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New Approach to Phosphinoalkynes Based on Pd- and Ni-Catalyzed Cross-Coupling of Terminal Alkynes with Chlorophosphanes

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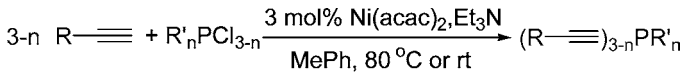
ABSTRACT



R=Ph, p-Tol, Pr, Am, Bu^t R'=Ph, Pr^i, Bu

The first example of direct phosphination of terminal alkynes with chlorophosphanes catalyzed by Ni or Pd complexes is described. Both aromatic and aliphatic terminal acetylenes undergo the coupling reaction to give corresponding coupling product in high yield.

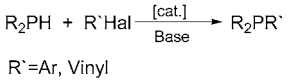
Alkynylphosphanes are an attractive and useful class of compounds in organic synthesis.[1] They can be identified as common building blocks in constructing a broad variety of alkenyl- and alkylphosphanes comprising functional groups[2] and phosphorus heterocycles.[3] Also, alkynylphosphanes are important ligands, forming complexes with transition metals through η^1-P-coordination, as well as by simultaneous participation of phosphorus UEP and acetylene π-orbitals in polydentate binding.[4]

Synthesis of alkynylphosphanes is usually accomplished by treating the respective P(III)-halide with acetylenides of sodium,[5a,b] lithium,[5a,b] magnesium,[5c,d] or titanium.[5e] Obviously, the use of the above active organometallic compounds substantially restricts their application in obtaining of tertiary alkynylphosphanes.

We report here a convenient and direct route to alkynylphosphanes by transition-metal-catalyzed cross-coupling reaction that eliminates these problems.

The reaction of R_2PH with aryl or vinyl halides catalyzed by Pd or Ni complexes is known to be a convenient procedure of obtaining tertiary phosphanes.[6] The reaction includes P−C bond formation as a result of nucleophilic substitution at the C-atom (Scheme 1).

Scheme 1



We proposed a novel catalytic method of synthesizing phosphinoalkynes by Pd- or Ni-catalyzed reaction between chlorophosphanes and alkynes in the presence of TEA, which is inversed (*Umpolung*) to the above process (Scheme 1) and can be considered as a nucleophilic substitution at the P-atom. (Scheme 2)

(1) (a) *The Chemistry of Organophosphorus Compounds*; Hartley, F. R.; Ed.; Wiley: Chichester, U.K., 1990−1996; Vols. 1−4. (b) Quin, L. D. *A Guide to Organophosphorus Chemistry*; Wiley: New York, 2000. (c) Muller, E. *Methoden der Organischen Chemie (Houben-Weyl)*; Georg Thieme Verlag: Stuttgart, 1977; Band 5/Teil 2.

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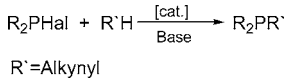
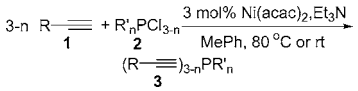
Scheme 2



The discovered transformations appeared to be a heteroanalogue of the Sonogashira reaction[7] in which the phosphorus−halide bond is activated. The reaction proceeds

Scheme 3



smoothly by heating a toluene solution of alkyne (**1**), chlorophosphane (**2**), Et_3N, and 3 mol % catalyst at 80 °C for 10−15 min or by allowing it to stand at room temperature for 6−8 h. The respective phosphanes (**3**) are formed in nearly quantitative yields.

Table 1. Effect of Catalyst, Solvent, and Temperature on Cross-Coupling of Phenylacetylene with Chlorodiphenylphosphane[a]

entry	catalyst	solvent	temp (°C)/time	conversion[b] (%)
1		PhMe	80/24 h	0
2	$Pd(PPh_3)_4$	MeCN	80/10 min	50
3	$(Ph_3P)_2PdCl_2$	PhMe	80/30 min	95
4	$Ni(PPh_3)_2Br_2$	PhH	80/10 min	97
5	$Ni(PPh_3)_2Br_2$	MeCN	80/10 min	99
6	$Ni(acac)_2$	PhMe	rt /10 h	95
7	$Ni(acac)_2$	CH_2Cl_2	80/10 min	99
8	$Ni(acac)_2$	PhMe	80/10 min	99
9	$Ni(cod)_2$	PhMe	80/10 min	99
10	$Ni(cod)_2$	PhMe	rt /6 h	98
11	$Ni[P(OEt)_3]_4$	PhH	120/15 min	98

[a] Reaction conditions: phenylacetylene, 1.25 mmol; Ph_2PCl, 1 mmol; catalyst, 3 mol %; Et_3N, 3 mmol; solvent, 2 mL; sealed tube. [b] Determined by ^{31}P NMR.

The choice of catalytic system is represented in Table 1. Various precursors of nickel catalyst were found to be effective (Table 1, entries 4−11). Complexes of palladium were found to be less active (Table 1, entries 2 and 3). In the absence of catalyst Ph_2PCl does not react with phenylacetylene in the presence of TEA even under heating at 80 °C for 24 h (Table 1, entry 1).[8] The best catalysts are $Ni(cod)_2$ and $Ni(acac)_2$, with which cross-coupling proceeds efficiently even at room temperature (Table 1, entries 6 and 10).

The nature of the solvent does not noticeably affect the rate of cross-coupling reaction. Thus, the cross-coupling proceeds with equal success both in nonpolar toluene (benzene) (Table 1, entries 4, 6, 8−11) and more polar CH_2Cl_2 or MeCN (Table 1, entries 5 and 7).

Under optimal conditions terminal alkynes easily react with diaryl- and dialkylchlorophosphanes (Table 2, entries

Table 2. Cross-Coupling of Chlorophosphanes with Alkynes[a]

entry	chlorophosphane	R−≡ R	product	time min	yield %[d]
1	Ph_2PCl[a] **2a**	Ph **1a**	Ph_2P−≡−Ph **3a**	10	99(95)
2	**2a**	p-Tol **1b**	Ph_2P−≡−Tol-p **3b**	10	99(96)
3	**2a**	Pr **1c**	Ph_2P−≡−Pr **3c**	10	98(91)
4	**2a**	Am **1d**	Ph_2P−≡−Am **3d**	10	99(93)
5	**2a**	Bu^t **1e**	Ph_2P−≡−Bu^t **3e**	30	96(87)
6	$Pr^i{}_2PCl$[a] **2b**	**1a**	$Pr^i{}_2P$−≡−Ph **3f**	10	98(79)
7	**2b**	**1d**	$Pr^i{}_2P$−≡−Am **3g**	10	99(82)
8	**2b**	**1e**	$Pr^i{}_2P$−≡−Bu^t **3h**	10	99(86)
9	$Pr^i(Ph)PCl$[a] **2c**	**1a**	$Pr^i(Ph)P$−≡−Ph **3i**	10	98(84)
10	Bu_2PCl[a] **2d**	**1a**	Bu_2P−≡−Ph **3j**	10	95(76)
11	**2d**	**1d**	Bu_2P−≡−Am **3k**	10	99(81)
12	$PhPCl_2$[b] **2e**	**1a**	$PhP(-≡-Ph)_2$ **3l**	10	99(96)
13	**2e**	**1d**	$PhP(-≡-Am)_2$ **3m**	10	98(95)
14	**2e**	**1e**	$PhP(-≡-Bu^t)_2$ **3n**	20	97(94)
15	PCl_3[c] **2f**	**1a**	$P(-≡-Ph)_3$ **3o**	15	98(78)
16	**2f**	**1b**	$P(-≡-Tol\text{-}p)_3$ **3p**	15	98(81)
17	**2f**	**1e**	$P(-≡-Bu^t)_3$ **3q**	30	94(84)
18	$Bu^t{}_2PCl$ **2g**	**1a**	$Bu^t{}_2P$−≡−Ph **3r**	e)	25

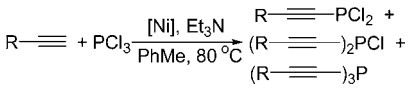
[a] Reaction conditions: 80 °C, toluene, 3 mol % $Ni(acac)_2$; (a) chlorophosphane 1 mmol, alkyne 1.25 mmol Et_3N 3 mmol, (b) dichlorophosphane 1 mmol, alkyne 2.5 mmol, Et_3N 6 mmol, (c) $PCl_3$1 mmol, alkyne 3.75 mmol, Et_3N 9 mmol; (d) based on ^{31}P NMR, value in parentheses is isolated yield, (e) 120 °C, 2 weeks.

(4) See for example: (a) Moldes, J.; De la Encarnacion, E.; Ros, J.; Alvarez-Larena, A.; Piniella, J. F. *J. Organomet. Chem.* **1998**, *566*, 165. (b) Rosa, P.; Le Floch, P.; Richard, L.; Mathey, F. *J. Am. Chem. Soc.* **1997**, *119*, 9417. (c) Jeffery, J. C.; Pereira R. M. S.; Vargas, M. D.; Went, M. J. *J. Chem. Soc., Dalton Trans.* **1995**, 1805. (d) Johnson, D. K.; Rukachasirikul, T.; Sun, Y.; Taylor, N. J.; Carty, A. J. *Inorg. Chem.* **1993**, *32*, 5544. (e) Berenguer, J. R.; Bernechea, M.; Fornies, J.; Gomes, J.; Lalinde, E. *Organometallics* **2002**, *21*, 2314. (f) Ara, J.; Falvello, L. R.; Fernandes, S.; Fornies, J.; Lalinde, E.; Martin, A.; Moreno, T. *Organometallics* **1997**, *16*, 5923. (g) Lauattani, E.; Suades, J.; Matheim, R. *J. Organomet. Chem.* **1991**, *421*, 335.

1−11), aryldichlorophosphanes (Table 2, entry 12), and PCl_3 (Table 2, entries 13−17). In all cases mono-, bis-, or tris-alkynylphosphanes are isolated in high yields, with the exception of bulky chlorodi(*tert*-butyl)phosphane, which forms the product of cross-coupling with phenylacetylene in 25% yield only after heating at 120 °C for 2 weeks (Table 2, entry 18).

It should be noted that selective substitution of one chlorine atom upon treatment of dichlorophosphanes or PCl_3 with 1 equiv of terminal alkyne proved problematic because a mixture of alkynylphosphanes with predominance of di- and trisubstituted derivatives is always formed. Terminal alkynes

Scheme 4

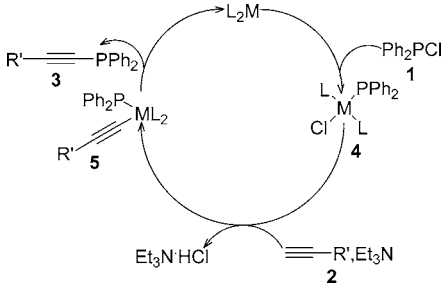


bearing alkyl and aryl substituents at the triple bond could be introduced into the reaction with halogenophosphanes under the stipulated conditions.

Unfortunately, the reaction of diphenylchlorophosphane with with *p*-anisyl-, *m*-trifluoromethylphenylacetylenes, methylpropargyl ether, and *N*,*N*-dimethylpropargylamine in the presence of Ni-catalysts led to the complex mixture of unidentified products.

The proposed mechanism of reaction is shown in Scheme 5. A first step of the catalytic cycle would be the oxidative addition of halogenophosphane (**1**) to the catalyst to give a phosphido complex (**4**). Subsequent transmetalation (exchange of halogen with acetylenide ion) led to complex (**5**),

Scheme 5



which was transformed into the product of cross-coupling (**3**) by reductive elimination.

Oxidative addition of the P−Cl bond to zerovalent Ni and Pd, unlike oxidative addition of the P−H bond, which is considered to be the key step in hydrophosphination of alkenes and alkynes,[9] according to our knowledge is not described in the literature.[10] However there are several examples of oxidative addition of the P−Cl bond to zerovalent Pt[11] and Fe[12] complexes, as well as of insertion of nontransition metal[13] to the P−Cl bond. Only one case of activation of a P(IV)−Cl bond by Pd(0)-complex, in hexaphosphazene, has been reported.[14]

In summary, we have developed a novel straightforward method of obtaining phosphinoalkynes via Pd- and Ni-catalyzed cross-coupling of terminal alkynes with chlorophosphanes, which can be treated as heteroanalogues of the Sonogashira reaction.

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Supporting Information Available: Detailed experimental procedures and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) For oxidative addition of phosphanes and phosphane oxides P−H bond to Pt(0), Pd(0), or Ni(0) centers, see: (a) Jasaka, C. A.; Dorn, H.; Lough, A. N.; Manners, L. *Chem. Eur. J.* **2003**, *9*, 271. (b) Han, L.-B.; Tanaka, M. *J. Am. Chem. Soc.* **1996**, *118*, 1571. (c) Gianandrea, R.; Mastrorilly, R.; Nolill, C. F.; Englert, U. *J. Chem. Soc., Dalton Trans.* **1997**, 1355. (d) Wicht, D. K.; Glueck, D. S. In *Catalytic Heterofunctionalization*; Togni, A., Grutzmacher, H., Eds.; Wiley-VCH: Weinheim, 2001; Chapter 5 and references therein.

(10) For oxidative addition of E-Hal bond, see for example: (a) Kuyper, J. *Inorg. Chem.* **1977**, *16*, 2171. (b) Kuyper, J. *Inorg. Chem.* **1978**, *17*, 77. (c) Butler, G.; Eaborn, C.; Pidcock, A. *J. Organomet. Chem.* **1978**, *144*, 23. (d) Yamashita, H.; Hayashi, T.; Kobayashi, T.; Tanaka, M.; Goto, M. *J. Am. Chem. Soc.* **1988**, *110*, 4417. (e) Chatani, N.; Amishiro, N.; Murai, S. *J. Am. Chem. Soc.* **1991**, *113*, 7778. (f) Chatani, N.; Amishiro, N.; Morii, T.; Yamashita, T.; Murai, S. *J. Org. Chem.* **1995**, *60*, 1834. (g) Yang, F.-Y.; Cheng, Ch.-H. *J. Am. Chem. Soc.* **2001**, *123*, 761.

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