

bonds. The resulting C_2 radicals proved to be effective in capturing the "hot" P^{32} atoms for formation of chemically stable C_2-P^{32} derivatives.

The possibility that the organic P^{32} compounds described in this paper are the chemical reaction products of P^{32} -oxyacids and glycerol was eliminated by the experimental observation that a mixture of glycerol and $H_3P^{32}O_3$ at room temperature yielded very little glycerophosphorous acid; no other compounds were observed. γ -Irradiation products of a $H_3P^{32}O_4$ -glycerol mixture contained unchanged $H_3P^{32}O_4$, some glycerophosphoric acid- P^{32} (probably in an equilibrium concentration), and other unrecognizable substances which were not identical with the neutron activation products. None of the neutron activation products was detectable by paper chromatographic spray reagents, whereas the starting materials, $H_3P^{31}O_4$ and glycerol, were easily detected by these reagents. Thus the organic products are considered to be products of "hot atom" reactions of P^{32} with the medium.

Nascent P^{31} atoms from related nuclear processes

have recoil energies comparable to those of P^{32} atoms. The products of their reactions would be organophosphorus compounds of P^{31} . One might consider the sources of the phosphate esters which could accumulate in extra-terrestrial²⁰ environments during chemical evolution²¹ and prior to origin of life. Some of these might result from nuclear processes on silicates to yield organophosphorus derivatives which could be oxidized by suitable minerals. The surprisingly rapid metabolism of phosphonic acids by primitive microorganisms²² and the occurrence of a phosphonic acid (2-aminoethanephosphonic acid)²³ in nature suggest synthetic applications and possible relationships of reactions revealed in this study.

(20) It is recognized that terrestrial conditions did not include an appreciable neutron flux during the era of chemical evolution.

(21) (a) M. Calvin, *American Scientist*, **44**, 248 (1956); (b) M. Calvin, *Naturwissenschaften*, **17**, 387 (1956).

(22) I. D. Zeleznick, T. C. Myers, and E. B. Titchener, *Federation Proc.*, **20**, 41 (1961).

(23) (a) M. Horiguchi and M. Kandatsu, *Nature*, **184**, 901 (1959); (b) J. S. Kittredge, E. Roberts, and D. G. Simonsen, *Biochem.*, **1**, 624 (1962).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE STATE UNIVERSITY OF NEW YORK AT STONY BROOK, N. Y.]

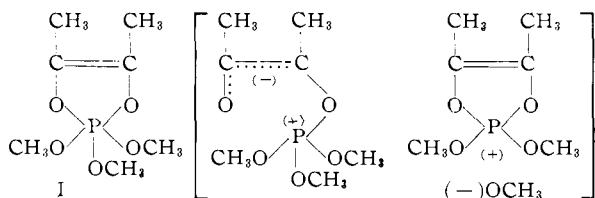
Cyclic Saturated Oxyphosphoranes and their Hydrolysis to Cyclic Phosphate Esters. The Diastereomeric 2:1 Biacetyl-Trimethyl Phosphite Adducts¹

BY FAUSTO RAMIREZ,² N. RAMANATHAN, AND N. B. DESAI

RECEIVED JUNE 6, 1963

Trimethyl phosphite reacts rapidly with the α -diketone biacetyl to form exclusively a 1:1 adduct having a cyclic unsaturated oxyphosphorane structure with the new 1,3-dioxaphospholene ring system. The 1:1 adduct reacts slowly with more biacetyl to form two diastereomeric forms of a 2:1 adduct having a cyclic saturated oxyphosphorane structure with the new 1,3-dioxaphospholane ring system. The pentavalent-phosphorus structures are based on: solubility in pentane, P^{31} n.m.r., H^1 n.m.r., and infrared spectra, and on the results of hydrolysis in aprotic solvents. The diastereomeric 2:1 adducts undergo a very rapid and exothermic reaction with one mole equivalent of water and yield diastereomeric cyclic phosphotriesters. A stereomutation at phosphorus was observed in the *meso*-cyclic phosphotriester.

We have described new organic compounds of phosphorus in which the phosphorus atom appears to be covalently bound to five oxygen atoms.^{1c} Typical of these substances is the biacetyl-trimethyl phosphite 1:1 adduct I. This is formed rapidly and exothermally when the diketone biacetyl is added to one mole equivalent of the phosphite ester at 10°. The properties of this pentane-soluble adduct are in better agreement with a *cyclic unsaturated oxyphosphorane* structure, I, derived from the 1,3-dioxaphospholene ring system, than with ionic structures.^{1c}



Experiments in which the biacetyl/phosphite mole ratio was greater than one, and in which the reaction was allowed to proceed for several hours, yielded a new substance. This observation was investigated in greater detail and the results are described in this paper.³

(1) (a) Organic Compounds with Pentavalent Phosphorus, Part X. (b) Part IX: F. Ramirez, N. B. Desai, and N. Ramanathan, *J. Am. Chem. Soc.*, **85**, 1874 (1963); (c) Part VIII: F. Ramirez and N. B. Desai, *ibid.*, **85**, 3252 (1963), and references therein.

(2) Alfred P. Sloan Fellow 1961-1963. Acknowledgment is made to the Cancer Institute of the National Institute of Health (CY-4769); the National Science Foundation (G 19509); and the Petroleum Research Fund of the A.C.S. (286-A) for generous support of this research.

(3) A preliminary account of parts of this work appeared in ref. 1b and in *J. Am. Chem. Soc.*, **84**, 1317 (1962).

Results

The biacetyl-trimethyl phosphite 1:1 adduct I reacted slowly with a second mole of biacetyl yielding a colorless, distillable oil. Analysis of this material agreed with the formula $C_{11}H_{21}O_7P$, which corresponds to a biacetyl-trimethyl phosphite 2:1 adduct. The data discussed below show that the oil is a mixture of the two possible diastereomeric forms of a *cyclic saturated oxyphosphorane*, IIa and IIb, a new type of organic compound with pentavalent phosphorus, derived from the 1,3-dioxaphospholane ring system. In one of the diastereomers, IIa, the two acetyl groups are *cis* to each other; in the other, IIb, they are *trans* to each other. The isomers are formed in the approximate proportion of 4:1, respectively.

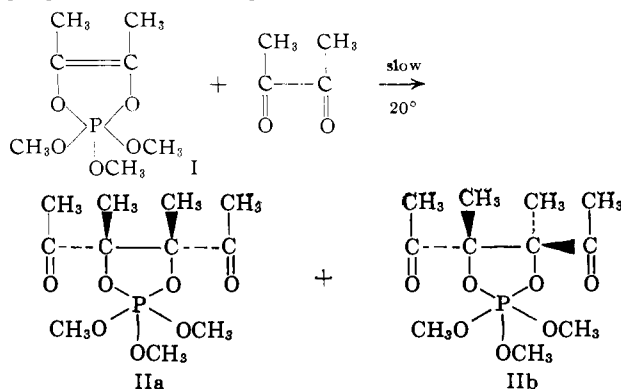


Table I (expt. 3 and 1) shows that an excess of biacetyl leads to higher yields of 2:1 adducts, IIa +

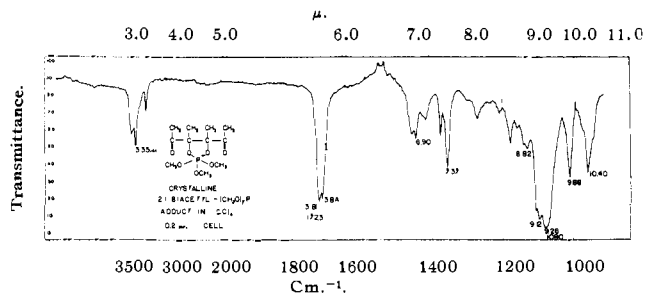


Figure 1.

I**b**. The reaction time is important, as seen in expt: 3 *vs.* 5, and 1 *vs.* 2.

The 1:1 adduct I need not be isolated in the preparation of the 2:1 adducts IIa and I**b**. This is shown in expt. 6-9 of Table I. For example, three moles of biacetyl were added, dropwise, with stirring, to one mole of trimethyl phosphite, the mixture being kept at 10° during the exothermic phase of the reaction. The second phase of the reaction was then allowed to proceed at 20° for 5 days (*cf.* expt. 7).

TABLE I

REACTION OF BIACETYL WITH THE BIACETYL-TRIMETHYL PHOSPHITE 1:1 Adduct I, AND WITH TRIMETHYL PHOSPHITE, AT 20°, IN A NITROGEN ATMOSPHERE

Expt.	Mole ratio ^a	Reacn. time, hr.	2:1 adduct, ^b %
1	1	120	67
2	1	96	52
3	3	120	91
4	3	48	87
5	3	24	40
6	2.5	72	83
7	3	120	87
8	3	170	87
9	4	96	92

^a Biacetyl/1:1 adduct (I) in expt. 1-5; biacetyl/trimethyl phosphite in expt. 6-9. ^b Distilled mixture of *meso* and *racemic* isomers (IIa + I**b**) of the biacetyl-trimethyl phosphite 2:1 adduct, *n*_D²⁵ 1.4471, collected at 65-75° (*ca.* 0.1 mm.); moisture must be excluded in handling the 1:1 and the 2:1 adducts.

The adducts IIa and I**b** are remarkably soluble in pentane; for instance, 40 g. of the original liquid mixture dissolved in 10 ml. of pentane. Crystals of the major isomer IIa separated from this solution in *ca.* 60% yield (or 53% yield based on trimethyl phosphite, in the case of expt. 7, Table I).

The minor isomer I**b** has not been isolated in a stereochemically pure form. The viscous oil which remained after removal of the crystalline isomer IIa consisted of approximately equal parts of both isomers IIa + I**b**. The yield of this enriched isomer mixture was 35% after distillation (or 30% yield based on trimethyl phosphite in expt. 7).

For reasons discussed below, the *meso*-configuration IIa with *cis*-acetyl groups is assigned to the major crystalline diastereomer. The *racemic* or DL configuration I**b** with *trans*-acetyl groups is assigned to the minor diastereomer.

Structure of the Biacetyl-Trimethyl Phosphite 2:1 Adducts Based on Physical Data.—Three types of materials must be discussed: (1) the original liquid mixture of isomers; (2) the crystalline major isomer which was obtained from this mixture by crystallization from pentane; (3) the liquid mixture of isomers which remained after the crystallization process.

(a) **The P³¹ n.m.r. spectra** of these three materials, (1), (2), and (3), gave one strong peak at +51 ± 2

(3a) NOTE ADDED IN PROOF.—The P³¹ n.m.r. spectra were initially obtained at 16 Mc./sec. The spectrum of the *meso* adduct IIa at 40.5 Mc./sec.

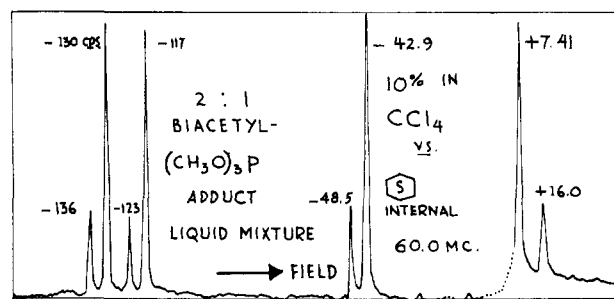


Fig. 2.—Proton n.m.r. spectrum of the original mixture of diastereomeric biacetyl-trimethyl phosphite adducts in CCl₄ solution at 60 Mc. The line of the cyclohexane used as internal reference has been omitted. The shifts relative to tetramethylsilane are: major isomer, 6.51 (*J*_{HP} 13 c.p.s.), 7.85, and 8.69 τ ; minor isomer, 6.40 (*J*_{HP} 13 c.p.s.), 7.75, and 8.83 τ .

p.p.m.^{3a} to high field of the external reference, 85% H₃PO₄. The liquids were examined neat, and the solid in a concentrated benzene solution. The P³¹ chemical shift of the 1:1 biacetyl-adduct I is +53 ± 2 p.p.m.^{3b} *vs.* 85% H₃PO₄.^{1c} These relatively large positive chemical shifts in the P³¹ n.m.r. spectra suggest penta-covalent phosphorus in the adducts, *i.e.*, oxyphosphorane structures.^{1c}

(b) **The infrared spectra** of the three materials, (1), (2), and (3), in CCl₄ solution were very similar. The spectrum of the crystalline major isomer IIa is reproduced in Fig. 1. The split band at 5.81 and 5.84 μ is due to C=O stretching vibrations. The very strong bands at 9.12 and 9.26 μ are due to POCH₃ stretching vibrations. The corresponding bands in the spectrum of the 1:1 biacetyl adduct I are found at 9.18 and 9.30 μ .^{1c}

(c) **The H¹ n.m.r. spectra** of the three materials, (1), (2), and (3), in CCl₄ solution showed significant differences. These spectra are reproduced in Fig. 2, 3, and 4, respectively. Figure 2 shows that the original

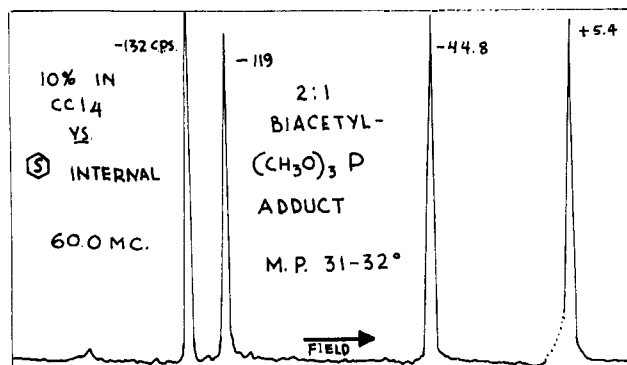


Fig. 3.—Proton n.m.r. spectrum of the crystalline major isomer of the biacetyl-trimethyl phosphite 2:1 adduct in CCl₄ solution at 60 Mc. The line of the cyclohexane used as internal reference has been omitted. The shifts relative to TMS are: 6.48 (*J*_{HP} 13 c.p.s.), 7.82, and 8.65 τ .

liquid mixture (1) consisted of approximately 80% of one isomer, IIa, and 20% of the other, I**b**. This mixture yielded *ca.* 60% of crystalline *meso* isomer IIa; *cf.* Fig. 3. The doublet at 6.48 τ in Fig. 3 is due to the

had eight of the expected ten lines due to the coupling between the phosphorus and the methoxyl protons, *J*_{PH} = 12.8 c.p.s. In CCl₄ solution δ _{PH} = +54.83 ± 0.04 p.p.m.; in a fresh CH₃OH solution, δ _{PH} = +54.26 ± 0.04 p.p.m. Measurements by Mr. S. R. Heller of this Department.

(3b) NOTE ADDED IN PROOF.—At 40.5 Mc./sec. the spectrum of the 1:1 biacetyl adduct I had eight of the expected ten lines, *J*_{PH} = 12.8 c.p.s.; δ _{PH} = +48.92 ± 0.02 p.p.m. (neat liquid), δ _{PH} = +48.89 ± 0.04 p.p.m. (fresh CH₃OH solution). For a recent compilation of P³¹ n.m.r. data see R. A. Y. Jones and A. R. Katritzky, *Angew. Chem. Int. Ed. Engl.*, **1**, 32 (1962).

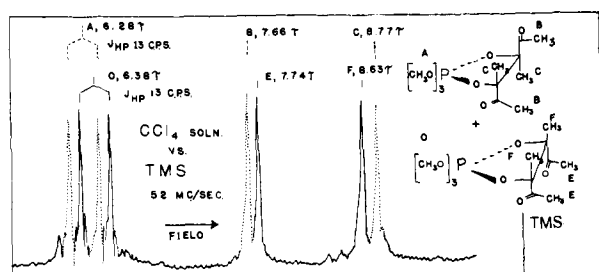


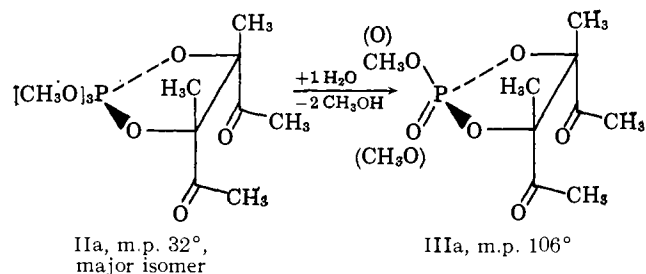
Figure 4.

protons of the CH_3OP groups, whose signals are split by the P^{31} nucleus, $J_{\text{HP}} = 13$ c.p.s. The appearance of *one doublet* only shows that the three methoxyl groups attached to the phosphorus are equivalent or, less likely, indistinguishable. The H^1 n.m.r. spectrum of the 1:1 adduct I showed also *one doublet* at 6.51τ , $J_{\text{HP}} = 13$ c.p.s., due to the three methoxyl groups attached to phosphorus.^{1c} The three methoxyl groups of $(\text{CH}_3\text{O})_3\text{PO}$ give rise to one doublet at 6.30τ , *i.e.*, its protons are somewhat less shielded than those in the oxyphosphoranes.

The singlet at 7.82τ in Fig. 3 is due to the protons of the two equivalent acetyl groups. The corresponding line in acetone⁴ is at 7.83τ . The singlet at 8.65τ is due to the protons of the two equivalent methyl groups attached to tetragonal carbon. The relative intensities are approximately 3:3:4:4, as expected. The two methyl groups of the 1:1 biacetyl adduct I give rise to a singlet at 8.25τ as expected from less shielded protons, *i.e.*, protons of methyl groups attached to trigonal carbon.^{1c}

Figure 4 confirms the estimate that both isomers IIa and IIb were present in the original mixture in the approximate proportion of 4:1, since removal of 60% of isomer IIa gave a mixture of roughly equal parts of IIa and IIb. An acetyl group has the property of shielding a methyl group *cis* to it (as in the racemic IIb), or an acetyl group *cis* to it (as in the *meso*-IIa), in the particular system under discussion.

Structure of the Biacetyl-Trimethyl Phosphite 2:1 Adducts Based on Chemical Data. Hydrolysis of Cyclic Saturated Oxyphosphoranes to Cyclic Phosphate Esters. Stereochemistry from H^1 N.m.r. Data.—The crystalline *meso* adduct IIa underwent a very rapid and exothermic reaction with *one* mole equivalent of water at 20° in aprotic solvents. The course of this hydrolysis was conveniently followed in carbon tetrachloride solution by means of quantitative infrared spectrometry: the first detectable products were the *meso*-diketol cyclic phosphate IIIa and two mole equivalents of methanol. The crystalline cyclic phos-



phate IIIa was isolated in *ca.* 80% yield when the hydrolysis of the oxyphosphorane was carried out in benzene or ether solution. Very little open-chain phosphate ester was produced as a result of the hydrolysis.

(4) "N.m.r. Spectra Catalog," compiled by N. S. Bhacca, I. F. Johnson, and J. N. Shoolery. Varian Associates, 1962, p. 7.

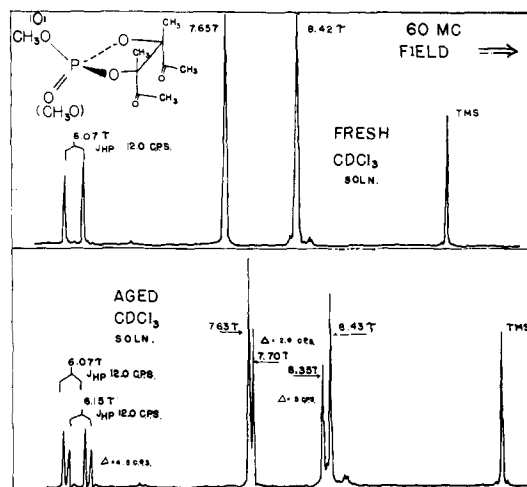
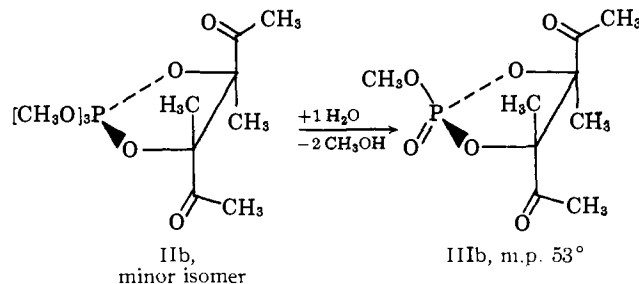


Figure 5.

The 50:50 mixture of *meso* and *racemic* adducts IIa + IIb was hydrolyzed with one mole equivalent of water in benzene solution. The *meso* and the *racemic* diketol cyclic phosphates IIIa and IIIb were separated by fractional crystallization from ether.



The cyclic phosphotriesters IIIa and IIIb are colorless crystalline substances which deteriorate on standing, even in dry air; they are extremely sensitive to moisture, but can be kept well under cold ether.

The infrared spectra of the diastereomeric phosphates IIIa and IIIb were very similar. Both had a strong, split band at $5.80, 5.83 \mu$ due to the $\text{C}=\text{O}$ stretching vibrations. Both had very strong and sharp bands at 7.70μ and at 9.52μ due to the PO and POCH_3 stretching vibrations, respectively (CCl_4 solutions). There was no absorption due to OH -groups.

The H^1 n.m.r. spectrum of a *freshly prepared solution* of the higher-melting cyclic phosphate IIIa is reproduced in the upper half of Fig. 5. This spectrum is consistent with the *meso* configuration IIIa, in which the methoxyl group attached to the phosphorus is on the same side *or* the opposite side of the two equivalent acetyl groups (or of the two equivalent methyl groups). The doublet at 6.07τ is due to the protons of the CH_3OP group, whose signals are split by the P^{31} nucleus, $J_{\text{HP}} = 12$ c.p.s. The singlet at 7.65τ is due to the two equivalent acetyl groups, and the singlet at 8.42τ is due to the two equivalent methyls attached to tetragonal carbon. The relative intensities are roughly 1:1:4:4 as expected.

The H^1 n.m.r. spectrum of the same solution of IIIa kept sealed for several days is reproduced in the lower half of Fig. 5. Two sets of four lines, one doublet and two singlets in each set, can be observed. The separation between the corresponding lines in the two sets is very small: 4.5 c.p.s. for the CH_3OP lines, 2.8 c.p.s. for the $\text{CH}_3\text{C}(\text{O})$ -lines, and 5 c.p.s. for the $\text{CH}_3\text{C} \leq$ lines. This behavior is consistent with a facile, but not instantaneous, stereomutation at phosphorus in

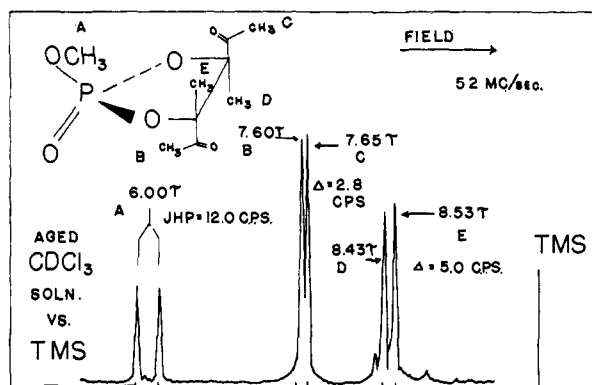


Figure 6.

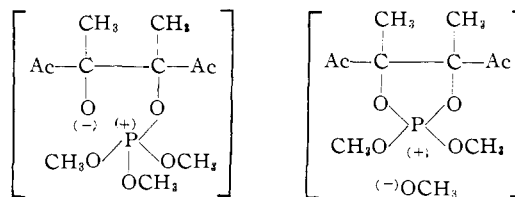
IIIa which should alter slightly the environment of the three different types of protons. This spectrum (Fig. 5) does not correspond to the final equilibrium position of the two isomers at phosphorus in the *meso*-phosphate IIIa: the intensities of the corresponding lines in the two sets became nearly equal on further aging of the solution. No major changes on aging were detectable in the infrared spectrum of the *meso*-diketol phosphate IIIa, if moisture was excluded.

The H^1 n.m.r. spectrum of a solution of the lower-melting cyclic phosphate IIIb is given in Fig. 6. This spectrum does not change with time, since now the stereomutation at phosphorus does not alter the environment of the five types of protons. The number of peaks, their positions, their relative intensities (1:1:2:2:2:2), and the invariance of the spectrum with time are uniquely consistent with the *racemic* configuration IIIb for the lower-melting cyclic phosphate. There is one doublet at 6.00 τ , $J_{HP} = 12.0$ c.p.s., due to the CH_3OP group. The singlet at 7.60 τ is tentatively assigned to the acetyl group which is adjacent to the phosphoryl oxygen, while the singlet at 7.65 τ is assigned to the acetyl group which is far from this oxygen atom. This assignment assumes that the phosphoryl group, $P=O$, has a deshielding effect.⁵ On the same basis, the singlets at 8.43 and 8.53 τ are assigned to the $CH_3-C\leftarrow$ groups in which the methyl is next to, and far from, the phosphoryl group, respectively.

The chemical shifts of the protons in the cyclic phosphates IIIa and IIIb should be compared with those in the cyclic oxyphosphoranes (IIa, IIb): the shielding of the protons is somewhat greater in the oxyphosphoranes.

Figures 5 and 6 provide one, but not the only, reason for the assignment of structure and configuration to the phosphates IIIa and IIIb. The formation of cyclic phosphotriesters IIIa and IIIb from the very mild hydrolysis of the 2:1 adducts IIa and IIb provides chemical evidence in favor of the pentacovalency of phosphorus in the latter. If the adducts IIa and IIb had an open-chain dipolar structure with tetravalent phosphorus the products of the hydrolysis should have been open-chain phosphate esters, since: (i) there is no reason to expect that the rate of hydrolysis of the open dipolar form should be any slower than the rate of hydrolysis of the oxyphosphorane structure and (ii) the open-chain phosphate esters, if formed, should not undergo an instantaneous cyclization under the experimental conditions. A cyclic ion-pair structure with tetravalent phosphorus is unlikely because: (i) the properties of the 2:1 adducts are not those to be expected from ion-pairs: *cf.* the P^{31} n.m.r. and H^1

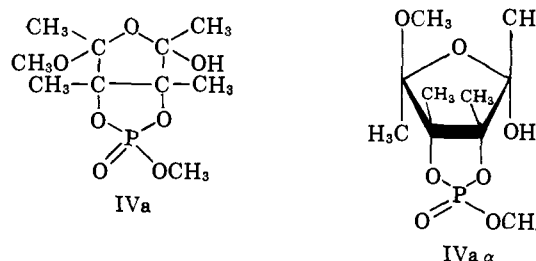
n.m.r. spectra and the solubility in cold pentane and (ii) if electronic effects in the adducts were to favor an ionic structure over an oxyphosphorane structure, that ionic structure probably should be of the open dipolar ion type rather than of the cyclic ion-pair type, for steric reasons (*cf.* open *vs.* cyclic phosphate esters).⁶



The synthesis of crystalline, stereochemically defined cyclic phosphate esters from α -diketones and trialkyl phosphites is a promising feature of oxyphosphorane chemistry. Cyclic phosphates, in particular those derived from ketols, are of considerable biological significance.

Stereochemistry from Chemical Data. Preparation of a Furanose-2,3-cyclic Phosphate.—The methanol which is formed in the hydrolysis of the crystalline *meso*-2:1 biacetyl adduct IIa adds slowly to the carbonyl function of the resulting *meso*-diketol cyclic phosphate IIIa. The product is a crystalline cyclic hemiketal cyclic phosphate ester IVa. Four diastereomers are possible; one of them is illustrated in formula IVa α , which emphasizes the features of a furanose-2,3-cyclic phosphate.

The ready formation of the hemiketal phosphate IVa suggests that the two acetyl groups in the high-melting diketol phosphate IIIa are *cis* to each other; *i.e.*, the latter has the *meso* configuration. Thus, the H^1 n.m.r. data and the chemical data on the stereochemistry of the phosphates are in agreement.



The hemiketal phosphate IVa had a characteristic infrared spectrum lacking $C=O$ absorption and having an OH band at 2.94 μ , a strong and sharp band at 7.73 μ due to cyclic $P=O$, and a very strong and sharp band at 9.53 μ typical of the monomethyl phosphates. The OH protons gave a signal at 5.77 τ , the CH_3OP gave a doublet at 6.15 τ , $J_{HP} 12$ c.p.s., and the hemiketal $CH_3OC\leftarrow$ protons were at 6.65 τ . In addition, the lines for three of the four different $CH_3C\leftarrow$ groups were resolvable: 8.50, 8.55 (double intensity, unresolved), and 8.58 τ . The elements of methanol can be removed from the hemiketal IVa by codistillation with benzene; the product is the diketol phosphate IIIa.

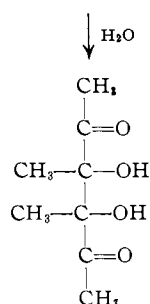
Hydrolysis of the Cyclic Phosphotriesters and of the Cyclic Oxyphosphoranes to Phosphorus-Free Diketols.—The cyclic phosphotriesters IIIa and IIIb were converted into diketols Va and Vb by an excess of water in benzene solution at 80°.

The higher-melting *meso*-phosphate IIIa gave a crystalline diastereomer of 8,4-dimethyl-3,4-dihydroxy-2,5-hexanedione, isolated in 90% yield; the *meso* configuration Va is assigned to it.

(5) E. T. Kaiser, M. Panar, and F. H. Westheimer, *ibid.*, **85**, 602 (1963);
(6) P. Haake and F. H. Westheimer, *ibid.*, **83**, 1102 (1961).

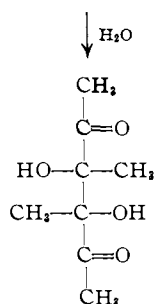
(5) See J. G. Pritchard and P. C. Lauterbur, *J. Am. Chem. Soc.*, **83**, 2105 (1961), for the effect of the $S=O$ group on chemical shifts of protons in cyclic sulfites.

IIIa, phosphate, m.p. 106°



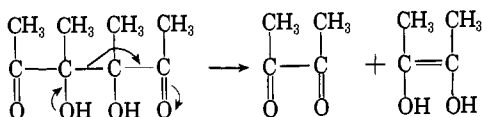
Va, m.p. 95°

IIIb, phosphate, m.p. 53°

Vb, n_D^{25} 1.4495

The lower-melting *racemic*-phosphate IIIb gave mainly a liquid diastereomer of the diketol, to which the *racemic* configuration Vb is assigned; Vb was isolated in ca. 60% yield; in addition, about 13% of the crystalline diketol Va was produced during the hydrolysis. Since the *racemic*-phosphate was free from *meso*-phosphate, some epimerization must have occurred. The second product of these hydrolyses was shown to be phosphoric acid and the partial epimerization of the tertiary alcohol is not unexpected, even though the hydroxyl group is adjacent to a carbonyl function.

Trimethyl phosphate was not affected by water in benzene solution under conditions which led to phosphorus-free diketols from the cyclic diketol phosphotriesters. The diketols cannot be obtained from the cyclic phosphate esters by hydrolyses in neutral or in alkaline aqueous media. Under these conditions biacetyl and acetoin are formed by dealdolization.



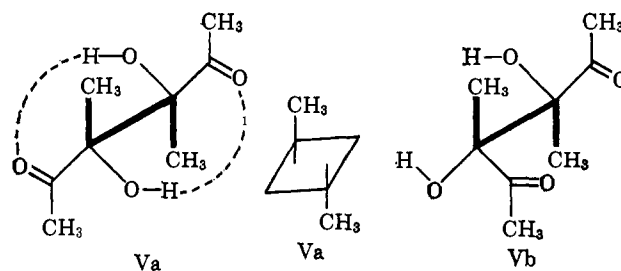
The adducts IIa and IIb were also converted into the diketols Va and Vb by an excess of water in benzene solution without isolation of intermediates.

The structure of the diketols Va⁷ and Vb is firmly established. Both isomers had bands in the C=O stretching and OH stretching regions of the infrared. The bands expected⁸ from OH deformation and C-O stretching vibrations in tertiary alcohols were also present. The H¹ n.m.r. spectrum of the crystalline diketol Va had a peak at 5.5 τ due to the OH protons, a singlet at 7.64 τ due to the protons of the two equivalent acetyl groups, and a singlet at 8.75 τ due to the protons of the two equivalent CH₃-C< groups. The corresponding signals of the liquid diketol Vb were at 5.5, 7.77, and 8.70 τ .

The relative positions (7.64 vs. 7.77 τ) of the acetyl protons of the *meso* and of the *racemic* isomers are opposite in the diketol series and in the cyclic oxyphosphorane series (7.85 vs. 7.75 τ); the latter corresponds with the cyclic phosphotriesters. The relative positions (8.75 vs. 8.70 τ) of the CH₃-C< protons of the *meso* and of the *racemic* isomers are also opposite in the diketol and in the cyclic oxyphosphorane series (8.69 vs. 8.83 τ); again, the latter corresponds with the cyclic phosphotriesters. These differences and similarities probably reflect the conformations, within each configuration, in the three structural types. Two extreme conformations for the diketols are as follows

(7) H. F. von Pechmann, *Ber.*, **21**, 1421 (1888), reported a compound that could be the *meso*-diketol.

(8) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 108.

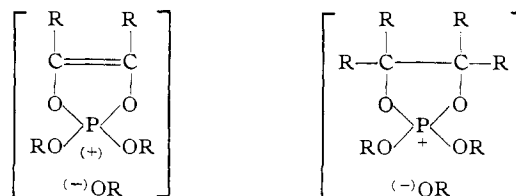


The diketols Va and Vb are freely soluble in both hexane and water, reflecting the intramolecular and intermolecular hydrogen-bonding possibilities. Both formed bis-2,4-dinitrophenylhydrazones, which, in conjunction with the analytical data, substantiates the structural assignment.

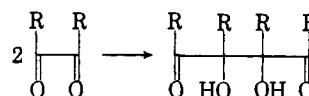
Discussion

The data presented in this paper strongly suggest that the phosphorus atom of the biacetyl-trimethyl phosphite 2:1 adducts IIa and IIb is covalently bound to five oxygen atoms. This conclusion is based on the formation of cyclic phosphate esters from the hydrolysis of the adducts and on the physical properties discussed in the previous section.^{8a} Some of the physical properties of the 2:1 biacetyl adducts are very similar to the corresponding properties of the 1:1 adducts derived from the reaction of tertiary phosphite esters with α -diketones and with *o*-quinones.^{1c} These similarities must reflect analogous structures. The 1:1 adducts themselves display certain characteristics which are not consistent with open-chain dipolar structures; for example, adduct I lacks carbonyl absorption but has olefin absorption in the infrared and Raman spectra. Therefore, the conclusion that the phosphorus is pentavalent in both types of adducts seems justified from several independent observations.

It should be emphasized that the distinction between cyclic oxyphosphorane (I, II) and cyclic ion-pair structures is a rather subtle one in the field of phosphorus chemistry. Further work aiming at an elucidation of the geometry of these adducts is in progress.



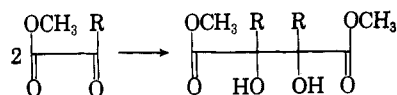
One of the significant results of this investigation is the discovery of a new pattern of carbon-carbon condensation induced by phosphite esters: the formation of a diketol from an α -diketone and a trialkyl phosphite (after hydrolysis)



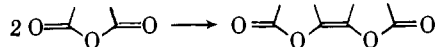
A related reaction is the formation of tartaric esters from α -ketoesters and trialkyl phosphites (after hydrolysis)⁹

(8a) NOTE ADDED IN PROOF.—The number and the positions of the lines in the P³¹ m.m.r. spectrum of the *meso* 2:1 biacetyl adduct IIa did not change significantly when the solvent was changed from carbon tetrachloride to methanol. Therefore, the cyclic oxyphosphorane did not open readily to a dipolar structure or to a noncyclic oxyphosphorane in methanol. A rapid exchange between the methoxyls and the solvent is possible.

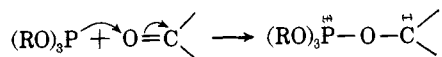
(9) F. Ramirez, N. B. Desai, and N. Ramanathan, *Tetrahedron Letters*, **No. 5**, 323 (1963).



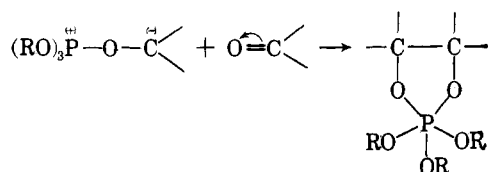
Another type of carbon-carbon condensation brought about by trialkyl phosphites is illustrated by the formation of biphtalyl from phthalic anhydride and trialkyl phosphites at elevated temperatures¹⁰



The common feature of these reactions seems to be an initial attack by the triply-connected phosphorus atom on the oxygen atom of a carbonyl function



Sometimes the intermediate 1:1 adduct is relatively stable and can be isolated. The stabilization could be due to the formation of a five-membered cyclic unsaturated oxyphosphorane. The next step is a nucleophilic addition of carbon to the carbonyl function.



The driving force could again be the formation of a five-membered cyclic oxyphosphorane, this time with a saturated ring.

The biphtalyl condensation requires elevated temperatures, and we have suggested alternative pathways for this reaction.¹⁰

The detailed mechanistic features of the hydrolysis of the cyclic saturated oxyphosphoranes (II \rightarrow III) remain to be elucidated. The essential questions are: (1) Is there incorporation of oxygen from the water into the resulting phosphate ester or into the methanol that is produced? This point is under investigation. (2) If the hydrolysis involves the replacement of a methoxyl by a hydroxyl: (a) is this replacement preceded by a P-O bond fission with transient formation of a cyclic ion-pair or (b) is there an increase in the coordination of the phosphorus from five to six during the substitution reaction?

Lastly, the H^1 n.m.r. spectra of the 1:1 and of the 2:1 trimethyl phosphite adducts I and II show that the three methoxyls are equivalent or, less likely, indistinguishable, since they give rise to one doublet only (the doublet is due to the H-P spin-spin coupling). This equivalence could result from a very rapid exchange among the methoxyl-group positions. The exchange may involve ionic structures as fleeting intermediates or may proceed without actual rupture of P-O bonds.¹¹ This question relates to the geometry of the adducts in different states and environments (crystals, solutions, etc.), about which nothing is as yet known.^{3a, 8a}

Experimental

The trimethyl phosphite was kept over sodium wire and used after distillation. The biacetyl was freshly distilled. Solvents were dried and distilled. All operations were carried out with precautions against moisture. The infrared spectra were taken in a Perkin-Elmer 21 spectrophotometer. The analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

(10) F. Ramirez, H. Yamanaka, and O. H. Basedow, *J. Am. Chem. Soc.*, **83**, 173 (1961).

(11) In a very recent paper, E. L. Muttarties, W. Mahler, and R. Schmutzler, *Inorg. Chem.*, **2**, 613 (1963), discuss the equivalence of the three fluorine atoms in $(\text{CH}_2)_3\text{PF}_3$.

1:1 Biacetyl-Trimethyl Phosphite Adduct (2,2,2-Trimethoxy-4,5-dimethyl-1,3-dioxaphospholene) (I).—Biacetyl (74 g.) was added dropwise to trimethyl phosphite (135 g.), under nitrogen, with stirring and cooling. The mixture was kept at 60° for 15 min. and then distilled. The colorless 1:1 adduct I was collected at 45–47° (0.5 mm.) and had n_D^{25} 1.4387, d_4^{25} 1.166 g./cc.; the yield was quantitative. The adduct is very sensitive to moisture.

Diastereomeric 2:1 Biacetyl-Trimethyl Phosphite Adducts (*meso*- and *racemic*-2,2,2-Trimethoxy-4,5-dimethyl-4,5-diacetyl-1,3-dioxaphospholanes) (IIa and IIb). (a) From Biacetyl and the 1:1 Adduct (I).—The adduct I (18.3 g.) and the biacetyl (22.5 g., 1:3 mole ratio) were allowed to react at 20° for 48 hr. under nitrogen, with stirring. The excess biacetyl was recovered by distillation, and the mixture of diastereomeric 2:1 adducts IIa and IIb was collected at 65–75° (ca. 0.1 mm.), yield 22.7 g., n_D^{25} 1.4471. Redistillation gave a colorless, viscous oil, n_D^{25} 1.4471, which according to the H^1 n.m.r. spectrum is a mixture of ca. 80% *meso*- and 20% *rac*-2,2,2-trimethoxy-4,5-dimethyl-4,5-diacetyl-1,3-dioxaphospholanes. The adducts are very sensitive to moisture.

Anal. Calcd. for $\text{C}_{11}\text{H}_{21}\text{O}_7\text{P}$: C, 44.6; H, 7.1; P, 10.4. Found: C, 44.6; H, 7.1; P, 10.6.

The P^{31} n.m.r. spectrum of this original mixture of diastereomeric 2:1 adducts (examined as neat liquid) had a line at $+51 \pm 2$ p.p.m. vs. 85% H_3PO_4 as external reference. The infrared spectrum (in CCl_4) had strong bands at 5.81 μ (shoulder at 5.84 μ) and 9.25 μ (shoulders at 9.12 and 9.00 μ); the spectrum was very similar to that of the crystalline isomer shown in Fig. 1. The H^1 n.m.r. spectrum (in CCl_4) had a doublet at 6.51 τ (J_{HP} 13 c.p.s.) and singlets at 7.85 and 8.69 τ due to the major isomer; it had also a doublet at 6.40 τ (J_{HP} 13 c.p.s.) and singlets at 7.75 and 8.83 τ due to the minor isomer; see Fig. 2.

(b) From Biacetyl and Trimethyl Phosphite without Isolation of the 1:1 Adduct (I).—Biacetyl (258 g.) was added dropwise to trimethyl phosphite (124 g., 3:1 mole ratio) with stirring and external cooling, under N_2 ; the addition required 3 hr. and the temperature was maintained at 15–20°. The mixture was then stirred at 20° for 5–7 days. The excess of biacetyl was removed at ca. 0.5 mm. Two fractions, (1) 152 g. and (2) 104 g., were arbitrarily collected in the boiling range 105–115° (0.5 mm.); these had very similar infrared spectra and n_D ; the yield of 2:1 adducts IIa + IIb was 87% based on trimethyl phosphite. The H^1 n.m.r. spectrum showed that the isomers were present in the approximate proportion 80:20 (cf. Fig. 2).

Fraction 1 was dissolved in 35 ml. of pentane, and the solution was kept at -10° for ca. 48 hr. The pentane mother liquid was decanted from the crystalline *meso*-2:1 adduct IIa (80 g.) with minimum exposure to moisture. Fraction 2 in 25 ml. of pentane gave, in this manner, 54 g. of crystalline IIa. In general, 1 ml. of pentane was employed per 4.3 g. of original mixture of diastereomers to obtain the crystalline *meso* isomer; the latter can be freed from traces of *racemic* isomer by one or two washings with small amounts of cold pentane. The analytical sample of *meso*-2,2,2-trimethoxy-4,5-dimethyl-4,5-diacetyl-1,3-dioxaphospholane (IIa) had m.p. 31–32° (pentane).

Anal. Calcd. for $\text{C}_{11}\text{H}_{21}\text{O}_7\text{P}$: C, 44.6; H, 7.1; P, 10.4; mol. wt., 296. Found: C, 44.4; H, 7.2; P, 9.8; mol. wt., 297 (isothermal distillation in dry benzene).

The P^{31} n.m.r. spectrum of this crystalline, major isomer IIa (examined in a 50% benzene solution) had a line at $+51$ p.p.m. vs. 85% H_3PO_4 as external reference. The infrared spectrum (in CCl_4) had bands at (μ): 3.31 (w) 3.35 (w), 3.50 (w), 5.81 (1720 cm^{-1}) and 5.84 (1712 cm^{-1}) (strong, split carbonyl), 6.83 (w), 6.90 (w), 7.05 (w), 7.25 (w), 7.35 (m), 8.45 (w), 9.00 (strong shoulder), 9.12 (strong shoulder), 9.26 (1080 cm^{-1} , very strong POCH_3), 9.88 (m), 10.40 (m); see Fig. 1. The H^1 n.m.r. (in CCl_4) had a doublet at 6.48 τ (J_{HP} 13 c.p.s.) and singlets at 7.82 and 8.65 τ ; see Fig. 3.

The two pentane mother liquids, from which most of the *meso* isomer had been removed, were combined and evaporated. The oily residue (ca. 130 g.) was redissolved in 10 ml. of pentane; more crystalline IIa separated after several days. The yield of crystalline *meso* isomer was 60% based on the distilled mixture of isomers, or 53% based on trimethyl phosphite. Pentane was removed from the mother liquid and the residue (116 g.) was submitted to short-path distillation at 0.5 mm. A forerun (ca. 6 g., up to 101°) was discarded and two fractions, (3) 35 g. and (4) 69 g., were arbitrarily collected in the boiling range 101–109° (0.5 mm.); these had virtually identical infrared spectra; the former had a slightly lower n_D^{25} than the latter (1.4475 and 1.4488). These two fractions (3 and 4) constituted a 40% yield based on the original distilled mixture of isomers, or 34% based on trimethyl phosphite. The H^1 n.m.r. spectrum showed that the stereoisomers were present in equal proportion (see Fig. 4). The analytical sample had n_D^{25} 1.4490 after one more distillation.

Anal. Found: C, 45.0; H, 7.2.

The infrared spectrum was indistinguishable from that of the original 80:20 mixture of diastereomers. The H^1 n.m.r. spec-

trum (in CCl_4) had one doublet at 6.38 τ (J_{HP} 13 c.p.s.) and singlets at 7.74 and 8.63 τ due to one isomer (IIa); it had also a doublet at 6.28 τ (J_{HP} 13 c.p.s.) and singlets at 7.66 τ and 8.77 τ due to the second isomer IIb.

Hydrolysis of the Crystalline meso-Oxyphosphorane (IIa) with One Mole Equivalent of Water. (a) In Ether Solution: Preparation of meso-Methyl (3,4-Dimethyl-3,4-dihydroxyhexanedione-2,5) Cyclic Phosphate (IIIa) and of Methyl (2,3,4,5-Tetramethyl-2,3,4,5-trihydroxy-5-methoxytetrahydrofuran) 3,4-Cyclic Phosphate (IVa).—The crystalline meso-2,2,2-trimethoxy-4,5-dimethyl-4,5-diacetyl-1,3-dioxaphospholane (IIa, 14.852 g., 50.2 mmoles) was dissolved in ether (28 ml.), dried over Na wire and distilled; the stirred solution was treated with water (0.900 ml., 50 mmoles) at 20°, under nitrogen. An exothermic reaction was noted within a few seconds; after 5 min., the clear solution was chilled (5°) and kept cold for 24 hr. Colorless rhombic plates of meso-methyl (3,4-dimethyl-3,4-dihydroxyhexanedione-2,5) cyclic phosphate (IIIa) crystallized out and were filtered in the absence of moisture: yield 5.35 g. (43%), m.p. range 106–112°, with some previous softening. This material was analyzed as such, and also after recrystallization from benzene-hexane; no significant differences were noted. The m.p. range was not narrowed by repeated crystallizations.

Anal. Calcd. for $\text{C}_9\text{H}_{18}\text{O}_8\text{P}$: C, 43.2; H, 6.0; P, 12.4; mol. wt., 250. Found: C, 43.2; H, 6.0; P, 12.4; mol. wt., 250 (titration with aq. NaOH at pH 7.0 and 25° until no more NaOH was consumed).

The infrared spectrum of a freshly prepared sample, taken in purified CHCl_3 (in μ) was: 5.80 (1720 cm^{-1}) (s), shoulder at 5.83, 6.90 (w), 7.02 (w), 7.22 (m), 7.33 (m), 7.70 (1295 cm^{-1}) (v. strong, sharp), 9.03 (m), 9.50 (1055 cm^{-1}) (v.s.); 9.95 (m), 10.4 (s); no OH stretching band. The spectrum was identical in CH_2Cl_2 (dried over P_2O_5 and distilled). No change in the spectra in these solvents was noted after 5 days if moisture was rigorously excluded.

The H^1 n.m.r. spectrum was taken of a freshly prepared solution of IIIa in CDCl_3 (in τ units): doublet at 6.07, J_{HP} 12 c.p.s.; singlets at 7.65 and 8.42; intensities 1:1:4:4; (Fig. 5); H^1 n.m.r. spectrum of the same solution, kept sealed for several days: doublet (τ) at 6.07, J_{HP} 12 c.p.s., singlets at 7.65 and 8.43; a second set of weaker lines: doublet at 6.15, J_{HP} 12 c.p.s., singlets at 7.70 and 8.35 (Fig. 5). More prolonged aging led to roughly equal intensities of the corresponding lines of the two sets.

The ether filtrate, from which diketol phosphate IIIa had been removed, was concentrated to ca. 10 ml. and the solution was kept 5–6 days at 5°. Colorless cubes of methyl (2,3,4,5-tetramethyl-2,3,4,5-trihydroxy-5-methoxytetrahydrofuran) 3,4-cyclic phosphate (IVa) crystallized out; yield 5.03 g. (35%), m.p. range 88–96°. The infrared spectrum of this material was very similar to that of an analytical sample, m.p. 104–105°, obtained by recrystallization from CH_2Cl_2 -hexane (*vide infra*); there was practically no C=O absorption.

The ether filtrate, from which hemiketal phosphate IVa had been removed, was evaporated to an oily residue (ca. 3.3 g., 20%), the infrared spectrum of which showed bands for hemiketal phosphotriester IVa and for acidic phosphodiester; weak carbonyl bands were also observed.

(b) In Ether Solution: Preparation of the Hemiketal Cyclic Phosphotriester IVa.—The hydrolysis of the oxyphosphorane IIa generates the diketol phosphate IIIa and two moles of methanol, which react further to form the cyclic hemiketal phosphate IVa. This secondary reaction is slow. In experiment (a), the original ether solution was immediately cooled and part of the material (ca. 43%) crystallized as the diketol phosphate IIIa. This was followed by the hemiketal phosphate IVa (35%). In experiment (b) most of the material was obtained as hemiketal IVa. (b) A solution of crystalline oxyphosphorane IIa (18.28 g.) in dry ether (55 ml.) was treated with water (1.11 ml.); the mixture was stirred vigorously for 5 min. at room temperature. The clear solution was kept undisturbed at 25° for 20 hr.; some ether was removed (ca. 20 ml.) and the mixture was cooled at 5° for 3 hr. The first crop of hemiketal phosphate IVa (9.0 g., 52%) had a m.p. range of 83–89°. The filtrate was concentrated further, affording (after prolonged cooling) a second crop (4.6 g.) of hemiketal phosphate IVa; yield ca. 78%. The elemental analysis, the infrared spectrum, and the H^1 n.m.r. spectrum of these samples of IVa, having a m.p. range of 83–91°, were indistinguishable from those of purified samples. Recrystallization from CH_2Cl_2 -hexane does not change the m.p. range appreciably. A filter paper spot test using a congo red spray revealed traces of an acid impurity. Consequently the following purification was performed: A solution containing 5.0 g. of phosphate IVa, 50 ml. of dry CH_2Cl_2 , and 1 ml. of piperidine was shaken (ca. 1 hr.) and then evaporated; the residue was triturated with ether (25 ml.) and the mixture kept 2 hr. at 5°. The insoluble crystals were collected and recrystallized from CH_2Cl_2 -hexane (1:2). The product (ca. 2 g.) had m.p. 103–105° and gave a negative im-

mediate spot test for acidity on filter paper when applied in CH_2Cl_2 solution and developed with a congo red spray.

Anal. Calcd. for $\text{C}_{10}\text{H}_{18}\text{O}_7\text{P}$: C, 42.6; H, 6.8; P, 11.0. Found: C, 42.6; H, 7.1; P, 11.0.

For methyl (2,3,4,5-Tetramethyl-2,3,4,5-trihydroxy-5-methoxytetrahydrofuran) 3,4-cyclic phosphate (IVa), the following properties were recorded on freshly-prepared solutions; infrared spectrum in purified CHCl_3 (in μ): broad OH with minimum at 2.94 (3400 cm^{-1}) and shoulder at 3.03; no C=O bands in the 5–6 μ region; characteristic weak band at 7.24 flanked by two weaker ones at 7.10 and 7.38; very strong and sharp 7.73 (1290 cm^{-1}); 8.47 (m), 8.60 (w), 9.10 (w), very strong and sharp 9.53 (1045 cm^{-1}), 10.1 (s); H^1 n.m.r. spectrum in CDCl_3 (in τ units): singlet at 5.77, doublet at 6.15, J_{HP} 12 c.p.s., singlet at 6.65, singlets at 8.50, 8.55 (double intensity indicating two unresolved lines), and 8.58.

In some samples of the hemiketal phosphate IVa, purified by the piperidine method, a m.p. of 114–115° was recorded immediately after purification. On standing, or after recrystallization (CH_2Cl_2 -hexane or CH_2Cl_2 -ether), the m.p. dropped to 104–105°. There is an "anomeric" carbon in this structure and four possible diastereomers at C₂ and C₅ which may account for this behavior.

(c) Diketol Cyclic Phosphate IIIa from Hydrolyses in Benzene Solution.—Water (0.678 ml.) was added to oxyphosphorane IIa (11.167 g.) in dry benzene (27 ml.) with stirring. The temperature of the solution rose from 26 to 37° in a few seconds. The benzene and the methanol were removed after 5 min. (bath at 70°; aspirator) and the residue was kept 20 hr. at 10°, under ether (20 ml.). The diketol phosphate IIIa was filtered; yield 7.7 g., 82%, m.p. range 90–100°, with previous softening; analysis and infrared spectrum very similar to those of analytical sample described in expt. (a).

The ether filtrate was concentrated and cooled to 10°; hemiketal phosphate IVa was filtered; yield 0.6 g., 6%, m.p. range 77–87; infrared spectrum very similar to that described in expt. (b). The second ether filtrate gave 0.95 g. (9%) of oil, the infrared spectrum of which shows bands for IIIa, IVa, and possibly some acid phosphodiester and open-chain triesters.

(d) Hemiketal cyclic phosphate IVa was obtained from hydrolyses in benzene solution as in expt. (c), but keeping the original solution 16 hr. at 20°. Removal of benzene (bath at 30°, vacuum) gave 75% of hemiketal phosphate IVa, m.p. 83–89°.

Conversion of Hemiketal Phosphate IVa into Diketol Phosphate IIIa.—Dry benzene (150 ml.) was added dropwise to a boiling solution of hemiketal phosphate IVa (2.64 g.) in benzene (50 ml.), from which solvent was being removed by distillation at a comparable rate. After 65 min., 150 ml. of benzene (containing methanol) had been removed. The solution was evaporated *in vacuo*; the residue (2.32 g. of crystals) showed the infrared spectrum of diketol phosphate IIIa. Trituration with ether left (1.8 g.) of diketol phosphate, m.p. 106–112°, as such and after recrystallization from benzene-hexane.

Spectrophotometric Study of the Hydrolysis of meso-Oxyphosphorane IIa in Carbon Tetrachloride.—One mole equivalent of water was added to a 1 M solution of the oxyphosphorane IIa in carbon tetrachloride (dried and distilled from P_2O_5), with vigorous stirring. The water was consumed immediately. The clear original solution was diluted fourfold with CCl_4 and rapidly examined in a Perkin-Elmer 21 spectrometer: the spectrum corresponded to that of a standard 0.5 M solution of methanol in CCl_4 and not to a standard 0.25 M solution of the latter, indicating that two mole equivalents of methanol were produced during the hydrolysis.

A second immediate fivefold dilution with CCl_4 gave a solution whose infrared spectrum corresponded to that of a standard 0.05 M solution of authentic diketol cyclic phosphate IIIa in CCl_4 . Thus, the hydrolysis proceeded rapidly and cleanly to one mole equivalent of cyclic phosphate.

The original 1 M solution was kept at 20° for 16 hr. after the hydrolysis. Twofold dilution with CCl_4 gave a solution whose infrared spectrum nearly coincided with that of the standard 0.5 M methanol- CCl_4 solution; *i.e.*, one mole equivalent of methanol had been consumed. A second tenfold dilution with CCl_4 produced a solution whose infrared spectrum was very close to that of a standard 0.05 M solution of authentic hemiketal cyclic phosphate IVa. Crystalline hemiketal phosphate IVa was isolated by evaporation of the CCl_4 .

Hydrolysis of the 50:50 Mixture of meso- and rac-Oxyphosphoranes IIa + IIb with One Mole Equivalent of Water. Preparation of Racemic Methyl (3,4-Dimethyl-3,4-dihydroxyhexanedione-2,5) Cyclic Phosphate (IIIb).—Water (1.885 ml.) was added to a solution of the 50:50 meso + rac-oxyphosphoranes (IIa + IIb, 31.034 g., n_D^{20} 1.4490) in benzene (80 ml.) with efficient stirring. The solvent was removed after 5 min. (bath at 70°, vacuum). The residue (28 g.) was immediately dissolved in ether (25 ml.); the solution was kept 20 hr. at 5° and 5 hr. at -15°. Some meso-diketol cyclic phosphate (IIIa, 5.2 g., 20%, m.p. range 85–103°) separated.

The ether filtrate was kept 66 hr. at -20° ; it deposited crystals of *rac*-methyl (3,4-dimethyl-3,4-dihydroxyhexanedione-3,5) cyclic phosphate (IIIb, 10.1 g., 39%, crude m.p. 45–50°). Recrystallization from dry ether (in the absence of moisture) gave colorless crystals of racemic diketol phosphate IIIb, m.p. 54–56°. Analysis was performed immediately. The solid phosphate deteriorates on standing, even under nitrogen, but is conveniently stored under ether at 5°.

Anal. Calcd. for $C_9H_{16}O_6P$: C, 43.2; H, 6.0; P, 12.4. Found: C, 42.5; H, 6.0; P, 11.6.

The infrared spectrum was taken in dry CCl_4 (μ): 5.80 (1725 cm^{-1}) (s) with shoulder at 5.83 [in CCl_4 the *meso* isomer shows a distinctly split carbonyl at 5.81, 5.84 μ]; 6.90 (w), 7.04 (w), 7.25 (m), 7.38 (m); 7.68 (1302 cm^{-1}) (v. s.); 8.93 (m); 9.51 (1052 cm^{-1}) (v. s.); 9.98 (m), 10.1 (shoulder), 10.4 (w). H^1 n.m.r. spectrum in $CDCl_3$ solution (τ): doublet at 6.00, J_{HP} 12 c.p.s., two singlets of equal intensities at 7.60 and 7.65 and two singlets of equal intensities at 8.43 and 8.53; see Fig. 6 (the spectrum does not change on standing, in the absence of moisture).

The ether filtrate from which the racemic diketol phosphate IIIb had separated was concentrated and cooled 24 hr. at -10° . Crystalline hemiketal cyclic phosphate IVa (2.4 g., 9%, m.p. 72–82°) separated out.

Hydrolysis of *meso*-Diketol Cyclic Phosphate (IIIa) to *meso*-3,4-Dimethyl-3,4-dihydroxyhexanedione-2,5 (Va).—A mixture of the *meso*-diketol phosphate IIIa (11.185 g., m.p. 105–110°), benzene (60 ml.), and water (4.02 ml., 5 mole equivalents) was kept 1.5 hr. at reflux temperature. The aqueous acid layer was separated, saturated with NaCl, and extracted with benzene. The combined benzene extracts and original layer were dried ($MgSO_4$) and evaporated *in vacuo*. Colorless needles of *meso*-3,4-dimethyl-3,4-dihydroxyhexanedione-2,5 (Va) (6.1 g., 80%, m.p. 89–92°) were obtained, analytical sample m.p. 95–96° (hexane).

Anal. Calcd. for $C_8H_{14}O_4$: C, 55.2; H, 8.1; mol. wt., 174. Found: C, 54.6; H, 8.2; mol. wt., 215.

The infrared spectrum was obtained in CCl_4 (μ): 2.90 (3460 cm^{-1}) (sharp) (m) (OH stretching); 3.34 (w), 3.40 (w), 5.86 (1707 cm^{-1}) (s) (C=O stretching); 6.85 (w), 7.02 (w), 7.30 (s) (OH deformation); 8.23 (s), 8.76 (s) (C—O stretching); 9.35 (m); H^1 n.m.r. spectrum (in CCl_4 , τ): singlets at 5.50, 7.64, and 8.75; intensities: 1:3:3; bis-2,4-dinitrophenyl-hydrazone m.p. 209–210° (chlorobenzene).

Anal. Calcd. for $C_{20}H_{22}O_{10}N_2$: C, 45.0; H, 4.1; N, 21.0. Found: C, 45.2; H, 4.0; N, 20.9.

Hydrolysis of *rac*-Diketol Cyclic Phosphate IIIb to *rac*-3,4-Dimethyl-3,4-dihydroxyhexanedione-2,5 (Vb).—A mixture of the *rac*-diketol phosphate IIIb (6.57 g., m.p. 50–52°), benzene (30 ml.), and water (1.9 ml., 4 mole equivalents) was kept 1.15 hr. at reflux temperature and worked up as for the *meso* isomer. A colorless oil (3.7 g., 80%) was obtained; this was stirred with 5 ml. of warm hexane and the mixture was kept 20 hr. at 5°. A

small amount of crystalline *meso*-diketol Va (600 mg., 13%) was filtered off. The hexane was evaporated and the residue (2.72 g., 60%) was submitted to short-path distillation; *rac*-3,4-dimethyl-3,4-dihydroxyhexanedione-2,5 (Vb) (2.21 g., 48%) had b.p. ca. 45–50° (0.3 mm.), n_D^{20} 1.4495.

Anal. Found: C, 55.7; H, 8.2.

The infrared spectrum in CCl_4 had bands at (μ): 2.87 (3480 cm^{-1}) (mw, broad) (OH stretching); 3.34 (w), 3.40 (w) 5.88 (1702 cm^{-1}) (s) (C=O stretching); 6.90 (w), 7.02 (w), 7.18 (ms), and 7.32 (ms) (OH deformations); 7.96 (w), 8.10 (w), 8.26 (m), 8.47 (m), 8.76 (s) with shoulder at 8.93 (s) (C—O stretching); 9.22 (m); H^1 n.m.r. spectrum (in CCl_4 , τ): singlets at 5.73, 7.77, and 8.70; bis-2,4-Dinitrophenylhydrazone, m.p. 200–202° (chlorobenzene). *Anal.* Found: C, 45.5; H, 4.3; N, 20.7.

Hydrolysis of the Crystalline *meso*-Oxyphosphorane (IIa) with an Excess of Water.—A solution of crystalline adduct IIa (10.08 g.) in benzene (50 ml.) containing some water (3 ml.) was kept 30 min. at reflux temperature under N_2 . The layers were separated; the water-acid layer was saturated with NaCl and extracted with benzene; the dried benzene layer plus extracts were evaporated. The crystalline residue was recrystallized from hexane; first crop of diketol Va, 4.81 g.; second crop, 0.34 g. (yield 93%; both melting at 94–95°).

This hydrolysis of IIa was repeated using water enriched with 10.61 atom % O^{18} , 0.179 atom % O^{17} , and an unspecified amount of deuterium (YEDA, Research and Development Co., Israel), in order to establish possible incorporation of O^{18} into the diketol during the hydrolysis.

The *meso*-diketol of normal isotope content was kept in contact with O^{18} -enriched water, in refluxing benzene containing some phosphoric acid, as in the hydrolysis experiment, in order to determine possible incorporation of O^{18} into the diketol as a result of an exchange with the water. The three samples of diketol were submitted to mass spectrometric analysis, with results which will be described elsewhere.

Hydrolysis of the Original Mixture of Diastereomeric Oxyphosphoranes IIa and IIb with an Excess of Water.—The original distilled mixture of *meso* and racemic adducts IIa and IIb (66.84 g.) was dissolved in benzene (350 ml.), treated with water (about 12 ml.), and carefully warmed up to initiate a vigorous reaction. The mixture was kept 1 hr. at reflux temperature and worked up as for the *meso* isomer. Fractional crystallization from hexane gave crystalline diketol Va, m.p. 94–95°, in 63% yield. Distillation of the liquid residue gave the *rac*-diketol Vb, n_D^{20} 1.4491 in about 20% yield. It is difficult to obtain *rac*-Vb completely free from *meso*-Va by this procedure (*vide supra*).

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Mechanisms of Reactions of Sulfinic Acids. V. The Mechanism of the Alkyl Sulfide-Sulfinic Acid Reaction¹

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The mechanism of the recently discovered² primary alkyl sulfide-*p*-toluenesulfinic acid reaction has now been determined. The relative reactivities of α,α -dideuteriobenzyl sulfide and its undeuterated analog show the reaction is subject to a large isotope effect ($k_H/k_D = 5.2$). This fact, combined with the variation of rate with sulfide structure for a series of sulfides (RCH_2)₂S and the previously reported² dependence of rate on other reaction variables, requires that the rate-determining step be eq. 2B. Experiments with butyl α -acetoxybutyl sulfide show that the cation $RCH=S-CH_2R^+$ produced in reaction 2B will be immediately hydrolyzed to RCHO and RCH₂SH, and that the mercaptan will then react extremely rapidly with some of the remaining sulfinic acid. Other experiments show that under the present reaction conditions this mercaptan-sulfinic acid ($ArSO_2H$) reaction gives as products, almost exclusively, the two thiol-sulfonates $ArSO_2SAR$ and $ArSO_2SCH_2R$. The course of the sulfide-sulfinic acid reaction subsequent to the rate-determining step is thus as shown in Chart I. Additional kinetic studies demonstrate that any small amount of disulfides produced along with the two thiol-sulfonates in the mercaptan-sulfinic acid reaction will be rapidly consumed by further reaction with sulfinic acid, in a process which also yields the two thiol-sulfonates above as products.

Kice and Bowers² recently described a new reaction between *p*-toluenesulfinic acid and primary alkyl

sulfides, which leads to the cleavage of the sulfide and the oxidation of one of its alkyl groups to the corresponding aldehyde. Other reaction products are the

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(2) J. L. Kice and K. W. Bowers, *J. Am. Chem. Soc.*, **84**, 2390 (1962).