

## Stereochemistry of Organophosphorus Cyclic Compounds. Part IV.<sup>1</sup> Synthesis and Geometrical Isomerism in Cyclic Five-Membered Phosphorus Thioacids. Crystal and Molecular Structure of the Imidazolium Salt of *r*-2-Hydroxy-*c*-4-methyl-1,3,2-dioxaphospholan-2-thione

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Several five-membered cyclic phosphorus monothioacid salts have been prepared by treatment of the corresponding cyclic thiophosphoryl chlorides with imidazole and water. The imidazolium salt of 2-hydroxy-4-methyl-1,3,2-dioxaphospholan-2-thione has been found to exist as a mixture of *cis* and *trans* isomers separable by crystallisation. The configurations of these diastereoisomers have been assigned on the basis of chemical correlations and X-ray analysis. The *cis*-isomer (with reference to the ring methyl group and the exocyclic oxygen atom) crystallises in space group  $P\bar{1}$  with  $a = 7.818(5)$ ,  $b = 9.736(5)$ ,  $c = 6.958(5)$  Å,  $\alpha = 76.42(20)$ ,  $\beta = 98.18(20)$ ,  $\gamma = 97.23(20)^\circ$ . The structural features of the 1,3,2-dioxaphospholan ring are discussed.

EFFORTS to determine the stereochemistry of five- and six-membered cyclic phosphorus compounds have increased over the past few years. As a part of our studies on the stereochemistry of phosphorus thioacids we have previously investigated<sup>2</sup> the geometrical isomerism in six-membered cyclic thio- and seleno-phosphorus acids and their derivatives by using the 4-methyl-1,3,2-dioxaphosphorinan system, which contains two chiral centres, one at phosphorus and one at carbon. Depending on the method of synthesis of these compounds, a mixture of geometrical isomers or a

single isomer can be obtained. A knowledge of the steric course of the reactions carried out and application of n.m.r. spectroscopy made it possible to determine the configuration and in some cases the conformation of these compounds.<sup>2-4</sup>

The studies were extended to analogous five-membered cyclic thio- and seleno-phosphorus acids, *e.g.* the corresponding 1,3,2-dioxaphospholans. The geometrical isomerism of a phosphorus monothioacid with the 1,3,2-dioxaphospholan ring built into a nucleoside system was first observed by Eckstein.<sup>5</sup> It was our aim to investigate this phenomenon in simpler five-membered

<sup>1</sup> Part III, W. Stec and A. Łopusiński, *Tetrahedron*, 1973, **29**, 547.

<sup>2</sup> M. Mikołajczyk and J. Łuczak, *Tetrahedron*, 1972, **28**, 5411.

<sup>3</sup> M. Mikołajczyk, J. Krzywański and B. Ziemnicka, *Phosphorus*, 1974, **5**, 67.

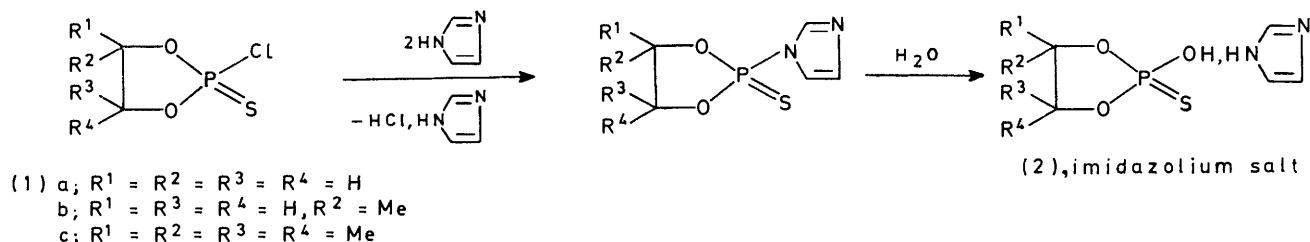
<sup>4</sup> M. Mikołajczyk, J. Krzywański, and B. Ziemnicka, *Tetrahedron Letters*, 1975, 1607.

<sup>5</sup> F. Eckstein and H. Gindl, *Chem. Ber.*, 1968, **101**, 1670; F. Eckstein, *FEBS Letters*, 1968, **2**, 85.

phosphorus monothioacid systems. The synthesis of 2-hydroxy-4-methyl-1,3,2-dioxaphospholan-2-thione (2b) as a mixture of geometrical isomers was reported in a preliminary communication.<sup>6</sup> This article presents the full details of this work as well as an X-ray determination of the structure of one isomer. The X-ray work

study the synthesis and hydrolysis of cyclic thiophosphorylimidazoles as a general route to five-membered cyclic phosphorus thioacids (see Scheme 1).

The starting 2-chloro-1,3,2-dioxaphospholan-2-thiones (1a) and (1b) were prepared in good yield from the thiophosphoryl chloride and the appropriate diols.<sup>8</sup>



SCHEME 1

confirmed the configurational assignments of the *cis*- and *trans*-2-hydroxy-4-methyl-1,3,2-dioxaphospholan-2-thione (2b) based on chemical correlations.

## RESULTS AND DISCUSSION

*Synthesis of Five-membered Cyclic Phosphorus Monothioacids.*—Alkaline hydrolysis of phosphorochloridothionates (=P(S)Cl), applicable to the synthesis of phosphorus monothioacids with a 1,3,2-dioxaphosphorinan ring,<sup>2,7</sup> could not be utilized for the preparation of the analogous five-membered derivatives, owing to the instability of the 1,3,2-dioxaphospholan ring under

However, with pinacol this reaction did not afford the expected chloride (1c). For this reason 2-chloro-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan-2-thione (1c) was synthesized by treatment of 2-mercapto-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan-2-thione<sup>9</sup> with phosphorus pentachloride.

As expected, the reaction of the cyclic chlorides (1) with imidazole in tetrahydrofuran afforded the corresponding thiophosphorylimidazoles, which, on account of their instability,\* were converted without isolation into crystalline imidazolium salts of 2-hydroxy-1,3,2-dioxaphospholan-2-thiones (2) by treatment with water.

TABLE 1

Salts of 2-hydroxy-1,3,2-dioxaphospholan-2-thiones and -2-selenones [(2) and (3)]

Salt	M.p. (°C) (from PrOH-Et <sub>2</sub> O)	Yield (%)	Formula	Elemental analyses (%)
(2a), imidazole	117—119	60	C <sub>8</sub> H <sub>9</sub> N <sub>2</sub> O <sub>3</sub> PS	Found: C, 28.9; H, 4.65; P, 14.9; S, 15.15; N, 13.35 Calc.: C, 28.85; H, 4.35; P, 14.9; S, 15.4; N, 13.45
(2b), imidazole	88—100 <sup>a</sup>	76	C <sub>6</sub> H <sub>11</sub> N <sub>2</sub> O <sub>3</sub> PS	Found: C, 32.35; H, 5.25; P, 13.65; S, 14.2; N, 12.55 Calc.: C, 32.45; H, 5.0; P, 13.95; S, 14.45; N, 12.6
(2c), imidazole	175—179.5	68(76) <sup>c</sup>	C <sub>9</sub> H <sub>17</sub> N <sub>2</sub> O <sub>3</sub> PS	Found: C, 41.0; H, 6.45; P, 11.5; S, 12.05; N, 10.35 Calc.: C, 40.9; H, 6.5; P, 11.7; S, 12.15; N, 10.6
(2c), dicyclohexylamine	212—215	88	C <sub>18</sub> H <sub>36</sub> NO <sub>3</sub> PS	Found: C, 57.4; H, 9.55; P, 8.25; S, 8.35; N, 3.7 Calc.: C, 57.25; H, 9.6; P, 8.2; S, 8.5; N, 3.7
(3), imidazole	177—180 <sup>b</sup>	78	C <sub>8</sub> H <sub>17</sub> N <sub>2</sub> O <sub>3</sub> PSe	Found: C, 34.85; H, 5.4; P, 10.0; N, 9.05 Calc.: C, 34.7; H, 5.5; P, 9.95; N, 9.0
(3), dicyclohexylamine	201—206	76	C <sub>18</sub> H <sub>36</sub> NO <sub>3</sub> PSe	Found: C, 51.3; H, 8.65; P, 7.5; N, 3.4 Calc.: C, 50.95; H, 8.55; P, 7.3; N, 3.3

<sup>a</sup> Two diastereoisomeric salts. <sup>b</sup> From propan-1-ol-pentane. <sup>c</sup> The yield in parentheses refers to addition of sulphur to the corresponding phosphite.

basic conditions. It was thus necessary to replace the chlorine atom with a better leaving group which would allow hydrolysis under neutral conditions. Since the imidazolyl group fulfils these conditions and since the last step in the synthesis of uridine 2',3'-cyclic phosphorothioate<sup>5</sup> was based on the hydrolysis of the corresponding thiophosphorylimidazole, we decided to

Neither the ring-opened product nor the sulphur-free acid was formed under the hydrolysis conditions.†

Another route to the thioacid (2c) and to its seleno-analogue (3) involved addition of sulphur and selenium to 4,4,5,5-tetramethyl-1,3,2-dioxaphospholan-2-one<sup>10</sup> in the presence of imidazole or dicyclohexylamine, resulting in the corresponding imidazolium or dicyclohexylammonium salt.

\* The thiophosphorylimidazole obtained from (1a) undergoes violent decomposition after removal of solvent.

† The formation of these products was observed by Eckstein<sup>5</sup> during the hydrolysis of the cyclic nucleoside thiophosphorylimidazoles.

<sup>6</sup> M. Mikołajczyk and H. M. Schiebel, *Angew. Chem. Internat. Edn.*, 1969, **8**, 511.

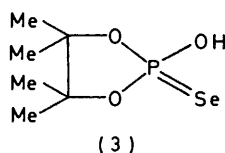
<sup>7</sup> R. S. Edmundson and A. J. Lambie, *J. Chem. Soc. (B)*, 1967, 977.

<sup>8</sup> N. J. Ziemiański and W. P. Kalaschnikow, *Zhur. obshchei Khim.*, 1967, **37**, 1141.

<sup>9</sup> R. S. Edmundson and A. J. Lambie, *J. Chem. Soc. (C)*, 1966, 1997.

<sup>10</sup> A. Zwierzak, *Canad. J. Chem.*, 1967, 2501.

The experimental results and some n.m.r. spectral data of the salts are summarised in Tables 1 and 2.



*Geometrical Isomerism in 2-Hydroxy-4-methyl-1,3,2-dioxaphospholan-2-thione (2b); Chemical Assignment of Stereochemistry.*—The compounds (2), containing two chiral centres in the molecule, would be expected to

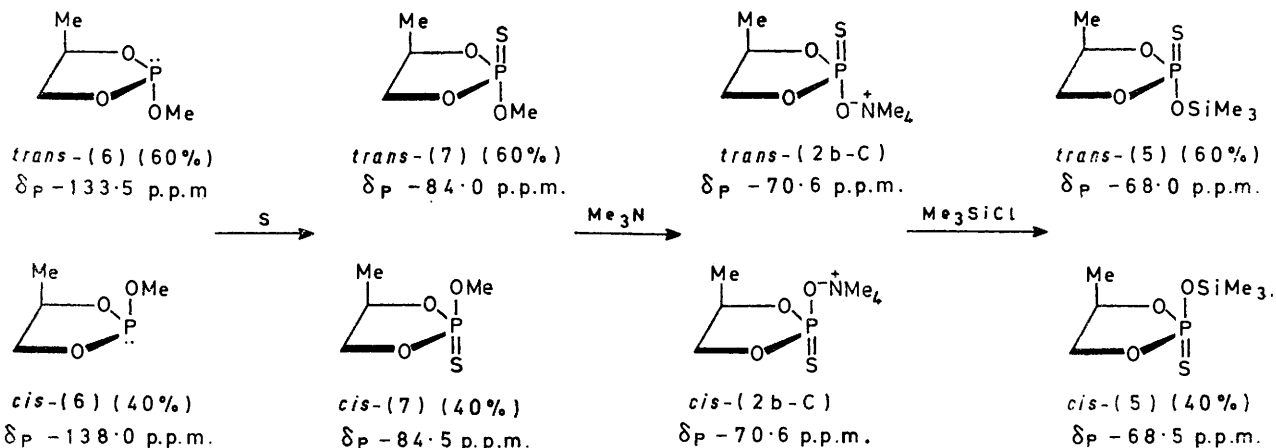
TABLE 2

N.m.r. data for imidazolium salts of 2-hydroxy-1,3,2-dioxaphospholan-2-thiones and -2-selenones [(2) and (3)]

Salt	$\delta_P$ (p.p.m.) <sup>a</sup>	$\delta_H$ <sup>b</sup>
(2a), imidazole	-71.5	4.38 (4 H, d), 7.63 (2 H, s), 8.9 (1 H, s)
(2b), imidazole	-71.25, -71.50	1.53 (3 H, d), 1.56 (3 H, d), 3.95-5.3 (3 H, m), 7.65 (2 H, s), 8.85 (1 H, s) ( $J_{CH_3,H}$ 6 Hz) <sup>c</sup>
(2c), imidazole	-64.0	1.4 (12 H, s), 7.53 (2 H, s), 8.75 (1 H, s) <sup>d</sup>
(3) imidazole	-53.3	1.4 (12 H, s), 7.53 (2 H, s), 8.8 (1 H, s) <sup>d</sup>

<sup>a</sup> Solvent H<sub>2</sub>O. <sup>b</sup> Solvent D<sub>2</sub>O. <sup>c</sup> Solvent CF<sub>3</sub>CO<sub>2</sub>H; mixture of diastereoisomers. <sup>d</sup> Magnetically non-equivalent methyl groups, owing to the prochiral nature of the phosphorus atom, are observed if the <sup>1</sup>H n.m.r. spectrum is run in Me<sub>2</sub>SO as solvent.

exist as a mixture of diastereoisomeric *cis*- and *trans*-forms. Thus the imidazolium salt (2b), prepared by the

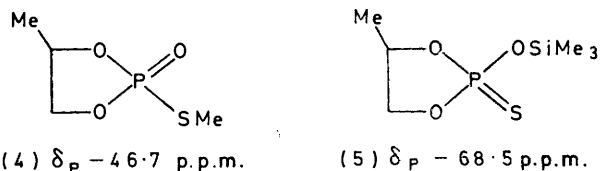


SCHEME 2

method described above, is a mixture of two diastereoisomeric salts, as evidenced by a broad m.p. and by analysis of its <sup>1</sup>H and <sup>31</sup>P n.m.r. spectra. The <sup>1</sup>H n.m.r. spectrum (100 MHz; D<sub>2</sub>O) exhibited two doublets of equal intensity at  $\delta$  1.40 and 1.41,\* corresponding to the methyl group in both diastereoisomers; accordingly in the <sup>31</sup>P{<sup>1</sup>H} n.m.r. spectrum two signals

\* Two diastereoisomeric imidazolium salts of (2b) may also be distinguished in the 60 MHz <sup>1</sup>H n.m.r. spectra (solvent trifluoroacetic acid) (see Table 2).

appeared at -71.25 and -71.50 p.p.m. By fractional crystallisation we were able to isolate one pure diastereoisomeric salt (2b-A), m.p. 121-123°,  $\delta_{Me}$  1.41,  $\delta_P$  -71.50 p.p.m. Since the differences in n.m.r. spectra between the two diastereoisomeric salts are small, the purity of the isomer isolated was further confirmed by its conversion into *S*-methyl and *O*-trimethylsilyl derivatives, (4) and (5), by treatment with



methyl iodide and trimethylsilyl chloride, respectively. Each compound was obtained as a pure diastereoisomer. However, in contrast to the configurationally stable (5), the *S*-methyl derivative (4) underwent slow epimerisation at phosphorus, resulting after a few days in a 1:1 mixture of diastereoisomeric esters (4),  $\delta_P$  -46.4 and -46.7 p.p.m.

An attempt to isolate the other diastereoisomeric imidazolium salt of (2b) in a pure state was only partly successful. Fractional crystallisation yielded the salt (2b-B), m.p. 77-82°, contaminated with 10% of the higher-melting isomer as determined by the <sup>1</sup>H n.m.r. spectrum.

In order to obtain further information concerning the geometry of the diastereoisomeric salts (2b-A) and (2b-B) we prepared the mixture of diastereoisomeric

tetramethylammonium salts of (2b) and their trimethylsilyl derivatives (5) in a stereospecific manner from the mixture of *cis*- and *trans*-2-methoxy-4-methyl-1,3,2-dioxaphospholans (6) (see Scheme 2). A large body of evidence<sup>11</sup> suggests that the isomer of (6) present in larger amounts (60%) has a *trans*-Me,OMe-relationship.

<sup>11</sup> D. Z. Denney, G. Y. Chen, and D. B. Denney, *J. Amer. Chem. Soc.*, 1969, **91**, 6838; R. H. Cox and M. G. Newton, *ibid.*, 1972, **94**, 4212; Han-Wan Ten and W. G. Bentrude, *Tetrahedron Letters*, 1975, 619.

Recently indirect support for this conclusion was provided<sup>12</sup> by an X-ray crystal structure determination of *trans*-2-methoxy-4,5-diphenyl-1,3,2-dioxaphospholan.

We found that addition of sulphur to the isomeric mixture of (6) (60% *trans* and 40% *cis*) affords a mixture of the corresponding 2-methoxy-4-methyl-1,3,2-dioxaphospholan-2-thiones (7) in the same ratio. Since this conversion is stereospecific and it undoubtedly proceeds with retention of configuration at phosphorus,<sup>13</sup> it is reasonable to assign the *trans*-geometry to the more abundant phosphorothioate (7),  $\delta_P$   $-84.0$  p.p.m., and the *cis*-configuration to the minor isomer,  $\delta_P$   $-84.5$  p.p.m. The diastereoisomeric phosphorothioates (7) were then treated with trimethylamine and the tetramethylammonium salt (2b-C) formed was in turn silylated with trimethylsilyl chloride to afford the trimethylsilyl ester (5) as a 60 : 40 mixture of diastereoisomers with  $\delta_P$   $-68.0$  and  $-68.5$  p.p.m., respectively.

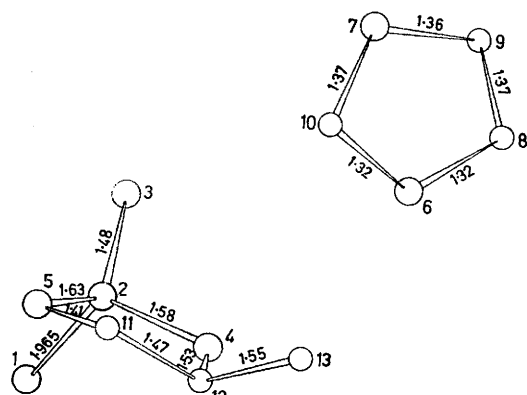


FIGURE 1 Conformation and bond lengths in the imidazolium salt (2b-A) of *r*-2-hydroxy-*c*-4-methyl-1,3,2-dioxaphospholan-2-thione

Since the configuration at phosphorus is unchanged during the demethylation as well as the silylation, the relationship between the ring methyl group and the exocyclic oxygen atom in the diastereoisomeric esters (5) is the same as that in the phosphorothioates (7). Therefore, the predominant isomer of (5),  $\delta_P$   $-68.0$  p.p.m., should have the *trans*-configuration and the *cis*-configuration should be assigned to the minor isomer. Consequently, the imidazolium salt (2b-A), which on silylation afforded *cis*-(5), should also have the *cis*-configuration and the imidazolium salt (2b-B) should have the *trans*-configuration.

Because the salt (2b-A) is crystalline and was obtained in a diastereoisomerically pure state, we determined its structure by X-ray analysis in order to confirm our assignments and to gain more detailed insight into the ring conformation.

<sup>12</sup> M. G. Newton and B. S. Campbell, *J. Amer. Chem. Soc.*, 1974, **96**, 7790.

<sup>13</sup> W. C. McEwen, *Topics Phosphorus Chem.*, 1965, **2**, 25.

<sup>14</sup> T. A. Steitz and W. N. Lipscomb, *J. Amer. Chem. Soc.*, 1965, **87**, 2488.

<sup>15</sup> H. Chiu and W. N. Lipscomb, *J. Amer. Chem. Soc.*, 1969, **91**, 4150.

<sup>16</sup> M. G. Newton, J. R. Cox, and J. A. Betrand, *J. Amer. Chem. Soc.*, 1966, **88**, 1503.

*Crystal Structure of the Imidazolium Salt (2b-A) of r*-2-Hydroxy-*c*-4-methyl-1,3,2-dioxaphospholan-2-thione.—The geometry of the molecule is shown in Figure 1. Bond lengths and angles are listed in Tables 3 and 4.

TABLE 3

Bond distances in Å (standard deviations in parentheses)

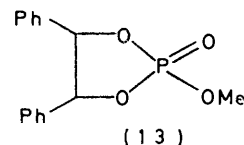
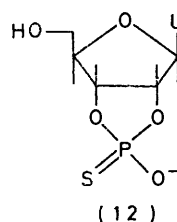
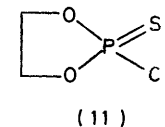
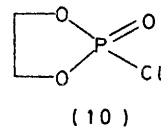
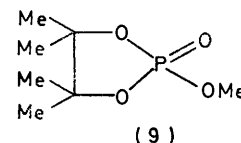
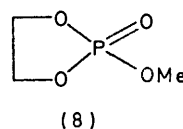
P(2)–S(1)	1.966(9)	C(12)–C(13)	1.554(28)
P(2)–O(3)	1.485(14)	N(6)–C(8)	1.311(25)
P(2)–O(4)	1.585(15)	N(6)–C(10)	1.315(25)
P(2)–O(5)	1.628(15)	C(7)–C(9)	1.391(20)
O(4)–C(12)	1.531(20)	C(7)–C(10)	1.342(21)
O(5)–C(11)	1.407(21)	C(8)–C(9)	1.364(28)
C(11)–C(12)	1.469(25)		

TABLE 4

Bond angles (°) (standard deviations in parentheses)

O(3)–P(2)–O(5)	111.2(7)	O(5)–P(2)–O(4)	97.5(9)
O(3)–P(2)–O(4)	107.2(7)	O(5)–C(11)–C(12)	107.4(11)
S(1)–P(2)–O(5)	109.0(5)	C(11)–C(12)–O(4)	106.8(10)
S(1)–P(2)–O(4)	114.5(5)	C(12)–O(4)–P(2)	109.6(9)
P(2)–O(5)–C(11)	112.2(9)		

Little information is available as to the structure and conformation of the phospholan ring. In all the studies published so far<sup>14–20</sup> the five-membered ring is described



as non-planar. It can adopt an envelope or a half-chair conformation. In Table 5 the most important geometric parameters of (2b-A) are compared with data for the related phospholans (8)–(13). A comparison of the bond lengths indicates that the C–C bond is slightly shortened and the corresponding C–O(4) and C–O(5) as well as the P–O(4) and P–O(5) bonds are not equivalent. This was also observed by Saenger and Eckstein<sup>19</sup> in the

<sup>17</sup> J. D. Lee, G. W. Goodacre, and S. C. Peake, *Naturwiss.*, 1970, **4**, 57, 195.

<sup>18</sup> W. A. Naumov, W. N. Siemashko, A. P. Zawialov, R. A. Czerkasov, and L. N. Grishyna, *Zhur. strukt. Khim.*, 1973, **14**, 787.

<sup>19</sup> W. Saenger and F. Eckstein, *J. Amer. Chem. Soc.*, 1970, **92**, 4712.

<sup>20</sup> D. Swank, Ch. N. Caughlan, F. Ramirez, and O. P. Madan, *J. Amer. Chem. Soc.*, 1967, **89**, 6503.

case of uridine 2',3'-cyclic phosphorothioate (12). These authors attributed it to steric interactions between the two rings, which does not apply in our case. Moreover, the effect of one methyl group on bond lengths should not be very important. It is likely that the observed ring distortion and bond shortening result from the considerable intermolecular forces.

The internal O-P-O bond angle ( $97.5^\circ \pm 0.9$ ) is very similar to the corresponding angle in other five-membered

shift of the electron cloud and some contribution of the mesomeric form of the monothioacid anion with the negative charge situated on the sulphur atom [ $\text{>P}(\text{:S})\cdot\text{O}^- \leftrightarrow \text{>P}(\text{:O})\cdot\text{S}^-$ ].

Dihedral angles between the plane O(4)-P-O(5) and the planes O(4)-C(11)-O(5) and O(4)-C(12)-O(5) are  $13.12^\circ$  and  $2.63^\circ$ , respectively. This indicates that the ring in its semi-chair conformation is folded similarly to the ring in compounds (9)–(11) (see Figure 2). The

TABLE 5  
Comparison of selected distances (Å) and dihedral angles ( $^\circ$ ) in some phospholans

	(2b-A)	(8)	(9)	(10)	(11)	(12)	(13)
C-C	1.47	1.56	1.59	1.547	1.525	1.55	1.551
C-O(4)(S)	1.53	1.42	1.49			1.50	1.470
C-O(5)(S)	1.41	1.44	1.50	1.49	1.88	1.41	1.449
P-S(O)	1.996	1.45	1.44	1.44	1.89	1.946	1.443
P-O(4)(S)	1.58	1.58	1.57	1.62	2.12	1.57	1.575
P-O(5)(S)	1.63	1.59	1.59			1.618	1.584
P-O(3)(Cl)	1.48	1.54	1.56	2.06	2.07	1.48	1.571
O(4)(S)-P-O(5)(S)	97.5	98.1	98.4	104.7	98.4	96.7	98.2
O(4)(S)-P-O(3)(Cl)	107.2	106.1	102.2			109.6	102.4
O(5)(S)-P-O(3)(Cl)	111.2	110.4	108.9	101.3	104.2	112.6	108.6
C-C-O(4)(S)	106.8	105.8	102.0			105.5	103.2
C-C-O(5)(S)	107.4	106.5	101.4	108.2	112.8	107.3	103.5
C-O(4)-P	109.6	114.4	112.3			113.4	111.8
C-O(5)-P	112.2	112.4	112.0	106.4	101.7	115.4	109.3
S=P-O(4)	114.5	115.3	119.4			112.6	117.5
S=P-O(5)	109.0	117.7	113.9	116.7	117.4	109.5	113.6

cyclic phosphorus esters: 2-methoxy-1,3,2-dioxaphospholan-2-one (8) ( $98.1^\circ$ <sup>15</sup>), 2-methoxy-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan-2-one (9) ( $98.4^\circ$ <sup>16</sup>), *trans*-2-methoxy-4,5-diphenyl-1,3,2-dioxaphospholan-2-one (13) ( $98.2^\circ$ <sup>12</sup>), and uridine 2',3'-cyclic phosphorothiate (12) ( $96.7^\circ$ <sup>19</sup>).

The three O(C)-P-O(C) angles in (2b-A) average  $105.3^\circ$ . In compounds (8) and (12) the corresponding values of  $104.9^\circ$  and  $106.3^\circ$ , respectively, were found. The sum of the three P-O bond lengths is 4.69 Å, in excellent agreement with the value (4.71 Å) observed by Steitz and Lipscomb<sup>14</sup> and that (4.67 Å) observed by Saenger and Eckstein.<sup>19</sup>

The elongation of the P=S bond to 1.965 Å [cf. 1.89 and 1.946 Å for compounds (11) and (12) (P=S double

angle between the C-C bond and its projection onto the O(4)-P-O(5) plane in (2b-A) is  $9.5^\circ$ , whereas in compounds (9)–(11) the corresponding values are 9.1, 14.5, and  $21.7^\circ$ , respectively.

The bond lengths in the imidazole ring are in accord with literature data<sup>22</sup> (within the limits of error). The position of the phospholan ring with respect to the imidazole ring makes possible the existence of a hydrogen bond (see Figure 3).

Finally, the ring methyl group in (2b-A) is confirmed to be *cis* with respect to the exocyclic oxygen atom.

#### EXPERIMENTAL

<sup>1</sup>H N.m.r. spectra were measured with a JEOL-JNM-C-60 HL instrument or a Varian 100 MHz spectrometer, with tetramethylsilane as internal standard. <sup>31</sup>P N.m.r. spectra were recorded with a JEOL-JNM-C-6 HL spectrometer at 24.3 MHz, with 85% phosphoric acid as external standard. A heteronuclear spin decoupler (INH-SD-HC) was used for precise <sup>31</sup>P chemical shift determination. Diastereoisomeric purities were determined from integrated <sup>1</sup>H and <sup>31</sup>P n.m.r. spectra. All solvents used were purified according to standard procedures.

*2-Chloro-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan-2-thione* (1c).—To a solution of 2-mercapto-4,4,5,5-tetramethyl-1,3,2-dioxaphospholan-2-thione<sup>9</sup> (10.6 g) in toluene (30 ml), a solution of phosphorus pentachloride (10.4 g) in toluene (30 ml) was added dropwise. The mixture was stirred at room temperature for 2 h and evaporated. The residue was crystallised from petroleum (b.p. 50–60°) below 0 °C to give the *chloro-derivative* (7.6 g, 70%), m.p.

<sup>22</sup> G. Will, *Kristallografiya*, 1963, **119**, 1; S. Garcia-Blanco and S. M. Carrera, *Anales real Soc. espan. Fis. Quim.*, 1958, **A54**, 75; G. Will, *Nature*, 1963, **198**, 575; S. Matinez-Carrera, *Acta Cryst.*, 1966, **20**, 783.

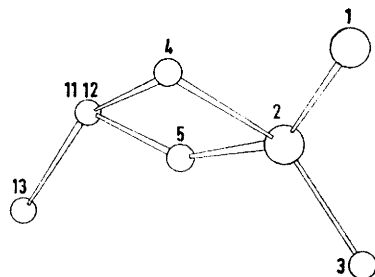


FIGURE 2 A view of *trans*-2-hydroxy-4-methyl-1,3,2-dioxaphospholan-2-thione (2b) down the 4,5- [C(11)-C(12)] bond in the five-membered ring

bond 1.91 Å<sup>21</sup>]) and the shortening of the P-O single bond (normal length 1.51 Å) to 1.485 Å may indicate a

<sup>21</sup> D. E. C. Cobridge, 'Phosphorus Chemistry,' vol. III, New York, 1966, pp. 211, 293.

62–64° (Found: C, 33.2; H, 5.55; P, 13.95; S, 15.0.  $C_6H_{12}ClO_2PS$  requires C, 33.55; H, 5.65; P, 14.45; S, 14.95%).

**General Procedure for Synthesis of Imidazolium Salts of 2-Hydroxy-1,3,2-dioxaphospholan-2-thiones (2).**—To a solution of the chloride (1) (0.05 mol) in tetrahydrofuran (50 ml), a solution of imidazole (6.8 g, 0.1 mol) in tetrahydrofuran (50 ml) was added dropwise with stirring. After 2 h the precipitated imidazolium hydrochloride was filtered off and the organic solution was treated with water (20 ml). The solvents were removed under reduced pressure and the residue was crystallised from propan-1-ol-ether to afford analytically pure *imidazolium salt*. Physical properties, yields, and some n.m.r. data are summarised in Tables 1 and 2.

**Addition of Sulphur and Selenium to 4,4,5,5-Tetramethyl-1,3,2-dioxaphospholan-2-one.**—To a mixture of the cyclic

amine (2 g) in benzene (10 ml) was added. After 48 h the precipitated *ammonium salt* was filtered off, washed with benzene, and crystallised from n-propanol-ether; yield 1.8 g (80%), m.p. 177–180° (Found: C, 37.05; H, 7.9; P, 13.6; N, 6.1.  $C_7H_{10}NO_3PS$  requires C, 37.0; H, 7.95; P, 13.65; N, 6.15%);  $\delta_H$  ( $D_2O$ ) 1.35 (3 H, d,  $J_{CH_3,H}$  6 Hz), 3.18 (12 H, s), and 3.6–4.7 (3 H, m);  $\delta_P$  ( $H_2O$ ) –70.6 p.p.m.

**4-Methyl-2-trimethylsilyloxy-1,3,2-dioxaphospholan-2-thione (5).**—A solution of the tetramethylammonium salt (2b-C) (2.27 g, 0.01 mol) in chloroform (20 ml) was treated with chloro(trimethyl)silane (1.08 g, 0.01 mol). The mixture was heated for 15 min at 50 °C and, after cooling, tetramethylammonium chloride was filtered off. Evaporation, and distillation of the residue gave a pure *product* (5) (1.8 g, 77%), b.p. 82–83° at 0.05 mmHg,  $n_D^{25}$  1.4650 (Found: C, 31.95; H, 6.75; P, 14.5.  $C_6H_{15}O_3PSSi$  requires C, 31.85; H, 6.65; P, 13.7%) as a mixture of

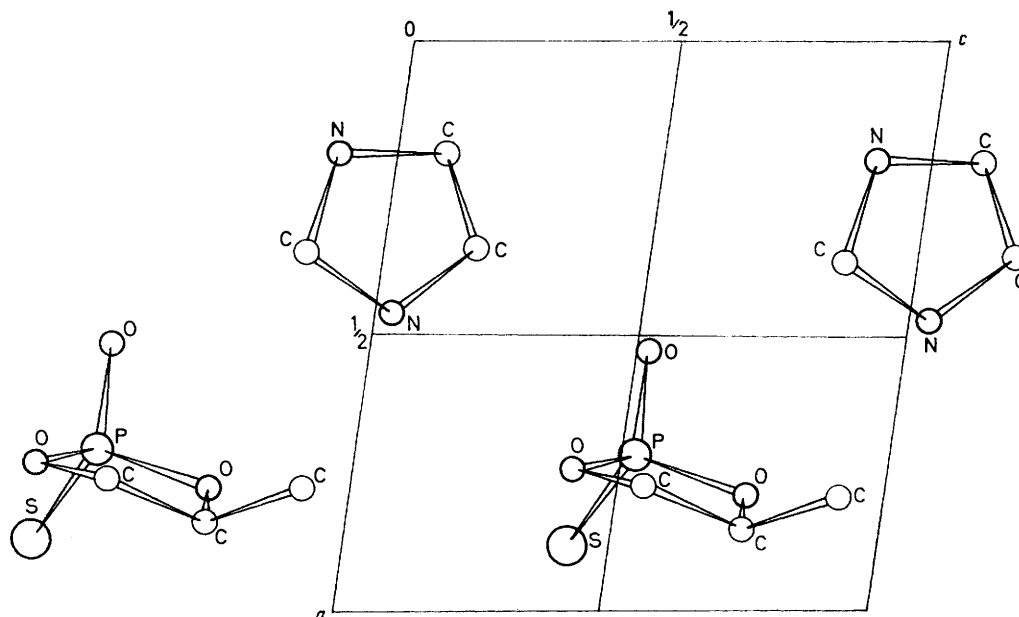


FIGURE 3 Stereoscopic packing diagram of one unit cell of (2b-A)

phosphite (1.64 g, 0.01 mol) and imidazole (0.68 g, 0.01 mol) or dicyclohexylamine (1.82 g, 0.01 mol) dissolved in benzene (15 ml), sulphur (0.3 g, 0.01 mol) or selenium (0.79 g, 0.01 mol) was added. The precipitated imidazolium or dicyclohexylammonium salt of (2c) or (3) was filtered off and recrystallised from n-propanol-ether (see Table 1).

**2-Methoxy-4-methyl-1,3,2-dioxaphospholan-2-thione (7).**—To the phosphite (6) (1.4 g, 0.01 mol; 60% *trans* and 40% *cis*), sulphur (0.32 g, 0.01 mol) was slowly added at 30–40 °C. After 4 h the mixture was heated at 50 °C under high vacuum to remove unchanged phosphite (6). The *product* (1.7 g, 99%;  $n_D^{25}$  1.4810) was a mixture of *trans*- and *cis*-isomers in the ratio 60 : 40 as determined by n.m.r. (Found: C, 28.65; H, 5.2; P, 18.25.  $C_4H_9O_3PS$  requires C, 28.6; H, 5.35; P, 18.45%); *trans*-(7)  $\delta_H$  ( $CCl_4$ ) 1.45 (3 H, d,  $J_{CH_3,H}$  6 Hz), 3.75 (3 H, d,  $J_{CH_2,P}$  15 Hz), and 3.7–5.2 (3 H, m);  $\delta_P$  (neat) –84.0 p.p.m.; *cis*-(7)  $\delta_H$  1.44 (3 H, d,  $J_{CH_3,H}$  6 Hz), 3.75 (3 H, d,  $J_{CH_2,O,P}$  15 Hz), and 3.7–5.2 (3 H, m);  $\delta_P$  –84.5 p.p.m.

**Tetramethylammonium Salt (2b-C) of 2-Hydroxy-4-methyl-1,3,2-dioxaphospholan-2-thione.**—To a solution of (7) (1.68 g, 0.01 mol) prepared as above in benzene (10 ml), trimethyl-

*trans*- and *cis*-isomers in the ratio 60 : 40 (n.m.r.); *trans*-(5)  $\delta_H$  ( $CCl_4$ ) 0.35 (9 H, s), 1.46 (3 H, d,  $J_{CH_3,H}$  6 Hz), and 3.77–4.9 (3 H, m);  $\delta_P$  (neat) –68.0 p.p.m.; *cis*-(5)  $\delta_H$  0.35 (9 H, s), 1.44 (3 H, d,  $J_{CH_3,H}$  6 Hz), and 3.77–4.99 (3 H, m);  $\delta_P$  –68.5 p.p.m. From the imidazolium salt (2b-A) (2.22 g, 0.010 mol), only the pure *cis*-isomer of (5) was obtained,  $\delta_P$  –68.5 p.p.m.

**4-Methyl-2-methylthio-1,3,2-dioxaphospholan-2-one (4).**—The reaction of the tetramethylammonium salt (2b-C) (2.27 g, 0.01 mol) with methyl iodide (4.25 g, 0.03 mol) in chloroform (20 ml) gave, after the usual work-up, the *ester* (4) as a mixture of diastereoisomers (1.0 g, 59%), b.p. 91–92° at 0.05 mmHg,  $n_D^{25}$  1.4902 (Found: C, 29.0; H, 5.5; P, 18.35.  $C_4H_9O_3PS$  requires C, 28.6; H, 5.35; P, 18.45%); *trans*-(4)  $\delta_H$  ( $CDCl_3$ ) 1.45 (3 H, d,  $J_{CH_3,H}$  6 Hz), 2.35 (3 H, d,  $J_{CH_3,S,P}$  17 Hz), and 3.69–5.10 (3 H, m);  $\delta_P$  (neat) –46.5 p.p.m.; *cis*-(4)  $\delta_H$  1.50 (3 H, d,  $J_{CH_3,H}$  6 Hz), 2.35 (3 H, d,  $J_{CH_3,S,P}$  17 Hz), and 3.69–5.10 (3 H, m);  $\delta_P$  –46.7 p.p.m.

The salt (2b-A) on methylation gave *cis*(4),  $\delta_P$  –46.7 p.p.m., which undergoes epimerisation.

**X-Ray Structure Determination of the Imidazolium Salt**

of *r*-2-Hydroxy-*c*-4-methyl-1,3,2-dioxaphospholan-2-thione (2b).—Approximate values of the unit cell parameters were determined from oscillation and rotation photographs by using copper radiation. Refinement of parameters was performed by the least squares method on the basis of 12 high angle reflections, measured with an automatic four-circle Hilger-Watts diffractometer controlled by a PDP-81 computer. Molybdenum radiation with graphite monochromator was used. These reflections were scanned by using the Peak Finder program<sup>23</sup> and parameters were calculated by use of Dobler's program.<sup>24</sup>

**Crystal Data.**—C<sub>6</sub>H<sub>11</sub>N<sub>2</sub>O<sub>3</sub>PS, *M* = 222.21. Triclinic, *a* = 7.818(5), *b* = 9.736(5), *c* = 6.958(5) Å, *U* = 507.27 Å,  $\alpha = 76.42(20)$ ,  $\beta = 98.18(20)$ ,  $\gamma = 97.23(20)^\circ$ , *D<sub>m</sub>* = 1.467, *Z* = 2, *D<sub>c</sub>* = 1.463, *F*(000) = 232. Space group *P* $\bar{1}$ . Mo-*K<sub>α</sub>* radiation.

The statistics of the normalized structure factors *E* and a negative piezo-effect test indicated the presence of a symmetry centre and hence the space group was defined as *P* $\bar{1}$ . The crystal employed had the dimensions 0.20 × 0.25 × 0.7 mm (elongated along the *c* axis). The intensities of the reflections were measured to a maximum  $\theta \leq 25^\circ$  by using the  $\theta$ - $2\theta$  scan technique according to the Watson program.<sup>25</sup> The number of independent reflections collected was about 1 600. The intensities were converted into structure amplitudes with no corrections for absorption in the crystal since the compound does not contain a heavy atom and the size of the crystal is insignificant. Only 1 247 reflections, for which  $F^2 \geq 5\sigma(F^2_{\min.})$ , were taken into consideration in further structure refinement.

In the first stage of the preparation of the structure model the direct methods of Sayre, Zacharaisen, and Cochran were utilized. Triple products were formed with a probability  $\geq 0.80$  by using 177 normalized amplitudes with  $|E| \geq 1.6$ . The basic group consisted of 7 reflections. All possible combinations of signs were subordinated to these seven reflections for which the *E* values were very large ( $2^7 = 128$  combinations). Each combination was used independently to define the signs of all normalized amplitudes. The estimations of three best combination of signs are as follows:<sup>26</sup>

$$\begin{array}{lll} N_1 = 31 & Q_1 = 174 & R_1 = 0.994 \\ N_2 = 23 & Q_2 = 174 & R_2 = 0.920 \\ N_3 = 29 & Q_3 = 174 & R_3 = 0.949 \end{array}$$

† For details see Notice to Authors No. 7, *J.C.S. Perkin I*, 1975, Index issue.

<sup>23</sup> Hilger and Watts, System Bulletin, N 3, September 1970.

<sup>24</sup> M. Dobler and B. Dneer, Least Squares Orientation Matrix Program, Zurich, 1968.

where *N* is the solution number, *Q* is the number of defined signs, and  $R = \Sigma^+ |E_h \cdot E_{h'} \cdot E_{h''}| / |\Sigma^+ |E_h \cdot E_{h'} \cdot E_{h''}|$  [ $\Sigma^+$  is the sum of triple products for which  $S(E_h) \cdot S(E_{h'}) \cdot S(E_{h''}) > 0$ ; in the denominator the sum of all triple products is given<sup>26</sup>].

The best *E* synthesis gives the model for the whole molecule with *R* 30.4%. Two subsequent approximations of the electron density map allowed further refinement of the atomic positions yielding *R* = 27.2%. The positions of all atoms were refined by least squares, and isotropic temperature factors were refined as the next stage. At this stage all weak reflections with  $F^2 \leq 5\sigma(F^2)$  were discarded. Further structure refinement was achieved by the full-matrix least squares method with weight according to Cruickshank.<sup>27</sup> Atomic co-ordinates and temperature factors are given in Table 6. Observed and calculated structure factors are available as Supplementary Publication No. SUP 21588 (5 pp.).†

TABLE 6

Atomic parameters (standard deviations in parentheses)

	<i>B</i> /Å <sup>2</sup>	<i>x</i>	<i>y</i>	<i>z</i>
S(1)	5.52(8)	0.360(4)	0.153(4)	0.425(5)
P(2)	3.76(6)	0.208(3)	0.259(3)	0.526(4)
O(3)	5.13(19)	0.022(9)	0.204(10)	0.522(10)
O(4)	5.90(21)	0.273(10)	0.281(11)	0.745(11)
O(5)	6.72(25)	0.231(11)	0.425(12)	0.411(13)
N(6)	6.53(30)	-0.035(14)	0.161(14)	1.031(15)
N(7)	7.00(32)	-0.299(15)	0.139(15)	0.889(16)
C(8)	3.28(21)	-0.137(11)	0.138(11)	1.172(12)
C(9)	6.08(34)	-0.306(17)	0.124(17)	1.092(18)
C(10)	2.79(18)	-0.131(11)	0.158(11)	0.860(11)
C(11)	7.18(42)	0.255(20)	0.517(20)	0.544(21)
C(12)	5.05(28)	0.330(14)	0.438(14)	0.738(15)
C(13)	8.68(51)	0.266(22)	0.478(23)	0.917(25)

The final divergence factor (*R*) with no allowances for hydrogen atoms was 16.2%. Owing to the pronounced mosaicity of the crystal and its instability the accuracy of the experimental data obtained is not precise enough for a more elaborate refinement. Therefore, no further refinements were carried out, especially in view of the fact that the stereochemical problem had been solved.

[5/1407 Received, 17th July, 1975]

<sup>25</sup> H. C. Watson, *Nature*, 1970, **225**, 806.

<sup>26</sup> All calculations were made according to the program prepared by B. L. Tarnopolski, W. I. Andrianov and Z. S. Safina, Institute of Chemical Physics of the Academy of Sciences (W. J. Andrianov, B. L. Tarnopolski, and R. Shibaeva, *Zhur. struki. Khim.*, 1969, **10**, 116).

<sup>27</sup> D. W. J. Cruickshank, in 'Computing Methods and Phase Problems in X-Ray Crystal Analysis,' Paper 6, Pergamon, Oxford, 1961.