Enantioselective Synthesis of *ansa*-Zirconocenes
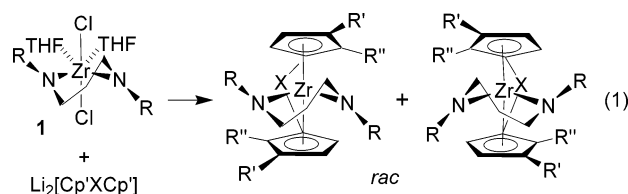
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Chiral "Brintzinger type" group 4 metal *ansa*-metallocene complexes exhibit high stereodirecting ability in many reactions.[1,2] However, *ansa*-metallocenes have been under-utilized in enantioselective catalysis, due in large part to the limited availability of enantiomerically pure catalysts.[3,4] Only a few *ansa*-metallocenes have been resolved, and most catalytic studies have used the original (EBTHI)ZrX$_2$ and (EBTHI)TiX$_2$ systems.[5] Here we describe a simple, efficient, and potentially general enantioselective synthesis of *ansa*-zirconocenes.
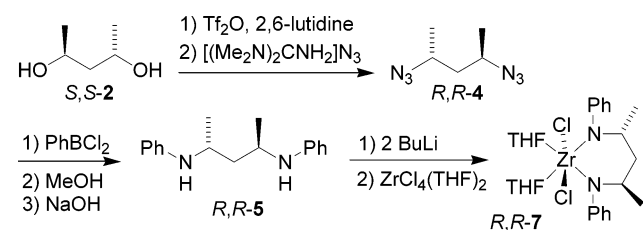
We recently reported a diastereoselective "chelate-controlled" synthesis of racemic *ansa*-zirconocenes, which is based on the reaction of Li$_2$[Cp′XCp′] salts with chelated bis-amide compounds Zr{RN(CH$_2$)$_3$NR}Cl$_2$(THF)$_2$ (**1**; R = Ph, SiMe$_3$), as shown in eq 1.[6] The twist conformation of the Zr{RN(CH$_2$)$_3$NR} ring in **1**

positions the N–R substituents on opposite sides of the N–Zr–N plane. This conformation is matched with the *rac*-metallocene structure but is incompatible with the *meso* isomer due to steric crowding between the N–R and Cp′ groups, which leads to complete selectivity for the *rac* product.
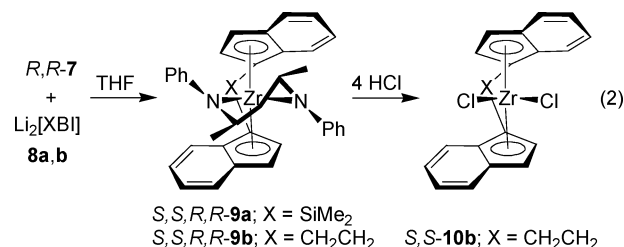
We reasoned that incorporation of substituents at C1 and C3 of the bis-amide ligand of **1** in a stereo-defined manner would favor one enantiomer of the twist conformation in the resulting metallocene, and possibly provide a means of controlling enantioselectivity. To test this concept, we prepared Zr{(2R,4R)-PhNCHMeCH$_2$-CHMeNPh}Cl$_2$(THF)$_2$ (*R,R*-**7**; Scheme 1), a chiral analogue of **1**.

Scheme 1

Conversion of (2S,4S)-pentanediol (*S,S*-**2**) to the ditriflate (*S,S*-**3**), followed by reaction with [(Me$_2$N)$_2$CNH$_2$]N$_3$, yields (2R,4R)-diazidopentane (*R,R*-**4**) quantitatively.[7] Reaction of (R,R)-**4** with PhBCl$_2$ followed by methanol workup and neutralization yields N,N′-diphenyl-(2R,4R)-pentanediamine (*R,R*-**5**, 76%, >99.5% ee).[8] Deprotonation of *R,R*-**5** with 2 equiv of *n*-BuLi yields Li$_2$[(2R,4R)-PhNCHMeCH$_2$CHMeNPh] (*R,R*-**6**) (99%). Reaction of ZrCl$_4$(THF)$_2$ and 1 equiv of *R,R*-**6** affords *R,R*-**7** (84% isolated).

The reaction of *R,R*-**7** with Li$_2$[SBI](Et$_2$O) (**8a**)[5] or Li$_2$[EBI]-(Et$_2$O) (**8b**)[5] in THF affords the corresponding metallocenes *S,S*-(SBI)Zr{(2R,4R)-PhNCHMeCH$_2$CHMeNPh} (*S,S,R,R*-**9a**) or *S,S*-(EBI)Zr{(2R,4R)-PhNCHMeCH$_2$CHMeNPh} (*S,S,R,R*-**9b**) in >95% isolated yield (eq 2). The ^{1}H NMR spectra of isolated **9a,b** display,

in each case, a single set of resonances and show that a single diastereomer is present. These results establish that the metallocene units of **9a,b** are formed in >99% ee. No significant side products were detected in these reactions. The use of THF as the solvent is important, as reactions of *R,R*-**7** with **8a,b** in Et$_2$O yielded mixtures of products. Compound **9b** was converted to the corresponding enantiomerically pure dichloride *S,S*-**10b** (91% isolated, >99% ee) by reaction with HCl in Et$_2$O. The chiral diamine *R,R*-**5** was recovered.

The configurations of *S,S,R,R*-**9a** and *S,S*-**10b** were established by X-ray crystallography. Additionally, *S,S*-**10b** was hydrogenated to the known *S,S*-(EBTHI)ZrCl$_2$ (*S,S*-**11b**), and the configuration and optical purity of *S,S*-**11b** were established from the optical rotation of this species and NMR analysis of its bis-(R)-O-acetyl-mandelate derivative.[3,5,9] These results confirm the configurations and optical purity of *S,S*-**10b** and *S,S,R,R*-**9b**.

The molecular structure of *S,S,R,R*-**9a** is shown in Figure 1. The Zr{PhNCHMeCH$_2$CHMeNPh} ring adopts a twist λ conformation,[10] which is matched to the *S,S*-metallocene unit. The C1 and C3 methyl groups (C(17) and C(17A)) occupy pseudoequatorial positions and point away from the metallocene unit, while, as illustrated in the space-filling view, the pseudoaxial C1–H and C3–H hydrogens point directly toward the indenyl rings. To form the *R,R*-metallocene without severe N–Ph/indenyl steric crowding, the bis-amide chelate ring would have to invert to the δ configuration. However, in this case, the C1 and C3 methyl groups would occupy pseudoaxial positions, and severe methyl/indenyl steric crowding would result.

While these structural data and steric arguments suggest that the matched metallocenes *S,S,R,R*-**9a** and *S,S,R,R*-**9b** may be more stable than the other stereoisomers of these complexes, the operative stereocontrol mechanism in eq 2 is unknown. X-ray crystallographic analyses show that the chelate rings of *R,R*-**7** and Cp$_2$Zr{(2R,4R)-PhNCHMeCH$_2$CHMeNPh} (*R,R*-**12**) adopt twist-boat conformations (Figure 2), suggesting that this may be the most stable conformation of these rings in the absence of significant steric interactions with other ligands. However, both *R,R*-**7** and *R,R*-**12** exhibit C$_2$ symmetry on the NMR time scale at 25 °C, which
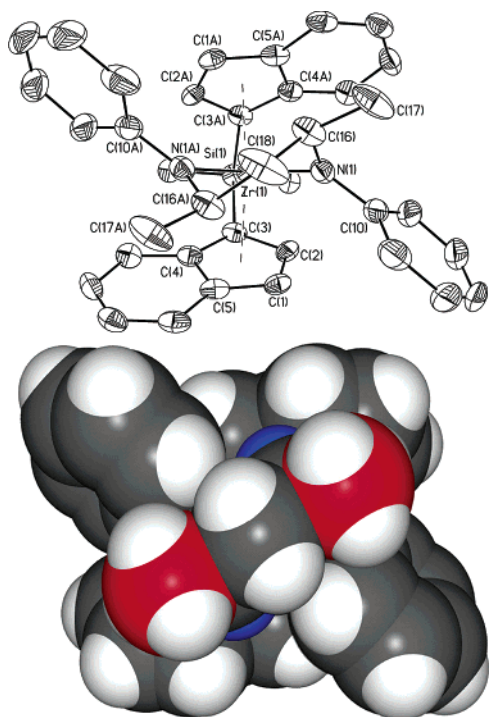
Figure 1. Molecular structure and space-filling view of *S*,*S*,*R*,*R*-**9a**. H atoms are omitted from the ORTEP view. The axial C1−H and C3−H hydrogen atoms are colored blue, and the equatorial methyl groups are colored red in the space-filling view. Bond distances (Å): Zr−N(1) 2.095(4), Zr−cent 2.301. Bond angles (deg): N(1)−Zr(1)−N(1A) 90.2(2), cent(1)−Zr(1)−cent(2) 125.5.
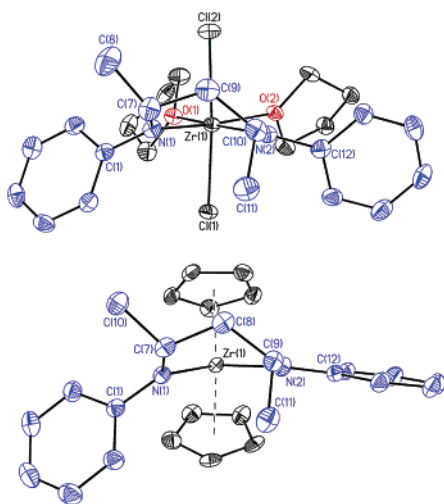

Figure 2. Molecular structures of *R*,*R*-**7** (top) and *R*,*R*-**12** (bottom). H atoms are omitted. Bond distances (Å) and angles (deg): *R*,*R*-**7**, Zr(1)−N(1) 2.028(2), Zr(1)−N(2) 2.046(2), Zr(1)−O(1) 2.348(2), Zr(1)−O(2) 2.319(2), Zr(1)−Cl(1) 2.484(2), Zr(1)−Cl(2) 2.504(2), N(1)−Zr(1)−N(2) 92.01(7), Cl(1)−Zr(1)−Cl(2) 161.91(2), O(1)−Zr(1)−O(2) 77.3(5); *R*,*R*-**12**, Zr−N(1) 2.087(2), Zr−N(2) 2.173(2), Zr−cent(1) 2.258, Zr−cent(2) 2.287, N(1)−Zr(1)−N(2) 91.62(8), cent(1)−Zr−cent(2) 124.1.

indicates that the chelate rings are flexible. Given the potential complexity of the mechanism of substitution of the chloride and

THF ligands of **7** by the incoming indenyl ligands,[11] more detailed studies will be required to understand the origin of stereocontrol in these reactions.

The methodology described here should be useful for the enantioselective synthesis of other bis-indenyl metallocenes and has the advantage that both enantiomers are available by using either *R*,*R*- or *S*,*S*-**7**. Tuning the steric interactions between the chiral bis-amide directing ligand and the metallocene framework by variation of the C1, C3, and N-substituents should enable broad application of this strategy.[6b]

Supporting Information Available: Experimental procedures and characterization data for new compounds (PDF); X-ray crystallographic data for *R*,*R*-**7**, *S*,*S*,*R*,*R*-**9a**, *S*,*S*-**10b**, and *R*,*R*-**12** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(5) Abbreviations: EBTHI, 1,2-ethylene-bis(tetrahydroindenyl); Cp′, generic cyclopentadienyl or indenyl; X, generic bridge; SBI, Me₂Si(indenyl)₂; EBI, 1,2-ethylene-bis(indenyl); cent, Cp′ ring centroid.

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