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Communications

Synthesis of Unsymmetrical Vicinal Diols Using Titanium Aminotroponimate Alkyl Complexes

Dietrich P. Steinhuebel and Stephen J. Lippard*

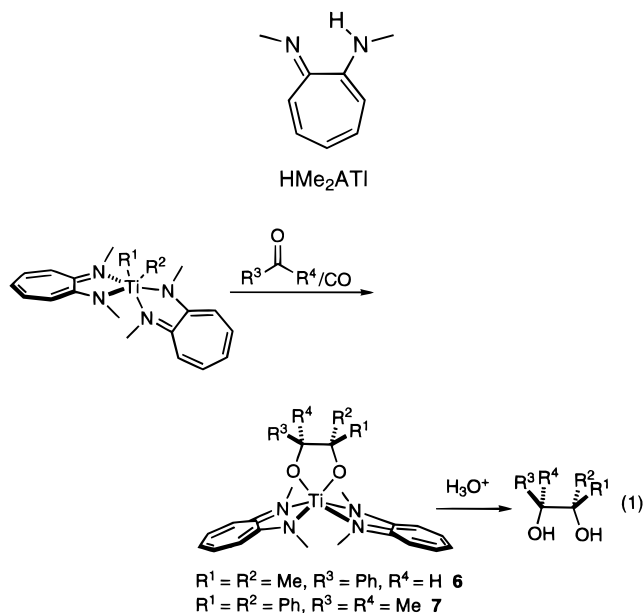
Department of Chemistry, Massachusetts Institute of Technology,
Cambridge, Massachusetts 02139

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Summary: A novel, multicomponent method to prepare vicinal diols from titanium dialkyl complexes, CO, and carbonyl compounds is presented. The reaction involves sequential coupling of aminotroponimate-supported titanium dialkyl complexes, carbon monoxide, and carbonyl compounds to yield vicinal diols following hydrolysis of the diolate complexes.

The coupling of aldehydes and/or ketones is a powerful method for the preparation of vicinal diols, an important class of compounds in synthetic chemistry.¹ Numerous methods exist that provide symmetrical diols via the homocoupling of aldehydes and ketones,²⁻⁴ but no general solutions exist for the synthesis of unsymmetrical diols.^{5,6} Here we describe a new approach, where titanium dialkyl complexes supported by aminotroponimate ligands (HMe₂ATI) are allowed to react with CO and carbonyl compounds. Subsequent acid treatment of the diolate complex releases the unsymmetrical, vicinal diol in better than 60% isolated yield (eq 1).

In one of the earliest examples involving the coupling of dissimilar carbonyl compounds to yield 1,2-diols, acetophenone reacted with a Me₂AlCl-stabilized η^2 -ketone zirconocene complex (A) to yield a zirconium



diolate complex (eq 2).⁷ This approach was extended by using anionic η^2 -aldehyde complexes (B) prepared by transmetalation of zirconocene α -stannylalkoxide complexes with methylolithium (eq 3).⁸

Recently, a vanadium(II) reagent and chelating, α -substituted aldehydes have been employed to effect a hetero-cross-coupling reaction.⁵ Although the mechanism of this process is unresolved, η^2 -aldehyde vanadium adducts were postulated as intermediates.

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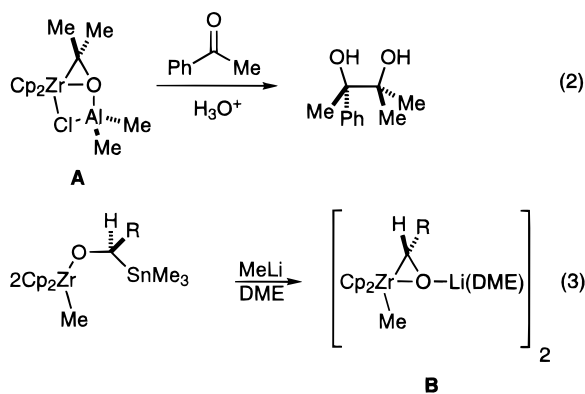


Table 1. Synthesis of Vicinal Diols with $[\text{TiR}^1\text{R}^2\{\text{Me}_2\text{ATI}\}_2]$, CO, and $\text{R}^3\text{R}^4\text{CO}$ According to Eq 1

| entry ^a | R ¹ | R ² | R ³ | R ⁴ | yield (%) ^b |
|--------------------|----------------|----------------|----------------|----------------------|------------------------|
| 8 | Me | Me | H | Ph | 60 |
| 9 | Me | Me | Me | Ph | 69 |
| 10 | Me | Me | H | (CH) ₂ Ph | 63 |
| 11 | Ph | Ph | H | Ph | 70 |
| 12 | Ph | Ph | Me | Me | 60 |
| 13 | Ph | Ph | H | (CH) ₂ Ph | 70 |
| 14 | Me | Ph | H | Ph | 66 |

^a Entries **8–10**, **14** were performed in toluene at 0 °C or –78 °C, whereas those for **11–13** were performed in CH₂Cl₂ at –78 °C. See Supporting Information for details. ^b Yield was determined on analytically pure material.

Previous work in our laboratory demonstrated that zirconium and hafnium tropocoronand dialkyl complexes react with CO to form isolable η^2 -ketone complexes, which add to chalcone, cyclohexenone, and cyclohexyl phenyl ketone to yield unsymmetrical zirconium diolates.^{9,10} We wished to explore the scope of this novel chemistry and to extend it to encompass a range of carbonyl compounds and dialkylmetal starting materials. Titanium was substituted for zirconium both to increase the nucleophilicity of the η^2 -complex and to allow for cleavage of the resultant metal diolate linkage under the reaction conditions. Several methods for cleaving titanium oxygen bonds in situ have recently been disclosed.^{3,4} To facilitate the carbonyl cross-coupling methodology, we decided to use aminotroponiminate (R_2ATI) ligands in place of tropocoronands due to their more facile synthesis and ease of derivatization.

Titanium aminotroponiminate complexes were prepared (Scheme 1) by reaction of $\text{TiCl}_2(\text{NMe}_2)_2$ with 2 equiv of HMe_2ATI in benzene to yield $[\text{TiCl}_2(\text{Me}_2\text{ATI})_2]$ (**1**) as an insoluble, dark purple powder. A more tractable derivative, $[\text{Ti}(\text{OTf})_2(\text{Me}_2\text{ATI})_2]$ (**2**), could be obtained by treating $[\text{TiCl}_2(\text{Me}_2\text{ATI})_2]$ with TMSOTf (2 equiv, CH_2Cl_2). This purple, crystalline material was characterized both spectroscopically and by X-ray crystallography. Reaction of $[\text{TiCl}_2(\text{Me}_2\text{ATI})_2]$ with either MeMgCl or PhMgBr (2 equiv, diethyl ether) yielded the dialkyl $[\text{Ti}(\text{CH}_3)_2\{\text{Me}_2\text{ATI}\}_2]$ (**3**) and diaryl $[\text{Ti}(\text{C}_6\text{H}_5)_2\{\text{Me}_2\text{ATI}\}_2]$ (**4**) complexes as dark red, crystalline solids in 83% and 40% yields, respectively. The mixed alkyl–aryl complex $[\text{Ti}(\text{CH}_3)(\text{C}_6\text{H}_5)\{\text{Me}_2\text{ATI}\}_2]$ (**5**) was prepared as a red crystalline solid by treating $[\text{TiCl}_2\{\text{Me}_2\text{ATI}\}_2]$ sequentially with MeMgCl (1 equiv, CH_2Cl_2) and PhMgBr (1 equiv, Et_2O). The solid-state structures of these alkyl and aryl complexes were determined by X-ray diffraction and confirm the expected six-coordinate titanium geometry.

Dialkyl complex **3** reacted readily with CO at room temperature; however, it was not possible to characterize any titanium-containing products. Reasoning that double alkyl migration to CO occurred in this reaction by analogy to previous Zr and Hf tropocoronand chem-

istry, we added benzaldehyde as an electrophilic trap for the putative η^2 -carbonyl intermediate. A dark red toluene solution of **3** and benzaldehyde reacted rapidly and cleanly at 0 °C with CO to yield a light red solution from which the unsymmetrical diolate complex **6** could be isolated (eq 1). Key ¹H NMR spectroscopic features of **6** include resonances at 1.49 and 1.38 ppm, which correspond to the diastereotopic methyl group protons on the diolate ligand. In addition, two broad resonances at 3.38 and 3.30 ppm were observed for the methyl groups of the ATI ligand. The formulation of **6** as the desired diolate complex was confirmed by X-ray crystallography. The free diol **8** could be isolated as a white, microcrystalline solid in 60% yield (Table 1) following treatment of **6** with 3 M aqueous HCl. Acetophenone also undergoes clean coupling with **3** and CO to afford diol **9**. No evidence for enolization of acetophenone was observed under the reaction conditions. Cinnamaldehyde could also be employed as a coupling partner to furnish the corresponding diol **10**. No product resulting from acetone addition to the γ position of cinnamaldehyde was observed, although a small amount (15%) of the diol resulting from homo-pinacol coupling of cinnamaldehyde was detected.

By analogy to the reactions performed with **3**, carbonylation of the diaryl complex **4** followed by trapping with benzaldehyde yielded diol **11**. Acetone also served as an electrophile to yield the diolate complex **7**, the structure of which was verified by X-ray crystallography (Figure 1).¹¹ The octahedral geometry and short Ti–O bond lengths, 1.8620(10) and 1.8747(10) Å, are very similar to those in **6**. Reaction of **4** with CO and cinnamaldehyde yielded diol **13**. In this case, however, no homocoupling product was detected. Use of a mixed alkyl complex of the type $[\text{Ti}(\text{R})(\text{R}')\{\text{Me}_2\text{ATI}\}_2]$ expanded the scope of diols that could be obtained by this chemistry. Reaction of benzaldehyde and CO afforded a 1:1 mixture of diastereomeric diols **14** in 66% yield.

The results presented are consistent with double alkyl migration to form a titanium η^2 -ketone complex that

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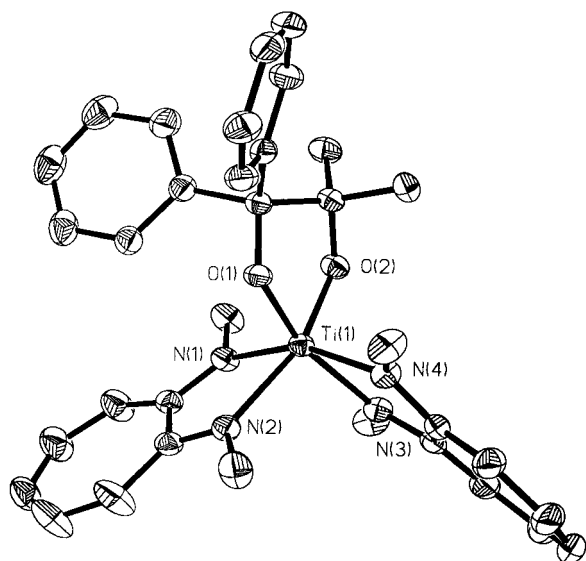


Figure 1. ORTEP diagram of **7** showing 50% thermal ellipsoids and selected atom labels.

subsequently reacts with either aldehyde or ketone to yield the diolate. This system 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 scrambling of the η^2 -ketone intermediate with the coupling partner is observed.^{12,13} It is noteworthy that previous examples of

(11) Crystal structure analysis of **7**: $C_{34}H_{38}N_4O_2Ti$, $M = 582.58$, monoclinic, space group $P2_1/c$, $a = 16.222(2) \text{ \AA}$, $b = 15.4521(16) \text{ \AA}$, $c = 11.8922(17) \text{ \AA}$, $\beta = 91.811(13)^\circ$, $V = 2979.4(7) \text{ \AA}^3$, $Z = 4$, $F(000) = 1232$, Mo $K\alpha$ radiation ($\lambda = 0.71073$), $\mu(\text{Mo } K\alpha) = 3.25 \text{ mm}^{-1}$; $T = 188 \text{ K}$, crystal dimensions $0.4 \text{ mm} \times 0.4 \text{ mm} \times 0.45 \text{ mm}$. The structure was solved by direct methods using XS and then refined by full-matrix least-squares and Fourier techniques using SHELXTL-PLUS. All non-hydrogen atoms were refined anisotropically; all hydrogens were located in the difference map and refined isotropically. The 5728 observed reflections [$I > 2\sigma(I)$] were collected on a Siemens CCD area detector ($1.82^\circ < \theta < 28.28^\circ$), corrected for absorption using the SADABS program and refined to an R value of 0.0349 ($wR^2 = 0.0928$). Crystallographic data including bond distances and angles in addition to positional and thermal parameters (excluding structure factors) for the structure can be found in the Supporting Information.

carbonyl insertion into preformed η^2 -carbonyl adducts relied on a Lewis acid additive (Li^+ , AlR_3) 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 neither the $\{\text{salenTi}\}$ nor $\{\text{Cp}_2\text{Ti}\}$ fragments will likely mediate this reaction. Titanium dialkyl complexes supported by the salen ligand yield products resulting from alkyl group migration to the imine carbons.¹⁴ Direct reaction of aromatic ketones with $[\text{Cp}_2\text{Ti}(\text{PMe}_3)_2]$ yields fulvenes, whereas the carbonylation of certain titanocene dialkyls affords $\text{Cp}_2\text{Ti}(\text{CO})_2$ and the corresponding dialkyl ketone.^{15,16}

In summary, we have described a novel, multicomponent, one-pot coupling reaction utilizing ATI-supported titanium dialkyl complexes, CO, and carbonyl compounds which results in the efficient synthesis of vicinal diols. Further studies are in progress to elucidate the mechanism, extend the scope, and develop asymmetric variants of this chemistry.

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Supporting Information Available: Experimental procedures for the preparation and characterization of compounds in addition to bond distances, angles, and positional and thermal parameters for compound **7** (14 pages). Ordering information is given on any current masthead page.

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