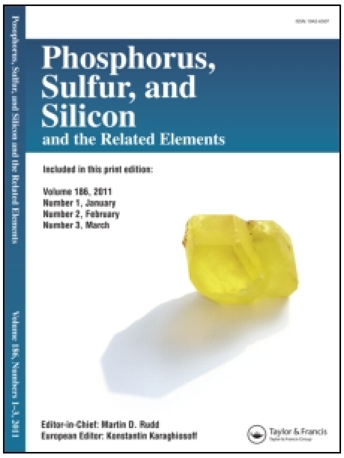

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N-ALKYL THIOCARBAMOYL PHOSPHONIC ACID ESTERS. 5[1]. DIMERIZATION THROUGH A TEN-MEMBERED HYDROGEN-BONDED RING

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N-ALKYL THIOCARBAMOYL PHOSPHONIC ACID ESTERS. 5[1]. DIMERIZATION THROUGH A TEN-MEMBERED HYDROGEN-BONDED RING

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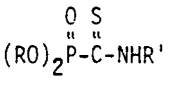
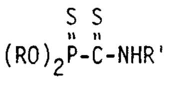
Thiocarbamoyl phosphonates, $(RO)_2PO—CS—NHR$, which are crystalline solids, were shown by X-ray crystallography to be associated in dimers. These dimers are held by two $P=O \cdots H—N$ bonds forming a ten-membered planar ring. In crystals of compounds containing an N-benzyl group, the aromatic rings are arranged symmetrically above and below the ten-membered ring. Thiophosphoryl analogs, $(RO)_2PS—CS—NHR$, do not seem to contain any hydrogen bonds in their crystals, thus explaining the fact that most of these compounds are liquids at room temperature. The findings seem to reinforce a previous argument that the different nmr behavior of compounds of the two sets, when dissolved in benzene, is due to the association of molecules of the phosphoryl series, through hydrogen bonding, in non-polar solvents.

Recently, the synthesis and properties of some esters of *N*-alkyl thiocarbamoyl phosphonic[2] and thiophosphonic[3] acids, series **1** and **2** (R = short alkyl, phenyl; R′ = methyl, benzyl), have been described.



$(\mathrm{RO})_2\overset{\mathrm{O}}{\overset{\|}{\mathrm{P}}}\text{-}\overset{\mathrm{S}}{\overset{\|}{\mathrm{C}}}\text{-NHR}'$

1



$(\mathrm{RO})_2\overset{\mathrm{S}}{\overset{\|}{\mathrm{P}}}\text{-}\overset{\mathrm{S}}{\overset{\|}{\mathrm{C}}}\text{-NHR}'$

2

It was noted that the chemical behaviour of the thioamide moieties was profoundly affected by the various groups attached to the molecules,[3,4] as were also some spectral properties of the compounds. A strong effect was observed in the upfield benzene shifts of the locations of the N—C<u>H</u> signals in the nmr spectra. When measured in benzene, these signals usually appeared at a higher magnetic field compared to their location in chloroform, but the magnitude of the shift varied considerably. In some cases an appreciable shift was found (nearly 1 ppm for **4**), while in others (mainly of series 1) the values were rather low. For compound **6** the value was even negative (i.e. a shift to a lower field!). The big difference in the magnitude of the shift could be explained either on the ground of differences between the geometries of the compounds, regarding the arrangement of the thioamide substituents, or alternatively as a result of different patterns of association

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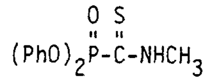
TABLE I

Crystallographic data for compounds **3**–**6**

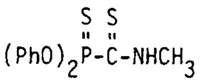
compound	**3**	**4**	**5**	**6**
formula	$C_{14}H_{14}O_3NPS$	$C_{14}H_{14}O_2NPS_2$	$C_{20}H_{18}O_3NPS$	$C_{12}H_{18}O_3NPS$
M	307.3	323.4	383.4	287.3
space group	C2/c	C2/c	$P\bar{1}$	$P\bar{1}$
a, A	12.400(2)	16.451(2)	10.174(2)	8.546(2)
b, A	14.196(2)	8.158(1)	10.863(2)	11.968(3)
c, A	17.972(3)	25.175(3)	10.096(2)	8.258(2)
α, deg			106.21(3)	106.75(3)
β, deg	108.17(4)	108.90(3)	94.73(3)	108.20(3)
γ, deg			65.63(2)	81.03(2)
V, A^3	3006 (1)	3197 (1)	975.3(6)	766.3(8)
z	8	8	2	2
ρ_{calc}, g cm^{-3}	1.36	1.34	1.31	1.25
$\mu(MoK_\alpha)$, cm^{-1}	2.77	3.78	2.21	2.68
No. of unique data	1940	2032	2479	1954
data with $I \geqslant 2\sigma(I)$	1654	1518	2074	1467
R	0.047	0.051	0.054	0.081
R_W	0.064	0.058	0.070	0.096

between the various molecules when they are dissolved in a non-polar solvent such as benzene.[1]



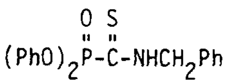
$(\mathrm{PhO})_2\overset{\mathrm{O}}{\overset{\|}{\mathrm{P}}}-\overset{\mathrm{S}}{\overset{\|}{\mathrm{C}}}-\mathrm{NHCH}_3$

3



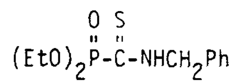
$(\mathrm{PhO})_2\overset{\mathrm{S}}{\overset{\|}{\mathrm{P}}}-\overset{\mathrm{S}}{\overset{\|}{\mathrm{C}}}-\mathrm{NHCH}_3$

4



$(\mathrm{PhO})_2\overset{\mathrm{O}}{\overset{\|}{\mathrm{P}}}-\overset{\mathrm{S}}{\overset{\|}{\mathrm{C}}}-\mathrm{NHCH}_2\mathrm{Ph}$

5



$(\mathrm{EtO})_2\overset{\mathrm{O}}{\overset{\|}{\mathrm{P}}}-\overset{\mathrm{S}}{\overset{\|}{\mathrm{C}}}-\mathrm{NHCH}_2\mathrm{Ph}$

6

We hoped that an X-ray crystallographic study of the compounds would clarify their conformation and would thus shed some light on their properties.

We were rather limited in the choice of our compounds; of the few thionophosphonates prepared only compound **4** was solid at room temperature. The analogous phosphonates, on the other hand, all crystallized nicely, but since some of them had melting points too low for crystallographic study at ambient temperature, only the aromatic esters **3** and **5**, and to a lesser extent the *N*-benzyl derivative **6**, were studied.

RESULTS AND DISCUSSION

The unit cell dimensions, as well as other pertinent crystallographic data, for compound **3**–**6** are presented in Table I. Positional and thermal parameters and important bond lengths and angles are presented as supplementary material. ORTEP stereodrawings of compounds **3**, **5** and **6**, the content of half a unit cell of **4** and a dimer of **3** are represented in Figures 1–5, respectively. It should be noted that due to its rather low melting point (75°C) compound **6** manifested a significant thermal motion, especially noticeable with its two ethoxy groups. The main features of its structure are, however, clear.

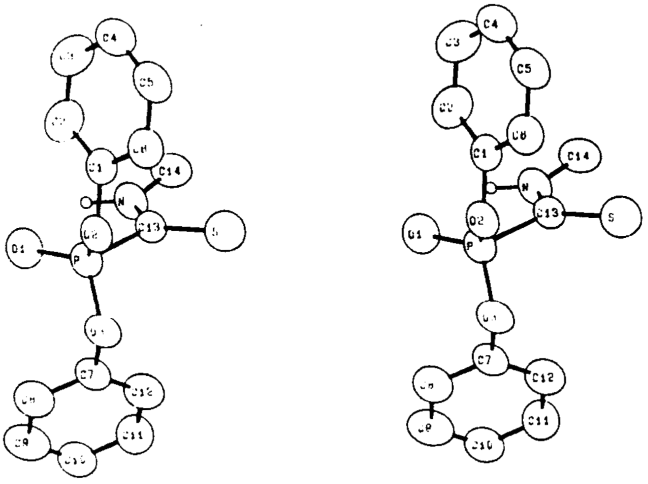


FIGURE 1 Stereoscopic view of **3**.

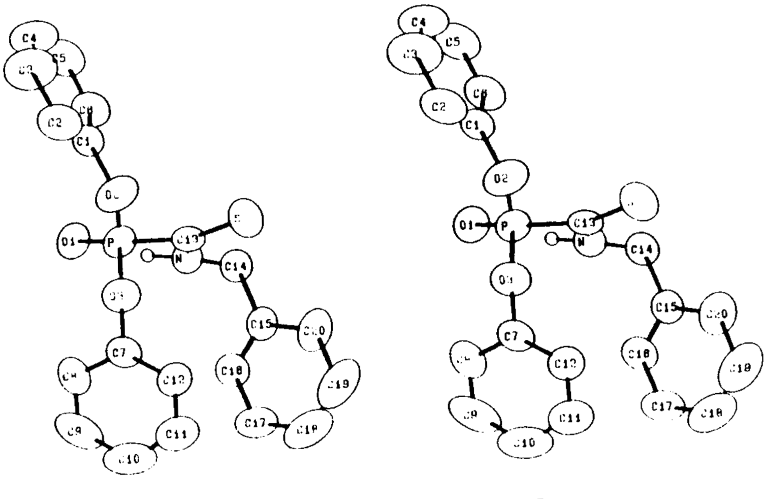


FIGURE 2 Stereoscopic view of **5**.

Intramolecular Geometry

The thioamide moieties were found to be practically planar, with a maximum deviation from planarity of only 0.07 Å (for C_{14} of **4**). The orientation of the nitrogen substituent around the C(S)—N bond was always (Z), i.e. R′ was located *cis* to the sulfur atom, in line with what is known for thioamides in general.[5] We believe that compounds **3**–**6** are all of a (Z) geometry in solution as well as in the solid, since the energy barrier to rotation around the thioamidic C—N bond in monoalkyl thioamides (e.g. $\Delta G^{\ddagger} = 23$ Kcal mol^{-1} for $CH_3(C{=}S)$—$NHCH_3$[6]) will probably prevent quick rotation, and since in the few cases where an (E) isomer was prepared,[6] its crystallization never caused the separation of the opposite isomer. The possibility that the large benzene-induced upfield shift of some of these compounds was a result of an (E) geometry[7] can thus be excluded.

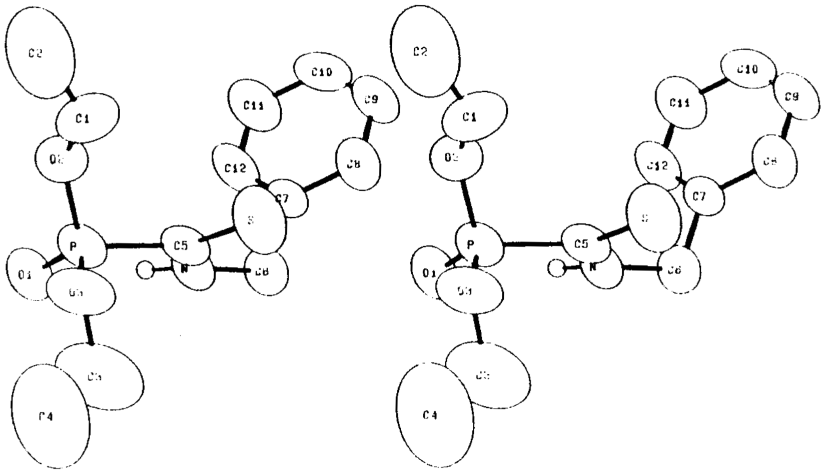


FIGURE 3 Stereoscopic view of **6**.

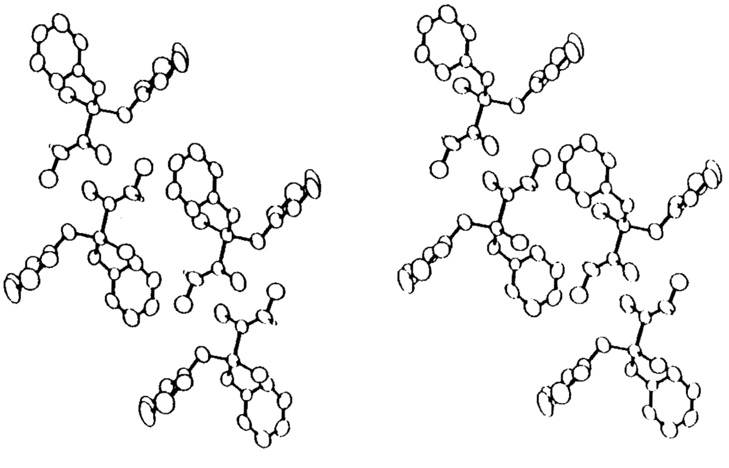


FIGURE 4 Stereoscopic view of the content of half a unit cell of **4**.

The P=O or P=S bonds of compounds **4**–**6** also lie in the plane of the thioamide (maximum deviation less than 0.1 Å for **3**, **4** and **6**, 0.50 Å for the hindered compound **5**), probably because of the conjugation between these bonds and the thioamide moiety. The existence of such a conjugation was also deduced[2] from the UV-visible spectra of the compounds, in which the typical thioamidic $n \rightarrow \pi^*$ band in ethanol occurred at 390–410 nm, whereas in nonconjugated molecules, such as $CH_3(C{=}S)$—$NHCH_3$, the same band appeared at 321 nm.[8] In spite of the conjugation, the length of the P—C bonds measured (1.82–1.83 Å) is not shorter than that of P—C not involved in conjugation (1.80–1.85 Å[9]). A similar finding has already been reported for another conjugated thioamide.[10]

An interesting feature in the structure of **5** is the nearly parallel arrangement of one of it's phenyl rings and the N-benzyl ring, the dihedral angle equals 19.8°, and the average distance between the rings is 4.58 Å.

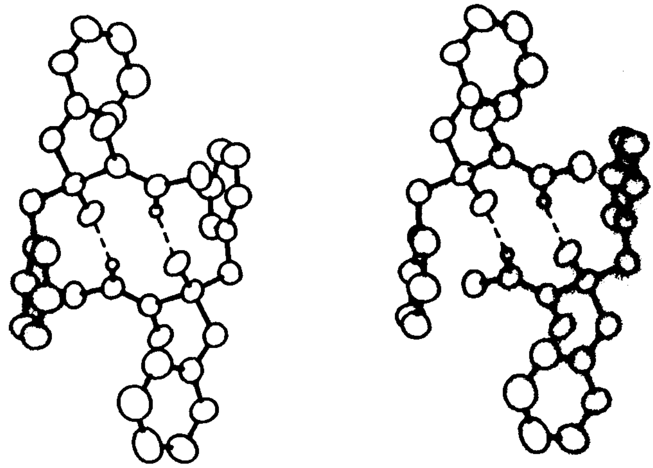
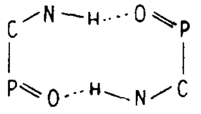


FIGURE 5 Stereoscopic view of a dimer of **3**.

Intermolecular Geometry

Looking at intermolecular distances and interactions, we found a major difference between our two series of compounds. The P=S compound **4** was monomeric, since the shortest distance between the atoms of neighbouring molecules (3.60 Å for P=S → S=C approach) equals the sum of the van-der-Vaals radii of the two sulfur atoms (about 1.72–1.85 Å for each).[11] The crystals of the phosphoryl compounds **3**, **5** and **6**, on the other hand, were composed of dimers which included a planar ten-membered ring, held by two hydrogen bonds which connected the nitrogen atom of one molecule to the phosphoryl oxygen atom of the other, as depicted in **7**.



7

The average deviation from planarity equals 0.01, 0.10 and 0.12 Å for **6**, **3** and **5**, respectively, indicating that there is some crowding above the central plane of the dimer in the phenoxy compounds **3** and **5**.

The existence of the N—H ··· O=P bridges is revealed by the short distances between the nitrogen and oxygen atoms, which are 2.80, 2.78 and 2.88 Å for compounds **3**, **5** and **6**. The bridges are not strictly colinear, forming angles of 147°, 148° and 142° for the same compounds.[12]

The type of hydrogen bonding found in our dimers is unusual for thioamides, which are known to aggregate in dimers or in chains through N—H ··· S=C bonds.[7] While the preference for the expanded dimers in the phosphonate series can be explained by assuming that the P=O ··· H—N hydrogen bond is energetically more favourable than a N—H ··· S=C bond, the behaviour of the P=S compound **4** is less readily understood. It is well known that the P=S moiety is considerably more hydrophobic than P=O, and thus is also less suitable to serve as an acceptor for the proton, but the non-existence of N—H ··· S═C bonds in **4**, and probably also in the other non-crystalline P═S derivatives which were prepared, is surprising.

It might be that the bulky phosphorus substituents hinder the mutual approach of the thioamide moieties. It might also be the result of the electron-withdrawing property of the P═S (and also of the P═O) group, which also renders the sulfur atom less nucleophilic compared to simple thioamides.[2-4]

While the carbon atom adjacent to the nitrogen is also located in the plane of the thioamide, the phenyl moiety attached to this carbon in compounds **5** and **6** is out of plane, forming dihedral angles of 67.2° and 107.5°, respectively. Thus, the benzylic ring and possibly one of the esterifying groups strongly hinder the approach to one of the thioamide surfaces, while the other surface is rather exposed, being somewhat disturbed only by the second esterifying group. In the dimer, on the other hand, the arrangement around a center of symmetry brings the benzyl and one of the esterifying groups of the neighbouring molecule above the exposed face of the thioamide, resulting in steric hinderance to the approach from either side.

Assuming that the crystallographic results showing the tendency of the P═O compounds to dimerize are also applicable to solutions in non-polar solvents, an explanation for their relatively low nmr benzene shifts can be offered. In benzene the non-polar environment causes molecules of series 1 (but not of series 2) to form dimers. This hinders the approach of benzene molecules, lowering, thus, both the specific[6] and the unspecific[13] shielding of the N—C$\underline{\underline{H}}$ protons. The surface of the central ring is even less accessible in the case of the *N*-benzyl compounds and this is reflected in their negligible upfield benzene shifts.

EXPERIMENTAL SECTION

X-ray crystal structure analysis. Data were measured on a PW 1100/20 four-circle computer-controlled diffractometer. MoK_α ($\lambda = 0.71069$ Å) radiation, with a graphite crystal monochromator in the incident beam, was used. The unit cell dimensions were obtained by a least square fit of 20 centered reflections in the range of $12° < \theta < 15°$. Intensity data were collected using the $\omega - 2\theta$ technique to a maximum 2θ of 45°. The scan width, $\Delta\omega$, for each reflection was 1° with a scan time of 20 seconds. Background measurements were made for a total of 20 seconds at both limits of each scan. Three standard reflections were monitored every 60 minutes. No systemic variations in intensities were found. Intensities were corrected for Lorentz and polarization effects. The positions of the hydrogen atoms, except for the H(N) one, were calculated. The position of the H(N) atom was found in a difference Fourier map. All non-hydrogen atoms were found by using the results of the MULTAN direct method analysis.[14] After several cycles of refinements,[15] the positions of the hydrogen atoms were introduced into the refinement process with a constant isotropic temperature factor of 0.5 Å^2. The refinement proceeded to covergence by minimizing the function $\Sigma w(|Fo| - |Fc|)^2$, where the weight w equals $\sigma(|Fo|)^{-2}$. The discrepancy indices, $R = \Sigma||Fo| - |Fc||/\Sigma|Fo|$ and $R_w = \{\Sigma w(|Fo| - |Fc|)^2/\Sigma w|Fo|^2\}^{1/2}$ are presented with other pertinent crystallographic data in Table I. A final difference Fourier map, showed several peaks of less than 0.4 e Å^{-3}, scattered about the unit cell without a significant feature.

ACKNOWLEDGMENT

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