C-Phosphorylated N^2-2-thiazolylformamidines

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C-Phosphorylation of 2-thiazolylformamidines by phosphorus tribromide was studied. It was shown that the 1,3-diazabut-1-enyl (formamidine) substituent can be used as both an activating and protective group. 5-Phosphorylated thiazoles containing either a formamidine fragment or an amino group were obtained. Some properties of the compounds synthesized were studied.

Key words: 2-thiazolylformamidines, phosphorus tribromide, activation of the formamidine fragment, phosphorylation, protection of the formamidine fragment, transamination.

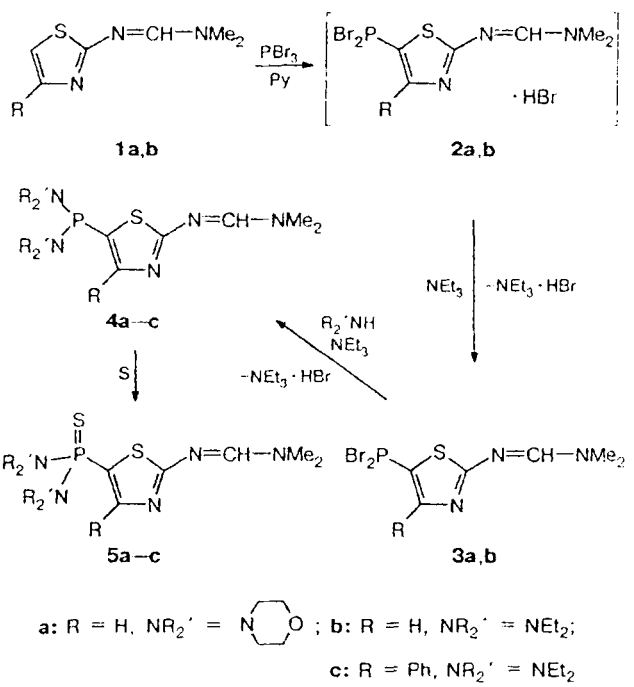
Polyfunctional organic systems containing both phosphorus and nitrogen functions have become available mostly thanks to M. I. Kabachnik's and Fields' works.[1,2] These compounds are of increasing interest because of their biological activity[3] and complexing properties.[4] That is why further development of the new approach found by us, *viz.*, the synthesis of such compounds by electrophilic phosphorylation of N^1,N^1-dimethyl-N^2-hetarylformamidines with phosphorus(III) halides, seems to be quite promising.[5,6]

In the present work, we study the possibility of using N^1,N^1-dimethyl-N^2-(thiazol-2-yl)formamidine (**1a**) and some of its derivatives in electrophilic phosphorylation of heterocycles. The electron-donor properties (σ° = −0.25)[7] of the 3-methyl-1,3-diazabut-1-enyl substituent (hereinafter referred to as formamidine) favor electrophilic introduction of a phosphorus-containing fragment into the thiazole ring at position 5 (activated by this substituent). Such an approach is convenient for synthesizing difficultly available and poorly studied 5-phosphorylated thiazole derivatives, obtained earlier only with the use of organolithium reagents[8] or by heterocyclization.[9,10]

Thiazolylformamidines **1a,b** were *C*-phosphorylated with phosphorus tribromide in pyridine at room temperature for 4 h (Scheme 1).

Because amidines are more basic than pyridine,[11,12] the resulting dibromophosphines exist in the reaction mixture in the form of salts, which are mainly precipitated. Under the action of an excess of triethylamine, these salts are transformed *in situ* into the corresponding dibromophosphines **3a,b**, key compounds for organophosphorus synthesis. Addition of triethylamine after completion of the phosphorylation substantially suppresses the occurrence of side reactions, including phosphorylation of the azomethine carbon atom,[13,14] because of a higher basicity of the reaction medium.

Scheme 1



a: R = H, NR_2' = morpholino; **b**: R = H, NR_2' = NEt_2; **c**: R = Ph, NR_2' = NEt_2

It should be noted that dibromophosphines **3** are poorly soluble in common organic solvents except for pyridine, which is due to their strong intermolecular association. Nevertheless, compound **3** was adequately soluble to be studied by ^1H and ^{31}P NMR spectroscopy, unlike imidazolyldihalophosphines, which are cyclic amidines and exist as very strong intermolecular associates so that only their derivatives can be specified.[15]

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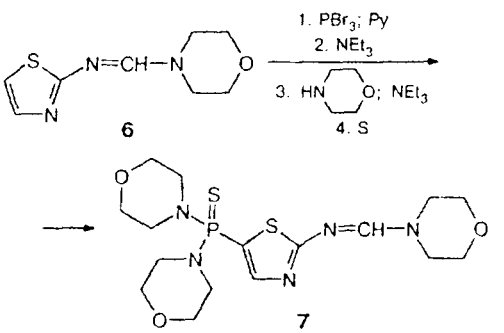
Reactions of dihalophosphines **3** with secondary amines yield the corresponding diamidophosphonites **4**, which further react with sulfur to give diamidothiophosphonates **5** (see Scheme 1).

Thiazol-2-yliminomethylmorpholine **6** undergoes similar transformations (Scheme 2), which shows that hetarylformamidines with a dimethylamino group at the formamidine carbon atom are not the sole compounds to be used in this reaction. It should be emphasized that the reactivity of the substrate decreases when the dimethylamino group in the formamidine substituent is replaced by a morpholine one.

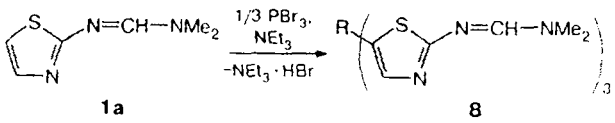
Scheme 2



When the most reactive N^1,N^1-dimethyl-N^2-(thiazol-2-yl)formamidine **1a** is phosphorylated, three thiazole fragments can be attached to one phosphorus atom (Scheme 3).

Reactions of compound **4a** with MeI and azides were studied (Scheme 4). Both of them involve the phosphorus atom of a molecule to give phosphonium salt **9**

Scheme 3



instead of an amidinium salt (reaction with MeI) or phosphazo compounds **10** and **11** according to the Staudinger reaction rather than products of cycloaddition to the amidine fragment of a molecule (reaction with azides).[16]

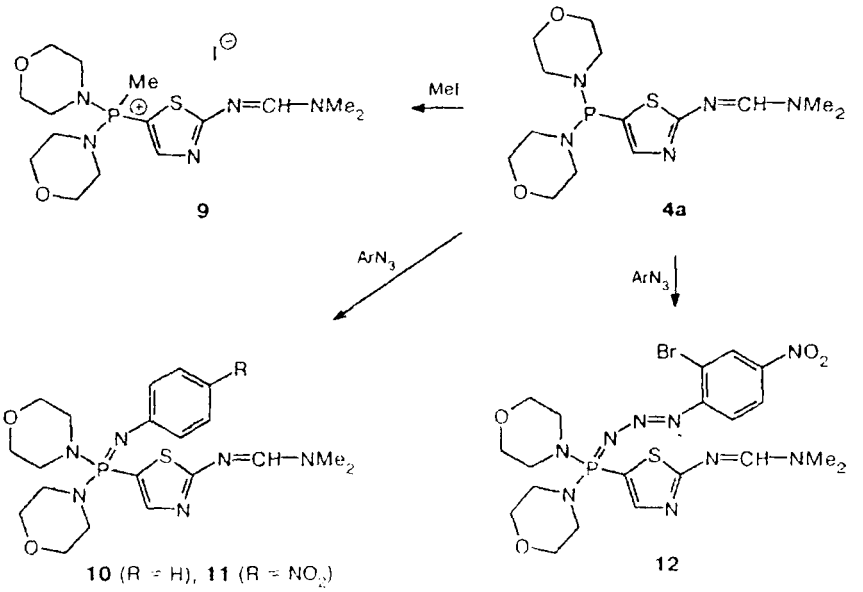
When diamidophosphonite **4a** reacts with an arylazide bearing two electron-acceptor substituents, one can isolate azophosphazo compound **12**. Chlorination of **4a** with hexachloroethane results in chlorophosphonium chloride **13**, whose hydrolysis gives diamidophosphonate **14** (Scheme 5).

Phosphine **8** was found to be quite resistant to oxidation. For example, it does not react with pyridine *N*-oxide and can be transformed into the corresponding phosphine oxide **15** only by heating with an excess of DMSO in DMF for several hours (Scheme 6).

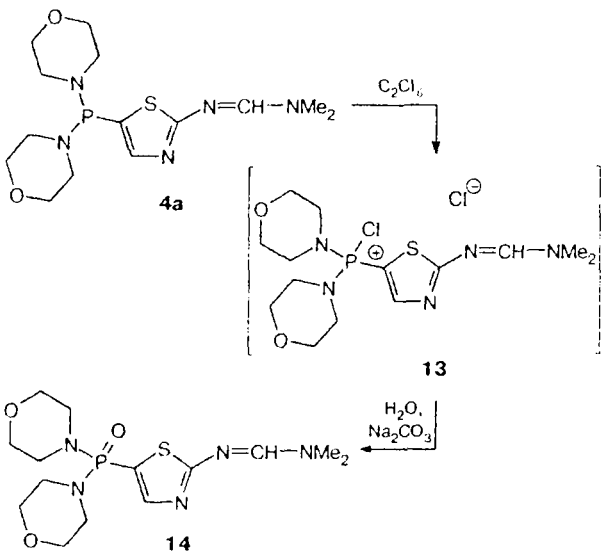
It is known that the amidine substituent easily reacts with various nitrogen- and oxygen-based nucleophiles. The former type reactions yield transamination products, while the latter type ones result in hydrolysis products.[17] Alternatively, compound **7** can be synthesized by reaction of **5a** with morpholine (Scheme 7).

Because the amino group can undergo soft transformation into the amidine group (by reaction with DMF dimethyl acetal or the Vilsmeier reagent), whose alkaline hydrolysis gives back the initial amines, the amidine group may be used as a protective function in electrophilic phosphorylation. Phosphorylated hetarylformamidines

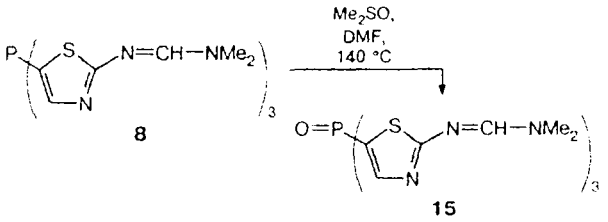
Scheme 4



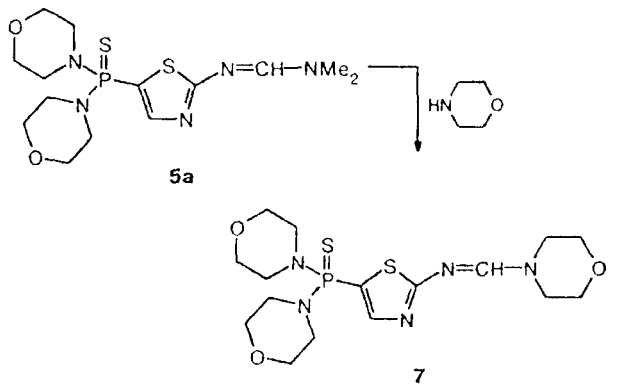
Scheme 5



Scheme 6



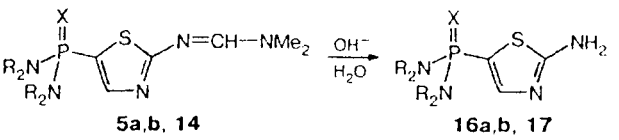
Scheme 7



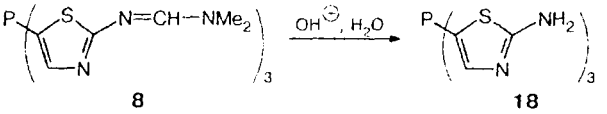
containing both a pentavalent phosphorus atom (**5a,b**, **14**) and a trivalent one (**8**) were transformed into the corresponding amines (Schemes 8 and 9).

It was shown with a reaction of compound **16a** with bromoacetone as an example that 5-phosphorylated 2-aminothiazoles can undergo heterocyclization (the

Scheme 8

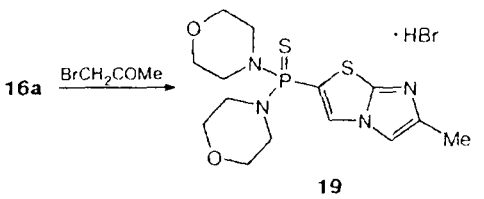


Scheme 9



Chichibabin reaction 2) to give 2-phosphorylated imidazo[2,1-*b*]thiazoles **19**, which cannot be obtained by direct phosphorylation (Scheme 10).

Scheme 10



Thus, the amidine substituent was shown to be used successfully as both an activating and protective group in electrophilic phosphorylation. The possibility of synthesizing new polyfunctional organic systems containing the phosphorus and nitrogen functions was demonstrated with the model thiazole system as the example.

Experimental

^{31}P and ^{1}H NMR spectra were recorded on a Varian VXR-300 instrument (131.31 and 300 MHz, respectively).

N^1,N^1-Dimethyl-N^2-(thiazol-2-yl)formamidine (1a) and N^1,N^1-dimethyl-N^2-(4-phenylthiazol-2-yl)formamidine (1b). DMF dimethyl acetal (0.012 mol) was added to a solution of 2-aminothiazole or 2-amino-4-phenylthiazole (0.01 mol), respectively, in 20 mL of anhydrous methanol. The reaction mixture was refluxed for 5 h and then concentrated to dryness. The product was purified by distillation *in vacuo*: **1a**, b.p. 140—142 (15 Torr); **1b**, b.p. 155—157 (15 Torr).

[2-(3-Methyl-1,3-diazabut-1-enyl)thiazol-5-yl]dibromophosphine (3a) and [2-(3-methyl-1,3-diazabut-1-enyl)-4-phenylthiazol-5-yl]dibromophosphine (3b). PBr_3 (0.01 mol) was added to a solution of amidine **1a** (or **1b**) (0.01 mol) in 15 mL of pyridine (25 mL in the case of **1b**). The reaction mixture was shaken at 10 °C for 10 min and kept for 4 h.

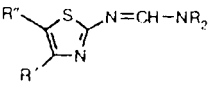
Table 1. Physicochemical constants and data of elemental analysis and ^{31}P NMR spectroscopy

Compound	M.p./°C	Yield (%)	Found / Calculated (%)				Molecular formula	^{31}P NMR, δ
			Br or I	N	P	S		
1a	36.5—37.5	92	—	27.07 27.07	—	20.67 20.66	$C_6H_9N_3S$	—
1b	85—86	91	—	18.19 18.17	—	13.82 13.86	$C_{12}H_{13}N_3S$	—
3a	110—111	76	46.40 46.32	12.12 12.18	8.96 8.98	9.20 9.29	$C_6H_8Br_2N_3PS$	125.9 (C_5H_5N)
3b	126—127	79	37.99 37.95	9.93 9.98	7.32 7.36	7.57 7.61	$C_{12}H_{12}Br_2N_3PS$	129.7 (C_5H_5N)
4a	Oil	75	—	19.50 19.59	8.53 8.67	8.88 8.97	$C_{14}H_{24}N_5O_2PS$	82.4 (C_6H_6)
4b	Oil	79	—	21.32 21.26	9.30 9.40	9.70 9.73	$C_{14}H_{28}N_5PS$	82.4 (C_5H_5N)
5a	172—173.5	90	—	17.89 17.98	7.99 7.95	16.40 16.47	$C_{14}H_{24}N_5O_2PS_2$	64.6 ($CHCl_3$)
5b	63—65	93	—	19.28 19.37	8.66 8.57	17.68 17.74	$C_{14}H_{28}N_5PS_2$	65.3 (C_6H_6)
5c	117—117.5	88	—	16.09 16.00	7.01 7.08	14.77 14.65	$C_{20}H_{32}N_5PS_2$	62.3 (C_6H_6)
6	118—120	80	—	21.35 21.30	— 16.26	16.20	$C_8H_{11}N_3OS$	—
7	157—159 (transamination: 86)	60	—	16.10 16.23	7.22 7.18	14.94 14.89	$C_{16}H_{26}N_5O_3PS_2$	64.8 ($CHCl_3$)
8	211—213	69	—	25.49 25.54	6.34 6.27	19.55 19.49	$C_{18}H_{24}N_9PS_3$	−62.2 (C_5H_5N)
9	192—194	85	25.41 25.43	14.00 14.02	6.16 6.20	6.37 6.42	$C_{15}H_{27}IN_5O_2PS$	43.4 (d, $J_{PH(Me)}$ = 14.1 Hz) (CH_3CN)
10	155—156	79	—	18.61 18.74	6.89 6.91	7.01 7.15	$C_{20}H_{29}N_6O_2PS$	4.7 (MePh)
11	157—158	84	—	19.96 19.87	6.23 6.28	6.58 6.50	$C_{20}H_{28}N_7O_4PS$	6.5 (C_6H_6)
12	108 (decomp.)	62	13.31 13.43	20.84 20.99	5.23 5.16	5.40 5.38	$C_{20}H_{27}BrN_9O_4PS$	33.4 (CH_3CN)
14	95—97	73	—	18.68 18.75	8.33 8.29	8.64 8.59	$C_{14}H_{24}N_5O_3PS$	18.8 (C_6H_6)
15	157—158	70	—	24.65 24.75	6.15 6.08	18.94 18.88	$C_{18}H_{24}N_9OPS_3$	1.1 (DMF)
16a	167—168.5	90	—	16.62 16.75	9.34 9.26	19.07 19.18	$C_{11}H_{19}N_4O_2PS_2$	64.9 (MeOH)
16b	136—137	94	—	18.20 18.28	10.00 10.11	20.86 20.93	$C_{11}H_{23}N_4PS_2$	65.7 (MeOH)
17	245—246	63	—	17.51 17.60	9.79 9.73	10.01 10.07	$C_{11}H_{19}N_4O_3PS$	20.2 (MeOH)
18	222—224	91	—	25.47 25.59	9.53 9.43	29.17 29.29	$C_9H_9N_6PS_3$	−61.1 (MeOH)
19	232—234	36	19.11 18.96	13.20 13.30	7.35 7.22	15.05 15.22	$C_{14}H_{25}BrN_4PS_2$	60.7 ($CHCl_3$)

Then, NEt_3 (0.02 mol) was added. After 20 min, the salts that formed were filtered off and washed with benzene. The filtrates were combined and concentrated to dryness. Dibromophosphines were recrystallized from octane.

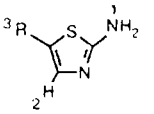
[2-(3-Methyl-1,3-diazabut-1-enyl)thiazol-5-yl]dimorpholidophosphonite (4a) and [2-(3-methyl-1,3-diazabut-1-enyl)thiazol-5-yl]tetraethyldiamidophosphonite (4b). NEt_3 (0.03 mol) and the corresponding secondary amine (0.021 mol)

Table 2. ^{1}H NMR spectral data for compounds **1**, **3**—**12**, **14**, **15**



Compound	Solvent	δ, *J*/Hz			
		NR_2	N=CH	R′	R″
1a	$(CD_3)_2CO$	3.15 (s, 3 H); 3.01 (s, 3 H)	8.32 (s, 1 H)	7.24 (d, 1 H, J_{34} = 3.6)	6.89 (d, 1 H)
1b	$CDCl_3$	3.10 (s, 3 H); 3.09 (s, 3 H)	8.26 (s, 1 H)	7.89 (d, 2 H, *o*-CH, *J* = 8.4); 7.37 (t, 2 H, *m*-CH); 7.26 (t, 1 H, *p*-CH, *J* = 6.6)	6.98 (s, 1 H)
3a	C_6D_6	2.33 (s, 3 H); 1.82 (s, 3 H)	8.08 (s, 1 H)	7.24 (d, 1 H, $J_{3\text{-}H,4\text{-}H}$ = 3.2)	—
3b	C_6D_6	2.31 (s, 3 H); 1.76 (s, 3 H)	8.02 (s, 1 H)	7.86 (m, 2 H, *o*-H); 7.0—7.2 (m, 3 H, *m*,*p*-H)	—
4a	$CDCl_3$	3.05 (s, 3 H); 3.08 (s, 3 H)	8.22 (s, 1 H)	7.20 (s, 1 H)	3.66 (t, 8 H, CH_2O, *J* = 4.5); 3.10 (m, 8 H, CH_2N)
4b	$CDCl_3$	3.06 (s, 3 H); 3.08 (s, 3 H)	8.25 (s, 1 H)	7.15 (s, 1 H)	1.08 (t, 12 H, Me, *J* = 7); 3.14 (m, 8 H, CH_2)
5a	$CDCl_3$	3.15 (s, 3 H); 3.11 (s, 3 H)	8.34 (s, 1 H)	7.85 (d, 1 H, $J_{3\text{-}P}$ = 5.1)	3.67 (t, 8 H, CH_2O, *J* = 4.5); 3.12 (m, 8 H, CH_2N)
5b	$CDCl_3$	3.22 (s, 3 H); 3.06 (s, 3 H)	8.40 (s, 1 H)	7.69 (d, 1 H, $J_{3\text{-}P}$ = 5.4)	1.08 (t, 12 H, Me, *J* = 7); 3.16 (m, 8 H, CH_2)
5c	$CDCl_3$	3.09 (s, 3 H); 3.11 (s, 3 H)	8.33 (s, 1 H)	7.89 (d, 2 H, *o*-CH, *J* = 8.4); 7.37 (t, 2 H, *m*-CH); 7.26 (t, 1 H, *p*-CH, *J* = 6.6)	1.04 (t, 12 H, Me, *J* = 6.9); 3.16 (m, 8 H, CH_2)
6	$CDCl_3$	3.75 (m, 6 H); 3.46 (t, 2 H)	8.28 (s, 1 H)	7.34 (m, 1 H)	6.82 (m, 1 H)
7	$CDCl_3$	3.77 (m, 6 H); 3.51 (t, 2 H, *J* = 5.4)	8.38 (s, 1 H)	7.85 (d, 1 H, $J_{3\text{-}P}$ = 5.1)	3.67 (t, 8 H, CH_2O, *J* = 4.5); 3.12 (m, 8 H, CH_2N)
8	CD_3SOCD_3	3.10 (s, 3 H); 3.07 (s, 3 H)	8.18 (s, 1 H)	7.49 (d, 1 H, $J_{3\text{-}P}$ = 4.8)	—
9	CD_3CN	3.18 (s, 3 H); 3.09 (s, 3 H)	8.43 (s, 1 H)	7.91 (d, 1 H, $J_{3\text{-}P}$ = 5.1)	3.67 (t, CH_2O, 8 H, *J* = 4.5); 3.19 (t, 8 H, CH_2N); 2.30 (d, 3 H, Me, J_{HP} = 14.1)
10	$CDCl_3$	3.14 (s, 3 H); 3.11 (s, 3 H)	8.29 (s, 1 H)	7.71 (d, 1 H, $J_{3\text{-}P}$ = 4.5)	3.64 (t, 8 H, CH_2O, *J* = 4.5); 3.18 (t, 8 H, CH_2N); 6.84 (d, 2 H, *o*-CH, *J* = 8.1); 7.12 (t, 2 H, *m*-CH); 6.73 (t, 1 H, *p*-CH, *J* = 6.6)
11	$CDCl_3$	3.16 (s, 3 H); 3.12 (s, 3 H)	8.33 (s, 1 H)	7.72 (d, 1 H, $J_{3\text{-}P}$ = 4.8)	3.66 (t, 8 H, CH_2O, *J* = 4.5); 3.18 (t, 8 H, CH_2N); 6.75 (d, 2 H, *o*-CH, *J* = 8.7); 8.02 (d, 2 H, *m*-CH, *J* = 8.7)
12	$CDCl_3$	3.18 (s, 3 H); 3.14 (s, 3 H)	8.39 (s, 1 H)	7.85 (d, 1 H, $J_{3\text{-}P}$ = 5.1)	3.68 (s, 8 H, CH_2O); 3.29 (s, 8 H, CH_2N); 7.47 (d, 1 H, *o*-CH, *J* = 9); 8.11 (d, 1 H, *m*-CH, *J* = 9); 8.51 (s, 1 H, *m*′-CH)
14	$CDCl_3$	3.15 (s, 3 H); 3.11 (s, 3 H)	8.35 (s, 1 H)	7.76 (d, 1 H, $J_{3\text{-}P}$ = 5.1)	3.65 (t, 8 H, CH_2O, *J* = 4.5); 3.15 (m, 8 H, CH_2N)
15	CD_3SOCD_3	3.00 (s, 3 H); 3.12 (s, 3 H)	8.27 (s, 1 H)	7.44 (d, 1 H, $J_{3\text{-}P}$ = 4.8)	—

Table 3. ^{1}H NMR spectral data (δ) of compounds **16**—**18**



Compound	Solvent	^{1}H NMR		
		NH_2	CH	R
16a	$CDCl_3$	1.70 (s, 1 H); 5.45 (s, 1 H)	7.35 (d, 1 H, J_{HP} = 5.1)	3.68 (t, 8 H, CH_2O, J = 4.8); 3.12 (m, 8 H, CH_2N)
16b	$CDCl_3$	5.53 (s, 2 H)	7.47 (d, 1 H, J_{HP} = 5.4)	1.09 (t, 12 H, Me, J = 7); 3.14 (m, 8 H, CH_2N)
17	$CDCl_3$	6.89 (s, 2 H)	7.35 (d, 1 H, J_{HP} = 4.5)	3.58 (t, 8 H, CH_2O, J = 4.5); 3.08 (m, 8 H, CH_2N)
18	CD_3SOCD_3	7.30 (s, 2 H)	7.08 (d, 1 H, J_{HP} = 5.1)	—

were added to a filtrate containing phosphine **3a** (obtained from amidine **1a** as described above). After 90 min, the salts that formed were filtered off and washed with benzene. The filtrates were combined, concentrated to dryness *in vacuo* (when concentrating **4a**, overheating should be avoided, otherwise transamination with excess morpholine takes place), dissolved in benzene, decanted (it is convenient to carry out the synthesis of compounds **9**—**14** with a benzene extract of **4a** because of lesser purification losses for the corresponding products), and again concentrated to dryness. The products were purified by extraction with anhydrous hexane (**4b**) and hot octane (**4a**).

[2-(3-Methyl-1,3-diazabut-1-enyl)thiazol-5-yl]dimorpholidothiophosphonate (5a) and 2-(3-methyl-1,3-diazabut-1-enyl)-tetraethyldiamidothiophosphonate (5b). Sulfur (0.001 mol) was added to a solution of amide **4a** (**4b**) (0.001 mol) in 4 mL of benzene. The reaction mixture was refluxed for 3 h, then cooled, and concentrated. The products were purified by recrystallization from propan-2-ol (**5a**) and hexane (**5b**).

[2-(3-Methyl-1,3-diazabut-1-enyl)-4-phenylthiazol-5-yl]tetraethyldiamidothiophosphonate (5c). PBr_3 (0.01 mol) was added to a solution of amidine **1b** (0.01 mol) in 15 mL of pyridine. The reaction mixture was shaken at 10 °C for 10 min. After 3 days, NEt_3 (0.04 mol) and the corresponding secondary amine (0.021 mol) were added. After 90 min, the salts that formed were filtered off and washed with benzene. The filtrates were combined and concentrated to dryness *in vacuo*. After addition of benzene (40 mL) and sulfur (0.01 mol), the mixture was refluxed for 3 h and concentrated to dryness. The product was recrystallized from octane.

(2-Morpholinomethaniminothiazol-5-yl)dimorpholidothiophosphonate (7). PBr_3 (0.01 mol) was added to a solution of amidine **6** (0.01 mol) in 15 mL of pyridine. The reaction mixture was shaken at 10 °C for 10 min. After 24 h, NEt_3 (0.04 mol) and the corresponding secondary amine (0.021 mol) were added. After 90 min, the salts that formed were filtered off and washed with benzene. Finely ground sulfur (0.01 mol) was added to the mother liquor, and the mixture was refluxed for 3 h and concentrated to dryness *in vacuo*. The product was recrystallized from propan-2-ol.

Thiazol-2-yliminomethylmorpholine (6) and (2-morpholinomethaniminothiazol-5-yl)dimorpholidothiophosphonate (7) (transamination). Morpholine (0.06 mol) was added to a solution of **1a** (or **5a**) (0.01 mol) in 15 mL of toluene (40 mL in the case of **5a**). The reaction mixture was refluxed until dimethylamine ceased to evolve and then concentrated to dryness. Compound **6** was crystallized from toluene (higher yields can be attained upon crystallization from large amounts of octane). Product **7** was purified by recrystallization from propan-2-ol.

Tris[2-(3-methyl-1,3-diazabut-1-enyl)thiazol-5-yl]phosphine (8). PBr_3 (0.01 mol) was added to a solution of amidine **1a** (0.03 mol) and NEt_3 (0.12 mol) in 45 mL of pyridine. The reaction mixture was shaken at 0 °C for 10 min. After 4 days, the product admixed with salts was filtered off. The precipitate was washed with benzene, and the salts were eluted with water. Phosphine **8** was purified by recrystallization from MeCN.

[2-(3-Methyl-1,3-diazabut-1-enyl)thiazol-5-yl]dimorpholidomethylphosphonium iodide (9). MeI (0.001 mol) was added to a solution of compound **4a** (0.001 mol) in 4 mL of benzene. After 5 days, the product was filtered off, washed with benzene, and recrystallized from propan-2-ol.

[2-(3-Methyl-1,3-diazabut-1-enyl)thiazol-5-yl]dimorpholido(phenyl)iminophosphonate (10) and [2-(3-methyl-1,3-diazabut-1-enyl)thiazol-5-yl]dimorpholido(*p*-nitrophenyl)-iminophosphonate (11). Azide (0.001 mol) was added to a solution of compound **4a** (0.001 mol) in 4 mL of benzene. The reaction mixture was kept for 1 h, refluxed for 3 h, and then concentrated to dryness. The product was recrystallized from propan-2-ol.

[2-(3-Methyl-1,3-diazabut-1-enyl)thiazol-5-yl]dimorpholido(4-nitro-2-bromophenylazo)iminophosphonate (12). Azide (0.001 mol) was added to a solution of compound **4a** (0.001 mol) in 4 mL of benzene. After 2 days, the product was filtered off and washed with benzene.

[2-(3-Methyl-1,3-diazabut-1-enyl)thiazol-5-yl]dimorpholidophosphonate (14). C_2Cl_6 (0.001 mol) in the form of a saturated solution in hexane was added to a solution of compound **4a** (0.001 mol) in 7 mL of benzene. After 2 days, chlorophosphonium chloride **13** was filtered off with precautions against moisture access, washed with hexane, and dissolved in CH_2Cl_2. Na_2CO_3 (0.003 mol) and then H_2O (0.0011 mol) were added. The reaction mixture was stirred with a magnetic stirrer for 6 h. The product was filtered off, concentrated to dryness, and recrystallized from EtOAc.

Tris[2-(3-methyl-1,3-diazabut-1-enyl)thiazol-5-yl]phosphine oxide (15). DMSO (0.025 mol) was added to a solution of compound **8** (0.001 mol) in 4 mL of DMF. The reaction mixture was kept at 140 °C for 15 h and then concentrated to dryness *in vacuo*. The product was recrystallized from Pr^{i}OH.

(2-Aminothiazol-5-yl)dimorpholidothiophosphonate (16a), (2-aminothiazol-5-yl)tetraethyldiamidothiophosphonate (16b), (2-aminothiazol-5-yl)dimorpholidophosphonate (17), and tris(2-aminothiazol-5-yl)phosphine (18). KOH (0.001 mol) and H_2O (0.016 mol) were added to a solution of amidine **5a** (**5b**, **14**, or **8**) (0.001 mol) in methanol. The reaction mixture was refluxed for 6 h (**5a**,**b** and **14**; 20 h in the case of **8**) and concentrated to dryness *in vacuo*. The products were purified by recrystallization from H_2O (**16a** and **18**), cyclohexane (**16b**), and DMF (**17**).

2-(6-Methylimidazo[2,1-*b*]thiazolyl)dimorpholidothiophosphonate (19). Bromoacetone (0.001 mol) was added to a solution of compound **16a** (0.001 mol) in 8 mL of acetone. After 24 h, the reaction mixture was concentrated to dryness, and PrⁱOH (15 mL) was added. The resulting solution was refluxed for 8 h and then concentrated to dryness. The product was recrystallized from $CHCl_3$. ^1H NMR ($CDCl_3$), δ: 2.57 (s, 3 H, Me); 3.18 (m, 8 H, CH_2N); 3.72 (t, 8 H, CH_2O, J = 4.5 Hz); 7.89 (s, 1 H, CHCMe); 8.73 (d, 1 H, CHCP, J_{HP} = 5.7 Hz).

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