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Dynamic Resolution of a Metallocene: Diastereoselective Assembly of an Early-Late Heterobimetallic Metal-Bridged *ansa*-Metallocene Opening a Route to Parallel Catalyst Synthesis

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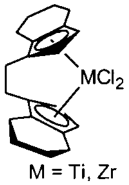
The efficient preparation of a diverse set of catalyst structures in a parallel combinatorial synthesis has been demonstrated as a powerful tool in enantioselective catalyst discovery.[1] Many of the examples to date involve the preparation of peptide libraries as ligands for transition metals, the systematic variation of substituents on ligands for coordination complexes, or the systematic variation of the metal in a coordination complex. Despite the successes of these approaches to combinatorial catalysis, not all catalysts can be prepared in a combinatorial manner by these routes. One such catalyst system is *ansa*-metallocenes, which stereoselectively catalyze a large array of important reactions from the isotactic polymerization of propylene[2] to enantioselective organic transformations.[3] Although catalyst **1** has been employed as the key enantioselective catalyst in at least two total syntheses,[4] *ansa*-metallocene methodology has not become a routinely employed synthetic method due in part to limited availability and limited structural variability in enantiopure form.



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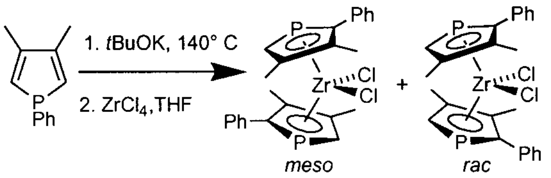
The preparation of novel *ansa*-metallocenes has been and continues to be the focus of numerous groups.[5] Brintzinger recently reported the asymmetric thermal transformation of biphenyl-bridged metallocenes that were achiral at the metal center, thus introducing a new route to enantiopure *ansa*-metallocenes with much potential.[6] Despite the importance of Brintzinger's catalyst **1** and the worldwide synthetic effort that has yielded some elegant synthetic routes such as those recently published by Jordan and co-workers,[7] a wide array of structurally diverse variants of *ansa*-metallocenes is not readily available.

If a route could be developed that would allow the efficient preparation of a diverse set of enantiopure *ansa*-metallocenes, they might become more broadly applied. Herein, we report the observation of the facile, thermal isomerization of chiral early transition metal phosphametallocenes. We have applied this observation to the design of a dynamic resolution of the phosphametallocene to yield an enantiopure, bimetallic *ansa*-metallocene.[8]

An unsymmetrical phospholyl anion, prepared from **2**,[9] was employed for the synthesis of phosphazirconocene **3**, which was obtained as a 63:37 mixture of racemic and meso isomers. Phosphole **2** had previously been used to prepare chiral phosphaferrocenes that were configurationally stable.[10] Our crude reaction product had a rac/meso isomer ratio of 63:37. After washing the crude reaction product with pentane an enhanced isomer ratio of 80:20 was found by ^{31}P NMR analysis. A solution of **3** and CDCl$_3$ was observed by ^{31}P NMR revealing that the isomer ratio changed over time, slowly returning to the thermodynamic equilibrium ratio of 63:37 (Figure 1).[11,12] Coordinating solvents, which presumably stabilize the coordinately unsaturated intermediates, greatly accelerate the rate of isomerization. Thus when a THF solution of **3** (rac/meso, 80:20) was prepared it had reached thermodynamic equilibrium in <15 min. Consistent with this hypothesis, a CDCl$_3$/14% THF (v/v) solution of **3** (80:20) was found to isomerize at an intermediate rate (Figure 1). The details of this isomerization remain to be elucidated, but we propose that the η^5-complex slips to an η^1-P-bound complex that undergoes inversion at P to interconvert the stereocenter with subsequent conversion back to an η^5-complex.[13]



(1)

2 **3m** **3r**

We have taken advantage of the isomerization of phosphazirconocene **3** to develop a dynamic resolution that produces an enantiopure bimetallic *ansa*-metallocene.[14,15]

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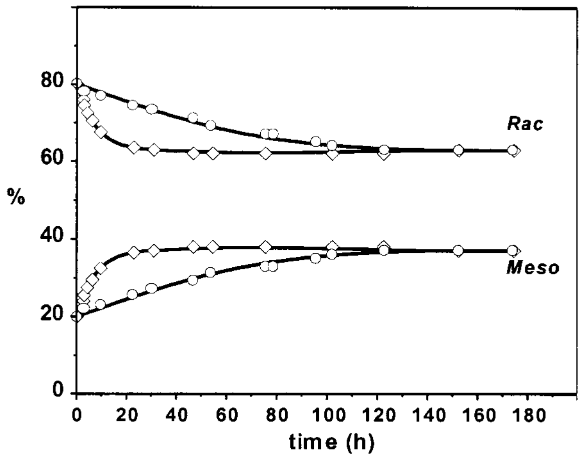
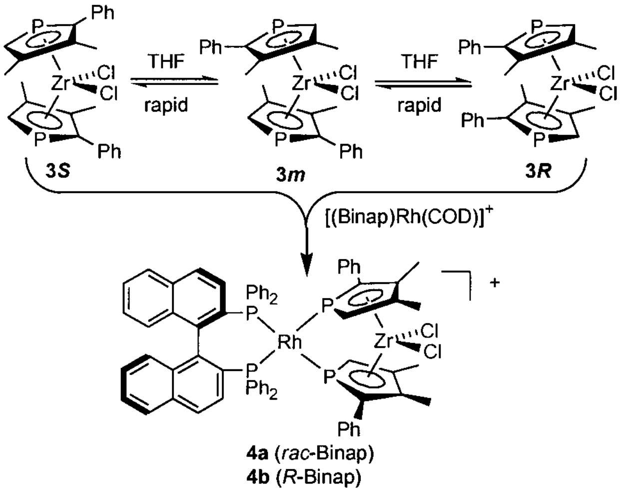


Figure 1. Percent rac (major)/meso (minor) isomers of **3** versus time (h) at room temperature in $CDCl_3$ (circle) and $CDCl_3$/14% THF (v/v) (diamond).

Scheme 1



Slow addition of a THF solution of [((*R*)-Binap)Rh(COD)]OTf to a THF solution of **3** produced a single diastereomer of the bimetallic *ansa*-metallocene **4b** as determined by ^{31}P NMR spectroscopy (Scheme 1). This experiment accomplished the dynamic resolution of phosphazirconocene **3**. The use of racemic Binap led to a material from which an X-ray quality crystal (vide infra) was obtained. Quantitative conversions to a single diastereomer were obtained in all cases as determined by ^{31}P NMR analysis. Racemic **4a** has been shown to polymerize ethylene thus establishing the viability of these complexes as catalysts.[16]

Although a single diastereomer had been formed, the stereochemistry at Zr remained to be determined. An X-ray crystal structure of **4a** revealed that the stereochemistry is C_2 symmetric at Zr. Figure 2 contains an ORTEP representation of the crystal structure of one of the molecules of **4a** in the unit cell, along with pertinent geometrical data. The molecule has a noncrystallographically imposed approximate C_2 axis if the chlorides are discounted. In solution, the molecule displays C_2 characteristics in the NMR spectra. Based on the crystals of **4a**, *S*-Binap yields the *R* absolute configuration of the metallocene.[17]

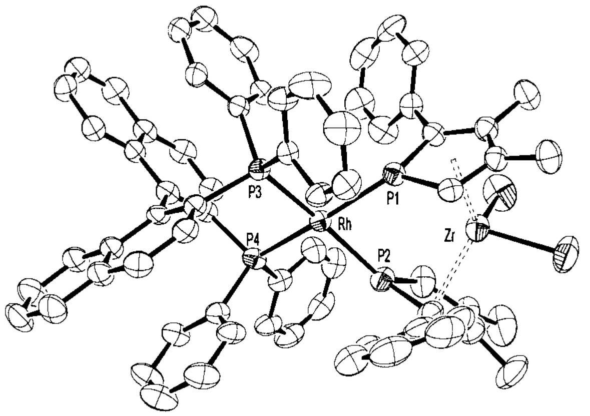


Figure 2. ORTEP view of the cation of **4a**. Representative geometrical data: Rh−P1, P2, 2.2897(14), 2.2840(14) Å; Rh−P3, P4, 2.2923(13), 2.2961(13) Å; P4−Rh−P3, 91.5°; P2−Rh−P1, 82.4°; P3−Rh−P1, 94.0°; P3−Rh−P2, 164.9°; Ct1−Zr−Ct2, 128.6°; Zr−Ct1, 2.27 Å; Zr−P1, 2.29 Å.

In conclusion, the synthesis and characterization of a chiral phosphazirconocene led to the unprecedented observation of the thermal, room-temperature isomerization of phosphazirconocene **3**. This isomerization was exploited to achieve a dynamic resolution of **3** with $[((R)\text{-Binap})Rh(COD)]^+$ producing enantiopure bimetallic *ansa*-metallocene **4b**. These experiments serve as proof of principle for the modular assembly of enantiopure bimetallic *ansa*-metallocenes, a prerequisite to developing a combinatorial approach to the preparation and evaluation of *ansa*-metallocenes as catalysts. While the applications of bimetallic *ansa*-metallocenes have yet to be fully developed,[12,18] the potential of this synthetic route to *ansa*-metallocenes will prompt further investigation. Further applications and structural variations of these complexes are underway.

Acknowledgment. We thank the University of California, Riverside and the University of California, Cancer Research Coordinating Committee for support of this work. We thank Dr. Richard Kondrat and Mr. Ron New for mass spectral analyses.

Supporting Information Available: Experimental details for the preparation of **3** and **4**, tables of positional parameters and their estimated deviations, tables of bond distances and bond angles for **4a**, along with the molecular structure including anion and solvent molecules (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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