Cyclopentadienyl Modification

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Alkyne Cycloaddition to a Titanocene Oxide as a Route to Cyclopentadienyl Modification**

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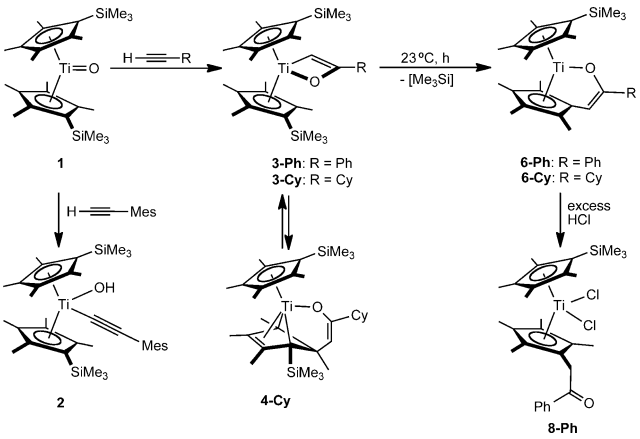
Abstract: *Addition of terminal or internal alkynes to a base-free titanocene oxide results in synthesis of the corresponding oxometallocyclobutene. With appropriate cyclopentadienyl substitution, these compounds undergo reversible C–C reductive elimination offering a unique approach to cyclopentadienyl modification.*

Bis(cyclopentadienyl)titanium and zirconium complexes bearing metal–ligand multiple bonds exhibit rich chemistry including olefin metathesis,[1] hydrogenation,[2] C–H activation,[3,4] cycloaddition,[5] and group transfer processes.[6] Monomeric titanocenes with terminal oxo ligands are a particularly interesting class of these compounds given the unique reactivity of the Ti=O π-system among early transition metal oxides. Cycloadditions of unsaturated organic molecules such as allenes and alkynes are well-established routes to oxatitanacyclobutanes and oxatitanacyclobutenes.[7,8] However, further elaboration of these products and incorporation into useful synthetic schemes has yet to be realized. As part of our effort to develop new methods for the cleavage of early transition metal–heteroatom bonds in the context of N_2 functionalization,[9] O-atom and related group transfer processes,[10] we have continued exploration of oxatitanacyclobutenes. Here we describe that cycloaddition of appropriate alkynes to the Ti=O bond of titanocenes with suitably electronically and sterically tuned cyclopentadienyl ligands triggers unique C–C reductive elimination chemistry, resulting in modification of one of the most ubiquitous ligands in organometallic chemistry.

Permethyltitanocene oxide, $[(\eta^5\text{-}C_5Me_5)_2TiO]$, is a rare and seminal example of a well-defined organometallic complex with a reactive Ti=O bond.[11] Unfortunately, this compound is metastable and undergoes facile decomposition by cyclopentadienyl ring ejection in the absence of a stabilizing ligand such as pyridine.[11] Replacement of one of the cyclopentadienyl methyl groups with a silyl substituent, as in the case of $[(\eta^5\text{-}C_5Me_4SiMe_3)_2TiO]$ (**1**) and $[(\eta^5\text{-}C_5Me_4SiMe_2Ph)_2TiO]$, has resulted in isolation and crystallographic characterization of base-free derivatives that enable chemistry unavailable to the base-stabilized complexes.[12] For example, addition of H_2 or silanes resulted in 1,2-addition across the Ti=O bond.[13] By using **1** as a representative example, the cycloaddition reactivity of these compounds with alkynes was studied to determine if unique reactivity was also available to the resulting oxatitanacycles.

Addition of one equivalent of PhCCH to **1** in $[D_6]$benzene at 23 °C resulted in immediate formation of a red solution. Analysis by ^{1}H NMR spectroscopy established the formation of a C_s symmetric product, consistent with formation of the expected oxatitanacycle, **3-Ph** (Scheme 1). Quantitation of



Scheme 1. Cycloaddition of terminal alkynes with **1** and subsequent reductive elimination reactivity.

the observed product by integration against an internal ferrocene standard established only 60% yield of **3-Ph** with no evidence for formation of other diamagnetic titanium products. Continued monitoring of the solution by NMR spectroscopy over the course of 24 h at 23 °C or heating to 50 °C for 2 h revealed complete disappearance of the resonances for **3-Ph** with no new peaks corresponding to diamagnetic titanium compounds. However, new singlets were observed in the vicinity of 0 ppm (see below). Repeating the reaction on a preparative scale in toluene at −35 °C resulted in deposition of red-green dichroic crystals suitable for X-ray diffraction. The solid-state structure, presented in Figure S1 (Supporting Information), verified the identity of the diamagnetic product as the oxatitanacyclobutene, **3-Ph**. The isomer with the phenyl substituent at the β-position of the metallocycle was the only one detected by NMR spectroscopy. Use of a terminal alkyne with a larger aryl substituent such as MesCCH (Mes = 2,4,6-Me_3-C_6H_2)) resulted in exclusive 1,2-addition of the C–H bond to form the hydroxyacetylide, **2** (Scheme 1, Figure S2).

To determine the fate of the titanium upon addition of PhCCH to **1**, a benzene solution of **3-Ph** was stirred for 24 h at

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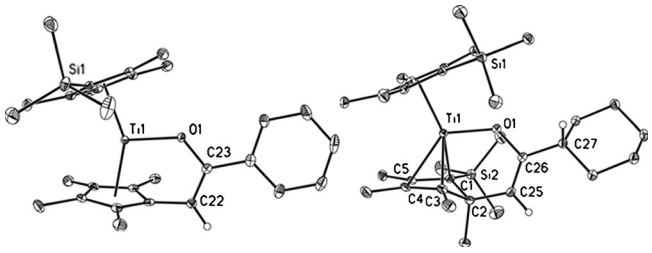


Figure 1. Representation of the molecular structure of **6-Ph** (left) and **4-Cy** (right) at 30% probability ellipsoids. Hydrogen atoms omitted for clarity.

23 °C followed by recrystallization from pentane at −35 °C. This procedure resulted in the isolation of red crystals suitable for X-ray diffraction in 77% yield. The solid-state structure of **6-Ph** (Figure 1) establishes formation of a titanium(III) compound in which the cyclopentadienyl ligand has been modified by replacement of the [$SiMe_3$] substituent with the carbon of the oxatitanacycle. Consistent with the Ti^{III} formulation, a solid-state magnetic moment of 1.6 μB was measured for **6-Ph** by magnetic susceptibility balance at 23 °C. A combination of ^{1}H NMR spectroscopic and GC-MS data confirmed formation of [D_5]trimethylsilylbenzene and [D_5]-2,5-cyclohexadienyl(trimethyl)silane as byproducts, likely resulting from trapping of an ejected [$SiMe_3$] radical by the [D_6]benzene solvent.[14]

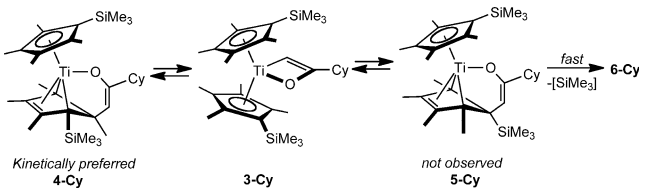
Addition of excess gaseous HCl to **6-Ph** resulted in protonolysis of the Ti–O bond and generation of the titanocene dichloride where the original [$SiMe_3$] substituent has been replaced by the 2-phenylethyl ketone (**8-Ph**). The identity of the product has been confirmed by NMR spectroscopy and X-ray diffraction (Figure S3). Thus oxatitanacycle group transfer has been used to modify the cyclopentadienyl ring.

The scope of the tandem cycloaddition–cyclopentadienyl modification sequence was explored with other terminal and internal alkynes. Addition of CyCCH to a [D_6]benzene solution of **1** induced an initial color change to red, then to green. Analysis of the green solution by ^{1}H NMR spectroscopy established formation of a C_1 symmetric, diamagnetic product identified as **4-Cy** (Scheme 1). A diagnostic resonance was located at 4.26 ppm in the ^{1}H NMR spectrum and assigned as a C-H derived from the terminal alkyne with long-range coupling (^{1}H-^{13}C HMBC) to a cyclopentadienyl carbon. Notably, two [$SiMe_3$] resonances are observed demonstrating that ejection of [$SiMe_3$] radical has not yet occurred. The identity of **4-Cy** was confirmed by single-crystal X-ray diffraction (Figure 1) and established formation of a titanium alkoxide complex where one of the cyclopentadienyl rings has been modified by C–C bond formation from formal reductive elimination from the unobserved oxatitanacycle, **3-Cy**. A short C4–C5 distance of 1.402(2) Å along with elongated C1–C2 and C3–C2 distances of 1.597(2) Å and 1.569(2) Å, respectively, indicate that the cyclopentadienyl ring has been reduced from a XL_2 to a X_2L ligand.[15] Modification of cyclopentadienyl ligands by C–H reductive elimination has been previously implicated by isotopic labeling experiments in zirconocene alkyl hydride complexes but to our knowledge these species have not been directly observed or isolated.[16] Carbon–carbon reductive elimination resulting in cyclopentadienyl ring modification is also rare. Green and Benfield reported that addition of phosphines to [$(\eta^5$-$C_5H_5)_2$MoEtCl] induced the reversible reductive elimination of an ethyl group forming a new ethyl-substituted η^4-cyclopentadiene ring.[17] Both Rosenthal[18a] and Takahashi[18b–d] have implicated C–C reductive elimination as part of net transformations that result in cyclopentadienyl modification.

To explore whether the oxatitanacyclobutene could be detected prior to C–C reductive elimination, the addition of cyclohexylacetylene to **1** was conducted at −70 °C in [D_8]toluene and monitored by ^{1}H NMR spectroscopy. Analysis of the low-temperature spectrum of the dark red solution revealed a new, diamagnetic complex with overall C_s symmetry, consistent with formation of the desired oxatitanacyclobutene, **3-Cy**. Warming the sample to −20 °C resulted in conversion to a new C_1 symmetric product, identified as **4-Cy**. In a separate experiment, **1** and cyclohexylacetylene were combined at −90 °C as frozen solutions in [D_8]toluene, transferred to the high-vacuum line, warmed to −78 °C and treated with 5 equivalents of gaseous HCl. Analysis of the resulting bright red solution by ^{1}H NMR spectroscopy established formation of [$(\eta^5$-$C_5Me_4SiMe_3)_2TiCl_2$] and cyclohexyl methyl ketone. The latter was also identified by GC-MS. This series of experiments confirms initial formation of the oxatitanacyclobutene **3-Cy** prior to C–C reductive elimination and modification of the cyclopentadienyl ring.

The thermal stability of **4-Cy** was studied to explore the reversibility of C–C reductive elimination and to gain insight into the preferences for [$SiMe_3$] radical ejection. Heating a [D_6]benzene solution of **4-Cy** at 50 °C for 2 h and monitoring by ^{1}H NMR spectroscopy resulted in disappearance of the resonances assigned to the **4-Cy** with concomitant appearance of new peaks in the vicinity of 0–0.5 ppm consistent with formation of **6-Cy**, arising from [$SiMe_3$] loss. Once **4-Cy** was consumed, the solution was treated with I_2 and formed a new, C_1 symmetric, diamagnetic product which was identified as the iodo titanocene alkoxide complex, **7-Cy**, resulting from [$SiMe_3$] radical ejection and new C–C bond formation. Furthermore, **6-Cy** was characterized by X-ray diffraction and the solid-state structure is presented in Figure S4. This sequence establishes that formation of **4-Cy** from **3-Cy** is reversible, ultimately forming a C–C bond at the silyl substituted carbon, which in turn undergoes irreversible loss of [$SiMe_3$] to form the resulting Ti^{III} alkoxide complex (Scheme 2).

As with aryl alkynes, introduction of a larger alkyl substituent results in competing 1,2-addition pathways. Addi-



Scheme 2. Reversible C–C reductive elimination and oxidative addition resulting in ejection of [$SiMe_3$] radical.

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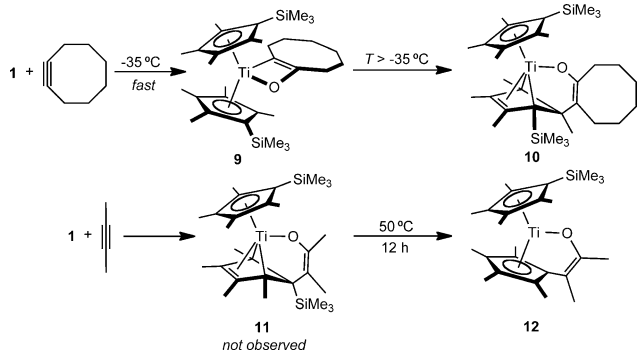
tion of *tert*-butyl acetylene to a [D_6]benzene solution of **1** yielded a mixture of products observable by ^{1}H NMR spectroscopy including the hydroxy titanocene acetylide and the C–C reductive elimination product. Heating this mixture at 50 °C for 12 h resulted in [$SiMe_3$] ejection, as determined by subsequent oxidation with I_2 and analysis by NMR spectroscopy (Figure S6).

Cyclooctyne, a strained, internal alkyne also underwent rapid cycloaddition with **1** to yield the anticipated oxatitanacyclobutene, **9** (Scheme 3). This product, characterized by



Scheme 3. Cycloaddition of internal alkynes with **1** and reductive elimination resulting in cyclopentadienyl modification.

NMR spectroscopy, combustion analysis and X-ray diffraction (Figure S7), proved stable only at −35 °C. Warming samples in a toluene solution formed **10**, the product of a bond-forming event between a carbon adjacent to the [$SiMe_3$] substituent and a carbon from the oxatitanacyclobutene (Figure S8). Heating a [D_6]benzene solution of **10** to 80 °C produced no change over the course of 5 days. Increasing the temperature of the thermolysis resulted in decomposition with no evidence of desilylation. It is likely that the additional substitution of the oxatitanacyclobutene resulting from cycloaddition of the internal alkyne increases the barrier for oxidative addition of the C–C bond. This in turn inhibits the reversible sequence necessary for reductive elimination involving the silylated carbon required for [$SiMe_3$] radical ejection.

Attempts to observe the oxatitanacyclobutene derived from cycloaddition of 2-butyne with **1** have been unsuccessful as no change was observed in the ^{1}H NMR spectrum when the reaction was conducted at 23 °C. Heating the sample to 50 °C for 12 h resulted in disappearance of all of the resonances of the titanocene with appearance of peaks in the vicinity of 0 ppm, signaling [D_6]benzene silylation and [$SiMe_3$] ejection. Oxidation of the paramagnetic titanium product with excess I_2 yielded the expected iodo alkoxide complex, establishing **12** as the product of thermolysis. Presumably, initial formation of the oxatitanacyclobutene is followed by reductive elimination to **11** (or isomers), which ultimately undergoes loss of [$SiMe_3$] to yield the observed products. This outcome also demonstrates that unactivated internal alkynes induce a higher barrier for both cycloaddition and initial C–C reductive elimination as no reaction was observed at 23 °C.

Additional studies were conducted to determine the origin of the unusual reductive elimination–cyclopentadienyl modification sequence. It is intriguing that analogous oxometallocyclobutenes of [$(\eta^5$-$C_5Me_5)_2$Ti] have not been reported to undergo similar chemistry. To further explore this possibility, the base free titanocene oxide, [$(\eta^5$-$C_5Me_4i Pr_2)_2$Ti] was generated in benzene solution[12] and treated with one equivalent PhCCH. This specific metallocene was chosen to the ability to generate a base free oxide and the similar steric profile of the alkylated cyclopentadienyl ligand to the silylated variants reported throughout. Recrystallization from pentane at −35 °C furnished the expected oxatitanacyclobutene (**13**) in 82 % yield as determined by NMR spectroscopy and X-ray diffraction (see Figure S5). Heating a [D_6]benzene solution at 60 °C for 5 days produced no change as judged by integration versus an internal ferrocene standard. Likewise, there was no evidence for formation of any C_1 symmetric products analogous to **4-Cy**, consistent with a higher kinetic barrier for the initial reductive elimination. This inertness contrasts the facile reductive elimination observed from **3-Cy** under identical conditions and can be traced to the electronic properties of the cyclopentadienyl ligands. Previous work from our laboratory[16b] and others[19] has demonstrated that introduction of relatively electron withdrawing silyl substituents onto cyclopentadienyl rings facilitates C–H reductive elimination as compared to the purely alkylated counterparts. The same effect is likely operative here as introduction of an [$SiMe_3$] substituent sufficiently destabilizes the Ti^{IV} ground state and facilitates C–C bond formation with the cyclopentadienyl ligand by reductive elimination.

In summary, cycloaddition of terminal and internal alkynes to a base-free titanocene oxide complex results in formation of the corresponding oxatitanacyclobutene derivatives which are poised for an unusual C–C reductive elimination to the cyclopentadienyl ring. The cyclopentadienyl ligand must be sufficiently electron poor to sufficiently destabilize the Ti^{IV} ground state to enable the initial C–C reductive elimination event. This process has proven reversible and when a carbon–carbon bond is formed to a carbon bearing a silyl substituent, facile and irreversible ejection of [$SiMe_3$] is observed and provides a unique method of cyclopentadienyl ring modification.

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[20] CCDC 988082 (**2-Mes**), 988076 (**3-Ph**), 992425 (**13**), 988081 (**4-Cy**), 988077 (**6-Ph**), 988080 (**6-Cy**), 988078 (**8-Ph**), 988079 (**9**), and 988075 (**10**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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