Geometry and Conformation of Crystalline Forms of β-Naphthoxy-Substituted 2-Thio-1,3,2-oxathiaphospholanes and 2-Thio-1,3,2-dithiaphospholanes

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ABSTRACT

Three compounds (1, 2, and 3) containing 1,3,2-oxathiaphospholane and 1,3,2-dithiaphospholane rings were subjected to structural studies by the X-ray method. Compounds 1 and 3 attain a half-chair conformation, whereas, for compound 2, an envelope conformation of the five-membered heterocyclic ring was found in the solid state. For all three compounds, a site occupation of some structural elements in a unit cell was observed.

INTRODUCTION

The phosphorothioate (Oligo-S) and phosphorodithioate (Oligo-S₂) analogues of oligonucleotides have recently drawn considerable attention as potent antisense inhibitors of expression of "unwanted" genes by virtue of their Watson–Crick hybridization properties combined with resistance to degradation by cellular nucleases [1]. In addition to numerous, more or less successful, approaches to the synthesis of Oligo-S and Oligo-S₂, the "thio-phospholane" method has recently been introduced by Stec et al. [2–5], involving the formation of a modified internucleotide bond by reaction of the base-activated 5'-OH component with, respectively, the appropriately protected nucleoside 3'-O-(2-thio-1,3,2-oxathiaphospholanes) (4) [2,3] or the nucleoside 3'-O-(2-thio-1,3,2-dithiaphospholanes) (5) [4,5]. The "oxathiaphospholane" route, by using diastereoisomerically pure 4, has allowed us, for the first time, to synthesize Oligo-S in a stereocontrolled manner, one possessing a predetermined absolute configuration at each P-chiral phosphorus center [2,3]. Recently introduced, appropriately protected nucleoside 3'-O-(2-thio-4,4-dimethyl-1,3,2-oxathiaphospholanes) (6) were found to be more easily separable into P-chiral diastereoisomers, thus being more efficient precursors of stereoregular Oligo-S [6]. The "dithiaphospholane" route has allowed us to effect an efficient synthesis of Oligo-S₂ [4,5] showing lower phosphoromonothioate contamination than found in oligo (nucleoside phosphorodithioates) obtained by alternative methods. An analogous approach has recently been applied for the synthesis of nucleoside-5'-O-(1,1-dithiotriphosphates) [7] and phosphorodithioate analogues of phospholipids [8].

The successful application of thiophospholane derivatives as reactive precursors of the above mentioned biophosphate analogues has raised in-
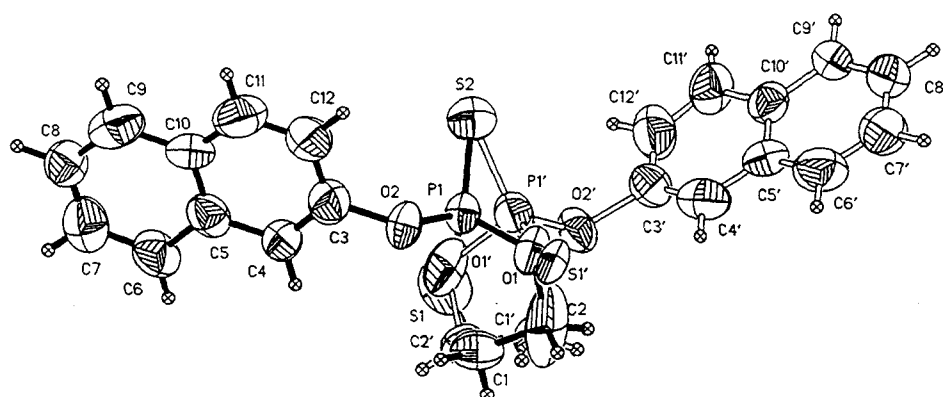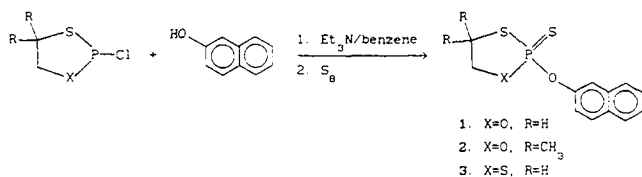

FIGURE 1 Thermal ellipsoidal plot of the asymmetric part of the unit cell of 1 with atom numbering scheme. Atoms from molecules with greater site-occupation factors are connected by full lines, and atoms with smaller occupation factors (primed) are connected by open lines.

SCHEME 1

terest in their molecular geometry and, in particular, in the conformation of oxathia- and dithiaphospholane rings. The knowledge of molecular structure of these compounds should give better insight into the molecular basis of their reactivity and, in particular, into the process of opening the five-membered heterocyclic ring accompanying their reaction with nucleophiles. Unfortunately, all attempts to crystallize nucleoside derivatives 4, 5, and 6 failed, and all reported compounds possessing either a oxathiaphospholane [9,10] or a dithia-
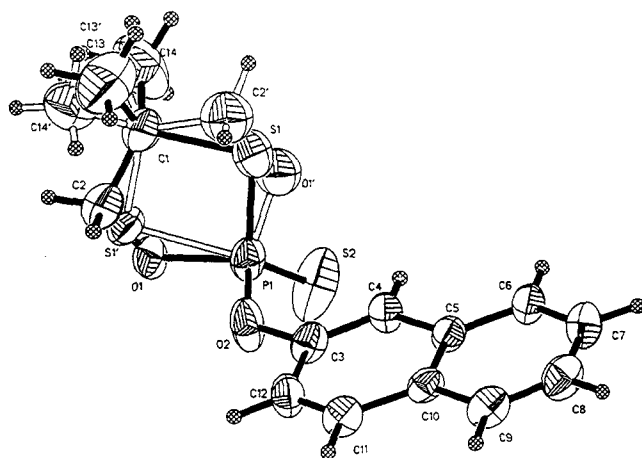

FIGURE 2 Thermal ellipsoidal plot of the molecule of 2 with atom numbering scheme. Atoms with greater site-occupation factors are connected by full lines, and atoms with smaller occupation factors (primed) are connected by open lines.

phospholane [11–15] ring, for which X-ray studies were performed, were rather distant analogues of 4–6. 2-Phenoxy-2-thiono-1,3,2-dithiaphospholane (7) was studied by 100 MHz ^{1}H NMR spectroscopy, and therefore only limited data regarding its conformation in solution were available [16]. Because of this, we decided to synthesize crystalline analogues of 4–6 and to perform studies of their crystal and molecular structures by the X-ray method. We have found that good candidates were the corresponding β-naphthoxy derivatives 1–3.

RESULTS AND DISCUSSION

2-(β-Naphthoxy)-2-thio-1, 3, 2-oxathiaphospholane (1), 2-(β-naphthoxy)-2-thio-4,4-dimethyl-1,3,2-oxathiaphospholane (2), and 2-(β-naphthoxy)-2-thio-1,3,2-dithiaphospholane (3) were synthesized in benzene solution from the corresponding phosphorochloridites and β-naphthol in the presence of triethylamine as a hydrogen chloride acceptor (Scheme 1). The intermediate P^{III} derivative was sulfurized with elemental sulfur. The addition of sulfur to the more sterically hindered 4,4-dimethyl derivative required heating for 2 hours in refluxing benzene. The crude compounds 1–3 were purified by flash chromatography on silica gel and then crystallized from benzene-hexane. Their purity and identity were confirmed by elemental analysis, TLC, ^{1}H and ^{31}P NMR, and mass spectrometry.

Compounds 1 and 3 crystallize in the monoclinic system, space group Cc, whereas compound 2 crystallizes in the orthorhombic system, space group $P2_12_12_1$. The X-ray analysis and crystallographic calculations allow us to conclude that, for compounds 1–3 in the crystalline form, a site occupation of some structural elements in a unit cell occurs. That phenomenon occurred in all three independent X-ray diffraction experiments performed for each of the structures (1, 2, and 3) on crystals obtained from the separate crystallizations. The site-occupation of some atoms in molecules containing the cyclic or acyclic –S(–O)P(=S)O– system was also observed for

FIGURE 3 Thermal ellipsoidal plot of the asymmetric part of the unit cell of **3** with atom numbering scheme. Atoms from molecules with greater site-occupation factors are connected by full lines, and atoms with smaller occupation factors (primed) are connected by open lines.
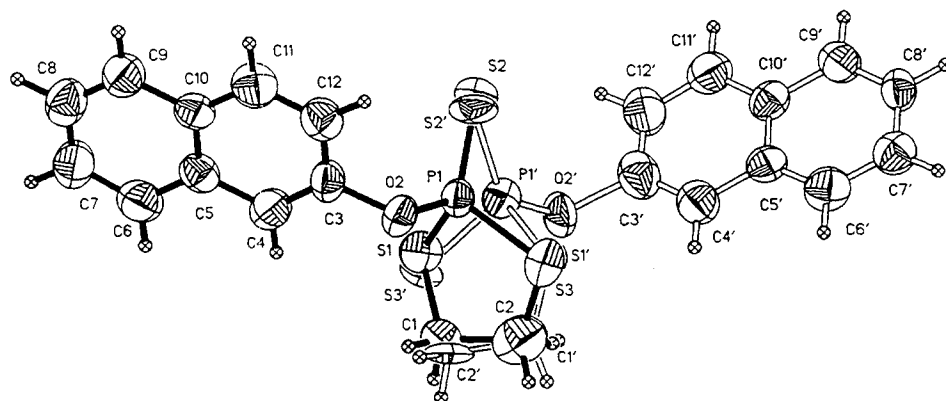
compounds possessing either ionic or covalent structures [17a–e]. Similar effects have been observed in our independent X-ray studies of the crystal and molecular structures of 2-thio-1,3,2-oxathia-and 2-thio-1,3,2-dithiaphospholane derivatives of cholesterol [18].

Figures 1, 2 and 3 show the molecular structure of **1**, **2**, and **3**, respectively, with their atom numbering schemes. The site occupation in the unit cells is represented in the following manner: atoms with greater site-occupation factors are connected by full lines, whereas atoms with smaller occupation factors (primed) are indicated by open lines. Tables 1–3 present the atom coordinates with

values of site-occupation factors for the corresponding atoms.

The naphthyl rings C3-C12 and C3'-C12' are in the unit cells of compounds **1** and **3** symmetrical (symmetry X − 1, 1 − Y, and Z − 0.5), but this symmetry could not be applied to the heterocyclic ring with exocyclic sulfur S2 and oxygen O2 and could not be applied, in detail, to respective atom names (nonprimed and primed) of naphthyl rings. The details are explained in Tables 1 and 3, respectively, for structures **1** and **3**, where the coordinates of C3 atom of naphthyl ring (with larger SOF) symmetrically correspond with the atom C8' of "primed" naphthyl ring (with smaller SOF).

TABLE 1 Atomic Coordinates (×10⁴), Equivalent Isotropic Displacement Coefficients (Å² × 10³), and Occupation Factors (%) for **1**

Atom		x	y	z	U (eq)	SOF	(%)
S2		3839ᵃ	4268(2)	2552ᵃ	103(1)	100.0	
P1		4063(6)	6098(3)	2979(4)	53(1)	67.2	
O2		4790(10)	6333(9)	4060(7)	63(2)	67.2	
S1		5166(8)	7225(8)	2097(5)	101(2)	67.2	
O1		2656(13)	7038(15)	2981(11)	67(4)	67.2	
C1		4364(19)	8642(14)	2600(12)	76(5)	67.2	
C2		2763(19)	8416(15)	2606(15)	151(9)	67.2	
P1'		3450(10)	6116(8)	2085(6)	71(2)	32.8	
O2'		2716(20)	6419(18)	1014(13)	72(5)	32.8	
S1'		2281(12)	7306(12)	2884(8)	57(2)	32.8	
O1'		4938(19)	6926(23)	2380(22)	86(8)	32.8	
C1'		3236(30)	8469(25)	2233(26)	81(9)	32.8	
C2'		4838(29)	8403(22)	2275(25)	64(8)	32.8	
C3	(C8')	6173(12)	5707(8)	4476(8)	79(3)	67.2	(32.8)
C4	(C9')	7433(11)	6222(9)	4317(8)	75(2)	67.2	(32.8)
C5	(C10')	8782(10)	5567(8)	4714(8)	70(2)	67.2	(32.8)
C6	(C11')	10135(11)	6070(12)	4549(9)	85(3)	67.2	(32.8)
C7	(C12')	11326(13)	5366(12)	4979(11)	98(4)	67.2	(32.8)
C8	(C3')	11271(12)	4265(9)	5516(8)	74(3)	67.2	(32.8)
C9	(C4')	9981(13)	3776(10)	5700(8)	90(3)	67.2	(32.8)
C10	(C5')	8686(11)	4415(8)	5280(7)	65(3)	67.2	(32.8)
C11	(C6')	7374(14)	3965(11)	5458(10)	106(4)	67.2	(32.8)
C12	(C7')	6101(13)	4566(9)	5075(10)	87(3)	67.2	(32.8)

ᵃCoordinates x and z were fixed to set the origin.

TABLE 2 Atomic Coordinates ($\times 10^4$), Equivalent Isotropic Displacement Coefficients ($\text{Å}^2 \times 10^3$), and Occupation Factors (%) When Not 100% (for **2**)

Atom	x	y	z	U (eq)	SOF (%)
P1	8336(3)	6565(2)	885(1)	46(1)	
S1	7839(7)	9216(5)	1071(1)	71(1)	76.1
S1'	6569(16)	7468(8)	400(2)	58(3)	23.9
S2	11012(4)	5479(5)	854(1)	90(1)	
O1	7192(13)	6606(12)	442(2)	49(2)	76.1
O1'	8754(57)	8625(18)	1052(10)	88(12)	23.9
O2	6690(9)	5405(8)	1145(1)	64(1)	
C1	6494(13)	9815(8)	583(2)	59(2)	
C2	5644(23)	8157(19)	412(4)	61(3)	76.1
C2'	7115(73)	10045(65)	1028(6)	91(15)	23.9
C3	6683(11)	5114(8)	1574(2)	43(1)	
C4	8277(10)	5600(8)	1825(2)	40(1)	
C5	8141(10)	5281(7)	2257(2)	38(1)	
C6	9746(10)	5779(9)	2533(2)	42(1)	
C7	9546(11)	5448(9)	2950(2)	50(2)	
C8	7739(12)	4635(9)	3103(2)	54(2)	
C9	6166(12)	4127(9)	2853(2)	48(1)	
C10	6293(9)	4470(7)	2420(2)	37(1)	
C11	4682(10)	3967(9)	2140(2)	43(1)	
C12	4879(11)	4283(10)	1727(2)	47(1)	
C13	4736(30)	11164(25)	696(6)	97(5)	76.1
C13'	7821(40)	10783(37)	245(7)	28(6)	23.9
C14	8153(26)	10839(30)	324(4)	110(6)	76.1
C14'	4248(42)	10545(92)	503(18)	125(22)	23.9

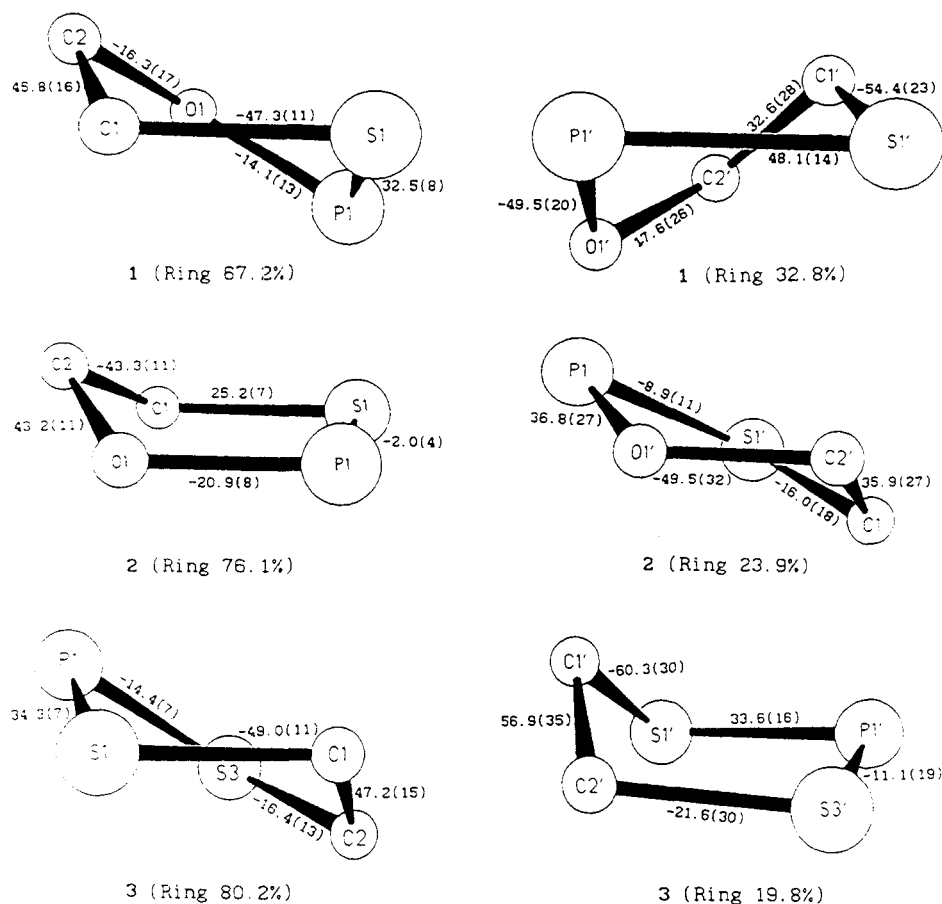Similarly, atom C4 (larger SOF) corresponds to C9' (smaller SOF), etc.

The obtained data allow us to draw interesting conclusions regarding the solid-state conformation and geometry of the five-membered heterocyclic rings. In compound **1**, the half-chair conformation of the oxathiaphospholane ring occurs for ring positions with larger, as well as for those with smaller, occupation factors. The other compounds adopt the following conformations for greater and less occupied positions: compound **2**—envelope and half-chair, compound **3**—half-chair and envelope. The results of detailed calculations of all asymmetry parameters are listed in Table H (given to the deposit agency). Figure 4 shows the conformation of five-membered rings (in both greater and less occupied positions) for compounds **1–3**, with torsion angles and asymmetry parameters (full tables were given to the deposit agency).

The exocyclic (double-bonded) sulfur atom is situated pseudoequatorially with regard to the five-membered ring in all three compounds for positions with a smaller, as well as those with a larger, occupation factors. The dihedral angles between least-squares planes passing through five atoms of the heterocyclic ring and naphthyl ring planes in **1**, **2**, and **3** are 34.9(3)°, 81.3(3)°, and 29.2(3)°, respectively. Thus, the presence of two methyl groups in position 4 of the heterocyclic ring in **2** has not only changed the conformation of the ring from half-

TABLE 3 Atomic Coordinates ($\times 10^4$), Equivalent Isotropic Displacement Coefficients ($\text{Å}^2 \times 10^3$), and Occupation Factors (%), for **3**

Atom		x	y	z	U (eq)	SOF (%)
S2		476[a]	−775(5)	4346[a]	87(2)	80.2
S1		1878(9)	2144(5)	3869(6)	58(1)	80.2
S3		−1054(10)	2326(7)	4734(6)	61(1)	80.2
P1		734(8)	1126(2)	4734(5)	46(1)	80.2
O2		1516(10)	1413(6)	5793(6)	53(1)	80.2
C1		1313(14)	3732(11)	4258(14)	68(3)	80.2
C2		−311(14)	3750(14)	4231(15)	90(5)	80.2
S2'		479(40)	−513(13)	4487(16)	72(4)	19.8
P1'		214(12)	1163(9)	3784(8)	51(2)	19.8
O2'		−569(28)	1504(27)	2718(18)	63(6)	19.8
S1'		−1066(23)	2266(22)	4518(13)	41(3)	19.8
S3'		1891(23)	2506(19)	3828(20)	59(3)	19.8
C1'		−453(35)	3768(33)	4030(34)	24(6)	19.8
C2'		1165(35)	3994(38)	4260(42)	75(18)	19.8
C3	(C8')	2859(10)	748(7)	6208(6)	55(2)	80.2 (19.8)
C4	(C9')	4137(11)	1260(9)	6068(7)	63(2)	80.2 (19.8)
C5	(C10')	5477(11)	564(7)	6471(7)	56(2)	80.2 (19.8)
C6	(C11')	6802(12)	1072(9)	6342(7)	71(2)	80.2 (19.8)
C7	(C12')	8024(12)	371(10)	6735(8)	75(2)	80.2 (19.8)
C8	(C3')	7940(12)	−797(9)	7264(7)	73(2)	80.2 (19.8)
C9	(C4')	6667(12)	−1300(10)	7398(7)	68(2)	80.2 (19.8)
C10	(C5')	5352(11)	−605(7)	6986(6)	53(2)	80.2 (19.8)
C11	(C6')	4000(12)	−1069(10)	7127(7)	71(2)	80.2 (19.8)
C12	(C7')	2740(12)	−416(8)	6742(7)	67(2)	80.2 (19.8)

[a]Coordinates x and z were fixed to set the origin.

FIGURE 4 Conformation of five-membered rings (in both greater and less occupied positions) for compounds **1–3**, with torsion angles and asymmetry parameters.

1 (Ring 67.2%)

1 (Ring 32.8%)

2 (Ring 76.1%)

2 (Ring 23.9%)

3 (Ring 80.2%)

3 (Ring 19.8%)

ASYMMETRY PARAMETERS

1: ΔCs(C1)	11.5(15)	ΔCs(S1')	12.8(20)
ΔC2(C1-S1)	9.5(15)	ΔC2(S1'-P1')	11.2(20)
2: ΔCs(C2)	3.0(10)	ΔCs(C2')	17.6(20)
ΔC2(C2-C1)	18.5(10)	ΔC2(O1'-C2')	5.1(20)
3: ΔCs(C1)	12.7(15)	ΔCs(C1')	8.8(20)
ΔC2(C1-S1)	9.2(15)	ΔC2(C1'-S1')	18.1(20)

chair into envelope, but has also made the naphthyl ring almost perpendicular to the heterocyclic oxathiaphospholane ring.

Table 4 contains the collection of bond lengths and bond angles of compounds **1–3**, including data only for atoms with larger site-occupation factors, and their comparison with literature data [11,12,22]. However, such comparison focused on a geometry of the 1,3,2-dithiaphospholane ring may only have a limited validity, since it is well known that bond lengths and angles in this type of ring are strongly influenced by the nature of substituents at the phosphorus atom. In this respect, two sets of literature data were chosen [11,12] describing the structure of 1,3,2-dithiaphospholanes substituted at phosphorus with groups or atoms of different size and electronegativity, e.g., the chlorine [11] and the phenyl group [12], as opposed to the β-naphthoxy group in **3**.

Comparing bond lengths obtained for com-

pound **3** with those obtained for **1** and **2** and using published data [11,12], one can conclude that existing differences may result from site-occupation and from the influence of other substituents attached to or present within the heterocyclic ring. On analysis of valence angles of five-membered heterocyclic oxathia- or dithiaphospholane rings in **1–3**, however, it is difficult to overlook the fact that at least one endocyclic valence angle at the sulfur atom is considerably smaller than the analogous angle at phosphorus. This phenomenon is also observed in compounds containing six-membered oxathia- and dithiaphosphorinane rings [19a–d]. It probably reflects the higher reactivity of this particular sulfur atom.

In the molecules of compounds **1–3**, no typical hydrogen bonds are observed. The shortest hydrogen contacts are the following:

H12···O2 = 2.74(4) Å with angle C1–H12···O2 102(3)° (**1**, intramolecular)

TABLE 4 Bond Lengths and Valence Angles in Examined Structures **1**, **2**, and **3**, Including Data Only for Atoms with Larger (or 100%) Site-Occupation Factors

			Compound **1** (SOF, 67.2%)	Compound **2** (SOF, 76.1%)	Compound **3** (SOF 80.2%)	Literature [22] (average)
P1		S1	2.046(9)	2.038(4)	2.046(11)	2.072
P1		O1	1.613(14)	1.610(7)	2.056(11)[a]	2.069[a]
S1		C1	1.788(18)	1.850(8)	1.792(14)	1.792
O1		C2	1.482(22)	1.503(17)	1.790(18)[a]	1.781[a]
C1		C2	1.511(25)	1.431(15)	1.512(19)	1.463
P1		S2	1.927(4)	1.890(3)	1.985(6)	1.924
P1		O2	1.598(11)	1.590(5)	1.612(11)	
O2		C3	1.483(14)	1.403(7)	1.459(12)	
C3		C4	1.327(15)	1.352(9)	1.345(14)	
C3		C12	1.423(15)	1.395(10)	1.411(12)	
C4		C5	1.463(13)	1.419(9)	1.467(13)	
C5		C6	1.404(15)	1.409(9)	1.379(15)	
C5		C10	1.408(13)	1.424(8)	1.401(11)	
C6		C7	1.385(16)	1.376(9)	1.380(14)	
C7		C8	1.338(17)	1.391(10)	1.405(14)	
C8		C9	1.353(17)	1.344(10)	1.335(16)	
C9		C10	1.424(15)	1.425(9)	1.451(14)	
C10		C11	1.356(17)	1.421(9)	1.392(15)	
C11		C12	1.376(17)	1.361(9)	1.381(14)	
C1		C13	—	1.536(20)	—	
C1		C14	—	1.544(19)	—	
S2	P1	O2	116.8(4)	114.2(2)	117.0(5)	
S2	P1	S1	112.1(3)	123.4(2)	110.7(4)	
S2	P1	O1	119.8(6)	112.0(3)	119.8(4)[a]	
O2	P1	S1	108.0(5)	103.8(2)	107.0(5)	
O2	P1	O1	99.1(7)	100.3(3)	97.9(5)[a]	
P1	S1	C1	85.9(6)	92.4(3)	92.1(6)	96.8
P1	O1	C2	116.6(12)	111.9(7)	95.4(7)[a]	98.7[a]
S1	P1	O1	98.8(6)	100.0(3)	102.5(4)[a]	103.4[a]
S1	C1	C2	110.3(12)	108.1(7)	110.4(11)	109.3
O1	C2	C1	104.6(14)	110.6(10)	115.8(12)[a]	110.4[a]
P1	O2	C3	123.6(8)	127.2(4)	122.4(7)	
O2	C3	C4	120.9(9)	123.5(6)	119.3(8)	
O2	C3	C12	117.7(9)	114.7(6)	117.5(8)	
C4	C3	C12	121.3(10)	121.8(6)	123.2(8)	
C3	C4	C5	119.9(9)	120.2(6)	118.7(9)	
C4	C5	C6	121.6(9)	122.5(6)	119.9(9)	
C4	C5	C10	117.8(9)	118.9(5)	117.8(8)	
C6	C5	C10	120.6(9)	118.6(5)	122.3(9)	
C5	C6	C7	115.7(11)	120.5(6)	117.2(9)	
C6	C7	C8	125.2(12)	120.0(6)	122.0(10)	
C7	C8	C9	120.3(11)	121.8(6)	121.5(10)	
C8	C9	C10	119.1(10)	120.0(6)	118.3(9)	
C5	C10	C9	119.2(9)	118.9(5)	118.6(8)	
C5	C10	C11	120.0(9)	118.3(5)	120.9(8)	
C9	C10	C11	120.8(10)	122.7(6)	120.5(9)	
C10	C11	C12	122.4(11)	121.0(6)	121.2(9)	
C3	C12	C11	118.4(11)	119.9(6)	118.2(9)	
S1	C1	C13	—	106.8(8)	—	
S1	C1	C14	—	104.7(8)	—	
C2	C1	C13	—	110.3(10)	—	
C2	C1	C14	—	117.2(10)	—	
C13	C1	C14	—	109.2(10)	—	

[a] In compound **3**, S3 except O1.

TABLE 5 Crystal Data and Experimental Details

	Compound 1	Compound 2	Compound 3
Molecular formula	$C_{12}H_{11}O_2S_2P$	$C_{14}H_{17}O_2S_2P$	$C_{12}H_{11}OS_3P$
Crystallographic system	monoclinic	orthorhombic	monoclinic
Space group	Cc	$P2_12_12_1$	Cc
$F(000)$	584	656	616
a (Å)	9.3224(8)	6.4111(7)	9.9439(9)
b (Å)	9.9881(8)	7.2478(5)	9.9932(9)
c (Å)	14.044(1)	32.341(3)	14.480(1)
β (°)	97.414(7)	—	99.469(8)
V (Å^3)	1297(2)	1502.8(2)	1334(2)
Z	4	4	4
D_c (g/cm^3)	1.446(2)	1.381(2)	1.486(2)
μ (cm^{-1})	47.6	41.5	60.2
Crystal dimensions (mm)	0.3, 0.3, 0.4	0.1, 0.15, 0.8	0.2, 0.3, 0.5
Maximum 2θ (°)	150	150	150
Radiation, λ (Å)	Cu K_α, 1.54178	Cu K_α, 1.54178	Cu K_α, 1.54178
Scan mode	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$
Scan width (°)	1.07 + 0.14 tan θ	1.22 + 0.14 tan θ	1.22 + 0.14 tan θ
hkl ranges $h=$	0 11	0 8	0 11
$k=$	−12 12	0 9	−12 12
$l=$	0 17	−40 0	−18 18
Number of reflections:			
unique	1028	1617	1447 integrated
with $l \geq 3\sigma(l)$	943	1371	1404
Number of parameters refined	207	205	217
Goodness-of-fit parameter	0.874	1.435	1.130
Largest difference peak (eÅ^{-3})	0.180	0.363	0.376
Largest difference hole (eÅ^{-3})	−0.150	−0.443	−0.313
R	0.044	0.058	0.043

H12··O2 = 2.77(4) Å with angle C1–H12··O2 108(3)° (**3**, intramolecular)

H22··O1 = 2.70(4) Å with angle C2–H22··O1 147(3)° (**2**, intermolecular, symmetry X − 0.5, 1.5 − Y, −Z)

H13··O2 = 2.66(4) Å with angle C1–H13··O2 177(3)° (**2**, intermolecular, symmetry X, 1 + Y, Z).

EXPERIMENTAL

Column chromatography and thin layer chromatography (TLC) were performed on Kieselgel 60, 230–400 mesh, and on Kieselgel 60 F 254 plates, respectively (both from E. Merck). For TLC, benzene was used as the developing system. The solvents were dried over calcium hydride and distilled before use. All reactions involving trivalent phosphorus compounds were performed under dry argon. Melting points were not corrected.

The NMR spectra were recorded on a Bruker AC 200 Spectrometer operating at 200.113 MHz for ^{1}H and 81.01 MHz (with broad band decoupling) for ^{31}P. Chemical shifts are given in parts per million with respect to TMS (internal standard) for ^{1}H and 85% H_3PO_4 (external standard) for ^{31}P. Chem-

ical shifts are positive when downfield from the standard. EI mass spectra were recorded on a Finnigan MAT 95 Spectrometer at 70 eV ionizing energy.

2-Chloro-1,3,2-oxathiaphospholane (**8**) [20] and 2-chloro-1,3,2-dithiaphospholane (**9**) [21] were prepared according to literature reports, whereas the synthesis of 2-chloro-4,4-dimethyl-1,3,2-oxathiaphospholane (**10**) will be described elsewhere [6].

2-(β-Naphthoxy)-2-thio-1,3,2-oxathiaphospholane (1)

Into a solution of β-naphthol (1.44 g, 10 mmol) and triethylamine (1.01 g, 10 mmol) in benzene (20 mL) was added freshly sublimed elemental sulfur (0.5 g), and to the resulting suspension was added dropwise, with stirring at 5°C, a solution of **8** (1.42 g, 10 mmol) in 10 mL of benzene. The reaction mixture was stirred overnight at room temperature and a solid deposit was filtered off. The solid was washed with benzene (2 × 10 mL) and the combined filtrates were evaporated. The residue was chromatographed on a column and eluted with a linear gradient of benzene in hexane (from 50 to 90%). The chromatography was followed by TLC.

The fractions containing product **1** (R_f = 0.53) were pooled and evaporated to give a white solid residue, which, upon crystallization from benzene-hexane, gave pure **1** in the form of colorless needles, mp 72–73°. Yield 2.48 g (88%).

Anal. calcd for $C_{12}H_{11}O_2S_2P$: C, 51.05; H, 3.93; P, 10.97. Found: C, 51.24; H, 3.84; P, 11.30. ^{31}P NMR (C_6D_6) δ 99.67. ^1H NMR (C_6D_6) δ 2.07–2.45 (m, 2H), δ 3.43–3.64 (m, 2H), δ 7.28–7.68 (m, 9H). MS m/z 282 (M$^+$, 100%), 222 (M$^+$ – C_2H_4S, 8%), 139 (M$^-$ – $C_{10}H_7O$, 25%).

2-(β-Naphthoxy)-2-thio-4,4-dimethyl-1,3,2-oxathiaphospholane (2)

The procedure as described previously for the synthesis of **1** was followed using chlorophosphite **10** in place of **8**, but with a difference in the sulfur addition step, one which required 2 hours of heating under reflux of a benzene solution. Colorless needles, mp 87–88°. TLC R_f = 0.58.

Anal. calcd for $C_{14}H_{15}O_2S_2P$: C, 54.18; H, 4.87; P, 9.98. Found: C, 54.14; H, 5.04; P, 10.32. ^{31}P NMR (C_6D_6) δ 101.95. ^1H NMR (C_6D_6) δ 0.99 (d, 6H, $^4J_{PH}$ = 7.0 Hz), δ 3.56 (d, 2H, $^3J_{PH}$ = 21.1 Hz), δ 7.14–7.74 (m, 9H). MS m/z 310 (M$^-$, 100%), 167 (M$^-$ – $C_{10}H_7O$, 6%).

2-(β-Naphthoxy)-2-thio-1,3,2-dithiaphospholane (3)

The same procedure as described previously was used for the synthesis of **1**, chlorophosphite **8** being replaced by **9**. Colorless needles, mp 122–123°. Yield 84%. TLC R_f = 0.63.

Anal. calcd for $C_{12}H_{11}OS_3P$: C, 48.30; H, 3.72; P, 10.38. Found: C, 48.68; H, 3.75; P, 10.35. ^{31}P NMR (C_6D_6) δ 118.74. ^1H NMR (C_6D_6) δ 2.43–2.62 (m, 4H), δ 7.34–7.76 (m, 9H). MS m/z 298 (M$^+$, 100%), 155 (M$^+$ – $C_{10}H_7O$, 55%).

X-Ray Measurements of 1, 2, and 3

Crystal and molecular structures of compounds 1, 2 and 3 were determined using of data collected on a CAD4 diffractometer. Crystal data and experimental details are shown in Table 5.

Intensity data were collected at room temperature using a diffractometer with graphite mono-chromatized Cu K_α radiation. Lattice constants were refined by the least-squares fit of 25 reflections in θ ranges: 19.9–29.9° for **1**, 15.5–30.4° for **2**, and 21.7–27.9° for **3**. Declines in intensities of three standard reflections (0, −4, −3; 0, −6, 0; −5, −1, 2 for **1** and 2, −1, 7; 2, −1, −12; 2, −2, 5 for **2** and −3, −5, 1; −3, 3, −2; −3, −5, −1 for **3**) were, respectively, 1.4, 6.1, and 1.7% during 44.4, 78.2, and 42.8 hours of exposure for compounds **1**, **2**, and **3** [23]. For compound **2**, intensities were corrected by use of the DECAY program [23] with the following correc-

tion coefficients: min 1.00005, max 1.03186, and av 1.01563. For compounds **1–3**, an absorption correction was applied [23,24] (see Table 5). A total of 943, 1371, and 1404 observed reflections, respectively, for **1**, **2**, and **3** (with $I \geq 3\sigma(I)$) were used to solve the structures by direct methods and to refine them by full-matrix least-squares using F's [25]. Hydrogen atoms were placed geometrically at idealized positions with fixed isotropic thermal parameters and set as riding. Anisotropic thermal parameters were refined for all nonhydrogen atoms in structures **1**, **2**, and **3**, except for atoms C2', O1', and C13' with smaller SOF in structure **2**, which were refined isotropically. The final refinement converged in **1** to R = 0.044 with a unit weight for 207 refined parameters, in **2** to R = 0.058 with weight $w = 1/(\sigma^2(F) + 0.006969F^2)$ for 205 refined parameters, and in **3** to R = 0.043 with unit weight for 217 refined parameters. All calculations (structure solution and refinement) were carried out with use of the SHELXTL package [25]. Scattering factors were taken from the International Tables for X-ray Crystallography [26]. Full crystallographic data, and values of F_{obs}, F_{calcd} are deposited at the Cambridge Crystallographic Data Centre [27].

The following crystallographic data are deposited at the Cambridge Crystallographic Data Centre [27]:

A-1, A-2, A-3: Hydrogen atom coordinates (for 1, 2, and 3)

B-1, B-2, B-3: Bond distances of nonhydrogen atoms (1, 2, and 3)

C-1, C-2, C-3: Valence angles including nonhydrogen atoms

D-1, D-2, D-3: Torsion angles including nonhydrogen atoms

E-1, E-2, E-3: Anisotropic displacement coefficients

F-1, F-2, F-3: Hydrogen contacts

G: Least-squares planes

H: Asymmetry parameters

I-1, I-2, I-3: Values of $10F_{obs}$ and $10F_{calcd}$

J-1, J-2, J-3: Additional figures presenting, separately, the molecules with larger as well as with smaller site-occupation factor.

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