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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.[1−3] We report that the substitution of Zr−Cl ligands by cyclopentadienyl ligands (Cp^-) is reversible and that this property can be exploited in the predictable synthesis of racemic *ansa*-zirconocenes.

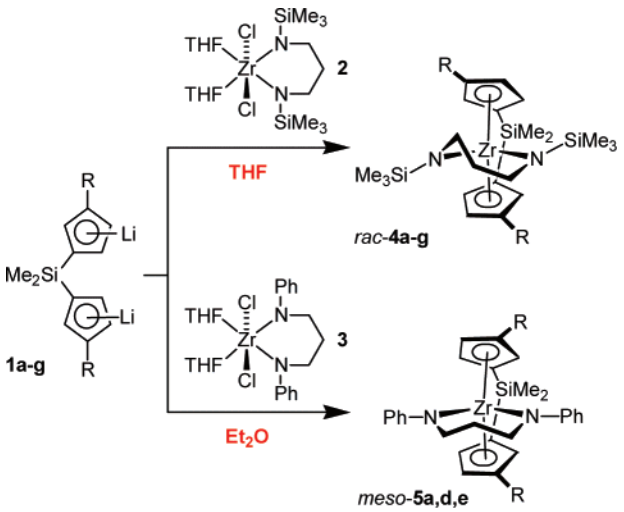
We reported the stereoselective synthesis of *ansa*-zirconocenes by the reaction of *ansa*-bis-Cp^- reagents (**1**) with $Zr\{RN(CH_2)_3NR\}Cl_2(THF)_2$ complexes (R = $SiMe_3$ (**2**), Ph (**3**)).[2b] As shown in Scheme 1, the reaction of $Li_2[Me_2Si(3\text{-}^tBu\text{-}C_5H_3)_2]$ (**1a**) with **2** *in THF* affords pure *rac*-$Me_2Si(3\text{-}^tBu\text{-}C_5H_3)_2Zr\{Me_3SiN(CH_2)_3NSiMe_3\}$ (*rac*-**4a**); metallocene products are not formed in Et_2O because of the insolubility of the reactants. In contrast, reaction of **1a** with **3** *in* Et_2O affords pure *meso*-$Me_2Si(3\text{-}^tBu\text{-}C_5H_3)_2Zr\{PhN(CH_2)_3NPh\}$ (*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*-$Me_2Si(3\text{-}R\text{-}C_5H_3)_2Zr\{Me_3SiN(CH_2)_3NSiMe_3\}$ (*rac*-**4b**−**g**) in quantitative isolated yield (Scheme 1). In contrast, the reaction of **1d**,**e** with **3** in Et_2O affords *meso*-$Me_2Si(3\text{-}R\text{-}C_5H_3)_2Zr\{PhN(CH_2)_3NPh\}$ (*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*-$Me_2Si(3\text{-}R\text{-}C_5H_3)_2ZrCl_2$ 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_8 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.[3−5] 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_8) 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 [a]



[a] R = ^{t}Bu (a), $SiMe_3$ (b), cyclohexen-1-yl (c), 1-Me-Cy (d), 1-Ph-Cy (e), 1-Me-*cyclo*-$C_{12}H_{22}$ (f), CMe_2Ph (g)

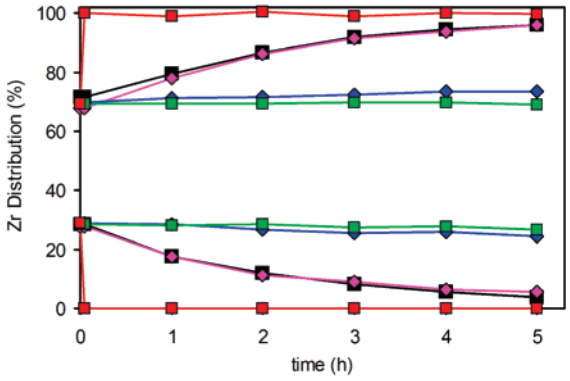


Figure 1. Time dependence of the concentrations of *rac*-**4c** (upper curves) and *meso*-**4c** (lower curves) measured relative to an internal standard starting from a 2/1 *rac*/*meso*-**4c** mixture (THF-d_8, 60 °C). Run i (black, squares), 2 equiv LiCl; run ii (violet, diamonds), 2 equiv LiCl and dark; run iii (blue, diamonds), no additive; run iv (green, squares), 2 equiv $Li[B(C_6F_5)_4]$; run v (red, squares), 2 equiv $[^nBu_4N]Cl$.

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 $Li[B(C_6F_5)_4]$ as a Li^+ source to the LiCl-free *rac*/*meso*-**4c** mixture had no effect (run iv). However, addition of $[^nBu_4N]Cl$ 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.[6] $[^nBu_4N]Cl$ is a more effective rac/meso isomerization catalyst than LiCl because it is less strongly ion-paired.

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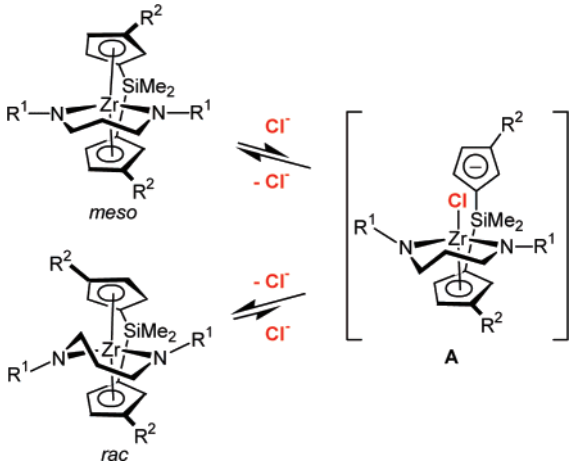
Scheme 2



The solubility of LiCl is very low *in Et_2O*, which should disfavor Cl^--catalyzed rac/meso isomerization in this solvent. NMR monitoring of the reaction of **1a** with **3** in Et_2O-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 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 [^{n}Bu$_4$N]Cl to a solution of *meso*-**5a** in 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 Et_2O is kinetically controlled.

The kinetics of isomerization of *meso*-**5a** to the equilibrium *rac*/*meso*-**5a** mixture in the presence of LiCl or [^{n}Bu$_4$N]Cl in THF-d_8 were measured by NMR and exhibit clean first-order approach-to-equilibrium kinetics (eq 1,2). k_{obs} is the sum of the forward (k_1, meso to rac) and reverse (k_{-1}, rac to meso) rate constants, and $K_{eq} = k_1/k_{-1}$. A series of approach-to-equilibrium experiments using varying concentrations of LiCl established that the isomerization is first order in [Cl^-]. The mechanism in Scheme 2, in which rac and meso interconvert via a transient "mono-Cp" η^5,η^0-Me_2Si(3-R-C_5H_3)$_2$Zr{$Me_3SiN(CH_2)_3NSiMe_3$}Cl^- intermediate (**A**), is consistent with these results.

$$meso\text{-}\mathbf{5a} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} rac\text{-}\mathbf{5a} \qquad (1)$$

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

To probe if a bis-amide ligand is required for chloride-catalyzed rac/meso isomerization, several $Me_2Si(\eta^5$-3-R-$C_5H_3)_2ZrCl_2$ complexes were examined. Reaction of *rac*-**6c** with [^{n}Bu$_4$N]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.[7] 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 [^{n}Bu$_4$N]Cl in 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 $SiMe_2$ bridge is required for facile displacement of Cp^- by chloride, a nonbridged system was investigated. The reaction of a 1/1 mixture of $(C_5H_5)_2ZrCl_2$ and $(C_5H_4Me)_2ZrCl_2$ with [^{n}Bu$_4$N]Cl in THF-d_8 afforded a 1/2/1 mixture of $(C_5H_5)_2ZrCl_2$, $(C_5H_5)(C_5H_4Me)ZrCl_2$, and $(C_5H_4Me)_2ZrCl_2$ 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.[4d]

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 Cp^-/Cl^- substitution is reversible under conditions where the displaced Cl^- remains in solution. (iii) In the case of *ansa*-zirconocene synthesis via the reaction of *ansa*-bis-Cp^- reagents with Zr{$RN(CH_2)_3NR$}$Cl_2(THF)_2$ or enantiopure Zr-{$RNCHMeCH_2CHMeNR$}$Cl_2(THF)_2$ compounds,[2c] N−R groups that deliver the desired {*ansa*-bis-Cp}Zr(bis-amide) stereoisomer in high yield can be chosen *in advance* based on the relative energies of the {*ansa*-bis-Cp}Zr(bis-amide) products, which can be computed (e.g., by DFT).[2e] 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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(7) No reaction was observed in the absence of [^{n}Bu$_4$N]Cl.

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