

Control of *ansa*-Zirconocene Stereochemistry by Reversible Exchange of Cyclopentadienyl and Chloride Ligands

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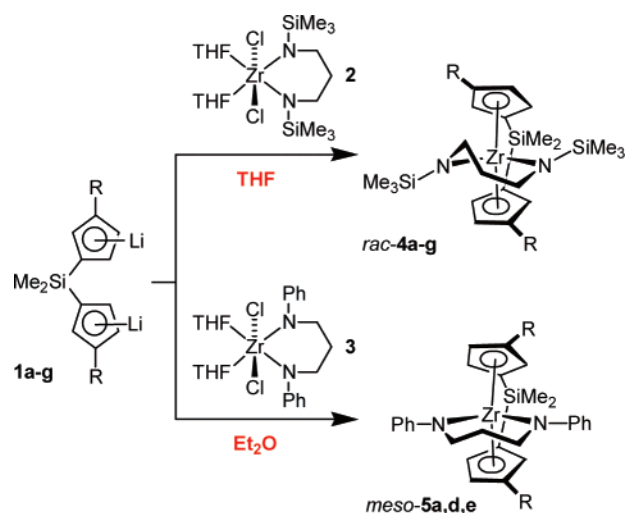
The development of efficient routes to chiral *ansa*-zirconocenes is important owing to the utility of these complexes in catalysis.<sup>1–3</sup> We report that the substitution of Zr–Cl ligands by cyclopentadienyl ligands (Cp<sup>–</sup>) is reversible and that this property can be exploited in the predictable synthesis of racemic *ansa*-zirconocenes.

We reported the stereoselective synthesis of *ansa*-zirconocenes by the reaction of *ansa*-bis-Cp<sup>–</sup> reagents (**1**) with Zr{RN(CH<sub>2</sub>)<sub>3</sub>–NR}Cl<sub>2</sub>(THF)<sub>2</sub> complexes (R = SiMe<sub>3</sub> (**2**), Ph (**3**)).<sup>2b</sup> As shown in Scheme 1, the reaction of Li<sub>2</sub>[Me<sub>2</sub>Si(3-*i*-Bu-C<sub>5</sub>H<sub>3</sub>)<sub>2</sub>] (**1a**) with **2** in THF affords pure *rac*-Me<sub>2</sub>Si(3-*i*-Bu-C<sub>5</sub>H<sub>3</sub>)<sub>2</sub>Zr{Me<sub>3</sub>SiN(CH<sub>2</sub>)<sub>3</sub>NSiMe<sub>3</sub>} (*rac*-**4a**); metallocene products are not formed in Et<sub>2</sub>O because of the insolubility of the reactants. In contrast, reaction of **1a** with **3** in Et<sub>2</sub>O affords pure *meso*-Me<sub>2</sub>Si(3-*i*-Bu-C<sub>5</sub>H<sub>3</sub>)<sub>2</sub>Zr{PhN(CH<sub>2</sub>)<sub>3</sub>NPh} (*meso*-**5a**), whereas *rac*/*meso*-**5a** mixtures are formed in THF. We studied the scope and mechanism of these reactions to understand these results.

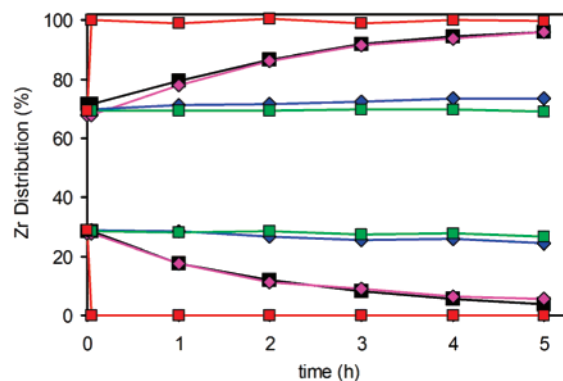
The reaction of **1b–g** with **2** in THF affords *rac*-Me<sub>2</sub>Si(3-*R*-C<sub>5</sub>H<sub>3</sub>)<sub>2</sub>Zr{Me<sub>3</sub>SiN(CH<sub>2</sub>)<sub>3</sub>NSiMe<sub>3</sub>} (*rac*-**4b–g**) in quantitative isolated yield (Scheme 1). In contrast, the reaction of **1d,e** with **3** in Et<sub>2</sub>O affords *meso*-Me<sub>2</sub>Si(3-*R*-C<sub>5</sub>H<sub>3</sub>)<sub>2</sub>Zr{PhN(CH<sub>2</sub>)<sub>3</sub>NPh} (*meso*-**5d,e**) in >95% NMR yield and 71–91% isolated yield. These results show that the behavior of **1a** in Scheme 1 is characteristic for this class of ligands. The reaction of *rac*-**4a–g** with HCl gives the corresponding *rac*-Me<sub>2</sub>Si(3-*R*-C<sub>5</sub>H<sub>3</sub>)<sub>2</sub>ZrCl<sub>2</sub> complexes (*rac*-**6a–g**) with retention of stereochemistry. Reaction of *meso*-**5d** with HCl gives **6d** with a slight loss in stereochemistry (*rac*/*meso* = 1/16).

To probe the mechanism of stereocontrol in the formation of *rac*-metallocenes in Scheme 1, the reaction of **1c** and **2** in THF-*d*<sub>8</sub> at 60 °C was monitored by NMR. These experiments showed that **1c** and **2** are completely converted within 5 min to a 2/1 *rac*/*meso*-**4c** mixture, which in turn converts to pure *rac*-**4c** in 6 h. No precipitates or intermediates were observed, and the sum of the concentrations of *rac*- and *meso*-**4c** remained constant after the consumption of **1** and **2** was complete. The conversion of *meso*-**4c** to *rac*-**4c** displays first-order behavior in metallocene (Figure 1, run i). Similar observations were made for the reaction of **1b** with **2**. These results show that the formation of *rac*-metallocenes by the reaction of **1** and **2** in THF is thermodynamically controlled.

The *meso* to *rac* isomerization requires cleavage of a Zr–Cp bond and re-coordination of the Cp through the opposite face. Several mechanisms for such Cp enantioface exchange processes have been identified in metallocenes, including photochemical, thermal, or radical-induced M–Cp bond homolysis, silatropic rearrangement, reversible amine elimination, heteroatom-assisted enantioface exchange, and LiCl-induced M–Cp bond heterolysis.<sup>3–5</sup> A series of experiments was performed to probe the mechanism in the present system. As shown in Figure 1, conversion of the 2/1 *rac*/*meso*-**4c** mixture (initially formed from **1c** and **2** in THF-*d*<sub>8</sub>) to pure *rac*-**4c** occurs at the same rate in ambient fluorescent light (run i) and in the dark (run ii), which is inconsistent with a photochemical *meso*/*rac* isomerization. To probe the role of the

Scheme 1<sup>a</sup>

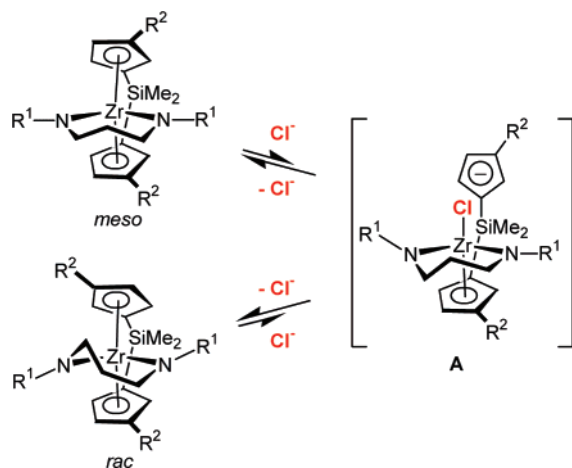
<sup>a</sup> R = *i*-Bu (a), SiMe<sub>3</sub> (b), cyclohexen-1-yl (c), 1-Me-Cy (d), 1-Ph-Cy (e), 1-Me-cyclo-C<sub>12</sub>H<sub>22</sub> (f), CMe<sub>2</sub>Ph (g)



**Figure 1.** Time dependence of the concentrations of *rac*-**4c** (upper curves) and *meso*-**4c** (lower curves) measured relative to an internal standard starting from a 2/1 *rac*/*meso*-**4c** mixture (THF-*d*<sub>8</sub>, 60 °C). Run i (black, squares), 2 equiv LiCl; run ii (violet, diamonds), 2 equiv LiCl and dark; run iii (blue, diamonds), no additive; run iv (green, squares), 2 equiv Li[B(C<sub>6</sub>F<sub>5</sub>)<sub>4</sub>]; run v (red, squares), 2 equiv [t-Bu<sub>4</sub>N]Cl.

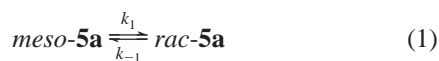
LiCl byproduct, which is soluble in THF, the LiCl was removed from the 2/1 *rac*/*meso*-**4c** mixture (see Supporting Information for details), and the sample was monitored by NMR. In this case, essentially no *rac*/*meso* isomerization occurred (run iii). Addition of Li[B(C<sub>6</sub>F<sub>5</sub>)<sub>4</sub>] as a Li<sup>+</sup> source to the LiCl-free *rac*/*meso*-**4c** mixture had no effect (run iv). However, addition of [t-Bu<sub>4</sub>N]Cl to the LiCl-free *rac*/*meso*-**4c** mixture resulted in rapid conversion (<5 min) to pure *rac*-**4c** (run v). Similar results were obtained for *rac*/*meso*-**4b**. These results show that the isomerization is catalyzed by chloride ion.<sup>6</sup> [t-Bu<sub>4</sub>N]Cl is a more effective *rac*/*meso* isomerization catalyst than LiCl because it is less strongly ion-paired.

Scheme 2



The solubility of LiCl is very low in  $\text{Et}_2\text{O}$ , which should disfavor  $\text{Cl}^-$ -catalyzed *rac/meso* isomerization in this solvent. NMR monitoring of the reaction of **1a** with **3** in  $\text{Et}_2\text{O}-d_{10}$  at 22 °C showed that the starting materials are completely converted to *meso*-**5a** within 2 h. No intermediates or further reaction were observed. In contrast, NMR monitoring of the same reaction in  $\text{THF}-d_8$  at 0 °C revealed the initial formation of a 1/3 *rac/meso*-**5a** mixture within 4 h and subsequent conversion to an equilibrium 3/1 *rac/meso*-**5a** mixture. Complex *meso*-**5a** is stable in THF, but addition of LiCl or  $[\text{tBu}_4\text{N}]\text{Cl}$  to a solution of *meso*-**5a** in  $\text{THF}-d_8$  results in conversion to the equilibrium 3/1 *rac/meso*-**5a** mixture. These results show that the formation of *meso*-metallocenes by the reaction of **1** and **3** in  $\text{Et}_2\text{O}$  is kinetically controlled.

The kinetics of isomerization of *meso*-**5a** to the equilibrium *rac/meso*-**5a** mixture in the presence of LiCl or  $[\text{tBu}_4\text{N}]\text{Cl}$  in  $\text{THF}-d_8$  were measured by NMR and exhibit clean first-order approach-to-equilibrium kinetics (eq 1,2).  $k_{\text{obs}}$  is the sum of the forward ( $k_1$ , *meso* to *rac*) and reverse ( $k_{-1}$ , *rac* to *meso*) rate constants, and  $K_{\text{eq}} = k_1/k_{-1}$ . A series of approach-to-equilibrium experiments using varying concentrations of LiCl established that the isomerization is first order in  $[\text{Cl}^-]$ . The mechanism in Scheme 2, in which *rac* and *meso* interconvert via a transient “mono-Cp”  $\eta^5, \eta^0\text{-Me}_2\text{Si}(3\text{-R-C}_5\text{H}_3)_2\text{Zr}\{\text{Me}_3\text{SiN}(\text{CH}_2)_3\text{NSiMe}_3\}\text{Cl}^-$  intermediate (**A**), is consistent with these results.



$$\ln \left( \frac{[\text{meso-5a}] - [\text{meso-5a}]_{\infty}}{[\text{meso-5a}]_0 - [\text{meso-5a}]_{\infty}} \right) = -k_{\text{obs}}t \quad (2)$$

To probe if a bis-amide ligand is required for chloride-catalyzed *rac/meso* isomerization, several  $\text{Me}_2\text{Si}(\eta^5\text{-3-R-C}_5\text{H}_3)_2\text{ZrCl}_2$  complexes were examined. Reaction of *rac*-**6c** with  $[\text{tBu}_4\text{N}]\text{Cl}$  under the conditions used for isomerization of *rac/meso*-**4c** (Figure 1, run v) afforded an equilibrium 0.9/1 *rac/meso*-**6c** mixture.<sup>7</sup> The isomerization of **6c** followed first-order approach-to-equilibrium kinetics and  $k_1$  (*meso* to *rac*) was >25 times slower than the value estimated for **4c**. Similarly, the isomerization of **6b** is much slower than that of **4b**. These results show that the bis-amide ligand accelerates but is not required for *rac/meso* isomerization. The strong donor ability of the bisamide ligand may stabilize the electron deficient intermediate **A**.

The kinetics of isomerization of *rac*-**6d**, and of a 1/16 *rac/meso*-**6d** mixture, catalyzed by  $[\text{tBu}_4\text{N}]\text{Cl}$  in  $\text{THF}-d_8$  were studied in detail. These reactions both afford a 1/2 equilibrium mixture of *rac/meso*-**6d** (2 d, 60 °C) and exhibit clean first-order approach-to-equilibrium kinetics. Identical kinetics are observed in ambient room light and in the dark, and no reaction occurs in the absence of chloride. These results are consistent with a mechanism analogous to that in Scheme 2.

To probe if the  $\text{SiMe}_2$  bridge is required for facile displacement of  $\text{Cp}^-$  by chloride, a nonbridged system was investigated. The reaction of a 1/1 mixture of  $(\text{C}_5\text{H}_5)_2\text{ZrCl}_2$  and  $(\text{C}_5\text{H}_4\text{Me})_2\text{ZrCl}_2$  with  $[\text{tBu}_4\text{N}]\text{Cl}$  in  $\text{THF}-d_8$  afforded a 1/2/1 mixture of  $(\text{C}_5\text{H}_5)_2\text{ZrCl}_2$ ,  $(\text{C}_5\text{H}_5)(\text{C}_5\text{H}_4\text{Me})\text{ZrCl}_2$ , and  $(\text{C}_5\text{H}_4\text{Me})_2\text{ZrCl}_2$  after 1 h at 60 °C. An identical dark reaction yielded the same 1/2/1 mixture. No reaction occurs in the absence of chloride.<sup>4d</sup>

Several conclusions emerge from these studies. (i) Cyclopentadienyl ligands are easily displaced from zirconocene species by chloride ion under mild conditions. (ii) As a result, the generation of zirconocenes by  $\text{Cp}^-/\text{Cl}^-$  substitution is reversible under conditions where the displaced  $\text{Cl}^-$  remains in solution. (iii) In the case of *ansa*-zirconocene synthesis via the reaction of *ansa*-bis- $\text{Cp}^-$  reagents with  $\text{Zr}\{\text{RN}(\text{CH}_2)_3\text{NR}\}\text{Cl}_2(\text{THF})_2$  or enantiopure  $\text{Zr}\{\text{RNCHMeCH}_2\text{CHMeNR}\}\text{Cl}_2(\text{THF})_2$  compounds,<sup>2c</sup> N–R groups that deliver the desired  $\{\text{ansa-bis-Cp}\}\text{Zr}(\text{bis-amide})$  stereoisomer in high yield can be chosen *in advance* based on the relative energies of the  $\{\text{ansa-bis-Cp}\}\text{Zr}(\text{bis-amide})$  products, which can be computed (e.g., by DFT).<sup>2e</sup> Thus *ansa*-zirconocenes can now be made with a high degree of predictability. (iv) Facile loss of metallocene stereochemistry can occur under conditions where free chloride or other nucleophilic species are present, which has important implications for stereoselective catalysis.

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**Supporting Information Available:** Experimental procedures, kinetic analyses, and data for new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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