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, Cp_2ZrCl_2 and $Cp^*_2ZrCl_2$. 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.

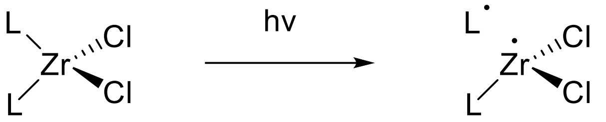
Introduction

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).[5c]

Investigation of metallocene complexes of titanium and zirconium bearing M–P bonds has uncovered rich chemistry.[7] Stephan has detailed the reactivity of Cp*Zr-phosphido derivatives, including insertion reactions, conversions to phosphinidene 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.[3a]

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.[10] 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•Cl_2], and a ligand-centered radical [L•] (Scheme 1).[10] This photochemistry has been exploited in photoinitiated radical polymerization of alkenes.[11]

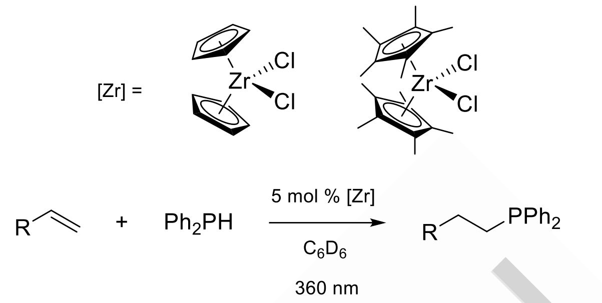


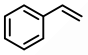
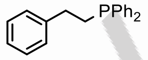
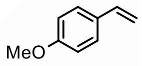
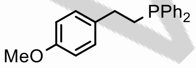
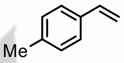
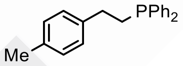
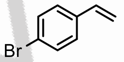
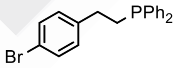
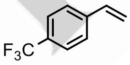
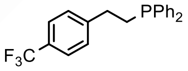
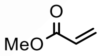
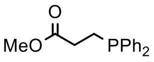
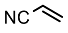
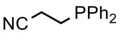
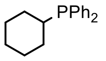
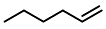
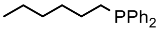
Scheme 1. Homolytic cleavage of L–Zr bond to generate radical species (L = Cp, Cp*).

Results and Discussion

Hydrophosphination with styrene and diphenylphosphine in the presence of 5 mol % of Cp_2ZrCl_2 (**1**) or $Cp^*_2ZrCl_2$ (**2**) resulted in modest to good conversion within 4 h. Catalyst **1** showed higher activity with 86% conversion to $PhCH_2CH_2PPh_2$, whereas **2** only afforded conversion of 36%. A variety of styrene derivates 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-d_6 using $SiMe_4$ as an internal standard (Table 1). The reaction was monitored via $^{31}P\{^1H\}$ 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 derivates 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. In some cases dehydrocoupling occurs, as evidenced by spectroscopic observation of Ph_2P-PPh_2, particularly when conversion to the hydrophosphination products is low.

Table 1. Hydrophosphination of alkenes with Cp_2ZrCl_2 (**1**) and $Cp^*_2ZrCl_2$ (**2**) at 4 h.[a]



Entry	Substrate	Product	Conversion with **1**	Conversion with **2**
1			86%	36%
2			91%	40%
3			94%	29%
4			90%	88%
5			98%	97%
6			>99%	>99%
7			96%	95%
8			-	-
9			trace	trace

Standard reaction conditions as described in text. The photoreactor temperature was 35 °C. Control reactions with styrene run in the dark at 35 °C showed no conversion after 5 h, and reactions run under UV-irradiation centered at 360 nm with no catalyst results in 22% conversion after 4 h. [a] Complete table with timepoints is detailed in the Supporting Information.

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 $^{31}P\{^{1}H\}$ and ^{1}H NMR at 2, 4, 6, and 24 h post-irradiation. After 15 min of irradiation, $\mathrm{Cp_2ZrCl_2}$ showed 13% conversion to the hydrophosphination products and $\mathrm{Cp*_2ZrCl_2}$ 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 (Figure 1). 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]

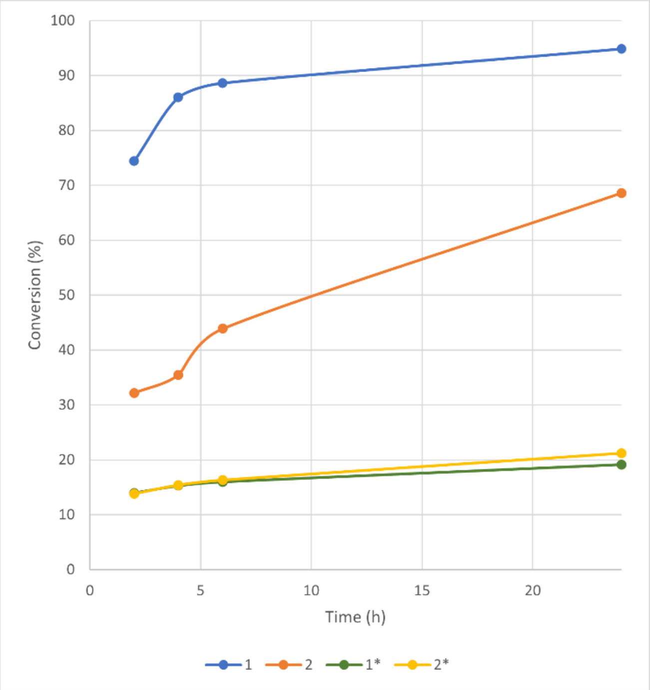


Figure 1. Comparison of conversion (%) between **1** (blue line, denoted as "1") and **2** (orange line, denoted as "2") under standard catalytic conditions with propagation experiments done with **1** (green line, denoted as "1*") and **2** (yellow line, denoted as "2*"). Tabulated data with conversions presented in the SI.

TEMPO has been used in previous reports to help determine if a reaction proceeds through an open- or closed-shell mechanism.[5c, 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 $\mathrm{PhCH_2CH_2PPh_2}$. In 4 h, with compound **1**, conversion is 78%, and with compound **2**, conversion is 73% ~~(Table 2).~~ 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. According to $^{31}P\{^{1}H\}$ NMR spectra, a mixture of products is formed. A report from Streubel highlights the reaction of diphenylphosphine with two equivalences of TEMPO.[13] The reaction produces a P-nitroxyl diphenylphosphine product which decomposes to P-nitroxyl diphenylphosphine oxide, diphenylphosphinylpiperidine oxide, and diphenylphosphine oxide. A different report by Yue also describes the behavior of diphenylphosphine oxide in the presence of TEMPO and styrene, yielding similar products as well as the formation of a TEMPO-trapped hydrophosphination product in low yields.[14] The formation of these products complicates the use of TEMPO as a potential radical mediator or trap, but these reactions have been detailed previously.[13-15] Stoichiometric TEMPO does not completely convert $\mathrm{Ph_2PH}$ to the nitroxyl compound, which would imply that hydrophosphination could still occur. As noted, however, the reaction is effectively inhibited under these conditions (Figure S4). Due to the complexity of TEMPO radical with phosphines, a more definitive—or at least less invasive experiment—was needed.

A strong technique in determining radical involvement during catalysis is monitoring 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 (Figure 2). This is similar with previous studies showcasing the homolytic cleavage of the Cp–Zr bond in $\mathrm{Cp_2ZrCl_2}$.[11b] The signal observed by Lalevee and coworkers was assigned as a zirconium-centered radical $[\mathrm{LZr{\bullet}Cl_2}]$, and a ligand-centered radical $[\mathrm{L{\bullet}}]$. Similarly, EPR signal appears when a solution of $\mathrm{Cp*_2ZrCl_2}$ is irradiated. Standard hydrophosphination reactions with **1** or **2** show no EPR signal prior to irradiation with signal appearing upon irradiation. The EPR spectra of **1** and **2** have apparent hyperfine coupling present, which can be attributed to the ligand-centered radical species. Additionally, an additional signal is present slightly upfield and overlapping with the hyperfine signals, which may be attributed to a zirconium-centered radical similar to what Lalevee observed and calculated. The EPR spectra of these complexes under catalytic conditions are complicated for assignment. Complex **1** under catalytic conditions shows the formation of a triplet or an overlapping doublet. While **2** under catalytic conditions show the formation of what seems to be a triplet with some complicated coupling occurring. The identity of these signals are most likely a mixture of radical species. Nevertheless, the observation of signals under catalytic conditions is clear evidence for radical formation during this transformation. These results establish that photodecomposition of these zirconocene compounds is occurring that generates radicals. Based on reactivity patterns, it is most that radical hydrophosphination of these substrates then occurs.

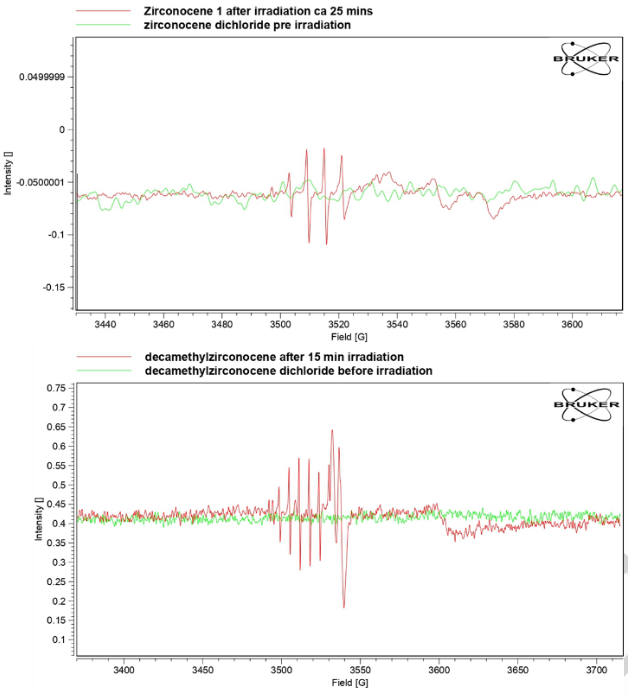
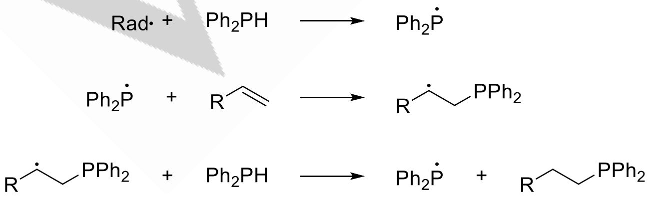


Figure 2. EPR spectra of compounds **1** (top) and **2** (bottom) before (green line) and after (red line) irradiation.

Radical-based hydrophosphination reactions are known, as a proposed mechanism for zirconocene-mediated radical hydrophosphination is presented in Scheme 2.[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.[4b]



Scheme 2. Proposed mechanism for zirconocene-mediated radical hydrophosphination. Rad• = [LZr•Cl$_2$] or [L•], where L = Cp or Cp*.

Conclusion

Compounds **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 [LZr•Cl$_2$] 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 N_2 atmosphere using standard Schlenk and glovebox techniques. Ph_2PH was prepared according to modified literature procedure.[16] Cp_2ZrCl_2 and $Cp^*_2ZrCl_2$ were prepared according to a modified literature procedure and recrystallized from hot $CHCl_3$.[17] Benzene-*d*$_6$ was subjected to three freeze-pump-thaw cycles and stored over activated 3 Å molecular sieves. Styrenes and its derivatives were passivated through a basic alumina column, subjected to three freeze-pump-thaw cycles, and passivated through activated basic alumina. Methyl acrylate, acrylonitrile, cyclohexene, and 1-hexene were distilled over CaH_2 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 $SiMe_4$ ($\delta = 0.00$) for ^{1}H NMR spectra or Ph_2PH ($\delta = -41$) for ^{31}P{^{1}H} NMR spectra. EPR measurements were collected on a Bruker EMXplus Spectrometer and samples irradiated with an ER 203UV irradiation system. Measurements were taken at ambient temperature. Parameters for EPR measurements are listed in the SI, as the parameters were varied depending on the sample.

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-*d*$_6$ with 0.1 M $SiMe_4$ 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 ^{31}P{^{1}H} and ^{1}H NMR spectroscopy at 0, 2, 4, 6, and 24 h intervals. Irradiation was done with a Rexim 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-*d*$_6$ was transferred to a quartz

EPR tube. Initial measurements were taken before irradiation. Samples were irradiated in the EPR cavity for ca. 15-25 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.[18]

Acknowledgements

This work was supported by the US National Science foundation through CHE-2101766 and CHE-1919417. The authors would like to thank Dr. Monika Ivancic for assistance in conducting EPR experiments.

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

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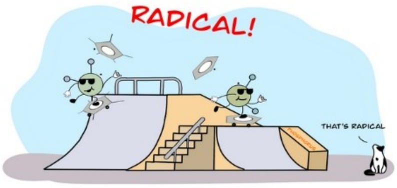

The parent and decamethyl zirconocene dichloride compounds are investigated as radical initiators for hydrophosphination. A radical process was uncovered by propagation, trapping, and EPR spectroscopy experiments.

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