# Asymmetric Synthesis of a Sterically Rigid Binaphthyl-Bridged Chiral Metallocene: Asymmetric Catalytic Epoxidation of Unfunctionalized Alkenes

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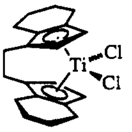
*Received December 9, 1992*

*Summary: The synthesis of the first enantiomerically enriched $C_2$-symmetrical bridged titanocene dichloride which incorporates homotopic cyclopentadienyl moieties is described, along with its application as an asymmetric epoxidation catalyst.*

The application of chiral metallocenes as catalysts for novel asymmetric catalytic and stoichiometric reactions is leading to an increase in the number and variety of enantiomerically enriched metallocene complexes.[1] The most widely and successfully used chiral metallocenes are Brintzinger's ethylene-bridged *ansa*-(bis(1-indenyl))metal complexes such as 1, which are synthesized from an achiral bis(indene) ligand as a mixture of meso and racemic metallocenes.[2] A synthetic drawback to obtaining metallocenes such as 1 in enantiomerically pure form is that a mixture of diastereomeric metallocenes must be first separated and the racemic $C_2$-symmetrical isomer resolved. We[3] and others[4] have previously employed a strategy of using a chiral bridging group to facilitate the isolation of single enantiomerically pure $C_2$-symmetrical *ansa*-(bis(1-indenyl))metal complexes such as **2** and **3**. Since the bridged 1-indenyl ligands in such complexes are still prochiral, mixtures of diastereomeric metallocenes may still ensue. A conceptually different ligand would have an indenyl-type ligand bridged at the 2-position by a chiral group. Since the ligand faces in such a ligand would be equivalent, only a single isomeric metallocene could inherently form and the asymmetry near the metal in such derived metallocenes would be due to an axially dissymmetric orientation of the indenyl ligands. The first complexes of this type, including the rigid metallocene 4, were recently reported.[5] We communicate herein the first preparation of an enantiomerically enriched, stereorigid metallocene complex incorporating non-prochiral indenyl-type ligands, 1,1′-binaphthalene-2,2′-diyl-bridged *ansa*-(bis(4,5,6,7-tetrahydro-2-indenyl))titanium dichloride complex **5**, along with its application in the catalytic asymmetric epoxidation of unfunctionalized alkenes.



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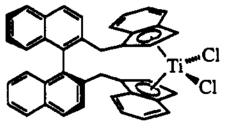

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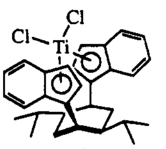

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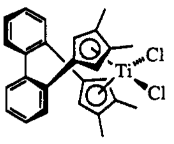

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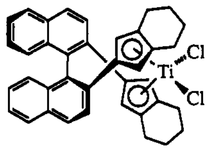

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**Ligand Synthesis and Metalation.** The synthesis of the enantiomerically enriched binaphthalene-derived bis(2-indene) ligand **10** needed for the formation of chiral metallocene complex **5** is straightforward and proceeds through known 1,1′-binaphthalene-2,2′-diamine (**7**) as illustrated in Scheme I. Diamine **7** is readily available in large amounts from the coupling of inexpensive 2-naphthol (**6**) in the presence of hydrazine and is readily resolved in large scale by recrystallization of diastereomeric salts of D-10-camphorsulfonic acid.[6] Obtaining the enantiomerically enriched 2,2′-dibromide **8** from diamine **7** is known to occur without loss of enantiomeric purity. Lithiation of dibromide **8** with alkyllithium is known to produce a 2,2′-dilithio species, which is configurationally stable when kept and reacted below −40 °C.[7] Addition of the readily available cyclopentenone **9**[8] to this dilithio species gave a modest yield of a diol which could be converted by acid-promoted dehydration to the bis(4,5,6,7-tetrahydro-2-indenyl) ligand **10**. The overall conversion of dibromide **8** to ligand **10** proceeds in 37% yield.

Since the two faces of the cyclopentadienyl ligands are homotopic, metalation of **10** can yield only a single $C_2$-symmetrical isomer of the *ansa*-metallocene dichlorides **5**. Thus, deprotonation of **10** could be effected with *n*-butyllithium in THF for 0.5 h at −78 °C and then for 0.5 h at 0 °C. Addition of $TiCl_3$ in THF at −10 °C, followed by heating under reflux for 6 h and then by treatment with HCl in $CHCl_3$ in air, gave after a simple extractive workup a single $C_2$-symmetric stereoisomeric titanocene dichloride complex whose structure was determined by spectroscopic characterization.[9] Recrystallization from solvents gave red microcrystals (mp >280 °C dec) in 68% yield. Attempts to obtain crystals large enough for X-ray diffraction studies were unsuccessful.[10]

**Asymmetric Epoxidation.** While many synthetic applications of the asymmetric epoxidation of functionalized alkenes catalyzed by titanium complexes in the presence of *tert*-butyl hydroperoxide (TBHP) have been

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[4] (a) Rheingold, A. L.; Robinson, N. P.; Whelan, J.; Bosnich, B. *Organometallics* **1992**, *11*, 1869. (b) Hollis, T. K.; Rheingold, A. L.; Robinson, N. P.; Whelan, J.; Bosnich, B. *Organometallics* **1992**, *11*, 2812. (c) Erickson, M. S.; Fronczek, F. R.; McLaughlin, M. L. *J. Organomet. Chem.* **1991**, *415*, 75.

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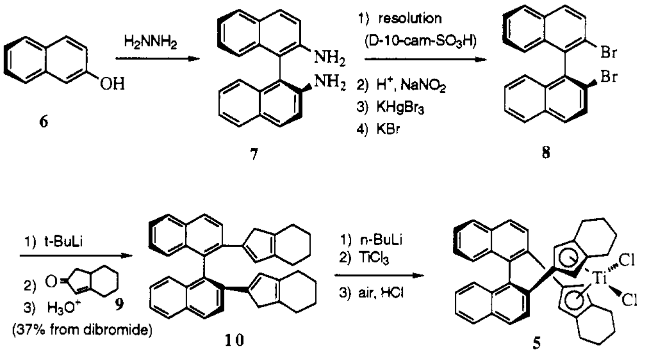
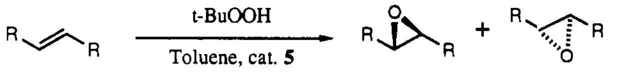
**Scheme I. Synthesis of Metallocene 5**

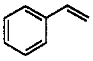
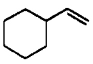
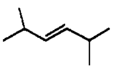
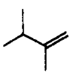


developed over the last several years,[11] only recently has the asymmetric titanocene-catalyzed epoxidation of unfunctionalized alkenes been reported[12]—in spite of the ability of polymer-supported titanocene complexes to catalyze the epoxidation of unfunctionalized alkenes being first reported in 1981.[13] In order to increase the scope of this reaction, we examined the ability of chiral titanocene dichloride complex **5** to function as a catalyst for the asymmetric epoxidation of unfunctionalized alkenes.

Epoxidation reactions were conducted by using 0.3% **5** in TBHP–toluene at substrate concentrations of 3.6 M for 15 h under argon at the highest temperature under which no epoxide formation was detected in the respective control reaction; *n*-decane was used as an internal standard.[10] When the temperature was raised, homogeneous solutions of the green titanocene dichloride **5** consistently turned yellow after about 10 min. After 15 h the reaction was stopped and the mixture analyzed by gas chromatography and $^1$H NMR spectroscopy. The epoxides were found as the sole detectable product; the results are summarized in Table I. From these results we note that the best selectivity was obtained with a sterically unhindered trans-disubstituted alkene. As the substituents become either more numerous or more encumbered, the selectivity drops. The ability to obtain better results with transoid alkenes sets these $C_2$-symmetric metallocene catalysts apart from the metalloporphyrin catalysts, which find greatest success in the enantioselective epoxidations of cisoid olefins.[15,16]

**Table I. Asymmetric Epoxidation of Aliphatic and Aromatic Alkenes Using 5**[a]



| substrate | temp (°C) | no. of turnovers | enantiomeric excess (% ee)[b] | major enantiomer[c] |
|---|---|---|---|---|
|  | 80 | 45 | 16 | (+) |
|  | 40 | 44 | 16 | (*R*)-(+) |
|  | 80 | 14 | 3 | (*S*)-(−) |
|  | 80 | 20 | 5 | |
|  | 80 | 18 | 2 | |

[a] Reactions were run with 0.3% catalyst, stoichiometric TBHP and 3.6 M alkene in toluene, for 15 h. No other byproducts were discovered by GC or $^1$H NMR. [b] Enantiomeric excess determined by GC analysis using a chiral β-cyclodextrin capillary column. [c] Assigned by comparison of polarimetry measurements with literature data.[12,14]

We have demonstrated that the enantiomerically enriched $C_2$-symmetric binaphthalene-derived titanium dichloride catalyst **5** can be used for the homogeneous asymmetric epoxidation of unfunctionalized alkenes. The sterically rigid, $C_2$-symmetrical chirality inherent in **5** has interesting ramifications in these and other enantioselective reactions of transoid or locally $C_2$-symmetric double bonds.

**Acknowledgment.** We thank the National Institutes of Health for support of this work (Grant No. GM 42735).

**Supplementary Material Available:** Text giving experimental procedures for the preparation of ligand **10** and titanocene dichloride **5** and their full spectroscopic data (2 pages). Ordering information is given on any current masthead page.

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(9) Selected characterization data for **5**: mp >280 °C; $[\alpha]^{23}_D = +895°$ ($c$ = 0.009, CHCl$_3$); $^1$H NMR (300 MHz, CDCl$_3$) δ 1.53 (m, 4H), 2.01 (m, 4H), 2.22 (ddd, $J$ = 17.0 Hz, $J$ = 6.0 Hz, $J$ = 6.0 Hz, 2H), 2.67 (ddd, $J$ = 17.0 Hz, $J$ = 6.0 Hz, $J$ = 6.0 Hz, 4H), 3.20 (ddd, $J$ = 17.0 Hz, $J$ = 6.5 Hz, $J$ = 6.5 Hz, 2H), 4.29 (d, $J$ = 2.5 Hz, 2H), 6.53 (d, $J$ = 2.5 Hz, 2H), 6.99 (d, $J$ = 8.5 Hz, 2H), 7.18 (t, $J$ = 9.0, 2H), 7.47 (t, $J$ = 9.0, 2H), 7.79 (d, $J$ = 8.5 Hz, 2H), 7.94 (d, $J$ = 8.5 Hz, 2H), 8.01 (d, $J$ = 8.5 Hz, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ 144.31, 136.63, 133.95, 133.53, 133.49, 131.87, 130.318, 127.97, 127.93, 126.85, 126.69, 126.41, 124.71, 120.36, 113.59, 25.60, 25.12, 21.79, 21.61; IR (thin film) 2928, 2290, 1590, 1497, 1273, 1261 cm$^{-1}$; FAB MS (100 mA, 8 kV) $m/z$ 608 (M$^+$, 2), 573 (M$^+$ − Cl, 12), 537 (M$^+$ − 2Cl, 4). Anal. Calcd for $C_{38}H_{32}TiCl_2 \cdot H_2O$: C, 72.97; H, 5.48. Found: C, 73.02; H, 5.24.

(10) The dilithio species derived from dibromide **8** also successfully added to 2-indanone, which after acid-promoted elimination gave a bis(indenyl) ligand analogous to tetrahydroindenyl ligand **10**, but attempts to form group 4 metallocene dichloride complexes from this bis(indenyl) ligand were unsuccessful.

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