INTERACTION OF DIETHYL THIOPHOSPHITE WITH PHENOLIC MANNICH BASES

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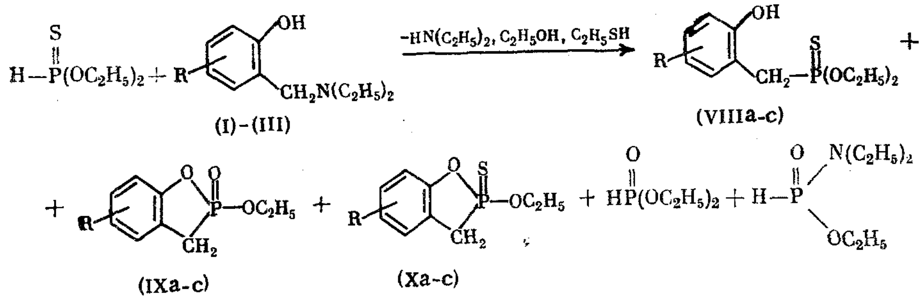
Phenolic Mannich bases (PMB) react with dialkyl phosphites to form o-hydroxybenzylphosphonate esters, which are converted at high temperatures to 2-oxo-2-alkoxy-1-oxaphosphaindans [1]. Dialkyl thiophosphites are known to behave like dialkyl phosphites in many reactions [2]. We have examined the interaction of diethyl thiophosphite (DTP) with o-(diethylaminomethyl)phenol (I), 2-(diethylaminomethyl)-4-methylphenol (II), 2-(diethylaminomethyl)-6-methylphenol (III), 2,5-bis(diethylaminomethyl)hydroquinone (IV), and some α-substituted methyldiethylamines of the type $(C_2H_5)_2N{-}CH_2{-}X$, where $X = OCH_3$ (V), $OCOCH_3$ (VI), and $N(C_2H_5)_2$ (VII).

The interaction of DTP with (I) in a stream of dry argon in absolute xylene at 140-145°C yielded several products; the ^{31}P NMR spectrum of the reaction mixture showed signals at δ −108, −116, and −46 ppm. The low-boiling fraction isolated during the reaction consisted of diethylamine, ethyl mercaptan, and ethanol, which were identified by GLC. Distillation of the residue under high vacuum gave in 30% yield OO-diethyl o-hydroxybenzylthiophosphonate (VIIIa), δ_P −108 ppm. During fractional distillation a cold trap collected diethyl phosphite and NN-diethyl O-ethyl amidophosphite [3] with δ_P −7 ppm, $J_{P-H} = 694$ Hz, and δ_P +1 ppm, $J_{P-H} = 612$ Hz, respectively.

Compound (VIIIa) rearranged over a period of 2-3 weeks. In the IR spectrum the P=S band in the 670 cm^{-1} region was joined by the bands of a phosphaindan heterocycle at 870 and 1180 cm^{-1} and a P=O band at 1250 cm^{-1}. Two triplets at δ 1.28 and 1.07 ppm appeared in the PMR spectrum. We assign the first to the phosphaindan structure and the second to phosphonate. After a month the product was crystalline 2-oxo-2-ethoxy-1-oxa-2-phosphaindan (IXa), δ_P −46 ppm.

On the basis of these considerations we suggest the following scheme for the interaction of DTP with (I):



R = H (I), 4-CH_3 (II), 5-CH_3 (III); R = H (VIIIa), 4-CH_3 (VIIIb), 5-CH_3 (VIIIc);
R = H (IXa) 5-CH_3 (IXb), 7-CH_3 (IXc); R = H (Xa), 5-CH_3 (Xb), 7-CH_3 (Xc)

The o- and p-substituted PMB's (II) and (III) reacted with DTP in the same way. The ^{31}P NMR spectrum of the reaction mixture showed signals at δ −108, −116, and −46 ppm. We were unable to isolate the products in the pure form by fractional distillation under high vacuum. The intensities in the ^{31}P NMR spectra of the fractions after distillation of the reaction mixture suggest that the first fraction contained mainly the products with chemical shifts δ_P −108 and −46 ppm but very little of the product with δ_P −116 ppm, whereas the second fraction was mostly the products with δ_P −116 and −46 ppm. These results were also

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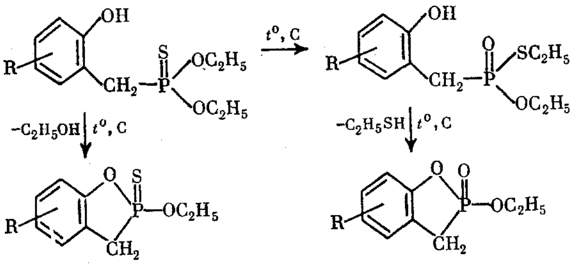
supported by TLC, since the number of products detected corresponded to the number of characteristic signals in the spectra.

Apparently the OO-diethyl o-hydroxybenzylthiophosphonates formed during the reaction can, under the forcing conditions of fractional distillation, undergo several transformations including thiono—thiolo isomerization

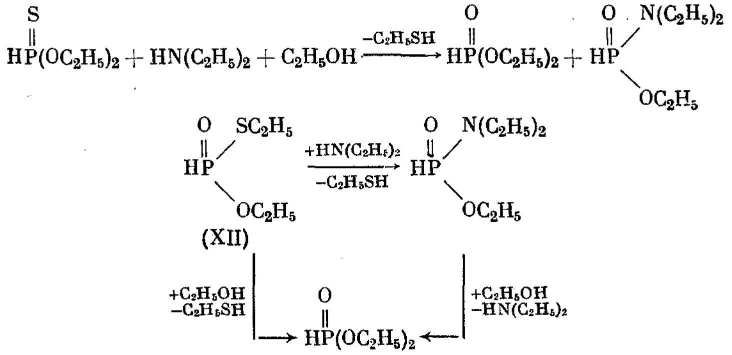


Examples of this kind of isomerization of thionophosphonate esters have been reported [4, 5].

We carried out the reaction of hydroquinone (IV) with DTP under equivalent conditions. Prolonged heating resulted in the formation of a high-melting precipitate. We were able to isolate from the reaction mixture after standing only tetraethyl 3,6-dihydroxy-1,4-xylylenediphosphonate (XI) with mp 180°C and δ_P −28 ppm [6].

The other concurrent process that reduces the yield of the sulfur-containing products is probably the disproportionation of DTP by reaction with the ethanol and diethylamine liberated during the reaction [7, 8]. To verify this conjecture we made a ^{31}P NMR study of the response of DTP to heating in sealed ampuls: a) of DTP itself at 140-160°C for 18 h; and b) with ethanol; c) with ethanol and diethylamine; and d) with diethylamine, all at 120-140°C for 5 h. In cases a) and b) DTP was unchanged, while in cases c) and d) we found almost complete disproportionation to form mainly NN-diethyl O-ethyl amidophosphite, δ_P +1 ppm, $J_{P-H} = 612$ Hz, and a small amount of diethyl phosphite, δ_P −7 ppm, $J_{P-H} = 694$ Hz.

We can write the reaction as



$$H\overset{S}{\overset{\|}{P}}(OC_2H_5)_2 + HN(C_2H_5)_2 + C_2H_5OH \xrightarrow{-C_2H_5SH} H\overset{O}{\overset{\|}{P}}(OC_2H_5)_2 + H\overset{O}{\overset{\|}{P}}(N(C_2H_5)_2)(OC_2H_5)$$

$$\underset{(XII)}{H\overset{O}{\overset{\|}{P}}(SC_2H_5)(OC_2H_5)} \xrightarrow[-C_2H_5SH]{+HN(C_2H_5)_2} H\overset{O}{\overset{\|}{P}}(N(C_2H_5)_2)(OC_2H_5)$$

$$\text{(XII)} \xrightarrow[-C_2H_5SH]{+C_2H_5OH} H\overset{O}{\overset{\|}{P}}(OC_2H_5)_2 \xleftarrow[-HN(C_2H_5)_2]{+C_2H_5OH} H\overset{O}{\overset{\|}{P}}(N(C_2H_5)_2)(OC_2H_5)$$

Apparently in the presence of diethylamine or the PMB itself product (XII) can be formed, and this is responsible for the formation of NN-diethyl O-ethyl amidophosphite and diethyl phosphite [4].

These processes did not take place in the interaction of DTP with α-substituted methyldiethylamines (V)-(VII). These reactions proceed in the same way as those with dialkyl phosphites [9] and gave in quantitative yield II-diethyl NN-diethylaminomethylthiophosphonate (XIII), which we were unable to prepare in the system amine—paraformaldehyde—diethyl thiophosphite. Mixing of the reactants caused the temperature of the reaction mixtures to rise to 40-50°C, while subsequent heating to 100°C resulted in reflux and the vigorous evolution of a low-boiling fraction, which GLC identified as methanol ($X = OCH_3$), diethylamine [$X = N(C_2H_5)_2$], and acetic acid ($X = OCOCH_3$); we removed acetic acid from the reaction mixture by pumping under 50-80 mm. We verified the structure of product (XIII) by elemental analysis and IR and ^{31}P NMR spectroscopy. Its IR spectrum showed the P=S band in the 620 cm^{-1} region but lacked absorption by the P=O group; the ^{31}P NMR spectrum had a signal at δ −94 ppm.

EXPERIMENTAL

The PMB's and DTP were synthesized by the methods of [10, 11]. The low-boiling fractions that distilled off in the course of the reaction were analyzed by GLC on a Khrom-3. The ^{31}P NMR spectra were recorded on a KGU instrument [10]. The reactions of the PMB's with DTP were carried out in a stream of dry argon; if an inert atmosphere was not used organophosphorus products not containing sulfur were formed. Resinification occurred in the absence of solvent.

Interaction of DTP with (I). Compound (I) (13.43 g) and DTP (11.55 g) were heated in absolute xylene (35 ml) at 148-150°C for 4 h. The low-boiling fraction (11 ml) contained diethylamine, ethyl mercaptan, and ethanol. After removal of the solvent fractional distillation under vacuum gave: 1) diethyl phosphite (3.5 g), bp 64°C (10 mm); n_D^{20} 1.4080; δ_P —7 ppm, $J_{P—H} = 694$ Hz [12]; 2) o-(diethylaminomethyl)phenol (3.2 g), bp 60-65°C (0.01 mm); n_D^{20} 1.5040; Found: N 7.62%. $C_{11}H_{17}NO$. Calculated: N 7.82%; 3) (VIIIa) (6 g, 31%), bp 103-105°C (0.001 mm); n_D^{20} 1.5530; δ_P —108 ppm, Found: P 11.87; S 11.87%. $C_{11}H_{17}O_3PS$. Calculated: P 11.92; S 11.30%; and 4) a fraction (2 g), bp 120-125°C (0.001 mm), n_D^{20} 1.5540; δ_P —108, —46 ppm.

The residue (4.2 g) was a solid bright orange mass, Found: S 11.09%. A trap cooled with liquid nitrogen collected a mixture (2.5 g) of diethyl phosphite (δ_P —7 ppm, $J_{P—H} =$ 694 Hz) and NN-diethyl O-ethyl amidophosphite (δ_P +1 ppm, $J_{P—H} = 612$ Hz).

Interaction of DTP with (II). Compound (II) (14.81 g) and DTP (11.85 g) were heated in absolute xylene (25 ml) at 150-155°C for 7 h. The low-boiling fraction (8 ml) contained diethylamine, ethyl mercaptan, and ethanol. After removal of the solvent fractional distillation of the reaction mixture under vacuum gave: 1) diethyl phosphite (3.2 g); 2) (IXb) (4.2 g), bp 120-121°C (0.001 mm); n_D^{20} 1.5230; δ_P —46 ppm; Found: C 55.87; H 6.30; P 14.90%. $C_{10}H_{13}O_3P$. Calculated: C 56.60; H 6.13; P 14.62%; and 3) a fraction (2 g), bp 135-136°C (0.001 mm); n_D^{20} 1.5385; δ_P —46 and —108 ppm, which precipitated (IXb) on standing for a month.

The residue (4 g) was a solid orange mass. A trap cooled with liquid nitrogen collected diethyl phosphite and NN-diethyl O-ethyl amidophosphite (1.5 g).

Interaction of DTP with (III). Compound (III) (19.3 g) and DTP (15.4 g) in absolute xylene (50 ml) were heated for 3 h under the conditions described above. The low-boiling fraction (9 ml) was distilled off and contained diethylamine, ethyl mercaptan, and ethanol. After removal of the solvent fractional distillation of the reaction mixture under vacuum gave: 1) diethyl phosphite (5.5 g); 2) (III) (7 g), bp 70-72°C (0.01 mm); n_D^{20} 1.5130; 3) a fraction (5.5 g), bp 100-110°C (0.001 mm); n_D^{20} 1.5500; δ_P —46, —108, and —116 ppm; and 4) a fraction (6 g), bp 110-115°C (0.001 mm); n_D^{20} 1.5740; δ_P —46 and —116 ppm; IR spectrum (ν, cm^{-1}): 1275 (P=O) and 680-690 (P=S).

On standing for a month (IXc) partially crystallized, mp 85-86°C [1].

A trap cooled with liquid nitrogen collected diethyl phosphite and NN-diethyl O-ethyl amidophosphite (1.8 g).

Interaction of DTP with (IV). Compound (IV) (14 g) and DTP (15.4 g) in absolute xylene (40 ml) were heated at 140-145°C for 7 h. The low-boiling fraction (6.5 ml) contained diethylamine, ethyl mercaptan, and ethanol. Heating was discontinued and xylene was stripped off. The residue was treated with alcohol and the dark gray precipitate with mp 230°C was filtered off. On standing white crystals of tetraethyl ester (XI) precipitated, yield 10.6 g (52%), mp 178-180°C (from ethanol) [6]. Found: C 46.87; H 6.80; P 14.86%. $C_{16}H_{28}O_8P_2$. Calculated: C 46.82; H 6.82; P 15.12%.

Interaction of DTP with (Methoxymethyl)diethylamine (V). To (V) (5.8 g) was added dropwise DTP (7.7 g). After the evolution of heat had ceased the reaction mixture was heated at 85°C for 20 min. The low-boiling fraction (1.8 ml) contained methanol. Fractional distillation gave (XIII) (9.3 g, 88.5%) with bp 120°C (10 mm); n_D^{20} 1.4661. Found: P 12.75; S 12.95%. $C_9H_{22}NPSO_2$. Calculated: P 12.97; S 13.38%.

Interaction of DTP with (Acetoxymethyl)diethylamine (VI). To (VI) (7.25 g) was added dropwise DTP (7.7 g). When the evolution of heat had ceased heating was continued at 80°C for 20 min, while CH_3COOH (2 g) was stripped off under 50-80 mm every 5 min. Fractional distillation gave (XIII) (9.64 g, 80%).

Interaction of Diethyl Thiophosphite with Bis(diethylamino)methane (VII). To (VII) (7.9 g) was added dropwise DTP (7.7 g); the temperature of the reaction mixture rose to 40°C. Subsequent heating to 130°C caused the mixture to reflux, which was continued for 40 min. The low-boiling fraction (4.5 ml) contained diethylamine. Fractional distillation gave (XIII) (11.47 g, 96%).

CONCLUSIONS

1. The interaction of phenolic Mannich bases with diethyl thiophosphite forms o-hydroxybenzylthiophosphonates, which undergo Pishchimuka rearrangement. Diethyl thiophosphite here disproportionates by reaction with diethylamine to form NN-diethyl O-ethyl amidophosphite and diethyl phosphite.

2. α-Substituted methyldiethylamines react with diethyl thiophosphite to form OO-diethyl NN-diethylaminomethylthiophosphonate.

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