Asymmetric Epoxidation of Unfunctionalized Alkenes Using the New C$_2$-Symmetrical 1,1'-Binaphthyl-2,2'-Dimethylene-Bridged *ansa*-Bis(1-indenyl)Titanium Dichloride Catalyst

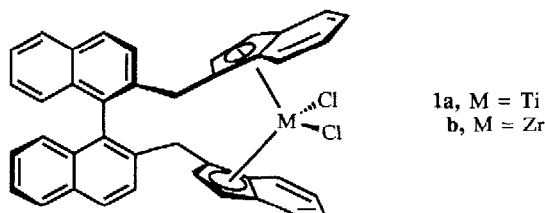Steven L. Colletti[†] and Ronald L. Halterman*

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Summary: The asymmetric catalytic epoxidation of various unfunctionalized alkyl and aryl alkenes has been accomplished using the new C$_2$-symmetrical 1,1'-binaphthyl-2,2'-dimethylene-bridged *ansa*-Bis(1-indenyl)titanium dichloride complex. Enantiomeric excesses of 22% and activities up to 61 turnovers were observed using the (R)(-)-BpDM-(1-ind)$_2$TiCl$_2$ catalyst.

The transition metal catalyzed epoxidation is a powerful and potentially asymmetric method in organic synthesis today.[1] The Sharpless asymmetric epoxidation of allylic alcohols is an example of how powerful these methods can become,[2] but is limited by the need for an allylic substituted hydroxyl functionality to precoordinate the metal and direct the attack of electrophillic oxygen upon the olefin. The potential for a general catalyst which epoxidizes olefins regardless of the functionality they possess,[3] lies in the development of chiral ligands which can impose asymmetry at the metal center through non-bonded interactions with the substrate. The development of such catalysts for epoxidation reactions has found the most activity in metalloporphyrin[4] and (salen)metal[5] chemistry. However, there has been no application of metallocene chemistry to the asymmetric catalytic epoxidation of unfunctionalized olefins. In the case of titanocene and zirconocene chemistry, the fate of postulated metal-oxo intermediates in the catalytic epoxidation of an alkene is to condense to insoluble (metal-oxygen-metal) polymers[6] which render the metallocene inactive. Brubaker and Grubbs have reported the catalytic epoxidation of cyclohexene and cyclooctene with the use of achiral heterogenous polymer-supported Cp$_2$TiCl$_2$ and Cp$_2$ZrCl$_2$ complexes in the presence of TBHP.[7] Presumably the attachment of these catalysts to a polymeric backbone prevented the metal centers from coming into bonding distance of each other and forming inactive (metal-oxygen-metal) polymers. Based on this result, we envisioned that sterically hindered chiral titanocene and zirconocene

complexes would not be prone to deactivation and could function as homogenous catalysts for the asymmetric epoxidation of unfunctionalized olefins.

We recently communicated the development of a new class of C_2-symmetrical binaphthyldimethylene-bridged bis(indene) *ansa*-metallocenes **1a** and **1b** (M=Ti, Zr).[8] We now report the use of the (R)(-)-2,2'-Bis(1-indenylmethyl)-1,1'-binaphthyldichlorotitanium complex **1a** as a homogenous catalyst for the asymmetric epoxidation of unfunctionalized trans and terminal alkenes.

1a, M = Ti
b, M = Zr

The epoxidation reactions were conducted by using 0.3% **1a** or **1b** in TBHP-toluene[9] 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] Upon warming, homogenous solutions of either the green titanium dichloride **1a** or colorless zirconium dichloride **1b** consistently turned yellow after about 10 min, presumably forming reactive metal-peroxo intermediates. The crude reaction mixtures were analyzed for both turnover number and enantiomeric excess (ee) via gas chromatography.[11] The results are shown in Table I for the asymmetric catalytic epoxidation of aliphatic and aromatic alkenes. Each authentic epoxide was subjected to the catalytic reaction conditions to insure that there was no Lewis acid catalyzed opening of the product in the epoxidation of alkene potentially causing kinetic resolution. These test reactions furnished ca. 100% recovery of epoxide with no detection of possible alcohol derivatives by GC or ^{1}H NMR.

From the results shown in Table I, it is apparent that the degree of asymmetric induction and catalytic activity is quite dependent upon the nature of the alkene substrate. Since the enantiofacial selectivity of (R)(-)-**1a** is determined by its C_2-symmetrically engineered cavity, the two possible stereofacial approaches of *trans*-3-hexene would appear to be the most defined for this C_2-symmetrical olefin compared to the other substrates tested.[12] Accordingly, the best enantioselectivity was obtained with *trans*-3-hexene (22% ee). The lower enantioselectivities found for the epoxidation of 1-substituted olefins, styrene and vinyl cyclohexane, could be attributed to the lack of *trans* geometry in these alkenes, resulting in less non-bonded interactions between the catalyst and the substrate. 1,1-disubstituted and trisubstituted olefins all gave the lowest enantioselectivities, a result apparently due to the steric bulkiness of these olefins preventing an efficient transfer of chirality from (R)(-)-**1a** to these alkenes. The catalytic epoxidation of 2,4,4-trimethyl-2-pentene was virtually non-enantioselective. From the results in Table I, it is also evident that in some cases, lowering the reaction temperature also lowered the stereodifferentiation besides decreasing the activity of the catalyst.

Table I.[a] Asymmetric Epoxidation of Aliphatic and Aromatic Alkenes Using (R)(-)-1a

entry	Alkene	Temperature	Number of Turnovers (% yield)[b]		enantiomeric excess	major[c] enantiomer
1		80 °C	40	(12)	22 %	(+)
2		60 °C	14	(4)	20 %	
3		40 °C	40	(12)	18 %	(R)(+)
4		23 °C	16	(5)	18 %	
5		80 °C	60	(15)	12 %	(S)(+)
6		60 °C	30	(7)	7 %	
7		80 °C	61	(25)	6 %	(S)(+)
8		60 °C	44	(19)	4 %	
9		80 °C	31	(8)	3 %	
10		60 °C	12	(4)	2 %	
11		40 °C	10	(6)	2 %	

[a] Reactions were run with 0.3% catalyst, stoichiometric TBHP, 3.6 M alkene in toluene, for 15 h. [b] Epoxidation yields correspond to the amount of alkene consumed with no other byproducts discovered by GC or ^{1}H NMR. [c] Assigned by comparison of polarimetry measurements with literature (ref 4a, 14).

Although there appears to be an electronic bias in the epoxidation of the two sterically similar terminal olefins, vinyl cyclohexane (15 % yield) and the more electron rich 2-methyl-1-heptene (25% yield), the sterics of an alkene seem to have a larger effect than the electronics of an alkene upon the catalytic activity of (R)(-)-1a.[13] Thus, the terminal olefin, vinyl cyclohexane, was epoxidized more efficiently (60 turnovers) than the internal olefin, *trans*-3-hexene (40 turnovers). As the steric bulk increases around the double bond, the ability of the substrate to enter the chiral pocket of catalyst (R)(-)-1a apparently diminishes. Comparing the epoxidations of entries 7 and 9, shows that the additional methyl group near the double bond in 2,3-dimethyl-1-butene essentially reduced the number of turnovers by 50% from 2-methyl-1-heptene. We have also observed remarkably lower catalyst activity with the less acidic zirconium analog rac-**1b** (*trans*-3-hexene, 80 °C, 1% yield, 3 turnovers), a result consistent with the polymer-supported zirconium complexes.[7b] The low activity of this zirconium catalyst discouraged examination of its asymmetric application. As the epoxidations progressed, the efficiency of (R)(-)-**1a** gradually decreased until the catalyst virtually became inactive at 15-18 h.

We have demonstrated that the enantiomerically enriched C_2-symmetric binaphthyl derived titanium dichloride catalyst (R)(-)-**1a** can be used for the homogeneous asymmetric epoxidation of unfunctionalized alkyl and aryl alkenes. The C_2-symmetrical chirality inherent in **1** has interesting ramifications in the enantioselective epoxidation of transoid or locally C_2-symmetric double bonds. This characteristic sets these C_2-symmetric metallocene catalysts apart from the metalloporphyrin catalysts which find greatest success in the enantioselective

epoxidations of cisoid olefins.[4,5] These promising preliminary results are leading to the development of other new C_2-symmetrical metallocene catalysts in our laboratory.

References and Notes

†   Work performed at the Department of Chemistry, Boston University, Boston, MA. 02215

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10.   All reactions were run under an inert atmosphere using dry, distilled and degassed reagents. For example: In a nitrogen-filled dry box (Vac Atmospheres), an oven-dried 2-neck 5 mL conical flask equipped with a vacuum adapter, stirbar and septum, was charged with **1a** (10 mg, 0.016 mmol) and transferred to a Schlenk line where it was brought under vacuum (< 0.001 mm Hg) and filled with argon 3X. n-Decane (103 μL, 0.526 mmol), *trans*-3-hexene (Aldrich, 99+%, 660 μL, 5.31 mmol), and TBHP (3.9 M in toluene, 1.36 mL, 5.31 mmol) were added sequentially via syringe. An aliquot (20 μL) of the reaction mixture was removed via syringe, diluted with toluene (50 μL), and analyzed by GC; *trans*-3-hexene (5.38 mmol). Under a positive pressure of argon (ca. 10 mm Hg) the septum was removed and replaced by a dry glass stopper. All greased joints were wrapped with teflon tape and secured, the vacuum adapter valve closed, and the reaction vessel heated at 80° C for 16 h in a closed system. After 10 min. the green homogenous reaction mixture turned yellow and stayed homogenous. The vessel was then opened and an aliquot again removed, diluted, and analyzed by GC; *trans*-3-hexene oxide (0.62 mmol).

11.   Hewlett-Packard 5890A gas chromatograph equipped with an achiral H-P fused silica capillary column (#19091J-102, 25 m X 0.20 mm i.d., 0.33 μm film) and a chiral CP-Cyclodex-B capillary column (Chrompack, Raritan, NJ. 08869, 50 m X 0.25 mm i.d., 0.25 μm film).

12.   Both *trans*-β-methylstyrene and *trans*-stilbene were epoxidized in control reactions.

13.   Under identical reaction conditions using 0.3% (R)(-)-**1a**, the catalytic epoxidation of cyclohexene was much more efficient (3-4X turnover/yield) than the catalytic epoxidation of *trans*-3-hexene.

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