

## Structure/Enantioselectivity Study of the Asymmetric Addition of Trimethylsilylcyanide to Benzaldehyde Catalyzed by Ti(IV)–Schiff Base Complexes

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In the presence of titanium tetraisopropoxide, tridentate salen ligands derived from *cis*-1-amino-2-indanol have been utilized in the asymmetric addition of trimethylsilylcyanide to benzaldehyde, which gave the cyanohydrins in up to 85% ee. We have examined the reaction of titanium tetraisopropoxide with these salen ligands by NMR spectrometry and X-ray crystallography. Reaction of ligands derived from salicylaldehydes with bulky substituents in the 3-position with titanium tetraisopropoxide gave the L<sup>\*</sup>Ti(O-*i*-Pr)<sub>2</sub> complexes, which are the proposed precatalysts in the asymmetric addition reaction. These ligands give good to very good enantioselectivity in the asymmetric trimethylsilylcyanation reaction. However, with groups smaller than *tert*-butyl in the 3-position, substantial amounts (up to 73%) of the catalytically inactive L<sub>2</sub><sup>\*</sup>Ti species are formed, resulting in large drops in the ee's of the cyanohydrins. The L<sub>2</sub><sup>\*</sup>Ti species were formed as mixtures of diastereomers, one of which has been characterized by X-ray crystallography. The crystal structure shows the titanium to be bonded to two ligands with a pseudo-octahedral coordination geometry. The ligands are bound in a meridional fashion and the complex is C<sub>2</sub>-symmetric. Use of 2 equiv of ligand relative to titanium tetraisopropoxide resulted in significant reductions in the ee of the cyanohydrin product, presumably due to formation of increased amounts of the inactive diastereomeric L<sub>2</sub><sup>\*</sup>Ti complexes.

Enantioselective carbon–carbon bond forming processes are at the heart of asymmetric catalysis.<sup>1–4</sup> Cyanohydrin formation is one such reaction that involves the creation of a new carbon–carbon bond between a carbonyl carbon and a cyanide ion.<sup>5</sup> In pioneering work, Evans and co-workers developed an elegant method for the cyanohydrin of carbonyl compounds using trimethylsilylcyanide in the presence of achiral Lewis acid catalysts.<sup>6</sup> Subsequent advances allow addition of trimethylsilylcyanide to carbonyl groups in an enantioselective fashion using chiral Lewis acid catalysts.<sup>7–9</sup> The products of this reaction, the

chiral cyanohydrins or cyanohydrin trimethylsilyl ethers, have been readily converted to  $\alpha$ -hydroxycarboxylic acids,<sup>10,11</sup>  $\alpha$ -hydroxyaldehydes,<sup>12,13</sup>  $\alpha$ -hydroxyketones,<sup>12,13</sup>  $\beta$ -amino alcohols,<sup>11–15</sup> and  $\alpha$ -amino acid derivatives.<sup>16</sup> In view of the increasing demand for intermediates of high optical purity, these versatile chiral cyanohydrins can serve as excellent synthetic precursors. Indeed, they have found applications as important intermediates in the synthesis of insecticides.<sup>17</sup>

In recent years,<sup>5</sup> synthetic methods have been reported for asymmetric or diastereoselective cyanohydrin employing catalysts containing magnesium,<sup>18,19</sup>

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boron,<sup>20</sup> aluminum,<sup>20–22</sup> tin,<sup>23</sup> bismuth,<sup>24</sup> rhenium,<sup>25</sup> titanium,<sup>26–28</sup> and lanthanide complexes.<sup>29</sup> Of these catalysts, the titanium-derived Lewis acids have attracted the most interest.<sup>5</sup> Titanium complexes supporting a variety of different classes of ligands catalyze the asymmetric trimethylsilylcyanation of aldehydes. For example, ligands such as TADDOLs,<sup>30,31</sup> tartrate esters,<sup>32</sup> BINOLs,<sup>22,29,33</sup> peptides,<sup>21,26</sup> sulfoximine,<sup>34,35</sup> and tridentate<sup>36–39</sup> and tetradentate<sup>28,40–42</sup> Schiff base ligands have been used with titanium to induce moderate to high enantioselectivities in the cyanohydration of aldehydes. Although substantial effort has been directed toward optimization of the catalysts through the modification of the ligand structures, investigations into the nature of the titanium complexes are less common. Noteworthy contributions to the study of the intermediate titanium complexes were made by Oguni and co-workers using NMR spectrometry, desorption mass spectrometry, and molecular weight determination.<sup>36,37</sup> Employing tridentate amino alcohol-based Schiff base ligands, they identified the active species as the 1:1 ligand to titanium adduct L\*Ti(O-*i*-Pr)<sub>2</sub>. They also determined that the bis(Schiff base) compounds L\*<sub>2</sub>-Ti were inactive in the catalytic hydrocyanation of aldehydes.

In this report we have used Schiff base ligands derived from commercially available *cis*-1-amino-2-

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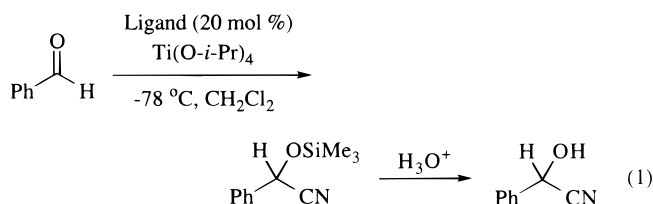
indanol.<sup>43</sup> Tridentate Schiff base ligands have been successfully used in several catalytic asymmetric reactions.<sup>44–47</sup> While this work was in progress, Jacobsen and co-workers used these and related ligands to make highly enantioselective Cr(III) catalysts for the asymmetric Diels–Alder reaction<sup>48</sup> and the asymmetric ring opening of meso aziridines.<sup>49</sup> The complexes formed on combination of titanium tetraisopropoxide and the tridentate Schiff base ligands catalyze the addition of trimethylsilyl cyanide to benzaldehyde with a wide range of enantioselectivities. We have performed a structure/enantioselectivity study that provides insight into the nature of the titanium Schiff base complexes. These results illustrate how ligand structure affects the nature of the titanium Schiff base complexes, which, in turn, influences the reactivity and enantioselectivity of the catalysts in this asymmetric C–C bond forming reaction.

## Results and Discussion

Oguni<sup>36,37</sup> and Jiang<sup>38,39</sup> have shown that the use of Schiff base ligands derived from chiral amino alcohols, in combination with titanium tetraisopropoxide, catalyze the cyanide addition to aldehydes with enantioselectivities ranging from 20 to 96%. They found that the size of substituents on the periphery of the ligand play a major role in determining the ee of the product. From these studies, no explanation emerged for this observation; however, our results suggest how ligand structure influences the catalyst composition, thus impacting enantioselectivities.

In the present investigation, we have focused on the use of *cis*-1-amino-2-indanol<sup>43</sup> to form the chiral backbone of the Schiff base ligands. It was hoped that the less conformationally mobile ligand would facilitate determination of structure/enantioselectivity relationships.

The ligands **1a–g** were readily prepared by the condensation of salicylaldehyde derivatives with the commercially available *cis*-1-amino-2-indanol in 70–99% yield (Figure 1, Table 1). For comparison Oguni's ligand **2c** was prepared in a similar fashion.<sup>36</sup>



The asymmetric trimethylsilylcyanations were performed employing conditions reported by Oguni and co-

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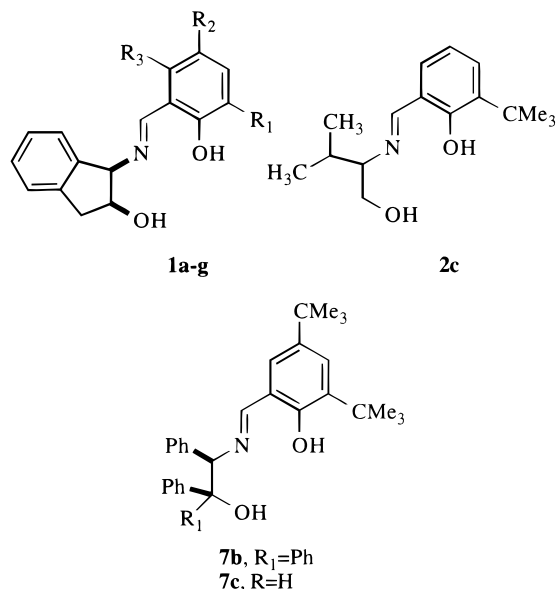
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**Figure 1.** Aminoalcohol-based ligands.**Table 1. Ligands 1a–g**

ligand	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>
<b>1a</b> ( <i>S,R</i> )	H	H	H
<b>1a</b> ( <i>R,S</i> )	H	H	H
<b>1b</b> ( <i>S,R</i> )	<i>tert</i> -Bu	<i>tert</i> -Bu	H
<b>1b</b> ( <i>R,S</i> )	<i>tert</i> -Bu	<i>tert</i> -Bu	H
<b>1c</b> ( <i>R,S</i> )	<i>tert</i> -Bu	H	H
<b>1d</b> ( <i>R,S</i> )	<i>tert</i> -Bu	CH <sub>3</sub>	H
<b>1e</b> ( <i>R,S</i> )	OCH <sub>3</sub>	H	H
<b>1f</b> ( <i>R,S</i> )	Br	Br	H
<b>1g</b> ( <i>R,S</i> )	H		C <sub>6</sub> H <sub>4</sub>

**Table 2. Conditions and Enantioselectivities of Ligands 1a–g in the Asymmetric Cyanohydrin of Benzaldehyde<sup>a</sup>**

entry	ligand	mol % ligand	yield (%)	enantioselective excess <sup>b</sup>	configuration
1	<b>1a</b> ( <i>S,R</i> )	20	48	34	( <i>S</i> )
2	<b>1a</b> ( <i>R,S</i> )	20	50	30	( <i>R</i> )
3	<b>1b</b> ( <i>S,R</i> )	20	67	70	( <i>S</i> )
4	<b>1b</b> ( <i>R,S</i> )	20	62	69	( <i>R</i> )
5	<b>1c</b> ( <i>R,S</i> )	20	64	85	( <i>R</i> )
6	<b>1d</b> ( <i>R,S</i> )	20	72	59	( <i>R</i> )
7	<b>1e</b> ( <i>R,S</i> )	20	73	38	( <i>R</i> )
8	<b>1f</b> ( <i>R,S</i> )	20	16	12	( <i>R</i> )
9	<b>1g</b> ( <i>R,S</i> )	20	62	37	( <i>R</i> )
10	<b>1a</b> ( <i>S,R</i> )	40	53	15	( <i>S</i> )
11	<b>1c</b> ( <i>S,R</i> )	40	23	19	( <i>S</i> )
12	<b>1f</b> ( <i>R,S</i> )	40	37	0	( <i>R</i> )
13	<b>1g</b> ( <i>R,S</i> )	40	37	12	( <i>R</i> )

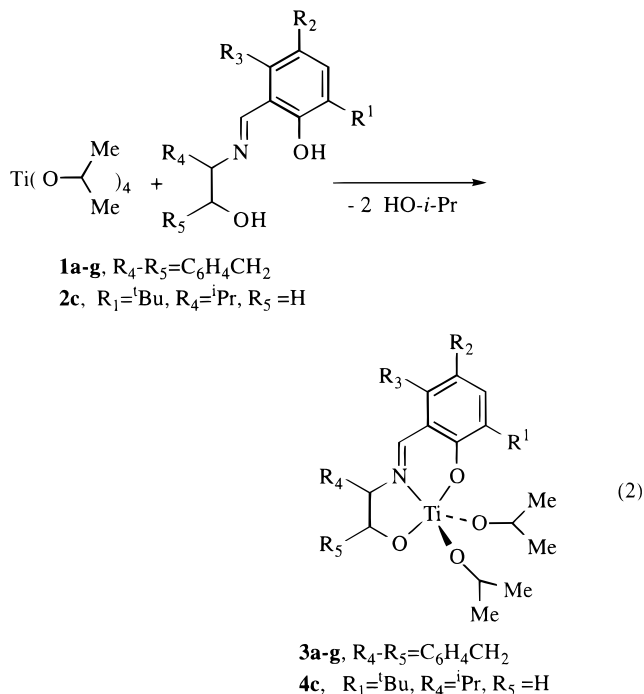
<sup>a</sup> All reactions were performed using 20 mol % titanium tetraisopropoxide at  $-78\text{ }^{\circ}\text{C}$  in dichloromethane for 36 h. Each ee is the result of a minimum of two runs. <sup>b</sup> Enantioselectivities were determined as described in the Experimental Section.

workers.<sup>36</sup> The reactions were run in dichloromethane at  $-78\text{ }^{\circ}\text{C}$  with 20 mol % ligand and were worked up after 36 h (eq 1, Table 2, entries 1–9). The cyanohydrin trimethylsilyl ethers were hydrolyzed on acidic workup, giving the cyanohydrins. The enantioselectivities were determined using chiral stationary phase GC of the acetylated cyanohydrins and were reproducible within  $\pm 2\%$  between runs. As will be seen below, the ee's determined in these experiments not only reflect the ability of the catalyst to discriminate between faces of the aldehyde but provide important information about the composition of the catalytic mixture. The results of

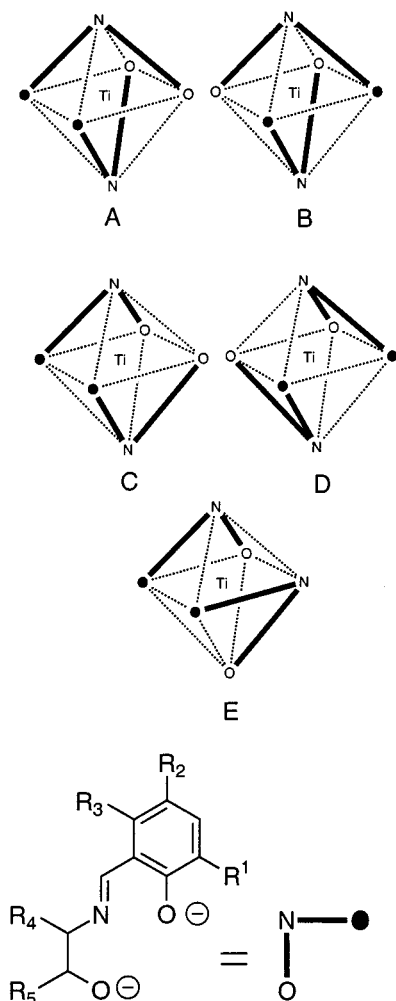
these experiments are shown in Table 2. Analysis of the ee's in Table 2 indicates that the enantioselectivity of catalysts derived from the ligands was highly dependent on the substituent at the 3-position (R<sub>1</sub>, Figure 1, Table 1). Ligands **1a**, **1e**, and **1g**, which contain small substituents in this position, gave poor ee's. However, incorporation of a bulky *tert*-butyl group at this site resulted in marked improvements in the enantioselectivities of these ligands (**1b–d**).

The enantioselectivity was also influenced by the substituent at the 5-position (R<sub>2</sub>). Both 5-*tert*-butyl (**1b**) and 5-methyl (**1d**) groups caused a drop in the enantioselectivity relative to **1c**, which has a hydrogen in this position. The enantioselectivity of **1c** is equal to that of Oguni's **2c** in the asymmetric hydrocyanation reaction.

In an effort to better understand the mechanism of the asymmetric hydrocyanation reaction and the factors that effect the enantioselectivity of this process, we chose to focus on the composition of the titanium–Schiff base complexes. It has been proposed that tridentate Schiff base ligands derived from amino alcohols react readily with titanium tetraisopropoxide to give the titanium Schiff base bis(isopropoxide) complexes, L<sup>\*</sup>Ti(O-*i*-Pr)<sub>2</sub> (eq 2, L<sup>\*</sup> = chiral Schiff base ligand **1a–g** and **2c**).<sup>36</sup> These complexes are believed to be involved in the catalysis for the asymmetric trimethylsilylcyanation of aldehydes. In important early work, Oguni and co-workers demonstrated that titanium tetraisopropoxide catalyzed the addition of trimethylsilylcyanide to benzaldehyde. However, moderate ligand acceleration<sup>50</sup> was observed upon addition of the chiral Schiff base ligands.<sup>36,37</sup>



Oguni and co-workers examined the reactivity of the chiral Schiff base ligand **2c** with titanium tetraisopropoxide employing a titanium:ligand ratio of either 1:1 or 1:2. When equal molar amounts of titanium tetrai-



**Figure 2.** The five possible coordination geometries of the tridentate ligands **1a–g** ( $L^*$ ) to titanium in the  $L^*_2Ti$  diastereomers. The bold lines indicate atoms that belong to the same ligand, and the dark circles represent the phenoxide oxygens.

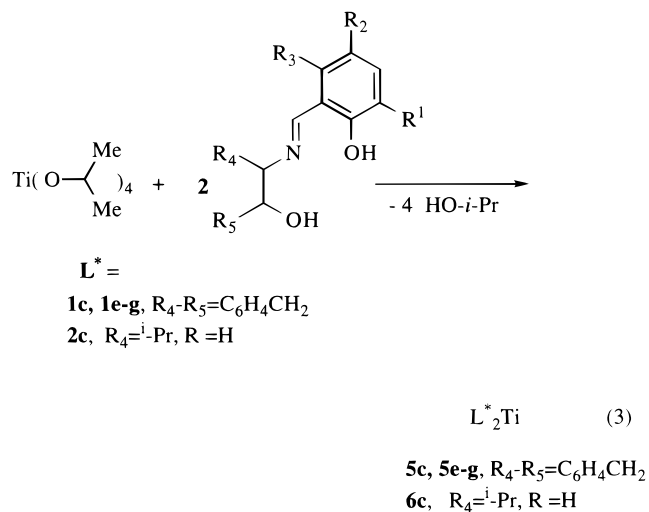
sopropoxide and the chiral ligand **2c** were combined, the complex  $L^*Ti(O-i-Pr)_2$  (**4c**) was cleanly formed (eq 2), as judged by NMR spectrometry, and further identified using field desorption mass spectrometry.

We have studied the reactions of the chiral 1-amino-2-indanol-derived ligands with titanium reagents, and in certain cases, our ligands behave similarly to **2c** of Oguni. We found that the aldimine C–H region of the  $^1H$  NMR spectrum was very useful for the identification of the ligand-containing products formed on reaction of **1a–g** with titanium tetraisopropoxide. The aldimine C–H resonances are well separated from each other and the remaining resonances of the ligand using a 500 MHz NMR spectrometer. Combination of the ligand **1c** and 1 equiv of titanium tetraisopropoxide resulted in the clean formation of the Schiff base complex  $L^*Ti(O-i-Pr)_2$  **3c** as determined by NMR spectrometry (eq 2). This observation paralleled that of Oguni using the ligand **2c**.<sup>36,37</sup>

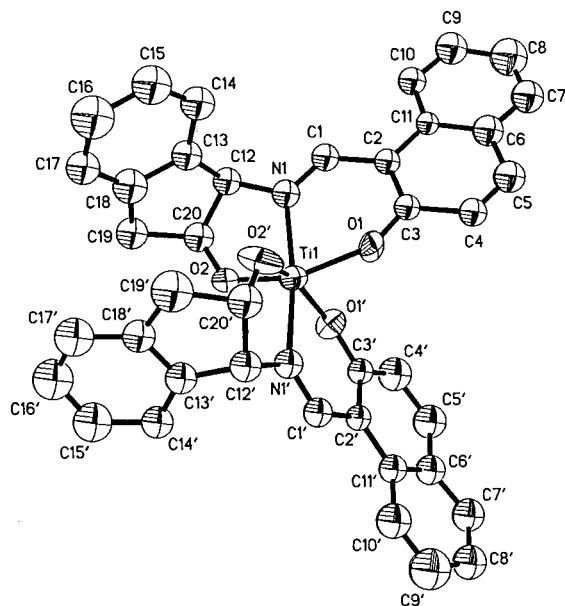
Ligands bearing smaller substituents at the 3-position of the salicylaldehyde moiety did not cleanly form  $L^*Ti(O-i-Pr)_2$  complexes but gave mixtures of products. On addition of titanium tetraisopropoxide to the naphthalene derivative **1g** in a 1:1 ratio in  $CH_2Cl_2$ , the initially insoluble ligand dissolved, giving a yellow solution. The

volatile components were removed, and the remaining material was dissolved in  $CDCl_3$ . The  $^1H$  NMR spectrum contained three singlets in the aldimine region at 9.64, 9.60, and 9.54 ppm in a ratio of 1:1:2. The absence of a signal at 8.80 ppm indicated that no unbound ligand **1g** remained. The presence of half of the initial titanium tetraisopropoxide (4.44 ppm) and the absence of free ligand suggested the formation of  $L^*_2Ti$  species (**5c**). Furthermore, integration of the diastereotopic isopropoxy methyldyne C–H resonances at 4.05 and 4.75 ppm indicated that these resonances belonged to the major product of the reaction,  $L^*Ti(O-i-Pr)_2$  (**3c**).

To identify and characterize the  $L^*_2Ti$  species, 2 equiv of the ligand **1g** was combined with titanium tetraisopropoxide as described above (eq 3). The  $^1H$  and  $^{13}C\{^1H\}$  NMR spectra indicated the presence of two different ligand environments in a 1:1 ratio within experimental error (with the imine C–H's at 9.64 and 9.60 ppm by  $^1H$  NMR, imine C=N's at 165.2 and 165.8 ppm by  $^{13}C\{^1H\}$  NMR). Oguni and co-workers also observed resonances for two inequivalent ligands (1:1 ratio) on combining 2 equiv of the ligand **2c** with 1 equiv of titanium tetraisopropoxide by NMR spectroscopy (with the imine C=N's at 165.2 and 165.8 ppm by  $^{13}C\{^1H\}$  NMR).



They logically concluded that an octahedral  $L^*_2Ti$  (**6c**) complex was formed with two inequivalent ligands (**E**, Figure 2, see discussion below). However, this structural assignment was inconsistent with our subsequent findings. The X-ray structure determination of **5g** (eq 3) was conducted at low temperature, and a drawing of the resulting structure is shown in Figure 3. Although the quality of the structure is marginal, it allows unambiguous assignment of the connectivity and the stereochemistry of the complex. The molecule contains two ligands bonded to titanium in a pseudo-octahedral coordination geometry with the imine nitrogens trans to each other. The meridional coordination imparts a  $C_2$ -symmetry axis on the compound (Figure 3). This symmetry operation interconverts the two ligands in the solid-state structure such that this compound would be expected to display a single set of resonances for the ligand by NMR spectrometry. The structure of **5g** is similar to a structure reported by Braun and co-workers



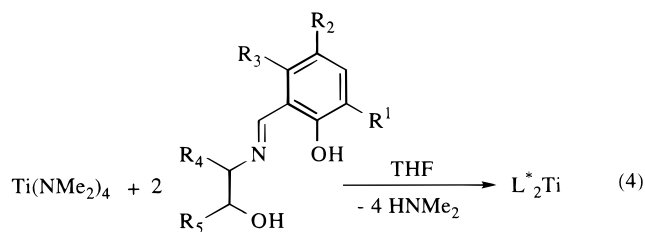
**Figure 3.** X-ray crystal structure of the  $C_2$ -symmetric  $L^*_2$ -Ti complex (**5g**) derived from ligand **1g**.

while this work was in progress.<sup>51</sup> Using the ligand **7b** (Figure 1), they were able to obtain an X-ray structure of one  $L^*_2$ Ti diastereomer (**8b**). This ligand is bonded to the titanium in a meridional fashion as in **5g**. Ligands of the type **7b** and their mono-Schiff base complexes  $L^*Ti(O-i-Pr)_2$  have been prepared and used in the asymmetric alkylation of aldehydes.<sup>52</sup> In the case of the ligand **1g**, the structure of **5g** alone does not explain the observed solution data for the  $L^*_2$ Ti species.

Coordination of two tridentate Schiff base ligands to titanium in an octahedral coordination geometry gives five possible geometrical isomers (Figure 2). In Figure 2, the dark circles represent the phenoxide oxygens and the open circles represent the alkoxide oxygens. The bold lines connecting the atoms in Figure 2 signify that the atoms are contained in the same ligand. In the structures **A** and **B** the ligand coordinates in a meridional fashion, while in structures **C–E** the ligands occupy a face of the octahedron. If the ligand were achiral, then coordination geometries **A** and **B** would be enantiomers, as would **C** and **D**. However, since the ligand bears stereogenic centers and is present in only one enantiomeric form, these structures are diastereomers. Structures **A–D** have  $C_2$ -symmetry axes, rendering the two ligands on each titanium center equivalent. Structure **E** is not  $C_2$ -symmetric, and the ligands are inequivalent. An NMR spectrum of this isomer would be expected to exhibit two sets of resonances for the inequivalent ligands in a 1:1 ratio.

One possible explanation for the observed solution and solid-state data is that the  $L^*_2$ Ti species consisted of two  $C_2$ -symmetric diastereomers in a 1:1 ratio. Although it seems unlikely that two diastereomers of this type would have equal energies, this hypothesis can be supported by preparing the diastereomers in a ratio other than 1:1. In an attempt to prepare the  $L^*_2$ Ti species under nonequilibrating conditions, the ligand **1g** was added to the titanium tetraamide  $Ti(NMe_2)_4$ , giving

a yellow solution (eq 4). The amides of titanium are very



basic and react rapidly with acidic hydrogens, expelling *N,N*-dimethylamine.<sup>53</sup> The volatile materials were removed, and a  $^1H$  NMR of the remaining yellow solid was taken in  $CDCl_3$ . Two aldimine resonances were observed at 9.64 and 9.60 ppm, which had chemical shifts identical to those generated on addition of 2 equiv of the ligand to titanium tetraisopropoxide (eq 3). The ratio of the integration of these resonances was 3:1, indicating that they indeed belonged to two diastereomeric  $C_2$ -symmetric  $L^*_2$ Ti complexes.

The X-ray study and the NMR data from reaction of **1g** with titanium tetraisopropoxide (1:1) strongly support the formation of three species in solution, two of which are the diastereomeric  $L^*_2$ Ti complexes and the third corresponding to  $L^*Ti(O-i-Pr)_2$ .

With this knowledge, we examined the interaction of 2-*tert*-butyl salicylaldehyde-based ligands **1c** and **2c** with  $Ti(NMe_2)_4$ . These ligands gave the highest enantioselectivities in the asymmetric trimethylsilylcyanoation reaction with titanium tetraisopropoxide (eq 1).<sup>36,37</sup> Unlike **1g**, both 2-*tert*-butyl-substituted ligands gave exclusively  $L^*Ti(O-i-Pr)_2$  upon reaction with titanium tetraisopropoxide. Oguni and co-workers reported that the product formed on reaction of 2 equiv of the ligand **2c** with titanium tetraisopropoxide was a single diastereomer (**E**, Figure 2). However, reaction of 2 equiv of the ligand **2c** with  $Ti(NMe_2)_4$  in THF followed by removal of the volatile materials gave a 1.9:1 ratio of the two diastereomers by  $^1H$  NMR spectrometry. The NMR spectrum of the two diastereomers formed from **2c** and  $Ti(NMe_2)_4$  indicated that imine C–H's were at 8.56 and 8.42 ppm by  $^1H$  NMR and the C=N's at 164.7 and 165.1 ppm by  $^{13}C\{^1H\}$  NMR spectrometry. These were very similar to the  $^{13}C\{^1H\}$  NMR spectrum reported by Oguni with the C=N's at 165.2 and 165.8 ppm by  $^{13}C\{^1H\}$  NMR. The remaining resonances also correlated (Experimental Section).<sup>36</sup> Employing the titanium tetraamide with indanol-derived ligand **1c** gave a 1.7:1 ratio of the two  $C_2$ -symmetric  $L^*_2$ Ti diastereomers. Braun also observed diastereomers of the  $L^*_2$ Ti complexes derived from ligand **7b** which were not generated in a 1:1 ratio.<sup>51</sup>

Subsequent examination of the reaction of methoxy ligand **1e** and the 3,5-dibromo ligand **1f** with titanium tetraisopropoxide gave results similar to those observed for **1g**. Reaction of **1e** with an equal molar amount of titanium tetraisopropoxide gave products with three aldimine resonances in the  $^1H$  NMR spectrum at 8.75, 8.70, and 8.64 ppm in a ratio of 1.1:1.7:1.0. These were determined to be the two  $C_2$ -symmetric  $L^*_2$ Ti diastereomers **5e** and  $L^*Ti(O-i-Pr)_2$  (**3e**), respectively, indicat-

(51) Fleischer, R.; Wunderlich, H.; Braun, M. *Eur. J. Org. Chem.* **1998**, 1063–1070.

(52) Fleischer, R.; Braun, M. *Synlett* **1998**, 1441–1443.

(53) Lappert, M. F.; Power, P. P.; Sanger, A. R.; Srivastava, R. C. *Metal and Metalloid Amides: Synthesis, Structure and Physical and Chemical Properties*; Halsted Press: New York, 1979.

ing that the  $L^*_2Ti$  diastereomers **5e** were formed preferentially to  $L^*Ti(O-i-Pr)_2$  **3e**. Similarly, reaction of the 3,5-dibromo ligand **1f** with 1 equiv of titanium tetraisopropoxide resulted in formation of a mixture of three Schiff base-containing products with aldimine resonances in the  $^1H$  NMR spectrum at 8.64, 8.53, and 8.47 ppm (in a ratio of 1.4:2.1:1). The two  $L^*_2Ti$  diastereomers **5f** exhibited aldimine resonances at 8.64 and 8.47 ppm. The results of these experiments indicate that more than half of the ligand is bound to the diastereomeric  $L^*_2Ti$  complexes (**5f**).

When tridentate Schiff base ligands **1e–g** are used with titanium tetraisopropoxide, the predominant products are the catalytically inactive  $L^*_2Ti$  diastereomers, which are formed at the expense of the desired  $L^*Ti(O-i-Pr)_2$  catalysts. Furthermore, the greater the percentage of diastereomeric  $L^*_2Ti$  complexes, the higher the ratio of  $Ti(O-i-Pr)_4$  to  $L^*Ti(O-i-Pr)_2$ . It has been shown that  $Ti(O-i-Pr)_4$  catalyzes the hydrocyanation of aldehydes.<sup>36</sup> It will compete with the asymmetric catalyst  $L^*Ti(O-i-Pr)_2$  for substrate, resulting in a decrease in the ee of the product. This point is emphasized in experiments involving 2 equiv of ligand per titanium (Table 2, entries 10–13). When the reaction was conducted using 20 mol % titanium tetraisopropoxide and 40 mol % ligand, the ee of the cyanohydrin dropped dramatically relative to when a 1:1 ratio of titanium tetraisopropoxide to ligand was used. The drop in ee on going from 1 equiv to 2 equiv of ligand per titanium was largest for ligand **1c**, which fell from 85% ee with 1 equiv of ligand to 19% ee with 2 equiv. Under the reaction conditions employing 2 equiv of **1c** it is likely that the ligand reacts with titanium tetraisopropoxide to establish an equilibrium between ligand **1c**, titanium tetraisopropoxide,  $L^*Ti(O-i-Pr)_2$  (**3c**), and  $L^*_2Ti$  (**5c**). In this mixture, the cyanohydrin was generated in 19% ee presumably via addition promoted by a combination of titanium tetraisopropoxide and  $L^*Ti(O-i-Pr)_2$  (**3c**). Since the ee is far below the 85% observed with  $L^*Ti(O-i-Pr)_2$  (**3c**), we hypothesize that the concentration of  $L^*Ti(O-i-Pr)_2$  is low due to formation of  $L^*_2Ti$ . This drop in ee upon using 40 mol % ligand observed with **1a**, **1f**, and **1g** is also consistent with increased formation of the catalytically inactive  $L^*_2Ti$  diastereomers. These results stand in sharp contrast to those reported by Jiang.<sup>38,39</sup> Using 2 equiv of the ligand **7c** with respect to titanium tetraisopropoxide, they report that the ee of the cyanohydrin was *higher* than when 1 equiv of ligand was used.<sup>38,39</sup> The observations reported by these authors are surprising given our results and those of Oguni.<sup>36</sup>

**Conclusions.** Studies with ligands **1c** and **2c**<sup>36</sup> indicate that use of 1 equiv of salicylaldehyde-based ligands with *tert*-butyl groups in the 3-position form exclusively the mono-Schiff base complexes,  $L^*Ti(O-i-Pr)_2$ , on reaction with 1 equiv of titanium tetraisopropoxide (eq 2). No  $L^*_2Ti$  complexes were detected by NMR spectrometry (500 MHz). In contrast, under the same conditions, ligands bearing smaller groups at the 3-position such as hydrogen, bromine, or methoxy (Figure 1) resulted in formation of significant amounts of the diastereomeric  $L^*_2Ti$  species along with  $L^*Ti(O-i-Pr)_2$ . Oguni has shown that  $L^*_2Ti$  complexes are catalytically inactive in the asymmetric trimethylsilylcyanation of aldehydes, which is supported by the

results of this study.<sup>36</sup> We found that when our ligands had small substituents in the 3-position of the salicylaldehyde moiety, the amount of ligand bound in the  $L^*_2Ti$  diastereomers ranged from 50% (for **1f**) to 73% (for **1e**). The ligands that form significant quantities of the diastereomeric  $L^*_2Ti$  complexes gave poor enantioselectivities in the asymmetric trimethylsilylcyanation of aldehydes (Table 2). An explanation for these observations is that the amount of catalytically active species present is reduced due to the formation of the diastereomeric  $L^*_2Ti$  complexes. Additionally, the greater the percentage of the  $L^*_2Ti$  complexes formed, the higher the concentration of unreacted titanium tetraisopropoxide, which catalyzes the addition reaction but gives racemic product.<sup>36</sup> Although the ligand acceleration by  $L^*Ti(O-i-Pr)_2$  is significant,<sup>36</sup> it is not sufficient to prevent erosion of the enantioselectivity through the titanium tetraisopropoxide-catalyzed addition.<sup>50</sup> Consistent with this hypothesis, we have found that employing 2 equiv of the chiral ligand with 1 equiv of titanium tetraisopropoxide resulted in a large drop in the enantioselectivities (Table 2, entries 10–13).

The role of achiral groups in asymmetric catalysts is often envisioned to be to direct the trajectory of the incoming substrate or to position the substrate for optimal enantiofacial differentiation in the selectivity-determining step. However, this study emphasizes the importance of achiral substituents in controlling the formation of the catalyst. The significance of this is apparent when it is considered that many asymmetric catalysts are formed *in situ* and the composition of the catalyst is often ill-defined or completely unknown. In the tridentate Schiff base–titanium tetraisopropoxide system investigated here, the position of achiral substituents on the ligand controls both the catalyst formation and the enantioselectivity.

## Experimental Section

**General Comments.** Details of the general experimental and X-ray structural determination are reported elsewhere.<sup>54</sup> All manipulations involving titanium complexes were carried out under an inert atmosphere in a Vacuum Atmospheres drybox with attached MO-40 Dritrain or by using standard Schlenk or vacuum line techniques.

High-resolution electron impact MS were obtained at 70 eV with a VG 7070 spectrometer at the University of California, Riverside Mass Spectrometry Facility. Elemental analyses were done by NuMega Resonance Labs, Inc., in San Diego, CA, or at the University of Pennsylvania.

Unless otherwise specified, all reagents were purchased from Aldrich Chemical Co. and used without further purification. Titanium tetraisopropoxide and benzaldehyde were distilled under vacuum and stored in glass reaction vessels fitted with Teflon stopcocks.

Enantiometric excesses were determined using a Hewlett-Packard 6890 gas chromatograph with a 30 m Supelco  $\beta$ -DEX column. The silyloxy cyanides were hydrolyzed to the alcohol and derivatized with acetic anhydride. The retention times of the enantiomers were 10.0 min (*R*) and 10.7 min (*S*).

**General Procedure for the Synthesis of the Ligands 1a–g: Synthesis of (1*S*,2*R*)-1-(*N*-Salicylideneamino)-2-indanol (**1a**).** A mixture of dry methanol (25 mL), (1*S*,2*R*)-(–)-*cis*-1-amino-2-indanol (0.50 g, 3.35 mmol), 2-hydroxybenzaldehyde (0.78 g, 3.35 mmol), and anhydrous  $Na_2SO_4$  (2 g)

(54) Pritchett, S.; Gantzel, P.; Walsh, P. J. *Organometallics* **1999**, *18*, 823–831.

was refluxed for 4 h. The solution was filtered, and the solvent was evaporated under reduced pressure, giving **1a** as a yellow solid (0.72 g, 70%): mp 114–116 °C;  $[\alpha]_D^{25} = -46.53^\circ$  ( $c = 0.5$ ,  $\text{CH}_2\text{Cl}_2$ ); IR (KBr) 3402, 3139, 1638, 743  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  8.56 (s, 1H), 7.38–7.14 (m, 6H), 7.00–6.84 (m, 2H), 4.79 (d, 1H,  $J = 6$  Hz), 4.68 (q, 1H,  $J = 6$  Hz), 3.24 (dd, 1H,  $J = 6$  Hz,  $J = 16$  Hz), 3.08 (dd, 1H,  $J = 6$  Hz,  $J = 18$  Hz) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  166.9, 161.1, 140.7, 140.7, 132.9, 131.9, 128.6, 127.1, 125.5, 124.8, 118.8, 118.7, 117.2, 75.6, 75.3, 39.6 ppm; EIMS  $m/z$  253 [ $\text{M}^+$ ] (100), 235-(23), 208(8), 133(39), 121(54), 104(38), 77(33); HREIMS  $m/z$  calcd for  $\text{C}_{16}\text{H}_{15}\text{NO}_2$  253.1103, found 253.1100. Anal. Calcd for  $\text{C}_{16}\text{H}_{15}\text{NO}_2$ : C, 75.88; H, 5.92. Found: C, 75.66; H, 5.73.

**(1*S*,2*R*)-1-[*N*-(3',5'-Di-*tert*-butylsalicylidene)amino]-2-indanol (1b)**: yellow solid (1.22 g, 99%); mp 65–68 °C;  $[\alpha]_D^{25} = -25.93^\circ$  ( $c = 0.5$ ,  $\text{CH}_2\text{Cl}_2$ ); IR (KBr) 3419, 2957, 1626, 755  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  8.57 (s, 1H), 7.42 (d, 1H,  $J = 2.6$  Hz), 7.30–7.14 (m, 5H), 4.75 (d, 1H,  $J = 6$  Hz), 4.64 (q, 2H,  $J = 4$  Hz,  $J = 8$  Hz), 3.37 (s, 1H), 3.21 (dd, 1H,  $J = 6$  Hz,  $J = 18$  Hz), 3.08 (dd, 1H,  $J = 6$  Hz,  $J = 16$  Hz), 1.43 (s, 9H), 1.33 (s, 9H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  168.0, 158.2, 141.0, 140.9, 140.4, 128.5, 127.6, 127.0, 126.5, 125.4, 124.9, 117.9, 75.4, 75.1, 39.4, 34.9, 34.0, 31.4, 29.3 ppm; EIMS  $m/z$  365 [ $\text{M}^+$ ] (100), 350(31), 218(55), 190(23); HREIMS  $m/z$  calcd for  $\text{C}_{24}\text{H}_{31}\text{NO}_2$  365.2355, found 365.2339. Anal. Calcd for  $\text{C}_{24}\text{H}_{31}\text{NO}_2$ : C, 78.90; H, 8.49. Found: C, 78.50; H, 8.39.

**(1*R*,2*S*)-1-[*N*-(3'-*tert*-Butylsalicylidene)amino]-2-indanol (1c)**: yellow solid (1.03 g, 99%); mp 75–78 °C;  $[\alpha]_D^{25} = +80.20^\circ$  ( $c = 0.5$ ,  $\text{CH}_2\text{Cl}_2$ ); IR (KBr) 3579, 2957, 1620, 748  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  8.59 (s, 1H), 7.38–7.16 (m, 6H), 6.85 (t, 1H,  $J = 7.6$  Hz), 4.77 (d, 1H,  $J = 5.2$  Hz), 4.67 (q, 2H,  $J = 5.2$  Hz,  $J = 10.8$  Hz), 3.24 (dd, 1H,  $J = 5.6$  Hz,  $J = 16$  Hz), 3.10 (dd, 1H,  $J = 5$  Hz,  $J = 16$  Hz), 1.41 (s, 9H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  167.9, 160.5, 141.0, 137.7, 130.3, 130.1, 128.6, 127.1, 125.5, 125.0, 118.7, 118.2, 75.6, 75.2, 39.6, 34.8, 29.3 ppm; EIMS  $m/z$  309 [ $\text{M}^+$ ] (100), 294-(22), 266(30), 176(43), 134(69), 105(30), 77(30); HREIMS  $m/z$  calcd for  $\text{C}_{20}\text{H}_{23}\text{NO}_2$  309.1729, found 309.1725. Anal. Calcd for  $\text{C}_{20}\text{H}_{23}\text{NO}_2$ : C, 77.66; H, 7.44. Found: C, 77.27; H, 7.51.

**(1*R*,2*S*)-1-[*N*-(3'-*tert*-Butyl-5'-methylsalicylidene)amino]-2-indanol (1d)**: yellow solid (0.92 g, 85%); mp 41–44 °C;  $[\alpha]_D^{25} = +48.50^\circ$  ( $c = 0.5$ ,  $\text{CH}_2\text{Cl}_2$ ); IR (KBr) 3397, 2952, 1626, 751  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  8.51 (s, 1H), 7.26–7.18 (m, 4H), 7.16 (s, 1H), 6.96 (s, 1H), 4.74 (d, 1H,  $J = 5.2$  Hz), 4.65 (q, 1H,  $J = 4.8$  Hz,  $J = 10.0$  Hz), 3.21 (dd, 1H,  $J = 6$  Hz and  $J = 16.4$  Hz), 3.08 (dd, 1H,  $J = 4.8$  Hz,  $J_2 = 16$  Hz), 2.29 (s, 3H), 1.39 (s, 9H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  167.8, 158.2, 141.0, 140.9, 137.4, 131.2, 130.1, 128.5, 127.0, 126.9, 124.5, 124.9, 118.4, 75.6, 75.2, 39.6, 34.6, 29.3, 20.5 ppm; EIMS  $m/z$  323 [ $\text{M}^+$ ] (100), 308(16), 280(15), 190(20), 176(52), 148(40), 133(27), 91(8); HREIMS  $m/z$  calcd for  $\text{C}_{21}\text{H}_{25}\text{NO}_2$  323.1885, found 323.1876. Anal. Calcd for  $\text{C}_{21}\text{H}_{25}\text{NO}_2$ : C, 78.01; H, 7.73. Found: C, 77.88; H, 8.10.

**(1*R*,2*S*)-1-[*N*-(3'-Methoxysalicylidene)amino]-2-indanol (1e)**: yellow solid (0.69 g, 73%); mp 107–110 °C;  $[\alpha]_D^{25} = +86.00^\circ$  ( $c = 0.5$ ,  $\text{CH}_2\text{Cl}_2$ ); IR (KBr) 3258, 2951, 1640, 1233, 738  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  8.54 (s, 1H), 7.28–7.18 (m, 4H), 6.95–6.82 (m, 3H), 4.80 (d, 1H,  $J = 5.4$  Hz), 4.68 (q, 1H,  $J = 5.6$  Hz,  $J_2 = 11$  Hz), 3.87 (s, 3H), 3.24 (dd, 1H,  $J = 5.8$  Hz,  $J = 15.8$  Hz), 3.09 (dd, 1H,  $J = 5.2$  Hz,  $J = 15.8$  Hz) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (50 MHz,  $\text{CDCl}_3$ )  $\delta$  166.6, 152.2, 148.6, 140.7, 140.4, 128.6, 127.0, 125.5, 124.8, 123.3, 118.4, 118.1, 114.6, 75.12, 74.8, 56.1, 39.5 ppm; EIMS  $m/z$  283 [ $\text{M}^+$ ] (100), 150(42), 133(34), 103(30), 77(30), 65(18), 51(12); HREIMS  $m/z$  calcd for  $\text{C}_{17}\text{H}_{17}\text{NO}_3$  283.1208, found 283.1214. Anal. Calcd for  $\text{C}_{17}\text{H}_{17}\text{NO}_3$ : C, 72.08; H, 6.00. Found: C, 72.16; H, 6.17.

**(*R*,*S*)-1-[*N*-(3,5-Dibromosalicylidene)amino]-2-indanol (1f)**: yellow solid (0.77 g, 86%); mp 205–208 °C;  $[\alpha]_D^{25} = +196.9^\circ$  ( $c = 0.5$ ,  $\text{CH}_3\text{OH}$ ); IR (KBr) 3325, 1639, 1498, 1212, 750, 691  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  8.57 (s, 1H), 8.77

(d, 1H,  $J = 2.4$  Hz), 7.35 (d, 1H,  $J = 2.2$  Hz), 7.26 (d, 4H,  $J = 11.2$  Hz), 4.98 (d, 1H,  $J = 6.0$  Hz), 4.64 (d, 1H,  $J = 4.6$  Hz), 3.17 (dd, 1H,  $J = 5.8$  Hz,  $J = 16$  Hz), 2.98 (dd, 1H,  $J = 4.8$  Hz,  $J = 15.8$  Hz) ppm;  $^{13}\text{C}\{^1\text{H}\}$  (50 MHz,  $\text{CDCl}_3$ )  $\delta$  163.1, 162.9, 139.7, 138.2, 136.7, 132.4, 127.1, 125.3, 123.7, 123.2, 116.3, 113.9, 103.2, 71.7, 68.9 ppm; EIMS  $m/z$  411 [ $\text{M}^+$ ] (4), 277(6), 133(43), 115(94), 103(74), 77(100). Anal. Calcd for  $\text{C}_{16}\text{H}_{13}\text{NO}_2\text{Br}_2$ : C, 46.71; H, 3.16. Found: C, 46.78; H, 3.10.

**(1*R*,2*S*)-1-(*N*-Naphthalidenamino)-2-indanol (1g)**: brown solid (0.75 g, 92%); mp 200–203 °C;  $[\alpha]_D^{25} = +139.9^\circ$  ( $c = 0.5$ ,  $\text{CH}_3\text{OH}$ ); IR (KBr) 3246, 1628, 1354, 743  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ )  $\delta$  8.90 (s, 1H), 7.85 (d, 1H,  $J = 8.4$  Hz), 7.64–7.15 (m, 8H), 6.77 (d, 1H,  $J = 9.6$  Hz), 4.99 (d, 1H,  $J = 12.64$  Hz), 4.71 (d, 1H,  $J = 4.39$  Hz), 3.21 (dd, 1H,  $J = 5.2$  Hz,  $J = 16.2$  Hz), 3.06 (dd, 1H,  $J = 3.4$  Hz,  $J = 16$  Hz) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR (125 MHz,  $\text{DMSO}-d_6$ )  $\delta$  178.8, 158.0, 140.8, 140.7, 137.4, 134.6, 128.9, 128.3, 127.9, 126.8, 126.2, 125.3, 125.0, 124.3, 122.0, 118.2, 105.7, 72.4, 67.5, 39.5 ppm; EIMS  $m/z$  303 [ $\text{M}^+$ ] (100), 258(8), 170(46), 115(28), 77(18); HREIMS  $m/z$  calcd for  $\text{C}_{20}\text{H}_{17}\text{NO}_2$  303.1259, found 303.1245. Anal. Calcd for  $\text{C}_{20}\text{H}_{17}\text{NO}_2$ : C, 79.20; H, 5.61. Found: C, 79.05; H, 5.55.

**Reaction of Titanium Tetraisopropoxide with 1 equiv of Ligand 1g. General Procedure.** Under a nitrogen atmosphere, the insoluble yellow naphthalene-derived ligand **1g** (74.5 mg,  $2.46 \times 10^{-4}$  mol) was stirred with 3 mL of  $\text{CH}_2\text{Cl}_2$  at 23 °C. One equiv of  $\text{Ti}(\text{O}-i\text{-Pr})_4$  (70.0 mg,  $2.46 \times 10^{-4}$  mol) was added dissolved in 0.5 mL of  $\text{CH}_2\text{Cl}_2$ . Within seconds of combining these reagents, the ligand dissolved, giving a clear yellow solution. After stirring for 15 min, the volatile materials were removed under reduced pressure, the remaining yellow solid was dissolved in  $\text{CDCl}_3$ , and an NMR spectrum was acquired. The NMR spectrum showed the presence of three aldimine C–H resonances at 9.58, 9.54, and 9.51 ppm in a ratio of 1:1:2. These resonances correspond to  $\text{L}^*_2\text{Ti}$  diastereomer 1,  $\text{L}^*_2\text{Ti}$  diastereomer 2, and  $\text{L}^*\text{Ti}(\text{O}-i\text{-Pr})_2$ , respectively, and indicate that 50% of the ligand was found in the inactive  $\text{L}^*_2\text{Ti}$  complexes. Additionally, 0.5 equiv of unreacted  $\text{Ti}(\text{O}-i\text{-Pr})_4$  was observed (determined by the position of the methyne hydrogen at 4.44 ppm).

**Reaction of Titanium Tetraisopropoxide with 1 equiv of Ligand 1c. Synthesis of 3c.** By subjecting the ligand **1c** (29.5 mg,  $9.55 \times 10^{-5}$  mol) and  $\text{Ti}(\text{O}-i\text{-Pr})_4$  (27.1 mg,  $9.55 \times 10^{-5}$  mol) to the procedure above, the following data were obtained:  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.81 (s, 1H), 7.46 (dd,  $J = 6.0$ ,  $J = 1.6$  Hz, 1H), 7.31 (m, 3H), 7.20 (m, 2H), 6.85 (t,  $J = 7.7$  Hz, 1H), 5.59 (td,  $J = 5.5$ ,  $J = 2.0$  Hz), 5.31 (d,  $J = 5.0$  Hz, 1H), 4.84 (m, 1H), 4.53 (m, 1H), 3.17 (dd,  $J = 16.8$ ,  $J = 5.3$  Hz, 1H), 3.10 (d,  $J = 16.6$  Hz, 1H), 1.48 (s, 9H), 2.22 (m, 6H), 0.87 (d,  $J = 5.4$  Hz, 3H), 0.76 (d,  $J = 4.9$  Hz, 3H);  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ )  $\delta$  165.3, 163.7, 142.5, 140.8, 139.4, 132.4, 131.6, 128.7, 126.7, 126.0, 125.0, 121.5, 117.8, 86.4, 82.2, 78.8, 76.4, 42.4, 35.3, 29.7, 26.7, 26.3, 25.7, 25.4 ppm. We were unable to crystallize this compound.

**Reaction of Titanium Tetraisopropoxide with 1 equiv of Ligand 2c. Synthesis of 4c.** Employing the ligand **2c** (29.8 mg,  $1.10 \times 10^{-4}$  mol) and  $\text{Ti}(\text{O}-i\text{-Pr})_4$  (31.2 mg,  $1.10 \times 10^{-4}$  mol) and the procedure above, the following data were obtained for  $\text{L}^*\text{Ti}(\text{O}-i\text{-Pr})_2$ , **4c**:  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  8.31 (s, 1H), 7.46 (dd,  $J = 5.9$ ,  $J = 1.7$  Hz, 1H), 7.22 (dd,  $J = 7.7$ ,  $J = 1.7$  Hz, 1H), 6.80 (t,  $J = 7.7$  Hz, 1H), 4.8 (m, 2H), 4.67 (dd,  $J = 10.3$ ,  $J = 4.6$  Hz, 1H), 4.38 (d,  $J = 10.4$  Hz, 1H), 3.39 (m, 1H), 2.45 (m, 1H), 1.48 (s, 9H), 1.25 (m, 12H), 1.04 (d,  $J = 6.7$  Hz, 3H), 0.88 (d,  $J = 6.8$  Hz, 3H) ppm;  $^{13}\text{C}\{^1\text{H}\}$  NMR ( $\text{CDCl}_3$ )  $\delta$  164.4, 163.3, 139.2, 132.1, 131.5, 121.3, 117.8, 82.8, 78.7, 77.6, 77.4, 74.1, 35.3, 30.5, 29.7, 26.7, 26.4, 26.2, 26.0, 20.5, 20.0 ppm.

**Reaction of Titanium Tetraisopropoxide with 1 equiv of Ligand 1e.** Employing the ligand **1e** (22.1 mg,  $7.46 \times 10^{-5}$  mol) and  $\text{Ti}(\text{O}-i\text{-Pr})_4$  (21.0 mg,  $7.46 \times 10^{-5}$  mol) and the procedure above, the following data were obtained. The  $^1\text{H}$  NMR of the aldimine region contained three resonances at  $\delta$

8.75, 8.70, and 8.64 ppm in a ratio of 1.1:1.7:1.0. These resonances correspond to L\*<sub>2</sub>Ti diastereomer 1, L\*<sub>2</sub>Ti diastereomer 2, and L\*Ti(O-*i*-Pr)<sub>2</sub>, respectively. These results indicate that 74% of the ligand is found in the inactive L\*<sub>2</sub>Ti complex.

**Reaction of Titanium Tetraisopropoxide with 1 equiv of Ligand 1f.** Employing the ligand **1f** (47.4 mg, 1.15 × 10<sup>-4</sup> mol) and Ti(O-*i*-Pr)<sub>4</sub> (32.7 mg, 1.15 × 10<sup>-4</sup> mol) and the procedure above, the following data were obtained. The <sup>1</sup>H NMR of the aldimine region contained three resonances at δ 8.64, 8.53, and 8.47 ppm in a ratio of 1.4:2.1:1.0. These resonances correspond to L\*<sub>2</sub>Ti diastereomer 1, L\*Ti(O-*i*-Pr)<sub>2</sub>, and L\*<sub>2</sub>Ti diastereomer 2, respectively, and indicate that 53% of the ligand is found in the inactive L\*<sub>2</sub>Ti complex.

**Reaction of Titanium Tetraisopropoxide with 2 equiv of Ligand 1g. Synthesis of L\*<sub>2</sub>Ti Diastereomers 5g.** Under a nitrogen atmosphere 2 equiv of the insoluble yellow naphthalene-derived ligand **1g** (61.7 mg, 1.02 × 10<sup>-4</sup> mol) was stirred with 2 mL of CH<sub>2</sub>Cl<sub>2</sub> at 23 °C. One equiv of Ti(O-*i*-Pr)<sub>4</sub> (30.0 mg, 6.10 × 10<sup>-5</sup> mol) was added as a solution in 1 mL of CH<sub>2</sub>Cl<sub>2</sub>. Within 5 min of combining these two solutions, the ligand had dissolved, giving a clear, pale yellow solution. After stirring for 2 h, the volatile materials were removed under reduced pressure, the remaining solid was dissolved in CDCl<sub>3</sub>, and an NMR spectrum was acquired. The NMR spectrum showed the presence of two C<sub>2</sub>-symmetric diastereomers in a 1:1 ratio. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) diastereomer 1: δ 9.64 (s, 1H), 8.25 (d, *J* = 8.4 Hz, 1H), 7.74 (m, 2H), 7.58 (m, 1H), 7.30 (m, 5H), 6.72 (d, *J* = 9.2 Hz, 1H), 5.58 (m, 1H), 5.38 (t, *J* = 5.0 Hz, 1H), 2.77 (dd, *J* = 17.0, *J* = 5.5 Hz, 1H), 1.92 (d, *J* = 16.9 Hz, 1H) ppm. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) diastereomer 2: δ 9.60 (s, 1H), 8.19 (d, *J* = 8.4 Hz, 1H), 7.74 (m, 1H), 7.68 (d, *J* = 9.15 Hz, 1H), 7.58 (m, 1H), 7.30 (m, 4H), 7.14 (d, *J* = 7.4 Hz, 1H), 5.98 (d, *J* = 9.3 Hz, 1H), 5.78 (d, *J* = 4.8 Hz, 1H), 5.58 (m, 1H), 3.07 (dd, *J* = 16.7, *J* = 5.4 Hz, 1H), 2.68 (d, *J* = 16.7 Hz, 1H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>) diastereomer 1: δ 166.95, 158.9, 142.3, 142.0, 136.4, 134.0, 129.3, 128.1, 128.0, 127.7, 126.8, 126.0, 124.6, 123.2, 122.0, 119.5, 111.1, 86.8, 85.9, 40.8 ppm. <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>) diastereomer 2: δ 166.93, 158.3, 142.9, 141.7, 136.0, 133.7, 129.2, 128.5, 128.0, 127.8, 126.7, 125.9, 124.7, 123.4, 121.7, 120.0, 112.6, 85.1, 84.9, 41.5 ppm. Anal. Calcd for C<sub>40</sub>H<sub>30</sub>N<sub>2</sub>O<sub>4</sub>Ti: C, 74.18; H, 4.66. Found: C, 73.88; H, 4.78.

**Reaction of Titanium Tetra(*N,N*-dimethylamide) with 2 equiv of Ligand 1g. General Procedure.** In a nitrogen-filled drybox 2 equiv of the naphthalene-derived ligand **1g** (39.8 mg, 1.32 × 10<sup>-4</sup> mol) was stirred with 2 mL of THF at 23 °C. One equiv of Ti(NMe<sub>2</sub>)<sub>4</sub> (14.7 mg, 6.58 × 10<sup>-5</sup> mol) was added as a solution in 1 mL of THF. On combining these two reagents, a yellow-orange solution was formed. After stirring for 15 min, the volatile materials were removed under reduced pressure. The remaining solid was dissolved in CDCl<sub>3</sub>, and a <sup>1</sup>H NMR spectrum acquired. The <sup>1</sup>H NMR spectrum showed the presence of two C<sub>2</sub>-symmetric diastereomers in a 1:3 ratio. The NMR characterization is listed above. The major diastereomer was diastereomer 2.

**Reaction of Titanium Tetra(*N,N*-dimethylamide) with 2 equiv of Ligand 1c.** The procedure described above was used. The ratio of diastereomer 1 to diastereomer 2 was found to be 1:2.3. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) diastereomer 1: δ 8.77 (s, 1H), 7.2 (m, 6H), 6.72 (t, *J* = 7.6 Hz, 1H), 5.70 (td, *J* = 5.1, *J* = 2.5 Hz, 1H), 5.65 (d, *J* = 5.1 Hz, 1H), 3.06 (dd, *J* = 16.5, *J* = 5.3 Hz, 1H), 2.88 (dd, *J* = 16.4, *J* = 2.0 Hz, 1H), 0.71 (s, 9H) ppm. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) diastereomer 2: δ 8.74 (s, 1H), 7.2 (m, 6H), 6.70 (t, *J* = 7.6 Hz, 1H), 5.42 (d, *J* = 5.0 Hz, 1H), 5.29 (td, *J* = 5.1, *J* = 1.8 Hz, 1H), 2.72 (dd, *J* = 16.6, *J* = 5.6 Hz, 1H), 2.35 (d, *J* = 16.6 Hz, 1H), 1.10 (s, 9H) ppm. <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>) diastereomer 1: δ 164.6, 164.1, 142.6, 140.6, 138.2, 132.2, 131.9, 128.7, 126.6, 126.2, 124.7, 121.4, 117.5, 85.4, 82.6, 40.8, 34.6, 29.1 ppm. <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>) diastereomer 2: δ 165.4, 165.0, 142.7, 141.4, 138.0, 132.3, 132.0, 128.3, 126.7, 125.8, 124.8, 120.7, 117.0, 86.4, 84.3, 40.4, 34.9, 29.5 ppm.

**Reaction of Titanium Tetra(*N,N*-dimethylamide) with 2 equiv of Ligand 2c.** The procedure described above was used. The ratio of diastereomer 1 to diastereomer 2 was found to be 1:1.9. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) diastereomer 1: δ 8.56 (s, 1H), 7.41 (dd, *J* = 7.6, *J* = 1.7 Hz, 1H), 7.32 (dd, *J* = 7.7, *J* = 1.6 Hz, 1H), 6.80 (t, *J* = 7.6 Hz, 1H), 4.55 (dd, *J* = 9.5, *J* = 4.5 Hz, 1H), 4.28 (dd, *J* = 9.4, *J* = 1.1 Hz, 1H), 3.70 (dd, *J* = 9.2, *J* = 4.3 Hz, 1H), 2.22 (sep, *J* = 6.8 Hz, 1H), 1.21 (s, 9H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H) ppm. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) diastereomer 2: δ 8.42 (s, 1H), 7.26 (dd, *J* = 7.6, *J* = 1.7 Hz, 1H), 7.17 (dd, *J* = 7.7, *J* = 1.6 Hz, 1H), 6.63 (t, *J* = 7.6 Hz, 1H), 4.86 (dd, *J* = 9.9, *J* = 4.6 Hz, 1H), 4.39 (dd, *J* = 9.9, *J* = 1.6 Hz, 1H), 3.78 (dd, *J* = 8.1, *J* = 4.5 Hz, 1H), 2.52 (sep, *J* = 6.8 Hz, 1H), 1.12 (d, *J* = 7.6 Hz, 3H), 1.04 (s, 9H), 1.02 (d, *J* = 6.8 Hz, 3H) ppm. <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>) diastereomer 1: δ 165.1, 163.7, 138.1, 134.4, 132.2, 121.4, 117.8, 82.7, 71.9, 35.0, 30.1, 29.4, 20.6, 20.0 ppm. <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>) diastereomer 2: δ 164.7, 164.4, 137.8, 132.4, 132.0, 120.6, 116.7, 84.3, 72.8, 34.7, 31.3, 29.8, 20.9, 19.6 ppm.

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**Supporting Information Available:** The X-ray crystal structure data for **5g**, <sup>1</sup>H NMR data of diastereomeric mixtures formed on reaction of **1c**, **1g**, and **2c** with Ti(NMe<sub>2</sub>)<sub>4</sub>, and <sup>1</sup>H data for **3c** are available. For the X-ray structures, tables of final atomic coordinates for the non-hydrogen atoms, anisotropic thermal parameters, complete list of bond distances and angles, and complete crystallographic data are included. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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