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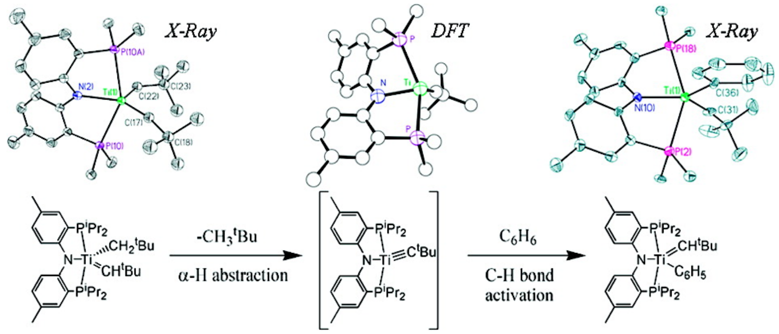

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Intermolecular C−H Bond Activation Promoted by a Titanium Alkylidyne

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The intermolecular activation of inert C−H bonds by organotransition metal complexes remains one of the most intensely studied areas in chemistry since these systems may allow for catalytically converting hydrocarbons from cheap sources to valuable, functionalized organic precursors.[1] Several strategies can lead to C−H bond activation reactions and include discrete oxidative addition, σ-bond metathesis, radical bond homolysis, electrophilic reactions, and 1,2-addition reactions across metal−ligand multiple bonded functionalities.[2] For the latter class of reactions, only a handful of M−L multiple bonded functionalities have been observed to perform *inter*molecular activation of inert C−H bonds.[3−7] We now report that transient titanium alkylidynes, which are generated by an abstraction reaction, can activate sp^2 and sp^3 C−H bonds under mild conditions. Experimental and theoretical studies were conducted in order to understand the mechanism and to deduce an energy profile for the C−H bond activation reaction.

Recently, our group reported the synthesis of a titanium alkylidene complex (PNP)Ti═CH^{t}Bu(OTf) supported by a pincer ligand (PNP = *N*-[2-P(CHMe$_2$)$_2$-4-methylphenyl]$_2^-$).[8] The triflate group can be readily substituted with stoichiometric LiCH$_2{}^t$Bu to afford the titanium alkylidene−alkyl (PNP)Ti═CH^{t}Bu(CH$_2{}^t$Bu) (**1**) (Scheme 1).[9,10] Compound **1** displays a ^{13}C NMR resonance at 260 ppm with a low $J_{\mathrm{C-H}}$ coupling of 86 Hz, consistent with an agostic α-H interaction taking place with the electron-deficient metal center.[7,11]

Compound **1** is a kinetic product inasmuch as it reacts with benzene over several hours at room temperature. As a result, compound **1** must be prepared in cyclohexane in order to avoid rapid C−H activation of benzene at 27 °C over 11.9 h (4.5 half-lives) to afford (PNP)Ti═CH^{t}Bu(C$_6$H$_5$) (**2**) in quantitative yield, and such a system can be independently prepared from (PNP)Ti═CH^{t}Bu(OTf) and ClMgPh (Scheme 1).[9]

To establish the connectivity and degree of α-H agostic interaction in these alkylidenes, we collected single-crystal X-ray diffraction data for compounds **1** and **2** (Scheme 1).[9] The structure for each reveals short Ti═C bonds (1.790(5) Å for **1**; 1.873(5) Å for **2**)[12] and a metal center residing in a pseudo trigonal bipyramidal geometry with "trans-like" phosphines (∼149°). These systems are impervious to intramolecular ancillary ligand degradation pathways when compared to other titanium alkylidene alkyl derivatives prepared by our group.[13]

To better understand the mechanism for conversion of **1** to **2**, by which the C−H bond of benzene is activated, we simulated the reaction using high-level density functional theory (DFT) at the B3LYP/cc-pVTZ(-f) level of theory[14] as implemented in the Jaguar program (Scheme 1).[15] Complex **1** first undergoes α-H abstraction concomitant with elimination of CH$_3{}^t$Bu to afford the titanium alkylidyne intermediate **A**, which embarks on an intermolecular 1,2-addition of the benzene C−H bond across the reactive Ti≡C linkage to provide product **2**. As shown in Scheme 1, the α-H abstraction step is rate-determining with a computed solution phase $\Delta G^\ddagger$ of 27.8 kcal/mol (**1-TS**), whereas C−H activation of the solvent is not predicted to be rate-limiting with the transition state, **A-TS**, found at 21.0 kcal/mol. Thus, the C−H activation barrier relative to the reactive alkylidyne intermediate is only 16.4 kcal/mol, a value which is remarkably low and justifies the titanium alkylidyne complex as a reactive intermediate. Both **1-TS** and **A-TS** feature structural elements that are intuitively expected for *σ-bond metathesis* transition states invoking the structural motif of a transient metallacycle.[9] We have also explored a number of plausible mechanistic alternatives theoretically and identified them all to not be viable.[9]

The proposal of the titanium alkylidyne intermediate and the reaction profile shown have been explored in a series of experimental studies. First, the reaction was carried out in C$_6$D$_6$ to confirm that **1** is quantitatively transformed to (PNP)Ti═CD^{t}Bu(C$_6$D$_5$) (**2**-d_6). Both ^{2}H and ^{2}H{^{1}H} NMR spectra of **2**-d_6 reveal >99+% ^{2}H incorporation into the α-carbon without any ^{2}H scrambling into the aryl or ^{i}Pr motifs of the PNP ligand. Most importantly, when complex **1** is thermolyzed in C$_6$D$_6$, we observe CH$_3{}^t$Bu as the sole byproduct (via ^{13}C and ^{1}H NMR spectroscopy), supporting our proposal that α-abstraction in **1** *precedes* the intermolecular C−H activation of benzene. Interestingly, the C−H and C−D activation steps are reversible since **2**-d_6 undergoes clean conversion to **2** in C$_6$H$_6$ (80 °C, 48 h, Scheme 1) and vice versa, thus linking intermediate **A** to **2**.[9] Our proposed reaction energy profile in Scheme 1 suggests that the reverse step of the C−H activation, that is, **2**→**A**, is associated with a barrier of 32.8 kcal/mol, which can be overcome at a slow, but reasonable rate under elevated temperature conditions.

Next, the kinetic parameters for the conversion of **1** to **2** were assessed experimentally by monitoring the decay of **1** using ^{31}P NMR spectroscopy in C$_6$D$_6$ to reveal a $k_{\mathrm{average}} = 6.5(4) \times 10^{-5}$ s^{-1} at 27 °C. The reaction was found to be pseudo-first-order in titanium, which is in good agreement with the reaction energy profile proposed based on DFT calculations. Under a depleted amount of benzene (e.g., C$_6$D$_{12}$), formation of **3** is not clean given the promiscuity of **A** to react with other solvent media. Temperature dependence studies of the **1**→**2** conversion (15−40 °C) allowed for extraction of the activation parameters[9] $\Delta H^\ddagger = 24.1(4)$ kcal/mol and $\Delta S^\ddagger = -2(1)$ cal/mol·K^{-1}, yielding a $\Delta G^\ddagger$ value of ∼24.7 kcal/mol at 298.15 K, which is in good agreement with the DFT prediction of 27.8 kcal/mol. There is insignificant change in the $k_{\mathrm{H}}/k_{\mathrm{D}}$ (1.04 at 27 °C) when examining the C−H activation reaction in C$_6$H$_6$ versus C$_6$D$_6$, but substantial $k_{\mathrm{H}}/k_{\mathrm{D}}$ discrepancy (3.7 at 27 °C) associated with the −CD$_2{}^t$Bu versus −CH$_2{}^t$Bu abstraction, thereby providing credence to a rate-determining step involving α-abstraction to generate a titanium alkylidyne linkage.

When compound (PNP)Ti═CH^{t}Bu(OTf) is treated with LiCH$_2$SiMe$_3$ in C$_6$D$_6$ at 40 °C for 24 h, complex (PNP)Ti═CDSiMe$_3$-(C$_6$D$_5$) (**3**-d_6) is formed quantitatively along with CH$_3{}^t$Bu. As

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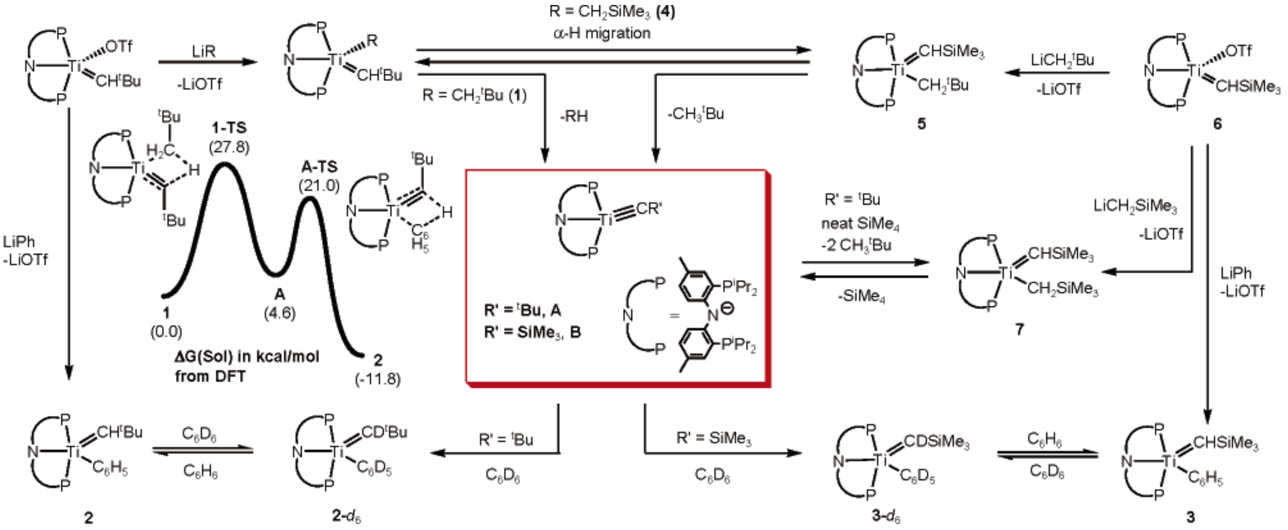
Scheme 1. Reactivity Studies of Titanium Alkylidene Complexes along with the Reaction Coordinate for the **1**→**2** Conversion in Benzene (ϵ = 2.284) (relative energies in kcal/mol are given in parentheses)



observed with isotopomer **2**-d_6, complex **3**-d_6 also experiences exchange with excess C_6H_6 to afford proteo **3** (Scheme 1). By analogy to the **1**→**2** conversion, we propose that the intermediate (PNP)Ti═CH^{t}Bu(CH$_2$SiMe$_3$) (**4**) undergoes α-H migration to generate (PNP)Ti═CHSiMe$_3$(CH$_2$^{t}Bu) (**5**), which then participates in C−H/C−D activation of solvent via the putative alkylidyne intermediate (PNP)Ti≡CSiMe$_3$ (**B**) (Scheme 1).[9] If the reaction is conducted in C_6D_{12}, the ^{1}H, ^{13}C, and ^{31}P NMR spectra indicate that both complexes **4** and **5** are present at 25 °C,[9] and when the mixture of **4**/**5** is thermolyzed in C_6D_6, only **3**-d_6 and CH$_3$^{t}Bu are formed. An independent synthesis of the **4**/**5** mixture can be generated from the transmetalation of (PNP)Ti═CHSiMe$_3$(OTf) (**6**)[9] and LiCH$_2$^{t}Bu, suggesting that **5** is likely the preferred isomer in the **4**↔**5** equilibrium, and that α-H migration in hypothetical **4** must precede both α-hydrogen abstraction and C−H activation of benzene. If complex (PNP)Ti═CHSiMe$_3$(CH$_2$SiMe$_3$) (**7**) is prepared from **6** and LiCH$_2$SiMe$_3$, thermolysis in C_6D_6 (88 °C, 12 h) also leads to quantitative C−H bond activation concurrent with formation of **3**-d_6 and SiMe$_4$ (Scheme 1). Independent synthesis of **3** can be accomplished with $^-$Ph and **6** (Scheme 1).[9] Most impressively, complex **1** transforms cleanly to **7** in neat SiMe$_4$ (35 °C, 48 h), further indicating that α-hydrogen abstraction, α-hydrogen migration, and 1,2-addition processes all play roles in these reaction profiles.

In summary, we combined extensive experimental and theoretical studies to examine the C−H activation mechanism involving the titanium alkylidene complex **1**. We found strong evidence for the existence of a thus far elusive terminal titanium alkylidyne intermediate, which has been shown to promote a number of diverse C−H activation reactions. Some of the transformations highlighted in this work are shown to be reversible, placing the key reaction steps in thermodynamic equilibrium scenarios that should allow for the rational design of systems capable of carrying important catalytic reactions.

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Supporting Information Available: Experimental preparation (compounds **1**−**9**), kinetic (conversion of **1** to **2**), crystallographic data (compound **1**, **2**, (PNP)Ti(CH$_2$Si(CH$_3$)$_3$)$_2$, and **6**), computational details, all calculated structures, and additional discussions. This material is available free of charge via the Internet at http://pubs.acs.org.

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