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Enantioselective Addition of Diethylzinc to Aldehydes Catalyzed by Titanium(IV) Complexes of Diol Derivatives of D-Mannitol and the Spectroscopic Study of the Catalytic System

Jing-Song You,[†] Ming-Yuan Shao, and Han-Mou Gau*

Department of Chemistry, National Chung-Hsing Univeristy, Taichung, Taiwan 402

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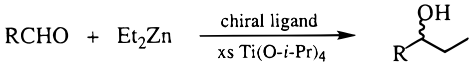
Enantioselective addition of diethylzinc to aldehydes catalyzed by Ti(IV) complexes of diol derivatives of D-mannitol was carried out. Good enantioselectivities were obtained with ee values up to 86% of *R*-configuration. A ^{1}H NMR study shows that the catalytic system in solution contains unreacted Ti(O-*i*-Pr)$_4$, a dimeric Ti(IV) complex [Ti(O-*i*-Pr)$_2$(μ-diolate)]$_2$ (**4**) containing two bridging diolate ligands, and a dimeric Ti(IV) complex [(diolate)(O-*i*-Pr)Ti(μ-O-*i*-Pr)$_2$Ti(O-*i*-Pr)$_3$] (**5**) containing one diolate ligand attached to only one Ti(IV) metal center. The complex **5** with the more electropositive Ti(IV) metal center is considered the most active catalyst in solution. The structure of **4** was determined by X-ray analysis, and the FAB-mass spectroscopic study confirms the existence of complex **5**. The role of excess Ti(O-*i*-Pr)$_4$ in the catalytic system is that Ti(O-*i*-Pr)$_4$ further reacts with the complex **4** to give the most active catalyst **5** in solution.

Introduction

More recently, titanium(IV) complexes containing C_2-symmetric bidentate chiral ligands, such as TADDOLs, TADDOL analogues,[1] sulfonamides,[2] or BINOLs,[3] have been found to be highly effective in catalytic enantioselective addition of diethylzinc to aldehydes (eq 1).[4] In previous studies, the active catalytic systems were in general generated in situ from mixing the chiral ligand with Ti(O-*i*-Pr)$_4$, and a common feature of excess Ti(O-*i*-Pr)$_4$ is required in order to obtain the best enantioselectivities.[1−3,5] However, there were not many discussions about the active catalyst in solution and about the role of excess Ti(O-*i*-Pr)$_4$ in these catalytic systems.[6]



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In this report, C_2-symmetric diol derivatives of D-mannitol were prepared and used as chiral ligand while mixing with Ti(O-*i*-Pr)$_4$ in enantioselective addition of diethylzinc to aldehydes. The spectroscopic study of the catalytic system was carried out, and the possible structure of the most active catalytic species in solution is proposed on the basis of the spectroscopic evidence. The role of excess Ti(O-*i*-Pr)$_4$ in the catalytic system is also discussed.

Results and Discussions

Synthesis. D-Mannitol (**1**), which is a relatively cheap and commercially available sugar, can be easily converted to C_2-symmetric 1,2:5,6-di-*O*-isopropylidene-D-mannitol (**2**) or 1,3:4,6-di-*O*-benzylidene-D-mannitol (**3**) according to literature procedures.[7] Due to the C_2-symmetric nature of diols and the inequivalent environments of the two hydrogens in the methylene group, ^{1}H NMR spectra reveal four sets of signals with equal intensities for the six CH/CH$_2$ groups at δ 4.20, 4.12, 3.97, and 3.75 ppm for **2** in CDCl$_3$ and at δ 4.14, 3.89, 3.78, and 3.52 ppm for **3** in DMSO-d_6.

[†] Postdoctoral research fellow from Department of Chemistry, Sichuan University, People's Republic of China.

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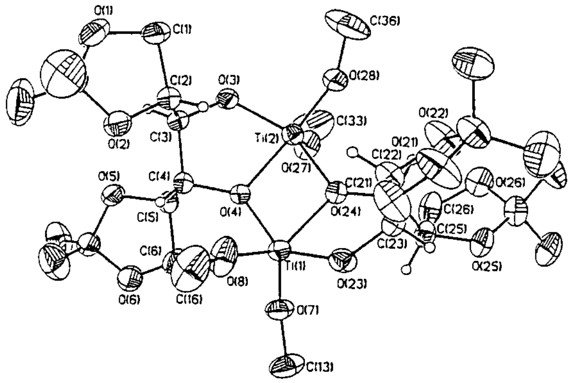
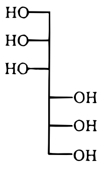


Figure 1. Molecular structure of **4**. The methyl groups of 2-propoxide ligands and the hydrogen atoms except those attached to chiral carbon atoms are omitted for clarity.

To explore the Ti(IV)-diolate complex system, the chiral diol **2** was reacted with 1 molar equiv of Ti(O-*i*-Pr)$_4$ (eq 2). The reaction released 2 molar equiv of HO-*i*-Pr, and a white powdered complex **4** was obtained after removing the volatile materials completely. The complex **4** is extremely soluble in hydrocarbons and can be crystallized from *n*-hexane as colorless crystals in 77% yield. The ^{1}H NMR spectrum reveals eight distinct sets of signals with equal intensities at δ 4.65, 4.36, 4.24, 4.22, 4.13, 4.09, 3.98, and 3.91 ppm for the six CH/CH$_2$ groups, indicating that the diolate ligand in complex **4** is no longer in C_2 symmetry. The X-ray structural analysis shows that the complex **4** is a dimeric Ti(IV) complex bridging through one alkoxy group of each diolate ligand, which makes all six CH/CH$_2$ groups structurally different.



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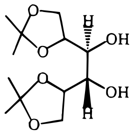

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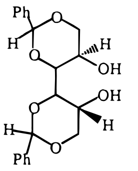

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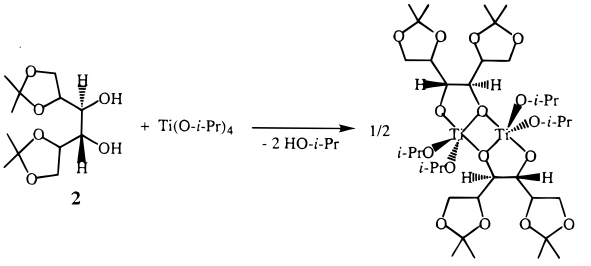

(2)

The Molecular Structure of 4. The molecular structure of **4** is shown in Figure 1, and selected bond lengths and bond angles are listed in Table 1. Complex **4** is a dimeric species bridging through one alkoxy donor of the diolate ligands with each Ti(IV) metal center having five coordinations. Although the chiral dimeric Ti(IV)-diolate complex [Ti(O-*i*-Pr)$_2$(μ-tartramide)]$_2$[8] was reported previously, the tartramide complex is six-coordinate around the Ti(IV) metal center due to further coordination of the amide carbonyl. Instead, the structure of **4** is similar to the chiral [TiX$_2$(μ-amino alcoholate)]$_2$[9] (X = NEt$_2$ or O-*i*-Pr) complexes and the nonchiral [Ti(ONp)$_3$(μ-ONp)]$_2$[10] complex (Np = neopentyl). In comparison with [Ti(ONp)$_3$(μ-ONp)]$_2$, the average Ti−OR distance at 1.751 Å in **4** is shorter by ~0.04 Å and the average Ti−O(diolate) distance, however, is longer by 0.04 Å. The bridging diolate ligands bond inequivalently to two Ti(IV) metal centers with bond lengths of 1.987(3) Å for the Ti(1)−O(4) bond, 2.036(3) Å for Ti(2)−O(4), 2.058(3) Å for Ti(1)−O(24), and 1.966(3) Å for Ti(2)−O(24). The average Ti−(μ-OR) distance at 2.012 Å is slightly shorter than the distance of 2.036 Å in [Ti(ONp)$_3$(μ-ONp)]$_2$.

Table 1. Selected Bond Lengths (Å) and Bond Angles (deg) for Complex 4

Ti(1)−O(7)	1.751(4)	Ti(2)−O(27)	1.766(3)
Ti(1)−O(8)	1.740 (4)	Ti(2)−O(28)	1.747(4)
Ti(1)−O(23)	1.828(4)	Ti(2)−O(3)	1.842(3)
Ti(1)−O(4)	1.987(3)	Ti(2)−O(4)	2.036(3)
Ti(1)−O(24)	2.058(3)	Ti(2)−O(24)	1.966(3)
Ti(1)···Ti(2)	3.290(1)		
Ti(1)−O(7)−C(13)	150.4(4)	Ti(2)−O(27)−C(33)	151.4(6)
Ti(1)−O(8)−C(16)	161.7(6)	Ti(2)−O(28)−C(36)	155.7(7)
Ti(1)−O(23)−C(23)	123.7(3)	Ti(2)−O(3)−C(3)	123.0(3)
O(4)−Ti(1)−O(23)	143.1(2)	O(3)−Ti(2)−O(24)	141.5(2)
O(8)−Ti(1)−O(24)	140.1(2)	O(28)−Ti(2)−O(4)	143.4(2)
O(7)−Ti(1)−O(8)	108.9(3)	O(27)−Ti(2)−O(28)	107.3(2)
O(4)−Ti(1)−O(24)	70.4(2)	O(4)−Ti(2)−O(24)	70.6(2)
Ti(1)−O(4)−Ti(2)	109.7(2)	Ti(1)−O(24)−Ti(2)	108.5(2)

Table 2. Enantioselective Addition of Diethylzinc to Aldehydes Catalyzed by 2 or 3/Ti(O-*i*-Pr)$_4$ in Situ-Formed Systems[a]

entry	compd	aldehyde	molecular sieves (4 Å, mg)	Ti(O-*i*-Pr)$_4$ (mmol)	yield (%)[b]	% ee[c]
1	**2**	benzaldehyde		0	0	
2	**2**	benzaldehyde		0.6	100	80(*R*)
3	**2**	benzaldehyde		1.0	100	85(*R*)
4	**2**	benzaldehyde		1.5	100	81(*R*)
5[d]	**2**	benzaldehyde		1.0	100	72(*R*)
6	**2**	4-methoxybenzaldehyde		1.0	100	84(*R*)
7[d]	**2**	benzaldehyde	200	1.0	100	86(*R*)
8[d]	**2**	4-methoxybenzaldehyde	200	1.0	100	83(*R*)
9	**3**	benzaldehyde		1.0	66	41(*R*)

[a] Reaction conditions: The ligand (0.2 mmol) and Ti(O-*i*-Pr)$_4$ were mixed in dry toluene at room temperature. After 1 h, the solution was dried in vacuo and 5 mL of toluene was then added. The resulting solution was chilled at 0 °C; Et$_2$Zn (3.0 mmol) and aldehyde(1.0 mmol) were added, and the mixture was allowed to react at 0 °C for 10 h. [b] The yields were based on the ^{1}H NMR spectra. [c] The ee values were determined by HPLC with a Chiralcel-OD column from Daicel. [d] The released 2-propanol was not removed prior to addition of diethylzinc.

Enantioselective Addition of Diethylzinc to Aldehydes Catalyzed by in Situ-Formed Titanium Complexes. Enantioselective additions of diethylzinc to aldehydes using catalytic systems prepared in situ from mixing Ti(O-*i*-Pr)$_4$ with **2** or **3** were carried out, and the results are listed in Table 2. The addition of diethylzinc to benzaldehyde in the presence of only **2** was examined first, but no reaction occurred, indicating that the chiral diol **2** itself is not a catalyst. However,

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Table 3. Enantioselective Addition of Diethylzinc to 4-Methoxybenzaldehyde Catalyzed by 4 with or without Addition of Ti(O-*i*-Pr)$_4$[a−c]

entry	time (h)	Ti(O-*i*-Pr)$_4$ (mmol)	yield (%)	ee (%)
1	10	0	16	50(*R*)
2	40	0	42	50(*R*)
3	10	0.2	100	76(*R*)
4	10	0.6	100	80(*R*)
5	10	0.8	100	85(*R*)

[a] Substrate/**4**/Et$_2$Zn = 1.0/0.1/3.0 (mmol). [b] See Table 1 for other conditions. [c] Solvent is toluene.

addition of Ti(O-*i*-Pr)$_4$ to the reaction system remarkably promoted the desired addition reaction. Our study shows that a large excess of Ti(O-*i*-Pr)$_4$ is required in order to obtain good enantioselectivities (entries 2−4), and the best ratio of **2**/Ti(O-*i*-Pr)$_4$ was found to be 1/5 with an ee value of 85% of *R* configuration (entry 3). In Table 2 except entries 5, 7, and 8, the catalytic systems were obtained by removing the generated 2-propanol prior to the addition of diethylzinc and aldehyde.[6b,11] Without removing the 2-propanol in the catalytic system, the ee value is lower at 72% (entry 5). Numerous reports had cited the use of molecular sieves to sequester the released 2-propanol, which serves as a competing ligand in the catalytic system.[12] Indeed, addition of powdered 4 Å molecular sieves was effective as an in situ trap of 2-propanol, resulting in high yields and good enantioselectivities (entries 7 and 8). In using **3** as the chiral diol ligand, however, the enantioselectivity was only 41% with 66% yield (entry 9). The solvent effects were also studied, and toluene was the best choice.

Enantioselective Addition of Diethylzinc to Aldehydes Catalyzed by the 4/Ti(O-*i*-Pr)$_4$ Catalytic System. The above results show that, as in many other catalytic systems, excess Ti(O-*i*-Pr)$_4$ was needed. To explore the role of excess Ti(O-*i*-Pr)$_4$ in solution, equal molar amounts of Ti(O-*i*-Pr)$_4$ and **2** were reacted in hexane, and a Ti(IV) complex **4** was obtained with a structure shown in Figure 1. In using **4** as catalyst and 4-methoxybenzaldehyde as substrate, the addition reaction was very slow, with only 16% yield in 10 h, and the ee value was only 50% of also *R* configuration (Table 3, entry 1). When the reaction time was increased to 40 h, the yield improved to only 42% (entry 2). Apparently, **4** itself is not an effective catalyst in solution. For the **2**/Ti(O-*i*-Pr)$_4$ catalytic system, there must be some species other than **4** that serves as the most effective catalyst in soltuion. With addition of Ti(O-*i*-Pr)$_4$ to **4**, the ee values improved to 85% (entry 5). In entry 5, the diolate/Ti ratio is 1/5, which is the same ratio as the best result for the in situ-formed **2**/Ti(O-*i*-Pr)$_4$ catalytic system.

NMR Study of the Catalytic System. To explore the solution structures of the catalytic system in solution, the ^{1}H NMR study of the catalytic system was carried out, and the spectra in the region from δ 4.95 to 3.70 ppm are shown in Figure 2. Figure 2a shows a spectrum of Ti(O-*i*-Pr)$_4$, and the spectrum of **4** is shown in Figure 2b. In Figure 2b, besides the methine signal at δ 4.45 ppm for Ti(O-*i*-Pr)$_4$, eight distinct CH/CH$_2$ signals for the chiral diolate ligands are observed, indicating different bonding modes of the two diolate oxygen donors. The observed ^{1}H NMR spectrum of **4** is consistent with the solid state structure with bridging diolate ligands. The ^{1}H NMR spectrum of the in situ-formed system with a **2**/Ti(O-*i*-Pr)$_4$ ratio of 1/5 is shown in Figure 2c. From the spectrum, besides the unreacted Ti(O-*i*-Pr)$_4$ and the compound **4**, the catalytic system contains also a species with a 2-propoxide methine peak at δ 4.75 ppm and with diolate CH/CH$_2$ signals around δ 4.09 ppm. The addition of 8-fold of Ti(O-*i*-Pr)$_4$ to complex **4** gave the same spectrum (Figure 2d) as the in situ formed catalytic system.

Subtracting intensities due to Ti(O-*i*-Pr)$_4$ and the compound **4** gives resonances corresponding to a dimeric titanium(IV) complex containing six 2-propoxide ligands and only one chiral diolate ligand. On the basis of the simpler diolate CH/CH$_2$ signals, two possible dimeric complexes, **5** and **6**, are proposed. Complex **5** is an unsymmetric dimeric species with the diolate ligand attached to only one Ti(IV) metal center and contains three types of 2-propoxide ligands, i.e., one terminal alkoxide on one metal center, two bridging alkoxides, and three terminal alkoxides on another metal center with a ratio of 1/2/3. On the other hand, complex **6** is a symmetric dimeric species bridging through the diolate ligand. The two Ti(O-*i*-R)$_3$ moieties in complex **6** are equivalent, and only one alkoxide NMR signal is expected. In Figure 2c, the observation of only one methine septet at δ 4.75 ppm may likely lead to a complex with symmetric alkoxides such as complex **6**. However, it is well known that titanium alkoxides are fluxional in solution with facile exchanges of terminal and bridging alkoxides, which give an averaged signal at room temperature.[13] To verify the structure of this new species, a variable-temperature ^{1}H NMR study was carried out. Resonances corresponding to complex **4** and Ti(O-*i*-Pr)$_4$ remained intact for temperatures down to −60.0 °C. However, the methine peak at δ 4.75 ppm started to broaden at 0.0 °C, and the broadened peak developed into two sets of signals at δ 4.82 and around δ 4.70 ppm at −20.0 °C. The ^{1}H NMR spectra of complex **4** and of the in situ-formed catalytic system in the methine region at −60.0 °C are shown in Figure 3. Figure 3a is a spectrum of complex **4** with the methine signal at δ 4.71 ppm corresponding to two hydrogens and one CH$_2$/CH doublet at δ 4.63 ppm corresponding to one hydrogen, and the spectrum confirms a relative intensity of 2/1. Figure 3b is a spectrum of the in situ-formed solution, and a downfield septet at δ 4.84 ppm and upfield septets around δ 4.70 ppm are clearly seen. Unfortunately, upfield septets were found to overlap with the methine septet of complex **4** at δ 4.71 ppm even with the use of a 600 MHz NMR spectrometer. Subtracting intensities arising from the methine signal of complex **4** from the overlapped resonances gives signals with intensities roughly equivalent to the downfield septet. The above observation suggests that the downfield septet corresponds to three terminal alkoxide ligands on one Ti(IV) metal center, and the upfield overlapped resonances are due to two bridging alkoxides

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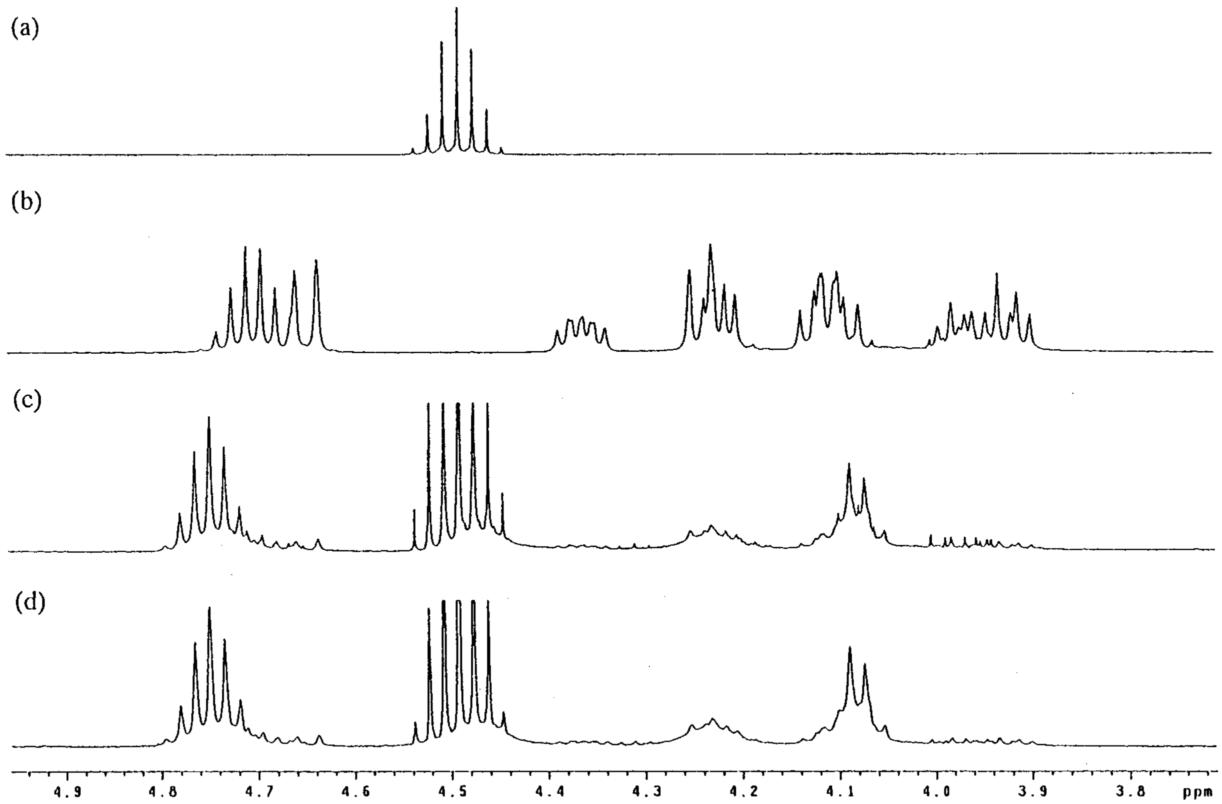


Figure 2. ^{1}H NMR spectra in $CDCl_3$: (a) Ti(O-*i*-Pr)$_4$; (b) complex **4**; (c) a 1:5 mixture of **2** with Ti(O-*i*-Pr)$_4$; (d) a 1:8 mixture of **4** with Ti(O-*i*-Pr)$_4$.

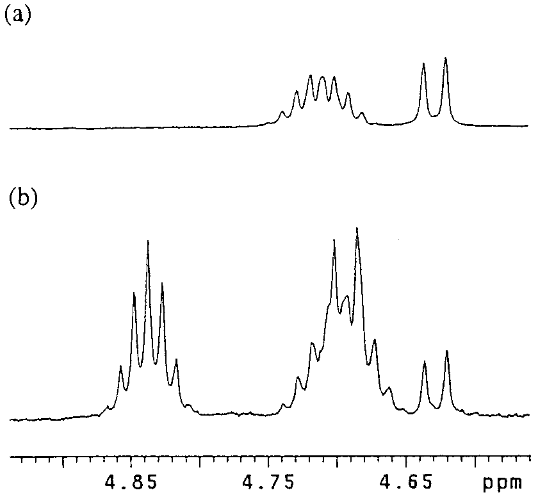
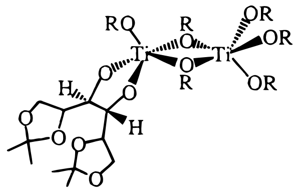


Figure 3. ^{1}H NMR spectra in the methine region in $CDCl_3$ at −60.0 °C at 600 MHz: (a) complex **4**; (b) a 1:5 mixture of **2** with Ti(O-*i*-Pr)$_4$.

and one terminal alkoxide on the Ti(IV) metal center containing the chiral diolate ligand. Besides the methine signal of complex **4** at δ 4.71 ppm, two septets at δ 4.70 and 4.69 ppm can be identified while closely inspecting the overlapped resonances. It seems that the septet at δ 4.70 ppm is a signal arising from the singly terminal alkoxide ligand, and thus, the split peaks show a relative intensity of 3/1/2. Based on the freezed low-temperature ^{1}H NMR spectrum, a symmetric structure like complex **6** giving only one alkoxide signal is ruled out. On the other hand, the VT NMR study supports the proposal of complex **5** as the new species formed in the catalytic system.



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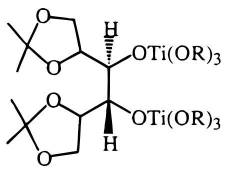

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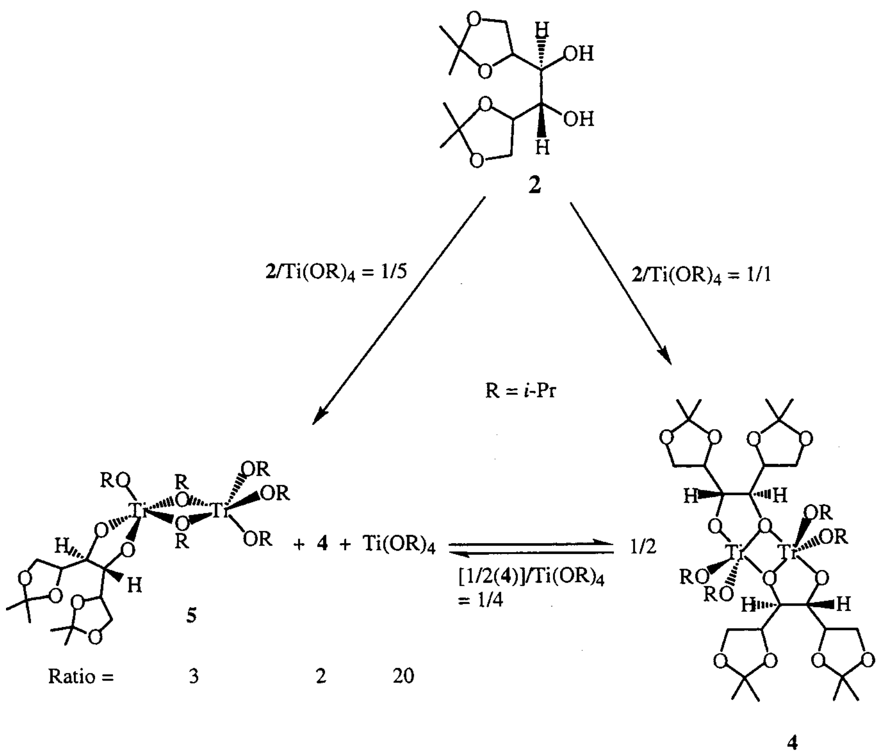
The ^{1}H NMR studies are summarized in Scheme 1. No matter whether the catalytic system was prepared from mixing **2** with Ti(O-*i*-Pr)$_4$ in a 1/5 ratio or from mixing **4** with Ti(O-*i*-Pr)$_4$ in 1/8 ratio, a similar relative ratio of **4**/**5**/Ti(O-*i*-Pr)$_4$ of roughly 2/3/20 was obtained. The role of Ti(O-*i*-Pr)$_4$ here is to react with **2** to give the dimeric complex **4** initially. Then the excess Ti(O-*i*-Pr)$_4$ reacts further with **4** to afford the active catalyst **5** in substantial amount in solution. The trend of increasing ee values of the desired chiral (*R*)-1-phenylpropanol product is parallel to the increasing addition of Ti(O-*i*-Pr)$_4$, which generates higher concentration of **5** in solution. However, a large excess of Ti(O-*i*-Pr)$_4$ would lower the ee values of the desired product, and the best ratio of **2**/Ti(O-*i*-Pr)$_4$ is determined to be 1/5. The ^{1}H NMR spectra show that the averaged methine signal of 2-propoxide ligands for complex **5** appears downfield relative to that for complex **4** and for Ti(O-*i*-Pr)$_4$. The observation indicates more electropositive nature, i.e., higher Lewis acidity, of the Ti(IV) metal center in complex **5**, which is likely a major reason for better catalytic behavior of the dimeric complex **5**.

FAB-Mass Spectroscopic Study of the Catalytic System. FAB-mass spectroscopy has been proven to be

Scheme 1



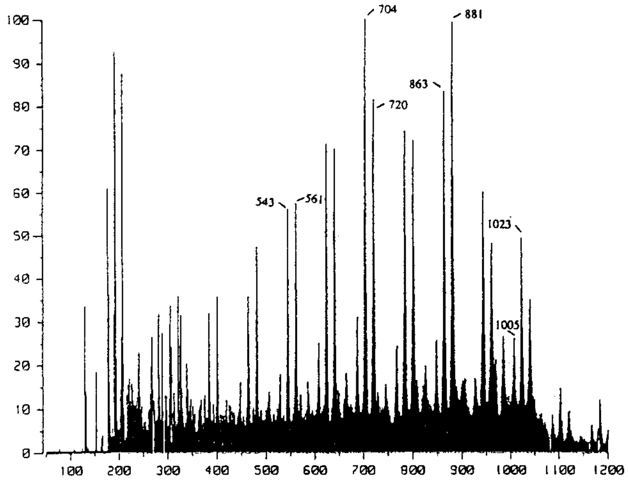


Figure 4. FAB-mass spectrum for complex **4** upon addition of 8 molar equiv of Ti(O-*i*- Pr)$_4$; 3-nitrobenzyl alcohol as matrix.

a good tool for identifying species in solution.[14] To further support our proposal of the dimeric complex **5**, an FAB-mass spectroscopic study was therefore carried out with the use of 3-nitrobenzyl alcohol (NBA) as matrix (Figure 4). Interactions of compounds **4** and **5** with NBA give rise to peaks of *m/z* 1005 for [**4**$\cdot OCH_2C_6H_4NO_2]^+$ and of 863 for [**5**$\cdot OCH_2C_6H_4NO_2]^+$, respectively. Reactions of these ions with water are responsible for the appearance of ions at *m/z* 1023 and 881. The observation of these peaks indicates the presence of complexes **4** and **5** in the catalytic system. Some of the other peaks arise from sequential loss of 2-propoxide ligand from complex **4** or **5** and also from the large excess of Ti(O-*i*-Pr)$_4$ reagent, which is likely to aggregate into dimers in solution.[15] For example, the base peak at *m/z* of 704 arises from loss of three 2-propoxide (MW = 59) fragments from the peak of 881. The peak with *m/z* 720 is due to $[\{Ti(O\text{-}i\text{-}Pr)_4\}_2\cdot OCH_2C_6H_4NO_2]^+$, and the peak with *m/z* 543 is due to a species after loss of three 2-propoxide fragments from the dimeric species. Interaction of the ion with *m/z* 543 with H_2O gives rise to the peak with *m/z* 561.

Conclusions

In summary, enantioselective additions of diethylzinc to aldehydes catalyzed by **2**/Ti(O-*i*-Pr)$_4$ catalytic system with good ee values are demonstrated. The ^1H NMR study suggests that the catalytic system in solution contains Ti(O-*i*-Pr)$_4$, complex **4**, and complex **5**. Complex **5** is considered as the most effective catalyst in this studied system. The FAB-mass spectroscopic study further confirms the existence of **5** in solution. On the basis of this study, similar reaction pathways for the generation of the most active species as illustrated in Scheme 1 are strongly suggested for other diol/Ti(O-*i*-Pr)$_4$ catalytic systems. Further investigations are currently underway.

Experimental Sections

Reagents and General Techniques. 1,2:5,6-di-*O*-isopropylidene-D-mannitol (**2**)[7d] and 1,3:4,6-di-*O*-benzylidene-D-mannitol (**3**)[7a] were prepared according to literature procedures. Ti(O-*i*-Pr)$_4$ was freshly distilled prior to use. Benzaldehyde and 4-methoxybenzaldehyde were distilled and stored over molecular sieves. *n*-Hexane and toluene were dried by refluxing for at least 24 h over sodium/benzophenone and freshly distilled prior to use. Deuterated chloroform was dried over molecular

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[14] Bonchio, M.; Licini, G.; Modena, G.; Bortolini, O.; Moro, S.; Nugent, W. A. *J. Am. Chem. Soc.* **1999**, *121*, 6258.

[15] Bradley, D. C.; Mehrotra, R. C.; Gaur, D. P. *Metal Alkoxides*; Academic Press: New York, 1978; p 68.

sieves. All syntheses and manipulations were carried out under a dry dinitrogen atmosphere.

Synthesis of [Ti(O-*i*-Pr)$_2$(μ-1,2:5,6-di-*O*-isopropylidene-D-mannitolate)]$_2$ (4). To a suspension of 1,2:5,6-di-*O*-isopropylidene-D-mannitol (**2**) (6.00 mmol, 1.58 g) in 30 mL of *n*-hexane was added Ti(O-*i*-Pr)$_4$ (6.00 mmol, 1.8 mL) at room temperature, and the solution became clear. The mixture was stirred for 1 h, and then the solution was concentrated in vacuo to 10 mL. The resulting solution was cooled at −20 °C for 10 h to get colorless crystals (2.0 g, 77%), mp 108−109 °C. ^{1}H NMR (CDCl$_3$): δ 1.21−1.41 (48H), 3.90−3.95 (m, 2H), 3.95−4.00 (m, 2H), 4.07−4.11 (m, 2H), 4.11−4.14 (m, 2H), 4.20−4.25 (m, 2H), 4.23−4.26 (m, 2H), 4.34−4.39 (m, 2H), 4.63−4.67 (m, 2H), 4.64−4.76 (m, 4H) ppm. ^{13}C {^{1}H} NMR (CDCl$_3$): δ 25.42, 25.73, 25.85, 26.87, 27.08, 67.59, 67.86, 75.87, 79.06, 79.45, 86.70, 90.19, 109.27, 109.33 ppm. Anal. Found: C, 51.22; H, 8.29. Calcd for $C_{36}H_{68}O_{16}Ti_2$: C, 50.71; H, 8.04.

General Procedures for the Addition of Et$_2$Zn to Aldehydes in the in Situ-Formed System. Under dry dinitrogen atmosphere, the diol (0.2 mmol) and Ti(O-*i*-Pr)$_4$ were mixed in 5 mL of dry toluene at room temperature. After the mixture was stirred for 1 h, the solvent was removed in vacuo, and 5 mL of toluene was then added. A 3.0 mmol sample of Et$_2$Zn (1.0 M solution in hexane) was injected at 0 °C. After 30 min, the orange-colored solution was treated with aldehyde (1.0 mmol) at 0 °C, stirred at this temperature for 10 h, and quenched with 1 N HCl. The aqueous phase was extracted with ethyl acetate (3 × 5 mL), dried over MgSO$_4$, filtered, and concentrated. Chromatography of the residue on silica gel (elution with 5:1 hexane/ethyl acetate) gave the carbinol as a colorless oil. The enantiomeric purity of the product was determined by HPLC with a Chiralcel-OD column from Daicel.

General Procedures for the Addition of Et$_2$Zn to Aldehydes Catalyzed by the 4/Ti(O-*i*-Pr)$_4$ System. Under dry dinitrogen atmosphere, to a stirred solution of 0.1 mmol of complex **4** and Ti(O-*i*-Pr)$_4$ in 5 mL of toluene was added 3.0 mmol of Et$_2$Zn (1.0 M solution in hexane) at 0 °C. After 30 min, the orange-colored solution was treated with aldehyde (1.0 mmol) at 0 °C, stirred at this temperature for 10 h, and quenched with 1 N HCl. The aqueous phase was extracted with ethyl acetate (3 × 5 mL), dried over MgSO$_4$, filtered, and concentrated. Chromatography of the residue on silica gel (elution with 5:1 hexane/ethyl acetate) gave the carbinol as a colorless oil. The enantiomeric purity of the product was determined by HPLC with a Chiralcel-OD column from Daicel.

Physical Measurements. ^{1}H NMR spectra were obtained with a Varian Mercury-400 (400 MHz) spectrometer, and ^{13}C NMR spectra were recorded with the Varian Mercury-400 (100.70 MHz) spectrometer. The variable-temperature NMR study was performed using a Varian Unity Inova 600 MHz spectrometer. The ^{1}H and ^{13}C chemical shifts were measured relative to tetramethylsilane as the internal reference. Melting points were taken on a Büchi 535 instrument and are uncorrected. Elemental analyses were performed using a Heraeus CHN-O-RAPID instrument. FAB-mass spectra were collected on a JEOL JMS-SX/SX 102A instrument. Test samples were prepared by dissolving the investigated precursor in 3-nitrobenzyl alcohol (NBA) as the liquid matrix.

Crystal Structure Determinations. A colorless crystal of **4** of size 0.4 × 0.6 × 0.6 mm in a sealed capillary under dinitrogen atmosphere was used for an X-ray diffraction study. The diffraction intensities were collected on a Bruker CCD Smart-1000 diffractometer equipped with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). All refinements and calculations were carried out with the Bruker AXS SHELXTL software package on a Pentium III-450 computer. The positions of heavy atoms for the structure were determined by direct methods and the remaining non-hydrogen atoms were located from successive difference Fourier map calculations. The refinements were carried out using full-matrix least-squares techniques. All non-hydrogen atoms were refined as individual anisotropic atoms. The hydrogen atoms were considered as the riding atom on a carbon atom with a C−H bond length of 0.96 Å, and the hydrogen atom temperature factors were fixed at 0.08 Å. The hydrogen atoms were included for refinements in the final cycles.

Acknowledgment. We would like to thank the National Science Council of Taiwan for financial support (NSC 89-2113-M-005-001).

Supporting Information Available: X-ray crystallographic data including final coordinates, bond lengths, bond angles, and anisotropic displacement coefficients for the complex **4** are available on the Internet only. This material is available free of charge via the Internet at http://pubs.acs.org.

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