Pergamon

Tetrahedron: *Asymmetry* 14 (2003) 3219–3224

TETRAHEDRON: *ASYMMETRY*

Synthesis of chiral 4,4′-disubstituted 1,1′-spirobiindane-7,7′-diols and related phosphoramidites: the substituent effect of SIPHOS ligands in Rh-catalyzed asymmetric hydrogenation

Shou-Fei Zhu, Yu Fu, Jian-Hua Xie, Bin Liu, Liang Xing and Qi-Lin Zhou*

State Key Laboratory and Institute of Elemento-organic Chemistry, Nankai University, Tianjin 300071, China

Received 25 June 2003; accepted 11 August 2003

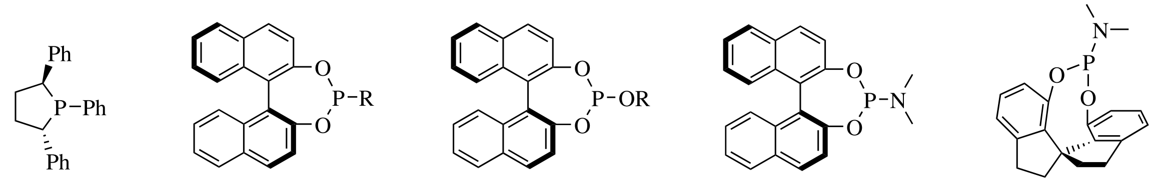
Abstract—Three chiral 4,4′-substituted 1,1′-spirobiindane-7,7′-diols and related monodentate spiro phosphoramidite ligands have been readily synthesized from enantiomerically pure 1,1′-spirobiindane-7,7′-diol. Excellent enantioselectivities were obtained with these new ligands in the rhodium-catalyzed asymmetric hydrogenation of dehydroamino acid derivatives and enamides. Comparing SIPHOS, ligands 4,4′-dibromo-SIPHOS and 4,4′-diphenyl-SIPHOS gave similarly high enantioselectivities although the rates in hydrogenations of enamides are somewhat slower. Methoxy substituents at the 4,4′-position of ligands slightly reduced enantioselectivities of hydrogenation reactions.

1. Introduction

Although the earliest chiral ligands used by Knowles[1] and Horner[2] in the rhodium-catalyzed asymmetric hydrogenation were monodentate phosphines, bidentate diphosphine ligands predominated in this area for almost 30 years since DIOP ligand was introduced by Dang and Kagan.[3] However, this situation has changed recently. It was Fiaud who reported in 1999 a rhodium complex of chiral monodentate ligand 1,2,5-triphenylphospholane **1**, achieving 82% ee in the hydrogenation of (*Z*)-2-acetaminocinnamic ester.[4] After that, several efficient chiral monodentate phosphorus ligands including BINOL-based phosphonites **2**,[5] phosphites **3**,[6] and phosphoramidites **4**[7] emerged (Scheme 1). With monodentate phosphorus ligands, extremely high enantioselectivities have been obtained in asymmetric hydrogenation of functional olefins.[8] We have recently developed a new class of phosphoramidite, SIPHOS, **5** containing a chiral 1,1′-spirobiindane-7,7′-diol backbone, and proved they were highly effective ligands in the rhodium-catalyzed asymmetric hydrogenations of itaconic acid, α-dehydroamino acid derivatives, and enamides.[9] It is of interest to study the substituent effect of SIPHOS ligand on the enantioselectivity. Herein we describe the synthesis of 4,4′-substituted SIPHOS ligands **6** and their applications in rhodium-catalyzed asymmetric hydrogenations.

2. Results and discussion

Ligands **6** were conveniently synthesized in good yields from enantiomerically pure (*S*)-1,1′-spirobiindane-7,7′-



1 2 3 4 5

Scheme 1.

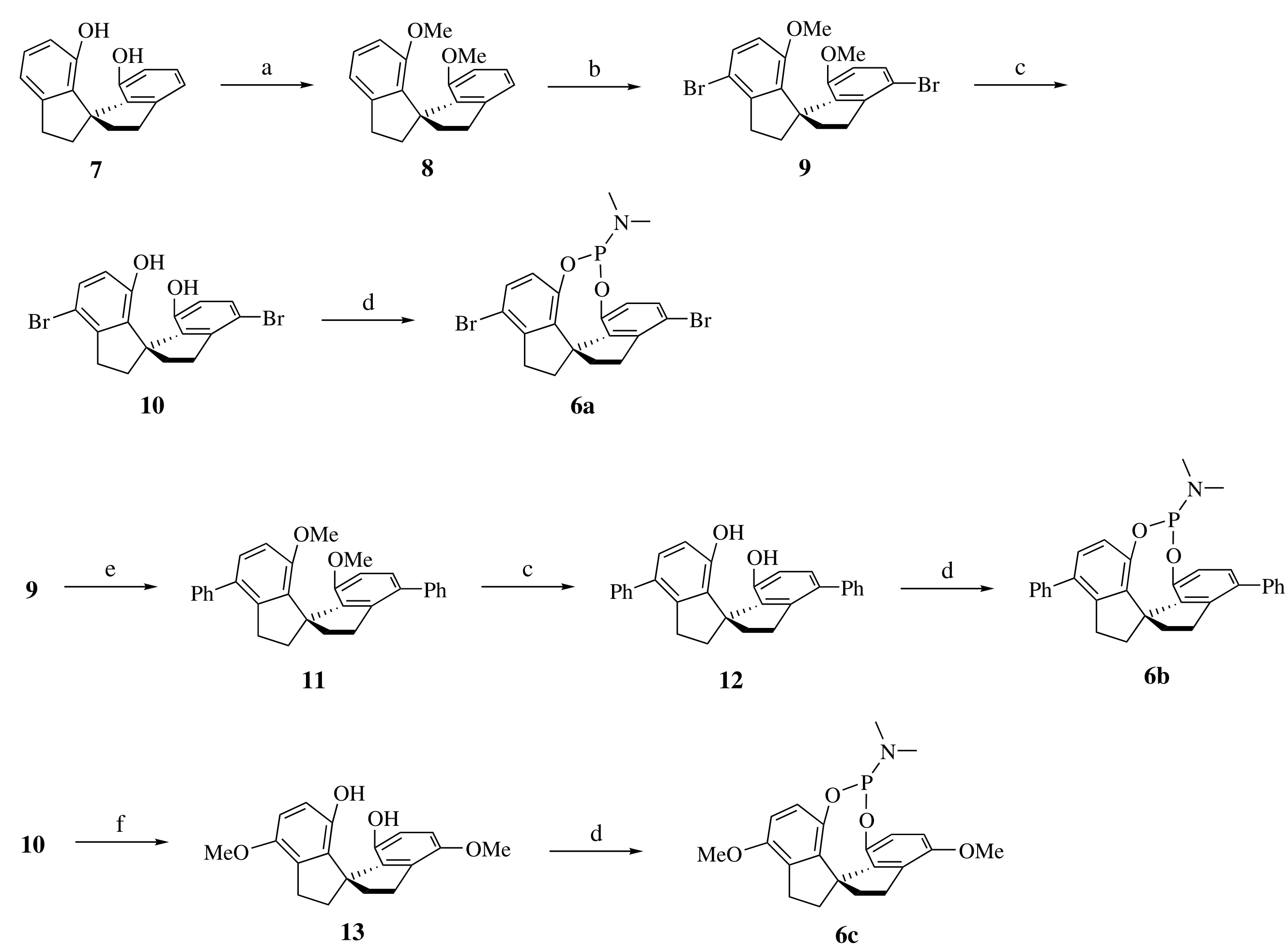
* Corresponding author. E-mail: qlzhou@nankai.edu.cn

0957-4166/$ - see front matter © 2003 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2003.08.017

diol [(*S*)-SPINOL] **7** which was easily prepared from 3-methoxybenzaldehyde[10] (Scheme 2). Thus, the protection of hydroxy groups of (*S*)-SPINOL, followed by bromination with NaBr in the presence of hydrogen peroxide provided compound **9** in nearly quantitative yield. Deprotection of hydroxy groups with boron tribromide in 92% yield and condensation with HMPT in refluxing toluene gave ligand (*S*)-DiBr-SIPHOS **6a** in 83% yield.[11] Ligand (*S*)-DiPh-SIPHOS **6b** was prepared by Suzuki coupling of compound **9** with phenylboronic acid catalyzed by $Pd(PPh_3)_4$,[12] deprotection of hydroxy group, and treatment with HMPT in 41% yield for three steps. Ligand (*S*)-DiMeO-SIPHOS **6c** was produced by methoxylation of compound **10** with NaOMe in the presence of CuCl and condensation with HMPT in 63% yield for two steps.[13]

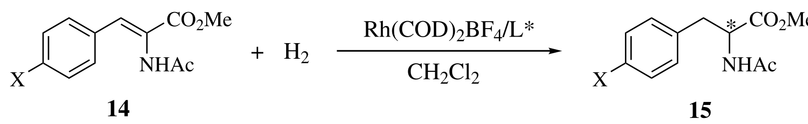
Rhodium-catalyzed asymmetric hydrogenation of α-dehydroamino esters and enamides were chosen to evaluate the substituent effect in ligands **6**. The hydrogenation of methyl 2-acetamidocinnamate **14a** was carried out in CH_2Cl_2 at 0°C under ambient H_2 pressure in the presence of 1 mol% catalyst formed in situ from $[Rh(COD)_2BF_4]$ and phosphoramidite ligands **6** (Rh/L = 1:2). As shown in Table 1, all 4,4′-substituted SIPHOS ligands **6** gave the rates which are similar to that with SIPHOS ligand **5**. Ligands 4,4′-dibromo-SIPHOS **6a** and 4,4′-diphenyl-SIPHOS **6b** produced hydrogenation product **14a** in 98.2% ee and 97.5% ee, respectively (entries 2 and 3), which are close to that obtained with ligand **5** (entry 1). In hydrogenations of other substituted 2-acetamidocinnamic esters **14b–d**, ligands **6a** and **6b** were also found to have similar enantioselectivities and rates to SIPHOS. However, 4,4′-dimethoxy-SIPHOS ligand **6c** provided somewhat lower enantioselectivities in the hydrogenations of all four 2-acetamidocinnamic esters, showing that the substitutions of electron-donating group at 4,4′-positions decreased the level of asymmetric reduction of SIPHOS ligands. In 2-acetamidocinnamic esters tested in hydrogenation, methyl 4′-methoxy-2-acetamidocinnamate **14c** gave lower rates and enantioselectivities than other substrates (entries 9–12).

Rhodium-catalyzed hydrogenation of enamides was performed in toluene at 50 atm of hydrogen. The



Scheme 2. Synthesis of 4,4′-substituted SIPHOS ligands. *Reagents and conditions*: (a) MeI, KOH, TBAB, CH_2Cl_2, rt, 5 h, quantitative; (b) NaBr, H_2O_2, HOAc, rt, 24 h, 98%; (c) BBr_3, CH_2Cl_2, −78°C to rt, 12 h, 92%; (d) HMPT, toluene, reflux, 3 h, 83% for **6a**, 75% for **6b**, 90% for **6c**; (e) $PhB(OH)_2$, $Pd(PPh_3)_4$, Na_2CO_3/H_2O, DME, reflux, 20 h, 65%; (f) NaOMe, CuCl, DMF, 120°C, 12 h, 70%.

Table 1. Rhodium-catalyzed asymmetric hydrogenation of 2-acetamidocinnamic esters[a]



Entry	Subs.	L*	Time (h)[b]	E.e. (%)[c]	Config.[d]
1	**14a** (X=H)	(*S*)-SIPHOS **5**	10	97.8	*S*
2	**14a** (X=H)	(*S*)-DiBr-SIPHOS **6a**	6	98.2	*S*
3	**14a** (X=H)	(*S*)-DiPh-SIPHOS **6b**	10	97.5	*S*
4	**14a** (X=H)	(*S*)-DiMeO-SIPHOS **6c**	8	96.5	*S*
5	**14b** (X=Cl)	(*S*)-SIPHOS **5**	8	98.8	*S*
6	**14b** (X=Cl)	(*S*)-DiBr-SIPHOS **6a**	6	98.5	*S*
7	**14b** (X=Cl)	(*S*)-DiPh-SIPHOS **6b**	10	98.0	*S*
8	**14b** (X=Cl)	(*S*)-DiMeO-SIPHOS **6c**	8	97.5	*S*
9	**14c** (X=OMe)	(*S*)-SIPHOS **5**	12	95.6	*S*
10	**14c** (X=OMe)	(*S*)-DiBr-SIPHOS **6a**	20	95.3	*S*
11	**14c** (X=OMe)	(*S*)-DiPh-SIPHOS **6b**	14	94.5	*S*
12	**14c** (X=OMe)	(*S*)-DiMeO-SIPHOS **6c**	12	93.7	*S*
13	**14d** (X=NO_2)	(*S*)-SIPHOS **5**	4	99.1	*S*
14	**14d** (X=NO_2)	(*S*)-DiBr-SIPHOS **6a**	4	98.7	*S*
15	**14d** (X=NO_2)	(*S*)-DiPh-SIPHOS **6b**	8	99.1	*S*
16	**14d** (X=NO_2)	(*S*)-DiMeO-SIPHOS **6c**	4	97.1	*S*

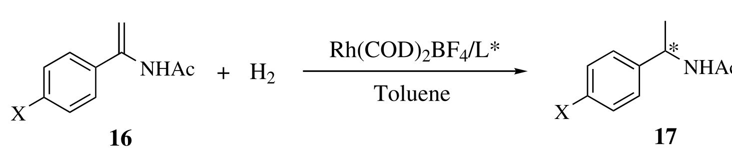
[a] The reactions were performed with 1 mol% of catalyst at 0°C under 1 atm of H_2. Yields were quantitative.
[b] Time for 100% conversion.
[c] Determined by chiral GC using Chrompack Chirasil-L-Val column.
[d] Assigned by comparing the specific rotation with reported values.

results were summarized in Table 2. Same as in the hydrogenation of α-dehydroamino esters, phosphoramidites **6a** and **6b** behaved very similar to their parental SIPHOS ligand, achieving high enantioselectivities in the hydrogenation of *N*-acetyl-α-arylenamides, although the rates were slower. In the hydrogenation of all three enanmides studied ligand **6c** once again afforded slightly lower enantioselectivities (by 3–4% ee) compared to SIPHOS ligand **5**.

3. Conclusion

We have developed a convenient method to introduce

Table 2. Rhodium-catalyzed asymmetric hydrogenation of enamides[a]



Entry	Subs.	L*	Time (h)[b]	E.e. (%)[c]	Config.[d]
1	**16a** (X=H)	(*S*)-SIPHOS **5**	24	98.0	*S*
2	**16a** (X=H)	(*S*)-DiBr-SIPHOS **6a**	30	97.1	*S*
3	**16a** (X=H)	(*S*)-DiPh-SIPHOS **6b**	30	97.7	*S*
4	**16a** (X=H)	(*S*)-DiMeO-SIPHOS **6c**	24	95.0	*S*
5	**16b** (X=Cl)	(*S*)-SIPHOS **5**	24	98.1	*S*
6	**16b** (X=Cl)	(*S*)-DiBr-SIPHOS **6a**	30	98.6	*S*
7	**16b** (X=Cl)	(*S*)-DiPh-SIPHOS **6b**	30	98.0	*S*
8	**16b** (X=Cl)	(*S*)-DiMeO-SIPHOS **6c**	24	93.7	*S*
9	**16c** (X=Me)	(*S*)-SIPHOS **5**	24	99.0	*S*
10	**16c** (X=Me)	(*S*)-DiBr-SIPHOS **6a**	30	97.8	*S*
11	**16c** (X=Me)	(*S*)-DiPh-SIPHOS **6b**	30	97.8	*S*
12	**16c** (X=Me)	(*S*)-DiMeO-SIPHOS **6c**	24	95.4	*S*

[a] The reactions were performed at 0°C in toluene, PH_2=50 atm. Yields were quantitative.
[b] Time for 100% conversion.
[c] Determined by chiral GC using Chrompack Chirasil-L-Val column.
[d] Determined by comparing the specific rotation with the reported values.

different substituents into 4,4′-positions of 1,1′-spirobiindane-7,7′-diols and related monodentate spiro phosphoramidite ligands. Ligands having electron-withdrawing bromo groups and conjugated phenyl groups displayed similar enantioselectivities and rates to SIPHOS ligand in the hydrogenation of α-dehydroamino esters and enamides. Introductions of electron-donating methoxy groups into SIPHOS reduced the enantioselectivity of ligands. These findings provided useful information for the design of new SPINOL-based ligands, which is ongoing in our laboratory.

4. Experimental

4.1. General

Toluene, DME, and THF were distilled from sodium–benzophenone ketyl under argon. Methylene chloride, ethyl acetate and DMF were distilled from CaH_2. 1,1′-Spirobiindane-7,7′-diol was prepared and resolved by previously reported methods.[10]

4.2. (*S*)-7,7′-Dimethoxy-1,1′-spirobiindane (*S*)-8

A mixture of (*S*)-**7** (1.0 g, 3.96 mmol), MeI (5.7 g, 39.60 mmol), tetrabutylammonium bromide (TBAB, 0.2 g, 0.62 mmol) and 20 mL of 3.5 M aqueous solution of potassium hydroxide was stirred for 5 h. The organic layer was separated and the water phase was extracted with CH_2Cl_2 (2×20 mL). The organic phases were combined and dried over anhydrous $MgSO_4$ and concentrated. The residue was chromatographed on silica gel column eluting with petroleum ether/EtOAc (5:1) to give compound **8** (1.16 g, 100%) as a white solid. Mp 153–154°C. $[\alpha]_D^{25}$ −40 (*c* 0.5, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ 7.16–7.11 (m, 2H), 6.87–6.84 (m, 2H), 6.62 (d, $J=8.4$ Hz, 2H), 3.53 (s, 6H), 3.06–2.98 (m, 4H), 2.35–2.28 (m, 2H), 2.20–2.16 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.5, 143.3, 136.9, 127.5, 116.8, 108.6, 59.2, 55.2, 38.8, 31.6. MS (*m*/*z*, %): 280 (M^+, 100). Anal. calcd for $C_{19}H_{20}O_2$: C, 81.04, H, 7.19. Found: C, 80.87, H, 7.24.

4.2.1. (*S*)-4,4′-Dibromo-7,7′-dimethoxy-1,1′-spirobiindane (*S*)-9.
To a suspension of (*S*)-**8** (330 mg, 1.2 mmol) and NaBr (247.8 mg, 2.4 mmol) in 7.2 mL glacial acetic acid, H_2O_2 (1.7 g, 14.7 mmol) was added dropwise at rt. The reaction mixture was stirred for 24 h, then diluted with 50 mL H_2O and extracted with EtOAc (3×30 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated. The residue was chromatographed on silica gel column eluting with petroleum ether/EtOAc (10:1) to afford compound **9** (506 mg, 98%) as a white solid. Mp 157–158°C. $[\alpha]_D^{25}$ +26 (*c* 0.5, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ 7.26 (d, $J=8.7$ Hz, 2H), 6.52 (d, $J=8.4$ Hz, 2H), 3.52 (s, 6H), 3.06–2.94 (m, 4H), 2.33–2.26 (m, 2H), 2.20–2.16 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.5, 144.8, 138.8, 130.3, 110.4, 61.8, 55.3, 37.8, 33.1. MS (*m*/*z*, %): 438 (M^+, 100). Anal. calcd for $C_{19}H_{18}Br_2O_2$: C, 52.08, H, 4.14. Found: C, 51.69, H, 4.43.

4.3. (*S*)-4,4′-Dibromo-7,7′-dihydroxy-1,1′-spirobiindane (*S*)-10

To a dried Schlenk tube equipped with septum and stirring bar (*S*)-**9** (300 mg, 0.69 mmol) was added. After two vacuum/nitrogen cycles, 3 mL CH_2Cl_2 was added by syringe. The solution was cooled to −78°C, treated with BBr_3 (156 μl, 1.7 mmol) in 2 mL CH_2Cl_2 and allowed to warm to rt. After stirring overnight, the reaction mixture was diluted with CH_2Cl_2 and washed sequentially with saturated $NaHSO_3$, $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was chromatographed on silica gel column eluting with petroleum ether/EtOAc (4:1) to provide compound **10** (260 mg, 92%) as a colorless oil which solidified slowly by standing. $[\alpha]_D^{25}$ +184 (*c* 0.5, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ 7.30 (d, $J=9.0$ Hz, 2H), 6.59 (d, $J=9.0$ Hz, 2H), 4.55 (s, 2H), 3.07–2.98 (m, 4H), 2.32–2.17 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.0, 145.4, 132.4, 116.5, 110.9, 60.3, 36.7, 32.7. MS (*m*/*z*, %): 410 (M^+, 100). HR-MS (FAB) calcd for $C_{17}H_{14}Br_2O_2$: 407.9360. Found: 407.9365.

4.4. (*S*)-4,4′-Diphenyl-7,7′-dimethoxy-1,1′-spirobiindane (*S*)-11

The suspension of $Pd(PPh_3)_4$ (78.9 mg, 0.14 mmol) and (*S*)-**9** (1.0 g, 2.28 mmol) in 10 mL anhydrous DME was stirred for 10 min at rt, then phenylboronic acid (0.98 g, 8.0 mmol) in a minimum of EtOH and aqueous Na_2CO_3 (2.0 M solution, 4.5 mL, 9.0 mmol) were added. The reaction mixture was refluxed for 20 h, cooled and filtrated. The filtrate was evaporated to dryness and the residue was resolved in CH_2Cl_2 and washed with saturated brine, dried over anhydrous Na_2SO_4 and concentrated. The residue was chromatographed on silica gel column eluting with petroleum ether/CH_2Cl_2 (4:1) to give (*S*)-**11** (650 mg, 65%) as a pale yellow solid. The compound was further purified by recrystallization from petroleum ether/EtOAc (7:1). Mp 220–221°C. $[\alpha]_D^{25}$ +6 (*c* 0.5, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ 7.50–7.18 (m, 12H), 6.74 (d, $J=8.1$ Hz, 2H), 3.60 (s, 6H), 3.12–3.08 (m, 4H), 2.38–2.31 (m, 2H), 2.26–2.20 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.1, 143.1, 141.8, 137.3, 131.0, 128.9, 128.4, 126.5, 109.5, 59.9, 55.5, 38.8, 31.9. MS (*m*/*z*, %): 432 (M^+, 100). Anal. calcd for $C_{31}H_{28}O_2$: C, 86.08, H, 6.52. Found: C, 85.86, H, 6.49.

4.5. (*S*)-4,4′-Diphenyl-7,7′-dihydroxy-1,1′-spirobiindane (*S*)-12

By the same procedure as that for (*S*)-**10**, compound (*S*)-**12** was synthesized from (*S*)-**11** (265 mg, 0.61 mmol) as a needle-like pale yellow crystal (210 mg, 85% from ethanol and EtOAc). Mp 192–193°C. $[\alpha]_D^{25}$ +142 (*c* 0.5, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ 7.47–7.24 (m, 14H), 6.81 (d, $J=8.1$ Hz, 2H), 4.75 (s, 2H), 3.20–3.00 (m, 4H), 2.44–2.18 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.2, 143.2, 140.6, 131.7, 130.6, 130.3, 128.5, 128.3, 126.6, 115.0, 57.8, 37.2, 31.3. MS (*m*/*z*,

%): 404 (M^+, 100). HR-MS (FAB) calcd for $C_{29}H_{24}O_2$: 404.1776. Found: 404.1776.

4.6. (*S*)-4,4′-Dimethoxy-7,7′-dihydroxy-1,1′-spirobiindane (*S*)-13

A 100 mL over dried Schlenk tube was flashed with nitrogen, charged with sodium (0.4 g, 18 mmol), and was added 5.5 mL methanol gently while stirring. After the sodium was completely dissolved, methanol was removed under vacuum. Then anhydrous CuCl (28 mg, 0.26 mmol), (*S*)-**10** (660 mg, 1.6 mmol) and dry DMF were added. After refluxed for 12 h with stirring at 120°C, the solvent was removed under vacuum. 20 mL cold water was then added with stirring to the residue in 15 min. The mixture was neutralized with 40 mL 2 N HCl to pH 2, stirred for another 15 min and extracted with chloroform (3×30 mL). The organic layers were combined and washed with brine, dried over anhydrous $MgSO_4$. After evaporation of solvent, the residue was chromatographed on silica gel column eluting with CH_2Cl_2 to afford (*S*)-**13** (350 mg, 70%) as a white solid. Mp 199–200°C. $[\alpha]_D^{25}$ −16 (*c* 0.5, CH_2Cl_2). ^1H NMR (200 MHz, $CDCl_3$): δ 6.66 (d, $J=1.9$ Hz, 4H), 4.26 (s, 2H), 3.80 (s, 6H), 3.19–2.97 (m, 4H), 2.29–2.19 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 146.7, 132.9, 132.4, 115.4, 114.8, 111.8, 111.2, 58.7, 56.0, 55.7, 37.7, 28.1, 28.0. MS (*m*/*z*, %): 312 (M^+, 100). Anal. calcd for $C_{19}H_{20}O_4$: C, 73.06, H, 6.45. Found: C, 72.92, H, 6.56.

4.7. (*S*)-*O*,*O*′-[4,4′-Dibromo-1,1′-spirobiindane-7,7′-diyl]-*N*,*N*-dimethylphosphoramidite (*S*)-6a

A mixture of (*S*)-**10** (410 mg, 1.0 mmol) and HMPT (0.3 mL, 1.5 mmol) in 5 mL dry toluene was heated at reflux under argon for 3 h. After cooling to rt, the mixture was concentrated and purified by chromatography on a silica gel column eluting with petroleum ether/EtOAc (15:1) to give (*S*)-**6a** as a white solid (400 mg, 83%). Mp 215.5–216°C. $[\alpha]_D^{25}$ −208 (*c* 0.5, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ 7.35–7.27 (m, 2H), 6.84 (d, $J=8.7$ Hz, 1H), 6.56 (d, $J=8.4$ Hz, 1H), 3.00–2.86 (m, 4H), 2.35 (d, $J=9.0$ Hz, 6H), 2.30–2.22 (m, 2H), 2.20–1.98 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.6, 147.5, 145.5, 144.9, 143.5, 142.2, 131.6, 131.4, 123.8, 123.4, 115.5, 114.8, 61.2, 37.6, 37.4, 35.6, 35.3, 32.4, 32.1. ^{31}P NMR (121 MHz, $CDCl_3$): δ 125.5. MS (*m*/*z*, %): 483 (M^+, 91), 60 (100). Anal. calcd for $C_{19}H_{18}Br_2NO_2P$: C, 47.23, H, 3.76, N, 2.90. Found: C, 47.23, H, 4.00, N, 3.04.

4.8. (*S*)-*O*,*O*′-[4,4′-Diphenyl-1,1′-spirobiindane-7,7′-diyl]-*N*,*N*-dimethylphosphoramidite (*S*)-6b

By the same procedure as that for (*S*)-**6a**, phosphoramidite (*S*)-**6b** was synthesized from (*S*)-**12** (404 mg, 1.0 mmol) as a white solid (358 mg, 75%). Mp 196.5–198°C. $[\alpha]_D^{25}$ −216 (*c* 0.5, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ 7.48–7.24 (m, 10H), 7.24–7.05 (m, 2H), 7.04 (d, $J=8.1$ Hz, 1H), 6.79 (d, $J=8.4$ Hz, 1H), 3.25–3.18 (m, 2H), 2.86–2.78 (m, 2H), 2.41 (d, $J=8.7$ Hz, 6H), 2.37–2.32 (m, 2H), 2.16–1.94 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.8, 145.5, 143.3, 142.7, 142.5, 141.3, 140.8, 140.7, 135.1, 134.7, 129.0, 128.8, 128.7, 128.6, 128.3, 128.2, 126.8, 122.4, 121.9, 121.8, 59.4, 38.3, 38.2, 35.6, 35.3, 31.1, 30.7. ^{31}P NMR (121 MHz, $CDCl_3$): δ 124.6. MS (*m*/*z*, %): 477 (M^+, 100). Anal. calcd for $C_{31}H_{28}NO_2P$: C, 77.97, H, 5.91, N, 2.93. Found: C, 77.83, H, 5.91, N, 2.94.

4.9. (*S*)-*O*,*O*′-[4,4′-Dimethoxy-1,1′-spirobiindane-7,7′-diyl]-*N*,*N*-dimethylphosphoramidite (*S*)-6c

By the same procedure as that for (*S*)-**6a**, phosporamidite (*S*)-**6c** was synthesized from (*S*)-**13** (190 mg, 0.6 mmol) as a white solid (200 mg, 90%). Mp 219-220°C. $[\alpha]_D^{25}$ −220 (*c* 0.5, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$): δ 6.91 (d, $J=9.0$ Hz, 1H), 6.72–6.62 (m, 3H), 3.83 (s, 6H), 2.87 (d, $J=7.2$ Hz, 4H), 2.34 (d, $J=9.3$ Hz, 6H), 2.30–2.10 (m, 2H), 2.06–1.85 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.9, 143.4, 142.2, 139.8, 132.9, 132.2, 122.3, 122.0, 110.0, 60.0, 55.7, 38.5, 38.3, 35.8, 35.5, 27.7, 27.4, 1.2. ^{31}P NMR (121 MHz, $CDCl_3$): δ 125.3. MS (*m*/*z*, %): 385 (M^+, 100). Anal. calcd for $C_{21}H_{24}NO_4P$: C, 65.45, H, 6.28, N, 3.63. Found: C, 65.45, H, 6.31, N, 3.53.

4.10. General procedure for asymmetric hydrogenation of methyl 2-acetamidocinnamates

To a Schlenk tube equipped with septum and stirring bar 2.0 mg (5 μmol) of $Rh(COD)_2BF_4$, 11 μmol of ligand and 0.5 mmol of substrate were added. After three vacuum/hydrogen cycles, 5 mL of solvent was added by a syringe and the reaction mixture was left stirring at 0°C under ambient H_2 pressure till the reaction was completed. The resulting mixture was filtered through a short silica gel column and concentrated under reduced pressure to give hydrogenation product in quantitative yield. The ee value of product was determined by chiral GC. The analytic conditions are as follows.

2-Acetamido-3-phenylpropanoate: Chrompack Chirasil-L-Val column (25 m×0.25 mm i.d.), programmed to increase at 4°C/min from 90°C to 190°C, $T_R=17.60$ and 18.34 min.

2-Acetamido-3-(4-chlorophenyl)propanoate: Chrompack Chirasil-L-Val column (25 m×0.25 mm i.d.), at 160°C constant, $T_R=13.79$ and 15.53 min.

2-Acetamido-3-(4-methoxylphenyl)propanoate: Chrompack Chirasil-L-Val (25 m×0.25 mm i.d.), at 160°C constant, $T_R=16.48$ and 18.34 min.

2-Acetamido-3-(4-nitrophenyl)propanoate: Chrompack Chirasil-L-Val (25 m×0.25 mm i.d.), programmed to increase at 2°C/min from 160 to 200°C, then at constant 200°C, $T_R=19.71$ and 20.62 min.

4.11. General procedure for asymmetric hydrogenation of 1-arylethenyl acetamides

1-Arylethenyl acetamide (0.5 mmol), $[Rh(COD)_2]BF_4$ (2.0 mg, 5 μmol) and 11 μmol of ligand were mixed together in autoclave in glove box, 5 mL of anhydrous toluene was introduced under nitrogen. After three vacuum/hydrogen cycles, the hydrogenation was performed at 0°C under 50 atm of hydrogen till complete conversion. The hydrogen pressure was released and reaction mixture was passed through a short silica gel column using petroleum ether/EtOAc (1:1 to 1:3) as eluent. After removal of solvent, the hydrogenation product was obtained in quantitative yield. The ee of product was determined by chiral GC. The analytic conditions are as follows.

1-Phenylethenyl acetamide: Chrompack Chirasil-L-Val (25 m×0.25 mm i.d.), programmed to increase at 1°C/min from 120 to 160°C, $T_R = 7.85$ and 8.49 min.

1-(4-Chlorophenyl)ethenyl acetamide: Chrompack Chirasil-L-Val (25 m×0.25 mm i.d.), at 150°C constant, $T_R = 12.26$ and 13.06 min.

1-(4-Methylphenyl)ethenyl acetamide: Chrompack Chirasil-L-Val (25 m×0.25 mm i.d.), at 130°C constant, $T_R = 15.31$ and 16.49 min.

Acknowledgements

Financial supports from the National Natural Science Foundation of China, the Major Basic Research Development Program (grant No. G2000077506), the Ministry of Education of China are gratefully acknowledged.

References

1. Knowles, W.; Sabacky, M. *J. Chem. Soc., Chem. Commun.* **1968**, 1445.
2. Horner, L.; Siegel, H.; Buthe, H. *Angew. Chem., Int. Ed.* **1968**, *7*, 942.
3. (a) Dang, T.-P.; Kagan, H. B. *J. Chem. Soc., Chem. Commun.* **1971**, 481; (b) Kagan, H. B.; Dang, T.-P. *J. Am. Chem. Soc.* **1972**, *94*, 6429.
4. Guillen, F.; Fiaud, J.-C. *Tetrahedron Lett.* **1999**, *40*, 2939.
5. Claver, C.; Fernandez, E.; Gillon, A.; Heslop, K.; Hyett, D. J.; Martorell, A.; Orpen, A. G.; Pringle, P. G. *Chem. Commun.* **2000**, 961.
6. (a) Reetz, M. T.; Sell, T. *Tetrahedron Lett.* **2000**, *41*, 6333; (b) Reetz, M. T.; Mehler, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 3889.
7. (a) Van den Berg, M.; Minnaard, A. J.; Schudde, E. P.; van Esch, J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *J. Am. Chem. Soc.* **2000**, *122*, 11539; (b) Van den Berg, M.; Haak, R. M.; Minnaard, A. J.; de Vries, A. H. M.; de Vries, J. G.; Feringa, B. L. *Adv. Synth. Catal.* **2002**, *334*, 1003.
8. (a) Komarov, I. V.; Borner, A. *Angew. Chem., Int. Ed.* **2001**, *40*, 1197; (b) Chen, W.; Xiao, J. *Tetrahedron Lett.* **2001**, *42*, 2897; (c) Zeng, Q.; Liu, H.; Mi, A.; Jiang, Y. Z.; Li, X. S.; Choi, M. C. K.; Chan, A. S. C. *Tetrahedron: Asymmetry* **2002**, *13*, 115; (d) Zeng, Q.; Liu, H.; Mi, A.; Jiang, Y.; Li, X. S.; Choi, M. C. K.; Chan, A. S. C. *Tetrahedron* **2002**, *58*, 8799; (e) Junge, K.; Oehme, G.; Monsees, A.; Riermeier, T.; Dingerdissen, U.; Beller, M. *Tetrahedron Lett.* **2002**, *43*, 4977; (f) Jia, X.; Guo, R.; Li, X.; Yao, X.; Chan, A. S. C. *Tetrahedron Lett.* **2002**, *43*, 5541; (g) Jia, X.; Li, X.; Xu, L.; Shi, Q.; Yao, X.; Chan, A. S. C. *J. Org. Chem.* **2003**, *68*, 4539.
9. (a) Fu, Y.; Xie, J.-H.; Hu, A.-G.; Zhou, H.; Wang, L.-X.; Zhou, Q.-L. *Chem. Commun.* **2002**, 480; (b) Hu, A.-G.; Fu, Y.; Xie, J.-H.; Zhou, H.; Wang, L.-X.; Zhou, Q.-L. *Angew. Chem., Int. Ed.* **2002**, *41*, 2348.
10. (a) Birman, V. B.; Rheingold, A. L.; Lam, K.-C. *Tetrahedron: Asymmetry* **1999**, *10*, 125; (b) Zhang, J.-H.; Liao, J.; Cui, X.; Yu, K.-B.; Deng, J.-G.; Zhu, S.-F.; Wang, L.-X.; Zhou, Q.-L.; Chung, L.-W.; Ye, T. *Tetrahedron: Asymmetry* **2002**, *13*, 1363.
11. Zhou, H.; Wang, W.-H.; Fu, Y.; Xie, J.-H.; Shi, W.-J.; Wang, L.-X.; Zhou, Q.-L. *J. Org. Chem.* **2003**, *68*, 1582.
12. Alo, B. I.; Kandil, A.; Patil, P. A.; Sharp, M. J.; Siddiqui, M. A.; Snieckus, V.; Josephy, P. D. *J. Org. Chem.* **1991**, *56*, 3763.
13. Chen, W.-M. *Indian J. Chem., Sect. B.* **1996**, *10*, 1085.