

Synthesis of Unsymmetrical Diolate, Oxametallacyclopentene, Amido-Alkoxide and Thiolato-Alkoxide Complexes Using Dialkyl and Diaryl Titanium Aminotroponimate Complexes: A Route to Unsymmetrical Vicinal Diols

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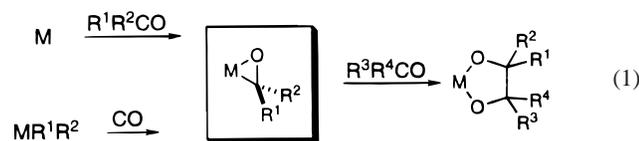
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Abstract: The reactivity of $[\text{TiR}_2(\text{Me}_2\text{ATI})_2]$ complexes, where $\text{Me}_2\text{ATI} = N,N'$ -dimethylaminotroponimate, or L, with CO or RNC in the presence of various organic electrophiles has been investigated. The compounds TiMe_2L_2 and TiPh_2L_2 react with CO and aldehydes or ketones to afford unsymmetrical diolate complexes that convert to the corresponding vicinal diols after hydrolysis. Phenyl acetylene also reacts to form the oxametallacyclopentene complex $[\text{Ti}(\text{OCMe}_2\text{CH}=\text{CPh})(\text{Me}_2\text{ATI})_2]$. Treatment of TiMe_2L_2 with RNC yields the free imine and a source of low-valent titanium. Trapping this intermediate with 2 equiv of benzaldehyde or benzil affords the titanium diolate or enediolate complex, respectively. When 1 equiv each of benzophenone and either *N*-tosylbenzaldimine or acetone were added to the intermediate, $[\text{Ti}(\text{Ph}_2\text{COCN}(\text{SO}_2\text{tol})\text{HPh})(\text{Me}_2\text{ATI})_2]$ and $[\text{Ti}(\text{Ph}_2\text{COCOMe}_2)(\text{Me}_2\text{ATI})_2]$, respectively, were obtained. The titanium thiolato-alkoxide complex $[\text{Ti}(\text{Ph}_2\text{CSCOMe}_2)(\text{Me}_2\text{ATI})_2]$ was prepared by use of thiobenzophenone and acetone. This chemistry allows for the preparation of unsymmetrical diols and oxametallacyclopentene complexes from Ti(IV) dialkyls, CO, and either carbonyl compounds or alkynes. Amido-alkoxide and thiolato-alkoxide complexes can be prepared by the reaction of Ti(IV) dialkyl complex, 2 equiv of benzophenone, and either an imine or thioketone.

Introduction

The facile preparation of unsymmetrical 1,2-diols and 2-amino alcohols is an important goal in synthetic chemistry.¹ The dihydroxylation and aminohydroxylation of olefins represents a powerful method for preparing these compounds.^{2,3} An alternative approach to the preparation of 1,2-functionalized hydrocarbons is the metal-mediated coupling of two dissimilar carbonyl compounds or the coupling of an imine with a carbonyl compound. These coupling methods rely on the formation of an η^2 -carbonyl complex, the metal–carbon bond of which possesses sufficient nucleophilicity to attack mild electrophiles. The requisite η^2 -carbonyl complex can be generated by treatment of a low-valent metal fragment with a carbonyl compound or by a multicomponent approach involving double alkyl migration to CO (eq 1). In this paper, we describe our use of both methods to prepare 1,2-diolate and amido-alkoxide complexes.



Several metal-mediated cross-coupling reactions of dissimilar carbonyl compounds have been reported (Figure 1). These methods employ low-valent group IV, group V, or lanthanide

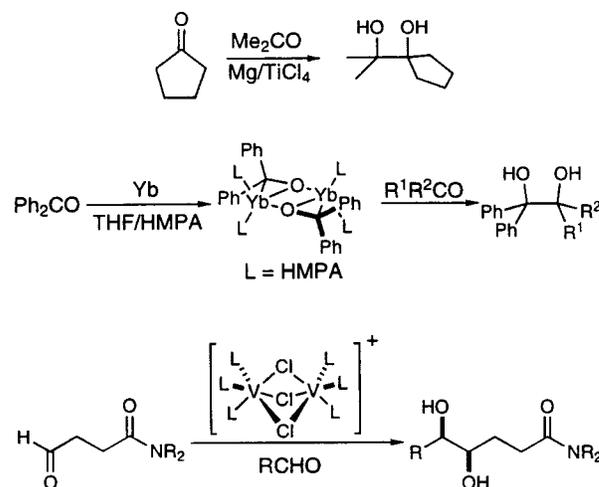


Figure 1. Representative metal-mediated syntheses of vicinal diols.

metals. In one of the first titanium-mediated syntheses of unsymmetrical diols, acetone was coupled with cyclic ketones to afford unsymmetrical diols.⁴ Little is known about the details of the titanium chemistry involved in this reaction. Subsequently, it was reported that treatment of equimolar amounts of Yb metal and benzophenone in THF and HMPA with carbonyl compounds or alkynes afforded unsymmetrical diols and allylic alcohols.⁵ The structurally characterized Yb(II) η^2 -benzophenone

(1) Wirth, T. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 61–63.
 (2) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483–2547.
 (3) Li, G.; Chang, H.-T.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 451–454.

(4) Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S. *J. Org. Chem.* **1976**, *41*, 260–265.

(5) Hou, Z.; Takamine, K.; Aoki, O.; Shiraiishi, H.; Fujiwara, Y.; Taniguchi, H. *J. Org. Chem.* **1988**, *53*, 6077–6084.

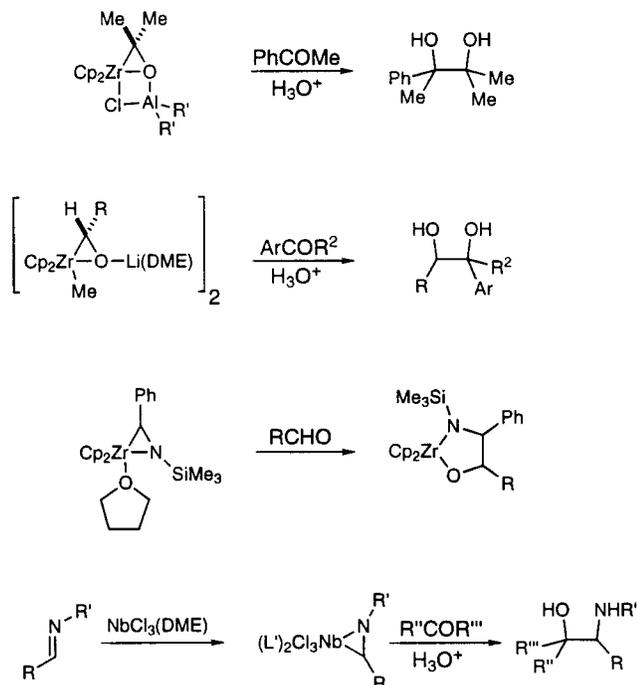


Figure 2. Syntheses of vicinal diols mediated by some well-defined carbonyl compounds and metal-mediated syntheses of amino-alcohols and amido-alkoxide complexes.

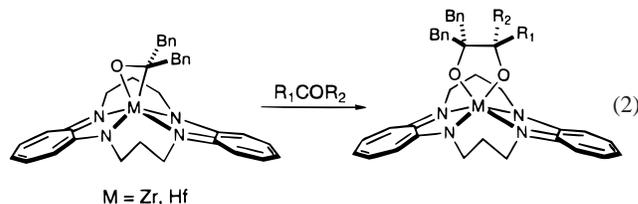
complex isolated from this reaction was a competent mediator of the coupling reactions.⁶ Finally, a vanadium(II) reagent and chelating, α -substituted aldehydes were employed to effect a hetero-*cross*-coupling reaction.⁷ Many mechanistic pathways can be envisioned for these transformations. Given the structure of the Yb η^2 -benzophenone complex, it is intriguing to consider that they all proceed by insertion of the electrophile into the metal-carbon bond of the early transition metal or lanthanide η^2 -carbonyl complex.

Two additional results support the notion that η^2 -carbonyl complexes are viable intermediates for coupling dissimilar carbonyl compounds. Acetophenone reacts with an Me₂AlCl-stabilized η^2 -ketone zirconocene complex to yield a zirconium diolate complex (Figure 2).⁸ In an extension of this work, lithium-stabilized zirconocene aldehyde complexes were allowed to react with aromatic aldehydes or ketones to afford vicinal diols in good isolated yield.⁹ An interesting feature of these two zirconocene systems is the presence of a Lewis acid (Li⁺ or Al³⁺) that could attenuate the reactivity of the carbonyl group prior to insertion. Substitution of an imine for the carbonyl group in this chemistry would afford 2-amino alcohols. The few methods reported to date for the metal-mediated synthesis of amino alcohols involve reaction of carbonyl compounds with early metal η^2 -imine complexes (Figure 2).¹⁰⁻¹²

We were interested to establish that the three-component coupling of a metal complex, CO, and carbonyl compound

would afford unsymmetrical diols. This approach offers versatility, since each of the reaction components can be varied. Moreover, it is not limited to the use of aromatic ketones, and the plentiful C₁ source, carbon monoxide, would be used. Electrophiles such as alkynes or imines would afford allylic alcohols and 2-amino alcohols, also useful materials. An alternative and complementary methodology that we wished to explore was the coupling of two distinct carbonyl compounds with a suitable low-valent metal complex.

Previous work in our laboratory demonstrated that zirconium and hafnium tropocoronand dialkyls react with CO to form isolable η^2 -ketone complexes. Chalcone, cyclohexenone, and cyclohexyl phenyl ketone react with these complexes to yield unsymmetrical zirconium diolates (eq 2).^{13,14} With this precedent



having been established, we wished to explore the scope of this chemistry and to extend it to a range of carbonyl compounds and other electrophiles as well as additional dialkylmetal starting materials. Titanium was substituted for zirconium to facilitate cleavage of the resultant metal diolate linkage under the reaction conditions. Aminotroponimate (R₂ATI) ligands were used in place of tropocoronands to facilitate the synthetic procedures and derivatization steps.

Here we describe two complementary methods for the in situ generation of titanium aminotroponimate η^2 -carbonyl complexes in order to prepare unsymmetrical diols and amido alkoxide complexes. The first procedure employs a multicomponent preparation of vicinal diols from titanium dialkyl complexes, CO, and carbonyl compounds. The second involves generation of transient low-valent titanium complexes to mediate the coupling of ketones with electrophiles such as an imine and other ketones. A portion of the former approach has been reported in preliminary form.¹⁵

Experimental Section

General Information. Hexane and benzene were distilled from sodium benzophenone ketyl under nitrogen. Toluene was distilled from sodium, and halogenated solvents were distilled from calcium hydride under nitrogen. Diethyl ether was passed through a column of activated alumina, and pentane was passed through a column of Ridox catalyst and alumina and then collected under vacuum. Benzaldehyde and *trans*-cinnamaldehyde were distilled from potassium carbonate, whereas acetophenone was distilled from calcium chloride; all three substrates were degassed three times and stored in a drybox over molecular sieves. Acetone was purified by preparation of the sodium iodide adduct, distillation, and degassing. Phenyl acetylene was distilled under reduced pressure and stored in a drybox. *tert*-Butyl isocyanide, xylol isocyanide, benzophenone, and benzil were used as received. CO gas (Airco) was used directly from the tank. TiR₂L₂,¹⁶ where L = Me₂ATI, thiobenzophenone,¹⁷ and the imines *N*-tosylbenzaldimine,¹⁸ *t*-BuN=CMe₂,^{19,20}

(13) Scott, M. J.; Lippard, S. J. *Organometallics* **1998**, *17*, 466-474.

(14) Scott, M. J.; Lippard, S. J. *J. Am. Chem. Soc.* **1997**, *119*, 3411-3412.

(15) Steinhuebel, D. P.; Lippard, S. J. *Organometallics* **1999**, *18*, 109-111.

(16) Steinhuebel, D. P.; Lippard, S. J. *Inorg. Chem.*, in press.

(17) Pedersen, B. S.; Scheibye, S.; Nilsson, N. H.; Lawesson, S.-O. *Bull. Soc. Chim. Belg.* **1978**, *87*, 223-228.

(6) Hou, Z.; Yamazaki, H.; Kobayashi, K.; Fujiwara, Y.; Taniguchi, H. *J. Chem. Soc., Chem. Commun.* **1992**, 722-724.

(7) Freudenberg, J. H.; Konradi, A. W.; Pedersen, S. F. *J. Am. Chem. Soc.* **1989**, *111*, 8014-8016.

(8) Waymouth, R. M.; Clauser, K. R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1986**, *108*, 6385-6387.

(9) Askham, F. R.; Carroll, K. M. *J. Org. Chem.* **1993**, *58*, 7328-7329.

(10) Buchwald, S. L.; Watson, B. T.; Wannamaker, M. W.; Dewan, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 4486-4494.

(11) Roskamp, E. J.; Pedersen, S. F. *J. Am. Chem. Soc.* **1987**, *109*, 6551-6553.

(12) Ito, H.; Taguchi, T.; Hanzawa, Y. *Tetrahedron Lett.* **1992**, *33*, 4469-4472.

and 2,6-Me₂C₆H₃N=CMe₂²¹ were prepared by following literature procedures. Experiments were either performed in a nitrogen-filled glovebox or by conventional Schlenk line techniques under argon. Chromatographic purification of products was accomplished using silica gel-60 (230–400 mesh) by a published method.²² Thin-layer chromatography (TLC) analyses were performed on silica plates and visualized by both aqueous ceric ammonium molybdate (CAM) stain and/or UV irradiation. Routine NMR spectra were recorded on a Bruker AC 250, Varian Unity, or Mercury 300 spectrometer at ambient probe temperature and referenced to the internal ¹H and ¹³C solvent peaks. NOESY experiments were performed on a Varian 501 at 283 K. Infrared spectra were recorded as pressed KBr disks with a BioRad FTS-135 FTIR spectrometer. Mass spectra were determined on a Finnegan 4000 mass spectrometer with 70-eV ionization.

Synthetic Procedures. [Ti(PhHCOCOMe₂)(Me₂ATI)₂] (**1**). A portion of TiMe₂L₂ (72 mg, 0.193 mmol) was dissolved in 15 mL of a 1:1 toluene–benzene mixture in a 25-mL Schlenk flask equipped with a stir bar and septum. This solution was cooled to –30 °C, and benzaldehyde (19.6 μL, 0.193 mmol) was added. The flask was quickly removed from the drybox, and CO was purged through the solution for 20 min (10–20 psi). The light red solution was stirred for an additional 1 h under a CO pressure. The solvent was evaporated and the flask brought into the drybox. Extraction with ether, filtration, and evaporation yielded a red solid. Diffusion of pentane into a saturated toluene solution at –30 °C yielded small red needles suitable for X-ray crystallography. ¹H NMR (C₆D₆): δ 7.52 (4H, d, *J* = 7.9 Hz), 7.13 (3H, m), 6.82 (4H, q, *J* = 9.3 Hz), 6.51 (1H, s), 6.27 (4H, m), 3.38 (3H, s), 3.20 (9H, s), 1.49 (3H, s), 1.38 (3H, s). ¹H NMR (CD₂Cl₂): δ 7.21 (9H, m), 6.49 (6H, m), 6.15 (1H, s), 3.44 (9H, s), 3.42 (3H, s), 1.28 (3H, s), 1.07 (3H, s). Anal. Calcd for TiC₂₈H₃₄N₄O₂: C, 66.40; H, 6.77; N, 11.06. Found: C, 66.21; H, 6.78; N, 11.38.

[Ti(Ph₂COCOME₂)(Me₂ATI)₂] (**2**). A portion of TiPh₂L₂ (100 mg, 0.201 mmol) was dissolved in 15 mL of toluene in a 25-mL Schlenk flask equipped with a stir bar and septum. Acetone (14.8 μL, 0.201 mmol) was dissolved in 5 mL of toluene in a vial capped by a septum, and both flasks were withdrawn from the drybox. The acetone solution was added to the titanium complex at –78 °C, and the solution was purged with CO for 20 min (10–20 psi); after 10 min, the cooling bath was removed. The light red solution was stirred for an additional 1.5 h under a positive pressure of CO, and the solvent was then removed. The dark red residue was extracted with benzene and then evaporated to dryness. Vapor diffusion of pentane into a saturated benzene solution yielded large red blocks (47 mg, 40%) suitable for X-ray crystallography. ¹H NMR (250 MHz, C₆D₆, 25 °C): δ 7.91 (4H, d, *J* = 7.1 Hz), 7.14 (8H, m), 6.85 (4H, t, *J* = 9.9), 6.28 (4H, m), 3.23 (12H, s), 1.78 (6H, s). Anal. Calcd for TiC₃₄H₃₈N₄O₂: C, 70.10; H, 6.57; N, 9.62. Found: C, 70.57; H, 6.90; N, 9.60.

[PhHC(OH)C(OH)Me₂] (**3**). A portion of TiMe₂L₂ (104 mg, 0.279 mmol) was dissolved in 15 mL of toluene in a 25-mL round-bottom flask equipped with a stir bar and rubber septum. This solution was cooled to –30 °C, and benzaldehyde (29 μL, 0.279 mmol) was added. The flask was quickly removed from the drybox, and CO was bubbled through the solution for 20 min at 0 °C (10–20 psi). The light red solution was stirred for an additional 2 h under positive CO pressure. The reaction was quenched with 3 M aqueous HCl and the biphasic mixture stirred for 1 h. The solution was extracted three times with CH₂Cl₂, dried with MgSO₄, filtered, and evaporated to dryness. Flash chromatography on silica gel (1:1:2 hexanes/EtOAc/CH₂Cl₂) yielded the product as a colorless, crystalline solid (28 mg, 60%). TLC: *R*_f = 0.26 (1:1:1 hexanes/EtOAc/CH₂Cl₂). ¹H NMR (250 MHz, CD₃OD, 25 °C): δ 7.33 (5H, m), 4.53 (1H, s), 1.20 (6H, s). ¹³C{¹H} (62.9 MHz,

CD₃OD, 25 °C) NMR: δ 143.1, 129.1, 128.6, 128.4, 81.9, 74.1, 26.3, 26.2. HRMS (EI): calcd for C₁₀H₁₄O₂ 166.0994, found 166.0994.

[PhMeC(OH)C(OH)Me₂] (**4**). A portion of TiMe₂L₂ (115 mg, 0.309 mmol) was dissolved in 15 mL of toluene in a 25-mL round-bottom flask equipped with a stir bar and septum. This flask was removed from the drybox and cooled to –78 °C, and acetophenone (32.5 μL, 0.309 mmol) was added. CO was purged through the solution for 20 min (10–20 psi), and at the 10 min point the cooling bath was removed. The light red solution was stirred for an additional 2 h under CO pressure. The reaction was worked up in a manner identical to that described for **3** to yield 44 mg (79%) of the crystalline diol. TLC: *R*_f = 0.29 (2:1:3 hexanes/EtOAc/CH₂Cl₂). ¹H NMR (250 MHz, CD₃OD): δ 7.51 (2H, dd, *J* = 8.7, 7.9 Hz), 7.21 (3H, m), 1.58 (3H, s), 1.11 (3H, s), 1.09 (3H, s). ¹³C{¹H} NMR (62.9 MHz, CD₃OD): δ 147.2, 128.3, 127.5, 79.3, 76.1, 25.6, 25.6, 24.7. Anal. Calcd for C₁₁H₁₆O₂: C, 73.30; H, 8.95. Found: C, 73.07; H, 8.58.

[PhCH=CH(H)C(OH)C(OH)Me₂] (**5**). A portion of TiMe₂L₂ (140 mg, 0.376 mmol) was dissolved in 15 mL of toluene in a 25-mL round-bottom flask equipped with a stir bar and septum. Cinnamaldehyde (47.4 μL, 0.376 mmol) was dissolved in 5 mL of toluene, and both vessels were removed from the drybox. The titanium complex was cooled to –78 °C, and the aldehyde was added under argon. CO was purged through the solution for 20 min (10–20 psi), and at the 10 min point the cooling bath was removed. The light red solution was stirred for an additional 2 h under a CO pressure, and TLC showed consumption of cinnamaldehyde. Identical workup to that described for **3** and flash chromatography (gradient elution, 3:2 to 1:1 hexanes/EtOAc) yielded 40 mg of the major product as a microcrystalline solid (55%) and 8 mg (15%) of a minor product. TLC (major): *R*_f = 0.37 (1:1 hexanes/EtOAc). ¹H NMR (250 MHz, CD₃OD): δ 7.38 (2H, d, *J* = 7.8 Hz), 7.21 (3H, m), 6.61 (1H, d, *J* = 16.0 Hz), 6.32 (1H, dd, *J* = 6.8, 16.0 Hz), 3.96 (1H, d, *J* = 7.3 Hz), 1.18 (3H, s), 1.17 (3H, s). ¹³C{¹H} NMR (62.9 MHz, CD₃OD): δ 138.7, 133.3, 130.2, 129.7, 128.7, 127.6, 80.7, 73.9, 26.5, 25.6. HRMS (EI): Calcd for C₁₂H₁₆O₂ 192.1150, Found 192.1149.

[PhHC(OH)C(OH)Ph₂] (**6**). A portion of TiPh₂L₂ (52 mg, 0.105 mmol) was dissolved in 15 mL of CH₂Cl₂ in a 25-mL round-bottom flask equipped with a stir bar and septum. This solution was cooled to –30 °C and benzaldehyde (11 μL, 0.105 mmol) added. The flask was quickly removed from the drybox, CO was purged through the solution for 15 min (10–20 psi), and the light red solution was stirred for an additional 4 h under a CO pressure. The reaction was worked up in a manner identical to that described for **3**, except that 5:1:0.5 hexanes/CH₂Cl₂/EtOAc was used, to yield 21.6 mg (70%) of the crystalline diol. Vapor diffusion of hexanes into a saturated chloroform solution at room temperature afforded colorless blocks that were used for elemental analysis. TLC: *R*_f = 0.28 (5:1:0.5 hexanes/CH₂Cl₂/EtOAc). ¹H NMR (250 MHz, CD₃OD): δ 7.60 (2H, d, *J* = 7.5 Hz), 7.15 (13H, m), 5.55 (1H, s). ¹³C{¹H} NMR (62.9 MHz, CD₃OD): δ 147.6, 146.5, 142.3, 129.9, 128.9, 128.8, 128.4, 128.0, 127.9, 127.8, 127.4, 82.0, 76.9. Anal. Calcd for C₂₀H₁₈O₂: C, 82.73; H, 6.25. Found: C, 82.82; H, 6.22.

[Me₂C(OH)C(OH)Ph₂] (**7**). TiPh₂L₂ (110 mg, 0.221 mmol) was dissolved in 15 mL of CH₂Cl₂ in a 25-mL round-bottom flask equipped with a stir bar and septum. Acetone (16.3 μL, 0.122 mmol) was dissolved in 5 mL of CH₂Cl₂ in a vial, and both flasks were withdrawn from the drybox. The acetone solution was added to the titanium complex at –78 °C, and CO was purged through the solution for 20 min; at the 10 min point the cooling bath was removed. The light red solution was stirred for an additional 3 h under a CO pressure (10–15 psi). The reaction was worked up in a manner identical to that described for **3** by using 5:1:0.5 hexanes/CH₂Cl₂/EtOAc to yield 27.4 mg (52%) of a crystalline diol. TLC: *R*_f = 0.21 (5:1:0.5 hexanes/CH₂Cl₂/EtOAc). ¹H NMR (250 MHz, CD₃OD): δ 7.67 (4H, d, *J* = 8.3 Hz), 7.18 (6H, m), 1.24 (6H, s). ¹³C{¹H} NMR (62.9 MHz, CD₃OD): δ 147.0, 129.8, 128.3, 127.6, 83.5, 77.4, 27.3. Anal. Calcd for C₁₆H₁₈O₂: C, 79.31; H, 7.49. Found: C, 79.03; H, 7.58.

[PhCH=CH(H)C(OH)C(OH)Ph₂] (**8**). A portion of TiPh₂L₂ (112 mg, 0.222 mmol) was dissolved in 10 mL of CH₂Cl₂ in a 25-mL round-bottom flask equipped with a stir bar and septum. Cinnamaldehyde (28.5 μL, 0.222 mmol) was dissolved in 5 mL of toluene, and both

(18) Jennings, W. B.; Lovely, C. J. *Tetrahedron Lett.* **1988**, *29*, 3725–3728.

(19) Quast, H.; Meichsner, G.; Seiferling, B. *Chem. Ber.* **1987**, *120*, 225–230.

(20) Weingarten, H.; Chupp, J. P.; White, W. A. *J. Org. Chem.* **1967**, *32*, 3246–3249.

(21) Walsh, P. J.; Baranger, A. M.; Bergman, R. G. *J. Am. Chem. Soc.* **1992**, *114*, 1708–1719.

(22) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

vessels were removed from the drybox. An analogous procedure to **5** was used, and flash chromatography (5:1:0.5 hexanes/CH₂Cl₂/EtOAc) yielded 50.0 mg of the product as a microcrystalline solid (70%). TLC: $R_f = 0.26$ (5:1:0.5 hexanes/CH₂Cl₂/EtOAc). ¹H NMR (250 MHz, CD₃OD): δ 7.59 (2H, d, $J = 8.6$ Hz), 7.43 (2H, d, $J = 8.8$ Hz), 7.23 (1H, m), 6.49 (1H, d, $J = 15.8$ Hz), 6.22 (1H, dd, $J = 15.8, 6.7$ Hz), 5.14 (1H, d, $J = 6.7$). ¹³C {¹H} NMR (125.77 MHz, CD₃OD): δ 144.8, 143.8, 136.7, 133.7, 128.7, 128.7, 128.4, 127.9, 127.6, 127.3, 126.9, 126.8, 126.7, 126.2, 80.3, 76.8.

[PhHC(OH)C(OH)MePh] (9). A portion of TiMePhL₂ (96 mg, 0.221 mmol) was dissolved in 15 mL of toluene in a 25-mL round-bottom flask equipped with a stir bar and septum. Benzaldehyde (22.5 μ L, 0.221 mmol) was added at -78 °C, and CO was purged through the solution for 15 min (10–20 psi). The light red solution was stirred for an additional 2 h under a CO pressure (10–15 psi). The reaction was worked up in a manner identical to that described for **3** using 3:1:0.5 hexanes/CH₂Cl₂/EtOAc to yield 33.5 mg (66%) of an equal mixture of diastereomeric diols that matched spectra reported in the literature.⁹ TLC: $R_f = 0.18$ (3:1:0.5 hexanes/CH₂Cl₂/EtOAc). ¹H NMR (250 MHz, CDCl₃): δ 7.23 (20H, m), 4.84 (1H, s), 4.76 (1H, s), 1.63 (3H, s), 1.38 (3H, s).

[Ti(Me₂C(O)HC=CPh)(Me₂ATI)₂] (10). A solution of TiMe₂L₂ (147 mg, 0.395 mmol) in benzene was treated with phenyl acetylene (47.7 μ L, 0.434 mmol) in a 25-mL Schlenk flask. The flask was removed from the drybox, and CO (10–20 psi) was carefully purged through the solution for 7 min and then stirred under a CO atmosphere for 1 h. The solvent was removed and the flask brought into the drybox. The red residue was extracted with Et₂O and filtered, and the ether was removed to yield a red foam. This material was dissolved in a minimum amount of CH₂Cl₂, and diffusion of pentane at -30 °C over 2 days yielded red microcrystalline material (110 mg, 2 crops, 54%). ¹H NMR (250 MHz, C₆D₆, 25 °C): δ 7.10 (2H, s), 6.97 (1H, m), 6.88 (6H, m), 6.57 (1H, s), 6.21 (6H, m), 3.12 (12H, s), 1.67 (6H, s). ¹³C {¹H} NMR (75 MHz, CD₂Cl₂, 25 °C): δ 207.0, 164.9, 152.9, 152.7, 135.9, 127.4, 125.9, 123.4, 120.8, 112.4, 88.0, 44.2, 30.5. IR (KBr, cm⁻¹) 3075, 3009, 2954, 2906, 2865, 2792, 1590, 1569, 1509, 1450, 1422, 1401, 1378, 1365, 1346, 1267, 1229, 1148, 1101, 1039, 981, 965, 909, 886, 807, 738, 759, 704, 645, 604, 570, 546, 594. The peak due to the dichloromethane solvate molecule is not included in the foregoing list. Anal. Calcd for TiC₂₉H₃₄N₄O·0.15CH₂Cl₂: C, 67.95; H, 6.71; N, 10.87. Found: C, 67.70; H, 6.36; N, 10.54.

[Ti(PhHCOCOPhH)(Me₂ATI)₂] (11). A benzene solution of *t*-BuNC (43.4 μ L, 0.384 mmol) was added dropwise to a -30 °C solution of TiMe₂L₂ (143 mg, 0.384 mmol) and benzaldehyde (78.0 μ L, 0.768 mmol) in benzene. The light red solution became slightly darker and was stirred for 4 h. The solution was then filtered and the solvent evaporated. The residue was dissolved in hot benzene, and after cooling to room temperature, pentane was layered on the solution. Red blocks (149 mg, 69%) formed that were suitable for X-ray crystallography. ¹H NMR (C₆D₆): δ 7.38 (4H, d, $J = 7.0$ Hz), 7.06 (6H, m), 6.85 (4H, t, $J = 10.2$ Hz), 6.55 (2H, s), 6.31 (6H, m), 3.35 (12H, s). ¹³C {¹H} NMR (75 MHz, C₆D₆, 25 °C): δ 165.5, 144.2, 136.2, 128.5, 127.7, 127.5, 120.6, 112.5, 102.8, 40.5. Anal. Calcd for TiC₃₂H₃₄N₄O₂: C, 69.31; H, 6.18; N, 10.10. Found: C, 68.89; H, 6.45; N, 10.15.

[Ti(PhCOCOPh)(Me₂ATI)₂] (12). A benzene solution of *t*-BuNC (28 μ L, 0.247 mmol) and benzil (52 mg, 0.247) was added to a cold solution of TiMe₂L₂ (92 mg, 0.247 mmol) in benzene. The brown solution was warmed to room temperature, stirred for 3 h, and then evaporated to dryness. Vapor diffusion of pentane into a saturated THF solution at -30 °C yielded a brown crystalline mass that was washed with pentane and dried (80 mg, 59%). ¹H NMR (250 MHz, C₆D₆, 25 °C): δ 7.85 (4H, d, $J = 7.5$ Hz), 7.11 (4H, t, $J = 7.4$ Hz), 6.96 (2H, m), 6.73 (4H, t, $J = 10.1$ Hz), 6.21 (6H, m), 3.35 (12H, s). ¹³C {¹H} NMR (75 MHz, C₆D₆): δ 164.2, 145.9, 137.4, 136.2, 127.9, 127.2, 126.1, 121.2, 112.7, 40.7. IR (KBr, cm⁻¹) 3061, 3004, 2869, 2801, 1958, 1871, 1758, 1686, 1600, 1588, 1512, 1425, 1427, 1400, 1357, 1267, 1229, 1149, 1135, 1101, 1067, 1037, 982, 925, 912, 888, 828, 730, 749, 722, 695, 657, 623, 531, 505, 488, 531, 419. Anal. Calcd for TiC₃₂H₃₂N₄O₂: C, 69.56; H, 5.84; N 10.14. Found: C, 69.68; H, 6.31; N, 9.62.

[Ti(Ph₂COCOPh₂)(Me₂ATI)₂] (13). A benzene solution of *t*-BuNC (33 μ L, 0.293 mmol) and benzophenone (106 mg, 0.586 mmol) was added to a solution of TiMe₂L₂ (109 mg, 0.293 mmol) in a 3:1 mixture of benzene–ether at -30 °C. The brown solution was warmed to room temperature and stirred for 1 h, and then the solvent was removed. Vapor diffusion of pentane into a saturated toluene solution at -30 °C yielded a red crystalline mass. ¹H NMR (250 MHz, C₆D₆, 25 °C): δ 7.75 (8H, d, $J = 6.7$ Hz), 6.98 (12H, m), 6.78 (4H, q, $J = 11.2$ Hz), 6.23 (4H, t, $J = 7.7$ Hz), 6.15 (2H, d, $J = 10.0$ Hz), 3.14 (12H, s). ¹³C {¹H} NMR (75 MHz, C₆D₆, 25 °C): δ 164.7, 149.9, 136.1, 129.3, 127.5, 126.5, 120.7, 105.5, 41.6. Anal. Calcd for TiC₄₄H₄₂N₄O₂: C, 74.78; H, 5.99; N 7.93. Found: C, 74.68; H, 6.25; N, 7.87.

[Ti(Ph₂COCN(SO₂tol)HPh)(Me₂ATI)₂] (14). To a benzene solution of benzophenone (50.96 mg, 0.269 mmol), *N*-tosylbenzaldimine (72.4 mg, 0.269 mmol), and *t*-BuNC (31.5 μ L, 0.269 mmol) was added a cold solution of TiMe₂L₂ (100 mg, 0.269 mmol) in benzene. The red-brown solution was stirred overnight and filtered, and then the solvent was removed. The dark solid was dissolved in hot benzene (8 mL) and filtered, and after cooling, pentane was carefully layered on the solution. Storage for 1 day at room temperature yielded large red blocks contaminated with a small amount of long red needles that could be separated by hand. The sample for elemental analysis and X-ray crystallography was crystallized a second time from benzene/pentane (75 mg, 36%). ¹H NMR (300 MHz, CDCl₃, 25 °C): δ 7.56 (2H, d, $J = 6.3$ Hz), 7.20 (4H, m), 7.0 (4H, m), 6.86 (2H, m), 6.75 (14H, m), 6.17 (2H, d, $J = 7.5$ Hz), 5.91 (2H, d, $J = 11.1$ Hz), 3.85 (3H, s), 3.29 (3H, s), 3.19 (3H, s), 2.72 (3H, s), 1.93 (3H, s). ¹³C {¹H} NMR (75 MHz, C₆D₆): δ 165.4, 165.2, 164.5, 163.9, 163.8, 163.3, 149.1, 146.8, 141.2, 139.4, 139.3, 136.8, 136.4, 136.3, 135.2, 134.9, 129.9, 127.8, 127.6, 127.2, 127.1, 126.9, 126.8, 126.5, 126.1, 125.3, 124.9, 123.0, 121.8, 118.7, 115.1, 114.1, 112.7, 112.1, 111.5, 109.9, 97.2, 80.1, 44.9, 43.9, 42.6, 42.1, 41.1, 38.6, 21.3. IR (KBr, cm⁻¹) 3064, 3031, 2867, 2813, 1567, 1512, 1452, 1420, 1402, 1355, 1304, 1264, 1230, 1172, 1141, 1087, 1038, 981, 947, 920, 887, 803, 793, 747, 699, 680, 669, 617, 591, 566, 530, 501, 421. Anal. Calcd for TiC₄₄H₄₅N₅SO₃: C, 68.95; H, 5.79; N 8.93. Found: C, 69.14; H, 6.51; N, 9.13.

[Ti(Ph₂CSCOME₂)(Me₂ATI)₂] (15). A portion of TiMe₂L₂ (59 mg, 0.158 mmol) was dissolved in 15 mL of benzene and frozen. In a separate vial, xylyl isocyanide (21 mg, 0.158) and thiobenzophenone (31 mg, 0.158) were dissolved in 5 mL of benzene. This solution was added to the thawed solution of metal complex, and stirring was continued for 1.5 h. Neat acetone (11.6 μ L, 0.158 mmol) was then added to the brown solution, which resulted in an immediate color change to red. The solution was stirred for an additional hour, filtered, and then evaporated to dryness. The red solid was dissolved in a minimum amount of warm benzene, and after cooling, pentane was diffused into the solution to yield red-brown crystals (45 mg, 42%) that were suitable for X-ray crystallography. ¹H NMR (300 MHz, C₆D₆, 25 °C): δ 7.84 (4H, m), 7.05 (6H, m), 6.84 (4H, t, $J = 10.8$ Hz), 6.29 (6H, m), 3.27 (6H, s), 3.09 (6H, s), 1.74 (6H, s). ¹³C {¹H} NMR (75 MHz, CDCl₃, 25 °C): δ 165.3, 164.1, 148.9, 135.6, 135.4, 128.5, 126.8, 125.2, 120.9, 113.6, 110.9, 98.3, 86.1, 44.0, 29.5. A benzene solvate molecule was identified by X-ray crystallography and ¹H NMR spectroscopy and the peaks are not listed above. Anal. Calcd for TiC₃₄H₃₈N₄O·C₆H₆: C, 70.99; H, 6.55; N, 8.28. Found: C, 71.10; H, 6.57; N, 8.40.

Collection and Reduction of X-ray Data. All crystals were covered with Paratone-N (Exxon) and then removed from the drybox for examination. Suitable single crystals were attached to the tips of quartz fibers and transferred to a Bruker CCD X-ray diffraction system with graphite-monochromatized Mo K α radiation ($\lambda = 0.71073$ Å) controlled by a pentium-based PC running the SMART software package. The temperature of the crystal was maintained with a Bruker LT-2A nitrogen cryostat. Procedures for data collection and reduction have been previously reported.²³ Space groups were determined by examining systematic absences and confirmed by the successful solution and refinement of the structures. The structures were solved by using either the direct methods program SIR-92,²⁴ XS, or Patterson methods and

(23) Feig, A. L.; Bautista, M. T.; Lippard, S. J. *Inorg. Chem.* **1996**, *35*, 6892–6898.

(24) Burla, M. C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Polidori, G.; Spagna, R.; Viterbo, D. *J. Appl. Crystallogr.* **1989**, *22*, 389–393.

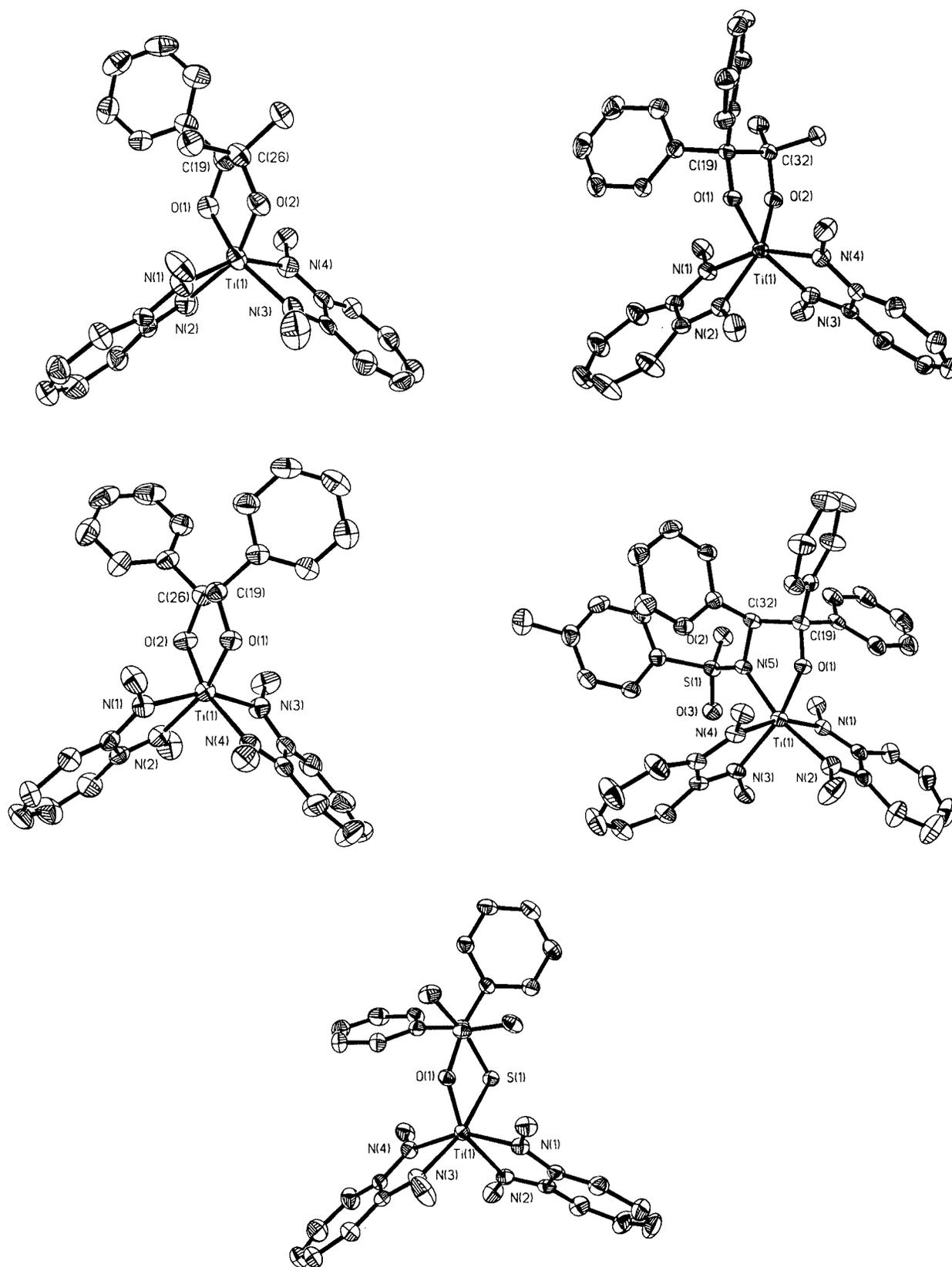


Figure 3. ORTEP diagrams (starting from left) of **1**, **2**, **11**, **14**, and **15** showing 50% thermal ellipsoids and selected atom labels.

then refined by full-matrix least-squares and Fourier techniques with SHELXTL-PLUS.²⁵ In general, all non-hydrogen atoms were refined anisotropically. Hydrogen atoms were either located from difference

(25) SHELXTL: Structure Analysis Program. 5.1; Bruker Analytical X-ray Systems; Madison, WI, 1997.

Fourier maps (**1** and **2**) and refined isotropically or assigned idealized positions and given a thermal parameter 1.2 times the thermal parameter of the carbon atom to which each was attached (**11**, **14**, and **15**). Absorption corrections were performed with the SADABS program.²⁶ Both **14** and **15** crystallize as benzene solvates. In **14**·C₆H₆ and **15**·

Table 1. Summary of X-ray Crystallographic Data

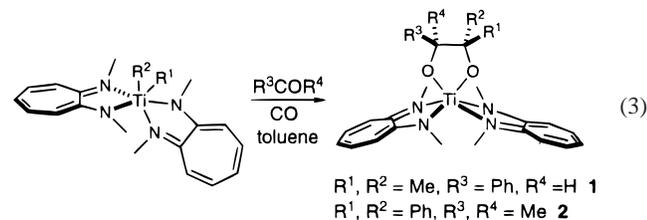
complex	1	2	11	14 ·C ₆ H ₆	15 ·C ₆ H ₆
formula	C ₂₈ H ₃₄ N ₄ O ₂ Ti	C ₃₄ H ₃₈ N ₄ O ₂ Ti	C ₃₂ H ₃₄ N ₄ O ₂ Ti	C ₅₁ H ₄₁ N ₅ O ₃ STi	C ₄₀ H ₄₄ N ₄ O ₂ STi
fw	506.49	582.58	554.53	861.93	676.75
space grp	<i>P</i> 2 ₁ / <i>n</i>	<i>P</i> 2 ₁ / <i>c</i>	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$
<i>a</i> , Å	13.336(11)	16.222(2)	10.384(3)	13.233(4)	10.9698(7)
<i>b</i> , Å	14.275(9)	15.452(2)	13.028(4)	13.823(4)	13.1873(9)
<i>c</i> , Å	14.095(8)	11.892(2)	13.305(5)	13.863(3)	14.6300(9)
α , deg			118.10(2)	60.514(15)	115.080(1)
β , deg	106.81(5)	91.81(1)	92.91(4)	88.66(2)	94.619(1)
γ , deg			110.73(2)	87.33(2)	109.801(2)
<i>V</i> , Å ³	2568(3)	2979.4(7)	1432.2(8)	2205.0(10)	1740.0(2)
<i>Z</i>	4	4	2	2	2
ρ_{calc} , g/cm ³	1.310	1.299	1.286	1.298	1.292
<i>T</i> , °C	−85	−85	−85	−85	−85
$\mu(\text{Mo K}\alpha)$, mm ^{−1}	0.365	0.325	0.334	0.291	0.344
2 θ limits, deg	3.70–46.54	3.64–56.56	3.60–56.56	3.08–56.46	3.18–56.46
total no. of data	10205	18065	8199	13993	11039
no. of unique data	3642	6876	5843	9759	7714
obsd data ^a	2167	5728	3282	5559	4813
no. of param	452	522	352	520	424
<i>R</i> ^b	0.0745	0.0349	0.0868	0.0595	0.0526
w <i>R</i> ^{2c}	0.1096	0.0928	0.1680	0.1577	0.1331
max, min peaks, e/Å ³	0.255, −0.292	0.295, −0.509	0.506, −0.454	0.761, −0.537	0.624, −0.539

^a Observation criterion: $I > 2\sigma(I)$. ^b $R = \sum||F_o| - |F_c||/\sum|F_o|$. ^c $wR^2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{1/2}$.

C₆H₆ the carbon atoms of the benzene molecule were refined anisotropically and hydrogen atoms were added. Partially labeled ORTEP plots of all structures displaying 50% thermal ellipsoids are presented in Figure 3. Crystallographic data including selected bond distances and angles can be found in Tables 1 and 2; full crystallographic details are included in the Supporting Information, Tables S1–S15.

Results and Discussion

Preparation of Unsymmetrical Diols. A three-component coupling of dialkyl titanium complexes, CO, and carbonyl compounds was achieved. Solutions of TiMe₂L₂ react rapidly with CO. By analogy with previous work on zirconium,¹³ we assume that double alkyl migration to CO occurs to produce [Ti(η^2 -Me₂CO)(Me₂ATI)₂], which could not be isolated. Upon addition of electrophiles, however, coupled products were obtained. A benzene solution of TiMe₂L₂ and 1 equiv of benzaldehyde reacted rapidly and cleanly with CO to afford a single product (eq 3). The ¹H NMR spectrum of this material



in C₆D₆ consisted of two 3H singlets at 1.49 and 1.38 ppm, assigned to the protons on inequivalent methyl groups of the diolate ligand. In addition to aromatic peaks, two broad resonances at 3.38 and 3.20 ppm were observed for the methyl groups of the ATI ligand. The formulation of this complex as the unsymmetrical diolate [Ti(PhHCOCOMe₂)(Me₂ATI)₂] (**1**) was confirmed by X-ray crystallography (Figure 3). The coordination geometry of **1** is nearly octahedral and the short Ti–O distances of 1.862(4) and 1.888(4) Å suggest that titanium–oxygen bond formation helps to drive this reaction.

(26) Program written by Professor George Sheldrick at University of Göttingen which corrects data collected on Bruker CCD and multiwire detectors for absorption and decay.

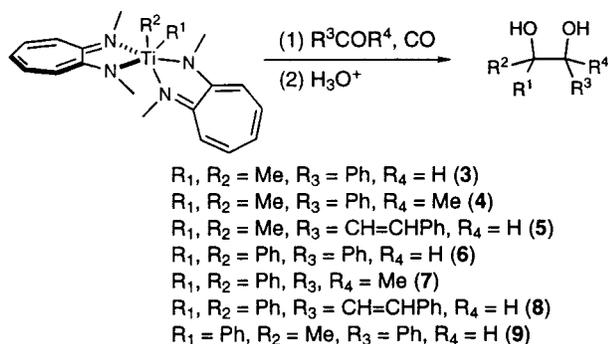
Table 2. Selected Bond Distances and Angles^a

complex	distances (Å)		angles (deg)		
1	Ti–O(1)	1.888(4)	N(1)–Ti–N(4)	155.0(2)	
	Ti–O(2)	1.862(4)	N(3)–Ti–O(1)	160.2(2)	
	Ti–N(1)	2.109(4)	O(2)–Ti–N(2)	155.7(2)	
	Ti–N(2)	2.104(4)	O(1)–Ti–O(2)	81.2(2)	
	Ti–N(3)	2.121(5)	N(3)–Ti–O(2)	94.8(2)	
	Ti–N(4)	2.106(4)			
	O(1)–C(19)	1.407(6)			
	O(2)–C(26)	1.417(6)			
	C(19)–C(26)	1.576(7)			
	C(26)–C(27)	1.509(8)			
	C(19)–C(20)	1.521(7)			
	2	Ti–N(1)	2.078(1)	N(4)–Ti–N(1)	157.24(5)
		Ti–N(2)	2.134(1)	O(2)–Ti–N(2)	161.08(5)
Ti–N(3)		2.139(1)	O(1)–Ti–N(3)	162.05(5)	
Ti–N(4)		2.079(1)	O(1)–Ti–O(2)	80.37(4)	
Ti–O(1)		1.875(1)	Ti–O(1)–C(19)	121.27(8)	
Ti–O(2)		1.862(1)	O(1)–Ti–N(4)	92.03(4)	
C(19)–C(32)		1.610(2)			
11		Ti–N(1)	2.085(4)	N(4)–Ti–O(2)	162.7(2)
		Ti–N(2)	2.109(4)	N(1)–Ti–N(3)	156.0(2)
	Ti–N(3)	2.086(4)	N(2)–Ti–O(1)	163.2(2)	
	Ti–N(4)	2.105(4)	O(1)–Ti–O(2)	81.5(1)	
	Ti–O(1)	1.878(3)	Ti–O(1)–C(19)	118.8(3)	
	Ti–O(2)	1.872(3)			
	14	Ti–N(1)	2.092(3)	N(4)–Ti–N(1)	160.9(1)
		Ti–N(2)	2.087(3)	N(3)–Ti–O(1)	162.3(1)
		Ti–N(3)	2.099(3)	N(2)–Ti–N(5)	165.5(1)
		Ti–N(4)	2.077(3)	Ti–N(5)–C(32)	114.7(2)
Ti–N(5)		2.110(3)	Ti–O(1)–C(19)	123.0(2)	
Ti–O(1)		1.864(2)			
C(19)–C(32)		1.568(5)			
15		Ti–N(1)	2.083(2)	N(1)–Ti–N(4)	155.07(9)
		Ti–N(2)	2.126(2)	N(3)–Ti–S(1)	163.77(7)
		Ti–N(3)	2.103(2)	N(2)–Ti–O(1)	155.28(9)
	Ti–N(4)	2.142(2)	O(1)–Ti–S(1)	79.85(6)	
	Ti–O(1)	1.831(2)	Ti–O(1)–C(20)	131.4(2)	
	Ti–S(1)	2.4245(9)	Ti–S(1)–C(19)	97.99(9)	

^a Numbers in parentheses are estimated standard deviations of the last significant figure. Atoms are labeled as indicated in Figure 3.

When the crude reaction mixture was treated with 3 M aqueous HCl, a single organic product was isolated in 60% yield after chromatography (Scheme 1). The spectroscopic features of this compound in C₆D₆ include two singlets for the inequivalent methyl groups and a singlet for the methine proton,

Scheme 1



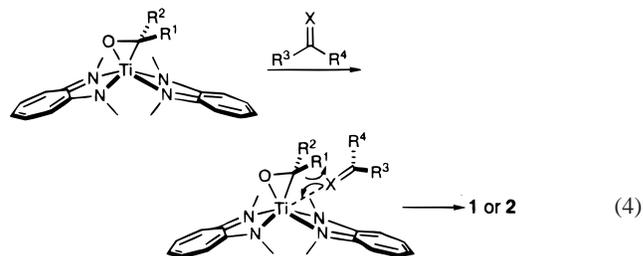
consistent with the diol [PhHC(OH)C(OH)Me₂] (3). Acetophenone also undergoes clean coupling with TiMe₂L₂ and CO under similar conditions to afford diol 4 in 79% yield after hydrolysis. In this case, however, the carbonyl was added at low temperature since TiMe₂L₂ will slowly transfer a methyl group to ketones.

Alkenes insert into η^2 -benzophenone zirconocene complexes.²⁷ We were therefore interested in determining the products of a reaction with an enone and a η^2 -carbonyl complex generated in situ. *trans*-Cinnamaldehyde was employed as the coupling partner to furnish the corresponding diol 5 in 55% yield. No product resulting from acetone addition to the γ position of cinnamaldehyde was observed, although a small amount of another product was observed; this material is the diol resulting from the homo-pinacol coupling of cinnamaldehyde.^{28,29}

By analogy to the reactions performed with TiMe₂L₂, carbonylation of TiPh₂L₂ followed by trapping with benzaldehyde and hydrolysis yielded diol 6 in 70% yield. The carbonyl coupling reactions mediated by TiPh₂L₂ complexes are clean, except for a small amount of biphenyl formed by decomposition of TiPh₂L₂, as detected by analysis of the crude reaction mixtures by TLC and ¹H NMR. The ¹H NMR spectrum of 6 consisted of a complicated aromatic region and a singlet for the methine proton at 5.55 ppm in CD₃OD. Acetone also served as an electrophile to yield the diolate complex 2. The ¹H NMR spectrum of this compound consisted of a broad 6H singlet at 1.78 ppm and an even broader 12H singlet at 3.23 ppm. The appearance of the inequivalent methyl groups of the ligand as a broad singlet could be the result of fluxional behavior. The structure has been verified by X-ray crystallography. The nearly octahedral geometry and short Ti–O bond lengths, 1.862(1) and 1.875(1) Å, compare well with the structural features of 1 (Figure 3). Hydrolysis of 2 yielded the expected diol 7. Reaction of TiPh₂L₂ with CO and *trans*-cinnamaldehyde yielded diol 8. In this case, however, no additional product could be detected by TLC or ¹H NMR spectroscopy. The spectroscopic properties of 8 are nearly identical to those of 5, consistent with *trans* olefin geometry. Curiously, it has been reported that mixtures of Mg, TiCl₄ and bulky diaryl ketones result in products consistent with 1,4-addition to enones.³⁰ Such a reaction has not been observed under our conditions.

The mixed alkyl–aryl complex TiMePhL₂ also reacts with benzaldehyde and CO to yield an equal mixture of diastereomeric diols 9 after hydrolysis. This assignment was based on comparison with previously reported spectra.⁹ Analysis of the TiMePhL₂ crude reaction mixture after hydrolysis by ¹H NMR spectroscopy and TLC did not reveal any other products.

These studies demonstrate that the multicomponent synthesis of unsymmetrical diols from CO, titanium dialkyl complexes and carbonyl compounds proceeds (Scheme 1) in good yield with few side products. In most cases, either the titanium diolate complex or free diol can be isolated. The results presented are consistent with double alkyl migration to form an unobserved, reactive titanium η^2 -ketone complex that subsequently couples with aldehydes and ketones (eq 4). The proposed intermediate η^2 -ketone complex must be a mild nucleophile, since no evidence for deprotonation of added ketones has been obtained. An important experimental feature of these reactions is that the electrophile be present in solution upon the addition of CO, which allows immediate trapping of the putative η^2 -ketone complex and avoids decomposition.



This coupling methodology is novel because both alkyl migration to CO and carbonyl coupling can occur in a single reaction sequence. Moreover, the Ti-ATI system appears to be unique in that no significant scrambling of the η^2 -ketone intermediate with the coupling partner is observed.^{31,32} It is noteworthy that previous examples of carbonyl insertion into preformed η^2 -carbonyl adducts relied on a Lewis acid additive (Li⁺, AlR₃) and utilized zirconium, the strong metal–oxygen bonds of which provide a significant driving force for the reaction. The present system does not require any additives and yields diolates directly from alkyl complexes. The unique nature of the ATI ligand system for this carbonyl coupling is further highlighted by the fact that the {Cp₂Ti}²⁺ fragment is not able to mediate this reaction. Direct reaction of aromatic ketones with [Cp₂Ti(PMe₃)₂] yields fulvenes, whereas [Cp₂Ti(CO)₂] converts enones to homopinacol coupling products.^{33,34} The carbonylation of certain titanocene dialkyls affords Cp₂Ti(CO)₂ and the corresponding dialkyl ketone.³⁵ The reaction described in the present work is stoichiometric in titanium but utilizes simple starting materials that should allow maximum flexibility in the synthesis of unsymmetrical diols.

Preparation of an Oxametallacyclopentene Complex. Use of an alkyne as coupling partner was examined in order to gauge the reactivity of the putative η^2 -carbonyl compound. The resultant oxametallacyclopentene complex should afford an allylic alcohol after hydrolysis. A benzene solution of TiMe₂L₂ and 1 equiv of phenyl acetylene reacted cleanly with CO to afford a red complex that could be recrystallized by diffusion of pentane into a dichloromethane solution at –35 °C (eq 5). The ¹H NMR spectrum of 10 in C₆D₆ consists of two singlets (6 and 12 protons) at 1.67 and 3.12 ppm in addition to a 1H singlet at 6.57 ppm. These spectral data are consistent with

(31) Giannini, L.; Solari, E.; De Angelis, S.; Ward, T. R.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *J. Am. Chem. Soc.* **1995**, *117*, 5801–5811.

(32) Giannini, L.; Caselli, A.; Solari, E.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C.; Re, N.; Sgamellotti, A. *J. Am. Chem. Soc.* **1997**, *119*, 9709–9719.

(33) Gleiter, R.; Wittwer, W. *Chem. Ber.* **1994**, *127*, 1797–1798.

(34) Schobert, R.; Maeref, F.; Dürr, S. *Synlett* **1995**, 83–84.

(35) Fachinetti, G.; Floriani, C. *J. Chem. Soc., Chem. Commun.* **1972**, 654–655.

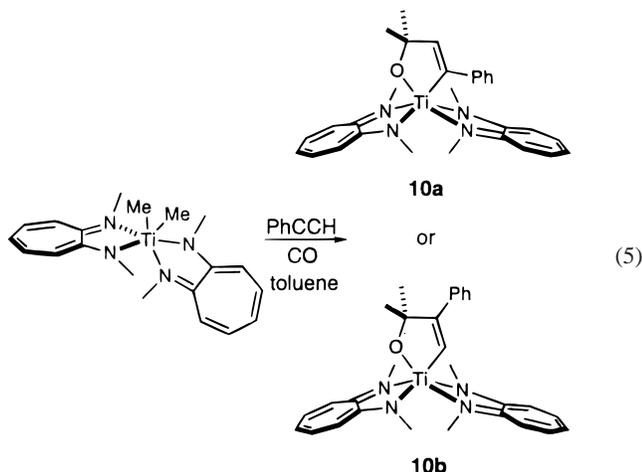
(27) Erker, G.; Rosenfeldt, F. *J. Organomet. Chem.* **1982**, *224*, 29–42.

(28) Chucho, J.; Wiemann, J. *Bull. Soc. Chim. Fr.* **1968**, 1497–1503.

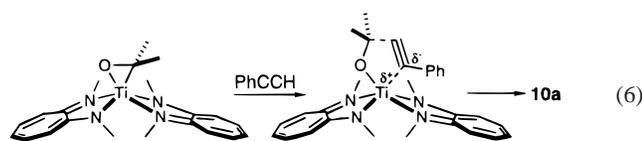
(29) Barden, M. C.; Schwartz, J. *J. Am. Chem. Soc.* **1996**, *118*, 5484–5485.

(30) Pons, J.-M.; Santelli, M. *Tetrahedron* **1990**, *46*, 513–522.

insertion of phenyl acetylene into the Ti–C bond of the η^2 -acetone complex.



Phenyl acetylene can insert into the Ti–C bond of an η^2 -acetone complex in either of two ways, depicted as **10a** or **10b**. If the insertion reaction is considered to proceed in a stepwise manner, electronic considerations favor attack β to the phenyl ring so that the developing negative charge can be stabilized at a benzylic position (eq 6). The effect of steric factors on the



regiochemistry is difficult to predict since it is not clear whether the acetone geminal methyl groups or the $\{\text{Ti}(\text{Me}_2\text{ATI})_2\}^{2+}$ fragment is sterically more demanding. The regiochemistry of alkyne insertion could not be determined solely by ^1H and ^{13}C NMR spectroscopy and it has not been possible to obtain X-ray diffraction quality crystals of **10**. A NOESY experiment in C_6D_6 , however, clearly revealed a cross-peak between the singlet at 1.67 ppm, which was assigned to the geminal methyl groups, and the vinylic methine singlet at 6.57 ppm. These data are consistent with alkyne insertion where the phenyl group is directed away from the two methyl groups of the η^2 -acetone unit (**10a**). Similar insertion regiochemistry has been observed for the reaction of hexyne with $[\text{Cp}_2\text{Zr}(\text{Ph}_2\text{CO})_2]$ and of phenyl acetylene with the zirconocene aluminum η^2 -carbonyl complex (Figure 4).^{8,27,36}

Attempts to hydrolyze **10** and isolate the corresponding allylic alcohol yielded mixtures of products under a variety of conditions, as determined by TLC and NMR spectroscopy. The reaction of iodine with oxametallacyclopentene complexes has been reported in the literature to afford the alkenyl iodide,³⁷ but treatment of **10** with I_2 in THF afforded multiple products.

There are numerous early metal-mediated syntheses of allylic alcohols. The thermolysis of a titanacyclopentadiene complex and benzophenone affords an oxametallacyclopentene insertion product or allylic alcohol after hydrolysis (Figure 4).³⁸ Treatment

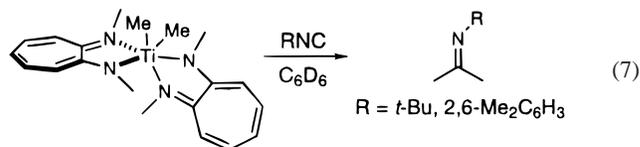
(36) Peulecke, N.; Ohff, A.; Tillack, A.; Baumann, W.; Kempe, R.; Burlakov, V. V.; Rosenthal, U. *Organometallics* **1996**, *15*, 1340–1344.

(37) Harada, K.; Urabe, H.; Sato, F. *Tetrahedron Lett.* **1995**, *36*, 3203–3206.

(38) Hill, J. E.; Balaich, G.; Fanwick, P. E.; Rothwell, I. P. *Organometallics* **1993**, *12*, 2911–2924.

of an aldehyde or ketone with a proposed η^2 -alkyne titanium complex, generated in situ by reacting an alkyne and $\text{Ti}(\text{O}-i\text{-Pr})_4$ with 2 equiv of $i\text{-PrMgCl}$, yields the corresponding allylic alcohol after hydrolysis; analogous chemistry has also been reported with tantalum and zirconium.^{37,39,40} Mixtures of Yb and benzophenone in HMPA/THF react with diphenylacetylene to yield allylic alcohols.⁵ Our multicomponent preparation of oxametallacyclopentene complexes provides a rare case where an alkyne inserts into an η^2 -ketone complex, that was derived from CO, with good regiochemistry at room temperature.

Reactivity of $[\text{TiMe}_2(\text{Me}_2\text{ATI})_2]$ with Isocyanides: Trapping with Benzaldehyde. Reaction of an imine with η^2 -ketone complexes generated in situ should afford amido-alkoxide complexes. Unlike reactions with other electrophiles that yielded clean products however, the imines did not. We therefore decided to reverse the order of the coupling reaction, by first forming an η^2 -imine complex and then treating the material with a carbonyl compound. A reaction of 1 equiv of 2,6- $\text{Me}_2\text{C}_6\text{H}_3\text{-NC}$ with TiMe_2L_2 in C_6D_6 solution gave a surprisingly simple ^1H NMR spectrum after about 1 h (eq 7). Similar results were



obtained with $t\text{-BuNC}$. The major product of this reaction has been identified as the imine 2,6- $\text{Me}_2\text{C}_6\text{H}_3\text{N}=\text{CMe}_2$, whereas with $t\text{-BuNC}$, $t\text{-BuN}=\text{CMe}_2$ was formed. The assignment of imine products was confirmed by independent synthesis.^{19,21}

The formation of imines suggested that reduction to afford low-valent titanium species had occurred. Reasoning that such a transient titanium species should be a reductant, we repeated the chemistry described in eq 7 in the presence of benzaldehyde as a trapping agent. A noticeable change in color to a much lighter red was apparent, and there was a new, diamagnetic Me_2ATI -containing product present in addition to $t\text{-BuN}=\text{CMe}_2$. The use of 2 equiv of benzaldehyde resulted in a clean NMR spectrum consisting of a 2H singlet at 6.55 ppm and a broad 12-proton singlet at 3.35 along with aromatic resonances. The resulting, crystalline complex (**11**) was identified by X-ray diffraction as the *anti*-pinacol coupling product of benzaldehyde (Figure 3). The Ti–O bond distances of 1.872(3) and 1.878(3) Å and the coordination geometry compare well with those in other Me_2ATI -containing titanium diolate complexes reported here. In this reaction, benzaldehyde most likely traps the low-valent titanium species formed after imine elimination. Insertion of another molecule of benzaldehyde accounts for the formation of **11**, although radical pathways are also possible.

These results demonstrate that imine elimination reactions provide a convenient source of low-valent titanium through reaction of isocyanides with TiR_2L_2 . In principle, this low-valent titanium source should allow the synthesis of unsymmetrical diols by reductive coupling of two dissimilar carbonyl compounds. Such an approach would complement our previously described three-component method. Compounds such as acetone, phenyl acetylene, and styrene either do not react with the species formed by reaction of TiMe_2L_2 with isocyanides or yield mixtures, however, as determined by ^1H NMR spectroscopy.

(39) Takai, K.; Ishiyama, T.; Yasue, H.; Nobunaka, T.; Itoh, M.; Oshiki, T.; Mashima, K.; Tani, K. *Organometallics* **1998**, *17*, 5128–5132.

(40) Buchwald, S. L.; Watson, B. T.; Huffman, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 2544–2546.

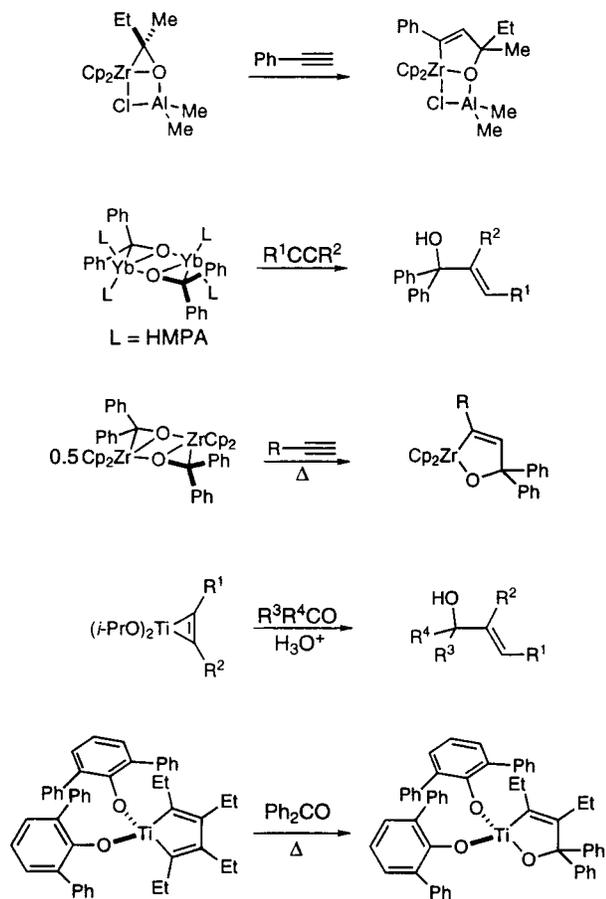


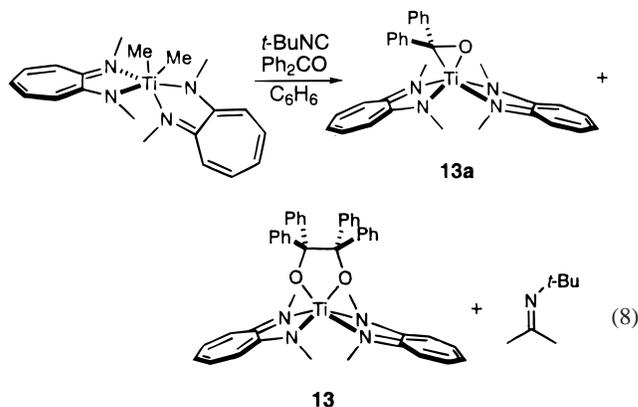
Figure 4. Selective metal-mediated synthesis of allylic alcohols and oxametallacyclopentenes.

The main problem is probably that it is difficult to reduce these substrates, and for this reason we turned to more potent oxidants.

Reactivity of [TiMe₂(Me₂ATI)₂] with Benzil: Preparation of an Eneiolate Complex. Addition of equimolar amounts of benzil and *t*-BuNC to a solution of TiMe₂L₂ in benzene yielded one new complex and *t*-BuN=CMe₂, as determined by NMR spectroscopy (**12**, Figure 5). This material can be crystallized by diffusion of pentane into a THF solution of the complex and the ¹H NMR spectrum of the solid in C₆D₆ consists of a 12H singlet and a complicated aromatic region integrating for 20H. The IR spectrum of solid **12** contains a weak stretch at 1600 cm⁻¹ and the ¹³C spectrum has a peak at 145.9 ppm consistent with the presence of an enediolate complex.⁴¹ Spectroscopic data and elemental analysis also confirm the formation of a titanium enediolate complex, **12**. Group IV enediolate complexes are common although titanium examples appear to be rare.⁴²

Reactivity of [TiMe₂(Me₂ATI)₂] with Isocyanides and Benzophenone. The addition of 2 equiv of benzophenone and *t*-BuNC to a solution of TiMe₂L₂ afforded a red solution that contained *t*-BuN=CMe₂. The ¹H NMR spectrum of the solid isolated from this reaction consisted of a singlet at 3.14 ppm and the aromatic region integrated for 30 protons. By analogy with the benzaldehyde reaction product, this complex was formulated as the diolate [Ti(Ph₂COCOPh₂)(Me₂ATI)₂] (**13**, Figure 5). When 1 equiv of benzophenone and *t*-BuNC were added slowly to a C₆D₆ solution of TiMe₂L₂, two complexes in

addition to *t*-BuN=CMe₂ were observed by ¹H NMR (eq 8).



One complex was assigned as **13** from its ¹H NMR spectrum. The other, **13a**, has a singlet at ~2.8 ppm, an unusual chemical shift region for the methyl groups of the Me₂ATI ligand. It has not been possible to purify this material since it can only be generated with **13**, from which it is difficult to separate. It was therefore characterized by its reactivity. The addition of an additional 1 equiv of benzophenone completely consumed **13a**, affording **13**. The addition of 1 equiv of acetone to a mixture of **13a** and **13** gave **2** and **13**. These two reactions strongly suggest that mixtures of the η²-benzophenone complex [Ti(Ph₂-CO)(Me₂ATI)₂] and **13** are generated when benzophenone is slowly added to TiMe₂L₂ and an isocyanide.

Reactivity of [TiMe₂(Me₂ATI)₂] with Isocyanides, Ketones, and Imines: Preparation of an Amido-Alkoxide Complex.

Since the reaction of 1 equiv of benzophenone with TiMe₂L₂ and isocyanides yielded mixtures of **13** and **13a**, we predicted that simultaneous addition of another trapping agent such as an imine would result in the formation of an amido-alkoxide complex. *N*-Tosylbenzalimine was selected because it is not sterically demanding, and the tosyl group increases both the electrophilicity and crystallinity of the imine. Equimolar amounts of *N*-tosylbenzalimine, benzophenone, and *t*-BuNC in C₆D₆ react with TiMe₂L₂ to yield a red-brown color and a complex NMR spectrum showing several products, although the major species had a spectrum consistent with a product having low symmetry (**14**). Free *t*-BuN=CMe₂ could also be detected in the reaction mixture.

When the reaction was scaled up, a red-brown crystalline complex could be isolated. The ¹H NMR spectrum of this material in C₆D₆ consisted of five 3H singlets and a complicated aromatic region. The ¹³C NMR spectrum also confirmed the low symmetry of the complex and the IR spectrum contained an intense band at 919 cm⁻¹ consistent with the presence of a sulfonamide group. This combination of spectral data supported the assignment of this material as the amido-alkoxide [Ti(Ph₂-COCN(SO₂tol)HPh)(Me₂ATI)₂] (**14**), which was confirmed by an X-ray crystallographic study that revealed nearly octahedral coordination geometry (Figure 3). As expected, the 2.110(3) Å Ti–N(tosyl) bond is slightly longer than the average Ti–N(Me₂-ATI) distance of 2.09 Å and the Ti–O distance of 1.864(2) Å is slightly shorter than the Ti–O distance in **2**. Although X-ray quality crystals of **14** can be readily obtained, preparing bulk samples completely free of impurities for elemental analysis has proved to be difficult. The insertion of an imine into η²-carbonyl complexes is not common. Metal-mediated preparations of 2-amino alcohols more commonly involve insertion of carbonyl compounds into Zr, Nb and Sm η²-imine complexes (Figure 2).^{43,44}

(41) Erker, G.; Czisch, P.; Schlund, R.; Angermund, K.; Krüger, C. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 364–365.

(42) Hofmann, P.; Stauffert, P.; Frede, M.; Tatsumi, K. *Chem. Ber.* **1989**, *122*, 1559–1577.

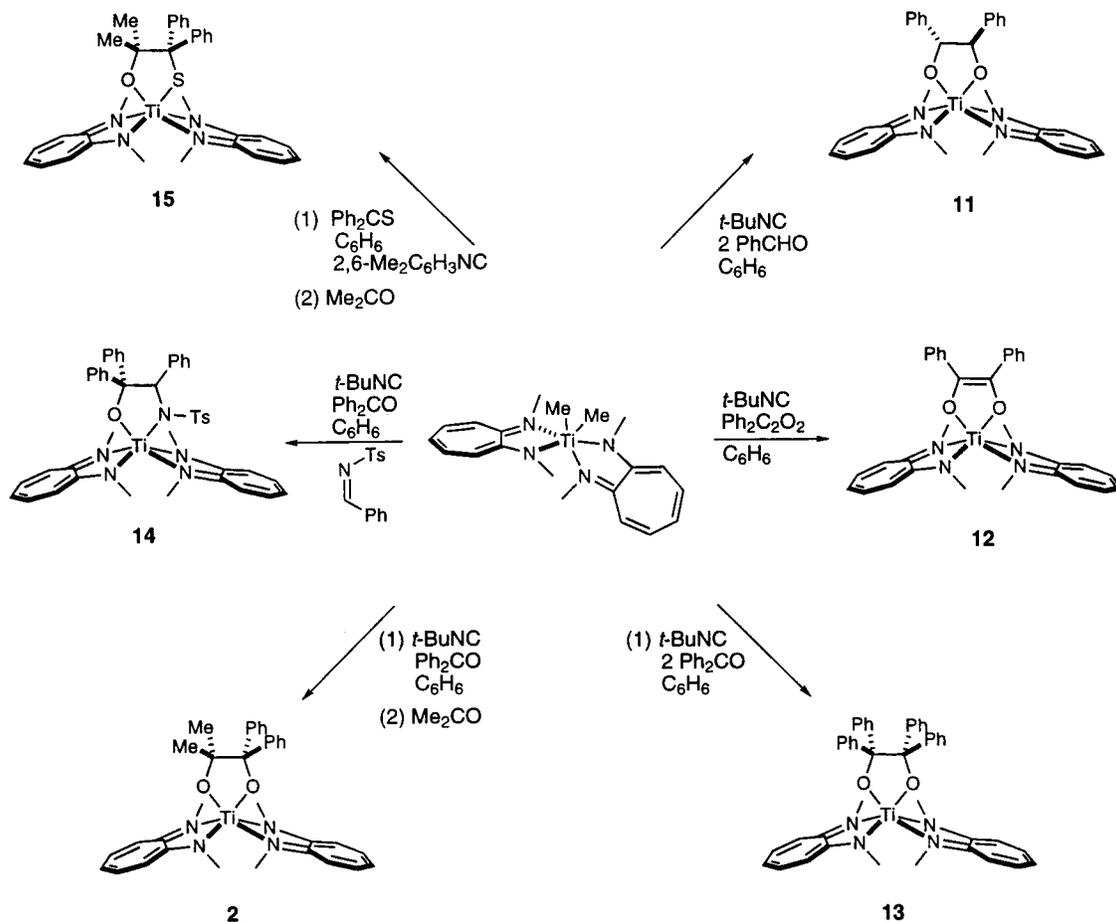
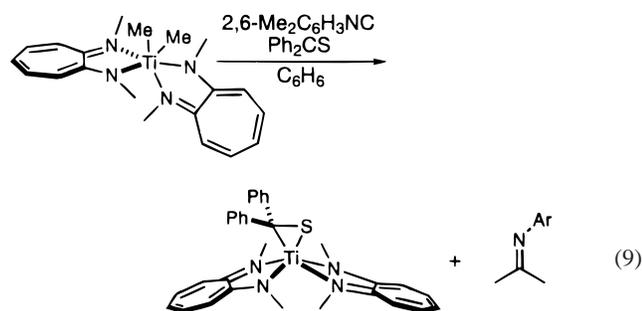


Figure 5. Carbonyl, imine, and thiocarbonyl coupling reactions mediated by $\text{TiMe}_2(\text{Me}_2\text{ATI})_2$ complexes and isocyanides.

Synthesis and Characterization of a Thiolato-Alkoxide Complex. The formation of two titanium–oxygen bonds provides a strong driving force for the formation of **13** even when only 1 equiv of benzophenone is added. Substitution of thiobenzophenone was therefore attempted to effect the formation of $[\text{Ti}(\text{SCPh}_2)(\text{Me}_2\text{ATI})_2]$. Addition of a blue C_6D_6 solution of thiobenzophenone and $2,6\text{-Me}_2\text{C}_6\text{H}_3\text{NC}$ to TiMe_2L_2 yielded a reddish solution that contained the free imine and a single, new titanium complex (eq 9). This complex has a ^1H NMR



signal at ~ 2.77 ppm, close to the chemical shift of the methyl groups in the putative $[\text{Ti}(\text{OCPh}_2)\{\text{Me}_2\text{ATI}\}_2]$ compound **13a**. Although it was encouraging that only one major product formed in this reaction, it has not been possible to purify it. As with $[\text{Ti}(\text{OCPh}_2)(\text{Me}_2\text{ATI})_2]$, its characterization was based on reactivity.

Addition of acetone yielded a light red solution, the ^1H NMR spectrum of which consisted of a 6H singlet at 1.74 ppm and two 6H singlets at 3.09 and 3.27 ppm (**15**, Figure 5). This spectrum was similar to that of **2**, the major difference being the resolution of the broad singlet corresponding to the four methyl groups of the ATI ligand in **2** into two, 6H singlets. This result is consistent with formation of the unsymmetrical thiolato-alkoxide complex $[\text{Ti}(\text{Ph}_2\text{CSCOMe}_2)(\text{Me}_2\text{ATI})_2]$ (**15**), an assignment verified by X-ray crystallography. The overall structural features of **15** are similar to those of **2** (Figure 3). The Ti–O distance of 1.831(2) Å is slightly shorter than the Ti–O distance in **2**, the stronger bond most likely compensating for weaker sulfur donation. The Ti–S distance of 2.4245(9) Å is slightly longer than representative Ti–S distances of 2.339(2) and 2.318(2) Å in $\text{CpTiOAr}(\text{SBn})_2$.⁴⁵ The isolation of **15** is consistent with the formation of $[\text{Ti}(\text{SCPh}_2)(\text{Me}_2\text{ATI})_2]$, as written in eq 9. Early transition metal thioaldehyde complexes have been isolated for both Ti and Zr and structurally characterized for Ti.^{46,47} The same β -hydroxy thiol has been prepared by the conceptually similar reaction of equimolar amounts of thiobenzophenone, acetone and Yb metal.⁴⁸ Reaction of $[\text{TiMe}_2(\text{Me}_2\text{ATI})_2]$ with thiobenzophenone and CO under our standard conditions generated **15**, as determined by ^1H NMR spectroscopy.

(45) Firth, A. V.; Stephan, D. W. *Organometallics* **1997**, *16*, 2183–2188.

(46) Park, J. W.; Henling, L. M.; Schaefer, W. P.; Grubbs, R. H. *Organometallics* **1990**, *9*, 1650–1656.

(47) Buchwald, S. L.; Nielsen, R. B. *J. Am. Chem. Soc.* **1988**, *110*, 3171–3175.

(48) Makioka, Y.; Uebori, S.-y.; Tsuno, M.; Taniguchi, Y.; Takaki, K.; Fujiwara, Y. *J. Org. Chem.* **1996**, *61*, 372–375.

(43) Imamoto, T.; Nishimura, S. *Chem. Lett.* **1990**, 1141–1142.

(44) Kataoka, Y.; Miyai, J.; Oshima, K.; Takai, K.; Utimoto, K. *J. Org. Chem.* **1992**, *57*, 1973–1981.

Mechanistic Considerations. The production of imine from TiMe_2L_2 and isocyanides occurs rapidly to generate a species that reacts like a source of low-valent titanium. Double alkyl migration with the isocyanide to generate an η^2 -imine complex is most likely the first step. There could be many factors that cause elimination of the imine. The electronic contributions that influence this reaction have been difficult to delineate. We focus our discussion on steric factors, which can play an important role in determining the stability of the imine complex. Molecular modeling of the putative intermediate $[\text{Ti}(\eta^2\text{-Me}_2\text{CN}(t\text{-Bu}))(\text{Me}_2\text{-ATI})_2]$ suggests that severe steric interactions take place between the methyl and *t*-Bu groups of the imine and the methyl groups of the ATI ligand. Thus, elimination of imine and formation of reduced titanium products appear to be more favorable than a sterically congested η^2 -imine complex.

Titanium η^2 -imine complexes have been prepared previously by the reaction of isocyanides with titanium dialkyl complexes. These compounds eliminate imine upon treatment with different pyridine bases, forming reduced titanium complexes.^{49,50} Titanocene metallacycles also react with isocyanides to yield isolable iminoacyl complexes that eliminate imine in solution.⁵¹ Such reductive elimination reactions have been used in the catalytic synthesis of cyclopentenones from enynes.⁵²

Attempts to trap these low-valent species with soft donors that stabilize Ti(II) complexes, such as PMe_3 , pyridine, or *t*-BuNC, have not been successful.^{53,54} The resulting paramagnetism makes rapid screening of reaction mixtures difficult.

(49) Durfee, L. D.; Fanwick, P. E.; Rothwell, I. P.; Foltz, K.; Huffman, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 4720–4722.

(50) Durfee, L. D.; Hill, J. E.; Kerschner, J. L.; Fanwick, P. E.; Rothwell, I. P. *Inorg. Chem.* **1989**, *28*, 3095–3096.

(51) Cámpora, J.; Buchwald, S. L.; Gutiérrez-Puebla, E.; Monge, A. *Organometallics* **1995**, *14*, 2039–2046.

(52) Grossman, R. B.; Buchwald, S. L. *J. Org. Chem.* **1992**, *57*, 5803–5805.

(53) Araya, M. A.; Cotton, F. A.; Matonic, J. H.; Murillo, C. A. *Inorg. Chem.* **1995**, *34*, 5424–5428.

Alkynes and azobenzenes do not yield diamagnetic products, consistent with our earlier observations that only good oxidants, or those that can form Ti–O bonds, react with the proposed low-valent titanium complex.

Conclusions

We have described a novel, multicomponent system for the preparation of unsymmetrical diols from carbonyl compounds, CO, and aminotroponimate ligated titanium dialkyl complexes. A reactive, titanium η^2 -carbonyl complex is proposed to be a key intermediate. Utilization of an alkyne as the electrophilic partner allows an oxametallacyclopentene complex to be prepared. All of these reactions proceed efficiently at ambient temperature and do not require the use of Lewis acid additives. In contrast, treatment of the dialkyl titanium complexes with isocyanides leads to elimination of imine and formation of one or more low-valent titanium complexes. This titanium species can be trapped either by 2 equiv of a readily oxidized carbonyl compound or by a dicarbonyl compound to yield stable Ti(IV) diolate complexes. Use of 1 equiv of benzophenone and either acetone or an imine results in the preparation of titanium diolate or amido-alkoxide complexes. Thiobenzophenone can also be coupled with acetone by this methodology.

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Supporting Information Available: Tables and figures reporting bond distances, angles, and positional and thermal parameters for compounds **1**, **2**, **11**, **14**, and **15**, including CIF files. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JA992662Y

(54) Wang, X.; Gray, S. D.; Chen, J.; Woo, L. K. *Inorg. Chem.* **1998**, *37*, 5–9.