

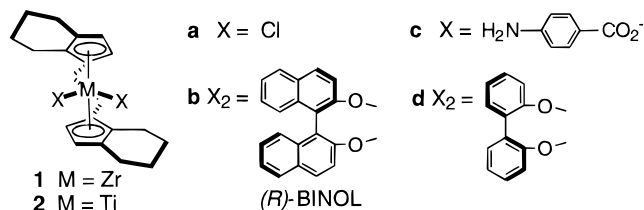
# Improved Procedure for the Preparation of Enantiomerically Pure Ethylenebis(tetrahydroindenyl)zirconium Derivatives

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Received October 8, 1996

Ethylenebis(tetrahydroindenyl)zirconocene complexes **1** have shown considerable utility in procedures that mediate and catalyze the enantioselective formation of carbon–carbon bonds.<sup>1</sup> Though it is possible to prepare enantiomerically pure **1** by resolution of the corresponding bis(*O*-acetyl mandelate) complex,<sup>2</sup> the more practical method involves the reaction of *rac*-**1a**<sup>3</sup> with the dilithio salt of optically pure 1,1'-binaphth-2-ol (BINOL) to yield 25–30% of optically pure **1b**.<sup>4</sup> This procedure is tedious, as it takes 3 days, and inefficient, as it wastes the unreacted enantiomer of **1a** that is lost or destroyed during the isolation procedure.



We recently disclosed a new method for the resolution of the titanium analogue **2** by simultaneous derivatization of *rac*-**2a** enantiomers to **2b** and **2c**, which could be separated by precipitation and filtration.<sup>5</sup> We now report an improved procedure for the preparation of both stereoisomers of **1**, **1b**, and **1d** in optically pure form from *rac*-**1a** (see Scheme 1). Analogous to the titanium procedure, the enantiomer of **1a** that is not converted to **1b** upon treatment with BINOL can be separated as the bis(4-aminobenzoate) complex **1c** by precipitation and filtration. In the present case, the lower stability of **1c** relative its titanium analogue to aqueous HCl necessitated the development of an alternative method for its derivatization. Complex **1c** is converted to the more stable **1d**,<sup>6</sup> which can be isolated by filtration followed by recrystallization.

In a typical procedure (Scheme 1), *rac*-ethylenebis(tetrahydroindenyl)zirconium dichloride, (*R,R,R*)-**1**,1'-binaphth-2-ol (0.5 equiv), 4-aminobenzoic acid (1.0 equiv), and NEt<sub>3</sub> (2.5 equiv) were stirred in CH<sub>2</sub>Cl<sub>2</sub> for 30 min. After addition of toluene and removal of the CH<sub>2</sub>Cl<sub>2</sub> *in vacuo*, hexane was added to induce the precipitation of (*S,S,S*)-**1c**. This solid was separated by filtration and washed with toluene and hexane to remove any trace (*R,R,R*)-**1b** (the absence of which was confirmed by <sup>1</sup>H NMR).

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(2) Schafer, A.; Karl, E.; Zsolnai, L.; Huttner, G.; Brintzinger, H. H. *J. Organomet. Chem.* **1987**, *328*, 87.

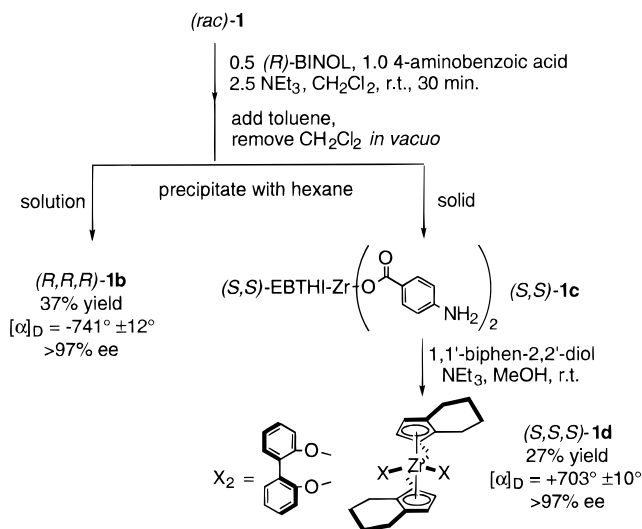
(3) Grossman, R. B.; Doyle, R. A.; Buchwald, S. L. *Organometallics* **1991**, *10*, 1501.

(4) (a) Grossman, R. B.; Davis, W. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1991**, *113*, 2321. (b) Wild, F. R. W. P.; Zsolnai, J.; Huttner, G.; Brintzinger, H. H. *J. Organomet. Chem.* **1982**, *232*, 233.

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(6) Habaue, S.; Sakamoto, H.; Okamoto, Y. *Chem. Lett.* **1996**, 383.

## Scheme 1



Evaporation of the filtrates followed by recrystallization yielded pure (*R,R,R*)-**1b**. Treatment of crude **1c** with 1,1'-biphen-2-ol and NEt<sub>3</sub> in MeOH gave (*S,S,S*)-**1d** as a white solid, which was isolated by filtration and recrystallized from MeOH and toluene. The ee of (*R,R,R*)-**1b** or (*S,S,S*)-**1d** were determined to be >97% by the <sup>1</sup>H NMR spectrum of their bis(*R*)-*O*-acetyl mandelate derivatives.<sup>2,4a</sup>

In summary, we have devised a single procedure that furnishes both enantiomers of **1** in enantiomerically pure form. The increased experimental simplicity of this protocol, relative to those previously reported, should lead to increased use of these enantiomerically pure zirconocene complexes. Future work will attempt to generalize this protocol to other metallocene derivatives.

## Experimental Section

**General Considerations.** All reactions were carried out under an atmosphere of Ar unless otherwise stated. Characterization was accomplished using instrumentation as previously described.<sup>5</sup> *rac*-**1a** was obtained from hydrogenation of *rac*-ethylene-1,2-bis(1-indenyl)zirconium dichloride<sup>3</sup> (Boulder Scientific Co., Mead, CO). (*R*)-1,1'-Binaphth-2-ol (Aldrich Chemical Co. and Strem Chemicals, Newburyport, MA), and all other reagents are commercially available and were used as received. Yields refer to isolated yields of products of greater than 95% purity as determined by <sup>1</sup>H NMR spectrometry and elemental analysis (E + R Microanalytical laboratory, Inc., Corona, NY).

**(*R,R*)-Ethylene-1,2-bis(η<sup>5</sup>-4,5,6,7-tetrahydro-1-indenyl)zirconium (*R*)-1,1'-Binaphth-2-olate, (*R,R,R*)-**1b**.** *rac*-Ethylene-1,2-bis(η<sup>5</sup>-4,5,6,7-tetrahydro-1-indenyl)zirconium dichloride (5.118 g, 12.0 mmol) was added to a solution of 4-aminobenzoic acid (1.646 g, 12.0 mmol), (*R*)-1,1'-binaphth-2-ol (1.735 g, 6.06 mmol), and triethylamine (4.2 mL, 30 mmol) in 100 mL of CH<sub>2</sub>Cl<sub>2</sub>. The reaction vessel was wrapped in aluminum foil to minimize exposure to light and stirred for 30 min at room temperature. Toluene (50 mL) was added, and the CH<sub>2</sub>Cl<sub>2</sub> was removed *in vacuo*. To the vigorously stirred solution was added hexane (200 mL) to precipitate **1c** as a white solid, which was isolated by filtration. The solid was stirred in toluene (50 mL) for 5 min, and hexane (200 mL) was added. The white solid was isolated again by filtration, checked for the absence of **1b** by <sup>1</sup>H NMR (CDCl<sub>3</sub>), and saved for the next step. The combined filtrates were concentrated *in vacuo* to give a yellow oil, which was dissolved in toluene (20 mL). MeOH (40 mL) was layered on top, and cooling at -20 °C gave yellow crystals of (*R,R*)-ethylene-1,2-bis(η<sup>5</sup>-4,5,6,7-tetrahydro-1-indenyl)zirconium (*R*)-1,1'-binaphth-2-olate (2.87 g, 37% yield, >97% ee): <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, TMS) δ 7.84 (d, 2H), 7.79 (d, 2H),

7.16–7.25 (m, 4H), 7.04 (td, 2H), 6.88 (d, 2H), 5.71 (d, 2H), 5.57 (d, 2H), 3.13–3.29 (m, 4H), 2.56–2.64 (m, 4H), 1.83 (m, 6H), 1.60 (m, 4H), 1.28 (m, 2H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  159.9, 134.9, 132.3, 130.4, 128.9, 128.6, 127.6, 126.7, 125.3, 123.2, 122.0, 122.0, 117.2, 113.8, 105.9, 27.6, 23.7, 22.6, 22.4, 22.1; IR (Nujol,  $\text{cm}^{-1}$ ) 1613 w, 1588 w, 1498 w, 1459 s, 1421 m, 1377 m, 1327 m, 1270 w, 1240 m, 1225 m, 1139 w, 1069 w, 987.8 w, 955.1 w, 855.6 w, 814.0 m, 784.1 m, 741.3 s, 579.9 m;  $[\alpha]_{\text{D}} = -741^\circ \pm 12^\circ$  ( $c = 0.085$  in  $\text{CH}_2\text{Cl}_2$ ) (lit.<sup>4a</sup> (*S,S,S*) isomer  $[\alpha]_{\text{D}} = +759^\circ$  ( $c = 0.08$  in  $\text{CH}_2\text{Cl}_2$ )). Anal. Calcd for  $\text{C}_{40}\text{H}_{36}\text{O}_2\text{Zr}$ : C, 75.08; H, 5.67. Found: C, 74.82; H 5.77. Derivatization of a small amount of (*R,R,R*)-**1b** to the bis-(*R*)-*O*-acetylmandelate complex formed only one diastereomer as determined by its  $^1\text{H}$  NMR spectrum, indicating that (*R,R,R*)-**1b** had an ee of >97%.<sup>2,4a</sup>

**(*S,S*)-Ethylene-1,2-bis( $\eta^5$ -4,5,6,7-tetrahydro-1-indenyl)zirconium (*S*)-1,1'-Biphen-2-olate, (*S,S,S*)-**1d**.**<sup>6</sup> The crude white solid from the first step of the above procedure was dissolved in MeOH (50 mL) in the air. A solution of 1,1'-biphen-2-ol (2.23 g, 12.0 mmol) and  $\text{NEt}_3$  (4.2 mL, 30 mmol) in MeOH (5 mL) was added. A white precipitate formed in 1 min, and water (20 mL) was added to complete the precipitation. The solid was isolated by filtration and dissolved in  $\text{CH}_2\text{Cl}_2$ . The organic phase was separated from the water trapped in the solid, dried over  $\text{MgSO}_4$ , and concentrated *in vacuo* to give a yellow oil. Crystallization was accomplished by layering MeOH (20 mL)

on top of a toluene solution (20 mL) of the yellow oil and cooling to  $-20^\circ\text{C}$ . Note: It is important *not* to heat the toluene to effect dissolution. This gave white crystals of (*S,S*)-ethylene-1,2-bis( $\eta^5$ -4,5,6,7-tetrahydro-1-indenyl)zirconium (*S*)-1,1'-biphen-2-olate (1.74 g, 27% yield):  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ , TMS)  $\delta$  7.2 (m, 4H), 6.85 (t, 2H), 6.70 (d, 2H), 5.70 (s, 4H), 3.3–3.1 (m, 4H), 2.57 (m, 4H), 2.05 (m, 4H), 1.47–1.85 (m, 6H), 1.45 (m, 2H);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ )  $\delta$  161.7, 131.9, 131.8, 130.3, 128.4, 128.3, 123.0, 119.2, 118.6, 114.6, 106.2, 27.4, 23.6, 22.8, 22.3, 22.3; IR (Nujol,  $\text{cm}^{-1}$ ) 1591 m, 1552 w, 1482 s, 1466 s, 1432 s, 1377 m, 1268 m, 1252 s, 1228 s, 1149 w, 1098 w, 1036 w, 1001 w, 863.6 s, 837.9 w, 802.0 s, 757.8 s, 733.4 m, 709.6 m, 618.9 s;  $[\alpha]_{\text{D}} = +703^\circ \pm 10^\circ$  ( $c = 0.101$  in  $\text{CH}_2\text{Cl}_2$ ). Anal. Calcd for  $\text{C}_{32}\text{H}_{32}\text{O}_2\text{Zr}$ : C, 71.20; H, 5.98. Found: C, 71.24; H 5.85. Derivatization of a small amount of (*S,S,S*)-**1d** to the bis(*R*)-*O*-acetyl mandelate complex formed only one diastereomer as determined by its  $^1\text{H}$  NMR spectrum, indicating that (*S,S,S*)-**1d** had an ee of >97%.<sup>2,4a</sup>

**Acknowledgment.** We thank the National Institutes of Health for support of this work. We are grateful to Boulder Scientific for a generous gift of *rac*-ethylene-1,2-bis(1-indenyl)zirconium dichloride.

JO961907B