Asymmetric Synthesis of Axially Chiral Biaryls by Nickel-Catalyzed Grignard Cross-Coupling of Dibenzothiophenes

Yong-Hwan Cho, Asato Kina, Toyoshi Shimada, and Tamio Hayashi*

Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo, Kyoto 606-8502, Japan

thayashi@kuchem.kyoto-u.ac.jp

Supporting Information

Experimental procedures for the determination of absolute configurations of the compounds 9am, 9an, and 19. S2-S5

Figure 1. Variable-temperature $^{31}$P NMR spectra of 21. S6
Determination of Absolute Configuration of 2,2'-Bis(4-methylphenyl)-6,6'-dimethyl-1,1'-biphenyl (9am).

(a) Preparation of an Authentic Sample, (S)-(+)-9am: The starting material, (S)-2,2'-bis(trifluoromethanesulfonyloxy)-6,6'-dimethyl-1,1'-biphenyl was prepared by the triflation of (S)-2,2'-dihydroxy-6,6'-dimethyl-1,1'-biphenyl\(^1\) with triflic anhydride and pyridine in 1,2-dichloroethane (96% yield). To a solution of the bis(triflate) (0.60 g, 1.2 mmol) and PdCl\(_2\)(dppf) (0.3 g, 0.3 mmol) in dry THF (50 mL) was slowly added 4-methylphenylzinc chloride solution which is a white slurry prepared from 4-methylphenylmagnesium bromide and ZnCl\(_2\) in THF (6.1 mL, 8.1 mmol) at 0 °C. The mixture was refluxed for 48 h. When the reaction was confirmed to be completed by a TLC analysis, the mixture was quenched with water at 0 °C. It was diluted with diethyl ether and the organic layer was washed with 10% HCl and brine. The organic layer was dried over anhydrous MgSO\(_4\) and evaporated under reduced pressure. Silica gel column chromatography (hexane/ethyl acetate = 98/2) gave 0.30 g (72% yield) of (S)-2,2'-bis(4-methylphenyl)-6,6'-dimethyl-1,1'-biphenyl (9am): \([\alpha]^{20}_D\) +75 (c 1.0, chloroform) for 9am of 97% ee; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 2.04 (s, 6H), 2.23 (s, 6H), 6.62 (d, \(J=8.0\) Hz, 4H), 6.83 (d, \(J=8.0\) Hz, 4H), 7.06 (d, \(J=7.6\) Hz, 2H), 7.13 (d, \(J=7.6\) Hz, 2H), 7.19 (t, \(J=7.6\) Hz, 2H); \(^{13}\)C NMR (CDCl\(_3\)) \(\delta\) 20.5, 21.0, 127.1, 127.8, 127.9, 128.6, 129.0, 135.5, 136.8, 138.2, 138.7, 141.1; Anal. Calcd for C\(_{28}\)H\(_{26}\): C, 92.77; H, 7.23. Found: C, 92.47; H, 7.35.

(b) Cross-Coupling of 8am with 4-Methylphenylmagnesium Bromide in the Presence of Ni(acac)\(_2\): To a solution of (S)-8am (81% ee, 100 mg, 0.33 mmol) and Ni(acac)\(_2\) (25 mg, 0.10 mmol) in dry benzene (6 mL) was added 4-methylphenylmagnesium bromide in Et\(_2\)O (2.6 mL, 3.3 mmol) at 0 °C. The reaction mixture was allowed to stir at 80 °C for 12 h and quenched with H\(_2\)O. It was diluted with CHCl\(_3\) and the organic layer was washed with 10% HCl, saturated aqueous NaHCO\(_3\), and aqueous sodium chloride. The organic layer was dried over anhydrous MgSO\(_4\) and evaporated under reduced pressure. Silica gel preparative thin layer chromatography (hexane/ethyl acetate = 98/2) gave 86 mg (72% yield, 81% ee) of (S)-
2,2'-bis(4-methylphenyl)-6,6'-dimethyl-1,1'-biphenyl (9am): [α]$_{20}^{D}$ +43 (c 1.0, chloroform) for 8am of 74% ee.

**Determination of Absolute Configuration of 2,2'-Diphenyl-6,6'-dimethyl-1,1'-biphenyl (9an).**

(a) **Preparation of an Authentic Sample, (S)-(+)9an:** (S)-2,2'-Diphenyl-6,6'-dimethyl-1,1'-biphenyl (9an) was prepared from (S)-2,2'-dihydroxy-6,6'-dimethyl-1,1'-biphenyl in a similar manner to the preparation of (S)-2,2'-bis(4-methylphenyl)-6,6'-dimethyl-1,1'-biphenyl (9am). [α]$_{20}^{D}$ +15 (c 0.8, chloroform) for 9an of 97% ee; 1H NMR (CDCl$_3$) δ 2.12 (s, 6H), 6.63 (d, $J$ = 7.4 Hz, 4H), 7.00 (t, $J$ = 7.5 Hz, 4H), 7.04 (d, $J$ = 7.4 Hz, 2H), 7.07 (t, $J$ = 7.5 Hz, 2H), 7.19 (d, $J$ = 7.4 Hz, 2H), 7.22 (t, $J$ = 7.5 Hz, 2H); 13C NMR (CDCl$_3$) δ 20.4, 125.9, 127.0, 127.2, 127.8, 128.7, 129.1, 137.0, 138.0, 141.1, 141.5; Anal. Calcd for C$_{26}$H$_{22}$: C, 93.37; H, 6.63. Found: C, 93.07; H, 6.72.

(b) **Cross-Coupling of 8an with Phenylmagnesium Bromide in the Presence of Ni(acac)$_2$:** To a solution of (S)-8an (81% ee, 12 mg, 0.04 mmol) and Ni(acac)$_2$ (3.2 mg, 0.01 mmol) in dry benzene (2 mL) was added phenylmagnesium bromide in THF (0.50 mL, 0.41 mmol) at 0 °C. The reaction mixture was allowed to stir at 80 °C for 12 h and quenched with H$_2$O at 0 °C. It was diluted with CHCl$_3$ and the organic layer was washed with 10% HCl, saturated NaHCO$_3$, and brine. The organic layer was dried over anhydrous MgSO$_4$ and evaporated under reduced pressure. Silica gel preparative thin layer chromatography (hexane/ethyl acetate = 98/2) gave 12 mg (87% yield) of (S)-2,2'-diphenyl-6,6'-dimethyl-1,1'-biphenyl (9an): [α]$_{20}^{D}$ +13 (c 1.0, chloroform) for 9an of 81% ee.

(c) **Cross-Coupling of 8cq with Methylmagnesium Iodide in the Presence of Ni(acac)$_2$:** To a solution of (S)-8cq (53% ee, 55 mg, 0.16 mmol) and Ni(acac)$_2$ (12 mg, 0.05 mmol) in dry benzene (4 mL) was added methylmagnesium iodide in Et$_2$O (0.70 mL, 1.3 mmol) at 0 °C. The reaction mixture was allowed to stir at 80 °C for 12 h and quenched with H$_2$O. It was diluted with CHCl$_3$ and the organic layer was washed with 10% HCl, saturated NaHCO$_3$, and brine. The organic layer
was dried over anhydrous MgSO₄ and evaporated under reduced pressure. Silica gel preparative thin layer chromatography (hexane/ethyl acetate = 98/2) gave 32 mg (61% yield) of (R)-2,2'-diphenyl-6,6'-dimethyl-1,1'-biphenyl (9an): [α]²⁰D –8 (c 1.0, chloroform) for 9an of 53% ee.

**Determination of Absolute Configuration of 2-(4-Methylphenyl)-1,1'-binaphthyl (19).**

(a) **Preparation of an Authentic Sample, (S)-(+)−19, from (S)-2-Trifluoromethanesulfonxyloxy-1,1'-binaphthyl:** The starting material, (S)-2-trifluoromethanesulfonxyloxy-1,1'-binaphthyl was prepared from (R)-binaphthol according to the reported procedures.² To a solution of the triflate (0.41 g, 1.0 mmol) and NiCl₂(dppe)³ (54 mg, 0.10 mmol) in dry THF (20 mL) was slowly added 4-methylphenylmagnesium bromide in THF (3.1 mL, 5.1 mmol) at 0 °C. The mixture was allowed to stir at 65 °C for 12 h, and quenched with H₂O at 0 °C. It was diluted with ether and the organic layer was washed with 10% HCl, saturated NaHCO₃ solution, and brine. The organic layer was dried over anhydrous MgSO₄ and evaporated under reduced pressure. Silica gel column chromatography (hexane/ethyl acetate = 98/2) gave 0.16 mg (45% yield) of (S)-2-(4-methylphenyl)-1,1'-binaphthyl (19).⁴ [α]²⁰D +96 (c 0.4, chloroform) for 19 of >99% ee; ¹H NMR (CDCl₃) δ 2.17 (s, 3H), 6.82 (d, J = 8.1 Hz, 2H), 6.96 (d, J = 8.1 Hz, 2H), 7.20 (d, J = 8.5 Hz, 1H), 7.25 (m, 3H), 7.36 (d, J = 8.1 Hz, 1H), 7.39 (t, J = 8.5 Hz, 1H), 7.41 (d, J = 8.1 Hz, 1H), 7.44 (ddd, J = 8.1, 6.6, 1.5 Hz, 1H), 7.64 (d, J = 8.5 Hz, 1H), 7.80 (d, J = 8.2 Hz, 1H), 7.86 (d, J = 8.2 Hz, 1H), 7.93 (d, J = 8.2 Hz, 1H), 7.99 (d, J = 8.5 Hz, 1H).

(b) **Cross-Coupling of 10 with 4-Methylphenylmagnesium Bromide in the Presence of Ni(acac)₂:** To a solution of (S)-2-mercapto-1,1'-binaphthyl (10) (43% ee, 21 mg, 0.07 mmol) and Ni(acac)₂ (2.0 mg, 0.01 mmol) in dry benzene (3.0 mL) was added 4-methylphenylmagnesium bromide in THF (0.5 mL, 0.73 mmol) at 0 °C. The reaction mixture was allowed to stir at 80 °C for 10 h and quenched with H₂O. It was diluted with CHCl₃ and the organic layer was washed with
10% HCl, saturated NaHCO₃ solution, and brine. The organic layer was dried over anhydrous MgSO₄ and evaporated under reduced pressure. Silica gel preparative thin layer chromatography (hexane/ethyl acetate = 98/2) gave 19 mg (75% yield, 44% ee) of (S)-2-(4-methylphenyl)-1,1'-binaphthyl (19): [α]₂⁰D +65 (c 0.5, chloroform) for 19 of 44% ee.

(c) Preparation from (S)-2-Mercapto-2'- (4-methylphenyl)-1,1'-binaphthyl (8dm): To a solution of (S)-2-methylsufinyl-2'- (4-methylphenyl)-1,1'-binaphthyl (0.12 g, 0.30 mmol), obtained by methylation of the mercapto group in (S)-2-mercapto-2'- (4-methylphenyl)-1,1'-binaphthyl (8dm) followed by oxidation of the sulfide with mCPBA according to the procedures described for the preparation of 12, in dry THF (10 mL) was slowly added ethylmagnesium bromide in diethyl ether (1.8 mL, 3.0 mmol) at 0 °C. The resulting mixture was stirred at room temperature for 35 min and quenched with 10% HCl at 0 °C. It was diluted with ether and the organic layer was washed with 10% HCl and saturated NaHCO₃ solution and brine, was dried over anhydrous MgSO₄, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (hexane/ethyl acetate = 98/2) to give 92 mg (90% yield) of (R)-2-(4-methyphenyl)-1,1'-binaphthyl (19): [α]₂⁰D −88 (c 0.3, chloroform) for 19 of 95% ee.

References


Figure 1. Experimental variable-temperature \(^{31}\)P NMR (202 Hz, left) spectra of 21 in CDCl\(_3\), and computer simulation of \(^{31}\)P NMR spectra with exchange rate constants (right).