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Regioselective Metal-Catalyzed Hydrophosphinylation of Alkynes: Synthesis of Enantiopure α- or β-Substituted Vinylphosphane Oxides

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Keywords: Alkynes / Homogeneous catalysis / Phosphorus heterocycles / Regioselectivity

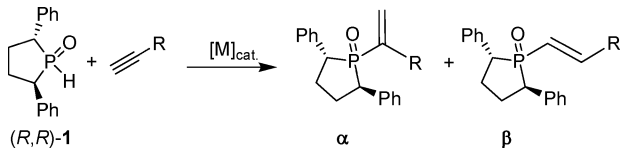
Palladium was found to catalyze regioselective Markovnikov addition of chiral enantiopure 1*r*-oxo-2*c*,5*t*-diphenylphospholane (**1**) to terminal alkynes, whereas rhodium catalysis offers selectively the (*E*)-anti-Markovnikov adduct. This strategy offers rapid access to chiral and enantiopure α- or β-substituted-1-alkenylphospholanes.

Introduction

Homogeneous catalysis is an increasingly useful and versatile alternative for the construction of C–P bonds. The addition of a P–H bond to an unsaturated carbon–carbon bond is, in terms of synthetic value and atom economy, a very attractive process for the construction of various organophosphorus compounds.[1] Particularly, metal-catalyzed addition of a P–H bond to alkynes results in the formation of P–alkene bonds.[2] This strategy has shown its potential in the synthesis of phosphanes,[3] phosphonates,[4] phosphinates,[5,4d] *H*-phosphinates[6] and phosphane oxides.[7] To the best of our knowledge, although appropriate catalyst or protocols are developed to produce the desired branched or linear α-β-unsaturated organophosphorus compounds, there are only two examples of synthesis of chiral enantioenriched vinylphosphane from hydrophosphination of alkynes. The first process is based on the stereospecific hydrophosphinylation of alkynes with *P*-chiral menthylphosphinate.[8] This strategy is regioselective but suffers from the use of a stoichiometric amount of menthyl chiral auxiliary. The second route is a palladium-catalyzed asymmetric hydrophosphination process with phosphane–borane.[9] In this case, *P*-chirogenic vinylphosphane–borane was obtained up to 42% *ee*.

Results and Discussion

In our group, we are interested in the preparation of organophosphorus compounds based on the chiral *trans*-2,5-diphenylphospholane[10] moiety and their applications as ligands[11] or chiral transfer agents.[12] With this in mind, we commenced our study by a strategy to produce chiral enantiopure vinylphosphane by metal-catalyzed hydrophosphinylation of alkynes (Scheme 1).



Scheme 1. Metal-catalyzed hydrophosphinylation of terminal alkyne with **1**.

This strategy is based on the metal-catalyzed reaction of enantiopure 1*r*-oxo-2*c*,5*t*-diphenylphospholane (**1**) with alkynes. Its offers some advantages: (i) Chiral enantiopure substituted vinylphosphane oxides can be accessed rapidly. (ii) The substrate possesses a nonstereogenic phosphorus atom, which avoids problems of stereochemical integrity. (iii) The chirality is provided by the phospholane moiety and not by the alkyne substrate. (iv) Either the α- or the β-substituted vinylic product can be obtained. Results of palladium-catalyzed hydrophosphinylation of various alkynes are collected in Table 1.

No reaction occurred in the absence of catalyst. Surprisingly, no product was obtained in the case of $Pd(OAc)_2$ and the diphosphane dppe, despite the usual good activity of this standard catalyst in hydrophosphinylation reactions.[7d] No better activity was observed with $Pd(dba)_2$ (Table 1, Entries 1 and 2). We found that hydrophosphinylation of phenylacetylene proceeded with total conversion at 80 °C to give vinylic phospholane oxide **2a** when the catalyst system used was composed of 5 mol-% of tetrakis(triphenylphosphane)palladium complex (Table 1, Entry 3). Under these conditions, only the α adduct was obtained, and no trace of the β isomer was detected by NMR spectroscopic analysis. This result indicates that the phosphorus attacks the internal carbon atom of the alkyne with total regioselec-

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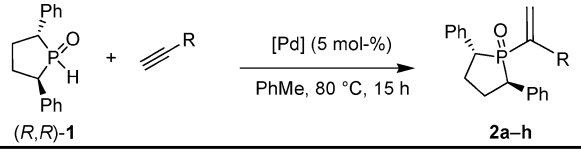
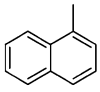
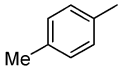
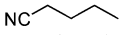
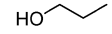
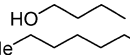
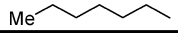
Table 1. Palladium-catalyzed hydrophosphinylation of alkynes.[a]



Entry	R	Product	Catalyst	Yield of α/β [%][b]
1	Ph	**2a**	$Pd(OAc)_2$, dppe	0
2	Ph	**2a**	$Pd(dba)_2$, dppe	0
3	Ph	**2a**	$Pd(PPh_3)_4$	>95 (40)/0[c]
4		**2b**	$Pd(PPh_3)_4$	>95 (45)/0[c]
5		**2c**	$Pd(PPh_3)_4$	>95 (50)/0[c]
6		**2d**	$Pd(PPh_3)_4$	>95 (60)/0[c]
7		**2e**	$Pd(PPh_3)_4$	>95 (63)/0[c]
8		**2f**	$Pd(PPh_3)_4$	>95 (60)/0[c]
9		**2g**	$Pd(PPh_3)_4$	>95 (33)/0[c]
10		**2h**	$Pd(PPh_3)_4$	>95 (31)/0[c]

[a] An equimolar mixture of **1** and an alkyne in toluene, in the presence of 5 mol-% of $Pd(PPh_3)_4$ (80 °C, 15 h). [b] Yields of α/β determined by ^1H and ^{31}P NMR spectroscopy. The isolated yields of pure products for analysis after column chromatography are reported in parentheses. [c] The β isomer was not detected by ^1H and ^{31}P NMR spectroscopy.

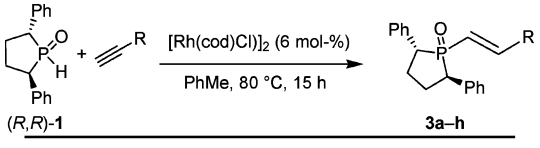
tivity. The results are similar for other alkynes and products **2a**–**g** were obtained with total conversion of starting material (^{31}P NMR).[13]

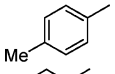
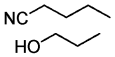
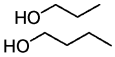
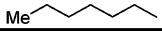
Conversely, rhodium-catalyzed hydrophosphinylation of alkynes led preferentially to the formation of the β adduct with total conversion of **1** (Table 2). The reaction is clean and highly selective for (*E*)-alkenylphospholane oxide isomer **3**. However, Rh catalysis seems to be slightly less regioselective than Pd catalysis for some alkynes.

Indeed, despite the absence of the α isomer for 4-butyn-1-ol, 4-pentyn-1-ol and 1-octyne (Table 2, Entries 6, 7 and 8), a trace amount of the α adduct was detected for phenyl and naphthylacetylene (Table 2, Entries 1 and 2). In some cases, the β adducts were contaminated by their corresponding α isomer, suggesting a decrease in the regioselectivity of the reaction (Table 2, Entries 3–5).

1-Ethynylcyclohexene selectively reacted at the triple bond under both palladium and rhodium catalysis. This proves the inertness of the internal double bond (Table 1, Entry 6 and Table 2, Entry 4). The reason for the total selectivity for the branched product under palladium catalysis is not clear. Indeed, it was demonstrated by Tanaka that hydrophosphinylation reactions of terminal alkynes with secondary phosphane oxides such as diphenylphosphane oxide, H–P(O)Ph_2, in the presence of $Pd(PPh_3)_4$ form linear products as the major products.[7a] In contrast, the same group demonstrated that it is possible to increase the formation of the α adduct or to switch completely the regioselectivity of this reaction in the presence of 5 mol-% of acidic

Table 2. Rhodium-catalyzed hydrophosphinylation of alkynes.[a]



Entry	R	Product	Yield of β/α [%][b]
1	Ph	**3a**	>95 (31)/trace
2		**3b**	>95 (50)/trace
3		**3c**	85 (60)/15
4		**3d**	57 (35)/43
5		**3e**	95 (45)/5
6		**3f**	>95 (25)/0[c]
7		**3g**	>95 (30)/0[c]
8		**3h**	>95 (25)/0[c]

[a] An equimolar mixture of **1** and an alkyne (0.5 mmol) in toluene (1 mL) in the presence of 6 mol-% of $[Rh(cod)Cl]_2$ (80 °C, 15 h). [b] Yields of α/β determined by ^1H and ^{31}P NMR spectroscopy. The isolated yields of pure products for analysis after column chromatography are reported in parentheses. [c] The α isomer was not detected by ^1H and ^{31}P NMR spectroscopy.

compounds like diphenylphosphinic acid [$Ph_2P(O)OH$] but in the presence of $PdMe_2L_2$ as catalyst.[7b] With this in mind, we observed, by NMR spectroscopy, a trace amount of *trans*-2,5-diphenylphospholanic acid (**4**) in the starting material, resulting of the slow oxidation of **1** (Figure 1). Total absence of phosphinic acid **4** in the substrate does not modify the selectivity, but the Pd-catalyzed reaction appears cleaner and proceeds with higher conversion. The presence or absence of **4** in the Rh-catalyzed hydrophosphination reaction did not alter the results.

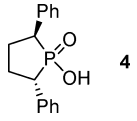


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Figure 1. Phospholanic acid **4**.

Mixing two equivalents of **1** with $[Rh(cod)Cl]_2$ in [D_8]-toluene gave immediately a complex showing a doublet at δ = 141 ppm ($J_{Rh,P}$ = 170 Hz) in the ^{31}P NMR spectrum, corresponding probably to the formation of $RhP_2(cod)Cl$ complex **A** (Figure 2). No other signals are detected. The presence of complex **A** is based on previous work.[11b,11c,14] Furthermore, we observed no signal in the range from 0 to –30 ppm in the ^1H NMR spectrum, corresponding to the [Rh]–H bond.[4a,7c,15] Monitoring the reaction with phenylacetylene at 80 °C by NMR spectroscopy revealed the slow disappearance of complex **A** and new signals over 3 h at 5.8–6.0 ppm, corresponding to the vinylic protons of compounds **3a**. The presence of the product was confirmed by ^{31}P NMR spectroscopy. In the case of palladium studies, no signal corresponding to the [Pd]–H bond was observed.

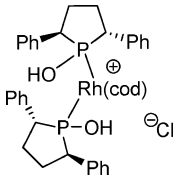
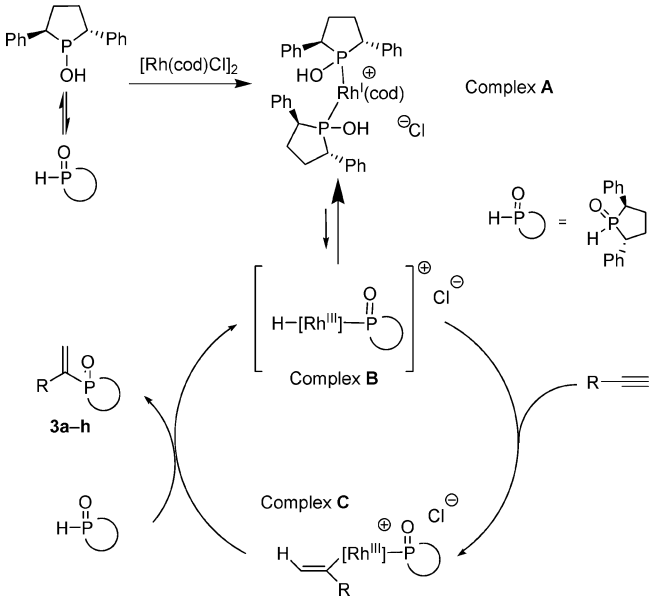


Figure 2. $RhP_2(cod)Cl$ complex **A**.

With this in mind, we tentatively propose the mechanism described in Scheme 2 for the rhodium-catalyzed hydrophosphinylation reaction. Complexes **A** and **B** resulting from coordination and oxidative addition of **1** to $[Rh(cod)Cl]_2$, respectively, would be in equilibrium. Insertion of the acetylenic substrate into the Rh–H bond of **B** would offer vinylic complex **C**. The [Rh]–C bond being cleaved by a further molecule of **1**. Complex **B** should be a minor and a very reactive complex rapidly undergoing alkyne insertion. This would explain the absence of the signal of the hydride proton in the spectra when monitoring the reaction by NMR spectroscopy.



Scheme 2. Proposed mechanism for hydrophosphinylation.

Conclusions

The mechanism of the hydrophosphinylation of alkynes by using chiral enantiopure phospholane oxide **1** is still not clear. However, in most cases, the reactions are selective particularly when catalyzed with a palladium complex. This strategy is applicable to a variety of alkynes and offers rapid access to chiral enantiopure α- or β-substituted vinylphospholane.

Supporting Information (see footnote on the first page of this article): Experimental procedures, characterization data and copies of the ^1H, ^{13}C and ^{31}P NMR spectra.

Acknowledgments

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[1] For recent reviews on metal-catalyzed P–H activation, see: a) O. Delacroix, A. C. Gaumont, *Curr. Org. Chem.* **2005**, *9*, 1851–1882; b) F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev.* **2004**, *104*, 3079–3160.

[2] L. Coudray, J.-L. Montchamp, *Eur. J. Org. Chem.* **2008**, 3601–3613.

[3] For examples of metal-catalyzed hydrophosphination, see: a) D. Mimeau, A.-C. Gaumont, *J. Org. Chem.* **2004**, *68*, 7016–7022; b) H. Ohmiya, H. Yorimitsu, K. Oshima, *Angew. Chem.* **2005**, *117*, 2420–2422; *Angew. Chem. Int. Ed.* **2005**, *44*, 2368–2370; c) A. M. Kawaoka, M. R. Douglas, T. J. Marks, *Organometallics* **2003**, *22*, 4630–4632; d) F. Jérôme, F. Monnier, H. Lawicka, S. Dérien, P. H. Dixneuf, *Chem. Commun.* **2003**, 696–697; e) M. Hayashi, Y. Matsuura, Y. Watanabe, *J. Org. Chem.* **2006**, *71*, 9248–9251.

[4] For the synthesis of phosphonates by metal-catalyzed hydrophosphorylation, see: a) C.-Q. Zhao, L. B. Han, M. Goto, M. Tanaka, *Angew. Chem.* **2001**, *113*, 1983–1986; *Angew. Chem. Int. Ed.* **2001**, *40*, 1929–1932; b) L. B. Han, M. Tanaka, *J. Am. Chem. Soc.* **1996**, *118*, 1571–1572; c) N. S. Goulioukina, T. M. Dolgina, I. P. Beletskaya, J.-C. Henry, D. Lavergne, V. Ratovelomanana-Vidal, J.-P. Genet, *Tetrahedron: Asymmetry* **2001**, *12*, 319–327; d) L. B. Han, C. Zhang, H. Yazawa, S. Shimada, *J. Am. Chem. Soc.* **2004**, *126*, 5080–5081.

[5] For the synthesis of phosphinates by metal-catalyzed hydrophosphinylation, see: a) S. Kumar Nune, M. Tanaka, *Chem. Commun.* **2007**, 2858–2860; b) L. B. Han, Y. Ono, H. Yazawa, *Org. Lett.* **2005**, *7*, 2909–2911.

[6] For the synthesis of *H*-phosphinates by metal-catalyzed hydrophosphinylation, see: a) S. Deprèle, J.-L. Montchamp, *J. Am. Chem. Soc.* **2002**, *124*, 9386–9387; b) P. Ribière, K. Bravo-Altamirano, M. I. Antczak, J. D. Hawkins, J.-L. Montchamp, *J. Org. Chem.* **2005**, *70*, 4064–4072; c) K. Bravo-Altamiraro, J.-L. Montchamp, *Tetrahedron Lett.* **2007**, *48*, 5755–5759.

[7] For the synthesis of phosphane oxides by metal-catalyzed hydrophosphinylation, see: a) L. B. Han, N. Choi, M. Tanaka, *Organometallics* **1996**, *15*, 3259–3261; b) L. B. Han, R. Huia, M. Tanaka, *Angew. Chem.* **1998**, *110*, 98–101; *Angew. Chem. Int. Ed.* **1998**, *37*, 94–96; c) L.-B. Han, C.-Q. Zhao, M. Tanaka, *J. Org. Chem.* **2001**, *66*, 5929–5932; d) N. Dobashi, K. Fuse, T. Hoshino, J. Kanada, T. Kashiwabara, C. Kobata, S. Nune, M. Tanaka, *Tetrahedron Lett.* **2007**, *48*, 4669–4673; e) M. Niu, H. Fu, Y. Jian, *Chem. Commun.* **2007**, 272–274; f) A. Allen, L. Ma, W. Lin, *Tetrahedron Lett.* **2002**, *43*, 3707–3710.

[8] L. B. Han, C.-Q. Zhao, S.-Y. Onozawa, M. Goto, M. Tanaka, *J. Am. Chem. Soc.* **2002**, *124*, 3842–3843.

[9] B. Join, D. Mimeau, O. Delacroix, A.-C. Gaumont, *Chem. Commun.* **2006**, 3249–3251.

[10] a) M. Toffano, C. Dobrota, J.-C. Fiaud, *Eur. J. Org. Chem.* **2006**, 650–656; b) F. Guillen, M. Rivard, M. Toffano, J.-Y. Legros, J.-C. Daran, J.-C. Fiaud, *Tetrahedron* **2002**, *58*, 5895–5904.

[11] a) C. Dobrota, M. Toffano, J.-C. Fiaud, *Tetrahedron Lett.* **2004**, *45*, 8153–8156; b) A. Galland, C. Dobrota, M. Toffano, J.-C. Fiaud, *Tetrahedron: Asymmetry* **2006**, *17*, 2354–2357; c) A. Galland, J.-M. Paris, T. Schlama, R. Guillot, J.-C. Fiaud, M. Toffano, *Eur. J. Org. Chem.* **2007**, 863–876.

[12] C. Dobrota, A. Duraud, M. Toffano, J.-C. Fiaud, *Eur. J. Org. Chem.* **2008**, 2439–2445.

[13] The isolated yields of pure product are low despite the high yields determined by NMR spectroscopy. This result is due to the degradation of product on silica gel.

[14] In solution, secondary phosphane oxides exist in equilibrium between pentavalent (phosphane oxide form) and trivalent

(phosphane form) tautomeric structures. At room temperature, the phosphane oxide form is the more stable, whereas the phosphane form coordinates transition metals: a) N. V. Dubrovina, A. Börner, *Angew. Chem.* **2004**, *116*, 6007–6010; *Angew. Chem. Int. Ed.* **2004**, *43*, 5883–5886; b) X.-B. Jiang, A. J. Minnaard, B. Hessen, B. L. Feringa, A. L. L. Duchateau, J. G. O. Andrien, J. A. F. Boogers, J. G. de Vries, *Org. Lett.* **2003**, *5*, 1503–1506; c) F. Wang, P. L. Polavarapu, J. Drabowicz, M. Mikolajczyk, *J. Org. Chem.* **2000**, *65*, 7561–7565.

[15] M. A. Bennet, T. R. B. Mitchel, *J. Organomet. Chem.* **1985**, *295*, 223–231.

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