Heteroatom Chemistry
Volume 13, Number 1, 2002

Intramolecular Cyclization of ω-Haloalkylsubstituted Thiophosphorylacetonitriles: Synthesis and Stereochemistry of 3-Cyano-2-oxo-1,2-thiaphosphacyclanes

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Received 31 January 2001; revised 19 April 2001

ABSTRACT: *Intramolecular S-alkylation in a series of* ω*-haloalkyl-substituted thiophosphorylacetonitriles* **5–7** *presents an effective synthetic route to the hitherto unknown 3-cyano-2-oxo-1,2-thiaphospholanes* **14** *and thiaphosphinanes* **15**. *The compounds were obtained as a mixture of* cis- *and* trans-*isomers that were resolved to individual stereoisomers in most cases. For some of them, X-ray diffraction analysis has been performed. It was shown that* ^{31}*P NMR spectroscopy can be used to assign the stereochemistry of 3-cyano-2-oxo-1,2-thiaphosphacyclanes.* © 2002 John Wiley & Sons, Inc. Heteroatom Chem 13:1–21, 2002; DOI 10.1002/hc.1101

INTRODUCTION

By now, many phosphorus-containing heterocycles have been described in the literature, among them phosphacyclanes with a single phosphorus heteroatom [1], and polyheteraphosphacyclanes and unsaturated derivatives [2–6] have been investigated most extensively. As regards saturated 1,2-heteraphosphacyclanes with oxygen, nitrogen, or sulfur as heteroatoms, 1,2-oxaphosphacyclanes have been studied sufficiently thoroughly, and some of them have found practical application in the industry, specifically as nonflammable hydraulic liquids and plasticizers [7,8], additives to oils, lubricants [9], flame retardants [10,11], thermostabilizing additives to fibers [12–14], and surfactants [15]. Moreover, despite the fact that 1,2-thiaphosphacyclanes should be of no less practical interest, at the beginning of the present investigation, only a few of the simplest, nonfunctionalized representatives of such types of compounds have been described. It was shown recently in our laboratory [16–19] that thiophosphoryl compounds **1**, with the phosphorus atom bearing the ω-haloalkyl moiety, rather easily undergo intramolecular S-alkylation reactions yielding five- and six-membered 1,2-thiaphosphacyclanium salts **2**. In the case of the presence of at least one alkoxy group at the phosphorus atom, a subsequent dealkylation takes place leading to formation of the 2-oxo-1,2-thiaphosphacyclanes **3** (Scheme 1).

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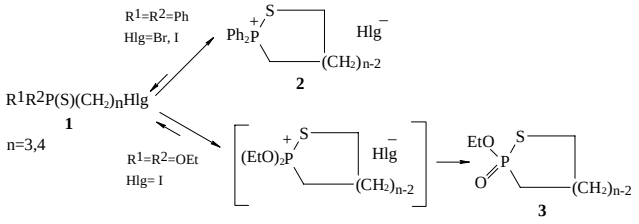
Contract Grant Sponsor: Russian Foundation of Basic Research.
Contract Grant Number: 99-03-033014.
Contract Grant number: 00-15-9738.
Contract Grant Number: 00-03-328079.



SCHEME 1

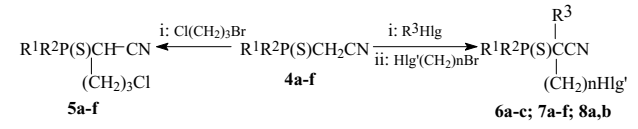
The subsequent functionalization of such compounds, with the introduction of substituents to the ring, represents, however, a rather complicated task. Nevertheless, such an S-alkylation must obviously be a general method of 1,2-thiaphosphacyclane structure formation. Therefore, one should strive to obtain the functional compounds of the said type starting from the functionalized thiophosphoryl compounds having an ω-haloalkyl group.

Earlier [20,21], we confirmed this assumption by the synthesis of a few (3-halopropyl)-substituted thiophosphonylacetonitriles and thiophosphinylacetonitriles. In this case, the intramolecular cyclizations proceeding under elevated temperatures, yielded the 2-ethoxy- and 2-methyl-3-cyano-2-oxo-1,2-thiaphosphinanes. To elucidate the limits of the application of the aforementioned synthetic scheme and to estimate the influence of the initial compound structures on the result and stereochemistry of the process, we have synthesized a variety of ω-haloalkyl-substituted compounds **5–8** and investigated their intramolecular transformations.

RESULTS AND DISCUSSION

Synthesis of ω-Halo-2-thiophosphorylalkanonitriles

Compounds **5–8**, having a terminal chlorine atom, were obtained as the result of an alkylation of thiophosphorylacetonitriles **4** under phase-transfer catalysis conditions based on the conditions of these reactions investigated by us earlier [22,23] (Scheme 2). Namely, it was established that C-monoalkylation of compounds **4** with monohaloalkanes and 1,3-bromochloropropane can be carried out in a 50% aq. $NaOH/CH_2Cl_2$ medium with high a degree of selectivity. The secondary alkylation of C-alkylated thiophosphorylacetonitriles with monohaloalkanes and unsymmetrical α, ω-dihaloalkanes, in turn, proceeded easily in the heterophase medium s. KOH/CH_3CN. It should be noted that the synthesis of disubstituted thiophosphorylacetonitriles **6–8** is most readily affected without



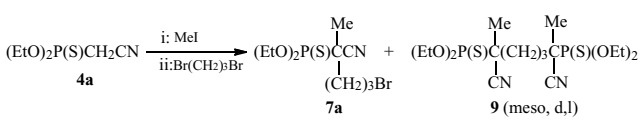
	R^1	R^2		R^1	R^2	R^3	n	Hlg'
4a,5a	OEt	OEt	**6a**	OEt	OEt	Me	2	Cl
4b,5b	OPr	OPr	**6b**	Ph	OEt	Me	2	Cl
4c,5c	Me	OPr^i	**6c**	Ph	OEt	Et	2	Cl
4d,5d	Me	OBu^i	**6d**	Ph	Ph	Me	2	Cl
4e,5e	Ph	OEt	**7a**	OEt	OEt	Me	3	Br
4f,5f	Ph	Ph	**7b**	OPr	OPr	Me	3	Cl
			7c	OEt	OEt	Pr	3	Cl
i: 50% aq. $NaOH/CH_2Cl_2$/TEBA			**7d**	Me	OPr^i	Me	3	Cl
ii: s.KOH/CH_3CN/TEBA			**7e**	Me	OBu^i	Me	3	Cl
Hlg = Br,I			**7f**	Ph	OEt	Me	3	Cl
			7g	Ph	Ph	Me	3	Cl
			8a	OEt	OEt	Me	4	Cl(Br)
			8b	Ph	Ph	Me	4	Cl

SCHEME 2

isolation of the intermediate alkylation products. The optimal catalyst for both biphasic systems is triethylbenzylammonium chloride (TEBA).

Use of the α, ω-dibromoalkanes for an alkylation of monoalkylsubstituted thiophosphorylacetonitriles, under the aforementioned conditions, could afford alkylation compounds having a terminal bromine atom. In this case, however, a side reaction proceeds to give symmetrical bis(thiophosphoryl) alkanedinitriles. For example, the reaction of diethylthiophosphorylpropionitrile with 1,3-dibromopropane to give **7a** is accompanied to a great extent by the formation of the heptanecarbodinitrile **9**, even with substantial dilution of the reaction mixture and with use of an excess of the alkylating agent (Scheme 3). When the said reaction was carried out under the standard dilution conditions suggested previously [23] for unsymmetric α, ω-bromochloroalkanes, **9** was found to be the main reaction product (yield 77%).

Compound **9** was obtained as a mixture with the statistical ratio of meso and racemic d,l-isomers and was almost insoluble in hexane. This allowed us to separate it readily from **7a**. Stereoisomers **9** were, in turn, separated by column chromatography. The structure of the meso-form **9** (R_C, S_C) was confirmed by single crystal X-ray diffraction analysis (Figure 1). The bond lengths and angles in **9** are characterized by the typical values for analogous



SCHEME 3

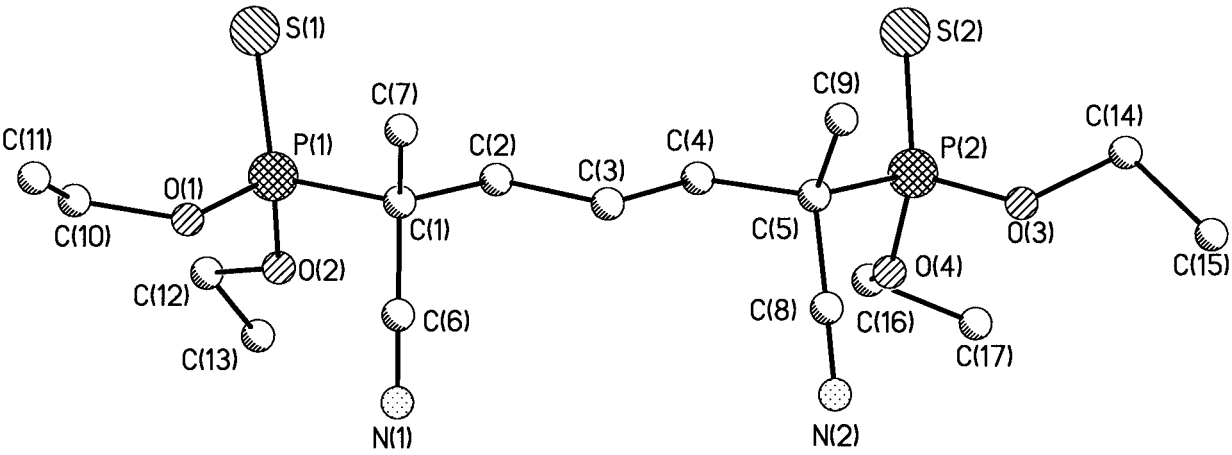


FIGURE 1 Molecular structure of meso-**9**. The disordering of OEt groups is omitted for clarity. Selected bond lengths (Å): P(1)-O(2) 1.561(3), P(1)-O(1) 1.571(3), P(1)-C(1) 1.849(3), P(1)-S(1) 1.917(2), P(2)-O(4) 1.562(3), P(2)-O(3) 1.565(3), P(2)-C(5) 1.838(3), P(2)-S(2) 1.915(2); Selected angles (deg.): O(2)-P(1)-O(1) 103.8(2), O(2)-P(1)-C(1) 101.0(2), O(1)-P(1)-C(1) 100.4(2), O(2)-P(1)-S(1) 116.7(2), O(1)-P(1)-S(1) 117.1(1), C(1)-P(1)-S(1) 115.3(1), O(4)-P(2)-O(3) 104.6(2), O(4)-P(2)-C(5) 101.9(1), O(3)-P(2)-C(5) 100.2(1), O(4)-P(2)-S(2) 116.8(1), O(3)-P(2)-S(2) 116.8(1), C(5)-P(2)-S(2) 114.3(1).

compounds [24]. In both of the $S{=}P(OEt)_2$ fragments, the P=S group is characterized by the antiperiplanar orientation with respect to the CN group. The slight shortening of P=S bonds, to 1.915(2)Å in **9**, is probably caused by the electron-withdrawing effect of the cyano group [24].

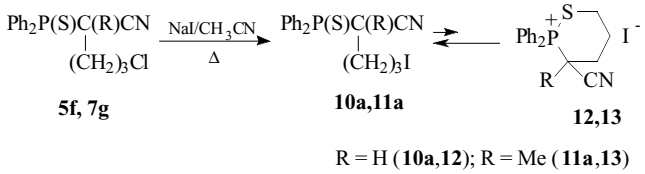
Yields, elemental analysis data, physicochemical constants, and spectroscopy data of the compounds **5–8** are summarized in Tables 1 and 2. It should be mentioned that, in order to accelerate the intramolecular S-alkylation, compounds with a terminal chlorine atom were transformed, in some cases, to the corresponding iodo-derivatives by the exchange reaction with NaI/CH_3CN.

Intramolecular S-Alkylation of ω-Halo-2-thiophosphorylalkanonitriles

Investigation of the intramolecular S-alkylation in a series of ω-halo-2-thiophosphorylalkanonitriles **5–8** (performed by the example of the compounds bearing the diphenylthiophosphinyl group **5f, 7g**) has demonstrated that the presence of the electron-withdrawing α-cyano group results in a regular decrease in the thione sulfur atom nucleophilicity, and, consequently, in an increase in ω-halo-2-thiophosphorylalkanonitriles stability.

Thus, unlike (3-iodobutyl)diphenylphosphine sulfide, which readily undergoes spontaneous intramolecular S-alkylation yielding diphenyl 1,2λ^5-thiaphosphinanium iodide [16], during the preparation from (3-chlorobutyl)diphenylphosphine sulfide by the exchange reaction with sodium iodide, its cyanosubstituted analogs **10a** and **11a** are stable and may be isolated. The corresponding cyclic forms **12** and **13** were formed slowly in acetonitrile solutions of **10a** and **11a**, the equilibrium between linear and cyclic forms (ring-chain halotropic tautomerism) being established in about six months (Scheme 4). After the equilibrium had been reached, the amounts of cyclic forms were found to be 14% (**12**) and 9% (**13**), according to the ^{31}P NMR data.

However, due to the subsequent irreversible dealkylation in the intermediate thiaphosphacyclanium salts, the cyclization of the initial compounds **5–7** proceeds rather readily, even for the compounds having a terminal chlorine atom, when there is at least one alkoxy group bonded to the phosphorus atom. Thus, **5–7** are only partly transformed to the five- and six-membered 3-cyano-2-oxo-1,2-thiaphosphacyclanes **14** and **15**, even under distillation *in vacuo* (Scheme 5, method I). Hence, although the introduction of the cyano group decreases the thione sulfur atom nucleophilicity, it promotes, at the same time, the dealkylation process in the intermediate thiaphosphacyclanium salt. It should be noted that the substituted thiophosphorylacetonitrile **8a**, bearing the 4-chlorobutyl moiety



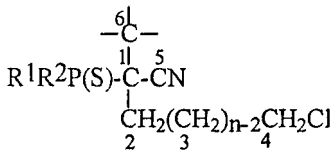
SCHEME 4

TABLE 1 Physical and Elemental Analyses Data for Compounds **5–9, 14** and **15**

Compound	Yield[a] (%)	m.p./°C or b.p./°C (mm Hg)	Formula	Found (%) Calculated (%) C	H	N	P
5a[b]	83 (46)	Oil	$C_9H_{17}ClNO_2PS$	40.11	6.28	5.35	11.58
				40.08	6.35	5.19	11.48
5b[b]	70 (41)	Oil	$C_{11}H_{21}ClNO_2PS$	43.67	7.13	—	10.12
				43.37	7.11	—	10.40
5c	82 (60)	170–175 (1)	$C_9H_{17}ClNOPS$	43.88	6.84	5.45	12.23
				43.60	6.75	5.52	12.20
5d[b]	65 (40)	Oil	$C_{10}H_{19}ClNOPS$	44.31	7.20	5.35	11.23
				44.86	7.15	5.23	11.57
5e[b]	87 (61)	Oil	$C_{13}H_{17}ClNOPS$	51.94	5.87	5.06	10.16
				51.74	5.64	4.64	10.28
5f[b]	75 (55)	88–89	$C_{17}H_{17}ClNPS$	62.68	4.98	4.29	9.26
				62.17	5.10	4.20	9.29
6a[b]	93 (70)	Oil	$C_9H_{17}ClNO_2PS$	40.55	5.87	5.38	—
				40.07	6.31	5.19	—
6b[b]	80 (69)	Oil	$C_{13}H_{17}ClNOPS$	51.88	5.42	4.83	—
				51.74	5.64	4.64	—
6c[b]	71 (60)	Oil	$C_{14}H_{19}ClNOPS$	53.18	5.93	4.68	—
				53.25	6.02	4.44	—
7a[c]	65 (57)[d]	165–175 (1)	—	—	—	—	—
7b	75 (63)	155–160 (1)	$C_{12}H_{23}ClNO_2PS$	47.10	7.93	—	—
				47.22	7.43		
7c[c]	85 (50)	150–165 (1)	$C_{12}H_{23}ClNO_2PS$	46.16	7.39	4.96	9.85
				46.23	7.38	4.49	9.95
7d	80 (64)	170–175 (1)	$C_{10}H_{19}ClNOPS$	47.19	7.69	—	11.31
				46.89	7.51		10.99
7e[b]	90 (68)	Oil	$C_{11}H_{21}ClNOPS$	47.10	7.69	—	11.31
				46.89	7.51		10.99
7f[b]	100 (83)	Oil	$C_{14}H_{19}ClNOPS$	53.22	6.03	4.36	9.55
				53.24	6.06	4.44	9.81
7g[b]	83 (65)	65–66	$C_{18}H_{19}ClNPS$	62.30	5.50	4.30	8.80
				62.15	5.50	4.03	8.90
8a[e]	92 (73)	150–195 (0.1)	—	—	—	—	—
8b	71 (59)	87–89 (Petrol. ether)	$C_{19}H_{21}ClNPS$	62.96	5.77	3.68	—
				63.06	5.85	3.87	
9		Oil (meso:D,L = 30:70)	$C_{17}H_{32}N_2O_4P_2S_2$	44.93	6.91	6.05	—
		94–95 (meso:D,L = 70:30)		44.93	7.05	6.17	
		93 (hexane, meso)					
14b	—	166–167 (**A:B** = 94:6)	$C_{11}H_{12}NOPS$	55.58	5.08	5.81	—
	61 (30)	108–109 (**B**)		55.70	5.06	5.91	
14c	95 (54)	101–102 (**A**)	$C_{12}H_{14}NOPS$	57.31	5.69	5.62	—
	Quant. (57)	71–72 (**B**)		57.37	5.58	5.58	
15a	75 (51)	65–70 (**A:B** = 50:50)	$C_7H_{12}NO_2PS$	40.60	5.93	6.70	15.12
	—	116–118 (**B**)		40.96	5.89	6.83	15.09
15b	55 (21)	73–74 (**A:B** = 50:50)[f]	—	—	—	—	—
	32 (17)						
15c	30 (18)	136–137 (**A**)	$C_6H_{10}NOPS$	41.73	5.72	7.78	—
	53 (25)	132–134 (**B**)		41.14	5.71	8.00	
15d	44 (21)	111–112 (**A**)	$C_{11}H_{12}NOPS$	55.56	5.06	5.70	—
	79 (34)			55.70	5.06	5.91	
15e	29 (10)	80–81 (**B**)	$C_9H_{16}NO_2PS$	46.36	7.08	5.99	13.05
				46.35	6.87	6.01	13.30
15f	19 (6)	134–136 (**A:B** = 84:16)	$C_{12}H_{14}NOPS$	56.44	5.82	5.44	11.77
	Quant. (24)			56.37	5.58	5.58	12.35
15g	15 (6)	Oil (**A:B** = 64:36)[g]	—	—	—	—	—
15h	64 (22)	151–152 (**B**)	$C_7H_{12}NOPS$	44.35	6.62	7.31	16.09
		—		44.44	6.35	7.41	16.40
15i	75 (45)	94–95 (**A:B** = 70:30)	$C_8H_{14}NO_2PS$	43.62	6.36	6.43	—
		107–108 (**A:B** = 5:95)		43.83	6.50	6.39	

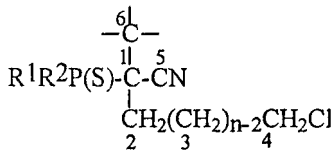
[a]According to ^{31}P NMR data (shown in parenthesis is the product yield after purification); for compounds **14** and, **15** the yield is based on the both diastereomers; shown first is the yield for chloroderivatives cyclization, the second is that for iododerivatives cyclization; for purification conditions, see Experimental section.
[b]Purified by column chromatography (silica gel 40-100 μm, hexane—acetone 100:4).
[c]Purified by distillation and column chromatography.
[d]86% Purity according to ^1H NMR data.
[e]A 85:15 mixture of compounds having terminal chlorine and bromine atoms according to ^1H NMR data.
[f]87% purity according to ^1H NMR data.
[g]86% purity according to ^1H NMR data.

TABLE 2 Selected ^{31}P, ^{1}H, and ^{13}C NMR and IR Data for Compounds **5–8**



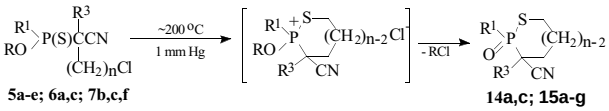
		NMR Spectra (δ ppm, J/Hz)[a,b]									
		^{1}H				^{13}C					
Compound	*IR ν_{CN} (cm^{-1})*	*$\delta^{31}P$ (ppm)*	*(NC)CH-P ddd ($^{2}J_{PH}$/$^{3}J_{HHA}$ / $^{3}J_{HHB}$)*	*C ^{6}H-C(CN)-P ($^{3}J_{PH}$)*	*CH_2C1 ($^{3}J_{HH}$)*	*C(1) ($^{1}J_{PC}$)*	*C(2) ($^{2}J_{PC}$)*	*C(3) ($^{3}J_{PC}$)*	*C(4)*	*C(5) ($^{2}J_{PC}$)*	*C(6) ($^{2}J_{PC}$)*
5a	2245	85.60	3.03 (21.2/10.3/3.9)	—	3.54 t (5.9)	36.00 d (113.7)	24.23	29.51 d (13.1)	34.08	115.28 d (7.8)	—
5b	2245	85.50	3.05 (21.2/9.6/4.0)	—	3.55 t (6.0)	36.36 d (113.8)	24.62	29.80 d (13.1)	43.23	115.57 d (8.0)	—
5c[c]	2235	89.54	2.95 (18.4/10.4/3.9)	—	3.56 t (5.6)	37.08 d (65.9)	23.78	29.72 d (12.0)	43.01	115.84 d (7.3)	
		88.87	2.93 (9.1/8.0/4.0)	—	3.57 t (6.0)	37.22 d (66.8)	23.18	29.67 d (11.9)	43.01	116.0 d (5.3)	
5d[c]	2235	90.20	2.50 (19.2/11.2/4.2)	—	—	—	—	—	—	—	
		90.10	2.29 (13.0/12.0/4.4)	—	2.94-2.99 br.t						
5e[c,d]	2240	84.70	3.21 (20.0/11.2/4.4)	—	3.52 t (6.4)	38.24 (73.5)	24.26	30.14 d (12.6)	43.24	116.11 d (6.2)	—
		84.66	3.01-3.10 m		3.53 t (6.0)	38.40 (73.1)	24.18	29.94 d (12.3)			
5f	2240	45.03	3.58 (14.0/11.6/4.0)	—	3.54 t (6.5)	34.72 (49.4)	28.12	29.81 d (11.5)	43.00	116.40 d (5.4)	—
6a	2240	90.68	—	1.55 d (18.0)	3.70 (H_A), 3.63 (H_B), ($^{2}J_{H_AH_B} = 10.8$)	40.14 d (114.9)	36.50	—	38.95 d (11.5)	118.11 d (6.9)	19.18 d (2.6)
6b[c]	2240	92.91	—	1.64 d (16.0)	3.54 (H_A), 3.50 (H_B), ($^{2}J_{H_AH_B} = 11.2$)	40.22 d (74.2)	36.03	—	38.73 d (13.5)	118.51 d (5.1)	17.94
		92.02	—	1.27 d (18.4)	3.77 (H_A), 3.69 (H_B), ($^{2}J_{H_AH_B} = 10.8$)	39.64 d (74.5)	35.29 d (2.3)	—	39.08 d (9.6)	118.54 d (5.4)	18.84
6c[c]	2235	93.04	—	1.38–1.47 m 1.59–1.68 m (CH_2(Et))	3.47 (H_A), 3.26 (H_B), ($^{2}J_{H_AH_B} = 10.4$)	44.81 d (74.4)	34.71	—	39.71 d (4.2)	117.72 d (5.0)	25.97 d (3.0)
		92.09			3.73 (H_A, H_B), ($^{2}J_{H_AH_B} = 11.2$)	45.28 d (74.0)	34.6 d (2.8)	—	38.84 d (8.5)	117.68 d (4.6)	25.72

TABLE 2 (continued) Selected ^{31}P, ^{1}H, and ^{13}C NMR and IR Data for Compounds **5–8**



		NMR Spectra (δ ppm, J/Hz)[a,b]									
		^{1}H				^{13}C					
Compound	*IR ν_{CN} (cm^{-1})*	*$\delta^{31}P$ (ppm)*	*(NC)CH-P ddd ($^{2}J_{PH}$/$^{3}J_{HHA}$/ $^{3}J_{HHB}$)*	*C ^{6}H-C(CN)-P ($^{3}J_{PH}$)*	*CH_2C1 ($^{3}J_{HH}$)*	*C(1) ($^{1}J_{PC}$)*	*C(2) ($^{2}J_{PC}$)*	*C(3) ($^{3}J_{PC}$)*	*C(4)*	*C(5) ($^{2}J_{PC}$)*	*C(6) ($^{2}J_{PC}$)*
7a[e]	2230	91.90	—	1.52 d (17.6)	3.49–3.54 m	40.35 d (115.2)	32.03	27.45 d (10.0)	32.20	118.54 d (6.9)	18.90
7b	2240	91.77	—	1.46 d (17.6)	3.49–3.55 m	40.90 d (115.2)	31.50	27.65 d (10.0)	43.82	118.54 d (6.8)	19.21
7c[f]	2240	92.2	—	1.86–2.10 m ($C\underline{H}_2CH_2CH_3$)	3.55 t (6.4)	45.48 d (112.4)	30.40	28.17 d (6.1)	44.24	118.5	18.28 d (7.7)
7d[c]	2235	98.06	—	1.53 d (15.6)	3.05–3.13 m	—	—	—	—	—	—
		97.55		1.52 d (17.6)							
7e[c]	2235	99.91	—	1.29 d (15.5)	3.09–3.14 m	41.03 d (69.4)	30.41	28.11 d (9.0)	44.13	119.90 d (3.9)	18.67
		99.33	—	1.18 d (17.4)		40.75 d (69.9)	31.42 d (2.0)	28.02 d (10.5)	44.01	113.81 d (4.4)	17.85
7f[c]	2240	93.61	—	—	—	40.78 d (75.4)	30.86	27.68 d (8.4)	43.71	119.39	18.85
		92.99	—	—	—	40.33 d (75.3)	30.30	27.19 d (11.0)	43.50	119.35	18.11
7g	2245	55.14	—	1.61 d (16.2)	3.50 t (7.8)	38.12 d (49.4)	31.3	27.84 d (9.1)	43.63	121.90	18.91 (3.9)
8a[g]	2235	92.34	—	1.46 d (17.2)	3.49 t (6.4)	41.22 d (115.2)	31.72	21.64 d (10.1)	44.36	119.21 d (6.6)	18.67
8b[h]	2240	56.10	—	—	—	—	—	—	—	—	—
11a	—	55.09	—	1.58 d (16.4)	3.10 t (8.0)	—	—	—	—	—	—

[a]Solvent $CDCl_3$; ^{1}H NMR (**5a–e; 6a–c; 7a–d,f,g; 11a**); NMR ^{13}C (**5a–c,e; 6a–c; 7a–d**).
[b]Solvent C_6D_6; ^{1}H NMR (**5f, 7e**); NMR ^{13}C (**5d,f , 7e,f,g**).
[c]Two diastereomers **A:B** = 1:1 (**5c,d**), 60:40 (**5e**), 57:43 (**6b**), 64:36 (**6c**), 1:1 (**7d**), 65:35 (**7e**), 64:36 (**7f**).
[d]In CH_3CN the diastereomers signals are interchanged (δ_P(**A**) 84.71, δ_P (**B**) 84.82).
[e]The compound having bromine terminal atom.
[f]The proton P–C–CH_2 (Pr) and $C\underline{H}_2CH_2CH_2Cl$ signals are overlapped.
[g]Solvent CD_3CN for ^{1}H, ^{31}P, ^{13}C NMR, spectrum is shown for the corresponding chlorine derivative.
[h]Solvent CH_2Cl_2.



	R^1	R^3	n
14a	OEt	Me	2
14c	Ph	Et	2
15a	OEt	H	3
15b	OPr	H	3
15c	Me	H	3
15d	Ph	H	3
15e	OPr	Me	3
15f	Ph	Me	3
15g	OEt	Pr	3

SCHEME 5

(the cyclization of which could afford only a seven-membered ring), does not cyclize under the aforementioned conditions. This can apparently be explained by the lesser thermodynamic stability of the said ring compared to the corresponding five- and six-membered analog.

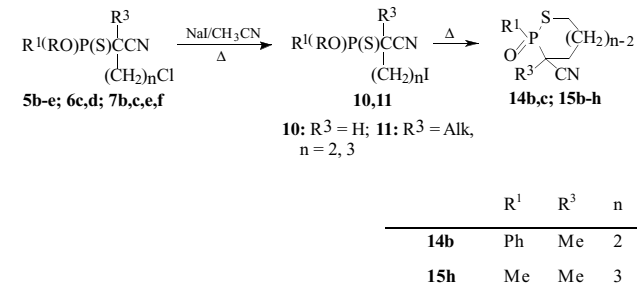
The yield of 3-cyano-2-oxo-1,2-thiaphosphacyclanes **15** under distillation *in vacuo* depends mainly on the easiness of dealkylation for the RO group (Table 3). In other words, it decreases with an increase of the volume of the radical (compare **15a** and **15b**) and also when passing from a primary radical to a secondary one (compare **15c**, obtained from **5c** and **5d**). Furthermore, the yields of the six-membered heterocycles are decreased drastically (up to 5–7%) with the insertion of the alkyl radical into the α-position to the phosphorus (compare **15b** and **15e**). Even **7a**, bearing a terminal bromine atom, transforms under distillation to the cyclic product with a yield of 7% only. Compounds **6**, when distilled, afforded the 3-alkyl-3-cyano-2-oxo-1,2-thiaphospholanes **14** far more readily and in considerably higher yields than observed for six-membered compounds, **15**, even in spite of the presence of an alkyl radical in the α-position to the phosphorus in the initial compounds **6a,c**. This fact corresponds to the general rule that five-membered rings are formed more readily than six-membered ones [25–27]. It should be mentioned that addition of catalytic amounts of TEBA to the initial compounds **5–7** increases the yields of the target compound **14** and **15**.

As one could expect, the intramolecular cyclization of the ω-iodoalkyl-substituted thiophosphinates and thiophosphonates **10** and **11** obtained from the corresponding chloroderivatives **5–7** in situ (with use of 2 equiv. NaI/CH_3CN and with 2 hours reflux, method II) proceeds under milder conditions. Intramolecular S-alkylation proceeds slowly even at room temperature. Thus, cyclic derivative **15c** is formed in 62% yield from the iodo derivative **5d** ($R^1 = Me$, $R^2 = Bu\text{-}i$, $R^3 = H$, $n = 3$) during one year at 20°C. Upon refluxing **5–7** in acetonitrile for 2–20 hours, 2-alkyl(phenyl)-3-cyano-2-oxo-1,2-thiaphosphacyclanes **14** and **15** are

TABLE 3 Dependence of Yields and Diastereomer Ratio of 3-Cyano-2-oxo-1,2-thiaphosphacyclanes **14** and **15** on the Initial Substrate Structure and Cyclization Method

		Yield **14** *and* **15**, *% (*^{31}*P NMR), Diastereomer Ratio*			
		Method I		*Method II*	
Substrate	*Thiaphosphacyclane*	*Distillation in vacuo*		*NaI/MeCN, Reflux*	
6a	**14a**	19 40[c]	**A** > **B** (60:40)	quant[a]	[b]
6b	**14b**	[b]	[b]	61	**A** < **B** (40:60)
6c	**14c**	95	**A** > **B** (70:30)	quant.	**A** < **B** (30:70)
5a	**15a**	75	**A** ≈ **B**	quant.[d]	[b]
5b	**15b**	55	**A** ≈ **B**	32	**A** ≈ **B**
5c	**15c**	7	**A** > **B** (60:40)	83	**A** < **B** (40:60)
5d	**15c**	30	**A** > **B** (60:40)	53	**A** < **B** (40:60)
5e	**15d**	44[c]	**A** > **B** (55:45)	79	**A** ≈ **B**
7a	**15i**	7	[b]	75[e]	**A** < **B** (40:60)
7b	**15e**	5.6 17[c]	**A** > **B** (60:40)	29	**A** < **B** (40:60)
7c	**15g**	15	**A** > **B** (60:40)	30	**A** < **B** (30:70)
7e	**15h**	[b]	[b]	64	**A** ≈ **B**
7f	**15f**	19	**A** > **B** (55:45)	quant.	**A** < **B** (40:60)

[a]Cyclic sodium salt **16**.
[b]The experiment was not carried out.
[c]Triethylbenzylammonium chloride addition (cat.) upon distillation.
[d]Cyclic sodium salt **17**.
[e]Cyclization of the compound having terminal bromine atom upon refluxion in the acetonitrile solution.



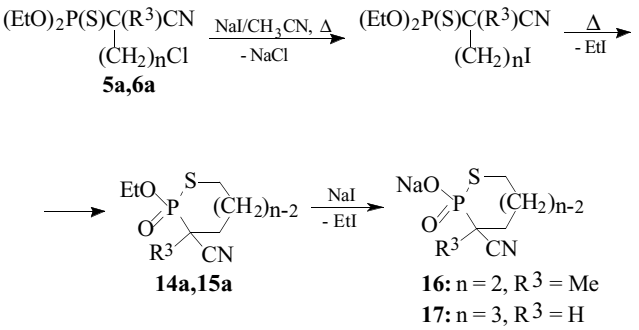
	R^1	R^3	n
14b	Ph	Me	2
15h	Me	Me	3

SCHEME 6

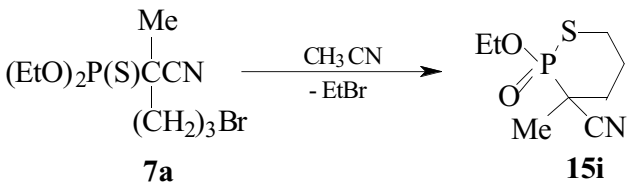
formed in yields up to quantitative (Scheme 6, Table 3).

It should be noted that cyclization of the thiophosphonates **5a** and **6a** occurred under such conditions (with an excess of NaI), followed by dealkylation of the second alkoxy group at the phosphorus atom in the desired 1,2-thiaphosphocyclanes **14a** and **15a**. As a result, the sodium salts of the corresponding cyclic acids **16** and **17** were obtained in practically quantitative yields. In the case of **8a**, this cyclization method resulted in a polymer product of nonidentified structure schemes.

To obtain 3-cyano-2-ethoxy-3-methyl-2-oxo-1,2-thiaphosphinane, **15i**, which is formed under thermal cyclization of the initial chloride in low yield (7%) and apparently could not be obtained from the corresponding iodo derivative (see Scheme 7), we have used S-alkylation of the corresponding ω-bromo-2-thiophosphorylalkanonitrile proceeding under reflux in the acetonitrile solution schemes.



SCHEME 7



SCHEME 8

The presence of two asymmetric centers—phosphorus and carbon C(3) atoms—in the 3-cyano-2-oxo-1,2-thiaphosphacyclanes determines their formation as a mixture of two diastereomers (**A** and **B**), each being a racemic mixture of the enantiomers. In the ^{31}P NMR spectrum (Table 4), two singlets correspond to these diastereomers **A** and **B** (with those denoted by diastereomer **A** showing a low-field chemical shift). The ratio of the diastereomers formed during the cyclization depends on the initial compound structure (mainly by the presence of the alkyl substituent in the α-position), the method of cyclization and the ring size. The influence of these factors on the diastereomeric composition of 3-cyano-2-oxo-1,2-thiaphosphacyclanes **14** and **15** obtained is shown in Table 3.

For 2-alkoxy-3-cyano-2-oxo-1,2-thiaphosphinanes, **15a,b**, without an alkyl substituent in the 3-position, the diastereomeric ratio is 1:1, while for their 3-alkylsubstituted analog, **15e–i**, the proportion of diastereomer **A** is generally higher when the cyclization is carried out by distillation *in vacuo* (Hlg = Cl), and diastereomer **B** is formed in a greater amount under milder conditions (when cyclizing 5-iodo(bromo)-2-thiophosphorylpentanonitriles). The same regularities may be observed for 3-cyano-2-oxo-1,2-thiaphospholanes, **14**. The preferential formation of one or another diastereomer obviously depends on steric and electronic factors determining the structure of the intermediate phosphonium salt and conditions of the cyclization as well.

The compounds **14** and **15** were isolated from the reaction mixtures as diastereomer mixtures (e.g., by precipitation using ether). These mixtures were resolved into the individual diastereomers in most cases by column chromatography and fractional crystallization. Satisfactory elemental analysis data were obtained both for the diastereomeric mixtures isolated and for the individual isomers (Table 1). The main spectral parameters of the heterocycles synthesized (^1H, ^{13}C, ^{31}P NMR and IR) are listed in Tables 4–6.

In the IR spectra, the absorption bands characteristic of P=O and CN groups are observed in the expected areas, and the difference for diastereomers **A** and **B** does not exceed 10 cm^{-1} (Table 5).

In the ^{31}P NMR spectra (Table 4), 1,2-thiaphospholanes **14** show signals in CH_2Cl_2 in the $\delta = 61–73$ ppm region. For compounds **15** the range of the chemical shift values in CH_2Cl_2 is 35–44 ppm for 2-alkoxyderivatives **15a,b,e,g**, 41–52 ppm for 2-methylsubstituted compounds **15c,h**, and 32–44 ppm for 2-phenylsubstituted analogs **15d,f**. Note that, as for the initial linear compounds **5–7**, the introduction of an alkyl substituent into the

TABLE 4 Chemical Shift Values (δ ppm) in ^{31}P NMR Spectra for 3-Cyano-2-oxo-1,2-thiaphosphacyclanes **14** and **15** (**A** and **B** diastereomers) in Different Solvents

Solvent	CH_3CN			CH_2Cl_2			$CDCl_3$			C_6H_6		
Compound	δ (**A**)	δ (**B**)	$\Delta\delta$	δ (**A**)	δ (**B**)	$\Delta\delta$	δ (**A**)	δ (**B**)	$\Delta\delta$	δ (**A**)	δ (**B**)	$\Delta\delta$
14a	—	—	—	69.62	68.12	1.50	—	—	—	—	—	—
14b	74.20	68.61	5.59	71.79	65.56	6.23	—	—	—	—	—	—
14c	73.83	66.14	7.69	72.21	61.79	10.42	72.71	65.11	7.60	70.62	62.87	7.75
15a	36.49	36.19	0.30	35.89	35.58	0.31	36.65	36.21	0.44	34.92	34.05	0.87
15b	37.06	36.58	0.48	36.00	35.55	0.45	36.54	36.16	0.38	—	—	—
15c	44.98	44.61	0.37	42.64	41.91	0.73	41.99	39.38	2.61	39.36	37.42	1.94
15d	35.44	34.56	0.88	35.05	34.29	0.76	35.15	34.57	0.58	—	—	—
15e	44.04	41.43	2.61	43.56	41.00	2.56	43.88	41.38	2.50	—	—	—
15f	—	—	—	43.98	40.05	3.93	44.51	40.54	3.97	—	—	—
15g	—	—	—	43.28	40.93	2.35	43.69	41.43	2.26	—	—	—
15h	52.48	47.64	4.84	51.67	47.45	4.22	—	—	—	51.43	45.50	5.93
15i	43.70	41.04	2.66	—	—	—	43.93	41.51	2.42	—	—	—

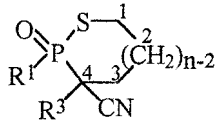
six membered heterocycles results in a considerable downfield shift ($\Delta\delta$ 7–9 ppm).

The difference between the chemical shifts of the 1,2-thiaphosphacyclanes **A** and **B** diastereomers ($\Delta\delta$) in the ^{31}P NMR spectra depends on the ring size, the presence of an alkyl substituent in the 3-position, and the solvent (Table 4). All other factors being the same, $\Delta\delta$ is generally higher for the compounds with a methyl or phenyl group bonded to the phosphorus atom. Furthermore, for the initial compounds **5–7** having two asymmetric centers, the change of the solvent often results in the change of the mutual signal positions of diastereomers **A** and **B** in ^{31}P NMR spectra, while for **14** and **15**, the mutual position of stereomers **A** and **B** remains unchangeable independently of the solvent in use, which is easy to follow in comparing their integral intensities.

In its ^{1}H NMR spectra, 3-cyano-2-oxo-1,2-thiaphosphacyclanes show the characteristic SCH_2 signal at the $\delta = 2.80$–3.60 region, which in some cases appears as an overall complex multiplet for both protons, and, for **14b,c**, and **15c-e,h**, two separate multiplets are observed corresponding to the protons in the *trans*- and *cis*-positions to the phosphoryl group oxygen atom. For 3-cyano-2-oxo-1,2-thiaphosphinanes, **15a–d**, the signal of the methine proton at the α-position to the phosphorus atom appears, as a rule, as a doublet of doublets of doublets, as it does for the initial compounds, **5**, but in lower field compared with the latter ones (Table 5).

In the ^{13}C NMR spectra of **14** and **15** (Table 6) the signals of the carbon atoms C(4) [28] bonded to the cyano-group are placed at $\delta = 31.49$–34.09 for 3-cyano-2-oxo-1,2-thiaphosphinanes **15a–d** and are shifted downfield (36.87–43.99) for their 3-alkyl-substituted analogs **15e–i**. In the case of the five-membered compounds **14**, the signals of the C(4) atom are placed at $\delta = 43.31$–50.11. It should be noted that, in six-membered ring compounds, the above C(4) signals are shifted upfield about 2–5 ppm compared to the P–C(CN) signal in the initial linear ω-haloalkyl-substituted thiophosphorylacetonitriles **5** and **7**. On the contrary, in the five-membered rings **14**, the signals of the C(4) atom are shifted about 3–10 ppm downfield with respect to the P–C(CN) signal in the initial **6**. Furthermore, the decrease of $^1J_{PC}$ (4–17 Hz) is noted in the cyclic compounds compared to the initial compounds **5–7**. This fact is explained logically by the change in the surroundings of the phosphorus atom attached to the aforementioned carbon atom (from R^1(RO)P(S)- to R^1(O)PSR-). It should be mentioned that $^1J_{PC}$ is generally less in case of the **A**-isomer both for five- and six-membered rings. In 1,2-thiaphosphinanes, the signal of the cyclic C(1) atom attached to sulfur appears as a doublet with $^2J_{PC}$ 3.7–5.9 Hz at $\delta = 24.85$–29.78 for **15a–d** and at $\delta = 33.45$–37.98 for their alkyl-substituted analogues **15e–i**. For 1,2-thiaphospholanes **14b,c**, the doublet of the C(1) atom is placed in the same region as for their 6-membered analogues, but with the $^2J_{PC}$ coupling constant increasing to 7.6–8.5 Hz. This constant is maximal for the cyclic salt **16** (9.2 Hz). Thus, alkyl substituent insertion into the α-position to the phosphorus atom results in a downfield shift of C(4), C(1), and C(6) signals. The signal of the CN-group carbon atom is located in the characteristic region of $\delta = 115$–120, appearing usually as a doublet for the **A**-isomer and as a singlet for the **B**-isomer. It should be noted that the signal of this group for the initial compounds **5–7** usually is situated in the same δ region as the doublet with $^2J_{PC}$ coupling constant equal to 4.4–8.0 Hz.

TABLE 5 Selected ^{1}H NMR and IR spectra parameters for 3-cyano-2-oxo-1,2-thiaphosphacyclanes **14** and **15**

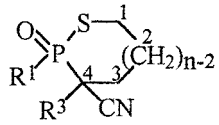


			IR Spectrum		^{1}H NMR Spectrum (δ, ppm, J Hz, $CDCl_3$)					
									C^4 (R^3)	
Compound	n	Diastereomer	ν/cm^{-1}, ν_{CN}	KBr ν_{PO}	δ_H (R^1)	C$^1H_2$	C$^2H_2$	C$^3H_2$	$R^3 = H$ ($^3J_{HH}$/$^3J_{HH}$/$^2J_{PH}$)	R^3 = Alk
14b	2	**A**	2240	1210	7.54–7.58 m 7.64–7.68 m 7.97–8.02 m (C_6H_5)	3.31 (H_C) 3.36 (H_D) ($^3J_{PH_C}$ 10.8, $^3J_{PH_D}$ 8.0, $^2J_{H_C H_D}$ 11.2)	—	2.37 (H_A) 2.91 (H_B) ($^3J_{PH_A}$ 20.0, $^3J_{PH_B}$ 23.6, $^2J_{H_C H_D}$ 14.0)		1.23 d ($^3J_{PH}$ 16.4)
14b	2	**B**	2235	1210	7.54–7.59 m 7.64–7.69 m 8.05–8.11 m (C_6H_5)	3.49–3.60 m	—	2.58 (H_A) 2.72 (H_B) ($^3J_{PH_A}$ 11.6, $^3J_{PH_B}$ 12.8, $^2J_{H_C H_D}$ 12.8)	—	1.66 d ($^3J_{PH}$ 13.6)
14c	2	**A**	2230	1200 1215[a]	7.50–7.56 m 7.62–7.65 m 7.93–8.10 m (C_6H_5)	3.24–3.60 m (H_A) 3.61–3.68 m (H_B)	—	2.24–2.35 m (H_C) 2.73–2.85 m (H_D)	—	1.21–1.48 m (CH_2(Et))
14c	2	**B**	2230	1210 1230[a]	7.48–7.53 m 7.58–7.62 m 8.03–8.09 m (C_6H_5)	3.46–3.54 m	—	2.64–2.69 m (H_C) 2.72–2.78 m (H_D)	—	1.91–2.10 m (CH_2(Et))
15a	3	**A**	2240	1245	4.05–4.09 m[b] (OCH_2)	2.92–3.06 m[c]	1.75–1.95, 2.12–2.23 two m	2.24–2.33, 2.43–2.60 two m	3.25 ddd (3.6/5.2/22.4)	—
15a	3	**B**	2240	1240	[b]	[c]	1.86–1.90, 2.15–2.10 two m	2.26–2.32, 2.50–2.54 two m	3.16 ddd (3.8/10.0/18.0)	—
15b[d]	3	**A**	2240	1245	4.02–4.28[b] (OCH_2)	2.82–2.92[c]	1.98–2.09, 2.12–2.28 2.32–2.48 three m[e]		3.27 ddd (3.6/4.8/22.8)	—
15b[d]	3	**B**	2245	1245	[b]	[c]			3.16 ddd (4.0/8.0/18.0)	—
15c	3	**A**	2245	1190	1.98 d (CH_3P) ($^3J_{PH}$ 13.4)	2.87–2.92, 3.36–3.58 two m	2.12–2.19 m	2.25–2.39, 2.52–2.56 two m	3.25 dt (3.9/16.7)	—

15c	3	**B**	—	—	1.96 d (CH_3P) ($^3J_{PH}$ 13.2)	2.88–2.92, 3.36–3.59 two m	2.21–2.32 m	2.27–2.42, 2.54–2.58 two m	3.02 ddd (4.8/6.1/11.6)	—
15d[d]	3	**A**[f]	2245	1210	7.50–7.88 m (C_6H_5)	2.91–3.03, 3.40–3.50 two m	1.85–2.01, 2.28–2.38 two m	2.47–2.55, 2.59–2.73 two m	3.24 ddd (4.8/8.0/12.4)	—
15d[d]	3	**B**[f]	—	—	7.53–7.58 m 7.63–7.67 m 7.88–7.94 m (C_6H_5)	2.61–2.78, 3.14–3.54 two m	1.90–2.01 m	2.12–2.48 m[e]	3.20–3.25 m	—
15e	3	**B**	2240	1240	4.08–4.16 m (OCH_2)	2.85–2.88 2.90–2.91 two m	1.98–2.33 m		—	1.66 d ($^3J_{PH}$ 14.8)
15f[d]	3	**A**	2240	1210	7.50–8.05 m (C_6H_5)	2.80–3.05 m[c]	2.20–2.30, 2.30–2.49 two m[e]		—	1.52 d ($^3J_{PH}$ 17.2)
15f[d]	3	**B**	—	—	7.50–7.65 m (C_6H_5)	[c]	1.96–2.08, 2.10–2.30 two m[e]		—	1.38 d ($^3J_{PH}$ 14.8)
15g[d,g]	3	**A**	—	—	4.07–4.25 m (OCH_2)	2.71–3.00 m	1.78–2.29 m		—	1.40–1.60 m (CH_2(Pr))
15h	3	**A**	2235	1245	1.84 (CH_3P) ($^2J_{PH}$ 13.2)	2.65–2.74, 3.21–3.30 two m	1.95–2.10, 2.74–2.84 two m[e]		—	1.71 d ($^3J_{PH}$ 16.4)
15i[d]	3	**A**	—	—	[b]	[c]	[e]		—	1.64 d ($^3J_{PH}$ 16.4)
15i[d]	3	**B**	2235	1245	4.19–4.32 m[b] (OCH_2)	2.84–2.90 m[c]	2.03–2.26 m[e]		—	1.62 d ($^3J_{PH}$ 14.8)
16[h]	2		2235, 2255	1230, 1240	—	1.98–2.03 2.92–2.97 two m	—	2.00 m (H_A) ($^3J_{HH}$ 6.6, $^3J_{HH}$ 6.8 $^3J_{PH_A}$ 14.8, $^2J_{H_A H_B}$ 13.2), 2.27 m (H_B) ($^3J_{HH}$ = 5.6), ($^3J_{PH}$ 23.2),	—	1.33 d ($^3J_{PH}$ 13.2)

[a] Two conformers.
[b] The signals of OCH_2 protones of **A** and **B** diastereomers are overlapped.
[c] The signals of C^1H_2 protones of **A** and **B** diastereomers are overlapped.
[d] **A** and **B** diastereomers mixture in 63:37 (**15b**), 29:71 (**15d**), 64:36 (**15g**), 5:95 (**15i**) ratio.
[e] The signals of C^2H_2 and C^3H_2 protones of **A** and **B** diastereomers are overlapped.
[f] Solvent CD_3CN.
[g] The signals of minor diastereomer **B** are overlapped by signal of major isomer **A**.
[h] Solvent DMSO-d_6.

TABLE 6 Selected ^{13}C NMR Data for 3-Cyano-2-oxo-1,2-thiaphosphacyclanes **14, 15** and **16**



			^{13}C NMR Spectrum (δ, ppm, J/Hz, $CDCl_3$)					
Compound	*n*	*Diastereomer*	*C(1)* $^2J_{PC}$	*C(2)* $^3J_{PC}$	*C(3)* $^2J_{PC}$	*C(4)* $^1J_{PC}$	*C(5)* $^2J_{PC}$	*C(6)* $^2J_{PC}$
14b	2	**A**	37.56 (8.5)	—	30.82 (1.1)	43.31 (60.4)	118.13 (4.7)	18.92
		B	37.73 (7.7)		31.42 (0.7)	44.09 (62.8)	118.86	17.04 (1.1)
14c	2	**A**	35.69 (8.5)	—	31.05	49.65 (59.5)	117.06 (5.6)	25.13
		B	35.96 (7.6)		31.18	50.11 (62.4)	117.63	24.73
15a	3	**A**	29.69 (5.8)	25.64 (4.5)	31.20 (3.6)	32.17 (96.8)	114.92 (11.2)	—
		B	29.08 (5.8)	23.14 (6.1)	29.45	31.73 (100.8)	115.22 (4.5)	—
15b	3	**A**	29.78 (5.7)	25.71 (4.6)	30.22 (3.6)	32.95 (96.9)	114.95 (11.7)	—
		B	29.17 (5.9)	23.48 (8.2)	30.15 (3.0)	32.53 (100.9)	115.24 (4.5)	—
15c	3	**A**	24.85 (5.0)	23.44 (4.9)	26.58	34.09 (62.3)	115.47	—
		B	26.34 (5.0)	23.44 (4.9)	27.12	31.49 (64.3)	116.56	—
15d[a]	3	**A**	26.90 (5.0)	26.47 (3.9)	27.27 (2.5)	33.74 (64.9)	117.24	—
		B	25.44 (5.0)	23.18 (5.1)	26.98 (2.5)	32.31 (67.0)	117.19	—
15e	3	**A**	36.70 (3.9)	23.55 (5.9)	29.99 (2.9)	39.30 (60.0)	119.14 (7.0)	18.75 (3.0)
		B	37.98 (4.9)	25.08 (5.0)	30.99 (3.5)	39.51 (103.8)	118.85	19.61 (6.0)
15f	3	**A**	33.45 (3.7)	21.51 (4.1)	26.37 (2.4)	36.87 (64.5)	116.80	19.91
		B	34.56 (4.0)	25.56 (4.0)	26.86 (2.4)	37.99 (68.9)	120.19	20.54 (2.0)
15g	3	**A**	35.07 (4.0)	22.84 (4.9)	33.67 (3.8)	41.67 (97.4)	117.92 (8.2)	29.88 (1.6)
		B	34.20 (5.4)	24.65 (5.2)	32.61	43.99 (102.0)	117.57	30.35 (2.8)
15h	3	**A**	33.93	22.50	27.50	36.88 (62.0)	119.42 (6.3)	19.99 (5.1)
15i	3	**B**	37.93 (4.8)	25.07 (5.0)	31.05 (3.4)	39.51 (103.7)	118.85	19.56 (6.0)
16b[b]	2		36.55 (9.2)	—	27.05 (3.8)	38.09	123.18 (3.8)	18.68 (2.1)

[a]Solvent CD_3CN.
[b]Solvent DMSO-d_6.

The structures of the series of the individual diastereomers **14** and **15** have been confirmed by the X-ray diffraction analysis. Important bond lengths and bond angles are shown in Table 7. According to the X-ray data, five-membered rings in **14** adopt the twist (deviation of the C(2), C(4) atoms) and the envelope conformation (deviation of the C(2) atom) (Figures 2 and 3), while all the six-membered rings, both reported herein and described by us previously [20,21], are characterized by chair conformations (Figures 4–6), with the axial position for the CN group in all molecules **14** and **15**. The phosphorus atoms are characterized by a slightly distorted tetrahedral configuration with the endocyclic C(4)P(1)S(1) angles in the ranges of 95.84(4) ÷ 97.87(3)° in five-membered rings **14** and 103.43(7) ÷ 105.79(5)° in six-membered rings **15**. The torsion angles C(5)C(4)P(1)O(1) are in the interval −35.0 to 55.2° for molecules having the equatorial position of the P=O group (synclinal conformation, *cis*-isomer), and from 147.6 to 170.6° for the axial P=O group (antiperiplanar conformation, *trans*-isomer).

The bond lengths and bond angles in five- and six-membered rings exhibit the expected values (Table 7). The P–S bond lengths in 1,2-thiaphosphinanes **15** (2.044(2) ÷ 2.065(2)Å) are slightly shortened in comparison with the typical single P–S bond (2.08 ÷ 2.10Å) [24] and are close to those observed earlier in the series of 1,2λ^5-thiaphosphinanium salts (2.05Å) [18,19]. Such similarity of thiaphosphinanium salts and cyanosubstituted cycles **14** and **15** means that the phosphorus atom in the latter compounds is characterized by a significant fractional positive charge, mainly due to the electron-withdrawing effect of both the CN group and the phosphoryl oxygen. The same conclusion can be made on the base of comparison of the P–S bond lengths in the nonfunctionalized 2-oxo-2-phenyl-1,2-thiaphosphinane [29] and **15d(A)** (Figure 5), where the P–S bond length is shortened by 0.02Å, while the P(1)–C(1) bond is elongated by 0.04Å due to the presence of the CN group (Table 7). Thus, one can conclude that, for the P–S bond, the presence of electron-withdrawing substituents leads not to an elongation

TABLE 7 Important Bond Lengths (Å) and Bond Angles (deg.) for Some Representatives of **14** and **15**

	14c(A)	**14c(B)**	**15a(B)**[a]	**15c(A)**[a]	**15c(B)**	**15d(A)**	**15i(B)**[a]	**15h(B)**[b]	**G**[a,c]
P(1)–S(1)	2.0778 (9)	2.0751 (4)[d] 2.0832 (4)	2.044 (2)	2.062 (2)	2.065 (2)	2.059 (1)[d] 2.061 (1)	2.0558 (7)	2.054 (1)	2.082 (1)
P(1)–O(1)	1.478 (2)	1.4805 (8) 1.4817 (8)	1.456 (3)	1.488 (2)	1.484 (2)	1.479 (2) 1.477 (2)	1.469 (1)	1.470 (4)	1.474 (2)
P(1)–R_1	1.793 (2)	1.800 (1) 1.801 (1)	1.573 (3)	1.785 (3)	1.788 (2)	1.797 (2) 1.801 (2)	1.572 (1)	1.785 (4)	1.801 (2)
P(1)–C(4)	1.857 (2)	1.869 (1) 1.873 (1)	1.817 (4)	1.838 (4)	1.833 (2)	1.839 (2) 1.832 (2)	1.836 (1)	1.852 (2)	1.790 (3)
S(1)–C(1)	1.837 (2)	1.840 (1) 1.834 (1)	1.807 (6)	1.835 (3)	1.845 (3)	1.838 (3) 1.827 (3)	1.832 (2)	1.837 (3)	1.828 (3)
C(4)P(1)S(1)	97.29 (8)	95.84 (4) 97.87 (3)	105.5 (1)	103.9 (1)	103.43 (7)	103.45 (8) 103.56 (8)	105.79 (5)	104.62 (9)	103.4 (1)
O(1)P(1)R^1	112.2 (1)	117.73 (5) 110.84 (5)	116.7 (2)	114.6 (1)	114.1 (1)	113.8 (1) 113.6 (1)	116.56 (8)	113.6 (4)	113.0 (1)
C(1)S(1)P(1)	95.7 (1)	94.93 (4) 95.20 (4)	105.5 (1)	97.9 (2)	100.13 (7)	99.1 (1) 97.96 (9)	99.54 (8)	100.2 (1)	96.8 (1)
C(5)C(4)P(1)O(1)	−35.0	165.4 147.6	170.6	170.6	50.0	167.9 170.00	55.2	50.5	n/a
Lp_SS(1)P(1)X[e]	118	−148 −124	175	176	177.1	173 175	175	176	176
Conformation[f]	Twist C(2),C(4) (0.52, −0.11E)	Twist C(2),C(4) (0.69, −0.13E) Envelope C(2) (0.64E)	chair	chair	chair	chair	chair	chair	chair

[a]The numbering of atoms in **15a(B), 15c(A), 15i(B),** and **G** is the same as for all other six-membered cycles in Figures 2–6.
[b]For **15h(B)** the bond lengths and angles are presented only for the molecule with the occupancy 0.80.
[c]**G** presents 2-oxo-2-phenyl-1,2-thiaphosphinane [29].
[d]For molecules **14c(B)** and **15d(A)** bond lengths and angles are indicated for two independent molecules.
[e]The torsion angle between the hypothetical sulfur electron lone pair (Lp_s) and the phosphorus axial subsistent (X is O(1) in diasteromer A and R^1 in **B**). The positions of Lp_s were calculated in the assumption of the tetrahedral arrangement of Lp_S's and C(1), P(1) atoms.
[f]For five-membered cycles the value in brackets corresponds to the deviation of the atom from the mean plane of remaining atoms of the cycle.

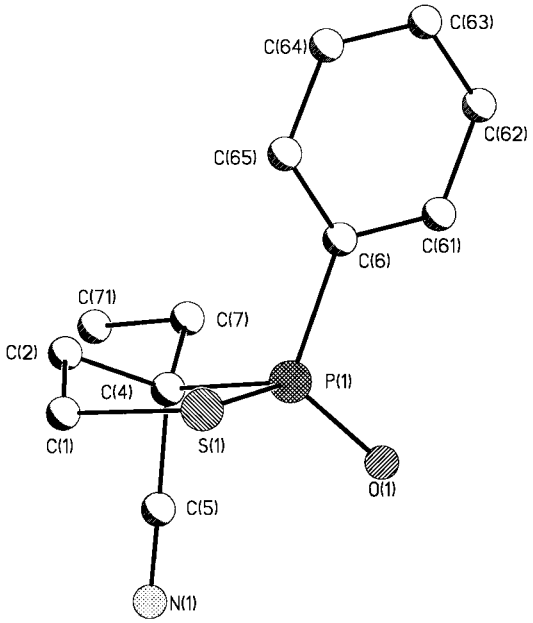


FIGURE 2 Molecular structure of **14c(A)**.

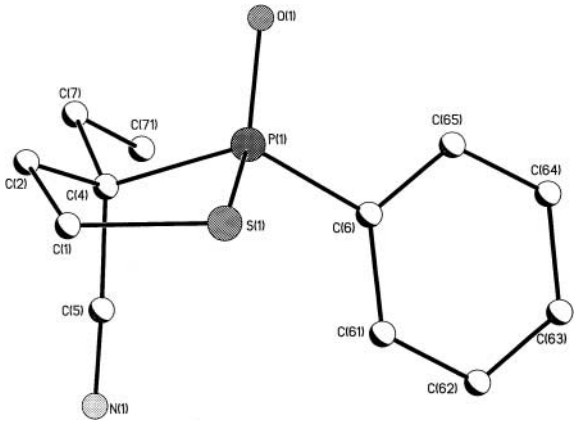


FIGURE 3 Molecular structure of **14c(B)**. Only one of two independent molecules is shown. The differences in their conformations are described in Table 7.

but to a shortening of the bond that is usual for the polar or ionic bonds.

Besides the inductive effects of the substituents, variation of the P–S bond can also be affected by the interaction between the lone pair (Lp_s) of the sulfur atom and the antibonding σ-orbital of the axial P–X bond (n-σ^* interaction), which differs for P=O, OAlk, and Alk groups [30]. The increase of a n-σ^* interaction must be reflected in the shortening of the P–S endocyclic bond and elongation of the axial exocyclic one.

Analysis of the important bond lengths and bond angles in the six-membered rings indicates clearly

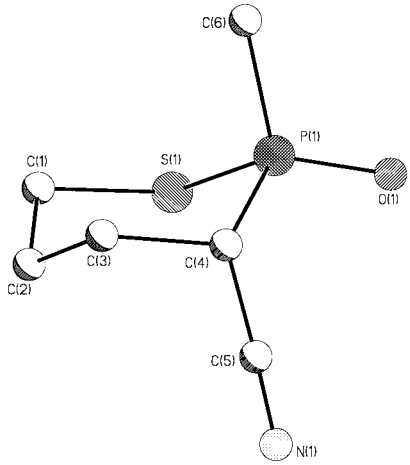


FIGURE 4 Molecular structure of **15c(B)**.

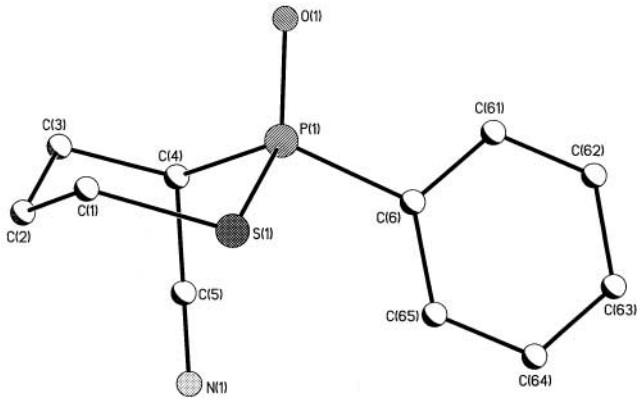


FIGURE 5 Molecular structure of **15d(A)**. Only one of two independent molecules is shown.

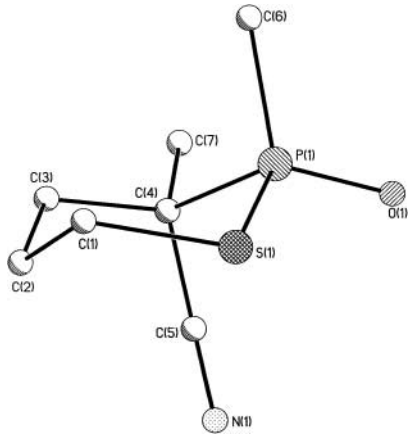


FIGURE 6 Molecular structure of **15h(B)**. The disordering is omitted for clarity.

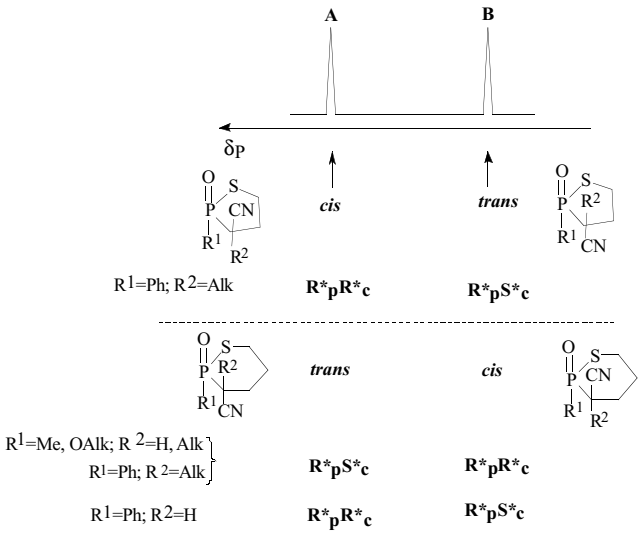
some influence of the n-σ^* interaction in the case of the OEt axial group in **15a(B)**, where not only the P–S bond attains the minimum value (2.044(2)Å), but also the S(1)-C(1) bond is the shortest one in the series of compounds studied (1.807(6)Å). In spite of pronounced shortening of the P–S bond in **15a(B)**, introduction of the Me group in the 3-position of the ring (compound **15i(B)**) causes an increase of the P–S bond length by 0.01Å, annulling, in fact, the influence of the n-σ^* interaction. It's noteworthy that the formal strength of the n-σ^* interaction, in accordance with the values of the pseudotorsion angle $Lp_sS(1)P(1)X$ and the length of the P(1)–O(2)(Et) bond in **15a(B)** and **15i(B)**, were found to be the same.

Opposite to the axial alkoxy group at the phosphorus atom, the influence of the n-σ^* interaction on the P–S bond is insignificant in the case of an axial P=O bond. For example, as it may be seen from Table 7, the P(1)–O(1) and P(1)–S(1) bonds in **15c(A)** and **15c(B)** are similar. The same situation is observed in the case of the 3-cyano-3-ethyl substituted 5-membered rings where the P(1)–S(1) and P(1)–O(1) bonds in **14c(B)**, with the axial position of the P=O group are close to the corresponding values in **14c(A)** with the equatorial P=O bond.

For the 1,2λ^5-thiaphosphacyclanium salts, the elongation of the P–S bond when passing from the five-membered rings to the six-membered ones (2.0751(4) ÷ 2.0832(4)Å) was not observed [18]. Therefore, taking into account the aforementioned influence of the alkyl substituent in the 3-position on the P–S bond length in **15a(B)** and **15i(B)**, one can suppose that the difference (0.019Å) between the P–S bond lengths in **14c(B)** and **15d(A)** is also caused mainly, not by the ring size change, but by introduction of the 3-ethyl substituent decreasing the fractional positive charge on the phosphorus atom.

Summarizing, the P–S bond length in 1,2-thiaphosphacyclanes is more affected by the inductive effects of the substituents at the phosphorus atom and in the 3-position of the ring than by the n-σ^* interaction.

Comparison of the ^{31}P NMR spectra and X-ray diffraction data allows one to conclude that for the 3-cyano-2-oxo-1,2-thiaphospholanes **14**, the isomer **A** (having a downfield chemical shift) is characterized by the synclinal conformation of the cyano group and phosphoryl oxygen atom (*cis*-isomer) with the identical configuration of the chiral centers (2*R**,3*R**), while diastereomer **B** is characterized by an antiperiplanar disposition of the said groups (*trans*-isomer) with the opposite configuration of the chiral centers (2*R**,3*S**). For the 2-



SCHEME 9

oxo-1,2-thiaphosphinanes, **15**, the situation changes to the opposite one: diastereomer **A** with a downfield shift in its ^{31}P NMR spectrum corresponds to the *trans*-disposition of the cyano group and phosphoryl oxygen atom with the opposite configuration of the chiral centers (2*R**,2S*), while the signal of the *cis*-isomer **B** with the identical configuration of the asymmetric centers is shifted upfield. The only exception is the 3-cyano-2-oxo-2-phenyl-1,2-thiaphosphinane **15f**, wherein the alteration of substituent precedence leads to the identical configuration of the chiral centers in the *trans*-**A** isomer and to the opposite one in the *cis*-**B** isomer. Scheme 9 illustrates stereoisomer **14** and **15** structures in comparison with δ ^{31}P.

Thus, ^{31}P NMR spectroscopy allows one to assign unambiguously the type of geometric isomer and the configuration of the asymmetric centers in 3-cyano-2-oxo-1,2-thiaphosphinanes **14** and **15**. To determine the stereochemical structures of phosphacyclanes and 1,2-oxaphosphacyclanes having a tetracoordinated phosphorus atom ^{1}H NMR spectra are commonly used [1,31]. This method of determination is based on the deshielding effect of the P=O bond on all kinds of protons in the *cis* position to the P=O group. Undoubtedly, this anisotropic effect allows the assignement of the *cis* and *trans* arrangements of the P=O group and C<u>H</u>-CN cyclic proton for the compounds **15a–d** or methyl [P–C(C<u>H</u>$_3$)CN-] or methylene [P–C(C<u>H</u>$_2$-R)CN-] group in 3-alkylsubstituted compounds, **14a–c** and **15e–i:** δ_H *trans*-isomer > δ_H *cis*-isomer [32]. Nevertheless, ^{31}P NMR spectroscopy is more preferable to determine the geometric structure of **14** and **15** as

having no need for chemically pure samples and allowing one to monitor the crude reaction mixtures. We believe that regularities described previously for the disposition of signals of *cis* and *trans* 2-oxo-1,2-thiaphosphacyclanes in ^{31}P NMR spectra have to be similar in passing to other 3-substituted 1,2-thiaphophacyclanes, provided that the 3-substituent will represent an electron-withdrawing group.

CONCLUSION

Thus, using as an example the ω-haloalkylsubstituted thiophosphorylalkanonitriles, the intramolecular S-alkylation has proven to be the general principle of the 1,2-thiaphosphacyclane ring construction which opens wide opportunities to synthesize different hitherto elusive 1,2-thiaphosphacyclanes, including functionalized ones.

EXPERIMENTAL

General

NMR spectra were recorded on Bruker WP-200SY and AMX-400 spectrometers in CH_2Cl_2, $CDCl_3$, C_6D_6, CD_3CN solutions using a deutero solvent as an internal standard (^1H, ^{13}C) and 85% H_3PO_4 as an external standard. IR spectra were recorded on a UR-20 spectrophotometer in a thin layer, in KBr pellets, or in vaseline oil. The starting thiophosphorylalkanonitriles **4** were obtained by the reaction of phosphorylacetonitriles with the Lawesson reagent according to the literature [33].

X-Ray Crystal Structure Determination

The crystallographic data for **9, 14c(A** and **B), 15c(B), 15d(A)** and **15h(B)** are presented in Table 8. All structures were solved by the direct method and refined by full-matrix least squares against F^2 in the anisotropic (H-atoms isotropic) approximation using the SHELXTL-97 package. Analysis of the electron density synthesis in **9** and **15h(B)** has revealed disordering of molecules in crystals. In the stucture of **9,** OEt groups were disordered by two positions, while in **15h(B)** the disordering was caused by the superposition of two molecules with the occupancies 0.8 and 0.2, respectively. The disorder in **15h(B)** with the same ratio of occupancies was observed for two independent single crystals. All hydrogen atoms in **9** and **14–15** were located from the electron density difference synthesis and were included in the refinement in isotropic approximation.

Supplementary Material

Crystallographic data, namely atomic coordinates, anisotropic parameters, a full list of the bond lengths, bond and torsion angles, and F_0/F_c values (excluding structure factors), reported in this article are given in the supplementary materials and have been deposited as supplementary nos. CCDC-154959 (**9**), CCDC-154958 (**14c(A)**), CCDC-154955 (**14c(B)**), CCDC-154956 (**15c(B)**), CCDC-154957 (**15d(A)**), and CCDC-154954 (**15h(B)**) at the Cambridge Crystallographic Data Centre. Copies of the data may be obtained free of charge on application to the CCDC,12 Union Road, Cambridge CB2 1EZ UK (Fax: [internat.] +44-1223/336-033; E-mail: deposit @ccdc.cam.ac.uk).

*5-Chloro-2-thiophosphorylpentanonitriles (**5**): General Procedure*

To a stirred solution of thiophosphorylacetonitrile **4** (10 mmol) and TEBA (200 mg) in CH_2Cl_2 (based on 15 mL of solvent for the solid **4f** and 5 mL for the liquid **4a–e**) NaOH (1.6 g, 40 mmol) was added as a 50% aqueous solution. To the reaction mixture, 1,3-bromochloropropane was added dropwise over 10 minutes. The reaction mixture was stirred for 3 hours at 20°C and diluted with water (15 mL); the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4) and concentrated *in vacuo*, and the residue was subjected to column chromatography (silica gel 40–100 μm; hexane–acetone elution) or distillation *in vacuo* (for **5c**).

*ω-Chloro-2-thiophosphorylalkanonitriles **6–8**: General Procedure*

Step a: To a stirred solution of thiophosphorylacetonitrile **4** (12 mmol) and TEBA (200 mg) in CH_2Cl_2 (20 mL), NaOH as a 50% aqueous solution (48 mmol) was added followed by the dropwise addition of the alkyl halide R^3Hlg (14.4 mmol). The reaction mixture was stirred for 3 hours at 20°C and diluted with water (15 mL); the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. The oil thus obtained, representing the intermediate thiophosphorylalkanonitrile of 87–96% purity (according to ^1H NMR spectrum), was used in the subsequent step without further purification.

Step b: To a stirred solution of the aforementioned oil and TEBA (200 mg) in CH_3CN (15 mL) $Br(CH_2)_nCl$ ($n = 2 - 4$) (15 mmol) was added, followed by powdered KOH (15 mmol) portionwise

TABLE 8 Crystal Data, Data Collection, and Structure Refinement Parameters for **9** and Some Representatives of **14** and **15**

Compound	**9**	**14c(A)**	**14c(B)**	**15c(B)**	**15d(A)**	**15h(B)**
Formula	$C_{17}H_{32}N_2O_4P_2S_2$	$C_{12}H_{14}NOPS$	$C_{12}H_{14}NOPS$	$C_6H_{10}NOPS$	$C_{11}H_{12}NOPS$	$C_7H_{12}NOPS$
Molecular weight	454.51	251.27	251.27	175.18	237.25	189.21
Crystal system, Space group	Monoclinic, $P\,2_1/c$	Monoclinic, $C\,2/c$	Triclinic, $P1$	Monoclinic, $P\,2_1/c$	Triclinic, $P1$	Orthorhombic, *Pbca*
a, Å	11.478 (4)	19.072 (4)	10.6650 (4)	9.113 (6)	10.312 (5)	12.4500 (9)
b, Å	17.654 (4)	12.890 (3)	10.9258 (4)	6.073 (5)	10.996 (5)	11.3047 (8)
c, Å	12.634 (4)	10.796 (2)	11.5450 (5)	15.077 (9)	11.523 (5)	13.1782 (10)
α (°)			72.467 (1)		65.13 (3)	
β (°)	95.78 (3)	98.99 (3)	71.922 (1)	98.62 (5)	89.34 (4)	
γ (°)			86.670 (1)		79.30 (4)	
V, Å^3	2547 (1)	2621.4 (9)	1218.52 (8)	825 (1)	1161 (1)	1854.7 (2)
Z	4	8	4	4	4	8
d (*calc.*), g cm^{-3}	1.185	1.273	1.370	1.410	1.357	1.355
μ (Mo Kα), cm^{-1}	3.56	3.48	3.75	5.19	3.88	4.67
Diffractometer	Siemens P3/C	Siemens P3/C	Smart 1000 CCD	Siemens P3/C	Siemens P3/C	Smart 1000 CCD
Temperature, (K)	298 (2)	153 (2)	110 (2)	298 (2)	298 (2)	100 (2)
$2\theta_{max}$(°)	50	50	60	64	50	60
No. collected refl., no. unique refl.	4684, 4454	2068, 1996	12751, 6760	3135, 2977	4371,4123	13466, 2666
(Rint)	(0.0318)	(0.0275)	(0.0128)	(0.0403)	(0.0582)	(0.0333)
R_1 (on *F* for refl. with $I > 2\sigma(I)$	0.0714	0.037	0.0321	0.0429	0.0425	0.0496
	(for 3537 refl.)	(for 1363 refl.)	(for 6173 refl.)	(for 1756 refl.)	(for 3754 refl.)	(for 2184 refl.)
wR_2 (on F^2 for all refl.)	0.1849	0.0920	0.0962	0.0950	0.1124	0.1252
	(for 4454 refl.)	(for 1996 refl.)	(for 6760 refl.)	(for 2977 refl.)	(for 4123 refl.)	(for 2666 refl.)
Goodness of fit on F^2	1.048	0.931	1.031	0.850	1.003	1.147

addition. The reaction mixture was stirred for 2 hours at 20°C, a further 15 mmol of the corresponding dihaloalkane was added, and stirring was continued for 1 hour. The reaction mixture was concentrated *in vacuo*, taken up in benzene (15 mL), and diluted with water (10 mL). The organic layer was separated, and the aqueous one was extracted with benzene. The combined organic fractions were dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by distillation or column chromatography.

*Interaction of the Methylated **4a** with $Br(CH_2)_3Br$*

The methylation of **4a** (14 mmol) was performed according to the aforementioned step a to give the intermediate product in quantitative yield with 96% purity (according to ^{1}H NMR spectroscopy). For the physicochemical and spectral parameters of the methylated **4a** see Ref. [22]. The substance was used for the subsequent stage without further purification.

The reaction of the latter compound with $Br(CH_2)_3Br$ (18.8 mmol) was carried out according to step b, using the standard workup of the reaction mixture. After concentration, hexane was added to the residue, and this was allowed to stand for 3 days at room temperature. The solid **9** (2.08 g, 64%; meso:d,l = 1:1) that precipitated was filtered off.

On attempted isolation of the isomers by column chromatography (100:1 to 100:13 hexane-acetone elution), two main fractions were obtained, the first (100:11 hexane-acetone) representing an oil (meso: d,l = 3:7) and the second (100:12 hexane-acetone) being a solid with m.p. 94–95°C (meso:d,l = 7:3). After recrystallization of the second fraction from hexane, the meso form was obtained in the pure state, (m.p. 93°C).

Anal. found (%): C, 44.93; H, 6.91; N, 6.05; Calcd. for $C_{17}H_{32}N_2O_4P_2S_2$ (%): C, 44.93; H, 7.05; N, 6.17.

Compound **9** (meso): ^{31}P NMR ($CDCl_3$) δ 92.3. ^{1}H NMR ($CDCl_3$) δ 1.35 (t, $^3J_{HH}$ 7.2 Hz, $C\underline{H}_3CH_2O$, 12H), 1.55 (d, $^2J_{PH}$ 17.6 Hz, $C(CN)CH_3$, 6H), 1.62–1.90 (m, $C(CN)CH_2$, 4H), 2.0–2.13 (m, $CH_2C\underline{H}_2CH_2$, 2H), 4.14–4.31 (m, OCH_2, 8H). ^{13}C NMR ($CDCl_3$) δ 15.94 and 16.05 ($\underline{C}H_3CH_2O$), 19.54 ($C(CN)\underline{C}H_3$), 20.44 (t, $CH_2\underline{C}H_2CH_2$, $^3J_{PC}$ 9.0 Hz), 34.0 ($\underline{C}H_2CH_2\underline{C}H_2$), 41.18 (d, $^1J_{PC}$ 114.6 Hz, P–C), 64.41–64.30 (two d, $^2J_{PC}$ 7.5 and 7.8 Hz, OCH_2), 119.24 (d, $^2J_{PC}$ 7.1 Hz, CN).

Compound **9** (**d,l**): ^{31}P NMR ($CDCl_3$) δ 92.1. ^{1}H NMR ($CDCl_3$) δ 1.36 (t, $^3J_{HH}$ 7.2 Hz, $C\underline{H}_3CH_2O$, 12H), 1.57 (d, $^2J_{PH}$ 17.6 Hz, $C(CN)CH_3$, 6H), 1.62–1.90 (m, $C(CN)CH_2$, 4H), 2.0–2.13 (m, $CH_2C\underline{H}_2CH_2$, 2H), 4.14–4.31 (m, OCH_2, 8H).

The reaction of methylated **4a** with $Br(CH_2)_3Br$ was carried out in the same manner, except that 25 mL of acetonitrile was used in the step of the reaction with $Br(CH_2)_3Br$; the residue obtained after the workup of the reaction mixture comprised (according to ^{31}P NMR spectroscopy) the target **7a** (65%); **9** (20%), and the C-methylation product **4a** (15%). The residue was distilled *in vacuo,* the fraction with b.p. 150– 165°C (1 mm Hg) being collected and comprising the target **7a** (86%); **15i** (8%) and the C- methylation product **4a** (6%). The fraction was used to produce 2-oxo-1,2-thiaphosphinane **15i** without further purification.

*2-Diphenylthiophosphinyl-5-iodopentanonitrile **10a***

The mixture of 5-chloro-2-diphenylthiophosphinylpentanonitrile **5f** (0.15 g, 0.45 mmol) and sodium iodide (81.36 mg, 0.54 mmol) in absolute acetonitrile was heated under reflux for 6 hours. After having been allowed to cool, the reaction mixture was concentrated, the residue was taken up in benzene, and sodium chloride was filtered off. The filtrate was concentrated to give the target compound **10a** (0.18 g, 94% purity according to ^{1}H NMR spectroscopy). ^{31}P NMR ($CDCl_3$) δ 45.69. ^{1}H NMR ($CDCl_3$) δ 1.85–1.87, 1.94–1.96 (two m, 1H + 1H, $CHC\underline{H}_2$), 2.11–2.17 (m, $C\underline{H}_2CH_2I$, 2H), 3.11–3.17 (m, $^3J_{HH_C} = {}^3J_{HH_D}$ 8.0, $^2J_{H_AH_B}$ 14 Hz,CH_2I, 2H, AB-system), 3.54–3.63 (m, CH, 1H), 7.52–7.88 (m, C_6H_5, 10H).

In the same manner from 5-chloro-2-diphenylthiophosphinyl-2-methylpentanonitrile **7g** (0.15 g, 0.43 mmol) and sodium iodide (77.5 mg, 0.52 mmol), **11a** (0.17 g) was obtained (the reaction mixture comprised about 20% **7g** according to ^{31}P NMR spectroscopy). ^{31}P NMR ($CDCl_3$) δ 55.09.^{1}H NMR ($CDCl_3$) δ 1.58 (d, $^3J_{PH}$ 16.4 Hz, $CH_3C(CN)$, 3H), 1.82–1.90, 1.98–2.04, 2.09–2.14 (three m, $C\underline{H}_2C\underline{H}_2CH_2I$, 1H + 1H + 2H), 3.10 (t, $^3J_{HH}$ 8.0 Hz, 2H, CH_2I), 7.52–7.58, 8.19–8.27 (two m, C_6H_5, 10H).

*^{31}P NMR Study of the Intramolecular **10a** and **11a** S-Alkylation*

A solution of 15 mg of the compound **10a, 11a** in absolute acetonitrile was placed in a 5 mm NMR ampule, which was sealed and stored at 20°C with the ^{31}P NMR spectra being recorded weekly.

TABLE 9 Methods of purification and isolation of cis- and trans-diastereomers **14** and **15**

Compound	*Cyclization Method*	*b.p. (1 mm Hg)* **(I)** *or the reflux duration (h)* **(II)**	*Methods of Purification and Isolation of Diastereomers*	*Yield (%)*[a] *According to the Reaction Mixture NMR ^{31}P*	*Yield (%)*[a] *After Purification*
14a[b]	I	150–170	Column chromatography (C_6H_{14}:Me_2CO = 10:4), **A:B** (60:40)	40	—
14b	II	18	Column chromatography (petrol. ether:Me_2 CO = 10:4), **B** = isomer, (petrol. ether:Me_2CO = 2:1), **A:B** (94:6)	61	30
14c	I	170–195	Column chromatography (C_7H_{16}:Me_2CO = 10:4), **B**-isomer, (C_7H_{16}:Me_2CO = 2:1), **A:B** (75:15) crystallization of **A** and **B** isomer mixture (Et_2O), **A**-isomer	95	54
14c	II	2	Column chromatography (petrol. ether:Me_2CO = 10:4), **B**-isomer, (petrol. ether:Me_2CO = 2:1), **A:B** (75:15), precipitation Et_2O - **A**-isomer	Quantitative	57
15a	I	140–200	Precipitation Et_2O-**A:B** (43:57), crystallization from C_6H_6-**B**-isomer; mother liquor crystallization (Et_2O), **A** and **B** isomer mixture (1:1)	75	51
15b	I	190–210	Column chromatography (petrol. ether:Me_2CO = 10:4), crystallization from C_6H_6, **B**-isomer)	55	21[b]
15b	II	32	Column chromatography (C_6H_{14}:Me_2CO = 10:4), **A:B** (63:37), crystallization from C_6H_{14}, **A:B** (47:53)	32	17
15c	I	210–220	Crystallization from C_6H_6 **A**-isomer, mother liquor crystallization (C_7H_{16}), **B**-isomer	30	18
15c	II	15	Reaction mixture crystallization from C_7H_{16} - **A:B** (74:26)	53	25
15d	I	202–210	Column chromatography (C_6H_{14}:Me_2CO = 10:4) - **A**-isomer	44	21
15d	II	22	Column chromatography (C_6H_{14}:Me_2CO = 10:4) - **A**-isomer	79	34
15e	II	40	Column chromatography (petrol. ether:Me_2CO = 10:1) - **A:B** (40:60), crystallization (C_6H_6: Et_2)-**B**-isomer	29	10
15f	I	193–210	Column chromatography (C_6H_{14}:Me_2CO = 10:4) - **A:B** (36:54); crystallization (C_6H_6: C_2H_{14}) - **A:B** (84:16)	19	6
15f	II	16	Column chromatography (petrol. ether:Me_2CO = 10:4) - **A**-isomer	Quantitative	24
15g	I	180–190	Column chromatography (C_6H_{14}:Me_2CO = 10:4) - **A:B** (36:54); crystallization (C_6H_6: Et_2O) - **A:B** (84:16)	15	6[h]
15h	II	25	Column chromatography (petrol. ether:Me_2CO = 10:1) - **A:B** (45:55), repeated column chromatography (petrol. ether: Me_2CO = 10:1) - **A:B** (73:27), 2:1 - **A**-isomer	64	22
15i	II	100	Precipitation by Et_2O - **A:B** (32:68), crystallization from Et_2O - **B**-isomer	75	45

[a]Based on both diastereomers.

[b]The compound decomposes during chromatographical purification yielding monobasic phosphonic acid EtO(HO)P(O)C(Me)(CN)CH_2CH_2SH (yield 5% after purification). ^{31}P NMR (δ ppm, DMSO-d_6) 17.2. ^1H NMR (δ ppm, **J** (Hz), DMSO-d_6): 1.23 **t** (3H, C$\underline{H}_3CH_2$, $^3\mathbf{J}_{HH}$ 7.2), 1.43 d (3H, CH_3C(CN), $^3\mathbf{J}_{PH}$ 14.4), 1.86–1.95, 2.06–2.15 two m (1H+1H, C$\underline{H}_2CH_2SH$), 2.59–2.69 m (2H, C$\underline{H}_2CH_2SH$), 4.02–4.11 m (2H, OCH_2).

*3-Cyano-2-oxo-1,2-thiaphosphacyclanes and 3-Alkyl-3-cyano-2-oxo-1,2-thiaphosphacyclanes **14,** and **15.***

Method I: The Intramolecular Cyclization of ω-Chloro-2-thiophosphorylalkanonitriles (General Procedure). ω-Chloro-2-thiophosphorylalkanonitriles **5–7** produced according to the aforementioned procedure as crude products without further purification [34] were distilled *in vacuo*. After low boiling alkyl halide (R^3Hlg) had been removed, the fraction was collected, boiling, in the ~160–210°C (1 mm Hg) range. The mixture of 3-cyano-2-oxo-1,2-thiaphosphacyclanes **14** and **15** diastereomers obtained was further purified and resolved by column chromatography, fractional crystallization, or by the combination of the previously mentioned methods (Table 9).

Method II: The Intramolecular Cyclization of ω-Iodo-2-thiophosphorylalkanonitriles (General Procedure). The mixture of ω-chloro-2-thiophosphorylalkanonitrile **5–7** (3.0 mmol) and sodium iodide (6.0 mmol) in absolute acetonitrile (20 mL) was heated under reflux for 2–40 hours (the course of the cyclization being monitored by the ^{31}P NMR spectroscopy). After cooling, the reaction mixture was filtered. The filtrate was concentrated *in vacuo*, and the residue was taken up in CH_2Cl_2 (15 mL) and filtered again. After concentration, the residue was purified as described in Table 9.

*3-Cyano-2-ethoxy-3-methyl-2-oxo-1,2-thiaphosphinane **15i***

The solution of 5-bromo-2-diethylthiophosphoryl-2-methylpentanonitrile **7a** (0.15 g, 0.46 mmol) in absolute acetonitrile (10 mL) was heated under reflux for 100 hours (by then the amount of the cyclic product was 75% according to ^{31}P NMR data and was not increasing under further heating). After cooling, the reaction mixture was concentrated *in vacuo* and crystallized from ether to give diastereomer **B** (45 mg, 45%) of the compound **15i**. The **15i (B)** was filtered off and the filtrate was concentrated and dried *in vacuo* (1 mm Hg) to give a 2:1 mixture of **A** and **B** diastereomers (40 mg).

*3-Cyano-3-methyl-1,2-thiaphospholane Acid Sodium Salt **16***

The mixture of 4-chloro-2-diethylthiophosphoryl-2-methylbutanonitrile **6a** (2.5 g, 9.78 mmol) and sodium iodide (3.0 g, 20,0 mmol) in absolute acetonitrile (15 mL) was heated under reflux for 10 hours. The solid that precipitated by then hampered the ability of the reaction mixture to boil uniformly. Thus, it was filtered, and heating was continued for 10 hours. After the standard work-up (see method II) the organic fraction (0.3 g) contained no phosphorus compounds (according to ^{31}P NMR). The solid obtained (2.5 g) representing a mixture of the sodium salt **16** and inorganic sodium salts was washed with CH_3CN (25 mL) and CH_2Cl_2 (2×25 mL), and the extract was dried *in vacuo*. ^{31}P NMR δ 47.89 (DMSO-d_6), 51.36 (Py). IR and ^{13}C and ^1H NMR spectroscopy data of the compound **16,** confirming the heterocycle formation, are shown in Tables 5 and 6. All attempts to isolate the corresponding acid by acidification, followed by extraction of the organic phase, resulted in the destruction of the ring compound.

In the same manner, the sodium salt of 3-cyano-1,2-thiaphosphinanic acid **17** (2.2 g) was obtained from 5-chloro-2-diethylthiophosphorylpentanonitrile **5a** (2.0 g, 7.42 mmol) and sodium iodide (2.36 g, 15.7 mmol). ^{31}P NMR δ 25.43 (CH_3CN), 25.75 (CH_2Cl_2).

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