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Phosphorylation of Imidazo[2,1-*b*]thiazoles with Phosphorus(III) Halides in the Presence of Bases

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ABSTRACT: *The reaction of phosphorus(III) halides with 6-substituted imidazo[2,1-b]thiazoles in the presence of bases proceeds regioselectively and affords 5-phosphinoimidazo[2,1-b]thiazoles, useful synthons for the preparation of various P(III) and P(V) derivatives. 5-Phosphinoimidazo[2,1-b]thiazoles are selectively alkylated at the phosphorus or heterocyclic nitrogen atom, depending on the alkylating agent.* Heteroatom Chem 16:648–655, 2005; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20166

INTRODUCTION

The previously developed new synthetic approach to C-phosphorylated N-alkylimidazoles and N-alkylbenzimidazoles through immediate phosphorylation of the substrates with phosphorus(III) [1] or phosphorus(V) [2] halides provided access to key phosphorus acid halides and dihalides, the valuable synthons for the preparation of various imidazole-containing phosphorus compounds. The high regioselectivity was also observed on phosphorylation of imidazoles fused to six-membered heterocycles, e.g. 2-substituted imidazo[1,2-*a*]pyridines, with phosphorus(III) halides [3]. Now we report on the extension of the reaction to imidazoles fused to five-membered rings, i.e., 6-substituted imidazo[2,1-*b*]thiazoles, the phosphorylated derivatives of which are unknown.

RESULTS AND DISCUSSION

The 6-substituted imidazo[2,1-*b*]thiazoles **1a–c** react regioselectively with P(III) halides in equimolar proportion to give 5-phosphino imidazo[2,1-*b*]thiazoles **2–4** (Scheme 1). The structure of the phosphorylation products was strictly confirmed by ^{1}H NMR spectra showing the absence of the singlet due to the C(5)–H proton (Table 2).

The phosphorylation rate substantially depends on the electronic nature of the R substituent and decreases in the order Me > Ph > Cl. Thus, with a donor methyl group (R = Me) the phosphorylation by PCl_3 is complete within a few minutes at room temperature, whereas with R = Ph or R = Cl it takes a day or a week, respectively. In this connection, it is worthwhile to use in the last case PBr_3 as the

*Phosphorylated Azoles. Part III.

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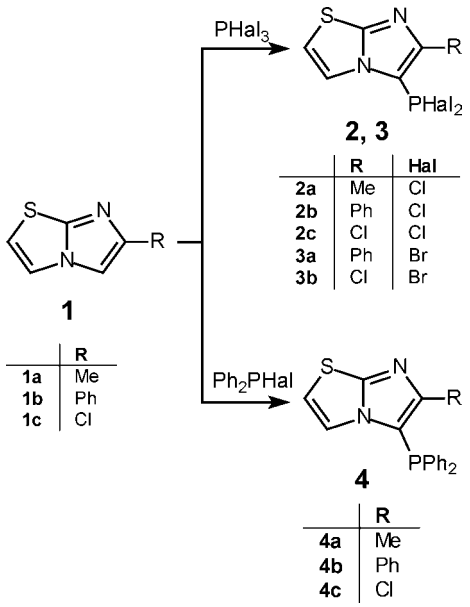
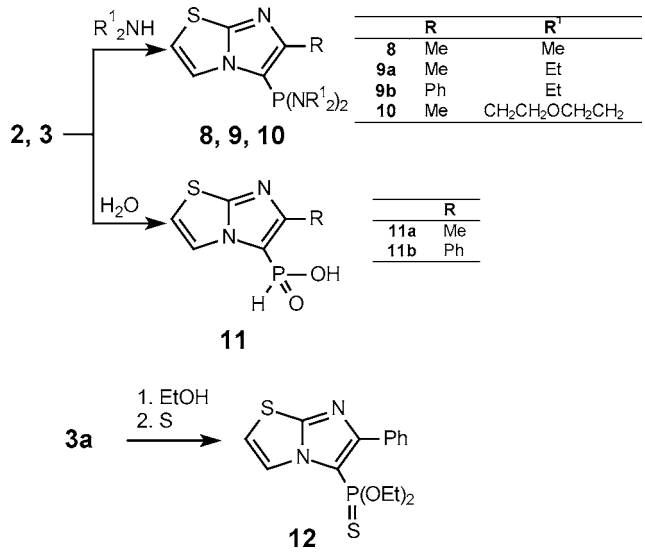


	R
1a	Me
1b	Ph
1c	Cl

	R	Hal
2a	Me	Cl
2b	Ph	Cl
2c	Cl	Cl
3a	Ph	Br
3b	Cl	Br

	R
4a	Me
4b	Ph
4c	Cl

SCHEME 1



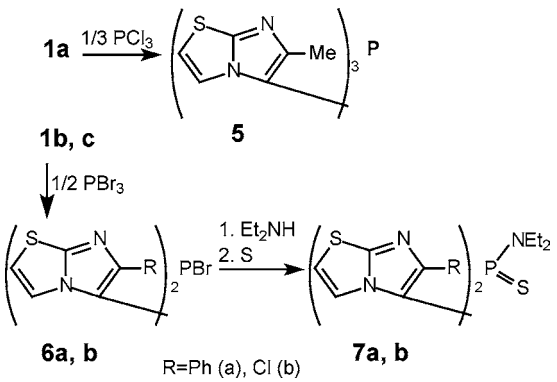
	R	R1
8	Me	Me
9a	Me	Et
9b	Ph	Et
10	Me	$CH_2CH_2OCH_2CH_2$

	R
11a	Me
11b	Ph

SCHEME 3

phosphorylating agent with which the reaction is completed within 2 h and affords dibromophosphine **3b** (δ ^{31}P = 90.92 ppm). The agent Ph_2PCl can be used for the preparation of phosphine **4a**, while for synthesis of phosphines **4b, c** it is necessary to use more reactive Ph_2PBr.

The influence of the substituent R in the starting compounds **1a–c** tells not only about the phosphorylation rate but also the number of heterocyclic residues which can be attached to the phosphorus atom. Thus, the phosphorylation in the system with the ratio **1** : $PHal_3$ = 3:1 gives the phosphine **5** if R = Me, whereas with R = Ph or Cl the end products are bromobisheteroarylphosphines **6a, b**. It is more convenient to prepare the latter at the 2:1 ratio of the reagents (Scheme 2). On treatment with diethylamine and sulfur, the bromophosphines **6a, b** are transformed into thiophosphinates **7a, b**.



SCHEME 2

Dihalogenophosphines **2, 3** are crystalline solids easily hydrolyzable in moist air. Compounds readily react with secondary amines to give diaminophosphines **8–10**. On hydrolysis **2, 3** are transformed into phosphinic acid **11**. By successive treatment with ethanol and sulfur, dibromophosphine **3a** was transformed into thiophosphonates **12** (Scheme 3).

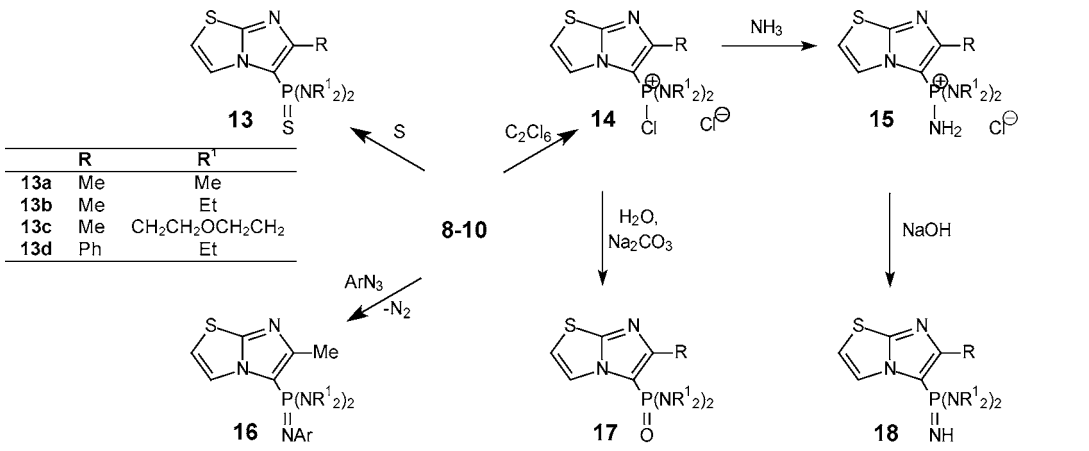
Phosphines **8–10** were oxidized into a series of phosphorylated imidazo[2,1-*b*]thiazole derivatives with P(V) atom **13–18** (Scheme 4).

Phosphines **4,8–10**, like phosphorylated imidazo[1,2-*a*]pyridines [3] and imidazoles [1], can be selectively alkylated at the phosphorus or heterocyclic nitrogen atom, depending on the alkylating agent. The first route is realized on alkylation with methyl iodide and the molar ratio of the reagents of 1:1 to give phosphonium salts **19**. With excess of methyl iodide both the phosphorus and the N(2) atom are methylated to yield salts **20**. The alkylation of phosphines **4**, **9** through the second route into the compounds **21** occurs when Meerwein salts are used as the alkylating agent (Scheme 5).

The P(V)-substituted imidazo[2,1-*b*]thiazoles are alkylated on the nitrogen atom with the formation of imidazo[2,1-*b*]thiazolium salts **22** (Scheme 6).

EXPERIMENTAL

All the manipulations with air-sensitive compounds were performed under dry argon. Solvents were purified by conventional procedures. Melting points were



	R	R^1
13a	Me	Me
13b	Me	Et
13c	Me	$CH_2CH_2OCH_2CH_2$
13d	Ph	Et

	R	Ar
16a	Et	Ph
16b	Et	*p*-MeC_6H_4
16c	Et	*p*-$MeC(O)C_6H_4$
16d	$CH_2CH_2OCH_2CH_2$	*p*-$NO_2C_6H_4$
16e	$CH_2CH_2OCH_2CH_2$	2-MeO-(5-NO_2-)C_6H_3

	R	R^1
14	Me	Me
17a	Me	Et
17b	Me	$CH_2CH_2OCH_2CH_2$
17c	Cl	Et

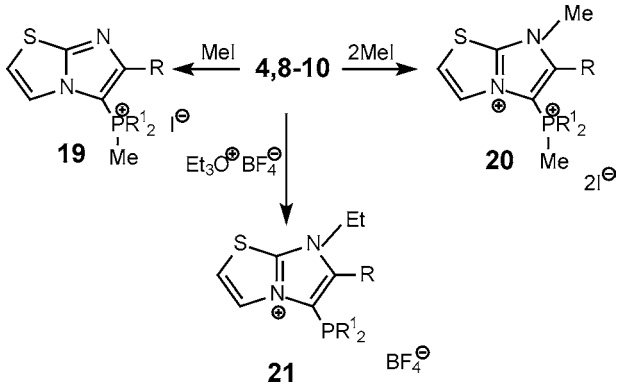
	R	R^1
15a	Me	Me
15b	Me	Et
18	Me	Et

SCHEME 4

determined with an electrothermal capillary melting point apparatus and were uncorrected.

The ^{31}P, ^{1}H, ^{13}C NMR spectra were measured on a spectrometer Varian VXR-300 (121, 300, and 75 MHz, respectively). Chemical shifts are reported relative to internal tetramethylsilane (^{1}H, ^{13}C) or external 85% H_3PO_4 (^{31}P).

All the analytical, spectral, and other physical data were collected in Tables 1, 2, and 3.



	R	R^1
19a	Me	NEt_2
19b	Me	N O
19c	Me	Ph
19d	Ph	Ph

	R	R^1
20a	Me	NEt_2
20b	Me	N O
21a	Me	NEt_2
21b	Me	Ph

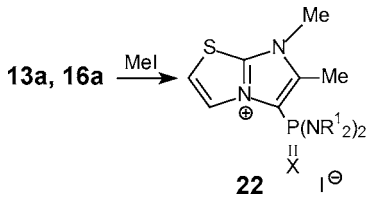
SCHEME 5

Synthesis of Dihalogenophosphines **2,3**

To a solution of compounds **1** (50 mmol) in pyridine (50 mL) was added triethylamine (60 mmol), then phosphorus trichloride or tribromide (50 mmol) was added dropwise under cooling at such a rate that the temperature was maintained at about 10°C, and the mixture was allowed to warm up to room temperature. After completion of the reaction, the solvent was evaporated in vacuo and benzene (50 mL) was added to the residue. The precipitated triethylamine hydrochloride was filtered off, and the filtrate was evaporated in vacuo.

Synthesis of Phosphines **4**

A mixture of compound **1** (20 mmol), triethylamine (20 mmol), and chloro- or bromodiphenylphosphine (20 mmol) in pyridine (20 mL) was allowed to stand for 24 h at room temperature, then the reaction mixture was diluted with benzene (60 mL); the precipitated triethylamine hydrochloride was removed by filtration, the filtrate was evaporated in vacuo, and



	R^1	X
22a	Me	S
22b	Et	NPh

SCHEME 6

TABLE 1 Yields, Analytical Data, and ^{31}P NMR Spectra

	Yield (%)	*Mp (°C) Bp/pressure, °C/Torr (cryst. solvent)*	*Mol. Formula*	*δ^{31}P(ppm) (Solvent)*	*Found (Calculated)(%)*	
					N	*P*
2a	93	100.5–102 137–140/0.14	$C_6H_5Cl_2N_2PS$	120.9 (C_6H_6)	11.53 (11.72)	12.57 (12.96)
2b	90	142–143 (C_6H_6)	$C_{11}H_7Cl_2N_2PS$	122.9 (C_6H_6)	9.21 (9.30)	10.03 (10.29)
2c	87	144–146 130/0.09[a]	$C_5H_2Cl_3N_2PS$	117.0 (C_6H_6)	10.53 (10.80)	11.51 (11.94)
3a	92	108–109	$C_{11}H_7Br_2N_2PS$	100.9 (C_5H_5N)	7.23 (7.18)	7.99 (7.94)
4a	69	138–139 135–138/0.01 (*n*-C_8H_{18})	$C_{18}H_{15}N_2PS$	−36.8 ($CHCl_3$)	8.39 (8.69)	9.51 (9.61)
4b	72	166–167 (C_2H_5OH)	$C_{23}H_{17}N_2PS$	−34.3 (C_5H_5N)	7.09 (7.29)	7.87 (8.06)
4c	70	127–128 (CH_3OH)	$C_{17}H_{12}ClN_2PS$	−35.4 ($CHCl_3$)	7.99 (8.17)	8.78 (9.04)
5	50	232–233 (C_6H_6)	$C_{18}H_{15}N_6PS_3$	−86.6 (C_5H_5N)	19.07 (18.99)	6.75 (7.00)
7a	67	150–151 (CH_3COOEt)	$C_{26}H_{24}N_5PS_3$	33.1 ($CHCl_3$)	12.89 (13.12)	5.59 (5.80)
7b	64	174–176 (CH_3COOEt)	$C_{14}H_{14}Cl_2N_5PS_3$	25.0 (C_6H_6)	15.61 (15.55)	6.93 (6.88)
8	68	45–46 139–142/0.01	$C_{10}H_{17}N_4PS$	88.3 (C_6H_6)	21.64 (21.86)	11.86 (12.08)
9a	72	150–155/0.04	$C_{14}H_{25}N_4PS$	82.0 (C_5H_5N)	18.03 (17.93)	9.97(9.91)
9b	70	Oil	$C_{19}H_{27}N_4PS$	82.5 (C_5H_5N)	15.03 (14.96)	8.07(8.27)
10	84	101–102 (*n*-C_7H_{16})	$C_{14}H_{21}N_4O_2PS$	83.4 ($C_6H_5CH_3$)	16.28 (16.46)	8.89 (9.10)
11a	83	157–158	$C_6H_7N_2O_2PS$	−3.6 d, $J = 562$ Hz (CH_3OH)	13.71 (13.86)	15.03 (15.32)
11b	87	149–151	$C_{11}H_9N_2O_2PS$	5.0 d, $J = 659$ Hz (H_2O)	10.41 (10.60)	11.56 (11.72)
12	64	81–82 (*n*-C_7H_{16})	$C_{15}H_{17}N_2O_2PS_2$	69.3 (C_6H_6)	8.03 (7.95)	8.62 (8.79)
13a	89	48–50 (*n*-C_7H_{16})	$C_{10}H_{17}N_4PS_2$	66.7 ($CHCl_3$)	19.03 (19.43)	10.49 (10.74)
13b	83	60–62 (*n*-C_6H_{14})	$C_{14}H_{25}N_4PS_2$	61.6 ($CHCl_3$)	16.07 (16.26)	9.09 (8.99)
13c	87	152–154	$C_{14}H_{21}N_4O_2PS_2$	62.1 (C_6H_6)	14.91 (15.04)	8.11 (8.32)
13d	85	67–68 (*n*-C_7H_{16})	$C_{19}H_{27}N_4PS_2$	58.0 (DMSO)	13.49 (13.78)	7.51 (7.62)
14	77	85–87	$C_{10}H_{17}Cl_2N_4PS$	46.2 ($CHCl_3$)	16.93 (17.12)	9.24 (9.47)
15a	73	197–198 (*i*-C_3H_7OH)	$C_{10}H_{19}ClN_5PS$	34.5 (CH_3CN)	22.51 (22.75)	9.87 (10.06)
15b	74	153–155 (CH_3COOEt:*i*-C_3H_7OH/1:1)	$C_{14}H_{27}ClN_5PS$	31.6 ($CHCl_3$)	19.01 (19.25)	8.38 (8.51)
16a	84	109–112 (*n*-C_7H_{16})	$C_{20}H_{30}N_5PS$	8.6 (C_6H_6)	17.11 (17.36)	7.51 (7.68)
16b	79	99–101 (*n*-C_7H_{16})	$C_{21}H_{32}N_5PS$	8.1 (C_6H_6)	16.69 (16.77)	7.31 (7.42)
16c	86	117–118 (*n*-C_7H_{16}: CH_3COOEt/1:1)	$C_{22}H_{32}N_5OPS$	10.8 (C_6H_6)	15.48 (15.72)	6.82 6.95)
16d	80	186–187 ($C_6H_5CH_3$)	$C_{20}H_{25}N_6O_4PS$	10.3 ($C_6H_5CH_3$)	17.51 (17.64)	6.41 (6.5)
16e	89	142–144 (*n*-C_7H_{16})	$C_{21}H_{27}N_6O_5PS$	8.1 ($C_6H_5CH_3$)	16.38 (16.59)	5.87 (6.11)
17a	81	Oil	$C_{14}H_{25}N_4OPS$	18.4 ($CHCl_3$)	16.87 (17.06)	9.13 (9.43)
17b	80	171–173 (*n*-C_7H_{16})	$C_{14}H_{21}N_4O_3PS$	15.9 (CH_2Cl_2)	15.43 (15.72)	8.39 (8.69)
17c	78	Oil	$C_{13}H_{22}ClN_4OPS$	15.5 ($CHCl_3$)	15.87 (16.06)	8.51 (8.88)
18	72	Oil	$C_{14}H_{26}N_5PS$	30.2 ($CHCl_3$)	21.08 (21.39)	9.26 (9.46)
19a	82	180–182 (*i*-C_3H_7OH)	$C_{15}H_{28}IN_4PS$	43.7 (CH_3CN)	12.27 (12.33)	6.54 (6.82)
19b	80	225–227 (C_2H_5OH)	$C_{15}H_{24}IN_4O_2PS$	42.4 (CH_3CN)	11.47 (11.62)	6.13 (6.42)
19c	75	210–121 (CH_3OH)	$C_{19}H_{18}IN_2PS$	7.6 ($CHCl_3$)	5.86 (6.03)	6.49 (6.67)
19d	79	208–209 (CH_3CN)	$C_{24}H_{20}IN_2PS$	12.5 ($CHCl_3$)	5.41 (5.32)	5.91 (5.88)
20a	52	261–262 (CH_3CN)	$C_{16}H_{31}I_2N_4PS$	39.2 (H_2O)	9.37 (9.4)	5.02 (5.19)
20b	56	254–256 (CH_3CN)	$C_{16}H_{27}I_2N_4O_2PS$	42.7 (CH_3CN)	8.64 (8.97)	4.51 (4.96)
21a	74	83–85	$C_{16}H_{30}BF_4N_4PS$	76.6 (CH_2Cl_2)	12.79 (13.08)	6.99 (7.23)
21b	61	172–173 (CH_3OH)	$C_{20}H_{20}BF_4N_2PS$	−32.5 (C_2H_5OH)	6.11 (6.39)	6.84 (7.07)
22a	79	219–221 (CH_3OH)	$C_{11}H_{20}IN_4PS_2$	63.5 ($CHCl_3$)	12.81 (13.02)	7.11 (7.20)
22b	74	231–232 (CH_3OH)	$C_{21}H_{33}IN_5PS$	6.0 ($CHCl_3$)	12.91 (12.84)	5.71 (5.68)

[a]Sublimation in vacuo.

TABLE 2 5-Phosphorylated Imidazo[2,1-*b*]thiazoles: ^{1}H NMR δ (Multiplicity), J (Hz)

	Solvent	*2-H*	*3-H*	*6-Me(Ph)*	*Other Signals*
2a	C_6D_6	5.73(t), 4.6	7.45(dd), 4.6, 1.4	2.2(d), 0.9	
2b	C_6D_6	5.78(d), 4.4	7.47(d), 4.4	7.83(m), *o*-Ph 7.05–7.14(m) *m,p*-Ph	
2c	C_6D_6	5.60(d), 4.5	7.22(d), 4.5		
3a	C_6D_6	5.76(d), 4.6	7.70(d), 4.6	7.84(m), *o*-Ph 7.05–7.14(m), *m,p*-Ph	
4a	$CDCl_3$	6.54(d), 4.5	6.67(d), 4.5	2.50(s)	7.25–7.35(m), Ph_2P
4b	$CDCl_3$		6.54(s)	7.90(d), 8.0, *o*-Ph 7.28–7.43(m), *m,p*-Ph+Ph_2P	7.28–7.43(m), Ph_2P+6-m,p-Ph
4c	$CDCl_3$	6.70(d), 4.5	6.74(d), 4.5		7.28–7.40(m), Ph_2P
5	$CDCl_3$		6.77(s)	2.19(s)	
7a	$CDCl_3$	6.84(d), 4.5	8.02(d), 4.5	7.15–7.35(m)	2.93(m), PN$\underline{CH_2}CH_3$ 0.87(t), 7.0, PN$C\underline{H_2}\underline{CH_3}$
7b	C_6D_6	5.67(d), 4.5	7.90(d), 4.5		3.18(m), PN$\underline{CH_2}CH_3$ 0.68(t), 6.9, PN$C\underline{H_2}\underline{CH_3}$
8	C_6D_6	6.05(d), 4.5	7.09(d), 4.5	2.47(s)	2.47(d), 9.6, PN$\underline{CH_3}$
9a	CD_3CN	6.86(d), 4.4	7.59(d), 4.4	2.31(s)	3.06(m), PN$\underline{CH_2}CH_3$ 1.07(t), 7.0, PN$C\underline{H_2}\underline{CH_3}$
9b	C_6D_6	5.98(d), 6.0	7.51(d), 6.0	8.04(d), 8.0, *o*-Ph 7.26(t), 8.0, *m*-Ph 7.14(t), 8.0, *p*-Ph	2.75(m), PN$\underline{CH_2}CH_3$ 0.78(t), 7.0, PN$C\underline{H_2}\underline{CH_3}$
10	CD_3CN	6.98(d), 4.5	7.82(d), 4.5	2.40(s)	3.67(m), PNCH$_2\underline{CH_2}$O 3.08(m), PN$\underline{CH_2}CH_2$O
11a	CF_3COOD	7.58(s)	8.45(s)	2.81(s)	
11b	CF_3COOD	7.60–7.80(m) +6-Ph	8.55(d), 4.0	7.60–7.80(m)+2-H	
12	$CDCl_3$	6.93(d), 4.5	8.37(d), 4.5	7.78(m), *o*-Ph 7.40(m), *m,p*-Ph	3.90(m), PO$\underline{CH_2}CH_3$ 1.10(t), 7.0, PO$C\underline{H_2}\underline{CH_3}$
13a	$CDCl_3$	6.81(d), 4.6	8.51(d), 4.6	2.57(d), 1.4	2.65(d), 12.8, PN$\underline{CH_3}$
13b	$CDCl_3$	6.80(d), 4.4	8.56(d), 4.4	2.55(d), 1.5	3.19(m), PN$\underline{CH_2}CH_3$ 1.08(t), 7.0, PN$C\underline{H_2}\underline{CH_3}$
13c	CD_3CN	7.05(d), 4.5	8.42(d), 4.5	2.56(d), 1.5	3.57(m), PNCH$_2\underline{CH_2}$O 3.03(m), PN$\underline{CH_2}CH_2$O
13d	$(CD_3)_2SO$	7.45(d), 4.5	7.97(d), 4.5	7.51(m), *o*-Ph 7.40(m), *m,p*-Ph	2.93(m), PN$\underline{CH_2}CH_3$ 0.91(t), 7.0, PN$C\underline{H_2}\underline{CH_3}$
14	CD_3CN	7.43(d), 4.4	8.28(d), 4.4	2.58(d), 1.5	2.64(d), 10.8, PN$\underline{CH_3}$
15a	CD_3CN	7.19(d), 4.4	8.03(d), 4.4	2.45(d), 1.5	5.96(br.s), P$\underline{NH_2}$ 2.75(d), 11.0, PN$\underline{CH_3}$
15b	$CDCl_3$	6.99(d), 4.5 +P$\underline{NH_2}$	8.69(m)	2.53(s)	6.99(br.s), P$\underline{NH_2}$+2-H 3.27(m) PN$\underline{CH_2}CH_3$ 1.20(t), 7.0, PN$C\underline{H_2}\underline{CH_3}$
16a	$CDCl_3$	6.80(d), 4.4	8.69(d), 4.4	2.52(d), 1.4	7.14(t), 7.2, *m*-Ph 6.71(m), *o,p*-Ph 3.17(m), PN$\underline{CH_2}CH_3$ 0.98(t), 7.0, PN$C\underline{H_2}\underline{CH_3}$
16b	$(CD_3)_2CO$	7.20(d), 4.4	8.64(d), 4.4	2.49(d), 1.5	7.73(dd), 8.8, 1.1, 3,5-$\underline{H}$-Ar 6.71(dd), 8.8, 1.1, 2,6-$\underline{H}$-Ar 3.22(m), PN$\underline{CH_2}CH_3$ 2.41(s), Ar$\underline{CH_3}$ 1.00(t), 7.0, PN$CH_2\underline{CH_3}$
16c	$CDCl_3$	6.83(d), 4.4	8.59(d), 4.4	2.53(d), 1.6	7.81(d), 8.7, 3,5-$\underline{H}$-Ar 6.69(d), 8.7, 2,6-$\underline{H}$-Ar 3.16(m), PN$\underline{CH_2}CH_3$ 2.51(s), Ar-CO$\underline{CH_3}$ 1.00(t), 7.0, PN$CH_2\underline{CH_3}$

(Continued)

TABLE 2 Continued

	Solvent	*2-H*	*3-H*	*6-Me(Ph)*	*Other Signals*
16d	$CDCl_3$	6.89(d), 4.5	8.41(d), 4.5	2.56(d), 1.5	8.08(d), 8.7, 3,5-H-Ar 6.81(d), 8.7, 2,6-H-Ar 3.63(m), $PNCH_2\underline{CH_2}O$ 3.16(m), $PN\underline{CH_2}CH_2O$
16e	$CDCl_3$	6.83(m)+3-H-Ar	9.22(d), 4.5	2.55(d), 1.5	7.72(m), 4,6-H-Ar 6.83(m), 3-H-Ar+2-H 3.95(s), $O\underline{CH_3}$ 3.65(m), $PNCH_2\underline{CH_2}O$ 3.18(m), $PN\underline{CH_2}CH_2O$
17a	$CDCl_3$	6.87(d), 4.4	8.18(d), 4.4	2.52(d), 1.4	3.18(m), $PN\underline{CH_2}CH_3$ 1.12(t), 7.2, $PNCH_2\underline{CH_3}$
17b	$CDCl_3$	6.84(d), 4.5	8.14(d), 4.5	2.49(s)	3.66(m), $PNCH_2\underline{CH_2}O$ 3.16(m), $PN\underline{CH_2}CH_2O$
17c	$CDCl_3$	6.84(dd), 4.6, 0.6	8.19(dd), 4.6, 0.6		3.08(m), $PN\underline{CH_2}CH_3$ 1.00(t), 7.0, $PNCH_2\underline{CH_3}$
18	$CDCl_3$	6.75(d), 4.4	8.43(d), 4.4	2.49(d), 1.5	3.12(m), $PN\underline{CH_2}CH_3$ 1.05(t), 7.0, $PNCH_2\underline{CH_3}$
19a	CD_3CN	7.31(d), 4.6	7.60(d), 4.6	2.46(d), 1.5	3.21(m), $PN\underline{CH_2}CH_3$ 2.27(d), 13.6, $P\underline{CH_3}$ 1.19(t), 7.0, $PNCH_2\underline{CH_3}$
19b	CD_3CN	7.35(d), 4.5	7.86(d), 4.5	2.52(s)	3.74(m), $PNCH_2\underline{CH_2}O$ 3.25(m), $PN\underline{CH_2}CH_2O$ 2.37(d), 13.8, $P\underline{CH_3}$
19c	$CDCl_3$	7.12(d), 4.3	7.27(d), 4.3	2.01(d), 1.4	7.70–7.95(m), Ph_2P 3.37(d), 13.5, $P\underline{CH_3}$
19d	$CDCl_3$	6.99(d), 4.2	7.18–7.26(m) +6-Ph	7.18–7.26(m)+3-H	7.61–7.83(m), Ph_2P 2.97(d), 13.5, $P\underline{CH_3}$
20a	D_2O	7.72(dd), 4.3, 0.9	7.86(dd), 4.3, 0.9	2.51(s)	3.81(s), 7-$\underline{CH_3}$ 3.23(m), $PN\underline{CH_2}CH_3$ 2.39(d), 13.5, $P\underline{CH_3}$ 1.13(t), 7.0, $PNCH_2\underline{CH_3}$
20b	D_2O	7.69(d), 4.4	8.00(d), 4.4	2.49(s)	3.74(s), 7-$\underline{CH_3}$ 3.64(m), $PNCH_2\underline{CH_2}O$ 3.22(m), $PN\underline{CH_2}CH_2O$ 2.43(d), 14.4, $P\underline{CH_3}$
21a	$CDCl_3$	7.59(d), 4.2	7.89(d), 4.2	2.51(s)	4.33(q), 7.2, 7-$\underline{CH_2}CH_3$ 3.16(m), $PN\underline{CH_2}CH_3$ 1.56(t), 7.2, 7-$CH_2\underline{CH_3}$ 1.14(t), 7.0, $PNCH_2\underline{CH_3}$
21b	$(CD_3)_2SO$	7.23(d), 4.1	7.63(d), 4.1	2.56(s)	7.36–7.52(m), Ph_2P 4.37(q), 7.2, 7-$\underline{CH_2}CH_3$ 1.47(t), 7.2, 7-$CH_2\underline{CH_3}$
22a	$CDCl_3$	7.82(d), 4.5	8.68(d), 4.5	2.78(s)	4.08(s), 7-$\underline{CH_3}$ 2.74(d), 13.2, $PN\underline{CH_3}$
22b	CD_3OD	7.72(d), 4.4	9.07(d), 4.4	2.70(s)	7.12(t), 7.7, 3,5-Ph 6.75(m), 2,4,6-Ph 3.94(s), 7-$\underline{CH_3}$ 3.23(m), $PN\underline{CH_2}CH_3$ 1.05(t), 7.0, $PNCH_2\underline{CH_3}$

the residue was crystallized from the appropriate solvent.

Tris(6-methylimidazo[2,1-b]thiazol-5-yl) phosphine **5**

To a solution of **1a** (15 mmol) in pyridine (15 mL) were successively added triethylamine (15 mmol) and phosphorus trichloride (5 mmol). After reacting for 24 h, the solution was evaporated to dryness and the residue was extracted with hot benzene (3 × 30 mL). The benzene extract was concentrated in vacuo to 20 mL, and phosphine **5** precipitated on cooling was separated and recrystallized.

Synthesis of Thiophosphinates **7**

To a solution of compound **1b, c** (20 mmol) in pyridine (20 mL) was added triethylamine (20 mmol)

TABLE 3 Phosphorylated Imidazo[2,1-*b*]thiazoles: ^{13}C NMR[a] δ (Multiplicity), ppm; J_{PC} (Hz)

	C^2	C^3	C^5	C^6	C^{7a}	6-CH_3	Others
4a	111.34 (s)	119.18 (d); 1.7	114.08 (d); 26.6	155.94 (d); 30.0	152.96 (s)	15.14 (d); 8.5	134.83 (d); 6.8, *ipso*-Ph 132.03 (d); 18.1, *o*-Ph 128.85 (d); 6.2, *m*-Ph 128.62 (s), *p*-Ph
13b	110.85 (s)	121.54 (s)	114.37 (d); 162.1	150.92 (d); 13.2	152.43 (d); 12.8	16.01 (s)	39.23 (d); 5.0, $N\underline{CH_2}CH_3$ 13.38 (d); 3.6, $NCH_2\underline{CH_3}$
19a	116.99 (s)	120.42 (s)	103.32 (d); 162.8	156.51 (d); 13.0	158.00 (d); 17.5	16.61 (s)	41.43 (d); 4.0, $N\underline{CH_2}CH_3$ 14.40 (d); 2.8, $NCH_2\underline{CH_3}$ 14.50 (d); 91.6, Me-P
21b	118.32 (s)	120.58 (d); 2.8	119.57 (d); 39.6	145.37 (d); 30.5	149.18 (s)	10.70 (d); 10.7	131.20 (d); 6.2, *ipso*-Ph 132.31 (d); 19.2, *o*-Ph 129.62 (d); 6.8, *m*-Ph 129.99 (s), *p*-Ph 43.40 (s), 7-$\underline{CH_2}CH_3$ 13.22 (s), 7-$CH_2\underline{CH_3}$
22a	119.44 (s)	122.48 (s)	117.10 (d); 151.5	142.79 (d); 15.8	149.64 (d); 6.8	12.01 (s)	37.04 (d); 3.4, $N\underline{CH_3}$ 36.27 (s), 7-CH_3

[a]All the spectra were taken in $CDCl_3$.

and phosphorus tribromide (10 mmol). ^{31}P NMR spectrum of the reaction mixture showed: δ ^{31}P = 7.85 ppm for **6a** after 24 h, or δ ^{31}P = 6.11 ppm for **6b** after 72 h. Diethylamine (30 mmol) and, 30 min later, finely crushed sulfur (10 mmol) were added and the mixture was stirred for 3 h, then the solvent was evaporated in vacuo and benzene (40 mL) was added to the residue. The insoluble salts were filtered off, the filtrate was evaporated, and the residue was crystallized.

Synthesis of Aminophosphines **8–10**

To a stirred solution of phosphines **2, 3** (10 mmol) in toluene (25 mL) cooled to 5°C was added dropwise a solution of the appropriate secondary amine (50 mmol) in toluene (15 mL). After reacting for 30 min, the precipitate was filtered off and the filtrate was evaporated in vacuo.

Synthesis of Imidazo[2,1-b]thiazol-5-yl-phosphinic Acids **11**

A solution of phosphines **2** or **3** (10 mmol) in benzene (30 mL) was left for 24 h in an open vessel under ambient atmosphere. The precipitated acid was separated and recrystallized.

Diethyl 6-Phenylimidazo[2,1-b]thiazol-5-ylthiophosphonate **12**

To a solution of phosphine **3a** (10 mmol) in benzene (20 mL) was added, at 5–10°C, triethylamine (20 mmol) and then, in a dropwise fashion, ethanol (20 mmol). After 0.5 h finely dispersed sulfur (10 mmol) was added and the mixture was stirred until the agent was completely dissolved. Then the triethylamine salt was separated, the filtrate was evaporated in vacuo, and the residue was crystallized.

Synthesis of Phosphine Sulfides **13**

To a solution of aminophosphines **8–10** (10 mmol) in benzene (10–20 mL) was added finely crushed sulfur (10 mmol), and the mixture was stirred until sulfur was completely dissolved. The residue after evaporation of the solvent was recrystallized.

Synthesis of Chlorophosphonium Chlorides **14**

Hexachloroethane (20 mmol) was dissolved in hexane (20 mL) and added to a solution of aminophosphine **8–10** (20 mmol) in benzene (20 mL). After 1 h, the precipitated product was filtered, washed with hexane and diethyl ether, and dried in vacuo.

Synthesis of Aminophosphonium Chlorides **15**

The appropriate chlorophosphonium chloride **14** (10 mmol) was dissolved in dichloromethane (20 mL), and ammonia gas was bubbled through the resulting solution until the precipitation ceased (for about 30 min). The precipitated ammonium chloride was separated by filtration, and the residue after evaporation of the filtrate was crystallized.

Synthesis of Aryliminophosphoranes **16**

To a solution of aminophosphine **8–10** (2 mmol) in toluene (30 mL) was added aryl azide (2 mmol) and the mixture was heated under reflux until the evolution of nitrogen ceased (1–2 h). After removal of the solvent, the residue was triturated with diethyl ether, to induce solidification, and recrystallized.

Synthesis of Phosphine Oxides **17**

The corresponding chlorophosphonium chloride **14** (5 mmol) was dissolved in dichloromethane (10 mL) and shaken with a saturated aqueous solution of sodium carbonate. The organic layer was separated, washed with water, dried over anhydrous sodium sulfate, and evaporated. The residue was held in vacuo (oily) or recrystallized (solid).

Synthesis of Iminophosphorane **18**

A solution of aminophosphonium chloride **15b** (5 mmol) in dichloromethane (50 mL) was shaken with 10% aq. NaOH (30 mL) in a separatory funnel. The organic layer was separated, dried (Na_2SO_4) and evaporated. The oily product was held in vacuo.

Synthesis of Phosphonium Salts **19**

To a solution of phosphine **4** or **8–10** (1 mmol) in benzene (30 mL) was added methyl iodide (1 mmol) and the reaction mixture was heated under reflux for 4–5 h. The precipitated product was filtered and crystallized.

Synthesis of Compound **20**

To a solution **8–10** (1 mmol) in acetonitrile (30 mL) was added methyl iodide (3 mmol) and the mixture was heated under reflux for 6–7 h. The product precipitated on cooling was filtered and crystallized.

Synthesis of Imidazo[2,1-b]thiazolium Tetrafluoroborates **21**

To a stirred solution of **4** or **8–10** (2 mmol) in dichloroethane (30 mL) was added dropwise, at −30°C, solution of thriethyloxonium tetrafluoroborate (2 mmol) in the same (20 mL). The reaction mixture was stirred at room temperature for 3 h, after which the solvent was evaporated. The residue was washed with diethyl ether until it solidified and then dried in vacuo. Product **21b** was purified by recrystallization.

Synthesis of Imidazo[2,1-b]thiazolium Iodides **22**

A mixture of corresponding substrate **13a** or **16a** (5 mmol) and methyl iodide (7 mmol) in benzene (20 mL) was heated under reflux for 10–16 h. The product precipitated after cooling was filtered and crystallized.

REFERENCES

[1] Tolmachev, A. A.; Yurchenko, A. A.; Merculov, A. S.; Semenova, M. G.; Zarudnitskii, E. V.; Ivanov, V. V.; Pinchuk, A. M. Heteroatom Chem 1999, 7, 585–597.

[2] Komarov, I. V.; Kornilov, M. Yu.; Turov, A. V.; Tolmachev, A. A.; Yurchenko, A. A.; Rusanov, E. V.; Chernega, A. N. Tetrahedron 1995, 51, 12417–12424.

[3] Tolmachev, A. A.; Yurchenko, A. A.; Kozlov, E. S.; Merkulov, A. S.; Semenova, M. G.; Pinchuk, A. M. Heteroatom Chem 1995, 6, 419–432.