schizophrenia, an appropriate multireceptor affinity profile might be required for efficacy against positive and negative signs and symptoms. Furthermore, an ideal drug against schizophrenia would preferably have a low dosage allowing once-per-day dosage, due to the low adherence of schizophrenic patients.

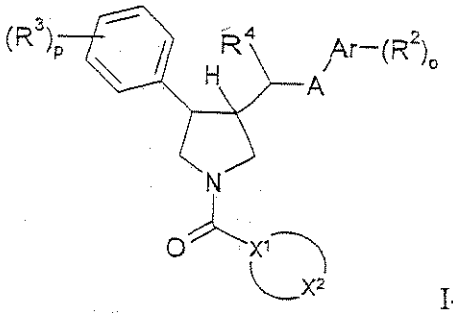
In recent years clinical studies with selective NK1 and NK2 receptor antagonists appeared in the literature showing results for the treatment of emesis, depression, anxiety, pain and migraine (NK1) and asthma (NK2 and NK1). The most exciting data were produced in the treatment of chemotherapy-induced emesis, nausea and depression with NK1 and in asthma with NK2- receptor antagonists. In contrast, no clinical data on NK3 receptor antagonists have appeared in the literature until 2000. Osanetant (SR 142,801) from Sanofi-Synthelabo was the first identified potent and selective non-peptide antagonist described for the NK3 tachykinin receptor for the potential treatment of schizophrenia, which was reported in the literature (*Current Opinion in Investigational Drugs, 2001, 2(7), 950-956 and Psychiatric Disorders Study 4, Schizophrenia, June 2003, Decision Recources, Inc., Waltham, Massachusetts).* The proposed drug SR 142,801 has been shown in a phase II trial as active on positive symptoms of schizophrenia, such as altered behaviour, delusion, hallucinations, extreme emotions, excited motor activity and incoherent speech, but inactive in the treatment of negative symptoms, which are depression, anhedonia, social isolation or memory and attention deficits.

The neurokinin-3 receptor antagonists have been described as useful in pain or inflammation, as well as in schizophrenia, *Exp. Opinion.Ther. Patents (2000), 10(6), 939-960 and Current Opinion in Investigational Drugs, 2001, 2(7), 950-956 956 and Psychiatric Disorders Study 4, Schizophrenia, June 2003, Decision Recources, Inc., Waltham, Massachusetts).*

~~Objects of the present invention~~ Objects of embodiments disclosed herein are novel compounds of formula I, their manufacture, medicaments based on a compound in accordance with the ~~invention~~ disclosure and their production as well as the use of compounds of formula I in the control or prevention of illnesses such as depression, pain, bipolar disorders, psychosis, Parkinson's disease, schizophrenia, anxiety and attention deficit hyperactivity disorder (ADHD).

The preferred indications using the compounds of the present ~~invention~~ disclosure are depression, psychosis, Parkinson's disease, schizophrenia, bipolar disorders, anxiety and attention deficit hyperactivity disorder (ADHD).

In a first aspect, there is provided a compound of formula I-A



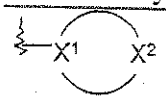
I-A

wherein

A is –NR'-;

R' is hydrogen or C_{1-7}-alkyl;

Ar is aryl or is a five or six membered heteroaryl group, containing one or two N-atoms;



is a 5 or 6 membered heterocyclic group wherein

X^1 is N or CH; and

X^2 is $-N(R^1)-$, $-CH_2-$, -O-, -S-, -S(O)-, or $-S(O)_2-$,

R^1 is hydrogen, C_{1-7}-alkyl, $S(O)_2$- C_{1-7}-alkyl, C(O)-C_{1-7}-alkyl, C(O)-cycloalkyl optionally substituted by C_{1-7}-alkyl;

with the proviso that at least one of X^1 or X^2 contains a heteroatom,

R^2 is C_{1-7}-alkyl substituted by halogen, halogen, cyano or nitro;

R^3 is halogen;

R^4 is hydrogen or C_{1-7}-alkyl;

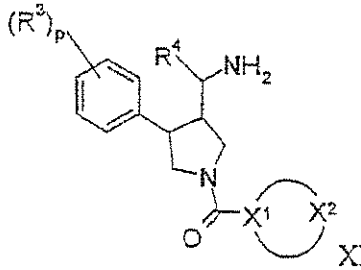
o is 1 or 2; in case o is 2, R^2 may be the same or different;

p is 1 or 2; in case p is 2, R^3 may be the same or different;

or a pharmaceutically active salt, a racemic mixture, an enantiomer, an optical isomer or a tautomeric form thereof.

In a second aspect, there is provided a process for preparing a compound of formula Ia as defined above, which process comprises

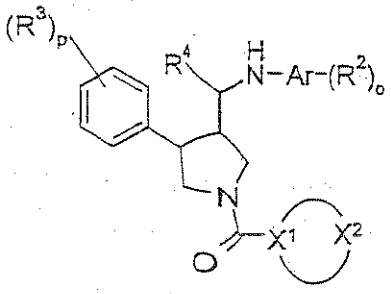
a) coupling a compound of formula



XXV

with hal-Ar-$(R^2)_o$

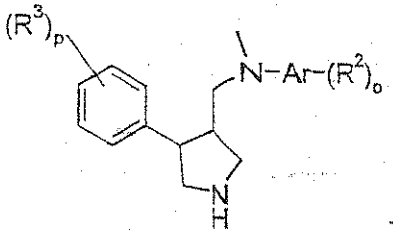
to a compound of formula



I-A4

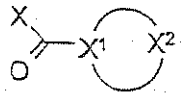
wherein the definitions are described in the first aspect, or

b) coupling a compound of formula

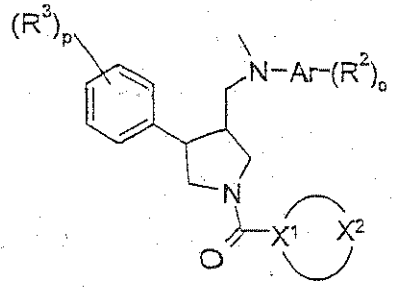


XXXVIII

with a compound of formula



to a compound of formula



I-A5

wherein the definitions are described in the first aspect, and

if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts.

In a third aspect, there is provided a medicament containing one or more compounds as defined above and pharmaceutically acceptable excipients.

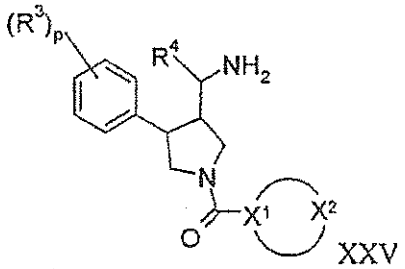
In a fourth aspect, there is provided the use of a compound as defined above for the manufacture of medicaments for the treatment of depression, pain, psychosis, Parkinson's disease, schizophrenia, bipolar disorder, anxiety and attention deficit hyperactivity disorder (ADHD).

The following definitions of the general terms used in the present description apply irrespective of whether the terms in question appear alone or in combination.

1-yl}-[1-(1-methyl-cyclopropanecarbonyl)-piperidin-4-yl]-methanone
(3SR,4RS) [4-(3-(4-fluoro-phenyl)-4-{[methyl-(5-trifluoromethyl-pyrimidin-2-yl)-amino]-methyl}-pyrrolidine-1-carbonyl)-piperidin-1-yl]-(1-methyl-cyclopropyl)-methanone
6-({(3S,4S)-4-(4-chloro-phenyl)-1-[1-(1-methyl-cyclopropanecarbonyl)-piperidine-4-carbonyl]-pyrrolidin-3-ylmethyl}-methyl-amino)-nicotinonitrile
[4-((3S,4S)-3-(4-chloro-phenyl)-4-{[methyl-(5-trifluoromethyl-pyridin-2-yl)-amino]-methyl}-pyrrolidine-1-carbonyl)-piperidin-1-yl]-(1-methyl-cyclopropyl)-methanone
((3S,4S)-3-(4-chloro-phenyl)-4-{[methyl-(5-trifluoromethyl-pyrimidin-2-yl)-amino]-methyl}-pyrrolidin-1-yl)-[1-(1-methyl-cyclopropanecarbonyl)-piperidin-4-yl]-methanone
{(3S,4S)-3-(3,4-dichloro-phenyl)-4-[(5-trifluoromethyl-pyrimidin-2-ylamino)-methyl]-pyrrolidin-1-yl}-[1-(1-methyl-cyclopropanecarbonyl)-piperidin-4-yl]-methanone
((3S,4S)-3-(3,4-dichloro-phenyl)-4-{[methyl-(5-trifluoromethyl-pyrimidin-2-yl)-amino]-methyl}-pyrrolidin-1-yl)-[1-(1-methyl-cyclopropanecarbonyl)-piperidin-4-yl]-methanone
[4-((3S,4S)-3-(3,4-dichloro-phenyl)-4-{[methyl-(5-trifluoromethyl-pyridin-2-yl)-amino]-methyl}-pyrrolidine-1-carbonyl)-piperidin-1-yl]-(1-methyl-cyclopropyl)-methanone
6-({(3S,4S)-4-(3,4-dichloro-phenyl)-1-[1-(1-methyl-cyclopropanecarbonyl)-piperidine-4-carbonyl]-pyrrolidin-3-ylmethyl}-methyl-amino)-nicotinonitrile or
{4-[(3S,4S)-3-{[(5-chloro-pyridin-2-yl)-methyl-amino]-methyl}-4-(3,4-dichloro-phenyl)-pyrrolidine-1-carbonyl]-piperidin-1-yl}-(1-methyl-cyclopropyl)-methanone.

8.~~7~~ A process for preparing a compound of formula Ia as defined in claim 1, which process comprises

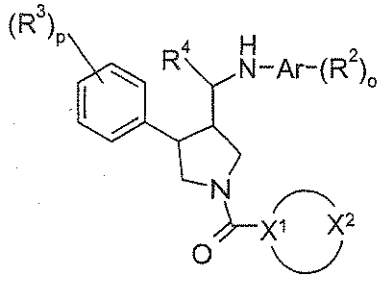
a) coupling a compound of formula



XXV

with hal-Ar-$(R^2)_o$

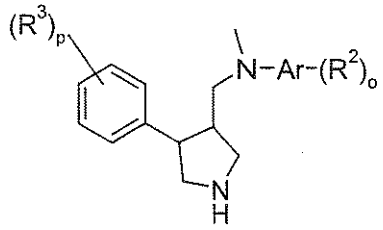
to a compound of formula



I-A4

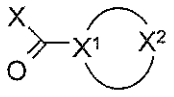
wherein the definitions are described in claim 1, or

b) coupling a compound of formula

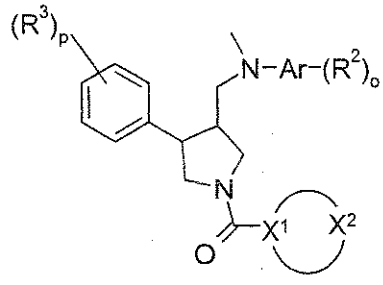


XXXVIII

with a compound of formula



to a compound of formula



I-A5

wherein the definitions are described in claim 1, and

if desired, converting the compounds obtained into pharmaceutically acceptable acid addition salts.

9. ~~8.~~ A medicament containing one or more compounds as claimed in any one of claims 1 – 6 and pharmaceutically acceptable excipients.

10. ~~9.~~ A medicament according to claim 8 for the treatment of depression, pain, psychosis, Parkinson's disease, schizophrenia, bipolar disorder, anxiety and attention deficit hyperactivity disorder (ADHD).

11. ~~10.~~ The use of a compound as claimed in any one of claims 1 – 6 for the manufacture of medicaments for the treatment of depression, pain, psychosis, Parkinson's disease, schizophrenia, bipolar disorder, anxiety and attention deficit hyperactivity disorder (ADHD).