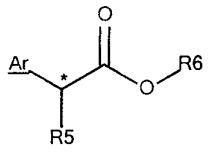
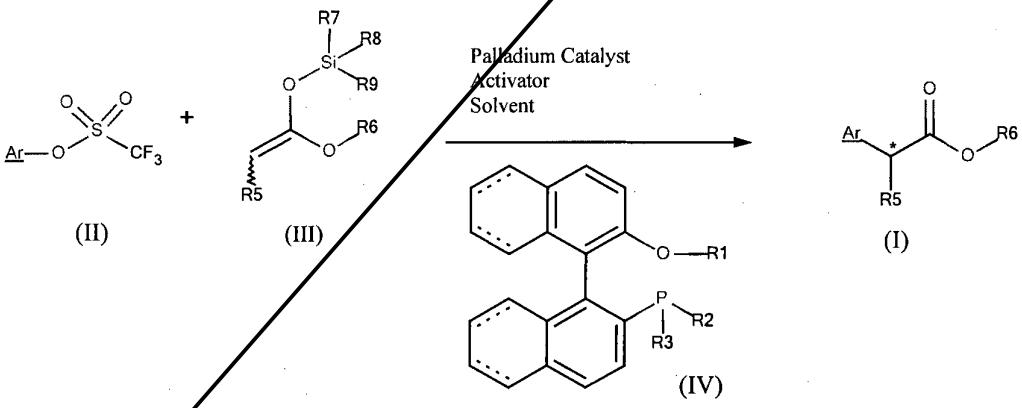
WHAT IS CLAIMED IS:

1. A method of asymmetrically synthesizing an α–aryl compound of Formula I:



(I),

or a pharmaceutically acceptable salt thereof, the method comprising the step of reacting a compound of Formula II with a compound of Formula III in the presence of a palladium catalyst, an activator, a compound of Formula IV, and optionally a solvent, to produce the asymmetric α–aryl compound of Formula I:



(II) (III) (IV) (I)

wherein:

* is an asymmetric carbon atom;

the compound of Formula III is the (E)- or (Z)-$OSiR^7R^8R^9$ isomer;

the palladium catalyst is selected from $PdMe_2(TMEDA)$, $Pd(dba)_2$, and $Pd(OAc)_2$;

the solvent is an aromatic solvent;

Ar is a substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl group, which is optionally independently substituted with 1, 2 or 3 R^4 groups;

 is a single or double bond, wherein either all of the  are single bonds or all of the  are double bonds;

R^1 is independently selected from hydrogen, alkyl, aryl, and arylalkyl;

R^2 and R^3 are each independently selected from alkyl, cycloalkyl, aryl and arylalkyl;

each R^4 is independently selected from hydrogen, amino, halogen, hydroxyl, nitro, cyano, alkyl, alkenyl, alkynyl, perfluoroalkyl, cycloalkyl, alkoxy, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, $(CH_2)_jOR^{11}$, $(CH_2)_jC(O)R^{11}$, $(CH_2)_jC(O)OR^{11}$, $(CH_2)_jOC(O)R^{11}$, $(CH_2)_jNR^{12}R^{13}$, $(CH_2)_jC(O)NR^{12}R^{13}$, $(CH_2)_jOC(O)NR^{12}R^{13}$, $(CH_2)_jN^{14}RC(O)R^{11}$, $(CH_2)_jN^{14}RC(O)OR^{11}$, $(CH_2)_jN^{14}RC(O)NR^{12}R^{13}$, $(CH_2)_jS(O)_mR^{11}$, and $(CH_2)_jS(O)_mNR^{12}R^{13}$, wherein each j is independently an integer selected from 0 to 6, and each m is independently an integer selected from 0 to 2;

R^5 is independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heteroarylalkyl, which is optionally independently substituted with 1, 2 or 3 R^{10} groups;

R^6 is independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted arylalkyl, which is optionally independently substituted with 1, 2 or 3 R^{10} groups;

R^7, R^8 and R^9 are each independently selected from alkyl, aryl and arylalkyl;

each R^{10} is independently selected from hydrogen, amino, halogen, hydroxyl, nitro, cyano, alkyl, alkenyl, alkynyl, perfluoroalkyl, cycloalkyl, alkoxy, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, $(CH_2)_jOR^{11}$, $(CH_2)_jC(O)R^{11}$, $(CH_2)_jC(O)OR^{11}$, $(CH_2)_jOC(O)R^{11}$, $(CH_2)_jNR^{12}R^{13}$, $(CH_2)_jC(O)NR^{12}R^{13}$, $(CH_2)_jOC(O)NR^{12}R^{13}$, $(CH_2)_jN^{14}RC(O)R^{11}$, $(CH_2)_jN^{14}RC(O)OR^{11}$, $(CH_2)_jN^{14}RC(O)NR^{12}R^{13}$, $(CH_2)_jS(O)_mR^{11}$, and $(CH_2)_jS(O)_mNR^{12}R^{13}$, wherein each j is independently an integer selected from 0 to 6, and each m is independently an integer selected from 0 to 2;

R^{11} is independently selected from hydrogen, alkyl, alkenyl, alkynyl, perfluoroalkyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, and heteroarylalkyl; and

R^{12}, R^{13}, R^{14} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, perfluoroalkyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, and heteroarylalkyl, or R^{14} is as described above, and R^{12} and R^{13} are joined together with the nitrogen atom to which they are attached, to form a substituted or unsubstituted 3- to 7-membered hetercycloalkyl or substituted or unsubstituted 5-membered heteroaryl, wherein the 3- to 7-membered hetercycloalkyl is selected from aziridine, azetidine, pyrrolidinyl, pyrazolidinyl, imidazolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, and azepanyl; and the 5-membered heteroaryl is selected from pyrrolyl, pyrazolyl, imidazolyl, pyridinyl, pyrazinyl, pyrimidinyl, indolyl, purinyl, benzimidazolyl, quinolinyl, and isoquinolinyl.

2. The method of claim 1, wherein:

* is an R or S asymmetric carbon atom, wherein the asymmetric α–aryl compound of Formula I is at least about 50% to about 60% enantiomeric excess;

the compound of Formula III is the (E)-$OSiR^7R^8R^9$ isomer;

the palladium catalyst is $PdMe_2(TMEDA)$;

the activator is $LiOC(O)CH_3$;

the aromatic solvent is selected from benzene, chlorobenzene, fluorobenzene, toluene, trifluorobenzene, dichloromethane, dichloroethane, tetrahydrofuran and mixtures thereof;

Ar is a substituted or unsubstituted phenyl, substituted or unsubstituted biphenyl, substituted or unsubstituted naphthalenyl, substituted or unsubstituted benzyl, substituted or unsubstituted CH_2(1-naphthalenyl), substituted or unsubstituted CH_2(2-naphthalenyl), substituted or unsubstituted furanyl, substituted or unsubstituted thiophenyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted pyridinyl, substituted or unsubstituted pyrazinyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted indolyl, substituted or unsubstituted purinyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzo[b]thiophenyl, substituted or unsubstituted quinolinyl, and substituted or unsubstituted isoquinolinyl;

R^1 is independently selected from hydrogen, $(C_1$-$C_6)$alkyl, phenyl, biphenyl, naphthalenyl, benzyl, CH_2(1-naphthalenyl) and CH_2(2-naphthalenyl);

R^2 and R^3 are each independently selected from $(C_1$-$C_6)$alkyl, $(C_3$-$C_6)$cycloalkyl, phenyl, biphenyl, benzyl, and naphthalenyl;

R^5 is independently selected from substituted or unsubstituted (C_{1-12})alkyl, substituted or unsubstituted phenyl, substituted or unsubstituted biphenyl, substituted or unsubstituted naphthalenyl, substituted or unsubstituted benzyl, substituted or unsubstituted CH_2(1-naphthalenyl), substituted or unsubstituted CH_2(2-naphthalenyl), substituted or unsubstituted furanyl, substituted or unsubstituted thiophenyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted pyridinyl, substituted or unsubstituted pyrazinyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted indolyl, substituted or unsubstituted purinyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzo[b]thiophenyl, substituted or unsubstituted quinolinyl, substituted or unsubstituted isoquinolinyl, substituted or unsubstituted aziridine, substituted or

unsubstituted oxiranyl, substituted or unsubstituted thiiranyl, substituted or unsubstituted azetidinyl, substituted or unsubstituted oxetanyl, substituted or unsubstituted thietanyl, substituted or unsubstituted pyrrolidinyl, substituted or unsubstituted pyrazolidinyl, substituted or unsubstituted imidazolidinyl, substituted or unsubstituted oxolanyl, substituted or unsubstituted thiolanyl, substituted or unsubstituted piperidinyl, substituted or unsubstituted oxanyl, substituted or unsubstituted thianyl, substituted or unsubstituted piperazinyl, substituted or unsubstituted morpholinyl, substituted or unsubstituted thiomorpholinyl, substituted or unsubstituted azepanyl, substituted or unsubstituted oxepanyl, and substituted or unsubstituted thiepinyl;

R^6 is independently selected from hydrogen, substituted or unsubstituted $(C_1\text{-}C_6)$alkyl, substituted or unsubstituted $(C_3\text{-}C_8)$cycloalkyl, phenyl, substituted or unsubstituted biphenyl, substituted or unsubstituted naphthalenyl, substituted or unsubstituted benzyl, substituted or unsubstituted CH_2(1-naphthalenyl), substituted or unsubstituted CH_2(2-naphthalenyl); and

R^7, R^8 and R^9 are each independently selected from $(C_1\text{-}C_6)$alkyl and phenyl.

3. The method of claim 2, wherein:

* is an R or S asymmetric carbon atom, wherein the asymmetric α–aryl compound of Formula I is at least about 60% to about 70% enantiomeric excess;

Ar is selected from substituted or unsubstituted phenyl, substituted or unsubstituted naphthalenyl, substituted or unsubstituted benzyl, substituted or unsubstituted CH_2(1-naphthalenyl), substituted or unsubstituted CH_2(2-naphthalenyl), substituted or unsubstituted furanyl, substituted or unsubstituted thiophenyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted pyridinyl, substituted or unsubstituted pyrazinyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted indolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzo[b]thiophenyl, substituted or unsubstituted quinolinyl, and substituted or unsubstituted isoquinolinyl;

R^1 is independently selected from hydrogen, methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, phenyl, benzyl, CH_2(1-naphthalenyl), and CH_2(2-naphthalenyl);

R^2 and R^3 are each independently selected from (C_1-C_6)alkyl and (C_3-C_6)cycloalkyl;

R^5 is independently selected from substituted or unsubstituted (C_1-C_{12})alkyl, substituted or unsubstituted phenyl, substituted or unsubstituted naphthalenyl, substituted or unsubstituted benzyl, substituted or unsubstituted CH_2(1-naphthalenyl), and substituted or unsubstituted CH_2(2-naphthalenyl);

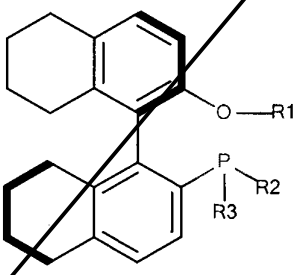
R^6 is independently selected from hydrogen, (C_1-C_6)alkyl, (C_3-C_8)cycloalkyl, phenyl, naphthalenyl, benzyl, CH_2(1-naphthalenyl), and CH_2(2-naphthalenyl); and

R^7, R^8 and R^9 are each independently selected from (C_1-C_6)alkyl.

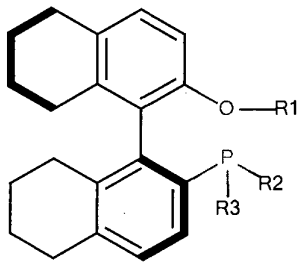
4. The method of claim 3, wherein:

* is an R or S asymmetric carbon atom, wherein the asymmetric α–aryl compound of Formula I is at least about 70% to about 80% enantiomeric excess; and

the compound of Formula IV has Formula IVa or IVb:



(IVa),

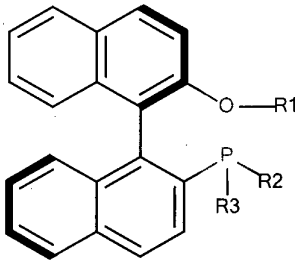


(IVb).

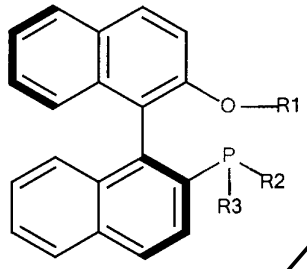
5. The method of claim 3, wherein:

* is an R or S asymmetric carbon atom, wherein the asymmetric α–aryl compound of Formula I is at least about 80% to about 90% enantiomeric excess; and

the compound of Formula IV has Formula IVc or IVd:



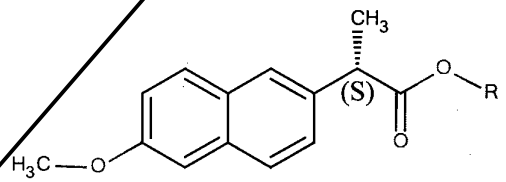
(IVc)



(IVd).

6. The method of any of claims 1 to 5, further comprising heating the compound of Formula II with the compound of Formula III in the presence of the palladium catalyst, the activator, the compound of Formula IV, and the solvent to produce the asymmetric α–aryl compound of Formula I.

7. The method of any of claims 1 to 6, wherein the compound of Formula I, or pharmaceutically acceptable salt thereof, is (S)-Naproxen or the tert-butyl ester thereof:



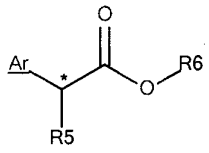
,

wherein R is H or $C(CH_3)_3$.

8. The method of any of claims 1 to 7, wherein the aromatic solvent is selected from the group consisting of benzene, chlorobenzene, fluorobenzene, toluene, trifluorobenzene, dichloromethane, dichloroethane, tetrahydrofuran, and combinations thereof.

9. The method of any of claom 1 to 8, wherein the activitator is selected from LiOC(O)CH3, LiOC(O)CF3, LiOS(O)2CH3, LiOC(O)C(CH3)3, LiF, NaOC(O)CH3, NaOC(O)CF3, Na2CO3, KOC(O)CH3, CsF, Cs2CO3, CsOC(O)CH3, ZnF2, Zn(OC(O)CH3)2, CuF2, and combinations thereof;

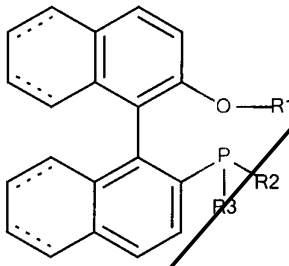
10. A compound of Formula I:



(I),

or a pharmaceutically acceptable salt thereof, prepared by the method of claim 1.

11. A compound having Formula IV:



(IV)

or a pharmaceutically acceptable salt thereof, wherein:

 is a single or double bond, wherein either all of the  are single bonds or all of the  are double bonds;

R^1 is independently selected from hydrogen, alkyl, aryl, and arylalkyl; and

R^2 and R^3 are each independently selected from alkyl, cycloalkyl, aryl and arylalkyl.

12. The compound of claim 10, wherein:

R^1 is independently selected from hydrogen, $(C_1\text{-}C_6)$alkyl, phenyl, biphenyl, naphthalenyl, benzyl, CH_2(1-naphthalenyl) and CH_2(2-naphthalenyl); and

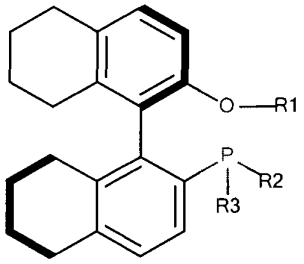
R^2 and R^3 are each independently selected from $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, phenyl, biphenyl, benzyl, and naphthalenyl.

13. The compound of claim 12, wherein:

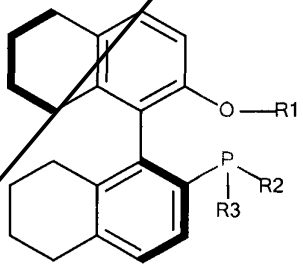
R^1 is independently selected from hydrogen, methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, phenyl, benzyl, CH_2(1-naphthalenyl), and CH_2(2-naphthalenyl); and

R^2 and R^3 are each independently selected from $(C_1\text{-}C_6)$alkyl and $(C_3\text{-}C_6)$cycloalkyl.

14. The compound of claim 11, wherein the compound of Formula IV has Formula IVa or IVb:

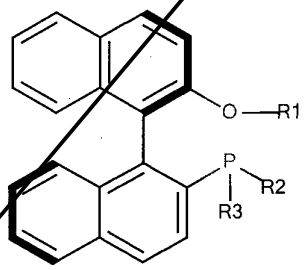


(IVa),

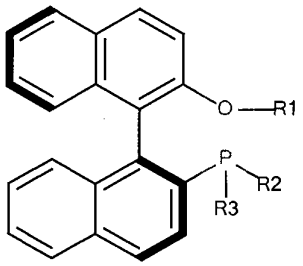


(IVb).

53. The compound of claim 11, wherein the compound of Formula IV has Formula IVc or IVd:

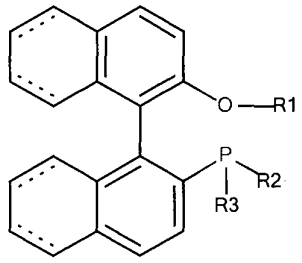


(IVc)



(IVd).

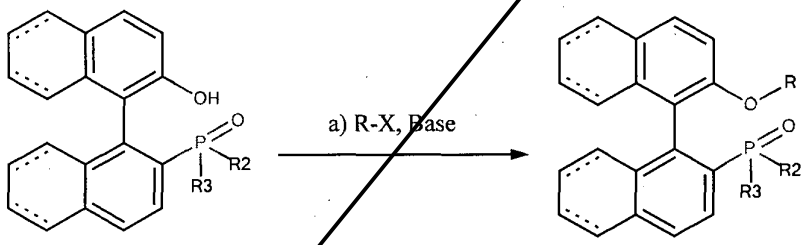
16. A method of preparing a compound of Formula IV:



(IV),

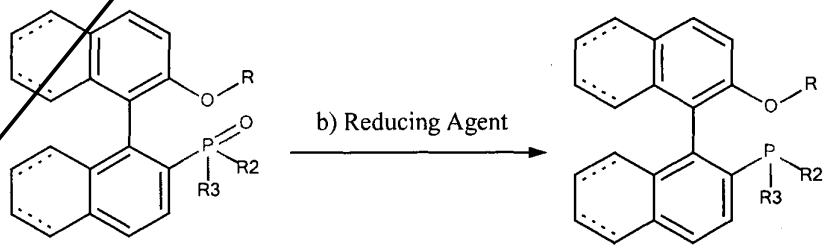
or a pharmaceutically acceptable salt thereof, the method comprising the steps of:

a) reacting a compound of Formula V with a compound R-X in the presence of a Base to provide a compound of Formula VI



(V) (VI) ; and

b) reducing the compound of Formula VI with a reducing agent to provide the compound of Formula IV:



(IV) ,

wherein:

R is selected from alkly, cycloalkyl, aryl, and arylalkyl;

 is a single or double bond, wherein either all of the  are single bonds or all of the  are double bonds;

R^1 is independently selected from hydrogen, alkyl, aryl, and arylalkyl; and

R^2 and R^3 are each independently selected from alkyl, cycloalkyl, aryl and arylalkyl.

17. The method of claim 16, wherein:

the base is selected from NaH, KH, NaOH, KOH, Na_2CO_3, K_2CO_3, Cs_2CO_3, $KOC(CH_3)_3$, NH_4OH, $NH_2(CH_3)$, $NH(CH_3)_2$, $N(CH_3)_3$, $((CH_3)_2CH)_2N(C_2H_5)$, and C_5H_5N;

the reducing agent is selected from $HSiCl_3$, $NaBH_4$, and KBH_4;

R is selected from methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, phenyl, benzyl, CH_2(1-naphthalenyl), and CH_2(2-naphthalenyl);

R^1 is independently selected from hydrogen, $(C_1\text{-}C_6)$alkyl, phenyl, biphenyl, naphthalenyl, benzyl, CH_2(1-naphthalenyl) and CH_2(2-naphthalenyl); and

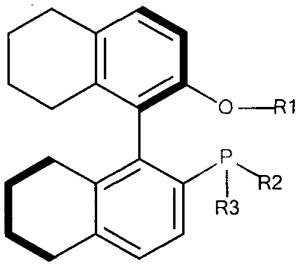
R^2 and R^3 are each independently selected from $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl, phenyl, biphenyl, benzyl, and naphthalenyl.

18. The method of claim 17, wherein:

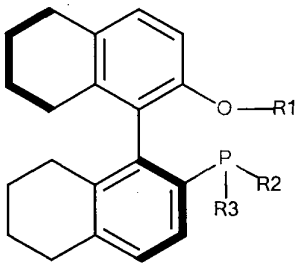
R^1 is independently selected from hydrogen, methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, phenyl, benzyl, CH_2(1-naphthalenyl), and CH_2(2-naphthalenyl); and

R^2 and R^3 are each independently selected from $(C_1\text{-}C_6)$alkyl and $(C_3\text{-}C_6)$cycloalkyl.

19. The method of claim 16, wherein the compound of Formula IV has Formula IVa or IVb:

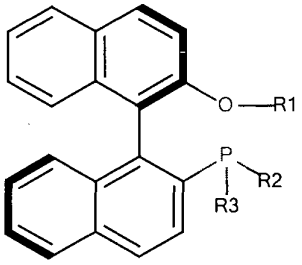


(IVa),

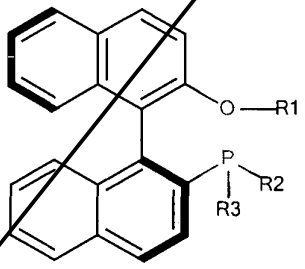


(IVb).

20. The method of claim 14, wherein the compound of Formula IV has Formula IVc or IVd:

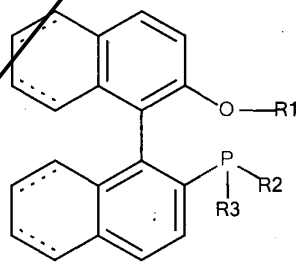


(IVc)



(IVd).

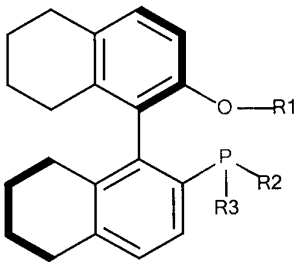
21. A compound of Formula IV:



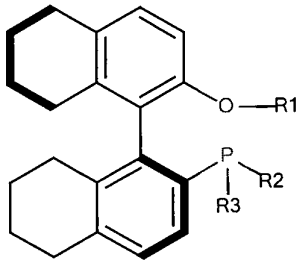
(IV),

or a pharmaceutically acceptable salt thereof, prepared by the method of claim 14.

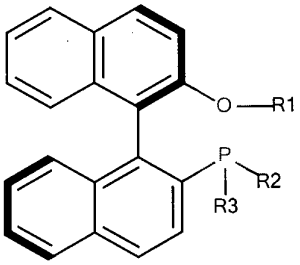
22. The compound of claim 21, wherein the compound of Formula IV has Formula Iva, IVb, IVc or IVd:



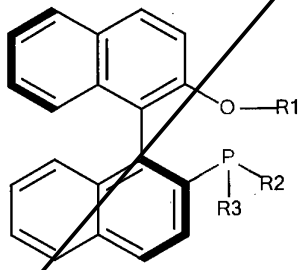
(IVa),



(IVb),



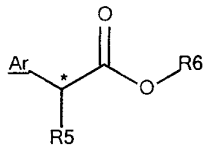
(IVc),



(IVd).

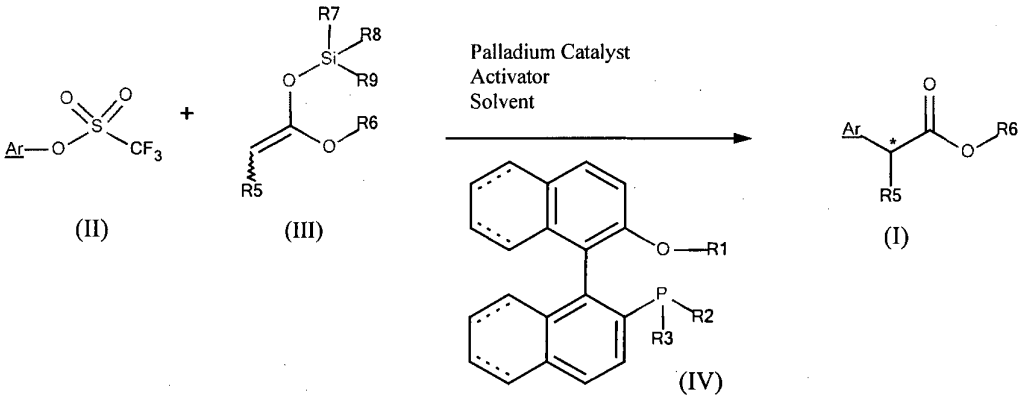
WHAT IS CLAIMED IS:

1. A method of asymmetrically synthesizing an α–aryl compound of Formula I:



(I),

or a pharmaceutically acceptable salt thereof, the method comprising the step of reacting a compound of Formula II with a compound of Formula III in the presence of a palladium catalyst, an activator, a compound of Formula IV, and optionally a solvent, to produce the asymmetric α–aryl compound of Formula I:



(II) (III) (I)

(IV)

wherein:

* is an asymmetric carbon atom;

the compound of Formula III is the (E)- or (Z)-$OSiR^7R^8R^9$ isomer;

the palladium catalyst is selected from $PdMe_2(TMEDA)$, $Pd(dba)_2$, and $Pd(OAc)_2$;

the solvent is an aromatic solvent;

Ar is a substituted or unsubstituted aryl or substituted or unsubstituted heteroaryl group, which is optionally independently substituted with 1, 2 or 3 R^4 groups;

 is a single or double bond, wherein either all of the  are single bonds or all of the  are double bonds;

R^1 is independently selected from hydrogen, alkyl, aryl, and arylalkyl;

R^2 and R^3 are each independently selected from alkyl, cycloalkyl, aryl and arylalkyl;

each R^4 is independently selected from hydrogen, amino, halogen, hydroxyl, nitro, cyano, alkyl, alkenyl, alkynyl, perfluoroalkyl, cycloalkyl, alkoxy, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, $(CH_2)_jOR^{11}$, $(CH_2)_jC(O)R^{11}$, $(CH_2)_jC(O)OR^{11}$, $(CH_2)_jOC(O)R^{11}$, $(CH_2)_jNR^{12}R^{13}$, $(CH_2)_jC(O)NR^{12}R^{13}$, $(CH_2)_jOC(O)NR^{12}R^{13}$, $(CH_2)_jN^{14}RC(O)R^{11}$, $(CH_2)_jN^{14}RC(O)OR^{11}$, $(CH_2)_jN^{14}RC(O)NR^{12}R^{13}$, $(CH_2)_jS(O)_mR^{11}$, and $(CH_2)_jS(O)_mNR^{12}R^{13}$, wherein each j is independently an integer selected from 0 to 6, and each m is independently an integer selected from 0 to 2;

R^5 is independently selected from substituted or unsubstituted alkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted arylalkyl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted heteroarylalkyl, which is optionally independently substituted with 1, 2 or 3 R^{10} groups;

R^6 is independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, and substituted or unsubstituted arylalkyl, which is optionally independently substituted with 1, 2 or 3 R^{10} groups;

R^7, R^8 and R^9 are each independently selected from alkyl, aryl and arylalkyl;

each R^{10} is independently selected from hydrogen, amino, halogen, hydroxyl, nitro, cyano, alkyl, alkenyl, alkynyl, perfluoroalkyl, cycloalkyl, alkoxy, heterocycloalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, $(CH_2)_jOR^{11}$, $(CH_2)_jC(O)R^{11}$, $(CH_2)_jC(O)OR^{11}$, $(CH_2)_jOC(O)R^{11}$, $(CH_2)_jNR^{12}R^{13}$, $(CH_2)_jC(O)NR^{12}R^{13}$, $(CH_2)_jOC(O)NR^{12}R^{13}$, $(CH_2)_jN^{14}RC(O)R^{11}$, $(CH_2)_jN^{14}RC(O)OR^{11}$, $(CH_2)_jN^{14}RC(O)NR^{12}R^{13}$, $(CH_2)_jS(O)_mR^{11}$, and $(CH_2)_jS(O)_mNR^{12}R^{13}$, wherein each j is independently an integer selected from 0 to 6, and each m is independently an integer selected from 0 to 2;

R^{11} is independently selected from hydrogen, alkyl, alkenyl, alkynyl, perfluoroalkyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, and heteroarylalkyl; and

R^{12}, R^{13}, R^{14} are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, perfluoroalkyl, cycloalkyl, heterocycloalkyl, aryl, arylalkyl, heteroaryl, and heteroarylalkyl, or R^{14} is as described above, and R^{12} and R^{13} are joined together with the nitrogen atom to which they are attached, to form a substituted or unsubstituted 3- to 7-membered hetercycloalkyl or substituted or unsubstituted 5-membered heteroaryl, wherein the 3- to 7-membered hetercycloalkyl is selected from aziridine, azetidine, pyrrolidinyl, pyrazolidinyl, imidazolidinyl, piperidinyl, piperazinyl, morpholinyl, thiomorpholinyl, and azepanyl; and the 5-membered heteroaryl is selected from pyrrolyl, pyrazolyl, imidazolyl, pyridinyl, pyrazinyl, pyrimidinyl, indolyl, purinyl, benzimidazolyl, quinolinyl, and isoquinolinyl.

2. The method of claim 1, wherein:

* is an R or S asymmetric carbon atom, wherein the asymmetric α–aryl compound of Formula I is at least about 50% to about 60% enantiomeric excess;

the compound of Formula III is the (E)-$OSiR^7R^8R^9$ isomer;

the palladium catalyst is $PdMe_2(TMEDA)$;

the activator is $LiOC(O)CH_3$;

the aromatic solvent is selected from benzene, chlorobenzene, fluorobenzene, toluene, trifluorobenzene, dichloromethane, dichloroethane, tetrahydrofuran and mixtures thereof;

Ar is a substituted or unsubstituted phenyl, substituted or unsubstituted biphenyl, substituted or unsubstituted naphthalenyl, substituted or unsubstituted benzyl, substituted or unsubstituted CH_2(1-naphthalenyl), substituted or unsubstituted CH_2(2-naphthalenyl), substituted or unsubstituted furanyl, substituted or unsubstituted thiophenyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted pyridinyl, substituted or unsubstituted pyrazinyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted indolyl, substituted or unsubstituted purinyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzo[b]thiophenyl, substituted or unsubstituted quinolinyl, and substituted or unsubstituted isoquinolinyl;

R^1 is independently selected from hydrogen, (C_1-C_6)alkyl, phenyl, biphenyl, naphthalenyl, benzyl, CH_2(1-naphthalenyl) and CH_2(2-naphthalenyl);

R^2 and R^3 are each independently selected from (C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, phenyl, biphenyl, benzyl, and naphthalenyl;

R^5 is independently selected from substituted or unsubstituted (C_1-$_{12}$)alkyl, substituted or unsubstituted phenyl, substituted or unsubstituted biphenyl, substituted or unsubstituted naphthalenyl, substituted or unsubstituted benzyl, substituted or unsubstituted CH_2(1-naphthalenyl), substituted or unsubstituted CH_2(2-naphthalenyl), substituted or unsubstituted furanyl, substituted or unsubstituted thiophenyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted pyridinyl, substituted or unsubstituted pyrazinyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted indolyl, substituted or unsubstituted purinyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzo[b]thiophenyl, substituted or unsubstituted quinolinyl, substituted or unsubstituted isoquinolinyl, substituted or unsubstituted aziridine, substituted or

unsubstituted oxiranyl, substituted or unsubstituted thiiranyl, substituted or unsubstituted azetidinyl, substituted or unsubstituted oxetanyl, substituted or unsubstituted thietanyl, substituted or unsubstituted pyrrolidinyl, substituted or unsubstituted pyrazolidinyl, substituted or unsubstituted imidazolidinyl, substituted or unsubstituted oxolanyl, substituted or unsubstituted thiolanyl, substituted or unsubstituted piperidinyl, substituted or unsubstituted oxanyl, substituted or unsubstituted thianyl, substituted or unsubstituted piperazinyl, substituted or unsubstituted morpholinyl, substituted or unsubstituted thiomorpholinyl, substituted or unsubstituted azepanyl, substituted or unsubstituted oxepanyl, and substituted or unsubstituted thiepinyl;

R^6 is independently selected from hydrogen, substituted or unsubstituted $(C_1\text{-}C_6)$alkyl, substituted or unsubstituted $(C_3\text{-}C_8)$cycloalkyl, phenyl, substituted or unsubstituted biphenyl, substituted or unsubstituted naphthalenyl, substituted or unsubstituted benzyl, substituted or unsubstituted CH_2(1-naphthalenyl), substituted or unsubstituted CH_2(2-naphthalenyl); and

R^7, R^8 and R^9 are each independently selected from $(C_1\text{-}C_6)$alkyl and phenyl.

3. The method of claim 2, wherein:

* is an R or S asymmetric carbon atom, wherein the asymmetric α–aryl compound of Formula I is at least about 60% to about 70% enantiomeric excess;

Ar is selected from substituted or unsubstituted phenyl, substituted or unsubstituted naphthalenyl, substituted or unsubstituted benzyl, substituted or unsubstituted CH_2(1-naphthalenyl), substituted or unsubstituted CH_2(2-naphthalenyl), substituted or unsubstituted furanyl, substituted or unsubstituted thiophenyl, substituted or unsubstituted pyrrolyl, substituted or unsubstituted pyrazolyl, substituted or unsubstituted imidazolyl, substituted or unsubstituted pyridinyl, substituted or unsubstituted pyrazinyl, substituted or unsubstituted pyrimidinyl, substituted or unsubstituted indolyl, substituted or unsubstituted benzimidazolyl, substituted or unsubstituted benzo[b]thiophenyl, substituted or unsubstituted quinolinyl, and substituted or unsubstituted isoquinolinyl;

R^1 is independently selected from hydrogen, methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, phenyl, benzyl, CH_2(1-naphthalenyl), and CH_2(2-naphthalenyl);

R^2 and R^3 are each independently selected from (C_1-C_6)alkyl and (C_3-C_6)cycloalkyl;

R^5 is independently selected from substituted or unsubstituted (C_1-C_{12})alkyl, substituted or unsubstituted phenyl, substituted or unsubstituted naphthalenyl, substituted or unsubstituted benzyl, substituted or unsubstituted CH_2(1-naphthalenyl), and substituted or unsubstituted CH_2(2-naphthalenyl);

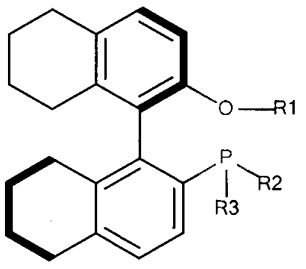
R^6 is independently selected from hydrogen, (C_1-C_6)alkyl, (C_3-C_8)cycloalkyl, phenyl, naphthalenyl, benzyl, CH_2(1-naphthalenyl), and CH_2(2-naphthalenyl); and

R^7, R^8 and R^9 are each independently selected from (C_1-C_6)alkyl.

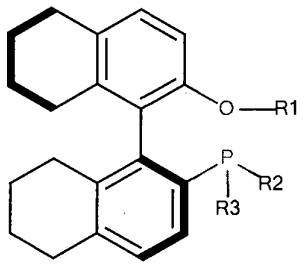
4. The method of claim 3, wherein:

* is an R or S asymmetric carbon atom, wherein the asymmetric α–aryl compound of Formula I is at least about 70% to about 80% enantiomeric excess; and

the compound of Formula IV has Formula IVa or IVb:



(IVa),

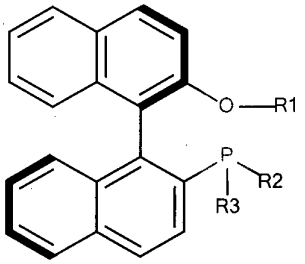


(IVb).

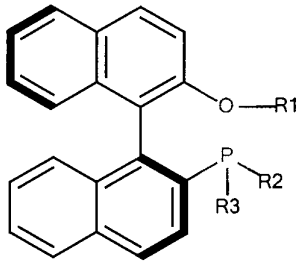
5. The method of claim 3, wherein:

* is an R or S asymmetric carbon atom, wherein the asymmetric α–aryl compound of Formula I is at least about 80% to about 90% enantiomeric excess; and

the compound of Formula IV has Formula IVc or IVd:



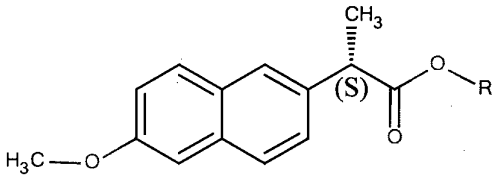
(IVc)



(IVd).

6. The method of any of claims 1 to 5, further comprising heating the compound of Formula II with the compound of Formula III in the presence of the palladium catalyst, the activator, the compound of Formula IV, and the solvent to produce the asymmetric α–aryl compound of Formula I.

7. The method of any of claims 1 to 6, wherein the compound of Formula I, or pharmaceutically acceptable salt thereof, is (S)-Naproxen or the tert-butyl ester thereof:



,

wherein R is H or $C(CH_3)_3$.

8. The method of any of claims 1 to 7, wherein the aromatic solvent is selected from the group consisting of benzene, chlorobenzene, fluorobenzene, toluene, trifluorobenzene, dichloromethane, dichloroethane, tetrahydrofuran, and combinations thereof.

9. The method of any of claom 1 to 8, wherein the activitator is selected from LiOC(O)CH3, LiOC(O)CF3, LiOS(O)2CH3, LiOC(O)C(CH3)3, LiF, NaOC(O)CH3, NaOC(O)CF3, Na2CO3, KOC(O)CH3, CsF, Cs2CO3, CsOC(O)CH3, ZnF2, Zn(OC(O)CH3)2, CuF2, and combinations thereof.