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Intermolecular Zirconium-Catalyzed Hydrophosphination of Alkenes and Dienes with Primary Phosphines

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Supporting Information

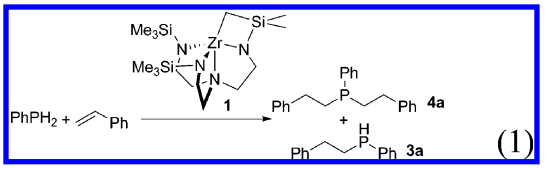
ABSTRACT: Catalytic hydrophosphination of terminal alkenes and dienes with primary phosphines (RPH_2; R = Cy, Ph) under mild conditions has been demonstrated using a zirconium complex, [κ^5-*N,N,N,N,C*-($Me_3SiNCH_2CH_2$)$_2$$NCH_2CH_2NSiMe_2CH$]Zr (**1**). Exclusively anti-Markovnikov functionalized products were observed, and the catalysis is selective for either the secondary or tertiary phosphine (i.e., double hydrophosphination) products, depending on reaction conditions. The utility of the secondary phosphine products as substrates for further elaboration was demonstrated with a platinum-catalyzed asymmetric alkylation reaction.

Despite the importance of organophosphines in a range of fields,[1] selective formation of P−C bonds remains a synthetic challenge.[2] For example, secondary phosphines are attractive compounds. These are precursors to tertiary phosphines, but these and their oxides are also useful as ligands[3] and have application in materials.[4] A leading metal-catalyzed route to organophosphines is hydrophopshination,[5−12] and despite success in the formation of tertiary phosphines, examples of selective formation of secondary phosphines have only been reported for limited substrates.[13−17]

Metal-catalyzed hydrophosphination has historically been dominated by the study of late transition metals,[5−12] but recent developments in early transition-metal, alkaline earth, and rare earth catalysts have shown great promise for the reaction.[14,18−27] Regardless, limitations in substrate remain. For example, unactivated alkenes are essentially absent from intermolecular hydrophopshination reactions.

Prior study of hydrophosphination and hydroarsination using traimidoamine-supported zirconium compounds was limited to terminal alkynes and carbodiimides.[28,29] Reinvestigation of these catalysis using primary phosphines has revealed greater reactivity than other systems for the hydrophosphination of alkene substrates, including unactivated alkenes. Additionally, these catalysts have high selectivity for either the secondary or tertiary phosphine product at ambient temperature, which may enable hydrophosphination to move from a specialty synthesis reaction to a broader commercial transformation.

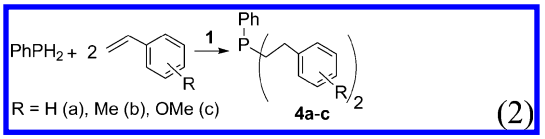
Treatment of styrene with 1 equiv of $PhPH_2$ at ambient temperature in the presence of 5 mol % of [κ^5-*N,N,N,N,C*-($Me_3SiNCH_2CH_2$)$_2$$NCH_2CH_2NSiMe_2CH$]Zr (**1**)[30] in benzene-d_6 solution completely consumed styrene to afford the single P−H addition product (PhC_2H_4)PHPh (**3a**) and the double P−H addition product (PhC_2H_4)$_2$PPh (**4a**) as a mixture in a 3:2 ratio as measured by ^{31}P NMR spectroscopy (eq 1).



(1)

Initial observation of the reaction by ^{31}P NMR spectroscopy showed the formation of (N_3N)ZrPHPh (**2**).[31] Hydrophosphination products **3a** and **4a** were identified by ^{1}H and ^{31}P NMR spectra and mass spectrometry and notably feature ^{31}P NMR chemical shifts of δ −52.2 and −24.1, respectively. These are anti-Markovnikov products based on ^{1}H NMR integrations, and compound **3a** displays J_{PH} = 205 Hz in both the ^{1}H and ^{31}P NMR spectra, consistent with a secondary phosphine.

Simple modification of this protocol allowed for a high isolated yield of either **3a** or **4a**. Reaction of $PhPH_2$ with 2 equiv of styrene in the presence of 5 mol % **1** gave exclusively tertiary product **4a** based on ^{31}P NMR spectroscopy (eq 2).



(2)

Furthermore, functionalized tertiary phosphines **4b** and **4c** can easily be prepared from 2 equiv of substituted styrene substrate and $PhPH_2$ in the presence of 5 mol % **1** under the same conditions as those for **4a** (eq 2).

More important, high selectivity for the *secondary* phosphine product was achieved by reacting styrene with 2 equiv of $PhPH_2$ and 5 mol % of **1**. The result was the desired secondary phosphine **3a** in a 9:1 ratio with **4a**. Careful distillation can return much (up to 75%) of unreacted $PhPH_2$, which affords pure secondary phosphine free from primary and tertiary derivatives. Though relatively few d^0 metal-catalyzed hydrophosphination reactions have been reported, the predominant substrate is Ph_2PH.[5−12] A notable exception here is Mindiola's titanium catalyst that uses a primary phosphine substrate and appears to proceed via [2 + 2] cycloaddition to a terminal phosphinidene.[14] However, this catalysis was only realized with an alkyne substrate. For these zirconium catalysts, selectivity for

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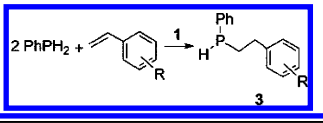
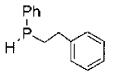
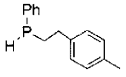
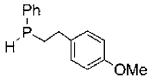
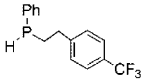
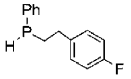
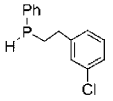
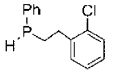
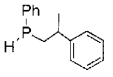
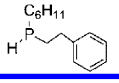
either the secondary or tertiary phosphine (i.e., single or double P−H addition) products by hydrophosphination under only slightly modified conditions represents a unique and convenient, atom-efficient method to obtain a variety of phosphine derivatives.

This transformation was readily elaborated to a variety of substituted styrene substrates with similar selectivity for the secondary product. Treatment of the styrene substrate with 2 equiv of primary phosphines using complex **1** as the catalyst gave functionalized secondary phosphines in good to excellent conversions (Table 1) and good isolated yields in several cases (Table 1, entries a, b, h, and i). The reactions are efficient (TON = 15−19) but at modest rates (TOF = 1.25−1.58 h^{-1}).

Table 1. Zirconium-Catalyzed Intermolecular Hydrophosphination of Styrenes with Primary Phosphines[a]



entry	Time/h	Product	Yield[b]
a	12		89 (72)
b	12		87 (69)
c	12		85
d	12		94
e	12		82
f	12		90
g	12		93
h	24		93 (80)
i[c]	60		74 (63)

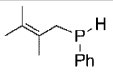
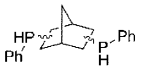
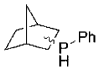
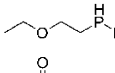
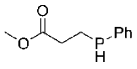
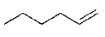
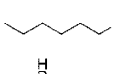
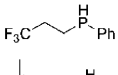
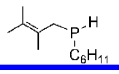
[a]Reaction conditions: 2.0 mmol of $PhPH_2$, 5 mol % of **1**, 1 mmol of styrene in 1 mL of benzene-d_6 at ambient temperature. [b]Yield was calculated from ^1H NMR of the crude product after complete conversion of alkene substrate. Isolated yields in parentheses are for reactions at 3 mmol scale. [c]$CyPH_2$ was used and required heating to 60 °C.

Halogenated styrene substrates react easily regardless the position of the halogen on the phenyl ring indicating some functional tolerance (Table 1, entries e−g). Hydrophosphination of a more sterically hindered styrene such as α-methylstyrene required longer reaction times (Table 1, entry h). Because the lowest yield in the hydrophosphination of functionalized styrenes was observed for *p*-methoxystyrene (Table 1, entry c), competition experiments were used to test electronic effects. Internal competition experiments favored styrene substrates bearing electron-withdrawing substituents, an observation that may suggest some degree of nucleophilic attack from the phosphide ligand.

Though primary phosphines are less bulky, these zirconium catalysts require no heating and achieve similar conversions with, in some cases, lower loadings than the perhaps most related rare earth and group 2 metal catalysts.[17,22−26] Because a myriad of primary phosphines are available, $CyPH_2$ (Cy = C_6H_{11}) was also tested as a substrate with styrene (Table 1, entry i). This reaction is qualitatively slower than that of $PhPH_2$, requiring elevated temperatures. However, $CyPH_2$ is the largest primary phosphine for which productive chemistry has been observed with these zirconium compounds.[31]

Given the initial success with styrene substrates, additional substrates, including both activated and unactivated alkenes, were targeted. Unactivated and cyclic alkenes as well as dienes were tested as hydrophosphination substrates using catalyst **1** and primary phosphines (Table 2). This catalyst was active for

Table 2. Zirconium-Catalyzed Intermolecular Hydrophosphination of Alkenes and Dienes with Primary Phosphines[a]

entry	Substrate	t/h	T/°C	Product	Yield[b]
a[c]		24	22		91(72)
b		24	22		40[d]
c[c]		24	22		88(82)
d		96	60		42[e]
e		6	22		96(90)
f		96	60		47[e]
g		120	90		~5[e]
h		120	90		22[e]
i[f]		96	60		85(63)

[a]Conditions: 2.0 mmol of $PhPH_2$, 5 mol % of **1**, 1 mmol of diene or alkene in 1 mL of benzene-d_6. [b]Yields determined using ^1H NMR after complete consumption of unsaturated substrate. Isolated yields in parentheses are reactions at 3 mmol scale. [c]Control reaction without **1** performed; detectable product observed after 3 d [d]Yield is estimated due to overlapping resonances with polymeric products. [e]Substrate was not completely consumed over the time noted. [f]$CyPH_2$ was used.

terminal alkenes and dienes but failed to catalyze the hydrophosphination of internal alkenes such as 3-hexene, *cis*-cyclooctene, or cyclohexene even at elevated temperatures and higher catalyst loadings.

The hydrophosphination of 2,3-dimethyl-1,3-butadiene with $PhPH_2$ gave the 1,4-addition product in good isolated yield with the same regioselectivity as found with calcium and titanium catalysts (Table 2, entry a).[26,27] Hydrophosphination

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of this substrate was also tested using $CyPH_2$, which required longer reaction times to give the same regioisomer of the secondary phosphine product (Table 2, entry i), similar to styrene hydrophosphination (*vide supra*).

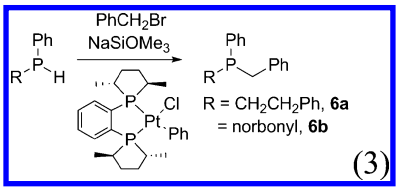
Cyclic but more strained alkenes such as norbornene and 2,5-norbornadiene proved to be successful in hydrophosphination with $PhPH_2$ using **1** (Table 2, entries b and c). Though the reaction with 2,5-norbornadiene underwent hydrophosphination to form functionalized secondary phosphines, a mixture of isomers was observed (Table 2, entry b). The yield for the hydrophosphination of 2,5-norbornadiene was low because of competing polymerization that hindered separation. Hydrophosphination of norbornene using **1** afforded a mixture of regioisomers, which are identical to the secondary phosphine reported in literature.[32] Simple unactivated alkenes were tested and were found to be successful substrates (TON ≈ 8−10), although longer times at higher temperatures were required (Table 2, entries d, f). Ethylene was a poor substrate (Table 2, entry g), and under these conditions, competing dehydrocoupling of $PhPH_2$ occurred.[31] However, the more facile hydrophosphination of 1-hexene and ethyl vinyl ether suggests that the solubility of ethylene in benzene may also have been a factor in the poor yield. Some improvement in conversion (TON ≈ 4) over that for ethylene was observed with the more soluble though electron-deficient 3,3,3-trifluoropropene (Table 2, entry h). The hydrophosphination of unactivated alkenes is significantly less efficient than that of styrenes and dienes, but these observations represent a substantial improvement over the current art. For example, calcium and ytterbium complexes failed to catalyze hydrophosphination of unactivated alkene substrates such as 1-hexene and norbornene with Ph_2PH despite success with styrene and diene substrates.[26]

Hydrophosphination reactions of Michael acceptors with phosphines can occur without a catalyst but suffer from lack of selectivity and require up to 30 d to reach completion.[33] Conversely, hydrophosphination of methyl acrylate with $PhPH_2$ using **1** readily formed the secondary phosphine after 6 h with high regioselectivity and isolated yield (Table 2, entry e).

Mechanistic aspects of hydrophosphination have been reviewed recently, and in general, d^0 metal catalysts are suggested to proceed via an insertion reaction.[9] This is consistent with a prior study of **1** in the catalytic hydrophosphination of terminal alkynes and carbodiimides that suggested insertion of the unsaturated substrate into the Zr−P bond was the P−C bond forming step in the catalysis.[29] A related mechanism can be tentatively proposed here for the hydrophosphination of alkenes with **1**, but it is important to underscore that not all observations (e.g., norbornadiene polymerization and 1,4-addition to butadiene) are accounted for in such a proposal. Reactions performed in the presence or absence of ambient light gave identical results, which is inconsistent with a radical reaction, though the product of norbornadiene polymerization here is similar to that initiated by radicals.[34] Tertiary hydrophosphination products would likely arise by the same catalytic cycle with the secondary phosphine as a substrate. Indeed, during the preparation of tertiary phosphines **4**, corresponding secondary phosphines **3** are observed but then diminish over time. These observations provide a convenient hypothesis that the selectivity is driven by kinetic factors in which secondary phosphines are simply slower substrates than the primary phosphine counterparts. However, greater mechanistic study of this system is warranted.

In nearly all examples, control reactions under the same conditions in the absence of **1** gave negligible product formation after 3 d. For the best substrates (e.g., styrene), up to 10% product formation can be observed after several days of heating. Hydrophosphination of methyl acrylate with $PhPH_2$ in the absence of **1** gave complete consumption in 3 d as a mixture of products, in contrast to the catalyzed reaction.

Initial demonstration of the synthetic utility of these secondary phosphine products was made through platinum-catalyzed asymmetric alkylation as reported by Glueck.[35] Reaction of **4** with benzyl bromide in the presence of $NaOSiMe_3$ and catalytic (*R*,*R*-Me-DuPhos)PtCl(Ph)[36] gave the tertiary product $(PhCH_2CH_2)PhP(CH_2Ph)$ (**6a**, eq 3). The



ee of the product was scarcely measurable, but sterically encumbered phosphines are required for optimal ee values in these transformations. Thus, reaction of **5c** under the same conditions gave (norbonyl)$PhP(CH_2Ph)$ (**6b**) in 98% yield with 61% ee as measured with a chiral reporter.[37]

In summary, triamidoamine-supported zirconium compounds catalyze the hydrophosphination of alkenes and dienes using primary phosphines. This catalyst can select for the tertiary or secondary phosphine products with simple modification of reaction conditions. Additionally, compound **1** shows activity for unactivated alkenes such as 1-hexene, substrates largely absent in prior reports. The ability to further elaborate on the secondary phosphine products suggests that this catalysis could have an impact on the commercial synthesis of phosphines. Further exploration of this catalysis is underway.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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