78. *The Reaction of Thiourea with Dialkyl Phosphites and Trialkyl Phosphates.*

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Treatment of thiourea with dialkyl hydrogen phosphites and trialkyl phosphates affords *N*-alkylthiouronium alkyl phosphites and *N*-alkylthiouronium dialkyl phosphates respectively. The infrared and ultraviolet spectra, electrical conductivity, and the properties of these compounds in aqueous solution have been studied.

The numerous reactions of the dialkyl phosphites show their versatility in the synthesis of organophosphorus compounds, but no previous studies of the reaction of dialkyl phosphites with thiourea have been noted. However, compounds of the general type $NRR'\cdot CX\cdot NR\cdot CH_2\cdot S\cdot PO(OR)_2$ ($X = O$ or S) have been prepared by reaction of the appropriate urea or thiourea having an active hydrogen atom with formaldehyde and dialkyl hydrogen thiophosphate.[1]

Fig. 1. (1) *Thiourea.* (2) *Tri-n-butyl phosphate.* (3) *Reaction product of thiourea with tri-n-butyl phosphate.* (4) *Reaction product of thiourea with di-n-butyl hydrogen phosphate.*

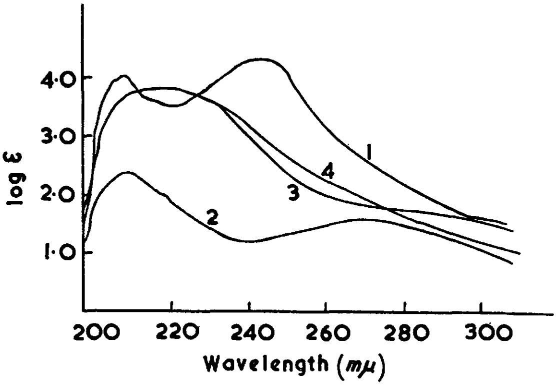
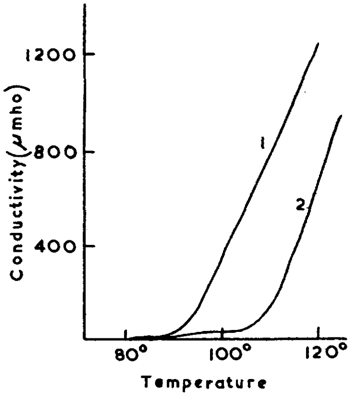


Fig. 2. *Electrical conductivity of: reaction product of thiourea* (1) *with tri-n-butyl phosphate and* (2) *with di-n-butyl hydrogen phosphite.*



Results.—A series of dialkyl hydrogen phosphites and trialkyl phosphates were mixed with thiourea in a 1 : 1 mole ratio. At room temperature no reaction took place but, on heating, the thiourea dissolved slowly to give a viscous brown oil which became dark brown above 150°. If heating was discontinued shortly after dissolution had just been effected, and the solution allowed to cool, crystalline products could be isolated in which the ratio of organic phosphorus residue to thiourea was 1 : 1. The ease of dissolution of thiourea increased on descent of homologous series and among isomers, *e.g.*, n- and iso-butyl compounds, the straight-chain compound dissolved the thiourea faster.

The solubility properties of the crystalline products varied considerably with the nature of the ester group in the parent phosphorus compound, a similar variation being noted in the carbamoyl phosphites formed by the base-catalysed reaction of dialkyl phosphites with isocyanates.[2]

Ultraviolet spectra. The ultraviolet spectra of typical compounds (in ethanol solution) are shown by Fig. 1, where the spectrum of the compound obtained from reaction of the dialkyl phosphite resembles that obtained from the trialkyl phosphate.

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[1] Hook and Moss, U.S.P. 2,566,288.

[2] Fox and Venezky, *J. Amer. Chem. Soc.*, 1956, **78**, 1664.

Conductivity. A further similarity in behaviour is shown in the conductivity and change in conductivity with temperature of the solid compounds (see Fig. 2). Both compounds have a very low conductance at room temperature, which increases on melting.

Infrared spectra. From a study of the infrared absorption bands for thiourea, Quagliano *et al.*[3] made the following assignments: NH_2 bending 1617 cm.$^{-1}$, NH_2 rocking 1450 cm.$^{-1}$, N–C–N stretching 1450 cm.$^{-1}$, C=S stretching 1059 and 757 cm.$^{-1}$. From a study of the infrared spectra of a number of dialkyl phosphites and trialkyl phosphates [4,5] the following assignments have been made: P–H stretching 2435 cm.$^{-1}$, P$\rightarrow$O stretching 1250—1300 cm.$^{-1}$, and P–O–C stretching 1030 cm.$^{-1}$ and 870 cm.$^{-1}$.

Both series of compounds obtained by reaction of thiourea with dialkyl phosphite and trialkyl phosphate were characterised by a P$\rightarrow$O absorption at 1200—1220 cm.$^{-1}$, a lower frequency than in the parent phosphite or phosphate. The band at 2435 cm.$^{-1}$ in the spectra of the present dialkyl phosphite suffered a shift to lower frequencies. The positions of the C=S bands were close to that in thiourea itself, and the NH_2 absorption was noted at 1695 cm.$^{-1}$.

In the region 950—1100 cm.$^{-1}$ a much greater resolution was achieved in the reaction products than in the parent phosphites or phosphates, though a lower intensity of absorption was obtained for the P–O–C band at 1030 cm.$^{-1}$.

Treatment of an aqueous solution of 0·1 mole of the product obtained from the reaction of thiourea with tri-n-butyl phosphate with 0·05 mole of uranyl nitrate acidified with a few drops of dilute nitric acid gave an almost quantitative precipitation of uranyl di-n-butyl phosphate. Evaporation of the filtrate gave a residue which after recrystallisation had m. p. 56°. Analyses for carbon, hydrogen, sulphur, and nitrogen indicated the residue to be *N*-n-butylthiouronium nitrate. A similar treatment of the products obtained from the dialkyl phosphites gave a uranyl precipitate which contained the thiourea residue, no thiourea compound being obtained from the filtrate. Treatment of both products obtained from the tri-n-butyl phosphate and di-n-butyl phosphite in sodium carbonate solution with sodium nitroprusside gave a red solution immediately, and with 3,5-dinitrobenzoic acid a derivative of m. p. 168° in each case.

Discussion.—The compounds isolated from the reaction of thiourea with dialkyl phosphites and trialkyl phosphates are formed by *N*-alkylation to form *N*-alkylthiouronium alkyl phosphites and *N*-alkylthiouronium dialkyl phosphates respectively. The dialkyl phosphites have been shown to react with cacotheline in sodium carbonate solution to give an intense red coloration.[6] The *N*-alkylthiouronium alkyl phosphites give no colour since monoalkyl phosphites give no reaction with cacotheline. Treatment of thiourea with trialkyl phosphites for 5 hr. did not result in *N*-alkylation. The shifts noted in the P$\rightarrow$O infrared absorption of the phosphate and phosphite compounds indicate considerable hydrogen bonding in these compounds and this doubtless plays an important part in the course of the reaction, allowing the possible formation of a hydrogen-bonded complex with the thiourea before alkylation takes place. Similar alkylations were attempted with urea but no reaction was noted, and use of thioacetamide instead of thiourea did not lead to *N*-alkylated products. The esters of sulphuric,[7] sulphurous,[8] and toluene-*p*-sulphonic [9] acids have been used frequently for the alkylation of amines, and Billman *et al.*[10] have described the alkylation of aromatic amines by trialkyl phosphates. In a study of the alkylation of phenols, Noller and Dutton[11] noted that alkyl borates, carbonates, nitrites, and

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[3] Yamaguchi, Penland, Mizushima, Lane, Curran, and Quagliano, *J. Amer. Chem. Soc.*, 1958, **80**, 527.

[4] Meyrick and Thompson, *J.*, 1950, 225.

[5] Bellamy and Beecher, *J.*, 1953, 728.

[6] Smith, *Analyt. Chim. Acta*, 1960, **22**, 249.

[7] Claesson and Lundwall, *Ber.*, 1880, **13**, 1700.

[8] Voss and Blanke, *Annalen*, 1931, **485**, 258.

[9] Marvel and Sekera, *J. Amer. Chem. Soc.*, 1933, **55**, 345.

[10] Billman, Radike, and Mundy, *J. Amer. Chem. Soc.*, 1942, **64**, 2977.

[11] Noller and Dutton, *J. Amer. Chem. Soc.*, 1933, **55**, 424.

phosphites were of no value though alkylation could be effected by trialkyl phosphates.

In order to assess the ability of thiourea and related compounds to undergo *N*-alkylation with other reagents and to form hydrogen-bonded compounds, thiourea was treated with dimethyl sulphoxide and dimethyl sulphite. In the former case a crystalline product was obtained, m. p. 55°, which decomposed immediately in water to give thiourea. Here alkylation did not take place and hydrogen-bonding forces alone were responsible for formation of the product. Dimethyl sulphite, on the other hand, as expected gave an analogous compound to that from trimethyl phosphate.

EXPERIMENTAL

The ultraviolet spectra were recorded in absolute ethanol solutions, a Unicam S.P. 500 spectrophotometer being used. The infrared spectra were recorded from Nujol mulls by use of a Perkin–Elmer Infra-cord spectrophotometer. The conductivity of the solid and fused compounds was recorded by melting the compound in a conductivity cell and allowing the melt to solidify. The conductance of the solid was then recorded at various temperatures up to the m. p., readings being made with a Wayne Kerr Universal bridge.

Reaction of Thiourea with Alkyl Phosphites and Alkyl Phosphates.—N-*n-Butylthiouronium n-butyl phosphite.* Thiourea (0·8 g.) was heated slowly with di-n-butyl phosphite (2·0 g.) to 135° and kept thereat until dissolution was complete. The temperature was then raised to 145°, and heating continued for 15 min. The mixture was cooled and extracted with hot carbon tetrachloride (3 × 50 ml.). The combined extract, on cooling, gave crude N-*n-butylthiouronium n-butyl phosphite* (1·40 g.) which, recrystallised from acetone, had m. p. 117° (Found: C, 39·2; H, 8·3; N, 9·95; S, 11·4; P, 11·9. $C_9H_{23}N_2O_3PS$ requires C, 40·0; H, 8·5; N, 10·4; S, 11·8; P, 11·9%).

N-*Alkylthiouronium salts*, $NHR{\cdot}CS{\cdot}NH_2,HX$.

R	X	Yield (%) *	M. p.†	R	X	Yield (%) *	M. p.†
(1) Pr^{i}	Pr^{i}O·PO·OH	39 ^{a}	165° ^{f}	(6) Pr^{n}	$(Pr^nO)_2PO_2$	32 ^{c}	124° ^{i}
(2) Et	EtO·PO(OH)	32 ^{a}	108 ^{g}	(7) Et	$(EtO)_2PO_2$	24 ^{a}	145 ^{g}
(3) Me	MeO·PO(OH)	34 ^{a}	112 ^{g}	(8) Me	$(MeO)_2PO_2$	27 ^{d}	138 ^{j}
(4) Bu^{n}	$(Bu^nO)_2PO_2$	33 ^{b}	97 ^{g}	(9) Allyl	$(Allyl)_2PO_2$	40 ^{b}	77 ^{k}
(5) Bu^{i}	$(Bu^iO)_2PO_2$	12 ^{c}	120 ^{h}				

	Found (%)						Required (%)				
	C	H	N	S	P	Formula	C	H	N	S	P
(1)	34·0	7·6	11·3	13·0	13·0	$C_7H_{19}N_2O_3PS$	34·7	7·85	11·6	13·2	12·8
(2)	27·8	7·0	12·8	14·5	14·9	$C_5H_{15}N_2O_3PS$	28·0	7·0	13·9	14·95	14·5
(3)	19·0	5·7	14·9	16·8	16·75	$C_3H_{11}N_2O_3PS$	19·4	5·9	15·05	17·2	16·7
(4)	44·5	8·9	8·1	9·3	9·15	$C_{13}H_{31}N_2O_4PS$	45·6	9·1	8·2	9·4	9·1
(6)	39·4	8·5	9·25	10·5	10·4	$C_{10}H_{25}N_2O_4PS$	40·0	8·3	9·3	10·7	10·3
(7)	32·0	7·3	10·6	12·2	12·1	$C_7H_{19}N_2O_4PS$	32·6	7·4	10·85	12·4	12·0
(8)	22·0	5·9	12·5	14·2	14·4	$C_4H_{11}N_2O_4PS$	22·2	6·0	13·0	14·8	14·35
(9)	40·1	6·4	9·4	10·8	10·6	$C_{10}H_{19}N_2O_4PS$	40·8	6·5	9·5	10·9	10·55

* Extracted by (*a*) hot $COMe_2$, (*b*) hot Et_2O, (*c*) cold Et_2O, (*d*) $CH_3{\cdot}CO_2Et$. † Crystallised from (*f*) $CHCl_3$, (*g*) $COMe_2$, (*h*) $Et_2O–CCl_4$, (*i*) $CH_3{\cdot}CO_2Et$, (*j*) $H_2O–COMe_2$, (*k*) Et_2O.

The reaction of thiourea with the other alkyl phosphites and alkyl phosphates was carried out in a similar manner, the salient features of the various syntheses being detailed in the annexed Table.

Reaction of Thiourea with Dimethyl Sulphoxide.—Thiourea (0·8 g.) was heated slowly with dimethyl sulphoxide (0·8 g.) for ½ hr. The mixture was cooled and washed with diethyl ether, and the *complex* crystallised from acetone; m. p. 55° (Found: C, 23·97; H, 6·64. $C_3H_{10}N_2OS_2$ requires C, 24·0; H, 6·7%). On treatment of the product with water, it dissociated completely, the resulting thiourea giving a precipitate immediately on addition of cupric chloride.

Reaction of Thiourea with Dimethyl Sulphite.—Thiourea (2·4 g.) was heated with dimethyl sulphite (3·30 g.) under reflux. The mixture was cooled and poured into acetone (200 c.c.); after standing, a crystalline product was obtained, which decomposed on standing. It dissolved in water, but no precipitate was obtained when cupric chloride was added to the solution. A crystalline derivative, m. p. 225°, was obtained on treatment with 3,5-dinitrobenzoic acid.

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