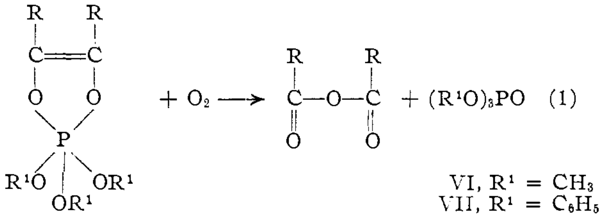
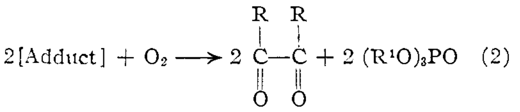
takes place when the 1:1 adducts[2,3] formed from tertiary phosphite esters $(R^1O)_3P$ and α-diketones, RCOCOR are allowed to react with dry molecular oxygen, in benzene solution at room temperature.

A stirred solution of the *colorless, crystalline* benziltrimethyl phosphite adduct[2a] I, m.p. 49°, in anhydrous benzene was kept at room temperature for five days under a slight pressure of dry oxygen. The mixture obtained upon removal of the benzene under reduced pressure contained benzoic anhydride (IV, *ca.* 30%), benzil (VIII, *ca.* 67%) and trimethyl phosphate (VI, *ca.* 94%).

The composition of the reaction mixture was ascertained by examination of its infrared spectrum and by actual isolation of the three substances in the stated yields. The presence of benzoic anhydride was confirmed by the direct formation, from the reaction mixture, of benzanilide and of benzoic acid. These results conform to the equations


VI, $R^1 = CH_3$
VII, $R^1 = C_6H_5$

I, R = C_6H_5; $R^1 = CH_3$ IV, R = C_6H_5
II, R = $R^1 = C_6H_5$ V, R = CH_3
III, R = $R^1 = CH_3$



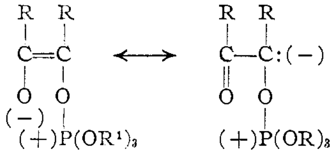
$$2[\text{Adduct}] + O_2 \longrightarrow 2\ \underset{O}{\overset{R}{C}}{-}\underset{O}{\overset{R}{C}} + 2\ (R^1O)_3PO \quad (2)$$

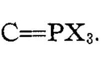
VIII, R = C_6H_5 VI, $R^1 = CH_3$
IX, R = CH_3 VII, $R^1 = C_6H_5$

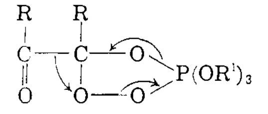
A similar, although faster, reaction was observed between molecular oxygen and the colorless, crystalline benzil-triphenylphosphite adduct,[2a] II, m.p. 99°. Benzoic anhydride (IV, *ca.* 25%), benzil (VIII) and triphenyl phosphate (VII) were isolated after three days.

Oxygen reacted also with the colorless, liquid biacetyl-trimethyl phosphite adduct[2a], III. The reaction appeared to be slower and gave acetic anhydride (V, at least 10–15%), biacetyl (IX, over 61%) and trimethyl phosphate (VI, *ca.* 80%) after nine days. A fourth substance, not yet identified, also was formed in *ca.* 15% yield.

In another communication[2a] we have summarized the evidence bearing on the structure of the α-diketone-tertiary phosphite adducts and of the *o*-quinone-tertiary phosphite adducts. The proton and phosphorus nuclear magnetic resonance spectra, the dipole moments and the infrared spectra are consistent only with cyclic structures I, II, III, for these adducts.[2a,3a] The results of the reactions of the adducts with anhydrous hydrogen chloride in ether solution and with bromine in carbon tetrachloride solution at low temperatures were also described.[2a] These reactions could be interpreted as attacks on the cyclic pentacovalent structures or on open dipolar forms such as Ia, IIa, IIIa. The latter could conceivably be present in small amounts in solutions of the adducts.


Ia, IIa, IIIa etc.

It seems possible that the oxygen-induced carbon-skeleton rearrangement, and the oxidative dephosphorylation observed with the adducts in benzene solution at room temperature, proceed via an intermediate such as X. X is essentially an "ozonide" derived from a phosphinemethylene,  $\overset{R}{\underset{R^1}{>}}C{=}PX_3$. It could decompose to the anhydride (IV or V) or could react with more adduct to give the original α-diketone (VIII or IX). These and other hypotheses are under investigation.


X

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Received March 23, 1960

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[3] For other reports on "liquid" α-diketone-*trialkyl* phosphite adducts see: (a) G. H. Birum and J. L. Dever, Abstracts, Div. of Org. Chem., A.C.S. Meeting, Chicago, Ill., Sept. 1958, p. 101-P; (b) V. A. Kukhtin, *Doklady Akad. Nauk, S.S.S.R.*, **121**, 466 (1958); *C. A.*, **53**, 1105b (1959).

CRYSTALLINE 1:1 ADDUCTS FROM THE REACTION OF TERTIARY PHOSPHITE ESTERS WITH *ortho*-QUINONES AND WITH *alpha*-DIKETONES. NEW ROUTES TO QUINOL-MONOPHOSPHATES AND TO KETOL-MONOPHOSPHATES[1]

Sir:

Extending our investigations[2] on the reactions of trivalent phosphorus compounds with quinones and with other carbonyl compounds (OAO), we have made observations which have a bearing on the problem of the pentacovalency of phosphorus, and which introduce new methods for the preparation of quinol-monophosphates.

(1) Trialkyl and triaryl phosphites react with *o*-quinones and with α-diketones[3] to form colorless, 1:1 adducts, $[(OAO{\cdot}P(OR)_3]$. Some of these adducts can be obtained in crystalline form and are stable in the absence of both air and moisture. Information derived from proton and phosphorus

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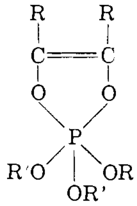
[1] Acknowledgment is made to the Donors of the Petroleum Research Fund Administered by the American Chemical Society for partial support of this Research (Grant 286-A), and to the National Cancer Institute of the National Institutes of Health (Grant CY-4769).

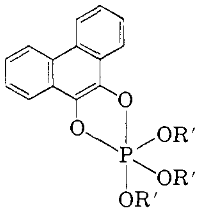
[2] (a) F. Ramirez and S. Dershowitz, This Journal, **78**, 5614 (1956); (b) *J. Org. Chem.*, **22**, 856 (1957); (c) **22**, 1282 (1957); (d) **23**, 778 (1958); (e) This Journal, **81**, 587 (1959); (f) F. Ramirez, E. H. Chen and S. Dershowitz, *ibid.*, **81**, 4338 (1959); (g) F. Ramirez, H. Yamanaka and O. H. Basedow, *J. Org. Chem.*, **24**, 1838 (1959).

[3] Other recent reports on the reaction of trialkyl phosphites with *α-diketones:* (a) G. H. Birum and J. L. Dever, Abstracts, Div. of Org. Chem., A.C.S. Meeting, Chicago, Ill., Sept., 1958, p. 101-P; (b) V. A. Kukhtin, *Doklady Akad. Nauk. S.S.S.R.*, **121**, 466 (1958); *C. A.*, **53**, 1105b (1959). The latter two mention "liquid" adducts only.

nuclear magnetic resonance spectra, dipole moments and infrared spectra is consistent only with cyclic structures containing pentacovalent phosphorus, such as I, II, III, IV and V.



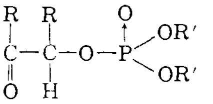
I, R = C_6H_5; R′ = CH_3; m.p. 49°
II, R = R′ = C_6H_5; m.p. 99°
III, R = R′ = CH_3; $n^{20}D$ 1.4391



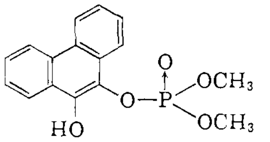
IV, R′ = CH_3; m.p. 74°
V, R′ = C_6H_5; m.p. 147°

(2) Evidently, the alkyl group translocation which takes place during the reaction of *p*-quinones with certain trialkyl phosphites[2e,f] and which gives rise to alkyl ethers of *p*-quinol monophosphates, *p*-$ROC_6H_4OP(O)(OR)_2$, does not occur with *o*-quinones. Contrary to a recent report,[3b] no alkyl group translocation has been observed in the reaction of α-diketones.

(3) The adducts react readily with *anhydrous hydrogen chloride* in ether solution. The trimethyl phosphite adducts, I, III and IV give α-ketol-monophosphates or *o*-quinol-monophosphates, VI, VII and VIII, respectively. This represents a convenient preparation of a type of compound of interest in biological chemistry.



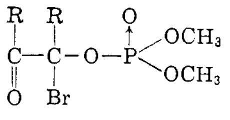
VI, R = C_6H_5; R′ = CH_3 (m.p. 78°)
VII, R = R′ = CH_3 ($n^{22}D$ 1.4215)



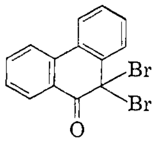
VIII, m.p. 132°

One of the *triphenyl* phosphite adducts (V) did not react with hydrogen chloride, while the other, II, afforded desyl chloride $C_6H_5COCHCl$-C_6H_5 and triphenyl phosphate $(C_6H_5O)_3PO$.

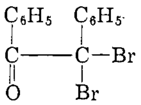
(4) The adducts react instantaneously with *bromine in carbon tetrachloride solution* at low temperatures. Two of the trimethyl phosphite adducts, I and III, gave α-bromo-α-ketol-monophosphates, IX and X, respectively. The third, IV, was converted into a dibromo ketone, XI. The triphenyl phosphite adducts, II and V, gave dibromoketones, XII and XI, respectively.



IX, R = C_6H_5; m.p. 118°
X, R = CH_3

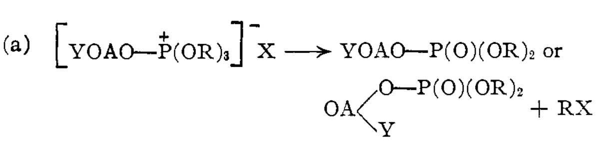


XI, m.p. 106°

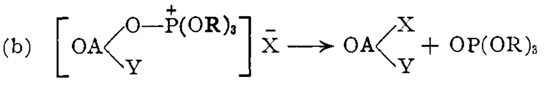


XII, m.p. 112°

These reactions could be interpreted as attacks of a reagent YX (HCl or Br_2) on the open, dipolar form of the adducts, $\overset{-}{O}AO-\overset{+}{P}(OR)_3$, or on the cyclic forms themselves. In any event, the reactions conform to the general expressions



$$\text{(a)}\quad \left[\text{YOAO}-\overset{+}{\text{P}}(\text{OR})_3\right]^{-}\text{X} \longrightarrow \text{YOAO}-\text{P(O)(OR)}_2 \text{ or } \text{OA}\genfrac{}{}{0pt}{}{\text{O}-\text{P(O)(OR)}_2}{\text{Y}} + \text{RX}$$



$$\text{(b)}\quad \left[\text{OA}\genfrac{}{}{0pt}{}{\text{O}-\overset{+}{\text{P}}(\text{OR})_3}{\text{Y}}\right]\overset{-}{\text{X}} \longrightarrow \text{OA}\genfrac{}{}{0pt}{}{\text{X}}{\text{Y}} + \text{OP(OR)}_3$$

Step (a) achieves the *reductive phosphorylation* of the carbonyl compound OAO, while step (b) effects its partial deoxygenation.

The trimethyl phosphite adducts were obtained in benzene solution at room temperature. The triphenyl phosphite adducts were prepared at 100° in the absence of solvent. Yields are nearly quantitative and the crystalline substances can be recrystallized from hexane. Some of the adducts (I and III) could be distilled unchanged, at reduced pressures.

Satisfactory elemental analyses were obtained for all new compounds. The molecular weight of the adducts corresponds to the monomeric formulas. The proton n.m.r. spectrum[4] of the biacetyl adduct, III, had one peak for the methyl group protons and one peak for the methoxyl group protons disclosing considerable symmetry. The phosphorus n.m.r. spectra[5] showed these chemical shifts (± 2 p.p.m.) relative to 85% H_3PO_4: I, +53, III, +53 and IV, +49. (The solids were examined in benzene solution.) The dipole moments[4] of the five adducts measured in benzene at 25° were very similar and close to 2 Debye units.

The characteristic feature of the infrared spectra[6] of the trimethyl phosphite adducts, I, III and IV, was a set of six bands in the 8.5–10.5μ region (P-O-C) with a very strong band at 9.40–9.45μ. The triphenyl phosphite adducts, II and V, had very strong bands at 8.25–8.30μ and 10.40–10.42μ.

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[4] We are grateful to Professor M. T. Rogers of Michigan State University for this determination. The dipole moments measured by Prof. Rogers will be described in detail elsewhere.

[5] Obtained through the courtesy of Drs. N. McKelvie and J. Lancaster of the American Cyanamid Co., Stamford, Conn. A detailed discussion will appear elsewhere.

[6] The adducts were examined as mineral oil mulls, as liquid films and in solutions in carbon tetrachloride and carbon disulfide. No significant differences were observed in the various media.

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RECEIVED MARCH 23, 1960

THE USE OF METABOLIC INHIBITORS IN THE STUDY OF MICROBIAL TRANSFORMATIONS OF ORGANIC COMPOUNDS

Sir:

In the study of microbiological transformations of organic compounds such as steroids, alkaloids, vitamins, amino acids, etc., one often observes that some microörganisms are capable of oxidizing organic compounds readily to carbon dioxide and water without the apparent accumulation of any intermediates. These intermediates are highly desirable not only because they are often biologically active (*e.g.*, hydrocortisone) but also because