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# Hydrophosphorylation of Alkynes Catalyzed by Palladium: Generality and Mechanism

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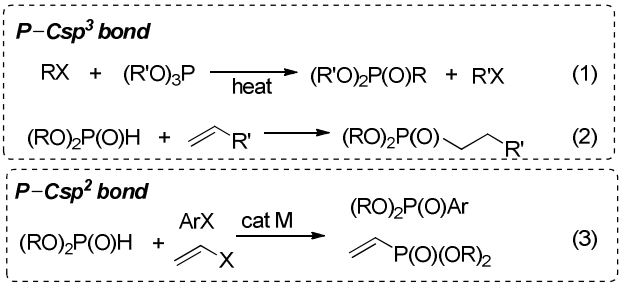
Supporting Information Placeholder

**ABSTRACT:** We carried out a comprehensive study on the generality, scope, limitation and mechanism of the palladium-catalyzed hydrophosphorylation of alkynes with P(O)-H compounds (i.e. H-phosphonates, H-phosphinates, secondary phosphine oxides, and hypophosphinic acid). For H-phosphonates, Pd/dppp was the best catalyst. Both aromatic and aliphatic alkynes, with a variety of functional groups, were applicable to produce the Markovnikov adducts in high yields with high *regio*-selectivity. Aromatic alkynes showed higher reactivity than aliphatic alkynes. Terminal alkynes reacted faster than internal alkynes. Sterically crowded H-phosphonates disfavored the addition. For H-phosphinates and secondary phosphine oxides, Pd/dppe/$Ph_2P(O)OH$ was the catalyst of choice, which led to highly *regio*-selective formation of the Markovnikov adducts. By using $Pd(PPh_3)_4$ as the catalyst, hypophosphinic acid added to terminal alkynes to give the corresponding Markovnikov adducts. Phosphinic acids, phosphonic acid and its monoester were not applicable to this palladium-catalyzed hydrophosphorylation. Mechanistic studies showed that, with a terminal alkyne, $(RO)_2P(O)H$ reacted, like a Brϕnsted acid, to selectively generate the $\alpha$-alkenylpalladium intermediate *via* hydropalladation. On the other hand, $Ph(RO)P(O)H$ and $Ph_2P(O)H$ gave a mixture of $\alpha$– and $\beta$- alkenylpalladium complexes. In the presence of $Ph_2P(O)OH$, hydropalladation with this acid took place first to selectively generate the α-alkenylpalladium intermediate. A subsequent ligand exchange with a P(O)H compound gave the phosphorylpalladium intermediate which produced the Markovnikov adduct *via* reductive elimination. Related intermediates in the catalytic cycle were isolated and characterized.

## INTRODUCTION

Because of the unique biological activity, organophosphorus compounds containing a phosphoryl P(O) group (phosphonates, phosphinates and phosphine oxides) have great applications in medicinal and agricultural chemistry.[1] For example, *fosfomycin* is a clinically used antibiotics,[2a] *glyphosate* ($(HO)_2P(O)CH_2NHCH_2CO_2H$)[2b] and *glufosinate* ($MeP(O)(OH)CH_2CH_2CH(NH_2)CO_2H$)[2c] are widely employed as herbicides. These organophosphoryl compounds are also widely used in organic synthesis.[1a,1h,1i,3] For instance, phosphonates are extensively used in Horner-Wadsworth-Emmons reactions for the selective preparation of olefins,[4a,4b] while phosphine oxides are good precursors to trivalent phosphines (including the chiral ones such as BINAP), which play a pivotal role as ligands in metal-catalyzed reactions.[4c] In addition, they also have wide applications in material chemistry.[5] Because a P(O) group is able to ligate to a variety of metal ions and acids, phosphoryl compound-based metal extractants (especially those for U and Pu) are well known.[5c,6a,6b] Fire retardancy is another unique feature of organophosphoryl compounds, and the development of an environment-benign phosphoryl compound-based fire retardant is of current concern.[5d,5e,6c,6d]

**Scheme 1. Well-Employed C-P(O) Bond-Forming Reactions**

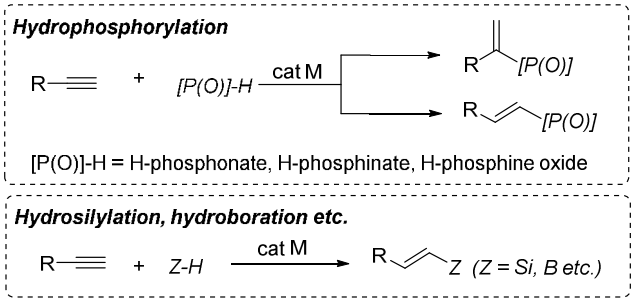



Despite the importance of organophosphoryl compounds, general and efficient methods for their preparation were rather limited.[7] Traditionally, the reaction of a halide RX with a phosphite $(RO)_3P$ at high temperatures (Michaelis-Arbuzov reaction) (Scheme 1, eq 1)[8] and the addition of a P(O)-H bond to an olefin[9] were the well-employed C-P(O) bond-forming reactions. However, these reactions were usually only effective for the generation of a P-C$sp^3$ bond. To solve this problem, the for-

mation of a P-C$sp^2$ bond *via* metal-catalyzed coupling of an alkenyl halide or ArX with a P(O)-H bond was then developed.[7a,10] However, the preparation of an alkenylphosphoryl compound by this method was often not practicable due to the difficult accessibility to alkenyl halides.

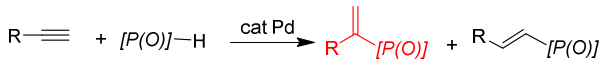
Metal-catalyzed addition of an H-heteroatom bond to a carbon-carbon unsaturated bond is one of the most straightforward and atom-efficient ways for the construction of a carbon-heteroatom bond (Scheme 2).[11] As represented by hydrosilylation and hydroboration reactions catalyzed by metals, nowadays, these addition reactions have tremendous applications in both laboratory and industry (Scheme 2).

**Scheme 2. Metal-Catalyzed Selective P(O)-H Addition to Alkynes (Hydrophosphorylation)**




Hydrogen phosphoryl compounds (H-phosphonate $(RO)_2P(O)H$, H-phosphinate (RO)RP(O)H and H-phosphine oxide $R_2P(O)H$) are a class of unique compounds. Firstly, a tautomerism exists between the P(V) and P(III) forms [P(O)H = P(OH)]. Therefore, they can ligate, like phosphines $R_3P$, to transition metals.[12] Secondly (and synthetically importantly), being different from the dangerous H-phosphines $R_2PH$ and phosphine halides $R_2PX$, P(O)H compounds are rather air- and moisture stable. They do not stink either. Thirdly, these chemicals are readily available, i.e. they can be easily prepared, or purchased since some $(RO)_2P(O)H$ are industrially manufactured . Therefore, the metal-catalyzed selective addition of P(O)-H compounds (hydrophosphorylation)[13] is no doubt an ideal way for the preparation of alkenylphosphoryl compounds which are extremely useful[14] but difficult to prepare by conventional methods.[15] However, different from their silicon and borane counterparts, P(O)-H compounds can coordinate to metals in their P(III) forms P(OH), and significantly deactivate the catalyst.[12] As a result, in a real sense, an efficient metal-catalyzed addition of $(RO)_2P(O)H$ to carbon-carbon unsaturated bonds under mild conditions was only realized in 1996 by employing a rather uncommon $Me_2Pd(PPh_2Me)_2$ complex as the catalyst.[16] Since then, this field has grown rapidly and a variety of alkenylphosphoryl compounds can now be prepared by metal-mediated *regio*- and *stereo*-selective hydrophosphorylation reactions.[7f,17] Because of their novel applications, some compounds (vinylphosphonates $CH_2$=CHP(O)$(OR)_2$, for example) are manufactured on industrial scale.[18]

**Scheme 3. Different Reactivity and Selectivity with P(O)-H Compounds**

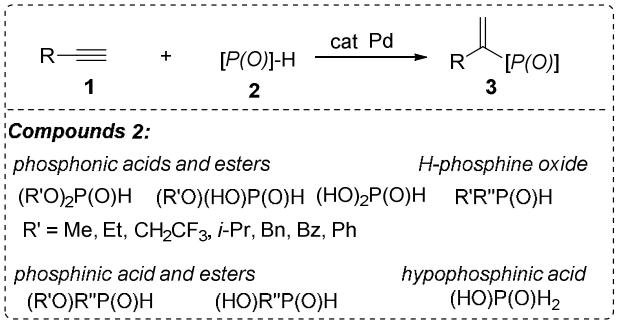



**1** **2** **3** **3'**

| P(O)-H compound | catalyst | major adduct |
|---|---|---|
| $(RO)_2P(O)H$ | Pd(0) | **3** |
| H-phosphonate | Pd(0)/$Ph_2P(O)OH$ | **3** |
| (RO)(R')P(O)H | Pd(0) | **3'** |
| H-phosphinate | Pd(0)/$Ph_2P(O)OH$ | **3** |
| $R_2P(O)H$ | Pd(0) | **3'** |
| H-phosphine oxide | Pd(0)/$Ph_2P(O)OH$ | **3** |

However, despite more than 20 years passed since the first palladium-catalyzed hydrophosphorylation,[16a] a full study on this reaction has not been conducted yet and a lot of puzzles remain unelucidated.[7f] For example, (1) why does the palladium-catalyzed addition of hydrogen phosphonates $(RO)_2P(O)H$ produce predominantly the Markovnikov adducts while (RO)PhP(O)H and $Ph_2P(O)H$ give a mixture of Markovnikov and *anti*-Markovnikov -adducts?[7f] (2) why can a trace amount of $Ph_2P(O)OH$ produce the Markovnikov adducts with higher selectivity (Scheme 3)?[7f,19] (3) How does the palladium complex work, i.e. hydropalladation (Pd-H addition) *vs* phosphorylpalladation (Pd-P(O)), and what are the reactive intermediates involved in the catalytic cycles? In addition, since the reaction was only briefly communicated,[16] information regarding generality, scope and limitations, which is pivotal to synthetic chemists, is not available.

**Scheme 4. Palladium-Catalyzed Selective Hydrophosphorylation of Alkynes with P(O)-H Compounds**




To celebrate its 20th anniversary of discovery, as the discoverer of the reaction, herein, we report a full study on the palladium-catalyzed hydrophosphorylation of alkynes with P(O)-H compounds. The results not only demonstrated the synthetic generality of the reaction (Scheme 4) but also answered the mechanistic puzzles associated with the reaction.[20,21]

## RESULTS AND DISCUSSION

### 1. Palladium-Catalyzed Hydrophosphorylation of Alkynes with H-phosphonates $(RO)_2P(O)H$.[22]

### 1.1. Efficiency of the Palladium Catalyst.

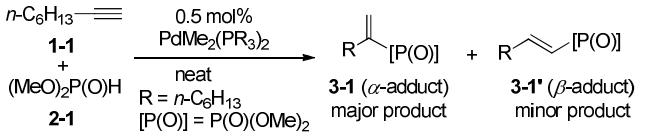
The early communication on the addition of $(RO)_2P(O)H$ to alkynes in the presence of a palladium catalyst provided a new way for the preparation of alkenylphosphonates under mild reaction conditions.[16a] However, the reaction conditions used are less practical since a rather special complex $Me_2Pd(PPh_2Me)_2$ and too much of the catalyst were used. Therefore, we decided to optimize the reaction conditions.[20]

**Effect of the Phosphine Ligand**. We first conducted a catalyst's screening by employing electronically and sterically different phosphines (Table 1). To minimize the effect of other factors, all these reactions were carried out by heating up an equimolar mixture of 1-octyne **1-1** with $(MeO)_2P(O)H$ **2-1** in the presence of 0.5 mol% $PdMe_2(PR_3)_2$.[23]

The efficiency of the catalysts strongly depends on the phosphine ligands used. As shown in Table 1, a tiny change of the structure of the phosphine could lead to a dramatic change (up or down) of the yields of the products. Among the phosphines investigated, *$PPh_2Me$ is the best monodentate ligand while dppp and dppb are the best bidentate ligands.*

Thus, while $PPh_3$ (run 1) only gave 10% yield of the products, $PPh_2Me$ could dramatically improve the catalyst`s efficiency to produce 78% yield of the adducts (run 2). However, surprisingly, a bulky alkyl group such as *i*-Bu (run 3) or cyclohexyl (run 4), produced a trace amount of the adducts. With $PPhMe_2$ and $PEt_3$, the addition only sluggishly proceeded (runs 5 and 6). A similar phenomenon was observed with bidentate phosphine ligands (runs 7-24). Thus, dppe (run 7, $Ph_2P(CH_2)_2PPh_2$) did not produce the adducts, while $Ph_2P(CH_2)_nPPh_2$ (run 10, dppp, n = 3; run 20, dppb, n = 4) could give excellent yields of the products with high *regio*-selectivity. However, the yields of the adducts decreased as the methylene chain of the bisphosphine ligand became longer (runs 21 and 22). Other bidentate phosphines such as dppf (run 23) and binap (run 24) could also produce the adducts. With dppp, the reaction could proceed efficiently with 0.25 mol% catalyst (run 11), and even 0.1 mol% of the catalyst could also produce the adducts in 77% yield after 20 h (run 12), and an almost quantitative yield after 48 h (run 13).

**Table 1. Hydrophosphorylation of 1-Octyne with $(MeO)_2P(O)H$ Catalyzed by $PdMe_2(PR_3)_2$[a]**




**3-1** ($\alpha$-adduct) major product **3-1'** ($\beta$-adduct) minor product

| run | phosphine | temp (°C) | time(h) | % yield($\alpha/\beta$)[b] |
|---|---|---|---|---|
| 1 | $PPh_3$ | 80 | 20 | 10(82/18) |
| 2 | **$PPh_2Me$** | 80 | 20 | 78(91/9) |
| 3 | $PPh_2$*i*-Bu | 80 | 20 | 9(88/12) |
| 4 | $PPh_2Cy$ | 80 | 20 | 7(87/13) |
| 5 | $PPhMe_2$ | 80 | 20 | 5(94/6) |
| 6 | $PEt_3$ | 80 | 20 | none |
| 7 | dppe | 80 | 20 | none |
| 8 | $Ph_2P(CH_2)_3PPh_2$ | 60 | 20 | 20(97/3) |
| 9 | $Ph_2P(CH_2)_3PPh_2$ | 70 | 20 | 85(98/2) |
| 10 | **$Ph_2P(CH_2)_3PPh_2$** | 80 | 20 | 100(98/2) |
| 11[c] | $Ph_2P(CH_2)_3PPh_2$ | 80 | 20 | 98 (97/3) |
| 12[d] | $Ph_2P(CH_2)_3PPh_2$ | 80 | 20 | 77 (97/3) |
| 13[d] | $Ph_2P(CH_2)_3PPh_2$ | 80 | 48 | 97 (97/3) |
| 14[e] | $Ph_2P(CH_2)_3PPh_2$ | 80 | 20 | 87(97/3) |
| 15[f] | $Ph_2P(CH_2)_3PPh_2$ | 80 | 20 | 78(96/4) |
| 16 | $Ph_2P(CH_2)_3PPh_2$ | 100 | 3 | 100(97/3) |
| 17[g] | $Ph_2P(CH_2)_3PPh_2$ | 100 | 5 | 100(97/3) |
| 18[h] | $Ph_2P(CH_2)_3PPh_2$ | 100 | 5 | 47(97/3) |
| 19[h] | $Ph_2P(CH_2)_3PPh_2$ | 120 | 2 | 100(96/4) |
| 20 | **$Ph_2P(CH_2)_4PPh_2$** | 80 | 20 | 95(94/6) |
| 21 | $Ph_2P(CH_2)_5PPh_2$ | 80 | 20 | 49(89/11) |
| 22 | $Ph_2P(CH_2)_{10}PPh_2$ | 80 | 20 | 28(88/12) |
| 23 | dppf | 80 | 20 | 73(95/5) |
| 24 | BINAP | 80 | 20 | 36(95/5) |

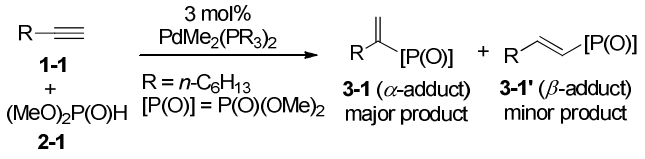
[a]All reactions were similarly conducted in a sealed tube using an equimolar $(MeO)_2P(O)H$ and 1-octyne (0.5 mmol) with or without a solvent (toluene) in the presence of 0.5 mol% the palladium catalyst. [b]Determined by $^1H$ NMR. $\alpha/\beta$ = the ratio of the $\alpha$-adduct (the branched one) to the $\beta$-adduct (the linear one) (this notation also applies to other tables and schemes in this article). [c]0.25 mol% Pd catalyst. [d]0.1 mol% Pd catalyst. [e]2.5 M toluene solution. [f]0.8 M toluene solution. [g]0.1 mol% Pd catalyst. [h]0.05 mol% Pd catalyst.

**Effect of Temperature and Concentration.** Although the addition proceeded efficiently at 80 °C (Table 1, run 10), it progressed slowly at 60 °C and 70 °C (runs 8 and 9). When the reaction was conducted at elevated temperatures 100 °C (run 16) and 120 °C (run 19), the reaction took place rapidly to produce the adduct in high yields and selectivity. The reaction also proceeded in a toluene solution (runs 14 and 15) to give good yields of the adducts.

**Effect of Impurities ($H_2O$ and $Ph_2P(O)OH$)**. During the course of the study, we occasionally found that the reaction could become considerably slow with carefully dried, freshly distilled materials. Since commercially supplied $(MeO)_2P(O)H$ usually contains water, we thought it might be water that made such a difference.

This is right. As shown in Table 2, hydrophosphorylation of 1-octyne with $(MeO)_2P(O)H$ using either $PdMe_2(PPh_2Me)_2$ or $PdMe_2$(dppp) as a catalyst was affected by water very much. With $PdMe_2(PPh_2Me)_2$, in the absence of water,[24] the reaction gave 46% and 71% yields of the adducts, respectively, after 5 h and 10 h (runs 1 and 2). However, the addition of a small amount of water accelerated the reaction. 3 mol% $H_2O$ (run 3)

**Table 2. Effect of Water on the Hydrophosphorylation of 1-Octyne with $(MeO)_2P(O)H$ Catalyzed by $PdMe_2(PR_3)_2$[a]**



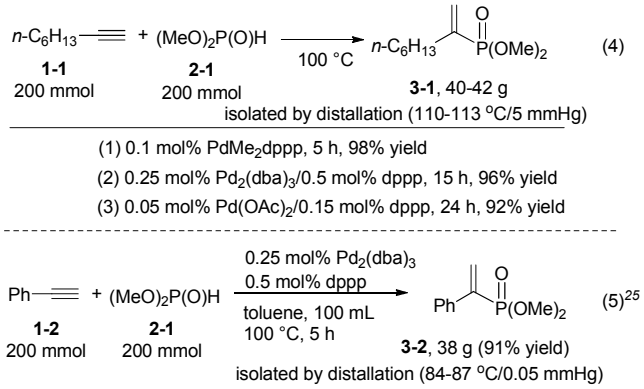

| run | $PR_3$ | mol% $H_2O$ | time (h) | % yield ($\alpha/\beta$)[b] |
|---|---|---|---|---|
| 1 | $PPh_2Me$, 67 °C | no | 5 | 46(87/13) |
| 2 | | no | 10 | 71(89/11) |
| 3 | | 3 | 6 | 88(94/6) |
| 4 | | 6 | 6 | 100(95/5) |
| 5 | | 12 | 1.5 | 100(96/4) |
| 6 | | 24 | 1.5 | 100(97/3) |
| 7 | | 36 | 5 | 38(98/2) |
| 8 | | | 10 | 45(97/3) |
| 9 | dppp, 80 °C | no | 0.5 | 62(95/5) |
| 10 | | 3 | 0.5 | 84(95/5) |
| 11 | | 6 | 0.5 | 94(96/4) |
| 12 | | 12 | 0.5 | 95(96/4) |
| 13 | | 22 | 0.5 | 95(95/5) |
| 14 | | 33 | 0.5 | 97(96/4) |
| 15[c] | | 3 | 0.5 | 75(96/4) |

[a]All reactions were similarly conducted in a sealed tube using an equimolar $(MeO)_2P(O)H$ and 1-octyne (0.5 mmol) dissolved in 0.5 mL toluene in the presence of 3 mol% palladium catalyst. [b]Determined by NMR. [c]3 mol% $Ph_2P(O)OH$ was used.

gave 88% yield of the adducts after 6 h, and 12 mol% $H_2O$ (run 5) gave a quantitative yield of the adducts after only 1.5 h! However, it was not that the more the water the higher the yield, because with 36 mol% water (runs 7 and 8), only 45% yield of the adducts was obtained after 10 h. Therefore, *a small amount of water accelerates the reaction, but too much water retards the reaction*. Water also improves the *regio*-selectivity. This phenomenon was also observed with $PdMe_2$(dppp) (runs 9 to 14). $Ph_2P(O)OH$ could also accelerate the reaction (run 15).

**A Large Scale Reaction**. By using the optimized reaction conditions, the hydrophosphorylation reaction could be easily carried out in a relatively large scale. As demonstrated in Scheme 5, the two starting materials (200 mmol 1-octyne and 200 mmol $(MeO)_2P(O)H$) were simply mixed together without purification,[25] and heated at 100 °C in the presence of a tiny amount of palladium catalyst (0.05 mol% ~ 0.5 mol%). The corresponding adducts were obtained in high yields with high *regio*-selectivity (97-98% selectivity) (SI). In addition to $PdMe_2$dppp, the commercially available catalyst precursors $Pd_2(dba)_3$/dppp and $Pd(OAc)_2$/dppp also worked efficiently. Therefore, ca. 40 g of **3-1** could be readily prepared (eq 4). Similarly, a mixture of phenylacetylene and $(MeO)_2P(O)H$ gave the corresponding alkenylphosphonate **3-2** in 91% isolated yield (eq 5) (*Caution*!).[25]

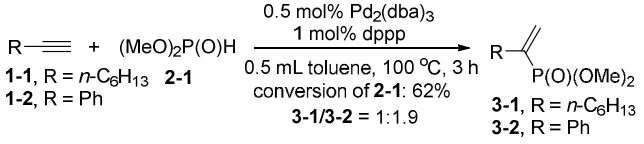
**Scheme 5. 200 mmol-Scale Reactions for an Aromatic and an Aliphatic Alkynes**




## 1.2. Reactivity of Alkynes.

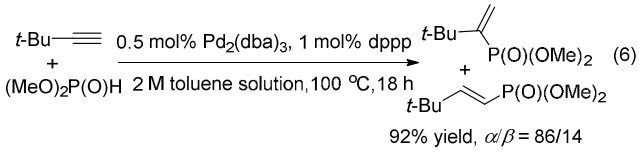
**Aliphatic Alkynes *vs* Aromatic Alkynes.** To compare the reactivity between an aliphatic and an aromatic alkyne, a competitive reaction between 1-octyne and phenylacetylene was carried out (Scheme 6). A mixture of

**Scheme 6. Reactivity of 1-Octyne *vs* Phenylacetylene**



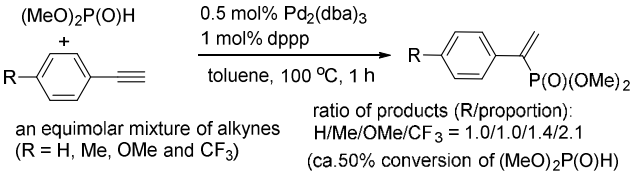

$(MeO)_2P(O)H$ (0.5 mmol), 1-octyne (0.25 mmol) and phenylacetylene (0.25 mmol) in toluene (0.5 mL) was heated at 100 °C for 3 h in the presence of a palladium catalyst. The $\alpha$-adducts **3-1** and **3-2** were generated in a ratio of 1:1.9. This result indicates that phenylacetylene reacts faster (*ca.* twice) than 1-octyne.

**Steric effect.** As might be expected, a sterically bulky alkyne might favor the formation of the $\beta$-adduct.[26] This is true. Although the above mentioned 1-octyne and phenylacetylene selectively gave the $\alpha$-adducts, under similar conditions, the steric bulky 3,3-dimethyl-1-butyne gave the adducts in 92% yield with a ratio $\alpha/\beta$ = 86/14 (eq 6).



**Electronic Effect.** The electronic effect on the reactivity was studied by conducting a competitive reaction of phenylacetylenes with $(MeO)_2P(O)H$ (acetylene 0.1 mmol each, $(MeO)_2P(O)H$ 0.4 mmol, toluene 0.5 mL) (Scheme 7). All gave the $\alpha$-adduct selectively, and the reactivity roughly follows an increasing order of H = Me < OMe < $CF_3$.

**Scheme 7. A Competitive Reaction of *p*-Substituted Phenylacetylenes**

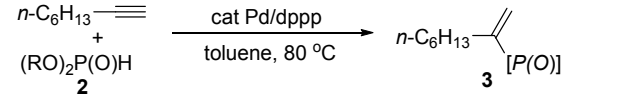


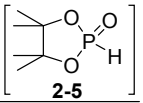

### 1.3. Reactivity of H-phosphonates.

Although no big difference in *regio*-selectivity (all gave the $\alpha$-adduct predominantly), as shown in Table 3, a strong steric effect was observed for $(RO)_2P(O)H$, i.e. the bulkier the R, the lower the reactivity of $(RO)_2P(O)H$. Competitive reactions of $(RO)_2P(O)H$, (R = Me, Et, *n*-Bu, *i*-Pr) and **2-5** with 1-octyne showed that the reactivity of H-phosphonates followed a decreasing order of **2-5** > $(MeO)_2P(O)H$ > $(EtO)_2P(O)H$ = $(n\text{-}BuO)_2P(O)H$ > $(i\text{-}PrO)_2P(O)H$. The difference of $(RO)_2P(O)H$ in reactivity can be simply attributed to the difference of their bulkiness, i.e. the smallest **2-5**,[27] reacted the fastest, and the most crowded $(i\text{-}PrO)_2P(O)H$ reacted the slowest. In fact, with a very bulky $(AdO)_2P(O)H$ (Ad = 1-adamantyl), no addition took place at all under similar conditions.

The additions to phenylacetylene and 1-octyne (representatives for terminal aromatic alkynes and terminal aliphatic alkynes, respectively) were summarized in Table 4. As to $(RO)_2P(O)H$ (where R = Me, Et, *n*-Bu, Bn and Ph) and the five-membered cyclic **2-5**, all could be used as the substrates to produce the corresponding $\alpha$-adducts selectively in high yields.

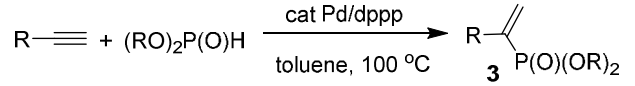
**Table 3. A Competitive Reaction of H-phosphonates: Yield of 3 *vs* Time.**[a]




| RO = MeO(**2-1**) | EtO(**2-2**) | *n*-BuO(**2-4**) | *i*-PrO(**2-3**) | **2-5** |
|---|---|---|---|---|
| 2h 34% | 7% | 7% | trace | 100% |
| 4h 88% | 32% | 32% | trace |  |
| 10h 100% | 72% | 72% | 15% | **2-5** |

[a]Reaction conditions: 0.5 mmol 1-octyne, an equimolar mixture of $(RO)_2P(O)H$ (0.1 mmol for each P(O)-H compound), 0.5 mol% $Pd_2(dba)_3$, 1 mol% dppp, 0.5 mL toluene-$d_8$, 80 °C. NMR yields based on $(RO)_2P(O)H$.

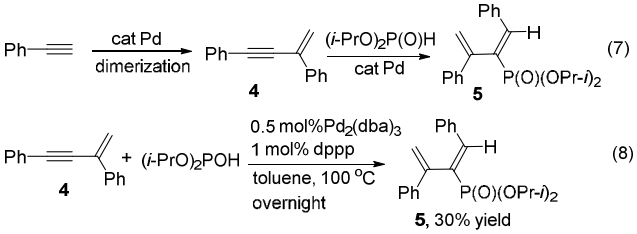
**Table 4. Palladium-Catalyzed Addition of H-phosphonates to Phenylacetylene and 1-Octyne**[a]



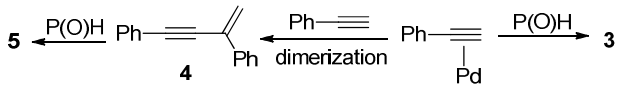

| run | alkynes | P(O)-H | product | yield (α/β) |
|---|---|---|---|---|
| 1 | Ph— | $(MeO)_2P(O)H$ | **3-2** | 90% (97/3) |
| 2 | | $(EtO)_2P(O)H$ | **3-3** | 80% (96:4) |
| 3 | | $(n\text{-}BuO)_2P(O)H$ | **3-4** | 94% (96:4) |
| 4[b] | | $(CF_3CH_2O)_2P(O)H$ | **3-5** | 85% (94:6) |
| 5 | | **2-5** | **3-6** | 96% (96:4) |
| 6 | | $(BnO)_2P(O)H$ | **3-7** | 70% (99:1) |
| 7[c] | | $(i\text{-}PrO)_2P(O)H$ | **3-8** | 30% (95/5) |
| 8 | 1-Octyne | $(MeO)_2P(O)H$ | **3-1** | 91% (95:5) |
| 9 | | $(EtO)_2P(O)H$ | **3-9** | 90% (96:4) |
| 10 | | $(n\text{-}BuO)_2P(O)H$ | **3-10** | 92% (96:4) |
| 11[b] | | $(CF_3CH_2O)_2P(O)H$ | **3-11** | 87% (90:10) |
| 12 | | $(i\text{-}PrO)_2P(O)H$ | **3-12** | 90% (96:4) |
| 13 | | **2-5** | **3-13** | 95% (95:5) |
| 14 | | $(PhO)_2P(O)H$ | **3-14** | 89% (95:5) |

[a]Reaction conditions: 0.5 mmol H-phosphonate, 0.5 mmol alkyne, 0.5 mol% $Pd_2(dba)_3$, 1 mol% dppp, 0.5 mL toluene, 100 °C, overnight. [b]$Pd(PPh_3)_4$ was used as the catalyst. [c]1 mmol phenylacetylene was added and 50% yield of **5** was produced.

As mentioned above, the bulky $(i\text{-}PrO)_2P(O)H$ is an exception (*vide infra*), which only gave 30% yield of **3-8** with phenylacetylene (run 7). However, interestingly, with 1-octyne, it could produce the corresponding adduct **3-12** in a high yield (run 12). Careful analysis of the products with phenylacetylene (run 7) revealed that, in addition to the *mono*-addition product **3-8**, a butadiene **5** was generated in 50% yield (run 7). Although the exact pathway for the formation of **5** was not clear, a stepwise path, firstly the generation of an enyne **4** by a head-to-tail dimerization of phenylacetylene,[28] followed by the addition of $(i\text{-}PrO)_2P(O)H$ to this enyne might account for its formation (eq 7). In support of this hypothesis, a separate reaction using enyne **4** did produce **5** *regio*-selectively (eq 8).

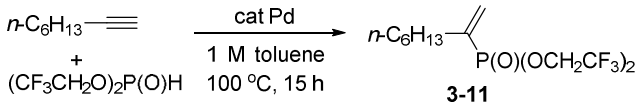



**Scheme 8. Hydrophosphorylation *vs* Dimerization**




Therefore, there are two competitive reactions: the dimerization of phenylacetylene and the addition of P(O)H to phenylacetylene (Scheme 8). With the bulky $(i\text{-PrO})_2P(O)H$, the addition of $(i\text{-PrO})_2P(O)H$ to phenylacetylene was slow and a considerable amount of phenylacetylene dimerized to generate **4** which eventually produced **5**. The addition of $(i\text{-PrO})_2P(O)H$ with 1-octyne could produce the corresponding alkenylphosphonate in a good yield because the dimerization of 1-octyne is slow compared to that of phenylacetylene.[28]

**Scheme 9. Palladium-Catalyzed Hydrophosphorylation of 1-Octyne with $(CF_3CH_2O)_2P(O)H$**



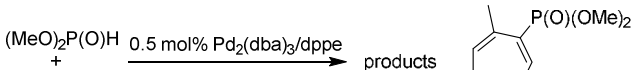

cat 2%$Pd(OAc)_2$ / 3%dppp (or 1%$Pd_2(dba)_3$ / 1%dppp), trace.
cat 1%$Pd_2(dba)_3$ / 2% $PPh_2Me$ (1%$Pd_2(dba)_3$ / 6% $PPh_2Me$), trace.
cat 1%$Pd_2(dba)_3$ / 3% $PPh_3$, 26% yield ($\alpha/\beta$ = 80/20).
cat 1%$Pd_2(dba)_3$ / 6% $PPh_3$, 53% yield ($\alpha/\beta$ = 90/10).
cat 1%$Pd_2(dba)_3$ / 8% $PPh_3$, 79% yield ($\alpha/\beta$ = 89/11).
cat 1 % $Pd(PPh_3)_4$, 87% yield ($\alpha/\beta$ = 90/10).

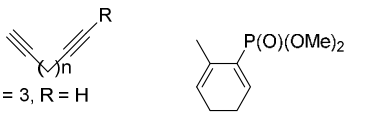
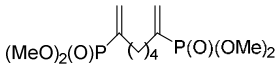
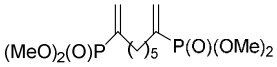
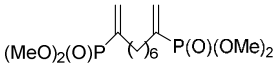
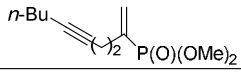
In addition to the above-mentioned steric effect, the electronic factor also significantly affects the addition. $(CF_3CH_2O)_2P(O)H$ **2-6**, is such an example (for discussions, see sections 6.2 and 6.3). As shown in Scheme 9, $(CF_3CH_2O)_2P(O)H$ did not efficiently produce the adducts using the Pd/dppp catalyst. Another catalyst $Pd/PPh_2Me$ that is effective for the hydrophosphorylation (Table 1) did not work either. Interestingly, by using $Pd(PPh_3)_4$, $(CF_3CH_2O)_2P(O)H$ reacted with both phenylacetylene and 1-octyne to produce the corresponding adducts in 85% and 87% yields, respectively (Table 4, runs 4 and 11).

### 1.4. Reactions with Diynes.

Diynes also react similarly to give the adducts. However, interestingly, they can generate different kinds of products with different length of the $(CH_2)_n$ linkage (Table 5). For example, hepta-1,6-diyne reacted with $(MeO)_2P(O)H$ smoothly to afford, not the expected addition product, but a six-membered cyclic **3-15** in 95% yield (run 1). With octa-1,7-diyne, the normal addition product **3-16** was produced in 80% yields and a seven-membered cyclic product **6** was generated in 15% yield (run 2). With nona-1,8-diyne, however, the normal hydrophosphorylation proceeded smoothly to give the addition product **3-17** in 91% yield and the expected eight-membered cyclic product was not detected (run 3). Deca-1,9-diyne reacted similarly to produce the corresponding addition product **3-18** in 93% yield (run 4). With deca-1,5-diyne, a mono-addition product **3-19** was obtained in 83% yield, and no cyclic phosphonates were detected (run 5).[29]

**Table 5. Palladium-Catalyzed Hydrophosphorylation of Diynes with $(MeO)_2P(O)H$[a]**



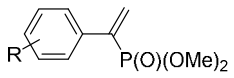

| run | alkynes | product | yield ($\alpha/\beta$)[b] |
|---|---|---|---|
| 1 | n = 3, R = H |  | **3-15**, 95%(-/-) |
| 2[c] | n = 4, R = H |  | **3-16**, 80%(91:9) |
| 3 | n = 5, R = H |  | **3-17**, 91%(96:4) |
| 4 | n = 6, R = H |  | **3-18**, 93%(92:8) |
| 5[d] | n = 2, R = *n*-Bu |  | **3-19**, 83%(95:5) |

[a]Reaction conditions: 0.5 mmol $(MeO)_2P(O)H$, 0.25 mmol alkynes, 0.5 mol% $Pd_2(dba)_3$, 1 mol% dppp, 0.5 mL toluene, 100 °C, overnight. [b]Isolated yield. [c]15% yield of the cyclized product **6** was produced. [d]0.25 mmol $(MeO)_2P(O)H$ was used.

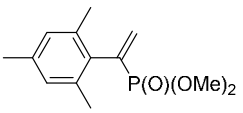
### 1.5. Scope and Limitations of the Palladium-Catalyzed Hydrophosphorylation of Alkynes with H-Phosphonates.

**Table 6. Palladium-Catalyzed Hydrophosphorylation of Alkynes with Hydrogen Phosphoryl Compounds**[a]

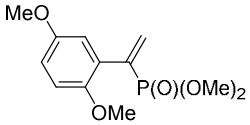
**H-phosphonates:**



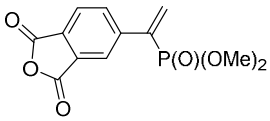
**3-20**, R = 4-Me, 93% (95/5)
**3-21**, R = 4-*t*-Bu, 92% (97/3)
**3-22**, R = 4-OMe, 93% (97/3)
**3-23**, R = 3-OMe, 90% (96/4)
**3-24**, R = 2-OMe, 91% (94/6)
**3-25**, R = 4-OPh, 82% (99/1)
**3-26**, R = 4-$NH_2$, 70% (99/1)[b]
**3-27**, R = 4-Ph, 93% (97/3)
**3-28**, R = 4-F, 90% (95/5)
**3-29**, R = 4-Cl, 90% (95/5)
**3-30**, R = 3-Cl, 89% (92/8)
**3-31**, R = 2-Cl, 86% (94/6)
**3-32**, R = 4-Ac, 93% (96/4)
**3-33**, R = 4-PhCO, 82% (95/5)
**3-34**, R = 4-$NO_2$, 90% (93/7)



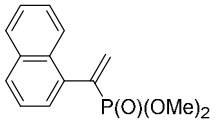
**3-35**, 89% (92/8)



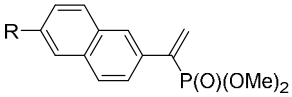
**3-36**, 91% (93/7)



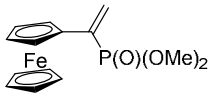
**3-37**, 75% (96/4)[c]



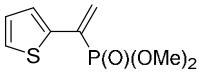
**3-38**, 75% (96/4)



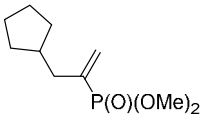
**3-39**, R = 6-H, 90% (90/10)
**3-40**, R = 6-OMe, 92% (97/3)



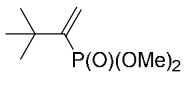
**3-41**, 87% (96/4)



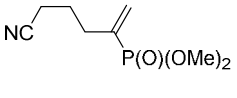
**3-42**, 89% (95/5)



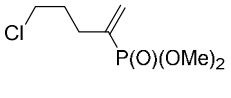
**3-43**, 92% (93/7)



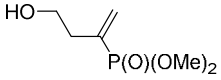
**3-44**, 92% (86/14)



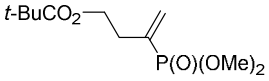
**3-45**, 93% (93/7)



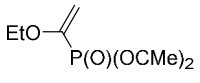
**3-46**, 85% (92/8)



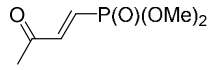
**3-47**, 82% (95/5)



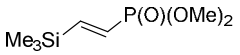
**3-48**, 92% (93/7)



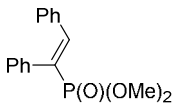
**3-49**, 85% (99/1)



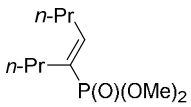
**3-50**, 91% (99/1)[d]



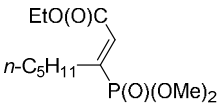
**3-51**, 78% (-/-)



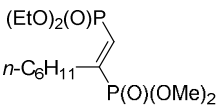
**3-52**, 97% (-/-)



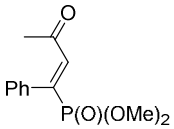
**3-53**, 89%(-/-)



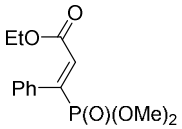
**3-54**, 94% (91/9)[e]



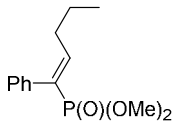
**3-55**, 94% (95/5)[e]



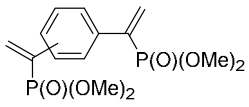
**3-56**, 95% (95/5)[e]



**3-57**, 96% (91/9)[e]

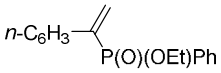


**3-58**, 95% (60/40)[e]

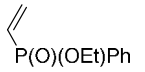


**3-59** (*p*-), 93% (97/3)
**3-60** (*m*-), 90% (96/4)
**3-61** (*o*-), 88% (95/5)

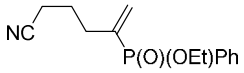
**H-phosphinates:**



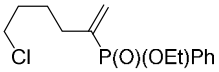
**3-62**, 92% (97/3)



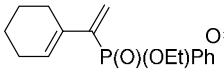
**3-63**, 76% (-/-)[f]



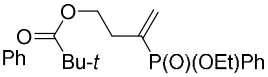
**3-64**, 95% (94/6)



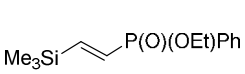
**3-65**, 95% (95/5)



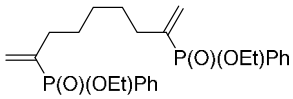
**3-66**, 91% (97/3)



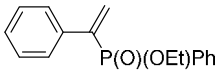
**3-67**, 93% (93/7)



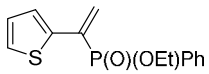
**3-68**, 63% (-/-)



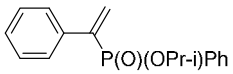
**3-69**, 85% (93/7)



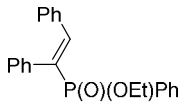
**3-70**, 99% (96/4)



**3-71**, 77% (96/4)

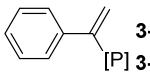


**3-72**, 90% (96/4)

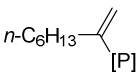


**3-73**, 99% (-/-)

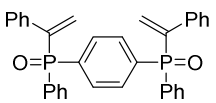
**H-secondary phosphine oxides:**



**3-74**, [P] = $P(O)Ph_2$, 91% (97/3)
**3-75**, [P] = $P(O)(C_6H_4OMe\text{-}p)_2$, 85% (95/5)
**3-76**, [P] = $P(O)(C_6H_4CF_3\text{-}p)_2$, 88% (94/6)
**3-77**, [P] = P(O)Ph(octyl-*n*), 90% (96/4)
**3-78**, [P] = P(O)Ph(Bu-*t*), trace (-/-)
**3-79**, [P] = $P(O)(C_4H_8Ph)_2$, 92% (97/3)
**3-80**, [P] = $P(O)(octyl\text{-}n)_2$, 80% (96/4)



**3-81**, [P] = $P(O)Ph_2$, 86% (95/5)
**3-82**, [P] = P(O)Ph(octyl-*n*), 87% (94/6)



**3-83**, 87% (94/6)

**Hypophosphinic acid:**[g]



**3-84**, 93% (97/3)



**3-85**, 83% (95/5)



**3-86**, 81% (95/5)



**3-87**, 92% (96/4)



**3-88**, 78% (95/5)



**3-89**, 77% (95/5)



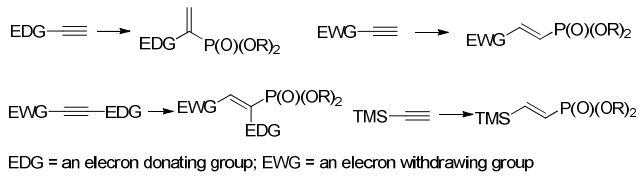
**3-90**, 65% (95/5)

[a]Reaction conditions: For H-phosphonates: 0.5 mmol H-phosphonate, 0.5 mmol alkynes, 0.5 mol% $Pd_2(dba)_3$, 1 mol% dppp, 0.5 mL toluene, 100 °C, 4 h~overnight; For H-phosphinates and H-phosphine oxides: 0.5 mmol H-phosphonate, 0.5 mmol alkynes, 1 mol% $Pd_2(dba)_3$, 2 mol% dppe, 4 mol% $Ph_2P(O)OH$, 0.5 mL toluene, 100 °C, overnight. For hypophosphinic acid: 10 mmol alkynes, 10 mmol $H_3PO_2$, 2

mol% $Pd(PPh_3)_4$, 10 mL THF, room temperature, overnight. [b] 1 mol% $Pd_2(dba)_3$, 2 mol% dppp, 0.5 mL dioanxe. [c] 2 mol% $Pd(OAc)_2$, 3 mol% dppp, 0.5 mL dioxane. [d] 3 equiv $(MeO)_2P(O)H$ (1.5 mmol) was used. With 1 equiv $(MeO)_2P(O)H$, the yield is *ca.* 51% due to polymerization of the alkyne. [e] Ratio of the two *regio*-isomers. [f] 1 atm acetylene gas. [g] NMR spectroscopically pure mixture of an H-alkenylphosphinate with its reduced form in a ratio shown in the parentheses.

To further disclose the scope and limitations of this palladium-catalyzed hydrophosphorylation reaction, the reactions of a wide range of alkynes and hydrogen phosphonates $(RO)_2P(O)H$ were conducted (Table 6). A variety of alkynes, i.e, aromatic and aliphatic, terminal and internal, electron-rich and electron-poor, all were readily hydrophosphorylated to produce the corresponding alkenylphosphonates in high yields with high *chemo*- and *stereo*-selectivity. The reaction features wide tolerance to a broad range of functional groups (i.e. the labile carbonyl, cyano, hydroxyl, halogens, free amine, anhydride and even $NO_2$ groups). Alkenylphosphonates of ferrocene and thiophene derivatives could also be prepared in high yields.

**Scheme 10. *Regio*-Selectivity of the Pd-Catalyzed Addition of $(RO)_2P(O)H$ to Alkynes Follows the Markovnikov`s Rule**




As judged from the *trans*-adducts with internal alkynes, this metal-catalyzed addition of a P(O)-H bond to the triple bond took place *via syn* addition to give the *trans*-adducts. As to the *regio*-selectivity, the addition well follows the Markovnikov`s rule to give the corresponding adducts selectively (Scheme 10). Therefore, a terminal alkyne with an electron donating group (EDG) produces the branched adduct while that with an electron withdrawing group (EWG) produces the linear one. For an internal alkyne having one electron-donating group and one electron-withdrawing group, the phosphoryl group selectively bonds to the same carbon with the EDG. For trimethylsilylacetylene, the phosphoryl group selectively bonds to the terminal carbon selectively.[30]

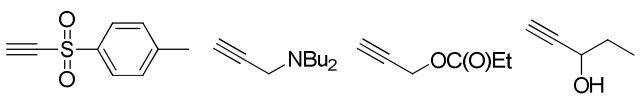



**Figure 1.** Alkynes not applicable to the reaction.

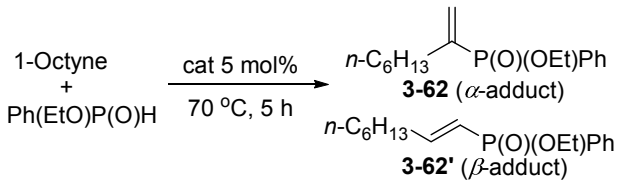
However, *limitations* do exist with alkynes (Figure 1). For example, 1-(ethynylsulfonyl)-4-methylbenzene did not produce the corresponding adduct because of the decomposition of the substrate under the present conditions. A few propargyl alkynes as shown in Figure 1 could not be hydrophosphorylated either.

## 2. Palladium-Catalyzed Hydrophosphorylation of Alkynes with H-Phosphinates R'(RO)P(O)H.[31]

H-phosphinates (RO)R'P(O)H can also add to alkynes catalyzed by a palladium catalyst. However, interestingly, *the best catalyst for their addition is different from that of H-phosphonates*, despite the structure`s similarity. In order to elucidate the *regio*- and *stereo*-selectivity of the addition of hydrogen phosphinates to alkynes, as a model reaction, we first investigated the addition of Ph(EtO)P(O)H **2-7** to 1-octyne (Table 7). None of the palladium catalysts tested was able to afford the corresponding adducts in satisfactory yields and selectivity. Thus, the common $Pd(PPh_3)_4$ only gave a trace amount of the product. $Me_2Pd(PPh_3)_2$, $Me_2Pd(PPh_2Me)_2$ and $Me_2Pd(PPhMe_2)_2$ could produce the adduct **3-62** in moderate yields. However, the selectivity was not satisfactory. Palladium complexes with a more basic phosphine $PEt_3$ and $PMe_3$ did not catalyze the addition satisfactorily. Remarkably, when a combination of $Me_2Pd(PPhMe)_2$ and $Ph_2P(O)OH$ was employed, an excellent yield of the $\alpha$-adduct **3-62** was obtained with a high *regio*-selectivity. A combination of 1 mol% $Pd_2(dba)_3$, 2 mol% dppe and 4 mol% $Ph_2P(O)OH$, could also give a good result (run 8).

As shown in Table 6, the reaction with Ph(EtO)P(O)H has a wide generality, and the Markovnikov adduct was generated selectively. Thus, with the exception of trimethylsilylacetylene which gave the $\beta$-*trans* adduct **3-68** selectively, both aliphatic and aromatic terminal alkynes tested all reacted efficiently, affording the $\alpha$-adducts selectively. In addition, a variety of functionalities such as chloro (**3-65**), cyano (**3-64**), ester (**3-67**), silyl (**3-68**), alkenyl (**3-66**), and thienyl (**3-71**) groups were well tolerant. Two P(O) groups were also easily introduced into nona-1,8-diyne (**3-69**). Though prolonged heating was needed compared with terminal alkynes, an internal alkyne like tolane could also be successfully hydrophosphorylated, producing the corresponding *trans*-adduct selectively (**3-73**). Acetylene gas was also hydrophosphorylated to give the corresponding vinylphosphinate **3-63** in 76% yield.

**Table 7. Pd-Mediated Addition of Ph(EtO)P(O)H to 1-Octyne**[a]

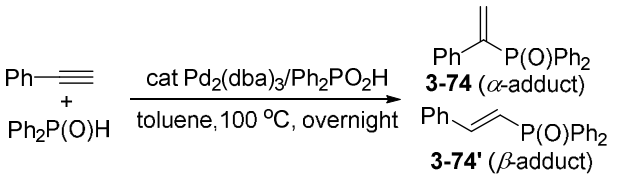



| run | catalyst | yield ($\alpha/\beta$)[b] |
|---|---|---|
| 1 | $Pd(PPh_3)_4$ | trace |
| 2 | $Me_2Pd(PPh_3)_2$ | 50% (66/34) |
| 3 | $Me_2Pd(PPh_2Me)_2$ | 52% (69/31) |
| 4 | $Me_2Pd(PPhMe_2)_2$ | 71% (72/28) |
| 5 | $Me_2Pd(PEt_3)_2$ | trace |
| 6 | $Me_2Pd(PMe_3)_2$ | trace |
| 7 | $Me_2Pd(PPhMe_2)_2$, 10% $Ph_2PO_2H$ | 100% (96/4) |
| 8[c] | $Pd_2(dba)_3$+dppe, 4% $Ph_2PO_2H$ | 90% (96/4) |
| 9[c] | $Pd_2(dba)_3$+dppp, 4% $Ph_2PO_2H$ | 71% (94/6) |

[a]Condition: 0.5 mmol 1-octyne, 0.5 mmol Ph(EtO)P(O)H, 5 mol% catalyst and 0.5 mL toluene, 70 °C, 5 h. [b]The yield and ratio were based on $^{31}P$ NMR spectra. [c]1 mol% $Pd_2(dba)_3$ (Pd/P = 1/2), 100 °C, overnight.

## 3. Palladium-Catalyzed Hydrophosphorylation of Alkynes with Secondary Phosphine Oxide R`RP(O)H.[32]

**Table 8. The Addition of $Ph_2P(O)H$ to Phenylacetylene Catalyzed by Palladium**[a]




| run | ligand | yield ($\alpha/\beta$) |
|---|---|---|
| 1 | dppe | 91% (97:3) |
| 2 | dppp | 66% (91:9) |
| 3 | dppb | 54% (93:7) |
| 4 | dppm | 46% (95:5) |
| 5 | $Ph_3P$ | 48% (95:5) |
| 6 | $Ph_2PMe$ | 56% (96:4) |
| 7 | $PhPMe_2$ | 62% (99:1) |
| 8 | dppf | 36% (95:5) |

[a]Condition: 0.5 mmol phenylacetylene, 0.5 mmol diphenylphosphine oxide, 1 mol% $Pd_2(dab)_3$, ligand (Pd/P = 1:2), 4 mol% $Ph_2P(O)OH$ and 0.5 mL toluene were mixed, 100 °C, overnight.

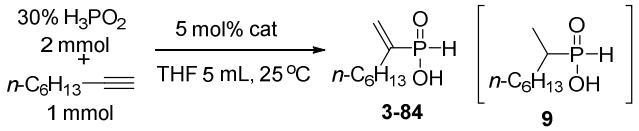
Addition of $Ph_2P(O)H$ **2-8** to terminal alkynes catalyzed by $Me_2Pd(PPhMe)_2/Ph_2P(O)OH$ selectively afforded the Markovnikov adducts.[19a,33] In order to generalize this reaction, a screening on the catalyst was carried out (Table 8). The addition proceeded smoothly to give the corresponding Markovnikov adduct using dppe as the ligand (run 1).

The results compiled in Table 6 showed that, in general, H-phosphine oxides could add to the alkynes *chemo*- and *regio*-selectively. With 1,4-bis(phenylphosphoryl)benzene, the corresponding adduct **3-83** was obtained in 87% yield. 1-Octyne also gave the alkenylphosphoryl oxides in high yields selectively (**3-81**, **3-82**). However, a bulky *tert*-butylphenylphosphine oxide only gave a trace amount of the adduct (**3-78**).

## 4. Palladium-Catalyzed Hydrophosphorylation of Alkynes with Hypophosphinic Acid $H_2P(O)(OH)$.[34]

The addition of hypophosphinic acid **2-9** to alkynes could also take place in the presence of a proper palladium catalyst. As shown in Table 9, $Pd(OAc)_2$ was reduced to the metallic palladium black and no addition products were detected (run 1). No addition took place either with $Pd_2(dba)_3$ or $Pd(PCy_3)_2$ (runs 2-3). Interestingly, however, the addition took place when $Me_2Pd(PPh_3)_2$ was used as the catalyst, and 75% yield of **3-84** was generated after 24 h (runs 4-6). A small amount of **9** (**3-84**/**9** > 95/5) *via* the reduction of **3-84** with $H_3PO_2$ was also detected.[35] Surprisingly, a similar addition did not occur with other palladium complexes (runs 7-9). Phosphine ligands $PPh_2R$ (R = Me, cyclohexanyl) were also effective for this reaction (runs 10-13). As to the bidentate ligand dppp, which is effective for the addition of $(MeO)_2P(O)H$ as described above, only gave a low yield of the product (run 14). On the other hand, dppf gave a quantitative yield of the adduct (run 21). Interestingly, an excess amount of 1-octyne slowed down the reaction (run 22), and only a low yield of the adduct was obtained with a dried $H_3PO_2$ (run 23). The common $Pd(PPh_3)_4$ or a combination of $Pd(OAc)_2$ (or $Pd_2(dba)_3$) with $PPh_3$ also well catalyzed this addition (runs 24-31). With 2 mol% $Pd(PPh_3)_4$, 95% yield of the adduct could be obtained (run 33).

**Table 9. The Addition of Hypophosphinic Acid to 1-Octyne Catalyzed by Palladium**



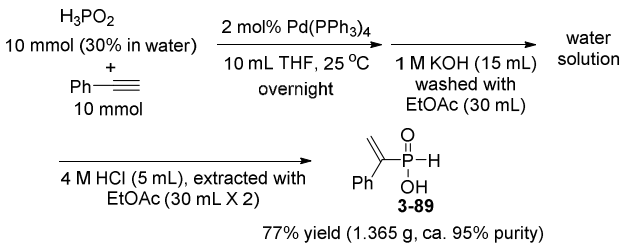

| run | cat | time | NMR yield (**3-84/9**) |
|---|---|---|---|
| 1 | $Pd(OAc)_2$ | 3 h | none |
| 2 | $Pd_2(dba)_3$ | 3 h | none |
| 3 | $Pd(PCy_3)_2$ | 24 h | none |
| 4 | **$Me_2Pd(PPh_3)_2$** | 3 h | 3% |
| 5 | | 6 h | 41% |
| 6 | | 24 h | 75% (92/8) |
| 7 | $Me_2Pd[P(o\text{-}Me\text{-}C_6H_4)_2]_2$ | 24 h | none |
| 8 | $Me_2Pd[P(1\text{-}naphthyl)_2]_2$ | 24 h | none |
| 9 | $Me_2Pd(binap)_2$ | 24 h | none |
| 10 | $Me_2Pd(PPh_2Me)_2$ | 3 h | 39% |
| 11 | | 7 h | 50% |
| 12 | | 24 h | 69% (94/6) |
| 13 | $Me_2Pd(PPh_2Cy)_2$ | 24 h | 55% (95/5) |
| 14 | $Me_2Pd(Ph_2P(CH_2)_3PPh_2)$ | 24 h | <10% |
| 15 | $Me_2Pd(Ph_2P(CH_2)_4PPh_2)$ | 3 h | 3% |
| 16 | | 24 h | 80% (90/10) |
| 17 | $Me_2Pd(Ph_2P(CH_2)_5PPh_2)$ | 3 h | 47% |
| 18 | | 24 h | 95% (94/6) |
| 19 | **$Me_2Pd(dppf)$** | 3 h | 64% |
| 20 | | 7 h | 95% |
| 21 | | 24 h | 100% (99/1) |
| 22[a] | $Me_2Pd(dppf)$ | 3 h | 18% |
| 23[b] | $Me_2Pd(dppf)$ | 24 h | 60% (98/2) |
| 24[c] | **$Pd(PPh_3)_4$** | 3 h | 48% |
| 25[c] | | 6 h | 61% |
| 26[c] | | 20 h | 91% (94/6) |
| 27 | $Pd(OAc)_2$/4 $PPh_3$ | 3 h | 47% |
| 28 | | 6 h | 66% |
| 29 | | 24 h | 95% (95/5) |
| 30 | $Pd_2(dba)_3$/4 $PPh_3$ | 3 h | 36% |
| 31 | | 24 h | 83% (94/6) |
| 32[c,d] | $Pd(PPh_3)_4$ | 3 h | 51% |
| **33[c,d]** | | 18 h | **95% (97/3)** |

[a]Molar ratio: alkyne/P(O)H = 2.5/1. [b]Dry $H_3PO_2$. [c]Molar ratio: alkyne/P(O)H = 1/1. [d]2 mol% Pd catalyst, 1M solution.

The results compiled in Table 6 showed that the addition of hypophosphinic acid to alkynes was a general reaction. Under the conditions of run 33, both aromatic and aliphatic alkynes could be hydrophosphorylated by hypophosphinic acid, producing the corresponding H-alkenylphosphinic acids in good yields with high *regio*-selectivity.

As described in SI, a very pure *H*-alkenylphosphinic acid is difficult to isolate by conventional $SiO_2$-column chromatography techniques because of the presence of the P(O)(OH) unit. However, as shown in Scheme 11, because of the high efficiency of the reaction, NMR spectroscopically pure *H*-alkenylphosphinic acid could be generated easily.

**Scheme 11. Hydrophosphorylation of Phenylacetylene with $H_2P(O)(OH)$ at 10 mmol Scale and Its Purification**




## 5. Hydrogen Phosphoryl Compounds not Applicable to the Reaction.

As described above, in addition to the esters of H-phosphonates, H-phosphinates, and secondary phosphine oxides, hypophosphinic acid could be used as the hydrogen phosphoryl compounds in the palladium-catalyzed addition of P(O)-H bonds to alkynes to produce the corresponding alkenylphsophorus compounds efficiently. However, a hydrogen phosphoryl compound bearing a free OH group (with the exception of $H_3PO_2$), i.e. phosphonic acid and phosphinic acids, could not be used in the reaction and no addition products were produced under similar conditions. (Figure 2. See 6.7 for discussions).

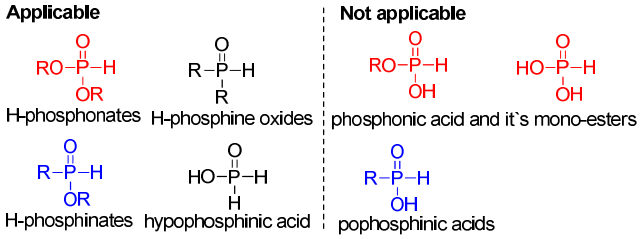



**Figure 2.** Hydrogen Phosphoryl Compounds Applicable and not Applicable to the Pd-Catalyzed Hydrophosphorylation of Alkynes.

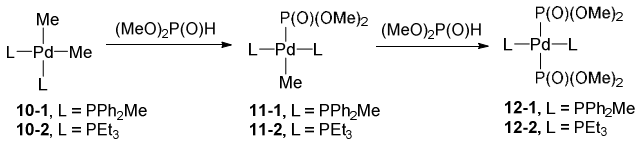
## 6. Mechanistic Insights.

### 6.1. Reactions Associated with $Me_2Pd(PR_3)_2$ in the Catalytic Reactions.

As reported earlier, a dimethylpalladium complex *cis*-$Me_2Pd(PPh_2Me)_2$[23] was initially used as a catalyst for the addition of $(MeO)_2P(O)H$ to alkynes.[16a] However, details about how this divalent Pd(II) complex catalyzed the addition were not known. To clarify the mechanism, several stoichiometric reactions were conducted. *cis*-$Me_2Pd(PPh_2Me)_2$ **10-1** (117.6 mg, 0.219 mmol) and $(MeO)_2P(O)H$ **2-1** (0.482 mmol) were dissolved in toluene (1.5 mL) at room temperature to give a transparent solution (Scheme 12). White solids gradually precipitated out from the solution which was determined to be the *trans*-$[(MeO)_2P(O)]_2Pd(PPh_2Me)_2$ **12-1** (129 mg, 81%

isolated yield).[36] Although a pure mono-methylpalladium complex **11-1** was not isolated, as described below, the formation of complex **12-1** was considered to take place through a stepwise protonolysis of *cis*-$Me_2Pd(PPh_2Me)_2$ with $(MeO)_2P(O)H$.

**Scheme 12. Reactions of Dimethylpalladium Complexes with P(O)-H Compounds**




By using a more stable *cis*-$Me_2Pd(PEt_3)_2$ **10-2**,[23] the stepwise protonolysis process could be confirmed clearly. Thus, at room temperature, $(MeO)_2P(O)H$ (0.267 mmol) was added to the solution of *cis*-$Me_2Pd(PEt_3)_2$ (0.089 mmol) in $C_6D_6$ (0.5 mL). Gas evolution was observed immediately. A new signal assigned to **11-2** emerged at δ 93.9 (P(O), *t*, $J_{PP}$ = 50.0 Hz, 1P) and δ 21.0 ($Et_3P$, *d*, $J_{PP}$ = 50.0 Hz, 2P) in $^{31}P$ NMR spectroscopy. As estimated from $^{31}P$ NMR spectroscopy, the ratio of **11-2** *vs* *cis*-$Me_2Pd(PEt_3)_2$ was 58/42 and 10/90 after 1.5 h and 3.5 h, respectively. The mono-methylpalladium complex **11-2** was rather stable under the current conditions, i.e. no thermal decomposition of **11-2** to $MeP(O)(OMe)_2$ was observed, and further protonolysis of **11-2** with $(MeO)_2P(O)H$ to form **12-2** (P(O), 81.0 ppm) was also negligible. However, further protonolysis of **11-2** with $(MeO)_2P(O)H$ did take place at a slightly elevated temperature. Thus, heating the solution at 60 °C for 3.5 h resulted in a complete disappearance of **11-2** and a quantitative formation of **12-2** (95% isolated yield).

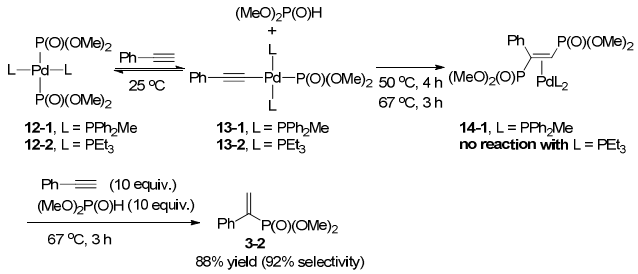
A separate experiment confirmed that the addition of free $PEt_3$ did not retard the protonolysis. However, interestingly, the two configuration isomers of $Me_2Pd(PEt_3)_2$ showed different reactivity towards $(MeO)_2P(O)H$, i.e *trans*-$Me_2Pd(PEt_3)_2$ was more reactive than the *cis*-$Me_2Pd(PEt_3)_2$ complex. For example, monitoring the reaction of $Me_2Pd(PEt_3)_2$ (*cis*/*trans* = 37/63, 33 mg, 0.089 mmol) with $(MeO)_2P(O)H$ (3 equiv) in $C_6D_6$ (0.5 mL) by $^{31}P$ NMR spectroscopy showed that the *trans*-$Me_2Pd(PEt_3)_2$ complex completely disappeared within 1 h and ca. 15% of *cis*-$Me_2Pd(PEt_3)_2$ remained.[37]

More interestingly, the above reaction was considerably accelerated by a trace amount of water. Thus, two reactions of *cis*-$Me_2Pd(PEt_3)_2$ (0.0693 mmol) with $(MeO)_2P(O)H$ (2.2 equiv) in $C_6D_6$ (0.4 mL) were carried out at room temperature, one had additional $H_2O$ (1.0 μL) and the other had not. The reaction of *cis*-$Me_2Pd(PEt_3)_2$ with water was completely consumed to give the corresponding palladium complexes, while 36% of *cis*-$Me_2Pd(PEt_3)_2$ remained without additional water after 80 minutes. This was consistent with the result in the catalytic reaction that a trace amount of water accelerated the $Me_2Pd(PPh_2Me)_2$-catalyzed addition of $(MeO)_2P(O)H$ to 1-octyne (see section 1.1. Effect of impurities).[38]

Complexes **12-1** and **12-2** are rather thermally stable since no decomposition was observed after heating their benzene solution at 80 °C for 5 h. Interestingly, however, they readily reacted with phenylacetylene (1 equiv) at room temperature *via* ligand exchange to liberate $(MeO)_2P(O)H$ (Scheme 13). This reaction seems reversible since the four chemicals were present in the mixture even after 24 h and no further formation of **13** was observed when the ratio of **12**/**13** reached ca. 1/1. Upon heating the mixture (50-67 °C), however, all these chemicals disappeared and a new complex **14-1** was formed quantitatively. With $PEt_3$, however, no corresponding olefin-coordinated complex could be detected under the current conditions.

No further reaction of complex **14-1** with an additional $(MeO)_2P(O)H$ (10 equiv) was observed at 67 °C. However, as phenylacetylene (10 equiv) was subsequently added, the addition of $(MeO)_2P(O)H$ to phenylacetylene took place to produce the adduct **3-2** in 88% yield after 3 h. As confirmed by NMR spectroscopy, complex **14-1** was also clearly observed in the mixture after the reaction.

**Scheme 13. The Role of Bisphosphorylpalladium Complexes in the Hydrophosphorylation**



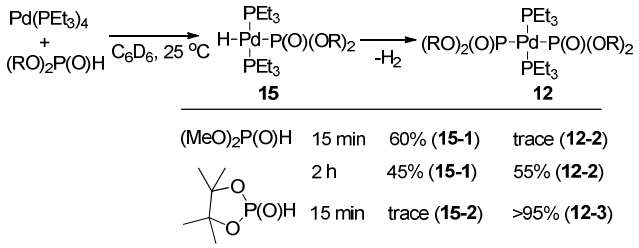

These results suggested that dimethylpalladium complex **10-1** only served as a catalyst precursor, which should change to zero-valent Pd(0) species through therm-decomposition of **10-1** [23] and/or a series of reactions as described above. These zero-valent Pd(0) acted as the catalyst for the hydrophosphorylation reaction.

### 6.2. The Reaction of $(RO)_2P(O)H$ with $Pd(PEt_3)_4$ and Phenylacetylene: H-Pd Addition *vs* P(O)-Pd Addition & the Acetylene Path *vs* the H-Pd Path.

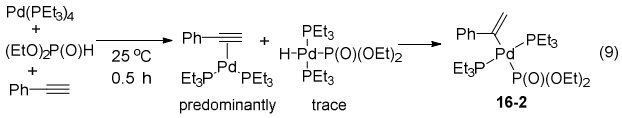
Oxidative addition of $(RO)_2P(O)H$ to $Pd(PEt_3)_4$ could generate the corresponding Pd-H species (Scheme 14). However, the Pd-H complex is rather unstable and decomposes easily at room temperature. For example, addition of $(MeO)_2P(O)H$ (0.2 mmol) to $Pd(PEt_3)_4$ (0.1 mmol) in $C_6D_6$ (0.5 mL) at room temperature could produce Pd-H in *ca*. 60% yield with a trace amount of the further reaction product P(O)-Pd-P(O) **12-2** in 15 min.

However, this Pd-H complex was not stable and further reacted with $(MeO)_2P(O)H$ to give the bisphosphorylpalladium complex **12-2** in 55% yield after 2 h. The more reactive five-membered P(O)-H compound produced the bisphosphorylpalladium complex predominantly and only a trace amount of Pd-H species could be detected from the reaction.

**Scheme 14. The Reactions of P(O)-H Compounds with Pd(0) Complex**



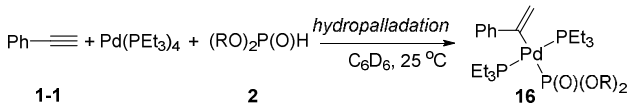

When $(EtO)_2P(O)H$ (0.05 mmol) was added to a mixture of $Pd(PEt_3)_4$ (0.05 mmol) and phenylacetylene (0.05 mmol) in $C_6D_6$, the color of the solution gradually turned from yellow to colorless. After 1 h, $^1H$ NMR showed that, while most of $(EtO)_2P(O)H$ remained unreacted, the free phenylacetylene almost disappeared because of its coordination to $Pd(PEt_3)_4$. Only a trace amount of Pd-H was detected (eq 9). Gradually, two characteristic vinyl proton signals at 6.50 ppm (d, $J_{P\text{-}H}$ = 30.4 Hz), 5.17 ppm (d, $J_{P\text{-}H}$ = 15.2 Hz), and two new phosphorus signals at 88.67 ppm (t, P(O), $J_{P\text{-}P}$ = 51.5 Hz), 13.99 (d, $PEt_3$, $J_{P\text{-}P}$ = 51.5 Hz) appeared, which, as described later, were due to a vinyl(phosphoryl)palladium complex **16-2**.[39] The starting materials disappeared after 30 h. Removal of the volatiles in *vacuo* gave **16-2** as a colorless oil (Table 10, run 2).




The above experiment in eq 9 revealed two facts regarding the reactivity and the selectivity of the palladium complexes: (1) formally, hydropalladation (H-Pd addition to the alkyne), rather than phosphorylpalladation (P(O)-Pd addition to the alkyne) took place, (2) hydropalladation took place predominantly with Pd moiety bond to the internal carbon of phenylacetylene.

As shown in Table 10, the reaction of phenylacetylene (0.05 mmol), *H*-phosphonate (0.05 mmol) and $Pd(PEt_3)_4$ (0.05 mmol) in $C_6D_6$ (0.5 mL) at room temperature was followed by NMR. Both steric and electronic factors of the substituent RO significantly affected this reaction: a *H*-phosphonate with an electron-withdrawing group reacts faster, while that with a steric bulky substituent reacts slower. For example, with $(CF_3CH_2O)_2P(O)H$, the reaction almost completed within 4 hours (run 3). On the other hand, with $(i\text{-}PrO)_2P(O)H$, the reaction required more than 4 days (run 4).

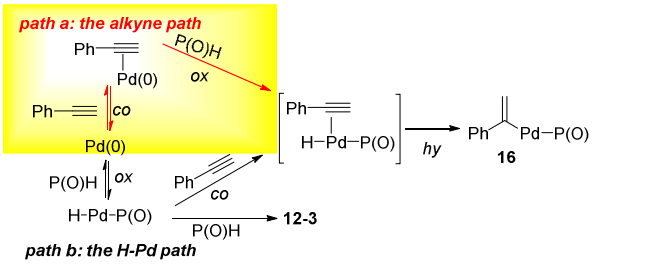
**Table 10. Generation of Alkenylpalladiums from Phenylacetylene, $Pd(PEt_3)_4$ and H-phosphonates**




| run | P(O)-H | product, yield/time |
|---|---|---|
| 1 | **2-1**, $(MeO)_2P(O)H$ | **16-1**, 50%/4 h, 95%/20 h |
| 2 | **2-2**, $(EtO)_2P(O)H$ | **16-2**, 15%/4 h, 70%/20 h, 93%/30 h |
| 3 | **2-6**, $(CF_3CH_2O)_2P(O)H$ | **16-3**, 92%/4 h |
| 4 | **2-3**, $(i\text{-}PrO)_2P(O)H$ | **16-4**, 6%/4 h, 26%/20 h, 67%/4 days |

These reactions with $(RO)_2P(O)H$ very much resembled that of carboxylic acids, that proceeds *via* the alkyne path (path a) rather than the hydride path (path b), to give the palladium complex with Pd attached to the internal carbon of the alkyne.[40] We assume that $(RO)_2P(O)H$ might similarly react *via* the alkyne path (path a) to produce the palladium complex (Scheme 15).[40]

**Scheme 15. Hydropalladation Paths of Alkynes with H-phosphonates.**




*co* = coordination; *ox* = oxidative addition; *hy* = hydropalladation; P(O)H = $(EtO)_2P(O)H$

## 6.3. Reductive Elimination of Alkenyl(phosphoryl)-palladium Complexes.

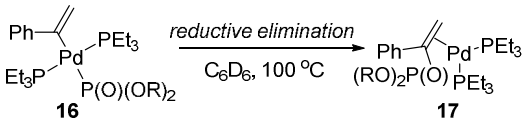
Complexes **16** are the first successfully isolated, structurally unambiguously determined (alkenyl)(phosphoryl)palladium complexes from the hydropalladation of alkynes. As described below, their isolation provides important clues to the catalytic cycle.

As shown in Table 11, although stable at room temperature, reductive elimination of complex **16-2** did take place at an elevated temperature (100 °C, 6 h), to generate the corresponding alkenylphosphonate that was isolated as an olefin-Pd(0) complex **17-2**.

Compared with the hydropalladation reactions of alkynes (see 6.2), where a significant steric effect was observed, the steric influence seems small with the reduc-

tive elimination since MeO and *i*-PrO all gave similar results (runs 1 and 4). However, a big electronic effect was observed.[21a] Thus, with $CF_3CH_2O$, the reductive elimination was slow compared to other RO groups (run 3).

**Table 11. Reductive Elimination of Alkenyl(phosphoryl)palladium Complexes.**[a]



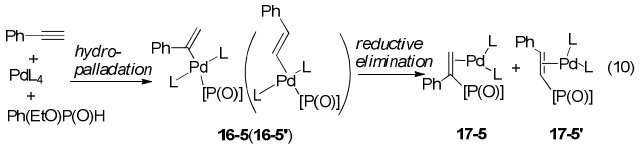

| run | RO | time | isolated yield |
|---|---|---|---|
| 1 | MeO | 6 h | **17-1**, 71% |
| 2 | EtO | 6 h | **17-2**, 78% |
| 3 | $CF_3CH_2O$ | (6) 15 h | **17-3**, (49) 80% |
| 4 | *i*-PrO | 6 h | **17-4**, 72% |

[a]Reaction conditions: 0.05 mmol complex **16** in 0.5 mL dry and degassed $C_6D_6$ was heated at 100 °C until the starting material was consumed, the reaction process was monitored by $^1H/^{31}P$ NMR spectroscopies.

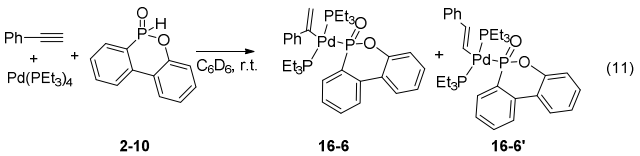
These results showed that the reductive elimination was slower and more difficult than the hydropalladation. Therefore, it is assumed that the reductive elimination step perhaps should be the rate-determining step in the palladium-catalyzed hydrophosphorylations.[41]

### 6.4. Reactions with Hydrogen Phosphinate Ph(EtO)P(O)H and H-phosphine Oxide $Ph_2P(O)H$.

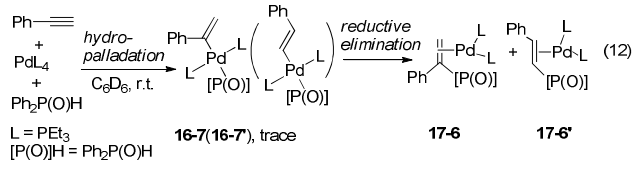
Very interestingly, the reaction is highly structure-sensitive with a P(O)-H compound, and the three compounds, i.e. H-phosphonates $(RO)_2P(O)H$, H-phosphinates Ph(RO)P(O)H and H-phosphine oxide $Ph_2P(O)H$, showed quite different behaviors under similar conditions.



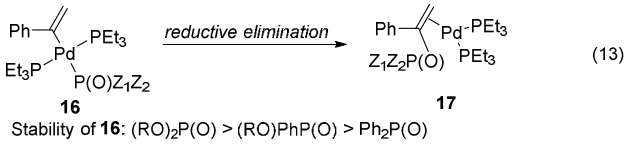

*H*-phosphinate Ph(EtO)P(O)H **2-7** gradually reacted at room temperature. However, being different from $(RO)_2P(O)H$, a *mixture* of alkenyl(phosphoryl)palladiums complexes **16-5** and **16-5'** were generated. In addition, these complexes were ***not stable*** at room temperature which decomposed slowly *via* reductive elimination to give a mixture of the corresponding olefin-palladium(0) complexes **17-5** and **17-5'** (eq 10). With a cyclic H-phosphinate **2-10**, the alkenyl(phosphoryl)palladiums **16-6** (**16-6'**) (generated in ca. 3:2 ratio) are stable (eq 11), and was successfully isolated and characterized (Table 13).




With $Ph_2P(O)H$ **2-8**, the corresponding alkenylpalladiums quickly decomposed to **17-6** (**17-6'**) at room temperature. Thus, only a trace amount of **16-7** (**16-7'**) could be detected by NMR from the reaction where the reductive elimination products **17-6** (**17-6'**) **(17-6/17-6'** = ca. 1:4) were generated predominantly (eq 12). When $Ph_2P(O)H$ with a trace amount of $Ph_2P(O)OH$ (*ca.* 5 mol%) was used, a mixture of **17-6** (**17-6'**) with a ratio of **17-6/17-6'** = ca. 11.5:1 was obtained (for the effect of $Ph_2P(O)OH$, see 6.6).



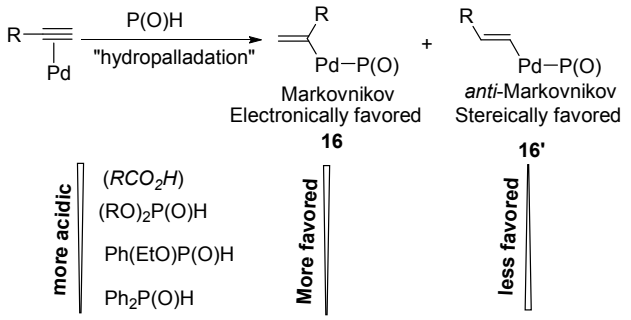

Therefore, the reductive elimination of complexes **16** follows an increasing order of $(RO)_2P(O)$ < (RO)PhP(O) < $Ph_2P(O)$ (eq 13).




### 6.5. An Explanation for the Difference in Reactivity between $(RO)_2P(O)H$, $Ph(EtO)P(O)H$ and $Ph_2P(O)H$.

Both electronic and steric factors affect the reactivity of the P(O)-H compounds. Consequently, the observed different behavior of the three kinds of P(O)-H compounds ($(RO)_2P(O)H$, $Ph(EtO)P(O)H$ and $Ph_2P(O)H$) reflect the results of the two factors. The formation of the Markovnikov intermediate **16** is more electronically favored, while the formation of the *anti*-Markovnikov intermediate **16'** is more sterically favored. Considering that a carboxyl acid $RCO_2H$ can predominantly generate the Markovnikov intermediate,[40] and the acidity of P(O)H compounds follows a decreasing order of $(RO)_2P(O)H$ > $Ph(EtO)P(O)H$ > $Ph_2P(O)H$,[42] we assume that, the more acidic $(RO)_2P(O)H$ might react, like $RCO_2H$, to predominantly give **16**, while steric factors weighted more with the less acidic $Ph(OEt)P(O)H$ and $Ph_2P(O)H$ which, consequently, gave a mixture of **16** and **16'** (Scheme 16).

**Scheme 16. "Acidity" Formally Determines the *regio*-Selectivity of the Hydropalladation**




### 6.6. The Role of a Brϕnsted Acid.

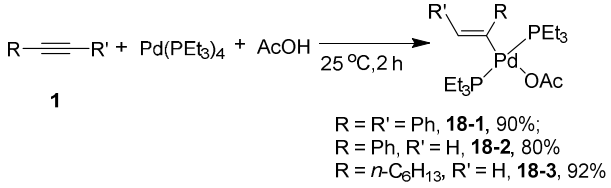
The addition of a trace amount of phosphinic acid $Ph_2P(O)OH$ could significantly enhance the reactivity and reverse the *regio*-selectivity of the palladium-catalyzed addition of $Ph_2P(O)H$ with a terminal alkyne.[19] However, the role of $Ph_2P(O)OH$ was not understood.

#### 6.6.1. *Regio*- and *Stereo*-selective Hydropalladition of an Alkyne with $Ph_2P(O)OH$.

Diphenylacetylene and phenylacetylene could be easily hydropalladated with the combination of carboxylic acid and $Pd(PEt_3)_4$.[40] The reaction took place *stereo*-selectively to produce the alkenylpalladium complexes in high yields (Scheme 17). With an aliphatic alkyne 1-octyne, the reaction also occurred to give the branched palladium complex *regio*-selectively in a high yield. Brϕnsted acids (acetic acid and $Ph_2P(O)OH$ as described below) were more reactive than P(O)-H compounds in the hydropalladation of alkyne.

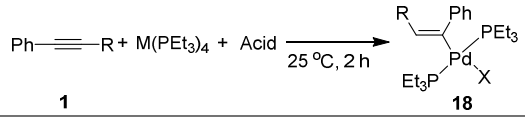
With $Ph_2P(O)OH$, a similar hydropalladation took place. Thus, as demonstrated in Table 12, diphenylacetylene was quickly hydropalladated generating the corresponding *cis*-alkenylpalladium complexes **18-4** at room temperature in 96% yield (run 1). With phenylacetylene, a Markovnikov-adduct alkenylpalladium complex **18-5** was readily generated *regio*-selectively (run 2). The structure of **18-5** was unambiguously confirmed by the X-ray analysis.[28a] Similarly, diphenylphosphoric acid $(PhO)_2P(O)OH$ also selectively gave the branched alkenylpalladium **18-6** in 85% yield (run 3). In addition, $Ni(PEt_3)_4$ was as reactive as $Pd(PEt_3)_4$ to afford the corresponding branched alkenylnickel complex **18-7** in 90% yield (run 4).

**Scheme 17. Hydropalladation of Alkynes with the Combination of Pd(0) Complex and Carboxylic Acids**



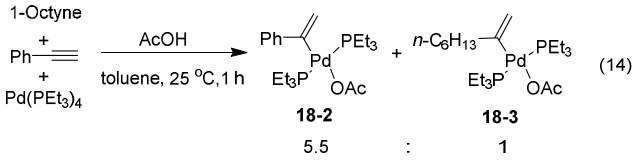

As to the reactivity of an alkyne, an aromatic alkyne is more reactive than an aliphatic alkyne. For example, the reaction of an equimolar mixture of phenylacetylene (0.05 mmol) and 1-octyne (0.05 mmol) with $Pd(PEt_3)_4$ (0.05 mmol) and acetic acid (0.1 mmol) in toluene-$d_8$ (0.5 mL) at room temperature, completed within one hour to generate **18-2** and **18-3** in the ratio of 5.5:1 (eq 14).

**Table 12. Hydrometalation of Alkynes with a Combination of $M(PEt_3)_4$ and P(O)(OH) Acid[a]**




| run | Ph–≡–R | $M(PEt_3)_4$ | acid | isolated yield |
|---|---|---|---|---|
| 1 | Ph–≡–Ph | $Pd(PEt_3)_4$ | $Ph_2P(O)OH$ | **18-4**, 96%[b] |
| 2 | Ph–≡–H | | $Ph_2P(O)OH$ | **18-5**, 82% (X-ray) |
| 3 | | | $(PhO)_2P(O)OH$ | **18-6**, 85% |
| 4 | | $Ni(PEt_3)_4$ | $Ph_2P(O)OH$ | **18-7**, 90% |

[a]Reaction conditions: 0.05 mmol alkynes, 0.05 mmol $M(PEt_3)_4$, 0.05 mmol acid and 0.5 mL $C_6D_6$ were mixed in the glove box at room temperature, 2 hours. The complex was isolated by recrystallization from hexane-toluene at -30 °C (if solid). [b]The complexes were colorless oil.

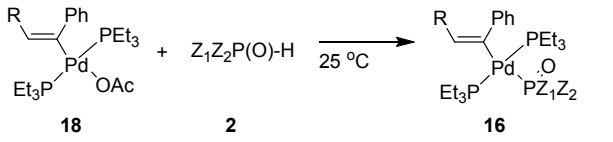



#### 6.6.2. Rapid Ligand-Exchange.

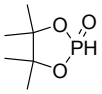
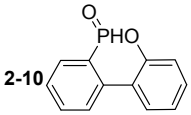
At room temperature, these alkenylpalladium complexes **18** react with P(O)-H compounds (H-phosphonates, H-phosphinates and H-phosphine oxides) quickly to give the corresponding alkenyl(phosphoryl)palladium complexes **16** in high yields *via* ligand-exchange reactions (Table 13). Thus, 0.05 mmol alkenylpalladium complex **18-1** and 0.05 mmol P(O)-H **2-5** were mixed in 0.5 mL $C_6D_6$ at room temperature, as indicated by NMR spectroscopies, the starting materials **18-1** and **2-5** were consumed in 2 hours, while a new characteristic alkenyl proton signal at 6.59 ppm (d, $J_{P\text{-}H}$ = 18.0 Hz) and two new phosphorus signals at 104.99 ppm (t, $J_{P\text{-}P}$ = 52.3 Hz), 9.29 ppm (d, $J_{P\text{-}P}$ = 52.3 Hz) were observed, indicative of the formation of a new alkenyl(phosphoryl)palladium complex **16-9**. Removal of the volatiles in *vacuo* afforded **16-9** as a white solid, which was recrystallized from toluene-hexane at -30 °C to give single crystals suitable for X-ray analysis (run 7). The ORTEP drawing of complex **16-9** was depicted in Figure 3, which unambiguously reveals the *trans* geometry of the carbon-carbon double bond as well as the *trans* geometry on Pd atom. The Pd

atom in complex **16-9** adopts a square-planar coordination geometry, which is ligated by two $PEt_3$ in a *trans* manner.

**Table 13. Ligand Exchange Reactions.**[a]

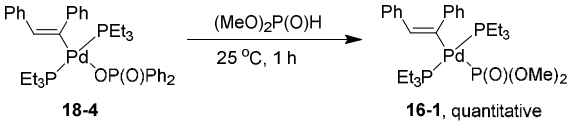



**18** **2** **16**

| run | alkenylpalladium | $Z_1Z_2P(O)$-H | isolated yield |
|---|---|---|---|
| 1 | R = H **18-2** | **2-1** $(MeO)_2POH$ | **16-1**, 72%[b,c] |
| 2 | | **2-2** $(EtO)_2POH$ | **16-2**, 92%[b,c] |
| 3 | | **2-4** $(CF_3CH_2O)_2POH$ | **16-3**, 90%[b,c] |
| 4 | | **2-3** $(i\text{-PrO})_2POH$ | **16-4**, 75%[b,c] |
| 5 | | **2-5**  | **16-8**, 80% (X-ray)[d] |
| 6 | | **2-10**  | **16-6**, 85% (X-ray)[e] |
| 7 | R = Ph **18-1** | **2-5**  | **16-9**, 81% (X-ray)[d] |

[a]Reaction conditions: 0.05 mmol alkynes, 0.05 mmol $M(PEt_3)_4$, 0.1 mmol HOAc and 0.5 mL $C_6D_6$ were mixed at room temperature for 20 h. Then, 0.05 mmol P(O)H compound was added. The mixture was kept at room temperature until the P(O)H compound was consumed. The complex was isolated by recrystallization from hexane-toluene at -30 °C (when solid). [b]The complexes were oil. [c]Toluene was used as solvent. [d]Those complexes contain HOAc. [e]Recrystallization from hexane-toluene at room temperature.

Complex **18-2** could also react with *H*-phosphonate **2-5** efficiently to give the corresponding alkenyl(phosphoryl)palladium complexes **16-8** in 80% isolated yields at room temperature (run 5). This ligand exchange reaction was significantly retarded with sterically bulky P(O)-H compounds (runs 1, 2, 3 and 4), i.e. the bulkier the substrate, the slower the reaction. With diethyl phosphonate **2-2**, the reaction required 9 h to give 92% yield of the complex. However, with diisopropyl phosphonate **2-3**, the reaction took several days (for details, see SI). With H-phosphinate **2-10**, the ligand exchange reaction also proceeded smoothly to afford the corresponding complex **16-6** in 85% isolated yield (run 6). The structures of complexes **16-6** and **16-8** were also unambiguously determined by X-ray analysis (Figures 4 and 5). As expected, complex **18-4** underwent similar ligand-exchange reaction with P(O)-H compounds to quantitatively give the phosphorylpalladium complex (eq 15).




**18-4** **16-1**, quantitative (15)

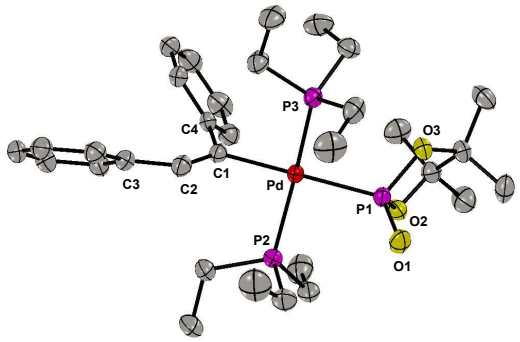



**Figure 3.** ORTEP Drawing of complex **16-9**. Thermal ellipsoids are drawn at 50% probability. H atoms and HOAc which was attached to the P=O by hydrogen bond are omitted for clarity. Selected bond lengths (Å) and angles (deg): C7-C8 = 1.335(2), C7-Pd1 = 2.0768(15), C7-C15 = 1.483(2), P2-Pd1 = 2.3492(5), P1-Pd1 = 2.3287(2); C8-C7-Pd1 = 126.41(12), C7-Pd1-P2 = 89.37(5), P1-Pd1-P2 = 88.882(16), P2-Pd1-P3 = 165.533(17).

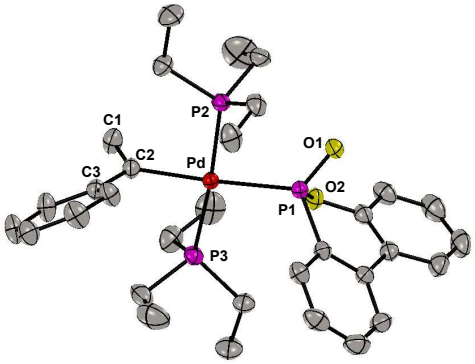
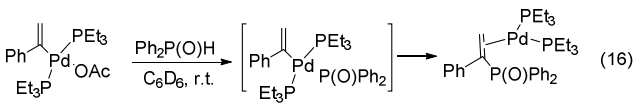



**Figure 4.** ORTEP Drawing of complex **16-6**. Thermal ellipsoids are drawn at 50% probability. H atoms are omitted for clarity. Selected bond lengths (Å) and angles (deg): C1-C2 = 1.336(2), C2-Pd = 2.0965(15), C2-C3 = 1.482(2), P2-Pd = 2.3240(5), P1-Pd = 2.3310(5); C1-C2-Pd = 118.72(12), C2-Pd-P2 = 90.23(4), P1-Pd-P2 = 88.779(15), P2-Pd-P3 = 174.047(15), O1-P1-Pd = 121.63(5).

When $Ph_2P(O)H$ was used as the substrate, the corresponding alkenylpalladium complex could not be isolated because of its rapid decomposition as described above (eq 12). Thus, **18-2** reacted with diphenylphosphine oxide **2-8** to produce, not the corresponding alkenyl(phosphoryl)palladium complex **16-7**, but the reductive elimination product **17-6** at room temperature in 80% isolated yield (eq 16, Figure 6).




**18-2** **16-7** **17-6** (16)

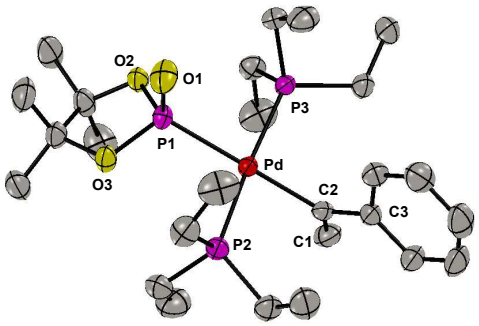



**Figure 5.** ORTEP Drawing of complex **16-8**. Thermal ellipsoids are drawn at 50% probability. H atoms and a HOAc attached to the P=O via hydrogen bond are omitted for clarity. Selected bond lengths (Å) and angles (deg): C1-C2 = 1.330(3), C2-C3 = 1.482(3), C2-Pd = 2.081(2), P2-Pd = 2.3362(7), P1-Pd = 2.3337(7); C1-C2-Pd = 120.27(18), C2-Pd-P2 = 88.36(6), P1-Pd-P2 = 90.36(2), P2-Pd-P3 = 175.37(2).

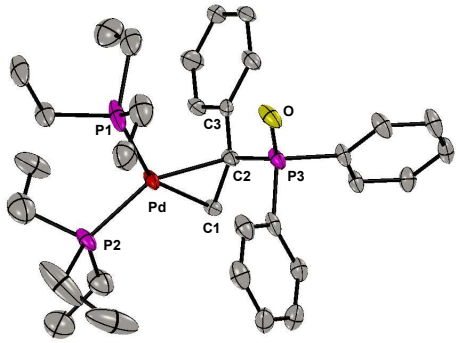
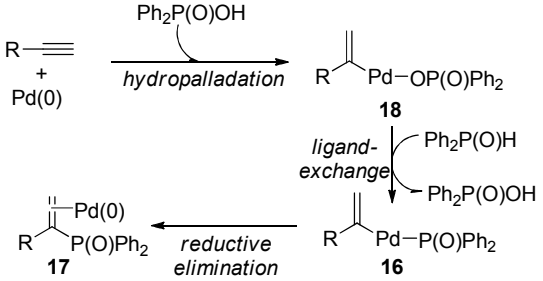



**Figure 6.** ORTEP Drawing of complex **17-6**. Thermal ellipsoids are drawn at 50% probability. H atoms are omitted for clarity. Selected bond lengths (Å) and angles (deg): C1-C2 = 1.431(8), C1-Pd1 = 2.090(6), C2-Pd1 = 2.162(6), P2-Pd1 = 2.2807(17), P1-Pd1 = 2.3291(19), C2-C3 = 1.508(9), C2-P3 = 1.781(6), O-P3 = 1.491(4); C1-Pd1-C2 = 39.3(2), C1-C2-Pd1 = 119.9(6), C1-Pd1-P2 = 99.69(16), C2-Pd1-P1 = 111.03(16), P1-Pd1-P2 = 109.71(6), C3-C2-Pd = 109.1(4), C2-P3-O = 116.1(3).

These elementary reactions can reasonably explain why in the presence of $Ph_2P(O)OH$, the palladium-catalyzed addition of $Ph_2P(O)H$ to alkynes selectively produces the Markovnikov adducts,[19] i.e. first, hydropalladation takes place selectively with $Ph_2P(O)OH$ to produce alkenylpalladium **18** which then reacts with $Ph_2P(O)H$ via a rapid ligand-exchange reaction to give the adduct **17** via an intermediate **16** (Scheme 18).

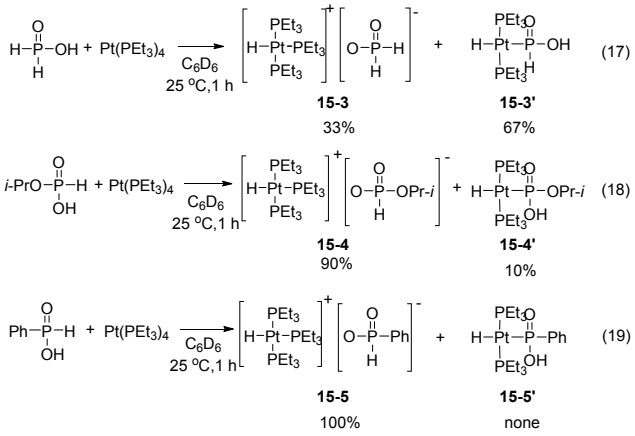
**Scheme 18. The Role of $Ph_2P(O)OH$.**




### 6.7. P(O)-H Compounds Applicable to Palladium-Catalyzed Hydrophosphorylation of Alkynes: P(O)-H Activation vs O-H Activation.

As described above, with the exception of hypophosphinic acid $H_3PO_2$, substrates with a hydroxyl OH group (P(O)OH) are not applicable to this palladium-catalyzed hydrophosphorylations (Figure 2). In order to understand this phenomenon, reactions of P(O)OH compounds with $Pt(PEt_3)_4$ were investigated (Scheme 19).[43]

**Scheme 19. Competitive Cleavage between P(O)-H Bond and O-H Bond with a Pt (0) Complex**



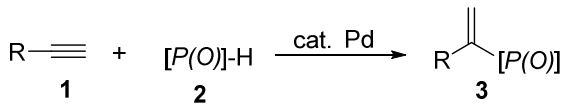

As shown in Scheme 19, 0.05 mmol $H_3PO_2$ (50% solution in water) reacted with 0.05 mmol $Pt(PEt_3)_4$ in 0.5 mL benzene-$d_6$ quickly at room temperature to give a mixture of Pt-H complexes **15-3** (*via* the activation of an O-H bond) and **15-3'** (*via* the activation of P(O)-H bond) with a ratio of *ca.* 0.5:1 (eq 17). Under similar conditions, phosphoric acid (*i*-PrO)P(O)(OH)H reacted quickly with $Pt(PEt_3)_4$ to give **15-4** *via* activation of an O-H bond in ca. 90% yield, whereas the product **15-4'** *via* activation of P(O)-H bond was generated in only *ca.* 10% yield (eq 18). When phosphoric acid PhP(O)(OH)H was used, only **15-5** *via* protonation of Pt(0) was detectable (eq 19).

The above results might indicate that except $H_3PO_2$, the reactive P(O)-Pd-H species could not be easily achieved with a P(O)(OH)H substrate, which may explain why the palladium-catalyzed addition of these P(O)OH compounds to alkynes hardly take place.[43]

## SUMMARY

In summary, the selective palladium-catalyzed addition of P(O)H compounds to alkynes (hydrophosphorylation) generating alkenylphosphoryl compounds was studied in detail. Four kinds of P(O)H compounds, H-phosphonate $(RO)_2P(O)H$, H-phosphinate $R(RO)P(O)H$, secondary phosphine oxide $R_2P(O)H$, and hypophosphinic acid $H_3PO_2$, can be used as the substrates for the hydrophosphorylation reactions to produce the corresponding Markovnikov adducts in high yields.

**Scheme 20. Preferred Catalyst for the Pd-Catalyzed Hydrophosphorylation of Alkynes**



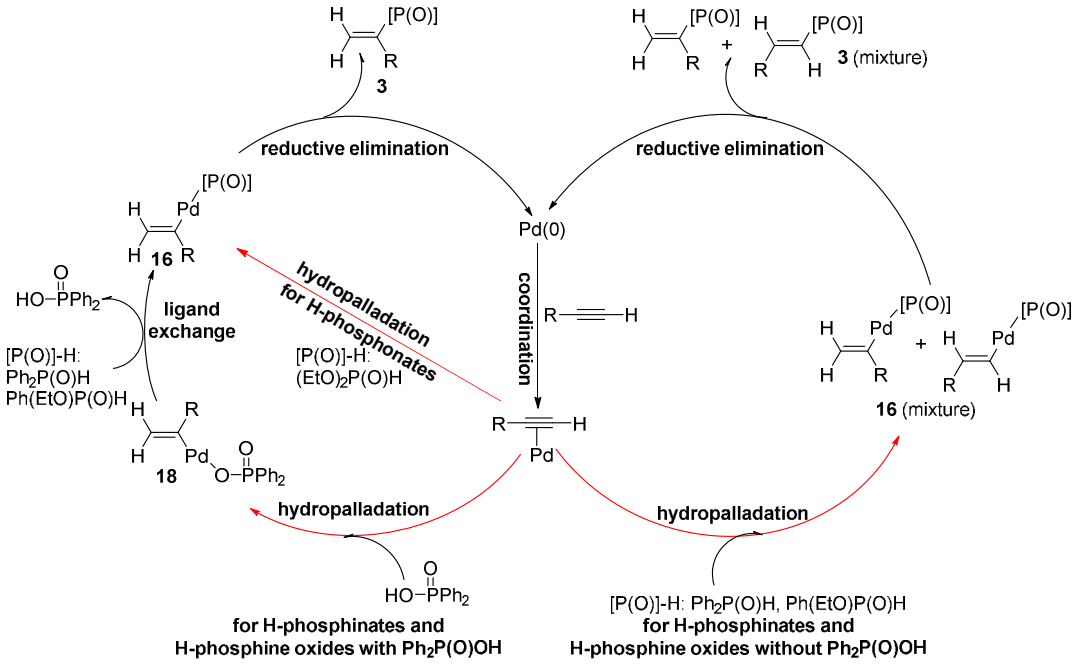

| [P(O)]-H | prefered catalyst |
|---|---|
| H-phosphonate $(R'O)_2P(O)H$ | **Pd/dppp** |
| H-phosphinate R'O)R''P(O)H | **Pd/dppe/$Ph_2P(O)OH$** |
| H-phosphine oxide R'R''P(O)H | **Pd/dppe/$Ph_2P(O)OH$** |
| hypophosphinic acid $(HO)P(O)H_2$ | **$Pd(PPh_3)_4$** |

The use of a right palladium catalyst is the key to a successful hydrophospholyation, because the best catalyst is different to each other for these P(O)H compounds (Scheme 20). For H-phosphonate $(RO)_2P(O)H$, Pd/dppp enables an efficient hydrophosphorylation. For H-phosphinate R(RO)P(O)H and secondary phosphine oxide $R_2P(O)H$, Pd/dppe/$Ph_2P(O)OH$ is the right catalyst. On the other hand, $Pd(PPh_3)_4$ is the catalyst for hypophosphinic acid $H_3PO_2$.

By using this hydrophosphorylation, dozens of grams of alkenylphosphonates can be readily prepared from commercially available starting materials (Scheme 5), showing that this hydrophosphorylation reaction is a powerful practical way for the preparation of these valuable organophosphorus compounds.[14,15]

This palladium-catalyzed hydrophosphorylation does have limitations. Firstly, it only produces the $\alpha$-adduct efficiently and selectively.[33] Secondly, except for $H_3PO_2$, P(O)H compounds having a free OH group, *i.e.* phosphinic acids, phosphonic acid and its mono-esters (Figure 2) are not applicable. A few alkynes cannot be used either (Figure 1).

**Scheme 21. Mechanism for the Palladium-Catalyzed Addition of P(O)-H Compounds to Alkynes**




Mechanistic studies allow us to draw an overall general catalytic cycle for this palladium-catalyzed hydrophosphorylation (Scheme 21). For $(RO)_2P(O)H$, it reacts like an Brϕnsted acid to produce the internal palladium intermediate **16** *via* hydropalladation which then produces the Markovnikov adduct selectively. On the other hand, for Ph(RO)P(O)H and $Ph_2P(O)H$, they produce a mixture of terminal and internal alkenylpalladium complexes, and consequently give a mixture of the adducts. In the presence of $Ph_2P(O)OH$, hydropalladation of alkynes with this acid takes place first to give an internal alkenylpalladium. A ligand exchange of this complex with a P(O)-H compound gives the internal phosphorylpalladium intermediate which produces the Markovnikov adduct *via* reductive elimination.

## ASSOCIATED CONTENT

General information, experimental procedures, characterization data, CIF files of **16-6, 16-8, 16-9** and **17-6,** copies of $^{1}H$, $^{13}C$ and $^{31}P$ NMR spectra for products. 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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(13) As to how to generally call this kind of metal-mediated additions of P(O)-H compounds, we noticed that currently there are several names for them, *i.e.* hydrophosphorylation, hydrophosphinylation etc.

Since the P(O) group is generally called a phosphoryl group, we prefer calling this kind of reactions hydrophosphorylation.
(14) Vinylphosphoryl compounds (taking vinylphosphonates $CH_2$=CHP(O)$(OR)_2$ as an example) are polar monomers similar to acrylates $CH_2$=$CHCO_2R$ etc. They are readily transformed to other functional compounds through the reactions of the reactive double bonds (addition, reduction, Diels-Alder reaction, epoxidation, dihydoxylation, Heck reaction and methathesis reaction etc.). Therefore, these compounds have vast applications in organic synthesis, medicinal & biochemistry, and material science. For *Applications in organic synthesis* (reviews), see: (a) Minami, T.; Motoyoshiya, J. *Synthesis* **1992**, 333. (b) Dembitsky, V. M.; Quantar, A. A. A. A.: Haj-Yehia, A.; Srebnik, M. *Mini-Rev. Org. Chem.* **2005**, *2*, 91. (c) Wang, H.; Liu, Z. *Chin. J. Org. Chem.* **2003**, *23*, 321. They are the key intermediates for the preparation of the clinically used antibacterial agent Fosfomycin. (d) Girotra, N. N.; Wendler, N. L. *Tetrahedron Lett.* **1969**, *10*, 4647. (e) Glamkowski, E. J.; Gal, G.; Purick, R.; Davidson, A. J.; Sletzinger, M. *J. Org. Chem.* **1970**, *35*, 3510. For *Applications in medicinal & biochemistry*: a few simple vinylphosphoryl compounds themselves are potential enzyme inhibitors, and show strong *anti*-proliferative activities, see: (f) Al-Quntar, A. A. A.; Baum, O.; Reich, R.; Srebnik, M. *Arch. Pharm.* **2004**, *337*, 76. (g) Wang, X.-H.; Han, L.-B. Jpn. Kokai Tokkyo Koho JP 200763168, 2007. (h) Wang, X.-H.; Han, L.-B. Jpn. Kokai Tokkyo Koho JP 2007137838, 2007. (i) Wang, X.-H.; Han, L.-B. Jpn. Kokai Tokkyo Koho JP 200770278, 2007. Examples for biological applications of their derivatives as *anti*-cancer, *anti*-viral and *anti*-bacterial compounds, see: (j) Liu, Z.; MacRitchie, N.; Pyne, S.; Pyne, N. J.; Bittman, R. *Bioorg. Med. Chem.* **2013**, *21*, 2503. (k) Tonelli, F.; Lim, K. G.; Loveridge, C.; Long, J.; Pitson, S. M.; Tigyi, G.; Bittman, R.; Pyne, S.; Pyne, N. J. *Cell. Signalling* **2010**, *22*, 1536. (l) Harnden, M. R.; Parkin, A.; Parratt, M. J.; Perkins, R. M. *J. Med. Chem.* **1993**, *36*, 1343. (m) Lazrek, H. B.; Rochdi, A.; Khaider, H.; Barascut, J. L.; Imbach, J. L.; Balzarini, J.; Witvrouw, M.; Pannecouque, C.; De Clercq, E. *Tetrahedron* **1998**, *54*, 3807. Because they can homo- or copolymerize to give functional polymers, huge applications in material chemistry are known, i.e. flame retardant materials, metal extractants, fuel cell membranes, thermoresponsive polymers, cement and dental materials etc., (n) David, G.; Negrell-Guirao, C. in *Phosphorus-Based Polymers: from Synthesis to Applications*; Monge S., David, G., Ed.s, RSC Polymer Chemistry Series, Royal Society of Chemistry: United Kingdom, 2014, Vol. 11, pp 35-50. (o) Soller, B. S.; Salzinger, S.; Rieger, B. *Chem. Rev.* **2016**, *116*, 1993. See also (p) Han, L.-B.; Uchimaru, Y.; Sasaki, S. Jpn. Kokai Tokkyo Koho JP 2013253816, 2013. (q) Han, L.-B.; Liu, R. Jpn. Kokai Tokkyo Koho JP 2010179287, 2010. (r) Han, L.-B.; Futamura, Y.; Fujino, H.; Watanabe, T. Jpn. Kokai Tokkyo Koho JP 2015110617, 2015. (s) Han, L.-B.; Futamura, Y.; Fujino, H.; Watanabe, T. Jpn. Kokai Tokkyo Koho JP 2014132089, 2014. (t) Han, L.-B.; Shinohara, Y. Jpn. Kokai Tokkyo Koho JP 2007145951, 2007. Recently, remarkable application that these vinylphosphoryl compounds can significantly improve the stability and performance of lithium battery even at high temperatures was discovered, (u) Han, J.; Lee, H.; Kim, H. US Patent US 7217480B2, 2007. (v) Han, L.-B; Matumoto, H.; Yoshinaga, M.; Yamashita, H. Jpn. Kokai Tokkyo Koho JP 2014205637, 2014. (w) Funada, Y.; Kubota, T. Jpn. Kokai Tokkyo Koho JP 201355031, 2013.
(15) A few methods for the preparation of vinylphosphoryl compounds are known, including A) the early dehydrobromination method of 2-bromoethylphosphonate which was prepared from $(EtO)_3P$ and $BrCH_2CH_2Br$ under high temperatures, (a) Kosolapoff, G. M. *J. Am. Chem. Soc.* **1948**, *70*, 1971. B) Metal-catalyzed couplings of halides (ref. 10). Recently, C-O, C-S, C-CN etc. bonds can also be converted to C-P bonds *via* this coupling method. (b) Yang, J.; Chen, T.; Han, L.-B. *J. Am. Chem. Soc.* **2015**, *137*, 1782. (c) Yang, J.; Xiao, J.; Chen, T.; Han, L.-B. *J. Org. Chem.* **2016**, *81*, 3911. (d) Yang, J.; Xiao, J.; Chen, T.; Yin, S.-F.; Han, L.-B. *Chem. Commun.* **2016**, *52*, 12233. (e) Zhang, J.-S.; Chen, T.; Yang, J.; Han, L.-B. *Chem. Commun.* **2015**, *51*, 7540. C) Other methods such as the transformation of alkynylphosphonates etc. (f) Mulla, K.; Aleshire, K. L.; Forster, P. M.; Kang, J. Y. *J. Org. Chem.* **2016**, *81*, 77 and references cited therein.
(16) (a) Han, L.-B.; Tanaka, M. *J. Am. Chem. Soc.* **1996**, *118*, 1571. It seems that there are two early examples of metal-mediated P(O)−H additions to carbon−carbon unsaturated bonds before this work: a U.S. patent claimed the addition of $(RO)_2P(O)H$ to alkynes by $Ni(PR_3)_2X_2$ at elevated temperatures, see: (b) Lin, K. U.S. Patent 3681481, 1972. Hirao and coworkers also very briefly claimed in their paper, describing the coupling of $(RO)_2P(O)H$ with organic halides, that $(RO)_2P(O)H$ added to isoprene, though the efficiency was low (10% yield, 150 °C, 20 h), see ref. 10a.
(17) (a) Delacroix, O.; Gaumont, A. C. *Curr. Org. Chem.* **2005**, *9*, 1851. (b) Wicht, D. K.; Glueck, D. S. Hydrophosphination and related reactions. In *Catalytic heterofunctionalization*. Togni, A., Grützmacher H., Eds., Weinheim, Wiley-VCH, 2001, Chapter 5, pp 143-170. (c) Greenberg, S.; Stephan, D. W. *Chem. Soc. Rev.* **2008**, *37*, 1482; (d) Beletskaya, I. P.; Kabachnik, M. M. *Mendeleev Commun.* **2008**, *18*, 113. (e) Coundray, L.; Montchamp, J.-L. *Eur. J. Org. Chem.* **2008**, *2008*, 3601.
(18) (a) http://www.katayamakagaku.co.jp/products/chemicalproducts/flameretardant/index.html. (b) Henkelmann, J.; Klass, K; Arndt, J. Eur. Patent 1203773, 2002. http://www.basf.de/en/intermed/products/vinylphosphonicacid/. (c) http://www.euticals.com/attachments/article/11/Euticals_VPA_final.pdf.
(19) (a) Han, L.-B.; Hua, R.; Tanaka, M. *Angew. Chem. Int. Ed.* **1998**, *37*, 94. (b) Han, L.-B.; Zhao, C.-Q.; Onozawa, S.-y.; Goto, M.; Tanaka, M. *J. Am. Chem. Soc.* **2002**, *124*, 3842. (c) Han, L.-B.; Zhang, C.; Yazawa, H.; Shimada, S. *J. Am. Chem. Soc.* **2004**, *126*, 5080. (d) Han, L.-B.; Ono, Y.; Yazawa, H. *Org. Lett.* **2005**, *7*, 2909. (e) Han, L.-B.; Choi, N.; Tanaka, M. *Organometallics* **1996**, *15*, 3259. (f) Kanada, J.; Tanaka, M. *Adv. Synth. Catal.* **2011**, *353*, 890. (g) Xu, Q.; Shen, R.; Ono, Y.; Nagahata, R.; Shimada, S.; Goto, M.; Han, L.-B. *Chem. Commun.* **2011**, *47*, 2333.
(20) Part of this work was reported in 225th National Meeting of the American Chemical Society: L.-B. Han, Abstracts of Papers of the American Chemical Society, U148, New Orleans, Louisiana, Mar. 23-27, 2003.
(21) Stockland, Jr. et al has investigated the reductive elimination step for the formation of the C-P(O) bonds using C-Pd-P(O) complexes. (a) Kohler, M. C.; Grimes, T. V.; Wang, X.; Cundari, T. R.; Stockland, R. A. *Organometallics* **2009**, *28*, 1193. (b) Kohler, M. C.; Stockland, R. A.; Rath, N. P. *Organometallics* **2006**, *25*, 5746. (c) Stockland, R. A.; Levine, A. M.; Giovine, M. T.; Guzei, I. A.; Cannistra, J. C. *Organometallics* **2004**, *23*, 647. (d) Levine, A. M.; Stockland, R. A.; Clark, R.; Guzei, I. *Organometallics* **2002**, *21*, 3278. The reaction has also been studied by calculation etc. (e) Wang, T.; Sang, S.; Liu, L.; Qiao, H.; Gao, Y.; Zhao, Y. *J. Org. Chem.* **2014**, *79*, 608. (f) Ananikov, V. P.; Khemchyan, L. L.; Beletskaya, I. P.; Starikova, Z. A. *Adv. Synth. Catal.* **2010**, *352*, 2979. For the reductive elimination of Ar-Pd-P(O)$(OEt)_2$, an electron-poor aryl reacted slower than that of an electron-rich aryl group (ref 21a).
(22) Previous communications related to cat Pd/$(RO)_2P(O)H$/alkyne generating alkenylphosphonates: (i) first communicated with the $Me_2Pd(PPh_2Me)_2$ mediated addition of $(RO)_2P(O)H$ (R = Me, Et) (ref 16a). (ii) an oxapalladacycle-mediated addition to 1-octyne and *t*-butylacetylene (ref 19g). (iii) reactions with α,ω-diynes generating cyclopentenes: (a) Kanada, J.; Yamashita, K.; Nune, S.; Tanaka, M. *Tetrahedron Lett.* **2009**, *50*, 6196.
(23) For the preparation and properties of these palladium complexes, see: (a) Ozawa, F.; Ito, T.; Nakamura, Y.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1868. (b) Graaf, W. D.; Boersma, J.; Smeets, W. J. J.; Spek, A. L.; Koten, G. V. *Organometallics* **1989**, *8*, 2907.
(24) The starting materials (1-octyne, $(MeO)_2P(O)H$ and toluene) used in this reaction were all dried and freshly distilled.
(25) 1-Octyne, phenylacetylene and $(MeO)_2P(O)H$ were purchased from TCI. *Caution*: for safety concern, the use of the catalyst $Pd(OAc)_2$/dppp without solvent should be avoided with the reaction of an aromatic alkyne because the author (L-BH) had observed an

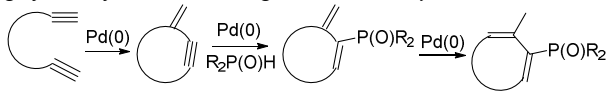
explosion when the reaction of phenylacetylene was carried out without solvent using $Pd(OAc)_2$/dppp as the catalyst. The reason was not clear. It was assumed that an explosive metal phenylacetylide was generated *via* the reaction of phenylacetylene with $Pd(OAc)_2$.

(26) Han, L.-B.; Ono, Y.; Xu, Q.; Shimada, S. *Bull. Chem. Soc. Jpn.* **2010**, *83*, 1086.

(27) This five-membered H-phosphonate was known to be more reactive than other $(RO)_2P(O)H$ compounds. For discussions, see, Han, L.-B.; Mirzaei, F.; Zhao, C.-Q.; Tanaka, M. *J. Am. Chem. Soc.* **2000**. *122*, 5407 and references cited therein.

(28) For Pd-catalyzed head-to-tail dimerization forming enynes, see: (a) Chen, T.; Guo, C.; Goto, M.; Han, L.-B. *Chem. Commun.* **2013**, *49*, 7498. (b) Trost, B. M.; Chan, C.; Ruther, G. *J. Am. Chem. Soc.* **1987**, *109*, 3486. (c) Trost, B. M.; Sorum, M. T.; Chan, C.; Harm, A. E.; Ruther, G. *J. Am. Chem. Soc.* **1997**, *119*, 698.

(29) We do not have evidences concerning the mechanism. However, as shown below, the terminal diyne may undergoes a similar intermolecular head-to-tail cyclization (see Scheme 8) generating an enyne **7**, which further reacts with $(MeO)_2P(O)H$ to give **8**. Isomerization of **8** by palladium would generate **6**. A Pd-catalyzed cyclization of aliphatic terminal diynes via intermolecular head-to-tail dimerization forming cyclic enynes, see: Lucking, U.; Pfaltz, A. *Synlett* **2000**, *9*, 1261.




**7** **8** **6**

(30) Because *t*-butylacetylene also gives the α-adduct as the major product (eq 6), this selectivity could not be simply due to steric reasons. The well-known feature that a silyl group stabilizes a α-anion and *β*-cation might contribute to this selectivity.

(31) Previous communications related to cat Pd/R´(RO)P(O)H/alkyne generating alkenylphosphinates: (i) first communicated by the $Me_2Pd(PPhMe_2)_2$ mediated addition of Ph(MenO)P(O)H (Men = menthyl) (ref 19b). (ii) an oxapalladacycle-mediated addition of Ph(EtO)P(O)H to 1-octyne and *t*-butylacetylene (ref 19g). (iii) $Pd(OAc)_2$/phosphine mediated additions: (a) Kumar, S.; Tanaka, M. *Chem. Commun.* **2007**, *50*, 2858.

(32) Previous communications related to cat Pd/RR´P(O)H/alkyne generating alkenylphosphine oxides: (i) first communicated with a $Pd(PPh_3)_4$ mediated addition of $Ph_2P(O)H$ (ref 19e). (ii) $Me_2Pd(PPhMe_2)$/$Ph_2P(O)OH$ mediated addition (ref 19a). (iii) an oxapalladacycle-mediated addition to 1-octyne, *t*-butylacetylene and diphenylacetylene (ref 19g). (iii) $Pd(OAc)_2$/phosphine mediated additions of $Ph_2P(O)H$ etc: Dobashi, N.; Fuse, K.; Hoshino, T.; Kanada, J.; Kashiwabara, T.; Kobata, C.; Tanaka, M. *Tetrahedron. Lett.* **2007**, *48*, 4669.

(33) Although $Pd(PPh_3)_4$ could catalyze the addition of $Ph_2P(O)H$ with terminal alkynes to give the *β*-adducts as the major products, these compounds were more conveniently prepared by the Rh-catalyzed P(O)-H additions which almost perfectly produce the *β*-adducts (ref 7f). A Cu-catalyzed addition also produces the *β*-adducts: Niu, M.; Fu, H.; Jiang, Y.; Zhao, Y. *Chem. Commun.* **2007**, 272.

(34) Previous communications related to cat Pd/$H_2P(O)(OH)$/alkyne generating hydrogen alkenylphosphinic acids: first communicated using a Pd/xantphos catalyst with 1-octyne, phenylacetylene, and 4-octyne: see: (a) Deprele, S.; Montchamp, J.-L. *J. Am. Chem. Soc.* **2002**, *124*, 9386. (b) Deprele, S.; Montchamp, J.-L. *Org. Lett.* **2004**, *6*, 3805.

(35) A separate experiment confirmed that the alkenylphosphoryl compounds can be reduced to the saturated **9**. $H_3PO_2$ is an efficient reductant, for transition metal-catalyzed transfer hydrogenation of unsaturated carbon-carbon bonds, see: (a) Guyon, C.; Metay, E.; Popowycz, F.; Lemaire, M. *Org. Biomol. Chem.* **2015**, *13*, 7879, and references therein. (b) Oliveira, M. C. F. *Appl. Catal. A: Gen.* **2007**, *329*, 7. (c) Kawasaki, T.; Tanaka, H.; Tsutsumi, T.; Kasahara, T.; Sato, I.; Soai, K. *J. Am. Chem. Soc.* **2006**, *128*, 6032.

(36) In contrast to *trans*-$[(MeO)_2P(O)]_2Pd(PEt_3)_2$, P-P couplings could not be clearly observed for *trans*-$[(MeO)_2P(O)]_2Pd(PPh_2Me)_2$, perhaps due to the weak ligating ability of $PPh_2Me$ that may dissociate from the complex in the solution. The combustion elemental analysis agrees with its composition.

(37) As confirmed separately, the possible isomerization between the *cis*- and *trans*-$Me_2Pd(PEt_3)_2$ in $C_6D_6$ is negligible under current conditions.

(38) Under similar conditions, in the absence of $(MeO)_2P(O)H$, *cis*-$Me_2Pd(PEt_3)_2$ is stable with water.

(39) The small germinal coupling between the two vinyl protons was not recognizable in the presence of a free $PEt_3$ due to rapid exchange reactions between the complex and $PEt_3$.

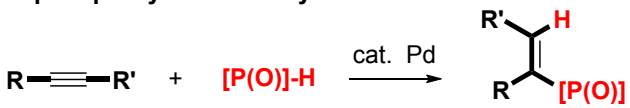
(40) For hydropalladation of carboxylic acids with the combination of $Pd(PEt_3)_4$ and alkynes, see: (a) Shen, R.; Chen, T.; Zhao, Y.; Qiu, R.; Zhou, Y.; Yin, S.; Wang, X.; Goto, M.; Han, L.-B. *J. Am. Chem. Soc.* **2011**, *133*, 17037. We noted that a protonation mechanism was proposed for the hydropalladation of Pd-alkyne complex with $Ph_2P(O)OH$ on the basis of DFT studies, see: (b) Zhang, H.; Bao, X. *RSC Adv.* **2015**, *5*, 84636. Although we do not have evidences excluding path b, its contribution should be small since it can hardly explain the high yields of the alkenylpalladium complexes *via* a long-time slow reaction, considering the rapid decomposition of the H-Pd complex (Scheme 14). Furthermore, the *regio*-selectivity of the hydropalladation is also similar to the reactions of carboxylic acids. Unfortunately, details on the insertion of an alkyne were not clear. We thank referees who suggested alternative mechanisms such as a nucleophilic addition of a hydride path. In addition, the alkyne path (path a) and the results of Scheme 7 would not be mutually exclusive considering an electron-poor alkyne coordinates easier with an alkyne.

(41) In a real sense, the results shown in Table 11 may only reflect the stability of complex **16**, because a reductive elimination required the isomerization of *trans*-**16** to *cis*-**16** or a dissociation of $PEt_3$ occurred first, that, unfortunately, was not available at this stage.

(42) Li, J.; Liu, L.; Fu, Y.; Guo, Q. *Tetrahedron* **2006**, *62*, 4453.

(43) This study was first conducted using $Pd(PEt_3)_4$. However, complicated results were obtained due to the rapid decomposition of the unstable Pd-H species.

**Hydrophosphorylation of alkynes**




**[P(O)]-H compounds:**

$(R'O)_2P(O)H$ $(R'O)(HO)P(O)H$ $(HO)_2P(O)H$ $R'R''P(O)H$

R' = Me, Et, $CH_2CF_3$, *i*-Pr, Bn, Bz, Ph

***H-phosphonic acids and esters***

***H-phosphine oxide***

$(R'O)R''P(O)H$ $(HO)R''P(O)H$

***H-phosphinic acid and esters***

$(HO)P(O)H_2$

***Hypophosphinic acid***