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Communication

Generation of Masked Ti^{II} Intermediates from Ti^{IV} Amides via β-H Abstraction or Alkyne Deprotonation: An Example of Ti-Catalyzed Nitrene-Coupled Transfer Hydrogenation

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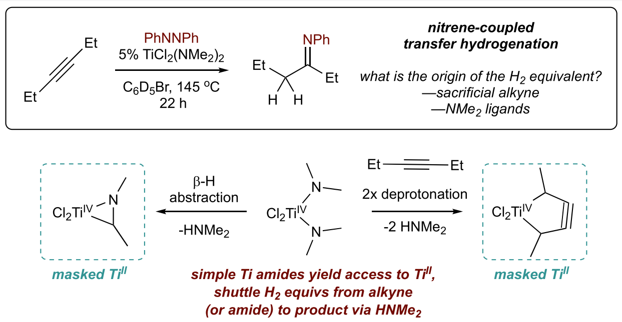
ABSTRACT: Simple Ti amide complexes are shown to act as sources for masked Ti^{II} intermediates via several pathways, as demonstrated through the investigation of a unique Ti-catalyzed nitrene-coupled transfer hydrogenation of 3-hexyne. This reaction proceeds through reduction of azobenzene by a masked Ti^{II} catalyst, wherein both amines and 3-hexyne can serve as the hydrogen source/reductant for Ti by forming putative titanaziridines via β-H abstraction or putative titanacyclopentynes via protonolysis, respectively.



Titanium(II) complexes and intermediates play important roles in various redox reactions,[1] such as Kulinkovich cyclopropanations,[2] alkyne cyclotrimerization,[3−5] and many other annulations.[6,7] Common methods for generating low-valent metals involve reduction of metal halides or β-H abstraction of alkyl ligands (Figure 1, top).[8−10] In many cases, these low-valent Ti^{II} intermediates are trapped or masked via backbonding into π-acidic ligands. In the interest of expanding the accessibility of Ti^{II} intermediates in catalysis, we herein report the reactivity of masked Ti^{II} intermediates generated from simple Ti amides via β-H abstraction or internal alkyne deprotonation (Figure 1, bottom).

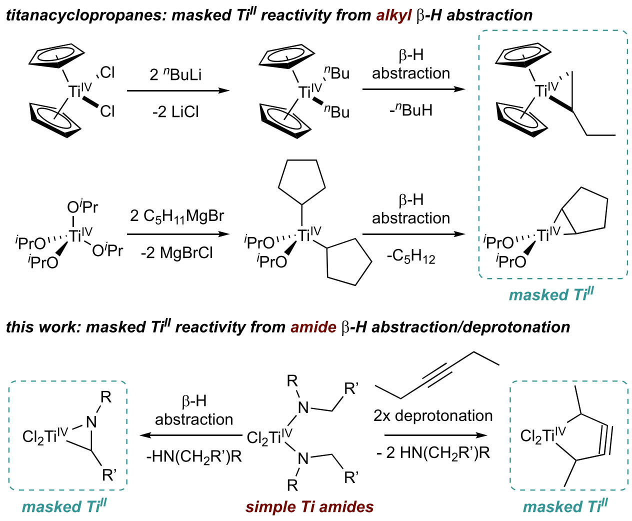


Figure 1. Masked Ti^{II} reagents generated via β-H abstraction by Ti alkyls (top) or Ti amides (bottom).

The η^2-titanaziridine complexes can be easily generated through β-H abstraction, and their insertion chemistry in the context of alkene hydroaminoalkylation catalysis is well-established.[11−13] We hypothesized that η^2-titanaziridine complexes could alternately be considered as masked Ti^{II} species for redox transformations, in direct analogy to chemistry mediated by η^2-olefin/titanacyclopropane complexes (Figure 1, bottom). In fact, Rothwell demonstrated that an η^2-titanaziridine could furnish a Ti imido upon stoichiometric reaction with azobenzene.[14,15] The use of diazenes to capture these reactive species could ultimately allow for catalytic nitrene transfer reactions[16−18] from simple and readily available Ti amide compounds.

Following this hypothesis, $TiCl_2(NMe_2)_2$ was examined as a catalyst for 3-hexyne cyclotrimerization[19] as well as [2 + 2 + 1] pyrrole synthesis.[16] 3-Hexyne underwent successful cyclotrimerization with 5 mol % of $TiCl_2(NMe_2)_2$ as the catalyst, yielding 58% of C_6Et_6 after 22 h at 145 °C (eq 1)—consistent with the hypothesis that Ti^{II} species could be accessed from

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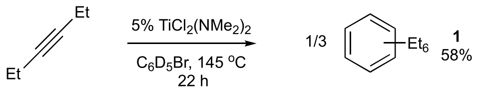
the amide, as cyclotrimerization typically occurs through a Ti^{II}/Ti^{IV} mechanism.[20−23]



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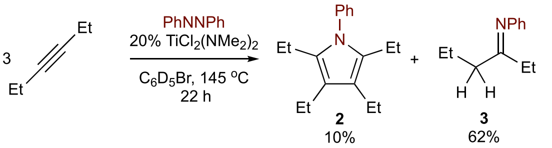

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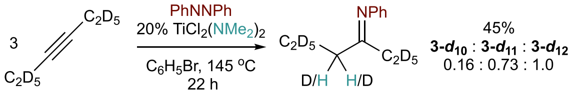


(3)

Surprisingly, the attempted [2 + 2 + 1] nitrene transfer reaction (eq 2) did not yield tetraethylpyrrole as the major product, instead generating a mixture of (*Z*)- and (*E*)-*N*-phenylhexan-3-imine in 62% yield—the product of formal nitrene-coupled hydrogenation of the alkyne. Although metallacycle protonation by free $HNMe_2$ resulting from β-H abstraction could account for some imine formation, yields in excess of the catalyst loading indicate that other mechanisms and chemical species must at least partly be involved in Ti redox and hydrogen transfer.

To investigate the source of hydrogen, the reaction was carried out with perdeuterated 3-hexyne-d_{10} (eq 3). This reaction yielded a mixture of **3**-d_{10}, **3**-d_{11}, and **3**-d_{12} in a ratio of 0.16:0.73:1.0 (eq 3). The predominance of **3**-d_{12} suggests that 3-hexyne is the major hydrogen source (vide infra). Meanwhile, the formation of **3**-d_{10} and mixed product **3**-d_{11} indicates that $HNMe_2$ (from β-H abstraction of dimethylamide ligand) also contributes a non-negligible amount of hydrogen. Notably, based on the catalyst loading, the dimethylamide ligands can account for the majority of hydrogen for **3**-d_{10} and **3**-d_{11}. However, as H/D scrambling of **3** with 3-hexyne can occur (see Supporting Information for a scrambling experiment), the approximate ratio of β-H abstraction versus alkyne deprotonation may be underestimated. This reaction is a rare example of Ti-catalyzed transfer hydrogenation[24,25] and a unique example of nitrene-coupled transfer hydrogenation.

Based on the information above, we propose the mechanism for nitrene-coupled transfer hydrogenation in Figure 2. Starting from $TiCl_2(NMe_2)_2$ (**A**), two pathways are possible: first, coordination of 3-hexyne to Ti and subsequent deprotonation of the propargylic C−H affords titanacyclopentyne complex **B** (pathway I). Coordination of another oxidizing π-acid such as azobenzene could then liberate 2,3,4-hexatriene to furnish a Ti η^2-hydrazido(2−) complex **C**. Although 2,3,4-hexatriene is not observed in reaction mixtures, metallacyclopentyne complexes of group 4 metals have been studied previously,[26−29] and this mechanism best accounts for the poor mass balance in 3-hexyne (despite 85% conversion of 3-hexyne, less than 50% 3-hexyne is converted to **3**), although we cannot rule out other dehydrogenation products of 3-hexyne being involved. Alternately, $TiCl_2(NMe_2)_2$ can undergo β-H abstraction to generate an η^2-titanaziridine **D** (pathway II), which could similarly undergo exchange with azobenzene to liberate *N*-methylformimine and generate the Ti η^2-hydrazido(2−) **C**. We have observed similar π-acid/azobenzene exchange with low-valent Ti halides during Ti-catalyzed isocyanide amination reactions.[30]

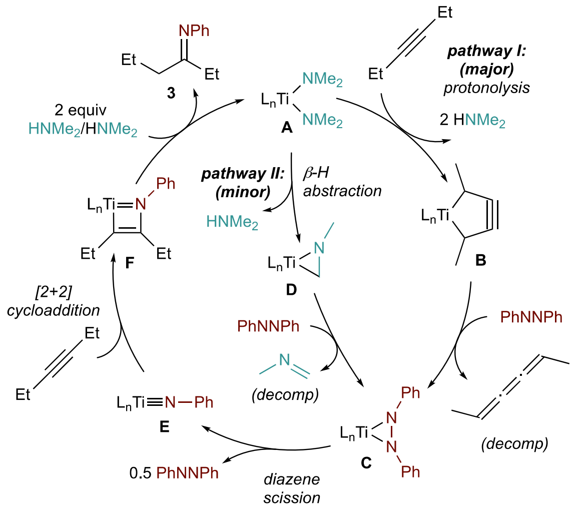
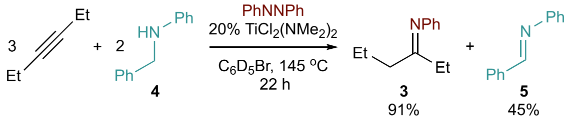


Figure 2. Plausible mechanism of hydroamination of 3-hexyne with azobenzene catalyzed by $TiCl_2(NMe_2)_2$. Teal and black hydrogens indicate their origin from $-NMe_2$ or 3-hexyne, respectively.

Ti η^2-hydrazido(2−) complexes like **C** are well-established to undergo bimetallic scission to Ti imido complexes (**E**).[16,31] From **E**, [2 + 2] cycloaddition of 3-hexyne yields azatitanacyclobutadiene **F**, which can undergo protonolysis by $HNMe_2$ to liberate the hydroaminated product[32−34] and regenerate $TiCl_2(NMe_2)_2$. $HNMe_2$ ultimately serves the role of a proton shuttle in the reaction, moving protons from either 3-hexyne or another equivalent of $-NMe_2$ to the imine product.



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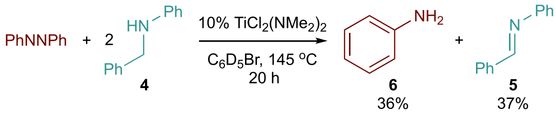

(5)

Prompted by these dual pathways, we hypothesized that secondary amines bearing more acidic α-hydrogens would be a more efficient source of hydrogen than 3-hexyne. In fact, reaction of 3-hexyne with *N*-benzylaniline (**4**) and azobenzene resulted in near quantitative (91% based on PhNNPh) formation of **3** (eq 4), along with significant formation of *N*-phenylaldimine dehydrogenated byproduct **5** (45%)—indicating that β-H abstraction from more reactive Ti-amides can occur at rates competitive with those of 3-hexyne deprotonation.

Following the success of *N*-benzylaniline in the nitrene-coupled transfer hydrogenation reaction, we also investigated simple azobenzene hydrogenation[35,36] using **4** as a direct probe of the efficiency of transfer hydrogenation via solely β-H abstraction (eq 5; see Supporting Information for the full proposed mechanism). In this case, good yield (36%) of $PhNH_2$ **6** could be achieved with prolonged heating, although the reaction was not as fast or efficient as those with 3-hexyne as a hydrogen source. Satisfyingly, the reactions in eqs 4 and 5 allowed observation of the dehydrogenated byproduct **5**: previously, *N*-methylformimine and 2,3,4-hexatriene were not detected, presumably due to their decomposition at elevated temperature.

Similar reactions catalyzed by other simple early transition metal amides, such as $Ti(NMe_2)_4$, $Zr(NMe_2)_4$, $V(NMe_2)_4$, and $Ta(NMe_2)_5$ (Tables S1 and S2), were not as effective as $TiCl_2(NMe_2)_2$, highlighting the sensitivity of this chemistry to the coordination environment and Lewis acidity of the metal.

In conclusion, we have discovered that Ti^{II} can be accessed from a simple Ti diamide via β-H abstraction or alkyne deprotonation, and these elementary steps can be incorporated into a unique Ti-catalyzed nitrene-coupled transfer hydrogenation reaction. An isotope labeling study indicates that alkyne deprotonation appears more facile than β-H abstraction. Although these catalytic reactions are likely not of practical value, the strategy for accessing Ti^{II} synthons from low-cost and stable Ti amide precursors will be of value for future endeavors in low-valent Ti catalysis,[10] surface organometallic chemistry of Ti,[37,38] and chemical vapor deposition of nitrogen-doped Ti thin films.[39,40]

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.organomet.0c00577.

Full experimental details (PDF)

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Notes

The authors declare no competing financial interest.

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