and routes of synthesis to obtain (I). In further embodiments, the use of 6-chloro-3-(phenyl-d_5)-inden-1-one (I) to obtain racemic 6-chloro-3-(phenyl-d_5)-indan-1-one (VIII) or (*S*)-6-chloro-3-(phenyl-d_5)-indan-1-one (IX) is disclosed.

Further the use of 6-chloro-3-(phenyl-d_5)-inden-1-one (I) to obtain 4-((1*R*,3*S*)-6-chloro-3-(phenyl-d_5)-indan-1-yl)-1(d_3),2,2-trimethyl-piperazine and pharmaceutically acceptable salts thereof is disclosed.

In another aspect, there is disclosed a process for production of Compound (I), the process comprising the following steps: a) 2,2'-azo-bis-isobutyronitrile and *N*-bromosuccinimide is added to a solution comprising 6-chloro-1-indanone; b) Triethylamine is added to the solution of step a) to obtain 3-bromo-6-chloro-inden-1-one; c) 3-bromo-6-chloro-inden-1-one is separated and reacted with 4,4,5,5-tetramethyl-2-d_5-phenyl-[1,3,2]dioxaborolane in the presence of an appropriate catalyst and base to obtain compound (I).

In a further aspect, there is disclosed a process for the production of Compound (I) comprising the steps of: 1. Synthesis of 6-chloro-3-(phenyl-d_5)-1*H*-indene (IV) by reaction between an organometallic species obtained from monohalogenated benzene-d_5 and 5-chloro-1-indanone (V) followed by dehydration; 2. Reaction of 6-chloro-3-(phenyl-d_5)-1*H*-indene (IV) to (*E*)-1-(6-chloro-3-phenyl(d_5)-1*H*-inden-1-ylidenemethyl)-*N*,*N*-dimethylamine (XIX) and further oxidative cleavage thereof to obtain compound (I).

Another aspect relates to a process comprising the steps a) Compound (I) as defined herein is reduced to obtain 6-chloro-3-(phenyl-d_5)-1H-inden-1-ol (VIa); b) Compound (VIa) is converted to 6-chloro-3-(phenyl-d_5)-indan-1-one (VIIIa) via base-induced rearrangement.

Another aspect relates to a process comprising the steps a) Compound (I) as defined herein is converted to (S)-6-chloro-3-(phenyl-d_5)-1H-inden-1-ol (VII) via enantioselective reduction in the presence of enantioselective catalyst and reductant; b) Compound (VII) is converted to (S)-6-chloro-3-(phenyl-d_5)-indan-1-one (IX) via base-induced rearrangement.

Another aspect relates to a process comprising conversion of Compound (I) as defined herein to obtain 6-chloro-3-(phenyl-d_5)-indan-1-one (VIIIa) via hydrogenation in the presence of a suitable catalyst, such as tris(triphenylphosphine)rhodium(I) chloride, in a suitable solvent, such as ethyl acetate.

Another aspect relates to a process comprising conversion of Compound (I) as defined herein to obtain (S)-6-chloro-3-(phenyl-d_5)-indan-1-one (IX) via asymmetric hydrogenation in the

presence of a suitable catalyst, such as a rhodium salt, and a chiral phosphine ligand and a suitable solvent, such as ethyl acetate.

Another aspect relates to a process wherein the compounds obtained in any of the processes described above are converted to 3,5-dichloro-1-(phenyl-d_5)-indan, in particular (±)-cis-3,5-dichloro-1-(phenyl-d_5)-indan or (1S,3S)-3,5-dichloro-1-(phenyl-d_5)-indan, the process comprising the following steps:

a) Reduction of (±)-6-chloro-3-(phenyl-d5)-indan-1-one (VIII), 6-chloro-3-(phenyl-d5)-indan-1-one (VIIIa) or (S)-6-chloro-3-(phenyl-d5)-indan-1-one (IX) to obtain the corresponding indanol: (±)-cis-6-chloro-3-(phenyl-d5)-indan-1-ol (X), 6-chloro-3-(phenyl-d_5)-indan-1-ol (Xb) or (1S,3S)-6-chloro-3-(phenyl-d5)-indan-1-ol (Xa) in the presence of a suitable reduction agent, such as $NaBH_4$;

b) Chlorination, e.g. in the presence thionyl chloride, of any of the compounds obtained in step a) to obtain the corresponding chlorinated indan compound (±)-cis-3,5-dichloro-1-(phenyl-d5)-indan (XI), 3,5-dichloro-1-(phenyl-d5)-indan (XIb) or (1S,3S)-3,5-dichloro-1-(phenyl-d5)-indan (XIa)

Yet another aspect relates to a process wherein the (±)-cis-3,5-dichloro-1-(phenyl-d5)-indan (XI), 3,5-dichloro-1-(phenyl-d5)-indan (XIb) or (1S,3S)-3,5-dichloro-1-(phenyl-d5)-indan (XIa) as obtained above are converted to a pharmaceutically acceptable salt of (±)-trans-1-(6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine, 1-(6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine or 1-((1R, 3S)-6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine, the process comprising the following steps:

a) reaction with 2,2-dimethylpiperazine;

b) formation and optionally precipitation of the pharmaceutically acceptable salt by addition of the corresponding acid.

Another aspect relates to a process wherein the pharmaceutically acceptable salt of (±)-trans-1-(6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine, 1-(6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine or 1-((1R, 3S)-6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine as obtained above is converted to a pharmaceutically acceptable salt of 4-((1R,3S)-6-chloro-3-(phenyl-d_5)-indan-1-yl)-1(d_3),2,2-trimethyl-piperazine, the process comprising the following steps:

a) alkylation in the presence of an active methyl-d_3 donor, such as methyl-iodide-d_3, and a base, such as potassium hydroxide, and

b) precipitation and optionally of the pharmaceutically acceptable salt by addition of the corresponding acid.

Another aspect relates to a process wherein the 3,5-dichloro-1-(phenyl-d_5)-indan, in particular (±)-cis-3,5-dichloro-1-(phenyl-d_5)-indan or (1S,3S)-3,5-dichloro-1-(phenyl-d_5)-indan, obtained as described above is converted to a pharmaceutically acceptable salt of 4-((1R,3S)-6-chloro-3-(phenyl-d_5)-indan-1-yl)-1(d_3),2,2-trimethyl-piperazine, the process comprising the following steps:

a) nucleophile substitution of 3,5-dichloro-1-(phenyl-d_5)-indan with 1(d_3),2,2-trimethylpiperazine bis-2,2,2-trifluoroacetate

b) precipitation and optionally of the pharmaceutically acceptable salt by addition of the corresponding acid.

DETAILED DESCRIPTION OF THE INVENTION

Compound list

(I): 6-chloro-3-(phenyl-d_5)-inden-1-one

(II): 6-chloro-1-indanone

(III): 3-bromo-6-chloro-inden-1-one

(IV): 6-chloro-3-(phenyl-d_5)-1*H*-indene

(V): 5-chloro-1-indanone

(VI): (±)-6-chloro-3-(phenyl-d_5)-1*H*-inden-1-ol

(VIa) 6-chloro-3-(phenyl-d_5)-1*H*-inden-1-ol

(VII): (*S*)-6-chloro-3-(phenyl-d_5)-1*H*-inden-1-ol

(VIII): (±)-6-chloro-3-(phenyl-d_5)-indan-1-one

(VIIIa): 6-chloro-3-(phenyl-d_5)-indan-1-one

(IX): (*S*)-6-chloro-3-(phenyl-d_5)-indan-1-one

(X): (±)-*cis*-6-chloro-3-(phenyl-d_5)-indan-1-ol

(Xa): (1*S*,3*S*)-6-chloro-3-(phenyl-d_5)-indan-1-ol

(Xb): 6-chloro-3-(phenyl-d_5)-indan-1-ol

(XI): (±)-*cis*-3,5-dichloro-1-(phenyl-d_5)-indan

(XIa): (1*S*,3*S*)-3,5-dichloro-1-(phenyl-d_5)-indan

and routes of synthesis to obtain (I). In further embodiments, the use of 6-chloro-3-(phenyl-d_5)-inden-1-one (I) to obtain racemic 6-chloro-3-(phenyl-d_5)-indan-1-one (VIII) or (*S*)-6-chloro-3-(phenyl-d_5)-indan-1-one (IX) is disclosed.

Further the use of 6-chloro-3-(phenyl-d_5)-inden-1-one (I) to obtain 4-((1*R*,3*S*)-6-chloro-3-(phenyl-d_5)-indan-1-yl)-1(d_3),2,2-trimethyl-piperazine and pharmaceutically acceptable salts thereof is disclosed.

In another aspect, there is disclosed a process for production of compound (I), wherein compound (I) is obtained via reaction of 3-bromo-6-chloro-inden-1-one with an arylboronic acid or an arylboronic ester.

Another aspect relates to a process comprising the steps a) Compound (I) as defined herein is reduced to obtain 6-chloro-3-(phenyl-d5)-1H-inden-1-ol (VIa); b) Compound (VIa) is converted to 6-chloro-3-(phenyl-d5)-indan-1-one (VIIIa) via base-induced rearrangement.

Another aspect relates to a process comprising the steps a) Compound (I) as defined herein is converted to (S)-6-chloro-3-(phenyl-d5)-1H-inden-1-ol (VII) via enantioselective reduction in the presence of enantioselective catalyst and reductant; b) Compound (VII) is converted to (S)-6-chloro-3-(phenyl-d5)-indan-1-one (IX) via base-induced rearrangement.

Another aspect relates to a process comprising conversion of Compound (I) as defined herein to obtain 6-chloro-3-(phenyl-d5)-indan-1-one (VIIIa) via hydrogenation in the presence of a suitable catalyst, such as tris(triphenylphosphine)rhodium(I) chloride, in a suitable solvent, such as ethyl acetate.

Another aspect relates to a process comprising conversion of Compound (I) as defined herein to obtain (S)-6-chloro-3-(phenyl-d5)-indan-1-one (IX) via asymmetric hydrogenation in the presence of a suitable catalyst, such as a rhodium salt, and a chiral phosphine ligand and a suitable solvent, such as ethyl acetate.

Another aspect relates to a process wherein the compounds obtained in any of the processes described above are converted to 3,5-dichloro-1-(phenyl-d5)-indan, in particular (±)-cis-3,5-dichloro-1-(phenyl-d5)-indan or (1S,3S)-3,5-dichloro-1-(phenyl-d5)-indan, the process comprising the following steps:

a) Reduction of (±)-6-chloro-3-(phenyl-d5)-indan-1-one (VIII), 6-chloro-3-(phenyl-d5)-indan-1-one (VIIIa) or (S)-6-chloro-3-(phenyl-d5)-indan-1-one (IX) to obtain the corresponding indanol: (±)-cis-6-chloro-3-(phenyl-d5)-indan-1-ol (X), 6-chloro-3-(phenyl-d5)-

indan-1-ol (Xb) or (1S,3S)-6-chloro-3-(phenyl-d5)-indan-1-ol (Xa) in the presence of a suitable reduction agent, such as NaBH4;

b) Chlorination, e.g. in the presence thionyl chloride, of any of the compounds obtained in step a) to obtain the corresponding chlorinated indan compound (±)-cis-3,5-dichloro-1-(phenyl-d5)-indan (XI), 3,5-dichloro-1-(phenyl-d5)-indan (XIb) or (1S,3S)-3,5-dichloro-1-(phenyl-d5)-indan (XIa)

Yet another aspect relates to a process wherein the (±)-cis-3,5-dichloro-1-(phenyl-d5)-indan (XI), 3,5-dichloro-1-(phenyl-d5)-indan (XIb) or (1S,3S)-3,5-dichloro-1-(phenyl-d5)-indan (XIa) as obtained above are converted to a pharmaceutically acceptable salt of (±)-trans-1-(6-chloro-3-(phenyl-d5)-indan-1-yl)-3,3-dimethyl-piperazine, 1-(6-chloro-3-(phenyl-d5)-indan-1-yl)-3,3-dimethyl-piperazine or 1-((1R, 3S)-6-chloro-3-(phenyl-d5)-indan-1-yl)-3,3-dimethyl-piperazine, the process comprising the following steps:

a) reaction with 2,2-dimethylpiperazine or a compound that subsequently can be transformed to to the 3,3-dimethylpiperazine moiety of (±)-trans-1-(6-chloro-3-(phenyl-d5)-indan-1-yl)-3,3-dimethyl-piperazine, 1-(6-chloro-3-(phenyl-d5)-indan-1-yl)-3,3-dimethyl-piperazine or 1-((1R, 3S)-6-chloro-3-(phenyl-d5)-indan-1-yl)-3,3-dimethyl-piperazine;

b) formation and optionally precipitation of the pharmaceutically acceptable salt by addition of the corresponding acid.

Another aspect relates to a process wherein the pharmaceutically acceptable salt of (±)-trans-1-(6-chloro-3-(phenyl-d5)-indan-1-yl)-3,3-dimethyl-piperazine, 1-(6-chloro-3-(phenyl-d5)-indan-1-yl)-3,3-dimethyl-piperazine or 1-((1R, 3S)-6-chloro-3-(phenyl-d5)-indan-1-yl)-3,3-dimethyl-piperazine as obtained above is converted to a pharmaceutically acceptable salt of 4-((1R,3S)-6-chloro-3-(phenyl-d5)-indan-1-yl)-1(d3),2,2-trimethyl-piperazine, the process comprising the following steps:

a) alkylation in the presence of an active methyl-d3 donor, such as methyl-iodide-d3, and a base, such as potassium hydroxide, and

b) precipitation and optionally of the pharmaceutically acceptable salt by addition of the corresponding acid.

Another aspect relates to a process wherein the 3,5-dichloro-1-(phenyl-d5)-indan, in particular (±)-cis-3,5-dichloro-1-(phenyl-d5)-indan or (1S,3S)-3,5-dichloro-1-(phenyl-d5)-indan, obtained as described above is converted to a pharmaceutically acceptable salt of 4-((1R,3S)-6-chloro-3-(phenyl-d5)-indan-1-yl)-1(d3),2,2-trimethyl-piperazine, the process comprising the following steps:

a) nucleophile substitution of 3,5-dichloro-1-(phenyl-d5)-indan with 1(d3),2,2-trimethylpiperazine bis-2,2,2-trifluoroacetate or a compound that subsequently can be transformed to the 1(d3),2,2-trimethyl-piperazine moiety of 4-((1R,3S)-6-chloro-3-(phenyl-d5)-indan-1-yl)-1(d3),2,2-trimethyl-piperazine

b) precipitation and optionally of the pharmaceutically acceptable salt by addition of the corresponding acid.

DETAILED DESCRIPTION OF THE INVENTION

Compound list

(I): 6-chloro-3-(phenyl-d_5)-inden-1-one

(II): 6-chloro-1-indanone

(III): 3-bromo-6-chloro-inden-1-one

(IV): 6-chloro-3-(phenyl-d_5)-1*H*-indene

(V): 5-chloro-1-indanone

(VI): (±)-6-chloro-3-(phenyl-d_5)-1*H*-inden-1-ol

(VIa) 6-chloro-3-(phenyl-d_5)-1*H*-inden-1-ol

(VII): (*S*)-6-chloro-3-(phenyl-d_5)-1*H*-inden-1-ol

(VIII): (±)-6-chloro-3-(phenyl-d_5)-indan-1-one

(VIIIa): 6-chloro-3-(phenyl-d_5)-indan-1-one

(IX): (*S*)-6-chloro-3-(phenyl-d_5)-indan-1-one

(X): (±)-*cis*-6-chloro-3-(phenyl-d_5)-indan-1-ol

(Xa): (1*S*,3*S*)-6-chloro-3-(phenyl-d_5)-indan-1-ol

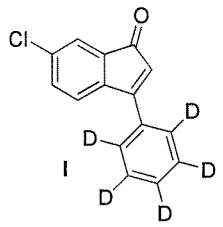
(Xb): 6-chloro-3-(phenyl-d_5)-indan-1-ol

(XI): (±)-*cis*-3,5-dichloro-1-(phenyl-d_5)-indan

(XIa): (1*S*,3*S*)-3,5-dichloro-1-(phenyl-d_5)-indan

Claims

1. A compound (Compound (I)) having the structure (I)



(I)

~~2. A process for production of compound (I), wherein compound (I) is obtained via reaction of 3-bromo-6-chloro-inden-1-one with an arylboronic acid or an arylboronic ester.~~

~~3. The process according to claim 2 wherein the arylboronic acid or arylboronic ester is 4,4,5,5-tetramethyl-2-d_5-phenyl-[1,3,2]dioxaborolane~~

~~4.~~2. ~~The~~A process for production of Compound (I), the process ~~of claims 1 or 2~~ comprising the following steps

a) 2,2'-azo-bis-isobutyronitrile and *N*-bromosuccinimide is added to a solution comprising 6-chloro-1-indanone

b) Triethylamine is added to the solution of step a) to obtain 3-bromo-6-chloro-inden-1-one

c) 3-bromo-6-chloro-inden-1-one is separated and reacted with 4,4,5,5-tetramethyl-2-d_5-phenyl-[1,3,2]dioxaborolane in the presence of an appropriate catalyst and base to obtain compound (I).

~~5.~~3. The process of claim ~~4~~2 wherein step c) is carried out in the presence of palladium acetate and triphenylphosphine.

~~6.~~4. ~~The~~ A process ~~according to claim 1~~for the production of Compound (I) comprising the steps of

~~3.~~ 1. Synthesis of 6-chloro-3-(phenyl-d_5)-1*H*-indene (IV) by reaction between an organometallic species obtained from monohalogenated benzene-d_5 and 5-chloro-1-indanone (V) followed by dehydration.

~~4.~~ 2. Reaction of 6-chloro-3-(phenyl-d_5)-1*H*-indene (IV) to (*E*)-1-(6-chloro-3-phenyl(d_5)-1*H*-inden-1-ylidenemethyl)-*N*,*N*-dimethylamine ~~compound~~ (XIX) and further oxidative cleavage thereof to obtain compound (I).

~~7.~~5. The process according to claim ~~6~~ 4 comprising the steps of

a) Synthesis of 6-chloro-3-(phenyl-d_5)-1*H*-indene (IV) by Grignard reaction between bromobenzene-d_5, magnesium and 5-chloro-1-indanone followed by dehydration.

b) Reacting 6-chloro-3-(phenyl-d_5)-1*H*-indene of step a) with 1,1-dimethoxy-*N*,*N*-dimethylmethanamine followed by oxidative cleavage of the formed enamine intermediate (XIX) to obtain compound (I).

~~8.~~6. The process of claims ~~6~~ 4 or ~~7~~ 5 wherein the oxidative cleavage in step b) is carried out by use of an oxidative agent selected from the group consisting of sodium metaperiodate, potassium metaperiodate, ozone, potassium dichromate, sodium dichromate, singlet oxygen and *m*-chloroperbenzoic acid.

~~9.~~7. A process comprising the steps

a) Compound (I) of claim 1 is reduced to obtain 6-chloro-3-(phenyl-d_5)-1*H*-inden-1-ol (VIa).

b) Compound (VIa) is converted to 6-chloro-3-(phenyl-d_5)-indan-1-one (VIIIa) via base-induced rearrangement.

~~10.~~8. A process comprising the steps

a) Compound (I) of claim 1 is converted to (*S*)-6-chloro-3-(phenyl-d_5)-1*H*-inden-1-ol (VII) via enantioselective reduction in the presence of enantioselective catalyst and reductant

b) Compound (VII) is converted to (*S*)-6-chloro-3-(phenyl-d_5)-indan-1-one (IX) via base-induced rearrangement.

~~11.~~9. A process comprising conversion of Compound (I) of claim 1 to obtain 6-chloro-3-(phenyl-d_5)-indan-1-one (VIIIa) via hydrogenation in the presence of a suitable catalyst, such as tris(triphenylphosphine)rhodium(I) chloride, in a suitable solvent, such as ethyl acetate.

~~12.~~10. A process comprising conversion of Compound (I) of claim 1 to obtain (*S*)-6-chloro-3-(phenyl-d_5)-indan-1-one (IX) via asymmetric hydrogenation in the

presence of a suitable catalyst, such as a rhodium salt, and a chiral phosphine ligand and a suitable solvent, such as ethyl acetate.

~~13.~~11. A process wherein the compounds obtained in any of claims ~~9~~ 7 to ~~12~~ 10 are converted to 3,5-dichloro-1-(phenyl-d_5)-indan, in particular (±)-*cis*-3,5-dichloro-1-(phenyl-d_5)-indan or (1*S*,3*S*)-3,5-dichloro-1-(phenyl-d_5)-indan, the process comprising the following steps

a) Reduction of (±)-6-chloro-3-(phenyl-d5)-indan-1-one (VIII), 6-chloro-3-(phenyl-d5)-indan-1-one (VIIIa) or (S)-6-chloro-3-(phenyl-d5)-indan-1-one (IX) to obtain the corresponding indanol:
(±)-cis-6-chloro-3-(phenyl-d5)-indan-1-ol (X), 6-chloro-3-(phenyl-d_5)-indan-1-ol (Xb) or (1S,3S)-6-chloro-3-(phenyl-d5)-indan-1-ol (Xa) in the presence of a suitable reduction agent, such as $NaBH_4$;

b) Chlorination, e.g. in the presence thionyl chloride, of any of the compounds obtained in step a) to obtain the corresponding chlorinated indan compound (±)-cis-3,5-dichloro-1-(phenyl-d5)-indan (XI), 3,5-dichloro-1-(phenyl-d5)-indan (XIb) or (1S,3S)-3,5-dichloro-1-(phenyl-d5)-indan (XIa)

~~14.~~12. A process wherein the (±)-cis-3,5-dichloro-1-(phenyl-d5)-indan (XI), 3,5-dichloro-1-(phenyl-d5)-indan (XIb) or (1S,3S)-3,5-dichloro-1-(phenyl-d5)-indan (XIa) as obtained in claim ~~13~~ 11 are converted to a pharmaceutically acceptable salt of (±)-*trans*-1-(6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine, 1-(6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine or 1-((1*R*, 3*S*)-6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine, the process comprising the following steps

a) reaction with 2,2-dimethylpiperazine ~~or a compound that subsequently can be transformed to to the 3,3-dimethylpiperazine moiety of (±)-*trans*-1-(6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine, 1-(6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine or 1-((1*R*, 3*S*)-6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine~~;

b) formation and optionally precipitation of the pharmaceutically acceptable salt by addition of the corresponding acid.

~~15.~~13. A process wherein the pharmaceutically acceptable salt of (±)-*trans*-1-(6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine, 1-(6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine or 1-((1*R*, 3*S*)-6-chloro-3-(phenyl-d_5)-indan-1-yl)-3,3-dimethyl-piperazine obtained in claim ~~14~~12 is converted to a pharmaceutically acceptable salt of 4-((1*R*,3*S*)-6-chloro-3-(phenyl-d_5)-indan-1-yl)-1(d_3),2,2-trimethyl-piperazine, the process comprising the following steps

a) alkylation in the presence of an active methyl-d_3 donor, such as methyl-iodide-d_3, and a base, such as potassium hydroxide, and

b) precipitation and optionally of the pharmaceutically acceptable salt by addition of the corresponding acid.

~~16.~~14. A process wherein the 3,5-dichloro-1-(phenyl-d_5)-indan, in particular (±)-*cis*-3,5-dichloro-1-(phenyl-d_5)-indan or (1*S*,3*S*)-3,5-dichloro-1-(phenyl-d_5)-indan, obtained in claim ~~13~~11 is converted to a pharmaceutically acceptable salt of 4-((1*R*,3*S*)-6-chloro-3-(phenyl-d_5)-indan-1-yl)-1(d_3),2,2-trimethyl-piperazine, the process comprising the following steps

a) nucleophile substitution of 3,5-dichloro-1-(phenyl-d_5)-indan with 1(d_3),2,2-trimethylpiperazine bis-2,2,2-trifluoroacetate ~~or a compound that subsequently can be transformed to the 1(d_3),2,2-trimethyl-piperazine moiety of 4-((1*R*,3*S*)-6-chloro-3-(phenyl-d_5)-indan-1-yl)-1(d_3),2,2-trimethyl-piperazine~~

b) precipitation and optionally of the pharmaceutically acceptable salt by addition of the corresponding acid.

~~17.~~15. A process according to any of ~~the preceding~~ claims 2 to 14 wherein the reactions are carried out with compounds comprising hydrogen (H) instead of deuterium (D) thus providing the corresponding non-deuterated compounds.