Tetrahedron 67 (2011) 9072–9079

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Determination of absolute configuration of 2-methyl-1-(*o*-tolyl)naphthalene and the related axially chiral biaryls

Lijie Sun, Wei-Min Dai *

Department of Chemistry, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong SAR, China

ARTICLE INFO

Article history:
Received 14 August 2011
Received in revised form 16 September 2011
Accepted 23 September 2011
Available online 29 September 2011

Keywords:
Asymmetric Suzuki–Miyaura cross-coupling
Atropisomeric naphthamide
Chemical resolution
Chiral biaryl
Chiral phosphine

ABSTRACT

An enantiomerically enriched sample (84.3% ee) of (a*S*)-2-methyl-1-[(((*o*-triisopropylsilyl)oxy)methyl) phenyl]naphthalene was produced via catalytic asymmetric Suzuki–Miyaura cross-coupling using an atropisomeric naphthamide-derived phosphine (A^2phos) as the chiral ligand. After one recrystallization, enantiopurity of the biaryl product was improved to 98.9% ee and its absolute configuration was determined by X-ray crystal structural analysis. Through chemical transformations, the (a*S*)-enantiomers of 1-[(*o*-hydroxymethyl)phenyl]-2-methylnaphthalene, 1-[(*o*-chloromethyl)phenyl]-2-methylnaphthalene, and 2-methyl-1-(*o*-tolyl)naphthalene were obtained. Several other chiral biaryls were synthesized and stereochemically assigned.

1. Introduction

Biaryls with three or more *ortho* substituents form stable atropisomers at ambient temperature as the result of high rotational energy barrier across the C_{Ar}–C_{Ar} single bond connected with the aryl rings.[1] Examples of configurationally stable biaryls are given in Fig. 1, including 2,2′,6′-trisubstituted biphenyls (**1**), 2,2′-disubstituted 1-phenylnaphthalenes (**2**), and 2,2′-substituted or 2,2′-unsubstituted 1,1′-binaphthyls (**3**). The Suzuki–Miyaura cross-coupling has been widely used for synthesis of biaryls starting from aryl halides or pseudohalides and arylboronic acids or equivalent boron-derived reagents.[2] It is believed that the catalytic enantioselective version of Suzuki–Miyaura cross-coupling using chiral ligand modified palladium catalysts is the most direct and efficient method for synthesis of the axially chiral biaryls.[3] Since the first reports in 2000,[3a,c] a number of chiral ligand types have been investigated for catalytic enantioselective formation of 1-arylnaphthalenes (**2**), and 1,1′-binaphthyls (**3**) according to the Suzuki–Miyaura protocol. However, the absolute configuration of some chiral biaryl products, such as 2-methyl-1-(*o*-tolyl)naphthalene **2** (X=Y=Me) remains unknown.[3o,q] In our previous work, we have developed a novel class of aromatic amide-derived phosphines (Aphos) for Suzuki–Miyaura cross-coupling of less reactive substrates.[4] An atropisomeric version, i.e., A^2phos **4**–**6**, possessing the atropisomeric 1-naphthamide scaffold has been applied to asymmetric allylic alkylation (AAA),[5a] asymmetric Heck reaction,[5b] and asymmetric Suzuki–Miyaura cross-coupling.[5c] We report here on synthesis and determination of the absolute configuration of 2-methyl-1-(*o*-tolyl)naphthalene and its related chiral biaryls. Our results are useful for future study of chiral 1-arylnaphthyls (**2**) as shown in Fig. 1.

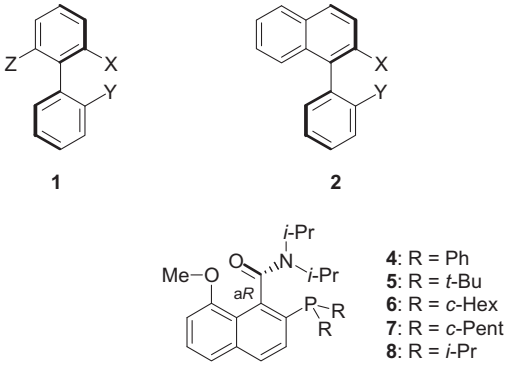

Fig. 1. Structures of axially chiral biphenyls (**1**), 1-arylnaphthyls (**2**), 1,1′-binaphthyls (**3**), and A^2phos **4**–**8**.

* Corresponding author. Tel.: +852 23587365; fax: +852 23581594; e-mail address: chdai@ust.hk (W.-M. Dai).

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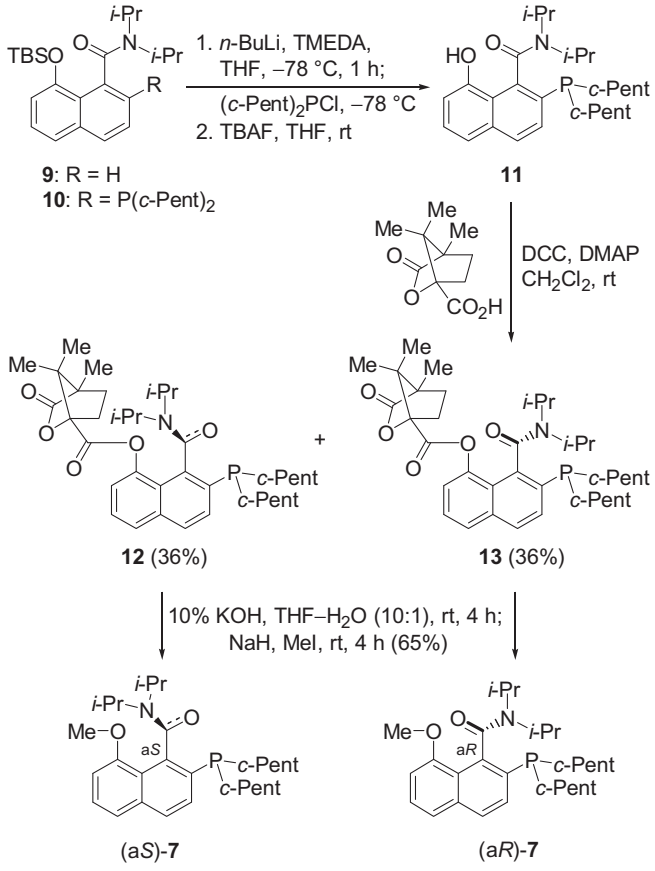
doi:10.1016/j.tet.2011.09.107

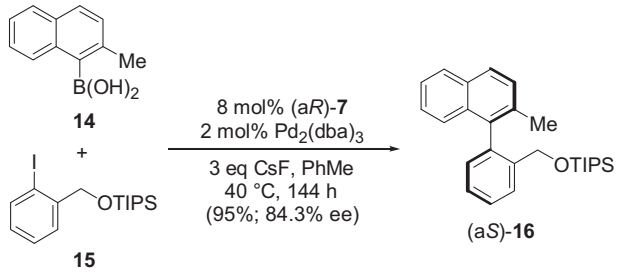
2. Results and discussion

We developed a chemical resolution process for synthesis of enantiomerically pure A^{2}phos **4**[5a] and **6**[5c] starting from the 8-TBSO-substituted 1-naphthamide **9**.[5a] By following the same procedure, A^{2}phos (a*R*)-**7** and (a*S*)-**7** were synthesized (Scheme 1). The naphthamide **9** was first subjected to standard *ortho*-lithiation using *n*-BuLi–TMEDA at −78 °C and the resultant aryllithium species was quenched with (*c*-Pent)$_2$PCl (−78 °C, 4 h) to form the racemic A^{2}phos **10** in 80% yield. Removal of the TBS protecting group in **10** was followed by esterification of the 8-hydroxy-1-naphthamide **11** with (1*S*)-(−)-camphanic acid in the presence of DCC–DMAP in CH_2Cl_2 at room temperature for 12 h, furnishing the diastereomeric esters **12** and **13** each in 36% isolated yield for the two steps from **10**. The isomer pure esters **12** and **13** obtained by column chromatographic separation over silica gel were converted into the target A^{2}phos without isolating the resolved 8-hydroxy intermediate **11** in order to minimize slow racemization. We also found that use of degassed solvents could improve the yield presumably due to suppression of oxidation of the phosphine moiety in the 8-hydroxide species. Thus, the ester **12** was treated with 10% KOH in mixed degassed THF–H_2O media at room temperature for 4 h and the extracted crude product was deprotonated using NaH, followed by reacting with MeI (rt, 4 h) in degassed THF to afford (a*S*)-**7** in 65% overall yield. The enantiomer (a*R*)-**7** was synthesized from **13** in the same manner. The absolute configuration of (a*R*)-**7** and (a*S*)-**7** is assigned by comparison of the sign of optical rotation data with reference to A^{2}phos **6**.[5c]

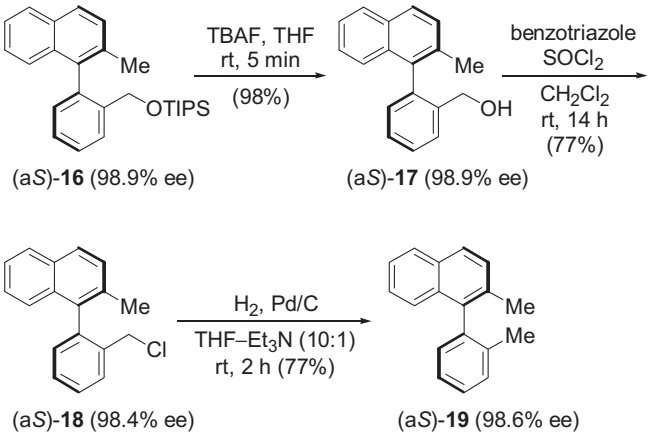


Scheme 1. Synthesis of A^{2}phos (a*R*)-**7** and (a*S*)-**7**.

We have demonstrated high efficiency of achiral Aphos–Pd catalyst system in catalyzing Suzuki–Miyaura cross-coupling reaction of electron-rich and bulky aryl chlorides at room temperature under mild basic conditions.[4e] Such catalytic profile is advantageous for catalytic formation of chiral biaryls from sterically bulky coupling partners at room temperature or under gentle heating conditions. We found that the coupling reaction of 2-methyl-1-naphthaleneboronic acid **14** with (2-iodobenzyloxy)triisopropylsilane **15**[6] took place at 40 °C in the presence of 8 mol % of A^{2}phos (a*R*)-**7**, 2 mol % $Pd_2(dba)_3$, and 3 equiv of CsF in toluene (Scheme 2). Use of 2:1 ratio of A^{2}phos to Pd was found to give better enantioselectivity. After heating at 40 °C for 144 h, the chiral biaryl (a*S*)-**16** was isolated in 95% chemical yield and in 84.3% ee as determined for its deprotected alcohol (a*S*)-**17** (see Scheme 3) by HPLC analysis over a chiral stationary phase. The chiral biaryl (a*S*)-**16** could be recrystallized from acetone to provide nearly enantiomerically pure materials (98.9% ee by HPLC). Its optical rotation data are given in entry 1 of Table 1. Furthermore, the absolute configuration was determined to be (a*S*) by X-ray crystal structural analysis[7] and the structural drawing is given in Fig. 2.



Scheme 2. Catalytic asymmetric Suzuki–Miyaura cross-coupling using Pd–A^{2}phos (a*R*)-**7**.



Scheme 3. Synthesis of 2-methyl-1-(*o*-tolyl)naphthalene (a*S*)-**19**.

Table 1
Optical rotation data of chiral biaryls

Entry	Chiral biaryl	$[\alpha]_D^{20}$ (*c*) in $CHCl_3$	ee[a] (%)
1	(a*S*)-**16**	+55.7 (1.00)	98.9[b]
2	(a*S*)-**17**	+27.4 (0.98)	98.9
3	(a*S*)-**18**	+74.5 (0.59)	98.4
4	(a*S*)-**19**	+3.75 (0.24)	98.6
5	(a*S*)-**19**	+2.4 (0.25)	73.1
6	(a*R*)-**23**	+12.4 (1.86)	71.7[b]
7	(a*R*)-**24**	+21.8 (0.86)	71.7
8	(a*R*)-**25**	+7.1 (1.01)	71.7[c]
9	(a*S*)-**26**	−37.5 (0.79)	72.9

[a] By HPLC analysis.
[b] By HPLC analysis of the desilylated alcohol (a*R*)-**24** in entry 7.
[c] Assumed based on the ee of the precursor (a*R*)-**24** in entry 7.

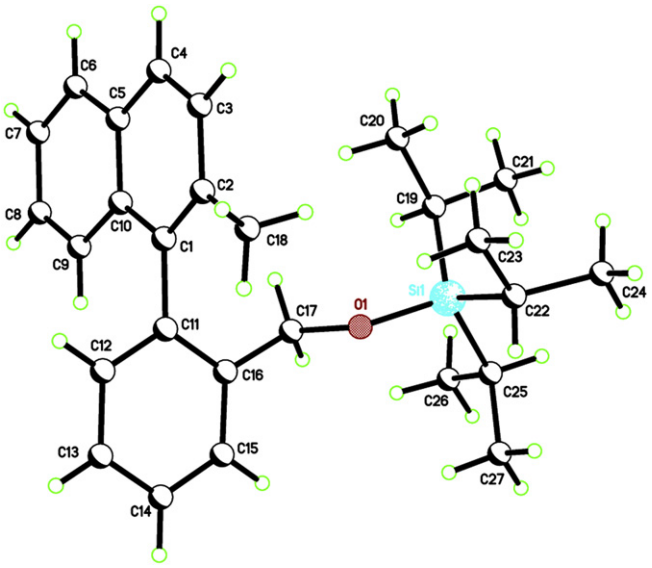
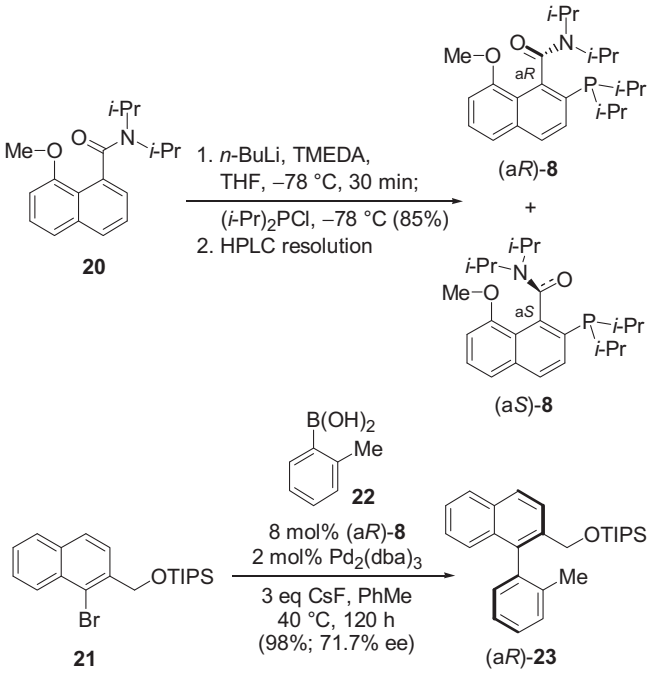


Fig. 2. X-ray crystal structure of chiral biaryl (a*S*)-**16**.

With enantiomerically pure (a*S*)-**16** in hand, some chemical transformations were carried out to form several related chiral biaryls as depicted in Scheme 3. Removal of the TIPS group in (a*S*)-**16** gave a 98% yield of the alcohol (a*S*)-**17** (98.9% ee by HPLC, entry 2, Table 1). Treatment of (a*S*)-**17** with $SOCl_2$–benzotriazole[8] in CH_2Cl_2 at room temperature for 14 h afforded the chloride (a*S*)-**18**[5c] (98.4% ee by HPLC, entry 3, Table 1). Finally, the chloride (a*S*)-**18** was reduced via hydrogenolysis in the presence of Pd/C in mixed THF–Et_3N (10:1) under a hydrogen atmosphere to furnish 2-methyl-1-(*o*-tolyl)naphthalene (a*S*)-**19**[3o,q,5c] in 77% yield. The optical rotation data of our synthesized (a*S*)-**19** (98.6% ee by HPLC, entry 4, Table 1) are close to the reported value of $[\alpha]_D^{20}$ +2.45 (*c* 1.00, $CHCl_3$, 83.6% ee) by Zhang[5c] and $[\alpha]_D^{20}$ +2.2 (*c* 2.48, $CHCl_3$, 84% ee) by Xu and Lin,[3q] but suggesting that the optical rotation data of $[\alpha]_D^{20}$ −92.7 (*c* 1.3, $CHCl_3$, 92% ee) for (a*R*)-**19** are problematic.[3o]

At this stage, we thought appropriate to doubly confirm our optical rotation value of (a*S*)-**19** by another sample synthesized from different starting materials (Scheme 4). Thus, the chiral biaryl (a*R*)-**23** was synthesized from ((1-bromo-2-naphthyl)methoxy)-triisopropylsilane **21** and *o*-tolylboronic acid **22** by a similar enantioselective Suzuki–Miyaura cross-coupling reaction using our A^{2}phos–Pd catalyst. The enantiomeric A^{2}phos (a*R*)-**8** and (a*S*)-**8**, possessing a slightly less bulky dialkylphosphino group, were obtained by HPLC resolution over a chiral stationary phase. The racemic sample was prepared from the 8-methoxy-1-naphthamide **20**[5b,9] and (*i*-Pr)$_2$PCl in 85% yield. The absolute configuration of (a*R*)-**8** was determined by X-ray crystal structural analysis[7] as depicted in Fig. 3. The chiral biaryl (a*R*)-**23** was obtained in 98% yield after heating at 40 °C for 120 h using 8 mol % (a*R*)-**8** and 2 mol % $Pd_2(dba)_3$. The coupling reaction gave 71.7% ee as determined by HPLC analysis of the corresponding alcohol (a*R*)-**24** (Scheme 5 and entry 6, Table 1). It should be mentioned that reversal in absolute configuration of the biaryls **23**–**25** is due to a change in priority order of the C2 substituents on the naphthalene ring.

Finally, the chiral biaryl (a*R*)-**23** was transformed into the alcohol (a*R*)-**24** in 98% yield by deprotecting the TIPS group (Scheme 5). This sample (a*R*)-**24** with 71.7% ee (entry 7, Table 1) was then treated with 2 equiv of BBr_3 in CH_2Cl_2 at 0 °C for 3 h to provide an 80% yield of the bromide (a*R*)-**25**,[5c] whose ee value was not directly analyzed by HPLC due to suspected lability toward the alcoholic eluate over silica gel column. Similar hydrogenolysis of (a*R*)-**25**



Scheme 4. Synthesis and Suzuki–Miyaura cross-coupling reaction of A^{2}phos (a*S*)-**8**.

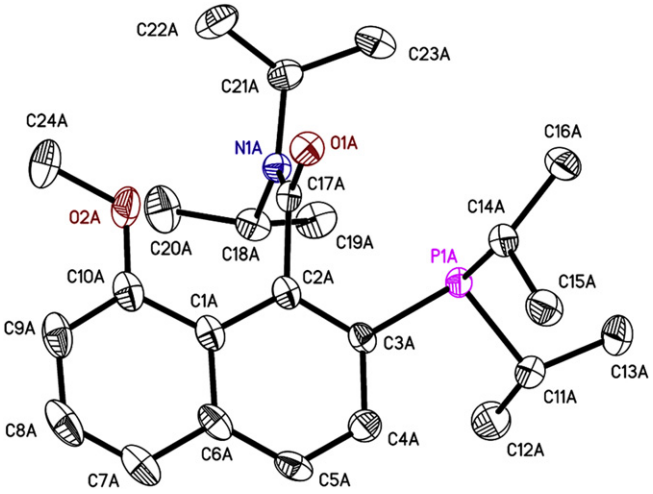
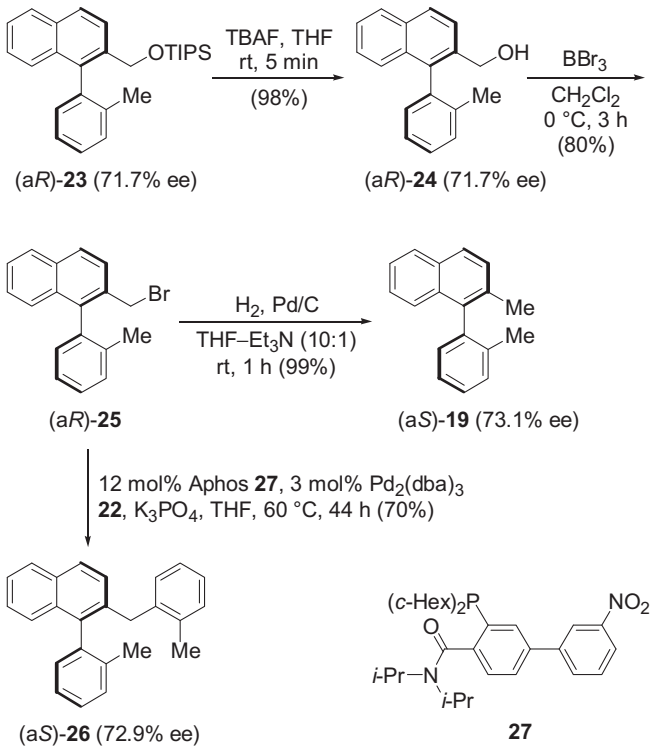


Fig. 3. X-ray crystal structure of A^{2}phos (a*R*)-**8**.

afforded 2-methyl-1-(*o*-tolyl)naphthalene (a*S*)-**19** in 99% yield and in 73.1% ee (entry 5, Table 1). The optical rotation data of this sample are consistent with our value measured for the sample prepared from (a*S*)-**16** (entry 4 vs entry 5, Table 1). Moreover, the bromide (a*R*)-**25** underwent Suzuki–Miyaura cross-coupling with *o*-tolylboronic acid **22** catalyzed by the achiral Aphos **27**[4e] and $Pd_2(dba)_3$ in the presence of K_3PO_4 as the mild base in THF at 60 °C for 44 h, giving the chiral biaryl (a*S*)-**26**[5c] in 70% yield with 72.9% ee by HPLC analysis (entry 9, Table 1).

3. Conclusion

In summary, we have synthesized eight axially chiral 1-arylnaphthalenes of the structural type **2** via A^{2}phos–Pd-catalyzed Suzuki–Miyaura cross-coupling reaction and subsequent chemical transformations. The absolute configuration of these



Scheme 5. Alternative synthesis of (a*S*)-**19**.

chiral biaryls has been carefully established on the basis of X-ray crystal structural analysis. Enantiopurity of these compounds has been measured by HPLC analysis over a chiral stationary phase and correlated to their optical rotation data. Our current work has clarified a dispute over the optical rotation data for 2-methyl-1-(*o*-tolyl)naphthalene.[3o,q] We believe our results are of useful reference for future study on this series of chiral 1-arylnaphthalenes.

4. Experimental

4.1. General methods

^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ (300 or 400 MHz for ^{1}H, 75 or 100 MHz for ^{13}C, and 162 MHz for ^{31}P, respectively) with residual $CHCl_3$ as the internal reference for ^{1}H (δ 7.26 ppm) and ^{13}C (δ 77.0 ppm) or a routine external reference for ^{31}P. IR spectra were taken on an FT-IR spectrophotometer. High-resolution mass spectra (HRMS) were measured by the CI^+ method. All reactions were carried out under a nitrogen atmosphere and monitored by thin-layer chromatography on 0.25-mm silica gel plates (60 F-254) using UV light, or 7% ethanolic phosphomolybdic acid and heating as the visualizing methods. Silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials. All reagents were obtained commercially and used as received.

HPLC analysis was performed on a Waters HPLC system equipped with a Waters 600 Controller, Waters 717 plus Autosampler, and 486 Tunable Absorbance Detector. HPLC setting for analysis of compounds **17**–**19** and **26**: Daicel chiralcel OJ column (0.46 cm×50 cm) eluting with 95:5 ratio of hexane–isopropanol at 0.5 mL/min and using UV detection at 254 nm. HPLC setting for analysis of compound **24**: Daicel chiralcel OD column (0.46 cm×50 cm) eluting with 90:10 ratio of hexane–isopropanol at 0.4–0.5 mL/min and using UV detection at 254 nm.

4.2. *N,N*-Diisopropyl-8-(((*tert*-butyldimethyl)silyl)oxy)-2-dicyclopentylphosphino-1-naphthamide (10)

To a flame-dried flask with a stirring bar were added the naphthamide **9**[5a] (3.080 g, 7.99 mmol), dry THF (50 mL), and TMEDA (1.44 mL, 9.58 mmol) under a nitrogen atmosphere. To the resultant solution cooled in a dry ice–acetone bath (−78 °C) was added *n*-butyllithium (1.6 M in hexane, 6 mL) dropwise followed by stirring at −78 °C for 1 h. Chlorodicyclopentylphosphine (1.84 mL, 9.58 mmol) was added to the mixture followed by stirring at −78 °C for another 4 h. The reaction was quenched with saturated aqueous NH_4Cl and the reaction mixture was filtered through a plug of silica gel with eluting by EtOAc (50 mL). The combined filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (silica gel, 4.8% EtOAc in hexane) to afford **10** (3.540 g, 80%) as colorless needles; mp 53–54 °C (hexane); R_f=0.31 (4.8% EtOAc in hexane); IR (film) 2954, 2862, 1636, 1438, 1298, 1260 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J=8.4 Hz, 1H), 7.60 (br d, J=7.2 Hz, 1H), 7.40 (d, J=7.6 Hz, 1H), 7.30 (dd, J=7.6, 7.6 Hz, 1H), 6.97 (dd, J=7.6, 0.8 Hz, 1H), 4.17 (br septet, J=6.8 Hz, 1H), 3.08 (septet, J=6.8 Hz, 1H), 2.49–2.31 (m, 1H), 2.08–1.93 (m, 2H), 1.89–1.76 (m, 1H), 1.76–1.40 (m, 14H), 1.61 (d, J=7.2 Hz, 3H), 1.56 (d, J=7.2 Hz, 3H), 1.00 (d, J=6.8 Hz, 3H), 0.92 (d, J=6.4 Hz, 3H), 0.84 (s, 9H), 0.45 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 152.8, 140.5 (d, J_{P-C}=32.1 Hz), 135.0, 128.7, 127.1, 126.3, 124.3 (d, J_{P-C}=7.7 Hz), 121.5 (2×), 115.9, 50.4, 45.7, 41.1 (br d, J_{P-C}=14.5 Hz), 35.6 (br d, J_{P-C}=12.7 Hz), 31.8 (d, J_{P-C}=26.6 Hz), 31.6 (d, J_{P-C}=14.9 Hz), 30.7 (d, J_{P-C}=12.2 Hz), 30.6 (d, J_{P-C}=17.6 Hz), 27.2 (3×), 27.0 (d, J_{P-C}=6.8 Hz), 26.2 (d, J_{P-C}=7.7 Hz), 26.1 (d, J_{P-C}=5.9 Hz), 25.4 (d, J_{P-C}=7.5 Hz), 22.9 (d, J_{P-C}=2.7 Hz), 21.8 (d, J_{P-C}=1.7 Hz), 21.6, 21.2 (d, J_{P-C}=5.2 Hz), 19.6, −1.8, −3.7; ^{31}P NMR (162 MHz, $CDCl_3$) δ −10.9; HRMS (CI^+) calcd for $C_{33}H_{53}NO_2PSi$ ($M+H^+$) 554.3583; found 554.3585. Anal. Calcd for $C_{33}H_{52}NO_2PSi$: C, 71.57; H, 9.46; N, 2.53; found: C, 71.88; H, 9.65; N, 2.35.

4.3. Procedure for synthesis of 11 and esterification with (1*S*)-(−)-camphanic acid

To a solution of the silyl ether **10** (2.220 g, 4.01 mmol) in THF (10 mL) under a nitrogen atmosphere was added TBAF (1.0 M in THF contained 5% water, 12.03 mL, 12.03 mmol) followed by stirring for 10 min. Saturated aqueous $NaHCO_3$ (30 mL) was added to the reaction mixture, and then extracted with CH_2Cl_2 (3×30 mL). The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the 8-hydroxy-1-naphthamide **11** as a non-crystalline solid, which was directly used for the next step.

To a solution of the above 8-hydroxy-1-naphthamide **11**, (1*S*)-(−)-camphanic acid (1.190 g, 6.01 mmol), and DMAP (97.9 mg, 0.80 mmol) in dry CH_2Cl_2 under a nitrogen atmosphere was added DCC (1.240 g, 6.01 mmol) followed by stirring at room temperature for 12 h. The reaction mixture was filtered though a plug of Celite with washing by cold CH_2Cl_2. The combined filtrate was concentrated under reduced pressure to give solid diastereomeric mixture, which was purified by flash column chromatography (silica gel, 2% EtOAc in CH_2Cl_2) to give **12** (0.893 g) and **13** (0.893 g) in 36% overall yield each from **10**.

*4.3.1. (aS,1′S,4′S)-(+)-N,N-Diisopropyl-2-dicyclopentylphosphino-8-{3′-oxo-4′,7′,7′-trimethyl-2′-oxabicyclo[2.2.2]heptane-1′-carbonyloxy}-1-naphthamide (**12**).* Prepared from **10** in 36% overall yield for the two steps as colorless needles (contaminated with some of the diastereomer **13**); mp 200 °C (dec; CH_2Cl_2–hexane); R_f=0.20 (2% EtOAc in CH_2Cl_2); $[\alpha]_D^{20}$ +21.9 (*c* 1.0, $CHCl_3$); IR (film) 2954, 1790, 1758, 1623, 1303, 1259, 1223, 1092, 1035 cm^{-1}; ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.79 (d, J=8.8 Hz, 1H), 7.75 (dd, J=8.4, 1.2 Hz, 1H), 7.67 (dd, J=8.8, 1.2 Hz, 1H), 7.46 (dd, J=7.6, 7.6 Hz, 1H), 7.01 (dd, J=7.6, 0.8 Hz, 1H), 4.75 (septet, J=7.2 Hz, 1H), 3.26 (septet, J=6.8 Hz, 1H), 2.57–2.31 (m, 3H), 2.06–1.90 (m, 3H), 1.83–1.40 (m, 16H), 1.55 (d, J=7.2 Hz, 6H), 1.20 (s, 3H), 1.18 (s, 3H), 1.15 (d, J=6.0 Hz, 3H), 1.14 (s, 3H), 0.95 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 168.7 (d, J_{P-C}=4.1 Hz), 167.8, 147.2, 139.3 (d, J_{P-C}=33.0 Hz), 136.6 (d, J_{P-C}=23.6 Hz), 135.0, 129.2 (d, J_{P-C}=2.9 Hz), 127.3, 127.1, 126.1, 123.7 (d, J_{P-C}=8.0 Hz), 120.0, 90.6, 54.9, 54.2, 50.6, 45.8, 40.7 (d, J_{P-C}=14.5 Hz), 35.0 (d, J_{P-C}=13.0 Hz), 32.2, 31.7 (d, J_{P-C}=26.8 Hz), 31.5 (d, J_{P-C}=14.3 Hz), 30.5 (d, J_{P-C}=12.4 Hz), 30.4 (d, J_{P-C}=16.1 Hz), 29.1, 27.0 (d, J_{P-C}=8.4 Hz), 26.1 (d, J_{P-C}=5.6 Hz), 26.1 (d, J_{P-C}=8.0 Hz), 25.3 (d, J_{P-C}=7.5 Hz), 22.8, 22.6 (d, J_{P-C}=4.4 Hz), 22.2 (d, J_{P-C}=3.0 Hz), 21.5 (d, J_{P-C}=2.7 Hz), 17.4, 17.2, 9.6; ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.3; HRMS (CI^+) calcd for $C_{37}H_{51}NO_5P$ ($M+H^+$) 620.3505; found 620.3503. Anal. Calcd for $C_{37}H_{50}NO_5P$: C, 71.70; H, 8.13; N, 2.26; found: C, 71.71; H, 8.16; N, 2.05.

*4.3.2. (aR,1′S,4′S)-(−)-N,N-Diisopropyl-2-dicyclopentylphosphino-8-{3′-oxo-4′,7′,7′-trimethyl-2′-oxabicyclo[2.2.2]heptane-1′-carbonyloxy}-1-naphthamide (**13**).* Prepared from **10** in 36% overall yield for the two steps as colorless needles; mp 240 °C (CH_2Cl_2–hexane); R_f=0.30 (2% EtOAc in CH_2Cl_2); $[\alpha]_D^{20}$ −25.9 (*c* 1.0, $CHCl_3$); IR (film) 2953, 1789, 1757, 1624, 1301, 1260, 1095, 1038 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J=8.4 Hz, 1H), 7.75 (d, J=8.0 Hz, 1H), 7.68 (d, J=8.0 Hz, 1H), 7.47 (dd, J=7.6, 7.6 Hz, 1H), 7.03 (d, J=7.6 Hz, 1H), 4.62 (septet, J=6.8 Hz, 1H), 3.23 (septet, J=6.8 Hz, 1H), 2.70–2.59 (m, 1H), 2.56–2.39 (m, 2H), 2.13–1.88 (m, 3H), 1.84–1.25 (m, 16H), 1.59 (d, J=7.6 Hz, 3H), 1.58 (d, J=6.8 Hz, 3H), 1.14 (s, 6H), 1.13 (d, J=6.4 Hz, 3H), 1.07 (s, 3H), 0.98 (d, J=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 169.0 (d, J_{P-C}=5.0 Hz), 167.8, 146.6, 139.3 (d, J_{P-C}=33.2 Hz), 136.6 (br, it was observed as doublet at 60 °C with J_{P-C}=24.8 Hz), 135.0, 129.2 (d, J_{P-C}=2.2 Hz), 127.3, 127.1, 126.2, 123.7 (d, J_{P-C}=8.5 Hz), 120.2, 90.8, 55.9, 55.0, 50.7, 46.1, 40.6 (d, J_{P-C}=13.7 Hz), 35.1 (d, J_{P-C}=12.0 Hz), 31.7 (d, J_{P-C}=27.6 Hz), 31.5 (d, J_{P-C}=13.7 Hz), 31.2, 30.5 (d, J_{P-C}=12.1 Hz), 30.5 (d, J_{P-C}=17.2 Hz), 29.2, 27.0 (d, J_{P-C}=6.8 Hz), 26.1 (d, J_{P-C}=7.2 Hz, 2×), 25.4 (d, J_{P-C}=6.7 Hz), 22.8 (d, J_{P-C}=3.1 Hz), 22.5, 22.1 (d, J_{P-C}=2.8 Hz), 21.3 (d, J_{P-C}=3.5 Hz), 16.8, 16.7, 9.8; ^{31}P NMR (162 MHz, $CDCl_3$) δ −11.2 (br); HRMS (CI^+) calcd for $C_{37}H_{51}NO_5P$ ($M+H^+$) 620.3505; found 620.3511. Anal. Calcd for $C_{37}H_{50}NO_5P$: C, 71.70; H, 8.13; N, 2.26; found: C, 71.70; H, 8.45; N, 2.03.

4.4. Procedure for synthesis of A^{2}phos (7)

To a solution of the camphanic ester **13** (700.0 mg, 1.13 mmol) in degassed THF (20 mL) cooled in an ice–water bath was added aqueous KOH (2 mL, 10% in degassed H_2O) under a nitrogen atmosphere followed by stirring at room temperature for 4 h. The reaction was quenched with degassed saturated aqueous NH_4Cl (10 mL), and the reaction mixture was then extracted with CH_2Cl_2 (3×20 mL). The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give the resolved chiral **11** as a non-crystalline solid, which was directly used for the next step.

To a suspension of NaH (60%, 135.5 mg, 3.39 mmol) in dry degassed THF (5 mL) cooled in an ice–water bath was added a solution of the resolved chiral 8-hydroxy-1-naphthamide **11** in dry degassed THF (10 mL) under a nitrogen atmosphere followed by stirring at room temperature for 30 min. To the resultant mixture was added MeI (0.28 mL, 4.52 mmol) followed by stirring at room temperature for 4 h. The reaction mixture was filtered through a plug of Celite with washing by EtOAc. The combined filtrate was concentrated under reduced pressure to give a residue, which was purified by flash column chromatography (silica gel, 16.6% EtOAc in hexane) to give (a*R*)-**7** (333.0 mg, 65%). The enantiomer (a*S*)-**7** was obtained from the camphanic ester **12** in the same manner.

*4.4.1. (aR)-(+)-N,N-Diisopropyl-2-dicyclopentylphosphino-8-methoxy-1-naphthamide [(aR)-**7**].* Colorless needles; mp 210–212 °C (CH_2Cl_2–hexane); R_f=0.31 (17% EtOAc in hexane); $[\alpha]_D^{20}$ +58.5 (*c* 1.0, $CHCl_3$); IR (film) 2953, 2865, 1628, 1451, 1304, 1259 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75–7.61 (m 2H), 7.42–7.37 (m, 2H), 6.86–6.82 (m, 1H), 3.90 (s, 3H), 3.60–3.47 (m, 2H), 2.58–2.34 (br m, 1H), 2.10–1.93 (br m, 2H), 1.87–1.30 (m, 15H), 1.70 (d, J=7.2 Hz, 3H), 1.68 (d, J=6.8 Hz, 3H), 1.15 (d, J=6.8 Hz, 3H), 0.93 (d, J=6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$ at 20 °C) δ 169.9 (d, J_{P-C}=3.5 Hz), 155.8, 140.7 (d, J_{P-C}=32.8 Hz), 135.3, 134.8 (br, it was observed as doublet at 60 °C with J_{P-C}=21.5 Hz), 129.2 (d, J_{P-C}=1.7 Hz), 127.1, 126.8, 121.6 (d, J_{P-C}=7.9 Hz), 120.7, 106.1, 55.0, 50.6, 46.0, 41.0 (br), 35.5 (br), 32.0 (d, J_{P-C}=26.9 Hz), 31.3 (d, J_{P-C}=12.1 Hz), 30.7 (d, J_{P-C}=16.8 Hz), 30.5 (d, J_{P-C}=11.6 Hz), 27.2 (d, J_{P-C}=8.4 Hz), 26.1 (d, J_{P-C}=7.8 Hz), 26.1 (d, J_{P-C}=5.4 Hz), 25.4 (d, J_{P-C}=7.1 Hz), 21.4 (d, J_{P-C}=4.4 Hz), 20.7, 20.3 (d, J_{P-C}=4.6 Hz), 19.8; ^{13}C NMR (100 MHz, $CDCl_3$ at 60 °C) δ 170.0 (d, J_{P-C}=4.6 Hz), 156.1, 141.0 (d, J_{P-C}=33.8 Hz), 135.4, 134.8 (d, J_{P-C}=21.5 Hz), 129.3 (d, J_{P-C}=2.2 Hz), 127.0, 126.7, 122.0 (d, J_{P-C}=8.1 Hz), 120.9, 106.4, 55.3, 50.6, 46.1, 41.1 (d, J_{P-C}=14.8 Hz), 35.9 (d, J_{P-C}=13.2 Hz), 32.0 (d, J_{P-C}=27.4 Hz), 31.6 (d, J_{P-C}=13.4 Hz), 30.8 (d, J_{P-C}=17.3 Hz), 30.6 (d, J_{P-C}=12.4 Hz), 27.2 (d, J_{P-C}=6.9 Hz), 26.2 (dd J_{P-C}=6.2 Hz), 26.2 (dd J_{P-C}=4.4 Hz), 25.5 (d, J_{P-C}=7.5 Hz), 21.4 (d, J_{P-C}=4.3 Hz), 20.9, 20.4 (d, J_{P-C}=4.1 Hz), 19.9; ^{31}P NMR (162 MHz, $CDCl_3$) δ −12.2 (br at 20 °C) or −12.3 (sharp at 60 °C); HRMS (CI^+) calcd for $C_{28}H_{41}NO_2P$ ($M+H^+$) 454.2875; found 454.2866. Anal. Calcd for $C_{28}H_{40}NO_2P$: C, 74.14; H, 8.89; N, 3.09; found: C, 74.12; H, 8.92; N, 2.96.

*4.4.2. (aS)-(+)-N,N-Diisopropyl-2-dicyclopentylphosphino-8-methoxy-1-naphthamide [(aS)-**7**].* Colorless needles; mp 211–212 °C (CH_2Cl_2–hexane); $[\alpha]_D^{20}$ −56.7 (*c* 0.8, $CHCl_3$). Other spectroscopic data are identical as those for (a*R*)-**7**.

4.5. Procedure for synthesis and HPLC resolution of A^{2}phos 8

To a flame-dried flask with a stirring bar were added 8-methoxy-1-naphthamide **20**[5b,9] (761.0 mg, 2.67 mmol), dry THF (20 mL), and TMEDA (0.48 mL, 3.20 mmol) under a nitrogen atmosphere. To the resultant solution cooled in a dry ice–acetone bath (−78 °C) was added *n*-butyllithium (1.6 M in hexane, 2 mL) dropwise followed by stirring at −78 °C for 30 min. Chlorodiisopropylphosphine (0.51 mL, 3.20 mmol) was added to the mixture followed by stirring at −78 °C for 4 h. The reaction was quenched with saturated aqueous NH_4Cl (1 mL). The reaction mixture was filtered through a plug of Celite with eluting by EtOAc (20 mL). The combined filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (silica gel, 16.6% EtOAc in hexane) to afford the racemic A^{2}phos **8** (910.0 mg, 85%) as a white solid.

The enantiomerically pure A^{2}phos (a*R*)-**8** and (a*S*)-**8** were obtained by HPLC resolution over a Chiralpak AD column. HPLC setting is: eluting with 90:10 ratio of hexane–isopropanol at 6 mL/min and using UV detection at 254 nm. Retention times are 2.82 and 3.58 min for (a*R*)-**8** and (a*S*)-**8**, respectively.

*4.5.1. (aR)-(+)-N,N-Diisopropyl-2-diisopropylphosphino-8-methoxy-1-naphthamide [(aR)-**8**].* Colorless needles; mp 139–141 °C (CH_2Cl_2–hexane); R_f=0.29 (17% EtOAc in hexane); $[\alpha]_D^{20}$ +68.4 (*c* 0.5, $CHCl_3$); IR (film) 2926, 2866, 1629, 1451, 1303, 1260 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J=8.4 Hz, 1H), 7.58 (d, J=8.0 Hz, 1H),7.43–7.35 (m, 2H), 6.88–6.82 (m, 1H), 3.90 (s, 3H), 3.55 (septet, J=6.8 Hz, 1H), 3.45 (septet, J=6.4 Hz, 1H), 2.44–2.35 (m, 1H), 2.03–1.92 (m, 1H), 1.75 (d, J=5.2 Hz, 3H), 1.69 (d, J=6.0 Hz, 3H), 1.28–1.18 (m, 3H), 1.16 (d, J=6.8 Hz, 3H), 1.14–0.93 (m, 9H),

0.92 (d, J=6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9 (d, J_{P-C}=4.7 Hz), 155.8, 141.3 (d, J_{P-C}=33.0 Hz), 135.2, 132.8 (d, J_{P-C}=23.8 Hz), 129.0 (d, J_{P-C}=2.4 Hz), 126.7 (2×), 122.0 (d, J_{P-C}=8.0 Hz), 120.7, 106.1, 55.1, 50.6, 45.9, 27.3 (d, J_{P-C}=16.4 Hz), 22.2 (d, J_{P-C}=13.2 Hz), 21.0 (d, J_{P-C}=5.0 Hz), 20.9 (d, J_{P-C}=15.2 Hz), 20.7, 20.6, 20.5 (d, J_{P-C}=12.7 Hz), 20.3 (d, J_{P-C}=4.4 Hz), 19.8, 19.4 (d, J_{P-C}=10.8 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ −1.6; HRMS (CI^+) calcd for $C_{24}H_{37}NO_2P$ ($M+H^+$) 402.2562; found 402.2565. Anal. Calcd for $C_{24}H_{36}NO_2P$: C, 71.79; H, 9.04; N, 3.49; found: C, 71.95; H, 9.08; N, 3.31.

*4.5.2. (aS)-(+)-N,N-Diisopropyl-2-diisopropylphosphino-8-methoxy-1-naphthamide [(aS)-**8**].* Colorless needles; mp 138–141 °C (CH_2Cl_2–hexane); $[\alpha]_D^{20}$ −63.1 (c 0.4, $CHCl_3$). Other spectroscopic data are identical as those for (a*R*)-**8**.

4.6. (2-Iodobenzyloxy)triisopropylsilane (15)[6]

To a solution of 2-iodobenzyl alcohol (0.500 g, 2.13 mmol) in dry CH_2Cl_2 (20 mL) cooled in an ice–water bath (0 °C) were added chlorotriisopropylsilane (0.69 mL, 3.20 mmol) and DBU[10] (0.48 mL, 3.20 mmol) followed by stirring at room temperature for 1 h. The reaction was quenched by saturated aqueous NH_4Cl (20 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×20 mL). The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 4.8% EtOAc in hexane) to afford the silyl ether **15** (0.790 mg, 95%) as a pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J=8.4 Hz, 1H), 7.63 (d, J=7.5 Hz, 1H), 7.40 (dd, J=7.5, 7.5 Hz, 1H), 6.98 (dd, J=7.5, 7.5 Hz, 1H), 4.74 (s, 2H), 1.35–1.05 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1, 138.5, 128.4, 128.1, 127.2, 95.6, 69.7, 18.0 (6×), 12.0 (3×).

4.7. [(1-Bromo-2-naphthyl)methoxy)]triisopropylsilane (21)

To a solution of 1-bromo-2-methylnaphthalene (5.08 g, 23.0 mmol) in CCl_4 (50 mL) were added NBS (4.13 g, 23.3 mmol) and benzoyl peroxide (0.10 g) followed by heating at reflux for 5 h. The reaction mixture was allowed to cool to room temperature, and filtered though a pad of silica gel with eluting by hexane. The combined filtrate was concentrated under reduced pressure and the residue was recrystallized from hexane to provide 1-bromo-2-(bromomethyl) naphthalene[11] (4.83 g, 70%) as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (d, J=8.7 Hz, 1H), 7.81 (d, J=7.5 Hz, 1H), 7.78 (d, J=8.4 Hz, 1H), 7.65–7.48 (m, 3H), 4.86 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.8, 134.0, 132.3, 128.2, 128.0, 127.7, 127.6, 127.5, 127.0, 124.8, 34.8.

To a solution of 1-bromo-2-(bromomethyl)naphthalene (4.83 g, 16.1 mmol) in THF (30 mL) were added water (30 mL) and $CaCO_3$ (8.05 g, 80.5 mmol). The mixture was refluxed for 10 h and the reaction mixture was allowed to cool to room temperature and filtered though a pad of Celite with eluting by EtOAc (50 mL). The combined filtrate was extracted with additional EtOAc (2×50 mL). The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 25% EtOAc–hexane) to give (1-bromo-2-hydroxymethyl)naphthalene[11a] (3.24 g, 85%) as a white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (d, J=8.1 Hz, 1H), 7.83 (d, J=8.1 Hz, 1H), 7.64–7.50 (m, 3H), 4.99 (s, 2H), 2.18 (br s, 1H).

To a solution of (1-bromo-2-hydroxymethyl)naphthalene (0.364 g, 1.54 mmol) in dry CH_2Cl_2 (15 mL) cooled in an ice–water bath (0 °C) were added chlorotriisopropylsilane (0.49 mL, 2.30 mmol) and DBU[10] (0.35 mL, 2.30 mmol) followed by stirring at room temperature for 1 h. The reaction was quenched by saturated aqueous NH_4Cl (15 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2×30 mL). The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 4.8% EtOAc–hexane) to give the silyl ether **21** (0.557 g, 92%) as a pale yellow oil; R_f=0.64 (4.8% EtOAc in hexane); IR (film) 2943, 2865, 1463, 1323, 1257, 1116 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (d, J=8.1 Hz, 1H), 7.87–7.81 (m, 3H), 7.59 (ddd, J=8.1, 7.2, 1.5 Hz, 1H), 7.50 (ddd, J=8.1, 7.2, 1.5 Hz, 1H), 5.08 (s, 2H), 1.32–1.12 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.6, 133.7, 131.8, 128.0, 127.4, 127.1, 126.4, 125.9, 124.7, 120.0, 65.6, 18.2 (6×), 12.2 (3×); HRMS (CI^+) calcd for $C_{20}H_{30}^{81}BrOSi^+$ ($M+2+H^+$) 395.1219 and $C_{20}H_{30}^{79}BrOSi^+$ ($M+H^+$) 393.1249; found 395.1203 and 393.1254.

4.8. General procedure for catalytic enantiomeric Suzuki–Miyaura cross-coupling reaction

A pressurized process vial (10 mL) with a magnetic stirring bar was charged with aryl halides (0.2 mmol), arylboronic acid (0.3 mmol, 1.5 equiv), $Pd_2(dba)_3$ (2 mol %), A^2phos (8 mol %), and CsF (0.6 mmol, 3 equiv). The vial was sealed with an aluminum crimp cap fitted with a silicon septum, and evacuated and back-filled with nitrogen (five times) through a needle. Degassed toluene (2 mL) was added through the septum using a syringe. The mixture was stirred at 40 °C for the indicated time. The reaction mixture was diluted with EtOAc (5 mL) and filtered through a pad of Celite with eluting by EtOAc (5 mL). The combined filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography over silica gel to give the chiral biaryl product. The ee of (a*S*)-**16** and (a*R*)-**23** was determined by HPLC analysis of the corresponding alcohols (a*S*)-**17** and (a*R*)-**24**, respectively, over a chiral stationary phase.

*4.8.1. (aS)-(+)-2-Methyl-1-[((o-triisopropylsilyl)oxy)methyl)phenyl] naphthalene [(aS)-**16**].* Prepared in 95% yield using A^2phos (a*R*)-**7** as the chiral ligand from 2-methyl-1-naphthaleneboronic acid **14** and aryl iodide **15** as colorless needles; mp 58–60 °C (acetone); R_f=0.28 (hexane); $[\alpha]_D^{20}$ +43.7 (c 1.0, $CHCl_3$, 84.3% ee). After one recrystallization from acetone the enantiopurity of (a*S*)-**16** was improved to 98.9%; $[\alpha]_D^{20}$ +55.7 (c 1.0, $CHCl_3$, 98.9% ee); IR (film) 2943, 2866, 1463, 1382, 1127, 1112, 1081, 1068 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (br t, J=8.4 Hz, 2H), 7.78 (d, J=8.0 Hz, 1H), 7.49 (ddd, J=7.6, 7.6, 1.6 Hz, 1H), 7.41 (d, J=8.4 Hz, 1H), 7.41–7.36 (m, 2H), 7.29 (ddd, J=8.0, 6.4, 1.2 Hz, 1H), 7.22 (br d, J=8.4 Hz, 1H), 7.11 (dd, J=7.6, 1.2 Hz, 1H), 4.35 and 4.28 (ABq, J=14.0 Hz, 2H), 2.16 (s, 3H), 0.98–0.89 (m, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.0, 136.7, 136.0, 133.2, 132.5, 131.9, 129.7, 128.5, 127.7, 127.6, 127.3, 126.8, 126.3, 125.9, 125.7, 124.8, 62.7, 20.4, 17.9 (6×), 11.9 (3×); HRMS (CI^+) calcd for $C_{27}H_{37}OSi$ ($M+H^+$) 405.2614; found 405.2603. Anal. Calcd for $C_{27}H_{36}OSi$: C, 80.14; H, 8.97; found: C, 80.16; H, 8.98. The absolute configuration of (a*S*)-**16** was established by X-ray crystal structural analysis as shown in Fig. 2.[7]

*4.8.2. (aR)-(+)-1-(o-Tolyl)-2-((triisopropyl)oxy)methylnaphthalene [(aR)-**23**].* Prepared in 98% yield using A^2phos (a*R*)-8 as the chiral ligand from aryl bromide **21** and *o*-tolylboronic acid **22** as a pale yellow oil; R_f=0.48 (hexane); $[\alpha]_D^{20}$ +12.4 (c 1.9, $CHCl_3$, 71.7% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96–7.86 (m, 3H), 7.48–7.24 (m, 6H), 7.12 (d, J=7.5 Hz, 1H), 4.63 and 4.50 (ABq, J=13.8 Hz, 2H), 1.92 (s, 3H), 1.15–1.00 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.5, 136.7, 136.2, 135.4, 132.5, 131.9, 129.9. 129.8, 127.8, 127.6, 127.3, 125.8, 125.8, 125.7, 125.1, 124.7, 63.2, 19.7, 18.1 (6×), 12.1 (3×).

4.9. (aS)-(+)-2-(2′-Methylnaphthalen-1′-yl)benzyl alcohol [(aS)-17]

To a solution of the silyl ether (a*S*)-**16** (20.2 mg, 0.05 mmol) in THF (10 mL) was added TBAF (1 mL, 1.0 M in THF, 1.0 mmol). The

resultant mixture was stirred at room temperature for 5 min. The mixture was filtered through a pad of silica gel with eluting by EtOAc (10 mL). The combined filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 16.7% EtOAc in hexane) to give the benzyl alcohol (a*S*)-**17** (12.2 mg, 98%) as a non-crystalline solid; R_f=0.29 (16.7% EtOAc in hexane); $[\alpha]_D^{20}$ +24.2 (*c* 1.0, $CHCl_3$, 84.3% ee) or $[\alpha]_D^{20}$ +27.4 (*c* 0.98, $CHCl_3$, 98.9% ee); IR (film) 3337 (br), 3054, 2921, 1447, 1380, 1031 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, *J*=8.7 Hz, 1H), 7.81 (d, *J*=8.7 Hz, 1H), 7.67 (dd, *J*=7.2, 0.9 Hz, 1H), 7.50 (ddd, *J*=7.2, 7.2, 1.8 Hz, 1H), 7.46–7.38 (m, 3H), 7.32 (ddd, *J*=8.4, 7.2, 1.5 Hz, 1H), 7.22 (d, *J*=8.4 Hz, 1H), 7.17 (dd, *J*=7.2, 0.9 Hz, 1H), 4.28 and 4.23 (ABq, *J*=12.9 Hz, 2H), 2.18 (s, 3H) (O*H* is not observed); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.3, 137.9, 135.9, 133.5, 132.7, 132.0, 130.3, 128.6, 127.9 (2×), 127.9, 127.7, 127.6, 126.2, 125.4, 125.0, 63.2, 20.5; HRMS (CI^+) calcd for $C_{18}H_{16}O$ (M^+) 248.1201; found 248.1201.

4.10. (a*S*)-(+)-1-(2′-Chloromethylphenyl)-2-methylnaphthalene [(a*S*)-18][5c]

Preparation of 1.0 M solution of $SOCl_2$–benzotriazole in CH_2Cl_2 was performed by following the literature procedure.[8] To a solution of benzotriazole (1.190 g, 10 mmol) in dry CH_2Cl_2 (10 mL) was added freshly distilled $SOCl_2$ (0.73 mL, 1.129 g, 10 mmol) under a nitrogen atmosphere. The resultant mixture was stirred for 10 min at room temperature to afford a solution (1.0 M) of $SOCl_2$–benzotriazole complex in CH_2Cl_2.

To a solution of the alcohol (a*S*)-**17** (24.8 mg, 0.1 mmol; 98.9% ee) in dry CH_2Cl_2 (5 mL) was added the above prepared $SOCl_2$–benzotriazole solution (0.50 mL, 1.0 M, 0.5 mmol) followed by stirring at room temperature for 14 h under a nitrogen atmosphere. The reaction was quenched by methanol (0.5 mL) and the reaction mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 100% hexane) to afford the benzyl chloride (a*S*)-**18**[5c] (20.5 mg, 77%) as a pale yellow oil; R_f=0.32 (hexane); $[\alpha]_D^{20}$ +74.5 (*c* 0.59, $CHCl_3$, 98.4% ee); IR (film) 2921, 1448, 1379 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J*=8.0 Hz, 1H), 7.83 (d, *J*=8.4 Hz, 1H), 7.68 (dd, *J*=7.6, 1.6 Hz, 1H), 7.52–7.39 (m, 4H), 7.32 (ddd, *J*=8.4, 6.8, 1.2 Hz, 1H), 7.20–7.16 (m, 2H), 4.25 and 4.16 (ABq, *J*=12.0 Hz, 2H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.1, 136.2, 135.3, 134.0, 132.7, 131.9, 130.6, 130.0, 128.8, 128.6, 128.2, 127.9, 127.8, 126.1, 125.6, 124.9, 44.1, 20.8; MS (CI^+) *m*/*z* 268 (M+2+H^+, 33), 266 (M+H^+, 100); HRMS (CI^+) calcd for $C_{18}H_{15}^{37}Cl$ (M^++2) 268.0832 and $C_{18}H_{15}^{35}Cl$ (M^+) 266.0862; found 268.0848 and 266.0882.

4.11. (a*S*)-(+)-2-Methyl-1-(*o*-tolyl)naphthalene [(a*S*)-19][3o,p,5c]

To a solution of the benzyl chloride (a*S*)-**18** (15.0 mg, 5.6×10^{-2} mmol; 98.4% ee) in THF–Et_3N (10:1, 5 mL) was added Pd/C (10%, 11.9 mg) followed by stirring for 2 h under a hydrogen atmosphere (1 atm). The reaction mixture was filtered through a pad of Celite with eluting by hexane. The combined filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (silica gel, 100% hexane) to give (a*S*)-**19** (10.0 mg, 77%) as a colorless oil; $[\alpha]_D^{20}$ +3.75 (*c* 0.24, $CHCl_3$, 98.6% ee), lit. $[\alpha]_D^{20}$ +2.45 (*c* 1.00, $CHCl_3$, 83.6% ee)[5c] and $[\alpha]_D^{20}$ +2.2 (*c* 2.48, $CHCl_3$, 84% ee)[3q] or $[\alpha]_D^{20}$ −92.7 (*c* 1.3, $CHCl_3$, 92% ee)[3o] for (a*R*)-**19**; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J*=8.4 Hz, 1H), 7.81 (d, *J*=8.8 Hz, 1H), 7.47–7.16 (m, 7H), 7.15 (d, *J*=6.8 Hz, 1H), 2.20 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 137.5, 136.8, 133.1, 132.5, 132.0, 130.0, 130.0, 128.6, 127.8, 127.4, 127.1, 125.9, 125.9, 125.7, 124.7, 20.3, 19.5; HRMS (CI^+) calcd for $C_{18}H_{16}$ (M^+) 232.1252; found 232.1259.

4.12. (a*R*)-(+)-[1-(*o*-Tolyl)naphthalen-2-yl]methanol [(a*R*)-24][12]

Prepared in 98% yield from (a*R*)-**23**, by following the same procedure as described for (a*S*)-**17**, as a non-crystalline solid; $[\alpha]_D^{20}$ +21.8 (*c* 0.86, $CHCl_3$, 71.7% ee); ^1H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J*=8.1 Hz, 1H), 7.86 (d, *J*=8.7 Hz, 1H), 7.68 (d, *J*=8.7 Hz, 1H), 7.46–7.40 (m, 1H), 7.35–7.22 (m, 5H), 7.12 (d, *J*=6.9 Hz, 1H), 4.47 (s, 2H), 1.90 (s, 3H) (O*H* is not observed).

4.13. (a*R*)-(+)-2-Bromomethyl-1-(*o*-tolyl)naphthalene [(a*R*)-25]

To a solution of the alcohol (a*R*)-**24** (118.0 mg, 0.47 mmol, 71.7% ee) in dry CH_2Cl_2 (20 mL) cooled in an ice–water bath (0 °C) was added BBr_3 (89 μL, 0.95 mmol) under a nitrogen atmosphere followed by stirring at the same temperature for 3 h. The reaction was quenched by methanol (1 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ (20 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, 100% hexane) to afford (a*R*)-**25** (115.8 mg, 80%) as a colorless oil; R_f=0.50 (3% EtOAc in hexane); $[\alpha]_D^{20}$ +7.1 (*c* 1.01, $CHCl_3$, 71.7% ee); IR (film) 2963, 1691, 1454, 1379, 1219 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J*=8.4 Hz, 1H), 7.89 (d, *J*=8.4 Hz, 1H), 7.66 (d, *J*=8.4 Hz, 1H), 7.52–7.48 (m, 1H), 7.46–7.34 (m, 4H), 7.30 (d, *J*=8.4 Hz, 1H), 7.26 (d, *J*=7.6 Hz, 1H), 4.49 and 4.36 (ABq, *J*=10.0 Hz, 2H), 1.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 137.1, 137.0, 133.2, 132.5, 132.3, 130.1, 130.1, 128.3, 128.1, 128.0, 127.5, 126.5, 126.5, 126.3, 125.9, 32.7, 19.9; HRMS (CI^+) calcd for $C_{18}H_{16}Br$ (M+H^+) 311.0435; found 311.0431.

4.14. Debromination of (a*R*)-25

To a solution of the bromide (a*R*)-**25** (30.0 mg, 9.6×10^{-2} mmol, 71.7% ee) in THF–Et_3N (10:1, 5 mL) was added Pd/C (10%, 10.2 mg). The resultant mixture was stirred for 1 h at room temperature under a hydrogen atmosphere (1 atm). The reaction mixture was filtered through a pad of Celite with eluting by hexane. The combined filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (silica gel, 100% hexane) to give (a*S*)-**19** (22.3 mg, 99%) as a colorless oil; $[\alpha]_D^{20}$ +2.40 (*c* 0.25, $CHCl_3$, 73.1% ee).

4.15. (a*S*)-(−)-2-(2′-Methylbenzyl)-1-(*o*-tolyl)naphthalene [(a*S*)-26][5c]

A pressurized process vial (10 mL) with a magnetic stirring bar was charged with the bromide (a*R*)-**25** (42.7 mg, 0.14 mmol, 71.7% ee), *o*-tolylboronic acid (28.0 mg, 0.21 mmol), $Pd_2(dba)_3$ (3.8 mg, 4.11×10^{-3} mmol), achiral Aphos **27**[4e] (8.6 mg, 1.64×10^{-2} mmol), and K_3PO_4 (87.6 mg, 0.41 mmol). The vial was sealed with an aluminum crimp cap fitted with a silicon septum, and evacuated and backfilled with nitrogen (five times) through a needle. Degassed THF (3 mL) was added through the septum using a syringe. The mixture was stirred at 60 °C for 44 h. The reaction mixture was allowed to cool to room temperature and filtered though a pad of Celite with eluting by hexane (10 mL). The combined filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography (silica gel, 100% hexane) to afford (a*S*)-**26**[5c] (31.0 mg, 70%) as a white solid; $[\alpha]_D^{20}$ −37.5 (*c* 0.79, $CHCl_3$, 72.9% ee); IR (film) 3056, 3017, 2923, 1490, 1461, 1381 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, *J*=8.1 Hz, 1H), 7.78 (d, *J*=8.4 Hz, 1H), 7.43 (ddd, *J*=8.4, 6.6, 1.5 Hz, 1H), 7.37–7.24 (m, 5H), 7.22 (d, *J*=8.7 Hz, 1H), 7.16–7.04 (m, 4H), 6.96 (br d, *J*=6.6 Hz, 1H), 3.81 (s, 2H), 2.07 (s, 3H), 1.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.8, 138.5, 137.8, 137.0, 136.4, 135.4, 132.5, 132.1, 130.0, 129.9, 129.9,

129.8, 127.7, 127.4, 127.4, 127.3, 126.0, 125.9, 125.9, 125.8, 125.7, 125.0, 37.1, 19.8, 19.7; MS (CI^+) *m*/*z* 322 ($M+H^+$, 100); HRMS (CI^+) calcd for $C_{25}H_{22}$ (M^+) 322.1721; found 322.1725.

Acknowledgements

This work is supported in part by a research grant (601003) from the Research Grant Council, The Hong Kong Special Administrative Region, China, and the Department of Chemistry, HKUST. The authors thank Dr. Herman Sung of the X-ray crystallographic facility of HKUST for assistance on the crystal structure analysis, and Dr. Ye Zhang for characterization of some biaryl compounds.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2011.09.107.

References and notes

1. For reviews on synthesis of axially chiral biaryls, see: (a) Bringmann, G.; Mortimer, A. J. P.; Keller, P. A.; Gresser, M. J.; Garner, J.; Breuning, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 5384–5427; (b) Baudoin, O. *Eur. J. Org. Chem.* **2005**, 4223–4229; (c) Wallace, T. W. *Org. Biomol. Chem.* **2006**, *4*, 3197–3210 and the references cited therein.
2. For reviews on Suzuki–Miyaura crosso-coupling, see: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483; (b) Stanforth, S. P. *Tetrahedron* **1998**, *54*, 263–303; (c) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633–9695; (d) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359–1469; (e) Bellina, F.; Carpita, A.; Rossi, R. *Synthesis* **2004**, 2419–2440; (f) Phan, N. T. S.; Sluys, M. V. D.; Jones, C. W. *Adv. Synth. Catal.* **2006**, *348*, 609–679.
3. For examples of catalytic enantioselective Suzuki–Miyaura cross-coupling to form axially chiral biaryls, see: (a) Cammidge, A. N.; Crépy, K. V. L. *Chem. Commun.* **2000**, 1723–1724; (b) Cammidge, A. N.; Crépy, K. V. L. *Tetrahedron* **2004**, *60*, 4377–4386; (c) Yin, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 12051–12052; (d) Castanet, A.-S.; Colobert, F.; Broutin, P.-E.; Obringer, M. *Tetrahedron: Asymmetry* **2002**, *13*, 659–665; (e) Jensen, J. F.; Johannsen, M. *Org. Lett.* **2003**, *5*, 3025–3028; (f) Herrbach, A.; Marinetti, A.; Baudoin, O.; Guénard, D.; Guéritte, F. *J. Org. Chem.* **2003**, *68*, 4897–4905; (g) Mikami, K.; Miyamoto, T.; Hatano, M. *Chem. Commun.* **2004**, 2082–2083; (h) Kasák, P.; Mereiter, K.; Widhalm, M. *Tetrahedron: Asymmetry* **2005**, *16*, 3416–3426; (i) Genov, M.; Almorín, A.; Espinet, P. *Chem.—Eur. J.* **2006**, *12*, 9346–9352; (j) Genov, M.; Almorín, A.; Espinet, P. *Tetrahedron: Asymmetry* **2007**, *18*, 625–627; (k) Bronger, R. P. J.; Guiry, P. J. *Tetrahedron: Asymmetry* **2007**, *18*, 1094–1102; (l) Takemoto, T.; Iwasa, S.; Hamada, H.; Shibatomi, K.; Kameyama, M.; Motoyama, Y.; Nishiyama, H. *Tetrahedron Lett.* **2007**, *48*, 3397–3401; (m) Sawai, K.; Tatumi, R.; Nakahodo, T.; Fujihara, H. *Angew. Chem., Int. Ed.* **2008**, *47*, 6917–6919; (n) Bermejo, A.; Ros, A.; Fernández, R.; Lassaletta, J. M. *J. Am. Chem. Soc.* **2008**, *130*, 15798–15799; (o) Uozumi, Y.; Matsuura, Y.; Arakawa, T.; Yamada, Y. M. A. *Angew. Chem., Int. Ed.* **2009**, *48*, 2708–2710; (p) Debono, N.; Labande, A.; Manoury, E.; Daran, J.-C.; Poli, R. *Organometallics* **2010**, *29*, 1879–1882; (q) Zhang, S.-S.; Wang, Z.-Q.; Xu, M.-H.; Lin, G.-Q. *Org. Lett.* **2010**, *12*, 5546–5549; (r) Yamamoto, T.; Akai, Y.; Nagata, Y.; Suginome, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 8844–8847 Also, see: (s) Willis, M. C.; Powell, L. H. W.; Claverie, C. K.; Watson, S. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 1249–1251.
4. (a) Dai, W.-M.; Li, Y.; Zhang, Y.; Lai, K. W.; Wu, J. *Tetrahedron Lett.* **2004**, *45*, 1999–2001; (b) Dai, W.-M.; Zhang, Y. *Tetrahedron Lett.* **2005**, *46*, 1377–1381; (c) Wu, J.; Nie, L.; Luo, J.; Dai, W.-M. *Synlett* **2007**, 2728–2732; (d) Jin, J.; Chen, Y.; Li, Y.; Wu, J.; Dai, W.-M. *Org. Lett.* **2007**, *9*, 2585–2588; (e) Dai, W.-M.; Li, Y.; Zhang, Y.; Yue, C.; Wu, J. *Chem.—Eur. J.* **2008**, *14*, 5538–5554; (f) Zheng, Y.; Yu, G.; Wu, J.; Dai, W.-M. *Synlett* **2010**, 1075–1080.
5. (a) Dai, W.-M.; Yeung, K. K. Y.; Liu, J.-T.; Zhang, Y.; Williams, I. D. *Org. Lett.* **2002**, *4*, 1615–1618; (b) Dai, W.-M.; Yeung, K. K. Y.; Wang, Y. *Tetrahedron* **2004**, *60*, 4425–4430; (c) Zhang, Y. Ph.D. Thesis, The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong SAR, China, 2005.
6. Martin, R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 3844–3845.
7. The X-ray crystal data (excluding structure factors) of compound (a*S*)-**16** (see Fig. 2) and A^2phos (a*R*)-**8** (see Fig. 3) have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no CCDC 809393 and CCDC 810280, respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).
8. Chaudhari, S. S.; Akamanchi, K. G. *Synlett* **1999**, 1763–1765.
9. Clayden, J.; Frampton, C. S.; McCarthy, C.; Westlund, N. *Tetrahedron* **1999**, *55*, 14161–14184.
10. For use of DBU as a base in formation of silyl ethers, see: Aizpurua, J. M.; Palomo, C. *Tetrahedron Lett.* **1985**, *26*, 475–476.
11. (a) Smith, J. G.; Dibble, P. W.; Sandborn, R. E. *J. Org. Chem.* **1986**, *51*, 3762–3768; (b) Chouhan, G.; Alper, H. *J. Org. Chem.* **2009**, *74*, 6181–6189.
12. Moleele, S. S.; Michael, J. P.; de Koning, C. B. *Tetrahedron* **2006**, *62*, 2831–2844.