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Phosphorylation of 2-(3-Methyl-1,3-diazabuten-1-yl)-3-Ethoxycarbonylthiophenes with Phosphorus(III) Halides

Alexandr M. Pinchuk, Svetlana A. Kovalyova, Sergey P. Ivonin, Anatoliy S. Merkulov, Tamara N. Kudrya, Alexandra A. Chaikovskaya, and Andrey A. Tolmachev

Institute of Organic Chemistry of National Academy of Sciences of Ukraine, Murmanskaya Street, 5, Kiev-94, 02056, Ukraine

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ABSTRACT: *2-(3-Methyl-1,3-diazabuten-1-yl)-3-ethoxycarbonylthiophenes are phosphorylated with phosphorus(III) halides in basic media at position 5 of the thiophene ring. Up to three heteroaromatic substituents can be introduced one by one at the same phosphorus atom. On this basis,* mono-, bis-, *and trishetaryl substituted P(III) and P(V) derivatives have been obtained. Phosphorylated 2-(*N,N-*dimethylformamidino)-3-ethoxycarbonylthiophenes provide a synthetic access to phosphorylated thienopyrimidines.* © 2001 John Wiley & Sons, Inc. Heteroatom Chem 12:641–651, 2001

INTRODUCTION

It is known that thienyl-2-dichlorophosphine can be obtained by phosphorylating thiophene with phosphorus trichloride in the presence of tin chloride(IV) [1]. However, running the reaction without the catalyst requires severe conditions, viz. 150–160°C in a sealed vial, even if phosphorus tribromide, a more reactive phosphorylating agent, is used [2]. Because of the electron-donor effect of the *N,N*-dimethylhydrazono group, thienylhydrazones are phosphorylated with phosphorus tribromide much more readily [3]. It might be expected that the electron-donor nature of the *N,N*-dimethylformamidino substituent in *N*-(thienyl-2)formamidines would also promote the course of the reaction under mild conditions, as in the phosphorylation of *N*-azolylformamidines [4]. The present work is focussed on the phosphorylation of 2-(3-methyl-1,3-diazabuten-1-yl)-3-ethoxycarbonylthiophenes with phosphorus(III) halides with a view to obtain multifunctional phosphorylated thiophenes and to study their properties.

RESULTS AND DISCUSSION

The activating effect of the *N,N*-dimethylaminomethylidenamino substituent at position 2 of the thiophene ring in the 2-(3-methyl-1,3-diazabuten-1-yl)-3-ethoxycarbonylthiophenes (**1a–c**) has appeared to be so great that despite the presence of an electron-acceptor group at position 3 of the thiophene moiety, the substances are phosphorylated easily at position 5 of the thiophene ring, when reacted with phosphorus(III) halides in benzene in the presence of triethylamine or in pyridine at room temperature (see Scheme 1). Thus, one, two, or even three (in the case of phosphorus tribromide) thienyl substituents may be successively provided at the

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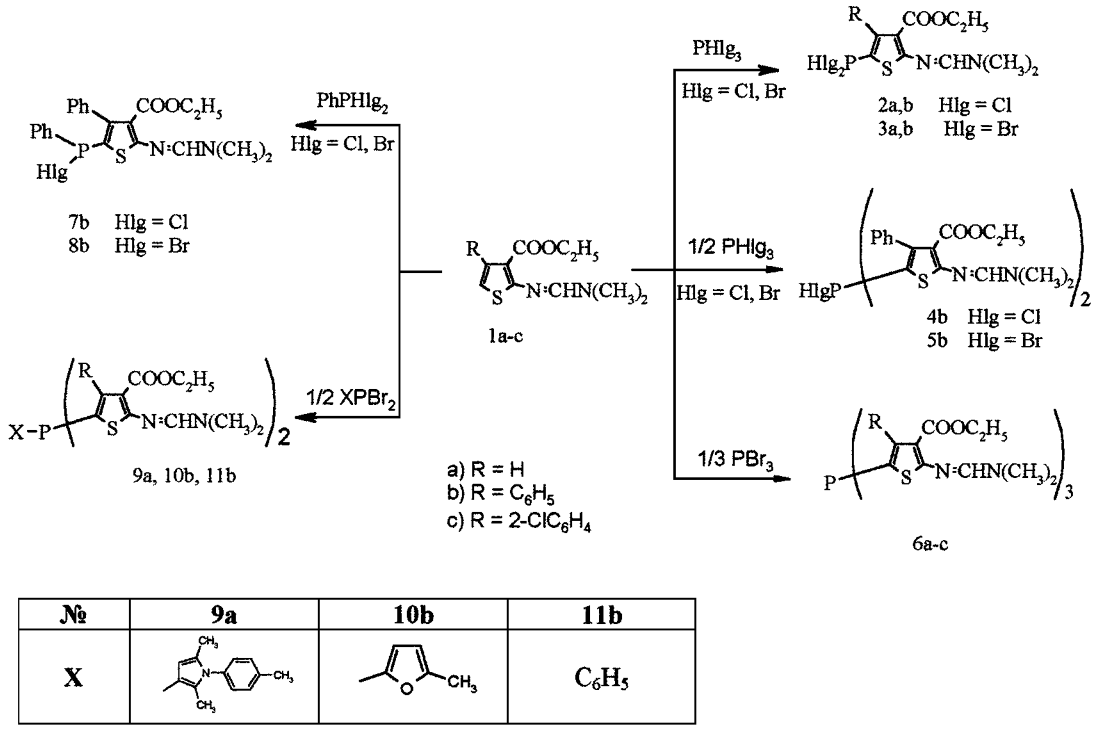
Correspondence to: Alexander M. Pinchuk; e-mail: hetfos@ukrpack.net.



SCHEME 1

same phosphorus atom, depending on the reagent ratio.

2-(3-Methyl-1,3-diazabuten-1-yl)-3-ethoxycarbonylthiophenes (**1a,b**) react easily with phosphorus tribromide and trichloride in the ratio of 1:1 and 2:1, respectively, to give thienyldihalogenophosphines (**2a,b, 3a,b**) and bisthienylhalogenophosphines (**4b, 5b**), respectively. Tristhienylphosphines (**6a–c**) are obtained when compounds **1a–c** react with phosphorus tribromide in the ratio of 3:1. It was found that the *tert*-phosphine **6c** needs a long period of heating (up to 50°C) of a mixture to be formed, and this apparently is connected to an increase of steric hindrance, if an *o*-chlorophenyl group is present at position 4.

Compounds **1a,b** react easily with phenyldibromophosphine and heteroaryldibromophosphines in the ratio of 1:1 and 2:1, respectively, to give halogenophosphines **7b, 8b** and *tert*-phosphines **9a, 10b, 11b**, respectively.

The structures of compounds **2a,b, 6a–c, 9a, 10b, 11b** were determined by ^{31}P (Table 1), ^{1}H (Table 2), and ^{13}C NMR spectroscopy (Table 3). For example, in the ^{1}H NMR spectrum of thienyldichlorophosphine (**2a**) there is no signal of the proton at the carbon atom 2 of the thiophene ring and the signal of the proton at the neighboring carbon atom 3 appears as a doublet (δH = 7.65 ppm; J_{HP} = 9,3 Hz). In the ^{13}C spectrum, resonances of carbon atoms 2 and 3 also appear as doublets with chemical shifts $\delta C = 127$ ppm ($J_{CP} = 72.2$ Hz) and $\delta C = 139$ ppm ($J_{CP} = 53.1$ Hz), respectively.

The halogenophospines **3a,b, 4b, 5b, 7b, 8b** were characterized by ^{31}P NMR spectroscopy only (Table 1) and were used in subsequent syntheses without additional purification.

The dihalogenophosphines **2a,b, 3a,b** and the halogenophosphines **4b, 5b, 7b, 8b** react with secondary amines to afford amidophosphonites **12a,b** and amidophosphinites **13b, 14b** (see Scheme 2). The structures of compounds **12b–14b** were determined by ^{31}P (Table 1), ^{1}H (Table 2), and ^{13}C NMR spectroscopy (Table 3). The amidophosphonite **12a** was characterized by ^{31}P NMR spectroscopy only (Table 1). Starting from phosphines **6a-c, 10b, 11b** and amides **12a,b, 13b, 14b**, standard procedures were employed to obtain compounds with a tetra- and pentacoordinated phosphorus atom, viz. methylphosphonium salts **15a–c, 19b, 20b, 23b, 24b**, oxides **16b, 21b, 25b**, thioxides **17a,b, 22b, 26a,b, 27b**, and imino derivatives **18a, 28b, 29b** (see Scheme 3). The structures of compounds **15–29** were determined by ^{31}P (Table 1) and ^{1}H NMR spectroscopy (Table 2).

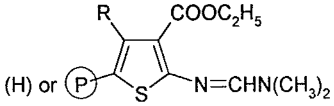
In the molecule of tristhienyl(methyl)phosphonium iodide(**15a**) containing no substituents at

TABLE 1 The Experimental Data of Compounds **1–43**

Compound	Yield (%)	mp (°C)	Formula	P(%) Calcd.	P(%) Found	N(%) Calcd.	N(%) Found	$\delta^{31}P$[a]
1a	60	–	$C_{10}H_{14}N_2O_2S$	–	–	12.38	12.11	–
1b	98	93–94[b]	$C_{16}H_{18}N_2O_2S$	–	–	9.26	9.42	–
1c	98	114–115[b]	$C_{16}H_{17}ClN_2O_2S$	–	–	8.32	8.48	–
2a	86	69–71[b]	$C_{10}H_{13}Cl_2N_2O_2PS$	9.47	9.25	8.56	8.42	144.8 (C_6H_6)
2b	70	146–147[b]	$C_{16}H_{17}Cl_2N_2O_2PS$	7.68	7.81	6.95	6.74	147.3 (C_6H_6)
3a	–	–	$C_{10}H_{13}Br_2N_2O_2PS$	–	–	–	–	131.1 (Py)
3b	–	–	$C_{16}H_{17}Br_2N_2O_2PS$	–	–	–	–	134.9 (Py)
4b	–	–	$C_{32}H_{34}ClN_4O_4PS_2$	–	–	–	–	53.9 (Py)
5b	–	–	$C_{32}H_{34}BrN_4O_4PS_2$	–	–	–	–	44.9 (Py)
6a	71	159–160[c]	$C_{30}H_{39}N_6O_6PS_3$	4.38	4.48	11.89	12.15	−43.1 (Py)
6b	82	230 (dec)[c]	$C_{48}H_{51}N_6O_6PS_3$	3.31	3.03	8.99	9.22	−56.2 (Py)
6c	75	215–216[c]	$C_{48}H_{48}Cl_3N_6O_6PS_3$	2.98	3.11	8.09	8.14	−59.7 (Py)
7b	–	–	$C_{22}H_{22}ClN_2O_2PS$	–	–	–	–	67.4 (Py)
8b	–	–	$C_{22}H_{22}BrN_2O_2PS$	–	–	–	–	60.8 (Py)
9a	70	80–82[c]	$C_{33}H_{40}N_5O_4PS_2$	4.65	4.71	10.52	10.23	−52.5 (Py)
10b	66	199–200[c]	$C_{37}H_{39}N_4O_5PS_2$	4.33	4.15	7.84	8.01	−64.1 (Py)
11b	78	177–178[c]	$C_{38}H_{39}N_4O_4PS_2$	4.36	4.23	7.88	7.62	−41.9 (Py)
12a	–	–	$C_{18}H_{29}N_4O_4PS$	–	–	–	–	85.4 (C_6H_6)
12b	70	112–113[b]	$C_{24}H_{33}N_4O_4PS$	6.14	6.11	11.10	11.23	88.9 (C_6H_6)
13b	70	178–179[b]	$C_{36}H_{44}N_5O_4PS_2$	4.39	4.51	9.92	10.14	28.42 (C_6H_6)
14b	68	115–116[b]	$C_{26}H_{30}N_3O_3PS$	6.25	5.98	8.48	8.62	42.9 (C_6H_6)
15a	74	113–115[d]	$C_{31}H_{42}IN_6O_6PS_3$	3.65	3.22	9.90	10.11	14.2 (C_6H_6)
15b	60	265 (dec)[d]	$C_{49}H_{54}IN_6O_6PS_3$	2.88	3.06	7.80	7.95	−2.5 (C_6H_6)
15c	84	260 (dec)[d]	$C_{49}H_{51}Cl_3IN_6O_6PS_3$	2.62	2.89	7.12	6.95	−3.8 (C_6H_6)
16b	71	279–280[c]	$C_{48}H_{51}N_6O_7PS_3$	3.26	3.33	8.84	9.12	−0.04 (C_6H_6)
17a	92	143–145[c]	$C_{30}H_{39}N_6O_6PS_4$	4.19	4.38	11.37	11.23	13.6 (C_6H_6)
17b	90	243(dec)[c]	$C_{48}H_{51}N_6O_6PS_4$	3.20	3.16	8.69	8.74	10.1 (C_6H_6)
18a	68	194–195[d]	$C_{37}H_{46}N_7O_6PS_3$	3.81	4.09	12.07	12.15	22.8 (C_6H_6)
19b	79	135(dec)[e]	$C_{39}H_{42}IN_4O_4PS_2$	3.63	3.72	6.57	6.22	−4.3 (C_6H_6)
20b	71	200–201[e]	$C_{37}H_{47}IN_5O_4PS_2$	3.65	3.42	8.26	8.43	31.4 (C_6H_6)
21b	52	101–102[c]	$C_{38}H_{39}N_4O_5PS_2$	4.26	4.11	7.71	7.66	9.9 (C_6H_6)
22b	72	177–178[c]	$C_{36}H_{44}N_5O_4PS_3$	4.20	4.44	9.49	9.61	44.6 (C_6H_6)
23b	40	203–204[e]	$C_{25}H_{36}IN_4O_4PS$	4.79	4.52	8.67	8.75	40.1 (CH_3OH)
24b	70	196–197	$C_{27}H_{33}IN_3O_3PS$	4.86	5.07	6.59	6.52	4.2 (C_6H_6)
25b	60	128–129[b]	$C_{24}H_{33}N_4O_5PS$	5.95	6.12	10.76	10.97	15.5 (C_6H_6)
26a	77	48–50[c]	$C_{18}H_{29}N_4O_4PS_2$	6.73	6.59	12.16	12.05	68.9 ($CHCl_3$)
26b	69	183–184[c]	$C_{24}H_{33}N_4O_4PS_2$	5.77	5.89	10.44	10.59	63.8 (C_6H_6)
27b	35	108–109[b]	$C_{26}H_{30}N_3O_3PS_2$	5.87	5.79	7.96	8.12	57.8 (C_6H_6)
28b	50	89–90[c]	$C_{30}H_{37}BrN_5O_4PS$	4.59	4.46	10.38	10.05	31.5 ($CHCl_3$)
29b	30	69–71[b]	$C_{32}H_{35}N_4O_3PS$	5.28	5.43	9.55	9.49	1.4 (C_6H_6)
30b	64	225–226[c]	$C_{20}H_{23}N_4O_3PS_2$	6.70	6.51	12.11	11.96	63.5 ($CHCl_3$)
31b	50	>320[c]	$C_{36}H_{21}N_6O_3PS_3$	4.35	4.17	11.79	7.45	−57.0 (C_6H_6)
32a	57	268–270[c]	$C_{18}H_9N_6O_3PS_4$	6.00	6.19	16.27	16.04	13.5 (DMSO)
33a	42	314–315[c]	$C_{18}H_{12}N_9O_3PS_4$	5.52	5.61	22.45	22.14	13.7 (DMSO)
34a	34	228–230[c]	$C_{25}H_{19}N_{10}O_3PS_3$	4.88	4.64	22.07	22.19	5.8 (DMSO)
35a	93	252–253	$C_{39}H_{24}N_9O_6PS_4$	3.54	3.46	14.42	14.55	13.5 (DMSO)
36b	80	177–179[c]	$C_{22}H_{28}N_3O_5PS_2$	6.08	5.96	8.25	8.14	64.7 (C_6H_6)
37b	70	186–187[c]	$C_{21}H_{28}N_3O_4PS_2$	6.43	6.67	8.73	8.59	64.2 (CH_3OH)
38a	54	133–135[c]	$C_{24}H_{24}N_3O_9PS_4$	4.71	5.09	6.39	6.25	13.4 ($CHCl_3$)
39a	47	148–150[c]	$C_{24}H_{24}N_3O_{10}PS_3$	4.83	5.11	6.55	6.59	−2.0 (DMSO)
40a	68	267–268[f]	$C_{15}H_9K_3N_3O_6PS_3$	5.42	5.29	7.35	7.39	−42.8 (H_2O)
41a	81	260 (dec)[f]	$C_{15}H_9K_3N_3O_6PS_4$	5.13	5.27	6.96	6.82	13.4 (H_2O)
42a	53	277–278[f]	$C_{22}H_{16}K_3N_4O_6PS_3$	4.58	4.67	8.28	8.37	20.8 (H_2O)
43a	67	210–212[f]	$C_{15}H_{12}N_3O_6PS_4$	6.33	6.58	8.58	8.71	13.5 ($CHCl_3$)

[a] Compounds within parentheses represent the solvents.
[b] Recrystallize from octane.
[c] Recrystallize from *i*-PrOH.
[d] Precipitated from benzene by hexane.
[e] Recrystallized from an ethylacetate–hexane mixture.
[f] Precipitated from ethanol by water.

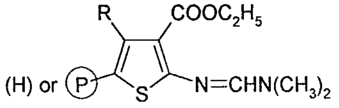
TABLE 2 The ^1H Data of Compounds **1**–**29** (δ, ppm; J, Hz)



	$CH_3CH_2—O$		$N{=}CHN(CH_3)_2$				
No.	$\underline{CH_3}\ CH_2$	$CH_2—O$	$N{=}CH—$	$N(CH_3)_2$	R	(H) or Ⓟ	Solvent
1a	1.33 (t, 3H, $J_{HH} = 7.2$)	4.25 (q, 2H, $J_{HH} = 7.2$)	7.65 (s, 1H)	3.09 (s, 6H)	7.21 (d, 1H, $J_{HH} = 3.8$)	6.52 (d, 1H, $J_{HH} = 3.8$)	$CDCl_3$
1b	1.03 (t, 3H, $J_{HH} = 7.2$)	4.10 (q, 2H, $J_{HH} = 7.2$)	7.69 (s, 1H)	3.06 (s, 6H)	7.28–7.35 (m, 5H)	6.48 (s, 1H)	$CDCl_3$
1c	1.08 (t, 3H, $J_{HH} = 7.2$)	4.13 (q, 2H, $J_{HH} = 7.2$)	7.67 (s, 1H)	3.06 (s, 6H)	7.37 (m, 4H)	6.46 (s, 1H)	$CDCl_3$
2a	0.8 (t, 3H, $J_{HH} = 7.2$)	3.84 (q, 2H, $J_{HH} = 7.2$)	6.87 (s, 1H)	1.83; 2.26 (s, 6H)	.57 (d, 1H, $J_{HP} = 9.3$)	–	C_6D_6
2b	0.67 (t, 3H, $J_{HH} = 7.2$)	3.90 (q, 2H, $J_{HH} = 7.2$)	7.20 (s, 1H)	1.93; 2.48 (s, 6H)	7.07–7.06 (m, 3H); 7.32–7.37 (m, 2H)	–	C_6D_6
6a	1.05 (t, 9H, $J_{HH} = 7.2$)	4.17 (q, 6H, $J_{HH} = 7.2$)	7.68 (s, 3H)	1.90; 2.52 (s, 18H)	8.13 (d, 3H, $J_{HP} = 9.6$)	–	C_6D_6
6b	0.75 (t, 9H, $J_{HH} = 7.2$)	3.98 (q, 6H, $J_{HH} = 7.2$)	8.04 (s, 3H)	2.59; 2.15 (s, 18H)	6.98–7.18 (m, 15H)	–	C_6D_6
6c	0.62–0.98 (m, 9H)	3.95–4.22 (m, 6H)	8.01 (br s, 3H)	2.01–2.16; 2.59–2.63 (m, 18H)	6.78–6.91; 7.11–7.22 (m, 12H)	–	C_6D_6
9a	1.34 (t, 3H, $J_{HH} = 7.2$)	4.26 (q, 2H, $J_{HH} = 7.2$)	8.57 (s, 2H)	3.12 (s, 12H)	7.71 (s, 1H)	1.79 (s, 3H, 5—CH_3); 1.79 (s, 3H, 2—CH_3); 2.40 (s, 3H, $\underline{CH_3}\ C_6H_4$); 7.08 (d, 2H, *o*-C_6H_4, $J_{HH} = 8.1$); 7.45 (d, 2H, m-C_6H_4, $J_{HH} = 8.1$)	$CDCl_3$
10b	0.68 (t, 6H, $J_{HH} = 7.2$)	3.93 (q, 4H, $J_{HH} = 7.2$)	7.34 (s, 2H)	1.89; 2.51 (s, 12H)	6.99–7.10; 7.34–7.39 (m, 10H)	2.01(s, 3H, CH_3); 5.77 (br s, 1H, $\underline{CH}{=}C(CH3)$); 6.63 (d, $\underline{CH}{=}C(P)$, $J_{HP} = 2.7$)	C_6D_6
11b	0.67 (t, 6H, $J_{HH} = 7.2$)	3.95 (q, 4H, $J_{HH} = 7.2$)	7.22 (s, 2H)	1.79; 2.48 (s, 12H)	7.61 (t, 2H, $J_{HH} = 7.2$); 7.57 (d, 4H, $J_{HH} = 7.2$)	7.02–7.12 (m, 9H, $\underline{C_6H_5}—C + \underline{C_6H_5}—P$)	C_6D_6
12b	0.73 (t, 3H, $J_{HH} = 7.2$)	3.97 (q, 2H, $J_{HH} = 7.2$)	7.46 (s, 1H)	1.93; 2.51 (s, 6H)	7.04 (d, 1H, $J_{HH} = 8$); 7.58 (d, 2H, $J_{HH} = 7$); 7.10–7.18 (m, 2H)	2.80 (m, 8H); 3.37 (m, 8H)	C_6D_6
13b	0.88 (t, 6H, $J_{HH} = 7.2$)	3.92 (m, 4H, $J_{HH} = 7.2$)	7.37 (s, 2H)	1.91; 2.52 (s, 6H)	7.24–7.38 (m, 6H); 7.75 (dd, 4H)	0.68 (t, 6H, $\underline{CH_3}CH_2$, $J_{HH} = 7.2$); 3.26–3.39 (m, 4H, $CH_3\underline{CH_2}$)	C_6D_6
14b	0.73 (t, 3H, $J_{HH} = 7.2$)	3.99 (q, 2H, $J_{HH} = 7.2$)	7.32 (s, 1H)	1.89; 2.51 (s, 6H)	aromatic: 7.03–7.22 (m, 6H); 7.14–7.64 (m, 4H); aliphatic: 2.87 (br s, 4H, —CH_2N); 3.45 (br s, 4H, —CH_2O)		C_6D_6
15a	1.35 (t, 9H, $J_{HH} = 7.2$)	4.30 (q, 6H, $J_{HH} = 7.2$)	8.19 (s, 3H)	3.16; 3.30 (s, 18H)	7.79 (d, 3H, $J_{HP} = 10.5$)	2.76 (d, 3H, CH_3—P, $J_{HH} = 19.2$)	$CDCl_3$
15b	0.93 (t, 9H, $J_{HH} = 6.9$)	4.02 (q, 6H, $J_{HH} = 6.9$)	8.62 (s, 3H)	3.15; 3.43 (s, 18H)	6.92 (d, 6H); 7.17–7.29 (m, 9H)	−0.14 (d, 3H, CH_3—P, $J_{HH} = 14$)	$CDCl_3$
15c	0.82–0.94 (m, 9H)	3.91–4.05 (m, 6H)	8.73 (br s, 3H)	3.17; 3.45 (s, 18H)	6.95–7.19 (m, 12H)	0.23 (d, 1H, $J_{HP} = 14$); 0.35 (d, 2H, $J_{HP} = 14$)	$CDCl_3$
16b	0.82 (t, 9H, $J_{HH} = 7.2$)	3.93 (q, 6H, $J_{HH} = 7.2$)	7.59 (s, 3H)	3.07; 3.11 (s, 18H)	7.17–7.26 (m, 15H)	–	$CDCl_3$
17a	1.31 (t, 9H, $J_{HH} = 6.9$)	4.23 (q, 6H, $J_{HH} = 6.9$)	7.83 (s, 3H)	3.08; 3.12 (s, 18H)	7.61 (d, 3H, $J_{HP} = 10.2$)	–	CD_3OD
17b	0.83 (t, 9H, $J_{HH} = 7.2$)	3.93 (q, 6H, $J_{HH} = 7.2$)	7.56 (s, 3H)	3.08; 3.11 (s, 18H)	7.12–7.22(m, 15H)	–	$CDCl_3$
18a	0.91 (t, 9H, $J_{HH} = 7.2$)	4.03 (q, 6H, $J_{HH} = 7.2$)	7.02 (m, 5H, *o*-C_6H_4 + $\underline{CH{=}N}$)	1.88; 2.48 (s, 18H)	8.51 (d, 3H, $J_{HH} = 9.3$)	2.15 (s, 3H, $\underline{CH_3}$); 7.53 (d, 2H, m-C_6H_4, $J_{HH} = 7.2$)	C_6D_6
19b	0.9 (t,6H, $J_{HH} = 7.2$)	3.98 (q, 4H, $J_{HH} = 7.2$)	8.28 (s, 2H)	3.11; 3.30 (s, 12H)	6.99 (d, 4H, m-C_6H_5 $J_{HH} = 7.2$)	7.2–7.4; 7.62–7.8 (m, 11H, *o,p*-C_6H_5+ C_6H_5—P); 0.11 (d, 3H, CH_3—P, $J_{HP} = 14.4$)	$CDCl_3$
20b	0.92 (t, 6H, $J_{HH} = 7.2$)	4.01 (q, 4H, $J_{HH} = 7.2$)	8.53 (s, 1H)	3.14; 3.39 (s, 12H)	7.03 (br s, 4H); 7.28–7.39 (m, 6H)	1.22 (t, 6H,$\underline{CH_3}CH_2$); 3.19–3.27 (m, 4H, $CH_3\underline{CH_2}$); 0.62 (d, 3H, CH_3-P,CH_3-P, $J_{HP} = 13.5$)	$CDCl_3$
21b	0.82 (t, 6H, $J_{HH} = 7.2$)	3.94 (q, 4H, $J_{HH} = 7.2$)	7.68 (s, 2H)	3.08; 3.09 (s, 12H)	6.98–7.2 (m, 15H, $\underline{C_6H_5} + \underline{C_6H_5}$—P)		$CDCl_3$
22b	0.91 (t, 6H, $J_{HH} = 7.2$)	3.94 (q, 4H, $J_{HH} = 7.2$)	7.65 (s, 2H)	3.08; 3.09 (s, 12H)	7.19 (br s, 10H)	0.86 (t, 6H); 2.83–2.94 (m, 4H)	$CDCl_3$
23b	0.90 (t, 3H, $J_{HH} = 7.2$)	3.98 (q, 2H, $J_{HH} = 7.2$)	7.98 (s, 1H)	3.13; 3.25 (s, 6H)	7.19–7.23 (m, 2H); 7.45–7.48 (m, 3H)	2.11 (t, 3H, CH_3—P, $J_{HH} = 10.2$); 3.18 (m, 8H); 3.75 (m, 8H)	$CDCl_3$

(Continued)

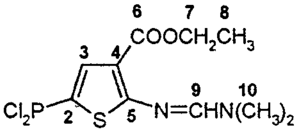
TABLE 2 Continued

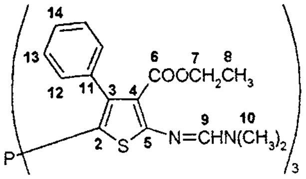


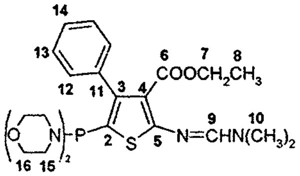
	$CH_3CH_2{-}O$		$N{=}CHN(CH_3)_2$				
No.	CH_3 CH_2	$CH_2{-}O$	$N{=}CH{-}$	$N(CH_3)_2$	*R*	*(H) or* P	*Solvent*
24b	0.88 (t, 3H, $J_{HH} = 7.2$)	3.87 (q, 2H, $J_{HH} = 7.2$)	8.12 (s, 1H)	3.15; 3.28 (s, 6H)	aromatic: 7.02 (br s, 2H,); 7.24–7.38(m, 3H); 7.63–7.92 (m, 5H); aliphatic: 3.00–3.12(m, 4H, $-CH_2N$); 3.77(br s, 4H,$-$ CH_2O); 2.22 (d, 3H, $CH_3{-}P$, $J_{HP} = 13.5$)		$CDCl_3$
25b	0.69 (t, 3H, $J_{HH} = 7.2$)	3.93 (q, 2H, $J_{HH} = 7.2$)	7.33 (s, 1H)	1.91; 2.47 (s, 6H)	7.16 (br s, 3H); 7.82 (d, 2H, $J_{HH} = 8.7$)	2.89 (m, 8H); 3.59 (m, 8H)	CD_3OD
26a	1.34 (t, 3H, $J_{HH} = 7.2$)	4.26 (q, 2H, $J_{HH} = 7.2$)	7.71 (s, 1H)	–	7.73 (d, 1H) $J_{HP} = 12$	3.13 (m, 14H, $-\underline{CH_2}N+N\underline{CH_3}$); 3.66 (m, 8H, $\overline{-CH_2O}$)	$CDCl_3$
26b	0.86 (t, 3H, $J_{HH} = 7.2$)	3.93 (q, 2H, $J_{HH} = 7.2$)	7.77 (s, 1H)	3.74 (s, 6H)	7.35 (br s, 5H)	2.95 (m, 8H, $-CH_2N$); 3.51 (m, 8H, $-CH_2O$)	$CDCl_3$
27b	0.80 (t, 3H, $J_{HH} = 7.2$)	3.90 (q, 2H, $J_{HH} = 7.2$)	7.87 (s, 1H)	3.69 (s, 6H)	aromatic: 6.89–6.92 (m, 2H); 7.13–7.53 (m, 8H); aliphatic: 2.78–3.00 (m, 4H, $-CH_2N$); 3.16 (br s, 4H, $-CH_2O$) $-CH_2O$)		$CDCl_3$
28b	0.86 (t, 3H, $J_{HH} = 7.2$)	3.92 (q, 2H, $J_{HH} = 7.2$)	7.73 (s, 1H)	3.08; 3.11 (s, 6H)	7.28–7.32 (m, 5H)	aromatic: 6.60 (d, 2H, $J_{HH} = 8.7$); 7.15 (d, 2H, $J_{HH} = 8.7$); aliphatic: 2.92 (br s, 8H, $-CH_2N$); 3.48 (br s, 8H, $-CH_2O$)	$CDCl_3$
29b	0.81 (t, 3H, $J_{HH} = 7.2$)	3.91 (q, 2H, $J_{HH} = 7.2$)	7.78 (s, 1H)	3.07 (t, 6H)	aromatic: 6.68–7.57 (m, 15H); aliphatic: 2.95 (br, s, 4H, $-CH_2N$); 3.8 (br, s, 4H, $-CH_2O$)		$CDCl_3$

position 3 of the thiophene rings (R = H), the signal of protons of the methyl group at the phosphorus atom gives rise to a ^1H NMR peak in the normal region, which appears as a doublet with the chemical shift $\delta H = 2.73$ ppm ($J_{HP} = 19$ Hz). At the same time, the protons of the methyl groups at the phosphorus atom in the methylphosphonium salts **15b, 19b, 20b, 23b, 24b** ($R = C_6H_5$) and **15c** ($R = 2\text{-}ClC_6H_4$) exhibit signals that are shifted to a stronger field (Table 2); for instance, the corresponding chemical shift for methylphosphonium iodide **15b** reaches the value $\delta H = -0.14$ ppm ($J_{HP} = 14.7$ Hz). In this case,

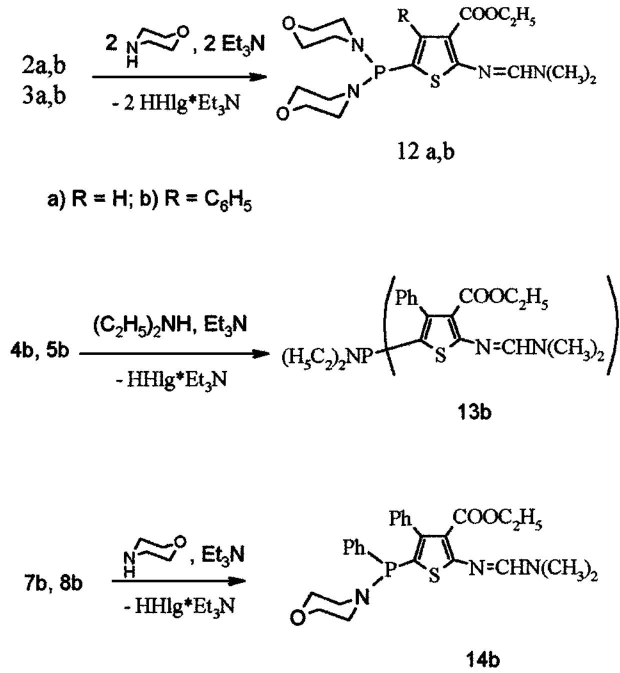
TABLE 3 The ^{13}C Data of Compounds **2a, 6b, 12b** (δ, ppm; J, Hz)







Carbon No.	**2a** C_6D_6/TMS	**6b** DMSO-d_6/TMS	**12b** C_6D_6/TMS
2	126.68 (d, $J_{CP} = 72.2$)	150.58 (d, $J_{CP} = 30.2$)	125.75 (d, $J_{CP} = 19.5$)
3	138.71 (d, $J_{CP} = 53.1$)	126.14 (d, $J_{CP} = 27.9$)	145.31 (d, $J_{CP} = 17.5$)
4	116.16 (d, $J_{CP} = 11.1$)	125.02 (d, $J_{CP} = 4.2$)	124.98 (s)
5	161.19 (s)	140.11 (d, $J_{CP} = 4.7$)	139.26 (s)
6	173.08 (s)	168.07 (s)	166.03 (s)
7	58.59 (s)	63.24 (s)	60.66 (s)
8	13.12 (s)	17.47 (s)	14.74 ((d, $J_{CP} = 24.7$)
9	154.01 (s)	158.48 (s)	154.68 (s)
10	33.03 (s); 38.25 (s)	38.10 (s)	23.65 (s); 32.58 (s)
11	–	167.35 (s)	141.7 (s)
12	–	132.47 (s)	130.59 (s)
13	–	131.03 (s)	–
14	–	130.78 (s)	127.68 (s)
15	–	–	50.53 (d, $J_{CP} = 14.2$)
16	–	–	68.44 (d, $J_{CP} = 6.5$)



SCHEME 2

the shift of the signal of the methyl group is evidently due to the symmetric screening of its protons by three phenyl groups, which are located in the "ortho" position to the phosphorus atom. In our opinion, the phenyl rings and the methyl group at the phosphorusatom are positioned on the same side of the conventional plane passing through the phosphorus atom perpendicular to the P—CH_3 bond. This conjecture is consistent with potential energy values computed by the molecular mechanics method (MM+) for the starting trisphosphine molecule **6b** with varied mutual arrangement of the lone electron pair of the phosphorus atom and the phenyl rings. As seen from the calculated data, the "crown-like" configuration of the phenyl rings relative to the lone electron pair is, on the average, 20–30% more energetically preferable than other configurations (see Fig. 1). With regard to the fact that the alkylation of tertiary phosphines is not accompanied by inversion at the phosphorus atom [5], one can expect that the "crown-like" configuration will be retained on alkylation. In the molecule of the more sterically hindered methylposphonium iodide (**15c**) (R = 2-ClC_6H_4), the arrangement of all *o*-chlorophenyl rings on the same side of the plane is hampered. In this case, the calculations suggest that the most energetically preferable configuration involves the disposition of the methyl group at the phosphorus atom and with only two *o*-chlorophenyl substituents on the same side of the plane. This arrangement will result in lesser screening of the methyl group as compared to the "crown-like" pattern, and the corresponding resonance will therefore occur at a weaker field. Besides, such a configuration allows for three possibilities for the mutual arrangement of chlorine atoms in the *o*-chlorophenyl groups lying on the same side of the plane as the methyl group, two of the three variants being identical as regards the disposition of the chlorine atoms relative to the methyl group. Thus, in the ^1H NMR spectrum, the P—CH_3 group should resonate in the form of two signals, with their integral intensities related as 2:1. This is the case for compound **15c**: the methyl group at the phosphorus atom shows the ^1H resonance as two doublets with the chemical shifts $\delta H = 0.35$ ppm ($J_{HP} = 14.7$ Hz) and $\delta H = 0.23$ ppm ($J_{HP} = 14.7$ Hz) and the integral intensity ratio equal to 2:1.

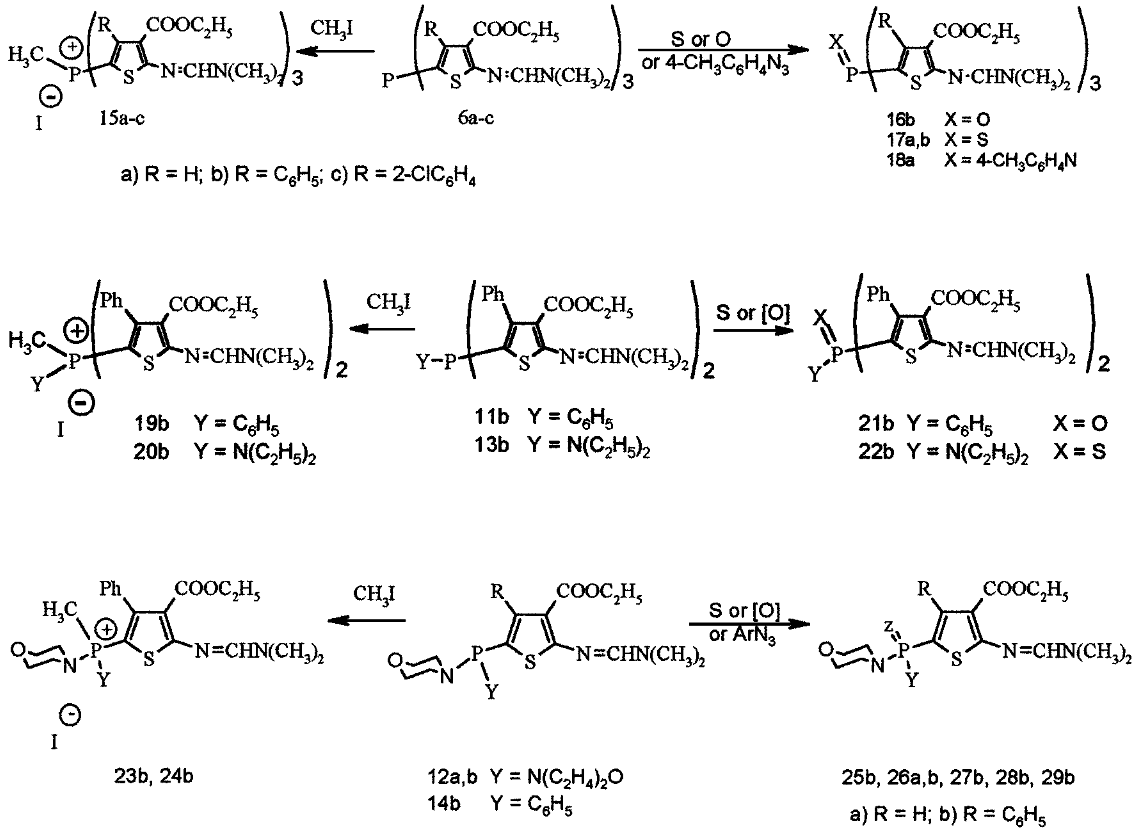
Steric hindrance caused by aryl groups at position 4 of the thiophene rings also exert an effect on the reactivity of phosphines **6b,c**. So, unlike the phosphine **6a**, the phosphines **6b,c** do not react with aryl azides, probably, due to increasing steric hindrance at the phosphorus atom.

Phosphine **6b**, phosphine thioxide **17a**, iminophospine **18a**, and diamidothiophosphonate **26b** react with formamide or hydrazine when heated to give phosphorylated thienopyrimidones **30b, 31b, 32a–34a** by means of heterocyclization with participation of amidine and ethoxycarbonyl groups. 3-Aminothienopyrimidone (**33a**) reacts easily with a substituted benzaldehyde to give a Shiffs base, as, for example, **35a** (see Scheme 4). Unsymmetrical phosphines **9a, 10b, 11b** by heating in formamide, do not react to form thienopyrimidones; this, apparently, is connected with their lower thermal stability.

The amidothiophosphonate **26b**, phosphine thioxide **17a**, and imino derivative **18a** under acidic hydrolysis conditions give derivatives of 5-(*N*-formyl)aminothiophenes **36b, 38a, 39a**. The compound **26b**, on heating with aqueous-alcoholic alkali, leads to phosphorylated 5-amino-4-ethoxycarbonylthiophene (**37b**), whereas phosphine **6a**, phosphine thioxide **17a**, and the imino derivative **18a** under the same conditions are hydrolized with participation of both ethoxycarbonyl and amidine groups, giving phosphorylated derivatives of 5-amino-4-thiophenecarboxylic acid (**40a–43a**) (see Scheme 5). The structures of compounds obtained as shown in Schemes 4 and 5 were determined by ^{31}P (Table 1) and ^1H NMR spectroscopy (Tables 4 and 5).

EXPERIMENTAL

All manipulations with moisture-sensitive compounds were performed under an atmosphere of dry



№	23b	24b	25b	26a	26b	27b	28b	29b
Y	N(C$_2$H$_4$)$_2$O	C$_6$H$_5$	N(C$_2$H$_4$)$_2$O	N(C$_2$H$_4$)$_2$O	N(C$_2$H$_4$)$_2$O	C$_6$H$_5$	N(C$_2$H$_4$)$_2$O	C$_6$H$_5$
Z	-	-	O	S	S	S	4-BrC$_6$H$_4$N	C$_6$H$_5$N

SCHEME 3

argon, standard Shlenk techniques being used. Solvents were purified by conventional procedures. The ^{31}P, ^{1}H, and ^{13}C NMR spectra were recorded on a Varian VXR-300 spectrometer (121, 300, and 75 MHz respectively). Chemical shifts are reported relative to internal tetramethylsilane (^{1}H, ^{13}C) or to external 85% H_3PO_4 (^{31}P).

*General Procedure for Synthesis of (2-Thienyl)dichlorophosphines (*2a,b*)*

The solutions of the corresponding compounds **1a,b** (0.013 mol) in pyridine (25 ml) were cooled to 10°C, and phosphorus trichloride (0.02 mol) was added dropwise. Each reaction mixture was stirred at 25°C for 2.5 h and then evaporated to dryness in vacuo. The residue was dissolved in benzene (25 ml), followed by addition of triethylamine (0.015 mol), filtration of the mixture, and evaporation of the filtrate to dryness in vacuo.

*General Procedure for Synthesis of (2-Thienyl)dibromophosphines (*3a,b*)*

The solution of each compound **1a,b** (0.013 mol) in pyridine (25 ml) was cooled to 10°C, and phosphorus tribromide (0.013 mol) was added dropwise. The reaction mixture was stirred at 25°C for 1.5 h and then evaporated to dryness in vacuo. The residue was dissolved in benzene, followed by addition of triethylamine (0.015 mol), filtration of the mixture, and evaporation of the filtrate to dryness in vacuo. The products **3a,b** were used without further purification.

*General Procedure for Synthesis of Bis-[3-phenyl-4-ethoxycarbonyl-5-(1-methyl-1,3-diazabuten-1-yl)-thienyl]halogenophosphines (*4b, 5b*)*

A solution of the compound **1b** (0.01 mol) in pyridine (20 ml) was cooled to 10°C, and phosphorus

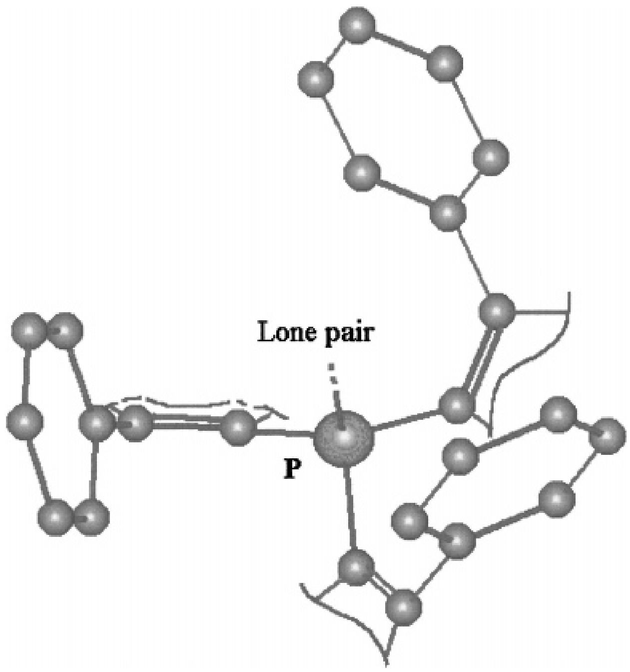


FIGURE 1 The spatial structure of the central moiety of the phosphine **6b** molecule corresponding to the potential energy minimum. (Calculated by the MM+ method).

trichloride (0.005 mol) or phosphorus tribromide (0.005 mol) was added dropwise. The reaction mixture was stirred at 25°C for 5 days (in the case of phosphorus trichloride) and for 20 h (in the case of phosphorus tribromide). Then it was evaporated to dryness in vacuo. The residue was dissolved in benzene, followed by addition of triethylamine (0.02 mol), filtration of the mixture, and evaporation of the filtrate to dryness in vacuo. The products were used without further purification.

General Procedure for Synthesis of the Tertiary Phosphines **6a,b**

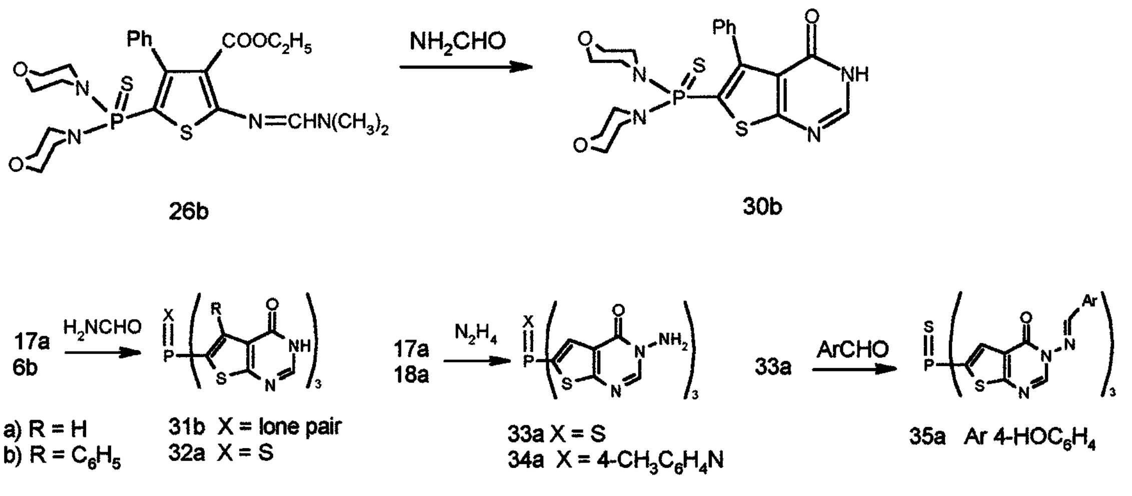
A solution of each compound **1a,b** (0.01 mol) in pyridine (20 ml) was cooled to 10°C and stirred, and phosphorus tribromide (0.0033 mol) was added dropwise. The mixture was stirred at 25°C for 28 h. Then it was diluted with benzene (10 ml), filtered, and evaporated to dryness in vacuo.

*Tris-[3-(2-chlorophenyl)-4-ethoxycarbonyl-5-(1-methyl-1,3-diazabuten-1-yl)-thienyl]phosphine (***6c***)*

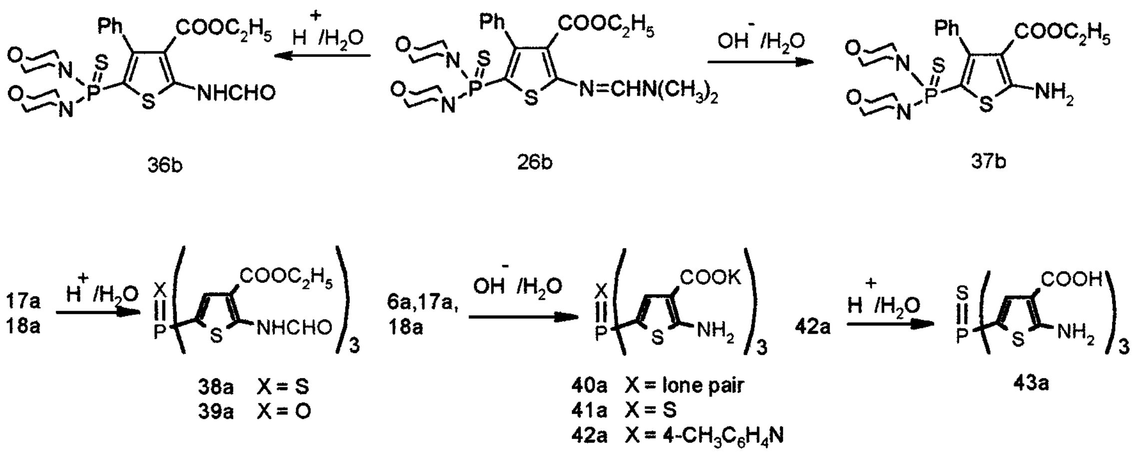
A solution of **1c** (0.01 mol) in pyridine (20 ml) was cooled to 10°C and stirred, and phosphorus tribromide (0.0033 mol) was added dropwise. The mixture was stirred at 50°C for 40 h. Then it was diluted with benzene (10 ml), filtered, and evaporated to dryness in vacuo.

*General Procedure for Synthesis of [3-Phenyl-4-ethoxycarbonyl-5-(1-methyl-1,3-diazabuten-1-yl)-thienyl]phenylhalogenophosphines (***7b, 8b***)*

A solution of the compound **1b** (0.01 mol) in pyridine (20 ml) was cooled to 10°C and stirred, and phenyldichlorophosphine (0.01 mol) or phenyldibromophosphine (0.01 mol) was added dropwise. The reaction mixture was stirred at 25°C for 5 days (in the case of phenyldichlorophosphine) and for 20 h (in the case of phenyldibromophosphine). Then it was evaporated to dryness in vacuo. The residue was dissolved in benzene, followed by addition of triethylamine (0.011 mol), filtration of the mixture,



SCHEME 4



SCHEME 5

and evaporation of the filtrate to dryness in vacuo. The compounds **7b, 8b** were used without further purification.

General Procedure for Synthesis of the Tertiary Phosphines **9a, 10b, 11b**

A solution of each compound **1a,b** (0.01 mol) in pyridine (20 ml) was cooled to 10°C and stirred, and the corresponding [1-(4-methylphenyl)-2,5-dimethylpirrolyl-3]- (0.005 mol), (2-methylfuryl-5)- (0.005 mol), or phenyldibromophosphine (0.005 mol) was added dropwise. The mixture was stirred at 25°C for 28 h. Then it was diluted with benzene (10 ml), filtered, and evaporated to dryness in vacuo.

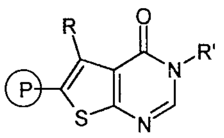
General Procedure for Synthesis of the Amidophosphonites **12a,b**

A solution of each compound **2a,b** (0.01 mol) or **3a,b** (0.01 mol) in benzene (25 ml) was cooled to 10°C and stirred; then morpholine (0.04 mol) was added dropwise. The mixture was stirred at 25°C for 1 h and then filtered. The filtrate was evaporated to dryness in vacuo. The compound **12a** was used without further purification.

General Procedure for Synthesis of the Amidophosphinites **13b, 14b**

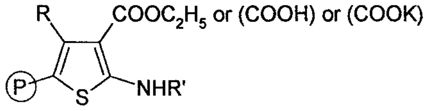
A solution of each compound **4b, 5b** (0.01 mol) or **7b, 8b** (0.01 mol) in benzene (25 ml) was cooled to

TABLE 4 The ^1H Data of Compounds **30–35** (δ, ppm; J, Hz)



No.	R′	N=CH—N	R	Ⓟ	Solvent
30b	8.28 (br s, 1H)	7.23 (s, 1H)	7.45–7.51 (m, 5H)	3.04 (m, 8H, —CH_2—N); 3.57 (m, 8H, —CH_2—O)	$CDCl_3$
31b	12.51 (br s, 1H)	8.19 (s, 1H)	6.93 (d, 2H, J_{HH} = 7); 7.21 (m, 3H)	–	DMSO-d_6
32a	12.7–12.9 (3H)	8.30 (s, 3H)	7.95 (d, 3H, , J_{HP} = 10.5)	–	DMSO-d_6
33a	7.74 (s, 6H)	9.28 (s, 3H)	7.52 (d, 3H, J_{HP} = 10.5)	–	DMSO-d_6
34a	7.73 (m, 10H, $\underline{NH_2 + C_6H_4}$)	9.28 (s, 3H)	7.56 (d, 3H, J_{HP} = 9.3)	2.53 (s, 3H, $\underline{CH_3}$)	DMSO-d_6
35a	6.79 (d, 6H, J_{HH} = 8.1); 7.49 (d, 6H, J_{HH} = 8.1); 8.25 (s, 1H, N—N=$\underline{CH}$); 11.3 (s, 3H)	9.89 (s, 3H)	7.72 (d, 3H, J_{HP} = 10.5)	–	DMSO-d_6

TABLE 5 The ^1H Data of Compounds **36–43**: δ (ppm), J (Hz)



		NHR′				
No.	*—OCH_2CH_3 or —OH*	*NH*	*R′*	*R*	Ⓟ	*Solvent*
36b	0.73 (t, 3H, $\underline{CH_3}CH_2$, $J_{HH} = 7.2$); 3.91 (q, 2H, $CH_3\underline{CH_2}$, $J_{HH} = 7.2$)	11.45 (s, 1H)	8.61 (s, 1H)	7.23 (m, 2H); 7.36 (m, 3H)	2.98 (m, 8H, —CH_2—N); 3.6 (m, 8H,—CH_2—O)	$CDCl_3$
37b	0.72 (t, 3H, $\underline{CH_3}CH_2$, $J_{HH} = 7.2$); 3.86 (q, 2H, $CH_3\underline{CH_2}$, $J_{HH} = 7.2$)	6.52 (s, 2H)		7.24 (m, 2H); 7.36 (m, 3H)	2.89 (m, 8H, —CH_2—N); 3.56 (m, 8H,—CH_2—O)	$CDCl_3$
38a	1.10 (t, 9H, $\underline{CH_3}CH_2$, $J_{HH} = 6.9$); 4.36 (q, 6H, $CH_3\underline{CH_2}$, $J_{HH} = 6.9$)	3.20 (s, 3H)	8.60 (s, 3H)	7.84 (d, 3H, $J_{HP} = 10.8$)	–	$CDCl_3$
39a	1.31 (t, 9H, $\underline{CH_3}CH_2$, $J_{HH} = 7.2$); 4.38 (q, 6H, $CH_3\underline{CH_2}$, $J_{HH} = 7.2$)	–	8.74 (s, 3H)	8.09 (d, 3H, $J_{HP} = 12.0$)	–	DMSO-d_6
40a	–	–		8.21 (br s, 3H)	–	D_2O
41a	–	–		7.72 (br s, 3H)	–	D_2O
42a	–	–		8.20 (s, 3H)	2.56 (s, 3H, CH_3); 7.20–7.30 (m, 4H, C_6H_4)	D_2O
43a	7.30–8.50 (9H, $\underline{NH_2}$ + $\underline{COOH}$)			7.21 (d, 3H, $J_{HP} = 12.3$)	–	DMSO-d_6

10°C and stirred, and then morpholine (0.02 mol) or diethylamine (0.02 mol) respectively was added dropwise. The mixture was stirred at 25°C for 1 h and then filtered. The filtrate was evaporated to dryness in vacuo.

General Procedure for Synthesis of the Methylphosphonium Iodides **15a–c, 19b, 20b, 23b, 24b**

To a solution of each compound **6a–c, 11b–14b** (0.005 mol) in benzene (10 ml), methyl iodide (0.02 mol) was added. The reaction mixture was refluxed for 4 h. Compounds **23b, 24b** precipitated. The solution was decanted. The product **24b** is sufficiently pure and does not need further purification.

General Procedure for Synthesis of the Phosphine Oxides **16b, 21b** *and the Amidophosphonate* **25b**

To a stirred and cooled to 10°C solution of each compound **6b, 11b, 12b** (0.01 mol) in benzene (20 ml), a 30% aqueous solution of hydrogen peroxide (5 ml) was added. After the reaction mixture had been stirred for 4 h, the organic layer was separated, washed with water twice, dried over sodium sulfate, and evaporated in vacuo.

General Procedure for Synthesis of the Phosphine Thioxides **17a,b**, *the Amidothiophosphinates* **22b, 27b**, *and the Amidothiophosphonates* **26a,b**

To a solution of each compound **6a,b, 12a,b, 13b, 14b** (0.01 mol) in benzene (20 ml), sulfur (0.01 mol) was added. The mixture was refluxed for 1h. Then it was evaporated to dryness in vacuo.

General Procedure for Synthesis of the Iminophosphine **18a**, *the Amidoiminophosphonate* **28b**, *and the Amidothiophosphinate* **29b**

To a solution of each compound **6a, 12b, 14b** (0.01 mol) in benzene (20 ml), a solution of the corresponding aryl azide (0.01 mol) in benzene (20 ml) was added. The mixture was refluxed for 1h. Then it was evaporated to dryness in vacuo.

General Procedure for Synthesis of the Thienopyrimidones **30b, 31b, 32a**

A suspension of each compound **6b, 17a, 26b** (0.01 mol) in formamide (10 ml) was heated on an oil bath at 145–150°C for 1 h. After the mixture had been cooled, the product was precipitated by addition of water. Then it was filtered off and washed with water.

General Procedure for Synthesis of the 3-Aminothienopyrimidones **33a, 34a**

To a solution of each compound **17a, 18a** (0.01 mol) in ethanol (30 ml), hydrazine 99% (0.03 mol) was added. The mixture was refluxed for 5 h. The reaction mixture was diluted with water, and the precipitated solid was filtered off.

*Tris-{3-[1-(4-hydroxyphenyl)methylideneamino]-4-oxo-3, 4-dihydrothieno[2, 3-d]pyrimidin-6-yl} phosphine thioxide (***35a***)*

To a suspension of compound **17a** (0.01 mol) in pyridine (5 ml), 4-hydroxybenzaldehyde (0.03 mol) and one drop of piperidine were added. The mixture was stirred at 80°C for 0.5 h. During this time a precipitate dissolved. Then pyridine was eveporated to dryness in vacuo. The product was washed with hot hexane (30 ml).

*[(3-Phenyl-4-ethoxycarbonyl-5-aminothienyl)] dimorpholidothiophosphonate (***37b***)*

To a suspension of compound **26b** (0.01 mol) in iso-propyl alcohol (30 ml), a solution of potassium hydroxide (0.05 mol) in water (5 ml) was added. The mixture was refluxed for 6 h. After it had cooled, the precipitate was filtered off.

*General Procedure for Synthesis of the 2-(N-formyl)-3-ethoxycarbonylthiophenes (***36b, 38a, 39a***)*

To a solution of each compound **17a, 18a, 26b** (0.01 mol) in ethanol (40 ml), hydrochloric acid 10% (4 ml) was added. The mixture was refluxed for 1 h. After the mixture had cooled, the precipitate was filtered off.

*General Procedure for Synthesis of the 2-Amino-3-carboxythiophenes (***40a–42a***)*

To a solution of the corresponding compound **6a, 17a, 18a** (0.01 mol) in ethanol (30 ml), potassium hydroxide (0.03 mol) was added. The mixture was refluxed for 5 h. After it had cooled, the precipitate was filtered off.

*Tris-[(5-amino-4-carboxy)thienyl-2]phosphine Thioxide (***43a***)*

To a solution of salt **42a** (0.01 mol) in water (5 ml), 10% hydrochloric acid (0.04 mol) was added. The precipitate was filtered off.

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