(12) PATENT
(19) AUSTRALIAN PATENT OFFICE

(11) Application No. AU 200113206 B2
(10) Patent No. 776118

(54) Title
Novel hydronaphtalene compounds, prepared by a rhodium catalyzed ring opening reaction in the presence of phosphine ligand

(51)6 International Patent Classification(s)
C07C 043/18 C07C 027/30
A61K 031/075 C07C 069/013
A61K 031/21 C07C 069/02
A61K 031/325 C07C 069/76
A61K 031/395 C07C 215/86
A61P 025/16 C07C 219/34
A61P 029/00 C07C 311/01
A61P 031/18 C07D 209/02
A61P 035/00 C07D 215/06

(21) Application No: 200113206 (22) Application Date: 2000.10.26

(87) WIPO No: WO01/30734

(30) Priority Data

(31) Number	(32) Date	(33) Country
9903930	1999.10.29	SE

(43) Publication Date : 2001.05.08
(43) Publication Journal Date : 2001.07.26
(44) Accepted Journal Date : 2004.08.26

(71) Applicant(s)
AstraZeneca AB

(72) Inventor(s)
Keith Fagnou; Mark Lautens

(74) Agent/Attorney
PHILLIPS ORMONDE and FITZPATRICK,367 Collins Street,MELBOURNE VIC 3000

(56) Related Art
FUNK ET AL J. CHROMATOGRAPHY 659(1), P 57-68, 1994
VON TUNGELN ET AL, CARCINOGENESIS, 7(7), P 1135-41, 1986
DUBEY ET AL, J. ORG. CHEM, VOL 51, NO 18, P 3407-3412, 1986

AU 200113206

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
3 May 2001 (03.05.2001)

PCT

(10) International Publication Number
WO 01/30734 A1

(51) International Patent Classification[7]: C07C 43/18, 69/013, 69/02, 69/76, 215/86, 219/34, 27/30, 311/01, C07D 209/02, 295/33, 215/06, A61K 31/075, 31/21, 31/325, 31/395, A61P 25/16, 29/00, 35/00, 31/18

(21) International Application Number: PCT/SE00/02090

(22) International Filing Date: 26 October 2000 (26.10.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
9903930-7 29 October 1999 (29.10.1999) SE

(71) Applicant *(for all designated States except US)*: **ASTRAZENECA AB** [SE/SE]; S-151 85 Södertälje (SE).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **FAGNOU, Keith** [CA/CA]; 30 Charles Street W., Apt. #823, Toronto, Ontario M4Y 1R5 (CA). **LAUTENS, Mark** [CA/CA]; Department of Chemistry, University of Toronto, 80 St. George Street, Toronto, Ontario M5S 3HC (CA).

(74) Agent: **ASTRAZENECA AB**; Global Intellectual Property, Patents, S-151 85 Södertälje (SE).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*
— *Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/30734 A1

(54) Title: NOVEL HYDRONAPHTALENE COMPOUNDS, PREPARED BY A RHODIUM CATALYZED RING OPENING REACTION IN THE PRESENCE OF PHOSPHINE LIGAND

(57) Abstract: The present invention is directed to a procedure for making an enantiomerically enriched compound containing a hydronaphthalene ring structure. The process involves reacting oxabenzonorbornadienes with nucleophiles using rhodium as a catalyst and in the presence of a phosphine ligand. The compounds synthesized may be used in pharmaceutical preparations for the treatment of a variety of diseases and conditions.

1

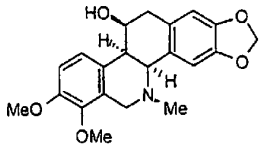
Novel hydronaphtalene compounds, prepared by a rhodium catalyzed ring opening reaction in the presence of phosphine ligand

Field of the Invention

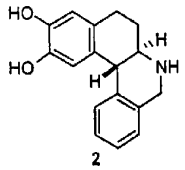
The present invention is directed to methods for chemically synthesizing compounds containing a hydronaphthalene ring structure. It encompasses the compounds made by the methods, pharmaceutical preparations containing the compounds, and methods for treating patients using these pharmaceutical preparations.

Background of the Invention

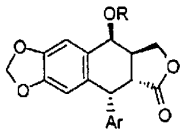
The hydronaphthalene structure can be found in many natural products and pharmaceutical agents. These include homochelidonine (structure 1 below; Slavik, J.; *et al.*, *Collect. Czech. Chem. Commun. 30*:3697 (1965); Spath, E., *et al.*, *Ber., 64*:1123 (1931); Bersch, H. W., *Arch. Pharm.* (Weinheim, Ger.), *291*:91 (1958)) an alkaloid isolated from Chelidonium plants, dihydrexidine (structure 2 below; Snyder, S. E., *J. Med. Chem., 38*:2395 (1995)) which shows antiparkinsonian character, etoposide (structure 3 below; Kamal, A., *et al.*, *Tetrahedron Lett. 37*:3359 (1996)) which is used in the treatment of various cancers, and SF-2315B (structure 4 below; Kim, K., *et al.*, *J. Org. Chem. 60*:6866 (1995)) which is a viral reverse transcriptase inhibitor. In addition, CNS agents, immunoregulatory agents and antibiotics contain variations on this framework (Perrone, R., *et al.*, *J. Med. Chem. 38*:942 (1995)).



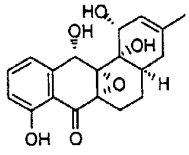
1



2

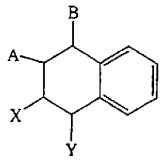


3



4

Given the large number of pharmaceutically useful compounds which contain this core skeleton, new methodology which produces functionalized hydronaphthalene skeletons (structure 1) would clearly be of value.



X, Y = O, N, C

Structure 1

Previous work on oxabicyclic ring opening reactions led to a catalytic enantioselective route to dihydronaphthol (Lautens, M., *et al., Tetrahedron 54*:1107 (1998)) which was a key step in the total synthesis of sertraline (Lautens, M., *et al., J. Org. Chem. 63*:5276 (1997)). However, little is known about the ring opening of oxabenzonorbornadiene or similar compounds with the incorporation of nucleophiles during the ring opening step. Duan and Chen developed a method of introducing aryl groups by using catalytic amounts of palladium (Duan, J.-P., *et al., Tetrahedron Lett., 34*:4019 (1993); Duan, J.-P., *et al., Organometallics* 14:1608 (1995)). Moinet *et al.*, later developed an enantioselective version of this reaction but the yields were low (*Tetrahedron Lett., 36*:2051 (1995)).

Catalytic organometallic processes that form carbon-heteroatom bonds are far fewer in number than those which form carbon-carbon bonds. The Wacker Process (Henry, P.M., Paladium Catalysed Oxidation of Hydrocarbons, vol. 2, Reidel, Boston, (1980)), oxidative carbonylations of amines and alcohols (Applied Homogeneous Catalysis with Organometallic Compounds: A Comprehensive Handbook in Two Volumes (eds.: B. Cornils, W.A. Herrmann), VCH, New York, (1984)) and the formation of arylamines and aryl ethers (Hartwig, J.F., *Agnew. Chem. Int. Ed. 37*:2046 (1998); Widenhoefer, R.A., *et al., J. Am. Chem. Soc. 119*:6787 (1997)) are a few that have been described to date.

The discussion of documents, acts, materials, devices, articles and the like is included in this specification solely for the purpose of providing a context for the present invention. It is not suggested or represented that any or all of these matters formed part of the prior art base or were common general knowledge in the field relevant to the present invention as it existed in Australia before the priority date of each claim of this application

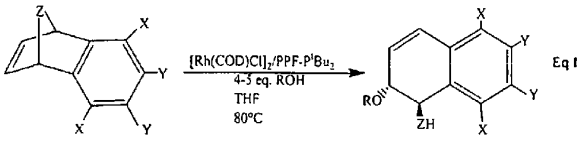
Throughout the description and claims of this specification, use of the word "comprise" and variations of the word, such as "comprising" and "comprises", is not intended to exclude other additives, components, integers or steps.

Summary of the Invention

The present invention is based upon the discovery of a rhodium catalyzed ring opening reaction of oxabenzonorbornadienes or azabicyclic compounds to produce a new carbon-oxygen bond via an intermolecular reaction with various alcohols. This reaction occurs in good yields with complete regio and diastereoselectivity and excellent enantioselectivity (*e.g.*, eq.1).

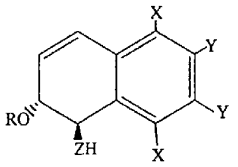
IPAU 20050901

W:\BA\687185\687185_P2A Speci.doc



In the reaction above, Z is O or NR_a. This reaction will work when oxabenzonorbornadienes or azabicyclic compounds are reacted with nitrogen nucleophiles, carboxylate nucleophiles, carbon nucleophiles or phenol nucleophiles. The invention encompasses not only the chemical reactions but also the compounds made by the reactions and the use of such compounds in the treatment of a variety of diseases and conditions.

In its first aspect, the invention is directed to a compound according to formula I:



(I)

in which R is selected from the group consisting of:

(a) H;

(b) a C_1-C_6 straight or branched alkyl;

(c) a straight or branched C_2-C_6 alkenyl;

(d) $-(CH_2)_nR_1$, wherein R_1 is a C_3-C_6 aryl, optionally substituted at one or more positions with a group selected from: Cl; F; NO_2; I; Br; a C_1-C_3 alkyl; and a C_1-C_3 alkoxy wherein n=0-3;

(e) $-C(O)R_2$, wherein R_2 is selected from the group consisting of: H; $-(CH_2)_nR_1$, wherein R_1 is as described above and n=0-3; and $-(CH_2)_nC(O)R_3$, wherein R_3 is a C_1-C_6 straight or branched alkyl and n=0-3;

(f) $-C(O)(CH_2)_p-C(O)-O-R_4$, wherein R_4 is a straight or branched C_1-C_6 alkyl and wherein p=0-3;

(g) $-R_d(CF_3)_j$, wherein R_d is a C_1-C_3 straight or branched alkyl and j=1-3;

(h) $-(CH_2)_j$-TMS, wherein TMS is trimethylsilyl, and j=1-3;

X and Y are independently selected from the group consisting of H; NH_2; F; Cl; Br; a C_1-C_3 alkyl; and a C_1-C_3 alkoxy;

or wherein the combination XY or YY together form a C_3-C_6 carbocyclic ring or a C_3-C_6 heterocyclic ring containing one or more heteroatoms selected from the group consisting of: O; N; and S; and

in which Z is selected from O or NR_a, wherein R_a is selected from:

(i) phenyl;

(j) (O)C-O-R_b, wherein R_b is a straight or branched C_1-C_6 alkyl;

(k) -SO_2-R_c, wherein R_c is selected from the group consisting of:

i) C_1-C_6 straight or branched alkyl;

ii) -$(CH_2)_q R_e$, wherein q=0-3 and R_e is a C_3-C_6 aryl, optionally substituted at one or more positions with a group selected from: Cl; F; NO_2; CN;I; Br; a straight or branched C_1-C_3 alkyl; a C_1-C_3 alkoxy; and –C(O)R_f, wherein R_f is a C_1-C_3 alkyl; -$(CH_2)_r CF_3$, wherein r=0-3;

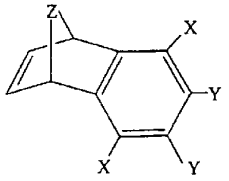
iii) –$R_g(CF_3)_s$, wherein R_g is a C_1-C_3 straight or branched alkyl and s=1-3;

iv) –$(CH_2)_s$-TMS, wherein TMS = trimethylsilyl and s= 1-3;

(l) -SO_2-$(CH_2)_q$- $Si(CH_3)_3$ wherein q is1-3.

Preferably, R in formula I is -$(CH_2)_n R_1$ and R_1 is a C_3-C_6 aryl optionally substituted at one or more positions with a group selected from: Cl; F; NO_2; I; Br; a C_1-C_3 alkyl; and a C_1-C_3 alkoxy and wherein n=0-3. When Z is NR_a, R_a is preferably phenyl; (O)C-O-C-$(CH_3)_3$; –SO_2-$(CH_2)_2$-$Si(CH_3)_3$; or -SO_2-R_c, wherein R_c is -$(CH_2)_q R_e$, wherein q=0-3 and R_e is a C_3-C_6 aryl, optionally substituted at one or more positions with a group selected from: Cl; F; NO_2; CN; I; Br; a straight or branched C_1-C_3 alkyl; a C_1-C_3 alkoxy; and –C(O)R_f, wherein R_f is a C_1-C_3 alkyl; -$(CH_2)_r CF_3$, wherein r=0-3.

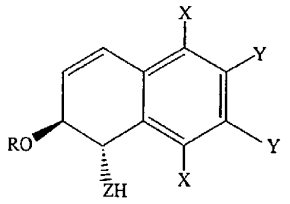
The compounds of formula I described above may be prepared by reacting a compound of formula ROH with a compound of formula V:



(V)

in which R, X, Y, and Z are as defined above. The reaction is catalyzed by $[Rh(COD)Cl]_2$ in the presence of a phosphine ligand, preferably selected from the group consisting of: DPPF; (R)-(S)-BPPFA; and (R)-(S)-PPF-P^{t}Bu$_2$. In prefered reactions: (a) the compound made is (1R*,2R*)-acetic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl ester and ROH is acetic acid; (b) the compound made is (1R*,2R*)-propionic acid 1-hydroxy-1,2--dihydro-naphthalen-2-yl ester and ROH is propionic acid; (c) the compound made is (1R,2R)-benzoic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester and ROH is benzoic acid; (d) the compound made is (1R*,2R*)-formic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester and ROH is formic acid; (e) the compound made is (1R*,2R*)-2-methyl acrylic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester and ROH is methacrylic acid; (f) the compound made is (1R*,2R*)-malonic acid ethyl-ester (1-hydroxy-1,2-dihydro-naphthalen-2-yl) ester and ROH is ethyl malonic acid; and (g) the compound made is (1R,2R)-2-(4-bromo-phenoxy)-1,2-dihydro-naphthalen-1-ol and ROH is p-bromophenol; (h) the compound made is *N*-[(1*R*,2*S*)-2-methoxy-1,2-dihydrohydro-1-naphthalenyl]-4-methylbenzene-sulfonamide and ROH is MeOH; (i) the compound made is 4-methyl-*N*-[(1*R*,2*S*)-2-phenoxy-1,2-dihydrohydro-1-naphthalenyl]benzenesulfonamide and the ROH is phenol; (j) the compound made is (1*R*,2*S*)-1-{[(4-methylphenyl)sulfonyl]amino}-1,2-dihydrohydro-2-naphthalenyl acetate and the ROH is acetic acid; (k) the compound made is (1*R*,2*S*)-1-{[(4-methylphenyl)-sulfonyl]amino}-1,2-dihydro-2-naphthalenyl benzoate and the ROH is benzoic acid; (l) the compound made is (1*R*,2*S*)-1-{[(4-methylphenyl)sulfonyl]amino}-1,2-dihydro-2-naphthalenyl pivalate and the ROH is pivalic acid; (m) the compound made is *N*-[(1*R*,2*S*)-2-methoxy-1,2-dihydro-1-naphthalenyl]-2-(trimethylsilyl)ethanesulfonamide and ROH is methanol.

In a second aspect the invention is directed to a compound according to formula II:



(II)

in which R is selected from the group consisting of:

(a) a C_1-C_6 straight or branched alkyl;

(b) -$(CH_2)_qR_5$, wherein q=0-3 and R_5 is a C_3-C_6 aryl optionally substituted at one or more positions with a group selected from: a straight or branched C_1-C_3 alkyl; a

C_1-C_3 alkoxy; Br; I; Cl; CN; F; NO_2; -$(CH_2)_rCF_3$, wherein r=0-3; and -$C(O)R_6$, wherein R_6 is a C_1-C_3 alkyl;

(c) -$R_7(CF_3)_s$, wherein R_7 is a C_1-C_3 straight or branched alkyl and s=1-3;

(d) -$(CH_2)_s$-TMS, wherein TMS=trimethylsilyl and s=1-3;

X and Y are independently selected from the group consisting of H; NH_2; F; Cl; Br; a C_1-C_3 alkyl; and a C_1-C_3 alkoxy;

or wherein the combination XY or YY together form a C_3-C_6 carbocyclic ring or a C_3-C_6 heterocyclic ring containing one or more heteroatoms selected from the group consisting of: O; N; and S; and

in which Z is selected from O or NR_a, wherein R_a is selected from:

(e) phenyl;

(f) (O)C-O-R_b, wherein R_b is a straight or branched C_1-C_6 alkyl;

(g) -SO_2-R_c, wherein R_c is selected from the group consisting of:

i) C_1-C_6 straight or branched alkyl;

ii) -$(CH_2)_qR_e$, wherein q=0-3 and R_e is a C_3-C_6 aryl, optionally substituted at one or more positions with a group selected from: Cl; F; NO_2; CN;I; Br; a straight or branched C_1-C_3 alkyl; a C_1-C_3 alkoxy; and –$C(O)R_f$, wherein R_f is a C_1-C_3 alkyl; -$(CH_2)_rCF_3$, wherein r=0-3;

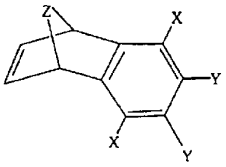
iii) –$R_g(CF_3)_s$, wherein R_g is a C_1-C_3 straight or branched alkyl and s=1-3;

iv) –$(CH_2)_s$-TMS, wherein TMS = trimethylsilyl and s= 1-3;

(h) -SO_2-$(CH_2)_q$- $Si(CH_3)_3$ wherein q is1-3.

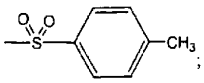
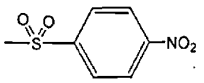
Preferably, R in formula II is -$(CH_2)_qR_5$ wherein q=0-3 and R_5 is a C_3-C_6 aryl optionally substituted at one or more positions with a group selected from: a straight or branched C_1-C_3 alkyl; a C_1-C_3 alkoxy; I; Cl; CN; F; NO_2; -$(CH_2)_rCF_3$, wherein r=0-3; and -$C(O)R_6$, wherein R_6 is a C_1-C_3 alkyl.

The compounds of formula II described above may be prepared by reacting a compound of formula ROH with a compound of formula V:

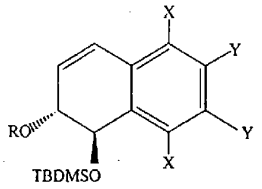


(V)

wherein R, X, Y, and Z are as defined above in connection with formula II and in which the reaction is catalyzed by $[Rh(COD)Cl]_2$ in the presence of a phosphine ligand, preferably (S)-(R)-PPF-P^{t}Bu$_2$. In preferred reactions: (a) the compound made is (1S,2S)-2-methoxy-1,2-dihydro-naphthalen-1-ol, and ROH is methanol; (b) the compound made is (1S,2S)-2-(ethoxy)-1,2-dihydro-naphthalen-1-ol, and ROH is ethanol; (c) the compound made is (1S,2S)-2-isopropoxy)-1,2-dihydro-naphthalen-1-ol and ROH is isopropanol; (d) the compound made is (1S,2S)-2-1-propenyloxy)-1,2-dihydro-naphthalen-1-ol, and ROH is allyl alcohol; (e) the compound made is (1S,2S)-2-(2-trimethylsilyl-ethoxy)-1,2-dihydro-naphthalen-1-ol, and ROH is trimethylsilyl-ethanol; (f) the compound made is (1S,2S)-2-benzyloxy-1,2-dihydro-naphthalen-1-ol, and ROH is benzylalcohol; (g) the compound made is (1S,2S)-2-4-methoxybenzyloxy-1,2-dihydro-naphthalen-1-ol, and ROH is anisylalcohol; (h) the compound made is (1S,2S)-2-(2,2,2-trifluoro-ethoxy)-1,2-dihydro-naphthalen-1-ol, and ROH is trifluoroethanol; (i) the compound made is (1S,2S)-2-(2,2,2-trifluoro-1-trifluoromethyl-ethoxy)-1,2-dihydro-naphthalen-1-ol and ROH is hexafluoro-isopropanol; (j) the compound made is (1S,2S)-6,7-difluoro-2-methoxy-1,2-dihydro-naphthalen-1-ol and ROH is methanol; (k) the compound made is (1S,2S)-6-methoxy-5,6-dihydro-naphtho[2,3-d][1,3]dioxol-5-ol and ROH is methanol; (l) the compound made is (1S,2S)-6,7-dibromo-2-methoxy-5,8-dimethyl-1,2-dihydro-naphthalen-1-ol and ROH is methanol; (m) the compound made is (1S,2S)-2-phenoxy-1,2-dihydro-naphthalen-1-ol and ROH is phenol; (n) the compound made is (1S,2S)-2-(4-nitrophenoxy)-1,2-dihydro-naphthalen-1-ol and ROH is 4-nitrophenol; (o) the compound made is (1S,2S)-2-(4-cyanophenoxy)-1,2-dihydro-naphthalen-1-ol and ROH is 4-cyanophenol; (p) the compound made is (1S,2S)-2-(4-acylphenoxy)-1,2,-dihydro-naphthalen-1-ol and ROH is 4-hydroxyaceto-phenone; (q) the compound made is (1S,2S)-2-(4-trifluoromethylphenoxy)-1,2,-dihydro-naphthalen-1-ol and ROH is 4-trifluoromethylphenyl; (r) the compound made is (1S,2S)-2-(4-fluorophenoxy)-1,2-dihydro-naphthalen-1-ol and ROH is 4-fluorophenol; (s) the compound made is (1S,2S)-2-(4-chlorophenoxy)-1,2-dihydro-naphthalen-1-ol and ROH is 4-chlorophenol; (t) the compound made is (1S,2S)-2-(4-iodophenoxy)-1,2-dihydro-naphthalen-1-ol and ROH is 4-iodophenol; (u) the compound made is (1S,2S)-2-(4-methylphenoxy)-1,2-dihydro-naphthalen-1-ol and ROH is p-cresol; (v) the compound made is (1S,2S)-2-(4-methoxyphenoxy)-1,2-dihydro-naphthalen-1-ol and ROH is 4-methoxyphenol; and (w) the compound made is (1S,2S)-2-(2-bromophenoxy)-1,2-dihydro-naphthalen-1-ol and ROH is 2-bromophenol. When Z is NR_3, R_3 is preferably phenyl; $(O)C\text{-}O\text{-}C\text{-}(CH_3)_3$;

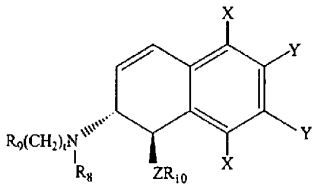


; ;or (O)S(O)-$(CH_2)_2$-$Si(CH_3)_3$.

The invention is also directed to a compound according to formula III:


(III)

wherein TBDMSO is a tert-butyldimethylsiloxy group, and R, X, and Y are as defined in above in connection with formula I. These compounds may be made by preparing a compound of formula I according to the process described above and then reacting the compound formed with a salt of tert-butyldimethylsilylic acid. Preferably, the compound formed is (1R*,2R*)-malonic acid (1-tert-butyldimethylsiloxy-1,2-dihydro-naphthalen-2-yl) ester ethyl ester and ROH is tert-butyldimethylsilylic acid.

In another aspect, the invention is directed to a compound according to formula IV:


(IV)

a) in which R_8 is H or CH_3;

b) t=0-3

c) R_9 is a C_3-C_6 aryl optionally substituted at one or more positions with a group selected from: a C_1-C_3 alkyl; a C_1-C_3 alkoxy; Cl; F; NO_2; and CF_3;
or R_9 together with N form a ring structure selected from: a phthalamide ring; a pyrrolidine ring; a piperidine ring; a tetrahydroquinoline ring; and an indole ring;

said ring structure being optionally substituted at one or more positions with a group selected from: a C_1-C_3 alkyl; a C_1-C_3 alkoxy; Cl; F; NO_2; and CF_3;

d) X and Y are independently selected from the group consisting of H; NH_2; F; Cl; Br; a C_1-C_3 alkyl; and a C_1-C_3 alkoxy; or wherein the combination XY or YY together form a C_3-C_6 carbocyclic ring or a C_3-C_6 heterocyclic ring containing one or more heteroatoms selected from the group consisting of: O; N; and S;

e) Z is selected from O or NR_a, wherein R_a is selected from:

(i) a straight or branched C_1-C_6 alkyl;

(ii) phenyl;

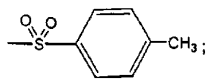
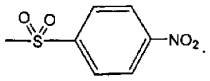
(iii) (O)C-O-R_b , wherein R_b is a straight or branched C_1-C_6 alkyl;

(iv) -SO_2-R_c, wherein R_c is an unsubstituted phenyl or a phenyl substituted with a C_1-C_3 alkyl or NO_2; and

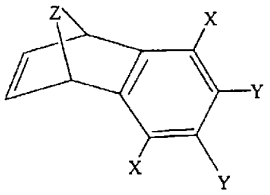
(v) -SO_2-$(CH_2)_q$- $Si(CH_3)_3$ wherein q is1-3; and

f) when Z is O, R_{10} is H; when Z is NR_a, R_{10} is either H or CH_3.

Preferably, R_8 in formula IV is H and R_9 together with N form a ring selected from the group consisting of a phthalamide ring; a pyrrolidine ring; a piperidine ring; a tetrahydroquinoline ring; and an indole ring; the ring being optionally substituted at one or more positions with a group selected from: a C_1-C_3 alkyl; a C_1-C_3 alkoxy; Cl; F; NO_2; and CF_3. When Z is NR_a, R_a is preferably methyl;


; or

.

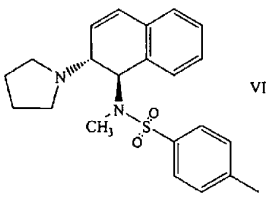
The compounds of formula IV described above may be prepared by reacting a compound of formula R_9-$(CH_2)_i$NHR_8 with a compound of formula V


(V)

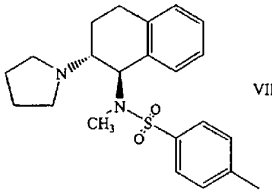
in which R_8, R_9, t, X, Y, and Z are as defined above in connection with compounds of formula IV and the reaction is catalyzed by $[Rh(COD)Cl]_2$ in the presence of a phosphine ligand; preferably selected from the group consisting of: DPPF; (R)-(S)-BPPFA; and (R)-(S)-PPF-P^{t}Bu$_2$. When Z is NR_a, the reaction will produce a product in which R_{10} is H. A subsequent reaction may be used to convert R_{10} to a methyl as set forth in the Examples section below. Most typically, the process will be used to produce products in which R_9 together with N form a ring selected from the group consisting of: a phthalamide ring; a pyrrolidine ring; a piperidine ring; a tetrahydroquinoline ring; and an indole ring; said ring structures being optionally substituted at one or more positions with a group selected from: a C_1-C_3 alkyl; a C_1-C_3 alkoxy; Cl; F; NO_2; and CF_3. In preferred reactions: (a) the compound made is (1R,2R)-2-(1-hydroxy-1,2-dihydro-naphthalen-2-yl) isoindole-1,3-dione and R_9-$(CH_2)_sNHR_8$ is phthalimide; (b) the compound made is (1R*,2R*)-2-pyrrolidin-1-yl-1,2-dihydro-naphthalen-1-ol and R_9-$(CH_2)_sNHR_8$ is pyrrolidine; (c) the compound made is (1R*,2R*)-2-piperidin-1-yl-1,2-dihydro-naphthalen-1-ol and R_9-$(CH_2)_sNHR_8$ is piperidine; (d) the compound made is (1R,2R)-2-(3,4-dihydro-2H-quinolin-1-yl)-1,2-dihydro-naphthalen-1-ol and R_9-$(CH_2)_sNHR_8$ is tetrahydroisoquin-oline; (e) the compound made is (1R,2R)-2(methyl-phenyl-amino)-1,2-dihydro-naphthalen-1-ol and R_9-$(CH_2)_sNHR_8$ is N-methylaniline; (f) the compound made is (1R*,2R*)-2-benzylamino-1,2-dihydro-naphthalen-1-ol and R_9-$(CH_2)_sNHR_8$ is benzyl-amine; (g) the compound made is (1R*,2R*)-2-(4-methoxy-benzylamino)-1,2-dihydro-naphthalen-1-ol and R_9-$(CH_2)_sNHR_8$ is p-methoxybenzylamine; and (h) the compound made is (1R,2R)-2-indol-1-yl-1,2-dihydro-naphthalen-1-ol and R_9-$(CH_2)_sNHR_8$ is indole; (i) the compound made is N-[1R,2R)-2(1-pyrrolidinyl)-1,2-dihydronaphthalenyl]-4-methylbenzenesulfonamide and the R_9-$(CH_2)_tNHR_8$ is pyrrolidine; (j) the compound made is *N*-[(1*R*,2*S*)-2-(1*H*-indol-1-yl)-1,2-dihydro-1-naphthalenyl]-4-methylbenzenesulfonamide and the R_9-$(CH_2)_tNHR_8$ is indole; (k) the compound made is *N*-[(1*R*,2*S*)-2-(3,4-dihydro-2(1*H*)-isoquinolinyl)-1,2-dihydro-1-naphthalenyl]-4-methylbenzenesulfonamide and the R_9-$(CH_2)_tNHR_8$ is tetrahydroisoquinoline; (l) the compound made is *N*-[(1*R*,2*S*)-2-(3,4-dihydro-1(2*H*)-quinolinyl)-1,2-dihydro-1-naphthalenyl]-4-methylbenzenesulfonamide and the R_9-$(CH_2)_tNHR_8$ is tetrahydroquinoline; (m) the compound made is 4-methyl-*N*-[(1*R*,2*S*)-2-(1-piperidinyl)-1,2-dihydro-1-naphthalenyl]-benzenesulfonamide and the R_9-$(CH_2)_tNHR_8$ is piperidine.

The invention also encompasses seven other processes. In the first (1S,2S)-N-(1-hydroxy-1,2-dihydro-naphthalen-2-yl)-benzene sulfonamide is formed by reacting oxabenzonorbornadiene with benzenesulfonamide. In the second, (1S*,2R*)-2-(hydroxy-1,2-dihydro-naphthalen-2-

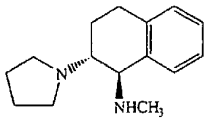
yl)malonic acid dimethyl ester is formed by reacting oxabenzonorbornadiene with dimethyl malonate. Both reactions are catalyzed by $[Rh(COD)Cl]_2$ in the presence of a phosphine ligand. In the third, the compound of formula VI is formed by reacting a compound of formula IV, which is produced as described above in connection with formation of compounds of formula IV, with iodomethane. In preferred reactions, the compound made is N,4-dimethyl-N-[(1R,2S)-2-(1-pyrrolidinyl)-1,2-dihydro-1-naphthalenyl]benzenesulfonamide. In the fourth, the compound of formula VII is formed by reacting compound of formula VI with hydrogen in the presence of palladium catalyst. The compound made is N,4-dimethyl-N-[(1R,2S)-2-(1-pyrrolidinyl)-1,2,3,4-tetrahydro-1-naphthalenyl]benzenesulfonamide. In the fifth, the compound of formula VIII is formed by reacting the compound of formula VII with sodium borohydride. The compound made using this reaction is (1*R*,2*S*)-*N*-methyl-2-(1-pyrrolidinyl)-1,2,3,4-tetrahydro-1-naphthalenamine. In the sixth, the compound of formula IX is formed by reacting a compound of formula IV which is produced as described above in connection with formation of compounds of formula IV, with iodomethane. The compound made using this reaction is N-methyl-4-nitro-N-[(1R,2S)-2-(1-pyrrolidinyl)-1,2-dihydro-1-naphthalenyl]benzenesulfonamide. In the seventh, the compound of formula X is formed by reacting a compound of formula I which is produced as described above in connection with formation of compounds of formula I, with iodomethane. The compound made using this reaction is (1*R*,2*S*)-1-{methyl[(4-methylphenyl)sulfonyl]amino}-1,2-dihydro-2-naphthalenyl acetate.



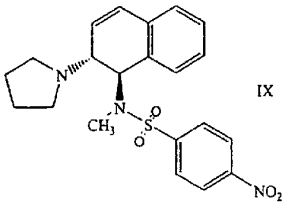
VI



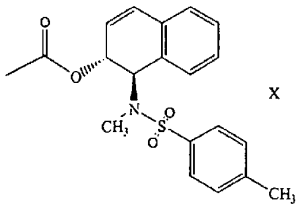
VII



VIII



IX



X

Overall, the most preferred compounds of the invention are:

a) (1S,2S)-2-methoxy-1,2-dihydro-naphthalen-1-ol;
b) (1S,2S)-2-(ethoxy)-1,2-dihydro-naphthalen-1-ol;
c) (1S,2S)-2-(isopropoxy)-1,2-dihydro-naphthalen-1-ol;
d) (1S,2S)-2-(1-propenyloxy)-1,2-dihydro-naphthalen-1-ol;
e) (1S,2S)-2-(2-trimethylsilyl-ethoxy)1,2-dihydro-naphthalen-1-ol;
f) (1S,2S)-2-benzyloxy-1,2-dihydro-naphthalen-1-ol;
g) (1S,2S)-2-(4-methoxybenzyloxy)-1,2-dihydro-naphthalen-1-ol;
h) (1S,2S)-2-(2,2,2-trifluoro-ethoxy)-1,2-dihydro-naphthalen-1-ol;
i) (1S,2S)-2-(2,2,2-trifluoro-1-trifluoromethyl-ethoxy)-1,2-dihydro-naphthalen-1-ol;
j) (1S,2S)-6,7-difluoro-2-methoxy-1,2-dihydro-naphthalen-1-ol;
k) (1S,2S)-6-methoxy-5,6-dihydro-naphthol[2,3-d][1,3]dioxol-5-ol;
l) (1S,2S)-6,7-dibromo-2-methoxy-5,8-dimethyl-1,2-dihydro-naphthalen-1-ol;
m) (1R*,2R*)-acetic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester;
n) (1R*,2R*)-propionic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester;
o) (1R,2R)-benzoic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester;
p) (1R*,2R*)-formic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester;
q) (1R*,2R*)-2-methyl acrylic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester;
r) (1R*,2R*)-malonic acid ethyl ester (1-hydroxy-1,2-dihydro-naphthalen-2-yl) ester;
s) (1R*,2R*)-malonic acid (1-tert-butylbimethylsiloxy-1,2-dihydro-naphthalen-2-yl) ethyl ester;
t) (1S*,2S*)4-tert-butyldimethylsiloxy-1,4-dihydro-naphthalen-2-yl) acetic acid ethyl ester;
u) (1R,2R)-2-(1-hydroxy-1,2-dihydro-naphthalen-2-yl)-isoindole-1,3-dione;
v) (1S,2S)-N-(1-hydroxy-1,2-dihydro-naphthalen-2-yl)-benzene sulfonamide;
w) (1R*,2R*)-2-pyrrolidin-1-yl-1,2-dihydro-naphthalen-1-ol;

x) (1R*,2R*)-2-piperidin-1-yl-1,2-dihydro-naphthalen-1-ol;
y) (1R,2R)-2-(3,4-dihydro-2H-quinolin-1-yl)-1,2-dihydro-naphthalen-1-ol;
z) (1R,2R)-2-(methyl-phenyl-amino)-1,2-dihydro-naphthalen-1-ol;
aa) (1R*,2R*)-2-benzylamino-1,2-dihydro-naphthalen-1-ol;
bb) (1R*,2R*)-2-(4-methoxy-benzylamino)-1,2-dihydro-naphthalen-1-ol;
cc) (1R,2R)-2-indol-1-yl-1,2-dihydro-naphthalen-1-ol;
dd) (1S*,2R*)-2-(hydroxy-1,2-dihydro-naphthalen-2-yl)malonic acid dimethyl ester;
ee) (1S,2S)-2-phenoxy-1,2-dihydro-naphthalen-1-ol;
ff) (1S,2S)-2-(4-nitrophenoxy)-1,2-dihydro-naphthalen-1-ol;
gg) (1S,2S)-2-(4-cyanophenoxy)-1,2-dihydro-naphthalen-1-ol;
hh) (1S,2S)-2-(4-acylphenoxy)-1,2-dihydro-naphthalen-1-ol;
ii) (1S,2S)-2-(4-trifluoromethylphenoxy)-1,2-dihydro-naphthalen-1-ol;
jj) (1S,2S)-2-(4-fluorophenoxy)-1,2-dihydro-naphthalen-1-ol;
kk) (1S,2S)-2-(4-chlorophenoxy)-1,2-dihydro-naphthalen-1-ol;
ll) (1S,2S)-2-(4-iodophenoxy)-1,2-dihydro-naphthalen-1-ol;
mm) (1R,2R)-2-(4-bromo-phenoxy)-1,2-dihydro-naphthalen-1-ol;
nn) (1S,2S)-2-(4-methylphenoxy)-1,2-dihydro-naphthalen-1-ol;
oo) (1S,2S)-2-(4-methoxyphenoxy)-1,2-dihydro-naphthalen-1-ol;
pp) (1S,2S)-2-(2-bromophenoxy)-1,2-dihydro-naphthalen-1-ol;
qq) 4-methyl-*N*-[(1*R*,2*S*)-2-(1-piperidinyl)-1,2-dihydro-1-naphthalenyl]benzenesulfonamide;
rr) *N*-[(1*R*,2*S*)-2-(3,4-dihydro-1(2*H*)-quinolinyl)-1,2-dihydro-1-naphthalenyl]-4-methylbenzenesulfonamide;
ss) *N*-[(1*R*,2*S*)-2-(3,4-dihydro-2(1*H*)-isoquinolinyl)-1,2-dihydro-1-naphthalenyl]-4-methylbenzenesulfonamide;
tt) *N*-[(1*R*,2*S*)-2-(1*H*-indol-1-yl)-1,2-dihydro-1-naphthalenyl]-4-methylbenzenesulfonamide;
uu) (1*R*,2*S*)-2-methoxy-*N*-phenyl-1,2-dihydro-1-naphthalenamine;
vv) *tert*-butyl (1*R*,2*S*)-2-methoxy-1,2-dihydro-1-naphthalenylcarbamate;
ww) *N*-[(1*R*,2*S*)-2-methoxy-1,2-dihydro-1-naphthalenyl]-2-(trimethylsilyl)ethanesulfonamide;
xx) *N*,4-dimethyl-*N*-[(1*R*,2*S*)-2-(1-pyrrolidinyl)-1,2,3,4-tetrahydro-1-naphthalenyl]-benzenesulfonamide;
yy) *N*,4-dimethyl-*N*-[(1*R*,2*S*)-2-(1-pyrrolidinyl)-1,2-dihydro-1-naphthalenyl]-benzenesulfonamide;
zz) *N*-hydroxy-4-({methyl[(1*R*,2*S*)-2-(1-pyrrolidinyl)-1,2-dihydro-1-naphthalenyl]amino}sulfonyl) -*N*-oxobenzenaminium;

aaa) *N*-methyl-4-nitro-*N*-[(1*R*,2*S*)-2-(1-pyrrolidinyl)-1,2-dihydro-1-naphthalenyl]-benzenesulfonamide;

bbb) (1*R*,2*S*)-*N*-methyl-2-(1-pyrrolidinyl)-1,2,3,4-tetrahydro-1-naphthalenamine;

ccc) *N*-[(1*R*,2*S*)-2-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl]-4-methylbenzenesulfonamide;

ddd) *N*-[(1*R*,2*S*)-2-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl]-4-methylbenzenesulfonamide;

eee) 4-methyl-*N*-[(1*R*,2*S*)-2-phenoxy-1,2,3,4-tetrahydro-1-naphthalenyl]benzenesulfonamide;

fff) (1*R*,2*S*)-1-{[(4-methylphenyl)sulfonyl]amino}-1,2,3,4-tetrahydro-2-naphthalenyl acetate;

ggg) (1*R*,2*S*)-1-{[(4-methylphenyl)sulfonyl]amino}-1,2-dihydro-2-naphthalenyl benzoate;

hhh) (1*R*,2*S*)-1-{[(4-methylphenyl)sulfonyl]amino}-1,2-dihydro-2-naphthalenyl pivalate;

iii) *N*-[(1*R*,2*S*)-2-methoxy-1,2-dihydro-1-naphthalenyl]-2-(trimethylsilyl)ethanesulfonamide;

jjj) *tert*-butyl (1*R*,2*S*)-2-methoxy-1,2-dihydro-1-naphthalenylcarbamate; and

kkk) 4-nitro-*N*-[(1*R*,2*S*)-2-(1-pyrrolidinyl)-1,2-dihydro-1-naphthalenyl]benzenesulfonamide.

Any of the compounds described above may be incorporated into a pharmaceutical preparation and administered to a patient in an amount effect for relieving one or more symptoms associated with a variety of diseases and conditions. Among the diseases that may be treated are Parkinson's disease, cancer and AIDS.

Detailed Description of the Invention

The present invention is based upon the discovery of a new process for the formation of enantiomerically enriched compounds containing the hydronaphthalene ring structure. The process involves reacting an aza- or oxabenzonorbornadiene compound with a nucleophile in the presence of a rhodium catalyst and a phosphine ligand. Detailed procedures for the formation of precursor compounds and their use in reactions are set forth in the Examples section below. Preferred nucleophiles are alcohols, phenols, amines, and stabilized carbanions such as malonates and malonate equivalents. In cases where simple aliphatic amines are used, reactions should be performed in the presence of a tertiary amine hydrochloride. This is not necessary for other types of amines. When carboxylic acids are used, reactions should be carried out in the presence of a tertiary amine, *e.g.*, triethylamine. Alternatively, the sodium or potassium salt of the carboxylic acid may be reacted in the presence of the hyrochloride of a tertiary amine, *e.g.* in the presence of triethylamine hydrochloride. It has been found that carboxylate ring-opened products can be made to undergo a subsequent transformation to produce 1,4-disubstituted dihyronaphthalenes. This is accomplished by an S_N2' addition of nucleophiles under catalytic or non-catalytic conditions to the allyl acetate functionality. For an example of the conversion of (1R*,2R*)-

Malonic acid (1-tert-butyldimethylsiloxy-1,2-dihydro-naphthalen-2-yl) ester ethyl ester to (1S*,2S*)-(4-Tert-butyldimethylsiloxy-1,4-dihydro-naphthalen-2-yl) acetic acid ethyl ester see the Examples section below.

The preferred catalyst is $[Rh(COD)Cl]_2$ and, depending upon the particular product desired, preferred ligands are DPPF or a chiral analogue of DPPF, (R)-(S)-BPPFA; (R)-(S)-PPF-P^tBu_2 and (S)-(R)-PPF-P^tBu_2. The ligands may be prepared by any process described in the literature (*see, e.g.*, Togni *et al.*, *J. Am. Chem. Soc. 116*:4062 (1994)). Reactions may be carried out using trifluoroethanol (TFE) or tetrahydrofuran (THF) as solvents under an inert atmosphere, preferably of nitrogen. The reaction temperature should typically be at least 60°C and preferably about 80°C.

The compounds formed may be incorporated into a pharmaceutical composition and used in the treatment of a variety of diseases and conditions. Specifically, the compounds may be used in the treatment of Parkinson's disease, cancers, and AIDS. The total daily dosage of compound administered to a patient should be at least the amount required to reduce or eliminate one or more symptoms associated with the condition being treated. For example, in the treatment of Parkinson's disease, sufficient agent should be administered to reduce the severity or frequency of tremors or other movement disorders associated with the disease. In treating cancers, agents should typically be given at a dosage sufficient to reduce tumor size or at a dosage sufficient to reduce the total number of cancerous cells in a patient. The actual dose selected for an individual patient will be determined by the attending physician based upon clinical conditions and using methods well known in the art. Agents may be provided in either a single or multiple dosage regimen, *e.g.*, a patient may be administered compounds twice a day.

Any route of administration and dosage form is compatible with the present invention, and therapeutic agents may be administered as either the sole active ingredient or in combination with other therapeutically active drugs. Routes of delivery compatible with the invention include parenteral, peroral, internal, pulmonary, rectal, nasal, vaginal, lingual, transdermal, intravenous, intraarterial, intramuscular, intraperitoneal, intracutaneous, and subcutaneous routes. Specific dosage forms that may be used include tablets, pills, capsules, powders, aerosols, suppositories, skin patches, parenterals, and oral liquids, including oil aqueous suspensions, solutions, and emulsions. Sustained release dosage forms may also be used. All dosage forms may be prepared

using methods that are standard in the art (*see, e.g.*, Remington's Pharmaceutical Sciences, 16th ed., A. Oslo, editor, Easton PA (1980)).

Therapeutic agents may be used in conjunction with any of the vehicles and excipients nly employed in pharmaceutical preparations, *e.g.*, talc, gum arabic, lactose, starch, magnesium stearate, cocoa butter, aqueous or non-aqueous solvents, oils, paraffin derivatives, glycols, etc. Coloring and flavoring agents may also be added to preparations designed for oral administration. Solutions can be prepared using water or physiologically compatible organic solvents such as ethanol, 1,2-propylene glycol, polyglycols, dimethyl sulfoxide, fatty alcohols, triglycerides, partial esthers of glycerine, and the like. Parenteral compositions containing compounds may be prepared using conventional techniques and include sterile isotonic saline, water, 1,3-butane diol, ethanol, 1,2-propylene glycol, polyglycols mixed with water, Ringer's solution, etc.

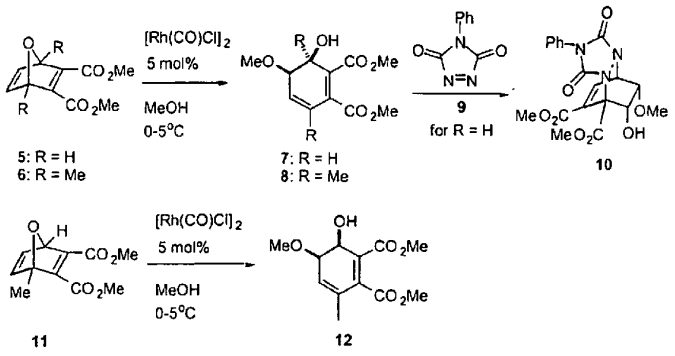
If desired, a patient may be initially given a relatively low dose of therapeutic agent in order to determine whether any adverse side effects are experienced. This may be particularly important in cases where a patient is taking other medications or has clinical characteristics that suggest that they may not be able to tolerate high drug dosages. If adverse side effects are not experienced by a patient, dosage may be gradually increased until a satisfactory alleviation of symptoms is achieved. For example, the dosage given to a patient with AIDS may be increased until blood counts return to a normal or more normal level.

Examples

I. Compounds Made Using Oxabenzonorbornadienes

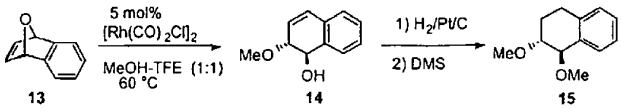
Example 1: Rhodium Catalysed Synthesis of Enatiomerically Enriched *trans*-2-Alkoxy-1,2-dihydro-naphthalen-1-ols

In 1973, Hogeveen and Middelkoop reported a $[Rh(CO)_2Cl]_2$ catalyzed ring opening reaction of **5** by reaction with methanol giving **6**. (Hogeveen, H., *et al.*, *Tetrahedron Lett. 190*:1 (1973)) Subsequently, Ashworth and Berchtold reported the stereochemistry of this reaction to be cis as shown after the formation of a Diels-Alder adduct with **9** (scheme 1) (Ashworth, R. W., *et al.*, *Tetrehedron Lett.* 339 (1977)). This stereochemistry is in keeping with the observation of exo attack by nucleophiles with other oxabicyclic starting materials (Lautens, M., *Synlett* 179 (1993)). Hogeveen and Middelkoop also reported that the reaction was regioselective when only one of the bridgehead positions was substituted, that is **11** gave only regioisomer **12**.



Scheme 1

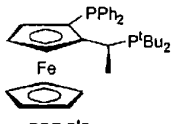
When **13** (Stiles, M., *e al., J. Am. Chem. Soc. 82*:3802 (1960)) was subjected to the Hogeveen and Middelkoop conditions, no reaction was observed. However, by changing the solvent system to a 1:1 mixture of trifluoroethanol (TFE):methanol and by increasing the temperature to 60°C, the desired product **14** was isolated in 70% yield. Remarkably, the stereochemistry of **14** was trans as proven by comparison with authentic samples of both stereoisomers of dimethoxytetrahydronaphthalene **15** (eq. 2) (The cis isomer of **15** was prepared by reaction of 1,2-dihydronaphthalene with OSO_4 followed by methylation with dimethylsulfate (DMS). The trans isomer was prepared by epoxidation of 1,2-dihydronaphthalene followed by ring opening with hyroxide and dimethylation with DMS).



Eq 2

Given the ability of this reaction to set up two stereocentres with complete regio and stereocontrol, the possibility of rendering it asymmetric was investigated. A serious drawback of the existing catalyst $[Rh(CO)_2Cl]_2$, however, was that the addition of phosphine ligands completely inhibited the reaction. By changing to a rhodium source possessing the more labile COD ligand, $[Rh(COD)Cl]_2$, it was possible to examine the catalytic ability of several chiral phosphine ligands. Not all rhodium-ligand combinations performed equally well. DPPE and BINAP did not produce the desired product, and phosphites resulted in poor yields. DPPF was

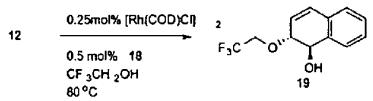
very efficient, however, giving **14** in 88% yield. One advantage of DPPF is that a number of chiral analogues have been prepared and could be studied to determine enantioselectivity. JOSIPHOS ligands (Togni, A.., *et al., J. Am. Chem. Soc. 116*:4062 (1994)) were among the chiral ligands examined which gave the most promising results. For example, PPF-P^{t}Bu$_2$ **16** gave **14** in 84% yield and 86% ee at 60°C. The ee could be significantly improved to 97% when the reaction temperature was increased by 20°C.



PPF-P^{t}Bu$_2$
18

These reactions were typically run as a 1:1 mixture of MeOH:TFE under a nitrogen atmosphere which gave **13** accompanied by small amounts of naphthol. In neat trifluoroethanol under a nitrogen atmosphere, naphthol is the major product with less than 5% conversion to the trifluoroethanol ring-opened product. Remarkably, this is not the case when the reaction is run under a carbon monoxide atmosphere. In the presence of CO, the reaction with neat TFE gives the TFE ring-opened product **17** in 70% yield after 3 hours. A colour change of the solution, from yellow to red was observed, suggesting that the CO was interacting with the rhodium metal. When the reaction was performed under asymmetric conditions using PPF-P^{t}Bu$_2$, **17** was obtained in 70% yield and 98% ee indicating that the ligand remains bound to the metal even if CO binding has occurred (table 1).

Table 1: Effects of Solvent and Atmosphere

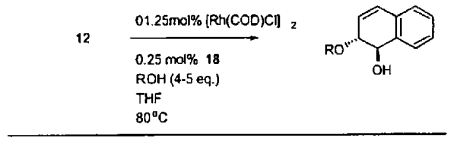


Atmosphere	Solvent / Equiv. TFE	Yield **19**	ee
N_2	TFE / neat	0%*	
CO	TFE / neat	70%	98%
N_2	THF / 5 eq. TFE	70%	98%

* only product observed is naphthol

Reactions run in alcohols other that TFE proceeded at a much slower rate. When the solvent was changed to THF, the reaction worked equally well with a broad range of alcohols under racemic and enantioselective conditions, and only five equivalents of the alcohol were required. THF also allowed the use of very low catalyst loadings, typically in the range of 0.125 mol% of $[Rh(COD)Cl]_2$ and 0.25 mol% of **16**. While TFE would only add to give **17** when the reaction was run under a CO atmosphere in neat TFE, this was not the case in THF. When THF was used as the solvent, TFE added efficiently under an inert nitrogen atmosphere to give **17** in 70% yield and 98% ee. Even the very weakly nucleophilic hexafluoroisopropanol (HFI) added under these reaction conditions to give **23** in 90% yield and 93% ee (table 2).

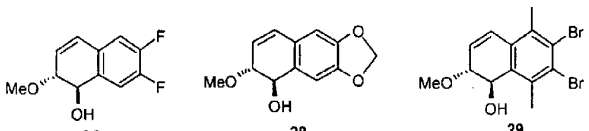
Table 2: Rhodium Catalysed Ring Opening of 12 with Various Alcohols



ROH	Product	Yield(%)	ee(%) [b]
MeOH [a]	**14**	96	97
EtOH [a]	**16**	84	97
^{i}PrOH [a]	**18**	94	93
Allyl Alcohol	**19**	92	>99
TMS Ethanol [a]	**20**	53	95
Benzyl Alcohol	**21**	66	>98
p-Methoxybenzyl Alcohol	**22**	87	97
TFE	**17**	70	98
HFI	**23**	90	93

[a] These reactions were performed under unoptimised conditions using 10 eq. ROH
[b] ee determined by formation of Moshers ester or by HPLC analysis with a Chiralcel OD column

In order to investigate the effects of substituents on the aromatic ring of **13**, difluoro (**24**), methylenedioxy (**25**), and dimethyldibromo (**26**) substrates were prepared (Hart, H., *Tetrahedron* *43*:5203 (1987)) and reacted them under the standard conditions. All gave the corresponding ring opened products in good yields and excellent ee's (chart 1) indicating that this reaction is not sensitive to remote substitution or electronic effects on the aromatic ring.



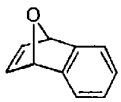
27
90% yield
95%ee

28
88% yield
96%ee

29
79% yield
97%ee

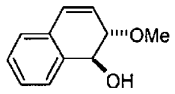
Chart 1

Example 2: Formation of 1,4-epoxy-1,4-dihydronaphthanlene (13)



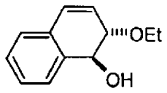
To furan (100 ml, 1.37 ml) in DME (100 ml) at 50°C in a flame dried three neck flask with a reflux condenser and two addition funnels attached was added simultaneously over two hours a solution of anthranilic acid (27.5 g, 200 mmol) in DME (100 ml) and a separate solution of isoamylnitrite (40 mL, 298 mmol) in DME (50 mL). Upon completion of addition, the reaction was allowed to stir at 50°C for 30 min until no further gas was evolved. The reaction mixture was then cooled to room temperature and portioned between Et_2O and saturated K_2CO_3 and the aqueous layer was extracted three times with Et_2O. The combined organic layer were washed with brine, dried over $MgSO_4$ and concentrated. Bulb to bulb distillation gave **13** (18.5 g, 64%) as a white solid. The spectral data correspond well with the literature data.[17]

Example 3: Compounds Formed by Reactions Involving Alcohols

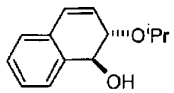


(1S,2S)-2-Methoxy-1,2-dihydro-naphthalen-1-ol (14) To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (0.5 mg, 0.0009 mmol), (R)-(S)-PPF-P^{t}Bu$_2$ (1.0 mg, 0.0018 mmol) and **13** (27 mg, 0.187 mmol) were added followed by addition of THF (0.5 mL) and methanol (0.5 mL). The mixture was heated for 15 hours and the solvents were removed *in vacuo*. The resulting solid

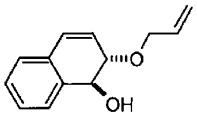
was purified by flash chromatography (20% ethyl acetate in hexanes) to give **14** a white crystalline solid (31.7 mg, 96%). The ee was determined to be 97% using HPLC analysis on a CHIRALCEL OD column, λ= 486 nm. Retention times in 4% isopropanol in hexanes were 10.1 min (major) and 11.1 min. R_f= 0.29 on silica gel (10% ethyl acetate:hexanes); mp 86-87° (Et_2O); $[\alpha]^{25}_D$= -208° (c= 10.1, $CHCl_3$); R_f= 0.39 on silica (20% ethyl acetate:hexanes). IR (KBr, cm^{-1}) 3277 (br), 2971 (m), 1466(m), 1285(m), 1114(s), 1048(m), 979(m), 775(s); ^{1}H NMR (400MHz, acetone-d) δ 7.60-7.62 (1H, m), 7.30-7.21 (2H, m), 7.13-7.11 (1H, m), 6.50 (1H, dd, J= 9.9,1.8 Hz), 6.04 (1H, dd, J= 9.9, 2.2 Hz), 4.85 (1H, dd, J= 9.9, 6.2 Hz), 3.50 (3H, s), 2.89 (1H, d, J= 12.8 Hz); ^{13}C NMR (400MHz, acetone-d) δ 138.5, 133.2, 129.1, 128.4, 128.3, 128.2, 126.8, 126.3, 83.1, 73.0, 57.1. HRMS calcd for $C_{11}H_{12}O_2$ (M^+): 176.0837. Found: 176.0835.



(1S,2S)-2-(Ethoxy)-1,2-dihydro-naphthalen-1-ol (16): : To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (2.1 mg, 0.043 mmol), (S)-(R)-PPF-P^{t}Bu$_2$ (3.8 mg, 0.087 mmol) and **13** (500 mg, 3.47 mmol) were added followed by addition of ethanol (4 mL) and THF (4 mL). The mixture was heated to reflux for five hours and the solvent was removed *in vacuo*. The resulting solid was purified by flash chromatography (20% ethyl acetate in hexanes) to give **16** as a white crystalline solid (553 mg, 84%). The ee was determined to be 97% using HPLC analysis on a CHIRALCEL OD column, λ = 254 nm. Retention times in 1.5% isopropanol in hexanes were 13.6 min and 14.2 min (major). R_f= 0.26 on silica gel (20% ethyl acetate:hexanes); mp 33° (Et_2O); $[\alpha]^{25}_D$= 185.9° (c= 9.6, $CHCl_3$); IR (KBr, cm^{-1}) 3601 (br), 3040 (m), 2977 (s), 1454 (s), 1396 (m), 1185 (s), 1104 (s); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.59-7.57 (1H, m), 7.27-7.20 (2H, m), 7.07-7.05 (1H, m), 6.43 (1H, dd, *J*= 9.9, 2.2 Hz), 6.01 (1H, dd, *J*= 9.9, 2.2 Hz), 4.90 (1H, d, *J*= 10.6 Hz), 4.18 (1H, ddd, *J*= 10.6, 2.2, 2.2 Hz), 3.79 (1H, AB, dq, *J*= 9.4, 6.9 Hz),), 3.58 (1H, AB, dq, *J*= 9.4, 6.9 Hz), 2.65 (1H, s), 1.27 (3H, t, *J*= 6.9 Hz),; ^{13}C NMR (400MHz, $CDCl_3$) δ 135.9, 131.9, 128.0, 127.8, 127.8, 126.1, 124.9, 80.7, 72.5, 64.6, 15.5. HRMS calcd for $C_{12}H_{14}O_2$ (M^+): 190.0994. Found: 190.0993.

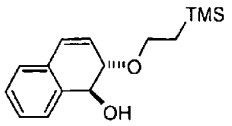


(1S,2S)-2-(Isopropoxy)-1,2-dihydro-naphthalen-1-ol (18): : To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (3.5 mg, 0.007 mmol), (S)-(R)-PPF-P^{t}Bu$_2$ (7.5 mg, 0.014 mmol) and **13** (100 mg, 0.694 mmol) were added followed by addition of THF (1.5 mL) and isopropanol (1.5 mL). The mixture was heated to 80°C for two hours and the solvent was removed *in vacuo*. The resulting oil was purified by flash chromatography (10% ethyl acetate in hexanes) to give **18** as a colourless oil (133.7 mg, 94%). The ee was determined to be 92% using HPLC analysis on a CHIRALCEL OD column, λ = 486 nm. Retention times in 1.5% isopropanol in hexanes were 9.7 min (major) and 10.7 min. R_f= 0.42 on silica gel (10% ethyl acetate:hexanes); $[\alpha]^{25}_D$= +154.0° (c= 12.6, $CHCl_3$); IR (KBr, cm^{-1}) 3435(br), 3038(w), 2952(s), 1454(m), 1249(s), 1087(s); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.61-7.58 (1H, m), 7.27-7.19 (2H, m), 7.06-7.04 (1H, m), 6.40 (1H, dd, *J*= 9.9, 2.0 Hz), 5.95 (1H, dd, *J*= 9.9, 2.2 Hz), 4.87 (1 H, d, *J*= 10.8 Hz), 4.24 (1H, ddd, *J*= 10.8, 2.2, 2.2 Hz), 3.85 (1H, h, *J* = 6.2 Hz), 2.98 (1H, s), 1.25 (6H, dd, *J*= 8.8, 6.2 Hz); ^{13}C NMR (400MHz, $CDCl_3$) δ136.2, 132.3, 129.6, 128.0, 127.9, 127.8, 126.3, 125.0, 78.9, 73.0, 71.1, 23.5, 22.4. HRMS calcd for $C_{13}H_{16}O_2$ (M^+): 204.1150. Found: 204.1150.

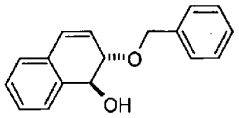


(1S,2S)-3-(1-propenyloxy)-1,2-dihydro-naphthalen-1-ol (19): : To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (9.1 mg, 0.018 mmol), (S)-(R)-PPF-P^{t}Bu$_2$ (15 mg, 0.028 mmol) and **13** (1.06 g, 7.35 mmol) were added followed by addition of THF (1.5 mL) and allyl alcohol (2 mL, 29.4 mmol). The mixture was heated to 80°C for two hours and the THF was removed *in vacuo*. The resulting oil was purified by flash chromatography (10% ethyl acetate in hexanes) to give **19** as a colourless oil (898mg, 60%) which solidified on sitting. The ee was determined to be >99% using HPLC analysis on a CHIRALCEL OD column, λ = 486 nm. Retention times in 1.5% isopropanol in hexanes were 15.2 min and 16.3 min (major). R_f= 0.17 on silica gel (10% ethyl acetate:hexanes); mp 25-26° (Et_2O); $[\alpha]^{25}_D$= +195.1° (c= 11.5, $CHCl_3$); IR (KBr, cm^{-1}) 3435(br), 3037(m), 2857(s), 1454(s), 1165(s), 1083(s); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.61-7.58 (1H, m), 7.27-7.20 (2H, m), 7.08-7.05 (1H, m), 6.44 (1H, dd, *J*= 9.9, 2.0 Hz), 6.00 (1H, dd, *J*= 9.9, 2.4 Hz), 6.00-5.92 (1H,m), 5.32 (1 H, ddd, *J*= 17.2, 3.3, 1.6 Hz), 5.21 (1H, ddd, *J*= 10.4, 2.9, 1.3 Hz), 4.94 (1H, d, *J* = 10.2 Hz), 4.27 (1H, ddd, *J* = 10.3, 2.2, 2.2 Hz),), 4.23 (1H, dddd, *J* = 12.8, 5.5, 1.5, 1.5 Hz), 4.12 (1H, dddd, *J* = 12.8, 5.9, 1.5, 1.5 Hz), 3.09 (1H, s); ^{13}C NMR

(400MHz, $CDCl_3$) δ135.8, 134.5, 131.8, 128.1, 127.7, 127.6, 127.4, 126.1, 125.0, 117.5, 80.1, 76.7, 72.4, 70.2. HRMS calcd for $C_{14}H_{14}O_2$ (M^+):202.0994. Found: 202.0994.

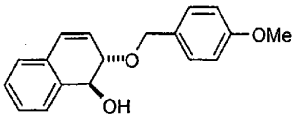


(1S,2S)-2-(2-Trimethylsilyl-ethoxy)-1,2-dihydro-naphthalen-1-ol (20): : To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (4.3 mg, 0.0087 mmol), (S)-(R)-PPF-P^{t}Bu$_2$ (9.4 mg, 0.0174 mmol) and **13** (100 mg, 0.694 mmol) were added followed by addition of THF (1.25 mL) and trimethylsilylethanol (1.25 mL). The mixture was heated to reflux for two hours and the THF was removed *in vacuo*. The resulting oil was purified by flash chromatography (10% ethyl acetate in hexanes) to give **20** as a colourless oil (84.7 mg, 53%). The ee was determined to be 95% using HPLC analysis on a CHIRALCEL OD column, λ = 486nm. Retention times in 0.5% isopropanol in hexanes were 17.9 min and 18.5 min (major). R_f= 0.25 on silica gel (10% ethyl acetate:hexanes); $[\alpha]^{25}_D$= +119.2° (c= 13.0, $CHCl_3$); IR (KBr, cm^{-1}) 3447(br), 3037(m), 2972(s), 1454(m), 1381(m), 1118(s), 1078(s); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.59-7.57 (1H, m), 7.28-7.21 (2H, m), 7.08-7.06 (1H, m), 6.43 (1H, dd, *J*= 9.9, 2.0 Hz), 6.03 (1H, dd, *J*= 9.9, 2.2 Hz), 4.89 (1 H, d, *J*= 10.6 Hz), 4.18 (1H, ddd, *J*= 10.6, 2.2, 2.2 Hz), 3.85-3.78 (2H, m), 3.63-3.56 (2H, m), 2.79 (1H, s), 1.05-0.97 (2H, m), 0.36 (9H, m); ^{13}C NMR (400MHz, $CDCl_3$) δ. 135.9, 132.0, 127.9, 127.9, 127.8, 127.6, 126.1, 124.9, 80.4, 72.6, 66.5, 18.6, -1.4. HRMS calcd for $C_{15}H_{22}O_2Si$ (M^+): 262.1389. Found: 262.1388.

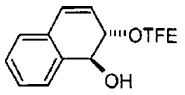


(1S,2S)-2-Benzyloxy-1,2-dihydro-naphthalen-1-ol (21): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (9.0 mg, 0.018 mmol), (S),(R)-PPF-P^{t}Bu$_2$ (19.0 mg, 0.035 mmol), and **13** (1.00 g, 6.94 mmol) were added followed by addition of THF (1.8 mL) and benzylalcohol (3.6 mL, 34.7 mmol) and heating to 80°C for 24 hours. The THF was then removed *in vacuo* and the resulting oil was purified by flash chromatography (10% ethyl acetate in hexanes) to give **21** as a crystalline solid (1.22 g, 70%). The ee was determined to be >98% using HPLC analysis on a CHIRALCEL OD column, λ = 486 nm. Retention times in 1.5% isopropanol in hexanes were

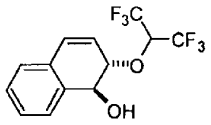
29.0 min and 32.5 min (major). R_f= 0.34 on silica gel (20% ethyl acetate:hexanes); mp 52-54° (Et_2O); $[\alpha]^{25}_D$= +167.3° (c= 10.0, $CHCl_3$); IR (KBr, cm^{-1}) 3305 (br), 3020 (w), 2876 (w), 1496 (m), 1352 (m), 1281 (m), 1169 (m), 1050 (s), 777 (s); ^1H NMR (400MHz, $CDCl_3$) δ 7.58-7.56 (1H, m), 7.41-7.22 (7H, m), 7.22-7.07 (1H, m), 6.46 (1H, dd, *J*= 9.9, 2.1 Hz), 6.05 (1H, dd, *J*= 9.9, 2.1 Hz), 4.98 (1H, d, *J*= 10.4 Hz), 4.78 (1H, d, *J*= 11.7 Hz), 4.63 (1H, d, *J*= 11.7 Hz), 4.33 (1H, ddd, *J*= 10.4, 2.2, 2.2 Hz), 2.61 (1H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 138.0, 135.9, 131.9, 128.5, 128.3, 128.1, 127.9, 127.9, 127.8, 127.4, 126.2, 125.1, 80.4, 72.6, 71.3. HRMS calcd for $C_{17}H_{16}O_2$ (M^+): 252.1150. Found: 252.1148.



(1S,2S)-2-(4-Methoxybenzyloxy-1,2-dihydro-naphthalen-1-ol (22): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (6.0 mg, 0.012 mmol), (S),(R)-PPF-P^{t}Bu$_2$ (13.0 mg, 0.024 mmol), and **13** (693 mg, 4.81 mmol) were added followed by addition of THF (1.5 mL) and anisyl alcohol (3.0 mL, 24.1 mmol) and heating to 80°C for 24 hours. . The THF was then removed *in vacuo* and the resulting oil was purified by flash chromatography (20% ethyl acetate in hexanes) to give **22** as a crystalline solid (1.18 g, 87%). The ee was determined to be 97% using HPLC analysis on a CHIRALCEL OD column, λ = 486 nm. Retention times in 1.5% isopropanol in hexanes were 37.1 min and 42.1 min (major). R_f= 0.53 on silica gel (30% ethyl acetate:hexanes); mp 63-64° (Et_2O); $[\alpha]^{25}_D$= +138.5° (c= 10.5, $CHCl_3$); IR (KBr, cm^{-1}) 3435(br), 3035(m), 2836(s), 1612(s), 1513(s), 1454(m), 1249(s), 1082(s); ^1H NMR (400MHz, $CDCl_3$) δ 7.59-7.57 (1H, m), 7.32 (2H, ddd, *J*= 8.7, 2.8, 1.9 Hz), 7.28-7.22 (1H, m),), 6.90 (2H, ddd, *J*= 8.7, 2.8, 1.9 Hz), 6.46 (1H, dd, *J*= 9.9, 2.1 Hz), 6.04 (1H, dd, *J*= 9.9, 2.4 Hz), 4.96 (1H, d, *J*= 10.1 Hz), 4.64 (1H, dd, *J*= 57.1, 11.4 Hz), 4.32 (1H, ddd, *J*= 10.2, 2.2, 2.2 Hz), 3.80 (1H, s), 2.96 (1H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 159.2, 135.9, 131.9, 129.9, 129.5, 128.1, 127.8, 127.6, 127.5, 126.1, 125.0, 113.8, 80.0, 72.5, 70.9, 55.1. HRMS calcd for $C_{17}H_{16}O_2$ (M^+): 252.1150. Found: 252.1148.

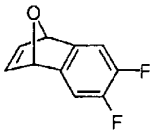


(1S,2S)-2-(2,2,2-Trifluoro-ethoxy)-1,2-dihydro-naphthalen-1-ol (17): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (2.1 mg, 0.043 mmol), (S)-(R)-PPF-P^{t}Bu$_2$ (3.8 mg, 0.087 mmol) and **13** (500 mg, 3.47 mmol) were added followed by addition of trifluoroethanol (4 mL) and THF (4 mL). The mixture was heated to reflux for three hours and the solvent was removed *in vacuo*. The resulting solid was purified by flash chromatography (10% ethyl acetate in hexanes) to give **17** as a white crystalline solid (594 mg, 70%). The ee was determined to be 98% using HPLC analysis on a CHIRALCEL OD column, λ = 254 nm. Retention times in 4% isopropanol in hexanes were 11.3 min (major) and 13.3 min. R_f= 0.41 on silica gel (20% ethyl acetate:hexanes); mp 79-80° (Et_2O); $[\alpha]^{25}_D$= 145.4° (c= 12.6, $CHCl_3$); IR (KBr, cm^{-1}) 3354 (br), 3036 (w), 2939 (w), 1455 (w), 1275 (s), 1169 (s), 1050(m), 977 (m); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.57-7.55 (1H, m), 7.30-7.23 (2H, m), 7.10-7.08 (1H, m), 6.48 (1H, dd, *J*= 9.9, 2.0 Hz), 5.94 (1H, dd, *J*= 9.9, 2.4 Hz), 4.96 (1 H, d, *J*= 2.2 Hz), 4.38 (1H, ddd, *J*= 9.9, 2.4, 2.2 Hz), 4.03 (2H, q, J^{H-F}= 8.6 Hz), 2.55 (1H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 135.5, 131.7, 129.2, 128.3, 128.1, 126.6, 125.9, 125.2, 122.4, 83.0, 72.8, 67.0 (q, J^{C-F}= 34.4 Hz). HRMS calcd for $C_{12}H_{11}O_2F_3$ (M^+): 244.0711. Found: 244.0720.

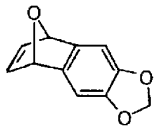


(1S,2S)-2-(2,2,2-Trifluoro-1-trifluoromethyl-ethoxy)-1,2-dihydro-naphthalen-1-ol (23): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (1.7 mg, 0.003 mmol),(S)-(R)-PPF-P^{t}Bu$_2$ (3.8 mg, 0.007 mmol) and **13** (55 mg, 0.382 mmol) were added followed by addition of THF (2.0 mL) and hexafluoroisopropanol (240 mg, 1.74 mmol). The mixture was heated to reflux for two hours and the solvent was removed *in vacuo*. The resulting solid was purified by flash chromatography (10% ethyl acetate in hexanes) to give **23** as a white solid (107.1mg, 90%). The ee was determined to be 93% using HPLC analysis on a CHIRALCEL OD column, λ = 486 nm. Retention times in 1.5% isopropanol in hexanes were 11.3 min and 17.6 min (major); R_f= 0.28 on silica gel (10% ethyl acetate:hexanes); mp 88.5-90° (Et_2O); $[\alpha]^{25}_D$= +101.8° (c= 10.9, $CHCl_3$); IR (KBr, cm^{-1}) 3191 (br), 2937 (m), 1379 (s), 1280 (s), 1247 (s), 1194 (s), 1100 (s), 954 (s), 753 (m); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.55-7.53 (1H, m), 7.31-7.26 (2H, m), 7.11-7.09 (1H, m), 6.49 (1H, dd, *J*= 9.9, 2.1 Hz), 5.92 (1H, dd, *J*= 9.9, 2.4 Hz), 5.07 (1H, dd, *J*= 9.7, 5.0 Hz), 4.63 (1H, ddd, *J*= 9.9, 1.5. 1.5 Hz), 4.58 (1H, h, J^{H-F}= 6.1 Hz), 2.50 (1H, d, *J*= 4.2 Hz); ^{13}C NMR

(400MHz, $CDCl_3$) δ 135.2, 131.5, 129.7, 128.5, 128.3, 126.7, 125.2, 122.9, 120.1, 85.4, 75.4 (h, J^{C-F}= 32.2 Hz), 73.5. HRMS calcd for $C_{13}H_{10}O_2F_6$ (M^+): 312.0585 Found: 312.0574.

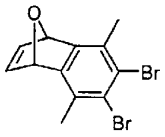


6,7-Difluoro-1,4-epoxy-1,4-dihydronaphthalene (24). To 3,4-difluoro-1,2-dibromobenzene (0.75 g, 2.78 mmol) and furan (1 mL, 14.7 mmol) in Et_2O (15 mL) at -78°C was added BuLi (1.1 mL, 2.5M in hexanes, 2.75 mmol) dropwise. The reaction was stirred for two hours at -78°C and then was allowed to warm to room temperature. After 2 hours, the reaction mixture was quenched with water dropwise and then was poured into water. The organic layer was separated and the aqueous layer was extracted three times with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, concentrated and chromatographed (25% ethyl acetate:hexanes) on silica gel to give **24** (350 mg, 70%) as a colourless oil. R_f= 0.21 on silica gel (20% ethyl acetate:hexanes); bp 40°C @ 0.5mmHg]; IR (neat, cm^{-1}), 3017 (M), 1624 (s), 1465 (s), 1365 (s), 1253 (s), 1190 (m), 1040 (s), 857 (s). ^1H NMR (400MHz, $CDCl_3$) δ 7.06 (2H, dd, J^{H-F}= 7.7, 7.7 Hz), 7.01 (2H, s), 5.67 (2H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 147.2 (dd, J^{C-F}= 247.9, 14.5 Hz), 145.1 (dd, J^{C-F}= 4.3, 4.3 Hz), 143.1, 110.8 (m), 82.1. HRMS calcd for $C_{10}H_6O$ (M^+): 180.0387. Found: 180.0394.

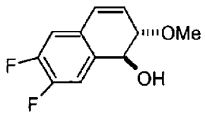


5,8-epoxy-5,8-dihydronaphtho[2,3-d][1,3]dioxole (25): To 3,4-dibromobenzo-1,3-dioxolane (1.54 g, 5.50 mmol) and furan (4 g, 58.8 mmol) in PhMe (55 mL) at -78°C was added BuLi (2.2 mL, 2.5M in hexanes, 5.5 mmol) dropwise. The reaction was stirred for two hours at -78°C and the allowed to warm to rt. After 3 hours, MeOH (2 mL) was added and the reaction mixture was poured into water. . The organic layer was separated and the aqueous layer was extracted three times with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. Recrystallization from hexanes gave **25** (560 mg, 54%) as white crystals). R_f= 0.47 on silica gel (30% ethyl acetate:hexanes); mp 111-112°C (Et_2O); IR (KBr, cm^{-1}) 2895, 1455, 1292, 1138, 1038, 1014, 848; ^1H NMR (400MHz, $CDCl_3$) δ 7.02 (2H, dd, *J*=

0.9,0.9 Hz), 6.82 (2H, s), 5.92 (1H, d, *J*= 1.5 Hz), 5.87 (1H, d, *J*= 1.5 Hz), 5.62 (2H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 144.3, 143.3, 103.9, 101.1, 82.4. HRMS calcd for $C_{11}H_8O_2$ (M^+): 188.0473. Found: 188.0463.

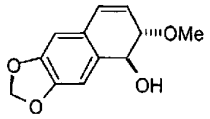


5,6-Dibromo-4,7-dimethyl-1,4-epoxy-1,4-dihydronaphthalene (26): To tetrabromo para-xylene (2.1 g, 5.0 mmol) and furan (4 g, 58.8 mmol) in PhMe (55 mL) at -78°C was added BuLi (2.2 mL, 2.5M in hexanes, 5.5 mmol) dropwise. The reaction was stirred for two hours at -78°C and the allowed to warm to rt. After 3 hours, MeOH (2 mL) was added and the reaction mixture was poured into water. . The organic layer was separated and the aqueous layer was extracted three times with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. Flash chromatography on silca gel gave **26** (185 mg, 50%) as a white solid. The spectral data correlates well with the literature values.[22]

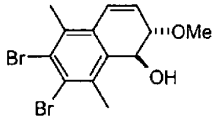


(1S,2S)-6,7-Difluoro-2-methoxy-1,2-dihydro-naphthalen-1-ol (27): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), (S)-(R)-PPF-P^{t}Bu$_2$ (5.4 mg, 0.010mmol) and **24** (72 mg, 0.40 mmol) were added followed by addition of THF (1.0 mL) and methanol (1.0 mL). The mixture was heated to reflux for 1 hour. The solvents were then removed *in vacuo*. The resulting solid was purified by flash chromatography (20% ethyl acetate in hexanes) to give **27** as a white crystalline solid (74.9 mg, 88%). The ee was determined to be 96.4% using HPLC analysis on a CHIRALCEL OD column, λ = 486 nm. Retention times in 4% isopropanol in hexanes were 8.9 min and 10.1 min (major). R_f= 0.27 on silica gel (30% ethyl acetate:hexanes); mp 129-131° (Et_2O); $[\alpha]^{25}_D$= +134.4° (c= 9.3, $CHCl_3$); IR (KBr, cm^{-1}) 3269 (br), 2937 (w), 1597 (m), 1503 (s), 1306 (s), 1103 (s), 893 (s); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.40 (1H, ddd, J^{H-F}= 10.8, 7.8 Hz, J^{H-H}=0.6 Hz), 6.85 (1H, dd, J^{H-F}= 10.9, 7.8 Hz), 6.31 (1H, dd, *J*= 10.0, 2.0 Hz), 6.05 (1H, dd, *J*= 10.0, 2.0 Hz), 4.79 (1H, d, *J*= 11.0 Hz), 4.05 (1H, ddd, *J*= 11.0, 2.0, 2.0 Hz), 3.49 (3H, s), 2.94 (1H, d, *J*= 2.2 Hz); ^{13}C NMR (400MHz, $CDCl_3$) δ 151.0 (d, J^{H-F}=

12.5 Hz), 148.5 (dd, J^{H-F}= 12.5,2.9 Hz), 133.2 (dd, J^{H-F}= 5.2, 3.6 Hz), 128.9 (dd, J^{H-F}= 6.6, 4.4 Hz), 128.0 (d, J^{H-F}= 2.2 Hz), 126.5 (dd, J^{H-F}= 2.2, 1.5 Hz), 115.1 (d, J^{H-F}= 18.3 Hz), 114.8 (d, J^{H-F}= 19.8 Hz), 82.3, 72.0, 57.0. HRMS calcd for $C_{11}H_{10}O_2F_2$ (M^+): 212.0649. Found: 212.0658.



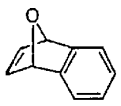
(1S,2S)-6-Methoxy-5,6-dihydro-naphtho[2,3-d][1,3]dioxol-5-ol (28): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (1.7 mg, 0.0035 mmol), (S)-(R)-PPF-P^{t}Bu$_2$ (3.8 mg, 0.0069 mmol) and **25** (100 mg, 0.694 mmol) were added followed by addition of THF (1.0 mL) and methanol (1.0 mL) and heating to reflux for 30 minutes. The solvents were then removed *in vacuo*. The resulting solid was purified by flash chromatography (30% ethyl acetate in hexanes) to give **28** as a white crystalline solid (127.5 mg, 90%). The ee was determined to be 95% using HPLC analysis on a CHIRALCEL OD column, λ = 486 nm. Retention times in 4% isopropanol in hexanes were 19.2 min (major) and 22.6 min. R_f= 0.24 on silica (30% ethyl acetate:hexanes); mp 117-119° (Et_2O); $[\alpha]^{25}_D$= +298.7° (c= 11.1, $CHCl_3$); IR (KBr, cm^{-1}) 3248 (br), 2926 (s), 1600 (m), 1483 (s), 1260 (s), 1113 (s), 941 (s), 876 (s); ^{1}H NMR (400MHz, acetone-d) δ 7.06 (1H, s), 6.65 (1H, s), 6.35 (1H, dd, J= 10.0, 2.0 Hz), 5.94 (2H, dd, J= 9.8, 1.0 Hz), 5.91 (1H, dd, J= 10.0, 2.5 Hz), 4.72 (1H, dt, J= 9.9 Hz), 4.02 (1H, dt, J= 10.3, 2.2 Hz), 3.48 (3H, s), 2.87 (1H, d, J= 13.2 Hz); ^{13}C NMR (400MHz, acetone-d) δ 147.8, 147.6, 133.0, 128.1, 127.2, 127.2, 107.5, 107.5, 101.9, 82.1, 73.0, 57.0. HRMS calcd for $C_{12}H_{12}O_4$ (M^+): 220.0736. Found: 220.0684.



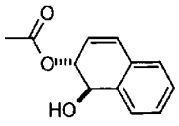
(1S,2S)-6,7-Dibromo-2-methoxy-5,8-dimethyl-1,2-dihydro-naphthalen-1-ol (29): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (1.5 mg, 0.0029 mmol), (R)-(S)-PPF-P^{t}Bu$_2$ (3.2 mg, 0.0059 mmol) and **26** (195 mg, 0.59 mmol) were added followed by addition of trifluoroethanol (1.0 mL) and methanol (1.0 mL). The mixture was heated to reflux for 20 hours. The solvents were then removed *in vacuo*. The resulting solid was purified by flash chromatography (50% ethyl acetate in hexanes) to give **29** as a white crystalline solid (171.6 mg, 79%). The ee was determined to be 97% using HPLC analysis on a CHIRALCEL OD column,

λ = 486 nm. Retention times in 4% isopropanol in hexanes were 16.8 min (major) and 19.3 min. R_f= 0.39 on silica gel (50% ethyl acetate:hexanes); mp 114-116° (Et_2O); $[\alpha]^{25}_D$= -197.1° (c= 10.0, $CHCl_3$); IR (KBr, cm^{-1}) 3349 (s), 2901 (m), 1700 (w), 1532 (w), 1404 (m), 1258 (m), 1081 (s), 936 (s); ^1H NMR (400MHz, $CDCl_3$) δ 6.96-6.93 (1H, m), 6.23-6.19 (1H, m), 4.89 (1H, s), 3.96-3.90 (1H, m), 3.38-3.35 (3H, m), 2.61-2.57 (3H, m), 2.54 (3H, s), 1.82-1.54 (1H, m); ^{13}C NMR (400MHz, $CDCl_3$) δ 137.3, 134.4, 133.2, 129.7, 129.5, 129.0, 128.1, 125.3, 75.3, 66.6, 56.6, 21.0, 20.6. HRMS calcd for $C_{13}H_{16}O_2Br_2$ (M^+): 361.9518. Found: 361.9335.

Example 4: Compounds Formed From Reactions Involving Carboxylate Nucleophiles

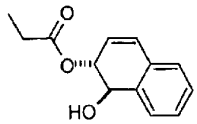


1



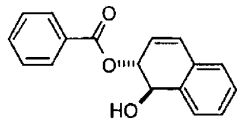
2

(1R*,2R*)-Acetic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester (2): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (4.3 mg, 0.008 mmol DPPF (9.6 mg, 0.017 mmol), 1 (50 mg, 1.39 mmol), and sodium acetate (142 mg, 1.74 mmol) were added followed by addition of THF (2 mL) and triethylamine hydrochloride (239 mg, 1.74 mmol). The mixture was heated at reflux for 3 hours and the solvents were removed *in vacuo*. The resulting mixture was purified by flash chromatography (30% ethyl acetate in hexanes) to give 2 as a crystalline solid (41 mg), 63%). R_f= 0.26 on silica gel (20% ethyl acetate:hexanes); mp 67-68° (Et_2O); IR (KBr, cm^{-1}) ^1H NMR (400MHz, $CDCl_3$) δ 7.54-7.53 (1H, m), 7.29-7.24 (2H, m), 7.10-7.08 (1H, m), 6.50 (1H, dd, *J*= 3.9, 1.3 Hz), 5.85 (1H, dd, *J*= 9.9, 3.1 Hz), 5.59 (1H, ddd, *J*= 9.0, 2.8, 1.9 Hz), 4.92 (1H, d, *J*= 9.0 Hz), 2.64 (1H, s), 2.12 (3H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 171.3, 135.2, 131.5, 129.5, 128.3, 126.7, 126.0, 125.4, 75.3, 71.7, 21.2. HRMS calcd for $C_{12}H_{12}O_3$ (M^+): 204.0786. Found: 204.0791.



3

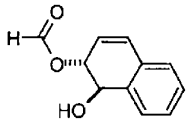
(1R*,2R*)-Propionic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester (3): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (4.3 mg, 0.0087 mmol), DPPF (9.6 mg, 0.017 mmol) and **1** (50 mg, 0.347 mmol) were added followed by addition of THF (2.5 mL), triethylamine (242 μL, 1.735 mmol) and propionic acid (130 μL, 1.735 mmol). The mixture was heated at reflux for 3 hours and the solvents were removed *in vacuo*. The resulting mixture was purified by flash chromatography (20% ethyl acetate in hexanes) to give **3** a white crystalline solid (50 mg, 66%). R_f= 0.24 on silica gel (% 20 ethyl acetate:hexanes); mp 55-56° (Et_2O); IR (KBr, cm^{-1}) 3491 (br), 3048 (w), 2984 (w), 1739 (s), 1454 (m), 1363 (w), 1182 (s), 1083 (m). ^1H NMR (400MHz, $CDCl_3$) δ 7.55-7.52 (1H, m), 7.29-7.24 (2H, m), 7.11-7.08 (1H, m), 6.50 (1H, dd, *J*= 10.0, 2.0 Hz), 5.85 (1H, dd, *J*= 12.8, 2.8 Hz), 5.61 (1H, ddd, *J*= 9.2, 2.8, 2.0 Hz), 4.93 (1H, d, *J*= 9.2 Hz), 2.40 (2H, qd, *J*= 7.6, 1.2 Hz), 1.16 (3H, t, *J*= 7.6 Hz); ^{13}C NMR (400MHz, $CDCl_3$) δ 174.8, 135.3, 131.5, 129.4, 128.3, 128.3, 126.7, 125.9, 125.5, 75.2, 71.9, 27.7, 9.0. HRMS calcd $C_{13}H_{14}O_3$ (M^-): 218.0943. Found: 218.0938



4

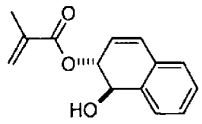
(1R,2R)-Benzoic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester (4): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (4.3 mg, 0.0087 mmol), (R)-(S)-BPPFA (9.6 mg, 0.017 mmol) and **1** (100 mg, 0.694 mmol) were added followed by addition of THF (4 mL), triethylamine (483 μL, 3.47 mmol) and benzoic acid (424 mg, 3.47 mmol). The mixture was heated at reflux for 6 hours and the solvents were removed *in vacuo*. The resulting mixture was purified by flash chromatography (20% ethyl acetate in hexanes) to give **4** a white crystalline solid (129 mg, 70%). The ee was determined to be 76% using HPLC analysis on a CHIRALCEL OD column, 10% isopropanol in hexanes, λ=254 nm. Retention times were 10.0 min (major) and

12.9 min. R_f= 0.3 on silica gel (10% ethyl acetate:hexanes); mp 107-109° (Et_2O); $[\alpha]^{25}_D$= -298.4° (c= 11.3, $CHCl_3$); IR (KBr, cm^{-1}) 3619 (br), 3071 (w), 2977 (w), 1724 (s), 1451 (m), 1324 (m), 1265 (s), 1110 (s). ^1H NMR (400MHz, $CDCl_3$) δ 8.10 (2H, d, *J*= 7.6 Hz), 7.64-7.59 (2H, m), 7.48-7.45 (2H, m), 7.34-7.32 (2H, m), 7.13-7.11 (1H, m), 6.55 (1H, d, *J*= 10.0 Hz), 5.97 (1H, dd, *J*= 9.8, 2.9 Hz), 5.86 (1H, ddd, *J*= 9.8, 2.0, 2.0 Hz), 5.11 (1H, d, *J*= 9.0 Hz), 2.84 (1H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 166.9, 135.3, 133.3, 131.6, 129.9, 129.8, 129.7, 128.4, 128.4, 128.4, 126.8, 126.1, 125.5, 76.1, 71.9. HRMS calcd for $C_{17}H_{14}O_3$ (M^+): 266.0943. Found: 266.0938.



5

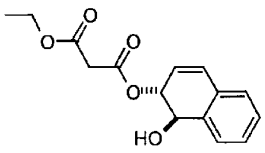
(1R*,2R*)-Formic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester (5): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (4.3 mg, 0.0087 mmol), DPPF (9.6 mg, 0.017 mmol), **1** (100 mg, 0.694 mmol), and ammonium formate (219 mg, 3.47 mmol), were added followed by addition of THF (5 mL). The mixture was heated at reflux for 3 hours and the solvents were removed *in vacuo*. The resulting mixture was purified by flash chromatography (30% ethyl acetate in hexanes) to give **5** a white crystalline solid (84 mg, 64%). R_f= 0.25 on silica gel (30% ethyl acetate:hexanes); mp 133-135° (Et_2O); IR (KBr, cm^{-1}) 3146 (br), 2935 (w), 1720 (s), 1482 (w), 1186 (s), 1049 (m), 968 (m); ^1H NMR (400MHz, $CDCl_3$) δ 8.17 (1H, d, *J*= 0.8 Hz), 7.52-7.50 (1H, m), 7.29-7.27 (2H, m), 7.13-7.11 (1H, m), 6.54 (1H, dd, *J*= 9.6, 1.6 Hz), 5.88 (1H, dd, *J*= 9.6, 2.8 Hz), 5.71-5.68 (1H, m), 4.96 (1H, d, *J*= 8.8 Hz), 2.8 (1H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 160.9, 134.8, 131.4, 130.0, 128.5, 126.9, 126.1, 124.6, 74.8, 71.4. HRMS calcd for $C_{11}H_{10}O_3$ (M^+): 190.0630. Found: 190.0625.



6

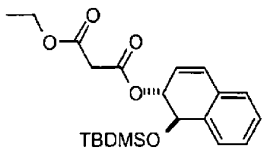
(1R*,2R*)-2-Methyl acrylic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester (6): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (4.3 mg, 0.0087 mmol), DPPF (9.6 mg, 0.017 mmol) and **1** (50 mg, 0.347 mmol) were added followed by addition of THF (2.5 mL),

triethylamine (242 μL, 1.735 mmol) and methacrylic acid (147 μL, 1.735 mmol). The mixture was heated at reflux for 3 hours and the solvents were removed *in vacuo*. The resulting mixture was purified by flash chromatography (30% ethyl acetate in hexanes) to give **6** a white crystalline solid (50 mg, 63%). R_f= 0.32 on silica gel (20% ethyl acetate:hexanes); mp 80-82° (Et_2O); IR (KBr, cm^{-1}) 3450 (br), 3030 (w), 2928 (w), 1722 (s), 1637 (m), 1454 (m), 1289 (m), 1163 (s); ^1H NMR (400MHz, $CDCl_3$) δ 7.56-7.55 (1H, m), 7.29-7.24 (2H, m), 7.10-7.09 (1H, m), 6.51 (1H, dd, *J*= 9.9, 1.9 Hz), 6.15 (1H, s), 5.87 (1H, dd, *J*= 9.9, 3.0 Hz), 5.67 (1H, ddd, *J*= 9.3, 2.1, 2.1 Hz), 5.61 (1H, s), 5.01 (1H, dd, *J*= 9.0, 5.7 Hz), 2.74 (1H, d, *J*= 6.1 Hz), 1.96 (3H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 167.6, 135.9, 135.3, 131.5, 129.4, 128.3, 128.2, 126.6, 126.4, 125.8, 125.5, 75.9, 71.9, 18.3. . HRMS calcd $C_{14}H_{12}O_2$ (M^+-H_2O): 212.0837. Found: 212.0831



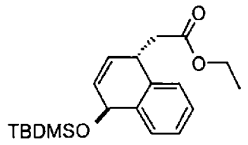
7

(1R*,2R*)-Malonic acid ethyl ester (1-hydroxy-1,2-dihydro-naphthalen-2-yl) ester (7): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (8.6 mg, 0.017 mmol DPPF (19.2 mg, 0.035 mmol), **1** (200 mg, 1.39 mmol), ethyl malonate potassium salt (590 mg, 3.47 mmol), and triethylamine hydrochloride (478 mg, 3.47 mmol) were added followed by addition of THF (8 mL). The mixture was heated at reflux for 3 hours and the solvents were removed *in vacuo*. The resulting mixture was purified by flash chromatography (30% ethyl acetate in hexanes) to give **7** a colourless oil (300 mg), 79%). R_f= 0.29 on silica gel (30% ethyl acetate:hexanes); IR (KBr, cm^{-1}) 3470 (br), 2983 (w), 1731 (s), 1453 (w), 1370 (m), 1150 (s), 1031 (m); ^1H NMR (400MHz, $CDCl_3$) δ 7.56-7.54 (1H, m), 7.27-7.21 (2H, m), 7.08-7.06 (1H, m), 6.48 (1H, dd, *J*= 9.9, 2.1 Hz), 5.83 (1H, dd, *J*= 9.7, 2.8 Hz), 5.70 (1H, ddd, *J*= 9.7, 2.5, 2.2 Hz), 4.97 (1H, d, *J*= 9.5 Hz), 4.18 (2H, q, *J*= 7.2 Hz), 3.43 (2H, dd, *J*= 23.6, 15.9 Hz), 3.21 (1H, s), 1.25 (3H, t, *J*= 7.1 Hz); ^{13}C NMR (400MHz, $CDCl_3$) δ 167.1, 166.5, 135.0, 131.5, 129.6, 128.3, 128.1, 126.6, 125.6, 125.1, 77.0, 71.6, 61.9, 41.6, 14.0. HRMS calcd for $C_{15}H_{14}O_4$ (M^+-H_2O): 258.0892. Found: 258.0899.



8

(1R*,2R*)-Malonic acid (1-tert-butyldimethylsiloxy-1,2-dihydro-naphthalen-2-yl) ester ethyl ester (8): To a dried round bottom flask, 7 (270 mg, 0.98 mmol), imidazole (134 mg, 1.96 mmol), dimethylaminopyridine (6 mg, 0.05 mmol) were dissolved in dichloromethane (4 mL). Tert-butyldimethylsilyl chloride (222 mg, 1.47 mmol) was then added portionwise and allowed to react for 24 hours. The reaction was then quenched with water, extracted with dichloromethane, dried over Na_2SO_4 and concentrated *in vacuo*. Flash chromatography (10% ethyl acetate in hexanes) gave a colourless oil **8** (343 mg, 90%). R_f= 0.48 on silica gel (10% ethyl acetate:hexanes. IR (KBr, cm-1) 2983 (w), 1731 (s), 1453 (w), 1370 (m), 1150 (s), 1031 (m); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.41-7.39 (1H, m), 7.24-7.22 (2H, m), 7.07-7.05 (1H, m), 6.47 (1H, dd, *J*= 9.9, 1.8 Hz), 5.83 (1H, dd, *J*= 9.7, 2.7 Hz), 5.60 (1H, ddd, *J*= 9.3, 2.9, 2.0 Hz), 5.00 (1H, dd, *J*= 9.3, 0.5 Hz), 4.22-4.15 (2H, m), 3.40 (2H, dd, *J*= 19.6, 16.0 Hz), 1.57 (1H, s), 1.25 (3H, t, *J*= 7.1 Hz), 0.92 (9H, s), 0.13 (3H, s), 0.09 (3H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 166.3, 166.2, 136.2, 132.1, 129.4, 128.0, 127.9, 126.5, 125.9, 125.7, 76.4, 71.6, 61.6, 41.7, 25.8, 18.1, 14.0, -4.3, -4.5. HRMS calcd for $C_{17}H_{21}O_5Si$ (M^+-C_4H_9): 333.1158. Found: 333.1149.

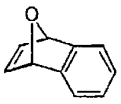


9

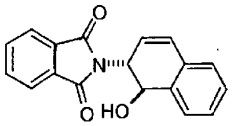
(1S*,2S*)-(4-Tert-butyldimethylsiloxy-1,4-dihydro-naphthalen-2-yl) acetic acid ethyl ester (9): To a dried round bottom flask, 8 (100 mg, 0.256 mmol) was dissolved in THF (4 mL). Potassium hydride (11.3 mg, 0.28 mmol) was then added portionwise and allowed to react for five minutes at room temperature. Triphenylphosphine (34.1 mg, 0.13 mmol) was then added followed by $Pd(PPh_3)_4$ (14.8 mg, 0.013 mmol). The reaction was then heated to reflux for two hours. The solvent was then removed *in vacuo* and the resulting oil purified by flash

chromatography (5% ethyl acetate in hexanes) giving **9** a colourless oil (54 mg, 61%). R_f= 0.27 on silica gel (5% ethyl acetate:hexanes); IR (KBr, cm^{-1}) 3036(w), 2956(s), 1735(s), 1472(m), 1257(s), 1077(s); ^1H NMR (400MHz, $CDCl_3$) δ 7.54-7.52 (1H, m), 7.30-7.23 (3H, m), 6.09 (1H, ddd, *J*= 2.4, 4.6, 10.2 Hz), 6.02 (1H, ddd, *J*= 10.2, 2.0, 0.5 Hz), 5.22-5.21 (1H, m), 4.15 (2H, q, *J*= 7.2 Hz), 3.92-3.87 (1H, m), 2.62 (1H, dd, *J*= 15.7, 5.7 Hz), 2.39 (1H, dd, *J*= 15.2, 9.0 Hz), 1.25 (3H, t, *J*= 7.2 Hz), 0.98 (9H, s), 0.21 (3H, s), 0.15 (3H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 171.7, 138.3, 136.1, 131.8, 128.2, 127.2, 127.0, 126.9, 126.6, 65.3, 60.5, 42.7, 36.5, 25.9, 18.2, 14.2, -4.2, -4.5. HRMS calcd $C_{17}H_{21}O_5Si$ (M^+-C_4H_9): 289.1260. Found: 289.1257

Example 5: Compounds Formed In Reactions Involving Nitrogen Nucleophiles



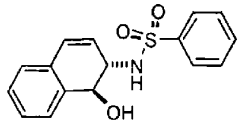
1



2

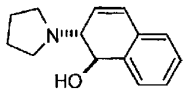
(1R,2R)-2-(1-hydroxy-1,2-dihydro-naphthalen-2-yl)-isoindole-1,3-dione (2): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (5.4mg, 0.011 mmol), (R)-(S)-BPPFA (12.2 mg, 0.022 mmol), phthalimide (510 mg, 3.47 mmol) and **1** (100 mg, 0.69 mmol) were added. THF (4 mL) was then added, followed by heating to 80°C for 3 days. The reaction mixture was then poured in to water and extracted three times with ethyl acetate. The organic layers were combined, washed with brine dried over Na_2SO_4, and concentrated *in vacuo*. The resulting solid was purified by flash chromatography (30% ethyl acetate in hexanes) to give **2** as a white crystalline solid (103.5 mg, 52%). The ee was determined to be 74% using HPLC analysis on a CHIRALCEL OD column, λ= 486nm. Retention times in 10% isopropanol in hexanes were 21.1 min (major)and 29.1 min. R_f= 0.36 on silica gel (30% ethyl acetate:hexanes); mp 175-176° (dec); $[\alpha]^{25}_D$= -6.1° (c= 12.9, $CHCl_3$); IR (KBr, cm^{-1}) 3536 (br), 3067 (w), 2921 (w), 1772 (m), 1693 (s), 1388 (s), 1084 (m), 955 (m), 719 (s); ^1H NMR (400MHz, $CDCl_3$) δ 7.78-7.75 (2H, m), 7.68-7.64 (2H, m), 7.57-7.55 (1H, m), 7.26-7.22 (2H, m), 7.09-7.07 (1H, m), 6.51 (1H, dd, *J*= 9.7, 2.7 Hz), 5.84 (1H, ddd, *J*= 9.7, 2.7, 2.2 Hz), 5.48 (1H, d, *J*= 12.8 Hz), 5.12 (1H, ddd, *J*= 12.8, 2.5, 2.4 Hz), 2.82 (1H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 168.6, 137.3, 134.2, 132.6, 132.1, 128.7, 128.2, 128.1, 126.9, 126.5, 124.4, 123.5, 70.9, 55.3. HRMS calcd for $C_{18}H_{11}NO_2$ (M^+-H_2O): 273.2939. Found: 273.0793.

35



3

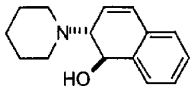
(1S,2S)-N-(1-Hydroxy-1,2-dihydro-naphthalen-2-yl)-benzene sulfonamide (3): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (4.3 mg, 0.0087 mmol), (S)-(R)-PPF-P^{t}Bu$_2$ (9.4 mg, 0.0173 mmol), benzenesulfonamide (545 mg, 3.47 mmol) and **1** (100 mg, 0.69 mmol) were added. THF (2 mL) was then added, followed by heating to 80°C for 12 hours. The reaction mixture was then poured into water and extracted three times with ethyl acetate. The organic layers were combined, washed with brine dried over Na_2SO_4, and concentrated *in vacuo*. The resulting solid was purified by flash chromatography (30% ethyl acetate in hexanes) to give **3** a white crystalline solid (223 mg, 96%). The ee was determined to be 95% by Mosher's ester formation and HPLC analysis on a CHIRALCEL OD column, λ= 486nm. Retention times in 10% isopropanol in hexanes were 26.6 min (major) and 39.4 min. R_f= 0.22 on silica gel (30% ethyl acetate:hexanes); mp 128-130° (dec); $[\alpha]^{25}_D$= 70° (c= 8.3, $CHCl_3$); IR (KBr, cm^{-1}) 3462 (br), 3200 (m), 2957 (w), 1447 (m), 1329 (m), 1329 (m), 1164 (s), 1093 (m). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.91-7.90 (2H, m), 7.62-7.58 (1H, m), 7.54-7.50 (2H, m), 7.47-7.45 (1H, m), 7.27-7.23 (2H, m), 6.40 (1H, dd, *J*= 9.7, 1.7 Hz), 5.55 (1H, dd, *J*= 9.7, 3.1 Hz), 5.26 (1H, s), 4.77 (1H, d, *J*= 8.8 Hz), 4.13-4.07 (1H, m), 2.91 (1H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 140.2, 134.9, 132.9, 131.3, 129.5, 129.2, 128.4, 128.4, 127.1, 126.4, 126.0, 72.0, 56.3. HRMS calcd for $C_{16}H_{15}NO_3S$ (M^+): 301.0773. Found: 301.0769.



4

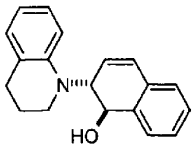
(1R*,2R*)-2-Pyrrolidin-1-yl-1,2-dihydro-naphthalen-1-ol (4): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (4.3mg, 0.009 mmol), DPPF (9.6 mg, 0.017 mmol), pyrrolidine (146 mg, 3.47 mmol), triethylamine hydrochloride (478 mg, 3.47 mmol) and **1** (125 mg, 0.865 mmol) followed by addition of THF (3 mL) and heating to reflux for 8 hours. The solvent was then removed *in vacuo* and the resulting mixture purified by flash chromatography (10% methanol in

acetone) to give **4** a white crystalline solid (119 mg, 80%). R_f= 0.14 on silica gel (10% methanol in acetone); mp 97-98° (Et_2O); IR (KBr, cm^{-1}) 3496 (br), 3035 (m), 2967 (s), 1454 (m), 1193 (s), 1117 (m), 1048 (s). ^1H NMR (400MHz, $CDCl_3$) δ 7.56 (1H, d, *J*= 7.1 Hz), 7.29-7.21 (2H, m), 7.08-7.06 (1H, m), 6.57 (1H, dd, *J*= 9.9, 2.4 Hz), 6.05 (1H, dd, *J*= 9.9, 2.4 Hz), 4.83 (1H, d, *J*= 11.3 Hz), 3.66 (1H, ddd, *J*= 11.3, 2.4, 2.4 Hz), 3.57 (1H, s), 2.81-2.79 (2H, m), 2.73-2.71 (2H, m), 1.84-1.80 (4H, m); ^{13}C NMR (400MHz, $CDCl_3$) δ 136.9, 131.8, 129.6, 127.7, 127.3, 126.1, 125.4, 124.7, 69.8, 63.3, 48.7, 23.8. HRMS calcd for $C_{14}H_{17}NO$ (M^+): 215.1310. Found: 215.1314.



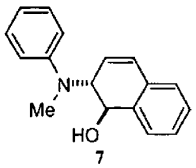
5

(1R*,2R*)-2-Piperidin-1-yl-1,2-dihydro-naphthalen-1-ol: To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (4.3 mg, 0.0087 mmol), DPPF (9.6 mg, 0.0173 mmol), piperidine hydrochloride (422 mg, 3.47 mmol), triethylamine (350 μL, 2.51 mmol) and **1** (100 mg, 0.69 mmol) were added followed by THF (3 mL) and heating to 80°C for 12 hours. The reaction mixture was then concentrated *in vacuo* and purified by flash chromatography (50% ethyl acetate, 48% hexanes, 2% methanol) to give **5** a white crystalline solid (130 mg, 82%). R_f= 0.24 on silica gel (50% ethyl acetate, 48% hexanes, 2% methanol); mp 62-64° (Et_2O); IR (KBr, cm^{-1}) 3482 (br), 3036 (w), 2937 (s), 2853 (m), 1453 (s), 1193 (s), 1109 (s), 1046 (s). ^1H NMR (400MHz, $CDCl_3$) δ 7.57 (1H, d, *J*= 7.1 Hz), 7.27-7.18 (2H, m), 7.05 (1H, dd, *J*= 6.9, 0.9 Hz), 6.49 (1H, dd, *J*= 9.9, 2.6 Hz), 6.12 (1H, dd, *J*= 9.9, 2.4 Hz), 4.87 (1H, d, *J*= 12.2 Hz), 3.58 (1H, s), 3.37 (1H, ddd, *J*= 12.2, 2.4, 2.4 Hz), 2.79-2.73 (2H, m), 2.48 (2H, m), 1.67-1.57 (4H, m), 1.56-1.46 (2H, m); ^{13}C NMR (400MHz, $CDCl_3$) δ 137.4, 131.8, 128.8, 127.1, 125.9, 125.2, 124.4, 68.2, 67.6, 50.4, 26.5, 24.6. HRMS calcd for $C_{15}H_{18}NO$ (M^+-H): 228.1388. Found: 228.1318.



6

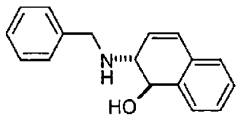
(1R,2R)-2-(3,4-Dihydro-2H-quinolin-1-yl)-1,2-dihydro-naphthalen-1-ol: To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (4.3 mg, 0.0087 mmol), (R)-(S)-BPPFA (9.6 mg, 0.0173 mmol), tetrahydroisoquinoline (231 mg, 1.735 mmol), **1** (60 mg, 0.416 mmol) and THF (2.5 mL) were added followed by heating to reflux for 3 hours. The solvent was then removed *in vacuo* and the resulting oil purified by flash chromatography (5% ethyl acetate in hexanes) to give **6** a colourless oil (114.1 mg, 98%). The ee was determined to be 65% using HPLC analysis on a CHIRALCEL OD column, λ= 254nm. Retention times in 10% isopropanol in hexanes were 10.3 min (major) and 11.2 min. R_f= 0.30 on silica gel (10% ethyl acetate:hexanes); $[\alpha]^{25}_D$= -30.0° (c= 13.8, $CHCl_3$); IR (KBr, cm^{-1}) 3588 (br), 3037 (w), 2932 (w), 1601 (s), 1495 (m), 1190 (m). ^1H NMR (400MHz, $CDCl_3$) δ 7.54-7.52 (1H, m), 7.31-7.29 (2H, m), 7.17-7.14 (1H, m), 7.10-7.09 (1H, m), 7.06-7.04 (1H, m), 6.94-6.93 (1H, m), 6.68-6-67 (1H, m), 6.65 (1H, dd, *J*= 9.4, 2.2 Hz), 5.96 (1H, dd, *J*= 9.9, 3.3 Hz), 5.13 (1H, d, *J*= 8.8 Hz), 4.78 (1H, ddd, *J*= 8.8, 2.5, 2.5 Hz), 3.31-3.26 (1H, m), 3.14-3.08 (1H, m), 2.81-2.80 (2H, m), 2.30 (1H, s), 1.95-1.89 (2H, m); ^{13}C NMR (400MHz, $CDCl_3$) δ 145.1, 136.5, 131.9, 129.7, 129.5, 128.0, 128.0, 128.0, 127.9, 127.0, 126.5, 125.9, 124.0, 116.8, 112.2, 69.5, 60.9, 44.1, 28.1, 22.5. HRMS calcd for $C_{19}H_{19}NO$ (M^+): 277.1467. Found: 277.1463.



7

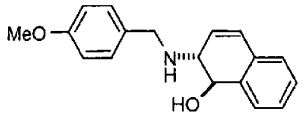
(1R,2R)-2-(Methyl-phenyl-amino)-1,2-dihydro-naphthalen-1-ol (7): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (3.5 mg, 0.007 mmol), (R)-(S)-BPPFA (7.7 mg, 0.014 mmol), N-methylaniline (372 mg, 3.47 mmol), **1** (105 mg, 0.728 mmol) and THF (3 mL) were added followed by heating to reflux for 3 hours. The solvent was then removed *in vacuo* and the resulting oil purified by flash chromatography (5% ethyl acetate in hexanes) to give **7** a white crystalline solid (176.3 mg, 96%). The ee was determined to be 74% using HPLC analysis on a CHIRALCEL OD column, λ= 254nm. Retention times in 10% isopropanol in hexanes were 11.1 min (major) and 13.3 min. R_f= 0.41 on silica gel (20% ethyl acetate:hexanes); mp 55-56° (Et_2O); $[\alpha]^{25}_D$= 50.4° (c= 11.8, $CHCl_3$); IR (KBr, cm^{-1}) 3594 (br), 3037 (m), 2884 (m), 1596 (s), 1503 (s), 1463 (m), 1186 (m), 935 (m). ^1H NMR (400MHz, $CDCl_3$) δ 7.57-7.55 (1H, m), 7.31-7.26 (4H, m), 7.15-7.13 (1H, m), 6.99-6.97 (2H, m), 6.84-6.81 (1H, m), 6.61 (1H, dd, *J*= 9.8, 2.6 Hz), 5.94 (1H, dd, *J*= 9.7, 2.9 Hz), 5.11 (1H, d, *J*= 9.8 Hz), 4.76 (1H, ddd, *J*= 9.7, 2.6, 2.6 Hz), 2.85

(3H, s), 2.50 (1H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 150.1, 136.4, 131.9, 129.6, 129.2, 128.0, 127.8, 127.7, 126.4, 125.5, 118.0, 114.5, 70.0, 63.3, 33.3. HRMS calcd for $C_{17}H_{17}NO$ (M^+): 251.1310. Found: 251.1307.



8

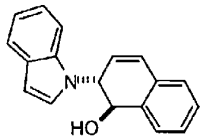
(1R*,2R*)-2-Benzylamino-1,2-dihydro-naphthalen-1-ol (8): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (4.3 mg, 0.009 mmol), DPPF (9.6 mg, 0.017 mmol), benzylamine hydrochloride (279 mg, 1.74 mmol), triethylamine (242 µL, 1.74 mmol) and 1 (50 mg, 0.347 mmol) followed by addition of THF (3 mL) and heating to reflux for 3 days. The solvent was then removed *in vacuo* and the resulting mixture purified by flash chromatography (50% ethyl acetate in hexanes) to give **8** a white crystalline solid (26.9 mg, 31%). R_f= 0.44 on silica gel (50% ethyl acetate, 48% hexanes, 2% methanol); mp 115-117° (dec) (Et_2O); IR (KBr, cm^{-1}) 3528 (br), 3030 (w), 2849 (w), 1455 (s), 1190 (m), 1112 (m), 1048 (m). ^{1}H NMR (400MHz, $CDCl_3$) δ 7.47-7.45 (1H, m), 7.29-7.24 (4H, m), 7.24-7.17 (3H, m), 7.02-7.01 (1H, m), 6.41 (1H, dd, *J*= 9.7, 2.0 Hz), 6.00 (1H, dd, *J*= 9.7, 2.5 Hz), 4.64 (1H, d, *J*= 9.0 Hz), 3.94 (1H, AB, *J*= 13.0 Hz), 3.75 (1H, AB, *J*= 13.0 Hz), 3.42 (1H, ddd, *J*= 11.0, 2.4, 2.4 Hz), 2.44 (1H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 139.8, 136.6, 132.1, 128.8, 128.5, 128.2, 127.9, 127.8, 127.6, 127.2, 126.1, 124.9, 72.1, 59.7, 50.7. HRMS calcd for $C_{17}H_{17}NO$ (M^+): 251.1310. Found: 251.1316.



9

(1R*,2R*)-2-(4-Methoxy-benzylamino)-1,2-dihydro-naphthalen-1-ol (9): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (4.3mg, 0.009 mmol), DPPF (9.6 mg, 0.017 mmol), p-methoxybenzylamine (238 mg, 1.74 mmol), triethylamine hydrochloride (239 mg, 1.74 mmol) and 1 (50 mg, 0.728 mmol) followed by addition of THF (3 mL) and heating to reflux for 3 days. The solvent was then removed *in vacuo* and the resulting mixture purified by flash chromatography (50% ethyl acetate in hexanes) to give 9 a white crystalline solid (43 mg, 44%).

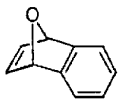
R_f= 0.27 on silica gel (50% ethyl acetate, 48% hexanes, 2% methanol); mp 96-98° (dec) (Et_2O); IR (KBr, cm^{-1}) 3528 (br), 3033 (w), 2835 (m), 1612 (m), 1512 (s), 1455 (m), 1248 (s), 1040 (m). ^1H NMR (400MHz, $CDCl_3$) δ 7.52-7.50 (1H, m), 7.26-7.22 (4H, m), 7.08-7.06 (1H, m), 6.85 (2H, d, *J*= 9.0 Hz), 6.47 (1H, dd, *J*= 9.7, 2.0 Hz), 6.05 (1H, dd, *J*= 9.9, 2.6 Hz), 4.68 (1H, d, *J*= 11.0 Hz), 3.95 (1H, d, *J*= 12.9 Hz), 3.79 (3H, s), 3.75 (1H, d, *J*= 2.9 Hz), 3.46 (1H, ddd, *J*= 11.0, 2.4, 2.4 Hz), 3.0-2.0 (2H, s (br)); ^{13}C NMR (400MHz, $CDCl_3$) δ 158.7, 136.7, 132.1, 131.9, 129.4, 128.9, 127.9, 127.7, 127.5, 126.0, 124.9, 113.9, 72.1, 59.6, 55.2, 50.1. HRMS calcd for $C_{18}H_{19}NO_2$ (M^+): 281.1416. Found: 281.1403.



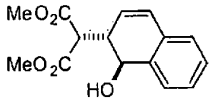
10

(1R,2R)-2-Indol-1-yl-1,2-dihydro-naphthalen-1-ol (10): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (4.3 mg, 0.009 mmol), (R)-(S)-BPPFA (9.6 mg, 0.017 mmol), indole (407 mg, 3.47 mmol) and **1** (100 mg, 0.69 mmol) were added. THF (4 mL) was then added, followed by heating to 80°C for 3 days. The reaction mixture was then concentrated *in vacuo*. The resulting oil was purified by flash chromatography (30% ethyl acetate in hexanes) to give **10** a colourless oil (147 mg, 81%). The ee was determined to be 79% using HPLC analysis on a CHIRALCEL OD column, λ= 254nm. Retention times in 10% isopropanol in hexanes were 28.5 min (major) and 30.1 min. R_f= 0.26 on silica gel (30% ethyl acetate:hexanes); $[\alpha]^{25}_D$= -46.7° (c= 11.3, $CHCl_3$); IR (KBr, cm^{-1}) 3485 (br), 3059 (m), 1592 (m), 1455 (s), 1414 (s), 1245 (m), 1091 (m), 908 (m); ^1H NMR (400MHz, $CDCl_3$) δ 8.13 (1H, s), 7.79 (1H, d, *J*= 7.8 Hz), 7.42 (1H, d, *J*= 7.3 Hz), 7.34-7.19 (6H, m), 6.85 (1H, d, *J*= 2.2 Hz), 6.69 (1H, dd, *J*= 9.5, 2.0 Hz), 6.20 (1H, dd, *J*= 9.5, 3.8 Hz), 5.06 (1H, d, *J*= 7.9 Hz), 4.12-4.08 (1H, m), 2.35 (1H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 136.5, 135.9, 132.5, 130.1, 128.0, 127.7, 126.9, 126.5, 126.4, 126.2, 122.6, 122.0, 119.3, 119.2, 113.9, 111.4, 72.7, 41.0. HRMS calcd for $C_{18}H_{15}NO$ (M^+): 261.1154. Found: 261.1141.

Example 6: Compounds Formed In Reactions Involving Carbon Nucleophiles



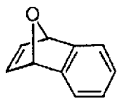
1



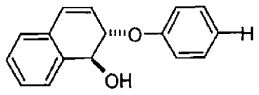
2

(1S*,2R*)-2-(Hydroxy-1,2-dihydro-naphthalen-2-yl)malonic acid dimethyl ester (2): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (8.6 mg, 0.0174 mmol), DPPF (19.2 mg, 0.0347 mmol), dimethyl malonate (137 mg, 1.041 mmol) and **1** (100 mg, 0.694 mmol) were added followed by addition of THF (1.5 mL) and heating to 80°C for 24 hours. The reaction mixture was then poured in to water and extracted three times with ethyl acetate. The organic layers were combined, washed with brine dried over Na_2SO_4, and concentrated *in vacuo*. The resulting oil was purified by flash chromatography (20% ethyl acetate in hexanes then increasing to 50% ethyl acetate in hexanes) to give **2** a colourless oil which crystallized on sitting (124.3 mg, 65%). R_f= 0.27 on silica gel (50% ethyl acetate:hexanes); mp 65-67° (Et_2O); IR (neat, cm^{-1}) 3490 (br), 3024 (m), 2954 (s), 1744 (s), 1436 (s), 1159 (s), 1026 (s), 913 (m), 783 (s); ^1H NMR (400MHz, $CDCl_3$) δ 7.40-7.38 (1H, m), 7.30-7.24 (2H, m), 7.13-7.11 (1H, m), 6.57 (1H, dd, *J*= 9.7, 1.5 Hz), 5.97 (1H, dd, *J*= 9.7, 4.2 Hz), 4.70 (1H, dd, *J*= 6.2, 6.2 Hz), 3.73 (3H, s), 3.70 (3H, s), 3.52 (1H, d, *J*= 7.6 Hz), 3.37-3.35 (1H, m), 2.09 (1H, d, *J*= 6.2 Hz); ^{13}C NMR (400MHz, $CDCl_3$) δ 168.6, 168.3, 135.4, 131.9, 128.3, 128.1, 126.8, 126.7, 70.3, 52.6, 52.6, 52.5, 42.3. HRMS calcd for $C_{15}H_{16}O_5$ (M^+): 276.0998. Found: 276.0104.

Example 7: Compounds Formed In Reactions Involving Phenol Nucleophiles



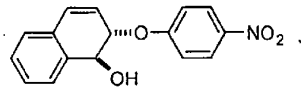
1



2

(1S,2S)-2-Phenoxy-1,2-dihydro-naphthalen-1-ol (2): To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (1.7 mg, 0.0035 mmol), (S)-(R)- PPF-P^{t}Bu$_2$ (3.8 mg, 0.0069 mmol, and **1** (100 mg, 0.694 mmol) were added. THF (2 mL) and phenol (327 mg, 3.47 mmol) were then added followed by heating to 80°C for 1.5 hours. The reaction mixture was then poured in to

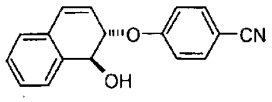
ether and washed three times with 5% aqueous Noah. The aqueous layers were combined and back extracted three times with ether. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The resulting solid was purified by flash chromatography (20% ethyl acetate in hexanes) to give **2** as a white crystalline solid (130.7 mg, 83%). The ee was determined to be 99.2% using HPLC analysis on a CHIRALCEL OD column, λ= 486 nm. Retention times in 4% isopropanol in hexanes were 15.2 min (major) and 17.8 min. F_r = 0.26 on silica gel (10% ethyl acetate:hexanes); mp 109-110°C (Et_2O); $[\alpha]^{25}_D$= +204.7° (c= 10.1, $CHCl_3$); IR (KBr, cm^{-1}) 3337 (br), 3029 (w), 2866 (w), 1600 (m), 1496 (s), 1249 (s), 1062 (s); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.63 (1H, m), 7.33-7.25 (4H, m), 7.13-7.11 (1H, m), 7.01-6.95 (3H, m), 6.51 (1H, dd, *J*= 9.9, 1.6 Hz), 6.02 (1H, dd, *J*= 9.9, 2.2 Hz), 5.19 (1H, d, *J*= 10.4 Hz), 5.11 (1H, ddd, *J*= 10.4, 2.0, 2.0 Hz), 2.66 (1H, s); ^{13}C NMR (400 MHz, $CDCl_3$) δ 157.4, 135.5, 131.9, 129.7, 129.0, 128.2, 128.0, 126.4, 126.1, 125.2, 121.5, 115.9, 79.1, 72.4. HRMS calcd for $C_{16}H_{14}O_2$ (M^+): 238.0994. Found: 238.0984.



3

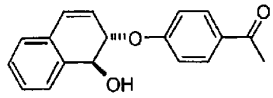
(1S,2S)-2-(4-nitrophenoxy)-1,2,-dihydro-naphthalen-1-ol (3): To a flame dried round-bottomed flask, $[Rh(COD)Cl]_2$ (1.7 mg, 0.0035 mmol), (S)-(R)-PPF-P^{t}Bu$_2$ (3.8 mg, 0.0069 mmol) and **1** (100 mg, 0.694 mmol) were added followed by addition of THF (2.5 mL) and 4-nitrophenol (483 mg, 3.47 mmol). The mixture was heated at 80°C for 45 minutes, then poured into diethyl ether and extracted 3 times with 10% aqueous sodium hydroxide solution. The aqueous extracts were combined and back-extracted three times with diethyl ether. The combined ether extracts were washed with brine and dried with anhydrous sodium sulfate. The solvents were removed *in vacuo*, yielding a solid which was purified by flash chromatography on silica gel (30% ethyl acetate in hexanes) giving a white crystalline solid **3** (184 mg, 94%). The ee was determined to be 97% by formation of Mosher's ester. F_r = 0.43 on silica (30% ethyl acetate:hexanes); mp 123-125°C (dec.); $[\alpha]^{25}_D$ = +169.9° (c = 10.3, $CHCl_3$); IR (KBr, cm^{-1}) 3351 (br), 3113 (w), 3071 (w), 2884 (w), 2843 (w), 1591 (s), 1503 (s), 1342 (s), 1295 (m), 1110 (m), 896 (w); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (2H, d, *J*=9.2 Hz), 7.62-7.60 (1H, m), 7.31-7.29 (2H, m), 7.15-7.13 (1H, m), 6.99 (2H, d, *J*= 9.2 Hz), 6.57 (1H, d, *J*= 9.9 Hz), 5.94 (1H, d, *J*= 9.9 Hz), 5.20 (2H, s), 2.61

(1H, s); ^{13}C NMR (400 MHz, $CDCl_3$): δ 162.6, 141.8, 135.0, 131.5, 130.2, 128.5, 128.4, 126.8, 126.0, 125.5, 124.1, 115.4, 79.6, 72.0.



4

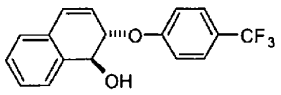
(1S,2S)-2-(4-Cyanophenoxy)-1,2,-dihydro-naphthalen-1-ol (4): To a flame dried round-bottomed flask, $[Rh(COD)Cl]_2$ (1.7 mg, 0.0035 mmol), (S)-(R)- PPF-P^{t}Bu$_2$ (3.8 mg, 0.0069 mmol) and 1 (100 mg, 0.694 mmol) were added followed by addition of THF (2.5 mL) and 4-cyanophenol (413 mg, 3.47 mmol). The mixture was heated at 80°C for 5 hours, then poured into diethyl ether and extracted 3 times with 10% aqueous sodium hydroxide solution. The aqueous extracts were combined and back-extracted three times with diethyl ether. The combined ether extracts were washed with brine and dried with anhydrous sodium sulfate. The solvents were removed *in vacuo*, yielding a solid which was purified by flash chromatography on silica gel (30% ethyl acetate in hexanes) giving a white crystalline solid **4** (160 mg, 88%). The ee was determined to be 97% by HPLC analysis on a CHIRALCEL OD column, λ= 256 nm. Retention times in 3% isopropanol in hexanes were 35.3 min and 37.7 min (major). F_r = 0.40 on silica (30% ethyl acetate in hexanes); mp 140-141°C (Et_2O); $[\alpha]^{25}_D$ = +182.3° (c = 11.2, $CHCl_3$) IR (KBr, cm^{-1}) 3303 (b) 3050 (w) 2210 (m) 1598 (s) 1503 (s) 1238 (s) 1025 (m) 859 (m) 778 (m); ^1H NMR (400 MHz, $CDCl_3$): δ 7.62-7.57 (3H, m), 7.33-7.27 (3H, m), 7.14-7.12 (1H, m), 6.56 (1H, dd, *J*= 1.4, 9.7 Hz), 5.93 (1H, dd, *J*= 1.4, 9.7 Hz), 5.20-5.13 (2H, m), 2.25 (1H, s). ^{13}C NMR (400 MHz, $CDCl_3$): δ 160.8, 135.0, 134.2, 131.5, 130.0, 128.5, 128.3, 126.7, 125.4, 124.4, 119.0, 116.2, 104.6, 79.2, 72.0. HRMS calcd for $(M-H_2O)^+$ ($C_{17}H_{11}ON$): 245.0841. Found: 245.0845.



5

(1S,2S)-2-(4-acylphenoxy)-1,2,-dihydro-naphthalen-1-ol (5): To a flame dried round-bottomed flask, $[Rh(COD)Cl]_2$ (1.7 mg, 0.0035 mmol), (S)-(R)- PPF-P^{t}Bu$_2$ (3.8 mg, 0.0069 mmol) and 1 (100 mg, 0.694 mmol) were added followed by addition of THF (2.5 mL) and 4-

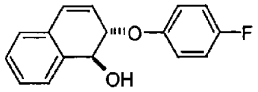
hydroxyacetophenone (472 mg, 3.47 mmol). The mixture was heated at 80° C for 2.5 hours, then poured into diethyl ether and extracted 3 times with 10% aqueous sodium hydroxide solution. The aqueous extracts were combined and back-extracted three times with diethyl ether. The combined ether extracts were washed with brine and dried with anhydrous sodium sulfate. The solvents were removed *in vacuo*, yielding a solid which was purified by flash chromatography on silica gel (30% ethyl acetate in hexanes) giving a white crystalline solid **5** (177 mg, 91%). The ee was determined to be > 99% by formation of Mosher's ester; R_f = 0.28 on silica (30% ethyl acetate in hexanes); mp 124-126°C (Et_2O); $[\alpha]^{25}_D$ = +153° (c = 9.8, $CHCl_3$). IR (KBr, cm^{-1}) 3367 (b), 3069 (w), 2916 (w), 1668 (s), 1601 (s), 1265 (s), 1053 (m), 835 (m), 779 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (2H, d, *J*=8.8 Hz), 7.66-7.64 (1H, m), 7.34-7.27 (2H, m), 7.16-7.14 (1H, m), 6.98 (2H, d, *J*= 8.8 Hz), 6.57 (1H, d, *J*= 9.9 Hz), 5.99 (1H, d, *J*= 9.9 Hz), 5.21 (2H, s), 2.85 (1H, s), 2.56 (3H, s); ^{13}C NMR (400 MHz, $CDCl_3$): δ 196.8, 161.4, 135.3, 131.7, 130.7, 130.6, 129.6, 128.3, 128.1, 126.6, 125.4, 125.0, 115.2, 79.0, 72.0, 26.3. HRMS calcd for $(M-H_2O)^+$ ($C_{18}H_{14}O_2$): 262.0994. Found: 262.0989.



6

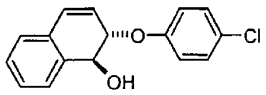
(1S,2S)- 2-(4-Trifluoromethylphenoxy)-1,2,-dihydro-naphthalen-1-ol (6): To a flame dried round-bottomed flask, $[Rh(COD)Cl]_2$ (1.7 mg, 0.0035 mmol), (S)-(R)- PPF-P^{t}Bu$_2$ (3.8 mg, 0.0069 mmol) and **1** (100 mg, 0.694 mmol) were added followed by addition of THF (2.5 mL) and4-trifluoromethylphenyl (563 mg, 3.47 mmol). The mixture was heated at 80° C for 8 hours, then poured into diethyl ether and extracted 3 times with 10% aqueous sodium hydroxide solution. The aqueous extracts were combined and back-extracted three times with diethyl ether. The combined ether extracts were washed with brine and dried with anhydrous sodium sulfate. The solvents were removed *in vacuo*, yielding a solid which was purified by flash chromatography on silica gel (10% ethyl acetate in hexanes) to give a white crystalline solid **6** (184 mg, 87%). The ee was determined to be 95% by HPLC analysis on a CHIRALCEL OD column, λ= 486 nm. Retention times in 4% isopropanol in hexanes were 14.8 min and 17.3 min (major). R_f = 0.46 on silica (20% ethyl acetate in hexanes); mp 118-119°C (Et_2O); $[\alpha]^{25}_D$ = +178° (c = 9.6, $CHCl_3$). IR (KBr, cm^{-1}) 3360 (br), 3061 (w), 2874 (w), 1617 (m), 1518 (m), 1326 (s), 1103 (s), 1051 (m), 839 (m), 782 (m), 745 (w); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63-7.54 (1H,

m), 7.55 (2H, d, J= 8.6 Hz), 7.33-7.24 (2H, m), 7.14-7.12 (1H, m), 7.01 (2H, d, J= 8.6 Hz), 6.55 (1H, dd, J= 1.6, 9.9 Hz), 5.97 (1H, dd, J= 2.0, 9.9 Hz), 5.21-5.13 (2H, m), 2.47 (1H, d, J= 3.6 Hz); ^{13}C NMR (400 MHz, $CDCl_3$): δ 159.9, 135.2, 131.7, 129.6, 128.4, 128.2, 127.1 (q, J^{C-F}= 3.6 Hz), 126.6, 125.4, 124.9, 123.4 (d, J^{C-F}= 33.0 Hz), 122.9 (d, J^{C-F}= 271.6 Hz), 115.6, 79.1, 72.1; HRMS calcd for (M^+) ($C_{17}H_{13}O_2F_3$): 306.0868. Found: 306.0852.



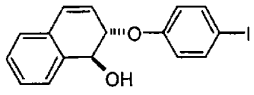
7

(1S,2S)-2-(4-Fluorophenoxy)-1,2,-dihydro-naphthalen-1-ol (7): To a flame dried round-bottomed flask, $[Rh(COD)Cl]_2$ (1.7 mg, 0.0035 mmol), (S)-(R)- PPF-P^{t}Bu$_2$ (3.8 mg, 0.0069 mmol) and **1** (100 mg, 0.694 mmol) were added followed by addition of THF (2.5 mL) and 4-fluorophenol (389 mg, 3.47 mmol). The mixture was heated at 80°C for 5 hours, then poured into diethyl ether and extracted 3 times with 10% aqueous sodium hydroxide solution. The aqueous extracts were combined and back-extracted three times with diethyl ether. The combined ether extracts were washed with brine and dried with anhydrous sodium sulfate. The solvents were removed *in vacuo*, yielding a solid which was purified by flash chromatography on silica gel (10% ethyl acetate in hexanes) giving a white crystalline solid **7** (163 mg, 92%). The ee was determined to be 97% by HPLC analysis on a CHIRALCEL OD column, λ= 486 nm). Retention times in 1.5% isopropanol in hexanes were 28.1 min (major) and 29.5 min. R_f = 0.39 on silica (20% ethyl acetate in hexanes); mp 127-129°C (Et_2O); $[\alpha]^{25}_D$ = +216° (c = 9.5, $CHCl_3$). IR (KBr, cm^{-1}) 3309 (b), 3071 (w), 2864 (w), 1504 (s), 1284 (m), 1052 (s), 781 (s), 692 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63-7.61 (1H, m), 7.31-7.26 (2H, m), 7.12-7.10 (1H, m), 7.00-6.95 (2H, m), 6.92-6.88 (2H, m), 6.51 (1H, dd, J= 2.1, 9.9 Hz), 5.98 (1H, dd, J= 2.2, 9.9 Hz), 5.15 (1H, dd, J= 3.6, 10.0 Hz), 5.01 (1H, ddd, J= 2.1, 2.1, 10.1 Hz), 2.54 (1H, d, J= 3.8 Hz); ^{13}C NMR (400 MHz, $CDCl_3$): δ 157.6 (d, J^{C-F}= 239 Hz), 156.4, 153.4, 135.4, 131.8, 129.1, 128.2, 126.5, 125.7, 125.2, 117.5 (d, J^{C-F}= 8 Hz), 116.1 (d, J^{C-F}= 23.5 Hz);. HRMS calcd for (M^+) ($C_{16}H_{13}O_2F$): 256.0810. Found: 256.0911.



8

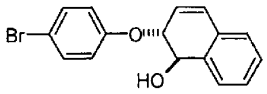
(1S,2S)-2-(4-Chlorophenoxy)-1,2,-dihydro-naphthalen-1-ol (8): To a flame dried round-bottomed flask, $[Rh(COD)Cl]_2$ (1.7 mg, 0.0035 mmol), (S)-(R)- PPF-P^{t}Bu$_2$ (3.8 mg, 0.0069 mmol) and **1** (100 mg, 0.694 mmol) were added followed by addition of THF (2.5 mL) and 4-chlorophenol (446 mg, 3.47 mmol). The mixture was heated at 80°C for 6 hours, then poured into diethyl ether and extracted 3 times with 10% aqueous sodium hydroxide solution. The aqueous extracts were combined and back-extracted three times with diethyl ether. The combined ether extracts were washed with brine and dried with anhydrous sodium sulfate. The solvents were removed *in vacuo*, yielding a solid which was purified by flash chromatography on silica gel (5% ethyl acetate in hexanes) giving a white crystalline solid **8** (169 mg, 89%). The ee was determined to be 92% by formation of Mosher's ester. R_f = 0.47 on silica (20% ethyl acetate in hexanes); mp 125-125.5°C (Et_2O); $[\alpha]^{25}_D$ = +150° (c = 10.6, $CHCl_3$). IR (KBr, cm^{-1}) 3302 (br), 3064 (w), 2874 (w), 1590 (m), 1489 (s), 1362 (w), 1230 (s), 1052 (m), 890 (w), 846 (m), 778 (s), 663 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65-7.64 (1H, m), 7.33-7.26 (4H, m), 7.16-7.13 (1H, m), 6.91(1H, ddd, *J*= 2.0, 2.0, 8.9 Hz), 6.55 (1H, dd, *J*= 1.8, 9.9 Hz), 5.99 (1H, dd, *J*= 2.2, 9.9 Hz), 5.19 (1H, dd, *J*= 3.8, 10.0 Hz), 5.07 (1H, ddd, *J*= 2.0, 2.0, 10.1 Hz), 2.56 (1H, d, *J*= 4.0 Hz); ^{13}C NMR (400 MHz, $CDCl_3$): δ 155.8, 135.2, 131.7, 129.5, 129.3, 128.2, 128.1, 126.5, 126.2, 125.3, 125.2, 116.9, 79.2, 72.1. HRMS calcd for $(M-H_2O)^+$ ($C_{16}H_{11}OCl$): 254.0498. Found: 254.0499.



9

(1S,2S)-2-(4-Iodophenoxy)-1,2,-dihydro-naphthalen-1-ol (9): To a flame dried round-bottomed flask, $[Rh(COD)Cl]_2$ (1.7 mg, 0.0035 mmol), (S)-(R)- PPF-P^{t}Bu$_2$ (3.8 mg, 0.0069 mmol) and **1** (100 mg, 0.694 mmol) were added followed by addition of THF (2.5 mL) and 4-iodophenol (763 mg, 3.47 mmol). The mixture was heated at 80°C for 12 hours, then poured into diethyl ether and extracted 3 times with 10% aqueous sodium hydroxide solution. The aqueous extracts were combined and back-extracted three times with diethyl ether. The combined ether extracts were washed with brine and dried with anhydrous sodium sulfate. The solvents were removed *in vacuo*, yielding a solid which was purified by flash chromatography on silica gel (10% ethyl acetate in hexanes) as a white crystalline solid **9** (193 mg, 73%). The ee was determined by deiodinating **9** (40 mg, 0.11 mmol) by reaction with t-BuLi (0.32 mL, 1.7M) in diethyl ether (2 mL) at -78°C followed by quenching with isopropanol. Extraction with ether from

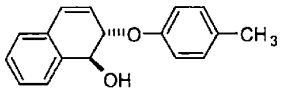
water, washing with brine, drying over anhydrous sodium sulfate and removal of the solvents *in vacuo* gave a white crystalline solid (24 mg, 92%). The ee was determined to be 98% by HPLC analysis on a CHIRALCEL OD column, λ= 256 nm. Retention times in 4% isopropanol in hexanes were 15.2 min (major) and 17.9 min; R_f = 0.44 on silica (20% ethyl acetate in hexanes); mp 160-162°C (Et_2O); $[\alpha]^{25}_D$ = +107° (c = 9.7, $CHCl_3$). IR (KBr, cm^{-1}) 3264 (br), 3050 (w), 2926 (w), 2843 (w), 1581 (m), 1485 (s), 1388 (w), 1279 (m), 1246 (s), 1046 (m), 824 (m), 780 (m), 571 (w); ^1H NMR (400 MHz, $CDCl_3$): δ 7.63-7.61 (1H, m), 7.58-7.55 (2H, m), 7.30-7.27 (2H, m), 7.13-7.11 (1H, m), 6.73 (2H, ddd, *J*= 2.2, 2.2, 9.0 Hz), 6.52 (1H, dd, *J*= 1.8, 9.8 Hz), 5.96 (1H,dd, *J*= 2.2, 9.8 Hz), 5.16 (1H, d, *J*= 10.0 Hz), 5.05 (1H, ddd, *J*= 2.0, 2.0, 10.0 Hz), 2.54 (1H, s); ^{13}C NMR (400 MHz, $CDCl_3$): δ 157.3, 138.5, 135.3, 131.7, 129.4, 128.3, 128.1, 126.6, 125.3, 125.3, 118.1, 83.6, 79.2, 72.2. HRMS calcd for $(M-H_2O)^+$ ($C_{16}H_{11}OI$): 345.9855. Found: 345.9849.



10

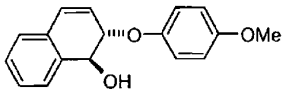
(1R,2R)-2-(4-Bromo-phenoxy)-1,2-dihydro-naphthalen-1-ol: To a flame dried round bottom flask, $[Rh(COD)Cl]_2$ (2.1 mg, 0.0043 mmol), (R)-(S)- PPF-P^{t}Bu$_2$ (4.6 mg, 0.0085 mmol, and **1** (122 mg, 0.85 mmol) were added.). THF (2 mL) and p-bromophenol (734 mg, 4.245 mmol) were then added followed by heating to 80°C for 1.5 hours. The reaction mixture was then poured in to ether and washed three times with 5% aqueous NaOH. The aqueous layers were combined and back extracted three times with ether. The organic layers were combined, washed with brine, dried over Na_2SO_4, and concentrated *in vacuo*. The resulting solid was purified by flash chromatography (20% ethyl acetate in hexanes) to give **10** a white crystalline solid (239.7 mg, 90%). The ee was determined by debrominating **10** (44 mg, 0.139 mmol) by reaction with t-BuLi (0.2 mL, 1.7M) in ether (2mL) at -78°C followed by quenching with isopropanol. Extraction with ether from water, washing with brine, drying over Na_2SO_4 and concentration gave a white crystalline solid **2** (31.5 mg, 95%). The ee was determined to be 96.8% by HPLC analysis on a CHIRALCEL OD column, λ= 486nm. Retention times in 4% isopropanol in hexanes were 15.2 min and 17.5 min (major). R_f= 0.26 on silica gel (10% ethyl acetate:hexanes); mp 145-146° (Et_2O); $[\alpha]^{25}_D$= -135.7° (c= 10.2, $CHCl_3$); IR (KBr, cm^{-1}) 3290 (br), 3060 (m), 2870 (w), 1583 (m), 1484 (s), 1227 (s), 1052 (m), 980 (s), 776 (s); ^1H NMR (400MHz, $CDCl_3$) δ 7.70-7.65 (1H,

m), 7.44-7.42 (2H, m), 7.35-7.32 (2H, m), 7.18-7.16 (1H, m), 6.88-6.86 (2H, m), 6.56 (1H, dd, *J*= 10.0, 2.0 Hz), 6.00 (1H, dd, *J*= 9.7, 2.2 Hz), 5.20 (1H, dd, *J*= 9.7, 3.6 Hz), 5.09 (1H, ddd, *J*= 10.0, 2.0, 2.0 Hz), 2.70 (1H, d, *J*= 3.9 Hz); ^{13}C NMR (400MHz, $CDCl_3$) δ 156.5, 135.3, 132.5, 131.7, 129.3, 128.3, 128.1, 126.5, 125.3, 117.6, 113.7, 79.4, 72.2. HRMS calcd for $C_{16}H_{11}OBr$ $(M-H_2O)^+$ 297.9994. Found: 297.9995.



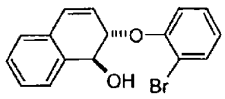
11

(1S,2S)-2-(4-Methylphenoxy)-1,2,-dihydro-naphthalen-1-ol (11): To a flame dried round-bottomed flask, $[Rh(COD)Cl]_2$ (1.7 mg, 0.0035 mmol), (S)-(R)- PPF-P^{t}Bu$_2$ (3.8 mg, 0.0069 mmol) and **1** (50 mg, 0.347 mmol) were added followed by addition of THF (2.5 mL) and p-cresol (188 mg, 1.74 mmol). The mixture was heated at 80°C for 24 hours, then poured into diethyl ether and extracted 3 times with 10% aqueous sodium hydroxide solution. The aqueous extracts were combined and back-extracted three times with diethyl ether. The combined ether extracts were washed with brine and dried with anhydrous sodium sulfate. The solvents were removed *in vacuo*, yielding a solid which was purified by flash chromatography on silica gel (5% ethyl acetate in hexanes) giving a white crystalline solid **11** (57 mg, 65%). The ee was determined to be 91% by HPLC analysis on a CHIRALCEL OD column, λ=256 nm. Retention times in 1% isopropanol in hexanes were 33.8 min (major) and 37.1 min. R_f = 0.49 on silica (20% ethyl acetate in hexanes); mp 80-81°C (Et_2O); $[\alpha]^{25}_D$ = +145° (c = 12.1, $CHCl_3$). IR (KBr, cm^{-1}) 3303 (br), 3050 (w), 2210 (m), 1598 (s), 1503 (s), 1238 (s), 1025 (m), 859 (m), 778 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67-7.65 (1H, m), 7.33-7.28 (2H, m), 7.14-7.11 (3H, m), 6.88 (2H, d, *J*= 8.4 Hz), 6.51 (1H, dd, *J*= 1.8, 9.9 Hz), 6.04 (1H, dd, *J*= 2.0, 9.9 Hz), 5.20 (1H, dd, *J*= 1.6, 10.2 Hz), 5.09 (1H, ddd, *J*= 1.8, 1.8, 10.2 Hz), 2.87 (1H, d, *J*= 2.7 Hz), 2.33 (3H, s). ^{13}C NMR (400 MHz, $CDCl_3$): δ 155.0, 135.4, 131.8, 130.7, 130.1, 128.8, 128.1, 127.9, 126.4, 126.2, 125.1, 115.6, 79.0, 72.3, 20.5. HRMS calcd for (M^+) $(C_{17}H_{16}O_2)$: 252.1150. Found: 252.1140.



12

(1S,2S)-2-(4-Methoxyphenoxy)-1,2,-dihydro-naphthalen-1-ol (12): To a flame dried round-bottomed flask, $[Rh(COD)Cl]_2$ (1.7 mg, 0.0035 mmol), (S)-(R)- PPF-P^{t}Bu$_2$ (3.8 mg, 0.0069 mmol) and **1** (100 mg, 0.694 mmol) were added followed by addition of THF (2.5 mL) and 4-methoxyphenol (431 mg, 3.47 mmol). The mixture was heated at 80°C for 6 hours, then poured into diethyl ether and extracted 3 times with 10% aqueous sodium hydroxide solution. The aqueous extracts were combined and back-extracted three times with diethyl ether. The combined ether extracts were washed with brine and dried with anhydrous sodium sulfate. The solvents were removed *in vacuo*, yielding a solid which was purified by flash chromatography on silica gel (10% ethyl acetate in hexanes) as a white crystalline solid **12** (159 mg, 85%). The ee was determined to be 95% by HPLC analysis on a CHIRALCEL OD column, λ= 256 nm. Retention times in 4% isopropanol in hexanes were 22.1 min (major) and 25.9 min. R_f = 0.33 on silica (20% ethyl acetate in hexanes); mp 91-92°C (Et_2O); $[\alpha]^{25}_D$ = +129° (c = 9.9, $CHCl_3$); IR (KBr, cm^{-1}) 3349 (br), 3050 (w), 2822 (w), 1508 (s), 1233 (s), 1046 (m), 825 (m), 751 (m), 695 (w); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66-7.64 (1H, m), 7.30-7.27 (2H, m), 7.12-7.10 (1H, m), 6.91 (2H, ddd, *J*= 2.3, 2.3, 9.1 Hz), 6.84 (2H, ddd, *J*= 2.4, 2.4, 9.2 Hz), 6.49 (1H, dd, *J*= 2.0, 9.9 Hz), 6.02 (1H, dd, *J*= 2.4, 9.9 Hz), 5.17 (1H, dd, *J*= 3.3, 10.1 Hz), 5.02 (1H, ddd, *J*= 2.0, 2.0, 10.3 Hz), 3.77 (3H, s), 3.12 (1H, d, *J*= 3.4 Hz). ^{13}C NMR (400 MHz, $CDCl_3$): δ 154.3, 151.2,135.5, 131.9, 128.7, 128.1, 127.9, 126.4, 126.3, 125.2, 117.2, 114.8, 80.0, 72.4, 55.7. HRMS calcd for (M^+) ($C_{17}H_{14}O_2$): 250.0994. Found: 250.1006.



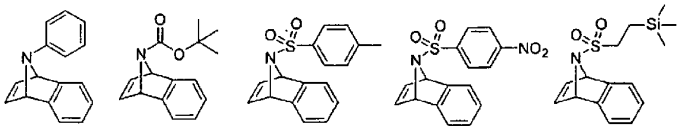
13

(1S,2S)-2-(2-Bromophenoxy)-1,2,-dihydro-naphthalen-1-ol (13): To a flame dried round-bottomed flask, $[Rh(COD)Cl]_2$ (1.7 mg, 0.0035 mmol), (S)-(R)- PPF-P^{t}Bu$_2$ (3.8 mg, 0.0069 mmol) and **1** (100 mg, 0.694 mmol) were added followed by addition of THF (2.5 mL) and 2-bromophenol (0.40 mL, 3.47 mmol). The mixture was heated at 80°C for 24 hours, then poured into diethyl ether and extracted 3 times with 10% aqueous sodium hydroxide solution. The aqueous extracts were combined and back-extracted three times with diethyl ether. The combined ether extracts were washed with brine and dried with anhydrous sodium sulfate. The solvents were removed *in vacuo*, yielding a solid which was purified by flash chromatography on silica

gel (5% ethyl acetate in hexanes) as a white crystalline solid **13** (75 mg, 37%). The ee was determined to be 81% by HPLC analysis on a CHIRALCEL OD column, λ= 486 nm. Retention times in 1.5% isopropanol in hexanes were 22.8 min and 32.1 min (major). R_f = 0.44 on silica (20% ethyl acetate in hexanes); mp 120-122°C (Et_2O); $[\alpha]^{25}_D$ = +254° (c = 9.2, $CHCl_3$). IR (KBr, cm^{-1}) 3341 (br), 3071 (w), 2884 (w), 1581 (m), 1472 (s), 1358 (m), 1237 (s), 1028 (s), 987 (s), 780 (s), 689 (m), 569 (m); ^1H NMR (400 MHz, $CDCl_3$): δ 7.67 (1H, d *J*= 6.8 Hz), 7.58 (1H, dd, *J*= 1.5, 7.9 Hz), 7.33-7.23 (3H, m), 7.14-7.12 (1H, m), 6.95(1H, dd, *J*= 1.1, 8.2 Hz), 6.92-6.87 (1H, m), 6.52 (1H, dd, *J*= 2.0, 9.9 Hz), 6.06 (1H, dd, *J*= 1.8, 9.9 Hz), 5.32 (1H, d, *J*= 11.0 Hz), 5.10 (1H, ddd, *J*= 2.0, 2.0, 11.0 Hz), 2.85 (1H, d, *J*= 3.2 Hz). ^{13}C NMR (400 MHz, $CDCl_3$): δ 154.3, 135.4, 133.6, 131.8, 129.1, 128.6, 128.3, 128.0, 126.4, 126.0, 124.9, 122.9, 115.6, 113.5, 82.2, 72.5. HRMS calculated for $(M-H_2O)^+$ ($C_{16}H_{11}OBr$): 297.9993. Found: 297.9976.

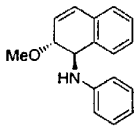
II. Compounds Made Using Azabicyclics

Example 8: Azabicyclic Starting Materials:



1 **2** **3** **4** **5**

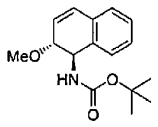
Example 9: Compounds Formed in Reactions Involving Alcohols



6

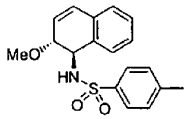
To a round bottomed flask was added **1** (44 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (1 ml) and MeOH (1 ml) were then added and the solution heated to reflux for 6 hours. The reaction mixture was then concentrated and chromatographed to give **6** (28 mg, 56%) a colourless oil. ^1H NMR (400MHz, $CDCl_3$) δ 7.35

(1H, d, *J*= 7.2Hz), 7.28-7.13 (4H, m), 6.76-6.68 (4H, m), 6.64 (1H, d, *J*= 9.9Hz), 6.11 (1H, dd, *J*= 4.0, 9.7Hz), 5.73 (1H, d, *J*= 6.0Hz), 4.21 (1H, dd, *J*= 4.3, 4.3Hz), 3.82 (1H, s), 3.42 (3H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 147.1, 135.2, 132.0, 129.9, 129.4, 129.3, 128.4, 128.3, 128.1, 127.0, 126.5, 126.5, 75.8, 56.1, 55.8. HRMS calcd for $C_{17}H_{17}NO$ (M^+): 251.1310. Found: 251.1315.



7

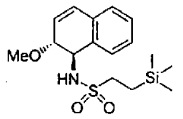
To a round bottomed flask was added **2** (49 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (1 ml) and MeOH (1 ml) were then added and the solution heated to reflux for 48 hours. The reaction mixture was then concentrated and chromatographed (10% ethyl acetate:hexanes) to give **7** (41 mg, 74%) a white solid. The regiochemistry and relative stereochemistry was proven by X-ray crystal diffraction. R_f= 0.25 on silica gel (10% ethyl acetate:hexanes); ^{1}H NMR (400MHz, $CDCl_3$) δ 7.35-7.34 (1H, m), 7.25-7.20 (2H, m), 7.10-7.08 (1H, m), 6.58 (2H, d, *J*= 9.7Hz), 6.07 (1H, dd, *J*= 4.3, 9.7Hz), 4.98 (1H, dd, *J*= 5.5, 8.0Hz), 4.61 (1H, d, *J*= 7.7Hz), 4.00 (1H, dd, *J*= 4.6, 4.6Hz), 3.45 (3H, s), 1.44 (9H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 155.3, 134.1, 131.9, 130.0, 130.0, 128.3, 128.3, 127.0, 125.9, 79.6, 56.3, 51.3, 28.4. HRMS calcd for $C_{16}H_{21}NO_3$ (M^+): 275.1521. Found: 275.1518.



8

To a round bottomed flask was added **3** (60 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (1 ml) and MeOH (1 ml) were then added and the solution heated to reflux for 9 hours (Note: **3** and **8** nearly co-spot by TLC but **8** stains red with permanganate whereas **3** stains white). The reaction mixture was then concentrated and chromatographed to give **8** (60 mg, 91%) a crystalline solid. mp 128-129°C; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.78 (2H, d, *J*= 8.0Hz), 7.33 (2H, d, *J*= 7.9Hz), 7.25-7.18 (1H, m), 7.11-7.04 (2H, m), 6.80 (2H, d, *J*= 7.5Hz), 6.60 (1H, d, *J*= 9.7Hz), 6.06 (1H, dd, *J*= 5.1, 9.2Hz), 4.50 (2H, s (br)), 3.98 (1H, s), 2.29 (3H, s), 2.47 (3H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 144.9, 137.2, 132.4, 131.7,

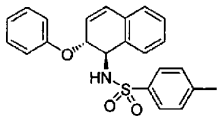
130.3, 129.6, 128.8, 128.4, 127.3, 124.9, 77.2, 56.5, 54.1, 21.6. Anal. Calcd for $C_{18}H_{19}NO_3S$: C, 65.63; H, 5.81; N, 4.25. Found: C, 65.74; H, 5.89; N, 4.19.



9

To a round bottomed flask was added **5** (61 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (1 ml) and MeOH (1 ml) were then added and the solution heated to reflux for 6 hours. The reaction mixture was then concentrated and chromatographed to give **9** (53 mg, 78%) a colourless oil. ^1H NMR (400MHz, $CDCl_3$) δ 7.51-7.47 (1H, m), 7.30-7.24 (2H, m), 7.14-7.10 (1H, m), 6.59 (1H, d, *J*= 9.9Hz), 6.10 (1H, dd, *J*= 3.7, 9.9Hz), 5.41 (1H, dd, *J*= 8.8, 8.8Hz), 4.55 (1H, d, *J*= 8.8Hz), 4.06 (1H, dd, *J*= 3.6, 6.9Hz), 3.45 (3H, s), 3.04-2.95 (2H, m), 1.07-0.85 (2H, m), 0.03 (6H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 133.7, 131.9, 129.9, 128.7, 128.4, 127.7,127.2, 125.5, 77.3, 56.5, 55.5, 50.2, 10.5, -2.0. HRMS calcd for $C_{16}H_{25}NO_3SSi$ (M^+): 339.1324. Found: 339.1327.

Example 10: Compounds Formed in Reactions Involving Phenol Nucleophiles

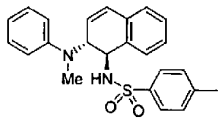


10

To a round bottomed flask was added **3** (60 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (2 ml) and PhOH (94 mg, 1.0 mmol) were added and the solution heated to reflux for 12 hours. The reaction mixture was then concentrated and chromatographed to give **10** (63 mg, 81%) a crystalline solid. ^1H NMR (400MHz, $CDCl_3$) δ 7.72 (2H, d, *J*= 8.2Hz), 7.30-7.20 (5H, m), 7.14-7.09 (2H, m), 6.98-6.92 (1H, m), 6.87 (1H, d, *J*= 7.4Hz), 6.77 (2H, d, *J*= 8.4Hz), 6.64 (1H, d, *J*= 10.2Hz), 6.06 (1H, dd, *J*= 4.6, 9.2Hz), 5.00 (1H, dd, *J*= 4.7, 4.7Hz), 4.71-4.64 (2H, m), 2.44 (3H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 156.8, 143.6, 137.5, 132.5, 131.7, 130.9, 129.7, 129.5, 128.9, 128.6, 128.2, 127.4, 127.4, 124.2, 121.4, 115.9,

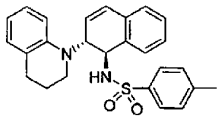
73.2, 54.4, 21.5. Anal. Calcd for $C_{23}H_{21}NO_3S$: C, 70.56; H, 5.41; N, 3.58. Found: C, 70.58; H, 5.43; N, 4.18.

Example 11: Compounds Formed in Reactions Involving Nitrogen or Carbon Nucleophiles



11

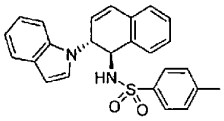
To a round bottomed flask was added **3** (60 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (2 ml) and N-methylaniline (107 mg, 1.0 mmol) were added and the solution heated to reflux for 8 hours. The reaction mixture was then concentrated and chromatographed to give **11** (72 mg, 89%) a crystalline solid. mp 136-142°C; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.62 (2H, d, *J*= 8.1Hz), 7.26-7.18 (4H, m), 7.14-7.08 (2H, m), 6.90 (1H, d, *J*= 7.3Hz), 6.80-6.68 (4H, m), 5.86 (1H, dd, *J*= 4.6, 9.9Hz), 4.73-4.53 (2H, m), 2.42 (3H, s), 2.34 (3H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 148.9, 143.4, 137.5, 133.7, 132.2, 130.4, 129.6, 129.2, 128.7, 128.4, 127.7, 127.3, 127.0, 126.0, 117.6, 113.8, 58.9, 54.6, 32.3, 21.5. Anal. Calcd for $C_{24}H_{24}N_2O_2S$: C, 71.26; H, 5.98; N, 6.93. Found: C, 71.32; H, 6.01; N, 4.16.



12

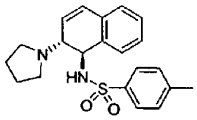
To a round bottomed flask was added **3** (60 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (2 ml) and tetrahydroquinoline (133 mg, 1.0 mmol) were added and the solution heated to reflux for 9 hours. The reaction mixture was then concentrated and chromatographed to give **12** (63 mg, 73%) a crystalline solid. mp 135-137°C; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.63 (2H, d, *J*= 8.2Hz), 7.25-7.20 (1H, m), 7.18 (2H, d, *J*= 8.2Hz), 7.11-7.00 (3H, m), 6.90 (1H, d, *J*= 6.4Hz), 6.83 (2H, d, *J*= 7.9Hz), 6.71 (1H, d, *J*= 9.7Hz), 6.64-6.58 (1H, m), 5.84 (1H, dd, *J*= 5.0, 9.7Hz), 4.83 (1H, d, *J*= 8.1Hz), 4.66 (1H, dd, *J*= 4.6, 4.6Hz), 4.58 (1H, dd, *J*= 4.7, 7.8Hz), 3.00-2.94 (1H, m), 2.62-2.40 (3H, m), 2.41 (3H, s), 1.60-1.52 (2H, m); ^{13}C NMR (400MHz, $CDCl_3$) δ 144.3, 143.2, 137.7, 133.8, 132.2, 130.7, 129.5, 129.5, 128.6,

128.2, 127.8, 127.1, 127.1, 127.0, 125.8, 123.3, 116.4, 111.7, 57.1, 53.9, 43.0, 28.0, 22.2, 21.5. Anal. Calcd for $C_{26}H_{26}N_2O_2S$: C, 72.53; H, 6.09; N, 6.51. Found: C, 72.55; H, 6.11; N, 6.50.



13

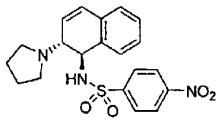
To a round bottomed flask was added 3 (60 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (2 ml) and indole (117 mg, 1.0 mmol) were added and the solution heated to reflux for 11 hours. The reaction mixture was then concentrated and chromatographed to give 13 (75 mg, 91%) a white solid. mp 132-135°C; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.84 (1H, s), 7.70-7.64 (3H, m), 7.24-7.07 (7H, m), 6.95-6.89 (1H, m), 6.65 (1H, d, *J*= 9.7Hz), 6.57 (1H, d, *J*= 2.4Hz), 6.50 (1H, d, *J*= 7.5Hz), 6.09 (1H, dd, *J*= 5.1, 9.5Hz), 4.99 (1H, d, *J*= 7.7Hz), 4.54 (1H, dd, *J*= 2.9, 7.7Hz), 4.26-4.22 (1H, m), 2.38 (3H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 143.2, 136.5, 132.4, 132.2, 132.2, 129.5, 128.9, 128.7, 128.6, 127.7, 127.1, 127.0, 126.4, 126.3, 122.5, 122.0, 119.5, 119.0, 112.2, 111.2, 56.0, 38.8, 21.5. HRMS calcd for $C_{25}H_{22}N_2O_2S$ (M^+): 414.1402. Found: 414.1407.



14

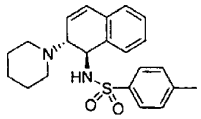
To a round bottomed flask was added 3 (60 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (2 ml) was then added followed by triethylamine hydrochloride (138 mg, 1.0 mmol) and pyrrolidine (83 µl, 1.0 mmol). The resulting heterogeneous mixture was heated to reflux for 14 hours. Upon completion, the reaction mixture was concentrated and chromatographed to give 14 (70 mg, 96%) a white solid. The regiochemistry and relative stereochemistry was proven by X-ray diffraction. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.74 (2H, d, *J*= 8.3Hz), 7.30 (2H, d, *J*= 8.2Hz), 7.22-7.17 (1H, m), 7.08-7.02 (2H, m), 6.84 (1H, d, *J*= 7.5Hz), 6.61 (1H, d, *J*= 9.7Hz), 5.93 (1H, dd, *J*= 4.9, 9.7Hz), 4.70 (1H, br s), 4.45 (1H, d, *J*= 3.7Hz), 3.89 (1H, dd, *J*= 4.2, 4.2Hz), 2.58-2.49 (2H, m), 2.45 (3H, s), 2.36-2.29 (2H,

m), 1.63-1.58 (4H, m); Anal. Calcd for $C_{21}H_{24}N_2O_2S$: C, 68.45; H, 6.56; N, 7.60. Found: C, 68.51; H, 6.62; N, 7.55.



15

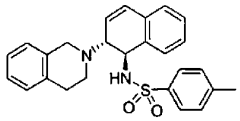
To a round bottomed flask was added **4** (66 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (2 ml) was then added followed by triethylamine hydrochloride (138 mg, 1.0 mmol) and pyrrolidine (83 µl, 1.0 mmol). The resulting heterogeneous mixture was heated to reflux for 16 hours. Upon completion, the reaction mixture was concentrated and chromatographed to give **15** (67 mg, 84%) a white solid. mp 142-145°C; ^{1}H NMR (400MHz, $CDCl_3$) δ 8.30 (2H, d, *J*= 8.8Hz), 7.99 (2H, d, *J*= 8.8Hz), 7.24-7.18 (1H, m), 7.10-7.04 (2H, m), 6.95-6.90 (1H, m), 6.63 (1H, d, *J*= 9.9Hz), 5.93 (1H, dd, *J*= 4.7, 9.7Hz), 5.20-4.80 (1H, br s), 4.60 (1H, d, *J*= 3.8Hz), 3.40-3.35 (1H, m), 2.58-2.50 (2H, m), 2.43-2.34 (2H, m), 1.64-1.57 (4H, m); ^{13}C NMR (400MHz, $CDCl_3$) δ 149.8,147.1, 132.8, 131.9, 129.7, 128.8, 128.2, 128.1, 128.0, 127.1, 125.0, 124.1, 61.4, 54.4, 50.0, 23.4. Anal. Calcd for $C_{20}H_{21}N_3O_4S$: C, 60.13; H, 5.30; N, 10.52. Found: C, 60.16; H, 5.33; N, 10.50.



16

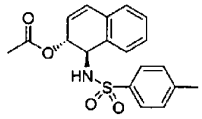
To a round bottomed flask was added **3** (60 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (2 ml) was then added followed by triethylamine (140 µl, 1.0 mmol) and piperidine hydrochloride (121 mg, 1.0 mmol). The resulting heterogeneous mixture was heated to reflux for 14 hours. Upon completion, the reaction mixture was concentrated and chromatographed to give **16** (72 mg, 94%) a white solid. mp 116-117°C; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.75 (2H, d, *J*= 8.2Hz), 7.30 (2H, d, *J*= 7.8Hz), 7.21-7.18 (1H, m), 7.10-7.05 (1H, m), 7.04 (1H, d, *J*= 7.5Hz), 6.94 (1H, d, *J*= 7.5Hz), 6.61 (1H, dd, *J*= 1.0, 9.7Hz), 5.91 (1H, dd, *J*= 4.8, 9.7Hz), 4.82 (1H, s (br)), 4.53 (1H, d, *J*= 4.4Hz), 3.38-3.35 (1H, m), 2.44 (3H, s), 2.41-2.34 (2H, m), 2.16-2.09 (2H, m), 1.40-1.26 (6H, m); ^{13}C NMR (400MHz, $CDCl_3$)

δ 143.3, 137.7, 134.2, 132.2, 129.6, 129.4, 128.2, 128.0, 127.7, 127.2, 126.6, 125.0, 64.2, 50.9, 49.6, 26.2, 24.3, 21.5. HRMS calcd for $C_{22}H_{26}N_2O_2S$ (M^+): 382.1715. Found: 382.1713.



17

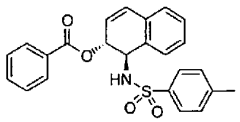
To a round bottomed flask was added **3** (60 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (2 ml) was then added followed by triethylamine hydrochloride (138 mg, 1.0 mmol) and tetrahydroisoqinoline (125 µl, 1.0 mmol). The resulting heterogeneous mixture was heated to reflux for 15 hours. Upon completion, the reaction mixture was concentrated and chromatographed to give **17** (70 mg, 81%) a white solid. mp 142-146°C; ^1H NMR (400MHz, $CDCl_3$) δ 7.73 (2H, d, *J*= 8.2Hz), 7.26-7.18 (3H, m), 7.12-6.98 (5H, m), 6.90 (1H, d, *J*= 8.1Hz), 6.80 (1H, d, *J*= 6.8Hz), 6.67 (1H, d, *J*= 9.7Hz), 5.95 (1H, dd, *J*= 4.7, 9.7Hz), 4.80 (1H, s), 4.62 (1H, s), 3.68 (1H, AB, d, *J*= 15.0Hz), 3.63 (1H, dd, *J*= 4.5, 4.5Hz), 3.40 (1H, AB, d, *J*= 15.0Hz), 2.68-2.56 (4H, m), 2.40 (3H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 143.4, 137.7, 137.7, 134.1, 133.8, 132.2, 129.9, 129.6, 128.6, 128.5, 128.3, 127.9, 127.2, 126.8, 126.5, 125.9, 125.4, 124.6. Anal. Calcd for $C_{26}H_{26}N_2O_2S$: C, 72.53; H, 6.09; N, 6.51. Found: C, 72.56; H, 6.12; N, 6.50.



18

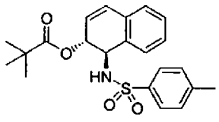
To a round bottomed flask was added **3** (60 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (1 ml) was then added followed by triethylamine hydrochloride (138 mg, 1.0 mmol) and potassium acetate (98 mg, 1.0 mmol). The resulting heterogeneous mixture was heated to reflux for 15 hours. Upon completion, the reaction mixture was concentrated and chromatographed to give **18** (63 mg, 88%) a white solid. ^1H NMR (400MHz, $CDCl_3$) δ 7.77 (2H, d, *J*= 8.3Hz), 7.31(2H, d, *J*= 8.2Hz), 7.27-7.22 (1H, m), 7.19-7.07 (3H, m), 6.54 (1H, d, *J*= 10.2Hz), 5.88 (1H, dd, *J*= 3.7, 10.2Hz), 5.48 –5.44 (1H, m), 4.90 (1H, d, *J*= 8.4Hz), 4.74-4.69 (1H, m), 2.44 (3H, s), 1.78 (3H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 170.6, 143.4, 138.2, 132.8, 131.9, 130.3, 129.7, 128.7, 128.5, 127.4, 127.1, 127.1, 125.0, 71.0, 55.7,

21.5, 20.7. Anal. Calcd for $C_{19}H_{19}NO_4S$: C, 63.85; H, 5.36; N, 3.92. Found: C, 63.88; H, 5.40; N, 3.81.



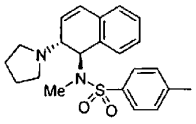
19

To a round bottomed flask was added **3** (60 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (1 ml) was then added followed by triethylamine (140 µl, 1.0 mmol) and benzoic acid (122 mg, 1.0 mmol). The resulting homogeneous solution was heated to reflux for 15 hours. Upon completion, the reaction mixture was concentrated and chromatographed to give **19** (73 mg, 87%) a white solid. mp 158-162°C; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.77 (2H, d, *J*= 7.1Hz), 7.65 (2H, d, *J*= 8.3Hz), 7.56-7.50 (1H, m), 7.40-7.32 (3H, m), 7.30-7.22 (2H, m), 7.11 (1H, dd, *J*= 1.3, 7.2Hz), 6.98 (2H, d, *J*= 8.1Hz), 6.56 (1H, dd, *J*= 1.3, 9.9Hz), 5.93 (1H, dd, *J*= 3.3, 9.7Hz), 5.79 (1H, ddd, *J*= 1.7, 3.3, 9.2Hz), 5.12 (1H, d, *J*= 8.4Hz), 4.90 (1H, dd, *J*= 8.8, 8.8Hz), 2.19 (3H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 166.4, 143.3, 138.0, 133.4, 133.3, 132.3, 130.4, 130.0, 129.7, 128.8, 128.8, 128.3, 127.5, 127.2, 126.9, 125.7, 72.3, 56.8, 21.6. HRMS calcd for $C_{24}H_{21}NO_4S$ (M^+): 419.1191. Found: 419.1997.



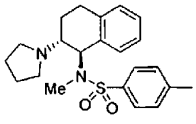
20

To a round bottomed flask was added **3** (60 mg, 0.2 mmol), $[Rh(COD)Cl]_2$ (2.5 mg, 0.005 mmol), and DPPF (5.5 mg, 0.01 mmol). THF (1 ml) was then added followed by triethylamine (140 µl, 1.0 mmol) and pivalic acid (102 mg, 1.0 mmol). The resulting homogeneous solution was heated to reflux for 15 hours. Upon completion, the reaction mixture was concentrated and chromatographed to give **20** (61 mg, 77%) a white solid. ^{1}H NMR (400MHz, $CDCl_3$) δ 7.75 (2H, d, *J*= 8.0Hz), 7.28 (2H, d, *J*= 8.0Hz), 7.16-7.00 (3H, m), 6.85 (1H, d, *J*= 7.6Hz), 6.55 (1H, d, *J*= 9.7Hz), 5.91 (1H, dd, *J*= 4.1, 9.7Hz), 5.34 (1H, dd, *J*= 5.9, 5.9Hz), 4.98 (1H, d, *J*= 8.4Hz), 4.70 (1H, dd, *J*= 7.3, 7.3Hz), 2.42 (3H, s), 1.07 (9H, s). HRMS calcd for $C_{22}H_{25}NO_4S$ (M^+): 399.1504. Found: 399.1507.



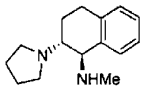
21

To a round bottomed flask was added **21** (100 mg, 0.27 mmol) and potassium carbonate (112 mg, 0.81 mmol). Acetone (3 ml) was then added followed by iodomethane (18 µl, 0.28 mmol). The mixture was stirred at room temperature for 4 hours then quenched with water. Extraction with ethylacetate, combining of the organic fractions and concentration gave a light yellow solid. Chromatography gave pure **21** (101 mg, 98%) a white crystalline solid. mp 109-111°C; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.86 (2H, d, *J*= 8.0Hz), 7.31 (2H, d, *J*= 8.0Hz), 7.26-7.12 (3H, m), 7.06 (1H, d, *J*= 6.9Hz), 6.58 (1H, d, *J*= 9.7Hz), 5.95 (1H, dd, *J*= 4.6, 9.9Hz), 5.35 (1H, d, *J*= 4.5Hz), 3.42 (1H, dd, *J*= 4.5, 4.5Hz), 2.62-2.48 (4H, m), 2.50 (3H, s), 2.45 (3H, s), 1.70-1.63 (4H, m); ^{13}C NMR (400MHz, $CDCl_3$) δ 143.0, 137.7, 133.6, 132.1, 129.5, 129.1, 128.9, 128.2, 128.1, 127.4, 126.5, 125.9, 58.2, 56.5, 48.6, 29.6, 23.5, 21.5. Anal. Calcd for $C_{22}H_{26}N_2O_2S$: C, 69.08; H, 6.85; N, 7.32. Found: C, 69.14; H, 6.91; N, 7.30.



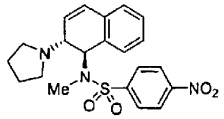
22

To a round bottomed flask was added **21** (100 mg, 0.26 mmol), ethylacetate (2 ml) and palladium on carbon (5mg). Hydrogen was added over this heterogeneous mixture via balloon for 15 hours. Upon completion, the mixture was filtred through celite and concentrated to give **22** a white solid. Crude ^{1}H NMR showed that this crude product was >95% pure. Further purification could be obtained by chromatography giving pure **22** (98 mg, 98%). mp 109-110°C; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.99 (2H, d, *J*= 8.1Hz), 7.30 (2H, d, *J*= 8.3Hz), 7.15-7.02 (4H, m), 5.29 (1H, d, *J*= 8.1Hz), 3.03-2.67 (5H, m), 2.65-2.52 (2H, m), 2.44 (3H, s), 2.43 (3H, s), 2.05-1.96 (1H, m), 1.90-1.80 (1H, m), 1.72-1.64 (4H, m); ^{13}C NMR (400MHz, $CDCl_3$) δ 142.8, 138.5, 137.5, 133.9, 129.2, 128.5, 127.7, 127.1, 126.4, 60.0, 59.3, 48.7, 30.3, 27.9, 23.6, 21.5, 21.4. Anal. Calcd for $C_{22}H_{28}N_2O_2S$: C, 68.72; H, 7.34; N, 7.29. Found: C, 68.79; H, 7.37; N, 7.22.



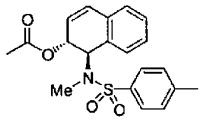
23

To a quartz tube was added **22** (80 mg, 0.2 mmol), 1,4-dimethoxybenzene (110 mg, 0.8 mmol) and sodium borohydride (76 mg, 2.0 mmol) followed by 90% aqueous ethanol solution (3 ml). The mixture was irradiated at 254 nm in a rayonet reactor for 2.5 hours. The crude mixture was concentrated azeotropically with ethanol and then chromatographed (90% acetone, 9% MeOH, 1% triethylamine) to give **23** (42 mg, 91%). Spectral data was identical to the literature data.



24

To a round bottomed flask was added **16** (100 mg, 0.25 mmol) and potassium carbonate (112 mg, 0.81 mmol). Acetone (3 ml) was then added followed by iodomethane (18 µl, 0.28 mmol). The mixture was stirred at room temperature for 4 hours then quenched with water. Extraction with ethylacetate, combining of the organic fractions and concentration gave a light yellow solid. Chromatography gave pure **24** (101 mg, 98%) a white crystalline solid. mp 139-141°C; ^{1}H NMR (400MHz, $CDCl_3$) δ 8.35 (2H, d, *J*= 8.8Hz), 8.22 (2H, d, *J*= 8.8Hz), 7.28-7.22 (3H, m), 7.09 (1H, d, *J*= 6.2Hz), 6.60 (1H, d, *J*= 9.9Hz), 5.95 (1H, dd, *J*= 4.0, 9.9Hz), 5.43 (1H, d, *J*= 6.6Hz), 3.54-3.49 (1H, m), 2.62 (3H, s), 2.60-2.54 (4H, m), 1.72-1.66 (4H, m); ^{13}C NMR (400MHz, $CDCl_3$) δ 149.8, 146.6, 133.6, 131.6, 129.5, 128.6, 128.3, 128.0, 126.8, 125.3, 124.0, 58.4, 58.0, 48.5, 29.8, 23.7. Anal. Calcd for $C_{21}H_{23}N_3O_4S$: C, 61.00; H, 5.61; N, 10.16. Found: C, 61.11; H, 5.65; N, 10.12.



25

To a round bottomed flask was added **18** (70 mg, 0.20 mmol) and potassium carbonate (110 mg, 0.80 mmol). Acetone (2.5 ml) was then added followed by iodomethane (15 µl, 0.24

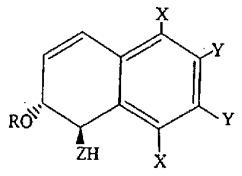
mmol). The mixture was stirred at room temperature for 4 hours then quenched with water. Extraction with ethylacetate, combining of the organic fractions and concentration gave a light yellow solid. Chromatography gave pure **25** (67 mg, 91%) a white crystalline solid. mp 113-116°C; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.78 (2H, d, *J*= 8.2Hz), 7.32 (2H, d, *J*= 8.2Hz), 7.25-7.17 (2H, m), 7.13-6.98 (2H, m), 6.46 (1H, dd, *J*= 1.8, 9.9Hz), 5.85 (1H, dd, *J*= 2.9, 9.9Hz), 5.71 (1H, ddd, *J*= 2.0, 2.6, 10.1Hz), 5.60 (1H, d, *J*= 10.1Hz), 2.69 (3H, s), 2.44 (3H, s), 1.90 (3H, s); ^{13}C NMR (400MHz, $CDCl_3$) δ 170.2, 143.4, 137.3, 133.2, 131.4, 129.6, 129.2, 128.4, 128.3, 127.1, 126.7, 126.4, 69.7, 60.0, 29.5, 21.4, 20.8. Anal. Calcd for $C_{20}H_{21}NO_4S$: C, 64.67; H, 5.70; N, 3.77. Found: C, 64.75; H, 5.77; N, 3.72.

Abbreviations

ee	"enantiomerically enriched," or "enantiomeric enrichment"
THF	tetrahydrofuran
DPPE	1,2-bis(diphenylphosphino)ethane
BINAP	2,2´-bis(diphenylphosphino)-1,1´-binaphthyl

The Claims Defining the Invention are as follows:

1. A compound according to formula I:



(I)

wherein R is $-(CH_2)_n R_1$ and R_1 is a C_3- C_6 aryl optionally substituted at one or more positions with a group selected from: Cl; F; NO_2; I; Br; a C_1-C_3 alkyl; and a C_1-C_3 alkoxy and wherein n=1-3; and

wherein X and Y are independently selected from the group consisting of H; NH_2; F; Cl; Br; a C_1-C_3 alkyl; and a C_1-C_3 alkoxy; or wherein adjacent X and Y or Y and Y together with the carbon atoms to which they are attached form a C_3-C_6 carbocyclic ring or a C_3-C_6 heterocyclic ring containing one or more heteroatoms selected from the group consisting of: O; N; and S; and

wherein Z is selected from O or NR_a, wherein R_a is selected from:

a) phenyl;

b) (O)C-O-R_b, wherein R_b is a straight or branched C_1-C_6 alkyl;

c) $-SO_2-R_c$, wherein R_c is selected from the group consisting of:

i) C_1-C_6 straight or branched alkyl;

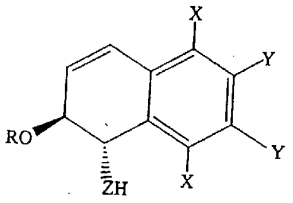
ii) $-(CH_2)_qR_e$, wherein q=0-3 and R_e is a C_3-C_6 aryl, optionally substituted at one or more positions with a group selected from: Cl; F; NO_2; CN; I; Br; a straight or branched C_1-C_3 alkyl; $-(CH_2)_rCF_3$ wherein r=0-3;

iii) $-R_g(CF_3)_s$, wherein R_g is a C_1-C_3 straight or branched alkyl and s=1-3;

iv) $-(CH_2)_s$-TMS, wherein TMS = trimethylsilyl and s= 1-3;

d) $-SO_2-(CH_2)_q-Si(CH_3)_3$ wherein q is 1-3.

2. A compound according to formula II:



(II)

wherein R $-(CH_2)_q$ R_5 wherein q is 0-3 and R_5 is a C_3-C_6 aryl optionally substituted at one of more positions with a group selected from; a straight or branched C_1-C_3 alkyl; a C_1-C_3 alkoxy; I; Cl; CN; F; NO_2; $-(CH_2)_r$ CF_3 wherein r is 0-3; and $C(O)R_6$ wherein R_6 is a C_1-C_3 alkyl; and

wherein X and Y are independently selected from the group consisting of H; NH_2, F; Cl; Br; a C_1-C_3 alkyl; and a C_1-C_3 alkoxy;

or wherein adjacent X and Y or Y and Y together with the carbon atoms to which they are attached form a C_3-C_6 carbocyclic ring or a C_3-C_6 heterocyclic ring containing one or more heteroatoms selected from the group consisting of : O; N; and S; and

wherein Z is selcted from O or NR_a, wherein R_a is selected from:

a) phenyl;

b) (O)C-O-R_b, wherein R_b is a straight of branched C_1-C_6 alkyl;

c) $-SO_2$-R_c, wherein R_c is selected from the group consisting of:

i) C_1-C_6 straight or branched alkyl;

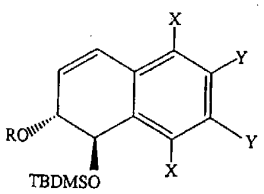
ii) $-(CH_2)_qR_e$, wherein q=0-3 and R_e is a C_3-C_6 aryl, optionally substituted at one or more positions with a group selected from: Cl; F; NO_2; CN; I; Br; a straight or branched C_1-C_3 alkyl; a C_1-C_3 alkoxy; and $-C(O)R_f$, wherein R_f is a C_1-C_3 alkyl; $-(CH_2)_rCF_3$, wherein r=0-3;

iii) $-R_g(CF_3)_s$, wherein R_g is a C_1-C_3 straight or branched alkyl and s=1-3;

iv) $-(CH_2)_s$-TMS, wherein TMS=trimethylsilyl and s= 1-3;

d) $-SO_2-(CH_2)_q-Si(CH_3)_3$ wherein q is 1-3.

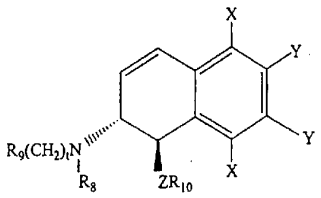
3. A compound according to formula III:



(III)

Wherein TBDMSO is a tert-butyldimethylsiloxy group, and R,X, and Y are as defined in claim 1.

4. A compound according to formula IV:



(IV)

wherein:

a) in which R_8 is H, or as defined in c);

b) t=0-3

c) R_9 is a C_3-C_6 aryl optionally substituted at one or more positions with a group selected from: a C_1-C_3 alkyl; a C_1-C_3 alkoxy; Cl; F; NO_2; and CF_3; or R_9 together with N, R_8 and $(CH_2)_t$ of formula IV form a ring structure selected from: a phthalimide ring; a pyrrolidine ring; a piperidine ring; a tetrahydroquinoline ring; and an indole ring; said ring structure being optionally substituted at one or more positions with a group selected from: a C_1-C_3 alkyl; a C_1-C_3 alkoxy; Cl; F; NO_2; and CF_3;

d) X and Y are independently selected from the group consisting of H; NH_2; F; Cl; Br; a C_1-C_3 alkyl; and a C_1-C_3 alkoxy; or wherein adjacent X and Y or Y and Y together with the carbon atom to which they are attached form a C_3-C_6 carbocyclic ring or a C_3-C_6 heterocyclic ring containing one or more heteroatoms selected from the group consisting of: O; N; and S;

e) Z is selected from O or NR_a, wherein R_a is selected from:

(i) a straight or branched C_1-C_6 alkyl;

(ii) phenyl;

(iii) (O)C-O-R_b, wherein R_b is a straight or branched C_1-C_6 alkyl;

(iv) $-SO_2$-R_c, wherein R_c is an unsubstituted phenyl or a phenyl substituted with a C_1-C_3 alkyl or NO_2; and

(v) $-SO_2$-$(CH_2)_q$-$Si(CH_3)_3$ wherein q is 1-3; and

f) when Z is O, R_{10} is H; when Z is NR_a, R_{10} is either H or CH_3.

tetrahydroquinoline ring; and an indole ring; said ring structure being optionally substituted at one or more positions with a group selected from: a C_1-C_3 alklyl; a C_1-C_3 alkoxy; Cl; F; NO_2; and CF_3.

5. A compound of any of claims 1-4, wherein X=H and Y=H.

6. A pharmaceutical composition comprising a compound according to any one of claims 1 to 5.

7. A method of treating a patient for pain, comprising administering to said patient an effective amount of the pharmaceutical compound of claim 6.

8. A method of treating a patient for Parkinson's disease, comprising administering an effective amount of the pharmaceutical composition of claim 6.

9. A method of treating a patient for cancer, comprising administering an effective amount of the pharmaceutical compound of claim 6.

10. A method of treating a patient for AIDS, comprising administering an effective amount of the pharmaceutical compound of claim 6.

11. A compound selected from the group consisting of:
(1S,2S)-2-methoxy-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(ethoxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(isopropoxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(1-propenyloxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(2-trimethylsilyl-ethoxy)1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-benzyloxy-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(4-methoxybenzyloxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(2,2,2-trifluoro-ethoxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(2,2,2-trifluoro-1-trifluoromethyl-ethoxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-6,7-difluoro-2-methoxy-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-6-methoxy-5,6-dihydro-naphthol [2,3-d] [1,3] dioxol-5-ol;
(1S,2S)-6,7-dibromo-2-methoxy-5,8-dimethyl-1,2-dihydro-naphthalen-1-ol;

(1R*,2R*)-acetic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester;
(1R*,2R*)-propionic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester;
(1R,2R)-benzoic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester;
(1R*,2R*)-formic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester;
(1R*,2R*)-2-methyl acrylic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester;
(1R*,2R*)-malonic acid ethyl ester (1-hydroxy-1,2-dihydro-naphthalen-2-yl) ester;
(1R*,2R*)-malonic acid (1-tert-butylbimethylsiloxy-1,2-dihydro-naphthalen-2-yl) ethyl ester;
(1S*,2S*)4-tert-butyldimethylsiloxy-1,4-dihydro-naphthalen-2-yl) acetic acid ethyl ester;
(1R,2R)-2-(1-hydroxy-1,2-dihydro-naphthalen-2-yl)-isoindole-1,3-dione;
(1S,2S)-N-(1-hydroxy-1,2-dihydro-naphthalen-2-yl)-benzene sulfonamide;
(1R*,2R*)-2-pyrrolidin-1-yl-1,2-dihydro-naphthalen-1-ol;
(1R*,2R*)-2-piperidin-1-yl-1,2-dihydro-naphthalen-1-ol;
(1R,2R)-2-(3,4-dihydro-2H-quinolin-1-yl)-1,2-dihydro-naphthalen-1-ol;
(1R,2R)-2-(methyl-phenyl-amino)-1,2-dihydro-naphthalen-1-ol;
(1R*,2R*)-2-benzylamino-1,2-dihydro-naphthalen-1-ol;
(1R*,2R*)-2-(4-methoxy-benzylamino)-1,2-dihydro-naphthalen-1-ol;
(1R,2R)-2-indol-1-yl-1,2-dihydro-naphthalen-1-ol;
(1S*,2R*)-2-(hydroxy-1,2-dihydro-naphthalen-2-yl)malonic acid dimethyl ester;
(1S,2S)-2-phenoxy-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(4-nitrophenoxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(4-cyanophenoxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(4-acylphenoxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(4-trifluoromethylphenoxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(4-fluorophenoxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(4-chlorophenoxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(4-iodophenoxy)-1,2-dihydro-naphthalen-1-ol;
(1R,2R)-2-(4-bromo-phenoxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(4-methylphenoxy)-1,2-dihydro-naphthalen-1-ol;
(1S,2S)-2-(4-methoxyphenoxy)-1,2-dihydro-naphthalen-1-ol; and
(1S,2S)-2-(2-bromophenoxy)-1,2-dihydro-naphthalen-1-ol.
4-methyl-*N*-[(1*R*,2*S*)-2-(1-piperidinyl)-1,2-dihydro-1-naphthalenyl]benzenesulfonamide;

N-[(1*R*,2*S*)-2-(3,4-dihydro-1(2*H*)-quinolinyl)-1,2-dihydro-1-naphthalenyl]-4-methylbenzenesulfonamide;

N-[(1*R*,2*S*)-2-(3,4-dihydro-2(1*H*)-isoquinolinyl)-1,2-dihydro-1-naphthalenyl]-4-methylbenzenesulfonamide;

N-[(1*R*,2*S*)-2-(1*H*-indol-1-yl)-1,2-dihydro-1-naphthalenyl]-4-methylbenzenesulfonamide;

(1*R*,2*S*)-2-methoxy-*N*-phenyl-1,2-dihydro-1-naphthalenamine;

tert-butyl (1*R*,2*S*)-2-methoxy-1,2-dihydro-1-naphthalenylcarbamate;

N-[(1*R*,2*S*)-2-methoxy-1,2-dihydro-1-naphthalenyl]-2-(trimethylsilyl)ethanesulfonamide;

N,4-dimethyl-*N*-[(1*R*,2*S*)-2-(1-pyrrolidinyl)-1,2,3,4-tetrahydro-1-naphthalenyl]-benzenesulfonamide;

N,4-dimethyl-*N*-[(1*R*,2*S*)-2-(1-pyrrolidinyl)-1,2-dihydro-1-naphthalenyl]-benzenesulfonamide;

N-hydroxy-4-({methyl[(1*R*,2*S*)-2-(1-pyrrolidinyl)-1,2-dihydro-1-naphthalenyl]amino}sulfonyl) -*N*-oxobenzenaminium;

N-methyl-4-nitro-*N*-[(1*R*,2*S*)-2-(1-pyrrolidinyl)-1,2-dihydro-1-naphthalenyl]-benzenesulfonamide;

(1*R*,2*S*)-*N*-methyl-2-(1-pyrrolidinyl)-1,2,3,4-tetrahydro-1-naphthalenamine;

N-[(1*R*,2*S*)-2-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl]-4-methylbenzenesulfonamide;

N-[(1*R*,2*S*)-2-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl]-4-methylbenzenesulfonamide;

4-methyl-*N*-[(1*R*,2*S*)-2-phenoxy-1,2,3,4-tetrahydro-1-naphthalenyl]benzenesulfonamide;

(1*R*,2*S*)-1-{[(4-methylphenyl)sulfonyl]amino}-1,2,3,4-tetrahydro-2-naphthalenyl acetate;

(1*R*,2*S*)-1-{[(4-methylphenyl)sulfonyl]amino}-1,2-dihydro-2-naphthalenyl benzoate;

(1*R*,2*S*)-1-{[(4-methylphenyl)sulfonyl]amino}-1,2-dihydro-2-naphthalenyl pivalate;

N-[(1*R*,2*S*)-2-methoxy-1,2-dihydro-1-naphthalenyl]-2-(trimethylsilyl)ethanesulfonamide;

tert-butyl (1*R*,2*S*)-2-methoxy-1,2-dihydro-1-naphthalenylcarbamate; and

4-nitro-*N*-[(1*R*,2*S*)-2-(1-pyrrolidinyl)-1,2-dihydro-1-naphthalenyl]benzenesulfonamide.

12. A pharmaceutical composition comprising a compound according to claim 11.

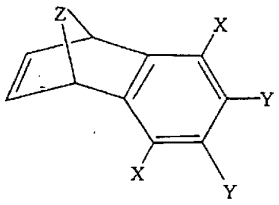
13. A method of treating a patient for pain, comprising administering to said patient an effective amount of the pharmaceutical of claim 12.

14. A method of treating a patient for Parkinson's Disease, comprising administering to said patient an effective amount of the pharmaceutical composition of claim 12.

15. A method of treating a patient for cancer, comprising administering to said patient an effective amount of the pharmaceutical composition of claim 12.

16. A method of treating a patient for AIDS, comprising administering to said patient and effective amount of the pharmaceutical composition of claim 12.

17. A process for preparing a compound according to formula I of claim 1, comprising reacting a compound of formula ROH with a compound of formula V:

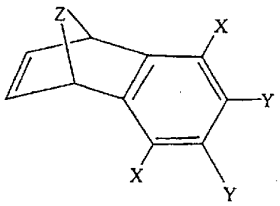


(V)

wherein R, X, Y, and Z are as defined in claim 1;
and wherein said reaction is catalyzed by $[Rh(COD)Cl]_2$ in the presence of a first chiral phosphine ligand.

18. A process of claim 17, wherein said first chiral phosphine ligand is selected from the group consisting of: DPPF; (R)-S)-BPPFA; and (R)-(S)-PPF-P^{t}Bu$_2$.

19. A process for preparing a compound according to formula II of claim 2, comprising reacting a compound of formula ROH with a compound of formula V:



(V)

wherein R, X, Y, and Z are as defined in claim 3;
and wherein said reaction is catalyzed by $[Rh(COD)Cl]_2$ in the presence of a second chiral phosphine ligand.

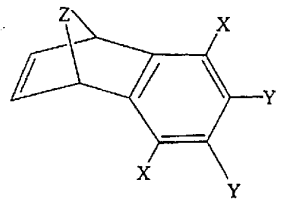
20. A process of claim 19, wherein said second chiral phosphine ligand is (S)-(R)-PPF-P^{t}Bu$_2$.

21. A process for preparing a compound according to formula III of claim 3, comprising:

a) preparing a compound of formula I according to the process of claim 17; and

b) reacting the compound formed in step (a) with a salt of tertbutyldimethylsilylic acid.

22. A process for preparing a compound of formula IV according to claim 4, comprising reacting a compound of formula R_9-$(CH_2)_t$NHR_8 with a compound of formula V.



(V)

wherein R_8, R_9, t, X, Y, and Z are as defined in claim 4 and wherein said reaction is catalyzed by $[Rh(COD)Cl]_2$ in the presence of a chiral phosphine ligand.

23. A process of claim 22, wherein said chiral phosphine ligand is selected from the group consisting of: DPPF; (R)-(S)-BPPFA; and (R)-(S)-PPF-P^{t}Bu$_2$.

24. A process of claim 23, wherein R_9 together with N form a ring selected from the group consisting of: a phthalamide ring; a pyrrolidine ring; a piperidine ring; a tetrahydroquinoline ring; and an indole ring; said ring structure being optionally substituted at one or more positions with a group selected from: a C_1-C_3 alkyl; a C_1-C_3 alkoxyl; Cl; F; NO_2; and CF_3.

25. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-methoxy-1,2-dihyddro-naphthalen-1-ol, and said compound of formula ROH is methanol.

26. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-(ethoxy)-1,2-dihydro-naphthalen-1-ol, and said compound of formula ROH is ethanol.

27. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-isopropoxy)-1,2-dihydro-naphthalen-1-o1 and said compound of formula ROH is isopropanol.

28. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-1-propenyloxy)-1,2-dihydro-naphthalen-1-o1, and said compound of formula ROH is allyl alcohol.

29. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-(2-trimethylsilyl-ethoxy)-1,2-dihydro-naphthalen-1-o1, and said compound of formula ROH is trimethylsilylethanol.

30. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-benzyloxy-1,2-dihydro-naphthalen-1-o1, and said compound of formula ROH is benzylalcohol.

31. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-4-methoxybenzyloxy-1,2-dihydro-naphthalen-1-ol, and said compound of formula of ROH is anisylalcohol.

32. A method of claim 19, wherein said compound of formula II is (1S,2S)-2-(2,2,2-trifluoro-ethoxy)-1,2-dihydro-naphthalen-1-o1, and said compound of formula ROH is trifluoroethanol.

33. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-(2,2,2-trifluoro-1-trifluoromethyl-ethoxy)-1,2-dihydro-naphthalen-1-o1 and said compound of formula ROH is hexafluoroisopropanol.

34. A process of claim 19, wherein said compound of formula II is (1S,2S)-6,7-difluoro-2-methoxy-1,2-dihydro-naphthalen-1-o1 and wherein said compound of formula ROH is methanol.

35. A method of claim 19, wherein said compound of formula II is (1S,2S)-6-methoxy-5,6-dihydro-naphtho[2,3-d] [1,3] dioxol-5-ol and wherein said compound of formula ROH is methanol.

36. A method of claim 19, wherein said compound of formula II is (1S,2S)-6,7-dibromo-2-methoxy-5,8-dimethyl-1,2-dihydro-naphthalen-1-ol and said compound of formula ROH is methanol.

37. A process of claim 17, wherein said compound of formula I is (1R*,2R*)-acetic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl ester and said compound of formula ROH is acetic acid.

38. A process of claim 17, wherein said compound of formula I is (1R*,2R*)-propionic acid 1-hydroxy-1,2—dihydro-naphthalen-2-yl ester and said compound of formula ROH is propionic acid.

39. A process of claim 17, wherein said compound of formula I is (1R,2R)-benzoic acid 1-hydroxy-1,2-dihydro-naphthalen-2yl-ester and said compound of formula ROH is benzoic acid.

40. A process of claim 17, wherein said compound of formula I is (1R*,2R*)-formic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester and said compound of formula ROH is formic acid.

41. A process of claim 17, wherein said compound of formula I is (1R*,2R*)-2-methyl acrylic acid 1-hydroxy-1,2-dihydro-naphthalen-2-yl-ester and said compound of formula ROH is methacrylic acid.

42. A process of claim 17, wherein said compound of formula I is (1R*,2R*)-malonic acid ethyl-ester (1-hydroxy-1,2-dihydro-naphthalen-2-yl) ester and said compound of formula ROH is ethyl malonic acid.

43. A method of claim 21, wherein said compound of formula III is (1R*,2R*)-malonic acid (1-tert-butyldimethylsiloxy-1,2-dihydro-naphthalen-2-yl) ester ethyl ester and said compound of formula ROH is tert-butyldimethylsilylic acid.

44. A method of claim 19, wherein said compound of formula II is (1S,2S)-2-phenoxy-1,2-dihydro-naphthalen-1-ol and said compound of formula ROH is phenol.

45. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-(4-nitrophenoxy)-1,2-dihydro-naphthalen-1-o1 and said compound of formula ROH is 4-nitrophenol.

46. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-(4-cycanophenoxy)-1,2-dihydro-naphthalen-1-o1 and said compound of formula ROH is 4-trifluoromethylphenyl.

47. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-(4-acylphenoxy)-1,2,-dihydro-naphthalen-1-o1 and said compound of formula ROH is 4-hydroxyacetophenone.

48. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-(4-trifluoromethylphenoxy)-1,2,-dihydro-naphthalen-1-o1 and said compound of formula ROH is 4-trifluoromethylphenyl.

49. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-(4-fluorophenoxy)-1,2-dihydro-naphthalen-1-o1 and said compound of formula ROH is 4-fluorophenol.

50. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-(4-chlorophenoxy)-1,2-dihydro-naphthalen-1-o1 and said compound of formula ROH is 4-chlorophenol.

51. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-(4-iodophenoxy)-1,2-dihydro-naphthalen-1-o1 and said compound of formula ROH is 4-iodophenol.

52. A process of claim 19, wherein said compound of formula I is (1R,2R)-2-(4-bromo-phenoxy)-1,2-dihydro-naphthalen-1-o1 and said compound of formula ROH is p-bromophenol.

53. A process of claim 19, wherein said compound of formula II is (1S,2S)-2-(4-methylphenoxy)-1,2-dihydro-naphthalen-1-ol and said compound of formula ROH is p-cresol.

54. A process of claim 19, wherein said compound of formula 11 is (1S,2S)-2-(4-methoxyphenoxy)-1,2-dihydro-naphthalen-1-ol and said compound of formula ROH is 4-methodyphenol.

55. A process of claim 19, wherein said compound of formula 11 is (1S,2S)-2-(2-bromophenoxy)-1,2-dihydo-naphthalen-1-ol and said compound of formula ROH is 2-bromophenol.

56. A process of claim 22, wherein said compound of formula IV is (1R,2R)-2-(1-hydroxy-1,2-dihydro-naphthalen-2-yl) isoindole-1,3-dione and said compound of formula R_9-$(CH_2)_5NHR_8$ is phthalimide.

57. A process of claim 22, wherein said compound of formula IV is (1R*,2R*)-2-pyrrolidin-1-yl-1,2-dihydro-naphthalen-1-ol and said compound of formula R_9-$(CH_2)_5NHR_8$ pyrrolidine.

58. A process of claim 22, wherein said compound of formula IV is (1R*,2R*)-2-piperidin-1-yl-1,2-dihydro-naphthalen-1-ol and said compound of formula R_9-$(CH_2)_5NHR_8$ is piperidine.

59. A process of claim 22, wherein said compound of formula IV is (1R,2R)-2-(3,4-dihydro-2H-quinolin-1-yl)-1,2-dihydro-naphthalen-1-ol and said compound of formula R_9-$(CH_2)_5NHR_8$ is tetrahydroisoquinoline.

60. A process of claim 22, wherein said compound of formula IV is (1R,2R)-2(methyl-phenyl-amino)-1,2-dihydro-naphthalen-1-ol and said compound of formula R_9-$(CH_2)_5NHR_8$ is N-methylaniline.

61. A process of claim 25, wherein said compound of formula IV is (1R*,2R*)-2-benzylamino-1,2-dihydro-naphthalen-1-ol and said compound of formula R_9-$(CH_2)_5NHR_8$ is benzylamine.

62. A process of claim 25, wherein said compound of formula IV is (1R*,2R*)-2-(4-methody-benzylamino)-1,2-dihydro-naphthalen-1-ol and said compound of formula R_9-$(CH_2)_5NHR_8$ is p-methoxybenzylamine.

63. A process of claim 25, wherein said compound of formula IV is (1R,2R)-2-indol-1-yl-1,2-dihydro-naphthalen-1-ol and said compound of formula R_9-$(CH_2)_5NHR_8$ is indole.

64. A process for preparing (1S,2S)-N-(1-hydroxy-1,2-dihydro-naphthalen-2-yl)-benzene sulfonamide, comprising reacting oxabenzonorbonadiene with benzenesulfonamide, wherein said reaction is catalyzed by $[Rh(COD)Cl]_2$ in the presence of a chiral phosphine ligand.

65. A process for preparing (1S*,2R*)-2-(hydroxy-1,2-dihydro-naphthalen-2-yl) malonic acid dimethyl ester, comprising reacting oxabenzonorbonadiene with dimethyl malonate, wherein said reaction is catalyzed by $[Rh(COD)Cl]_2$ in the presence of a chiral phosphine ligand.

66. A compound according to any one of claims 1 to 4, substantially as hereinbefore described with reference to any one of the examples.

67. A process according to any one of claims 17,19 or 22, substantially as hereinbefore described with reference to any one of the examples.

Dated: 2 July 2004

PHILLIPS ORMONDE & FITZPATRICK

Attorneys for: AstraZeneca AB

David B Fitzpatrick

W:\BA\667185\667185_P74 Claims.doc