

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

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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'-biphenyl¹ 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 PdCl₂(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 ZnCl₂ 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 MgSO₄ 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**): [α]_D²⁰ +75 (*c* 1.0, chloroform) for **9am** of 97% ee; ¹H NMR (CDCl₃) δ 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); ¹³C NMR (CDCl₃) δ 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 C₂₈H₂₆: 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 Et₂O (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 H₂O. It was diluted with CHCl₃ and the organic layer was washed with 10% HCl, saturated aqueous NaHCO₃, and aqueous sodium chloride. 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 86 mg (72% yield, 81% ee) of (S)-

2,2'-bis(4-methylphenyl)-6,6'-dimethyl-1,1'-biphenyl (**9am**): $[\alpha]^{20}_{\text{D}} +43$ (*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'-biphenyl¹ in a similar manner to the preparation of (*S*)-2,2'-bis(4-methylphenyl)-6,6'-dimethyl-1,1'-biphenyl (**9am**). $[\alpha]^{20}_{\text{D}} +15$ (*c* 0.8, chloroform) for **9an** of 97% ee; ¹H NMR (CDCl₃) 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 (CDCl₃) 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 C₂₆H₂₂: 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 H₂O at 0 °C. It was diluted with CHCl₃ and the organic layer was washed with 10% HCl, saturated NaHCO₃, 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 12 mg (87% yield) of (*S*)-2,2'-diphenyl-6,6'-dimethyl-1,1'-biphenyl (**9an**): $[\alpha]^{20}_{\text{D}} +13$ (*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 Et₂O (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 H₂O. It was diluted with CHCl₃ and the organic layer was washed with 10% HCl, saturated NaHCO₃, 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 32 mg (61% yield) of (*R*)-2,2'-diphenyl-6,6'-dimethyl-1,1'-biphenyl (**9an**): $[\alpha]^{20}_{\text{D}} -8$ (*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-Trifluoromethanesulfonyloxy-1,1'-binaphthyl: The starting material, (*S*)-2-trifluoromethanesulfonyloxy-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 $\text{NiCl}_2(\text{dppe})^3$ (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 H_2O at 0 °C. It was diluted with ether and the organic layer was washed with 10% HCl, saturated NaHCO_3 solution, 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 0.16 mg (45% yield) of (*S*)-2-(4-methylphenyl)-1,1'-binaphthyl (**19**).⁴ $[\alpha]^{20}_{\text{D}} +96$ (*c* 0.4, chloroform) for **19** of >99% ee; ^1H NMR (CDCl_3) 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 $\text{Ni}(\text{acac})_2$: To a solution of (*S*)-2-mercapto-1,1'-binaphthyl (**10**) (43% ee, 21 mg, 0.07 mmol) and $\text{Ni}(\text{acac})_2$ (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 H_2O . It was diluted with CHCl_3 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]_D²⁰ +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 *m*CPBA 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-methylphenyl)-1,1'-binaphthyl (**19**): [α]_D²⁰ –88 (*c* 0.3, chloroform) for **19** of 95% ee.

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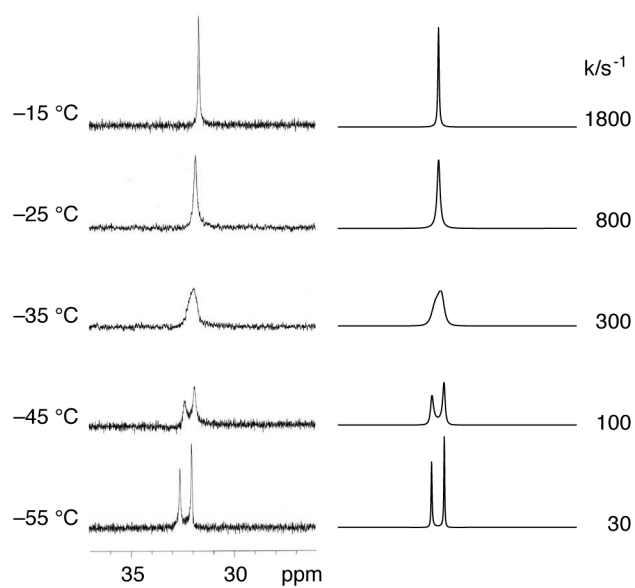


Figure 1. Experimental variable-temperature ^{31}P NMR (202 Hz, left) spectra of **21** in CDCl_3 , and computer simulation of ^{31}P NMR spectra with exchange rate constants (right).