Substituted 2-thio-3,5-dicyano-4-aryl-6-aminopyridines and their use

The present invention relates to substituted 2-thio-3,5-dicyano-4-aryl-6-aminopyridines, to a process for their preparation and to their use as active compounds for medicaments.

The present invention furthermore provides the use of adenosine-receptor-selective ligands for the prophylaxis and/or treatment of various disorders.

Adenosine, a nucleoside consisting of adenine and D-ribose, is an endogenous factor having cell-protective activity, in particular under cell-damaging conditions with limited oxygen and substrate supply, such as, for example, in the case of ischemia in various organs (for example heart and brain).

Adenosine is formed intracellularly as an intermediate during the degradation of adenosine 5'-monophosphate (AMP) and S-adenosylhomocysteine, but it can be released from the cell, in which case it acts as a hormone-like substance or neurotransmitter by binding to specific receptors.

Under normoxic conditions, the concentration of free adenosine in the extracellular space is very low. However, under ischemic or hypoxic conditions, the extracellular concentration of adenosine in the affected organs is increased dramatically. Thus, it is known, for example, that adenosine inhibits platelet degradation and increases the blood supply to the coronary vessels of the heart. Furthermore, it acts on the heart rate, on the release of neurotransmitters and on lymphocyte differentiation.

The aim of these actions of adenosine is to increase the oxygen supply of the affected organs and/or to reduce the metabolism of these organs in order to adjust the metabolism of the organ to the blood supply of the organ under ischemic or hypoxic conditions.

The action of adenosine is mediated via specific receptors. To date, subtypes A1, A2a, A2b and A3 are known. The actions of these adenosine receptors are mediated intracellularly by the messenger cAMP. In the case of the binding of adenosine to the A2a or A2b receptors, the intracellular cAMP is increased via activation of the membrane-bond adenylate cyclase, whereas binding of adenosine to A1 or A3 receptors results in a decrease of the intracellular cAMP concentration via inhibition of adenylate cyclase.

According to the invention, "Adenosine-receptor-selective ligands" are substances which bind selectively to one or more subtypes of the adenosine receptors, thus either mimicking the action of adenosine (adenosine agonists) or blocking its action (adenosine antagonists).

According to their receptor selectivity, adenosine-receptor-selective ligands can be divided into different categories, for example ligands which bind selectively to the A1 or A2 receptors of adenosine and in the case of the latter also, for example, those which bind selectively to the A2a or the A2b receptors of adenosine. Also possible are adenosine receptor ligands which bind selectively to a plurality of subtypes of the adenosine receptors, for example ligands which bind selectively to the A1 and the A2, but not to the A3 receptors of adenosine.

The abovementioned receptor selectivity can be determined by the effect of the substances on cell lines which, after stable transfection with the corresponding cDNA, express the receptor subtypes in question (see the publication M.E. Olah, H. Ren, J. Ostrowski, K.A. Jacobson, G.L. Stiles, "Cloning, expression, and characterization of the unique bovine A1 adenosine receptor. Studies on the ligand binding site by site-directed mutagenesis." in *J. Biol. Chem.* **267** (1992) pages 10764-10770, the disclosure of which is hereby fully incorporated by way of reference).

The effect of the substances on such cell lines can be monitored by biochemical measurement of the intracellular messenger cAMP (see the publication K.N. Klotz,

J. Hessling, J. Hegler, C. Owman, B. Kull, B.B. Fredholm, M.J. Lohse, "Comparative pharmacology of human adenosine receptor subtypes - characterization of stably transfected receptors in CHO cells" in *Naunyn Schmiedebergs Arch. Pharmacol.* **357** (1998) pages 1-9, the disclosure of which is hereby fully incorporated by way of reference).

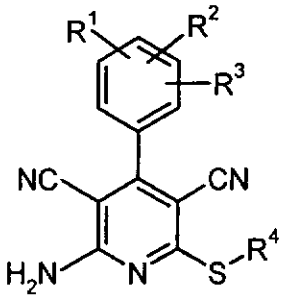
The "adenosine-receptor-specific" ligands known from the prior art are mainly derivatives based on natural adenosine (S.-A. Poulsen and R.J. Quinn, "Adenosine receptors: new opportunities for future drugs" in *Bioorganic and Medicinal Chemistry* **6** (1998) pages 619-641). However, most of the adenosine ligands known from the prior art have the disadvantage that their action is not really receptor-specific, that their activity is less than that of natural adenosine or that they have only very weak activity after oral administration. Thus, because of the disadvantages mentioned above, they are mainly only used for experimental purposes.

It is now an object of the following invention to find or provide compounds which have a wide therapeutic range and can serve as active compounds for the prophylaxis and/or treatment of various diseases.

In particular, it is an object of the present invention to find or provide substances which preferably act as adenosine-receptor-selective ligands and are suitable for the prophylaxis and/or treatment of various disorders, in particular disorders of the cardiovascular system (cardiovascular disorders) or inflammatory disorders, but additionally also disorders of the urogenital system, the respiratory tract, the central nervous system, the diabetes (in particular diabetes mellitus) and cancer.

It is a further object of the present invention to find or provide adenosine-receptor-selective ligands having a high specificity of action for the abovementioned purposes.

Accordingly, the present invention relates to compounds of the general formula (I)



(I),

in which :

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:

hydrogen;

hydroxyl;

optionally substituted (C_1-C_8)-alkyl;

optionally substituted (C_6-C_{10})-aryl;

optionally substituted (C_1-C_8)-alkoxy;

-O-$(CH_2)_n$-CH=CH_2 where n = 0, 1 or 2;

halogen;

nitro;

cyano;

-C(O)-R^5;

-C(O)-NR^6R^7;

-NR^6R^7;

-NR^6-C(O)-R^8;

-O-C(O)-R^8;

-SO_2-NR^6R^7; and

-NR^6-SO_2R^8,

where:

R^5 denotes:

hydrogen;

hydroxyl;
optionally substituted (C_1-C_8)-alkyl;
optionally substituted (C_3-C_7)-cycloalkyl;
optionally substituted (C_1-C_8)-alkoxy;
optionally substituted (C_6-C_{10})-aryl;
optionally substituted (C_6-C_{10})-aryloxy; or
-O-$(CH_2)_n$-[(C_6-C_{10})-aryl] where n = 1, 2 or 3,

where the (C_6-C_{10})-aryl group may be fused via two adjacent ring atoms to optionally substituted (C_4-C_7)-cycloalkyl,

or

R^5 represents a 5- to 7-membered saturated or unsaturated heterocycle which for its part may be mono- or polysubstituted by
an oxo group (=O);
halogen;
optionally substituted (C_1-C_8)-alkyl;
nitro;
cyano;
hydroxyl;
optionally substituted (C_6-C_{10})-aryl; or
by (C_1-C_8)-alkoxy,

or

R^5 represents optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted (C_6-C_{10})-aryl or optionally substituted (C_4-C_7)-cycloalkyl,

and

R^6 and R^7 are identical or different and represent

hydrogen;

optionally substituted (C_1-C_8)-alkyl;

optionally substituted (C_6-C_{10})-aryl; or

represent optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S

or

R^6 and R^7 together with the nitrogen atom to which they are optionally attached form a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of

an oxo group (=O);

halogen;

(C_1-C_8)-alkyl;

nitro;

cyano;

hydroxyl;

(C_6-C_{10})-aryl; or

(C_1-C_8)-alkoxy,

and

R^8 represents hydroxyl;
NR^6R^7 where R^6 and R^7 are as defined above;
optionally substituted (C_1-C_8)-alkyl;
(C_1-C_8)-alkoxy;
optionally substituted (C_6-C_{10})-aryl;
(C_6-C_{10})-aryloxy; or
$-O-(CH_2)_n-[(C_6-C_{10})\text{-aryl}]$ where n = 1, 2 or 3,

and

R^4 represents straight-chain or branched (C_1-C_8)-alkyl or (C_2-C_8)-alkenyl which are optionally mono- or polysubstituted by
hydroxyl;
halogen;
cyano;
$-C(O)-R^5$ where R^5 is as defined above;
$-C(O)-NR^6R^7$ where R^6 and R^7 are as defined above;
$-NR^6R^7$ where R^6 and R^7 are as defined above;
$-NR^6-C(O)-R^8$ where R^6 and R^8 are as defined above;
$-SO_2-NR^6R^7$ where R^6 and R^7 are as defined above;
$-NR^6-SO_2-R^8$ where R^6 and R^8 are as defined above;
$-C(O)-(CH_2)_n-C(O)-R^8$ where n = 0 to 2 and R^8 is as defined above;
(C_1-C_8)-alkoxy;
optionally substituted (C_6-C_{10})-aryloxy;
optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S;
optionally substituted (C_6-C_{10})-aryl; or
by a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents

from the group consisting of an oxo group (=O); halogen; (C_1-C_8)-alkyl; nitro; cyano; hydroxyl; (C_6-C_{10})-aryl; or by (C_1-C_8)-alkoxy,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted (C_6-C_{10})-aryl,

or

R^4 represents a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S, which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); halogen; (C_1-C_8)-alkyl; nitro; cyano; hydroxyl; (C_6-C_{10})-aryl; or by (C_1-C_8)-alkoxy, and which may optionally be fused via two adjacent ring atoms to optionally substituted (C_6-C_{10})-aryl or optionally substituted (C_4-C_7)-cycloalkyl,

and their tautomers and their respective salts, hydrates and alkoxides,

except for the following compounds of the general formula (I), in which the radicals R^1, R^2, R^3 and R^4 are as defined below:

- $R^1 = R^2 = H$; R^3 = para-OH; R^4 = -CH_2-Z where Z = CN, C(O)-OC_2H_5, 4-Br-C_6H_4-CO, 4-n-butyl-C_6H_4-CO, H, C_6H_5, C(O)-O-CH_2-C_6H_5, C(O)-OCH_3, C(O)-OH, 2-oxo-benzo-pyranyl-3-carbonyl, 4-Cl-C_6H_4-CO, 3-Br-C_6H_4-CO, 4-C_6H_5-C_6H_4-CO, 4-CH_3-C_6H_4-CO, 3,4-Cl_2-C_6H_3-CO;
- $R^1 = R^2 = H$; R^3 = meta-OH; R^4 = -CH_2-Z where Z = 4-Br-C_6H_4-NH-CO, 2-oxo-benzo-pyranyl-3-carbonyl, 4-Cl-C_6H_4-CO;
- $R^1 = R^2 = H$; R^3 = para-O-C(O)-CH_3; R^4 = -CH_2-Z where Z = 4-CH_3-C_6H_4-CO, H, 2-oxo-benzopyranyl-3-carbonyl, $(CH_2)_3$-CH_3, 4-C_6H_5-C_6H_4;
- $R^1 = R^2 = R^3 = H$; R^4 = -CH_2-Z where Z = CH_3, CN , 2-naphthyl;
- $R^1 = R^2 = H$; R^3 = para-butoxy; R^4 = -CH_2-Z where Z = 4-Cl-C_6H_5, C(O)-OCH_3, C(O)-C_6H_5, CH=CH_2, C(O)-NH_2, H, 4-Br-C_6H_4-CO, 4-Cl-C_6H_4-CO, C(O)-

OC_2H_5, C(O)-O-CH_2-C_6H_5, 2-oxo-benzopyranyl-3-carbonyl, C(O)-NH-C_6H_5, CN;

- $R^1 = R^2 = H$; R^3 = para-bromo; R^4 = -CH_2-Z where Z = 4-Br-C_6H_4-CO, 4-Cl-C_6H_4-CO, C(O)-NH_2, C(O)-OCH_3, 4-Cl-C_6H_5, 4-Br-C_6H_4-NH-CO;
- $R^1 = R^2 = H$; R^3 = meta-fluoro; R^4 = -CH_2-Z where Z = 4-Br-C_6H_4-CO, C(O)-NH_2, C(O)-O-CH_2-C_6H_5, CN;
- $R^1 = R^2 = H$; R^3 = para-chloro; R^4 = -CH_2-Z where Z = 2-naphthyl, CH_3;
- $R^1 = R^2 = H$; R^3 = para-OCH_3; R^4 = -CH_2-Z where Z = 2-naphthyl, CH_3;
- $R^1 = R^2 = H$; R^3 = meta-NO_2; R^4 = -CH_2-Z where Z = CH_3.

Some of the abovementioned substances which can be used in accordance with the present invention for the prophylaxis and/or treatment of disorders are novel, and some are also known from the literature (see *Dyachenko et al.*, Russian Journal of Chemistry, Vol. 33, No. 7, 1997, pages 1014-1017 and Vol. 34, No. 4, 1998, pages 557-563; *Dyachenko et al.*, Chemistry of Heterocyclic Compounds, Vol. 34, 1998, pages 188-194; *Elnagdi et al.*, Zeitschrift für Naturforschung, Vol. 47b, 1992, pages 572-578; *Riguera et al.*, Eur. J. Med. Chem. 33, 1998, pages 887-897; *J. Vaquero, Thesis,* University of Alcala de Henares, Madrid, Spain, 1981). However, in the literature, a therapeutic use of the known compounds has hitherto not been described. The first time this has happened is in the context of the present invention.

Accordingly, the present invention also provides the use of the abovementioned compounds of the general formula (I), including the compounds excluded above, for the prophylaxis and/or treatment of disorders.

Depending on the substitution pattern, the compounds of the formula (I) can exist in stereoisomeric forms which are either like image and mirror image (enantiomers) or not like image and mirror image (diastereomers). The invention relates both to the enantiomers or diastereomers and to their respective mixtures. The racemic forms, like the diastereomers, can be separated in a known manner into the stereoisomerically uniform components. Likewise, the present invention also relates to the other tautomers of the compounds of the formula (I) and their salts.

Physiologically acceptable salts of the compounds of the formula (I) can be salts of the substances according to the invention with mineral acids, carboxylic acids or sulfonic acids. Particular preference is given, for example, to salts with hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, ethanesulfonic acid, toluenesulfonic acid, benzenesulfonic acid, naphthalene disulfonic acid, trifluoroacetic acid, acetic acid, propionic acid, lactic acid, tartaric acid, citric acid, fumaric acid, maleic acid or benzoic acid.

Salts which may be mentioned include salts with customary bases, such as, for example, alkali metal salts (for example sodium or potassium salts), alkaline earth metal salts (for example calcium or magnesium salts) or ammonium salts, derived from ammonia or organic amines such as, for example, diethylamine, triethylamine, ethyldiisopropylamine, procaine, dibenzylamine, N-methylmorpholine, dihydroabietylamine, 1-ephenamine or methylpiperidine.

Definitions in the context of the present invention:

- Halogen generally represents fluorine, chlorine, bromine or iodine. Preference is given to fluorine, chlorine or bromine. Very particular preference is given to fluorine or chlorine.

- In the context of the present invention, (C_1-C_8)-alkyl, (C_1-C_6)-alkyl and (C_1-C_4)-alkyl represent a straight-chain or branched alkyl radical having 1 to 8; 1 to 6 and 1 to 4 carbon atoms, respectively. Examples which may be mentioned are: methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, n-pentyl, isopentyl, n-hexyl, isohexyl, n-heptyl and n-octyl. Preference is given to a straight-chain or branched alkyl radical having 1 to 6 carbon atoms. Particular preference is given to a straight-chain or branched alkyl radical having 1 to 4 carbon atoms.

- Optionally substituted (C_1-C_8)-alkyl, (C_1-C_6)-alkyl and (C_1-C_4)-alkyl, as used in the present invention, denotes an above-defined straight-chain or branched alkyl radical having 1 to 8; 1 to 6 and 1 to 4 carbon atoms, respectively, which for its part can be mono- or polysubstituted by identical or different substituents. Substituents which may be mentioned are in particular the following substituents: halogen (fluorine, chlorine, bromine, iodine); cyano; nitro; carboxyl; hydroxyl; straight-chain or branched (C_1-C_8)-alkoxy, preferably (C_1-C_6)-alkoxy, in particular (C_1-C_4)-alkoxy, where the alkoxy radical for its part may optionally be substituted; straight-chain or branched (C_2-C_8)-alkenyl, preferably (C_2-C_6)-alkenyl, in particular (C_2-C_4)-alkenyl, where the alkenyl radical for its part may optionally be substituted; (C_6-C_{10})-aryl, in particular phenyl or naphthyl, where the (C_6-C_{10})-aryl radical for its part may optionally be substituted; (C_1-C_4)-alkylsulfonyloxy, where the (C_1-C_4)-alkylsulfonyloxy radical for its part may optionally be substituted; phenylsulfonyl or p-tolylsulfonyl; straight-chain or branched (C_1-C_8)-thioalkyl, where the thioalkyl radical for its part may optionally be substituted; straight-chain or branched mono-, di- and/or trihalogeno-(C_1-C_8)-alkyl, in particular trifluoromethyl; straight-chain or branched mono-, di- and/or trihalogeno-(C_1-C_8)-alkoxy, in particular trifluoromethoxy; acyl; amino, N-[(C_1-C_8)-alkyl]-amino and/or N-di-[(C_1-C_8)-alkyl]-amino, where the alkyl radical for its part may optionally be substituted; and (C_1-C_8)-alkoxycarbonyl, where the alkoxycarbonyl radical for its part may optionally be substituted.

- In the context of the present invention, (C_6-C_{10})-aryl represents an aromatic radical having 6 to 10 carbon atoms. Preferred aryl radicals are phenyl and naphthyl.

- In the context of the present invention, the term optionally substituted (C_6-C_{10})-aryl represents an aromatic radical as defined above having 6 to 10 carbon atoms which for its part may be mono- or polysubstituted by identical or different substituents, in particular by: halogen (fluorine, chlorine, bromine, iodine); cyano; nitro; carboxyl; hydroxyl; straight-chain or branched (C_1-C_8)-alkyl, preferably (C_1-C_6)-alkyl, in particular (C_1-C_4)-alkyl, where the alkyl radical for its part may optionally be substituted; straight-chain or branched (C_1-C_8)-alkoxy, preferably (C_1-C_6)-alkoxy, in particular (C_1-C_4)-alkoxy, where the alkoxy radical for its part may optionally be substituted; straight-chain or branched (C_2-C_8)-alkenyl, preferably (C_2-C_6)-alkenyl, in particular (C_2-C_4)-alkenyl, where the alkenyl radical for its part may optionally be substituted; straight-chain or branched (C_1-C_8)-thioalkyl, where the thioalkyl radical for its part may optionally be substituted; straight-chain or branched mono-, di- and/or trihalogeno-(C_1-C_8)-alkyl, in particular trifluoromethyl; straight-chain or branched mono-, di- and/or trihalogeno-(C_1-C_8)-alkoxy, in particular trifluoromethoxy; acyl; amino, N-[(C_1-C_8)-alkyl]-amino and/or N-di-[(C_1-C_8)-alkyl]-amino, where the alkyl radical for its part may optionally be substituted; N-[(C_1-C_6)-alkoxy]-aldimino; (C_1-C_8)-alkoxycarbonyl, where the alkoxycarbonyl radical for its part may optionally be substituted; and (C_6-C_{10})-aryl, in particular phenyl or naphthyl, where the (C_6-C_{10})-aryl radical for its part may optionally be substituted.

- (C_6-C_{10})-Aryloxy represents a group -O-(C_6-C_{10})-aryl, in particular a group -O-phenyl or -O-naphthyl, where otherwise reference may be made to the above definition of (C_6-C_{10})-aryl.

- Optionally substituted (C_6-C_{10})-aryloxy denotes a group -O-(C_6-C_{10})-aryl as defined above where, with respect to the substituents of the (C_6-C_{10})-aryl group, reference may be made to the above definition under optionally substituted (C_6-C_{10})-aryl.

- $\underline{(C_1\text{-}C_8)\text{-Alkoxy, }(C_1\text{-}C_6)\text{-alkoxy and }(C_1\text{-}C_4)\text{-alkoxy}}$, as used in the present invention and also in the definitions of $(C_1\text{-}C_8)$-alkoxycarbonyl represents a straight-chain or branched alkoxy radical having 1 to 8; 1 to 6 and 1 to 4 carbon atoms, respectively. Examples which may be mentioned are: methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, tert-butoxy, n-pentoxy, isopentoxy, n-hexoxy, isohexoxy, n-heptoxy and n-octoxy. Preference is given to a straight-chain or branched alkoxy radical having 1 to 6 carbon atoms. Particular preference is given to a straight-chain or branched alkoxy radical having 1 to 4 carbon atoms.

- In the context of the present invention, $\underline{\text{optionally substituted }(C_1\text{-}C_8)\text{-alkoxy, }(C_1\text{-}C_6)\text{-alkoxy and }(C_1\text{-}C_4)\text{-alkoxy}}$ denotes a straight-chain or branched alkoxy radical as defined above having 1 to 8, 1 to 6 and 1 to 4 carbon atoms, respectively, which may optionally be mono- or polysubstituted by identical or different substituents, in particular by the following substituents: halogen (fluorine, chlorine, bromine, iodine); cyano; nitro; carboxyl; hydroxyl; straight-chain or branched $(C_2\text{-}C_8)$-alkenyl, preferably $(C_2\text{-}C_6)$-alkenyl, in particular $(C_2\text{-}C_4)$-alkenyl, where the alkenyl radical for its part may optionally be substituted; straight-chain or branched $(C_1\text{-}C_8)$-thioalkyl, where the thioalkyl radical for its part may optionally be substituted; straight-chain or branched mono-, di- and/or trihalogeno-$(C_1\text{-}C_8)$-alkyl, in particular trifluoromethyl; straight-chain or branched mono-, di- and/or trihalogeno-$(C_1\text{-}C_8)$-alkoxy, in particular trifluoromethoxy; acyl; amino, N-[$(C_1\text{-}C_8)$-alkyl]-amino and/or N-di-[$(C_1\text{-}C_8)$-alkyl]-amino, where the alkyl radical for its part may optionally be substituted; or $(C_1\text{-}C_8)$-alkoxycarbonyl, where the alkoxycarbonyl radical for its part may optionally be substituted.

- In the context of the invention, $\underline{(C_3\text{-}C_7)\text{-Cycloalkyl}}$ generally represents a carbon ring having 3 to 7 carbon atoms, such as, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl.

- In the context of the invention, optionally substituted (C_3-C_7)-cycloalkyl generally represents a (C_3-C_7)-cycloalkyl radical as defined above which may optionally be mono- or polysubstituted by identical or different substituents, in particular by a (C_1-C_8)-alkyl radical, preferably a (C_1-C_6)-alkyl radical, very particularly preferably a (C_1-C_4)-alkyl radical, which for its part may in turn be mono- or polysubstituted as defined above.

- In the context of the invention, a 5- to 6-membered aromatic heterocycle having up to 3 heteroatoms from the group consisting of S, N and O generally represents a monocyclic heteroaromatic radical which is attached via a ring carbon atom of the heteroaromatic radical and, if appropriate, also via a ring nitrogen atom of the heteroaromatic radical. Examples which may be mentioned are: furanyl (for example furan-2-yl, furan-3-yl), pyrrolyl (for example pyrrol-1-yl, pyrrol-2-yl, pyrrol-3-yl), thienyl, thiazolyl, oxazolyl, imidazolyl, triazolyl, pyridyl, pyrimidyl, pyridazinyl. Preference is given to pyridyl, pyrimidyl, pyridazinyl, furanyl, imidazolyl and thiazolyl.

- In the context of the invention, an optionally substituted 5- to 6-membered aromatic heterocycle having up to 3 heteroatoms from the group consisting of S, N and O generally represents a heterocycle as defined above which may be mono- or polysubstituted by identical or different substituents from the group consisting of nitro; amino; guanidino; aminocarbonyl; halogen, preferably chlorine or fluorine; (C_1-C_6)-alkyl, preferably (C_1-C_4)-alkyl, as defined above, which for its part may optionally be substituted; or by (C_6-C_{10})-aryl as defined above which for its part may optionally be substituted.

Compounds which are preferred in the context of the invention are compounds of the general formula (I),

in which:

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:

hydrogen;

hydroxyl;

optionally substituted (C_1-C_6)-alkyl;

optionally substituted phenyl or naphthyl;

optionally substituted (C_1-C_6)-alkoxy;

-O-$(CH_2)_n$-CH=CH_2 where n = 1 or 2;

fluorine, chlorine, bromine;

nitro;

cyano;

-C(O)-R^5;

-C(O)-NR^6R^7;

-NR^6R^7;

-NR^6-C(O)-R^8;

-O-C(O)-R^8;

-SO_2-NR^6R^7; and

-NR^6-SO_2R^8,

where:

R^5 denotes:

hydrogen;

hydroxyl;

optionally substituted (C_1-C_6)-alkyl;

optionally substituted (C_3-C_7)-cycloalkyl;

optionally substituted (C_1-C_6)-alkoxy;

optionally substituted phenyl or naphthyl;

optionally substituted phenyloxy or naphthyloxy; or

-O-$(CH_2)_n$-phenyl where n = 1, 2 or 3,

where the phenyl or naphthyl group may be fused via two adjacent ring atoms to optionally substituted (C_4-C_7)-cycloalkyl,

or

R^5 represents a 5- to 7-membered saturated or unsaturated heterocycle which for its part may be mono- or polysubstituted by
an oxo group (=O);
fluorine, chlorine, bromine;
optionally substituted (C_1-C_6)-alkyl;
nitro;
cyano;
hydroxyl;
optionally substituted phenyl or naphthyl; or
by (C_1-C_6)-alkoxy,

or

R^5 represents optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted phenyl or naphthyl or optionally substituted (C_4-C_7)-cycloalkyl,

and

R^6 and R^7 are identical or different and represent
hydrogen;
optionally substituted (C_1-C_6)-alkyl;
optionally substituted phenyl or naphthyl; or
represent optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S

or

R^6 and R^7 together with the nitrogen atom to which they are optionally attached form a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of
an oxo group (=O);
fluorine, chlorine, bromine;
(C_1-C_6)-alkyl;
nitro;
cyano;
hydroxyl;
phenyl or naphthyl; or
(C_1-C_6)-alkoxy,

and

R^8 represents NR^6R^7 where R^6 and R^7 are as defined above;
optionally substituted (C_1-C_6)-alkyl;
(C_1-C_6)-alkoxy;
optionally substituted phenyl or naphthyl;
phenyloxy or naphthyloxy; or
$-O-(CH_2)_n$-phenyl where n = 1, 2 or 3,

and

R^4 represents straight-chain or branched (C_1-C_6)-alkyl or (C_2-C_6)-alkenyl which are optionally mono- or polysubstituted by
hydroxyl;
fluoro, chloro, bromine;
cyano;

-C(O)-R^5 where R^5 is as defined above;
-C(O)-NR^6R^7 where R^6 and R^7 are as defined above;
-NR^6R^7 where R^6 and R^7 are as defined above;
-NR^6-C(O)-R^8 where R^6 and R^8 are as defined above;
-SO_2-NR^6R^7 where R^6 and R^7 are as defined above;
-NR^6-SO_2-R^8 where R^6 and R^8 are as defined above;
-C(O)-$(CH_2)_n$-C(O)-R^8 where n = 0 to 2 and R^8 is as defined above;
$(C_1$-$C_6)$-alkoxy;
optionally substituted phenyloxy or naphthyloxy;
optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S;
optionally substituted phenyl or naphthyl; or
by a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S, which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); fluorine, chlorine, bromine; $(C_1$-$C_6)$-alkyl; nitro; cyano; hydroxyl; phenyl or naphthyl; or by $(C_1$-$C_6)$-alkoxy,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted phenyl or naphthyl,

or

R^4 represents a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S,
which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); fluorine, chlorine, bromine; $(C_1$-$C_6)$-alkyl; nitro; cyano; hydroxyl; phenyl or naphthyl; or by $(C_1$-$C_6)$-alkoxy and
which may optionally be fused via two adjacent ring atoms to optionally substituted phenyl or naphthyl or optionally substituted $(C_4$-$C_7)$-cycloalkyl,

and their tautomers and their respective salts, hydrates and alkoxides,

except for the following compounds of the general formula (I), in which the radicals R^1, R^2, R^3 and R^4 are as defined below:

- $R^1 = R^2 = H$; R^3 = para-OH; R^4 = $-CH_2-Z$ where Z = CN, C(O)-OC_2H_5, 4-Br-C_6H_4-CO, 4-n-butyl-C_6H_4-CO, H, C_6H_5, C(O)-O-CH_2-C_6H_5, C(O)-OCH_3, C(O)-OH, 2-oxo-benzo-pyranyl-3-carbonyl, 4-Cl-C_6H_4-CO, 3-Br-C_6H_4-CO, 4-C_6H_5-C_6H_4-CO, 4-CH_3-C_6H_4-CO, 3,4-Cl_2-C_6H_3-CO;
- $R^1 = R^2 = H$; R^3 = meta-OH; R^4 = $-CH_2-Z$ where Z = 4-Br-C_6H_4-NH-CO, 2-oxo-benzo-pyranyl-3-carbonyl, 4-Cl-C_6H_4-CO;
- $R^1 = R^2 = H$; R^3 = para-O-C(O)-CH_3; R^4 = $-CH_2-Z$ where Z = 4-CH_3-C_6H_4-CO, H, 2-oxo-benzopyranyl-3-carbonyl, $(CH_2)_3$-CH_3, 4-C_6H_5-C_6H_4;
- $R^1 = R^2 = R^3 = H$; R^4 = $-CH_2-Z$ where Z = CH_3, CN, 2-naphthyl;
- $R^1 = R^2 = H$; R^3 = para-butoxy; R^4 = $-CH_2-Z$ where Z = 4-Cl-C_6H_5, C(O)-OCH_3, C(O)-C_6H_5, CH=CH_2, C(O)-NH_2, H, 4-Br-C_6H_4-CO, 4-Cl-C_6H_4-CO, C(O)-OC_2H_5, C(O)-O-CH_2-C_6H_5, 2-oxo-benzopyranyl-3-carbonyl, C(O)-NH-C_6H_5, CN;
- $R^1 = R^2 = H$; R^3 = para-bromo; R^4 = $-CH_2-Z$ where Z = 4-Br-C_6H_4-CO, 4-Cl-C_6H_4-CO, C(O)-NH_2, C(O)-OCH_3, 4-Cl-C_6H_5, 4-Br-C_6H_4-NH-CO;
- $R^1 = R^2 = H$; R^3 = meta-fluoro; R^4 = $-CH_2-Z$ where Z = 4-Br-C_6H_4-CO, C(O)-NH_2, C(O)-O-CH_2-C_6H_5, CN;
- $R^1 = R^2 = H$; R^3 = para-chloro; R^4 = $-CH_2-Z$ where Z = 2-naphthyl, CH_3;
- $R^1 = R^2 = H$; R^3 = para-OCH_3; R^4 = $-CH_2-Z$ where Z = 2-naphthyl, CH_3;
- $R^1 = R^2 = H$; R^3 = meta-NO_2; R^4 = $-CH_2-Z$ where Z = CH_3.

Particularly preferred compounds are the compounds of the general formula (I)

in which:

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:

hydrogen;

hydroxyl;

optionally substituted (C_1-C_4)-alkyl;

optionally substituted phenyl;

optionally substituted (C_1-C_4)-alkoxy;

-O-$(CH_2)_n$-CH=CH_2 where n = 1;

fluorine, chlorine;

nitro;

cyano;

-C(O)-R^5;

-C(O)-NR^6R^7;

-NR^6R^7;

-NR^6-C(O)-R^8;

-O-C(O)-R^8;

-SO_2-NR^6R^7; and

-NR^6-SO_2R^8,

where:

R^5 denotes:

hydrogen;

hydroxyl;

optionally substituted (C_1-C_4)-alkyl;

optionally substituted (C_3-C_7)-cycloalkyl;

optionally substituted (C_1-C_4)-alkoxy;

optionally substituted phenyl;

optionally substituted phenyloxy; or

-O-$(CH_2)_n$-phenyl where n = 1,

where the phenyl group may be fused via two adjacent ring atoms to optionally substituted (C_5-C_6)-cycloalkyl,

or

R^5 represents a 5- to 7-membered saturated or unsaturated heterocycle which for its part may be mono- or polysubstituted by
an oxo group (=O);
fluorine, chlorine;
optionally substituted (C_1-C_4)-alkyl;
nitro;
cyano;
hydroxyl;
optionally substituted phenyl; or
by (C_1-C_4)-alkoxy,

or

R^5 represents optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S, selected from the group consisting of furanyl, pyrrolyl, thienyl, thiazolyl, oxazolyl, imidazolyl, triazolyl, pyridyl, pyrimidyl and pyridazinyl,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted phenyl or optionally substituted (C_5-C_6)-cycloalkyl,

and

R^6 and R^7 are identical or different and represent
hydrogen;
optionally substituted (C_1-C_4)-alkyl;

optionally substituted phenyl; or

represent optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S selected from the group consisting of furanyl, pyrrolyl, thienyl, thiazolyl, oxazolyl, imidazolyl, triazolyl, pyridyl, pyrimidyl and pyridazinyl,

or

R^6 and R^7 together with the nitrogen atom to which they are optionally attached form a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of

an oxo group (=O);

fluorine, chlorine;

(C_1-C_4)-alkyl;

nitro;

cyano;

hydroxyl;

phenyl; or

(C_1-C_4)-alkoxy,

and

R^8 represents NR^6R^7 where R^6 and R^7 are as defined above;

optionally substituted (C_1-C_4)-alkyl;

(C_1-C_4)-alkoxy;

optionally substituted phenyl;

phenyloxy; or

$-O-(CH_2)_n$-phenyl where n = 1,

and

R^4 represents straight-chain or branched (C_1-C_4)-alkyl or (C_2-C_4)-alkenyl which are optionally mono- or polysubstituted by

hydroxyl;

fluorine, chlorine;

cyano;

-C(O)-R^5 where R^5 is as defined above;

-C(O)-NR^6R^7 where R^6 and R^7 are as defined above;

-NR^6R^7 where R^6 and R^7 are as defined above;

-NR^6-C(O)-R^8 where R^6 and R^8 are as defined above;

-SO_2-NR^6R^7 where R^6 and R^7 are as defined above;

-NR^6-SO_2-R^8 where R^6 and R^8 are as defined above;

-C(O)-$(CH_2)_n$-C(O)-R^8 where n = 0 to 2 and R^8 is as defined above;

(C_1-C_4)-alkoxy;

optionally substituted phenyloxy;

optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S selected from the group consisting of furanyl, pyrrolyl, thienyl, thiazolyl, oxazolyl, imidazolyl, triazolyl, pyridyl, pyrimidyl and pyridazinyl;

optionally substituted phenyl; or

by a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); fluorine, chlorine; (C_1-C_4)-alkyl; nitro; cyano; hydroxyl; phenyl; or by (C_1-C_4)-alkoxy,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent rings atoms to optionally substituted phenyl,

or

R^4 represents a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S,
which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); fluorine, chlorine; (C_1-C_4)-alkyl; nitro; cyano; hydroxyl; phenyl; or by (C_1-C_4)-alkoxy and
which may optionally be fused via two adjacent ring atoms to optionally substituted phenyl or optionally substituted (C_5-C_6)-cycloalkyl,

and their tautomers and their respective salts, hydrates and alkoxides,

except for the following compounds of the general formula (I), in which the radicals R^1, R^2, R^3 and R^4 are as defined below:

- $R^1 = R^2 = H$; R^3 = para-OH; $R^4 = -CH_2-Z$ where Z = CN, C(O)-OC_2H_5, 4-Br-C_6H_4-CO, 4-n-butyl-C_6H_4-CO, H, C_6H_5, C(O)-O-CH_2-C_6H_5, C(O)-OCH_3, C(O)-OH, 2-oxo-benzo-pyranyl-3-carbonyl, 4-Cl-C_6H_4-CO, 3-Br-C_6H_4-CO, 4-C_6H_5-C_6H_4-CO, 4-CH_3-C_6H_4-CO, 3,4-Cl_2-C_6H_3-CO;
- $R^1 = R^2 = H$; R^3 = meta-OH; $R^4 = -CH_2-Z$ where Z = 4-Br-C_6H_4-NH-CO, 2-oxo-benzo-pyranyl-3-carbonyl, 4-Cl-C_6H_4-CO;
- $R^1 = R^2 = H$; R^3 = para-O-C(O)-CH_3; $R^4 = -CH_2-Z$ where Z = 4-CH_3-C_6H_4-CO, H, 2-oxo-benzopyranyl-3-carbonyl, 4-C_6H_5-C_6H_4;
- $R^1 = R^2 = R^3 = H$; $R^4 = -CH_2-Z$ where Z = CH_3, CN;
- $R^1 = R^2 = H$; R^3 = para-butoxy; $R^4 = -CH_2-Z$ where Z = 4-Cl-C_6H_5, C(O)-OCH_3, C(O)-C_6H_5, CH=CH_2, C(O)-NH_2, H, 4-Br-C_6H_4-CO, 4-Cl-C_6H_4-CO, C(O)-OC_2H_5, C(O)-O-CH_2-C_6H_5, 2-oxo-benzopyranyl-3-carbonyl, C(O)-NH-C_6H_5, CN;
- $R^1 = R^2 = H$; R^3 = meta-fluoro; $R^4 = -CH_2-Z$ where Z = 4-Br-C_6H_4-CO, C(O)-NH_2, C(O)-O-CH_2-C_6H_5, CN;
- $R^1 = R^2 = H$; R^3 = para-chloro; $R^4 = -CH_2-Z$ where Z = CH_3;
- $R^1 = R^2 = H$; R^3 = para-OCH_3; $R^4 = -CH_2-Z$ where Z = CH_3;

- $R^1 = R^2 = H$; R^3 = meta-NO_2; $R^4 = -CH_2-Z$ where Z = CH_3.

Particular preference according to the invention is given to compounds of the general formula (I)

in which:

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:

hydrogen;

hydroxyl;

methyl;

trifluoromethyl;

methoxy;

radicals of the formulae $-O-CH_2-CH_2-OH$, $-O-CH_2-COOH$ or $-O-CH_2-CH=CH_2$;

fluorine, chlorine or bromine;

nitro;

cyano;

$-C(O)OH$ or $-C(O)OCH_3$;

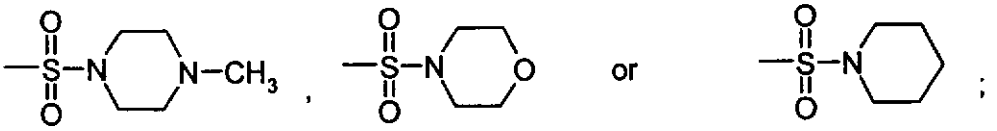
$-C(O)NH_2$;

$-NH_2$;

$-NH-C(O)-CH_3$;

$-O-C(O)-CH_3$ or $-O-C(O)-C_2H_5$;

radicals of the formulae



;

and

$-NH-SO_2CH_3$ or $-NH-SO_2C_6H_5$,

and

R^4 represents straight-chain or branched (C_1-C_4)-alkyl which is optionally mono- or polysubstituted by

hydroxyl;

amino;

-C(O)-OCH_3;

-C(O)-NH_2, -C(O)-$HNCH_3$, -C(O)-HNC_2H_5, or -C(O)-HNC_6H_5;

-$NHC(O)NH_2$, -$NHC(O)NHCH_3$, -$NHC(O)NHC_2H_5$, -$NHC(O)OCH_3$ or -$NHC(O)OC_2H_5$;

-SO_2-NH_2;

-NH-SO_2-CH_3 or -NH-SO_2-C_2H_5;

-OCH_3;

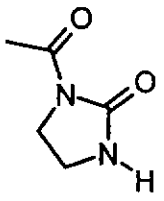
phenyl, which may be substituted by nitro, cyano, fluorine, methoxy, difluoromethoxy, methoxycarbonyl or p-tolylsulfonylmethyl;

pyridyl, furyl, imidazolyl, benzimidazolyl or thiazolyl, which may in each case be mono- or disubstituted by identical or different substituents from the group consisting of methyl, nitro and chlorine;

oxadiazolyl which may be substituted by phenyl or methoxyphenyl;

or

a radical of the formula



or

R^4 represents allyl or 3,3-dimethylallyl,

and their tautomers and their respective salts, hydrates and alkoxides,

except for the following compounds of the general formula (I), in which the radicals R^1, R^2, R^3 and R^4 are as defined below:

- $R^1 = R^2 = H$; R^3 = para-OH; $R^4 = -CH_2-Z$ where Z = H, C_6H_5, C(O)-OCH_3;
- $R^1 = R^2 = H$; R^3 = para-O-C(O)-CH_3; $R^4 = -CH_2-Z$ where Z = H;
- $R^1 = R^2 = R^3 = H$; $R^4 = -CH_2-Z$ where Z = CH_3;
- $R^1 = R^2 = H$; R^3 = meta-fluoro; $R^4 = -CH_2-Z$ where Z = C(O)-NH_2;
- $R^1 = R^2 = H$; R^3 = para-chloro; $R^4 = -CH_2-Z$ where Z = CH_3;
- $R^1 = R^2 = H$; R^3 = para-OCH_3; $R^4 = -CH_2-Z$ where Z = CH_3;
- $R^1 = R^2 = H$; R^3 = meta-NO_2; $R^4 = -CH_2-Z$ where Z = CH_3.

Very particular preference according to the invention is given to compounds of the general formula (I)

in which:

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:

hydrogen;

hydroxyl;

methyl;

methoxy;

radicals of the formulae -O-CH_2-CH_2-OH, -O-CH_2-COOH or -O-CH_2-CH=CH_2;

fluorine or chlorine;

nitro;

cyano;

-C(O)OH or –C(O)OCH_3;

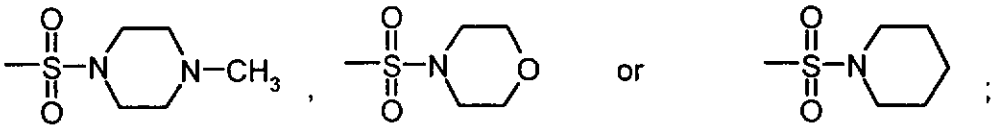
-C(O)NH_2;

$-NH_2$;

$-NH-C(O)CH_3$;

$-O-C(O)-CH_3$ or $-O-C(O)-C_2H_5$;

radicals of the formulae



and

$-NH-SO_2CH_3$ or $-NH-SO_2C_6H_5$,

and

R^4 represents straight-chain or branched (C_1-C_4)-alkyl which is optionally mono- or polysubstituted by

hydroxyl;

amino;

$-C(O)-OCH_3$;

$-C(O)-NH_2$, $-C(O)-HNCH_3$, $-C(O)-HNC_2H_5$, or $-C(O)-HNC_6H_5$;

$-NHC(O)NH_2$, $-NHC(O)NHCH_3$, $-NHC(O)NHC_2H_5$, $-NHC(O)OCH_3$ or $-NHC(O)OC_2H_5$;

$-SO_2-NH_2$;

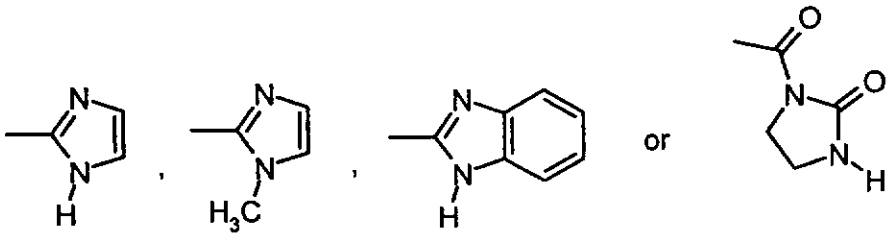
$-NH-SO_2-CH_3$ or $-NH-SO_2-C_2H_5$;

$-OCH_3$;

phenyl;

ortho-nitrophenyl; or

a radical of the formula



or

R^4 represents allyl,

and their tautomers and their respective salts, hydrates and alkoxides,

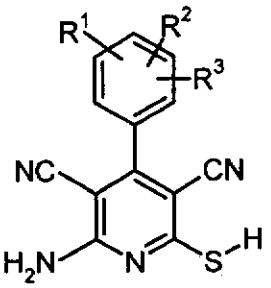
except for the following compounds of the general formula (I), in which the radicals R^1, R^2, R^3 and R^4 are as defined below:

- $R^1 = R^2 = H$; R^3 = para-OH; $R^4 = -CH_2-Z$ where Z = H, C_6H_5, $C(O)-OCH_3$;
- $R^1 = R^2 = H$; R^3 = para-$O-C(O)-CH_3$; $R^4 = -CH_2-Z$ where Z = H;
- $R^1 = R^2 = R^3 = H$; $R^4 = -CH_2-Z$ where Z = CH_3;
- $R^1 = R^2 = H$; R^3 = meta-fluoro; $R^4 = -CH_2-Z$ where Z = $C(O)-NH_2$;
- $R^1 = R^2 = H$; R^3 = para-chloro; $R^4 = -CH_2-Z$ where Z = CH_3;
- $R^1 = R^2 = H$; R^3 = para-OCH_3; $R^4 = -CH_2-Z$ where Z = CH_3;
- $R^1 = R^2 = H$; R^3 = meta-NO_2; $R^4 = -CH_2-Z$ where Z = CH_3.

The present invention also provides a process for preparing the compounds of the general formula (I).

According to a first variant of the process according to the invention, the compounds of the general formula (I) are prepared by

reacting compounds of the general formula (II)



(II),

in which the radicals R^1, R^2 and R^3 are as defined above

with compounds of the general formula (III)

$$R^4\text{-}X \quad \text{(III)},$$

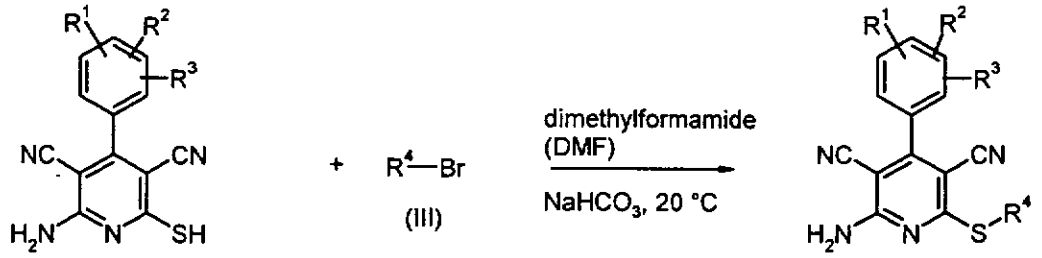
in which R^4 is as defined above

and

X represents a nucleofugic group (preferably halogen, in particular chlorine, bromine or iodine, or mesylate, tosylate, triflate or 1-imidazolyl),

in inert solvents, if appropriate in the presence of a base.

The process described above can be illustrated in an exemplary manner by the equation below:



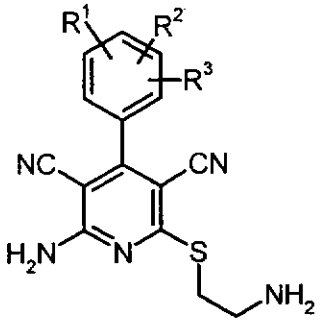
(II) (I)

If the radical R^4 in the general formula (I) has the meaning of

alkyl, substituted by the radicals $-NR^6\text{-}C(O)\text{-}R^8$, $-NR^6\text{-}C(O)\text{-}NR^6R^7$, $-NR^6\text{-}SO_2\text{-}R^8$,

where the radicals R^6, R^7 and R^8 are as defined above,

it is alternatively, according to a second variant of the process according to the invention, also possible to prepare the compounds of the general formula (I) by initially reacting the compounds of the general formula (II) with 2-bromoethylamine to give compounds of the general formula (IV)



(IV)

which are then reacted with compounds of the general formula

R^9-Y (V),

in which

R^9 has the meaning -C(O)-R^8, -C(O)-O-R^8, -C(O)-NR^6R^7, -SO_2-R^8 where R^8 is as defined above

and

Y represents a nucleofugic group, preferably halogen, in particular chlorine, bromine or iodine, or mesylate, tosylate, triflate or 1-imidazolyl,

or else

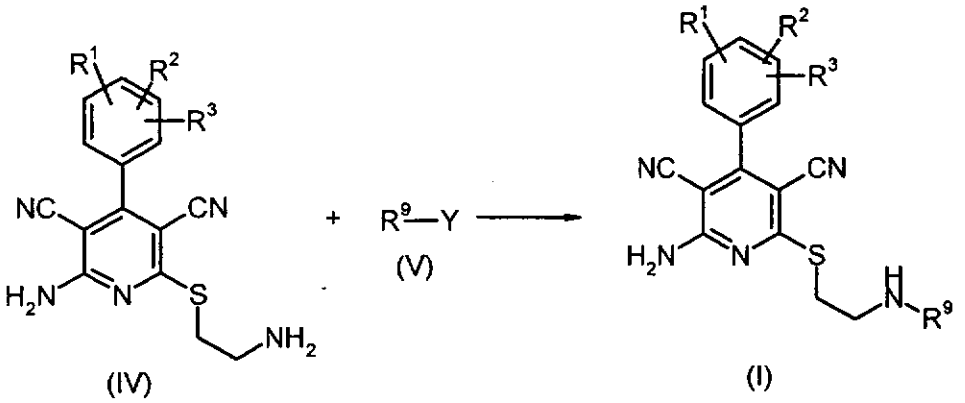
R^9 has the meaning R^6

and

Y represents the group O=C=N-,

in inert solvents, if appropriate in the presence of a base.

The second variant, described above, of the process according to the invention can be illustrated in an exemplary manner by the following equation:



The nucleofugic group X, which is sometimes also referred to as leaving group, can be introduced into the reaction separately or else be generated in situ by customary methods, for example by the "Mitsunobu reaction".

Suitable solvents for the process according to the invention are all organic solvents which are inert under the reaction conditions. These include alcohols such as methanol, ethanol and isopropanol, ketones such as acetone and methyl ethyl ketone, acyclic and cyclic ethers such as diethyl ether and tetrahydrofuran, esters such as ethyl acetate or butyl acetate, hydrocarbons such as benzene, xylene, toluene, hexane or cyclohexane, dimethylformamide, acetonitrile, pyridine, dimethyl sulfoxide (DMSO), chlorinated hydrocarbons such as dichloromethane, chlorobenzene or dichloroethane or hexamethylphosphoric triamide. Water is also suitable for use as solvent. Particular preference is given to dimethylformamide. It is also possible to use mixtures of the solvents mentioned above.

Suitable bases are the customary inorganic or organic bases. These preferably include alkali metal hydroxides, such as, for example, sodium hydroxide or potassium hydroxide, or alkali metal carbonates, such as sodium carbonate or potassium carbonate or sodium bicarbonate or potassium bicarbonate, or sodium methoxide or potassium methoxide or sodium ethoxide or potassium ethoxide or potassium tert-butoxide, or else amides, such as sodium amide, lithium bis-(trimethylsilyl)amide or lithium diisopropylamide, or organometallic compounds, such as butyllithium or phenyllithium, or else amines, such as triethylamine and pyridine. Preference is given to the alkali metal carbonates and alkali metal bicarbonates.

Here, the base can be employed in an amount of from 1 to 10 mol, preferably from 1 to 5 mol, in particular from 1 to 4 mol, based on 1 mol of the compounds of the general formula (II) or (IV).

The reaction generally takes place in a temperature range of from -78°C to reflux temperature. preferably in the range from –78°C to +40°C, in particular at room temperature.

The reaction can be carried out at atmospheric, elevated or reduced pressure (for example in the range from 0.5 to 5 bar). In general, the reaction is carried out at atmospheric pressure.

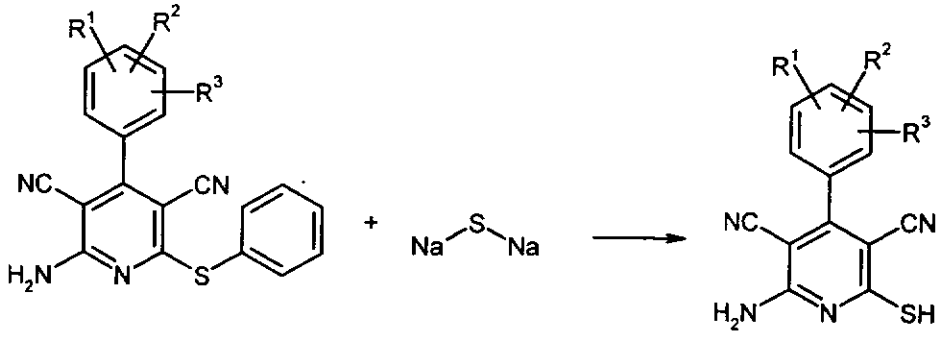
The person skilled in the art is familiar with numerous modifications of the conditions mentioned above which are within the knowledge of the average expert and within the scope of the present invention.

The compounds of the general formulae (II) are likewise known per se to the person skilled in the art or can be prepared by customary methods known from the literature. Reference may be made in particular to the following publications, the respective content of which is expressly incorporated herein by way of reference:

- *Dyachenko et al.*, Russian Journal of Chemistry, Vol. 33, No. 7, 1997, pages 1014-1017 and Vol. 34, No. 4, 1998, pages 557-563;

- *Dyachenko et al.*, Chemistry of Heterocyclic Compounds, Vol. 34, No. 2, 1998, pages 188-194;
- *Qintela et al.*, European Journal of Medicinal Chemistry, Vol. 33, 1998, pages 887-897;
- *Kandeel et al.*, Zeitschrift für Naturforschung 42b, 107-111 (1987).

It is also possible to prepare the compounds of the general formula (II) from compounds of the general formula (VI) by reaction with an alkali metal sulfide. This preparation method can be illustrated in an exemplary manner by the equation below:



(VI) (II)

The alkali metal sulfide used is preferably sodium sulfide in an amount of from 1 to 10 mol, preferably from 1 to 5 mol, in particular from 1 to 4 mol, based on 1 mol of the compounds of the general formula (VI).

Suitable solvents are all organic solvents which are inert under the reaction conditions. These include N,N-dimethylformamide, N-methylpyrrolidinone, hexamethylphosphoric triamide, pyridine and acetonitrile. Particularly preference is given to N,N-dimethylformamide. It is also possible to use mixtures of the solvents mentioned above.

The reaction is generally carried out in a temperature range of from +20°C to reflux temperature, preferably in the range from +20°C to +120°C, in particular at from +60°C to +100°C.

The reaction can be carried out at atmospheric, elevated or reduced pressure (for example in the range from 0.5 to 5 bar). In general, the reaction is carried out at atmospheric pressure.

The person skilled in the art is familiar with numerous modifications of the conditions mentioned above which are within the knowledge of the average expert and within the scope of the present invention.

The compounds of the general formulae (VI) are likewise known per se to the person skilled in the art or can be prepared by customary methods known from the literature. Reference may be made in particular to the publication *Kambe et al., Synthesis, 531 (1981)* the content of which is expressly incorporated herein by way of reference.

The compounds of the general formulae (III) or (V) are either commercially available or known per se to the person skilled in the art or can be prepared by customary methods.

Surprisingly, the compounds of the general formula (I) have an unforeseeable useful pharmacological activity spectrum and are therefore suitable in particular for the prophylaxis and/or treatment of disorders.

This is because it has now been found, unexpectedly, that the substances of the formula (I) above are suitable for the prophylaxis and/or treatment of a large number of disorders, i.e. in particular, for example, disorders of the cardiovascular system (cardiovascular disorders); urogenital disorders; respiratory disorders; inflammatory and neuroinflammatory disorders; diabetes, in particular diabetes mellitus; cancer; and finally also neurodegenerative disorders, such as, for example, Parkinson's disease, and also pain.

In the context of the present invention, cardiovascular disorders are to be understood as meaning, in particular, for example the following disorders: coronary heart disease; hypertension (high blood pressure); restinosis such as, for example,

restinosis after balloon dilatation of peripheral blood vessels; arteriosclerosis; tachycardia; arrhythmias; peripheral and cardiovascular disorders; stable and unstable angina pectoris; and atrial fibrillation.

The compounds of the general formula (I) are furthermore also suitable for reducing the myocardial area effected by an infarct.

The compounds of the general formula (I) are furthermore suitable for the treatment and prophylaxis of thromboembolic disorders and ischemias such as myocardial infarction, stroke and transitory ischemic attacks.

A further area of indication for which the compounds of the general formula (I) are suitable is the prophylaxis and/or therapy of urogenital disorders, such as, for example, irritable bladder, erectile dysfunction and female sexual dysfunction, and additionally also the prophylaxis and/or treatment of inflammatory disorders, such as, for example, asthma and inflammable dermatoses, of neuroinflammatory disorders of the central nervous system, such as, for example, conditions after cerebral infarction, Alzheimer's disease, furthermore also neurodegenerative disorders such as Parkinson's disease, and also pain.

A further area of indication is respiratory disorders such as, for example, asthma, chronic bronchitis, pulmonary emphysema, bronchiectases, cystic fibrosis (mucoviscidosis) and pulmonary hypertension.

The compounds of the general formula (I) are furthermore also suitable for the prophylaxis and/or therapy of hepatic fibrosis and cirrhosis of the liver.

Finally, the compounds of the general formula (I) are also suitable for the prophylaxis and/or therapy of diabetes, in particular diabetes mellitus.

Accordingly, the present invention also relates to the use of the substances of the general formula (I) for preparing medicaments and pharmaceutical compositions for the prophylaxis and/or treatment of the clinical features mentioned above.

The present invention furthermore relates to a method for the prophylaxis and/or the treatment of the clinical pictures mentioned above using substances of the general formula (I).

The pharmaceutical activity of the abovementioned compounds of the general formula (I) can be explained by their action as selective ligands on individual subtypes or a plurality of subtypes of the adenosine receptors, in particular as selective ligands on adenosine A1, adenosine A2a and/or adenosine A2b receptors, preferably as selective ligands on adenosine A1 and/or adenosine A2b receptors.

In the context of the present invention, "selective" are adenosine receptor ligands where, firstly, a clear effect on one or more adenosine receptor subtypes and, secondly, no or a considerably weaker effect on one or more other adenosine receptor subtypes can be observed, where, with respect to the test methods for the selectivity of action, reference is made to the test methods described in section A. II.

Compared to adenosine receptor ligands of the prior art, the substances of the general formula (I) are much more selective. Thus, for example, compounds of the general formula (I) in which R^4 represents $(C_1\text{-}C_4)$-alkyl which is substituted by a group of the formula $-C(O)NR^6R^7$, where R^6 and R^7 are identical or different and are hydrogen or optionally substituted $(C_1\text{-}C_3)$-alkyl, are generally selective on adenosine A2b receptors.

On the other hand, compounds of the general formula (I) in which R^4 represents $(C_1\text{-}C_4)$-alkyl substituted by one or more hydroxyl groups generally act selectively on adenosine A1 receptors.

Compounds of the general formula (I) in which R^4 represents (C_1-C_4)-alkyl substituted by imidazolyl or optionally substituted benzyl, in turn, generally act selectively on adenosine A1 and adenosine A2b receptors.

This receptor selectivity can be determined by biochemical measurement of the intracellular messenger cAMP in cells which specifically only express one subtype of the adenosine receptors. In the case of agonists, an increase in the intracellular cAMP concentration is observed; in the case of antagonists, a decrease in the intracellular cAMP concentration after prior stimulation with adenosine or adenosine-like substances is observed (see the publications B. Kull, G. Arslan, C. Nilsson, C. Owman, A. Lorenzen, U. Schwabe, B.B. Fredholm, "Differences in the order of potency for agonists but not antagonists at human and rat adenosine A2A receptors", *Biochem. Pharmacol.*, **57** (1999) pages 65-75; and S.P. Alexander, J. Cooper, J. Shine, S.J. Hill, "Characterization of the human brain putative A2B adenosine receptor expressed in Chinese hamster ovary (CHO.A2B4) cells", *Br. J. Pharmacol.*, **119** (1996) pages 1286-90, the respective disclosure of which is hereby expressly incorporated by way of reference).

Accordingly, the present invention also provides the use of selective adenosine receptor ligands, in particular of selective adenosine A1, adenosine A2a and/or adenosine A2b receptor ligands, for preparing medicaments and pharmaceutical compositions for the prophylaxis and/or treatment of disorders, in particular, for example, disorders of the cardiovascular system (cardiovascular disorders); urogenital disorders; inflammatory and neuroinflammatory disorders; neurodegenerative disorders; respiratory disorders; hepatic fibrosis, cirrhosis of the liver; cancer; and finally diabetes, in particular diabetes mellitus, where, with respect to the individual areas of indication, reference is also made to what has been said above.

Thus, compounds of the general formula (I) which bind selectively to adenosine A1 receptors are preferably suitable for myocardial protection and for the prophylaxis and/or treatment of tachycardias, atrial arrhythmias, cardiac insufficiency, of acute

kidney failure, diabetes and of pain. Compounds of the general formula (I) which bind selectively to adenosine A2a receptors, on the other hand, are preferably suitable for the prophylaxis and/or treatment of thromboembolic disorders, of neurodengenerative disorders such as Parkinson's disease and also for wound healing. Compounds of the general formula (I) which bind selectively to adenosine A2b receptors, in turn, are preferably suitable for the prophylaxis and/or therapy of hepatic fibrosis, of myocardial infarction, of neuroinflammatory disorders, Alzheimer's disease, of urogenital incontinence and also of respiratory disorders such as, for example, asthma and chronic bronchitis.

The present invention also provides medicaments and pharmaceutical compositions comprising at least one selective adenosine and/or adenosine A2b receptor ligand, preferably at least one compound of the general formula (I), together with one or more pharmacologically acceptable excipients or carriers, and their use for the purposes mentioned above.

Suitable for administering the compounds of the general formula (I) are all customary administration forms, i.e. oral, parenteral, inhalative, nasal, sublingual, rectal or external, such as, for example, transdermal, with particular preference oral or parenteral. In the case of parenteral administration, particular mention may be made of intravenous, intramuscular and subcutaneous administration, for example as a subcutaneous depot. Very particular preference is given to oral administration.

Here, the active compounds can be administered on their own or in the form of preparations. Suitable preparations for oral administration are inter alia tablets, capsules, pellets, sugar-coated tablets, pills, granules, solid and liquid aerosols, syrups, emulsions, suspensions and solutions. Here, the active compound has to be present in such a quantity that a therapeutic effect is obtained. In general, the active compound can be present in a concentration of from 0.1 to 100% by weight, in particular from 0.5 to 90% by weight, preferably from 5 to 80% by weight. In particular, the concentration of the active compound should be 0.5-90% by weight,

i.e. the active compound should be present in quantitites sufficient to achieve the dosage range mentioned.

To this end, the active compounds can be converted in a manner known per se into the customary preparations. This is achieved using inert nontoxic pharmaceutically suitable carriers, excipients, solvents, vehicles, emulsifiers and/or dispersants.

Excipients which may be mentioned are, for example: water, nontoxic organic solvents such as, for example, paraffins, vegetable oils (for example sesame oil), alcohols (for example ethanol, glycerol), glycols (for example polyethylene glycol), solid carriers, such as natural or synthetic ground minerals (for example talc or silicates), sugars (for example lactose), emulsifiers, dispersants (for example polyvinylpyrrolidone) and glidants (for example magnesium sulfate).

In the case of oral administration, tablets may, of course, also contain additives such as sodium citrate, together with adjuvants such as starch, gelatin and the like. Aqueous preparations for oral administration may furthermore be admixed with flavor enhancers or colorants.

In general, it has been found to be advantageous to administer, in the case of parenteral administration, quantities of from about 0.1 to about 10 000 µg/kg, preferably from about 1 to about 1 000 µg/kg, in particular from about 1 µg/kg to about 100 µg/kg, of bodyweight, to obtain effective results. In the case of oral administration, the quantity is from about 0.1 to about 10 mg/kg, preferably from about 0.5 to about 5 mg/kg, in particular from about 1 to about 4 mg/kg, of bodyweight.

In spite of this, it may still be required, depending on bodyweight, administration route, individual response to the active compound, the type of preparation and the time or interval at which administration takes place, to deviate from the quantities mentioned.

The present invention is illustrated by the examples below; however, these examples are only intended to facilitate a better understanding of the invention and not to restrict the invention in any way.

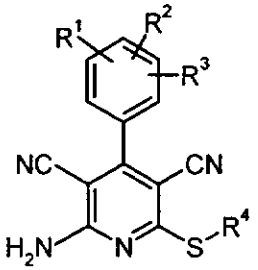
A. Evaluation of the physiological activity

I. Demonstration of the cardiovascular action

Langendorff heart of the rat:

After opening the thoracic cage of anesthetized rats, the heart is removed quickly and introduced into a conventional Langendorff apparatus. The coronary arteries are perfused at a constant volume (10 ml/min), and the resulting perfusion pressure is recorded via an appropriate pressure sensor. In this arrangement, a decrease of the perfusion pressure corresponds to a relaxation of the coronary arteries. At the same time, the pressure which is developed by the heart during each contraction is measured via a balloon introduced into the left ventricle and a further pressure sensor. The frequency of the isolated beating heart is calculated from the number of contractions per time unit.

In this test arrangement, the following values were obtained for the coronary perfusion pressure (the stated percentage refers to the reduction of the coronary perfusion pressure in percent at the respective concentration):

	Reduction of the coronary perfusion pressure in percent at a concentration of	
Compound of the formula (I) used 	**10^{-7} g/ml**	**10^{-6} g/ml**
$R^1 = R^2 = H$ R^3 = para-CH_3 R^4 = -CH_2-CH(OH)(CH_2OH) (compound of example A 198)	no effect observed	about 26%
$R^1 = R^2 = H$ R^3 = para-CH_3 R^4 = -CH_2-phenyl (compound of example A 189)	no effect observed	about 37%
$R^1 = R^2 = H$ R^3 = meta-OH R^4 = -CH_2-CH_2OH (compound of example A 43)	about 42%	about 68%
$R^1 = R^2 = H$ R^3 = para-OH R^4 = -CH_2-CH_2OH (compound of example 21)	about 40%	about 75%
$R^1 = R^2 = H$ R^3 = para-OH R^4 = 2-imidazolylmethyl (compound of example A 379)	about 64%	about 63%

At the stated concentrations, the substances tested had no effect on the pressure developed during the contraction in the left ventricle and no effect on the heart rate. Thus, it was demonstrated that the substances act selectively only on coronary perfusion.

II. Demonstration of the receptor selectivity (adenosine A1, A2a, A2b and A3 receptor selectivity)

Cells of the permanent line CHO (Chinese Hamster Ovary) were stably transfected with cDNA for the adenosine receptor subtypes A1, A2a, A2b and A3. Binding of the substances to the A2a or A2b receptor subtypes was determined by measuring the intracellular cAMP concentration in these cells using a conventional radioimmunological assay (cAMP-RIA, IBL GmbH, Hamburg, Germany).

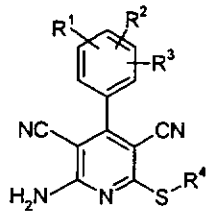
In the case of the action of the substances as agonists, binding of the substances is expressed in an increase of the intracellular cAMP concentration. In these experiments, the adenosine analogue NECA (5-N-ethylcarboxamido-adenosine), which binds unselectively, but with high affinity, to all adenosine receptor subtypes and has agonistic action (Klotz, K.N., Hessling, J., Hegler, J., Owman, C., Kull, B., Fredholm, B.B., Lohse, M.J., Comparative pharmacology of human adenosine receptor subtypes - characterization of stably transfected receptors in CHO cells, Naunyn Schmiedebergs Arch Pharmacol, 357 (1998), 1-9) was used as reference compound.

The adenosine receptors A1 and A3 are coupled to a Gi protein, i.e. stimulation of these receptors results in an inhibition of adenylate cyclase and thus a reduction of the intracellular cAMP level. To identify A1/A3 receptor agonists, the adenylate cyclase is stimulated using forskolin. However, additional stimulation of the A1/A3 receptors inhibits adenylate cyclase, so that it is possible to detect A1/A3 receptor agonists by a comparatively low concentration of cAMP in the cell.

To demonstrate an antagonistic effect on adenosine receptors, the recombinant cells transfected with the corresponding receptor were prestimulated with NECA, and the effect of the substances on a reduction of the intracellular cAMP concentration by this prestimulation was examined. In these experiments, XAC (xanthine amine congener), which binds unselectively, but with high affinity, to all adenosine receptor subtypes and has antagonistic action (Müller, C.E., Stein, B., Adenosine receptor

antagonists: structures and potential therapeutic applications, Current Pharmaceutical Design, 2 (1996), 501-530) was used as reference compound.

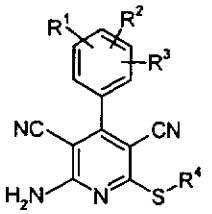
In the experiments below, the intracellular cAMP concentration in CHO cells which had been transfected with cDNA for the A2b receptor was determined. What is stated is the cAMP concentration in percent in all cells in a well of a microtiter plate, based on the control value obtained without any substances acting on the cells:

	Concentration of intracellular cAMP in percent at a concentration of				
Compound of the formula (I) used 	**10^{-9} M**	**10^{-8} M**	**10^{-7} M**	**10^{-6} M**	**10^{-5} M**
NECA (reference)	363	340	858	1226	1263
$R^1 = R^2 = H$ R^3 = para-OH $R^4 = -CH_2-C(O)NH_2$ (compound of example A 1)			837	947	900
$R^1 = R^2 = H$ R^3 = para-OH $R^4 = -CH_2-CH_2OH$ (compound of example 21)			253	432	384
$R^1 = R^2 = H$ R^3 = meta-OH $R^4 = -CH_2-CH_2OH$ (compound of example A 43)			347	674	784
$R^1 = R^2 = H$ R^3 = meta-OH $R^4 = -CH_2-CH(CH3)OH$ (compound of example A 46)			463	716	753
$R^1 = R^2 = H$ $R^3 = H$ $R^4 = -CH_2-CH_2OH$ (compound of example A 104)	100	178	438	586	571
$R^1 = R^2 = H$ R^3 = para-OH R^4 = 2-imidazolylmethyl (compound of example A 379)	870	846	861	936	1140

In these experiments, it was possible to block the action of all substances by the antagonist XAC, which is unselective, but highly specific for adenosine receptors.

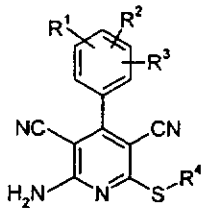
In the experiments below, the intracellular cAMP concentration in CHO cells which had been transfected with cDNA for the A2a receptor was determined. What is stated is the cAMP concentration in percent in all cells in a well of a microtiter plate, based on the control value obtained without any substances acting on the cells:

5

	Concentration of intracellular cAMP in percent at a concentration of				
Compound of the formula (I) used 	**10^{-9} M**	**10^{-8} M**	**10^{-7} M**	**10^{-6} M**	**10^{-5} M**
NECA (reference)	585	800	1301	1992	2075
$R^1 = R^2 = H$ R^3 = para-OH R^4 = $-CH_2-C(O)NH_2$ (compound of example A 1)			92	117	208
$R^1 = R^2 = H$ R^3 = para-OH R^4 = $-CH_2-CH_2OH$ (compound of example 21)			143	117	
$R^1 = R^2 = H$ R^3 = meta-OH R^4 = $-CH_2-CH_2OH$ (compound of example A 43)			117	200	317
$R^1 = R^2 = H$ R^3 = meta-OH R^4 = $-CH_2-CH(CH3)OH$ (compound of example A 46)			67	108	183
$R^1 = R^2 = H$ $R^3 = H$ R^4 = $-CH_2-CH_2OH$ (compound of example A 104)	104	107	107	146	212
$R^1 = R^2 = H$ R^3 = para-OH R^4 = 2-imidazolylmethyl (compound of example A 379)	93	160	218	235	291

In these experiments, it was possible to block the action of all substances by the antagonist XAC, which is unselective, but highly specific for adenosine receptors.

In the following experiments, the intracellular cAMP concentration in CHO cells transfected with the cDNA for the A1 receptor was determined. What is stated is the cAMP concentration in percent in all cells of a well of a microtiter plate, based on the control value obtained without the action of any substance but after prestimulation with 1 µM of forskolin for 15 min (in these measurements, the cAMP concentration without prestimulation with forskolin is 18%):

	Concentration of intracellular cAMP in percent at a concentration of		
Compound of the formula (I) used 	**10^{-7} M**	**10^{-6} M**	**10^{-5} M**
NECA (reference)	24	24	28
$R^1 = R^2 = H$ R^3 = meta-OH R^4 = $-CH_2-CH_2OH$ (compound of example A 43)	18	24	22
$R^1 = R^2 = H$ $R^3 = H$ R^4 = $-CH_2-CH_2OH$ (compound of example A 104)	28	23	21
$R^1 = R^2 = H$ R^3 = para-OH R^4 = 2-imidazolylmethyl (compound of example A 379)	34	34	35

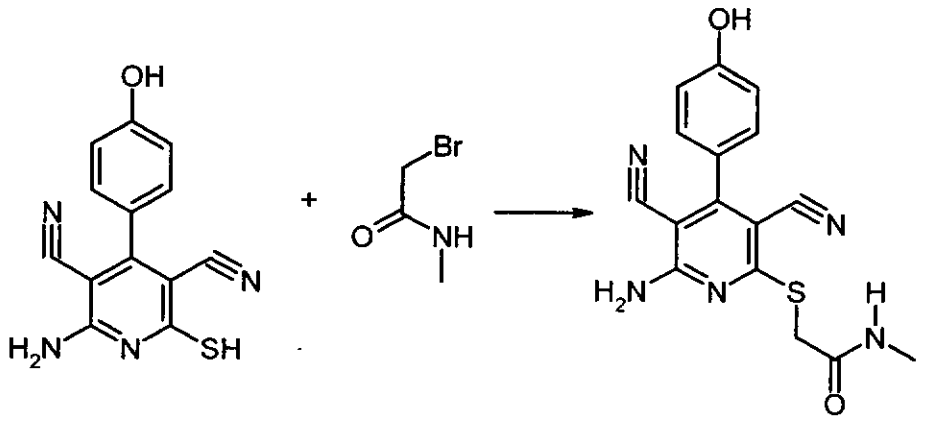
Thus, the compound of example A 1 has a clear agonistic effect on cells which express the adenosine receptor A2b and virtually no effect on cells with the A2a receptor. In contrast, the compounds from example A 43 and A 104 have a clear agonistic effect on cells with the A 1 receptor, virtually no effect on cells with A2a receptors and a considerably weaker effect on cells with the A2b receptor and are therefore selective adenosine A1 receptor agonists. The compound of example A 379, on the other hand, has a clear agonistic effect on cells with the A2b receptor,

virtually no effect on cells with A2a receptors and a comparably weaker effect on cells with the A1 receptor and is thus a selective adenosine A2b receptor agonist.

B. Synthesis examples

Example 1

2-{[6-Amino-3,5-dicyano-4-(4-hydroxyphenyl)-2-pyridinyl]sulfanyl}-N-methyl-acetamide



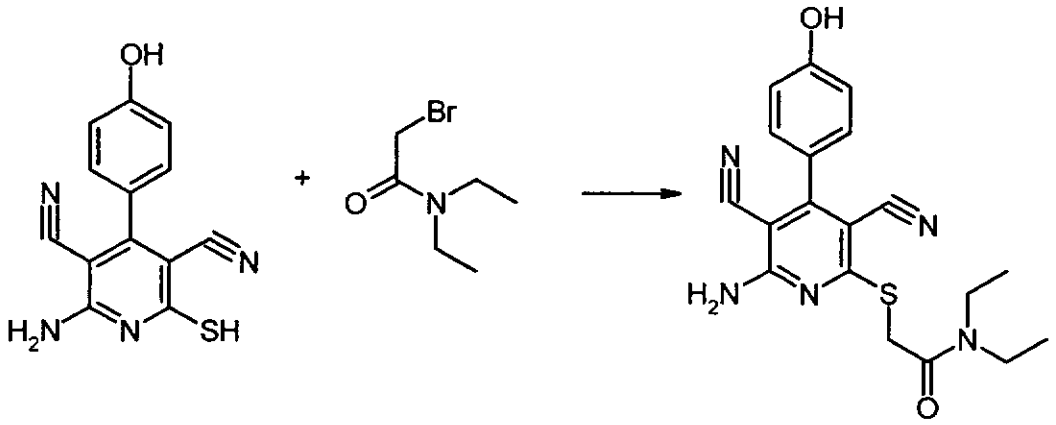
At room temperature (RT), 53.6 mg (0.2 mmol) of 2-amino-4-(4-hydroxyphenyl)-6-sulfanyl-3,5-pyridinedicarbonitrile and 45.6 mg (0.3 mmol) of N-methylbromo-acetamide are stirred in 0.5 ml of dimethylformamide (DMF) together with 33.6 mg (0.4 mmol) of $NaHCO_3$ for 4 hours. Thin-layer chromatography (TLC) (CH_2Cl_2/CH_3OH 10:1) shows complete conversion. The entire mixture is diluted with water and ethyl acetate (EA) and the EA phase is dried with $MgSO_4$ and concentrated under reduced pressure. The residue crystallizes from methanol.

Yield: 45 mg (66.3% of theory), white crystals

Mass spectrum: molecular mass calculated: 339, found $[M+H]^+$=340.3

Example 2

2-{[6-Amino-3,5-dicyano-4-(4-hydroxyphenyl)-2-pyridinyl]sulfanyl}-N,N-diethylacetamide



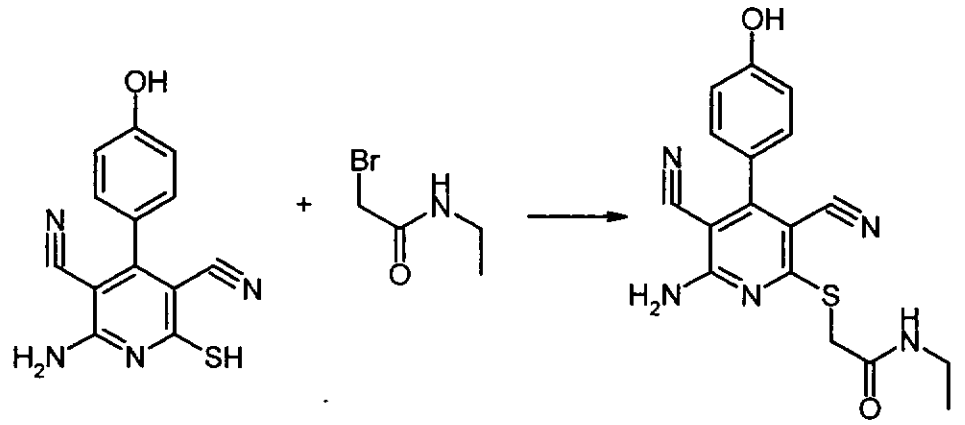
At RT, 53.6 mg (0.2 mmol) of 2-amino-4-(4-hydroxyphenyl)-6-sulfanyl-3,5-pyridinedicarbonitrile and 58.2 mg (0.3 mmol) of N,N-diethylbromoacetamide are stirred in 0.5 ml of DMF together with 33.6 mg (0.4 mmol) of $NaHCO_3$ for 4 hours. TLC (CH_2Cl_2/CH_3OH 10:1) shows complete conversion. The entire mixture is diluted with water and ethyl acetate and the EA phase is dried with $MgSO_4$ and concentrated under reduced pressure. The residue crystallizes from methanol.

Yield: 50 mg (65.5% of theory), white crystals

Mass spectrum: molecular mass calculated: 381, found $[M+H]^+=382$

Example 3

2-{[6-Amino-3,5-dicyano-4-(4-hydroxyphenyl)-2-pyridinyl]sulfanyl}-N-ethylacetamide



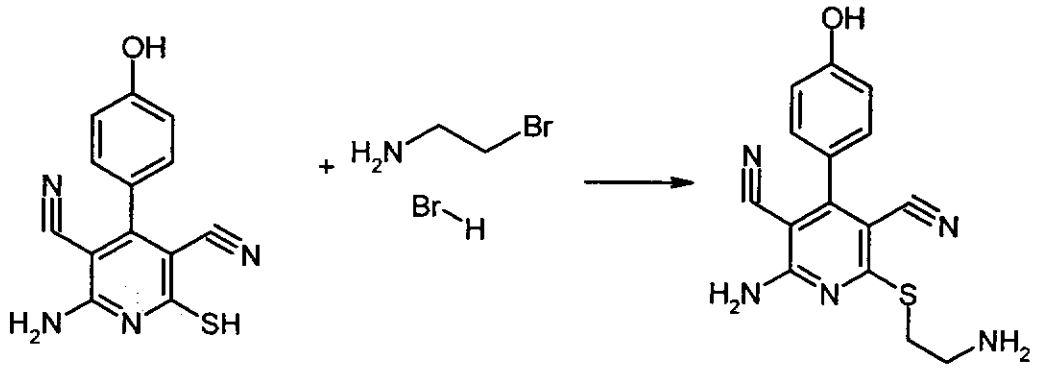
At RT 0.76 g (2 mmol) of 2-amino-4-(4-hydroxyphenyl)-6-sulfanyl-3,5-pyridinedicarbonitrile and 0.5 g (3 mmol) of N-ethylbromoacetamide are stirred in 5 ml of DMF together with 0.34 g (4 mmol) of $NaHCO_3$ for 4 hours. After dilution with water, the mixture is extracted with ethyl acetate and the ethyl acetate phase is dried with $MgSO_4$ and concentrated under reduced pressure. The solid residue obtained after concentration is stirred with methanol. The crystals are filtered off with suction and dried under reduced pressure.

Yield: 0.49 g (69.5% of theory), crystals

Mass spectrum: molecular mass calculated: 353, found $[M+H]^+$=354.2

Example 4

2-Amino-6-[(2-aminoethyl)sulfanyl]-4-(4-hydroxyphenyl)-3,5-pyridinedicarbonitrile



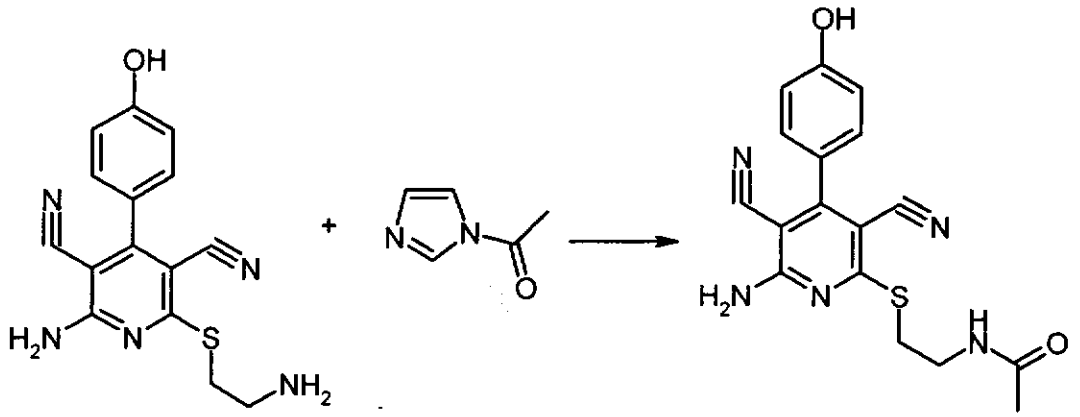
268 mg (1 mmol) of 2-amino-4-(4-hydroxyphenyl)-6-sulfanyl-3,5-pyridinedicarbonitrile, 105 mg (1 mmol) of 2-bromoethylamine hydrobromide and 168 mg (2 mmol) of $NaHCO_3$ are stirred in 1 ml of DMF for 1 hour. The entire mixture is diluted with a few milliliters of 1N HCl. The crystals are filtered off with suction and dried under reduced pressure.

Yield: 200 mg (64.2% of theory), yellow crystals

Mass spectrum: molecular mass calculated: 311, found $[M+H]^+=312$

Example 5

N-(2-{[6-Amino-3,5-dicyano-4-(4-hydroxyphenyl)-2-pyridinyl]sulfanyl}ethyl)-acetamide



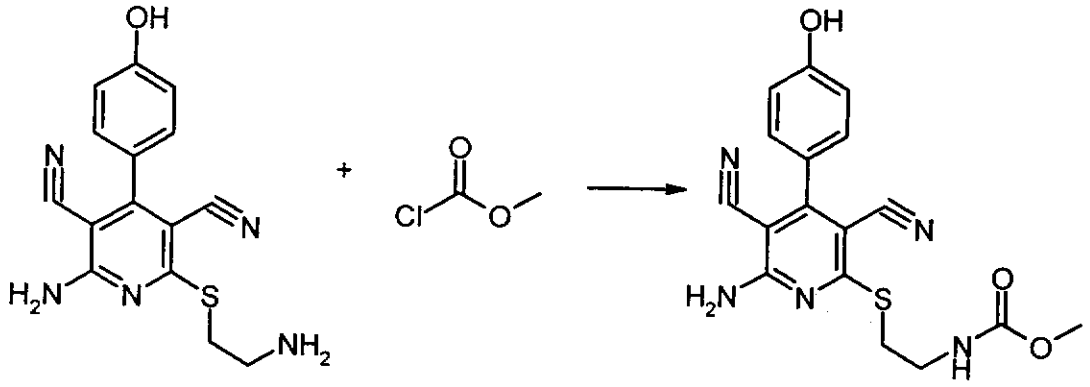
At RT 60 mg (0.2 mmol) of 2-amino-6-[(2-aminoethyl)sulfanyl]-4-(4-hydroxyphenyl)-3,5-pyridinedicarbonitrile and 30 mg (0.3 mmol) of N-acetylimidazole are stirred in 0.5 ml of DMF for 1 hour. Water is slowly added dropwise, the mixture becomes slightly turbid and the crude product crystallizes out. The product is filtered off with suction, washed with water and dried under reduced pressure. This gives 53 mg of yellow crystals. The crystals are dissolved in 1 ml of a 1:1 mixture of CH_2Cl_2/CH_3OH, and a few drops of concentrated ammonia are added (removal of diacetylated byproduct). The mixture is stirred at RT for 5 hours. The product crystallizes out when the reaction solution is concentrated. The product is filtered off with suction and washed with methanol.

Yield: 37 mg (52.3% of theory), almost white crystals

Mass spectrum: molecular mass calculated: 353, found $[M+H]^+=354$

Example 6

2-{[6-Amino-3,5-dicyano-4-(4-hydroxyphenyl)-2-pyridinyl]sulfanyl}methyl-carbamate



Under argon, 31.1 mg (0.1 mmol) of 2-amino-6-[(2-aminoethyl)sulfanyl]-4-(4-hydroxyphenyl)-3,5-pyridinedicarbonitrile are suspended at RT in 1 to 2 ml of dichloromethane, and the mixture is cooled to from -20 to –25°C. At this temperature, 30.3 mg (0.3 mmol) of triethylamine and 28,3 mg (0.3 mmol) of methyl chloroformate are added. The mixture is stirred at –20 C for 30 minutes and then allowed to warm to 0°C over a period of 1 hour. The mixture is concentrated under reduced pressure, 4 ml of a 2 molar NH_3 solution in methanol are added and the mixture is stirred at RT for 1 hour. The mixture is then concentrated, dissolved in 600 µl of DMSO and purified by preparative HPLC.

HPLC conditions:

Column: GROM-SIL 120 ODS 4 HE 5µ 50 X 20 mm

Precolumn: GROM-SIL ODS 4 HE 15µ 10 X 20 mm

Wavelength: 220 nm

Flow rate: 25 ml/min

Gradient: A = acetonitrile + 0.1% trifluoroacetic acid

B = water + 0.1% trifluoroacetic acid

0 min: 10% A; 1.75 min. 10% A; 5.5 min. 90% A; 8 min. 90% A;

8.1 min. 10% A; 9 min. 10% A

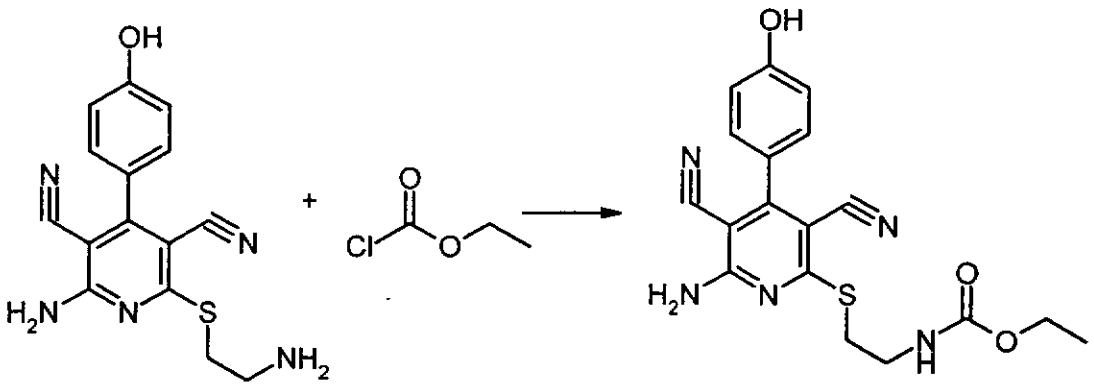
Injection volume: 600 µl of DMSO solution

Yield: 21.7 mg (58.7% of theory) of product

Mass spectrum: molecular mass calculated: 369, found $[M+H]^+$=370.1

Example 7

2-{[6-Amino-3,5-dicyano-4-(4-hydroxyphenyl)-2-pyridinyl]sulfanyl}ethyl-carbamate



Under argon, 31.1 mg (0.1 mmol) of 2-amino-6-[(2-aminoethyl)sulfanyl]-4-(4-hydroxyphenyl)-3,5-pyridinedicarbonitrile are suspended at RT in 1 to 2 ml of dichloromethane, and the mixture is cooled to from -20 to -25°C. At this temperature, 30.3 mg (0.3 mmol) of triethylamine and 32.6 mg (0.3 mmol) of ethyl chloroformate are added. The mixture is stirred at -20°C for 30 minutes and then allowed to warm to 0°C over a period of 1 hour. The mixture is concentrated under reduced pressure, 4 ml of a 2 molar NH_3 solution in methanol are added and the mixture is stirred at RT for 1 hour. The mixture is then concentrated, dissolved in 600 µl of DMSO and purified by preparative HPLC.

HPLC conditions:

Column: GROM-SIL 120 ODS 4 HE 5µ 50 X 20 mm

Precolumn: GROM-SIL ODS 4 HE 15µ 10 X 20 mm

Wavelength: 220 nm

Flow rate: 25 ml/min

Gradient: A = acetonitrile + 0.1% trifluoroacetic acid

B= water + 0.1% trifluoroacetic acid

0 min: 10% A; 1.75 min. 10% A; 5.5 min. 90% A; 8 min. 90% A;

8.1 min. 10% A; 9 min. 10% A

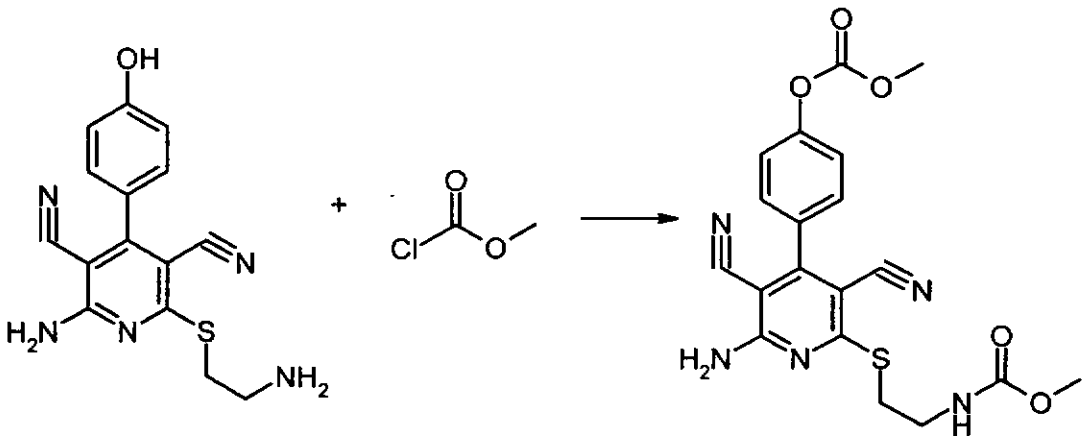
Injection volume: 600 µl of DMSO solution

Yield: 20.5 mg (53.5% of theory) of product

Mass spectrum: molecular mass calculated: 383, found $[M+H]^+$=384.2

Example 8

4-[2-Amino-3,5-dicyano-6-({2-[(methoxycarbonyl)amino]ethyl}sulfanyl)-4-pyridinyl]phenyl-methylcarbonate



Under argon, 31.1 mg (0.1 mmol) of 2-amino-6-[(2-aminoethyl)sulfanyl]-4-(4-hydroxyphenyl)-3,5-pyridinedicarbonitrile are suspended at RT in 1 to 2 ml of dichloromethane, and the mixture is cooled to from -20 to -25°C. At this temperature, 10.1 mg (0.1 mmol) of triethylamine and 9.4 mg (0.1 mmol) of methyl chloroformate are added. The mixture is stirred at -20°C for 30 minutes and then allowed to warm to 0°C over a period of 1 hour. The mixture is then concentrated dissolved in 600 µl of DMSO and purified by preparative HPLC.

HPLC conditions:

Column: GROM-SIL 120 ODS 4 HE 5µ 50 X 20 mm

Precolumn: GROM-SIL ODS 4 HE 15µ 10 X 20 mm

Wavelength: 220 nm

Flow rate: 25 ml/min

Gradient: A = acetonitrile + 0.1% trifluoroacetic acid

B= water + 0.1 % trifluoroacetic acid

0 min: 10% A; 1.75 min. 10% A; 5.5 min. 90% A; 8 min. 90% A;

8.1 min. 10% A; 9 min. 10% A

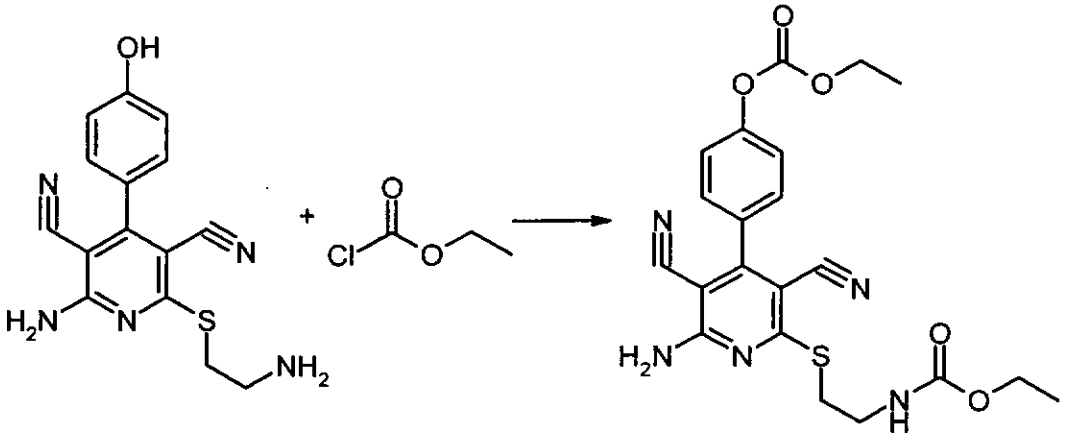
Injection volume: 600 µl of DMSO solution

Yield: 11.2 mg (26.2% of theory) of product

Mass spectrum: molecular mass calculated: 427, found $[M+H]^+$= 428.2

Example 9

4-[2-Amino-3,5-dicyano-6-({2-[(methoxycarbonyl)amino]ethyl}sulfanyl)-4-pyridinyl]phenyl-ethylcarbonate



Under argon 31.1 mg (0.1 mmol) of 2-amino-6-[(2-aminoethyl)sulfanyl]-4-(4-hydroxyphenyl)-3,5-pyridinedicarbonitrile are suspended at RT in 1 to 2 ml of dichloromethane, and the mixture is cooled to from -20 to –25°C. At this temperature, 10.1 mg (0.1 mmol) of triethylamine and 10.9 mg (0.1 mmol) of ethyl chloroformate are added. The mixture is stirred at–20°C for 30 minutes and then allowed to warm to 0°C over a period of 1 hour. The mixture is then concentrated, dissolved in 600 µl of DMSO and purified by preparative HPLC.

HPLC conditions:

Column: GROM-SIL 120 ODS 4 HE 5µ 50 X 20 mm

Precolumn: GROM-SIL ODS 4 HE 15µ 10 X 20 mm

Wavelength: 220 nm

Flow rate: 25 ml/min

Gradient: A = acetonitrile + 0.1% trifluoroacetic acid

B= water + 0.1% trifluoroacetic acid

0 min: 10% A; 1.75 min. 10% A; 5.5 min. 90% A; 8 min. 90% A;

8.1 min. 10% A; 9 min. 10% A

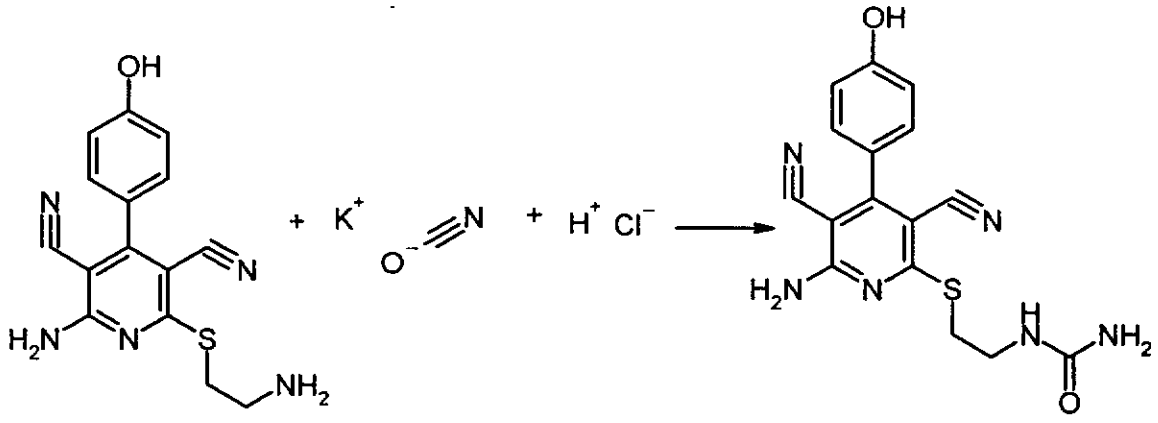
Injection volume: 600 µl of DMSO solution

Yield: 15.2 mg (33.4% of theory) of product

Mass spectrum: molecular mass calculated: 455, found $[M+H]^+$= 456.2

Example 10

N-(2-{[6-Amino-3,5-dicyano-4-(4-hydroxyphenyl)-2-pyridinyl]sulfanyl}-ethyl)urea



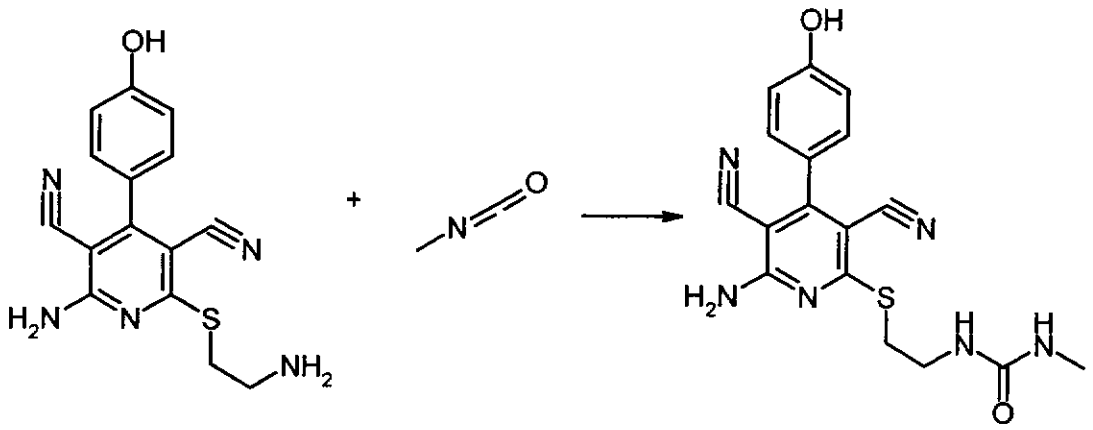
31.1 mg (0.1 mmol) of 2-amino-6-[(2-aminoethyl)sulfanyl]-4-(4-hydroxyphenyl)-3,5-pyridinedicarbonitrile are suspended in 0.91 ml of 1N HCl, and 8.1 mg (0.1 mmol) of potassium cyanate are added. After the addition of a few drops of methanol, the mixture is stirred at 50°C for a total of 10 hours. The crystals are filtered off with suction and washed with water and ether.

Yield: 16 mg (45.1% of theory) of product

Mass spectrum: molecular mass calculated: 354, found $[M+H]^+$= 355.1

Example 11

N-(2-{[6-Amino-3,5-dicyano-4-(4-hydroxyphenyl)-2-pyridinyl]sulfanyl}ethyl)-N'-methylurea



62.2 mg (0.2 mmol) of 2-amino-6-[(2-aminoethyl)sulfanyl]-4-(4-hydroxyphenyl)-3,5-pyridinedicarbonitrile are suspended in 0.4 ml of DMF, and 11.4 mg (0.2 mmol) of methyl isocyanate are added at room temperature. The mixture is stirred overnight, filtered and purified by preparative HPLC.

HPLC conditions:

Column: GROM-SIL 120 ODS 4 HE 5µ 50 X 20 mm

Precolumn: GROM-SIL ODS 4 HE 15µ 10 X 20 mm

Wavelength: 220 nm

Flow rate: 25 ml/min

Gradient: A = acetonitrile + 0.1% trifluoroacetic acid

B= water + 0.1% trifluoroacetic acid

0 min: 10% A; 1.75 min. 10% A; 5.5 min. 90% A; 8 min. 90% A;

8.1 min. 10% A; 9 min. 10% A

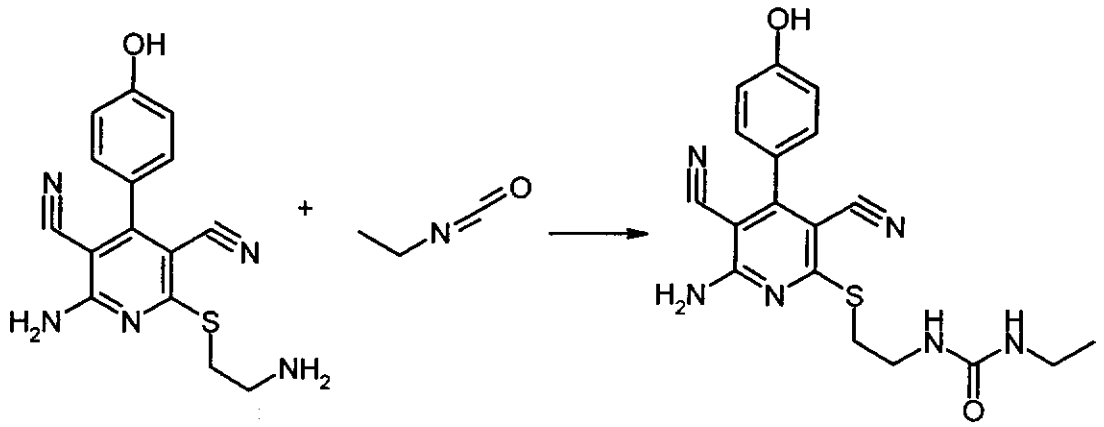
Injection volume: 400 µl of DMF solution

Yield: 45.9 mg (62.3% of theory) of product

Mass spectrum: molecular mass calculated: 368, found $[M+H]^+$=369.2

Example 12

N-(2-{[6-amino-3,5-dicyano-4-(4-hydroxyphenyl)-2-pyridinyl]sulfanyl}ethyl)-N'-methylurea



62.2 mg (0.2 mmol) of 2-amino-6-[(2-aminoethyl)sulfanyl]-4-(4-hydroxyphenyl)-3,5-pyridinedicarbonitrile are suspended in 0.4 ml of DMF, and 14.2 mg (0.2 mmol) of ethyl isocyanate are added at room temperature. The mixture is stirred overnight, filtered and purified by preparative HPLC.

HPLC conditions:

Column: GROM-SIL 120 ODS 4 HE 5µ 50 X 20 mm

Precolumn: GROM-SIL ODS 4 HE 15µ 10 X 20 mm

Wavelength: 220 nm

Flow rate: 25 ml/min

Gradient: A = acetonitrile + 0.1% trifluoroacetic acid

B= water + 0.1% trifluoroacetic acid

0 min: 10% A; 1.75 min. 10% A; 5.5 min. 90% A; 8 min. 90% A;

8.1 min. 10% A; 9 min. 10% A

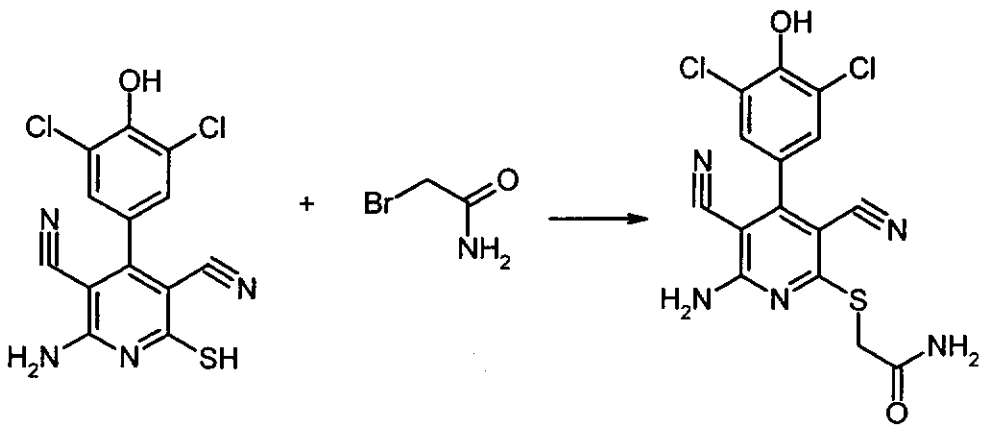
Injection volume: 400 µl of DMF solution

Yield: 37.6 mg (49.2 % of theory) of product

Mass spectrum: molecular mass calculated: 382, found $[M+H]^+$=383.2

Example 13

3,5-Dicyano-4-(3,5-dichloro-4-hydroxyphenyl)-2-carbamoylmethyl-6-amino-pyridine



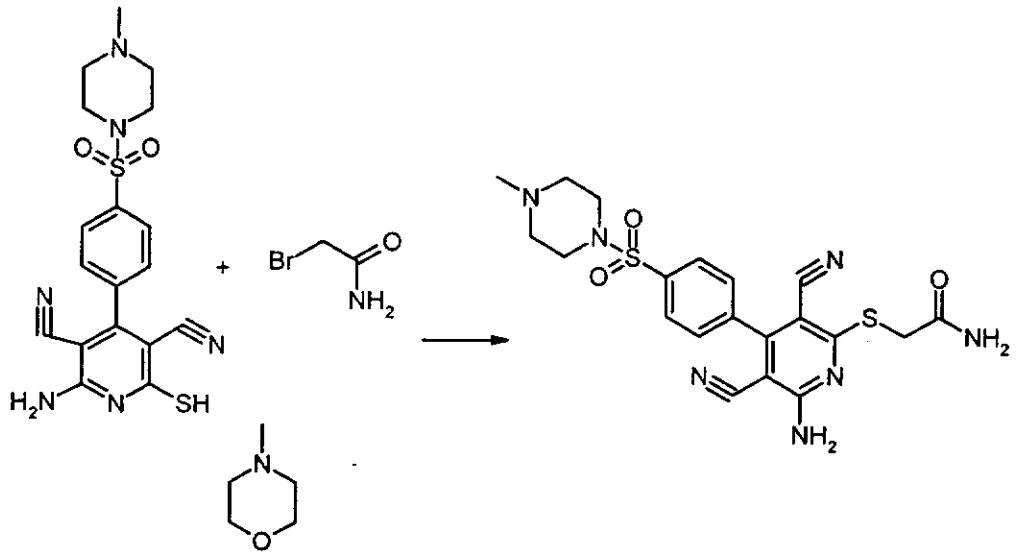
337.2 mg (1 mmol) of 2-amino-4-(3,5-dichloro-4-hydroxyphenyl)-6-sulfanyl-3,5-pyridinedicarbonitrile and 207 mg (1.5 mmol) of bromoacetamide are dissolved in 4 ml of DMF, 336 mg (4 mmol) of $NaHCO_3$ are added and the mixture is stirred at RT for 8 hours. The mixture is diluted with water and washed with ethyl acetate. The aqueous phase is acidified with 1N HCl and the resulting crystals are filtered off with suction and dried.

Yield: 180 mg (45.7 % of theory) of product

Mass spectrum: molecular mass calculated: 393, found $[M+H]^+$=394.1

Example 14

2-[(6-Amino-3,5-dicyano-4-{4-[(4-methylpiperazino)sulfonyl]phenyl}-2-pyridinyl)sulfanyl]acetamide



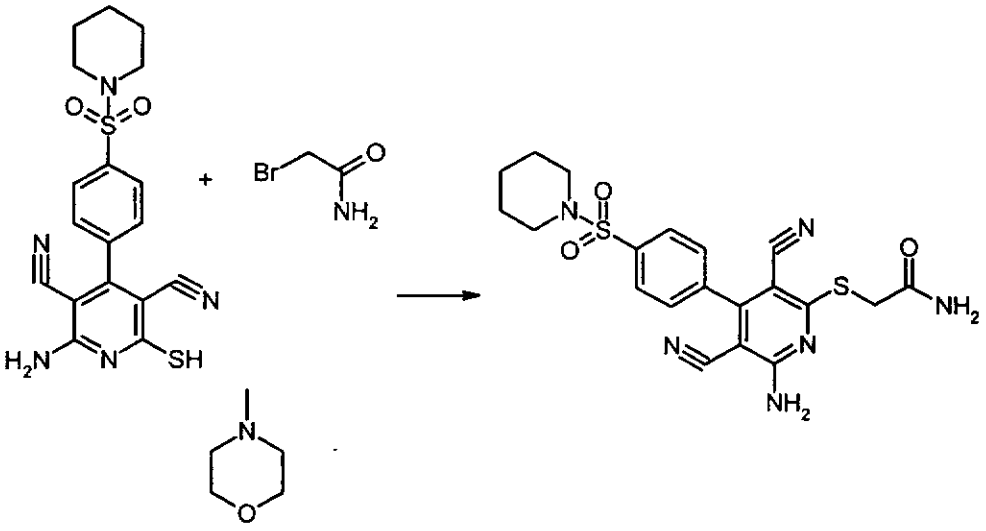
84 mg (0.163 mmol) of 2-amino-4-{4-[(4-methylpiperazino)sulfonyl]phenyl}-6-sulfanyl-3,5-pyridinedicarbonitrile N-methylmorpholinium salt together with 53.3 mg (0.244 mmol) of bromoacetamide and 54.7 mg (0.65 mmol) of $NaHCO_3$ are stirred in 0.5 ml of DMF overnight. After filtration, the reaction solution is initially purified by preparative HPLC. The isolated fraction is reconcentrated under reduced pressure and the residue is purified by preparative thin-layer chromatography.

Yield: 14 mg (18.2 % of theory) of product

Mass spectrum: molecular mass calculated: 471, found $[M+H]^+$=472.1

Example 15

2-({6-Amino-3,5-dicyano-4-[4-(piperidinosulfonyl)phenyl]-2-pyridinyl}-sulfanyl)acetamide



82 mg (0.164 mmol) of 2-amino-4-{4-(piperidinosulfonyl)phenyl}-6-sulfanyl-3,5-pyridinedicarbonitrile N-methylmorpholinium salt together with 53.5 mg (0.246 mmol) of bromoacetamide and 55 mg (0.65 mmol) of $NaHCO_3$ are stirred in 0.5 ml of DMF overnight. After filtration, the reaction solution is purified by preparative HPLC.

HPLC conditions:

Column: GROM-SIL 120 ODS 4 HE 5µ 50 x 20 mm

Precolumn: GROM-SIL ODS 4 HE 15 µ 10 x 20 mm

Wavelength: 220 mm

Flow rate: 25 ml/min

Gradient: A = acetonitrile + 0.1% trifluoroacetic acid

B = water + 0.1% trifluoroacetic acid

0 min: 10%; 1.75 min. 10% A; 5.5 min. 90% A; 8 min. 90% A;

8.1 min. 10% A; 9 min. 10% A

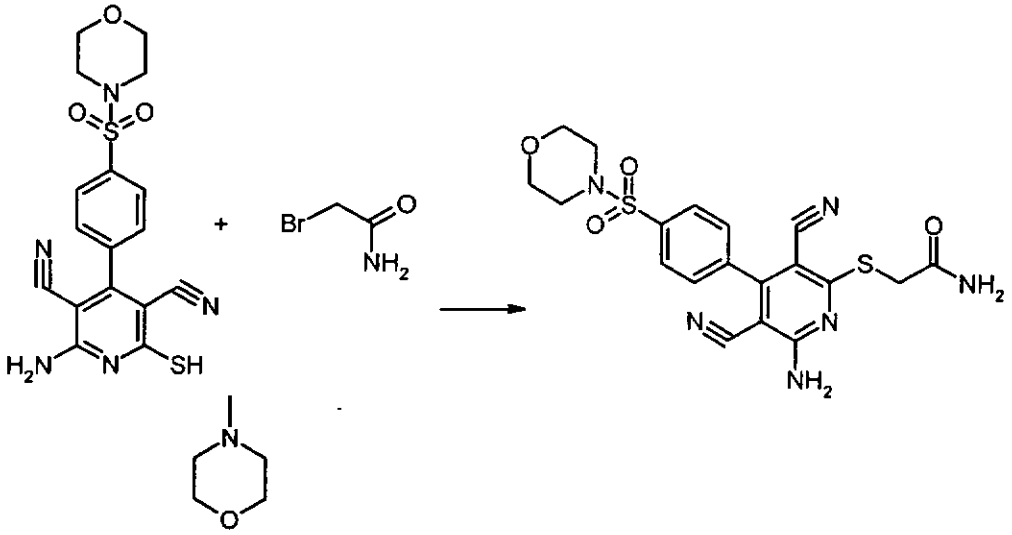
Injection volume: 400 µl of DMF solution

Yield: 42.8 mg (57.2% of theory) of product

NMR [400 MHz, DMSO-d_6]: 1.4 m (2H), 1.6 m (4H), 3.0 tr (4H), 3.9 s (2H), 7.25 s (1H), 7.5 s (1H), 7.8 d (2H), 7.9 d (2H), 8.1 s broad (2H)

Example 16

2-({6-Amino-3,5-dicyano-4-[4-(morpholinosulfonyl)phenyl]-2-pyridinyl}-sulfanyl)acetamide



90 mg (0.179 mmol) of 2-amino-4-{4-(morpholinosulfonyl)phenyl}-6-sulfanyl-3,5-pyridinedicarbonitrile N-methylmorpholinium salt together with 58.5 mg (0.269 mmol) of bromoacetamide and 60 mg (0.71 mmol) of $NaHCO_3$ are stirred in 0.5 ml of DMF overnight. After filtration, the reaction solution is purified by preparative HPLC.

HPLC conditions:

Column: GROM-SIL 120 ODS 4 HE 5µ 50 x 20 mm

Precolumn: GROM-SIL ODS 4 HE 15 µ 10 x 20 mm

Wavelength: 220 mm

Flow rate: 25 ml/min

Gradient: A = acetonitrile + 0.1% trifluoroacetic acid

B = water + 0.1% trifluoroacetic acid

0 min: 10%; 1.75 min. 10% A; 5.5 min. 90% A; 8 min. 90% A; 8.1 min. 10% A; 9 min. 10% A

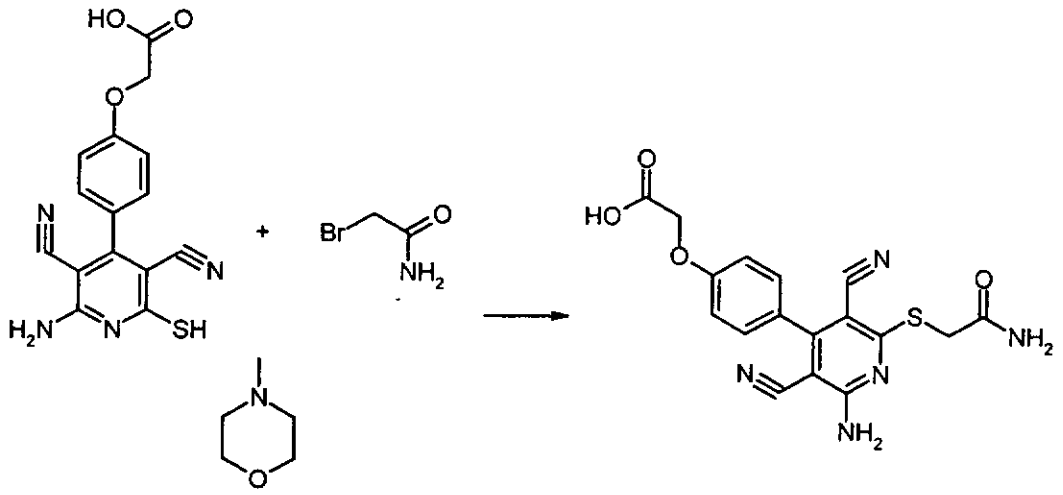
Injection volume: 400 µl of DMF solution

Yield: 43.7 mg (53.2% of theory) of product

NMR[400 MHz, DMSO-d_6]: 2.9 tr (4H), 3.65 tr (4H), 3.9 s (2H), 7.25 s (1H), 7.5 s (1H), 7.85 d (2H), 7.95 d (2H), 8.15 s broad (2H)

Example 17

2-(4-{2-Amino-6-[(2-amino-2-oxoethyl)sulfanyl]-3,5-dicyano-4-pyridinyl}-phenoxy)acetic acid



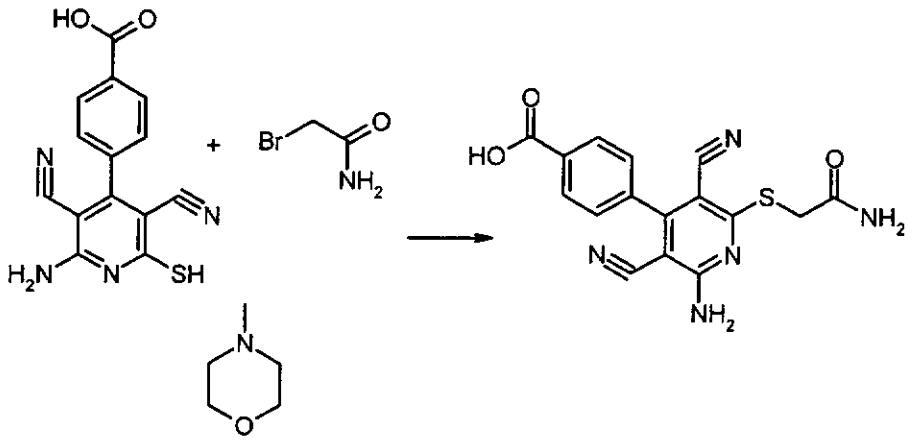
135 mg (0.316 mmol) of 2-[4-(2-amino-3,5-dicyano-6-sulfanyl-4-pyridinyl)-phenoxy]acetic acid N-methylmorpholinium salt together with 103.3 mg (0.474 mmol) of bromoacetamide and 106.1 mg (1.263 mmol) of $NaHCO_3$ are stirred in 0.5 ml of DMF overnight. After filtration, the reaction solution is prepurified by preparative HPLC. The isolated fraction is reconcentrated under reduced pressure and the residue is purified by preparative thin-layer chromatography.

Yield: 14 mg (11.6 % of theory) of product

Mass spectrum: molecular mass calculated: 383, found $[M+Na]^+$=406.2

Example 18

4-{2-Amino-6-[(2-amino-2-oxoethyl)sulfanyl]-3,5-dicyano-4-pyridinyl}-benzoic acid



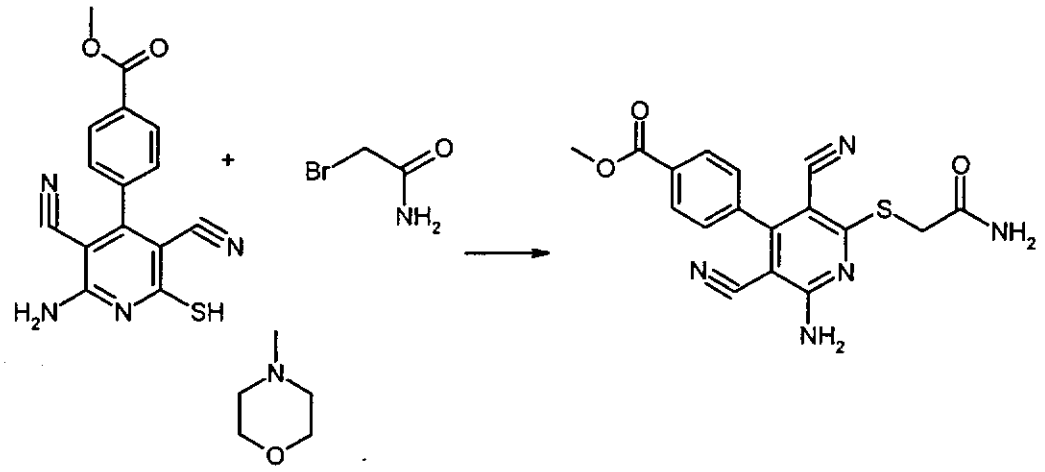
72 mg (0.18 mmol) of 2-[4-(2-amino-3,5-dicyano-6-sulfanyl-4-pyridinyl)benzoic acid N-methylmorpholinium salt together with 59.2 mg (0.27 mmol) of bromo-acetamide and 60.9 mg (0.72 mmol) of $NaHCO_3$ are stirred in 0.5 ml of DMF overnight. After filtration, the reaction solution is prepurified by preparative HPLC. The isolated fraction is reconcentrated under reduced pressure and the residue is purified by preparative thin-layer chromatography.

Yield: 11 mg (17.2 % of theory) of product

Mass spectrum: molecular mass calculated: 353, found $[M+H]^+$=353.9

Example 19

Methyl 4-{2-amino-6-[(2-amino-2-oxoethyl)sulfanyl]-3,5-dicyano-4-pyridinyl}-benzoate



89 mg (0.216 mmol) of methyl 4-(2-amino-3,5-dicyano-6-sulfanyl-4-pyridinyl)-benzoate N-methylmorpholinium salt together with 70.7 mg (0.324 mmol) of bromoacetamide and 72.7 mg (0.86mmol) of $NaHCO_3$ are stirred in 0.5 ml of DMF overnight. After filtration, the reaction solution is purified by preparative HPLC.

HPLC conditions:

Column: GROM-SIL 120 ODS 4 HE 5µ 50 x 20 mm

Precolumn: GROM-SIL ODS 4 HE 15 µ 10 x 20 mm

Wavelength: 220 mm

Flow rate: 25 ml/min

Gradient: A = acetonitrile + 0.1% trifluoroacetic acid

B = water + 0.1% trifluoroacetic acid

0 min: 10%; 1.75 min. 10% A; 5.5 min. 90% A; 8 min. 90% A;

8.1 min. 10% A; 9 min. 10% A

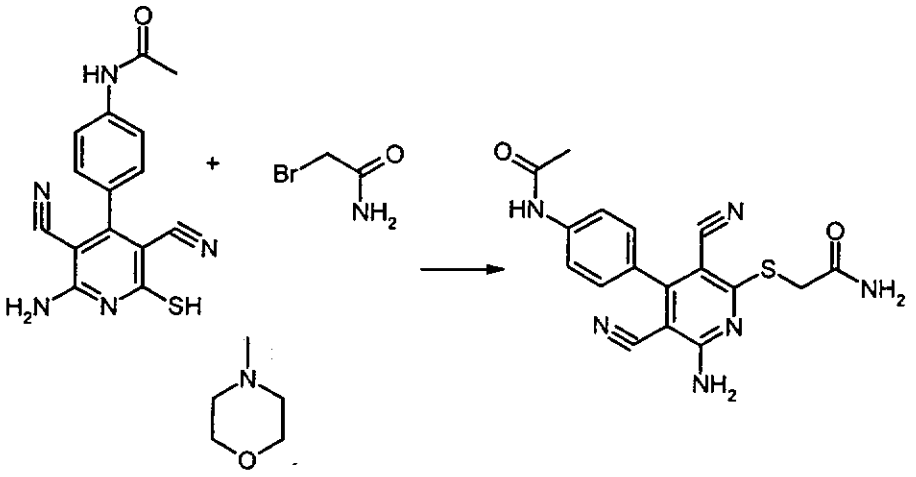
Injection volume: 400 µl of DMF solution

Yield: 40.4 mg (50.8% of theory) of product

NMR [400 MHz, DMSO-d_6]: 3.9 s (2H), 7.25 s (1H), 7.5 s (1H), 7.7 d (2H), 8.1 d (2H), 8.1 s broad (2H)

Example 20

2-({4-[4-(Acetylamino)phenyl]-6-amino-3,5-dicyano-2-pyridinyl}sulfanyl)-acetamide



44 mg (0.11 mmol) of N-[4-(2-amino-3,5-dicyano-6-sulfanyl-4-pyridinyl)phenyl]-acetamide N-methylmorpholinium salt together with 35 mg (0.16 mmol) of bromoacetamide and 36 mg (0.43 mmol) of $NaHCO_3$ are stirred in 0.5 ml of DMF overnight. After filtration, the reaction solution was purified by preparative HPLC.

HPLC conditions:

Column: GROM-SIL 120 ODS 4 HE 5µ 50 x 20 mm

Precolumn: GROM-SIL ODS 4 HE 15 µ 10 x 20 mm

Wavelength: 220 mm

Flow rate: 25 ml/min

Gradient: A = acetonitrile + 0.1% trifluoroacetic acid

B = water + 0.1% trifluoroacetic acid

0 min: 10%; 1.75 min. 10% A; 5.5 min. 90% A; 8 min. 90% A;

8.1 min. 10% A; 9 min. 10% A

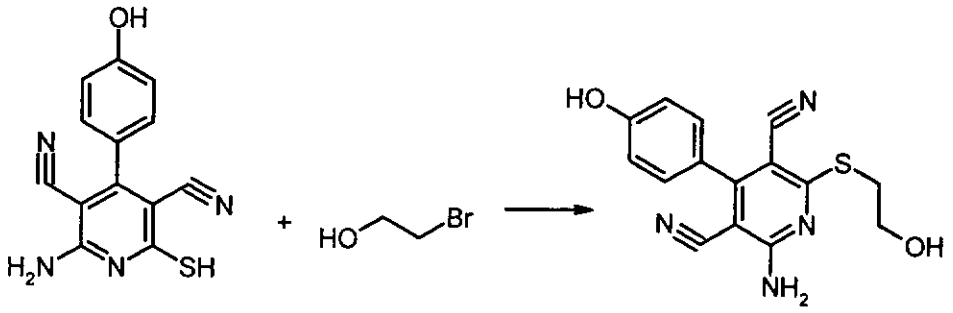
Injection volume: 400 µl of DMF solution

Yield: 18.3 mg (46.6% of theory) of product

NMR [400 MHz, DMSO-d_6]: 2.1 s (3H), 3.9 s (2H), 7.25 s (1H), 7.5 d (3H), 7.7 d (2H), 8.0 s broad (2H), 10.25 s (1H)

Example 21

2-Amino-6-[(2-hydroxyethyl)sulfanyl]-4-(4-hydroxyphenyl)-3,5-pyridinedicarbonitrile



26.8 mg (0.1 mmol) of 2-amino-4-(4-hydroxyphenyl)-6-sulfanyl-3,5-pyridinedicarbonitrile are dissolved in 0.2 ml of dimethylformamide. 20 mg (0.238 mmol) of solid sodium bicarbonate are added, followed by a solution of 18.74 mg (0.15 mmol) of 2-bromoethanol in 0.06 ml of dimethylformamide. The reaction mixture is shaken overnight and, after filtration, purified by preparative HPLC.

HPLC conditions:

Column: GROM-SIL 120 ODS 4 HE 5µ 50 X 20 mm

Precolumn: GROM-SIL ODS 4 HE 15µ 10 X 20 mm

Wavelength: 220 nm

Flow rate: 25 ml/min

Gradient: A = acetonitrile + 0.1% trifluoroacetic acid

B= water + 0.1% trifluoroacetic acid

0 min: 10% A; 1.75 min. 10% A; 5.5 min. 90% A; 8 min. 90% A; 8.1 min. 10% A; 9 min. 10% A

Injection volume: 300 µl of DMSO solution

Retention time: 3.97 min

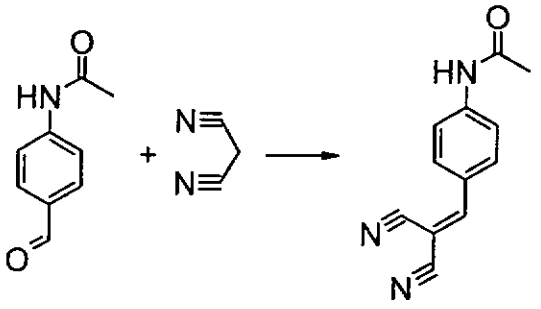
Yield: 14.1 mg (45.1% of theory)

Mass spectrum: molecular mass calculated: 312, found $[M+H]^+$=313

Example 22

1. Step:

N-[4-(2,2-Dicyanovinyl)phenyl]acetamide



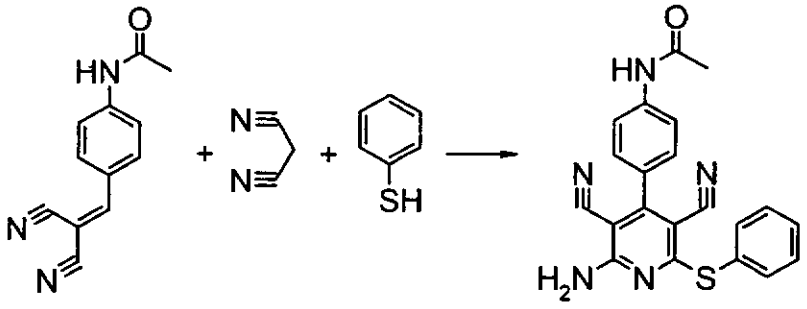
32.6 g (0.2 mol) of 4-acetaminobenzaldehyde and 13.74 g (0.208 mol) of malononitrile are initially charged in 140 ml of ethanol, and 24 drops of piperidine are added. The mixture is stirred at reflux for 30 min. After cooling, the crystals are filtered off with suction and dried.

Yield: 38.6 g (90.6% of theory) of product

Mass spectrum: molecular mass calculated: 211, found $[M+H]^+ = 212$

2. Step

N-{4-[2-Amino-3,5-dicyano-6-(phenylsulfanyl)-4-pyridinyl]phenyl}acetamide



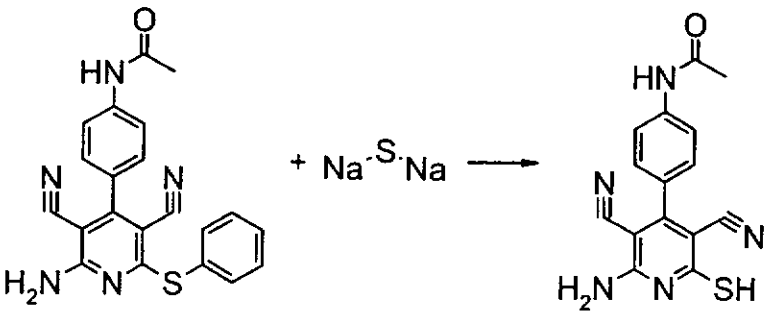
19 g (0.09 mol) of N-[4-(2,2-dicyanovinyl)phenyl]acetamide, 5.95 g (0.09 mol) of malononitrile and 9.91 g (0.09 mol) of thiophenol are initially charged in 120 ml of ethanol, and 0.4 ml of triethylamine are added. The mixture is stirred at reflux for 2 h, during which the product crystallizes. After cooling, the product is filtered off with suction and dried under reduced pressure.

Yield: 10.25 g (29.6% of theory) of product

Mass spectrum: molecular mass calculated: 385, found $[M+H]^+ = 386$

3. Step

N-[4-(2-Amino-3,5-dicyano-6-sulfanyl-4-pyridinyl)phenyl]acetamide



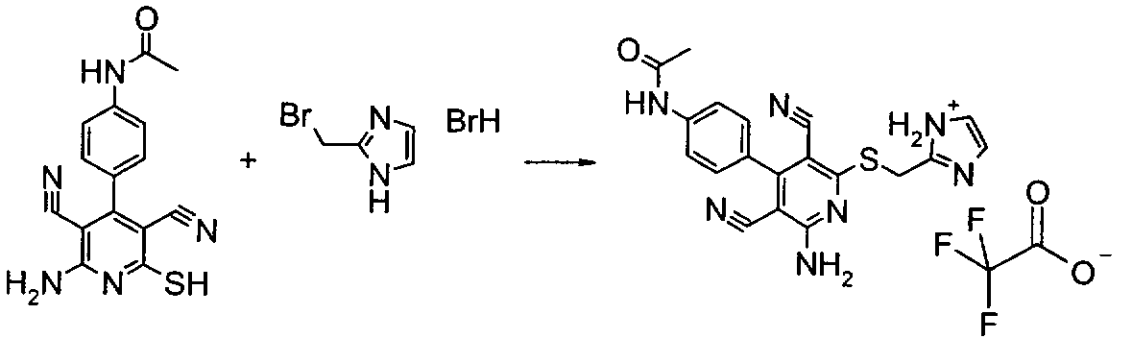
Under argon, 1.16 g (3 mmol) of N-{4-[2-amino-3,5-dicyano-6-(phenylsulfanyl)-4-pyridinyl]phenyl}-acetamide are dissolved in 10 ml of DMF, 0.78 g (10 mmol) of sodium sulfide are added and the mixture is stirred at 80°C for 2 h. 20 ml of 1N HCl are then added and the resulting crystals are filtered off with suction and dried under reduced pressure.

Yield: 428 mg (46.1 % of theory) of product

Mass spectrum: molecular mass calculated: 309, found $[M+H]^+ = 310.1$

4. Step

2-[({4-[4-(Acetylamino)phenyl]-6-amino-3,5-dicyano-2-pyridinyl}sulfanyl)-methyl]-1H-imidazol-1-ium trifluoracetate



309 mg (1 mmol) of N-[4-(2-amino-3,5-dicyano-6-sulfanyl-4-pyridinyl)phenyl]-acetamide, 241 mg (1 mmol) of 2-(bromomethyl)-1H-imidazole hydrobromide and 336 mg (4 mmol) of $NaHCO_3$ in 2 ml of DMF are stirred at RT. After 2 h, 4 to 5 ml of water are added and the beige crystals are filtered off with suction and dried under reduced pressure. The crystals (310 mg) are dissolved in DMSO and purified by prep. HPLC using 9 injections. The corresponding fraction is concentrated under reduced pressure and the crystalline residue is suspended in water, filtered off with suction and dried under reduced pressure.

HPLC conditions:

Column: Kromasil 100 C18 5µm 50 X 20 mm

Precolumn: GROM-SIL ODS 4 HE 15µ 10 X 20 mm

Wavelength: 220 nm

Flow rate: 25 ml/min

Gradient: A = acetonitrile + 0.1% trifluoroacetic acid

B= water + 0.1% trifluoroacetic acid

0 min: 10% A; 2 min. 10% A; 6 min. 90% A; 7 min. 90% A;

7.1 min. 10% A; 8 min. 10% A

Injection volume: 500 µl of DMSO solution

Retention time: 3.6 min

Yield: 234 mg (60% of theory) of product

Mass spectrum: molecular mass calculated: 389, found $[M+H]^+ = 390.1$

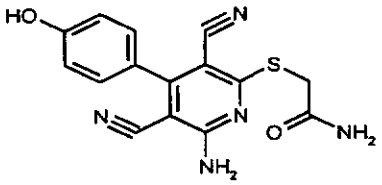
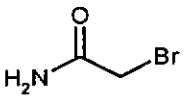
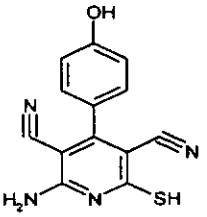
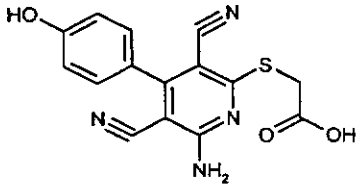
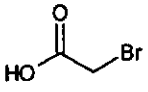
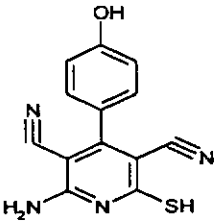
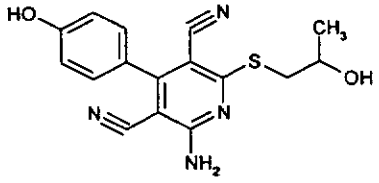
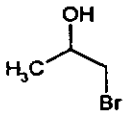
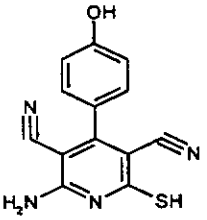
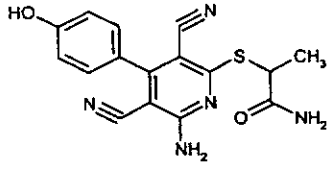
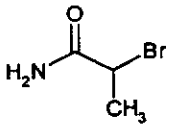
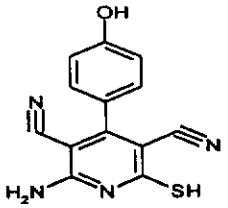
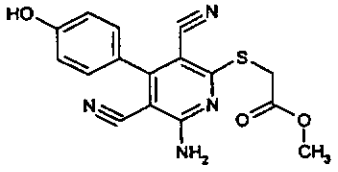
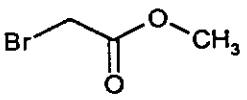
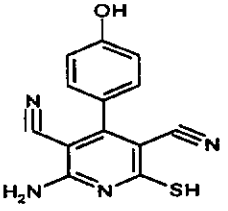
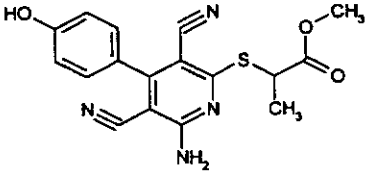
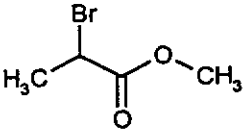
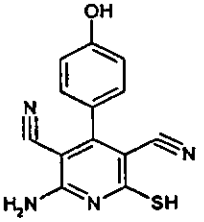
^{1}H-NMR (300 MHz, DMSO-d_6): δ = 2.1 s (3H), 4.7 s (1H), 7.4 d (2H), 7.55 s (1H), 7.7 d (2H), 8.1 s broad (2H), 10.25 s (1H), 14.2 s broad (1H)

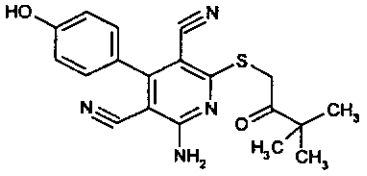
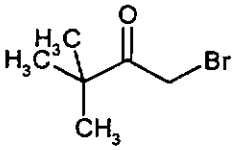
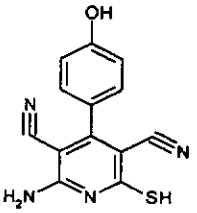
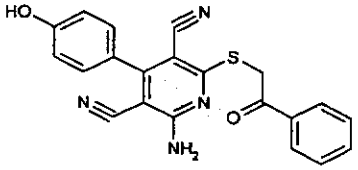
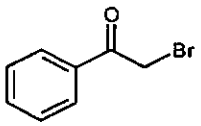
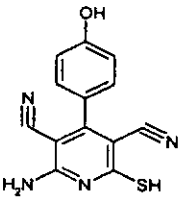
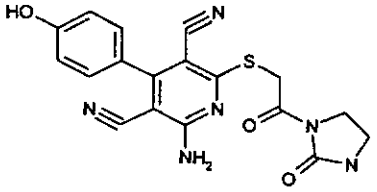
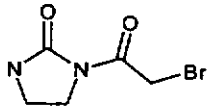
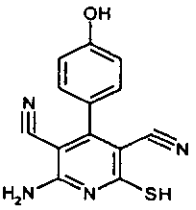
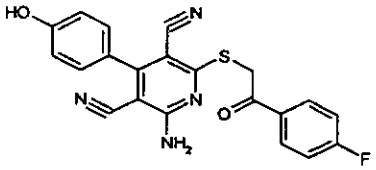
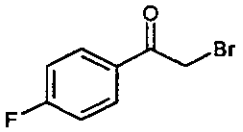
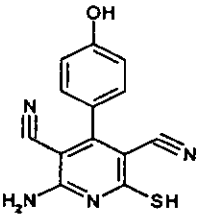
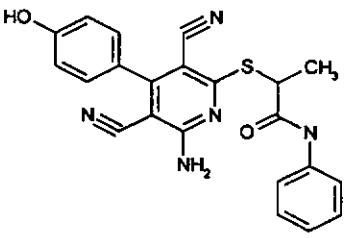
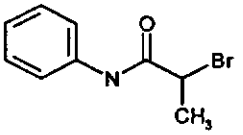
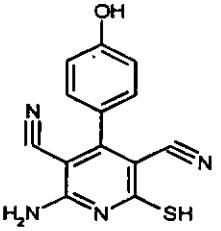
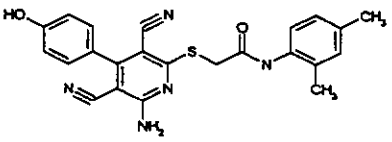
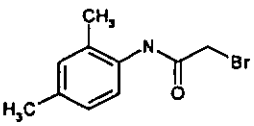
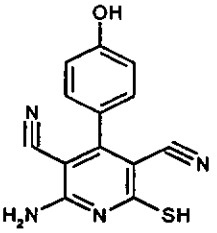
The compounds listed in the tables below (examples A 1 to A 377, A 378 to A 413 and B 1 to B 375) were prepared analogously to the procedures given above. Identity and purity of the compounds was demonstrated by LC-MS.

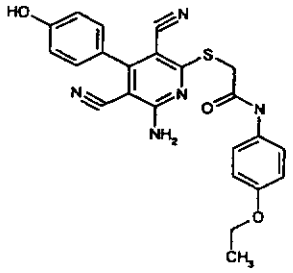
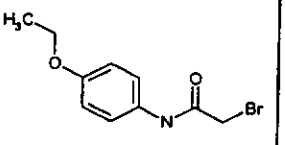
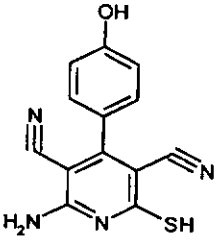
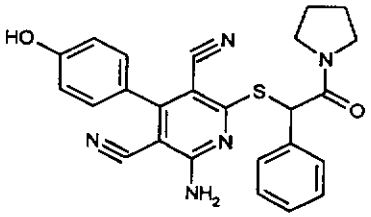
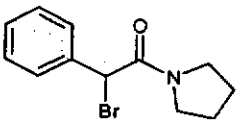
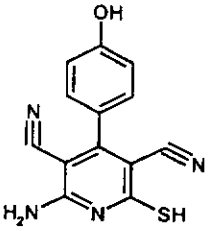
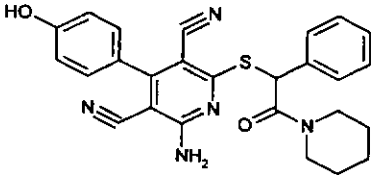
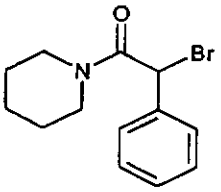
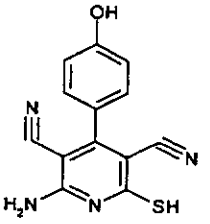
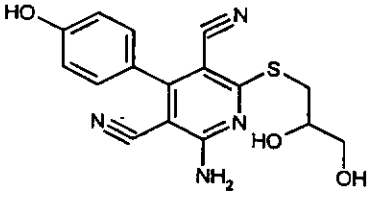
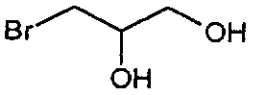
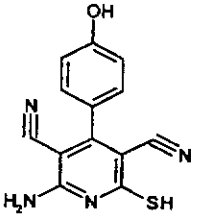
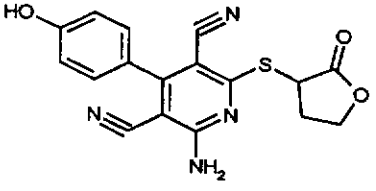
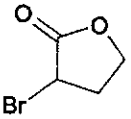
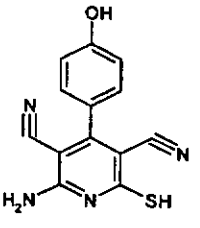
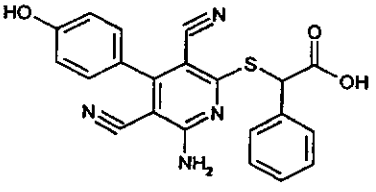
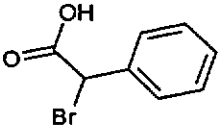
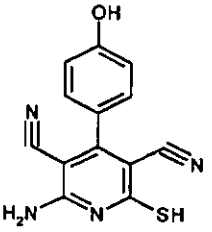
The compounds of examples A 1 to A 413 were either isolated as crystals or, if they did not crystallize directly from the reaction solution, purified by preparative HPLC.

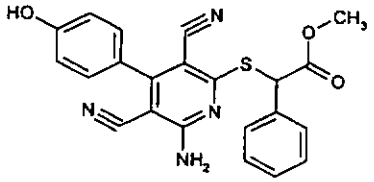
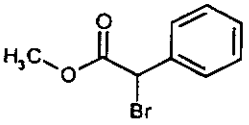
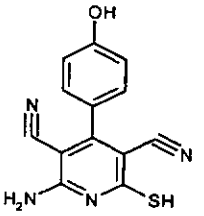
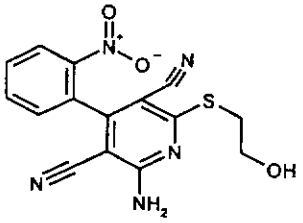
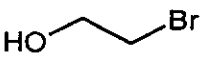
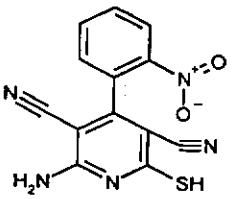
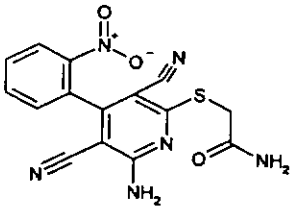
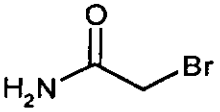
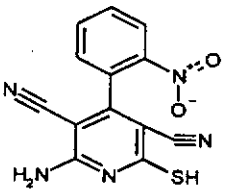
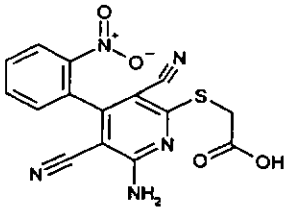
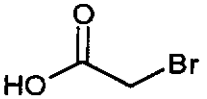
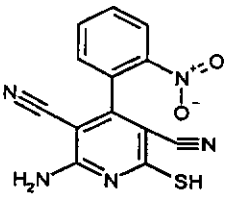
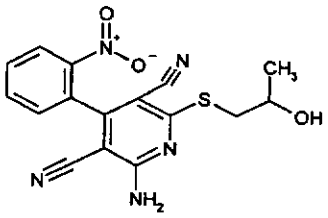
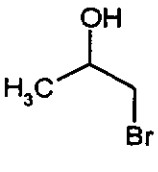
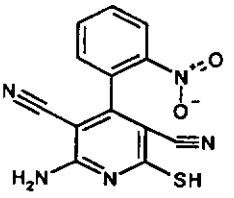
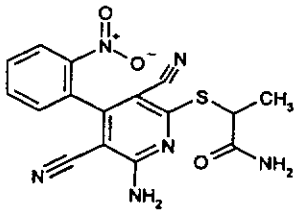
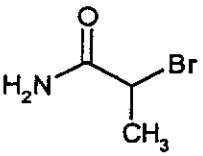
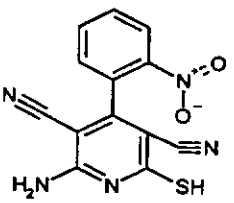
The compounds of examples B 1 to B 375 were prepared on a 10 µmol scale, analogously to the procedures above. These compounds were purified and identified by a preparative HPLC-MS system.

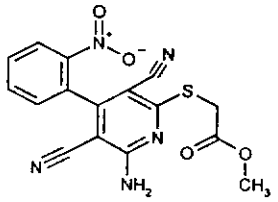
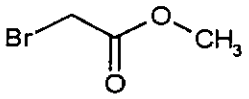
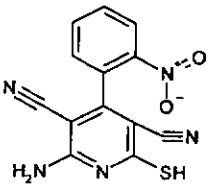
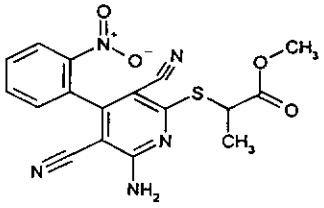
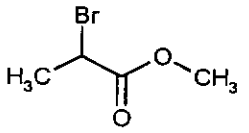
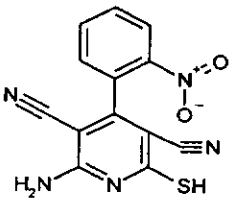
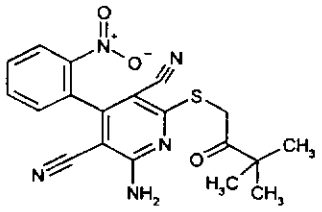
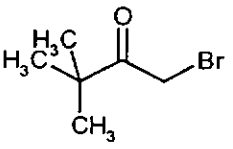
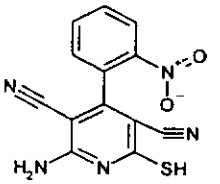
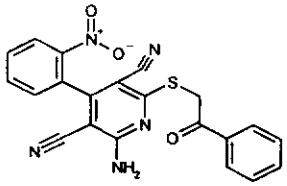
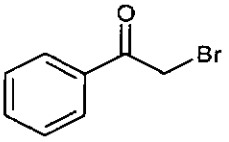
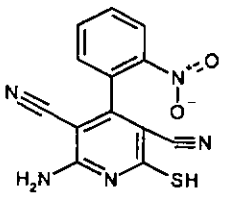
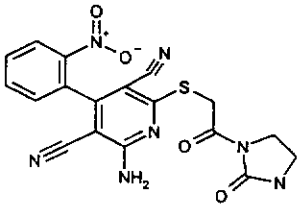
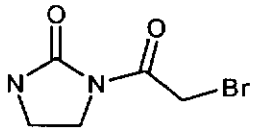
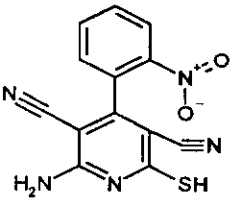
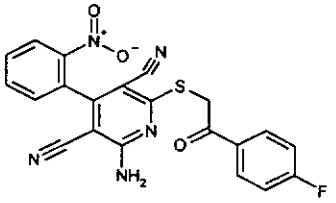
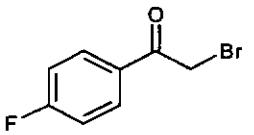
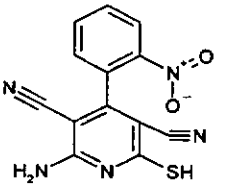
In the tables below, structures having a group –N- are in each case understood to contain a group –NH- and structures having a group –N are in each case to be understood as containing a group $-NH_2$.

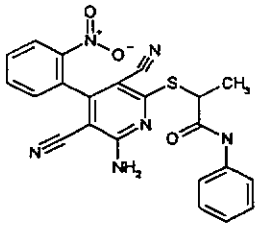
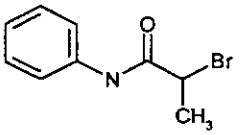
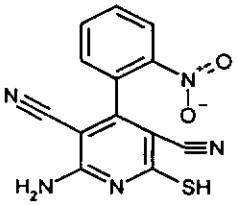
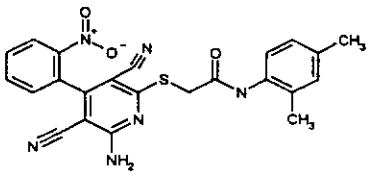
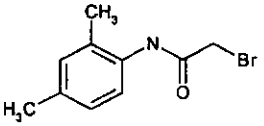
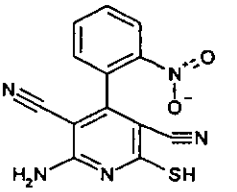
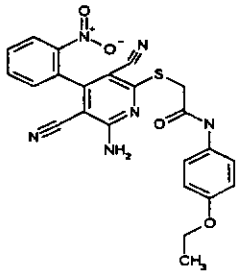
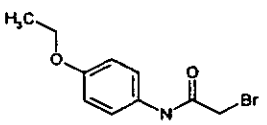
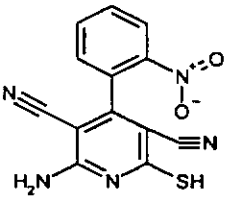
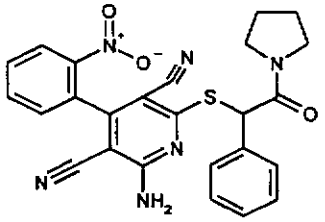
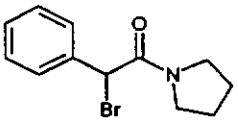
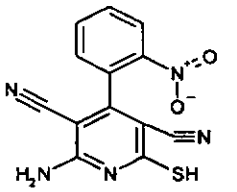
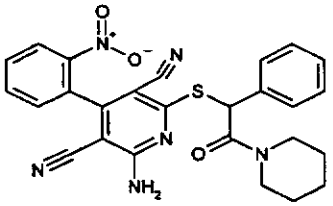
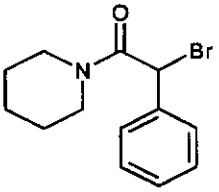
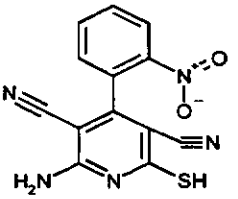
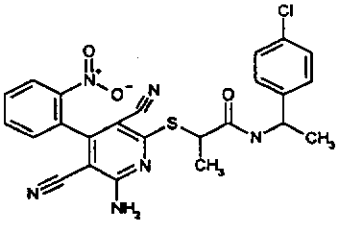
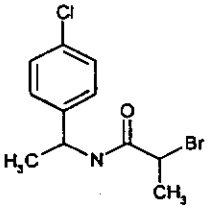
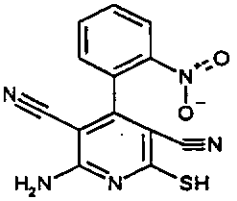
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A1				325	326	57.5
A2				326	327	7.0
A3				326	327	52.7
A4				339	340	67.5
A5				340	341	60.8
A6				354	355	53.6

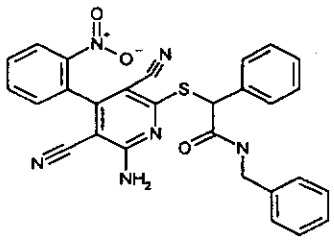
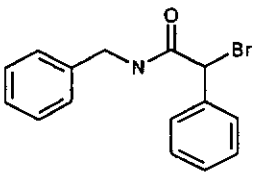
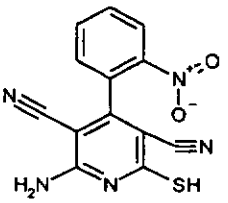
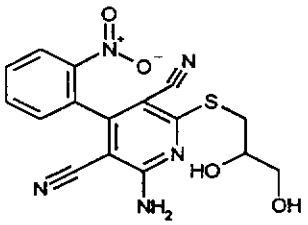
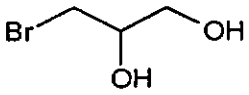
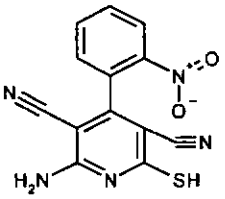
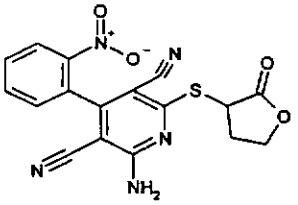
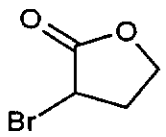
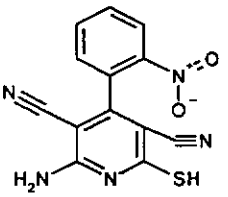
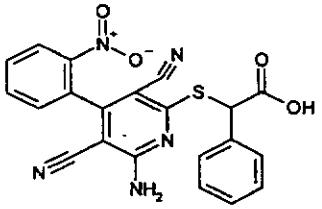
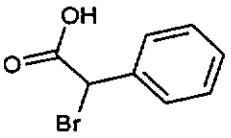
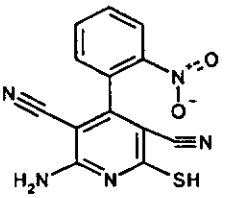
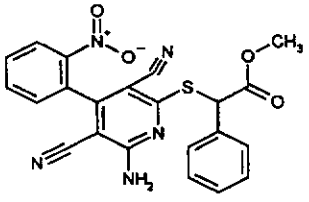
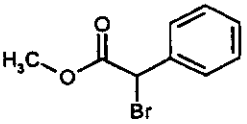
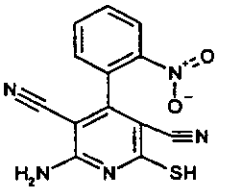
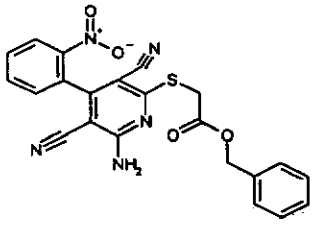
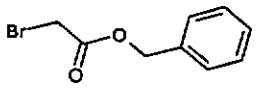
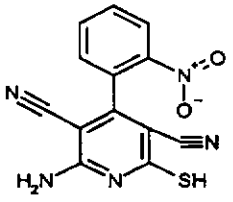
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A7				366	367	30.0
A8				386	387	57.2
A9				394	395	12.2
A10				404	405	39.3
A11				415	416	58.2
A12				430	431	25.1

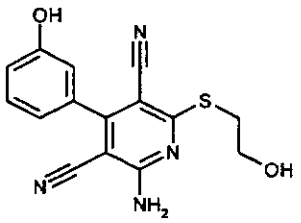
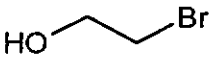
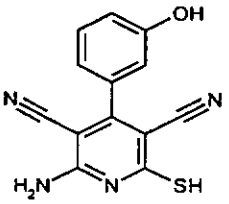
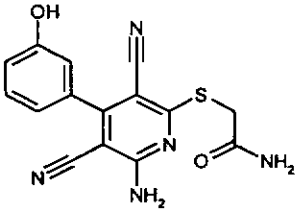
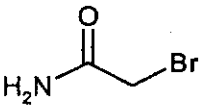
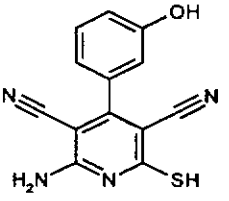
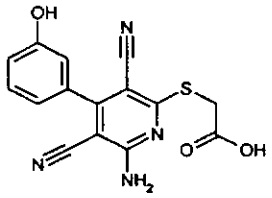
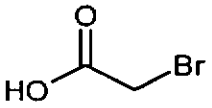
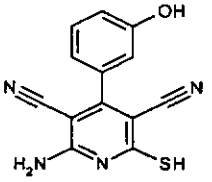
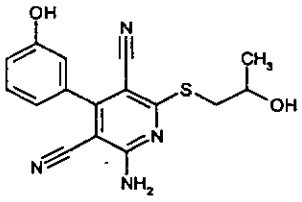
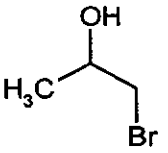
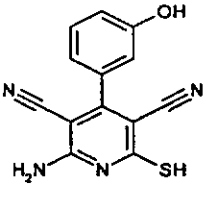
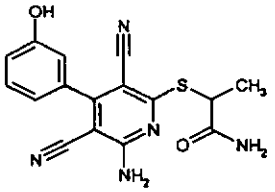
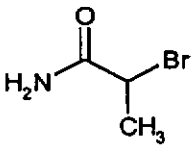
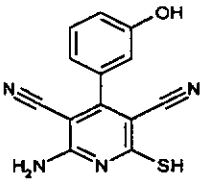
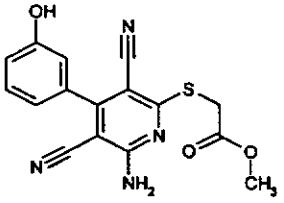
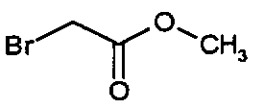
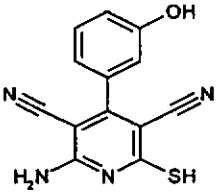
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A13				446	447	28.1
A14				456	457	29.6
A15				470	471	62.2
A16				342	343	54.0
A17				352	353	73.8
A18				402	403	65.6

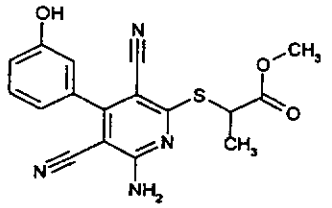
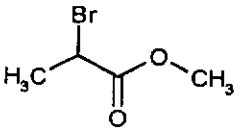
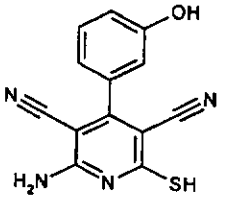
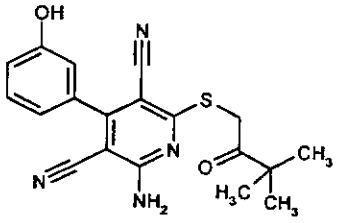
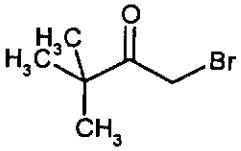
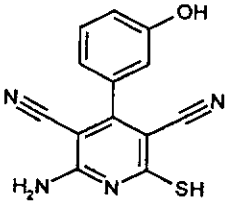
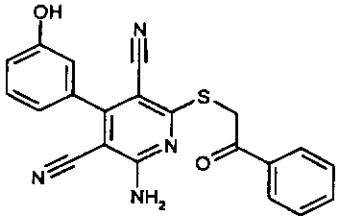
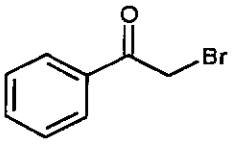
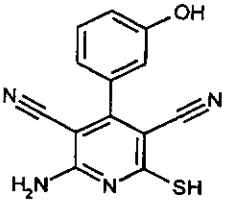
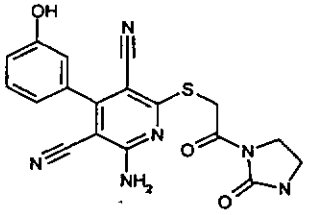
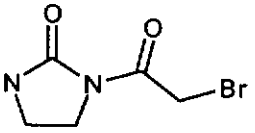
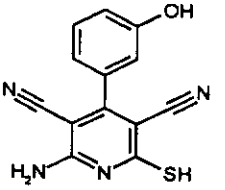
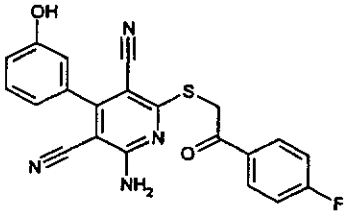
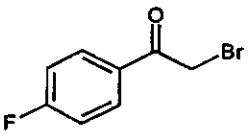
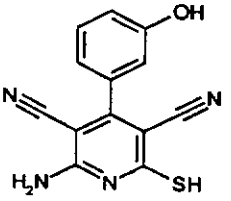
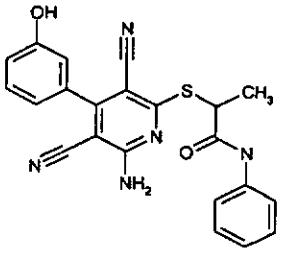
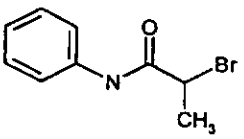
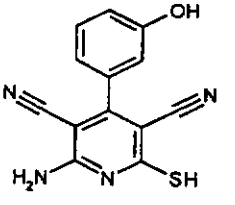
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A19				416	417	51.9
A20				341	342	29.7
A21				354	355	84.4
A22				355	356	10.0
A23				355	356	35.2
A24				368	369	77.1

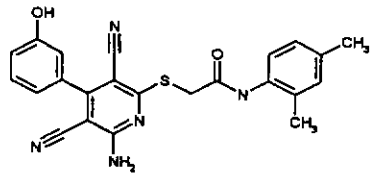
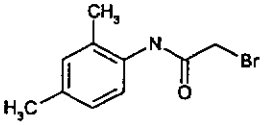
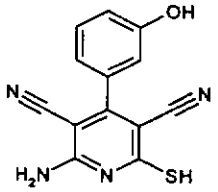
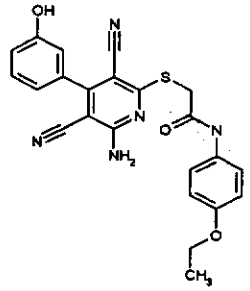
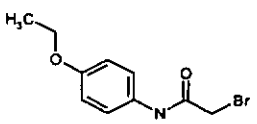
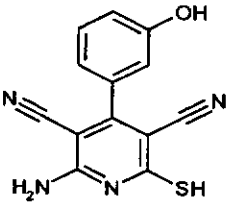
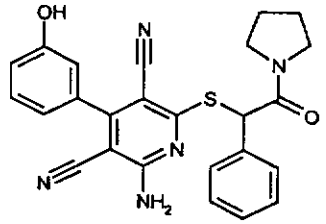
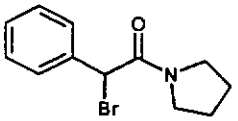
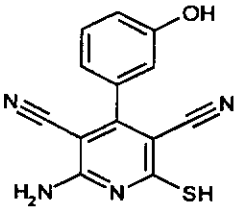
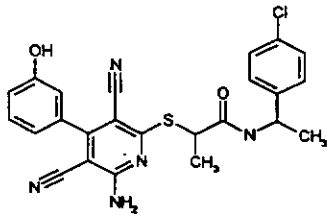
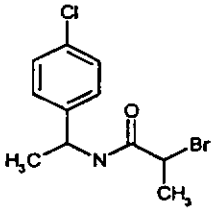
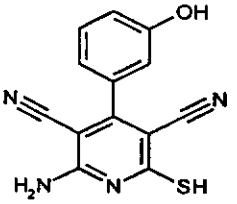
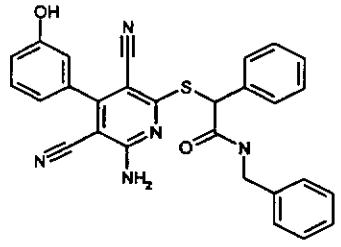
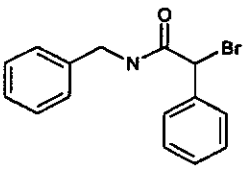
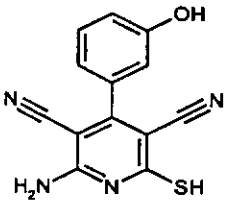
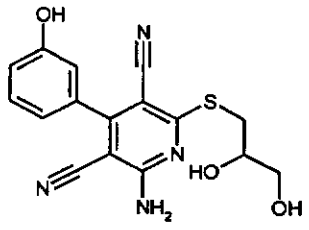
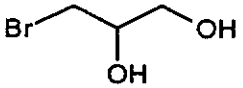
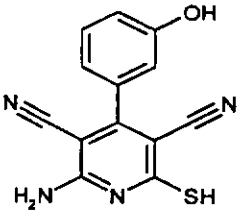
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A25				369	370	70.9
A26				383	384	68.1
A27				395	396	60.2
A28				415	416	58.0
A29				423	424	31.2
A30				433	434	36.2

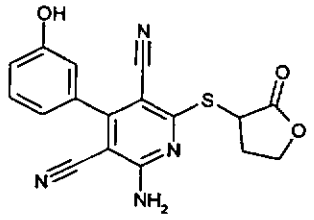
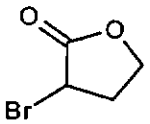
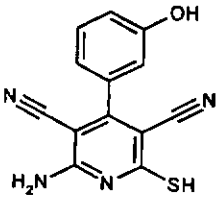
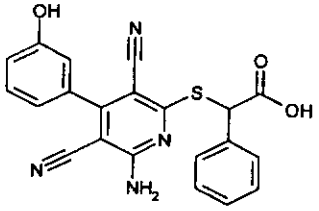
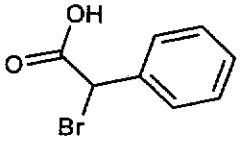
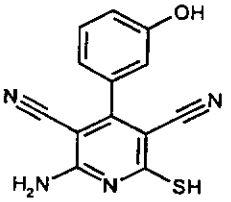
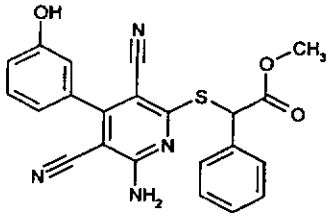
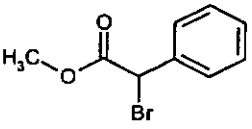
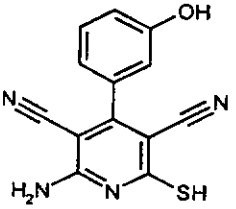
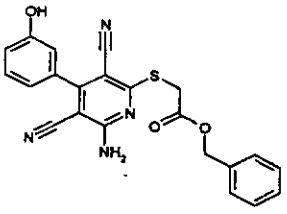
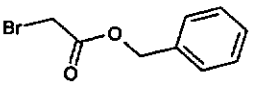
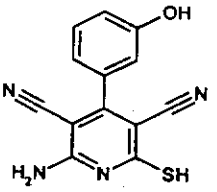
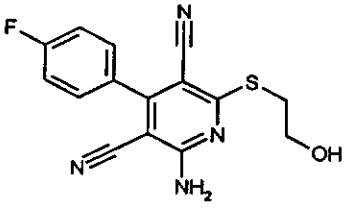
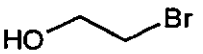
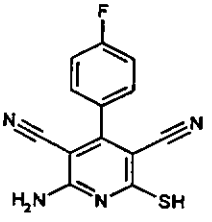
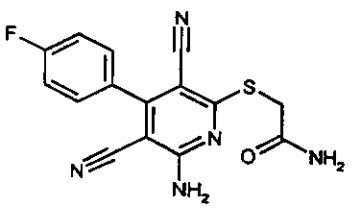
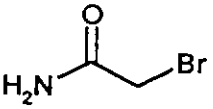
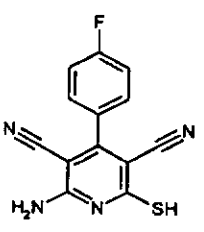
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A31				444	445	51.1
A32				459	460	46.7
A33				475	476	49.7
A34				485	486	47.1
A35				499	500	64.0
A36				507	508	37.5

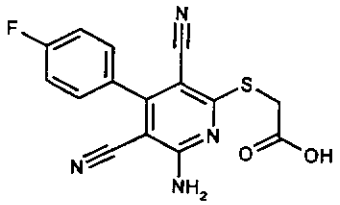
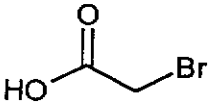
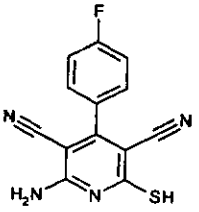
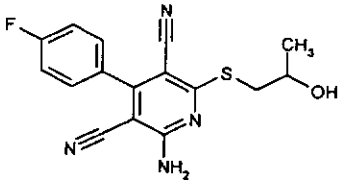
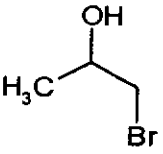
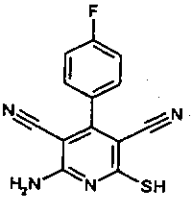
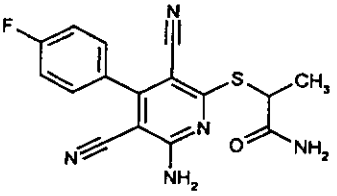
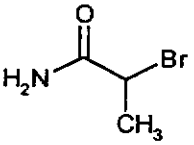
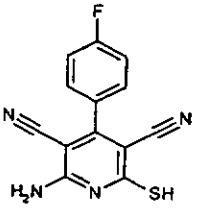
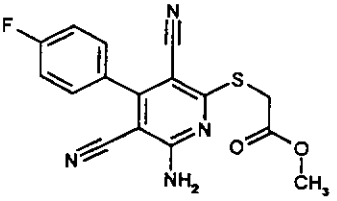
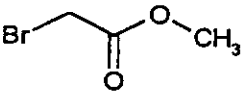
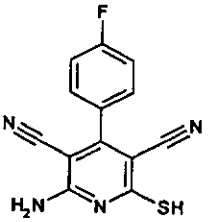
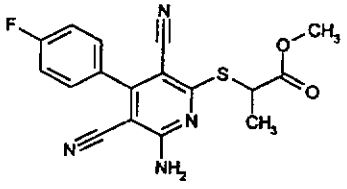
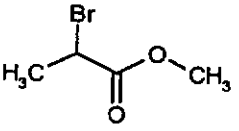
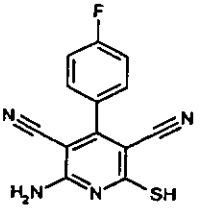
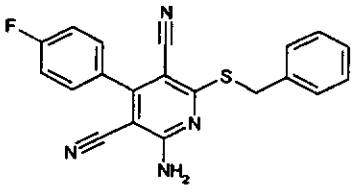
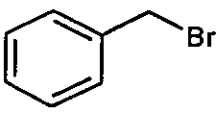
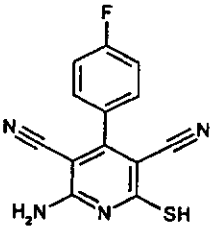
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A37				521	522	61.5
A38				371	372	63.8
A39				381	382	50.3
A40				431	432	40.8
A41				445	446	71.9
A42				445	446	32.6

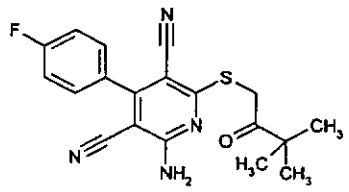
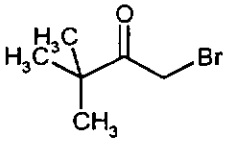
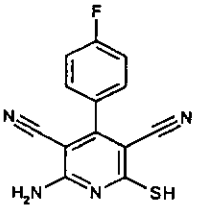
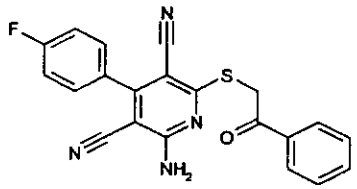
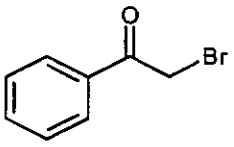
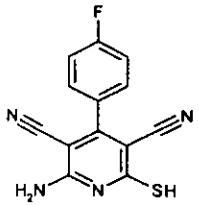
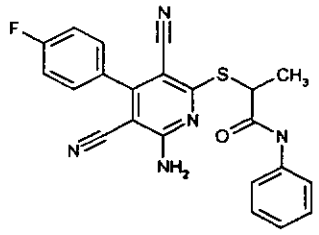
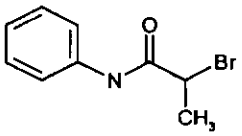
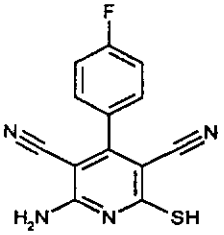
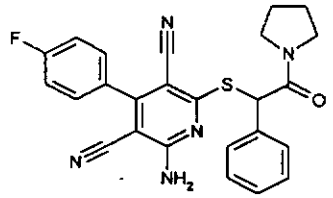
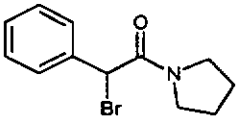
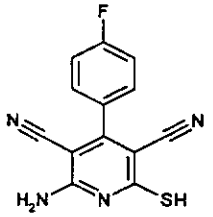
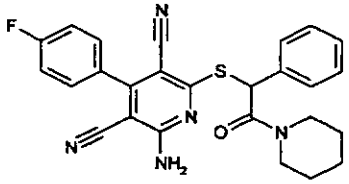
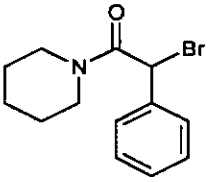
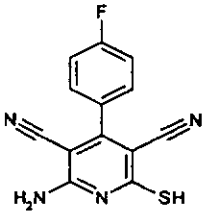
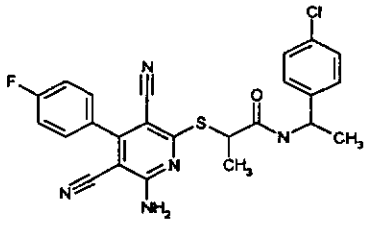
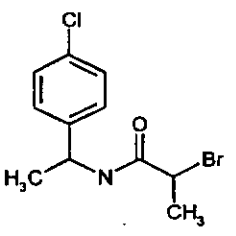
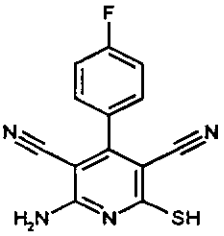
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A43				312	313	60.8
A44				325	326	78.4
A45				326	327	13.9
A46				326	327	17.8
A47				339	340	89.6
A48				340	341	77.6

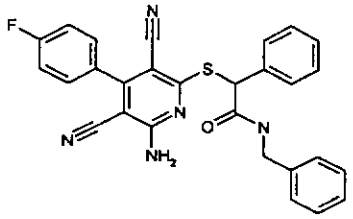
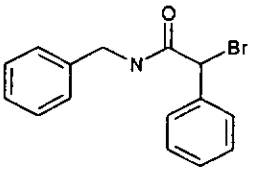
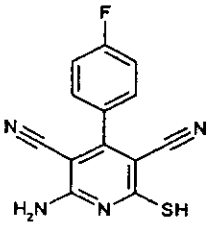
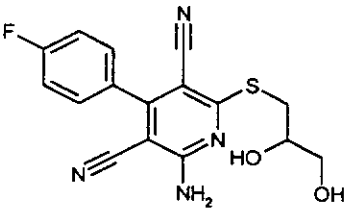
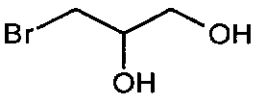
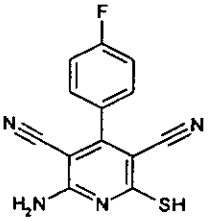
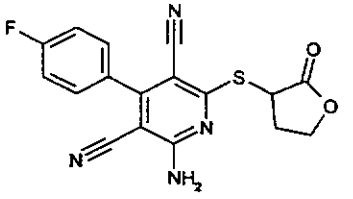
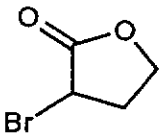
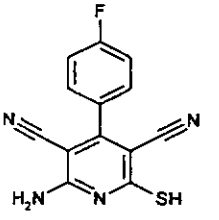
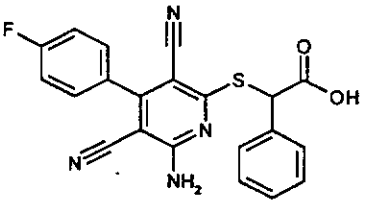
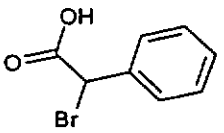
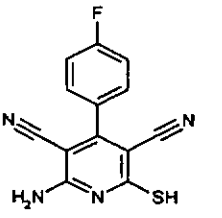
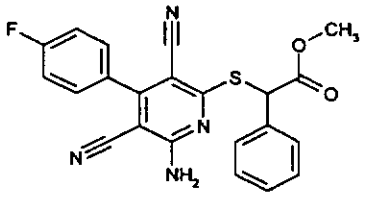
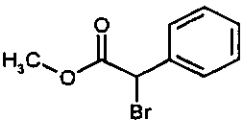
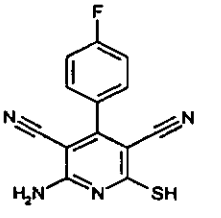
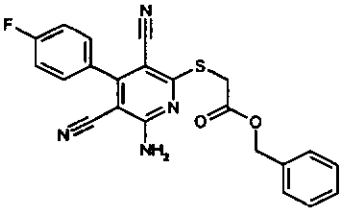
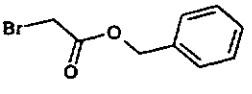
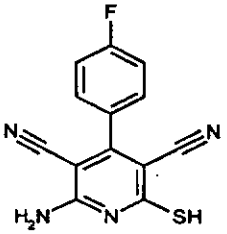
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A49				354	355	56.2
A50				366	367	47.5
A51				386	387	36.5
A52				394	395	20.5
A53				404	405	58.8
A54				415	416	18.3

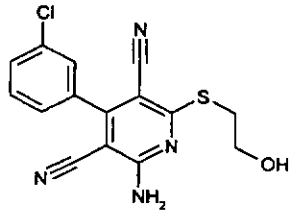
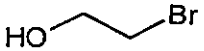
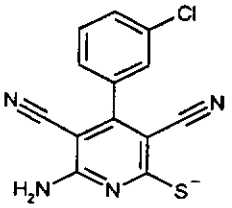
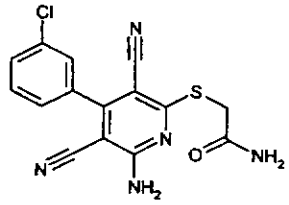
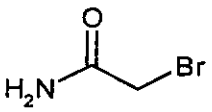
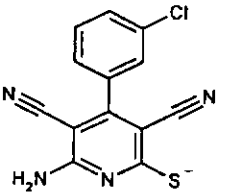
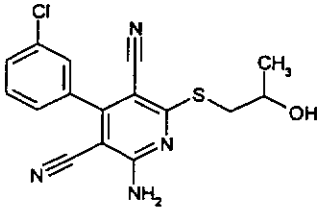
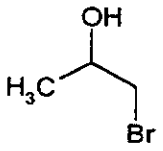
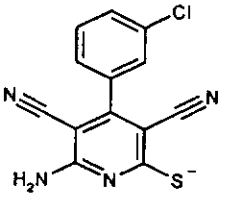
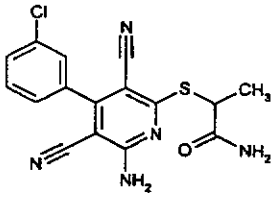
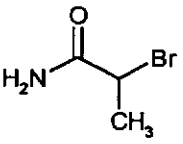
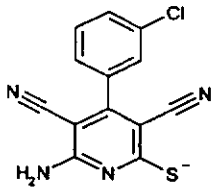
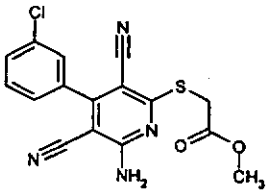
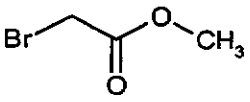
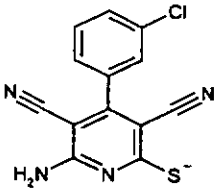
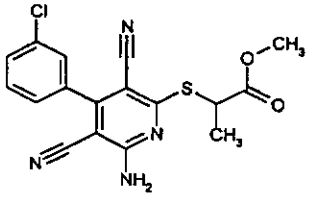
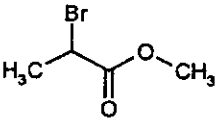
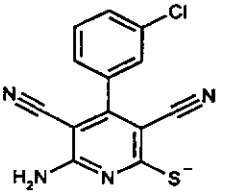
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A55				430	431	29.8
A56				446	447	42.2
A57				456	457	9.2
A58				478	479	54.2
A59				492	493	66.3
A60				342	343	73.6

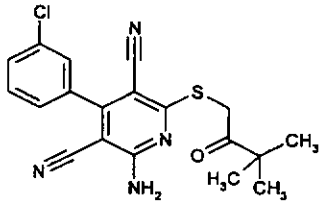
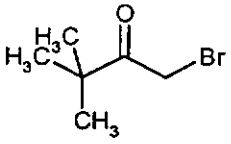
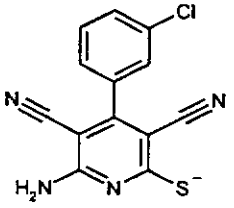
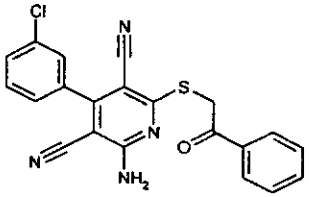
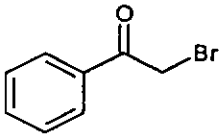
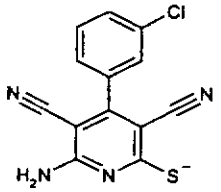
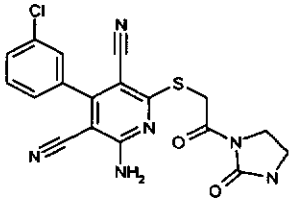
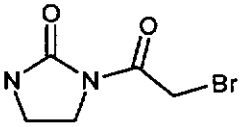
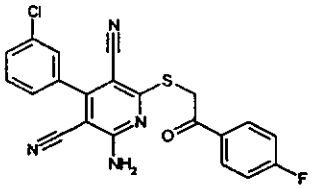
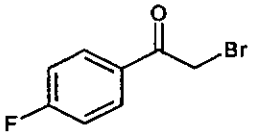
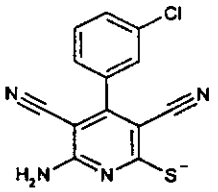
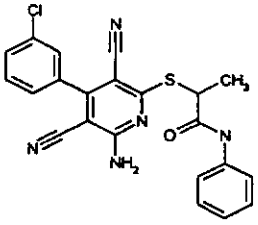
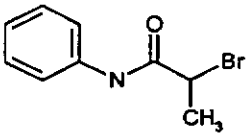
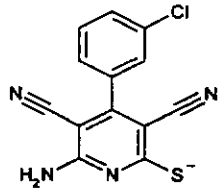
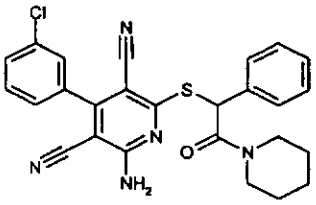
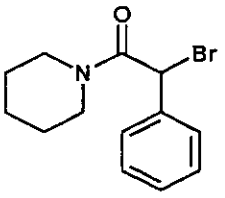
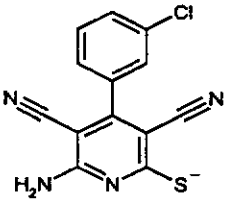
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A61				352	353	68.1
A62				402	403	41.2
A63				416	417	52.1
A64				416	417	52.6
A65				314	315	62.7
A66				327	328	58.0

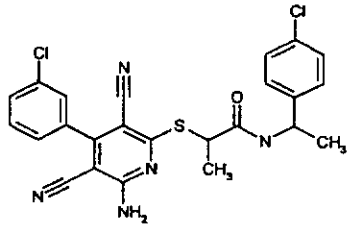
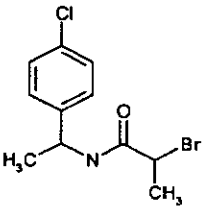
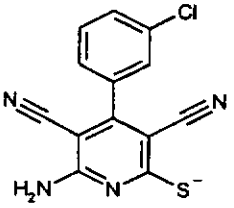
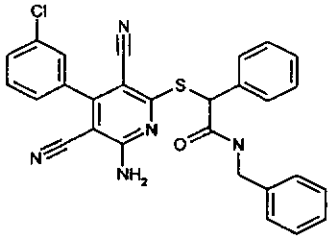
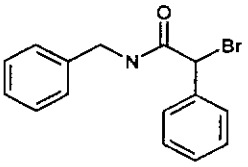
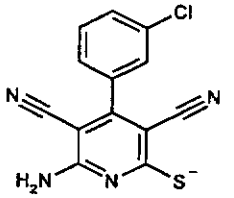
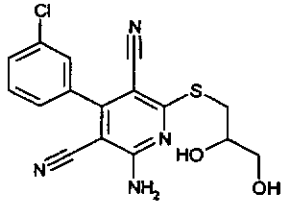
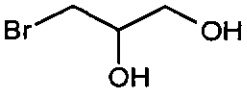
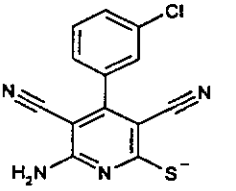
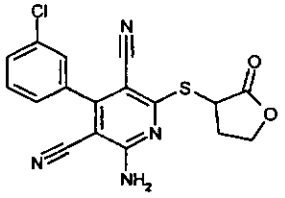
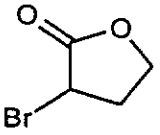
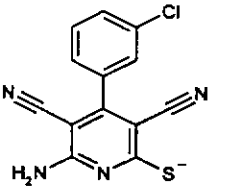
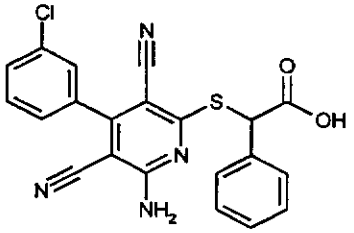
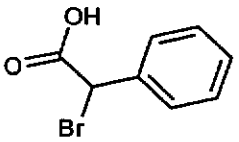
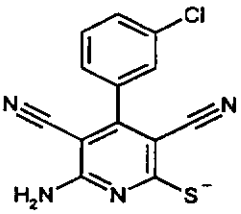
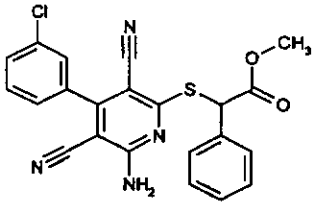
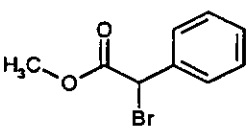
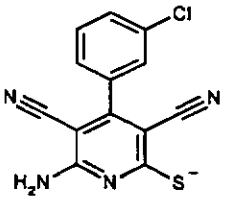
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A67				328	329	17.1
A68				328	329	53.9
A69				341	342	57.7
A70				342	343	35.6
A71				356	357	49.7
A72				360	361	43.3

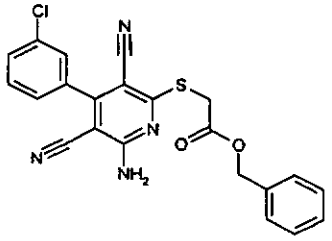
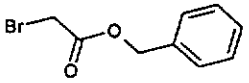
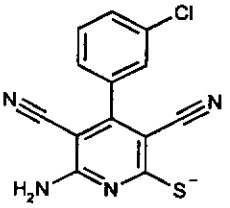
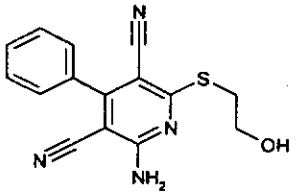
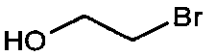
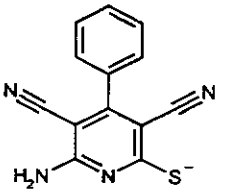
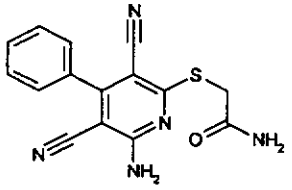
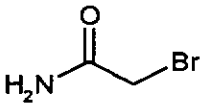
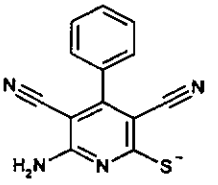
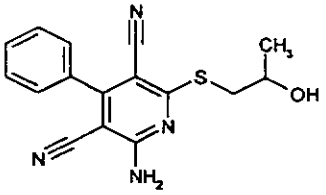
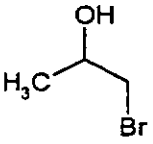
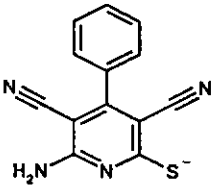
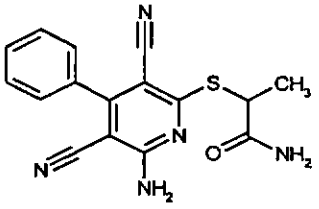
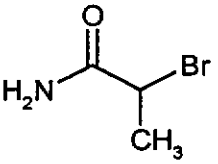
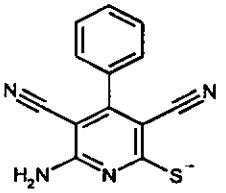
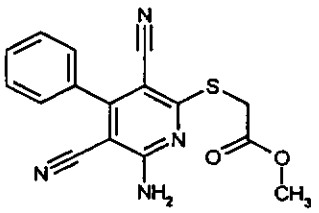
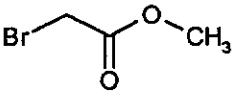
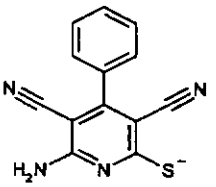
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A73				368	369	14.7
A74				388	389	17.5
A75				417	418	31.1
A76				458	459	19.5
A77				472	473	41.8
A78				480	481	32.9

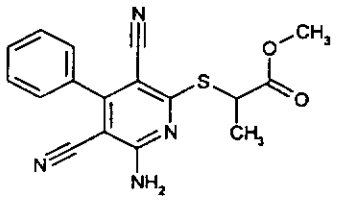
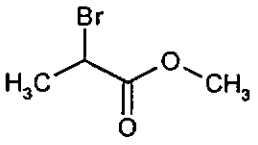
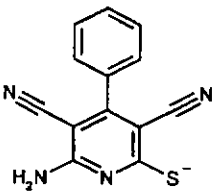
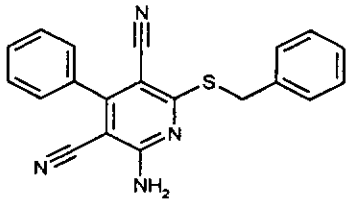
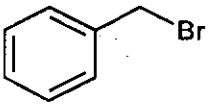
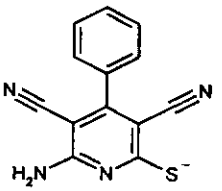
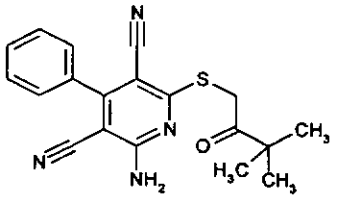
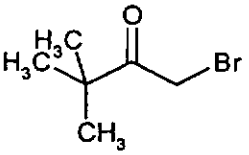
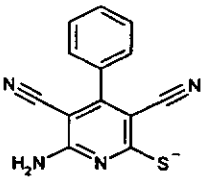
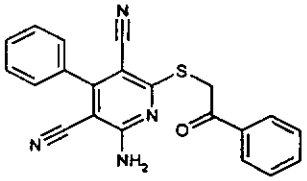
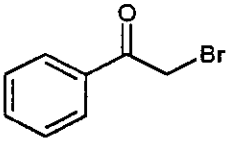
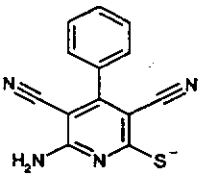
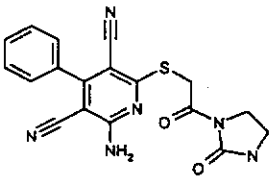
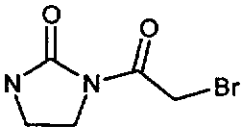
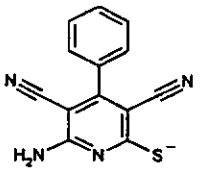
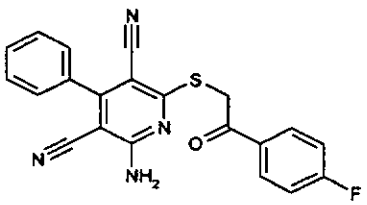
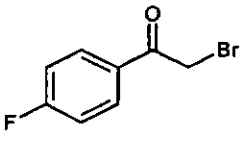
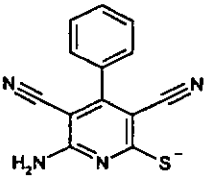
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A79				494	495	29.0
A80				344	345	45.6
A81				354	355	37.2
A82				404	405	37.6
A83				418	419	63.3
A84				418	419	21.5

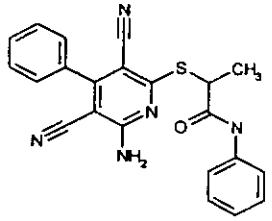
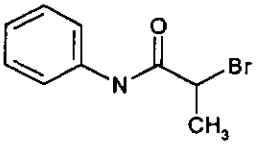
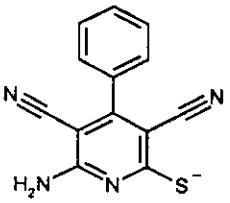
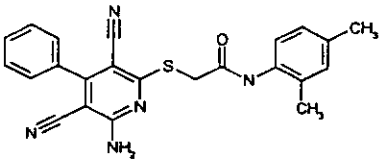
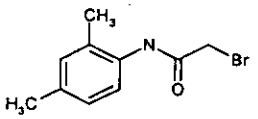
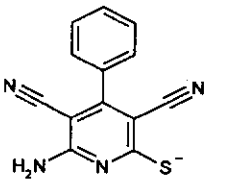
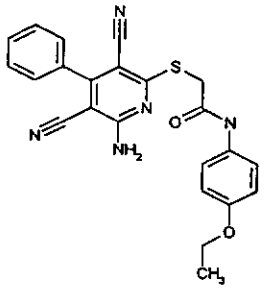
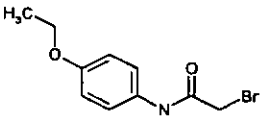
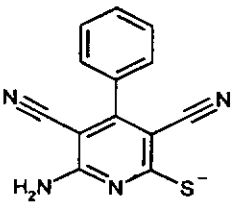
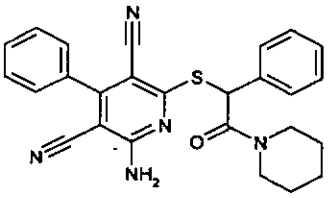
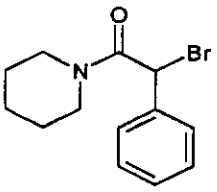
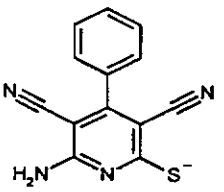
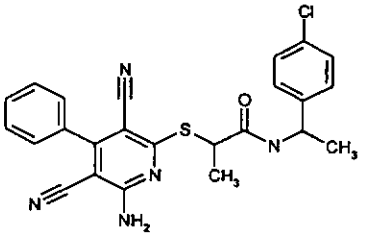
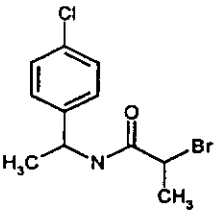
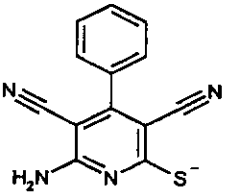
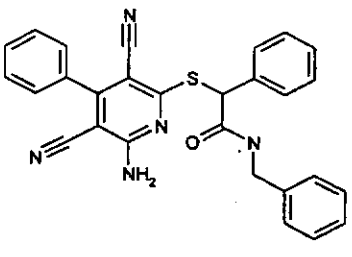
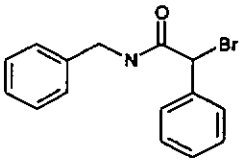
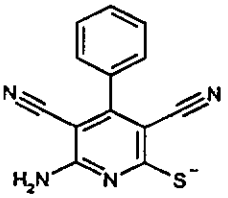
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A85				331	332	71.3
A86				344	345	66.9
A87				345	346	76.3
A88				358	359	83.8
A89				359	360	89.7
A90				373	374	70.5

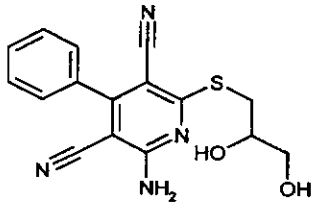
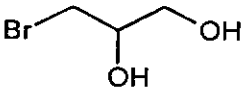
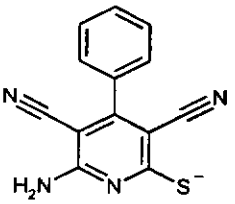
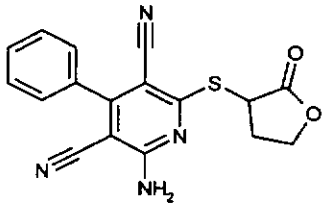
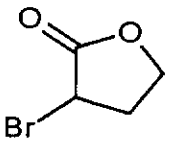
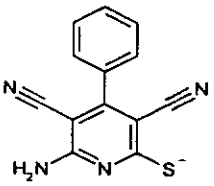
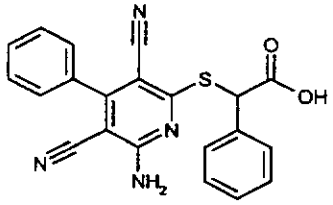
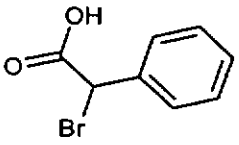
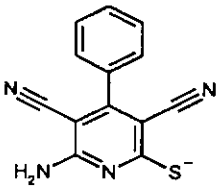
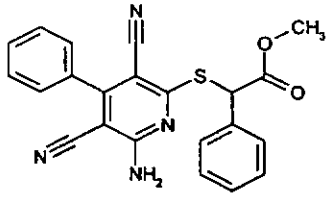
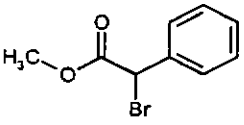
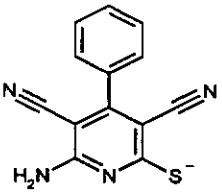
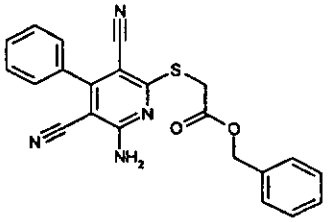
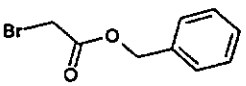
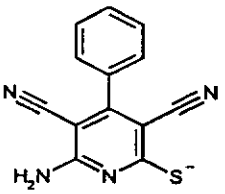
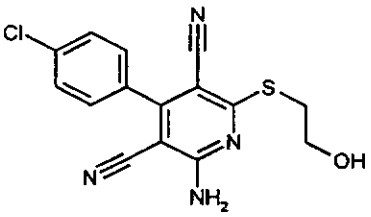
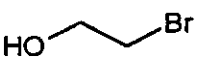
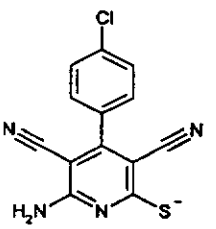
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A91				385	386	12.2
A92				405	406	84.0
A93				413	414	12.1
A94				423	424	23.6
A95				434	435	67.3
A96				488	489	67.4

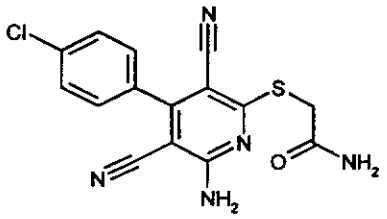
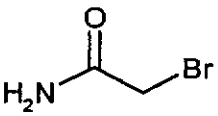
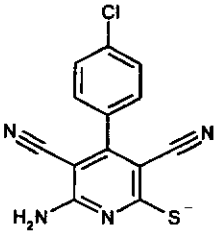
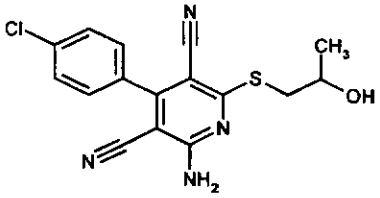
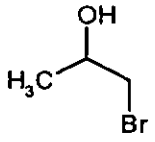
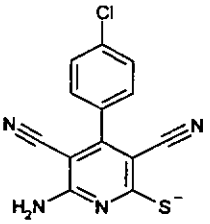
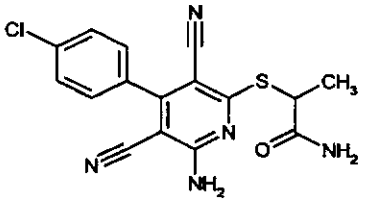
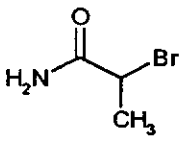
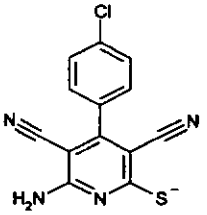
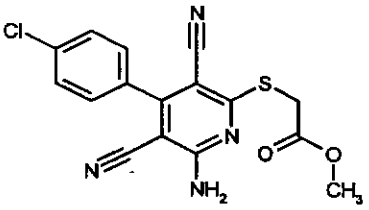
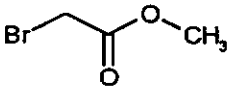
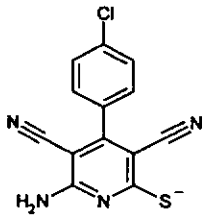
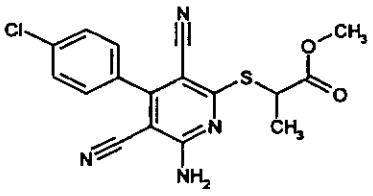
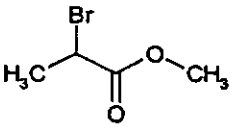
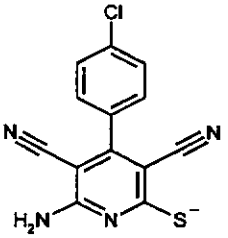
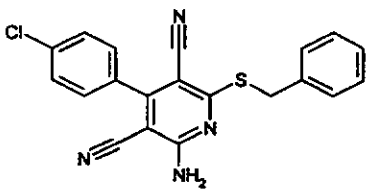
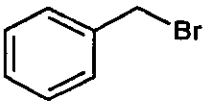
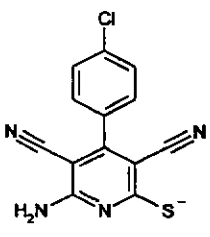
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A97				496	497	90.2
A98				510	511	55.7
A99				361	362	103.1
A100				371	372	48.3
A101				421	422	97.9
A102				435	436	51.7

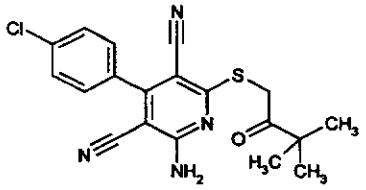
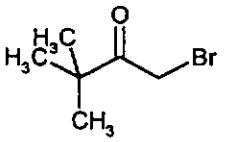
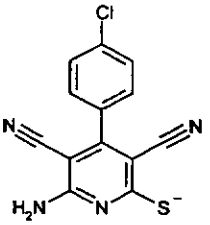
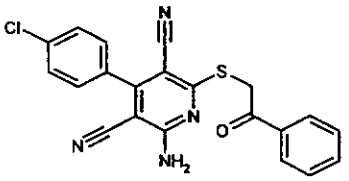
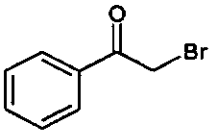
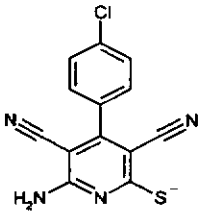
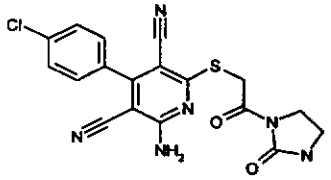
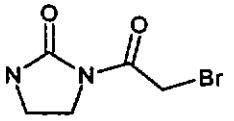
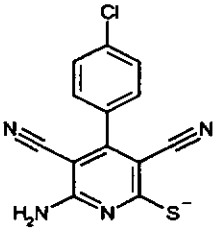
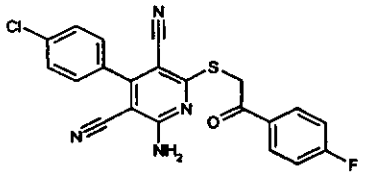
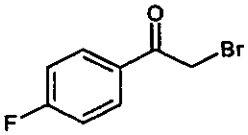
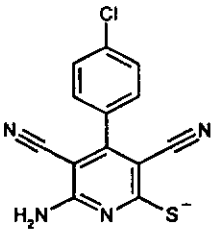
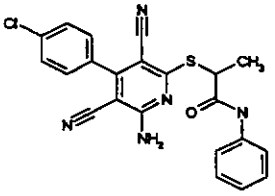
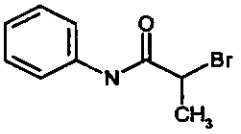
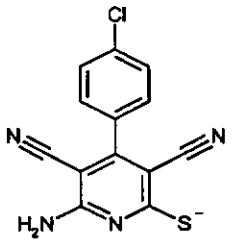
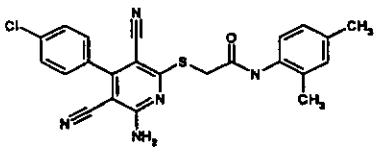
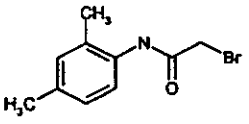
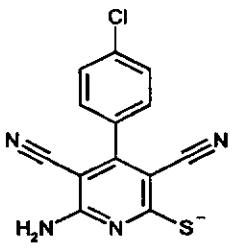
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A103				435	436	63.7
A104				296	297	82.0
A105				309	310	75.6
A106				310	311	72.5
A107				323	324	84.4
A108				324	325	67.8

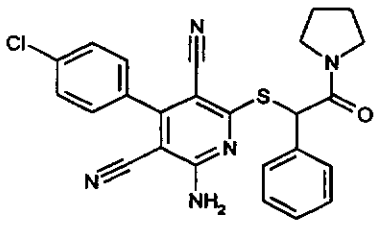
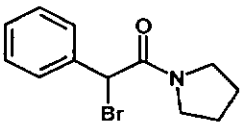
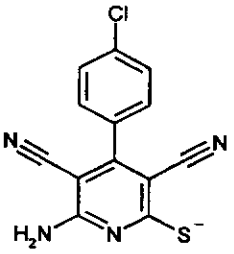
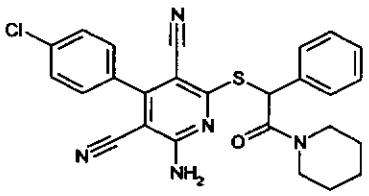
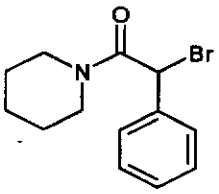
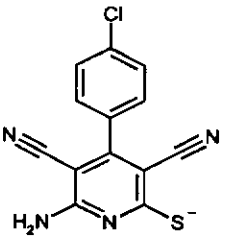
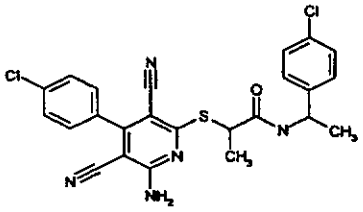
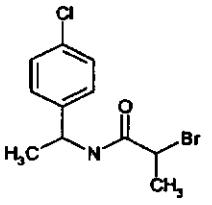
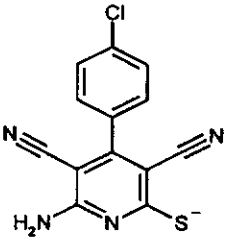
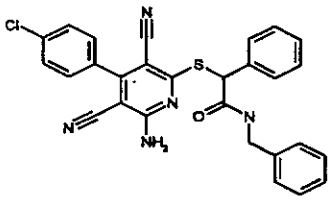
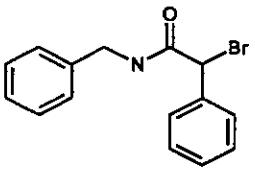
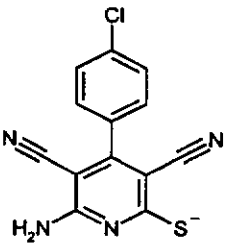
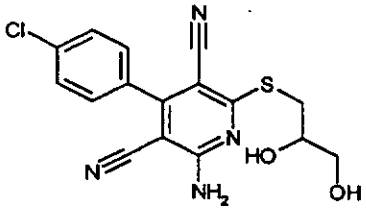
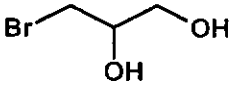
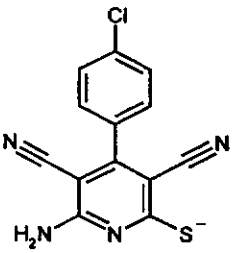
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A109				338	339	71.8
A110				342	343	44.7
A111				350	351	18.5
A112				370	371	73.2
A113				378	379	46.8
A114				388	389	91.4

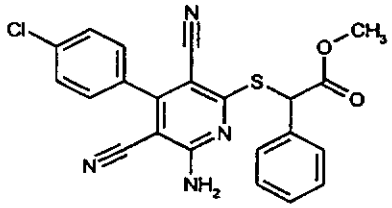
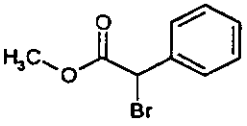
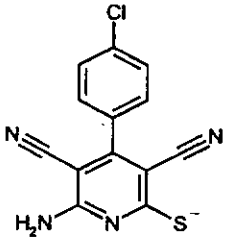
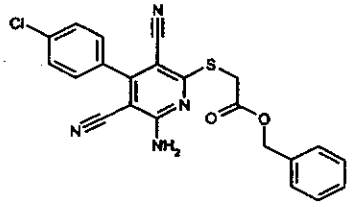
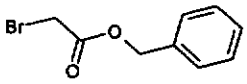
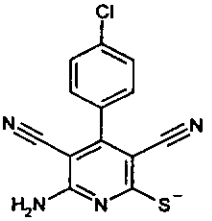
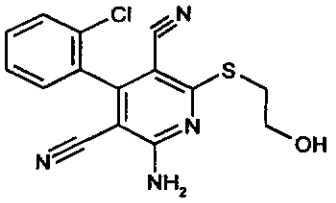
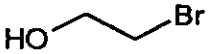
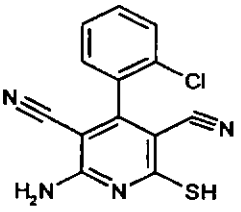
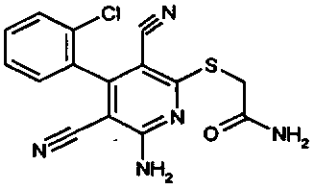
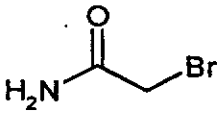
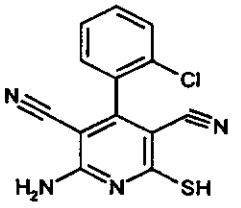
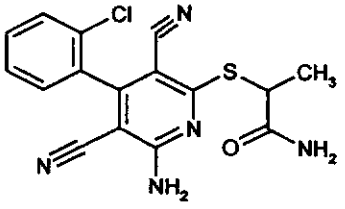
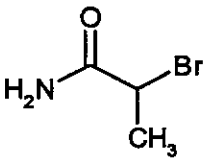
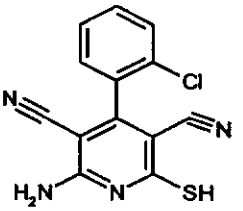
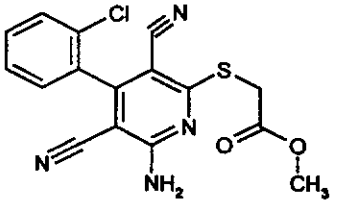
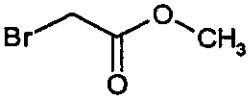
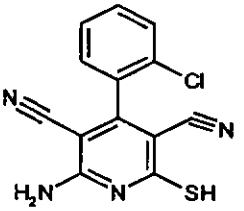
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A115				399	400	17.5
A116				414	415	16.7
A117				430	431	31.4
A118				454	455	58.4
A119				462	463	77.1
A120				476	477	13.0

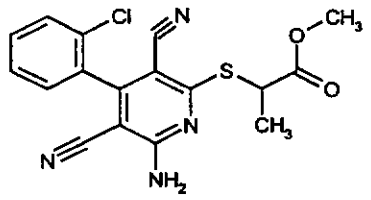
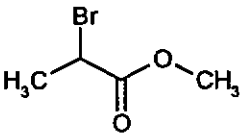
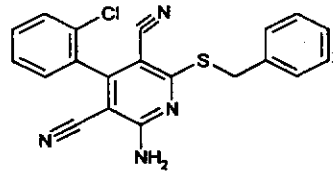
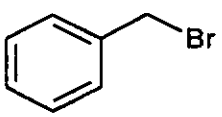
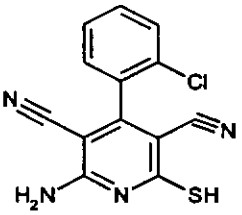
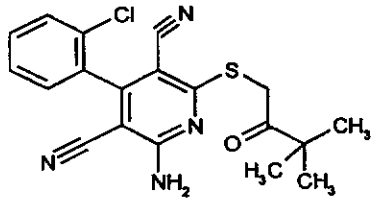
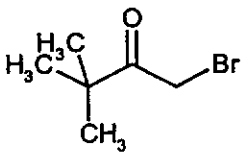
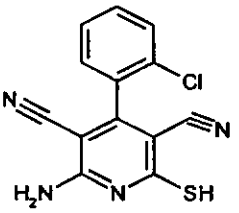
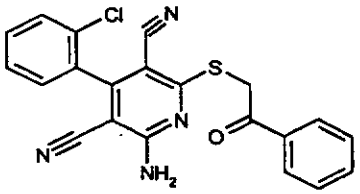
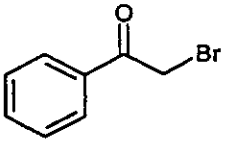
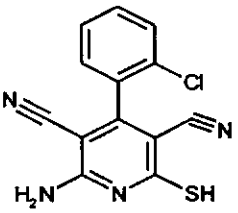
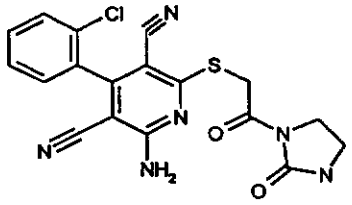
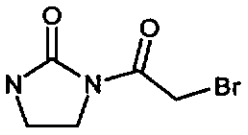
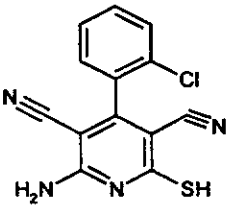
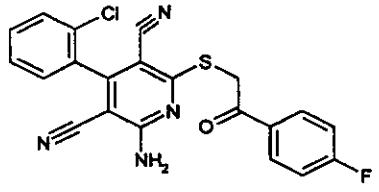
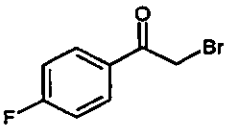
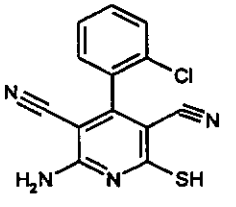
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A121				326	327	89.8
A122				336	337	69.3
A123				386	387	73.2
A124				400	401	66.9
A125				400	401	74.2
A126				331	332	72.6

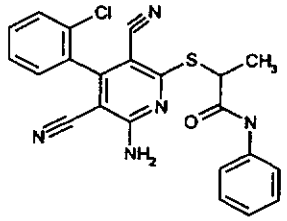
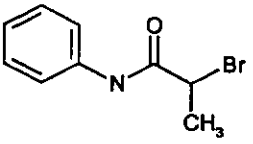
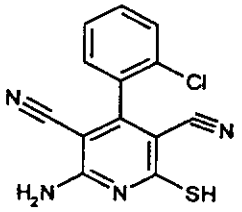
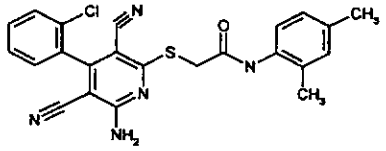
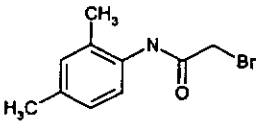
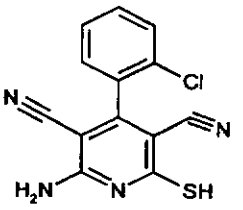
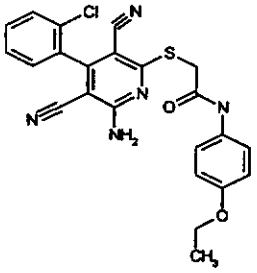
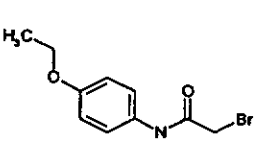
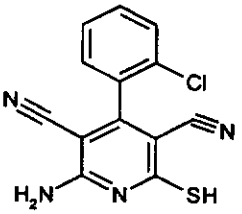
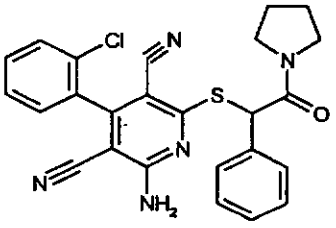
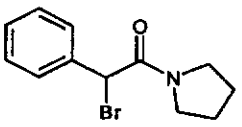
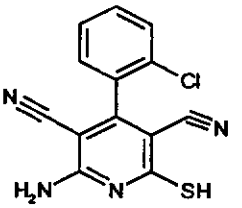
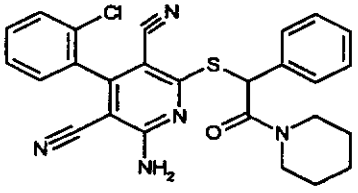
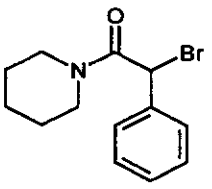
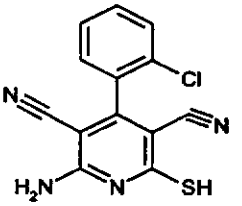
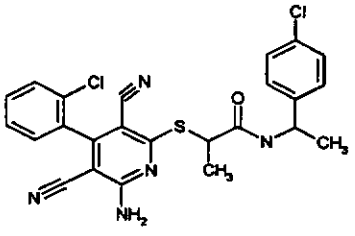
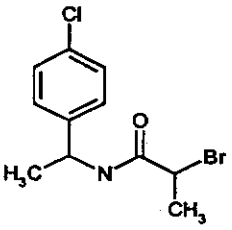
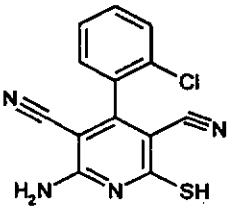
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A127				344	345	68.1
A128				345	346	70.2
A129				358	359	72.4
A130				359	360	44.3
A131				373	374	57.7
A132				377	378	17.2

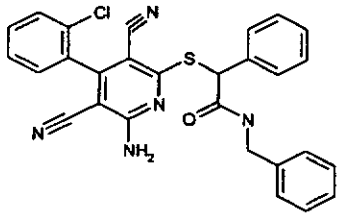
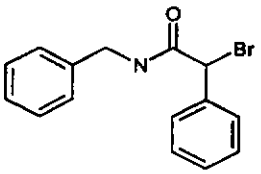
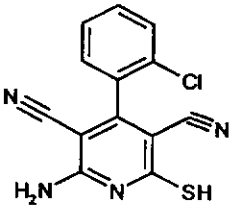
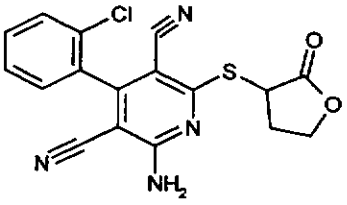
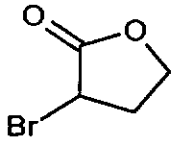
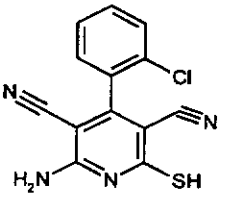
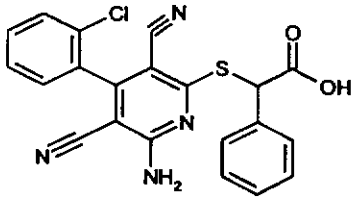
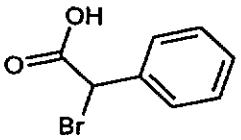
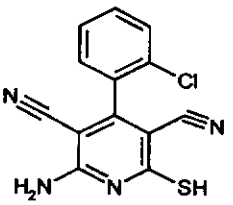
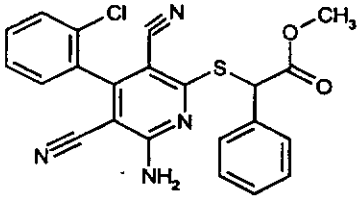
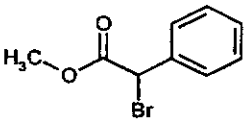
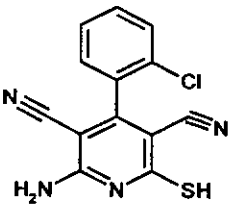
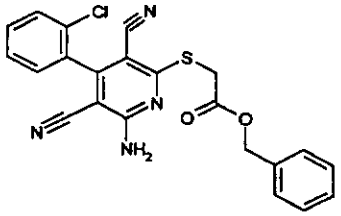
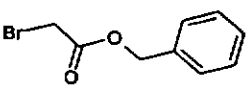
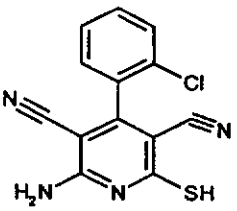
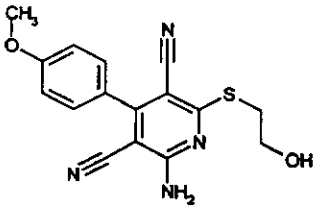
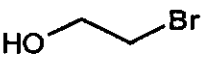
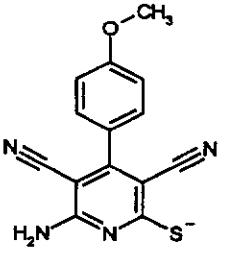
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A133				385	386	14.0
A134				405	406	8.9
A135				413	414	17.2
A136				423	424	12.8
A137				434	435	10.1
A138				448	449	10.0

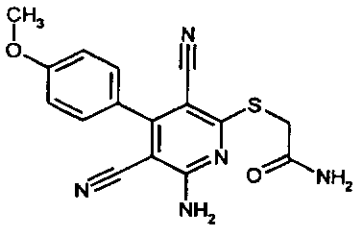
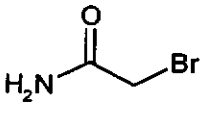
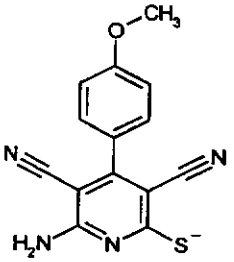
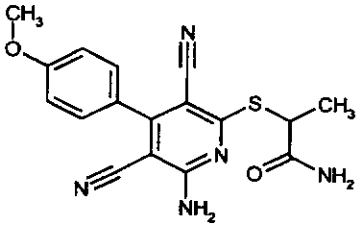
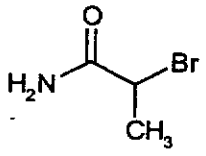
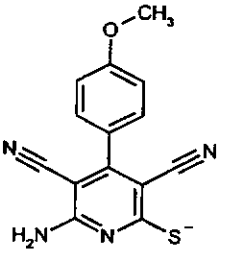
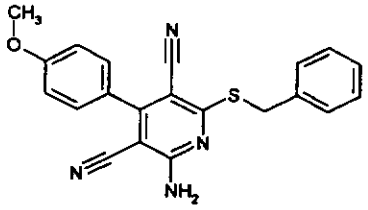
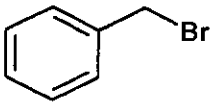
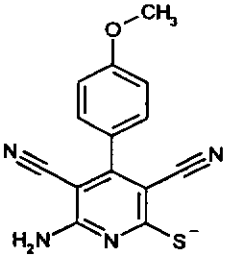
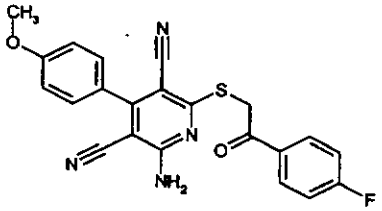
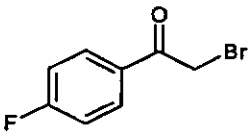
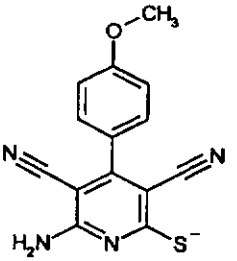
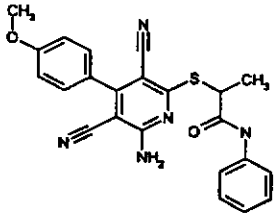
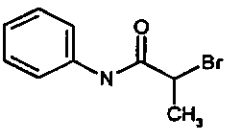
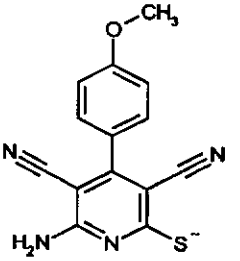
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A139				474	475	52.1
A140				488	489	52.3
A141				496	497	50.2
A142				510	511	43.5
A143				361	362	56.0

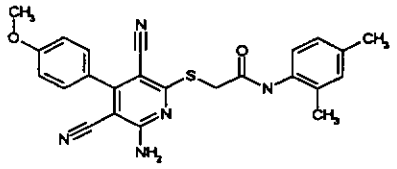
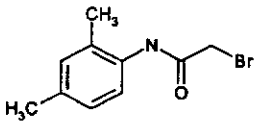
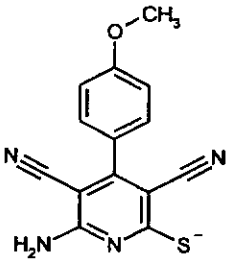
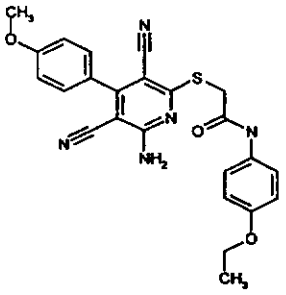
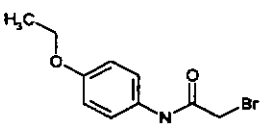
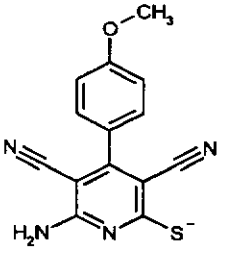
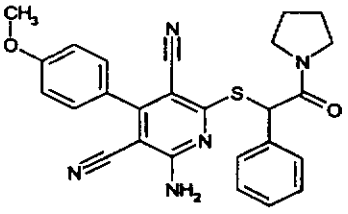
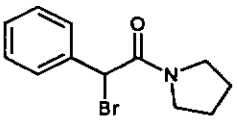
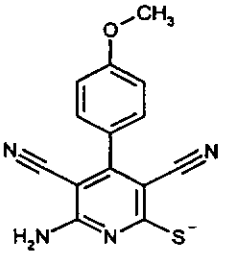
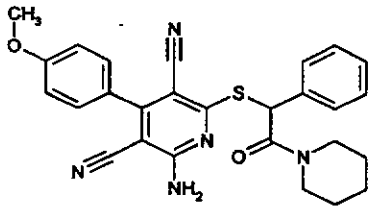
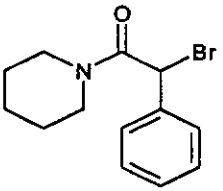
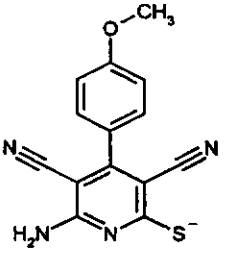
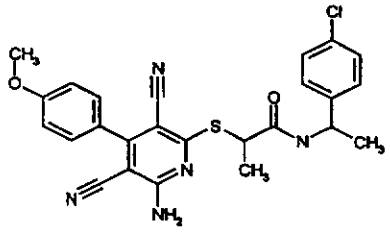
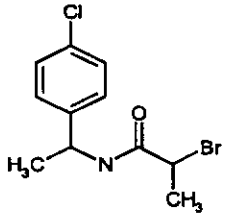
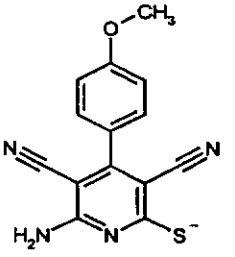
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A144				435	436	3.7
A145				435	436	67.4
A146				331	332	64.1
A147				344	345	70.7
A148				358	359	72.7
A149				359	360	58.8

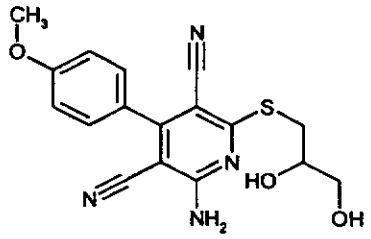
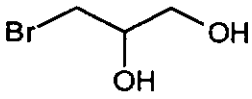
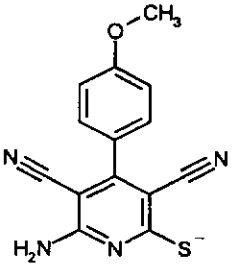
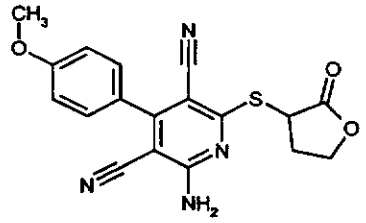
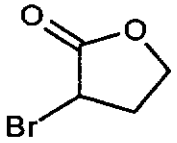
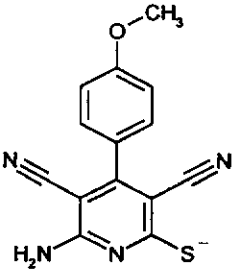
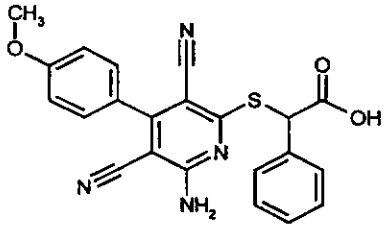
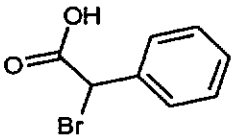
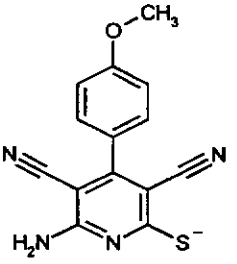
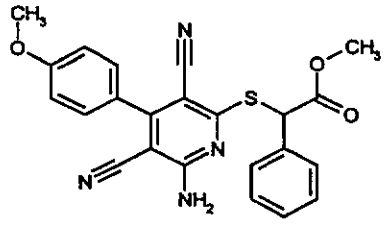
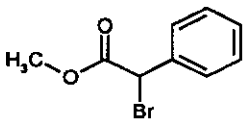
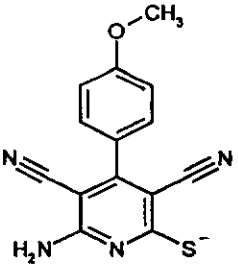
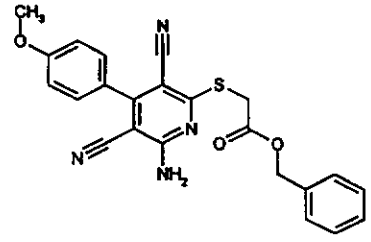
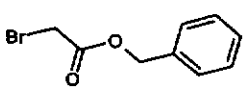
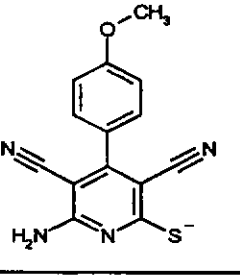
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A150				373	374	56.3
A151				377	378	55.5
A152				385	386	64.2
A153				405	406	32.4
A154				413	414	55.7
A155				423	424	53.9

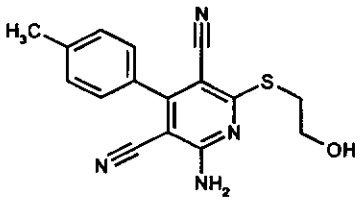
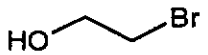
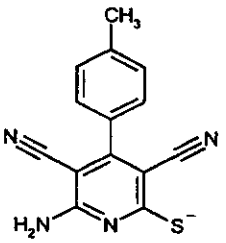
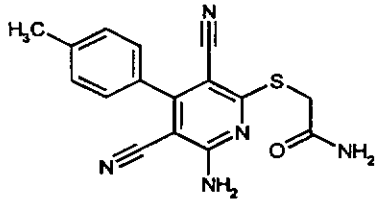
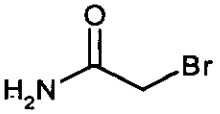
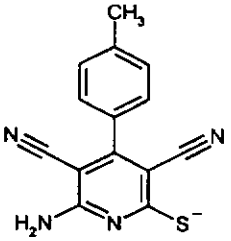
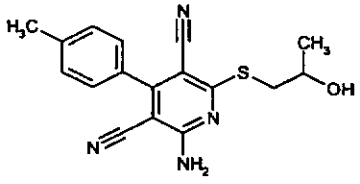
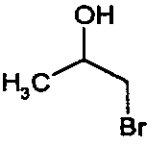
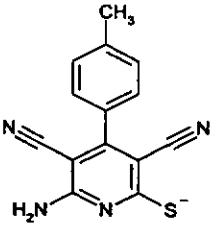
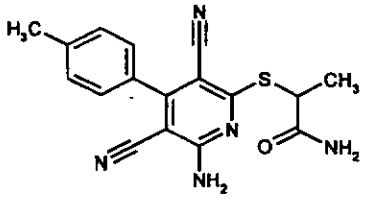
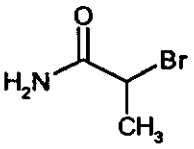
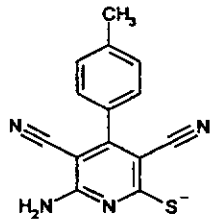
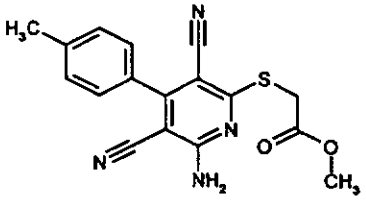
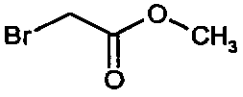
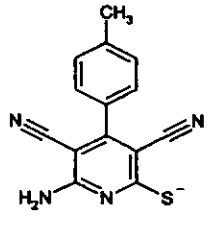
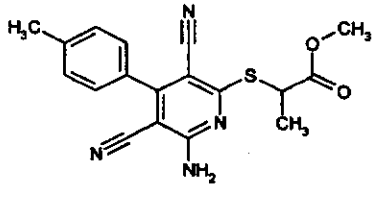
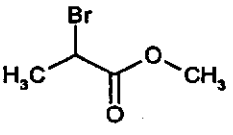
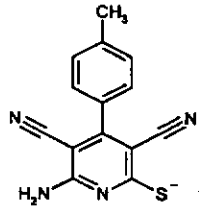
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A156				434	435	74.9
A157				448	449	69.0
A158				464	465	72.0
A159				474	475	73.0
A160				488	489	75.2
A161				496	497	75.5

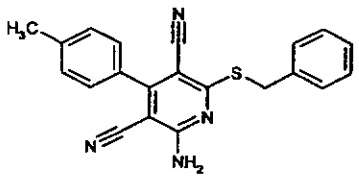
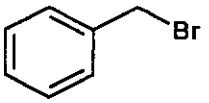
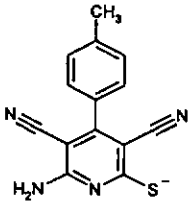
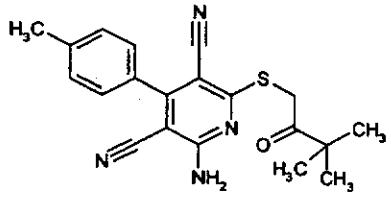
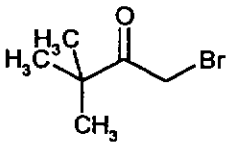
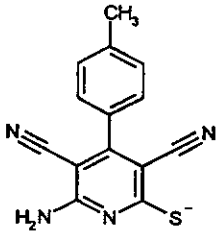
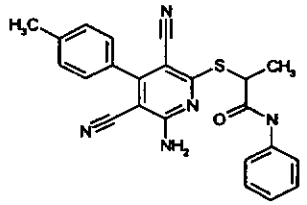
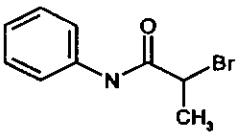
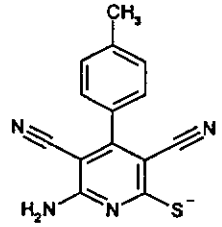
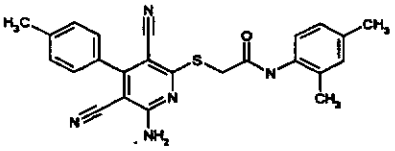
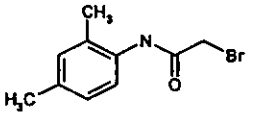
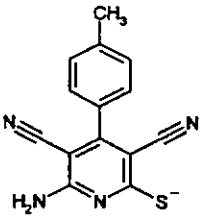
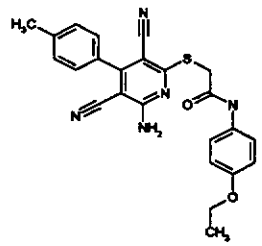
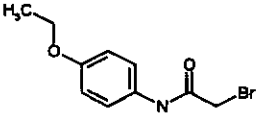
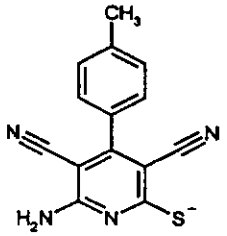
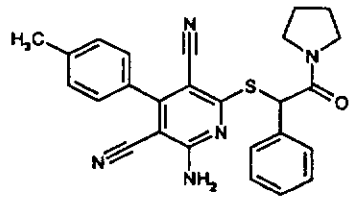
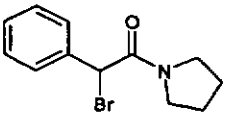
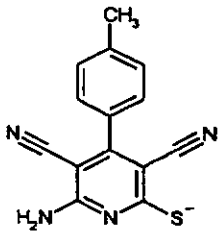
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A162				510	511	67.4
A163				371	372	75.2
A164				421	422	57.7
A165				435	436	71.3
A166				435	436	54.0
A167				326	327	50.9

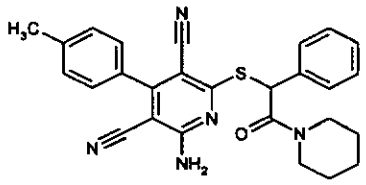
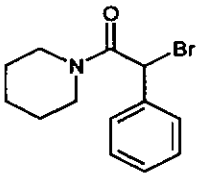
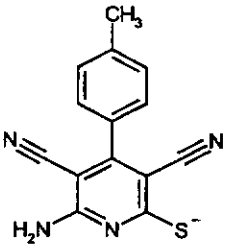
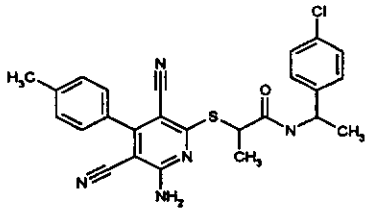
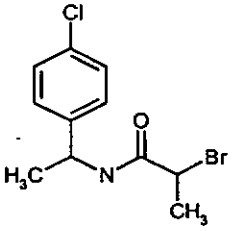
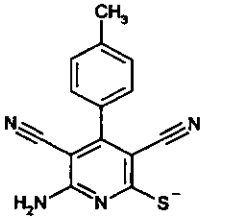
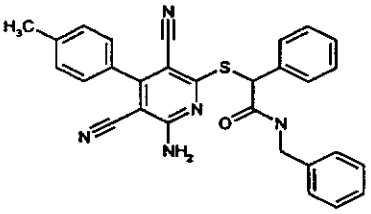
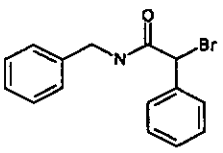
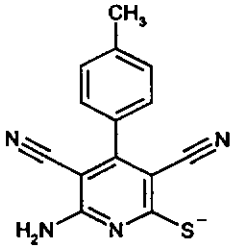
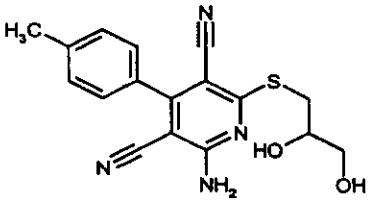
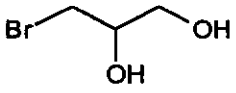
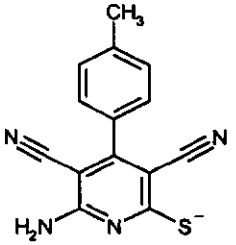
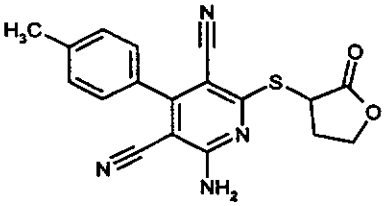
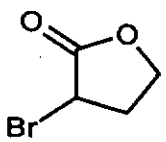
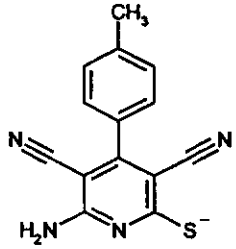
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A168				339	340	76.3
A169				353	354	50.4
A170				372	373	30.6
A171				418	419	13.6
A172				430	431	63.8

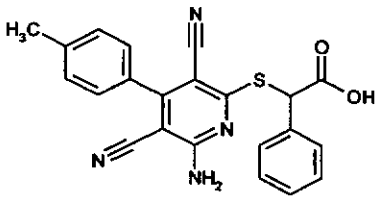
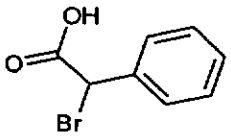
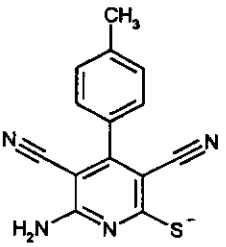
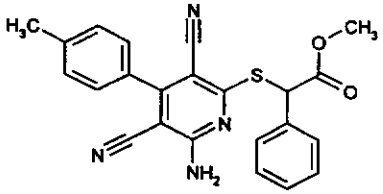
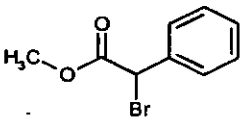
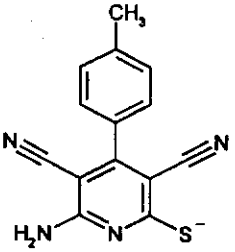
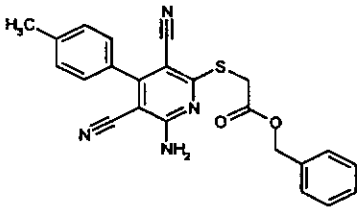
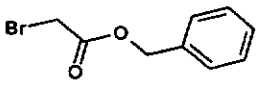
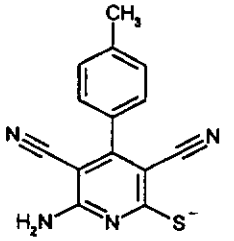
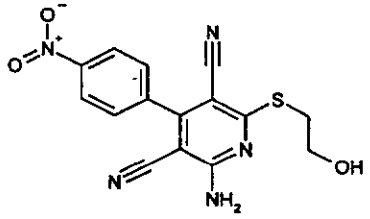
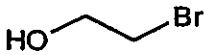
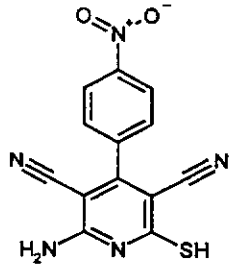
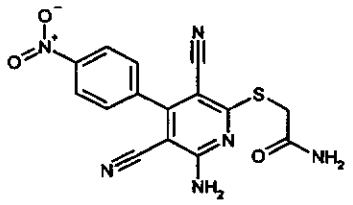
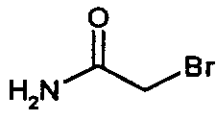
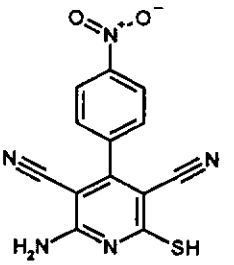
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A173				444	445	26.2
A174				460	461	32.2
A175				470	471	96.9
A176				484	485	18.2
A177				492	493	78.5

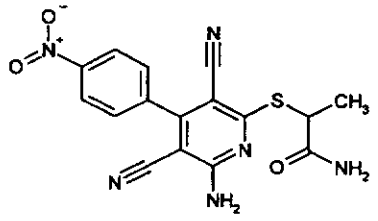
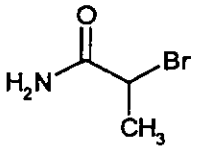
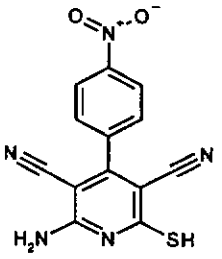
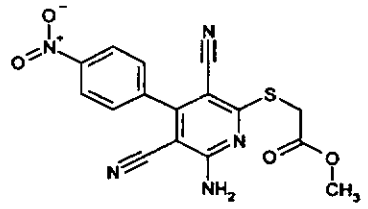
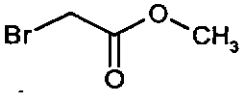
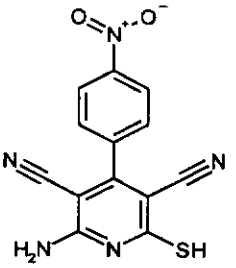
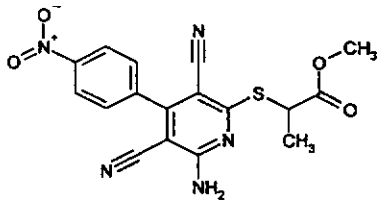
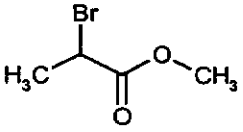
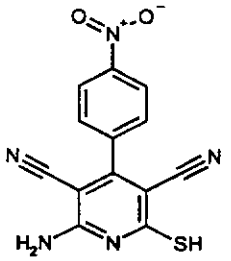
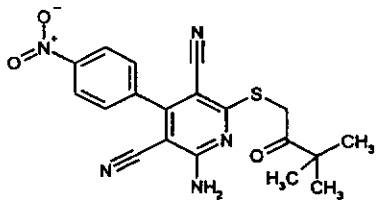
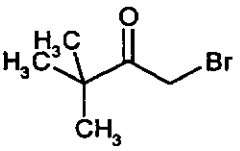
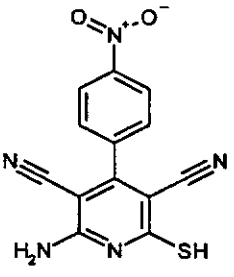
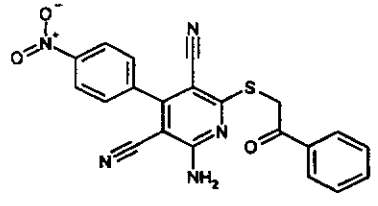
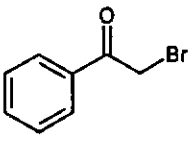
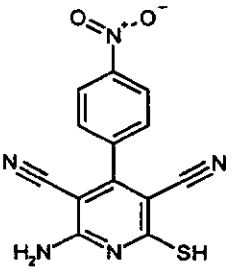
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A178				356	357	17.1
A179				366	367	31.1
A180				416	417	80.0
A181				430	431	66.2
A182				430	431	73.6

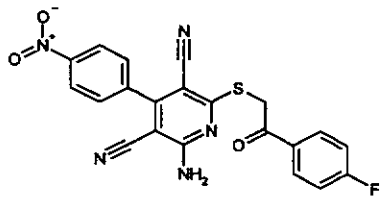
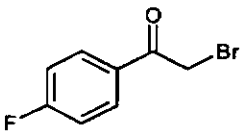
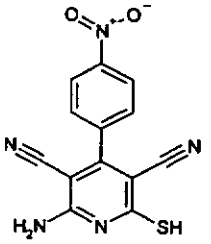
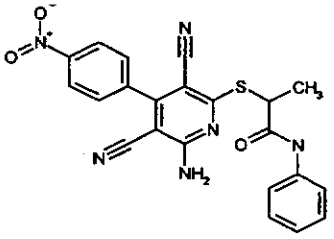
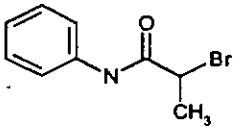
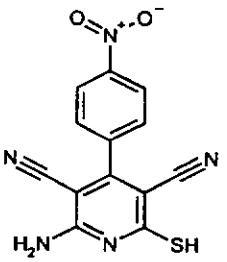
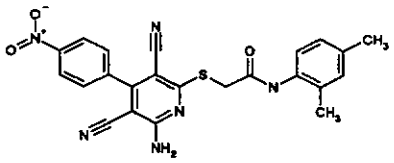
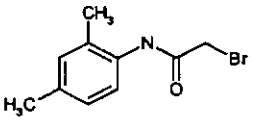
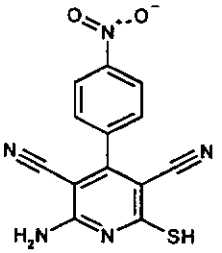
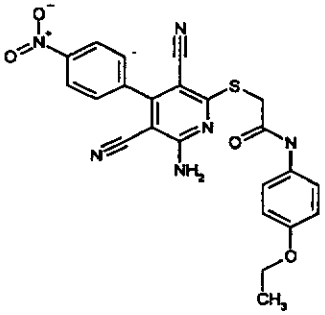
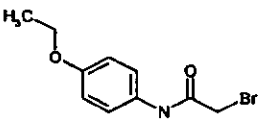
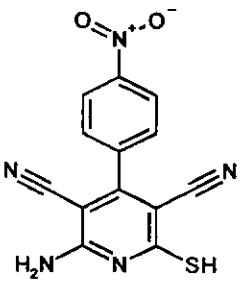
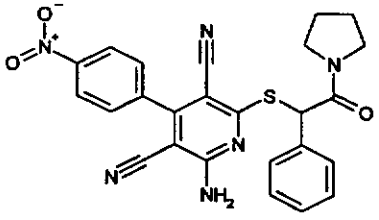
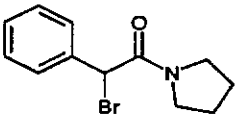
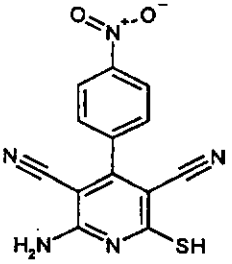
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A183				310	311	28.4
A184				323	324	39.3
A185				324	325	41.9
A186				337	338	40.9
A187				338	339	11.5
A188				352	353	29.2

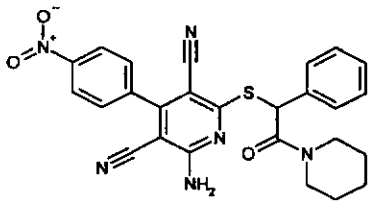
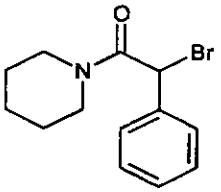
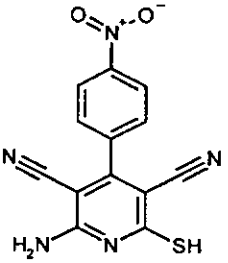
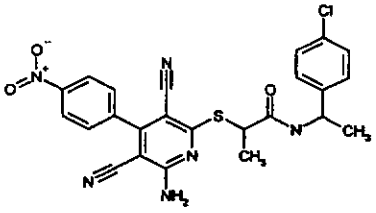
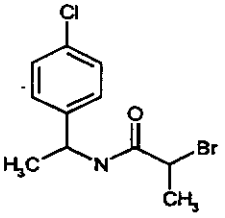
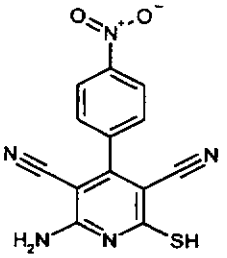
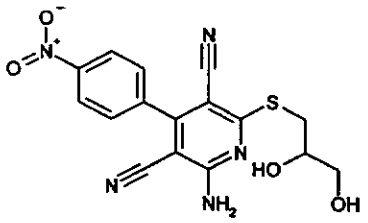
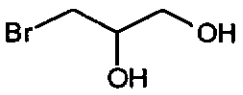
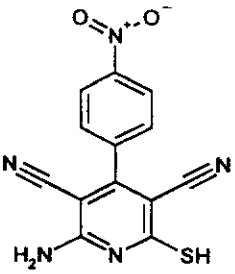
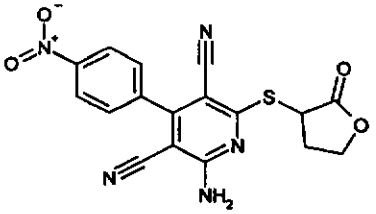
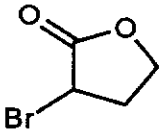
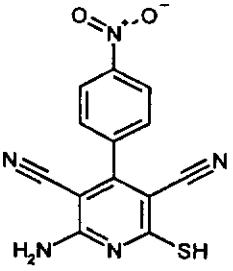
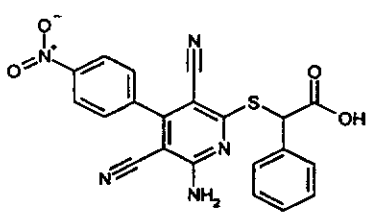
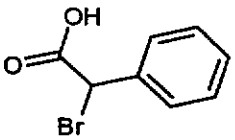
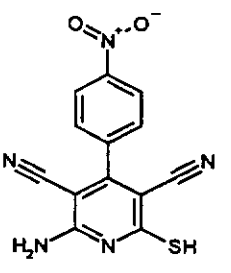
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A189				356	357	51.9
A190				364	365	77.4
A191				414	415	51.8
A192				428	429	58.2
A193				444	445	58.2
A194				454	455	29.5

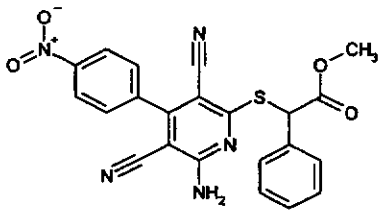
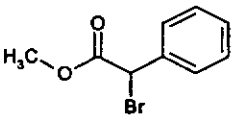
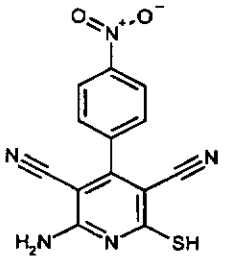
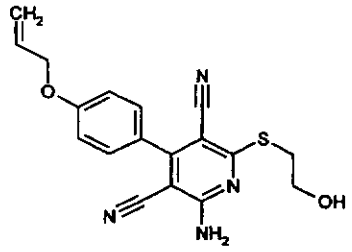
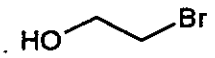
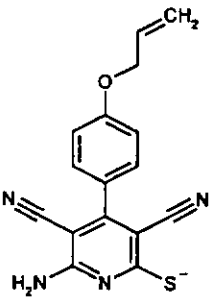
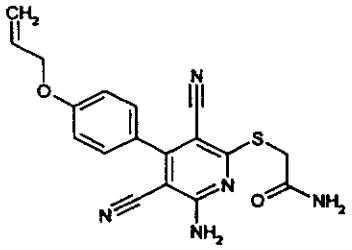
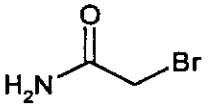
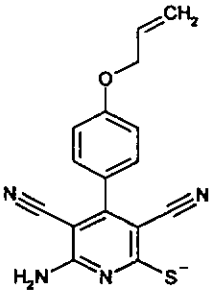
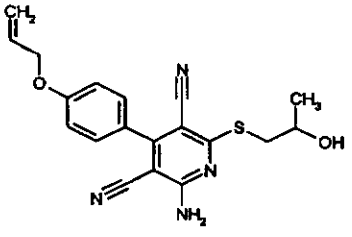
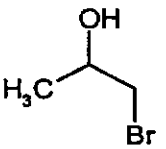
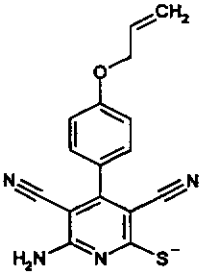
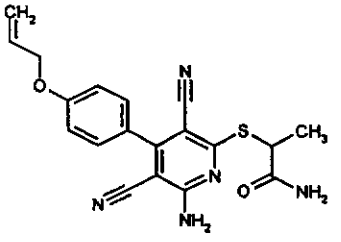
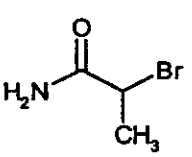
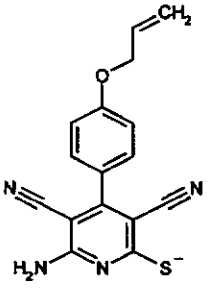
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A195				468	469	43.8
A196				476	477	51.7
A197				490	491	73.9
A198				340	341	37.9
A199				350	351	80.8

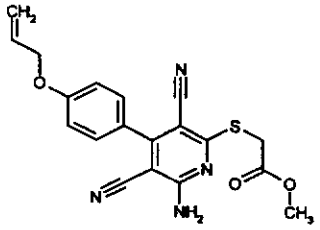
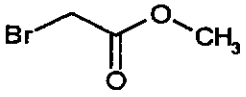
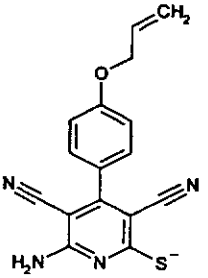
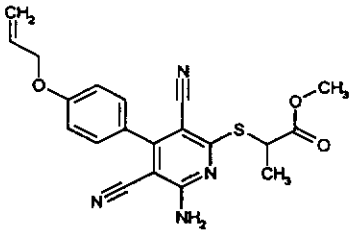
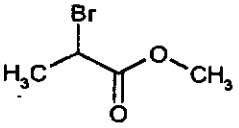
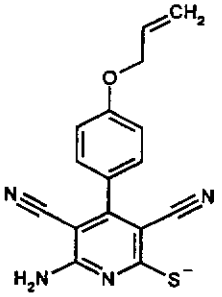
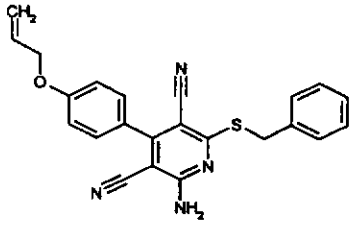
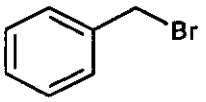
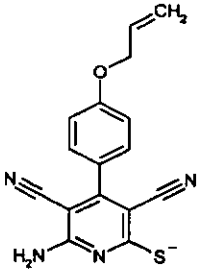
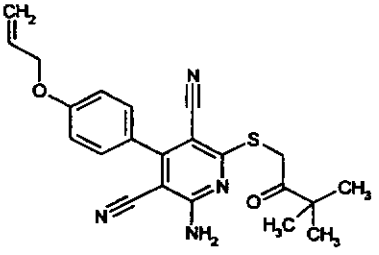
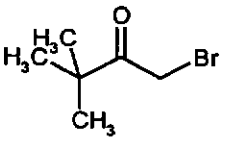
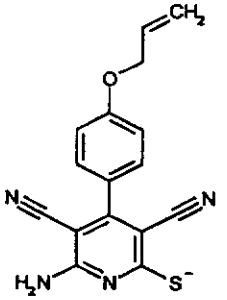
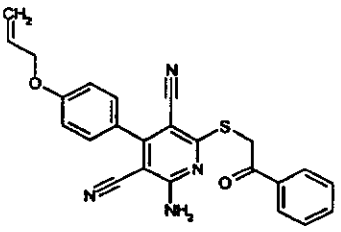
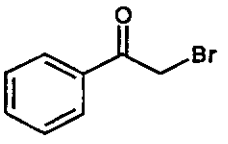
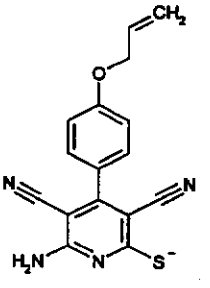
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A200				400	401	48.4
A201				414	415	20.7
A202				414	415	61.0
A203				341	342	55.4
A204				354	355	38.4

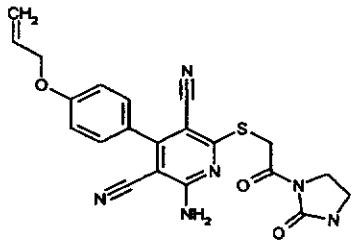
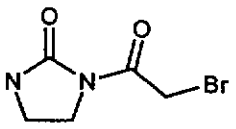
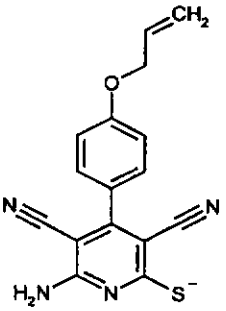
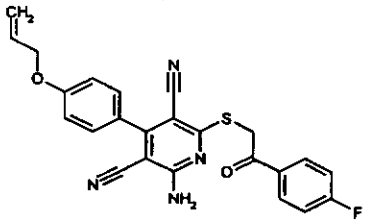
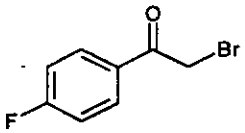
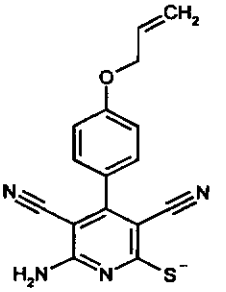
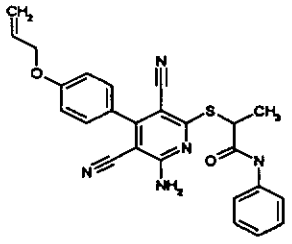
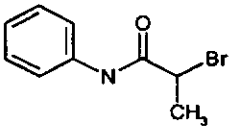
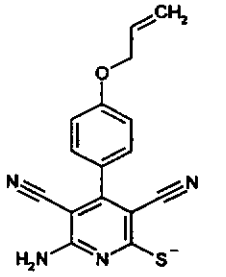
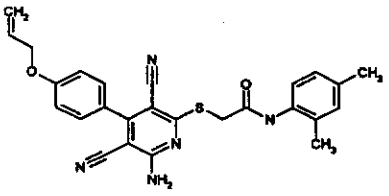
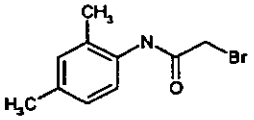
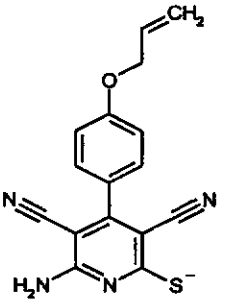
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A205				368	369	70.6
A206				369	370	49.5
A207				383	384	65.5
A208				395	396	14.2
A209				415	416	22.9

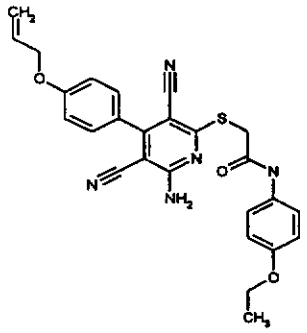
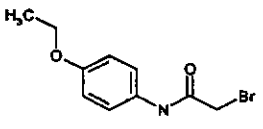
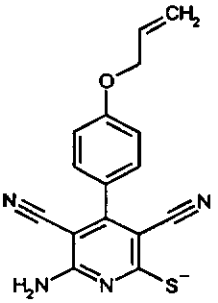
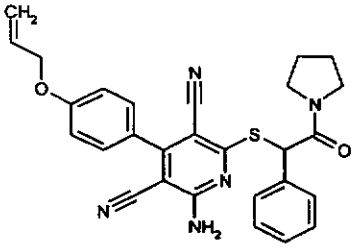
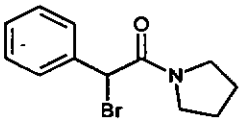
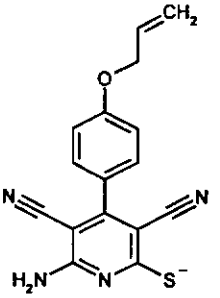
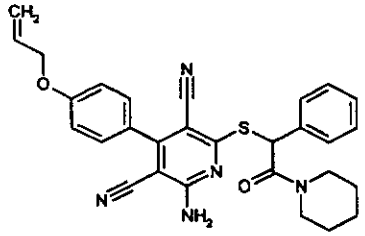
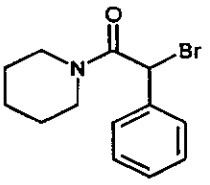
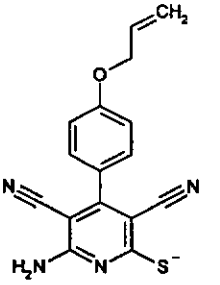
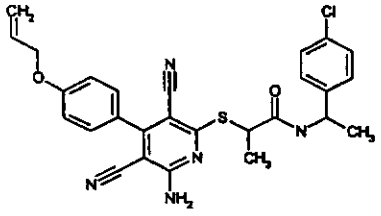
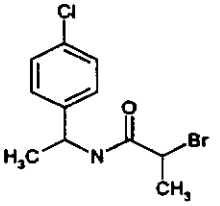
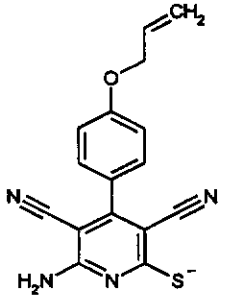
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A210				433	434	40.8
A211				444	445	70.2
A212				459	460	21.6
A213				475	476	57.5
A214				485	486	41.5

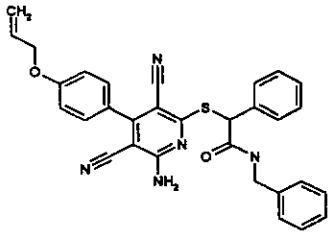
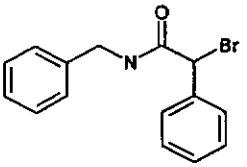
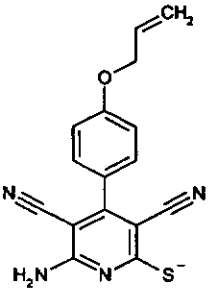
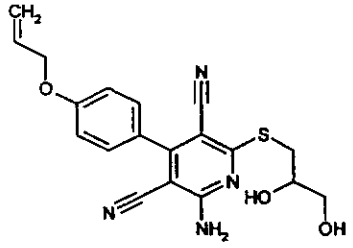
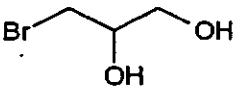
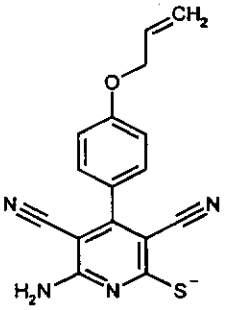
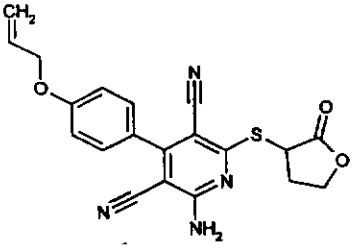
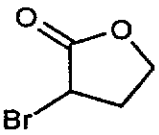
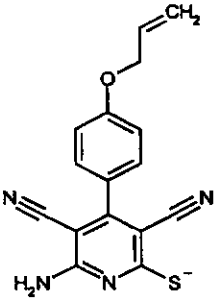
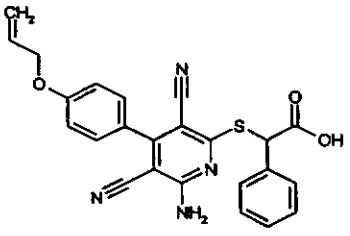
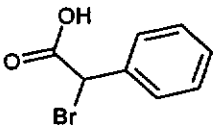
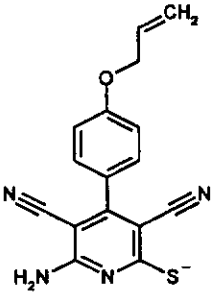
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A215				499	500	43.1
A216				507	508	56.2
A217				371	372	62.5
A218				381	382	39.9
A219				431	432	55.6

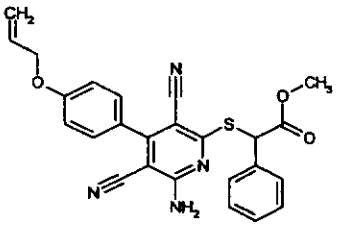
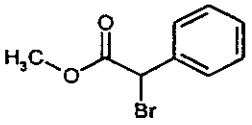
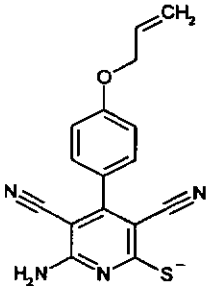
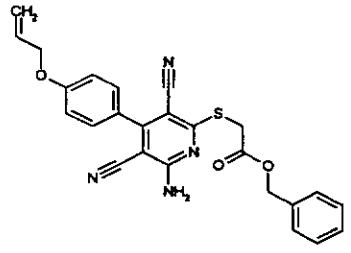
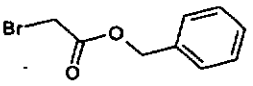
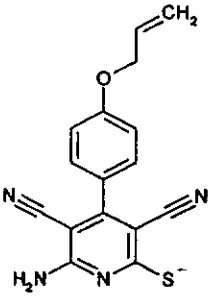
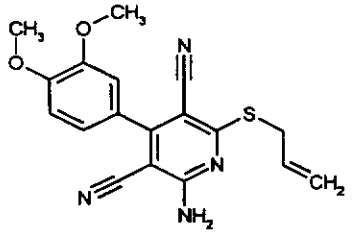
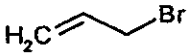
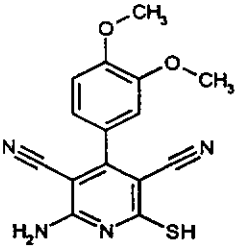
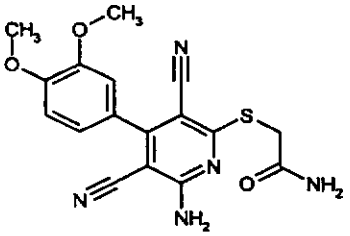
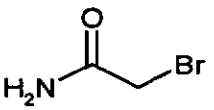
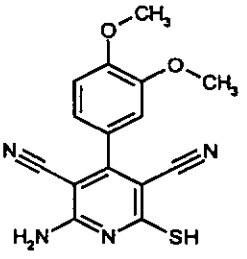
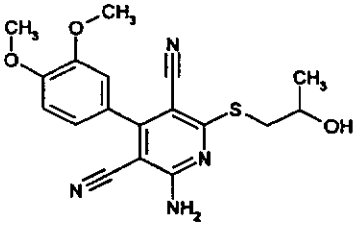
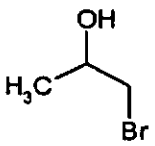
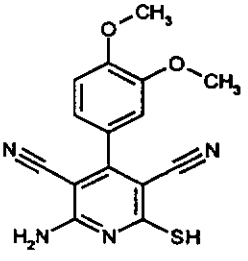
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A220				445	446	32.6
A221				352	353	61.3
A222				365	366	80.2
A223				366	367	73.1
A224				379	380	81.7

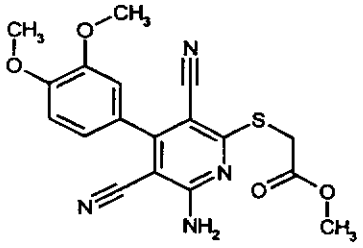
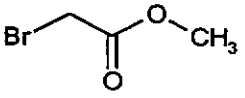
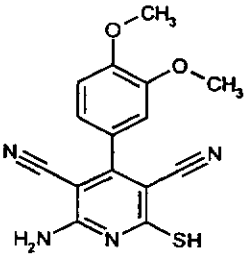
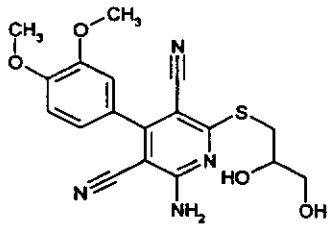
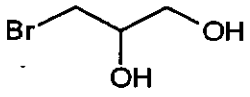
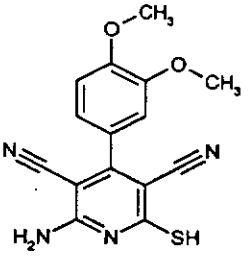
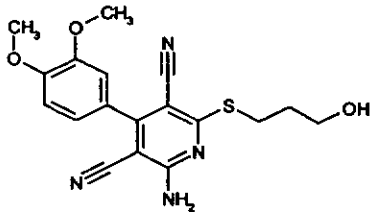
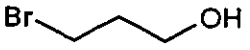
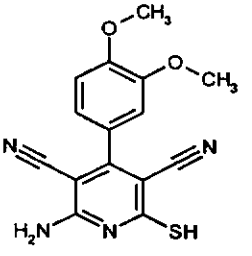
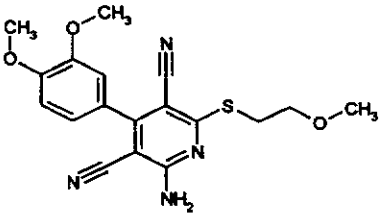
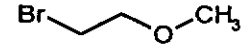
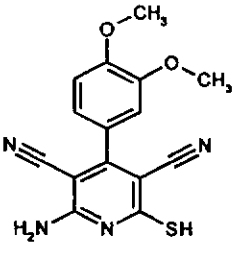
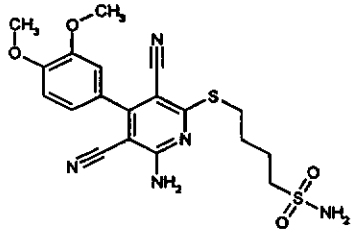
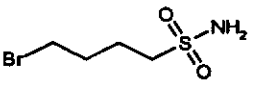
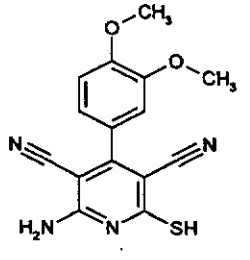
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A225				380	381	71.0
A226				394	395	65.9
A227				398	399	76.3
A228				407	408	79.7
A229				427	428	40.8

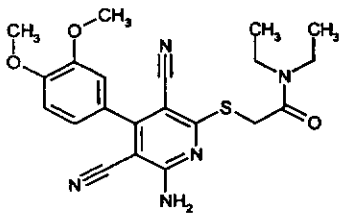
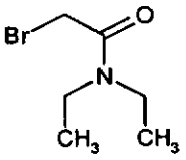
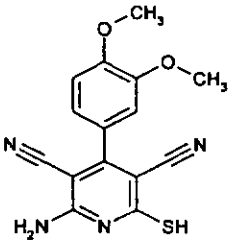
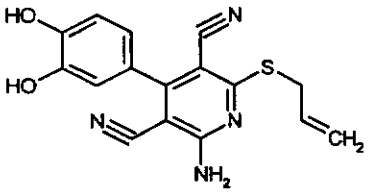
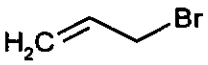
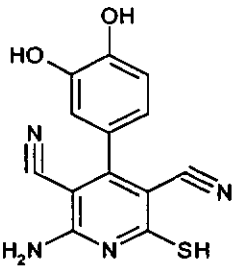
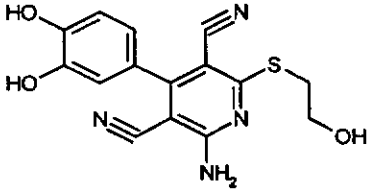
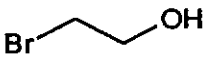
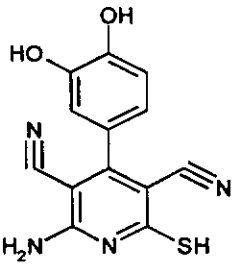
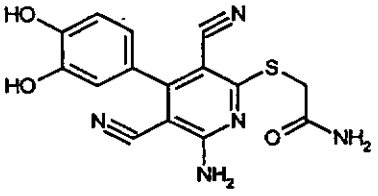
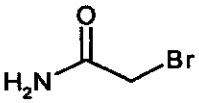
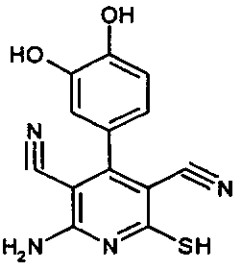
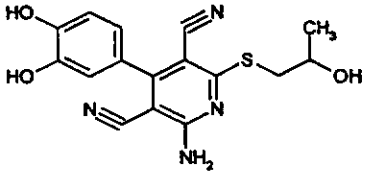
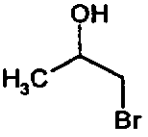
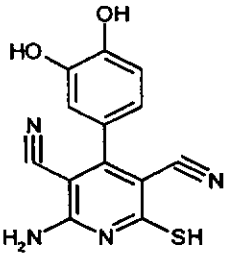
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A230				434	435	22.1
A231				444	445	9.7
A232				456	457	15.6
A233				470	471	43.7

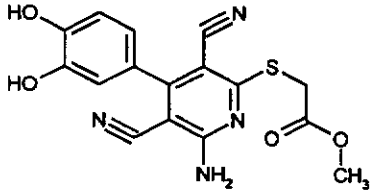
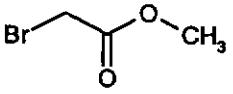
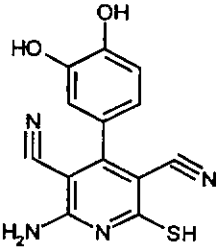
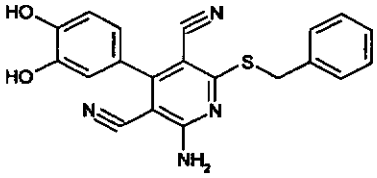
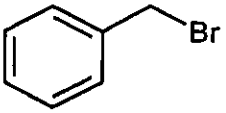
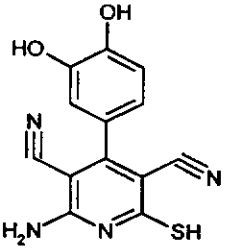
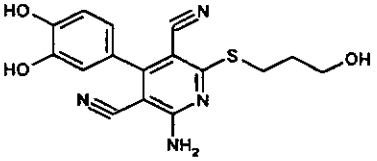
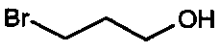
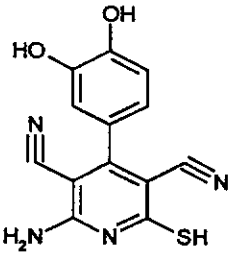
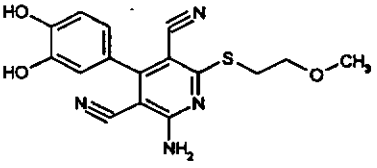
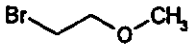
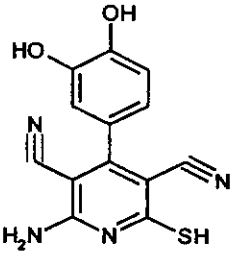
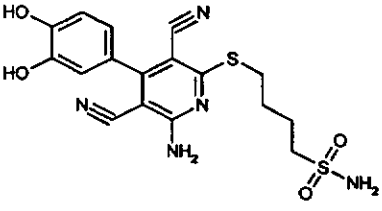
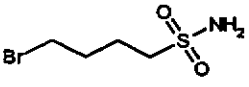
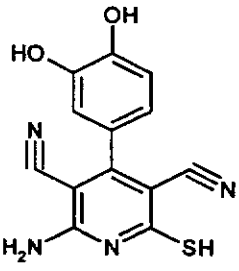
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A234				486	487	71.1
A235				496	497	96.4
A236				510	511	84.6
A237				518	519	41.7

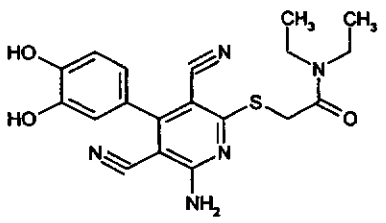
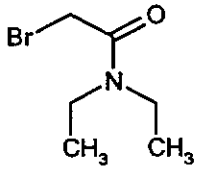
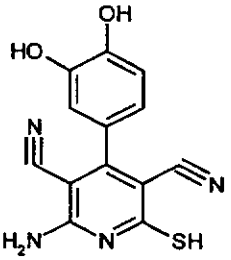
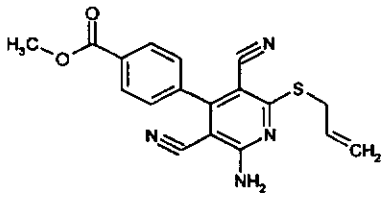
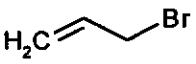
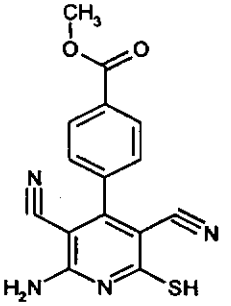
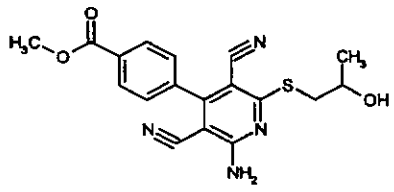
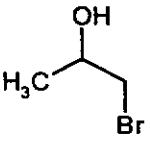
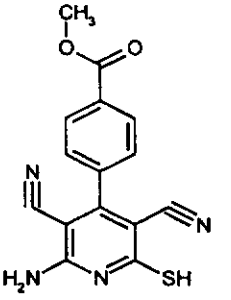
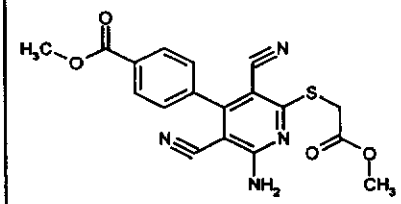
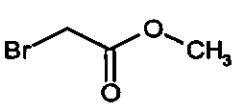
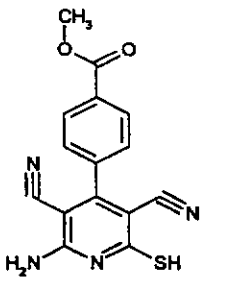
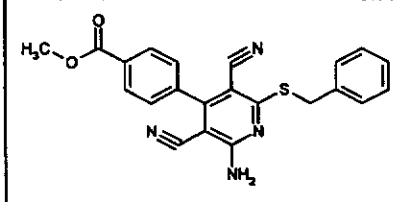
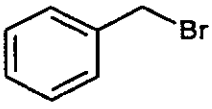
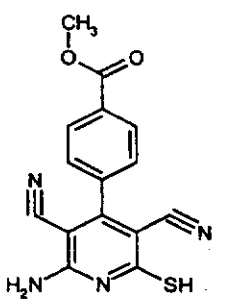
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A238				532	533	28.8
A239				382	383	83.7
A240				392	393	54.8
A241				443	444	75.0

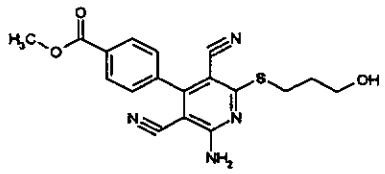
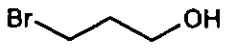
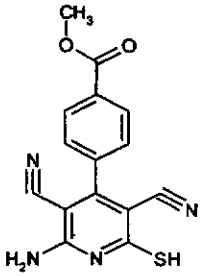
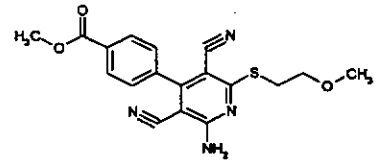
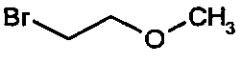
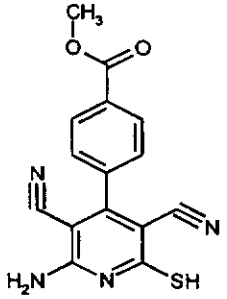
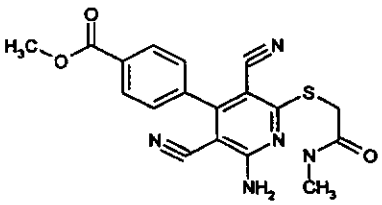
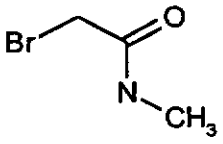
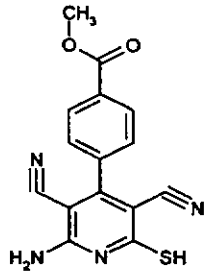
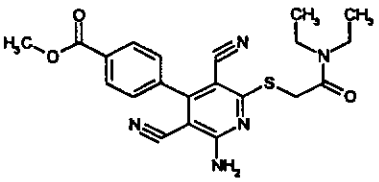
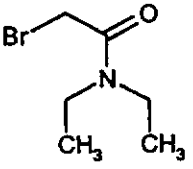
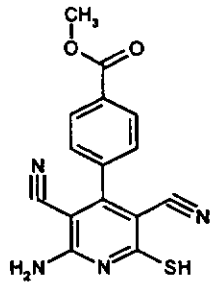
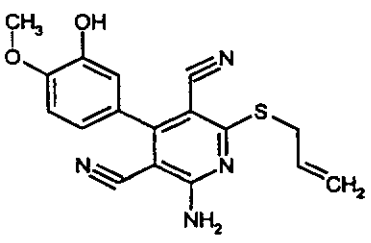
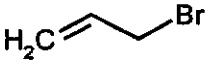
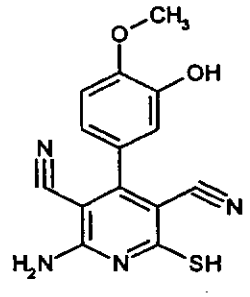
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A242				457	458	50.2
A243				457	458	44.9
A244				352	353	54.5
A245				369	370	85.5
A246				370	371	60.7

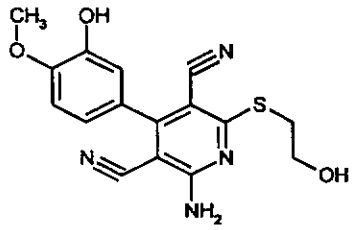
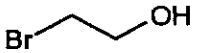
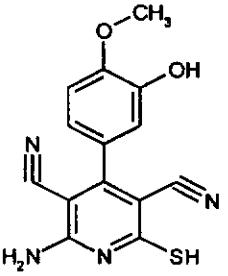
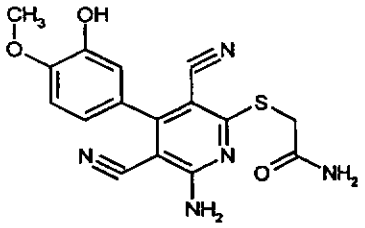
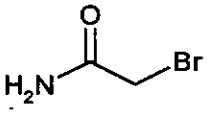
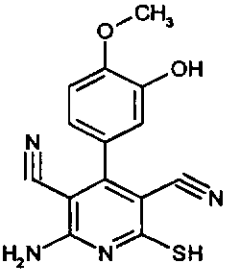
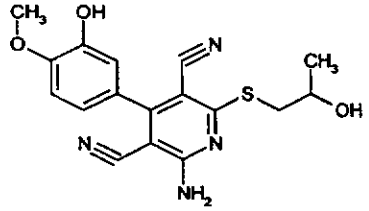
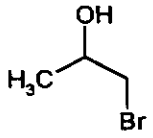
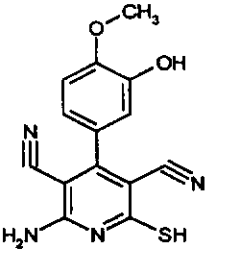
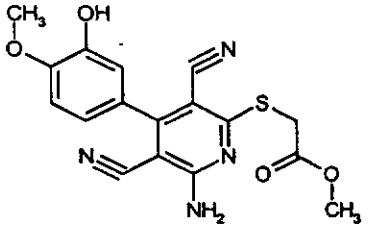
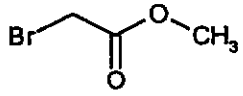
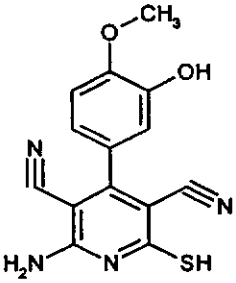
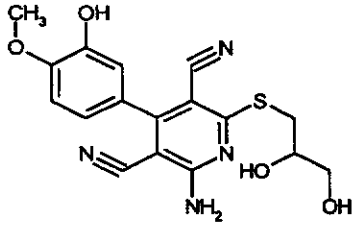
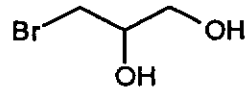
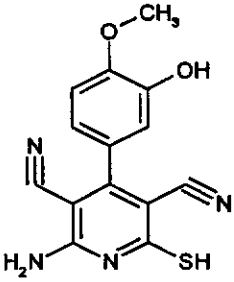
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A247				384	385	59.1
A248				386	387	79.7
A249				370	371	51.6
A250				370	371	49.4
A251				448	449	70.4

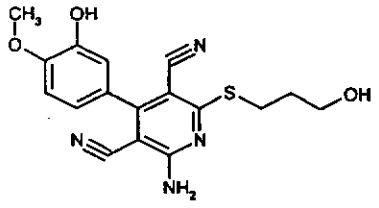
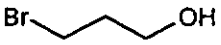
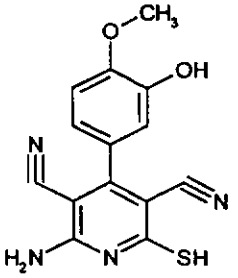
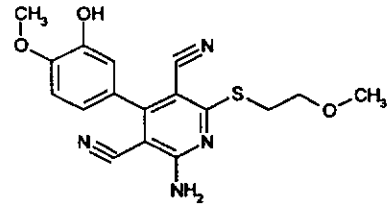
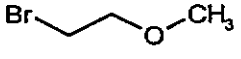
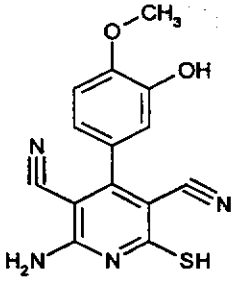
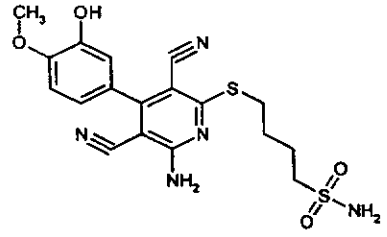
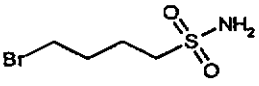
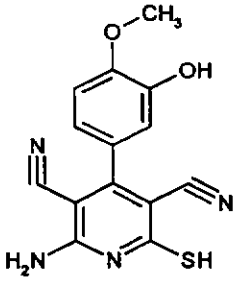
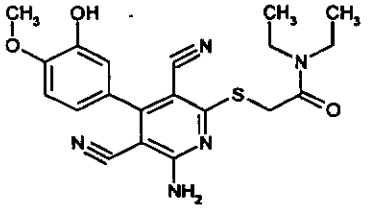
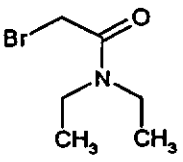
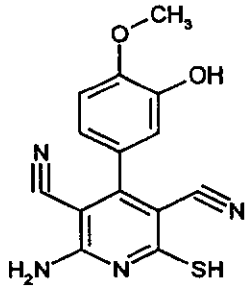
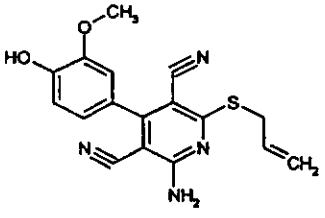
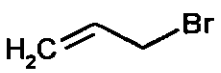
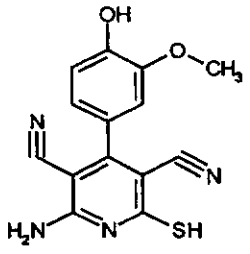
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A252				426	427	39.0
A253				324	325	66.9
A254				328	329	90.1
A255				341	342	114.5
A256				342	343	70.7

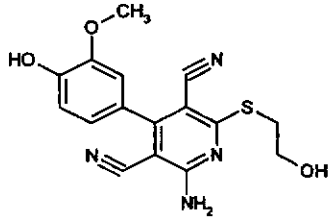
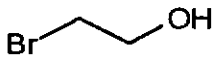
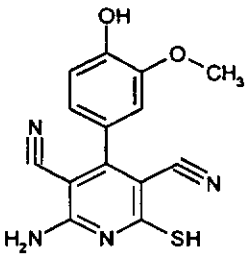
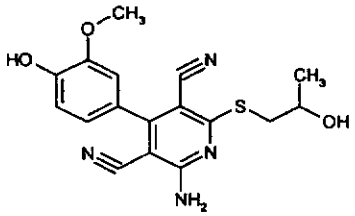
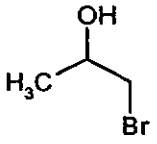
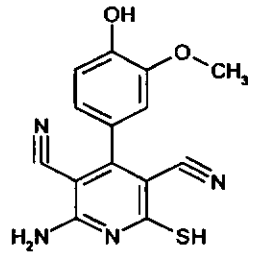
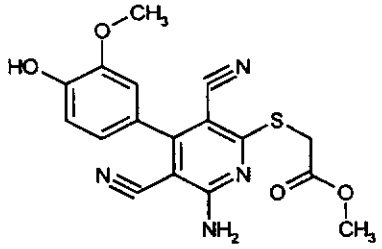
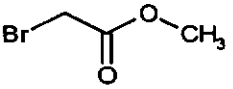
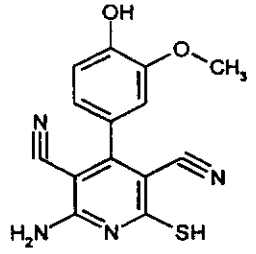
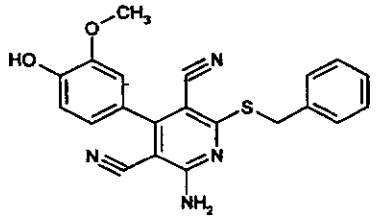
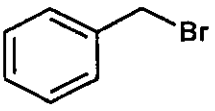
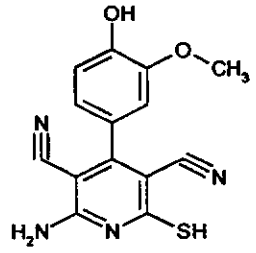
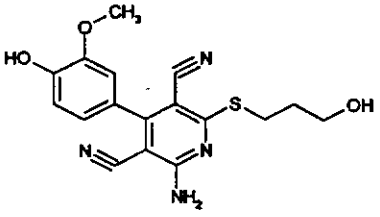
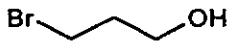
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A257				356	357	77.7
A258				374	375	87.1
A259				342	343	85.3
A260				342	343	73.3
A261				419	420	91.3

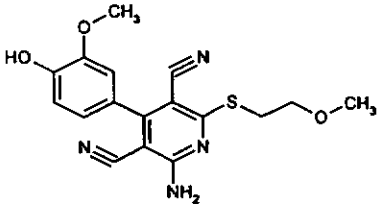
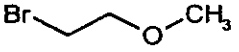
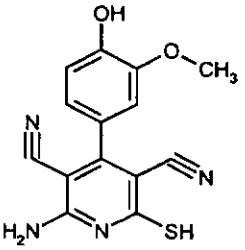
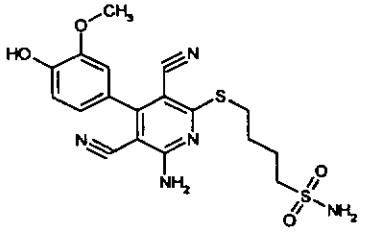
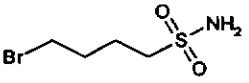
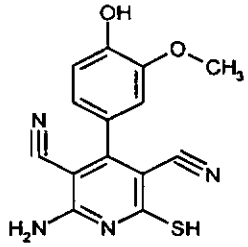
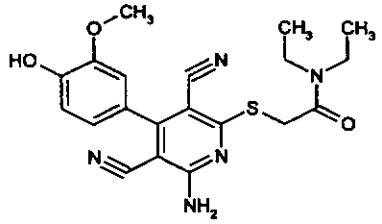
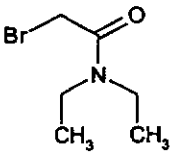
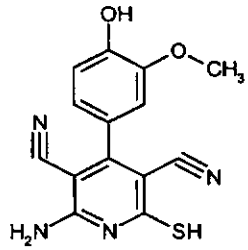
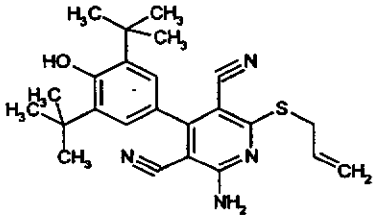
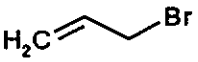
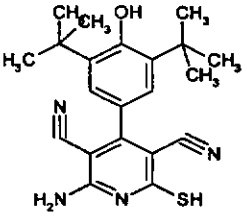
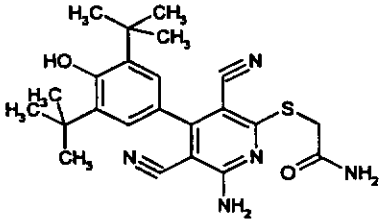
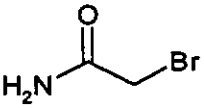
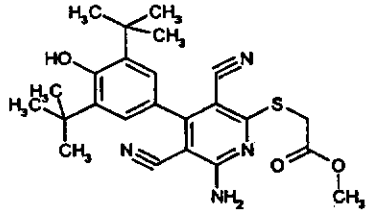
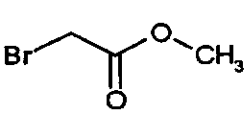
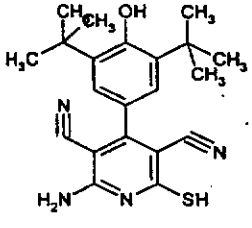
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A262				397	398	66.2
A263				350	351	50.5
A264				368	369	49.1
A265				382	383	58.6
A266				400	401	53.4

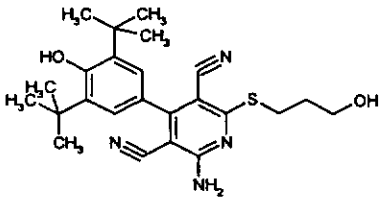
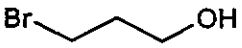
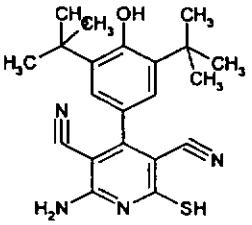
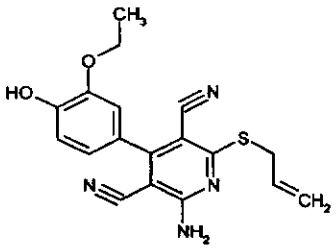
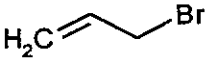
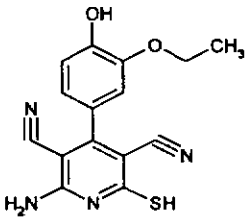
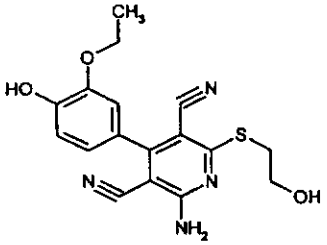
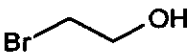
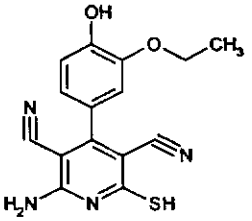
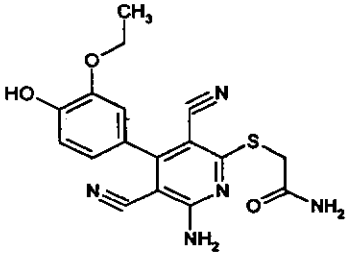
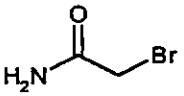
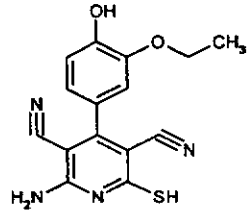
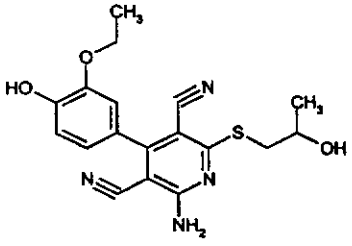
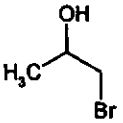
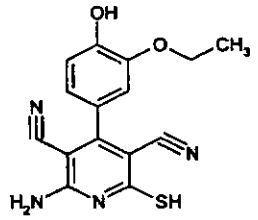
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A267				368	369	48.9
A268				368	369	31.8
A269				381	382	30.2
A270				423	424	17.0
A271				338	339	71.2

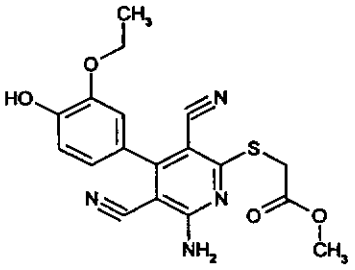
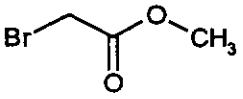
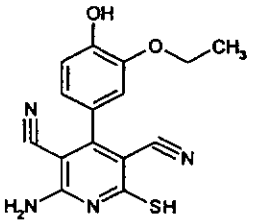
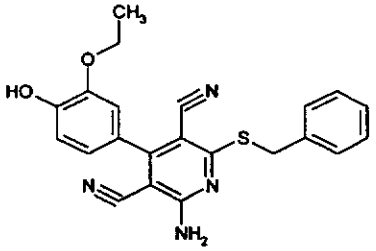
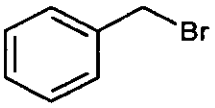
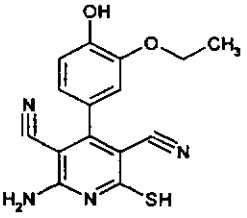
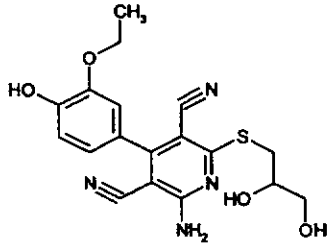
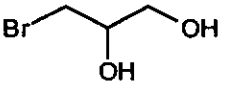
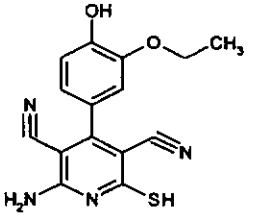
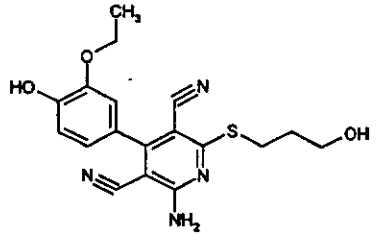
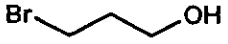
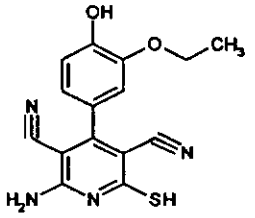
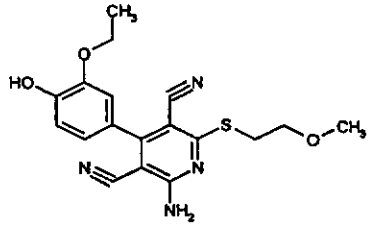
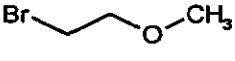
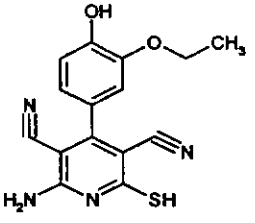
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A272				342	343	50.8
A273				355	356	96.0
A274				356	357	69.0
A275				370	371	80.5
A276				372	373	85.4

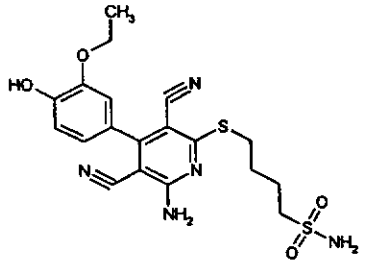
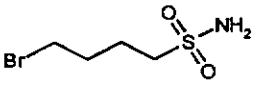
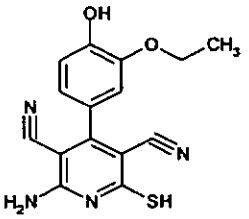
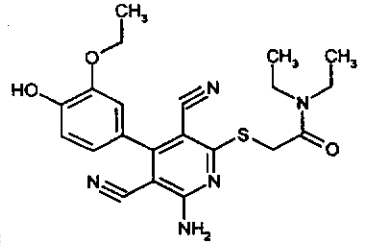
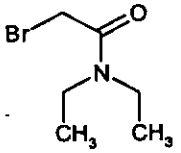
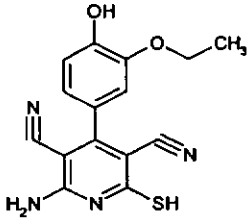
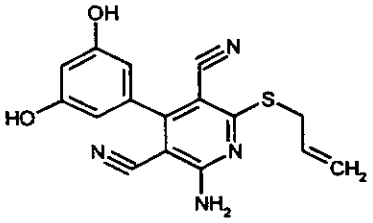
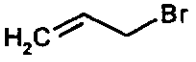
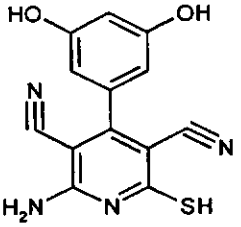
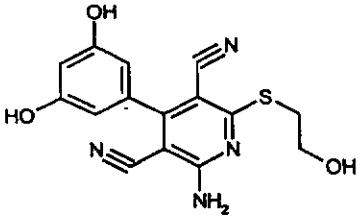
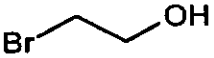
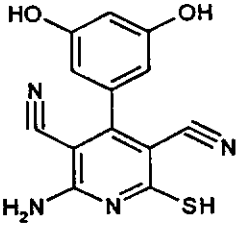
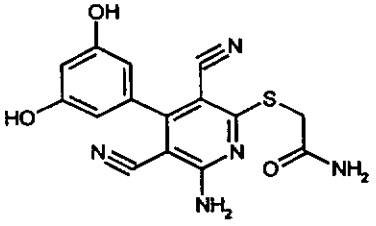
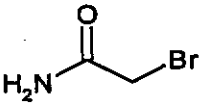
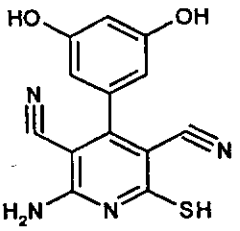
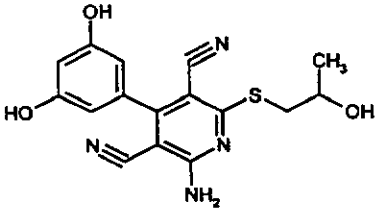
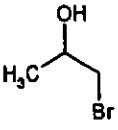
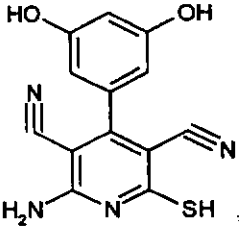
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A277				356	357	69.3
A278				356	357	58.9
A279				434	435	84.4
A280				411	412	80.2
A281				338	339	60.6

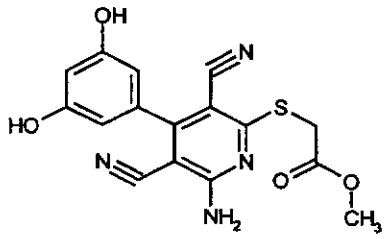
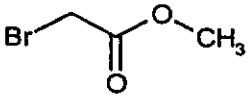
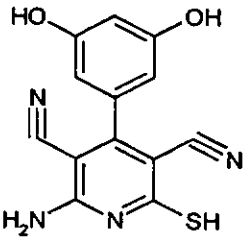
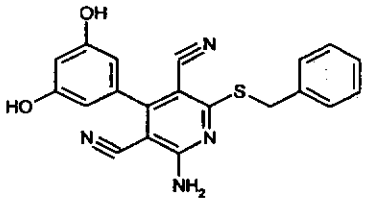
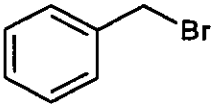
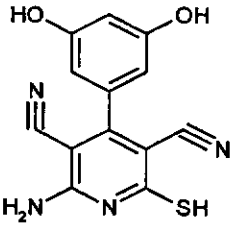
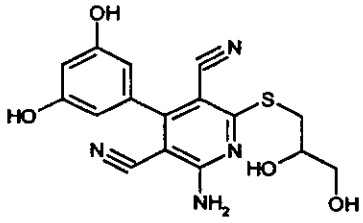
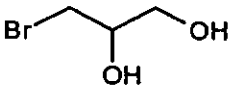
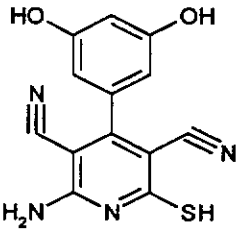
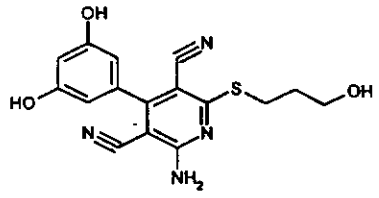
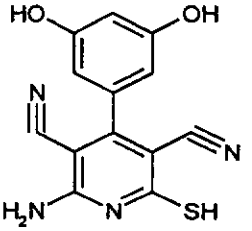
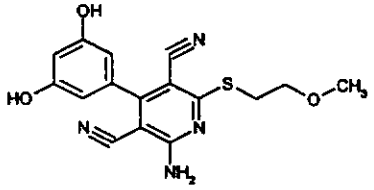
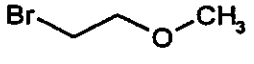
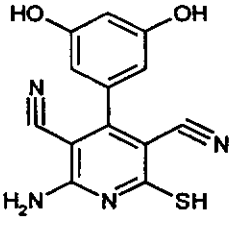
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A282				342	343	59.3
A283				356	357	62.0
A284				370	371	55.3
A285				388	389	59.0
A286				356	357	43.2

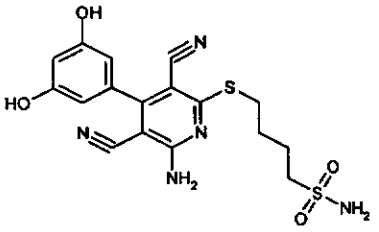
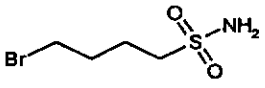
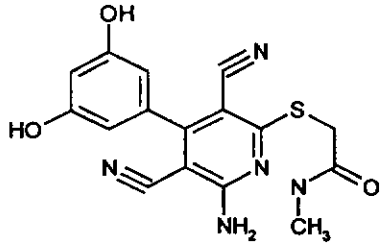
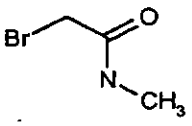
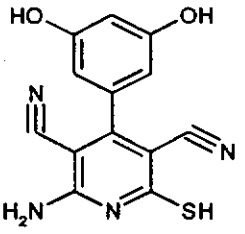
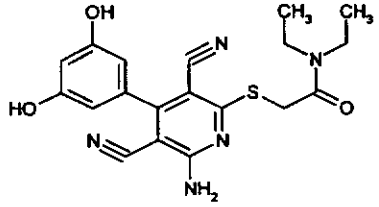
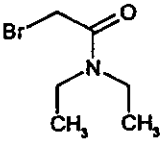
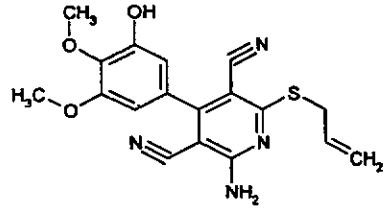
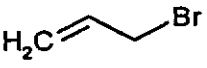
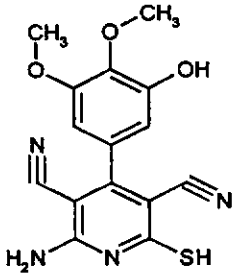
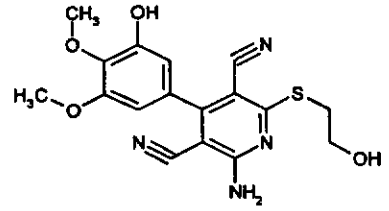
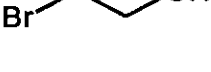
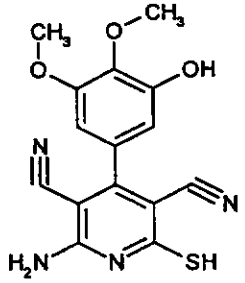
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A287				356	357	46.6
A288				434	435	62.5
A289				411	412	24.5
A290				421	422	100.6
A291				438	439	75.4
A292				453	454	58.8

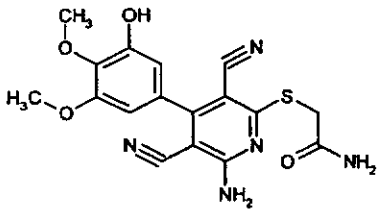
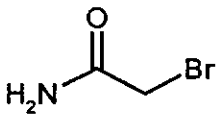
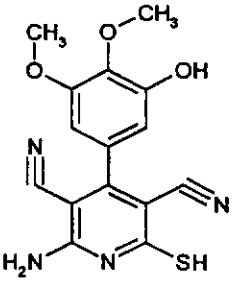
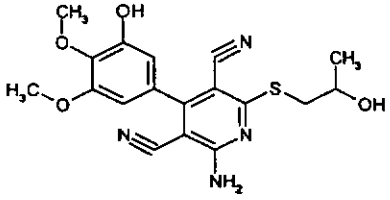
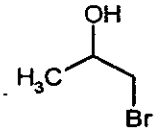
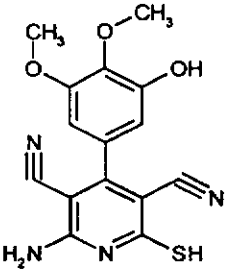
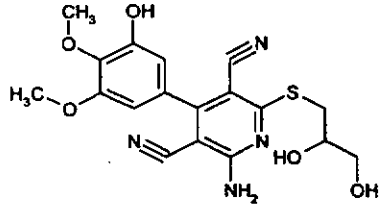
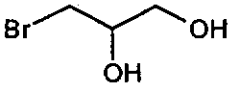
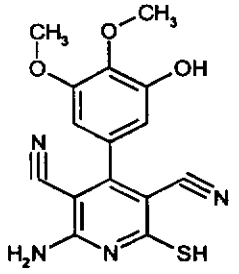
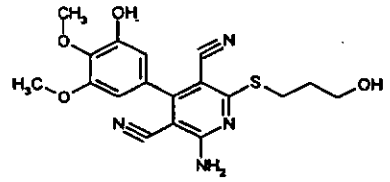
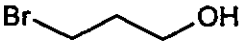
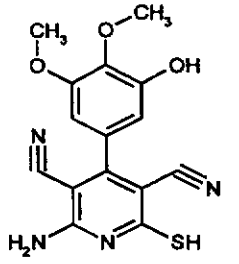
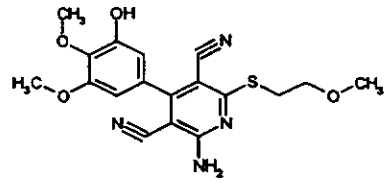
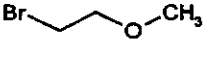
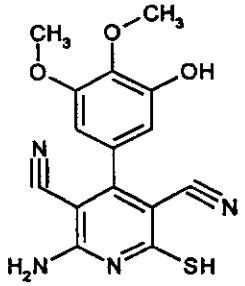
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A293				439	440	50.2
A294				352	353	68.7
A295				356	357	73.5
A296				369	370	92.9
A297				370	371	78.6

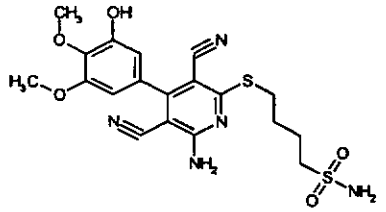
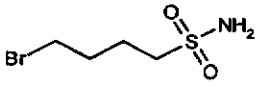
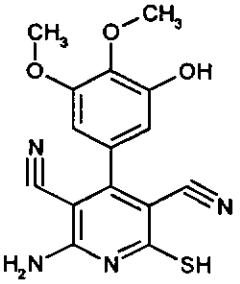
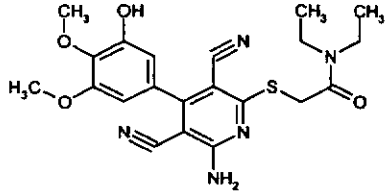
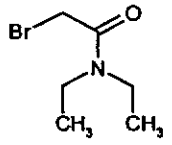
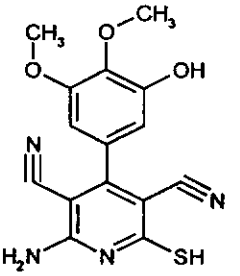
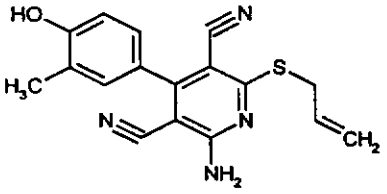
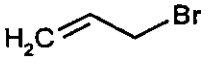
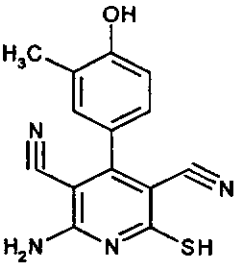
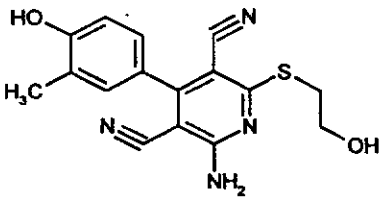
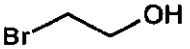
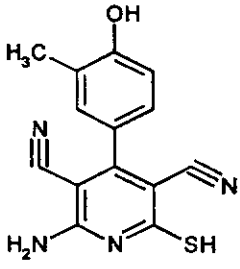
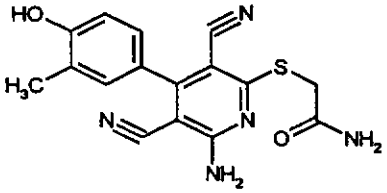
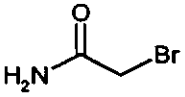
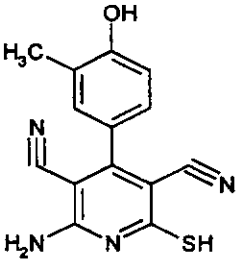
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A298				384	385	71.0
A299				402	403	84.2
A300				386	387	100.9
A301				370	371	100.4
A302				370	371	82.3

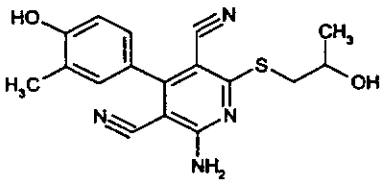
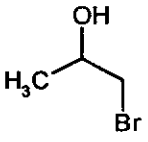
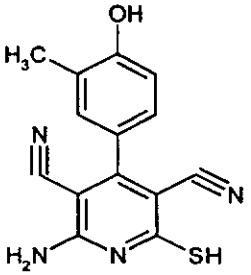
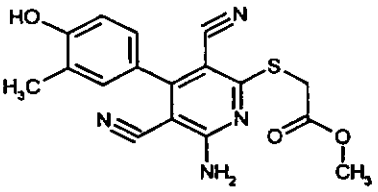
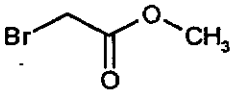
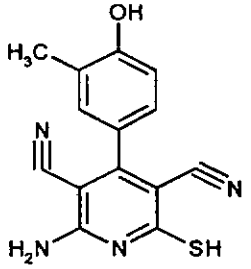
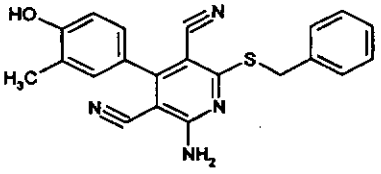
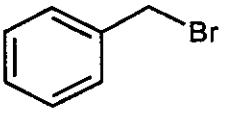
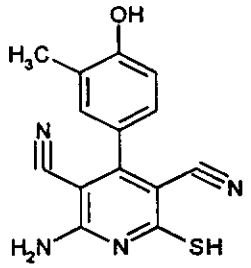
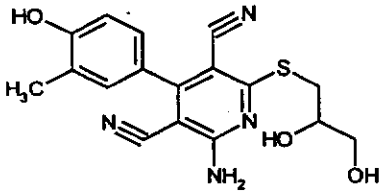
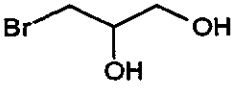
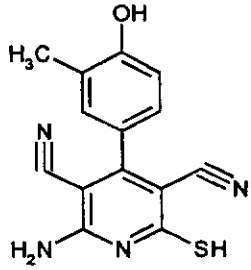
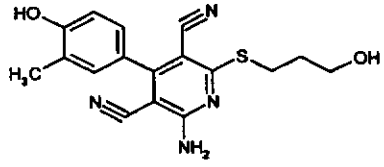
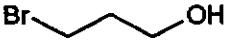
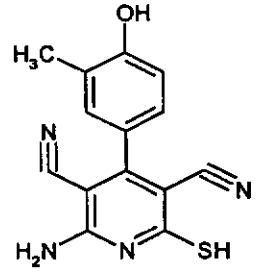
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A303				448	449	82.0
A304				426	427	60.2
A305				324	325	26.8
A306				328	329	33.8
A307				341	342	43.1
A308				342	343	34.2

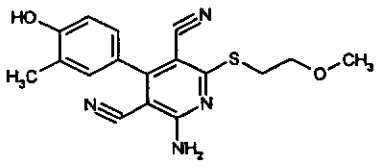
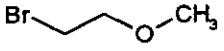
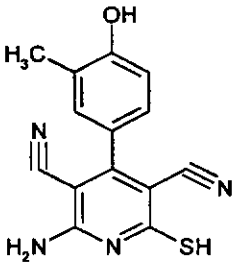
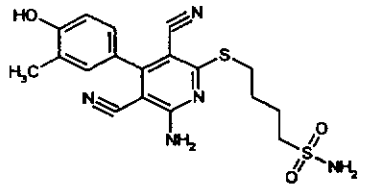
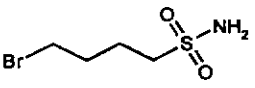
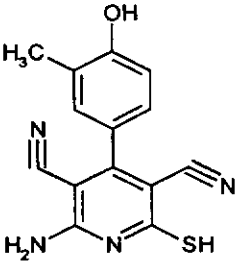
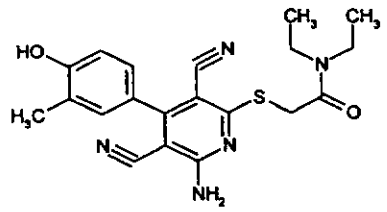
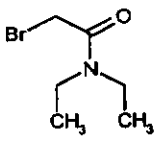
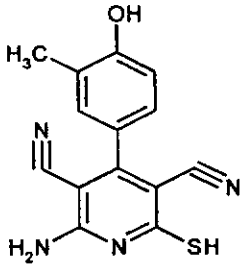
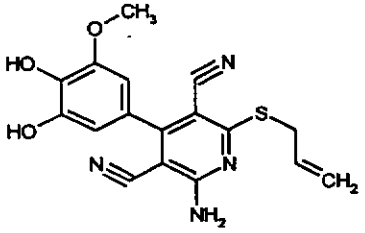
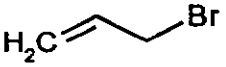
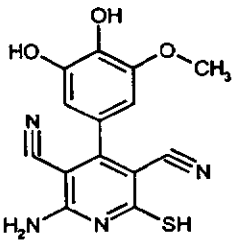
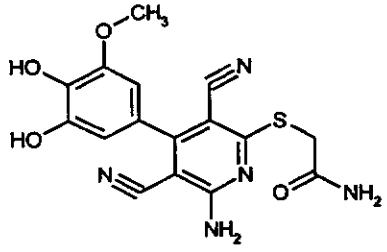
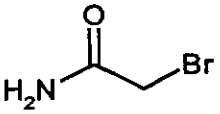
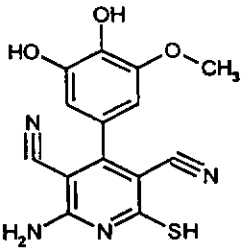
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A309				356	357	30.9
A310				374	375	34.7
A311				358	359	41.0
A312				342	343	33.3
A313				342	343	25.1

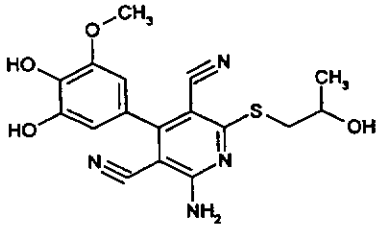
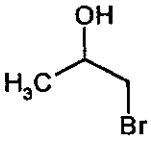
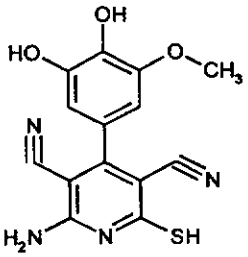
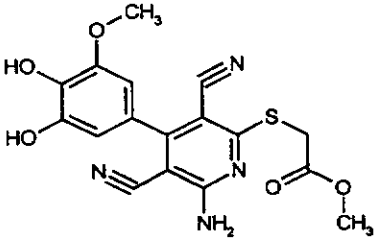
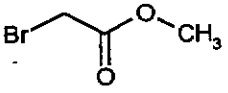
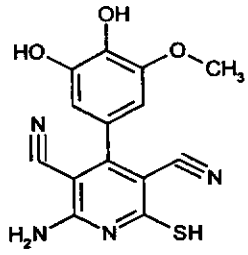
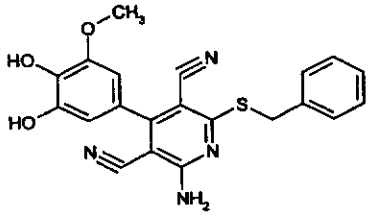
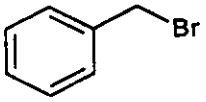
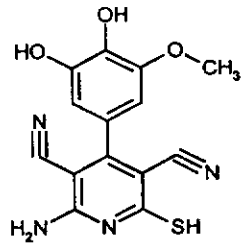
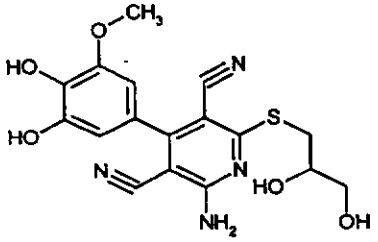
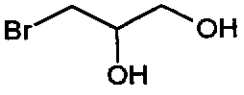
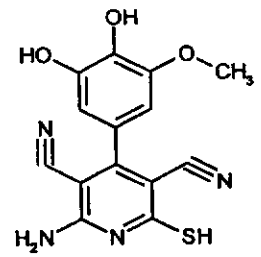
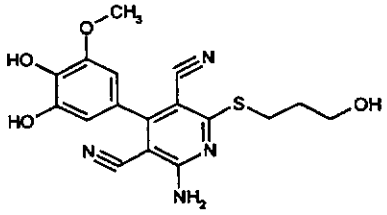
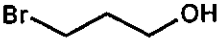
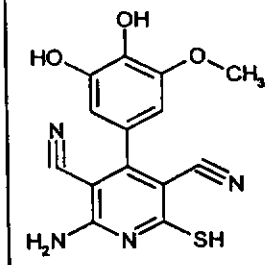
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A314				419	420	30.3
A315				355	356	36.3
A316				397	398	30.7
A317				368	369	68.9
A318				372	373	77.6

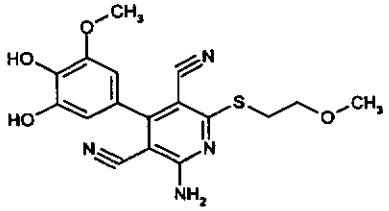
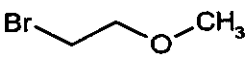
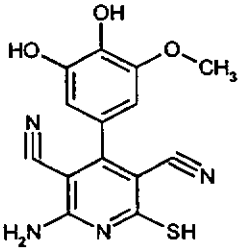
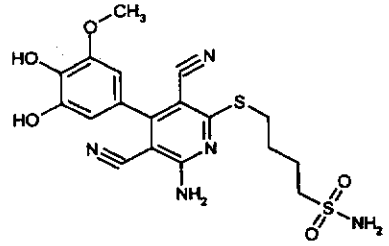
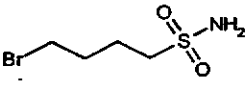
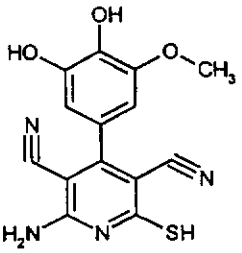
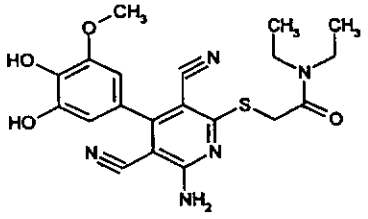
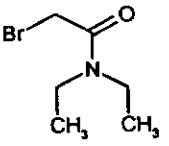
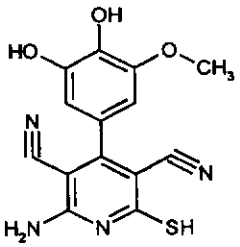
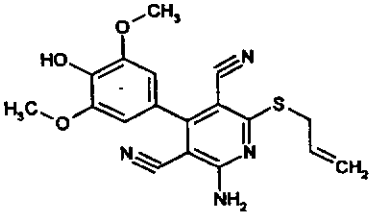
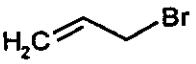
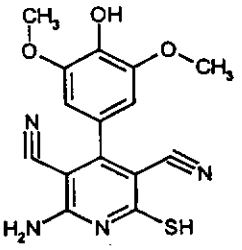
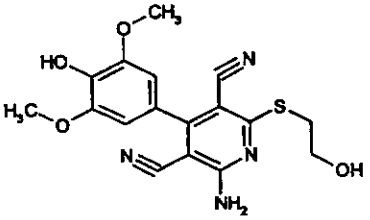
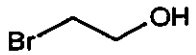
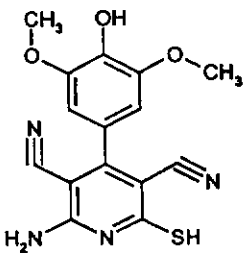
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A319				385	386	107.4
A320				386	387	64.2
A321				402	403	88.7
A322				386	387	73.8
A323				386	387	74.5

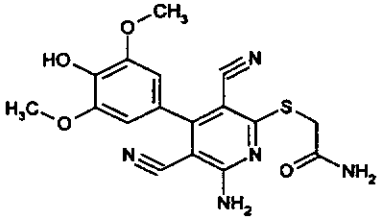
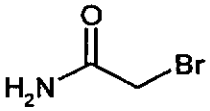
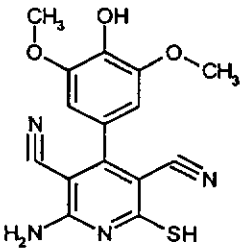
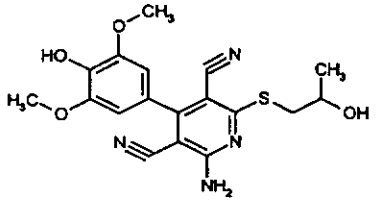
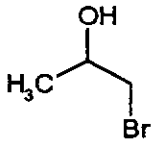
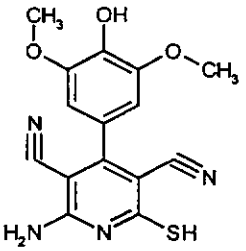
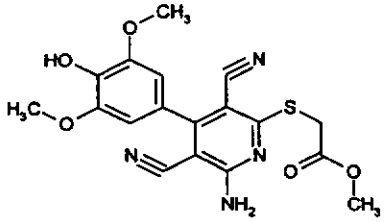
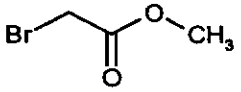
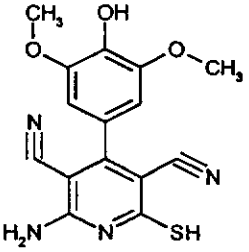
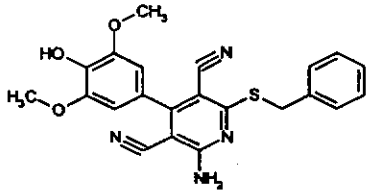
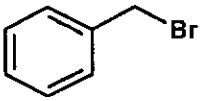
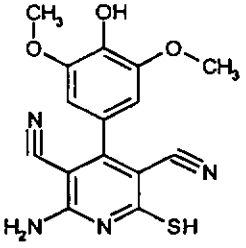
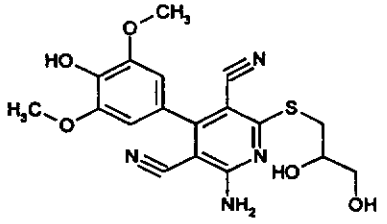
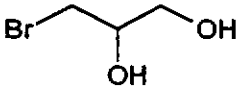
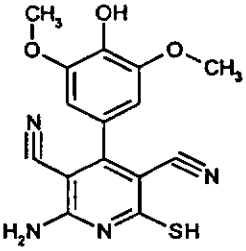
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A324				464	465	83.3
A325				442	443	85.6
A326				322	323	53.0
A327				326	327	19.3
A328				339	340	88.1

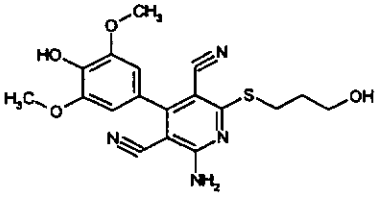
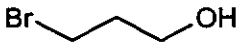
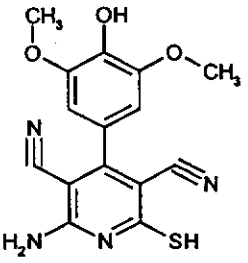
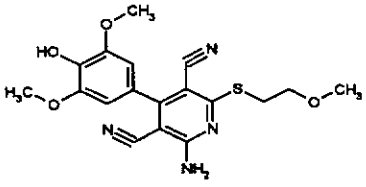
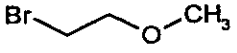
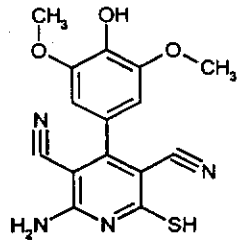
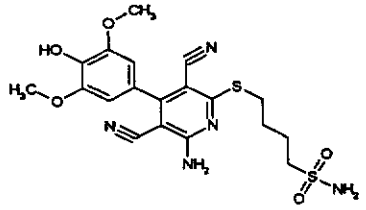
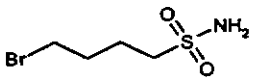
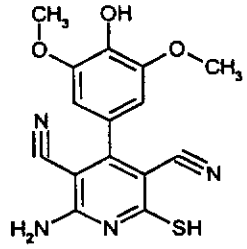
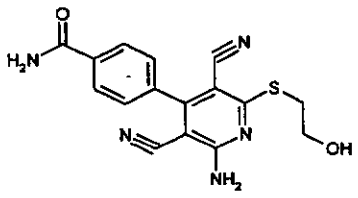
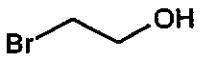
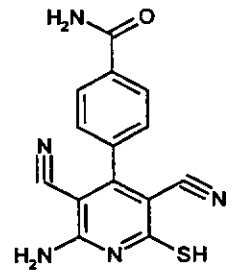
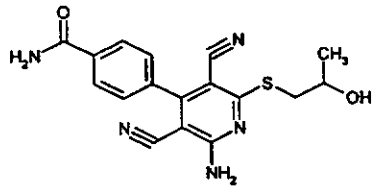
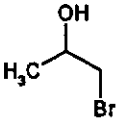
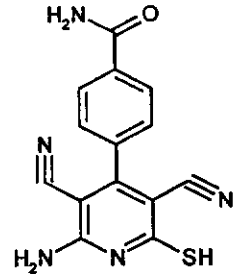
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A329				340	341	77.3
A330				354	355	68.3
A331				372	373	59.3
A332				356	357	75.2
A333				340	341	47.0

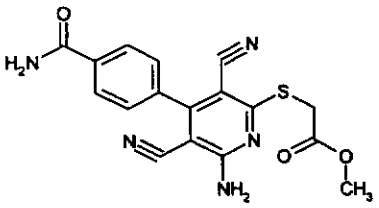
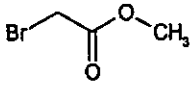
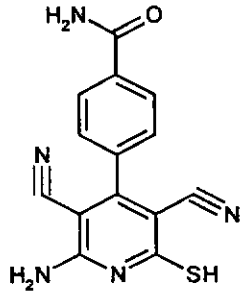
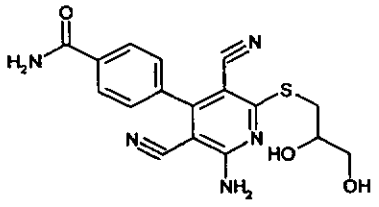
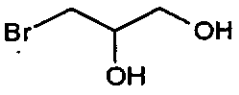
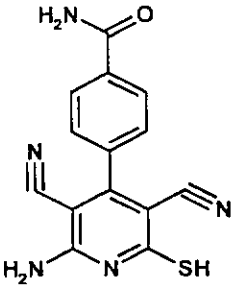
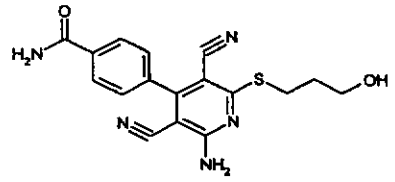
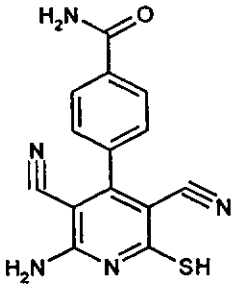
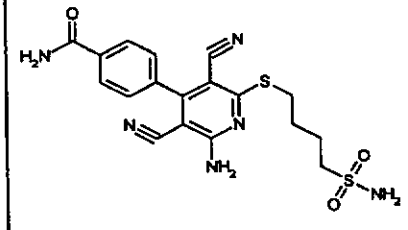
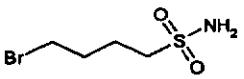
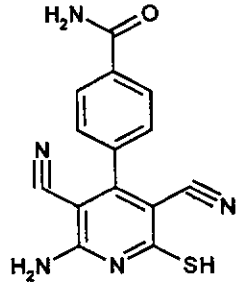
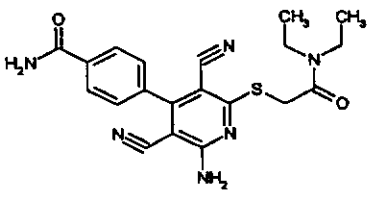
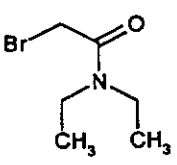
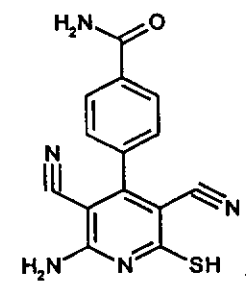
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A334				340	341	60.5
A335				418	419	80.5
A336				395	396	74.6
A337				354	355	56.4
A338				371	372	47.4

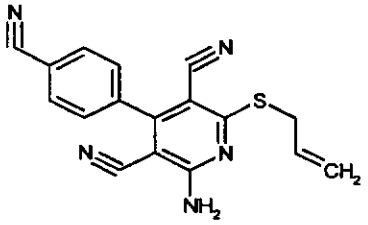
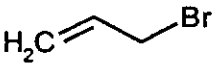
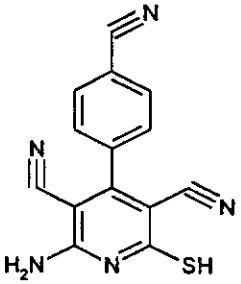
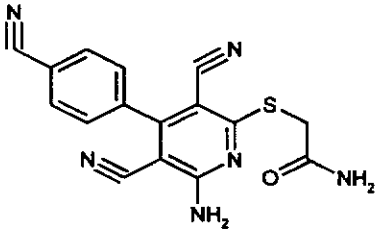
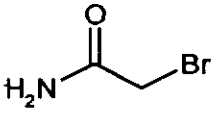
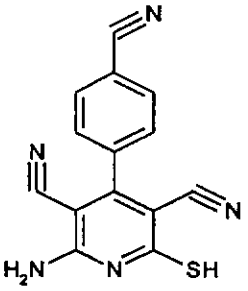
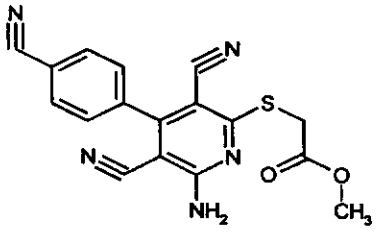
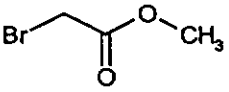
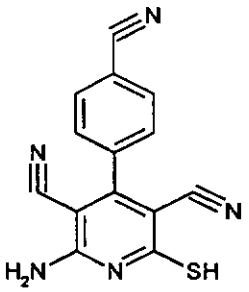
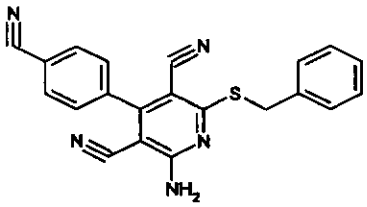
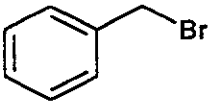
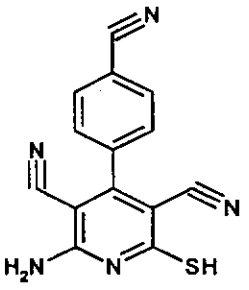
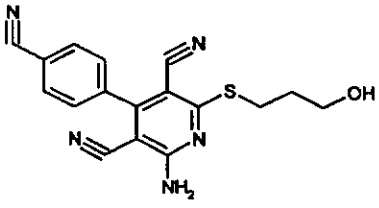
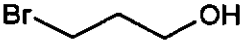
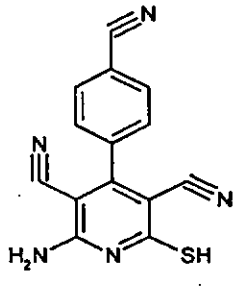
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A339				372	373	68.5
A340				386	387	81.0
A341				404	405	77.1
A342				388	389	64.1
A343				372	373	65.5

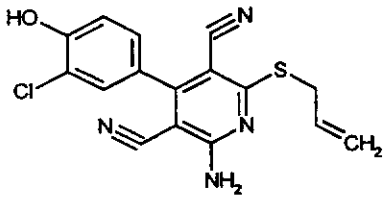
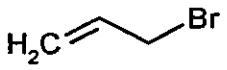
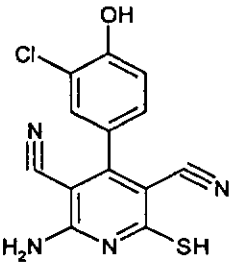
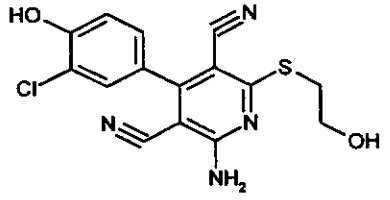
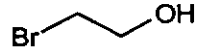
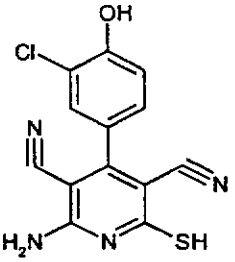
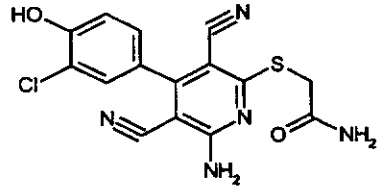
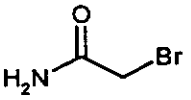
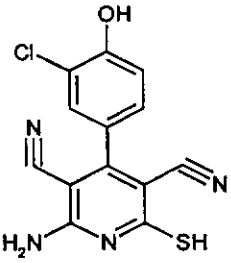
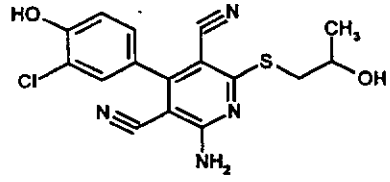
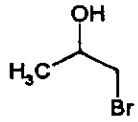
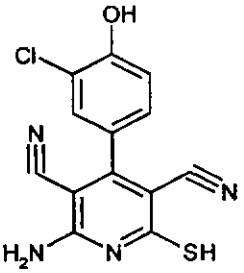
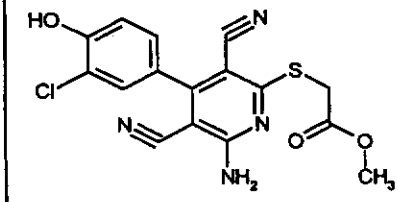
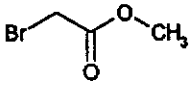
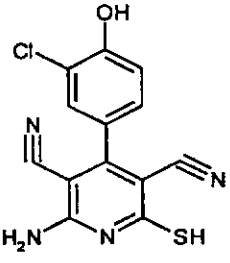
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A344				372	373	67.9
A345				450	451	77.0
A346				427	428	77.2
A347				368	369	69.5
A348				372	373	10.7

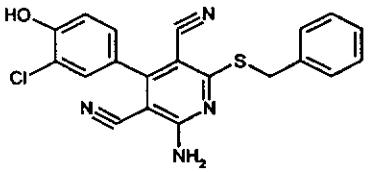
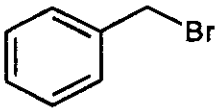
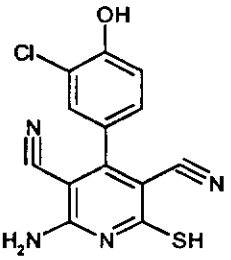
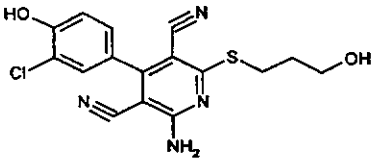
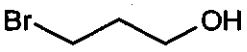
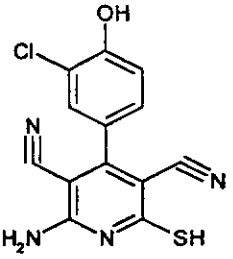
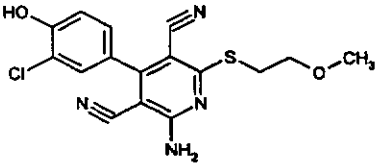
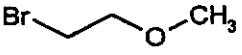
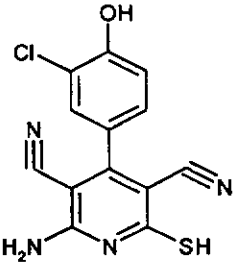
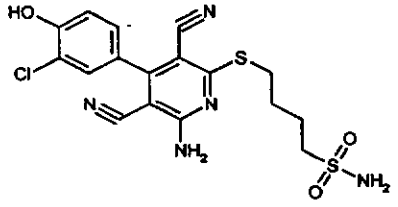
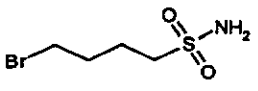
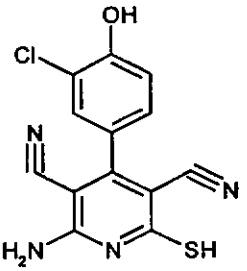
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A349				385	386	46.2
A350				386	387	75.6
A351				400	401	31.7
A352				418	419	90.8
A353				402	403	92.4

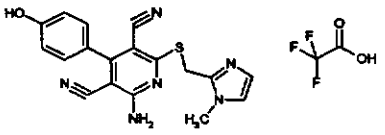
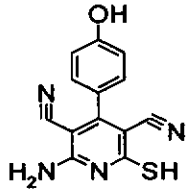
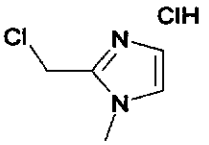
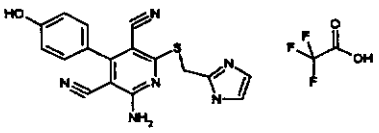
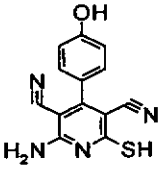
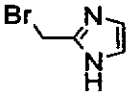
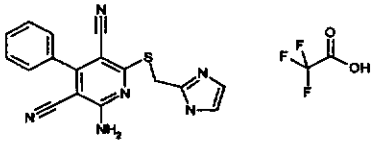
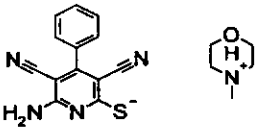
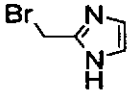
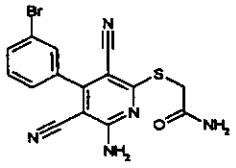
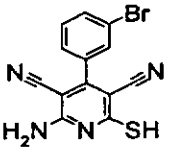
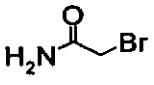
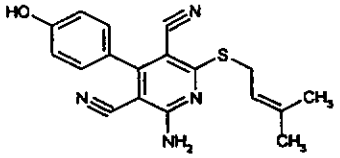
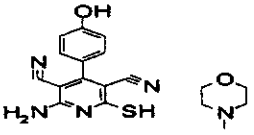
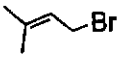
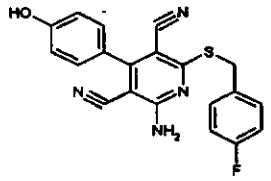
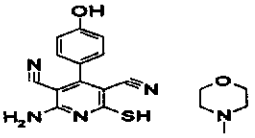
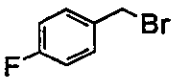
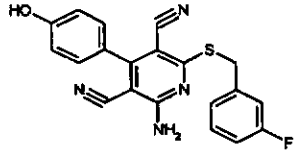
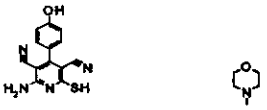
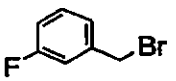
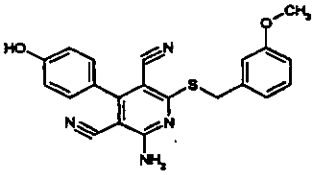
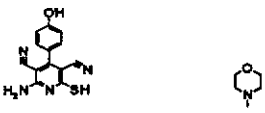
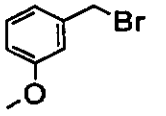
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A354				386	387	73.2
A355				386	387	55.6
A356				464	465	85.4
A357				339	340	58.9
A358				353	354	89.1

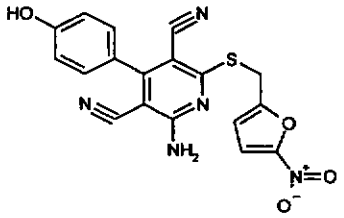
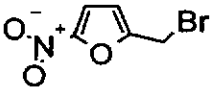
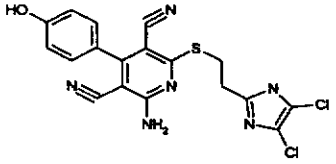
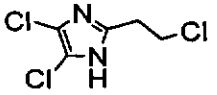
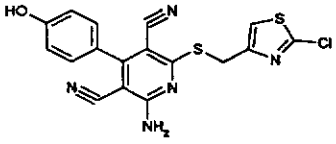
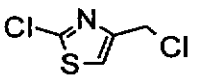
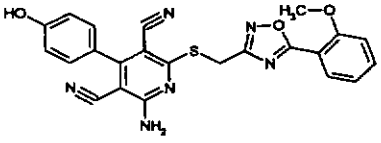
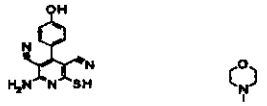
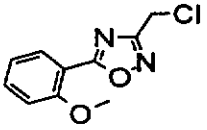
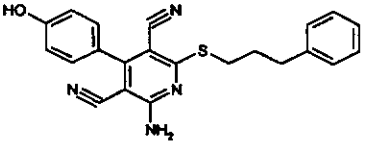
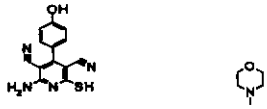
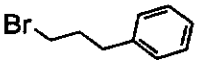
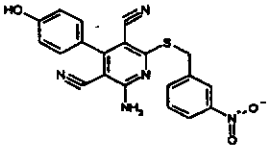
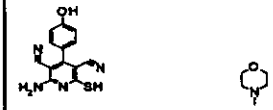
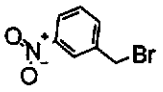
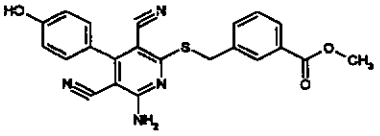
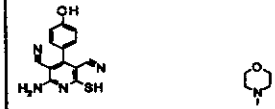
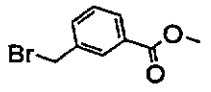
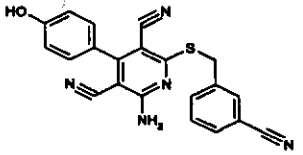
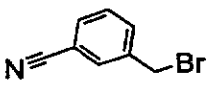
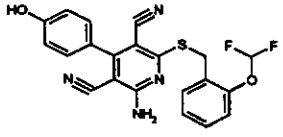
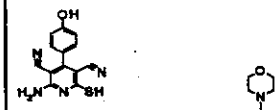
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A359				367	368	61.5
A360				369	370	65.2
A361				353	354	61.7
A362				431	432	53.9
A363				408	409	61.7

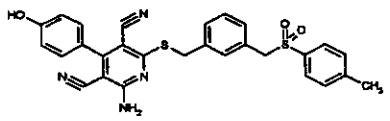
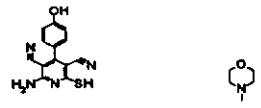
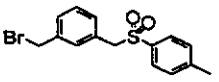
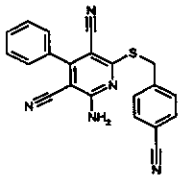
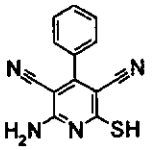
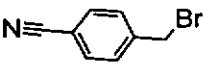
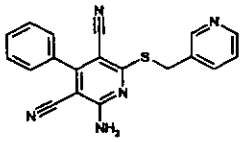
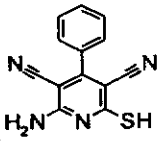
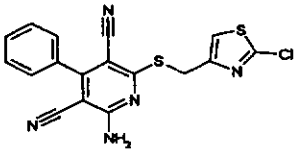
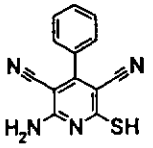
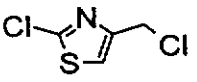
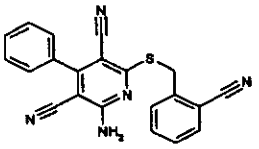
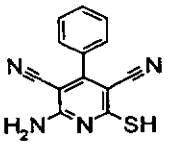
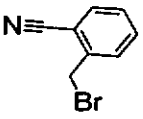
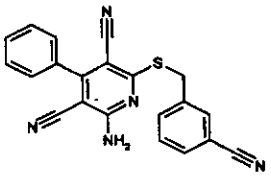
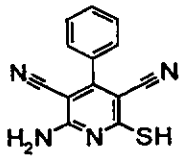
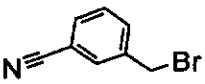
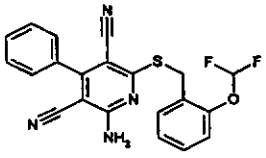
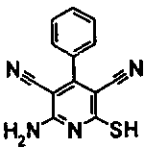
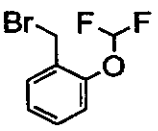
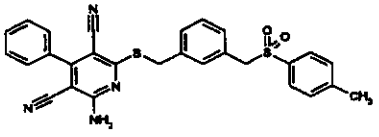
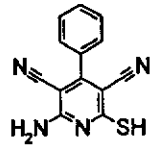
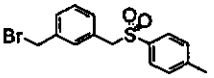
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A364				317	318	35.9
A365				334	335	24.5
A366				349	350	41.2
A367				367	368	45.2
A368				335	336	50.1

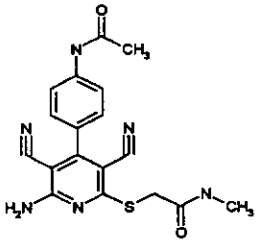
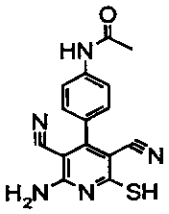
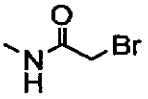
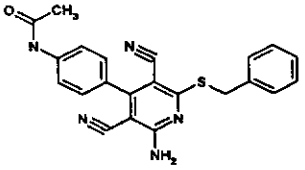
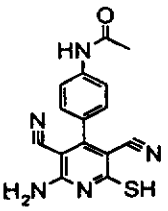
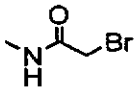
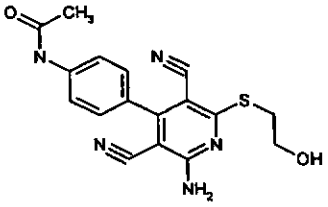
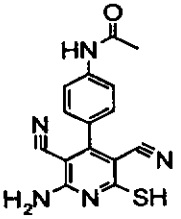
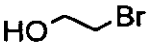
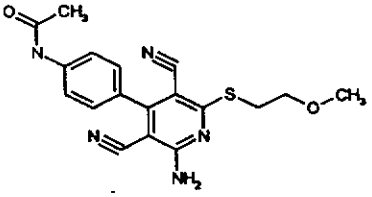
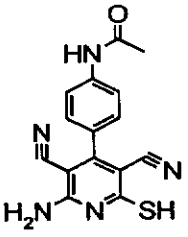
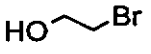
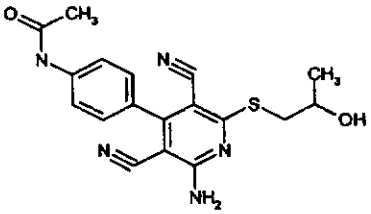
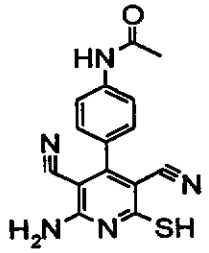
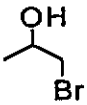
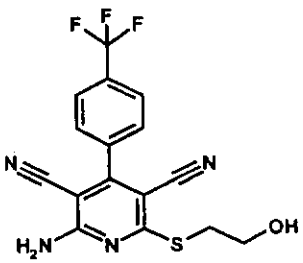
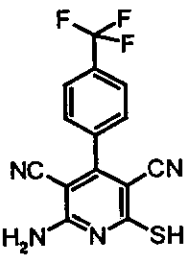
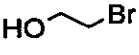
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A369				343	344	75.6
A370				347	348	89.4
A371				360	361	81.7
A372				361	362	89.0
A373				375	376	60.8

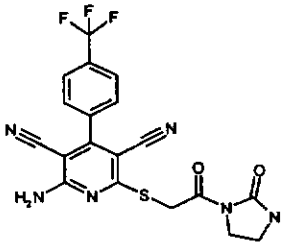
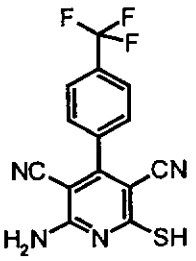
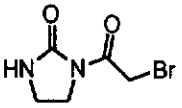
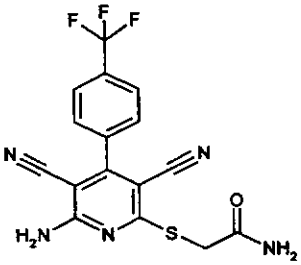
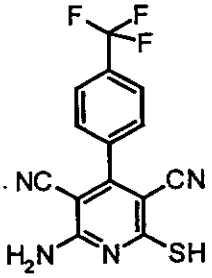
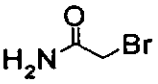
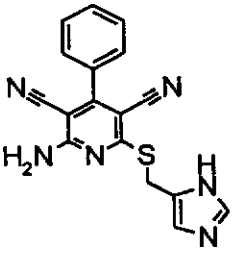
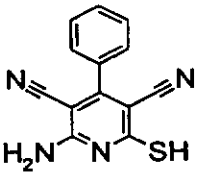
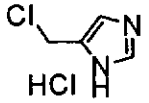
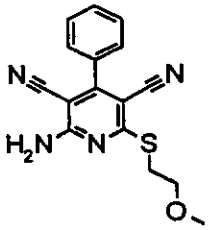
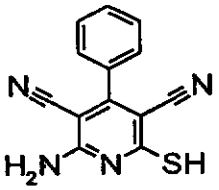
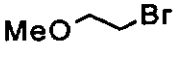
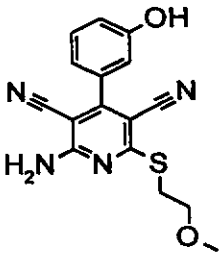
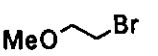
Ex. No.	Product	Starting material A	Starting material B	Molecular mass calculated	[M+H]+ found	Yield (% of theory)
A374				393	394	69.5
A375				361	362	21.9
A376				361	362	56.5
A377				438	439	90.7

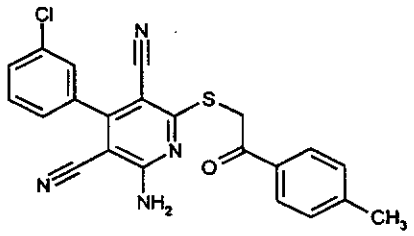
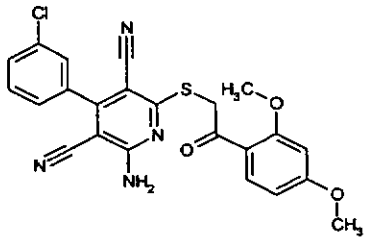
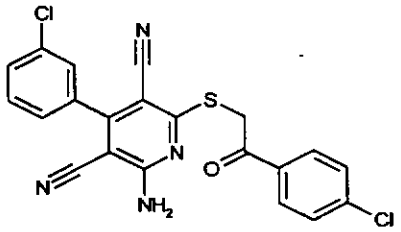
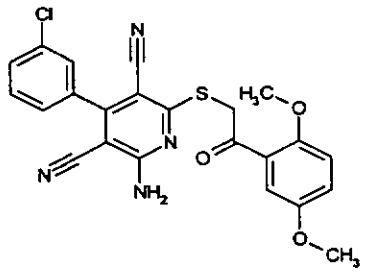
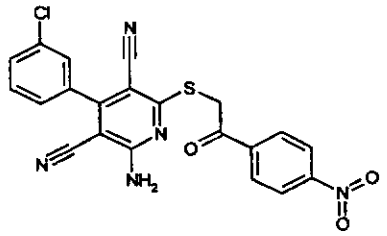
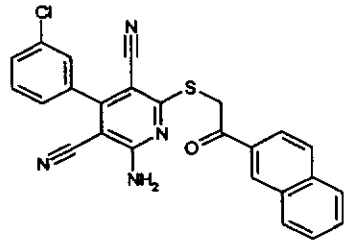
Ex. No.	Product	Starting material A	Starting material B	Molar mass calculated	[M+H]+ found	Yield (% of theory)
A 378				476	477	40.3
A 379				462	463	16.4
A 380				446	447	71.7
A 381				388	389	74.2
A 382				336	337	76.4
A 383				376	377	68.3
A 384				376	377	66.4
A 385				388	389	64.9

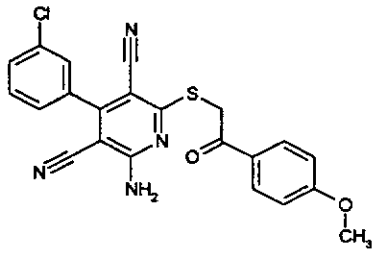
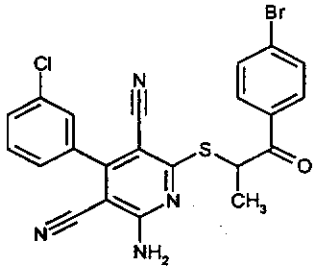
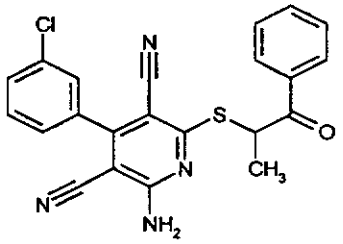
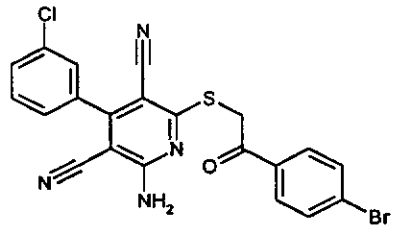
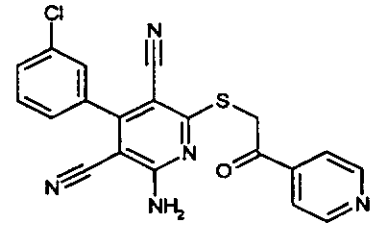
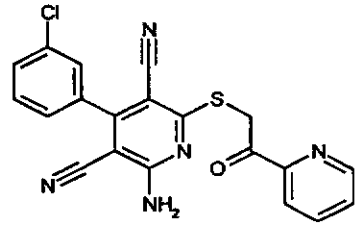
Ex. No.	Product	Starting material A	Starting material B	Molar mass calculated	[M+H]+ found	Yield (% of theory)
A 386				393	394	57.7
A 387				431	432	23.4
A 388				400	401	46.5
A 389				456	457	5.5
A 390				386	387	62.9
A 391				403	404	60.2
A 392				416	417	18.0
A 393				383	384	55.6
A 394				424	425	56.5

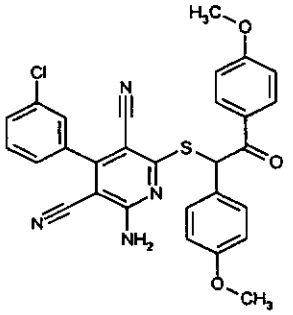
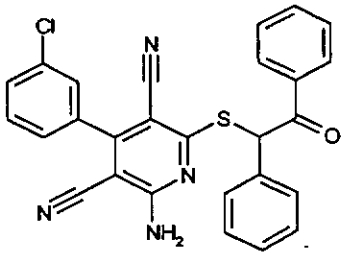
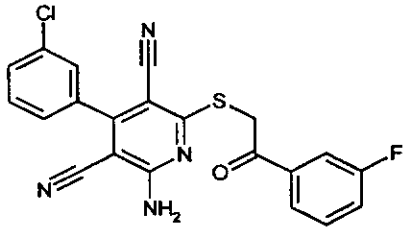
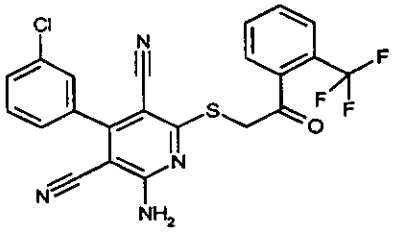
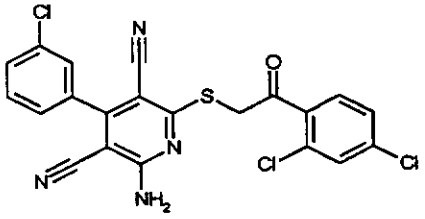
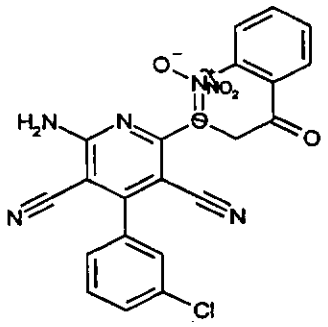
Ex. No.	Product	Starting material A	Starting material B	Molar mass calculated	[M+H]+ found	Yield (% of theory)
A 395				527	528	67.8
A 396				367	368	13.6
A 397				343	344	23.6
A 398				384	385	15.6
A 399				367	368	72.4
A 400				367	368	7.1
A 401				408	409	78.1
A 402				511	512	45.0

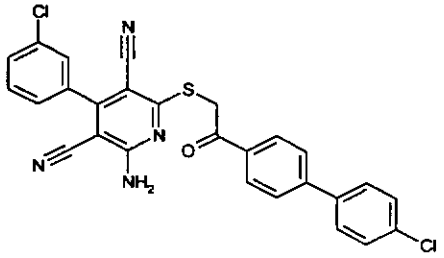
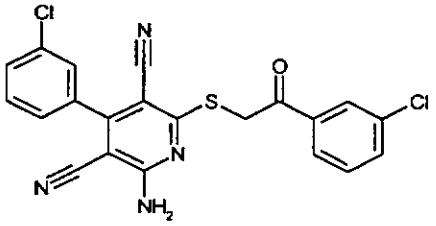
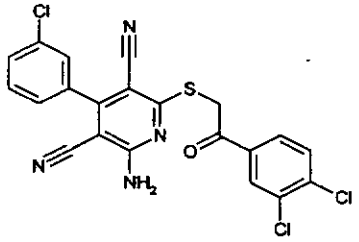
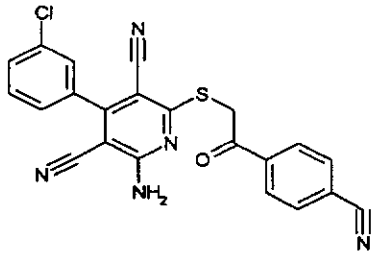
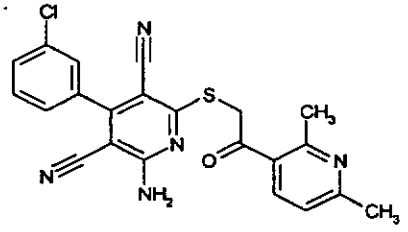
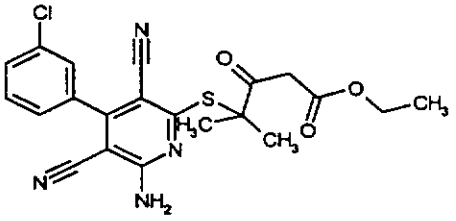
Ex. No.	Product	Starting material A	Starting material B	Molar mass calculated	[M+H]+ found	Yield (% of theory)
A 403				380	381	21.8
A 404				399	400	47.3
A 405				353	354	56.6
A 406				367	368	43.3
A 407				367	368	49.8
A 408				364	365	68.6

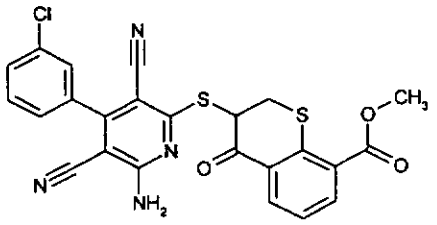
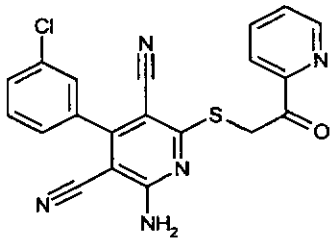
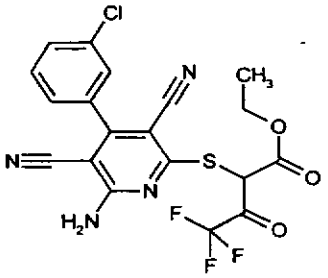
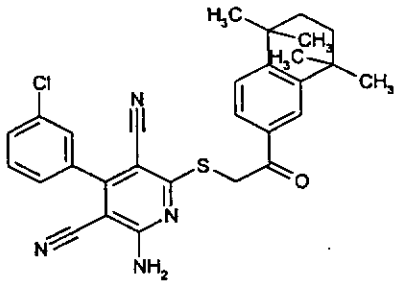
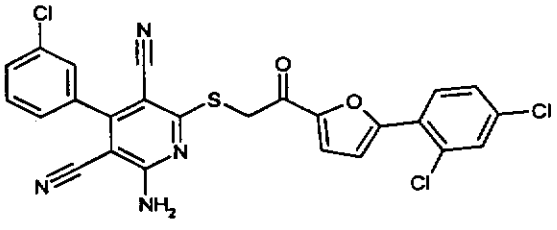
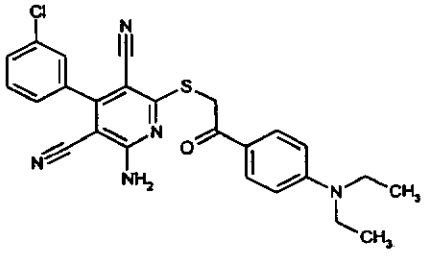
Ex. No.	Product	Starting material A	Starting material B	Molar mass calculated	[M+H]+ found	Yield (% of theory)
A 409				446	447	57.3
A 410				377	378	15.5
A 411				332	333	35.4
A 412				310	311	86.4
A 413				326	327	46.4

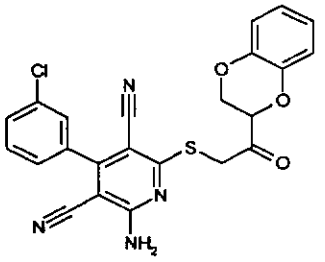
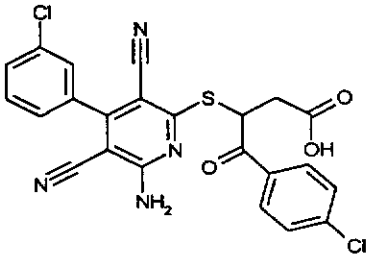
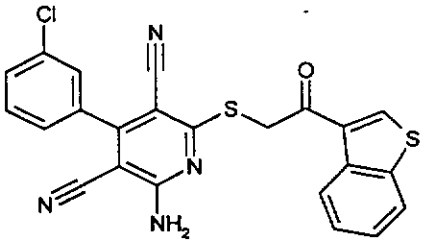
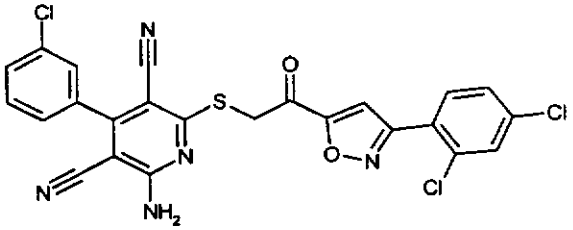
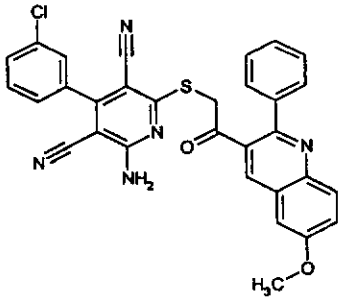
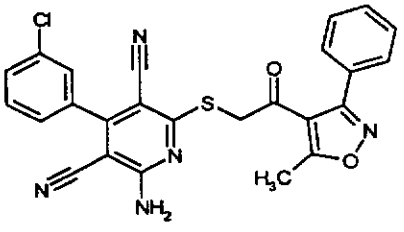
Ex. No.	Product	Molecular weight
B1		419
B2		465
B3		439
B4		465
B5		450
B6		455

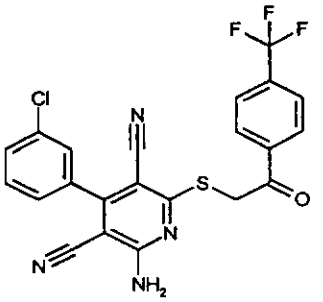
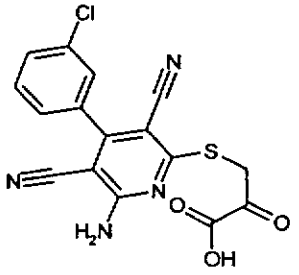
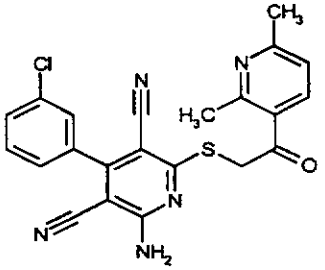
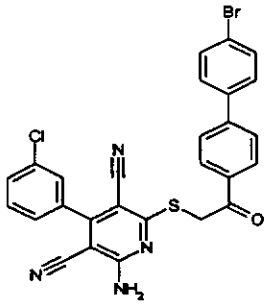
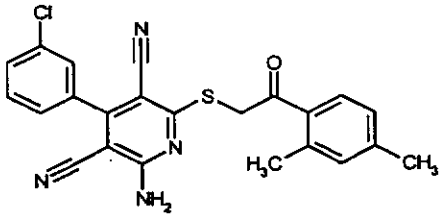
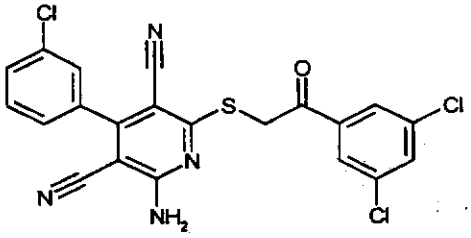
Ex. No.	Product	Molecular weight
B7		435
B8		498
B9		419
B10		484
B11		406
B12		406

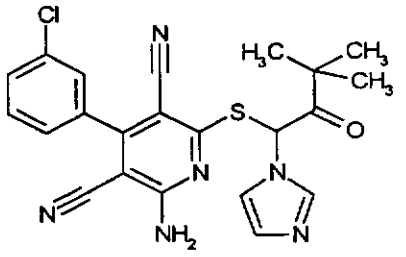
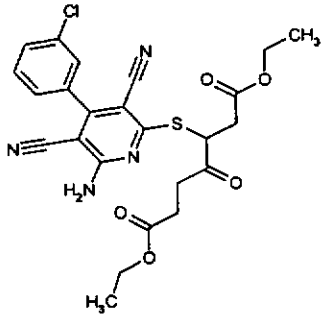
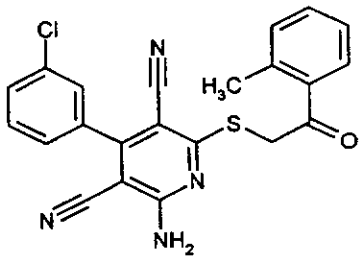
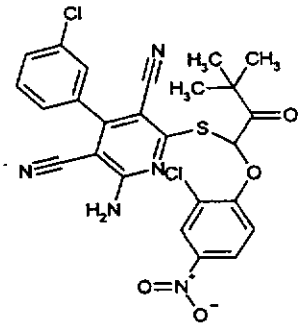
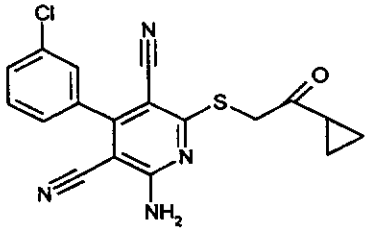
Ex. No.	Product	Molecular weight
B13		541
B14		481
B15		423
B16		473
B17		474
B18		450

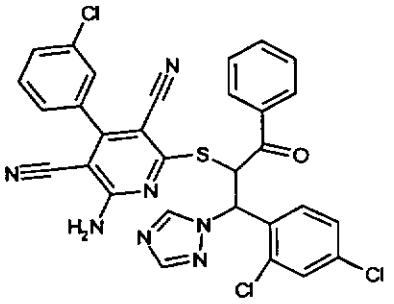
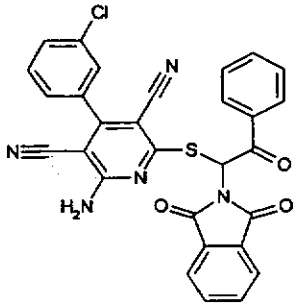
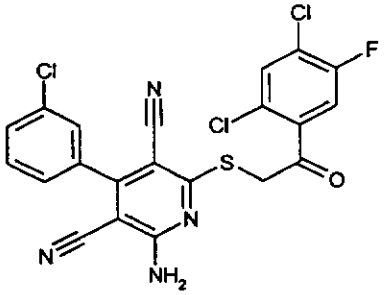
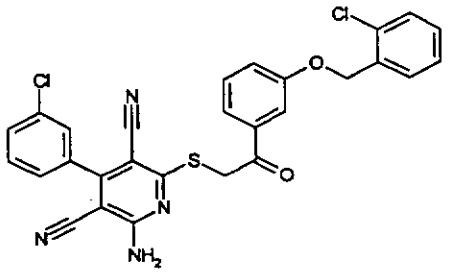
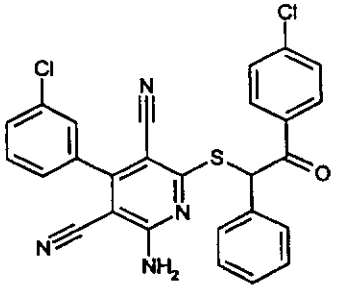
Ex. No.	Product	Molecular weight
B19		515
B20		439
B21		474
B22		430
B23		434
B24		443

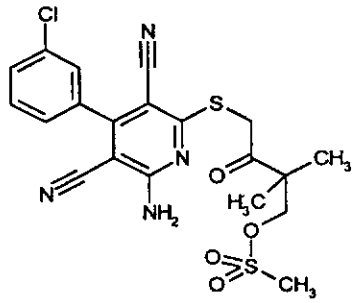
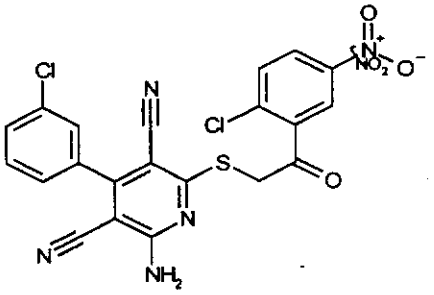
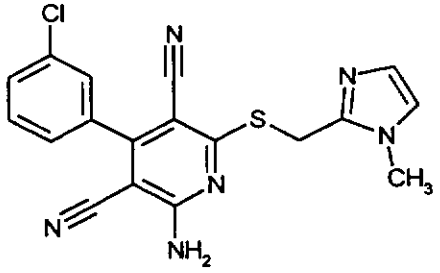
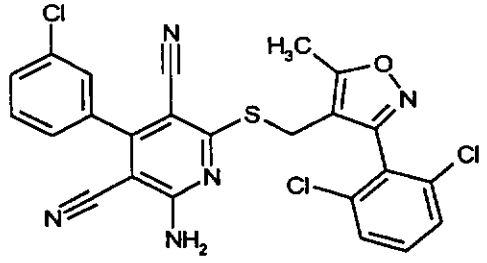
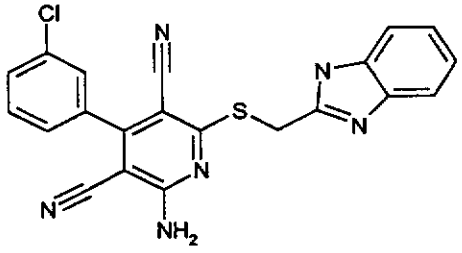
Ex. No.	Product	Molecular weight
B25		507
B26		406
B27		469
B28		515
B29		540
B30		476

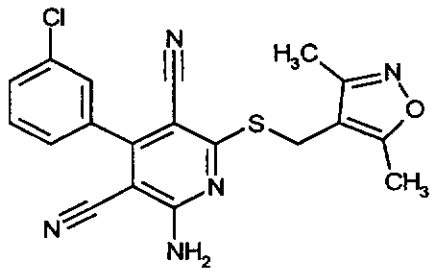
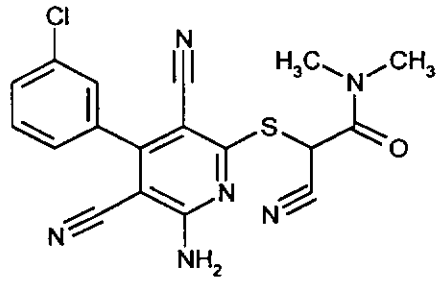
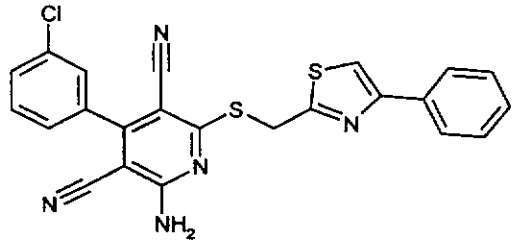
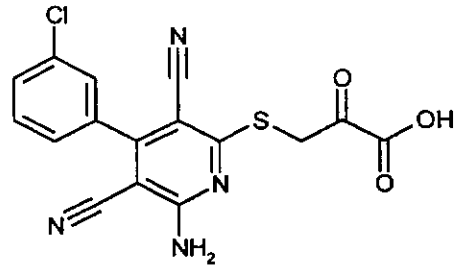
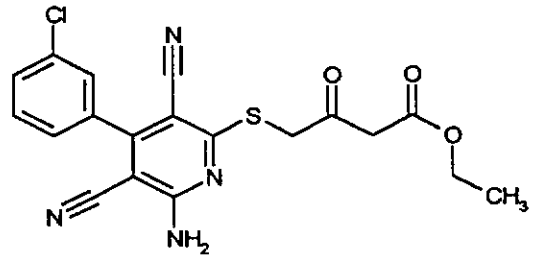
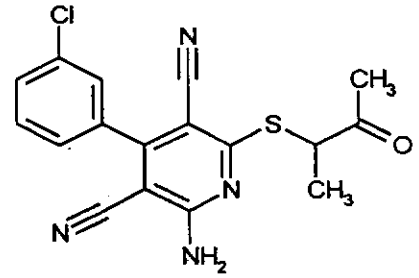
Ex. No.	Product	Molecular weight
B31		463
B32		497
B33		461
B34		541
B35		562
B36		486

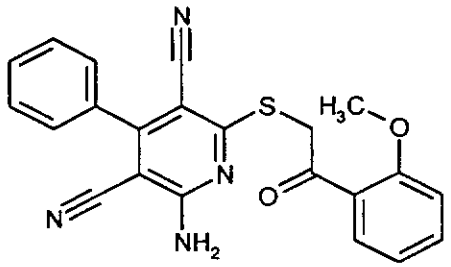
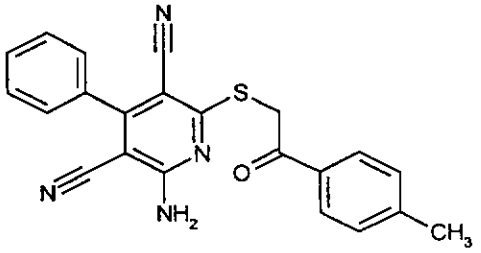
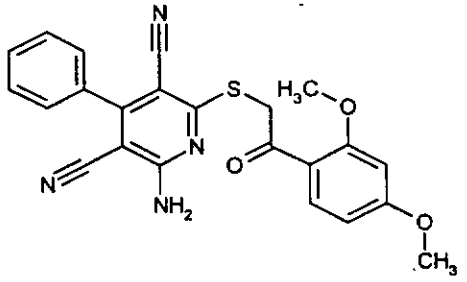
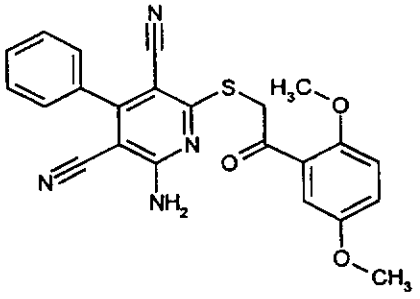
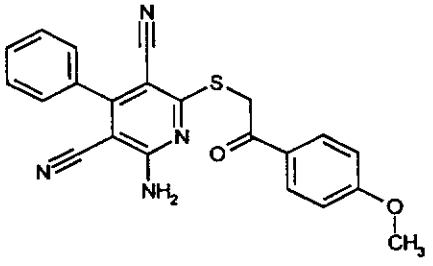
Ex. No.	Product	Molecular weight
B37		473
B38		373
B39		434
B40		560
B41		433
B42		474

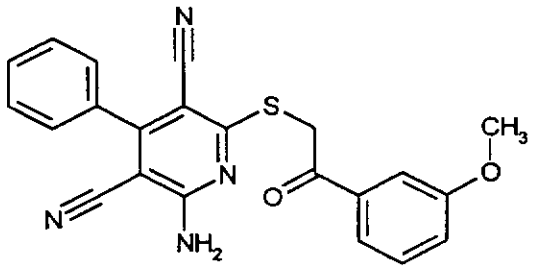
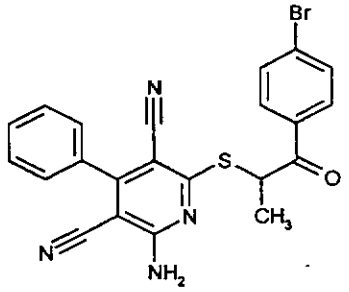
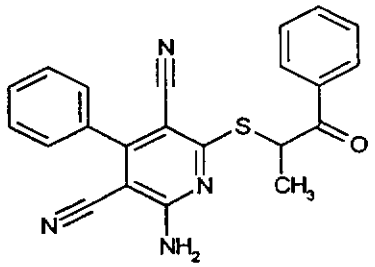
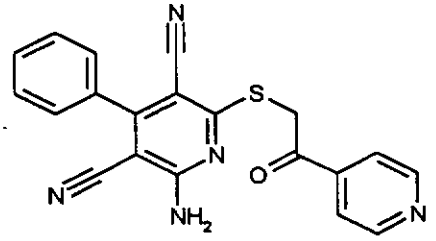
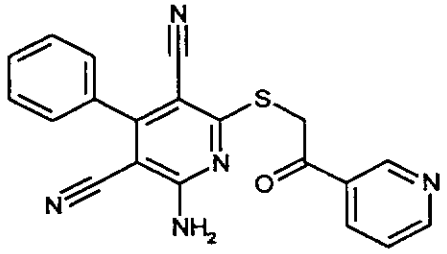
Ex. No.	Product	Molecular weight
B43		451
B44		515
B45		419
B46		556
B47		369

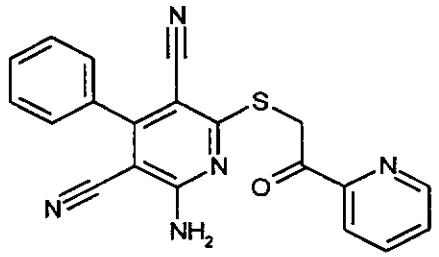
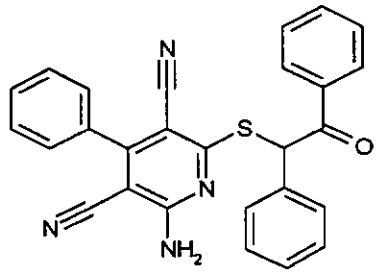
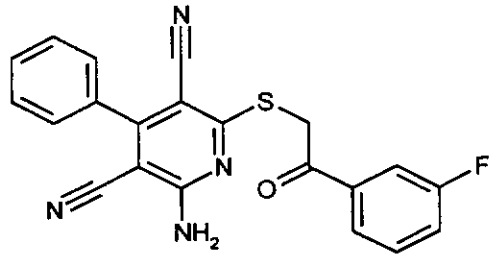
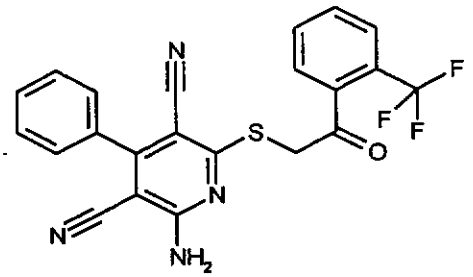
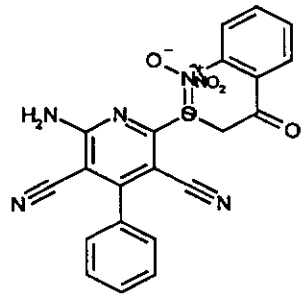
Ex. No.	Product	Molecular weight
B48		631
B49		550
B50		492
B51		545
B52		515

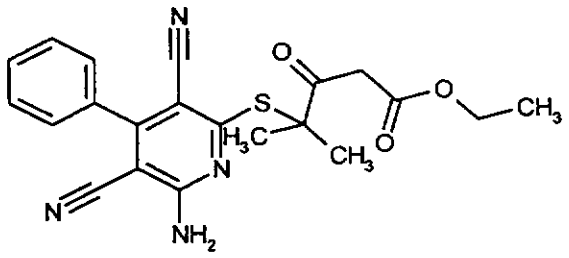
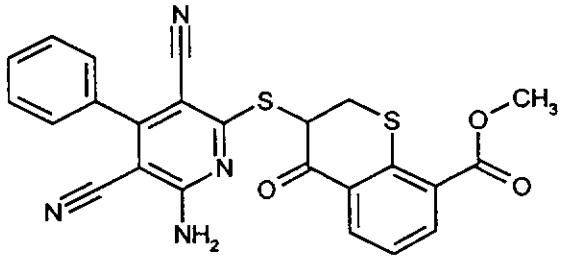
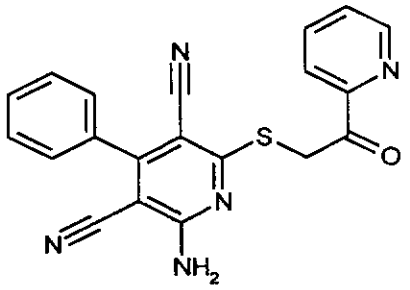
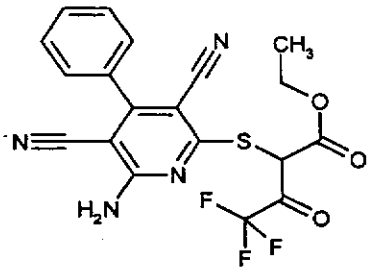
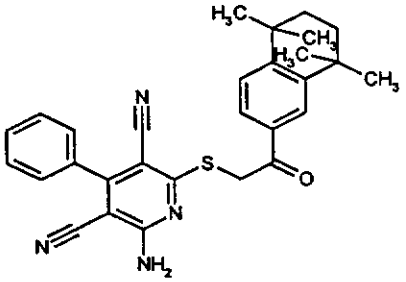
Ex. No.	Product	Molecular weight
B53		479
B54		484
B55		381
B56		527
B57		417

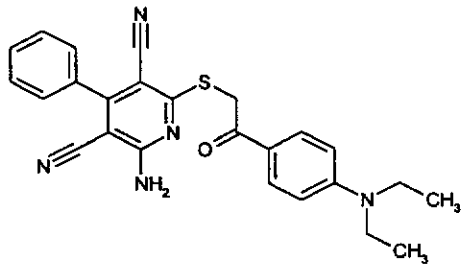
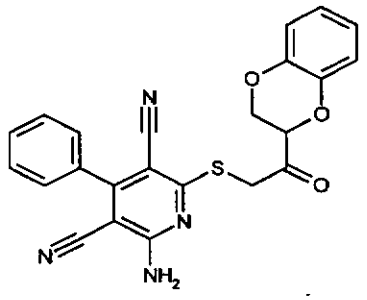
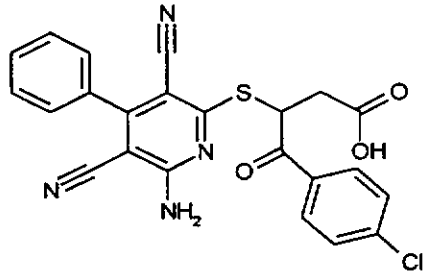
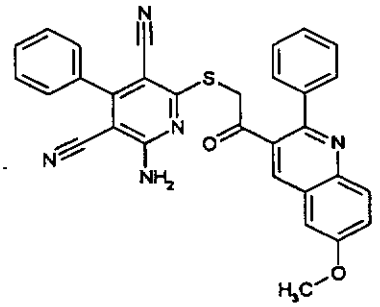
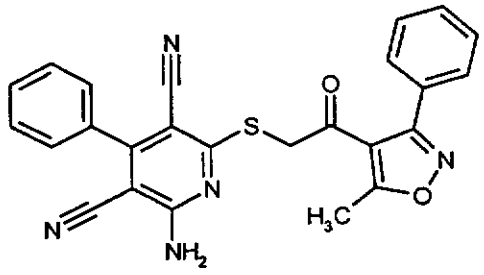
Ex. No.	Product	Molecular weight
B58		396
B59		397
B60		460
B61		373
B62		415
B63		357

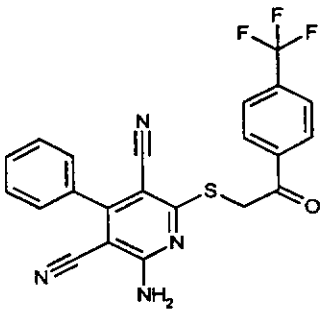
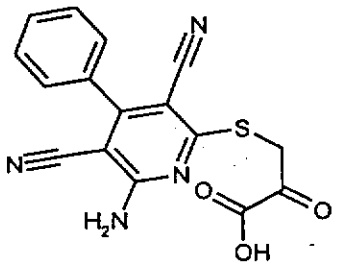
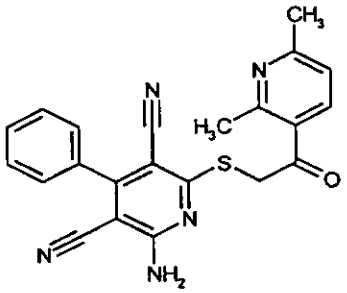
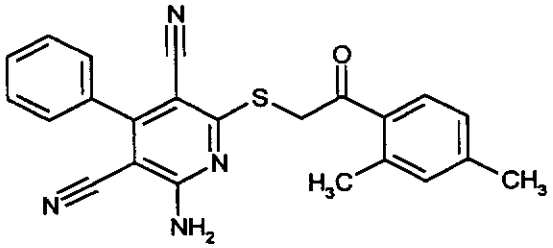
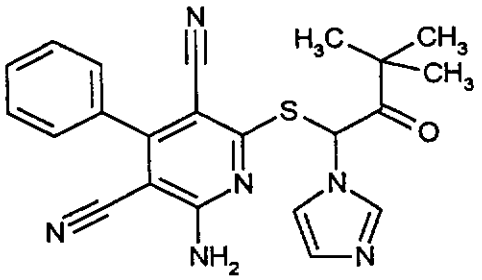
Ex. No.	Product	Molecular weight
B64		400
B65		384
B66		430
B67		430
B68		400

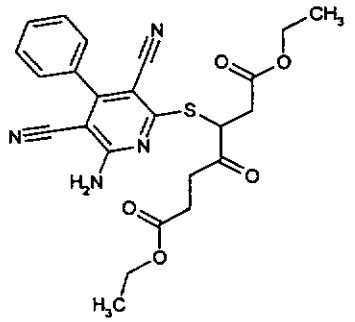
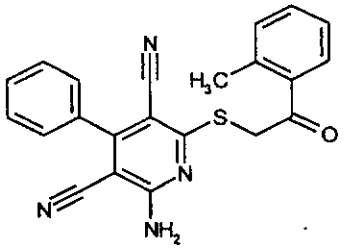
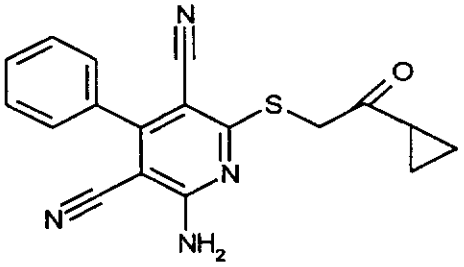
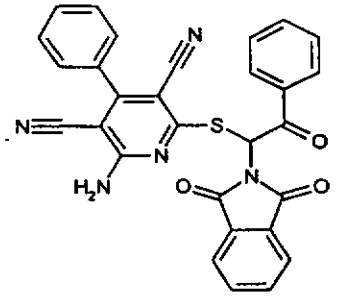
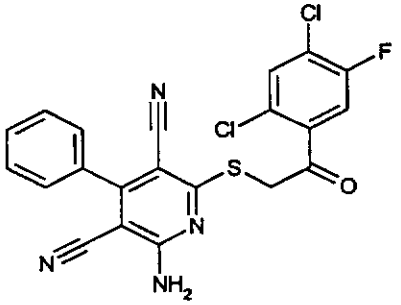
Ex. No.	Product	Molecular weight
B69		400
B70		463
B71		384
B72		371
B73		371

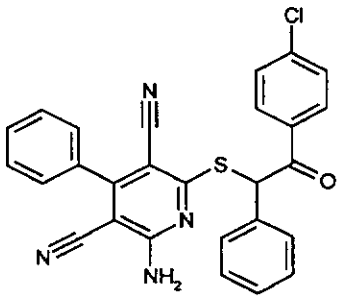
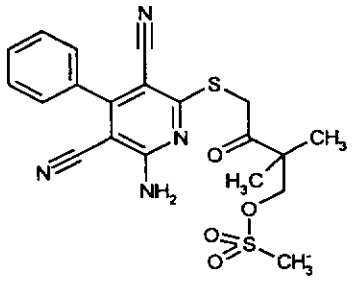
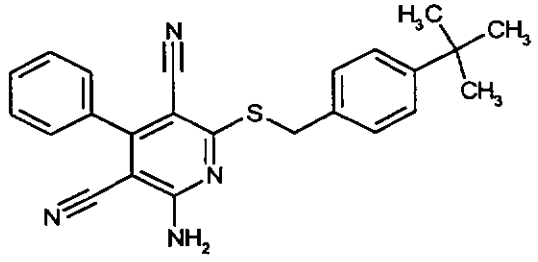
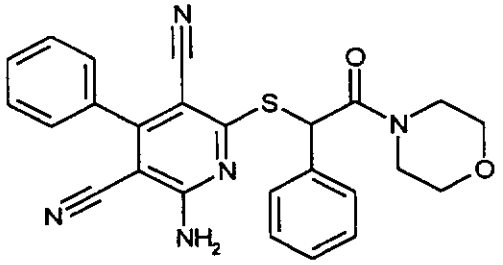
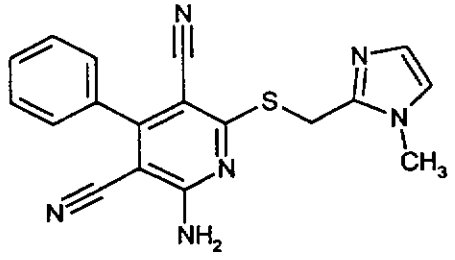
Ex. No.	Product	Molecular weight
B74		371
B75		447
B76		388
B77		438
B78		415

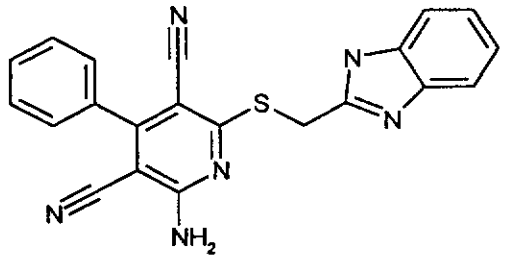
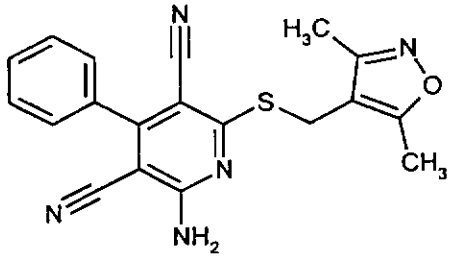
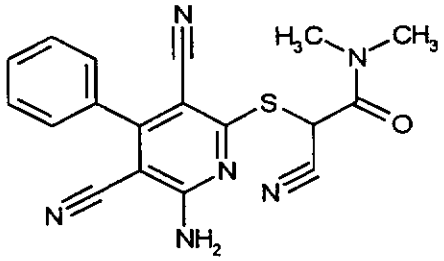
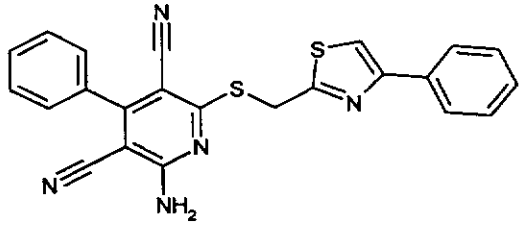
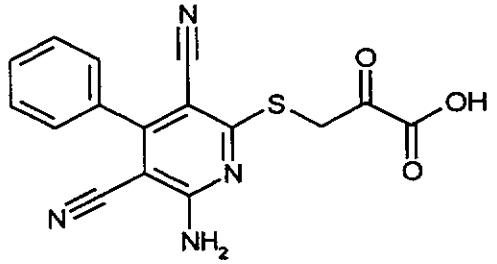
Ex. No.	Product	Molecular weight
B79		408
B80		473
B81		371
B82		434
B83		481

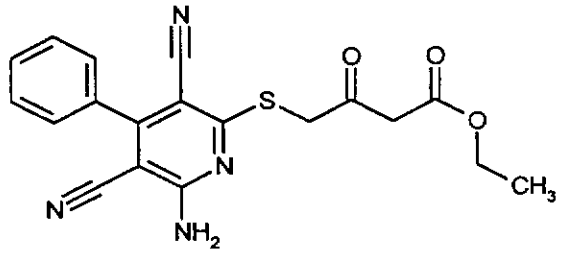
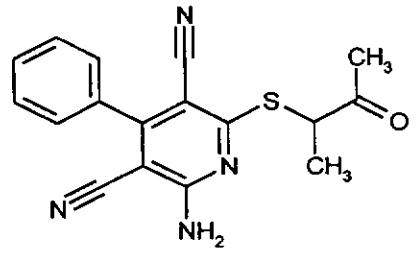
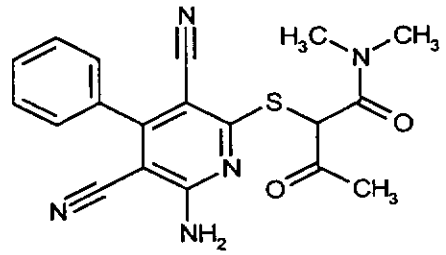
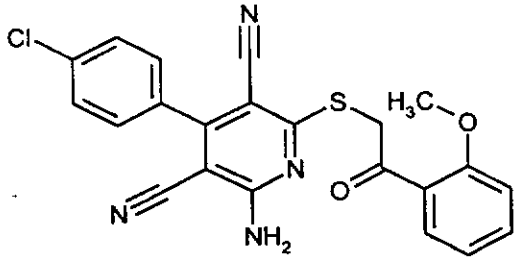
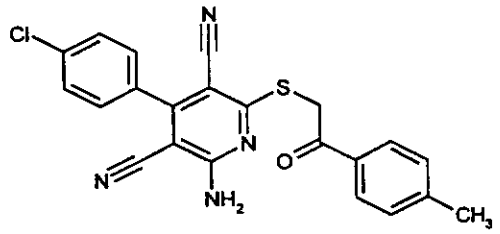
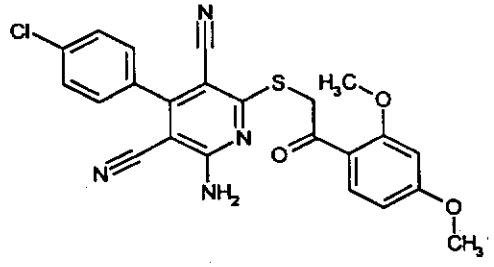
Ex. No.	Product	Molecular weight
B84		442
B85		428
B86		463
B87		528
B88		452

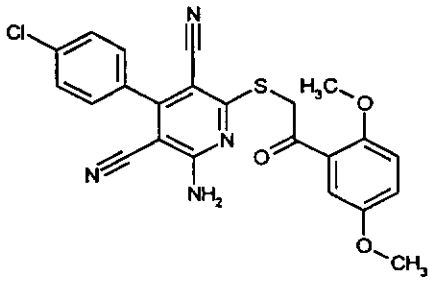
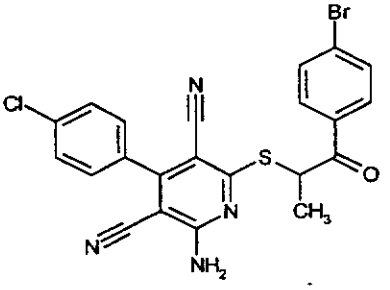
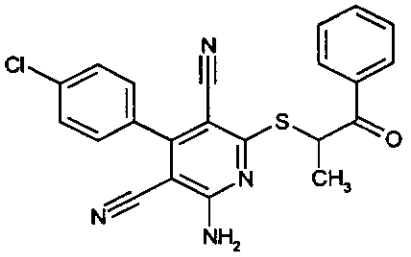
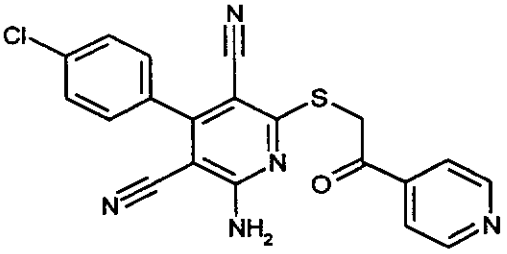
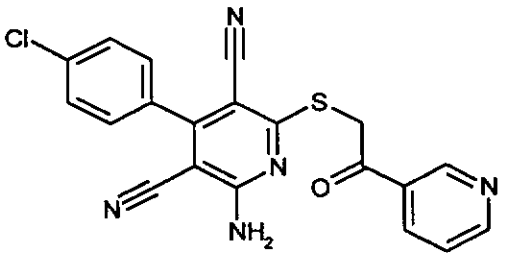
Ex. No.	Product	Molecular weight
B89		438
B90		338
B91		399
B92		398
B93		417

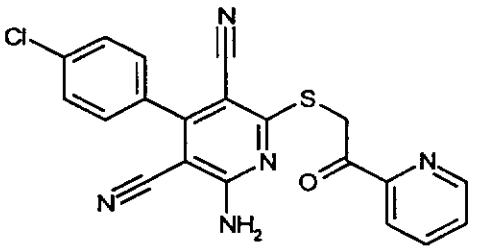
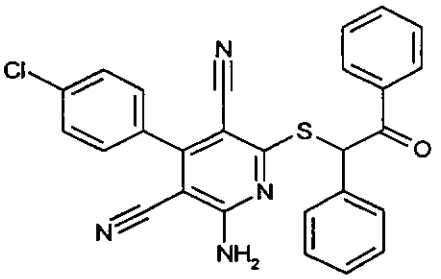
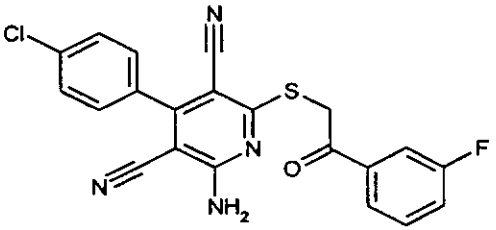
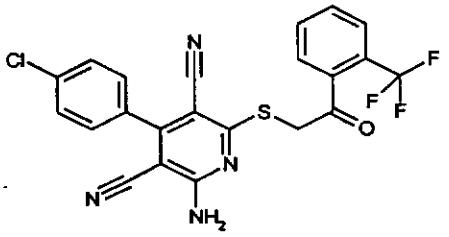
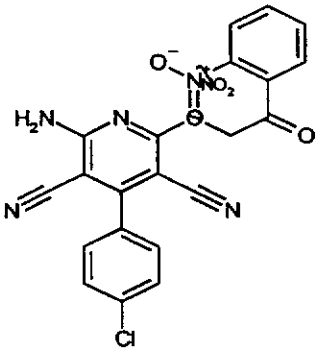
Ex. No.	Product	Molecular weight
B94		481
B95		384
B96		334
B97		516
B98		457

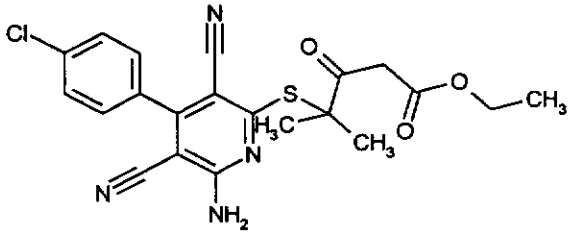
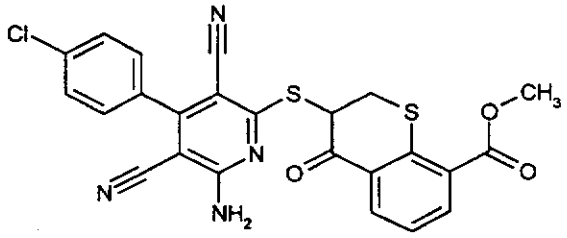
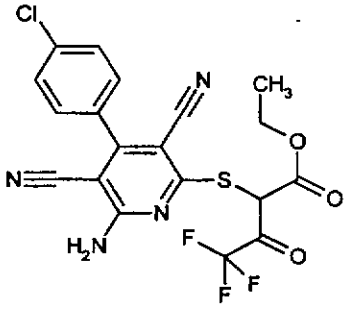
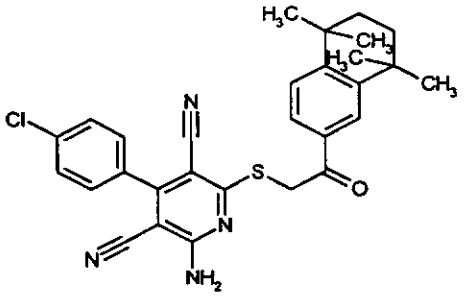
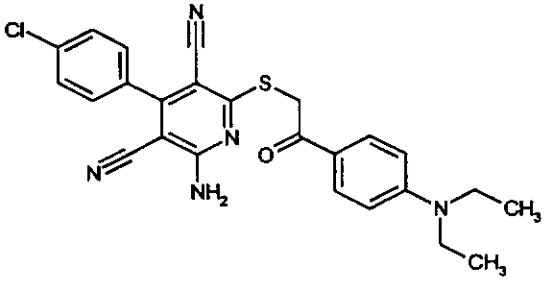
Ex. No.	Product	Molecular weight
B99		481
B100		445
B101		399
B102		456
B103		346

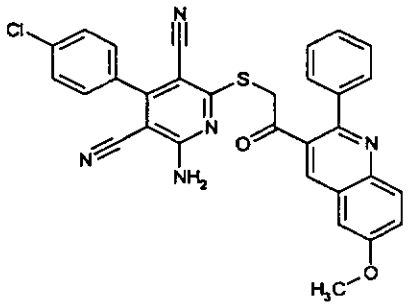
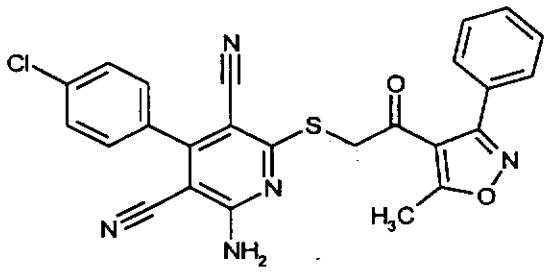
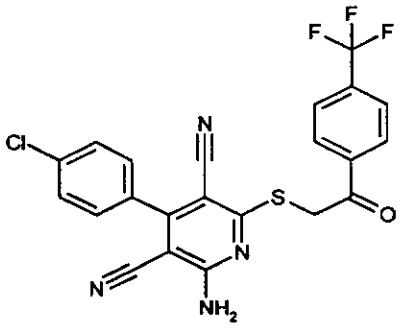
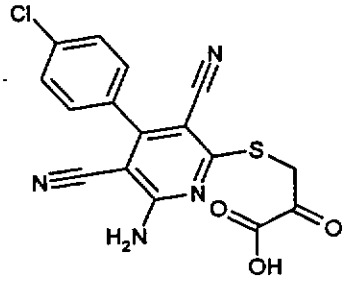
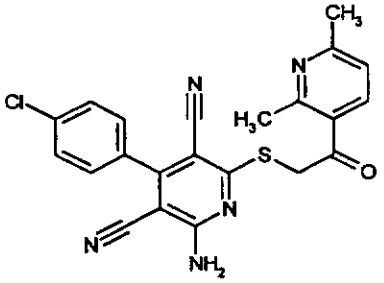
Ex. No.	Product	Molecular weight
B104		382
B105		361
B106		362
B107		426
B108		338

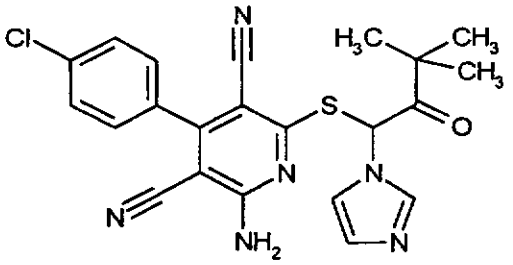
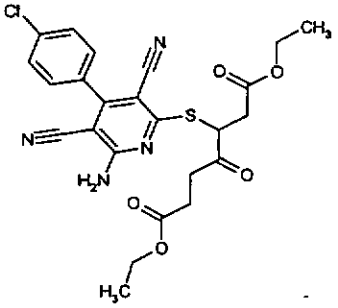
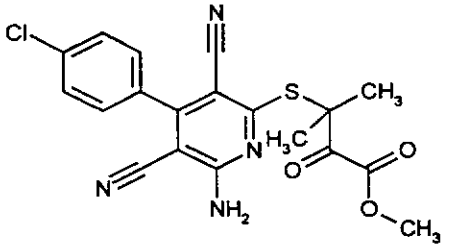
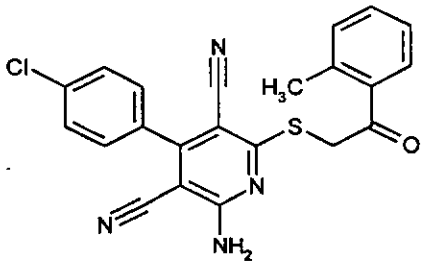
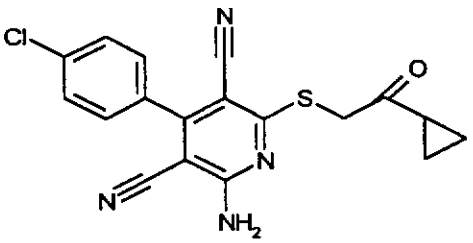
Ex. No.	Product	Molecular weight
B109		380
B110		322
B111		379
B112		435
B113		419
B114		465

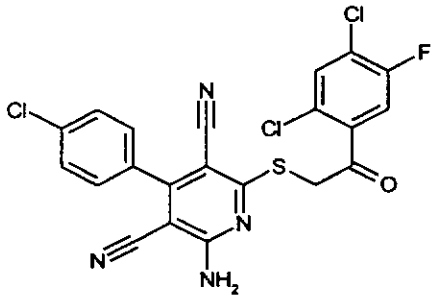
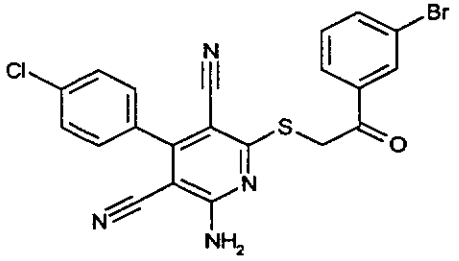
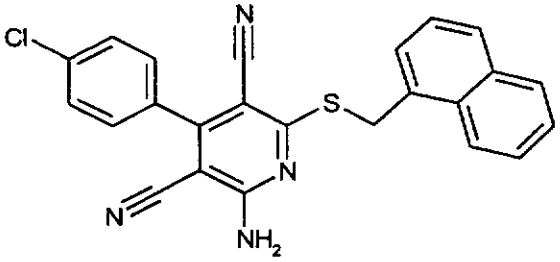
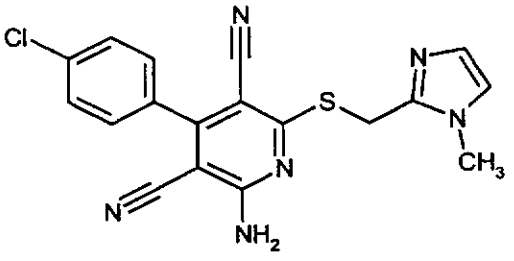
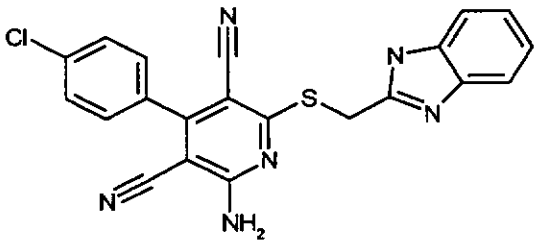
Ex. No.	Product	Molecular weight
B115		465
B116		498
B117		419
B118		406
B119		406

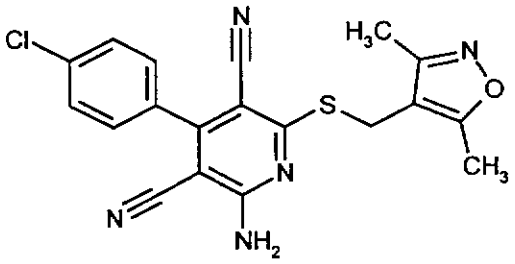
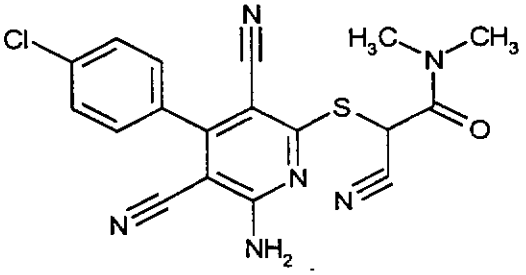
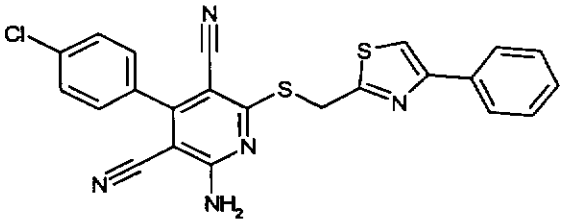
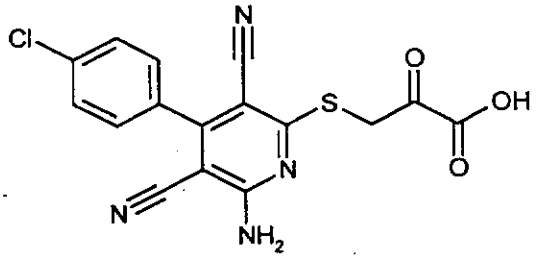
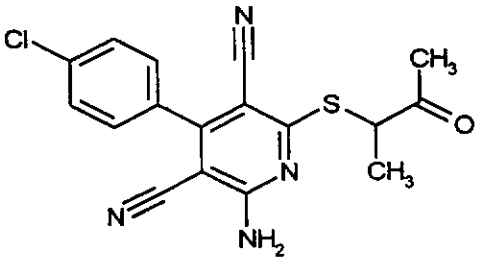
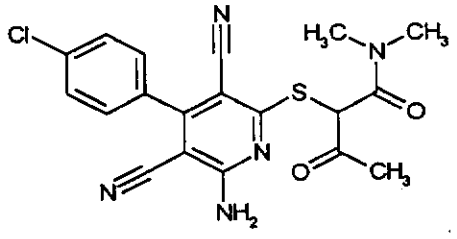
Ex. No.	Product	Molecular weight
B120		406
B121		481
B122		423
B123		473
B124		450

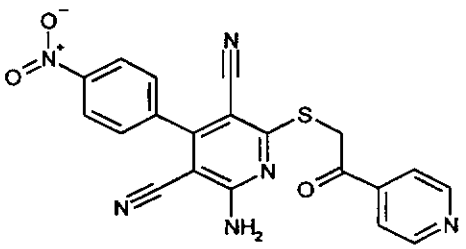
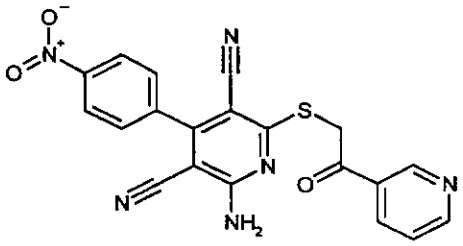
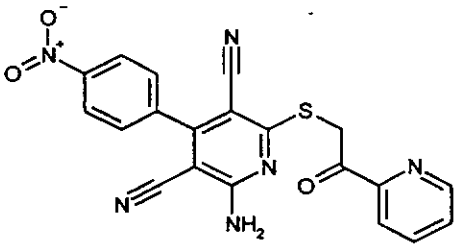
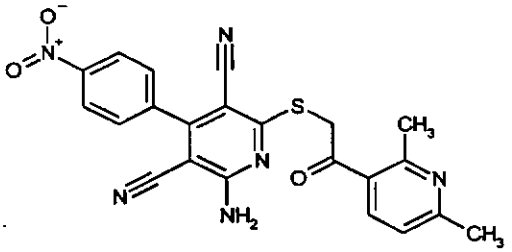
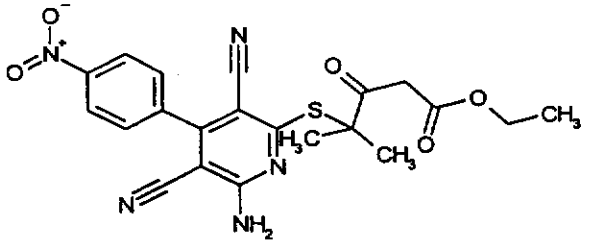
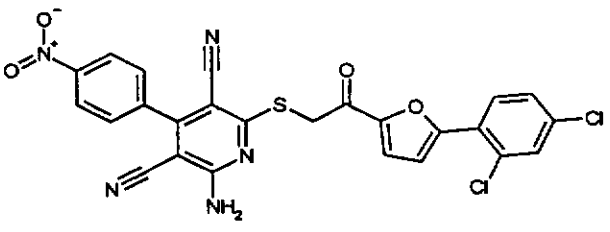
Ex. No.	Product	Molecular weight
B125		443
B126		507
B127		469
B128		515
B129		476

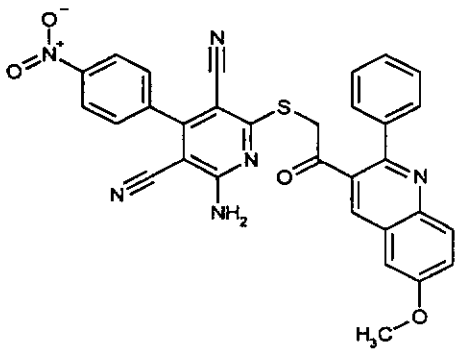
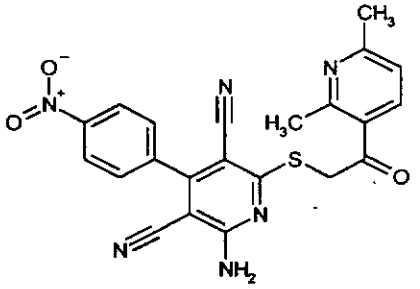
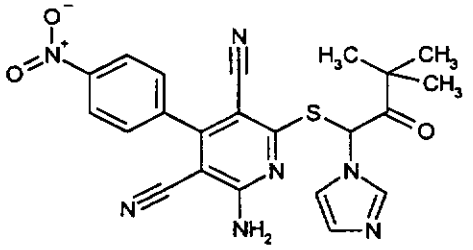
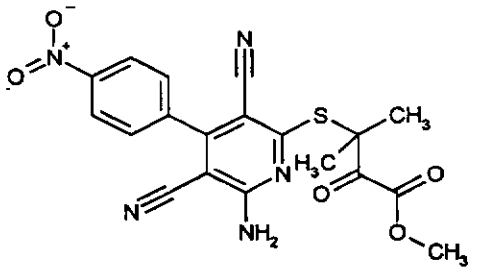
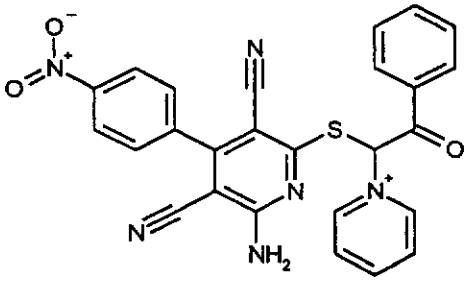
Ex. No.	Product	Molecular weight
B130		562
B131		486
B132		473
B133		373
B134		434

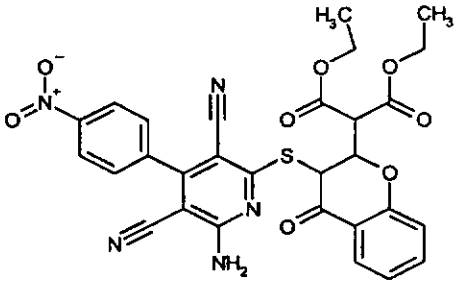
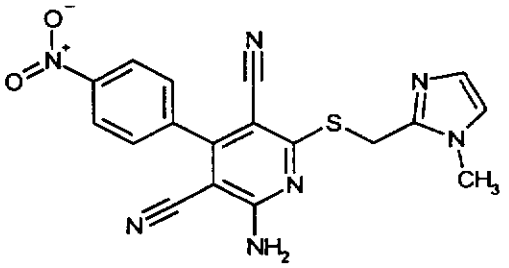
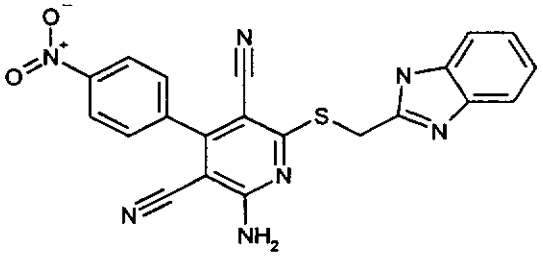
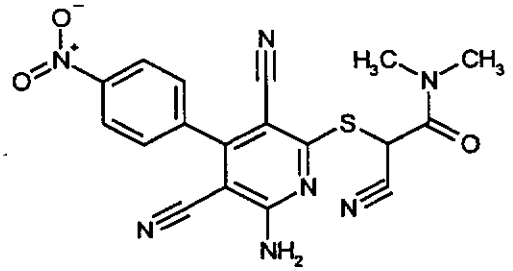
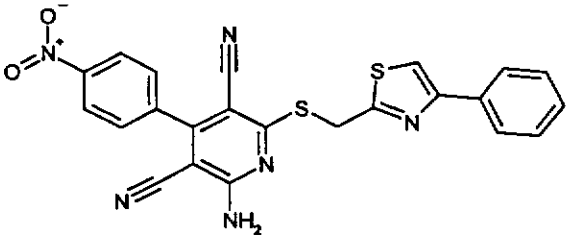
Ex. No.	Product	Molecular weight
B135		451
B136		515
B137		415
B138		419
B139		369

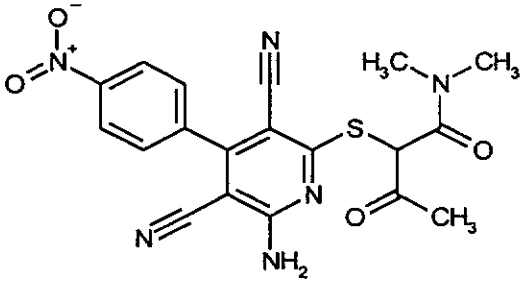
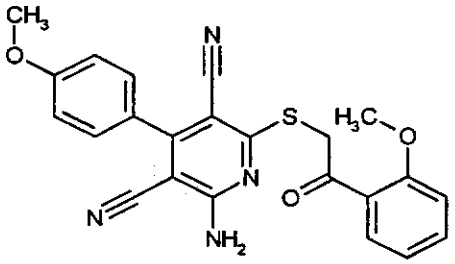
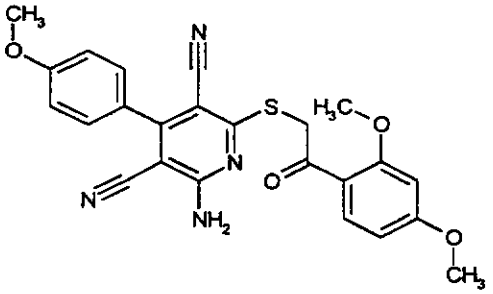
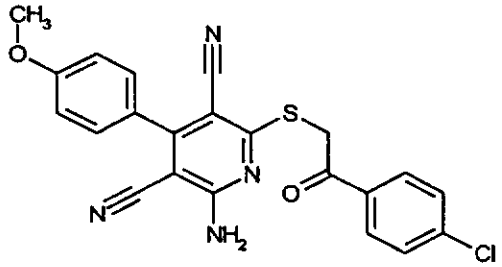
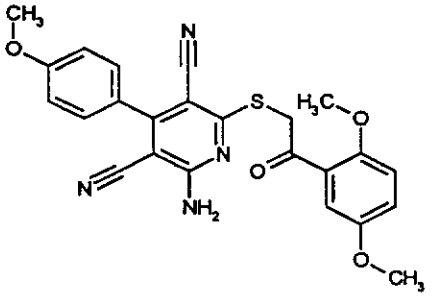
Ex. No.	Product	Molecular weight
B140		492
B141		484
B142		427
B143		381
B144		417

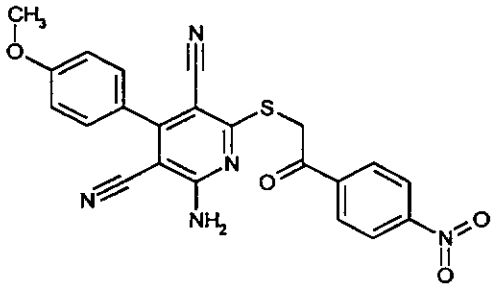
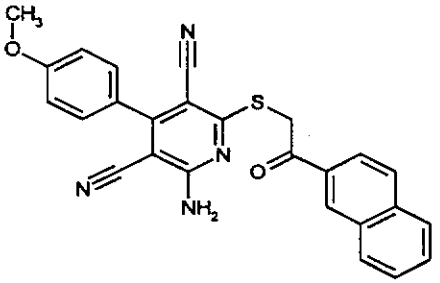
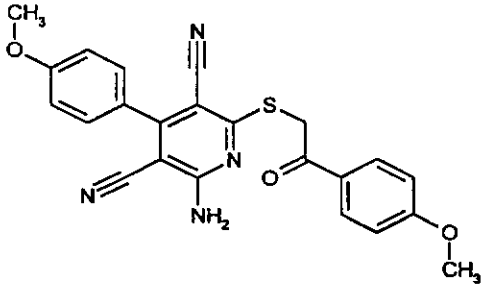
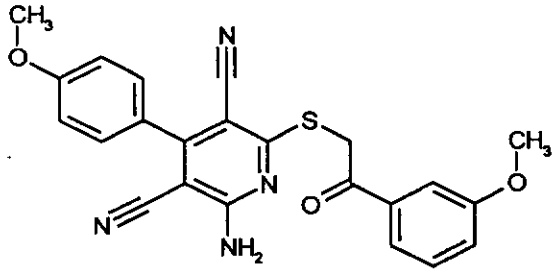
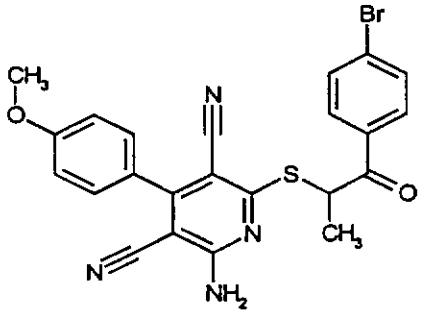
Ex. No.	Product	Molecular weight
B145		396
B146		397
B147		460
B148		373
B149		357
B150		414

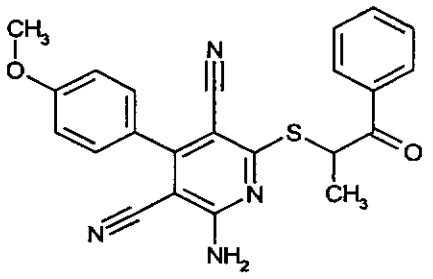
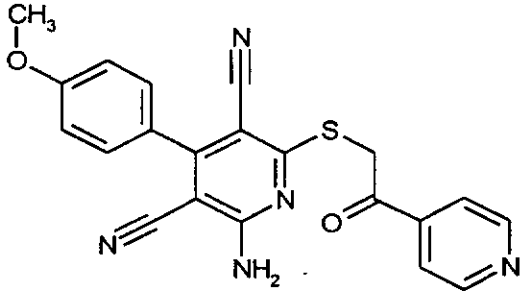
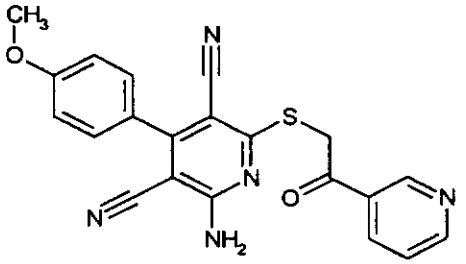
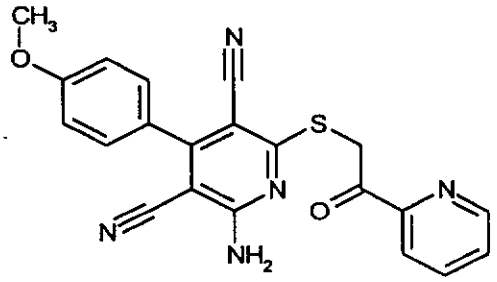
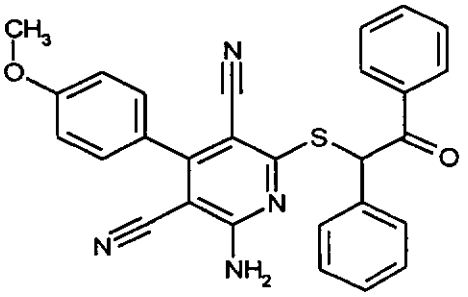
Ex. No.	Product	Molecular weight
B151		416
B152		416
B153		416
B154		444
B155		453
B156		550

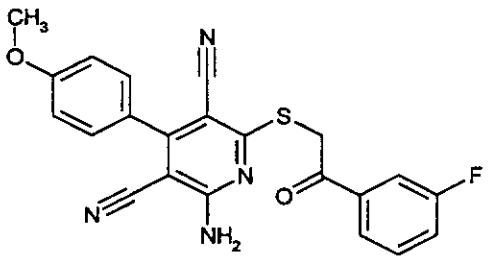
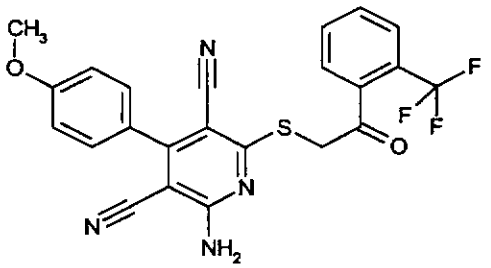
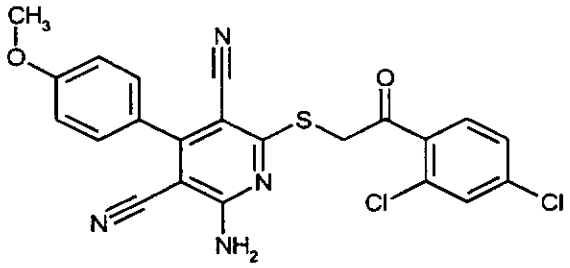
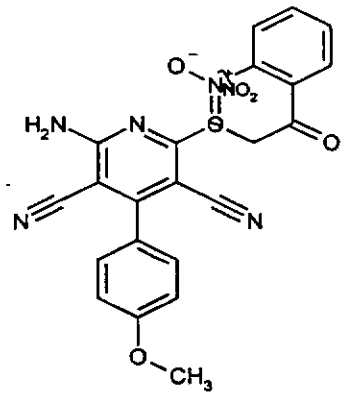
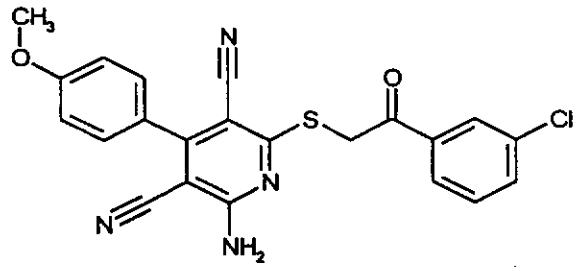
Ex. No.	Product	Molecular weight
B157		573
B158		444
B159		462
B160		425
B161		494

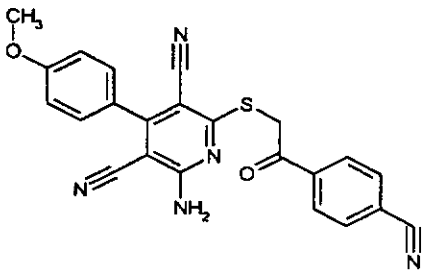
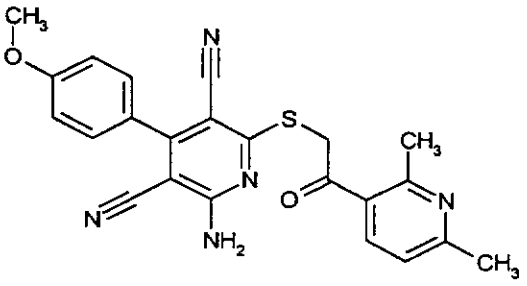
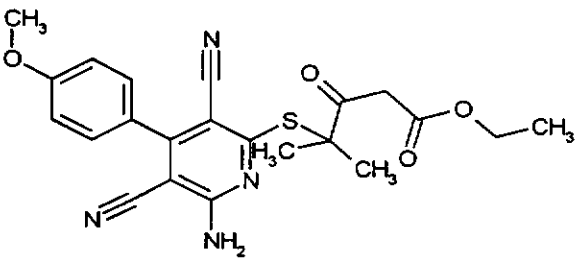
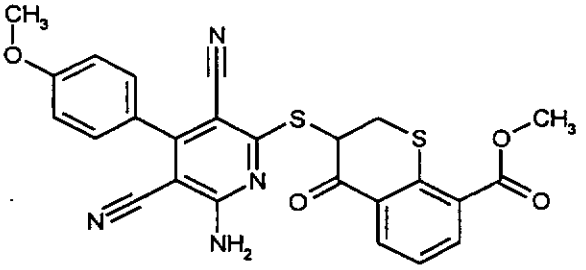
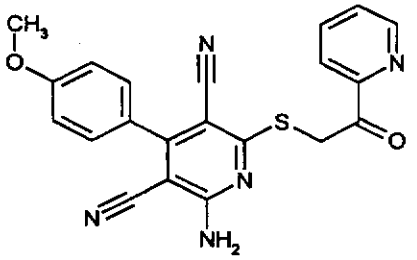
Ex. No.	Product	Molecular weight
B162		602
B163		391
B164		427
B165		407
B166		471

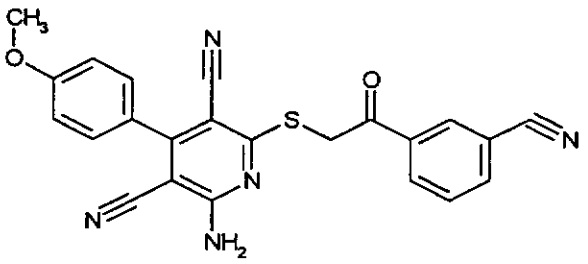
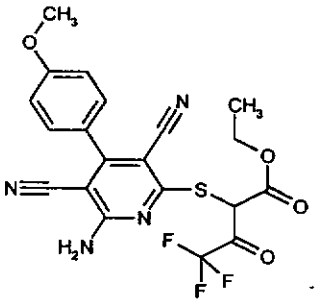
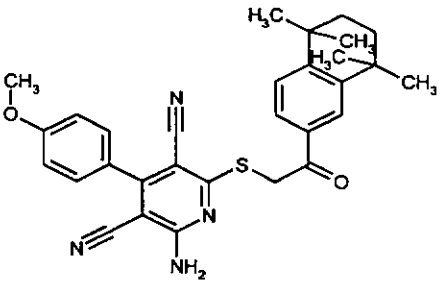
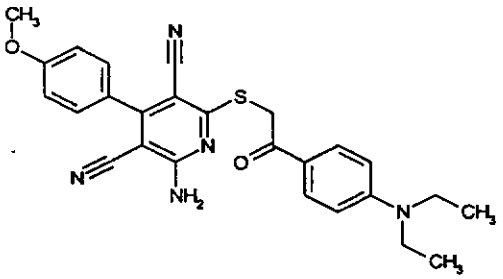
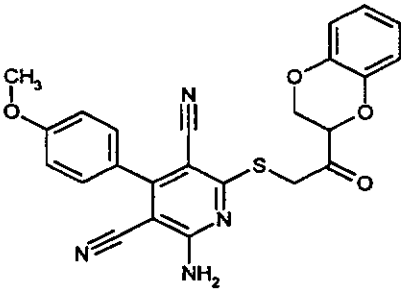
Ex. No.	Product	Molecular weight
B167		424
B168		430
B169		461
B170		435
B171		461

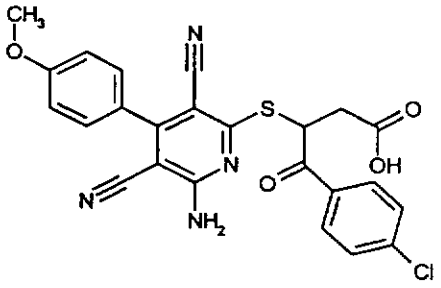
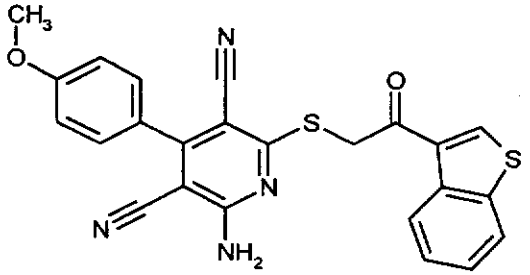
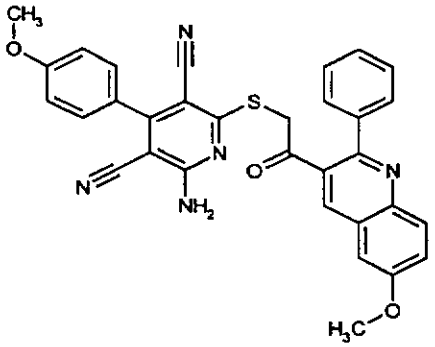
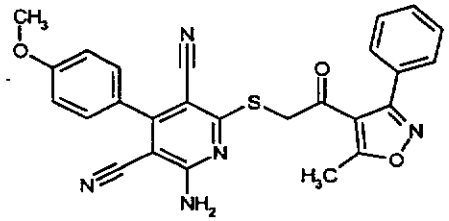
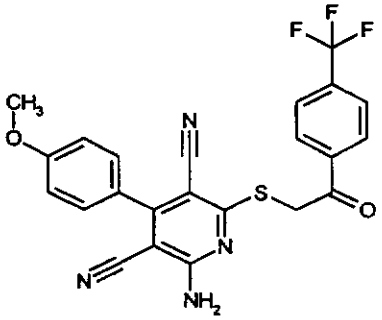
Ex. No.	Product	Molecular weight
B172		445
B173		451
B174		430
B175		430
B176		493

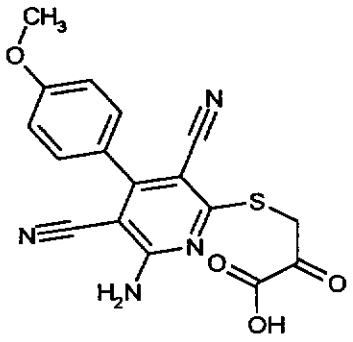
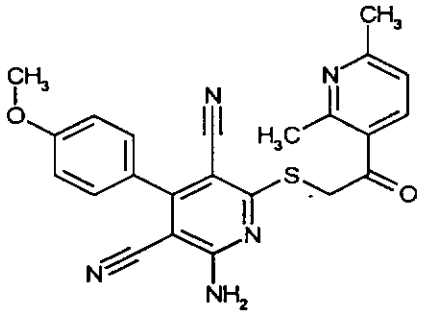
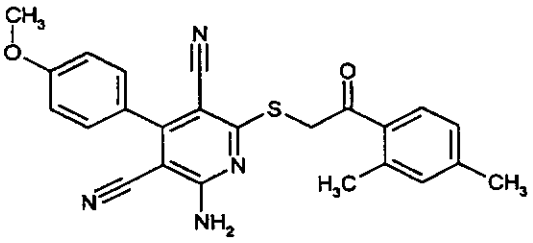
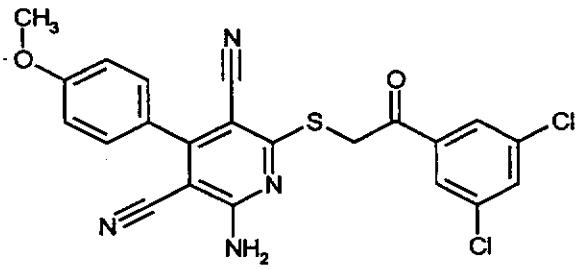
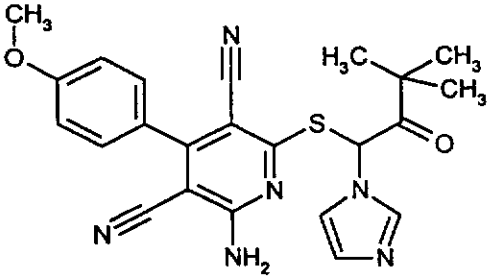
Ex. No.	Product	Molecular weight
B177		414
B178		401
B179		401
B180		401
B181		477

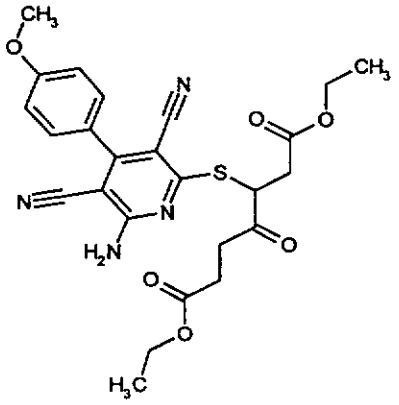
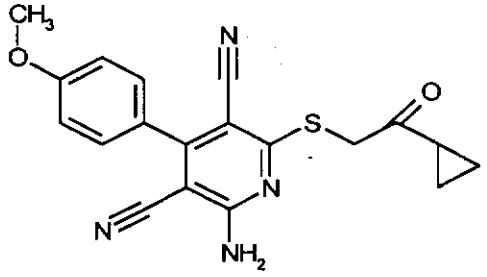
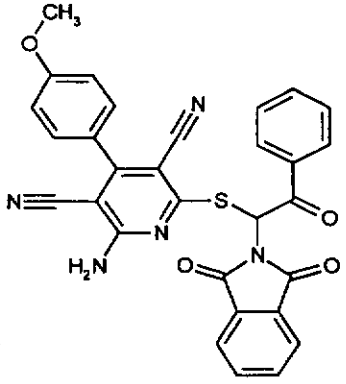
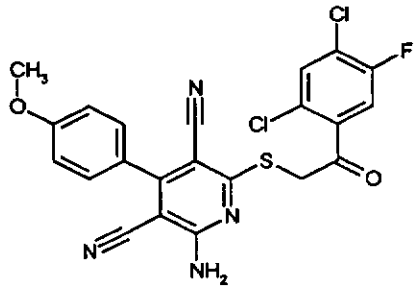
Ex. No.	Product	Molecular weight
B182		418
B183		468
B184		469
B185		445
B186		435

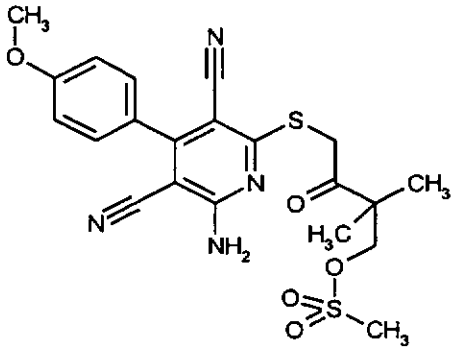
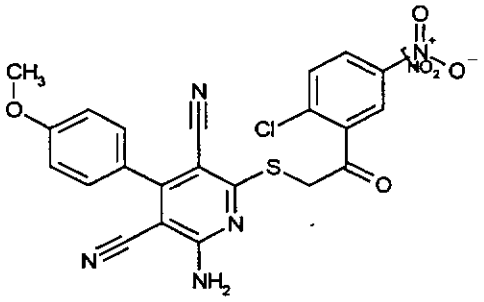
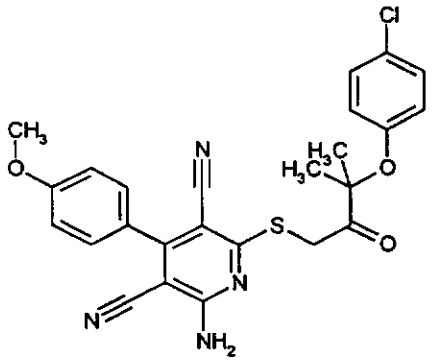
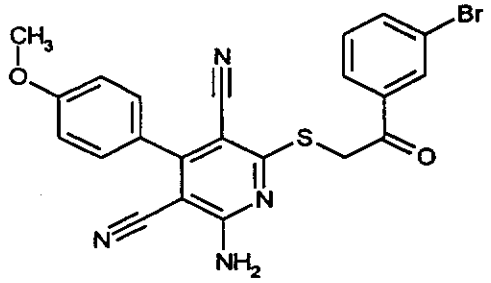
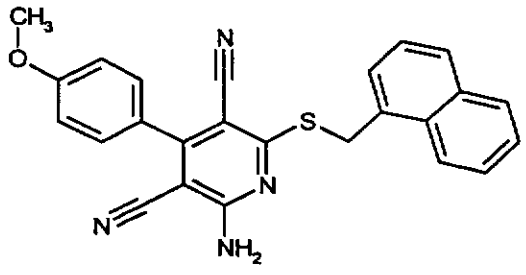
Ex. No.	Product	Molecular weight
B187		425
B188		430
B189		439
B190		503
B191		401

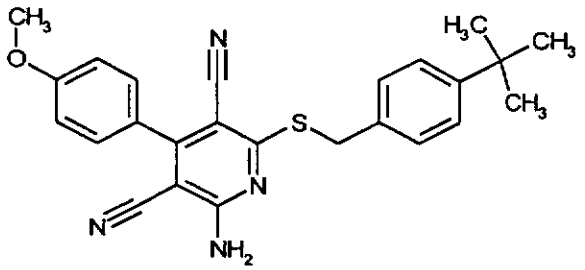
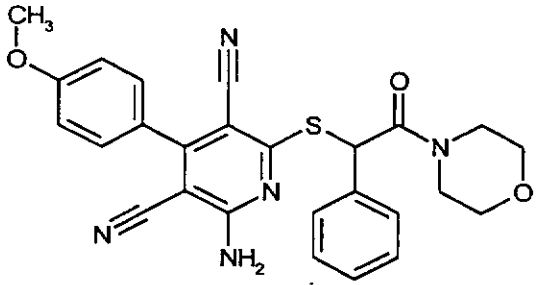
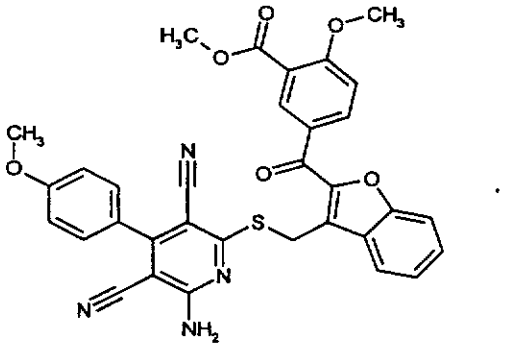
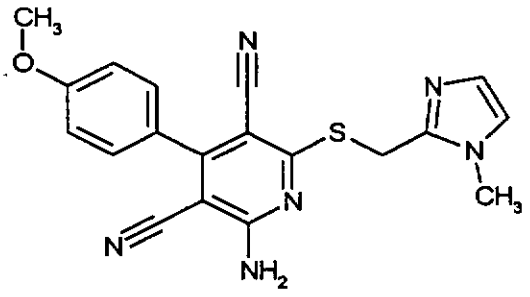
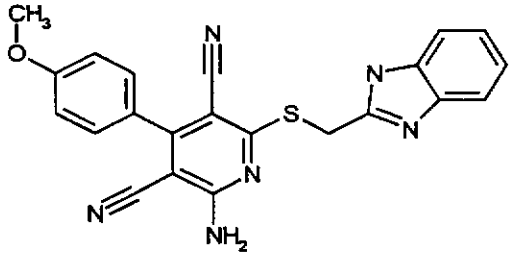
Ex. No.	Product	Molecular weight
B192		425
B193		464
B194		511
B195		472
B196		458

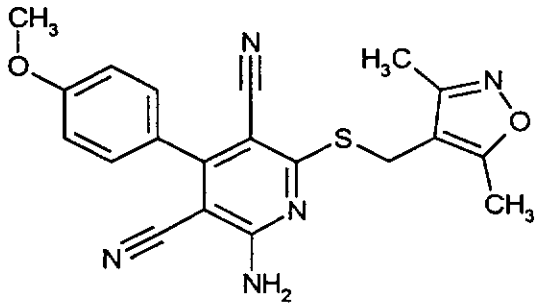
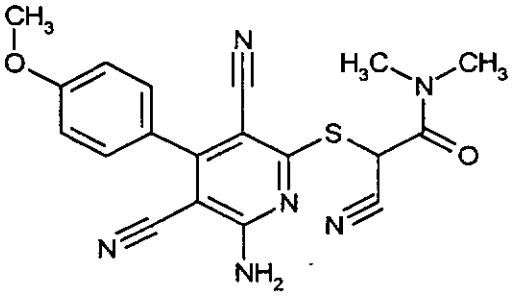
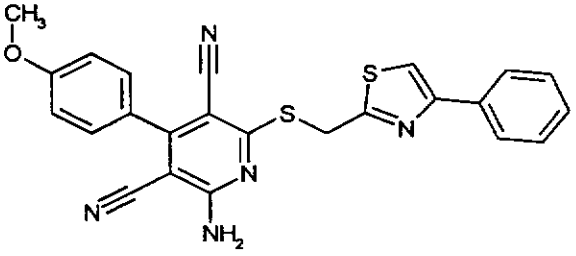
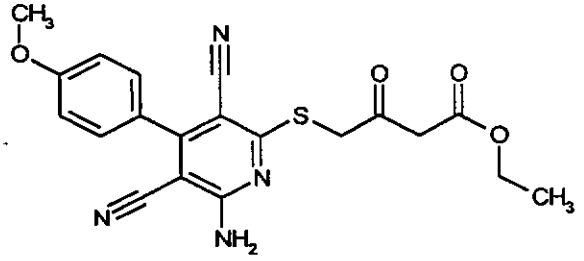
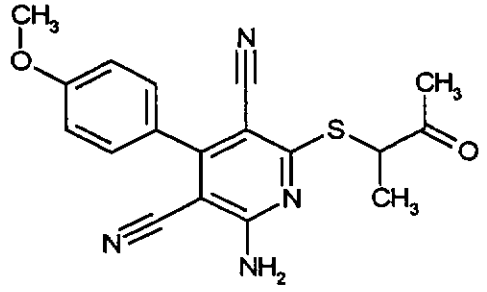
Ex. No.	Product	Molecular weight
B197		493
B198		457
B199		558
B200		482
B201		468

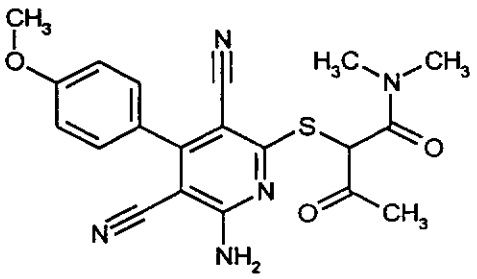
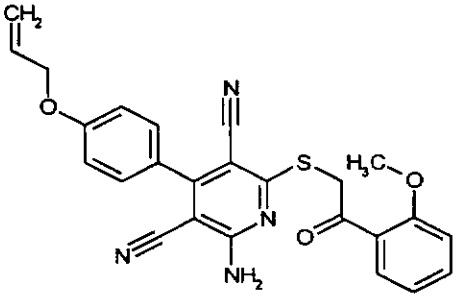
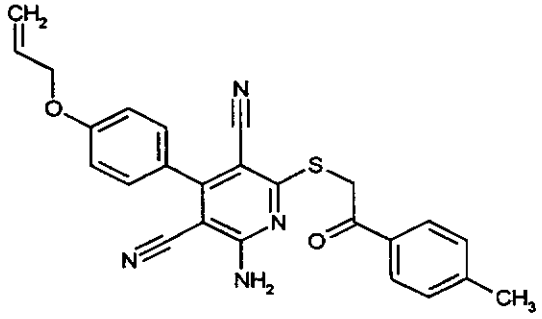
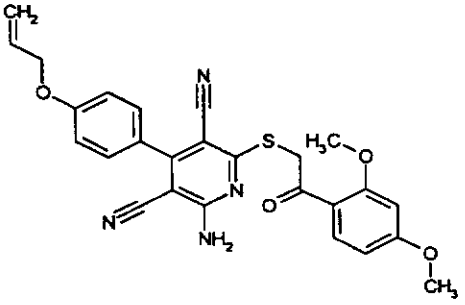
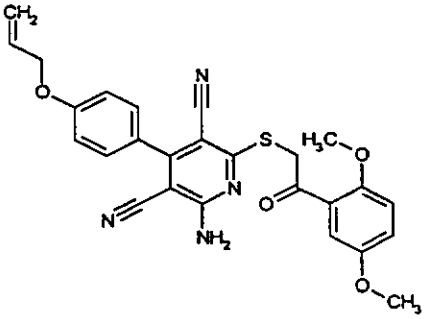
Ex. No.	Product	Molecular weight
B202		368
B203		430
B204		429
B205		469
B206		447

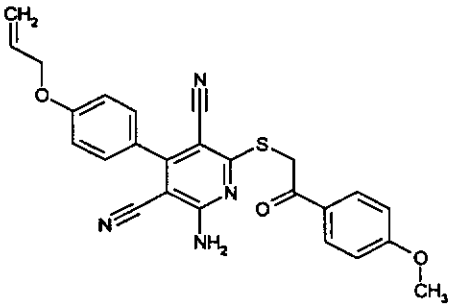
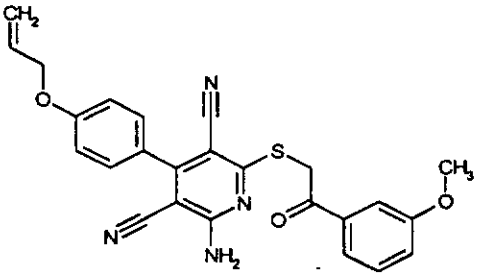
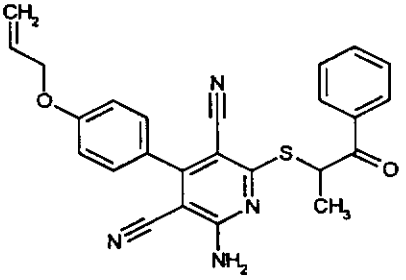
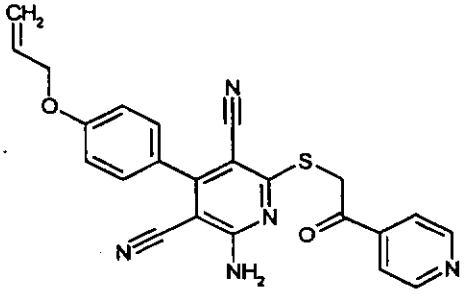
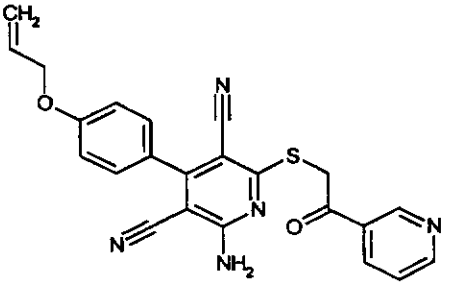
Ex. No.	Product	Molecular weight
B207		511
B208		364
B209		546
B210		487

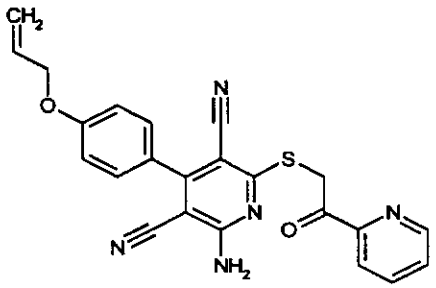
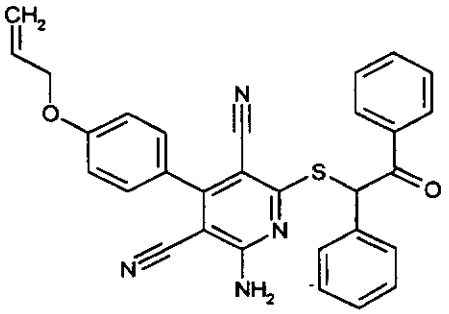
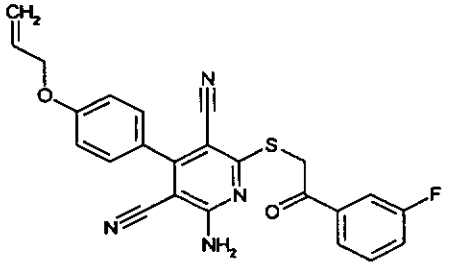
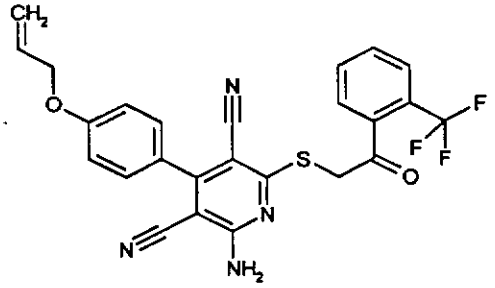
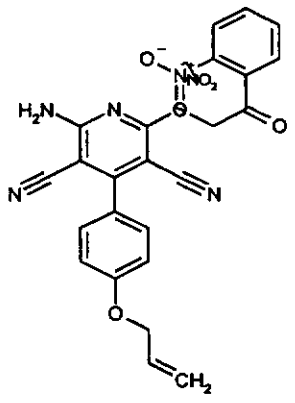
Ex. No.	Product	Molecular weight
B211		475
B212		480
B213		493
B214		479
B215		423

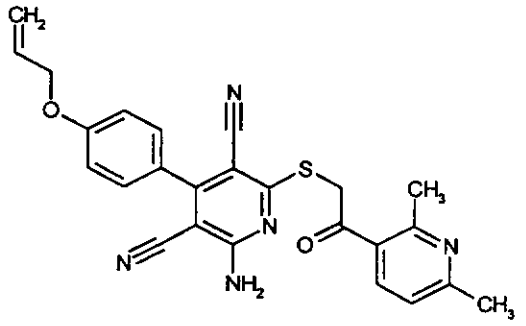
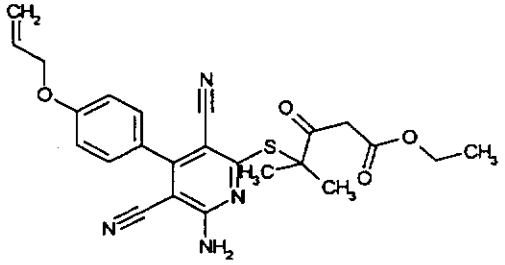
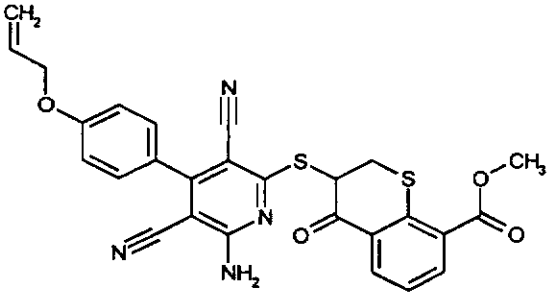
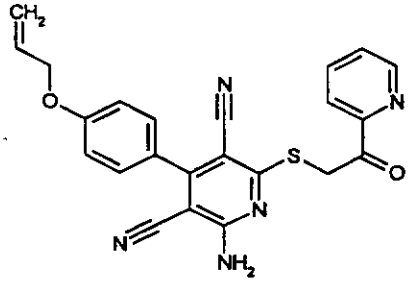
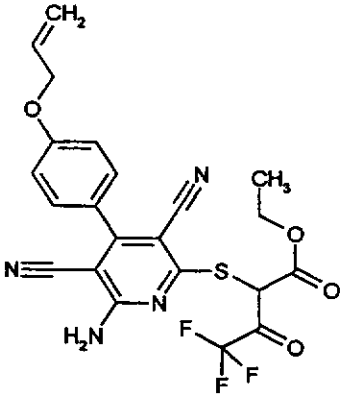
Ex. No.	Product	Molecular weight
B216		429
B217		486
B218		605
B219		376
B220		412

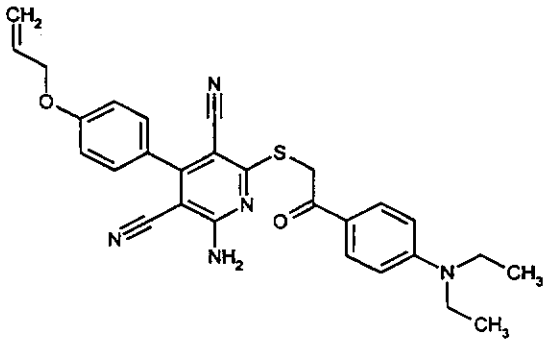
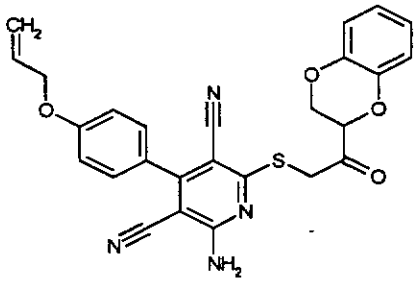
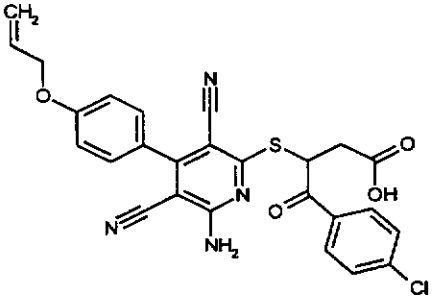
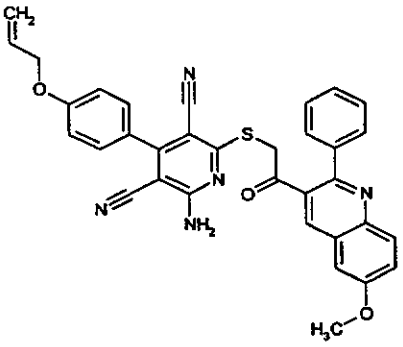
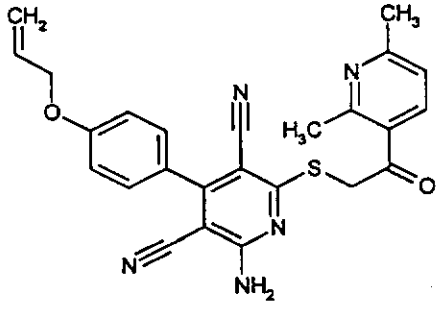
Ex. No.	Product	Molecular weight
B221		391
B222		392
B223		456
B224		410
B225		352

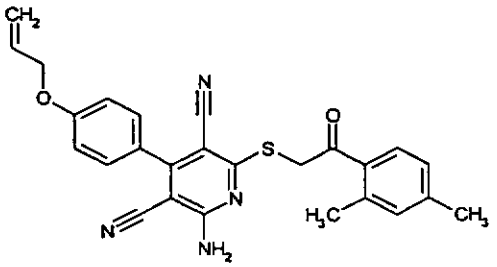
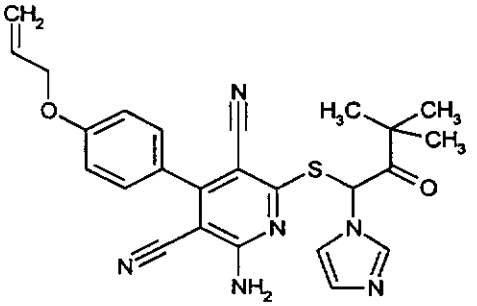
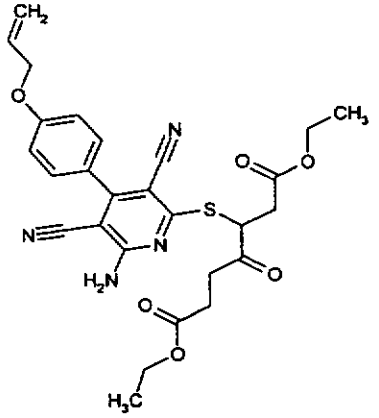
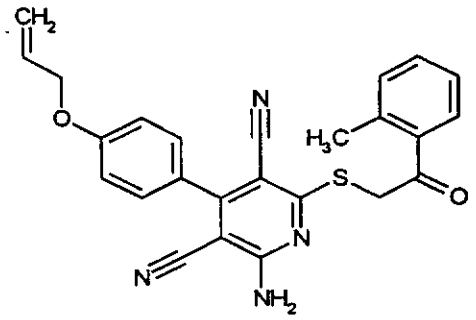
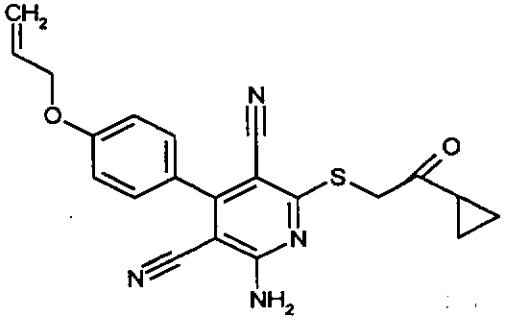
Ex. No.	Product	Molecular weight
B226		409
B227		457
B228		441
B229		487
B230		487

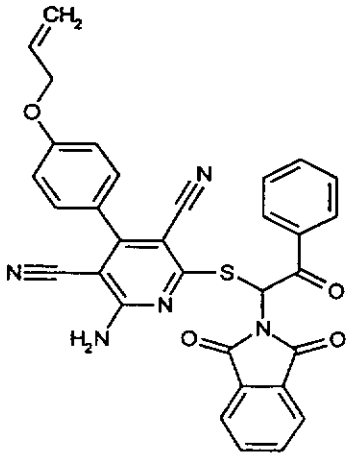
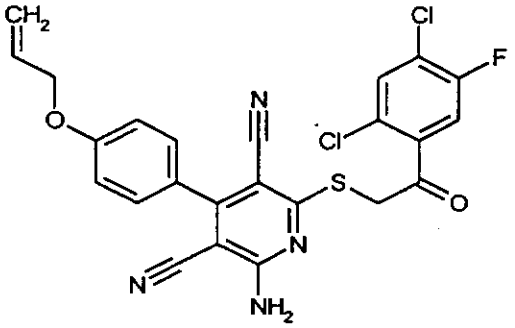
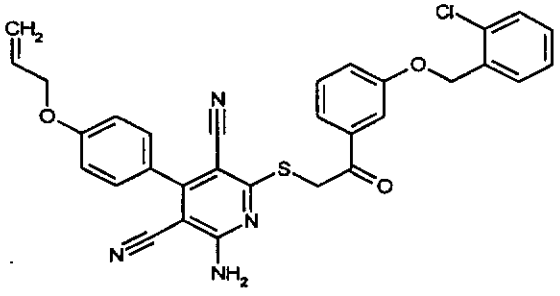
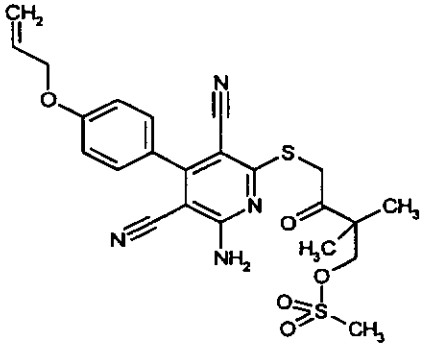
Ex. No.	Product	Molecular weight
B231		457
B232		457
B233		441
B234		427
B235		427

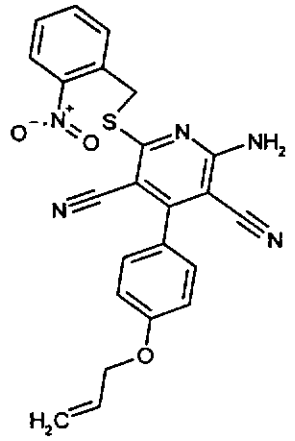
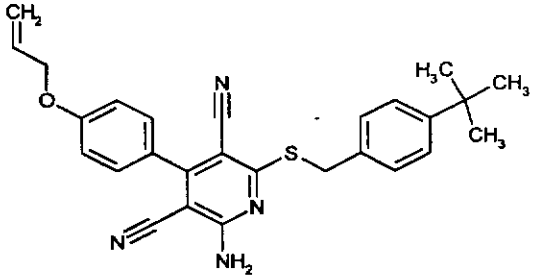
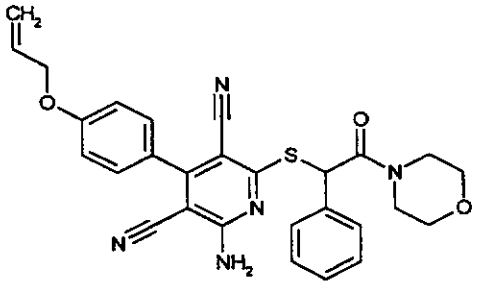
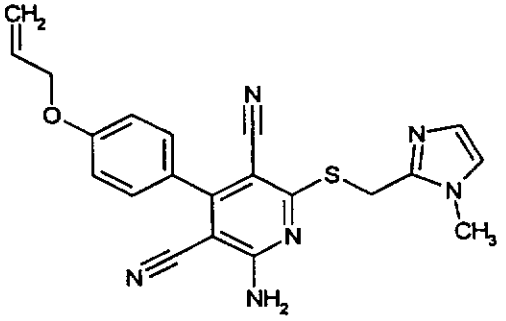
Ex. No.	Product	Molecular weight
B236		427
B237		503
B238		444
B239		494
B240		471

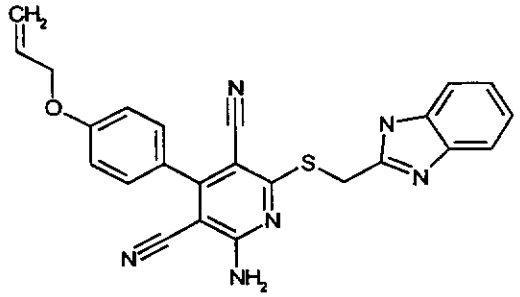
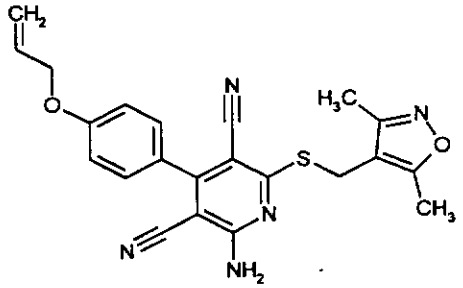
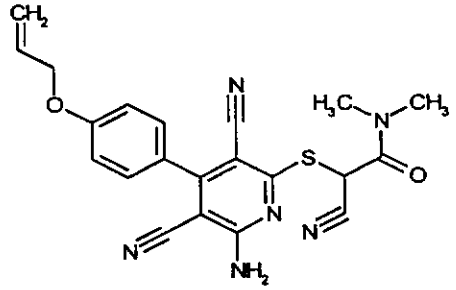
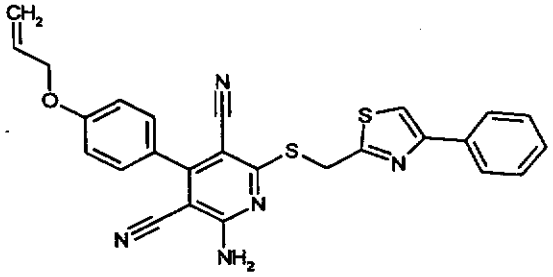
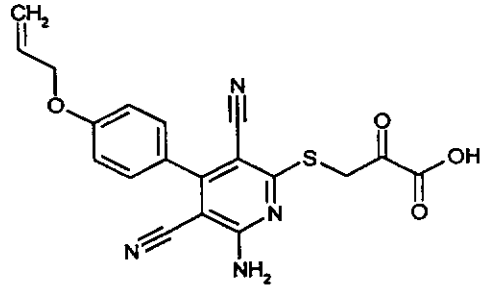
Ex. No.	Product	Molecular weight
B241		456
B242		465
B243		529
B244		427
B245		490

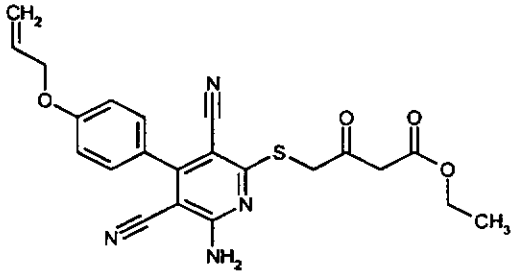
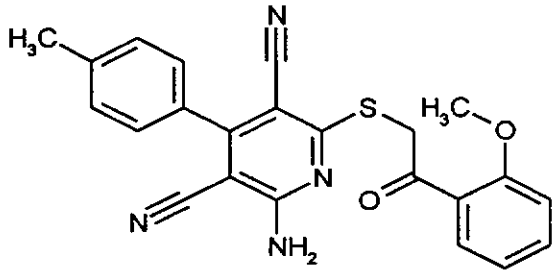
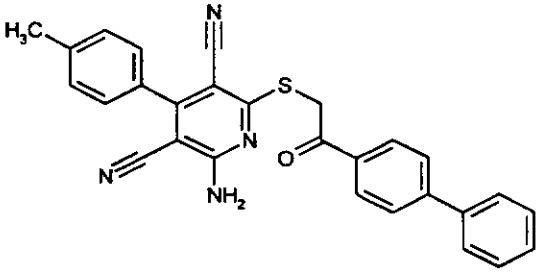
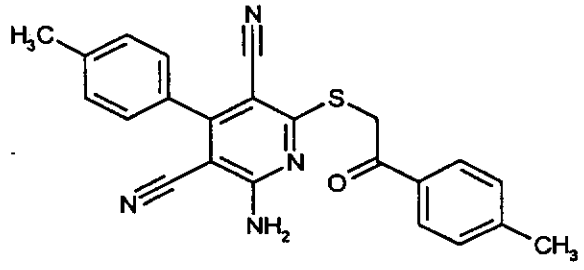
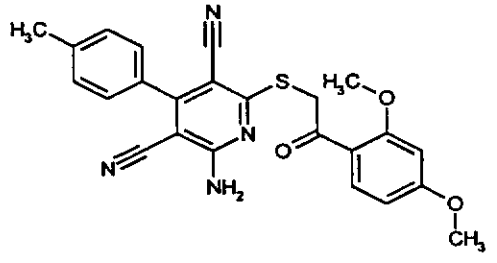
Ex. No.	Product	Molecular weight
B246		498
B247		485
B248		519
B249		584
B250		456

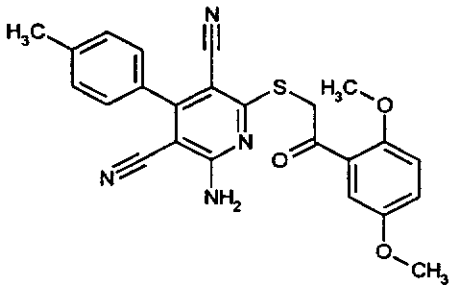
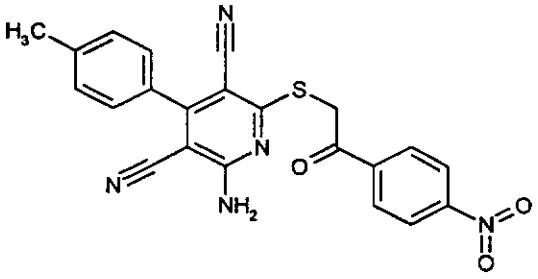
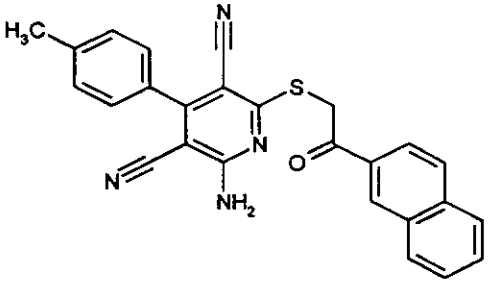
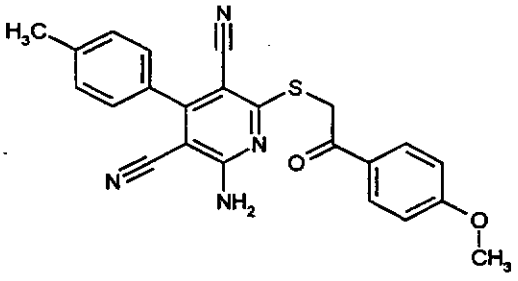
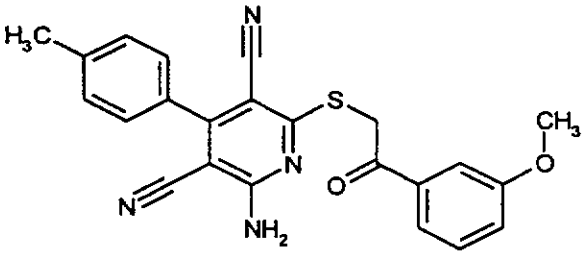
Ex. No.	Product	Molecular weight
B251		455
B252		473
B253		537
B254		441
B255		390

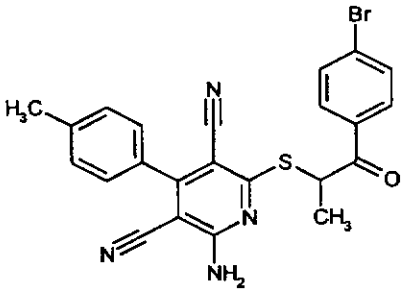
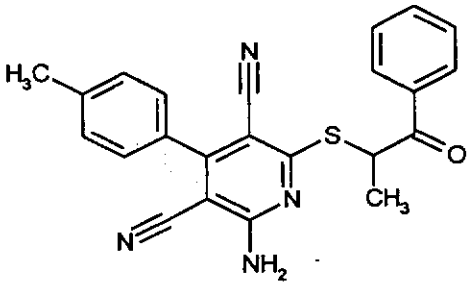
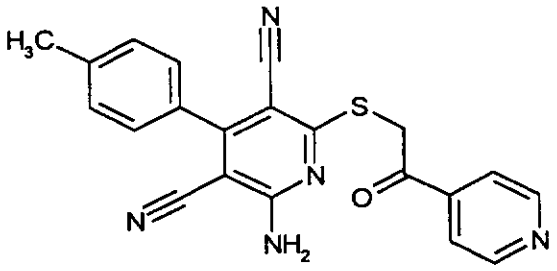
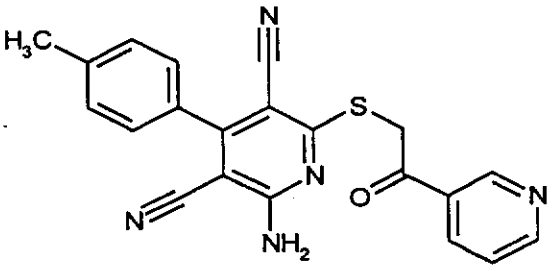
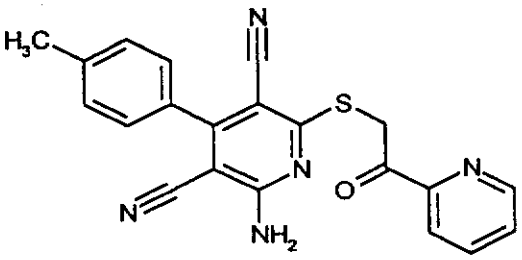
Ex. No.	Product	Molecular weight
B256		572
B257		513
B258		567
B259		501

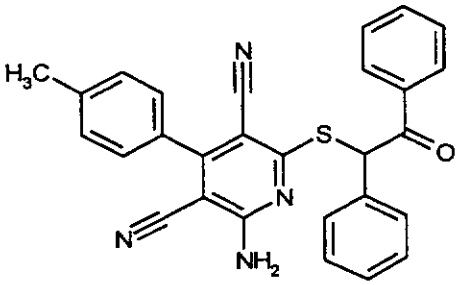
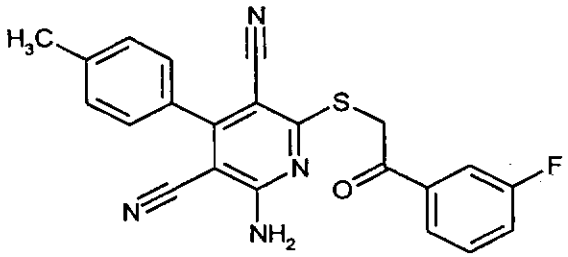
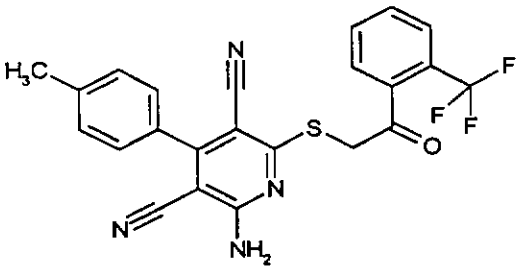
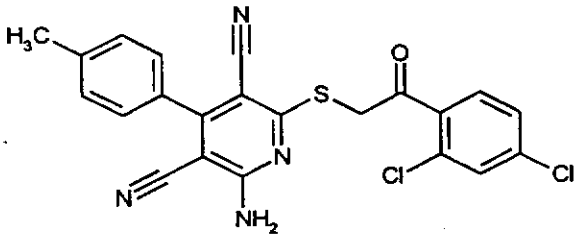
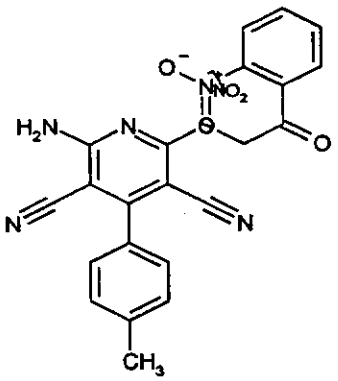
Ex. No.	Product	Molecular weight
B260		443
B261		455
B262		512
B263		402

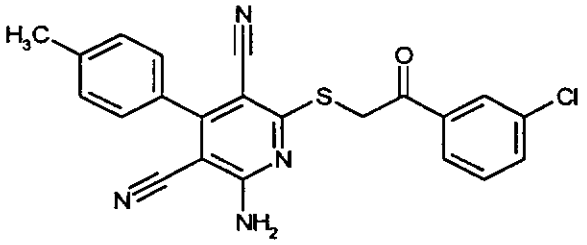
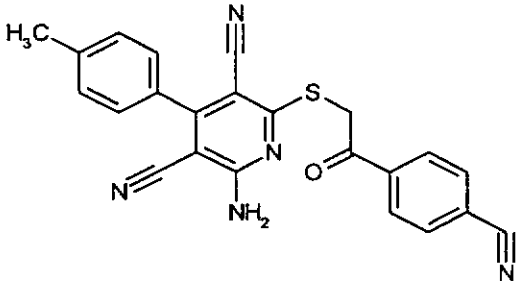
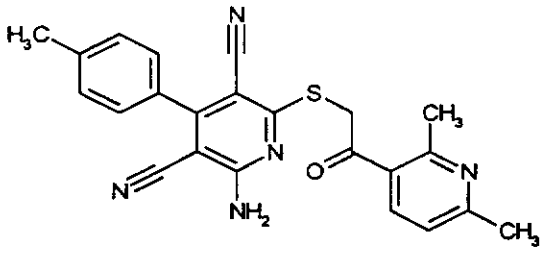
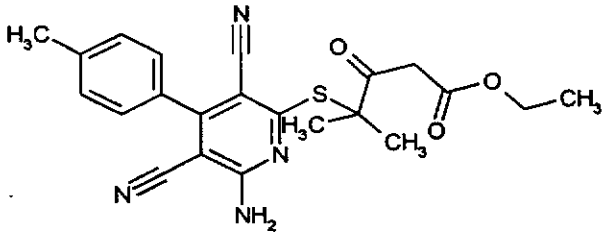
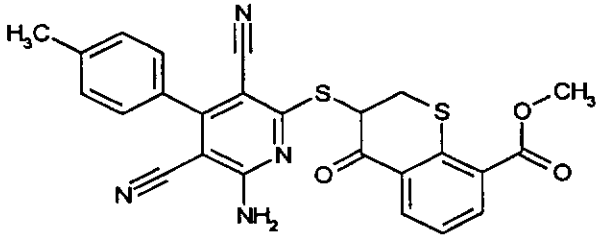
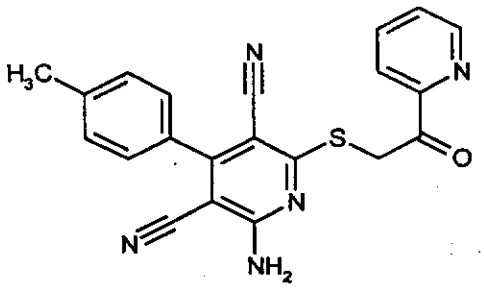
Ex. No.	Product	Molecular weight
B264		439
B265		417
B266		418
B267		482
B268		394

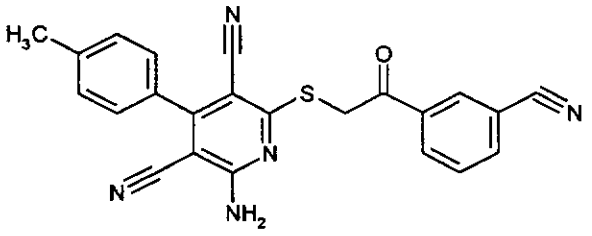
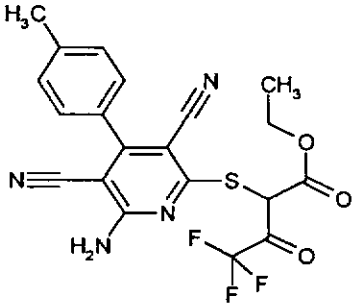
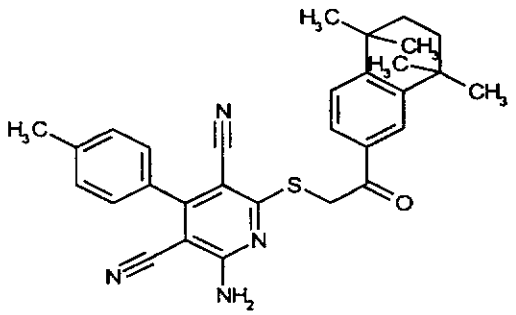
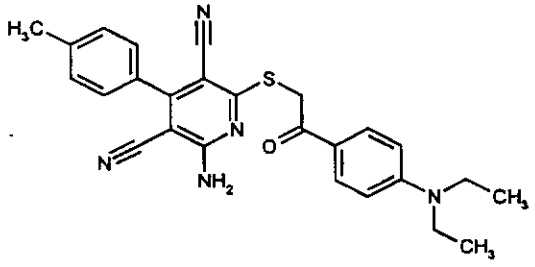
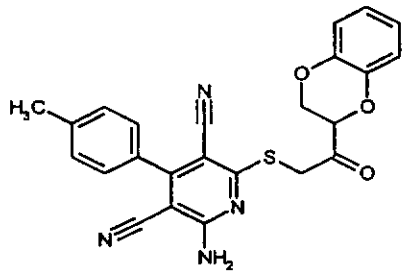
Ex. No.	Product	Molecular weight
B269		436
B270		414
B271		461
B272		398
B273		445

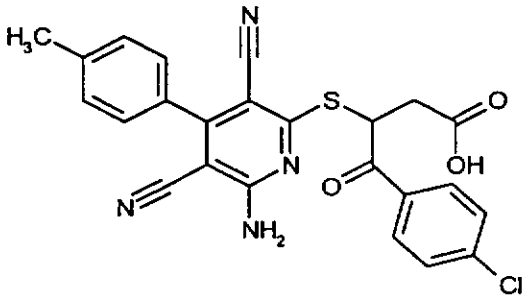
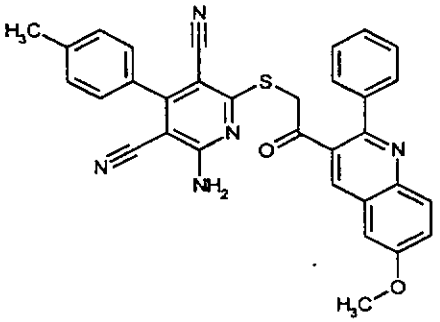
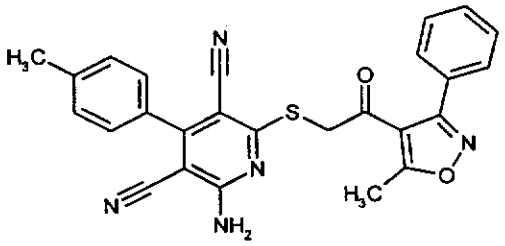
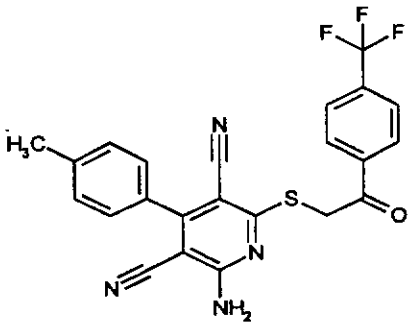
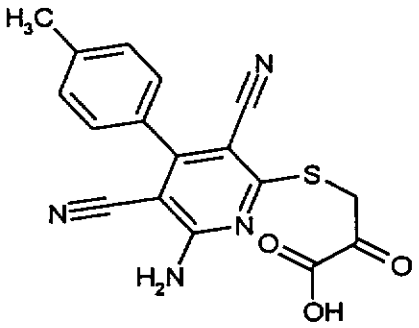
Ex. No.	Product	Molecular weight
B274		445
B275		429
B276		435
B277		414
B278		414

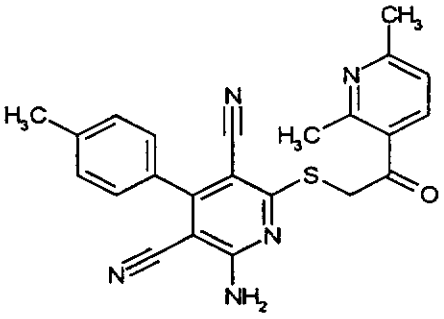
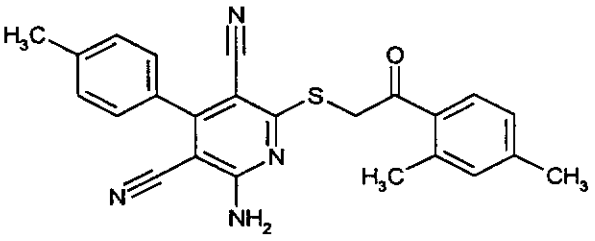
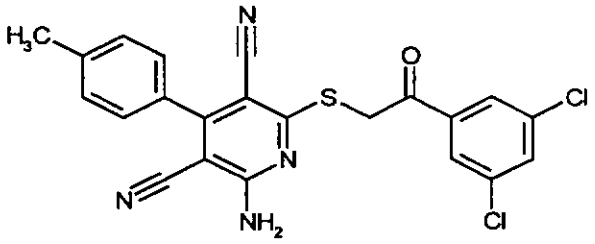
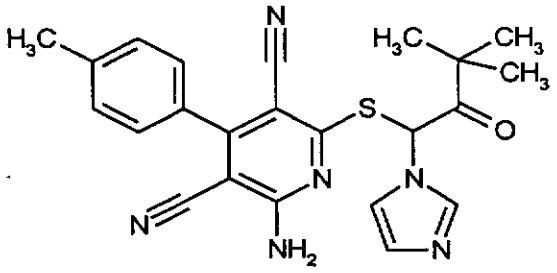
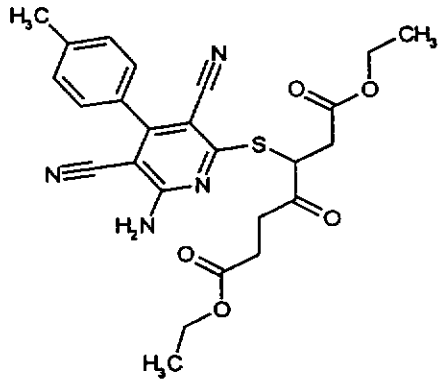
Ex. No.	Product	Molecular weight
B279		477
B280		398
B281		385
B282		385
B283		385

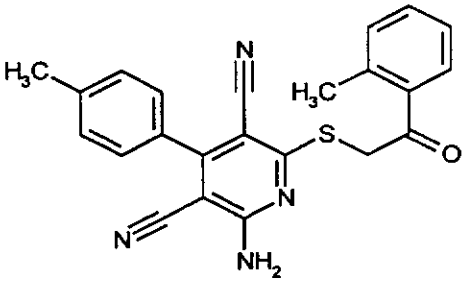
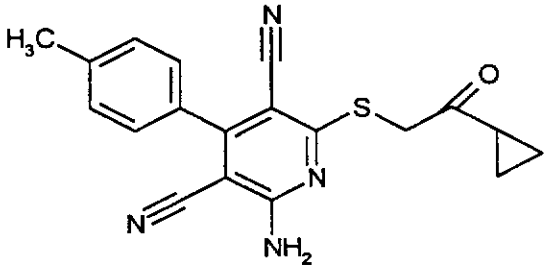
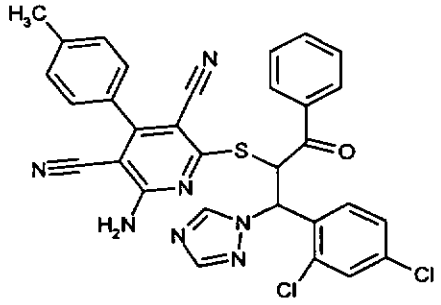
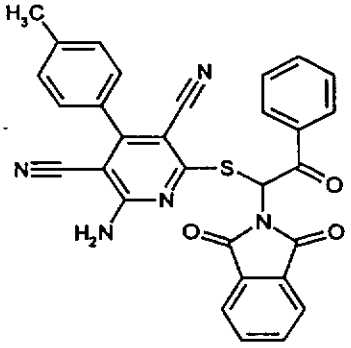
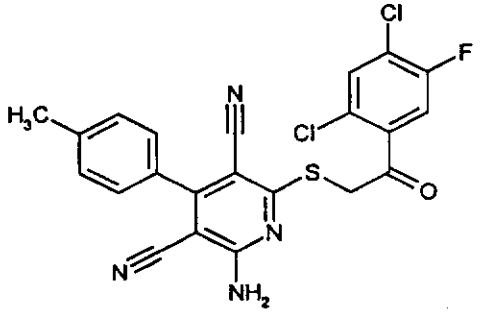
Ex. No.	Product	Molecular weight
B284		461
B285		402
B286		452
B287		453
B288		429

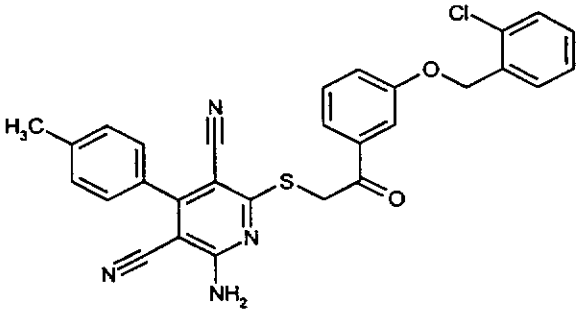
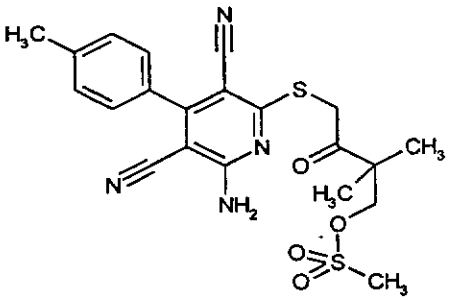
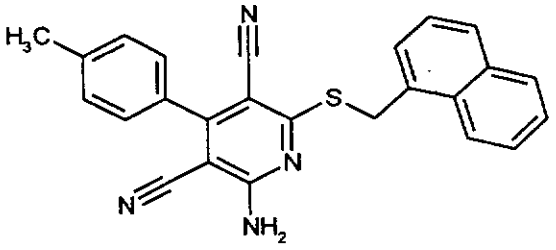
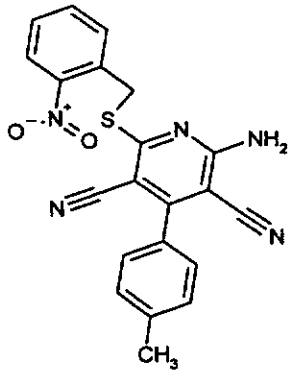
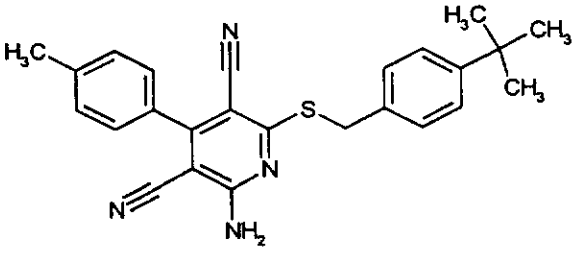
Ex. No.	Product	Molecular weight
B289		419
B290		409
B291		414
B292		423
B293		487
B294		385

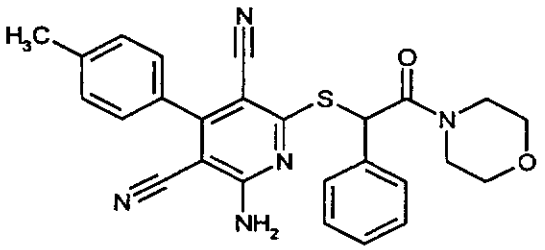
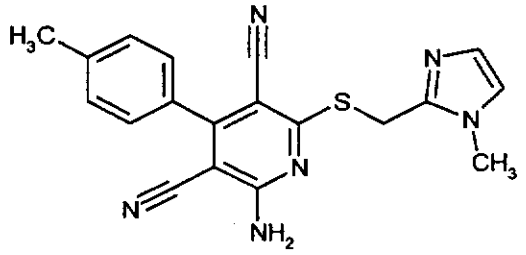
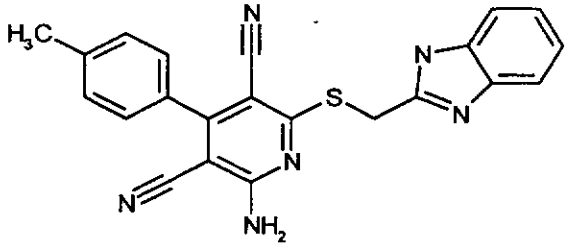
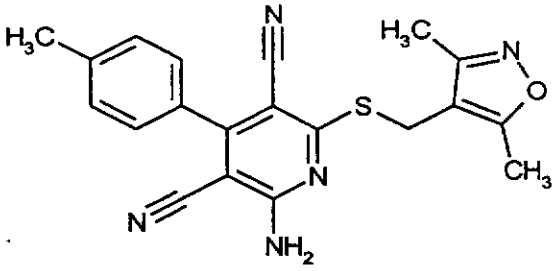
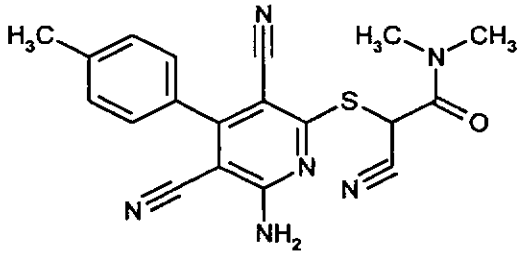
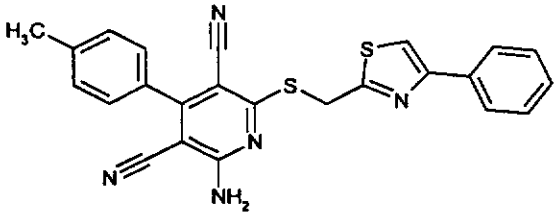
Ex. No.	Product	Molecular weight
B295		409
B296		448
B297		495
B298		456
B299		443

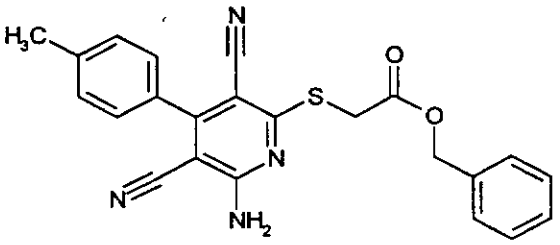
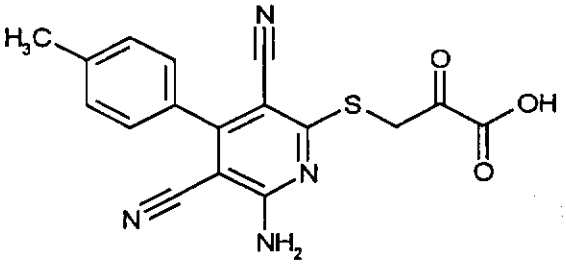
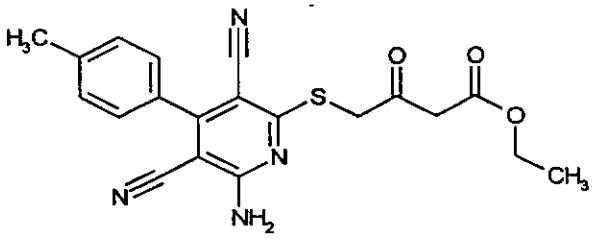
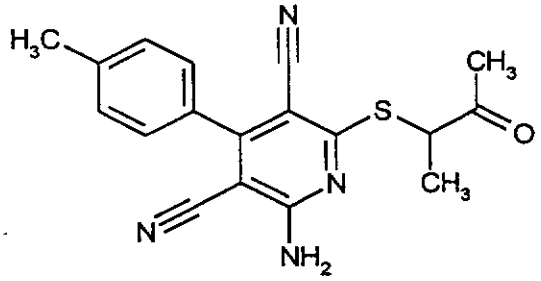
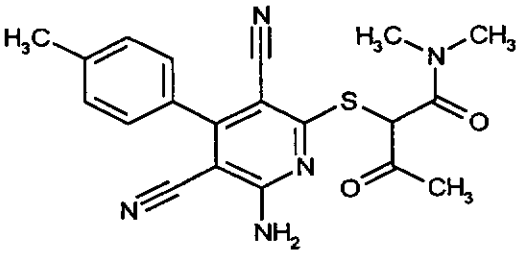
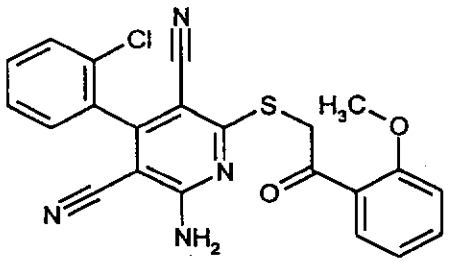
Ex. No.	Product	Molecular weight
B300		477
B301		542
B302		466
B303		452
B304		352

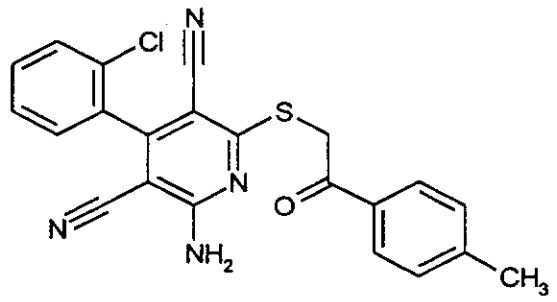
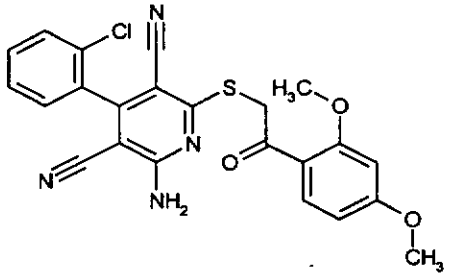
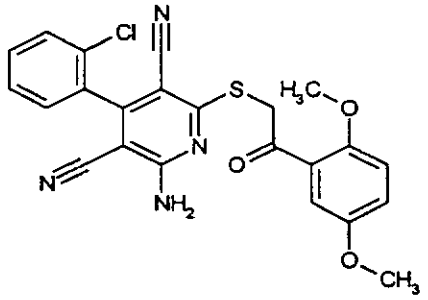
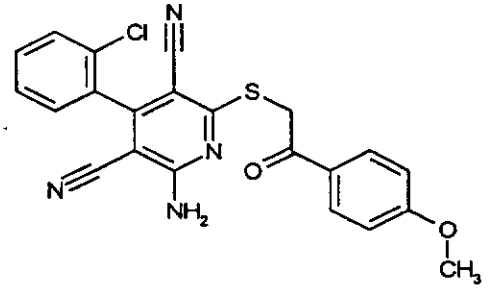
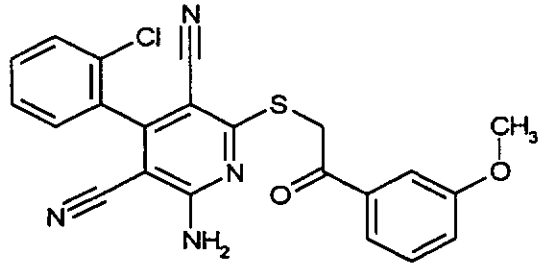
Ex. No.	Product	Molecular weight
B305		414
B306		413
B307		453
B308		431
B309		495

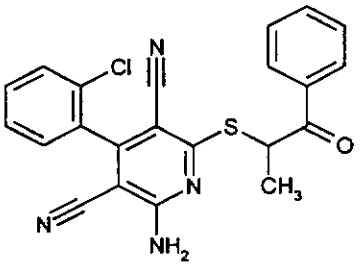
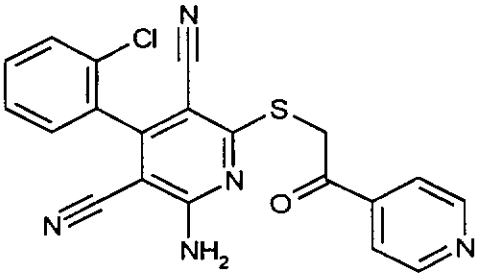
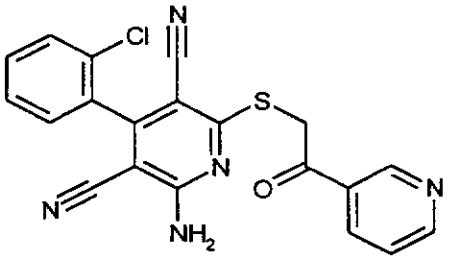
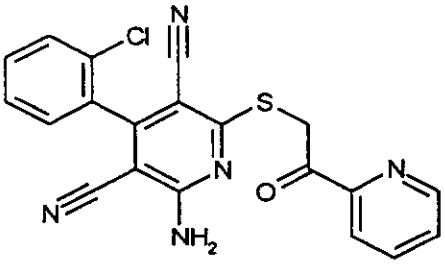
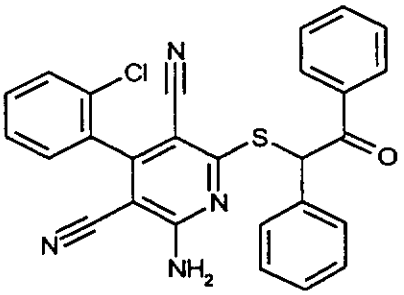
Ex. No.	Product	Molecular weight
B310		398
B311		348
B312		611
B313		530
B314		471

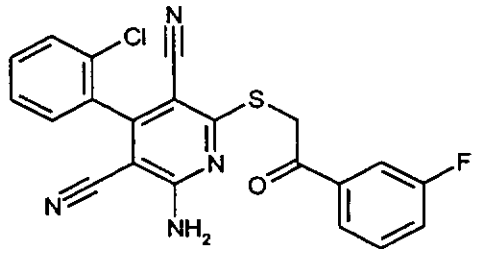
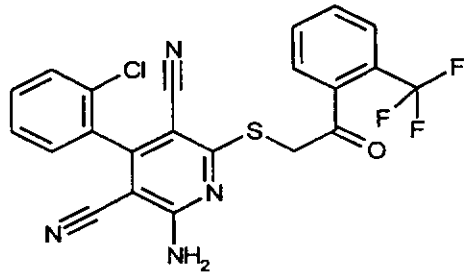
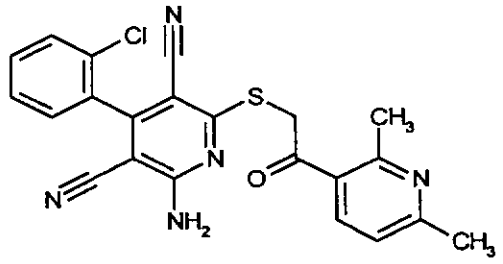
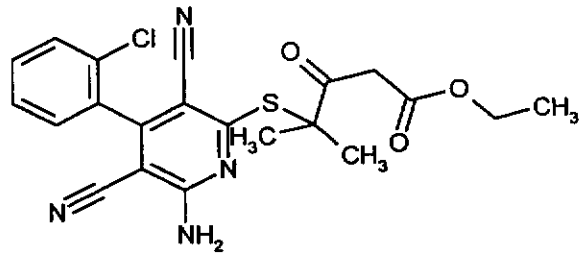
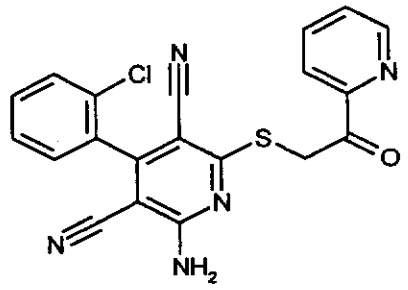
Ex. No.	Product	Molecular weight
B315		525
B316		459
B317		407
B318		401
B319		413

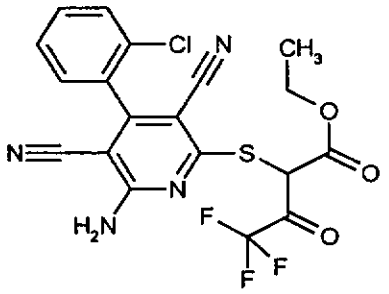
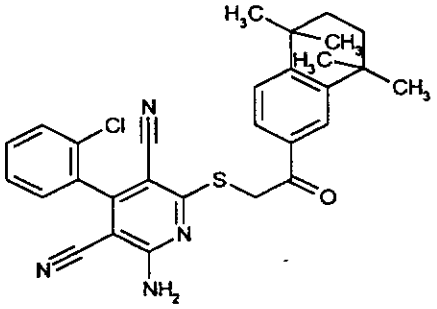
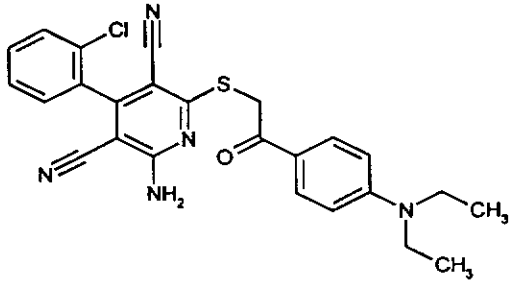
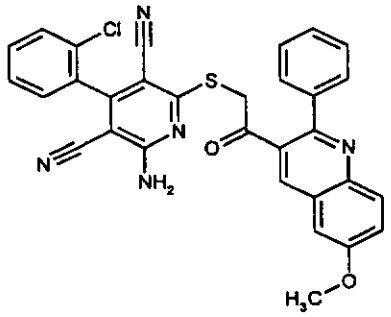
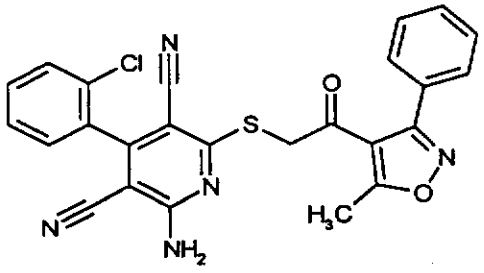
Ex. No.	Product	Molecular weight
B320		470
B321		360
B322		396
B323		375
B324		376
B325		440

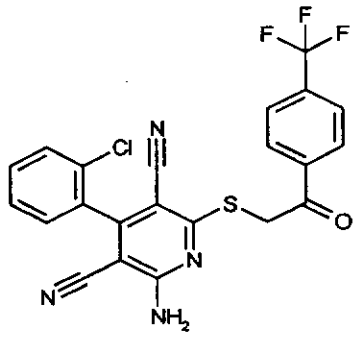
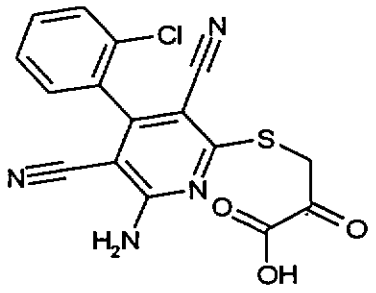
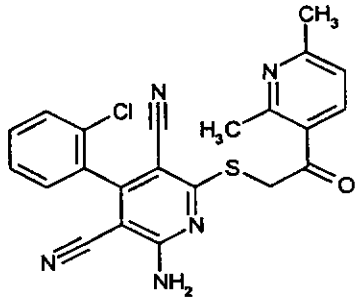
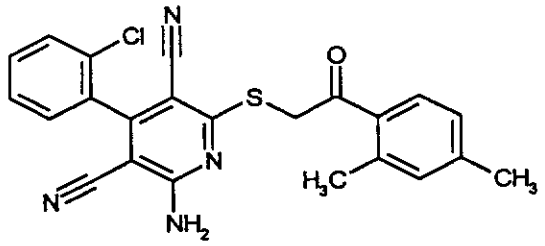
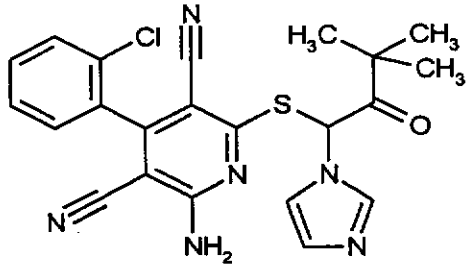
Ex. No.	Product	Molecular weight
B326		414
B327		352
B328		394
B329		336
B330		393
B331		435

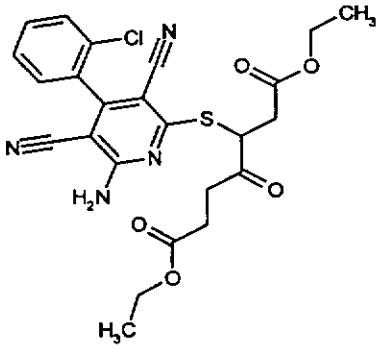
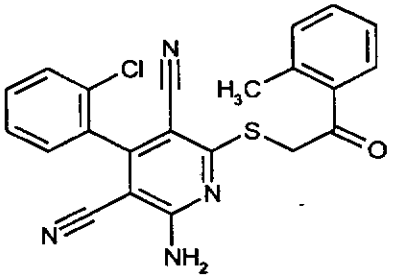
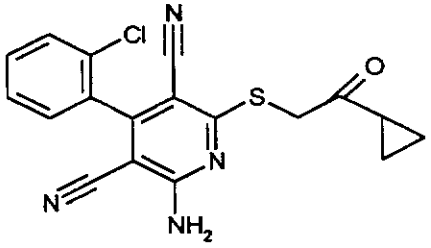
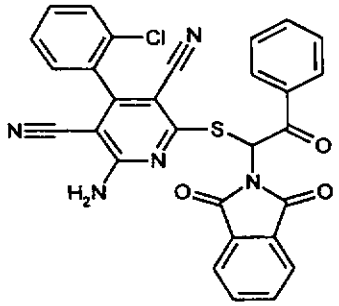
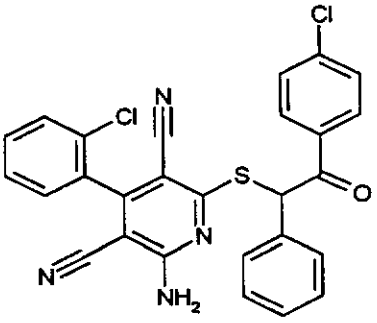
Ex. No.	Product	Molecular weight
B332		419
B333		465
B334		465
B335		435
B336		435

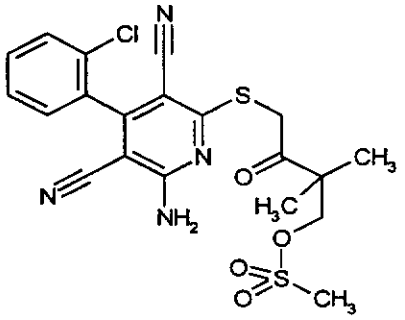
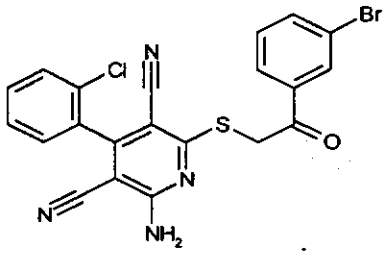
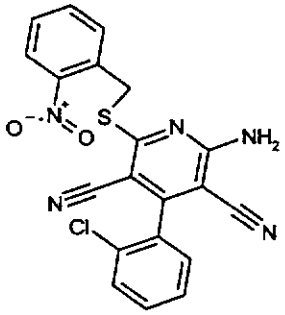
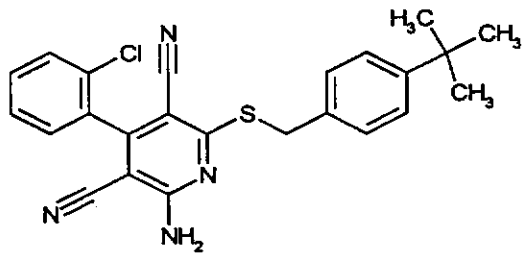
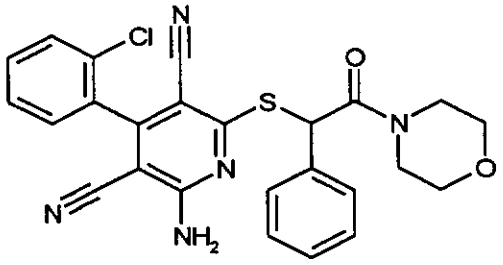
Ex. No.	Product	Molecular weight
B337		419
B338		406
B339		406
B340		406
B341		481

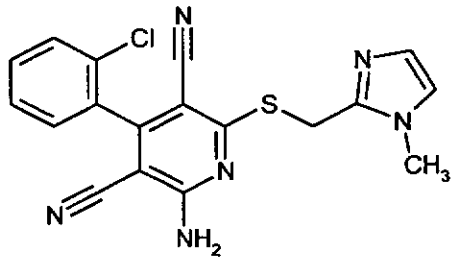
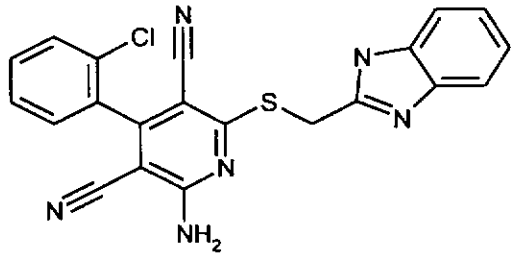
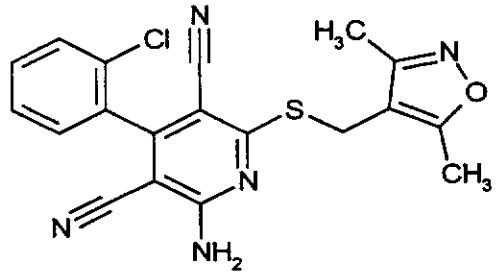
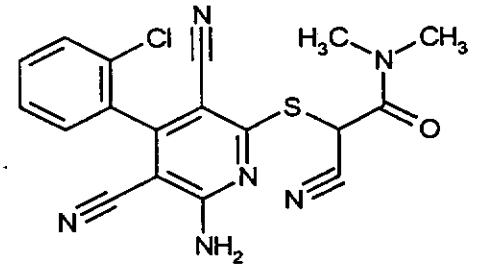
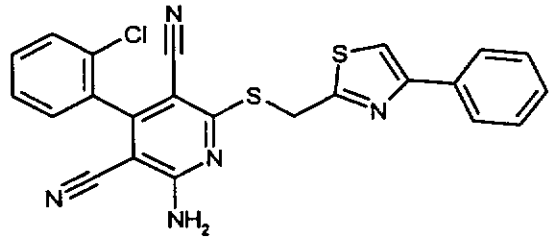
Ex. No.	Product	Molecular weight
B342		423
B343		473
B344		434
B345		443
B346		406

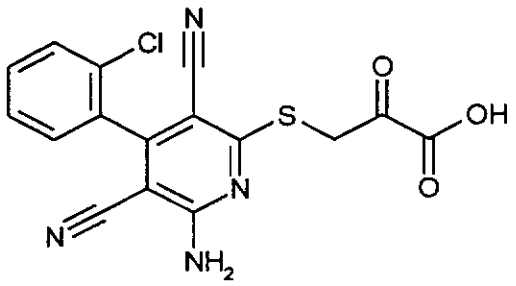
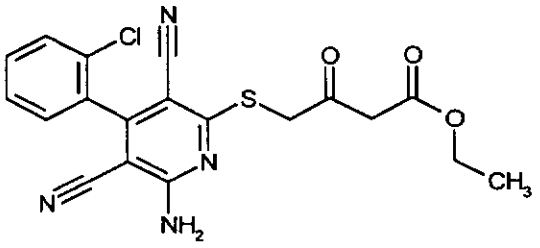
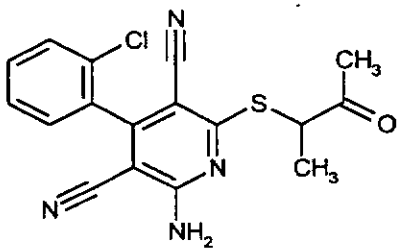
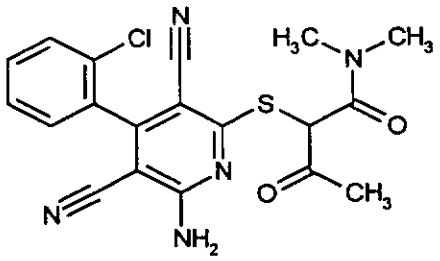
Ex. No.	Product	Molecular weight
B347		469
B348		515
B349		476
B350		562
B351		486

Ex. No.	Product	Molecular weight
B352		473
B353		373
B354		434
B355		433
B356		451

Ex. No.	Product	Molecular weight
B357		515
B358		419
B359		369
B360		550
B361		515

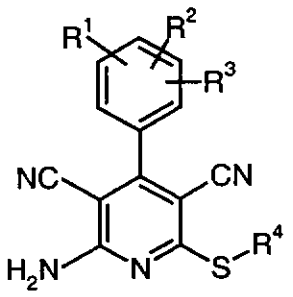
Ex. No.	Product	Molecular weight
B362		479
B363		484
B364		422
B365		433
B366		490

Ex. No.	Product	Molecular weight
B367		381
B368		417
B369		396
B370		397
B371		460

Ex. No.	Product	Molecular weight
B372		373
B373		415
B374		357
B375		414

Patent Claims

1. A compound of the general formula (I)



(I),

characterized in that :

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:

hydrogen;

hydroxyl;

optionally substituted (C_1-C_8)-alkyl;

optionally substituted (C_6-C_{10})-aryl;

optionally substituted (C_1-C_8)-alkoxy;

-O-$(CH_2)_n$-CH=CH_2 where n = 0, 1 or 2;

halogen;

nitro;

cyano;

-C(O)-R^5;

-C(O)-NR^6R^7;

-NR^6R^7;

-NR^6-C(O)-R^8;

-O-C(O)-R^8;

-SO_2-NR^6R^7; and

-NR^6-SO_2R^8,

where:

R^5 denotes:

hydrogen;

hydroxyl;

optionally substituted (C_1-C_8)-alkyl;

optionally substituted (C_3-C_7)-cycloalkyl;

optionally substituted (C_1-C_8)-alkoxy;

optionally substituted (C_6-C_{10})-aryl;

optionally substituted (C_6-C_{10})-aryloxy; or

-O-$(CH_2)_n$-[(C_6-C_{10})-aryl] where n = 1, 2 or 3,

where the (C_6-C_{10})-aryl group may be fused via two adjacent ring atoms to optionally substituted (C_4-C_7)-cycloalkyl,

or

R^5 represents a 5- to 7-membered saturated or unsaturated heterocycle which for its part may be mono- or polysubstituted by

an oxo group (=O);

halogen;

optionally substituted (C_1-C_8)-alkyl;

nitro;

cyano;

hydroxyl;

optionally substituted (C_6-C_{10})-aryl; or

by (C_1-C_8)-alkoxy,

or

R^5 represents optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted $(C_6$-$C_{10})$-aryl or optionally substituted $(C_4$-$C_7)$-cycloalkyl,

and

R^6 and R^7 are identical or different and represent
hydrogen;
optionally substituted $(C_1$-$C_8)$-alkyl;
optionally substituted $(C_6$-$C_{10})$-aryl; or
represent optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S

or

R^6 and R^7 together with the nitrogen atom to which they are optionally attached form a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of
an oxo group (=O);
halogen;
$(C_1$-$C_8)$-alkyl;
nitro;
cyano;

hydroxyl;
$(C_6$-$C_{10})$-aryl; or
$(C_1$-$C_8)$-alkoxy,

and

R^8 represents hydroxyl;
NR^6R^7 where R^6 and R^7 are as defined above;
optionally substituted $(C_1$-$C_8)$-alkyl;
$(C_1$-$C_8)$-alkoxy;
optionally substituted $(C_6$-$C_{10})$-aryl;
$(C_6$-$C_{10})$-aryloxy; or
$-O-(CH_2)_n-[(C_6$-$C_{10})$-aryl] where n = 1, 2 or 3,

and

R^4 represents straight-chain or branched $(C_1$-$C_8)$-alkyl or $(C_2$-$C_8)$-alkenyl which are optionally mono- or polysubstituted by
hydroxyl;
halogen;
cyano;
$-C(O)-R^5$ where R^5 is as defined above;
$-C(O)-NR^6R^7$ where R^6 and R^7 are as defined above;
$-NR^6R^7$ where R^6 and R^7 are as defined above;
$-NR^6-C(O)-R^8$ where R^6 and R^8 are as defined above;
$-SO_2-NR^6R^7$ where R^6 and R^7 are as defined above;
$-NR^6-SO_2-R^8$ where R^6 and R^8 are as defined above;
$-C(O)-(CH_2)_n-C(O)-R^8$ where n = 0 to 2 and R^8 is as defined above;
$(C_1$-$C_8)$-alkoxy;
optionally substituted $(C_6$-$C_{10})$-aryloxy;
optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S;

optionally substituted (C_6-C_{10})-aryl; or

by a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); halogen; (C_1-C_8)-alkyl; nitro; cyano; hydroxyl; (C_6-C_{10})-aryl; or by (C_1-C_8)-alkoxy,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted (C_6-C_{10})-aryl,

or

R^4 represents a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S, which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); halogen; (C_1-C_8)-alkyl; nitro; cyano; hydroxyl; (C_6-C_{10})-aryl; or by (C_1-C_8)-alkoxy, and

which may optionally be fused via two adjacent ring atoms to optionally substituted (C_6-C_{10})-aryl or optionally substituted (C_4-C_7)-cycloalkyl,

and their tautomers and their respective salts, hydrates and alkoxides,

except for the following compounds of the general formula (I), in which the radicals R^1, R^2, R^3 and R^4 are as defined below:

- $R^1 = R^2 = H$; R^3 = para-OH; $R^4 = -CH_2-Z$ where Z = CN, C(O)-OC_2H_5, 4-Br-C_6H_4-CO, 4-n-butyl-C_6H_4-CO, H, C_6H_5, C(O)-O-CH_2-C_6H_5, C(O)-OCH_3, C(O)-OH, 2-oxo-benzo-pyranyl-3-carbonyl, 4-Cl-

C_6H_4-CO, 3-Br-C_6H_4-CO, 4-C_6H_5-C_6H_4-CO, 4-CH_3-C_6H_4-CO, 3,4-Cl_2-C_6H_3-CO, C(O)-NH_2;

- $R^1 = R^2 = H$; R^3 = meta-OH; R^4 = -CH_2-Z where Z = 4-Br-C_6H_4-NH-CO, 2-oxo-benzo-pyranyl-3-carbonyl, 4-Cl-C_6H_4-CO;
- $R^1 = R^2 = H$; R^3 = para-O-C(O)-CH_3; R^4 = -CH_2-Z where Z = 4-CH_3-C_6H_4-CO, H, 2-oxo-benzopyranyl-3-carbonyl, $(CH_2)_3$-CH_3, 4-C_6H_5-C_6H_4, $(CH_2)_4$-CH_3, CH_3, 2-CH_3-C_6H_4;
- $R^1 = R^2 = R^3 = H$; R^4 = -CH_2-Z where Z = CH_3, CN, 2-naphthyl, 4-Br-C_6H_4-CO; C(O)-OCH_3, C(O)-OCH_2-C_6H_5, H, C(O)-C_6H_5, 4-Cl-C_6-H_4-CO;
- $R^1 = R^2 = H$; R^3 = para-butoxy; R^4 = -CH_2-Z where Z = 4-Cl-C_6H_5, C(O)-OCH_3, C(O)-C_6H_5, $CH=CH_2$, C(O)-NH_2, H, 4-Br-C_6H_4-CO, 4-Cl-C_6H_4-CO, C(O)-OC_2H_5, C(O)-O-CH_2-C_6H_5, 2-oxo-benzo-pyranyl-3-carbonyl, C(O)-NH-C_6H_5, CN;
- $R^1 = R^2 = H$; R^3 = para-bromo; R^4 = -CH_2-Z where Z = 4-Br-C_6H_4-CO, 4-Cl-C_6H_4-CO, C(O)-NH_2, C(O)-OCH_3, 4-Cl-C_6H_5, 4-Br-C_6H_4-NH-CO;
- $R^1 = R^2 = H$; R^3 = meta-fluoro; R^4 = -CH_2-Z where Z = 4-Br-C_6H_4-CO, C(O)-NH_2, C(O)-O-CH_2-C_6H_5, CN;
- $R^1 = R^2 = H$; R^3 = para-chloro; R^4 = -CH_2-Z where Z = 2-naphthyl, CH_3, 4-Cl-C_6H_4-CO, C_6H_5-CO;
- $R^1 = R^2 = H$; R^3 = para-OCH_3; R^4 = -CH_2-Z where Z = 2-naphthyl, CH_3;
- $R^1 = R^2 = H$; R^3 = meta-NO_2; R^4 = -CH_2-Z where Z = CH_3,
- $R^1 = R^2 = H$; R^3 = ortho-OCH_3; R^4 = -CH_2-Z where Z = 4-Cl-C_6H_4-CO;
- $R^1 = R^2 = H$; R^3 = ortho-chloro; R^4 = -CH_2-Z where Z = 4-Cl-C_6H_4-CO, C_6H_5-CO, $CH = CH_2$;
- $R^1 = R^2 = H$; R^3 = ortho-iodo; R^4 = -CH_2-Z where Z = C = CH_2.

2. The compound of the general formula (I) as claimed in claim 1, characterized in that:

R^1, R^2, R^3 are identical or different and independently of one another are

selected from the group of the following substituents:

hydrogen;

hydroxyl;

optionally substituted (C_1-C_6)-alkyl;

optionally substituted phenyl or naphthyl;
optionally substituted (C_1-C_6)-alkoxy;
-O-$(CH_2)_n$-CH=CH_2 where n = 1 or 2;
fluorine, chlorine, bromine;
nitro;
cyano;
-C(O)-R^5;
-C(O)-NR^6R^7;
-NR^6R^7;
-NR^6-C(O)-R^8;
-O-C(O)-R^8;
-SO_2-NR^6R^7; and
-NR^6-SO_2R^8,

where:

R^5 denotes:
hydrogen;
hydroxyl;
optionally substituted (C_1-C_6)-alkyl;
optionally substituted (C_3-C_7)-cycloalkyl;
optionally substituted (C_1-C_6)-alkoxy;
optionally substituted phenyl or naphthyl;
optionally substituted phenyloxy or naphthyloxy; or
-O-$(CH_2)_n$-phenyl where n = 1, 2 or 3,

where the phenyl or naphthyl group may be fused via two adjacent ring atoms to optionally substituted (C_4-C_7)-cycloalkyl,

or

R^5 represents a 5- to 7-membered saturated or unsaturated heterocycle which for its part may be mono- or polysubstituted by

an oxo group (=O);

fluorine, chlorine, bromine;

optionally substituted (C_1-C_6)-alkyl;

nitro;

cyano;

hydroxyl;

optionally substituted phenyl or naphthyl; or

by (C_1-C_6)-alkoxy,

or

R^5 represents optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted phenyl or naphthyl or optionally substituted (C_4-C_7)-cycloalkyl,

and

R^6 and R^7 are identical or different and represent

hydrogen;

optionally substituted (C_1-C_6)-alkyl;

optionally substituted phenyl or naphthyl; or

represent optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S

or

R^6 and R^7 together with the nitrogen atom to which they are optionally attached form a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of

an oxo group (=O);
fluorine, chlorine, bromine;
(C_1-C_6)-alkyl;
nitro;
cyano;
hydroxyl;
phenyl or naphthyl; or
(C_1-C_6)-alkoxy,

and

R^8 represents NR^6R^7 where R^6 and R^7 are as defined above;
optionally substituted (C_1-C_6)-alkyl;
(C_1-C_6)-alkoxy;
optionally substituted phenyl or naphthyl;
phenyloxy or naphthyloxy; or
$-O-(CH_2)_n$-phenyl where n = 1, 2 or 3,

and

R^4 represents straight-chain or branched (C_1-C_6)-alkyl or (C_2-C_6)-alkenyl which are optionally mono- or polysubstituted by
hydroxyl;

fluoro, chloro, bromine;

cyano;

-C(O)-R^5 where R^5 is as defined above;

-C(O)-NR^6R^7 where R^6 and R^7 are as defined above;

-NR^6R^7 where R^6 and R^7 are as defined above;

-NR^6-C(O)-R^8 where R^6 and R^8 are as defined above;

-SO_2-NR^6R^7 where R^6 and R^7 are as defined above;

-NR^6-SO_2-R^8 where R^6 and R^8 are as defined above;

-C(O)-$(CH_2)_n$-C(O)-R^8 where n = 0 to 2 and R^8 is as defined above;

$(C_1$-$C_6)$-alkoxy;

optionally substituted phenyloxy or naphthyloxy;

optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S;

optionally substituted phenyl or naphthyl; or

by a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S, which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); fluorine, chlorine, bromine; $(C_1$-$C_6)$-alkyl; nitro; cyano; hydroxyl; phenyl or naphthyl; or by $(C_1$-$C_6)$-alkoxy,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted phenyl or naphthyl,

or

R^4 represents a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S, which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo

group (=O); fluorine, chlorine, bromine; (C_1-C_6)-alkyl; nitro; cyano; hydroxyl; phenyl or naphthyl; or by (C_1-C_6)-alkoxy and
which may optionally be fused via two adjacent ring atoms to optionally substituted phenyl or naphthyl or optionally substituted (C_4-C_7)-cycloalkyl,

and their tautomers and their respective salts, hydrates and alkoxides,

except for the following compounds of the general formula (I), in which the radicals R^1, R^2, R^3 and R^4 are as defined below:

- $R^1 = R^2 = H$; R^3 = para-OH; R^4 = -CH_2-Z where Z = CN, C(O)-OC_2H_5, 4-Br-C_6H_4-CO, 4-n-butyl-C_6H_4-CO, H, C_6H_5, C(O)-O-CH_2-C_6H_5, C(O)-OCH_3, C(O)-OH, 2-oxo-benzo-pyranyl-3-carbonyl, 4-Cl-C_6H_4-CO, 3-Br-C_6H_4-CO, 4-C_6H_5-C_6H_4-CO, 4-CH_3-C_6H_4-CO, 3,4-Cl_2-C_6H_3-CO, C(O)-NH_2;
- $R^1 = R^2 = H$; R^3 = meta-OH; R^4 = -CH_2-Z where Z = 4-Br-C_6H_4-NH-CO, 2-oxo-benzo-pyranyl-3-carbonyl, 4-Cl-C_6H_4-CO;
- $R^1 = R^2 = H$; R^3 = para-O-C(O)-CH_3; R^4 = -CH_2-Z where Z = 4-CH_3-C_6H_4-CO, H, 2-oxo-benzopyranyl-3-carbonyl, $(CH_2)_3$-CH_3, 4-C_6H_5-C_6H_4, $(CH_2)_4$-CH_3, CH_3, 2-CH_3-C_6H_4;
- $R^1 = R^2 = R^3 = H$; R^4 = -CH_2-Z where Z = CH_3, CN, 2-napthyl, 4-Br-C_6H_4-CO, C(O)-OCH_3, C(O)-OCH_2-C_6H_5, H, C(O)-C_6H_5, 4-Cl-C_6H_4-CO;
- $R^1 = R^2 = H$; R^3 = para-butoxy; R^4 = -CH_2-Z where Z = 4-Cl-C_6H_5, C(O)-OCH_3, C(O)-C_6H_5, CH=CH_2, C(O)-NH_2, H, 4-Br-C_6H_4-CO, 4-Cl-C_6H_4-CO, C(O)-OC_2H_5, C(O)-O-CH_2-C_6H_5, 2-oxo-benzopyranyl-3-carbonyl, C(O)-NH-C_6H_5, CN;
- $R^1 = R^2 = H$; R^3 = para-bromo; R^4 = -CH_2-Z where Z = 4-Br-C_6H_4-CO, 4-Cl-C_6H_4-CO, C(O)-NH_2, C(O)-OCH_3, 4-Cl-C_6H_5, 4-Br-C_6H_4-NH-CO;

- $R^1 = R^2 = H$; R^3 = meta-fluoro; R^4 = $-CH_2-Z$ where Z = 4-Br-C_6H_4-CO, C(O)-NH_2, C(O)-O-CH_2-C_6H_5, CN;
- $R^1 = R^2 = H$; R^3 = para-chloro; R^4 = $-CH_2-Z$ where Z = 2-napthyl, CH_3, 4-Cl-C_6H_4-CO, C_6H_5-CO;
- $R^1 = R^2 = H$; R^3 = para-OCH_3; R^4 = $-CH_2-Z$ where Z = 2-naphthyl, CH_3;
- $R^1 = R^2 = H$; R^3 = meta-NO_2; R^4 = $-CH_2-Z$ where Z = CH_3.
- $R^1 = R^2 = H$; R^3 = ortho-OCH_3; R^4 = $-CH_2-Z$ where Z = 4-Cl-C_6H_4-CO;
- $R^1 = R^2 = H$; R^3 = ortho-chloro; R^4 = $-CH_2-Z$ where Z = 4-Cl-C_6H_4-CO, C_6H_5-CO, $CH=CH_2$;

3. The compound of the general formula (I) as claimed in claim 1 or 2, characterized in that:

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:

hydrogen;

hydroxyl;

optionally substituted (C_1-C_4)-alkyl;

optionally substituted phenyl;

optionally substituted (C_1-C_4)-alkoxy;

$-O-(CH_2)_n-CH=CH_2$ where n = 1;

fluorine, chlorine;

nitro;

cyano;

$-C(O)-R^5$;

$-C(O)-NR^6R^7$;

$-NR^6R^7$;

$-NR^6-C(O)-R^8$;

$-O-C(O)-R^8$;

$-SO_2-NR^6R^7$; and

$-NR^6-SO_2R^8$,

where:

R^5 denotes:

hydrogen;

hydroxyl;

optionally substituted (C_1-C_4)-alkyl;

optionally substituted (C_3-C_7)-cycloalkyl;

optionally substituted (C_1-C_4)-alkoxy;

optionally substituted phenyl;

optionally substituted phenyloxy; or

-O-$(CH_2)_n$-phenyl where n = 1,

where the phenyl group may be fused via two adjacent ring atoms to optionally substituted (C_5-C_6)-cycloalkyl,

or

R^5 represents a 5- to 7-membered saturated or unsaturated heterocycle which for its part may be mono- or polysubstituted by

an oxo group (=O);

fluorine, chlorine;

optionally substituted (C_1-C_4)-alkyl;

nitro;

cyano;

hydroxyl;

optionally substituted phenyl; or

by (C_1-C_4)-alkoxy,

or

R^5 represents optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S, selected from the group consisting of furanyl, pyrrolyl,

thienyl, thiazolyl, oxazolyl, imidazolyl, triazolyl, pyridyl, pyrimidyl and pyridazinyl,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted phenyl or optionally substituted (C_5-C_6)-cycloalkyl,

and

R^6 and R^7 are identical or different and represent

hydrogen;

optionally substituted (C_1-C_4)-alkyl;

optionally substituted phenyl; or

represent optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S selected from the group consisting of furanyl, pyrrolyl, thienyl, thiazolyl, oxazolyl, imidazolyl, triazolyl, pyridyl, pyrimidyl and pyridazinyl,

or

R^6 and R^7 together with the nitrogen atom to which they are optionally attached form a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of

an oxo group (=O);

fluorine, chlorine;

(C_1-C_4)-alkyl;

nitro;

cyano;

hydroxyl;
phenyl; or
(C_1-C_4)-alkoxy,

and

R^8 represents NR^6R^7 where R^6 and R^7 are as defined above;
optionally substituted (C_1-C_4)-alkyl;
(C_1-C_4)-alkoxy;
optionally substituted phenyl;
phenyloxy; or
$-O-(CH_2)_n$-phenyl where n = 1,

and

R^4 represents straight-chain or branched (C_1-C_4)-alkyl or (C_2-C_4)-alkenyl which are optionally mono- or polysubstituted by
hydroxyl;
fluorine, chlorine;
cyano;
$-C(O)-R^5$ where R^5 is as defined above;
$-C(O)-NR^6R^7$ where R^6 and R^7 are as defined above;
$-NR^6R^7$ where R^6 and R^7 are as defined above;
$-NR^6-C(O)-R^8$ where R^6 and R^8 are as defined above;
$-SO_2-NR^6R^7$ where R^6 and R^7 are as defined above;
$-NR^6-SO_2-R^8$ where R^6 and R^8 are as defined above;
$-C(O)-(CH_2)_n-C(O)-R^8$ where n = 0 to 2 and R^8 is as defined above;
(C_1-C_4)-alkoxy;
optionally substituted phenyloxy;
optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S selected from

the group consisting of furanyl, pyrrolyl, thienyl, thiazolyl, oxazolyl, imidazolyl, triazolyl, pyridyl, pyrimidyl and pyridazinyl;
optionally substituted phenyl; or
by a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); fluorine, chlorine; (C_1-C_4)-alkyl; nitro; cyano; hydroxyl; phenyl; or by (C_1-C_4)-alkoxy,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent rings atoms to optionally substituted phenyl,

or

R^4 represents a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S,
which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); fluorine, chlorine; (C_1-C_4)-alkyl; nitro; cyano; hydroxyl; phenyl; or by (C_1-C_4)-alkoxy and
which may optionally be fused via two adjacent ring atoms to optionally substituted phenyl or optionally substituted (C_5-C_6)-cycloalkyl,

and their tautomers and their respective salts, hydrates and alkoxides,

except for the following compounds of the general formula (I), in which the radicals R^1, R^2, R^3 and R^4 are as defined below:

- $R^1 = R^2 = H$; R^3 = para-OH; $R^4 = -CH_2-Z$ where Z = CN, C(O)-OC_2H_5, 4-Br-C_6H_4-CO, 4-n-butyl-C_6H_4-CO, H, C_6H_5, C(O)-O-CH_2-

C_6H_5, C(O)-OCH_3, C(O)-OH, 2-oxo-benzo-pyranyl-3-carbonyl, 4-Cl-C_6H_4-CO, 3-Br-C_6H_4-CO, 4-C_6H_5-C_6H_4-CO, 4-CH_3-C_6H_4-CO, 3,4-Cl_2-C_6H_3-CO, C(O)-NH_2

- $R^1 = R^2 = H$; R^3 = meta-OH; R^4 = -CH_2-Z where Z = 4-Br-C_6H_4-NH-CO, 2-oxo-benzo-pyranyl-3-carbonyl, 4-Cl-C_6H_4-CO;
- $R^1 = R^2 = H$; R^3 = para-O-C(O)-CH_3; R^4 = -CH_2-Z where Z = 4-CH_3-C_6H_4-CO,H,2-oxo-benzopyranyl-3-carbonyl, 4-C_6H_5-C_6H_4, CH_3, 2-CH_3-C_6H_4;
- $R^1 = R^2 = R^3 = H$; R^4 = -CH_2-Z where Z = CH_3, CN, 4-Br-C_6H_4-CO, C(O)-OCH_3, C(O)-OCH_2-C_6H_5, H, C(O)-C_6H_5, 4-Cl-C_6H_4-CO;
- $R^1 = R^2 = H$; R^3 = para-butoxy; R^4 = -CH_2-Z where Z = 4-Cl-C_6H_5, C(O)-OCH_3, C(O)-C_6H_5, CH=CH_2, C(O)-NH_2, H, 4-Br-C_6H_4-CO, 4-Cl-C_6H_4-CO, C(O)-OC_2H_5, C(O)-O-CH_2-C_6H_5, 2-oxo-benzopyranyl-3-carbonyl, C(O)-NH-C_6H_5, CN;
- $R^1 = R^2 = H$; R^3 = meta-fluoro; R^4 = -CH_2-Z where Z = 4-Br-C_6H_4-CO, C(O)-NH_2, C(O)-O-CH_2-C_6H_5, CN;
- $R^1 = R^2 = H$; R^3 = para-chloro; R^4 = -CH_2-Z where Z = CH_3, 4-Cl-C_6H_4-CO, C_6H_5-CO;
- $R^1 = R^2 = H$; R^3 = para-OCH_3; R^4 = -CH_2-Z where Z = CH_3;
- $R^1 = R^2 = H$; R^3 = meta-NO_2; R^4 = -CH_2-Z where Z = CH_3;
- $R^1 = R^2 = H$; R^3 = ortho-OCH_3; R^4 = -CH_2-Z where Z = 4-Cl-C_6H_4-CO;
- $R^1 = R^2 = H$; R^3 = ortho-chloro; R^4 = -CH_2-Z where Z = 4-Cl-C_6H_4-CO, C_6H_5-CO, CH=CH_2.

4. The compound of the general formula (I) as claimed in any of claims 1 to 3, characterized in that

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:

hydrogen;

hydroxyl;

methyl;

trifluoromethyl;

methoxy;

radicals of the formulae $-O-CH_2-CH_2-OH$, $-O-CH_2-COOH$ or $-O-CH_2-CH=CH_2$;

fluorine, chlorine or bromine;

nitro;

cyano;

-C(O)OH or $-C(O)OCH_3$;

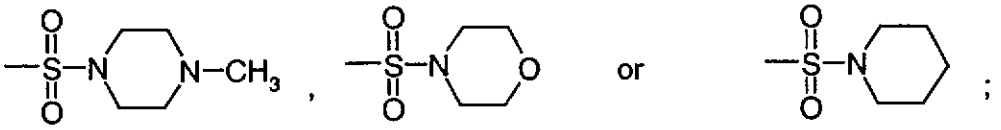
$-C(O)NH_2$;

$-NH_2$;

$-NH-C(O)-CH_3$;

$-O-C(O)-CH_3$ or $-O-C(O)-C_2H_5$;

radicals of the formulae



and

$-NH-SO_2CH_3$ or $-NH-SO_2C_6H_5$,

and

R^4 represents straight-chain or branched (C_1-C_4)-alkyl which is optionally mono- or polysubstituted by

hydroxyl;

amino;

$-C(O)-OCH_3$;

$-C(O)-NH_2$, $-C(O)-HNCH_3$, $-C(O)-HNC_2H_5$, or $-C(O)-HNC_6H_5$;

$-NHC(O)NH_2$, $-NHC(O)NHCH_3$, $-NHC(O)NHC_2H_5$, $-NHC(O)OCH_3$ or $-NHC(O)OC_2H_5$;

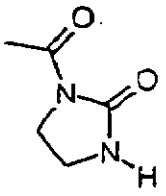
$-SO_2-NH_2$;

$-NH-SO_2-CH_3$ or $-NH-SO_2-C_2H_5$;

$-OCH_3$;

phenyl, which may be substituted by nitro, cyano, fluorine, methoxy, difluoromethoxy, methoxycarbonyl or p-tolylsulfonylmethyl;

pyridyl, furyl, imidazolyl, benzimidazolyl or thiazolyl, which may in each case be mono- or disubstituted by identical or different substituents from the group consisting of methyl, nitro and chlorine;
oxadiazolyl which may be substituted by phenyl or methoxyphenyl;
or
a radical of the formula



or

R^4 represents allyl or 3,3-dimethylallyl,

and their tautomers and their respective salts, hydrates and alkoxides,

except for the following compounds of the general formula (I), in which the radicals R^1, R^2, R^3 and R^4 are as defined below:

- $R^1 = R^2 = H$; R^3 = para-OH; $R^4 = -CH_2-Z$ where Z = H, C_6H_5, C(O)-OCH_3, C(O)-NH_2;
- $R^1 = R^2 = H$; R^3 = para-O-C(O)-CH_3; $R^4 = -CH_2-Z$ where Z = H, CH_3;
- $R^1 = R^2 = R^3 = H$; $R^4 = -CH_2-Z$ where Z = CH_3, C(O)-OCH_3;
- $R^1 = R^2 = H$; R^3 = meta-fluoro; $R^4 = -CH_2-Z$ where Z = C(O)-NH_2;
- $R^1 = R^2 = H$; R^3 = para-chloro; $R^4 = -CH_2-Z$ where Z = CH_3;
- $R^1 = R^2 = H$; R^3 = para-OCH_3; $R^4 = -CH_2-Z$ where Z = CH_3;
- $R^1 = R^2 = H$; R^3 = meta-NO_2; $R^4 = -CH_2-Z$ where Z = CH_3.

5. The compound of the general formula (I) as claimed in any of claims 1 to 4, characterized in that,

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:

hydrogen;

hydroxyl;

methyl;

methoxy;

radicals of the formulae $-O-CH_2-CH_2-OH$, $-O-CH_2-COOH$ or $-O-CH_2-CH=CH_2$;

fluorine or chlorine;

nitro;

cyano;

$-C(O)OH$ or $-C(O)OCH_3$;

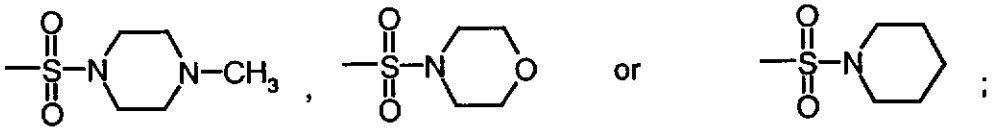
$-C(O)NH_2$;

$-NH_2$;

$-NH-C(O)CH_3$;

$-O-C(O)-CH_3$ or $-O-C(O)-C_2H_5$;

radicals of the formulae



;

and

$-NH-SO_2CH_3$ or $-NH-SO_2C_6H_5$,

and

R^4 represents straight-chain or branched (C_1-C_4)-alkyl which is optionally mono- or polysubstituted by

hydroxyl;

amino;

$-C(O)-OCH_3$;

$-C(O)-NH_2$, $-C(O)-HNCH_3$, $-C(O)-HNC_2H_5$, or $-C(O)-HNC_6H_5$;

$-NHC(O)NH_2$, $-NHC(O)NHCH_3$, $-NHC(O)NHC_2H_5$, $-NHC(O)OCH_3$ or $-NHC(O)OC_2H_5$;

$-SO_2-NH_2$;

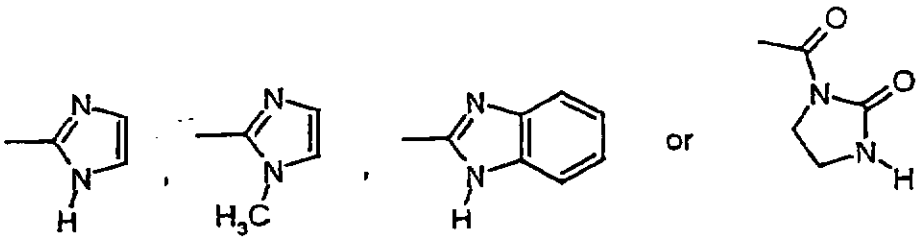
$-NH-SO_2-CH_3$ or $-NH-SO_2-C_2H_5$;

$-OCH_3$;

phenyl;

ortho-nitrophenyl; or

a radical of the formula



or

R^4 represents allyl,

and their tautomers and their respective salts, hydrates and alkoxides,

except for the following compounds of the general formula (I), in which the radicals R^1, R^2, R^3 and R^4 are as defined below:

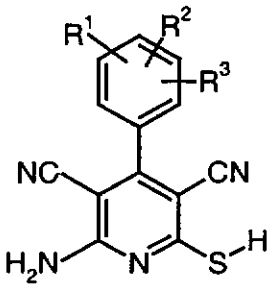
- $R^1 = R^2 = H$; R^3 = para-OH; $R^4 = -CH_2-Z$ where Z = H, C_6H_5, C(O)-OCH_3, $C(O)-NH_2$;
- $R^1 = R^2 = H$; R^3 = para-O-C(O)-CH_3; $R^4 = -CH_2-Z$ where Z = H, CH_3;
- $R^1 = R^2 = H$; $R^3 = H$; $R^4 = -CH_2-Z$ where Z = CH_3, C(O)-OCH_3;
- $R^1 = R^2 = H$; R^3 = meta-fluoro; $R^4 = -CH_2-Z$ where Z = $C(O)-NH_2$;
- $R^1 = R^2 = H$; R^3 = para-chloro; $R^4 = -CH_2-Z$ where Z = CH_3;
- $R^1 = R^2 = H$; R^3 = para-OCH_3; $R^4 = -CH_2-Z$ where Z = CH_3;

- $R^1 = R^2 = H$; R^3 = meta-NO_2; $R^4 = -CH_2-Z$ where Z = CH_3.

6. A process for preparing the compounds of the general formula (I) as claimed in any of claims 1 to 5,

characterized in that:

compounds of the general formula (II)



(II),

in which the radicals R^1, R^2 and R^3 are as defined above,

are reacted with compounds of the general formula (III)

$$R^4\text{-}X \quad \text{(III)},$$

in which R^4 is as defined above

and

X represents a nucleofugic group (preferably halogen, in particular chlorine, bromine or iodine, or mesylate, tosylate, triflate or 1-imidazolyl),

in inert solvents, if appropriate in the presence of a base.

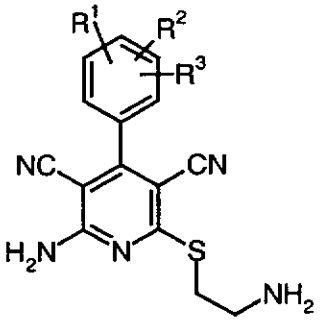
7. The process for preparing the compounds of the general formula (I) as claimed in any of claims 1 to 5 in the case that in the general formula (I) the radical R^4 has the meaning of

alkyl, substituted by the radicals $-NR^6-C(O)-R^8$, $-NR^6-C(O)-NR^6R^7$, $-NR^6-SO_2-R^8$

where the radicals R^6, R^7 and R^8 are as defined above,

characterized in that:

initially the compounds of the above general formula (II) are reacted with 2-bromoethylamine to give the compounds of the general formula (IV)



(IV)

which are then reacted with compounds of the general formula

$$R^9\text{-}Y \quad (V),$$

in which

R^9 has the meaning $-C(O)-R^8$, $-C(O)-O-R^8$, $-C(O)-NR^6R^7$, $-SO_2-R^8$ where R^8 is as defined above

and

Y represents a nucleofugic group, preferably halogen, in particular chlorine, bromine or iodine, or mesylate, tosylate, triflate or 1-imidazolyl,

or else

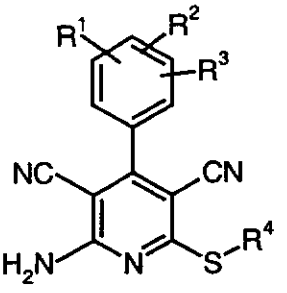
R^9 has the meaning R^6

and

Y represents the group O=C=N-,

in inert solvents, if appropriate in the presence of a base.

8. A compound of the general formula (I)



(I),

characterized in that:

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:
hydrogen;
hydroxyl;
optionally substituted (C_1-C_8)-alkyl;
optionally substituted (C_6-C_{10})-aryl;
optionally substituted (C_1-C_8)-alkoxy;
-O-$(CH_2)_n$-CH=CH_2 where n = 0, 1 or 2;

halogen;
nitro;
cyano;
$-C(O)-R^5$;
$-C(O)-NR^6R^7$;
$-NR^6R^7$;
$-NR^6-C(O)-R^8$;
$-O-C(O)-R^8$;
$-SO_2-NR^6R^7$; and
$-NR^6-SO_2R^8$,

where:

R^5 denotes:
hydrogen;
hydroxyl;
optionally substituted (C_1-C_8)-alkyl;
optionally substituted (C_3-C_7)-cycloalkyl;
optionally substituted (C_1-C_8)-alkoxy;
optionally substituted (C_6-C_{10})-aryl;
optionally substituted (C_6-C_{10})-aryloxy; or
$-O-(CH_2)_n-[(C_6-C_{10})$-aryl] where n = 1, 2 or 3,

where the (C_6-C_{10})-aryl group may be fused via two adjacent ring atoms to optionally substituted (C_4-C_7)-cycloalkyl,

or

R^5 represents a 5- to 7-membered saturated or unsaturated heterocycle which for its part may be mono- or polysubstituted by
an oxo group (=O);

halogen;
optionally substituted (C_1-C_8)-alkyl;
nitro;
cyano;
hydroxyl;
optionally substituted (C_6-C_{10})-aryl; or
by (C_1-C_8)-alkoxy,

or

R^5 represents optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted (C_6-C_{10})-aryl or optionally substituted (C_4-C_7)-cycloalkyl,

and

R^6 and R^7 are identical or different and represent
hydrogen;
optionally substituted (C_1-C_8)-alkyl;
optionally substituted (C_6-C_{10})-aryl; or
represent optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S

or

R^6 and R^7 together with the nitrogen atom to which they are optionally attached form a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of

an oxo group (=O);

halogen;

$(C_1$-$C_8)$-alkyl;

nitro;

cyano;

hydroxyl;

$(C_6$-$C_{10})$-aryl; or

$(C_1$-$C_8)$-alkoxy,

and

R^8 represents hydroxyl;

NR^6R^7 where R^6 and R^7 are as defined above;

optionally substituted $(C_1$-$C_8)$-alkyl;

$(C_1$-$C_8)$-alkoxy;

optionally substituted $(C_6$-$C_{10})$-aryl;

$(C_6$-$C_{10})$-aryloxy; or

$-O-(CH_2)_n-[(C_6$-$C_{10})$-aryl] where n = 1, 2 or 3,

and

R^4 represents straight-chain or branched $(C_1$-$C_8)$-alkyl or $(C_2$-$C_8)$-alkenyl which are optionally mono- or polysubstituted by

hydroxyl;

halogen;

cyano;

-C(O)-R^5 where R^5 is as defined above;
-C(O)-NR^6R^7 where R^6 and R^7 are as defined above;
-NR^6R^7 where R^6 and R^7 are as defined above;
-NR^6-C(O)-R^8 where R^6 and R^8 are as defined above;
-SO_2-NR^6R^7 where R^6 and R^7 are as defined above;
-NR^6-SO_2-R^8 where R^6 and R^8 are as defined above;
-C(O)-$(CH_2)_n$-C(O)-R^8 where n = 0 to 2 and R^8 is as defined above;
(C_1-C_8)-alkoxy;
optionally substituted (C_6-C_{10})-aryloxy;
optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S;
optionally substituted (C_6-C_{10})-aryl; or
by a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); halogen; (C_1-C_8)-alkyl; nitro; cyano; hydroxyl; (C_6-C_{10})-aryl; or by (C_1-C_8)-alkoxy,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted (C_6-C_{10})-aryl,

or

R^4 represents a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S, which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); halogen; (C_1-C_8)-alkyl; nitro; cyano; hydroxyl; (C_6-C_{10})-aryl; or by (C_1-C_8)-alkoxy, and

which may optionally be fused via two adjacent ring atoms to optionally substituted (C_6-C_{10})-aryl or optionally substituted (C_4-C_7)-cycloalkyl,

and their tautomers and their respective salts, hydrates and alkoxides,

for the prophylaxis and/or treatment of disorders.

9. The compound of the general formula (I) as claimed in claim 8,

characterized in that:

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:
hydrogen;
hydroxyl;
optionally substituted (C_1-C_6)-alkyl;
optionally substituted phenyl or naphthyl;
optionally substituted (C_1-C_6)-alkoxy;
-O-$(CH_2)_n$-$CH=CH_2$ where n = 1 or 2;
fluorine, chlorine, bromine;
nitro;
cyano;
-C(O)-R^5;
-C(O)-NR^6R^7;
-NR^6R^7;
-NR^6-C(O)-R^8;
-O-C(O)-R^8;
-SO_2-NR^6R^7; and
-NR^6-SO_2R^8,

where:

R^5 denotes:

hydrogen;

hydroxyl;

optionally substituted (C_1-C_6)-alkyl;

optionally substituted (C_3-C_7)-cycloalkyl;

optionally substituted (C_1-C_6)-alkoxy;

optionally substituted phenyl or naphthyl;

optionally substituted phenyloxy or naphthyloxy; or

-O-$(CH_2)_n$-phenyl where n = 1, 2 or 3,

where the phenyl or naphthyl group may be fused via two adjacent ring atoms to optionally substituted (C_4-C_7)-cycloalkyl,

or

R^5 represents a 5- to 7-membered saturated or unsaturated heterocycle which for its part may be mono- or polysubstituted by

an oxo group (=O);

fluorine, chlorine, bromine;

optionally substituted (C_1-C_6)-alkyl;

nitro;

cyano;

hydroxyl;

optionally substituted phenyl or naphthyl; or

by (C_1-C_6)-alkoxy,

or

R^5 represents optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted phenyl or naphthyl or optionally substituted (C_4-C_7)-cycloalkyl,

and

R^6 and R^7 are identical or different and represent
hydrogen;
optionally substituted (C_1-C_6)-alkyl;
optionally substituted phenyl or naphthyl; or
represent optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S

or

R^6 and R^7 together with the nitrogen atom to which they are optionally attached form a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of
an oxo group (=O);
fluorine, chlorine, bromine;
(C_1-C_6)-alkyl;
nitro;
cyano;

hydroxyl;
phenyl or naphthyl; or
(C_1-C_6)-alkoxy,

and

R^8 represents NR^6R^7 where R^6 and R^7 are as defined above;
optionally substituted (C_1-C_6)-alkyl;
(C_1-C_6)-alkoxy;
optionally substituted phenyl or naphthyl;
phenyloxy or naphthyloxy; or
$-O-(CH_2)_n$-phenyl where n = 1, 2 or 3,

and

R^4 represents straight-chain or branched (C_1-C_6)-alkyl or (C_2-C_6)-alkenyl which are optionally mono- or polysubstituted by
hydroxyl;
fluoro, chloro, bromine;
cyano;
$-C(O)-R^5$ where R^5 is as defined above;
$-C(O)-NR^6R^7$ where R^6 and R^7 are as defined above;
$-NR^6R^7$ where R^6 and R^7 are as defined above;
$-NR^6-C(O)-R^8$ where R^6 and R^8 are as defined above;
$-SO_2-NR^6R^7$ where R^6 and R^7 are as defined above;
$-NR^6-SO_2-R^8$ where R^6 and R^8 are as defined above;
$-C(O)-(CH_2)_n-C(O)-R^8$ where n = 0 to 2 and R^8 is as defined above;
(C_1-C_6)-alkoxy;
optionally substituted phenyloxy or naphthyloxy;
optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S;
optionally substituted phenyl or naphthyl; or

by a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S, which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); fluorine, chlorine, bromine; (C_1-C_6)-alkyl; nitro; cyano; hydroxyl; phenyl or naphthyl; or by (C_1-C_6)-alkoxy,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted phenyl or naphthyl,

or

R^4 represents a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S, which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); fluorine, chlorine, bromine; (C_1-C_6)-alkyl; nitro; cyano; hydroxyl; phenyl or naphthyl; or by (C_1-C_6)-alkoxy and which may optionally be fused via two adjacent ring atoms to optionally substituted phenyl or naphthyl or optionally substituted (C_4-C_7)-cycloalkyl,

and their tautomers and their respective salts, hydrates and alkoxides,

for the prophylaxis and/or treatment of disorders.

10. The compound of the general formula (I) as claimed in claim 8 or 9,

characterized in that:

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:

hydrogen;

hydroxyl;

optionally substituted (C_1-C_4)-alkyl;

optionally substituted phenyl;

optionally substituted (C_1-C_4)-alkoxy;

-O-$(CH_2)_n$-CH=CH_2 where n = 1;

fluorine, chlorine;

nitro;

cyano;

-C(O)-R^5;

-C(O)-NR^6R^7;

-NR^6R^7;

-NR^6-C(O)-R^8;

-O-C(O)-R^8;

-SO_2-NR^6R^7; and

-NR^6-SO_2R^8,

where:

R^5 denotes:

hydrogen;

hydroxyl;

optionally substituted (C_1-C_4)-alkyl;

optionally substituted (C_3-C_7)-cycloalkyl;

optionally substituted (C_1-C_4)-alkoxy;

optionally substituted phenyl;

optionally substituted phenyloxy; or

-O-$(CH_2)_n$-phenyl where n = 1,

where the phenyl group may be fused via two adjacent ring atoms to optionally substituted (C_5-C_6)-cycloalkyl,

or

R^5 represents a 5- to 7-membered saturated or unsaturatedheterocycle which for its part may be mono- or polysubstituted by
an oxo group (=O);
fluorine, chlorine;
optionally substituted (C_1-C_4)-alkyl;
nitro;
cyano;
hydroxyl;
optionally substituted phenyl; or
by (C_1-C_4)-alkoxy,

or

R^5 represents optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S, selected from the group consisting of furanyl, pyrrolyl, thienyl, thiazolyl, oxazolyl, imidazolyl, triazolyl, pyridyl, pyrimidyl and pyridazinyl,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent ring atoms to optionally substituted phenyl or optionally substituted (C_5-C_6)-cycloalkyl,

and

R^6 and R^7 are identical or different and represent

hydrogen;
optionally substituted (C_1-C_4)-alkyl;
optionally substituted phenyl; or
represent optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S selected from the group consisting of furanyl, pyrrolyl, thienyl, thiazolyl, oxazolyl, imidazolyl, triazolyl, pyridyl, pyrimidyl and pyridazinyl,

or

R^6 and R^7 together with the nitrogen atom to which they are optionally attached form a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of
an oxo group (=O);
fluorine, chlorine;
(C_1-C_4)-alkyl;
nitro;
cyano;
hydroxyl;
phenyl; or
(C_1-C_4)-alkoxy,

and

R^8 represents NR^6R^7 where R^6 and R^7 are as defined above;
optionally substituted (C_1-C_4)-alkyl;
(C_1-C_4)-alkoxy;
optionally substituted phenyl;

phenyloxy; or

-O-$(CH_2)_n$-phenyl where n = 1,

and

R^4 represents straight-chain or branched (C_1-C_4)-alkyl or (C_2-C_4)-alkenyl which are optionally mono- or polysubstituted by

hydroxyl;

fluorine, chlorine;

cyano;

-C(O)-R^5 where R^5 is as defined above;

-C(O)-NR^6R^7 where R^6 and R^7 are as defined above;

-NR^6R^7 where R^6 and R^7 are as defined above;

-NR^6-C(O)-R^8 where R^6 and R^8 are as defined above;

-SO_2-NR^6R^7 where R^6 and R^7 are as defined above;

-NR^6-SO_2-R^8 where R^6 and R^8 are as defined above;

-C(O)-$(CH_2)_n$-C(O)-R^8 where n = 0 to 2 and R^8 is as defined above;

(C_1-C_4)-alkoxy;

optionally substituted phenyloxy;

optionally substituted 5- to 6-membered heteroaryl having up to 3 heteroatoms from the group consisting of N, O and S selected from the group consisting of furanyl, pyrrolyl, thienyl, thiazolyl, oxazolyl, imidazolyl, triazolyl, pyridyl, pyrimidyl and pyridazinyl;

optionally substituted phenyl; or

by a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); fluorine, chlorine; (C_1-C_4)-alkyl; nitro; cyano; hydroxyl; phenyl; or by (C_1-C_4)-alkoxy,

where the heterocycle and the heteroaryl ring may each optionally be fused via two adjacent rings atoms to optionally substituted phenyl,

or

R^4 represents a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of N, O and S, which for its part may optionally be mono- or polysubstituted by identical or different substituents from the group consisting of an oxo group (=O); fluorine, chlorine; (C_1-C_4)-alkyl; nitro; cyano; hydroxyl; phenyl; or by (C_1-C_4)-alkoxy and
which may optionally be fused via two adjacent ring atoms to optionally substituted phenyl or optionally substituted (C_5-C_6)-cycloalkyl,

and their tautomers and their respective salts, hydrates and alkoxides,

for the prophylaxis and/or treatment of disorders.

11. The compound of the general formula (I) as claimed in any of claims 8 to 10, characterized in that:

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:
hydrogen;
hydroxyl;
methyl;
trifluoromethyl;
methoxy;
radicals of the formulae -O-CH_2-CH_2-OH, -O-CH_2-COOH or -O-CH_2-CH=CH_2;
fluorine, chlorine or bromine;

nitro;

cyano;

-C(O)OH or –C(O)OCH_3;

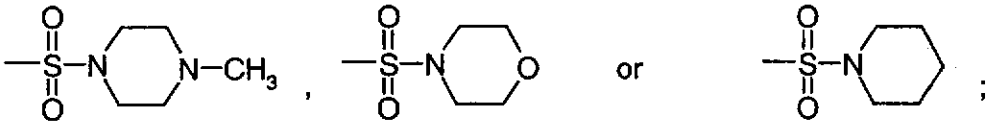
-C(O)NH_2;

-NH_2;

-NH-C(O)-CH_3;

-O-C(O)-CH_3 or -O-C(O)-C_2H_5;

radicals of the formulae



and

-NH-SO_2CH_3 or -NH-$SO_2C_6H_5$,

and

R^4 represents straight-chain or branched (C_1-C_4)-alkyl which is optionally mono- or polysubstituted by

hydroxyl;

amino;

-C(O)-OCH_3;

-C(O)-NH_2, -C(O)-$HNCH_3$, -C(O)-HNC_2H_5, or -C(O)-HNC_6H_5;

-$NHC(O)NH_2$, -$NHC(O)NHCH_3$, -$NHC(O)NHC_2H_5$, -$NHC(O)OCH_3$ or -$NHC(O)OC_2H_5$;

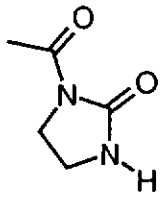
-SO_2-NH_2;

-NH-SO_2-CH_3 or -NH-SO_2-C_2H_5;

-OCH_3;

phenyl, which may be substituted by nitro, cyano, fluorine, methoxy, difluoromethoxy, methoxycarbonyl or p-tolylsulfonylmethyl;

pyridyl, furyl, imidazolyl, benzimidazolyl or thiazolyl, which may in each case be mono- or disubstituted by identical or different substituents from the group consisting of methyl, nitro and chlorine;
oxadiazolyl which may be substituted by phenyl or methoxyphenyl;
or
a radical of the formula



or

R^4 represents allyl or 3,3-dimethylallyl,

and their tautomers and their respective salts, hydrates and alkoxides,

for the prophylaxis and/or treatment of disorders.

12. The compound of the general formula (I) as claimed in any of claims 8 to 11, characterized in that:

R^1, R^2, R^3 are identical or different and independently of one another are selected from the group of the following substituents:
hydrogen;
hydroxyl;
methyl;
methoxy;
radicals of the formulae $-O-CH_2-CH_2-OH$, $-O-CH_2-COOH$ or $-O-CH_2-CH=CH_2$;

fluorine or chlorine;

nitro;

cyano;

-C(O)OH or –$C(O)OCH_3$;

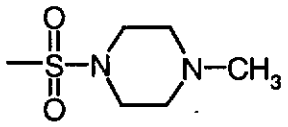
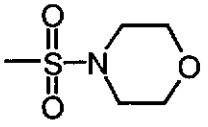
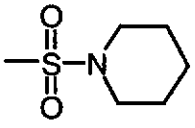
-$C(O)NH_2$;

- NH_2;

-NH-$C(O)CH_3$;

-O-$C(O)$-CH_3 or -O-$C(O)$-C_2H_5;

radicals of the formulae



or

;

and

–NH-SO_2CH_3 or –NH-$SO_2C_6H_5$,

and

represents straight-chain or branched (C_1-C_4)-alkyl which is optionally mono- or polysubstituted by

hydroxyl;

amino;

-$C(O)$-OCH_3;

-$C(O)$-NH_2, -$C(O)$-$HNCH_3$, -$C(O)$-HNC_2H_5, or -$C(O)$-HNC_6H_5;

-$NHC(O)NH_2$, -$NHC(O)NHCH_3$, -$NHC(O)NHC_2H_5$, -$NHC(O)OCH_3$ or -$NHC(O)OC_2H_5$;

-SO_2-NH_2;

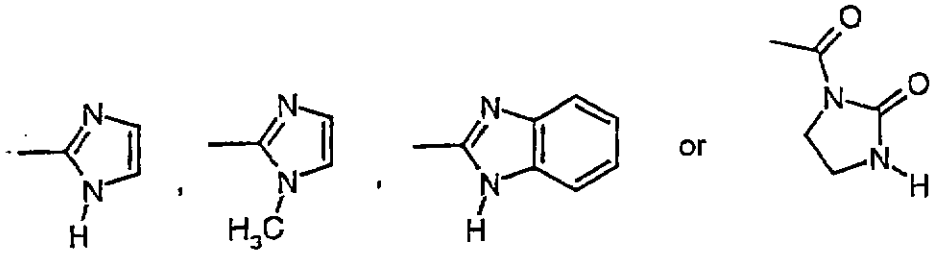
-NH-SO_2-CH_3 or -NH-SO_2-C_2H_5;

-OCH_3;

phenyl;

ortho-nitrophenyl; or

a radical of the formula



or

R^4 represents allyl,

and their tautomers and their respective salts, hydrates and alkoxides,

for the prophylaxis and/or treatment of disorders.

13. A medicament or pharmaceutical composition, comprising at least one compound of the general formula (I) as claimed in any of claims 8 to 12.

14. A medicament as claimed in claim 13 furthermore comprising pharmacologically acceptable carriers and excipients.

15. A medicament as claimed in claim 13 or claim 14 for the prophylaxis and/or treatment of disorders, in particular cardiovascular disorders; urogenital disorders; respiratory disorders; inflammatory and neuroinflammatory disorders; diabetes, in particular diabetes mellitus; neurodegenerative disorders; pain; cancer; and also hepatic fibrosis and cirrhosis of the liver.

16. The use of selective adenosine receptor ligands of the general formula (I) as claimed in any of claims 8 to 12 for the preparation of a medicament for the prophylaxis and/or treatment of disorders, in particular cardiovascular disorders; urogenital disorders; respiratory disorders; inflammatory and neuroinflammatory disorders; diabetes, in particular diabetes mellitus; neurodegenerative disorders; pain; cancer; and also hepatic fibrosis and cirrhosis of the liver.