Solid State Structures and Solution Behavior of Titanium(IV) Octahydrobinaphtholate Complexes. Examination of Nonlinear Behavior in the Asymmetric Addition of Ethyl Groups to Benzaldehyde

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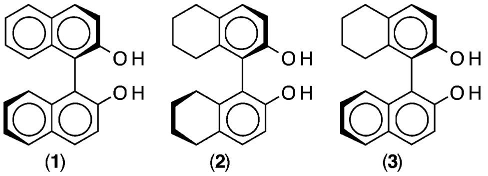
In several asymmetric reactions, H_8-BINOL-based catalysts (H_8-BINOL = 5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-bi-2-naphthol) exhibit higher levels of enantioselectivity than analogous catalysts based on BINOL. A comparison of structures of titanium complexes prepared from H_8-BINOL and BINOL was, therefore, undertaken. Reaction of (*rac*)-H_8-BINOL with 1 equiv of titanium tetraisopropoxide resulted in formation of the dimer (*meso*)-[(H_8-BINOLate)Ti(O-*i*-Pr)$_2$]$_2$ [(*meso*)-**6**], which was characterized crystallographically. In a similar fashion, use of (*rac*)-BINOL led to formation of the dimer (*meso*)-[(BINOLate)Ti(O-*i*-Pr)$_2$]$_2$ [(*meso*)-**7**]. The torsional angles between the aryl rings of the H_8-BINOLate and BINOLate ligands in these complexes were 63.2(5)° and 55.7(4)°, respectively. The larger torsional angle of the H_8-BINOLate ligand results in an increase in the bite angle of the ligand by just over 2°. Upon dissolving dimers (*meso*)-**6** and (*meso*)-**7**, equilibria between the homo- and heterochiral dimers were observed. Reaction of H_8-BINOL with an excess of titanium tetraisopropoxide provided crystals of the dinuclear complex [(H_8-BINOLate)Ti(O-*i*-Pr)$_2$]·Ti(O-*i*-Pr)$_4$ (**8**). Likewise, reaction of 2 equiv of Ti(OCy)$_4$ (Cy = cyclohexyl) with H_8-BINOL furnished [(H_8-BINOLate)Ti(OCy)$_2$]·Ti(OCy)$_4$ (**9**). These compounds were characterized by X-ray crystallography and compared to the known [(BINOLate)Ti(O-*i*-Pr)$_2$]·Ti(O-*i*-Pr)$_4$, a proposed intermediate in the asymmetric addition of alkyl groups to aldehydes. The solution behavior of **8** and **9** was studied by NMR spectroscopy, revealing that both complexes in solution are in equilibrium with dimers and free titanium tetraisopropoxide. Nonlinear studies with catalytic H_8-BINOL and an excess of titanium tetraisopropoxide in the asymmetric addition of ethyl groups to benzaldehyde showed no nonlinearity, suggesting that the equilibrium strongly favors formation of dinuclear **8** under the conditions of the asymmetric addition.

Introduction

BINOL (1,1′-bi-2-naphthol, **1**, Figure 1) is one of the most effective chiral ligands in asymmetric catalysis.[1−4] It has been successfully employed with a wide range of metal centers in a variety of Lewis acid-catalyzed processes. Recently, hydrogenated derivatives of BINOL, such as H_8-BINOL (5,5′,6,6′,7,7′,8,8′-octahydro-1,1′-bi-2-naphthol, **2**)[5] and H_4-BINOL (5,6,7,8-tetrahydro-1,1′-bi-2-naphthol, **3**)[6] have been used to facilitate asymmetric reactions with better efficiency and enantioselectivity than reactions utilizing BINOL as a chiral ligand.[7] Some examples of the successful use of hydrogenated BINOL ligands in asymmetric catalysis include nucleophilic epoxide opening reactions catalyzed by (H_8-BINOLate)$_2$GaNa,[8] sulfide oxidation with a titanium 3,3′-dinitro-H_8-BINOLate complex,[9] asymmetric olefin metathesis with molybdenum 3,3′-dialkyl-H_8-BINOLate catalysts,[10,11] hetero-Diels−Alder reaction



(**1**)
(*R*)-BINOL

(**2**)
(*R*)-H_8-BINOL

(**3**)
(*R*)-H_4-BINOL

Figure 1. BINOL (**1**), H_8-BINOL (**2**), and H_4-BINOL (**3**).

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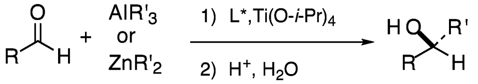
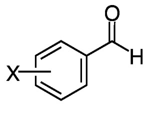
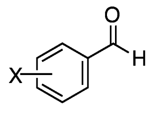
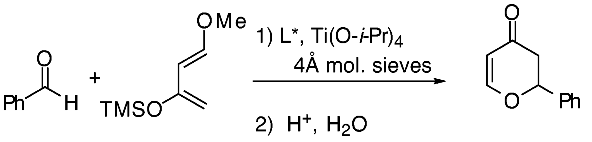
Scheme 1. Comparison of BINOL and H_8-BINOL-Based Titanium Catalysts in the Asymmetric Addition of Alkylzinc and Alkylaluminum Reagents to Aldehydes

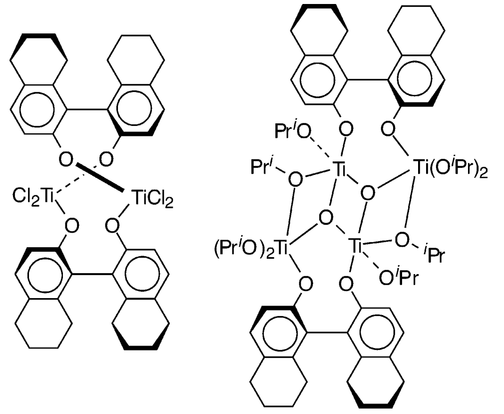


reagent	aldehyde		enantioselectivity L* = BINOL	H_8-BINOL
$ZnEt_2$		X = H	92	98
		X = *ortho*-F	73	94
		X = *ortho*-Br	59	85
		X = *para*-OMe	79	95
		X = *meta*-NO_2	70	88
$AlEt_3$		X = H	81	96
		X = *ortho*-F	52	91
		X = *ortho*-Cl	62	91
		X = *para*-OMe	67	93
		X = *meta*-OMe	71	94

Scheme 2. Comparison of BINOL, H_4-BINOL, and H_8-BINOL-Based Titanium Catalysts in the Asymmetric Hetero-Diels−Alder Reaction



L*	enantioselectivity
BINOL	87
H_4-BINOL	95
H_8-BINOL	97



4 5

Figure 2. Structurally characterized (H_8-BINOLate)Ti complexes.

using titanium-H_8-BINOLate catalysts,[12,13] and alkyl addition to aldehydes via (H_8-BINOLate)Ti complexes.[14,15] The (H_8-BINOLate)Ti-based catalysts used in the asymmetric addition of alkylzinc and alkylaluminum reagents by Chan and co-workers[14,15] and the asymmetric hetero-Diels−Alder reaction of Jiang and co-workers[13] are most relevant to the present study and are illustrated in Schemes 1 and 2. A comparison of the enantioselectivities with BINOL-, H_4-BINOL-, and H_8-BINOL-based catalysts is presented. These reactions employ precatalysts derived from titanium tetraisopropoxide and BINOL derivatives.

While the improved performance of the H_8-BINOLate ligands is often attributed to the increased steric requirement of the ligand as a result of the larger dihedral angle between the aromatic rings, only a handful of transition metal H_8-BINOLate complexes have been crystallographically characterized. Heppert and co-workers reported the first two X-ray structures of H_8-BINOL bound to a metal.[16,17] One complex is a titanium chloride dimer (**4**) that forms a 14-membered ring with two bridging H_8-BINOLate ligands, while the other is a tetranuclear titanium isopropoxide di-μ_3-oxo complex (**5**), also with two bridging H_8-BINOLate ligands (Figure 2). In both structures, each oxygen atom of the H_8-BINOLate ligand bonds to only one titanium center, so that the ligand spans two titanium atoms instead of chelating to one metal. The dihedral angles of the ligand were found to be 93° in the dimer and 80° and 88° in the tetranuclear complex. On the basis of these structures, it was suggested that the large dihedral angle of the H_8-BINOLate ligand is incompatible with a chelation binding mode to titanium.[17]

More recently, Schrock, Hoveyda, and co-workers reported the structural characterization of 3,3′-dialkyl-H_8-BINOLate molybdenum complexes, which are catalysts for the asymmetric ring-closing metathesis reaction.[10,11] All three of these structures are monomeric molybdenum imido alkylidene complexes with chelating H_8-BINOLate ligands. The dihedral angle for the 3,3′-di-*tert*-butyl H_8-BINOLate ligand bound to molybdenum was found to be 88.6°, which is comparable to the dihedral angles of the bridging H_8-BINOLate ligand in Heppert's titanium structures.

Because of the successful application of titanium BINOL-based catalysts to several reactions in asymmetric catalysis and the lack of structural information of such species, we have studied the solution and solid state structures of this class of compounds.[18,19] In the present study we compare the structures of titanium BINOL and H_8-BINOL derivatives. Herein, we report crystal structures of H_8-BINOLate-Ti complexes in which both oxygens of the H_8-BINOLate ligand are bound to a single titanium center. The gross structural features of these compounds are similar to previously reported titanium BINOLate structures;[18,19] however, the dihedral angles between the aryl rings are larger in the H_8-BINOLate complexes. Compounds derived from H_8-BINOL exhibit complex equilibria involving dimeric and dinuclear species. The nonlinear behavior of these compounds was examined in the asymmetric addition of ethyl groups to benzaldehyde.

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Table 1. Selected Bond Distances [Å] and Angles [deg] for (*meso*)-6 and (*meso*)-7

	(*meso*)-**6**	(*meso*)-**7**		(*meso*)-**6**	(*meso*)-**7**
Ti−O(1)	1.858(3)	1.864(3)	Ti−Ti′	3.3552(14)	3.382(2)
Ti−O(2)	2.138(3)	2.140(2)	O(1)−Ti−O(2)	85.43(11)	83.31(10)
Ti′−O(2)	1.947(3)	1.965(2)	Ti−O(2)−Ti′	110.37(11)	110.86(10)
Ti−O(3)	1.756(3)	1.753(3)	C(1)−C(10)−C(11)−C(20)	63.2(5)	55.7(4)
Ti−O(4)	1.779(3)	1.764(3)			

Results and Discussion

Synthesis and Structure of H_8-BINOLate- and BINOLate-Titanium Complexes. Heterochiral dimer (*meso*)-**6** was prepared by combining 1 equiv each of Ti(O-*i*-Pr)$_4$ and (*rac*)-H_8-BINOL[5] in dichloromethane, resulting in a bright yellow solution (eq 1). Removal of the solvent and liberated 2-propanol under reduced pressure gave a pale yellow solid that was crystallized by dissolution in dichloromethane, layering with pentane, and cooling to −35 °C. Thus, X-ray quality crystals were obtained, and the structure of heterochiral dimer (*meso*)-**6** is shown in eq 1. An ORTEP diagram is illustrated in Figure 3. Two dichloromethane solvent molecules crystallized in the unit cell. For the purpose of comparison, the analogous reaction was performed using (*rac*)-BINOL and titanium tetraisopropoxide (eq 1). Crystals were grown at −35 °C from a mixture of dichloromethane and 2-propanol layered with hexanes, and an ORTEP diagram of (*meso*)-**7** is shown in Figure 4.

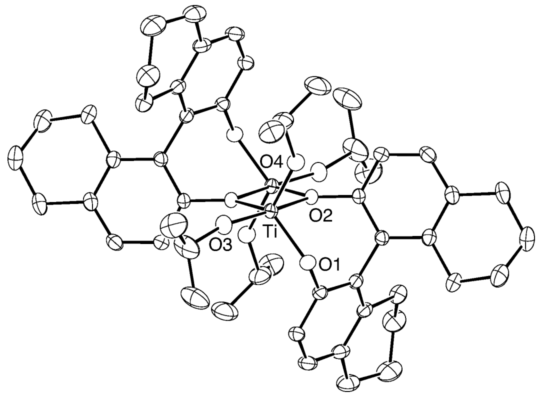


Figure 3. Thermal ellipsoid plot of (*meso*)-**6**. Ellipsoids are at the 30% probability level. Bond distances and angles are given in Table 1.

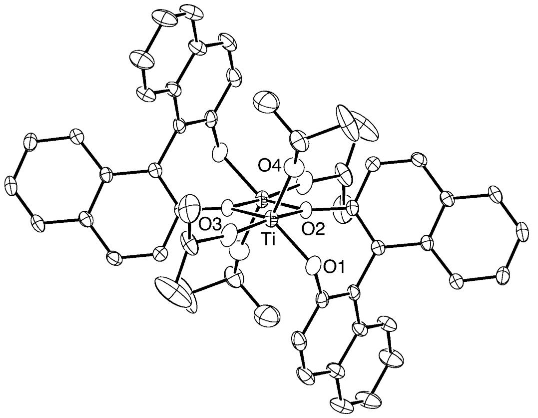
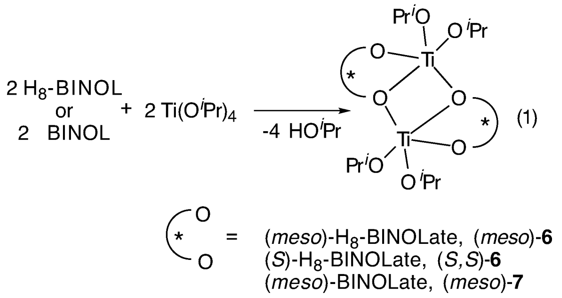


Figure 4. Thermal ellipsoid plot of (*meso*)-**7**. Ellipsoids are at the 30% probability level. Bond distances and angles are given in Table 1.



(1)

The gross structural features of heterochiral dimers (*meso*)-**6** and (*meso*)-**7** are similar, consisting of [(*R*)-bis-aryloxide]Ti(O-*i*-Pr)$_2$ and [(*S*)-bis-aryloxide]Ti(O-*i*-Pr)$_2$ dimerized through one oxygen of each of the bridging aryloxide moieties. Selected bond lengths and angles are given in Table 1. The Ti−alkoxide bond lengths of 1.756(3) and 1.779(3) Å in (*meso*)-**6** and 1.753(3) and 1.764(3) Å in (*meso*)-**7** are similar to those of related compounds.[18−20] The terminal O(1) and bridging O(2) aryloxide oxygens have significantly different bond lengths to titanium, with Ti−O(1) and Ti−O(2) bond lengths of 1.858(3) and 2.138(3) Å in (*meso*)-**6** and 1.864(3) and 2.140(2) Å in (*meso*)-**7**. The Ti′−O(2) bond lengths of 1.947(3) Å in (*meso*)-**6** and 1.965(2) Å in (*meso*)-**7** are shorter than the bond between the bridging oxygen O(2) and Ti, the first titanium center. The dihedral angle of the H_8-binaphthyl rings in the H_8-BINOLate ligand is 63.2(5)° in (*meso*)-**6**, while the BINOL derivative (*meso*)-**7** has a smaller dihedral angle of 55.7(4)°. Correspondingly, the O(1)−Ti−O(2) angle of 85.43(11)° in (*meso*)-**6** is somewhat larger than that of 83.31(10)° in (*meso*)-**7**.

Use of (*S*)-H_8-BINOL to prepare the homochiral dimer (*S*,*S*)-**6** did not result in crystalline material, and we were not able to purify this compound by crystallization. Nonetheless, the NMR spectral data of this complex are informative and discussed below. In contrast to the structure of (*meso*)-**7**, use of resolved BINOL ligand under the conditions of eq 1 and crystallization results in formation of the trimer [(BINOLate)Ti(O-*i*-Pr)$_2$]$_3$.[18,19,21]

Our previous studies in the asymmetric addition of alkyl groups to aldehydes with (BINOLate)Ti catalysts indicated that the dinuclear complex (BINOLate)Ti(O-*i*-Pr)$_2$·Ti(O-*i*-Pr)$_4$ was an important intermediate.[19] We set out to synthesize and characterize analogous compounds prepared from H_8-BINOL. Complex **8** was prepared by reaction of 6 equiv of Ti(O-*i*-Pr)$_4$ with 1 equiv of (*rac*)-H_8-BINOL in dichloromethane (eq 2). The resulting yellow oil was crystallized from pentane at

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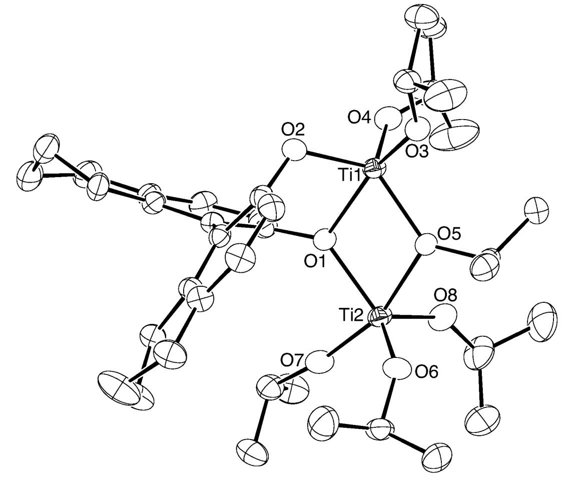
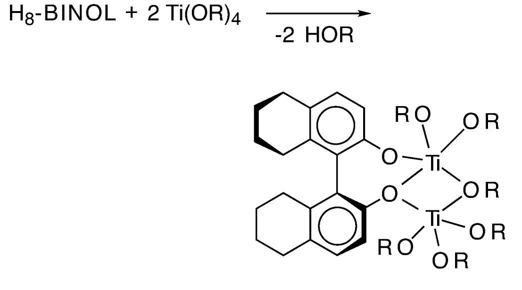


Figure 5. Thermal ellipsoid plot of **8**. Ellipsoids are at the 30% probability level. Bond distances and angles are given in Table 2.

Table 2. Selected Bond Distances [Å] and Angles [deg] for 8, 9, and (BINOLate)Ti_2(O-*i*-Pr)$_6$

	8	**9**	(BINOLate)-Ti_2(O-*i*-Pr)$_6$
Ti(1)−O(1)	2.117(2)	2.139(3)	2.111(3)
Ti(1)−O(2)	1.862(3)	1.885(4)	1.861(3)
Ti(1)−O(3)	1.802(3)	1.775(4)	1.781(3)
Ti(1)−O(4)	1.773(3)	1.754(4)	1.779(3)
Ti(1)−O(5)	1.931(2)	1.923(3)	1.921(3)
Ti(2)−O(1)	1.988(2)	1.976(3)	1.980(3)
Ti(2)−O(5)	2.110(2)	2.122(3)	2.120(3)
Ti(2)−O(6)	1.790(3)	1.800(4)	1.794(3)
Ti(2)−O(7)	1.763(3)	1.769(4)	1.765(3)
Ti(2)−O(8)	1.784(3)	1.785(4)	1.805(3)
Ti(1)−Ti(2)	3.3156(8)	3.3224(12)	3.3085(10)
O(1)−Ti(1)−O(2)	84.29(10)	84.26(13)	82.78(11)
Ti(1)−O(1)−Ti(2)	107.70(11)	107.64(14)	107.90(11)
Ti(1)−O(5)−Ti(2)	110.18(11)	110.33(14)	109.80(12)
C(1)−C(10)−C(11)−C(20)	61.7(4)	61.6(6)	54.1(5)

−35 °C, affording X-ray quality crystals of the dinuclear **8**. This complex crystallized as a pair of enantiomers in the unit cell. The (*S*)-enantiomer is shown in the ORTEP diagram in Figure 5. Selected bond lengths and angles are given in Table 2.



(2)

8, R = *i*-Pr
9, R = Cy

Analogous to complex **8**, dinuclear complex **9** was prepared by reaction of 2 equiv of Ti(OCy)$_4$ (Cy = cyclohexyl) and 1 equiv of (*S*)-H_8-BINOL in dichloromethane (eq 2). X-ray quality crystals were grown from a pentane solution at −35 °C, and the resulting ORTEP diagram is shown in Figure 6. A molecule of cyclohexanol cocrystallized in the unit cell but has been omitted from the figure. Selected bond lengths and angles are given in Table 2. Three of the cyclohexyl groups are disordered as detailed in the Supporting Information. The disorder is not shown in Figure 6.

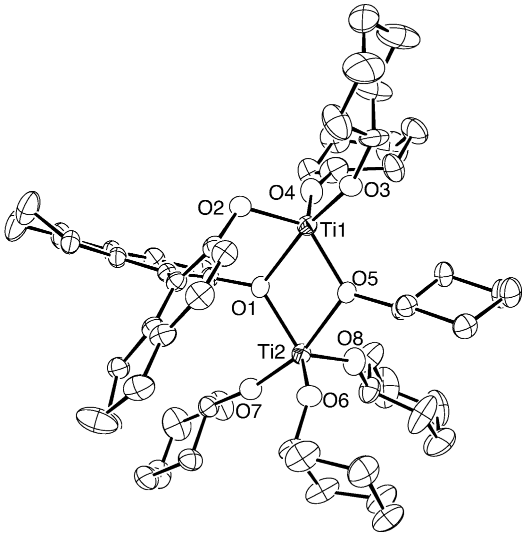


Figure 6. Thermal ellipsoid plot of **9**. Ellipsoids are at the 30% probability level. Bond distances and angles are given in Table 2.

Dinuclear complexes **8** and **9** can be envisioned as an (H_8-BINOLate)Ti(OR)$_2$ fragment bound to a molecule of Ti(OR)$_4$ through one bridging H_8-BINOLate oxygen and one bridging alkoxide oxygen. The structural features of **8** and **9** are similar to those of the parent BINOL analogue (BINOLate)Ti(O-*i*-Pr)$_2$·Ti(O-*i*-Pr)$_4$,[18,19] as illustrated by comparison of selected bond lengths and angles in Table 2. The Ti−alkoxide bond lengths in **8** and **9** range from 1.763(3) to 1.802(3) Å and from 1.754(4) to 1.800(4) Å, respectively. The related (BINOLate)Ti(O-*i*-Pr)$_2$·Ti(O-*i*-Pr)$_4$ and (H_8-BINOLate)-Ti(O-*i*-Pr)$_2$·Ti(O-*i*-Pr)$_4$ show similar Ti_2O_2 core structures. In **8** and **9**, the bridging alkoxide oxygen O(5) has a shorter bond with Ti(1), which is bound to the H_8-BINOLate ligand, than with Ti(2). Similarly, the H_8-BINOLate oxygens O(2) and O(1) have notably different bond lengths to Ti(1) of 1.862(3) and 2.117(2) Å in **8** and 1.885(4) and 2.139(3) Å in **9**. The bridging H_8-BINOLate oxygen O(1) has a shorter bond with Ti(2) than with Ti(1). These bond lengths are similar to those for the analogous BINOL complex.[18,19] The dihedral angle of the H_8-BINOLate rings is 61.7(4)° in **8** and 61.6(6)° in **9**, whereas the BINOL complex has a smaller dihedral angle of 54.1(5)°. The larger dihedral angle in the H_8-BINOLate derivative also results in an increase in the O−Ti−O bond angle. In the dinuclear H_8-BINOLate derivatives **8** and **9**, the O(1)−Ti−O(2) bond angle is 84.29(10)° and 84.26(13)°, respectively, while the same angle in the BINOLate analogue is 82.78(11)°. Thus, the H_8-BINOLate ligand has a slightly larger bite angle than the BINOLate ligand. The dihedral angles in **8** and **9** are slightly smaller than the dihedral angle observed in the structure of the heterochiral dimer (*meso*)-**6**.

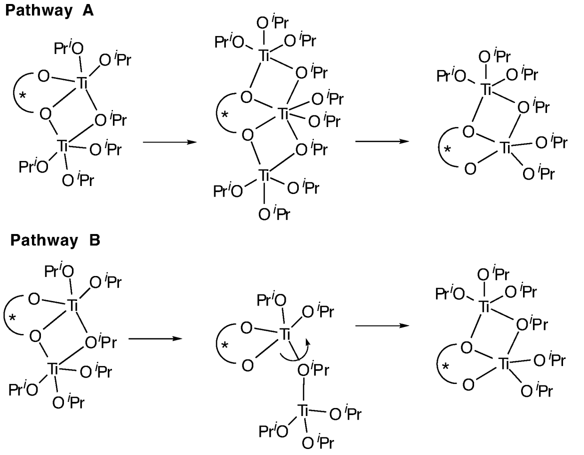
The dihedral angles of 61−63° in complexes (*meso*)-**6**, **8**, and **9** are significantly smaller than those of 80−93° in the reported H_8-BINOLate complexes of titanium[17] and molybdenum.[10,11] The larger dihedral angle in Heppert's H_8-BINOLate-titanium complexes can be explained by the fact that the H_8-BINOLate ligand bridges two titanium centers, so that each H_8-BINOLate oxygen is bound to a different titanium atom, requiring a larger dihedral angle for this configuration. The reported molybdenum complexes do have a chelated H_8-BINOLate ligand bound to one metal center through both oxygens. However, the ligand is substituted at the 3,3′ position with bulky alkyl groups that serve to increase the dihedral angle through steric interactions and inhibit dimerization through steric shielding. In addition, the larger size of the molybdenum center allows for chelation of the H_8-BINOLate ligand, thus accommodating a larger dihedral angle, whereas the smaller titanium center in (*meso*)-**6**, **8**, and **9** forces the ligand to adopt a smaller dihedral angle in order to retain bonding in a chelating fashion.

The titanium-H_8-BINOLate complexes (*meso*)-**6**, **8**, and **9** all have similar structural features. The H_8-BINOLate oxygens are bound unequally to one titanium center, and the bridging H_8-BINOLate oxygen forms a shorter bond with the second titanium center. For compounds **8** and **9** with bridging alkoxide groups, the bridging alkoxide oxygen has a shorter bond with the titanium center that is bound to both H_8-BINOLate oxygens. These trends have been observed previously for BINOLate-titanium-isopropoxide complexes in the literature.[18,19,22] Given the enhanced performance of H_8-BINOL over BINOL in certain catalytic asymmetric reactions, complexes (*meso*)-**6**, **8**, and **9** are surprisingly similar in structure to the analogous BINOLate derivatives.[18] While the dihedral angles of all three H_8-BINOLate complexes are roughly the same, they are approximately 7° larger than those of their BINOLate derivatives. Increasing the dihedral angle of the ligand results in a small increase in the bite angle of the ligand. Thus, an increase in the O−Ti−O bond angle may also be important. This difference in the dihedral angle and the bite angle is likely responsible for the observed difference in catalytic performance, since the structural features of the H_8-BINOLate complexes are similar to those of the BINOLate complexes.

Solution NMR Spectra of 6−9. The ^{1}H NMR spectrum of the material formed on reaction of (*S*)-H_8-BINOL with 1 equiv of $Ti(O\text{-}i\text{-}Pr)_4$ (eq 1) shows two aromatic doublets and one isopropoxide methyne resonance, all of equal integration. This simplicity is also observed in the $^{13}C\{^1H\}$ NMR spectrum, which shows one isopropoxide methyne resonance and six aromatic carbon resonances. The C_2-symmetry implied by these simple NMR spectra may arise in solution by the dimer (*S*,*S*)-**6** undergoing an intramolecular exchange of H_8-BINOLate ligands via cleavage of one bond between each titanium and bridging oxygen, as proposed by Heppert and co-workers to explain the C_2-symmetry observed in the solution spectra of the similar homochiral dimer $[(3,3'\text{-}Me_2\text{-BINOLate})Ti(O\text{-}i\text{-}Pr)_2]_2$.[22]

Unlike the simple solution spectra of homochiral dimer (*S*,*S*)-**6**, the spectra of (*meso*)-**6** appear more complex. When crystals of (*meso*)-**6** are dissolved in $CDCl_3$, the solution appears to contain an equilibrium mixture of the hetero- and homochiral dimers, as evidenced by the ^{1}H and $^{13}C\{^1H\}$ NMR spectra. The aromatic region of the ^{1}H NMR spectrum of (*meso*)-**6** shows four doublets of equal integration. The isopropoxide methyne hydrogens appear as three resonances in a 2:1:1 ratio. The $^{13}C\{^1H\}$ NMR spectrum of (*meso*)-**6** shows two downfield resonances for the aromatic *ipso*-carbons and three resonances for the isopropoxy O*C*HMe$_2$. All of the resonances that appear in the ^{1}H and $^{13}C\{^1H\}$ NMR spectra for the homochiral dimer (*S*,*S*)-**6** match perfectly with peaks that appear in the spectra of (*meso*)-**6** in solution, which is evidence that an equilibrium mixture is established in solution. Similar to that of (*meso*)-**6**, the ^{1}H NMR spectrum of the BINOL derivative (*meso*)-**7** also shows three resonances for the isopropoxide methyne hydrogens in a 2:1:1 ratio. Solution molecular weight studies of $(\text{BINOLate})Ti(O\text{-}i\text{-}Pr)_2$ indicated that it is a dimer,[21] although it is a trimer in the solid state.[18,21] All of the resonances in the ^{1}H and $^{13}C\{^1H\}$ NMR spectra of the homochiral dimer $[(\text{BINOLate})Ti(O\text{-}i\text{-}Pr)_2]_2$ also appear in the solution spectra of (*meso*)-**7**, which indicates that an equilibrium mixture of homo- and heterochiral dimers exists.

Scheme 3. Proposed Mechanism for Rearrangement of Heterobinuclear Compound 8



Since crystals of dinuclear complex **8** were difficult to grow without 6 equiv of $Ti(O\text{-}i\text{-}Pr)_4$, the excess $Ti(O\text{-}i\text{-}Pr)_4$ swamped the alkyl and alkoxide regions of the ^{1}H NMR spectrum, leaving a clear view of only the aromatic region, which shows six doublets in a 1:2:1:1:2:1 ratio. The two large doublets are most likely the dinuclear **8**, although we would expect to see four doublets for the static structure shown in eq 2. The $(H_8\text{-BINOLate})Ti(O\text{-}i\text{-}Pr)_2$ moiety probably undergoes a rapid exchange of the bound $Ti(O\text{-}i\text{-}Pr)_4$ with free $Ti(O\text{-}i\text{-}Pr)_4$ that exists in excess in the solution, resulting in two sets of equivalent aromatic hydrogens. This could be an associative process, going through an intermediate of the type $(H_8\text{-BINOLate})Ti(O\text{-}i\text{-}Pr)_2{\cdot}2[Ti(O\text{-}i\text{-}Pr)_4]$. The BINOL derivative $(\text{BINOLate})Ti(O\text{-}i\text{-}Pr)_2{\cdot}2[Ti(O\text{-}i\text{-}Pr)_4]$ is stable in the solid state, and the structure has been reported.[18] On dissolving, this compound loses 1 equiv of $Ti(O\text{-}i\text{-}Pr)_4$ to give $(\text{BINOLate})Ti(O\text{-}i\text{-}Pr)_2{\cdot}Ti(O\text{-}i\text{-}Pr)_4$ and free $Ti(O\text{-}i\text{-}Pr)_4$. It is also possible that the dinuclear species undergoes an intramolecular rearrangement by breaking the Ti(2)−O(1) bond, pseudorotation about the five-coordinate Ti(1), and recoordination of an alkoxide by Ti(1). Both of these mechanisms depicted in Scheme 3 have been suggested by Heppert to explain the C_2-symmetry observed in the room-temperature solution NMR spectra of the dinuclear $(3,3'\text{-}Me_2\text{BINOLate})Ti(O\text{-}i\text{-}Pr)_2{\cdot}Ti(O\text{-}i\text{-}Pr)_4$.[22]

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[22] Boyle, T. J.; Barnes, D. L.; Heppert, J. A.; Morales, L.; Takusagawa, F.; Connolly, J. C. *Organometallics* **1992**, *11*, 1112−1126.

The four smaller aromatic doublets in the solution spectrum of crude **8** match those seen in the ^{1}H NMR spectrum of the heterochiral dimer (*meso*)-**6**, consisting of (*meso*)-**6** and (*S,S*)-**6**. Thus, **8** is in equilibrium with small amounts of hetero- and homochiral dimers and free Ti(O-*i*-Pr)$_4$. This result is in contrast to earlier results with the BINOL derivative (BINOLate)Ti(O-*i*-Pr)$_2$•Ti(O-*i*-Pr)$_4$, where only the dinuclear complex is observed.[18] A ^{1}H NMR spectrum matching that of **8** was obtained from titrating (*meso*)-**6** with Ti(O-*i*-Pr)$_4$ in 2 equiv increments. The spectrum gradually changed from that described for (*meso*)-**6** to the spectrum matching that described above for **8** after about 8 equiv of Ti(O-*i*-Pr)$_4$ with respect to (*meso*)-**6** had been added. After addition of 4 equiv of Ti(O-*i*-Pr)$_4$, roughly equal amounts of dinuclear **8**, (*meso*)-**6**, and (*S,S*)-**6** existed in solution. After 14 equiv of Ti(O-*i*-Pr)$_4$ had been added to (*meso*)-**6**, the product was predominately the dinuclear complex. This result suggests that excess Ti(O-*i*-Pr)$_4$ breaks up the dimeric (*meso*)-**6** and (*S,S*)-**6** to establish an equilibrium between dinuclear **8**, (*meso*)-**6**, and (*S,S*)-**6**. A similar experiment involving titration of (*S,S*)-**6** with excess Ti(O-*i*-Pr)$_4$ also results in the conversion of the majority of the homochiral dimer to the dinuclear species with the same two large doublets in the ^{1}H NMR spectrum as was seen for **8**. Reaction of resolved and racemic H$_8$-BINOL with 2 equiv of Ti(O-*i*-Pr)$_4$ results in mostly homochiral and a mixture of homo- and heterochiral dimers, respectively, in solution by ^{1}H NMR and only a small amount of dinuclear species. These NMR experiments show that the dimeric complexes form preferentially over the dinuclear species, which require an excess of added Ti(O-*i*-Pr)$_4$. This result is in contrast to the behavior of the structurally similar dinuclear complex (BINOLate)Ti(O-*i*-Pr)$_2$•Ti(O-*i*-Pr)$_4$, which forms as the major product upon reaction of (*rac*)-BINOL with 2 equiv of Ti(O-*i*-Pr)$_4$.[18]

The ^{1}H NMR spectrum of crystals of dinuclear complex **9**, prepared from the resolved H$_8$-BINOL ligand, shows two aromatic doublets in a 1:1 ratio. The alkoxide methyne protons appear as two resonances in a 1:2 ratio, the smaller resonance belonging to the (H$_8$-BINOLate)Ti(OCy)$_2$ portion and the larger resonance attributed to the Ti(OCy)$_4$ moiety. The ^{13}C{^{1}H} NMR spectrum shows one aromatic *ipso*-carbon resonance and three alkoxide O*C*HMe$_2$ resonances. The simplicity of these spectra suggests a high degree of symmetry that does not exist in the static dinuclear structure in eq 2. The dinuclear species **9** most likely exists in solution as the homochiral dimer [(H$_8$-BINOLate)Ti(OCy)$_2$]$_2$ and free Ti(OCy)$_4$. The NMR spectra of a 1:1 mixture of Ti(OCy)$_4$ and (*S*)-H$_8$-BINOL, which presumably form the homochiral dimer [(H$_8$-BINOLate)Ti(OCy)$_2$]$_2$, exhibit the same ^{1}H and ^{13}C{^{1}H} NMR resonances as the solution spectra of **9**. Rearrangement processes such as those described for (*S,S*)-**6** may account for the observed C_2-symmetry of **9** in solution, which appears to exist as the homochiral dimer and free Ti(OCy)$_4$. No dinuclear species is observed by NMR when crystals of **9** are dissolved in CDCl$_3$. Unlike **8**, which was prepared with 6 equiv of Ti(O-*i*-Pr)$_4$ and whose NMR was obtained in the presence of the unreacted Ti(O-*i*-Pr)$_4$, crystalline **9** in solution contains no extra Ti(OCy)$_4$, which would otherwise act to break up the dimer and form the dinuclear species.

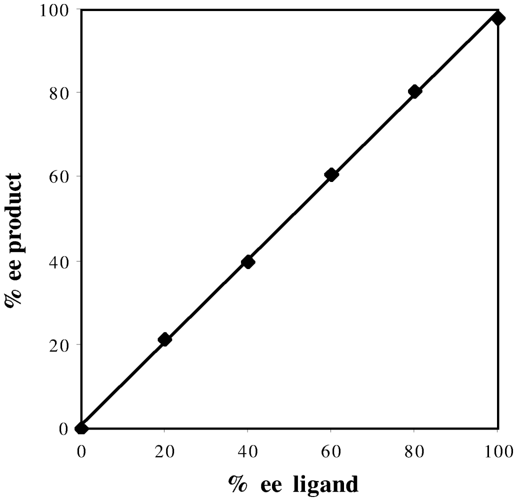

Figure 7. Plot of data from nonlinear effect experiments.

Mechanistic Studies of Diethylzinc Addition to Aldehydes Mediated by H$_8$-BINOL/Ti(O-*i*-Pr)$_4$. H$_8$-BINOL recently has been shown to give better enantioselectivity than BINOL in the diethylzinc addition to aldehydes (97.6 vs 91.9% ee for benzaldehyde, Scheme 1), yet little is known about the mechanism.[15] Given the complex equilibrium observed in the NMR spectra of **6**, **8**, and **9**, we investigated the nonlinear behavior of these compounds in the asymmetric addition of ethyl groups to benzaldehyde. Following the general procedure of Zhang and Chan,[15] we examined the asymmetric addition reaction with H$_8$-BINOL of varying ee to determine if a nonlinear effect exists under catalytic conditions. The experiment was run with H$_8$-BINOL of 20, 40, 60, 80, and 100% ee, in addition to 1.6 equiv of Ti(O-*i*-Pr)$_4$ and 3 equiv of ZnEt$_2$ with respect to benzaldehyde substrate. A ligand loading of 10 mol % H$_8$-BINOL was used for these experiments, as this amount was found to be the lowest that still gives the maximum ee of 98% reported in the literature. The nonlinear effect experiments were performed at −20 °C so that the reaction would be slow enough to monitor by removing aliquots at varying time points. The reactions reached completion at 4 h, and the ee's were constant over time. No nonlinear effects were observed for this catalytic system, as can be seen by the straight-line plot of the data in Figure 7.

The absence of nonlinear effects in the catalytic addition of ZnEt$_2$ to benzaldehyde makes it unlikely that dimeric species are involved in the reaction. Instead, the dinuclear species **8** may be formed as a result of the excess Ti(O-*i*-Pr)$_4$, which is critical to the efficiency and enantioselectivity of the reaction. As illustrated by the NMR titration experiment described above, the presence of about 7 equiv of Ti(O-*i*-Pr)$_4$ with respect to H$_8$-BINOL is necessary to convert the majority of the dimeric species into the dinuclear complex in solution. This observation would explain Zhang and Chen's finding that a 1:7 ratio of H$_8$-BINOL to Ti(O-*i*-Pr)$_4$ was optimal in their diethylzinc additions to aldehydes.[15] It must be noted that an absence of nonlinear effect may be observed even though dimers are formed during the asymmetric reaction. As seen in the NMR studies described above, the homo- and heterochiral dimers exist in solution in roughly equal amounts ($K_{eq} \approx 1$). This equilibrium would result in no observable nonlinear behavior in the asymmetric reaction if monomers are the reactive species or if the diastereomeric dimers have the same reactivity. This scenario is unlikely, however, due to the large excess of Ti(O-*i*-Pr)$_4$ in the reaction which would react with monomer and dimers to form the dinuclear species (H$_8$-BINOLate)Ti(O-*i*-Pr)$_2$·Ti(O-*i*-Pr)$_4$. Interestingly, the same lack of nonlinear effects was observed for the asymmetric addition reaction to aldehydes under similar conditions, using BINOL as the chiral ligand and 120 mol % Ti(O-*i*-Pr)$_4$.[19]

Conclusions

Three new structures of titanium-H$_8$-BINOLate-isopropoxide were studied crystallographically in the solid state and in solution by NMR spectroscopy. These structures were compared to their BINOLate analogues that were previously published and (*meso*)-**7**, which is reported here. Excess Ti(O-*i*-Pr)$_4$ breaks up the dimeric species to form the dinuclear species in solution. These dimeric and dinuclear titanium complexes show that even though the H$_8$-BINOLate ligand has a larger dihedral angle and steric requirement than the more common BINOLate ligand, the H$_8$-BINOLate ligand can bind in a chelating fashion to one titanium center to form complexes that are very similar in structure to those obtained from the BINOLate ligand. In addition, the fact that both H$_8$-BINOL- and BINOL-based catalysts show no nonlinear effects for the catalytic asymmetric addition reaction to aldehydes suggests that these two catalysts may react in a mechanistically similar fashion, possibly forming a dinuclear species containing two titanium atoms but only one bisphenoxide ligand. Given the similarity in solid state structure of known (BINOLate)Ti complexes and the (H$_8$-BINOLate)Ti derivatives described here, the difference in dihedral angle (about 7°) may account for the enhanced performance of H$_8$-BINOL over BINOL as a chiral ligand for some catalytic asymmetric reactions. The differences in catalytic activity of H$_8$-BINOLate versus BINOLate complexes may also be the result of differing solution behavior of these compounds. While the BINOLate and H$_8$-BINOLate complexes appear to have similar solid state structures, the solution behavior illustrates some differences. In solution, the dinuclear BINOLate complex forms easily with stoichiometric amounts of starting materials and does not require excess titanium alkoxide. On the other hand, the addition of excess titanium alkoxide is necessary to form the dinuclear H$_8$-BINOLate complex, which establishes an equilibrium in solution with both homo- and heterochiral dimeric species and free titanium alkoxide. In the absence of excess titanium alkoxide, the dimeric H$_8$-BINOLate species appears to be more stable and form in preference to the dinuclear form containing two titanium atoms but only one H$_8$-BINOLate ligand. The opposite is true of the BINOLate compounds, where the dinuclear form appears to be more stable than the dimeric form in solution. These differences in solution behavior, coupled with the difference in dihedral angles for H$_8$-BINOLate and BINOLate titanium alkoxide complexes, may provide some insight into the differing enantioselectivity of these ligands in asymmetric catalysis.

Experimental Section

General Methods. All reactions were carried out in dry glassware under nitrogen using standard glovebox or Schlenk line techniques. All solvents were dried and distilled prior to use. Titanium tetraisopropoxide and benzaldehyde were distilled prior to use. NMR spectra were recorded on a Bruker 360 MHz or AM500 MHz NMR spectrometer. Chemical shifts are reported relative to residual protiated solvent or tetramethylsilane. Enantiomeric excesses were determined on a Hewlett-Packard 6890 gas chromatograph with a 30 m Supelco β-DEX. H$_8$-BINOL was prepared according to the literature procedure.[5] Tetrakis(cyclohexyloxy)titanium was prepared from cyclohexanol and titanium tetraisopropoxide.

[(*R*)-H$_8$-BINOLate][(*S*)-H$_8$-BINOLate]Ti$_2$(O-*i*-Pr)$_4$ [(*meso*)-6]. To a stirred suspension of racemic H$_8$-BINOL (125.0 mg, 0.425 mmol) in 5 mL of dichloromethane was added 1 equiv of Ti(O-*i*-Pr)$_4$ (120.7 mg, 0.425 mmol) in 5 mL of dichloromethane. The resulting bright yellow solution was stirred for 30 min, and the volatiles were removed under vacuum. The pale yellow residue was redissolved in dichloromethane, and the volatiles were again removed under vacuum. This process was repeated a third time to ensure complete removal of the liberated 2-propanol. X-ray quality crystals were grown by dissolving the pale yellow solid in dichloromethane and layering with pentane at −35 °C. ^{1}H NMR (500 MHz, CDCl$_3$): δ 6.83 (d, J = 8.2 Hz, 2H), 6.71 (d, J = 8.2 Hz, 2H), 6.65 (d, J = 8.1 Hz, 2H), 6.47 (d, J = 7.8 Hz, 2H), 4.50 (quin, J = 6.0 Hz, 2H), 4.35 (quin, J = 6.1 Hz, 1H), 4.10 (quin, J = 6.0 Hz, 1H), 2.72 (m, 6H), 2.63 (m, 2H), 2.49 (m, 2H), 2.41 (m, 2H), 2.13 (m, 4H), 1.73 (m, 2H), 1.68 (m, 10H), 1.51 (m, 4H), 1.15 (2H), 1.07 (m, 10H), 1.03 (d, J = 5.3 Hz, 6H), 0.68 (d, J = 5.2 Hz, 6H). ^{13}C{^{1}H} NMR (360 MHz, CDCl$_3$): δ 158.94, 157.79, 136.44, 136.36, 130.83, 130.64, 128.24, 128.10, 126.08, 125.56, 117.58, 117.10, 80.95, 80.48, 79.65, 29.62, 29.59, 27.97, 25.97, 25.78, 25.69, 25.23, 23.46, 23.38, 23.31.

[(*S*)-H$_8$-BINOLate]$_2$Ti$_2$(O-*i*-Pr)$_4$ [(*S,S*)-6]. To a stirred suspension of (*S*)-H$_8$-BINOL (125.5 mg, 0.426 mmol) in 5 mL of dichloromethane was added 1 equiv of Ti(O-*i*-Pr)$_4$ (121.2 mg, 0.426 mmol) in 5 mL of dichloromethane. The resulting amber solution was stirred for 30 min, and the volatiles were removed under vacuum. The orange-yellow solid was redissolved in dichloromethane, and the volatiles were again removed under vacuum. This process was repeated a third time to ensure complete removal of the liberated 2-propanol. The resulting compound is presumably the homochiral dimer, but we were not able to obtain crystalline material for a structural determination. ^{1}H NMR (360 MHz, CDCl$_3$): δ 6.71 (d, J = 8.1 Hz, 4H), 6.47 (d, J = 7.4 Hz, 4H), 4.49 (m, 4H), 2.70 (m, 8H), 2.40 (m, 4H), 2.12 (m, 4H), 1.69 (m, 12H), 1.50 (m, 4H), 1.06 (m, 24H). ^{13}C{^{1}H} NMR (360 MHz, CDCl$_3$): δ 157.75, 136.28, 130.54, 128.04, 125.50, 117.03, 80.38, 29.55, 27.89, 25.89, 25.62, 23.39, 23.31.

[(*R*)-BINOLate][(*S*)-BINOLate]Ti$_2$(O-*i*-Pr)$_4$ [(*meso*)-7]. To a stirred suspension of racemic BINOL (9.5 mg, 0.0332 mmol) in 0.2 mL of dichloromethane was added 1 equiv of Ti(O-*i*-Pr)$_4$ (9.8 μL, 0.0332 mmol) and 25 equiv of 2-propanol (64 μL, 0.836 mmol). After stirring for 15 min, the orange solution was layered with hexanes and cooled to −35 °C, affording X-ray quality crystals. This compound can also be prepared without 2-propanol and crystallized from a dichoromethane solution layered with hexanes. ^{1}H NMR (500 MHz, CDCl$_3$): δ 7.86 (m, 8H), 7.49 (d, J = 8.6 Hz, 2H), 7.36 (m, 5H), 7.30 (m, 5H), 7.17 (m, 8H), 6.77 (br m, 2H), 4.52 (quin, J = 5.8 Hz, 2H), 4.40 (br s, 1H), 3.65 (br s, 1H), 1.11 (d, J = 6.0 Hz, 9H), 1.05 (d, J = 6.1 Hz, 9H), 1.03 (m, 6H), 0.28 (d, J = 4.1 Hz, 6H). Strongest resonances in ^{13}C{^{1}H} NMR (500 MHz,

$CDCl_3$): δ 159.15, 133.31, 130.30, 129.05, 128.25, 128.17, 127.14, 125.61, 123.55, 121.39, 81.21, 77.44, 25.89, 25.63.

(H_8-BINOLate)Ti_2(O-*i*-Pr)$_6$ (8). To a stirred suspension of racemic H_8-BINOL (10.0 mg, 0.0340 mmol) in 5 mL of dichloromethane was added 6 equiv of Ti(O-*i*-Pr)$_4$ (57.9 mg, 0.204 mmol) in 5 mL of dichloromethane. The resulting yellow solution was stirred for 30 min, and the volatiles were removed under vacuum. The pale yellow residue was redissolved in dichloromethane, and the volatiles were again removed under vacuum. This process was repeated a third time to ensure complete removal of the liberated 2-propanol. X-ray quality crystals were grown from pentane at −35 °C. The unit cell contains cocrystallized enantiomers. ^1H NMR of crude material, aromatic region (360 MHz, $CDCl_3$): δ 6.83 (d, $J = 8.2$ Hz, 1H), 6.78 (d, $J = 8.2$ Hz, 2H), 6.71 (d, $J = 8.2$ Hz, 1H), 6.66 (d, overlapping, 1H), 6.62 (d, $J = 8.2$ Hz, 2H), 6.47 (d, $J = 7.8$ Hz, 1H).

[(*S*)-H_8-BINOLate]Ti_2(OCy)$_6$ (9). To a stirred suspension of (*S*)-H_8-BINOL (100.0 mg, 0.340 mmol) in 5 mL of dichloromethane was added 2 equiv of Ti(OCy)$_4$ (302.0 mg, 0.679 mmol) in 5 mL of dichloromethane. The resulting yellow solution was stirred for 30 min, and the volatiles were removed under vacuum. X-ray quality crystals were grown from pentane at −35 °C. A molecule of cyclohexanol cocrystallized with the titanium complex. ^1H NMR (360 MHz, $CDCl_3$): δ 6.71 (d, $J = 8.1$ Hz, 2H), 6.48 (d, $J = 7.5$ Hz, 2H), 4.20 (br s, 2H), 4.05 (br s, 4H), 3.54 (br s, 1H, CyOH), 2.70 (m, 4H), 2.38 (m, 2H), 2.10 (m, 2H), 1.83 (br s, 14H) 1.66 (m, 22H), 1.48 (m, 8H), 1.20 (m, 35H). $^{13}C\{^1H\}$ NMR (360 MHz, $CDCl_3$): δ 157.79, 136.31, 130.58, 128.02, 125.54, 117.16, 86.34, 82.66, 70.56, 64.87, 36.91, 35.79, 35.57, 29.62, 27.91, 25.90, 25.82, 25.68, 24.41, 23.91, 23.85, 23.48, 23.41.

[(*S*)-H_8-BINOLate]$_2Ti_2$(OCy)$_4$. To a stirred suspension of (*S*)-H_8-BINOL (125.0 mg, 0.425 mmol) in 5 mL of dichloromethane was added 1 equiv of Ti(OCy)$_4$ (188.7 mg, 0.425 mmol) in 5 mL of dichloromethane. The solution was stirred for 30 min, and the volatiles were removed under vacuum. The resulting oil is presumably the homochiral dimer plus free cyclohexanol, but we were not able to obtain crystalline material for a structural determination. ^1H NMR (360 MHz, $CDCl_3$): δ 6.71 (d, $J = 8.1$ Hz, 4H), 6.48 (d, $J = 7.6$ Hz, 4H), 4.20 (br s, 4H), 3.53 (br s, 4H, free CyOH), 2.70 (m, 8H), 2.44 (m, 4H), 2.10 (m, 4H), 1.65 (m, 54H), 1.14 (m, 42H). $^{13}C\{^1H\}$ NMR (360 MHz, $CDCl_3$): δ 157.73, 136.26, 130.52, 128.00, 125.48, 117.08, 86.30, 80.37, 70.54 (br), 64.7 (br), 35.73, 35.55, 29.56, 27.87, 25.73, 25.58, 24.6 (br), 23.88 (br), 23.42, 23.35.

NMR Titration Experiments. Crystals of heterochiral dimer (*meso*)-**6** (10.0 mg, 0.0109 mmol) and noncrystalline homochiral dimer (*S*,*S*)-**6** (10.0 mg, 0.0109 mmol) were each dissolved in 0.4 mL of $CDCl_3$ and transferred to separate NMR tubes. After the ^1H NMR spectra were recorded, Ti(O-*i*-Pr)$_4$ (6.5 μL, 0.0217 mmol) was added to each tube, which was inverted several times to ensure dissolution. The ^1H NMR spectra were recorded, and Ti(O-*i*-Pr)$_4$ was added in 6.5 μL increments, with the ^1H NMR spectra being recorded after each addition. A total of 45.5 μL (0.152 mmol) of Ti(O-*i*-Pr)$_4$ was added to each tube.

Table 3. Amounts of Ligand for Nonlinear Effect Experiment

% ee H_8-BINOL	(*S*)-H_8-BINOL	(*rac*)-H_8-BINOL
20	5.0 mg	20.0 mg
40	10.0 mg	15.0 mg
60	15.0 mg	10.0 mg
80	20.0 mg	5.0 mg

Reaction of (*R*)- and (*rac*)-H_8-BINOL with 2 Equiv Ti(O-*i*-Pr)$_4$. To each stirred suspension of (*R*)-H_8-BINOL (40.0 mg, 0.136 mmol) and (*rac*)-H_8-BINOL (40.0 mg, 0.136 mmol) in 5 mL of dichloromethane was added 2 equiv of Ti(O-*i*-Pr)$_4$ (77.2 mg, 0.272 mmol) in 5 mL of dichloromethane. The resulting solutions were stirred for 30 min, and the volatiles were removed under vacuum. The residues were redissolved in dichloromethane, and the volatiles were again removed under vacuum. This process was repeated a third time to ensure complete removal of the liberated 2-propanol. The ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded in $CDCl_3$.

Nonlinear Effect Experiment. (*S*)-H_8-BINOL and (*rac*)-H_8-BINOL were weighed in the amounts shown above in Table 3 into four 10 mL Schlenk flasks equipped with stirbars to give 20, 40, 60, and 80% ee of (*S*)-H_8-BINOL (0.0849 mmol total). Dichloromethane (6.8 mL) was added to each flask, followed by titanium tetraisopropoxide (407 μL, 1.36 mmol), and the resulting orange solutions were stirred for several minutes. A 1.0 M solution of diethylzinc (2.55 mL, 2.55 mmol) in hexanes was added to each flask via syringe. The solutions were then cooled to −20 °C, benzaldehyde (87 μL, 0.853 mmol) was added, and the solutions were stirred for 4 h. Samples of each of the four reactions were quenched with 1 M HCl, extracted with pentane, dried over magnesium sulfate, filtered through Celite, and analyzed by chiral GC.

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Supporting Information Available: Detailed information on the crystal structure determinations, including tables of data collection parameters, final atomic positional and thermal parameters, and interatomic distances and angles as well as ORTEP diagrams of (*meso*)-**6**, (*meso*)-**7**, **8**, and **9**. NMR spectra of (*meso*)-**6**, (*S*,*S*)-**6**, (*meso*)-**7**, **8**, **9**, titration experiments, reaction of (*R*)- and (*rac*)-H_8-BINOL with 2 equiv Ti(O-*i*-Pr)$_4$, and reaction of (*S*)-H_8-BINOL with 1 equiv Ti(OCy)$_4$. This material is available free of charge via the Internet at http://pubs.acs.org.

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