Selective *C*-mono- and *C,C*-dialkylation of thiophosphorylacetonitriles

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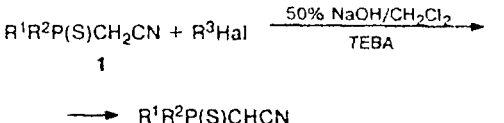
Alkylation of thiophosphorylacetonitriles under phase transfer catalysis conditions in the 50% $NaOH/CH_2Cl_2$ system proceeds as monoalkylation, whereas alkylation in MeCN with the use of solid KOH as a base gives a disubstituted product. The order in which the reagents were added as well as dilution of the reaction mixture affected substantially the yields of the target compounds. X-ray diffraction analysis of a single crystal of dibutyl(diphenylthiophosphoryl)acetonitrile was carried out.

Key words: thiophosphorylacetonitriles, alkylation; haloalkanes; phase transfer catalysis; NMR spectra; dibutyl(diphenylthiophosphoryl)acetonitrile, X-ray diffraction analysis.

It is known[1] that classical methods of alkylation of compounds that contain the activated methylene group (phosphorus-substituted acetonitriles belong to these compounds) usually afford a mixture of products of mono- and dialkylation. However, when the method of phase transfer catalysis (PTC) is used, the selectivity of the reactions can be often achieved by changing the reaction conditions. Thus, monoalkylation of dialkoxyphosphorylacetonitriles with iodoalkanes was carried out under the conditions of ion-pair extraction in CH_2Cl_2 at 45 °C (1 h) in the presence of a 0.5 *N* NaOH solution (the yields of the products were 30—80%).[2] Monoalkylation of the analogs of these compounds that contain dialkylamide groups at the P atom proceeded under the conditions of both ion-pair extraction (at 20 °C) and PTC (10 mol.% of triethylbenzylammonium chloride (TEBA)) in the absence of a solvent.[3] *C,C*-Dialkylation of dialkoxyphosphorylacetonitriles proceeded under the action of chloro-, bromo-, and iodoalkanes in the conditions of ion-pair extraction without a solvent at 60 °C in the presence of a 50% NaOH solution (the yields were 46—88%).[4] Alkylation with dibromomethane under these conditions yielded the product of cycloalkylation, namely, 1-diethoxyphosphoryl-1-cyanocyclopropane.[4] Cycloalkylation of phosphoryl- and thiophosphorylacetonitriles with α,ω-dihaloalkanes under the phase transfer catalysis conditions (K_2CO_3/DMSO) has been studied in detail previously.[5,6]

With the aim of developing simple methods for the preparative synthesis of *C*-mono- and *C,C*-dialkyl-substituted thiophosphorylacetonitriles, we studied their alkylation under the PTC conditions. It was found that the reactions of thiophosphorylacetonitriles (**1**) with bromo- and iodoalkanes in a mixture of 50% aqueous NaOH and CH_2Cl_2 at 20 °C using 5 mol.% TEBA* as a catalyst proceeded readily to form products of monoalkylation (**2**) in high yields (83—93%, Table 1). The ratio of the reagents under these conditions had virtually no effect on the direction of the reaction (Table 2; see, for example, runs *6* and *7*). Only methylation of compounds **1** with a more than twofold excess of MeI afforded the product of dialkylation (**3**) in a yield of up to 15% (see Table 2, runs *1* and *2*). The yields of monoalkyl-substituted thiophosphorylacetonitriles **2** were substantially affected by the amount of the solvent used. Thus, when the reaction mixture was diluted, the reaction did not proceed to completion, and therefore, the yields of the target compounds decreased (*cf.* Table 2, runs *3* and *4* and runs *5* and *6*).



$R^1 = R^2 = OBu^n$, Ph; R^1 = Me, $R^2 = OPr^i$, OBu^i; R^3 = Me, Et, Bu^n; Hal = Br, I

When the phosphoryl compounds $R^1R^2P(O)CH_2CN$ (R^1 and $R^2 = OPr^n$ or Ph) reacted with haloalkanes under the conditions that are optimum for thiophosphorylacetonitriles **1**, the major direction of the reaction was also monoalkylation** (the yields of the

† Deceased.

* In the presence of other ammonium salts as a catalyst under PCT conditions, the yields of compounds **2** decreased (see Table 2, run *10*).

** According to the data of ^{31}P NMR spectroscopy of the organic phase.

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Table 1. Yields, physicochemical characteristics, and data of elemental analysis of the $R^1R^2P(S)C(R^3)(R^4)CN$ compounds (**2—4**)

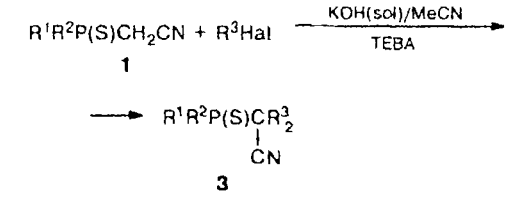
Compound	R^1R^2	R^3	R^4	Yield[a] (%)	M.p./°C (solvent) [B.p./°C (*p*/Torr)]	n_D^{20}	Found / Calculated (%) C	H	N	P	S	Molecular formula
2a	$(BuO)_2$	Me	H	90 (74)	[145—150 (1)]	1.4740	50.55 50.17	8.71 8.42	5.49 5.32	11.99 11.76	12.05 12.18	$C_{11}H_{22}NO_2PS$
2b	$Me(OBu^i)$	Me	H	87 (65)[b]	[117 (0.1)]	1.4918	47.14 46.81	7.63 7.86	—	15.09 15.09	15.47 15.62	$C_8H_{16}NOPS$
2c	Ph_2	Me	H	93 (81)	78—79 (EtOH)	—	66.48 66.42	5.63 5.17	5.00 5.17	—	—	$C_{15}H_{14}NPS$
2d	$Me(OPr^i)$	Et	H	88 (76)	[115 (0.1)]	1.4961	46.61 46.82	7.84 7.86	—	—	—	$C_8H_{16}NOPS$
2e	$Me(OBu^i)$	Et	H	90 (81)	[115 (0.1)]	1.4920	49.14 49.30	8.00 8.27	6.40 6.39	13.89 14.12	14.68 14.62	$C_9H_{18}NOPS$
2f	Ph_2	Et	H	84 (75)	135 (EtOH)	—	68.16 67.35	5.90 5.65	4.96 4.91	—	—	$C_{16}H_{16}NPS$
2g	Ph_2	Bu	H	83 (71)	93—94 (heptane)	—	69.58 69.01	6.50 6.39	4.48 4.47	—	—	$C_{18}H_{20}NPS$
3a	$(BuO)_2$	Me	Me	Quantitative (80)	[148—150 (1)]	1.4719	52.33 51.96	9.05 8.72	4.89 5.05	11.14 11.17	11.07 11.56	$C_{12}H_{24}NO_2PS$
3b[c]	Ph_2	Me	Me	Quantitative (85)	124 (EtOH)	—	67.06 67.37	5.86 5.61	4.86 4.91	10.69 10.88	11.29 11.23	$C_{16}H_{16}NPS$
3c	$(BuO)_2$	Et	Et	Quantitative (77)	[130 (0.5)]	1.4750	54.61 55.06	9.07 9.24	4.36 4.59	9.69 10.14	10.84 10.50	$C_{14}H_{28}NO_2PS$
3d	Ph_2	Et	Et	Quantitative (64)	69—70 (heptane)	—	69.38 68.98	6.78 6.43	4.33 4.47	9.45 9.88	10.14 10.23	$C_{18}H_{20}NPS$
3e	Ph_2	Bu	Bu	51 (37)	101—102 (EtOH)	—	71.76 71.54	7.82 7.59	3.76 3.79	—	—	$C_{22}H_{28}NPS$
4a	$Me(OPr^i)$	Me	Et	Quantitative (82)	[126—128 (0.1)]	1.4946	48.90 49.32	8.23 8.22	6.37 6.39	13.79 14.16	15.07 14.61	$C_9H_{18}NOPS$
4b	Ph_2	Me	Et	85 (65)[b]	112—114 (EtOH)	—	68.55 68.23	6.22 6.02	4.40 4.68	—	—	$C_{17}H_{18}NPS$

[a] According to the data of ^{31}P NMR spectroscopy (the yield of the purified product is given in parentheses).
[b] Purified by chromatography (40—100 silica gel, a hexane—acetone (**2b**) or pentane—ether (**4b**) mixture was used as the eluent).
[c] Published data:[14] the yield was 33%, m.p. 125—127 °C.

dialkylated products were 15—20%). However, the yields of the target compounds decreased substantially due to the cleavage of the P—C bond and hydrolysis of the alkoxy groups at the P atom as a result of which salts of the corresponding phosphorus acids of the $R^1(NaO)P(O)CH_2CN$ and $R^1R^2P(O)ONa$ types (these salts remained in the aqueous phase) were obtained. This is in agreement with the published data.[7]

The KOH(sol)/MeCN system appeared to be most efficient in the preparation of products of *C,C*-dialkylation of thiophosphorylacetonitriles **3** (method *A*).

It should be noted that for all haloalkanes, except for MeI, the order in which the reagents were added played a decisive role. Products of dialkylation **3** were obtained in high yields (84—100%, see Tables 1 and 2, runs *12* and *13*) when dry powdered KOH was added portionwise to a mixture of the initial reagents (taken in a **1** : R^3Hal ratio of 1.0 : 2.5) in MeCN. The reactions with iodoalkanes gave products in the highest yields. However, an increase in the alkyl chain length of the alkylat-



$R^1 = R^2 = OBu^n$, Ph; R^1 = Me, $R^2 = OPr^i$, OBu^i; R^3 = Me, Et, Bu^n; Hal = Br, I

Table 2. Effect of the reaction conditions on the yields of the alkylation products

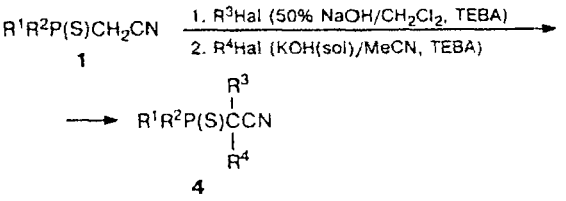
Run	R^1R^2	R^3Hal	Reaction conditions			Yield (%)[a]		
			1 : R^3Hal	1/solvent	order in which the reagents were added	1	2	3
				In the 50% NaOH/CH_2Cl_2 mixture				
1	$(BuO)_2$	MeI	1.0 : 1.2	0.01 mol/10 mL	Addition of RHal to a mixture of the reagents	—	94	6
2	$(BuO)_2$	MeI	1.0 : 2.5	The same	The same	—	85	15
3	Me(OPr^i)	MeI	1.0 : 1.5	0.01 mol/20 mL	The same	20	80	—
4	Me(OPr^i)	EtI	1.0 : 1.5	The same	The same	43	57	—
5	Me(OPr^i)	MeI	1.0 : 1.5	0.01 mol/10 mL	The same	—	Quantitative	—
6	Me(OPr^i)	EtI	1.0 : 1.5	The same	The same	12	88	—
7	Me(OPr^i)	EtI	1.0 : 2.5	The same	The same	13	87	—
8	Ph_2	MeI	1.0 : 1.2	The same	The same	—	Quantitative	—
9	Ph_2	EtI	1.0 : 1.2	The same	The same	5	95	—
10[b]	Ph_2	EtI	1.0 : 1.2	The same	The same	31	69	—
11	Ph_2	BuI	1.0 : 1.2	The same	The same	5	95	—
				In the KOH(sol)/MeCN system				
12	Ph_2	EtBr	1.0 : 2.5	1 g/10 mL	Portionwise addition of KOH to a mixture of the reagents (method *A*)	16	—	84
13	Ph_2	EtI	1.0 : 2.5	The same	The same	—	—	Quantitative
14	Ph_2	BuI	1.0 : 2.5	The same	The same	10	39	51
15	Ph_2	BuI	1.0 : 2.5	1 g/40 mL	The same	10	52	38
16	Ph_2	EtBr	1.0 : 2.5	1 g/10 mL	Rapid addition of RHal to a mixture of the reagents	12	33	55
17	Ph_2	EtI	1.0 : 2.5	The same	The same	4	42	54
18	Ph_2	BuBr	1.0 : 2.5	The same	The same	14	66	20
19	Ph_2	$C_7H_{15}Br$	1.0 : 2.5	The same	The same	14	69	17
20	Ph_2	EtBr	1.0 : 2.5	The same	Slow addition of RHal to a mixture of the reagents	22	64	14
21	Ph_2	MeI	1.0 : 1.2	1 g/40 mL	Mixture of all reagents	50	—	50
22	Ph_2	MeI	1.0 : 2.2	The same	The same	—	—	Quantitative

[a] The yield according to the data of ^{31}P NMR spectroscopy.
[b] Bu_4NCl as a catalyst.

ing reagent resulted in a decrease in the yield of the target product (see Table 2, runs *13* and *14*). In this case, when the reaction mixture was diluted, the yield of the product of dialkylation **3** also decreased (see Table 2, runs *14* and *15*). A different situation was observed when haloalkane was rapidly added to a mixture of the initial compound, KOH, and TEBA in MeCN. The reaction yielded a mixture of products of monoalkylation **2** and dialkylation **3**. In this case, the yields of compounds **2** increased as the length of the alkyl radical of the alkylating reagent increased (see Table 2, runs *16*, *18*, and *19*) as well as when iodoalkanes were used (see Table 2, runs *16* and *17*). Slow addition of haloalkane resulted in an increase in the yield of the product of monosubstitution **2** (see Table 2, run *20*). However, alkylation of thiophosphorylacetonitriles with more electrophilic MeI afforded dimethylated compounds **3** regardless of the order in which the reagents were added, their ratio, and their concentrations in the solution (see Table 2, runs *21* and *22*).

Interestingly, we failed to perform alkylation of phosphorylacetonitriles under these conditions, and only the products of the cleavage of the P—C bond, $R^1R^2P(O)OH$, were obtained.

When the reaction was carried out successively in CH_2Cl_2 and MeCN, we succeeded in synthesizing disubstituted products **4** that contain different alkyl substituents at the central carbon atom (method *B*).



R^1 = Me, R^2 = OPr^i; R^1 = R^2 = Ph; R^3 = Me; R^4 = Et

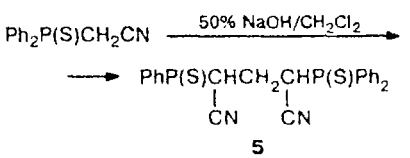
It is known[8,9] that generally, alkylation with secondary haloalkanes proceeds more slowly to form products

Table 3. Selected parameters of the ^1H, ^{31}P, and ^{13}C NMR spectra (δ, *J*/Hz) of compounds **2—4**

Compound	δ ^{31}P	δ ^1H			δ ^{13}C		
		CH ($^2J_{PH}/^3J_{HH}$)[b] or ($^2J_{PH}/^3J_{HHA}/^3J_{HHB}$)[c]	CH_3—C—P ($^3J_{PH}$)	CH_2—C—P ($^3J_{PH}$)	P—C—CN ($^1J_{PC}$)	P—C(CN)—C	CN ($^3J_{PC}$)
2a	87.2	2.66 (dq, *J* = 20.4/7.2)	1.25 (dd, *J* = 19.0)	—	—	—	—
2b[d]	93.5	2.99 (dq, *J* = 12.4/7.3)	1.56 (dd, *J* = 16.3)	—	32.1 (d, *J* = 67.3)	12.7 (s)	117.8 (s)
	91.3	3.04 (dq, *J* = 16.3/7.3)	1.58 (dd, *J* = 15.4)		31.5 (d, *J* = 66.6)	12.2 (s)	117.7 (d, *J* = 1.5)
2c	47.2	3.60 (dq, *J* = 14.2/7.2)	1.54 (dd, *J* = 16.4)	—	29.90 (d, *J* = 49.6)	12.2 (s)	117.9 (d, *J* = 4.0)
2d[d]	89.6	2.54 (ddd, *J* = 13.3/11.1/4.1)	—	1.53—1.67 (m, H_A);[e] 1.76—1.84 (m, H_B)	—	—	—
	88.1	2.64 (ddd, *J* = 18.8/11.2/4.2)	—				
2e[d]	91.6	2.25 (m)	—	1.60—1.68 (m, H_A);[e] 1.77—1.90 (m, H_B)	—	—	—
	89.8	2.48 (ddd, *J* = 19.6/11.1/4.2)	—				
2f	45.0	3.43 (ddd, *J* = 14.6/11.5/3.8)	—	1.68—1.75 (m, H_A); 2.05—2.10 (m, H_B)	—	—	—
2g	45.6	3.46 (ddd, *J* = 14.8/11.4/3.4)	—	1.62—1.69 (m, H_A); 1.97—2.03 (m, H_B)	—	—	—
3a	93.6	—	1.40 (d, *J* = 17.3)	1.62—1.69 (m, H_A); 1.97—2.03 (m, H_B)	—	—	—
3b	55.1	—	1.58 (d, *J* = 15.4)	—	33.6 (d, *J* = 49.7)	21.9 (s)	123.0 (d, *J* = 2.0)
3c	92.8	—	—	—	—	—	—
3d	53.3	—	—	1.95 (H_A, *J* = 13.0);[f] 2.04 (H_B, *J* = 12.3)	38.0 (d, *J* = 49.0)	26.9 (s)	121.3 (s)
3e	53.4	—	—	—	—	—	—
4a	98.2		1.35 (d, *J* = 17.5)	1.59—1.65 (m, H_A);[e] 1.82—1.90 (m, H_B)	41.3 (d, *J* = 71.4)	16.7 (s, $\underline{C}H_3$—C—P); 26.4 (s, $\underline{C}H_2$—C—P)	119.6 (d, *J* = 3.8)
	98.0		1.37 (d, *J* = 15.8)		41.5 (d, *J* = 70.7)	17.7 (s, $\underline{C}H_3$—C—P); 25.3 (s, $\underline{C}H_2$—C—P)	119.5 (d, *J* = 4.0)
4b	54.9	—	1.52 (d, *J* = 16.1)	1.68—1.92 (m, H_A); 1.94—2.14 (m, H_B)	38.8 (d, *J* = 50.1)	18.1 (s, $\underline{C}H_3$—C—P); 26.5 (s, $\underline{C}H_2$—C—P)	121.6 (s)

[a] The ^{31}P and ^1H NMR spectra were recorded in C_6D_6 (**2a,e, 3a,c,d**) and $CDCl_3$ (**2b—d,f,g, 3b—e, 4a,b**); and the ^{13}C NMR spectra were obtained in C_6D_6 (**2b, 3b,d**) and $CDCl_3$ (**2c, 4a,b**).
[b] For compounds **2a—c**.
[c] For compounds **2d—g**.
[d] Two racemic mixtures of diastereomers in a ratio of 56 : 44.
[e] The signals of the methylene protons of the diastereomers overlap.
[f] $^2J_{HH}$ = 14.3 Hz.

in lower yields compared to the corresponding reactions with primary haloalkanes both under the classical conditions and under the conditions of phase transfer catalysis. It should be noted that thiophosphorylacetonitriles **1** did not undergo alkylation with secondary haloalkanes in any of the above-described systems. When the reaction with diphenylthiophosphorylacetonitrile was carried out in CH_2Cl_2, the product of interaction with the solvent, namely, 2,4-bis(thiophosphoryl)glutaronitrile (**5**), was formed in a yield of 10%.



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The compositions and structures of compounds **2—4** were confirmed by the data of elemental analysis and ^1H, ^{31}P, and ^{13}C NMR spectroscopy (Tables 1 and 3). In the ^{31}P NMR spectra, the δP signal shifts downfield

compared to unsubstituted compounds **1** as thiophosphorylacetonitriles **1** are alkylated, *i.e.*, as the number of alkyl groups at the α-C atom increases. For monoalkylated derivatives **2**, $\Delta\delta P$ = 5.3—11.0. For dialkyl-substituted products **3**, $\Delta\delta P$ = 11.2—18.9. The maximum shift of the signal is observed for the derivatives of diphenylthiophosphorylacetonitrile (for $Ph_2P(S)CH_2CN$, δP is 36.0[10]). In the ^{13}C NMR spectra of compounds **2**—**4**, the doublet of the central C atom and the signal of the C atom of the nitrile group also shift downfield in the course of alkylation of the compounds, while the value of the spin-spin coupling constant $^1J_{PC}$ remains virtually unchanged.

In the ^1H NMR spectra of monoalkylated products **2**, the signals of the methine proton appear as a doublet of quadruplets in the case of R^3 = Me (**2a—c**) or as a doublet of doublets of doublets when the number of carbon atoms in the alkyl substituent increases, which is attributable to the magnetic nonequivalence of the protons of the methylene group of the substituents at the α-C atom. It should be noted that the value of the spin-spin coupling constant $^3J_{PH}$ is comparable with (and in some cases, are larger than) the value of $^2J_{PH}$.

Table 4. Bond lengths and bond angles in the structure of 3e

Bond	*d*/Å	Bond	*d*/Å
P(1)—C(9)	1.822(3)	C(7)—C(8)	1.385(4)
P(1)—C(3)	1.822(3)	C(9)—C(10)	1.389(4)
P(1)—C(1)	1.899(3)	C(9)—C(14)	1.400(4)
P(1)—S(1)	1.9447(9)	C(10)—C(11)	1.377(5)
N(1)—C(2)	1.136(4)	C(11)—C(12)	1.382(5)
C(1)—C(2)	1.470(4)	C(12)—C(13)	1.382(5)
C(1)—C(15)	1.543(4)	C(13)—C(14)	1.382(5)
C(1)—C(19)	1.563(4)	C(15)—C(16)	1.523(5)
C(3)—C(8)	1.389(4)	C(16)—C(17)	1.514(6)
C(3)—C(4)	1.390(4)	C(17)—C(18)	1.500(6)
C(4)—C(5)	1.394(5)	C(19)—C(20)	1.521(4)
C(5)—C(6)	1.382(6)	C(20)—C(21)	1.515(4)
C(6)—C(7)	1.383(5)	C(21)—C(22)	1.520(5)

Angle	ω/deg	Angle	ω/deg
C(9)—P(1)—C(3)	105.7(1)	C(5)—C(6)—C(7)	119.5(3)
C(9)—P(1)—C(1)	104.4(1)	C(6)—C(7)—C(8)	120.4(3)
C(3)—P(1)—C(1)	108.6(1)	C(7)—C(8)—C(3)	119.9(3)
C(9)—P(1)—S(1)	114.2(1)	C(10)—C(9)—C(14)	119.3(3)
C(3)—P(1)—S(1)	112.9(1)	C(10)—C(9)—P(1)	119.0(2)
C(1)—P(1)—S(1)	110.5(1)	C(14)—C(9)—P(1)	121.6(2)
C(2)—C(1)—C(15)	111.9(2)	C(11)—C(10)—C(9)	120.4(3)
C(2)—C(1)—C(19)	108.5(2)	C(10)—C(11)—C(12)	120.3(3)
C(15)—C(1)—C(19)	113.5(2)	C(11)—C(12)—C(13)	119.7(3)
C(2)—C(1)—P(1)	108.7(2)	C(14)—C(13)—C(12)	120.7(3)
C(15)—C(1)—P(1)	108.9(2)	C(13)—C(14)—C(9)	119.6(3)
C(19)—C(1)—P(1)	105.1(2)	C(16)—C(15)—C(1)	116.7(3)
N(1)—C(2)—C(1)	178.2(3)	C(17)—C(16)—C(15)	113.9(3)
C(8)—C(3)—C(4)	120.1(3)	C(18)—C(17)—C(16)	113.8(4)
C(8)—C(3)—P(1)	123.4(2)	C(20)—C(19)—C(1)	117.3(3)
C(4)—C(3)—P(1)	116.5(2)	C(21)—C(20)—C(19)	111.3(3)
C(3)—C(4)—C(5)	119.2(3)	C(20)—C(21)—C(22)	112.8(3)
C(6)—C(5)—C(4)	120.8(3)		

In the case of different substituents at the P atom, the molecules of compounds **2** and **4** (**2b,d,e** and **4a**) contain two asymmetric atoms (α-C and P). This is responsible for the presence of two diastereomers, each is a racemic mixture of two enantiomers (in the ^{31}P NMR spectra, two singlets correspond to these diastereomers). In the ^1H and ^{13}C NMR spectra, the numbers of the signals are doubled. The ratio of the enantiomeric pairs of compounds **2** is close to the statistical value (56 : 44).

The structure of dibutyl(diphenylthiophosphoryl)-acetonitrile (**3e**) in the crystal was established by X-ray diffraction analysis. The overall view of molecule **3e** and the atomic numbering scheme are shown in Fig. 1. The bond lengths and bond angles are given in Table 4. The principal torsion angles are listed in Table 5. The geometric parameters of molecule **3e** are close to the expected values.[11] The phosphorus atom has a somewhat distorted tetrahedral configuration: the bond angles at the P atom are in the range of 104.4(1)—114.2(1)°. As is usually the case in the structures of α-phosphorus-substituted ω-haloalkanes,[12] the S=P—C angles are slightly larger than the C—P—C angles (see Table 4). The P—S and P—C bond lengths in the diphenylthiophosphoryl fragment (P—S is 1.9447(9) Å, and P(1)—C(Ph) is 1.822(3) Å) in dibutyl-substituted thiophosphorylacetonitrile **3e** are close to the analogous values in the molecule of triphenylphosphine sulfide

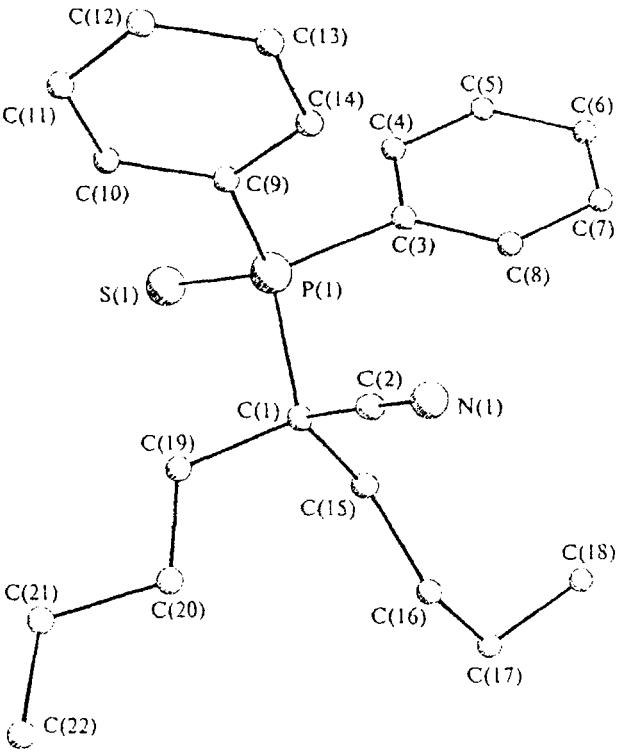

Fig. 1. Structure of the molecule of dibutyl(diphenylthiophosphoryl)acetonitrile (**3e**).

Table 5. Principal torsion angles (τ) in the structure of **3e**

Angle	τ/deg	Angle	τ/deg	Angle	τ/deg
C(9)—P(1)—C(1)—C(2)	−43.4(2)	P(1)—C(1)—C(2)—N(1)	133.12(9)	S(1)—P(1)—C(9)—C(14)	−158.6(2)
C(3)—P(1)—C(1)—C(2)	69.0(2)	C(9)—P(1)—C(3)—C(8)	84.8(3)	C(2)—C(1)—C(15)—C(16)	42.4(4)
S(1)—P(1)—C(1)—C(2)	−166.6(2)	C(1)—P(1)—C(3)—C(8)	−26.7(3)	C(19)—C(1)—C(15)—C(16)	−80.8(4)
C(9)—P(1)—C(1)—C(15)	−165.5(2)	S(1)—P(1)—C(3)—C(8)	−149.6(2)	C(12)—C(15)—C(16)—P(1)	162.5(3)
C(3)—P(1)—C(1)—C(15)	−53.1(2)	C(9)—P(1)—C(3)—C(4)	−94.9(2)	C(1)—C(15)—C(16)—C(17)	−177.9(3)
S(1)—P(1)—C(1)—C(15)	71.3(2)	C(1)—P(1)—C(3)—C(4)	153.5(2)	C(15)—C(16)—C(17)—C(18)	69.7(6)
C(9)—P(1)—C(1)—C(19)	72.6(2)	S(1)—P(1)—C(3)—C(4)	30.6(3)	C(2)—C(1)—C(19)—C(20)	−47.3(4)
C(3)—P(1)—C(1)—C(19)	−175.0(1)	C(1)—P(1)—C(9)—C(10)	−97.5(2)	C(15)—C(1)—C(19)—C(20)	77.8(3)
S(1)—P(1)—C(1)—C(19)	−50.6(2)	S(1)—P(1)—C(9)—C(10)	23.2(3)	P(1)—C(1)—C(19)—C(20)	−163.4(3)
C(15)—C(1)—C(2)—N(1)	−106.7(4)	C(3)—P(1)—C(9)—C(14)	−33.9(3)	C(1)—C(19)—C(20)—C(21)	176.3(3)
C(19)—C(1)—C(2)—N(1)	19.4(5)	C(1)—P(1)—C(9)—C(14)	80.6(2)	C(19)—C(20)—C(21)—C(22)	−174.2(3)

$Ph_3P{=}S$ (1.950(2) Å and 1.817(6) Å, respectively).[12] However, in molecule **3e**, the P(1)—C(1) bond (1.899(3) Å) is substantially elongated. For example, the length of the analogous bond between the P and C atoms of the alkyl fragment in diphenylphosphine sulfide $Ph_2P(S)Alk$ is 1.815(5) Å (Alk = $(CH_2)_3OH$).[13] Apparently, the P(1)—C(1) bond in the molecule of the compound under study is elongated due to the steric repulsion between the phenyl rings and the cyano group.

The thiophosphoryl and cyano groups are in the mutually antiperiplanar orientations (the S(1)—P(1)—C(1)—C(2) torsion angle is −166.6(2)°). The orientation of the phenyl rings relative to the thiophosphoryl group is characterized by the S(1)—P(1)—C(3)—C(8) and S(1)—P(1)—C(9)—C(10) torsion angles (−149.7(2)° and 23.2(3)°, respectively). It should be noted that the butyl substituents in molecule **3e** adopt different conformations. Thus, the C(19)C(20)C(21)C(22) fragment adopts the transoid conformation, and the second butyl group, C(5)C(16)C(17)C(18), adopts the *trans-gauche* conformation (the C(1)—C(15)—C(16)—C(17) and C(15)—C(16)—C(17)—C(18) torsion angles are −177.9(3)° and 69.7(6)°, respectively).

Analysis of the crystal packing of molecules **3e** demonstrated that the intermolecular and intramolecular distances correspond to the normal van der Waals interactions.

To summarize, we have developed simple and convenient methods for the synthesis of *C*-mono and *C,C*-dialkyl-substituted thiophosphorylacetonitriles, which allow one to prepare these compounds in high yields. The structures of the resulting compounds were established.

Experimental

The NMR spectra were recorded on Bruker WP-200SY and AMX-400 instruments in $CDCl_3$ and C_6D_6 relative to $SiMe_4$ (^1H and ^{13}C) and a 85% H_3PO_4 solution (^{31}P); the concentrations of the solvents were 0.05—0.2 mol L^{-1}. Initial compounds **1** were prepared by the reaction of the corresponding phosphorylacetonitriles with the Lawesson's reagent according to a procedure developed previously.[10]

***C*-Monoalkyl-substituted thiophosphorylacetonitriles (2a—g) (general procedure).** A mixture of an 50% aqueous solution of NaOH (0.06 mol) and TEBA (5 mol.%) was added to a solution of thiophosphorylacetonitrile **1** (0.01 mol) in CH_2Cl_2* (10 mL). Haloalkane (0.015 mol) was added slowly with stirring to the reaction mixture. After completion of addition, the reaction mixture was stirred at 20 °C for 3 h. Then H_2O (10 mL) was added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined extracts were dried with Na_2SO_4. The solvent and the volatile products were distilled off *in vacuo*. The residue was distilled or recrystallized. The constants, yields, and data of elemental analysis of compounds **2a—g** are given in Table 1.

***C,C*-Dialkyl-substituted thiophosphorylacetonitriles (3a—e) (method *A*).** A solution of thiophosphorylacetonitrile **1** (0.01 mol), haloalkane (0.025 mol), and TEBA (200 mg) in MeCN (10 mL) was stirred for 5 min. Finely powdered dry KOH (0.025 mol) was added portionwise. After completion of addition, the reaction mixture was stirred at 20 °C for 3 h and concentrated *in vacuo*. Then H_2O (10 mL) was added to the residue, and the mixture was extracted with benzene. Further workup was carried out as described previously. The constants, yields, and data of elemental analysis of compounds **3a—e** are given in Table 1.

***C,C*-Alkyl(alkyl')-substituted thiophosphorylacetonitriles (4a,b) (method *B*).** A 50% aqueous solution of NaOH (0.06 mol) was added to a solution of thiophosphorylacetonitrile **1** (0.01 mol) and TEBA (100 mg) in CH_2Cl_2 (10 mL). Then MeI (0.02 mol in the case of R^1 = Me and R^2 = OPr^i and 0.012 mol in the case of R^1 = R^2 = Ph) was added slowly with stirring. After completion of addition, the reaction mixture was stirred for 3 h. Then H_2O (10 mL) was added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined extracts were dried with Na_2SO_4 and concentrated *in vacuo*. A solution of solid KOH (0.015 mol) in MeCN (10 mL) was added to the reaction mixture, and then a solution of haloalkane (0.015 mol) in MeCN (1 mL) was added portionwise with stirring. The reaction mixture was stirred for 2.5 h and concentrated. Then H_2O (8 mL) was added, and the reaction mixture was extracted with benzene. The combined extracts were dried with Na_2SO_4 and concentrated. The residue was distilled *in vacuo* or recrystallized.

Reaction of diphenylthiophosphorylacetonitrile with cyclohexyl bromide. A 50% aqueous solution of NaOH (0.06 mol) was added to a solution of diphenylthiophosphorylacetonitrile

* In the case of solid diphenylthiophosphorylacetonitrile, 5 mL of the solvent were taken per 0.5 g of the compound under the conditions of both mono- and dialkylation.

Table 6. Coordinates of nonhydrogen atoms ($\times 10^4$) and equivalent thermal parameters ($U_{eq} \times 10^3$) in the structure of **3e**

Atom	x	y	z	U_{eq}/Å^2
P(1)	1808(1)	8186(1)	1886(1)	25(1)
S(1)	2938(1)	8785(1)	243(1)	38(1)
N(1)	−1242(3)	6101(3)	4294(2)	37(1)
C(1)	777(3)	6489(3)	2215(2)	27(1)
C(2)	−346(3)	6274(3)	3394(3)	29(1)
C(3)	3052(3)	7839(3)	2769(2)	27(1)
C(4)	4341(3)	8648(3)	2338(3)	34(1)
C(5)	5330(4)	8439(4)	2978(3)	43(1)
C(6)	5054(4)	7429(4)	4022(3)	43(1)
C(7)	3777(4)	6618(4)	4437(3)	40(1)
C(8)	2763(3)	6833(3)	3823(3)	33(1)
C(9)	267(3)	9499(3)	2444(3)	28(1)
C(10)	−376(4)	10500(3)	1688(3)	35(1)
C(11)	−1584(4)	11469(4)	2090(3)	43(1)
C(12)	−2156(4)	11469(4)	3248(3)	43(1)
C(13)	−1511(4)	10488(4)	4005(3)	42(1)
C(14)	−312(4)	9496(4)	3617(3)	34(1)
C(15)	1998(4)	5195(3)	2072(3)	34(1)
C(16)	1405(5)	3689(4)	2626(4)	52(1)
C(17)	2670(6)	2473(4)	2489(5)	54(1)
C(18)	2371(5)	3714(6)	3175(6)	66(1)
C(19)	−137(4)	6834(4)	1348(3)	35(1)
C(20)	−1423(4)	5864(4)	1609(3)	34(1)
C(21)	−2270(4)	6387(4)	740(3)	38(1)
C(22)	−3667(4)	5536(4)	1040(4)	44(1)

(0.01 mol) and TEBA (50 mg) in CH_2Cl_2 (20 mL). Then cyclohexyl bromide (0.015 mol) was added. The reaction mixture was stirred for 3 h, and H_2O (8 mL) was added. The reaction mixture was extracted with CH_2Cl_2. The combined extracts were dried with Na_2SO_4, concentrated, and washed with hot benzene. The residue was recrystallized from a CH_2Cl_2–C_6H_6 mixture. Compound **5** was obtained in a yield of 0.25 g (10%), m.p. 256–257 °C. Found (%): C, 66.11; H, 4.53; N, 5.28; P, 11.92. $C_{29}H_{24}N_2P_2S_2$. Calculated (%): C, 66.14; H, 4.59; N, 5.32; P, 11.76. ^{31}P NMR, δ: 48.7 (Me_2CO); 45.6 (CH_2Cl_2). ^{1}H NMR (CD_2Cl_2), δ: 2.28 (m, 2 H, CH_2); 4.0 (ddd, 2 H, CH, $^2J_{PH}$ = 12.9 Hz, $^3J_{HH}$ = 6.7 Hz, $^3J_{HH}$ = 8.7 Hz); 7.18–8.04 (m, 20 H, C_6H_5). ^{13}C NMR (CD_2Cl_2), δ: 25.6 (t, CH_2, $^2J_{PC}$ = 1.9 Hz); 34.9 (dd, CH, $^1J_{PC}$ = 46.8 Hz, $^3J_{PC}$ = 10.6 Hz); 115.7 (d, CN, $^2J_{PC}$ = 1.5 Hz). MS, *m/z*: 527/2 $[M+H]^+$, 526/5 $[M]^+$.

X-ray diffraction study of dibutyl(diphenylthiophosphoryl)-acetonitrile (3e). Single crystals of **3e** were prepared by crystallization from EtOH. X-ray diffraction study was carried out on an automated four-circle Syntex $P2_1$ diffractometer (Mo-Kα radiation, graphite monochromator, θ/2θ scanning technique, 2θ < 50°) at −80 °C. Crystals are triclinic, a = 9.267(2) Å, b = 9.639(2) Å, c = 12.797(3) Å, α = 73.82(2)°, β = 68.79(2)°, γ = 80.50(2)°, V = 1020.9(5) Å^3, M = 369.48, space group $P\bar{1}$, d_{calc} = 1.202 g cm^{-3}, $F(000)$ = 396, μ = 0.241 mm^{-1}. Of a total of 3985 measured reflections, 3727 independent reflections were used in calculations and the refinement.

The structure was solved by direct methods and refined anisotropically by the full-matrix least-squares method based on F^2. The hydrogen atoms were revealed from the difference electron density syntheses and were included in the refinement with isotropic thermal parameters. The final values of the R factors calculated with the use of 2856 reflections with $I > 2\sigma(I)$ were as follows: R_1 = 0.0547; wR_1 = 0.1348, GOF = 1.061 using 3424 measured reflections. All calculations were carried out on an IBM-PC/AT computer using the SHELXTL PLUS program package (version 3). The coordinates of the nonhydrogen atoms and isotropic thermal parameters are given in Table 6.

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