Synthesis, Structure, and Catalytic Properties of Bis[bis(sulfonamido)] Titanium Complexes

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Synthesis, Structure, and Catalytic Properties of Bis[bis(sulfonamido)] Titanium Complexes

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Reaction of the titanium tetraamide $Ti(NMe_2)_4$ with 2 equiv of racemic or resolved bis(sulfonamide) ligand resulted in the formation of the [bis(sulfonamido)]$_2$Ti complexes (TiL_2) and *N*,*N*-dimethylamine. We have characterized the resulting TiL_2 complexes by X-ray crystallography and variable-temperature NMR spectrometry to explore differences in the bonding and geometry of the bis(sulfonamido) ligand in these complexes. When racemic ligand was used, the resulting TiL_2 complexes consisted of the homochiral and heterochiral diastereomers. One of these heterochiral diastereomers was characterized by X-ray crystallography (**7hetero**). When resolved ligand was employed, it was found that the product composition was dependent on the size of the bis(sulfonamide) ligand employed in the synthesis. When the aryl group of the bis(sulfonamide) ligand was tolyl (**1res**), two diastereomeric compounds were observed that were in equilibrium. These complexes were the **C_2-6homo** and **C_s-6homo** diastereomers. When the aryl group was 2,5-dimethylphenyl (Xyl) (**3rac**), the major product was determined to be the homochiral diastereomer, **C_2-8homo**, by X-ray crystallography. The homochiral diastereomer generated from the bis(sulfonamide) ligand with the aryl group 5-chloro-2-methoxy phenyl (**4res**) also gave the homochiral diastereomer **C_2-9homo**. By NMR spectrometry both **C_2-8homo** and **C_2-9homo** were found to be single diastereomers, and no signals that could be attributed to the C_s-symmetric counterparts to **C_s-6homo** were observed. The structures of **C_2-6homo, 7hetero**, **C_2-8homo**, and **C_2-9homo** were determined. Although the geometries between the homochiral and heterochiral diastereomers are very different, the metrical parameters are not. Each of the titanium centers in these structures is eight-coordinate. The ligand was found to bind through one of the sulfonyl oxygens of each sulfonyl group as well as the sulfonamido nitrogens. The Ti−N distances of the sulfonamido groups range from 2.070(3) to 2.095(3) Å, while Ti−O sulfonyl distances range from 2.159(2) to 2.328(3) Å. The bis(sulfonamide) ligands used in this work have also been used in the asymmetric addition of diethylzinc to aldehydes. This reaction is very efficient and gives excellent enantioselectivity with a wide variety of aldehydes. To determine if the TiL_2 complexes were involved in the catalysis, an equilibrium mixture of the diastereomers **C_2-6homo/C_s-6homo** was used in the asymmetric addition and compared with the catalyst generated under the reaction conditions from the ligand **1res**. Although the mixture of **C_2-6homo/C_s-6homo** gave high enantioselectivity, it exhibited different enantioselectivity and turnover frequency from the catalyst generated from **1res**.

Introduction

Chiral sulfonamide- and bis(sulfonamide)-based ligands have been successfully used in a variety of catalytic asymmetric transformations.[1−3] Efficient enantioselective catalytic processes have been developed for the asymmetric reduction of ketones employing aminosulfonamido ruthenium complexes[4−8] and the asymmetric addition of alkyl groups to ketones employing sulfonamide-alcohol ligands.[9,10] Chiral bis(sulfonamide) ligands have been used in the asymmetric Diels−Alder cycloaddition,[11−13] [2+2] cycloaddition,[14] Claisen rear-

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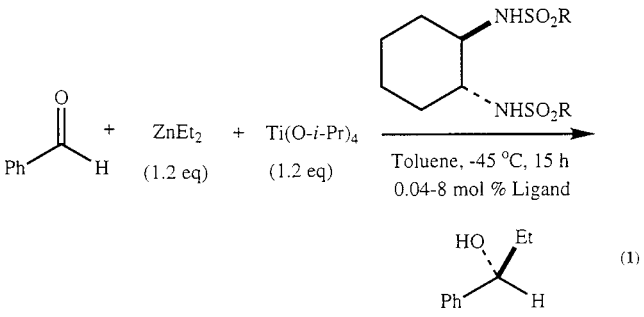
rangement,[15,16] enolization−amination reactions,[17] the cyclopropanation of allylic alcohols,[18−20] and the addition of alkyl groups to aldehydes (eq 1).[19,21−26] The later reaction is one of the most efficient and highly enantioselective carbon−carbon bond forming processes and has attracted our attention.



(1)

The initial studies of the asymmetric addition reaction (eq 1) using bis(sulfonamide)-based ligands by Ohno and Kobayashi[22−24] were primarily concerned with development of enantioselective catalysts. Subsequently, Knochel and co-workers explored the scope of this process and found that a wide variety of functionalized secondary alcohols could be prepared with high enantioselectivity.[27−31] In these studies catalysts were generated in situ from the ligand, dialkylzinc reagents, and titanium tetraisopropoxide.[26] As a result, little was known about the structure of the active species or how it functioned. Recent work directed toward understanding eq 1 has begun to illuminate the bonding of the bis(sulfonamide) ligand to titanium and some of the steps involved in related asymmetric reactions.[20,25,32−34]

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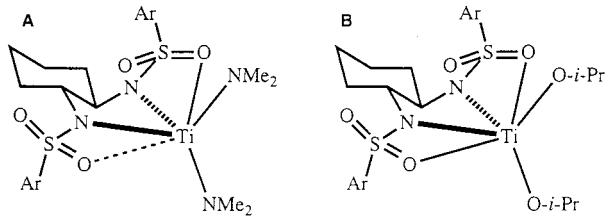


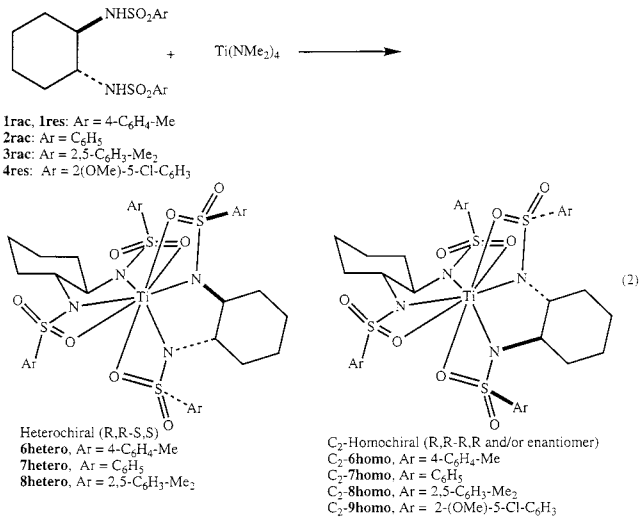
Figure 1.

In titanium bis(sulfonamido) bis(amide) complexes, $LTi(NMe_2)_2$, where L = bis(sulfonamido) ligand (Figure 1, **A**), we[25,32] and Gagné and co-workers[34] have shown that the ligand can bind in a tridentate or a tetradentate fashion by X-ray crystallography. In the solid-state structures of titanium bis(sulfonamido) bis(alkoxide) complexes, $LTi(O\text{-}i\text{-}Pr)_2$, (Figure 1, **B**) the ligands bind to titanium in a tetradentate fashion. We have recently demonstrated that these complexes are catalytically competent in the asymmetric addition of alkyl groups to aldehydes (eq 1).[25]

The present study concerns the bis[bis(sulfonamido)] titanium complexes, TiL_2. Initially we considered the TiL_2 species as possible intermediates in eq 1. However, research outlined here indicates that the TiL_2 complexes are not the active catalysts in the asymmetric addition.[25] Described herein is the rich stereochemical and structural properties of TiL_2 complexes.

Results

Synthesis of TiL_2 Complexes. The TiL_2 complexes **6**−**9** were prepared by dropwise addition of the tetraamide $Ti(NMe_2)_4$ to the ligands **1**−**4** (eq 2). The designation rac and res attached to the compound number signify that the ligand was either racemic or resolved (eq 2). On addition of $Ti(NMe_2)_4$ to **1**−**4**, the color of the reaction mixture turned dark and then lightened after approximately 1 h to give a yellow homogeneous solution. In reactions of $Ti(NMe_2)_4$ with the ligands **1rac**, **1res**, **2rac**, and **3rac** the resultant products were isolated as a mixture of diastereomers (^{1}H NMR spectrometry).



(2)

The ratios of the diastereomeric hetero- and homochiral TiL_2 complexes formed from **1rac** and **2rac** were found to be dependent on the solvent employed in the

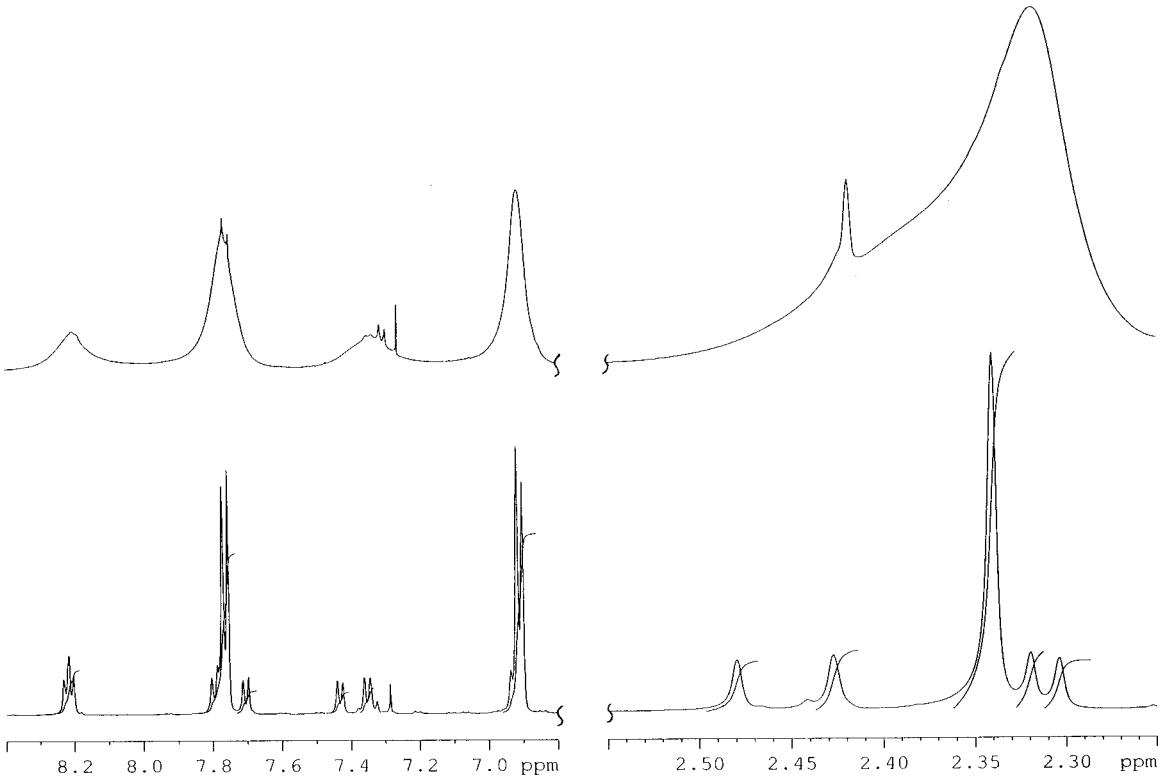


Figure 2. ^{1}H NMR spectra of **C_2-6homo/C_s-6homo** equilibrium in $CDCl_3$ at 23 °C (top) and at −15 °C (bottom).

synthesis as detailed below. We were able to enhance the amount of one of the diastereomers by fractional recrystallization and to grow X-ray quality crystals of four of the diastereomeric TiL_2 complexes. However, we were not able to isolate substantial quantities of the single diastereomers for mixtures made with **1rac** or **2rac** because the diastereomers had similar solubilities and cocrystallized. Samples for crystallographic studies were obtained by separating the crystals of the diastereomers manually.

Reaction of **1rac** with $Ti(NMe_2)_4$ initially appeared to give a mixture of the two diastereomeric TiL_2 complexes (eq 2, also see below). As outlined below, these products were determined to be the heterochiral diastereomer **6hetero** (containing two ligands of opposite configuration) and the C_2-symmetric homochiral diastereomer **C_2-6homo** (composed of two ligands of the same configuration). When the reaction was conducted in toluene, the ratio of the heterochiral to the homochiral diastereomers was 9:1, while in THF it was 7:3. The ratios of these diastereomers did not change over time, in different solvents, or when briefly heated, indicating that the diastereomers are not in equilibrium. The broad lines in the ^{1}H and $^{13}C\{^1H\}$ NMR spectra of the diastereomers indicated that both compounds were fluxional. The major diastereomer consisted of broadened resonances that exhibited splitting between the aromatic protons, while the minor diastereomer had only broad, featureless resonances in the aromatic region. Two broad partially overlapping resonances were observed for the para-methyl groups of the two diastereomers. The resonances for the cyclohexane ring protons were not resolved.

To confirm that the minor component obtained from **1rac** was the C_2-symmetric homochiral diastereomer, we conducted the reaction of the resolved ligand **1res** with $Ti(NMe_2)_4$. The resulting mixture consisted of the expected diastereomer (**C_2-6homo**) and a new diastereomer as judged by the aromatic region of the ^{1}H NMR spectrum, which contained two pairs of broad resonances with a ratio of the diastereomers of 6:4. In the room-temperature ^{1}H NMR spectrum in $CDCl_3$ the aromatic C−H's of the major diastereomer resonated at 7.74 and 6.90 ppm and the minor at 8.17 and 7.32 ppm (see Figure 2). The major diastereomer formed in the reaction of **1res** with $Ti(NMe_2)_4$ was identical to the minor diastereomer formed from **1rac** and $Ti(NMe_2)_4$ and was identified as **C_2-6homo**. The second diastereomer that formed on reaction of **1res** with $Ti(NMe_2)_4$ had not been observed in the reaction of **1rac** with $Ti(NMe_2)_4$ because its resonances were obscured by **6hetero**.

To understand the relationship between the diastereomers formed from **1res**, variable-temperature NMR experiments were conducted. A sealed NMR tube containing a C_6D_6 solution of the TiL_2 diastereomers from **1res** was heated in the probe of a 200 MHz NMR spectrometer, and ^{1}H NMR spectra were recorded. On heating the mixture to 50 °C in C_6D_6 the aromatic resonances further broaden and started to merge. At 70 °C resonances of the major diastereomer (6.58 and 8.01 ppm) and the minor diastereomer (6.99 and 8.60 ppm) coalesced into broad resonances at 6.77 and 8.15 ppm. These studies indicated that the two diastereomers were in equilibrium.

We next cooled a sample of the two diastereomers from **1res** in $CDCl_3$ and monitored the mixture using a 500 MHz NMR spectrometer. On cooling to −15 °C the resonances in the ^{1}H NMR spectra became sharp and well defined (Figure 2). The symmetry of the major diastereomer did not change from C_2-symmetric in the range of −15 to −65 °C. Two doublets were observed

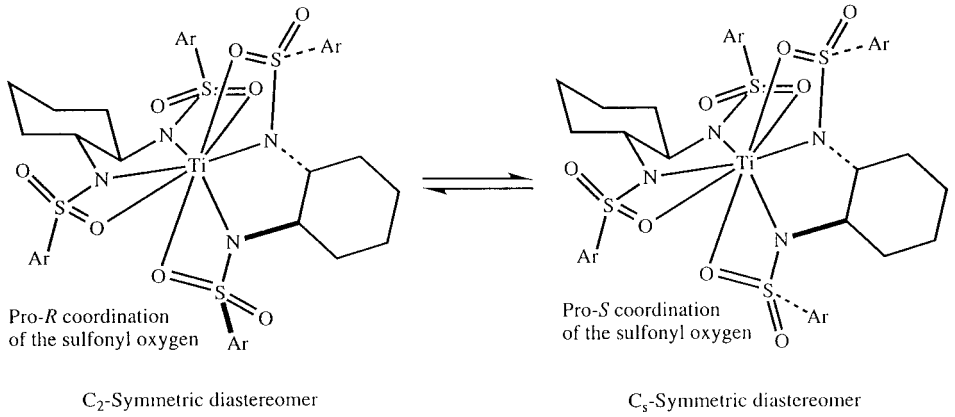


Figure 3. Proposed equilibrium between C_2- and C_s-symmetric diastereomers.

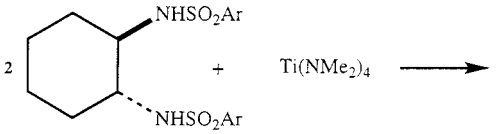
for the aromatic C−H's at 6.91 and 7.77 ppm and a singlet for the methyl group at 2.34 ppm in a ratio of 2:2:3. In contrast, the symmetry of the minor diastereomer changed on cooling to −15 °C. In the aromatic region of the minor diastereomer two doublets (integration of 1H each) were partially overlapping at 8.23 and 8.21 ppm. Doublets were also found at 7.79, 7.72, 7.42, and 7.34 ppm, and two resonances at 6.93 ppm partially overlapped with the upfield resonance of the major diastereomer as illustrated in Figure 2. At −15 °C four singlets in a ratio of 1:1:1:1 (Figure 2) were observed for the para-methyl groups at 2.30, 2.32, 2.43, and 2.48 ppm, which indicated that the minor diastereomer was the C_s-symmetric homochiral diastereomer **C_s-6homo** (Figure 3).

We were unable to grow X-ray quality crystals from the mixture of **6hetero**, **C_2-6homo**, and **C_s-6homo**. We therefore prepared the phenyl derivatives with **2rac** (eq 2). Reaction of **2rac** with $Ti(NMe_2)_4$ gave two detectable diastereomers which were formed in a ratio of 8:2 in benzene and 6:4 in THF. In analogy with the diastereomers formed with **1rac**, the major diastereomer is believed to be the heterochiral diastereomer **7hetero** and the minor product the C_2-symmetric homochiral diastereomer **C_2-7homo**. Due to the broad resonances in the ^{1}H NMR spectra of these diastereomers, no resonances could be assigned to the C_s-homochiral diastereomer **C_s-6homo**.

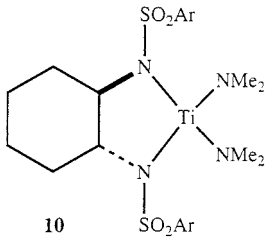
On reaction of **3rac** with $Ti(NMe_2)_4$, a 5:1 ratio of the diastereomers was observed by ^{1}H NMR spectroscopy (eq 2). The major diastereomer was isolated by recrystallization from toluene and ether. The resonances of this diastereomer in the ^{1}H NMR spectrum were sharp. The structure of this complex is discussed in the next section.

Upon reaction of **4res** with $Ti(NMe_2)_4$ a single product was isolated in 51% yield after dissolving the crude product in THF and precipitating with diethyl ether. NMR spectroscopy indicated that there was only one ligand environment on this complex, and its structure was therefore assigned as the C_2-symmetric homochiral complex **9homo** (eq 2). No resonances that could be attributed to **C_s-9homo** were observed by NMR spectrometry. Additionally, unlike the diastereomeric mixture of **C_2-6homo** and **C_s-6homo**, the resonances of **C_2-9homo** were well resolved with the expected coupling.

In contrast to studies with ligands **1rac**−**3rac**, the reaction of **5rac** with $Ti(NMe_2)_4$ did not result in the formation of the TiL_2 complex. Instead, examination of the reaction mixture (NMR) indicated that only 1 equiv of the ligand had been consumed and the product was the known $LTi(NMe_2)_2$.[32]



5rac: Ar = 2,4,6-C_6H_2-Me_3



10 (3)

X-ray Structure Determinations of C_2-6homo, 7hetero, C_2-8homo, and C_2-9homo. To gain a better understanding of the bonding in these TiL_2 complexes, their structures were determined by X-ray diffraction. Gold-colored X-ray quality crystals of heterochiral diastereomer **7hetero**, the predominant diastereomer on reaction of the ligand **2rac** with $Ti(NMe_2)_4$, were grown by vapor diffusion of diethyl ether into a THF solution. ORTEP diagrams are illustrated in Figure 4. Crystals of **C_2-6homo** formed on gas-phase diffusion of hexanes into a toluene solution of **C_2-6homo/C_s-6homo**. The structure of **C_2-6homo** is illustrated in Figure 5. Additionally, crystals of **C_2-8homo** were grown by vapor diffusion of diethyl ether into a toluene solution of **C_2-8homo**, and the structure is shown in Figure 6. Crystals of **C_2-9homo** were grown by dissolving the compound in a toluene solution containing a small amount of dichloromethane. Into this solution was vapor diffused diethyl ether. An ORTEP diagram is illustrated in Figure 7. Bond distances and bond angles for all compounds can be found in Tables 1 and 2, respectively. In the case of **C_2-9homo**, there were three independent molecules in the asymmetric unit that possess the same gross structural features. The bond distances and bond angles for molecule 1 are listed in Tables 1 and 2, and the data for molecules 2 and 3 can be found in the Supporting Information. Details of the structure deter-

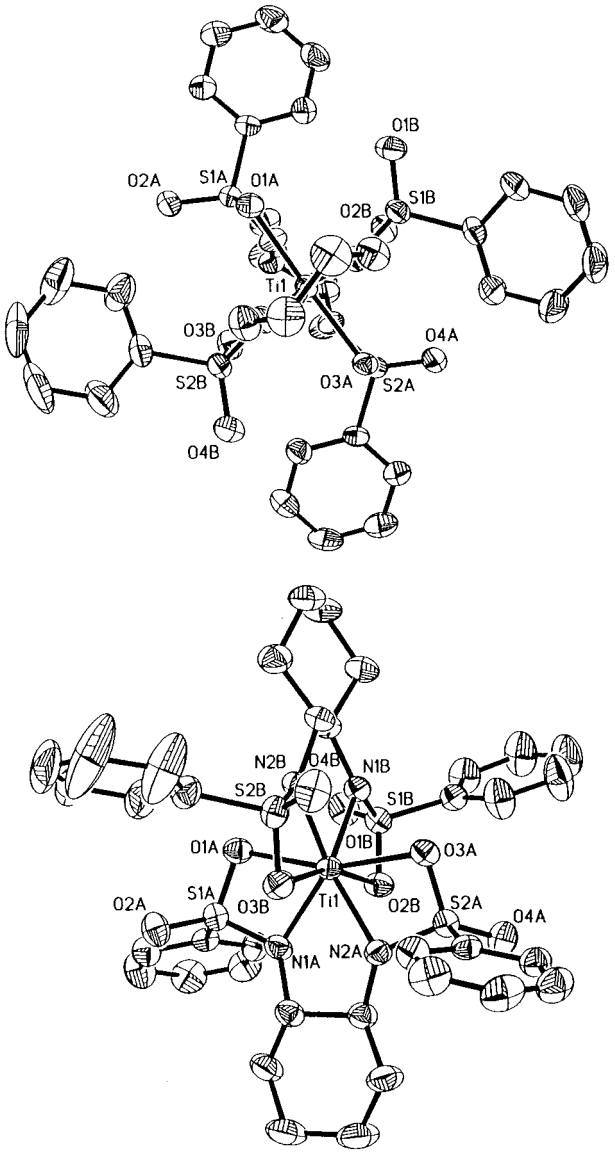


Figure 4. Two views of the structure of **7hetero** are shown. The atoms are shown at 30% probability. Bond lengths and bond angles are shown in Tables 1 and 2.

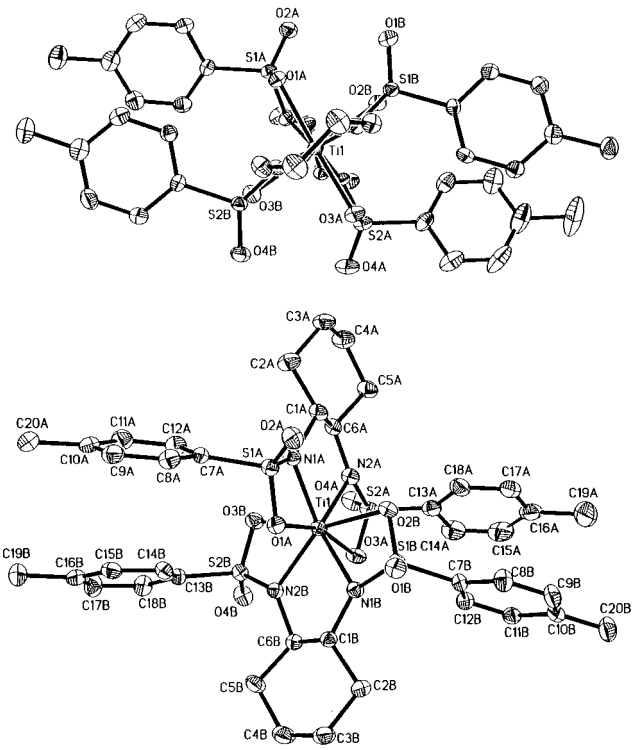


Figure 5. Two views of the structure of **C_2-6homo** are shown. The atoms are shown at 30% probability. Bond lengths and bond angles are shown in Tables 1 and 2.

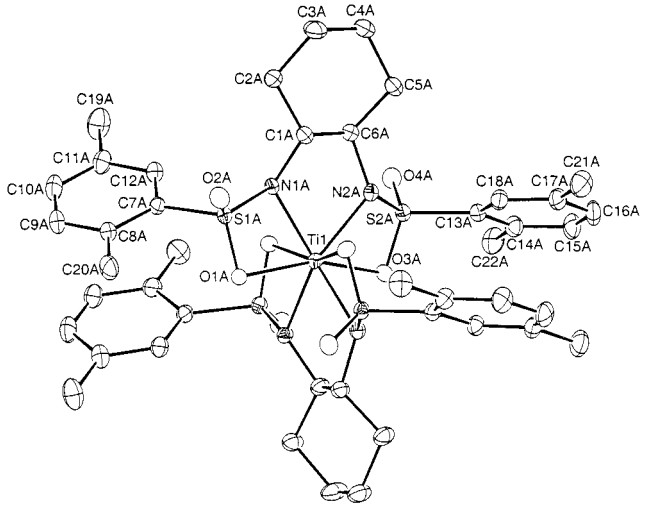


Figure 6. ORTEP drawing of **C_2-8homo** is shown. The atoms are shown at 30% probability. Bond lengths and bond angles are shown in Tables 1 and 2.

mination are located in the Experimental Section, and crystal data and collection parameters are listed in Table 3.

All four structures contain eight-coordinate titanium centers with the titanium bonded to one sulfonyl oxygen from each sulfonyl group and the sulfonamido nitrogens. In all the structures the Ti−O distances range from 2.159(2) to 2.328(2) Å and the Ti−N distances range from 2.070(3) to 2.095(3) Å (Table 1). The Ti−N distances in the bis(sulfonamido) complexes are between 0.1 and 0.2 Å longer than Ti−N distances to silylamides[35] and about 0.3 Å longer than Ti−NMe_2 distances in the bis(sulfonamido)Ti(NMe_2)$_2$ complexes.[32] As noted in Tables 1 and 2, significant differences in S−O bond lengths and O−S−N bond angles are observed between coordinated and noncoordinated sulfonyl oxygens. Coordination of the sulfonyl oxygen to titanium results in a lengthening of the S−O bond distance of about 0.05 Å and in a decrease in the N−S−O bond angle by approximately 20° with respect to N−S−O bond angle of the uncoordinated sulfonyl oxygen. Similar observations have been noted in the bis(amide) complexes LTi(NMe_2)$_2$ structures.[32−34] It is interesting that the metrical parameters of **7hetero** and **C_2-6homo** are very similar, although their gross structural features are quite different.

Catalytic Behavior of the TiL_2 Complexes under the Conditions of the Asymmetric Addition Reaction. The bis(sulfonamide) ligand **1res** has been used in the asymmetric addition of ethyl groups to benzaldehyde to give 1-phenyl-1-propanol with 97% ee.[25] We therefore examined the ability of the TiL_2 complexes to act as precatalysts or catalysts in the asymmetric

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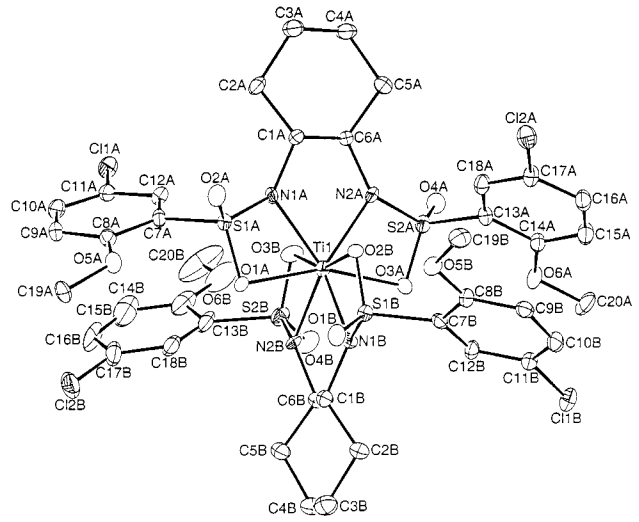
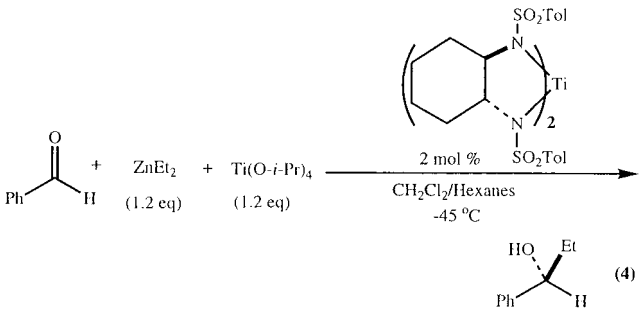


Figure 7. ORTEP drawing of **C_2-9homo** is shown. The atoms are shown at 30% probability. Bond lengths and bond angles are shown in Tables 1 and 2.

Table 1. Selected Bond Distances for C_2-6homo, 7hetero, C_2-8homo, and C_2-9homo (Å)

	C_2-6homo	7hetero	C_2-8homo	C_2-9homo
Ti(1)−N(1A)	2.095(3)	2.074(3)	2.087(2)	2.091(6)
Ti(1)−N(2A)	2.085(2)	2.085(2)	2.073(2)	2.080(6)
Ti(1)−N(1B)	2.081(3)	2.071(3)	2.073(2)	2.073(6)
Ti(1)−N(2B)	2.070(3)	2.077(3)	2.087(2)	2.078(6)
Ti(1)−O(1A)	2.232(2)	2.279(3)	2.159(2)	2.248(5)
Ti(1)−O(2B)	2.217(2)	2.231(3)	2.328(2)	2.217(5)
Ti(1)−O(3A)	2.205(2)	2.209(3)	2.328(2)	2.178(5)
Ti(1)−O(3B)	2.256(2)	2.238(3)	2.159(2)	2.238(5)
S(1A)−O(1A)	1.492(2)	1.483(3)	1.495(2)	1.487(5)
S(1A)−O(2A)	1.437(2)	1.433(3)	1.431(2)	1.430(5)
S(2A)−O(3A)	1.498(2)	1.493(2)	1.470(2)	1.489(5)
S(2A)−O(4A)	1.431(3)	1.435(3)	1.435(2)	1.431(5)
S(1B)−O(1B)	1.435(2)	1.432(3)	1.435(2)	1.419(5)
S(1B)−O(2B)	1.496(2)	1.489(2)	1.470(2)	1.497(5)
S(2B)−O(3B)	1.489(2)	1.492(3)	1.495(2)	1.492(5)
S(2B)−O(4B)	1.435(2)	1.430(3)	1.431(2)	1.425(6)
S(1A)−N(1A)	1.566(2)	1.565(3)	1.561(2)	1.550(5)
S(2A)−N(2A)	1.557(3)	1.557(4)	1.583(2)	1.558(6)
S(1B)−N(1B)	1.562(3)	1.565(3)	1.583(2)	1.533(6)
S(2B)−N(2B)	1.560(3)	1.556(3)	1.561(2)	1.554(6)

alkylation of aldehydes and compared it to **1res**. Crystals of **C_2-6homo/C_s-6homo** were used in the asymmetric addition under conditions designed to accommodate the solubility of **C_2-6homo/C_s-6homo** (dichloromethane was used in place of toluene). The addition was conducted as illustrated in eq 4 using 2 mol % TiL_2. In



(4)

a separate flask under identical conditions the ligand **1res** was examined (eq 1). The reactions were followed by removing aliquots that were rapidly quenched with 2 M HCl and extracted into pentane. For each sample,

Table 2. Selected Bond Angles for C_2-6homo, 7hetero, C_2-8homo, and C_2-9homo (deg)

	C_2-6homo	7hetero	C_2-8homo	C_2-9homo
N(1A)−S(1A)−O(1A)	98.26(13)	97.2(2)	98.39(10)	99.8(3)
N(1A)−S(1A)−O(2A)	118.23(14)	118.2(2)	117.07(11)	116.5(3)
N(2A)−S(2A)−O(3A)	97.91(13)	96.8(1)	99.43(10)	98.5(3)
N(2A)−S(2A)−O(4A)	118.3(2)	118.6(2)	114.60(11)	117.3(3)
N(1B)−S(1B)−O(1B)	118.64(14)	118.4(2)	114.60(11)	117.0(3)
N(1B)−S(1B)−O(2B)	97.26(13)	96.6(1)	99.43(10)	98.5(3)
N(2B)−S(2B)−O(3B)	97.66(13)	96.5(1)	98.39(10)	99.2(3)
N(2B)−S(2B)−O(4B)	117.90(14)	118.3(2)	117.07(11)	117.0(3)
N(1A)−Ti(1)−N(2A)	70.81(10)	70.3(1)	73.21(7)	71.5(2)
N(1B)−Ti(1)−N(2B)	70.82(10)	70.8(1)	73.21(7)	71.8(2)
N(1A)−Ti(1)−N(1B)	138.08(10)	131.2(2)	140.62(8)	139.3(2)
N(1A)−Ti(1)−N(2B)	125.21(10)	129.1(1)	129.69(1)	121.9(2)
N(2A)−Ti(1)−N(2B)	137.76(10)	133.5(1)	140.62(8)	139.2(2)
N(2A)−Ti(1)−N(1B)	126.59(10)	133.3(1)	110.59(11)	125.8(2)

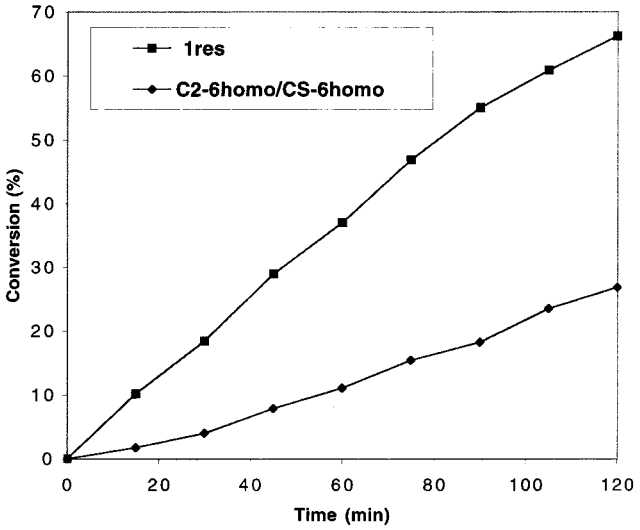


Figure 8. Plot of percent conversion vs time for ligands **1res** (eq 1) and the diastereomeric mixture **C_2-6homo/C_s-6homo** (eq 4).

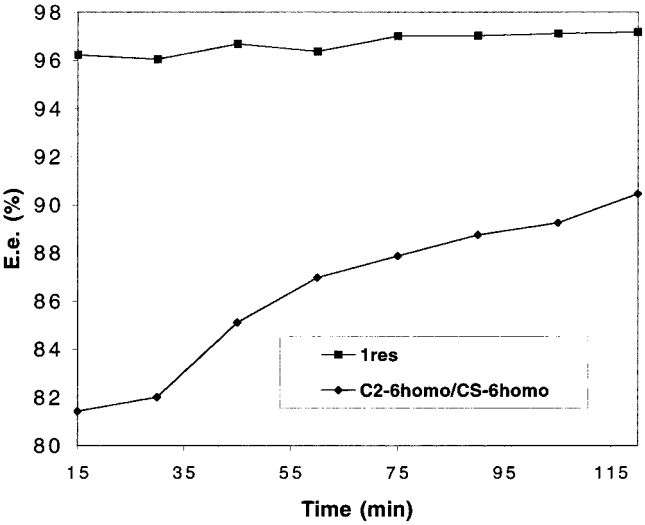


Figure 9. Plot of the enantiomeric excess of 1-phenyl-1-propanol with **1res** (eq 1) and the diastereomeric mixture **C_2-6homo/C_s-6homo** (eq 4) as a function of time.

the percent conversion and ee were determined by GC using a chiral stationary phase column. The results of this study are depicted graphically in Figures 8 and 9. In Figure 8 is plotted the percent conversion as a function of time. This graph indicates that the catalyst derived from the bis(sulfonamide) ligand is significantly

Table 3. Crystal Data and Structure Refinement Parameters for C_2-6homo, 7hetero, C_2-8homo, and C_2-9homo

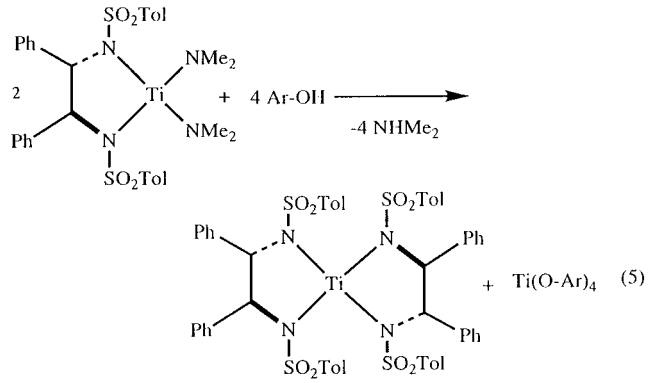
	C_2-6homo	7hetero	C_2-8homo	C_2-9homo
empirical formula	$C_{40}H_{48}N_4O_8S_4Ti$	$C_{40}H_{50}N_4O_9S_4Ti$	$C_{44}H_{56}N_4O_8S_4Ti$	$C_{40}H_{44}Cl_4N_4O_{12}S_4Ti$
fw	888.96	907.0	945.07	1090.76
a (Å)	12.3260(4)	11.848(5)	13.7561(2)	14.8889(4)
b (Å)	12.3260(4)	12.062(6)	21.5632(4)	37.7574(10)
c (Å)	55.025(3)	17.081(8)	15.4853(2)	15.5479(5)
α (deg)	90	103.17(4)	90	90
β (deg)	90	93.51(4)	93.453(1)	101.2440(10)
γ (deg)	90	111.82(4)	90	90
V (Å^3)	8360.0(6)	2178(2)	4585.00(12)	8572.7(4)
Z	8	2	4	2
space group	$P4_32_12$	$P\bar{1}$	$C2/c$ (#15)	$P2_1$ (#4)
T (°C)	−100	−80	−83	−153
radiation, λ (Å)	Mo Kα, 0.71073	Mo Kα, 0.71073	Mo Kα, 0.71069	Mo Kα, 0.71069
$\rho_{(calcd)}$ g/cm^3	1.413	1.383	1.369	1.443
μ (mm^{-1})	0.461	0.445	0.425	0.576
final R indices[a]	R1=0.0505	R1=0.0485	R1=0.0464	R1=0.0717
[$I>2\sigma(I)$]	wR2=0.1049	wR2=0.0686	wR2=0.1091	wR2=0.1873
R indices	R1=0.0542	R1=0.0604	R1=0.0501	R1=0.0806
(all data)	wR2=0.1191	wR2=0.0716	wR2=0.1114	wR2=0.1961

more efficient than the catalyst formed when **C_2-6homo/C_s-6homo** was employed. Furthermore, as shown in Figure 9, the enantiomeric excess of the product is constant over time with **1res** while the enantiomeric excess of the product generated in the reaction using **C_2-6homo/C_s-6homo** increases with time. These results indicate that **C_2-6homo/C_s-6homo** is not the active catalyst formed when the ligand **1res** is employed in the asymmetric addition reaction.

Discussion

Titanium Bis(sulfonamido) Complexes. The bis(sulfonamide) ligands have been found to generate highly enantioselective catalysts in the asymmetric addition of dialkylzinc reagents to aldehydes (eq 1).[19,22−26,30,31,36−38] Their Lewis acidity arises as a result of the electron-withdrawing nature of the sulfonyl groups, which render the N−H's of the bis(sulfonamide) ligands considerably more acidic than those of alkylamines. The pK_a of the sulfonamide N−H is approximately 10,[39] which is comparable with that of a phenol. The presence of the sulfonyl groups stabilizes negative charge on the sulfonamido nitrogen, leaving much less electron density on the N that is available to be donated to titanium. As a result, the bis(sulfonamido) titanium complexes are significantly more Lewis acidic than their dialkyl amide counterparts. The electron-deficient nature of group IV bis(sulfonamido) metal complexes, combined with the oxophillicity of these elements, results in the coordination of one or two of the sulfonyl oxygens to the metal.[25,32,33]

Elimination of amines from titanium amide complexes is a convenient method for the synthesis of a variety of titanium compounds.[40,41] We[25,33] and Gagné[34] have shown that the bis(sulfonamide) ligands readily react with basic titanium amide groups, Ti−NR_2, liberating amine and cleanly generating the bis(sulfonamido) titanium complexes. When only 1 equiv of the bis(sulfonamide) ligand was added relative to the titanium amide complex, the product was L$Ti(NR_2)_2$ (Figure 1, A). When 2 equiv of the ligand was added, however, complexes with two bis(sulfonamido) ligands bound to the metal form, provided the that ligand is not too sterically hindered to preclude reaction of the intermediate L$Ti(NMe_2)_2$ with the second equivalent of ligand. While we were working on this study, Gagné and coworkers reported the only other example of a TiL_2 complex.[34] The diamine used in this system was derived from 1,2-diphenyl-1,2-diaminoethane. Gagné's TiL_2 compound was generated from resolved L$Ti(NMe_2)_2$ complex through an interesting comproportionation reaction illustrated in eq 5. The spectral data suggested that the compound was the C_2-symmetric homochiral diastereomer and that it was formed exclusively. No structural information is available for this compound.

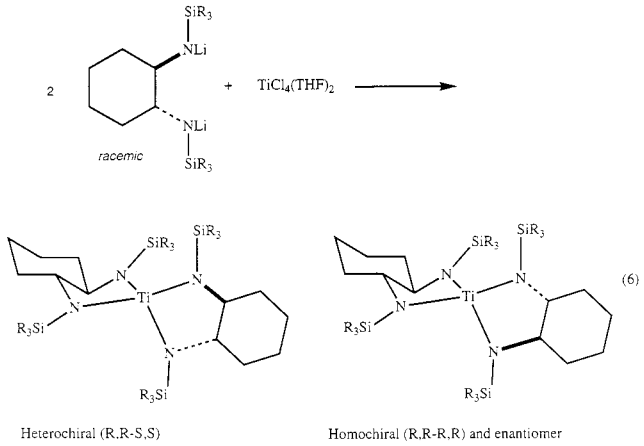


(5)

Conformational Analysis of TiL_2 Complexes. To simplify the discussion, we initially consider coordination of only the sulfonamide nitrogens to the titanium center and not the sulfonyl oxygens. In the reaction involving use of 2 equiv of the racemic bis(sulfonamide) ligand with the $Ti(NMe_2)_4$, two diastereomers can be imagined. The heterochiral complex can be formed on reaction of the titanium tetraamide with one ligand of *R*,*R* configuration and one of *S*,*S* configuration. The

(36) Vettel, S.; Lutz, C.; Diefenbach, A.; Harderlein, G.; Hammerschmidt, S.; Kühling, K.; Mofid, M.-R.; Zimmermann, T.; Knochel, P. *Tetrahedron: Asymmetry* **1997**, *8*, 779−800.
(37) Lütjens, H.; Nowotny, S.; Knochel, P. *Tetrahedron: Asymmetry* **1995**, *6*, 2675−2678.
(38) Lutz, C.; Knochel, P. *J. Org. Chem.* **1997**, *62*, 7895−7898.
(39) Gordon, A. J.; Ford, R. A. *The Chemist's Companion*; John Wiley & Sons: New York, 1972.
(40) Diamond, G. M.; Jordan, R. F.; Petersen, J. L. *Organometallics* **1996**, *15*, 4038−4044.
(41) Diamond, G. M.; Jordan, R. F.; Petersen, J. L. *Organometallics* **1996**, *15*, 4045−4053.

homochiral complex incorporates 2 equiv of the same configuration of the ligand. A similar system was investigated by Jordan and co-workers involving silyl derivatives of racemic *trans*-1,2-diaminocyclohexane and its complexes with titanium as shown in eq 6.[35] This reaction resulted in the generation of a mixture of diastereomers.



(6)

Another related report involved silicone bis[bis(sulfonamido)] complexes, SiL_2, using achiral sulfonamide ligands. These complexes have been characterized by X-ray diffraction methods and contain four-coordinate silicon. It is proposed that there is a weak interaction between the silicon and the sulfonyl oxygens; however, the O···Si distances are 2.85−3.02 Å, whereas the Si−N distances are on the order of 1.7−1.8 Å.[42]

The TiL_2 sulfonamide system becomes more complex when coordination of the sulfonyl oxygens is considered. The oxygens of each sulfur are diastereotopic, and coordination of one of the sulfonyl oxygens to titanium makes the sulfur a stereogenic center. This coordination is thought to be important in the asymmetric addition reaction (eq 1).[25,43] To understand the relationship between the diastereomers formed on coordination of the sulfonyl oxygens, it is helpful to use a model to represent the shape of the bound bis(sulfonamido) ligand (Figure 10). The horizontal and vertical lines represent the cyclohexane ring and the sulfonyl groups. The H's shown are the axial methine C−H's of the cyclohexane ring. The slanted lines represent the aromatic rings. In the model, the bold lines indicate that the cyclohexyl group (not shown) is coming out of the page toward the reader, while the thin lines represent the ligand going back into the page.

The simplified model of the ligand is useful to understand the formation of diastereomers and conformational preferences in this system (Figure 10). It is important to note that in the structures of the $LTi(NMe_2)_2$ and $LTi(O\text{-}i\text{-}Pr)_2$ (Figure 1), the aryl rings are directed away from the axial methine C−H on the carbon to which the sulfonamido group is attached. In the model system the H's are shown to illustrate this relationship. When the bis(sulfonamido) ligand coordinated to the metal has the *R,R* configuration, the pro-*R* sulfonyl oxygens will preferentially coordinate to give the *R* configuration at both sulfurs. The origin of this preference is not clear but appears to be uniformly observed in the solid-state structures of the bis(sulfonamido) titanium complexes in Figure 1 and in the four structures reported here.[25,32−34]

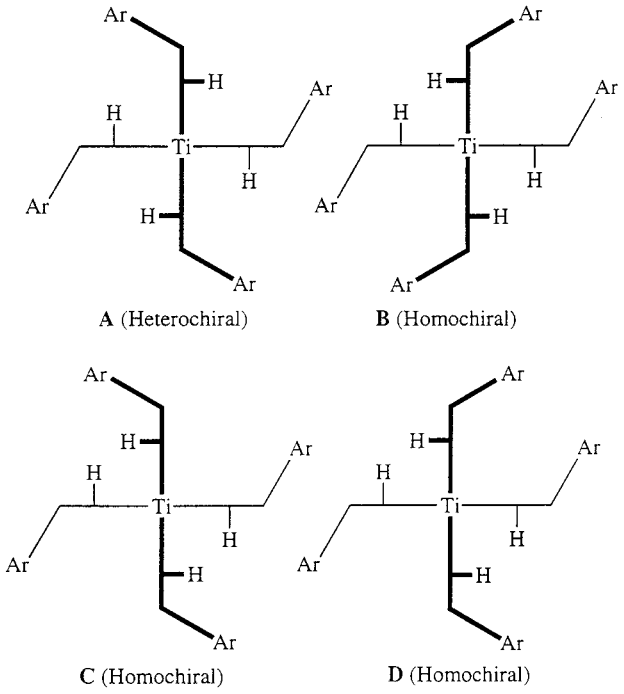


Figure 10. Simplified geometries and conformations of bis[bis(sulfonamido)] complexes of titanium.

From the models of the diastereomeric TiL_2 complexes illustrated in Figure 10 it seems likely that the heterochiral complex (model diastereomer **A**) will be the most stable as a result of minimization of interligand repulsion. In diastereomer **A**, the aryl groups are well separated and there is one aryl group in each of the four quadrants defined by the N−Ti−N plane of the ligands. This is in contrast with the homochiral diastereomer **B**. In the homochiral diastereomer, formed from the *R,R* configuration of the ligand, the coordination of the pro-*R* oxygens of the sulfonyl groups gives diastereomer **B**. To minimize the Ar−Ar interactions in **B**, both of the pro-*S* sulfonyl oxygens of one of the ligands could preferentially coordinate while the second ligand remained unchanged, giving the diastereomer **C** (Figure 10). In **C**, the two ligands have different geometries and would be inequivalent by NMR spectrometry. Finally, it is also possible that the titanium could coordinate a pro-*R* and a pro-*S* sulfonyl oxygen from one of the ligands and the pro-*R* oxygens of the other to give the diastereomer **D**. All of the aryl groups are inequivalent in **D**. Thus, it should be possible to discriminate between **B** and **C** by NMR.

The TiL_2 complexes were prepared as outlined in eq 2. We found that the type of product formed [TiL_2 vs $LTi(NMe_2)_2$] as well as the ratios of the diastereomers observed were dependent on the size of the aryl groups of the bis(sulfonamide) ligands. Reaction of the tetraamide with the racemic ditolyl ligand **1rac** in benzene gave a mixture of two diastereomeric products (eq 2). Both diastereomers have the same symmetry by ^1H NMR spectroscopy at room temperature and each

(42) Rong, G.; Keese, R.; Stoeckli-Evans, H. *Eur. J. Inorg. Chem.* **1998**, 1967−1973.
(43) Balsells, J.; Betancort, J. M.; Walsh, P. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 3428−3430.

showed only one environment for the aryl groups. The structures proposed for these compounds were the heterochiral diastereomer **6hetero** and C_2-symmetric homochiral diastereomer **C_2-6homo**. We then attempted to synthesize the homochiral complex **C_2-6homo** by reaction of the resolved ligand **1res** with $Ti(NMe_2)_4$. However, two diastereomeric products were formed in this reaction in a ratio of 6:4. The major diastereomer formed with **1res** was identical to the minor product observed on reaction of $Ti(NMe_2)_4$ with **1rac**. Heating the mixture of diastereomers to 70 °C in a sealed NMR tube resulted in coalescence of the sets of aromatic and methyl resonances of the diastereomers by ^{1}H NMR spectroscopy (200 MHz). These results indicate that the compounds were interconverting on the NMR time scale. Cooling the sample in $CDCl_3$ and monitoring the solution by ^{1}H NMR spectroscopy (500 MHz) resulted in a sharpening of the resonances of the major diastereomer, but no change in symmetry was observed down to −65 °C. In the case of the minor diastereomer from **1res**, cooling the sample to −15 °C resulted in the four aromatic rings becoming inequivalent (Figure 2). All four methyl groups were also inequivalent at −15 °C, appearing as four singlets in the ^{1}H NMR spectrum (Figure 2). The only diastereomer with this symmetry in Figure 10 is **D**. The interconversion of **C_2-6homo** and **C_s-6homo** can be envisioned to occur by dissociation of a pro-*R* sulfonyl oxygen from **C_2-6homo** followed by rotation about the N−S bond and coordination of the pro-*S* sulfonyl oxygen giving **C_s-6homo** (diastereomer **D**). Apparently, in the equilibrium between **C_2-6homo** and **C_s-6homo** (structures **B** and **D** in Figure 10) the relief of the aryl−aryl interactions on going from **C_2-6homo** to **C_s-6homo** is insufficient to override the stabilization afforded by coordination of the pro-*R* sulfonyl oxygen. It is not clear at this time why there is a strong preference for the titanium-bearing (*R*,*R*)-bis(sulfonamido) ligand to coordinate the pro-(*R*) sulfonyl oxygen. The behavior of complexes prepared from **2rac** was found to parallel those synthesized from **1rac**.

Reaction of $Ti(NMe_2)_4$ with **3rac** gave two diastereomers in a ratio of 5:1. Recrystallization of this mixture gave a single diastereomer, which was determined to be the major diastereomer by NMR spectroscopy of the crystals. We predicted that this compound would be the heterochiral complex, in analogy with the reactivity of **1rac**. As will be discussed below in the section on structure determinations, to our surprise this compound was the homochiral diastereomer **C_2-8homo**.

In the reaction of **4res** with $Ti(NMe_2)_4$ (eq 2) only one diastereomer was obtained by precipitation of the crude reaction mixture from THF with diethyl ether. From the X-ray analysis it was determined that the structure of the product was **C_2-9homo**.

In contrast with **1rac-3rac**, the reaction of the racemic mesityl ligand **5rac** with the $Ti(NMe_2)_4$ does not give the TiL_2 complex. In this reaction only 1 equiv of the ligand was consumed per titanium and the product was $LTi(NMe_2)_2$, **10** (eq 3).[32,33] The difference in reactivity between **1rac**−**3rac** and **5rac** with $Ti(NMe_2)_4$ was attributed to the increased size of the aryl rings of **5rac**, which precluded reaction of $LTi(NMe_2)_2$ with the second equivalent of free ligand.

X-ray Structural Determinations of C_2-6homo, 7hetero, C_2-8homo, and C_2-9homo. To aid in understanding the structure and bonding in the TiL_2 complexes and their fluxional properties, we determined the structures of four TiL_2 complexes. Two views of the structure of the diastereomer **7hetero** are illustrated in Figure 4. From these ORTEP drawings the bonding of the bis(sulfonamido) ligands to the titanium and the spatial arrangement of the ligands can be seen. The planes that are defined by the N1A−Ti1−N2A and N1B−Ti1−N2B are orthogonal to minimize ligand−ligand interactions. In each of the sulfonamido groups the phenyl rings are oriented opposite the axial methine C−H at the junction of the sulfonamide and the cyclohexyl ring. As a result, each phenyl group occupies a separate quadrant, thus minimizing the interactions between these groups. To our knowledge, this orientation of the aryl group has been observed for all crystallographically characterized early transition metal complexes containing the bis(sulfonamide) ligand.[25,32−34]

The bond distances and bond angles for all the structures are listed in Tables 1 and 2, respectively. In the structure of **7hetero** the sulfonyl oxygens are bonded to the titanium with Ti−O distances between 2.209(3) and 2.279(3) Å. These distances can be compared with those of the related $LTi(NMe_2)_2$ and $LTi(O\text{-}i\text{-}Pr)_2$ complexes. In the amide complexes, the titanium center is bonded to one or two sulfonyl oxygens (Figure 1, **A**). When bonded to only one sulfonyl oxygen, the Ti−O distances range from 2.167(2) to 2.219(3) Å.[32] When the titanium is bonded to two sulfonyl groups, the distances are considerably longer [2.447(4) and 2.434(4) Å].[33] In the alkoxide complexes, $LTi(O\text{-}i\text{-}Pr)_2$ (Figure 1, **B**), one of the sulfonyl oxygens from each SO_2 group is bonded to titanium. The Ti−O distances range from 2.249(3) to 2.390(3) Å.[32] This trend suggests that the better the donor ability of the ligands on titanium, the longer the sulfonyl oxygen−titanium (Ti−O) bond distances. The effect of coordination of the sulfonyl oxygens to titanium is reflected in the differences in the sulfur−oxygen distances of the bound and unbound sulfonyl groups. The S−O distance in the free ligand **2rac** ranges from 1.437 to 1.443 Å.[32] In the heterochiral derivative **7hetero**, the unbound S−O distances are very similar to the S−O distances in the free ligand **2rac** and range from 1.430(3) to 1.435(3) Å. The titanium-bound sulfonyl oxygens have S−O distances that are considerably longer, falling between 1.483(3) and 1.493(2) Å. The shortening of the Ti−O bond distances and the greater lengthening of the S−O bonds on coordination of the oxygen to titanium in **7hetero** with respect to $LTi(NMe_2)_2$ and $LTi(O\text{-}i\text{-}Pr)_2$ attest to the electron-deficient nature of the titanium center in this eight-coordinate complex. The increased interaction between the titanium and the sulfonyl oxygens does not affect the Ti−N distances, which fall between 2.071(3) and 2.085(3) Å. These distances are typical of bis(sulfonamido) nitrogens bonded to titanium.

The bond distances and bond angles in the C_2-symmetric homochiral complex **C_2-6homo** are very similar to those of **7hetero** (Tables 1 and 2) even though the geometries are very different. Unlike **7hetero**, where the aryl groups are well separated, the structure of **C_2-6homo** has one tolyl group from each ligand

sharing a quadrant. As is illustrated in Figure 5, the tolyl rings in the homochiral **C_2-6homo** are much closer than in the heterochiral **7hetero**. The closest carbon−carbon interactions in **C_2-6homo** are between carbons C(12A) and C(14B) (3.340 Å) and C(11A) and C(15B) (3.455 Å). In this structure the aryl rings are offset and the overlap of the rings is minimal, unlike that observed for **C_2-8homo** and **C_2-9homo**. Despite the aryl−aryl interactions in the geometry of **C_2-6homo**, the titanium center preferentially coordinates the pro-*R* oxygens of the sulfonyl groups to give diastereomer **B** (Figure 10) when bound to the (*R*,*R*)-ligand. In this conformation the tolyl groups are oriented opposite the axial methine C−H of the cyclohexane ring.

The structure of the major diastereomer obtained from the reaction of 2 equiv of **3rac** with $Ti(NMe_2)_4$ was obtained. We had anticipated that the predominant product formed in this reaction would be **8hetero** (eq 2) in analogy with the reactivity of **1rac** and **2rac**. However, we were surprised to find that the crystal contained a racemic mixture of **C_2-8homo** (Figure 6). The ^{1}H NMR of the remaining crystals indicated that they were the same as the major diastereomer. It is not clear why the ligand **3rac** preferentially forms the homochiral rather than the heterochiral TiL_2 complex. One difference in the structures of **C_2-6homo** and **C_2-8homo** is the extent of overlap between the aromatic rings. In **C_2-6homo** the aryl rings have little overlap, with only two carbons of each ring held in proximity. In the structure of **C_2-8homo** the aromatic rings containing carbons C7A−C12A and C13B−C18B are only slightly offset in position and the carbon atoms of these rings are staggered with respect to the adjacent ring. The distances between carbons on adjacent rings range from 3.67 to 3.858 Å. In contrast, the rings containing carbons C13A−C18A and C10B−C15B do not overlap. It is not clear if or how the interligand interaction between aryl rings can influence formation of **C_2-8homo** over **8hetero**.

The structure of **C_2-9homo**, which was formed from **4res**, was also examined and is shown in Figure 7. The unit cell of **C_2-9homo** contains three molecules in the asymmetric unit which are very similar. The bond distances and angles of molecule 1 are presented in Tables 1 and 2 with metrical parameters of molecules 2 and 3 listed in the Supporting Information. The gross structural features are similar to **C_2-6homo** and **C_2-8homo**. The aromatic rings of **C_2-9homo** are slightly offset, with distances between the closest carbons on adjacent rings ranging from 3.532 to 3.695 Å for rings C7A−C12A and C13B−C18B and 3.466−3.674 Å for rings containing carbons C7B−C12B and C13A−C18A. In this structure both rings are held in close proximity, whereas only one set of rings had close contacts in the structure of **C_2-8homo**.

Examination of the TiL_2 Complexes in the Asymmetric Addition of Alkyl Groups to Aldehydes. To determine if the TiL_2 complexes could be involved in the asymmetric addition of alkyl groups to aldehydes (eq 1), we conducted the asymmetric addition using the diastereomers **C_2-6homo/C_s-6homo** (eq 4). In these experiments, the ligand **1res** [(*R*,*R*)-configuration] was compared with diastereomers **C_2-6homo/C_s-6homo** [prepared from (*R*,*R*)-**1res**] in terms of both enantioselectivity and turnover frequency. Both **1res** and **C_2-6homo/C_s-6homo** were used at 2 mol % loading, which is equivalent to using twice as much ligand in the case of the TiL_2 diastereomers**.** The two reactions were run side by side, and aliquots were periodically removed and rapidly quenched with 2 M HCl. Each sample was then analyzed using chiral stationary phase GC to determine the ee of the 1-phenyl-1-propanol and the percent conversion (integration against an internal standard). The results of these experiments are shown in Figures 8 and 9. In Figure 8 is plotted the conversion as a function of time for **1res** and **C_2-6homo/C_s-6homo**. Even though the total amount of ligand in **C_2-6homo/C_s-6homo** is twice that of **1res**, the conversion is significantly faster with **1res**. Additionally, the ee of the product was constant over time in the reaction employing **1res** but increased with time with the **C_2-6homo/C_s-6homo** diastereomers (Figure 9). These results suggest that a single species was responsible for the catalysis with **1res** and that the catalyst was changing with time when **C_2-6homo/C_s-6homo** were used. Furthermore, the enantioselectivity observed starting with the TiL_2 diastereomers is approaching that of the catalyst formed from **1res**. It is likely that the diastereomers **C_2-6homo/C_s-6homo** undergo decomposition in the course of the reaction to generate the same catalyst that is formed with **1res**. At early reaction times, the percentage of decomposition of **C_2-6homo/C_s-6homo** is low and the amount of the catalyst formed as a result is small. This reaction is an example of ligand-accelerated catalysis,[44] and therefore there are two competing pathways for product formation. One of these is the formation of product by the chiral catalyst giving nonracemic product. The other pathway is the background reaction, which is the addition of the alkyl group to the aldehyde promoted by the weak Lewis acid titanium tetraisopropoxide. This pathway gives racemic product since there is no chiral ligand involved. As the amount of the catalyst formed on decomposition of the diastereomers **C_2-6homo/C_s-6homo** increases, more catalyst is generated. Thus, more product is formed through the ligand-accelerated pathway and the ee of the product rises.

The chemistry and the catalysis in the asymmetric addition of alkyl groups to aldehydes with the LTi(O-*i*-Pr)$_2$ and TiL_2 complexes described here is reminiscent of the pioneering work of Seebach.[45−50] Seebach and coworkers have developed the TADDOL ligands, which have been used successfully in a variety of asymmetric transformations. They have synthesized the (TADDOLate)Ti(O-*i*-Pr)$_2$ and the spirotitanate (TADDOLate)$_2$Ti, both of which can be used in the asymmetric addition of alkyl groups to aldehydes and give the same

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highly enantioselective catalyst.[46] One difference between these systems is that the TiL_2 complexes derived from the bis(sulfonamide) ligands are more stable with respect to reaction with titanium tetraisopropoxide to generate the $LTi(O\text{-}i\text{-}Pr)_2$ complexes. In contrast, $(TADDOLate)_2Ti$ readily reacts with titanium tetraisopropoxide to generate 2 equiv of $(TADDOLate)Ti(O\text{-}i\text{-}Pr)_2$, which is believed to be responsible for the catalysis in the asymmetric addition of alkyl groups to aldehydes. The increased stability of the TiL_2 complexes is due to the lack of available coordination sites in the eight-coordinate TiL_2 complexes.

Conclusions

We have developed a synthetic methodology for the synthesis of the TiL_2 complexes by reaction of bis(sulfonamide) ligand with the titanium tetraamide. We have found that the bis(sulfonamido) ligand exhibits a strong preference to be C_2-symmetric with the aryl groups oriented away from the axial methine C−H's of the cyclohexane ring. The ligand is held firmly in this position by the stereospecific coordination of the sulfonyl oxygens to titanium. We believe that these interactions are vital to obtain high enantioselectivity in the asymmetric addition of alkyl groups to aldehydes.[25,43] An investigation into the possibility that the TiL_2 complexes were involved in the asymmetric alkylation of aldehydes indicated that they are not the active catalysts but that they most likely undergo a slow decomposition under the reaction conditions of the asymmetric addition to generate $LTi(O\text{-}i\text{-}Pr)_2$.

Experimental Section

General Comments. The general Experimental Section has been previously described.[32] Enantiomeric excesses were determined using GC methods. GC analyses were carried on a Hewlett-Packard 6890 gas chromatograph with a 30 m Supelco β-DEX column.

Synthesis and Characterization of the Heterochiral and Homochiral Diastereomers C_2-6homo and 6hetero. Under an inert atmosphere, the powdered ligand **1rac** (780 mg, 1.85×10^{-3} mol) was stirred in 5 mL of benzene at room temperature. To this slurry was added $Ti(NMe_2)_4$ (210 mg, 9.25×10^{-4} mol, 0.5 equiv) as a solution in 1 mL of benzene dropwise. On addition of the titanium complex, the ligand dissolved to give a yellow-brown solution, which was stirred until a yellow solid formed (5 h). This solid was isolated after decanting the solvent and washing with diethyl ether. In this manner a mixture of **6hetero** and **C_2-6homo** was isolated in 89% yield (730 mg, 8.22×10^{-4} mol) as a mixture of two diastereomers in a ratio **6hetero**/**C_2-6homo** = 6:1. Crystallization of this mixture from THF/Et_2O gave a similar mixture of diastereomers. When the reaction was carried out in THF, the resulting solution afforded a yellow solid, which was washed with diethyl ether and allowed to dry. In this manner, the two diastereomers were isolated in a ratio **6hetero**/**C_2-6homo** = 7:3.

Data for 6hetero and C_2-6homo. ^{1}H NMR ($CDCl_3$, 200 MHz) **6hetero**: δ 8.25 (d, J = 8 Hz, 8H); 7.32 (d, J = 8 Hz, 8H); 3.66 (br, 4H); 2.42 (s, 12H); 1.73 (br, 4H); 1.48 (br, 4H); 1.02 (br, 8H) ppm; **C_2-6homo**: δ 7.74 (d, J = 8 Hz, 8H); 6.90 (br, 8H); 3.66 (b, 4H); 2.32 (s, 12H); 1.73 (br, 4H); 1.48 (br, 4H); 1.02 (br, 8H) ppm; $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, 23 °C) **6hetero**: δ 143.8, 139.3. 129.3, 128.2, 66.7, 30.2, 23.8, 21.5 ppm.

Synthesis and Characterization of C_2-6homo/C_s-6homo. The procedure was identical to that employing **1rac** in benzene but with the resolved ligand **1res**. The product was isolated by diffusion of diethyl ether into a benzene solution of the compound at room temperature. The yield was 81%. The ratio of the two diastereomers did not change when the reaction was performed in different solvents. However, the ratio was 3:1 in C_6D_6 and 6:4 in $CDCl_3$, as determined by ^{1}H NMR spectrometry.

Data in $CDCl_3$. ^{1}H NMR ($CDCl_3$, 23 °C, 200 MHz) **C_2-6homo**: δ 7.74 (br, J = 8 Hz, 8H); 6.90 (br, 8H); 3.70 (br, 4H); 2.33 (s, 12H); 1.76 (br, 4H); 1.51 (br, 4H); 1.11 (br, 8H) ppm. ^{1}H NMR ($CDCl_3$, 23 °C, 200 MHz) **C_s-6homo**: δ 8.18 (br, 8H), 7.32 (br, 8H), 3.70 (br, 4H), 2.33 (br, 12H), 1.76 (br, 4H), 1.51 (br, 4H), 1.11 (br, 8H) ppm.

Data in C_6D_6. ^{1}H NMR (C_6D_6, 23 °C, 200 MHz) **C_2-6homo**: δ 8.01 (br, 8H); 6.57 (br, 8H); 4.30 (br, 4H); 1.86 (br, 12H); 1.14 (br, 8H); 0.82 (br, 4H) ppm. ^{1}H NMR (C_6D_6, 23 °C, 200 MHz) **C_S-6homo**: δ 8.60 (br, 8H), 6.99 (br, 8H), 3.92 (br, 4H), 1.86 (br, 16H); 1.14 (br, 8H); 0.82 (br, 4H) ppm.

C_2-6homo/C_s-6homo. IR (CH_2Cl_2): 2938, 2862, 1597, 1445, 1311, 1274, 1207, 1105, 990, 897, 818 cm^{-1}. MS (ES+, 30 eV), *m/e* (relative intensity): 889 $(M + H)^+$ (46), 524 (29), 468 (100). HRMS calcd for $C_{40}H_{49}N_4O_8S_4Ti$ $(M + H)^+$: 889.191274. Found: 889.189955.

Variable-Temperature NMR of C_2-6homo/C_s-6homo. ^{1}H NMR (C_6D_6, 70 °C, 200 MHz): δ 8.15 (b, 8H); 6.77 (b, 8H); 4.12 (b, 4H); 1.89 (b, 16H); 1.19 (b, 8H); 0.86 (b, 4H) ppm. $^{13}C\{^1H\}$ NMR (C_6D_6, 60 °C, 125 MHz): 143.1, 139.3, 128.8, 127.4, 67.8, 31.1, 23.9, 21.4 ppm.

Synthesis and Characterization of 7homo and 7hetero. Under an inert atmosphere, the insoluble ligand **2rac** (353 mg, 8.95×10^{-4} mol, 2 equiv) was stirred in 5 mL of benzene at room temperature. To this mixture was added $Ti(NMe_2)_4$ (100 mg, 4.47×10^{-4} mol) dropwise as a solution in 1 mL of benzene. On addition of the titanium complex, the ligand dissolved to give a clear yellow-brown solution. When no undissolved ligand remained, stirring was discontinued. The solution was allowed to stand at room temperature, resulting in the formation of yellow crystals after 12−24 h. The solution was decanted and the crystals washed with diethyl ether. The product was isolated in 79% yield as a mixture of the heterochiral **7hetero** and the homochiral **C_2-7homo**. The ratio of the two diastereomers **7hetero**/**C_2-7homo** was determined to be 4:1.

Data in $CDCl_3$. ^{1}H NMR ($CDCl_3$, 200 MHz, 23 °C) **7hetero**: δ 8.38 (b, 8H); 7.56 (b, 12H); 3.69 (b, 4H); 1.77 (b, 4H); 1.49 (b, 4H); 1.04 (b, 8H) ppm; **C_2-7homo**: δ 7.89 (b, 8H); 7.41 (b, 4H); 7.14 (b, 8H); 3.69 (b, 4H); 1.77 (b, 4H); 1.49 (b, 4H); 1.04 (b, 8H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, 23 °C) **7hetero**: δ 142.1, 133.1, 128.8, 128.2, 66.9, 30.3, 23.8 ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz, 23 °C) **C_2-7homo**: δ 141.9, 132.7, 128.8, 127.3, 65.9, 31.2, 23.9 ppm. IR (Nujol) 1281, 1211, 1165, 1123, 1105, 976, 897 cm^{-1}.

Synthesis and Characterization of C2-8homo. Under an inert atmosphere, the insoluble ligand **3rac** (200 mg, 4.44×10^{-4} mol, 2 equiv) was stirred in 2 mL of toluene at room temperature. To this mixture was added $Ti(NMe_2)_4$ (54 mg, 2.41×10^{-4} mol) with stirring. On addition of the titanium complex, the ligand dissolved to give a clear brown solution. When no undissolved ligand remained, stirring was discontinued. The solution was allowed to stand at room temperature, resulting in the formation of yellow crystals after 24 h. The solution was decanted and the crystals washed with diethyl ether. The product was isolated in 75% yield.

Data for C_2-8homo. ^{1}H NMR ($CDCl_3$, 500 MHz, 23 °C): δ 7.32 (s, 4H), 6.99 (d, J = 7.1 Hz, 4H), 6.88 (d, J = 7.1 Hz, 4H), 3.81 (m, 4H), 2.72 (s, 12H), 1.84 (m, 4H), 1.82 (s, 12H), 1.61 (m, 4H), 1.25 (m, 8H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 140.7, 134.9, 133.3, 132.3, 131.4, 128.5, 66.1, 31.8, 24.2, 20.6, 20.5 ppm. IR (CH_2Cl_2): 2940, 2826, 1490, 1448, 1312, 1283,

1208, 1076, 992, 902 cm^{-1}. MS (ES+, 30 eV), *m/e* (relative intensity): 945 $(M + H)^+$ (100), 496 (12). HRMS calcd for $C_{44}H_{57}N_4O_8S_4Ti$ $(M + H)^+$: 945.253874. Found: 945.255335.

Synthesis and Characterization of C_2-9homo. Under an inert atmosphere, the insoluble ligand **4res** (1.12 g, 2.13×10^{-3} mol, 2 equiv) was stirred in 5 mL of toluene at room temperature. To this mixture was added $Ti(NMe_2)_4$ (239 mg, 1.06×10^{-3} mol) as a solution in 5 mL of toluene. On addition of the titanium complex, the ligand dissolved to give a yellow-brown solution, which was allowed to stir overnight. During this time, the product precipitated as a yellow solid and was isolated by decanting the solvent and washing with diethyl ether. The product was allowed to dry under reduced pressure. In this manner **C_2-9homo** was isolated as a 1:1 mixture with toluene (640 mg, 51%).

Data for C_2-9homo. ^1H NMR ($CDCl_3$, 500 MHz): 7.44 (d, $J = 2.5$ Hz, 4H); 7.08 (dd, $J = 2.5$ Hz, $J = 8.8$ Hz, 4H); 6.80 (d, $J = 8.8$ Hz, 4H); 3.97 (s, 12H); 3.85 (m, 4H); 2.05 (m, 4H); 1.70 (m, 4H); 1.40 (m, 8H) ppm. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): 155.6, 133.2, 131.2, 128.8, 123.5, 113.4, 66.3, 56.3, 31.9, 24.1 ppm. IR (CH_2Cl_2) 2942, 2862, 1588, 1570, 1479, 1289, 1167, 1075, 1019, 901, 812 cm^{-1}. MS (ES+, 30 eV), *m/e* (relative intensity): 1089 $(M + H)^+$ (36), 843 (20), 568 (100). HRMS calcd for $C_{40}H_{45}Cl_4N_4O_{12}S_4Ti$ $(M + H)^+$: 1089.015043. Found: 1089.014140.

Procedure for the Asymmetric Additions of Diethylzinc to Aldehydes. Inside the drybox, the complex **C_2-6homo/ C_s-6homo** (14.8 mg, 1.7×10^{-5} mol, 2 mol %) was introduced in a 10 mL Schlenk flask equipped with a stir bar. The flask was removed from the drybox and a 1.0 M solution of diethylzinc in dichloromethane (1 mL, 1×10^{-3} mol, 1.2 equiv) was added under a nitrogen atmosphere. The resulting yellow solution was stirred for 15 min and cooled to −45 °C. Titanium tetraisopropoxide in hexanes (1 M, 1×10^{-3} mol, 1.2 equiv) was added slowly by syringe. The solution was stirred for 10 min and benzaldehyde was added (84.7 μL, 8.3×10^{-4} mol). The progress of the reaction was monitored by GC. Aliquots of 0.1−0.2 mL of the reaction mixture were removed periodically, quenched with 2 mL of 2 M HCl, extracted with 1 mL of pentane, and filtered through a plug of Celite. The samples were analyzed by GC using a chiral stationary phase 30 m Supelco β-DEX column as described previously.[25]

X-ray Crystallographic Procedures. Crystals were grown at room temperature, isolated from the mother liquor, and immediately immersed in paratone under a nitrogen atmosphere in a drybox. A crystal was selected for the X-ray diffraction study, mounted in paratone on a quartz fiber, and rapidly placed in a nitrogen gas cold stream of the cryostat of the Siemans P3/PC diffractometer or a Rigaku R-AXIS IIc area detector. The crystal was indexed and data were collected at low temperature. Corrections for the effects of absorption anisotropy were done. Structure solutions were performed by direct methods, and structure refinement was done with the programs SHELXS and SHELXL.[25] Crystallographic parameters are given in Table 3, and selected bond distances and angles are provided in Tables 1 and 2, respectively.

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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. This material is available free of charge via the Internet at http://pubs.acs.org.

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