A Convenient and Direct Route to Phosphinoalkynes via Copper-Catalyzed Cross-Coupling of Terminal Alkynes with Chlorophosphanes

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Abstract: A new efficient method to obtain various alkynylphosphanes $R_nP(==-R')_{3-n}$ [R = Ar, Alk, alkoxy, amido R' = Ar, Het, Alk, CH₂Z (Z = OMe, NMe₂), n = 0–2] has been developed by means of cross-coupling reaction of chlorophosphanes R_nPCl_{3-n} (R = Ar, Alk, Alkoxy) with terminal alkynes catalyzed by cuprous salts.

Key words: phosphorus, cross-coupling, alkynes, copper, homogenous catalysis

Alkynylphosphanes are an attractive class of compounds useful in organic synthesis.¹ They can be identified as common building blocks in constructing a broad variety of alkenyl- and alkylphosphanes² bearing functional groups and phosphorus heterocycles.³ Also alkynylphosphanes can be utilized for the preparation of neutral and cationic, homo- and hetero-bridged complexes,⁴ metallacycles,⁵ and transition metal clusters bearing polyyne ligand.⁶

We have previously shown that alkynylphosphanes comprising one, two or three acetylenic substitutes at phosphorus atom, could be obtained by cross-coupling reaction between terminal alkynes and aryl (or alkyl) chlorophosphanes catalyzed by Ni or Pd complexes.⁷ The reaction represents the heteroanalog of Sonogashira reaction.⁸

We report here a convenient method of preparing alkynylphosphanes which is based on utilizing Cu(I) salts as catalyst in the reaction between terminal alkynes and chlorophosphanes (Equation 1).

$$R_{n}PCI_{3-n} + R' = \frac{1 \text{ mol% CuX, Et_{3}N}}{MePh, r.t.}$$

$$R_{n}P(- R')_{3-n}$$

Equation 1

The reaction proceeds smoothly by stirring a toluene solution of chlorophosphane 1, alkyne 2, Et_3N and CuI or CuBr (1 mol%) under argon at room temperature for 1–6

hours. The resulting phosphanes **3** are formed in nearly quantitative yields.

Under optimal conditions terminal alkynes easily react with diaryl- and dialkylchlorophosphanes (Table 1, entries 1–12), aryldichlorophosphanes (Table 1, entry 14) and PCl₃ (Table 1, entries 15, 16). In all cases mono-, bisor tris(alkynyl)phosphanes are isolated in high yields with the exception of phosphane **3m**, which is formed from bulky *t*-Bu₂PCl in 50% yield only after heating at 120 °C for 24 hours (Table 1, entry 13). Poor electrophiles such as (RO)₂PCl, (R₂N)₂PCl and R₂NPCl₂ also reacted with terminal alkynes in the presence of Cu catalyst to give alkynyl phosphonites and phosphinites in high yields.

Terminal alkynes bearing alkyl and aryl substitutes at the triple bond could be introduced using this reaction with halogenophosphanes under the above conditionsThe use of Cu(I) catalyst makes it possible to carry out the reaction with alkynes containing sensitive functional groups (Table 1, entries 3, 10, 11) as well as alkynes bearing heteroaryl substituents (Table 1, entries 7–9). One should notice that the reaction with alkynes (Table 1, entries 3, 6, 10, 11) in the presence of Ni or Pd catalysts failed to provide efficiently products of cross-coupling since the reaction led to complex mixture of unidentified compounds.⁷

The mechanism of Cu-catalyzed cross-coupling may include either P–Cl bond activation as it proceeds under catalysis by Ni complexes⁷ or formation of copperacetylenic intermediate by reacting a Cu complex with a terminal alkyne in the presence of Et_3N .

We have demonstrated that the interaction of Ph₂PCl with CuI in toluene led to the formation of a complex. By performing an X-ray analysis it was shown that the above complex proved to be a tetrahedral complex bearing three molecules of chlorophosphane (Ph₂PCl)₃CuI (Figure 1).⁹ Assuming the above intermediate, the mechanism of Castro reaction looks most reasonable¹⁰ (Scheme 1).

Phosphinoalkynes 3; General Procedure

Chlorophosphane **1**, CuI (1 mol%), Et₃N, alkyne **2**, and solvent were mixed in a Schlenk flask and stirred for an appropriate period of time at r.t. (see Table 1 for molar amounts used). The progress of the reaction was monitored by ³¹P NMR measurements every hour. After completion of the reaction (disappearance of the signal of chlorophosphane), the ammonium salt was removed by filtration, and the solvent was evaporated under reduced pressure. The crude product was then purified by passing through a silica gel column (CH₂Cl₂–hexane) or distilled under reduced pressure (Table 1).

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Table 1 Cross-Coupling Chlorophosphanes and Chlorophosphites with Terminal Alkynes^a

Entry	Chlorophosphane	R' in	Product	Yield (%) ^b
		R'		
1	Ph_2PCl (1a)	Ph	Ph ₂ P— <u>—</u> Ph 3 a	99 (95) ^c
2	1a	$4-\text{MeC}_6\text{H}_4$	$Ph_2P \longrightarrow C_6H_4Me-4$	95 (92) ^c
3	1a	$4-MeOC_6H_4$	3 b Ph₂P─ ── C ₆ H₄OMe-4	99 (96) ^c
4	1a	$4-Me_2NC_6H_4$	3c Ph ₂ P $ -$ C ₆ H ₄ NMe ₂ -4	96 (93) ^c
5	1a	$2-Me_2NC_6H_4$	3d Ph₂P - C ₆ H₄NMe₂-2	98 (94) ^c
6	1a	$3-CF_3C_6H_4$	3e Ph₂P─ ── C ₆ H₄CF ₃ -3	95 (92) ^c
7	1a	2-pyridyl	3f Ph ₂ P- <u>-</u> -Py-2	99 (93) ^c
8	1a	2-thienyl	3g Ph₂P − Thienyl-2	94 (90) ^c
9	1a	6-quinolinyl	3h Ph ₂ P———Quinol6	96 (92) ^c
10	1a	MeOCH ₂	3i Ph ₂ P———CH ₂ OMe	83 (49) ^c
11	1a	Me ₂ NCH ₂	3j Ph ₂ P- \equiv -CH ₂ NMe ₂	96 (92) ^c
12	<i>i</i> -Pr ₂ PCl (1b)	Ph	3k ⊬Pr₂P────Ph	98 (80) ^c
13	t-Bu ₂ PCl (1c)	Ph	3I <i>t</i> -Bu ₂ P————————————————————————————————————	50 ^{c,d}
14	$PhPCl_2$ (1d)	Ph	3m PhP(Ph) ₂	99 (96) ^e
15	PCl ₃ (1e)	Ph	3n P(────Ph) ₃	98 (78) ^f
16	PCl ₃ (1e)	$4-MeC_6H_4$	30 P(95 (81) ^f
17		Ph	$3p$ $\begin{bmatrix} 0\\ 0 \end{bmatrix} P = Ph$	96 (42) ^{c.g}
18	1f (<i>i</i> -PrO) ₂ PCl (1g)	Ph	3q ^{i-PrO} PPh i-PrO	98 (36) ^{c,g}
19	$(Et_2N)_2PCl$ (1h)	Ph	$3\mathbf{r}$ (Et ₂ N) ₂ P———Ph	98 ^{c,g}
20	Et_2NPCl_2 (1i)	Ph	3s Et ₂ NP(Ph) ₂ 3t	99 ^{c,g}

^a Reaction conditions: chlorophosphane (1 mmol), CuI (1 mol%), toluene, r.t.

^b Based on ³¹P NMR spectrum, isolated yields are given in parentheses. ^c Alkyne (1.25 mmol), Et₃N (3 mmol), 6–8 h.

^d 120 °C, 24 h.

^e Alkyne (2.5 mmol), Et₃N (6 mmol), 4 h.

 $^{\rm f}$ Alkyne (3.75 mmol), Et₃N (9 mmol), 45 min.

^g Decomposes during distillation.







Figure 1 X-ray crystal structure of (Ph₂PCl)₃CuI⁹

Compounds were obtained in sufficiently pure state as indicated by their $^1\!H$ and $^{13}\!C$ NMR spectra. 11

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- As found from X-ray data (Figure 1), the copper atom in the (9)structure of (Ph₂PCl)₃CuI adopts a tetrahedral coordination. The copper and chlorine atoms are situated on either sides of the plane of phosphorus atoms. The Cu(1) atom is deviated from the plane of P(1), P(2) and P(3) atoms to 0.75 Å. Also, the chlorine atoms are antiperiplanar to the iodine atom, the torsion angle ClPCuI is equal to 167° on an average. X-ray investigation of structure 1 was carried out on Bruker Smart CCD 1000 diffractometer at 293 K. Crystals are monoclinic, $a = 20.381(4), b = 9.462(2), 20.411(4) \text{ Å}, \beta = 112.395(4)^{\circ},$ space group P21/c, Z = 4 M = 852.3, F(000) = 1696, μ [MoK& agr;] = 18.25 cm⁻¹. Intensities of 27979 reflections were measured and 10473 independent reflections were used for further refinement. The refinement was converged to wR2 = 0.0623 and GOF = 0.980 for all independent reflections [R1 = 0.0325 was calculated against F2 for 5790 observed reflections with $I > 2 \sigma(I)$]. Experimental and crystal data were submitted to Cambridge Crystallographic Data Centre.

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- (11) For example: 2-(2-Pyridyl)ethynyldiphenylphosphane(**3g**): Yield: 93%; light yellow solid; mp 32 °C. ³¹P{H} NMR (162.6 MHz, CDCl₃): $\delta = -34.44$ (s). ¹H NMR (400 MHz, CDCl₃): $\delta = 6.98$ (m, 1 H), 7.19 (m, 1 H), 7.21 (m, 7 H), 7.37 (m, 1 H), 7.61 (dt, 4 H, J = 1.4 Hz), 8.43 (m, 1 H). ¹³C NMR (100.6 MHz, CDCl₃): $\delta = 86.11$ (d, J = 9.8 Hz), 106.22,
- 122.74, 126.78, 128.15 (d, J = 7.6 Hz), 128.69, 132.30 (d, J = 21.3 Hz), 134.79 (d, J = 7.5 Hz), 135.55, 142.04, 149.46. (3-Methoxyprop-1-ynyl)(diphenyl)phosphane(**3j**): Yield: 49%; light yellow oil; bp 160 °C/0.1 Torr. ³¹P{H} NMR (162.6 MHz, CDCl₃): $\delta = -34.62$ (s). ¹H NMR (400 MHz, CDCl₃): $\delta = 3.31$ (s, 3 H), 4.17 (s, 2 H), 7.24 (m, 6 H), 7.61 (dt, 4 H, J = 1.7 Hz). ¹³C NMR (100.6 MHz, CDCl₃): $\delta =$ 57.23, 60.20, 83.22 (d, J = 7.6 Hz), 104.36, 128.26 (d, J = 7.6 Hz), 128.72, 132.14 (d, J = 21.3 Hz), 135.59.