Letter

Zirconium-catalyzed intermolecular double hydrophosphination of alkynes with a primary phosphine

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ACS Catal., **Just Accepted Manuscript** • DOI: 10.1021/acscatal.6b01850 • Publication Date (Web): 25 Aug 2016

Zirconium-Catalyzed Intermolecular Double Hydrophosphination of Alkynes with a Primary Phosphine

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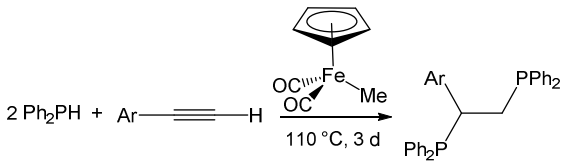
Supporting Information Placeholder

ABSTRACT: Catalytic double hydrophosphination of internal alkynes and primary phosphines is possible using a zirconium complex, [κ^5-*N,N,N,N,C*-($Me_3SiNCH_2CH_2)_2NCH_2CH_2NSiMe_2CH$]Zr (**1**). The reaction proceeds via stepwise hydrophosphination to give vinyl phosphine products, which can be isolated or further converted to the respective 1,2-bis(phosphino)ethane (i.e., double hydrophosphination). The catalysis is highly selective for formation of secondary phosphine products.

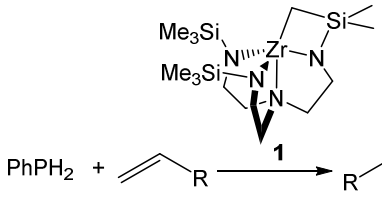
Keywords: Hydrophosphination, double hydrophosphination, primary phosphine, zirconium, internal alkynes, acetylene

Despite advances in selective P–C bond formation,[1-10] significant hurdles remain.[11] Metal-catalyzed hydrophosphination has been under scrutiny for more than 25 years owing to its potential to address challenges in the selective synthesis of materials, biomolecules, and ligands for catalysis. Substrates remain a particular challenge in metal-catalyzed hydrophosphination. For example, there are only a limited set of metal catalysts that engage in the hydrophosphination of alkynes, despite the greater reactivity of these molecules over alkenes.[12-20] Among those reactions, Nakazawa's reports of a simple iron catalyst for the intermolecular double hydrophosphination of terminal alkynes stands out (Eq 1).[12, 17] That unique chemistry provided direct access to 1,2-bis(diphosphino)ethanes, privileged architectures for late transition-metal catalysis. This iron catalysis and a recent report from Di Giuseppe et al. are the two known metal-catalyzed *double* hydrophosphination reactions to date.[12, 17, 21]



(1)

There are challenges with the phosphine substrate as well. Primary phosphines have received limited attention as substrates due to the potential for mixtures of secondary and tertiary phosphine products, despite early successes with these substrates.[22-23] In recent years, primary phosphines have been under more intense reinvestigation due to the potential to further functionalize the secondary phosphine products, which can be prepared selectively using range of catalysts.[24] Among those, zirconium catalysts have been particularly successful with primary phosphine substates,[25-26] providing substantial, albeit not ideal, conversions with even unactivated alkenes—a substrate class all but untouched by intermolecular hydrophosphination (Eq 2).

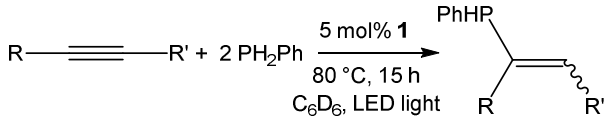


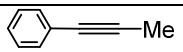
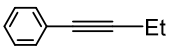
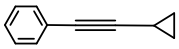
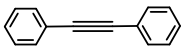
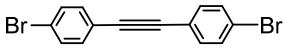
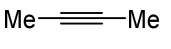
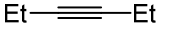
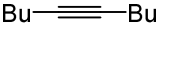
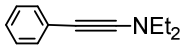
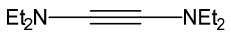
(2)

Investigation of zirconium-catalyzed intermolecular hydrophosphination of alkynes has yielded unique reactivity. The zirconium compound **1** ([κ^5-*N,N,N,N,C*-($Me_3SiNCH_2CH_2)_2NCH_2CH_2NSiMe_2CH$]Zr) has good reactivity for the intermolecular hydrophosphination and double hydrophosphination of internal alkynes, a category of substrates not successful for Nakazawa[12, 17] or Di Giuseppe et al.,[21] suggesting these are highly complementary systems. The net result is that these catalysts now avail the full suite of alkyne substrates for hydrophosphination and *double* hydrophosphination.

Treatment of alkyne substrate with two equivalents of $PhPH_2$ and 5 mol % of **1** results in hydrophosphination to give the vinyl phosphine product after 15 h at 80 °C under irradiation by an 830 lumen, 9-Watt LED lamp (Table 1). Light is important for catalysis. Reactions run under ambient light proceeded with consistent conversions, whereas reaction run in the absence of light resulted in no hydrophosphination under identical conditions. Thus, direct irradiation with visible photons appears to be necessary to activate alkyne substrates. The product phosphines are formed as a mixture of *E* and *Z* isomers and can be isolated in yields up to 78%. Vinyl phosphine **2d** and **2h** are stable for at least 14 d at ambient temperature under a nitrogen atmosphere. Hydrophosphination in the absence of **1** under otherwise identical conditions fails to provide detectable amounts of hydrophosphination products.

Table 1: Hydrophosphination of internal alkynes with $PhPH_2$[a]



entry	alkyne substrate	NMR conv. (%)	*E*:*Z* ratio
2a		99 (78)	5.1 : 1
2b		99	1.9 : 1
2c		96	1.8 : 1
2d		89 (64)	3.1 : 1
2e		75	3.7 : 1
2f		96 (76)	3.5 : 1
2g		88 (70)	1 : 1.5
2h		59 (41)	1 : 1.8
2i		46	1 : 1.2
2j[b]		80	15.5 : 1

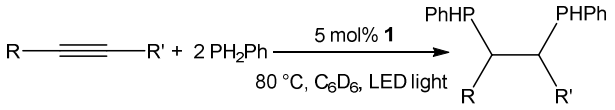
[a] Reactions run in a PTFE-valved NMR tube, heated to 80 °C under visible irradiation. Conversion to product phosphines determined by ^{31}P NMR integration. Values in parenthesis represent isolated yields. [b]Reaction ran at ambient temperature.

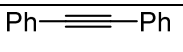
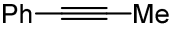
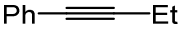
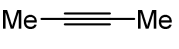
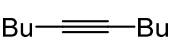
Hydrophosphination of unsymmetrical aryl/alkyl-substituted alkynes provides the secondary phosphine products with complete selectivity for the new P–C bond at the alkyl-substituted position (i.e., R = alkyl and R' = aryl in the equation with Table 1) and no detectable amounts of P–C bond formation at the aryl-substituted position (Table 1, **2a**–**2c**, **2i**). The observed selectivity may be governed by steric effects because the alkyl substituents employed are limited in size. Indeed, hydrophosphination of diarylacetylenes proceeded smoothly, indicating that the reaction is not in some way limited by an aromatic substituent (Table 1, **2d** and **2e**).

Unactivated alkynes react readily to provide the corresponding vinyl phosphines (Table 1, **2f**–**2h**). Hydrophosphination of 2-butyne provides the greatest conversion under these conditions as compared to related dialkyl-substituted alkynes, which demonstrates a steric dependence. The longer chain alkyls also favored the *Z* isomer, which may be an expression of the decrease in steric hindrance of alkyl groups interacting on the same side of the molecule. Alkynes possessing aryl groups favor the *E* isomer likely due to a decreased steric interaction between the phenylphosphino group and the aryl substituent.

The highest selectivity was observed for bis(diethylamino)acetylene (Table 1, **2j**), which readily provided the single hydrophosphination products after 15 h at ambient temperature with a 15.5 : 1 selectivity for the *Z* isomer. Experiments in which only one equivalent of $PhPH_2$ was added to bis(diethylamido)acetylene to purposely form the single hydrophosphination products resulted in a 78 : 1 formation of the *E* : *Z* isomers (Table S1). Unlike the other vinyl phosphines (Table 1), these (**2j** *E* & *Z*) products readily isomerized in the presence of excess primary phosphine. Control experiments indicated that **1** is not responsible for isomerization (see Supporting Information for details).

Table 2: Double hydrophosphination of internal alkynes with $PhPH_2$[a]



entry	alkyne	t/d	NMR conv. (%)
3a		9 (62)	78
3b		3 (71)	92
3c		6	88
3d		4	96
3e		4 (55)	78
3f		7	73

[a] Reactions run in a PTFE-valved NMR tube, heated to 80 °C under visible irradiation. Conversion to product phosphines determined by ^{31}P NMR integration.

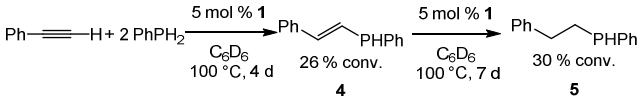
Treatment of a vinyl phosphine product with a second equivalent of $PhPH_2$ provides the corresponding 1,2-bis(phosphino)ethane as a mixture of *rac* and *meso* isomers in high yields with ^{31}P NMR chemical shifts in the range of –28 to –41 ppm. The reaction proceeds with regioselective addition of the P–H bond across the alkyne such that no formation of the 1,1 addition product is observed. Notably, the second hydrophosphination product can be obtained either by reaction of the isolated vinyl phosphine or in a one-pot procedure by reacting alkyne with two equivalents of the primary phosphine.

Unactivated alkynes are a challenging class of hydrophosphination substrates. However, these are converted by **1** to both the single hydrophosphination products (vide supra) and double hydrophosphination products (Table 2, **3d**-**3f**). The TONs for these unactivated substrates (TON = 14–19) are nearly identical to the TON of aryl alkynes (TON = 15–18), suggesting that unactivated substrates are no less efficient than their activated counterparts. This similarity may represent inhibition only by steric factors as hydrophosphination of diphenylacetylene had both a lower TON and TOF (TOF = 8.7 d^{-1}) than all other internal alkynes tested (TOF = 10.4–30.7 d^{-1}). The observation that hydrophosphination catalysis with **1** has comparable activity for both activated and unactivated alkynes represents a rare exception in this field.

Although double hydrophosphination of terminal alkynes has been demonstrated,[12, 17, 21] those substrates were not com-

patible with **1**. Attempted hydrophosphination of 1-hexyne with 5 mol % **1** provided 5% conversion after 8 d at 80 °C with a loss of anti-Markovnikov selectivity. Control reactions without **1** provide virtually identical results, indicating that this reaction is a thermal process rather than a catalytic one.

Previous investigation of heterofuctionalization using **1** as a catalyst with terminal alkynes were successful with diphenylphosphine and diphenylarsine.[27-28] In those reactions, it was established that phenylacetylene inhibited catalysis such that extended reaction times at relatively high temperatures were required. Treatment of one equivalent of phenylacetylene with two equivalents of $PhPH_2$ in the presence of **1** provided 26% conversion to the single hydrophosphination product **4** after four days at 100 °C (eq. 3). Extended reaction times failed to deliver the second hydrophosphination product and provided the *hydrogenation* product, $PhCH_2CH_2PHPh$ (**5**), in 30 % conversion instead. Product **5** is the known hydrophosphination product of styrene with $PhPH_2$.[25]

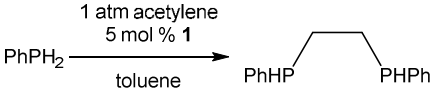


(3)

Attempted hydrophosphination catalysis of phenylacetylene with **1** at these high temperatures and extended reaction times gives, as anticipated, competitive dehydrocoupling of the primary phosphine. Analysis of the crude $^{31}P\{^1H\}$ NMR spectrum after seven days revealed a 20% conversion of $PhPH_2$ to dehydrocoupled products,[29] allowing for a buildup of hydrogen gas in the sealed NMR tube. Thus, it is hypothesized that **5** arises from the hydrogenation of **4** by **1** or hydrogenation of phenylacetylene to styrene with this ambient hydrogen atmosphere. It has, however, been demonstrated that **1** is a poor hydrogenation catalyst with a hydrogen atmosphere, though such forcing conditions were not explored in those studies.[30] A related hydrophosphination system also suffered from competitive hydrogenation during catalytic hydrophosphination of phenylacetylene.[21] Attempts to isolate the vinyl phosphine intermediate by vacuum distillation were hindered by the similar volatilities of both the vinyl and saturated phosphines. Isolation of **5** by vacuum distillation provided identical spectroscopic data as that for the authentic compound.[25, 31]

Nakazawa's iron catalyst that successfully engages in double hydrophosphination of terminal aryl alkynes has not been demonstrated to be effective with internal alkyne substrates.[12, 17] In this regard, compound **1** and $CpFeMe(CO)_2$ represent a highly complementary pair of catalysts in this exceedingly rare double hydrophosphination reaction. Double hydrophosphination with terminal alkynes were also noted in Oro's report.[21]

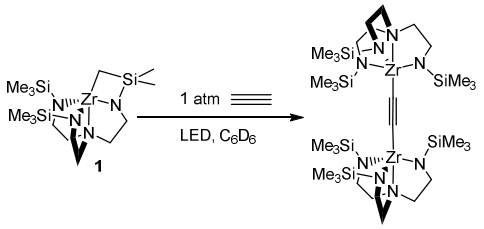
Secondary phosphines,[32-34] and primary phosphines[25] have been known to undergo hydrophosphination with ethylene, but so far there has been no report of hydrophosphination reactions involving acetylene. However, functionalization of the parent molecule offers an unparalleled opportunity for further synthesis of specialized diphosphines that are employed in an array of conventional transformations. Heating a solution of $PhPH_2$ in toluene with catalytic amounts of **1** under an 1 atm of acetylene results in 65% yield of 1,2-bis(phenylphosphino)ethane[35] after 18 h (Eq. 4).



(4)

Removal of **1** by filtration through Celite® followed by distillation affords the product as a 1:1 mixture of *rac* and *meso* isomers. Control experiments in which $PhPH_2$ is heated under acetylene gas in the absence of **1** fails to convert measureable amounts of 1,2-bis(phenylphosphino)ethane under identical conditions. It should be noted that the quality of the acetylene gas is crucial for hydrophosphination to occur, as acetylene samples of lesser purity failed to provide detectable hydrophosphination products.

Conversion of acetylene to 1,2-bis(phenylphosphino)ethane[35] was surprising based on the lack of catalytic reactivity with terminal alkynes. It was anticipated that acetylene would readily ring open **1** and form an alkynyl compound related to those known for terminal alkynes,[27, 29] a risk that seemed amplified by acetylene's ability to act as a bridging ligand between two zirconium centers. Indeed, reaction of **1** with 1 atm of acetylene results in immediate formation of bimetallic **6**, in which acetylene bridges the two zirconium centers (Eq 5).



(5)

Compound **6** displays four resonances in the ^{13}C NMR spectrum, including a single alkyne peak at δ 94.2, indicating a symmetric complex. Sublimation returns **6** as an off-white solid, which is highly related to terminal alkynyl derivatives by conventional spectroscopic interrogation.[27, 29] Treatment of **6** with one equivalent of $PhPH_2$ results in no detectable ligand exchange after two days at 80 °C, which is similar to the lethargic reactivity of $(N_3N)ZrC{\equiv}CPh$ toward Ph_2PH, despite the fact that both $(N_3N)ZrC{\equiv}CPh$ and **1** are active catalysts for the hydrophosphination of phenylacetylene with Ph_2PH.[29]

In summary, we have reported the first example of a double hydrophosphination of internal alkynes in a simple, one-pot procedure. This is also the first example of a double hydrophosphination of alkynes to use a primary phosphine and a rare example of a hydrophosphination of internal alkynes. Acetylene gas was also shown to undergo hydrophosphination with **1** to provide the common moiety 1,2-bis(phosphino)ethane. Hydrophosphination of acetylene, also a unique substrate, by **1** results in the formation of **6**, a bimetallic zirconium species. These double hydrophosphination reactions provide a significant complement to the only other known catalysts for this reaction, Nakazawa's iron compounds,[12, 17] and a rhodium *N*-heterocyclic carbene compound[21] that afford similar reactivity with terminal alkynes. The zirconium-catalyzed reactions occur in a stepwise fash-

ion, which has allowed for the convenient isolation of a family of vinyl phosphines. Further exploration of this catalysis is currently underway.

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Notes

The authors declare no competing financial interest.

ASSOCIATED CONTENT

Supporting Information

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

ACKNOWLEDGMENT

This work was supported by the U.S. National Science Foundation (CHE- 1265608 and CHE- 1565658).

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