Radical Hydrophosphination Initiated by Triamidoamine-Supported Titanium Despite Insertion into the Ti–P Bond

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Supporting Information Placeholder

ABSTRACT: Titanium compounds supported by the triamidoamine ligand (N₃N, N(CH₃CH₃NSiMe₃)₃) have been investigated for hydrophosphination catalysis. The simple titanium alkyl compound (N₃N)TiMe (2) demonstrate modest activity as a precatalyst for the photocatalytic hydrophosphination of styrene, but the terminal phosphido compound, (N₃N)TiPHPh (4), is inactive. Analysis of these reactions by EPR spectroscopy indicates that (N₃N)TiMe undergoes homolytic Ti–C bond cleavage to achieve radical hydrophosphination. This pathway was further supported in a radical trapping experiment. The phosphido derivative 4 does not produce radicals under similar conditions, despite undergoing facile migratory insertion reactions with polar substrates featuring C–N and C–O multiple bonds. Both nitrile and isonitrile substrates insert with ultimate formation of phosphaalkene products, a change in reactivity as compared to the zirconium congener. Molecular structures of (N₃N)TiPHPh (4), (N₃N)TiNBnC=PPh (5), and (N₃N)Ti(CH₃)(C(Ph)=PPh) (6) are reported.

INTRODUCTION

The efficient use of phosphorus is quickly becoming one of the most pressing issues of our time.⁷ Among methods of producing phosphorus-containing products, hydrophosphination stands strong as one of the most atom-economical and efficient reactions available, but unmet challenges loom for the transformation.² Despite a wide range of catalysts for the reaction,³ activity among catalysts has been modest in many cases with reactions requiring high reaction temperatures and extended times in many instances. Recently, a series of studies has demonstrated that irradiation of hydrophosphination is capable of not only accelerating this transformation but providing access to relatively inert substrates with zirconium- and copper-based catalysts.⁴,⁵ Extending this methodology to other earth-abundant metals is thus a driving force in this field. Early work involving iron has been shown to be promising, with thermal hydrophosphination⁶ being greatly enhanced by photolysis.⁷ Thermal hydrophosphination using an iron β-diketiminate has also been shown to go through a radical-based mechanism.⁸ Initial exploration of titanium catalysts for hydrophosphination encourages greater use of this highly abundant transition metal. Mindiola reported a titanium phosphinidene compound that appears to operate through a [2+2] cycloaddition mechanism in the hydrophosphination of alkynes.⁹ LeGendre expanded on the substrate scope with titanium with the 1,4-hydrophosphination of 1,3-dienes with a Ti(II) catalyst.¹⁰ These examples also illustrate there is ample space for development of titanium-catalyzed hydrophosphination. In this report, we explore chemistry of triamidoamine-supported titanium compounds, based on those initially reported by Verkade¹¹,¹² and Schrock,¹³,¹⁴ respectively, due to their similarity to familiar zirconium congeners.¹⁵ Because photocatalytic hydrophosphination with zirconium compounds appears general,⁴,¹⁶ catalysis under these conditions was of particular interest. While the Ti-P in this system is subject to migratory insertion, a new phosphido derivative is not an active hydrophosphination catalyst. Unlike zirconium, the Ti–Me derivative promotes radical hydrophosphination under photolysis. This reactivity is more akin to radical hydrophosphination initiated by iron compounds as reported recently by Webster.⁸

RESULTS AND DISCUSSION

Treatment of (N₃N)TiCl (1, N₃N = N(CH₃CH₃NSiMe₃)₃) with 1 equiv of ethereal MeLi affords (N₃N)TiMe (2) in 91% yield as yellow crystals (eq. 1). The NMR spectra of 2 are simple, featuring an indicative methyl resonance at δ = 1.00 and methylene triplets at δ = 3.35, 2.16 in the ¹H NMR spectrum. Spectra of 2 are consistent with related derivatives.¹¹,¹³,¹⁴,¹⁷

![Chemical structure of (N₃N)TiMe (2)]

Initial hydrophosphination reactions were undertaken with styrene and phenylphosphine as substrates using 5 mol % 2 (Table 1). While catalysis was observed under ambient conditions (light and temperature), conversions were substantially higher under irradiation in both the visible and near ultraviolet. The reaction exclusively affords the anti-Markovnikov product. Decreasing the excess of phosphine lead to a mild decrease in selectivity, but the reaction remains selective to the single activation product. Control reactions demonstrated that light, and in particular photon density, is a critical factor in the observed reactivity.
It was initially hypothesized that catalysis would occur via substrate insertion into a Ti–P bond. Observation of this catalysis by $^{31}$P NMR spectroscopy did not reveal an apparent titanium-phosphido intermediate, despite the relatively high loading. Indeed, the high loading was deliberate to potentially observe such an intermediate. The absence of a clear phosphido compound is consistent with a developing hypothesis that many hydroposphination precatalysts would have greater reactivity if not for limited conversion to an active metal-phosphido derivative.\(^{15}\) To test both of these hypotheses, the preparation of a phosphido derivative was undertaken.

Treatment of 2 with either 1 equiv. or excess phenylphosphine failed to form a titanium phosphido product, and the only new resonances observed in $^{31}$P NMR spectra of these attempts were small amounts of dehydrocoupling products. For (N\(\text{N}\))Zr derivatives, the alkyl compounds do not directly react with P–H bonds because cyclometalation of the triamidoamine ligand occurs faster to afford \([\kappa^2-N,N,N,N-C-(\text{Me}_2\text{SiNCH}_2\text{CH}_2\text{NCH}_2\text{CH}_2\text{NSiMe}_2\text{CH}_2)]\text{Zr}\) than direct reaction with phosphine.\(^{18}\) Thus, (N\(\text{N}\))Ti(Bu) (3), a precursor known to cyclometallate and eliminate alkane,\(^{13}\) was used instead. Treatment of 3 with 1.1 equiv. of phenylphosphine in hexanes solution resulted in a color change to a deep red upon heating to 50 °C. Analytically pure, deep red crystals of (N\(\text{N}\))TiPPh$_2$ (4) were obtained in 88% yield upon crystallization from pentane solution at -40 °C (eq. 2). Spectroscopic data confirms the formulation, featuring diagnostic resonances at $\delta = 9.1$ and $\delta = 4.59$ in the $^{31}$P[\(\text{H}\)] and $^1$H NMR spectra, respectively, associated with the phenylphosphido ligand, and $v_{\text{PH}} = 2293$ cm$^{-1}$ was measured in the infrared. An expected LMCT band was observed at $\lambda = 508$ nm ($\varepsilon = 2300$ M$^{-1}$cm$^{-1}$) with an intense feature in the near UV $\lambda = 322$ nm ($\varepsilon = 110000$ M$^{-1}$cm$^{-1}$).

Crystals suitable for X-ray analysis were obtained by slow crystalization from cold pentane solution of 4, and molecular structure is shown in Figure 1. The key bond of 4, Ti1–P1 = 2.563(1) Å, is significantly longer than that of the cationic titanocene phosphido reported by LeGendre (Ti–P = 2.3599(14) Å).\(^{19}\) This increased bond length is consistent with the upfield shift of the $^{31}$P NMR resonance of 4 and with the limited ligand-to-metal $\pi$-bonding found for (N\(\text{N}\))ZrPRR’ compounds, though charge may play a role in these bond lengths as well.\(^{18}\) Comparison of geometry index\(^ {20}\) calculations at the metal center shows $\tau_{\text{Ti}} = 0.955$ versus $\tau_{\text{Zr}} = 1.02$,\(^ {23}\) but it is important to note that these calculations are not fully indicative of the geometry at these metals where study of zirconium compounds indicate significant deviation from a trigonal bipyramidal geometry.\(^ {18}\)

With a titanium phosphido in hand, catalysis testing was performed to determine the role of 4 for catalytic hydroposphination under irradiation. A reaction of phenylphosphine with styrene with 5 mole % of 4 was prepared and divided into four equal parts, with deliberate irradiation in each the visible (LED lamp) and near-UV centered at 360 nm, under ambient light, and a control in the dark. In the dark, no appreciable reactivity was observed over extended reaction times (24 h). Ambient lighting saw no conversion under similar reaction times to those for 2. After 1 h, both LED and 360 nm light showed no appreciable conversion to a hydroposphination product, though 4 did disappear to produce an as-yet unidentified resonance at $\delta \sim -121.3$.

\begin{table}[h]
\centering
\caption{Reaction Condition Screening for Hydroposphination of Styrene with Phenylphosphate}
\begin{tabular}{|c|c|c|c|}
\hline
conditions & t & X & Y \\
\hline
Dark & 5 h & < 1 % & 0 % \\
Dark, 75°C & 5 h & 16 % & 0 % \\
Ambient & 5 h & 36 % & 5 % \\
360 nm UV & 1 h & 22 % & trace \\
Blue LED can & 1 h & 63 % & 2 % \\
LED Lamp & 1 h & 40 % & 4 % \\
\hline
\end{tabular}
\end{table}

\textsuperscript{a}All reactions were run in benzene-$d_6$ solvent and temperature was monitored such that no runs were greater than 35 °C unless noted. Conversions were determined by integrating the $^1$H and $^{31}$P[\(\text{H}\)] NMR spectra.
isostructural zirconium compounds. The short C1–N1 bond length of 1.385 Å as well as the near-planarity of the Ti1–N1–C1–P1 system, as shown by dihedral angle of −168.54°, indicates significant conjugation. The phosphaalkene moiety is confirmed spectroscopically with diagnostic resonances at δ = 10.55, δ = 198.6, and δ = 92.5 for 1H, 13C{1H}, and 31P{1H} NMR spectra, respectively. Unfortunately, the predicted P=O stretch (~900 cm⁻¹) appears to be obscured by the triamidoamine backbone in the infrared.

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Alternatively, the reaction of 4 with benzonitrile in benzene-d6 occurred slowly over approximately 18 h. The product of the insertion, (N3N)TiN(H)(C(Ph)=PPh) (6) is shown in Figure 3. In this instance, a 1,2-insertion product forms, but somewhat surprisingly, the phosphaalkene tautomer is favored as the product. This was identified by the imine νN≡N = 3247 cm⁻¹ in the infrared. Diagnostic resonances in the NMR spectra are also seen including the imine hydrogen at δ = 9.02 and the phosphorus resonance δ = 86.74. The spectroscopic assignment was confirmed through X-ray crystallographic analysis. Like compound 5, a P1–C1–N1–Ti1 dihedral angle = −169.02°(8) and P1–C1 = 1.735(1) Å indicate the phosphaalkene moiety and extended conjugation. This reactivity is in stark contrast with the zirconium analog, which prefers the other tautomer, but is more consistent with analogous thorium reactivity.

Finally, a simple reaction between phosphido 4 and pivaldehyde was conducted in benzene-d6. The solution immediately became light yellow upon addition of the pivaldehyde, and yellow crystals were collected by crystallization from concentrated pentane solution (Scheme 1). The insertion product was assigned, in part, by νP=O = 2310 cm⁻¹ observed in the infrared, a indicative secondary 31P NMR resonance at δ = −51.8 (cf. PhMePCH has δ = −68.4),26 and a corresponding phosphine resonance in the 1H NMR spectrum at δ = 4.76 with diagnostic couplings (JPH = 203.6, 4.5 Hz). Unfortunately, single crystals of 7 were not able to provide satisfactory diffraction data for a molecular structure to confirm the spectroscopic data.

In light of insertion into the Ti–P bond, additional investigation of the hydrophosphination catalysis with 2 was undertaken. The first hypothesis was the potential for radical chemistry due to the facile Ti(III/IV) couple for many organometallic compounds. Webster has recently demonstrated effective use of the cyclopropyl substituent as a radical trap to corroborate radical-based mechanism.

A final experiment established that open-shell compounds are indeed being generated during catalysis. Reaction of 8 with
phenylphosphine in the presence of 10 mol % of 2 in pentane solution was conducted in an EPR tube. At the onset of the reaction, there were no signals in an ambient temperature EPR spectrum. When the reaction mixture was illuminated with a broadband UV lamp in the EPR spectrometer; however, features appear immediately, indicating that radicals are generated under reaction conditions (Figure S27). It is known that group 4 methyl compounds shows that they are capable of homolytic cleavage under light, and it is proposed that a similar Ti–C cleavage event is occurring in this system that leads to radical hydrophosphination.

**CONCLUSION**

Titanium compounds were known to engage in catalytic hydrophosphination, and the activity with styrene represents the most challenging substrate for this category of catalyst to date. However, the triamidoamine-supported titanium methyl precatalyst 2 appears to undergo Ti–C bond cleavage upon irradiation that generates radical intermediates that initiate hydrophosphination. Because similar metal-initiated radical hydrophosphination reactivity has already been reported for iron compounds by Webster, such reactivity may be a general pitfall for these most abundant 3d metals. Titanium compounds were known to engage in catalytic hyphosphination. Encouraging for identifying uniquely titanium-bonding, the difference from zirconium is, however, envisioned at this point as well. The most abundant 3d metals—however, the triamidoamine—like crystals that were isolated from the mother liquor. Repeated efforts for satisfactory analysis failed, despite apparently pure compound by NMR spectroscopy. The triamidoamine-supported titanium methyl precatalyst 2 appears to undergo Ti–C bond cleavage upon irradiation that generates radical intermediates that initiate hydrophosphination. Because similar metal-initiated radical hydrophosphination reactivity has already been reported for iron compounds by Webster, such reactivity may be a general pitfall for these most abundant 3d metals. Titanium compounds were known to engage in catalytic hyphosphination. Encouraging for identifying uniquely titanium-bonding, the difference from zirconium is, however, envisioned at this point as well. The most abundant 3d metals—however, the triamidoamine—like crystals that were isolated from the mother liquor. Repeated efforts for satisfactory analysis failed, despite apparently pure compound by NMR spectroscopy. The triamidoamine-supported titanium methyl precatalyst 2 appears to undergo Ti–C bond cleavage upon irradiation that generates radical intermediates that initiate hydrophosphination. Because similar metal-initiated radical hydrophosphination reactivity has already been reported for iron compounds by Webster, such reactivity may be a general pitfall for these most abundant 3d metals. Titanium compounds were known to engage in catalytic hyphosphination. Encouraging for identifying uniquely titanium-bonding, the difference from zirconium is, however, envisioned at this point as well. The most abundant 3d metals—however, the triamidoamine—like crystals that were isolated from the mother liquor. Repeated efforts for satisfactory analysis failed, despite apparently pure compound by NMR spectroscopy. The triamidoamine-supported titanium methyl precatalyst 2 appears to undergo Ti–C bond cleavage upon irradiation that generates radical intermediates that initiate hydrophosphination. Because similar metal-initiated radical hydrophosphination reactivity has already been reported for iron compounds by Webster, such reactivity may be a general pitfall for these most abundant 3d metals.
benzene-d₆, and 18 μL of pivaldehyde (0.1656 mmol, 1.02 eq.), to be monitored by NMR over time. The solution immediately lightened to a clear brown, and NMR indicated complete conversion. The tube was transferred back into the glovebox, and the solution was lyophilized, dissolved into pentane and stuck in the freezer to yield 74.5 mg (74.7%) of yellow crystals. ¹H NMR (500 MHz, CD₆D₆) δ 7.66 (dd, J₁ = 10.1, 4.0 Hz, 2 H, 2 aryl), 7.15–7.11 (m, 2 H, 2 aryl), 7.05 (t, J₂ = 7.4 Hz, 1 H, aryl), 5.45 (dd, J₁ = 4.4, 2.9 Hz, 1 H, CH₂), 4.76 (dd, J₁ = 203.6, 4.5 Hz, 1H, PH), 3.18 (qdd, J₁ = 13.5, 6.2, 4.8 Hz, 6H, CH₃), 2.50 (m, 6 H, CH₃), 1.22 (s, 9 H, CH₃), 0.38 (s, 27 H, SiCH₃). ¹³C NMR (126 MHz, CD₆D₆) δ 137.06 (arly), 134.58 (arly), 127.94 (arly), 97.79 (OCC), 62.88 (CH₂), 49.44 (CH), 39.40 (CH₂), 28.28 (CH₂), 1.75 (SiCH₃). ¹⁹F NMR (202 MHz, CD₆D₆) δ 51.85 (s). IR (KBr): 3068.92 (w), 3052.17 (w), 2994.30 (w), 2889.47 (m), 2849.38 (m), 2310.22 (m), 1294.49 (s), 870.55 (s), 825.89 (s), 781.03 (s), 734.07 (s), 712.06 (m).

Synthesis of α-cyclopropyl styrene (8) Prepared by a modification of literature procedure. To a 50 mL round bottom flask in the glovebox was added 4.110 g of methyl triphenylphosphonium bromide (11.51 mmol), 1.286 g of potassium tert-butoxide (11.48 mmol), and 1.33 g of cyclopropyl phenyl ketone (9.11 mmol, 0.8 equiv.) to yield 1.19 g (91%) of light yellow liquid. Spectra of the product matched literature values.

Synthesis of phenyl-2-phenylpent-2-en-1-ylphosphine (9) In the glovebox, to a 2 dram shell vial was added 213 μL of phenylphosphine (1.94 mmol), 139 mg 8 (0.969 mmol), 40.8 mg 2 (10 mol %), and 0.5 mL benzene-d₆. The reaction was transferred into an NMR tube and monitored by ¹H and ³¹P [¹H] NMR. The reaction was placed into a blue LED photoreactor, and after 1 hour all of the reactant alkene was consumed by ¹H NMR. Attempted purification by adding methanol and 30% hydrogen peroxide yielded yellow foam and decomposition. Partial characterization is as follows: ¹H NMR (500 MHz, CD₆D₆) δ 5.56 (t, J = 6.2 Hz, 1H), 4.11 (dt, J = 207.7, 7.4 Hz, P-H), 2.88 (m, 2H), 1.84 (m, 3H), 0.80 (t, J = 7.5 Hz, 3H). ³¹P [¹H] NMR (202 MHz, CD₆D₆) δ -55.26 (s).

General Protocol for Catalytic Runs
To a two-dram shell vial was added 35 μL of styrene, 0.5 mL benzene-d₆ spiked with 1.3,5-trimethoxybenzene, 67 μL phenylphosphine, and 6 mg 2. The mixture was transferred to an NMR tube and subject to reaction conditions, irradiation, dark, or ambient light, and monitored by ¹H and ³¹P [¹H] NMR spectroscopy. Completion was measured by the disappearance of styrene resonances, and conversion to hydrophosphination products were determined by integrating the phosphine signals. Thermal trials were done in a J-Young style NMR tube.

General Protocol for EPR Experiment
Prepared according to general procedure with the exception that the reaction mixture was in an EPR tube, the solvent was pentane, and the reaction mixture was irradiated with a Bruker ER 203V lamp accessory and monitored by EPR spectroscopy.

ASSOCIATED CONTENT
Supporting Information
Representative spectra of compounds and crystallographic data table (PDF). Full crystallographic data for compounds 4, 5, and 6 as CCDC 2237685–2237687, respectively (CIF).

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ACKNOWLEDGMENT
This research was supported by the U. S. National Science Foundation through CHE-2101766, and by the Japan Society for the Promotion of Science. EPR measurements were conducted in a spectrometer with optical cavity that was obtained through CHE-1919417.

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