

Phosphinodithioformates

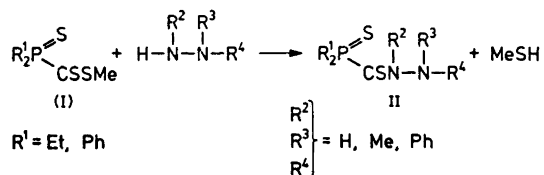
V. *P,P*-Disubstituted Thiophosphinoylthioformhydrazides

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The title compounds II have been prepared from $R_2P(S)CSSMe$ (I), $R = Et, Ph$) and hydrazine, various methyl-substituted hydrazines, and phenylhydrazine. The structures of these compounds have been studied by IR and 1H NMR spectroscopy. The reaction of (I) with methylhydrazine gives rise to a mixture of $R_2P(S)CSN(Me)NH_2$ and (mostly) $R_2P(S)CSNHNHMe$. In addition these and other compounds II exhibit *E-Z* isomerism about the C(S)-N bond. Tautomerism between apolar and dipolar isomers has been demonstrated for the compounds II derived from 1,1-dimethylhydrazine. Shielding effects from phenyl groups and the magnitude of coupling constants have been used in the assignment of 1H NMR signals to *E-Z* isomers. The pK_A values of several of the compounds and the barrier to rotation about the C(S)-N bond of one of the compounds II have been estimated.

As part of a study of the chemistry of derivatives of phosphinodithioformic acid¹ we have investigated the preparation and properties of *P,P*-disubstituted thiophosphinoylthioformhydrazides (II). This type of compound,



which to our knowledge has not been described previously, was obtained from methyl *P,P*-disubstituted thiophosphinoyldithioformates (I)² and hydrazines. The reaction of (I) with hydrazine and methylhydrazine is fast at room temperature, whereas 1,1- and 1,2-dimethylhydrazine and phenylhydrazine react more slowly. Trimethylhydrazine, 1-methyl-2-phenylhydrazine and 1,1-diphenylhydrazine do not give detectable amounts of II. The reaction probably

Table 1. Yields, melting points and elemental analyses for thiophosphinoylthioformhydrazides.

No.	Compound	Method	Yield, %	M.p., °C	Formula	Analyses (C, H, N, S)
IIa	Et ₂ P(S)CSNHNH ₂	A	70 ^a	66.5—67.5	C ₆ H ₁₃ N ₂ PS ₂	Found: 30.67; 14.26; 32.88 Calc.: 30.59; 14.28; 32.67
IIb	Et ₂ P(S)CSNHNHMe	B	50 ^b	49.5—50.5	C ₆ H ₁₅ N ₂ PS ₂	Found: 34.38; 13.36; 30.40 Calc.: 34.26; 13.32; 30.49
IIc	Et ₂ P(S)CSN(Me)NH ₂	B+C	20 ^b	76—77	[†]	Found: 33.98; 13.22; 30.35
IId	Et ₂ P(S)CSN(Me)NHMe	C	35 ^c	48—49	C ₇ H ₁₇ N ₂ PS ₂	Found: 37.38; 12.48; 28.31 Calc.: 37.47; 12.49; 28.59
IIe	Et ₂ P(S)CSNHN(Me) ₂	B'	45 ^c	<i>ca.</i> 55 ^e	[†]	Found: 37.46; 12.42; 28.33
IIf	Et ₂ P(S)CS ⁻ NN ⁺ H(Me) ₂	B'	40 ^a	62—63	[†]	Found: 37.43; 12.38; 28.68
IIg	Et ₂ P(S)CSNHNHPh	A'	75 ^d	107—108	C ₁₁ H ₁₇ N ₂ PS ₂	Found: 48.30; 6.37; 10.13; 23.40 Calc.: 48.50; 6.29; 10.29; 23.54
IIh	Ph ₂ P(S)CSNHNH ₂	A	80 ^e	153.5—154.5	C ₁₃ H ₁₃ N ₂ PS ₂	Found: 53.42; 4.57; 9.60; 21.73 Calc.: 53.39; 4.48; 9.58; 21.93
IIi	Ph ₂ P(S)CSNHNHMe	B	50 ^e	159—160	C ₁₄ H ₁₅ N ₂ PS ₂	Found: 54.80; 5.04; 9.05; 20.70 Calc.: 54.88; 4.94; 9.14; 20.93
IIj	Ph ₂ P(S)CSN(Me)NH ₂	B+C	10 ^e	154—155	[†]	Found: 54.95; 5.05; 9.07; 20.71
IIk	Ph ₂ P(S)CSN(Me)NHMe	C	35 ^e	145—146	C ₁₅ H ₁₇ N ₂ PS ₂	Found: 56.45; 5.44; 8.87; 19.86 Calc.: 56.22; 5.35; 8.74; 20.01
IIl	Ph ₂ P(S)CS ⁻ NN ⁺ H(Me) ₂	B'	30 ^f	150.5—151.5	[†]	Found: 56.35; 5.41; 8.76; 19.92
IIm	Ph ₂ P(S)CSNHNHPh	D	60 ^e	133.5—134	C ₁₉ H ₁₇ N ₂ PS ₂	Found: 62.05; 4.71; 7.67; 17.34 Calc.: 61.93; 4.65; 7.61; 17.40

Recrystallized from ^a 2-propanol, ^b 80% methanol, ^c hexane, ^d methanol, ^e ethanol, ^f 1-propanol. [†] When quickly heated. Tautomerize to IIf upon melting.

fails with the higher substituted hydrazines due to steric hindrance from the $R_2P(S)$ group. Steric hindrance likewise explains the product distribution of the reaction of (I), $R^1 = Et$ and Ph with methylhydrazine. The main product is the 3-methylhydrazide instead of the 2-methylhydrazide * expected³ from considerations of the relative nucleophilic reactivity of the two nitrogen atoms of methylhydrazine. This steric control prevails even in the case of (I), $R^1 = Me$.⁴ The hydrazides were isolated in variable yields (Table 1) due to side reactions, *e.g.* between (I) and the reaction product methanethiol. These side reactions are under further investigation. The hydrazides II were characterized by elemental analyses (Table 1), and by IR and 1H NMR spectroscopy (Table 2).

Table 2. 1H NMR chemical shifts ^a (τ) and coupling constants (J , Hz) of thiophosphinoylthioformhydrazides (ca. 5 % solutions in $CDCl_3$ at ca. 40°C).

Compound	$N(2)CH_3$	J_{PCNCH}	$N(3)CH_3$	J_{PCNCH}	J_{HNCH}	NH ^b	% ^c
IIa						2.7	
IIb	Z		7.14 (d) ^d	ca. 0.7 ^d	not obs.	-0.5	
						3.5	
IIc	Z	5.88 (d ^e)				3.7	65
	E	6.35 (d)				4.2	35
II d ^f	Z	5.97 (d)	7.31 (dd)	1.1	6.1	2.3 (q)	40
	E	6.44 (d)	7.21 (d)	< 0.3	5.9	4.0 (q)	60
IIe	Z		7.22 (s)			-0.1	
IIg						-1.4	
						1.7	
IIh						3.3	
IIi	Z		7.10 (d) ^d	ca. 0.8 ^d	not obs.	-1.1	
						3.3	
IIj	Z	6.40 (d)				3.9	75
	E	6.37 (d)				4.9	25
IIk ^f	Z	6.49 (d)	ca. 0.7	7.33 (dd)	1.2	6.1	not obs. ^g
	E	6.51 (d)	ca. 1.2	7.79 (d)	< 0.3	5.8	5.5 (q)
IIl ^h	Z			7.18 (s)			not obs.
IIm						-1.9	
						1.7 ^g	

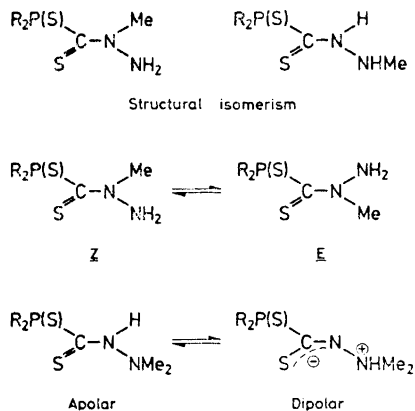
^a The values given are the centres of the multiplets. ^b In order to obtain separate NH signals from *E* and *Z* isomers or from $N(2)$ -H and $N(3)$ -H's the solution was shaken with solid Na_2CO_3 in the NMR tube. ^c Estimated from the integral values. ^d Doublet only when $N(3)$ -H exchange rapidly (a little water added). ^e Multiplicity of signals, s=singlet, d=doublet, q=quartet. ^f Obtained at 90 MHz because of overlapping signals at 60 MHz. ^g Covered or partly covered by the phenyl signals. ^h Apolar isomer.

STRUCTURE OF II

Three types of isomerism are possible for compounds with a thiohydrazide structure,⁵ namely structural isomerism when the reacting hydrazine is unsymmetrical, *E-Z* isomerism due to hindered rotation about the $C(S)-N$

* The IUPAC numbering $\overset{1}{C}(S)-\overset{2}{N}-\overset{3}{N}$ has been used throughout this work.

bond, and tautomerism (between apolar and dipolar isomers) due to the simultaneous presence of an acidic proton (II, $R^2=H$) and a basic nitrogen atom:



The occurrence of isomerism of these types is demonstrated in this series by IR and ¹H NMR spectroscopy.

The *N*-unsubstituted hydrazides IIa and IIh are at least 90 % apolar in the solid state and in CHCl₃ solution, as shown by the absence of NH⁺ bands (2500–2800 cm⁻¹) in the IR spectra.⁵ The ¹H NMR spectra (CDCl₃) showed only one, broad signal from the NH protons, leaving the question of *E-Z* isomerism open for these compounds.

The products from methylhydrazine and (I) are mixtures of 2- and 3-methylhydrazides. These isomers were separated by utilization of the fact that only the last type has acidic properties and dissolves in aqueous NaOH. This extraction procedure established IIb and IIIi as the 3- and IIc and IIj as the 2-methylhydrazides.

The 3-methylhydrazides IIb and IIIi were shown by IR spectroscopy to be apolar in the solid state and in CHCl₃ solution. The ¹H NMR spectra (CDCl₃) show two NH signals and one broadened *N*-CH₃ signal. On addition of a little water the NH signals collapse to one signal, and the *N*-CH₃ signal becomes narrower and shows a splitting. The splitting of the *N*-CH₃ signal is due to a coupling to phosphorus ($J = 0.7 - 0.8$ Hz), because it collapses to a singlet on strong irradiation at the ³¹P frequency. Long-range couplings from phosphorus spanning 4 or 5 bonds are known in similar systems.^{2,6} The fact that different *N*-CH₃ signals from *E* and *Z* isomers are not observed may be due to (i) accidental coincidence of signals, (ii) a low barrier for rotation about the C(S)–N bond, or (iii) the presence of only one of the *E-Z* isomers. The first possibility is considered unlikely since only one set of signals was observed when the spectra of IIb and IIIi were recorded in C₆D₆. The second possibility is also unlikely since the barrier for rotation probably is comparable to that for IIc (21.1 kcal/mol, see below). Although IIb and IIIi, contrary to IIc, are capable of dissociate the *N*(2)-H, the anions formed are expected to have higher bar-

riers for rotation than IIc. A dissociation would therefore, if anything, rise the barrier. It is therefore likely that one isomer prevails in the equilibrium mixture. Consequently the two NH signals observed must arise from the *N*(2)-H and the *N*(3)-H in the same isomer. The low field signal is assigned the more acidic *N*(2)-H.

The ^1H NMR spectra (CDCl_3) of the 2-methylhydrazides IIc and IIj show two NH signals and two *N*- CH_3 doublets. Since dipolar forms are impossible for these hydrazides the two set of signals must arise from the presence of *E*-*Z* isomers. When comparing the *N*- CH_3 signals from IIc with those from IIj (Fig. 1) it is seen that one of the doublets has approximately the same

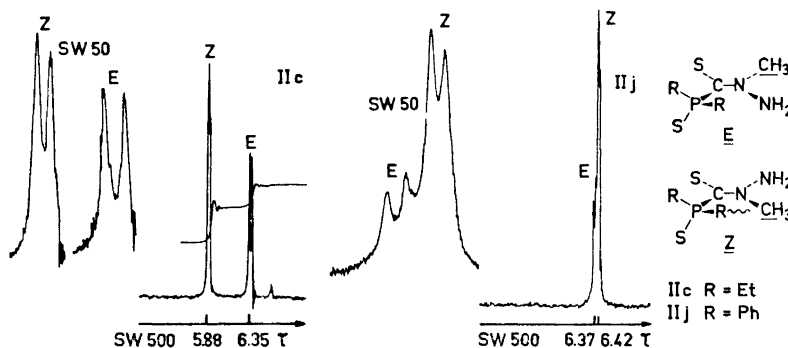


Fig. 1. Part of the ^1H NMR spectra (60 MHz) of the thiophosphinoylthioformhydrazides IIc and IIj showing the *N*- CH_3 signals. At the left: Signals expanded ten times.

chemical shift for both compounds, whereas the other is shifted upfield for IIj. Inspection of models of *E* and *Z* isomers suggests that this upfield shift may be explained by phenyl group shielding of the *N*- CH_3 protons of the *Z* isomer, whereas the *N*- CH_3 group of the *E* isomer is well away from the shielding area above the planes of the phenyl groups. Furthermore the coupling constants J_{PCNCH} are very similar for the doublets so correlated, and largest when phosphorus is *trans* to the *N*- CH_3 group (*E* isomers). The assignments of signals from IIc and IIj to *E* and *Z* isomers given in Table 2 are based on these arguments.

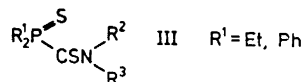
The 2,3-dimethylhydrazides IIId and IIk also exist as equilibrium mixtures of *E* and *Z* isomers in CDCl_3 . The ^1H NMR spectra show signals due to the *N*(2)- CH_3 groups which correspond well with the analogous signals from the 2-methylhydrazides IIc and IIj, and the shielding effect and the magnitude of the coupling constants J_{PCNCH} allow likewise the assignment to *E* and *Z* isomers (Table 2). The *N*(3)- CH_3 signals are doublets due to coupling to *N*(3)-H, one of the doublets being further splitted due to long-range coupling to phosphorus. The assignment to *E* and *Z* isomers follows from the integral values. A shielding is found for the *N*(3)- CH_3 group of the *E* isomer of IIk relative to IIId, in accordance with models which show that this methyl group is close to a phenyl group in the most probable conformations. The finding of a shielding effect for *N*(3)- CH_3 groups indicate that the 3-methylhydrazides, the

structures of which was discussed above, are *Z* isomers, because the methyl group of IIIi is not shielded relative to that of IIb.

The 3,3-dimethylhydrazides II f and III are dipolar in the solid state as shown by the broad IR NH⁺ bands in the 2550–2750 cm⁻¹ region and the absence of bands above 3050 cm⁻¹. In CHCl₃ the apolar isomers prevail (NH bands in the 3070–3150 cm⁻¹ region (CDCl₃) and absence of bands in the 2500–2780 cm⁻¹ region). By recrystallizing II f from hexane the apolar isomer II e could be isolated (NH band at 3130 cm⁻¹ (KBr)), whereas 2-propanol gave the dipolar II f. Isomerization of II e to II f in the solid state took place within a few hours at room temperature, but II e was rather stable at -25°C. All attempts to isolate the apolar isomer of III were fruitless. The ¹H NMR spectra (CDCl₃) of II e and II f are identical in accord with rapid isomerization of II f to II e in this solvent. The spectra of II e and III show one broadened *N*-CH₃ signal and a very broad NH signal. The lack of shielding of the *N*-CH₃ group of III indicate that II e and apolar III are *Z* isomers.

The phenylhydrazides II g and II m are apolar in the solid state and in CHCl₃ solution (IR). The compounds are soluble in 2 N NaOH and are therefore 3-phenylhydrazides, as found for other thiohydrazides prepared from phenylhydrazine.³ The two NH signals observed in the ¹H NMR spectra most likely arise from *N*(2)-H and *N*(3)-H of one isomer, as found for II b and IIIi, although the presence of *E*-*Z* isomerism cannot be excluded.

The assignment of ¹H NMR signals to *E* and *Z* isomers, which is based primarily on the observed shielding of *N*-CH₃ groups by *P*-phenyl groups, is supported by several other observations: (1) The 3-methyl- and 3,3-dimethylhydrazides exist mainly as the sterically least hindered *Z* isomers. (2) The J_{PCNCH} coupling constant is largest when the *N*(2)-CH₃ group is *trans* to phosphorus about the C(S)-N bond (*E* isomers). This is in accord with the findings for the analogous J_{HCNCH} coupling constants in *N*-methyl thioformamides.^{7,8} (3) The ¹H NMR spectra of the closely related thioamides III



described earlier⁶ may be assigned similarly. Thus (III, R²=R³=Me) shows a large upfield shift of one of the *N*-CH₃ signals and virtually no shift of the other *N*-CH₃ signal when R¹ is changed from Et to Ph.⁶ The *N*-CH₃ group, the signal of which is shifted, is assigned *cis* to the R₂P(S) group and shows accordingly the smallest J_{PCNCH} value (1.0 Hz; the other is 1.6 Hz). No shielding is observed for (III, R²=H, R³=Me, Et) when R¹ is changed from Et to Ph and J_{PCNCH} is rather large (1.7–1.9 Hz). These findings are in agreement with the alkyl group being *trans* to the R₂P(S) group, which is also the sterically least hindered position.

PROPERTIES OF II

The thiohydrazides II are colourless or yellow solids, *e.g.* the dipolar II f is colourless and the apolar isomer II e is sulfur yellow. The compounds are nearly insoluble in water except II a and the dipolar II f. All the thiohydrazides

Table 3. Dissociation constants for thiophosphinoylthioformhydrazides, determined by potentiometric titration of the hydrazides (ca. 5×10^{-4} mol in 50 ml, 20°C) with 0.1 M aqueous NaOH.

Compound	pK_A, H_2O	$pK_A, 1:1$ (vol.) EtOH-H ₂ O
Et ₂ P(S)CSNHNH ₂	5.6 ^a	6.6 ^a
Et ₂ P(S)CSNHNHMe		6.4 ^a
Et ₂ P(S)CS ⁻ NN ⁺ H(Me) ₂	9.5 ^a	10.0 ^a
Et ₂ P(S)CSNHNHPh		4.9 ^b
Ph ₂ P(S)CSNHNH ₂		7.1 ^a

^a pH at half-neutralisation. ^b Calc. from $pK_A = 2pH - 14 - \log C_B$ at the equivalence point, since the hydrazide was poorly soluble.

with an *N*(2)H are freely soluble in 2 N NaOH showing the acidic character general for such thiohydrazides.³ Apart from the dipolar IIf, however, their pK_A -values are 4–5 p*K*-units lower than those for simple thiohydrazides³ (Table 3). This remarkable acid strength reflects the electron-attracting power of the R₂P(S) group. It is obscure to us that such strong acids are not isomerized to their dipolar isomers irrespectively of the degree of substitution at *N*(3). The compounds are somewhat weaker bases than simple thiohydrazides and could not be titrated as bases in 1:1 ethanol-water, although salts are formed with HCl in ether.

The barrier for rotation about the C(S)–N bond in dimethyl sulfoxide has been estimated for the thiohydrazide IIc. From the coalescence temperature for the *N*-CH₃ signals ($140 \pm 2^\circ\text{C}$) and the chemical shift difference at slow exchange (26.5 Hz at 40°C) an approximate ΔG^\ddagger value of 21.1 kcal/mol is calculated. This value is close to the two ΔG^\ddagger values published for the isomerization of *E* to *Z* (21.0) and *Z* to *E* isomers (22.4 kcal/mol) of 3-methyl-3-phenylthioformhydrazide.⁹ The R₂P(S) group thus seems to have no significant effect on the barrier for rotation about the C(S)–N bond in the thiohydrazides II.

EXPERIMENTAL

Analyses were carried out by the Microanalysis Department of this laboratory. Infrared spectra were recorded on a Perkin Elmer 337 Grating Infrared Spectrophotometer, and the proton magnetic resonance spectra on a Varian A-60 A or (in case of IIId and IIk) a Bruker HX-90 E instrument. The ΔG^\ddagger was calculated by the method given by Kessler.¹⁰

S-Methyl *P,P*-diethylthiophosphinoyldithioformate (Ia) was prepared as previously described.² *S*-Methyl *P,P*-diphenylthiophosphinoyldithioformate (Ib) was prepared from reaction of potassium diphenylthiophosphinoyldithioformate² suspended in ether with methyl iodide. Filtration and evaporation of the solvent gave (Ib) (ca. 70 %) which was sufficiently pure for preparation of the hydrazides.

Thiophosphinoylthioformhydrazides IIa-m. The following methods A–D have been used for the preparations. The choice of method and of solvent for recrystallization is shown in Table 1.

A. The ester (10^{-2} mol) in acetonitrile (50 ml) was mixed with an equimolar amount of the hydrazine at room temperature. After one minute the red colour of the reaction mixture had disappeared, and the mixture was evaporated to dryness at reduced pressure to give the crude product.

A'. The procedure is identical to A except that the reaction mixture was allowed to stand for 24 h before evaporation.

B. The ester (10^{-2} mol) in methylene chloride (50 ml) and the hydrazine (2×10^{-2} mol) were mixed at room temperature. The red colour disappeared immediately. The solution was extracted with 2 M aqueous NaOH (3×25 ml), the aqueous phase acidified (conc. HCl), extracted with methylene chloride (3×50 ml), and dried (MgSO_4). Evaporation of the solvent gave the crude product.

B'. The procedure is identical to B except that the reaction mixture was allowed to stand for 24 h before extraction.

C. The ester (10^{-2} mol) in dry ether (150 ml) was mixed with the hydrazine (2×10^{-2} mol) at room temperature. After 30 min the reaction mixture was evaporated to dryness in order to remove methanethiol. The residue was redissolved in dry ether (75 ml), and a solution of HCl in dry ether (ca. 4 M, 10 ml) was added with stirring. The precipitated hydrochloride was isolated by filtration, washed with HCl-ether, and dried. Treatment at 0°C with 2 M NaOH liberated the hydrazide, which was extracted with methylene chloride and isolated by evaporation of the solvent.

B + C. The reaction was performed as described in B, but the compound was isolated from the reaction mixture after the extraction with NaOH. The reaction mixture was evaporated to dryness, the residue dissolved in ether, and the hydrazide precipitated with HCl as described in C.

D. The ester (10^{-2} mol) in acetonitrile (70 ml) was mixed with phenylhydrazine (5×10^{-2} mol) at room temperature. After 10 min 4 M aqueous HCl (20 ml) was added with stirring, and the resulting precipitate was isolated by filtration, washed several times with 4 M HCl and then water to give the crude product.

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