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# Designing the Chiral Ligand Space around an Early Transition Metal: Myrtanyl Zirconocene

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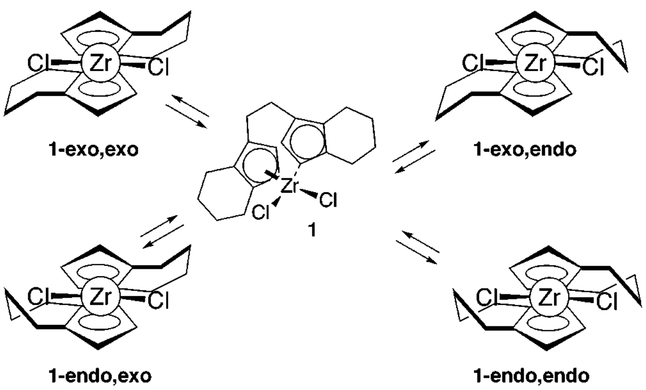
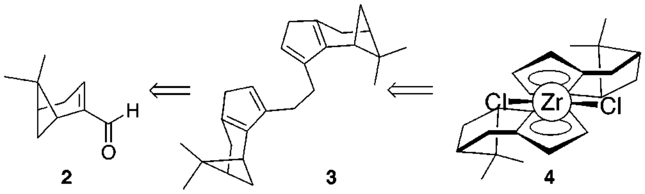
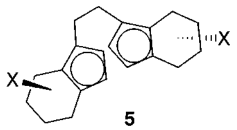
There have been many reports in recent years of catalytic applications[2] of the inherently chiral $C_2$-symmetrical zirconocene complex **1**[3] and its Ti counterpart.[4] There are practical limits on the use of **1**, however, as the complex is produced[5] in its racemic form and must therefore be resolved[6] before use. In particular, it should be noted that although **1** is usually portrayed with its cyclohexene rings planar, as illustrated, in fact these will exist as half chairs. Complex **1** and its derivatives will therefore be fluxional, equilibrating between **1-exo,exo**, in which the metal center is more exposed, and **1-endo,endo**, in which the metal center is more encumbered. While this fluxional ability may help to make **1** an outstanding polymerization catalyst[7]—open to accept the next alkene or closed and therefore protected when coordinatively unsaturated—there are many catalytic applications for which the permanently "exo,exo" active site would be desirable.

Several alternatives to **1**, many of them inherently chiral and so not requiring resolution as part of the preparation, have been put forward,[8] but none mimics well the open, nicely $C_2$-symmetric active site of **1-exo,exo**. We now report the design and preparation from myrtenal **2** of the inherently chiral zirconocene **4**, which quite rigidly replicates the key structural features of **1-exo,exo**.





The starting point for our approach was the observation, in cartoon form, that a bis-Cp ligand such as **5**, in which the "X" group blocks one face of each cyclopentadienyl in such a way that the metal complexes selectively to the other, would only be able to adopt a single coordination geometry around a group-4 metal. If the faces were blocked as indicated, in a chiral rather than a meso fashion, then the resulting single complex would be inherently chiral.



The first question was, how could one effectively block one face of each cyclopentadienyl ring? One solution could be found in the elegant work of Paquette,[9] who nicely demonstrated that cyclopentadienyls such as **6** derived from pinene selectively complex metals on the face away from the *gem*-dimethyl group, as shown. It then remained to be determined how long the linkage between the Cp ligands should be and whether it should be at "a", at "b", or at "c".

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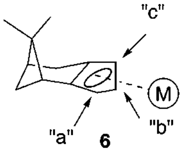


**6**

Simple molecular modeling[10–12] suggested that the bis-Cp derived from a two-carbon link attached at “a” should lead to a chiral complex that would closely replicate the active site of the resolved complex **1-exo,exo**. Alternatively, bridging at “c” would have replicated the more congested **1-endo,endo**. Our preparation of the “exo,-exo” ligand began with the commercially available (*R*)-myrtenal **2** (Scheme 1).[13]

We planned to prepare the cyclopentadienyl rings of **2** by double Skattebol rearrangement,[14–16] by way of the symmetrical tetraene **9**. To this end, we homologated myrtenal **2** to the methyl ketone **7**, by addition of methyllithium followed by Swern oxidation.[17] The use of methyllithium proved critical. The diastereomeric methyl carbinol from methylmagnesium bromide addition oxidized only very sluggishly.

Oxidation[18] of the lithium enolate of **7** with $CuCl_2$ proceeded smoothly, to give the symmetrical diketone **8**. Although the dimerization could only be induced to proceed to about 80% conversion, the residual monomeric ketone was easily distilled away from the product. Wittig condensation in refluxing THF then provided the tetraene **9**.

In the event, dibromocarbene addition, by the method of Seyferth,[19] followed by exposure to $CH_3Li/Et_2O$ did indeed serve well to establish the two cyclopentadiene rings of **3**. The bis-cyclopentadienyl intermediate was most easily isolated as the derived dianion **10**.

The conversion of dianion **10** to myrtanyl zirconocene **4** was accomplished most efficiently by following the procedure of Jordan.[5] Thus, exposure of the neutral hydrocarbon to $Zr(NMe_2)_4$ gave an intermediate, presumably the bis-dimethylamide. Stirring of this intermediate with anhydrous $Et_3N{\cdot}HCl$ then gave the nicely crystalline zirconocene dichloride **4**.

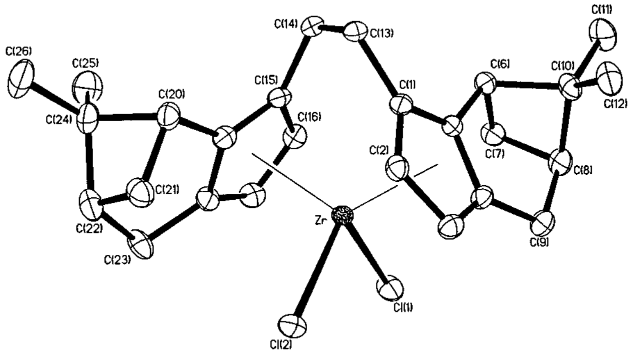
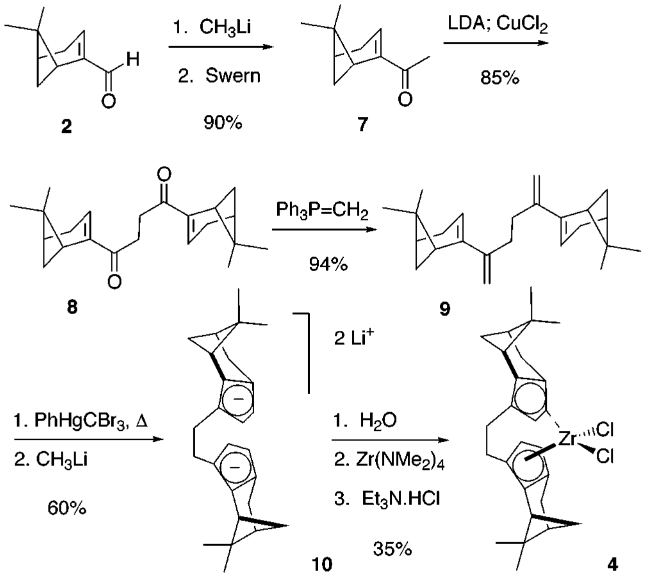


**Figure 1.** Molecular structure of **4** drawn with 50% probability thermal ellipsoids. Zr–Cl(1), 2.449(2); Zr–Cl(2), 2.437(2), Zr–CNT(1–5), 2.219(5); Zr–CNT(15–19), 2.233(5) Å. CNT–Zr–CNT, 124.3(2); Cl(1)–Zr–Cl(2), 93.6(1). Torsion angle (1,13,14,15), 43.4.

### Scheme 1



Our interest in the design of **4** was to replicate the steric environment around the metal in **1-exo,exo**. As can be seen from the X-ray structure of **4** (Figure 1), the complex is indeed nicely $C_2$-symmetric.[20] The cyclopentadienyl-fused cyclohexane rings of **4** are more rigidly fixed than those of **1**, making them effectively somewhat more bulky.

An inherent assumption in the synthetic approach outlined here is that the metalation/complexation protocol developed by Jordan[5] either shows a substantial kinetic preference for formation of the more stable product or that it is easily reversible and that the more stable product is formed under equilibrium control. We have not yet made any attempt to distinguish experimentally between these possibilities.

We expect that **4** should mimic many of the catalytic applications of the more difficult to prepare **1**, as it

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(10) Both ZINDO and molecular mechanics were used as implemented on the Tektronix CAChe workstation. For leading references to ZINDO, a semiempirical program that has been parametrized for the first two rows of transition metals, see: (a) Zerner, M. C.; Loew, G. W.; Kirchner, R. F.; Mueller-Westerhoff, U. T. *J. Am. Chem. Soc.* **1980**, *102*, 589. (b) Anderson, W. P.; Cundari, T. R.; Drago, R. S.; Zerner, M. C. *Inorg. Chem.* **1990**, *29*, 1.

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(20) Crystal data for **4**: $C_{26}H_{32}Cl_2Zr$, orthorhombic, $P2_12_12_1$, $a = 10.763(3)$ Å, $b = 14.283(3)$ Å, $c = 15.638(3)$ Å, $V = 2404.1(9)$ Å$^3$, $Z = 4$, $T = 232$ K. $R(F) = 3.64\%$, $R(wF) = 3.55\%$.

provides such a similar chiral environment around the metal center.

## Experimental Section[21]

**Methyl Ketone 7.** (*R*)-Myrtenal **2** (30.0 g, 0.2 mol) in 30 mL of $Et_2O$ was added via cannula to methyllithium (1.4 M in $Et_2O$, 220 mL, 308 mmol) in a 500 mL Schlenk flask with external ice−water cooling. After addition, the reaction mixture was allowed to warm to room temperature for 30 min. The reaction mixture was partitioned between 1 M aqueous HCl and $Et_2O$. The combined organic extract was dried ($Na_2SO_4$) and concentrated, and the residue was distilled through a short path apparatus to give the alcohol (30.4 g) as a colorless oil, bp (0.1 mm) = 78−84 °C.

Neat DMSO (26.1 mL) was added dropwise over 5 min to oxalyl chloride (2.0 M in $CH_2Cl_2$, 92 mL, 184 mmol) and methylene chloride (200 mL) in a 500 mL Schlenk flask at −60 °C. Two minutes after the addition of DMSO, the above alcohol (27.8 g) diluted in 30 mL of $CH_2Cl_2$ was added via cannula. After 15 min, triethylamine (120 mL) was added dropwise over 10 min. The mixture was stirred an additional 10 min and then was allowed to come to room temperature over 30 min. The reaction mixture was partitioned between $CH_2Cl_2$ and, sequentially, water, 1% aqueous HCl, and saturated aqueous $NaHCO_3$. The combined organic extract was dried ($Na_2SO_4$) and concentrated, and the residue was distilled through a short path apparatus to give ketone **7** (27.1 g, 90% from myrtenal) as a colorless oil, bp (0.1 mm) = 55−60 °C. $^1H$ NMR ($\delta$): 6.69 (bs, 1 H); 2.89 (t, $J$ = 5.6 Hz, 1H); 2.41 (m, 3 H); 2.22 (s, 3H); 2.09 (bs, 1H); 1.25 (s, 3H); 0.95 (d, $J$ = 9.0 Hz, 1H); 0.67 (s, 3H); $^{13}C$ NMR ($\delta$): u, 196.7, 149.5, 39.3, 37.2, 32.4, 30.9; d, 137.3, 40.1, 25.7, 24.8, 20.7.

**Diketone 8.** Lithium diisopropylamide (1.5 M in THF, 113 mL) was added dropwise over 10 min to the methyl ketone (25.9 g, 158 mmol) in 250 mL of THF in a 1 L Schlenk flask at −78 °C. After 45 min, a solution of $CuCl_2$ (23.4 g, 174 mmol) in DMF (117 mL) was added via cannula. After 30 min the cooling bath was removed. After an additional 30 min the reaction mixture was partitioned between $Et_2O$ and 1.0 M aqueous HCl. The combined organic extract was dried ($Na_2SO_4$) and concentrated, and the residual ketone monomer (4.5 g) was removed by distillation as above. The residue was purified by chromatography to give the diketone (18.1 g, 85% yield from **7**) as a pale yellow oil. TLC: $R_f$ (20% EtOAc/hexanes) = 0.67. $^1H$ NMR ($\delta$): 6.80 (bs, 1H); 2.96 (m, 6H); 2.41 (m, 6H); 2.09 (bs, 2H); 1.28 (s, 6H); 1.01 (d, $J$ = 9.9 Hz, 2H); 0.71 (s, 6H). $^{13}C$ NMR ($\delta$): u, 197.3, 148.6, 40.1, 39.5, 39.2, 37.0, 32.2, 30.9, 30.8, 25.6, 20.6; d, 136.0.

**Tetraene 9.** A solution of *n*-butyllithium (1.6 M in hexanes, 46.2 mL, 73.9 mmol) was added over 2 min to a suspension of methyl triphenylphosphonium bromide (27.0 g, 73.7 mmol) in THF (175 mL) in a 500 mL Schlenk flask with ice−water cooling. After 45 min, the reaction mixture was cooled to −78 °C and diketone **8** (11.3 g, 34.4 mmol) in 25 mL of THF was added via cannula. The mixture was warmed to reflux overnight and then partitioned between water and $Et_2O$. The combined organic extract was dried ($Na_2SO_4$) and concentrated, and the residue was filtered through silica gel to give tetraene **9** (10.5 g, 94%) as a light brown oil. TLC: $R_f$ (hexanes) = 0.80. $^1H$ NMR ($\delta$): 5.64 (bs, 2H); 4.91 (s, 2H); 4.78 (s, 2H); 2.52 (m, 2H); 2.41 (m, 10H); 2.05 (bs, 2H); 1.15 (s, 6H); 1.08 (d, $J$ = 5.5 Hz, 2H); 0.79 (s, 6H). $^{13}C$ NMR ($\delta$): 147.6, 146.9, 119.2, 108.8, 43.1, 40.8, 37.6, 33.6, 31.9, 31.4, 26.5, 20.8.

**Dianion 10.** Tetraene **9** (10.5 g, 32.6 mmol), $PhHgCBr_3$ (36.0 g, 68 mmol), and 100 mL of benzene were combined and warmed to reflux for 3 h. The mixture was filtered and the filtrate was concentrated to dryness. The residue was extracted into hexane and filtered again. The filtrate was concentrated and the residue was filtered through silica gel with hexane to give 17.5 g (26.4 mmol, 81%) of the tetrabromo compound as a mixture of diastereomers, TLC: $R_f$ (hexane) = 0.76. $^1H$ NMR ($\delta$): 5.35 (m, 2H); 2.35 (m, 4H); 2.18 (m, 8H); 1.96 (m, 4H); 1.65 (m, 4H); 1.21 (m, 6H); 0.78 (m, 6H).

Methyllithium (1.4 M in $Et_2O$, 137 mL, 192 mmol) was added dropwise over 10 min with ice−water cooling to the tetrabromo compound (16.0 g, 24.1 mmol) in 1 L of $Et_2O$. After stirring at room temperature overnight, the reaction mixture was partitioned between ice−water and $Et_2O$. The combined organic extract was dried ($Na_2SO_4$) and concentrated to give the crude tetraene as a gum (7.0 g).

In a controlled atmosphere box, the crude tetraene (7.0 g, 20.0 mmol) was taken up in $Et_2O$ (60 mL). BuLi (1.6 M in hexanes, 32 mL, 50 mmol) was added dropwise at room temperature. After stirring overnight, the suspension was filtered, and the resulting light yellow solid dianion **10** (7.0 g, 19.6 mmol, 60% from **8**) was vacuum-dried. $^1H$ NMR (THF-$d_8$) ($\delta$): 5.11 (d, $J$ = 2.3 Hz, 2H); 5.09 (d, $J$ = 2.3 Hz, 2H); 2.78 (m, 10H); 2.41 (m, 4H); 2.04 (m, 2H); 1.16 (s, 6H); 0.68 (s, 6H). $^{13}C$ NMR (THF-$d_8$) ($\delta$): 98.1, 97.7, 44.1, 42.6, 37.3, 32.9, 30.3, 28.0, 22.4.

**Myrtanyl Zirconocene 4.** In a 100 mL Schlenk flask, $Zr(NMe_2)_4$ (1.0 g, 3.7 mmol) was dissolved in 20 mL of toluene. Dianion **10** (1.29 g, 3.6 mmol) was partitioned between $Et_2O$ and saturated aqueous $NaHCO_3$. The combined organic extract was dried ($Na_2SO_4$) and concentrated, and the residue was taken up in toluene and cannulated into the $Zr(NMe_2)_4$ solution at room temperature. After addition, the reaction mixture was refluxed for 16 h with the bubbler open and no nitrogen flow. Anhydrous triethylamine hydrochloride (2 equiv) in toluene was introduced and the mixture was stirred for another 30 min. The solvent was evaporated, and the residue was taken up in 10 mL of hexane and filtered to remove LiCl. The filtrate was evaporated and the residue was extracted with 5 mL of nitromethane. The nitromethane solution was filtered and evaporated to leave 640 mg (1.3 mmol, 35% from dianion **10**) of myrtanyl zirconocene dichloride **4** as a light brown solid. This was stored in the drybox until further use. $^1H$ NMR ($\delta$): 6.27 (d, $J$ = 2.8 Hz, 2H); 5.43 (d, $J$ = 2.8 Hz, 2H); 3.31 (dd, $J$ = 16.4, 1.6 Hz, 2H); 3.14 (dd, 16.4, 1.6 Hz, 2H); 2.94 (d, $J$ = 7.5 Hz, 2H); 2.85 (t, $J$ = 5.4 Hz, 2H); 2.72 (dd, $J$ = 16.4, 2.9 Hz, 2H); 2.45 (m, 2H); 2.15 (bs, 2H); 1.95 (d, $J$ = 10.0 Hz, 2H); 1.35 (s, 6H); 0.38 (s, 6H). $^{13}C$ NMR ($\delta$): 134.8, 133.5, 132.5, 115.2, 109.9, 43.4, 41.5, 41.1, 29.8, 29.5, 27.3, 25.9, 20.7.

X-ray-quality crystals were obtained by sublimation of the crude material (oil diffusion pump at 150 °C). The sublimed complex was then dissolved in $Et_2O$/pentane, and the pentane was allowed to evaporate slowly overnight, delivering pale yellow spars.

**Acknowledgment.** We thank the National Science Foundation, CHE-9215196, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work. We thank Professor Michael H. Nantz for a helpful discussion of the Skattebol rearrangement.

**Supporting Information Available:** Spectroscopic data ($^1H$, $^{13}C$) for all new compounds (10 pages). Full crystallographic details including atomic coordinates, thermal parameters, bond lengths and angles, and atomic displacement parameters. This material is available free of charge via the Internet at http://pubs.acs.org.

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[21] For general experimental procedures, see: Taber, D. F.; Meagley, R. P.; Doren, D. J. *J. Org. Chem.* **1996**, *61*, 5723.