

Highly Selective Markovnikov Addition of Hypervalent *H*-Spirophosphoranes to Alkynes Mediated by Palladium Acetate: Generality and Mechanism

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Palladium acetate efficiently catalyzes the addition of an *H*-spirophosphorane (pinacolato)₂PH to alkynes to give Markovnikov addition products highly selectively. The addition products can be easily converted to the corresponding alkenylphosphonates and phosphonic acids via simple hydrolysis or thermal decomposition. This new reaction is a general method for the introduction of phosphorus functionality to the internal carbons of terminal alkynes, resolving the problem of the regioselectivity associated with hydrophosphorylation reactions so far reported. Mechanistic studies confirmed that (a) palladium acetate was reduced to metallic palladium by *H*-spirophosphorane, (b) the P–H bond of *H*-spirophosphorane could be activated by zero-valent platinum complexes to give the corresponding hydridoplatinum complexes, and (c) an alkenylpalladium species was identified from the reaction of palladium acetate with *H*-spirophosphorane and diphenylacetylene. These results support a reaction mechanism that palladium acetate was first reduced by *H*-spirophosphorane to give zero-valent palladium. This zero-valent palladium might insert into the P–H bond of the *H*-spirophosphorane to give a hydridopalladium species which then added to alkyne via the addition of H–Pd bond to form an alkenylpalladium species with the hydrogen atom added to the terminal carbon of alkynes. Reductive elimination of the alkenylpalladium affords the addition product.

Alkenylphosphinyl compounds (C=C–P(O)Z¹Z², where Z¹ and Z² represent an alkoxy, alkyl, or aryl group, respectively) are versatile synthetic reagents for the preparation of bidentate phosphorus ligands,¹ flame retardants, and polymers,² etc.³ For example, they are the key intermediates for the preparation of the clinically used antibacterial agent Fosfomycin ((1*R*,2*S*)-(1,2-epoxypropyl)phosphonic acid) and analogs.⁴ In addition to their synthetic applications, some alkenylphosphorus compounds also show interesting biological activity.⁵ Thus, alkenylphosphonates are potential enzyme inhibitors,⁶ and their strong antiproliferative activities were also discovered recently.⁷ A representative example of such compounds is Midafotel ((*R*)-4-[(2*E*)-3-phosphono-2-propenyl]-2-piperazine-carboxylic acid) which is a potent and competitive *N*-methyl-D-aspartate (NMDA) antagonist developed for the treatment of neurodegenerative diseases.⁸

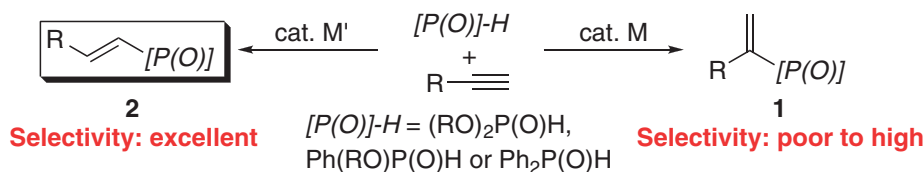
Although a few methods for the preparation of alkenylphosphinyl compounds are available,³ the transition-metal-mediated regio- and stereoselective addition of P(O)–H bonds to alkynes (hydrophosphorylation) initiated by us^{9,10} appears to be one of the most direct and efficient ways.^{9,11,12} Some alkenylphosphorus compounds are now commercially prepared by this method.¹³

As summarized in Scheme 1, by using a suitable catalyst, both the Markovnikov adduct **1** (catalysts: Me₂Pd(PPh₂Me)₂,⁹ Me₂Pd(PPhMe)₂/Ph₂P(O)OH,^{12c,12n} or Ni(PPhMe)₂/Ph₂P–O₂H¹²ⁱ) and the *anti*-Markovnikov regioisomer **2** (catalysts: Ni(PPh₂Me)₄,¹²ⁱ Pd(PPh₃)₄,^{12b} or RhCl(PPh₃)₃,^{12e}) have been prepared by the addition of the corresponding H–P(O) compound to an alkyne. However, whereas the addition reaction

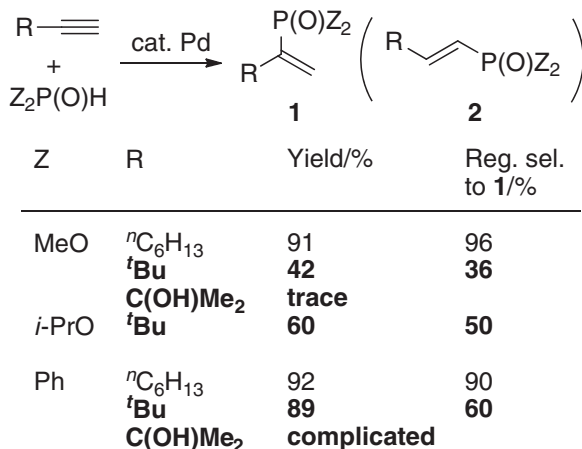
generating the *anti*-Markovnikov regioisomer **2** is general and the selectivity is excellent, the preparation of **1** is usually accompanied by the *anti*-Markovnikov regioisomer **2** which can even become the major product when bulky substrates are used. For example, although the PdMe₂(PPh₂Me)₂ catalyzed addition of hydrogen phosphonates to 1-octyne gave **1** with ca. 90%–96% regioselectivity,⁹ a similar addition to 3,3-dimethyl-1-butyne only proceeded sluggishly to give 42% yield of the adducts with 36% regioselectivity to **1**. A similar result was obtained when a catalyst^{11f} Pd₂(dba)₃/Ph₃P/CF₃CO₂H was employed (Scheme 2). On the other hand, the addition to 2-methyl-3-butyne-2-ol hardly proceeded. A similar phenomenon was observed in the addition of Ph₂P(O)H to alkynes. Thus by employing PdMe₂(PPhMe)₂/Ph₂PO₂H,^{12c,12n} Ph₂P(O)H added to 1-octyne to give the corresponding adduct **1** in 92% yield with 90% selectivity. However, under similar reaction conditions, the addition of Ph₂P(O)H to 3,3-dimethyl-1-butyne only gave **1** in 60% selectivity and the addition to 2-methyl-3-butyne-2-ol produced a complicated mixture. Therefore, the regioselectivity to **1** is highly substrate dependent and a general method for its preparation is required.

In addition to substrate limitations, the purification of the alkenylphosphorus products by conventional silica gel column chromatography techniques can be difficult, because of the structural similarity of alkenylphosphorus compounds with the phosphine oxide impurities, generated from the phosphine ligands of the catalysts via air oxidation.

In order to overcome these drawbacks of the current metal-mediated P(O)–H additions, studies on the development of a new general method for the preparation of the Markovnikov



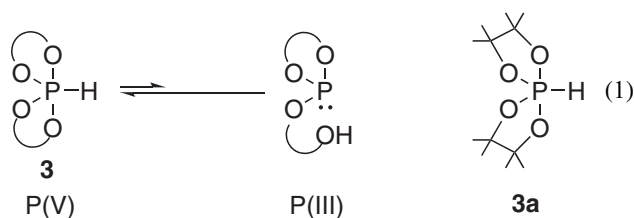
Scheme 1. Metal-mediated P(O)–H additions to alkynes forming alkenylphosphorus compounds.



Scheme 2. Strong substrate dependency of hydrophosphorylation reactions.

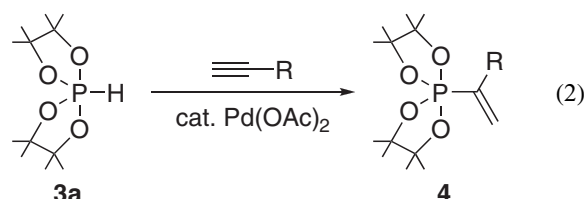
adduct **1** via a *phosphine-free* metal-catalyzed selective hydrophosphorylation of alkynes were carried out, which we believe, once achieved can complete the metal-mediated hydrophosphorylation of alkynes enabling the selective preparation of both isomers **1** and **2**.

Pentacoordinated *H*-spiroposphoranes **3** are easily prepared and handled.¹⁴ Although compound **3** was known three decades ago,^{14a} studies on its reactivity were unexplored. Thus, only a few Michael-type additions of these compounds were reported,^{14c} and no transition metal catalyzed transformations of **3** were known. Being similar to $(\text{RO})_2\text{P}(\text{O})\text{H}$, compound **3** can exist as a tautomeric mixture of P(V) and P(III) species with the latter being able to ligate the metal and thus can potentially deactivate the catalysts (eq 1).¹⁵ However, quite different from $(\text{RO})_2\text{P}(\text{O})\text{H}$, this equilibrium is easily affected by the substituents on **3**. In fact, it was known that **3a** bearing two pinacolato substituents solely exists in the P(V) form.¹⁶ Therefore, we surmised that because of this noteworthy feature (the absence of a lone electron pair on phosphorus and hence the inability of the P(V) form of **3** to coordinate a metal) different behaviors of **3a** from $(\text{RO})_2\text{P}(\text{O})\text{H}$ should be expected in the metal-catalyzed hydrophosphorylation reactions.



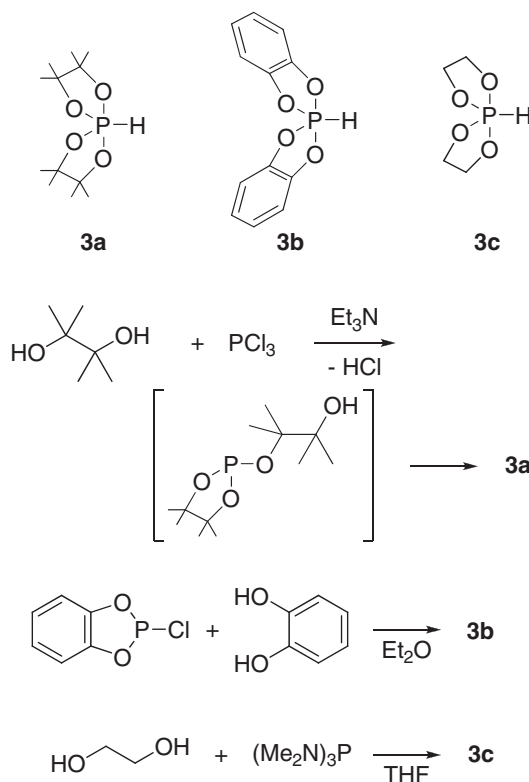
Herein we disclose the details of a *general* palladium-catalyzed addition of an *H*-spiroposphorane **3a** to alkynes leading to the Markovnikov adduct **4** in high yields (eq 2).¹⁷ To

the best of our knowledge such a metal-mediated addition reaction of **3** has never been reported.¹⁸



Results and Discussion

Preparation of 3. Hypervalent phosphorus compounds that contain P–C bonds are known as labile species and their synthetic procedures are usually complicated. On the other hand, $\lambda^5\delta^5$ phosphoranes built up with an oxo-spirocyclic skeleton are very easy to prepare and handle.¹⁴ They can be obtained by a simple reaction of PCl_3 with the corresponding diols. *H*-Spiroposphorane **3a** was prepared using a modified procedure of the literature,¹⁶ via a slow addition of PCl_3 to 2 molar equivalents of pinacol in Et_2O at 0°C in the presence of Et_3N (Scheme 3). A P(III) phosphite intermediate $(\text{CMe}_2\text{O})_2\text{-POCMe}_2\text{CMe}_2\text{OH}$ formed during the reaction isomerizes to the cyclic P(V) **3a** having a P–H bond. Thus, at 0°C , PCl_3



Scheme 3. Preparation of *H*-spiroposphoranes.

(0.05 mol) was added to a mixture of pinacol (0.1 mol) and triethylamine (0.15 mol) dissolved in dry ether (300 mL). The reaction mixture was stirred overnight at room temperature. The reaction mixture was washed with water and recrystallization of the crude product gave pure **3a** as a white solid in good yield (65%–75%). Spirophosphorane **3a** is stable toward air and water at ambient temperature, though it is hygroscopic. For the preparation of other *H*-spirophosphoranes using catechol and ethylene glycol, a modified method was used. Thus, **3b** was synthesized from catechol and 2-chloro-1,3,2-benzodioxaphosphole, while **3c** was prepared by a reaction of (Me₂N)₃P with ethylene glycol. These compounds are rather unstable toward water.

We also confirmed the result of Burgada by ³¹P NMR spectroscopy that **3a** exists exclusively in the P(V) form, while **3b** and **3c** exist as a mixture of P(V) and P(III) species in solution.¹⁶

Metal-Catalyzed Addition of **3** to 1-Octyne: Catalyst Screening and Optimization of the Reaction Conditions.

The addition of **3a** (0.25 mmol) to 1-octyne (0.25 mmol) was thoroughly investigated in toluene (0.5 mL) at 80 °C in the presence of a metal catalyst (10 mol %). As determined by ¹H and ³¹P NMR spectroscopy, the simple palladium acetate produced a quantitative yield of **4a** after 0.5 h with ≥96% regioselectivity. Other metals showing catalytic activity were as follows (catalyst, time/h, NMR yield of **4a**): Pd(PPh₃)₄, 4 (18) h, 18 (98)%; Pd₂(dba)₃, 18 h, 55%; Pd/Al₂O₃, 72 h, 54%; Pd(OCOPh)₂, 2 h, 88%; Pd(NO₃)₂, 2 h, 67%. However, metal-complexes such as PdCl₂, PdBr₂, PdSO₄, Pd(acac)₂, PdCl₂(PhCN)₂, PdCl₂(PPh₃)₂, PdCl₂(P-*i*-Pr)₂, PdCl₂(dppe), PdCl₂(dppb), (η³-C₃H₅PdCl)₂, NiCl₂, NiCl₂(PPh₃)₂, Ni(PR₃)₄ (PR₃ = PPh₃, PPh₂Me, and PPhMe₂), Ni(cod)₂, RhCl(PPh₃)₃, and [Rh(cod)Cl]₂ either gave a complicated result or did not catalyze the addition at all. These results clearly demonstrated a different chemical behavior of **3a** from the 4-coordinate (RO)₂P(O)H. For example, Pd(OAc)₂ did not catalyze a similar addition of (MeO)₂P(O)H,⁹ whereas Ni(PR₃)₄ which can efficiently catalyze the addition of (MeO)₂P(O)H¹²ⁱ did not show catalytic activity with **3a**.

This Pd(OAc)₂-mediated addition was optimized (Table 1). Thus, under nitrogen, by using 3 mol % of Pd(OAc)₂ (Run 1), 95% yield of **4a** was generated after heating **3a** and an equivalent amount of 1-octyne dissolved in toluene for 2 h. Interestingly, this Pd(OAc)₂-catalyzed addition can be conducted without the pre-exclusion of air. For example, the Pd(OAc)₂-catalyzed addition of **3a** to 1-octyne conducted under air also gave 93% yield of **4a** (Run 2). The addition of water lowered the yield of **4a** (Run 3), whereas additives such as Et₃N (Run 4) and Ph₃P (Run 5) did not significantly affect the reaction. However, the addition of Et₃P could completely stop the catalytic addition (Run 6). The amount of Pd(OAc)₂-catalyst used could be reduced, albeit a longer reaction time was required. For example, the reaction with 0.5 mol % Pd(OAc)₂ gave 71% yield of **4a** after 14 h (Run 7). Trifluoroacetate palladium also catalyzed the reaction, which also proceeded under air, though a considerable amount of **5a** was observed due to the hydrolysis of **4a** (vide infra) (Runs 8 and 9).

Scope and Limitations. As demonstrated in Table 2, this is a highly general regioselective addition reaction which is

Table 1. Optimization of the Addition of **3a** to 1-Octyne Forming **4a**^{a)}

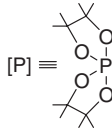
Run	Catalyst (mol %)	Time/h	Yield/(% ^{b)})
1	Pd(OAc) ₂ (3)	2	95
2 ^{c)}	Pd(OAc) ₂ (3)	2	93
3	Pd(OAc) ₂ (3)/H ₂ O (10)	2	45
4	Pd(OAc) ₂ (3)/Et ₃ N (6)	2	75
5	Pd(OAc) ₂ (3)/Ph ₃ P (6)	2	88
6	Pd(OAc) ₂ (3)/Et ₃ P (6)	16	0
7	Pd(OAc) ₂ (0.5)	14	71
8	Pd(OCOCF ₃) ₂ (3)	2	96 ^{d)}
9 ^{c),e)}	Pd(OCOCF ₃) ₂ (0.1)	14	88 ^{f)}

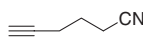
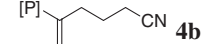
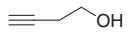
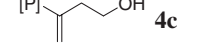
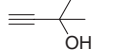
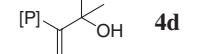
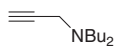
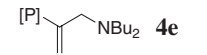
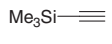
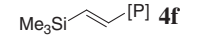
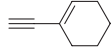
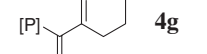
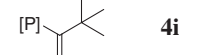
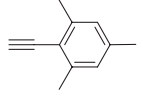
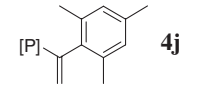
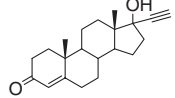
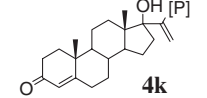
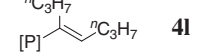
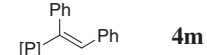
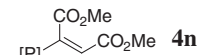
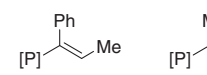
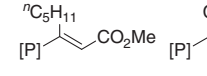
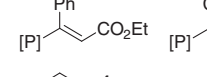
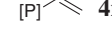
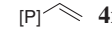
a) Reactions were carried out using **3a** (0.25 mmol) and 1-octyne (0.25 mmol) with palladium catalyst in toluene (0.5 mL) at 80 °C under nitrogen. b) Yields were determined by ³¹P NMR spectroscopy. c) Reaction was carried out under air. d) **4a**/**5a** = 78/22. e) In the absence of a solvent. f) **4a**/**5a** = 89/11.

applicable to a variety of alkynes bearing functionalities. Thus, as shown by Runs 1–6, the reaction of **3a** with alkynes having cyano, hydroxy, amino, silyl,¹⁹ or alkenyl groups smoothly proceeded to produce good yields of the adduct **4** with excellent regioselectivity. Aromatic acetylenes such as phenylacetylene also gave 86% yield of the corresponding adduct selectively (Run 7). The results with bulky alkynes are particularly noteworthy. Thus, an excellent regioselectivity and high yields of the adducts were obtained from 3,3-dimethyl-1-butyne (Run 8), 2-methyl-3-butyne-2-ol (Run 3), mesitylacetylene (Run 9), and the biologically active ethisterone (Run 10). It was reminded that similar reactions of these bulky alkynes with (RO)₂P(O)H hardly proceeded to produce a mixture of terminal and internal adducts in low regioselectivity (vide supra). Not only terminal alkynes, this addition also took place efficiently with internal alkynes to give the *trans*-adducts selectively. Thus, both dialkyl (Run 11) and diphenyl (Run 12) acetylenes successfully gave the corresponding adducts in high yields and selectivity. An alkyne with two electron-withdrawing methoxycarbonyl groups also afforded the corresponding adduct efficiently (Run 13). Finally, the reaction of **3a** with an atmosphere of industry-grade acetylene gas²⁰ in the presence of 0.3–1 mol % of Pd(OAc)₂ produced the corresponding vinyl-spirophosphorane **4r** in nearly a quantitative yield (Runs 17 and 18).

From unsymmetrical alkynes, good regioselectivities, following the Markovnikov rule, could be observed when the two substituents are substantially electronically different. Thus, methyl 2-octynoate (Run 15) and ethyl 3-phenylpropiolate (Run 16) gave a mixture of **4p**/**4p'** and **4q**/**4q'** in 86% and 81% yields, respectively. In both cases, isomers with phosphorus attached to the side of the less electron-withdrawing substituent were predominantly formed. On the other hand, the

Table 2. Pd(OAc)₂-Mediated Addition of **3a** with Alkynes^{a)}

$$\mathbf{3a} + \text{R}^1\text{—}\equiv\text{R}^2 \xrightarrow[\text{toluene, 80 } ^\circ\text{C}]{3 \text{ mol\% Pd(OAc)}_2} [\text{P}]\text{—}\text{C}(\text{R}^1)=\text{C}(\text{R}^2) \quad \mathbf{4}$$


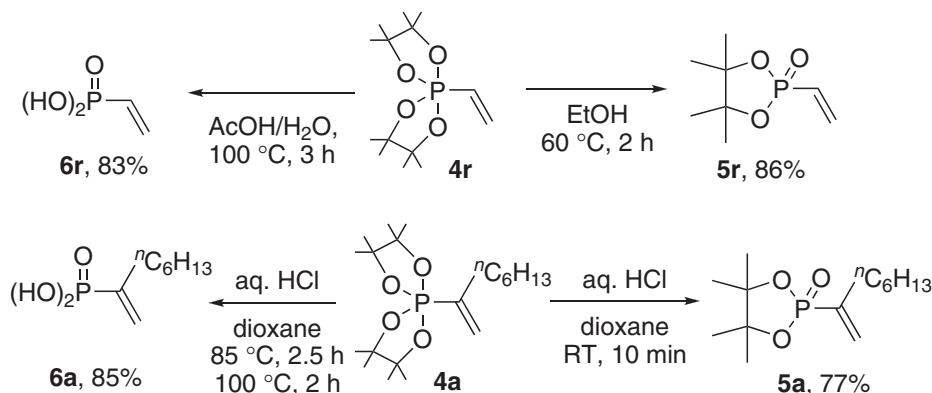
Run	Alkyne	Time/h	Product	Yield/% ^{b)}
1		2	 4b	83 (84)
2		4	 4c	73 (79)
3		5	 4d	73 (78)
4		4	 4e	73 (79)
5 ^{c),d)}		2	 4f	74 (90)
6		8	 4g	76 (76)
7 ^{c)}		4	 4h	86 (86)
8		4	 4i	88 (91)
9		4	 4j	91 (91)
10 ^{e)}		7	 4k	84 ^{d)} (84)
11	$n\text{C}_3\text{H}_7\text{—}\equiv\text{—}n\text{C}_3\text{H}_7$	1	 4l	95 (97)
12	$\text{Ph—}\equiv\text{—Ph}$	2	 4m	95 (95)
13	$\text{MeO}_2\text{C—}\equiv\text{—CO}_2\text{Me}$	2	 4n	91 (91)
14	$\text{Ph—}\equiv\text{—Me}$	2	 4o/4o' (48/52)	95 (98)
15	$n\text{C}_5\text{H}_{11}\text{—}\equiv\text{—CO}_2\text{Me}$	22	 4p/4p' (90/10)	86 (95)
16	$\text{Ph—}\equiv\text{—CO}_2\text{Et}$	9	 4q/4q' (88/12)	81 (92)
17 ^{e),f)}		1.5	 4r	94 (100)
18 ^{e),g)}		16	 4r	98 (100)

a) Reactions were carried out by heating a toluene solution (0.5 M) of an equimolar ratio of **3a** and an alkyne in the presence of 3 mol % Pd(OAc)₂. Regioselectivity for terminal alkynes $\geq 96\%$. Only *trans*-adduct was obtained for internal alkynes. b) Isolated yields (those in parentheses refer to NMR yields). c) Ph₂P(O)OH (1–6 mol %) was added. d) Only *trans*-adduct was obtained.¹⁹ e) Under 1 atm acetylene gas atmosphere. f) 1 mol % Pd(OAc)₂. g) 0.3 mol % Pd(OAc)₂.

addition of **3a** to 1-propynylbenzene (Run 14) gave an almost equimolar mixture of the two regioisomers **4o/4o'**.

In sharp contrast to the high reactivity of alkynes, alkenes such as 1-octene, acrylonitrile, styrene, and α -ethylstyrene did

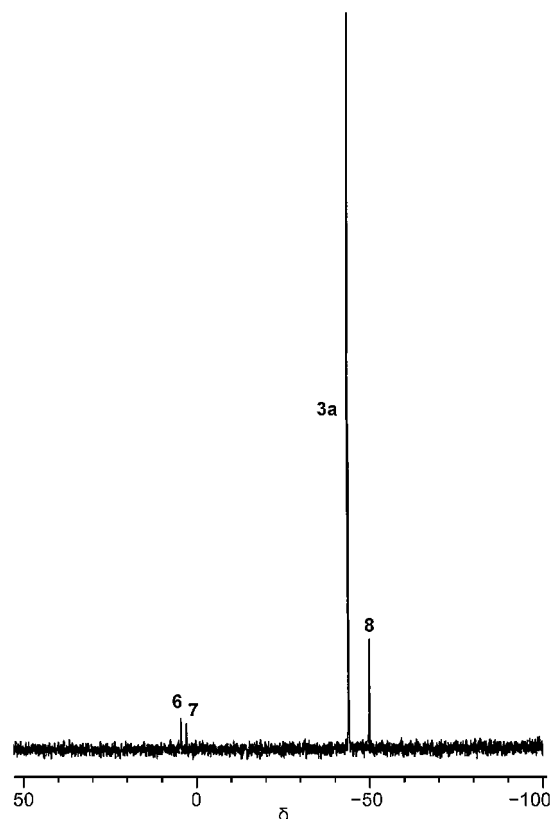
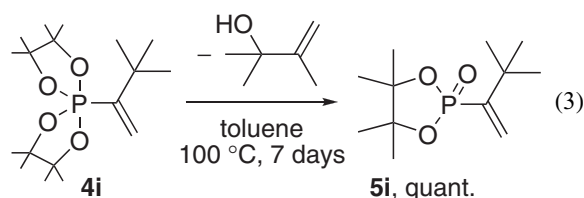
not react with **3a** under similar reaction conditions. In addition, a remarkable difference in reactivity between **3a** with **3b** (**3c**) was observed. Thus, although *H*-spirophosphorane **3a** efficiently reacts with a variety of alkynes to give the addition

Scheme 4. Easy conversion of **4** to alkenylphosphonates.

products, no addition products are obtained at all with *H*-spiroposphoranes **3b** and **3c** under similar reaction conditions even after heating at 80 °C for 24 h. The structural difference mentioned above that **3a** takes the P(V) form while **3b** (**3c**) exists as a mixture of P(V) and P(III) tautomers,¹⁶ was assumed to be the first reason for this big difference in reactivity.

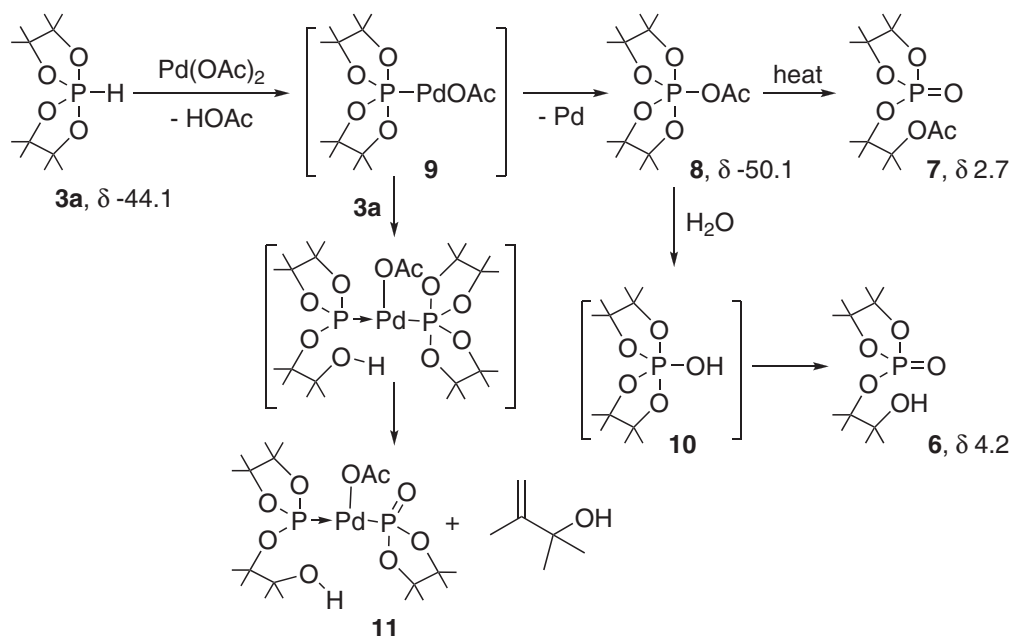
Hydrolysis and Thermal Decomposition of Alkenylspiroposphoranes **4 to Phosphonate Derivatives.** Though compound **4** is stable toward moisture and air at room temperature, the spiro ring collapses smoothly at an elevated temperature or in the presence of an acid to give the corresponding phosphonate derivatives. Thus, heating **4r** in EtOH at 60 °C for 2 h produced 1,3-dioxo-2-phosphorane 2-oxide derivative **5r** in 86% yield (Scheme 4). If the reaction is conducted in an acidic medium **4r** can be further hydrolyzed to give the corresponding vinylphosphonic acid. For example, after heating **4r** in a 1:1 mixture of AcOH/H₂O at 100 °C for 3 h, vinylphosphonic acid was obtained in 83% yield. The hydrolysis can be carried out stepwise under acidic conditions. Similarly, with hydrochloric acid, alkenylspiroposphorane **4a** produced phosphonate **5a** in 77% yield at room temperature, and produced 85% yield of alkenylphosphonic acid **6a** on heating.

A bulky substituent in **4** accelerates this hydrolysis. Thus, although other alkenylspiroposphoranes **4** are stable toward purification on silica gel, **4i** with a *tert*-butyl group was completely converted to 1,3-dioxo-2-phosphorane **5i** when being stirred with silica gel in hexane at room temperature for 0.5 h. Interestingly, although in the absence of an acid and water no decomposition of **4i** took place at 80 °C, a simple thermal decomposition of **4i** to **5i** takes place at an elevated temperature (eq 3). Thus, heating **4i** in toluene at 100 °C for 3 days could generate **5i** in 62% yield (a quantitative amount of **5i** was obtained after 7 days). The formation of the counterpart 2,3-dimethyl-3-buten-2-ol during this thermal decomposition could be confirmed by ¹H NMR spectrum (ca. 87% NMR yield).

Chart 1. ³¹P NMR chart of a reaction mixture of Pd(OAc)₂ with **3a** in THF-*d*₈ at 25 °C overnight.

Hydrolysis of an alkylspiroposphorane with water affording the corresponding alkylphosphonate was briefly described by Burgada in the literature.²¹ However, such a thermal decomposition of **4i** generating **5i** seems to have not been recognized before.

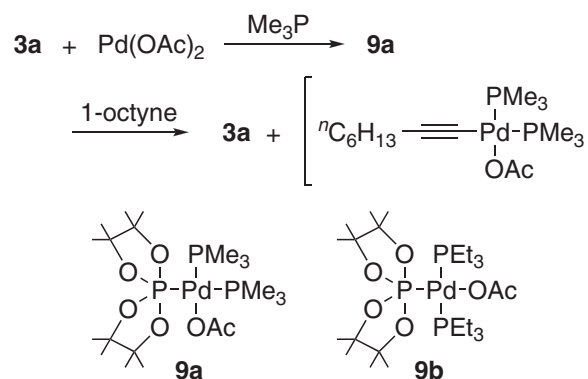
Reaction of Pd(OAc)₂ and Pd(OCOCF₃)₂ with **3a.** A mixture of Pd(OAc)₂ (0.1 mmol) and **3a** (0.1 mmol) dissolved in THF-*d*₈ (0.5 mL) produced a brown transparent solution. However, after 2 h at room temperature, no other signals except that for **3a** (δ −44.1) could be detected by ³¹P NMR spectroscopy. Significant changes were observed after standing the solution overnight, i.e., metallic palladium came out from the solution and several new signals were detected by ³¹P NMR spectroscopy (³¹P integration ratios: **6**/**7**/**3a**/**8** = 0.5/0.2/10/

Scheme 5. Reduction of palladium acetate by **3a**.

1.4) (Chart 1). As expected, heating the solution at 50 °C accelerated this process (20 min: **6/7/3a/8** = 0.12/0.12/1/0.3 and 3 h: **6/7/3a/8** = 0.29/1.22/1/0.93). Similar results were observed when excess **3a** was used ($\text{Pd}(\text{OAc})_2/\mathbf{3a} = 1/2$) except more starting material **3a** remained unreacted. The reaction proceeded faster in toluene: metallic palladium came out from the initially brown transparent solution after 0.5 h and the reaction almost completed after 3 h (**6/7/3a/8** = 4.6/0.2/1/7). Compounds corresponding to δ 2.74 and δ 4.28 were successfully isolated from the reaction mixture and were identified as phosphates **7** and **6**. The compound corresponding to δ -50.1 could not be isolated in pure form because it gradually decomposed at room temperature to **6** and **7** (vide infra). As shown below, filtration and evaporation of the above reaction mixture in toluene gave a yellow oil containing **6**, **7**, and **8** with a ratio, initially **6/7/8** = 0.5/0.2/1, and then became to **6/7/8** = 2.4/2.4/1 after 1 h at room temperature. No other signals except those for **6**, **7**, and **8** could be detected. However, no deposition of metallic palladium was observed from this mixture even on heating at 100 °C for 1 h, indicating that **8** is not a palladium-containing species. On the other hand, as judging from its ^{31}P NMR chemical shift, compound **8** should have a similar spiro structure to compound **3a**.

These results agreed with a two-step reaction sequence in which compound **8** was first generated, and it decomposed subsequently to give **6** and **7**. Thus, the reaction of **3a** with $\text{Pd}(\text{OAc})_2$ was rationalized as follows: **3a** reacted with $\text{Pd}(\text{OAc})_2$ to give **9** with the liberation of acetic acid (the formation of AcOH could be identified by ^1H NMR); **9** subsequently decomposed, formally via a reductive elimination pathway, to give **8** and liberate metallic Pd. This spirophosphorus compound **8** collapsed to **7** or **6** via hydrolysis with water.²²

In addition to the above phosphorus compounds, tiny signals displayed at ^{31}P NMR at 99.7 ppm (dd, $J_{\text{PP}} = 90.2$ Hz) and 50.3 (dd, $J_{\text{PP}} = 99.2$ Hz) (ca. 2% of all phosphorus compounds as

Scheme 6. Trapping the intermediate **9** by a phosphine ligand.

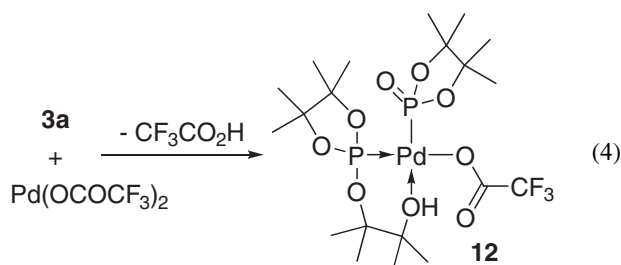
estimated from ^{31}P NMR) could also be observed. Although this complex has not been isolated, as described below (the reaction of **3a** with $(\text{CF}_3\text{CO}_2)_2\text{Pd}$), it is reasonable to assume it has a structure depicted as **11** by comparing to a similar complex generated from **3a** with $(\text{CF}_3\text{CO}_2)_2\text{Pd}$ which was unambiguously established by an X-ray analysis.

Although palladium complex **9** could not be isolated, complex **9a** and **9b** stabilized by a phosphine ligand were successfully isolated (Scheme 6), supporting the mechanism proposed in Scheme 5. A high yield of complex **9a** was isolated from a reaction of **3a** with $\text{Pd}(\text{OAc})_2$ in the presence of Me_3P . Thus, a mixture of **3a**, $\text{Pd}(\text{OAc})_2$, and PMe_3 (**3a**/ Pd / $\text{PMe}_3 = 1/1/3$) in THF at room temperature gave a transparent yellow solution, in which a new complex **9a** was formed. ^{31}P NMR showed that the reaction completed after 4 h and complex **9a** having a *cis*-structure was generated quantitatively. THF and other volatiles were removed under reduced pressure to obtain the crude complex **9a**. By recrystallization from pentane pure **9a** was obtained as a white solid in 82% yield. Similarly was prepared complex **9b** by a reaction of **3a** with

$\text{Pd}(\text{OAc})_2$ in the presence of Et_3P . In contrast with **9**, the phosphine-ligated complex **9a** is thermally stable at 80 °C in toluene or THF under nitrogen, and no decomposition could be observed after heating for 20 h. However, it completely decomposed at elevated temperature (0.05 M in toluene, 110 °C, 3 h) or when exposed to air at room temperature for 2 h.

Heating a mixture of **9a** with 1-octyne in toluene at 80 °C for 2 h resulted in the complete disappearance of the complex. However, the reaction did not produce the addition product **4a** but afforded **3a** via, formally, a protonolysis of **9a** with 1-octyne.

In contrast to the above reaction of **3a** with $\text{Pd}(\text{OAc})_2$, a similar reaction with $(\text{CF}_3\text{CO}_2)_2\text{Pd}$ did not produce metallic palladium, but gave colorless needles of **12** in high yields. Thus, $(\text{CF}_3\text{CO}_2)_2\text{Pd}$ (0.5 mmol) and **3a** (1.0 mmol) dissolved in CH_2Cl_2 was mixed at room temperature. The resulting pale yellow suspension was stirred until solid was dissolved (ca. 24 h). Removal of the solvent followed by recrystallization of the residue from CH_2Cl_2 gave complex **12** as white crystals in 83% yield (eq 4). The structure of complex **12** was determined by X-ray crystallography (Figure 1).²³ The complex has a square-planar configuration surrounding Pd. The bond length of P2–O7 is 1.483(2) Å, which is a typical value for P=O bond rather than a value for a single P–O bond.²⁴ Therefore, the structure for **12** is depicted as shown below where the spiro ring of O–P bond was cleft to a P(III) phosphite species bearing an OH group. The phosphorus atom of the phosphite and the oxygen atom of the OH group coordinate to the Pd(II) center.



The exact pathway for the formation of **12** is not clear (Scheme 7). It is reasonable to assume that a palladium species **9'** was generated first by a similar protonolysis observed for the reaction of **3a** with $\text{Pd}(\text{OAc})_2$ (Scheme 5). Since hydrogen

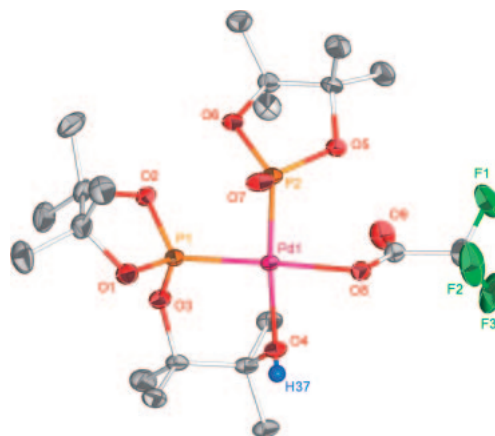
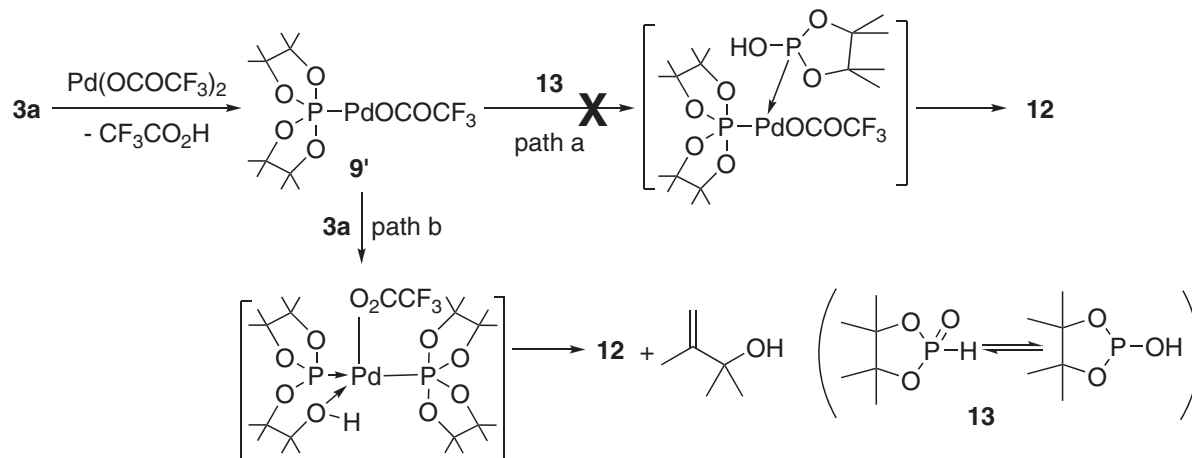
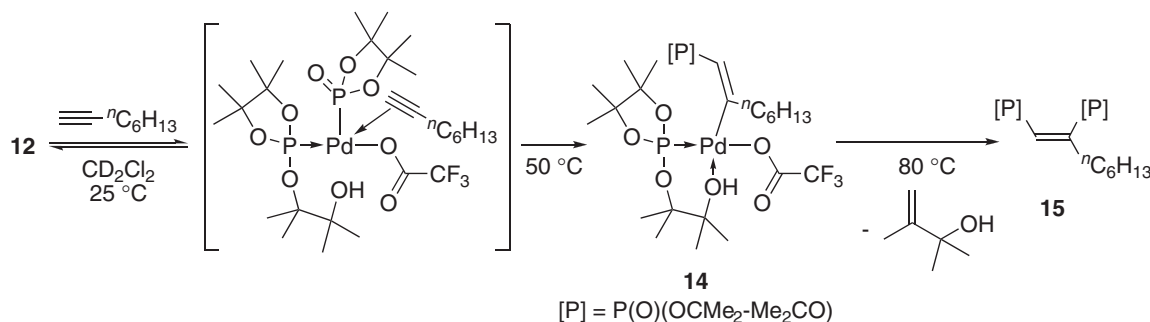


Figure 1. Molecular structure of complex **12** (50% probability level). Hydrogen atoms bound to carbons are omitted for clarity. Selected bond lengths (Å) and angles (°): P2–O7 = 1.483(2), Pd–P1 = 2.1869(6), Pd–P2 = 2.2211(6), Pd–O4 = 2.1313(2), Pd–O8 = 2.0881(2), P1–Pd–P2 = 94.76(2), P1–Pd–O4 = 90.90(5), P2–Pd–O8 = 86.87(5), O4–Pd–O8 = 87.42(7).

phosphonate **13** could be generated by the hydrolysis of **3a**,¹⁴ a reaction path a in which **13** coordinates to **9'** via the phosphite form¹⁵ might be proposed. However, as described below, this possibility seems low since **13** could not be detected during the reaction. Thus, as shown by ^{31}P NMR spectroscopy, no detectable five-membered P–H compound **13** could be found during the reaction, and when an extra amount of **3a** was used in the reactions, it remained unchanged, i.e., **3a** does not decompose to **13** under the present conditions. A separate experiment using a mixture of **3a** and 5 mol % $(\text{CF}_3\text{CO}_2)_2\text{Pd}$ in toluene also showed that no **13** was formed at room temperature for 24 h. As confirmed by ^{31}P NMR spectroscopy, no reaction took place between **3a** and $(\text{CF}_3\text{CO}_2)_2\text{Pd}$ at –30 °C for 2 h. The reaction slowly proceeded at 0 °C to produce a trace amount of **12** after 1 h as the only product detectable by ^{31}P NMR spectroscopy. On the other hand, the formation of 2,3-dimethyl-3-buten-2-ol was confirmed by ^1H NMR spectroscopy. Therefore, the formation of **12** may take place via the coordination of **3a**¹⁸ to **9'** which collapsed to give **12** (path b).



Scheme 7. Reaction of **3a** with $(\text{CF}_3\text{CO}_2)_2\text{Pd}$ leading to **12**.



Scheme 8.

Complex **12** catalyzed the addition of **3a** to 1-octyne to produce adducts **4a** and **5a** as efficiently as $(\text{CF}_3\text{CO}_2)_2\text{Pd}$ (3 mol % Pd catalyst, toluene, 80°C , 6 h. Complex **12**: 79% **4a**, 16% **5a** and $\text{Pd}(\text{OCOCF}_3)_2$: 75% **4a**, 21% **5a**). However, being similar to $\text{Pd}(\text{OCOCF}_3)_2$, it does not catalyze the addition of $(\text{MeO})_2\text{P}(\text{O})\text{H}$ to 1-octyne and only sluggishly catalyzed the addition of the more reactive five-membered P–H compound **13** to produce a trace amount of the corresponding adduct (ca. 3% yield). This fact can be an indication that the formation of the five-membered adduct **5a** obtained from the addition of **3a** to 1-octyne is not due to a simple addition of **13** to alkyne, but due to other paths such as the protonolysis of the adduct **4a**.

Nevertheless, as described below, complex **12** is apparently not the real catalyst for the formation of adducts **4a** and **5a**. Complex **12** reacted with 1-octyne to give quantitatively a new complex **14** via a *cis*-insertion of the Pd–P(O) bond of **12** to 1-octyne with P(O) bonding to the terminal carbon and Pd bonding to the internal carbon, showing that the reaction of **12** with 1-octyne could not lead to adducts **4a** and **5a**. Thus, 1-octyne (1.9 mg, 0.017 mmol) was added to a suspension of **12** (4.4 mg, 0.007 mmol) in CD_2Cl_2 (0.5 mL) in an NMR tube. The suspension turned clear upon standing at room temperature for 1 h, and a new compound was formed as confirmed by ^{31}P NMR spectroscopy (δ 55.6 (d, $J = 79$ Hz) and 100.0 (d, $J = 79$ Hz), which was assumed to be an alkyne-coordinated complex (ratio to **12** = 66/34) (Scheme 8). The ratio of **12** to the new complex did not change upon further standing for 4 h, indicating that the reaction reached equilibrium. However, interestingly, when this solution was heated to 50°C , a new complex **14** was formed quantitatively. The structure of complex **14** was unambiguously determined by X-ray crystallography (Figure 2).

Heating **14** at 80°C for 36 h in CD_2Cl_2 in a sealed tube resulted in the formation of bisphosphinylalkene **15** in 75% yield accompanied by the generation of 81% yield of 2,3-dimethyl-3-buten-2-ol as determined by ^1H NMR spectroscopy.

Reactions of $\text{Pd}(\text{OAc})_2$ with **3a in the Presence of an Alkyne: Determining the Real Catalysts.** In order to determine the real catalysts in this palladium acetate-mediated additions of **3a** to alkynes, a similar reaction to Scheme 5 in the presence of an alkyne (molar ratios of $\text{Pd}(\text{OAc})_2/\mathbf{3a}/\text{alkyne} = 1/1/1$ to $1/4/4$) was conducted and the reaction was monitored by ^1H and ^{31}P NMR spectroscopies. The following five alkynes were used as substrates: 1-octyne, $\text{CH}_2=\text{C}(\text{Me})\text{C}\equiv\text{CH}$, 4-octyne, $\text{MeO}_2\text{C}\equiv\text{CCO}_2\text{Me}$, and $\text{PhC}\equiv\text{CPh}$. As indicated by ^1H and ^{31}P NMR spectra, in all cases, consumption of the

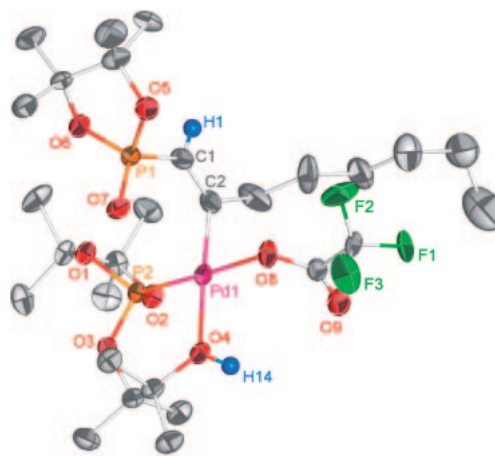
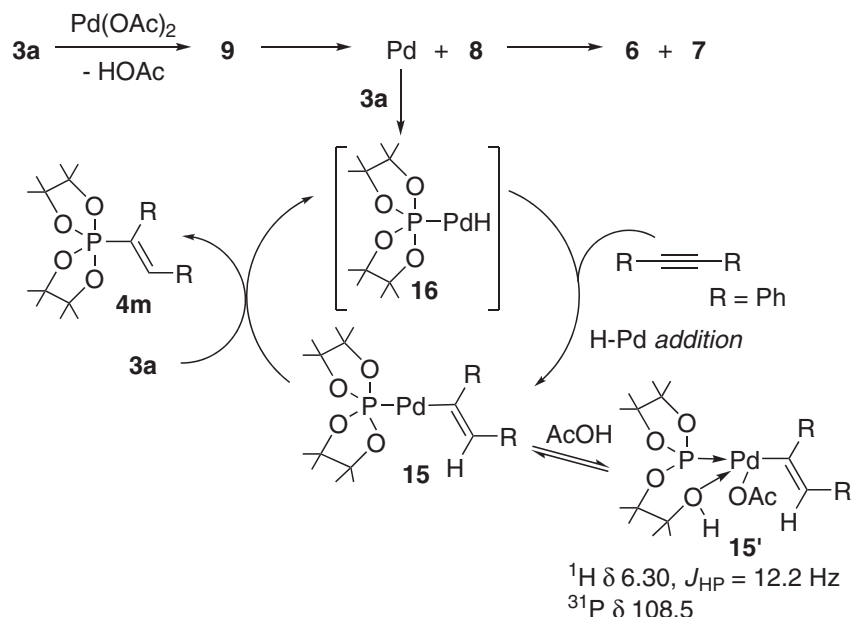
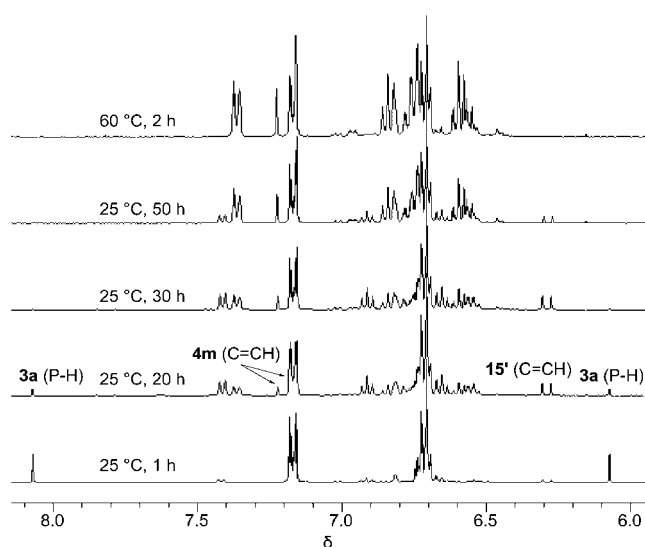
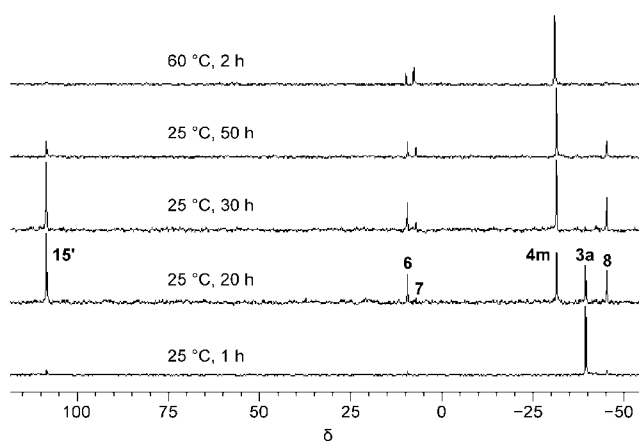


Figure 2. Molecular structure of complex **14** (40% probability level). Hydrogen atoms except the vinyl proton are omitted for clarity. Selected bond lengths (Å) and angles (°): P1–O7 = 1.467(3), P2–O1 = 1.583(7), Pd–P2 = 2.717(11), Pd–C2 = 1.977(5), Pd–O4 = 2.150(3), Pd–O8 = 2.110(3), P2–Pd–C2 = 88.57(15), P2–Pd–O4 = 94.46(8), C2–Pd–O8 = 89.04(18), O4–Pd–O8 = 87.92(13).

starting materials **3a** and alkyne was observed at room temperature to produce a transparent solution, where, in sharp contrast to reactions in the absence of an alkyne, no decomposition to metallic palladium was observed after 20 h. Although no valuable information on the possible reactive catalytic species was obtained with the former three alkynes, fortunately, an alkenylpalladium species **15'** (see below for its structure assignment) was clearly observed with $\text{MeO}_2\text{C}\equiv\text{CCO}_2\text{Me}$ and $\text{PhC}\equiv\text{CPh}$ (Scheme 9). Thus, at room temperature, a mixture of $\text{Pd}(\text{OAc})_2$, **3a**, and diphenylacetylene (0.02 mmol for each substrate) was dissolved in 0.5 mL toluene- d_8 to get a pale yellow transparent solution (Charts 2 and 3). As shown in Chart 2, in ^1H NMR, a doublet was observed at δ 6.30 ($J_{\text{HP}} = 12.2$ Hz), assignable to an alkenylpalladium species **15'** (see below for its assignment), which increased as the reaction progressed for 30 h. Formation of the addition product **4m** was also observed (a doublet at δ 7.21) which increased constantly. The solution remained transparent during these times. Noted however, as **3a** was completely consumed after ca. 50 h, precipitation of metallic palladium was observed, and the doublet at δ 6.30 also gradually disappeared. Upon heating the solution at 60°C for 2 h, complex **15'** completely

Scheme 9. Reaction of Pd(OAc)₂ with **3a** and diphenylacetylene.Chart 2. Time course of ¹H NMR spectra for a mixture of Pd(OAc)₂, **3a**, and diphenylacetylene in toluene-*d*₈.

disappeared to leave the addition product **4m** as the sole product. In agreement with ¹H NMR spectroscopy, similar phenomena were observed with ³¹P NMR spectroscopy (Chart 3). The signal at δ 108.5 was due to **15'**, others signals could be assigned to **6**, **7**, **4m**, **3a**, and **8**, respectively. As the reaction progressed, **15'** gradually increased, however, as **3a** was completely consumed after 30 h, **15'** decreased to deposit metallic palladium and afforded the adduct **4m** (amounts (μmol) of **15'** and **4m**) calculated on the basis of ³¹P NMR (time, **15'**, **4m**): 1 h: **15'**, trace; **4m**, trace. 20 h: **15'**, 7.1; **4m**, 4.6. 30 h: **15'**, 7.3; **4m**, 6.3. 50 h: **15'**, 2.0; **4m**, 11). As estimated from ¹H NMR spectroscopy, 29% of Pd(OAc)₂, 74% of PhC $\equiv$ CPh, and 100% **3a** were consumed, respectively, and ca. 70% yield of the adduct **4m** was generated from the above reaction after heating at 60 °C. Similar results were also

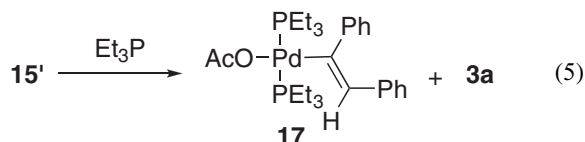
Chart 3. Time course of ³¹P NMR spectra for a mixture of Pd(OAc)₂, **3a**, and diphenylacetylene in toluene-*d*₈.

obtained from ³¹P NMR spectroscopy (73% yield of **4m**, a total yield of 23% for compounds **6** and **7** (**6/7** = 1/2)).

These results very well reflect a reaction process shown in Scheme 9: Pd(OAc)₂ was reduced by **3a** to generate zero-valent palladium and **8** (which subsequently decomposed to **6** and **7**); this palladium reacted with **3a** and PhC $\equiv$ CPh to afford the adduct **4m** via an alkenylpalladium intermediate **15**, which was assumed to be generated through an H-Pd addition of an hydridopalladium species **16**. This complex **16** could be formed via an oxidative addition of **3a** to palladium. Although direct evidence for its formation was not available, as described below a similar oxidative addition of **3a** to Pt(PEt₃)_n did take place to give the corresponding hydridoplatinum species (eq 6), which supports this possibility.

As described above, an alkenylpalladium species assigned to **15'** was observed by NMR spectroscopies. The structural assignment was based on the following observations. First, its ³¹P signal appeared in the low magnetic field at δ 108.5

indicating that this alkenylpalladium intermediate has a structure of **15'** where a phosphite ligates to Pd rather than a spirophosphane configuration as shown in complexes **15** and **16**. The isolation of this alkenylpalladium was not successful due to its decomposition at room temperature. However, it was trapped with Et₃P to give an alkenylpalladium complex **17** and **3a** (eq 5). The successful isolation of complex **17** from a mixture of complexes shown in Scheme 9 deduces the structures of **15** and **15'**.



Therefore, Pd(OAc)₂ is a precursor for the catalytic addition of **3a** to alkynes. In the catalytic cycle, Pd(OAc)₂ may be first reduced by **3a** to form zero-valent palladium which generates a hydridopalladium catalytic species such as **16** to start the catalytic cycle. Indeed, an induction period (ca. 5 min) for the catalytic addition reaction of **3a** to diphenylacetylene was observed (Figure 3), which agrees with the mechanism proposed.

Reaction of Spirophosphorane 3a with Zero-Valent Pd and Pt Complexes. No reaction was observed between **3a** and the following metal-complexes at room temperature in toluene: Pd(PCy₃)₂, Pd(PEt₃)₄, Pt(PPh₃)₃, and Pt(cod)₂. However, an oxidative addition of the P–H bond of **3a** to Et₃P-ligated Pt(0)

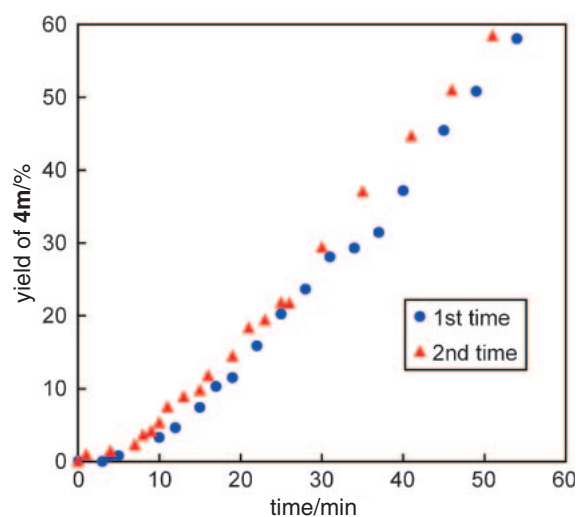
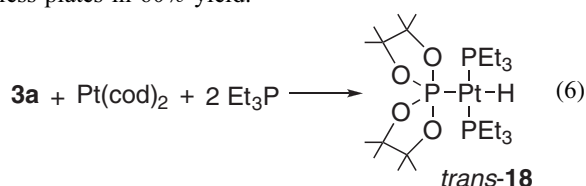


Figure 3. Yields of **4m** vs. time for a reaction of diphenylacetylene (0.2 mmol) with **3a** (0.2 mmol) in the presence of palladium acetate (0.01 mmol) in toluene (0.5 mmol) followed by ³¹P NMR spectroscopy.

complexes does proceed at room temperature to give the corresponding hydridoplatinum complex *trans*-**18** (94% NMR yield based on Pt(cod)₂) (eq 6). Thus, NMR spectroscopy of a 1:1:2 mixture of **3a**, Pt(cod)₂, and Et₃P in toluene after standing overnight clearly showed the formation of a P–Pt–H species as the result of oxidative addition of **3a** to platinum. The ¹H NMR spectroscopy exhibited a dt signal with Pt satellites centered at δ –8.40 with coupling constants of ¹J_{HPt} = 723 Hz, ²J_{HP} = 291 Hz, and ²J_{HP} = 19.8 Hz, respectively. In ³¹P NMR, a set of a doublet and a triplet displayed at δ 17.9 (*J*_{PP} = 36.0 Hz, *J*_{PPt} = 2837 Hz) and 40.1 (*J*_{PP} = 36.0 Hz, *J*_{PPt} = 4055 Hz), respectively, with a 2:1 integration ratio. Noted that the H–Pt coupling constant is relatively small compared to other P(O)–Pt–H complexes (Table 3). At the same time, the *J*_{PPt} value of the spirophosphoranyl group *trans* to hydride is considerably larger than that of other P(O)–Pt bonds which ranges from 1308 to 3288 Hz. These facts indicate a larger *trans* influence of the spirophosphoranyl group than P(O) groups. The complex was isolated by recrystallization from pentane to give *trans*-**18** as colorless plates in 60% yield.



Oxidative addition of **3a** to Pt(PEt₃)₄ also took place to give the corresponding hydridoplatinum complexes, though the reaction was slow compared to the above reaction using a combination of Pt(cod)₂ and Et₃P. Thus a mixture of Pt(PEt₃)₄ and 4 equivalents of **3a** in toluene at room temperature only produced 26% yield (based on Pt) of the corresponding hydridoplatinum complexes after 2 days (eq 7). In addition, the hydrido complex was obtained as a mixture of *cis*- and *trans*-hydridoplatinums with the *cis* one being predominantly formed (a ratio of *cis*/*trans* = 7/3). After further standing the mixture at room temperature for 5 days, *cis*-**18** completely disappeared leaving *trans*-**18** as the sole hydrido complex (31% yield). Therefore, the *cis*-**18** hydrido complex perhaps is the first product of the oxidative addition reaction which isomerizes to the thermodynamically more stable *trans*-**18**.

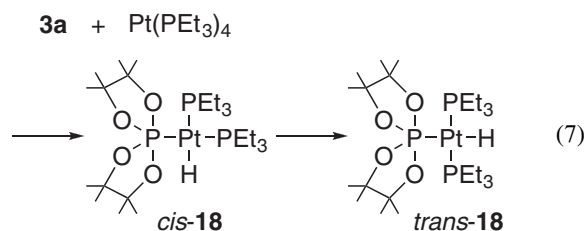
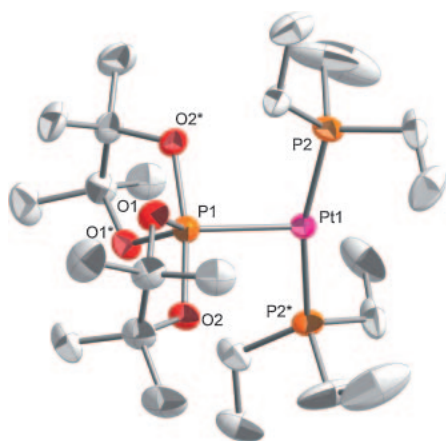
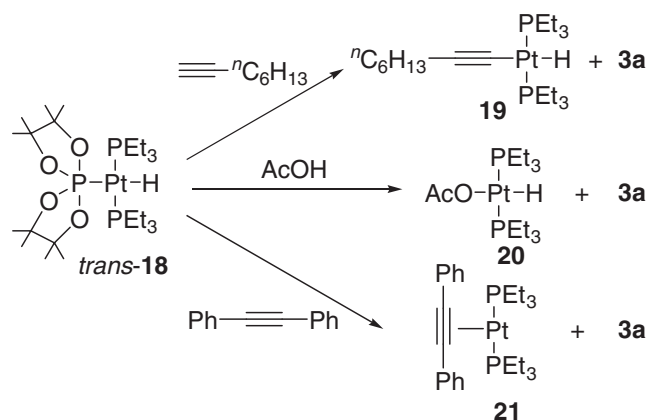


Table 3. NMR Spectra Data for Complexes *trans*-HPt[P][P']₂

P	P'	δ _H	<i>J</i> _{HPt}	<i>J</i> _{HP}	<i>J</i> _{HP'}	δ _P	<i>J</i> _{PPt}	δ _{P'}	<i>J</i> _{P'Pt}	<i>J</i> _{PP'}
(pinacolato) ₂ P (18)	PEt ₃	–8.40	723	291	20	40.1	4055	17.9	2837	36
Ph(MenO)P(O) ¹²ⁿ	PEt ₃	–5.23	720	193	19	100.1	2803	20.0	2671	28
(EtO) ₂ P(O) ⁹	PEt ₃	–5.23	737	226	18	95.1	3288	22.3	2630	33
PhPH•BH ₃ ²⁵	PEt ₃	–5.74	872	125	15	–48.7	1440	17.9	2572	19
Ph ₂ P•BH ₃ ²⁵	PEt ₃	–6.75	805	124	17	–3.7	1575	16.7	2648	17
PH ₂ •W(CO) ₅ ²⁶	PPh ₃	–4.59	812	120	13	–176.7	1308	29.7	2892	15

Table 4. Bond Lengths (Å) and Angles (°) for Complexes *trans*-HPT[P][P']₂

P	P'	Pt–P	Pt–P'	P–Pt–P'		P'–Pt–P'	
(pinacolato) ₂ P (18)	PEt ₃	2.351(5)	2.272(3)	97.56(10)		164.87(17)	
PhPH•BH ₃ ²⁵	PEt ₃	2.3477(14)	2.2863(13)	2.2771(14)	98.87(5)	92.83(5)	168.26(5)
Ph ₂ P•BH ₃ ²⁵	PEt ₃	2.331(3)	2.253(3)	2.256(2)	98.72(9)	99.10(9)	160.22(12)
PH ₂ •W(CO) ₅ ²⁶	PPh ₃	2.359(2)	2.278(2)	2.282(2)	98.01(8)	96.87(8)	161.43(8)

**Figure 4.** Molecular structure of *trans*-**18** (40% probability level). Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (°): Pt1–P1 = 2.351(5), Pt1–P2 = 2.272(3), P1–O1 = 1.654(7), P1–O2 = 1.751(5), P1–Pt1–P2 = 97.56(10), P2–Pt1–P2* = 164.87(17), P2–Pt1–P1–O1 = 46.0(2).**Scheme 10.** Reaction of *trans*-**18**.

X-ray crystallographic analysis of the crystal of *trans*-**18** unambiguously confirmed the structure (Figure 4). To the best of our knowledge, this is the first isolation of a transition metal hydride complex having a spirophosphorane framework.¹⁸ The complex has a slightly distorted square-planar geometry in which the spirophosphoranyl group and PEt₃ are placed at the mutually *cis*-positions with bond lengths being Pt1–P1 = 2.351(5) Å and Pt1–P2 = 2.272(3) Å, respectively. Interestingly, the Pt1–P1 bond length has a similar value to other Pt–P bonds (Table 4).^{25,26}

Protonolysis rather than addition of the Pt–H bond were observed when a mixture of *trans*-**18** with 1-octyne in toluene

was heated at 80 °C for 18 h. The complex *trans*-**18** completely disappeared to generate an alkynylplatinum complex **19** (86% yield) and a quantitative yield of **3a** (Scheme 10). The expected alkenylplatinum species via the addition of H–Pt bond to the alkyne could not be observed. Such a protonolysis can even proceed faster with acetic acid. Thus, 75% yield of complex **20** was generated after mixing **18** and an equivalent amount of acetic acid in toluene at room temperature for 10 min. On the other hand, heating a mixture of diphenylacetylene with *trans*-**18** at 80 °C for 16 h produced complex **21**, in which, no alkenylplatinum species by the addition of the H–Pt bond could be recognized either.

Summary and Conclusion

Palladium acetate catalyzed the addition of spirophosphorane **3a** with alkynes to give the Markovnikov isomers predominantly. The reaction is general and is tolerant toward a variety of functionalities. The reaction is also easily carried out and it could even be performed under air. There is a short induction period for the addition reaction of **3a** with alkynes catalyzed by palladium acetate, during which the addition reaction almost did not take place. Rapid addition occurred after this short induction period.

A stoichiometric reaction of Pd(OAc)₂ with **3a** gave metallic palladium which was formed first by the substitution of an OAc of Pd(OAc)₂ by **3a** to give a spirophosphoranyl palladium **9** and AcOH. Spirophosphoranyl palladium **9** subsequently decomposed to give metallic palladium and other phosphorus compounds (Scheme 5). This reduction of palladium acetate to zero-valent metallic palladium corresponds to the induction period observed for palladium acetate catalyzed addition of **3a** with alkynes.

An alkenylpalladium species **15'** was identified from the reaction of Pd(OAc)₂ with **3a** and diphenylacetylene (Scheme 9). In addition, the P–H bond of spirophosphorane **3a** could be activated by zero-valent platinum complexes to give the corresponding hydridoplatinum complexes **18** (eq 6). These facts indicate a reaction mechanism that Pd(OAc)₂ was first reduced by **3a** to produce zero-valent palladium. This palladium may insert into the P–H bond of spirophosphorane **3a** to give a hydridopalladium species. This hydridopalladium **16** added to alkynes via the addition of H–Pd bond to give an alkenylpalladium species **15** with the hydrogen atom added to the terminal carbon of terminal alkynes. Reductive elimination of complex **15** gave the addition product **4**.

This new reaction reported provides a general methodology for the introduction of phosphorus functionality to the internal carbon of a terminal alkyne, resolving the problem of the regioselectivity associated with hydrophosphorylation reactions so far reported. The adduct **4**, when necessary, can be readily converted to the corresponding alkenylphosphonates

and phosphonic acids via a simple hydrolysis or a thermal decomposition process. Therefore, this new reaction is a perfect complement to the hitherto known hydrophosphorylation reactions.

The new reaction is featured by its high generality and simplicity: it does not require a phosphine–palladium complex but the simple palladium acetate; moreover, in contrast to hitherto reported metal-catalyzed P(O)–H additions^{9,11,12} that require oxygen-free reaction conditions, this new addition reaction could even be conducted under air. In addition, these alkenyl spiroposphoranes **4** are a new class of phosphorus containing heterocyclic compounds and there are no alternative ways for their preparation.¹⁷ The high potential of these compounds as starting reagents for the synthesis of diverse novel phosphorus heterocyclic compounds, which are of current interest,^{14c} though the chemical transformations of their reactive carbon–carbon double bonds can be readily expected.

Experimental

General. Unless otherwise noted all reactions were carried out under dry nitrogen atmosphere. Solvents were dried and purified under nitrogen before use by standard procedures. Chemical reagents were purchased and used as received. ¹H, ¹³C, and ³¹P NMR spectra were recorded on a JEOL LA-500 instrument (500 MHz for ¹H, 125.4 MHz for ¹³C, and 201.9 MHz for ³¹P NMR spectroscopy). Unless otherwise noted, CDCl₃ was used as the solvent. Chemical shift values for ¹H and ¹³C were referred to internal Me₄Si (0 ppm), and that for ³¹P was referred to H₃PO₄ (85% solution in D₂O, 0 ppm). Mass spectra were measured on a Shimadzu GCMS-QP2010 spectrometer (EI). HRMS analysis was performed by the Analytical Center at the National Institute of Advanced Industrial Science and Technology.

Crystallographic data have been deposited with Cambridge Crystallographic Data Centre: Deposition number CCDC-765608 for compound *trans*-**18**. Copies of the data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html> (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, U.K.; Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).

Pd(OAc)₂-Catalyzed Addition of **3a to Alkynes: A Representative Procedure.** 1-Octyne (27.6 mg, 0.25 mmol), **3a** (66.1 mg, 0.25 mmol), and Pd(OAc)₂ (1.7 mg, 3 mol %) were dissolved in 0.5 mL of dry toluene. The mixture was heated at 80 °C for 2 h in a sealed tube and evaporated in vacuo. The residues were passed through a short silica gel column (CH₂Cl₂ solvent) to remove the catalyst, and was subjected to bulb-to-bulb distillation under vacuum (1.2 × 10^{−3} mmHg) to obtain pure **4a** as colorless oil (82.4 mg, 0.22 mmol, 88% yield).

4a: Colorless oil; bp 128–130 °C/1.2 × 10^{−3} mmHg (bulb-to-bulb distillation); ¹H NMR: δ 0.88 (3H, t, *J* = 6.9 Hz), 1.14 (12H, s), 1.24–1.39 (6H, m), 1.26 (12H, s), 1.52 (2H, quint, *J* = 7.5 Hz), 2.38 (2H, dd, *J*_{HP} = 10.2 Hz, *J*_{HH} = 6.7 Hz), 5.38 (1H, dd, *J*_{HP} = 55.3 Hz, *J*_{HH} = 1.5 Hz), 5.76 (1H, dd, *J*_{HP} = 25.0 Hz, *J*_{HH} = 0.9 Hz); ¹³C NMR: δ 14.0, 22.6, 23.7 (d, *J*_{CP} = 7.1 Hz), 24.4 (d, *J*_{CP} = 5.1 Hz), 28.1 (d, *J*_{CP} = 8.3 Hz), 29.1, 31.8, 32.8 (d, *J*_{CP} = 11.4 Hz), 78.2, 120.5 (d, *J*_{CP} = 8.3 Hz), 150.3 (d, *J*_{CP} = 204.7 Hz); ³¹P NMR δ −31.6. Anal. Calcd

for C₂₀H₃₉O₄P: C, 64.14; H, 10.50%. Found: C, 63.95; H, 10.49%.

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Supporting Information

Determination of the regioselectivity, experimental procedure, copies of NMR spectra and analytical data for adducts **4** and other compounds. This material is available free of charge on the Web at: <http://www.csj.jp/journals/bcsj/>.

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