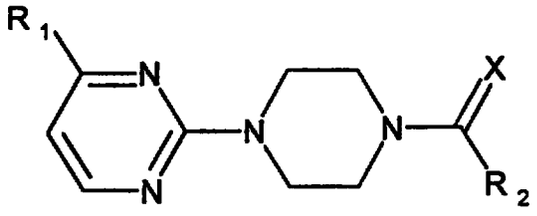
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DERIVATIVES OF ACYL-PIPERAZINYL-PYRIMIDINES, THEIR PREPARATION AND APPLICATION AS MEDICAMENTS

FIELD OF THE INVENTION

The present invention relates to new acyl-piperazinyl-pyrimidines of the general formula (I), to their physiologically acceptable salts, to procedures for their preparation, to their application as medicaments in therapy for humans and/or as veterinary medicaments and to the pharmaceutical compositions which contain said compounds.



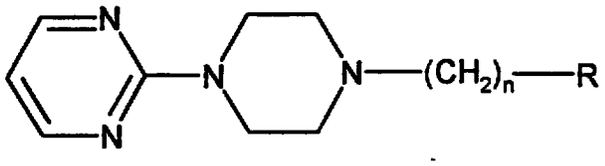
(I)

The new compounds object of the present invention can be used in the pharmaceutical industry as intermediates and for the preparation of medicaments.

BACKGROUND OF THE INVENTION

In our patents EP 382 637 and EP 497 659 we have described different derivatives of alkyl-piperazinyl-pyrimidines of the general formula (II) with ansiolytic and or tranquillising properties.

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(II)

We have now discovered that the addition of a substituent to position 4 of the pyrimide and the substitution of an alkyl radical with an acyl radical gives rise to the new compounds of general formula (I). Said compounds show useful biological properties which makes them especially useful for their use in therapy in humans and veterinary therapy. The compounds of the present invention are useful as agents which act on the central nervous system in mammals including humans. In particular, the new compounds are useful as sedatives, anti-convulsants, sleep-inducing agents and general anaesthetics.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 shows the results of the sedative activity of some of the compounds of the invention, as determined by reduction in locomotive activity.

DETAILED DESCRIPTION OF THE INVENTION

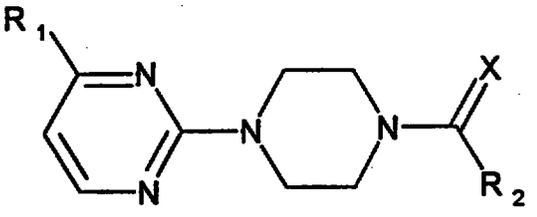
The present invention provides new compounds capable of inducing conscious sedation, of acting as sleep-inducing agents, anti-convulsants, analgesics, muscular relaxants, anti-tusigenics, ansiolytics, anti-psychotics, anti-depressants, anti-cerebral ischeamics, anti-migraine agents, agents useful for sleep disorders, agents for neurodegenerative diseases, agents for cognitive disorders and Alzheimer's disease, and

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capable of inducing or maintaining general anaesthesia, when administered by an appropriate method at a suitable dosage level.

The compounds of the present invention are represented by the general formula (I)

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(I)

where

X is an oxygen or sulphur atom;

R_1 is a C_{1-4} alkoxy or trifluoromethyl radical;

R_2 is a C_{1-6} alkoxy radical; C_{3-6} saturated cycloalkyl; heterocycloalkyl consisting of a ring of 3 to 6 atoms in which the heteroatom is selected from an atom of oxygen, sulphur or nitrogen, optionally N-substituted; phenyl optionally substituted with 1, 2 or 3 identical or different substituents selected from fluorine, chlorine, bromine, amino, acetamido, nitro, methyl, trifluoromethyl and methoxy; arylalkyl consisting of a C_{1-3} alkyl group substituted by a phenyl radical optionally substituted by 1, 2 or 3 identical or different substituents selected from fluorine, chlorine, bromo, amino, acetamido, nitro, methyl, trifluoromethyl and methoxy; heteroaryl consisting of a 5 or 6 heteroatom ring, optionally substituted, or of fused heteroaromatic systems optionally substituted, of 9 or 10 atoms consisting of 1 or 2 heteroatoms selected from oxygen, sulphur and nitrogen, selecting the aforementioned substituents from flourine, chlorine, bromine, amino, acetamido, nitro, methyl, trifluoromethyl and methoxy; and heteroarylalkyl consisting of an alkyl group of 1 to 3 carbon atmos substituted with a heteroaryl radical consisting of a 5 or 6 member heteroaromatic ring, optionally substituted, or of fused 9 to 10 member heteroaromatic systems, optionally substituted with 1 or 2 heteroatoms selected from oxygen, sulphur and nitrogen, selected the aforementioned substituents from fluorine, chlorine, bromine, amino, acetamido, nitro, methyl, trifluoromethyl and methoxy; and their physiologically acceptable salts.

In the present invention, the term C_{1-4} "alkoxy" represents a radical OR_3 in which R_3 is a saturated linear or branched carbon chain containing 1 to 4 atoms, such as methoxy, ethoxy, propoxy, isopropoxy, butoxy, *sec*-butoxy o *tert*-butoxy for example.

The term "alkyl" represents a radical derived from a saturated linear or branched hydrocarbon. The term C_{1-6} alkyl represents a linear or branched chain alkyl radical containing 1 to 6 atoms of carbon, such as methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *sec*-butyl, *tert*-butyl, pentyl, isopentyl, neopentyl and hexyl for example.

The term C_{3-6} saturated "cycloalkyl" represents a saturated ring of 3 to 6 atoms of carbon, such as cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl for example.

The term "heterocycloalkyl" represents a ring of 3 to 6 atoms of which there is a heteroatom such as an oxygen atom or an atom of sulphur, such as a 2-aziridinyl, 2-tetrahydrofuryl, 3-tetrahydrofuryl, 2-tetrahydrothienyl, 3-tetrahydrothienyl for example, or an atom of nitrogen which may or may not be substituted, such as 2-azetidinyl, 2-piperidinyl, 3-piperidinyl or 4-piperidinyl for example.

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The term "aryl" represents an unsubstituted or substituted phenyl radical, with 1, 2 or 3 identical or different substituents such as fluorine, chlorine, bromine, amino, acetamido, nitro, methyl, triflouromethyl or methoxy, such as 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-bromophenyl, 3-bromorophenyl, 4-bromophenyl, 2-aminophenyl, 3-aminophenyl, 4-aminophenyl, 2-nitrophenyl, 3-nitrophenyl, 4-nitophenyl, 2-acetamidophenyl, 3-acetamidophenyl, 4-acetamidophenyl, 2-nitrophenyl, 3-nitrophenyl, 4-nitrophenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-(trifluoromethyl)phenyl, 3-(trifluoromethyl)phenyl, 4-(trifluoromethyl)phenyl, 2-metoxyphenyl, 3-metoxyphenyl, 4-metoxyphenyl, 2,3-difluorophenyl, 3,4-difluorophenyl, 2,4-difluorophenyl, 2,3-dibromophenyl, 3,4-dibromophenyl, 2,4-dibromophenyl, 2,3-dimethylphenyl, 3,4-dimethylphenyl, 2,4-dimethylphenyl, 2,3-dimethoxyphenyl, 3,4-dimethoxyphenyl, 2,4-dimethoxyphenyl for example.

The term "arylalkyl" represents a linear or branched chain of 1 to 3 atoms of carbon which is substituted with an aryl radical, according to the hereinbefore definition of "aryl", and which includes substituents such as phenylmethyl, 1-phenylethyl, 2-phenylethyl, 3-phenylethyl, 3-phenylpropyl, as well as other radicals in which the aromatic ring is substituted with groups such as fluorine, chlorine, bromine, amino, acetamido, nitro, methyl, trifluoromethyl or methoxy.

The term "heteroaryl" represents a substituted or unsubstituted heteraromatic ring of 5 or 6 members or unsubstituted or substituted fused heteroaromatic systems of 9 or 10 members consisting of 1 or 2 heteroatoms such as nitrogen, oxygen or sulphur, with the substituent groups being groups such as fluorine, chlorine, bromine, amino, acetamido, nitro, methyl, trifluoromethyl or methoxy, such as 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 3-methyl-2-thienyl, 5-methyl-2-thienyl, 3-methoxy-2-thienyl, 3-chloro-2-thienyl, 5-chloro-2-thienyl, 2-pyrrolyl, 3-pyrrolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-indolyl, 3-indolyl, 2-benzo[b]thienyl, 3-benzyo[b]thienyl, 3-chloro-2-benzo[b]thienyl, pirazolyl, imidazolyl, pyrimidinyl, piridazinyl, pirazinyl, benzimidazolyl, quinolyl, oxazolyl and thiazolyl for example.

The term "heteroarylalkyl" represents an alkyl group of 1 to 3 atoms of carbon which is substituted with a heteroaryl radical, according to the hereinbefore definition of "heteroaryl", and which includes substituents such as 2-thienylmethyl, 2-benzo[b]thienylmethyl and 3-(4-chloropyrazolyl)propyl.

The new compounds of general formula (I) may contain an asymmetric carbon atom and can therefore be prepared as optical isomers or racemates. The racemates of compounds (I) can be resolved into their optical isomers using conventional methods, such as separation by chiral chromatography or fractionated crystallisation from their diasteroisomer salts for example. Similarly, they can also be obtained from asymmetric synthesis using chiral precursors.

The present invention also relates to physiologicaly acceptable salts of the compounds of general formula (I), in particular addition salts of mineral acids such as hydrochloric acid, hydrobromic acid, phosphoric acid, sulphuric acid, nitric acid and addition salts of organic acids such as *p*-toluensulphonic acid or methansulphonic acid.

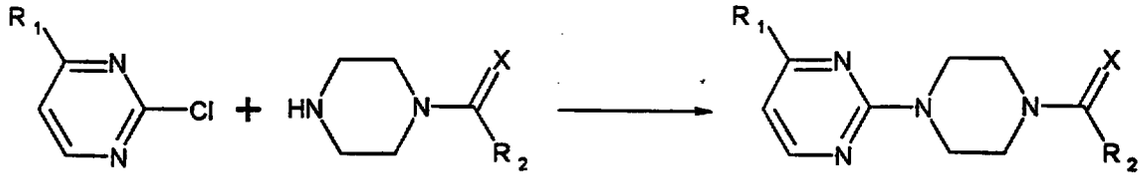
The new derivatives of general formula (I), in which X is an atom of oxygen and R_1 and R_2 have the hereinbefore defined meaning, can be prepared according to methods A or B which are described below.

METHOD A:

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The compounds of general formula (I) can be prepared by reacting the derivative of chloropyrimidine (III), where R_1 has the hereinbefore defined meaning, with a derivative of piperazine of general formula (IV) in which X and R_2 have the hereinbefore defined meaning.

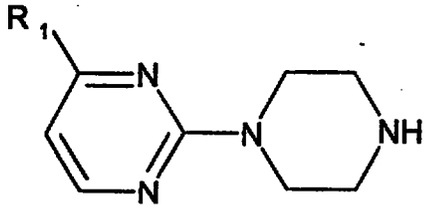


(III) (IV) (I)

The reaction is carried out in an organic solvent, for example in an chlorinated hydrocarbon such as dichloromethane or chloroform, a linear or cyclic ether such as 1,2-dimethoxyethane, tetrahydrofurane or dioxane, a aprotic polar solvent such as pyridine, dimethylsulphoxide or dimethylformamide or any other type of solvent appropriate for carry out a aromatic nucleophilic substitution reaction. The reaction can be carried out in the presence of a mineral or organic base such as an aliphatic amine, preferably triethylamine or M-methylmorphine by stirring at a temperature lying between room temperature and the boiling point of the solvent for a period of time lying between ten minutes and twenty-four hours, the preferring conditions being a period of time between thirty minutes and five hours.

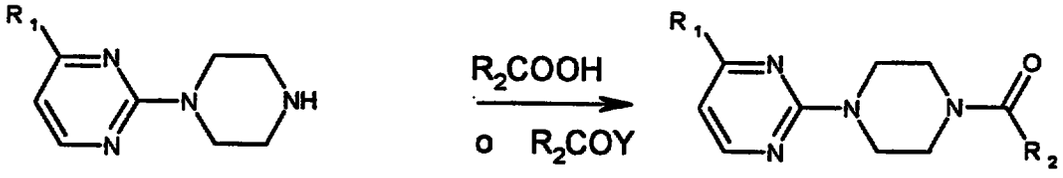
METHOD B:
By reaction of the amine of formula (V):

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(V)

in which R_1 has the hereinbefore defined meaning with a carboxylic acid of the general formula R_2COOH (VI), in which R_2 has the hereinbefore defined meaning, or with a salt of said acid or also with a derivative reagent R_2COY (VII).



(V) (I)

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Examples of salts include salts of alkali metals such as sodium salts and potassium salts, alkaline earth salts such as calcium salts and magnesium salts, ammonium salts, and salts of organic bases such as triethylamine, trimethylamine, pyridine and picoline.

Examples of derivative reagents of general formula R_2COY (VII) in which Y is a halogen atom preferably a chlorine atom or a bromine atom, an azide group ($-N_3$), a 1-imidazolyl, a O-CO-R_4, in which R_4 can be an alkyl or aryl radical of 1 to 6 carbon atoms, preferably substituted with one or several halogen atoms, or a group OR_5 where R_5 represents an aromatic group of one or two rings substituted with one or several halogen atoms or nitro radicals, the preferred groups being 4-nitrophenyl, 2,4-dinitrophenyl, pentachlorophenyl, pentafluorophenyl, 1-benzotriazolyl o N-succinimide. Similarly, instead of using the aforementioned derivative reagents, compounds of general formula (I) can be prepared directly by reaction of the amine (V) with the carboxylic acid or general formula (VI). In this case it is preferable that the reaction proceeds in the presence of reagents that activate the carbonyl groups such as N.N'-dicyclohexylcarbodiimide, diisopropylcarbondiimide or 3-(3-dimethylamino)propyl-1-ethycarbodiimide. This reaction can also be carried out using the said carbodiimidas in the presence of 1-benzotriazol or N-hydroxysuccinimide. The acids of general formula (VI) and the amine of formula (V) also react directly in the presence of N,N'-carbonyldiimidazol or of propanophosphonic acid anhydride.

The reaction is carried out in an organic solvent, for example in an chlorinated hydrocarbon such as dichloromethane or chloroform, a linear or cyclic ether such as 1,2-dimethoxyethane, tetrahydrofurane or dioxane, a aprotic polar solvent such as pyridine, dimethylsulphoxide or dimethylformamide or any other type of solvent appropriate for carry out a aromatic nucleophilic substitution reaction. The reaction can be carried out in the presence of a mineral or organic base such as an aliphatic amine, preferably triethylamine or M-methylmorphine by stirring at a temperature lying between room temperature and the boiling point of the solvent for a period of time lying between ten minutes and twenty-four hours, the preferring conditions being a period of time between thirty minutes and five hours.

METHOD C

The new derivatives of general formula (I), in which X is an atom of sulphur and R_1 and R_2 have the hereinbefore defined meaning, can be prepared according to the following method.

By treating a compound of a compound of general formula (I), in which R_1 and R_2 have the hereinbefore defined meaning and in which X is an atom of oxygen, with Lawesson's reagent (2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphaethano-2,4-disulphuro) or with phosphorous pentasulphide, the corresponding thioamides are obtained in which X is a sulphur atom:



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The reaction is carried out in an organic solvent such as toluene, benzene, heptane, pyridine or tetrahydrofurane. The reaction is continually shaken at a temperature lying between room temperature and the boiling point of the solvent for a period of time of between one hour and twenty-four hours, preferably carrying out the reaction at 80°C for a time between one hour and sixteen hours.

METHOD D:

The salts of the compounds of general formula (I) can be prepared by reaction with a mineral acid such as hydrochloric acid, hydrobromic acid, phosphoric acid, sulphuric acid, nitric acid or with an organic acid such as *p*-toluensulphonic acid or methansulphonic acid in an appropriate solvent such as methanol, ethanol, ethyl ether, ethyl acetate, acetonitrile or acetone, being obtained with the normal precipitation techniques or crystallisation of the corresponding salts.

The invention provides pharmaceutical compositions which comprise, as well as a pharmaceutically acceptable excipient, at least one compound of general formula (I) or one of their physiologically acceptable salts. The invention also relates to the use of a compound of general formula (I) and their physiologically acceptable salts in the elaboration of a medicament with activity in the mammalian, central nervous system, including activity in the human central nervous system in particular, in the manufacture of a medicament with sedative, anticonvulsive, sleep-inducing and general anaesthetic activity.

In the examples which follow the preparation of new compounds according to the invention is indicated. Also described are some typical forms of use for the different fields of application, as well as medicinal formulas applicable to the compounds of the invention.

METHOD A:

Example 1. Preparation of 2-[4-(2-furylcarbonyl)-1-piperazinyl]-4-methoxy-pyrimidine.

A solution of 1.0 g (6.92 mmol) of 2-chloro-4-methoxypyrimidine, 1.49 g (8,30 mmol) of 1-(2-furylcarbonyl)piperazine and 1.39 g (13.84 mmol) of triethylamine in 20 mL of n-butanol is maintained under gentle reflux conditions overnight. The solvent is evaporated off under reduced pressure and the crude residue is diluted in chloroform and washed in water. The organic phase is dried over $NaSO_4$ and evaporated to dryness to give a crude product which is purified using silica-gel chromatography eluting with ethyl acetate/petroleum ether 70:30 to yield an oil which solidifies when left to stand. The solid is suspended in petroleum ether to yield 1.4 g (4.86 mmol) of 2-[4-(2-furylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine. m.p. = 85-86°C.

METHOD B:

Example 3. Preparation of 4-methoxy-2-`4-(2-thienylcarbonyl)-1-piperazinyl] pyrimidine

A solution of 1.0 g (5.15 mmol) of 4-methoxy-2-(1-piperazinyl)pyrimidine and 1 mL (7.18 mmol) of triethylamine in 30 mL of CH_2Cl_2 is cooled to 0° C and 0.76 g (5.18 mmol) of 2-thienylcarbonyl chloride slowly added. The solution is kept at 0° C for an hour and then the temperature allowed to rise to room temperature. The organic phase is washed with H_2O, dried over $NaSO_4$ and the solvent removed under reduced pressure.

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The crude residue is dissolved in ethyl ether crystallising 1.0 g (3.28 mmol) of 4-methoxy-2-[4-(2-thiencarbonyl)-1-piperazinyl]pryimidine. m.p. = 71-73° C

Example 12. Preparation of 4-methoxy-2-[4-(3-thienylcarbonyl)-1-piperazinyl] pyrimidine.

To a solution of 1.0 g (7.81 mmol) of 3-thienylcarboxylic acid and 1 mL (7.86 mmol) of triethylamine in 30 mL of CH_2Cl_2 cooled to 0° C 0.84 g (7.81 mmol) of ethyl chloroformiate are added. The mixture is maintained at 0° C for 20 minutes and then 1.5 g (7.81 mmol) of 4-methoxy-2-(1-piperazinyl) pyrimidine dissolved in 10 mL of CH_2Cl_2 are added to the solution. The temperature is allowed to rise to room temperature and the solution continually stirred for 2 hours and the organic phase is washed with H_2O, dried over $NaSO_4$ and the solvent evaporated off under reduced pressure. The resulting oil is treated with ethyl ether to yield a solid which is recrystallised from ethanol/H_2O to give 0.8 g (2.63 mmol) of 4-methoxy-2-[4-(3-thienylcarbonyl)-1-piperazinyl]pyrimidine. m.p. = 90-92° C.

Example 20. Preparation of 2-[4-(2-inolylcarbonyl)-1-piperazinyl]-4-methoxy pyrimidine.

To a solution of 0.83 g (5.15 mmol) of indol-2-carboxylic acid in 15 mL of dry THF 0.83 g (5.15 mmol) of N,N'-carbonyldiimidazol is added. After 30 minutes 1.0 g (5.15 mmol) of 4 methoxy-2-(1-piperazinyl) pyrimidine is added to the solution and it is left overnight with continuous stirring. The solvent is eliminated under reduced pressure and H_2O added. This produces a precipitate which is filtered and dried, to give 1.7 g (5.04 mmol) of 2-[4-(2-indolylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine. m.p. = 202-203° C.

METHOD C

Example 54. Preparation of 4-methoxy-2-(4-thiobenzoyl-1-piperazinyl) pyrimidine.

0.56 g (1.9 mmol) of 2-(4-benzoyl-1-piperazinyl)-4-methoxypyrimidine are dissolved in 25 mL of dry toluene, and 0.46 g (1.14 mmol) of Lawesson's reagent (2,4-bis(4-methoxyphenyl)-1,32,4-dithiadiphosphaethano-2,4-disulphide) added. The mixture is heated to 80-90° C for 16 hours. Ethyl ether is added, basic water is used to wash the residue and the organic extract is dried with $NaSO_4$ and the solvent evaporated off under reduced pressure. The resulting crude residue is crystallised with ethyl ether-petroleum ether to give 160 mg (0.5 mmol) of 2-(4-thiobenzoyl-1-piperazinyl)-4-methoxypyrimidine. m.p. = 125-129° C.

METHOD D:

Example 2. Preparation of 2-[4-(2-furylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate.

1.0 g (3.47 mmol) of 2-[4-(2-furylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine in ethyl acetate and a few drops of a solution of ethyl ether/hydrochloric acid are added, thus obtaining a precipitate which is filtered and dried, to yield 1.07 g (3.29 mmol) of 2-[4-(2-furylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate. m.p. = 162-164° C.

Example 4. Preparation of 4-methoxy-2-[4-(2-thienylcarbonyl)-1-piperazinyl] pyrimidine chlorohydrate.

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28014 MADRID

1.0 g (3.29 mmol) of 4-methoxy-2-[4-(2-thienylcarbonyl)-1-piperazinyl] pyrimidine is dissolved in acetone and a few drops of a solution of ethyl ether/hydrochloric acid are added, thus obtaining a precipitate which is filtered and dried, to yield 1.05 g (3.08 mmol) of 4-methoxy-2-[4-(2-thienylcarbonyl)-1-piperazinyl] pyrimidine chlorohydrate. m.p. = 143-145° C.

Example 13. Preparation of 4-methoxy-2-[4-(3-thienylcarbonyl)-1-piperazinyl] pyrimidine chlorohydrate..

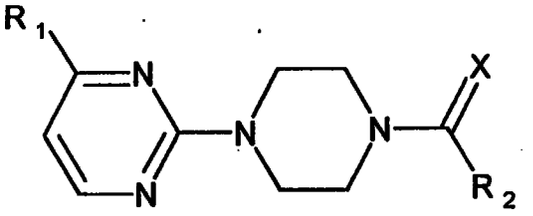
0.8 g (2.63 mmol) of 4-methoxy-2-[4-(3-thienylcarbonyl)-1-piperazinyl] pyrimidine is dissolved in ethanol and a few drops of a solution of ethanol/hydrochloric acid are added, thus obtaining a precipitate which is filtered and dried, to yield 0.6 g (1.76 mmol) of 4-methoxy-2-[4-(3-thienylcarbonyl)-1-piperazinyl] pyrimidine chlorohydrate. m.p. = 154-156° C.

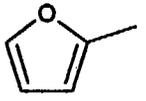
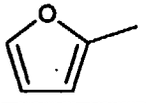
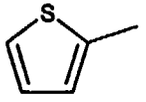
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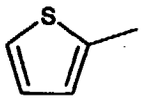
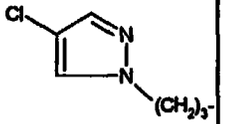
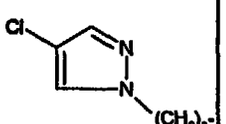
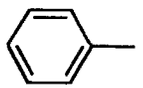
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TABLE 1

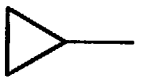
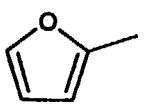
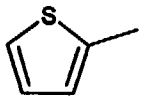
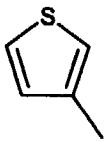
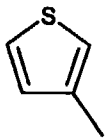


Example	R_1	R_2	X	Base or Salt	Procedure	m.p. (°C)	^{1}H RMN (MHz) (Solvent) δ	IR, cm^{-1}
1	CH_3O-		O	base	A	85-86	(300 MHz) ($CDCl_3$) 3.90 (broad singlet, 11H), 6.04 (d, J=5.5 Hz, 1H), 6.51 (dd, J= 3.5 Hz, J'= 1.7 Hz, 1H). 7.05 (d, J= 3.5 Hz, 1H), 7.51 (broad singlet, 1H). 8.07 (d, J= 5.5 Hz, 1H).	(KBr) 1623, 1598, 1583, 1561, 1502, 1439, 1264, 1025.
2	CH_3O-		O	HCl	D	162-164	(300 MHz) (DMSO-d_6) 3.83 (m, 4H), 3.91 (m, 4H), 3.95 (s. 3H), 6.36 (d, J= 6.3 Hz, 1H), 6.66 (m, 1H), 7.07 (m, 1H), 7.88 (m, 1H), 8.16 (d, J= 6.3 Hz, 1H).	(KBr) 2800-2200 (broad), 1642, 1605, 1483, 1262.
3	CH_3O-		O	base	B	71-73	(300 MHz) ($CDCl_3$) 3.83 (m, 4H), 3.89 (a.c., 7H,(δ= 3.89, s)), 6.04 (d, J= 5.7 Hz, 1H), 7.07 (dd, J= 5.1 Hz, J'= 3.9 Hz, 1H), 7.33 (d, J= 3.9 Hz, 1H), 7.48 (d, J= 5.1 Hz, 1H), 8.07 (d, J= 5.7 Hz, 1H).	(KBr) 1598, 1561, 1432, 1257, 989.

4	CH_3O-		O	HCl	D	143-145	(300 Mhz) (DMSO-d_6) 3.80 (m, 4H), 3.91 (m, 4H), 3.95 (s, 3H), 6.37 (d, J= 6.5 Hz, 1H), 7.15 (dd, J= 4.9 Hz, J'= 3.6 Hz, 1H), 7.49 (dd, J= 3.6 Hz, J'= 1.2 Hz, 1H), 7.80 (dd, J= 4.9 Hz, J'= 1.2 Hz, 1H), 8.15 (d, J= 6.5 Hz, 1H).	(KBr) 2800-2200 (broad), 1637, 1611, 1597, 1484, 1437, 1409, 1210.
5	CH_3O-	CH_3	O	base	A	119-120	(300 MHz) ($CDCl_3$) 2.15 (s, 3H), 3.52 (m, 2H), 3.68 (m, 2H), 3.83 (m, 4H), 3.89 (s, 3H), 6.02 (d, J= 5.7 Hz, 1H), 8.06 (d, J= 5.7 Hz, 1H).	(KBr) 1654, 1595, 1561, 1423, 1345, 1249, 988.
6	CH_3O-		O	base	B	aceite	(300 MHz) ($CDCl_3$) 2.21 (m, 2H), 2.32 (m, 2H), 3.45 (m, 2H), 3.68 (m, 2H), 3.80 (m, 4H), 3.89 (s, 3H), 4.20 (t, J= 6.5 Hz, 2H), 6.03 (d, J= 5.7 Hz, 1H), 7.40 (s, 1H), 7.42 (s, 1H), 8.05 (d, J= 5.7 Hz, 1H).	(film) 1651, 1644, 1588, 1470, 1339.
7	CH_3O-		O	HCl	D	148-149	(300 MHz) (DMSO-d_6) 1.98 (q, J= 6.9 Hz, 2H), 2.33 (t, J= 7.0 Hz, 2H), 3.57 (m, 4H), 3.82 (m, 4H), 3.95 (s, 3H), 4.10 (t, J= 6.9 Hz, 2H), 6.36 (d, J=6.6 Hz, 1H), 7.50 (s, 1H), 7.98 (s, 1H), 8.14 (d, J= 6.6 Hz, 1H).	(KBr) 2800-2200 (broad), 1641, 1610, 1484, 1437, 1353, 1270, 1216.
8	CH_3O-		O	base	B	99-102	(300 MHz) ($CDCl_3$) 3.52 (m, 2H), 3.73-4.00 (a.c., 9H, (δ= 3.88, s)), 6.03 (d, J= 5.5 Hz, 1H), 7.44 (s, 5H), 8.06 (d, J= 5.5 Hz, 1H).	(KBr) 1625, 1606, 1597, 1558, 1461, 1428, 1266, 988.

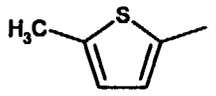
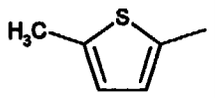
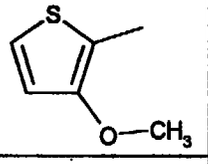
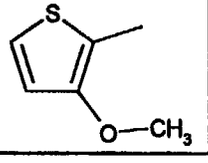
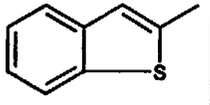
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9	CH_3O-		O	base	B	76-78	(300 MHz) ($CDCl_3$) 0.80 (m, 2H), 1.02 (m, 2H), 1.78 (m, 1H), 3.68-3.92 (a.c., 11H, (δ= 3.89, s)), 6.02 (d, J= 5.7 Hz, 1H), 8.06 (d, J= 5.7 Hz, 1H).	(KBr) 1638, 1589, 1567, 1470, 1414, 1335, 1235, 1225.
10	CF_3-		O	base	A	112-113	(300 MHz) ($CDCl_3$) 3.84-4.00 (a.c., 8H), 6.51 (dd, J= 3.5 Hz, J'= 1.7 Hz, 1H), 6.82 (d, J=, 4.8 Hz, 1H), 7.06 (dd, J= 3.5 Hz, J'= 1.0 Hz, 1H), 7.51 (dd, J= 1.7 Hz, J'= 1.0 Hz, 1H), 8.51 (d, J= 4.8 Hz, 1H).	(KBr) 1620, 1592, 1509, 1332, 1268, 1138.
11	CF_3-		O	base	B	136-137	(300 MHz) ($CDCl_3$) 3.86 (a.c., 4H), 3.96 (a.c., 4H), 6.82 (d, J= 4.8 Hz, 1H), 7.08 (dd, J= 5.0 Hz, J'= 3.7 Hz, 1H), 7.34 (dd, J= 3.7 Hz, J'= 1.1 Hz, 1H), 7.48 (dd, J= 5.0 Hz, J'= 1.1 Hz, 1H), 8.52 (d, J= 4.8 Hz, 1H).	(KBr) 1594, 1521, 1430, 1336, 1262, 1151.
12	CH_3O-		O	base	B	90-92	(300 MHz) ($CDCl_3$) 3.72 (m, 4H), 3.80-3.96 (a.c., 7H, (δ= 3.89, s)), 6.03 (d, J= 5.6 Hz, 1H), 7.22 (d, J= 5.0 Hz, 1H), 7.36 (m, 1H), 7.56 (broad singlet, 1H), 8.06 (d, J= 5.6 Hz, 1H).	(KBr) 1623, 1595, 1582, 1561.
13	CH_3O-		O	HCl	D	154-156	(300 MHz) (DMSO-d_6) 3.66 (m, 4H), 3.87 (m, 4H), 3.92 (s, 3H), 6.32 (d, J=6.1 Hz, 1H), 7.24 (m, 1H), 7.63 (broad singlet, 1H), 7.85 (broad singlet, 1H), 8.14 (d, J= 6.1 Hz, 1H).	(KBr) 2800-2200 (broad), 1642, 1617, 1598.

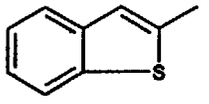
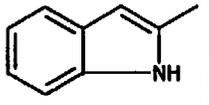
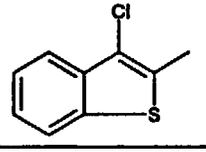
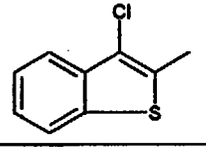
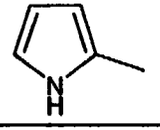
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14	CH_3O-		O	base	B	90-92	(300 MHz) ($CDCl_3$) 2.51 (s, 3H), 3.79-3.93 (a.c., 11H, (δ= 3.89, s)), 6.03 (d, J= 5.6 Hz, 1H), 6.72 (m, 1H), 7.15 (d, J= 3.5 Hz, 1H), 8.06 (d, J= 5.6 Hz, 1H).	(KBr) 1625, 1562, 1510, 1414, 1261.
15	CH_3O-		O	HCl	D	115-119	(300 Mhz) ($CDCl_3$) 2.46 (s, 3H), 3.79 (m, 4H), 3.91 (m, 4H), 3.95 (s, 3H), 6.37 (d, J= 6.4 Hz, 1H), 6.84 (m, J= 3.6 Hz, 1H), 7.29 (d, J= 3.6 Hz, 1H), 8.14 (d, J= 6.4 Hz, 1H).	(KBr) 2800-2200 (broad), 1641, 1615, 1602, 1488, 1412, 1260.
16	CH_3O-		O	base	B	99-101	(300 MHz) ($CDCl_3$) 3.69 (a.c., 4H), 3.85-3.93 (a.c., 10H, (δ= 3.90, two singlets)), 6.02 (d, J= 5.7 Hz, 1H), 6.80 (d, J= 5.6 HZ, 1H), 7.37 (d, J= 5.6 Hz, 1H), 8.07 (d, J= 5.7 Hz, 1H).	(KBr) 1623, 1594, 1656.
17	CH_3O-		O	HCl	D	162-165	(300 MHz) (DMSO-d_6) 3.60 (a.c., 4H), 3.82-3.90 (a.c., 7H, (δ= 3.88, s)), 3.94 (s, 3H), 6.33 (d, J= 6.3 Hz, 1H), 7.04 (d, J= 5.6 Hz, 1H), 7.69 (d, J= 5.6 Hz, 1H), 8.14 (d, J= 6.3 Hz, 1H).	(KBr) 2800-2200 (broad), 1640, 1610, 1479, 1442, 1406.
18	CH_3O-		O	base	B	173-174	(300 MHz) ($CDCl_3$) 3.86 (m, 4H), 3.90 (s, 3H), 3.92 (m, 4H), 6.05 (d, J= 5.7 Hz, 1H), 7.42 (a.c., 2H), 7.53 (s, 1H), 7.85 (a.c., 2H), 8.07 (d, J= 5.7 Hz, 1H).	(KBr) 1604, 1589, 1559, 1459, 1259, 991.

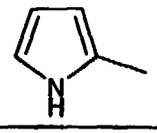
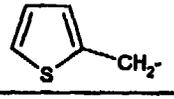
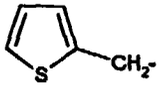
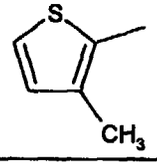
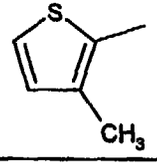
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19	CH_3O-		O	HCl	D	155-156	(300 MHz) (DMSO-d_6) 3.84 (m, 4H), 3.89-3.97 (a.c., 7H, (δ= 3.93, s)), 6.32 (d, J= 6.3 Hz,1H), 7.45 (a.c., 2H), 7.81 (s, 1H), 7.94 (m, 1H), 8.02 (m, 1H), 8.15 (d, J= 6.3 Hz, 1H).	(KBr) 2800-2200 (broad), 1644, 1615, 1487.
20	CH_3O-		O	base	B	202-203	(300 MHz) ($CDCl_3$) 3.92 (s, 3H), 3.93-4.10 (a.c., 8H), 6.05 (d, J= 5.6 Hz, 1H), 6.83 (d, J= 1.4 Hz, 1H), 7.15 (t, J= 7.3 Hz, 1H), 7.30 (t, J= 7.3 Hz, 1H), 7.45 (d, J= 8.3 Hz, 1H), 7.67 (d, J= 8.3 Hz, 1H), 8.09 (d, J= 5.6 Hz, 1H), 9.42 (broad singlet, 1H).	(KBr) 3260, 1605, 1578, 1571, 1438, 1336, 1251.
21	CH_3O-		O	base	B	175-176	(300 MHz) ($CDCl_3$) 3.59 (m, 2H), 3.88 (s, 3H), 3.92 (m, 6H), 6.04 (d, J= 5.6 Hz, 1H), 750 (a.c., 2H), 7.86 (a.c., 2H) 8.06 (d, J= 5.6 Hz, 1H).	(KBr) 1638, 1588, 1564, 1263.
22	CH_3O-		O	HCl	D	164-165	(300 MHz) (DMSO-d_6) 3.45-4.00 (a.c., 11H, (δ= 3.91, s)), 6.31 (d, J= 6.4 Hz, 1H), 7.60 (a.c., 2H), 7.88 (m, 1H). 8.12-8.18 (a.c., 2H, (δ=8.15, d, J= 6.4 Hz)).	(KBr) 2800-2200 (broad), 1640, 1629, 1625, 1609, 1418, 1219.
23	CH_3O-		O	base	B	142-143	(300 MHz) ($CDCl_3$) 3.90 (s, 3H), 3.92 (a.c., 8H), 6.03 (d, J= 5.6 Hz, 1H), 6.26 (m, 1H), 6.56 (m, 1H), 6.94 (m, 1H), 8.07 (d, J= 5.6 Hz, 1H), 9.87 (m, 1H).	(KBr) 3258, 1586, 1566, 1467, 1433.

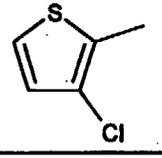
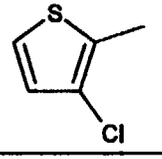
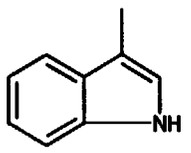
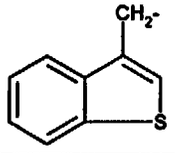
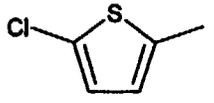
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24	CH_3O-		O	HCl	D	180-182 (dec)	(300 MHz) (DMSO-d_6) 3.86 (a.c., 4H), 3.94 (m, 4H), 3.97 (s, 3H), 6.13 (m, 1H), 6.41 (d, J= 6.7 Hz, 1H), 6.56 (m, 1H), 6.90 (m, 1H), 8.15 (d, J= 6.7 Hz, 1H), 11.52 (m, 1H).	(KBr) 3162, 2800-2200 (broad), 1633, 1605, 1487, 1428.
25	CH_3O-		O	base	B	69-71	(300 MHz) ($CDCl_3$) 3.57 (m, 2H), 3.72 (m, 4H), 3.80 (m, 2H), 3.88 (s, 3H), 3.97 (s, 2H), 6.02 (d, J= 5.7 Hz, 1H), 6.95 (m, 2H), 7.21 (m, 1H), 8.05 (d, J= 5.7 Hz, 1H).	(KBr) 1634, 1561, 1440, 1337, 1236.
26	CH_3O-		O	HCl	D	172-175	(300 MHz) (DMSO-d_6) 3.63 (m, 2H), 3.70 (m, 2H), 3.83 (m, 4H), 3.96 (s, 3H), 4.03 (s, 2H), 6.38 (d, J= 6.6 Hz, 1H), 6.96 (m, 2H), 7.39 (dd, J= 4.8 Hz, J'= 1.7 Hz, 1H), 8.15 (d, J= 6.6 Hz, 1H).	(KBr) 2800-2200 (broad), 1667, 1636, 1606, 1411, 1216, 1208.
27	CH_3O-		O	base	B	87-89	(300 MHz) ($CDCl_3$) 2.,29 (s, 3H), 3.,68 (m, 4H), 3.86 (m, 4H), 3.88 (s, 3H), 6.03 (d, J= 5.6 Hz, 1H), 6.86 (d, J= 5.0 Hz, 1H), 7.30 (d, J= 5.0 Hz, 1H) 8.06 (d, J= 5.7 Hz, 1H).	(KBr) 1634, 1586, 1567, 1468, 1453, 1260.
28	CH_3O-		O	HCl	D	144-146	(300 MHz) (DMSO-d_6) 3.62 (m, 4H), 3.89 (m, 4H), 3.94 (s, 3H), 6.37 (d, J= 6.6 Hz, 1H), 6.95 (d, J= 4.9 Hz, 1H), 7.60 (d, J= 4.9 Hz, 1H), 8.14 (d, J= 6.6 Hz, 1H).	(KBr) 2800-2200 (broad), 1617, 1604, 1486, 1427, 1413, 1258.

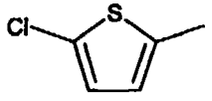
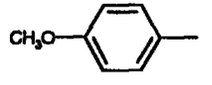
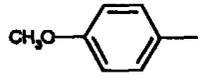
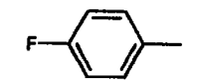
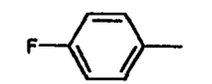
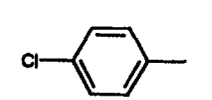
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29	CH_3O-		O	base	B	86-88	(300 MHz) ($CDCl_3$) 3.55-3.85 (a.c., 4H), 3.89 (s, 3H), 3.91 (m, 4H), 6.04 (d, J= 5.7 Hz, 1H), 6.94 (d, J= 5.1 Hz, 1H), 7.40 (d, J= 5.1 Hz, 1H), 8.07 (d, J= 5.7 Hz, 1H).	(KBr) 1622, 1561, 1509.
30	CH_3O-		O	HCl	D	144-147	(300 MHz) (DMSO-d_6) 3.50-3.70 (a.c., 4H), 3.87 (m, 4H), 3.91 (s, 3H), 6.31 (d, J= 6.2 Hz, 1H), 7.14 (d, J= 5.4 Hz, 1H), 7.85 (d, J= 5.4 Hz, 1H), 8.14 (d, J= 6.2 Hz, 1H).	(KBr) 2800-2200 (broad), 1636, 1608, 1481, 1443, 1407.
31	CH_3O-		O	base	B	229-231	(300 MHz) ($CDCl_3$) 3.80 (m, 4H), 3.84-3.93 (a.c., 7H, (δ= 3.88, s)), 6.03 (d, J= 5.7 Hz, 1H), 7.22 (m, 2H), 7.38 (m, 1H), 7.46 (d, J= 2.8 Hz, 1H), 7.73 (m, 1H), 8.07 (d, J= 5.7 Hz, 1H), 8.96 (broad singlet, 1H).	(KBr) 3181, 1610, 1590, 1559, 1467, 1339, 998.
32	CH_3O-		O	base	B	135-137	(300 MHz) ($CDCl_3$) 3.53 (m, 2H), 3.66 (m, 2H), 3.78 (a.c., 4H), 3.86 (s, 3H), 3.98 (s, 2H), 6.01 (d, J= 5.6 Hz, 1H), 7.26 (s, 1H), 7.40 (m, 2H), 7.85 (m, 2H), 8.03 (d, J= 5.6 Hz, 1H).	(KBr) 1619, 1590, 1561, 1553, 1454, 990.
33	CH_3O-		O	base	B	99-100	(300 MHz) ($CDCl_3$) 3.81 (m, 4H), 3.89 (m, 4H), 3.90 (s, 3H), 6.04 (d, J= 5.7 Hz, 1H), 6.89 (d, J= 4.0 Hz, 1H), 7.13 (d, J= 4.0 Hz, 1H), 8.07 (d, J= 5.7 Hz, 1H).	(KBr) 1610, 1594, 1584, 1561, 1442, 1258.

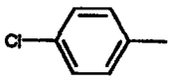
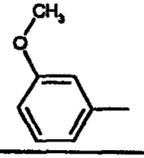
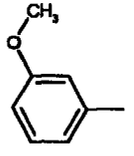
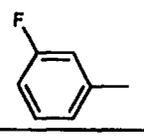
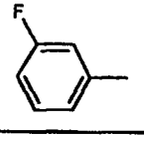
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34	CH_3O-		O	HCl	D	159-162	(300 MHz) (DMSO-d_6) 3.80 (m, 4H), 3.91 (m, 4H), 3.94 (s, 3H), 6.35 (d, J= 6.3 Hz, 1H), 7.18 (d, J= 4.0 Hz, 1H), 7.40 (d, J= 4.0 Hz, 1H) 8.15 (d, J= 6.3 Hz, 1H).	(KBr) 2800-2200 (broad), 1639, 1615, 1592, 1436.
35	CH_3O-		O	base	B	127-129	(300 MHz) ($CDCl_3$) 3.58-3.96 (a.c., 14H, (δ= 3.84, s, y δ= 3.87, s)), 6.02 (d, J= 5.7 Hz, 1H), 6.92 (m, J= 8.8 Hz, 2H), 7.41 (m, J= 8.8 Hz, 2H), 8.05 (d, J= 5.7 Hz, 1H).	(KBr) 1624, 1587, 1562, 1433, 1252.
36	CH_3O-		O	HCl	D	162-164	(300 MHz) ($CDCl_3$) 3.76-3.88 (a.c., 7H, (δ= 3.85, s)), 3.93-4.36 (a.c., 7H, (δ= 4.07, s)), 6.29 (d, J= 6.8 Hz, 1H), 6.93 (d, J= 8.6 Hz, 2H), 7.40 (d, J=8.6 Hz, 2H), 8.10 (d, J= 6.8 Hz, 1H).	(KBr) 2800-2200 (broad), 1631, 1615, 1484, 1428, 1413, 1260, 1244.
37	CH_3O-		O	base	B	123-126	(300 MHz) ($CDCl_3$) 3.37-4.03 (a.c., 11H, (δ= 3.89, s)), 6.04 (d, J= 5.7 Hz, 1H), 7.12 (m, J= 8.8 Hz, 2H), 7.46 (m, J= 8.8 Hz, J'= 5.4 Hz, 2H), 8.06 (d, J= 5.7 Hz, 1H).	(KBr) 1631, 1584, 1565, 1428, 1340, 1249.
38	CH_3O-		O	HCl	D	152-156	(300 MHz) ($CDCl_3$) 3.80 (m, 4H), 3.98-4.28 (a.c., 7H, (δ= 4.07, s)), 6.31 (d, J= 6.8 Hz, 1H), 7.13 (t, J= 8.6 Hz, 2H), 7.44 (dd, J= 8.6 Hz, J'= 5.3 Hz, 2H), 8.11 (d, J= 6.8 Hz, 1H).	(KBr) 2800-2200 (broad), 1630 (banda intensa), 1485, 1439, 1415, 1355, 1266, 1005.
39	CH_3O-		O	base	B	143-144	(300 MHz) ($CDCl_3$) 3.50 (m, 2H), 3.66-4.01 (a.c., 9H, (δ= 3.89, s)), 6.04 (d, J= 5.6 Hz, 1H), 7.40 (system AB, J= 8.7 Hz, 4H), 8.06 (d, J= 5.6 Hz, 1H).	(KBr) 1630, 1580, 1558, 1470, 1439, 1262.

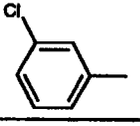
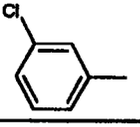
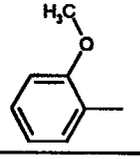
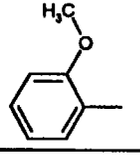
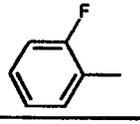
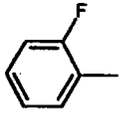
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40	CH_3O-		O	HCl	D	166-168	(300 MHz) ($CDCl_3$) 3.80 (m, 4H), 3.97-4.38 (a.c., 7H, (δ= 4.09, s)), 6.32 (d, J= 6.9 Hz, 1H), 7.37 and 7.43 (system AB, J= 8.6 Hz, 4H), 8.11 (d, J= 6.9 Hz, 1H).	(KBr) 2800-2200 (broad), 1631, 1609, 1492, 1431, 1420,1359, 1262.
41	CH_3O-		O	base	B	78-81	(300 MHz) ($CDCl_3$) 3.50 (m, 2H), 3.66-4.02 (a.c., 12H,(δ= 3.83, s y δ= 3.88, s)), 6.03 (d, J= 5.6 Hz, 1H), 6.99 (a.c., 3H), 7.33 (t, J= 8.0 Hz, 1H), 8.06 (d, J= 5.6 Hz, 1H).	(KBr) 1630, 1584, 1562, 1430, 1338, 1236.
42	CH_3O-		O	HCl	D	158-161	(300 MHz) ($CDCl_3$) 3.61-4.38 (a.c., 14H, (δ= 3.83, s and δ= 4.08, s)), 6,30 (d, J= 6.9 Hz, 1H), 6.96 (a.c.. 3H), 7.34 (t, J= 8.1 Hz, 1H), 8.10 (d, J= 6.9 Hz, 1H),	(KBr) 2800-2200 (broad), 1636, 1605, 1490, 1418, 1270.
43	CH_3O-		O	base	B	106-107	(300 MHz) ($CDCl_3$) 3.49 (m, 2H), 3.66-4.02 (a.c., 9H, (δ= 3.89, s)), 6.04 (d, J= 5.6 Hz, 1H), 7.19 (a.c., 3H), 7.41 (m, 1H), 8.06 (d, J= 5.6 Hz, 1H).	(KBr) 1639, 1593, 1582, 1459, 1439, 1342.
44	CH_3O-		O	HCl	D	153-156	(300 MHz) ($CDCl_3$) 3.56-4.43 (a.c., 11H, (δ= 4.09, s)), 6,32 (d, J= 6.9 Hz, 1H), 7.18 (a.c., 3H), 7.43 (m, 1H), 8.11 (d, J= 6.9 Hz, 1H).	(KBr) 2800-2200 (broad), 1639, 1610, 1489, 1415, 1288, 1266.

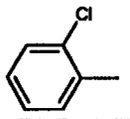
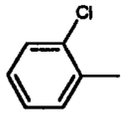
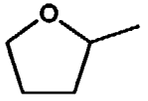
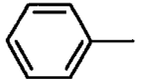
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45	CH_3O-		O	base	B	94-96	(300 MHz) ($CDCl_3$) 3.49 (m, 2H), 3.70-4.00 (a.c., 9H, (δ= 3.89, s)), 6,04 (d, J= 5.7 Hz, 1H), 7.29-7.45 (a.c., 4H), 8.07 (d, J= 5.7 Hz, 1H).	(KBr) 1645, 159[illegible] 1561, 1433, 1256.
46	CH_3O-		O	HCl	D	166-170	(300 MHz) ($CDCl_3$) 3.60-3.97 (a.c., 4H), 3.98-4.37 (a.c., 7H, (δ= 4.08, s)), 6.31 (d, J= 7.0 Hz, 1H), 7.29 (m, 1H), 7.42 (a.c., 3H), 8.11 (d, J= 7.0 Hz, 1H).	(KBr) 2800-2200 (broad), 1632, 1611, 1597, 1488, 1414, 1286.
47	CH_3O-		O	base	B	113-115	(300 MHz) ($CDCl_3$) 3.33 (m, 2H), 3.72-3.99 (a.c., 12H, (δ= 3.84, s y δ= 3.88, s)), 6.02 (d, J= 5.6 Hz, 1H), 6.93 (d, J= 8.6 Hz, 1H), 7.02 (m, 1H), 7.28 (m, 1H), 7.38 (m, 1H), 8.05 (d, J= 5.6 Hz, 1H).	(KBr) 1619, 1584, 1562, 1241.
48	CH_3O-		O	HCl	D	163-164	(300 MHz) ($CDCl_3$) 3.51 (m, 2H), 3.75-4.33 (a.c., 12 H, (δ= 3.85, s and δ= 4.09, s)), 6.28 (d, J= 7.0 Hz, 1H), 6.95 (d, J= 8.3 Hz, 1H), 7.02 (m, 1H), 7.25 (m, 1H), 7.40 (m, 1H), 8.10 (d, J= 8.3 Hz, 1H).	(KBr) 2800-2200 (broad), 1644, 1628, 1611, 1490, 1261.
49	CH_3O-		O	base	B	102-103	(300 MHz) ($CDCl_3$) 3.40 (broad, 2H), 3.77-3.98 (a.c., 9H, (δ= 3.89, s)), 6.03 (d, J= 5.6 Hz, 1H), 7.12 (m, 1H), 7.23 (m, 1H), 7.42 (m, 2H), 8.06 (d, J= 5.6 Hz, 1H).	(KBr) 1641, 1595, 1561, 1466.
50	CH_3O-		O	HCl	D	148-152	(300 MHz) ($CDCl_3$) 3.58 (broad, 2H), 3.82-4.39 (a.c., 9H, (δ= 4.08, s)), 6.31 (d, J= 6.9 Hz, 1H), 7.13 (m, 1H), 7.25 (m, 1H), 7.44 (m, 2H), 8.11 (d, J= 6.9 Hz, 1H).	(KBr) 2800-2200 (broad), 1643, 1612, 1490, 1430, 1418, 1287, 1260.

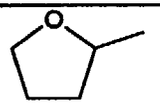
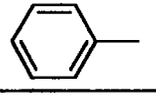
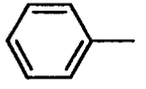
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51	CH_3O-		O	base	B	112-115	(300 MHz) ($CDCl_3$) 3.32 (m, 2H), 3.71-4.00 (a.c., 9H, (δ= 3.88, s)), 6.03 (d, J= 5.6 Hz, 1H), 7.30-7.46 (a.c., 4H), 8.06 (d, J= 5.6 Hz, 1H).	(KBr) 1640, 1561.
52	CH_3O-		O	HCl	D	152-154	(300 MHz) ($CDCl_3$) 3.49 (m, 2H), 3.73-4.40 (a.c., 9H, (δ= 4.08, s)), 6.30 (d, J= 6.7 Hz, 1H), 7.25-7.48 (a.c., 4H), 8.10 (d, J= 6.7 Hz, 1H).	(KBr) 2800-2200 (broad), 1643, 1609, 1492, 1431, 1415, 1288, 1258.
53	CH_3O-		O	base	B	90-91	(300 MHz) ($CDCl_3$) 1.82-2.13 (a.c., 3H), 2.31 (m, 1H), 3.58 (m, 2H), 3.67-3.82 (a.c., 4H), 3.82-3.98 (a.c., 7H, (δ= 3.87, s)), 4.63 (dd, J= 7.4 Hz, J'= 5.3 Hz, 1H), 6.00 (d, J= 5.6 Hz, 1H), 8.03 (d, J= 5.6 Hz, 1H)	(KBr) 1653, 1596, 1586, 1564, 1505, 1239, 987.
54	CH_3O-		S	base	C	125-129	(300 Mhz) ($CDCl_3$) 3.68 (m, 2H), 3.82 (m, 2H), 3.88 (s,3H), 4.07 (m, 2H), 4.48 (m, 2H), 6.06 (d, J= 5.7 Hz, 1H), 7.29-7.41 (a.c., 5H), 8.08 (d, J= 5.7 Hz, 1H).	(KBr) 1589, 1561, 1470, 1233.

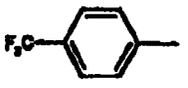
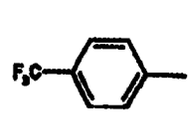
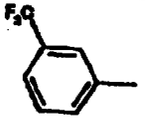
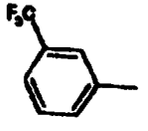
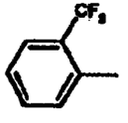
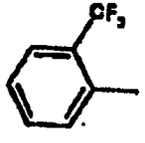
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Example	R_1	R_2	X	Base or Salt	Procedure	m.p. (°C)	^{1}H RMN (MHz) (Solvent) δ	IR cm^{-1}
55	CH_3O-		O	HCl	D	149-151	(300 MHz) ($CDCl_3$) 1.84-2.14 (a.c., 2H), 2.30 (m, 1H) , 3.41-4.53 (a.c., 13H, (δ=4.06, s)), 4.57 (t, J=6.3 Hz, 1H), 6.29 (d, J=6.9 Hz, 1H), 8.12 (d, J=6.9 Hz, 1H).	(KBr) 2800-2200 (broad) , 1644, 1609, 1491, 1241, 1217.
56	CH_3O-		S	HCl	D	151-154	(300 MHz) ($CDCl_3$) 3.87 (broad, 2H), 4.09 (s,3H), 4.22 (broad, 4H), 4.53 (broad. 2H), 6.33 (d, J=6,2 Hz, 1H), 7.27-7.44 (a.c., 5H), 8.12 (d, J=6.2 Hz, 1H).	(KBr) 2800-2200 (broad) 1637, 1604, 1494, 1212.
57	CH_3O-		O	HCl	D	136-138	(300 Mhz) ($CDCl_3$) 3.61-4.37 (a.c., 11H, (δ=4.08, s)), 6.30 (d, J= 7.2 Hz, 1H), 7.43 (m, 5H), 8.10 (d, J=7.2 Hz, 1H).	(KBr) 2800-2200 (broad), 1643, 1637, 1629, 1611, 1488, 1265.

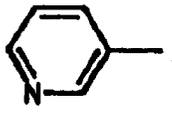
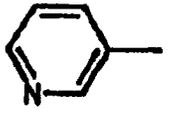
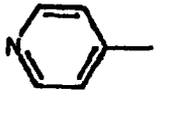
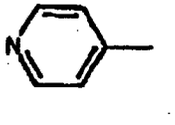
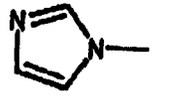
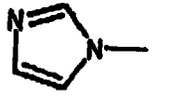
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58	CH_3O-		O	base	B	123-126	(300 MHz) ($CDCl_3$) 3.45 /m, 2H), 3.74-3.99 (a.c., 9H, (δ=3.88, s)), 6.04 (d, J=5.6 Hz, 1H), 7.56 and 7.71 (system AB, J=8,0 Hz, 4H), 8.06 (d, J=5.6 Hz, 1H).	(KBr) 1645, 159[illegible] 1561, 1433, 1256.
59	CH_3O-		O	HCl	D	140-143	(300 MHz) ($CDCl_3$) 3.57-4.29 (a.c., 11H, (δ=4.08, s)), 7.31 (d, J= 6.7 Hz, 1H), 7.55 and 7.73 (system AB, J= 8.2 Hz, 4H), 8.11 (d, J=6.7 Hz, 1H).	(KBr) 2800-2200 (broad), 1640, 1611, 1491, 1327, 1264.
60	CH_3O-		O	base	B	oil	(300 MHz) ($CDCl_3$)) 3.49 (m, 2H), 3.73- 4.00 (a.c., 9H, (δ=3.88, s)), 6.04 (d, J=5.6 Hz, 1H), 7.53-7.78 (a.c., 4H), 8.06 (d, J= 5.6 Hz, 1H).	(film) 1643, 1587, 1567, 1332.
61	CH_3O-		O	HCl	D	177-179	(300 MHz) ($CDCl_3$) 3.55-4.40 (a.c. 11H, (δ=4.08, s)). 6.32 (d. J= 7.1 Hz, 1H), 7.60 (m, 2H), 7.72 (m, 2H), 8.11 (d, J= 7.1 Hz, 1H).	(KBr) 2800-2200 (broad), 1637, 1611, 1490, 1333, 1322, 1264.
62	CH_3O-		O	base	B	93-97	(300 MHz) ($CDCl_3$) 3.24 (m, 2H), 3.75 (m, 2H), 3.82-3.96 (a.c., 7H, (δ=3.87, s)), 6.03 (d, J= 5.6 Hz, 1H), 7.36 (d, J= 7.3 Hz, 1H), 7.54 (t, J=7.6 Hz, 1H), 7.62 (t, J= 7.6 Hz, 1H), 7.73 (d, J= 7.3 Hz, 1H), 8.05 (d, J= 5.6 Hz, 1H).	(KBr) 1641, 1587, 1569, 1436, 1341, 1314, 1251
63	CH_3O-		O	HCl	D	155-158	(300 MHz) ($CDCl_3$) 3.42 (broad singlet, 2H), 3.70-4.43 (a.c., 9H, (δ=4.07, s)), 6.30 (d, J= 7.1 Hz, 1H), 7.33 (d, J= 7.2 Hz, 1H), 7,60 (m, 2H), 7.74 (d, J= 7.2 Hz, 1H), 8.08 (d, J= 7.1 Hz, 1H).	(KBr) 2800-2200 (banda ancha), 1645, 1604, 1486, 1317, 1126.

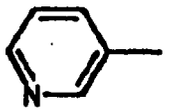
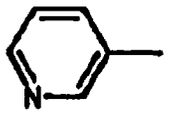
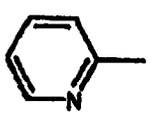
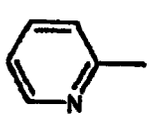
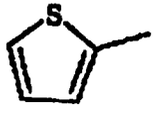
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64	CH_3O-		O	base	B	102-105	(300 MHz) ($CDCl_3$) 3.51 (m, 2H), 3.69-4.00 (a.c., 9H, (=3.88,s)), 6.04 (d, J= 5.6 Hz, 1H), 7.39 (dd, J= 7.7 Hz, J'=5.0 Hz, 1H), 7.79 (d, J= 7.7 Hz, 1H), 8.06 (d, J=5.6 Hz, 1H), 8.70 (m, 2H).	(KBr) 1623, 1589, 1566,1439.
65	CH_3O-		O	2 HCl	D	148-151	(300 MHz) (DMSO-d_6) 3.66-4.42 (a.c., 11H, (δ=3.92, s)), 6.32 (d, J= 6.3 Hz, 1H), 7.78 (dd, J= 7.9 Hz, J'= 5.4 Hz, 1H), 8.14 (d, J= 6.3 Hz, 1H), 8.22 (d, J= 7.9 Hz, 1H), 8.81 (d, J= 5.4 Hz, 1H), 8.85 (s, 1H).	(KBr) 2800-2200 (broad), 1641, 1609, 1493, 1442, 1268
66	CH_3O-		O	base	B	149-152	(300 MHz) ($CDCl_3$) 3.43 (m, 2H), 3.75-3.98 (a.c., 9H, (δ=3.88,s)), 6.05 (d, J= 5.7 Hz, 1H), 7.32 (m, 2H), 8.06 (d, J= 5,7 Hz, 1H), 8.73 (m, 2H).	(KBr) 1638, 1589, 1561, 1340.
67	CH_3O-		O	2 HCl	D	157-161	(300 MHz) (DMSO-d_6) 3.42 (m, 2H), 3.73-4.05 (a.c., 9H, (δ=3.94, s)), 6.37 (d, J= 6.5 Hz, 1H), 7.98 (d, J= 5.5 Hz, 2H), 8.14 (d, J= 6.5 Hz, 1H), 8.96 (d, J= 5.5 Hz, 1H).	(KBr) 2800-2200 (broad), 1634, 1610, 1488, 1415, 1356, 1287, 1265.
68	CH_3O-		O	base	B	127-131	(300 MHz) ($CDCl_3$) 3.68 (m, 4H), 3.89 (s, 3H), 3.92 (m, 4H), 6.06 (d, J= 5.7 Hz, 1H), 7.12 (s, 1H), 7.24 (s, 1H), 7.91 (s, 1H), 8.07 (d, J= 5.7 Hz, 1H).	(KBr) 1691, 1599, 1556, 1430, 1418, 1241, 988
69	CH_3O-		O	HCl	D	160-163	(300 MHz) (DMSO-d_6) 3.68 (m, 4H), 3.95 (s, 3H), 3.98 (m, 4H), 6.35 (d, J= 6.0 Hz, 1H), 7.82 (s, 1H), 8.05 (s, 1H), 8.17 (d, J= 6,0 Hz, 1H), 9.54 (s, 1H).	(KBr) 2800-2200 (broad), 1733, 1639, 1612, 1490, 1416

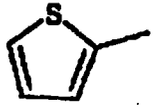
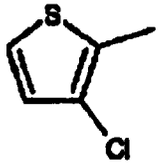
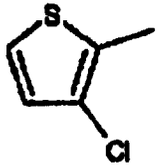
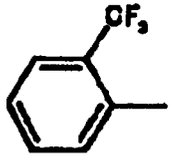
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70	CF_3-		O	base	B	125-126	(300 MHz) ($CDCl_3$) 3.41-4.15 (a.c., 8H), 6.84 (d, J=4.8 Hz, 1H), 7.40 (ddd, J=7.9 Hz, J'= 4.8 Hz, J''= 0.9 Hz, 1H), 7.80 (ddd, J= 7.9 Hz, J'= 2.1 Hz, J''= 1.8 Hz, 1H), 8.53 (d, J= 4.8 Hz, 1H), 8.71 (m, 2H).	(KBr) 1631, 1502, 1434, 1257, 1158.
71	CF_3-		O	HCl	D	149-154	(300 MHz) (DMSO-d_6, TFA) 3.46 (m, 2H), 3.67-4.03 (a.c., 6H), 7.03 (d, J= 4.8 Hz, 1H), 8.05 (dd, J= 8,0 Hz, J'= 5.6 Hz, 1H), 8.56 (d, J= 8.0 Hz, 1H), 8.68 (d, J= 4.8 Hz, 1H), 8.95 (d, J= 5.6 Hz, 1H), 9.04 (s, 1H).	(KBr) 2800-2200 (broad), 1634, 1595, 1524, 1435, 1338, 1273, 1186, 981.
72	CH_3O-		O	base	B	108-111	(300 MHz) ($CDCl_3$) 3.69 (m, 2H), 3.81-4.02 (a.c., 9H, (δ= 3.88, s)), 6.02 (d, J= 5.7 Hz, 1H), 7.37 (m, 1H), 7.70 (d, J= 8.0 Hz, 1H), 7.82 (dt, J= 8.0 Hz, J'= 1.7 Hz, 1H), 8.06 (d, J= 5.7 Hz, 1H), 8.61 (d, J= 5.1 Hz, 1H).	(KBr) 1623, 1595, 1585, 1565, 1473, 1263.
73	CH_3O-		O	2HCl	D	157-161	(300 MHz) (DMSO-d_6, TFA) 3.67 (broad), 3.79-4.07 (a.c., 9H, (δ=3.99, s)), 6.48 (d, J= 6.5 Hz, 1H), 7.63 (m, 1H), 7.78 (m, 1H), 8.09 (m, 1H), 8.19 (d. J= 6.5 Hz. 1H), 8.68 (d, J= 4.6 Hz, 1H).	(KBr) 2800-2200 (broad), 1650, 1606, 1495, 1444, 1265
74	C_2H_5O-		O	base	B	97-99	(300 MHz) ($CDCl_3$) 1.37 (t, J= 7.1 Hz, 3H), 3.77-3.93 (a.c., 8H), 4.33 (q, J= 7.1 Hz, 2H), 6.01 (d, J= 5.6 Hz, 1H), 7.07 (m, 1H), 7.33 (d, J= 3.4 Hz, 1H), 7.47 (d, J= 4.9 Hz, 1H), 8.06 (d, J=5.6 Hz, 1H).	(KBr) 1605, 1583, 1560, 1449, 1438, 1258, 1237.

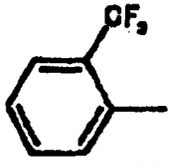
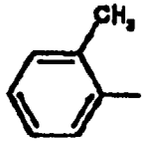
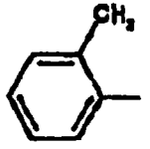
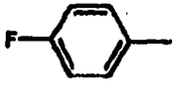
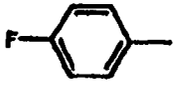
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75	C_2H_5O-		O	HCl	D	138-139	(300 MHz) ($CDCl_3$) 1.45 (t, J=7.1 Hz, 3H), 3.80-4.40 (a.c., (H), 4.50 (q,J= 7.1 Hz, 2H), 6.27 (d, J= 6.9 Hz, 1H), 7.08 (dd, J= 4.9 Hz, J'= 3.8 Hz, 1H), 7.33 (d, J= 3.8 Hz, 1H), 7.50 (d, J= 4.9 Hz, 1H), 8.10 (d, J= 6.9 Hz, 1H).	(KBr) 2800-2200 (broad), 1609, 1434, 1257, 994
76	C_2H_5O-		O	base	B	91-94	(300 MHz) ($CDCl_3$) 1.36 (t, J= 7.1 Hz, 3H), 3.45-3.97 (a.c., 8H). 4.32 (q, J= 7.1 Hz, 2H), 6.01 (d, J= 5.6 Hz, 1H), 6.93 (d, J= 5.2 Hz, 1H), 7.40 (d, J=5.2 Hz, 1H), 8.06 (d, J=5.6 Hz, 1H).	(KBr) 1625, 1558, 1436, 1255
77	C_2H_5O-		O	HCl	D	167-169	(300 MHz) ($CDCl_3$) 1.46 (t, J= 7.0 Hz, 3H), 3.81 (broad, 4H), 3.93-4.42 (a.c., 4H), 4.51 (q, J= 7.0 Hz, 2H), 6.28 (d, J=6.9 Hz, 1H), 6.95 (d, J=5.3 Hz, 1H), 7.44 (d, J= 5.3 Hz, 1H), 8.10 (d, J= 6.9 Hz, 1H).	(KBr) 2800-2200 (broad) 1639, 1617, 1604, 1460, 1440, 1292, 1260, 1203.
78	C_2H_5O-		O	base	B	99-101	(300 MHz) ($CDCl_3$) 1.36 (t, J= 7.1 Hz, 3H), 3.23 (m, 2H), 3.73 (m, 2H), 3.88 (a.c., 4H), 4.31 (q, J= 7.1 Hz, 2H). 6.00 (d, J= 5.6 Hz, 1H), 7.36 (d, J= 7.2 Hz, 1H), 7.54 (m, 1H), 7.62 (m, 1H), 7.73 (m, 1H), 8.05 (d. J= 5.6 Hz, 1H).	(KBr) 1624, 1582, 1437, 1258

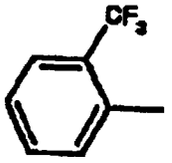
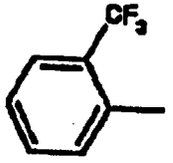
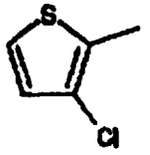
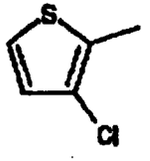
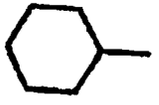
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79	C_2H_5O-		O	HCl	D	146-148	(300 MHz) ($CDCl_3$) 1.45 (t, J= 7.1 Hz, 3H), 3.42 (broad, 2H), 3.68-4.41 (a.c., 6H), 4.50 (m, 2H), 6.27 (d, J= 6.7 Hz, 1H), 7.33 (d, J=7.1 Hz, 1H), 7.61 (m, 2H), 7.74 (d, J= 7.9 Hz, 1H), 8.07 (d, J=6.7 Hz, 1H).	(KBr) 2800-2200 (broad), 1640, 1602, 1437, 1320, 1259
80	CH_3O-		O	base	B	70-73	(300 MHz) ($CDCl_3$) 2.33 (s, 3H), 3.30 (broad, 2H), 3.74 (broad, 2H), 3.83-3.98 (a.c., 7H, (δ=3.87, s)), 6.03 (d, J= 5.5 Hz, 1H), 7.15-7.34 (m. 4H), 8.05 (d, J= 5.5 Hz, 1H).	(KBr) 1621, 1598, 1559, 1430, 1263
81	CH_3O-		O	HCl	D	151-153	(300 MHz) ($CDCl_3$) 2.30 (s, 3H), 3.48 (broad, 2H), 3.90-4.35 (a.c., 9H, (=4.08, s)), 6.29 (d, J= 6.0 Hz. 1H), 7.13-7.32 (a.c., 4H), 8.10 (d, J= 6.0 Hz, 1H).	(KBr) 2800-2200 (broad), 1643, 1630, 1610, 1491, 1415, 1263
82	$(CH_3)_2CHO$		O	base	B	112-115	(300 MHz) ($CDCl_3$) 1.31 (d, J= 6.0 Hz, 6H), 3.40-4.00 (a.c., 8H). 5.24 (h, J= 6.0 Hz, 1H), 5.96 (d, J= 5.7 Hz, 1H), 7.13 (t, J= 7.8 Hz, 2H), 7.46 (m, J= 8.8 Hz, J'= 5.4 Hz, 2H), 8.03 (d, J= 5.7 Hz, 1H).	(KBr) 1632, 1583, 1557, 1450, 1236
83	$(CH_3)_2CHO$		O	HCl	D	163-166	(300 MHz) ($CDCl_3$) 1.41 (d, J= 6.0 Hz, 6H), 3.65-4.40 (a.c., 8H), 5.39 (m, 1H), 6.22 (d, J= 6.9 Hz, 1H), 7.13 (m, 2H), 7.43 (m, 2H), 8.07 (d, J=6.9 Hz, 1H).	(KBr) 2800-2200 (broad) 1636, 1608, 1458, 1432, 1259

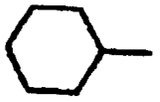
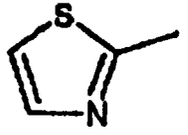
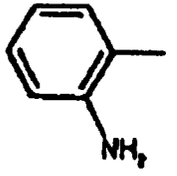
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84	$(CH_3)_2CHO$		O	base	B	---	(300 MHz) ($CDCl_3$) 1.29 (d, J= 6.0 Hz, 6H), 3.24 (m, 2H), 3.72 (m, 2H), 3.89 (m, 4H), 5.24 (h, J= 6.0 Hz, 1H), 5.97 (d, J=5.7 Hz, 1H), 7.36 (d, J= 7.2 Hz, 1H), 7.58 (m, 2H), 7.73 (d, J= 7.8 Hz, 1H), 8.04 (d, J= 5.7 Hz, 1H).	(KBr) 1651, 1581, 1563, 1317
85	$(CH_3)_2CHO$		O	HCl	D	159-161	(300 MHz) ($CDCl_3$) 1.42 (d, J=5.6 Hz, 6H), 3.43 (broad, 2H), 3.67-4.44 (a.c., 6H), 5.40 (m, 1H), 6.22 (d, J= 6.8 Hz, 1H), 7.33 (d, J= 6.9 Hz, 1H), 7.61 (m, 2H), 7.75 (d, J= 7.5 Hz, 1H), 8.05 (d, J= 6.9 Hz, 1H).	(KBr) 2800-2200 (broad), 1640, 1604, 1473, 1317, 1122
86	$(CH_3)_2CHO$		O	base	B	68-70	(300 MHz) ($CDCl_3$) 1.33 (d, J= 6.1 Hz, 6H), 3.40-4.07 (a.c., 8H), 5.26 (h, J= 6.1 Hz, 1H), 5.97 (d, J= 5.7 Hz, 1H), 6.93 (d, J= 5.3 Hz, 1H), 7.39 (d, J= 5.3 Hz, 1H), 8.05 (d, J= 5,7 Hz, 1H).	(KBr) 1631, 1583, 1557, 1445
87	$(CH_3)_2CHO$		O	HCl	D	148-150	(300 MHz) ($CDCl_3$) 1.42 (d, J= 6.1 Hz, 6H), 3.66-4.44 (a.c., 8H), 5.39 (h, J= 6.1 Hz, 1H), 6.23 (d, j= 5.7 Hz, 1H), 6.95 (d, J= 5.3 Hz, 1H), 7.44 (d, J= 5.3 Hz, 1H), 8.08 (d, J= 5.7 Hz, 1H).	(KBr) 2800-2200 (broad) 1644, 1612, 1462, 1446, 1313, 1282, 1250
88	CH_3O-		O	base	B	109-111	(300 MHz) ($CDCl_3$) 1.28 (m, 3H), 1.46-1.89 (a.c., 7H), 2.50 (tt, J= 11,2 Hz, J'= 3.3 Hz, 1H), 3.56 (m, 2H), 3.69 (m, 2H), 3.81 (m, 4H), 3.89 (s, 3H), 6.02 (d, J= 5.5 Hz, 1H), 8.06 (d, J=5.5 Hz, 1H).	(KBr) 1629, 1591, 1556, 1339, 1239, 992

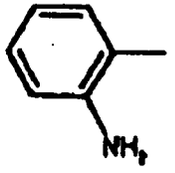
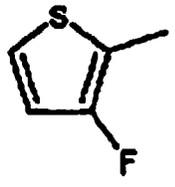
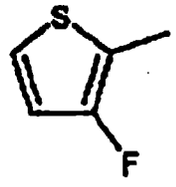
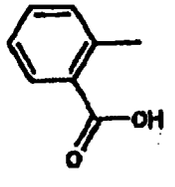
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89	CH_3O-		O	HCl	D	121-124	(300 MHz) ($CDCl_3$) 1.27 (m, 3H), 1.53 (m, 2H), 1.75 (a.c., 5H), 2.47 (m, 1H), 3.75 (broad singlet, 4H), 3.92 (m, 2H), 4.07 (s, 3H), 4.29 (m, 2H), 6.30 (d, J= 7.0 Hz, 1H), 8.11 (d, J= 7.0 Hz, 1H).	(KBr) 2800-2200 (broad), 1632, 1604, 1487, 1431, 1212
90	C_2H_5O-		O	base	B	136-138	(300 MHz) ($CDCl_3$) 1.37 (t, J= 7.0 Hz, 3H), 3.38-4.00 (a.c., 8H), 4.32 (q, J= 7.0 Hz, 2H), 6.01 (d, J= 5.7 Hz, 1H), 7.12 (t, J= 8.5 Hz, 2H), 7.45 (m, 2H), 8.06 (d. J= 5.7 Hz, 1H).	(KBr) 1616, 1590, 1557, 1432
91	C_2H_5O-		O	HCl	D	155-157	(300 MHz) ($CDCl_3$) 1.46 (t, J= 7.0 Hz, 3H), 3.67-4.38 (a.c., 8H), 4.51 (q, J= 7.0 Hz, 2H), 6,28 (d, J= 6.8 Hz, 1H), 7.14 (t, J= 8.8 Hz, 2H), 7.45 (m, 2H), 8.11 (d, J= 6.8 Hz, 1H).	(KBr) 2800-2200 (broad), 1636, 1606, 1458, 1436, 1258
92	CH_3O-		O	base	B	106-108	(300 MHz) ($CDCl_3$) 3.85-3.99 (a.c., 9H, (δ=3.90, s)), 4.50 (m, 2H), 6.03 (d, J= 5.7 Hz, 1H), 7.56 (d, J= 3.2 Hz, 1H), 7.91 (d, J= 3.2 Hz, 1H), 8.07 (d, J= 5.7 Hz, 1H)	(KBr) 1596, 1565, 1496, 1442, 1257, 1004
93	CH_3O-		O	base	B	145-147	(300 MHz) ($CDCl_3$) 3.70 (broad, 4H), 3.83-3.90 (a.c., 7H, (δ=3.88, s)), 4.35 (s, 2H), 6.03 (d, J= 5.6 Hz, 1H), 6.74 (m, 2H), 7.11 (m, 1H), 8.06 (d, J= 5.6 Hz, 1H).	(KBr) 3444, 3323, 1617, 1586, 1566, 1498, 1467, 1260

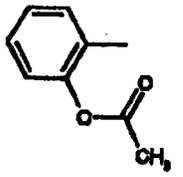
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94	CH_3O-		O	2 HCl	D	155-157	(300 MHz) (DMSO-d_3) 3.61 (broad, 4H), 3.94 (s, 7H), 6.37 (d, J= 6.5 Hz, 1H), 7.10 (t, J= 7.5 Hz, 1H), 7.20 (d, J= 7.5 Hz, 1H), 7.32 (d, J= 7.5 Hz, 1H), 7.38 (t, j= 7.5 Hz, 1H), 8.14 (d, J= 6.5 Hz, 1H).	(KBr) 3700-2200 (broad), 1614, 1491, 1439, 1257.
95	CH_3O-		O	base	B	oil	(300 MHz) ($CDCl_3$) 3.73 (broad, 4H), 3.86-3.99 (a.c., 7H, (δ=3.89,s)), 6.03 (d, J= 5.7 Hz, 1H), 6.78 (d, J= 5.4 Hz, 1H), 7.37 (dd, J= 5.4 Hz, J'= 3.7 Hz, 1H), 8.06 (d, J= 5.7 Hz, 1H).	(KBr) 1626, 1586, 1469, 1443
96	CH_3O-		O	HCl	D	156-157	(300 MHz) ($CDCl_3$) 3.86 (broad singlet, 4H), 4.08 (s, 5H), 4.23-4.45 (m, 2H), 6.31 (d, J= 6.9 Hz, 1H), 6.80 (d, J=5.5 Hz, 1H), 7.41 (dd, J= 5.5 Hz, J'= 3.7 Hz, 1H), 8.12 (d, J= 6.9 Hz, 1H).	(KBr) 2800-2200 (broad), 1618, 1482, 1413, 1262, 995
97	CH_3O-		O	---	B	186-188	(300 MHz) ($CDCl_3$) 3.25 (m, 2H), 3.65-3.99 (a.c., 9H, (δ=3.86,s)), 6.02 (d, J= 5.8 Hz, 1H), 7.30 (d, J= 7.6 Hz, 1H), 7.45 (t, J= 7.6 Hz, 1H=, 7.57 (t, J= 7.6 Hz, 1H), 8.06 (m, 2H).	(KBr) 3600-2500 (broad), 1711, 1583, 1444, 1342, 1266

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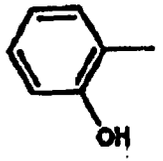
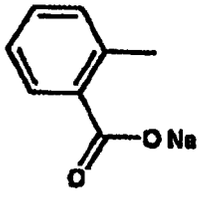
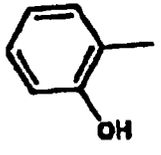
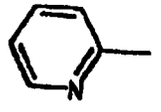
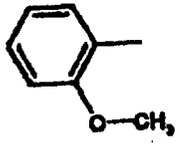
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98	CH_3O-		O	base	B	139-142	(300 Mhz) ($CDCl_3$) 2.27 (s, 3H), 3.38 (m, 2H), 3.74-3.94 (a.c., 9H, (=3,87, s)), 6.03 (d, J= 5.7 Hz, 1H), 7.18 (d, J= 8.2 Hz, 1H), 7.32 (m, 2H), 7.44 (m, 1H), 8.05 (d, J= 5.7 Hz, 1H)	(KBr) 1764, 1566, 1429, 1259, 1194	

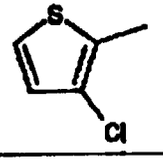
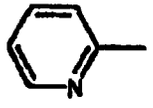
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99	CH_3O-		O	base	B	186-188	(300 MHz) ($CDCl_3$) 3.80 (m, 4H), 3.86-3.95 (a.c., 7H), (δ=3.89)), 6.04 (d, J=5,7 Hz, 1H), 6.87 (t, J=7.5 Hz, 1H), 7.03 (d, J=8.1 Hz, 1H), 7.28 (m, 1H), 7.35 (m, 1H), 8.06 (d, J=5.7 Hz, 1H).	KBr (3500-2500 (broad), 1566, 1443, 1335, 1229.
100	CH_3O-		O	---	D	---	(300 MHz) (DMSO-d_6) 3.06 (m, 2H), 3.38-3.72 (a.c., 4H), 3.79 (s, 3H), 3.92 (m, 2H), 6.04 (d, J=5.4 Hz, 1H), 7.02 (m, 1H), 7.27 (m, 2H), 7.79 (m, 1H), 8.06 (d, J=5,4 Hz, 1H).	(KBR) 1624, 1588, 1563, 1382.
101	CH_3O-		O	HCl	D	158-159	(300 MHz) (DMSO-d_6) 3.34 (m, 2H), 3.62-4.01 (a.c., 9H, (δ=3.93)), 6.36 (d, J=6.3 Hz, 1H), 6.84 (t, J=7.2 Hz. 1H), 6.91 (d, J=8.1 Hz, 1H), 7.15 (m, 1H), 7.23 (m. 1H), 8.13 (d, J=6.3 Hz, 1H).	(KBr) 3500-2500 (broad), 1622, 1493, 1361,1289, 1211.
102	CH_3O-		O	HCl	D	151-153	(300 MHz) ($CDCl_3$) 3.93 (broad s, 4H), 4.00-4.40 (a.c., 7H, (δ=4.07, s)), 6.29 (d, J=6.8 Hz, 1H), 7.40 (m, 1H), 7.72 (broad d, J=7.2 Hz, 1H), 7.84 (dt, J=7.6 Hz, J'=1.7 Hz, 1H), 8.11 (d, J=6.8 Hz, 1H), 8.59 (d, J=5.0 Hz, 1H).	(KBr) 3500-2500 (broad), 1616, 1486, 1413, 1311, 1212.
103	CH_3O-		O	NO_3H	D	137-139	(300 MHz) ($CDCl_3$) 3.31-3.64 (a.c., 2H), 3.70-4.24 (a.c., 12H, (δ=3.85, s)(δ=4.08, s)), 6.30 (d, J=6.9 Hz, 1H), 6.95 (8.2 Hz, 1H), 8.23 (d, J=6.9 Hz, 1H).	(KBr) 3500-2500 (broad), 1646, 1485, 1281, 1000, 750.

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104	CH_3O-		O	NO_3H	D	129-131	(300 Mhz) ($CDCl_3$) 3.81 (broad, 4H), 4.02 (broad, 4H), 4.08 (s, 3H), 6.33 (d, J= 7.0 Hz, 1H), 6.95 (d, J= 5.0 Hz, 1H), 8.25 (d, J= 7.0 Hz, 1H)	(KBr) 3500-2900 (broad), 1643, 1456, 1411, 1258, 077
105	CH_3CH_2O-		O	base	B	87-900	(300 Mhz) ($CDCl_3$) 1.36 (t, J= 7.0 Hz, 3H), 3.68 (m, 2H), 3.78-3.99 (a.c., 6H), 4.33 (q, J= 7.0 Hz, 2H), 6.00 (d, J= 5,6 Hz, 1H), 7.69 (d, J= 7.9 Hz, 1H), 7.82 (dt, J= 7.9 Hz, J'= 1.5 Hz, 1H), 8.05 (d, J= 5.6 Hz, 1H), 8.60 (d, J= 4.8 Hz, 1H).	(KBr) 1634, 1578, 1557, 1447, 1237, 1000

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Sleep-inducing activity in mice

The sleep-inducing activity of the products of the present invention have been studied, evaluating the their capacity to increase the sleep time induced by barbital, according to a modification of the method described by David Sudgen (*J. Pharmacol. Exp. Ther.*, **1983**, 227, 3).

Fifteen minutes after the administration of barbital (150 mg/Kg, i.v.), the mice were treated with the product of the study at an initial dose of 100 mg/Kg (i.p.). For the most active products a dosage efficacy 50 (DE_{50}) was determined. The results for some of the products of the invention are shown in Table 2, taking meprobamate as the reference product.

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Table 2. Capacity to increase the sleep time induced by barbital

Example	% Activity (sleep) Dosage 100 mg/kg	DE_{50} (mg/kg)
2	93	14.4
4	100	8.7
8	97	9.7
9	67	28.1
10	74	11.6
11	89	10.5
13	77	41.3
15	86	8.2
17	56	84.2
18	82	27.3
22	57	75
24	69	41.5
26	60	74.1
30	75	37.2
32	73	56.5
34	98	7
55	70	31
57	100	1.6
59	101	14
61	102	4.5
63	103	4
65	100	7.7
67	96	15
69	97	10
73	98	9.5
81	99	8.3
83	100	5.3
87	101	10
89	102	8
91	81	10
92	98	8
94	84	5.2
96	97	3
Meprobamate	54	84.5

General anaesthetic activity

The general anaesthetic activity was study in mice, injecting the product of the study in the caudal vein. The start and duration time of sleep were recorded. The results for some of the products of the patent are shown in Table 3 and it can be seen that they show a clear anaesthetic activity with respect to the reference compound (Propofol), with the animals recovering later.

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Table 3 Anaesthetic activity in mice. I.V. administration.

Example	Dosage (mg/kg)	Start (s)	Duration (min)
2	80 40	Immediate 12	5.3 0.6
4	80 40	Immediate 15	7.4 1.3
15	80 40	20 15	1.9 1.4
30	80 40	30 30	7.9 1.8
34	80 40	Immediate No	1.5 0
57	80	Immediate	11
59	80	20	3.4
61	80	10	1.6
65	80	20	8.6
63	80	Immediate	14.8
71	80	60	5.6
73	80	Immediate	9
77	80	Immediate	10
79	80	Immediate	19
81	80	Immediate	10
85	80	Immediate	8.4
87	80	Immediate	10
89	80	Immediate	4
91	80	Immediate	7
92	80	Immediate	5
96	80	Immediate	6
101	80	Immediate	2
Propofol	106 120 80	30 20 No	6.2 3.9 0

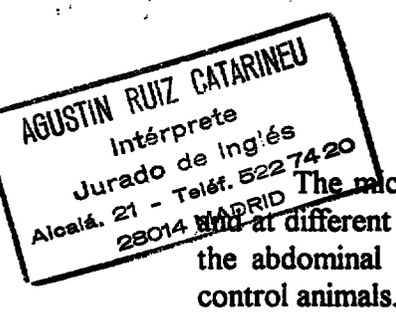
Sedative activity

The sedative activity of some of the products on the locomotive activity of mice at different dosages has been studied. The technique described by T.G. Heffneren *J. Pharm. Exp. Ther.*, **1989**, 251, 105-112 has been followed. The measurement of the locomotive activity is carried out by dividing the rats into groups of four and determining the movement of the animals in an automated fashion using a video installation and the SMART program (Letica S.A.) for image analysis. The measurement of activity started 5 minutes after the administration of the product via i.p. and continued for twenty minutes. The results (Figure 1) show the sedative effect of the compounds tested.

Muscular relaxant activity

The muscular relaxant activity has been studied in the products of the invention by evaluated their effect on the abdominal body tone of mice, following the method described by S. IRWING (Gordon Res. Conf. On Medicinal Chem., 1959, p. 133).

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The mice received the products under study at a dosage of 80 mg/kg, via I.p., and at different times after administration (1/2, 1, 2, 3, 4 and 5 hours) the body tone and the abdominal tone was evaluated looking at the muscular tension compared to the control animals.

The results listed in Table 4 show that many of the products are noticeably active as muscular relaxants. This effect lasts longer than for propofol or zolpidem, which were used as reference products.

Table 4. Miorelaxant activity in the Irwing mouse test. [Dosage = 80 mg/kg, i.p.]

Example	% muscular relaxation at a time of:					
	1/2 H	1 H	2 H	3 H	4 H	5 H
4	100	90	10	0	0	0
34	60	70	80	85	40	40
57	100	100	100	80	55	0
63	100	100	90	75	20	0
71	100	100	100	40	10	0
73	100	100	100	0	0	0
75	100	100	100	80	80	60
77	100	100	100	60	0	0
79	100	100	100	65	0	0
83	90	90	90	70	50	0
92	100	100	100	0	0	0
propofol	100	100	70	0	0	0

Analgesic activity

The analgesic activity of the products of the invention have been studied by evaluation of their effect in the test of contortions induced by phenylbenzoquinone in mice, following the method described by Siegmund E., and coworkers (Proc. Soc. Exp. Biol. Med. 1957, 95: 729-731).

The mice received the products of the study, a different dosage levels, and one hour later they received an injections i.p. of 5 mg/kg of phenylbenzoquinone. The contortions of the mice were registered for the following fifteen minutes and compared with the contortions of the control group. The DE_{50} (dosage efficacy 50) of the compound of Example 4 is shown. This compound showed a better analgesic activity than aspirin, both when administered subcutaneously and orally.

Table 5. Analgesic activity. Protection from contortions induced by phenylbenzoquinone in mice.

Example	DE_{50} (mg/kg, s.c.)	DE_{50} (mg/kg, o.a.)
Aspirin	84	120
4	48	72

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Pharmaceutical formulations

1. For injections (im/iv):

Compound of Example 4	5 mg
Sodium chloride	c.s.
HCl 0.1 N or NaOH	c.s.
Water for injection c.s.p.	3 ml

2. Capsules

Compound of Example 4	0.5 to 4.0 mg
Colloidal silicon dioxide	0.5 mg
Magnesium stearate	1.0 mg
Lactose c.s.p.	100 mg

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3. Tablets

Compound of Example 4	0.5 to 4.0 mg
Colloidal silicon dioxide	0.5 mg
Magnesium stearate	1.0 mg
Sodium croscarmelose	60 mg
Lactose c.s.p.	100 mg

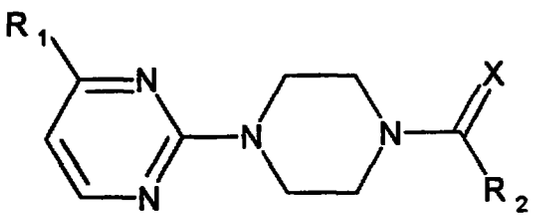
Formula B (humid granulation)

Compound of Example 4	0.5 to 4.0 mg
Colloidal silicon dioxide	0.5 mg
Magnesium stearate	1.0 mg
Povidone K-30	5.0 mg
Sodium carboxymethylstarch	5.0 mg
Microcrystalline cellulose	20 mg
Lactose c.s.p.	100 mg

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CLAIMS

1. A derivative of acyl-piperazinyl-pyrimidine of general formula (I)



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(I)

where

X is an oxygen or sulphur atom;

R_1 is a C_{1-4} alkoxy or trifluoromethyl radical;

R_2 is a C_{1-6} alkoxy radical; C_{3-6} saturated cycloalkyl; heterocycloalkyl consisting of a ring of 3 to 6 atoms in which the heteroatom is selected from an atom of oxygen, sulphur or nitrogen, optionally N-substituted; phenyl optionally substituted with 1, 2 or 3 identical or different substituents selectred from fluorine, chlorine, bromine, amino, acetamido, nitro, methyl, trifluoromethyl and methoxy; arylalkyl consisting of a C_{1-3} alkyl group substituted by a phenyl radical optionally substituted by 1, 2 or 3 identical or different substituents selected from fluorine, chlorine, bromo, amino, acetamido, nitro, methyl, trifluoromethyl and methoxy; heteroaryl consisting of a 5 or 6 heteroatom ring, optionally substituted, or of fused heteroaromatic systems optionally substituted, of 9 or 10 atoms consisting of 1 or 2 heteroatoms selected from oxygen, sulphur and nitrogen, selecting the aforementioned substituents from flourine, chlorine, bromine, amino, acetamido, nitro, methyl, trifluoromethyl and methoxy; and heteroarylalkyl consisting of an alkyl group of 1 to 3 carbon atmos substituted with a heteroaryl radical consisting of a 5 or 6 member heteroaromatic ring, optionally substituted, or of fused 9 to 10 member heteroaromatic systems, optionally substituted with 1 or 2 heteroatoms selected from oxygen, sulphur and nitrogen, selected the aforementioned substituents from fluorine, chlorine, bromine, amino, acetamido, nitro, methyl, trifluoromethyl and methoxy; and their physiologically acceptable salts.

2. A compound according to claim 1, in which R_1 is methoxy, ethoxy, propoxy, isopropoxy, butoxy, *sec*-butoxy or *tert*-butoxy.

3. A compound according to claim 1, in which R_2 is methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *sec*-butyl, *tert*-butyl, pentyl, isopentyl, neopentyl or hexyl.

4. A compound according to claim 1, in which R_2 is cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl.

5. A compound according to claim 1, in which R_2 is 2-azyridinyl, 2-tetrahydrofuryl, 3-tetrahydrofuryl, 2-tetrahydrothienyl, 3-tetrahydrothienyl, 2-azetidinyl, 2-pyrrolidinyl, 3-pyrrolidinyl, 2-piperidinyl, 3-piperidinyl or 4-piperidinyl.

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6. A compound according to claim 1, in which R_2 is 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-clorophenyl, 3-clorophenyl, 4-clorophenyl, 2-bromophenyl, 3-bromophenyl, 4-bromophenyl, 2-aminophenyl, 3-aminophenyl, 4-aminophenyl, 2-nitrophenyl, 3-nitrophenyl, 4-nitrophenyl, 2-acetamidophenyl, 3-acetamidophenyl, 4-acetamidophenyl, 2-nitrophenyl, 3-nitrophenyl, 4-nitrophenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-(trifluoromethyl)phenyl, 3-(trifluoromethyl)phenyl, 4-(trifluoromethyl)phenyl, 2-metoxyphenyl, 3-metoxyphenyl, 4-metoxyphenyl, 2,3-difluorophenyl, 3,4-difluorophenyl, 2,4-difluorophenyl, 2,3-dibromophenyl, 3,4-dibromophenyl, 2,4-dibromophenyl, 2,3-dimethylphenyl, 3,4-dimethylphenyl, 2,4-dimethylphenyl, 2,3-dimethoxyphenyl, 3,4-dimethoxyphenyl, 2,4-dimethoxyphenyl.

7. A compound according to claim 1, in which R_2 is phenylmethyl, 1-phenylethyl, 2-phenylethyl, 3-phenylpropyl, optionally substituted at the aromatic ring.

8. A compound according to claim 1, in which R_2 is 2-furyl, 3-furyl, 2-thienyl, 3-thienyl, 3-methyl-2-thienyl, 5-methyl-2-thienyl, 3-methoxy-2-thienyl, 3-chloro-2-thienyl, 5-chloro-2-thienyl, 2-pyrrolyl, 3-pyrrolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, 2-indolyl, 3-indolyl, 2-benzo[b]thienyl, 3-benzyo[b]thienyl, 3-chloro-2-benzo[b]thienyl, pirazolyl, imidazolyl, pyrimidinyl, piridazinyl, pirazinyl, benzimidazolyl, quinolyl, oxazolyl or thiazolyl

9. A compound according to claim 1, in which R_2 is 2-thienylmethyl, 2-benzo[b]thienmethyl or 3-(4-chloropirazolyl)propyl.

10. A compound according to claim 1, selected from the following group:

- 2-[4-(2-furylcarbonyl)-1-piperazinyl]-4-methoxypirimidine,
- 2-[4-(2-furylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 4-methoxy-2-[4-(2-thienylcarbonyl)-1-piperazinyl]pyrimidine,
- 4-methoxy-2-[4-(2-thienylcarbonyl)-1-piperazinyl]pyrimidine chlorohydrate,
- 2-(4-acetyl-1-piperazinyl)-4-methoxypyrimidine,
- 2-{4-[4-(4-chloropyrazolyl)butanoyl]-1-piperazinyl}-4-methoxypyrimidine,
- 2-{4-[4-(4-chloropyrazolyl)butanoyl]-1-piperazinyl}-4-methoxypyrimidine chlorohydrate,
- 2-(4-benzoyl-1-piperazinyl)-4-methoxypyrimidine,
- 2-(4-cyclopropylcarbonyl-1-piperazinyl)-4-methoxypyrimidine,
- 2-[4-(2-furylcarbonyl)-1-piperazinyl]-4-(trifluoromethyl)pyrimidine,
- 2-[4-(2-thienylcarbonyl)-1-piperazinyl]-4-(trifluoromethyl)pyrimidine,
- 4-methoxy-2-[4-(3-thienylcarbonyl)-1-piperazinyl]pyrimidine,
- 4-methoxy-2-[4-(3-thienylcarbonyl)-1-piperazinyl]pyrimidine chlorohydrate,
- 2-[4-(5-methyl-2-thienylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(5-methyl-2-thienylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine chlroohydrate,
- 4-methoxy-2-[4-(3-methoxy-2-thienylcarbonyl)-1-piperazinyl]pyrimidine,
- 4-methoxy-2-[4-(3-methoxy-2-thienylcarbonyl)-1-piperazinyl]pyrimidine chlorohydrate,
- 2-[4-(2-benzo[b]thienylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine,

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2-[4-(2-benzo[b]thienylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,

- 2-[4-(2-indolylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(3-chloro-2-benzo[b]thienylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(3-chloro-2-benzo[b]thienylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 4-methoxy-2-[4-(2-pyrrolylcarbonyl)-1-piperazinyl]pyrimidine,
- 4-methoxy-2-[4-(2-pyrrolylcarbonyl)-1-piperazinyl]pyrimidine chlorohydrate,
- 4-methoxy-2-[4-(2-thienylacetyl)-1-piperazinyl]pyrimidine,
- 4-methoxy-2-[4-(2-thienylacetyl)-1-piperazinyl]pyrimidine chlorohydrate,
- 2-[4-(3-methyl-2-thienylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(3-methyl-2-thienylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine clorohydrate,
- 2-[4-(3-chloro-2-thienylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(3-chloro-2-thienylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 2-[4-(3-indolylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(3-benzo[b]thienylacetyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(5-chloro-2-thienylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(5-chloro-2-thienylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 4-methoxy-2-[4-(4-chlorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine,
- 4-methoxy-2-[4-(4-chlorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 2-[4-(4-fluorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(4-fluorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 2-[4-(4-chlorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(4-chlorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 4-methoxy-2-[4-(3-methoxybenzoyl)-1-piperazinyl]pyrimidine,
- 4-methoxy-2-[4-(3-methoxybenzoyl)-1-piperazinyl]pyrimidine chlorohydrate,
- 2-[4-(3-fluorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(3-fluorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 2-[4-(3-chlorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(3-chlorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 4-methoxy-2-[4-(2-methoxybenzoyl)-1-piperazinyl]pyrimidine,
- 4-methoxy-2-[4-(2-methoxybenzoyl)-1-piperazinyl]pyrimidine chlorohydrate,
- 2-[4-(2-(fluorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(2-(fluorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 2-[4-(2-(chlorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(2-(chlorobenzoyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 4-methoxy-2-[4-(2-tetrahydrofurylcarbonyl)-1-piperazinyl]pyrimidine,
- 4-methoxy-2-(4-thiobenzoyl-1-piperazinyl)pyrimidine,
- 4-methoxy-2-[4-(2-tetrahydrofurylcarbonyl)-1-piperazinyl]pyrimidine chlorohydrate,
- 4-methoxy-2-(4-thiobenzoyl-1-piperazinyl)pyrimidine chlorohydrate,
- 2-(4-benzoyl-1-piperazinyl)-4-methoxypyrimidine,
- 4-methoxy-2-{4-[4-(trifluoromethyl)benzoyl]-1-piperazinyl}pyrimidine,

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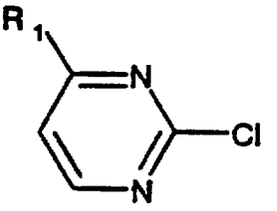
- 4-methoxy-2-{4-[4-(trifluoromethyl)benzoyl]-1-piperazinyl}pyrimidine chlorohydrate,
- 4-methoxy-2-{4-[3-(trifluoromethyl)benzoyl]-1-piperazinyl}pyrimidine,
- 4-methoxy-2-{4-[3-(trifluoromethyl)benzoyl]-1-piperazinyl}pyrimidine chlorohydrate,
- 4-methoxy-2-{4-[2-(trifluoromethyl)benzoyl]-1-piperazinyl}pyrimidine,
- 4-methoxy-2-{4-[2-(trifluoromethyl)benzoyl]-1-piperazinyl}pyrimidine chlorohydrate,
- 4-methoxy-2-(4-nicotinoyl-1-piperazinyl)pyrimidine,
- 4-methoxy-2-(4-nicotinoyl-1-piperazinyl)pyrimidine dichlorohydrate,
- 2-(4-isonicotinoyl-1-piperazinyl)-4-methoxypyrimidine,
- 2-(4-isonicotinoyl-1-piperazinyl)-4-methoxypyrimidine dichlorohydrate,
- 2-[4-(1-imidazolylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(1-imidazolylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 2-(4-nicotinoyl-1-piperazinyl)-4-(trifluoromethyl)pyrimidine,
- 2-(4-nicotinoyl-1-piperazinyl)-4-(trifluoromethyl)pyrimidine chlorohydrate,
- 4-methoxy-2-`4-(2-pyridylcarbonyl)-1-piperazinyl]pyrimidine,
- 4-methoxy-2-`4-(2-pyridylcarbonyl)-1-piperazinyl]pyrimidine dichlorohydrate,
- 4-ethoxy-2-[4-(2-thienylcarbonyl)-1-piperazinyl]pyrimidine,
- 4-ethoxy-2-[4-(2-thienylcarbonyl)-1-piperazinyl]pyrimidine chlorohydrate,
- 2-[4-(3-chloro-2-thienylcarbonyl)-1-piperazinyl]-4-ethoxypyrimidine,
- 2-[4-(3-chloro-2-thienylcarbonyl)-1-piperazinyl]-4-ethoxypyrimidine chlorohydrate,
- 4-ethoxy-2-{4-[2-(trifluoromethyl)benzoyl]-1-piperazinyl}pyrimidine,
- 4-ethoxy-2-{4-[2-(trifluoromethyl)benzoyl]-1-piperazinyl}pyrimidine chlorohydrate,
- 2-[4-(2-methylbenzoyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(2-methylbenzoyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 2-[4-(4-fluorobenzoyl)-1-piperazinyl]-4-isopropoxypyrimidine,
- 2-[4-(4-fluorobenzoyl)-1-piperazinyl]-4-isopropoxypyrimidine chlorohydrate,
- 4-isopropoxy-2-{4-[2-(trifluoromethyl)benzoyl]-1-piperazinyl]pyrimidine,
- 4-isopropoxy-2-{4-[2-(trifluoromethyl)benzoyl]-1-piperazinyl]pyrimidine chlorohydrate,
- 2-[4-(3-chloro-2-thiencarbonyl)-1-piperazinyl]-4-isopropoxypyrimidine,
- 2-[4-(3-chloro-2-thiencarbonyl)-1-piperazinyl]-4-isopropoxypyrimidine chlorohydrate
- 2-[4-(cyclohexylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(cyclohexylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 4-ethoxy-2[4-(4-fluorobenzoyl]-1-piperazinyl}pyrimidine,
- 4-ethoxy-2[4-(4-fluorobenzoyl]-1-piperazinyl}pyrimidine chlorohydrate,
- 2-[4-(2-thiazolylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(2-aminobenzoyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(2-aminobenzoyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 2-[4-(3-fluoro-2-thieylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(3-fluoro-2-thieylcarbonyl)-1-piperazinyl]-4-methoxypyrimidine chlorohydrate,
- 2-[4-(4-methoxy-2-pyrimidinyl)-1-piperazinylcarbonyl]benzoic acid,

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- 2-[4-(2-acetoxybenzoyl)-1-piperazinyl]-4-methoxypyrimidine,
- 2-[4-(2-hydroxybenzoyl)-1-piperazinyl]-4-methoxypyrimidine,
- sodium 2-[4-(4-methoxy-2-pyrimidinyl)-1-piperazinylcarbonyl]benzoate,
- 2-[4-(2-hydroxybenzoyl)-1-piperazinyl]-4-methoxypyrimidine hydrochlorate,
- 4-methoxy-2-[4-(2-methoxybenzoyl)-1-piperazinyl]-4-methoxypyrimidine, and
- 4-ethoxy-2[4-(2-pyridylcarbonyl]-1-piperazinyl}pyrimidine.

11. Procedure for the preparation of a compound of general formula (I), in which X represents an atom of oxygen, according to claim 1, which comprises reacting a derivative of the chloropyrimidine of formula (III)



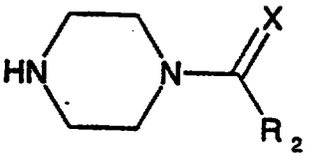
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(III)

where R_1 has the meaning defined in claim 1,

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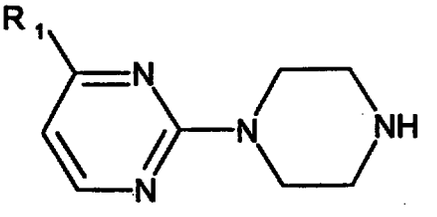
with a derivative of piperazine of general formula (IV)



(IV)

where R_2 has the meaning defined in claim 1 and X represents an oxygen atom.

12. Procedure for the preparation of a compound of general formula (I) in which X represents an atom of oxygen, according to claim 1, which comprises reacting an amine of formula (V)



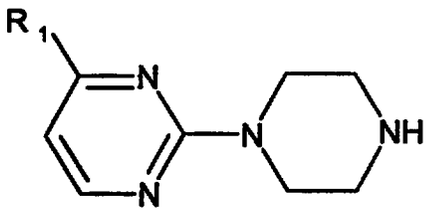
(V)

where R_1 has the meaning defined in claim 1,

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with a carboxylic acid of formula R_2COOH (VI) or with a salt of said acid, in which R_2 has the meaning defined in claim 1.

13. Procedure for the preparation of a compound of general formula (I) in which X represents an oxygen atom, according to claim 1, which comprises reacting an amine of formula (V)



(V)

where R_1 has the meaning defined in claim 1
with a derivative reagent R_2COY (VII), in which R_2 has the meaning defined in claim 1 and Y represents a halogen atom, an azide group, a 1-imidazolyl group, a O-CO-R_4 group, where R_4 represents an alkyl radical of 1 to 6 atoms of carbon or an aryl radical, optionally substituted with one or several halogen atoms, or an OR_5 group where R_5 represents an aromatic group or one or two rings substituted with one or several halogen atoms or nitro radicals, or N-succinimide.

14. Procedure for the preparation of a compound of general formula (I) in which X represents a sulphur atom, according to claim 1, which comprises reacting a compound of general formula (I) in which X represents an oxygen atom, with Lawesson's reagent, (2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphaethano-2,4-disulphuride), or with phosphorous pentasulphide.

15. Procedure for the preparation of the physiologically acceptable salts of the compounds of general formula (I), according to claim 1, which comprises reacting a compound of general formula (I) with a mineral acid or an organic acid in an appropriate solvent.

16. A pharmaceutical composition characterised in that it contains, in addition to a pharmaceutically acceptable excipient, at least one compound of general formula (I) or one of its physiologically acceptable salts, according to claims 1 to 10.

17. Use of a compound of general formula (I) or their pharmaceutically acceptable salts, according to any one of the claims 1 to 10, in the fabrication of a medicament with activity in the central nervous system of mammals, including man.

18. Use of a compound of general formula (I) or their pharmaceutically acceptable salts, according to any one of the claims 1 to 10, in the fabrication of a medicament with sedative, anticonvulsants, analgesic, muscular relaxant, antitusigenic, ansiolytic, antipsicotic, antidepressant, anti-cerebral ischeamic, anti-migraine activity, in the fabrication of a medicament for treating sleep disorders, neurodegenerative diseases, cognitive disorders and Alzheimer's disease, sleep-inducing or general anaesthetic agents, for mammals, including man.

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