ORGANIC
LETTERS

2001
Vol. 3, No. 5
699−702

Snapshots of Titanium BINOLate Complexes with Diverse Solid State Structures[†]

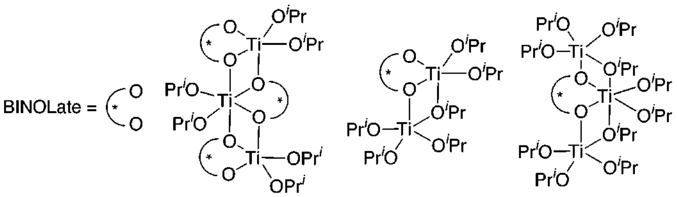
Timothy J. Davis, Jaume Balsells, Patrick J. Carroll, and Patrick J. Walsh*

*Department of Chemistry, University of Pennsylvania, 231 South 34th Street,
Philadelphia, Pennsylvania 19104-6323*

pwalsh@sas.upenn.edu

Received December 21, 2000

ABSTRACT



Many important asymmetric reactions are catalyzed by (BINOLate)Ti species with unknown structures. Reported here are three structures of BINOLate titanium complexes that show an interesting aggregation of (BINOLate)Ti(OiPr)$_2$ with itself and with titanium tetraisopropoxide. These complexes are potential intermediates in the asymmetric addition of alkyl groups to aldehydes.

Of the multitude of ligands that have been prepared and screened in asymmetric catalysis, BINOL (**1**, Figure 1) is perhaps the most effective across a broad spectrum of transformations.

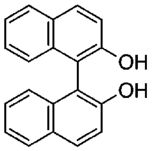


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Figure 1.

BINOL has been shown to form very enantioselective catalysts with main group elements,[1,2] transition metals,[2] f-block elements,[3] and heterobimetallic combinations[4,5] from these groups.[2,6−8]

In concert with various titanium precursors, BINOL forms highly enantioselective catalysts that have been employed in many asymmetric processes.[2,6−15] Considering the importance of titanium BINOL complexes in asymmetric catalysis,

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[†] Dedicated to Professor K. Barry Sharpless, a pioneer in asymmetric catalysis, on the occasion of his 60th birthday.

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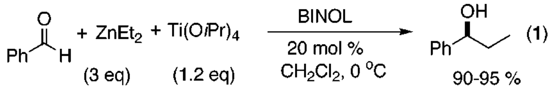
10.1021/ol0070381 CCC: $20.00

there is little information regarding the structures of these species. With this in mind we initiated research designed to elucidate the solid state interactions between BINOL and varying amounts of titanium tetraisopropoxide. The resulting structures provide insight into possible intermediates in the asymmetric addition of alkyl groups to aldehydes catalyzed by (BINOLate)Ti-based complexes in the presence of excess titanium tetraisopropoxide (eq 1).



The asymmetric addition of alkyl groups to aldehydes employing BINOL and titanium tetraisopropoxide (eq 1) was introduced independently by Nakai[16] and Chan.[17] On the basis of their results, other groups have examined related additions including use of modified[18] and hetero-substituted BINOL analogues,[19] fluorinated BINOL derivatives,[20] dendrimers containing BINOL,[21] poly BINOLs,[15,22] polymer-supported BINOL,[23−25] and even fluorous BINOL derivatives in organic/fluorous biphasic systems.[26]

Despite the flurry of recent interest in this reaction, little concrete mechanistic information has been reported. The proposed intermediates include (BINOLate)Ti(O*i*Pr)$_2$[17,22] and (BINOLate)Ti(O*i*Pr)(Et) (Figure 2).[16] Upon combining 6 equiv of titanium tetraisopropoxide with BINOL, Nakai and Mori observed formation of a complex proposed to be (BINOLate)Ti$_2$(O*i*Pr)$_6$ (Figure 2), on the basis of the ^{1}H NMR of this mixture. Importantly, to obtain high enantioselectivity and turnover frequency in eq 1, an excess of titanium tetraisopropoxide must be used [Ti(O*i*Pr)$_4$:BINOL is 6:1]. Although the role of the excess titanium tetraisopropoxide is not clear, the results of Nakai and Mori suggest that interaction of titanium tetraisopropoxide with (BINOLate)Ti species must be considered in any mechanistic investigation.

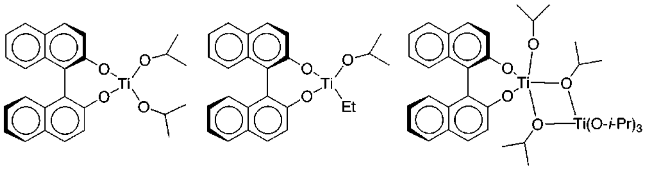


Figure 2. Proposed intermediates in the asymmetric addition of alkyl groups to aldehydes (eq 1).

Our study began with synthesis of titanium BINOLate complexes with BINOL to titanium tetraisopropoxide ratios of 1:1, 1:2, and 1:6. All reactions were stirred at room temperature for 1 h and the volatile materials removed under reduced pressure. Combination of equal molar amounts of BINOL and titanium tetraisopropoxide followed by recrystallization of the resulting compound from chloroform at −30 °C provided crystals for a low-temperature structural determination (90% isolated yield). The structure is the trimeric [(BINOLate)Ti(O*i*Pr)$_2$]$_3$·CHCl$_3$ (**2**, Figure 3).[27] For the purpose of comparison, bond lengths for all the structures are given in Table 1. A structure differing in the absence of the CHCl$_3$ found in **2** was reported in the Ph.D. Thesis of Dr. C. Martin from the laboratory of Prof. K. B. Sharpless.[28] The spectroscopic data of **2** are identical to that reported by Martin and Sharpless.[28] Our structure is presented here because the quality of the original structure was low and this important structure has been misrepresented in the literature several times,[16,29−32] including in an excellent recent review.[7]

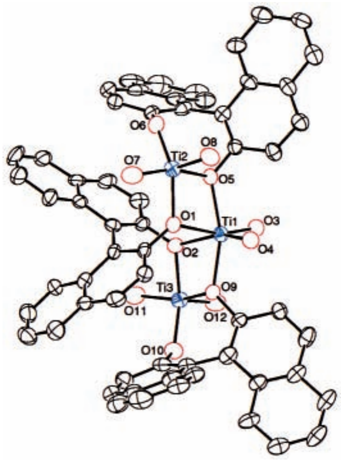


Figure 3. Structure of the trimeric **2**. The isopropoxy groups have been removed for clarity. Bond distances are located in Table 1.

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(27) Crystal structure data for $C_{79}H_{79}Cl_3O_{12}Ti_3$ (**2**): crystal size 0.32 × 0.22 × 0.08 mm, orthorhombic, space group $P2_12_12_1$ (No. 19), $a = 18.9384(3)$, $b = 22.5807(6)$, and $c = 17.8197(4)$ Å, $V = 7620.5(3)$ Å^3, $Z = 4$, $\rho_{calc} = 1.282$ g/cm^{-3}, $2q_{max} = 50.7°$, Mo Kα radiation, scan mode image plate φ-oscillations, $T = 220$ K, $m = 4.70$ cm^{-1}. Refinement on F^2 for 1130 reflections and 839 parameters gave R1 = 9.06 and wR2 = 24.76 for $I > 2\sigma(I)$. Residual electron density $-0.364 < \Delta\rho < 0.567$ e Å^{-3}.

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Table 1. Selected Bond Distances for **2**−**4** [Å]

	2	**3**	**4**
Ti(1)−O(1)	2.117(5)	2.111(3)	2.147(2)
Ti(1)−O(2)	2.097(5)	1.861(3)	2.156(2)
Ti(1)−O(3)	1.775(5)	1.781(3)	1.779(2)
Ti(1)−O(4)	1.776(5)	1.779(3)	1.778(2)
Ti(1)−O(5)	2.046(5)	1.921(3)	1.999(2)
Ti(1)−O(9)	2.062(5)		1.997(2)
Ti(2)−O(1)	1.992(5)	1.980(3)	2.041(2)
Ti(2)−O(5)	2.119(4)	2.120(3)	2.073(2)
Ti(2)−O(6)	1.853(5)	1.794(3)	1.801(2)
Ti(2)−O(7)	1.752(6)	1.765(3)	1.779(2)
Ti(2)−O(8)	1.772(5)	1.805(3)	1.791(2)
Ti(3)−O(2)	2.011(5)		2.020(2)
Ti(3)−O(9)	2.093(5)		2.087(2)
Ti(3)−O(10)	1.847(5)		1.792(2)
Ti(3)−O(11)	1.762(5)		1.780(2)
Ti(3)−O(12)	1.776(6)		1.794(2)
Ti(1)−Ti(2)	3.334(2)	3.309 (1)	3.348(1)
Ti(1)−Ti(3)	3.339(2)		3.346(1)

The central titanium in **2** is in a distorted octahedral environment while the remaining titanium centers have distorted trigonal-bipyramidal geometries. Importantly, *the naphthylate oxygens bridge the metal centers and the isopropoxy groups are terminal*. For comparison, the analogous 3,3′-dimethyl BINOLate derivative [(Me$_2$-BINOL)Ti(O*i*Pr)$_2$]$_2$ is dimeric, showing the sensitivity of these complexes to small changes in the chiral ligand.[33] It is unlikely that trimer **2** is involved in the asymmetric addition reaction in eq 1 on the basis of the absence of nonlinear effects[34,35] under the conditions of the addition reaction (eq 1).[16]

When 2 equiv of titanium tetraisopropoxide was combined with *racemic* BINOL under the conditions outlined above and the resulting solid recrystallized from dichloromethane at −30 °C, X-ray quality crystals formed in 70% yield.[36] The structure of **3** is illustrated in Figure 4.[37]

The structure contains two inequivalent titanium centers and one BINOLate ligand. To a first approximation it appears as if a (BINOLate)Ti(O*i*Pr)$_2$ has bound to a molecule of Ti(O*i*Pr)$_4$. Both titanium centers have distorted trigonal-bipyramidal geometries and again the naphthylate oxygen bridges to the second titanium center. The room temperature ^{1}H NMR spectrum has three types of methyl resonances in an approximate ratio of 1:1:10 (the latter of which is very broad), indicating that one of the isopropoxy groups does not readily exchange with the others. The ^{13}C{^{1}H} NMR contains 20 aromatic resonances indicating that the C_2-symmetry of the BINOLate ligand has been lost, consistent with the solid state structure. The structure can be contrasted with the product formed on reaction of the monomeric substituted 3,3′-derivative [(^{t}BuMe$_2$Si)$_2$-BINOLate]Ti(O*i*Pr)$_2$ with titanium tetraisopropoxide. This reaction gave [(^{t}BuMe$_2$Si)$_2$-BINOLate]Ti$_2$(O*i*Pr)$_6$ in which the naphthylate oxygens each interact with *only one* titanium center.[33]

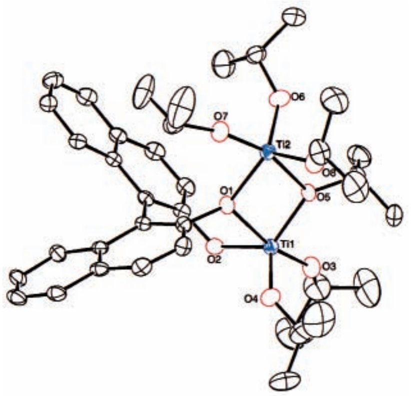

Figure 4. Structure of the dinuclear **3**. Bond distances are located in Table 1.

In the asymmetric addition reaction in eq 1, titanium tetraisopropoxide is in 6-fold excess with respect to BINOL. We therefore combined 6 equiv of titanium tetraisopropoxide with 1 equiv of (*S*)-BINOL.[36]

After removal of the volatile materials under reduced pressure, crystals were grown in pentane at −30 °C (isolated yield 79%). Data for the structure were collected at low temperature and an ORTEP diagram of **4** is depicted in Figure 5.[38]

The structure consists of a trinuclear arrangement of titanium metals with a single BINOLate ligand, as would

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(36) Compounds **3** and **4** were synthesized as outlined below employing (*S*)-BINOL in the synthesis of **4**. The ^{1}H and ^{13}C{^{1}H} NMR spectra of **3** and **4** indicate that **4** dissociates to form **3** and Ti(O*i*Pr)$_4$ in solution. **Preparation of 3.** Racemic BINOL (286 mg, 1.0 mmol) was dissolved in 10 mL of dichloromethane, and titanium tetraisopropoxide (568 mg, 2.0 mmol) was added at 23 °C. The resulting mixture was stirred for 60 min, and volatile materials were removed under reduced pressure. Recrystallization of the remaining solid from dichloromethane at −30 °C yielded X-ray quality crystals of **3** in 70% yield (512 mg, 0.7 mmol). ^{1}H NMR (CDCl$_3$, 500 MHz) δ 1.04 (d, $J = 5.7$ Hz, 3H), 1.10 (d, $J = 5.6$ Hz, 3H), 1.21 (s (broad), 30H), 4.51 (b, 6H), 6.75 (b, 1H), 7.1−7.2 (m, 3H), 7.2−7.3 (m, 3H), 7.3−7.4 (m, 1H), 7.47 (d, $J = 8.6$ Hz, 1H), 7.75 (d, $J = 8.8$ Hz, 1H), 7.78 (d, $J = 8.1$ Hz, 1H), 7.86 (d, $J = 8.1$ Hz, 1H) ppm; ^{13}C{^{1}H} NMR (CDCl$_3$, 125 MHz) δ 25.4, 25.6, 26.3 (b), 76.3 (b), 81.0, 118.5, 119.4, 121.1, 122.6, 122.8, 123.3, 125.1, 125.4, 126.9, 127.0, 127.8, 128.0, 128.1, 128.8, 129.9, 130.1, 133.1, 133.5, 158.9, 159.9 ppm.

(37) Crystal structure data for $C_{38}H_{54}O_8Ti_2$ (**3**): crystal size 0.44 × 0.32 × 0.02 mm, monoclinic, space group $P2_1/c$ (No. 14), $a = 18.9125(2)$, $b = 12.9863(1)$, and $c = 17.2672(2)$ Å, $b = 109.651(1)$, $V = 3993.89(7)$ Å^3, $Z = 4$, $\rho_{\text{calc}} = 1.222$ g/cm^{-3}, $2q_{\max} = 50.7°$, Mo Kα radiation, scan mode image plate φ-oscillations, $T = 210$ K, $m = 4.46$ cm^{-1}. Refinement on F^2 for 6334 reflections and 445 parameters gave R1 = 8.26 and wR2 = 15.16 for $I > 2\sigma(I)$. Residual electron density $-0.345 < \Delta\rho < 0.467$ e Å^{-3}.

(38) Crystal structure data for $C_{50}H_{82}O_{12}Ti_3$ (**4**): crystal size 0.35 × 0.18 × 0.12 mm, orthorhombic, space group $P2_12_12_1$ (No. 19), $a = 22.0884(1)$, $b = 24.2202(1)$, and $c = 10.2972(1)$ Å, $V = 5508.85(6)$ Å^3, $Z = 4$, $\rho_{\text{calc}} = 1.228$ g/cm^{-3}, $2q_{\max} = 50.7°$, Mo Kα radiation, scan mode image plate φ-oscillations, $T = 210$ K, $m = 4.79$ cm^{-1}. Refinement on F^2 for 9983 reflections and 623 parameters gave R1 = 4.45 and wR2 = 10.63 for $I > 2\sigma(I)$. Residual electron density $-0.325 < \Delta\rho < 0.533$ e Å^{-3}.

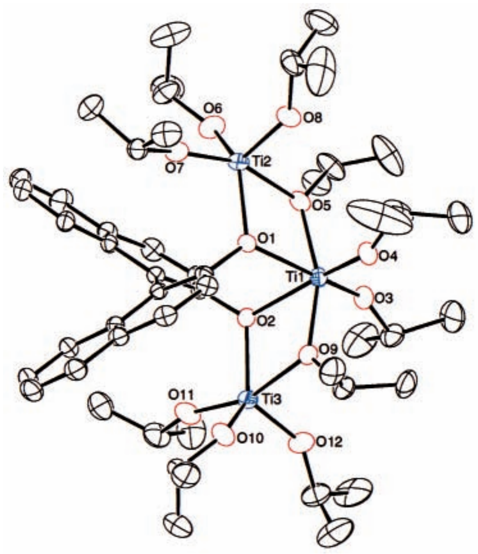

Figure 5. Structure of the trinuclear **4**. Bond distances are located in Table 1.

be expected if binuclear **3** had reacted with another equivalent of titanium tetraisopropoxide. Like trimer **2**, the central titanium in **4** has a distorted octahedral geometry and the terminal titanium centers have distorted trigonal-bipyramidal geometries. The naphthylate oxygens O(1) and O(2) bridge to Ti(2) and Ti(3) and exhibit shorter Ti−O distances to these centers than to Ti(1). Conversely, isopropoxy oxygens O(5) and O(9) form shorter distances to Ti(1) than to Ti(2) or Ti(3) (Table 1). When **4** is dissolved in $CDCl_3$, the $^{13}C\{^1H\}$ NMR spectrum is identical to binuclear **3** with excess titanium tetraisopropoxide, suggesting that loss of one titanium tetraisopropoxide from **4** is facile in solution.

In summary, the three structures of BINOLate−titanium complexes reported here present insight into the association of titanium and BINOL in the solid state. These aggregates are being considered in mechanistic studies that are currently ongoing in our laboratories.

Acknowledgment. This work was supported by the National Science Foundation (CHE-9733274).

Supporting Information Available: The X-ray data. This material is available free of charge via the Internet at http//pubs.acs.org.

OL0070381