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Bis(binaphthylcyclopentadienyl)-derived metallocene peroxide complexes: catalysts for the enantioselective epoxidation of unfunctionalized alkenes

Steven L. Colletti and Ronald L. Halterman

Department of Chemistry and Biochemistry, University of Oklahoma, 620 Parrington Oval, Norman, OK 73019-0370 (USA)

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Abstract

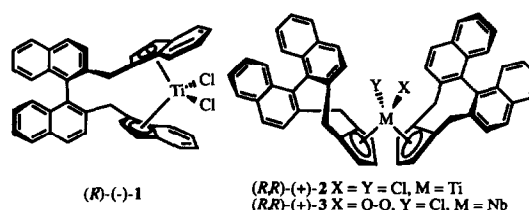
The enantioselective catalytic epoxidation of unfunctionalized alkyl and aryl olefins was conducted using titanocene and niobocene peroxide complexes incorporating a C_2 -symmetrical binaphthylcyclopentadienyl ligand (BpDMCp). Enantiomeric excesses up to 20% and activities up to 55 turnovers were obtained with the application of our chiral bis(binaphthylcyclopentadienyl)-derived metallocenes. A significant decrease in the enantioselectivity for the epoxidation of *trans*-3-hexene was observed when the metal was changed from titanium to niobium in these binaphthyl-derived C_2 -symmetrical complexes. The preparation of the bis(binaphthylcyclopentadienyl)-chloroniobium peroxide complexes and bis(indenyl)chloroniobium peroxide is described.

1. Introduction

Throughout the last fifteen years there has been a limited number of systems investigated which concern the enantioselective catalytic epoxidation of unfunctionalized alkenes. Over that period many of the systems which have been presented require a specific functional group such as chalcones or prochiral halohydrins to generate enantiomerically enriched epoxides as with the alkaloid-based [1] and polyaminoacid-based [2] phase transfer catalysts or Co^{II} (salen) complexes [3]. The vanadium [4], molybdenum [5], and the very successful titanium–tartrate [6] systems all require the application of allylic alcohols to achieve good enantioselectivity. The most effective means to achieve substantial enantioselectivity in the asymmetric epoxidation of *unfunctionalized* olefins has been the use of the metalloporphyrin [7] or (salen)manganese [8] systems. The success of these systems appears to be limited to the epoxidation of cisoid olefins due to the inherent planarity of these catalysts.

We have recently communicated the development of an entirely new class of chiral epoxidation catalyst [9a], namely the binaphthyl-bridged bis(indenyl) titanocene

dichloride 1 [9b] which provides interesting ramifications in the asymmetric epoxidation of *trans*-alkenes due to its C_2 -symmetric cleft. The C_2 -symmetrical chirality associated with such metallocene complexes



complement the metalloporphyrin and (salen)metal catalysts. We have also described the preparation and structure elucidation of the binaphthyl-based C_2 -symmetrical titanocene dichloride 2 [10a]. Herein we present our results of the asymmetric catalytic epoxidation of *trans* and terminal alkenes using our bis(binaphthylcyclopentadienyl)titanium dichloride 2, abbreviated (BpDMCp) $_2$ TiCl $_2$, with comparison to the bis(binaphthylcyclopentadienyl)chloroniobium peroxide 3, abbreviated (BpDMCp) $_2$ Nb(O $_2$)Cl. The preparation of the previously unreported bis(indenyl)chloroniobium peroxide 4 is also described, a complex which has demonstrated inferior activity in the catalytic epoxidation of cyclohexene relative to parent niobocene chloroperoxide [11].

Correspondence to: Professor R.L. Halterman.

2. Experimental details [12]

2.1. (*R,R*)-(+)-Bis[2,3-(1,1'-binaphthyl-2,2'-dimethyl)cyclo-2,4-dienyl]dichloroniobium (6)

A solution of (*R*)-(+)-binaphthylcyclopentadiene **5** [10] (180 mg, 0.523 mmol) in THF (2.6 ml) was cooled to -78°C under argon. *n*-Butyllithium (1.48 M in heptane, 0.371 ml, 0.549 mmol) was introduced dropwise and the resulting dark yellow solution was stirred at -78°C over 0.5 h. The anion solution was then added dropwise to a pale yellow solution of $\text{NbCl}_4(\text{THF})_2$ [13] (99 mg, 0.261 mmol) in THF (2.6 ml) at -10°C via syringe. The reaction mixture was then warmed to room temperature and stirred for 3 h at 23°C during which the color changed from green to black-green. The reaction mixture was concentrated *in vacuo* and upon complete solvent removal, the dark green residue was dissolved in distilled-degassed CH_2Cl_2 (6 ml) and distilled-degassed hexane (12 ml) was introduced dropwise at room temperature via syringe. The heterogeneous solution was then Schlenk-filtered to remove inorganic entities leaving a green filtrate which was concentrated *in vacuo* to a green crystalline solid **6** (138 mg, 62%), m.p. 200°C dec; $[\alpha]_{\text{D}}^{23} + 78.1^{\circ}$ (*c* 0.105, CH_2Cl_2); IR (KBr) 3051, 2958, 2928, 1620, 1593, 1507, 1420, 1363, 1260, 1095, 1022, 864, 821, 800, 756, 685, 622, 573, 515 cm^{-1} .

2.2. (*R,R*)-(+)-Bis[2,3-(1,1'-binaphthyl-2,2'-dimethyl)cyclopenta-2,4-dienyl]chloroniobium(V) peroxide (3)

In a nitrogen-filled dry box, a 25 ml Schlenk tube was charged with (*R,R*)-(+)-dichloride **6** (138 mg, 0.162 mmol) and transferred to a Schlenk line (under argon) where 10 ml of distilled-degassed CH_2Cl_2 was introduced via syringe. Degassed H_2O_2 (30% in H_2O , 0.667 ml, 6.52 mmol) was added dropwise to the dark green solution at room temperature *via* syringe. The reaction mixture began frothing during which a color change from dark green to light green to red to orange to light yellow occurred. After 30 min the reaction mixture was opened to air and extracted with CH_2Cl_2 and H_2O . **Caution!** Niobium peroxides are known to be occasionally explosive when exposed to air [11]. One instance of an excessive evolution of gas occurred upon opening the reaction vessel to air. The CH_2Cl_2 partition was dried over Na_2SO_4 , concentrated via rotary evaporation and the yellow residue was further dried under vacuum. The crude product was purified open to air via precipitation of the niobocene from distilled methylene chloride by dropwise addition of distilled hexane. The precipitated fine yellow powder was isolated as a mixture of *ca.* 10% oxo **7** and *ca.* 90% peroxy **3** (113 mg, 83%), m.p. 240°C dec; $[\alpha]_{\text{D}}^{23} + 127^{\circ}$ (*c* 0.074, CH_2Cl_2); ^1H NMR (500 MHz, CDCl_3) δ 8.04 (d, $J = 9.0$ Hz,

1H), 8.01 (d, $J = 9.0$ Hz, 1H), 7.96 (d, $J = 8.5$ Hz, 1H), 7.87 (m, 6H), 7.82 (d, $J = 9.0$ Hz, 1H), 7.42 (m, 5H), 7.34 (d, $J = 8.5$ Hz, 1H), 7.19 (m, 6H), 7.06 (d, $J = 8.5$ Hz, 1H), 6.97 (d, $J = 8.5$ Hz, 1H), 6.10 (dd, $J = 3.0, 3.0$ Hz, 1H), 6.02 (dd, $J = 3.0, 3.0$ Hz, 1H), 5.66 (dd, $J = 3.0, 3.0$ Hz, 1H), 5.56 (dd, $J = 3.0, 3.0$ Hz, 1H), 5.51 (s, 1H), 5.05 (s, 1H), 4.11 (d, $J = 16.0$ Hz, 1H), 3.92 (d, $J = 16.0$ Hz, 1H), 3.45 (m, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 140.00 - 95.00 (obscured by *minor* oxoniobocene), 35.53 ($-\text{CH}_2-$), 34.70 ($-\text{CH}_2-$), 33.93 ($-\text{CH}_2-$), 33.87 ($-\text{CH}_2-$); IR (KBr) 3052, 2954, 2926, 1508, 1424, 1362, 1258, 1026, 866, 822, 800, 757, 517 cm^{-1} .

2.3. (*R,R*)-Bis[2,3-(1,1'-binaphthyl-2,2'-dimethyl)cyclopenta-2,4-dienyl]chloroniobium(V) oxide (7)

Open to air, an NMR tube was charged with a *ca.* (90:10) mixture of peroxy **3** to oxo **7** respectively (15 mg, *ca.* 0.018 mmol), PPh_3 (116 mg, 0.443 mmol), dissolved in CDCl_3 (0.400 ml) and purged with argon. The solution changed color from light yellow to gold. ^1H NMR analysis (sp^2 region, 5.00–6.50 ppm) of the solution showed a complete reversal of the peroxy **3** to oxo **7** ratio (10:90) respectively. For oxo **7**; ^1H NMR (300 MHz, CDCl_3) δ 6.39 (dd, $J = 3.0, 3.0$ Hz, 1H), 5.98 (m, 1H), 5.91 (dd, $J = 3.0, 3.0$ Hz, 1H), 5.85 (dd, $J = 3.0, 3.0$ Hz, 1H), 5.22 (m, 1H), 5.08 (m, 1H).

2.4. Bis(η^5 -indenyl)chloroniobium(V) peroxide (4)

Freshly distilled indene (0.315 ml, 2.70 mmol) was diluted with THF (27 ml) and cooled to -78°C . *n*-Butyllithium (1.48 M in heptane, 1.82 ml, 2.70 mmol) was added dropwise to form a yellow solution of the indenyl anion which was warmed to 0°C over 0.5 h. The anion solution was then re-cooled to -78°C and introduced dropwise via syringe to neat $\text{NbCl}_3(\text{DME})$ (391 mg, 1.35 mmol) also pre-cooled to -78°C . The reaction mixture was allowed to warm to room temperature and was stirred at 23°C for 3 h producing a brown solution. The mixture was concentrated *in vacuo* to a brown residue which upon complete removal of solvent was dissolved in degassed CH_2Cl_2 (54 ml) followed by dropwise addition of degassed H_2O_2 (30% in H_2O , 3.40 ml, 33.75 mmol) via syringe at 23°C . The reaction mixture was stirred for 30 min upon which the color turned yellow. Concentration *in vacuo* afforded a dark yellow residue which upon drying was dissolved in degassed CH_2Cl_2 (25 ml), Schlenk filtered to remove inorganic byproducts, and the orange filtrate concentrated *in vacuo*. The residue was then rapidly stirred in degassed hexane (25 ml) under argon and the organic residues were Schlenk filtered-decanted through. The remaining orange residue was dried *in vacuo* and purified open to air by heating into solution with either

1-chlorobutane or 1-chloropentane (solvents bubbled with argon for *ca.* 15 min). The hot filtered solution was purged with argon and cooled to -30°C for 2–3 h upon which peroxo niobocene **4** precipitated as an orange glassy solid (192 mg, 38%), ^1H NMR (300 MHz, CDCl_3) δ 7.45 (m, 8H), 5.38 (d, $J = 5.0$ Hz, 2H), 5.26 (d, $J = 5.0$ Hz, 2H), 4.39 (dd, $J = 5.0, 5.0$ Hz, 2H); IR (neat film) 3067, 2962, 1713, 1696, 1603, 1460, 1402, 1260, 1093, 1020, 860, 799, 758, 602 cm^{-1} .

2.5. Catalytic epoxidation using niobocene peroxides (*R,R*)-(+)-(**3**) and (**4**)

In a nitrogen-filled dry box, an oven-dried 25 ml Schlenk tube equipped with a stirbar and septum, was charged with *ca.* 0.03% **3** or **4** (1–5 mg) and transferred to a Schlenk line where it was brought under vacuum (< 0.001 mmHg) and filled three times with argon. Acetonitrile (6.6 M in olefin), *n*-decane (75 equiv.), olefin (2940 equiv.), and H_2O_2 (30% in H_2O , 294 equiv.) were added sequentially via syringe. An aliquot (80 μl) of the reaction mixture was removed via syringe and analyzed by GC. Under a positive pressure of argon (*ca.* 10 cmHg) the reaction mixture was heated at 70°C for *ca.* 4 h after which the yellow catalyst **3** solution turned nearly colorless and the light orange catalyst **4** solution turned yellow. Both catalyst solutions **3** and **4** were homogenous throughout. The reaction mixture was then cooled to room temperature and the reaction vessel opened. A pipette was used to decant the organic phase of the reaction mixture which was transferred to a vial and dried with Na_2SO_4 , filtered over celite. The crude solution was analyzed by GC for yield-turnover and where appropriate, enantiomeric excess.

2.6. Asymmetric catalytic epoxidation using titanocene dichlorides (*R,R*)-(+)-(**2**)

In a nitrogen-filled dry box, an oven-dried two-neck 5 ml conical flask equipped with a vacuum adapter, stirbar and septum, was charged with *ca.* 0.3% **2** (4–10 mg) and transferred to a Schlenk line where it was brought under vacuum (< 0.001 mmHg) and filled with argon 3X. *n*-Decane (33 equiv.), olefin (333 equiv.), and TBHP (3.9 M in toluene, 333 equiv.) [14] 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. Under a positive pressure of argon (*ca.* 10 cm 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 in a closed system for *ca.* 16 h at different temperatures depending upon the olefin used. After 10–30 min the red homogenous reaction mixture

turned yellow and stayed homogeneous. The vessel was then opened and an aliquot again removed, diluted, and analyzed by GC for yield-turnover and enantiomeric excess. Where enantiomeric excesses were above 5%, absolute configuration was determined by comparison of polarimetry measurements with the literature. Thus the crude reaction mixture was loaded onto a preparative thin layer chromatography glass plate (SiO_2 , petroleum ether) and developed five times. The pure epoxides were isolated as colorless oils which were dissolved in toluene (2 ml) and examined for sign of optical rotation typically $> 0.010^{\circ}$ (α). As a check for the removal of any chiral impurities, the catalytic epoxidation of cyclohexene with (*R,R*)-(+)–**2** afforded cyclohexene oxide which was purified as above providing an optical rotation of 0.000° (α).

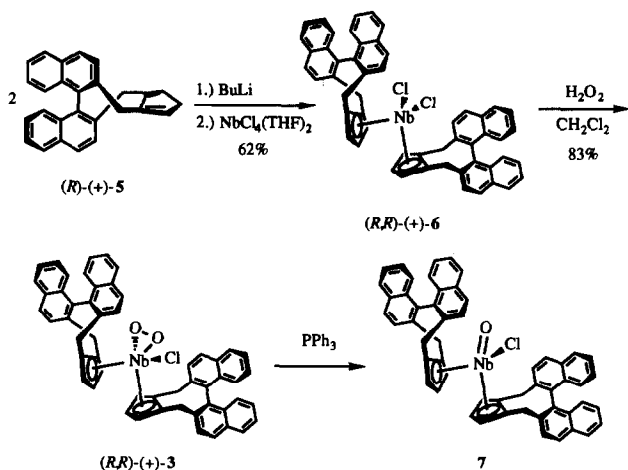
2.7. Test for kinetic resolution in epoxide opening

In a nitrogen-filled dry box, an oven-dried 1/2 dram screw-cap vial equipped with a flybar was charged with *ca.* 1% titanocene dichloride **2** (*ca.* 2 mg) and then *n*-decane (0.077 mmol), authentic epoxide (0.234 mmol), and TBHP (3.9 M in toluene, 0.78 mmol) were added sequentially via microsyringe. An aliquot (20 μl) was removed for GC analysis and the vial was sealed with teflon tape, the screw-cap, teflon tape, and then parafilm. The reaction mixture was heated in an oil bath at the temperature for the respective catalytic epoxidation of olefin. After 15 h the mixture was cooled and analyzed by GC resulting in *ca.* 100% of oxirane in all epoxide systems.

3. Results

3.1. Niobocene syntheses

Treatment of the *n*-butyllithium generated anion of (*R*)-(+)–BpDMCp **5** with $\text{NbCl}_4(\text{THF})_2$ in THF at -10°C with warming to room temperature for 3 h produced a black-green reaction mixture [15]. After solvent removal *in vacuo* the green product was freed of inorganic residue by precipitation with CH_2Cl_2 -hexane, leaving a green mother liquor which was concentrated *in vacuo* to provide green crystalline paramagnetic niobocene dichloride **6** in 62% yield. In the absence of diamagnetic NMR spectra, the identity of niobocene(IV) dichloride **6** was determined from its IR spectrum which displayed nearly identical absorbances to its titanocene dichloride **2** counterpart [10a,16]. Niobocene dichloride **6** would not succumb to mass spectral analysis, displaying only the BpDMCp ligand **5** fragment in 100% relative intensity. However, the conclusive identification of the chloro peroxide derivative **3** synthesized in high yield from this putative dichloride strongly implicates the presence of **6**.



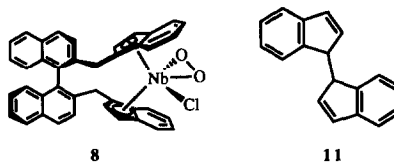
Scheme 1. Niobocene formations with binaphthylcyclopentadiene 5.

Oxidation of niobocene(IV) dichloride 6 to niobocene(V) chloro peroxide 3 was accomplished by using 30% aqueous hydrogen peroxide [11]. Thus the dark green reaction mixture of dichloride 6 faded to light yellow with the introduction of H₂O₂ providing niobocene peroxide 3 as a fine yellow powder in 83% yield after precipitation from CH₂Cl₂-hexane. The product was observed to be 90% peroxide 3 and 10% niobocene chloro oxide 7 by ¹H NMR, a mixture whose ratio was subsequently reversed by the addition of excess PPh₃. Thus the oxidation of PPh₃ to P(O)Ph₃ with peroxide 3 induced the formation of excess oxo niobocene 7 [11,17].

The oxidation of triphenylphosphine by (R,R)-(+)-3 supports our assignment of the niobocene peroxide structure. We also based the presence of a peroxide moiety in 3 upon its IR spectrum which revealed a characteristic peroxide oxygen-oxygen stretch ($\nu(\text{O}-\text{O})$) of 866 cm⁻¹ and a NbO₂ (ν_{sym}) absorbance of 517 cm⁻¹ [11,18]. Owing to the incorporation of the additional chiral niobium atom in complex 3, the C₂-symmetry that was observed in titanocene dichloride 2 is lost, and the ¹H NMR spectrum therefore revealed six different cyclopentadienyl resonances at 6.10, 6.02, 5.66, 5.56, 5.51, and 5.05 ppm for niobocene chloro peroxide 3.

Having demonstrated the facile preparation of niobocene peroxide 3, we knew of no report of a chiral bridged bis(indenyl) niobocene peroxide such as 8, nor for that matter, the *parent* bis(indenyl)chloroniobium peroxide 4. Although the synthesis of *ansa*-niobocene 8 did not bear fruit, we ultimately succeeded in the preparation of unknown *parent* bis(indenyl)chloroniobium peroxide 4. Concurrent with our efforts toward the synthesis of *ansa*-niobocene peroxide 8 we explored the preparation of the *parent* peroxide 4. Our

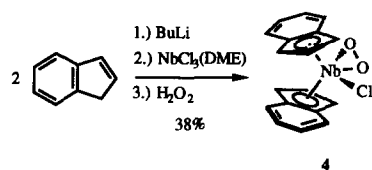
initial attempts at preparing peroxide 4 involved the preliminary formation of bis(indenyl)niobium(IV) dichloride 9 and its subsequent oxidation to 4 [11,15]. Although (indenyl)₂NbCl₂ 9 has been reported, its preparation and characterization is quite precarious [19]. We found that treatment of NbCl₄(THF)₂ with indenyllithium formed a brown solid which was purified to afford paramagnetic niobocene dichloride 9 in 30% yield. Green and Hughes recently reported the synthesis of bis(indenyl)niobium dichloride 9 by this same method providing similar results in 30–35% yield [20]. The oxidation of dichloride 9 with either H₂O₂ [11] or DMSO [21] (various reaction times, molar equivalents, anaerobic or aerobic, 23°C) did not furnish niobocene(V) peroxide 4 nor bis(indenyl)niobium(V) chloro oxide 10 respectively including the attempted oxidation of dichloride 9 with TBHP or basic aqueous hydrogen peroxide.



During this study, however, we discovered that the major isolated product from dichloride 9 formation was a mixture of *meso* and *dl* 1,1'-Bi-1H-indenes 11 [22] by ¹H NMR spectroscopy, indicating that reductive elimination of 1,1'-Bi-1H-indene 11 was mediated by NbCl₄(THF)₂. Indeed, high yields (66 to 82%) of 11 could be obtained by the reaction of indenyllithium with 50% NbCl₄(THF)₂ depending upon the reaction temperature (23 to -10°C respectively). No coupling product was observed upon allowing indenyllithium to react with itself under the reaction conditions and the unexplained characteristic low yields of bis(indenyl)niobium dichloride 9 formation observed by us and the Green group [20] appears to be a direct result of the propensity of higher valent niobium species [23] to reductively eliminate 1,1'-Bi-1H-indene. Consequently, Cp₂NbCl₂ (78%) [15a] and other substituted *cyclopentadienyl*-derived niobocene dichlorides (62–95%) [15b] are associated with much higher synthetic yields.

A one-pot synthesis of peroxide 4 was ultimately possible via metalation with niobium(III) chloride followed by immediate oxidation. The use of NbCl₃(DME) at -78°C with warming to 23°C for 3 h produced a brown residue which was immediately treated with H₂O₂ for 30 min at 23°C providing after purification bis(η^5 -indenyl) niobium chloro peroxide 4 in 38% yield as an orange glassy solid. A significant change in the IR spectrum was observed between dichloride 9 and peroxide 4 in the region of 500 to 1300 cm⁻¹. The IR spectrum of 4 displays the characteristic *sharp* perox-

ide oxygen–oxygen stretch ($\nu(\text{O}-\text{O})$) of 860 cm^{-1} and a NbO_2 (ν_{sym}) absorbance of 602 cm^{-1} [11,18]. Due to the incorporation of a mirror plane which includes

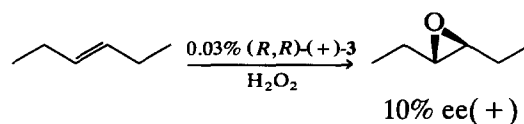


both oxygen atoms, the chlorine atom and the niobium atom in the node of the plane [24], both indenyl ligands are thus equivalent by C_s -symmetry. The ^1H NMR spectrum therefore revealed three different 5.0 Hz coupled cyclopentadienyl resonances at 5.38, 5.26 and 4.39 ppm for $(\eta^5\text{-indenyl})_2\text{Nb}(\text{O})_2\text{Cl}$ 4.

3.2. Asymmetric catalytic epoxidations

In 1980 Sala-Pala *et al.* reported that $\text{Cp}_2\text{Nb}(\text{O})_2\text{Cl}$ could be used catalytically in the presence of H_2O_2 for the low-yield epoxidation of cyclohexene [11]. As a preliminary study, we chose to incorporate our chiral cyclopentadienyl ligand BpDMCp 5 into this catalytic epoxidation scheme. The homogenous epoxidation reaction was conducted by using 0.03% (R,R) -(+)-peroxoniobocene 3 with 10% oxidant (30% H_2O_2 in water) and a *trans*-3-hexene concentration of 6.6 M in acetonitrile. *n*-Decane was used as an internal standard. After 4 h at 70°C the initial yellow reaction mixture turned colorless. The crude reaction mixtures were analyzed for both turnover number and enan-

tiomeric excess *via* gas chromatography. *trans*-3-Hexene oxide was produced in 10% ee with 35



turnovers (1.2% yield). The *parent* bis(indenyl)niobium peroxide 4 was also tested for use as an epoxidation catalyst. Under identical reaction conditions, the reproduction of the $\text{Cp}_2\text{Nb}(\text{O})_2\text{Cl}$ system [11] afforded cyclohexene oxide with 75 turnovers and 2.6% yield in our hands, but the $(\text{indene})_2\text{Nb}(\text{O})_2\text{Cl}$ 4 complex produced cyclohexene oxide in only trace amounts as observed by GC. The use of TBHP instead of H_2O_2 resulted in no epoxidation of cyclohexene at all.

For the titanium series, the epoxidation reactions were conducted by using 0.3% (R,R) -(+)- $(\text{BpDM-Cp})_2\text{TiCl}_2$ 2 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 (alkene, TBHP, no precatalyst 2). *n*-Decane was used as an internal standard. Upon warming, homogeneous solutions of the red titanium dichloride 2 consistently turned yellow after about 10 min, presumably forming reactive metal–peroxo intermediates such as 12. The crude reaction mixtures were analyzed for both turnover number and enantiomeric excess *via* gas chromatography. The results are shown in Table 1 for the asymmetric catalytic epoxidation of aliphatic and aro-

TABLE 1. Asymmetric epoxidation catalyzed by (R,R) -(+)-2

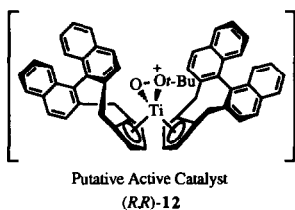
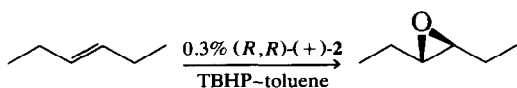
Entry	Alkene	Temperature ($^\circ\text{C}$)	Number of turnovers	(% yield)	Enantiomeric excess (%)	Major enantiomer
1		80	45	(11)	20	(+)
2		40	38	(12)	16	(R)(+)
3		80	55	(14)	6	(S)(+)
4		80	36	(19)	4	(S)(+)
5		80	43	(13)	6	
6		80	17	(5)	4	
7		40	10	(3)	2	

matic alkenes. Absolute configurations were assigned by comparison of polarimetry measurements with the literature [7a,25]. As the epoxidations progressed, the efficiency of the titanocene catalyst **12** gradually decreased until it virtually became inactive after 15–18 h.

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 were run in both the absence and presence of one molar equivalent of *t*-butanol to the authentic epoxide. The reactions furnished *ca.* 100% recovery of epoxide with no detection of possible alcohol derivatives by GC or ¹H NMR spectroscopy.

4. Discussion

Prior to our research there had been no application of chiral metallocenes to the asymmetric catalytic epoxidation of olefins. In the case of titanocene chemistry, the fate of postulated metal–oxo intermediates in the catalytic epoxidation of an alkene is to condense to insoluble (metal–oxygen–metal) polymers [26] which render the metallocene inactive. In contrast to the catalytic inactivity of *parent* titanocene dichloride, Lau *et al.* have reported the catalytic epoxidation of cyclohexene and cyclooctene with the use of achiral heterogeneous polymer-(polystyrene-divinylbenzene beads)-supported Cp₂TiCl₂ in the presence of TBHP [27]. We have shown that sterically hindered chiral titanocene complexes suppress the formation of insoluble metal–oxygen polymers thus enabling their application as homogenous catalysts for the asymmetric epoxidation of unfunctionalized olefins [9a].



The results shown in Table 1 follow the same trends observed with our *ansa*-bis(indenyl) titanocene (*R*)-(-)-**1** [9a]. Accordingly, the best enantioselectivities were obtained with *trans*-3-hexene in which two non-bonded interactions between the olefin and the C₂-symmetrical catalyst are possible. Both *trans*- β -methylstyrene and *trans*-stilbene were epoxidized in their

control reactions and therefore were not investigated in these systems. 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 one non-bonded interaction between the catalyst and the substrate. 2,5-Dimethyl-*trans*-3-hexene and the 1,1-disubstituted and trisubstituted olefins all gave the lowest enantioselectivities, a result possibly due to the excessive steric bulk of these olefins preventing a close interaction with the catalyst to induce stereodifferentiation. Consequently the activity with these substrates was also lower. Comparing the epoxidations of 2-methyl-1-heptene with 2,3-dimethyl-1-butene, shows that the additional methyl group near the double bond in 2,3-dimethyl-1-butene (13% yield) reduces the yield compared to 2-methyl-1-heptene (19% yield). Remarkably, under identical reaction conditions the catalytic epoxidation of the sterically devoid disubstituted olefin, cyclohexene (*ca.* 40% yield), provided three to four times the yield than the catalytic epoxidation of the sterically laden disubstituted olefin, *trans*-3-hexene.

A comparison of the niobocene catalyst (*R,R*)-(+)-(BpDMCp)₂Nb(O)₂Cl **3** with the titanocene catalyst (*R,R*)-(+)-(BpDMCp)₂TiCl₂ **2** in the epoxidation of *trans*-3-hexene shows that the enantioselectivity of the former achieved 10% ee and the latter 20% ee. This marked change in enantioselectivity for the same ligand system apparently arises from the differences between niobium(V) and titanium(IV) metallocenes. The longer (BpDMCp)–metal bond length and the presumed five coordinate transition state for niobocene **3** could be factors that result in a more open chiral cleft of this metallocene resulting in diminished stereodifferentiation [11,24].

The result that the absolute configurations of the major epoxide enantiomers were the same for both (*R,R*)-(+)-**2** and (*R*)-(-)-**1** [9a] catalyst systems is supported by the fact that these two catalysts possess the same enantiomeric C₂-symmetrical cleft. The binaphthyl-bridged bis(indenyl) titanium catalyst **1** provided slightly higher enantiomeric excesses (2%–6% ee) [9a] than the unbridged bis(cyclopentadienyl) titanium catalyst **2** reported here, but the general similarity in the degree of stereodifferentiation of the two titanocenes is promising for the unbridged complex (*R,R*)-(+)-**2**. This result exemplifies the efficiency of the BpDMCp **5** ligand to impose asymmetry even without the aid of a bridging fragment between the two BpDMCp ligands in (*R,R*)-(+)-(BpDMCp)₂TiCl₂ **2** to reduce cyclopentadienyl–metal rotation [28]. Further structural tuning of the BpDMCp **5** ligand to increase its stereodifferentiation efficiency is surely a bright prospect.

In an attempt to achieve higher yields in this epoxidation scheme the catalyst concentrations were raised to 1.5%–2.0%. This change did not furnish reaction completion but resulted in similar to lower yields with consistently fewer turnovers. As the catalyst concentrations were further increased the reaction mixtures became heterogeneous resulting in the need for more dilute (0.7 M) substrate concentrations which ultimately destroyed catalytic activity. Monitoring the epoxidation of vinylcyclohexane with 1.5% (BpDMCp)₂TiCl₂ **2** showed that 11% epoxide formation had occurred after *ca.* 5 h and the yield had reached only 12% after 17–33 h. Therefore there had to be an extreme excess of alkene present at the *start* of the catalytic reaction to afford respectable turnover numbers. This effect translates into low catalyst concentrations. It has been speculated that autoretardation of the titanocene catalysts occurs as the amount of *t*-butanol increases [27]. Thus the formation of titanocene bis-*t*-butoxide would presumably be inactive toward metal peroxide formation with TBHP. Since *t*-butanol is inevitably produced via the TBHP oxidant, the epoxidations were also attempted with an H₂O₂–H₂O oxidant under phase transfer catalysis employing 5% benzyldimethyltetradecyl or tetrapentyl ammonium chloride in chloroform and 1.5% (BpDMCp)₂TiCl₂ **2**. No epoxidation of vinylcyclohexane or 1-octene was observed although the reaction mixtures did possess the characteristic yellow color of the putative metal peroxide.

In conclusion, we have demonstrated the ability of a chiral binaphthyl-derived bis(cyclopentadienyl)titanium complex to catalyze the asymmetric epoxidation of unfunctionalized alkenes with virtually the same selectivity as a previously reported bridged chiral bis(indenyl)titanium catalyst. A chiral bis(indenyl)chloroniobium peroxide also functions as an epoxidation catalyst, albeit with lower turnovers and lower enantioselectivity.

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