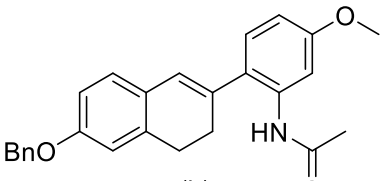
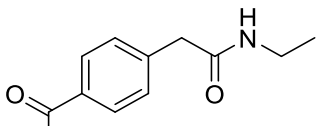


(a)

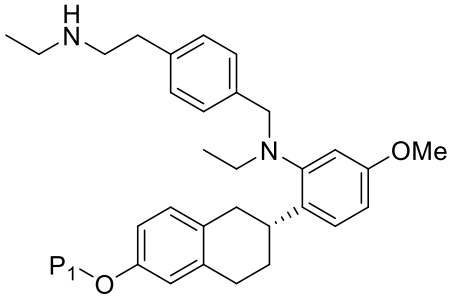


(b) and



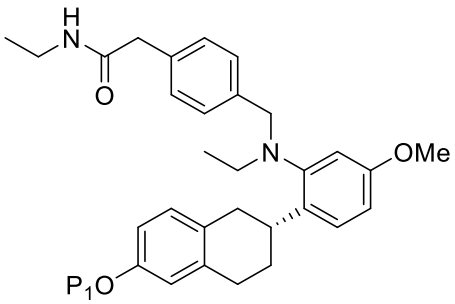
(f) .

[0004b] In another aspect of the present disclosure, there is provided a process of preparing a compound of formula (VIII)



(VIII) ,

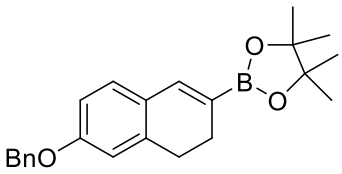
comprising the reduction of a compound of formula (VII)



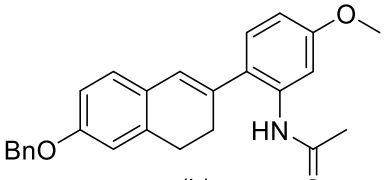
(VII)

CLAIMS:

1. A compound selected from:

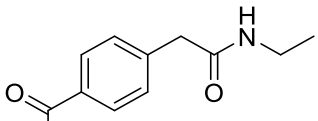


(a)



(b)

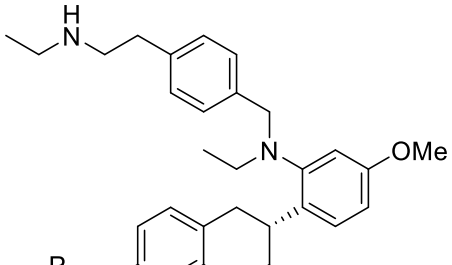
and



(f)

.

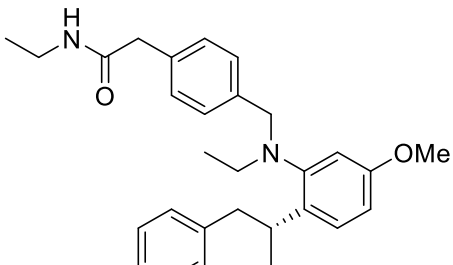
2. A process of preparing a compound of formula (VIII)



(VIII)

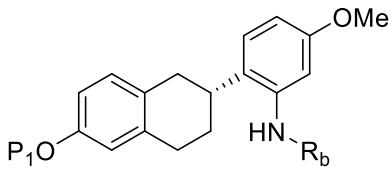
,

comprising the reduction of a compound of formula (VII)



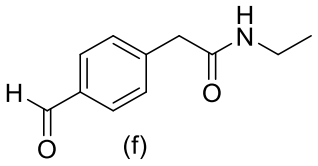
(VII)

wherein said compound of formula (VII) is prepared by a reductive amination of a compound of formula (VI)



(VI)

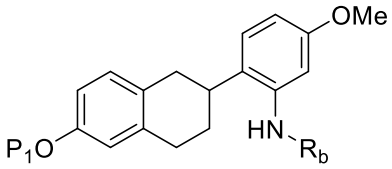
in the presence of a compound of formula (f)



(f)

,

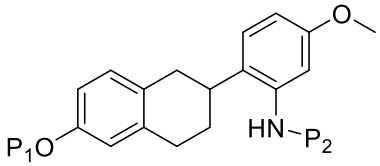
wherein said compound of formula (VI) is prepared by contacting a compound of formula (V)



(V)

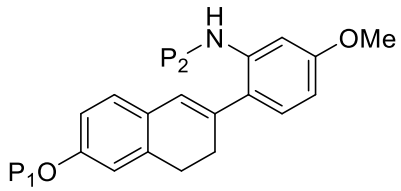
with a chiral acid to form an enantiomerically enriched salt, crystallizing the enantiomerically enriched salt, and freeing the compound of formula (VI),

wherein said compound of formula (V) is prepared by treatment of a compound of formula (IV) with a reducing agent;



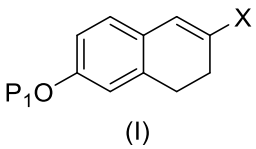
(IV)

wherein said compound of formula (IV) is prepared by reduction of a compound of formula (III)



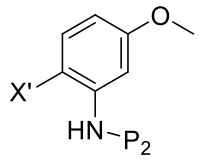
(III)

wherein said compound of formula (III) is prepared by the coupling of a compound of formula (I)



(I)

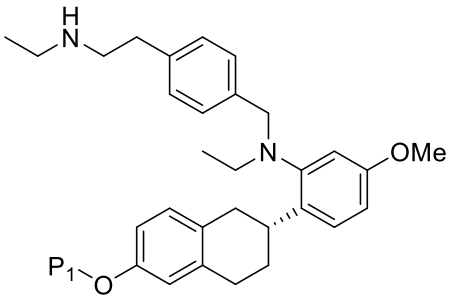
with a compound of formula (II)



(II)

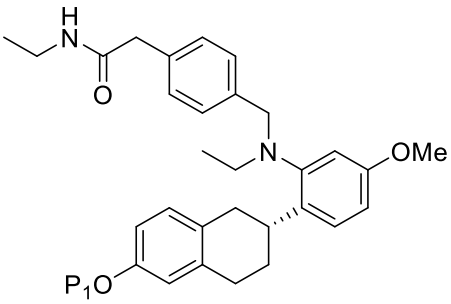
and wherein P_1 is H, or a phenol protecting group; R_b is H or Et; P_2 is (C=O)-CH_3; X is a halogen, transition metal-containing functional group, or boron-containing functional group; and X' is a halogen, transition metal-containing functional group, or boron-containing functional group; and wherein said X and X' are suitable for cross-coupling of compound (I) with compound (II).

3. A process of preparing a compound of formula (VIII):



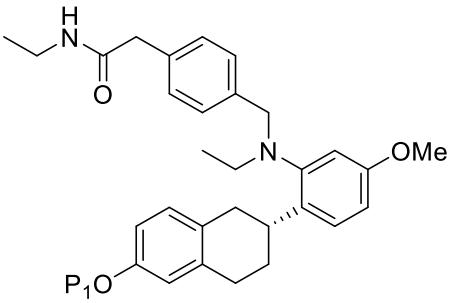
(VIII)

comprising the reduction of a compound of formula (VII):



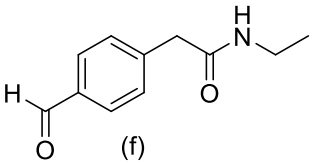
(VII)

wherein P_1 is H or a phenol protecting group;



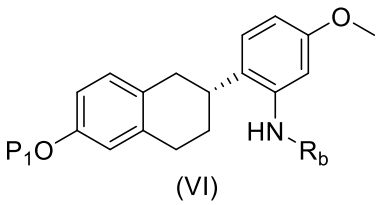
(VII)

comprising the reaction of a compound of formula (f);



(f)

with a compound of formula (VI)



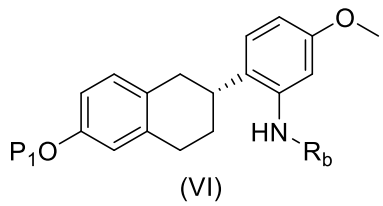
(VI) ,

in the presence of a reducing agent wherein Rb is H or Et.

4. The process of claim 3, conducted in the presence of AlH_3, AlH_2Cl, $AlHCl_2$, $NaBH_4$, $LiAlH_4$, $LiBH_4$, $LiEt_3BH$, BH_3, $BH_3.THF$, $CH_3CH_2C(O)OBH_3Na$, $Zn(OAc)_2/(EtO)_3SiH$, $Mg/TiCL_4$, (HBpin)/tris(4,4-dimethyl-2-oxazolinyl)phenylborateMgMe or combinations thereof.

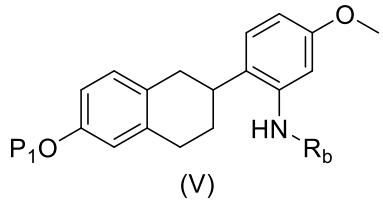
5. The process of claim 3 wherein the reducing agent used to react Compound (f) with a compound of Formula VI is $NaBH(OAc)_3$.

6. The process of claim 3, further comprising a process for increasing the enantiomer excess of a compound of formula (VI):



(VI)

comprising contacting a compound of formula (V) with a chiral acid to form an enantiomerically enriched salt,



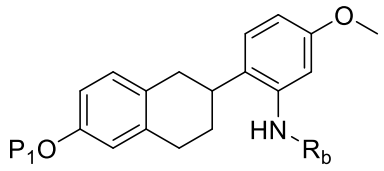
(V)

crystallizing the enantiomerically enriched salt, and freeing the compound of formula (VI).

7. The process of claim 6, wherein said enantiomeric excess of the compound of formula (VI) is >50%.

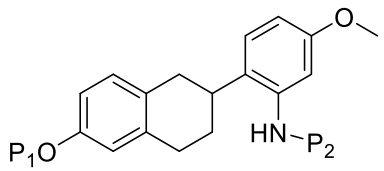
8. The process of claim 6 or claim 7, wherein said processes uses a (+) or (-) chiral acid selected from Aspartic acid, O-Acetyl-Mandelic acid, cis-2-Benzamidocyclohexanecarboxylic acid, 1,1'-Binapthyl-2,2'-diyl hydrogen phosphate, Camphoric acid, 10-Camphorsulfonic acid, trans-1,2-Cyclohexanedicarboxylic acid, Dibenzoyl-Tartaric acid, Diacetyl-tartaric acid, Di-p-toluoyl-tartaric acid, N-(3,5-Dinitrobenzoyl)-α-phenylglycine, Diacetyl-tartaric anhydride, Diacetyl-tartaric acid, Glutamic acid, Malic acid, Mandelic acid, N-(α-methylbenzyl)phthalamic acid, 2-(6-Methoxy-2-napthyl)propionic acid, Pyroglutamic acid, Quinic acid and Tartaric acid, or combinations thereof.

9. The process of claim 6, further comprising a process of preparing a compound of formula (V):



(V)

comprising the reaction of a compound of formula (IV):



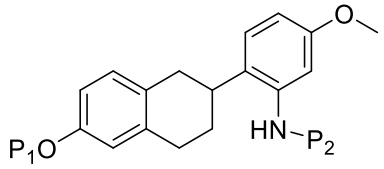
(IV)

with an acid, base, nucleophile or reducing agent wherein P_2 is an amino-protecting group selected from (C=O)-C_1-C_8 alkyl, (C=O)-aryl, (C=O)-heteroaryl, (C=O)-O-C_1-C_8 alkyl, (C=O)-O-aryl, (C=O)-O-heteroaryl, or (C=O)-O-C_1-C_8 alkylaryl.

10. The process of claim 9, wherein the compound of formula (IV) is treated with a hydride-containing reducing agent.

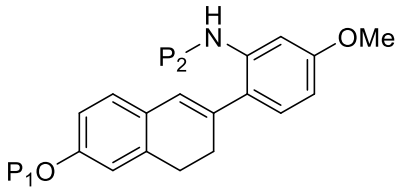
11. The process of claim 9 wherein R_b is H; and the compound according to formula (IV) is treated with an acid, base or nucleophile.

12. The process of claim 9, further comprising a process of preparing a compound of formula (IV):



(IV)

comprising the reduction of a compound of formula (III):

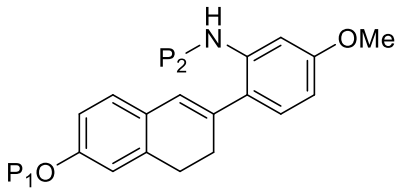


(III)

in the presence of a reducing agent.

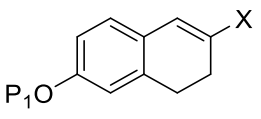
13. The process of claim 12, wherein P_1 is H, (C=O)-C_1-C_8 alkyl, (C=O)-aryl, (C=O)-heteroaryl, Si(C_1-C_5 alkyl)$_3$, Si(aryl)$_2$(C_1-C_5 alkyl) or CH_2Aryl.

14. The process of claim 12, further comprising a process of preparing a compound of formula (III):



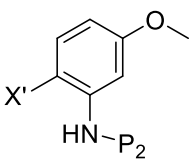
(III)

comprising the reaction of a compound of formula (I):



(I)

with a compound of formula (II):



(II)

in the presence of a base and a transition metal catalyst;

wherein

X is $B(OR)_2$, $B(-O-(C(R_a)_2)_n-O-)$, Cl, Br, I, OSO_2CF_3 or OSO_2(aryl);

X' is $B(OR)_2$, $B(-O-(C(R_a)_2)_n-O-)$, Cl, Br, I, OSO_2CF_3 or OSO_2(aryl);

each R is independently H, C_{1-3} alkyl or aryl;

each R_a is independently C_{1-3} alkyl or aryl; and

each n is independently an integer of 2 or 3,

wherein when X is $B(OR)_2$ or $B(-O-(C(R_a)_2)_n-O-)$, X' is Cl, Br, I, OSO_2CF_3 or OSO_2(aryl).

15. The process of claim 14, wherein P_1 is H, or a protecting group selected from (C=O)-C_1-C_8 alkyl, (C=O)-aryl, (C=O)-heteroaryl, $Si(C_1$-C_5 alkyl$)_3$, $Si(aryl)_2(C_1$-C_5 alkyl) and CH_2Aryl;

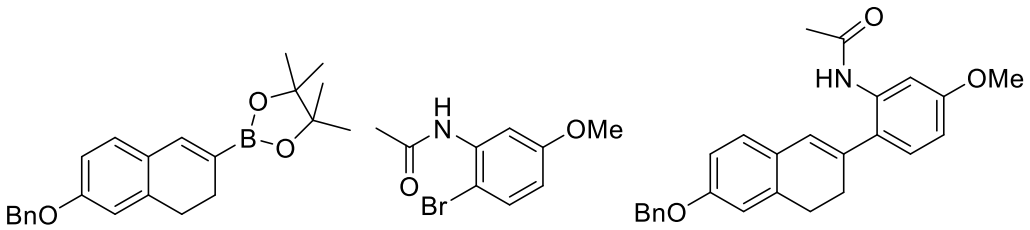
P_2 is $(C=O)-CH_3$;

X is $B(OR)_2$, or $B(-O-(C(R_a)_2)_n-O-)$; and

X' is Cl, Br, I, OSO_2CF_3 or OSO_2(aryl).

16. The process of claim 14 or claim 15, conducted in the presence of a transition metal catalyst selected from the group consisting of $Pd(OAc)_2$, $Pd(PPh_3)_4$, $PdCl_2(PPh_3)_2$, $Pd(dppf)Cl_2$, $Pd_2(Dba)_3$, Cu(0), $Pd(PCy_3)_2$, and any combinations thereof.

17. The process of any one of claims 2, or 14-16, wherein the compounds of formulas (I), (II) and (III) are (a), (aa') and (b):



(a) (aa') (b)