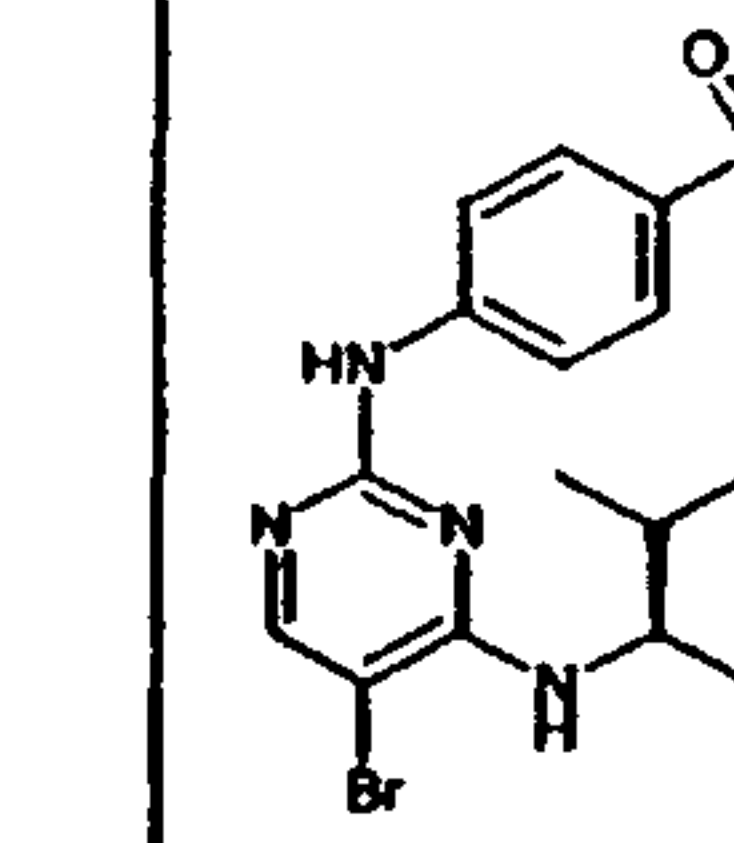
				
Beispiel Nr.	231	232	233	234
	10.3 (s, 1H) 8.34 (tr, 1H) 8.2 (s, 1H) 7.9 (m, 4H) 4.3 (q, 2H) 4.2 (m, 2H) 3.23 (tr, 1H) 1.32 (tr, 3H)	9.28 (s, 1H) 8.0 (s, 1H) 7.73 (d, 2H) 7.63 (tr, 1H) 7.18 (d, 2H) 5.0 (m, 1H) 4.3 (s, 2H) 4.14 (m, 2H) 3.11 (tr, 1H)	10.48 (s, 1H) 8.25 (s, 1H) 7.85 (m, 4H) 7.25 (m, 1H) 7.15 (s, 1H) 5.1 (m, 1H) 3.58 (m, 4H)	9.63 (s, 1H) 8.12 (s, 1H) 7.65 (m, 4H) 7.42 (d, 2H) 7.35 (tr, 2H) 7.21 (m, 1H) 7.16 (s, 1H) 5.35 (m, 1H) 1.55 (d, 3H)
Aus- beute	85%	35%	33%	25%
Schmp.				
Masse	330 (EI)	288 (EI)	389 (CI)	448 (ESI)

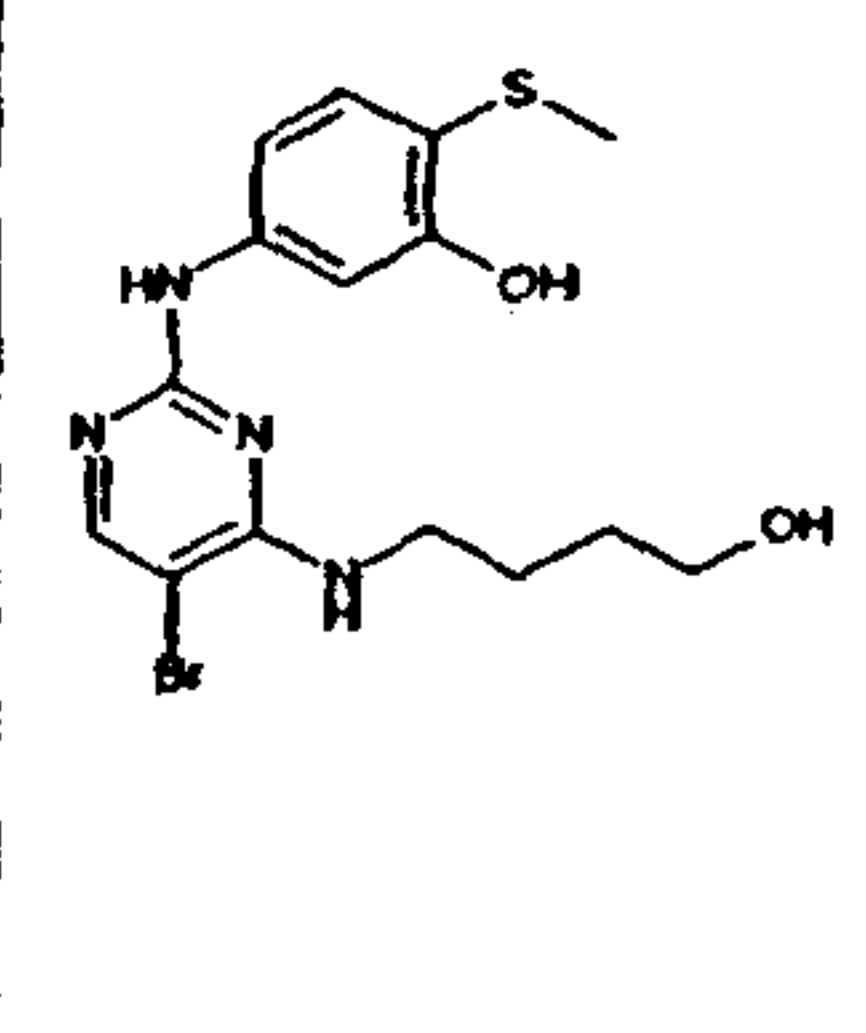
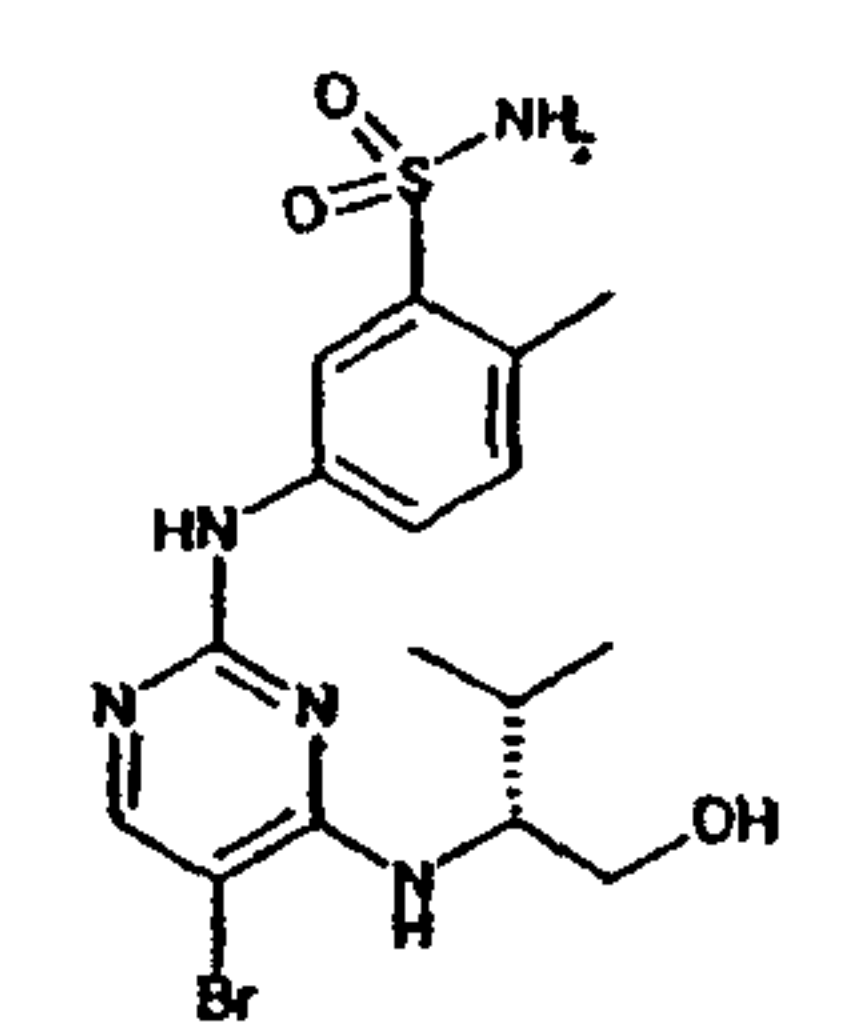
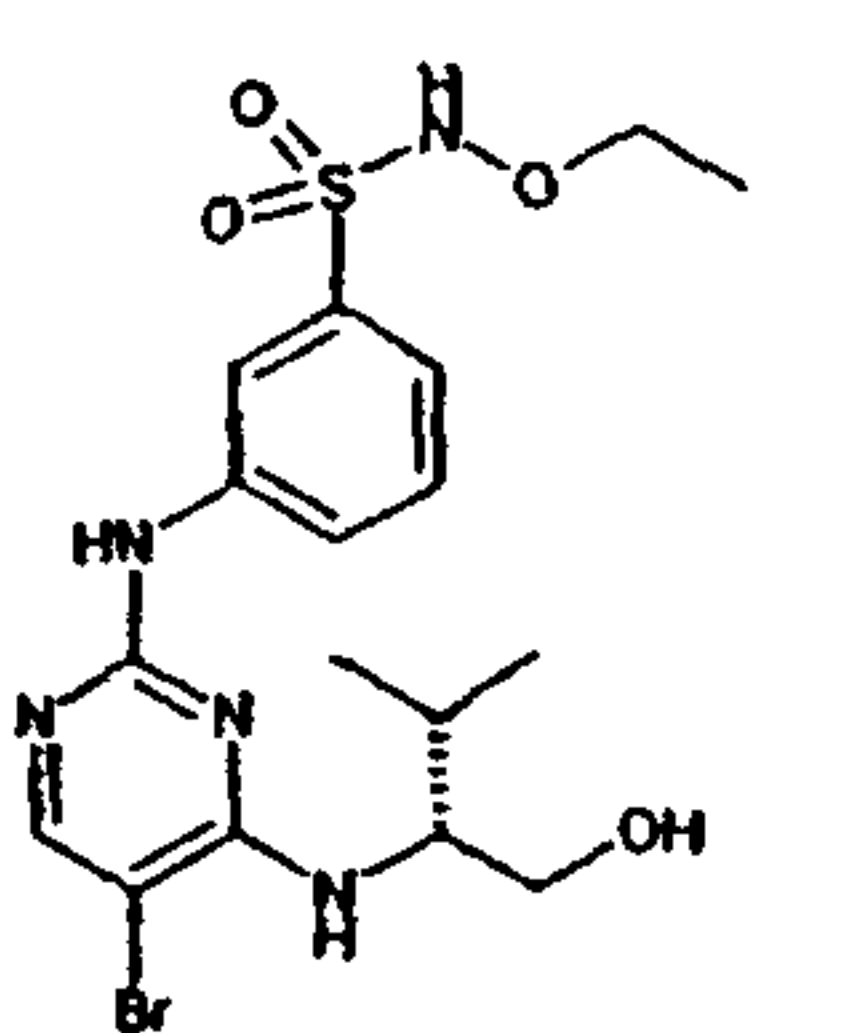
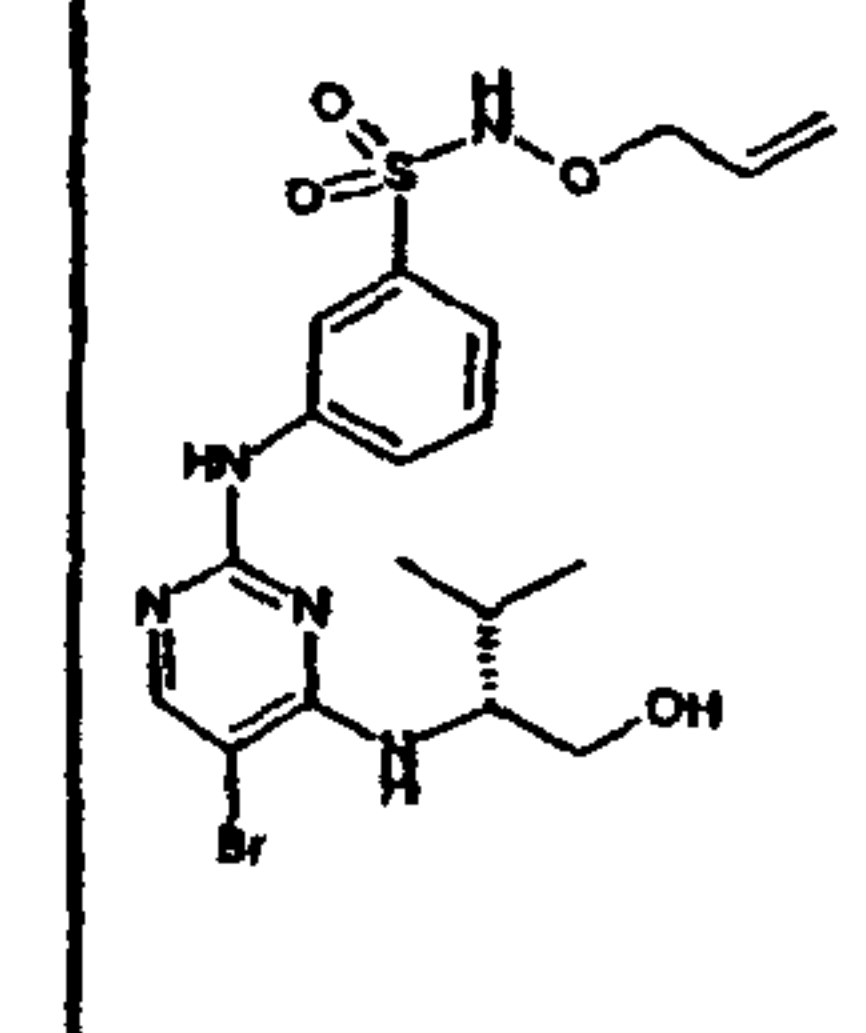
				
Beispiel-Nr.	235	236	237	238
Schmp. [°C]				
Masse	486 (ES)	516 (ES)	504 (ES)	488 (ES)

				
Beispiel-Nr.	239	240	241	242
Schmp. [°C]				
Masse	536 (ES)	502 (ES)	484 (ES)	551 (ES)

			
Beispiel-Nr.	243	244	245
Schmp. [°C]			
Masse	516 (ES)	514 (ES)	433 (ES)

				
Beispiel-Nr.	246	247	248	249
Schmp. [°C]			205	>300
Masse	446 (ES)	415 (EI)	504 (ES)	431 (ES)

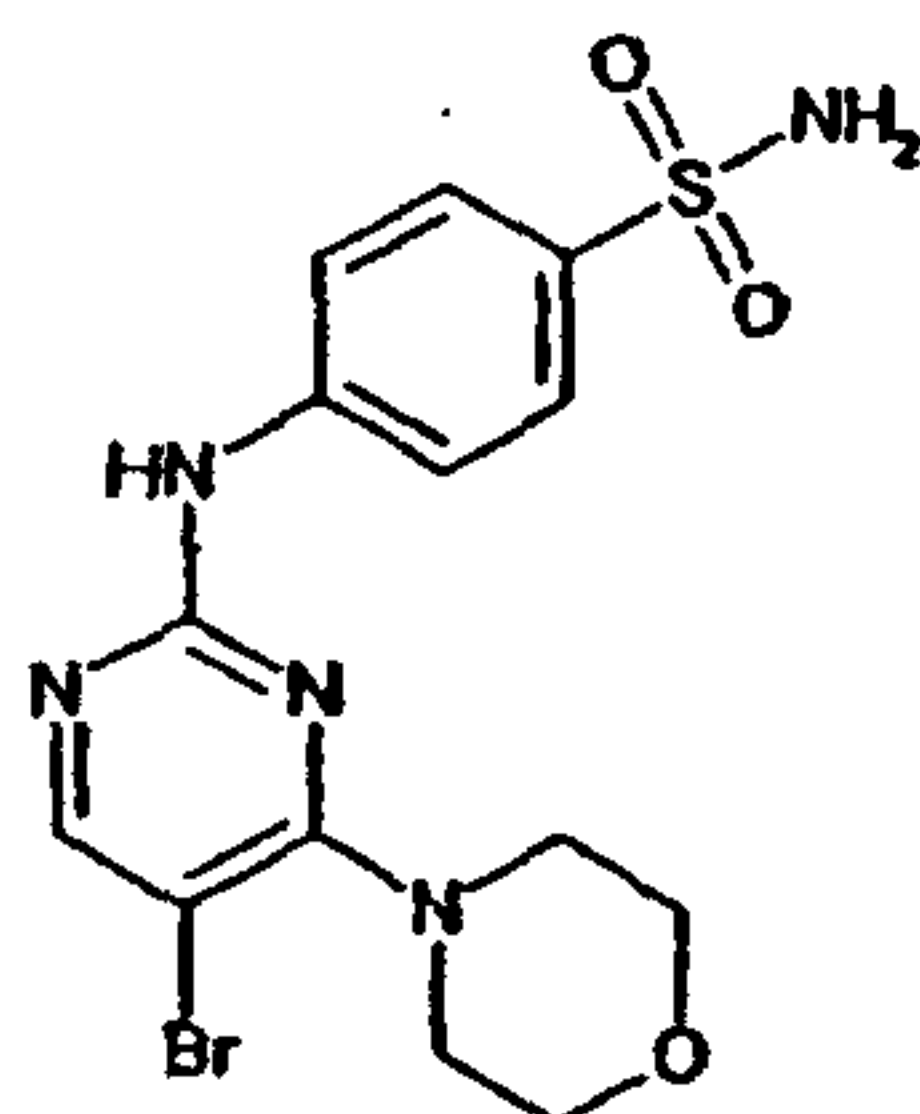
				
Beispiel-Nr.	250	251	252	253
Schmp. [°C]	113	231	187	
Masse	488 (ES)	446 (ES)	433 (ES)	

				
Nr.	254	255	256	257
Schmp. [°C]				
Masse	399 (ES)	444 (ES)	474 (ES)	486 (ES)

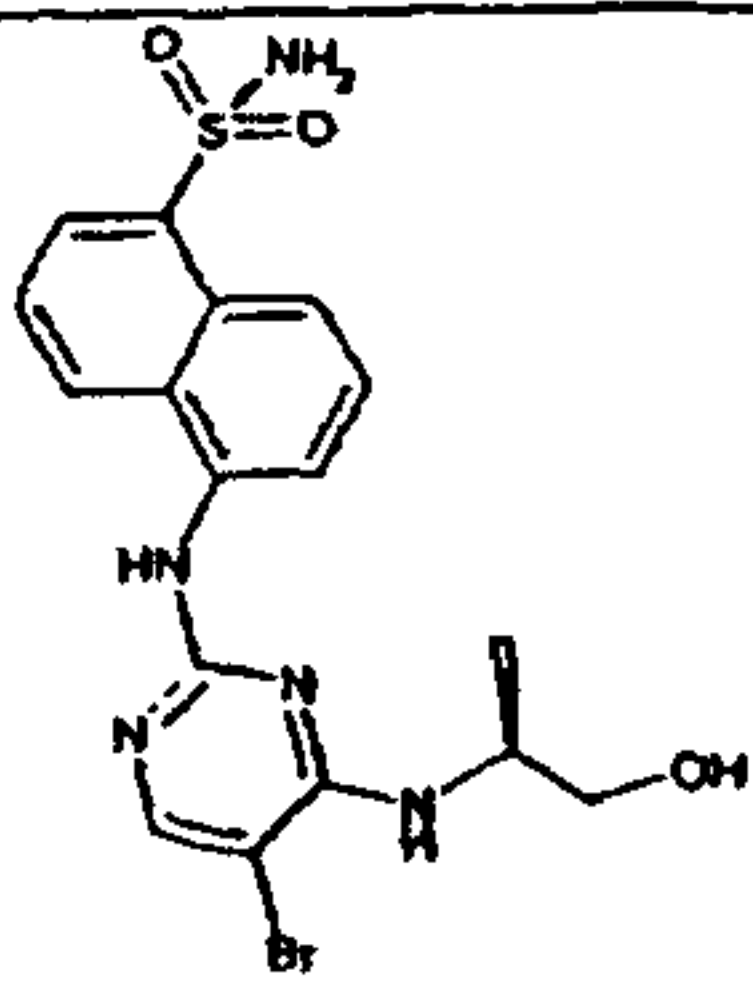
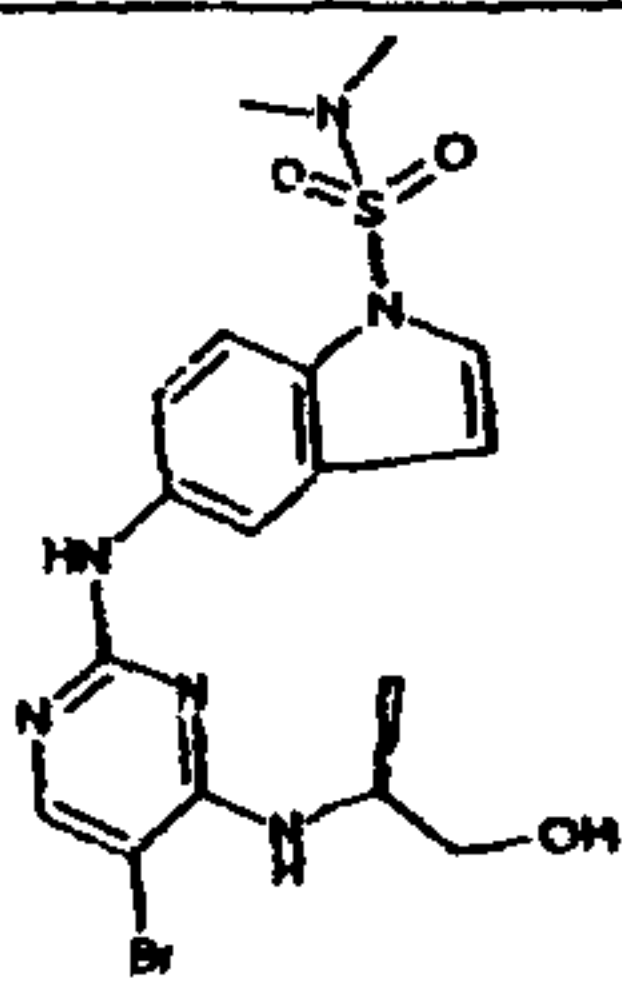
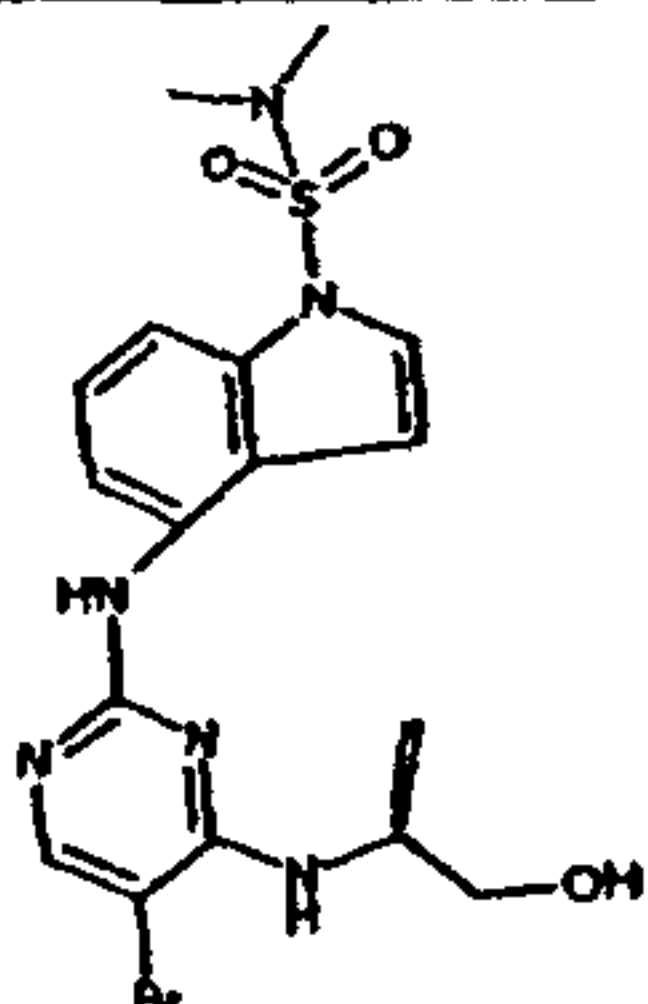
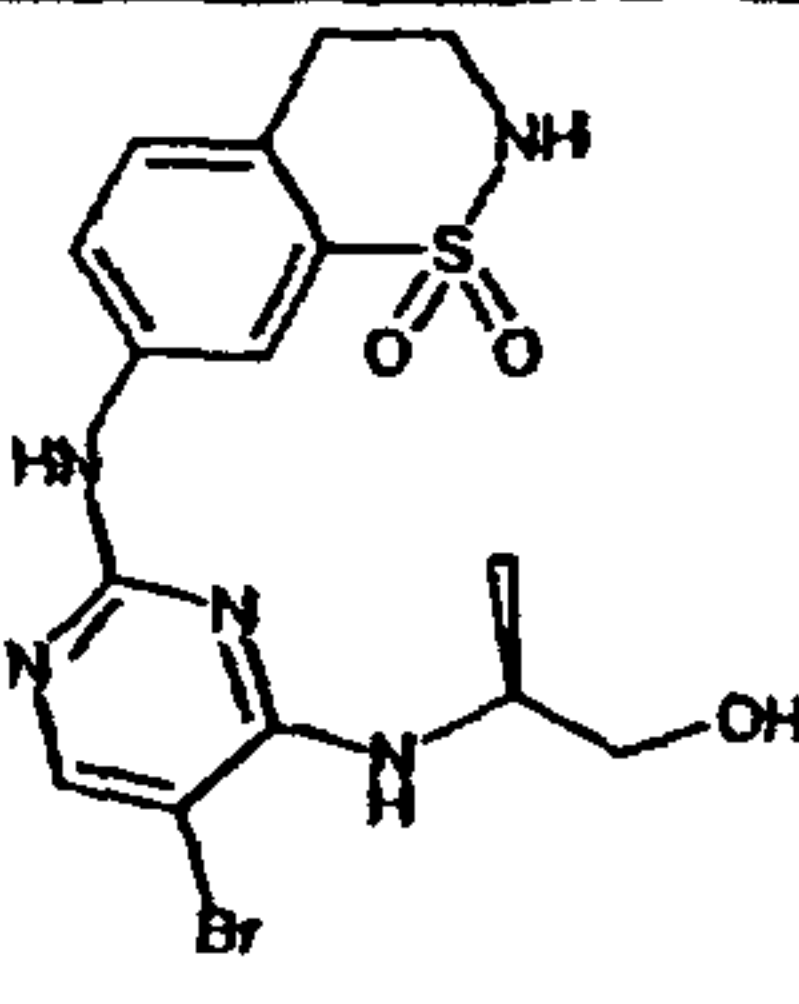
Compounds Nos. 159, 160, 161, 163, 167, 168, 170, 174, 175, 191, 192, 203 and 204 that are identified with *) can be produced by the process variants that are described under Example No. 295.

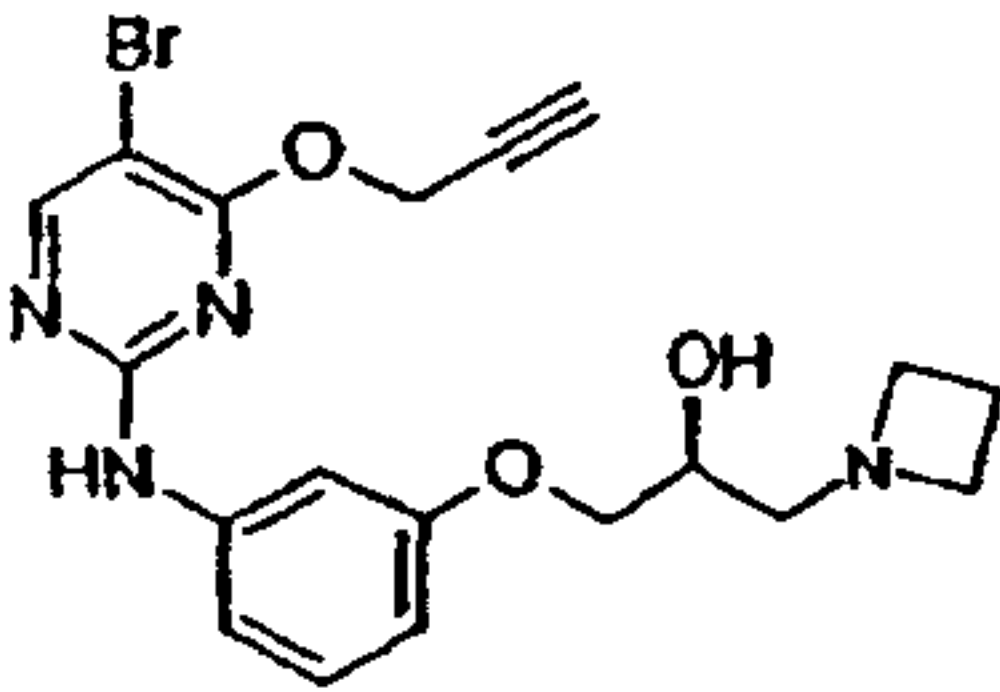
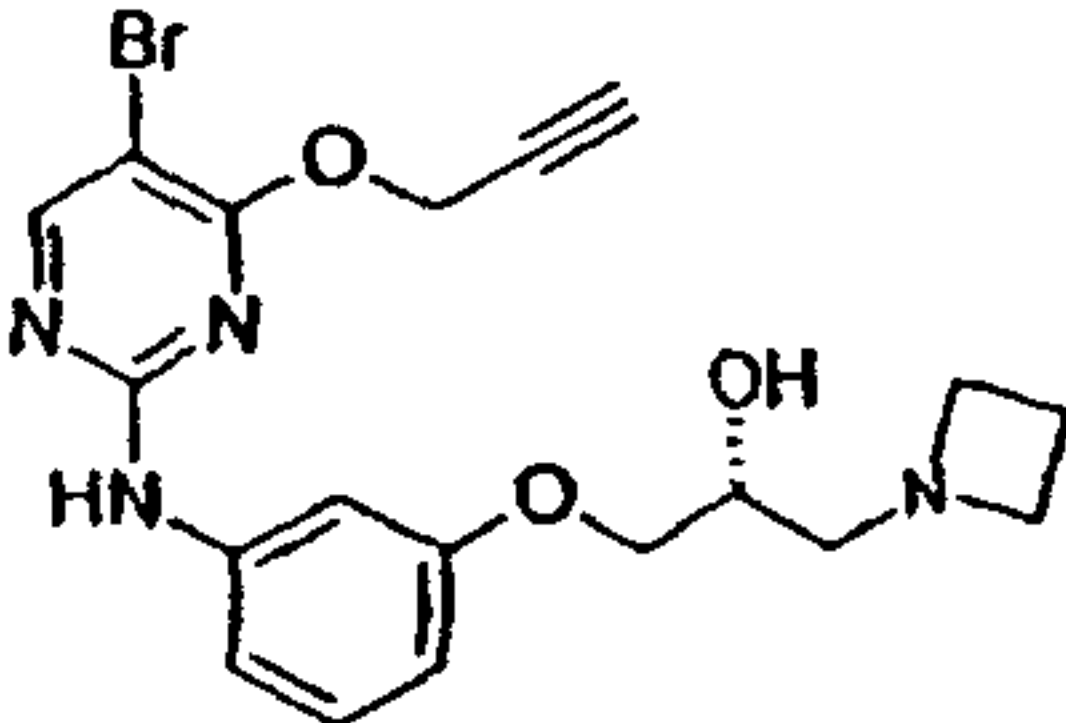
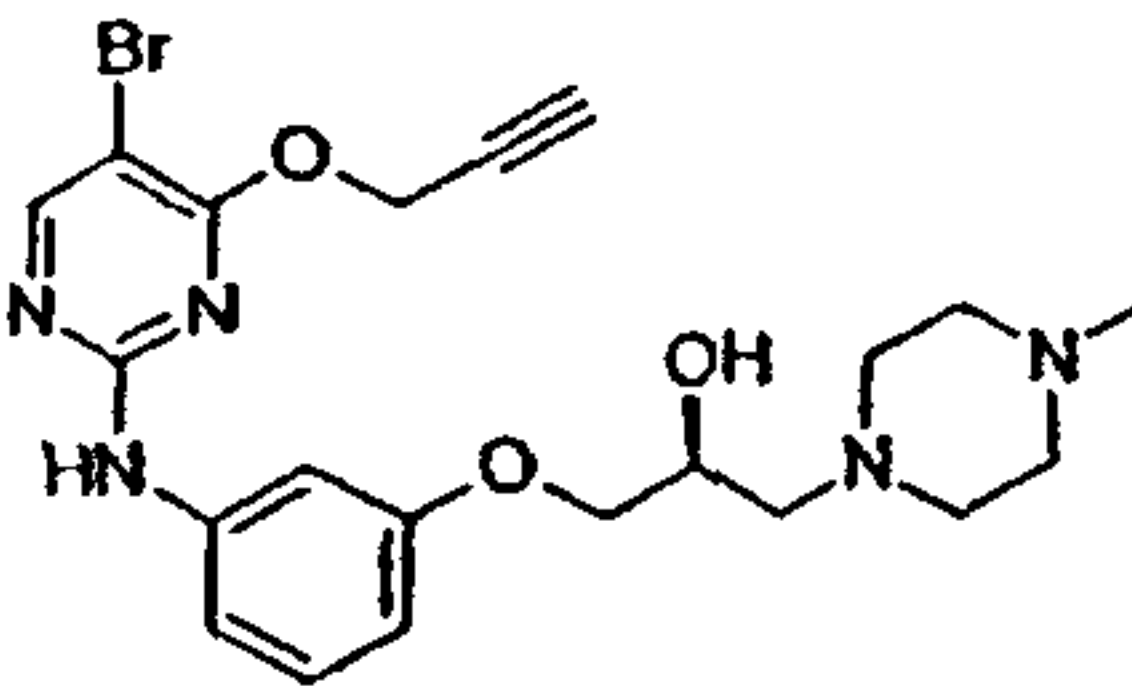
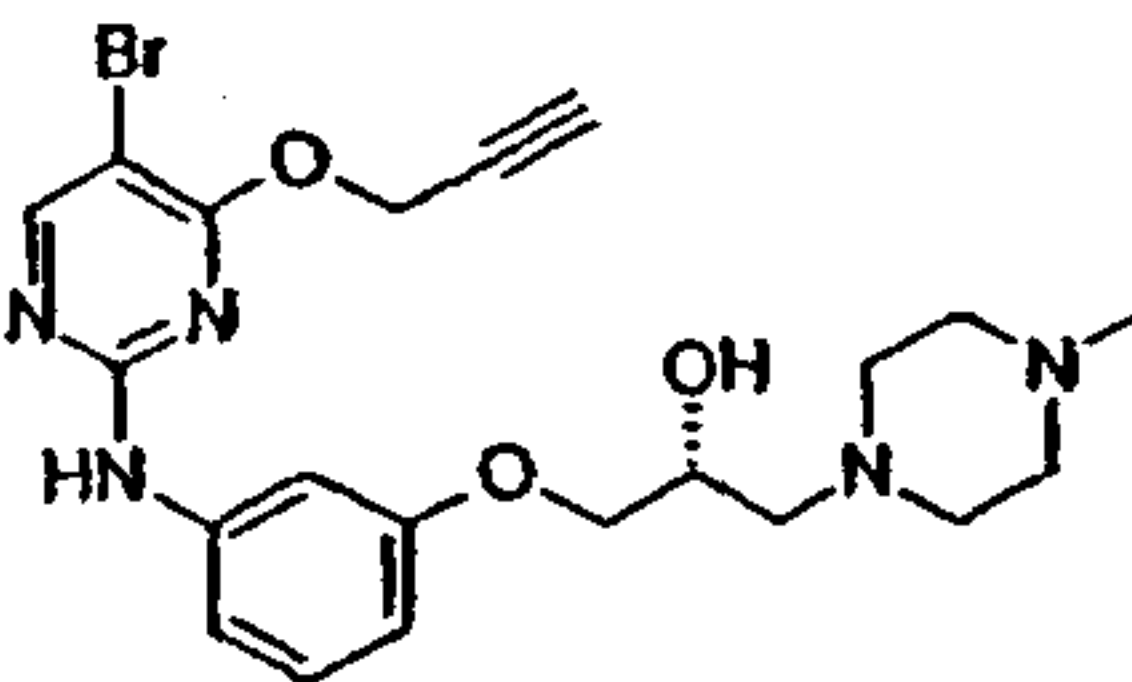
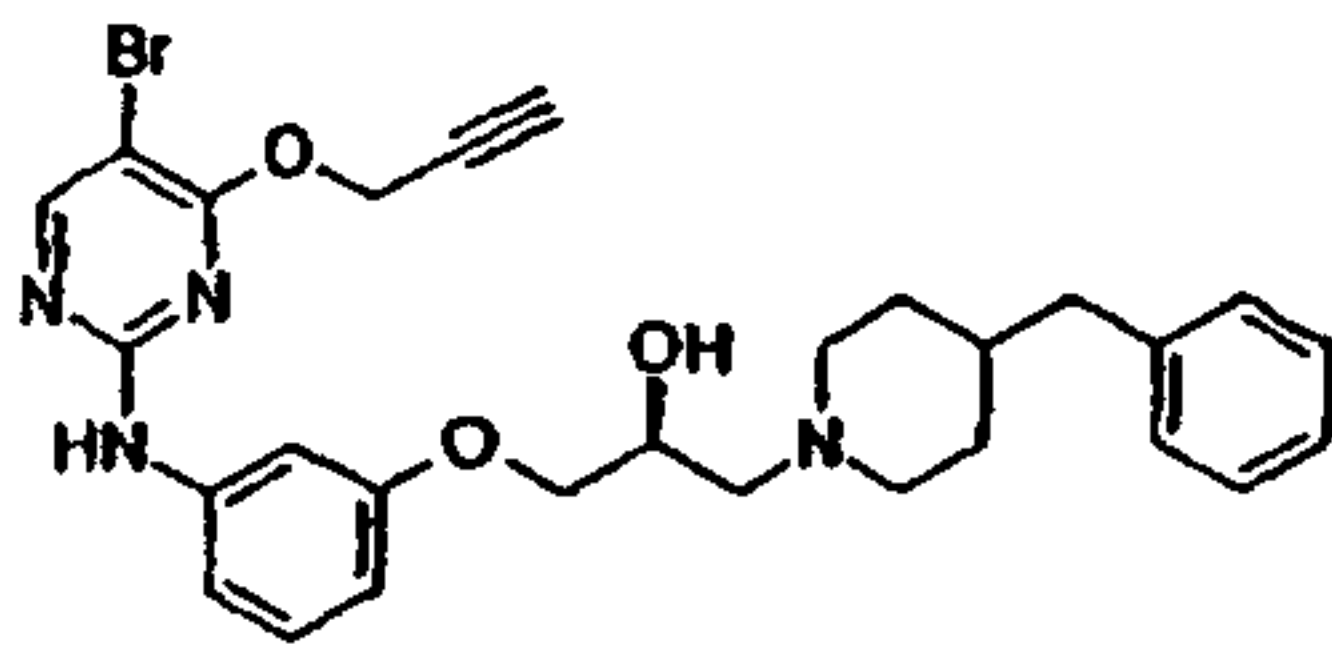
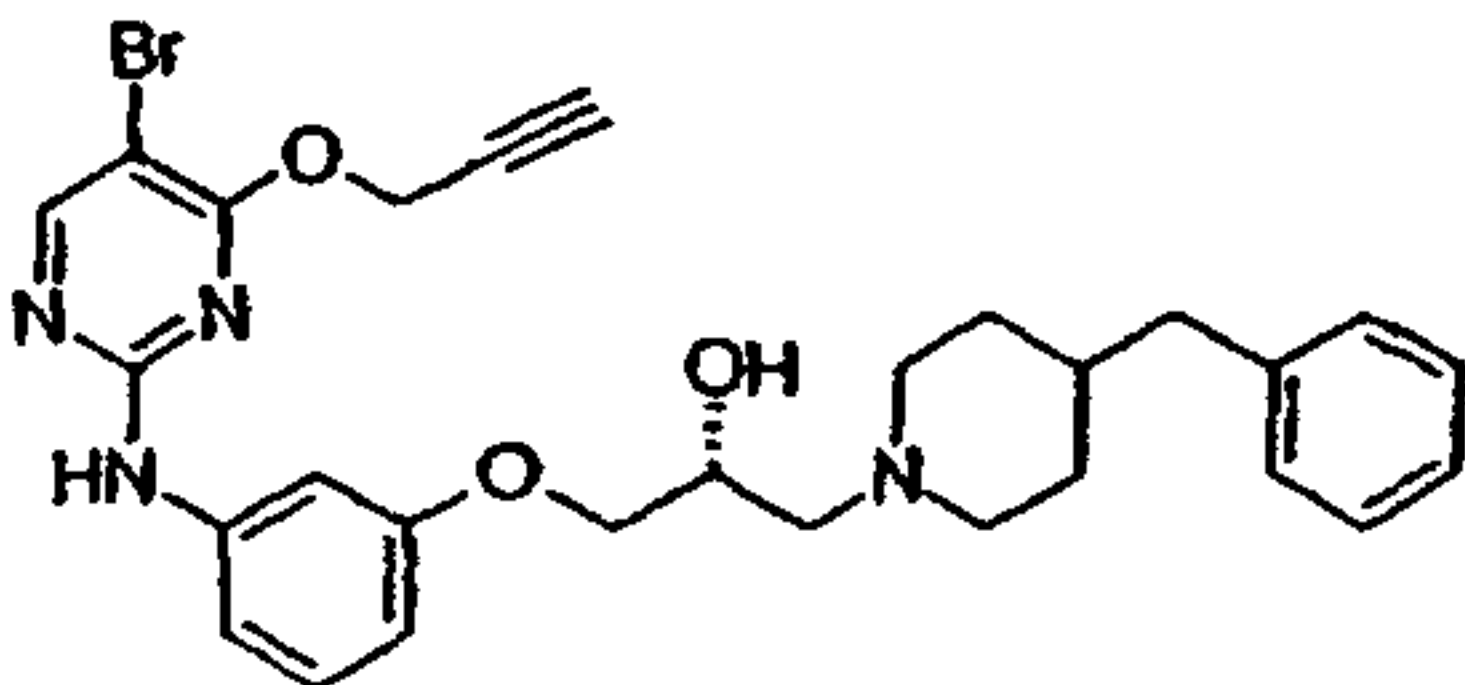
Example 258

Production of 4-(5-bromo-4-morpholin-4-yl-pyrimidin-2-ylamino)-phenylsulfonamide

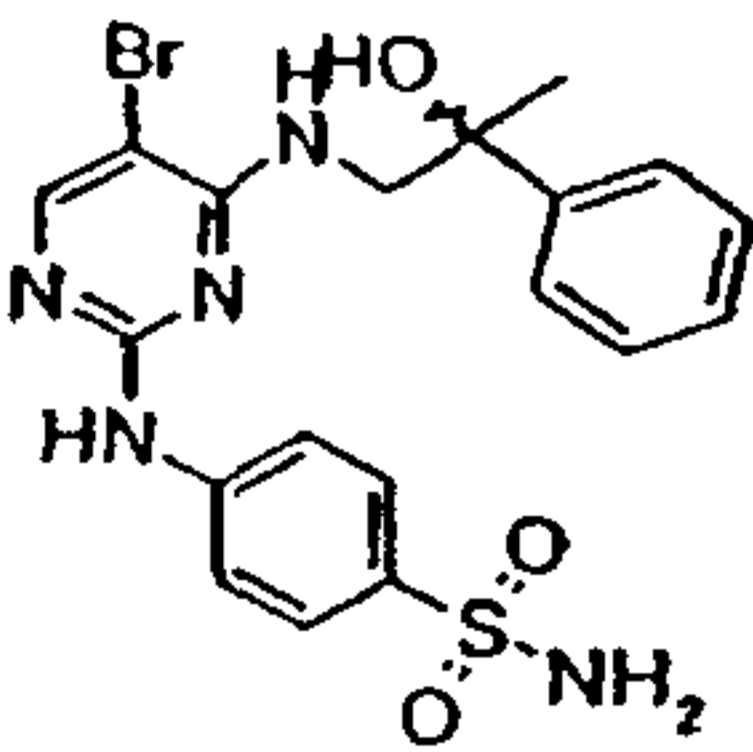
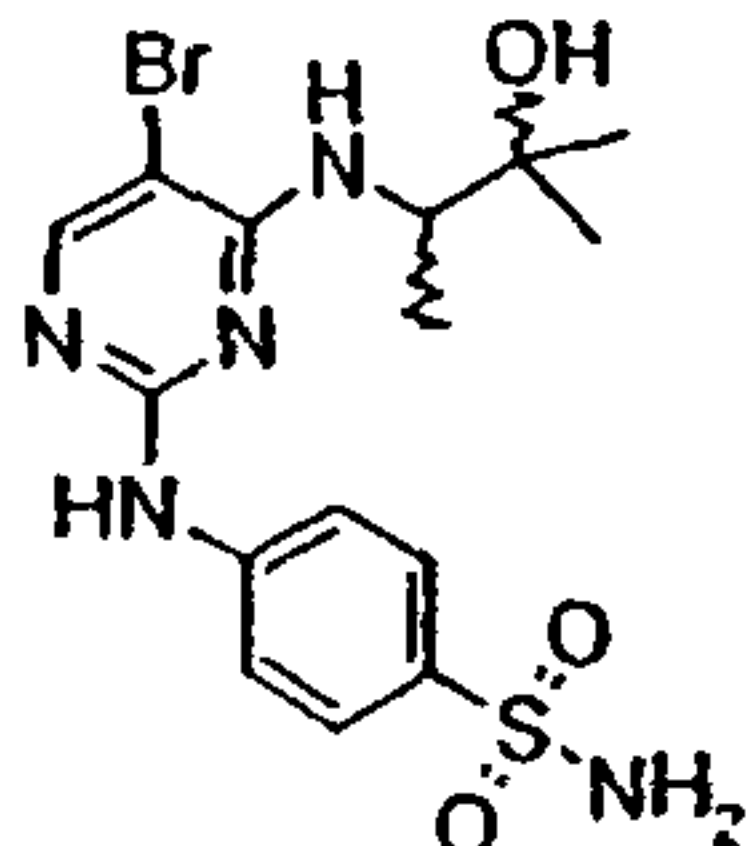
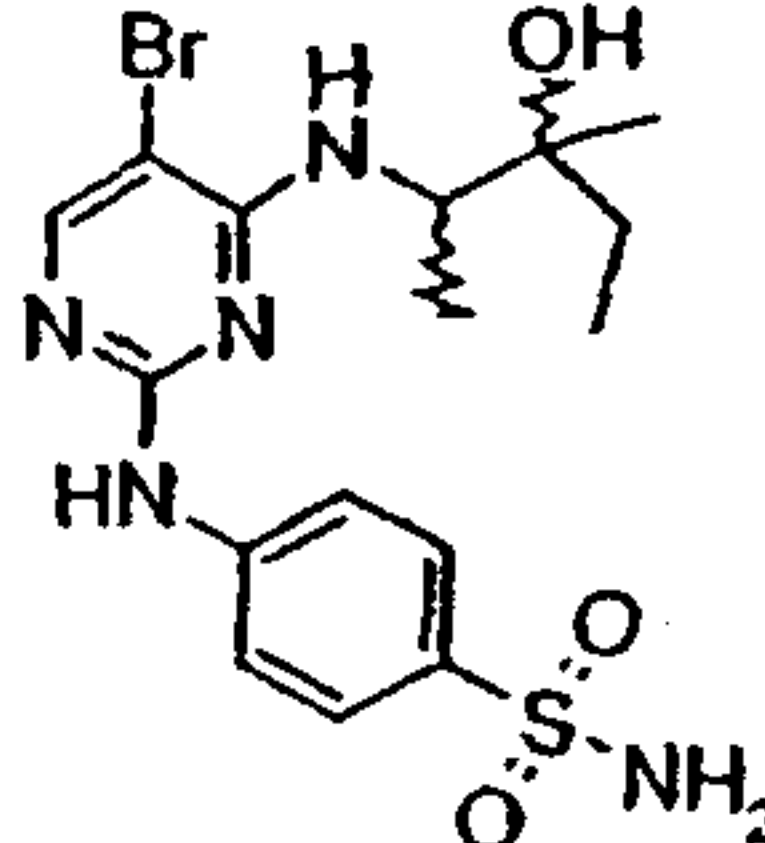


202 mg (0.60 mmol) of the compound of Example No. 122 is mixed with 1 ml of water and 0.2 g (1.2 mmol) of bromine and stirred at room temperature. After 24 hours, 0.2 g (1.2 mmol) of bromine is added again, and it is stirred for another 24 hours at room temperature. The solvent is evaporated by means of underpressure, and the remaining residue is purified by chromatography (Flashmaster II, DCM/MeOH 7:3). 17 mg (0.04 mmol, 7%) of the product is obtained as a white solid.

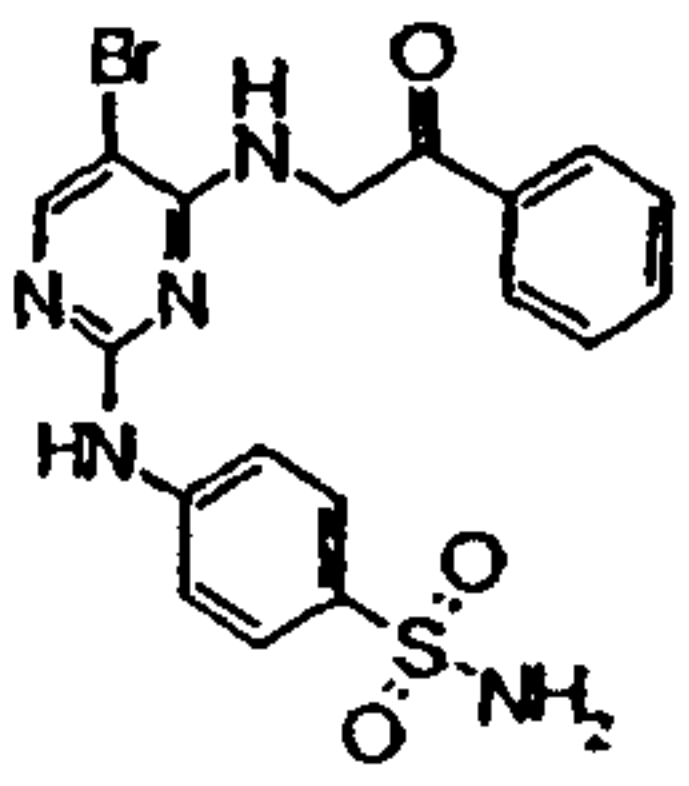
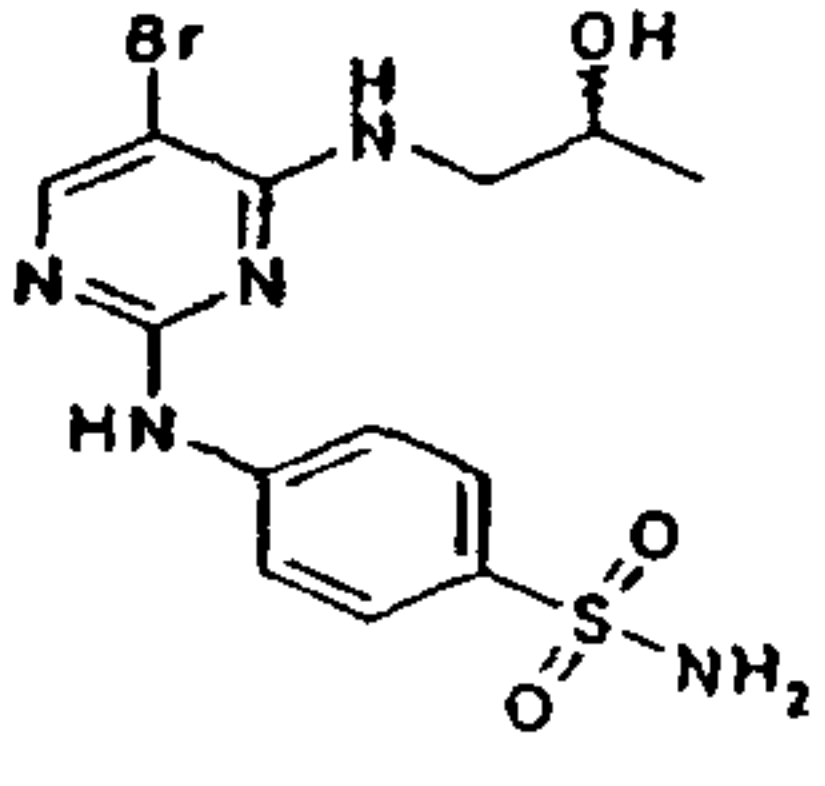
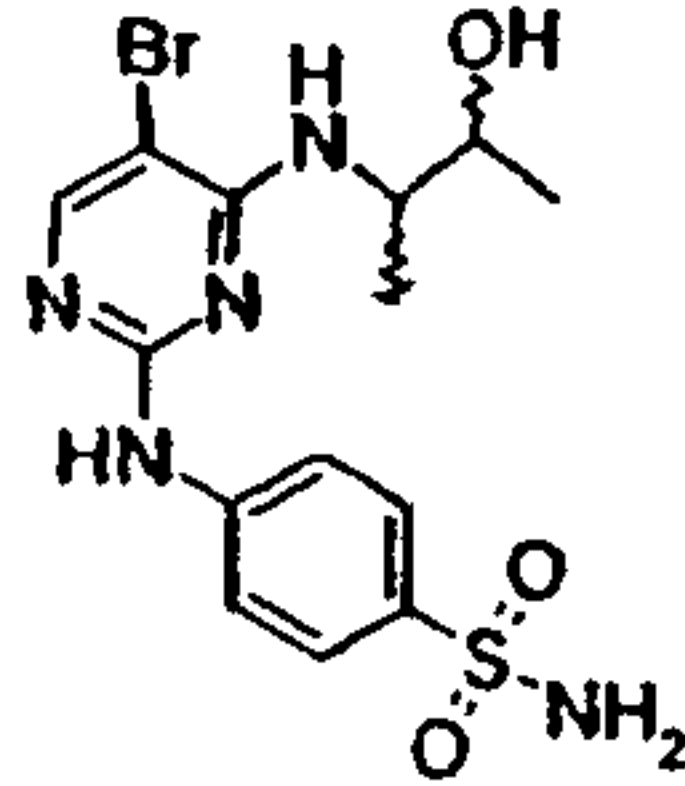
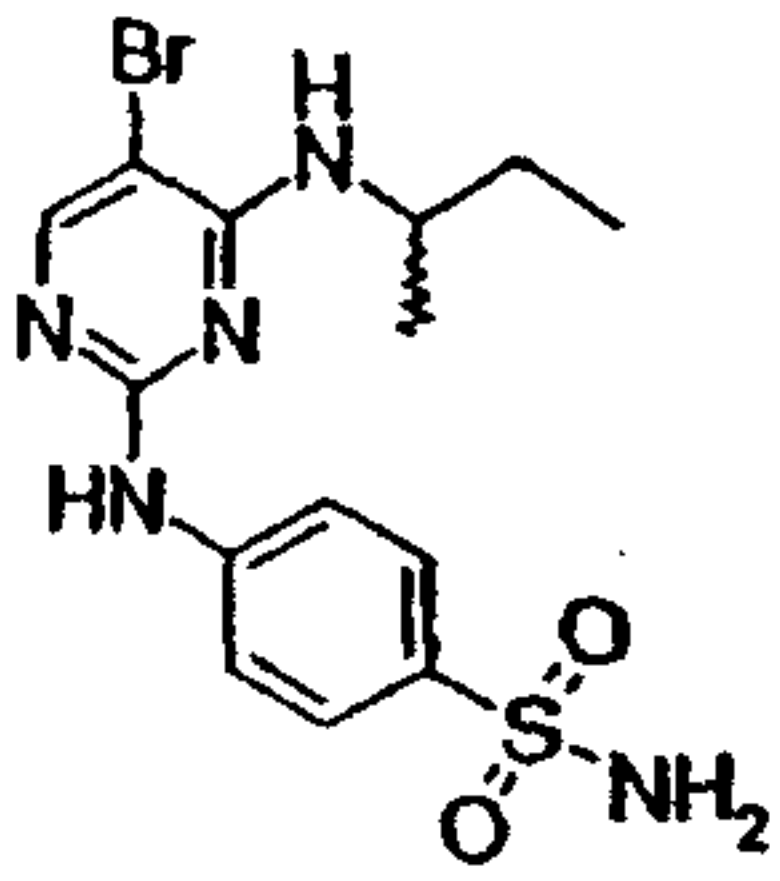
				
Beispiel-Nr.	259	260	261	262
Schmp. [°C]		205-207	202-203	
Masse	MS (ES) 452, 454 (M+ H, 100 %)			428 (ES)

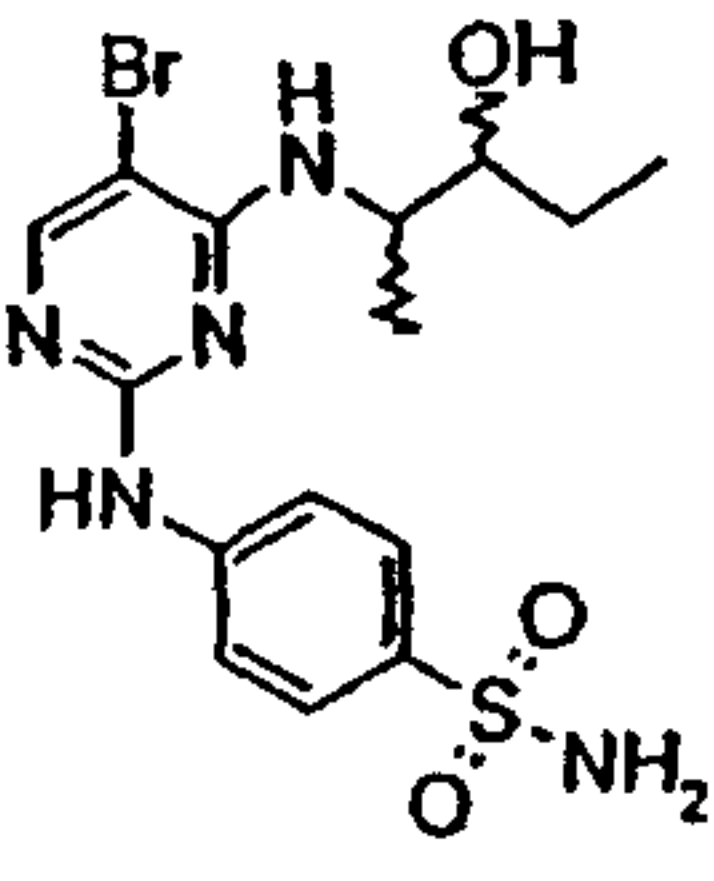
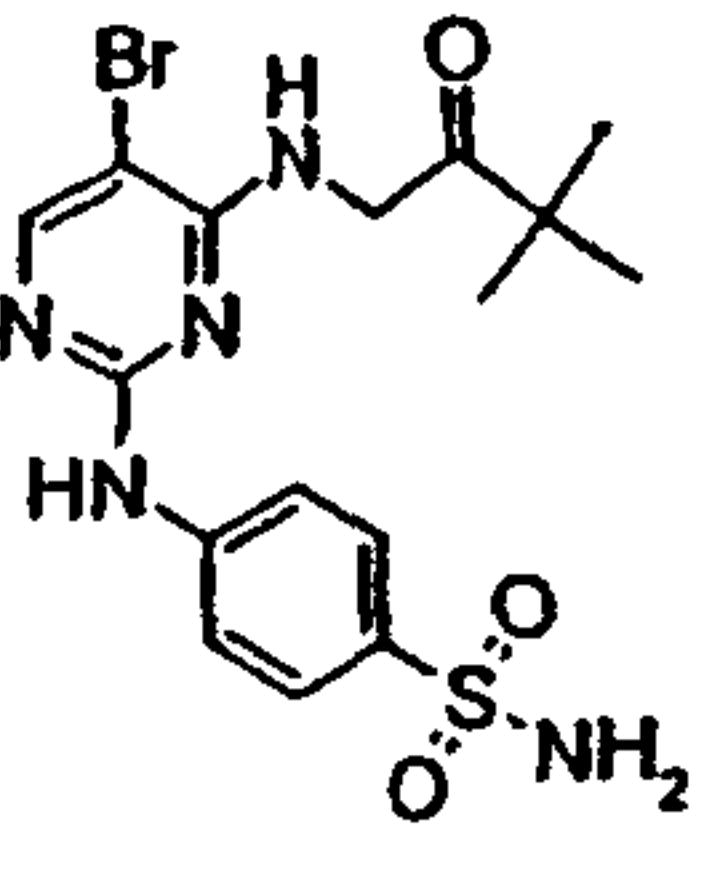
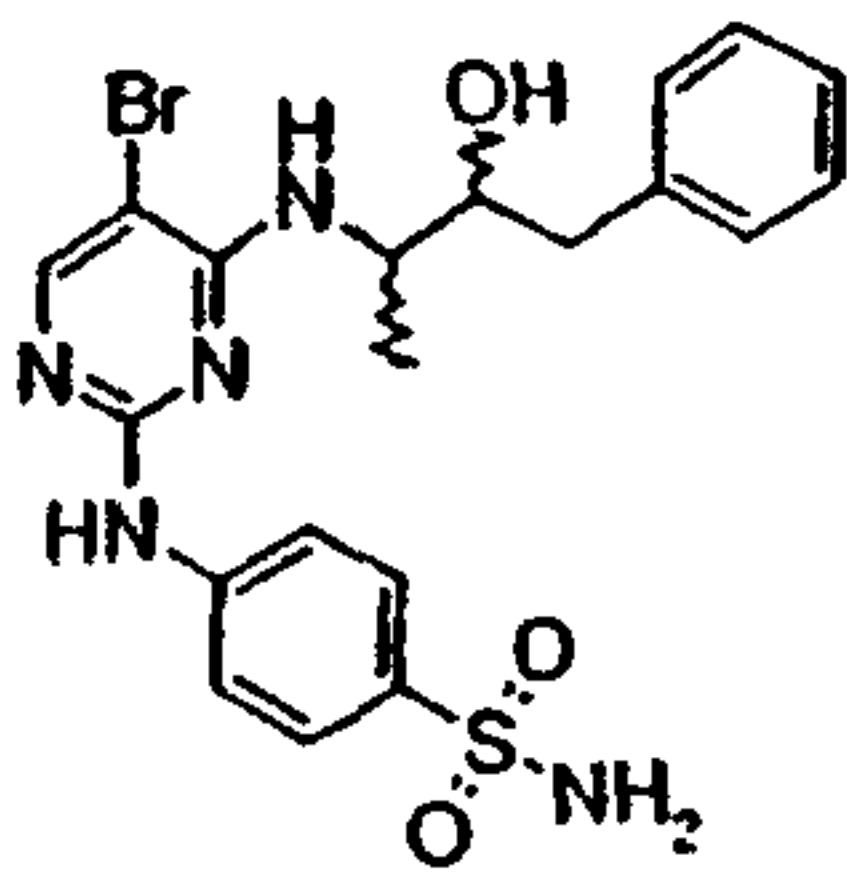
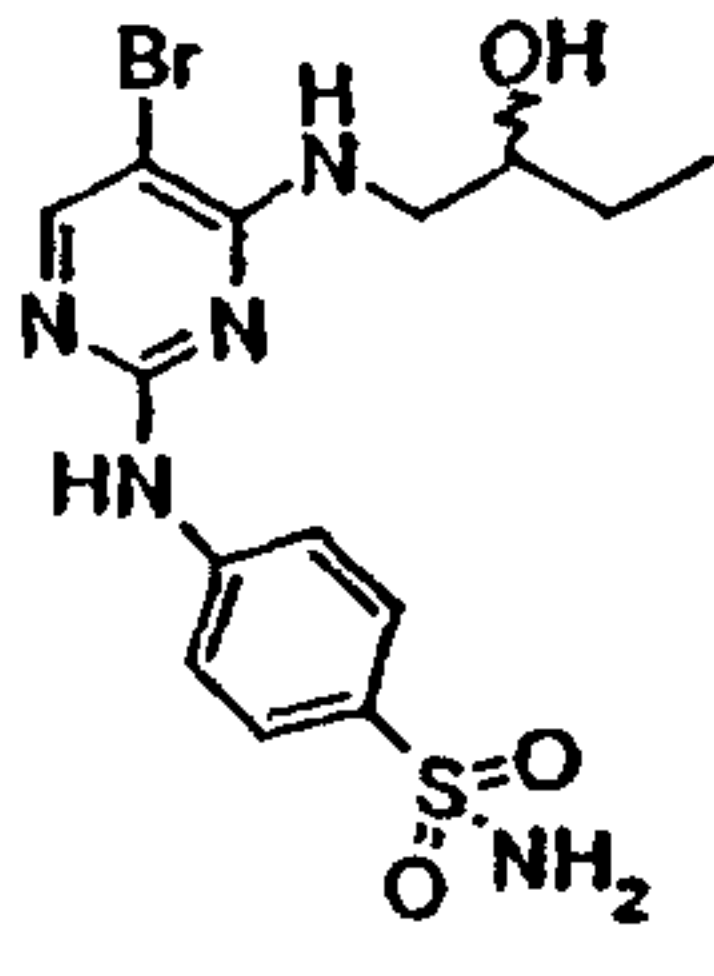
Beispiel-Nr.	Verbindung	ESI-MS
263		434
264		434
265		477
266		477
267		552
268		552

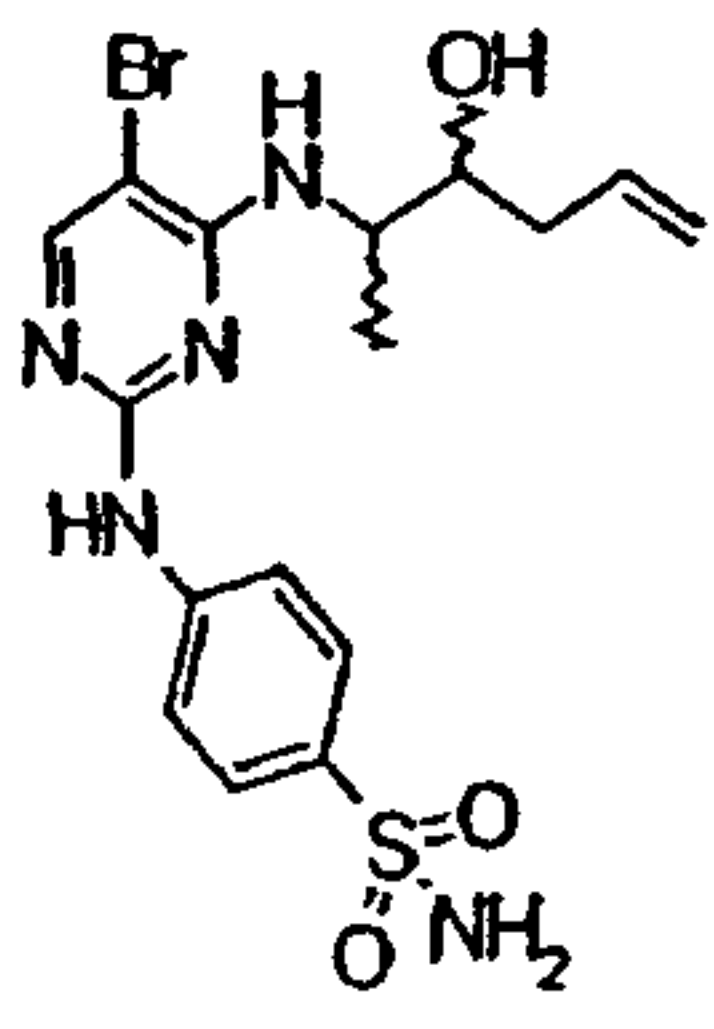
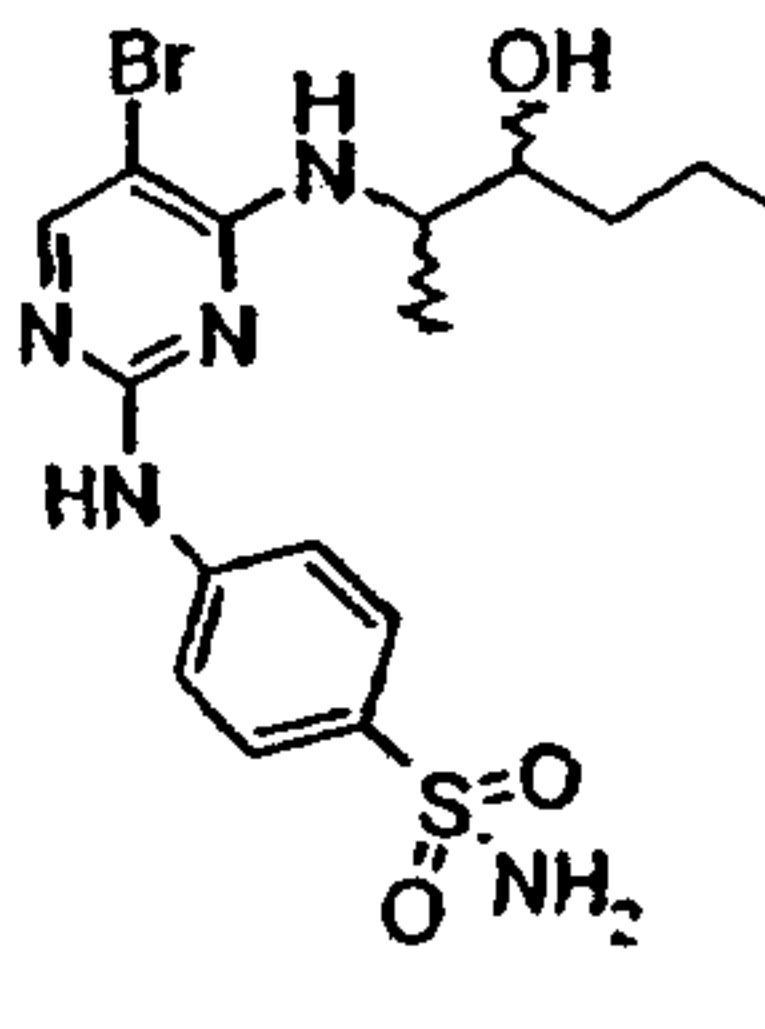
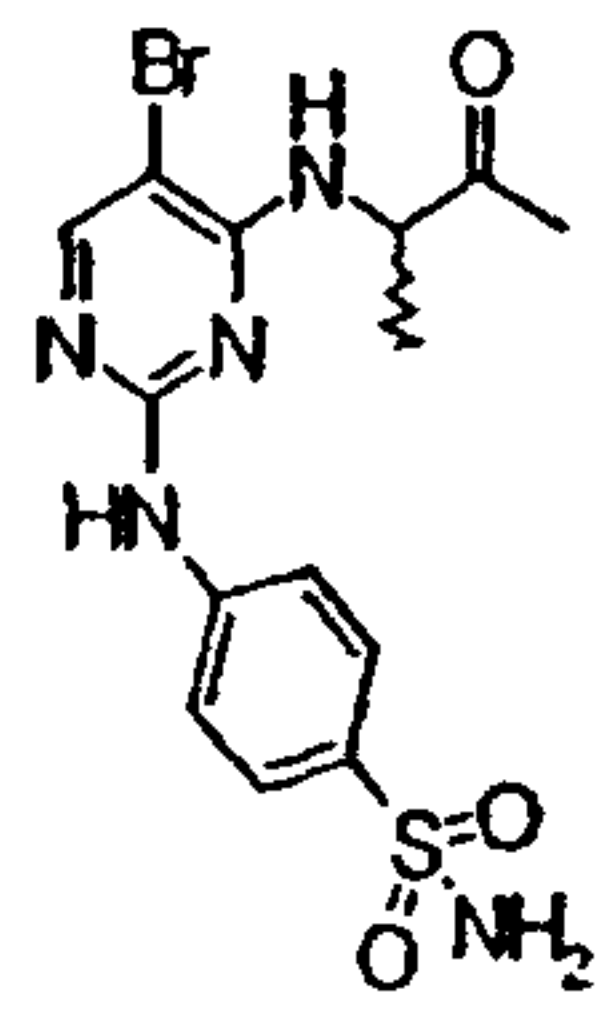
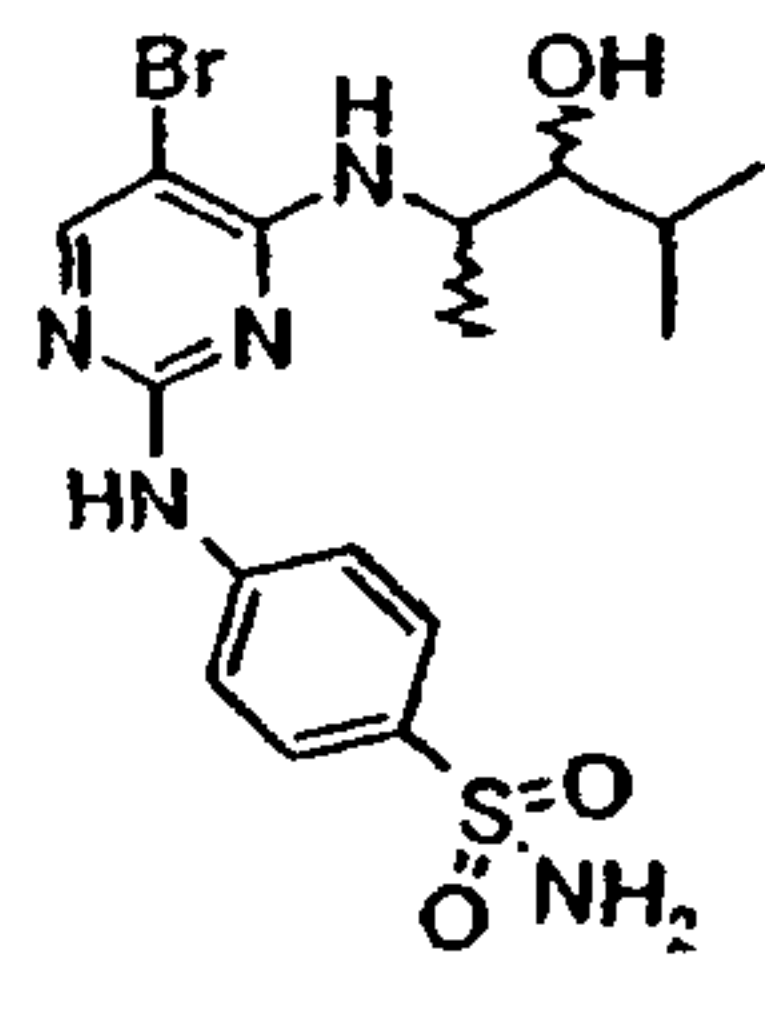
Analogously to the process for the production of intermediate products that is described under Example 6.0, the following compounds were also produced:

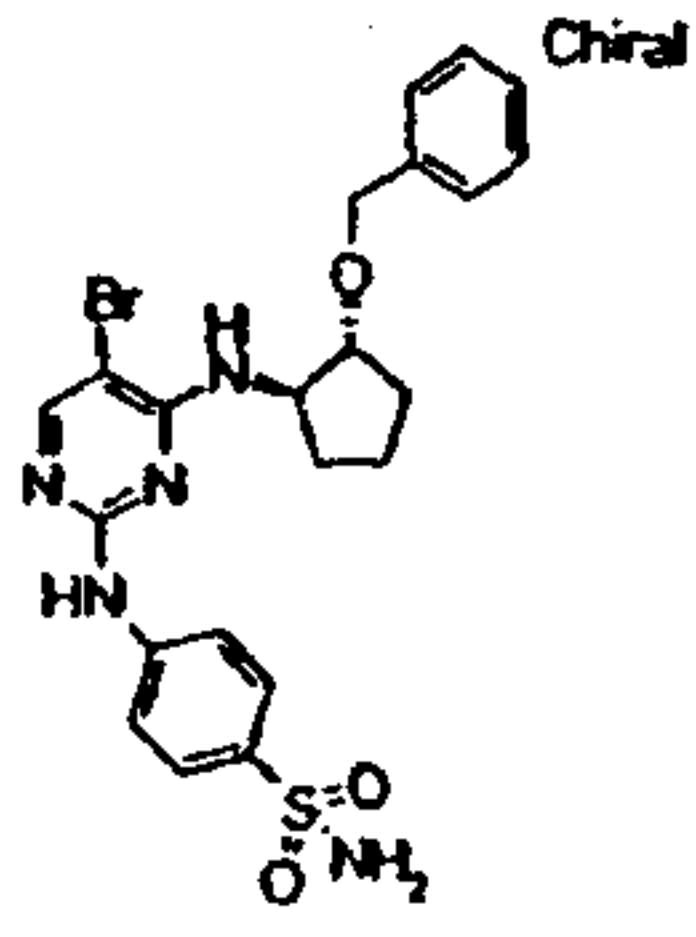
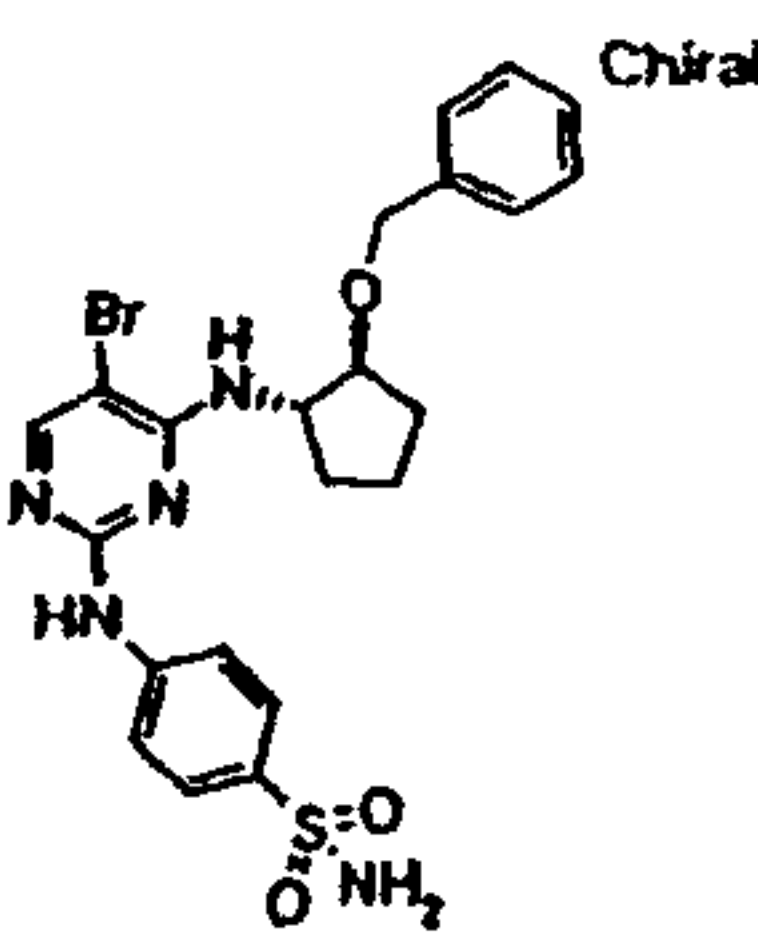
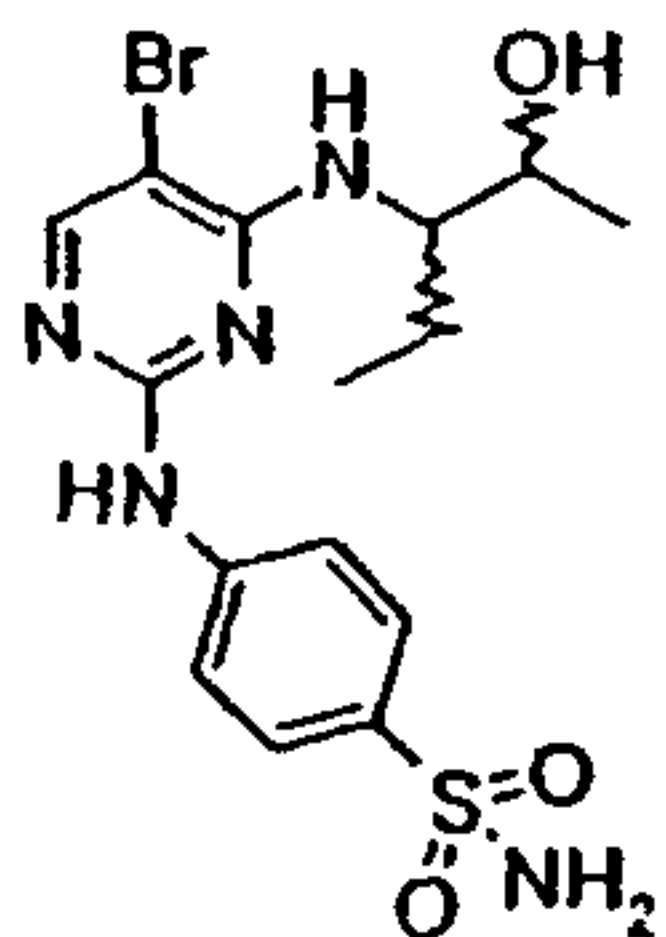
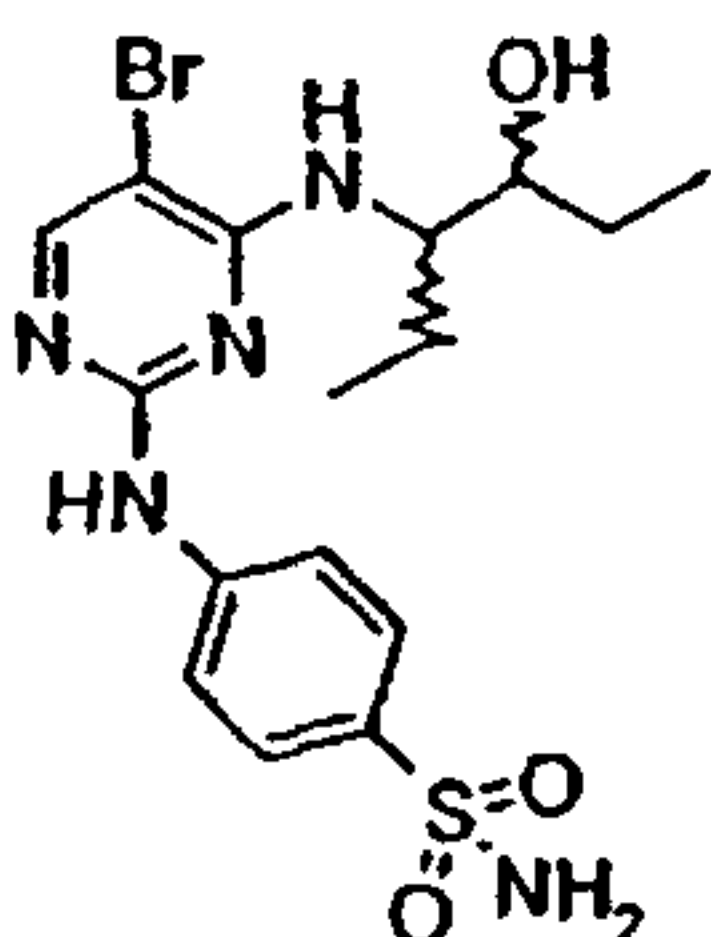
Beispiel-Nr.	269	270	271
			
Ausbeute	47%	90%	
Masse	ESI : MH ⁺ 480 (100%) 478 (97%) 115 (30%)	ESI : MH ⁺ 432 (100%) 430 (94%) 157 (43%)	ESI : MH ⁺ 446 (18%)

Analogously to production example 1, the following compounds were also produced:

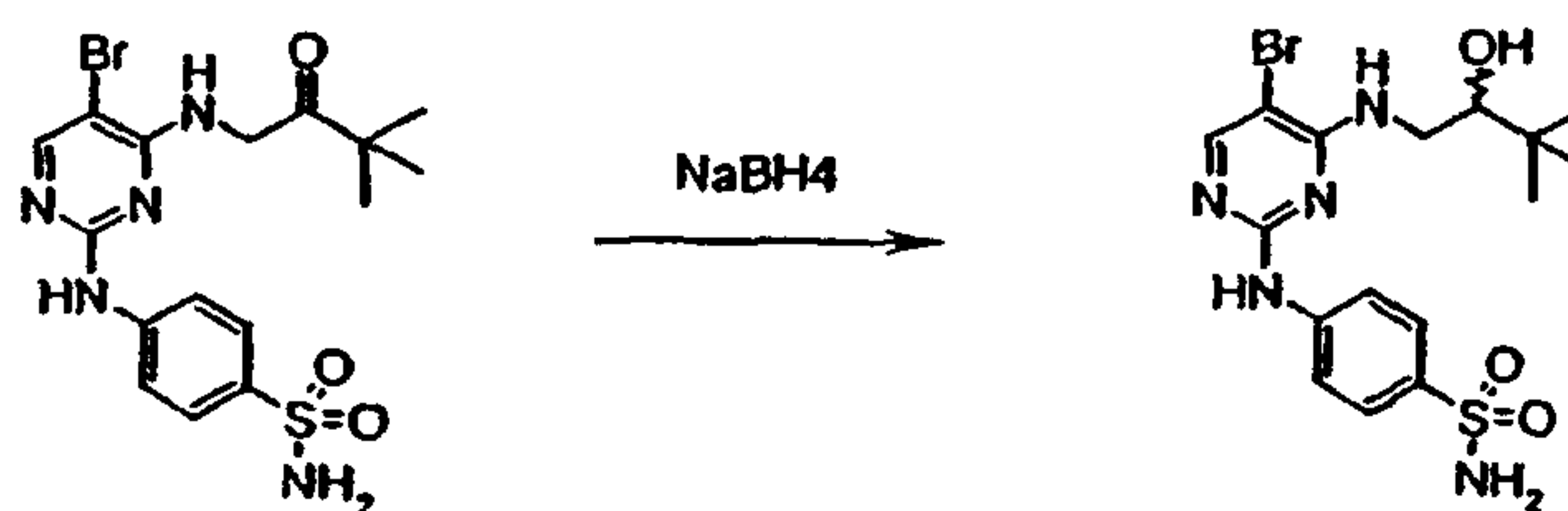
				
Beispiel -Nr.	272	273	274	275
Aus- beute	61%	44%	42%	68%
Masse	El : M ⁺ 463 (4%) 277 (8%) 105 (100%)	El : M ⁺ 403 (24%) 358 (100%) 277 (52%)	ESI : MH ⁺ 418 100% 416 (94%) 346 (8%)	El : M ⁺ 401 (33%) 372 (100%) 344 (38%)

				
Beispiel -Nr.	276	277	278	279
Aus- beute	81%	58%	~20%	30%
Masse	El : M ⁺ 431 (5%) 372 (100%) 291 (46%)	ESI : MH ⁺ 444 (100%) 442 (97%) 115 (20%)	ESI : MH ⁺ 494 (75%) 346 (18%) 214 (55%)	ESI : MH ⁺ 418 (100%) 416 (97%) 310 (27%)

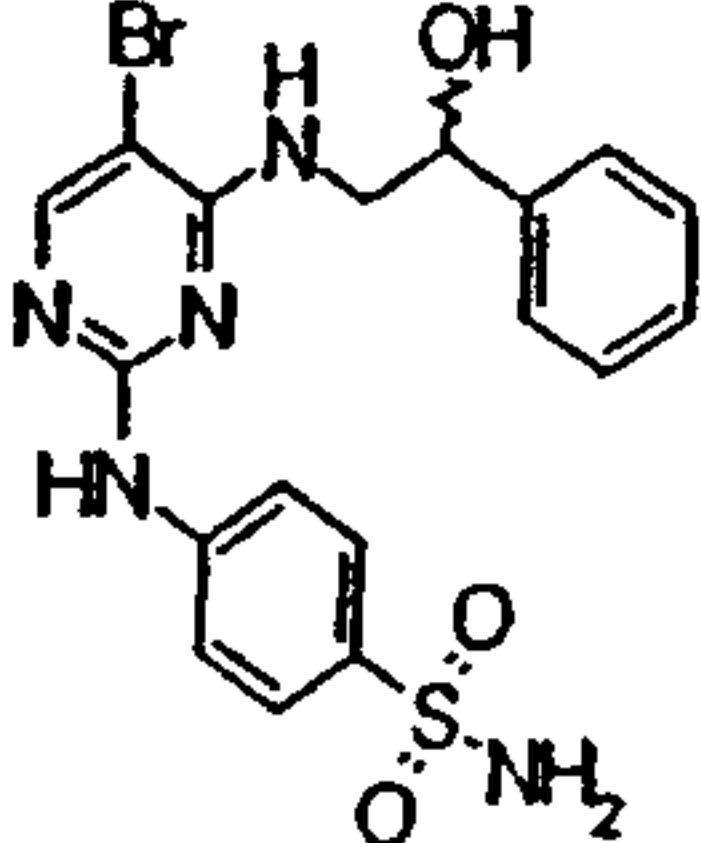
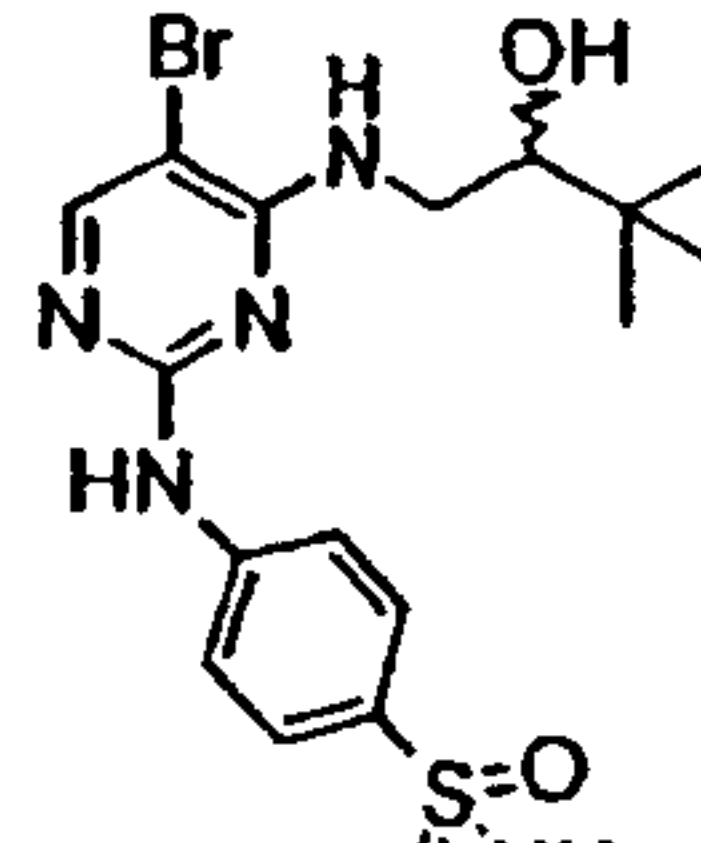
				
Beispiel -Nr.	280	281	282	283
Aus- beute	55%	43%	~18%	35%
Masse	ESI : MH ⁺ 444 (100%) 442 (97%) 214 (12%)	ESI : MH ⁺ 446 (100%) 444 (95%) 346 (5%)	ESI : MH ⁺ 416 (100%) 414 (96%) 317 (4%)	ESI : MH ⁺ 446 (100%) 444 (90%)

				
Beispiel -Nr.	284	285	286	287
Aus- beute	51%	46%	47%	61%
Masse	ESI : MH ⁺ 520 (100%) 518 (97%) 115 (27%)	ESI : MH ⁺ 520 (100%) 518 (97%) 115 (23%)	ESI : MH ⁺ 432 (100%) 430 (95%) 346 (5%)	ESI : MH ⁺ 446 (100%) 444 (93%) 115 (13%)

According to the production variants below, the following compounds are also synthesized:

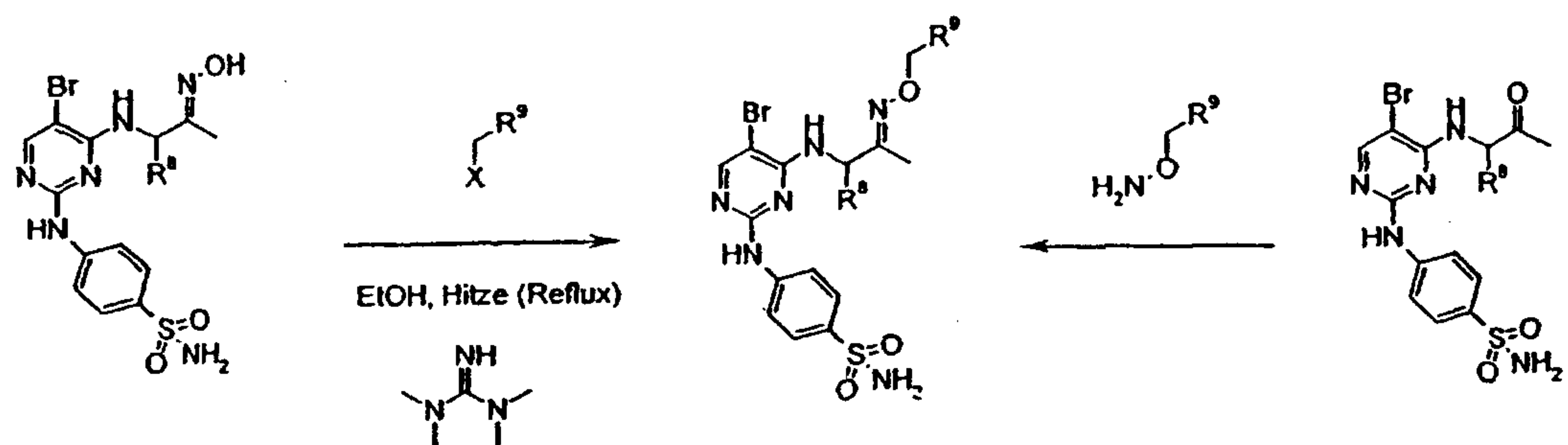


30 mg (0.0678 mmol) of compound No. 278 is dissolved in 1 ml of methanol/tetrahydrofuran 1:1. After adding ≈ 10 mg of sodium borohydride, stirring is continued for 2 hours. Then, it is quenched with ≈ 3 -4 drops of glacial acetic acid while being cooled, and it is concentrated by evaporation. Below, the crude product is taken up with a little water, suctioned off, rewashed with acetonitrile and dried in a vacuum at 60°C . Yield: 21 mg (70% of theory) of the desired compound.

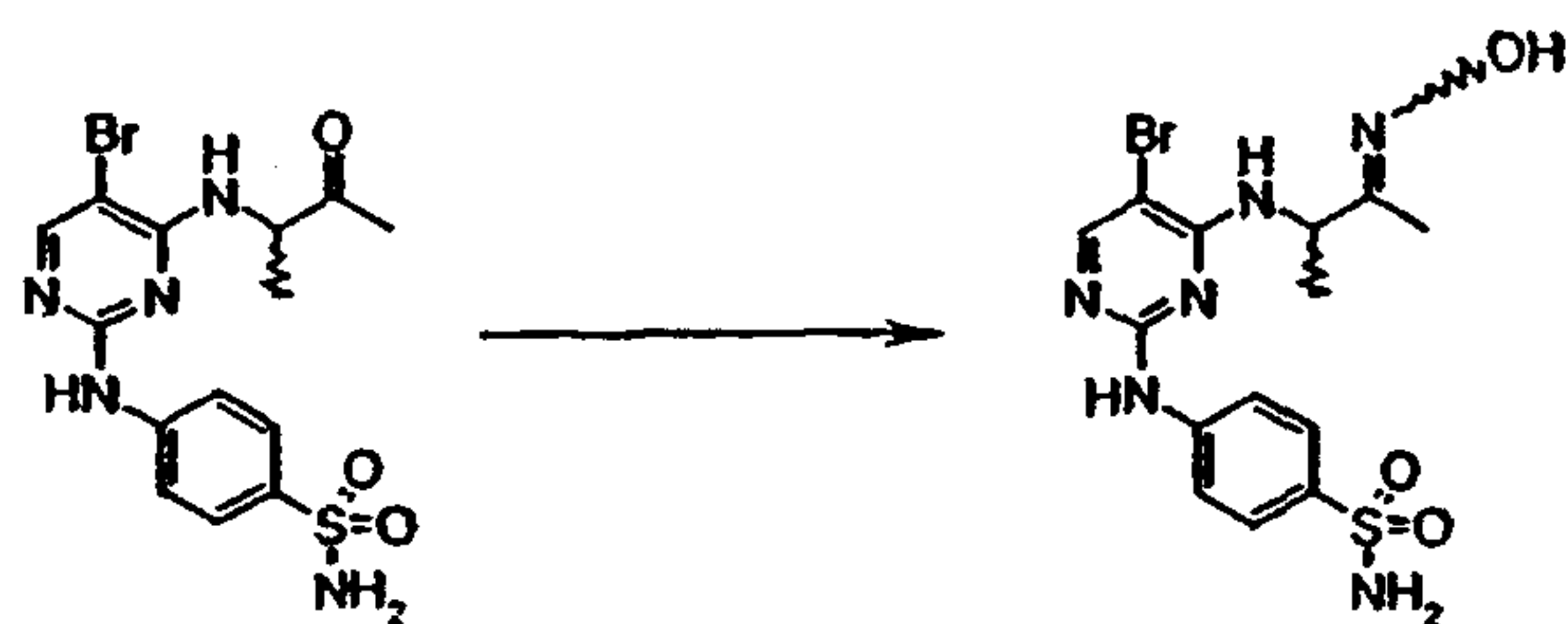
		
Beispiel -Nr.	288	289
Aus- beute	52%	70%
Masse	EI: M^+ 465 (5%) 358 (40%) 207 (31%)	ESI: MH^+ 446 (100%) 444 (93%) 117 (20%)

Example 290**Production of the Oxime Ether-Pyrimidine Compounds of General Formula I**

The production of the oxime ether is carried out according to the following general reaction diagram:



R⁸ and R⁹ have the meanings that are indicated in general formula I.

Production of Example 290

50 mg (0.12 mmol) of compound No. 282, 34 mg of hydroxylammonium chloride and 150 mg of pulverized KOH are refluxed for 2 hours in 2 ml of ethanol. Then, it is

poured onto ice water and acidified with glacial acetic acid, extracted 3 times with dichloromethane/isopropanol 4:1, dried with magnesium sulfate and concentrated by evaporation. The residue is suspended with acetonitrile, suctioned off and dried at 60°C. Yield: 28 mg (54% of theory) of the desired compound.

Mass

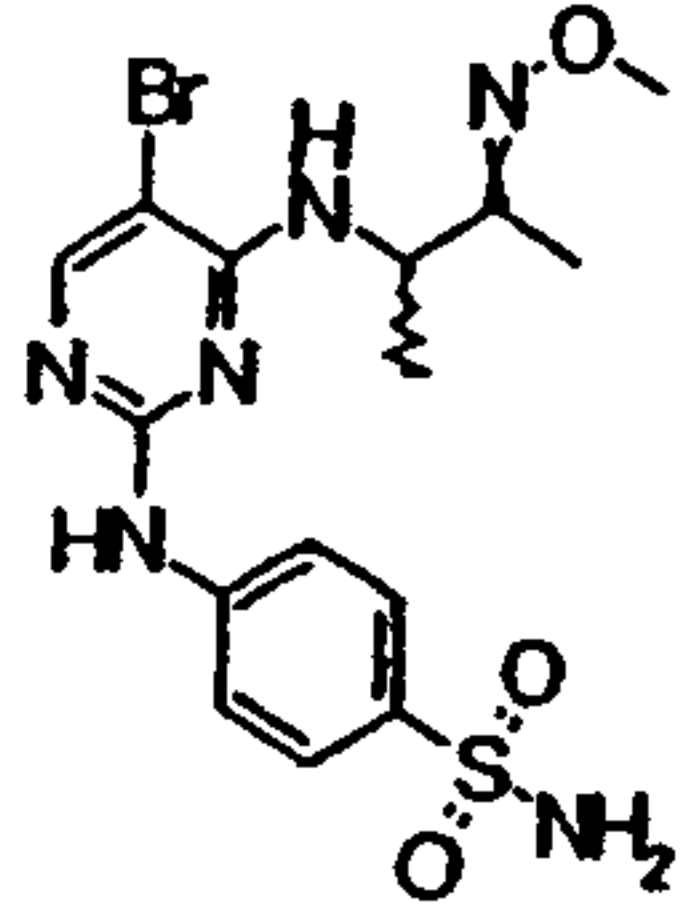
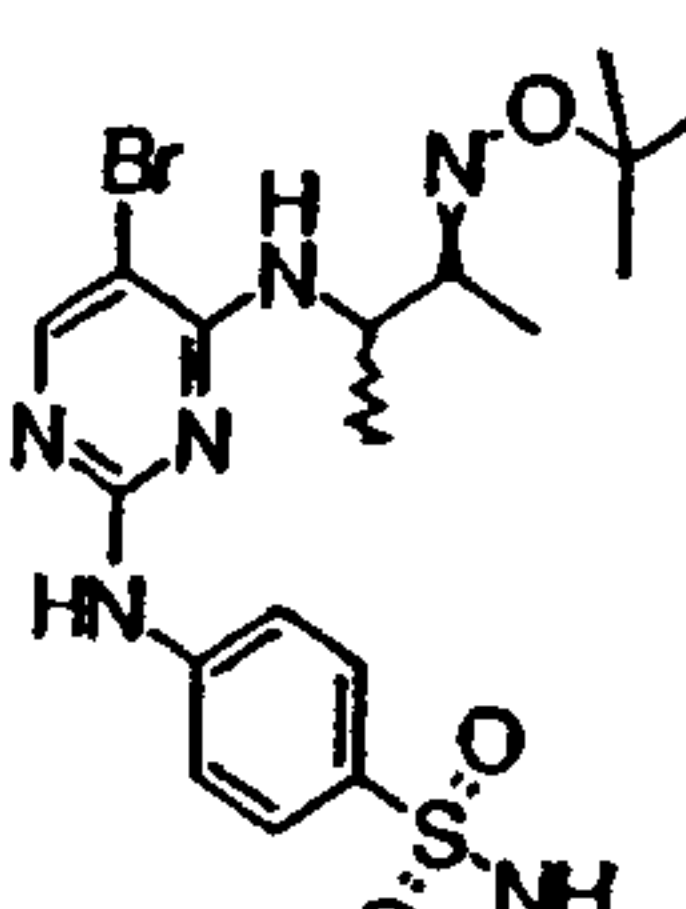
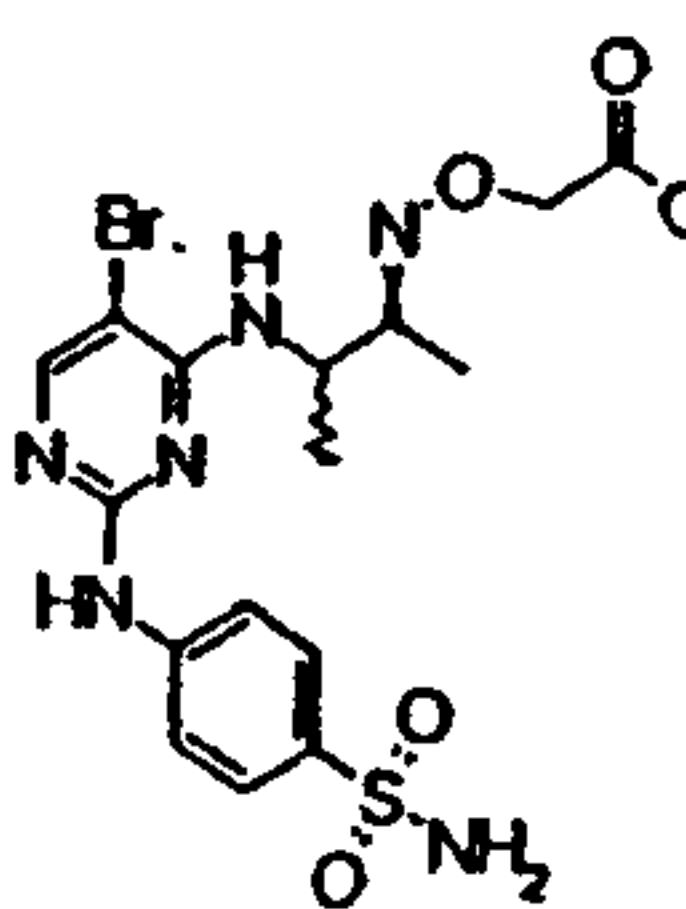
ESI:

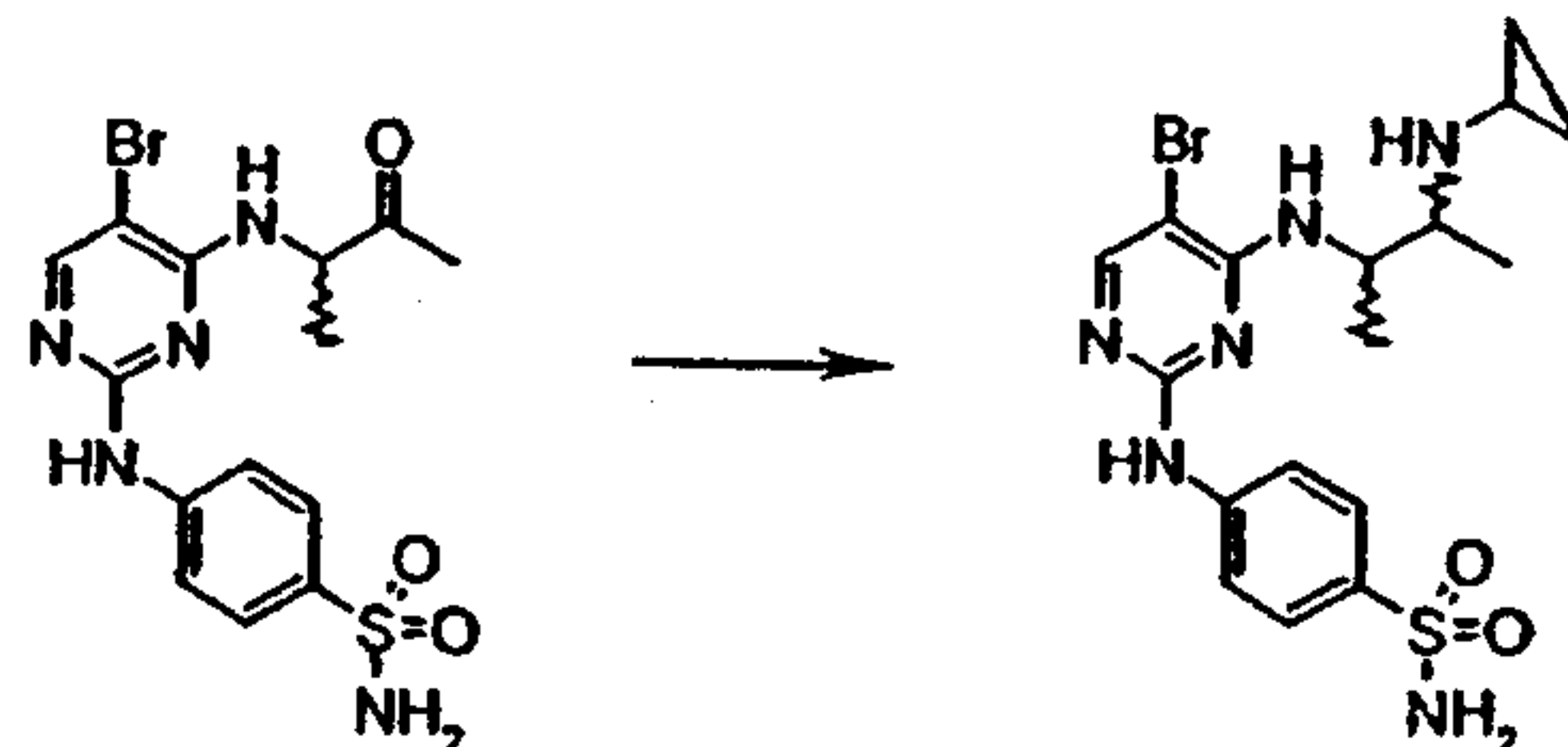
MH^+ 429 (29%)

371 (61%)

289 (91%)

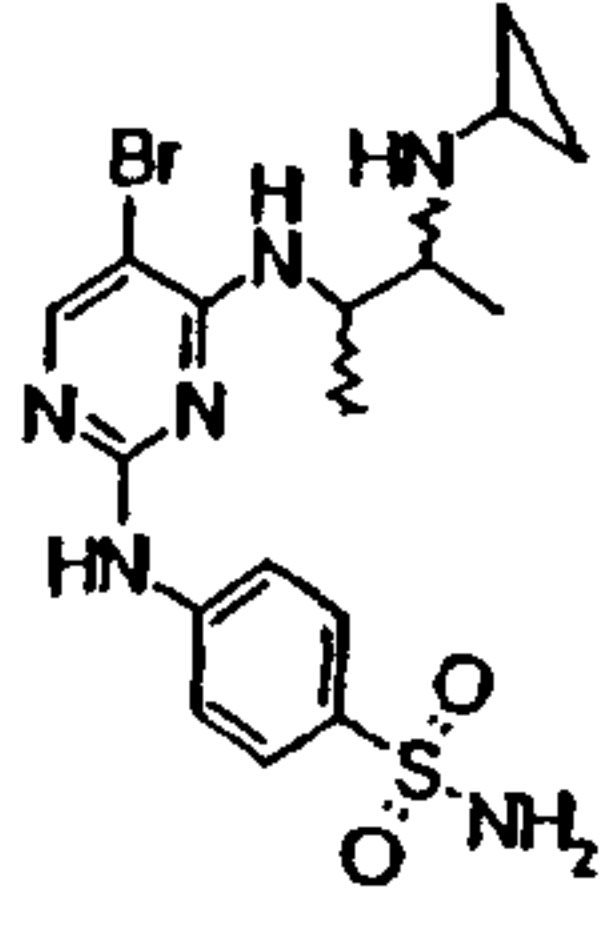
Similarly produced were also the following compounds:

			
Bispiel-Nr.	291	292	293
Ausbeute	34%	36%	40%
Masse	ESI : MH^+ 443 (95%) 445 (99%) 373 (32%)	ESI : MH^+ 485 (92%) 487 (99%)	ESI : MH^+ 487 (91%) 489 (89%) 373 (32%)

Example 294**Reduced Amination**

50 mg (0.12 mmol) of compound No. 282 and 7.5 mg (0.132 mmol) of cyclopropylamine are dissolved in 2 ml of 1,2-dichloroethane. After 9.1 mg (0.144 mmol) of sodium cyanoborohydride is added, it is allowed to stir for 12 more hours. Then, it is diluted with dichloromethane/isopropanol 4:1, washed 2 x with water, dried with magnesium sulfate and concentrated by evaporation. The residue is chromatographed on silica gel with dichloromethane/methanol 95:5. Yield: 18 mg (33% of theory) of the desired compound.

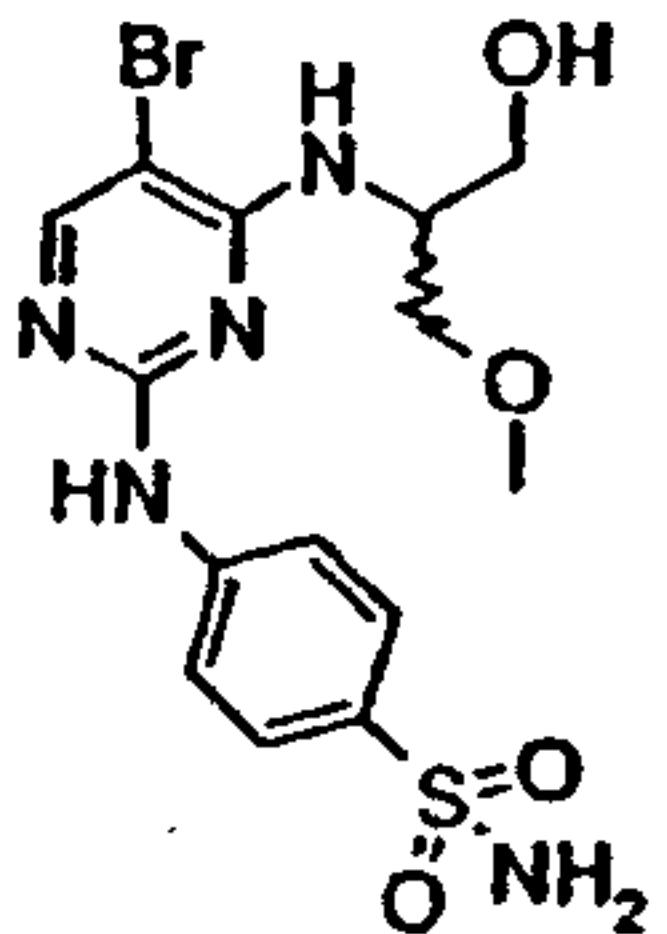
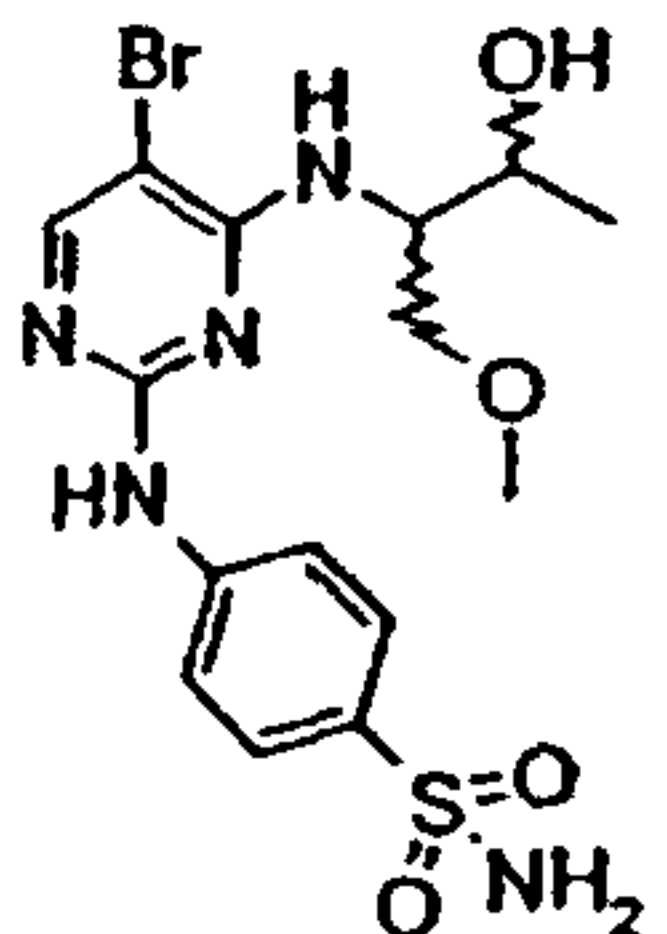
111

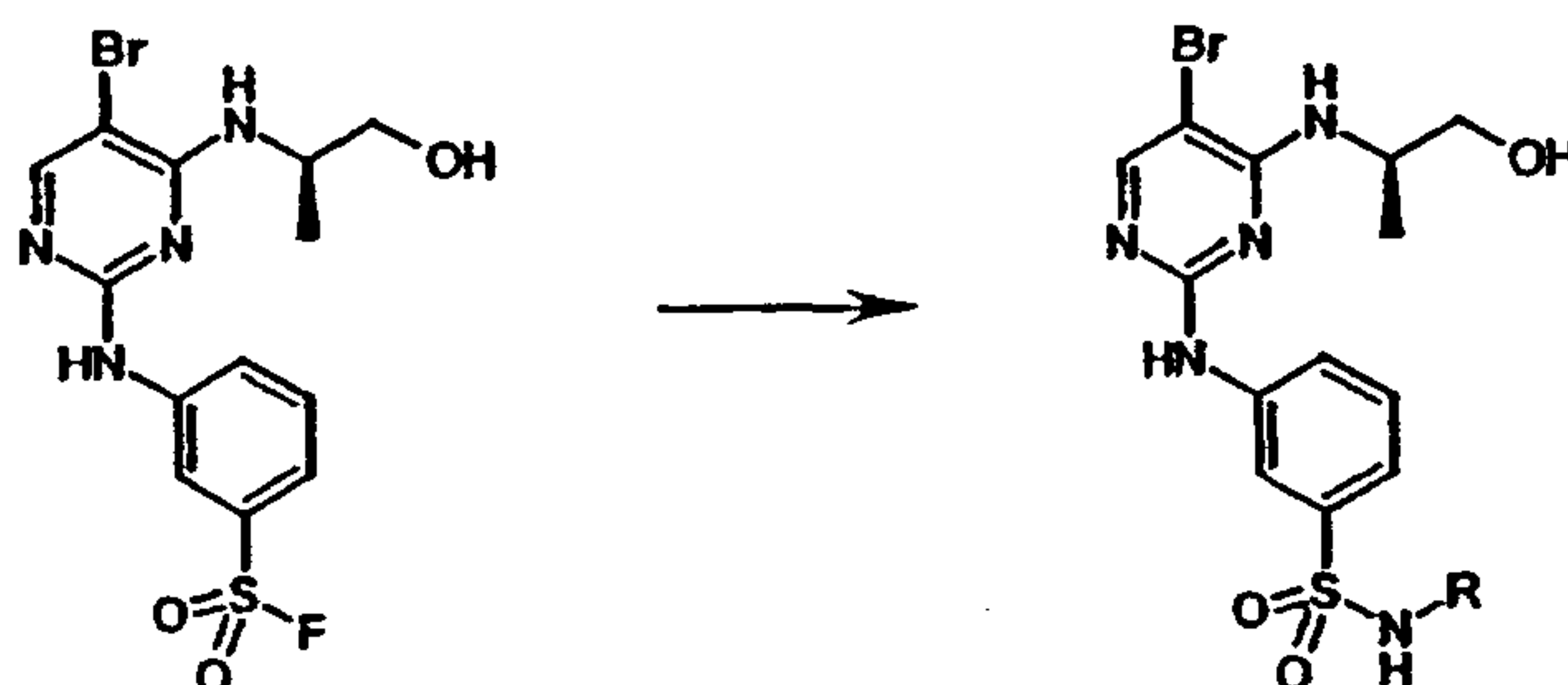
	
Aus- beute	33%
Masse	ESI : MH ⁺ 457 (98%) 455 (93%) 249 (55%)

Produced similarly are also compounds Nos. 159, 160, 161, 163, 167, 168, 170, 174, 175, 191, 192, 203 and 204.

Examples 295 and 296

Produced similarly to Example 1 are also the following two compounds:

		
Beispiel	295	296
Ausbeute	46 %	47 %
Masse	ESI : MH ⁺ 432 (30%) 434 (31%) 123 (100%)	ESI : MH ⁺ 446 (45%) 448 (49%) 123 (90%)

Production of Sulfonamides of General Formula I

0.2 mmol of sulfonic acid fluoride is introduced into the reactor of a synthesizer. 1.0 ml of solvent, preferably 2-butanol, is added. 0.2 ml (0.2 mmol) of DMAP – dissolved in a solvent, for example DMSO or 2-butanol – and 0.2 ml (0.2 mmol) of the amine, dissolved in 2-butanol, are added in succession via a pipette. The reaction mixture is then stirred for 20 hours at 80°C. After the reaction is completed, the crude product is pipetted off, and the reactor is rewashed with 1.0 ml of THF. The solution of the crude product is then concentrated by evaporation and purified by HPLC.

The compounds below were produced:

[Key to subsequent tables:]

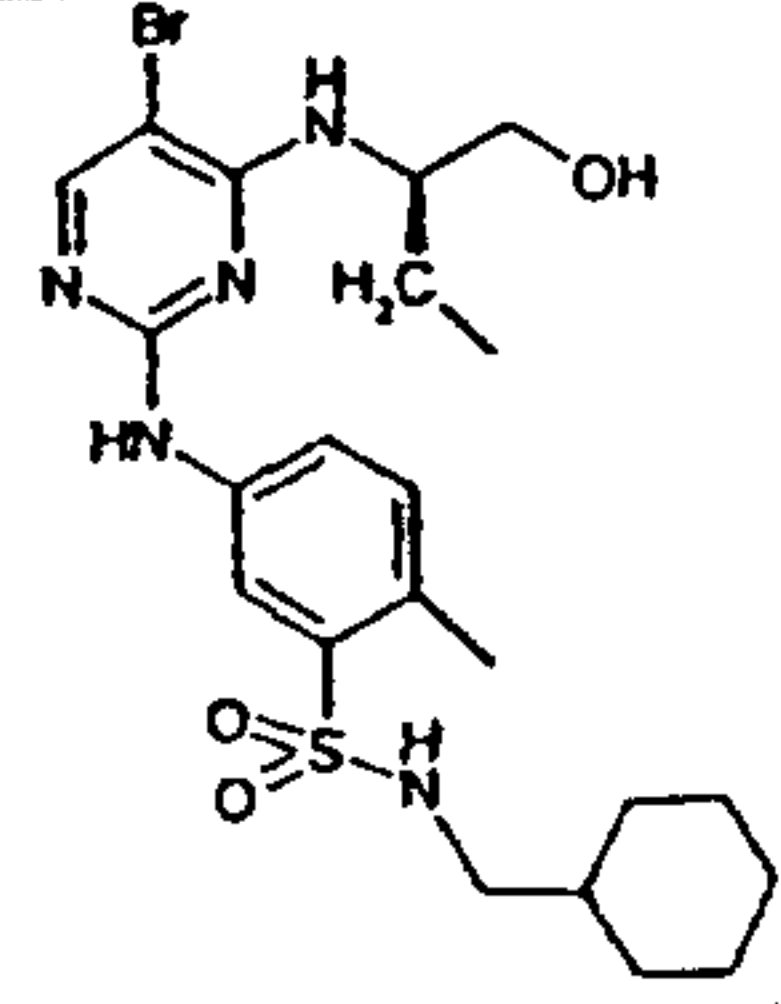
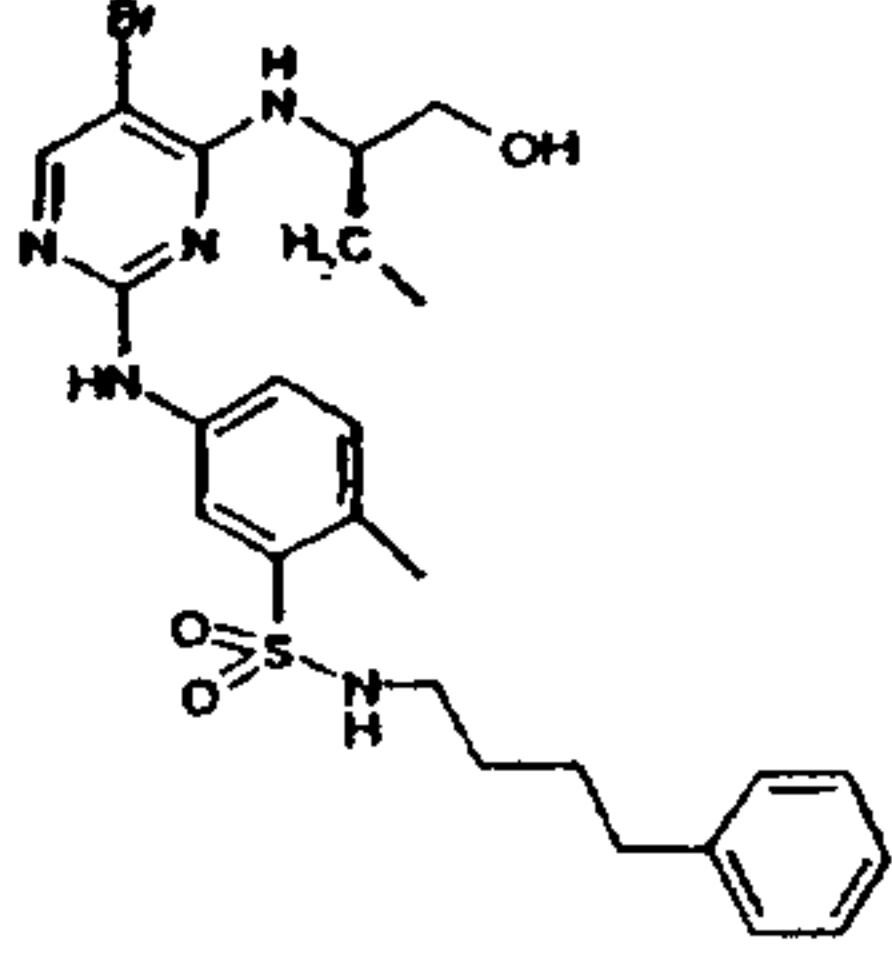
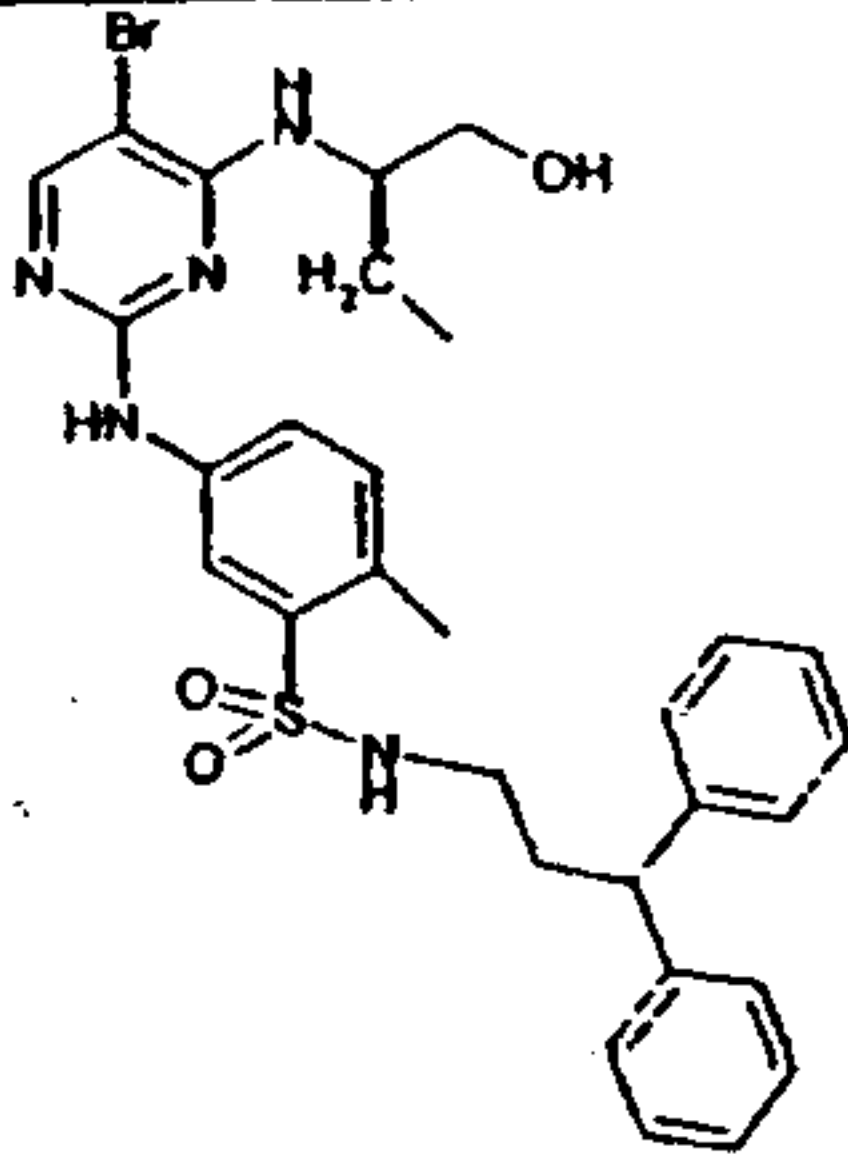
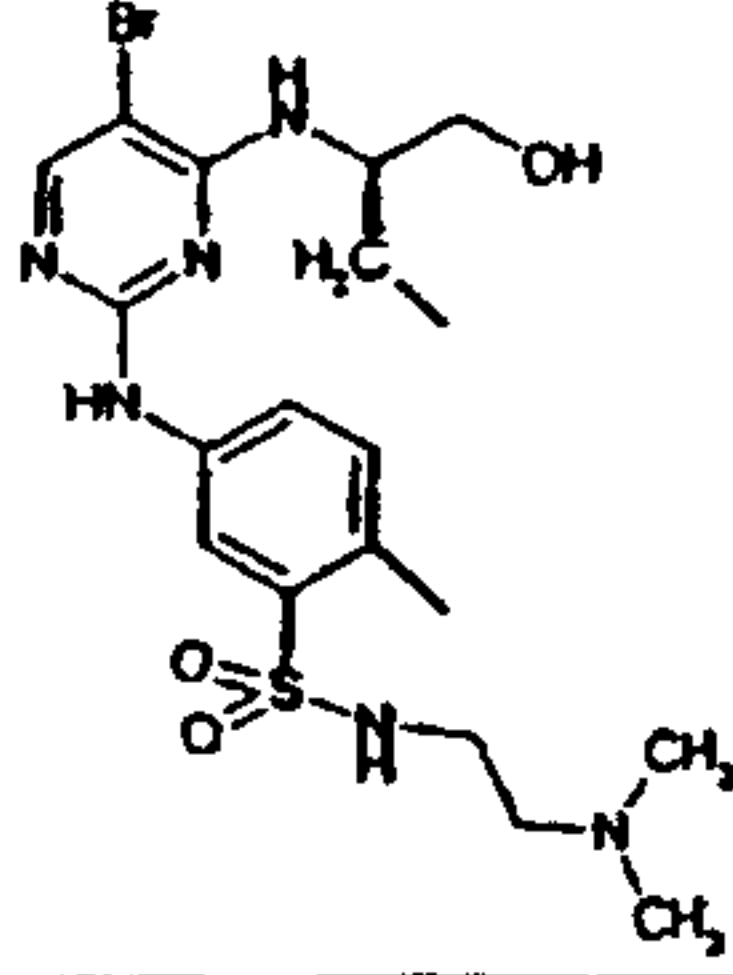
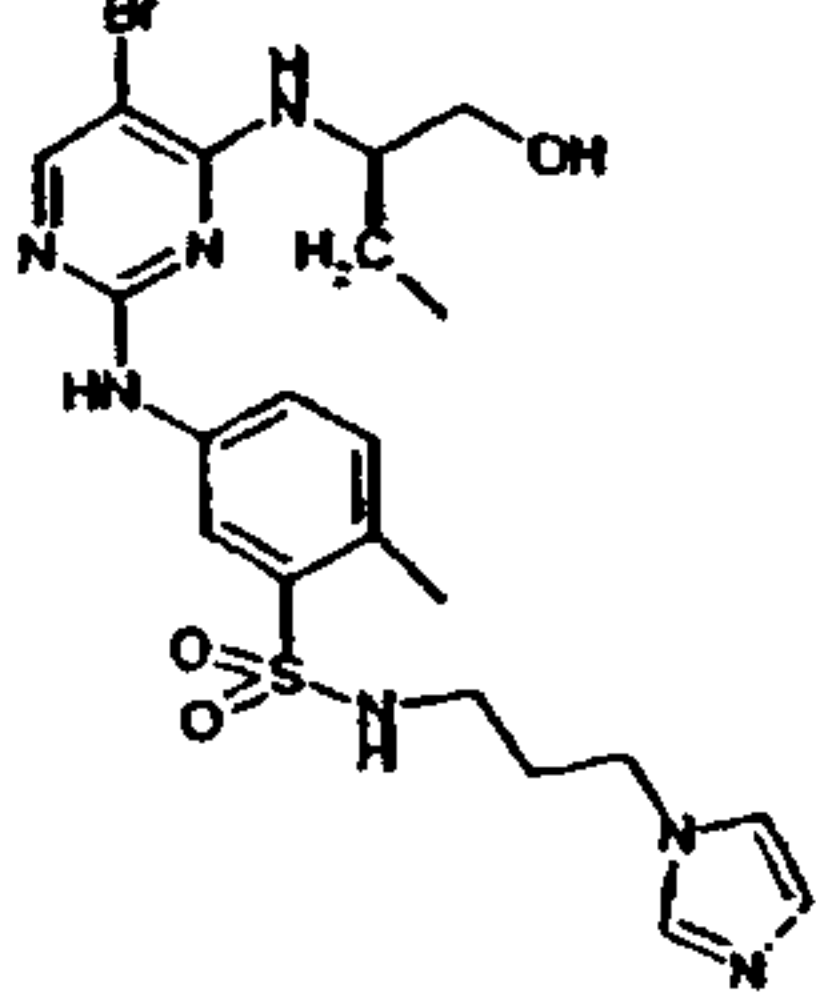
Beispiel-Nr. = Example No.

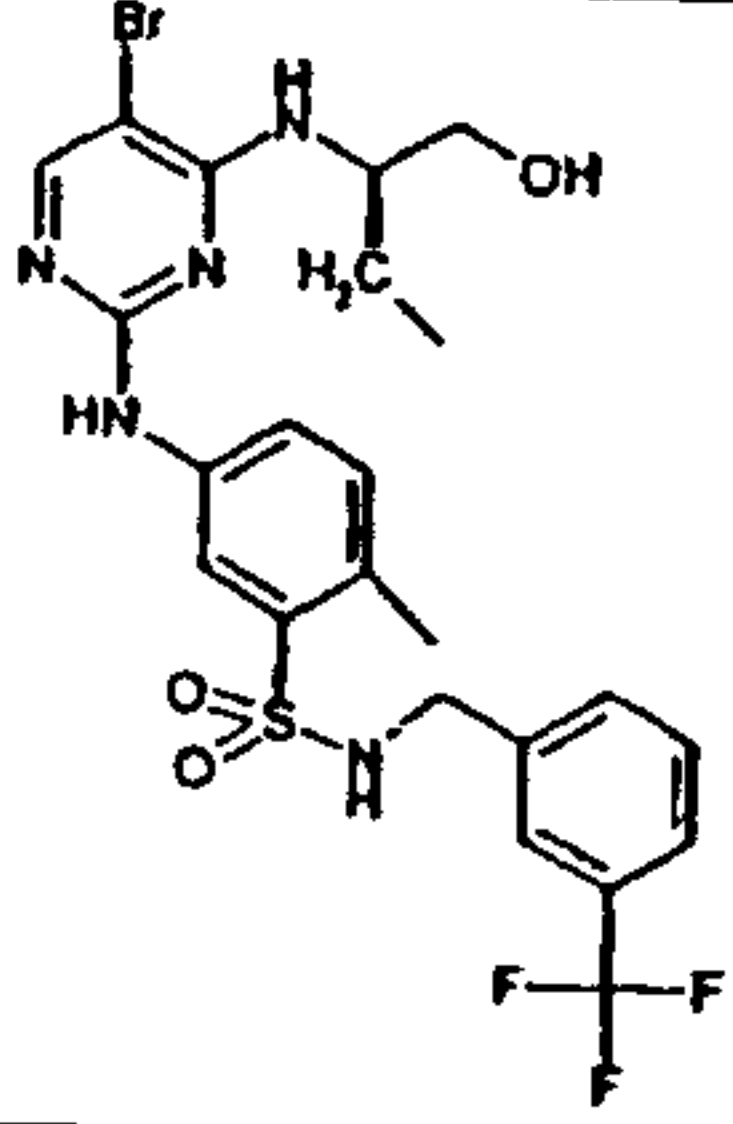
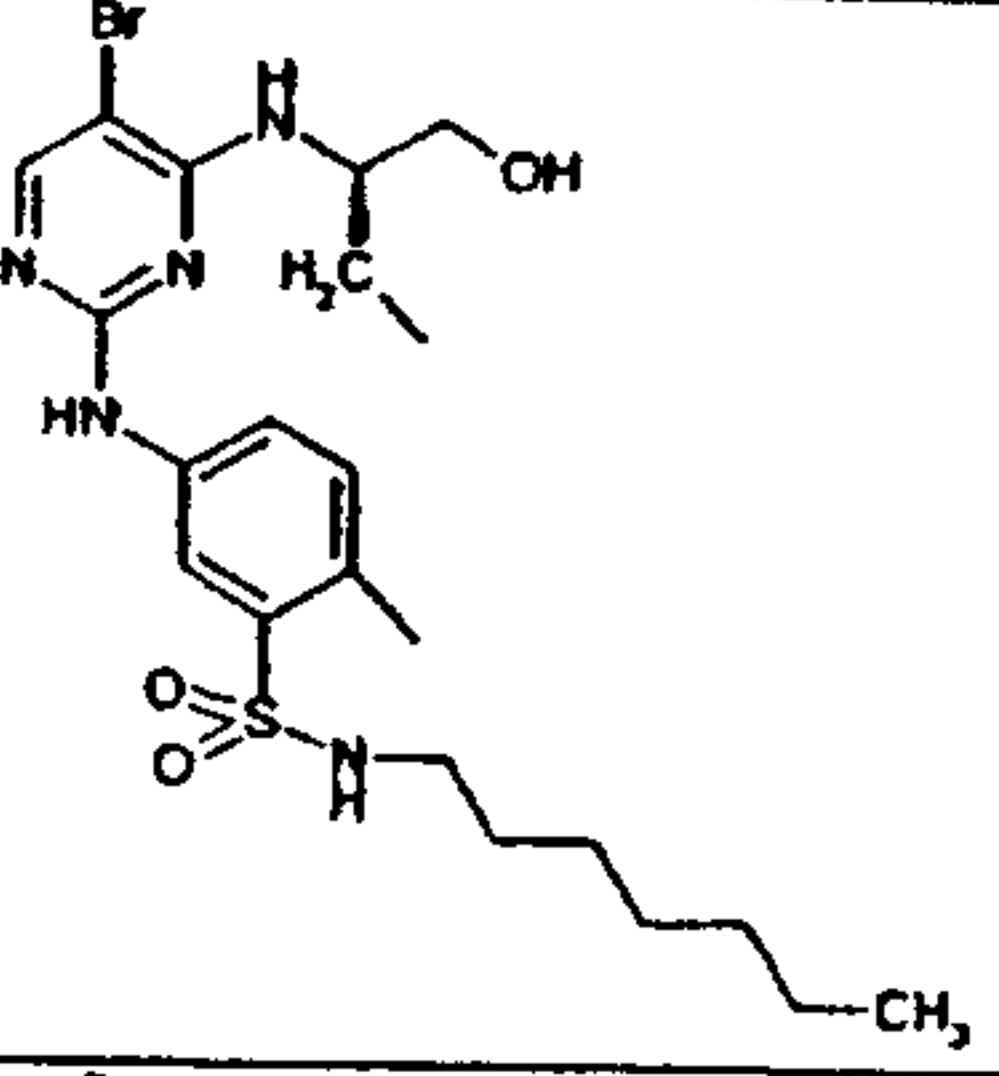
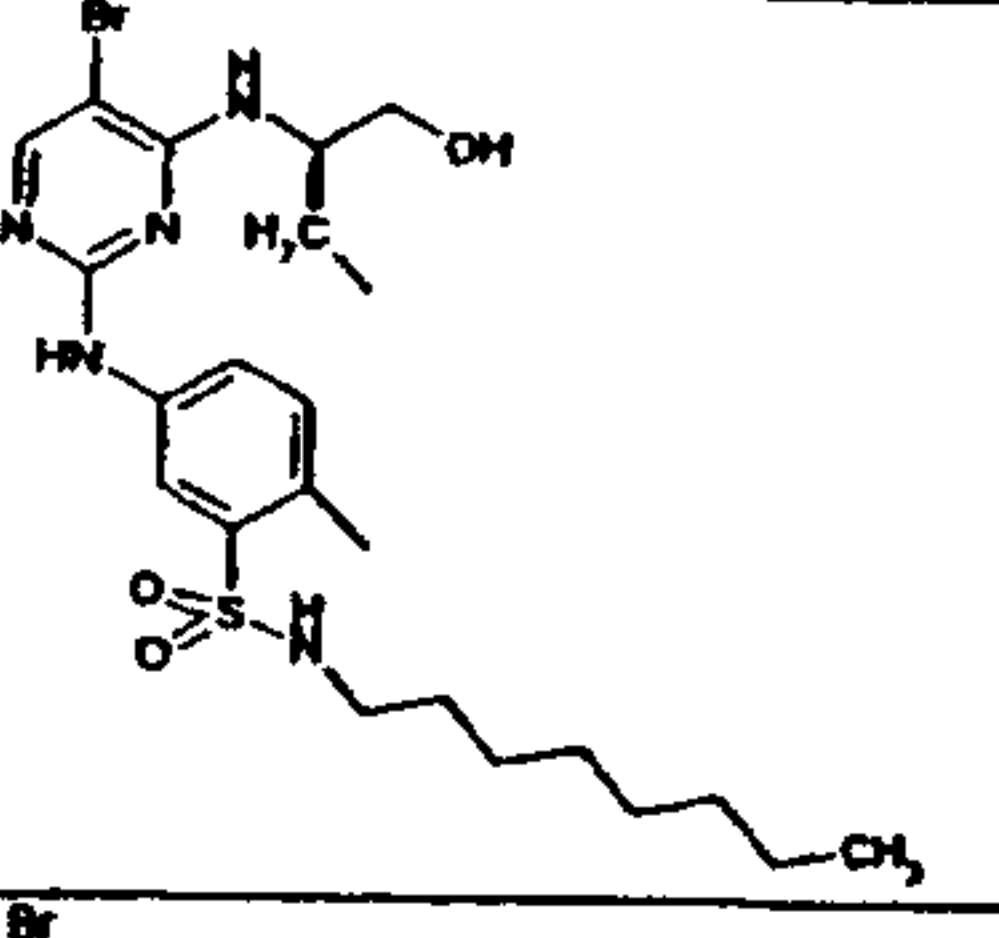
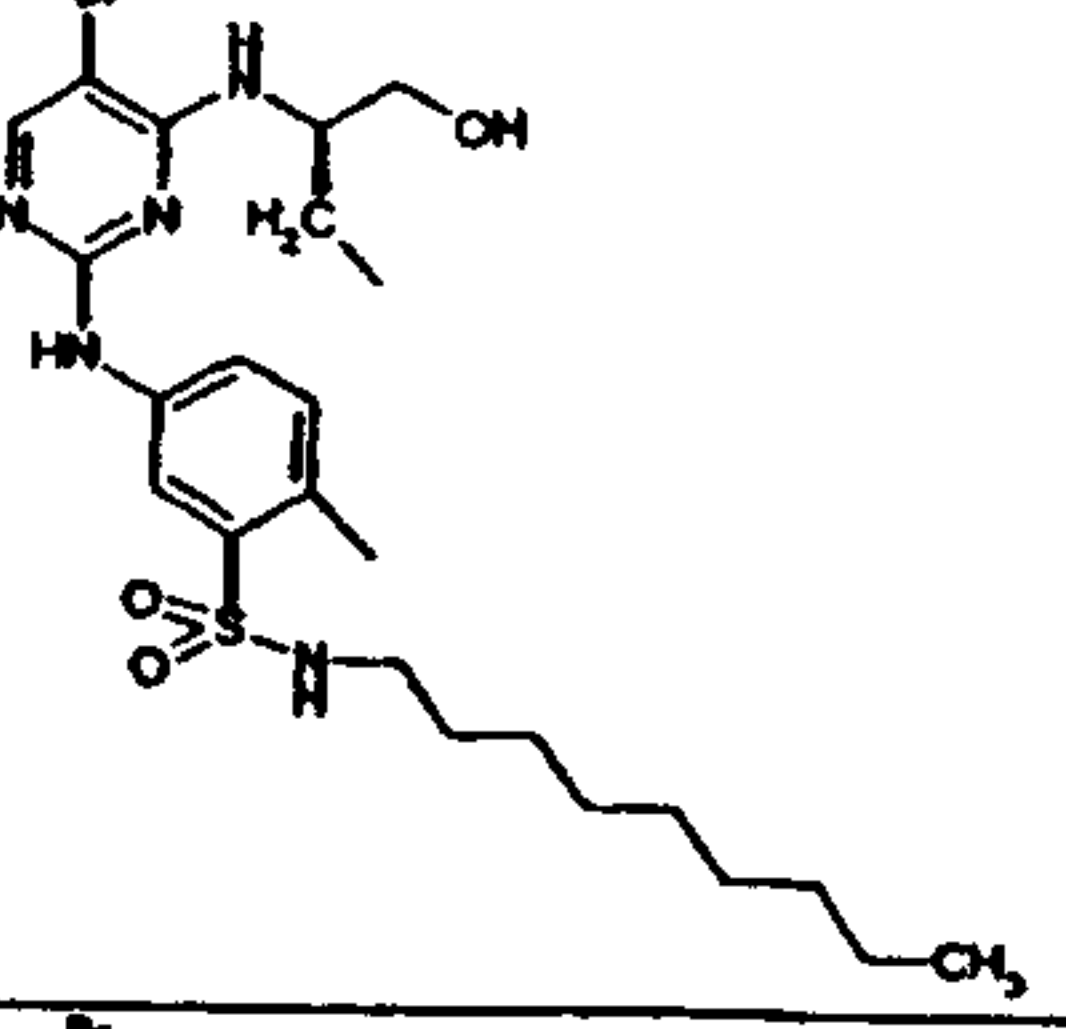
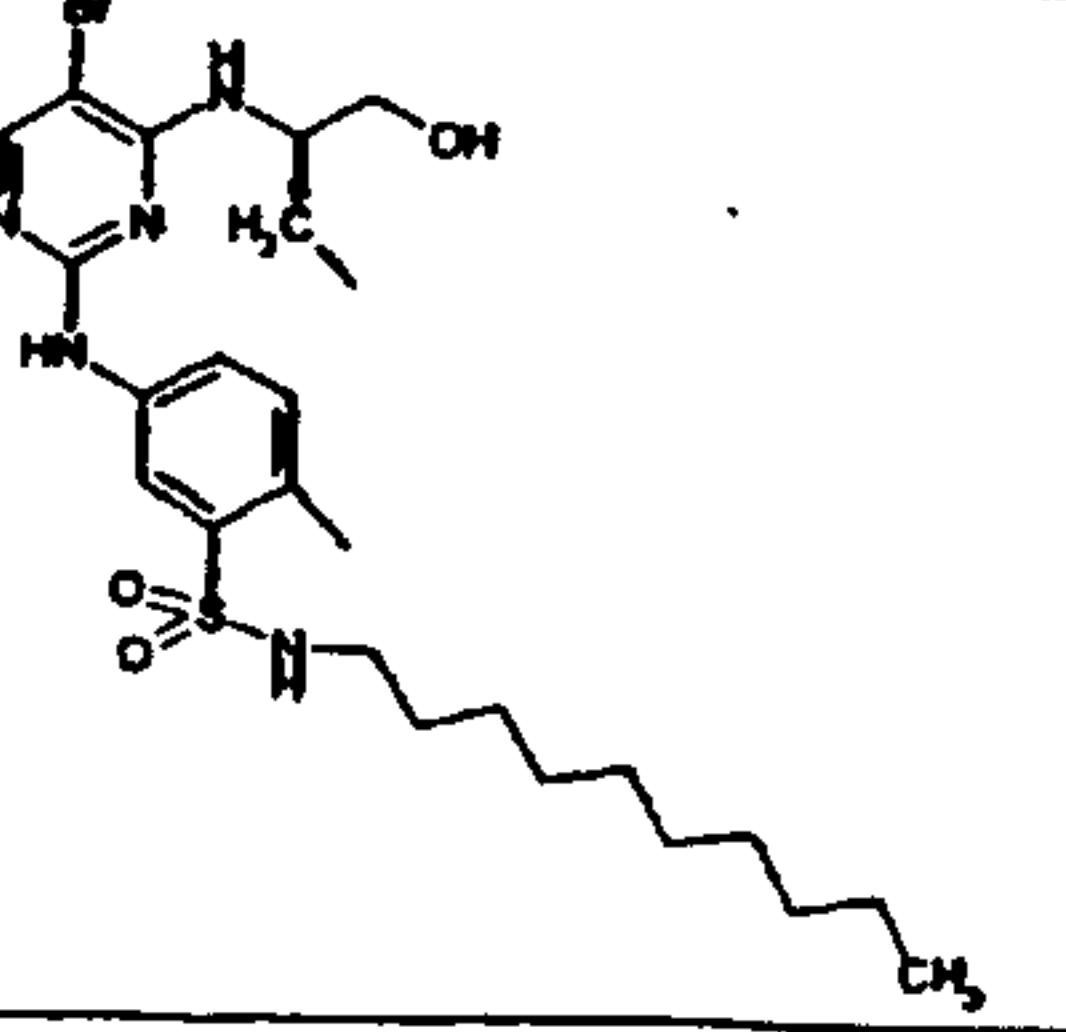
Verbindung = Compound

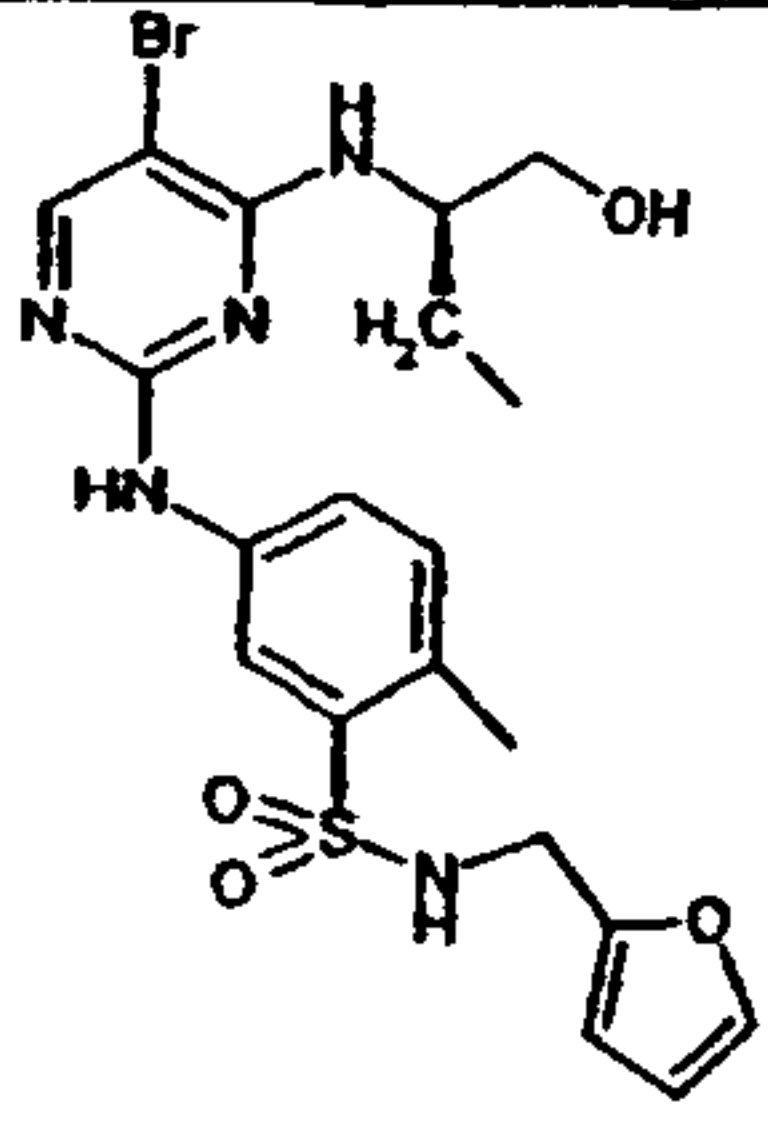
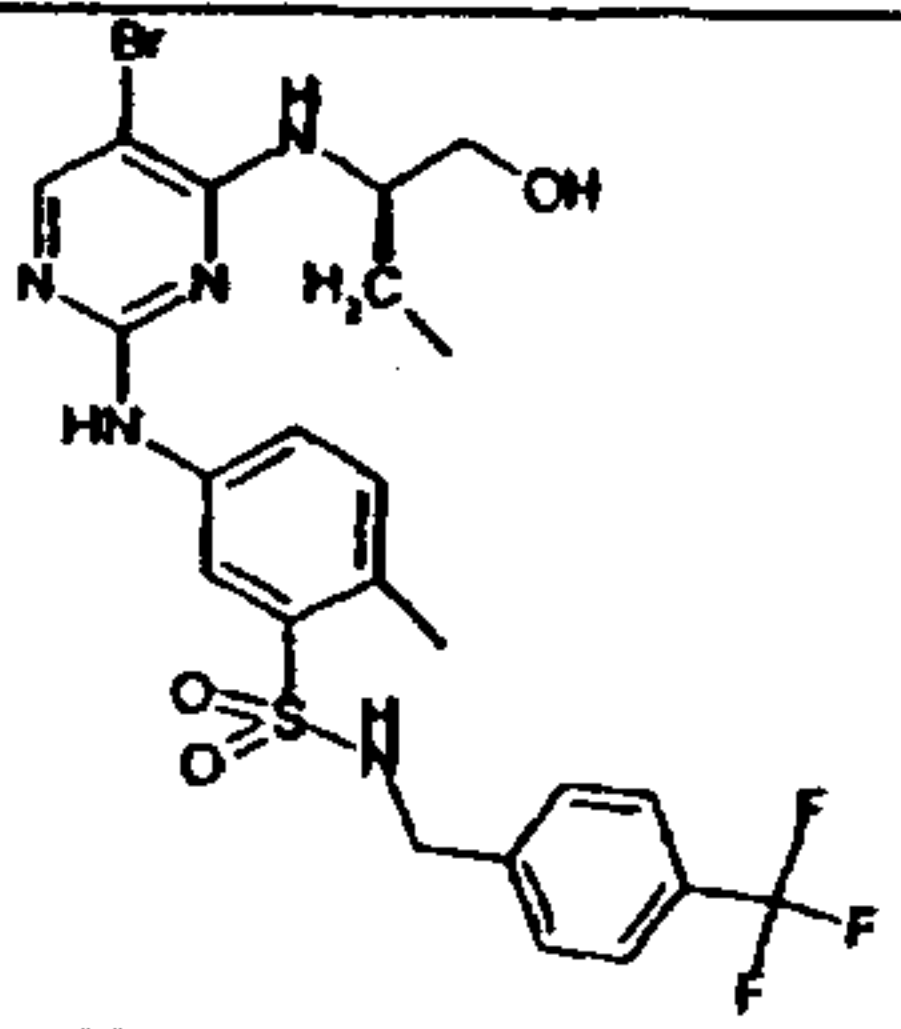
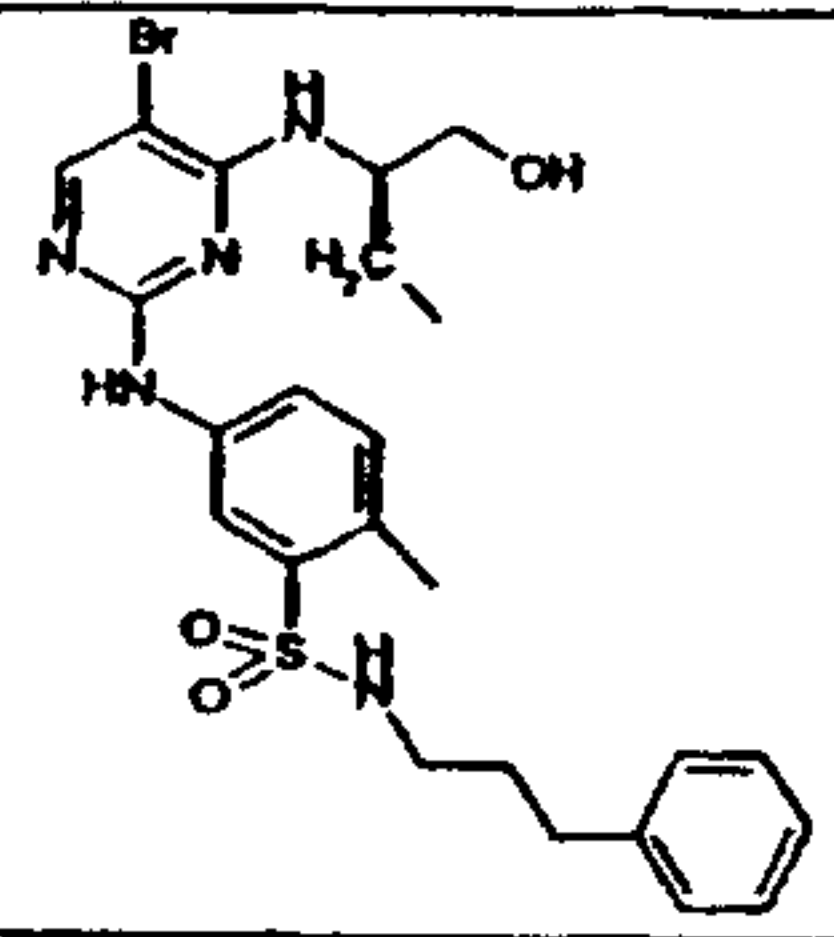
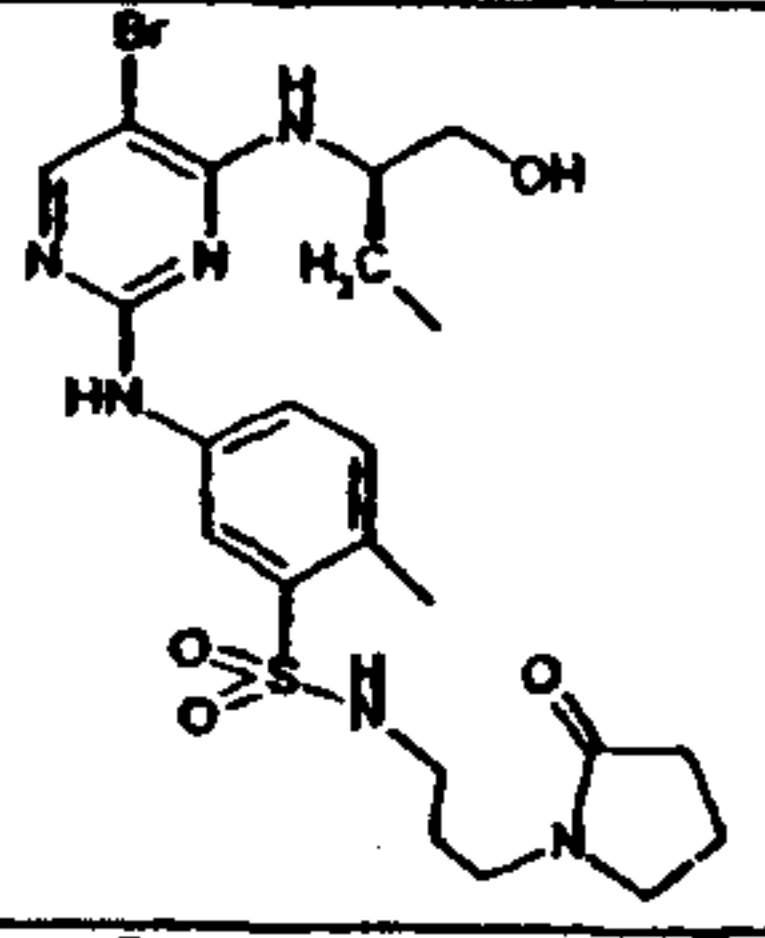
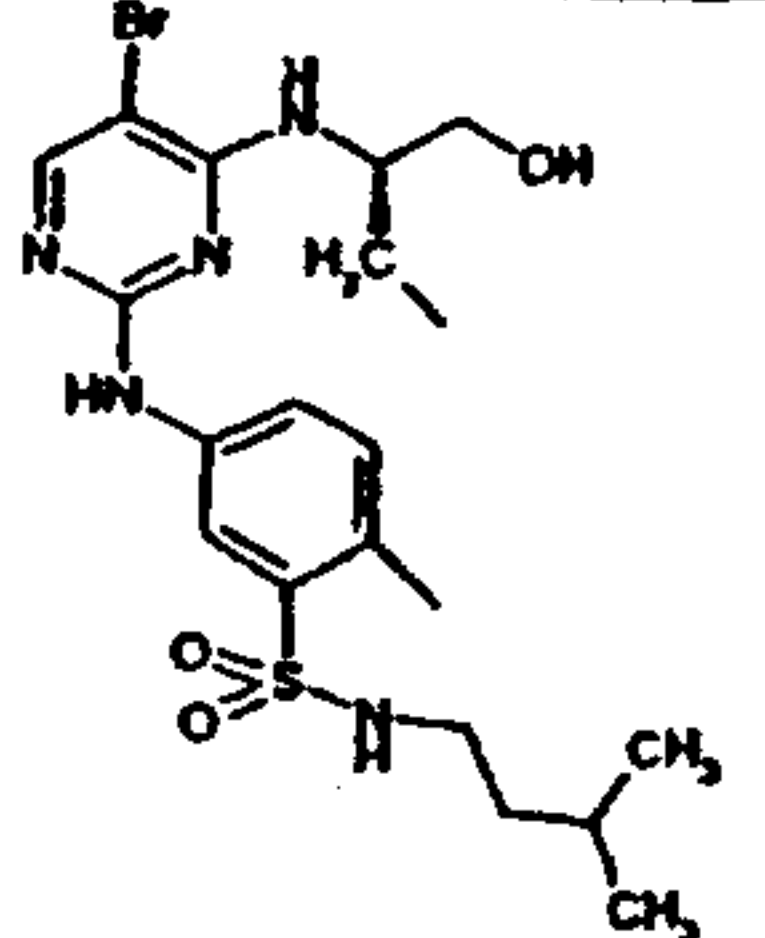
Molgewicht = Molecular Weight

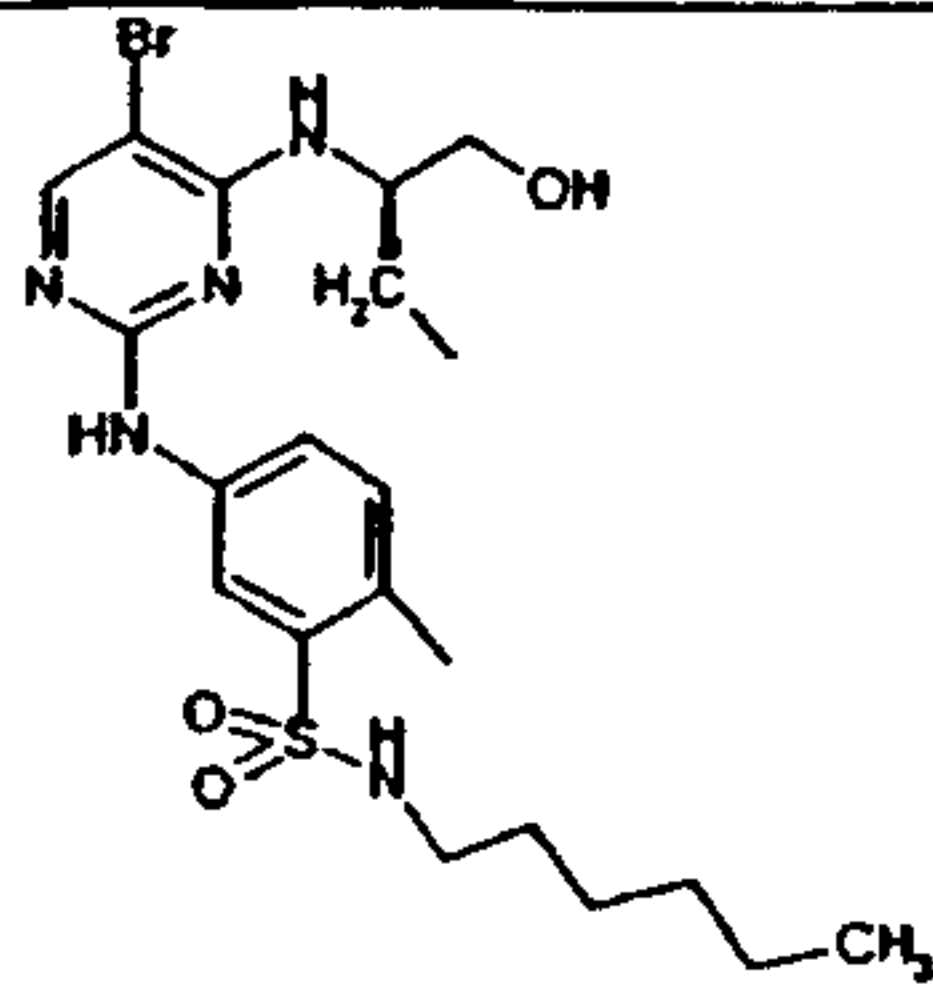
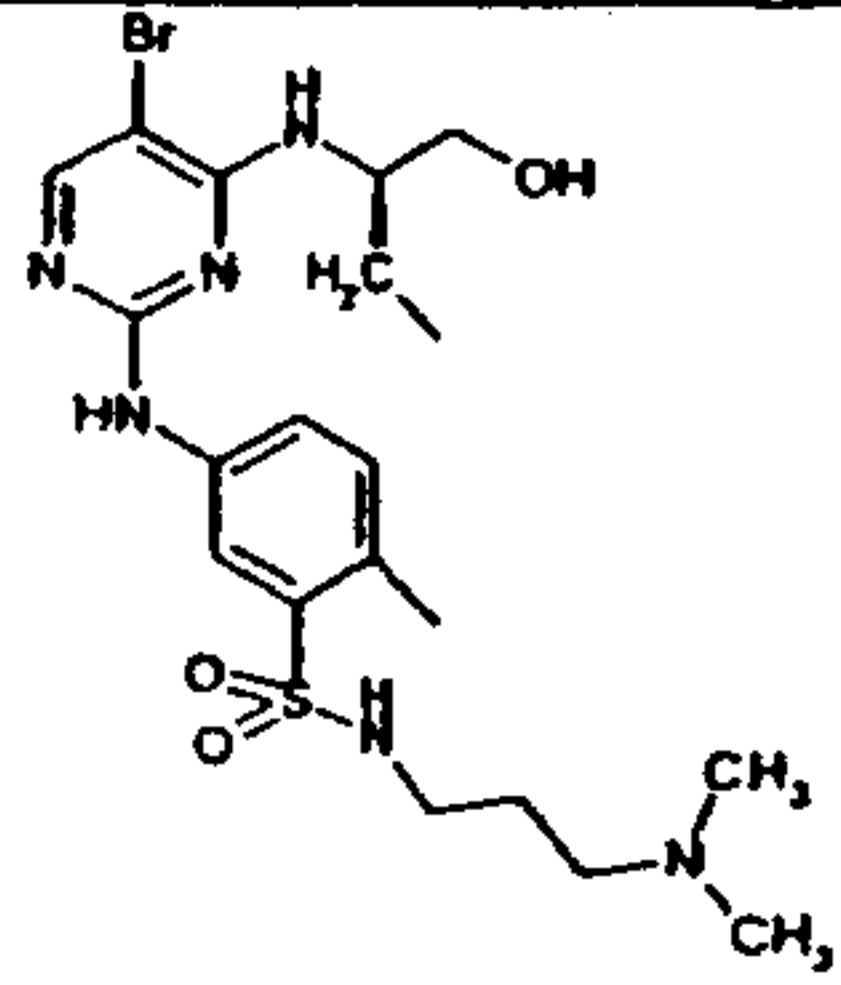
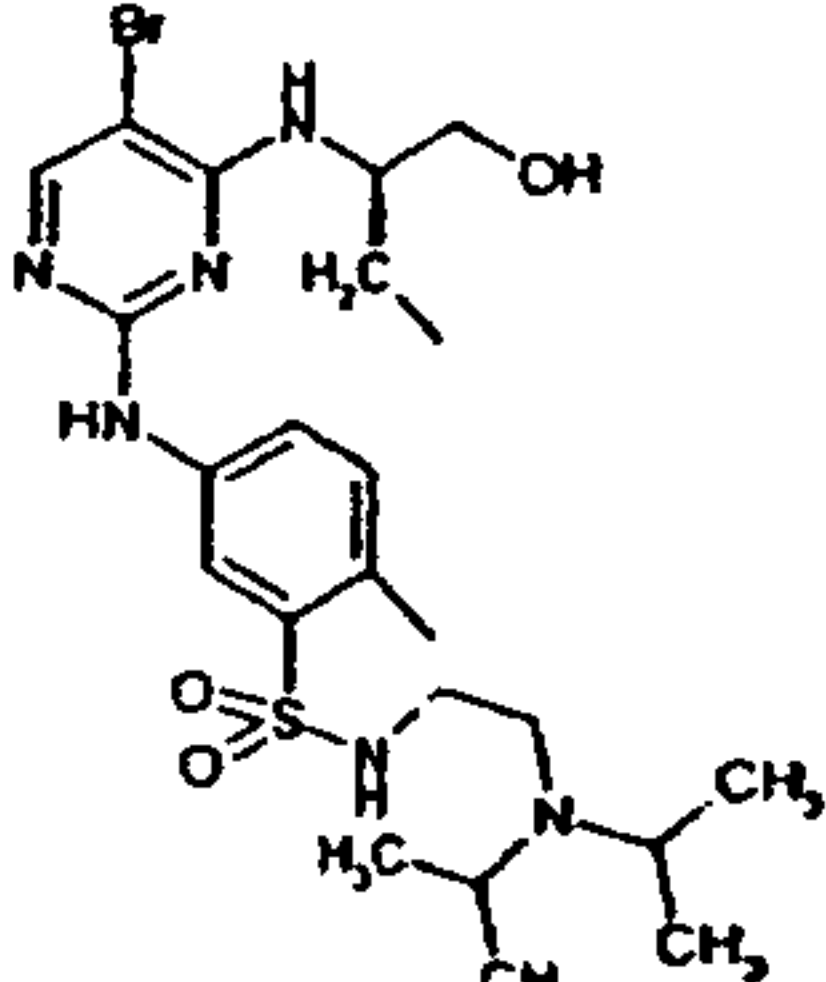
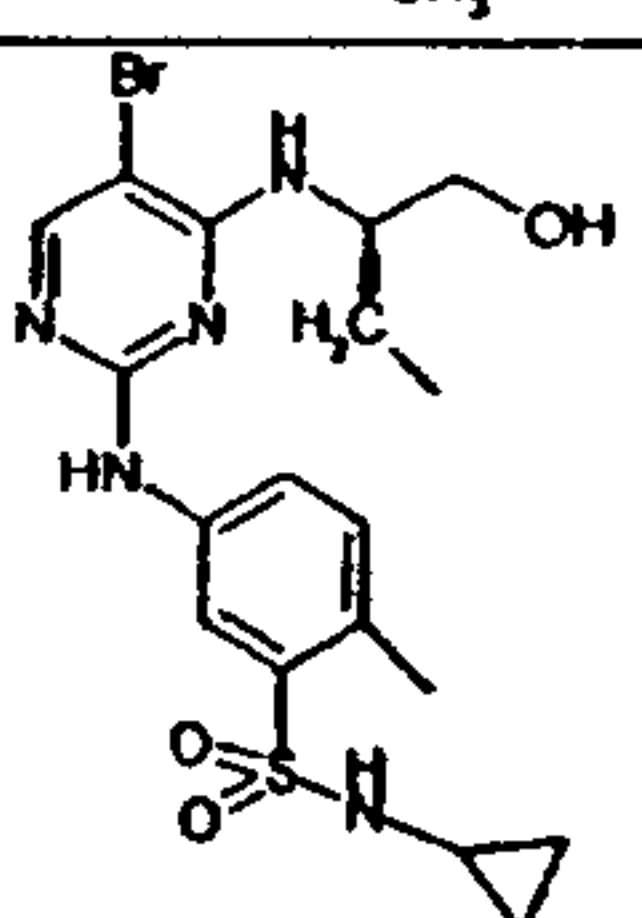
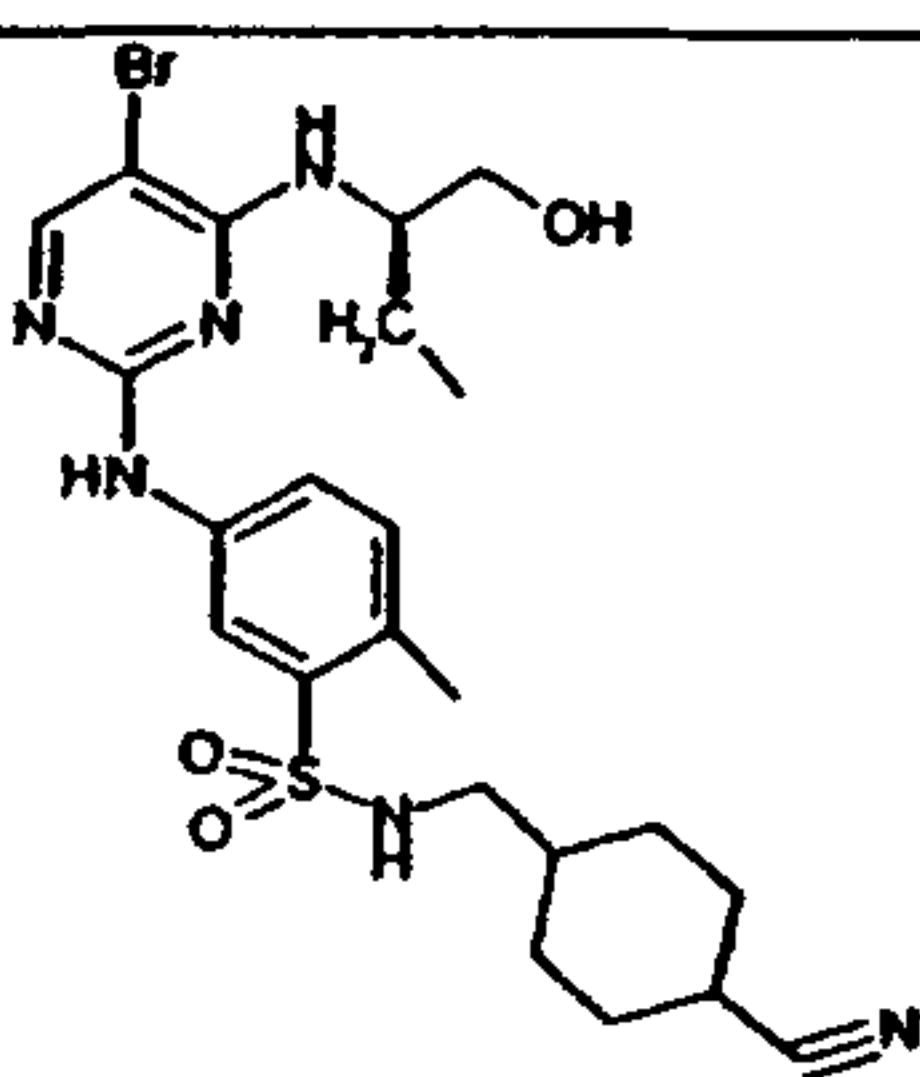
Schmelzpunkt = Melting point

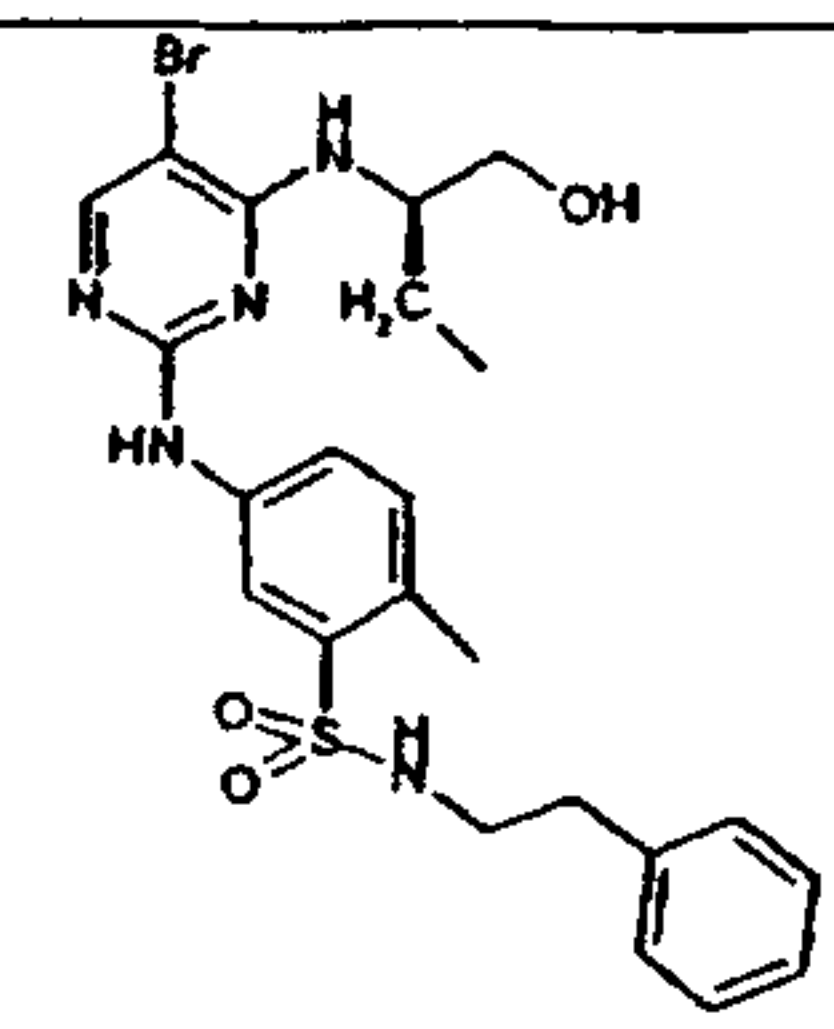
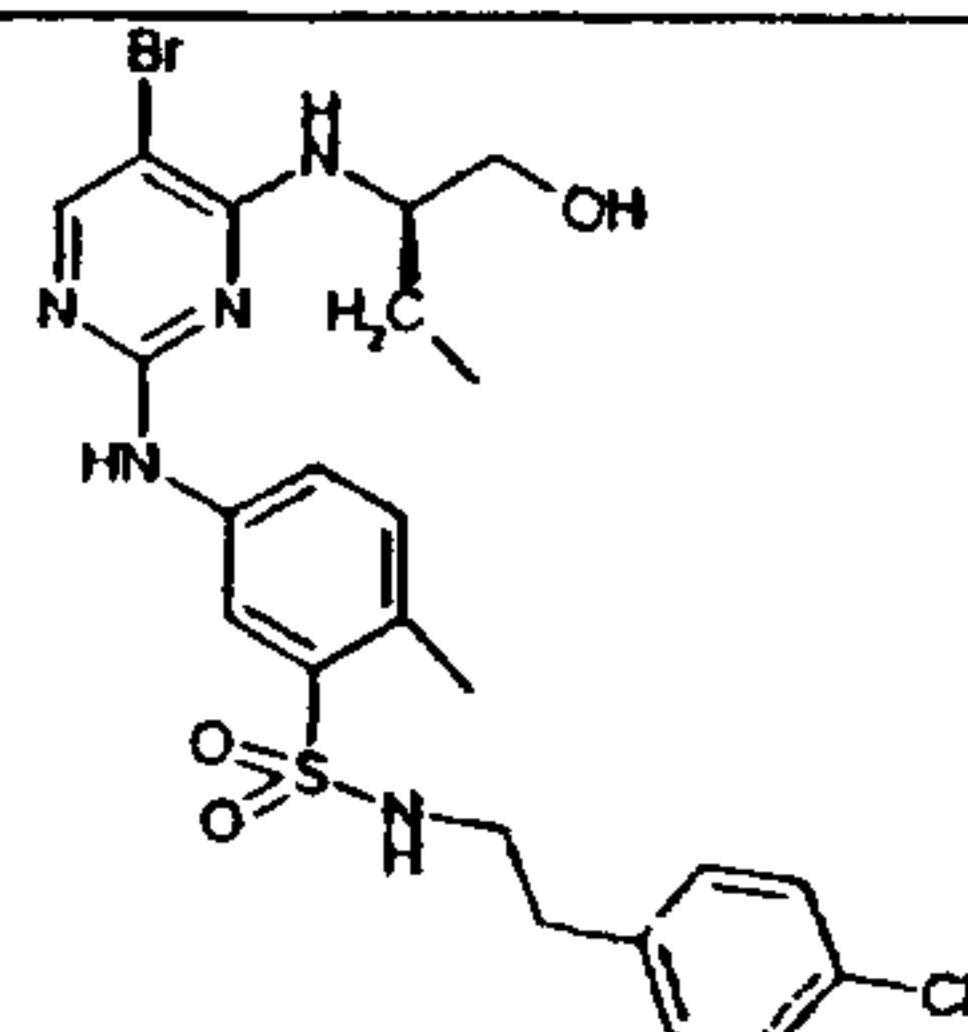
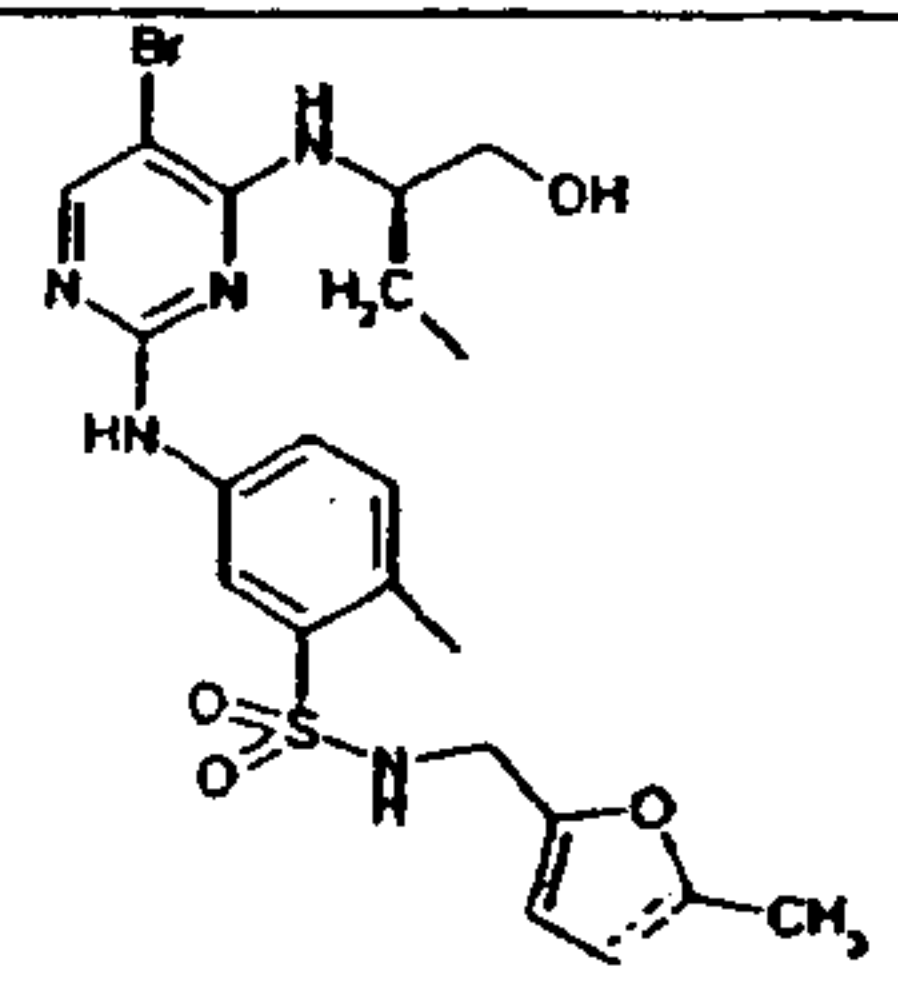
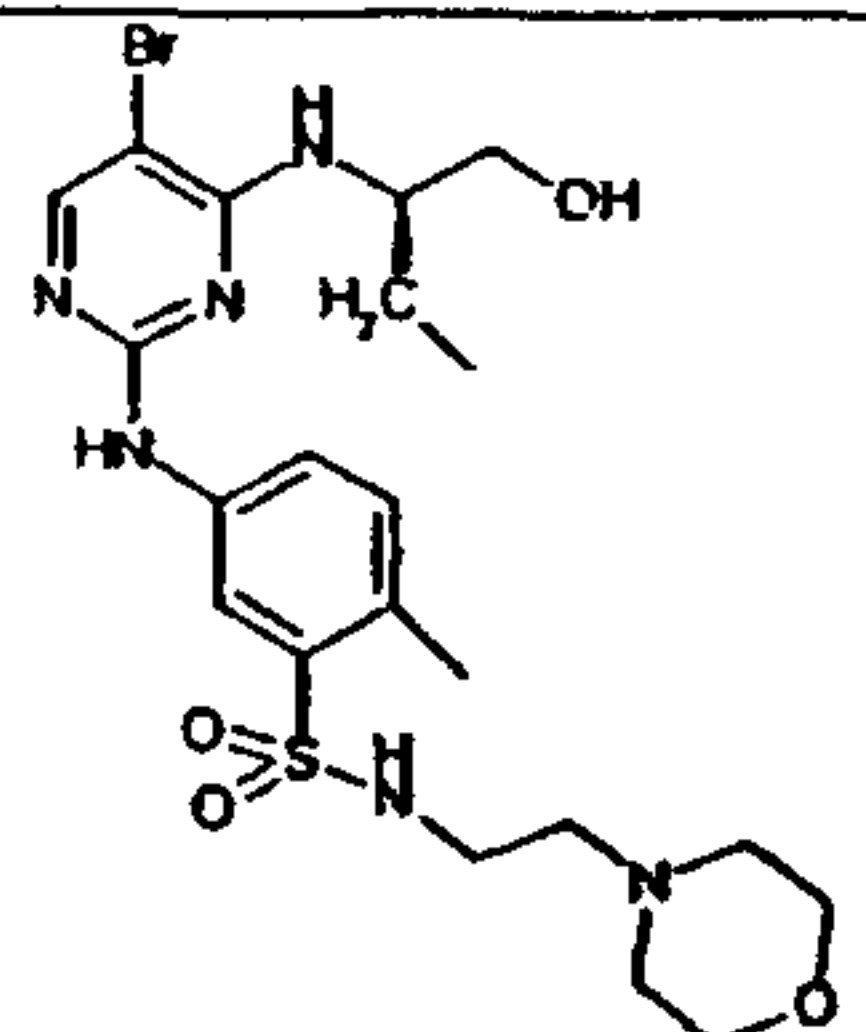
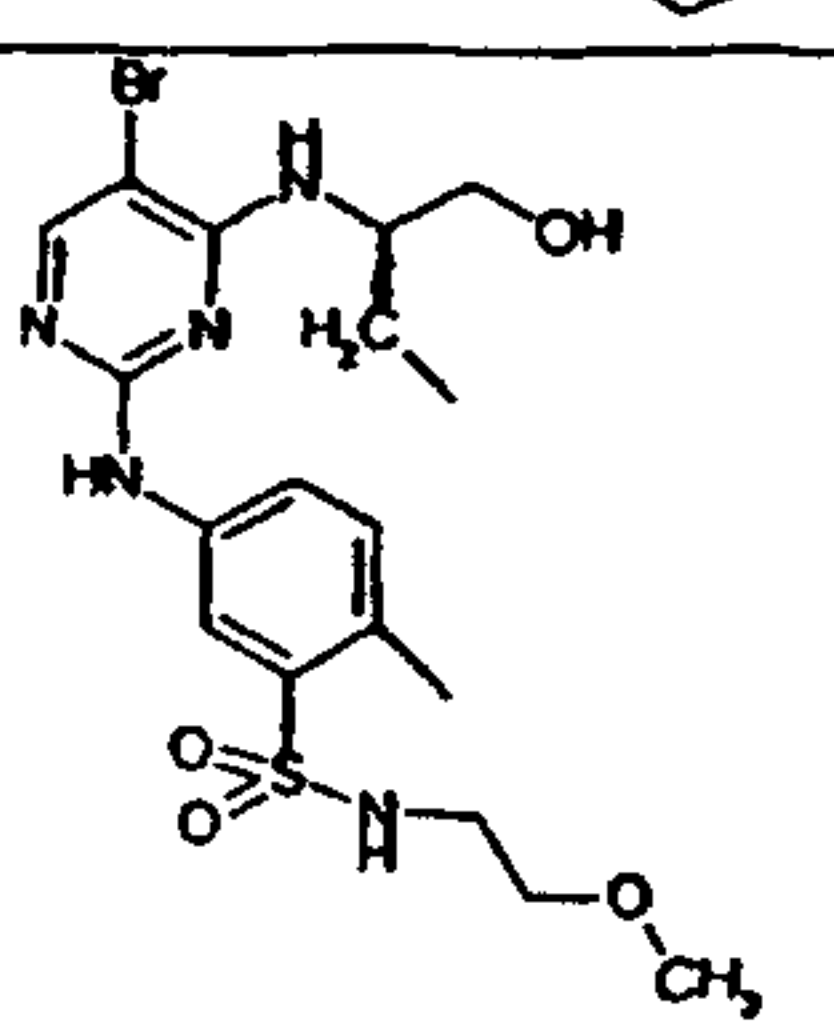
und = and

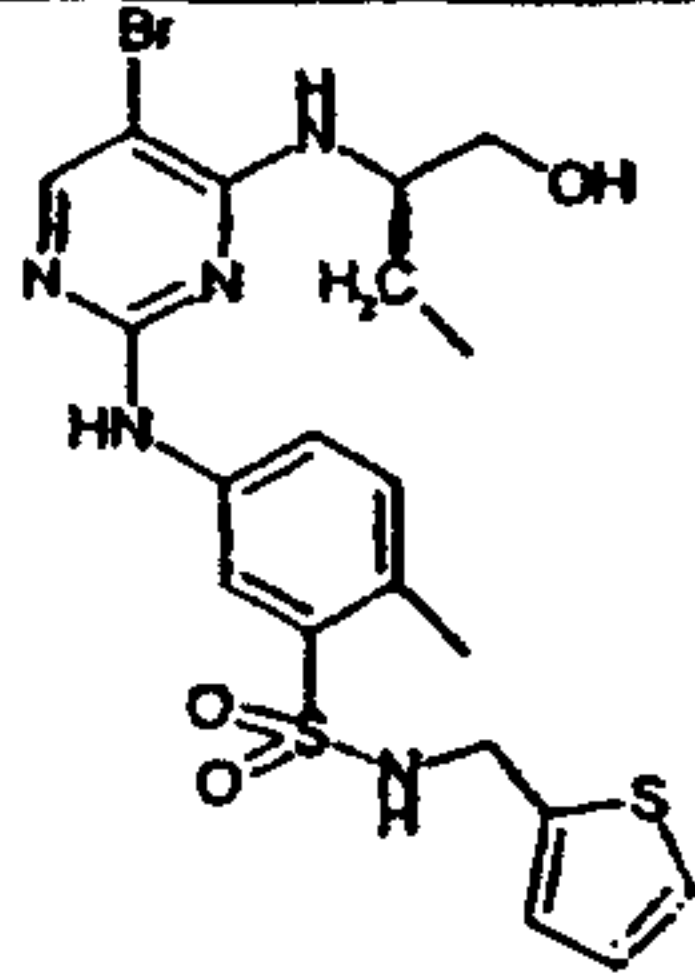
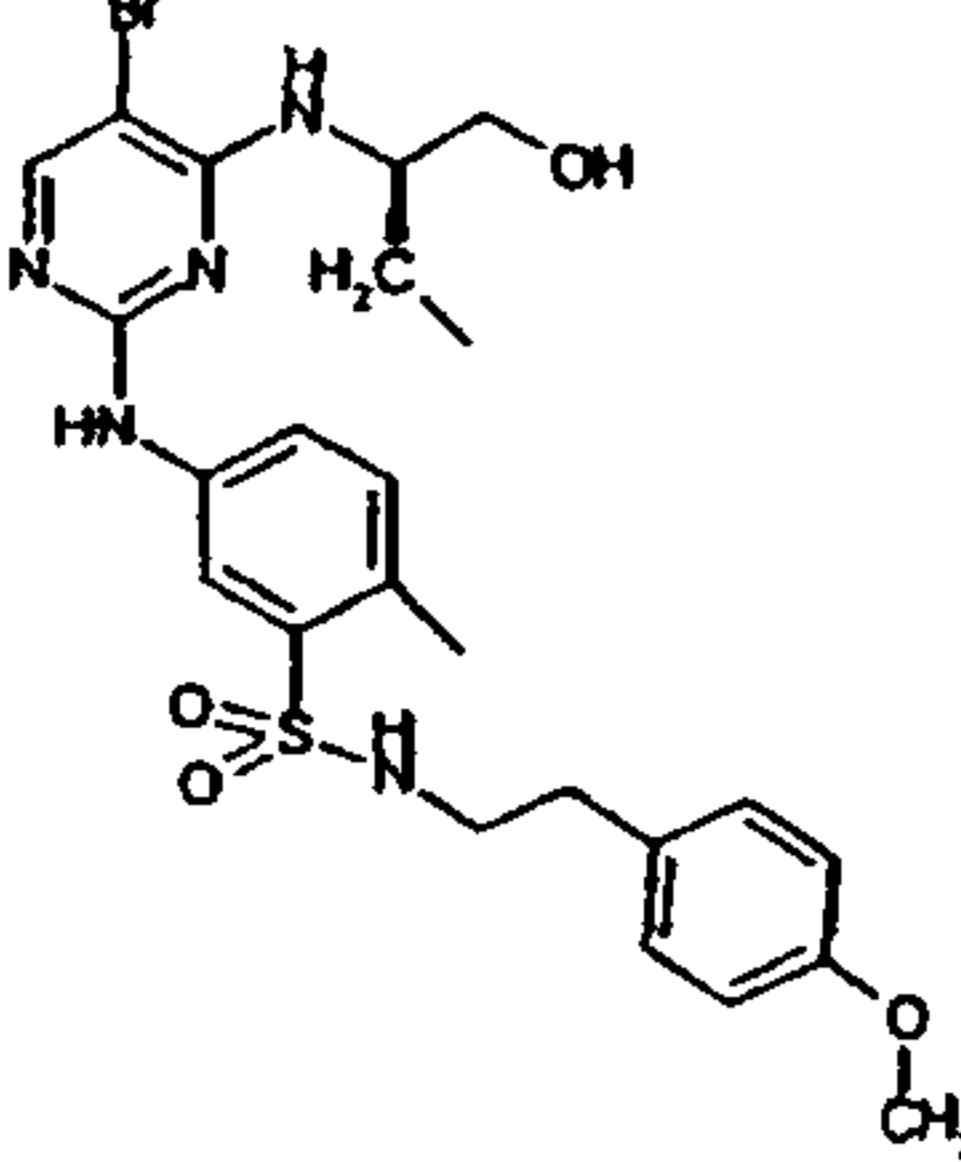
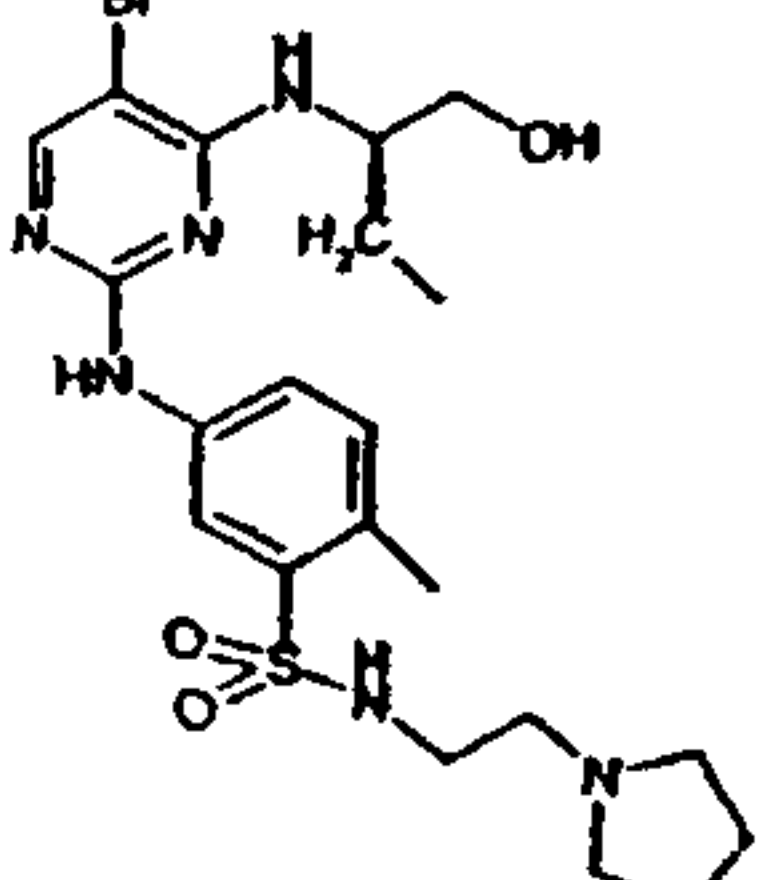
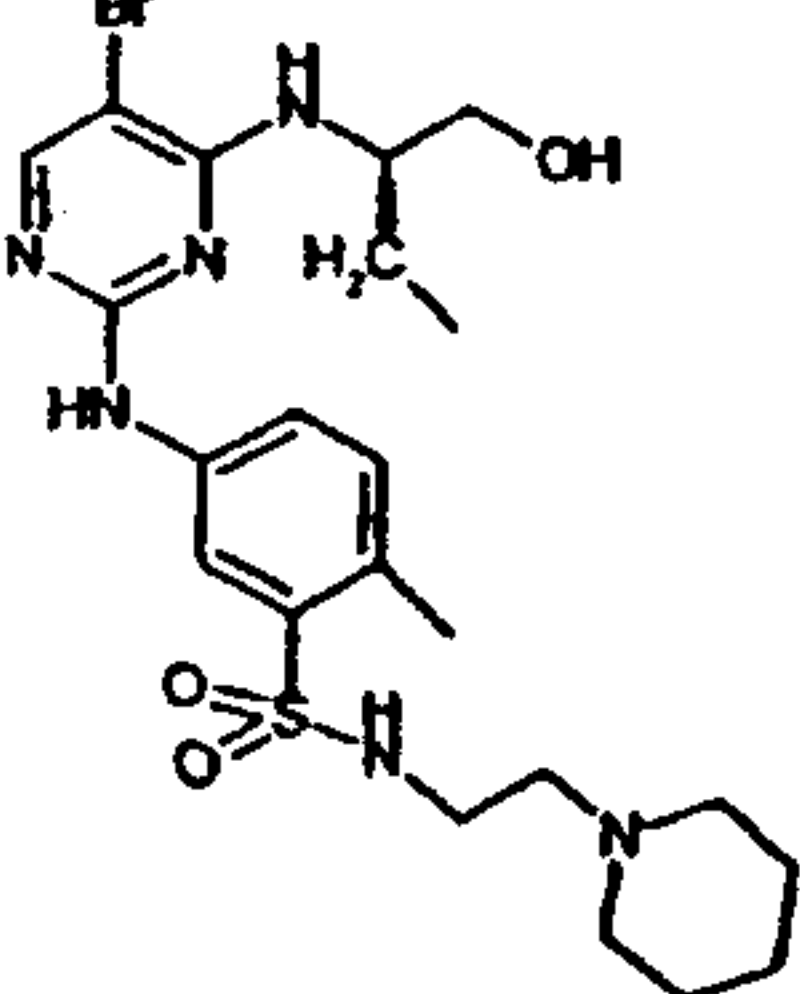
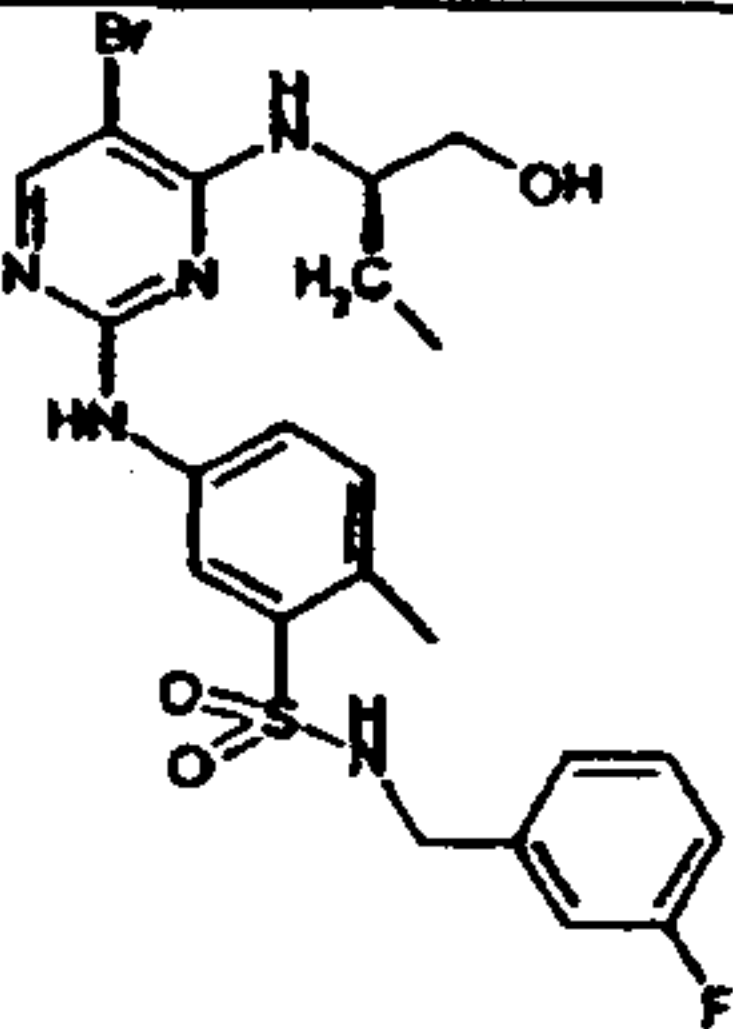
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
297		526,4968	526/528
298		562,5298	562/564
299		624,6006	624/626
300		501,4471	501/503
301		538,4682	538/540

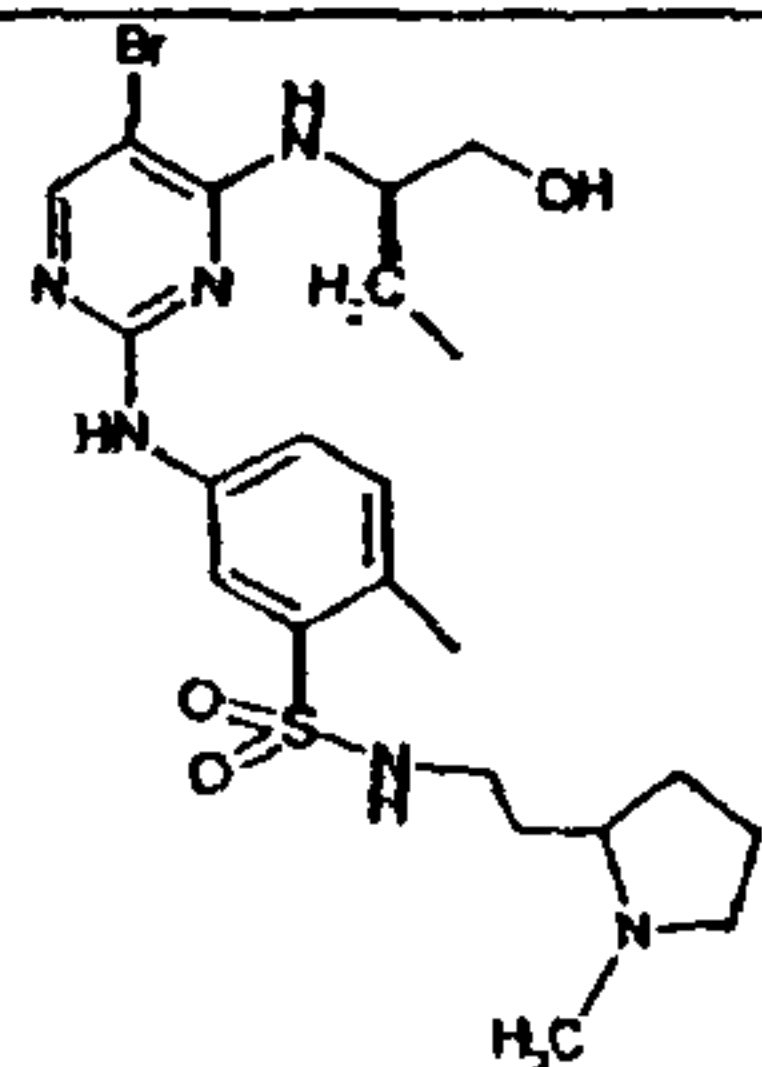
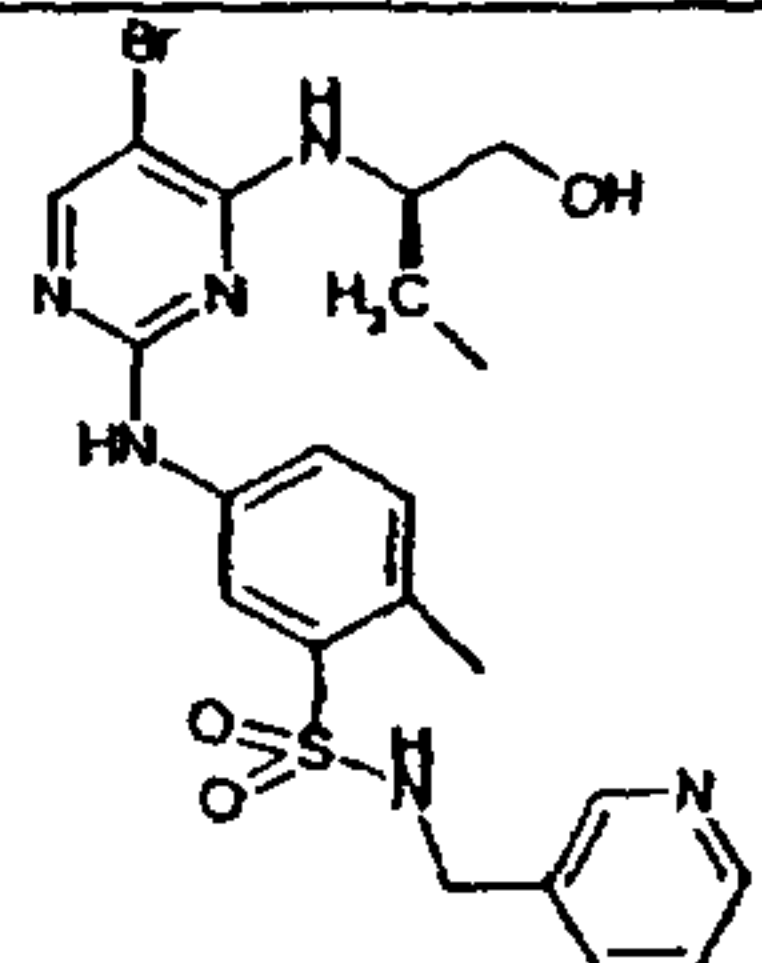
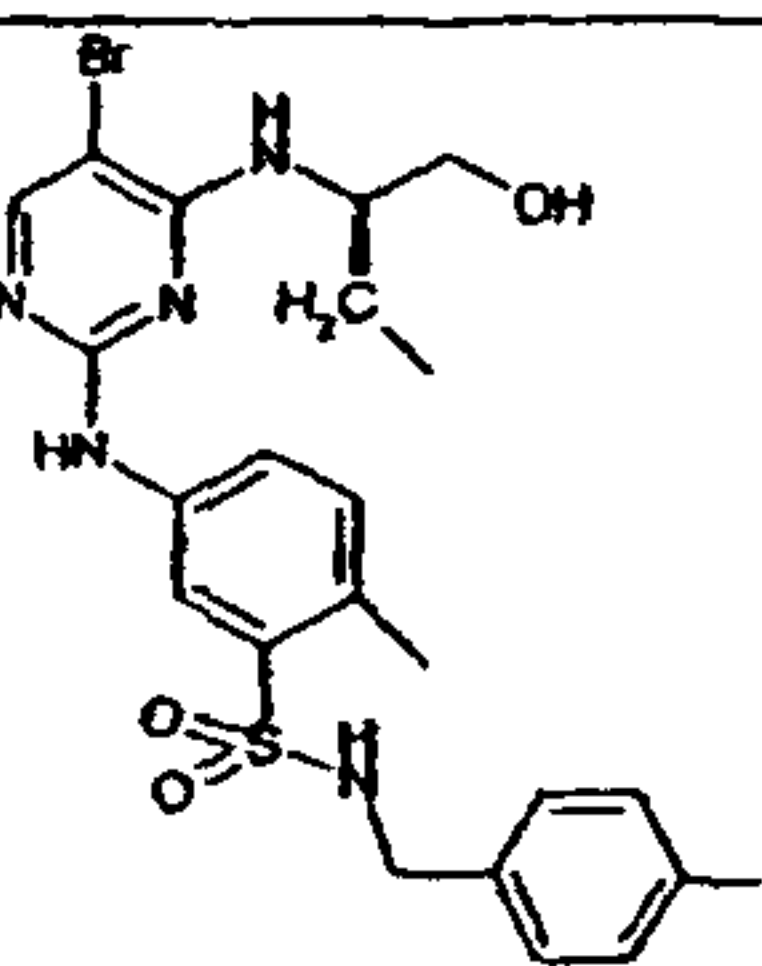
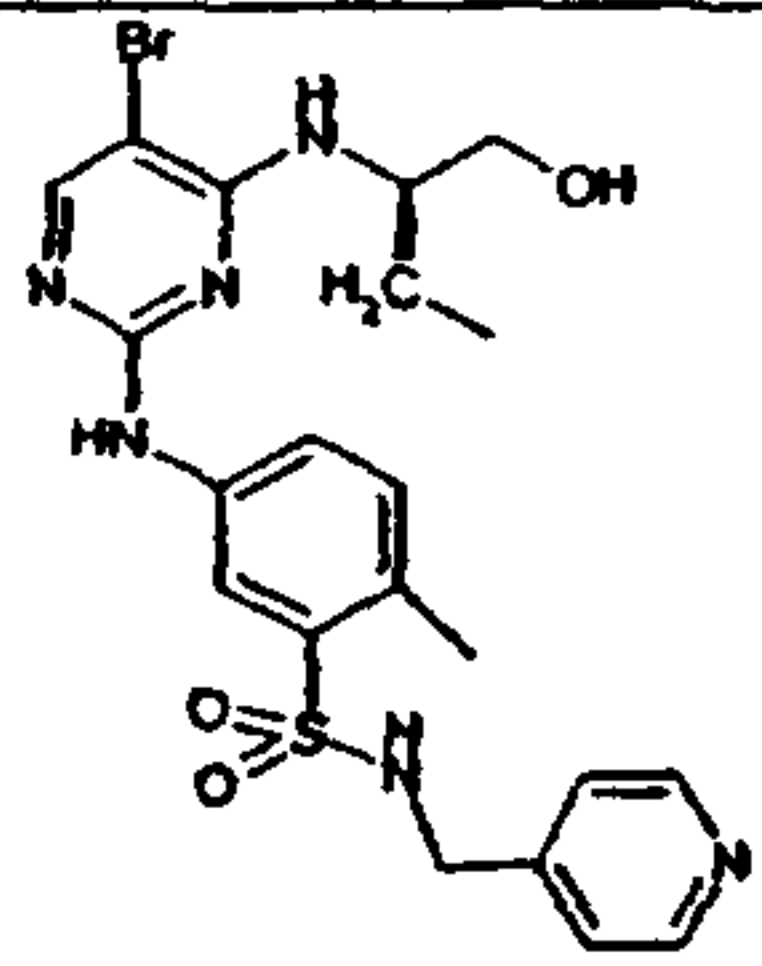
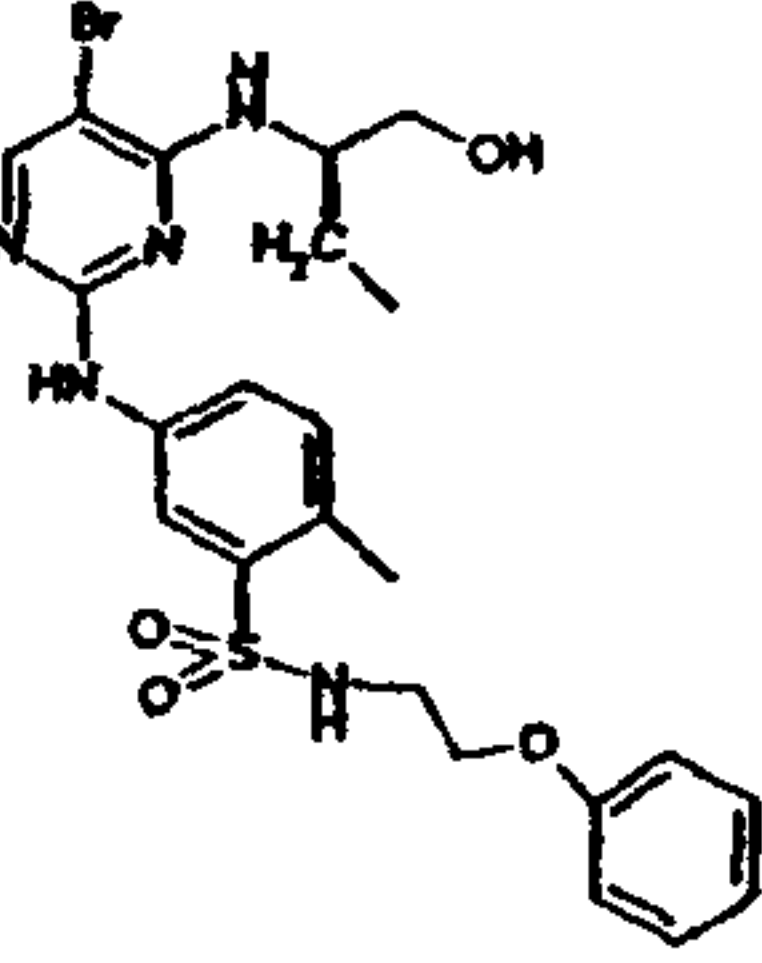
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
302		588,4465	588/590
303		528,5126	528/530
304		542,5394	542/544
305		556,5662	556/558
306		570,593	570/572

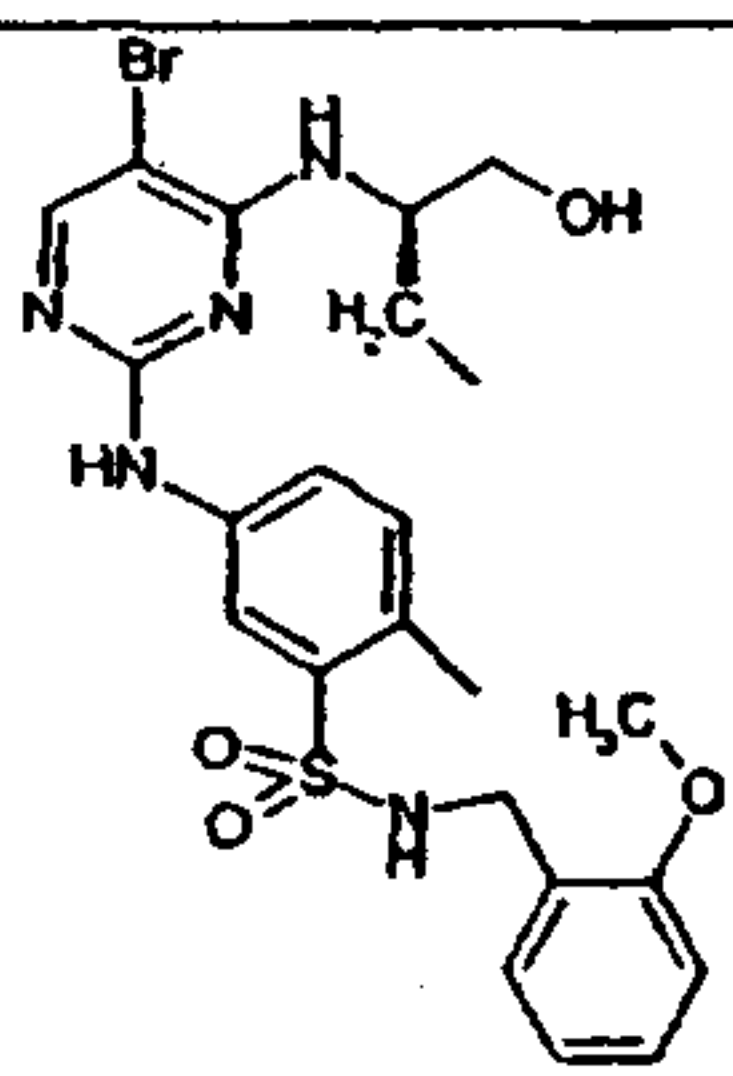
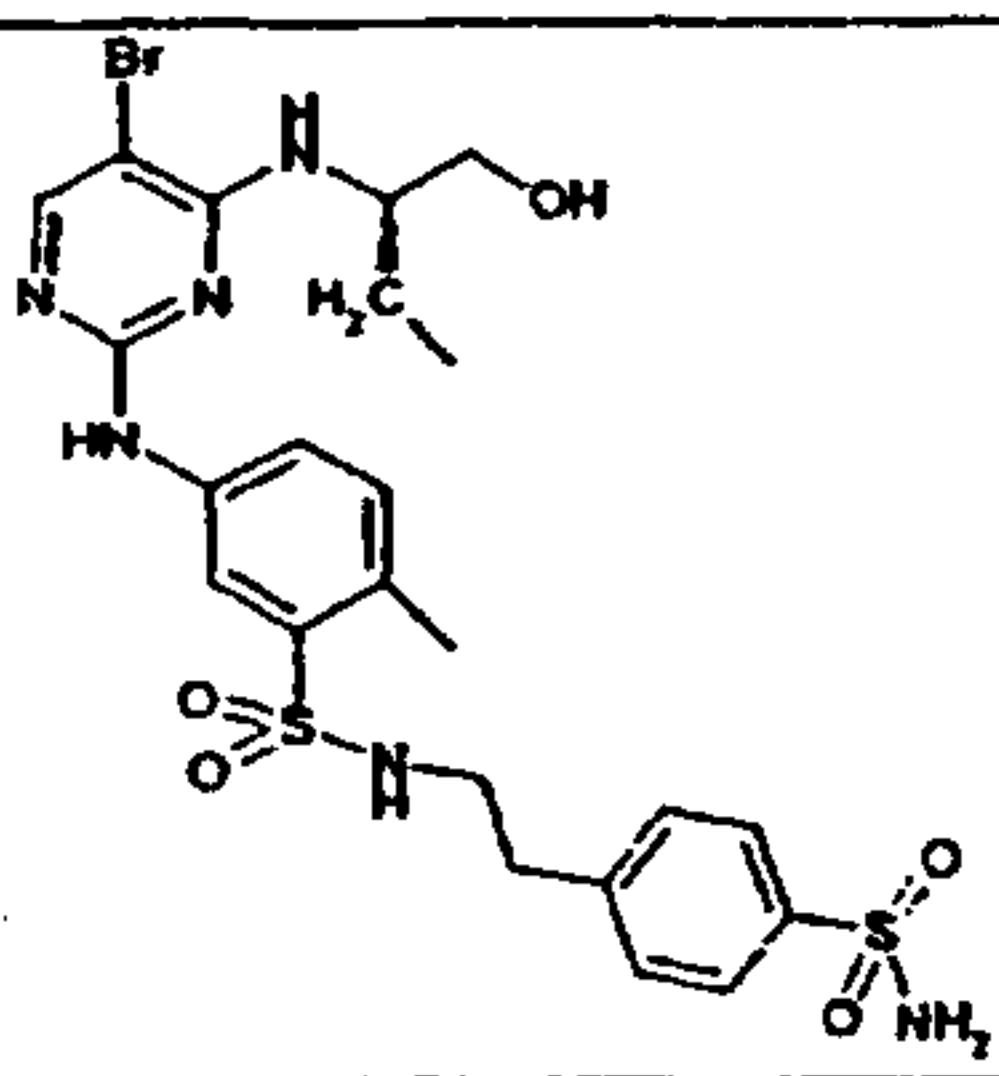
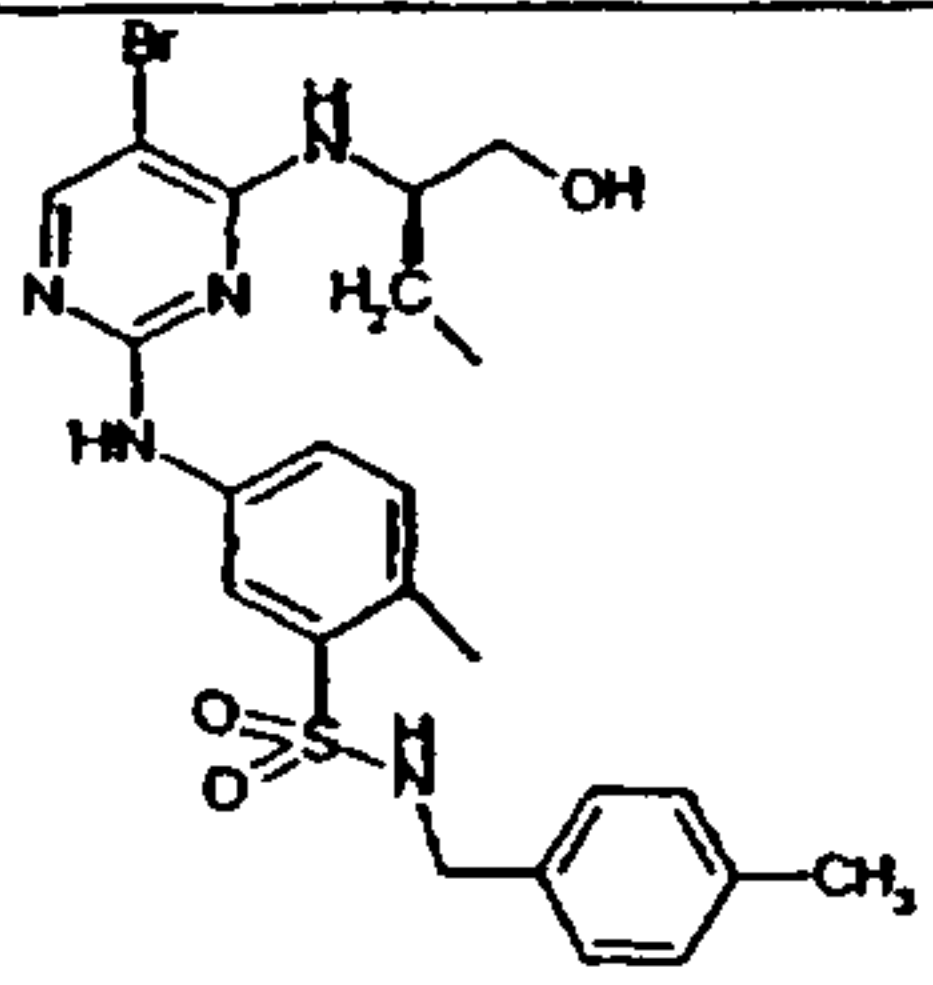
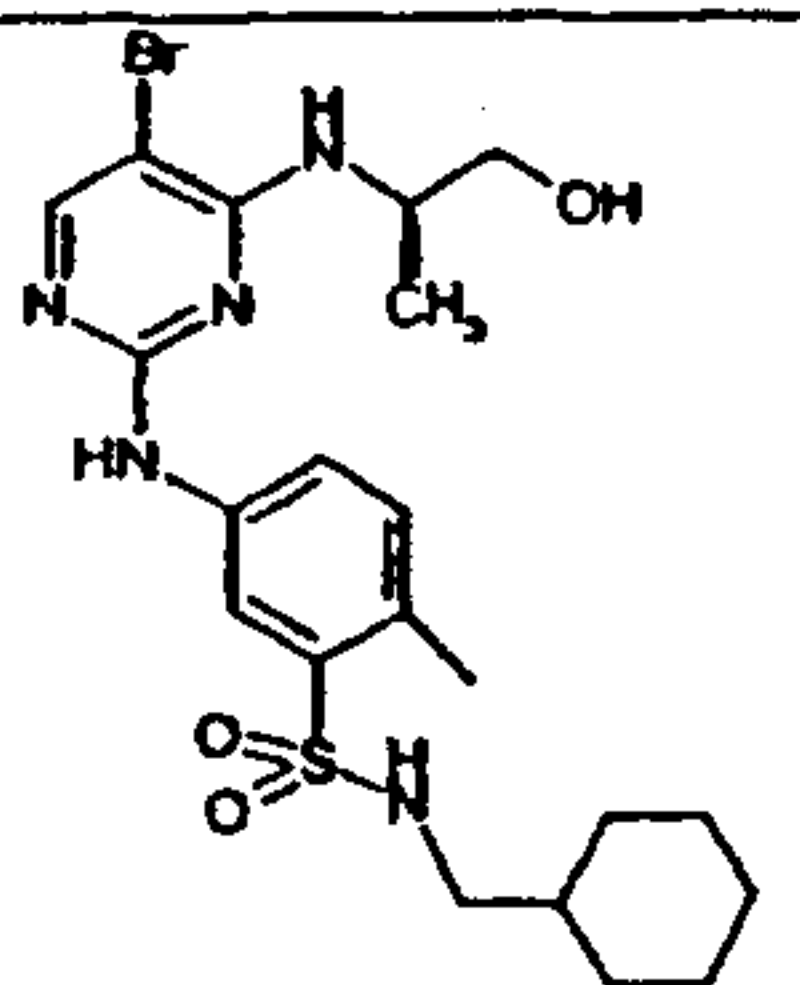
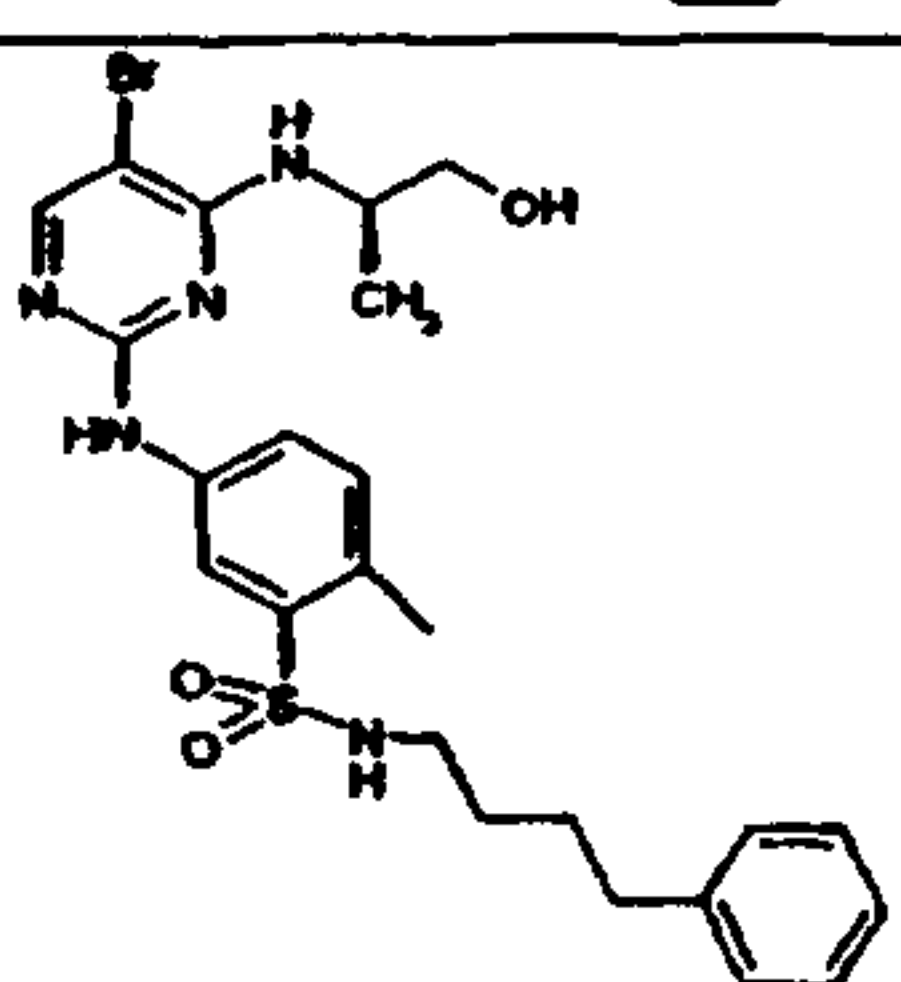
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
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308		588,4465	588/590
309		548,503	548/550
310		555,4949	555/557
311		500,459	500/502

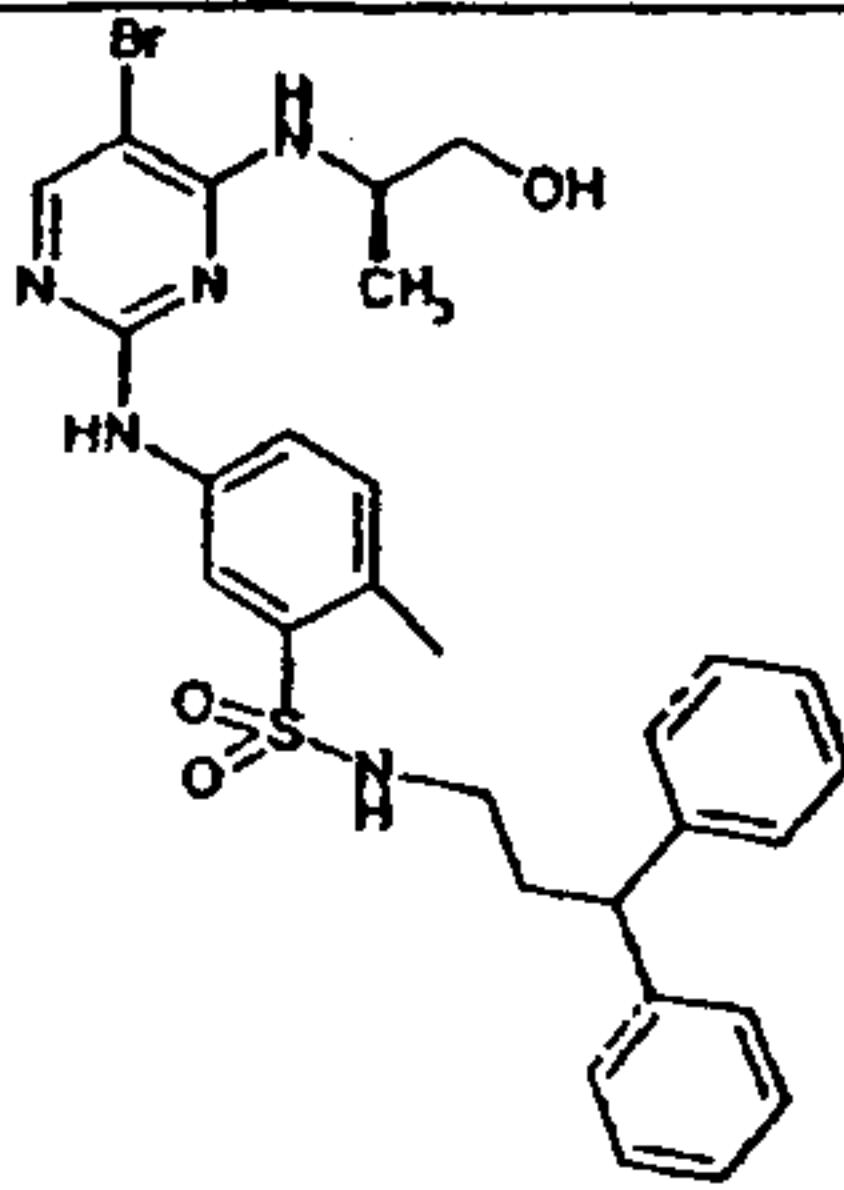
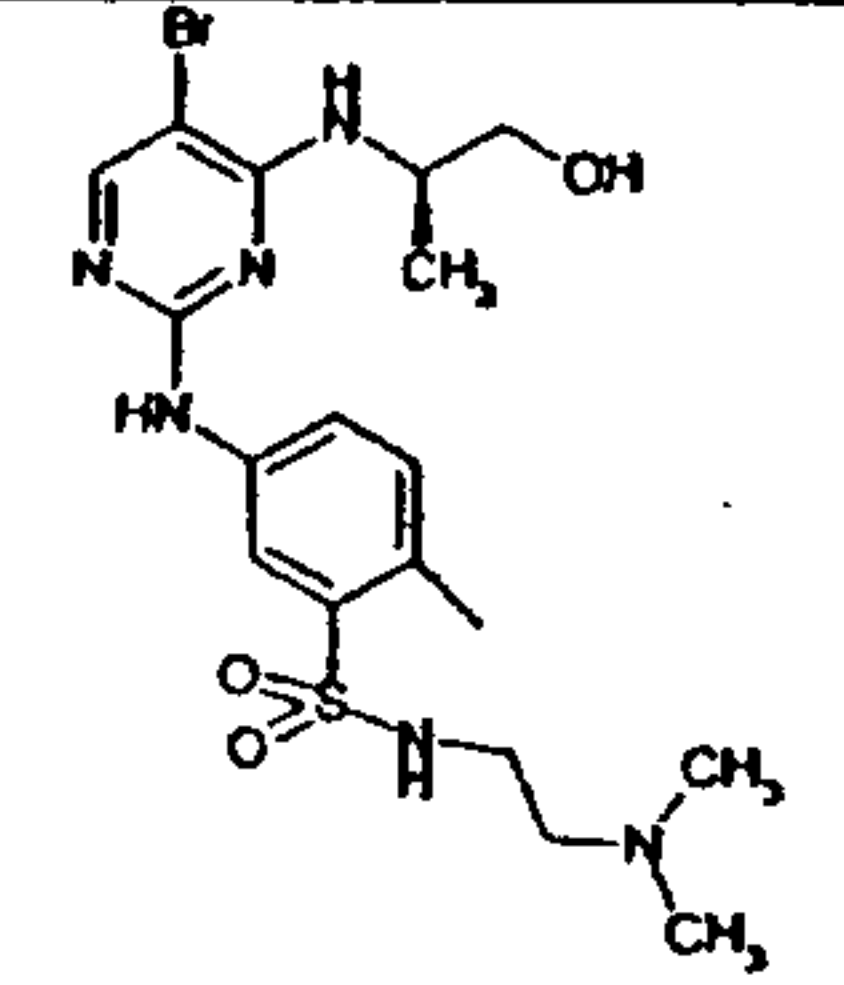
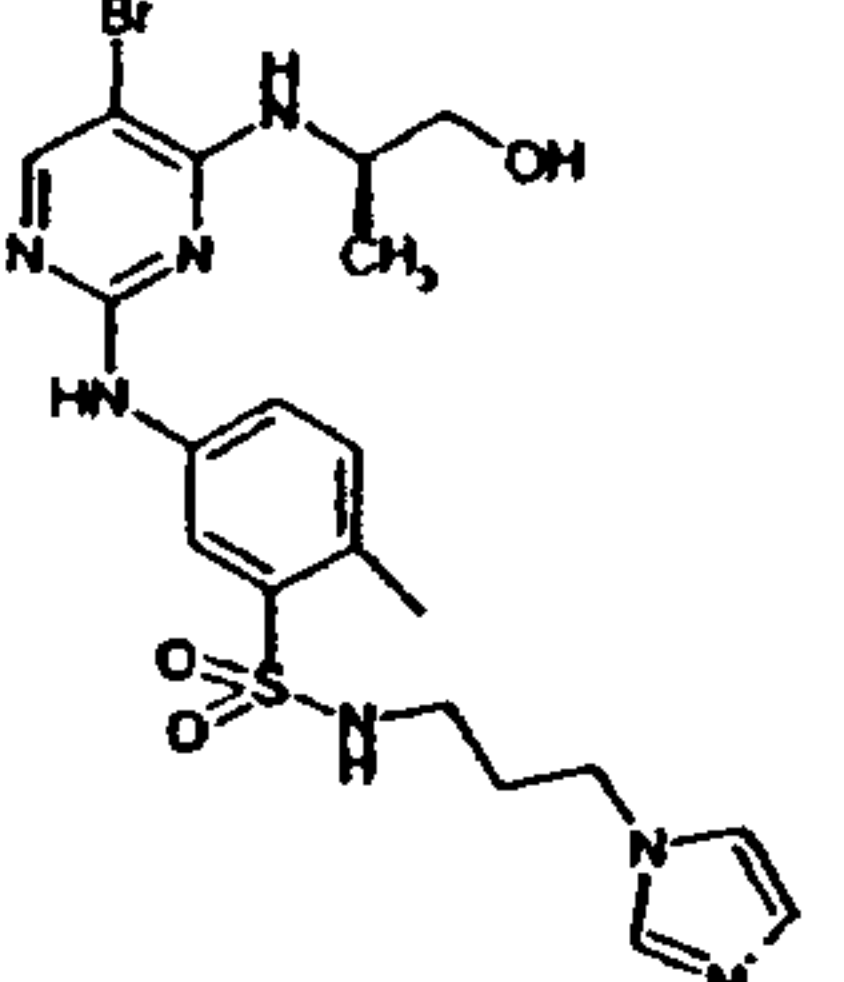
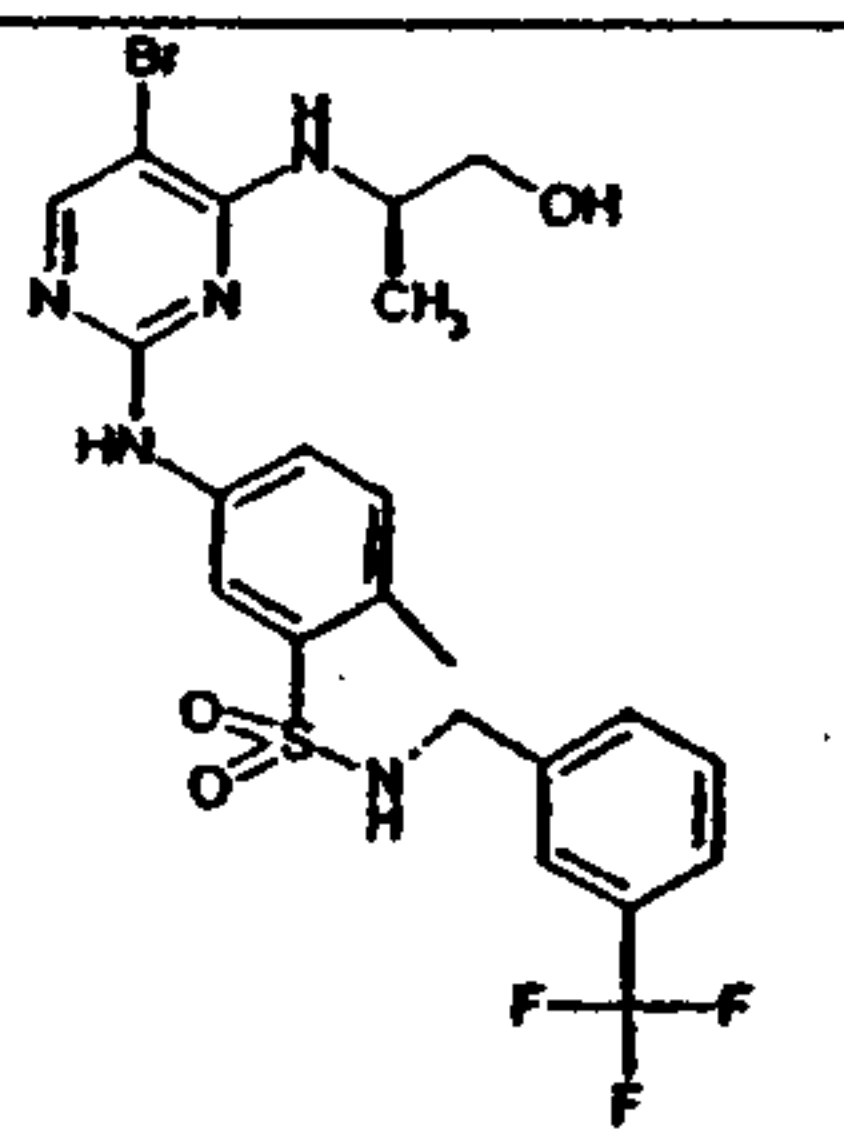
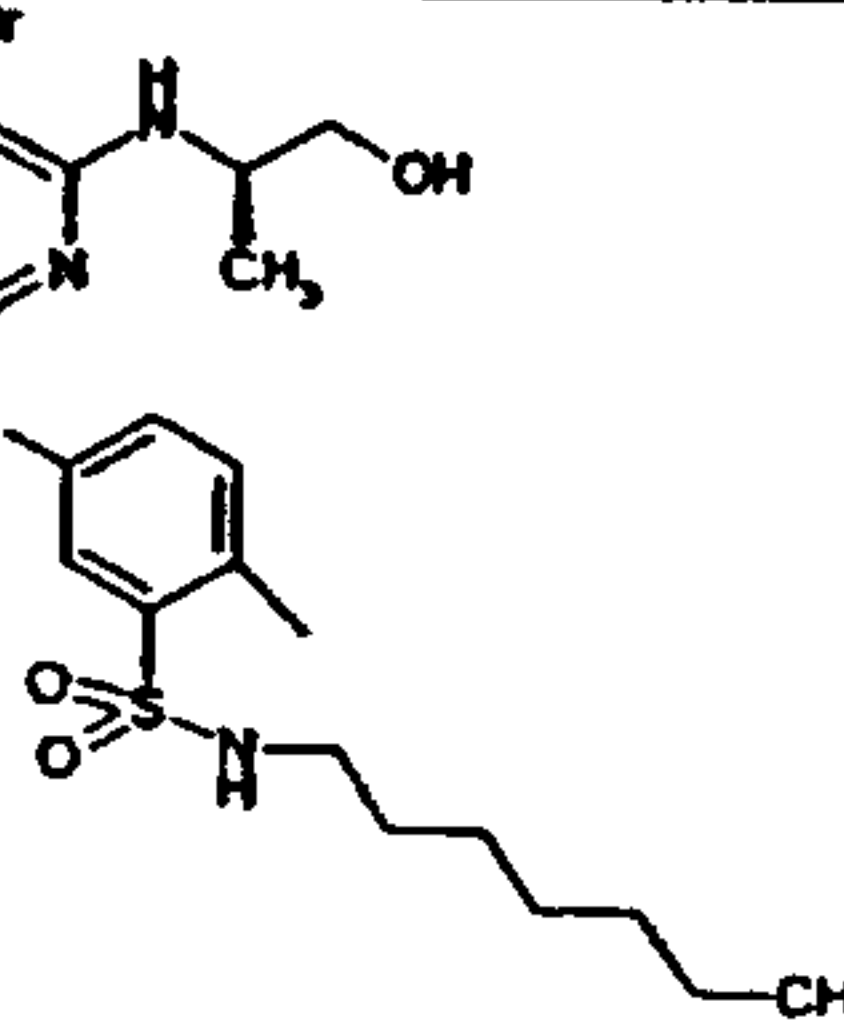
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
312		514,4858	514/516
313		515,4739	515/517
314		557,5543	557/559
315		470,3896	470/472
316		551,5069	551/553

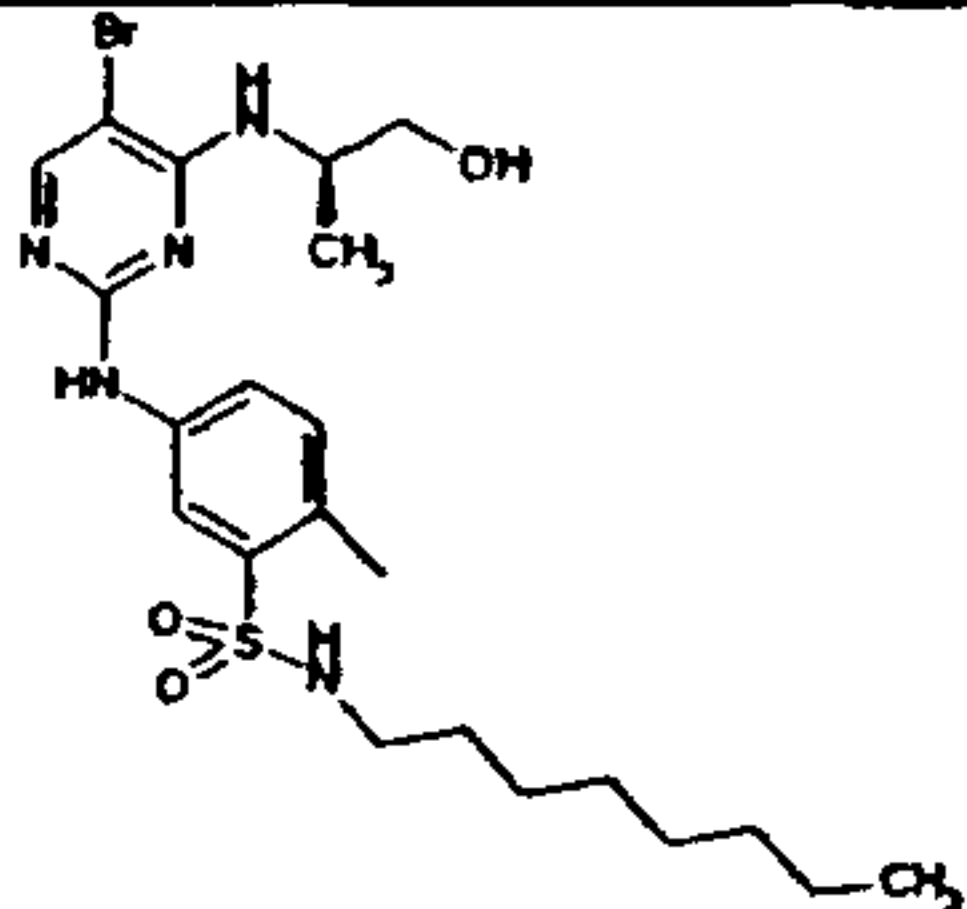
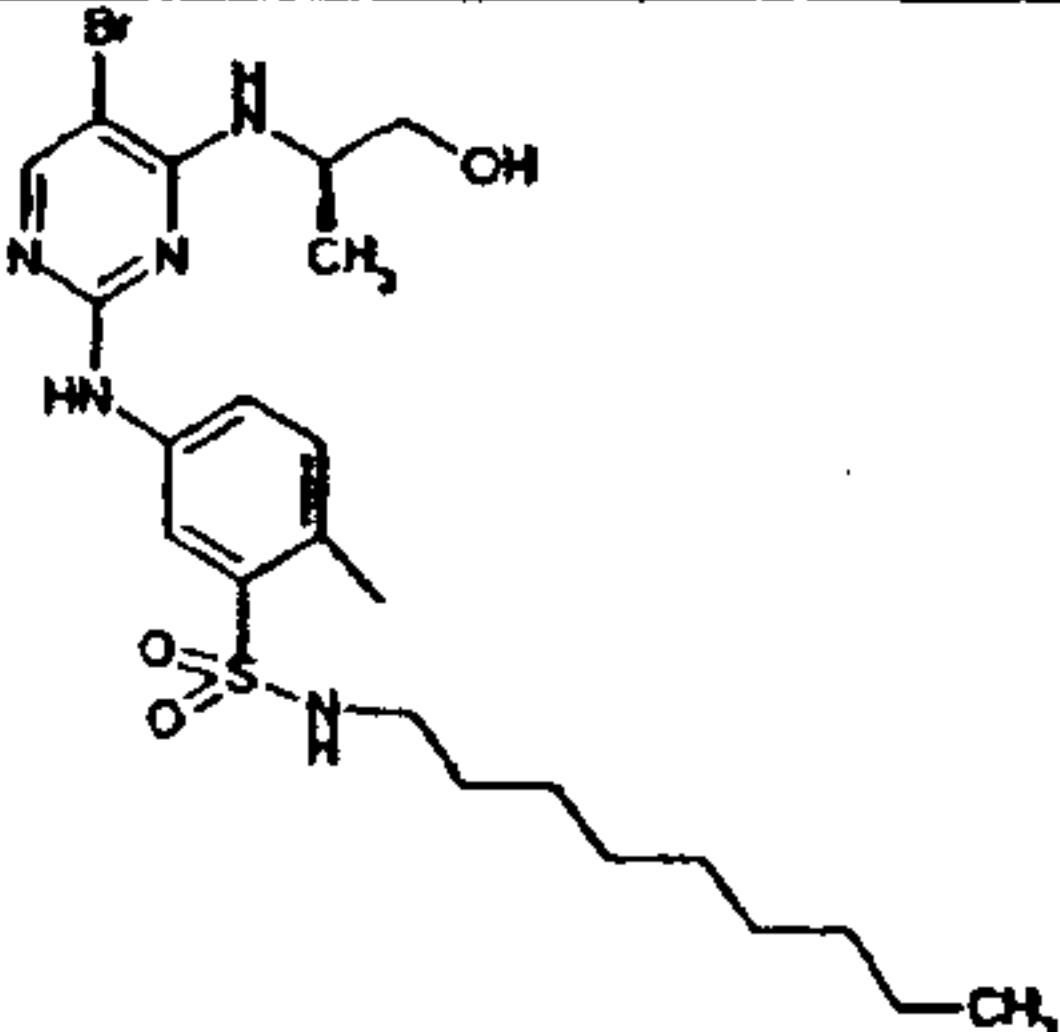
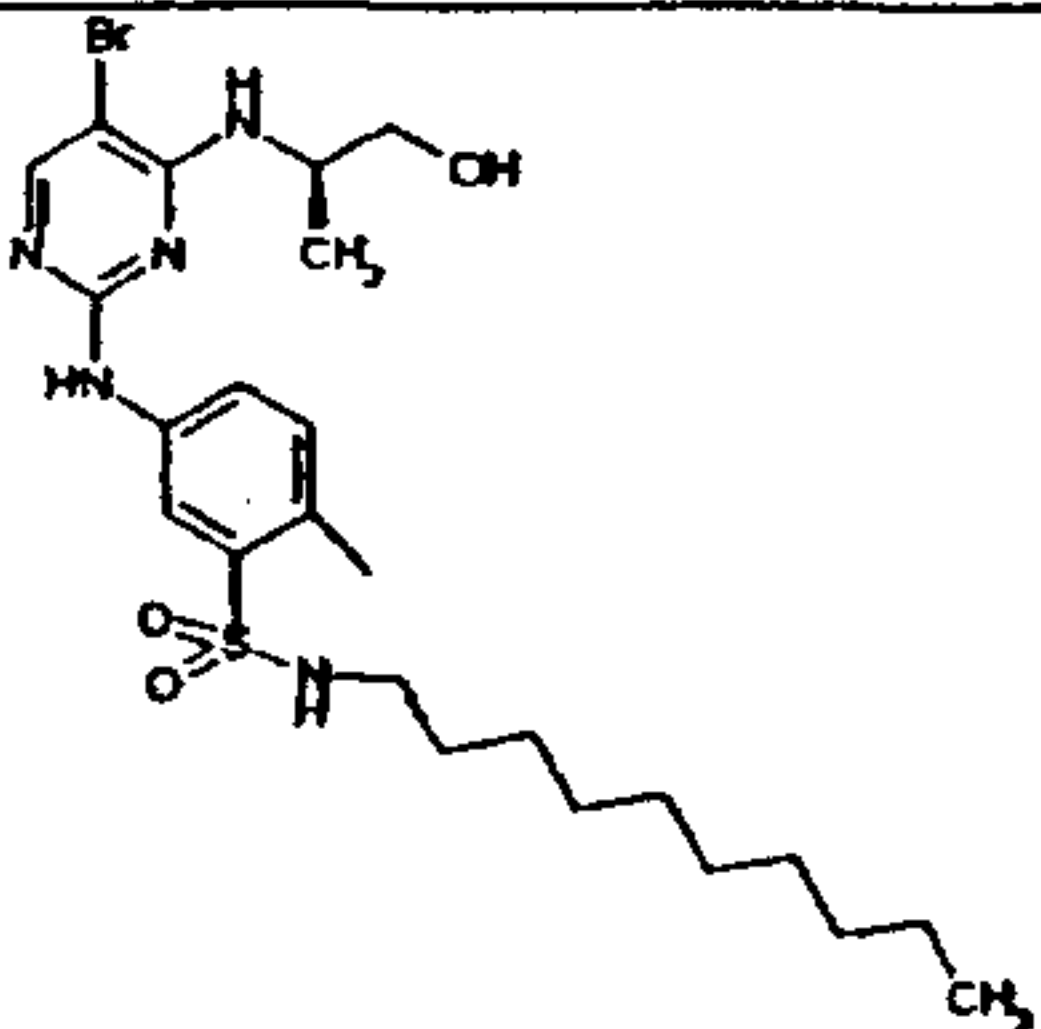
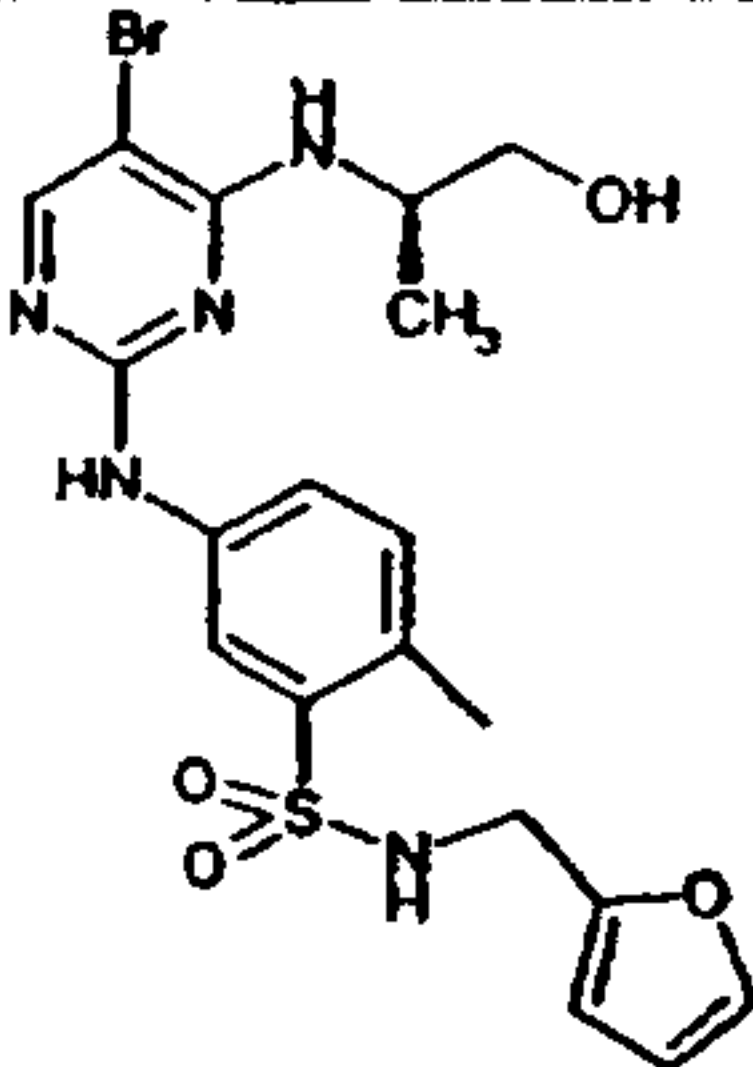
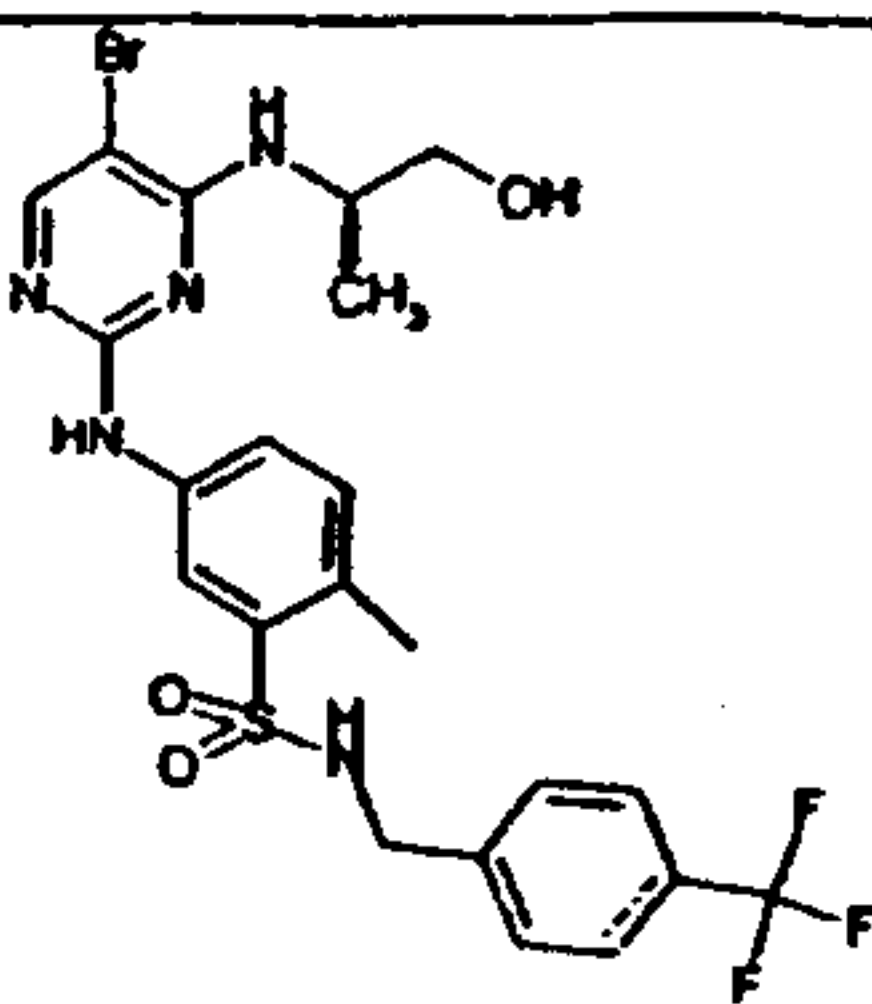
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
317		534,4762	534/536
318		568,9213	568/570
319		524,4374	524/526
320		543,4839	543/545
321		488,4044	488/490

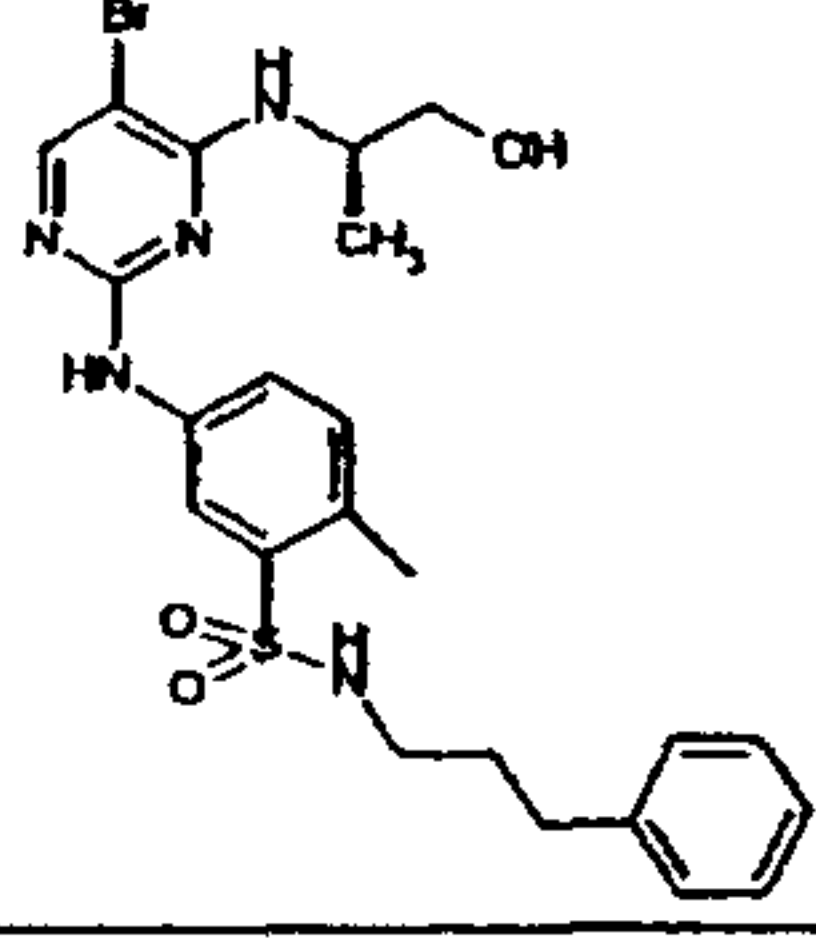
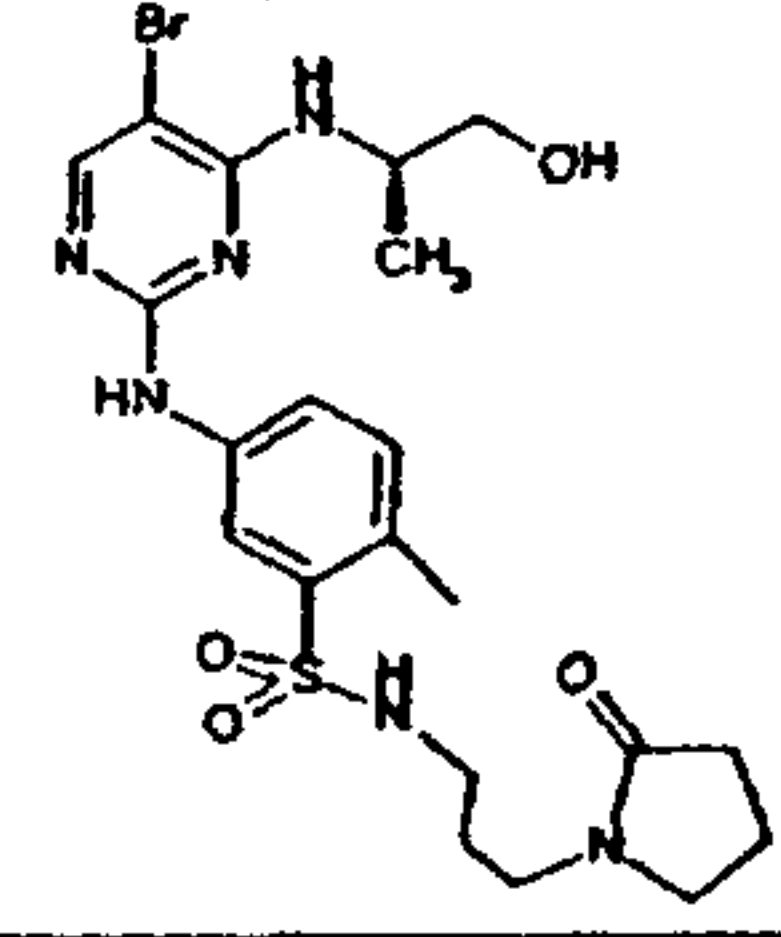
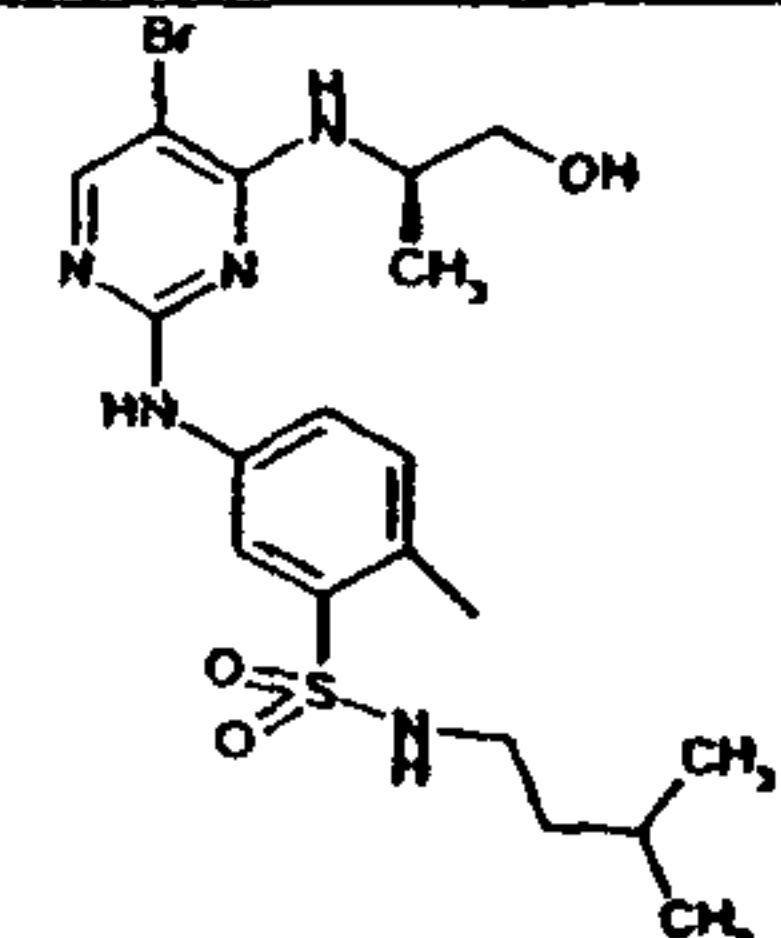
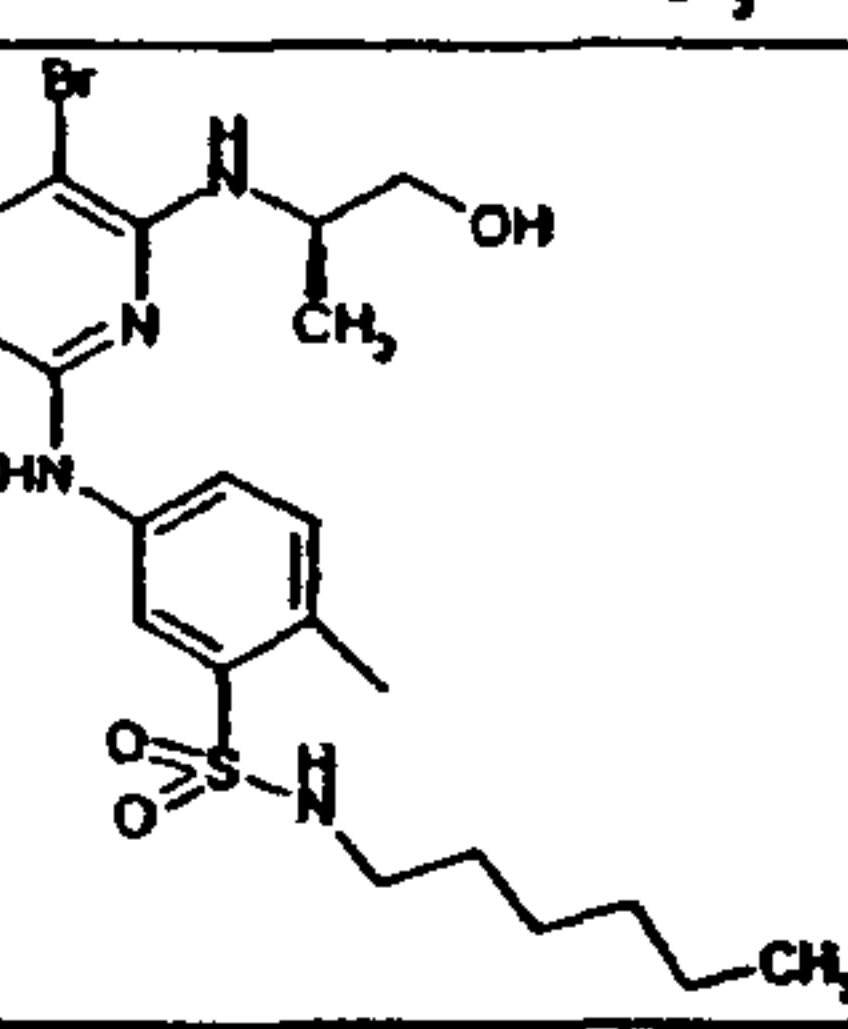
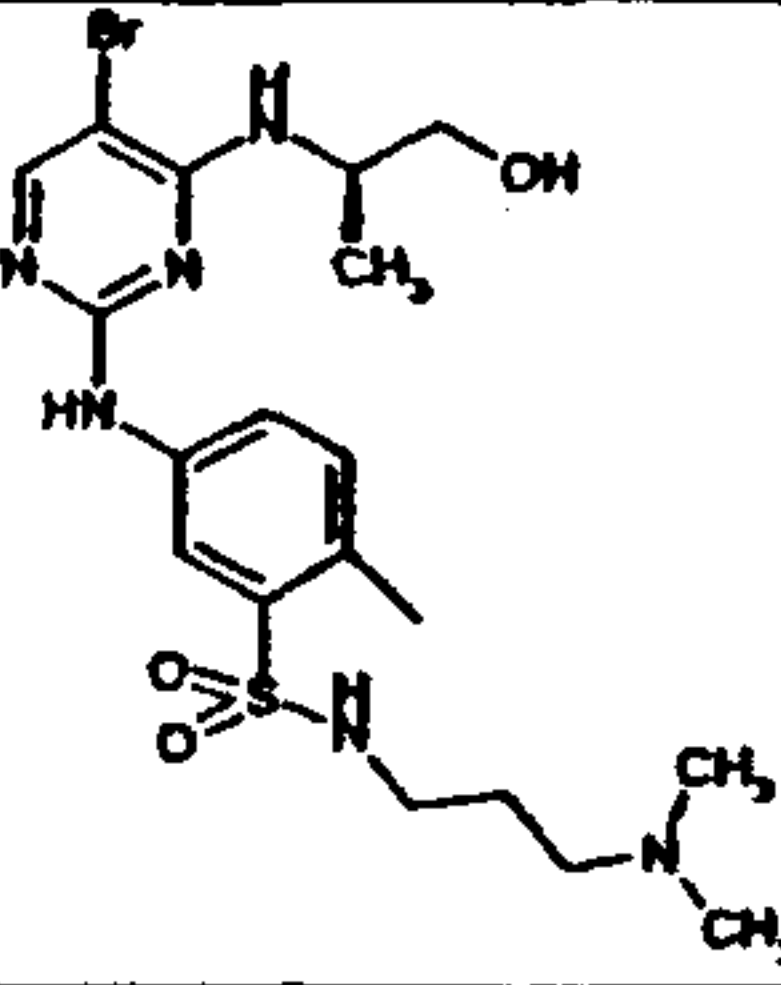
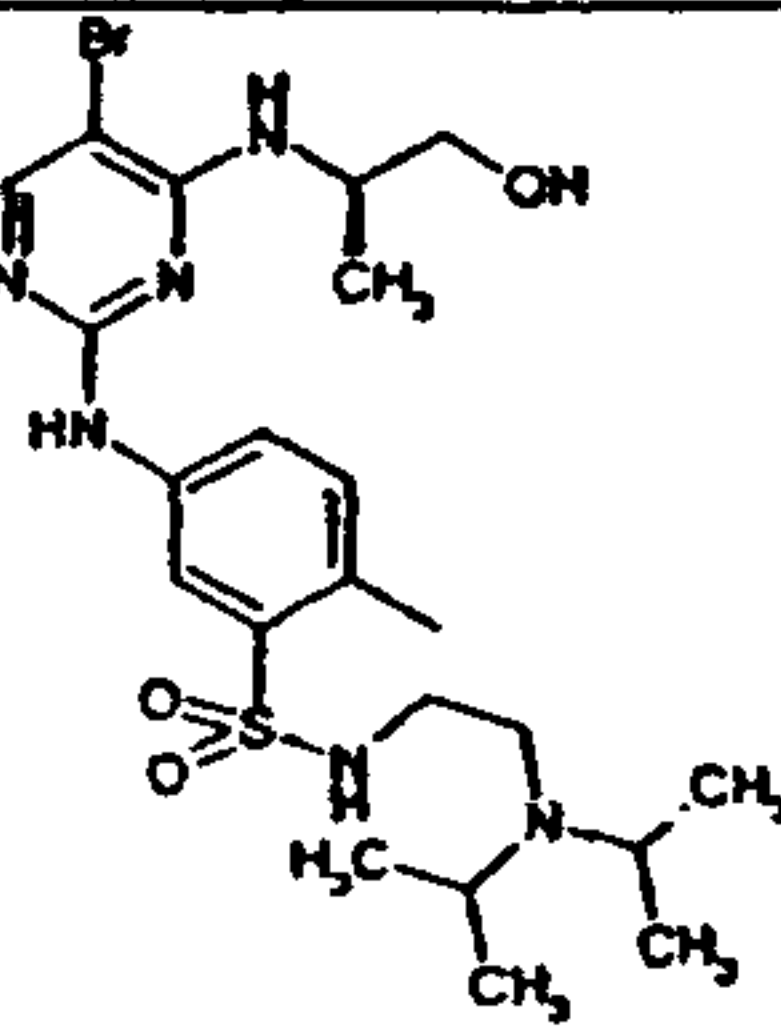
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
322		526,4776	526/528
323		564,502	564/566
324		527,4849	527/529
325		541,5117	541/543
326		538,4395	538/540

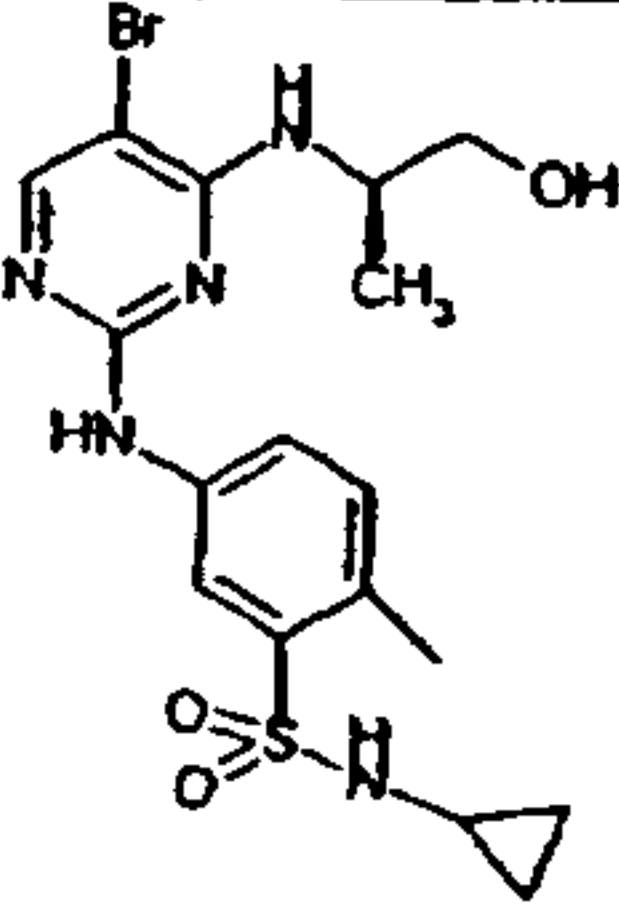
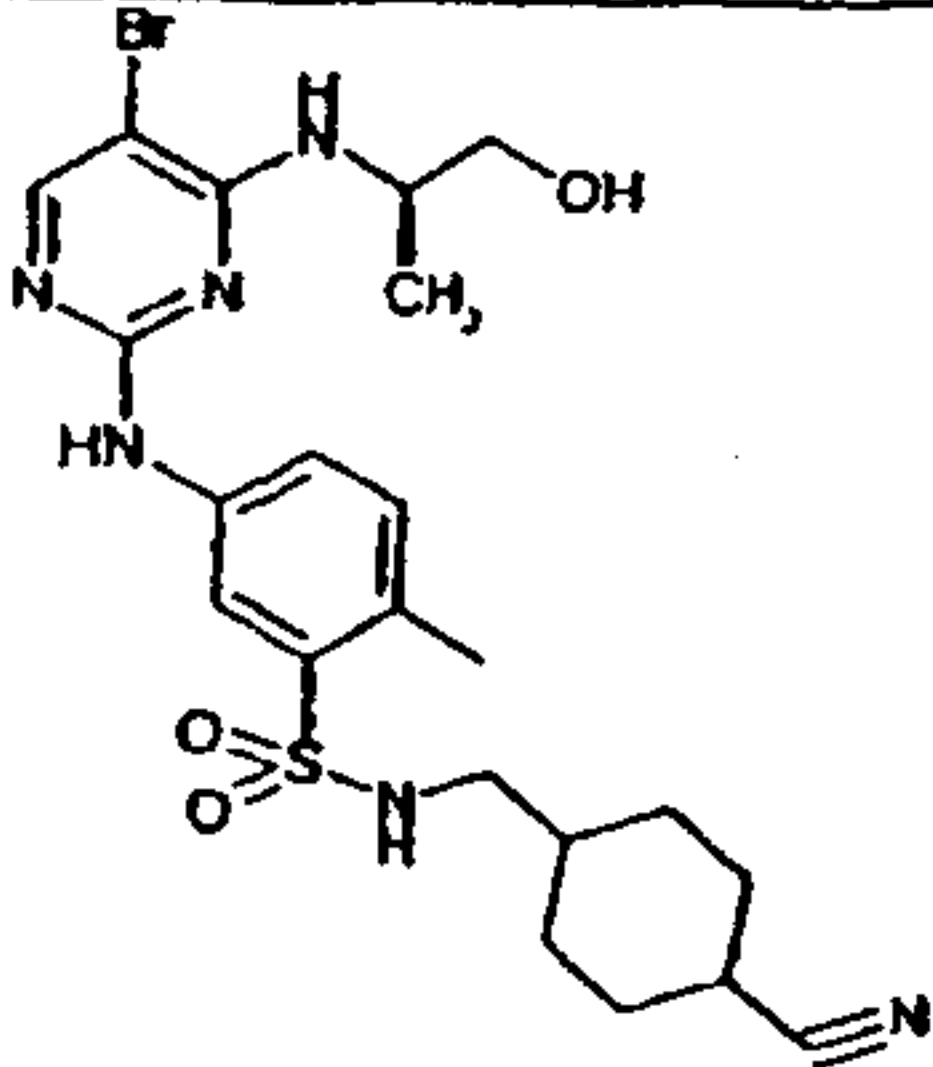
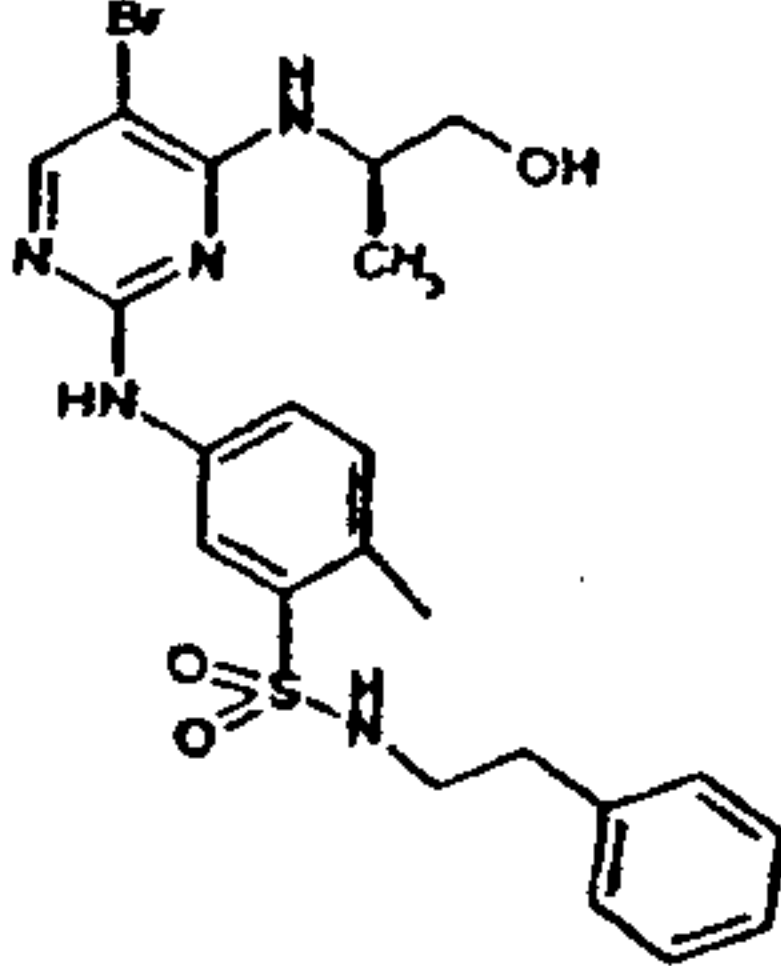
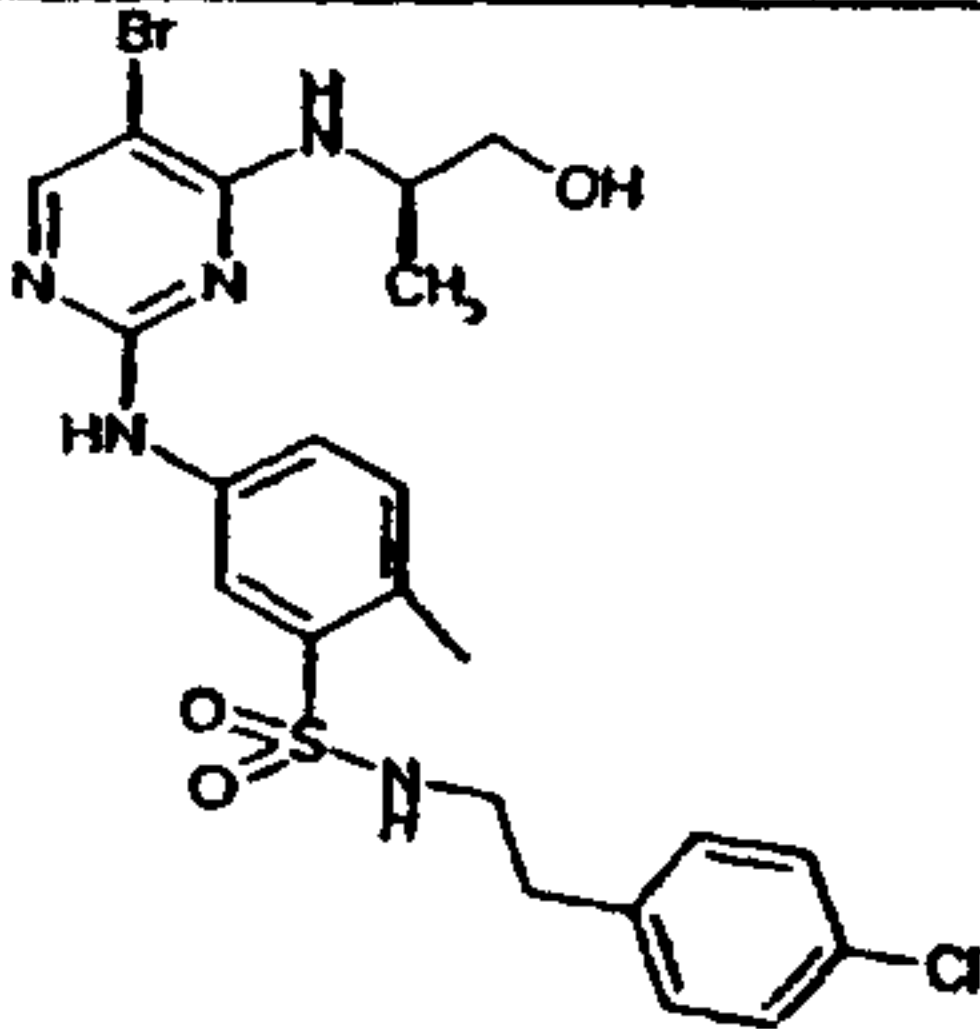
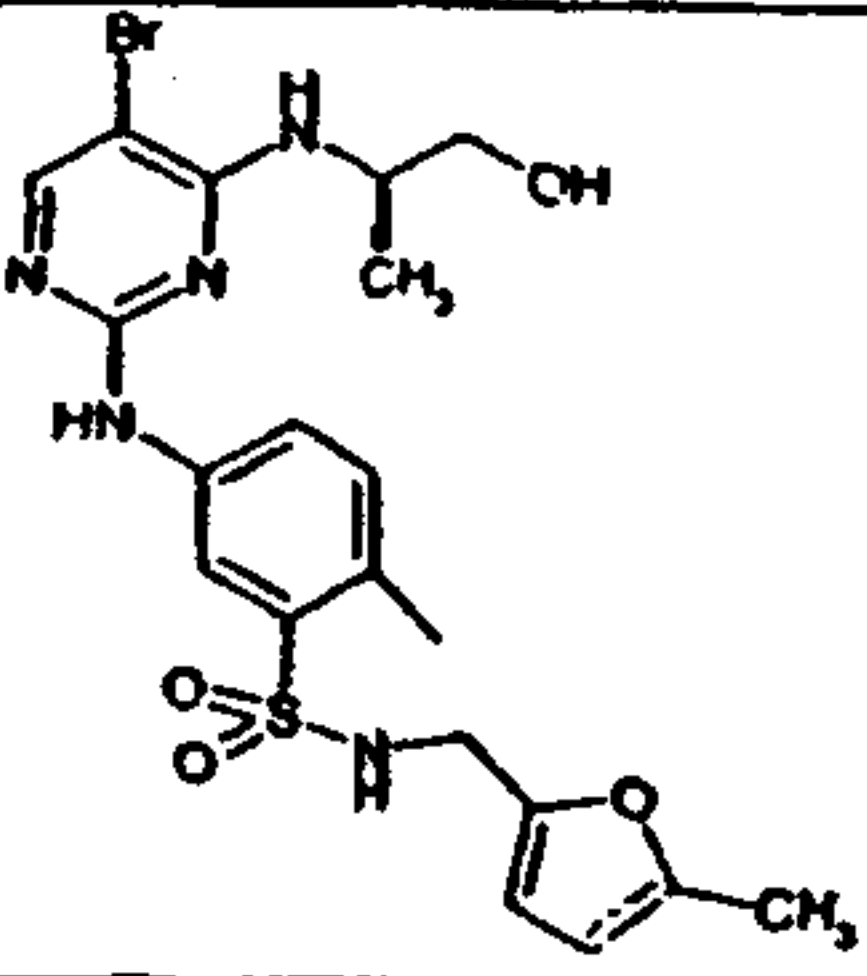
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
327		541,5117	541/543
328		521,4375	521/523
329		538,4395	538/540
330		521,4375	521/523
331		550,4752	550/552

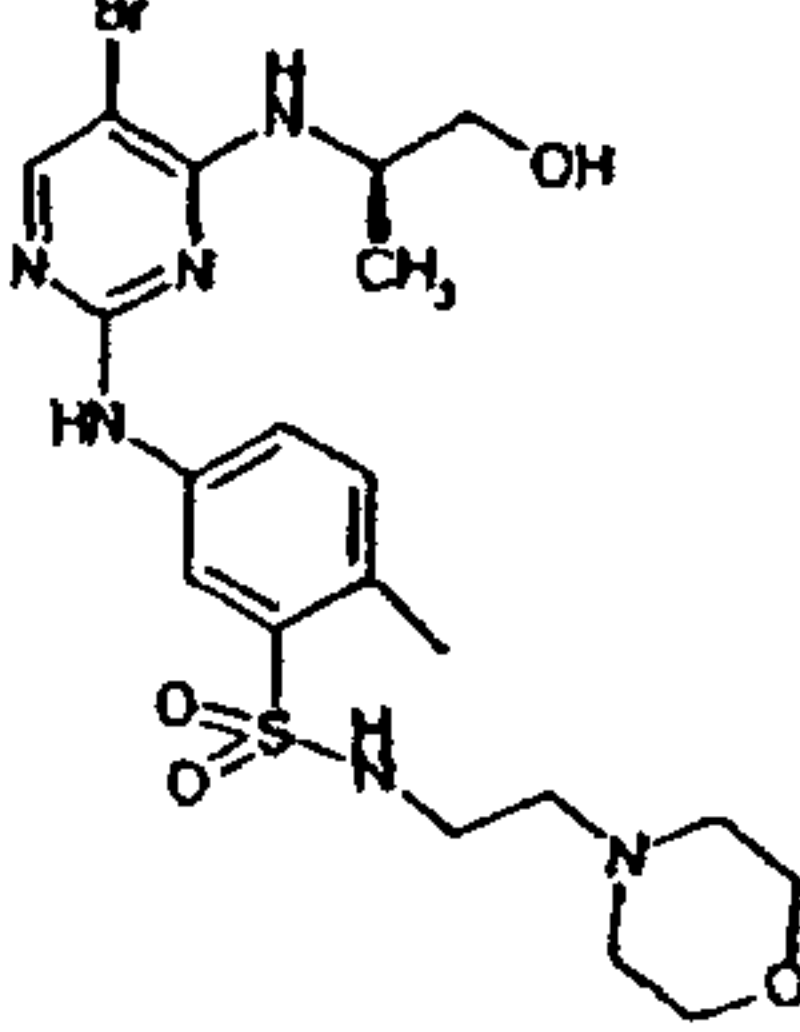
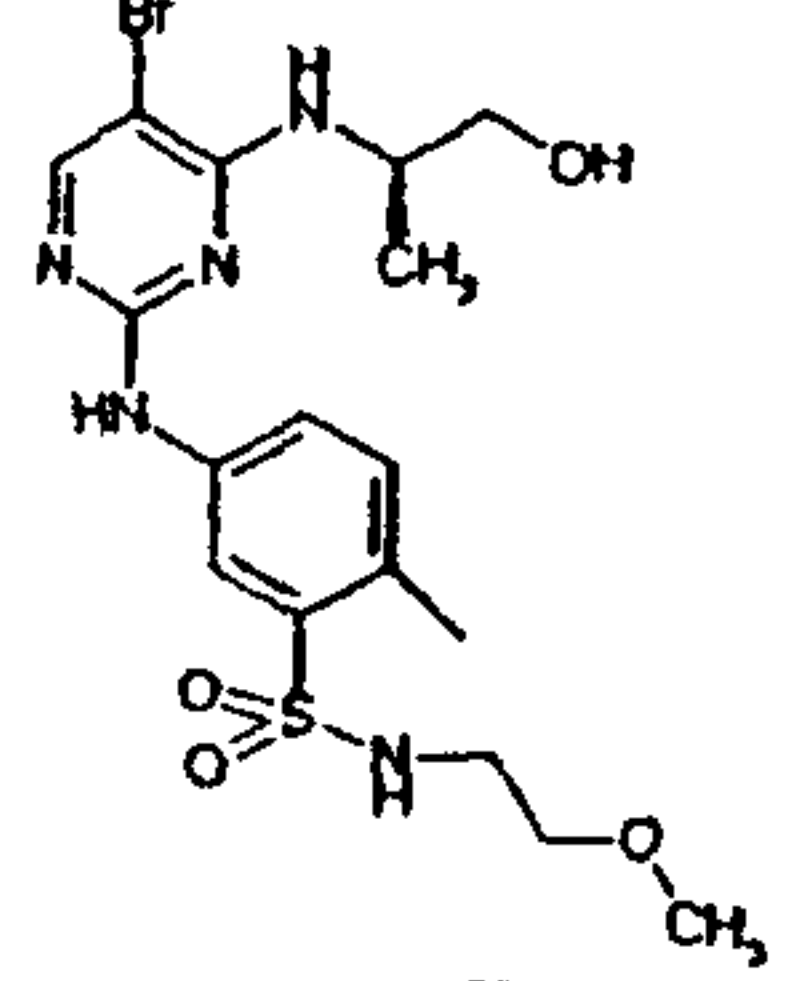
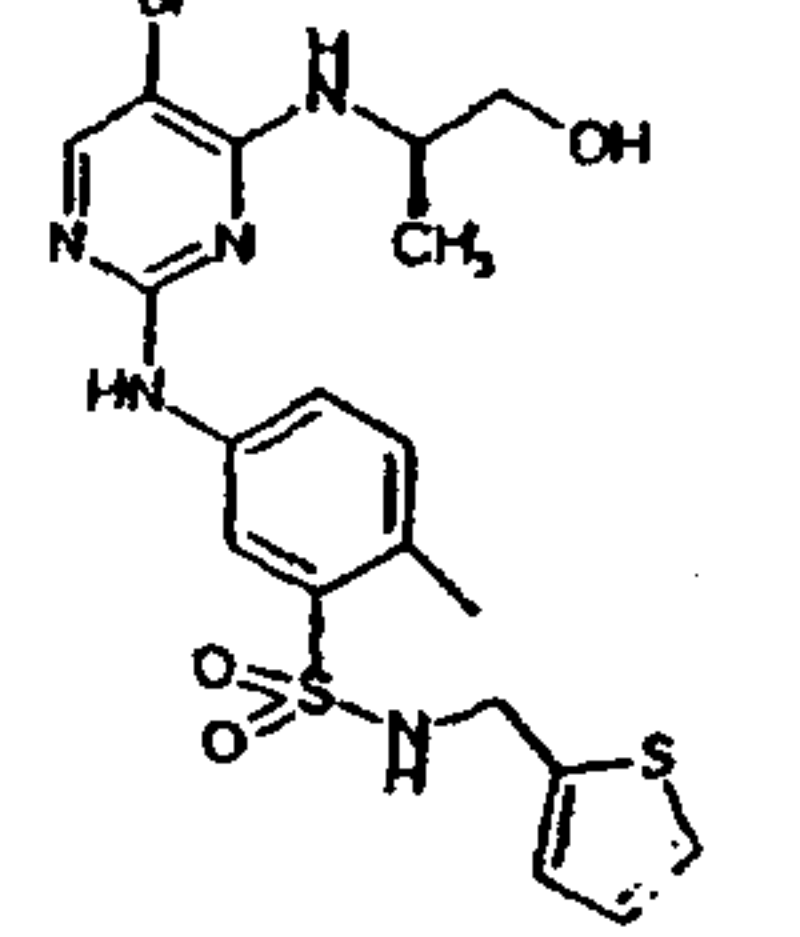
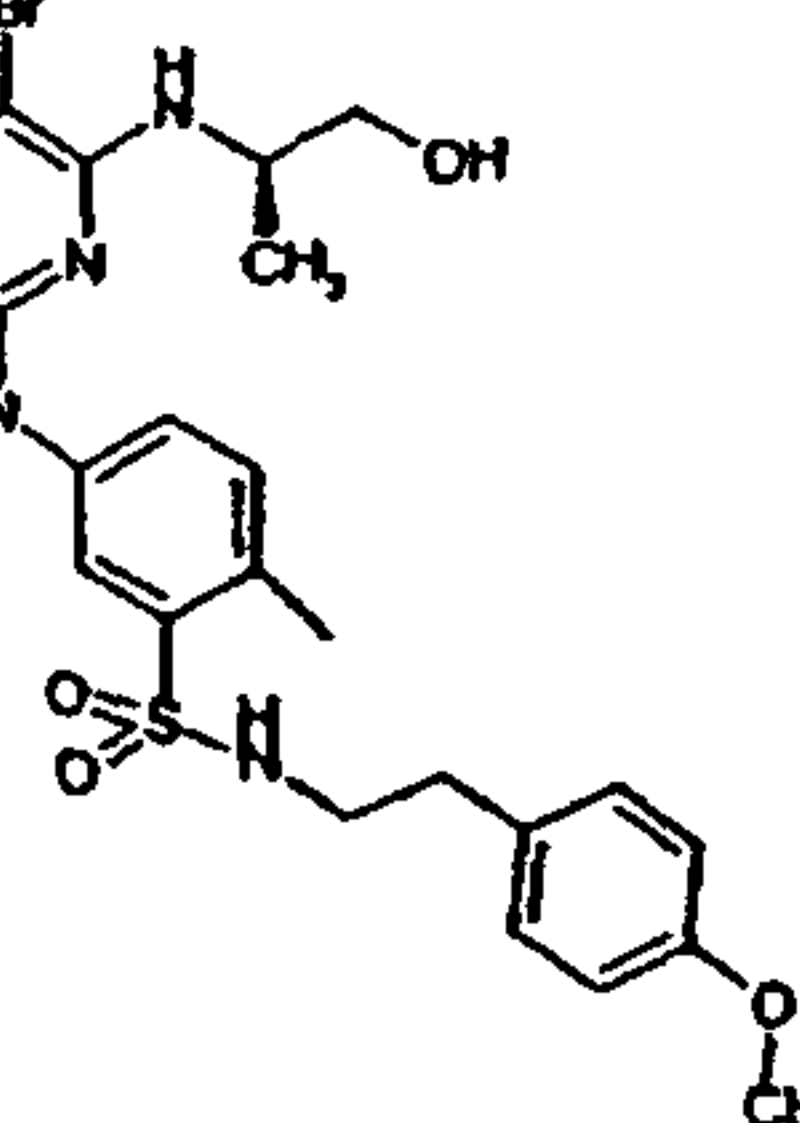
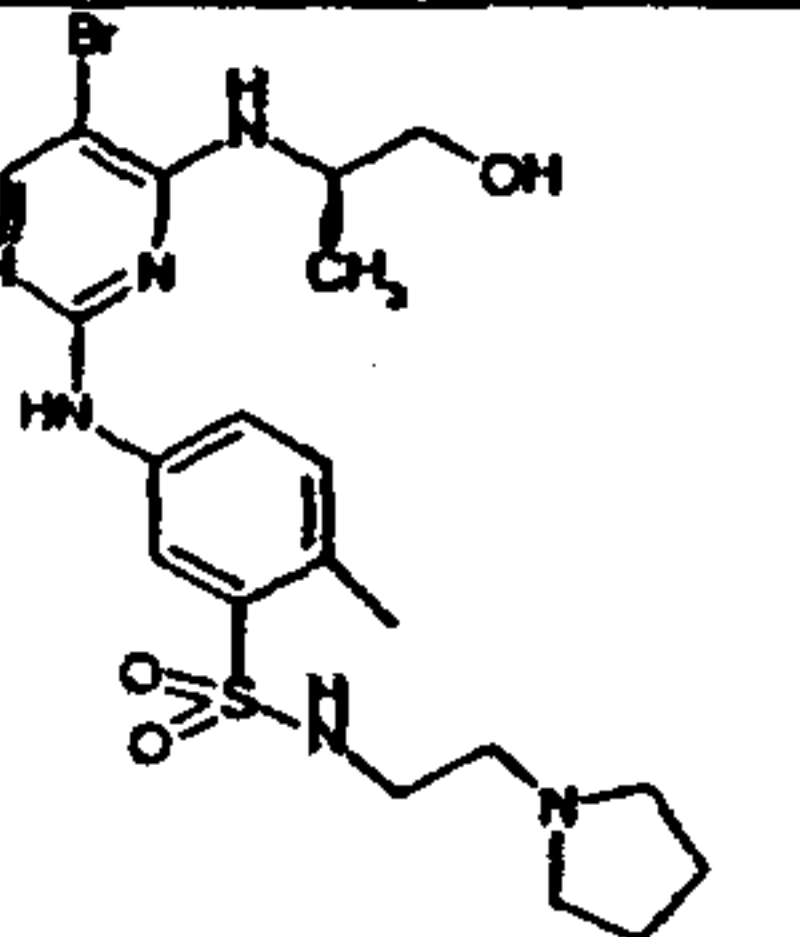
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
332		550,4752	550/552
333		613,5551	613/615
334		534,4762	534/536
335		512,47	512/514
336		548,503	548/550

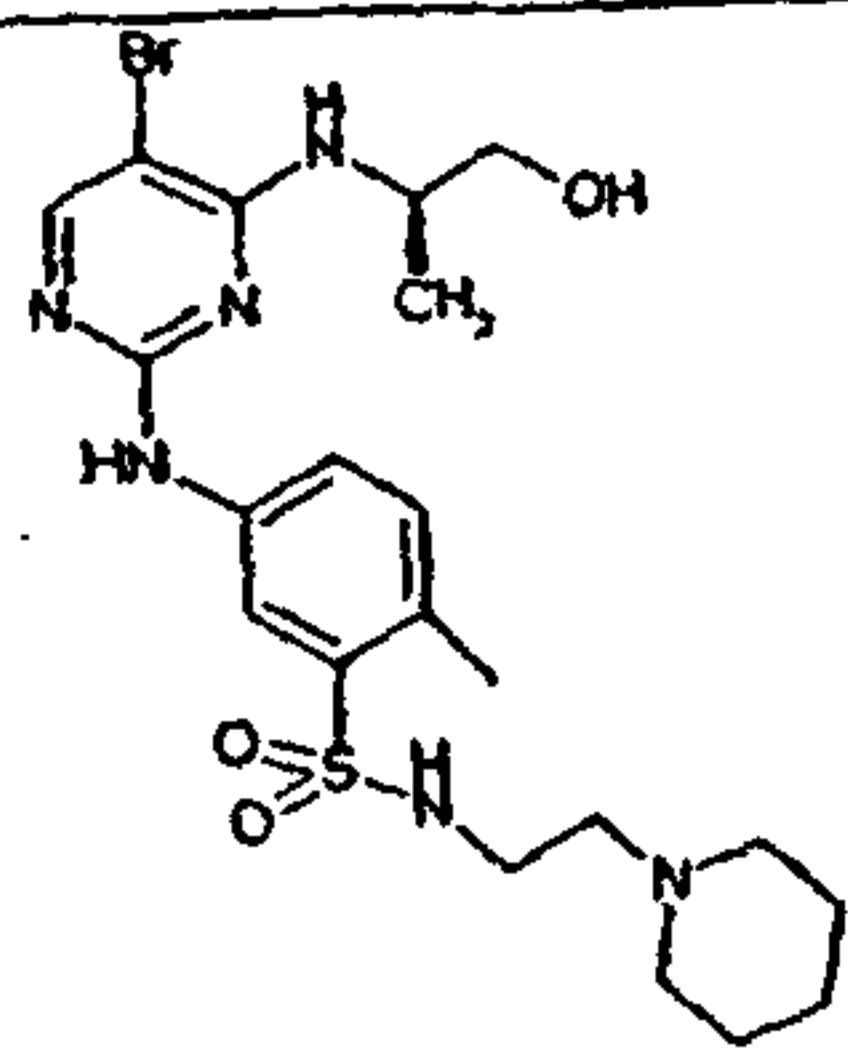
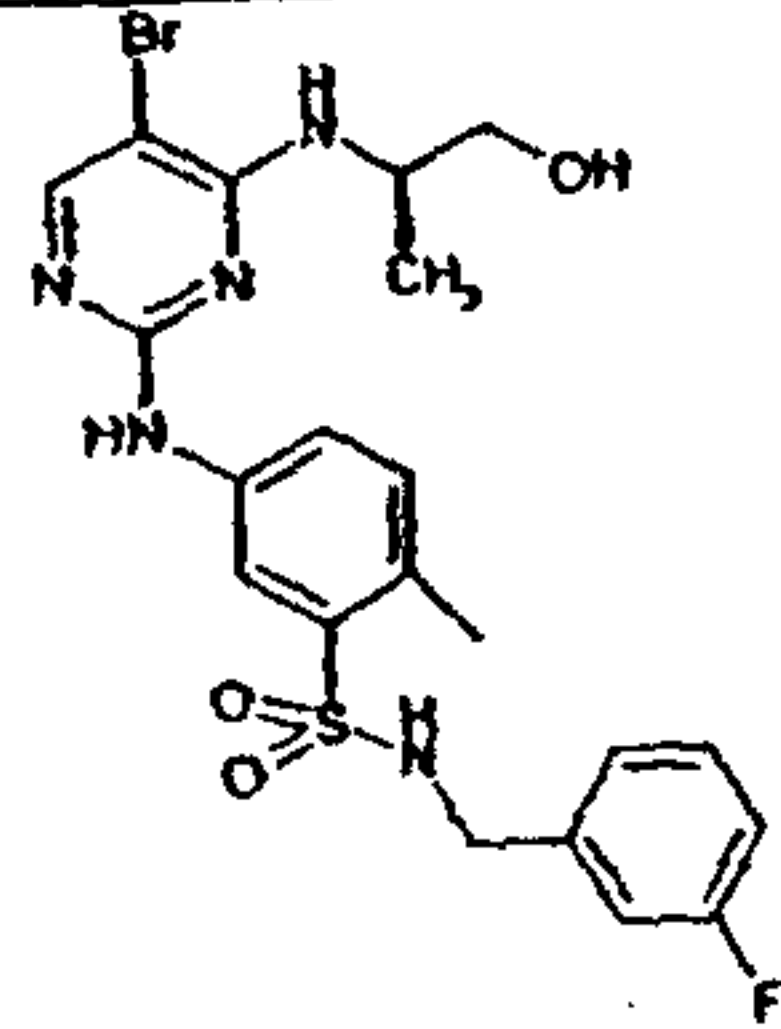
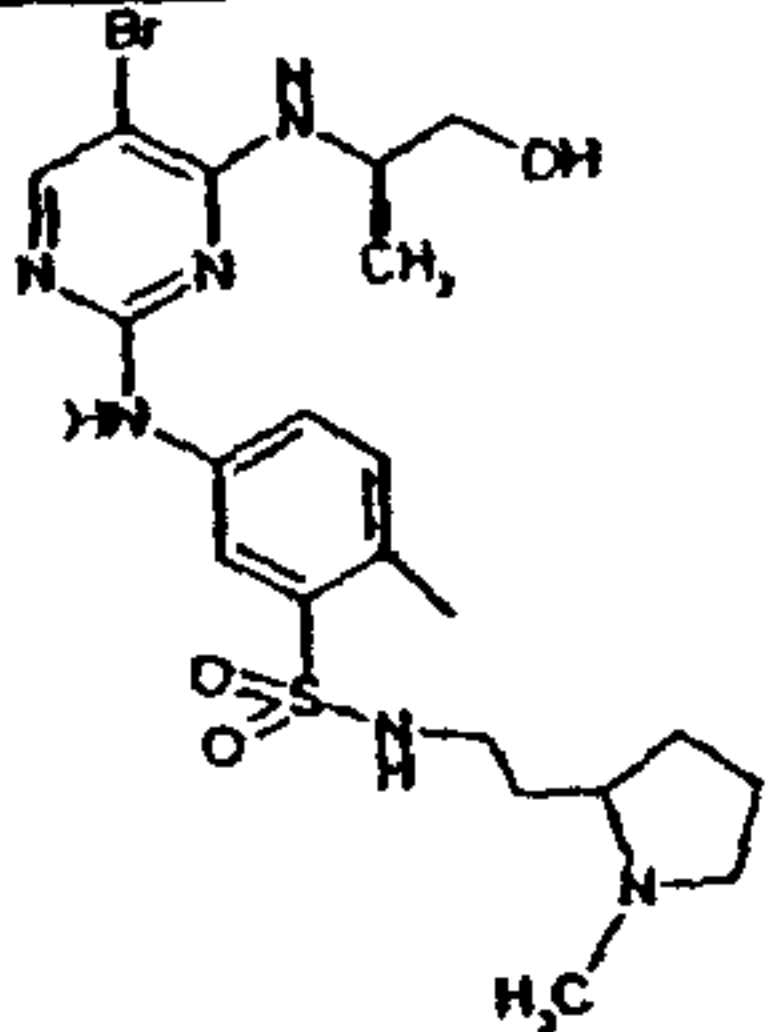
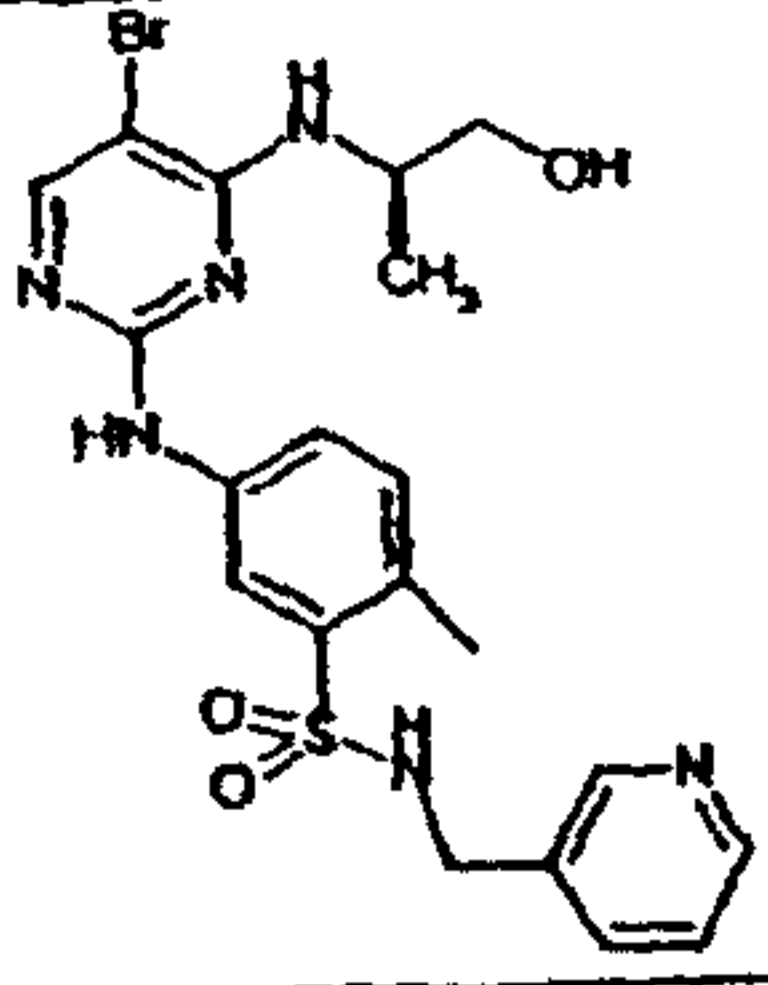
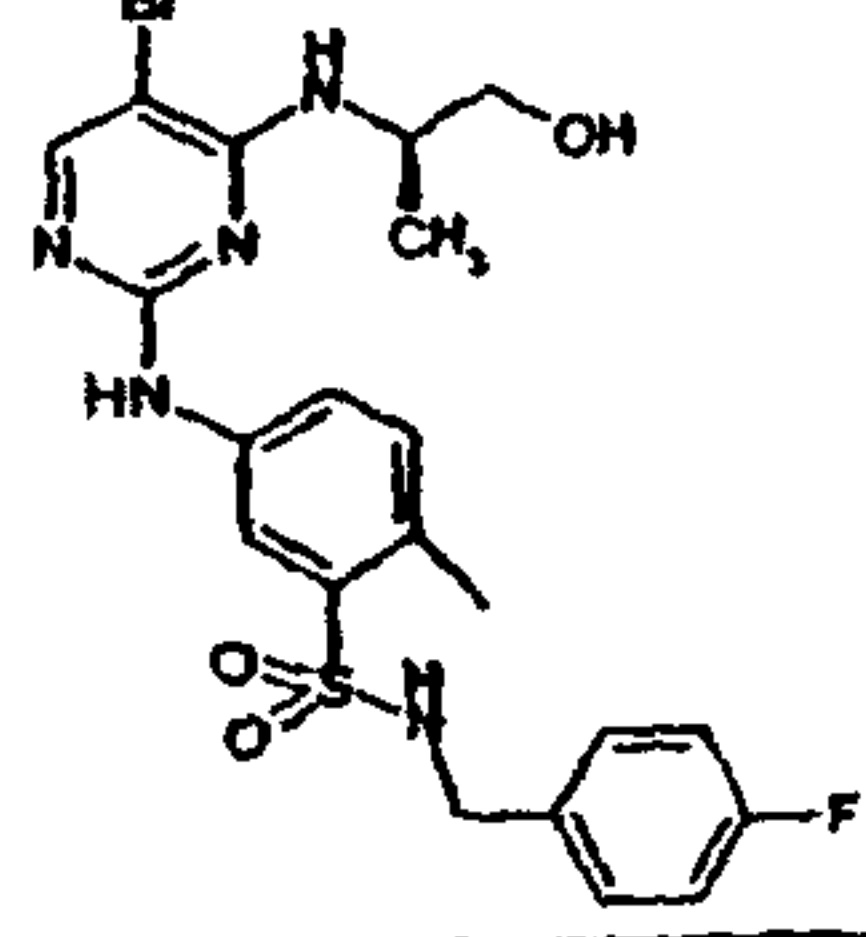
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
337		610,5738	610/612
338		487,4203	487/489
339		524,4414	524/526
340		574,4197	574/576
341		514,4858	516/514

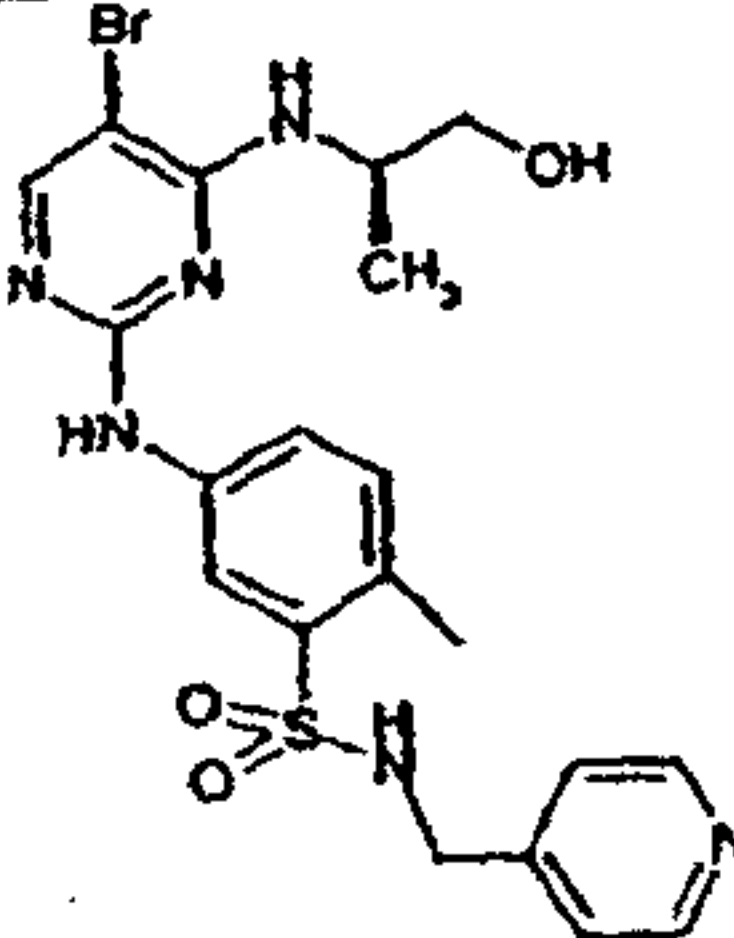
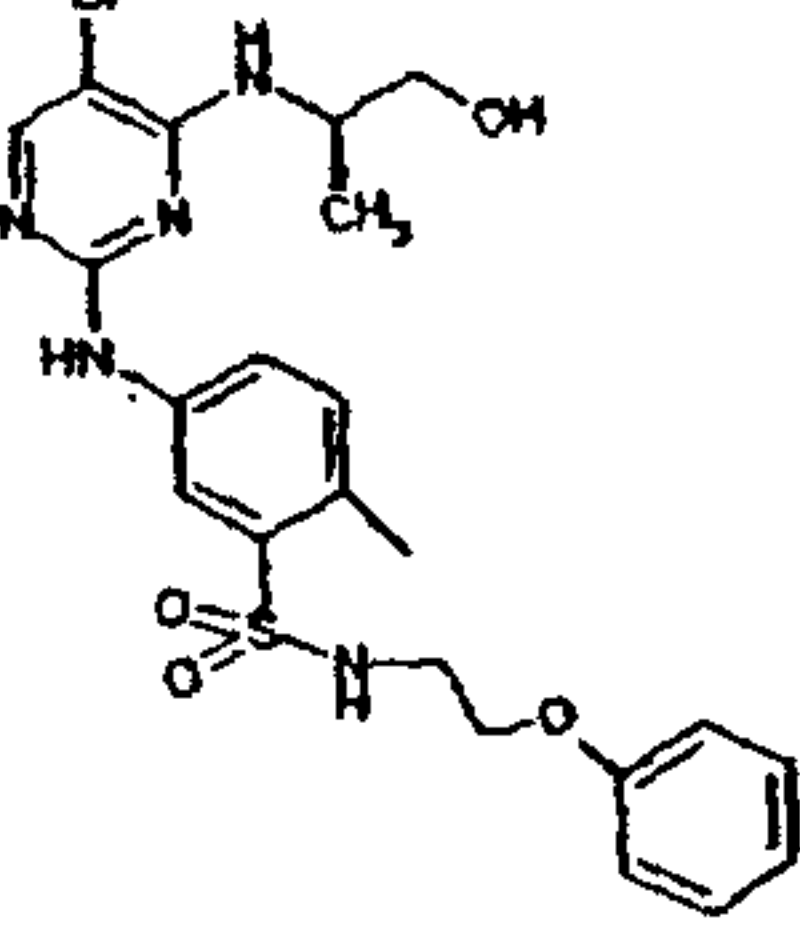
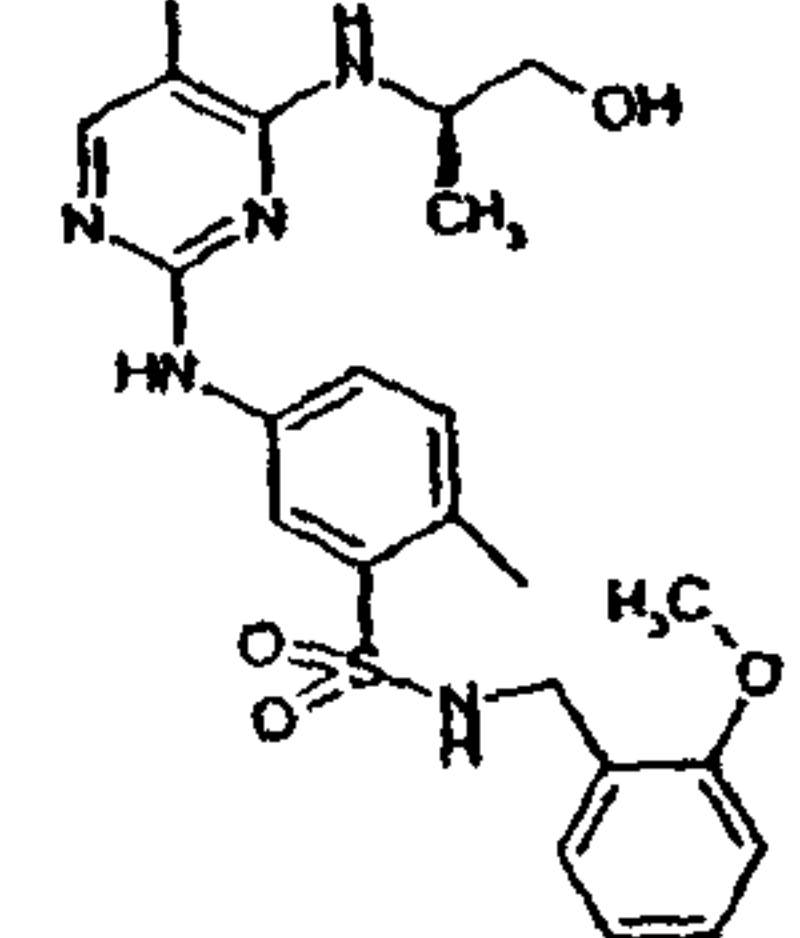
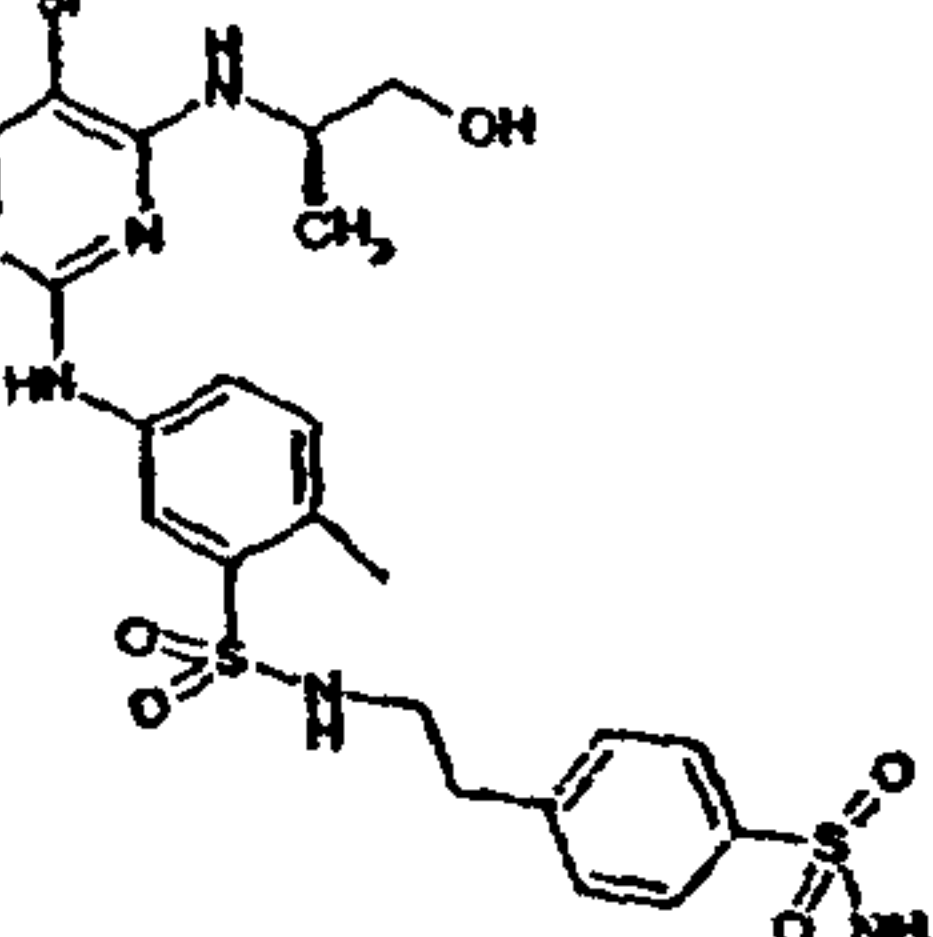
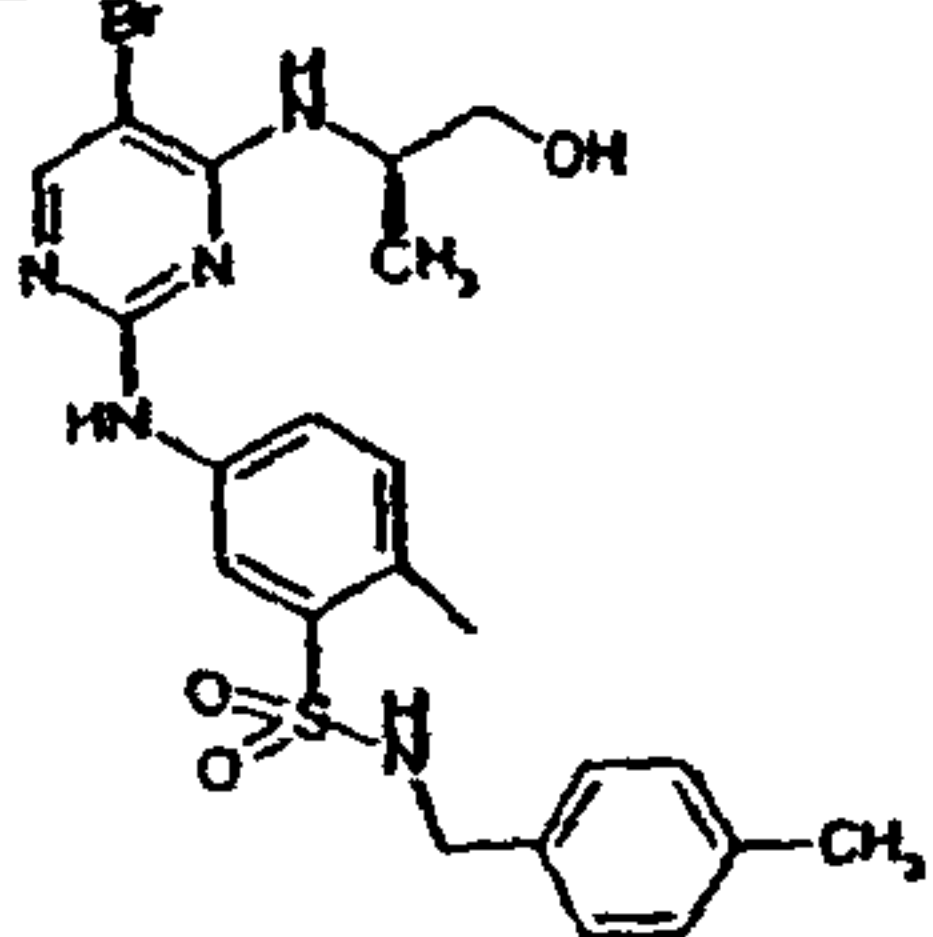
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
342		528,5126	528/530
343		542,5394	542/544
344		556,5662	556/558
345		496,3838	496/498
346		574,4197	574/576

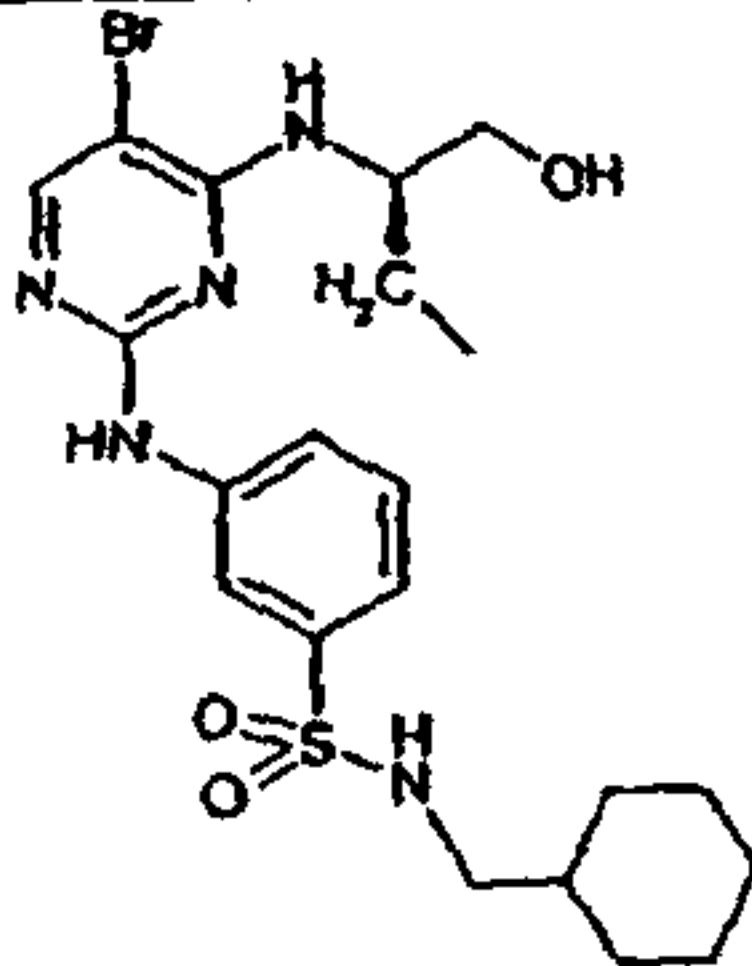
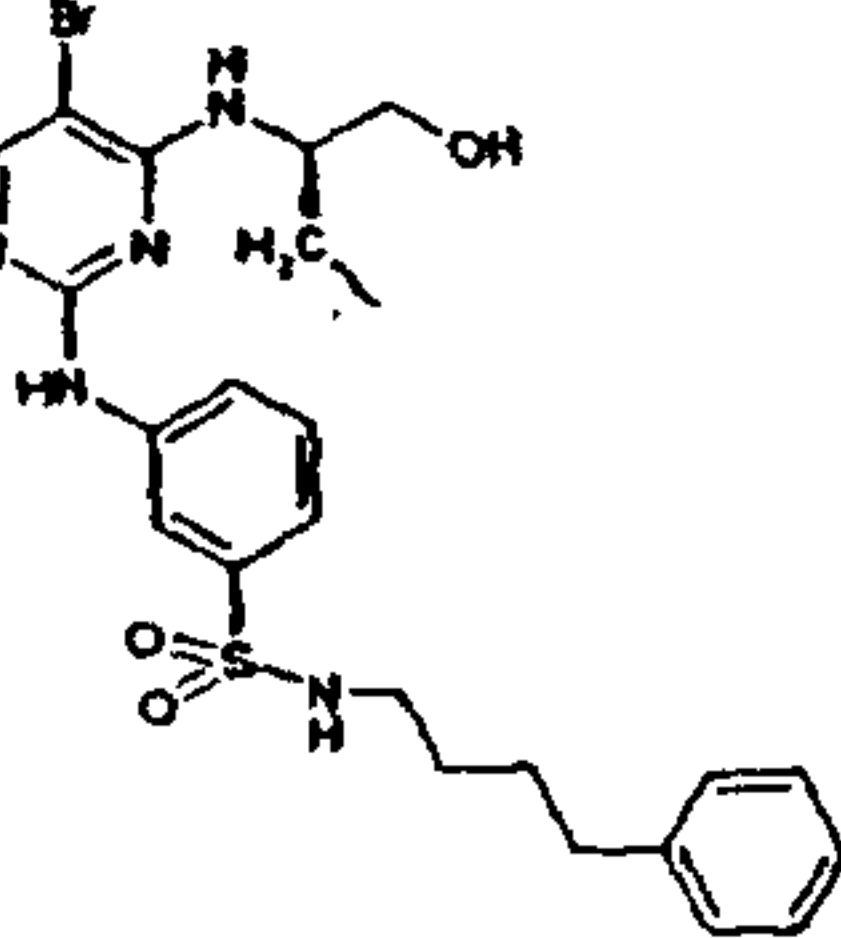
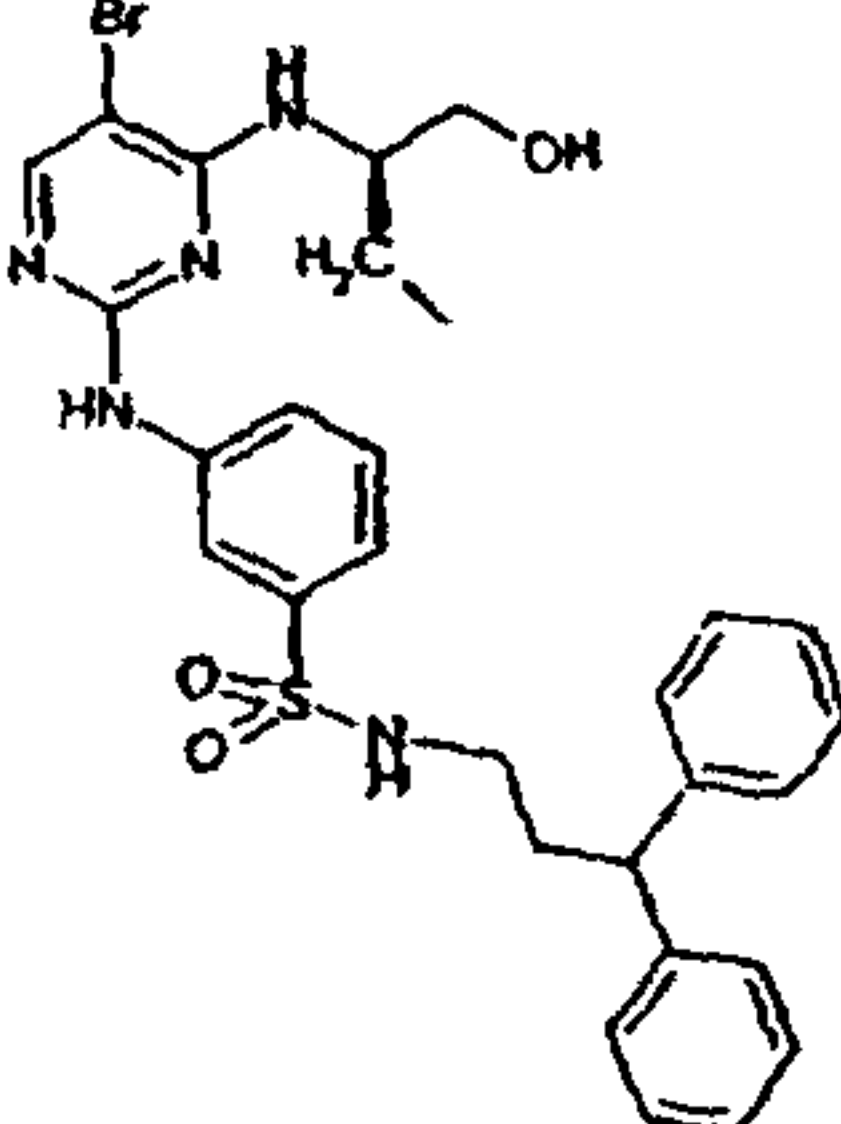
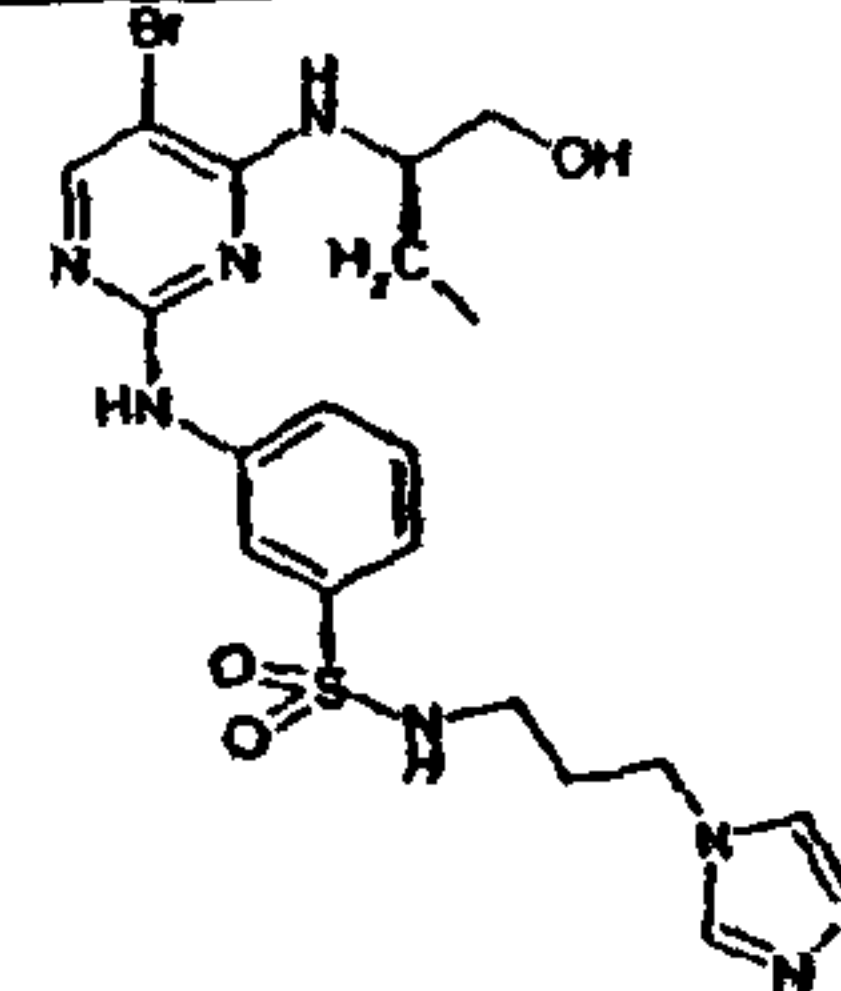
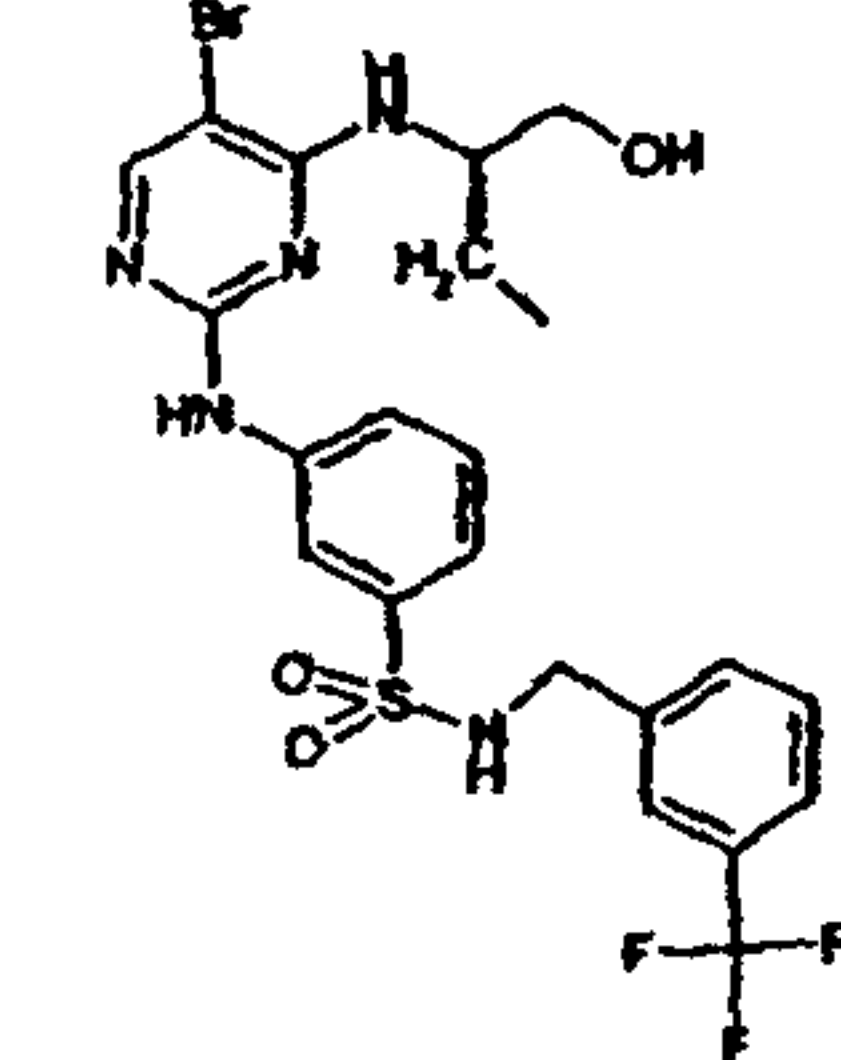
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
347		534,4762	534/536
348		541,4681	541/543
349		486,4322	486/488
350		500,459	500/502
351		501,4471	501/503
352		543,5275	543/545

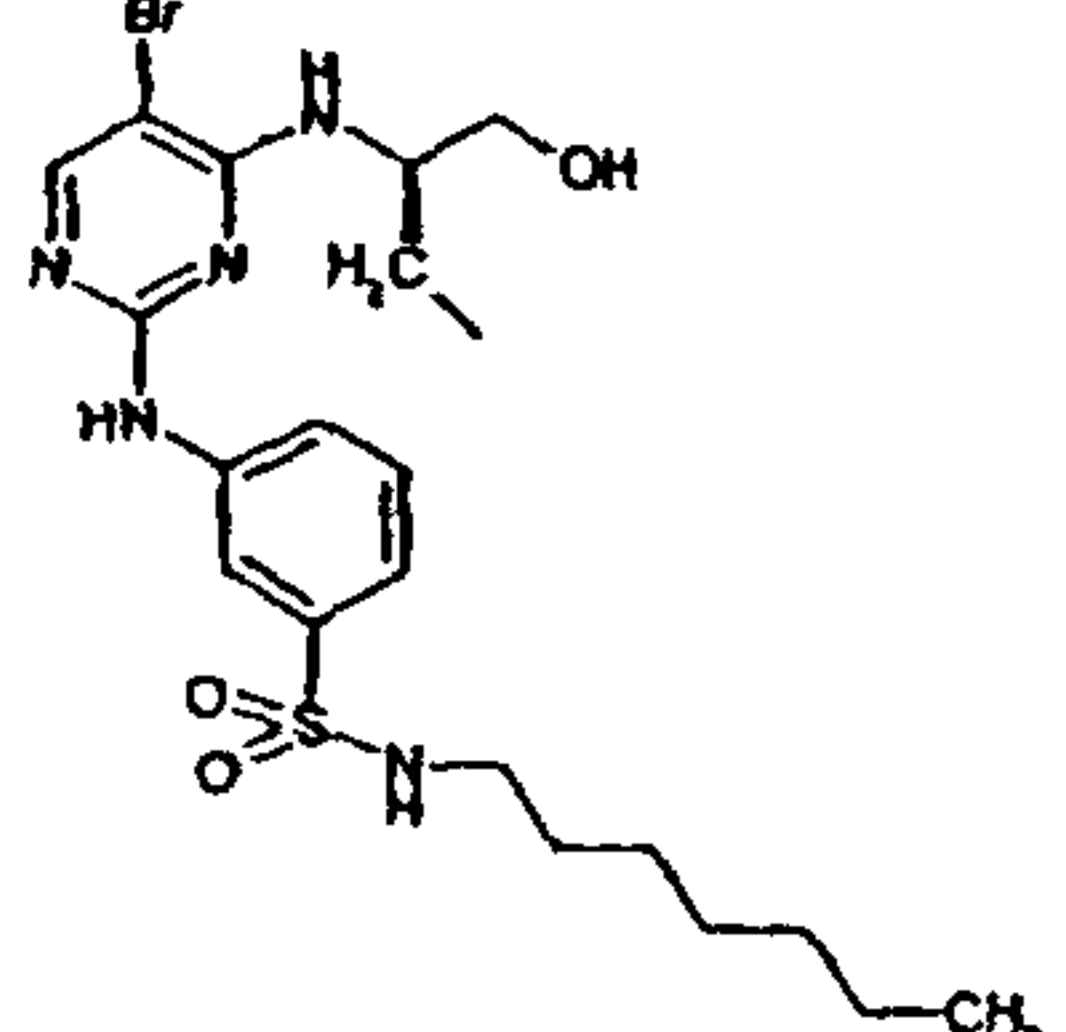
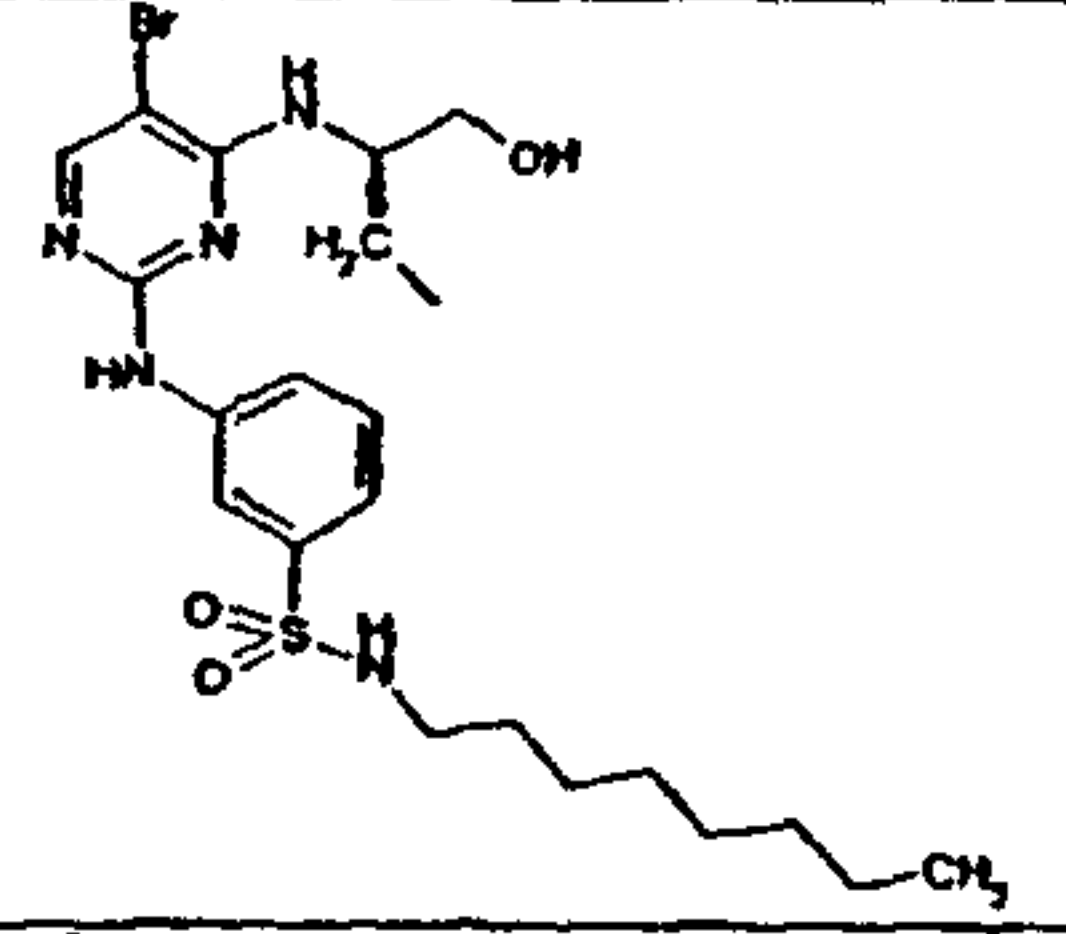
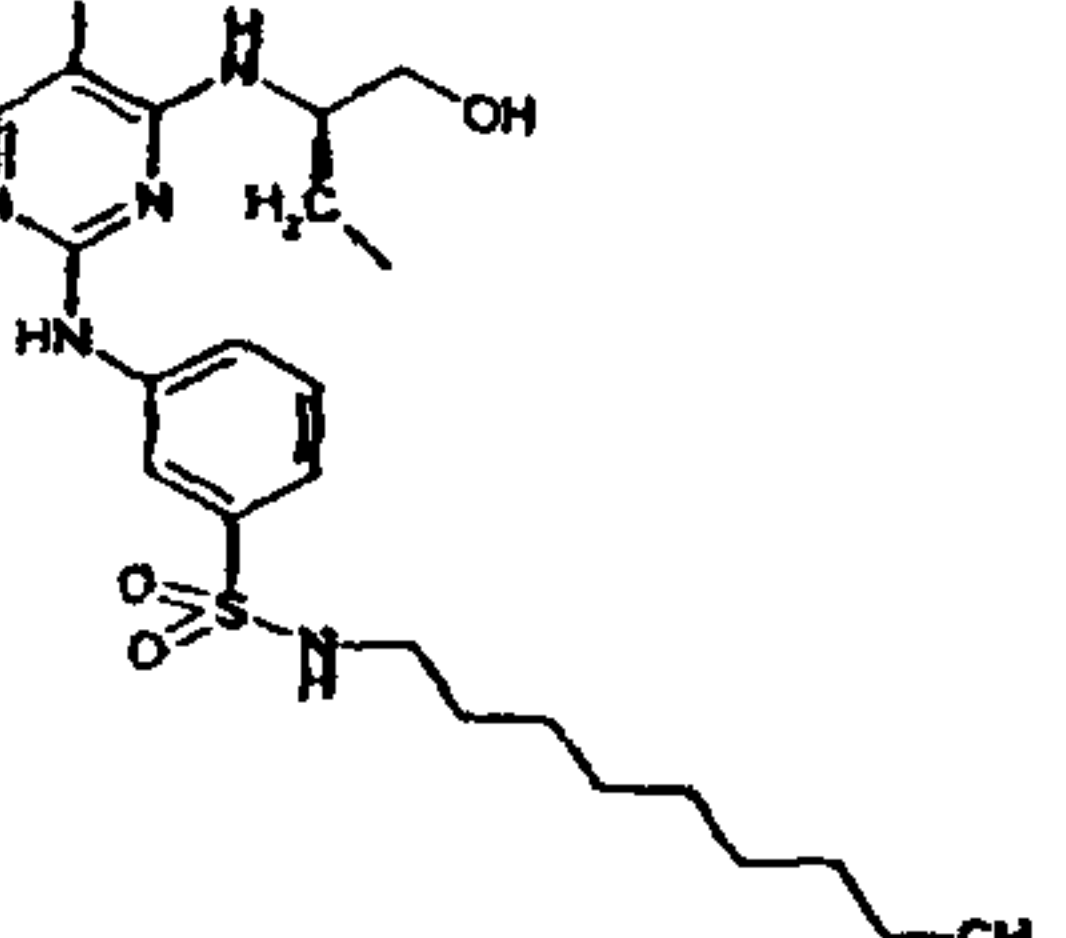
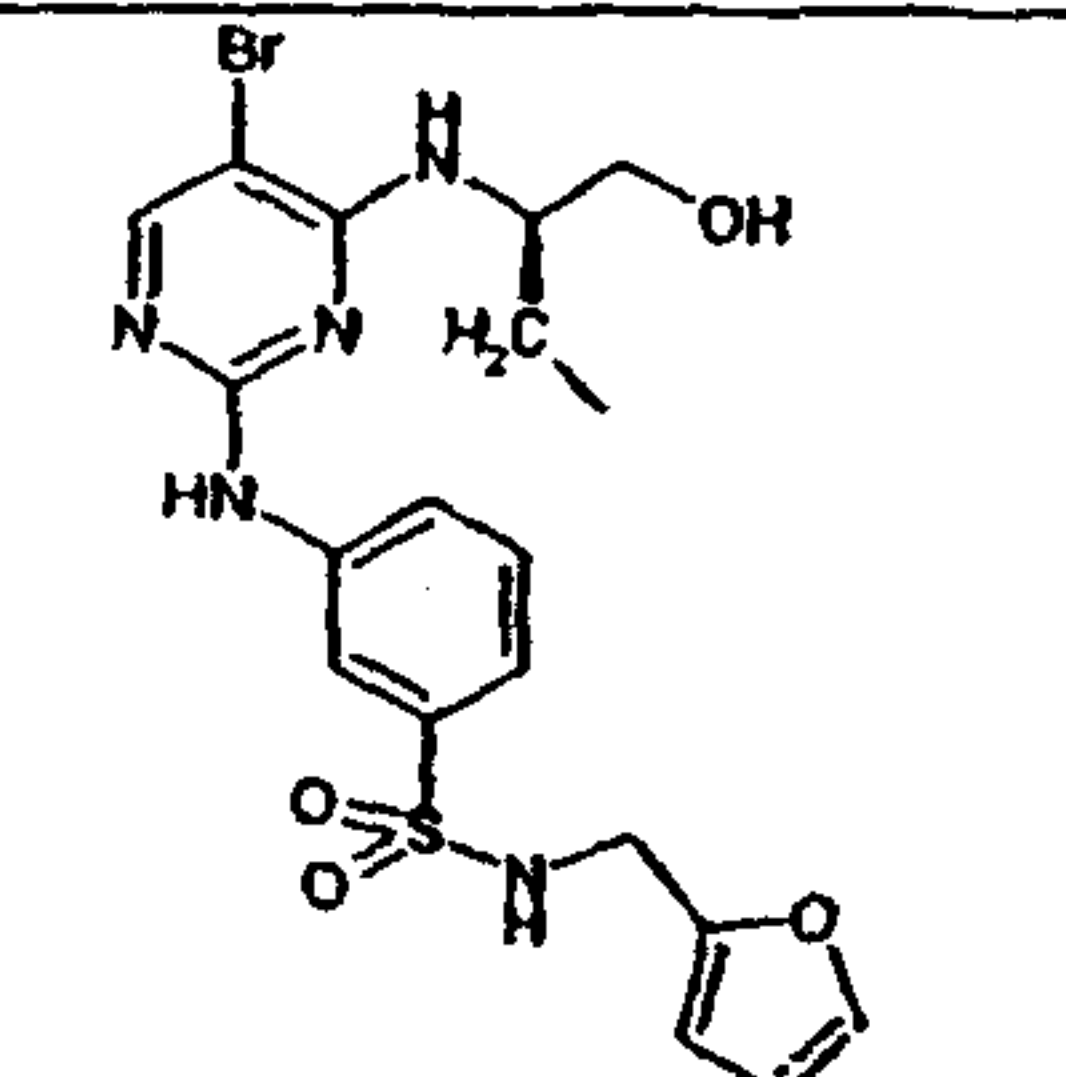
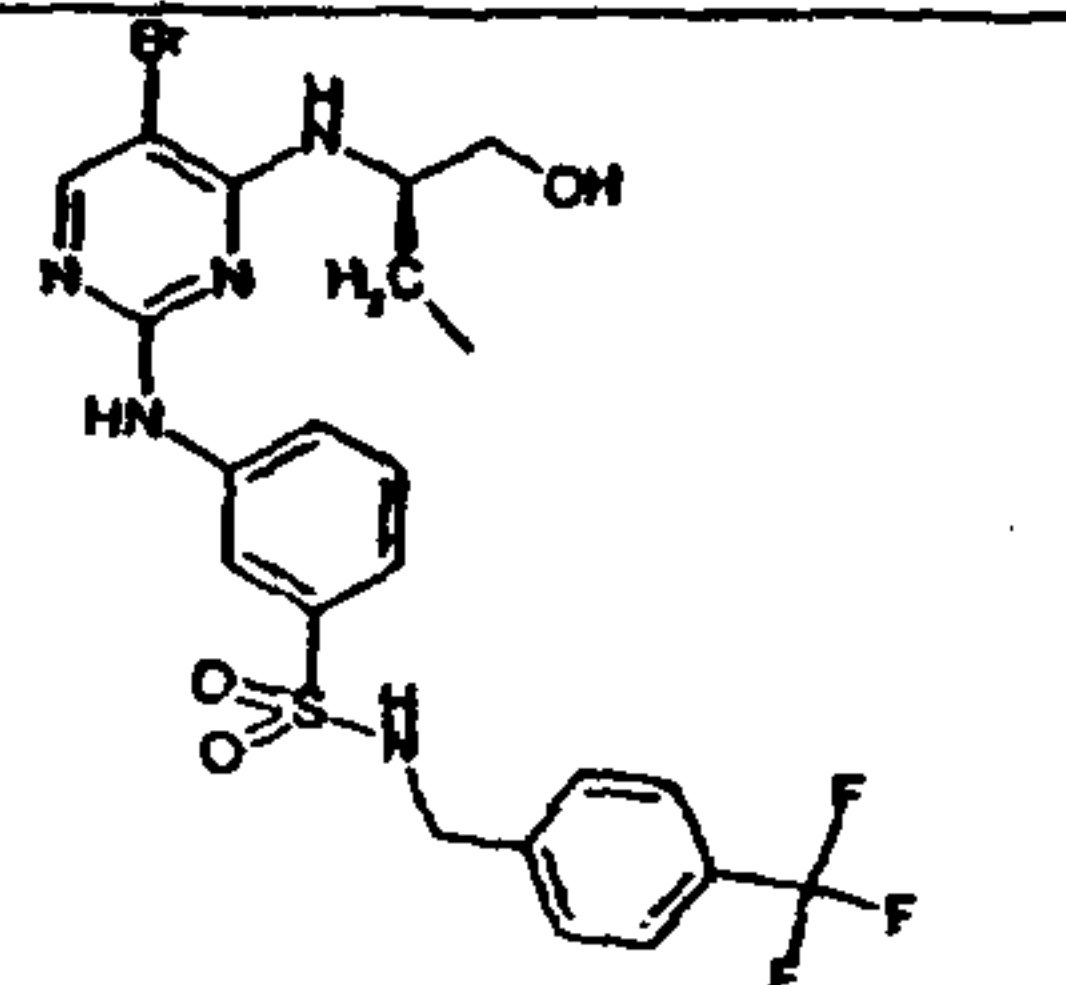
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
353		456,3628	456/458
354		537,4801	537/539
355		520,4494	520/522
356		554,8945	554/556
357		510,4106	510/512

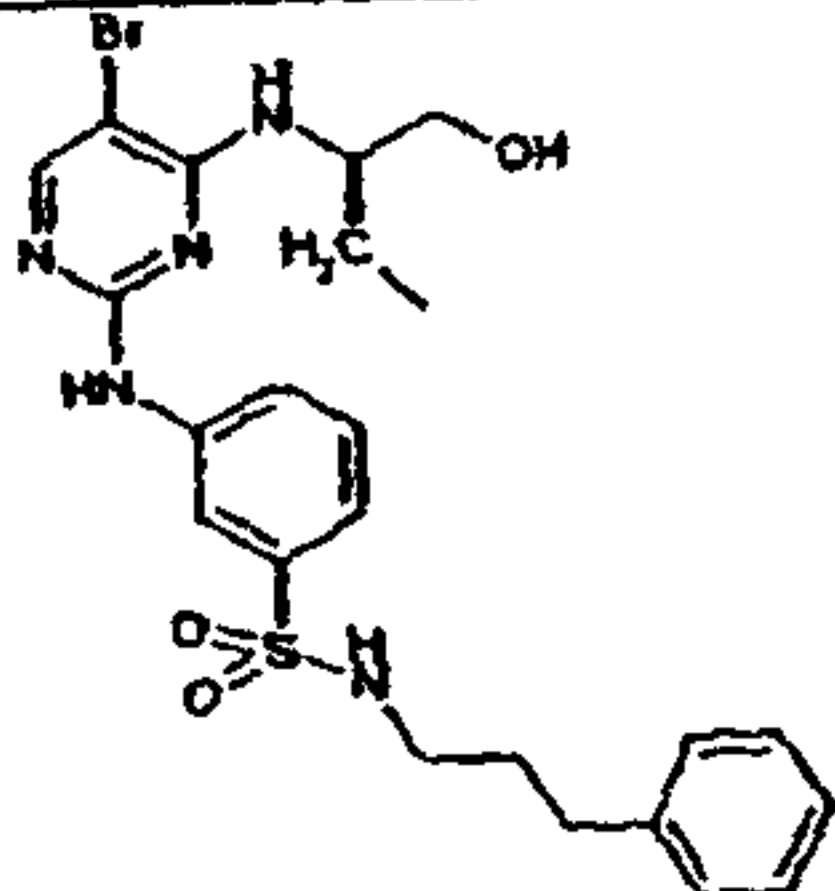
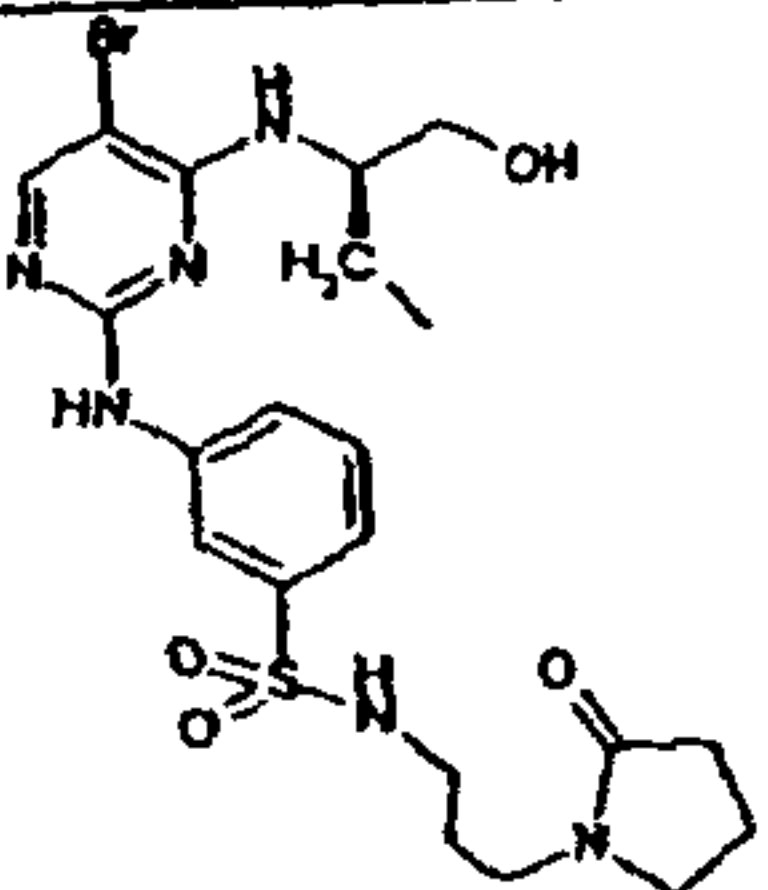
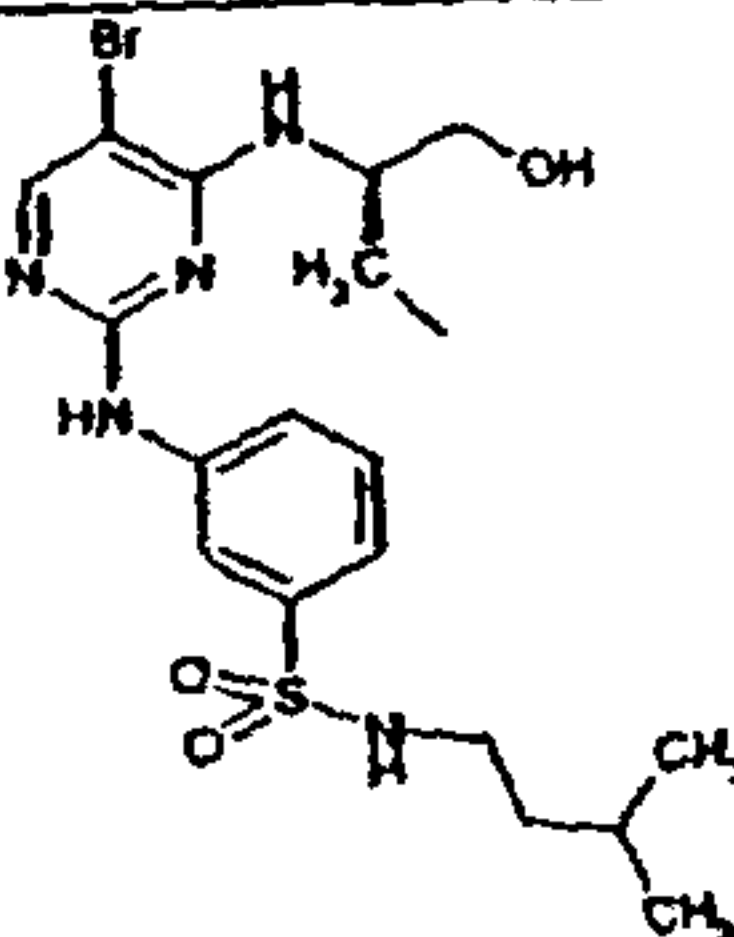
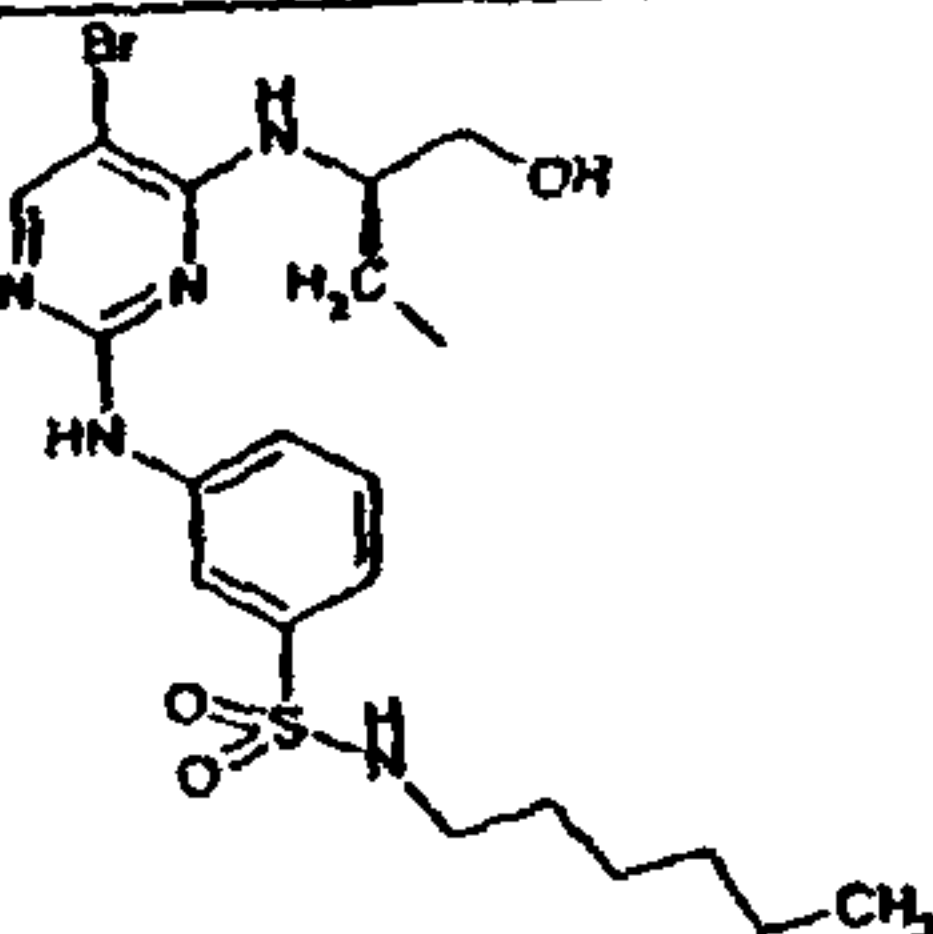
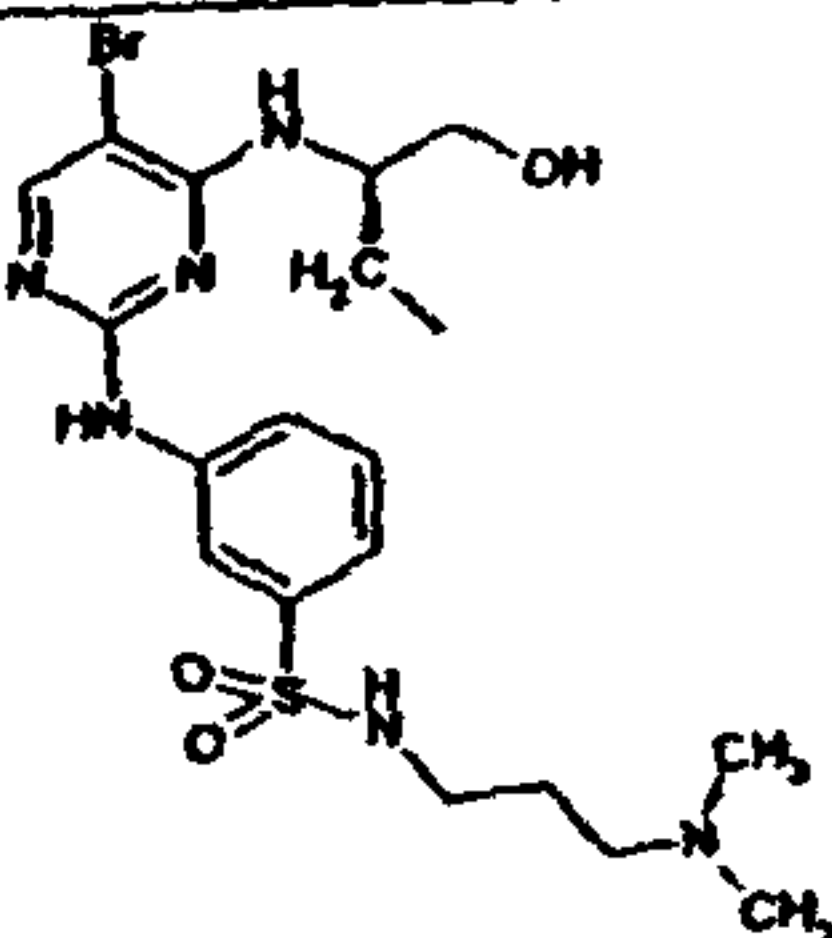
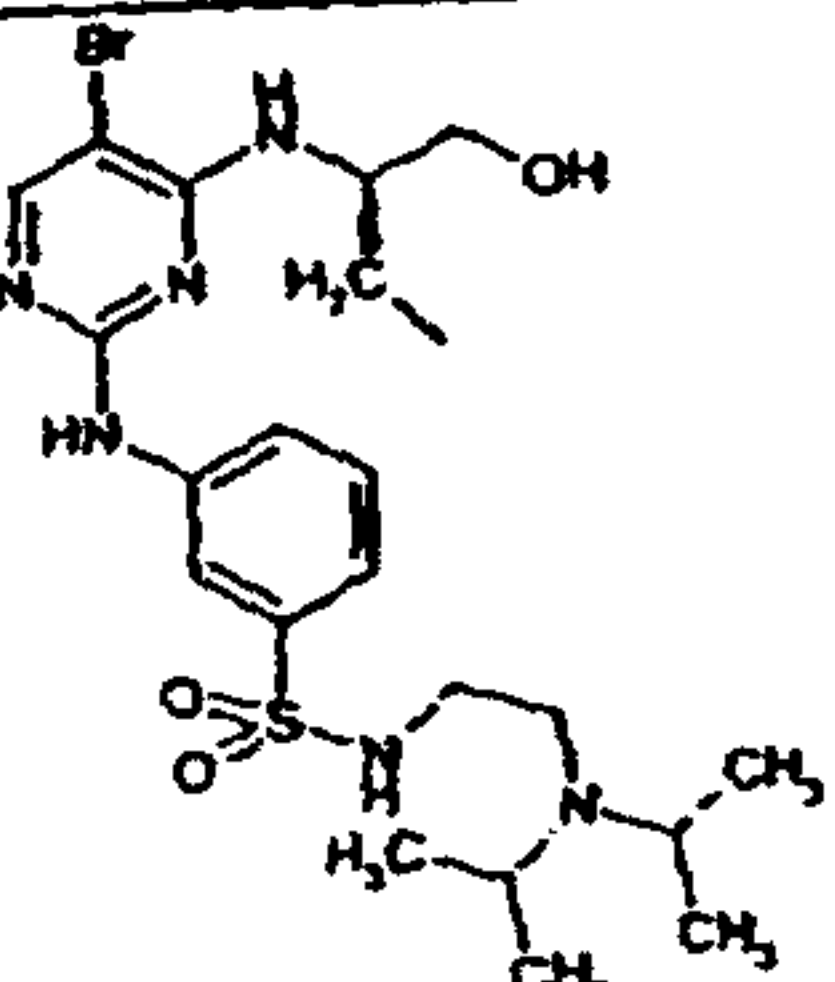
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
358		529,4571	529/531
359		474,3776	474/476
360		512,4508	541/514
361		550,4752	550/552
362		513,4581	513/515

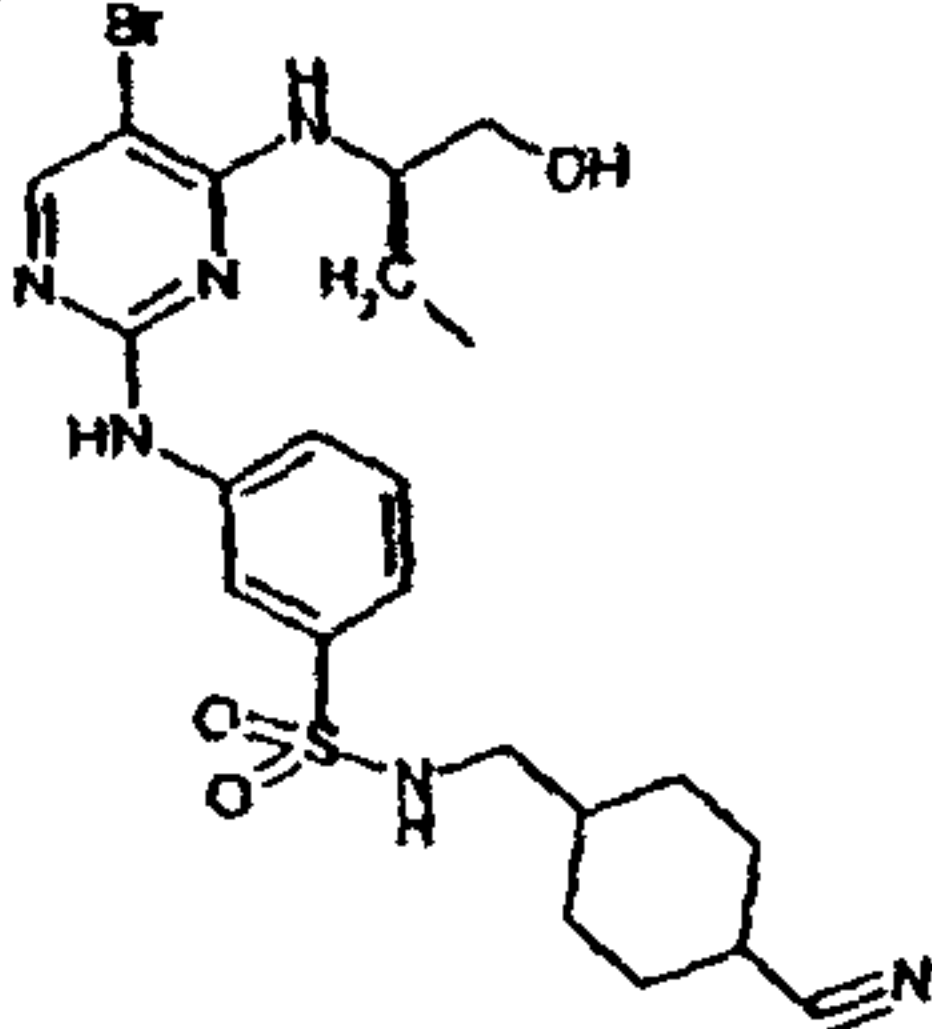
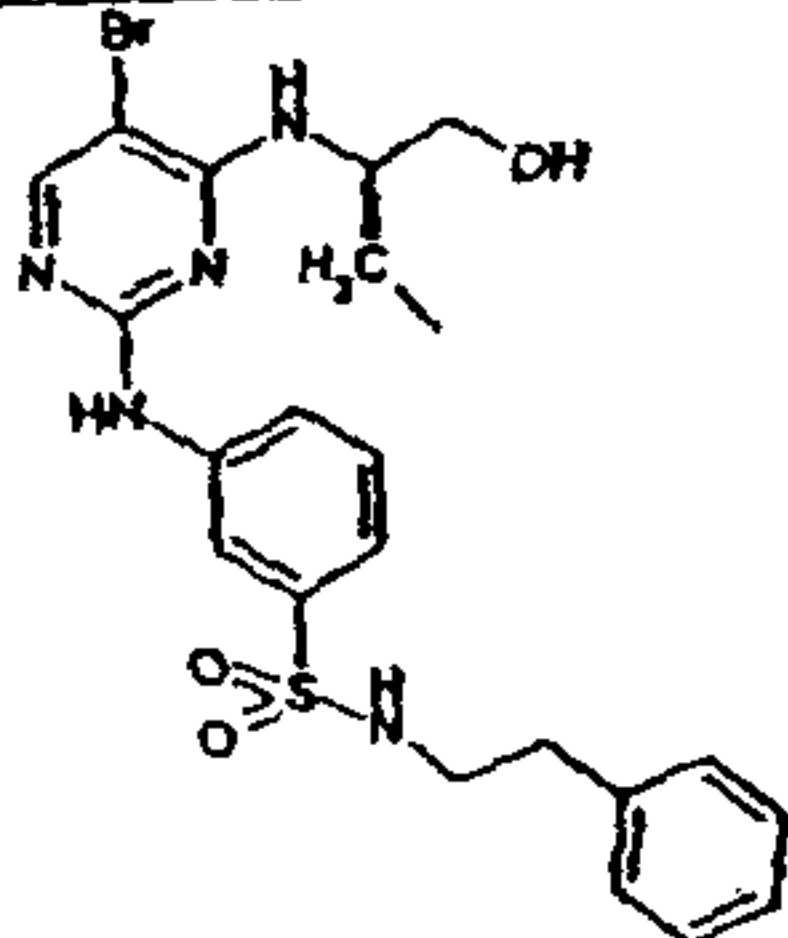
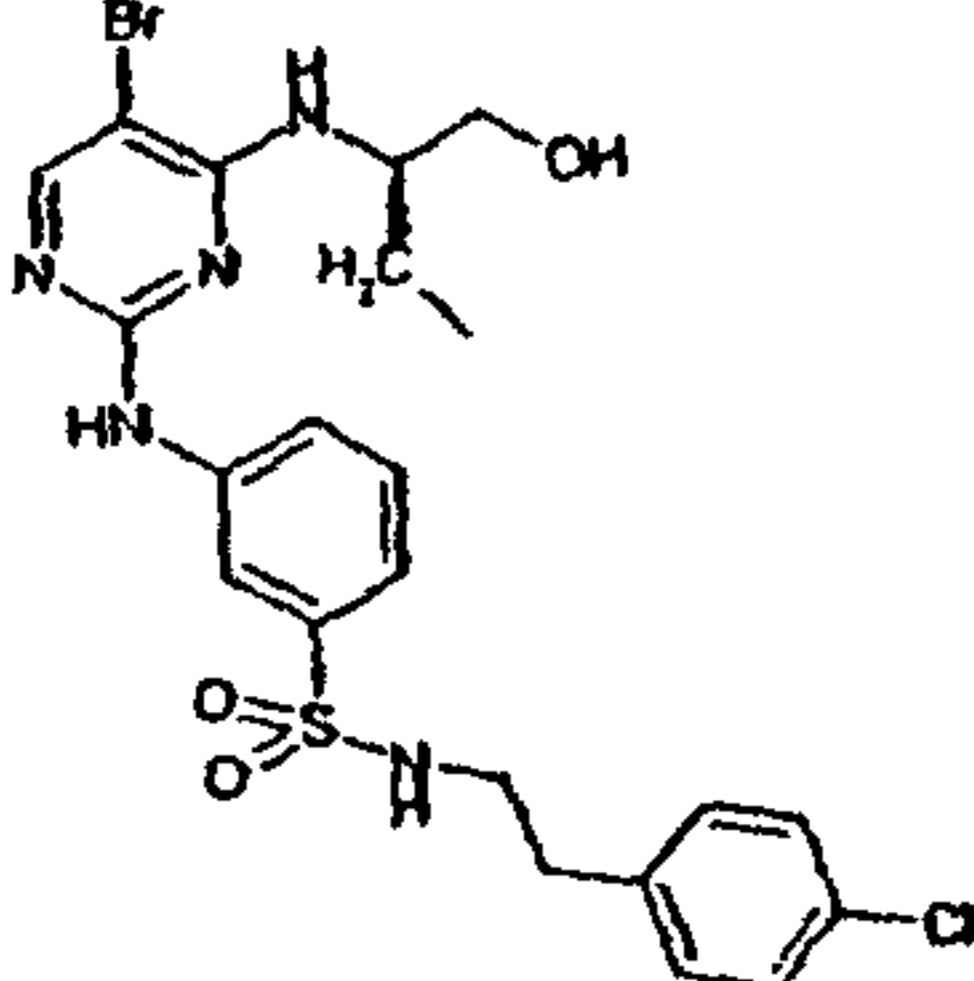
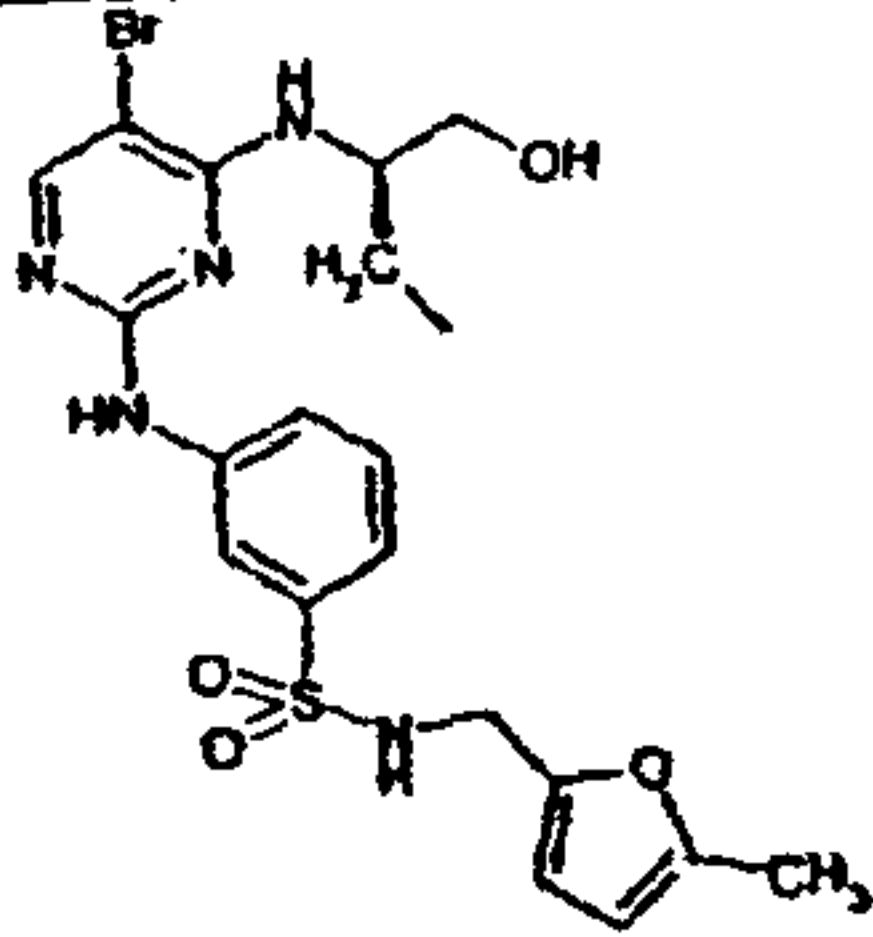
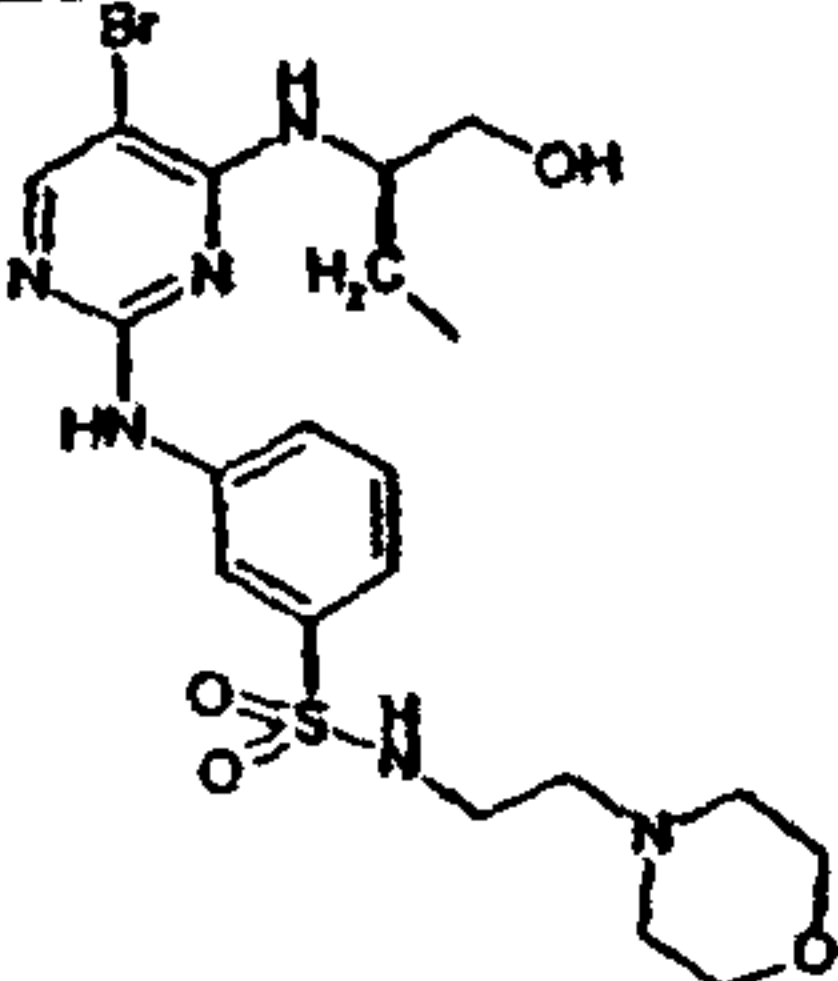
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
363		527,4849	527/529
364		524,4127	524/526
365		527,4849	527/529
366		507,4107	507/509
367		524,4127	524/526

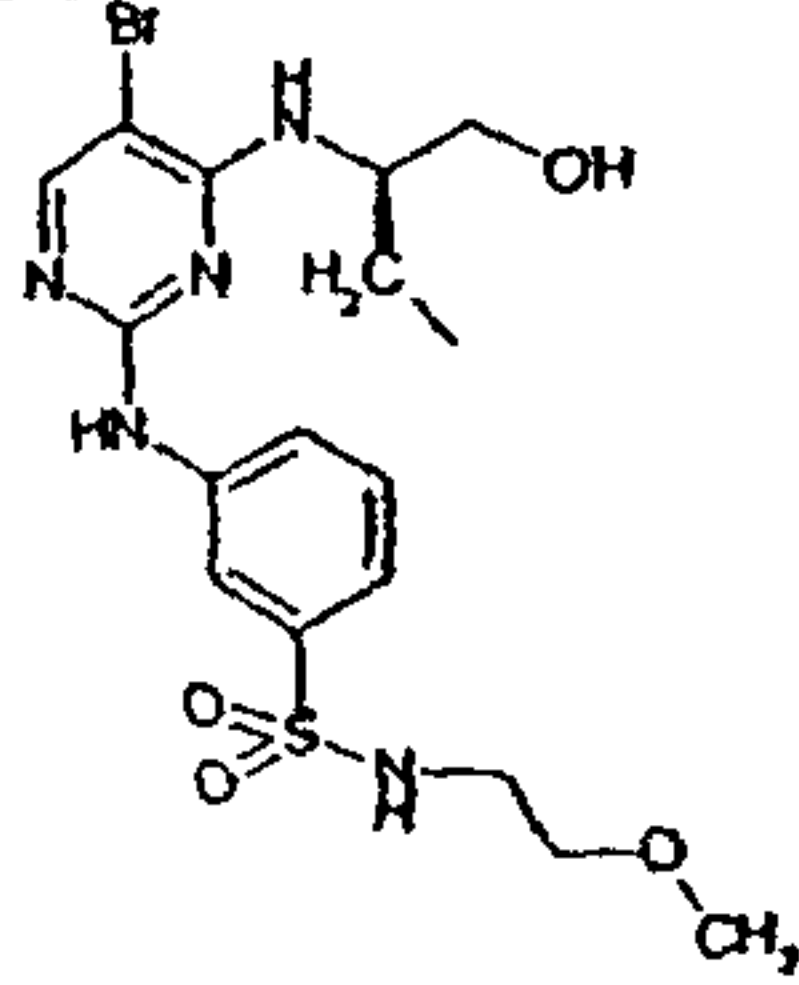
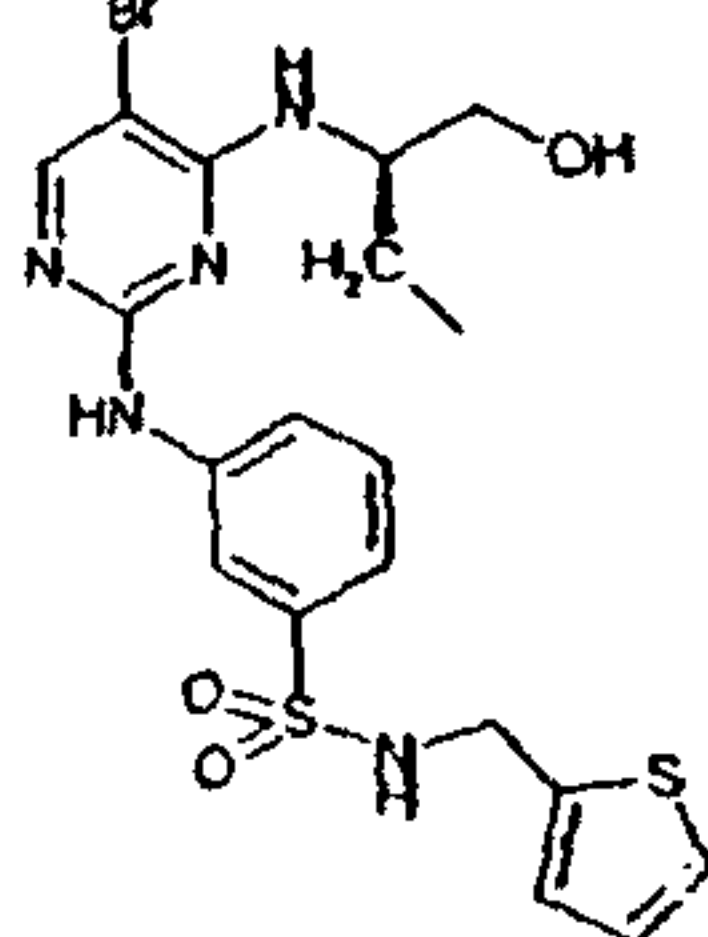
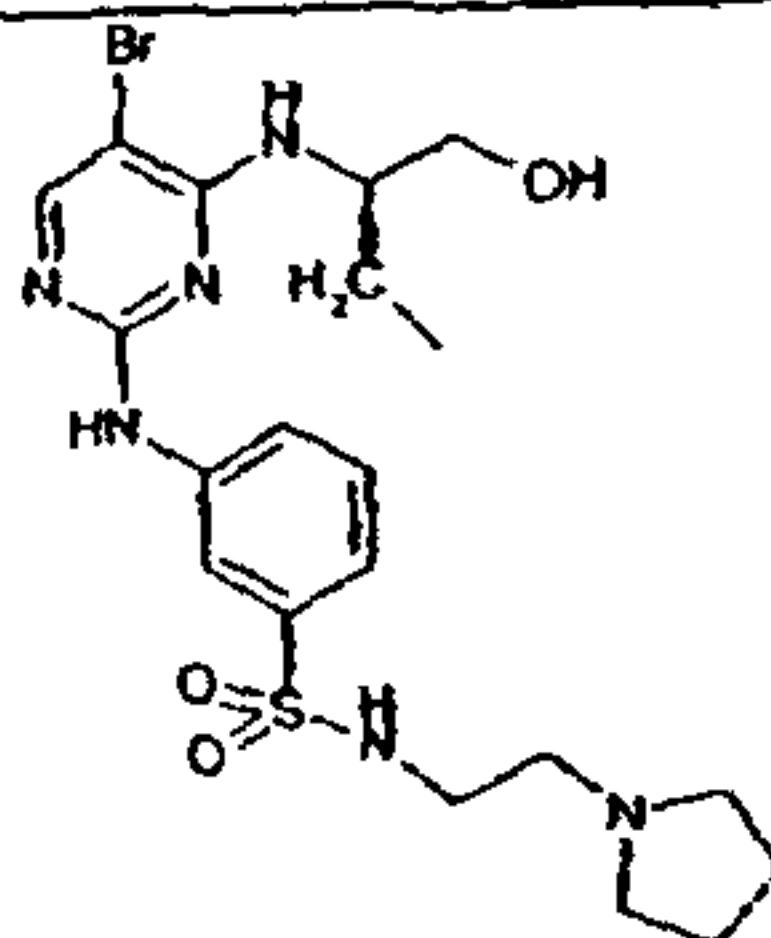
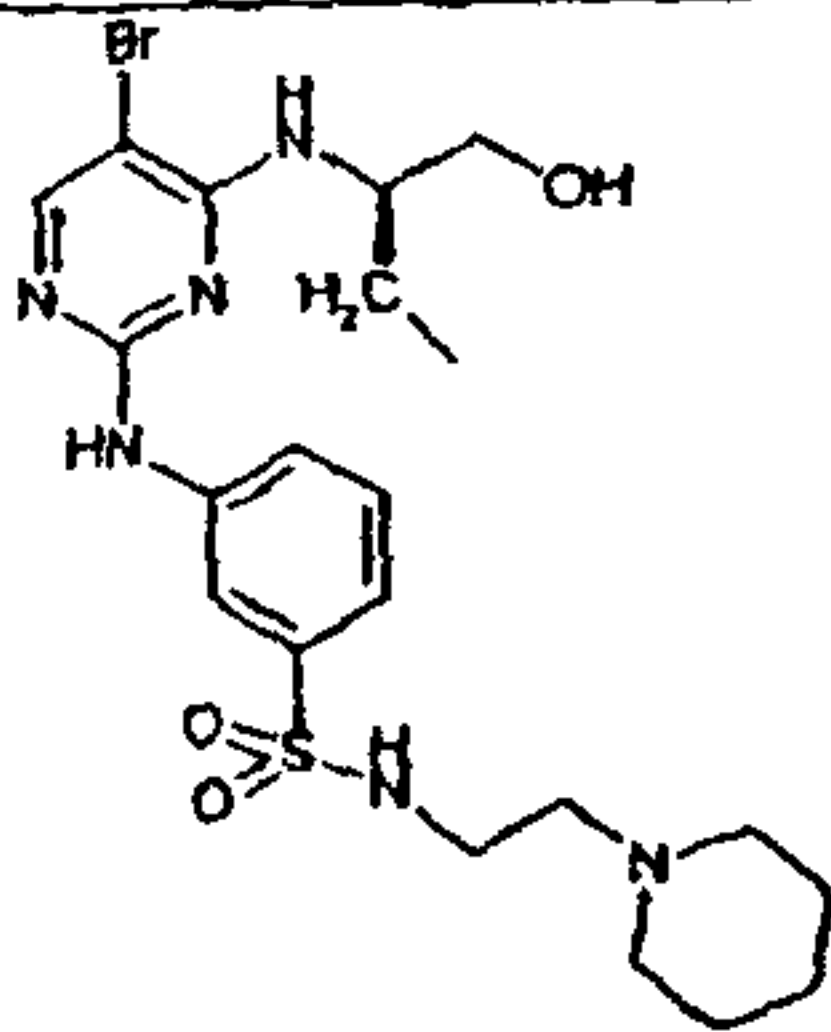
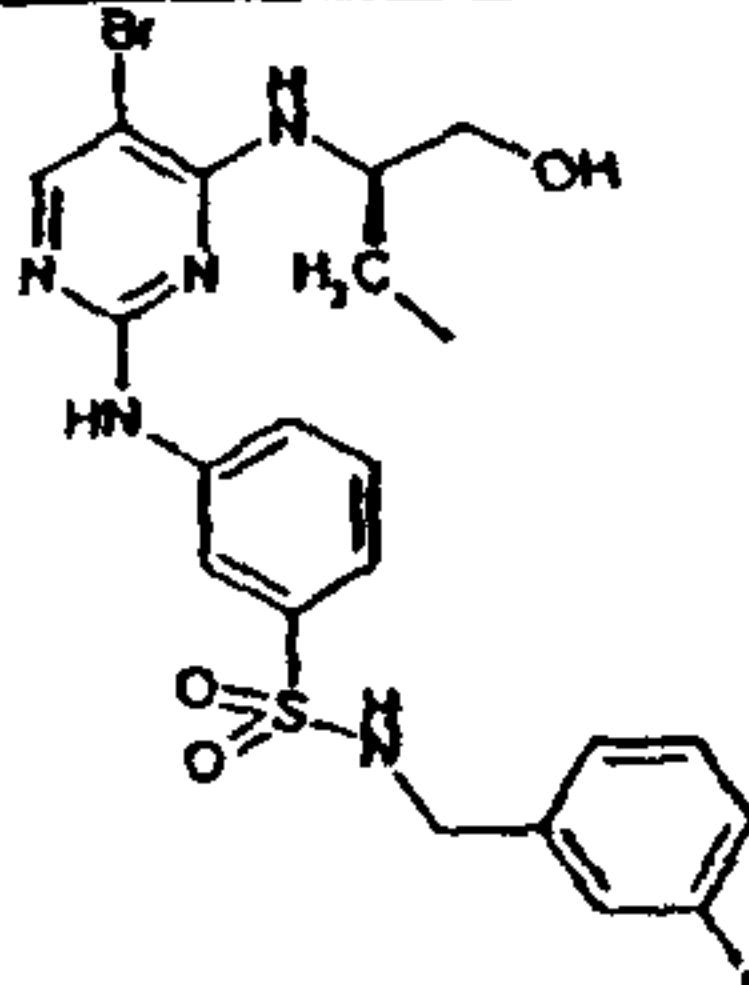
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
368		507,4107	507/509
369		536,4484	536/538
370		536,4484	536/538
371		599,5283	599/601
372		520,4494	520/522

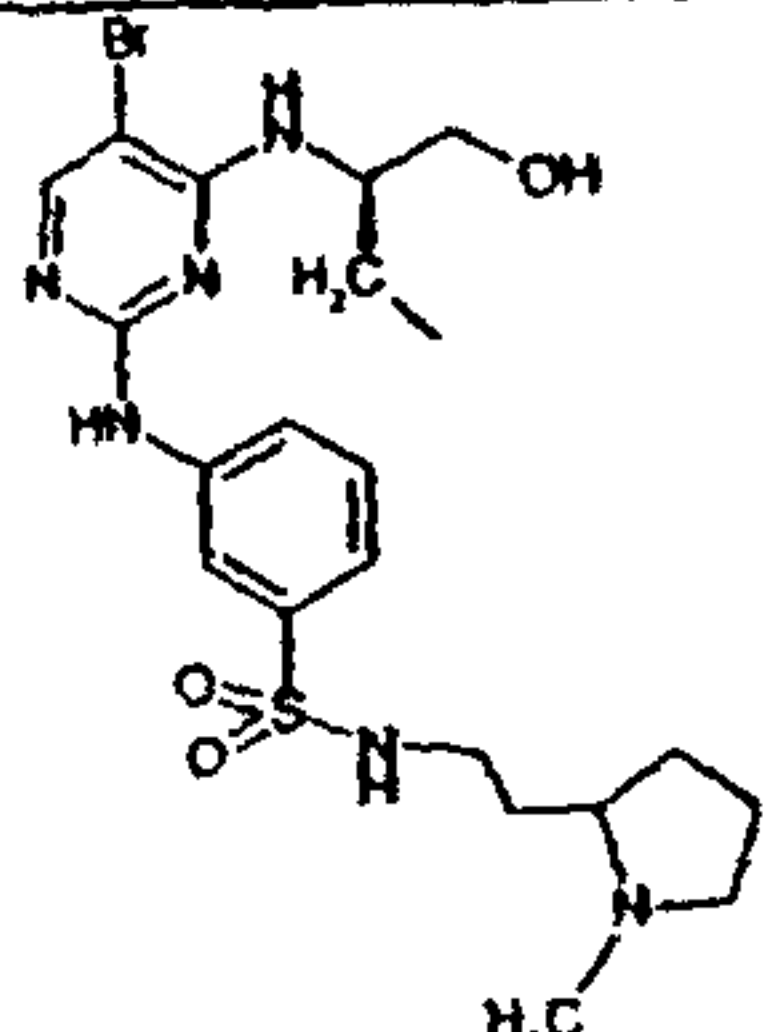
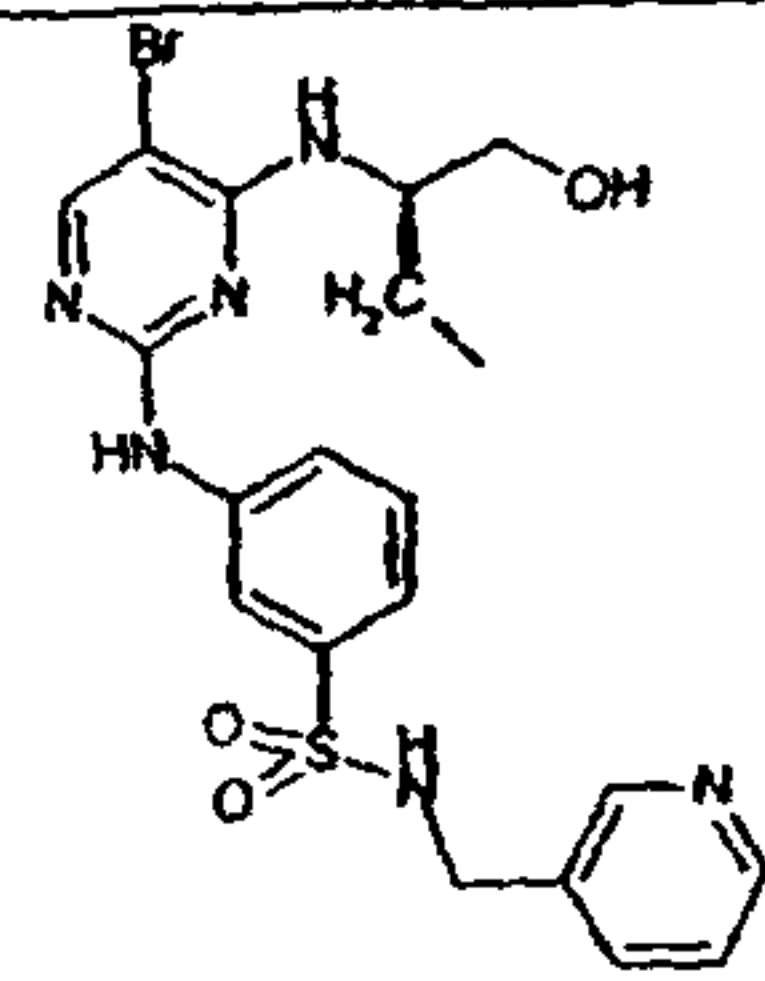
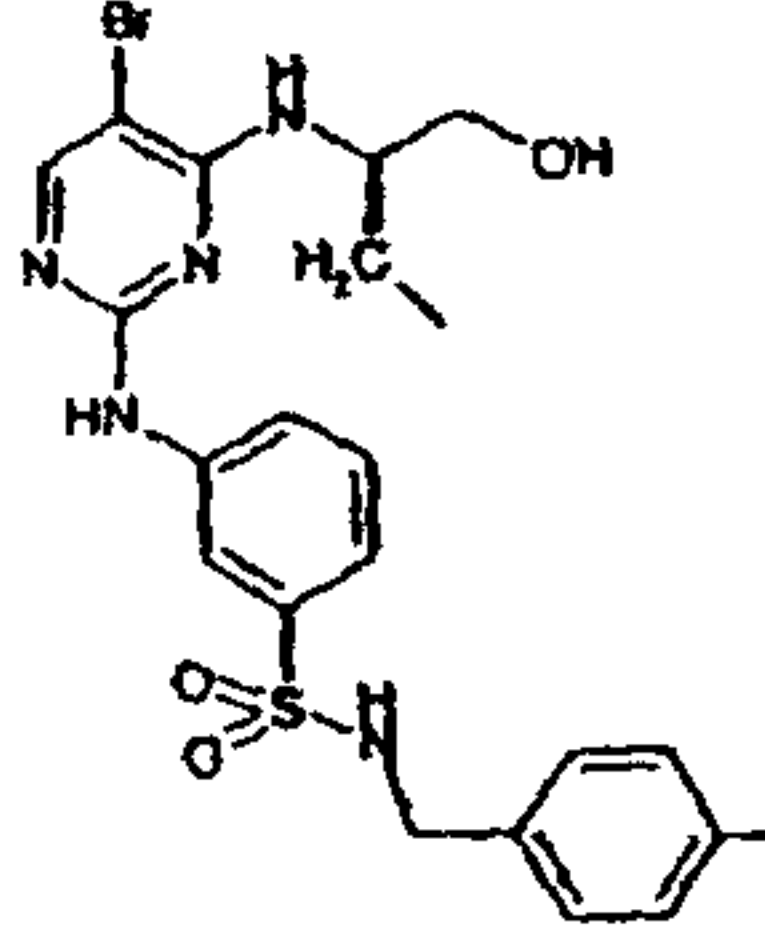
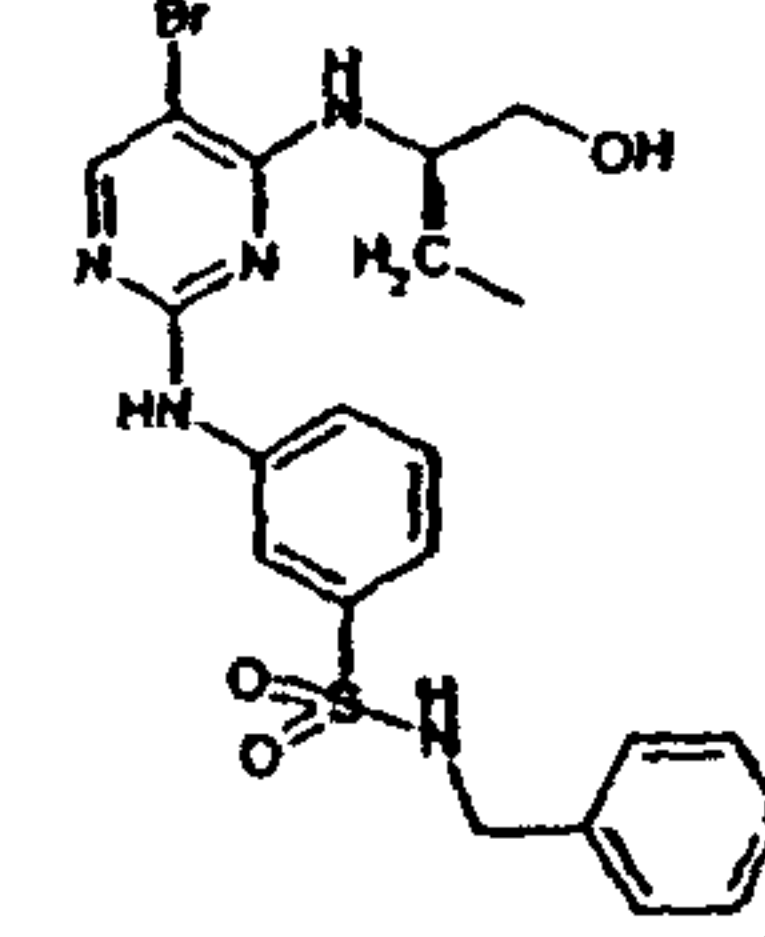
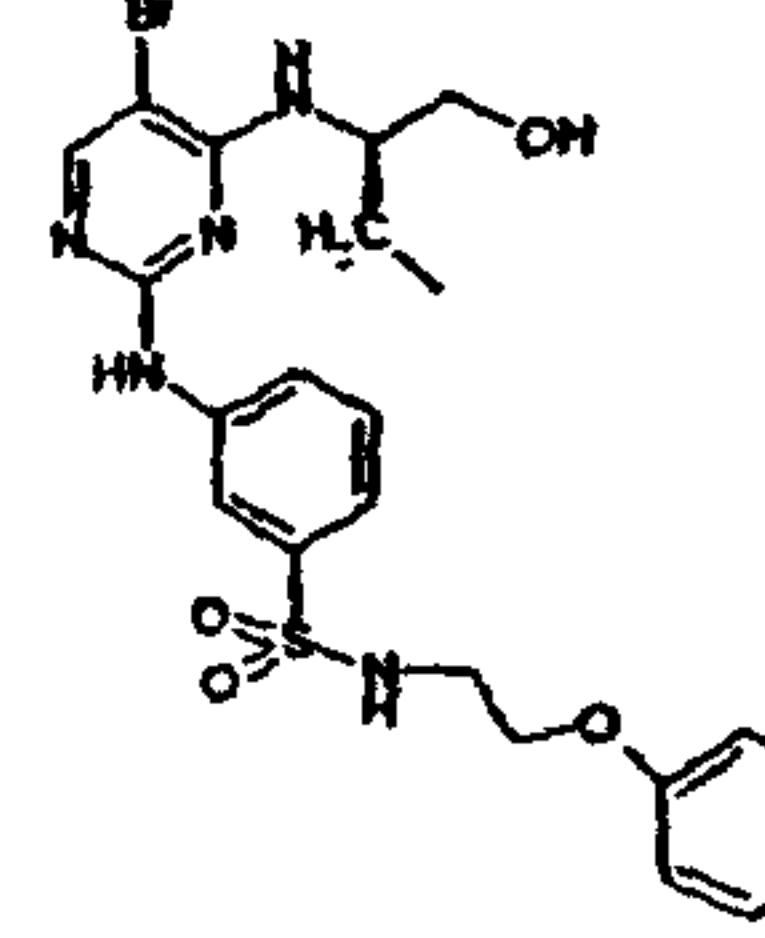
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
373		512,47	512/514
374		548,503	548/550
375		610,5738	610/612
376		524,4414	524/526
377		574,4197	574/576

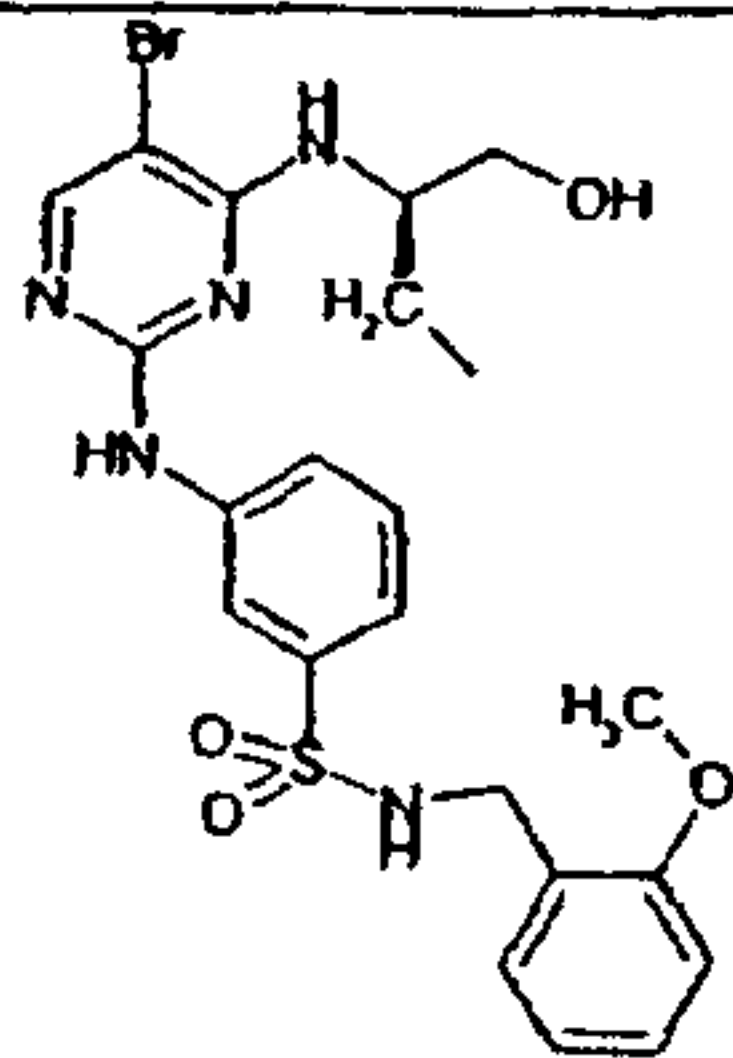
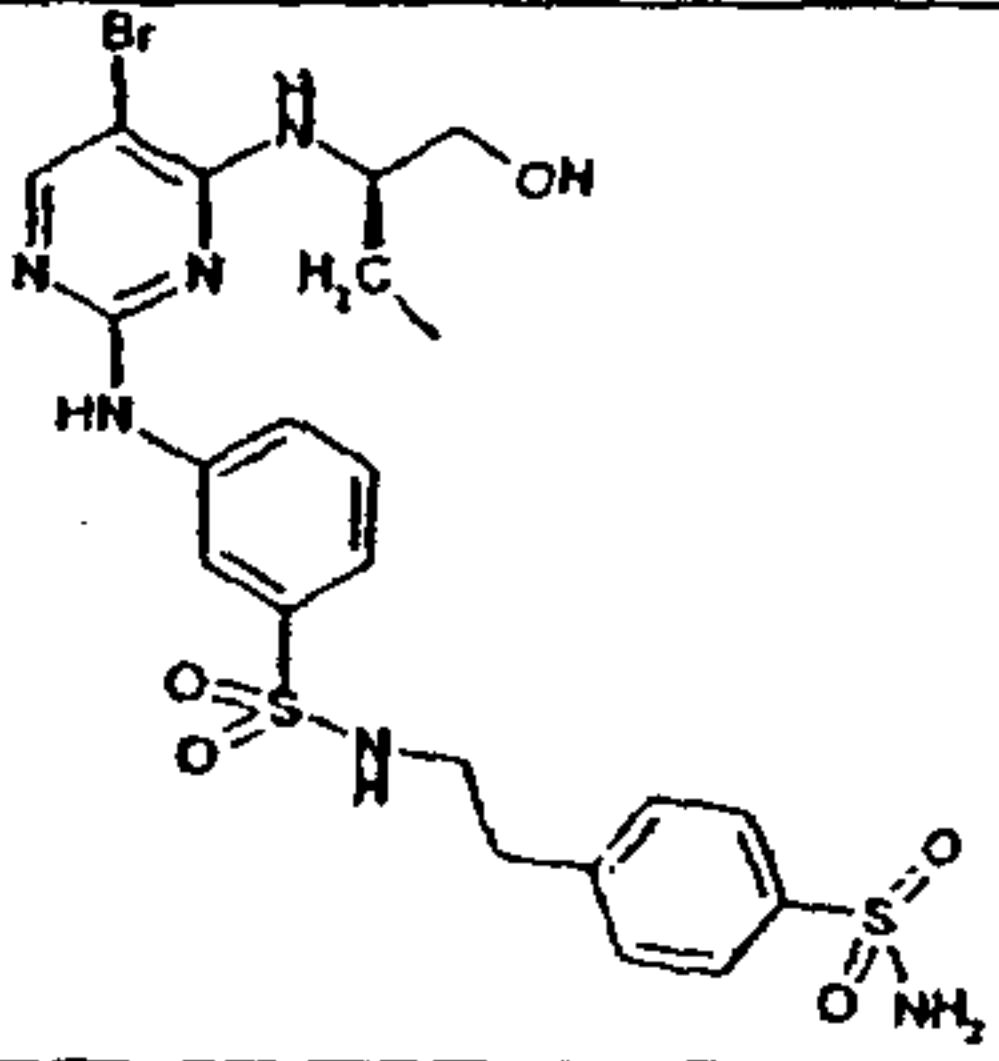
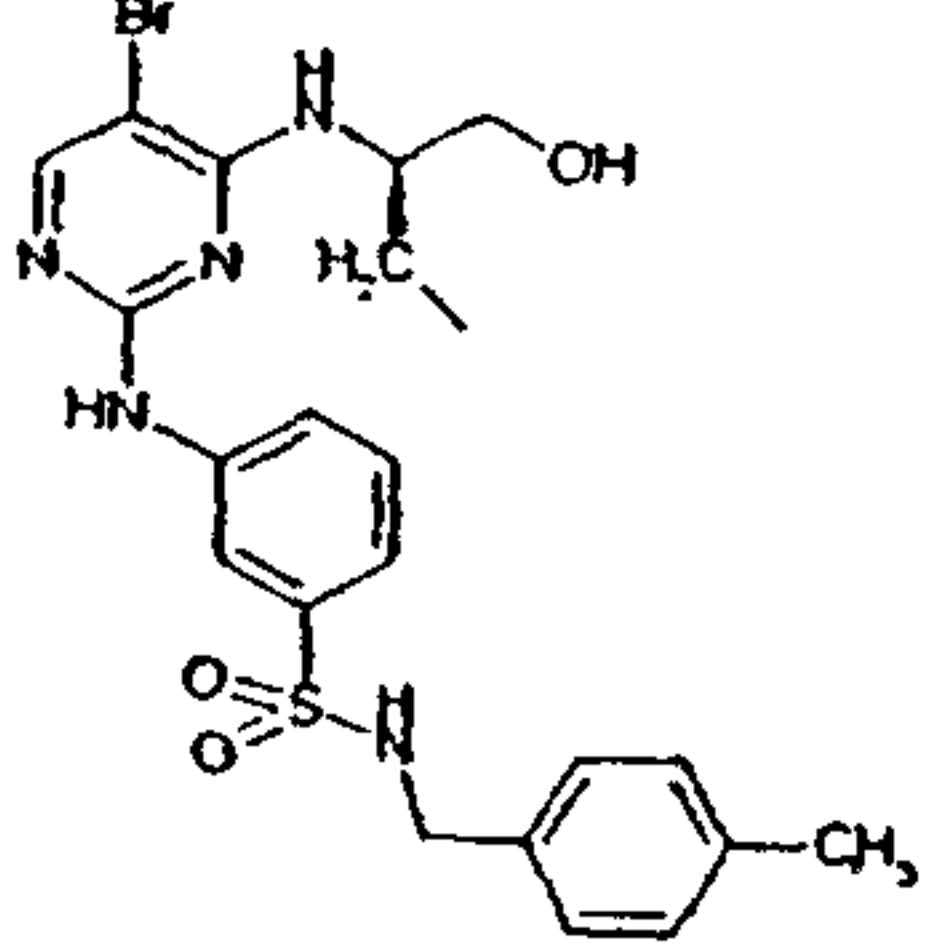
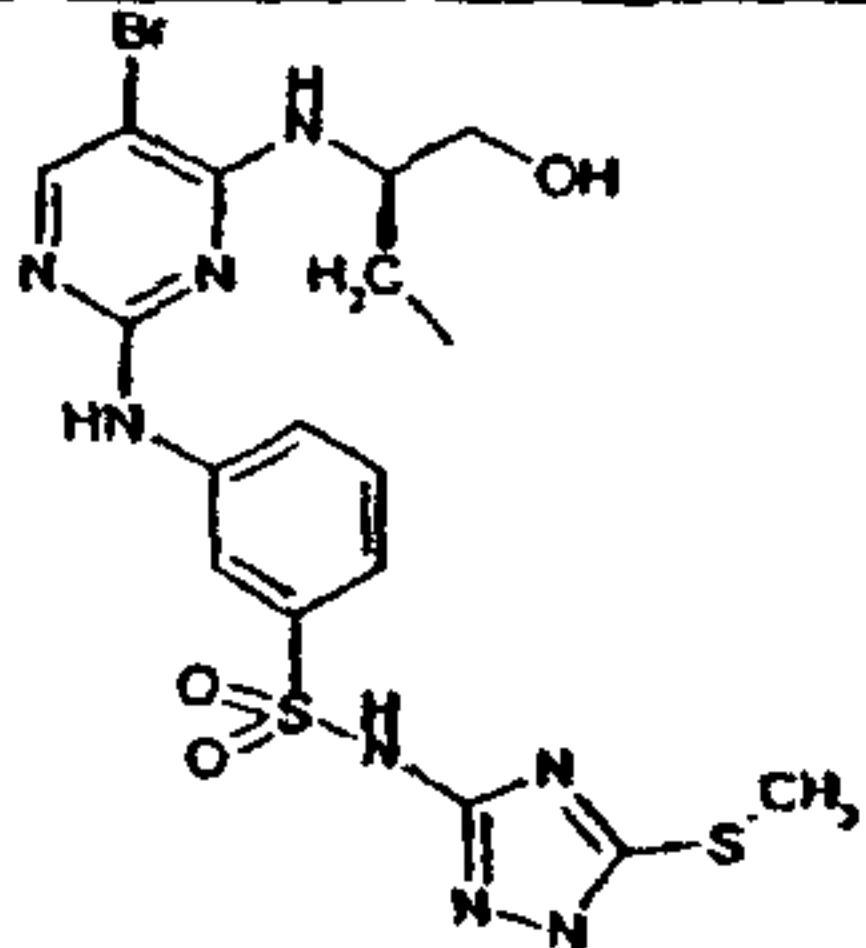
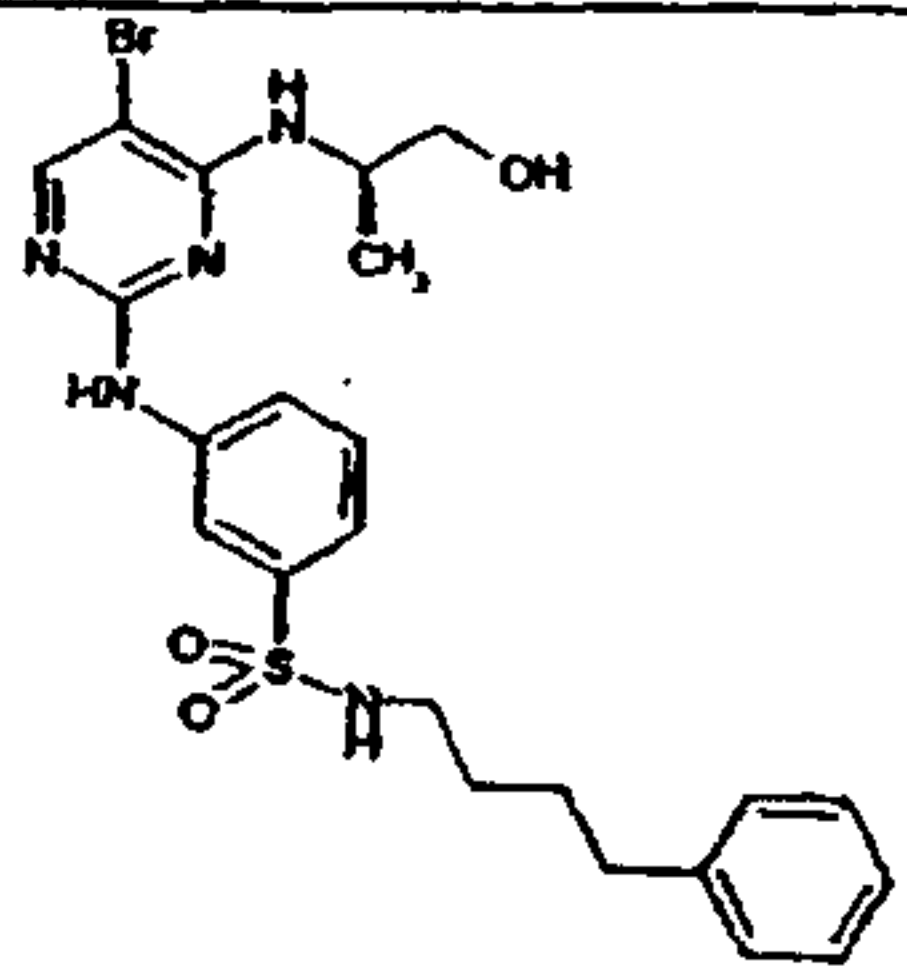
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
378		514,4858	514/516
379		528,5126	528/530
380		542,5394	542/544
381		496,3838	496/498
382		574,4197	574/576

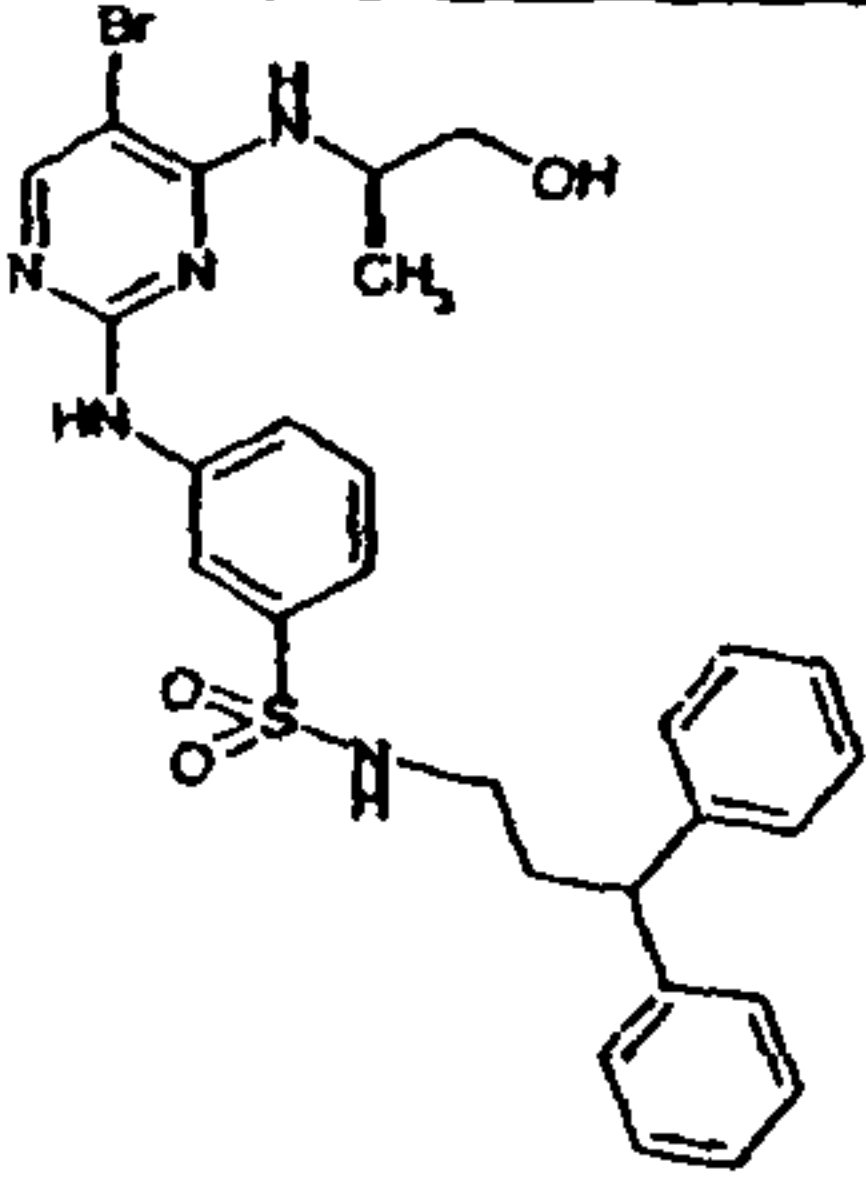
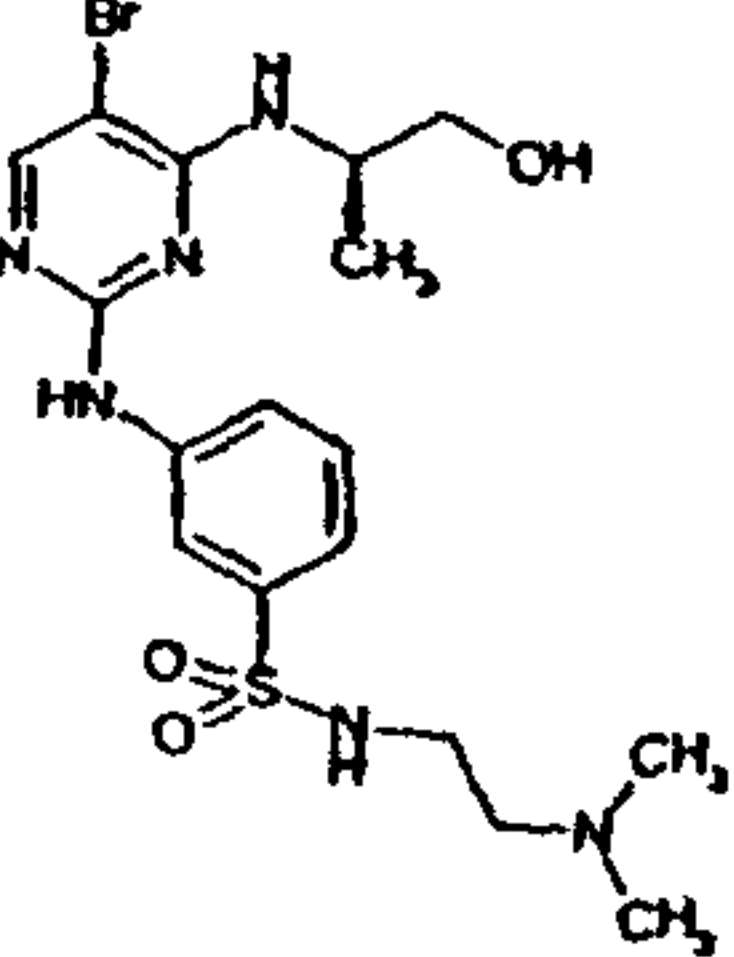
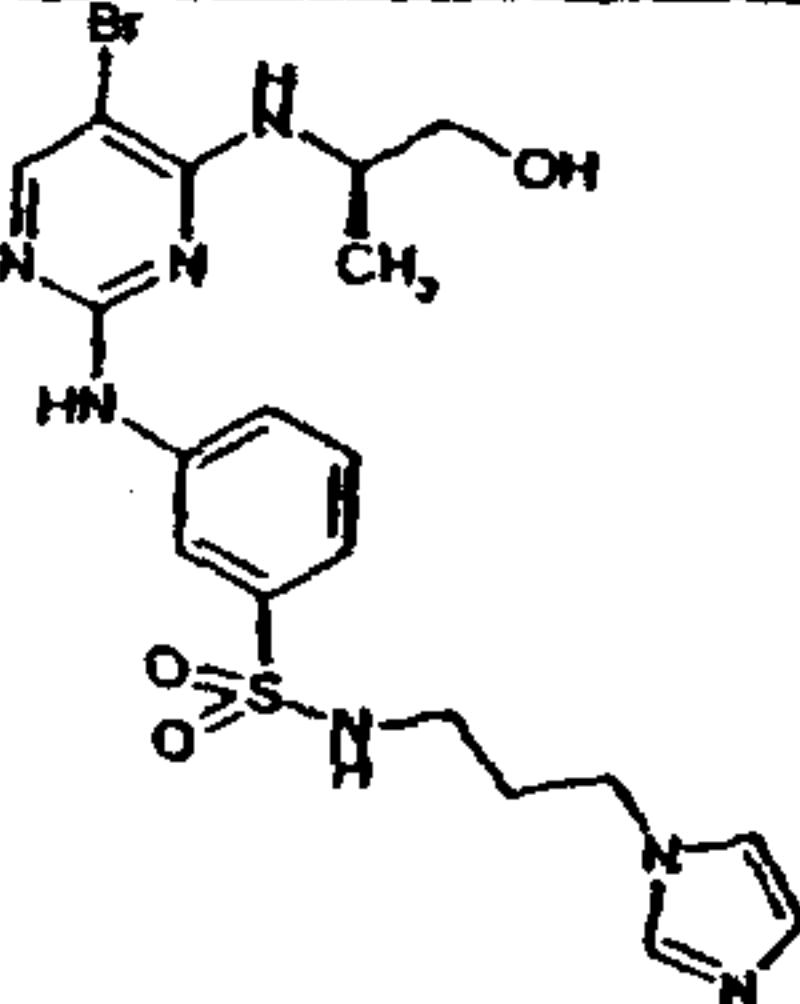
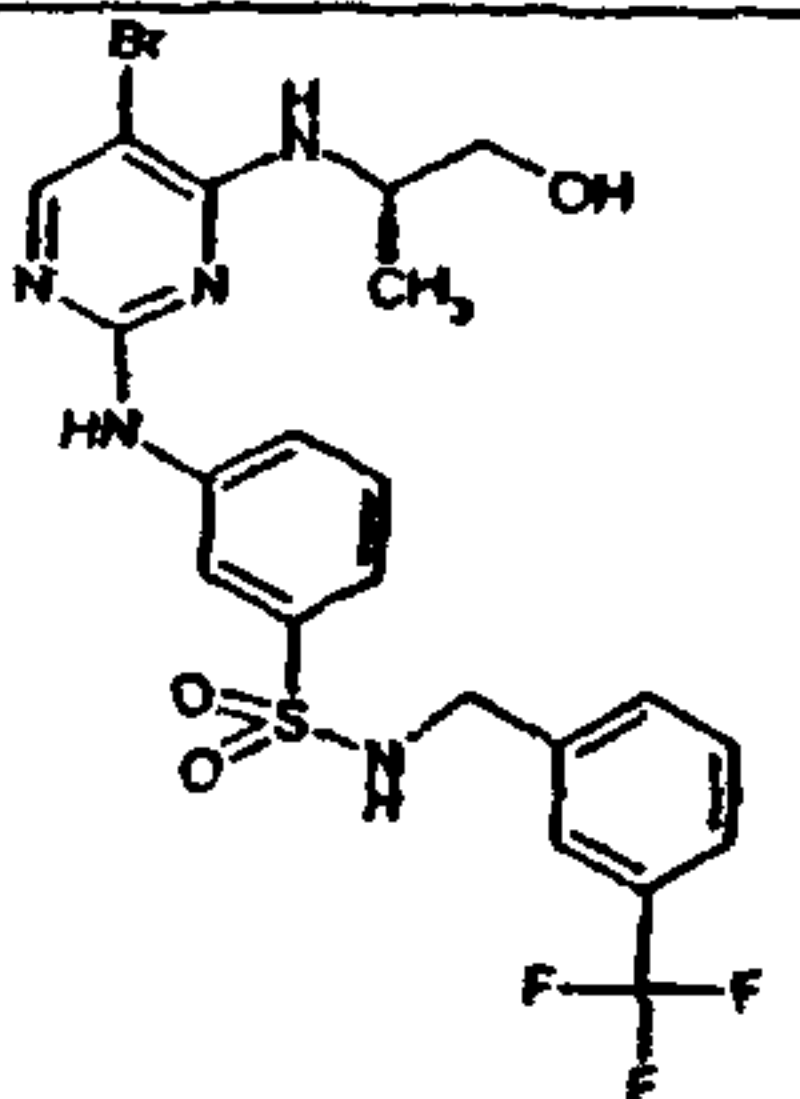
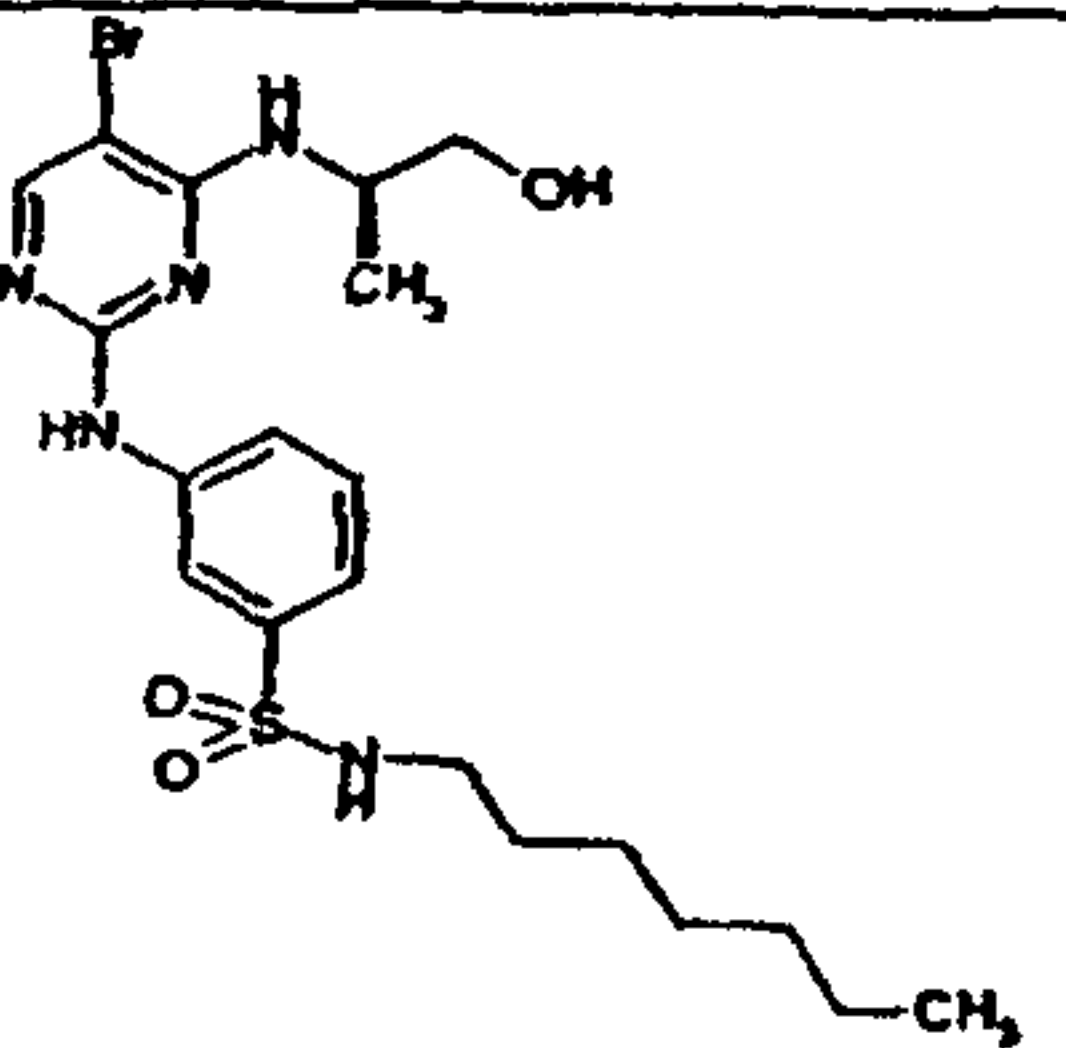
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
383		534,4762	534/536
384		541,4681	541/543
385		486,4322	486/488
386		500,459	500/502
387		501,4471	501/503
388		543,5275	543/545

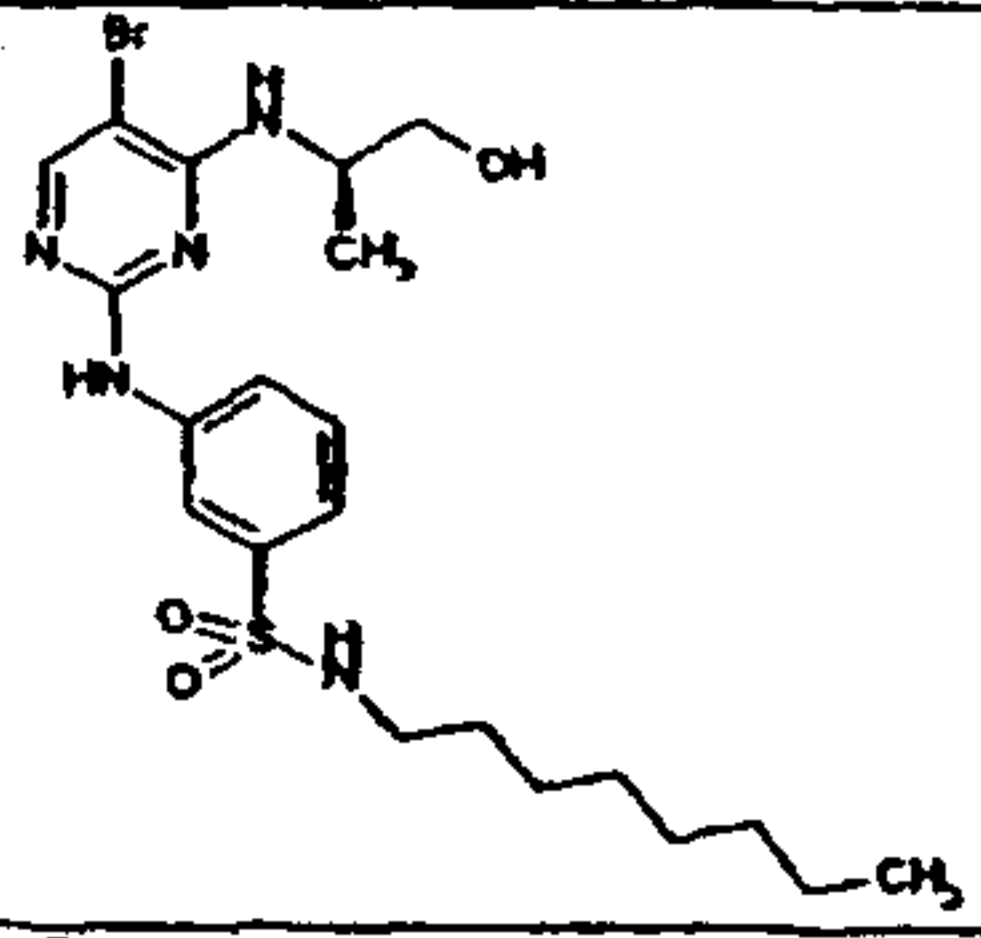
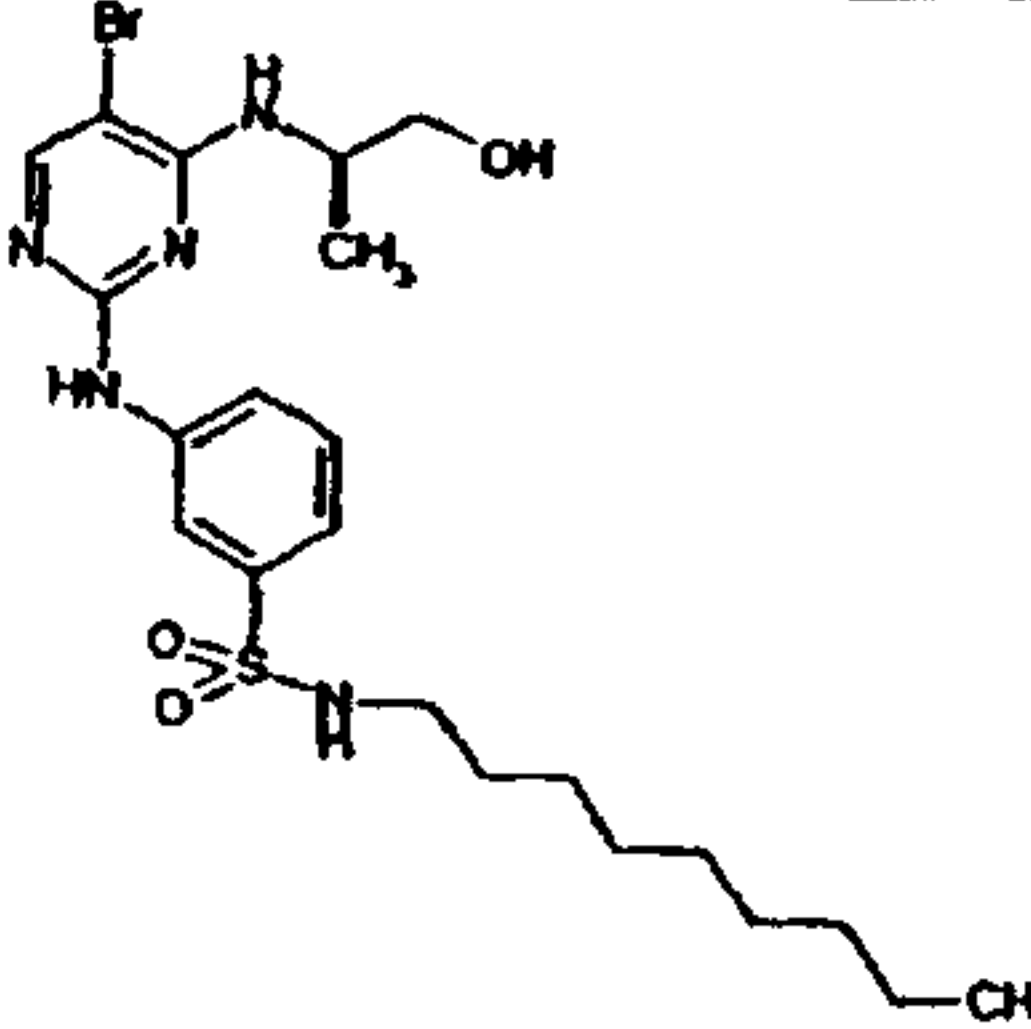
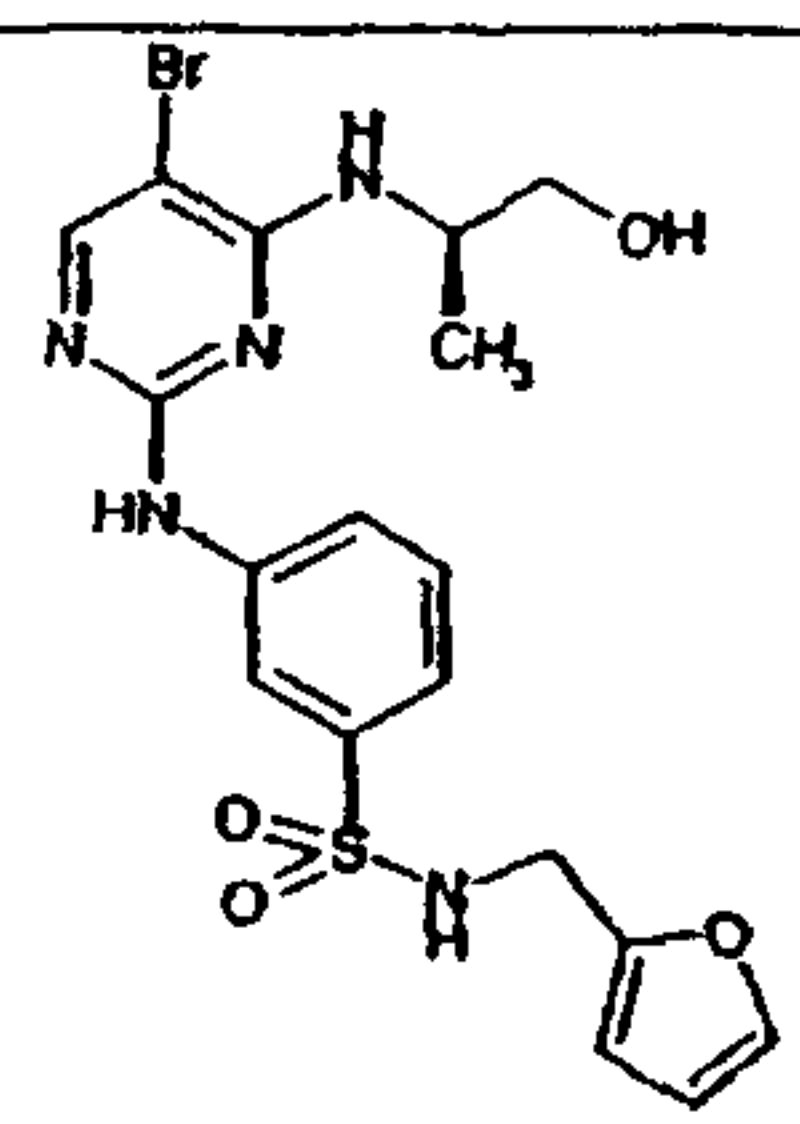
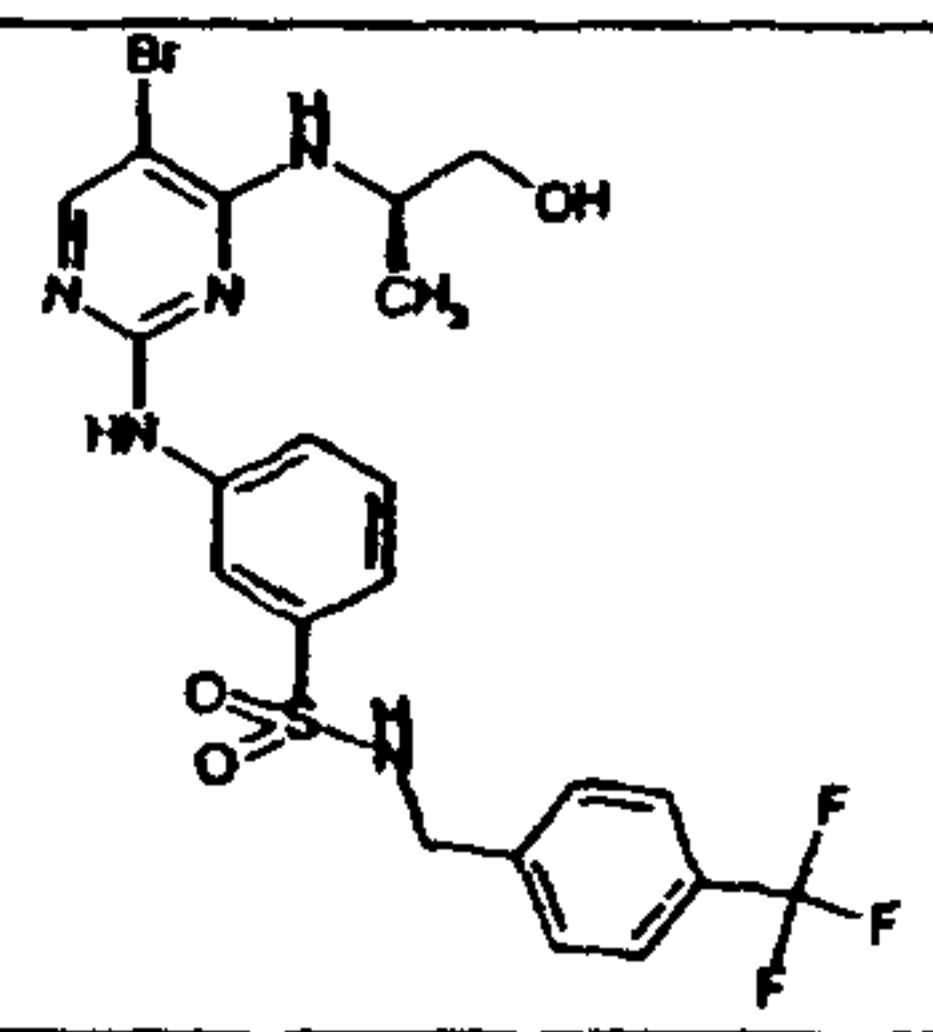
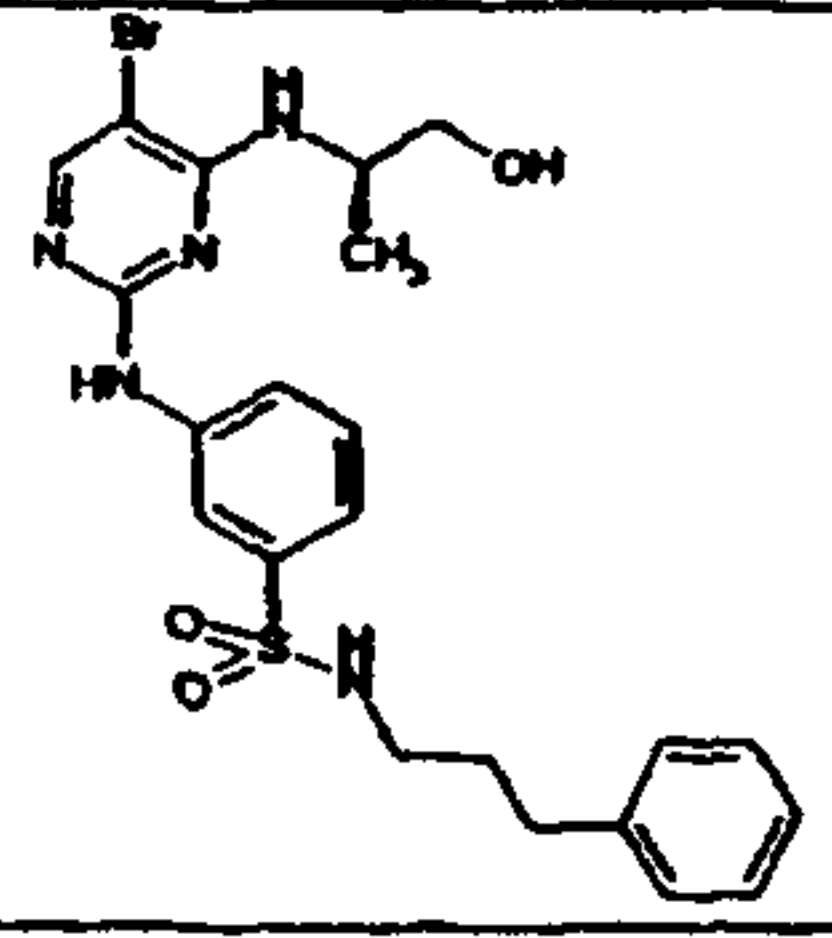
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
389		537,4801	537/539
390		520,4494	520/522
391		554,8945	554/556
392		510,4106	510/512
393		529,4571	529/531

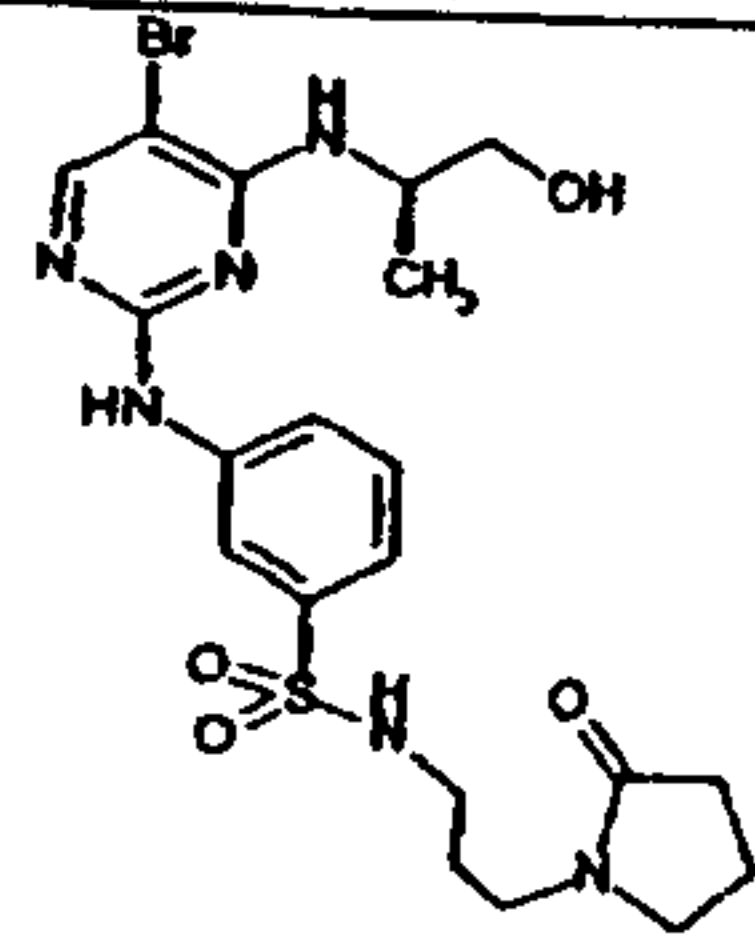
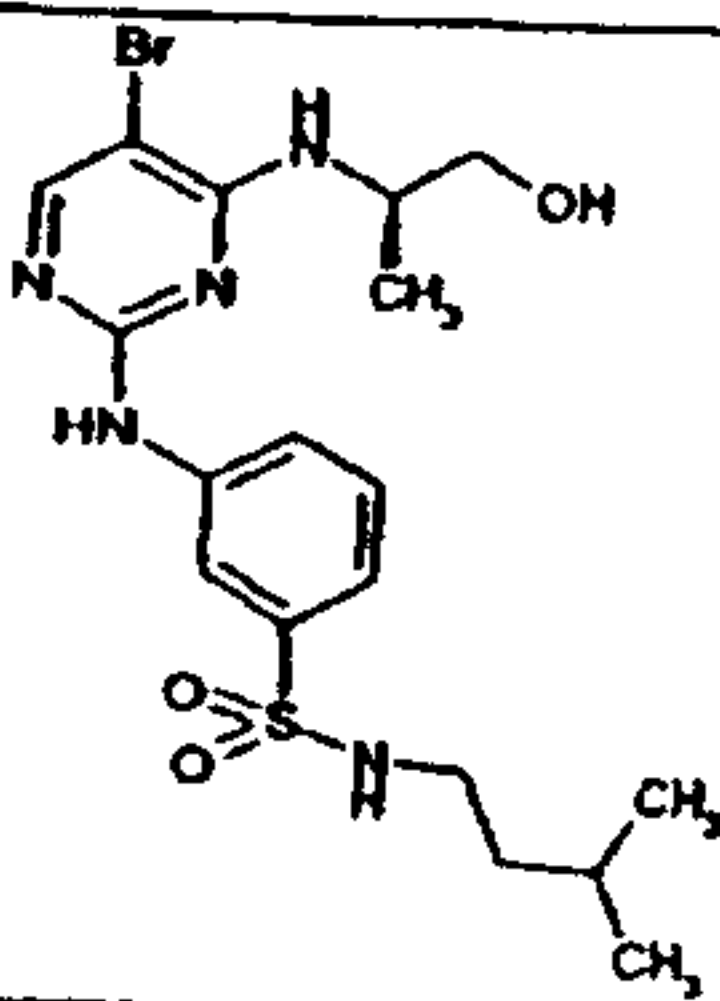
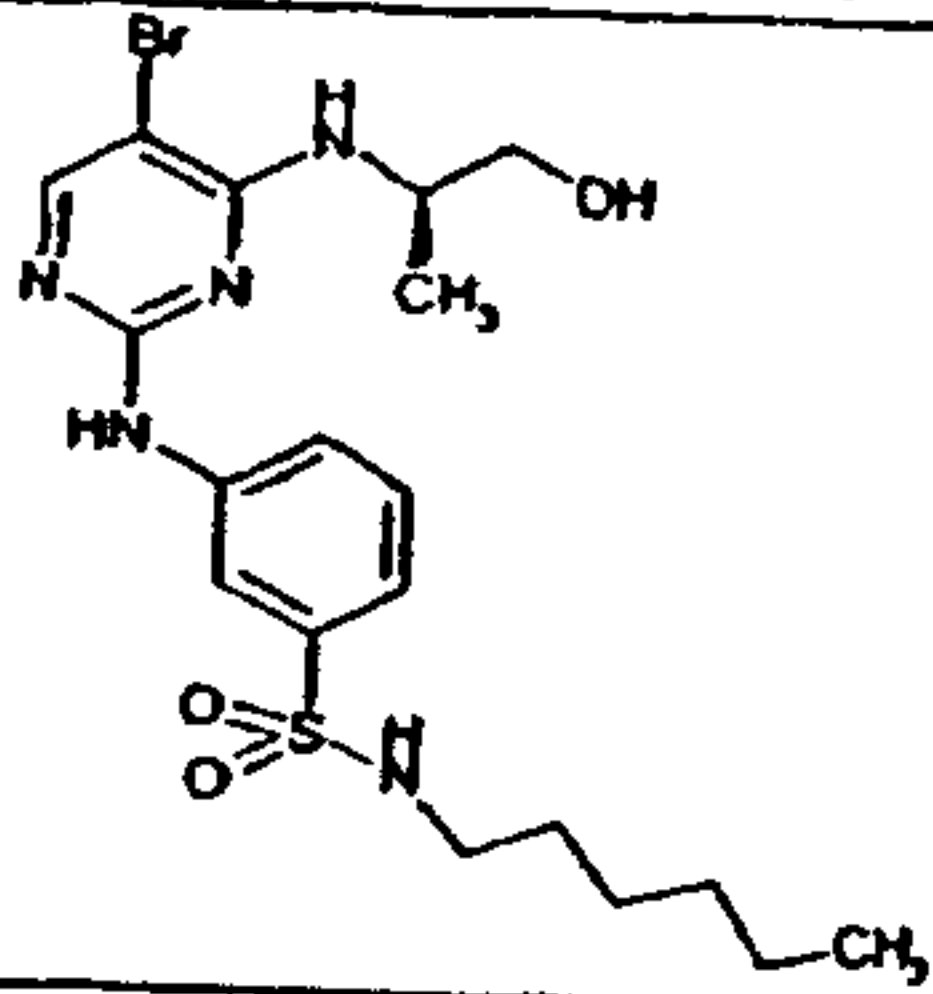
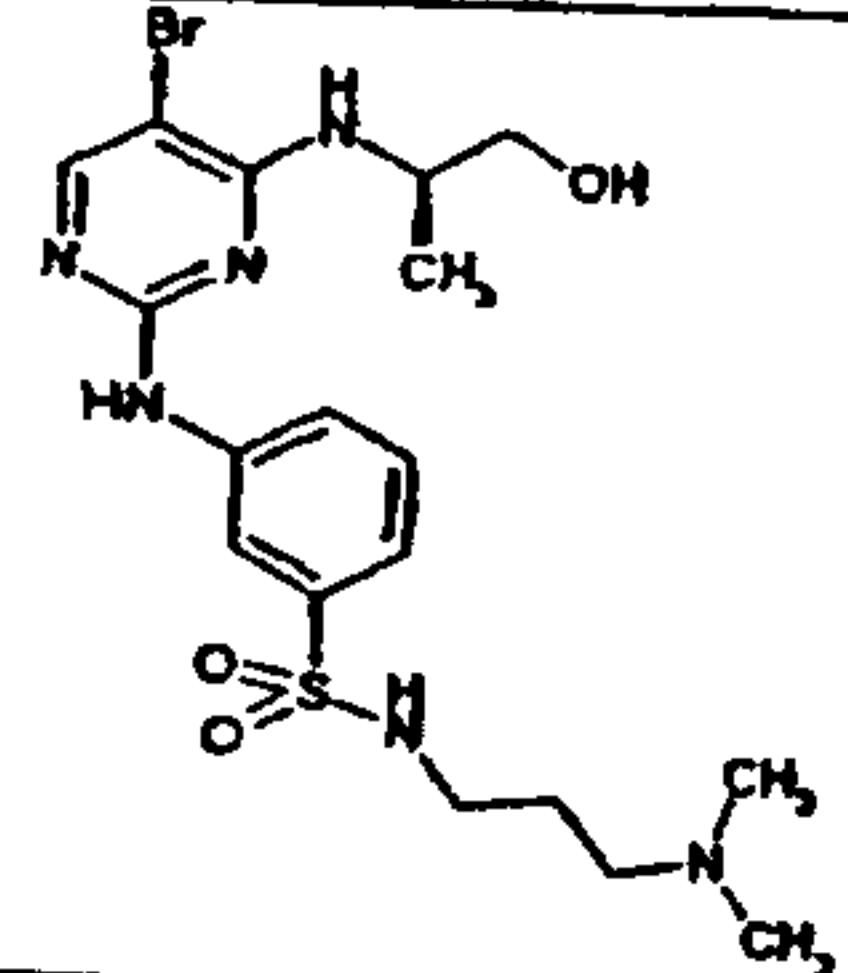
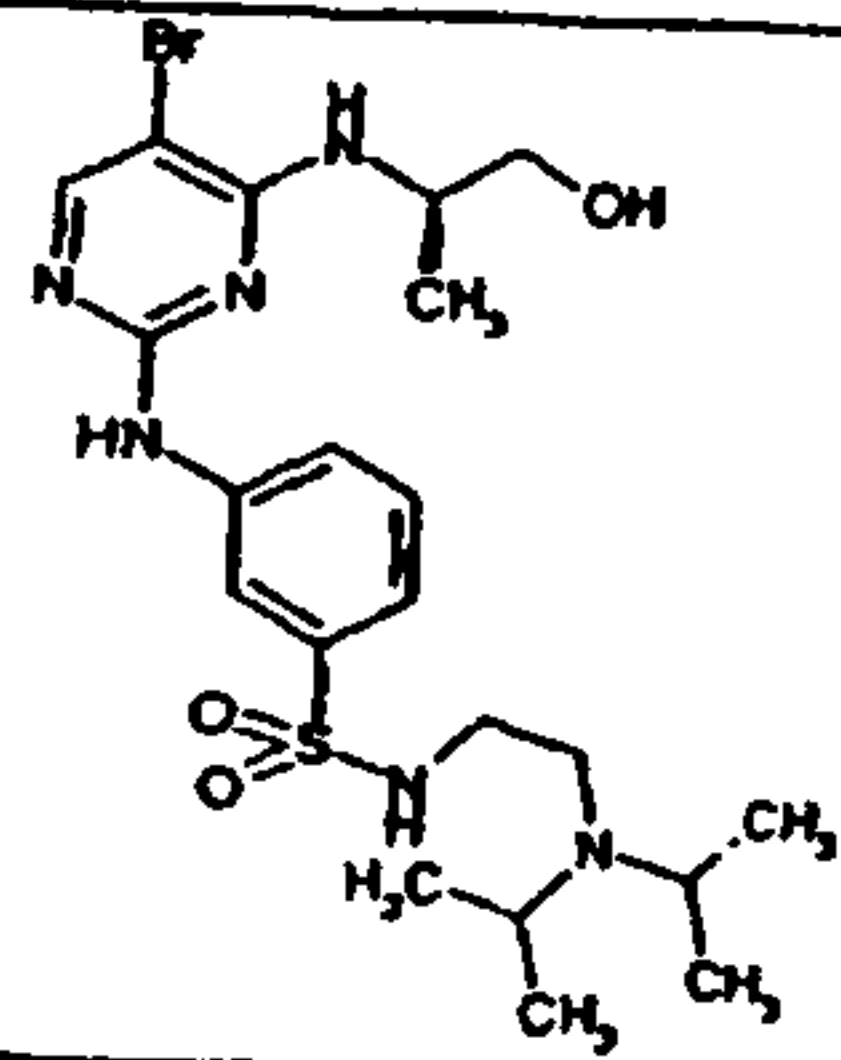
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
394		474,3776	474/476
395		512,4508	512/514
396		513,4581	513/515
397		527,4849	527/529
398		524,4127	524/526

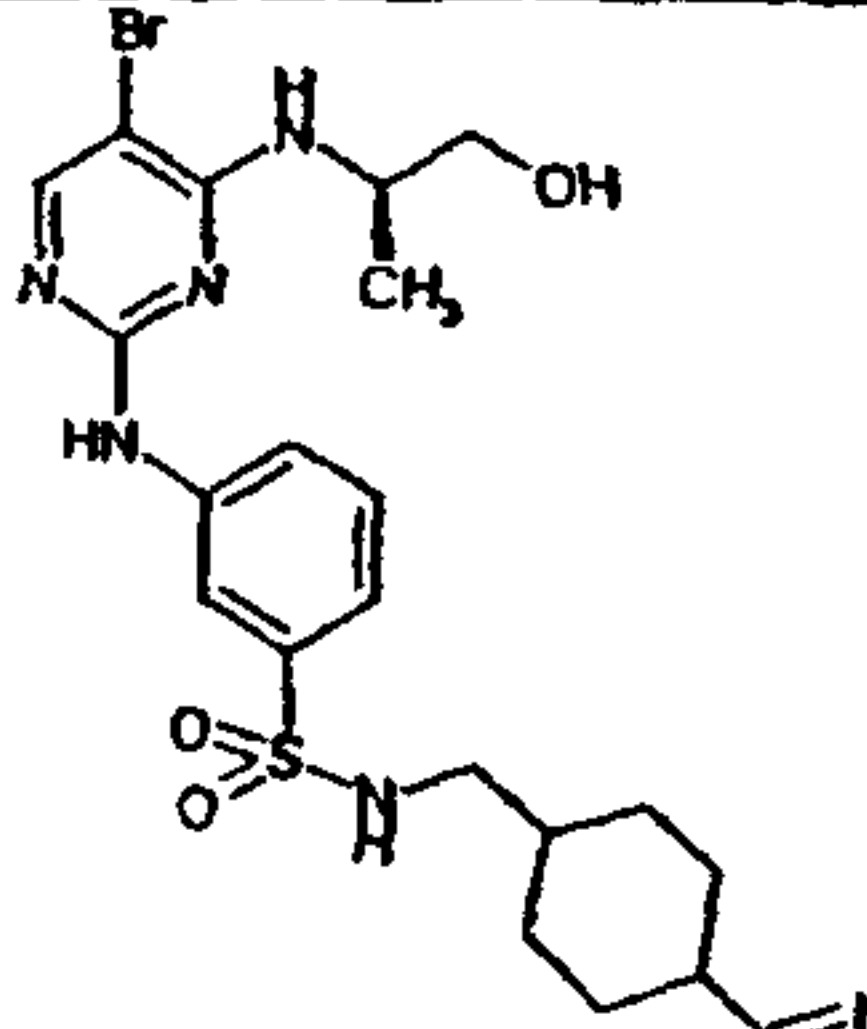
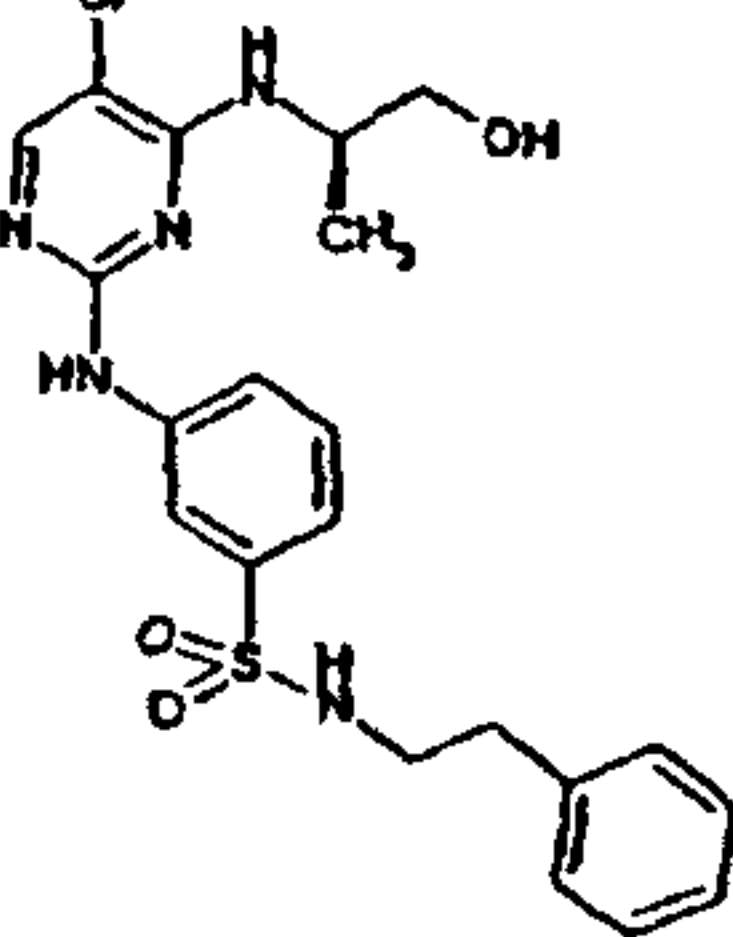
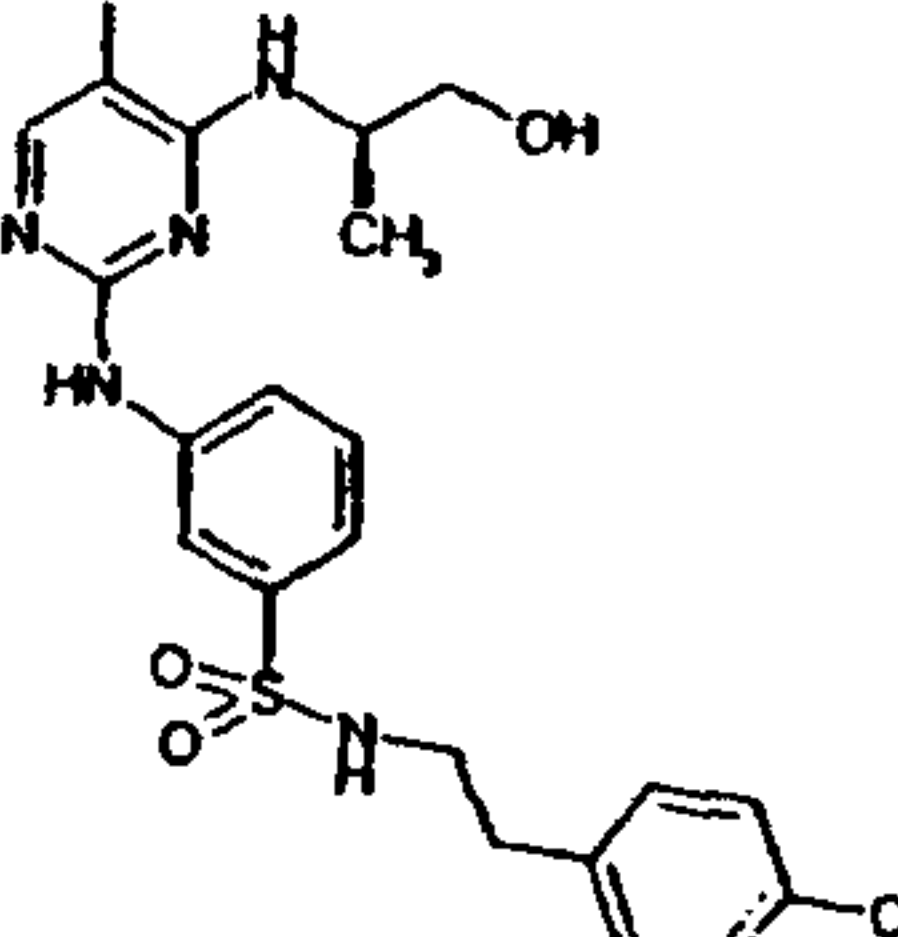
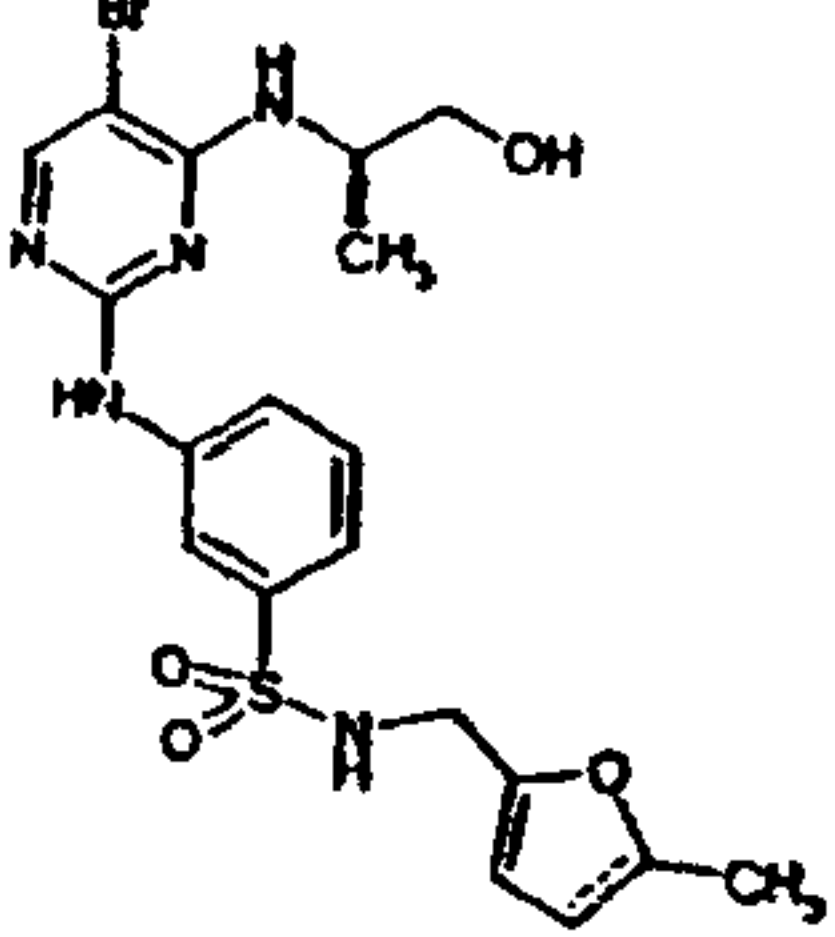
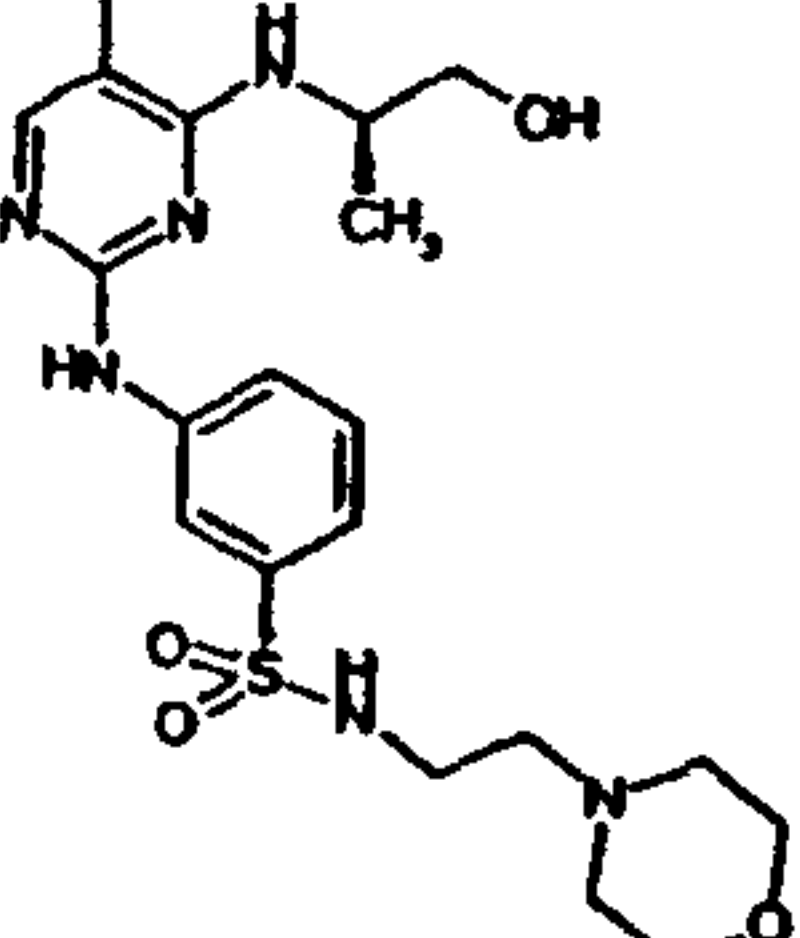
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
399		527,4849	527/529
400		507,4107	507/509
401		524,4127	524/526
402		507,4107	507/509
403		536,4484	526/538

Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
404		536,4484	536/538
405		599,5283	599/601
406		520,4494	520/522
407		529,4419	529/531
408		534,4762	534/536

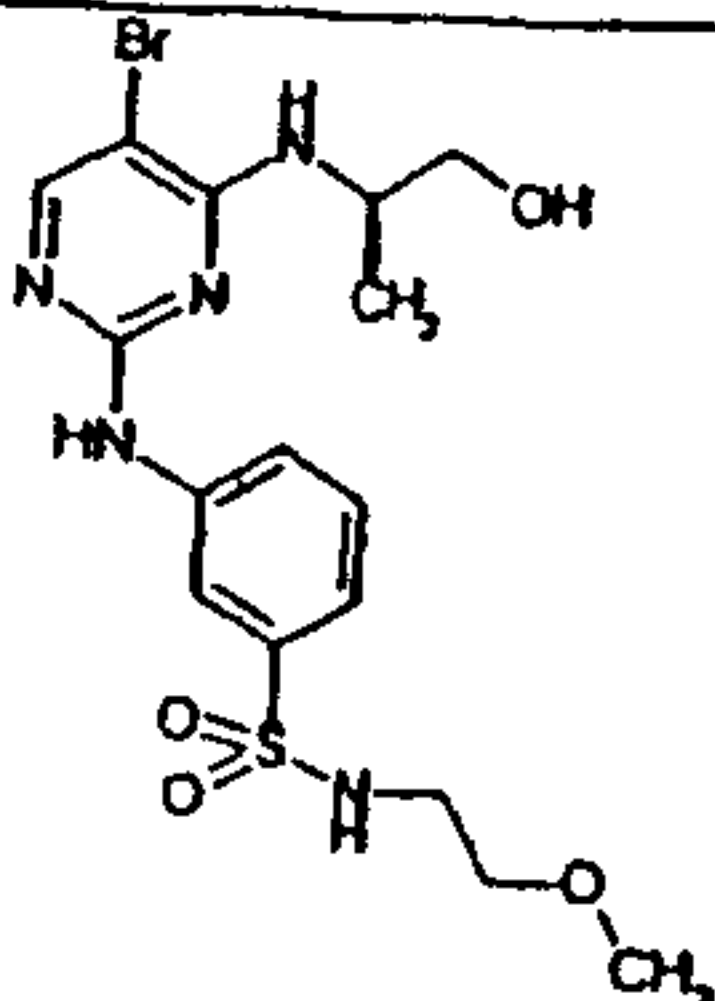
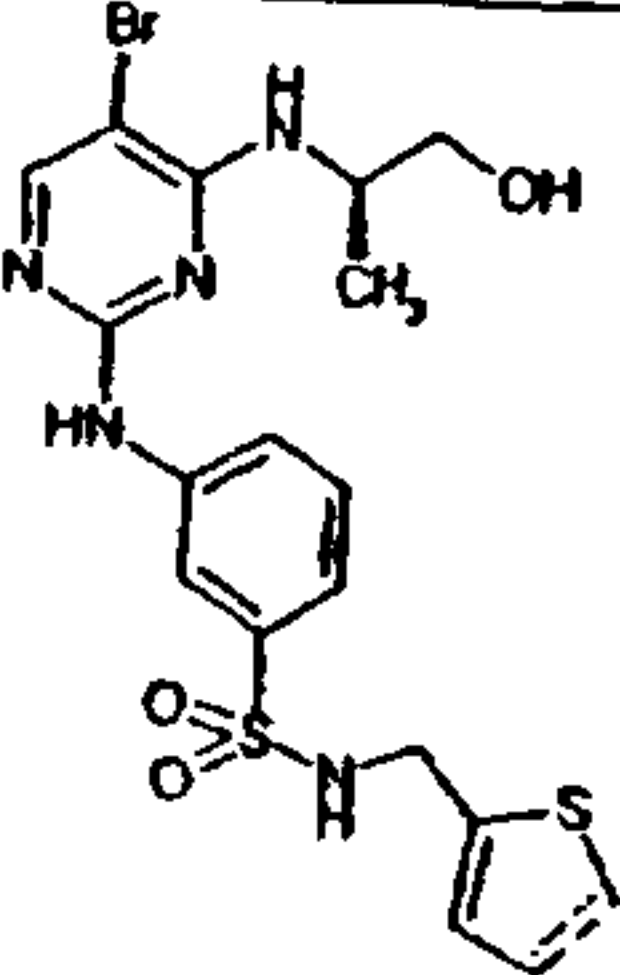
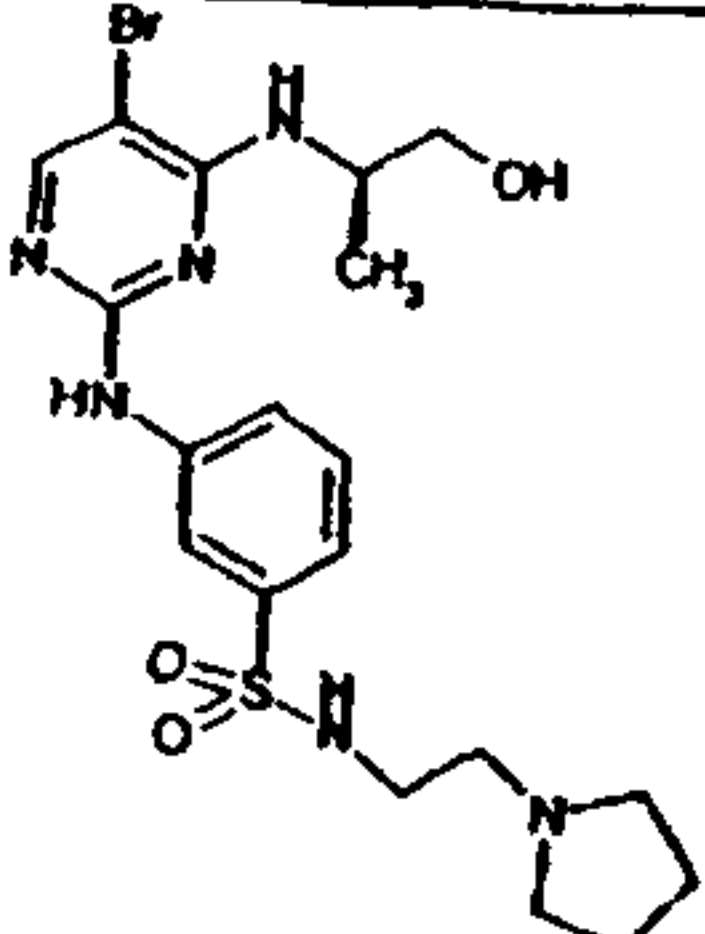
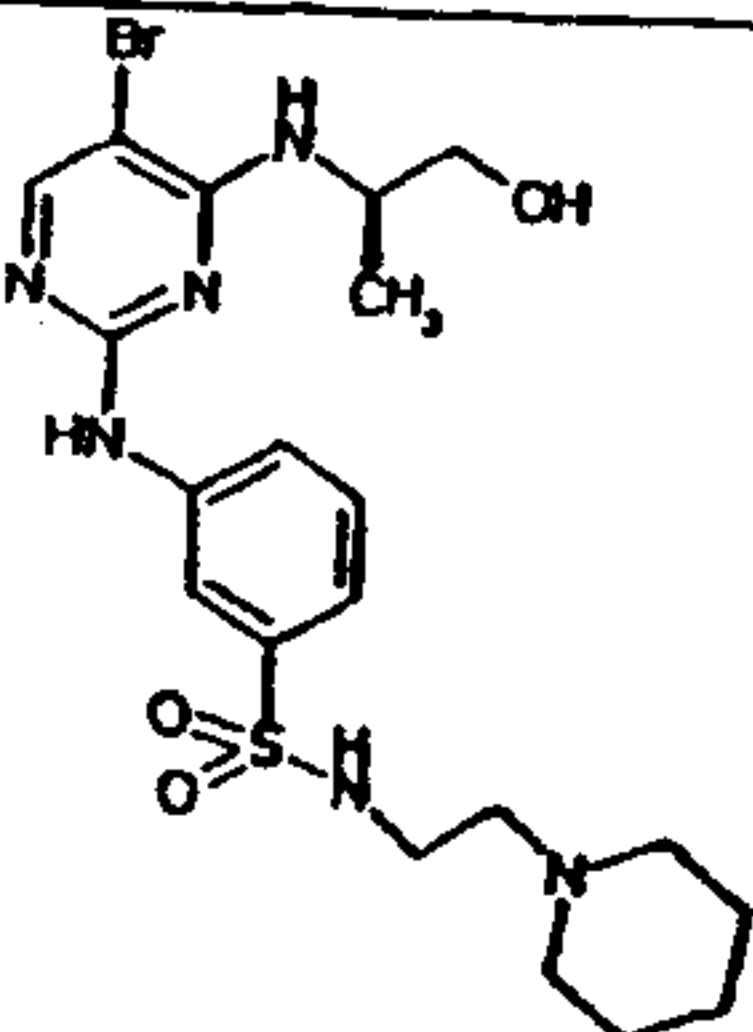
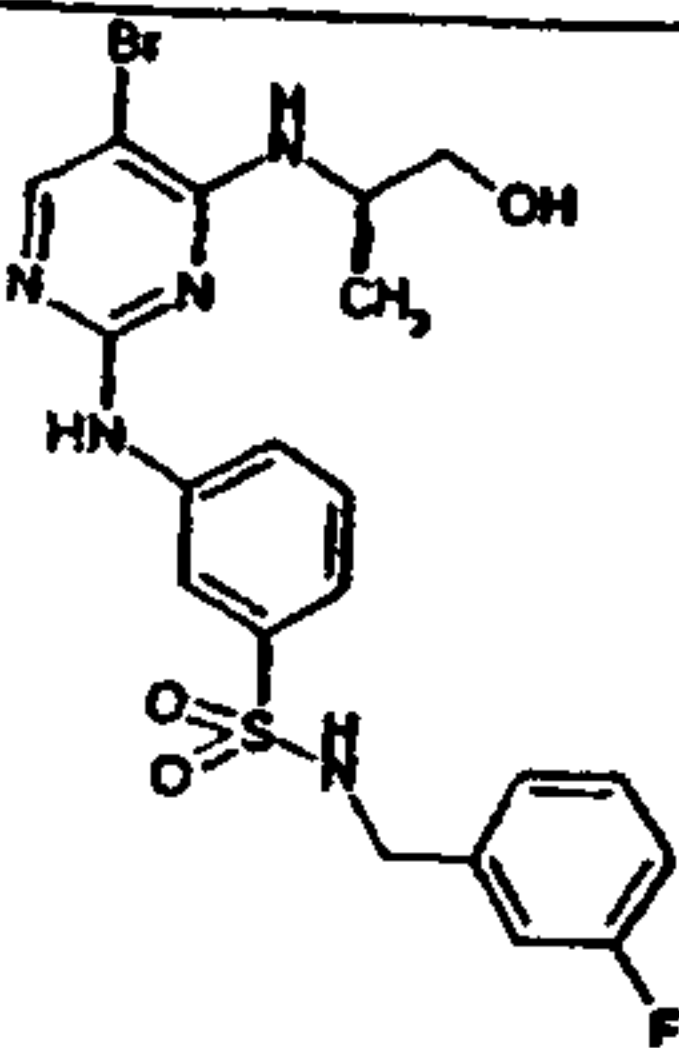
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
409		596,547	596/598
410		473,3935	473/475
411		510,4146	510/512
412		560,3929	560/562
413		500,459	500/502

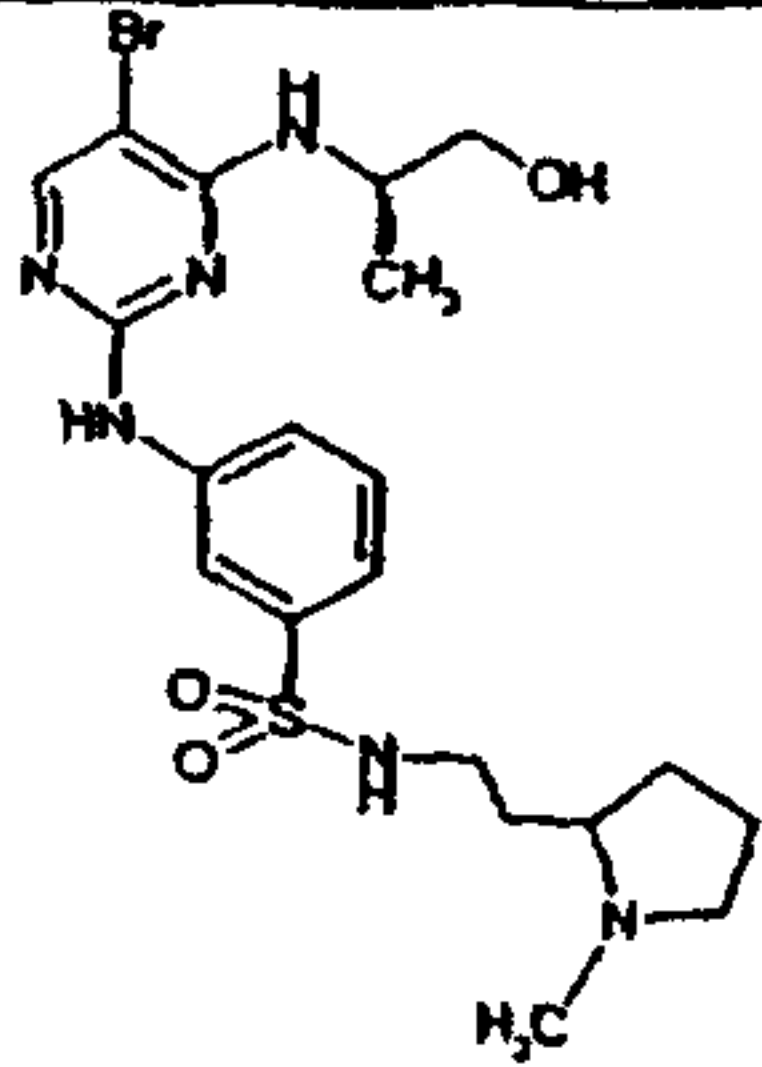
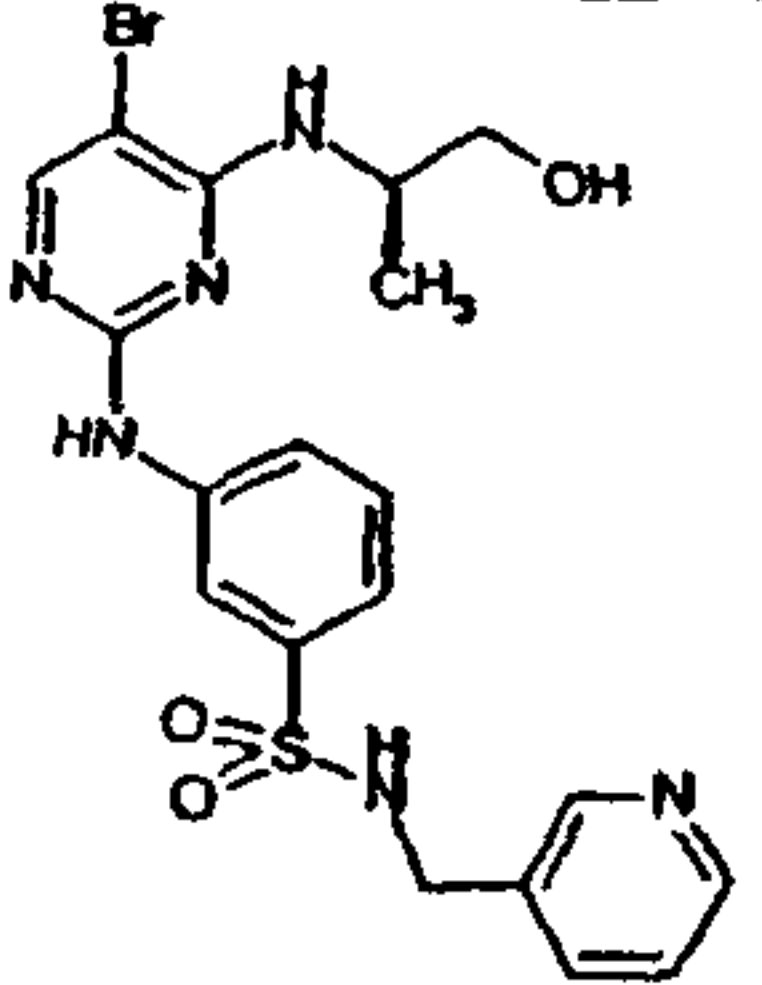
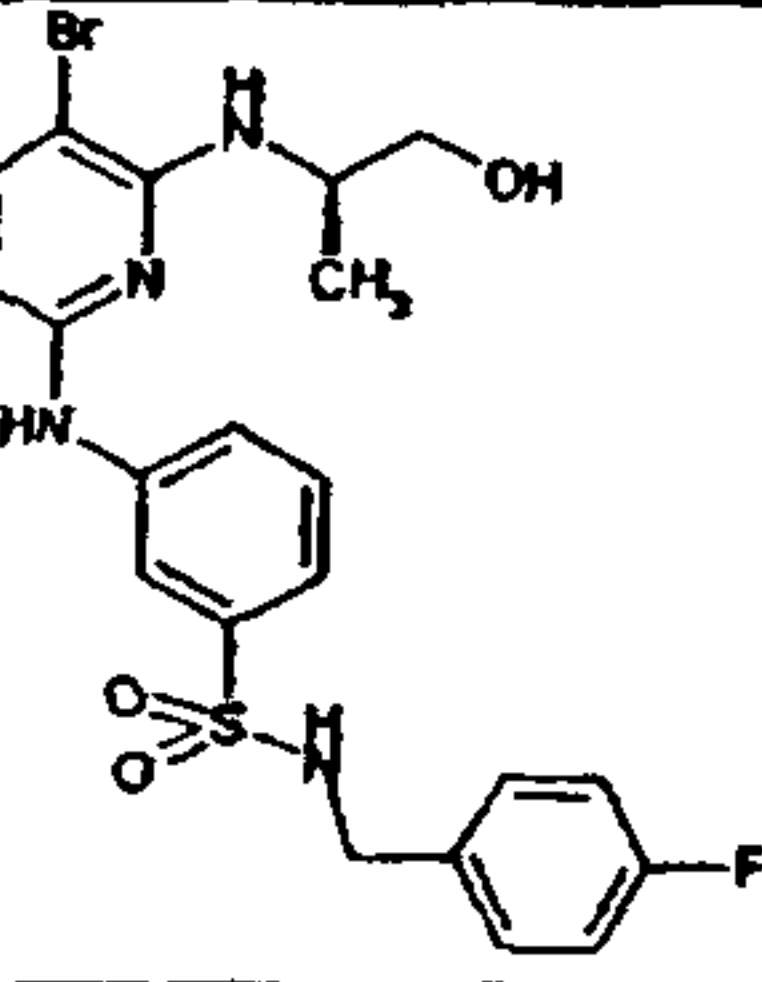
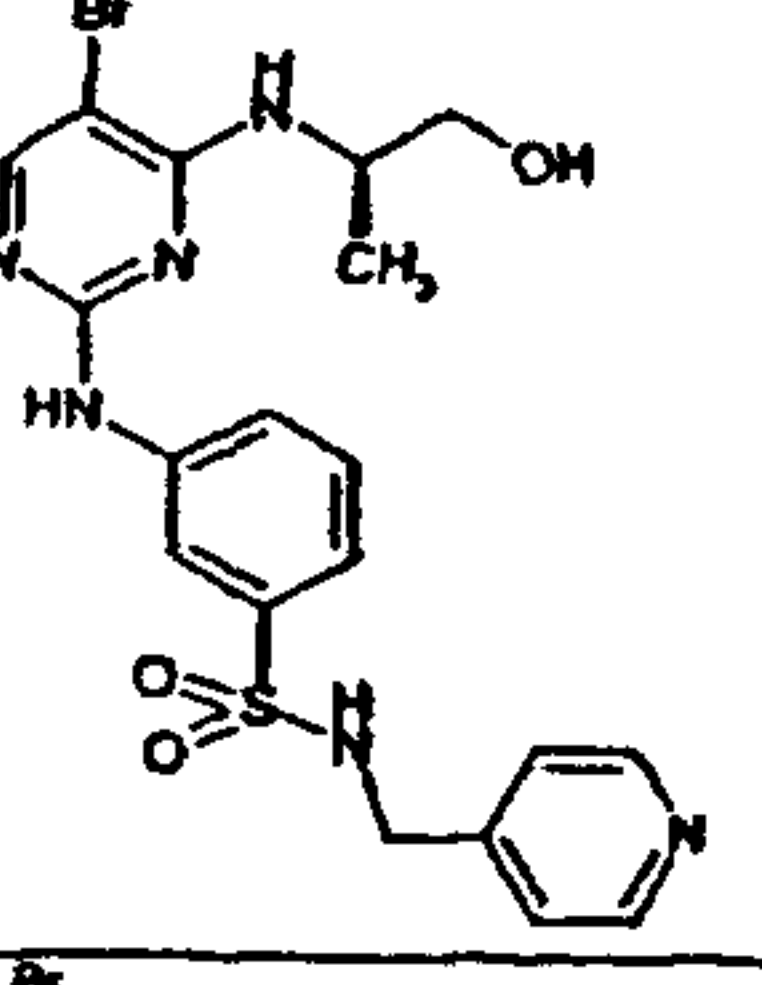
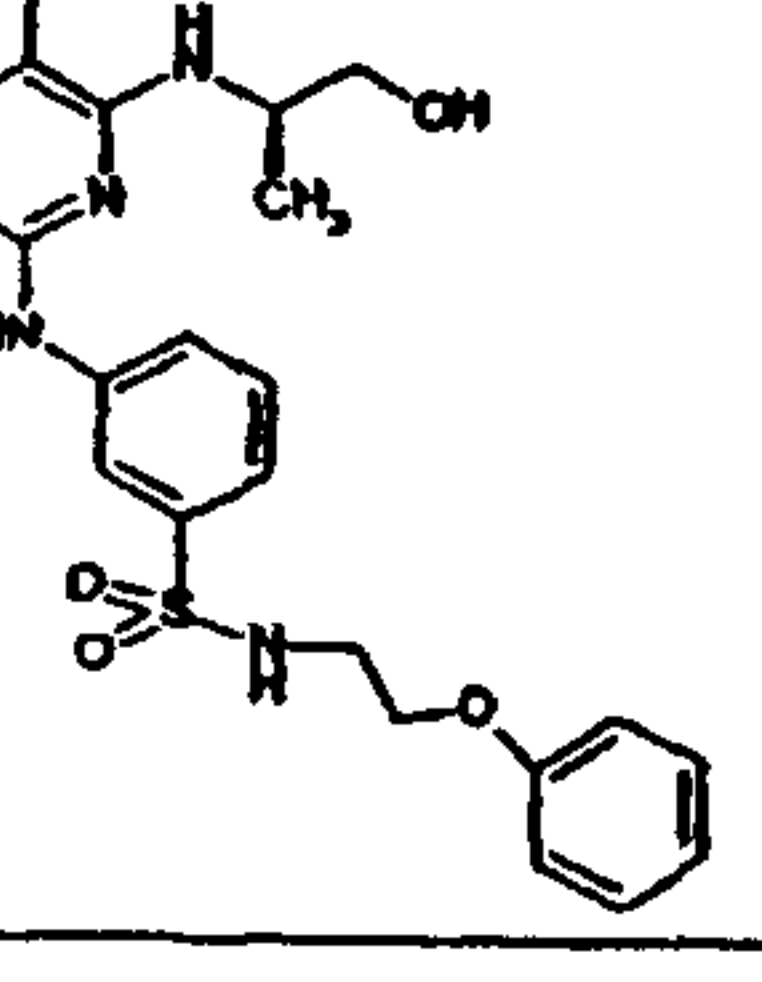
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
414		514,4858	514/516
415		528,5126	528/530
416		482,357	482/484
417		560,3929	560/562
418		520,4494	520/522

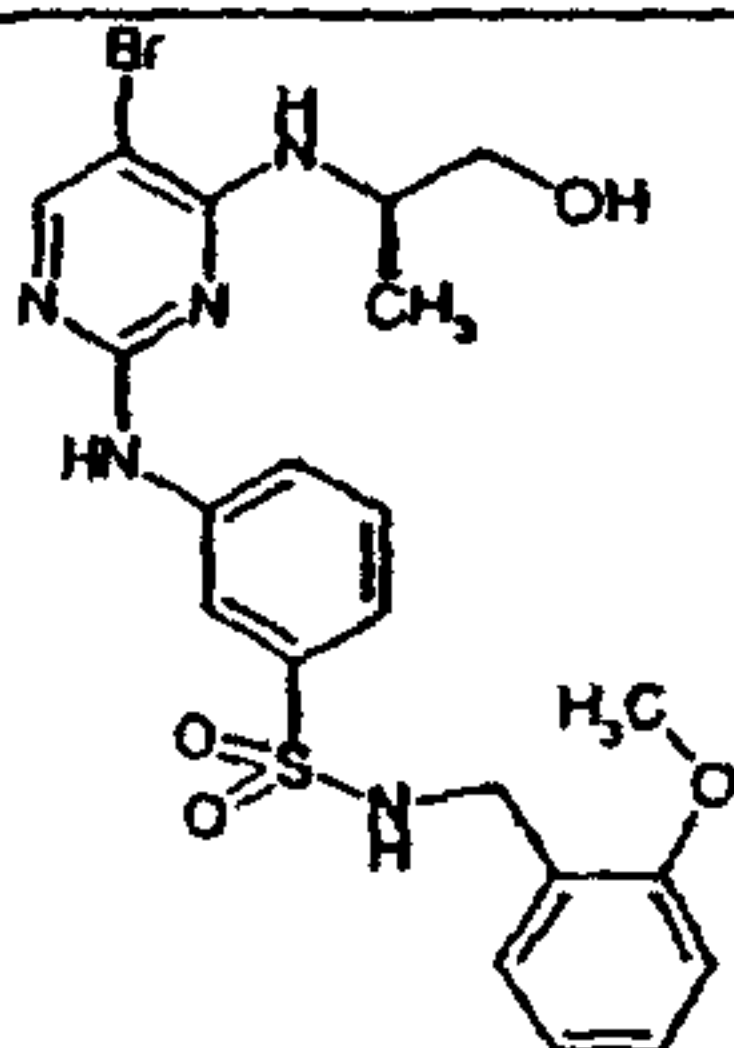
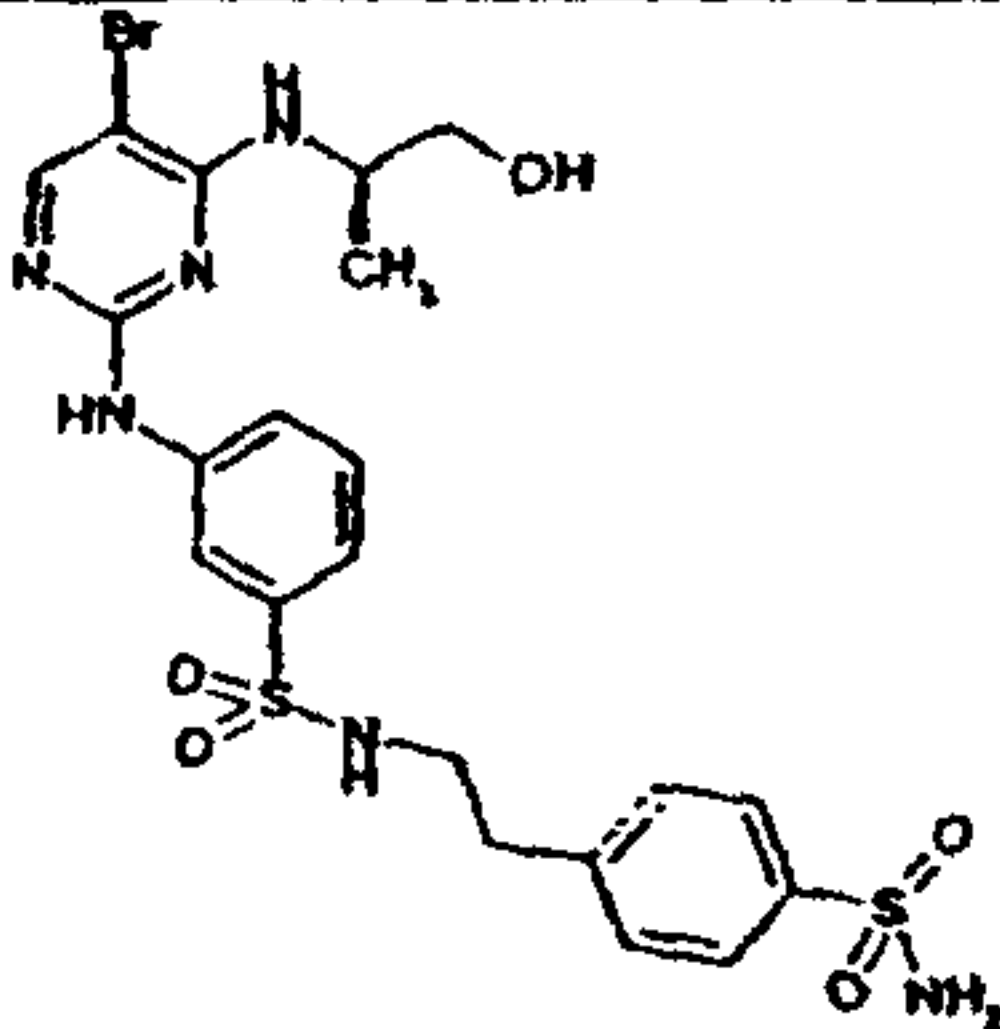
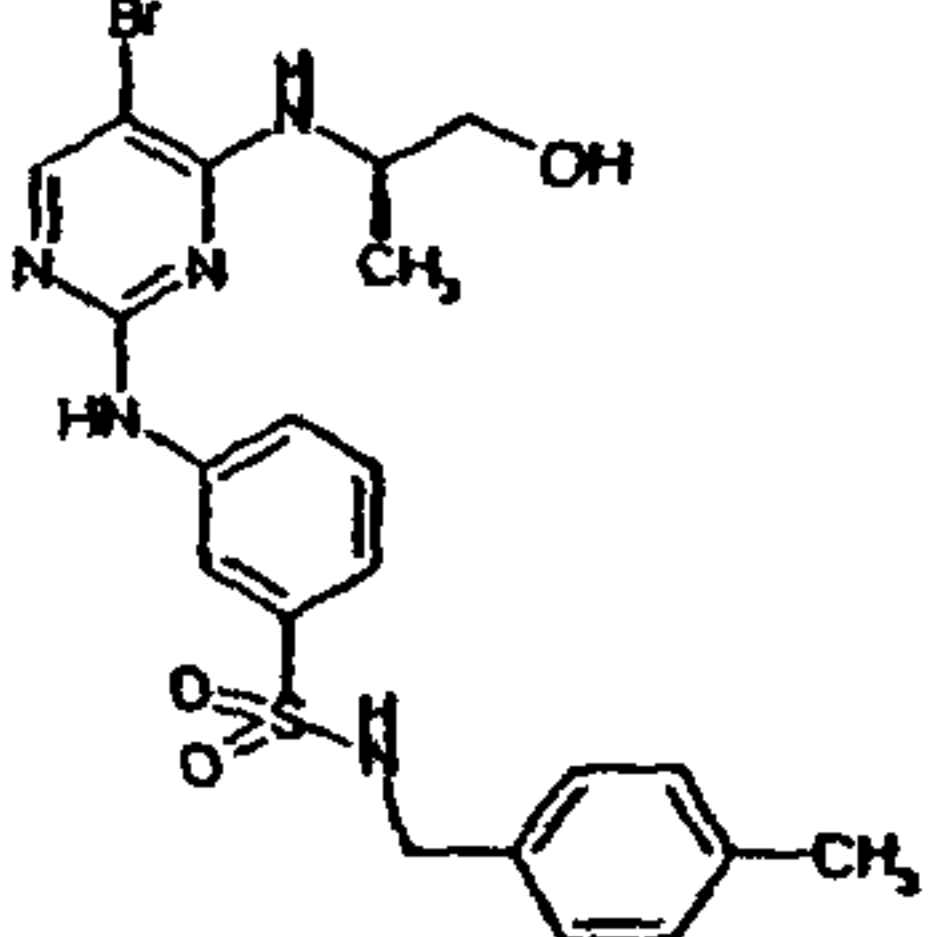
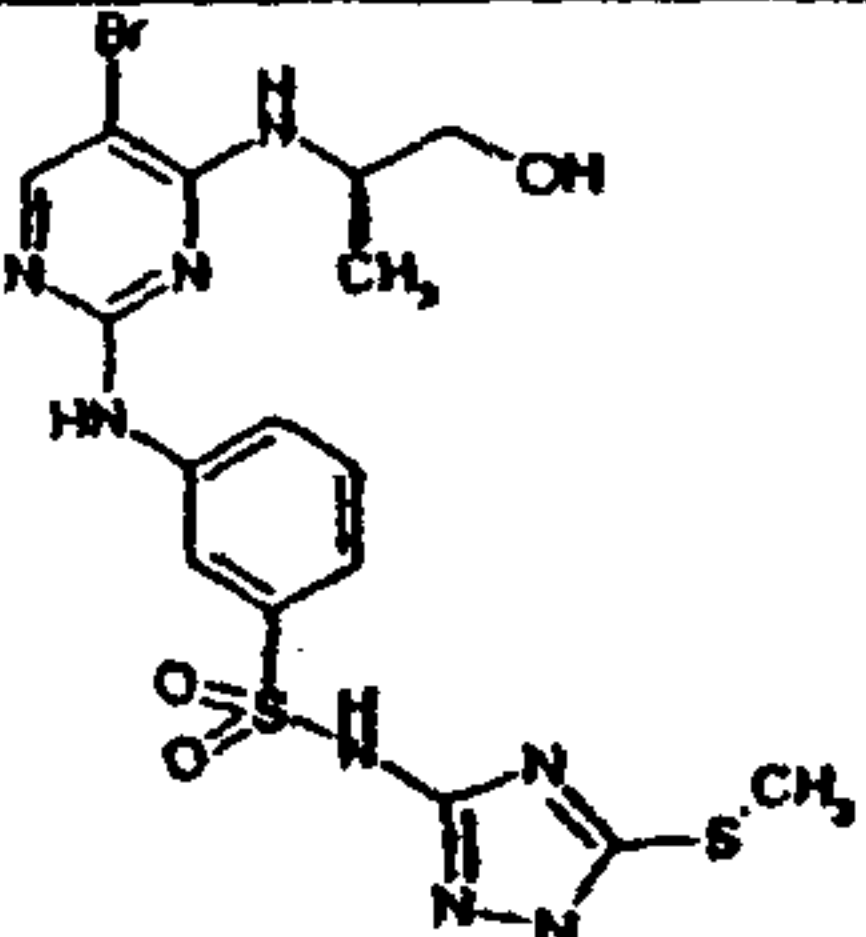
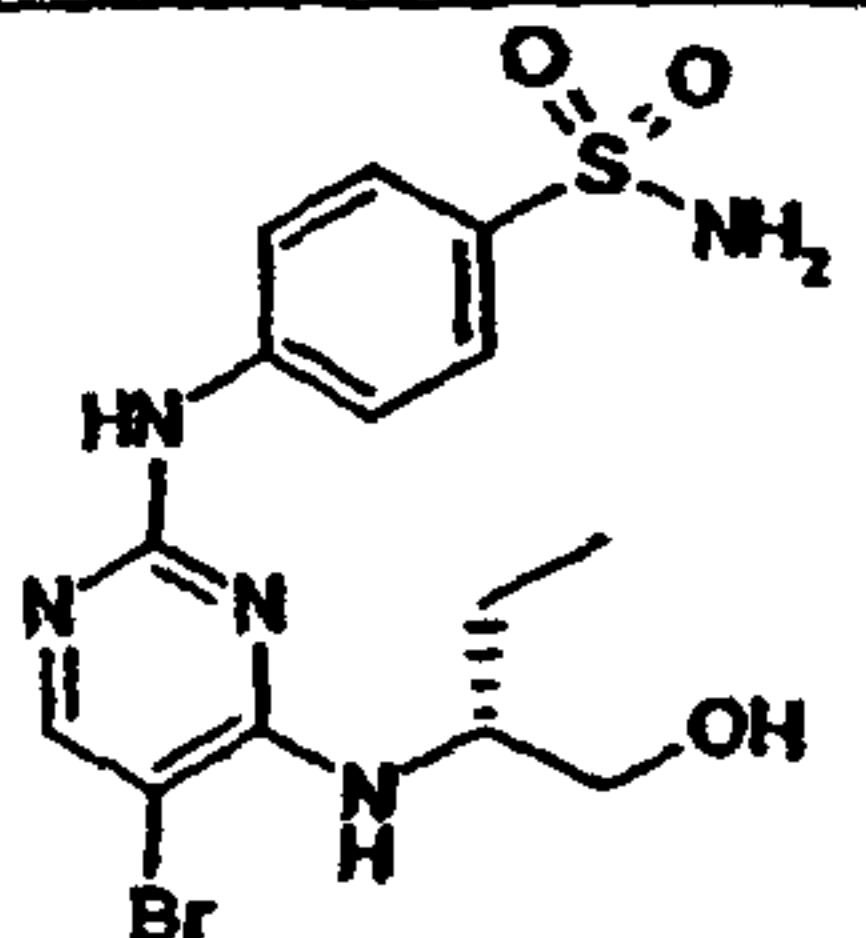
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
419		527,4413	527/529
420		472,4054	472/474
421		486,4322	486/488
422		487,4203	487/489
423		529,5007	529/531

Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
424		523,4532	523/525
425		506,4226	506/508
426		540,8677	540/542
427		496,3838	496/498
428		515,4303	515/517

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Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
429		460,3508	460/462
430		498,424	498/500
431		499,4313	499/501
432		513,4581	513/515
433		510,3859	510/512

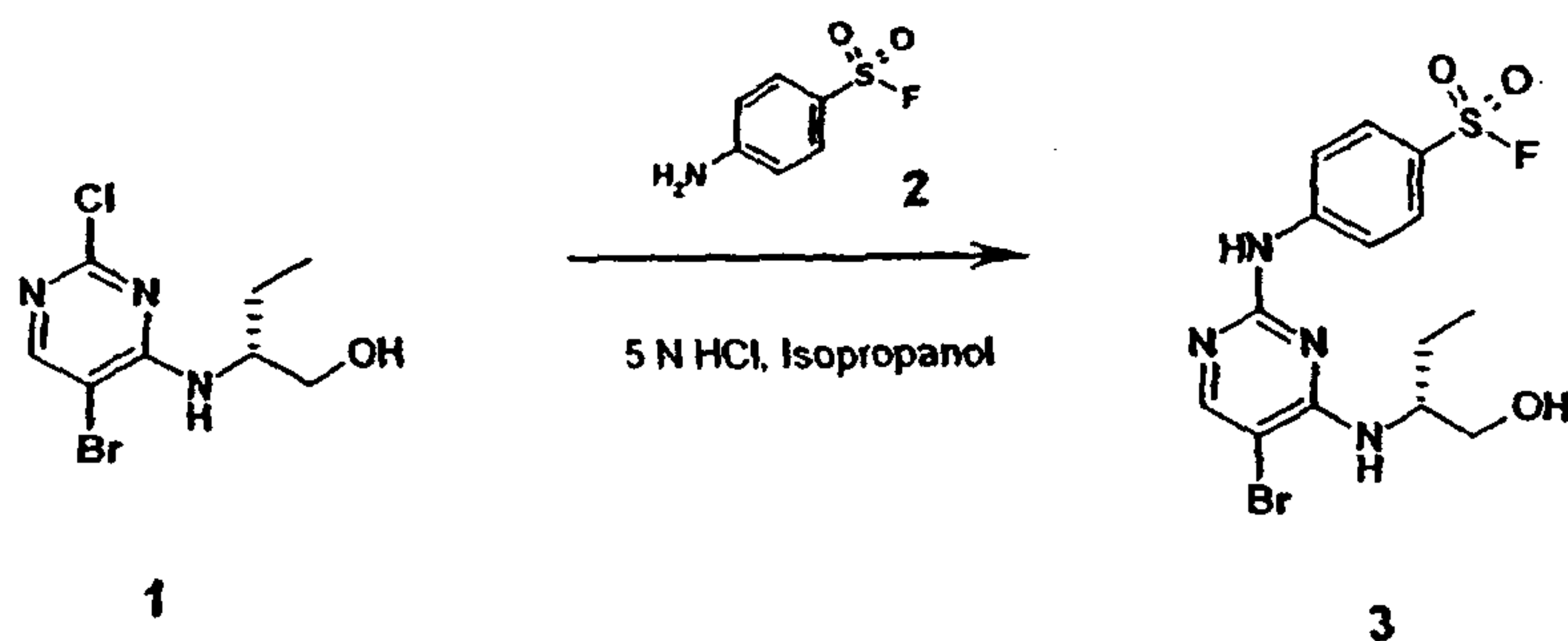
Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
434		513,4581	513/515
435		493,3839	493/495
436		510,3859	510/512
437		493,3839	493/495
438		522,4216	522/524

Beispiel-Nr.	Verbindung	Molgewicht	ESI-MS
439		522,4216	522/524
440		585,5015	585/587
441		506,4226	506/508
442		515,4151	515/517
443 *)		416,30	416/418

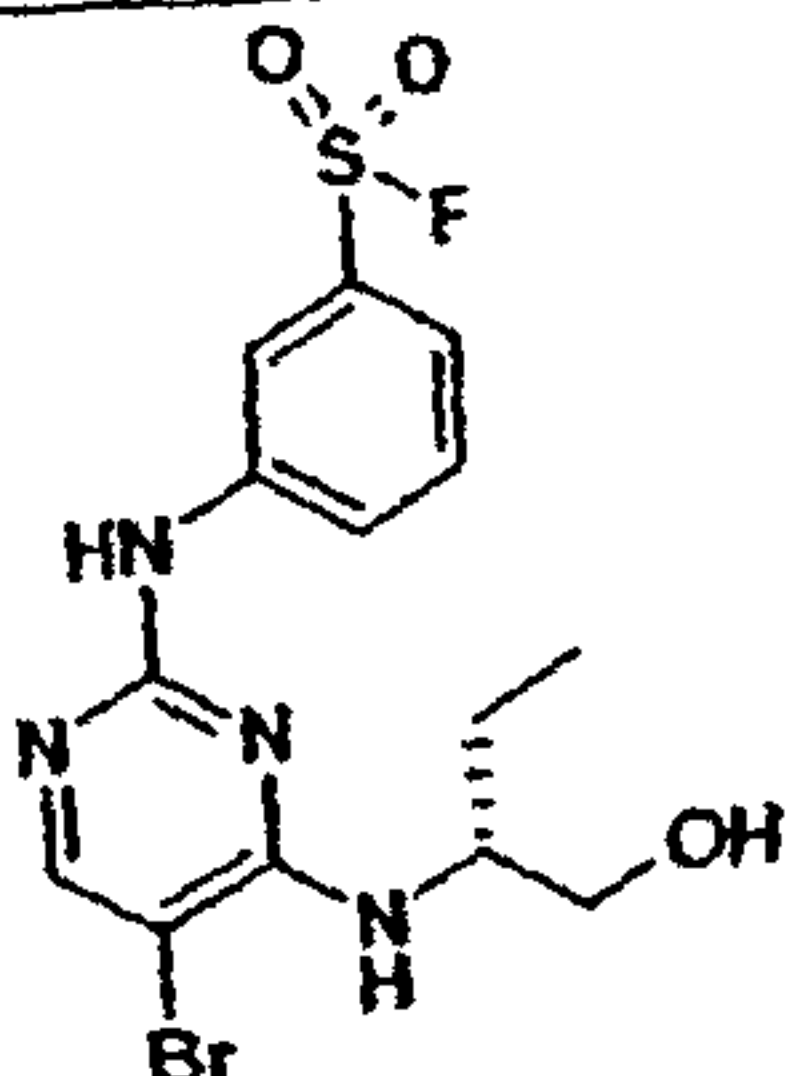
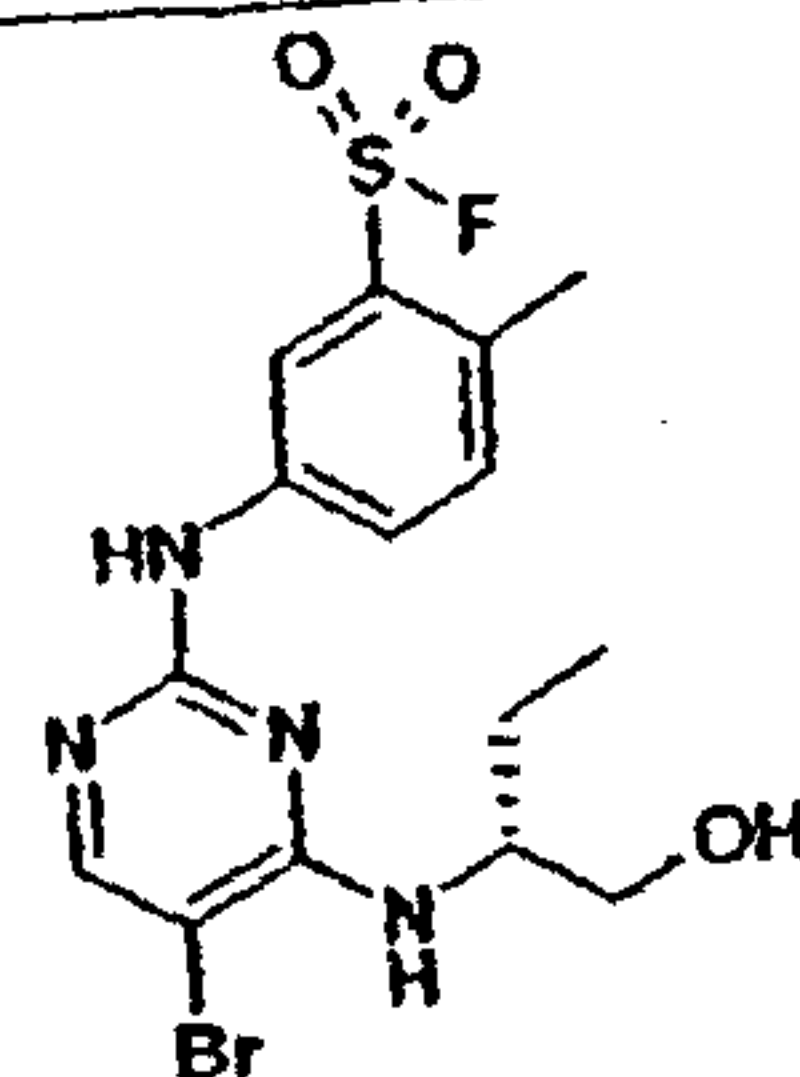
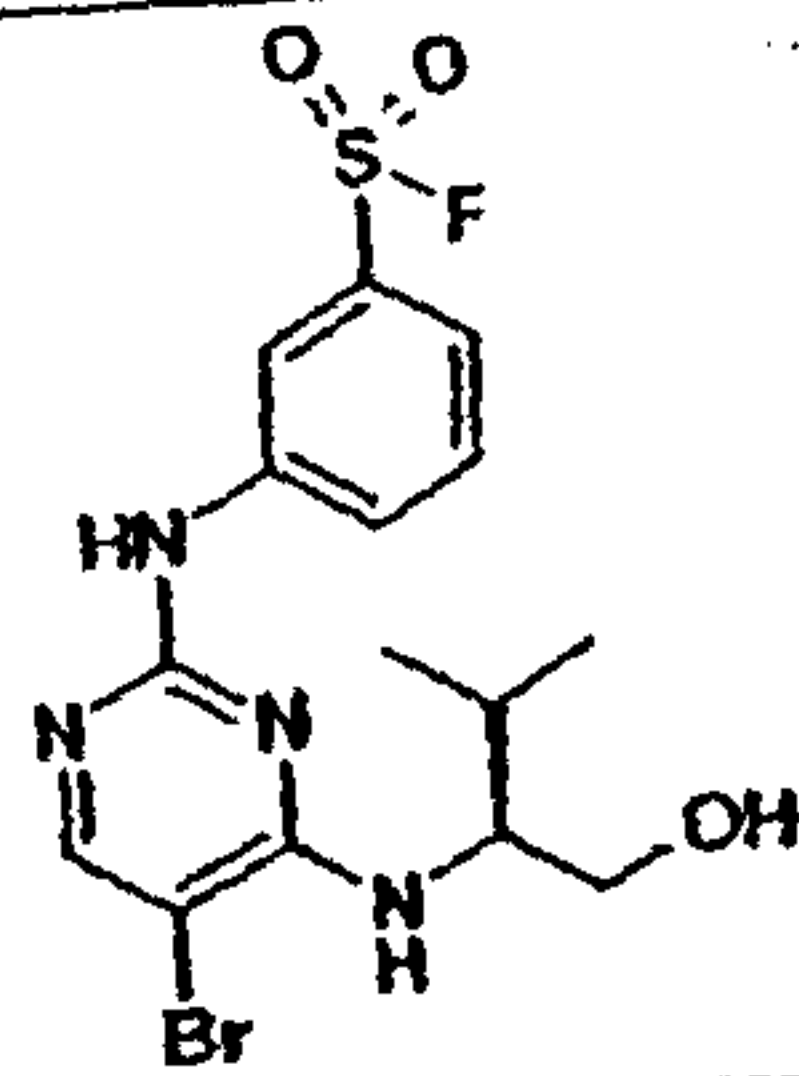
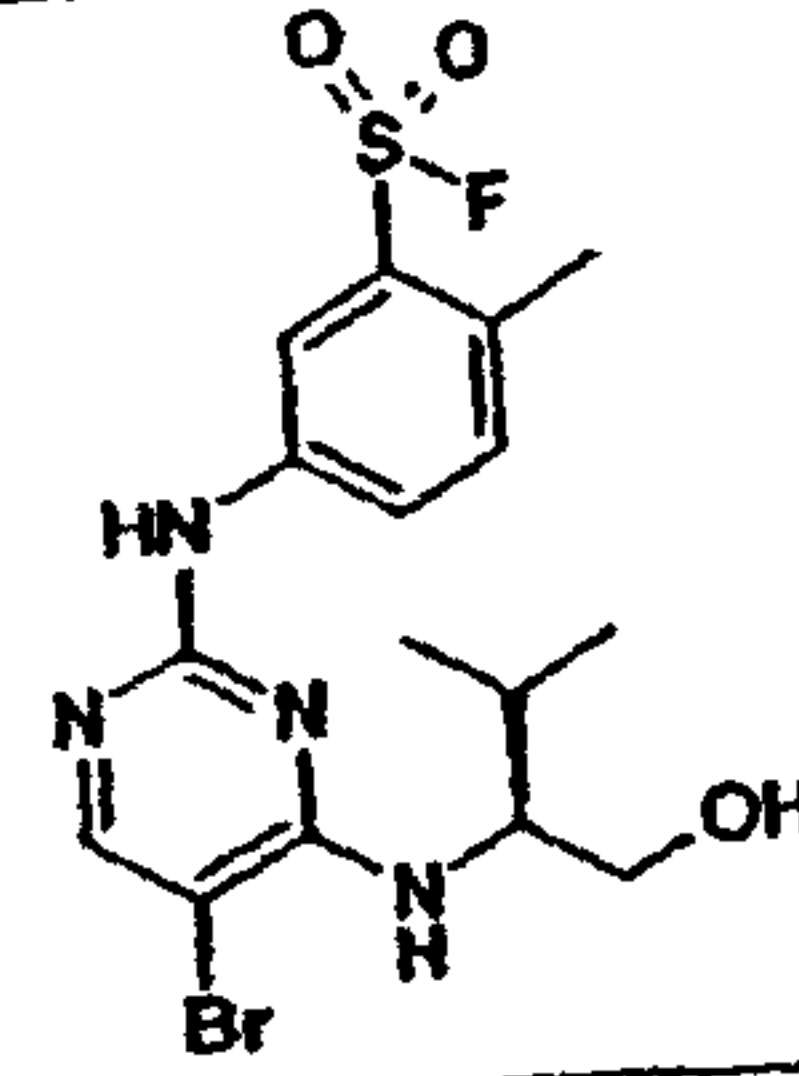
*) produced in accordance with the described sulfonamide process

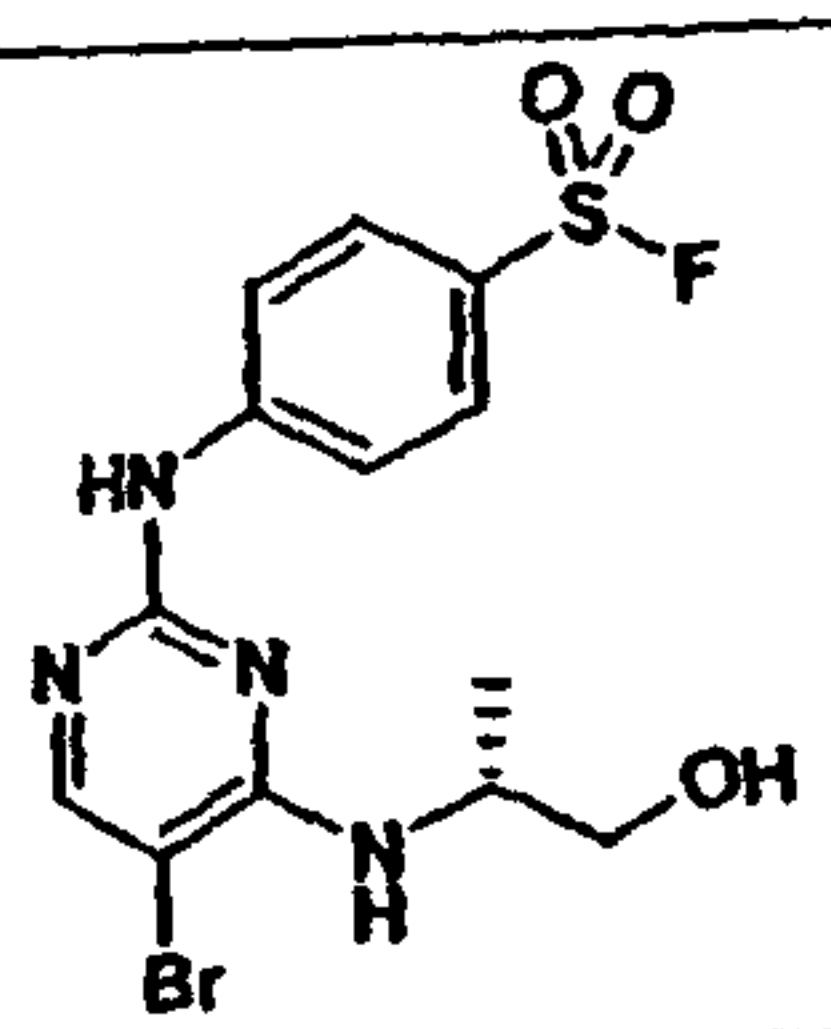
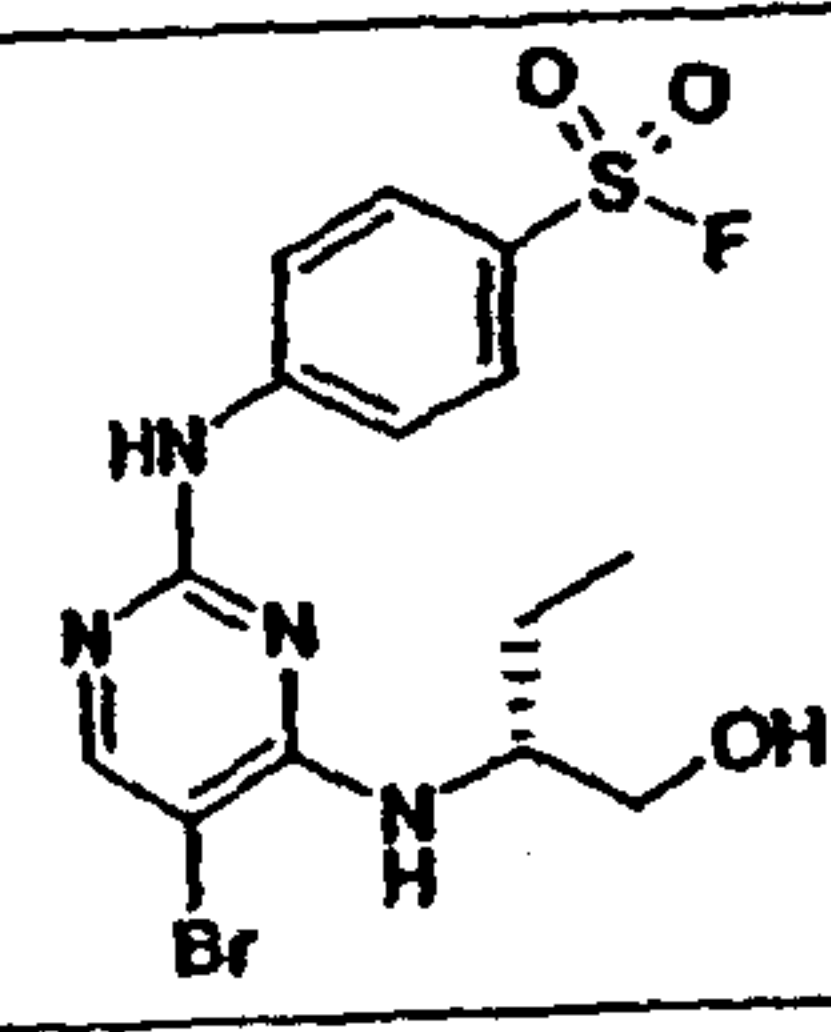
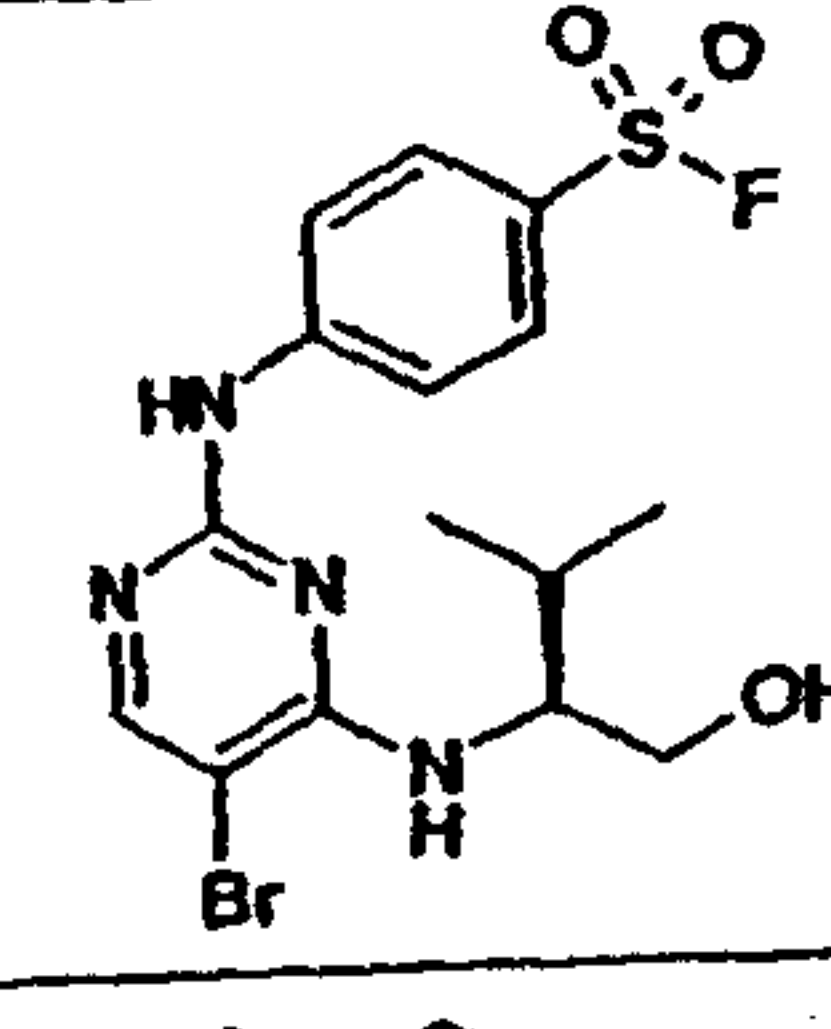
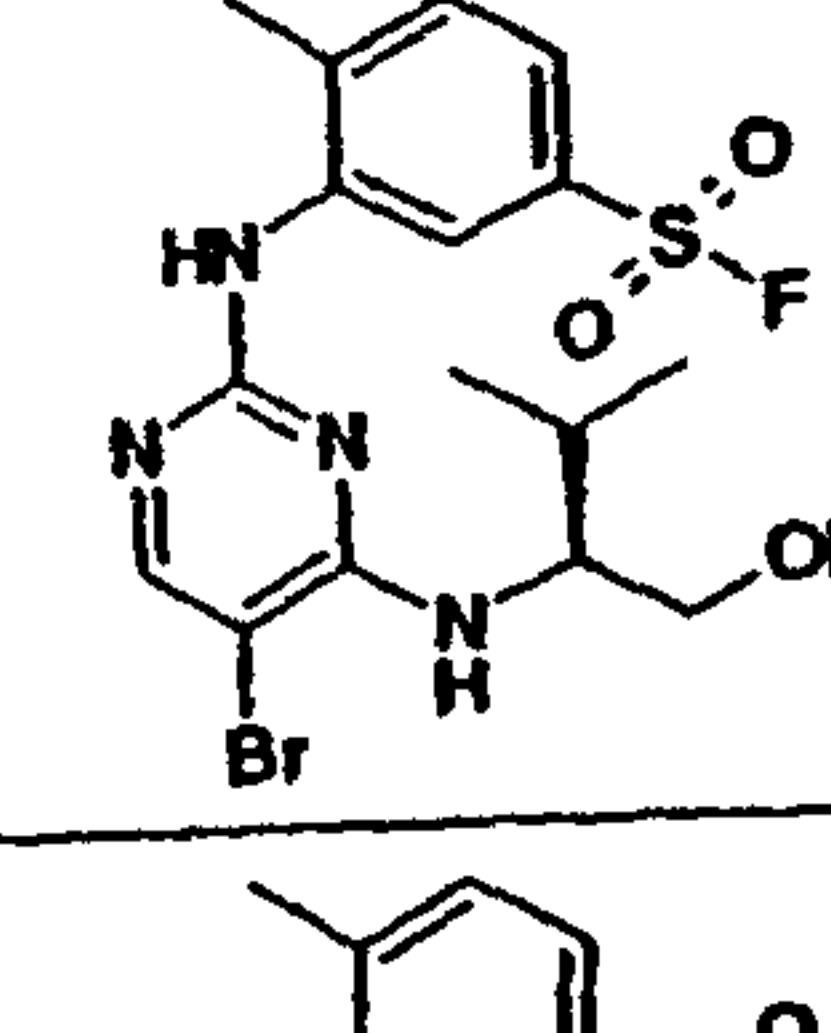
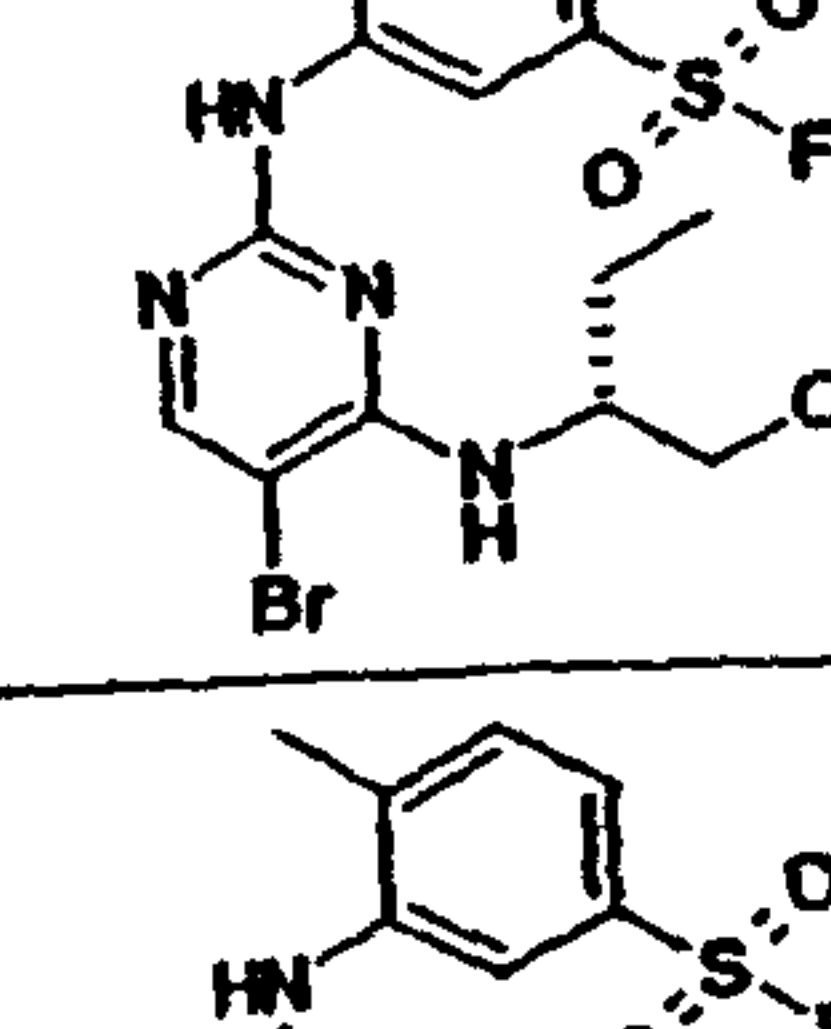
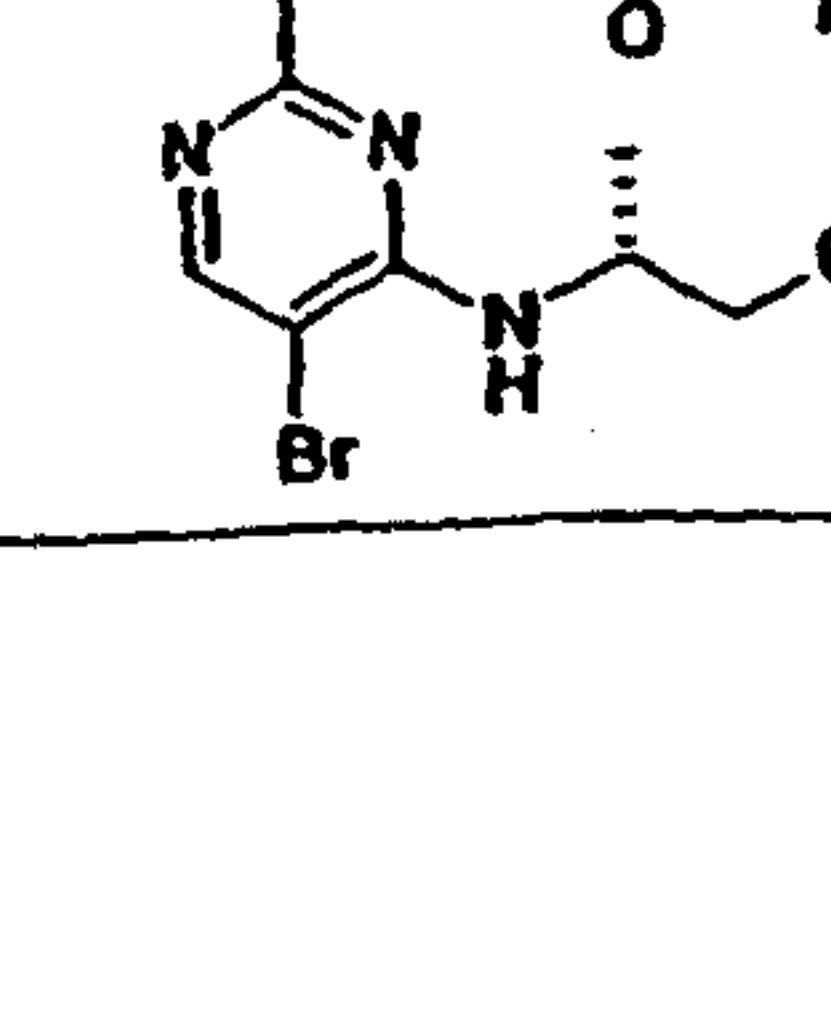
Production of the Pyrimidine-Sulfonyl Fluorides of General Formula I

The production of the pyrimidine-sulfonic acid fluorides is carried out analogously to the production of the sulfonic acid amides.

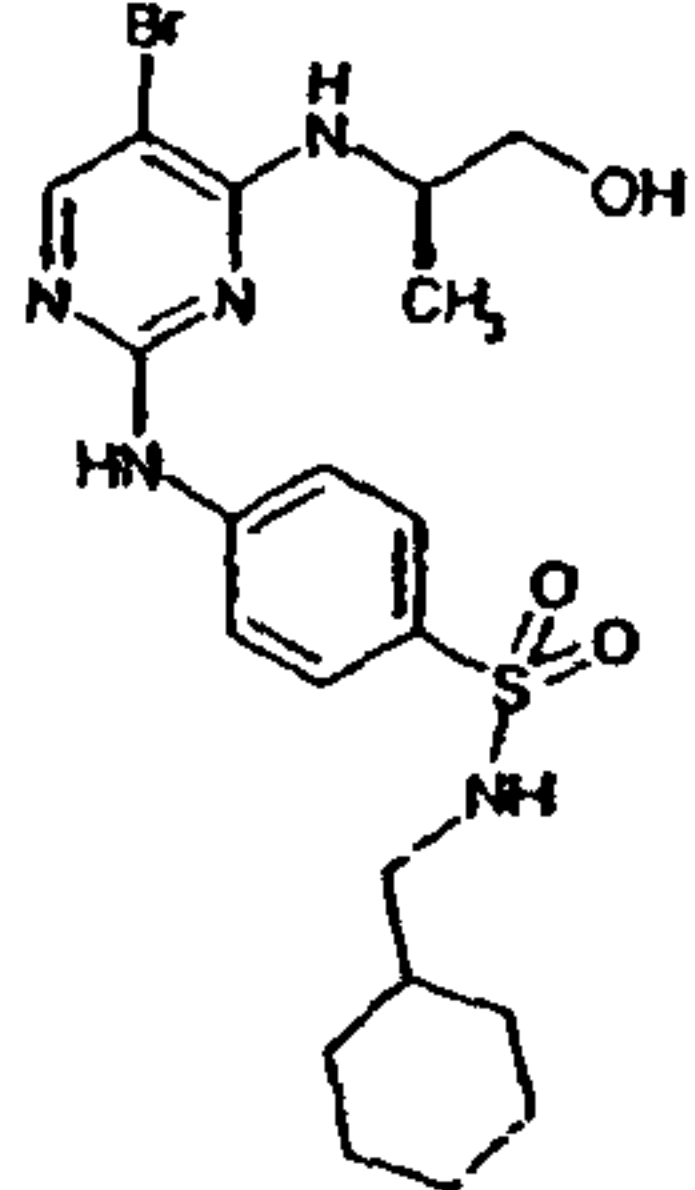
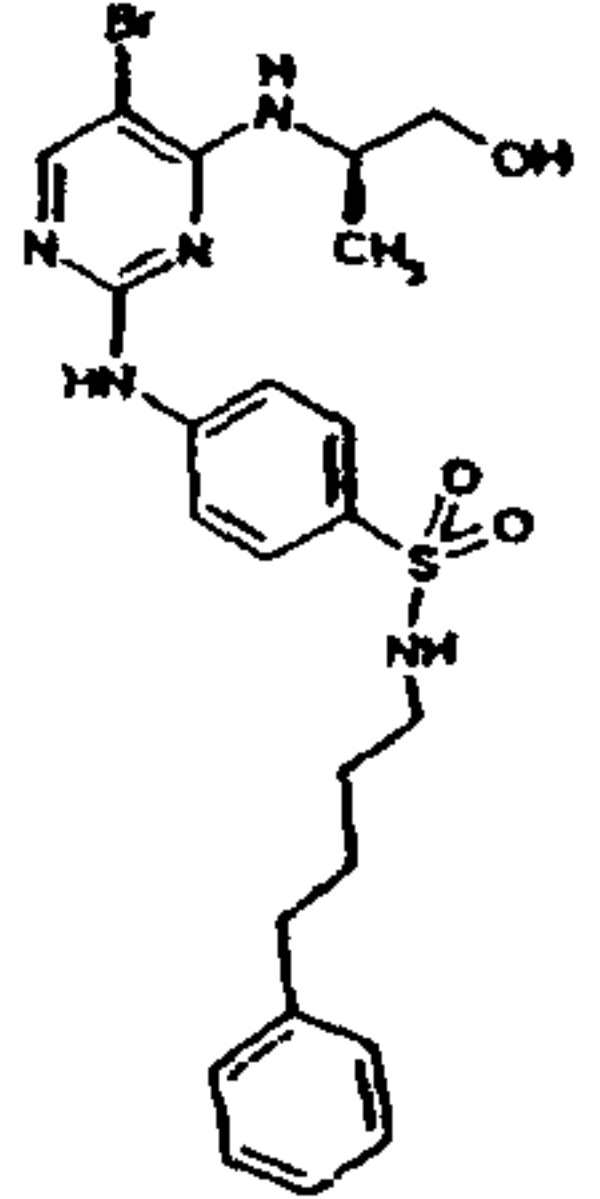
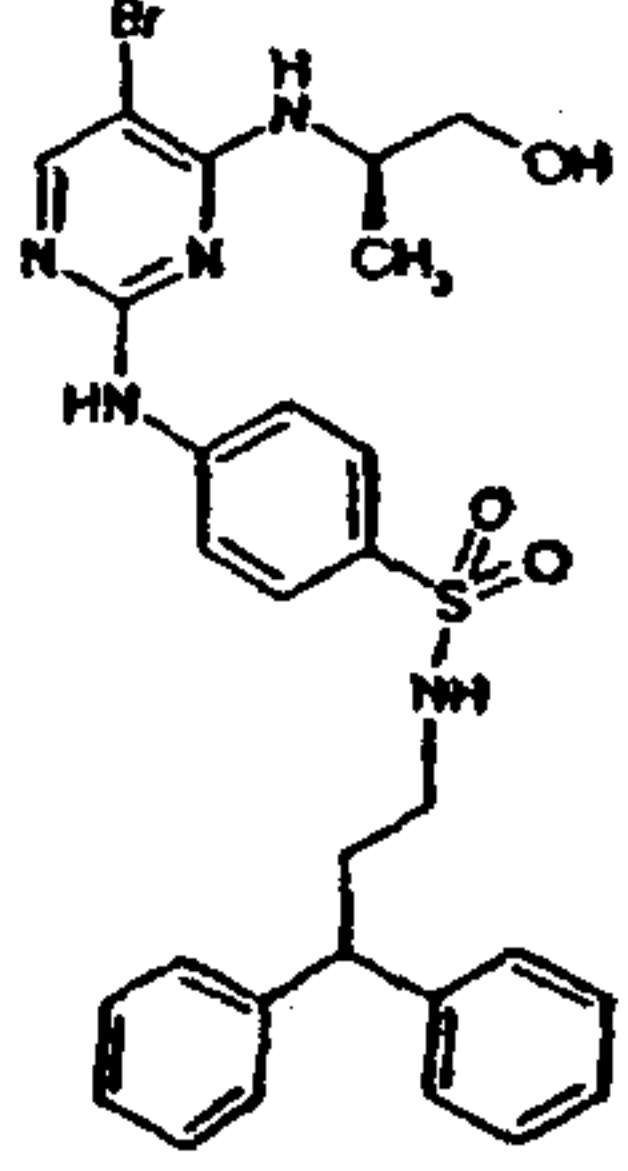
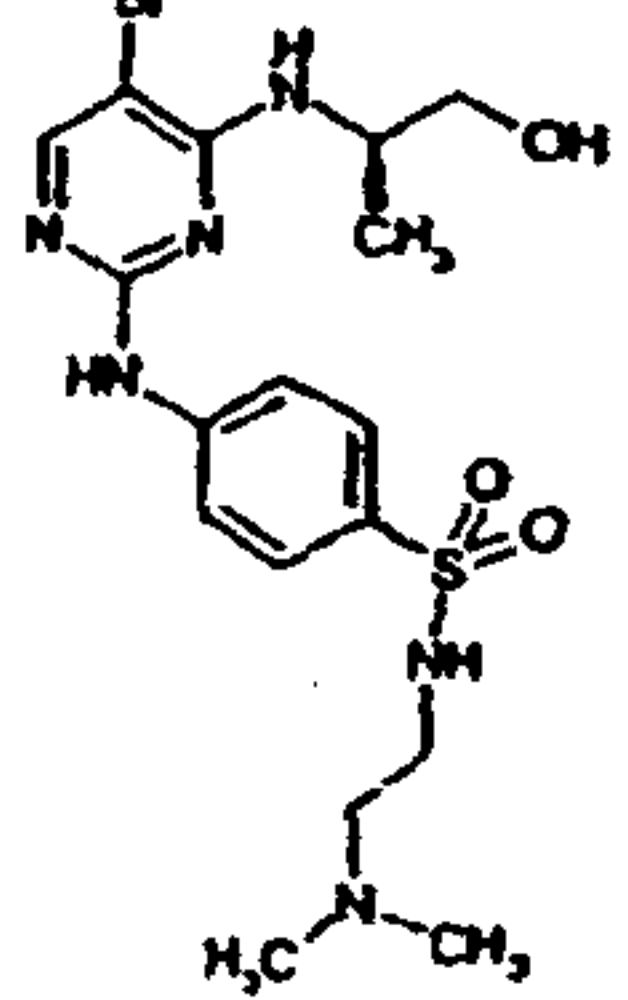


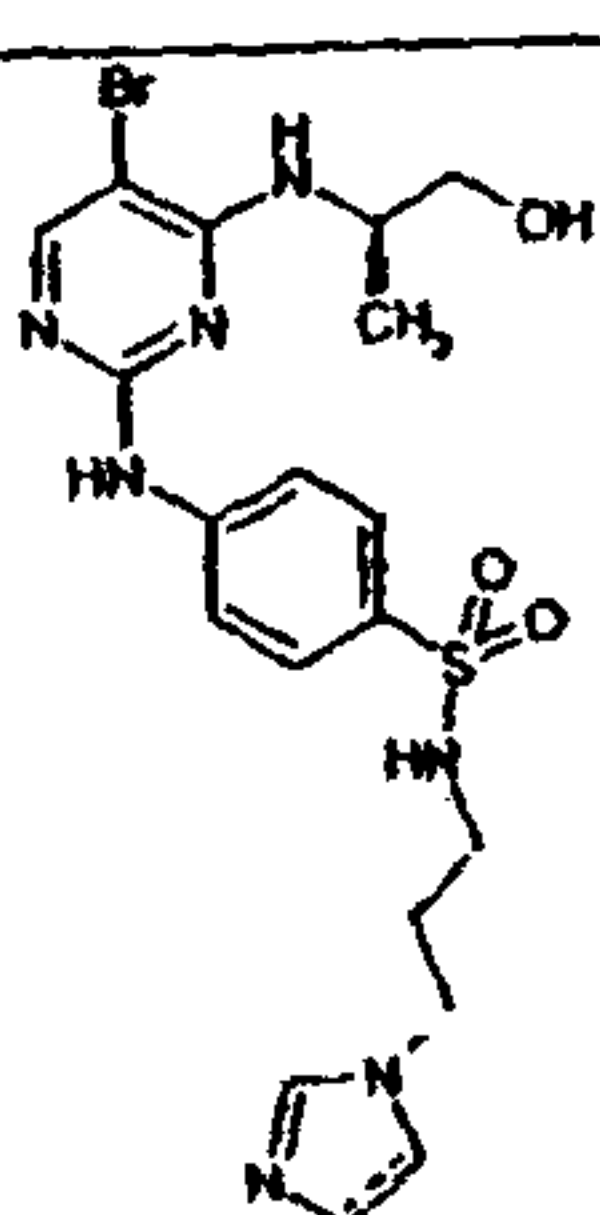
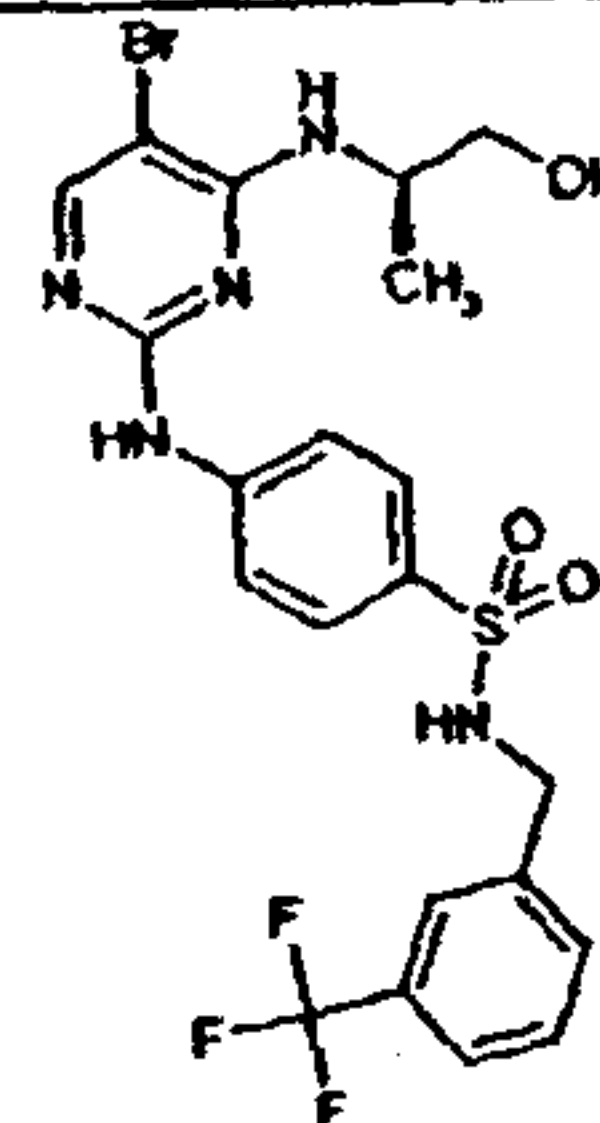
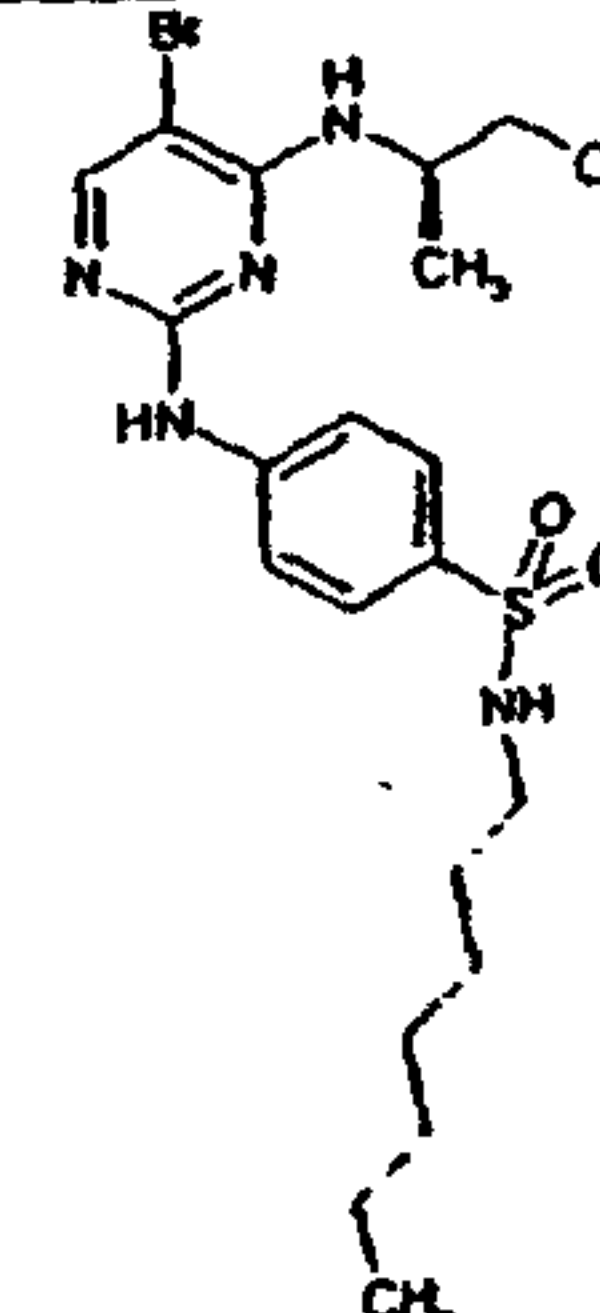
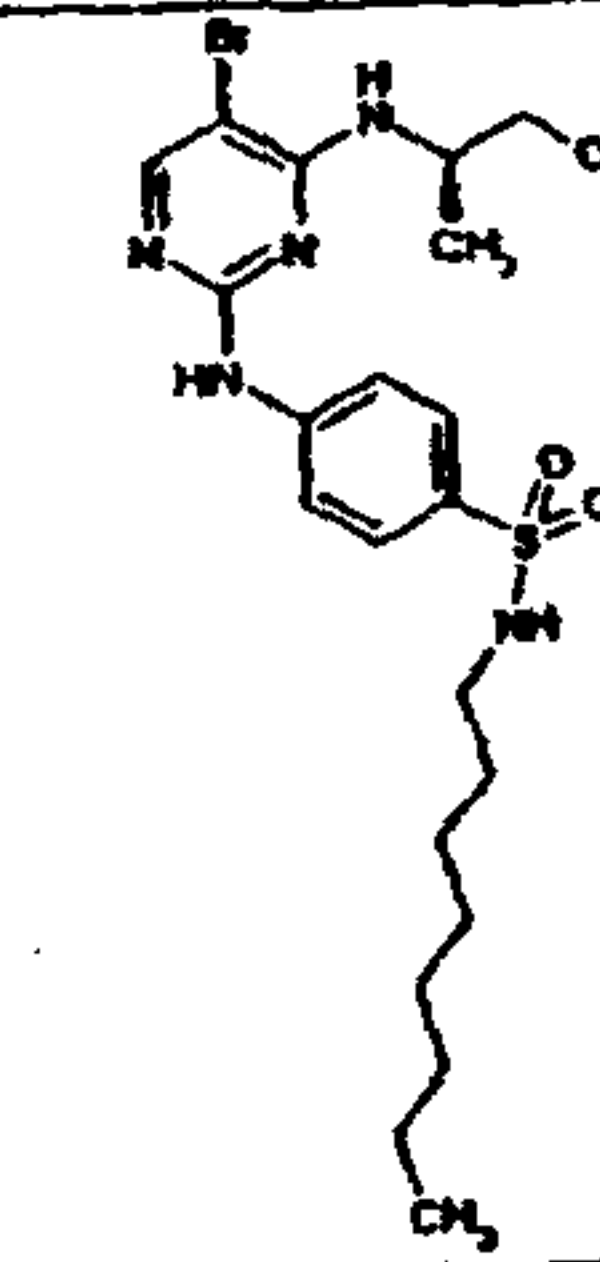
Beispiel-Nr.	Verbindung	Molgewicht	Schmelzpunkt [°C] und ESI-MS
444		405,25	217-220 405/407
445		419,27	196-202 419/421

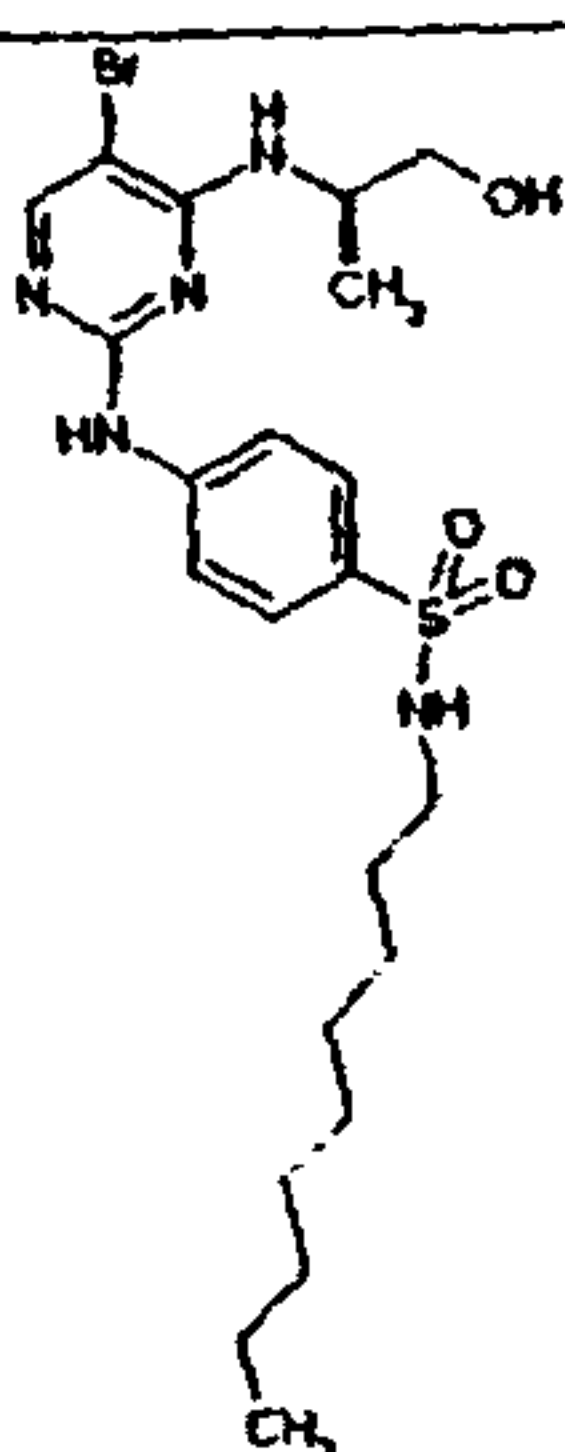
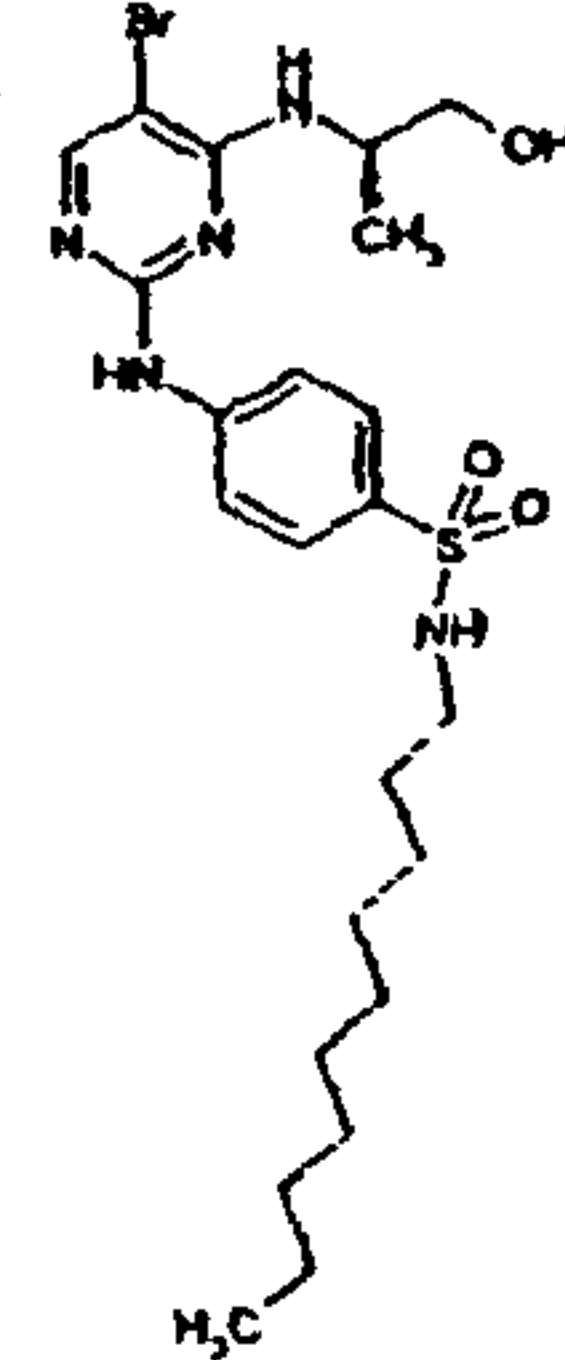
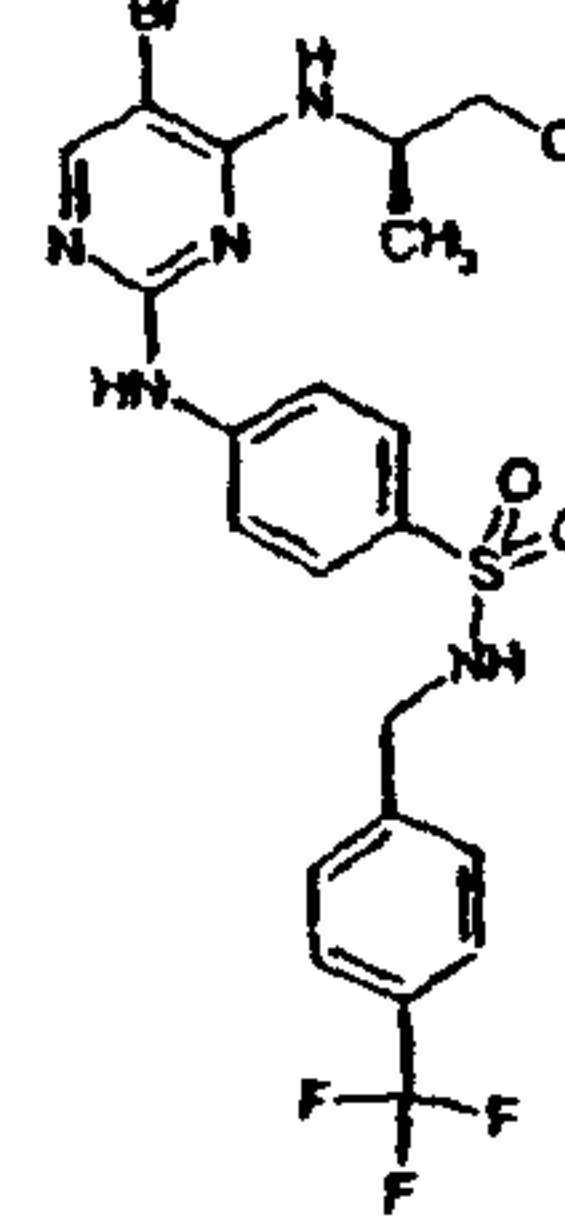
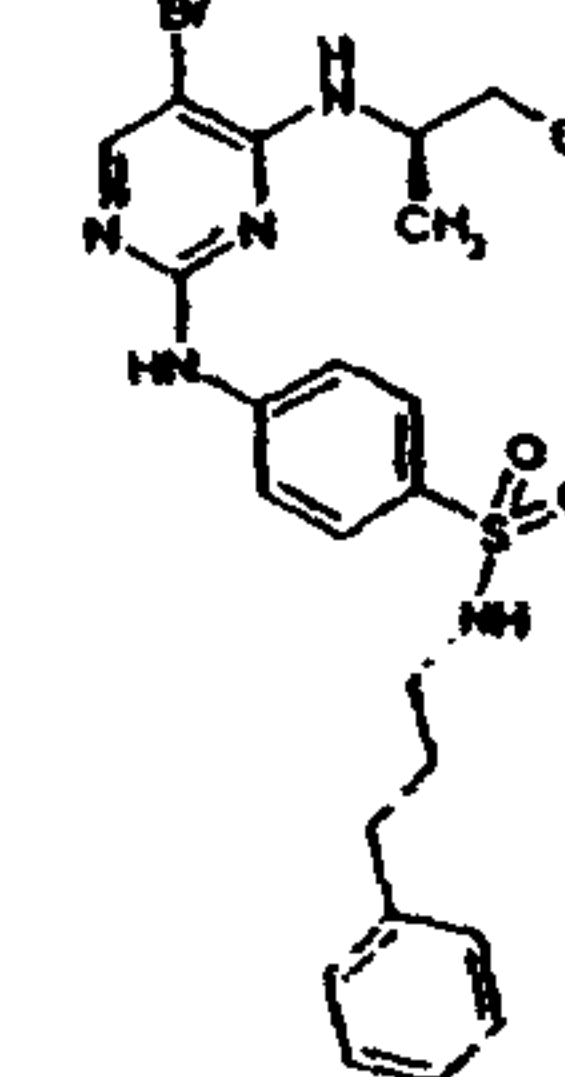
Beispiel-Nr.	Verbindung	Molgewicht	Schmelzpunkt [°C] und ESI-MS
446		419,27	165-196 419/421
447		433,30	198-204 433/435
448		433,30	144-149 433/435
449		447,33	219-222 447/449

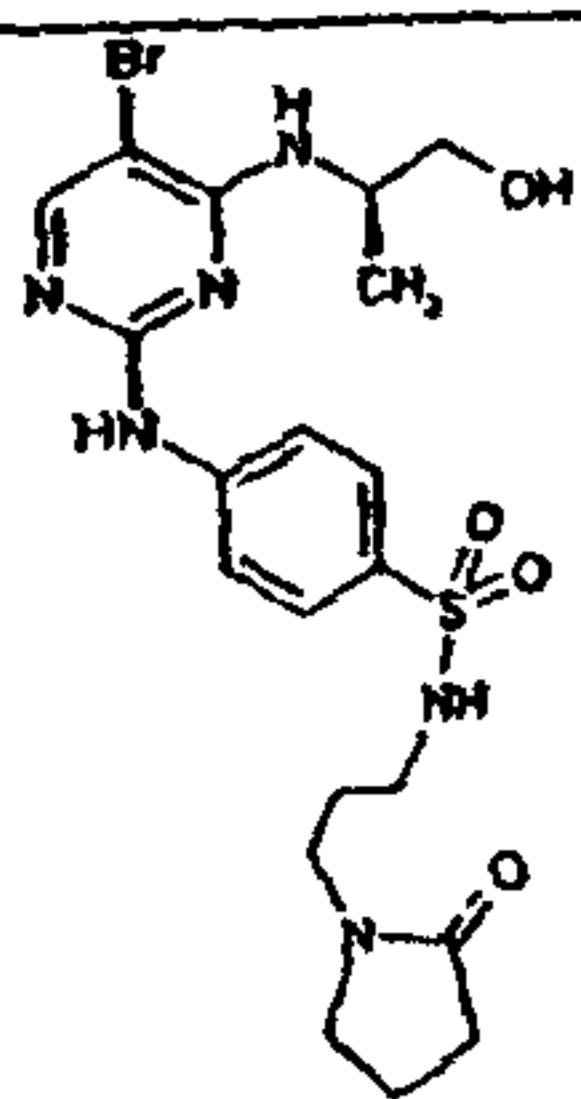
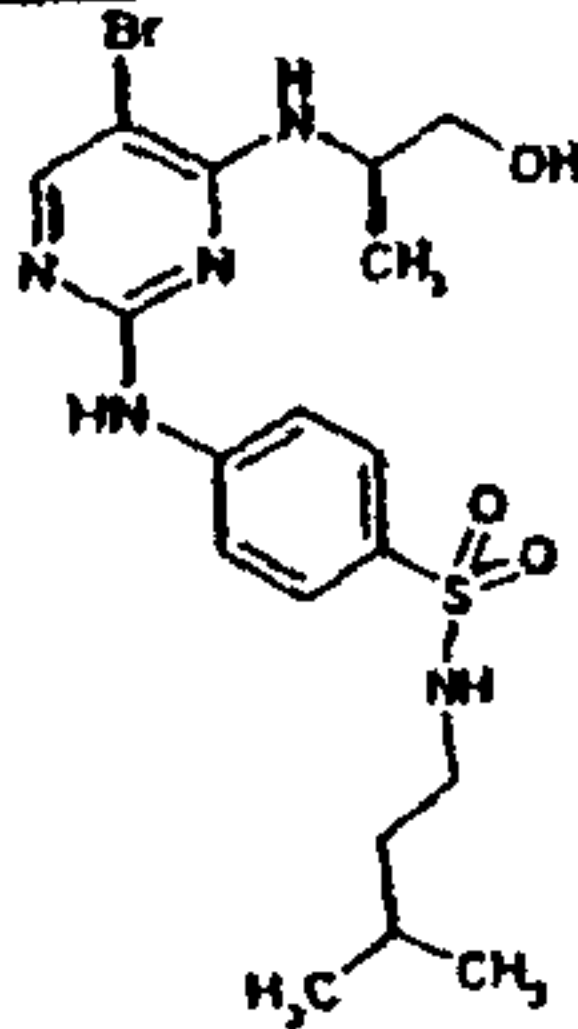
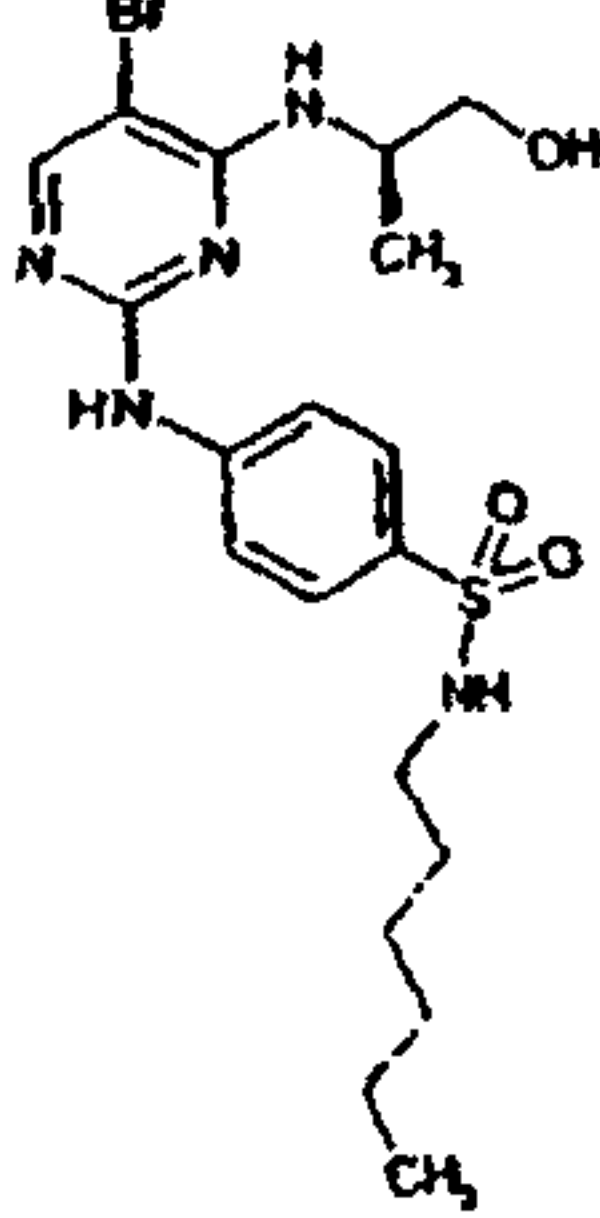
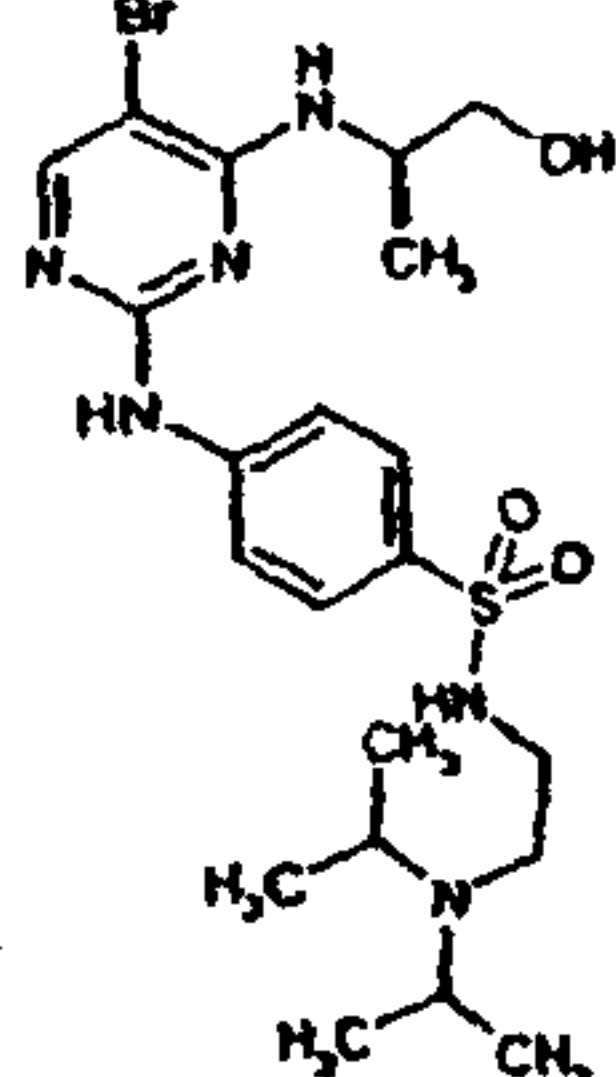
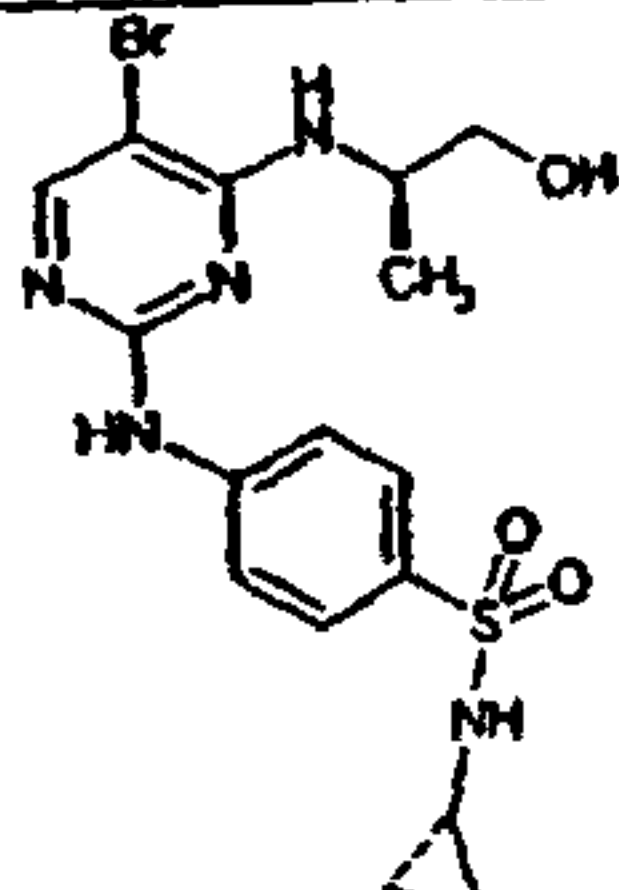
Beispiel-Nr.	Verbindung	Molgewicht	Schmelzpunkt [°C] und ESI-MS
450		405,25	170-173 405/407
451		419,27	226-228 419/421
452		433,30	 433/435
453		447,33	 447/449
454		433,30	 433/435
455		419,27	 419/421

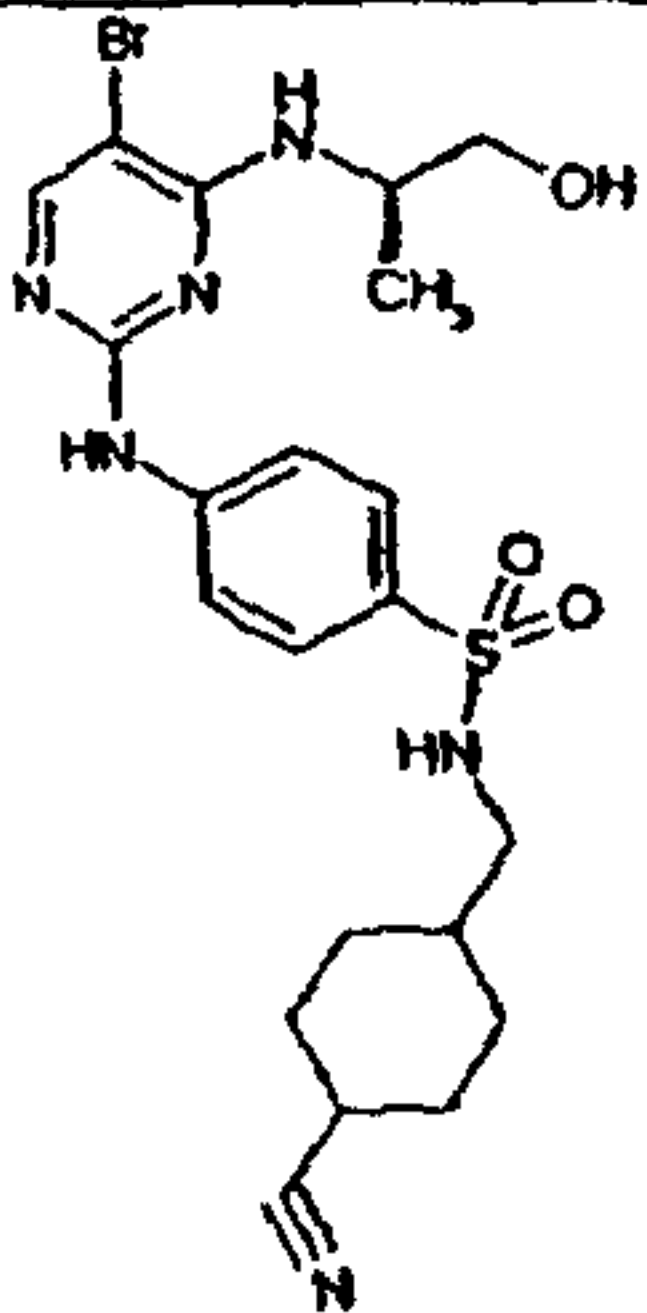
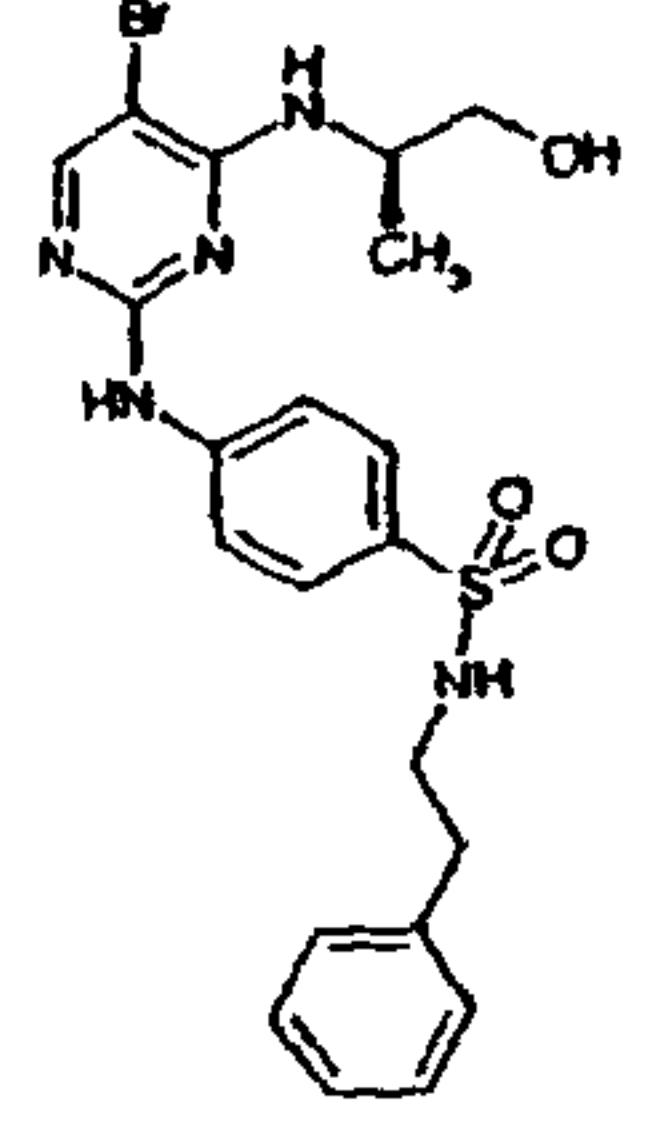
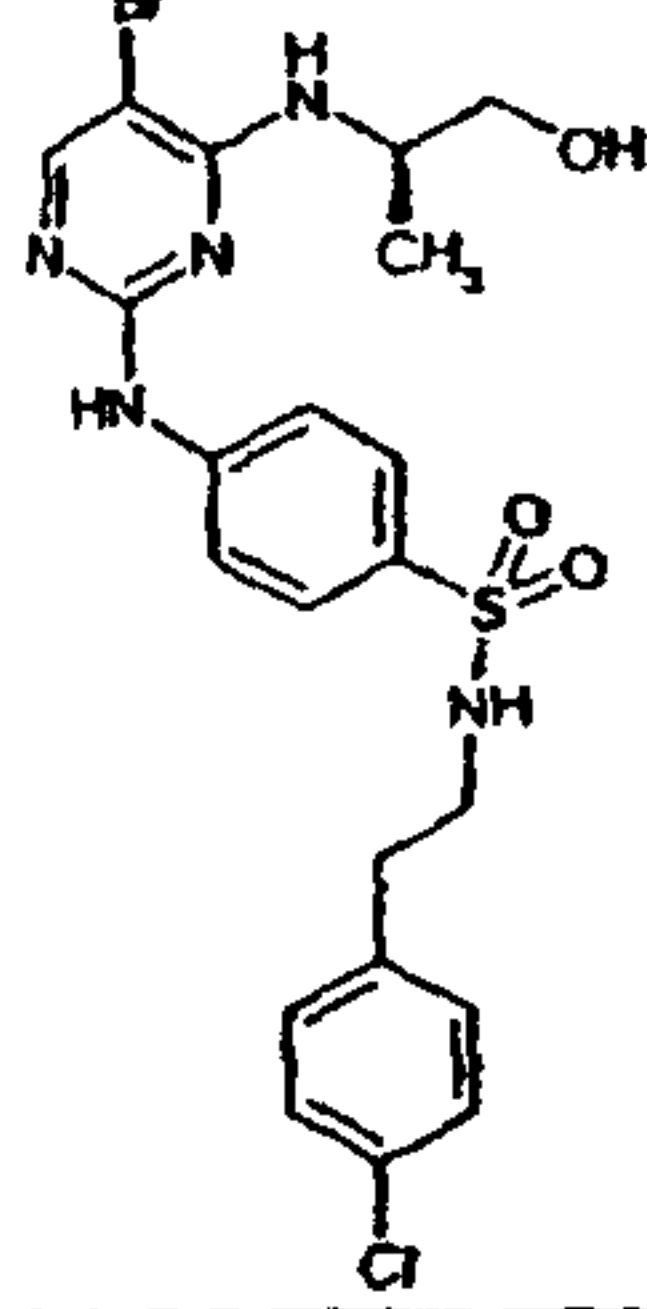
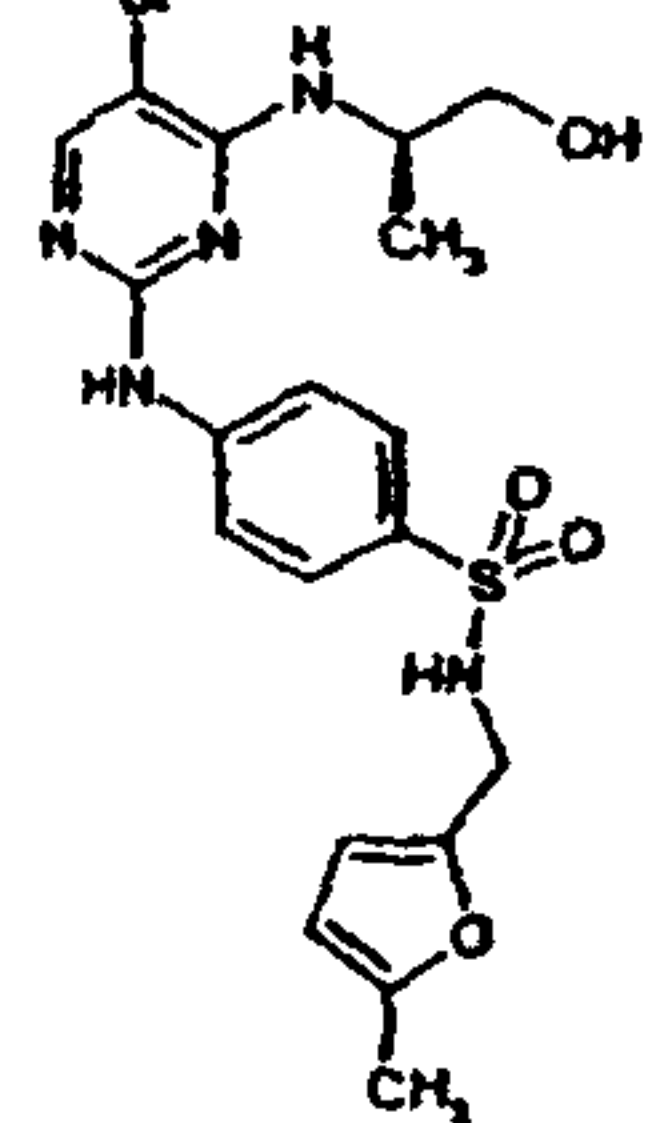
Similarly produced to the above-described examples were also the following para-compounds:

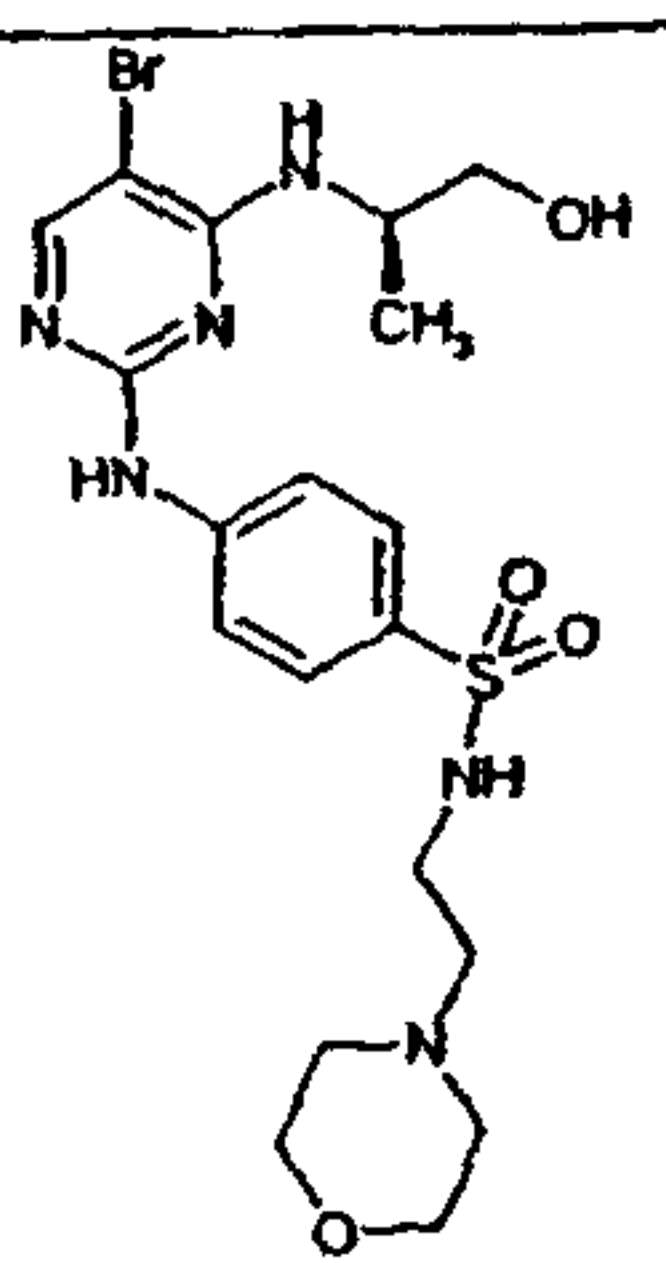
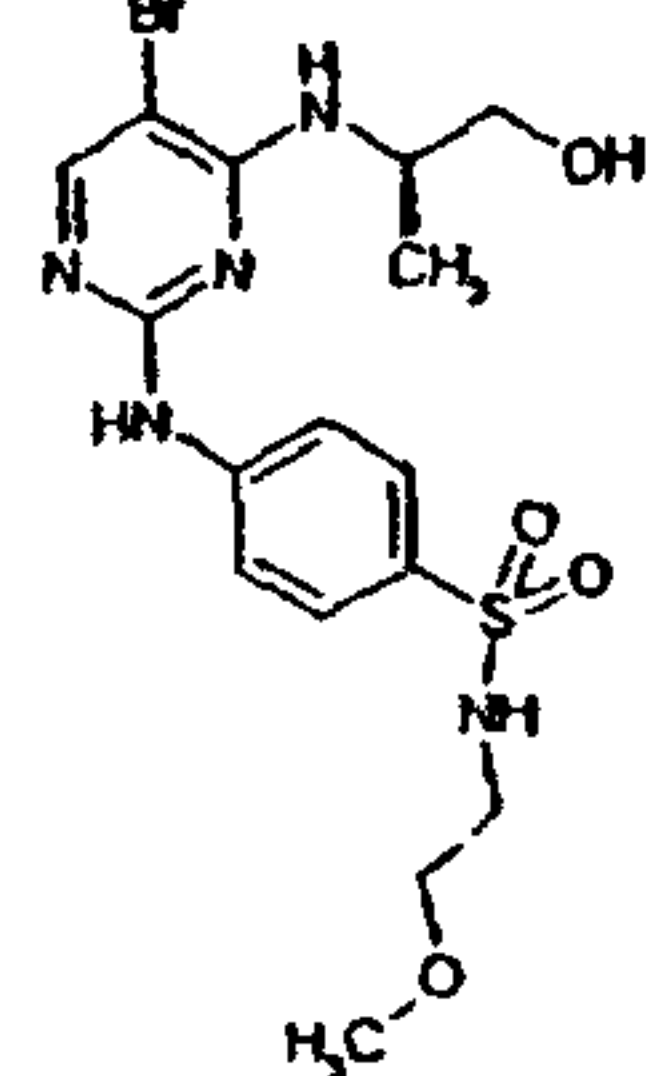
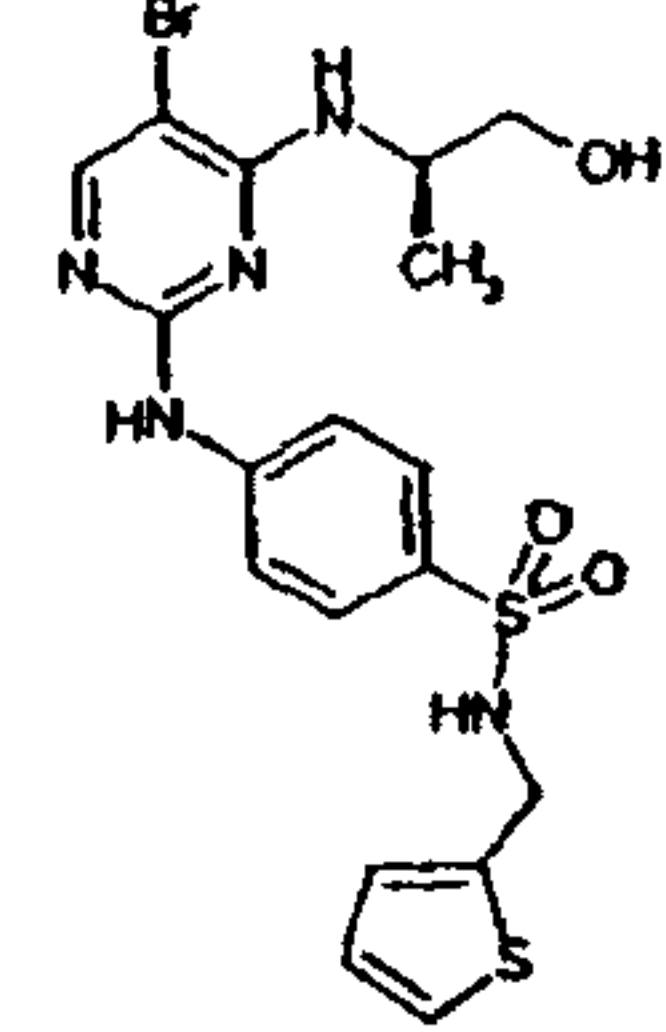
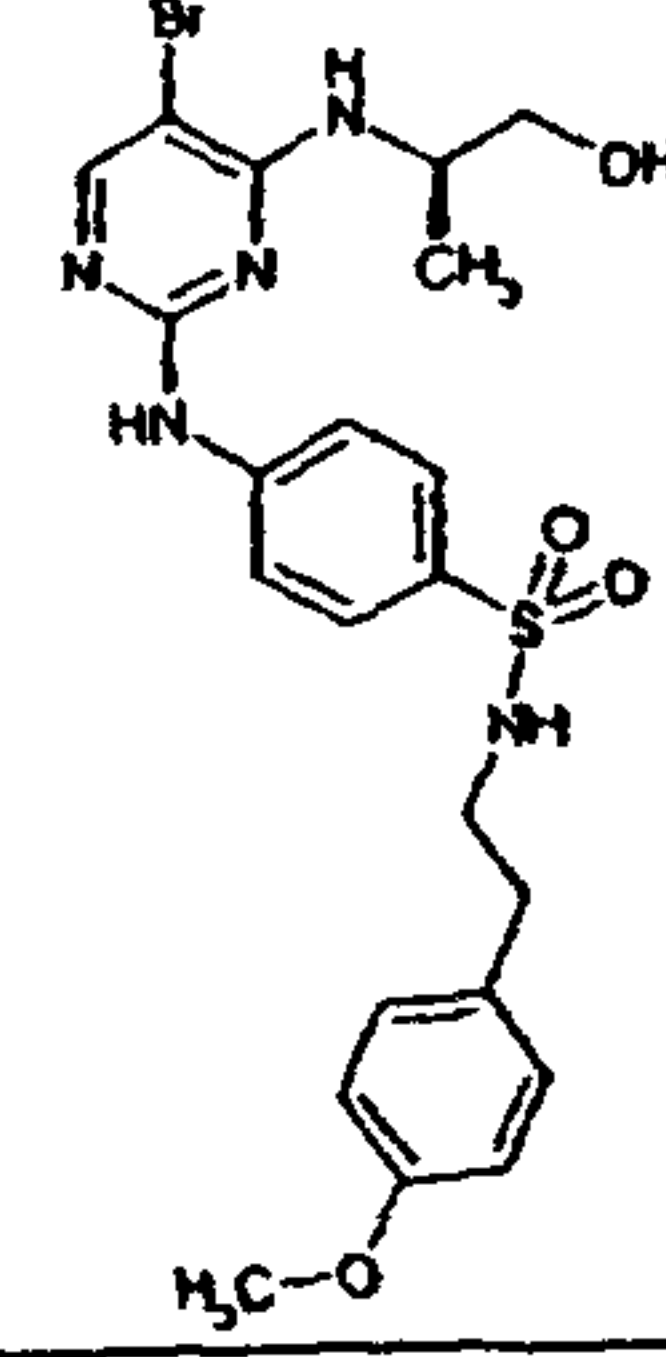
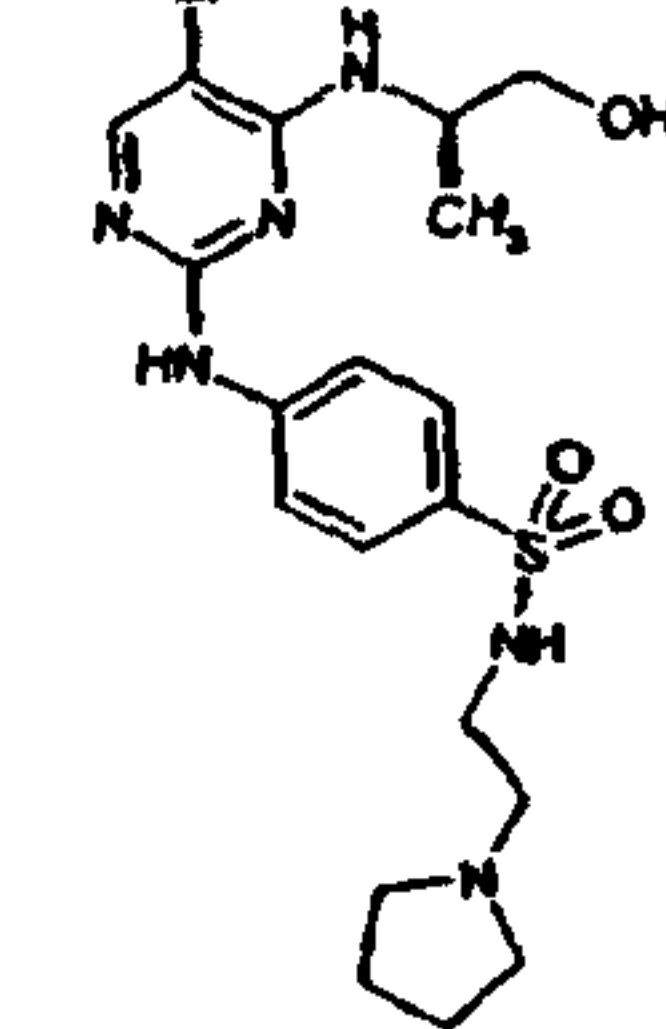
Beispiel-Nr.	Verbindung	Molekular-gewicht	ESI-MS
456		498,4432	498/500
457		534,4762	534/536
458		596,547	596/598
459		473,3935	473/475

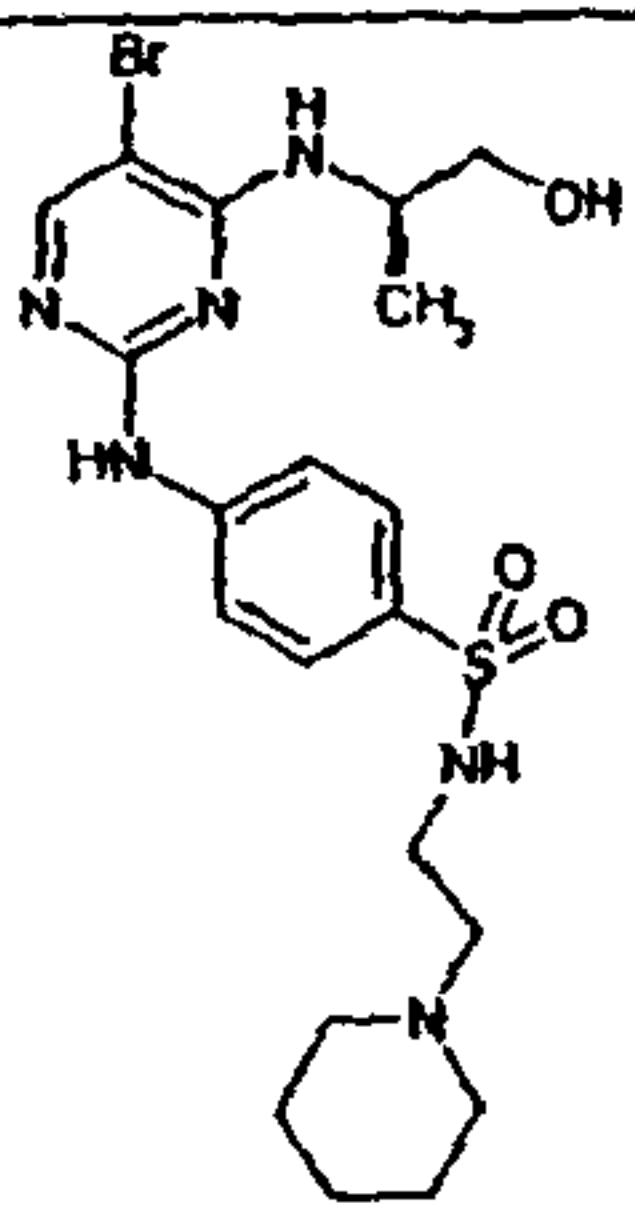
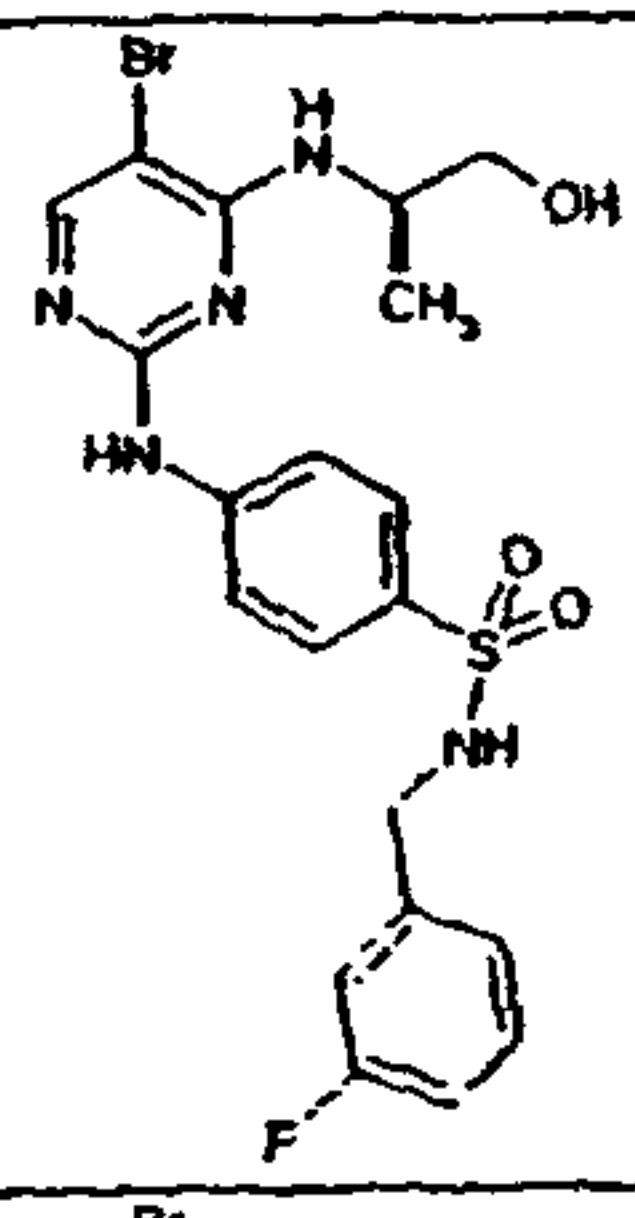
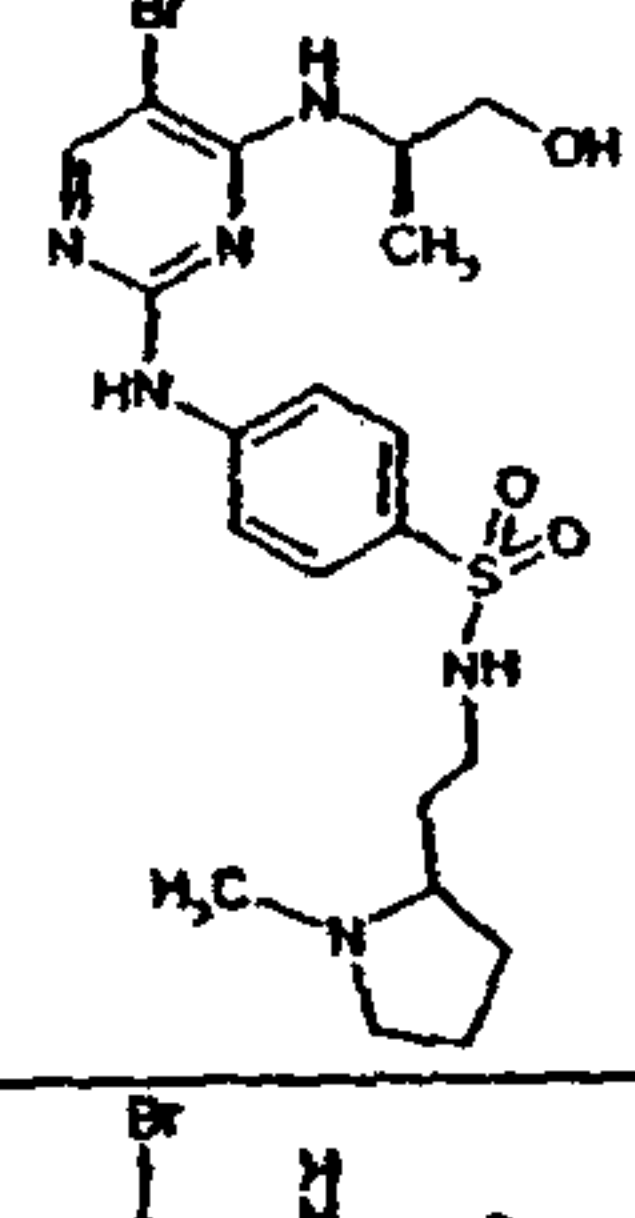
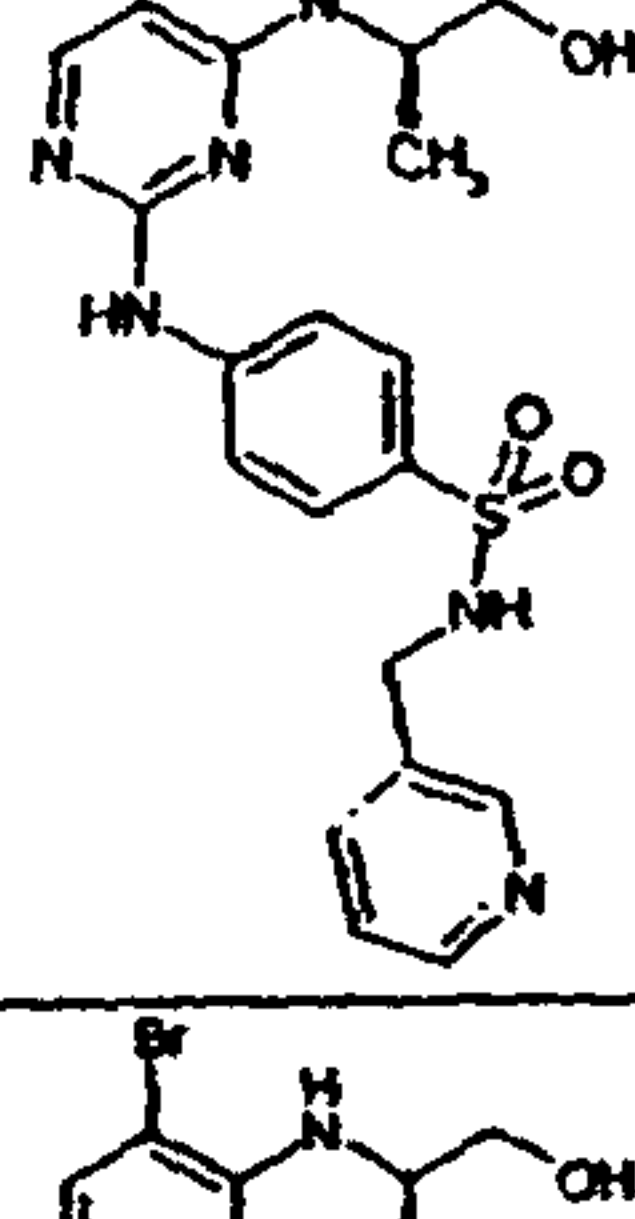
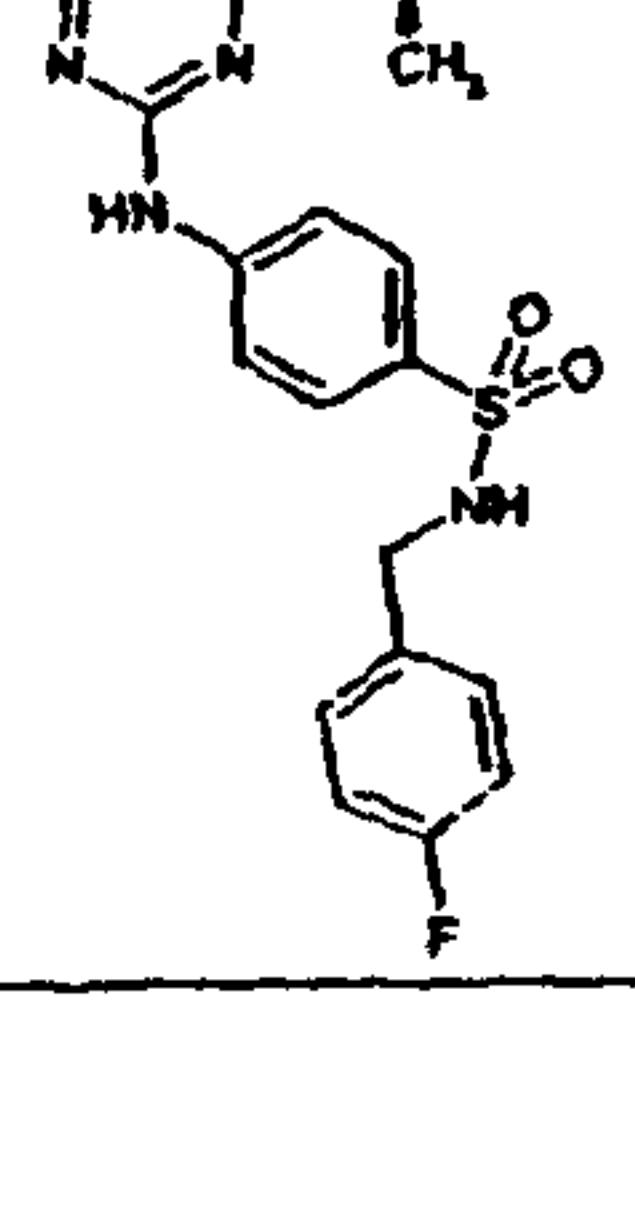
Beispiel-Nr.	Verbindung	Molekular- gewicht	ESI-MS
460		510,4146	510/512
461		560,3929	560/562
462		500,459	500/502
463		514,4858	514/516

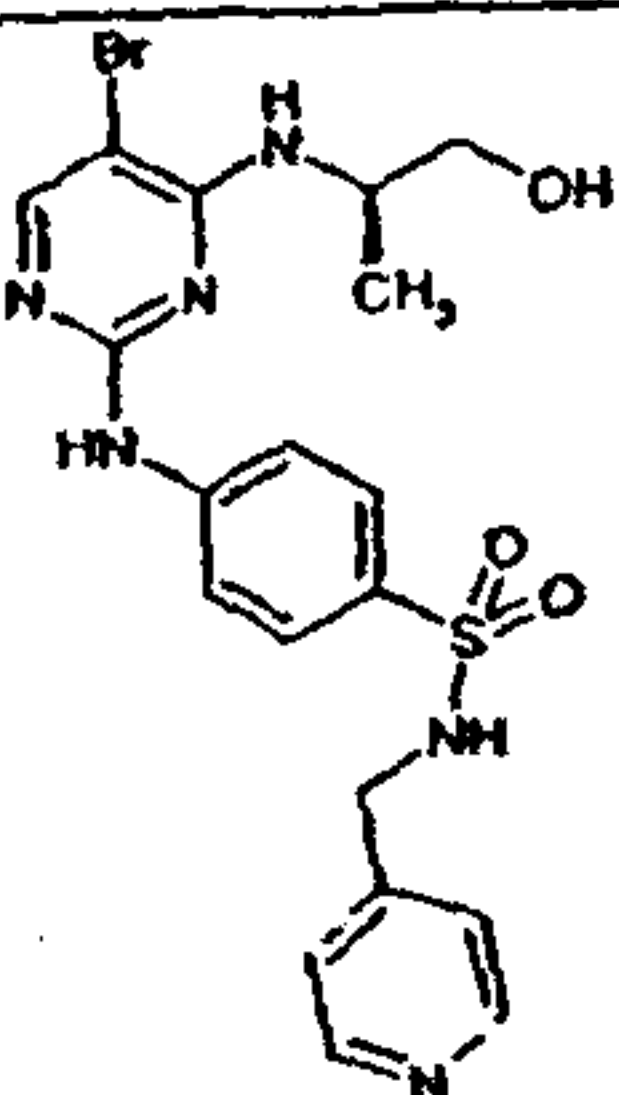
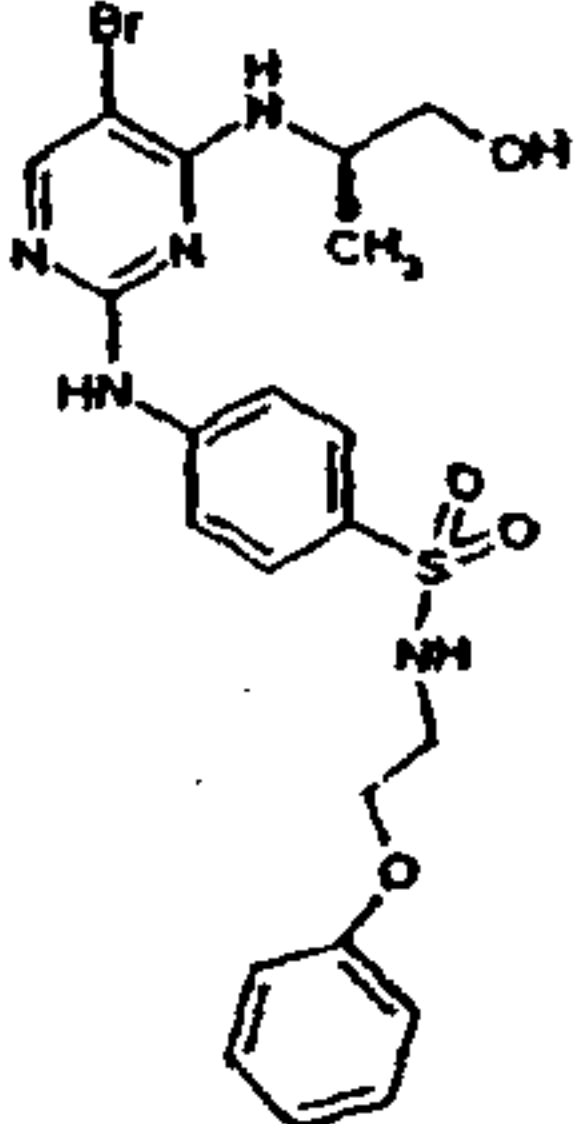
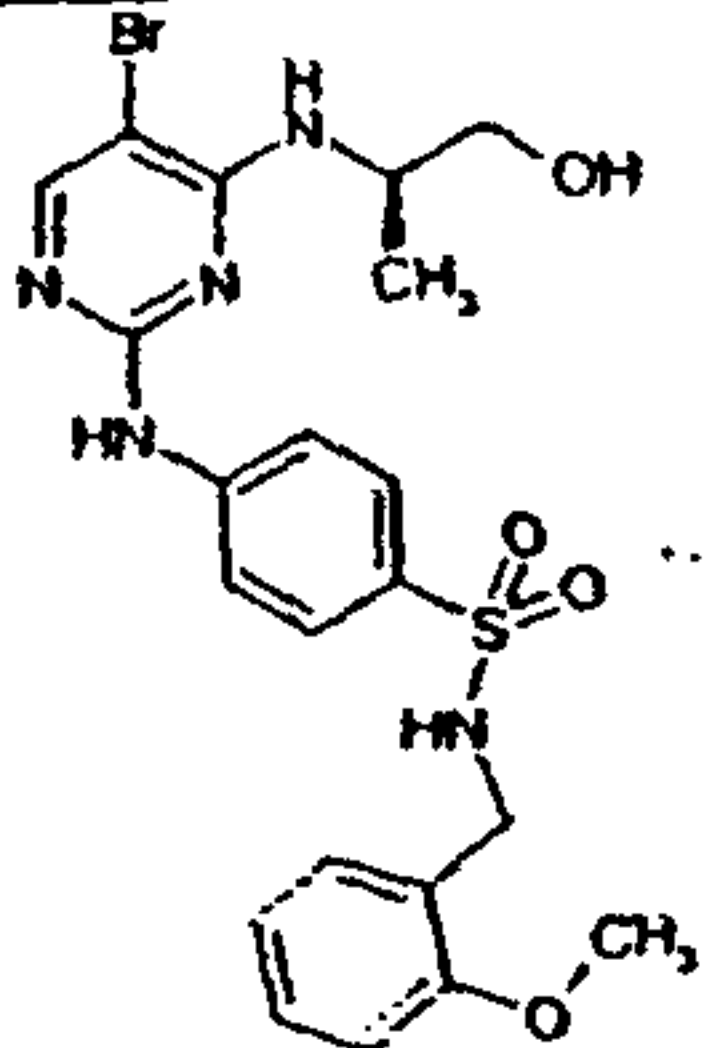
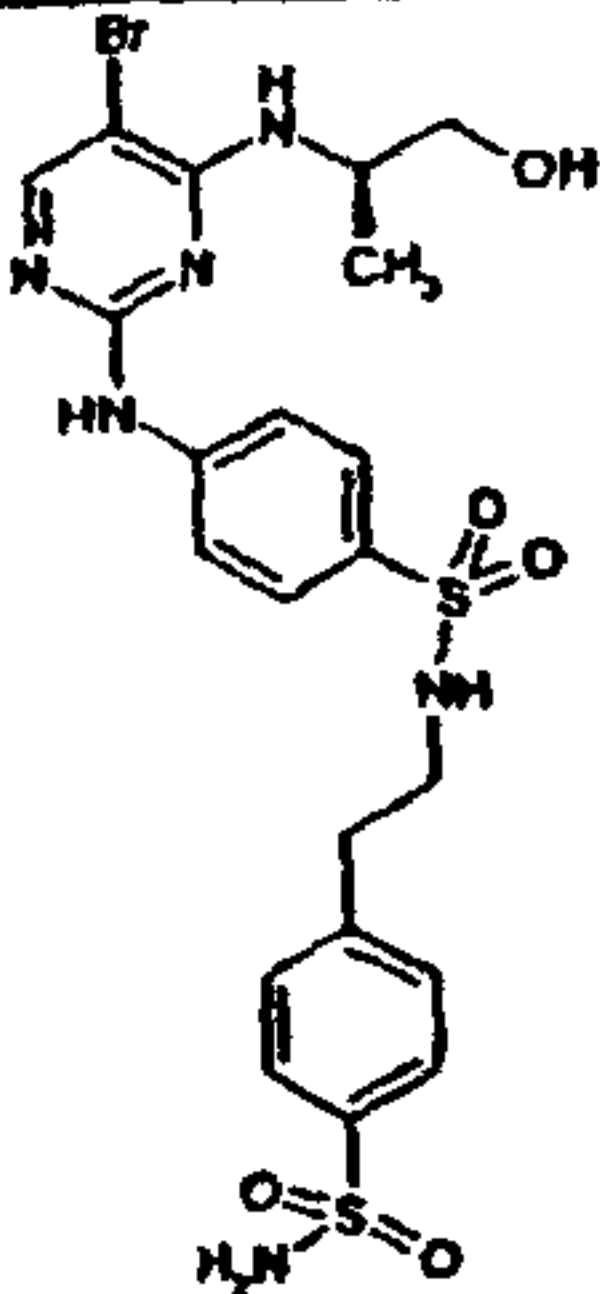
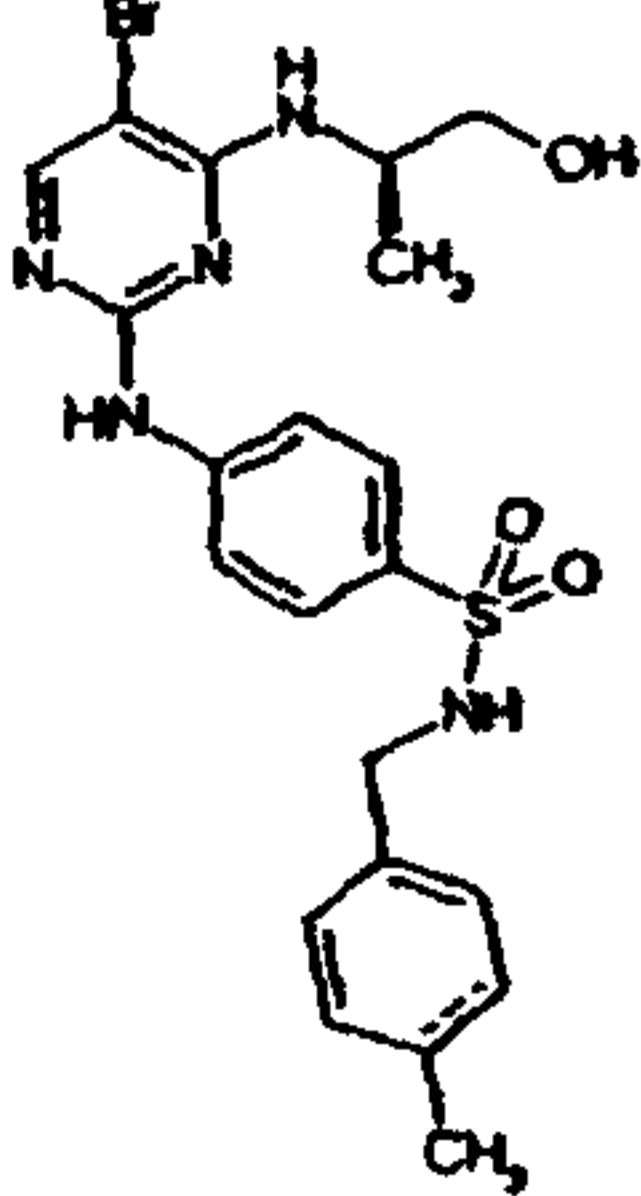
Beispiel-Nr.	Verbindung	Molekular- gewicht	ESI-MS
464		528,5126	528/530
465		542,5394	542/544
466		560,3929	560/562
467		520,4494	520/522

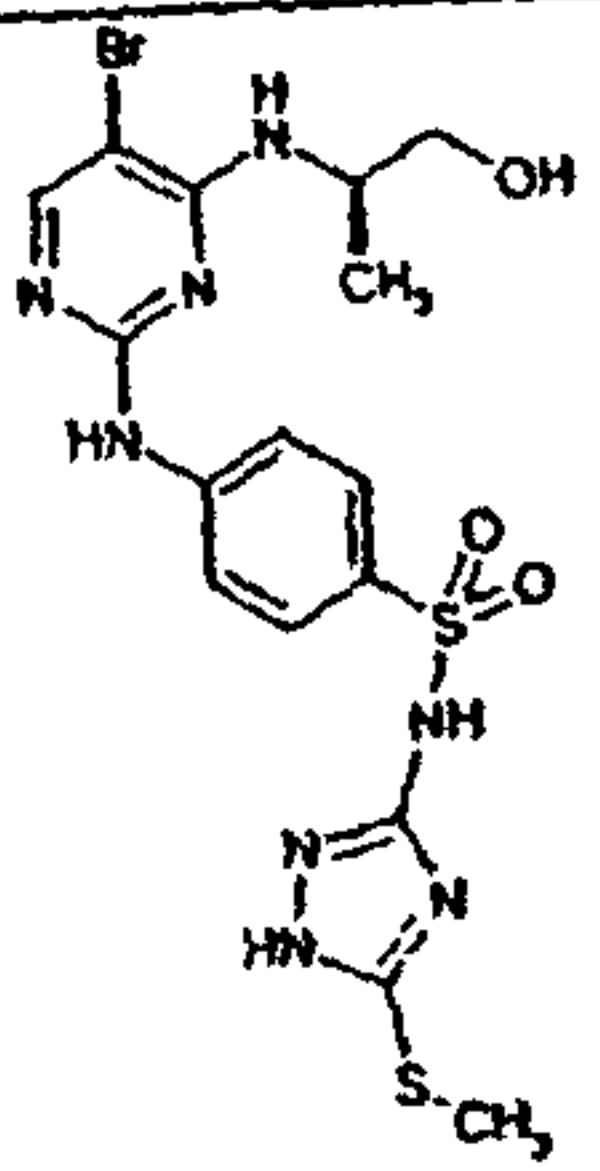
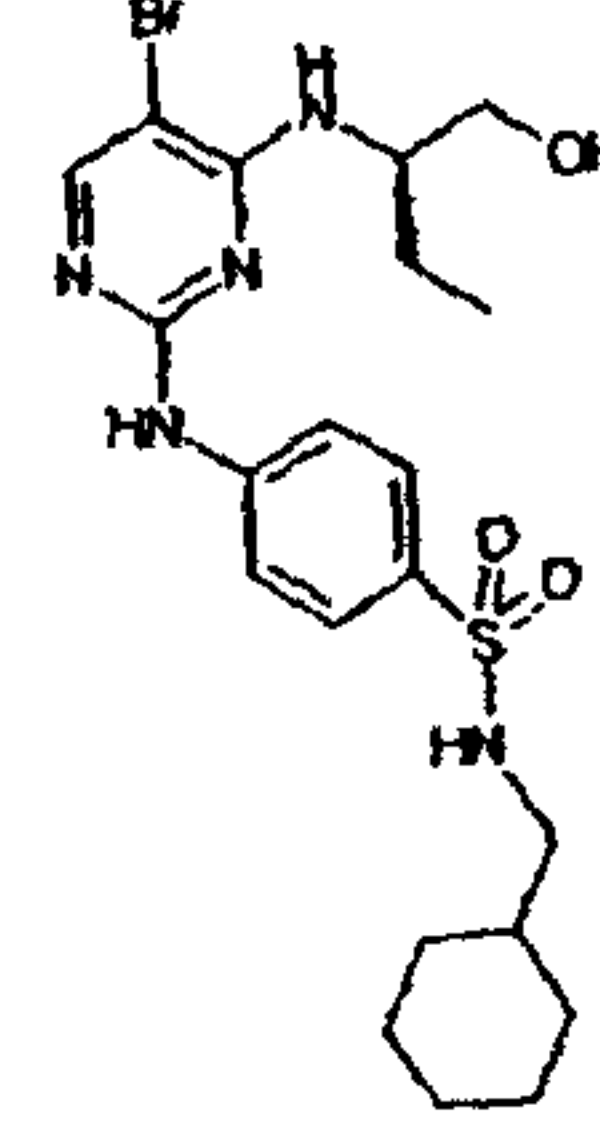
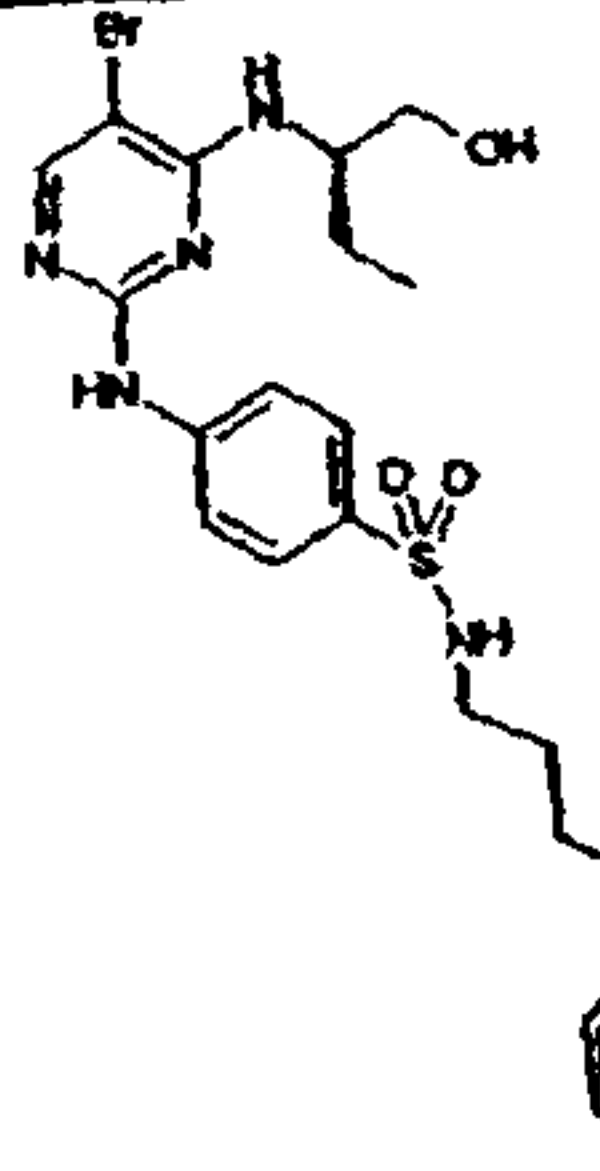
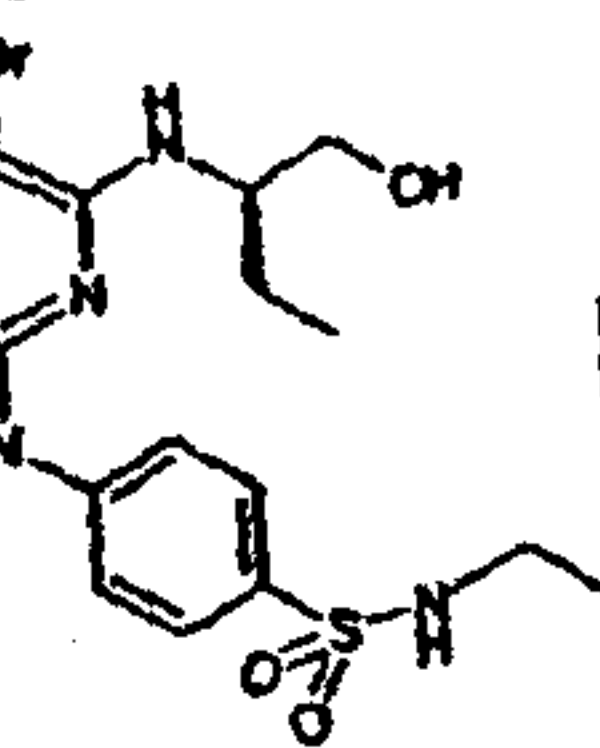
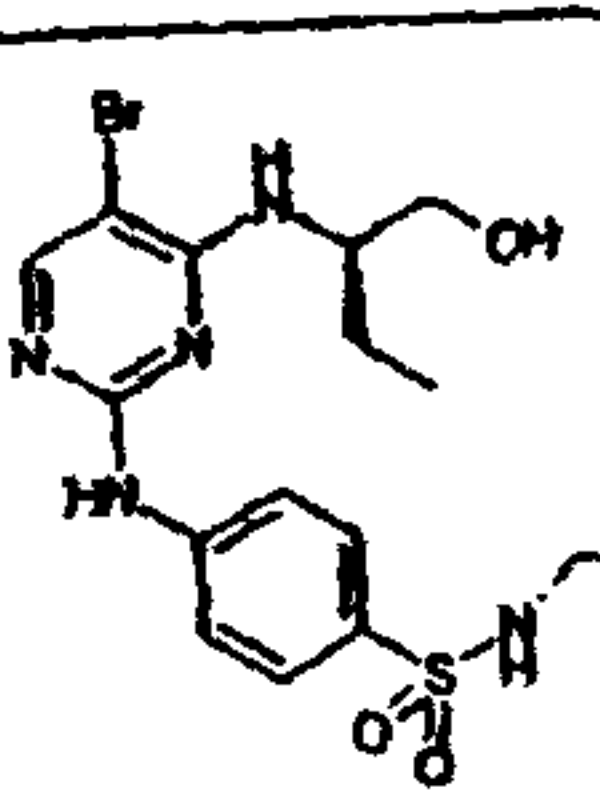
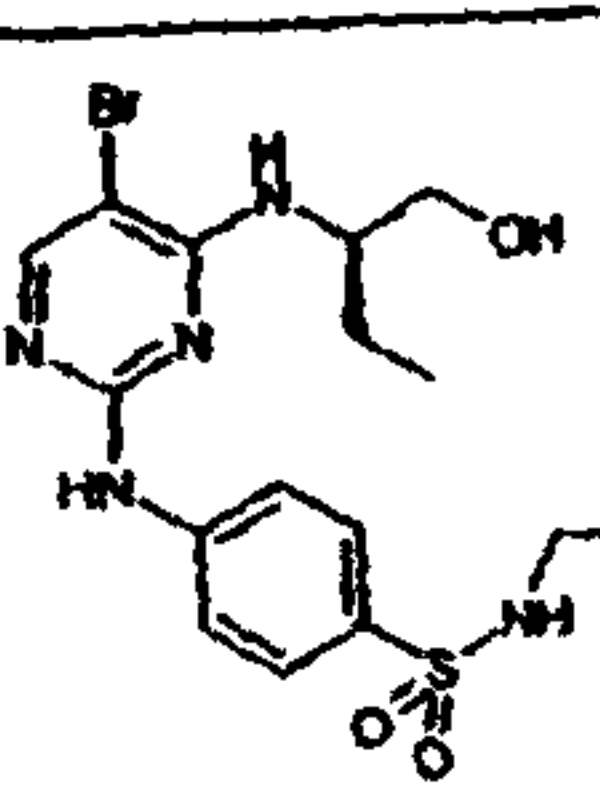
Beispiel-Nr.	Verbindung	Molekular- gewicht	ESI-MS
468		527,4413	527/529
469		472,4054	472/474
470		486,4322	486/488
471		529,5007	529/531
472		442,336	442/444

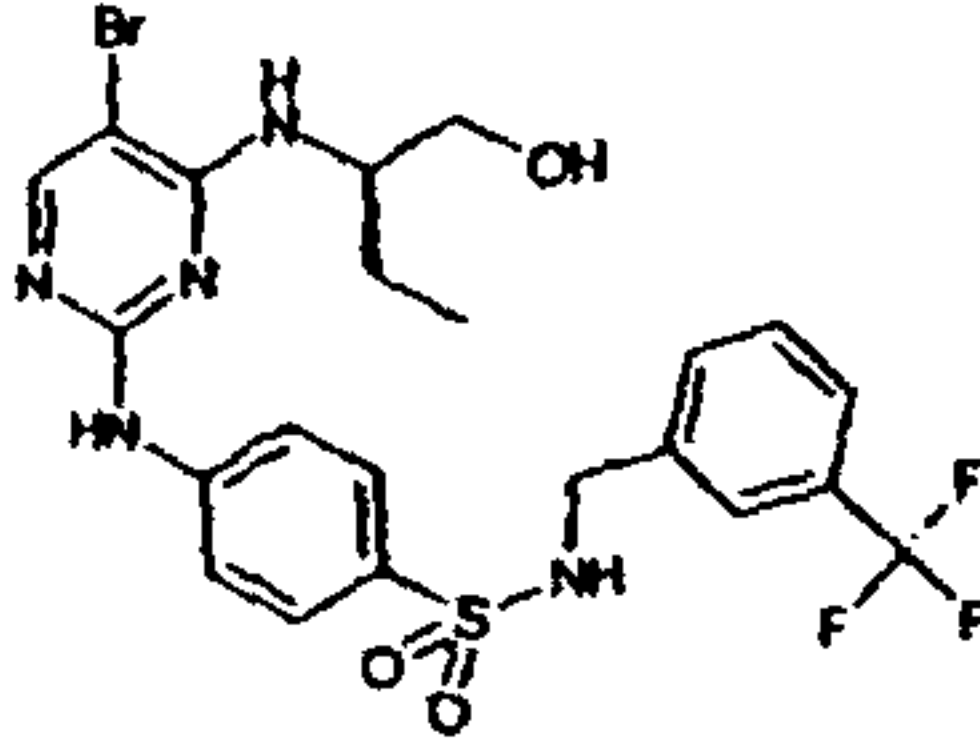
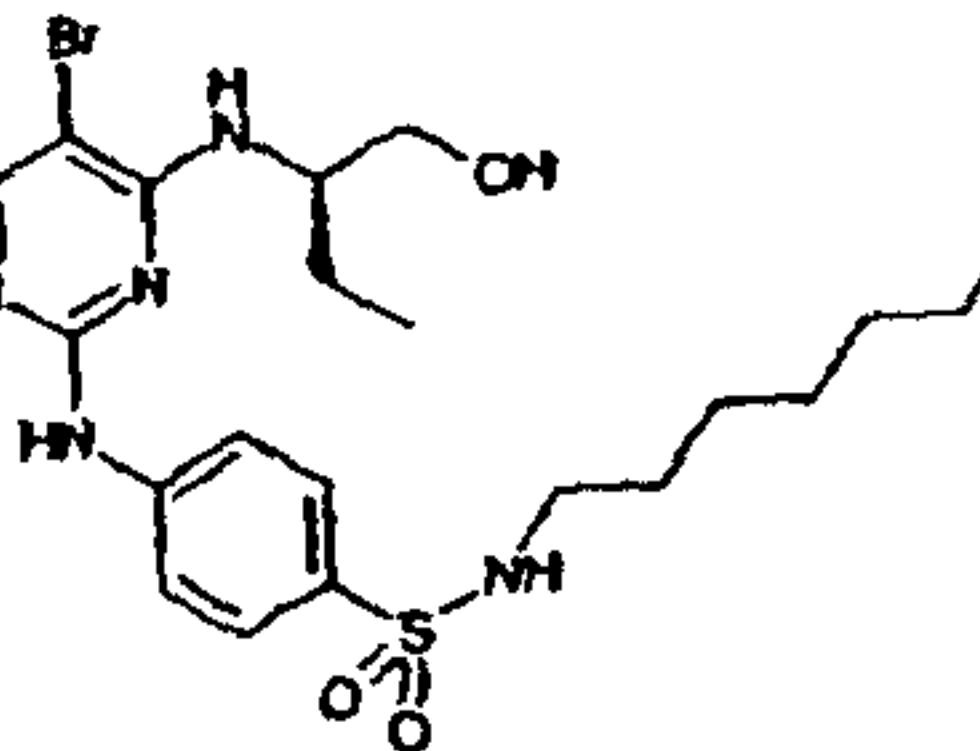
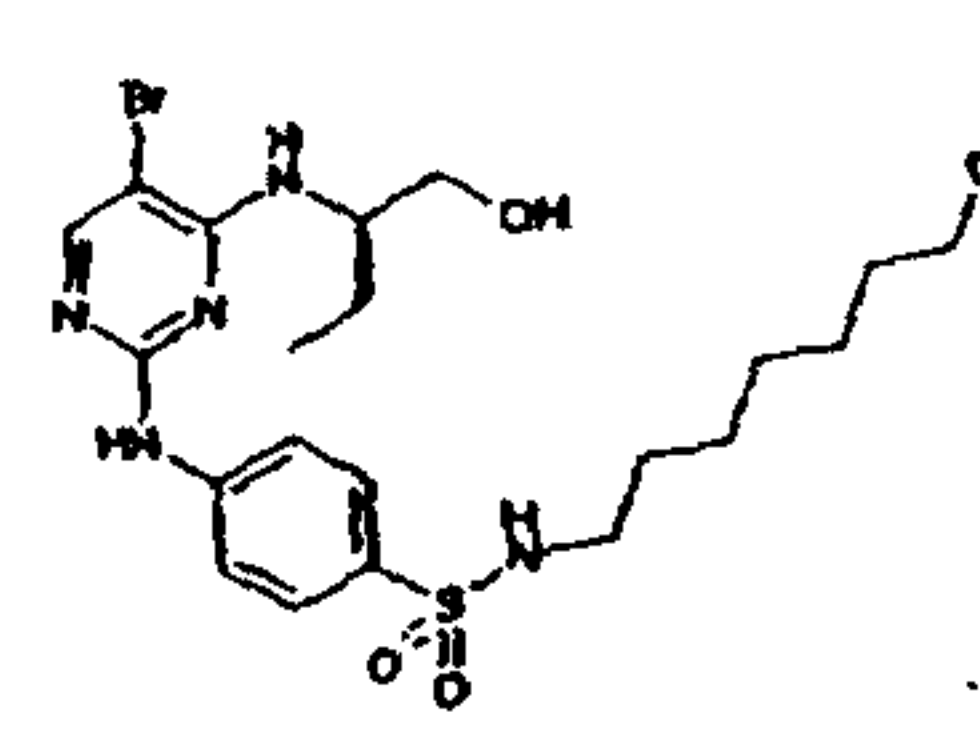
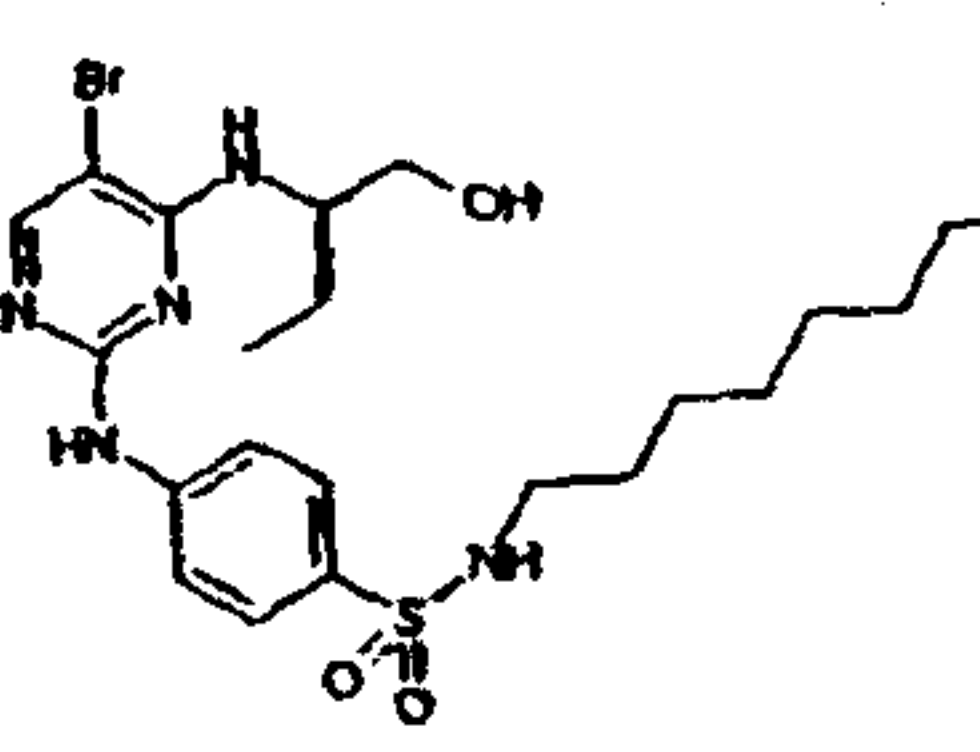
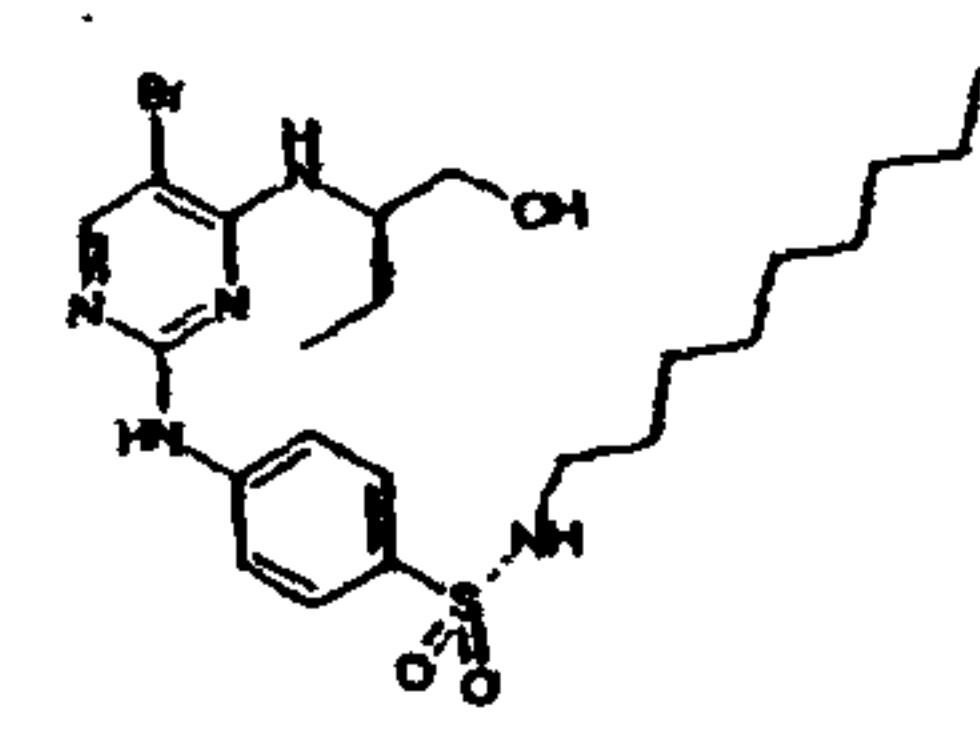
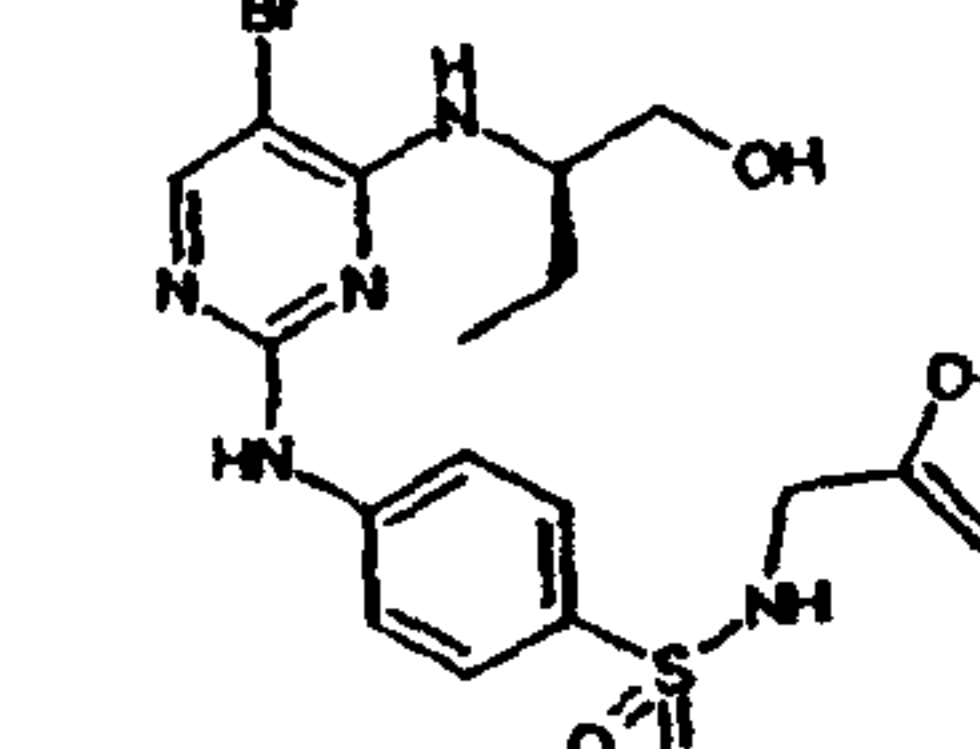
Beispiel-Nr.	Verbindung	Molekular- gewicht	ESI-MS
473		523,4532	523/525
474		506,4226	506/508
475		540,8677	540/542
476		496,3838	496/498

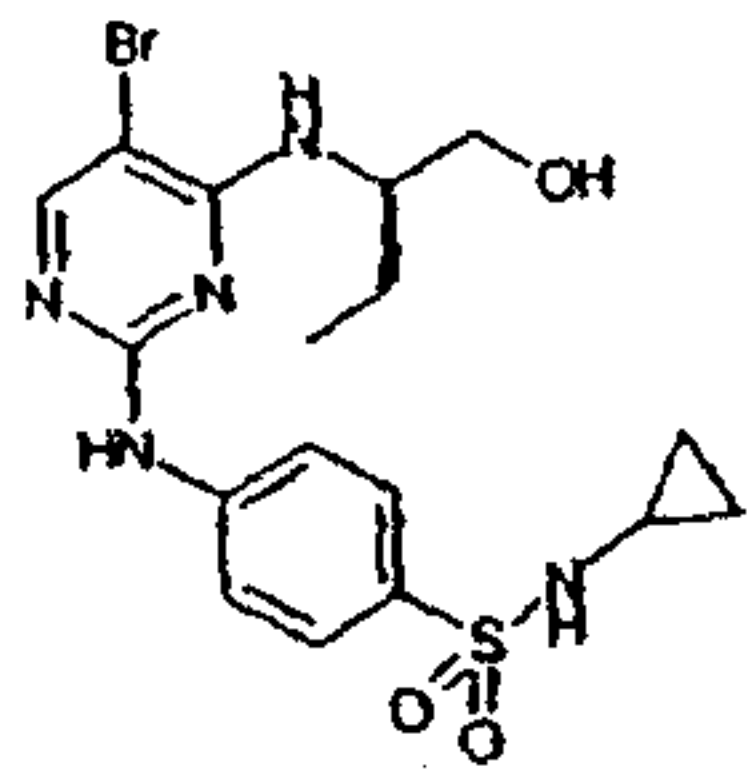
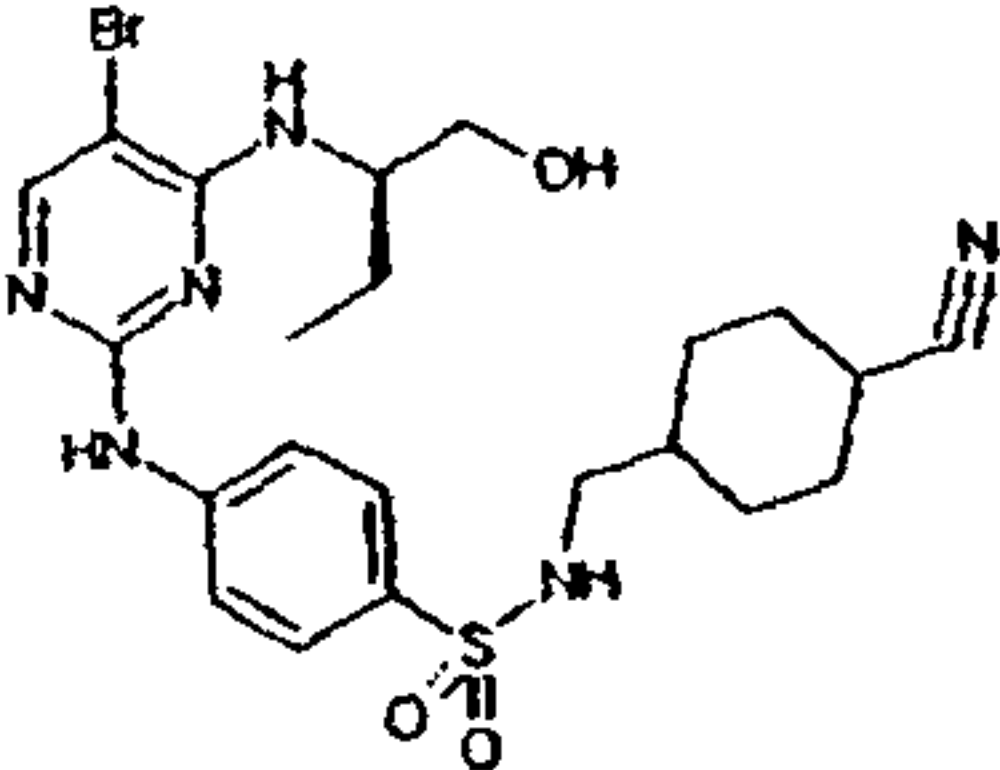
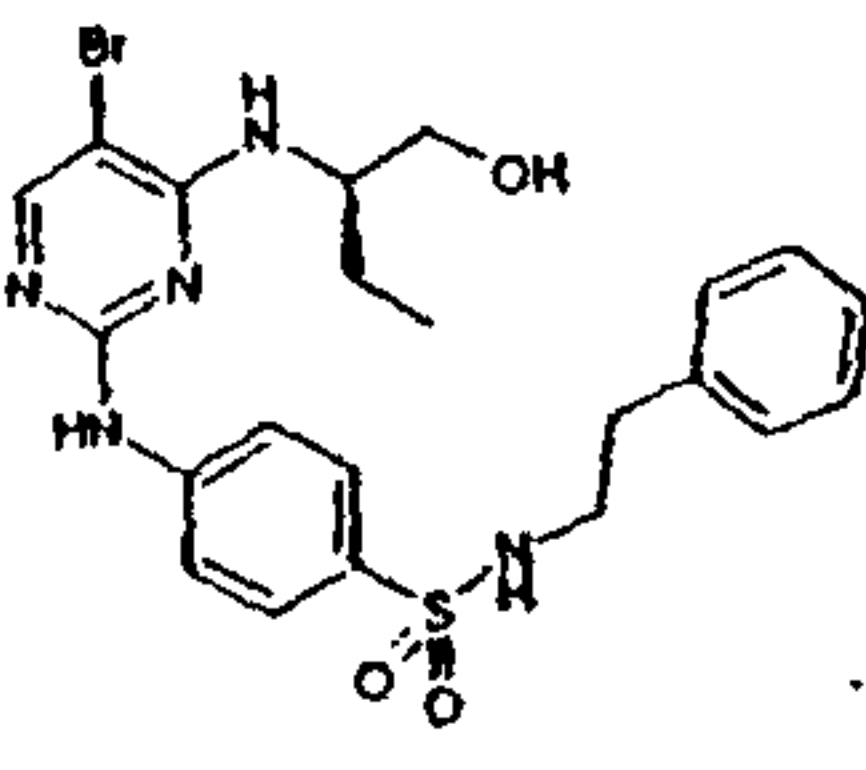
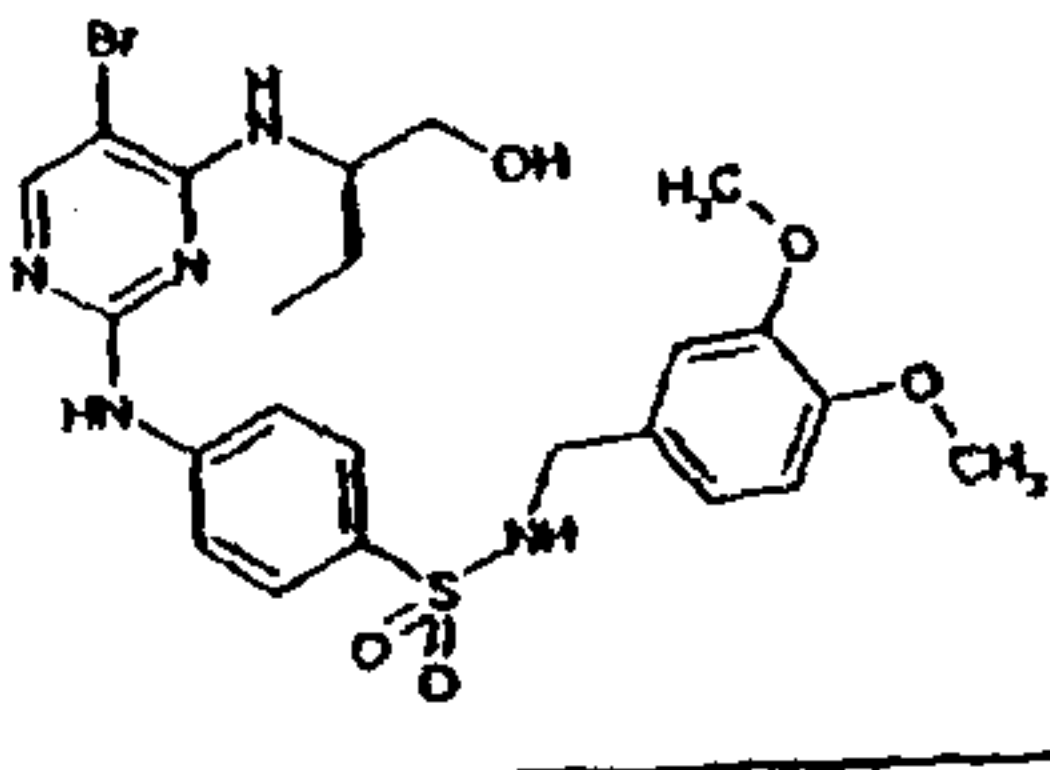
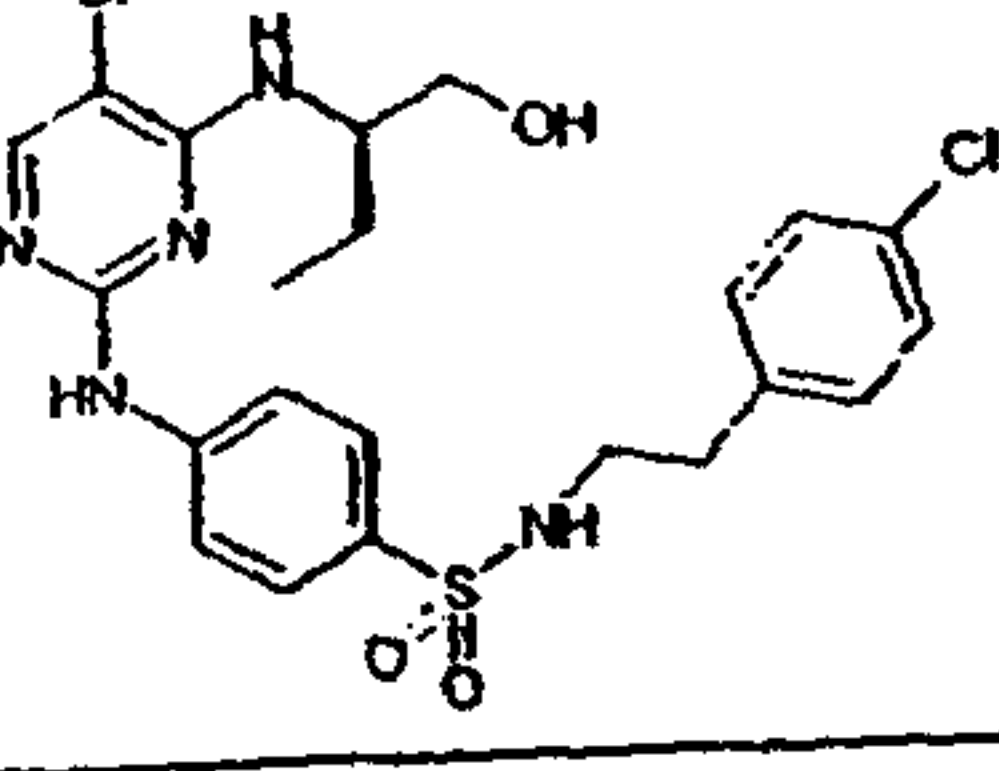
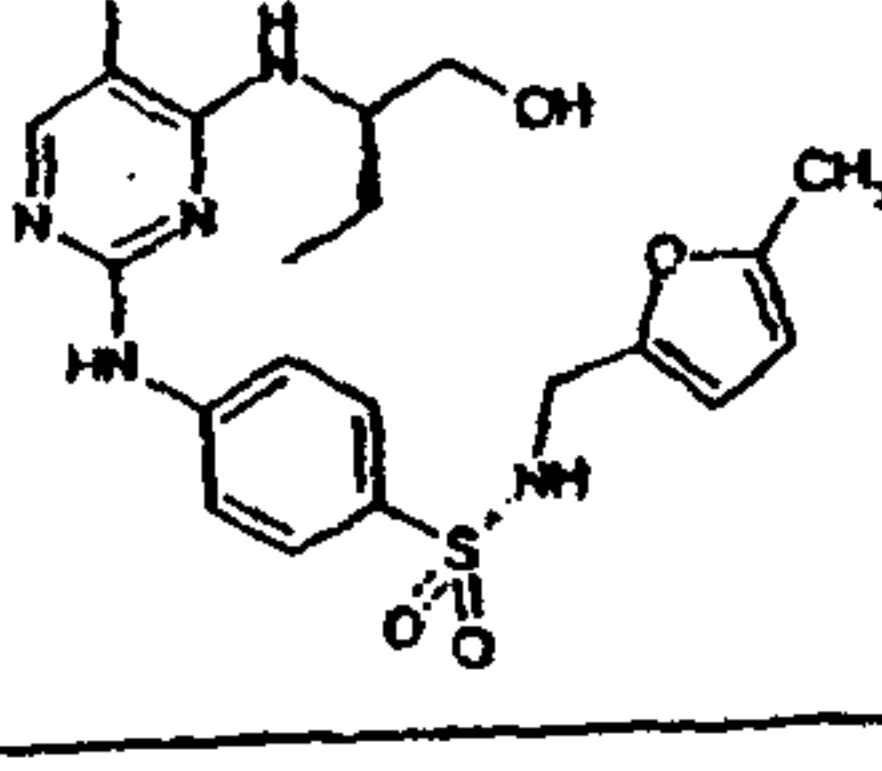
Beispiel-Nr.	Verbindung	Molekular- gewicht	ESI-MS
477		515,4303	515/517
478		460,3508	460/462
479		498,424	498/500
480		536,4484	536/538
481		499,4313	499/501

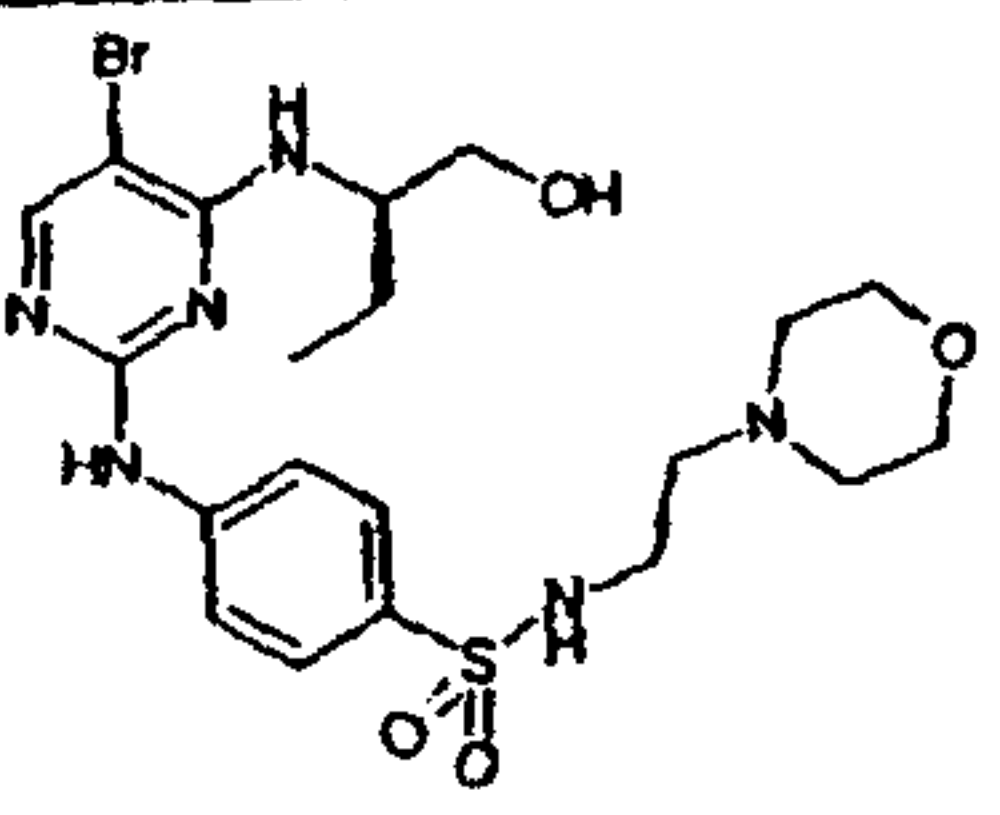
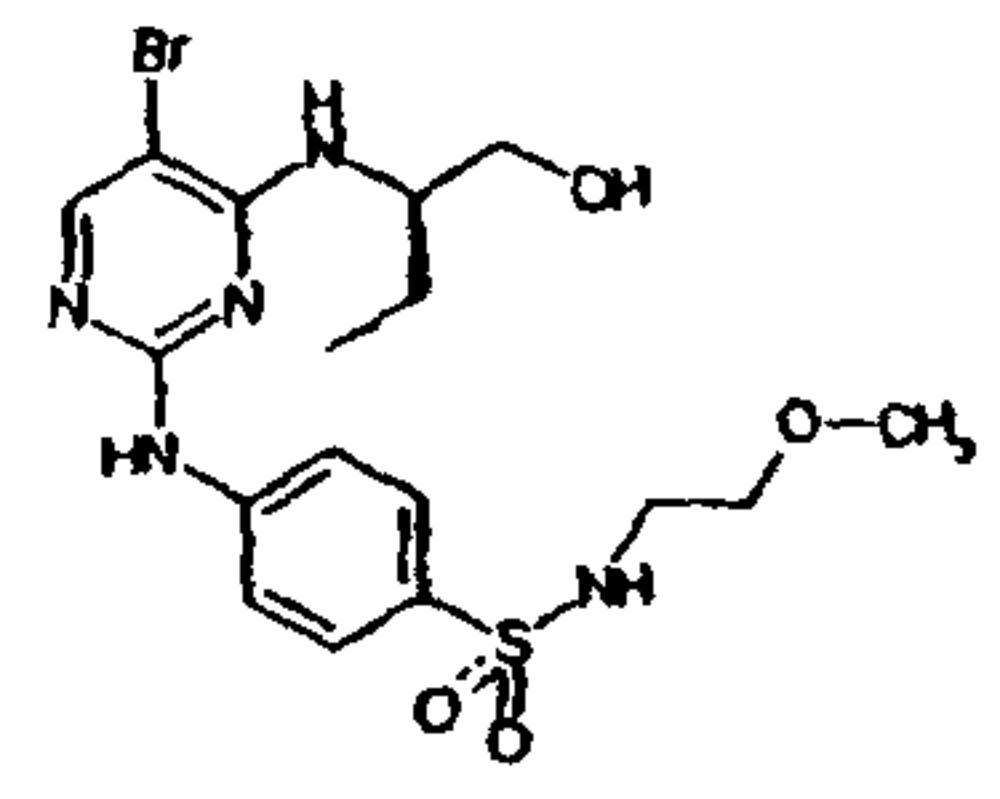
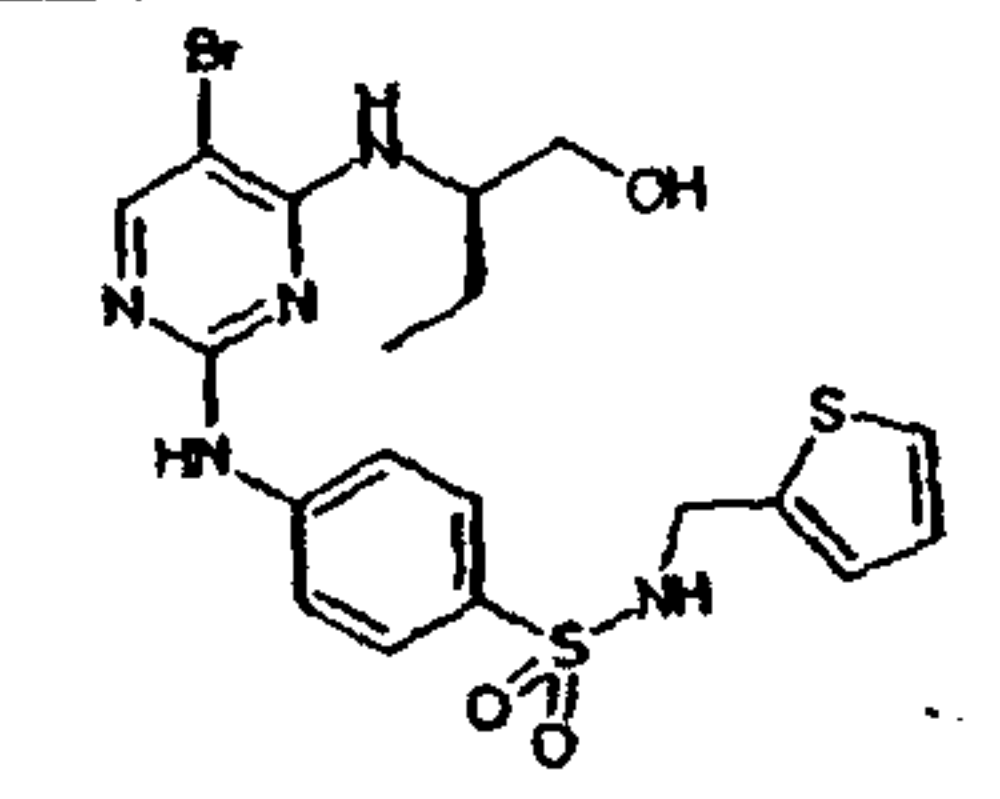
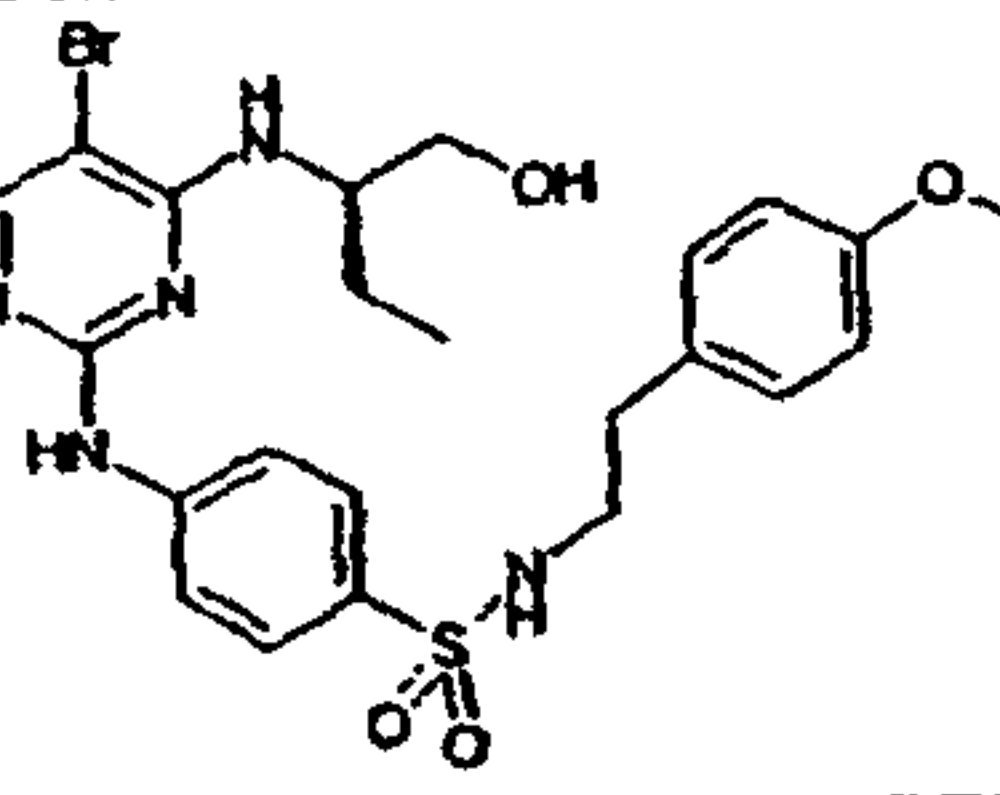
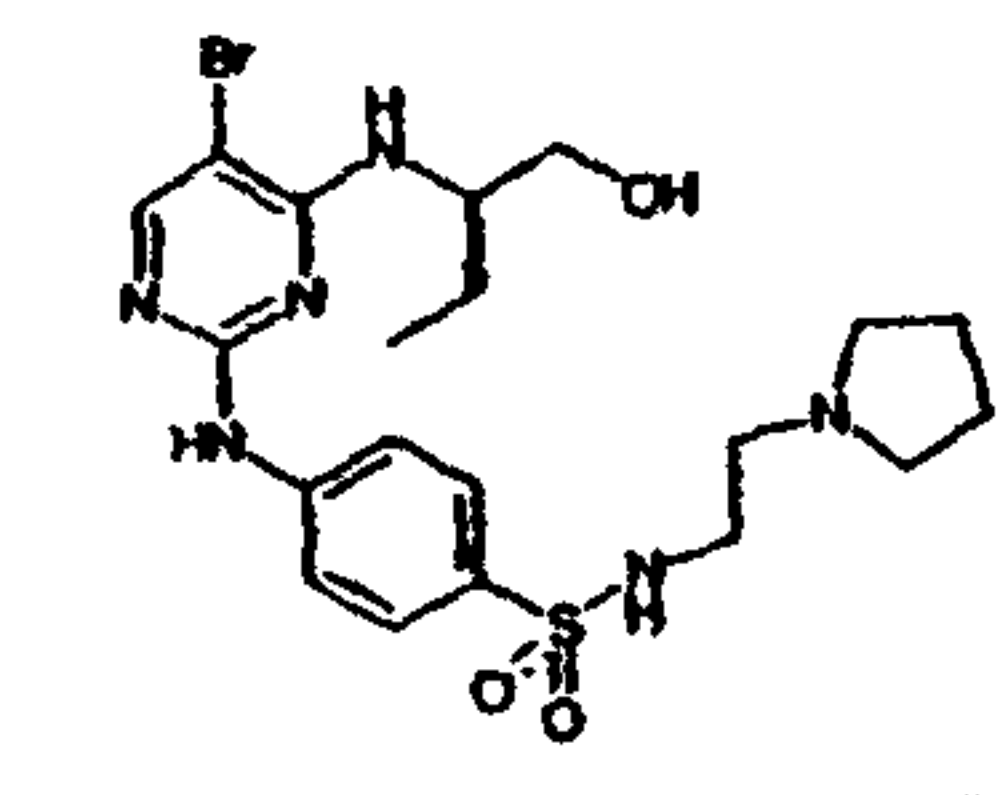
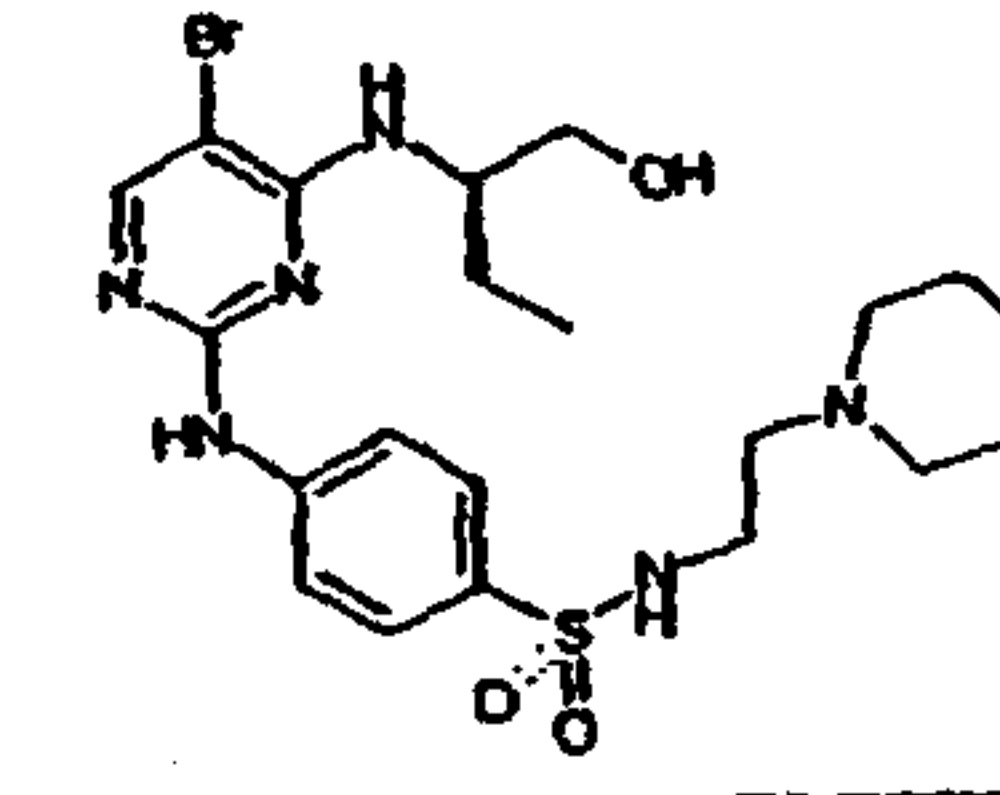
Beispiel-Nr.	Verbindung	Molekular- gewicht	ESI-MS
482		513,4581	513/515
483		510,3859	510/512
484		513,4581	513/515
485		493,3839	493/495
486		510,3859	510/512

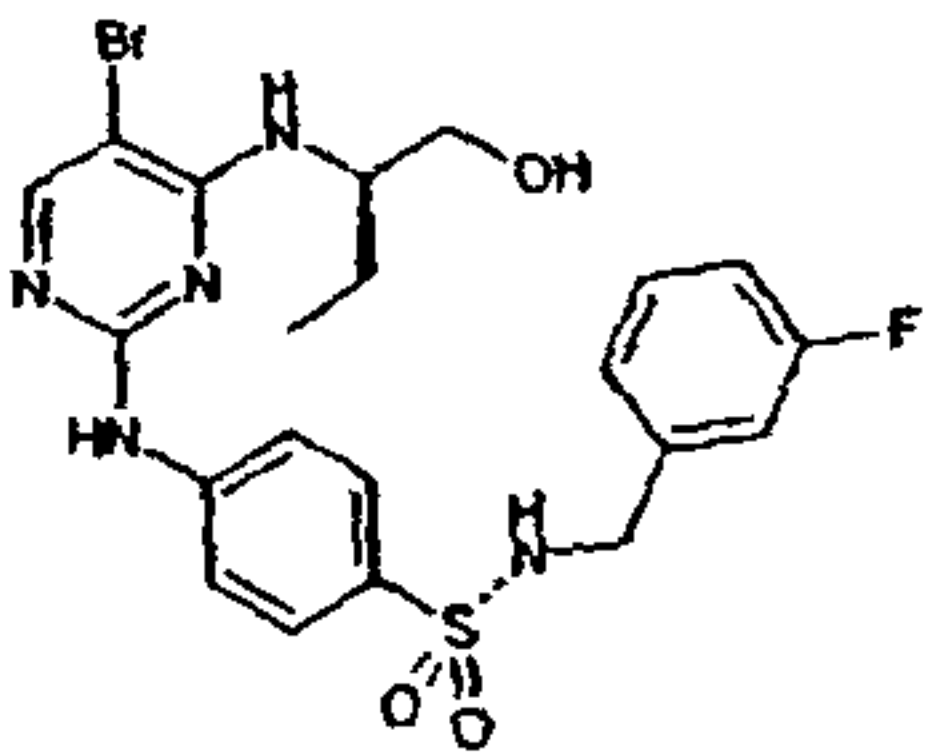
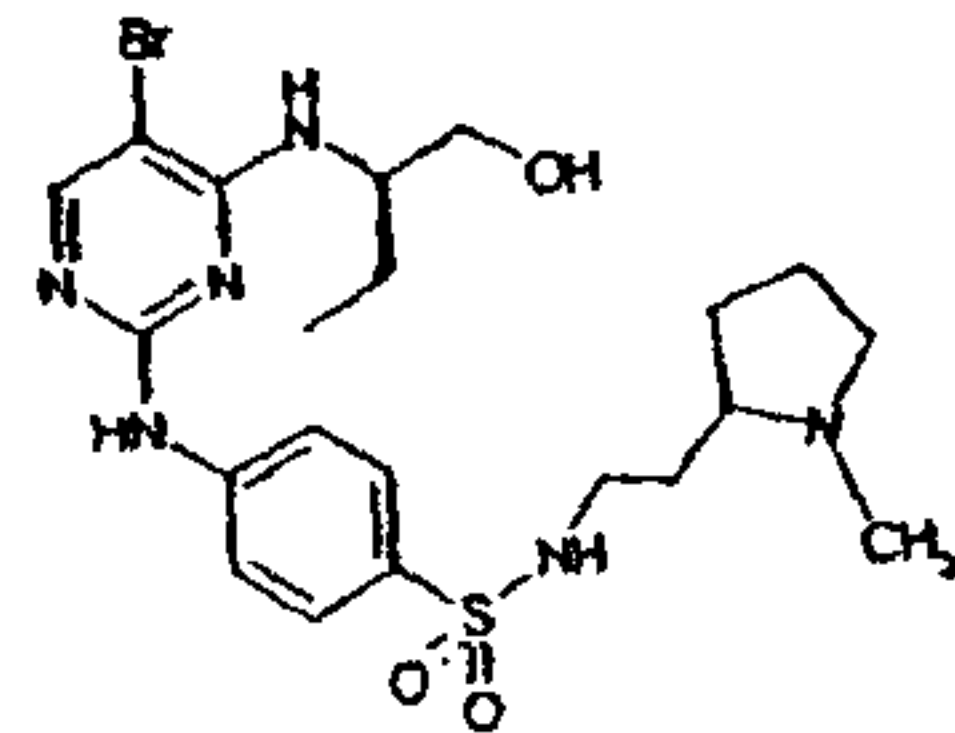
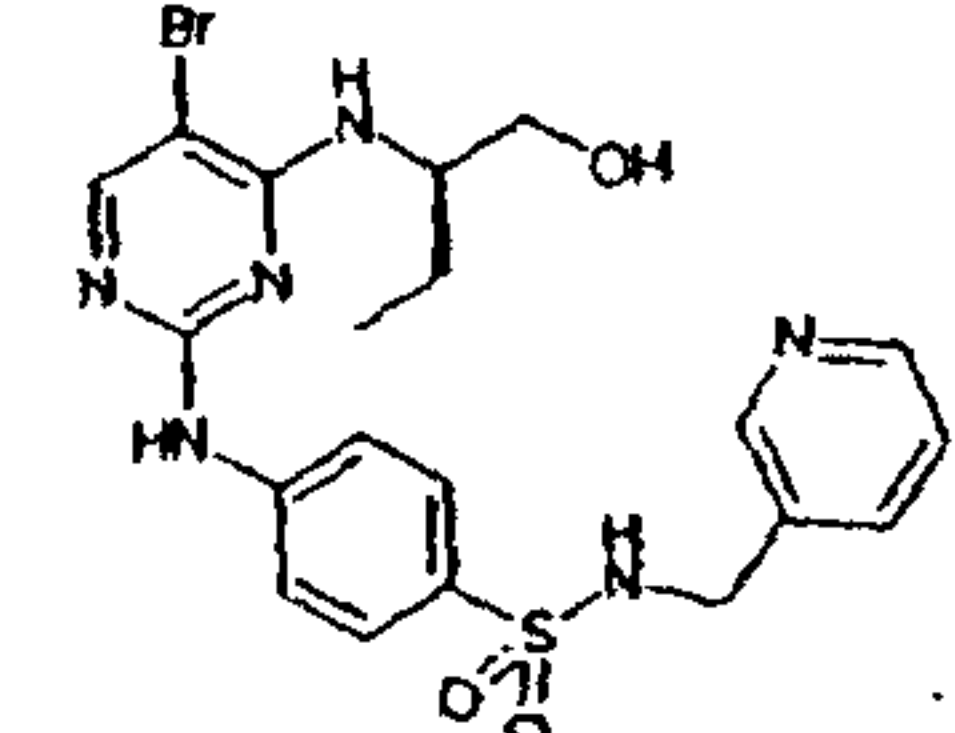
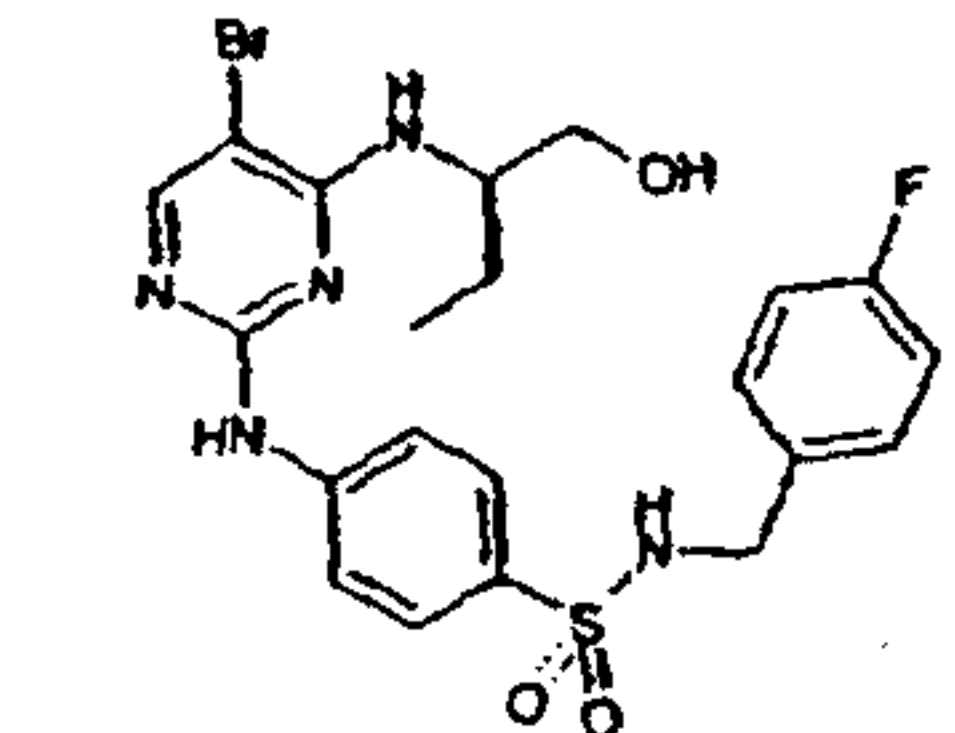
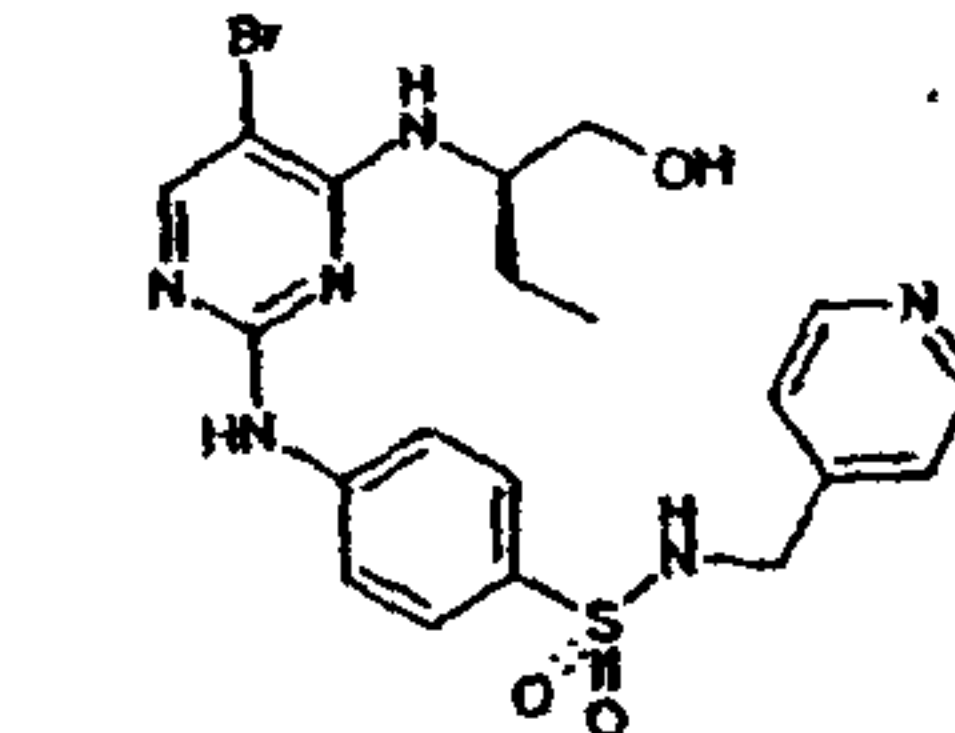
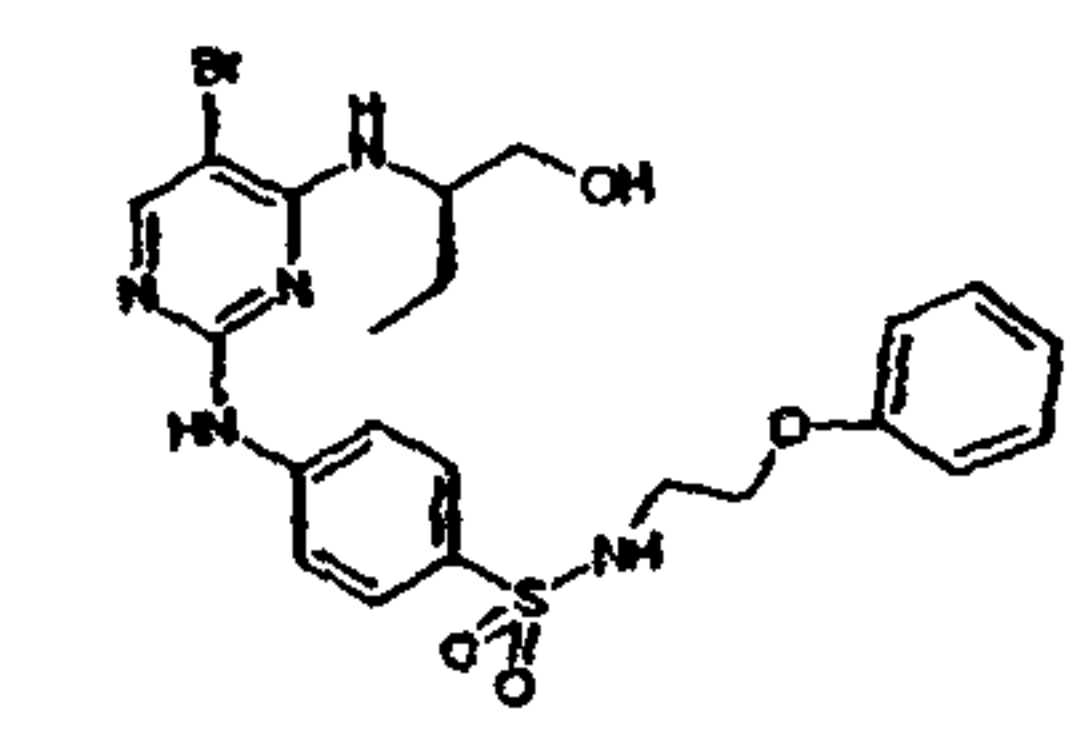
Beispiel-Nr.	Verbindung	Molekular- gewicht	ESI-MS
487		493,3839	493/495
488		522,4216	522/524
489		522,4216	522/524
490		585,5015	585/587
491		506,4226	506/508

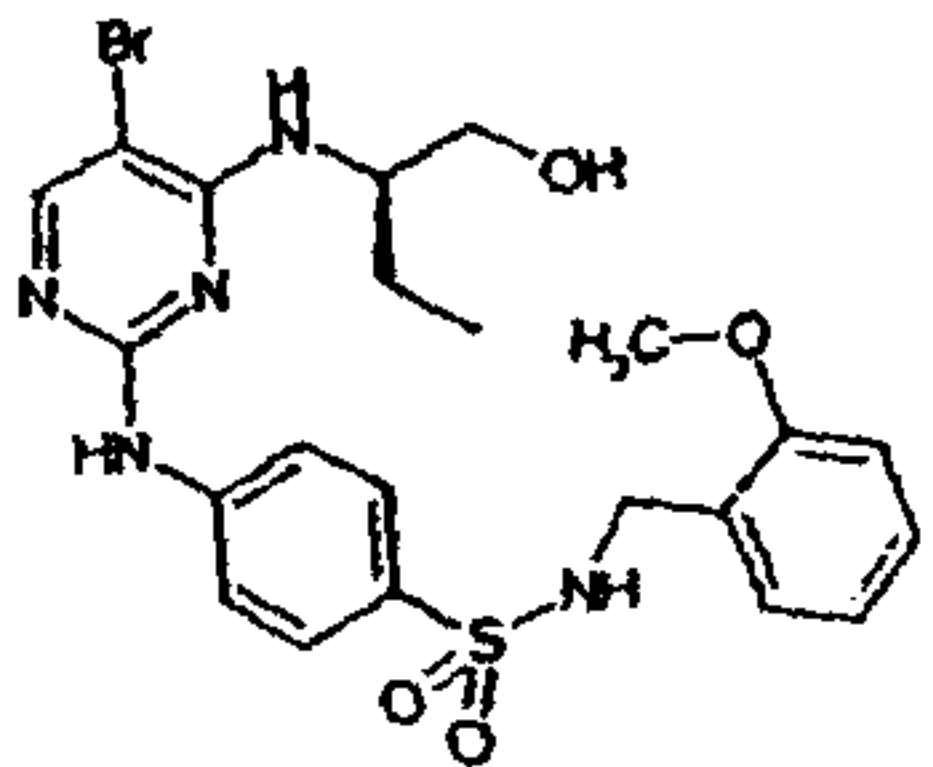
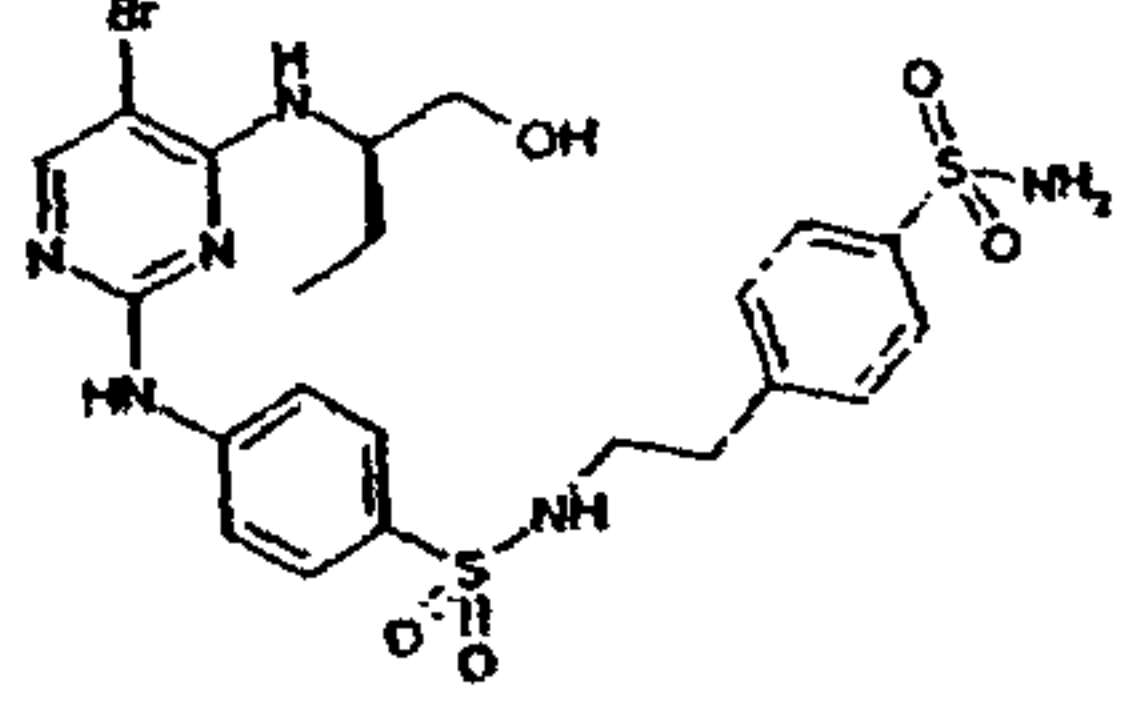
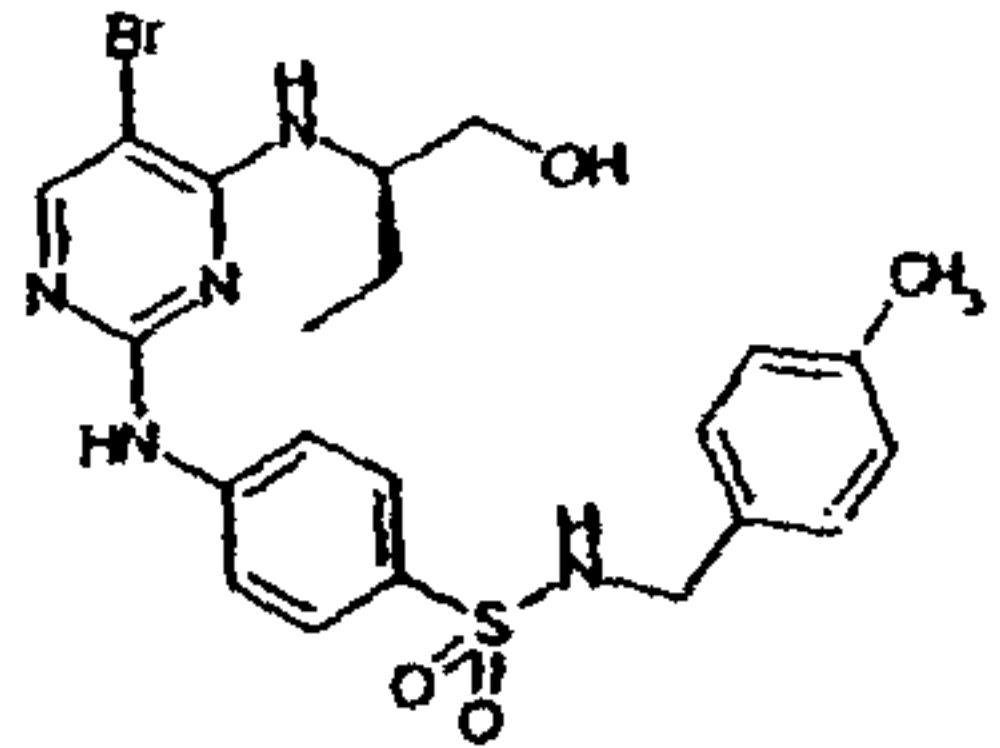
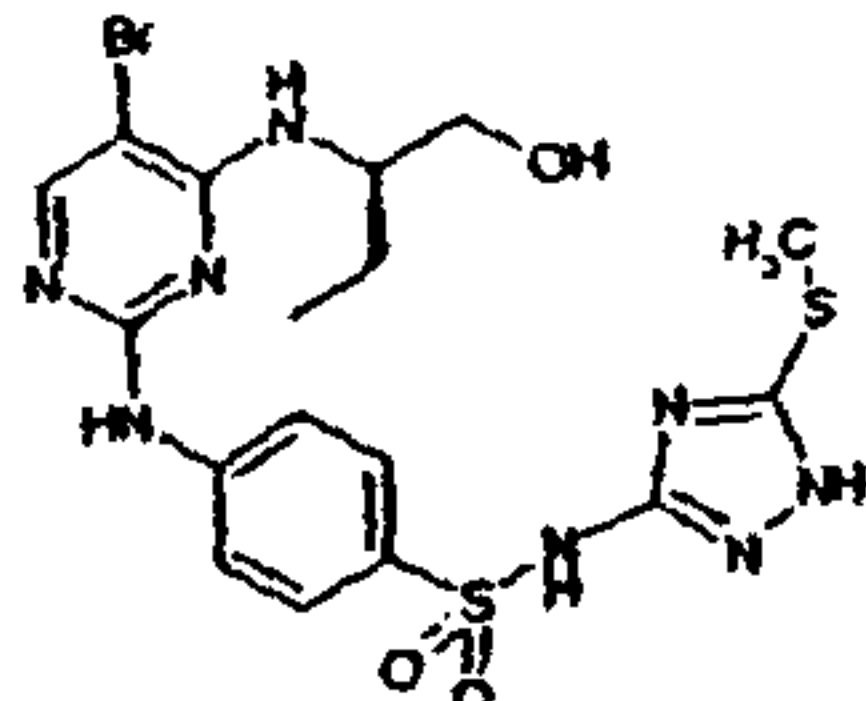
Beispiel-Nr.	Verbindung	Molekulargewicht	ESI-MS
492		515,4151	515/517
493		512,47	
494		548,503	
495		610,5738	
496		487,4203	
497		524,4414	

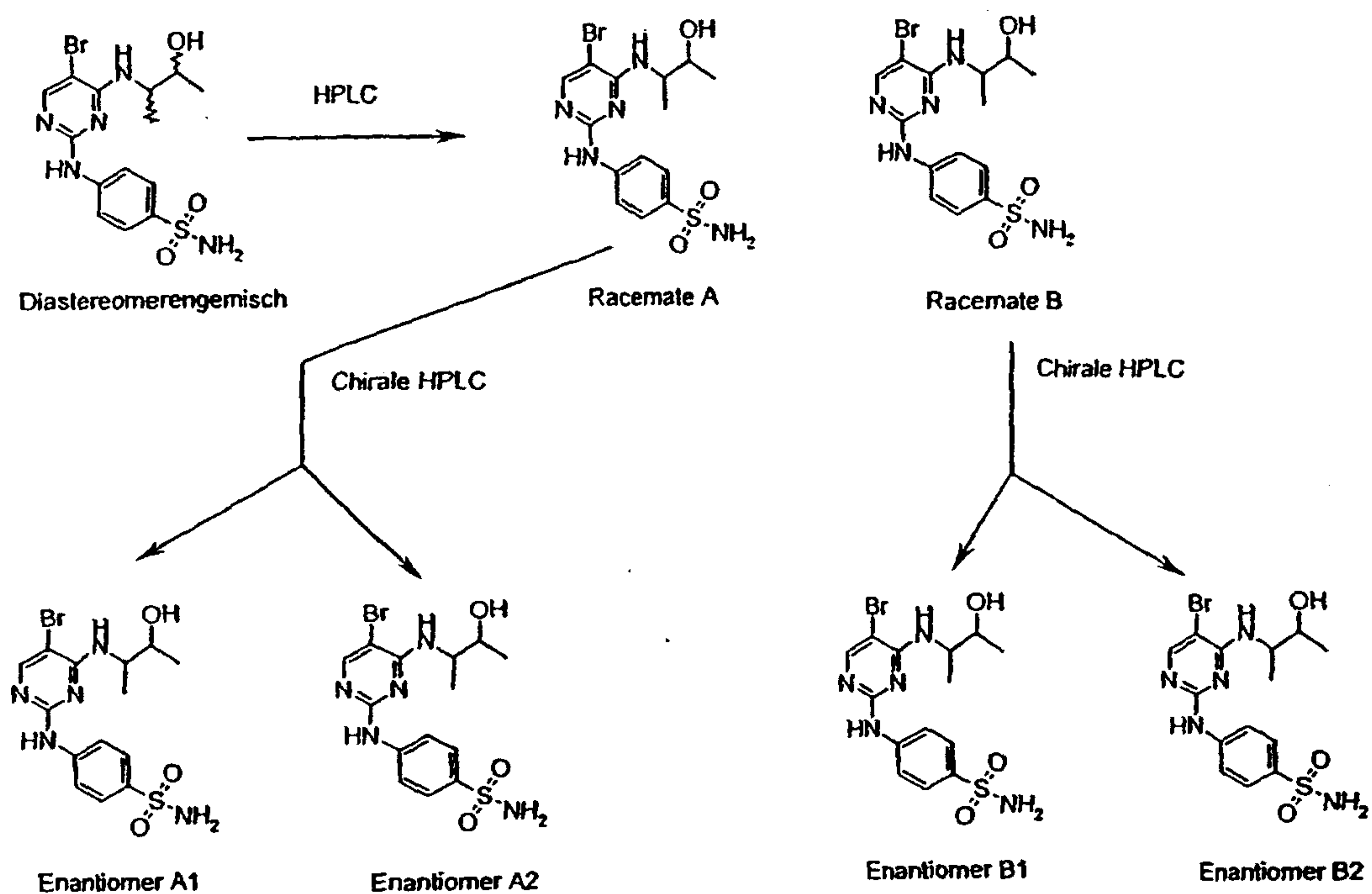
Beispiel-Nr.	Verbindung	Molekulargewicht	ESI-MS
498		574,4197	
499		514,4858	
500		528,5126	
501		542,5394	
502		556,5662	
503		496,3838	

Beispiel-Nr.	Verbindung	Molekulargewicht	ESI-MS
511		456,3628	
512		537,4801	
513		520,4494	
514		566,4742	
515		554,8945	
516		510,4106	

Beispiel-Nr.	Verbindung	Molekulargewicht	ESI-MS
517		529,4571	
518		474,3776	
519		512,4508	
520		550,4752	
521		513,4581	
522		527,4849	

Beispiel-Nr.	Verbindung	Molekulargewicht	ESI-MS
523		524,4127	
524		527,4849	
525		507,4107	
526		524,4127	
527		507,4107	
528		536,4484	

Beispiel-Nr.	Verbindung	Molekulargewicht	ESI-MS
529		536,4484	
530		599,5283	
531		520,4494	
532		529,4419	

Separation of Diastereomer Mixtures of the Compounds According to the Invention**Separation in the Example of the Diastereomer Mixture of Compound No. 274**

[Key:]

Diastereomerengemisch = Diastereomer mixture

Chirale HPLC = Chiral HPLC

The diastereomer mixture was separated in the two corresponding racemates (A and B) by means of HPLC. Conditions:

Column: Kromasil C18 (5 μ m) 150 x 4.6 mm

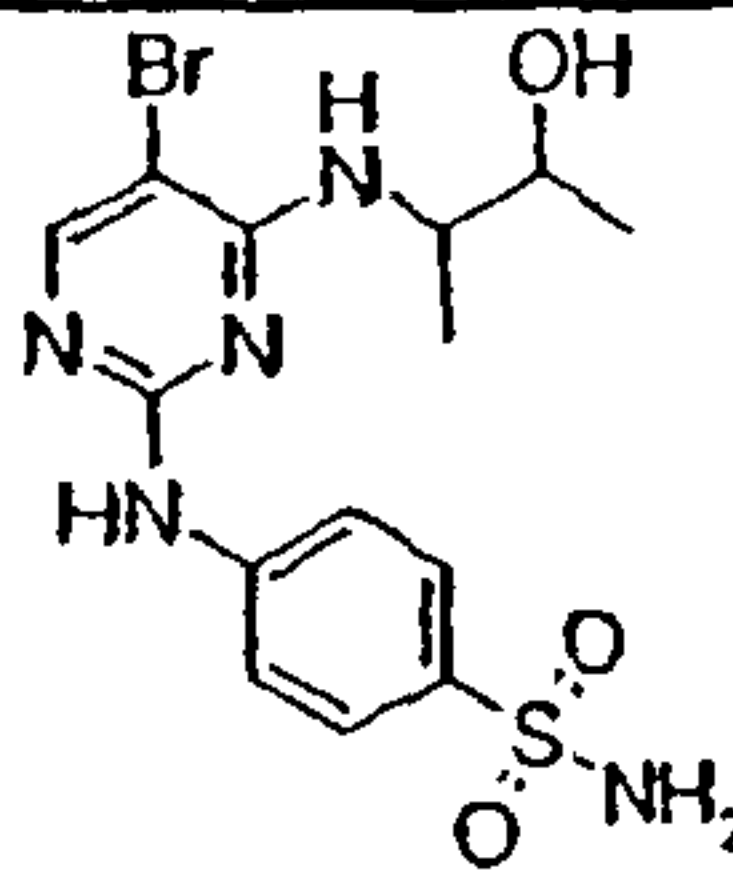
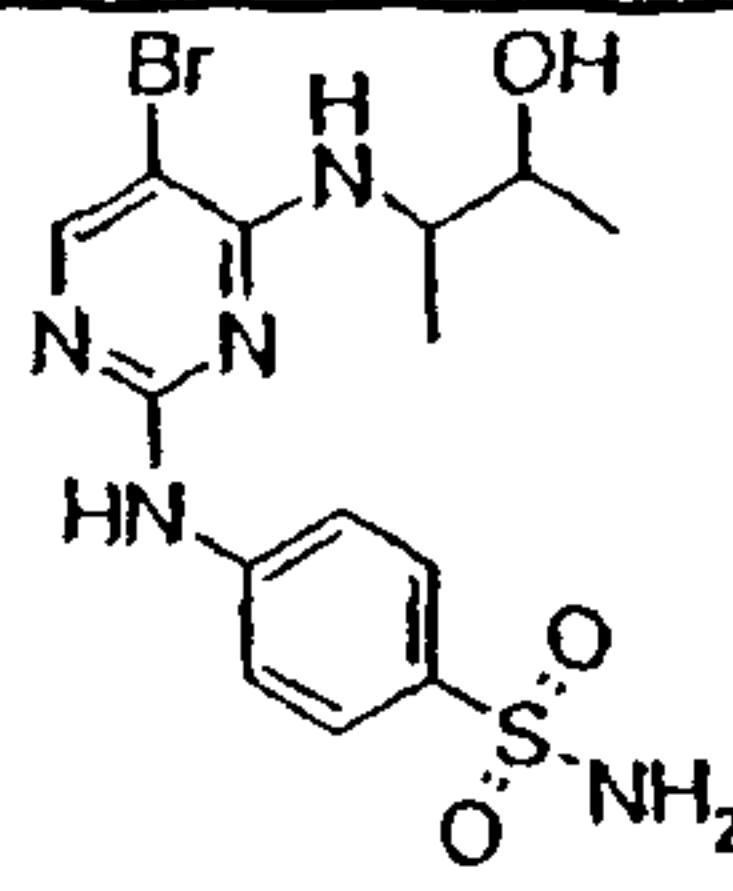
Eluant: 25% acetonitrile/water with 1 ml of NH₃/l;

Flow: 1.0 ml/min

Detection: PDA 300 nm

Retention times: Racemate A – 11.6 minutes

Racemate B – 12.4 minutes

	 Racemate B	 Racemate A
NMR	DMSO-d6: 9.68, s, 1 H 8.12, s, 1 H 7.87, d, 2 H 7.70, d, 2 H 7.14, s, 2 H 6.15, d, 1 H 5.01, d, 1 H 4.10, m, 1 H 3.80, m, 1 H 1.22, d, 3 H 1.1, d, 3 H	DMSO-d6: 9.68, s, 1 H 8.11, s, 1 H 7.85, d, 2 H 7.69, d, 2 H 7.16, s, 2 H 6.35, d, 1 H 4.90, d, 1 H 4.08, m, 1 H 3.80, m, 1 H 1.18, d, 3 H 1.12, d, 3 H

Below, racemates A and B in each case were separated by means of chiral HPLC.

Conditions:

Column: Chiralpak AD (10 μ m) 250 x 4.6 mm

Eluant: Hexane/ethanol 80:20

Flow: 1.0 ml/min

Detection: PDA 300 nm

Retention times: Enantiomer A1 – 16.6 minutes

Enantiomer A2 – 19.6 minutes

Enantiomer B1 – 16.0 minutes

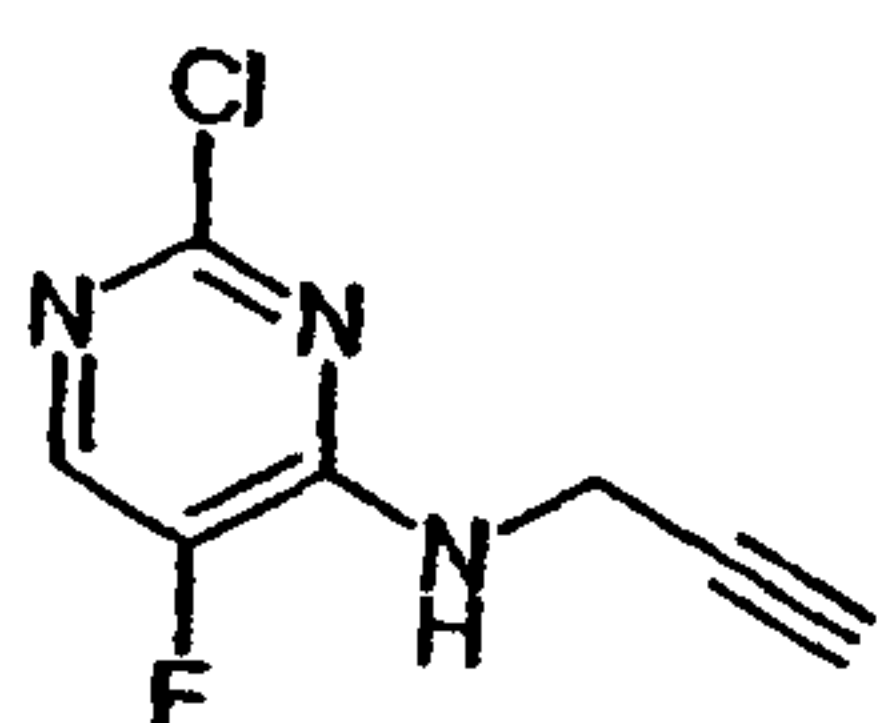
Enantiomer B2 – 17.8 minutes

Production of the intermediate stages preferably used for the synthesis of the compounds of general formula I according to the invention.

Example 1.0

Production of N-(2-chloro-5-fluoro-4-pyrimidinyl)-N-2-propynylamine

11.1 g (66 mmol) of 2,4-dichloro-5-fluoropyrimidine is dissolved in 60 ml of acetonitrile, and 10.2 ml (73 mmol) of triethylamine and 6.0 ml (86 mmol) of propynylamine are added. The reaction mixture is stirred overnight at room temperature and then poured into water. The mixture is extracted by means of ethyl acetate, the combined organic phases are dried on MgSO_2 , and the solvent is evaporated by means of underpressure. After the remaining material is recrystallized with diisopropyl ether/hexane, the yield is 10.6 g (87% of theory) of the product.



5-H	8.18 (3.3Hz, 1H)	Solvent: DMSO
4CH	4.14 (dd, 2H)	Yield: 87%
	3.20 (t, 1H)	Melting point: 96°C
NH	8.65 (tb, 1H)	

The 4-(diaminocyclohexyl) derivatives that are described below are synthesized via reductive aminations of the described keto derivative with use of triacetoxy borohydride (Abdel-Magid, Carson, Harris, Maryanoff, Sha, *J. Org. Chem.* 1996, 61, 3849). The keto derivative is obtained by TPAP oxidation (Griffith, Ley, *Aldrichimica Acta* 1990, 23, 13) of the corresponding alcohol.

Similarly produced are also the following intermediate compounds:

[Key to subsequent tables:]

Beispiel-Nr. = Example No.

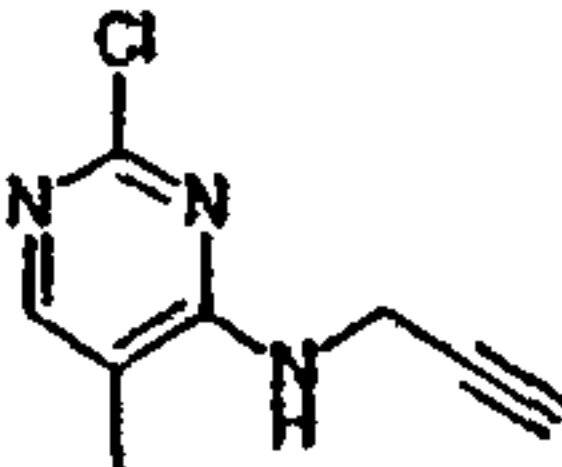
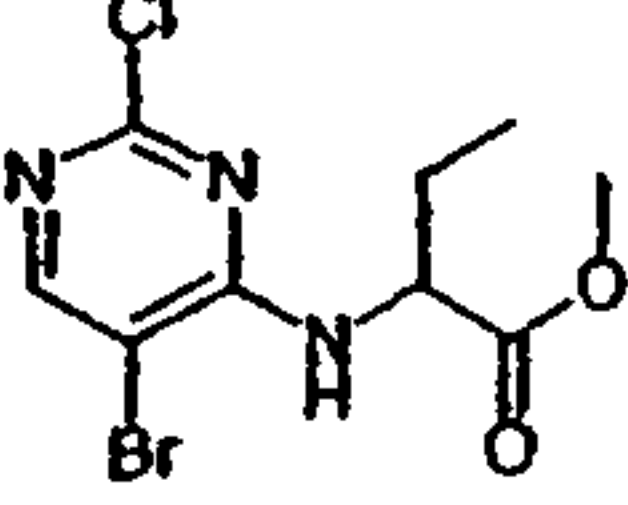
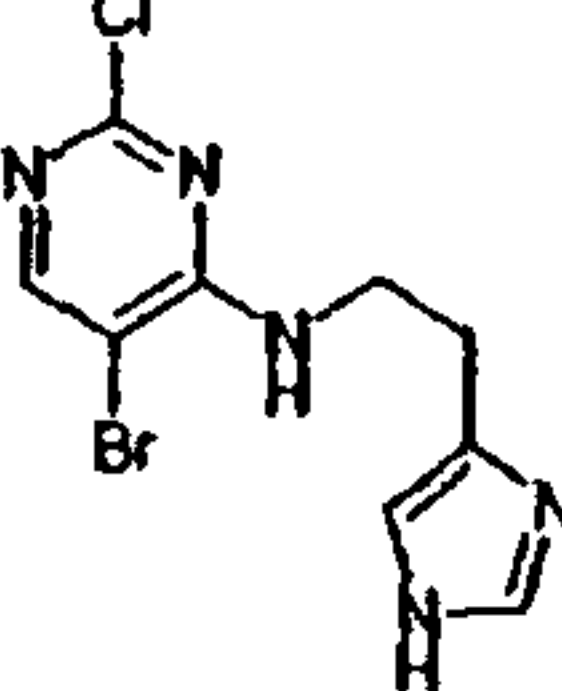
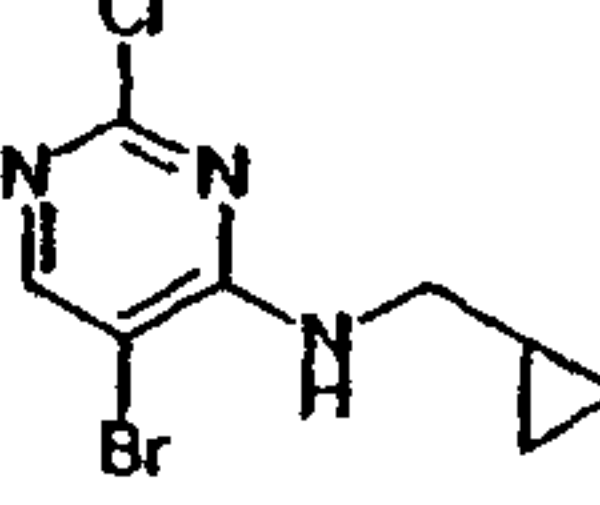
Lösemittel = Solvent

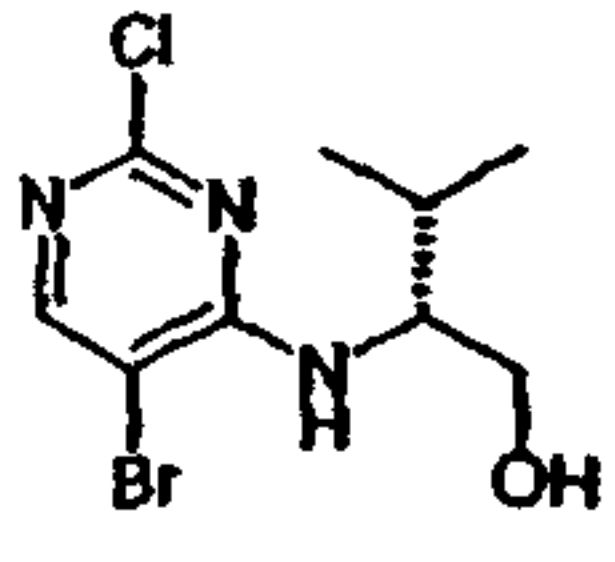
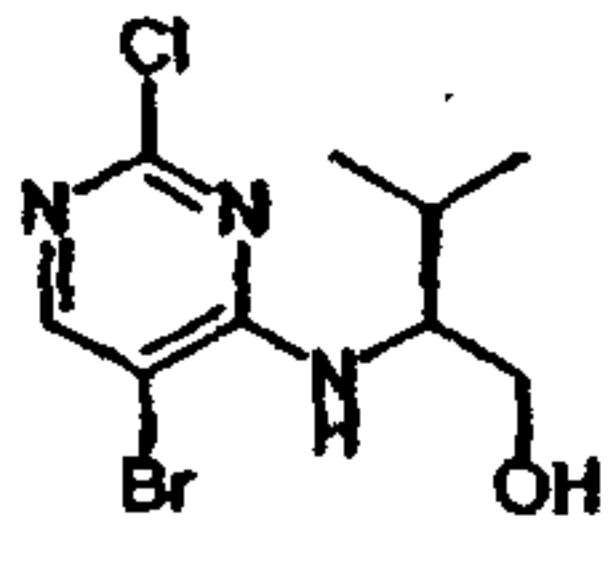
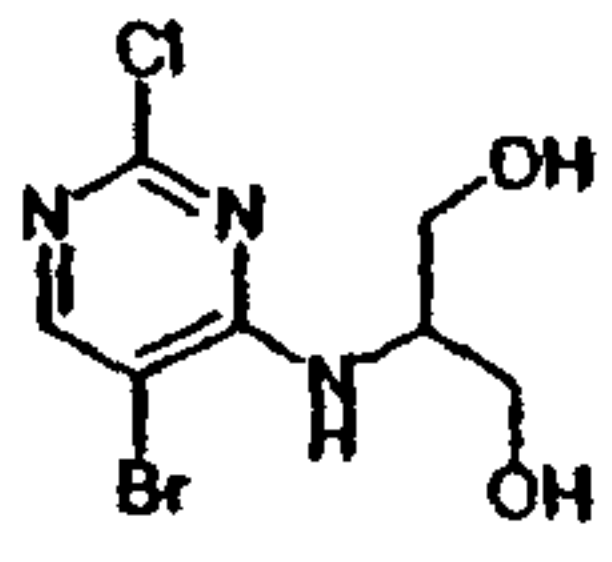
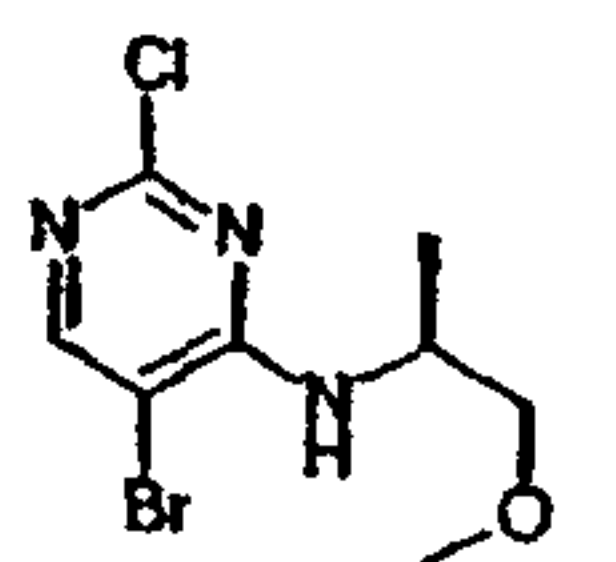
Ausbeute = Yield

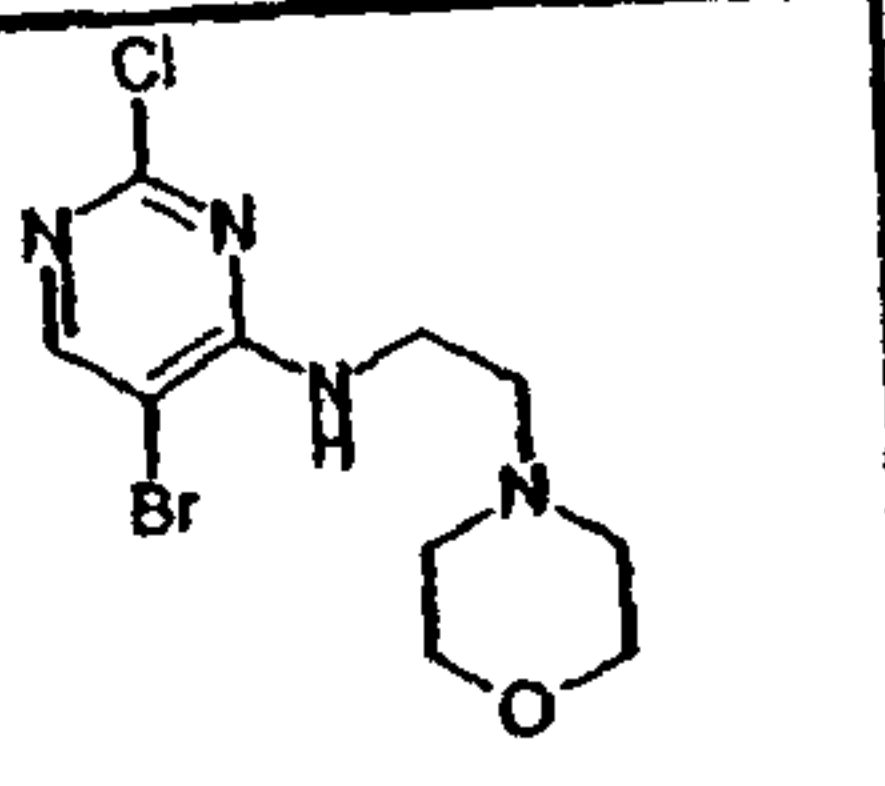
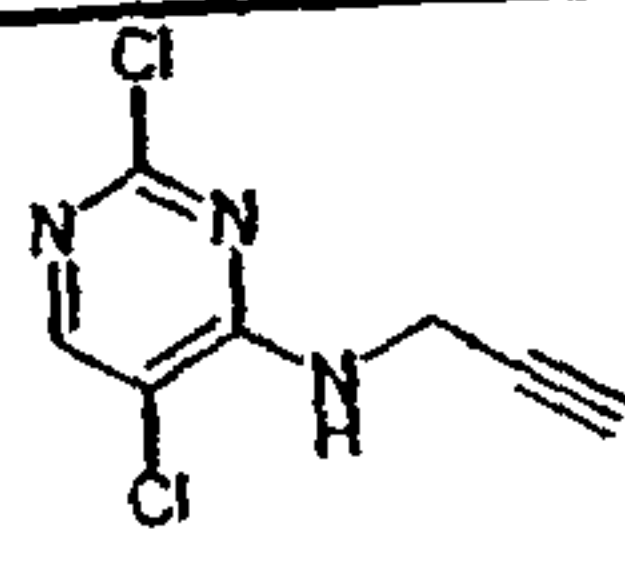
Schmp. = Melting point

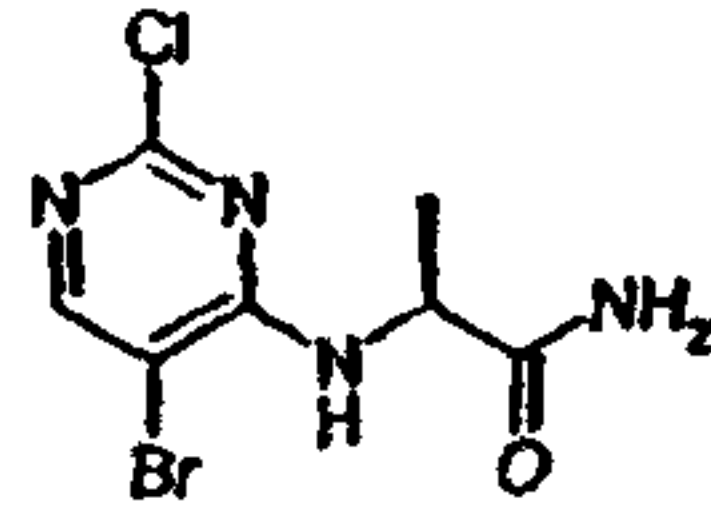
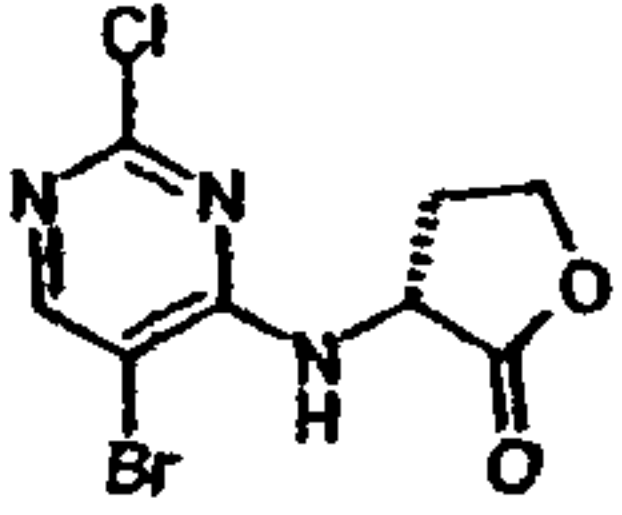
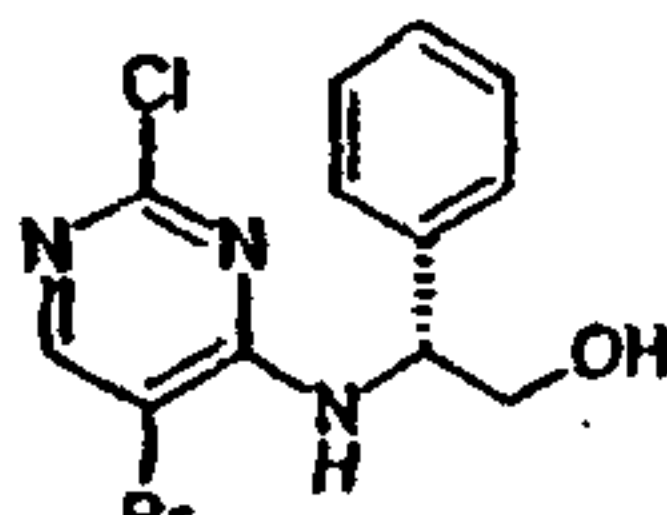
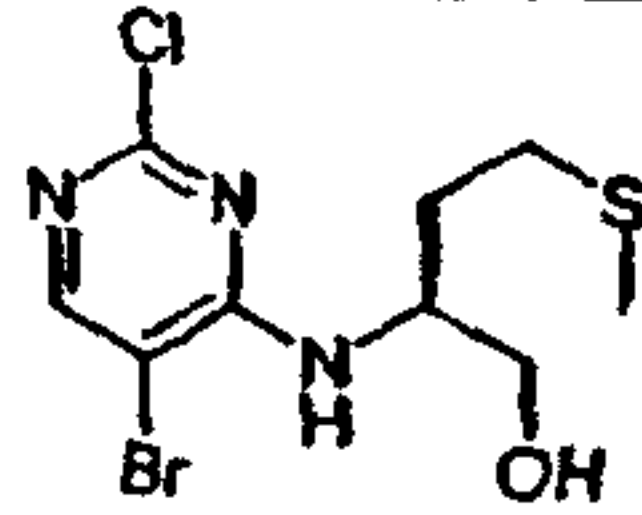
Masse = Mass

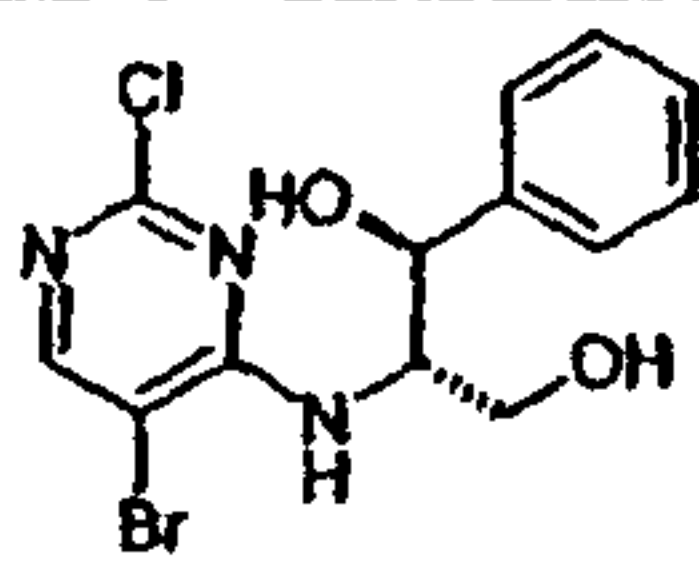
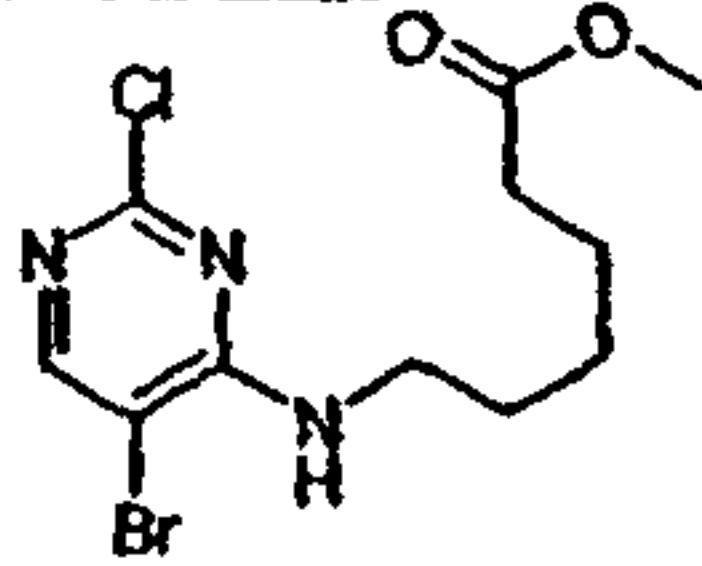
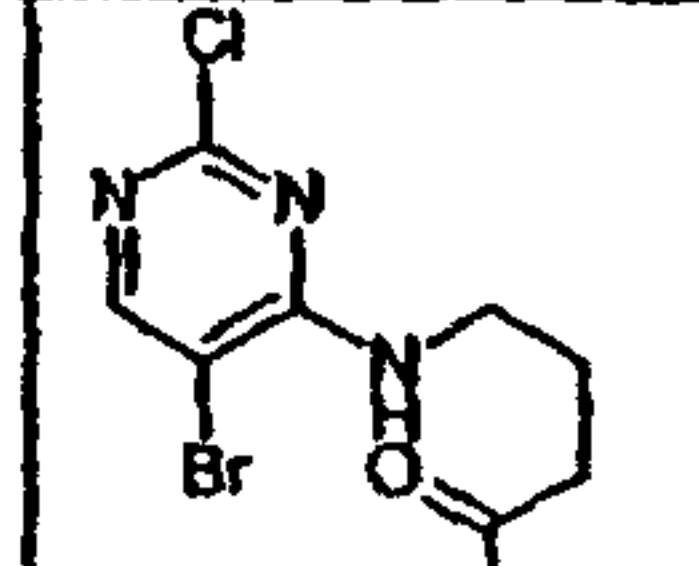
Chrom. Ausbeute = Chromatography yield

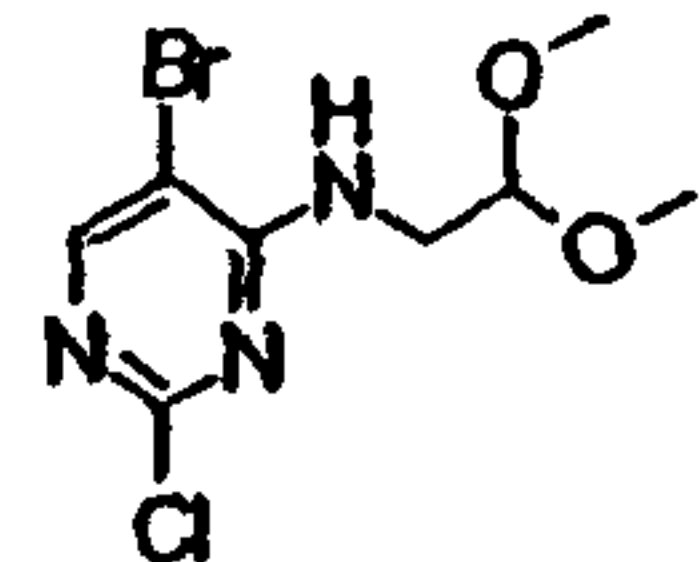
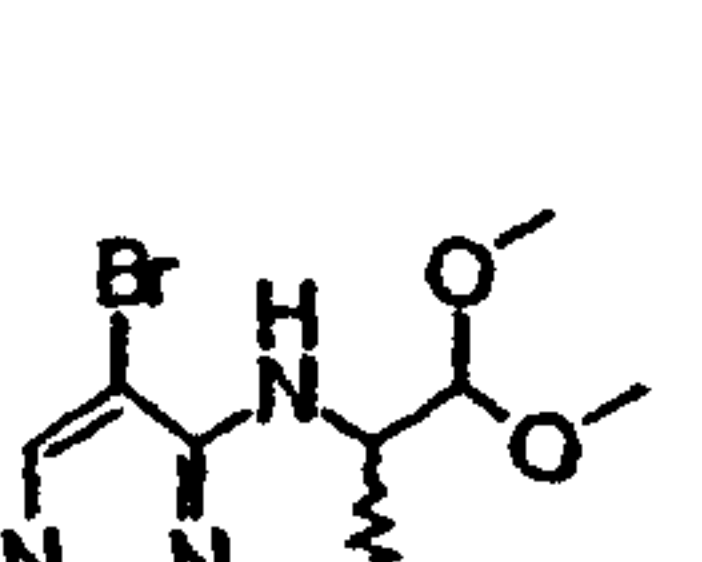
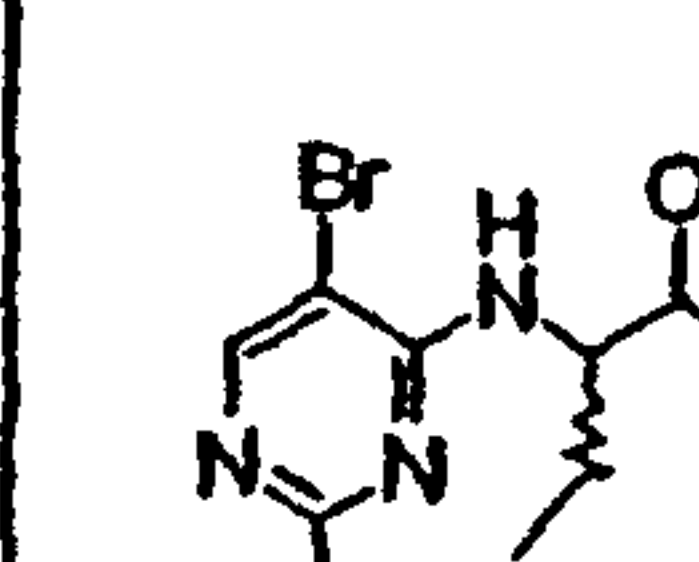
				
Beispiel -Nr.	1.1	1.2	1.3	1.4
Löse- mittel	CDCl ₃	DMSO	DMSO	DMSO
5-H	7.87 (s,1H)	8.34 (s,1H)	8.24 (s,1H)	8.23 (s,1H)
4CH	4.32 (dd,2H)	4.48 (q,1H)	3.59 (td,2H)	3.21 (t,2H)
	2.30 (t,1H)	1.93 (dq,2H)	2.78 (t,2H)	1.10 (mc,1H)
5CH	2.03 (s,3H)	0.92 (t,3H)	7.57 (s,1H)	0.42 (mc,2H)
		3.66 (s,3H)	6.85 (s,1H)	0.37 (mc,2H)
NH	4.91 (sb,1H)	7.69 (d,1H)	7.90 (tb,1H)	7.84 (t,1H)
			11.92 (sb,1H)	
Aus- beute	80%	42%	33%	74%
Schmp.	121-121.5°C	73°C	90°C	98°C

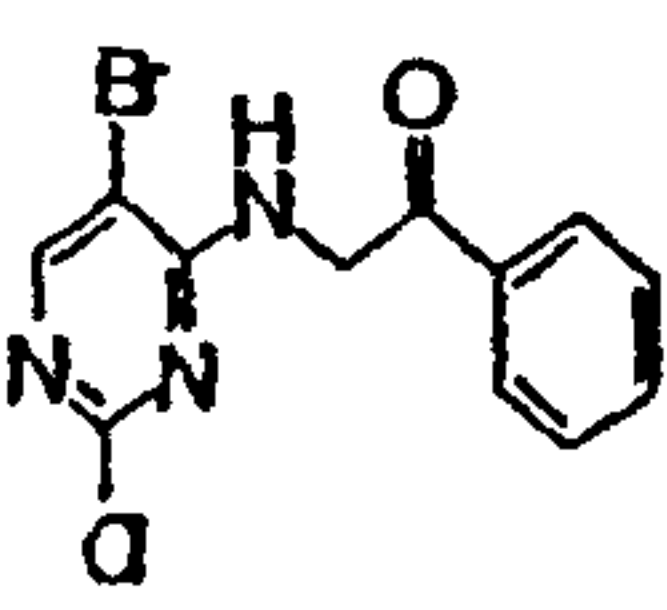
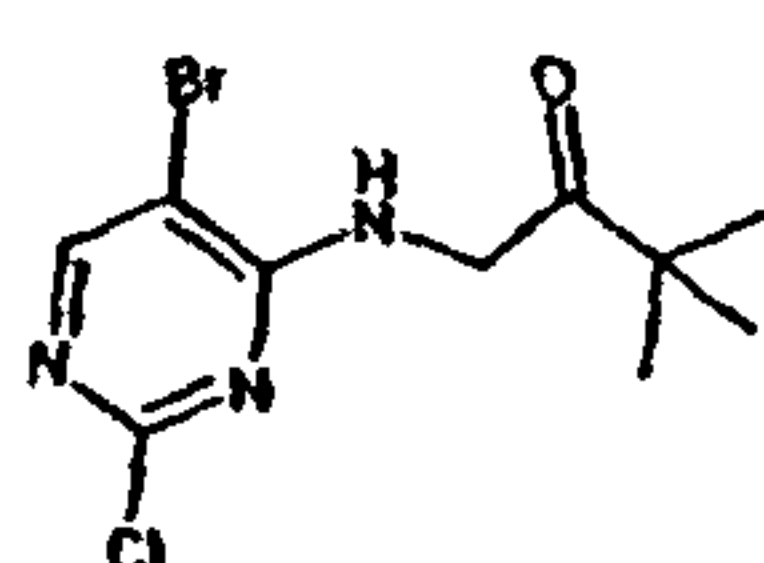
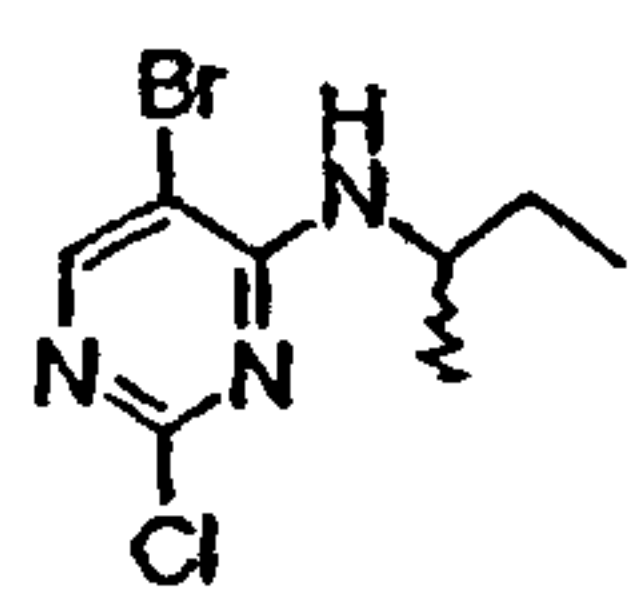
				
Beispiel -Nr.	1.5	1.6	1.7	1.8
Löse- mittel	DMSO	DMSO	DMSO	DMSO
6-H	8.26 (s,1H)	8.26 (s,1H)	8.27 (s,1H)	8.37 (s,1H)
4CH	3.59 (mc,2H)	3.58 (mc,2H)	3.58 (sb,4H)	4.40 (m, 1H)
	3.90 (mc,1H)	3.97(mc,1H)	4.14 (mc,1H)	3.49 (dd,1H)
	1.98 (mc,1H)	1.96 (mc,1H)		3.33 (dd,1H)
	0.94 (d,3H)	0.92 (d,3H)		3.26 (s,3H)
	0.86 (d,3H)	0.84 (d,3H)		1.15 (d,3H)
OH	4.67 (mb,1H)	4.74 (t,1H)	4.78 (sb,2H)	
NH	6.75 (sb,1H)	6.87 (d,1H)	6.73 (sb,1H)	7.29 (d, 1H)
Aus- beute	82%	91%	41%	74%
Schmp.	113-114°C	121 – 122°C	155-156°C	Öl

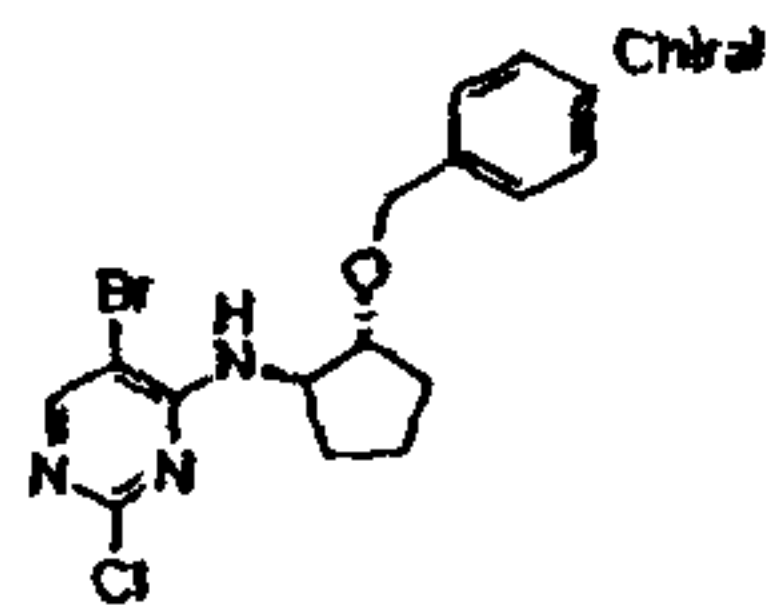
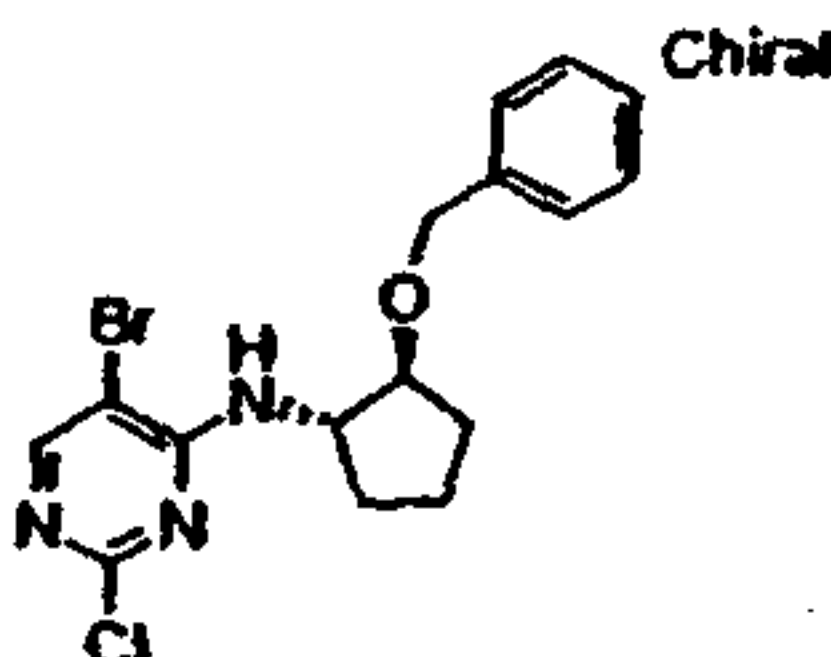
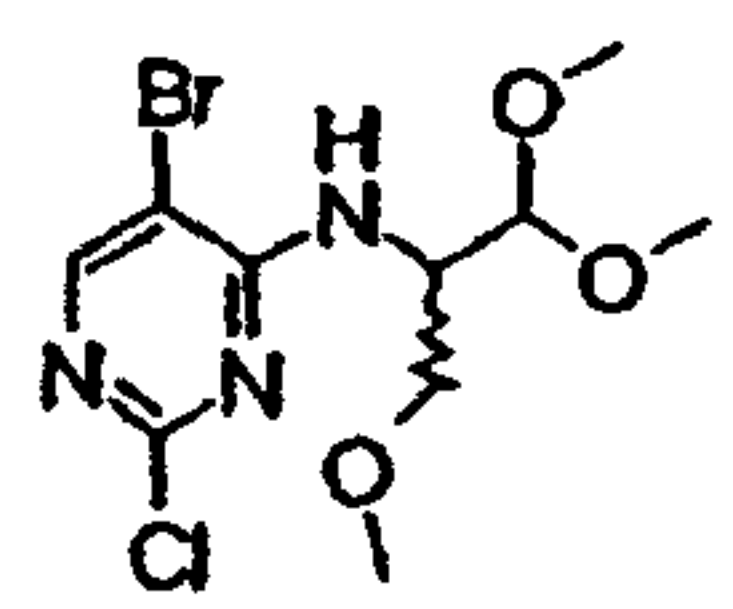
		
Beispiel-Nr.	1.9	1.10
Lösemittel	DMSO	DMSO
6-H	8.24 (s, 1H)	8.36 (s, 1H)
4CH	3.49 (q, 2H)	4.14 (d, 2H)
	2.50 (t, 2H)	3.18 (t, 1H)
	2.42 (t, 4H)	
	3.56 (t, 4H)	
OH		
NH	7.57 (sb, 1H)	8.40 (s, 1H)
Ausbeute	31%	73
Schmp.	118 – 119°C	103 – 104°C

				
Beispiel -Nr.	1.11	1.12	1.13	1.14
Löse- mittel	DMSO	DMSO	DMSO	DMSO
6-H	8.30 (s,1H) 4.46 (dq,1H) 1.38 (d,3H)	8.32 (s,1H) 5.04 (q,1H) 2.39 (m,2H)	8.29 (s,1H) 3.7-3.9 (2H) 5.19 (m,1H) 7.2-7.4 (5H)	8.24 (s,1H) 4.25 (m,1H) 3.48 (m,2H)
NH	7.60 (sb,1H)	4.31 (q,1H)	7.72 (d,1H) 5.09 (t,1H)	1.86 (m,2H)
OH	7.29 (sb,1H) 7.21 (d,1H)	4.40 (t,1H) 8.13 (d,1H)		2.43 (m,2H) 2.03(s,3H) 7.13 (d,1H) 4.88 (t,1H)
Aus- beute	87%	63%	99%	78%
Schmp.	234°C Zers.	210°C Zers.	152-153°C	130°C

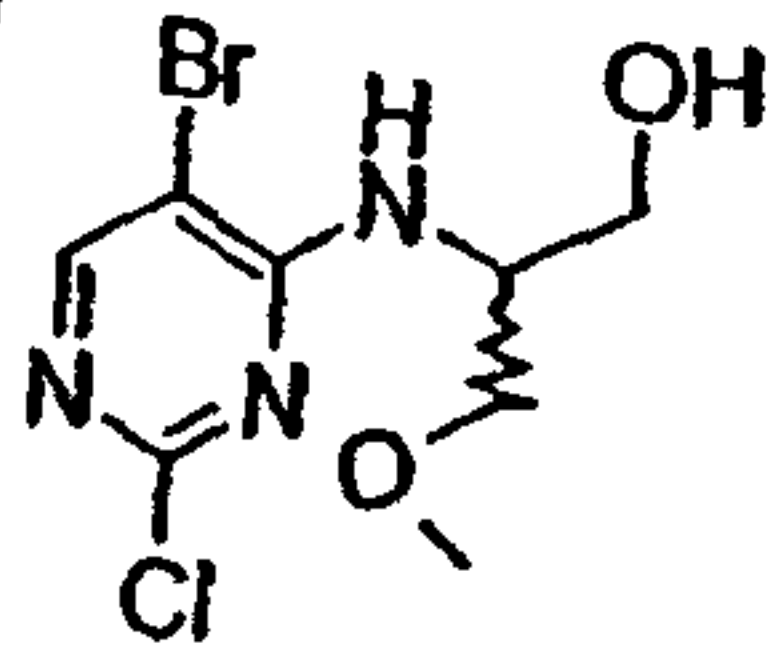
			
Beispiel-Nr.	1.15	1.16	1.17
Lösemittel	DMSO	DMSO	DMSO
6-H	8.20 (s, 1H) 3.55 (m, 2H) 4.22 (m, 1H) 5.03 (m, 2H) 7.1-7.4 (5H)	8.21 (s, 1H) 3.33 (q, 2H) 1.53 (m, 4H) 1.28 (m, 2H) 2.29 (t, 2H)	8.22 (s, 1H) 3.39 (q, 2H) 2.26 (t, 2H) 1.79 (q, 2H)
NH	6.53 (d, 1H) 5.93 (d, 1H)	7.74 (t, 1H)	7.78 (t, 1H) 12.11 (sb, 1H)
Ausbeute	93%	99%	11%
Schmp.	Öl	Öl	Öl

			
Beispiel-Nr.	1.18	1.19	1.20
Ausbeute	86 %	64 %	87%
Masse	ESI : MH ⁺ 297(2%) 266 (22%) 234 (30%)	ESI : MH ⁺ 311 (2%) 248 (20%) 236 (18%)	CI : M ⁺ 354 (100%) 352 (72%) 308 (54%)

			
Beispiel-Nr.	1.21	1.22	1.23
Ausbeute	26 %	~20%	89%
Masse	EI : M ⁺ 327 (10%) 222 (36%) 105 (100%)	NMR, CDCl ₃ 8,16 (s, 1H) 6,55 (s, 1H) 4,43 (d, 2H) 1,29 (s, 9H)	EI : M ⁺ 265 (15%) 236 (100%) 209 (18%)

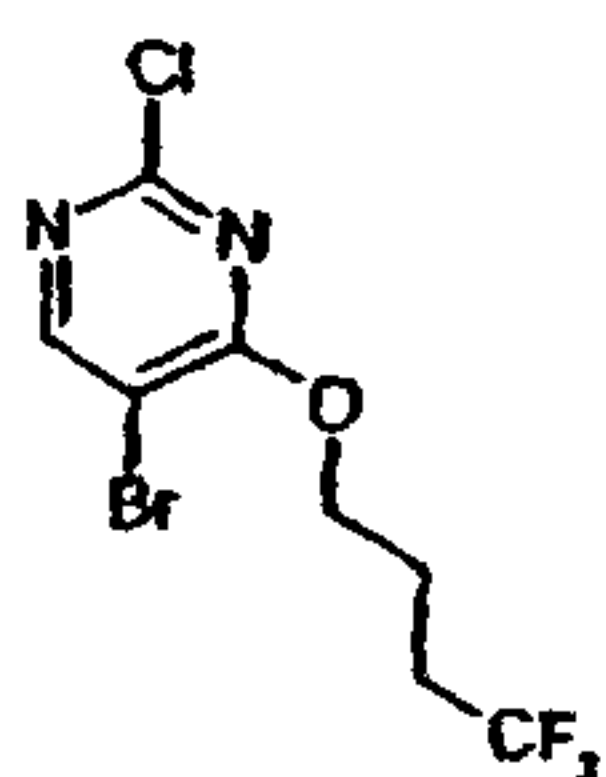
			
Beispiel-Nr.	1.24	1.25	1.26
Ausbeute	75 %	70 %	83 %
Masse	CI : M ⁺ 384 (100%) 212 (21%) 91 (7%)	CI M ⁺ 384 (100%) 212 (21%) 91 (7%)	ESI : 319 3% 278 100% 220 68%

174

	
Beispiel-Nr.	1.27
Ausbeute	98 %
Masse	ESI: MH ⁺ 296 (90%) 298 (100%) 210 (12%)

Example 2.0**Production of 5-Bromo-2-chloro-4-(4,4,4-trifluorobutoxy)pyrimidine**

3.19 g (14 mmol) of 5-bromo-2,4-dichloropyrimidine is mixed with 8.06 g (63 mmol) of 4,4,4-trifluorobutanol, and 0.74 ml (8.4 mmol) of trifluoromethanesulfonic acid is slowly added to it. The reaction mixture is stirred overnight at room temperature and then poured into water. The mixture is extracted by means of ethyl acetate, the combined organic phases are dried on MgSO_2 , and the solvent is evaporated by means of underpressure. The product is always contaminated with varying amounts of 2,4-bisalkoxypyrimidine. The remaining material is therefore purified by means of gradient chromatography with silica gel as a carrier medium (eluant: hexane and hexane/ethyl acetate at a 9:1 ratio). This process results in a yield of 1.70 g (38%) and also yields 1.93 g (34%) of 5-bromo-2,4-bis-(4,4,4-trifluorobutoxy)pyrimidine (starting compound).



5-H 8.74 (s, 1H) Chromatography: H to H/EA 9:1

4C 4.48 (t, 2H) Yield: 38%

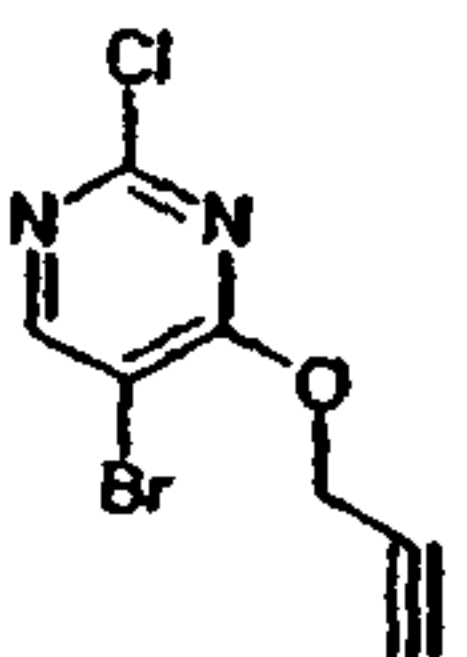
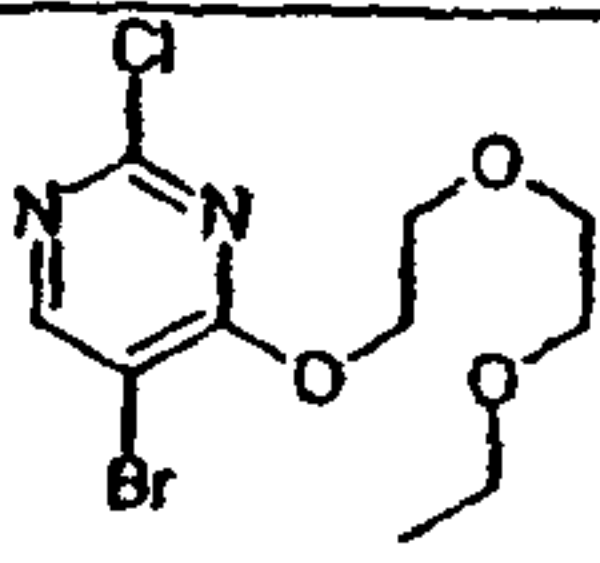
H 2.00 (mc, 2H) Melting point: 66.5-67.5°

2.44 (mc, 2H)

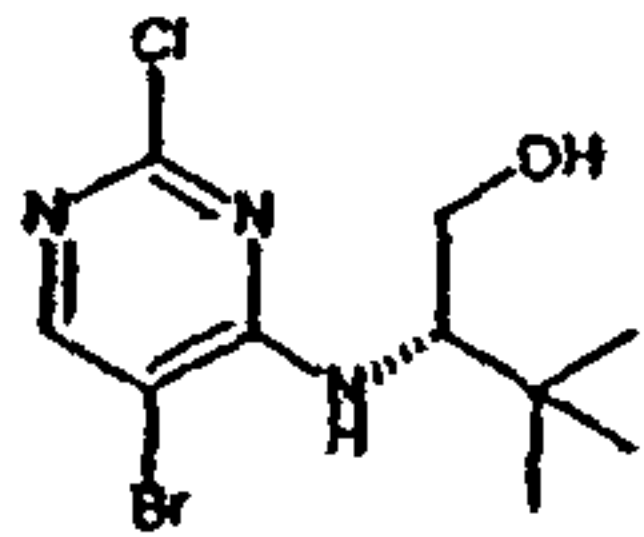
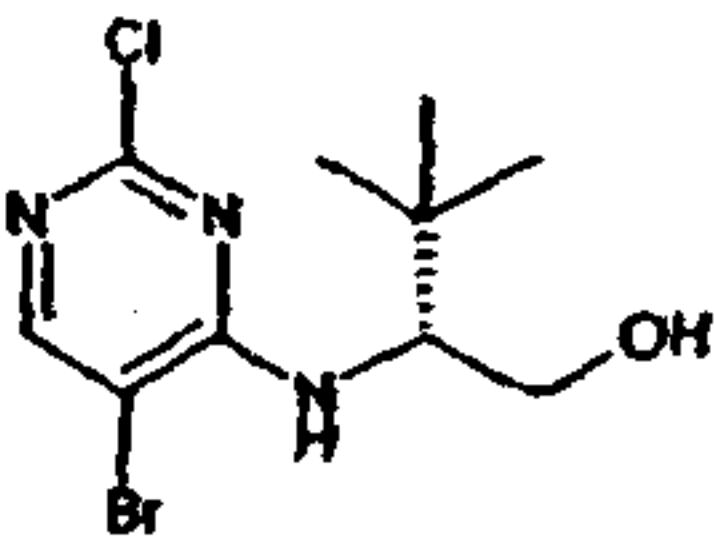
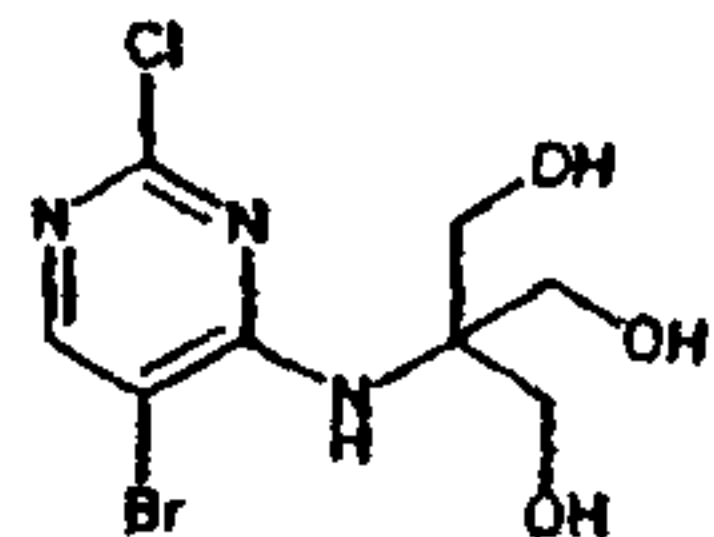
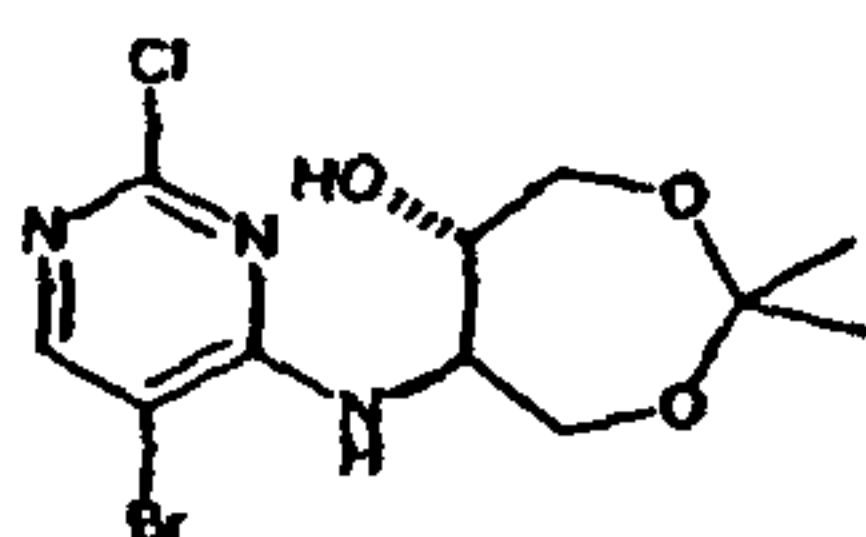
5C

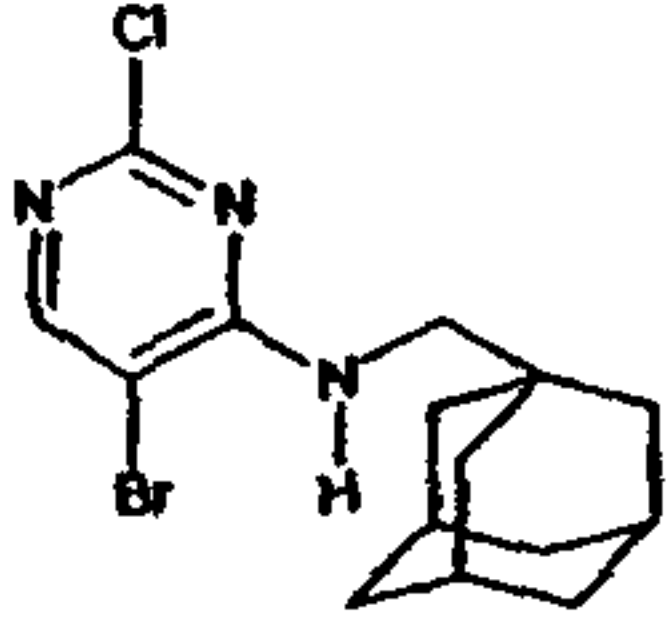
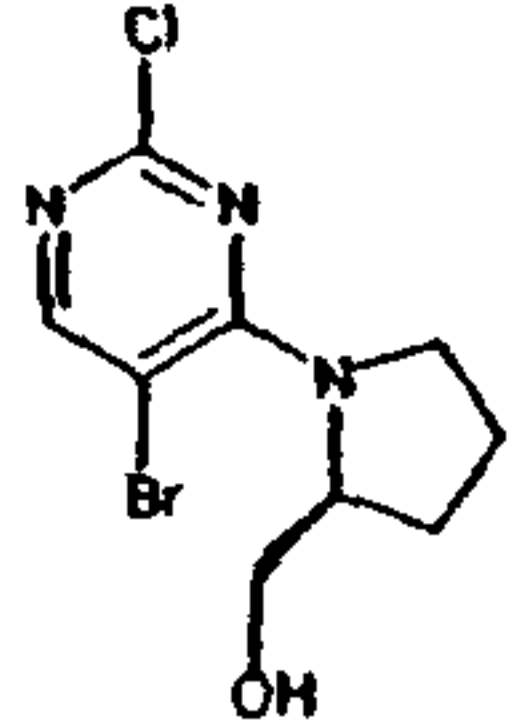
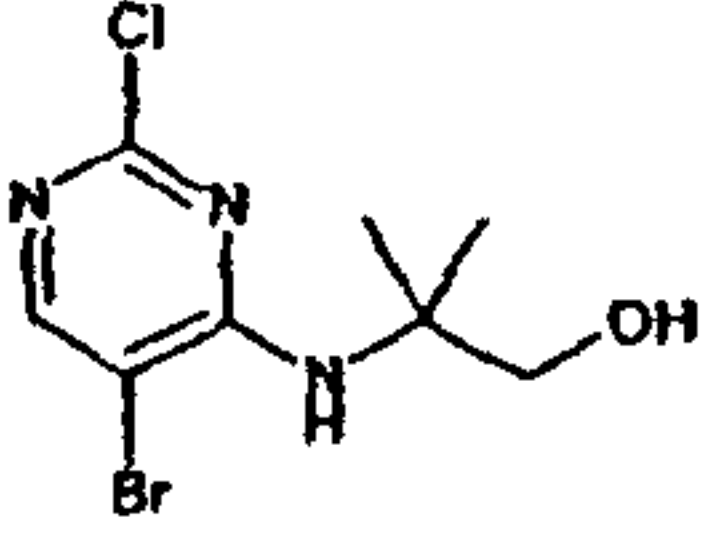
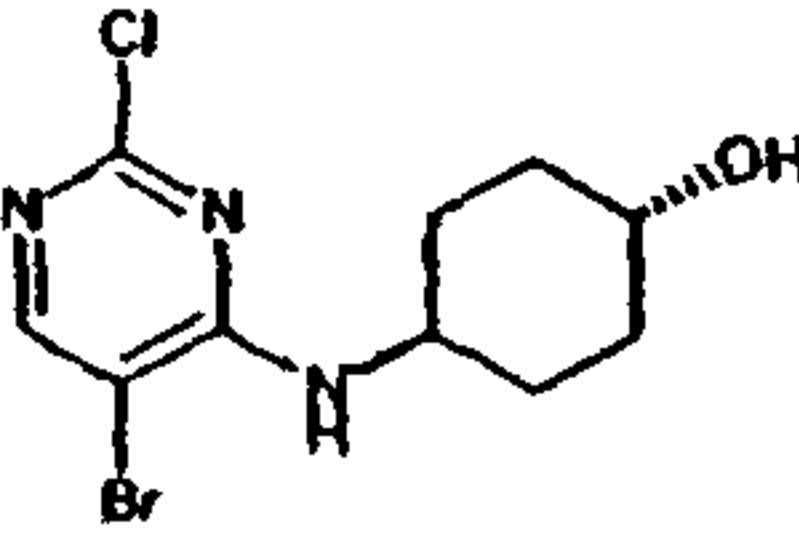
H-

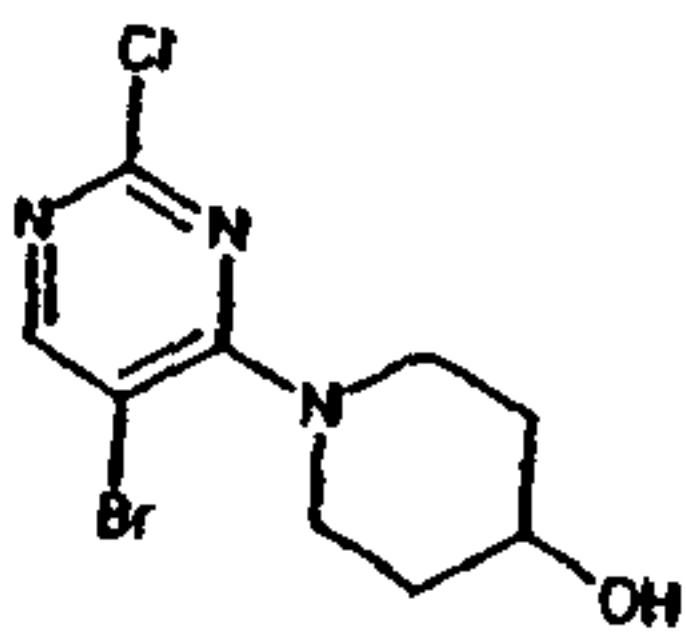
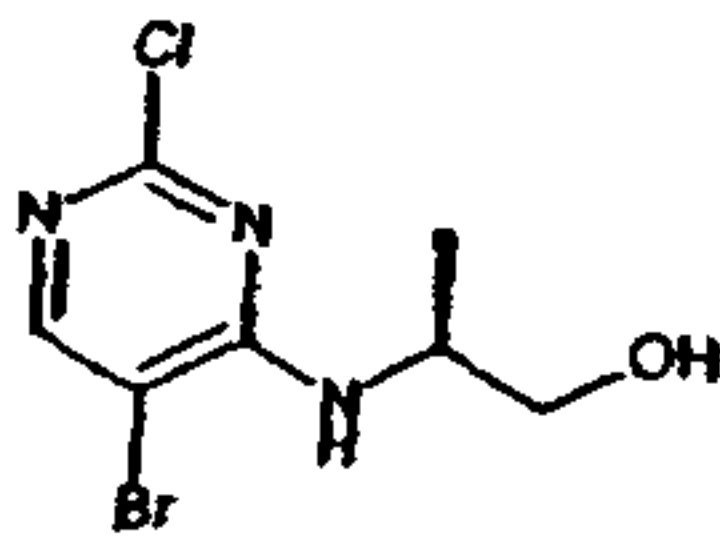
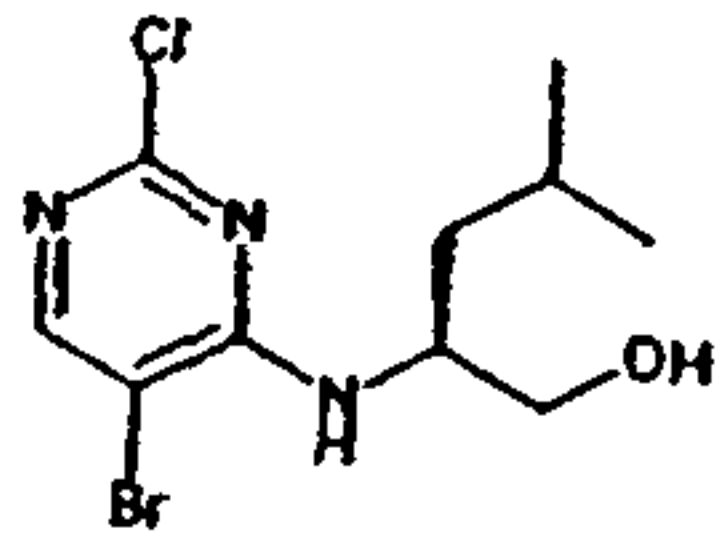
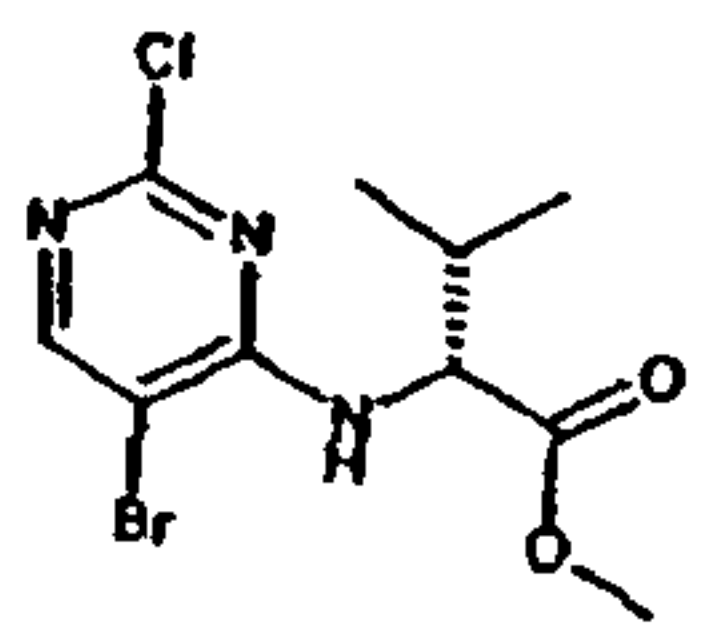
Similarly produced are also the following compounds:

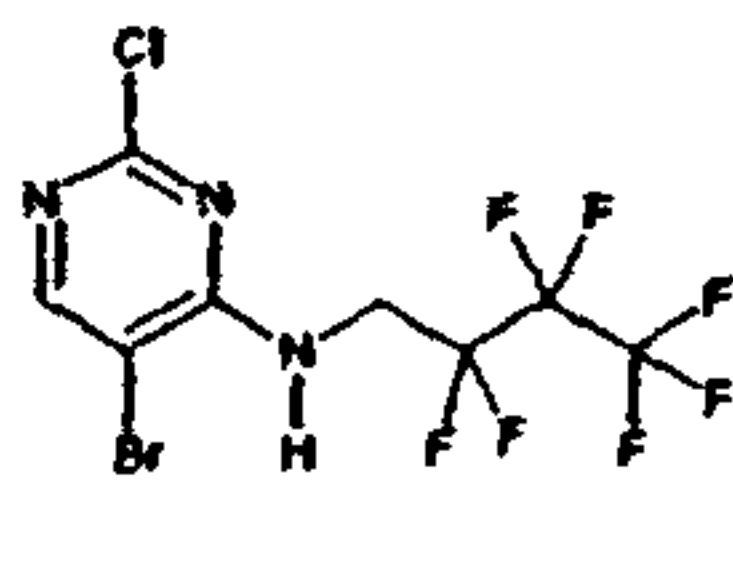
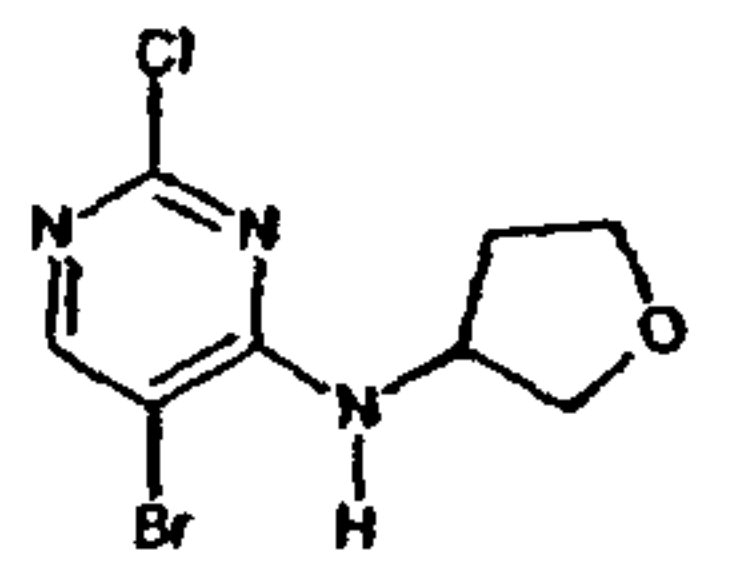
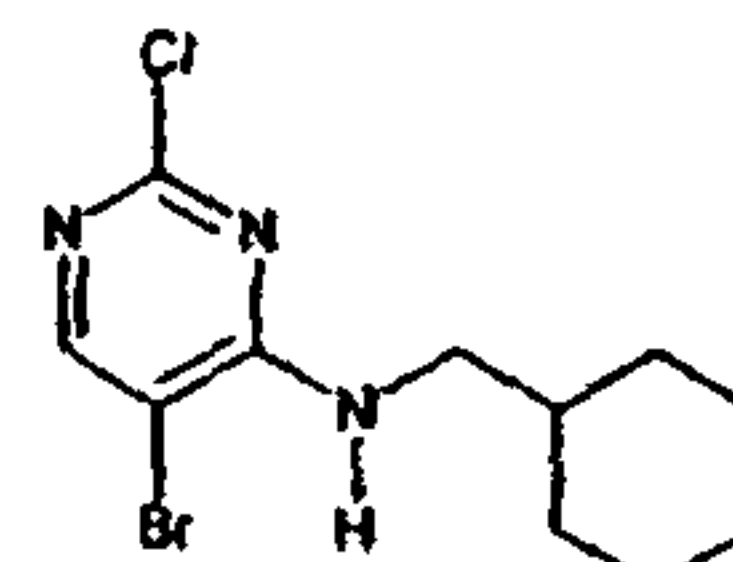
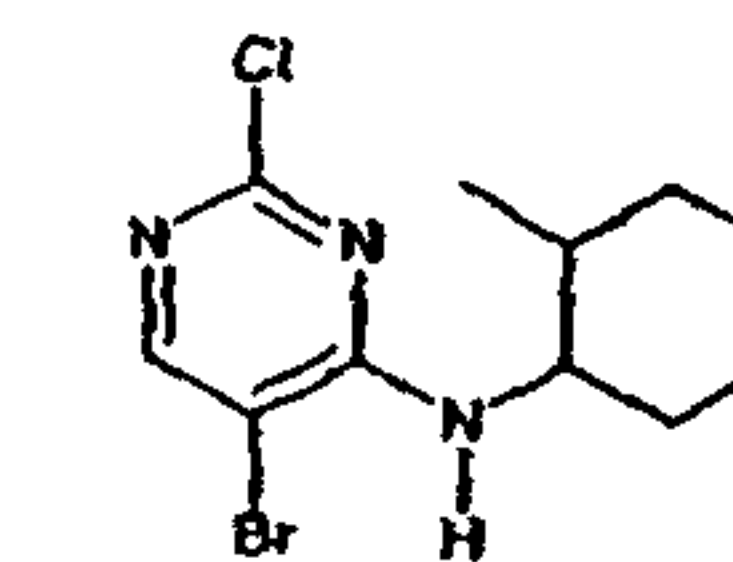
		
Beispiel-Nr.	2.1	2.2
	CDCl ₃	DMSO
5-H	8.49 (s,1H)	8.75 (s,1H)
4CH	5.10 (d,2H)	4.05 (mc,2H)
		3.79 (mc,2H)
5CH	2.59 (t,1H)	3.60 (mc,2H)
		3.48 (mc,2H)
		3.40 (t,2H)
		1.07 (t,3H)
Chrom.	H to H/EA 4:1	DCM to DCM/MeOH 95:5
Ausbeute	78%	11%
Schmp.	55°C	OI

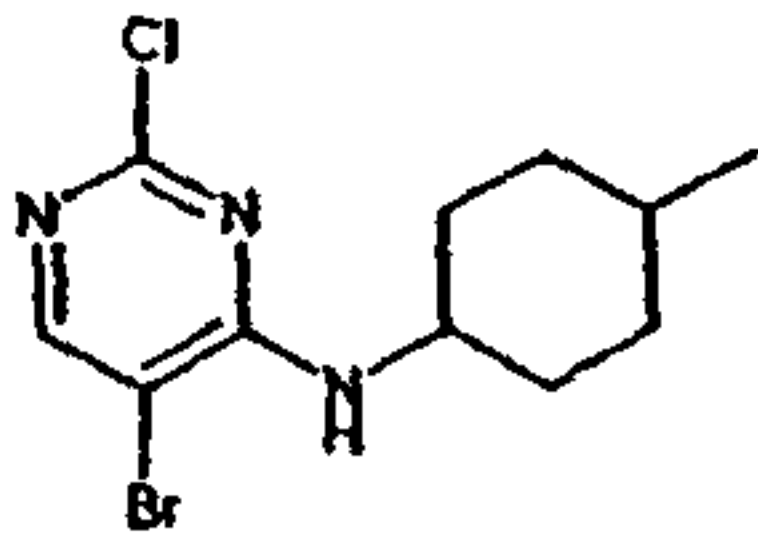
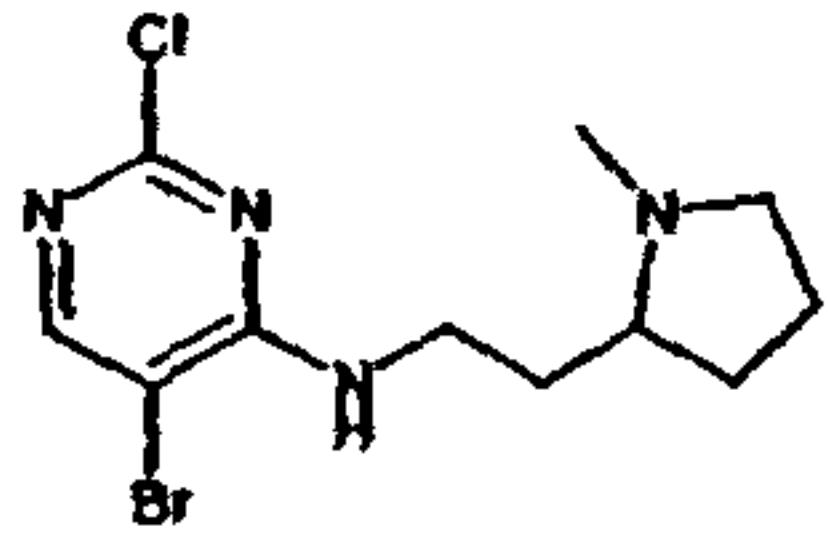
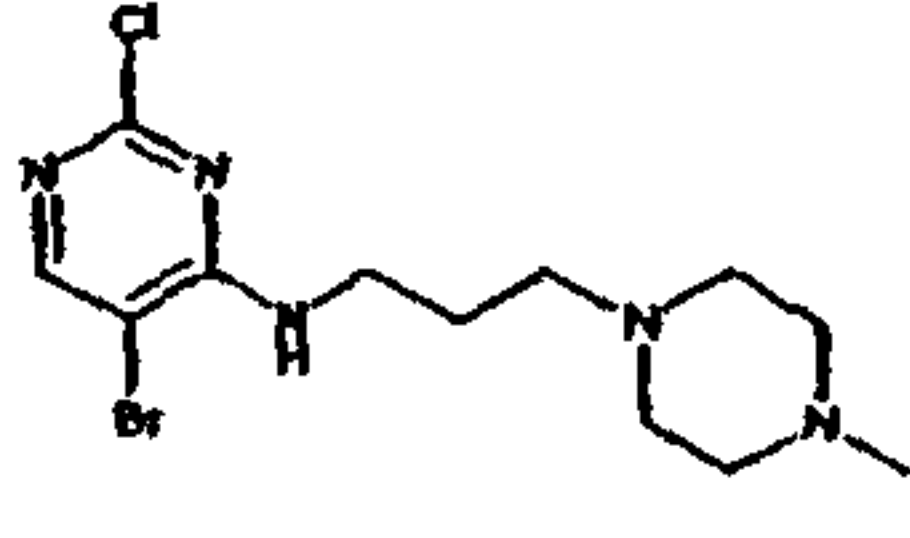
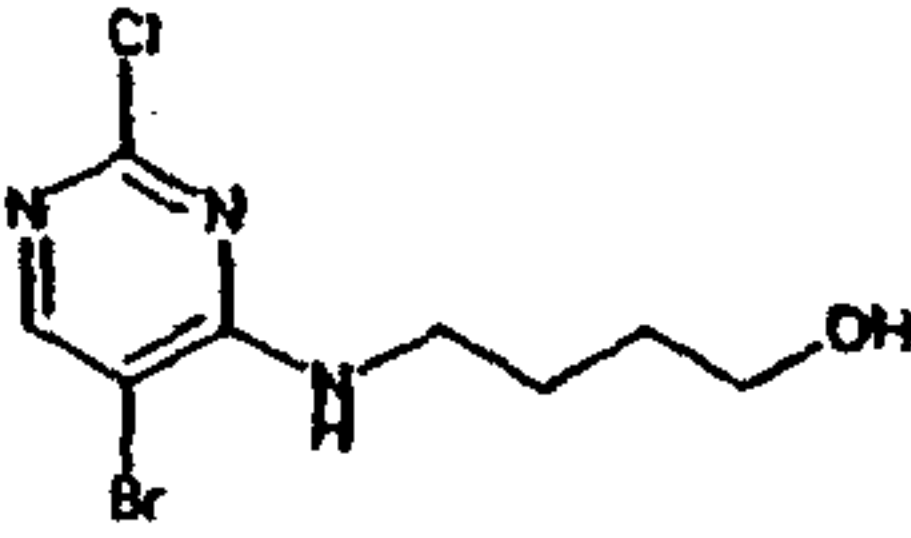
Analogously to process examples 1 and 2, the following intermediate products are also produced:

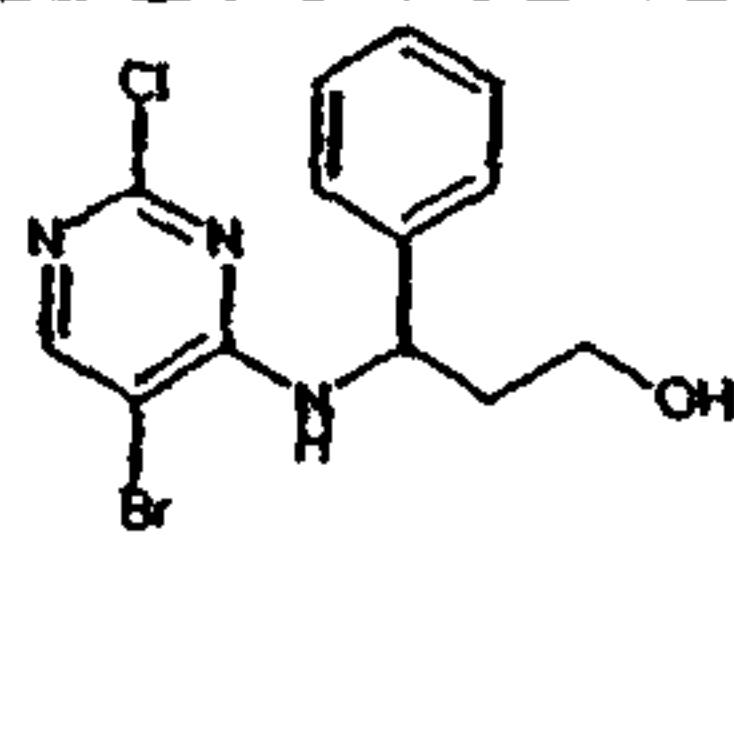
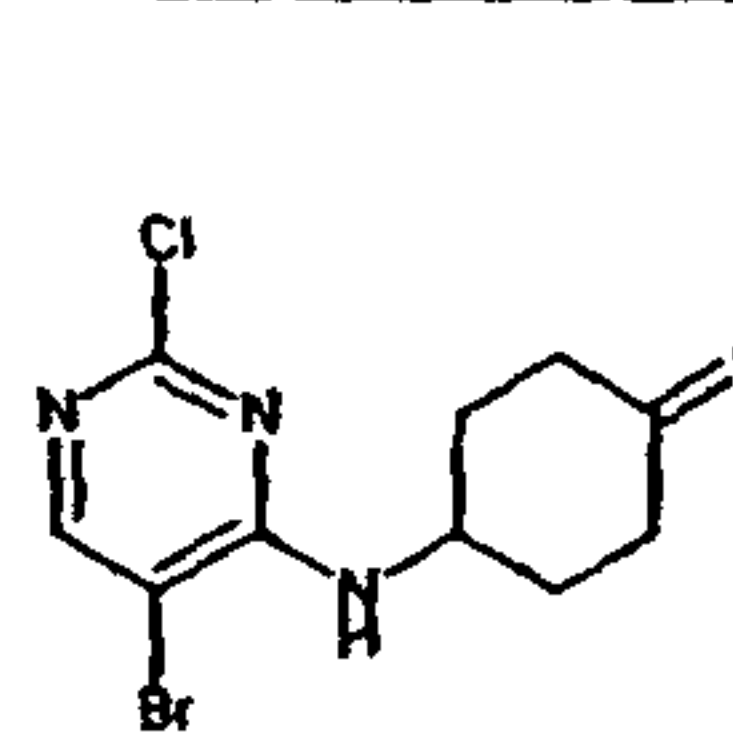
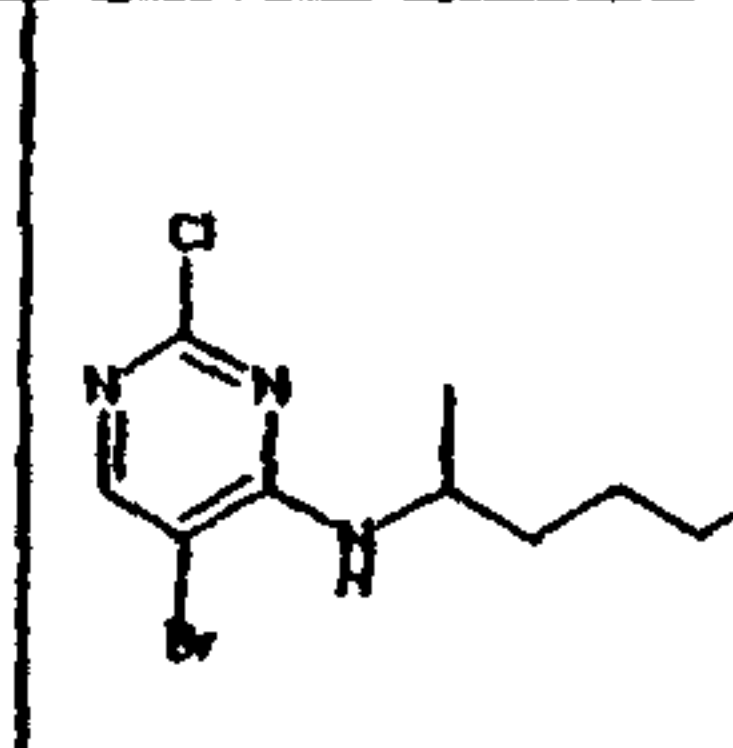
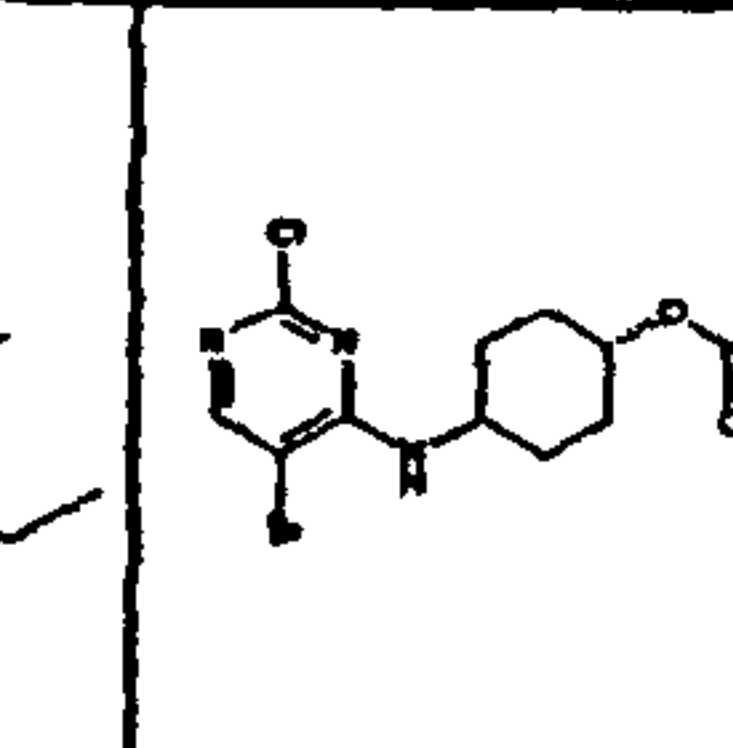
				
Beispiel -Nr.	1-2.1	1-2.2	1-2.3	1-2.4
Löse- Mittel	DMSO	DMSO	DMSO	DMSO
	8.26 (s, 1H) 6.65 (d, 1H) 4.70 (t, 1H) 4.10 (dt, 1H) 3.65 (at, 2H) 0.90 (s, 9H)	8.26 (s, 1H) 6.65 (d, 1H) 4.70 (t, 1H) 4.10 (dt, 1H) 3.65 (at, 2H) 0.90 (s, 9H)	8.29 (s, 1H) 6.32 (s, 1H) 4.89 (t, 3H) 3.74 (d, 6H)	8.28 (s, 1H) 7.09 (d, 1H) 5.05 (d, 1H) 3.95 (m, 1H) 3.60 (m, 5H) 1.30 (s, 3H) 1.28 (s, 3H)
Aus- beute	49%	70%	16%	92%
Masse	309 (EI)	309 (EI)	314 (EI)	354 (EI)

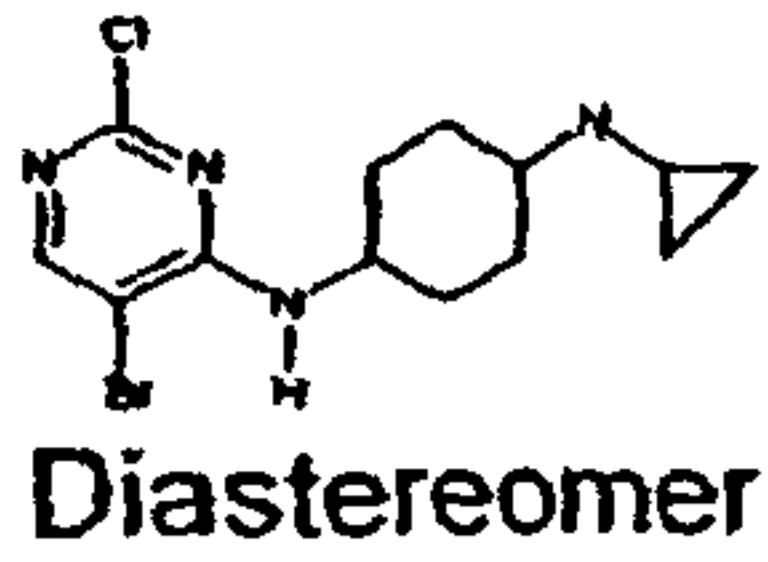
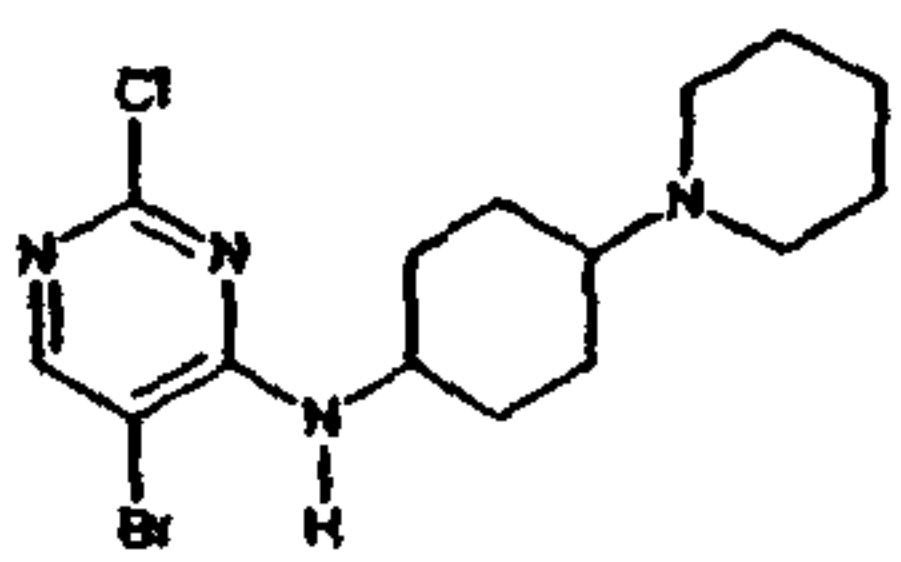
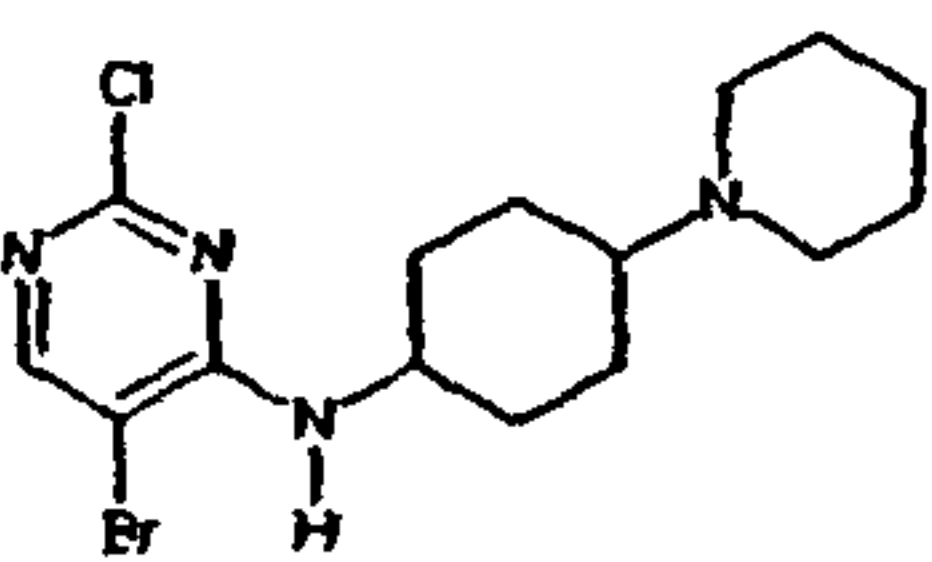
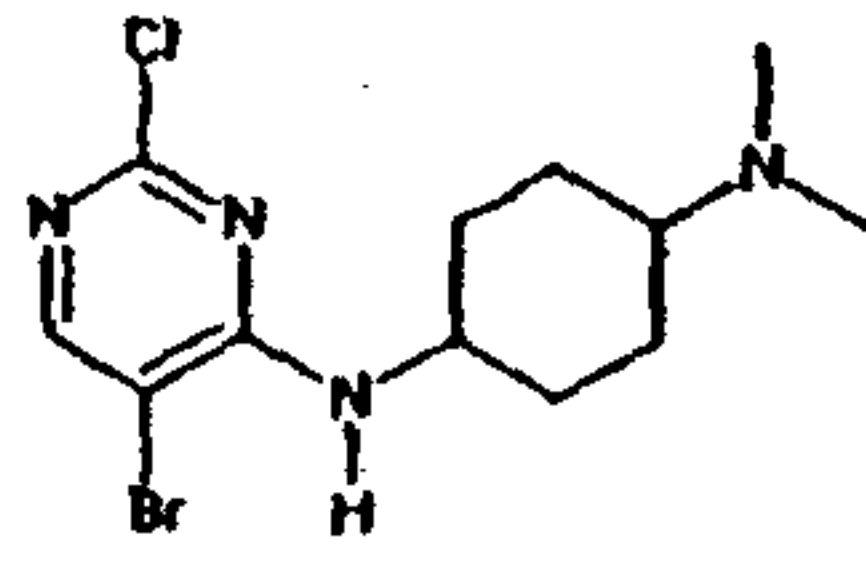
				
Beispiel -Nr.	1-2.5	1-2.6	1-2.7	1-2.8
Löse- mittel	DMSO	DMSO	DMSO	DMSO
	8.15 (s,1H) 7.25 (t,1H) 3.16 (s,2H) 1.90 (s,3H) 1.61 (q,6H) 1.41 (s,6H)	8.22 (s,1H) 4.82 (t,1H) 4.49 (br,1H) 3.85 (m,1H) 3.76 (m,1H) 3.54 (m,1H) 3.40 (m,1H) 1.93 (m,3H) 1.80 (m,1H)	8.28 (s,1H) 6.29 (s,1H) 5.31 (t,1H) 3.39 (d,2H) 1.39 (s,6H)	8.22 (s,1H) 7.23 (d,1H) 4.60 (d,1H) 3.85 (m,1H) 3.35 (m,1H) 1.80 (m,4H) 1.53 (m,2H) 1.20 (m,2H)
Aus- beute	70%	75%	46%	24%
Masse	357 (EI)	293 (EI)	281 (EI)	305 (EI)

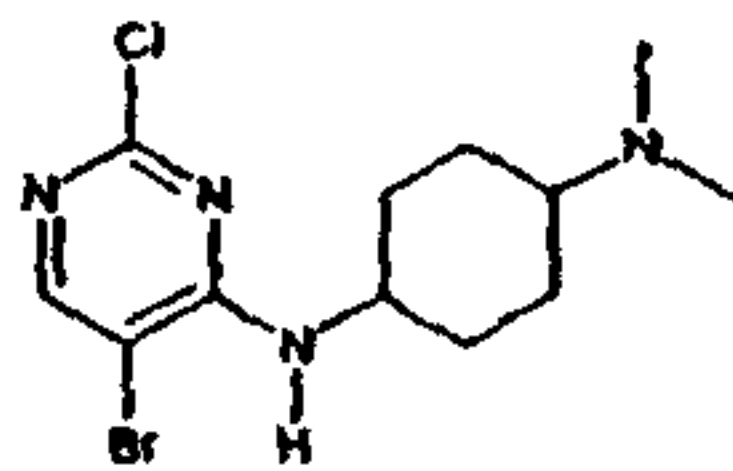
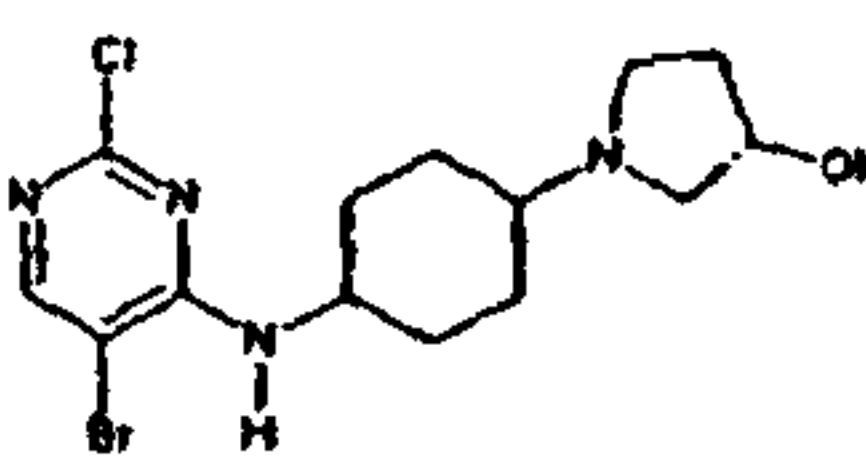
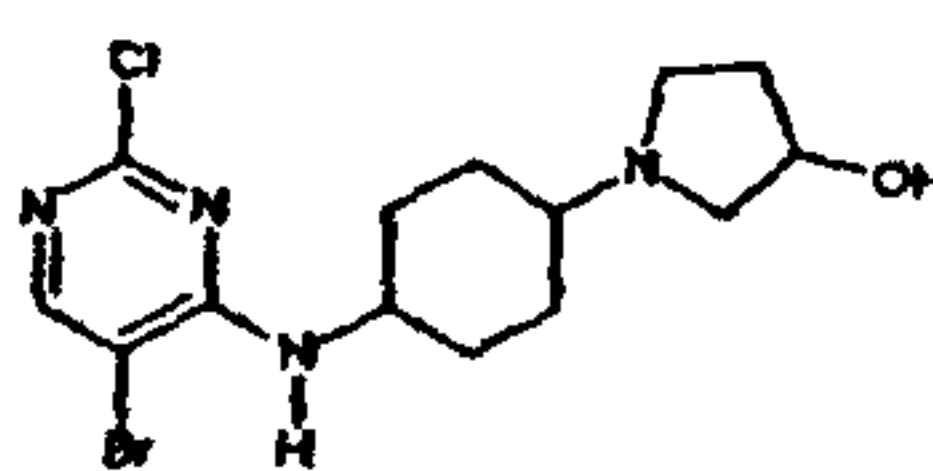
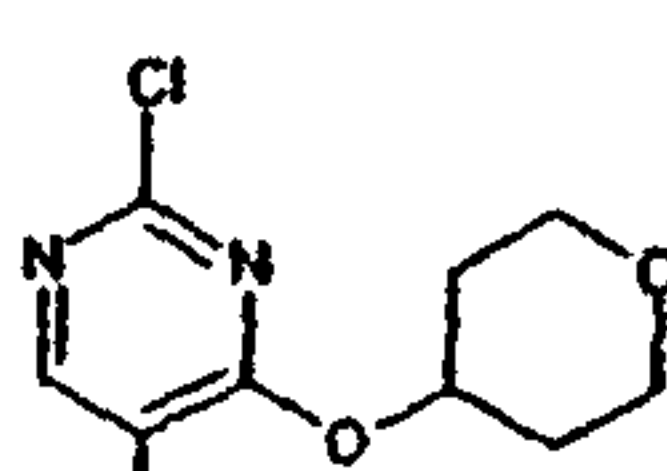
				
Beispiel -Nr.	1-2.9	1-2.10	1-2.11	1-2.12
Löse- mittel	DMSO	DMSO	DMSO	DMSO
	8.38 (s, 1H) 4.81 (br, 1H) 3.96 (m, 2H) 3.72 (m, 1H) 3.30 (m, 2H) 1.81 (m, 2H) 1.48 (m, 2H)	8.22 (s, 1H) 7.05 (d, 1H) 4.82 (t, 1H) 4.18 (m, 1H) 3.42 (m, 2H) 1.15 (d, 3H)	8.21 (s, 1H) 7.06 (d, 1H) 4.81 (t, 1H) 4.22 (m, 1H) 3.47 (m, 2H) 1.51 (m, 2H) 1.37 (m, 1H) 0.88 (m, 6H)	8.31 (s, 1H) 7.32 (d, 1H) 4.35 (s, 1H) 3.68 (s, 3H) 2.32 (m, 1H) 0.90 (dd, 6H)
Aus- beute	19%	71%	99%	77 %
Masse	292 (EI)	266 (EI)	308 (EI)	322 (ES)

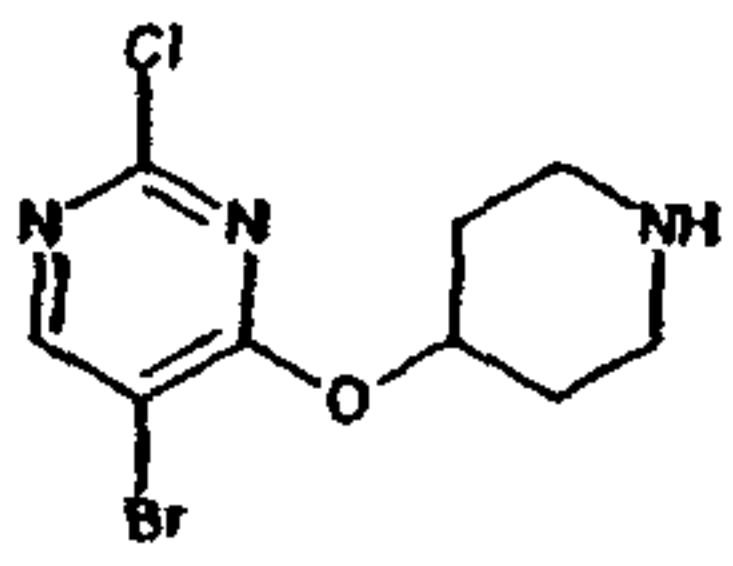
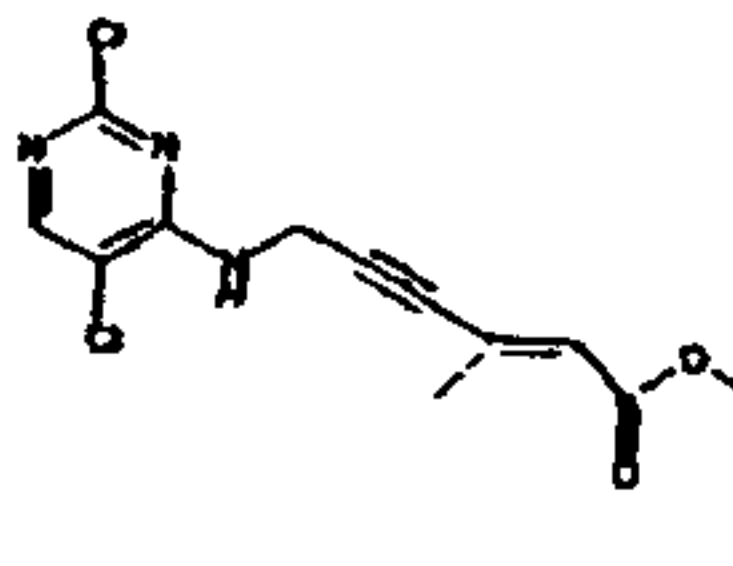
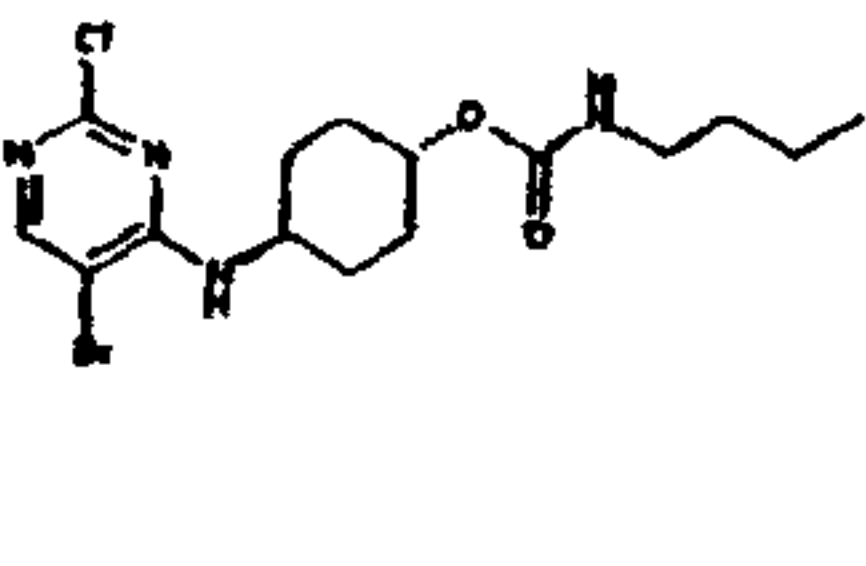
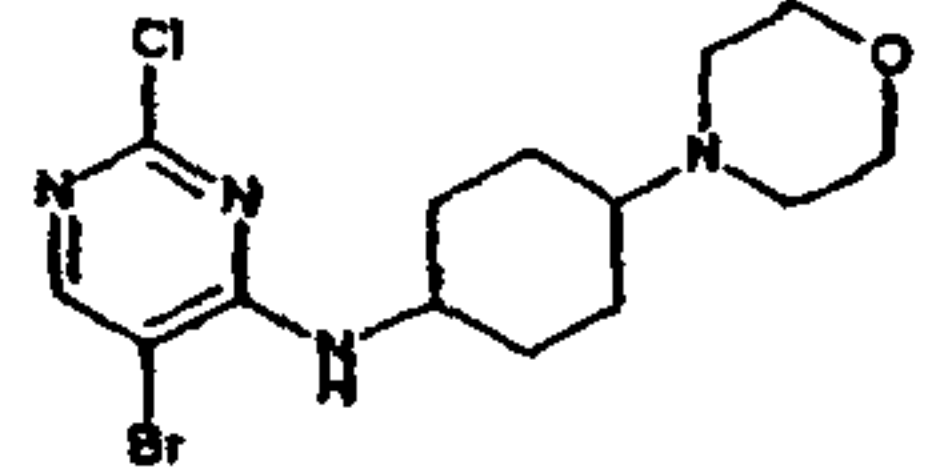
				 trans
Beispiel -Nr.	1-2.13	1-2.14	1-2.15	1-2.16
Löse- mittel	DMSO	DMSO	DMSO	DMSO
	8.41 (s,1H) 8.11 (s,1H) 4.28 (t,2H)	8.25 (s,1H) 4.53 (m,1H) 3.88 (m,2H) 3.70 (dd,1H) 3.62 (dd,1H) 2.16 (m,1H) 2.02 (m,1H) 7.56 (d,1H)	8.19 (s,1H) 7.65 (t,1H) 3.18 (t,2H) 1.62 (m,6H) 1.16 (m,3H) 0.90 (m,2H)	8.19 (s,1H) 7.30 (d,1H) 3.65 (m,1H) 1.68 (m,5H) 1.25 (m,4H) 0.78 (d,3H)
Aus- beute	46%	72%	68%	31%
Masse	390 (FAB)	277 (EI)	303 (EI)	305 (EI)

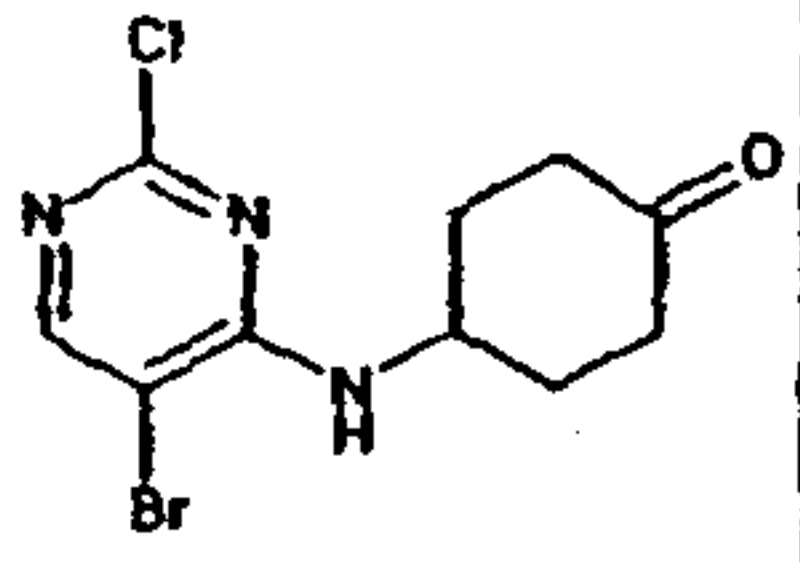
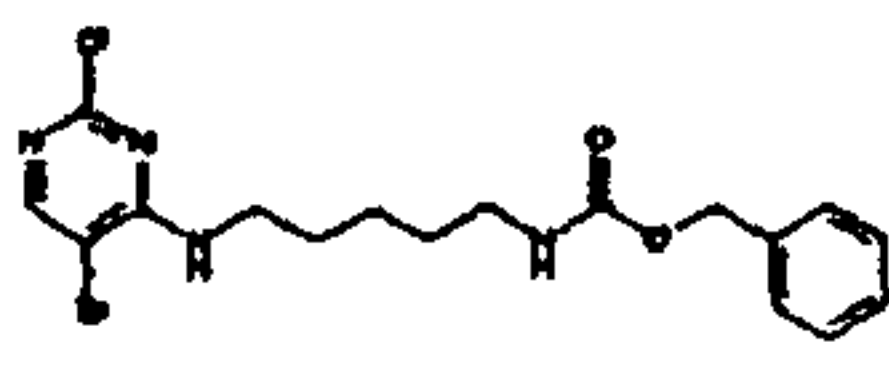
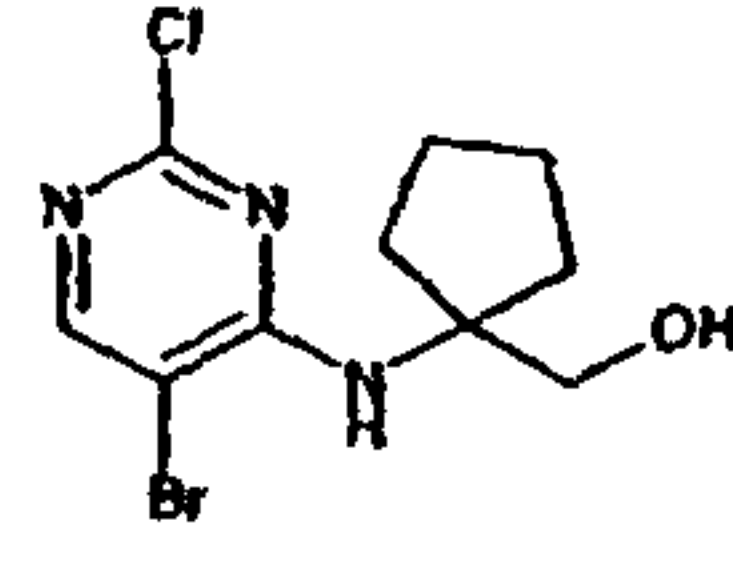
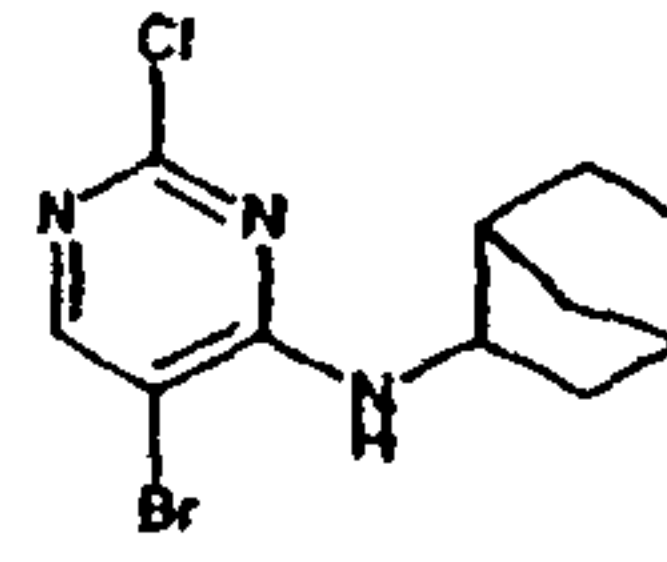
				
Beispiel -Nr.	1-2.17	1-2.18	1-2.19	1-2.20
Löse- mittel	DMSO	DMSO	DMSO	DMSO
	8.21 (s,1H) 7.22 (d,1H) 3.88 (m,1H) 1.70 (m,4H) 1.50 (m,2H) 1.28 (m,1H) 1.01 (m,2H) 0.82 (d,3H)	8.35 (t,1H) 8.19 (s,1H) 3.40 (m,2H) 2.97 (p,1H) 2.22 (m,4H) 2.08 (dd,1H) 1.70 (m,6H)	8.21 (s,1H) 7.81 (t,1H) 3.41 (dd,2H) 2.31 (m,10H) 2.13 (s,3H) 1.70 (p,2H)	8.20 (s,1H) 7.71 (t,1H) 4.45 (br,1H) 3.40 (m,4H) 1.60 (m,2H) 1.44 (m,2H)
Aus- beute	22%	32%	28%	98%
Masse	303 (EI)	320 (EI)	349 (EI)	281 (EI)

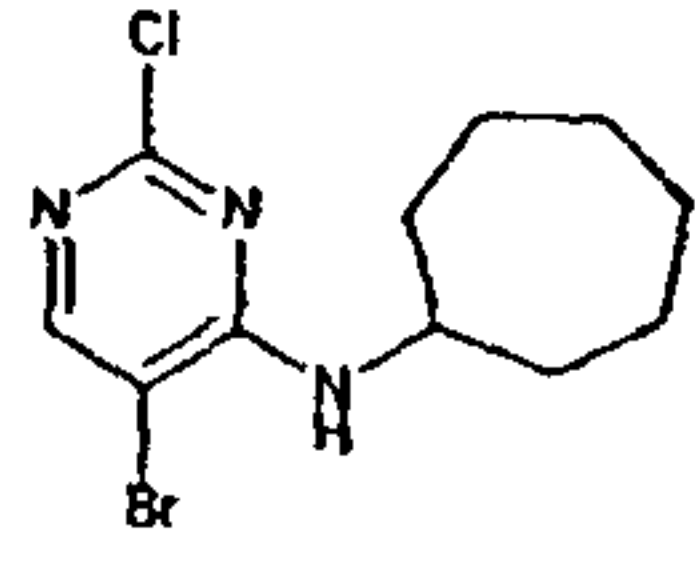
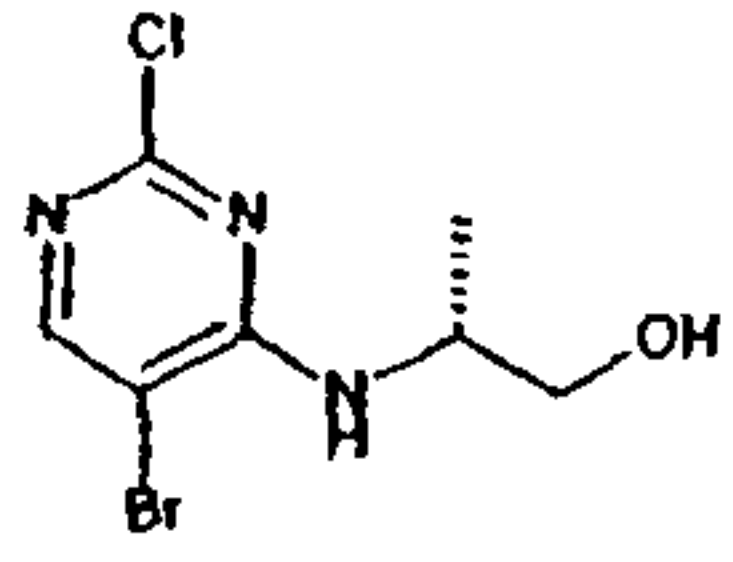
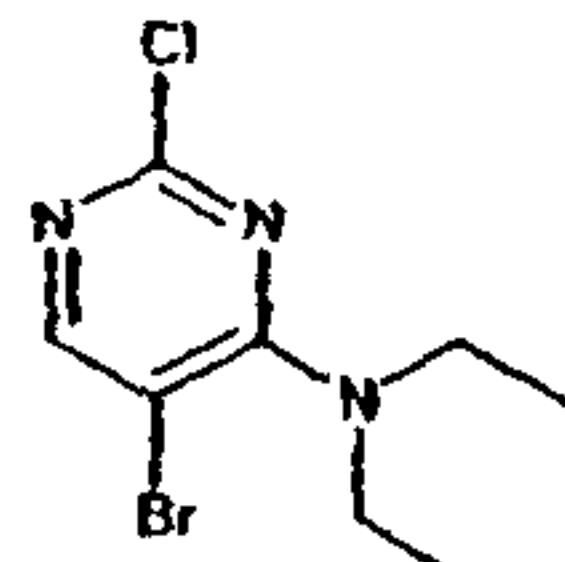
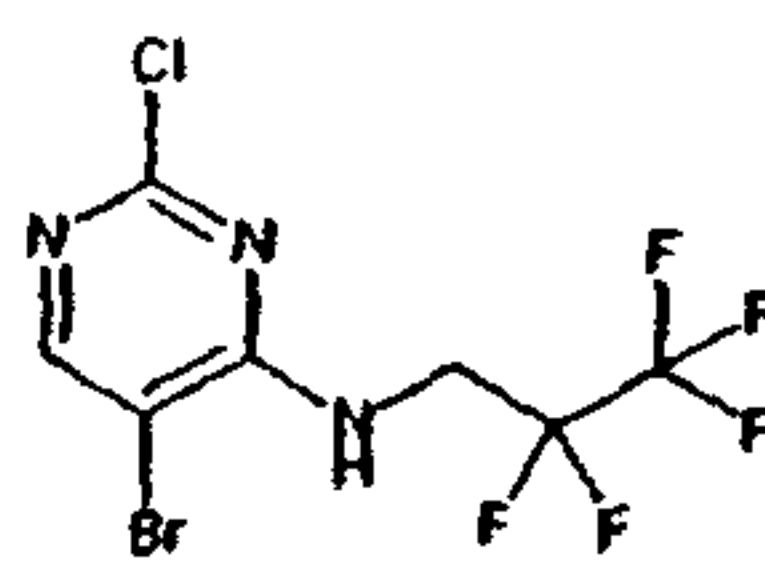
				
Beispiel -Nr.	1-2.21	1-2.22	1-2.23	1-2.24
Löse- mittel	DMSO	DMSO	DMSO	DMSO
	8.25 (s,1H) 8.08 (d,1H) 7.35 (m,5H) 5.30 (m,1H) 4.81 (t,1H) 3.45 (m,2H) 2.05 (m,2H)	8.25 (s,1H) 7.38 (d,1H) 4.44 (m,1H) 2.60 (m,2H) 2.24 (m,2H) 2.07 (m,2H) 1.90 (m,2H)	8.20 (s,1H) 7.28 (d,1H) 4.19 (m,1H) 2.40 (m,6H) 1.50 (m,4H) 1.15 (d,3H) 0.91 (t,6H)	8.21 (s,1H) 7.24 (d,1H) 7.02 (t,1H) 4.40 (m,1H) 3.92 (m,1H) 2.95 (q,2H) 1.95 (m,2H) 1.82 (m,2H) 1.59 (m,2H) 1.3 (m,6H) 0.82 (t,3H)
Aus- beute	97%	58%	52%	70%
Masse	343 (EI)	304 (ES)	348 (EI)	

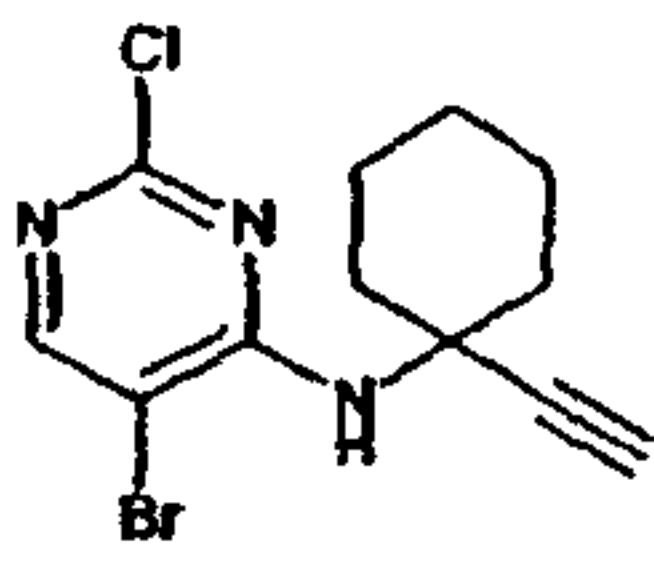
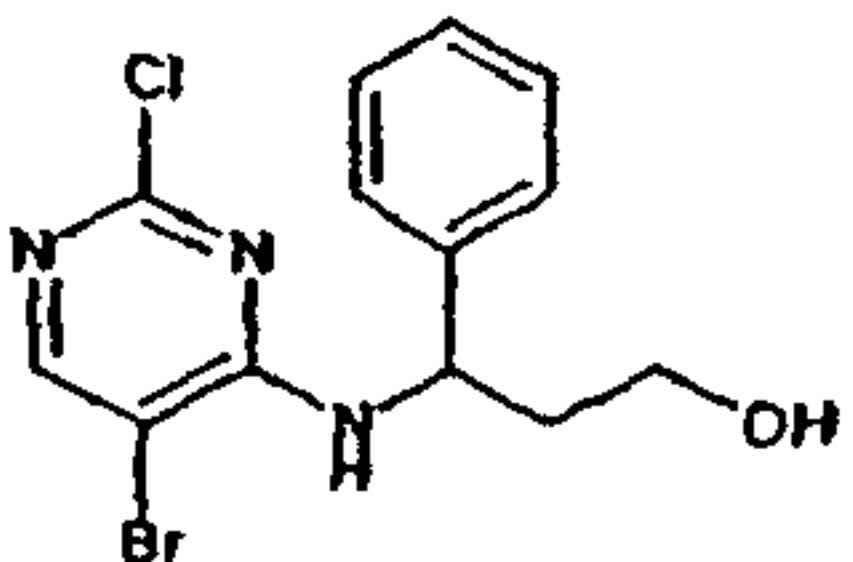
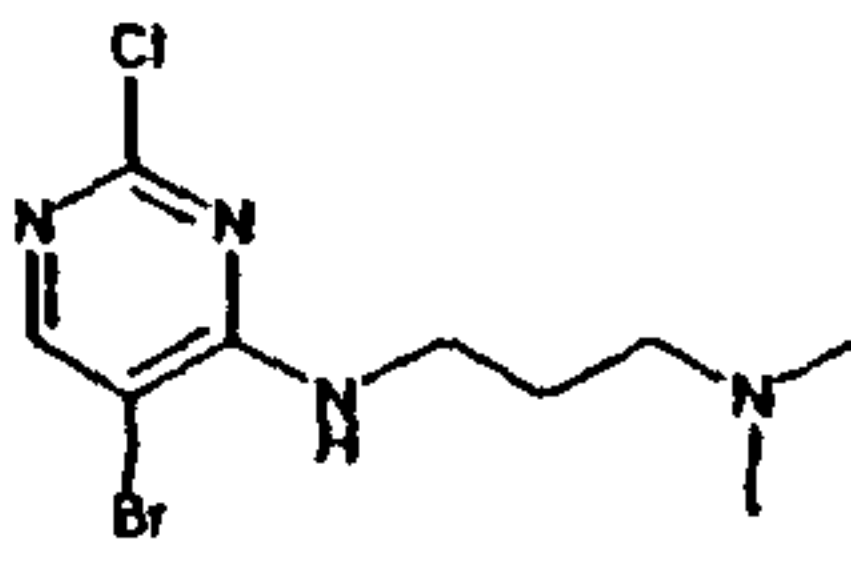
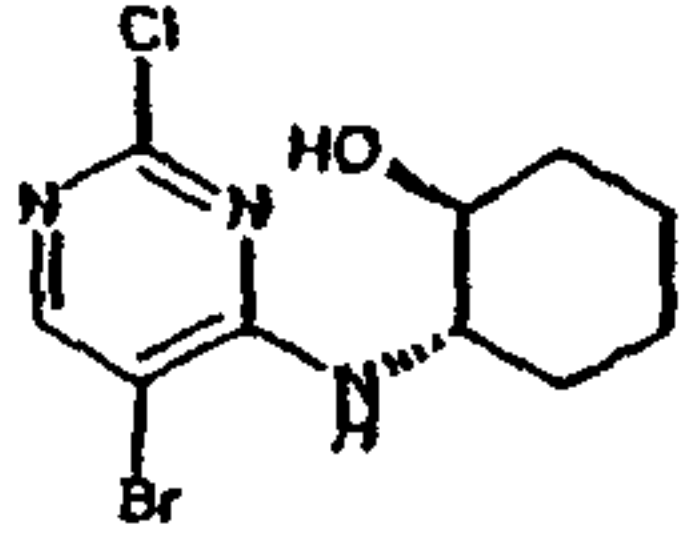
	 Diastereomer 1/2	 Diastereomer 1	 Diastereomer 2	 Diastereomer 1
Beispiel -Nr.	1-2.25	1-2.26	1-2.27	1-2.28
Löse- mittel	DMSO	DMSO	DMSO	DMSO
		8.22 (s,1H) 7.21 (d,1H) 3.82 (m,1H) 2.45 (m,4H) 2.22 (m,1H) 1.78 (m,8H) 1.45 (m,6H)	8.25 (s,1H) 6.87 (d,1H) 4.02 (m,1H) 2.45 (m,4H) 2.22 (m,1H) 1.78 (m,8H) 1.45 (m,6H)	8.22 (s,1H) 7.28 (d,1H) 3.85 (m,1H) 2.19 (s,6H) 2.15 (m,1H) 1.82 (m,4H) 1.50 (m,2H) 1.25 (m,2H)
Aus- beute	n.b.	26%	23%	51%
Masse	344 (EI)	374 (EI)	374 (EI)	334 (EI)

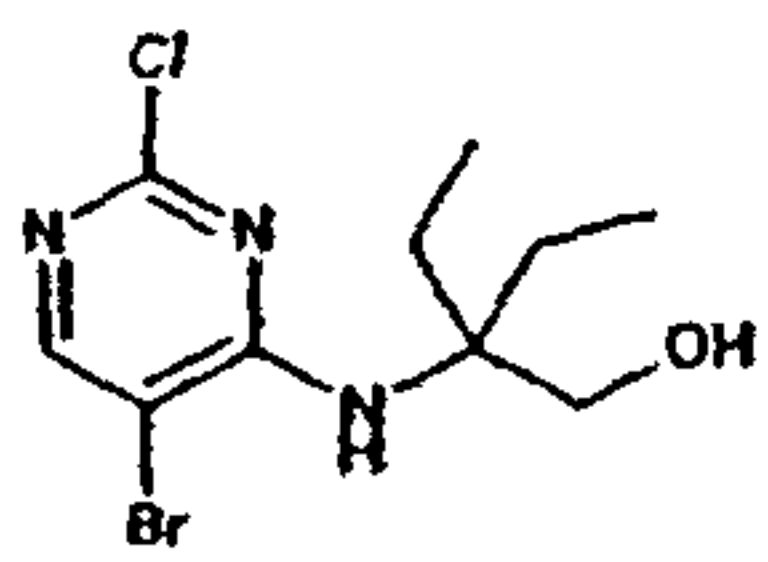
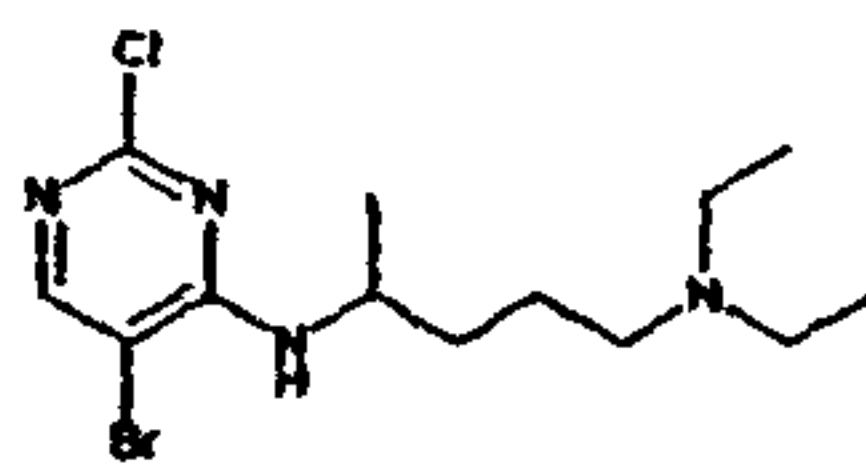
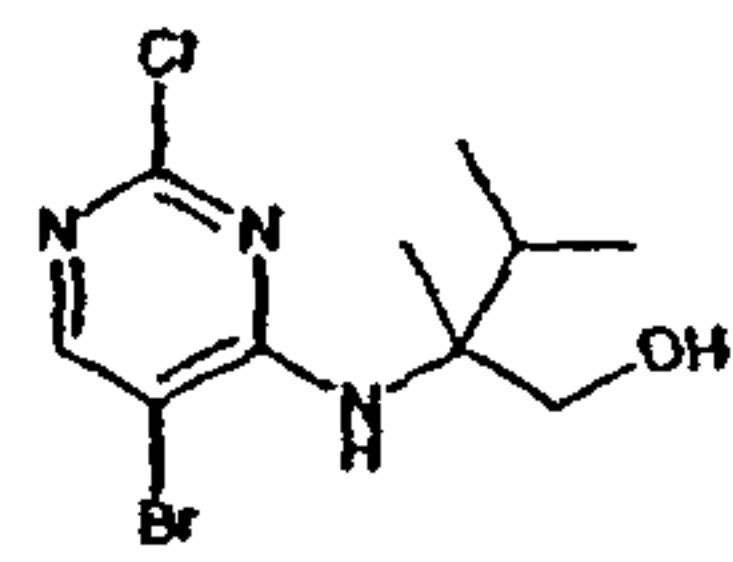
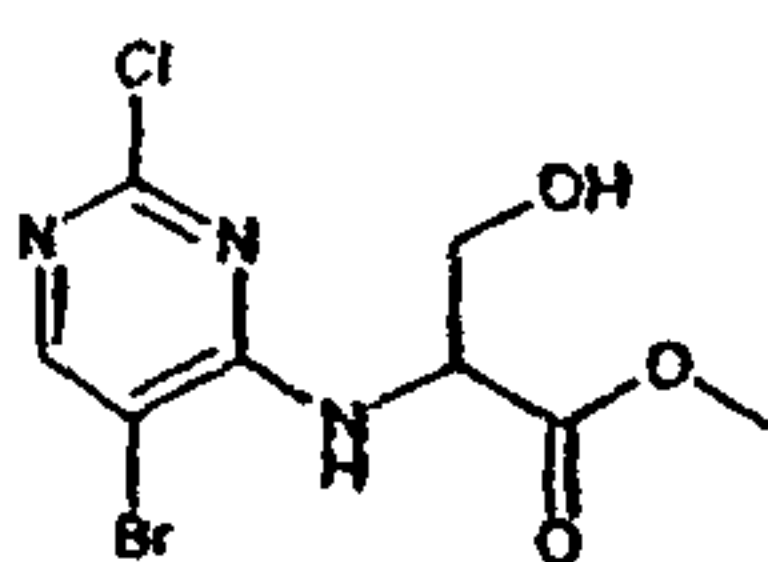
	 Diastereomer 1+2 (ca. 1:1)	 Diastereomer 1+2 (ca. 1:1)	 Diastereomer 3+4 (ca. 1:1)	
Beispiel -Nr.	1-2.29	1-2.30	1-2.31	1-2.32
Löse- mittel	DMSO	DMSO	DMSO	DMSO
	8.22 (s,2H) 7.28 (d,1H) 7.10 (d,1H) 4.00 (m,1H) 3.85 (m,1H) 2.19 (s,6H) 2.17 (s,6H) 2.15 (m,1H) 2.00 (m,1H) 1.82 (m,8H) 1.50 (m,6H) 1.25 (m,2H)	8.21 (s,1H) 7.18 (d,1H) 4.62 (s,1H) 4.20 (m,1H) 3.95 (m,1H) 2.75 (dd,1H) 2.50 (m,2H) 2.31 (dd,1H) 2.15 (s,1H) 2.00 (m,1H) 1.82 (m,4H) 1.55 (m,5H)	8.21 (s,1H) 7.22 (d,1H) 4.65 (s,1H) 4.15 (m,1H) 3.85 (m,1H) 2.78 (m,1H) 2.60 (m,1H) 2.38 (dd,1H) 1.95 (m,3H) 1.80 (m,2H) 1.52 (m,3H) 1.20 (m,2H)	8.71 (s,1H) 5.32 (m,1H) 3.82 (m,2H) 3.55 (m,2H) 2.00 (m,2H) 1.70 (m,2H)
Aus- beute	13%	35%	21%	40%
Masse	334 (EI)	374 (EI)	374 (EI)	292 (EI)

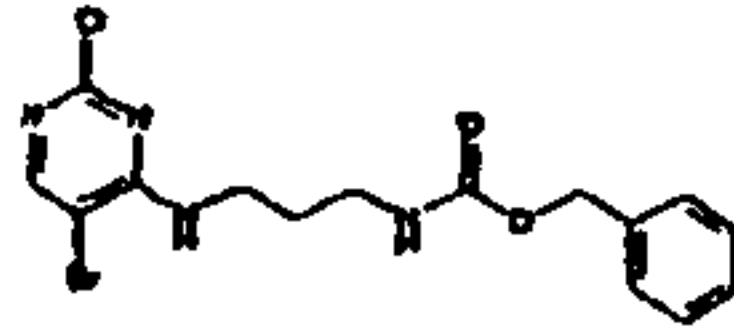
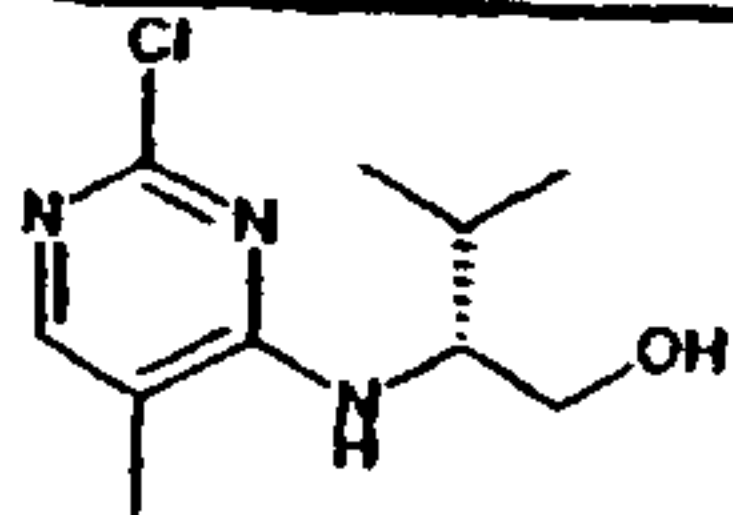
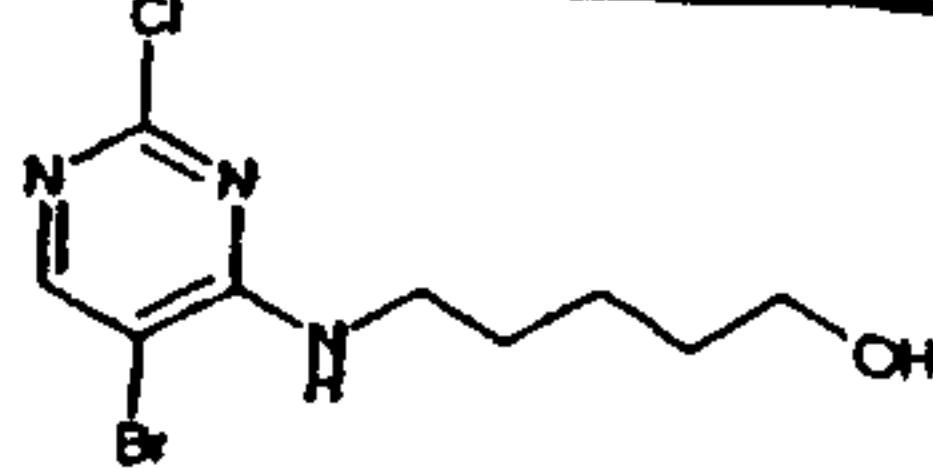
				 Diastereomere 1+2 (ca.1:1)
Beispiel -Nr.	1-2.33	1-2.34	1-2.35	1-2.36
Löse- mittel	DMSO	CDCl ₃	DMSO	CDCl ₃
	8.50 (s,1H) 4.10 (m,2H) 3.72 (m,1H) 3.30 (m,2H) 1.75 (m,2H) 1.35 (m,2H)	8.08 (s,1H) 6.04 (m,1H) 5.71 (br,1H) 4.48 (d,2H) 3.71 (s,3H) 2.25 (s,3H)	8.23 (s,1H) 7.27 (d,1H) 7.04 (t,1H) 4.46 (m,1H) 3.95 (m,1H) 2.94 (m,2H) 1.92 (m,4H) 1.62 (m,2H) 1.32 (m,6H) 0.84 (t,3H)	8.11 (s,2H,1+2) 5.55 (m,1H,1) 5.29 (m,1H,2) 4.25 (m,1H,1) 3.98 (m,1H,2) 3.72 (m,8H,1+2) 2.65 (m,8H,1+2) 1.70 (m,18H,1+2)
Aus- beute	3%	30%	70%	66%
Masse	291 (EI)	300 (ES)	405 (ES)	375 (ES)

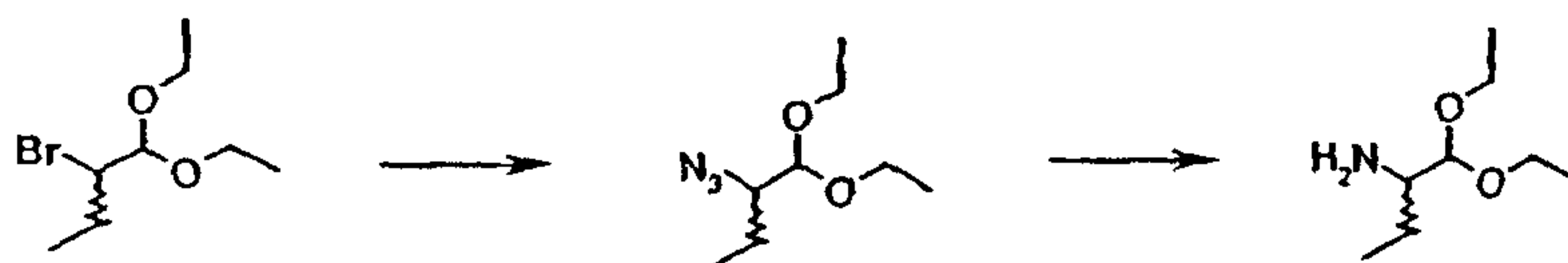
				
Beispiel -Nr.	1-2.37	1-2.38	1-2.39	1-2.40
Löse- mittel	CDCl ₃	CDCl ₃	DMSO	DMSO
	8.14 (s,1H) 5.41 (m,1H) 4.49 (m,1H) 2.44 (m,6H) 1.79 (m,2H)	8.20 (s,1H) 7.71 (m,1H) 7.30 (m,6H) 4.97 (s,2H) 3.00 (m,2H) 1.40 (m,8H)	8.22 (s,1H) 6.35 (s,1H) 5.19 (t,1H) 3.54 (d,2H) 2.00 (m,2H) 1.75 (m,4H) 1.53 (m,2H)	8.22 (s,1H) 7.12 (d,1H) 4.10 (m,1H) 2.20 (m,1H) 1.89 (m,1H) 1.35 (m,8H)
Aus- beute	58%	77%	48%	60%
Masse	304 (ES)	427 (ES)	308 (EI)	301 (EI)

				
Beispiel -Nr.	1-2.41	1-2.42	1-2.43	1-2.44
Löse- mittel	DMSO	DMSO	DMSO	DMSO
	8.19 (s, 1H) 7.21 (d, 1H) 4.03 (m, 1H) 1.60 (m, 12H)	8.21 (s, 1H) 7.03 (d, 1H) 4.83 (t, 1H) 4.13 (m, 1H) 3.47 (m, 2H) 1.12 (d, 3H)	8.28 (s, 1H) 3.62 (q, 4H) 1.18 (t, 6H)	8.41 (s, 1H) 8.15 (t, 1H) 4.21 (td, 2H)
Aus- beute	73%	61%	13%	21%
Masse	303 (EI)	267 (EI)	265 (EI)	339 (EI)

				
Beispiel -Nr.	1-2.45	1-2.46	1-2.47	1-2.48
Löse- mittel	DMSO	DMSO	DMSO	DMSO
	8.36 (s,1H) 6.56 (s,1H) 3.81 (s,1H) 2.28 (m,2H) 1.83 (m,2H) 1.58 (m,6H)	8.26 (s,1H) 8.06 (d,1H) 7.30 (m,5H) 5.29 (m,1H) 4.81 (t,1H) 3.42 (m,2H) 2.10 (m,2H)	8.32 (t,1H) 8.15 (s,1H) 3.40 (m,2H) 2.34 (m,2H) 2.18 (s,6H) 1.69 (m,2H)	8.15 (s,1H) 7.06 (d,1H) 4.65 (br,1H) 3.79 (m,1H) 3.52 (m,1H) 1.86 (m,2H) 1.61 (m,2H) 1.25 (m,4H)
Aus- beute	84%	97%	22%	53%
Masse	314 (EI)	343 (EI)	294 (EI)	307 (EI)

				
Beispiel -Nr.	1-2.49	1-2.50	1-2.51	1-2.52
Löse- mittel	DMSO	DMSO	DMSO	
	8.29 (s,1H) 6.05 (s,1H) 5.18 (m,1H) 3.54 (s,2H) 1.92 (m,2H) 1.70 (m,2H)	8.18 (s,1H) 7.25 (d,1H) 4.15 (m,1H) 2.40 (m,6H) 1.50 (m,4H) 1.17 (d,3H) 0.90 (dd,6H)	8,29 (s,1H) 6.18 (s,1H) 5.15 (t,1H) 3.70 (m,1H) 3.49 (m,1H) 2.60 (m,1H) 0.92 (d,3H) 0.83 (d,3H)	8.38 (s,1H) 7.28 (d,1H) 5.28 (t,1H) 4.65 (m,1H) 3.86 (m,2H) 3.65 (s,3H)
Aus- beute	16%	52%	27%	63%
Masse	308 (EI)	350 (EI)	308 (EI)	309 (EI)

			
Beispiel -Nr.	1-2.53	1-2.54	1-2.55
Löse- mittel	DMSO	DMSO	DMSO
	8.22 (s, 1H) 7.65 (t, 1H) 7.30 (m, 6H) 5.01 (s, 2H) 3.38 (m, 2H) 3.04 (m, 2H) 1.68 (m, 2H)	7.75 (s, 1H) 6.55 (d, 1H) 4.54 (m, 1	8.18 (s, 1H) 7.69 (t, 1H) 4.32 (br, 1H) 3.35 (m, 4H) 1.40 (m, 6H)
Aus- beute	77%	50%	43%
Masse	398 (EI)	229 (EI)	295 (EI)

Example 3.0**Production of Amines**

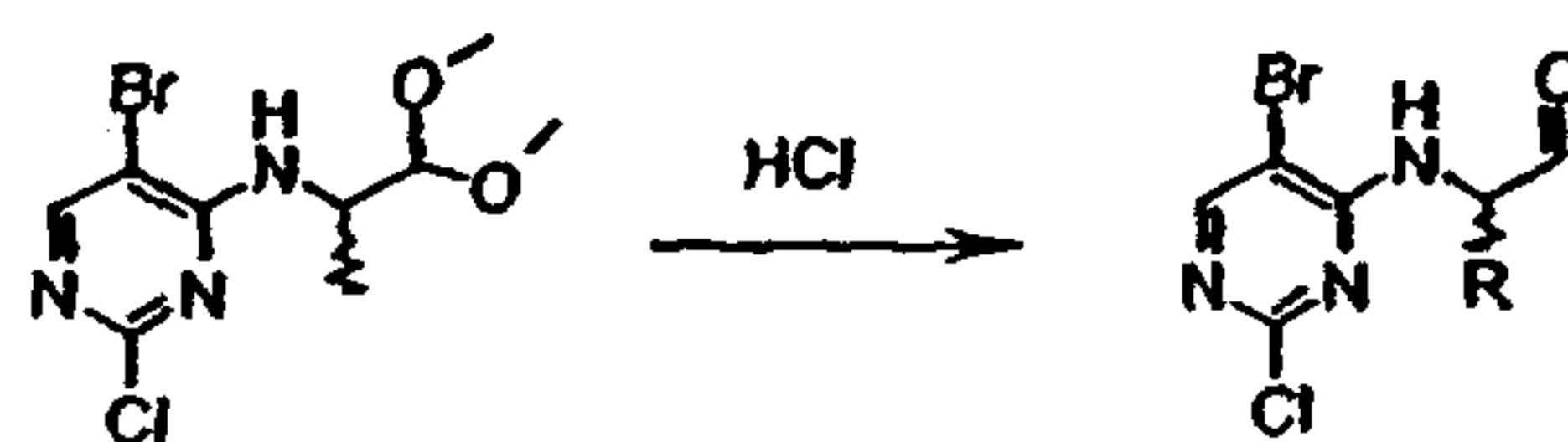
4.5 g (20 mmol) of 2-bromobutyraldehyde diethyl acetyl (Pfaltz-Bauer Company) and 5.2 g (80 mmol) of sodium azide are stirred for 5 days in 15 ml of DMF at 100°C. Then, it is poured onto cold dilute sodium bicarbonate solution, extracted 3 x with ether, the organic phase is dried with magnesium sulfate and concentrated by evaporation: raw yield 1.87 g (50% of theory).

936 mg of the crude product is dissolved in 50 ml of methanol, mixed with palladium on carbon (10%) and stirred for 12 hours under H₂ atmosphere. After the catalyst is filtered off and after concentration by evaporation, 457 mg (57% of theory) of the desired amine remains.

Beispiel-Nr.	3.0	3.1	3.2	3.3
Ausbeute	50%	57%	50 %	71 %
NMR CDCl3	4,38 (d , 1H) 3,72 (m , 2H) 3,6 (m , 2H) 3,25 (m , 1H) 1,7 (m , 1H) 1,46 (m , 1H) 1,25 (trtr , 6H) 1,0 (tr , 3H)	4,19 (d , 1H) 3,68 (m , 2H) 3,52 (m , 2H) 2,7 (m , 1H) 1,60 (m , 1H) 1,25 (m , 1H) 1,2 (trtr , 6H) 0,95 (tr , 3H)	4,38 (d , 1H) 3,58 (m , 2H) 3,5 (m , 1H) 3,49 (s , 3H) 3,43 (s , 3H) 3,39 (s , 3H)	4,25 (d , 1H) 3,5 (m , 1H) 3,42 (s , 3H) 3,41 (s , 3H) 3,40 (m , 1H) 3,08 (m , 1H)

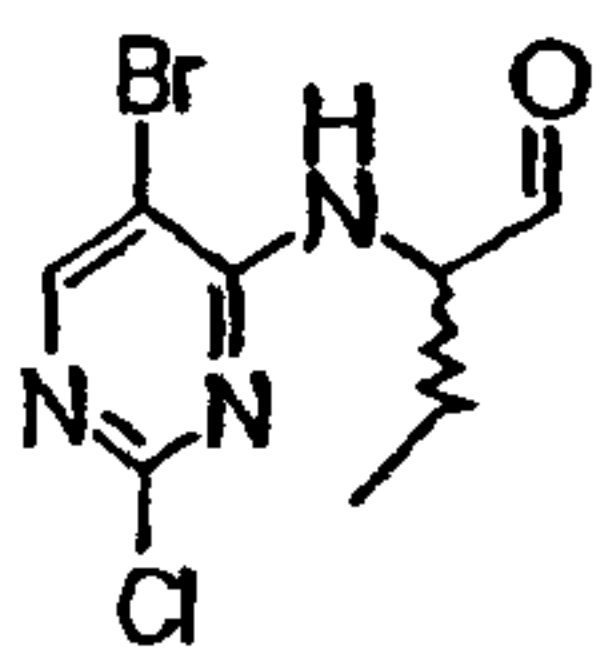
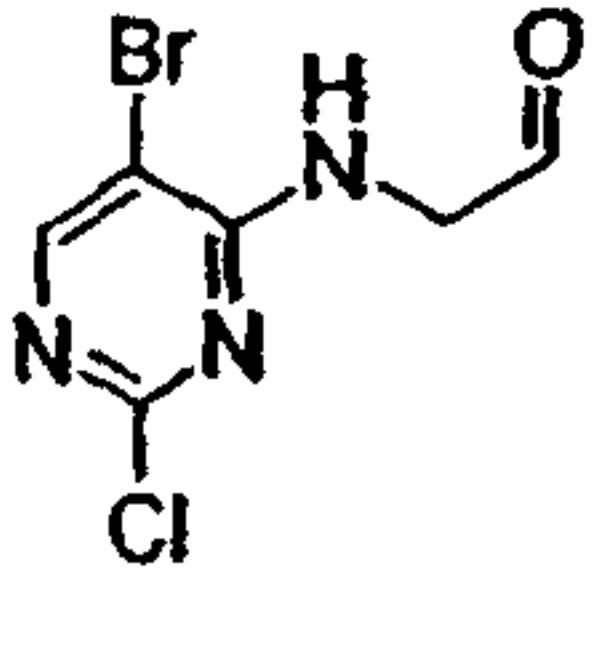
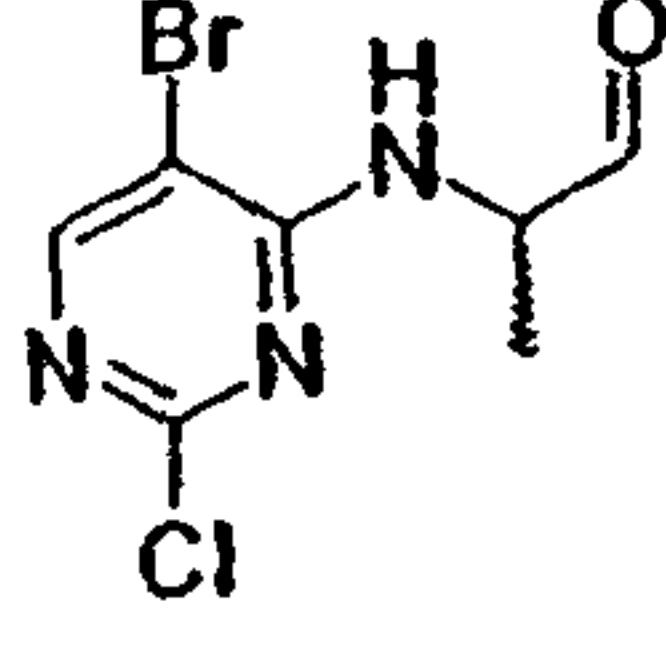
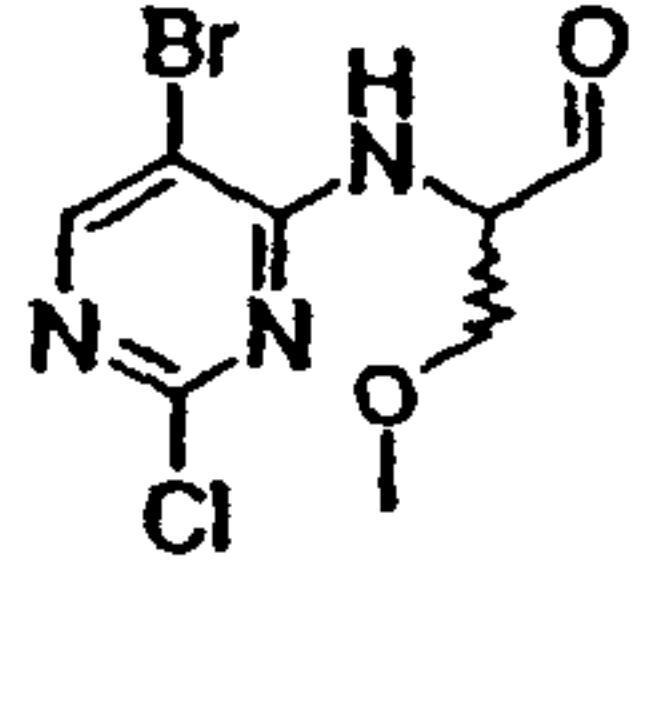
Example 4.0

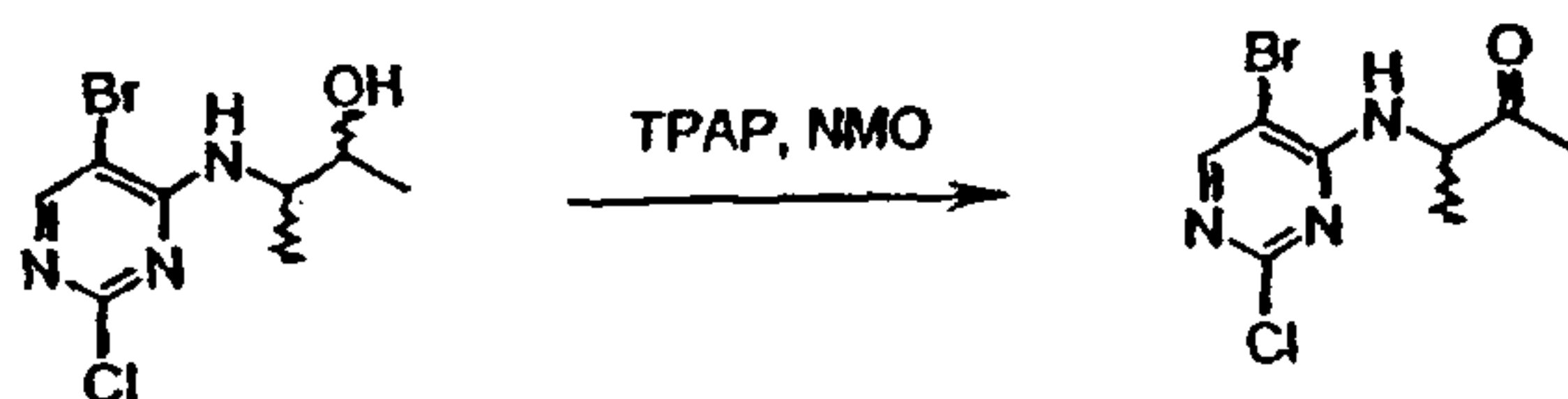
Production of the Free Aldehydes



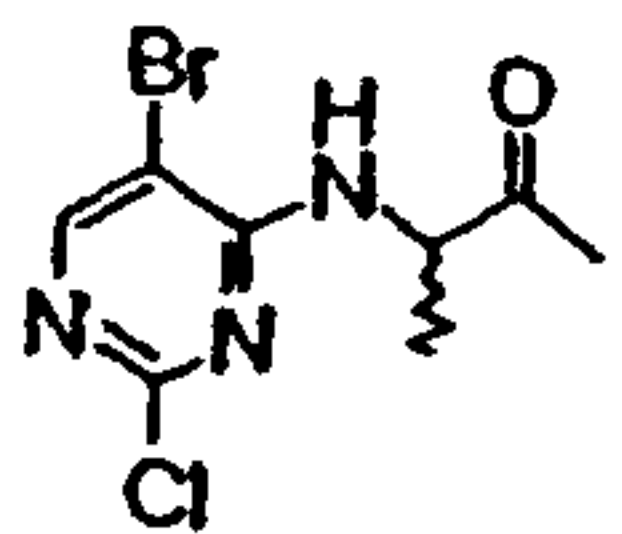
148 mg (0.5 mmol) of intermediate product compound 1.18 is dissolved in 1 ml of glacial acetic acid. At room temperature, 0.5 ml of 1N hydrochloric acid is added, and it is stirred for 12 hours. For working-up, it is poured onto ice water and carefully

neutralized with pulverized sodium bicarbonate. Then, it is extracted 3 x with ethyl acetate, the organic phase is dried with magnesium sulfate and concentrated by evaporation, crude product 104 mg (83% of theory) of the aldehyde of compound 4.0. The crude product can be used without further purification.

				
Beispiel -Nr.	4.1	4.0	4.2	4.3
Aus- beute	82 %	83 %	89 %	79 %
Masse	ESI : MH ⁺ 278 (39%) 210 (100%)	ESI : MH ⁺ 250 (9%)	ESI: MH ⁺ 266 (8%)	ESI: MH ⁺ 294 (10%)

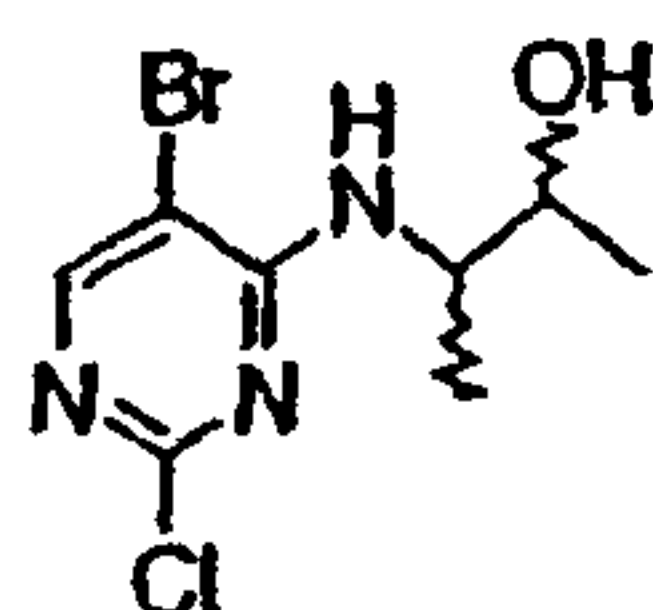
Example 5.0**Production of Ketones**

100 mg (0.356 mmol) of compound 6.0 and 126 mg of N-methylmorpholine-N-oxide are dissolved in 5 ml of dichloromethane and stirred for 10 minutes with pulverized molecular sieve (4 Å). Then, 6 mg of tetrapropylammonium perruthenate is added, and it is stirred for 4 more hours at room temperature. After concentration by evaporation, it is chromatographed on silica gel (hexane/ethyl acetate 4:1 > 2:1). Yield: 75 mg (76% of theory) of the ketone of compound 5.0.

	
Beispiel -Nr.	5.0
Aus- beute	76%
Masse	ESI : MH ⁺ 280 (100%) 200 (37%) 156 (30%)

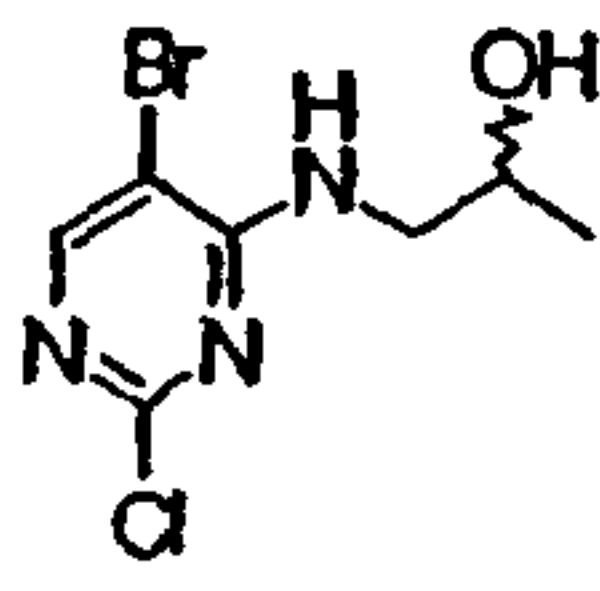
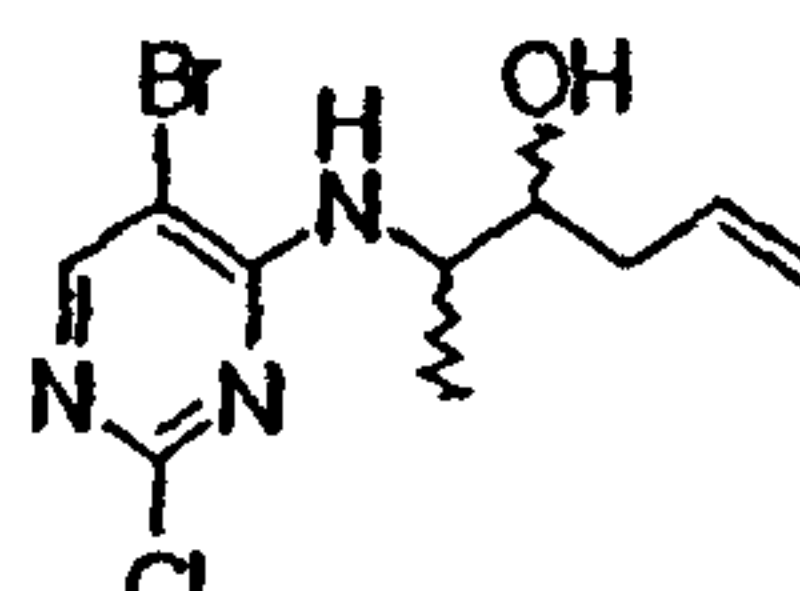
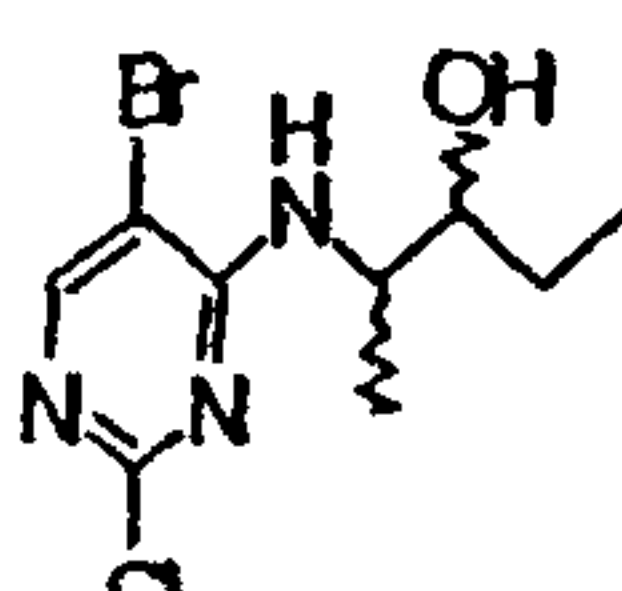
Example 6.0**Production of Alcohols**

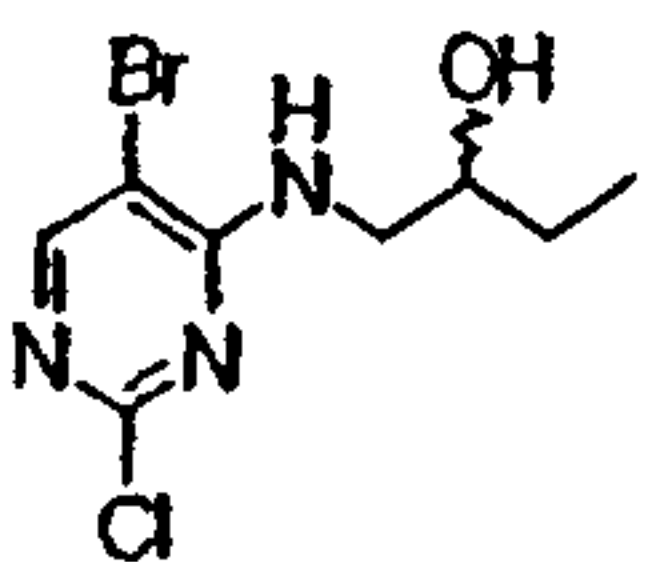
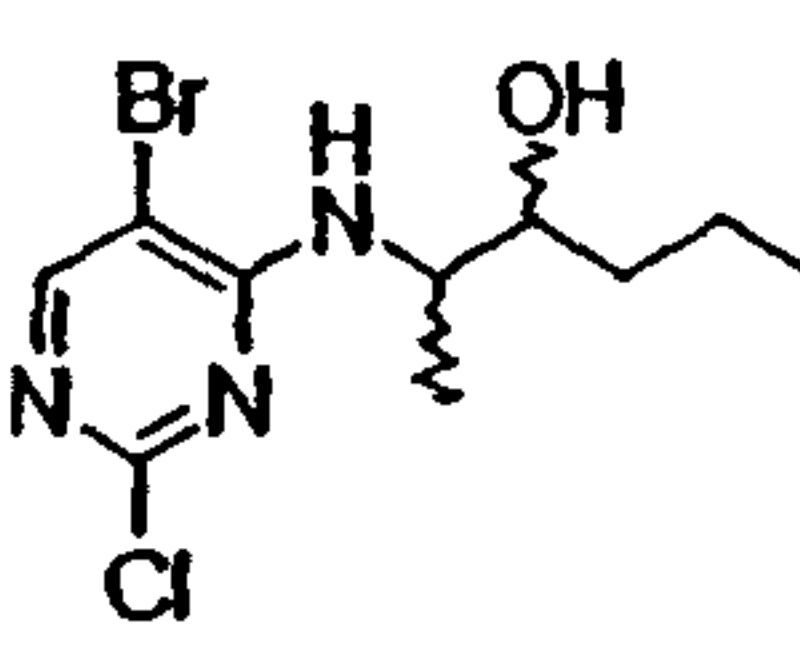
265 mg (1 mmol) of compound 4.2 is dissolved in 20 ml of tetrahydrofuran. While being cooled in an ice bath, 5 equivalents of methylmagnesium bromide (3 molar solution in ether) is added in portions. Then, it is stirred for 3 more hours at room temperature and then quenched with water while being cooled. Then, it is mixed with ammonium chloride solution, extracted 3 x with ethyl acetate, the organic phase is dried with magnesium sulfate and concentrated by evaporation. Flash chromatography (hexane/ethyl acetate 2:1) yields 213 mg (76% of theory) of the alcohol of compound 6.0.

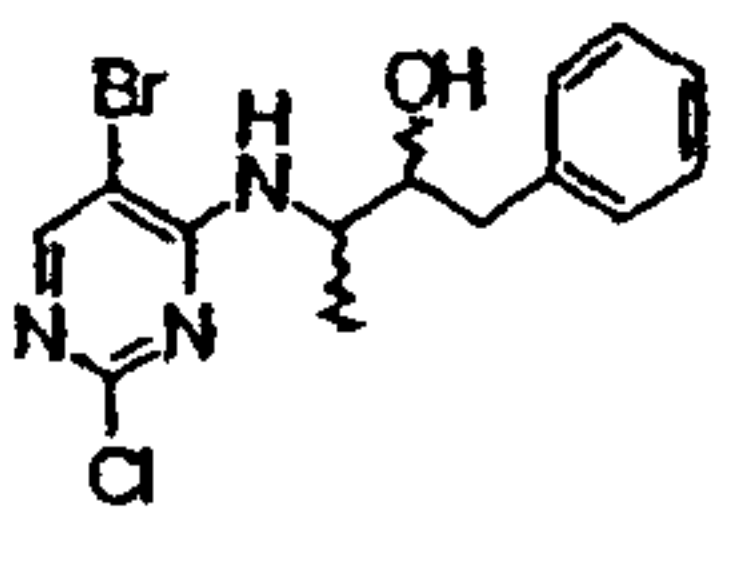
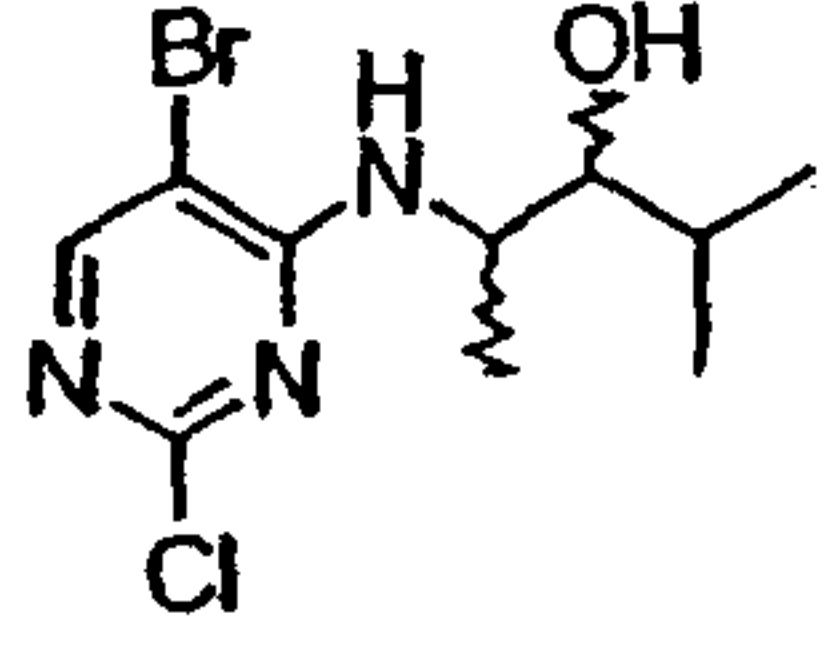
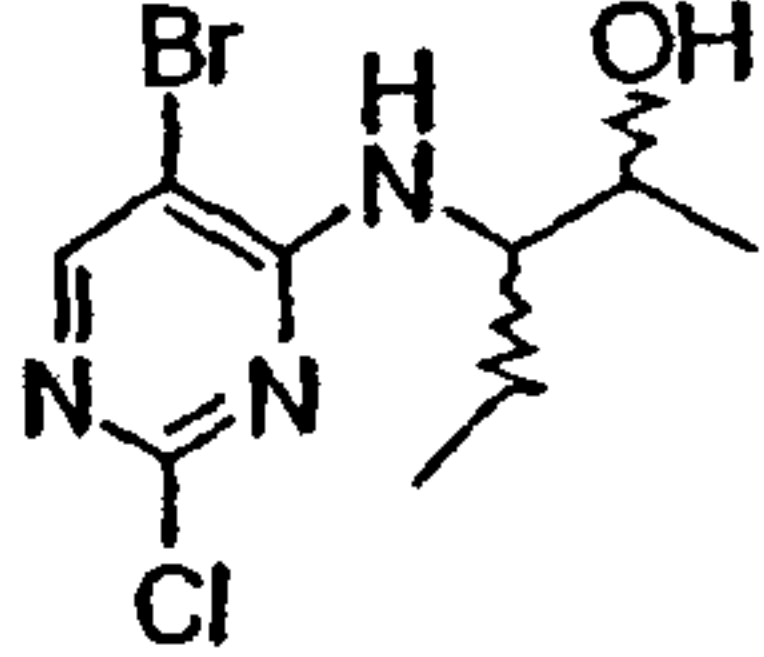


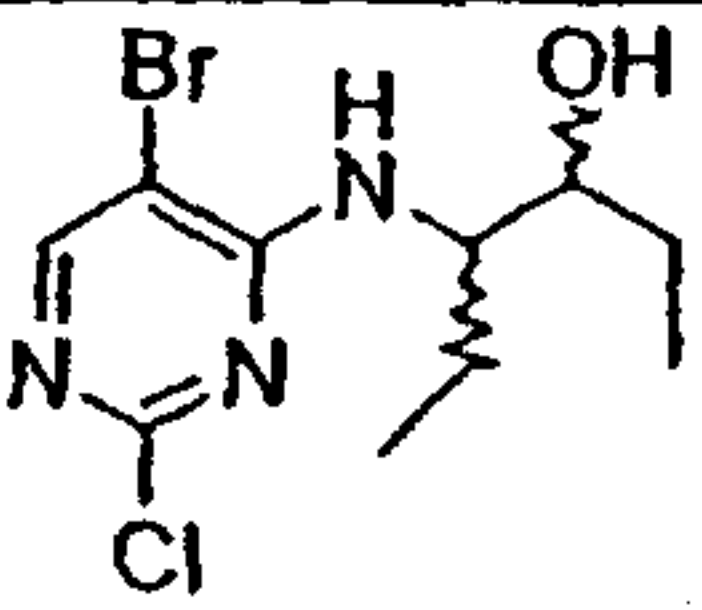
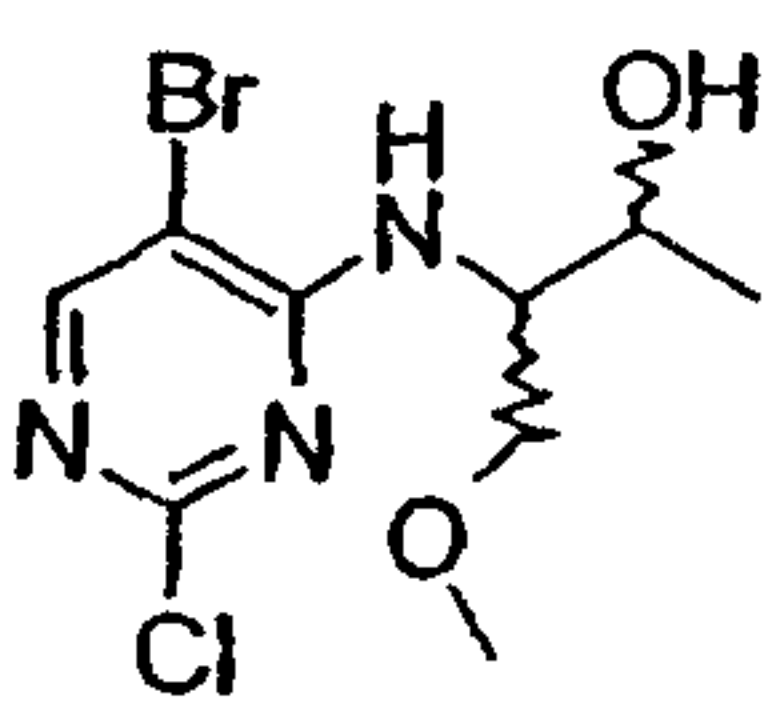
ESI:MH⁺ 282 (100%) 276 (5%)

Similarly produced are also the following intermediate products:

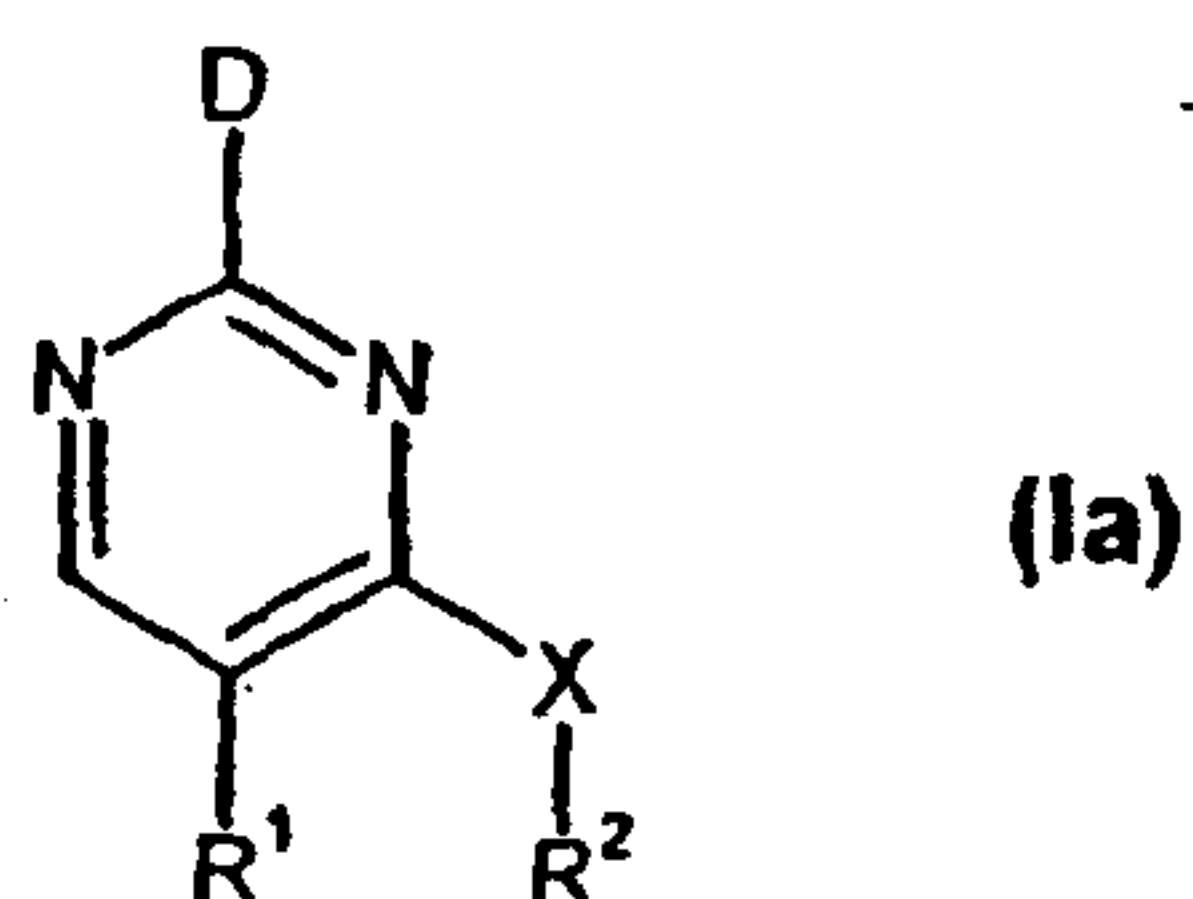
			
Beispiel -Nr.	6.1	6.2	6.3
Aus- beute	46%	32%	39%
Masse	El: M^+ 267 (3%) 223 (100%) 132 (27%)	ESI: MH^+ 308 (100%) 306 (71%) 268 (31%)	ESI: MH^+ 296 (100%) 294 (73%) 217 (4%)

		
Beispiel -Nr.	6.4	6.5
Aus- beute	36%	50%
Masse	El : M+ 281 (3%) 223 (100%) 114 (38%)	ESI: MH ⁺ 310 (100%) 308 (87%) 298 (9%)

			
Beispiel -Nr.	6.6	6.7	6.8
Aus- beute	40%	~20%	35%
Masse	El : M ⁺ 358 (100%) 356 (97%) 277 (29%)	Cl: M ⁺ 310 (100%) 308 (84%) 130 (54%)	ESI : MH ⁺ 294 (28%) 296 (36%) 210 (100%)

		
Beispiel -Nr.	6.9	6.10
Aus- beute	29 %	67 %
Masse	ESI : MH ⁺ 308 (28%) 310 (38%) 210 (100%)	ESI: MH ⁺ 310 (87%) 312 (100%) 123 (24%)

Subjects of this invention are thus also compounds of general formula Ia

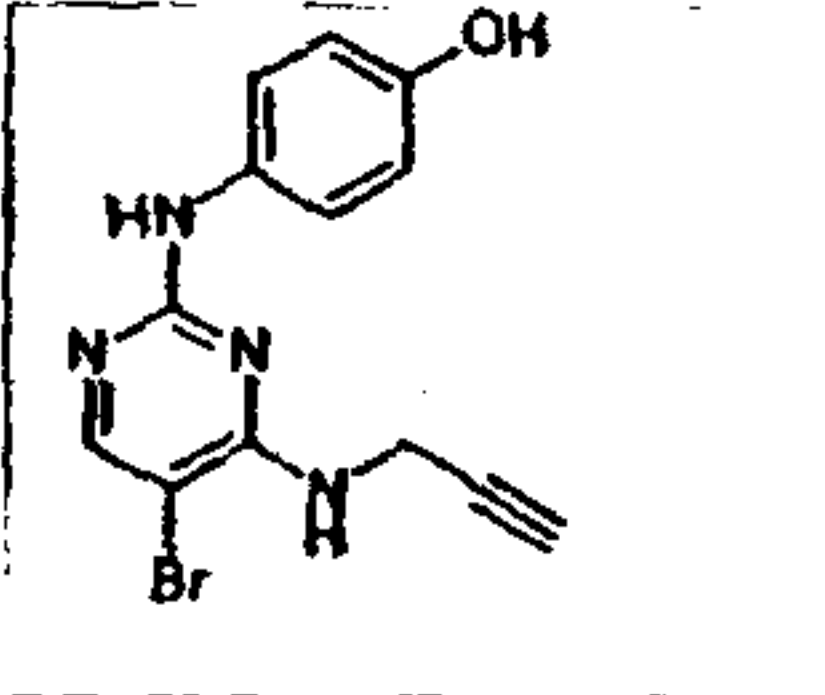
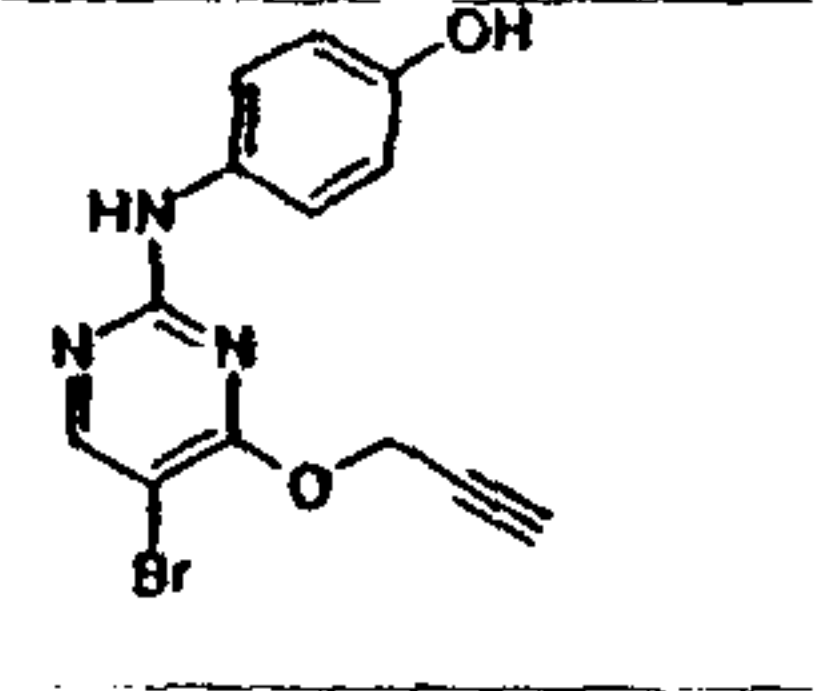
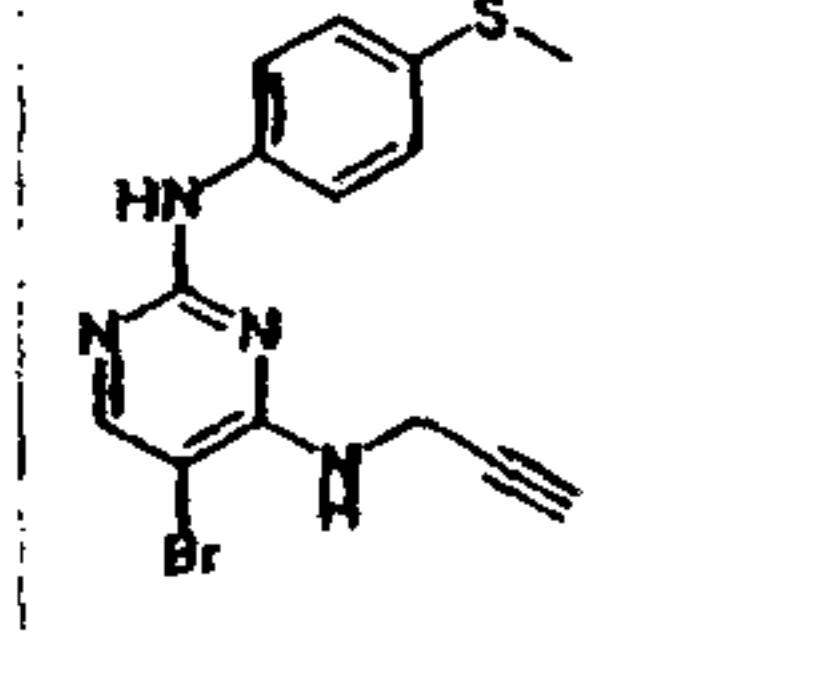
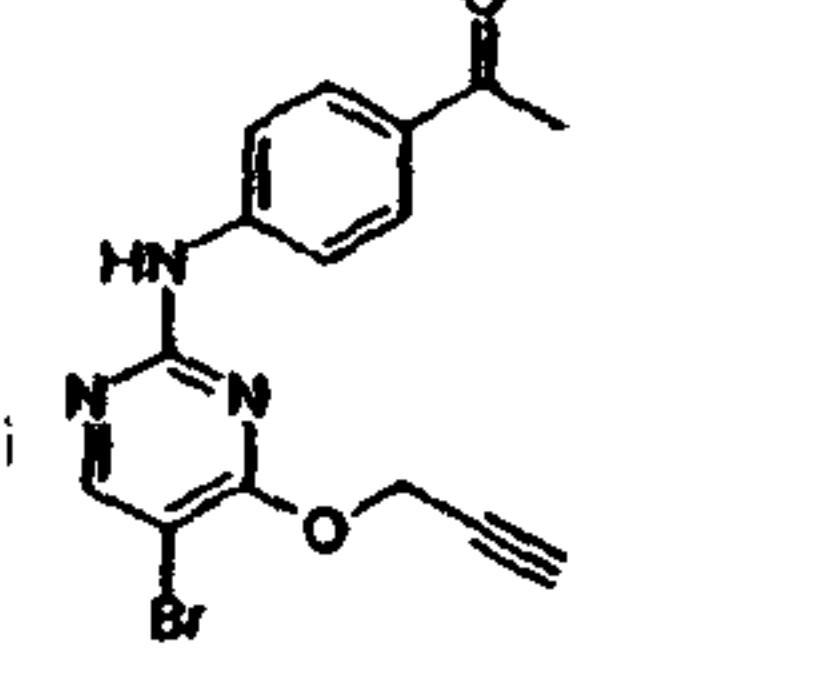
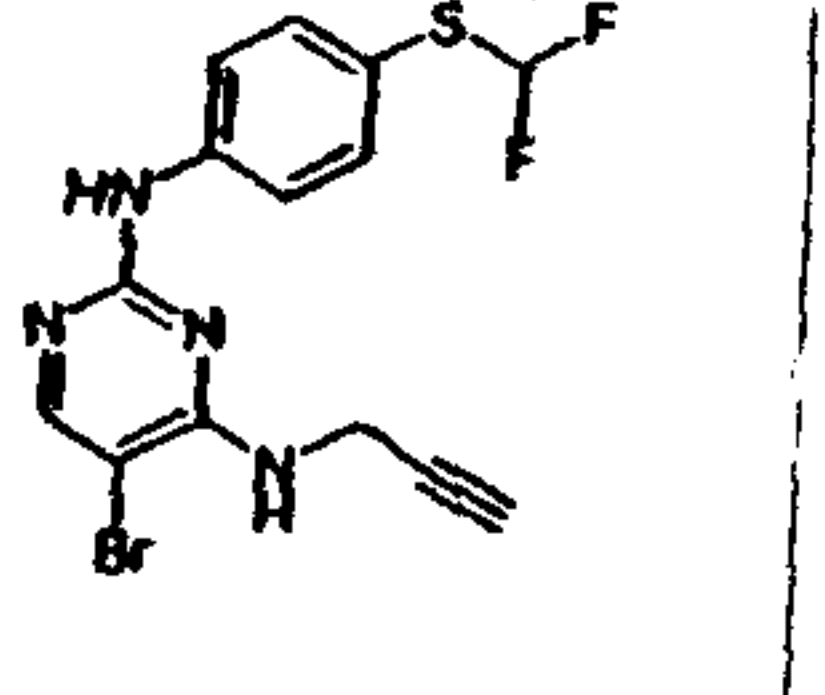


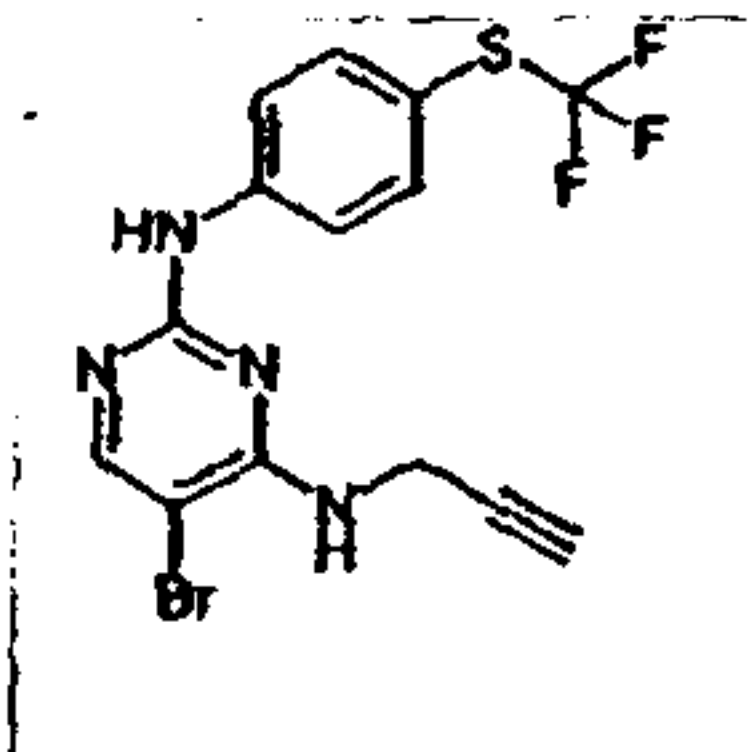
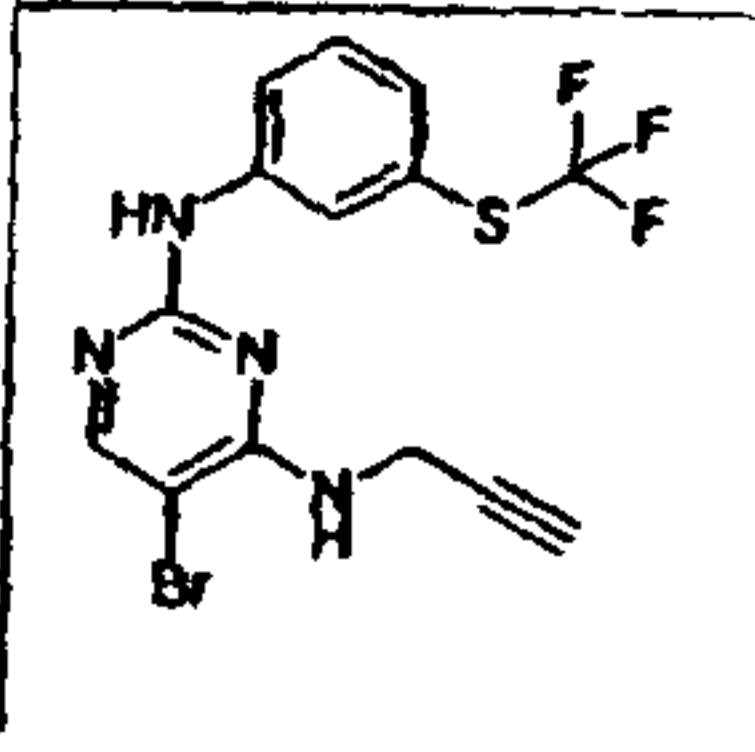
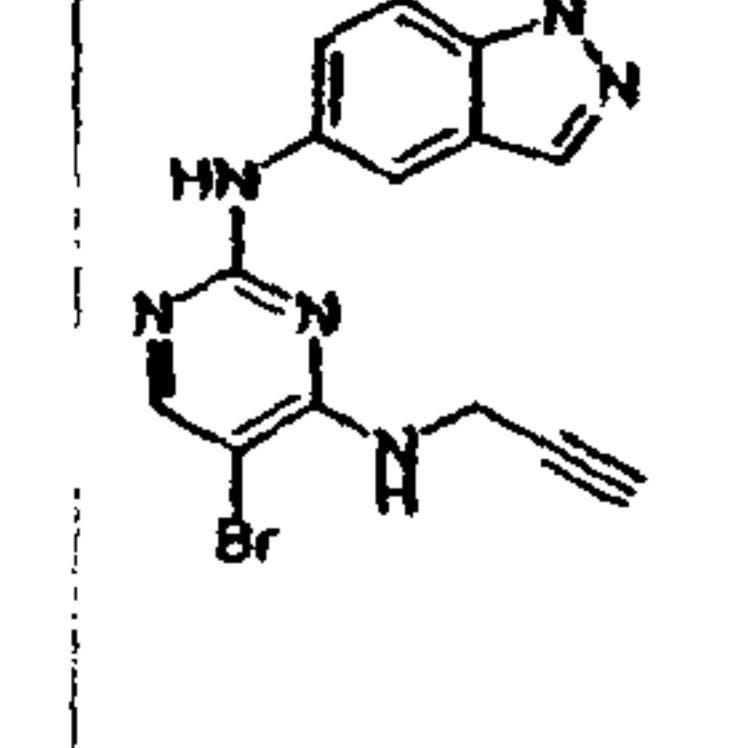
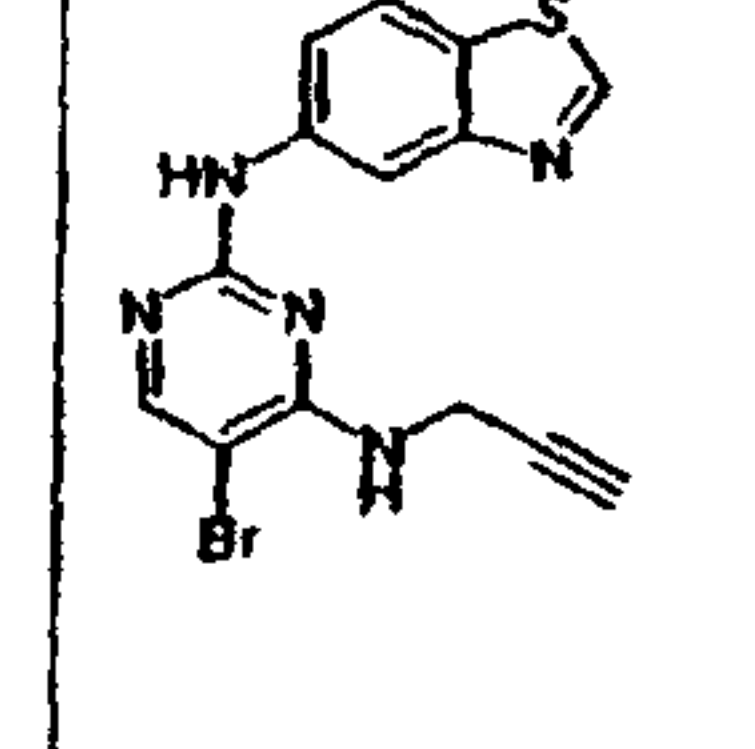
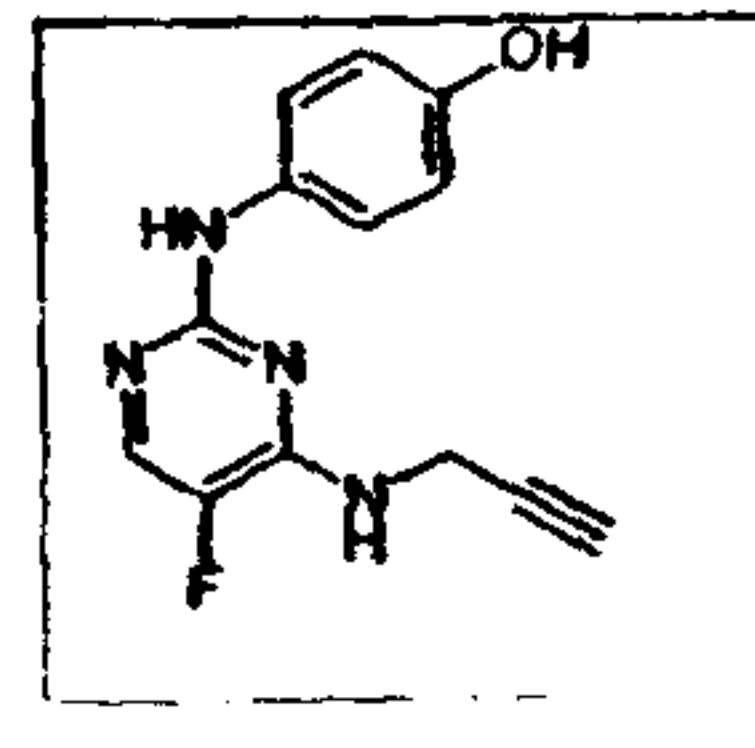
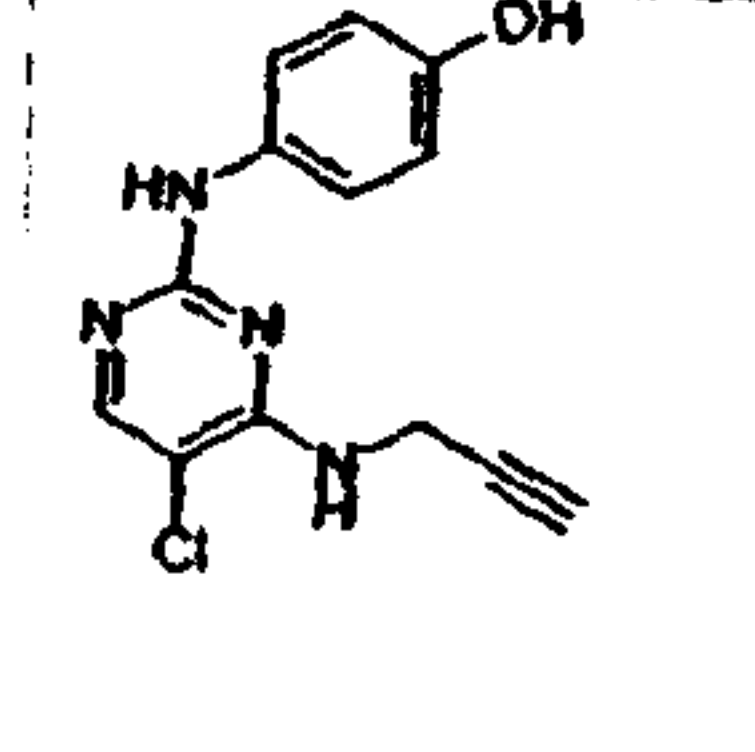
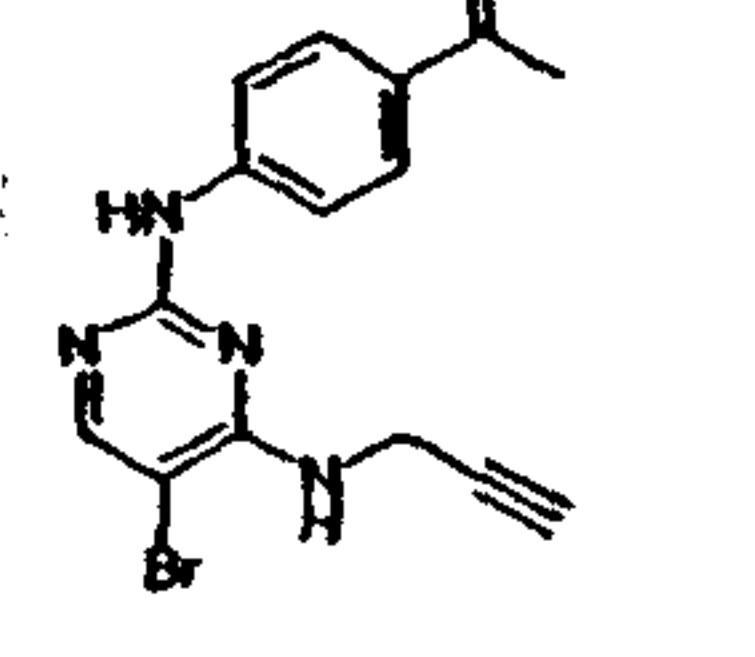
in which

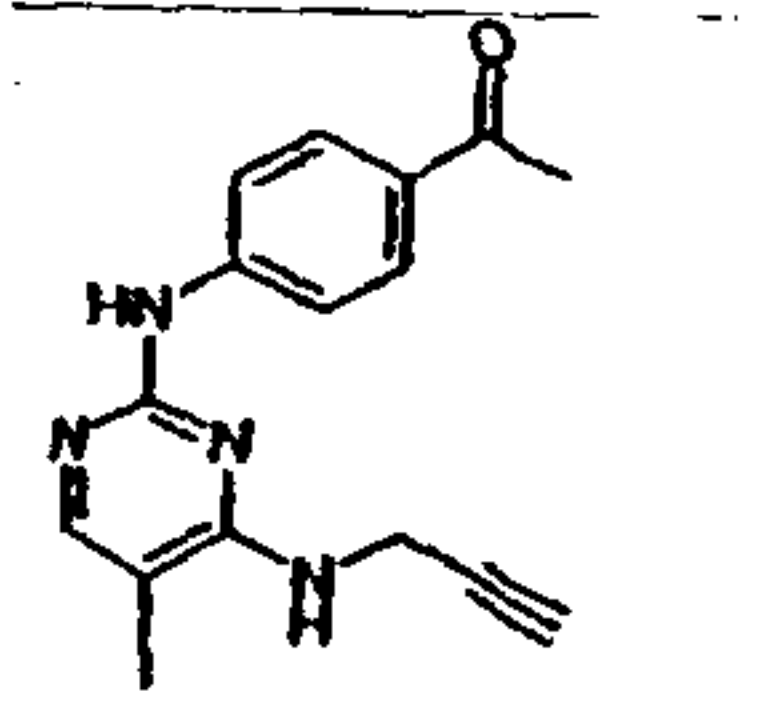
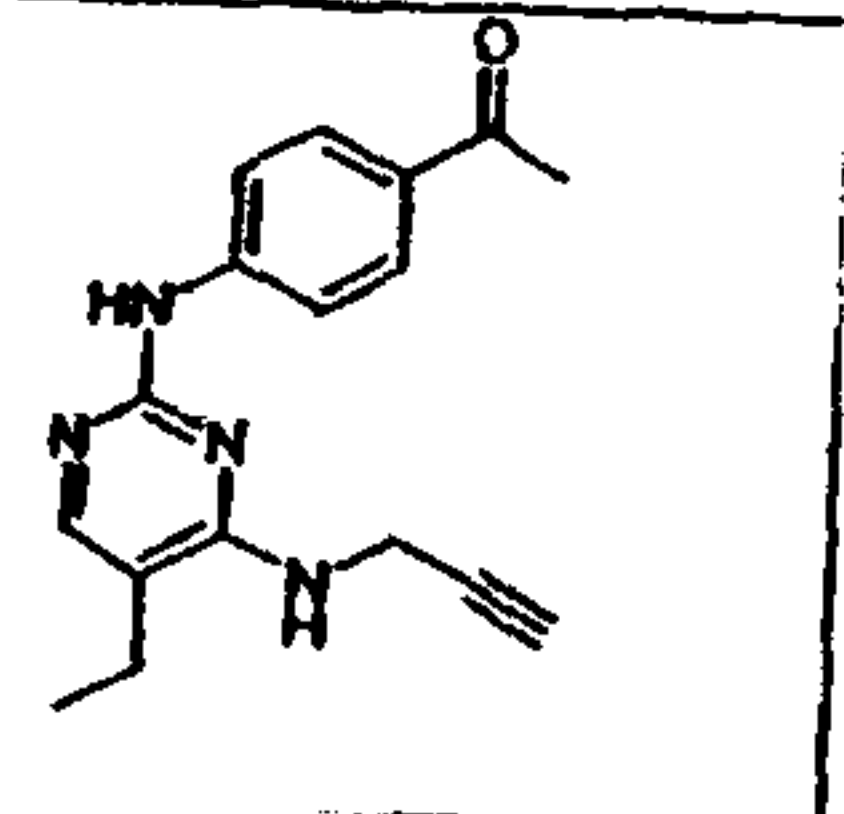
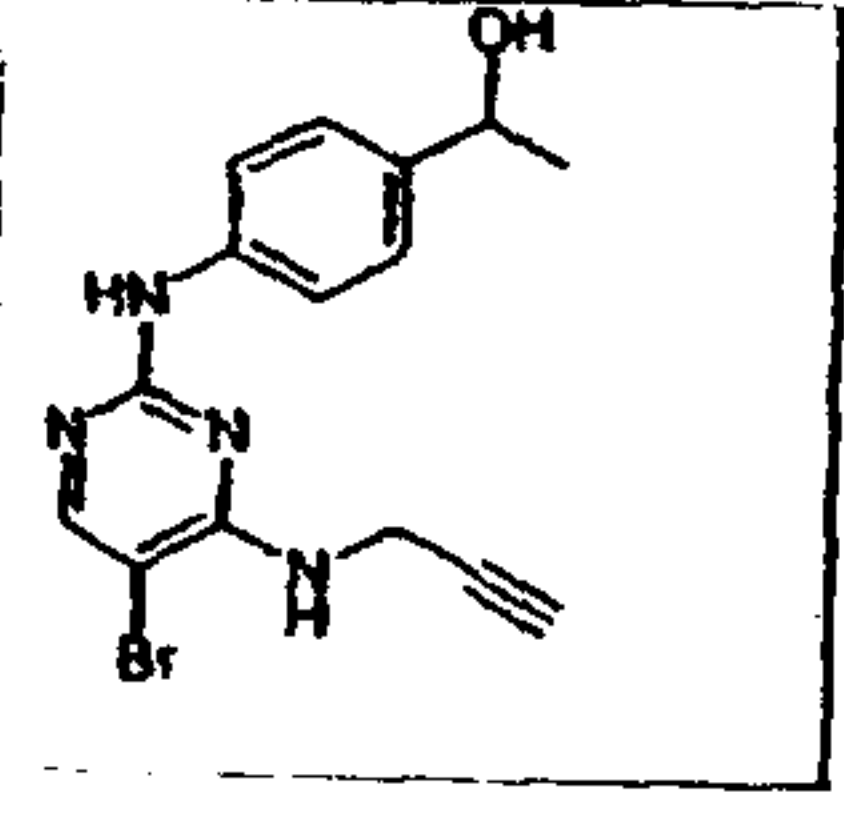
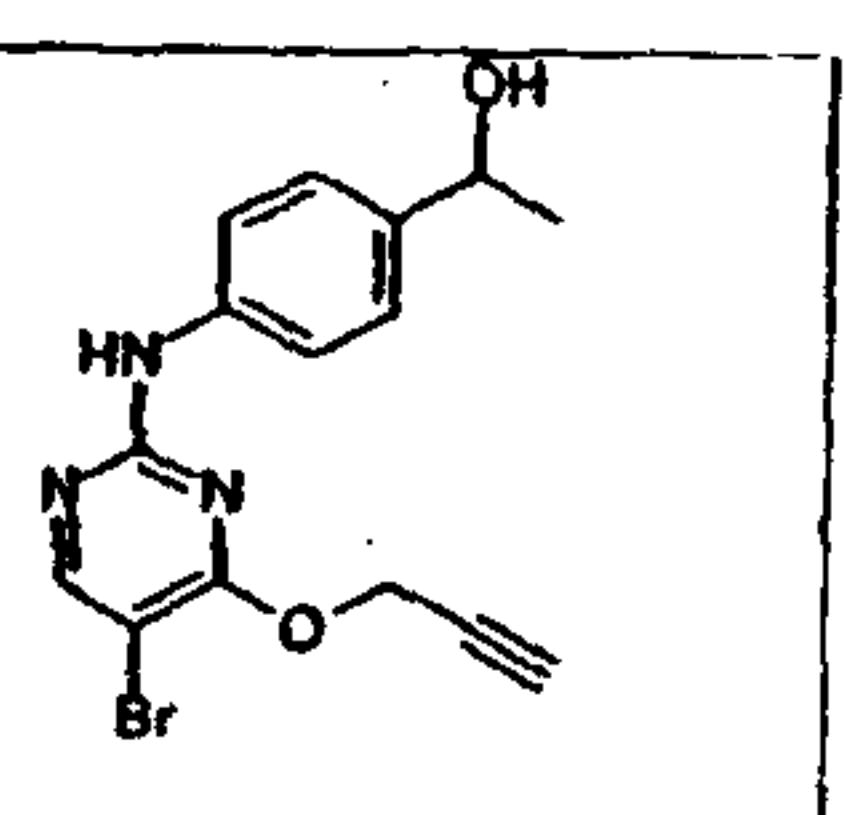
D stands for halogen, and X, R¹, and R² have the meanings that are indicated in general formula (I).

Those intermediate products of general formula Ia, in which D stands for chlorine and X, R¹ and R² have the meanings that are indicated in the general formula, are especially valuable.

Another subject of this invention are also those compounds that fall under industrial property right DE 4029650, whose action is in the fungicide range and which are not described as CDK inhibitors, however, and also their use for treating cancer is not described.

No.	Structure	Name
5		4-[[5-Bromo-4-(2-propynylamino)-2-pyrimidinyl]amino]-phenol
6		4-[[5-Bromo-4-(2-propynyloxy)-2-pyrimidinyl]amino]-phenol
16		5-Bromo-N2-(4-methylthiophenyl)-N4-2-propynyl-2,4-pyrimidine diamine
22		1-[4-[(5-Bromo-4-(2-propynyloxy)-2-pyrimidinyl)amino]phenyl]-ethanone
23		5-Bromo-N2-(4-difluoromethylthiophenyl)-N4-2-propynyl-2,4-pyrimidine diamine

No.	Structure	Name
24		5-Bromo-N4-2-propynyl-N2-(4-trifluoromethylthiophenyl)-2,4-pyrimidine diamine
35		5-Bromo-N4-2-propynyl-N2-(3-trifluoromethylthiophenyl)-2,4-pyrimidine diamine
37		N-[5-Bromo-4-(2-propynylamino)-2-pyrimidinyl]-indazol-5-amine
38		N-[5-Bromo-4-(2-propynylamino)-2-pyrimidinyl]-benzothiazole-5-amine
42		4-[[5-Fluoro-4-(2-propynyloxy)-2-pyrimidinyl]amino]phenol
43		4-[[5-Chloro-4-(2-propynyloxy)-2-pyrimidinyl]amino]phenol
50		1-[4-[(5-Bromo-4-(2-propynylamino)-2-pyrimidinyl)amino]phenyl]-ethanone

No.	Structure	Name
54		1-[4-[(5-Iodo-4-(2-propynylamino)-2-pyrimidinyl)amino]phenyl]-ethanone
70		1-[4-[(5-Ethyl-4-(2-propynylamino)-2-pyrimidinyl)amino]phenyl]-ethanone
81		1-[4-[(5-Bromo-4-(2-propynylamino)-2-pyrimidinyl)amino]phenyl]-ethanol
82		1-[4-[(5-Bromo-4-(2-propynyloxy)-2-pyrimidinyl)amino]phenyl]-ethanol

The invention thus relates in addition to pharmaceutical agents that comprise a compound of general formula I

in which

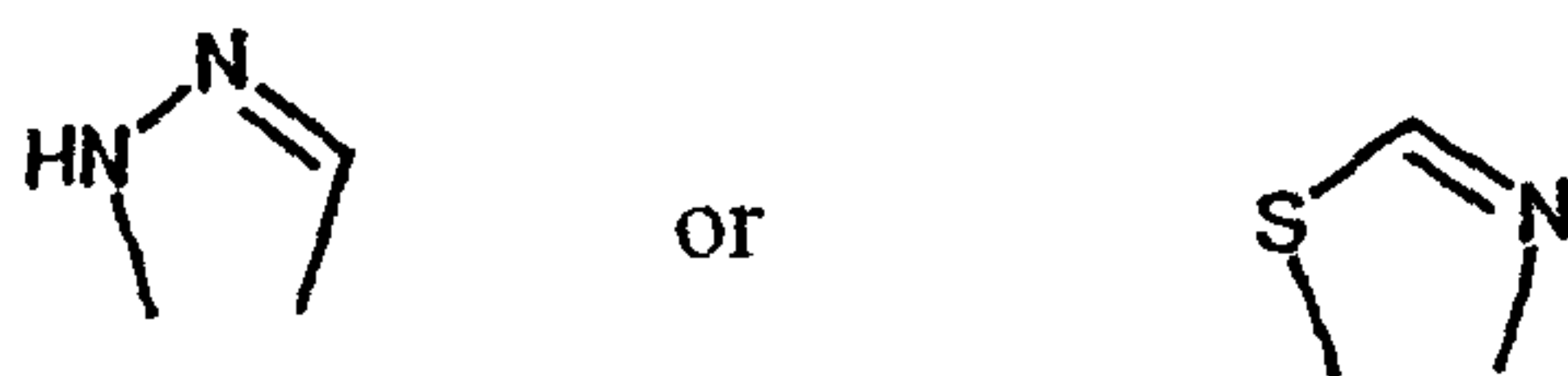
R^1 stands for halogen or C_1 - C_3 -alkyl

X stands for oxygen or $-NH$,

A stands for hydrogen

B stands for hydroxy, $-CO$ -alkyl- R^7 , $-S-CHF_2$, $-S-(CH_2)_nCH(OH)CH_2N-R^3R^4$, $-S-CF_3$, or $-CH(OH)-CH_3$, or

A and B, independently of one another, can form a group



R^2 , R^3 , R^4 , R^7 and R^8 have the meanings that are indicated in general formula I, as well as isomers, diastereomers, enantiomers and salts thereof.

The agents according to the invention can also be used for treating cancer, autoimmune diseases, cardiovascular diseases, chemotherapy agent-induced alopecia and mucositis, infectious diseases, nephrological diseases, chronic and acute neurodegenerative diseases and viral infections, whereby cancer is defined as solid tumors and leukemia; autoimmune diseases are defined as psoriasis, alopecia and multiple sclerosis; cardiovascular diseases are defined as stenoses, arterioscleroses and restenoses; infectious diseases are defined as diseases that are caused by unicellular parasites; nephrological diseases are defined as glomerulonephritis; chronic neurodegenerative diseases are defined as Huntington's disease, amyotrophic lateral

sclerosis, Parkinson's disease, AIDS dementia and Alzheimer's disease; acute neurodegenerative diseases are defined as ischemias of the brain and neurotraumas; and viral infections are defined as cytomegalic infections, herpes, hepatitis B or C, and HIV diseases.

The following examples describe the biological action of the compounds according to the invention without limiting the invention to these examples.

Example 1

CDK2/CycE Kinase Assay

Recombinant CDK2- and CycE-GST-fusion proteins, purified from baculovirus-infected insect cells (Sf9), were obtained by Dr. Dieter Marmé, Klinik für Tumorbologie [Clinic for Tumor Biology], Freiburg. Histone H1, which was used as a kinase substrate, was purchased by the Sigma Company.

CDK2/CycE (50 ng/measuring point) was incubated for 15 minutes at 22°C in the presence of various concentrations of test substances (0 μ M, as well as within the range of 0.01-100 μ M) in assay buffer [50 mmol of Tris/HCl pH 8.0, 10 mmol of $MgCl_2$, 0.1 mmol of Na ortho-vanadate, 1.0 mmol of dithiothreitol, 0.5 μ M of adenosine triphosphate (ATP), 10 μ g/measuring point of histone H1, 0.2 μ Ci/measuring point of ^{33}P -gamma ATP, 0.05% NP40, 12.5% dimethyl sulfoxide]. The reaction was stopped by adding EDTA solution (250 mmol, pH 8.0, 14 μ l/measuring point).

From each reaction batch, 10 μ l was applied to P30 filter strips (Wallac Company), and non-incorporated ^{33}P -ATP was removed by subjecting the filter strips to three washing cycles for 10 minutes each in 0.5% phosphoric acid. After the filter strips were dried for one hour at 70°C, the filter strips were covered with scintillator strips (MeltiLexTM A, Wallac Company) and baked for one hour at 90°C. The amount of incorporated ^{33}P (substrate phosphorylation) was determined by scintillation measurement in a gamma-radiation measuring device (Wallac).

Example 2**Proliferation Assay**

Cultivated human tumor cells (as indicated) were flattened out at a density of 5000 cells/measuring point in a 96-hole multititer plate in 200 μ l of the corresponding growth medium. After 24 hours, the cells of one plate (zero-point plate) were colored with crystal violet (see below), while the medium of the other plates was replaced by fresh culture medium (200 μ l), to which the test substances were added at various concentrations (0 μ m, as well as in the range of 0.01-30 μ m; the final concentration of the solvent dimethyl sulfoxide was 0.5%). The cells were incubated for 4 days in the presence of test substances. The cell proliferation was determined by coloring the cells with crystal violet: the cells were fixed by adding 20 μ l/measuring point of a 11% glutaric aldehyde solution for 15 minutes at room temperature. After three washing cycles of the fixed cells with water, the plates were dried at room temperature. The cells were colored by adding 100 μ l/measuring point of a 0.1% crystal violet solution (pH was set at 3 by adding acetic acid). After three washing cycles of the colored cells with water, the plates were dried at room temperature. The dye was dissolved by adding 100 μ l/measuring point of a 10% acetic acid solution. The extinction was determined by photometry at a wavelength of 595 nm. The change of cell growth, in percent, was calculated by standardization of the measured values to the extinction values of the zero-point plate (=0%) and the extinction of the untreated (0 μ m) cells (=100%).

The results of Examples 1 and 2 are cited in the following tables.

[Key to subsequent tables:]

Beispiel Nummer = Example Number

Beispiel Nummer	Inhibition IC ₅₀ [nM]	Proliferation IC ₅₀ [μM]				Sw
	CDK2/CycE	MCF7	H460	HCT116	DU145	(g/l)
22	40	1,2	1,5	1,5	1,5	0.003
37	70	4				0.006
6	70	4	6			0.008
40	20	1	3	3	9	0.002
51	70	8				
20	60	4				
21	400	2				
1	300	8				
2	700					
16	300	3				
24	400	5				
26	300	3				
35	120	>10				
23	180	3				
11	6	0,2	0,5	0,3	0,2	
38	80	>10				
34	1800					
10	4	0,2	0,5	0,5	0,5	
12	400	4				
25	70	1,2	1,5	1,1	1,2	0.017
9	7	0,9		3	3	
7	6	0,7	1,5	1,2	0,5	0.028
31	800	7				0.0023
14	200	3				0.013
18	2000					0.039
3	200	8				0.039
19	800	>10				0.041
13	2000	>10				

Beispiel Nummer	Inhibition IC ₅₀ [nM]	Proliferation IC ₅₀ [μM]				Sw
	CDK2/CycE	MCF7	H460	HCT116	DU145	(g/l)
17	1000	>10				0.04
4	40	8				0.042
15	300	>10				0.024
8	<10	4				0.007
43	200	6				0.04
36	30	0,4	0,6	0,5	0,6	0.018
27	>10000					
42	2000					0.043
39	300					0.0016
44	8	1,2	0,4	0,4	0,3	0.005
45	10	2	1,7	1,2	0,5	0.0094
50	150					
5	90	10				0.043
46	7	2				0.0069
52	200	0,2	1,6	1,2	2	0.0005
53	300	1,6				0.026
54	100	1,1				0.0015
47	12	0,7	1,8	1,3	0,9	
56	80	4				0.023
49	50	>10				0.044
48	4	0,2	1	0,4	0,3	0.042
96	400					0.0005
98	2000					
85	2000					0.001
84	400					0.0005
86	3000					
87	250	0,8				0.003
22	40	1,2	1,5	1,5	1,5	0.003

Beispiel Nummer	Inhibition IC ₅₀ [nM]	Proliferation IC ₅₀ [μM]				Sw
	CDK2/CycE	MCF7	H460	HCT116	DU145	(g/l)
37	70	4				0.006
6	70	4	6			0.008
16	300	3				
24	400	5				
35	120	>10				
23	180	3				
38	80	>10				
43	200	6				0.04
42	2000					0.043
50	150					
5	90	10				0.043
54	100	1,1				0.0015

Proof of Superiority of the Compounds According to the Invention Compared to the Known Compounds

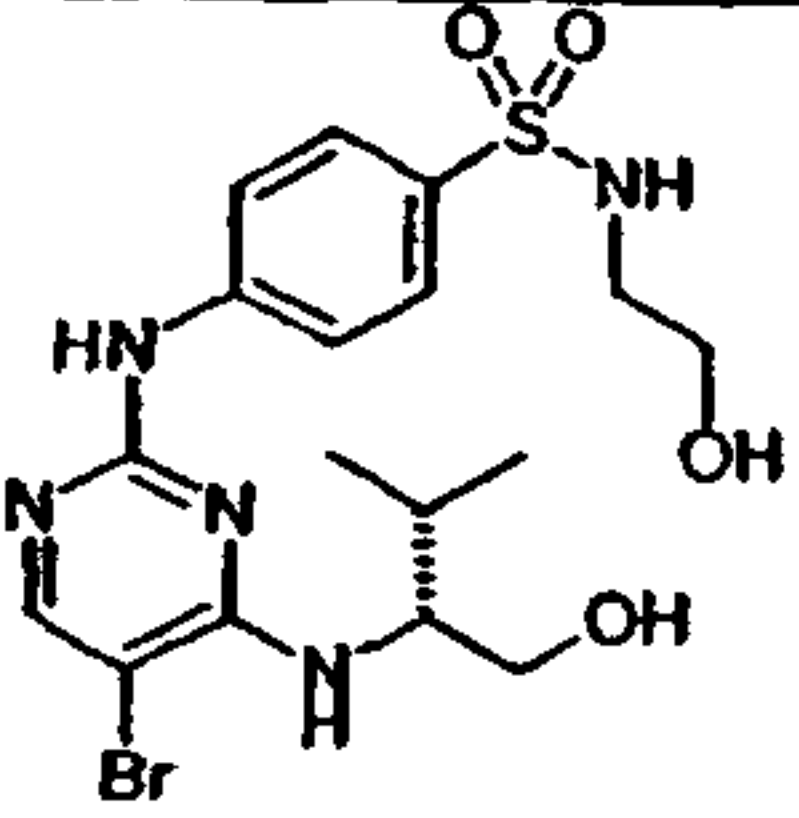
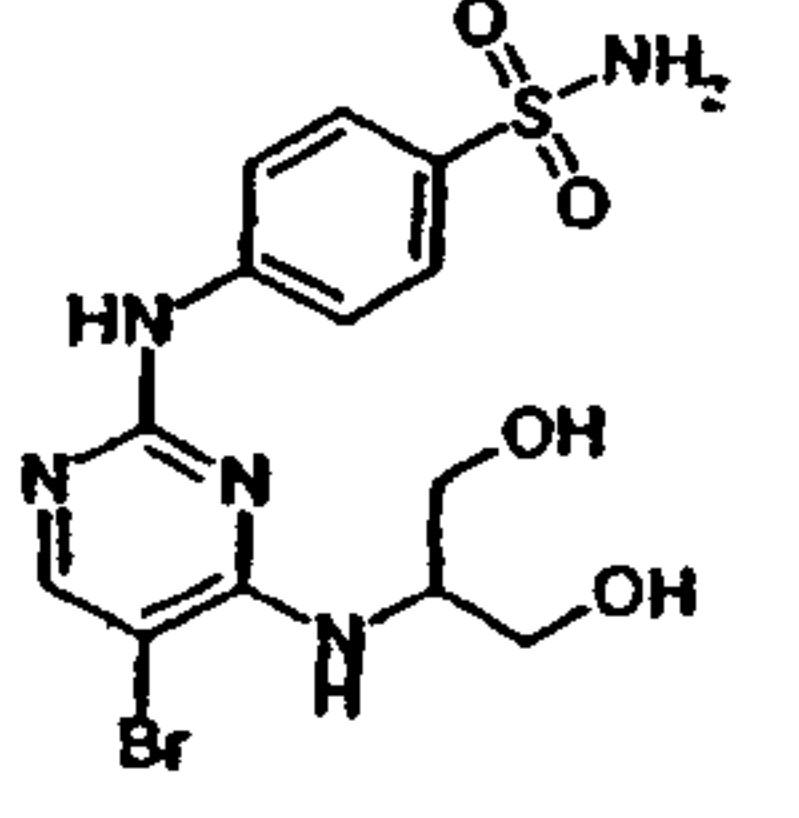
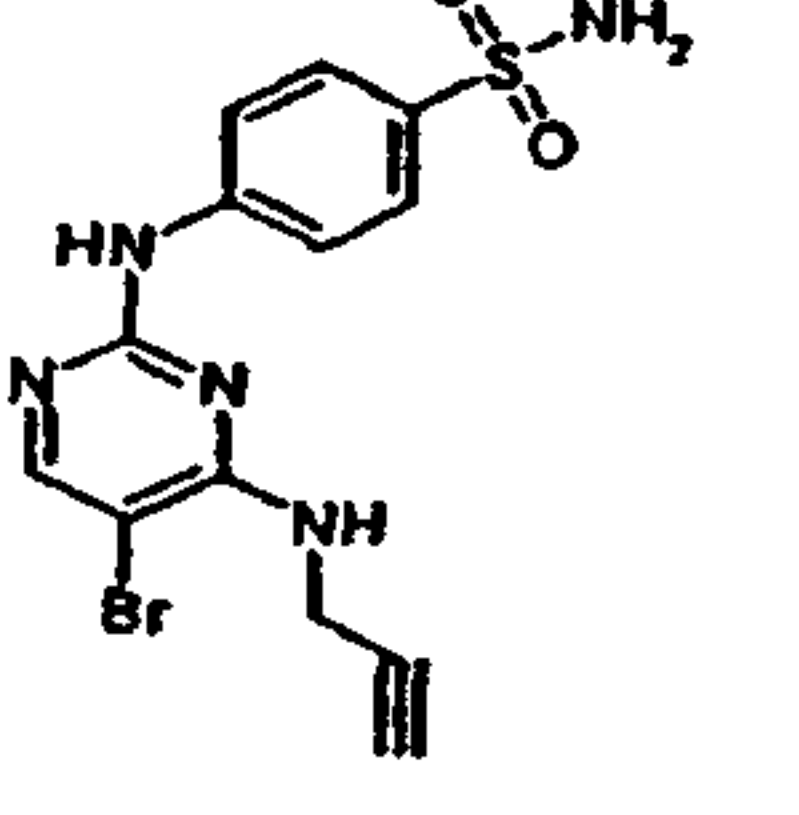
To prove the superiority of the compounds according to the invention compared to the known compounds, the compounds according to the invention were compared to known reference compounds and structurally-similar known compounds in the enzyme test. The result is cited in the following table:

[Key to the following tables:]

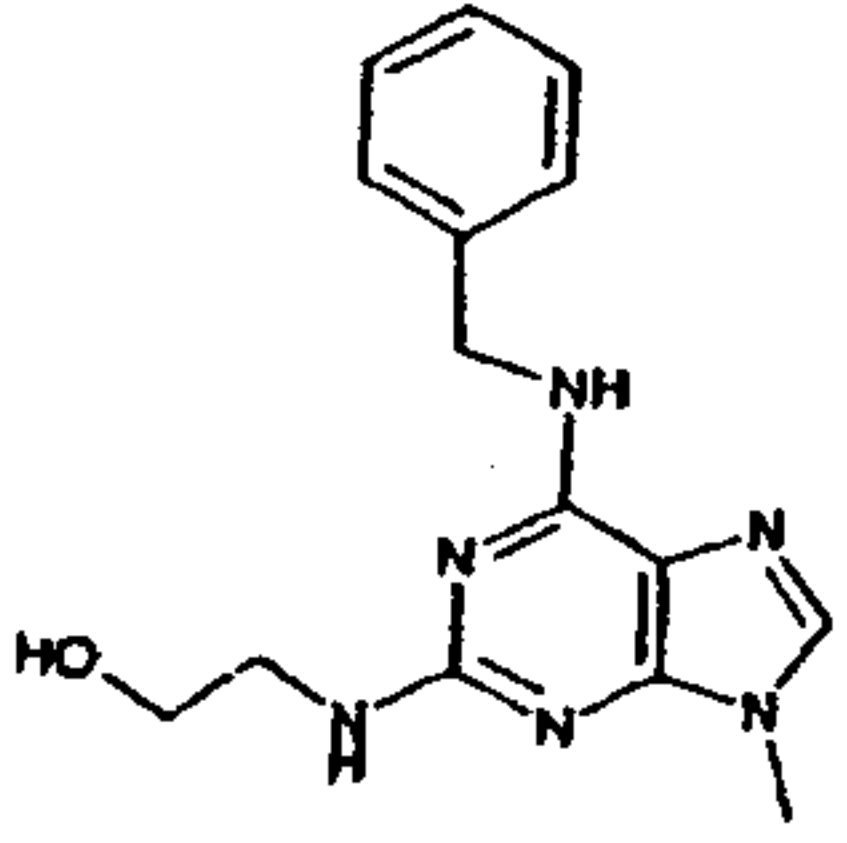
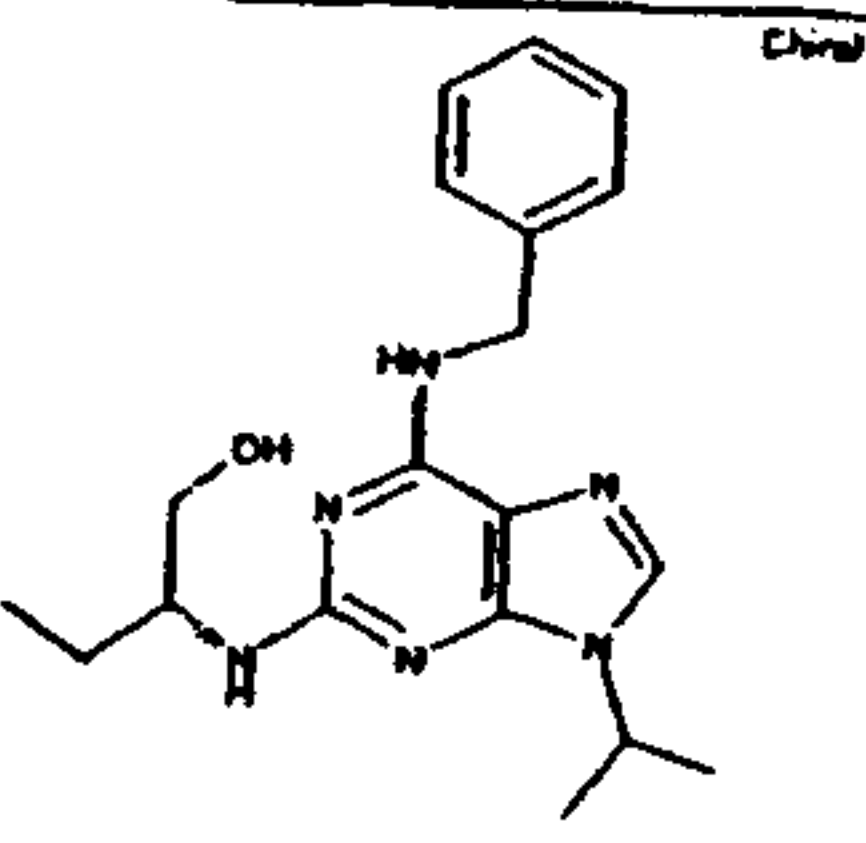
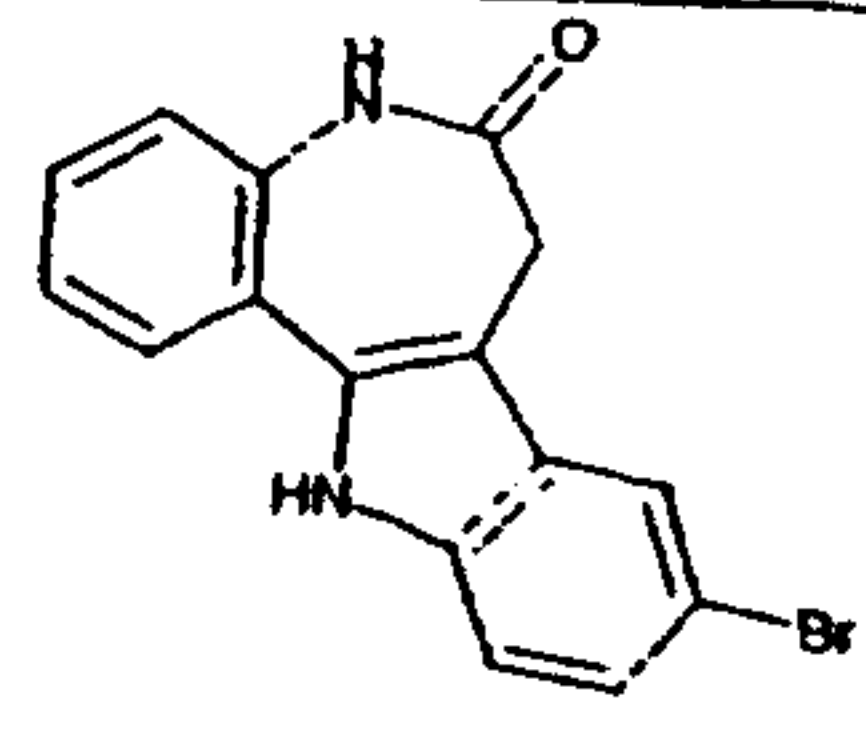
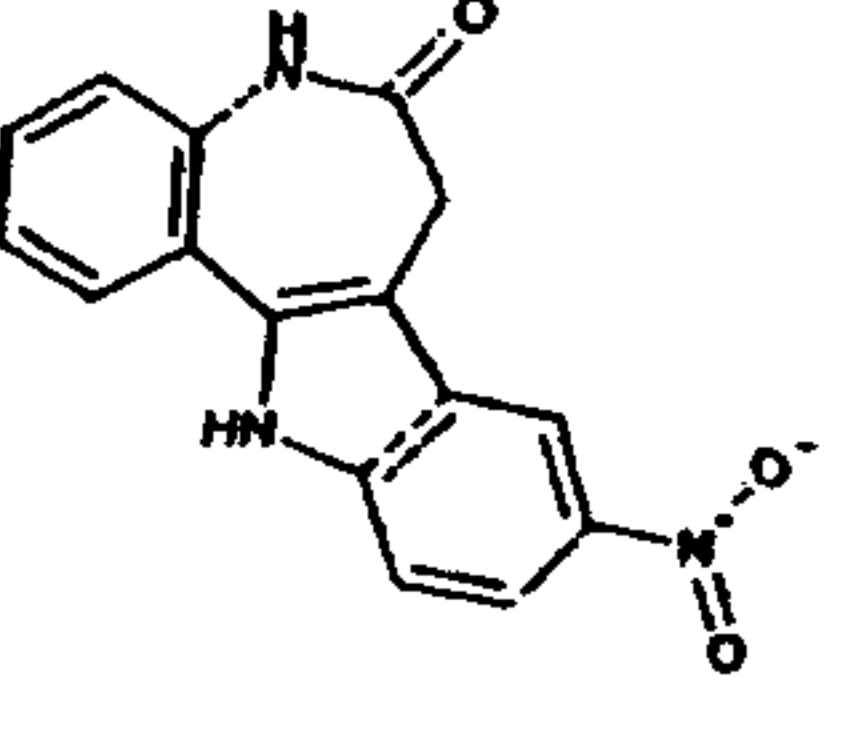
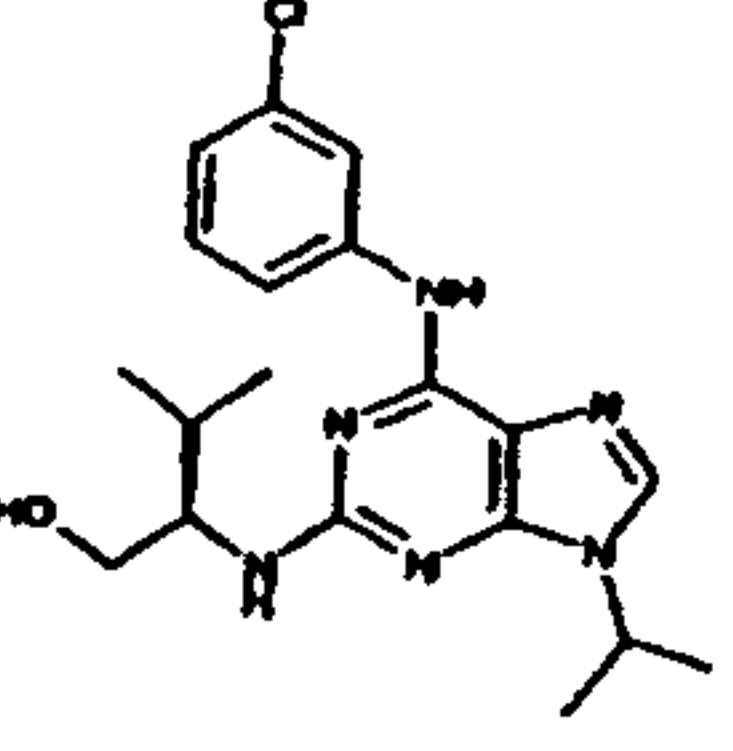
Beispiel-Nr. = Example No.

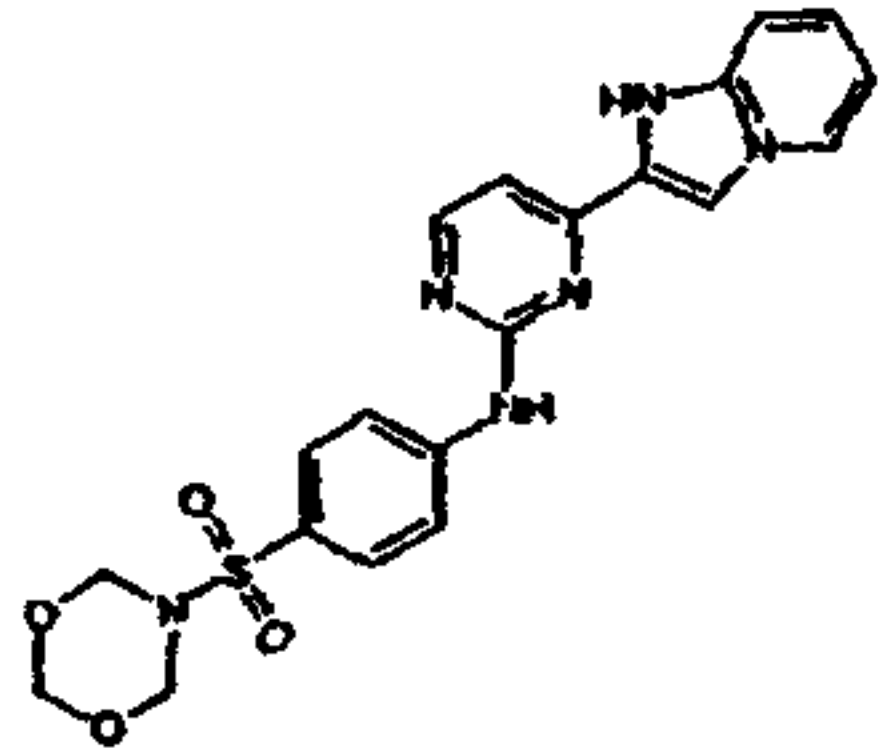
Löslichkeit (g/l) = Solubility (g/l)

Beispiel 11 aus WO01/14375 (Seite 38) = Example 11 from WO01/14375 (page 38)

Beispiel-Nr.	R ²	A	CDK2/ CycE IC ₅₀ [nM]	MCF-7 IC ₅₀ [μM]	Löslich- keit (g/l)
 Nr. 48	CH(C ₃ H ₇)- CH ₂ -OH-	-SO ₂ -N- (CH ₂) ₂ -OH	4	0.2	0,042
 Nr. 9	CH(CH ₂ OH) ₂	SO ₂ NH ₂	7	0,9	0,009
 Nr. 11	Propargyl- NH-	SO ₂ NH ₂	6	0,2	

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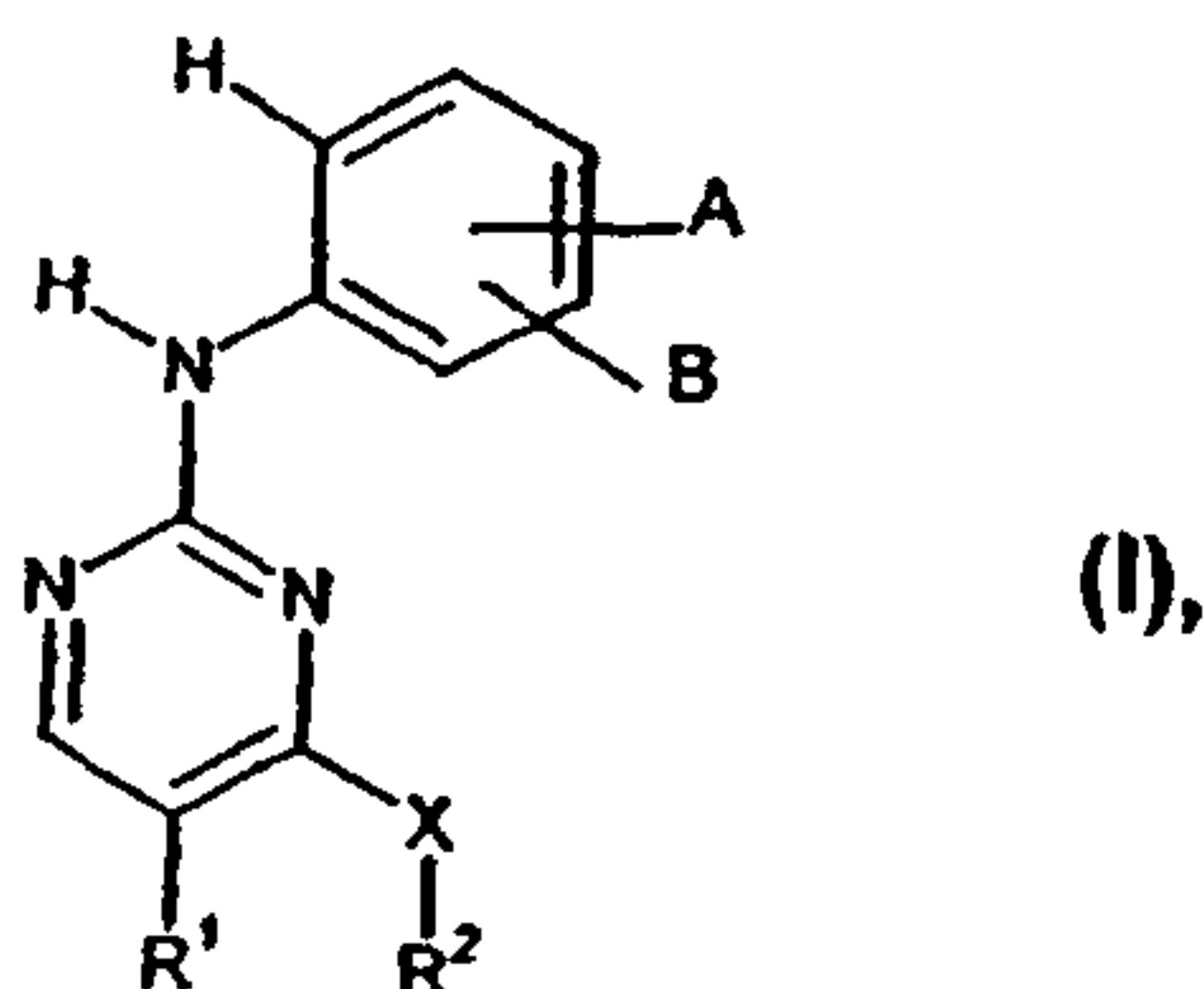
Beispiel-Nr.	R ²	A	CDK2/ CycE IC ₅₀ [nM]	MCF-7 IC ₅₀ [μM]	Löslich- keit (g/l)
 Olomoucine			7000	30	
 Roscovitine			1500	8	
 Kenpaullone			1800	6	
 Alsterpaullone			90	1.2	
 Purvalanol A			10	2	

Beispiel-Nr.	R ²	A	CDK2/ CycE IC ₅₀ [nM]	MCF-7 IC ₅₀ [μM]	Löslich- keit (g/l)
Beispiel 11 aus WO01/14375 (Seite 38) 			190		

It can be seen from the results of the table that both in the enzyme test and in the cell test, the compounds according to the invention have significantly higher activities in the enzyme and in the MCF-7 cells than the compounds that are known from the prior art. The compounds according to the invention are thus far superior to the known compounds.

Claims

1. Compounds of general formula I

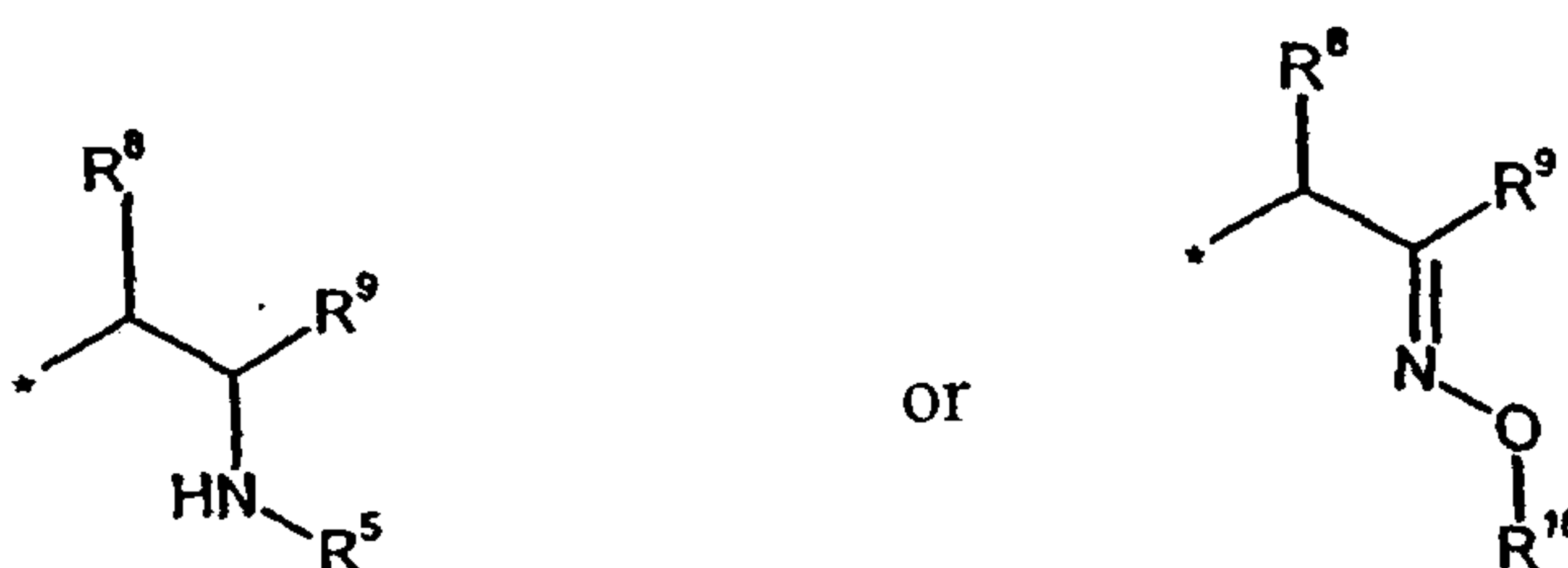


in which

- R^1 stands for hydrogen, halogen, C_1 - C_6 -alkyl, nitro, or for the group $-COR^5$, $-OCF_3$, $-(CH_2)_nR^5$, $-S-CF_3$ or $-SO_2CF_3$,
- R^2 stands for C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl, C_2 - C_{10} -alkinyl, or C_3 - C_{10} -cycloalkyl or for C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl, C_2 - C_{10} -alkinyl, or C_3 - C_{10} -cycloalkyl that is substituted in one or more places in the same way or differently with hydroxy, halogen, C_1 - C_6 -alkoxy, C_1 - C_6 -alkylthio, amino, cyano, C_1 - C_6 -alkyl, $-NH-(CH_2)_n-C_3$ - C_{10} -cycloalkyl, C_3 - C_{10} -cycloalkyl, C_1 - C_6 -hydroxyalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkinyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, $-NHC_1$ - C_6 -alkyl, $-N(C_1$ - C_6 -alkyl) $_2$, $-SO(C_1$ - C_6 -alkyl), $-SO_2(C_1$ - C_6 -alkyl), C_1 - C_6 -alkanoyl, $-CONR^3R^4$, $-COR^5$, C_1 - C_6 -alkylOAc, carboxy, aryl, heteroaryl, $-(CH_2)_n$ -aryl, $-(CH_2)_n$ -heteroaryl,

phenyl-(CH₂)_n-R⁵, -(CH₂)_nPO₃(R⁵)₂ or with the group -R⁶ or -NR³R⁴, and the phenyl, C₃-C₁₀-cycloalkyl, aryl, heteroaryl, -(CH₂)_n-aryl and -(CH₂)_n-heteroaryl itself optionally can be substituted in one or more places in the same way or differently with halogen, hydroxy, C₁-C₆-alkyl, C₁-C₆-alkoxy, heteroaryl, benzoxy or with the group -CF₃ or -OCF₃, and the ring of the C₃-C₁₀-cycloalkyl and the C₁-C₁₀-alkyl optionally can be interrupted by one or more nitrogen, oxygen and/or sulfur atoms and/or can be interrupted by one or more =C=O groups in the ring and/or optionally one or more possible double bonds can be contained in the ring, or

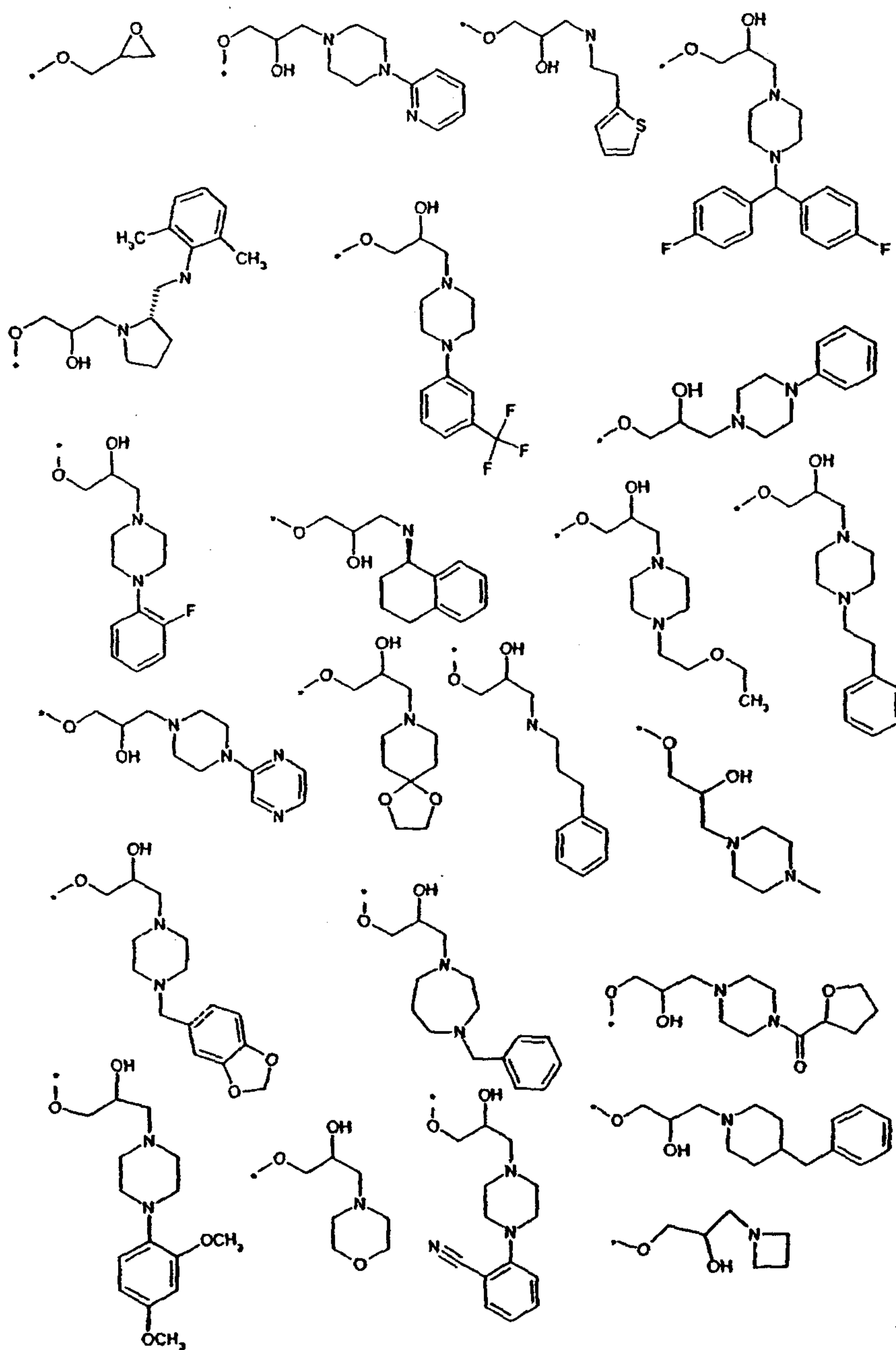
R² stands for the group



X stands for oxygen or for the group -NH-, -N(C₁-C₃-alkyl) or for -OC₃-C₁₀-cycloalkyl, which can be substituted in one or more places in the same way or differently with a heteroaromatic compound, or

X and R² together form a C₃-C₁₀-cycloalkyl ring, which optionally can contain one or more heteroatoms and optionally can be substituted in one or more places with hydroxy, C₁-C₆-alkyl, C₁-C₆-alkoxy or halogen,

A and B, in each case independently of one another, stand for hydrogen, hydroxy, C₁-C₃-alkyl, C₁-C₆-alkoxy or for the group -SR⁷, -S(O)R⁷, -SO₂R⁷, -NHSO₂R⁷, -CH(OH)R⁷, -CR⁷(OH)-R⁷, C₁-C₆-alkylP(O)OR³OR⁴ or -COR⁷, or for



or

A and B together form a C₃-C₁₀-cycloalkyl ring that optionally can be interrupted by one or more nitrogen, oxygen and/or sulfur atoms and/or can be interrupted by one or more =C=O or =SO₂ groups in the ring and/or optionally one or more possible double bonds can be contained in the ring, and the C₃-C₁₀-cycloalkyl ring optionally can be substituted in one or more places in the same way or differently with hydroxy, halogen, C₁-C₆-alkoxy, C₁-C₆-alkylthio, amino, cyano, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₃-C₁₀-cycloalkyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, -NHC₁-C₆-alkyl, -N(C₁-C₆-alkyl)₂, -SO(C₁-C₆-alkyl), -SO₂R⁷, C₁-C₆-alkanoyl, -CONR³R⁴, -COR⁵, C₁-C₆-alkoxyOAc, phenyl or with the group R⁶, whereby the phenyl itself optionally can be substituted in one or more places in the same way or differently with halogen, hydroxy, C₁-C₆-alkyl, C₁-C₆-alkoxy or with the group -CF₃ or -OCF₃, R³ and R⁴, in each case independently of one another, stand for hydrogen, phenyl, benzyloxy, C₁-C₁₂-alkyl, C₁-C₆-alkoxy, C₂-C₄-alkenyloxy, C₃-C₆-cycloalkyl, hydroxy, hydroxy-C₁-C₆-alkyl, dihydroxy-C₁-C₆-alkyl, heteroaryl, heterocyclo-C₃-C₁₀-alkyl, heteroaryl-C₁-C₃-alkyl, C₃-C₆-cycloalkyl-C₁-C₃-alkyl that is optionally substituted with cyano, or for C₁-C₆-alkyl that is optionally substituted in one or more places in the same way or differently with phenyl, pyridyl, phenyloxy, C₃-C₆-cycloalkyl, C₁-C₆-alkyl or C₁-C₆-alkoxy,

whereby the phenyl itself can be substituted in one or more places in the same way or differently with halogen, C₁-C₆-alkyl, C₁-C₆-alkoxy or with the group -SO₂NR³R⁴,

or for the group -(CH₂)_nNR³R⁴, -CNHNH₂ or -NR³R⁴,

or

- R³ and R⁴ together form a C₃-C₁₀-cycloalkyl ring that optionally can be interrupted by one or more nitrogen, oxygen and/or sulfur atoms and/or can be interrupted by one or more =C=O groups in the ring and/or optionally one or more possible double bonds can be contained in the ring,
- R⁵ stands for hydroxy, phenyl, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, benzoxy, C₁-C₆-alkylthio or C₁-C₆-alkoxy,
- R⁶ stands for a heteroaryl or C₃-C₁₀-cycloalkyl ring, whereby the ring has the above-indicated meaning,
- R⁷ stands for halogen, hydroxy, phenyl, C₁-C₆-alkyl, C₂-C₆-alkenyl, C₂-C₆-alkinyl, C₃-C₁₀-cycloalkyl, with the above-indicated meaning, or for the group -NR³R⁴, or for a C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl, C₂-C₁₀-alkinyl or C₃-C₇-cycloalkyl that is substituted in one or more places in the same way or differently with hydroxy, C₁-C₆-alkoxy, halogen, phenyl, -NR³R⁴ or phenyl, which itself can be substituted in one or more places in the same way or differently with halogen, hydroxy, C₁-C₆-alkyl, C₁-C₆-alkoxy, halo-C₁-C₆-alkyl, halo-C₁-C₆-alkoxy, or R⁷ stands for phenyl, which itself can be substituted in one or more places in the same way or differently

with halogen, hydroxy, C₁-C₆-alkyl or C₁-C₆-alkoxy, halo-C₁-C₆-alkyl, or halo-C₁-C₆-alkoxy,

R⁸, R⁹ and

R¹⁰, in each case independently of one another, stand for hydrogen, hydroxy, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl, C₂-C₁₀-alkinyl, C₃-C₁₀-cycloalkyl, aryl, heteroaryl or for C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl, C₂-C₁₀-alkinyl or C₃-C₁₀-cycloalkyl that is optionally substituted in one or more places in the same way or differently with hydroxy, halogen, C₁-C₆-alkoxy, C₁-C₆-alkylthio, amino, cyano, C₁-C₆-alkyl, -NH-(CH₂)_n-C₃-C₁₀-cycloalkyl, C₃-C₁₀-cycloalkyl, C₁-C₆-hydroxyalkyl, C₂-C₆-alkenyl, C₂-C₆-alkinyl, C₁-C₆-alkoxy-C₁-C₆-alkyl, C₁-C₆-alkoxy-C₁-C₆-alkoxy-C₁-C₆-alkyl, -NHC₁-C₆-alkyl, -N(C₁-C₆-alkyl)₂, -SO(C₁-C₆-alkyl), -SO₂(C₁-C₆-alkyl), C₁-C₆-alkanoyl, -CONR³R⁴, -COR⁵, C₁-C₆-alkylOAc, carboxy, aryl, heteroaryl, -(CH₂)_n-aryl, -(CH₂)_n-heteroaryl, phenyl-(CH₂)_n-R⁵, -(CH₂)_nPO₃(R⁵)₂ or with the group -R⁶ or -NR³R⁴, and the phenyl, C₃-C₁₀-cycloalkyl, aryl, heteroaryl, -(CH₂)_n-aryl and -(CH₂)_n-heteroaryl itself optionally can be substituted in one or more places in the same way or differently with halogen, hydroxy, C₁-C₆-alkyl, C₁-C₆-alkoxy or with the group -CF₃ or -OCF₃, and the ring of C₃-C₁₀-cycloalkyl and the C₁-C₁₀-alkyl optionally can be interrupted by one or more nitrogen, oxygen and/or sulfur atoms and/or can be interrupted by one or more =C=O groups in the ring and/or optionally one or more possible double bonds can be contained in the ring, and

n stands for 0-6,

as well as isomers, diastereomers, enantiomers and salts thereof.

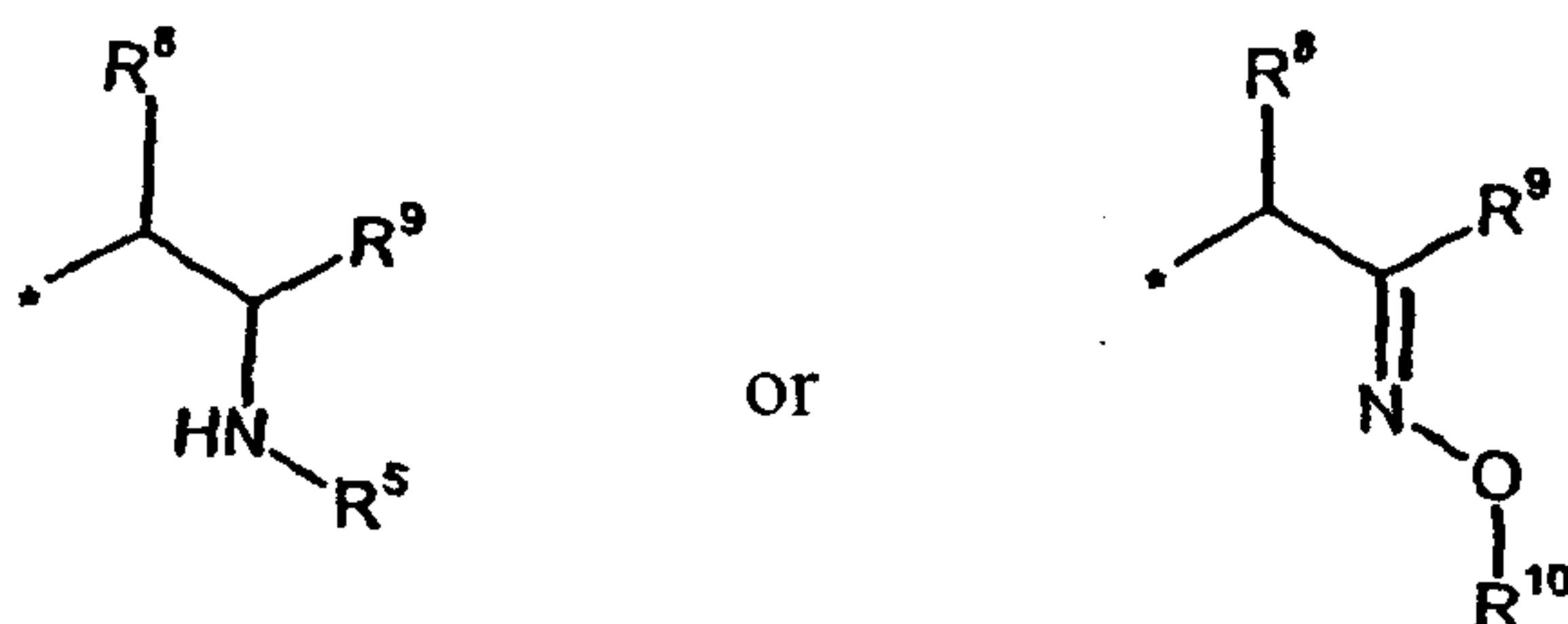
2. Compounds of general formula I, according to claim 1, in which

R^1 stands for hydrogen, halogen, C_1 - C_6 -alkyl, nitro, or for the group $-COR^5$, $-OCF_3$, $-(CH_2)_nR^5$, $-S-CF_3$ or $-SO_2CF_3$,

R^2 stands for C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl, C_2 - C_{10} -alkinyl, or C_3 - C_{10} -cycloalkyl or for C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl, C_2 - C_{10} -alkinyl, or C_3 - C_{10} -cycloalkyl that is substituted in one or more places in the same way or differently with hydroxy, halogen, C_1 - C_6 -alkoxy, C_1 - C_6 -alkylthio, amino, cyano, C_1 - C_6 -alkyl, $-NH-(CH_2)_n-C_3$ - C_{10} -cycloalkyl, C_3 - C_{10} -cycloalkyl, C_1 - C_6 -hydroxyalkyl, C_2 - C_6 -alkenyl, C_2 - C_6 -alkinyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy- C_1 - C_6 -alkoxy- C_1 - C_6 -alkyl, $-NHC_1$ - C_6 -alkyl, $-N(C_1$ - C_6 -alkyl) $_2$, $-SO(C_1$ - C_6 -alkyl), $-SO_2(C_1$ - C_6 -alkyl), C_1 - C_6 -alkanoyl, $-CONR^3R^4$, $-COR^5$, C_1 - C_6 -alkylOAc, carboxy, aryl, heteroaryl, $-(CH_2)_n$ -aryl, $-(CH_2)_n$ -heteroaryl, phenyl- $(CH_2)_n-R^5$, $-(CH_2)_nPO_3(R^5)_2$ or with the group $-R^6$ or $-NR^3R^4$, and the phenyl, C_3 - C_{10} -cycloalkyl, aryl, heteroaryl, $-(CH_2)_n$ -aryl and $-(CH_2)_n$ -heteroaryl itself optionally can be substituted in one or more places in the same way or differently with halogen, hydroxy, C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy, heteroaryl, benzyloxy or with the group $-CF_3$ or $-OCF_3$, and the ring of the C_3 - C_{10} -cycloalkyl and the C_1 - C_{10} -alkyl optionally can be interrupted by one or more nitrogen, oxygen and/or sulfur atoms and/or can be

interrupted by one or more $=C=O$ groups in the ring and/or optionally one or more possible double bonds can be contained in the ring, or

R^2 stands for the group



X stands for oxygen or for the group $-NH-$, $-N(C_1-C_3\text{-alkyl})$ or for $-OC_3-C_{10}\text{-cycloalkyl}$, which can be substituted in one or more places in the same way or differently with a heteroaromatic compound,
or

X and R^2 together form a $C_3-C_{10}\text{-cycloalkyl}$ ring, which optionally can contain one or more heteroatoms and optionally can be substituted in one or more places with hydroxy, $C_1-C_6\text{-alkyl}$, $C_1-C_6\text{-alkoxy}$ or halogen,

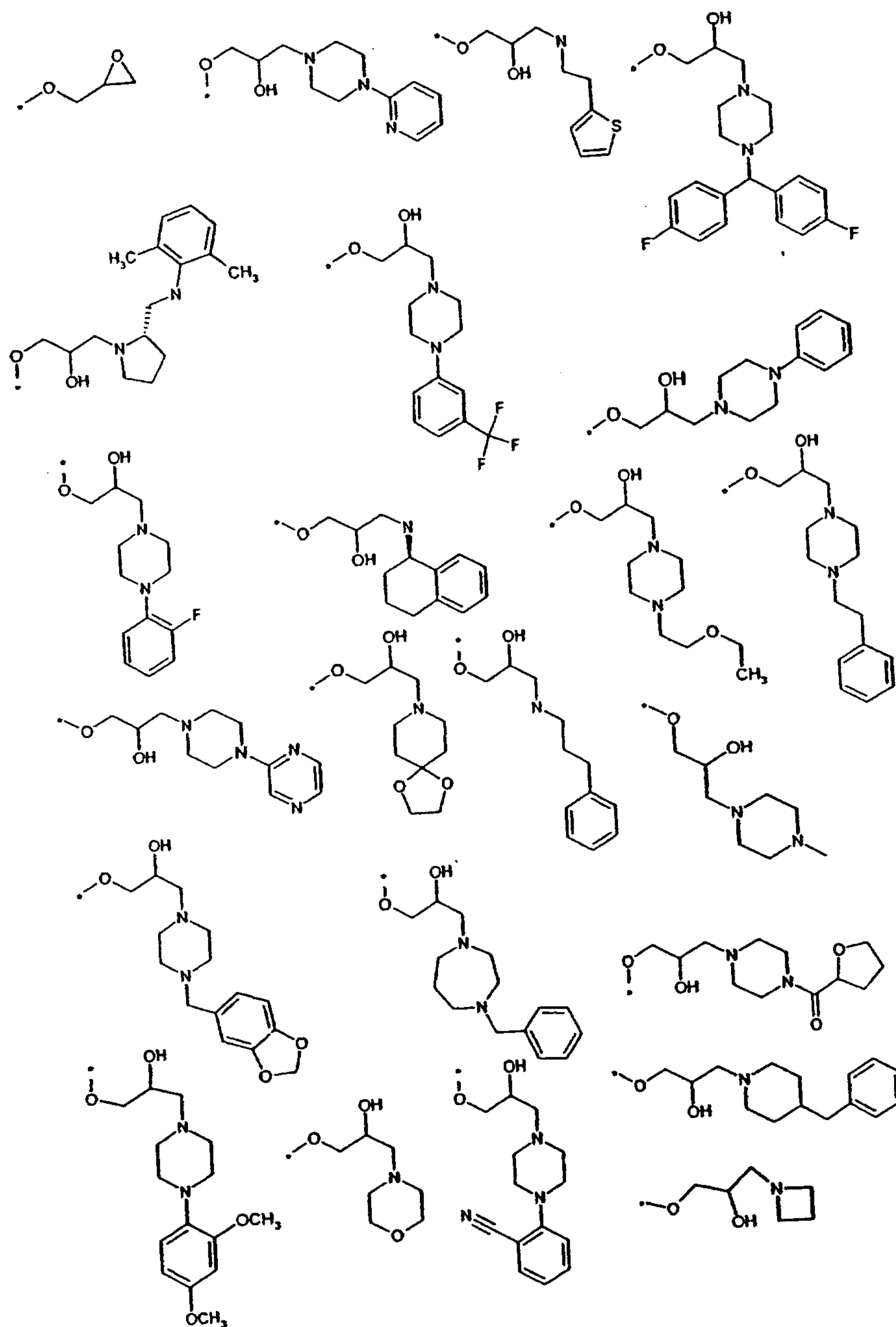
A and B , in each case independently of one another, stand for hydrogen,

hydroxy, $C_1-C_3\text{-alkyl}$, $C_1-C_6\text{-alkoxy}$ or for the group $-S-CH_3$,

$-SO_2-C_2H_4-OH$, $-CO-CH_3$, $-S-CHF_2$, $-S-(CH_2)_nCH(OH)CH_2N-R^3R^4$,

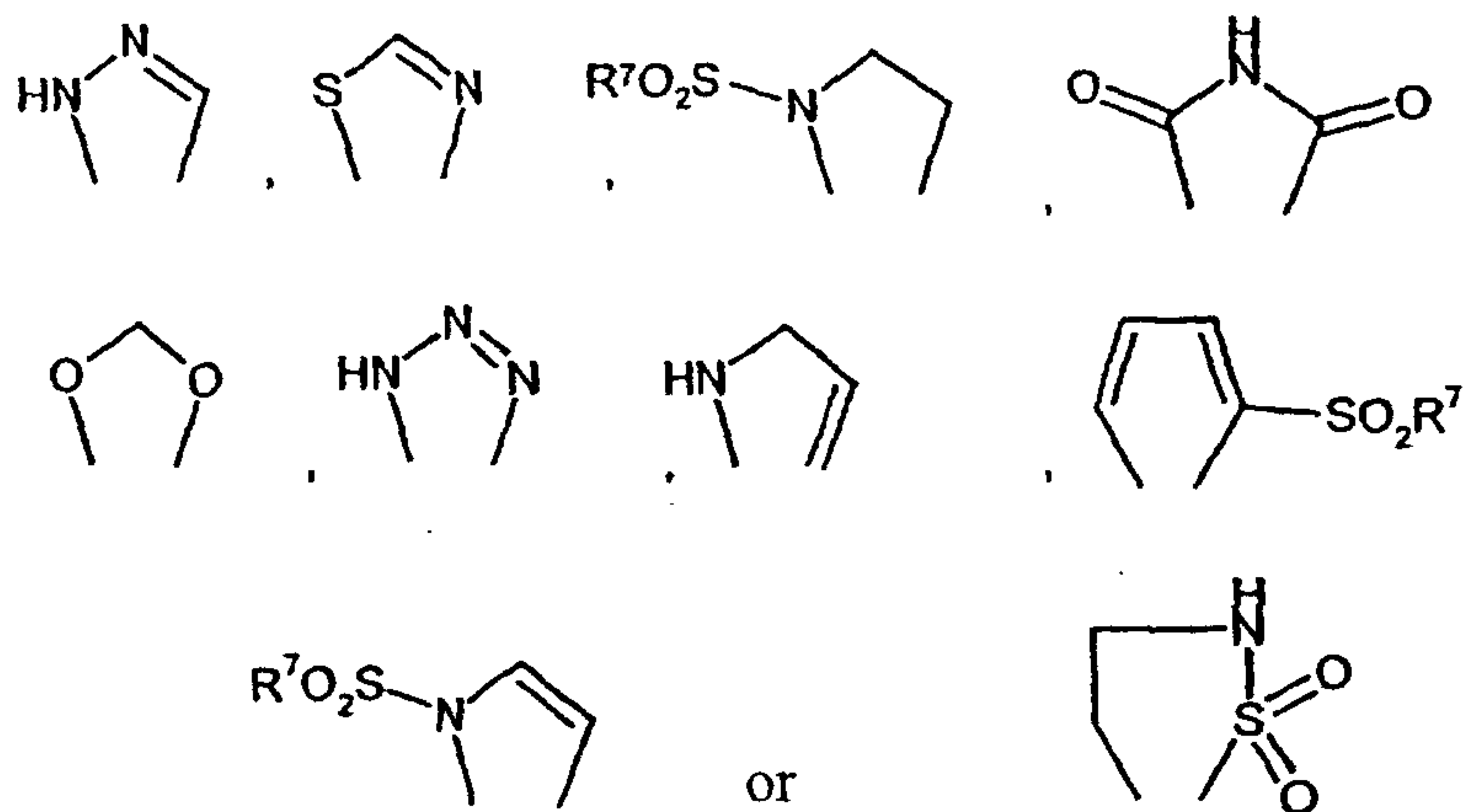
$-CH_2P(O)OR^3OR^4$, $-S-CF_3$, $-SO-CH_3$, $-SO_2CF_3$, $-SO_2-(CH_2)_n-N-R^3R^4$,

$-SO_2-NR^3R^4$, $-SO_2R^7$, $-CH(OH)-CH_3$ or for

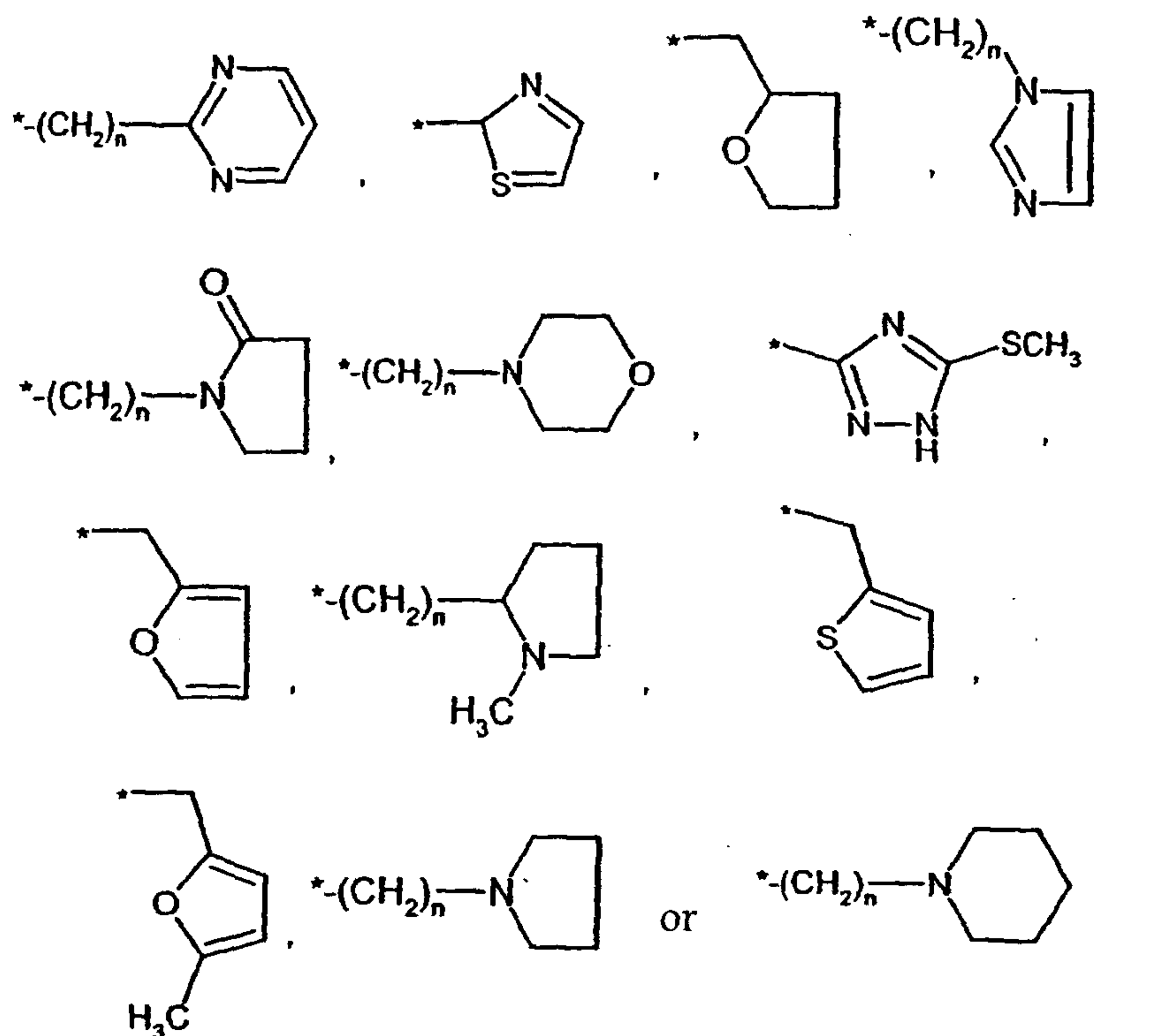


or

A and B together can form a group



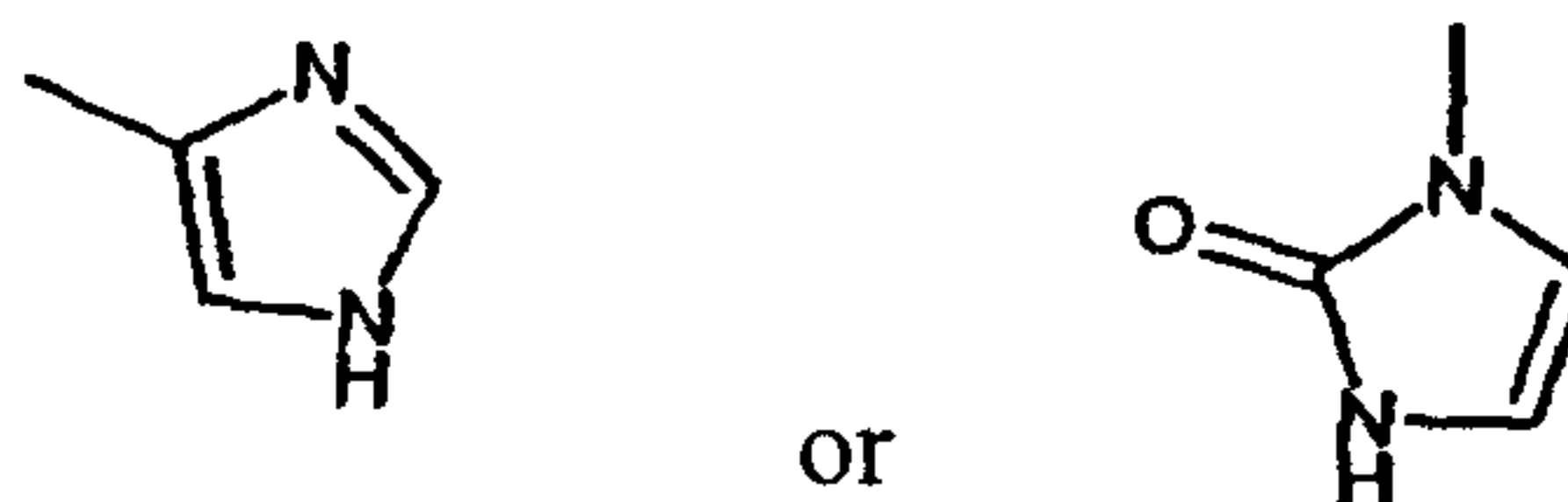
R^3 and R^4 , in each case independently of one another, stand for hydrogen, phenyl, benzyloxy, C_1 - C_{12} -alkyl, C_1 - C_6 -alkoxy, C_2 - C_4 -alkenyloxy, C_3 - C_6 -cycloalkyl, hydroxy, hydroxy- C_1 - C_6 -alkyl, dihydroxy- C_1 - C_6 -alkyl, heteroaryl, heterocyclo- C_3 - C_{10} -alkyl, heteroaryl- C_1 - C_3 -alkyl, C_3 - C_6 -cycloalkyl- C_1 - C_3 -alkyl optionally substituted with cyano, or for C_1 - C_6 -alkyl that is optionally substituted in one or more places in the same way or differently with phenyl, pyridyl, phenyloxy, C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkyl or C_1 - C_6 -alkoxy, whereby the phenyl itself can be substituted in one or more places in the same way or differently with halogen, trifluoromethyl, C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy or with the group $-SO_2NR^3R^4$, or for the group $-(CH_2)_nNR^3R^4$, $-CNHNH_2$ or $-NR^3R^4$ or for



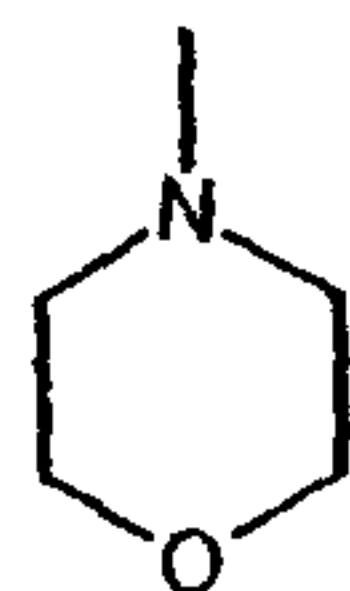
which optionally can be substituted with C₁-C₆-alkyl,

R⁵ stands for hydroxy, phenyl, C₁-C₆-alkyl, C₃-C₆-cycloalkyl, benzoxy, C₁-C₆-alkylthio or C₁-C₆-alkoxy,

R⁶ stands for the group



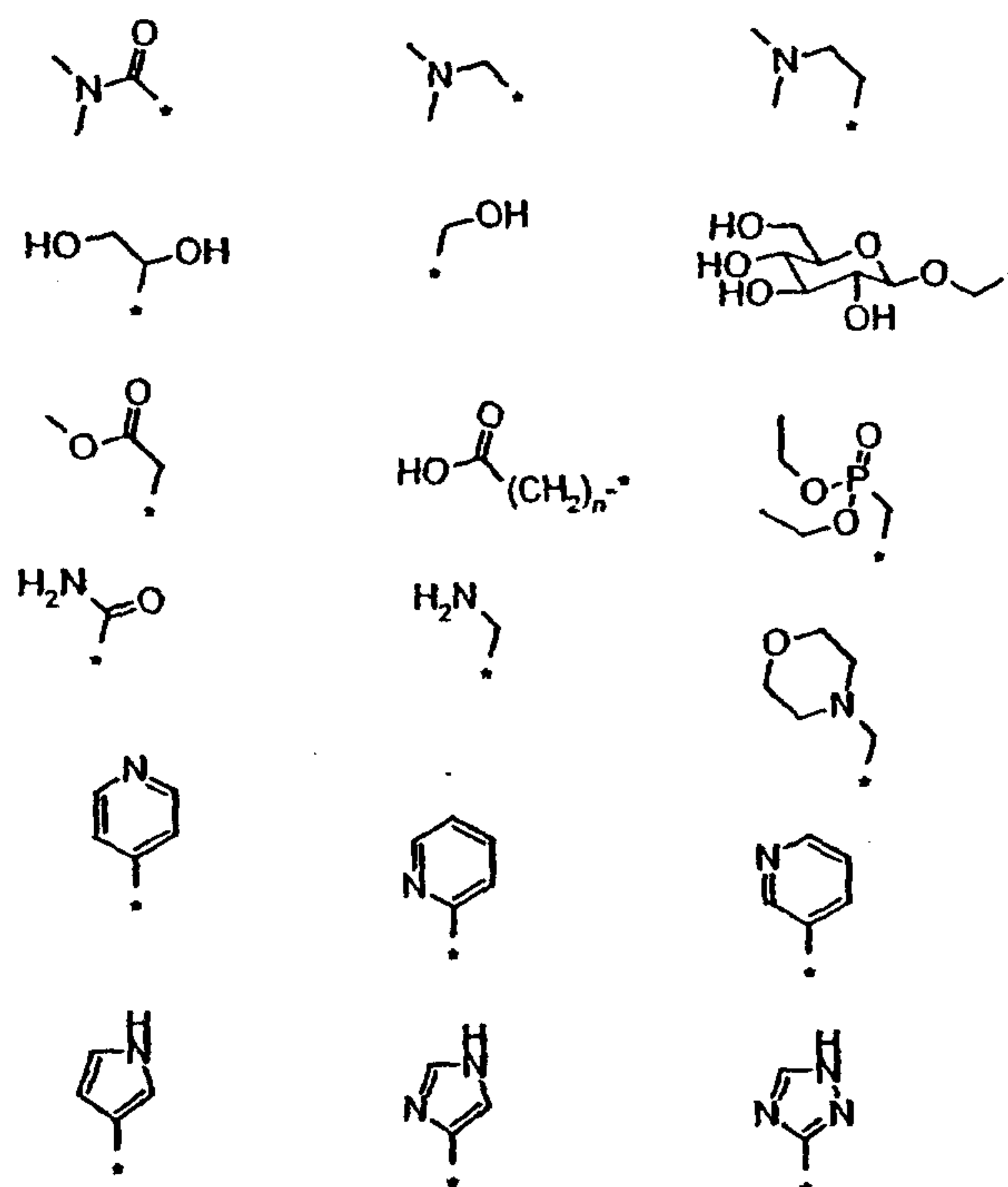
R^7 stands for halogen, hydroxy, phenyl, C_1 - C_6 -alkyl, $-C_2H_4OH$, $-NR^3R^4$, or the group



R^8 , R^9 and

R^{10} , in each case independently of one another, stand for hydrogen, hydroxy,

C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl or for the group



and

n stands for 0-6,

as well as isomers, enantiomers, diastereomers, and salts thereof.

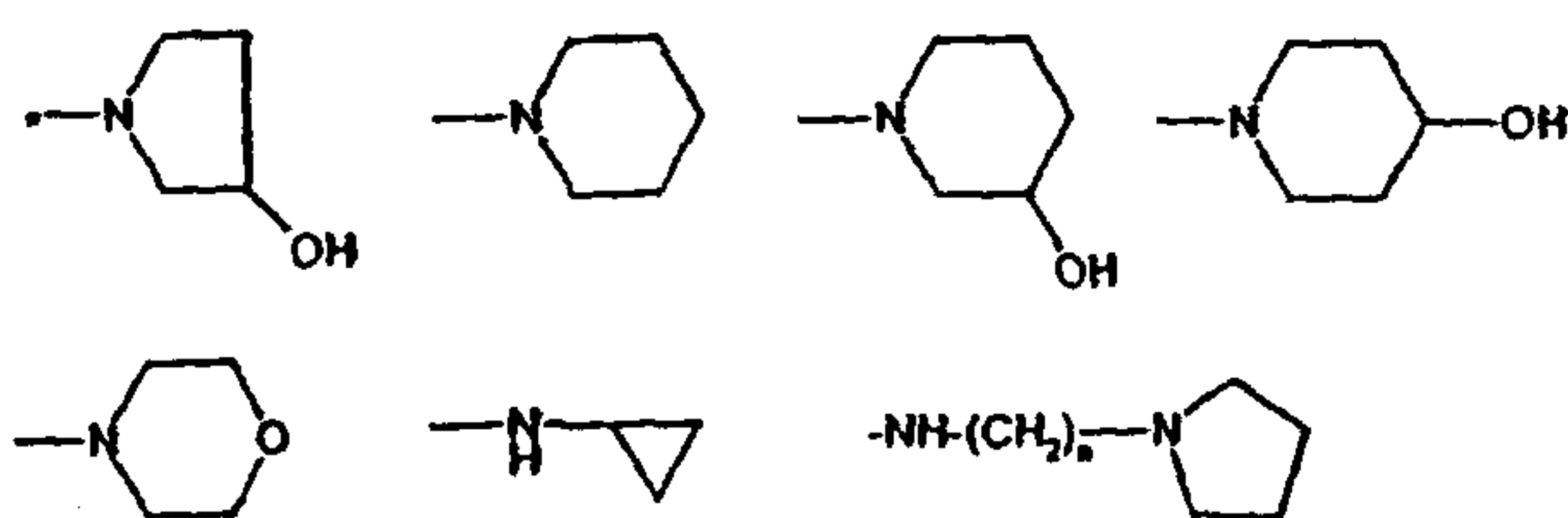
3. Compounds of general formula I, according to claims 1 and 2, in which

R^1 stands for hydrogen, halogen, C_1 - C_3 -alkyl, or for the group

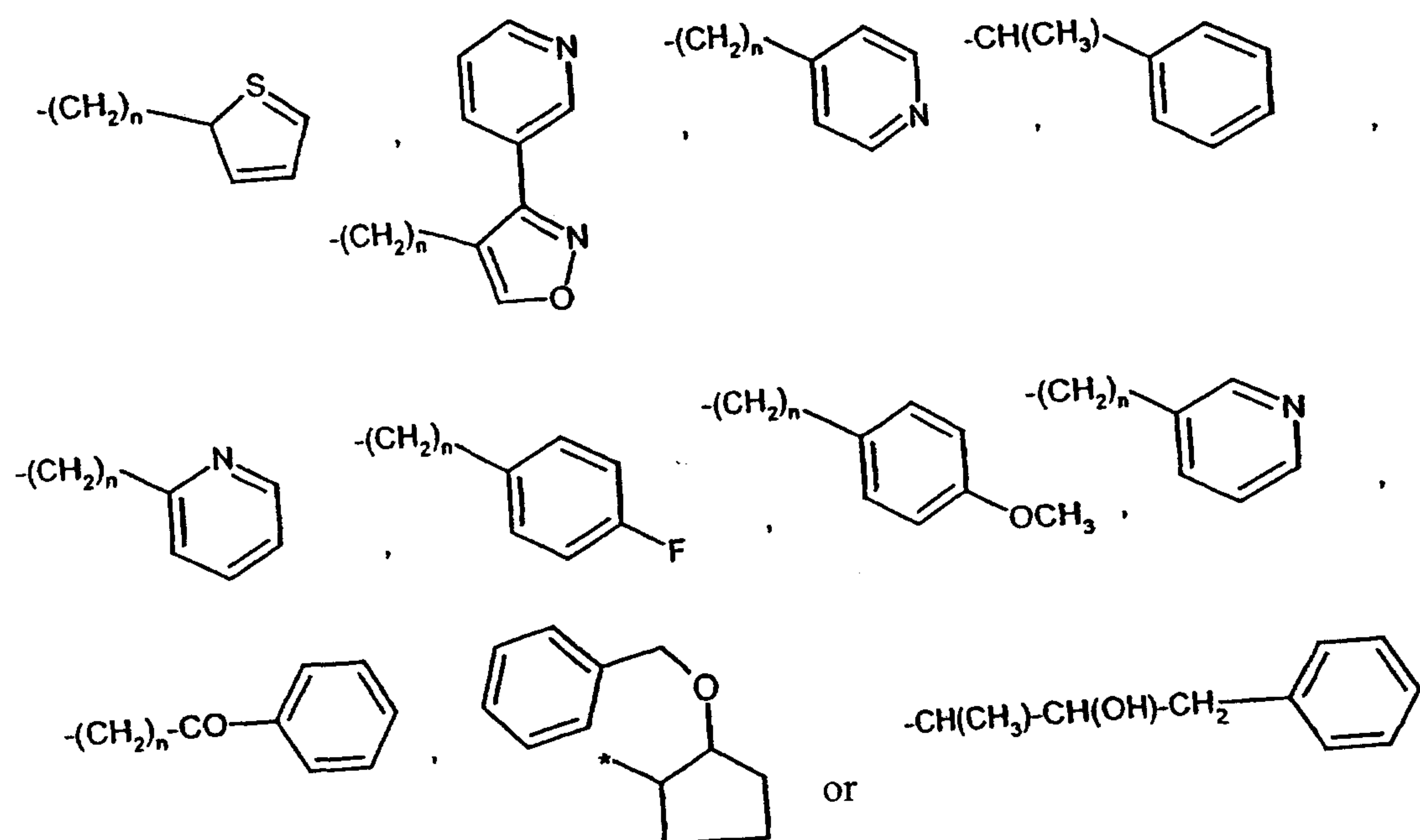
$-(CH_2)_nR^5$,

R^2 stands for $-\text{CH}(\text{CH}_3)-(\text{CH}_2)_n-R^5$, $-\text{CH}-(\text{CH}_2\text{OH})_2$, $-(\text{CH}_2)_nR^7$, $-\text{CH}(\text{C}_3\text{H}_7)-(\text{CH}_2)_n-R^5$, $-\text{CH}(\text{C}_2\text{H}_5)-(\text{CH}_2)_n-R^5$, $-\text{CH}_2-\text{CN}$, $-\text{CH}(\text{CH}_3)\text{COCH}_3$, $-\text{CH}(\text{CH}_3)-\text{C}(\text{OH})(\text{CH}_3)_2$, $-\text{CH}(\text{CH}(\text{OH})\text{CH}_3)\text{OCH}_3$, $-\text{CH}(\text{C}_2\text{H}_5)\text{CO}-R^5$, C_2 - C_4 -alkynyl, $-(\text{CH}_2)_n-\text{COR}^5$, $-(\text{CH}_2)_n-\text{CO}-C_1$ - C_6 -alkyl, $-(\text{CH}_2)_n-\text{C}(\text{OH})(\text{CH}_3)$ -phenyl, $-\text{CH}(\text{CH}_3)-\text{C}(\text{CH}_3)-R^5$, $-\text{CH}(\text{CH}_3)-\text{C}(\text{CH}_3)(\text{C}_2\text{H}_5)-R^5$, $-\text{CH}(\text{OCH}_3)-\text{CH}_2-R^5$, $-\text{CH}_2-\text{CH}(\text{OH})-R^5$, $-\text{CH}(\text{OCH}_3)-\text{CHR}^5-\text{CH}_3$, $-\text{CH}(\text{CH}_3)-\text{CH}(\text{OH})-\text{CH}_2-\text{CH}=\text{CH}_2$, $-\text{CH}(\text{C}_2\text{H}_5)-\text{CH}(\text{OH})-(\text{CH}_2)_n-\text{CH}_3$, $-\text{CH}(\text{CH}_3)-\text{CH}(\text{OH})-(\text{CH}_2)_n-\text{CH}_3$, $-\text{CH}(\text{CH}_3)-\text{CH}(\text{OH})-\text{CH}(\text{CH}_3)_2$, $(\text{CH}_2\text{OAC})_2$, $-(\text{CH}_2)_n-R^6$, $-(\text{CH}_2)_n-(\text{CF}_2)_n-\text{CF}_3$, $-\text{CH}(\text{CH}_2)_n-R^5)_2$, $-\text{CH}(\text{CH}_3)-\text{CO}-\text{NH}_2$, $-\text{CH}(\text{CH}_2\text{OH})$ -phenyl, $-\text{CH}(\text{CH}_2\text{OH})-\text{CH}(\text{OH})-(\text{CH}_2)_nR^5$, $-\text{CH}(\text{CH}_2\text{OH})-\text{CH}(\text{OH})$ -phenyl, $-\text{CH}(\text{CH}_2\text{OH})-\text{C}_2\text{H}_4-R^5$, $-(\text{CH}_2)_n-\text{C}\equiv\text{C}-\text{C}(\text{CH}_3)=\text{CH}-\text{COR}^5$, $-\text{CH}(\text{Ph})-(\text{CH}_2)_n-R^5$, $-(\text{CH}_2)_n-\text{COR}^5$, $-(\text{CH}_2)_n\text{PO}_3(\text{R}^5)_2$, $-(\text{CH}_2)_n-\text{COR}^5$, $-\text{CH}((\text{CH}_2)_n\text{OR}^5)\text{CO}-R^5$, $-(\text{CH}_2)_n\text{CONHCH}((\text{CH}_2)_nR^5)_2$, $-(\text{CH}_2)_n\text{NH}-\text{COR}^5$, $-\text{CH}(\text{CH}_2)_nR^5-(\text{CH}_2)_nC_3$ - C_{10} -cycloalkyl, $-(\text{CH}_2)_nC_3$ - C_{10} -cycloalkyl, C_3 - C_{10} -cycloalkyl; C_1 - C_6 -alkyl, C_3 - C_{10} -cycloalkyl,

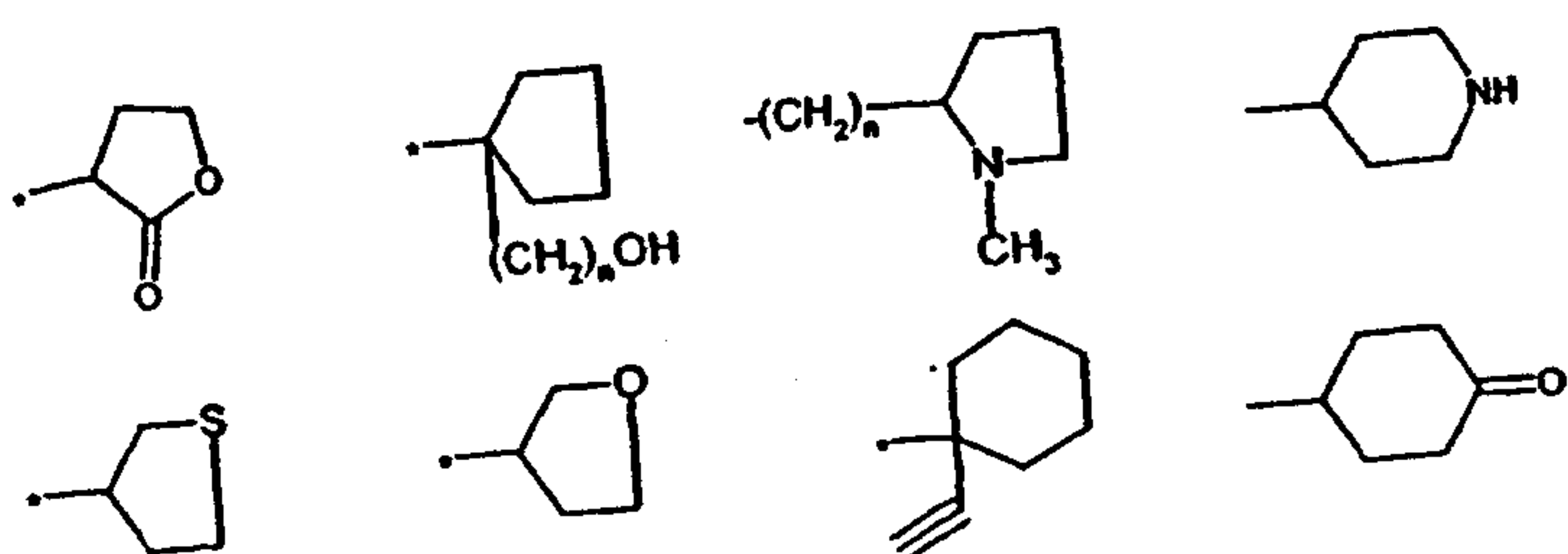
$-(\text{CH}_2)_n\text{-O-}(\text{CH}_2)_n\text{-R}^5$, $-(\text{CH}_2)_n\text{-NR}^3\text{R}^4$ that is optionally substituted in one or more places in the same way or differently with hydroxy, $\text{C}_1\text{-C}_6\text{-alkyl}$ or the group $-\text{COONH}(\text{CH}_2)_n\text{CH}_3$ or $-\text{NR}^3\text{R}^4$,
 $-\text{CH}(\text{C}_3\text{H}_7)\text{-(CH}_2)_n\text{-OC(O)-}(\text{CH}_2)_n\text{-CH}_3$, $-(\text{CH}_2)_n\text{-R}^5$,
 $-\text{C}(\text{CH}_3)_2\text{-(CH}_2)_n\text{-R}^5$, $-\text{C}(\text{CH}_2)_n(\text{CH}_3)\text{-(CH}_2)_n\text{R}^5$,
 $-\text{C}(\text{CH}_2)_n\text{-(CH}_2)_n\text{R}^5$, $-\text{CH}(\text{t-butyl})\text{-(CH}_2)_n\text{-R}^5$,
 $-\text{CCH}_3(\text{C}_3\text{H}_7)\text{-(CH}_2)_n\text{R}^5$, $-\text{CH}(\text{C}_3\text{H}_7)\text{-(CH}_2)_n\text{-R}^5$,
 $-\text{CH}(\text{C}_3\text{H}_7)\text{-COR}^5$, $-\text{CH}(\text{C}_3\text{H}_7)\text{-(CH}_2)_n\text{-OC(O)-NH-Ph}$,
 $-\text{CH}((\text{CH}_2)_n(\text{C}_3\text{H}_7))\text{-(CH}_2)_n\text{R}^5$,
 $-\text{CH}(\text{C}_3\text{H}_7)\text{-(CH}_2)_n\text{-OC(O)-NH-Ph(OR}^5)_3$, $-\text{NR}^3\text{R}^4$,
 $-\text{NH-}(\text{CH}_2)_n\text{-NR}^3\text{R}^4$, $\text{R}^5\text{-(CH}_2)_n\text{-C}^*\text{H-CH(R}^5)\text{-(CH}_2)_n\text{-R}^5$,
 $-(\text{CH}_2)_n\text{-CO-NH-}(\text{CH}_2)_n\text{-CO-R}^5$, $-\text{OC(O)NH-C}_1\text{-C}_6\text{-alkyl}$ or
 $-(\text{CH}_2)_n\text{-CO-NH-}(\text{CH}_2)_n\text{-CH-}((\text{CH}_2)_n\text{R}^5)_2$,
 or for $\text{C}_3\text{-C}_{10}\text{-cycloalkyl}$, which is substituted with the group



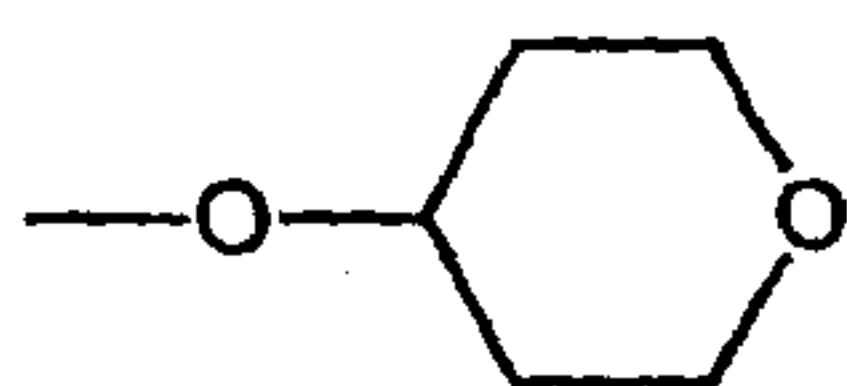
or for the group



or for

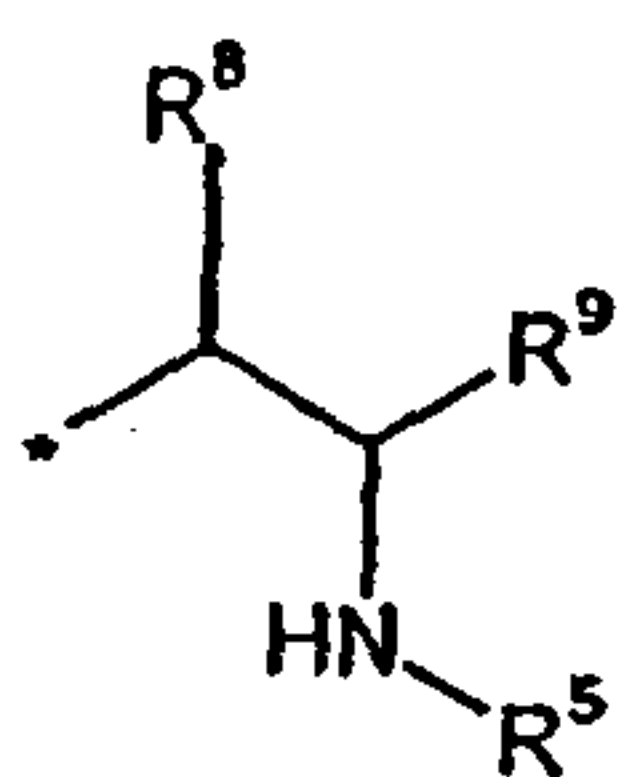


X stands for oxygen or for the group -NH- , $\text{-N(C}_1\text{-C}_3\text{-alkyl)}$ or

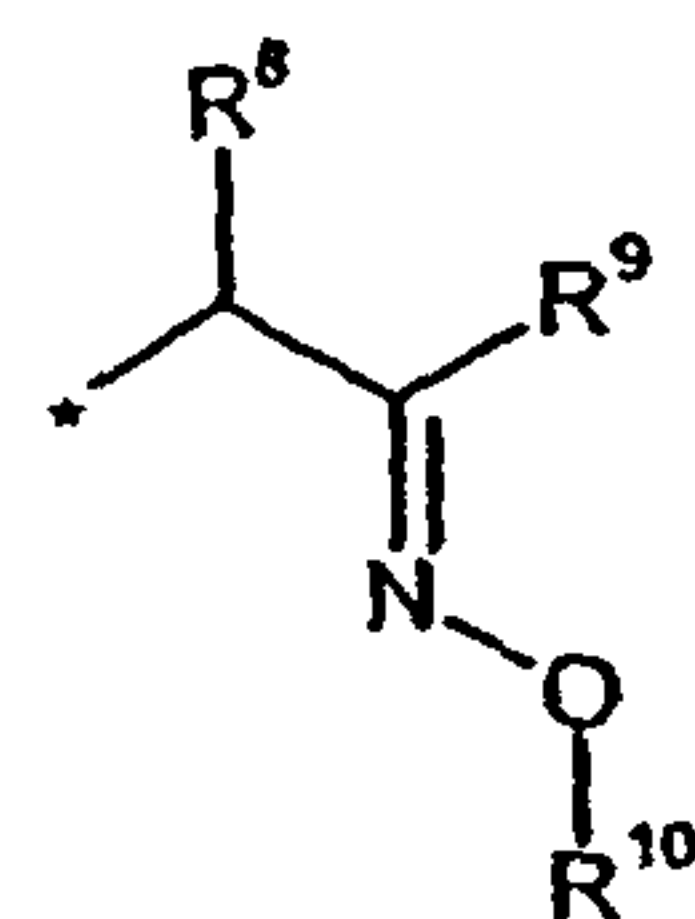


or

R^2 stands for the group

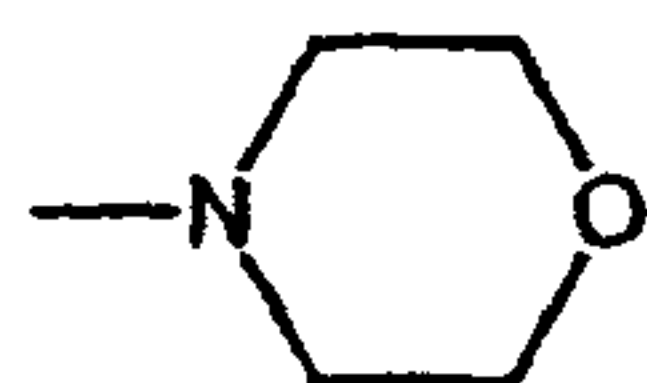


or

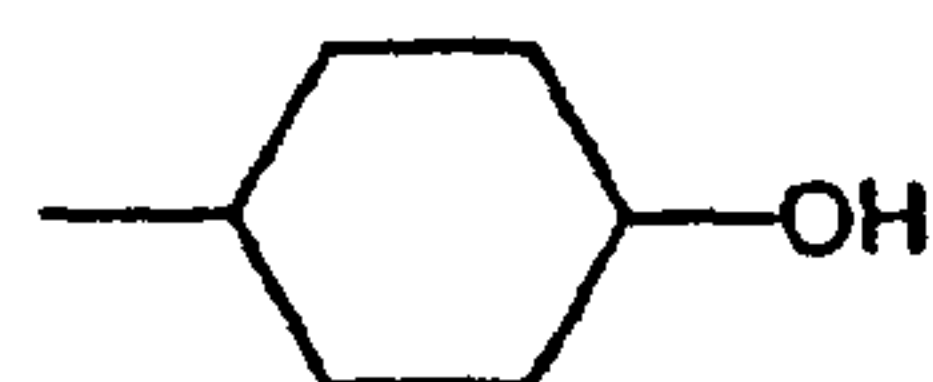


or

X and R^2 together form a group



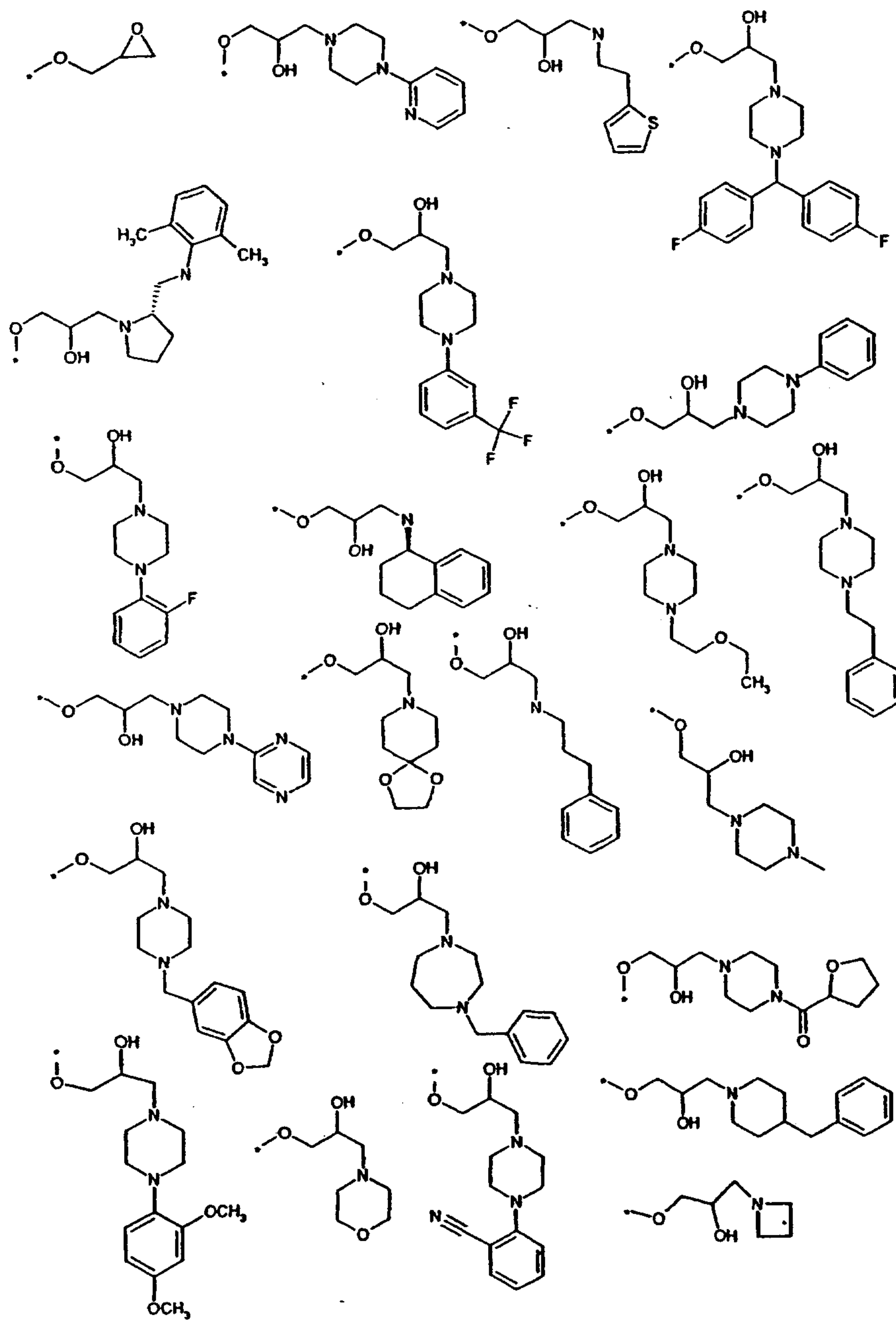
or



A and B, in each case independently of one another, stand for hydrogen,

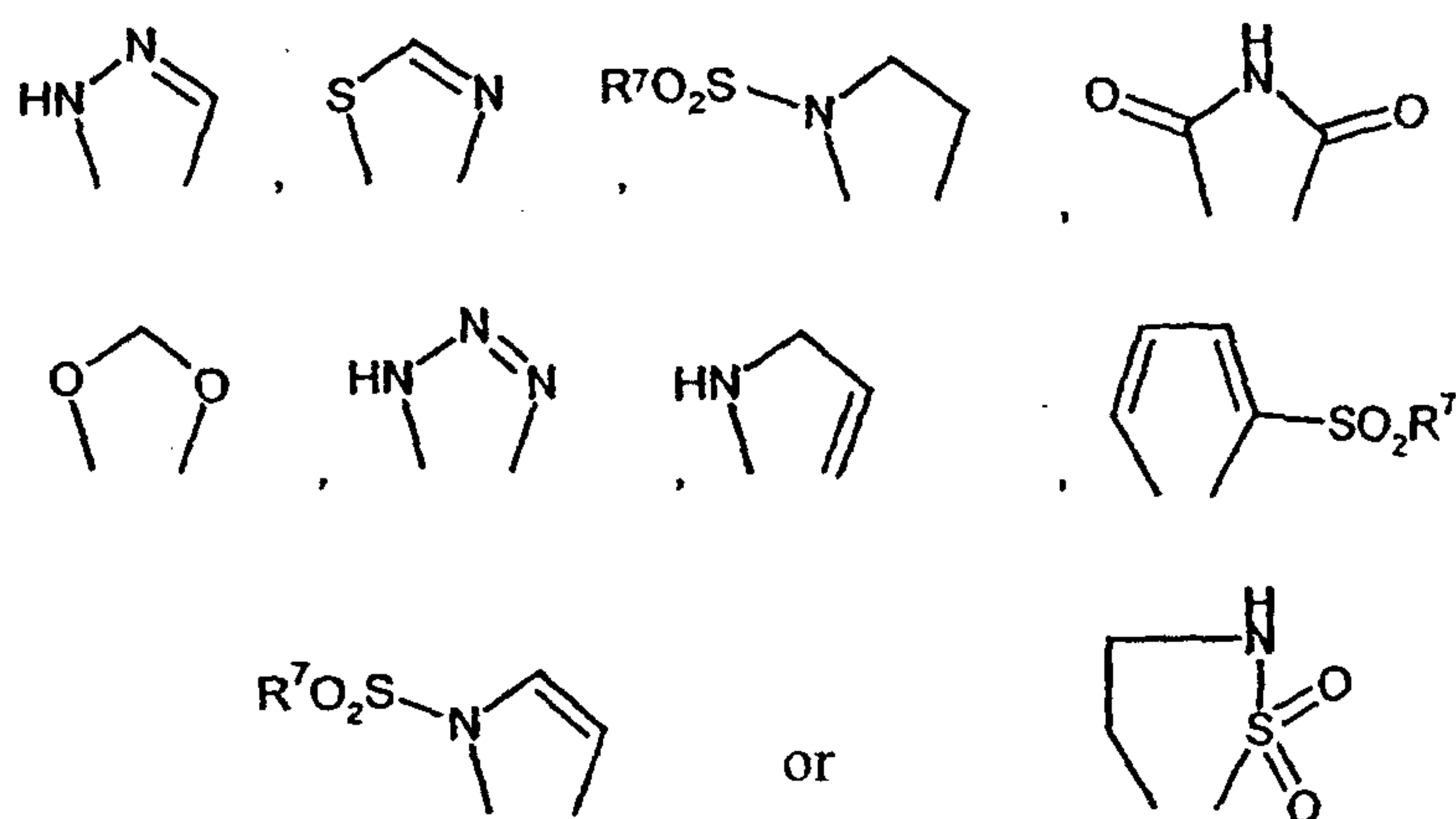
hydroxy, $\text{C}_1\text{-C}_3\text{-alkyl}$, $\text{C}_1\text{-C}_6\text{-alkoxy}$ or for the group -S-CH_3 , $\text{-SO}_2\text{-C}_2\text{H}_4\text{-OH}$, -CO-CH_3 , -S-CHF_2 , $\text{-S(CH}_2)_n\text{CH(OH)CH}_2\text{N-R}^3\text{R}^4$, $\text{-CH}_2\text{PO(OC}_2\text{H}_5)_2$, -S-CF_3 , -SO-CH_3 , $\text{-SO}_2\text{CF}_3$, $\text{-SO}_2\text{-(CH}_2)_n\text{-N-R}^3\text{R}^4$, $\text{-SO}_2\text{-NR}^3\text{R}^4$, $\text{-SO}_2\text{R}^7$, -CH(OH)-CH_3 , -COOH , $\text{-CH((CH}_2)_n\text{R}^5)_2$, $\text{-(CH}_2)_n\text{R}^5$, $\text{-COO-C}_1\text{-C}_6\text{-alkyl}$, $\text{-CONR}^3\text{R}^4$ or for

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OR

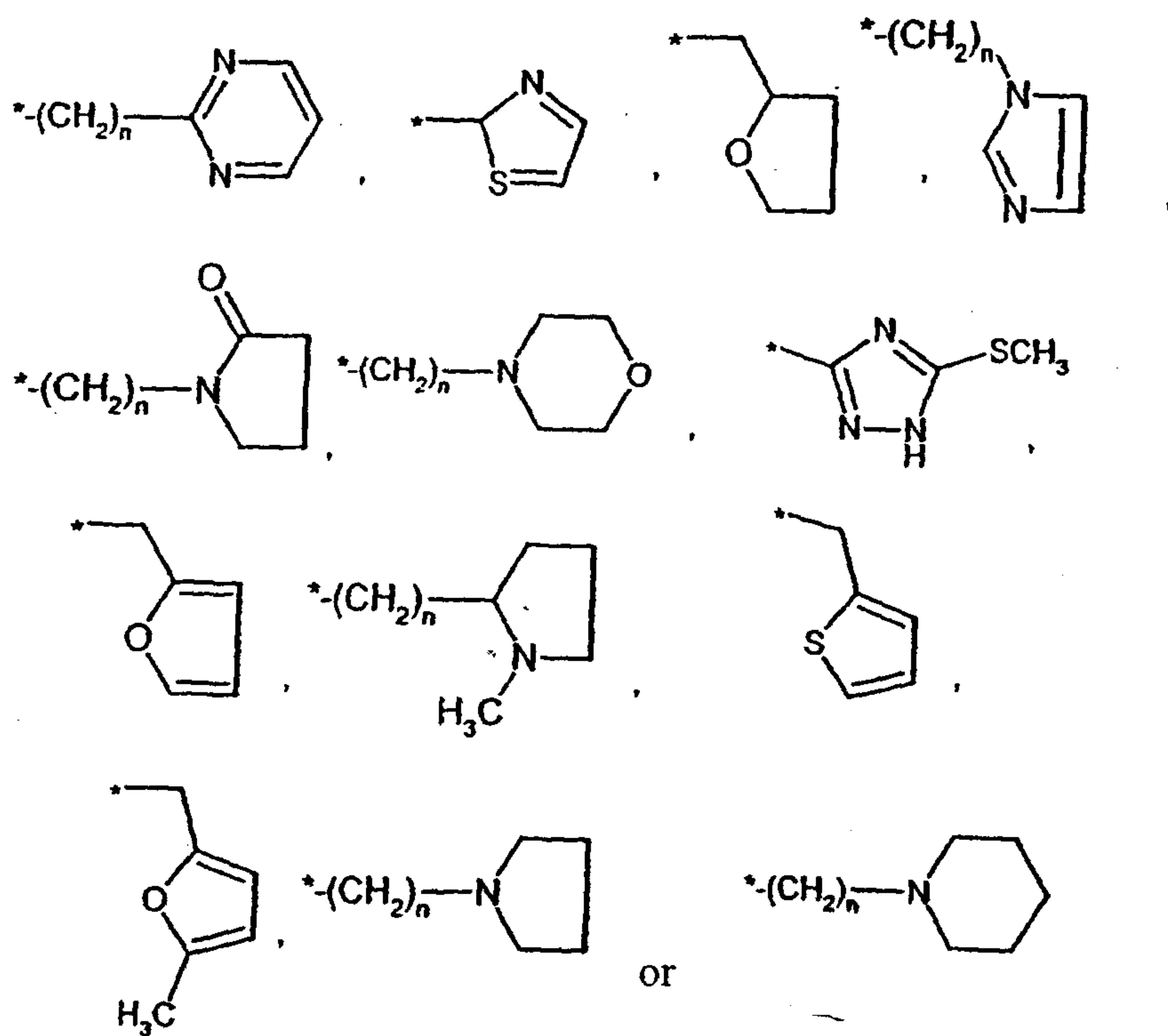
A and B together can form a group



R^3 and R^4 , in each case independently of one another, stand for hydrogen, phenyl, benzyloxy, C_1 - C_{12} -alkyl, C_1 - C_6 -alkoxy, C_2 - C_4 -alkenyloxy, C_3 - C_6 -cycloalkyl, hydroxy, hydroxy- C_1 - C_6 -alkyl, dihydroxy- C_1 - C_6 -alkyl, heteroaryl, heterocyclo- C_3 - C_{10} -alkyl, heteroaryl- C_1 - C_3 -alkyl, C_3 - C_6 -cycloalkyl- C_1 - C_3 -alkyl that is optionally substituted with cyano, or for C_1 - C_6 -alkyl that is optionally substituted in one or more places in the same way or differently with phenyl, pyridyl, phenyloxy, C_3 - C_6 -cycloalkyl, C_1 - C_6 -alkyl or C_1 - C_6 -alkoxy, whereby the phenyl itself can be substituted in one or more places in the same way or differently with halogen, trifluoromethyl, C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy or with the group

$-\text{SO}_2\text{NR}^3\text{R}^4$,

or for the group $-(\text{CH}_2)_n\text{NR}^3\text{R}^4$, $-\text{CNHNH}_2$ or $-\text{NR}^3\text{R}^4$ or for



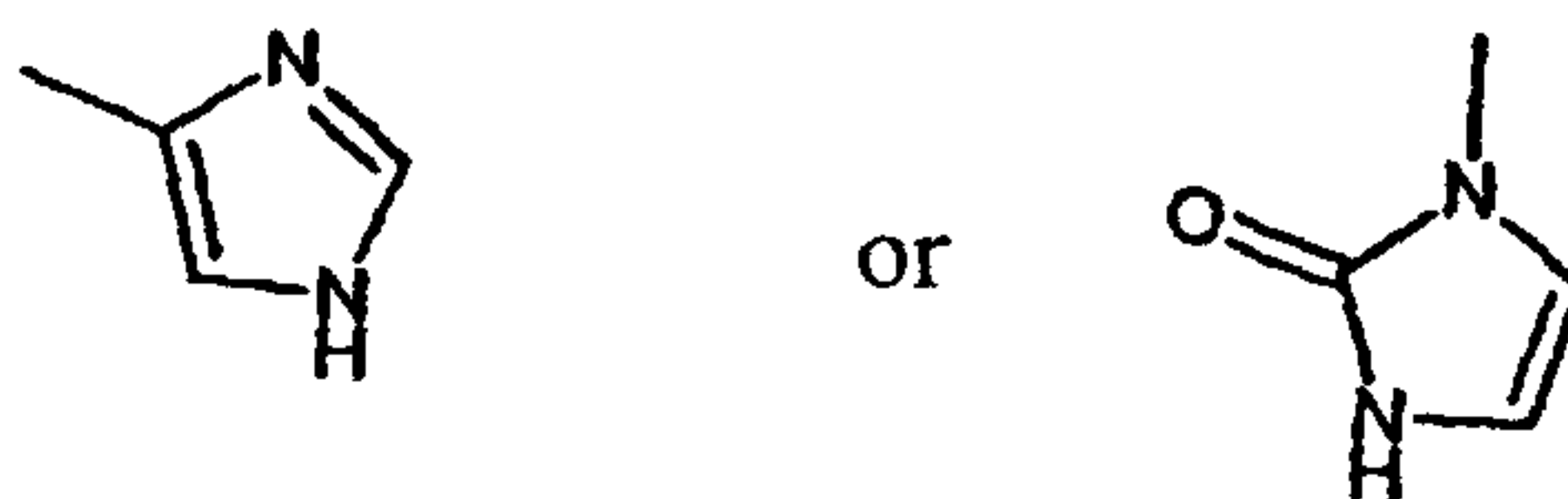
which optionally can be substituted with C_1 - C_6 -alkyl,

R^5 stands for hydroxy, phenyl, C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl, benzoxy,

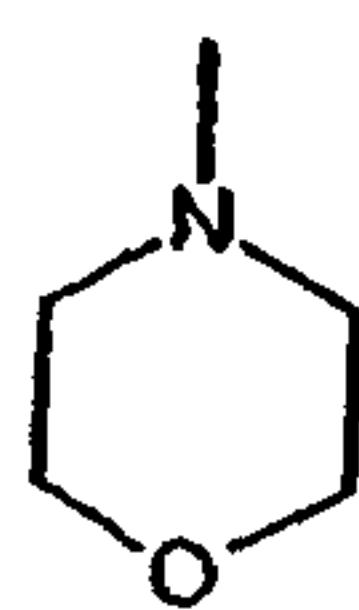
C_1 - C_6 -alkylthio or C_1 - C_6 -alkoxy,

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R^6 stands for the group



R^7 stands for halogen, hydroxy, phenyl, C_1 - C_6 -alkyl, $-(CH_2)_nOH$, $-NR^3R^4$ or the group



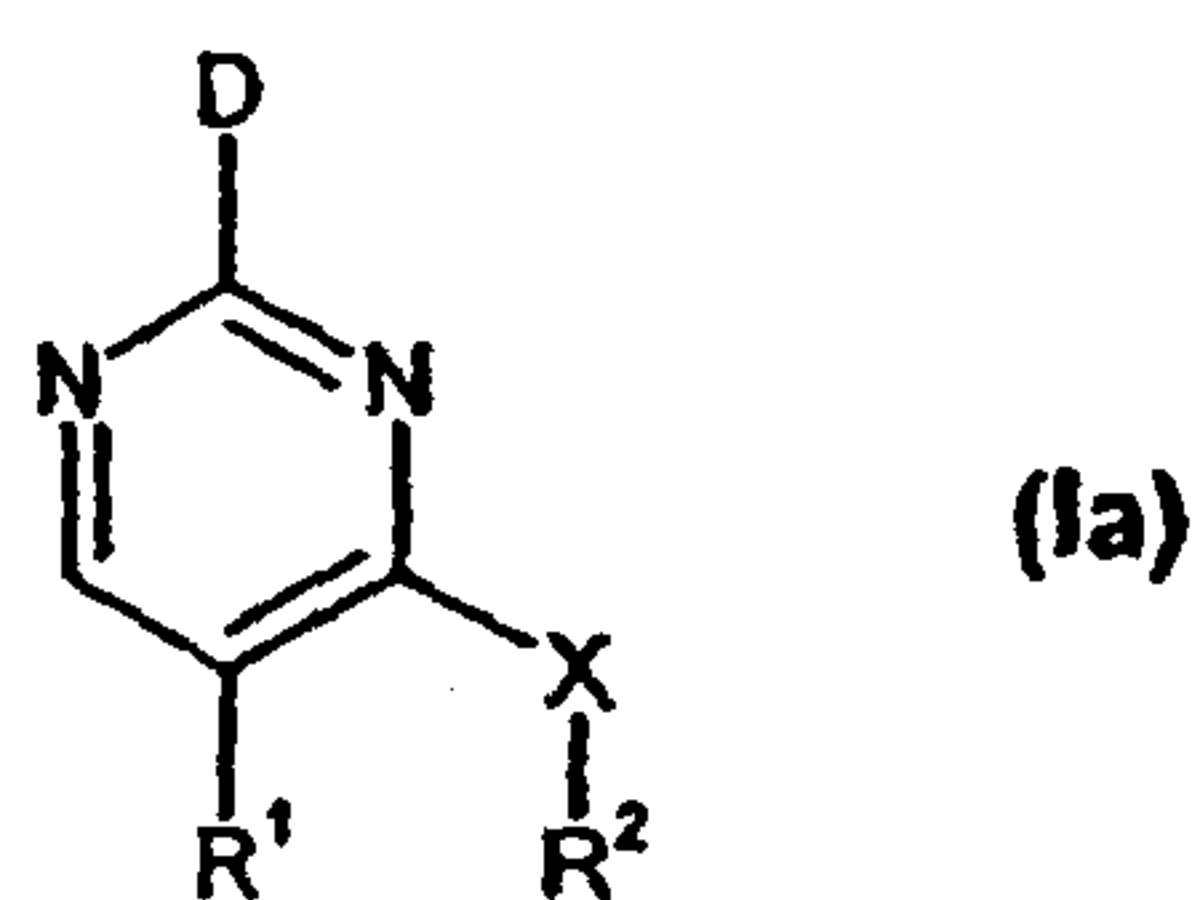
R^8 , R^9 and

R^{10} stand for hydrogen, hydroxy, C_1 - C_6 -alkyl or for the group $-(CH_2)_n-COOH$, and

n stands for 0-6,

as well as isomers, diastereomers, enantiomers and salts thereof .

4. Use of the compound of general formula Ia



In which D stands for halogen, and X, R^1 , and R^2 have the meanings that are indicated in general formula (I), as intermediate products for the production of the compound of general formula I.

5. Use of the compounds of general formula Ia, according to claim 4, in which D stands for chlorine and X, R¹ and R² have the meanings that are indicated in the general formula.

6. Pharmaceutical agents that comprise a compound of general formula I in which

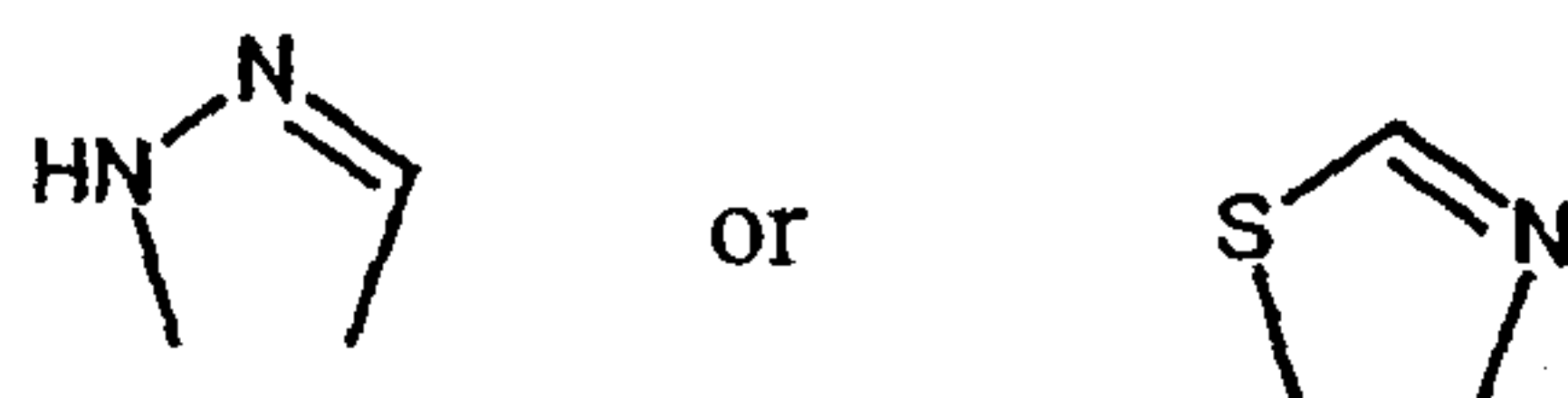
R¹ stands for halogen or C₁-C₃-alkyl

X stands for oxygen or -NH,

A stands for hydrogen

B stands for hydroxy, -CO-alkyl-R⁷, -S-CHF₂, -S-(CH₂)_nCH(OH)CH₂N-R³R⁴, -S-CF₃, or -CH-(OH)-CH₃, or

A and B, independently of one another, can form a group



R², R³, R⁴, R⁷ and R⁸ have the meanings that are indicated in general formula I, as well as isomers, diastereomers, enantiomers and salts thereof.

7. Use of the compounds of general formula I, according to claims 1 to 3, for the production of a pharmaceutical agent for treating cancer, auto-immune diseases, chemotherapy agent-induced alopecia and mucositis, cardiovascular diseases, infectious diseases, nephrological diseases, chronic and acute neurodegenerative diseases and viral infections.

8. Use according to claim 7, wherein cancer is defined as solid tumors and

leukemia; auto-immune diseases are defined as psoriasis, alopecia and multiple sclerosis; cardiovascular diseases are defined as stenoses, arterioscleroses and restenoses; infectious diseases are defined as diseases that are caused by unicellular parasites; nephrological diseases are defined as glomerulonephritis; chronic neurodegenerative diseases are defined as Huntington's disease, amyotrophic lateral sclerosis, Parkinson's disease, AIDS dementia and Alzheimer's disease; acute neurodegenerative diseases are defined as ischemias of the brain and neurotraumas; and viral infections are defined as cytomegalic infections, herpes, hepatitis B and C, and HIV diseases.

9. Pharmaceutical agents that contain at least one compound according to claims 1 to 3.

10. Pharmaceutical agent according to claim 9 for treating cancer, auto-immune diseases, cardiovascular diseases, infectious diseases, nephrological diseases, neurodegenerative diseases and viral infections.

11. Compounds according to claims 1 to 3 and pharmaceutical agents according to claims 6 to 7, with suitable formulation substances and vehicles.

12. Use of the compounds of general formula I and the pharmaceutical agents, according to claims 1 to 3 and 6, as inhibitors of the cyclin-dependent kinases.

13. Use according to claim 12, wherein the kinase is CDK1, CDK2, CDK3, CDK4, CDK5, CDK6, CDK7, CDK8 or CDK9.

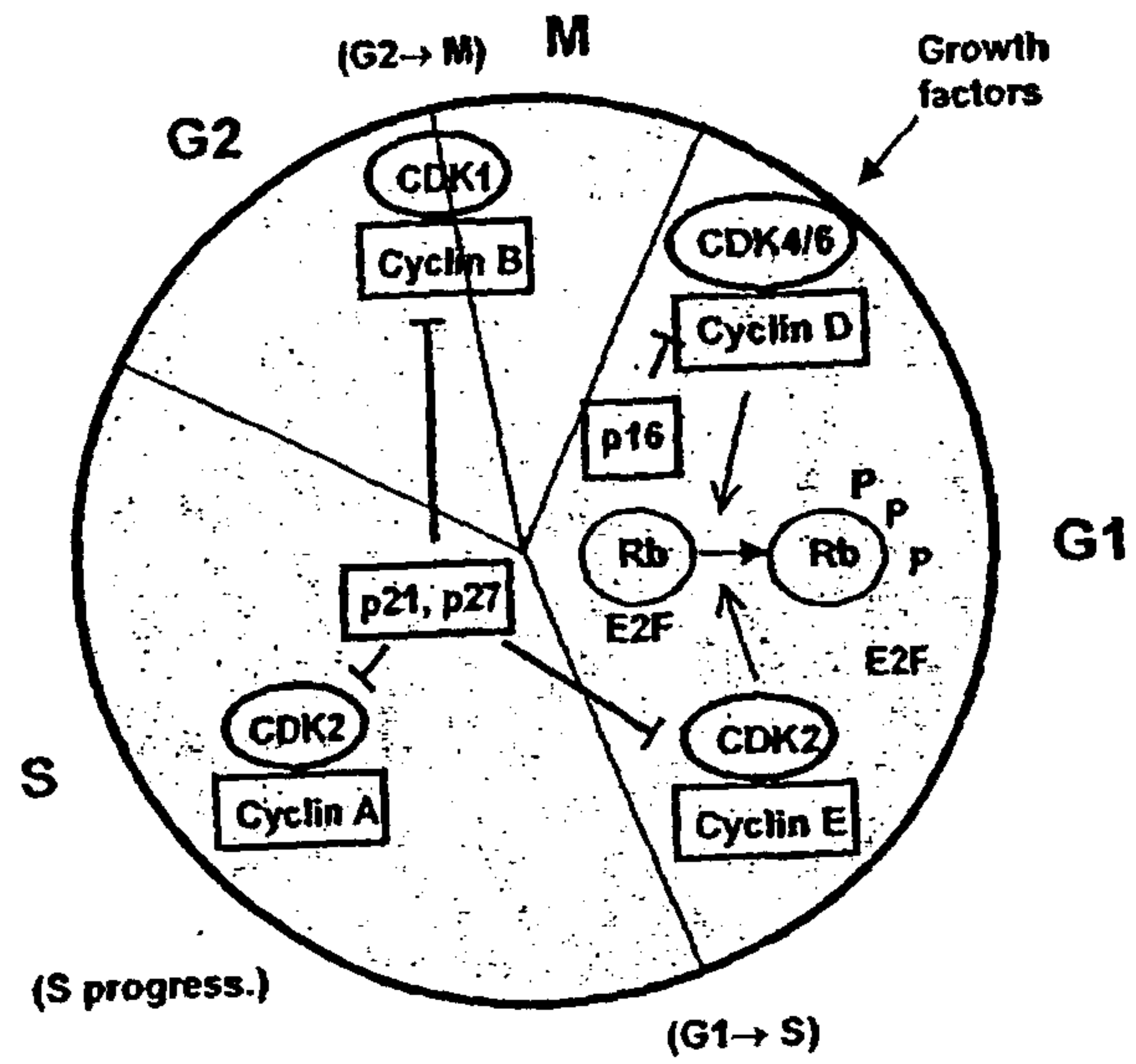
14. Use of the compounds of general formula I and the pharmaceutical agents, according to claims 1 to 3 and 6, as inhibitors of the glycogen-synthase-kinase (GSK-3 β).

15. Use of the compounds of general formula I, according to claims 1 to 3, in the form of a pharmaceutical preparation for enteral, parenteral and oral administration.

16. Use of the agent according to claim 6, in the form of a preparation for enteral, parenteral and oral administration.

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Fig 1

*Mark & Clerk*