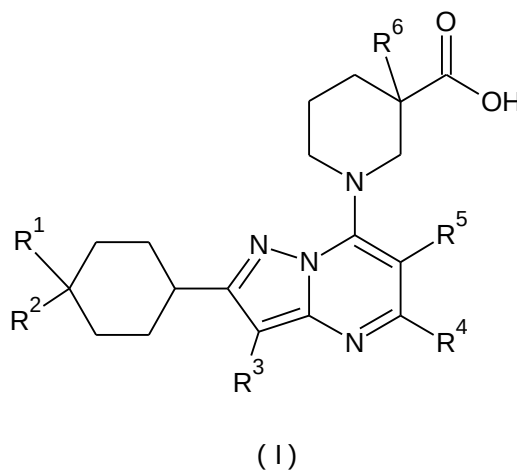


Claims

1. A compound of formula (I) wherein:



R^1 and R^2 are independently selected from hydrogen, halogen atom, C_{1-6} alkyl, halo C_{1-6} alkyl;

R^3 is hydrogen, halogen atom, C_{1-6} alkyl, cyano group;

R^4 is C_{1-6} alkyl;

R^5 is C_{1-6} alkyl optionally substituted by a halogen atom or halogen atoms, C_{3-5} cycloalkyl;

C_{3-5} cycloalkyl C_{1-6} alkyl, dialkylamino, C_{1-6} alkoxy, C_{1-6} alkoxy C_{1-6} alkyl, C_{1-6} alkylthio group, tetrahydrofuranyl, tetrahydrofuranyl C_{1-6} alkyl, tetrahydropyranyl, tetrahydropyranyl C_{1-6} alkyl;

or R_4 and R_5 together form an unsubstituted or substituted by one or more C_{1-3} alkyl, C_{1-3} alkoxy, halo C_{1-3} alkyl, C_{1-3} alkylcarbonyl 3 to 7-membered saturated ring, wherein the members of the ring are selected from the group consisting of carbon, nitrogen, oxygen, and sulphur;

R^6 is hydrogen, halogen atom or C_{1-6} alkyl, hydroxyl, C_{1-6} alkoxy, C_{1-6} alkoxy C_{1-6} alkyl, halo C_{1-6} alkyl, amino group; or pharmaceutically acceptable salts, enantiomers, diastereomers, solvates and hydrates thereof.

2. A compound according to claim 1 wherein

R^1 and R^2 are independently selected from hydrogen, halogen atom, C_{1-6} alkyl, halo C_{1-6} alkyl;

R^3 is hydrogen, halogen atom, C_{1-6} alkyl, cyano group;

R^4 is C_{1-6} alkyl;

R⁵ is C₁₋₆alkyl optionally substituted by a halogen atom or halogen atoms, C₃₋₅ cycloalkyl; C₃₋₅ cycloalkylC₁₋₆alkyl, dialkylamino, C₁₋₆alkoxy, C₁₋₆alkoxyC₁₋₆alkyl, C₁₋₆alkylthio group, tetrahydrofuranyl, tetrahydrofuranylC₁₋₆alkyl, tetrahydropyranyl, tetrahydropyranylC₁₋₆alkyl; R⁶ is hydrogen, halogen atom or C₁₋₆alkyl, hydroxyl, C₁₋₆alkoxy, C₁₋₆alkoxyC₁₋₆alkyl, haloC₁₋₆alkyl, amino group; or pharmaceutically acceptable salts, racemates, enantiomers, diastereomers, solvates and hydrates thereof.

3. A compound according to claim 1 wherein

R¹ and R² are independently selected from hydrogen, halogen atom, C₁₋₆alkyl, haloC₁₋₆alkyl;

R³ is hydrogen, halogen atom, C₁₋₆alkyl, cyano group;

R₄ and R₅ together form an unsubstituted or substituted by one or more C₁₋₃alkyl, C₁₋₃alkoxy, haloC₁₋₃alkyl, C₁₋₃alkylcarbonyl 3 to 7-membered saturated ring, wherein the members of the ring are selected from the group consisting of carbon, nitrogen, oxygen, and sulphur;

R⁶ is hydrogen, halogen atom or C₁₋₆alkyl, hydroxyl, C₁₋₆alkoxy, C₁₋₆alkoxyC₁₋₆alkyl, haloC₁₋₆alkyl, amino group or pharmaceutically acceptable salts, enantiomers, diastereomers, solvates and hydrates thereof.

4. A compound according to claim 1 wherein R⁴ is methyl; and R⁵ is isopropyl or C₁₋₆alkoxyC₁₋₆alkyl.

5. A compound according to claim 1 selected from the group of

(3S)-1-[5-Methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]piperidine-3-carboxylic acid

(3S)-1-[5-Methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]-3-(propan-2-yl)piperidine-3-carboxylic acid

(3R)-3-Methyl-1-[5-methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]piperidine-3-carboxylic acid

(3R)-1-[5-Methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]-3-propylpiperidine-3-carboxylic acid

(3S)-1-[5-Methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]-3-propylpiperidine-3-carboxylic acid

(3R)-3-(Fluoromethyl)-1-[5-methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]piperidine-3-carboxylic acid

(3S)-3-(Fluoromethyl)-1-[5-methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]piperidine-3-carboxylic acid

(3R)-3-Methyl-1-[(8S)-8-methyl-2-[trans-4-(trifluoromethyl)cyclohexyl]-5H,6H,7H,8H-pyrazolo[3,2-b]quinazolin-9-yl]piperidine-3-carboxylic acid

(3R)-3-Methyl-1-[(8R)-8-methyl-2-[trans-4-(trifluoromethyl)cyclohexyl]-5H,6H,7H,8H-pyrazolo[3,2-b]quinazolin-9-yl]piperidine-3-carboxylic acid

(3R)-1-[5-Methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]piperidine-3-carboxylic acid

(3S)-3-Methyl-1-[5-methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]piperidine-3-carboxylic acid

(3S)-3-Ethyl-1-[5-methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]piperidine-3-carboxylic acid

(3R)-3-Ethyl-1-[5-methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]piperidine-3-carboxylic acid

(3R)-1-[5-Methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]-3-(propan-2-yl)piperidine-3-carboxylic acid

(3S)-1-[3-Fluoro-5-methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]-3-methylpiperidine-3-carboxylic acid

(3R)-1-[3-Fluoro-5-methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]-3-methylpiperidine-3-carboxylic acid

(3S)-3-Ethyl-1-[3-fluoro-5-methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]piperidine-3-carboxylic acid

(3R)-3-Ethyl-1-[3-fluoro-5-methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]piperidine-3-carboxylic acid

(3S)-1-{3-Fluoro-6-methoxy-5-methyl-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl}-3-methylpiperidine-3-carboxylic acid

(3R)-1-{3-Fluoro-6-methoxy-5-methyl-2-[trans-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl}-3-methylpiperidine-3-carboxylic acid

(3S)-3-Ethyl-1-{6-methoxy-5-methyl-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl}piperidine-3-carboxylic acid

(3R)-3-Ethyl-1-{6-methoxy-5-methyl-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl}piperidine-3-carboxylic acid

(3S)-1-{3-Fluoro-6-methoxy-5-methyl-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl}-3-methylpiperidine-3-carboxylic acid

(3R)-1-{3-Fluoro-6-methoxy-5-methyl-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl}-3-methylpiperidine-3-carboxylic acid

(3S)-3-Ethyl-1-{3-fluoro-6-methoxy-5-methyl-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl}piperidine-3-carboxylic acid

(3R)-3-Ethyl-1-{3-fluoro-6-methoxy-5-methyl-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl}piperidine-3-carboxylic acid

(3R)-1-{6-Ethyl-5-methyl-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl}-3-methylpiperidine-3-carboxylic acid

(3R)-3-Ethyl-1-{6-ethyl-5-methyl-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl}piperidine-3-carboxylic acid

(3S)-1-[2-(4,4-Difluorocyclohexyl)-5-methyl-6-(propan-2-yl)pyrazolo[1,5-a]pyrimidin-7-yl]-3-methylpiperidine-3-carboxylic acid

(3R)-1-[2-(4,4-Difluorocyclohexyl)-5-methyl-6-(propan-2-yl)pyrazolo[1,5-a]pyrimidin-7-yl]-3-methylpiperidine-3-carboxylic acid

(3S)-1-[2-(4,4-Difluorocyclohexyl)-5-methyl-6-(propan-2-yl)pyrazolo[1,5-a]pyrimidin-7-yl]-3-ethylpiperidine-3-carboxylic acid

(3R)-1-[2-(4,4-Difluorocyclohexyl)-5-methyl-6-(propan-2-yl)pyrazolo[1,5-a]pyrimidin-7-yl]-3-ethylpiperidine-3-carboxylic acid

(3R)-1-[2-(4,4-Difluorocyclohexyl)-5,6-diethylpyrazolo[1,5-a]pyrimidin-7-yl]-3-methylpiperidine-3-carboxylic acid

(3R)-3-Methyl-1-{2-[trans-4-(trifluoromethyl)cyclohexyl]-5H,6H,7H,8H-pyrazolo[3,2-b]quinazolin-9-yl}piperidine-3-carboxylic acid

(3R)-3-Methyl-1-{5-[trans-4-(trifluoromethyl)cyclohexyl]-2,6,7-triazatricyclo[7.5.0.0^{3,7}]tetradeca-1,3,5,8-tetraen-8-yl}piperidine-3-carboxylic acid

(3R)-3-Methyl-1-{5-[trans-4-(trifluoromethyl)cyclohexyl]-11-oxa-2,6,7-triazatricyclo[7.4.0.0^{3,7}]trideca-1,3,5,8-tetraen-8-yl}piperidine-3-carboxylic acid

(3S)-3-Methyl-1-{5-[trans-4-(trifluoromethyl)cyclohexyl]-12-oxa-2,6,7-triazatricyclo[7.4.0.0^{3,7}]trideca-1,3,5,8-tetraen-8-yl}piperidine-3-carboxylic acid

(3S)-1-[3-Cyano-5-methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]-3-methylpiperidine-3-carboxylic acid

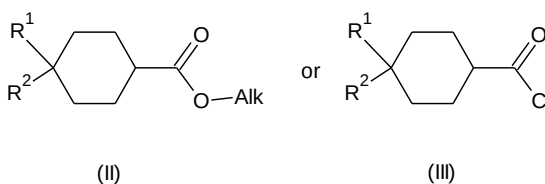
(3R)-1-[3-Cyano-5-methyl-6-(propan-2-yl)-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]-3-methylpiperidine-3-carboxylic acid

(3R)-1-[2-(4,4-Difluorocyclohexyl)-3-fluoro-5-methyl-6-(propan-2-yl)pyrazolo[1,5-a]pyrimidin-7-yl]-3-methylpiperidine-3-carboxylic acid

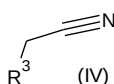
(3R)-1-[6-(2-methoxyethyl)-5-methyl-2-[trans-4-(trifluoromethyl)cyclohexyl]pyrazolo[1,5-a]pyrimidin-7-yl]-3-methylpiperidine-3-carboxylic acid

6. Process for preparing the compounds of formula (I) according to claim 1 characterized by

step 1) reacting an carboxylic acid ester derivative of formula (II) or carboxylic acid chloride derivative of formula (III)

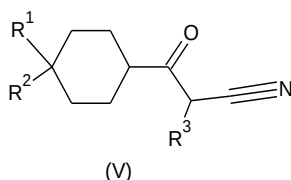


- wherein the meaning of R^1 and R^2 is described above for compound of formula (I) with an acetonitrile derivative of formula (IV)

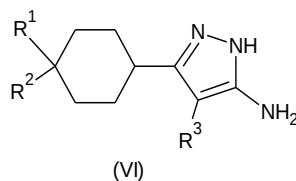


- wherein the meaning of R^3 is described above for compound of formula (I), then

step 2) the so obtained acylacetonitrile derivative of formula (V) is reacted

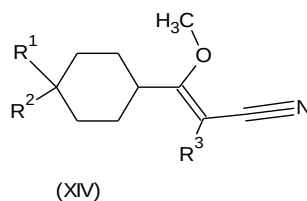


2a) with hydrazine hydrate to provide a compound of formula (VI)

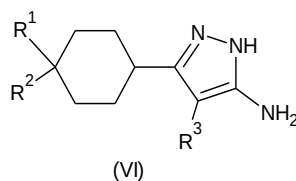


- wherein the meaning of R^1 , R^2 is as described above and R^3 is hydrogen, halogen atom, C_{1-6} alkyl group or

2b) with trimethyl orthoformate to provide the malononitrile derivative of formula (XIV)

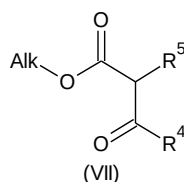


- wherein the meaning of R^1 , R^2 is as described above and R^3 is cyano group which is reacted with hydrazine hydrate to provide a compound of formula (VI)



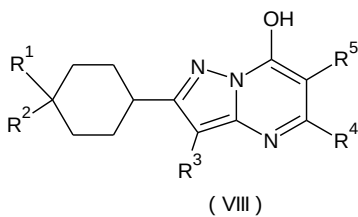
then

step 3) the compound of formula (VI) wherein the meaning of R^1 , R^2 , R^3 is as described above for the formula (I) – obtained according to the steps described in 2a) or 2b) is reacted with acylacetic ester derivative of formula (VII)

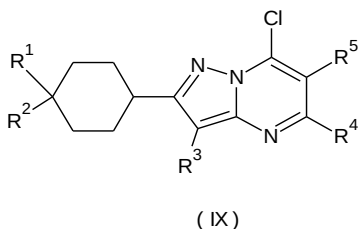


- wherein the meaning of R^4 and R^5 is as described above for the formula (I), then

step 4) the so obtained compound of formula (VIII)

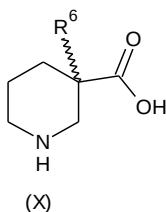


- wherein the meaning of R^1 , R^2 , R^3 , R^4 , and R^5 is as described above for the formula (I) - is chlorinated to furnish a chloro derivative of formula (IX)



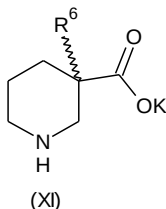
- wherein the meaning of R^1 , R^2 , R^3 , R^4 , and R^5 is as described above for the formula (I) - and
step 5) the latter is reacted with either

5c) a nipecotic acid derivative of formula (X)



- wherein the meaning of R^6 is as described above for the formula (I) – and the obtained derivative of formula (I) and optical antipodes or racemates and/or salts thereof in given case can be transformed into an other compound of formula (I) and optical antipodes or racemates and/or salts thereof by introducing new substituents and/or modifying or removing the existing ones, or

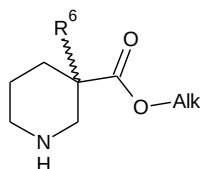
5d) its alkali salt of formula (XI)



- wherein the meaning of R^6 is as described above for the formula (I) – and the obtained compound of formula (I) and optical antipodes or racemates and/or salts thereof optionally can be transformed into an other compound of formula (I) and optical

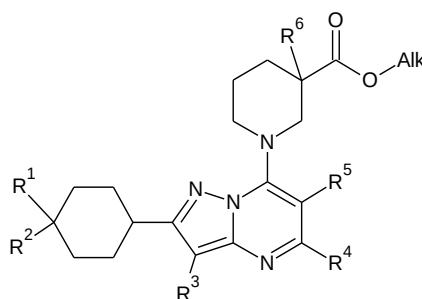
antipodes or racemates and/or salts thereof by introducing new substituents and/or modifying or removing the existing ones, or

5e) a nipecotic acid ester derivative of formula (XII)



(XII)

- wherein the meaning of R^6 is as described above for the formula (I) – to provide the ester derivative of formula (XIII)



(XIII)

- wherein the meaning of R^1 , R^2 , R^3 , R^4 , R^5 and R^6 is as described above for the formula (I) finally the latter is saponified with a strong base or acid – and the obtained derivative of formula (I) and optical antipodes or racemates and/or salts thereof optionally can be transformed into an other compound of formula (I) and optical antipodes or racemates and/or salts thereof by introducing new substituents and/or modifying or removing the existing ones.

7. A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (I) or pharmaceutically acceptable salts, racemates, enantiomers, diastereomers, solvates and hydrates thereof according to claim 1 as active ingredient and pharmaceutically acceptable carrier.

8. A combination comprising a therapeutically effective amount of a compound of formula (I) or pharmaceutically acceptable salts, racemates, enantiomers, diastereomers, solvates and hydrates thereof according to claim 1 and one or more therapeutically active co-agents.

9. A compound of formula (I) or pharmaceutically acceptable salts, racemates, enantiomers, diastereomers, solvates and hydrates thereof according to claim 1 for use in the treatment or prevention of a disorder selected from the group of psychiatric disorders (such as anxiety, panic disorder, posttraumatic disorder, depression, schizophrenia), neurodevelopmental disorders (such as autism spectrum disorder, obsessive-compulsive disorder, Fragile X syndrome), cognitive disorders, epilepsy, spasticity, skeletal muscle rigidity, spinal cord injury, multiple sclerosis, amyotrophic lateral sclerosis, cerebral palsy, essential tremor, pain (neuropathic, visceral, osteoarthritic), substance abuse (cocaine, nicotine, alcohol), obesity, binge eating, asthma, cough, urinary incontinence, gastroesophageal reflux disease, transient lower esophageal sphincter relaxation, irritable bowel syndrome.