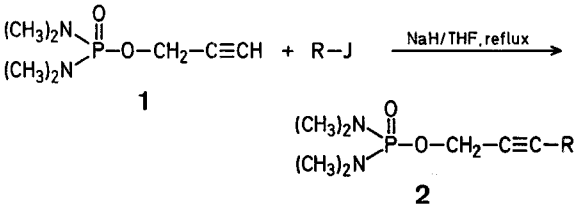
Synthesis of 2-Alkynyl Tetramethylphosphorodiamidates; A New Route to 1-Bromo-2-alkynes

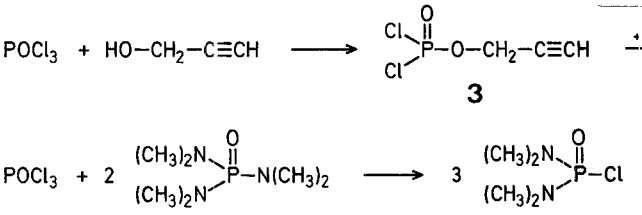
G. Sturtz, J. P. Paugam, B. Corbel

Laboratoire de Chimie Hétéroorganique, Faculté des Sciences, F-29283 Brest Cedex, France

During our studies on the synthetic potential of certain organophosphorus compounds we observed that 2-propynyl tetramethylphosphorodiamidate (**1**) can be C-alkylated with alkyl iodides in the presence of sodium hydride in tetrahydrofuran.



Compound **1** was prepared either from 2-propynyl phosphorodichloridate (**3**) and dimethylamine or from bis[dimethylamino]-chlorophosphine oxide and sodium 2-propynoxide.



The latter method is experimentally more convenient and gives better yields; it is carried out in tetrahydrofuran at −10°.

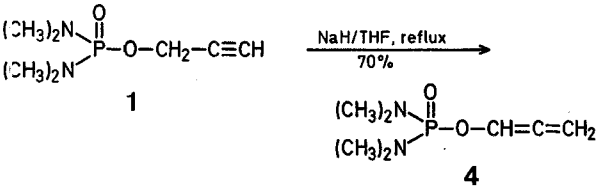
A few years ago, the metallation of alkynes by metal amides in hexamethylphosphoric triamide (HMPT) has been reported[1,2], and this method has also been used to alkylate terminal alkynes[3]. In view of the structural analogy of **1** with HMPT we assume that in our reaction compound **1** is not only a reaction partner but also plays in important role as solvent. In Table 1 are summarized the results obtained in the preparation of compounds **3**, **1**, and **2**.

All compounds **2** listed in Table 1 were prepared using the one-step alkylation procedure described in the experimental part. The two-step metallation-alkylation of compound **1** is not applicable, due to propargylic rearrangement caused by sodium hydride; the product is propadienyl tetramethylphosphorodiamidate (**4**), 30% of **1** being recovered unchanged.

Table 1. Yields and Physical Data of Compounds **3**, **1**, and **2** prepared

Compound	R	Yield (%)	b.p./ 0.01 torr	n_D^{20}
3	—	72	62°	n_D^{25}: 1.4625
1	—	95[a]	91°	1.4609
2a	CH_3	95	94°	1.4660
2b	C_2H_5	77[b]	99°	1.4638
2c	n-C_3H_7	59[b]	106°	1.4647
2d	n-C_4H_9	59[b]	112°	1.4651
2e	n-C_5H_{11}	34[b]	124°	1.4647

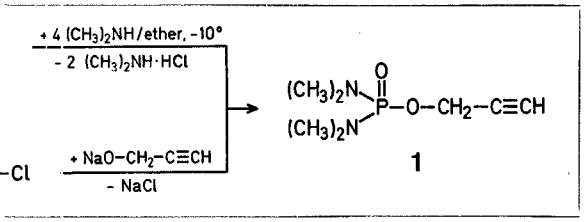
[a] Prepared by method B.
[b] Partial decomposition during distillation.



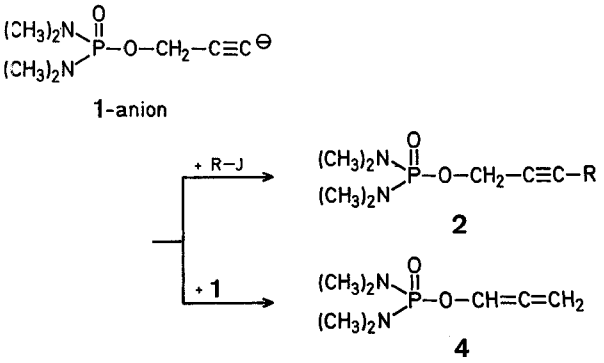
Compound **4** is also a by-product in our alkylation reaction; its yield increases with decreasing reactivity of the alkyl halide and with decreasing reagent: solvent ratio (see Table 2).

Table 2. Formation of Propadienyl Tetramethylphosphorodiamidate (**4**) in the Reaction of **1**-Anion with Alkyl Halides in Tetrahydrofuran

X–$(CH_2)_n$–CH_3	n=0	n=1	n=2		n=3	n=4	
	X=J	X=J	X=J	X=Br	X=J	X=J	
Yield (%) of **4**	0	1	8	65	10	15 (conc. solution)	26 (dil. solution)



The course of the reaction is thus determined by the rates of nucleophilic and electrophilic substitution.



The scope of the reaction is limited by the alkylating properties of the alkyl halide; i.e., the alkyl halide should

preferentially react with the carbanion of **1** and not undergo side reactions in the presence of the base.

Cleavage of the 2-alkynyl tetramethylphosphorodiamidates (**2**) with 48% hydrobromic acid or, better, freshly distilled phosphorus(III) bromide affords the corresponding 1-bromo-2-alkynes (**5**) in yields of ~50% and up to 80%, respectively.

$Br-CH_2-C\equiv C-(CH_2)_n-CH_3$ n = 0,1,2,3,4

5

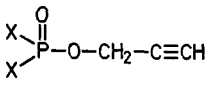
In the case of the cleavage with hydrobromic acid, addition of hydrogen bromide to the C≡C triple bond occurs as a side reaction.

Table 3. 1-Bromo-2-alkynes (**5**) by Brominative Cleavage of 2-Alkynyl Tetramethylphosphorodiamidates (**2**)

R	R	Yield (%) using HBr	Yield (%) using PBr_3	b.p./ 15 torr	n_D^{21}
a	CH_3	55	72	36°	1.5062
b	C_2H_5	53	72	44°	1.4971
c	n-C_3H_7	56	80	54°	1.4922
d	n-C_4H_9	57	73	76°	1.4889
e	n-C_5H_{11}	46	78	92°	1.4871

Using the method described here, 1-bromo-2-alkynes (**5**) may be prepared from the corresponding propargylic alcohols in yields ranging from 55 to 65% by treatment of the crude 2-alkynyl tetramethylphosphorodiamidates (**2**) with phosphorus(III) bromide (after removal of excess alkyl iodide in vacuo). Our new method might in some cases be advantageous over other known methods for the preparation of **5**, e.g., methods involving reaction of acetylenides with formaldehyde[4,5,6] or alkylation of other derivatives of propargyl alcohol in liquid ammonia[7,8,9].

We also carried out the alkylation-brominative cleavage reaction with 2-propynyl tetraalkylphosphorodiamidates other than **1**;



X = $(C_2H_5)_2N-$, $(n\text{-}C_4H_9)_2N-$,  ,  , 

there was, however, no improvement in yield[10].

The structures of all products obtained were established by I.R.- and N.M.R. spectrometry. The I.R. spectra were recorded on a Perkin Elmer model, type 257. The ^{1}H-N.M.R. spectra were recorded on a JEOL C 60 HL model, using 30% solutions in chloroform, and TMS as internal standard. G.L.C. analysis of the products was carried out on a Girdel 75 FD gas chromatograph. A 1/8 in ×5 ft column of 10% SE 30 on chromosorb W-HMDS 80–100 mesh was used for purity control of the products.

2-Propynyl Phosphorodichloridate (3):
Phosphoryl chloride (460 g, 3 mol) is placed in a 500-ml three-necked flask equipped with a mechanical stirrer, a thermometer, and a dropping funnel. The flask is cooled to 10° and propargyl alcohol (112 g, 2 mol) is added dropwise with stirring. After the addition is complete, the mixture is allowed to warm to room temperature and stirring is continued for 5 h. Hydrogen chloride is removed under reduced pressure and the residual black liquid is distilled in vacuo; yield: 72%; b.p. 62°/0.01 torr.

I.R. (film): $\nu_{C-H(ass)}$ = 3255 (s), $\nu_{C-H(free)}$ = 3295 (s), $\nu_{C\equiv C}$ = 2110 (m), ν_{P-O} = 1215 cm^{-1} (s).

^{1}H-N.M.R. ($CDCl_3$): δ = 4.75 (CH_2, J_{HP} = 14 Hz), 2.86 ppm (C≡CH, J_{HH} = 2.50 Hz).

2-Propynyl Tetramethylphosphorodiamidate (1):

Method A, from 2-Propynyl Phosphorodichloridate (**3**): A solution of dimethylamine (0.9 mol) in ether is placed in a 500-ml three-necked flask equipped with stirrer, thermometer, dropping funnel, and condenser. The flask is cooled to 10° and 2-propynyl phosphorodichloridate (**1**; 34.6 g) is added dropwise with stirring. The reaction is strongly exothermic, and dimethylamine hydrochloride precipitates. Stirring is continued at room temperature for 2 h. The amine hydrochloride is removed by filtration through a Büchner funnel. The solid on the filter is washed with chloroform and the filtrate is dried with sodium sulfate. The solvent is removed at reduced pressure and the residue is distilled in vacuo; yield: 85%; b.p. 91°/0.01 torr.

I.R. (film): $\nu_{C-H(ass)}$ = 3185 (s), $\nu_{C-H(free)}$ = 3285 (m), $\nu_{C\equiv C}$ = 2120 (m), ν_{P-O} = 1215 (s), ν_{P-N} = 755 cm^{-1} (s).

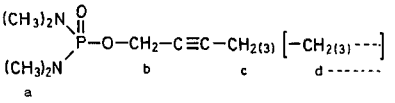
^{1}H-N.M.R. ($CDCl_3$): δ = 2.63 (CH_3, J_{HP} = 9.75 Hz), 4.54 (CH_2, J_{HP} = 10.35 Hz), 3.00 ppm (C≡CH, J_{HH} = 2.55 Hz).

Method B, from Bis[dimethylamino]-chlorophosphine Oxide and Propargyl Alcohol: A dry 1000-ml three-necked flask equipped with stirrer, thermometer, and dropping funnel is purged with dry nitrogen and charged with a 50% dispersion (48 g, 1 mol) of sodium hydride in mineral oil and with dry tetrahydrofuran (250 ml). A solution of propargyl alcohol (61.6 g, 1.1 mol) in tetrahydrofuran is then added with stirring dropwise at such a rate as to maintain the mixture at gentle reflux. After the addition is complete, the mixture is refluxed until the evolution of hydrogen has ceased (1–2 h). The mixture is then cooled to −20° and bis-[dimethylamino]-chlorophosphine oxide (170.5 g, 1 mol) is added dropwise with stirring. After the addition is complete, the mixture is allowed to warm to room temperature. Water (500 ml) is cautiously added, the mixture is extracted with chloroform, and the extracts are dried with sodium sulfate. The solvent is removed under reduced pressure and the residue is distilled in vacuo; yield: 95%.

Alkylation of 2-Propynyl Tetramethylphosphorodiamidate (2): General Procedure:
A suspension of sodium hydride (1 mol) in anhydrous tetrahydrofuran (200 ml) is placed in a 1000-ml three-necked flask equipped with stirrer, dropping funnel, and condenser. A solution of 2-propynyl tetramethylphosphorodiamidate (1 mol) and the alkyl iodide (1.2 mol) in anhydrous tetrahydrofuran (100 ml) is added dropwise with stirring at room temperature, gas evolution being controlled carefully. After the addition is complete, the mixture is refluxed. The reaction suddenly becomes violent and has to be slowed down by cooling the mixture with Dry Ice. The mixture is then held at gentle reflux until the evolution of hydrogen has ceased. Water (300 ml) is added, the mixture extracted with chloroform, and the extract dried with sodium sulfate. The solvent is removed at reduced pressure and the residual product distilled in vacuo.

I. R. (film): characteristic bands; $\nu_{C\equiv C}$ = 2236 (m), ν_{P-O} = 1220 (s), ν_{P-N} = 755 cm^{-1} (s).

^{1}H-N.M.R. ($CDCl_3$):



2a: δ_a = 2.65 (J_{H_aP} = 9.75 Hz), δ_b = 4.52 (J_{H_bP} = 9.90 Hz), δ_c = 1.88 ppm ($J_{H_bH_c}$ = 2.40 Hz).

2b: δ_a = 2.65 (J_{H_aP} = 9.75 Hz), δ_b = 4.52 (J_{H_bP} = 9.90 Hz), δ_c = 2.25 ($J_{H_bH_c}$ = 2.15 Hz), δ_d = 1.13 ppm ($J_{H_cH_d}$ = 7.50 Hz).

2c; $\delta_a = 2.65$ ($J_{H_aP} = 9.75$ Hz), $\delta_b = 4.52$ ($J_{H_bP} = 9.90$ Hz), $\delta_c = 2.15$ ($J_{H_bH_c} = 2.15$), $\delta_d = 1.47$, $\delta_e = 1.00$ ppm.

2d; $\delta_a = 2.65$ ($J_{H_aP} = 9.75$ Hz), $\delta_b = 4.52$ ($J_{H_bP} = 9.90$ Hz), $\delta_c = 2.15$ ($J_{H_bH_c} = 2.15$ Hz), $\delta_d + \delta_e = 1.45$, $\delta_f = 0.92$ ppm.

2e; $\delta_a = 2.65$ ($J_{H_aP} = 9.75$ Hz), $\delta_b = 4.52$ ($J_{H_bP} = 9.90$ Hz), $\delta_c = 2.25$ ($J_{H_bH_c} = 2.15$ Hz), $\delta_d + \delta_e + \delta_f = 1.40$, $\delta_g = 0.92$ ppm.

Preparation of 1-Bromo-2-alkynes (5); General Procedure:

Method A; Cleavage of **2** with Hydrobromic Acid: In a three-necked flask fitted with stirrer, dropping funnel, and condenser, 48% hydrobromic acid (60 ml) is added with stirring to a solution of the 2-alkynyl tetramethylphosphorodiamidate (**2**; 0.1 mol) in ether (120 ml) at 5°. The reaction is strongly exothermic. The mixture is stirred for 2 h. The layers are then separated, the aqueous phase is extracted with ether, the organic phases are washed with aqueous sodium hydrogen carbonate, and dried with sodium sulfate. The solvent is removed and the residual product distilled in vacuo.

Method B; Cleavage of **2** with Phosphorus(III) Bromide: A solution of the 2-alkynyl tetramethylphosphorodiamidate (**2**; 0.1 mol) in anhydrous ether (75 ml) is placed in a 250-ml three-necked flask fitted with stirrer, dropping funnel, and condenser. To this is added freshly distilled phosphorus(III) bromide (10 ml) dropwise with stirring at room temperature. The mixture is heated to reflux for 4 h. It is then allowed to cool to room temperature: water (50 ml) is added and the mixture extracted with ether. The organic phases are washed with saturated aqueous sodium hydrogen carbonate and dried with sodium sulfate. The solvent is evaporated and the residual product distilled in vacuo.

I.R. (film):

5a; $\nu_{C\equiv C} = 2240$ (s), $\nu_{C-Br} = 1215$ cm^{-1} (s).

5b; $\nu_{C\equiv C} = 2240$ (s), $\nu_{C-Br} = 1205$ cm^{-1} (s).

5c; $\nu_{C\equiv C} = 2235$ (s), $\nu_{C-Br} = 1205$ cm^{-1} (s).

5d; $\nu_{C\equiv C} = 2235$ (s), $\nu_{C-Br} = 1205$ cm^{-1} (s).

5e; $\nu_{C\equiv C} = 2235$ (s), $\nu_{C-Br} = 1205$ cm^{-1} (s).

^{1}H-N.M.R. ($CDCl_3$):

$$\underset{a}{Br-CH_2}-C\equiv C-\underset{b}{CH_{2(3)}}\left[-\underset{c}{CH_{2(3)}}\cdots\right]$$

5a; $\delta_a = 3.92$ ($J_{H_aH_b} = 2.65$ Hz), $\delta_b = 1.91$ ppm.

5b; $\delta_a = 3.95$ ($J_{H_aH_b} = 2.32$ Hz), $\delta_b = 2.31$ ($J_{H_bH_c} = 7.50$ Hz), $\delta_c = 1.13$ ppm.

5c; $\delta_a = 4.00$ ($J_{H_aH_b} = 2.40$ Hz), $\delta_b = 2.27$, $\delta_c = 1.58$, $\delta_d = 1.03$ ppm.

5d; $\delta_a = 3.96$ ($J_{H_aH_b} = 2.40$ Hz), $\delta_b = 2.27$, $\delta_c + \delta_d = 1.46$, $\delta_e = 0.95$ ppm.

5e; $\delta_a = 3.87$ ($J_{H_aH_b} = 2.40$ Hz), $\delta_b = 2.25$, $\delta_c + \delta_d + \delta_e = 1.47$, $\delta_f = 0.94$ ppm.

Received: June 26, 1974

[1] H. Normant, *Angew. Chem.* **79**, 1029 (1967); *Angew. Chem. Internat. Edit.* **6**, 1046 (1967).

[2] T. Cuvigny, *Bull. Soc. Chim. France* **1965**, 1872.

[3] J. F. Normant, *Bull. Soc. Chim. France* **1965**, 859.

[4] G. Smets, *Mem. Acad. Belg.* [8] **21**, 51 (1947); *C.A.* **44**, 8315 (1950).

[5] C. Michel, S. Tchelitcheff, *Bull. Soc. Chim. France* **1964**, 2230.

[6] A. Schaap, L. Brandsma, J. F. Arens, *Rec. Trav. Chim.* **84**, 1200 (1965).

[7] W. H. Kunau, *Chem. Phys. Lipids* **7**, 101 (1971).

[8] J. M. Conia, *Bull. Soc. Chim. France* **1955**, 1449.

[9] R. Couffignal, M. Gaudemar, P. Perriot, *Bull. Soc. Chim. France* **1967**, 3909.

[10] G. Sturtz, J. P. Paugam, B. Corbel, P. Vuillefroy de Silly, *French Patent* 7325634 (1973), Anvar.