

## Efficient and Selective Nickel-Catalyzed Addition of H–P(O) and H–S Bonds to Alkynes

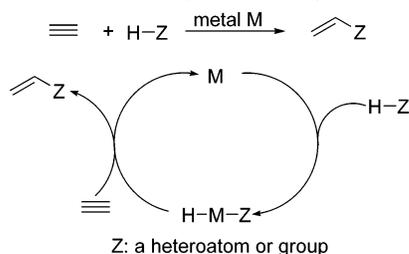
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Metal complex-catalyzed additions of a heteroatom compound H–Z (Z = a heteroatom or group) to a carbon–carbon unsaturated bond (Scheme 1) is one of the most straightforward ways for the preparation of heteroatom compounds, which have wide applications in organic synthesis and industrial processes.<sup>1</sup> Whereas the second and third row VIII B metals have been frequently used as the catalysts for these reactions, the corresponding first row metals were often known to show lower catalytic activity and/or give unsatisfactory results.<sup>2</sup> For example, nickel did not catalyze the hydrosilylation reactions as efficiently as platinum or rhodium and gave a rather complex result.<sup>3</sup> Similarly, nickel showed poor catalytic activity in the additions of thiols<sup>4b</sup> and P(O)–H compounds,<sup>5b</sup> where noble metals efficiently promote the reactions.<sup>4,5</sup> However, the replacement of these noble metals by cheaper ones is highly desirable since it can directly lead to a large cost reduction for the preparation of the products, which is crucial for an industry process.

### Scheme 1. Simplified Mechanism for the Metal-Catalyzed Addition of H-Heteroatom Compounds to Alkynes<sup>a</sup>



<sup>a</sup> For clarity, ligands on the metal M were eliminated.

Since a hydrido metal complex generated by the oxidative addition of H–Z to the metal is a key intermediate in the metal-catalyzed additions (Scheme 1) and since a hydrido nickel complex is probably more reactive than its noble metal analogues,<sup>6</sup> we surmise that catalyst nickel should not be inherently inferior to the noble metals.<sup>2</sup> We disclose herein that, to our surprise, by only slightly adjusting the structure of the phosphine ligand, nickel(0) can catalyze, more efficiently than the noble metals,<sup>4,5</sup> the addition of a variety of H–P(O) and H–S bonds to alkynes, *at room temperature*. Moreover, both the Markovnikov and the anti-Markovnikov adducts can be generated selectively by this single nickel-catalyzed reaction.

As demonstrated in Table 1, Ni(cod)<sub>2</sub> did not catalyze the addition of (MeO)<sub>2</sub>P(O)H to 1-octyne even on heating. The addition reaction slowly proceeded when Ni(PPh<sub>3</sub>)<sub>4</sub>, in situ generated from Ni(cod)<sub>2</sub> and PPh<sub>3</sub>, was used as the catalyst to produce 25% yield of the adducts after being stirred at room temperature for 2 h. *Dramatically, however, as PPh<sub>3</sub> was replaced by PPh<sub>2</sub>Me, the addition took place readily to afford the adducts in a high combined yield within 2 h!* It is clear from Table 1 that both alkyl- and aryl-substituted phosphines can be used as ligands and a steric crowdedness on the phosphine is the key factor determining the

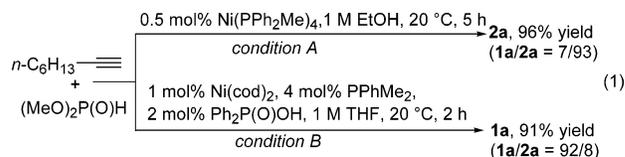
**Table 1.** Nickel-Catalyzed Addition of (MeO)<sub>2</sub>P(O)H to 1-Octyne<sup>a</sup>

PR <sub>3</sub>	% yield (1a/2a)	PR <sub>3</sub>	% yield (1a/2a)
none <sup>b</sup>	none	PPhCy <sub>2</sub> <sup>c</sup>	trace
PPh <sub>3</sub>	25 (36/64)	PPhMe <sup>t</sup> -Bu	23 (44/56)
PPh <sub>2</sub> Me	93 (35/65)	PMe <sub>3</sub>	93 (62/38)
PPh <sub>2</sub> Bu	79 (53/47)	PEt <sub>3</sub>	69 (31/69)
PPh <sub>2</sub> <i>i</i> -Pr	4 (62/38)	PBu <sub>3</sub>	40 (35/65)
PPhMe <sub>2</sub>	98 (55/45)	P( <i>t</i> -Bu) <sub>3</sub>	none
PPhEt <sub>2</sub>	96 (24/76)		

<sup>a</sup> Reaction conditions: 0.05 mmol Ni(cod)<sub>2</sub>, 0.2 mmol PR<sub>3</sub>, 1.0 mmol (MeO)<sub>2</sub>P(O)H, and 1.0 mmol 1-octyne in 1 mL of THF. Yields and ratios of the adducts were determined by GC. <sup>b</sup> Conducted at 67 °C for 5 h. <sup>c</sup> Cy = cyclohexyl.

catalyst's activity. Thus, although PPh<sub>2</sub>Bu worked similarly, in sharp contrast, a bulkier PPh<sub>2</sub>*i*-Pr only promoted the reaction sluggishly. The less sterically hindered but more basic PPhMe<sub>2</sub> and PPhEt<sub>2</sub> could work more efficiently than PPh<sub>2</sub>Me to give nearly quantitative yields of the products. Furthermore, *these additions are so clean that even the highly expected nickel-catalyzed oligomerization products<sup>7</sup> could not be detected from the reaction mixture.* However, once again, the bulkier PPhCy<sub>2</sub> (Cy = cyclohexyl) and PPhMe<sup>t</sup>-Bu did not work well. This steric effect was also clearly demonstrated by using trialkylphosphines. Thus, though the small PMe<sub>3</sub> can trigger the reaction as efficiently as PPhMe<sub>2</sub>, the product's yields decrease as the phosphine goes down from PEt<sub>3</sub> to PBu<sub>3</sub>, and P(*t*-Bu)<sub>3</sub> failed to promote the addition. It was noted that the corresponding palladium, platinum, and rhodium complexes do not catalyze this addition under similar reaction conditions.<sup>1d,5,8</sup>

Although a mixture of regioisomers **1** and **2** was obtained from above reactions, interestingly we found, for the first time, that selective generation of both **1** and **2** could be achieved via this single nickel-catalyzed reaction by slightly tuning the reaction conditions (eq 1), which undoubtedly provides a powerful tool for



the preparation of the synthetically and biologically valuable alkenylphosphonates.<sup>8</sup> Thus, in the presence of a tiny amount of Ni(PPh<sub>2</sub>Me)<sub>4</sub>, the reaction carried out in EtOH at room temperature proceeded rapidly to afford the adducts in high yield with 93% regioselectivity to adduct **2a** (condition A). On the other hand, when the same reaction was conducted in THF in the presence of a

**Table 2.** Nickel-Mediated Selective P–H Addition to Alkynes
$$\text{R}-\text{C}\equiv\text{C} + [\text{P}]-\text{H} \xrightarrow{\text{cat. Ni}} \begin{matrix} [\text{P}] \\ | \\ \text{R}-\text{C}=\text{C} \\ | \\ \text{1} \end{matrix} \quad \left( \text{R}-\text{C}=\text{C}-[\text{P}] \right) \\ \text{2}$$

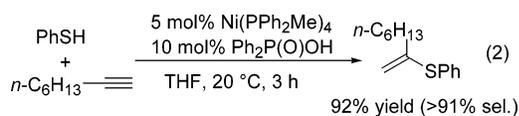
R	[P]–H	condition	% yield (1/2) <sup>a</sup>
Ph	(MeO) <sub>2</sub> P(O)H	A	91 (1/99)
Ph	(MeO) <sub>2</sub> P(O)H	B	72 (90/10) <sup>b</sup>
<i>n</i> -C <sub>6</sub> H <sub>13</sub>	Ph(EtO)P(O)H	A	95 (5/95)
<i>n</i> -C <sub>6</sub> H <sub>13</sub>	Ph(EtO)P(O)H	B	93 (92/8)
Ph	Ph(EtO)P(O)H	A	87 (1/99)
Ph	Ph(EtO)P(O)H	B	89 (94/6)
<i>n</i> -C <sub>6</sub> H <sub>13</sub>	Ph <sub>2</sub> P(O)H	A	96 (12/88)
<i>n</i> -C <sub>6</sub> H <sub>13</sub>	Ph <sub>2</sub> P(O)H	B	93 (88/12)
Ph	Ph <sub>2</sub> P(O)H	A	81 (4/96)
Ph	Ph <sub>2</sub> P(O)H	B	79 (93/7)

<sup>a</sup> Isolated combined yield of the adducts. Ratios of **1** to **2** were determined by <sup>1</sup>H NMR. <sup>b</sup> Conducted at 67 °C for 3 h.

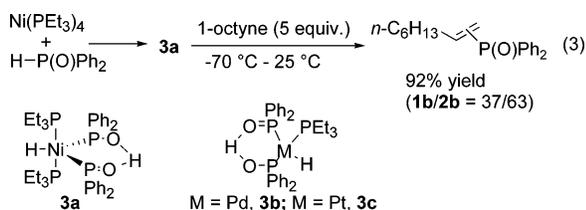
combination of Ni(cod)<sub>2</sub>/PPhMe<sub>2</sub>/Ph<sub>2</sub>P(O)OH (condition B),<sup>9</sup> a high yield of the adducts with a regioselectivity of 92% to **1a** was obtained.

The nickel-catalyzed reaction is highly general. As demonstrated by Table 2, hydrogen phosphinate Ph(EtO)P(O)H, diphenylphosphine oxide Ph<sub>2</sub>P(O)H, aliphatic alkyne 1-octyne, and aromatic alkyne phenylacetylene all can be used as the substrates of the reaction to produce the corresponding adducts selectively in high yields.

Worth noting is that a preliminary study also showed that this nickel-catalyzed addition could be successfully applied to other H-heteroatom compounds. For example, it efficiently catalyzes the addition of PhSH to alkynes at room temperature (eq 2) to produce the corresponding vinylsulfide selectively in a high combined yield. Similar reactions using palladium catalysts required heating for a long time.<sup>4b</sup>



Mechanistic studies on the addition of Ph<sub>2</sub>P(O)H unambiguously revealed the formation of a novel five-coordinate hydrido nickel complex **3a** in the catalysis formed via the oxidative addition of Ph<sub>2</sub>P(O)H to NiP(Et<sub>3</sub>)<sub>4</sub> (eq 3). Thus, when Ph<sub>2</sub>P(O)H (0.5 mmol)



was added to Ni(PEt<sub>3</sub>)<sub>4</sub> (0.25 mmol) in toluene-*d*<sub>8</sub> (1 mL) at 0 °C, the color of the solution turned from red-brown to deep orange immediately. <sup>1</sup>H NMR spectroscopy showed the disappearance of Ph<sub>2</sub>P(O)H within 5 min and displayed a new triplet at –16.3 ppm (*J*<sub>PH</sub> = 33.6 Hz), clearly indicating the formation of a Ni–H species.<sup>6c</sup> Although the hydrido nickel complex slowly decomposes, by keeping the solution at –30 °C, pure **3** was obtained as deep orange solids in 62% yield. At room temperature, its <sup>31</sup>P NMR spectroscopy only displayed two broad singlets at δ 92.5 (P(O)) and –2.2 (PEt<sub>3</sub>), respectively. However, by cooling the solution to –70 °C, two triplets with an integration ratio of 1/1 could be clearly recognized (*J*<sub>PP</sub> = 58.2 Hz). Moreover, in the <sup>1</sup>H NMR spectroscopy,

the initially observed triplet of Ni–H at room temperature became a quintet, and a new singlet emerged at 18.7 ppm (OH) (see Supporting Information for details). These NMR observations, together with the results of our preliminary X-ray analysis,<sup>10</sup> indicate that complex **3a** is a five-coordinate 18-electron hydrido complex, perhaps adopting a trigonal bipyramidal structure.

Complex **3a** is so reactive that even at –70 °C the formation of **1b** and **2b** was observed from a mixture of 1-octyne and **3a** in toluene. The reaction completed rapidly as the reaction temperature was raised to 25 °C to give a mixture of **1b** and **2b** in 92% combined yield (based on Ph<sub>2</sub>P(O)H; **1b/2b** = 37/63) (eq 3). Note that although oxidative additions of Ph<sub>2</sub>P(O)H to Pd(PET<sub>3</sub>)<sub>4</sub> and Pt(PET<sub>3</sub>)<sub>4</sub> also proceeded rapidly to give the corresponding four-coordinate 16-electron hydrido metal complexes **3b** and **3c**, respectively, the reactivity of these complexes toward 1-octyne is considerably lower than that of **3a**. Thus, **3b** only slowly reacted with 1-octyne at room temperature, while a similar reaction did not take place with **3c** even after a long time of heating.<sup>11</sup> These results are consistent with the observations of the catalytic behaviors of these metals and may indicate that the higher catalytic activity of the nickel complex is due to the higher reactivity of the corresponding hydrido nickel intermediates.

Studies on the mechanism and applications of the current Ni-catalyzed additions to other heteroatom compounds are under way.

**Supporting Information Available:** Full characterization of new **1**, **2**, and complex **3a** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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