RESEARCH ARTICLE

Zirconocene-Mediated Radical Hydrophosphination
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This work is dedicated to Rainer Streubel—a kind, supportive, and insightful colleague—on the bittersweet occasion of his retirement.

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Abstract: Hydrophosphination activity has been solicited from the parent and decamethyl zirconocene dichloride compounds, Cp₂ZrCl₂ and Cp₃*ZrCl₂. Given recent reports of photocatalytic hydrophosphination, these compounds were irradiated in the near ultraviolet (UV) as precatalysts resulting in the successful hydrophosphination of styrene substrates and activated alkenes. Irradiation appears to induce homolysis of the Cp or Cp* ligand, resulting in radical hydrophosphination. Successful detection of this radical reactivity was achieved by monitoring for EPR signals with in situ irradiation, a methodology proving to be general for the determination of radical versus closed-shell reactivity in transition-metal photocatalysis.

Introduction

Molecules containing P–C bonds are prevalent in pharmaceuticals, agriculture, polymers, and other materials.[1] An efficient way to form these bonds is through hydrophosphination, which leverages commodity alkene substrates in an atom-economical P–C bond forming step. Such efficiency is particularly attractive due to the diminishing supply of readily available phosphorus under consistently increasing global demand.[2] Hydrophosphination is, effectively, an example of a Michael addition for adequately activated unsaturated substrates. However, a Michael addition framework represents a narrow scope of substrates, and examples of base, acid, or transition-metal catalysis that expand substrate scope have been reported.[3] Likewise, direct photolysis to promote hydrophosphination is known, and these reactions are consistent with radical initiation.[4]

Recent reports demonstrate the efficacy of irradiation on accelerating metal-catalyzed hydrophosphination, which offers access to challenging unactivated substrates.[5] Irradiation of triamidoamine-supported zirconium under catalytic hydrophosphination conditions results in an enhancement of activity as well as facile access to unactivated alkene substrates. The increase in relative rate was attributed to a P n → Zr d charge transfer that elongates the Zr–P bond allowing for a more facile alkene insertion.[5a] Irradiation of catalytic systems can also lead to open-shell (radical) reactivity instead of closed-shell transformation. In contrast to zirconium, triamidoamine-supported titanium compounds undergo a homolytic cleavage of a titanium–alkyl bond to achieve modest hydrophosphination of styrene.[6] Successful detection of the radical species arose from trapping experiments that were buttressed by EPR measurements under direct irradiation. However, copper compounds, which are also accelerated in hydrophosphination by irradiation, do not form radicals according to EPR spectroscopy under catalytic conditions (i.e., irradiation).[5b]

Investigation of metallocene complexes of titanium and zirconium bearing M–P bonds has uncovered rich chemistry.[7] Stephan has detailed the reactivity of Cp₂Zr-phosphido derivatives, including insertion reactions, conversions to phosphinidine ligands, and catalytic P–H bond activation in the form of dehydrocoupling.[8] Of course, zirconocene-phosphido compounds were known far longer, and Baker’s studies provided key structural insight on zirconium-phosphorus multiple bonding.[9] While zirconocene-phosphido chemistry has been well documented, the absence of hydrophosphination with these compounds was odd in the literature, despite the success of related zirconium compounds in this transformation.[10a]

It was hypothesized that zirconocene compounds could be activated for hydrophosphination by photolysis if excitation that favored Zr–P bond elongation/weakening could be achieved. In the course of studying photolysis of zirconocene precatalysts for hydrophosphination, a radical-based hydrophosphination reaction was discovered. Previous reports on zirconocene complexes elucidate that ultraviolet (UV) irradiation leads to generation of two distinct radical species.[10c] Photolysis at the absorption band for zirconocenes leads to a ligand to metal charge transfer (LMCT) which produces a reactive excited state.
The L→Zr excited state leads to homolytic cleavage of the ligand and metal center, generating two radical species, a zirconium-centered radical [LZr•Cl₂] and a ligand-centered radical [L*] (Scheme 1). This photochemistry has been exploited in photoinitiated radical polymerization of alkenes.[11]

Scheme 1. Homolytic cleavage of L–Zr bond to generate radical species (L = Cp, Cp*).

**Results and Discussion**

Hydrophosphination with styrene and diphenylphosphine in the presence of 5 mol % of Cp₂ZrCl₂ (1) or Cp*₂ZrCl₂ (2) resulted in modest to good conversion within 4 h. Catalyst 1 showed higher activity with 86% conversion to PhCH₂CH₂PPh₂, whereas 2 only afforded conversion of 36%. A variety of styrene derivatives and other alkenes were tested for hydrophosphination. Standard catalytic reaction conditions were an equimolar mixture of alkene and diphenylphosphine in the presence of 5 mol % of either 1 or 2 in benzene-δ₆ using SiMe₄ as an internal standard (Table 1). The reaction was monitored via ³¹P and ¹H NMR spectroscopy at 2, 4, 6, and 24 h intervals. Both 1 and 2 showed good to high activity towards electron-withdrawing styrene substrates within 4 h (Table 1). The activity between these two catalysts diverges when using styrene derivatives bearing electron-donating groups at the para position. Complex 1 showed good conversion of 4-methoxystyrene and 4-methylstyrene within 4 h with conversions of 91% and 94%, respectively. In contrast, 2 afforded only 40% and 29% conversion for 4-methoxystyrene and 4-methylstyrene, respectively. The decrease in activity for 2 is most likely a combination of the C=C bond of these substrates being more difficult to activate, but photodecomposition of the catalyst may play a role as well. In contrast, activated alkenes gave near-quantitative conversion within 2 h, with only a slight increase after 4 h, while unactivated substrates gave, at best, trace conversion after 24 h of irradiation.

A report by Green and coworkers describes the decomposition of zirconocenes in different solvents under UV irradiation.[11a] When compared to 1, the degradation of 2 occurs at a faster rate. The decay of 2 occurred faster in the presence of THF. The basicity of diphenylphosphine may contribute to faster degradation of 2 under catalytic conditions, hence lower product conversion. Additionally, trace conversion of unactivated substrates is likely due to catalyst degradation before successful hydrophosphination of these substrates can occur.

It has been reported that irradiation of both 1 and 2 centered at 360 nm results in homolysis of the L–Zr bond, a process that was studied and exploited for radical alkene polymerization.[11] It was hypothesized that L–Zr cleavage may be faster than Zr–P photochemical activation, and efforts to identify radical reactivity were undertaken. First, radical reactivity was probed with propagation and (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) reactions. Propagation reactions were performed with styrene as
a substrate. Standard reaction mixtures were irradiated for 15 min followed by rigorous exclusion of light. The reaction was then monitored via $^{31}$P and $^1$H NMR at 2, 4, 6, and 24 h post-irradiation. After 15 min of irradiation, Cp$_2$ZrCl$_2$ showed 13% conversion to the hydrophosphination products and Cp$^+$ZrCl$_2$ showed 10% conversion, consistent with reactions run entirely under irradiation. After 24 h however, runs with compound 1 only gave 19% and compound 2 gave 21% conversion. At each interval of time taken, both catalysts displayed only a gradual increase in conversion (Table 2). These experiments demonstrate that continued irradiation is necessary but do not strongly support a radical or closed shell process. Previous study on the photochemistry of zirconocenes monitored via UV-vis spectroscopy demonstrates that photodecomposition under irradiation is a gradual process and occurs under constant irradiation.$^{[11a]}$ When samples are irradiated and left in the dark, the photodecomposition was noted to be reversible. Complete photodecomposition required exposure times greater than 15 min. Therefore, it appears possible that 15 min of irradiation time is sufficient to generate a limited quantity of active species, and some of that compound may revert to the ground state in the absence of light. This supposition helps understand why continuous irradiation is required to achieve high conversions during catalysis.$^{[11a]}$

| Table 2. Propagation experiments with 1 and 2.$^{[b,c,d]}$ |
|-----------------|-----------------|-----------------|
| Catalyst       | Conversion after | Conversion after |
|                | 0.25 h           | 4 h             |
| 1              | 13 %            | 19 %            |
| 2              | 10 %            | 20 %            |

$^{[b]}$ Complete table with timepoints is detailed in the Supporting Information. $^{[c]}$ Reactions ran in standard reaction conditions with the exception that samples were irradiated for only 15 min and then covered in aluminium foil and placed in the dark.

TEMPO has been used in previous repos to help determine if a reaction proceeds through an open- or closed-shell mechanism.$^{[8c, 12]}$ Trapping experiments were done utilizing catalytic (0.02 mmol, 10 mol %) and stoichiometric (0.2 mmol) amounts of TEMPO. Addition of 10 mol % of TEMPO to the hydrophosphination of styrene under otherwise standard conditions affords PhCH$_2$CH$_2$PPh$_2$. In 4 h, with compound 1, conversion is 86%, and with compound 2, conversion is 82% (Table 3). When comparing the reaction of 1 and 2 for hydrophosphination with an addition of 10 mol % of TEMPO, the conversions are effectively identical at each time point (Table S4). When stoichiometric TEMPO is added to the hydrophosphination of styrene, reactivity with 1 is inhibited and 2 shows trace only conversion to the hydrophosphination product over 24 h. These experiments highlight the use of TEMPO as a potential radical mediator in hydrophosphination for catalytic amounts, but the added TEMPO may act as a radical trap when used in stoichiometric amounts. These are still challenging results because it is already known that TEMPO reacts directly with phosphines, and the stoichiometric chemistry may merely reflect that background reactivity.$^{[13]}$

| Table 3. TEMPO experiments with 1 and 2 at 4 h under irradiation.$^{[b,d]}$ |
|-----------------|-----------------|
| Catalyst       | TEMPO           |
|                | TEMPO           |
| 1              | 86 %            | Trace %         |
| 2              | 82 %            | 14 %            |

$^{[b]}$ Complete table with timepoints is detailed in the Supplementary Information. $^{[d]}$ Reactions run in standard reaction conditions, with the exception of added TEMPO. Column 2 denotes the use of 10% (0.02 mmol) TEMPO and column 3 denotes the use of 1 equiv. (0.2 mmol) TEMPO.

The results garnered from the propagation and trapping reactions continued to tease at radical hydrophosphination with 1 or 2, but a more definitive experiment was needed. A strong technique in determining radical involvement during catalysis if to monitor the reaction via EPR during irradiation.$^{[5c, 6]}$ Control spectra of 1 or 2 shows no EPR signal. However, an EPR signal is observed when these samples were irradiated with UV light. This is similar with previous studies showcasing the homolytic cleavage of the Cp–Zr bond in Cp$_2$ZrCl$_2$.$^{[11b]}$ The signal observed by Laevlee and coworkers was assigned as a zirconium-centered radical [LZr•Cl]. and a ligand-centered radical [L•]. Similarly, EPR signal appears when a solution of Cp$^+$ZrCl$_2$ is irradiated. Standard hydrophosphination reactions with 1 or 2 show no EPR signal prior to irradiation with signal appearing upon irradiation. These results clearly establish that photodecomposition of these zirconocene compounds is occurring to generate radicals and that these are likely to initiate radical hydrophosphination of these substrates. Radical-based hydrophosphination reactions are known, as a proposed mechanism for zirconocene-mediated radical hydrophosphination is presented in Scheme 3.$^{[3b]}$ Metal-initiated radical hydrophosphination has been reported with iron by Webster. The reactivity patterns of these zirconocene precatalysts are similar to those observed by Webster and coworkers, further supporting the radical-based process for P–C bond formation.$^{[b,h]}$

\[ \text{Ph}_3\text{P} + \text{Ph}_2\text{PH} \rightarrow \text{Ph}_3\text{PPH}_2 \]

\[ \text{Ph}_3\text{PPH}_2 + \text{Ph}_2\text{PH} \rightarrow \text{Ph}_3\text{P} + \text{Ph}_2\text{PPH}_2 \]

**Scheme 3. Proposed mechanism for zirconocene-mediated radical hydrophosphination. I = [LZrCl] or [L•], where L = Cp or Cp\(^+\).**

**Conclusion**

Complexes 1 and 2 are photoinitiators for radical hydrophosphination, which was partially supported by propagation and radical trapping experiments. Observation of EPR signals under catalytic conditions, however, provides strong
evidence for the formation of radicals. Unlike other reports of light-enhanced zirconium-mediated hydrophosphination that operate via an elongation of the Zr–P bond due to a P n → Zr d transition, the zirconocene compounds in this study initiate reactivity via the homolysis of the L–Zr bond generating [LZrCl2] and[L]. This radical precursor affords reactivity similar to prior reported radical initiators.

Experimental Section

General considerations: Air- and moisture-sensitive reactions were carried out under purified N2 atmosphere using standard Schlenk and glovebox techniques. Ph3PH was prepared according to modified literature procedure. CP2ZrCl2 and CP2′ZrCl2 were prepared according to a modified literature procedure and recrystallized from hot CHCl3. Benzene-d6 was subjected to three freeze-pump-thaw cycles and stored over activated 3 Å molecular sieves. Styrenes and its derivatives were subjected to three freeze-pump-thaw cycles and passivated through activated basic alumina. Methyl acrylate, acrylonitrile, cylohexene, and 1-hexene were distilled over CaH2 or sodium metal. All alkenes were stored at −30 °C after purification. TEMPO was sublimed at 35 °C under dynamic vacuum. All NMR data was collected at 298 K on a Bruker AXR 500 MHz spectrometer. Spectra recorded were referenced to SiMe4 (δ = 0.00) for 1H NMR spectra or Ph3PH (δ = −41) for 31P NMR spectra. EPR measurements were collected on a Bruker EMX plus Spectrometer and samples irradiated with an ER 203UV irradiation system. Measurements were taken at ambient temperature. Microwave frequency = 9.85 GHz, microwave power = 0.6325 mW, modulation amplitude = 3 G, modulation frequency = 100.00 kHz, time constant = 0.01 ms, conversion time = 90 ms.

General procedure for hydrophosphination reactions: A scintillation vial was charged with 0.5 mL of a 0.02 M (0.01 mmol) zirconocene solution (in benzene-d6 with 0.1 M SiMe4 standard), 0.2 mmol of diphenylphosphine, and followed by 0.2 mmol of alkene. Contents were mixed then transferred to a PTFE-valved J-Young type-NMR tube, and the solution irradiated with a UV bulb centered at 360 nm. Reactions were monitored by 31P and 1H NMR spectroscopy at 0, 2, 4, 6, and 24 h intervals. Irradiation was done with a Rexam G23 UV-A (9 W) lamp. Photoreactor temperature was at 35 °C, control reactions done in the dark at 35 °C showed no conversion to the tertiary phosphine product.

General procedure for EPR measurements: 0.5 mL of a 0.02 M zirconocene solution in benzene-d6 was transferred to a quartz EPR tube. Initial measurements were taken before irradiation. Samples were irradiated in the EPR cavity for ca. 15 min, then the EPR measurement was retaken. Hydrophosphination reactions were also monitored via EPR before and after irradiation.

Supporting Information

The authors have cited additional references within the Supporting Information.

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Keywords: EPR Spectroscopy • Hydrophosphination • Photocatalysis • Radicals • Zirconium

References:


The parent and decamethyl zirconocene dichloride compounds are investigated as radical initiators for hydrophosphination. A radical process was uncovered by propagation, trapping, and EPR spectroscopy experiments.

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