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Oxidation of Phosphites by Means of *p*-Quinones and Benzyl Alcohol

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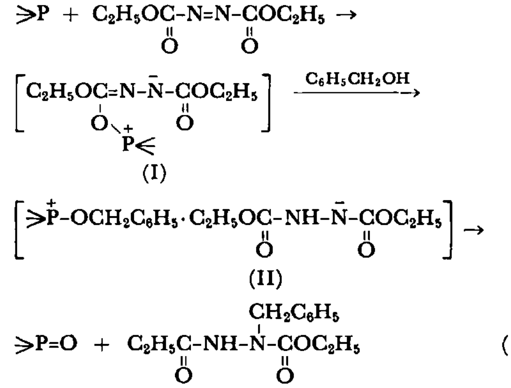
Triethyl phosphite and tri-*n*-butyl phosphite were oxidized to the corresponding trialkyl phosphates by means of *p*-quinones and benzyl alcohol. On the other hand, when diethyl (*N*-diethyl)phosphoroamidite was treated with *p*-benzoquinone and benzyl alcohol, 4-ethoxyphenyl ethyl (*N*-diethyl)phosphoroamidate was obtained in a 69% yield and no diethyl (*N*-diethyl)-phosphoroamidate was isolated. The reaction of 2, 3, 5, 6-tetrachloroquinone with diethyl benzyl phosphite in the presence of ethanol resulted in the formation of triethyl phosphate and 4-benzyloxy-2, 3, 5, 6-tetrachlorophenyl diethyl phosphate in 16% and 68% yields respectively.

Preceding paper[1] describes the oxidation of phosphites or phosphines to the corresponding phosphates or phosphine oxides by means of diethyl azodicarboxylate and benzyl alcohol. The reaction proceeds through the proposed intermediates of an imidoyl phosphonium salt (I) and benzyloxy phosphonium salt (II) from which the corresponding pentavalent phosphorus compound and diethyl *N*-benzylhydrazodicarboxylate were formed (Eq. (1)).



$$>P + C_2H_5O\underset{\overset{\|}{O}}{C}{-}N{=}N{-}\underset{\overset{\|}{O}}{C}OC_2H_5 \rightarrow$$

$$\left[\begin{array}{c}C_2H_5O\underset{\overset{|}{O}}{C}{=}N{-}\overset{-}{N}{-}\underset{\overset{\|}{O}}{C}OC_2H_5\\ \diagdown\overset{+}{P}<\end{array}\right] \xrightarrow{C_6H_5CH_2OH}$$

(I)

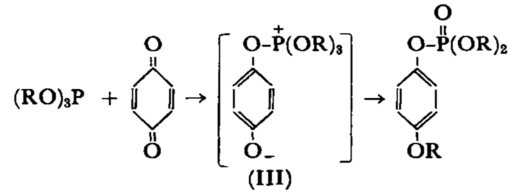
$$\left[>\overset{+}{P}{-}OCH_2C_6H_5\cdot C_2H_5O\underset{\overset{\|}{O}}{C}{-}NH{-}\overset{-}{N}{-}\underset{\overset{\|}{O}}{C}OC_2H_5\right] \rightarrow$$

(II)

$$>P{=}O + C_2H_5\underset{\overset{\|}{O}}{C}{-}NH{-}\overset{\overset{CH_2C_6H_5}{|}}{N}{-}\underset{\overset{\|}{O}}{C}OC_2H_5 \qquad (1)$$

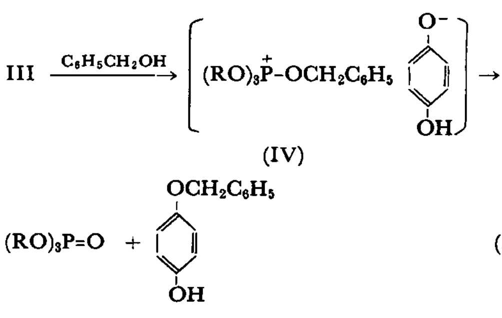
In the course of work aimed at the synthesis o esters of phosphoric acid, first objective of the present study was the oxidation of phosphites by the use of *p*-quinones and benzyl alcohol.

The reactions of quinones with trivalent phosphorus compounds have been investigated in considerable detail.[2] For example, Ramirez[3] demonstrated that the reaction of *p*-quinones with trialkyl phosphites resulted in the formation of the corresponding dialkyl 4-alkoxyaryl phosphates *via* quaternary phosphonium salt (III) (Eq. (2)).



(2)

Since the intermediate (III) is analogous in structure to I, III may be expected to react with benzyl alcohol to give benzyloxy phosphonium salt (IV). On the basis of the results reported earlier,[1,4] the phosphonium salt (IV) would decompose with the formation of trialkyl phosphate and 4-benzyloxyphenol (Eq. (3)).



(3)

When triethyl phosphite was treated with equimolar amounts of *p*-benzoquinone and benzyl alcohol in benzene at room temperature, triethyl phosphate, hydroquinone and hydroquinone dibenzyl ether were obtained in 80%, 71% and 44%

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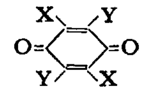
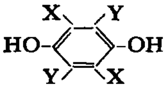
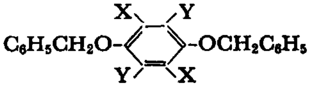
[1] O. Mitsunobu, M. Yamada and T. Mukaiyama, This Bulletin, **40**, 935 (1967).

[2] R. G. Harvey and R. DeSombre, "Topics in Phosphorus Chemistry (Edited by M. Grayson and E. J. Griffith), Vol. 1," Interscience Publishers, New York (1964), p. 96.

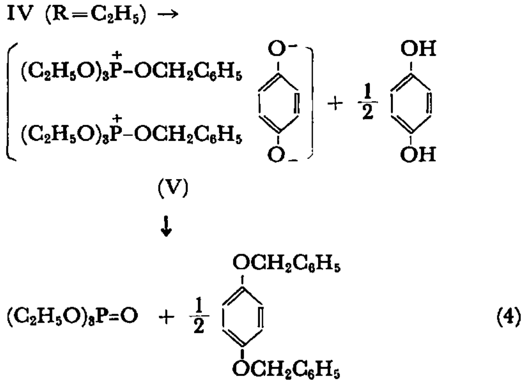
[3] F. Ramirez and S. Dershowitz, *J. Am. Chem. Soc.*, **81**, 587 (1959); F. Ramirez, E. H. Chen and S. Dershowitz, *ibid.*, **81**, 4338 (1959).

[4] T. Mukaiyama, O. Mitsunobu and T. Obata, *J. Org. Chem.*, **30**, 101 (1965).

Table 1. The oxidation of trialkyl phosphites by the use of *p*-quinones and benzyl alcohol

			Product		
		$(RO)_3P$	$(RO)_3P=O$		
X	Y	R	Yield, %	Yield, %	Yield, %
H	H	C_2H_5	80	71	44
H	H	n-C_4H_9	88		46
CH_3	H	C_2H_5	66	55	26
CH_3	H	n-C_4H_9	53		
Cl	Cl	C_2H_5	72	50	44
Cl	Cl	n-C_4H_9	47	53	54

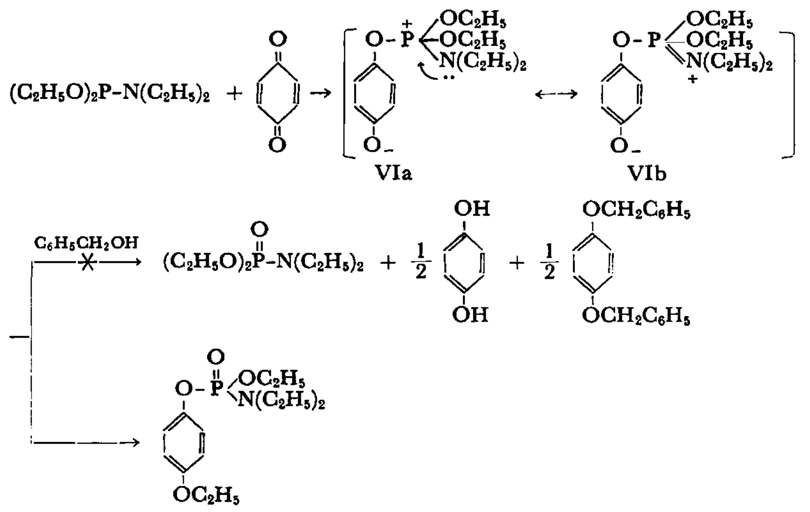
yields, respectively. No benzyloxyphenol, an expected product, could be isolated. The result suggests that an initially formed intermediate of benzyloxy phosphonium salt (IV) converts into a second quaternary phosphonium salt (V) and hydroquinone. The quaternary phosphonium salt (V) then in turn decomposes into the phosphate and the hydroquinone dibenzyl ether (Eq. (4)).



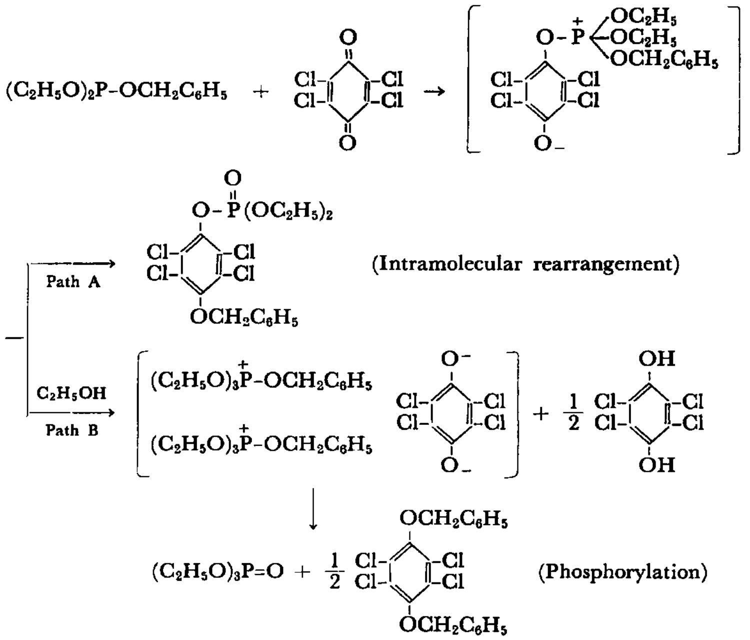
(4)

Similarly, triethyl phosphite and tri-*n*-butyl phosphite were oxidized to triethyl phosphate and tri-*n*-butyl phosphate by means of either 2, 3, 5, 6-tetrachloroquinone or 2, 5-dimethylquinone in the presence of benzyl alcohol. The results are summarized in Table 1.

Contrary to the successful oxidation of trialkyl phosphites by the use of *p*-quinones and benzyl alcohol, diethyl (*N*-diethyl)phosphoroamidate could not be obtained by the oxidation of diethyl (*N*-diethyl)phosphoroamidite by the present method. When diethyl (*N*-diethyl)phosphoroamidite was treated with equimilar amounts of *p*-benzoquinone and benzyl alcohol in refluxed benzene, 4-ethoxyphenyl ethyl (*N*-diethyl)phosphoroamidate was obtained in a 69% yield and benzyl alcohol(89%) was recovered. This result may be explained as follows. The positive charge of the initially formed phosphonium salt (VI) is not located on the phosphorus atom, but also resides partially on the nitrogen atom (VIa, b). Consequently, nucleophilic attack of the benzyl alcohol on the phosphorus atom becomes slower than the rearrangement of ethyl group and 4-ethoxyphenyl (*N*-diethyl)phosphoroamidate was predominantly formed (Eq. (5)).



(5)



(6)

As shown above, the reactions of *p*-quinones with trivalent phosphorus compounds in the presence of benzyl alcohol show close resemblance to those of diethyl azodicarboxylate and either benzyl or allyl alcohol.(1) Thus, the reaction of diethyl benzyl phosphite with 2, 3, 5, 6-tetrachloroquinone and ethyl alcohol was attempted with the assumption that the ethyl alcohol may be phosphorylated to give triethyl phosphate(1) (Eq. (6), Path B). However, contrary to our expectation, the main product of the reaction was 4-benzyloxy-2, 3, 5, 6-tetrachlorophenyl diethyl phosphate (68%) and triethyl phosphate was obtained only in 16% yield. This observation shows that the intramolecular rearrangement of the benzyl group of an intermediate (Eq. (6), Path A) take place more easily than the displacement of the aryloxy anion by the ethoxy anion (Eq. (6), Path B).

Experimental

Triethyl phosphite, tri-*n*-butyl phosphite and *p*-quinones were obtained from commercial sources. The solvents and alcohols were purified and dried by ordinary procedures. Diethyl benzyl phosphite was prepared by the procedure given in literature.(5)

Oxidation of Triethyl Phosphite by Means of *p*-Benzoquinone and Benzyl Alcohol. A solution of triethyl phosphite (8.30 g, 0.05 mol) in 10 m*l* of benzene was added drop by drop to a stirring solution of *p*-benzoquinone (5.40 g, 0.05 mol) and benzyl alcohol (5.40 g, 0.05 mol) in 100 m*l* of benzene at room temperature under nitrogen. Immediately, quinhydrone began to precipitate. After the reaction mixture was kept standing for 6 days at room temperature, quinhydrone was removed by filtration (0.32 g, 5.8%, mp 166—167°C, a mixture melting point with an authentic material was not depressed). The solvent was evaporated from the filtrate and hydroquinone dibenzyl ether thus formed was removed by filtration (3.17 g, 44%, an analytical sample was obtained by recrystallization from alcohol, mp 126—127°C. Found: C, 82.68; H, 6.39%). The filtrate was fractionated to give triethyl phosphate (7.30 g, 80%, bp 51—83°C/2 mmHg, redistillation nallowed the boiling point to 62—64°C/3 mmHg). The triethyl phosphate was shown to be identical with the authentic sample by comparison of infrared spectra. The residue of the fractionation was solidified on standing and washed with 10 m*l* of benzene-petroleum (1 : 1) to give hydroquinone (1.95 g, 71%).

Similarly, tributyl phosphate was obtained by the reaction of tri-*n*-butyl phosphite with *p*-quinone and benzyl alcohol.

Oxidation of Triethyl Phosphite by Means of 2, 3, 5, 6-Tetrachloroquinone and Benzyl Alcohol. A solution of triethyl phosphite (1.66 g, 0.01 mol) in 10 m*l* of benzene was added drop by drop to a stirring mixture of 2, 3, 5, 6-tetrachloroquinone (2.46 g, 0.01 mol) and benzyl alcohol (1.08 g, 0.01 mol) in 30 m*l* of benzene at room temperature. A red color appeared instantaneously together with dissolution of the quinone and faded after *ca.* 15 min. The mixture was refluxed for 100 min. After removal of the solvent, 2, 3, 5, 6-tetrachlorohydroquinone dibenzyl ether was obtained by filtration (0.95 g, 44%). An analytical sample was obtained by recrystallization from benzene, mp 174°C (Found: C, 55.37; H, 3.50%). Triethyl phosphate was obtained by fractionation of the filtrate (1.30 g, 72%). The residual oil which solidified on standing was taken up in benzene-ether (1 : 1). The solution was extracted with 5% aqueous sodium hydroxide. The aqueous solution was acidified to give 2, 3, 5, 6-tetrachlorohydroquinone (0.62 g, 50%, mp 234°C, undepressed by the admixture with an authentic sample).

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5) F. W. Hofmann and R. J. Ess, *J. Am. Chem. Soc.*, **78**, 5817 (1956).

Reaction of Diethyl (*N*-Diethyl)phosphoroamidite with *p*-Benzoquinone and Benzyl Alcohol. A solution of diethyl (*N*-diethyl)phosphoroamidite (1.93 g, 0.01 mol) in 10 m*l* of benzene was added to a solution of *p*-benzoquinone (1.08 g, 0.01 mol) and benzyl alcohol (1.08 g, 0.01 mol) in 20 m*l* of benzene. Immediately, the orange color of the solusolution changed to a deep red. The solution was refluxed for 2 hr. After the solvent was removed, the residue was fractionated to give recovered benzyl alcohol (0.96 g, 89%, bp 100—104°C/14 mmHg, redistillation gave bp 100—101°C/8 mmHg) and ethyl 4-ethoxyphenyl (*N*-diethyl)phosphoroamidate (2.08 g, 69.0%, bp 120—130°C/0.03 mmHg. An analytical sample was obtained by redistillation, bp 115—120°C/0.05 mmHg).

Found: N, 4.42%. Calcd for $C_{14}H_{24}NO_4P$: N, 4.65%.

Reaction of Diethyl Benzyl Phosphite with 2, 3, 5, 6-Tetrachloroquinone and Ethyl Alcohol. A solution of diethyl benzyl phosphite (2.28 g, 0.01 mol) in 10 m*l* of benzene was added to the mixture of 2, 3, 5, 6-tetrachloroquinone (2.46 g, 0.01 mol) and ethyl alcohol (2 m*l*) in 40 m*l* of benzene. The solution was allowed to stand for 24 hr at room temperature. After the removal of the solvent, the residue was fractionated to give triethyl phosphate (0.29 g, 16%, bp 69—74°C/2 mmHg) and 2, 3, 5, 6-tetrachlorohydroquinone (0.11 g, 8.9%) deposited on the inner wall of condenser. The remaining oil crystallized on standing (3.20 g, 67.6%, mp 68—86°C, an analytical sample was obtained by recrystallization from ether, mp 95—96°C). The crystalline compound was shown to be 4-benzyloxy-2, 3, 5, 6-tetrachlorophenyl diethyl phosphate on the bases of elemental analysis and its conversion into 2, 3, 5, 6-tetrachlorohydroquinone monobenzyl ether as outlined below.

Found: C, 42.84; H, 3.87%. Calcd for $C_{17}H_{17}Cl_4O_5P$: C, 43.07; H, 3.59%.

Reaction of 4-Benzyloxy-2, 3, 5, 6-tetrachlorophenyl Diethyl Phosphate with Sodium Ethoxide. The white crystalline compound obtained in the above experiment was added to a solution of sodium ethoxide (0.12 g of sodium was dissolved in 5 m*l* of ethyl alcohol) and was refluxed for 1 hr. After removal of the solvent from the red colored solution, the residue was dissolved in water and acidified with hydrochloric acid. The mixture was filtered to give 2, 3, 5, 6-tetrachlorohydroquinone monobenzyl ether (mp 130—136°C). Recrystallization from benzene-petroleum ether gave an analytical sample, mp 136—138°C.

Found: C, 46.15; H, 3.10%. Calcd for $C_{13}H_8Cl_4O_2$: C, 46.16; H, 2.37%.

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