and the noncoincidence of the wavelength values with the standard values for an α helix (233 and 222 mμ, respectively).

The problem of the unambiguous assignment of the optically active transition in the 225–235-mμ range is so far unsolved, and the possibility that chromophores other than the amide group or the thioether function are involved must not be neglected.

The comparison of the enzymic activity of the [Orn[10],-Nle[13]]-RNase S′, against RNA, with that of the [Orn[10]]-RNase S′[7a] shows that the replacement of methionine by norleucine does not significantly affect the ability of the modified synthetic eicosapeptide to give an enzymatically active complex with S-protein.

These findings provide independent support for the proposed[4,5] hydrophobic contribution of methionine side chain to the S-peptide–S-protein binding and suggest that such an interaction is not highly specific for the thioether function but may more generally involve other hydrophobic residues.

Moreover, while one should be cautious about interpreting results obtained from studies with enzymes in the same light as those obtained with hormones one may suppose that the methionyl residue plays a similar role in the S-peptide and in the above-mentioned polypeptide hormones.

Acknowledgments. The authors are indebted to Professor E. R. Blout for giving permission to A. S. to carry out the ORD and CD measurements in his laboratory. They also wish to thank Dr. E. Celon for carrying out the microanalyses, Professor J. Steigman for reading the manuscript, and Mr. U. Anselmi and Mr. D. Stivanello for the skillful technical assistance.

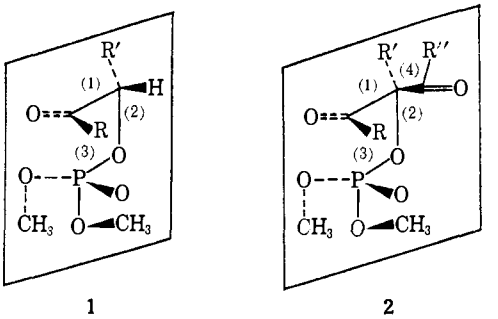
Synthesis of Sugar-Like Phosphates by the Oxyphosphorane Condensation. Reaction of Glyoxal with Trialkyl Phosphites and Preparation of Phosphate Esters of Glycolaldehyde, α-Hydroxy β-Keto Aldehydes, and Hydroxymalonaldehyde Chloride

Fausto Ramirez,[1] S. L. Glaser, A. J. Bigler, and J. F. Pilot

Contribution from the Department of Chemistry, State University of New York at Stony Brook, Stony Brook, New York 11790. *Received August 19, 1968*

Abstract: Commercially available "glyoxal trimer dihydrate" was converted into monomeric anhydrous glyoxal which was allowed to react with trimethyl phosphite to form 2,2,2-trimethoxy-2,2-dihydro-1,3,2-dioxaphospholene. The phospholene was transformed into dimethyl 2-oxoethyl phosphate ("diose phosphate") by anhydrous HCl, and into a series of α-hydroxy β-keto aldehyde phosphates by carboxylic acid chlorides. The reaction of the phospholene with phosgene, $COCl_2$, gave dimethyl phosphohydroxymalonaldehyde chloride. The ^{31}P and ^{1}H nmr and infrared spectra were studied.

This research was undertaken to provide general procedures for the synthesis of polyfunctional carbonyl-containing phosphate esters of biological interest.[2] The phosphates can be represented schematically[3] by formulas **1** and **2**. These are arbitrarily chosen conformations which can serve as a basis for discussion of the possible interactions between the polar groups, P=O and C=O, and the effects of other groups, R, R′, and R″, on these interactions.



1 **2**

R and R′ = H, alkyl, or aryl; R″ = H, Cl, alkyl, aryl

The availability of pure anhydrous samples[4,5] of these low molecular weight highly reactive phosphates is

(1) John Simon Guggenheim Fellow, 1968. This work was supported by Public Health Service Grant No. CA-04769-09 from the National Cancer Institute, and by National Science Foundation Grant GP-6690.

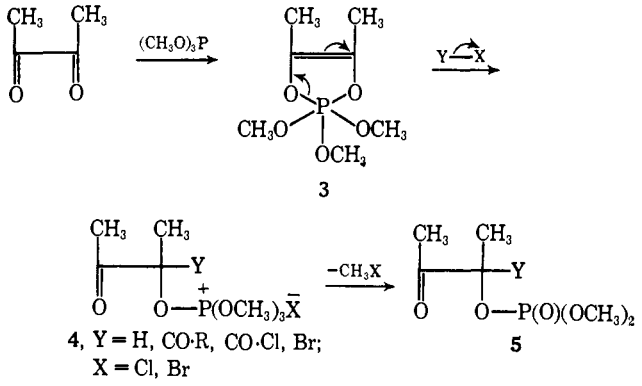
(2) (a) T. C. Bruice and S. J. Benkovic, "Biorganic Mechanisms," Vol. 2, W. A. Benjamin, Inc., New York, N. Y., 1966; (b) H. Khorana, "Some Recent Developments on the Chemistry of Phosphate Esters of Biological Interest," John Wiley & Sons, Inc., New York, N. Y., 1961; (c) M. Calvin and J. A. Bassham, "The Photosynthesis of Carbon Compounds," W. A. Benjamin, Inc., New York, N. Y., 1962; (d) D. M. Brown, *Advan. Org. Chem.*, 2, 141 (1963); (e) F. Cramer, *Angew. Chem.*, 72, 236 (1960); (f) J. R. Cox, Jr., and B. Ramsay, *Chem. Rev.*, 64, 317 (1964).

(3) Four atoms are placed on the plane indicated, *i.e.*, aldehyde C, alcohol C and O, and phosphoryl P. Wedges and dashes denote group in front and back of plane, respectively.

(4) The preparation of aqueous solutions of the dicyclohexylammonium salt of glycolaldehyde dihydrogen phosphate has been thoroughly described by Ballou and MacDonald.[5] The "hydrate" of the diethyl acetal derivative of this material is offered commercially at $6 per 25 mg (Calbiochem, Los Angeles, Calif.).

(5) C. E. Ballou and D. L. MacDonald in "Methods in Carbohydrate Chemistry," Vol. II, R. L. Whistler, M. L. Wolfrom, and J. N. BeMiller, Ed., Academic Press, New York, N. Y., 1963, p 272.

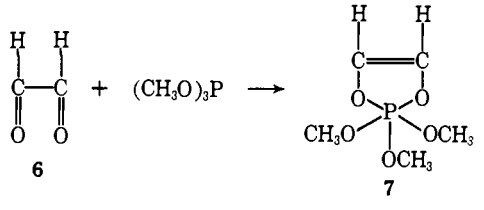
desirable for studies of the mechanisms of their nonenzymatic reactions,[2,5-7] and for examination of their physical properties in various media (vapor, solution, crystal). New synthetic approaches to these compounds have been developed in this laboratory.[8] One of these approaches[9] involves the reaction of a cyclic oxyphosphorane, **3**, with a reagent, Y–X, made up of an electrophilic, Y, and a nucleophilic, X, portion. The result is a transient intermediate **4** which is readily transformed into the desired phosphate **5** under anhydrous conditions.



The present paper deals with the utilization of monomeric anhydrous glyoxal for the synthesis of phosphate esters of types **1** and **2**.

Results

Reaction of Glyoxal with Trimethyl Phosphite. The commercially available[10] crystalline "glyoxal trimer dihydrate" was converted into anhydrous monomeric glyoxal (**6**) upon heating with P_2O_5 at 135° in an adaptation of the procedure of Harries and Temme.[11] The anhydrous glyoxal was allowed to react with trimethyl phosphite in benzene solution (hexane is preferable as the solvent in this reaction) to give 2,2,2-trimethoxy-2,2-dihydro-1,3,2-dioxaphospholene (**7**). The conditions given in the Experimental Section permitted the utilization of about 25–30% of the reported glyoxal content of the "trimer dihydrate" in the formation of the phosphite adduct **7**, without the troublesome formation of insoluble "polyglyoxal."



(6) P. Fleury and J. Courtois, *Bull. Soc. Chim. France*, **8**, 397 (1941).
(7) (a) E. Juni and G. Heym, *Arch. Biochem. Biophys.*, **67**, 410 (1957); (b) E. Juni and G. Heym, *J. Biol. Chem.*, **218**, 365 (1956).
(8) (a) F. Ramirez, K. Tasaka, N. B. Desai, and C. P. Smith, *J. Org. Chem.*, **33**, 25 (1968); (b) D. Swank, C. N. Caughlan, F. Ramirez, O. P. Madan, and C. P. Smith, *J. Am. Chem. Soc.*, **89**, 6503 (1967), and references therein; (c) F. Ramirez and K. Tasaka, to be published.
(9) (a) F. Ramirez, S. B. Bhatia, A. J. Bigler, and C. P. Smith, *J. Org. Chem.*, **33**, 1192 (1968); (b) F. Ramirez, H. J. Kugler, A. V. Patwardhan, and C. P. Smith, *ibid.*, **33**, 1185 (1968); (c) F. Ramirez, H. J. Kugler, and C. P. Smith, *Tetrahedron*, **24**, 3153 (1968).
(10) This material is manufactured by Nobel-Bozel (Paris, France), and was obtained from Centerchem, Inc., New York, N. Y. It is reported to contain 98% of $(CHOCHO)_3 \cdot 2H_2O$ and "less than 2.0% moisture."
(11) C. Harries and P. Temme, *Ber.*, **40**, 166 (1907).

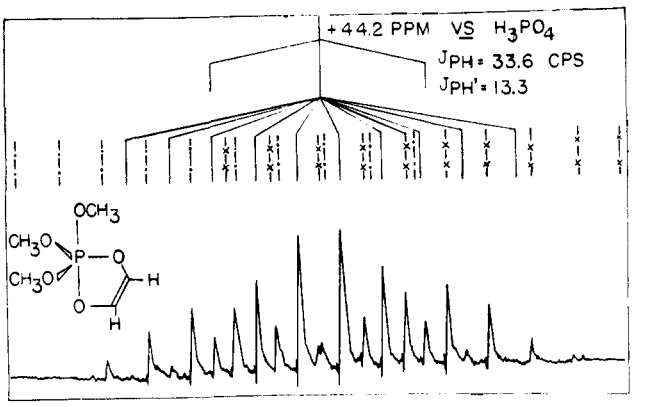
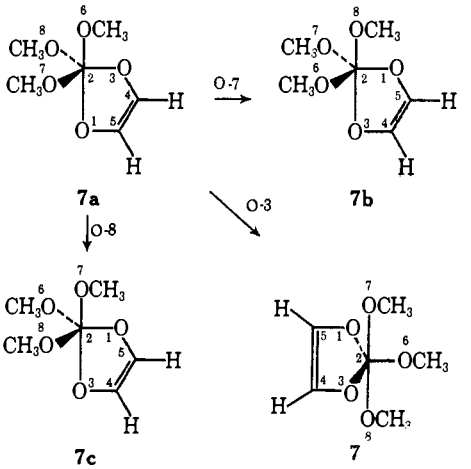


Figure 1. Observed and calculated ^{31}P nmr spectrum of the glyoxal–trimethyl phosphite 1:1 adduct in CH_2Cl_2 solution at 40.5 Mcps. The signal is a triplet of decets centered at +44.2 ppm *vs.* H_3PO_4.

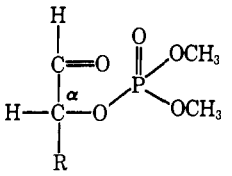
The structure of the phospholene **7** was based mainly on the position[12] and on the pattern of the ^{31}P nmr signal reproduced in Figure 1. The ^1H nmr spectrum in $CDCl_3$ solution at +30° had *one doublet* at τ 3.37, J_{HP} = 33.6 cps, due to the vinyl protons, and *one doublet* at τ 6.43, J_{HP} = 13.3 cps, due to the methoxy protons. *The spectrum was not changed significantly when examined at −70°.* As discussed[12,13] in connection with other derivatives of the 2,2-dihydro-1,3,2-dioxaphospholene[12] ring system, the apparent equivalency of the three methoxy groups and of the two vinyl protons is reasonable in terms of a rapid positional exchange of the groups attached to trigonal-bipyramidal phosphorus by the mechanism of pseudorotation.[14] Note that pseudorotation of the bipyramid **7a** using one or the other of the equatorial methoxy groups result in the same bipyramid **7b** and **7c**, respectively, with "scrambled" methoxy groups and vinyl protons. Further scrambling by subsequent pseudorotations is possible. A pseudorotation of the original bipyramid



7a using a ring oxygen as pivot leads to a new diastereomer, **7d** (also a *meso* form), in which the angle in

(12) (a) F. Ramirez, *Accounts Chem. Res.*, **1**, 168 (1968); (b) F. Ramirez, J. F. Pilot, O. P. Madan, and C. P. Smith, *J. Am. Chem. Soc.*, **90**, 1275 (1968); (c) F. Ramirez, *Trans. N. Y. Acad. Sci.*, **30**, 410 (1968).
(13) (a) F. H. Westheimer, *Accounts Chem. Res.*, **1**, 70 (1968); (b) D. G. Gorenstein and F. H. Westheimer, *Proc. Natl. Acad. Sci. U. S.*, **58**, 1747 (1967).
(14) (a) R. S. Berry, *J. Chem. Phys.*, **32**, 933 (1960); (b) E. L. Muetterties and R. A. Schunn, *Quart. Rev.* (London), **20**, 245 (1966); (c) E. L. Muetterties, *Inorg. Chem.*, **6**, 635 (1967); (d) P. C. Lauterbur and F. Ramirez, *J. Am. Chem. Soc.*, **90**, 6722 (1968).

Table I. Analyses of Phosphate Esters Derived from Glycolaldehyde, α-Hydroxy β-Keto Aldehydes, and α-Hydroxymalonaldehyde Chloride

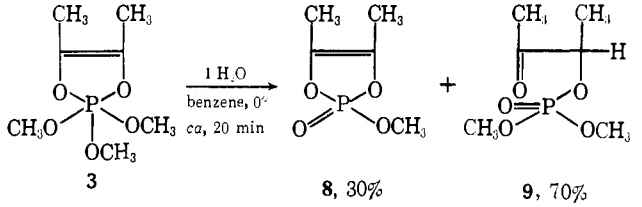


Compd	R	Bp, °C (mm)	Molecular formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H	Yield, %	Conditions Temp, °C	Conditions Time, hr	Solv
11	H	77–78 (0.05)	$C_4H_9O_5P$[a]	28.6	5.4	28.3	5.4	75	0	1	C_6H_6
18	$COCH_3$	120–122 (0.2)	$C_6H_{11}O_6P$	34.3	5.3	34.1	5.3	70	25	3	CH_2Cl_2
19	$COCF_3$	83–84 (0.2)	$C_6H_8O_6PF_3$	27.3	3.1	27.8	3.6	65	0	1	CH_2Cl_2
20	COC_6H_5	148–149 (0.2)	$C_{11}H_{13}O_6P$	48.5	4.8	49.0	4.8	85	75	1	None
22	COCl	82–83 (0.2)	$C_5H_8O_6PCl$[b]	26.0	3.5	25.9	3.7	80	0	1	CH_2Cl_2

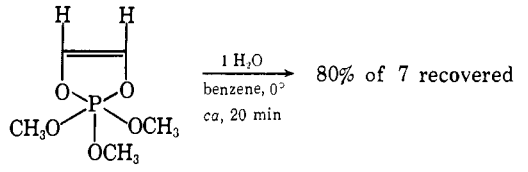
[a] *Anal.* Calcd for phosphorus: 18.4. Found: 18.0. [b] *Anal.* Calcd for phosphorus: 13.4. Found: 13.3. *Anal.* Calcd for Cl: 15.4. Found: 15.2.

the ring has been expanded from 90 to 120°. The relative energies of the diastereomers, and the changes associated with their interconversion by pseudorotation, have not been estimated as yet. However, X-ray data for an analogous cyclic phospholene disclosed a structure of type **7a** (≡**7b**, **7c**) with the phospholene ring in an apical-equatorial plane.[12a]

The glyoxal–phosphite adduct **7** *was much less sensitive to water than the analogous biacetyl–phosphite adduct* **3**. About 85% of the former, **7**, was recovered unchanged[8c] when its benzene solution was treated with 1 mol equiv of water at 0°, under conditions which completely hydrolyzed the latter, **3**, to a mixture of acetoinenediol cyclophosphate (**8**) and dimethyl phosphoacetoin[8b] (**9**). These hydrolyses are being studied further.

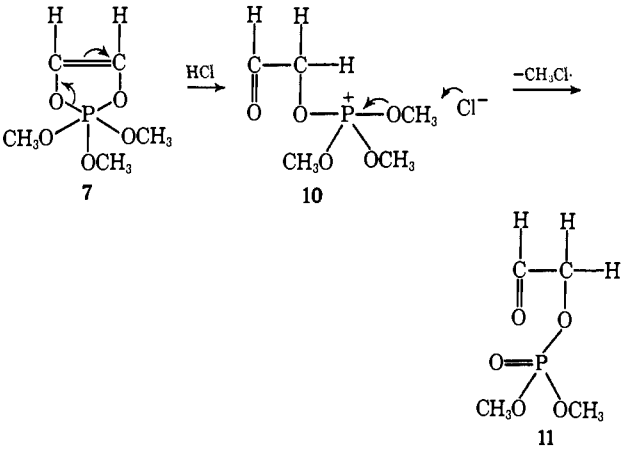


3 **8**, 30% **9**, 70%



7

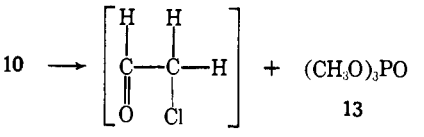
Reaction of the Glyoxal–Trimethyl Phosphite 1:1 Adduct 7 with Hydrogen Chloride, with Carboxylic Acid Chlorides, and with Phosgene. The phospholene **7** was easily transformed into dimethyl 2-oxoethyl phosphate (**11**) ("diose phosphate")[6] by hydrogen chloride. The properties of the phosphate **11** are summarized in Tables I and II. A probable mechanism for this reaction involves the tetraoxyphosphonium chloride **10** as an intermediate. A small amount of trimethyl phosphate (**13**, *ca.* 5%) was detected as a by-product of the reaction. Probably, it is formed together with



7 **10** **11**

α-chloroacetaldehyde (**12**) as a result of a nucleophilic attack by chloride on the α-carbon of intermediate **10**.

Acetyl chloride (**14**) was allowed to react with the phospholene **7** and gave dimethyl 2-(1,3-dioxobutyl) phosphate (**18**). The trifluoro analog **19** was made from trifluoroacetyl chloride (**15**) and the phospholene **7**. Benzoyl chloride (**16**) was somewhat less reactive toward the phospholene **7**, but it afforded dimethyl 2-(1,3-dioxo-3-phenylpropyl) phosphate (**20**).

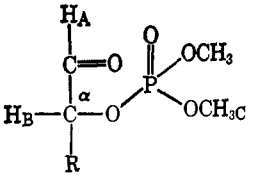


10 **12** **13**

It is assumed that the phospholene **7** performed a nucleophilic substitution on the acid chloride to yield the tetraoxyphosphonium chloride **17** which then lost methyl chloride and formed the phosphates **18**–**20**. Very little trimethyl phosphate was formed as by-product in these reactions.

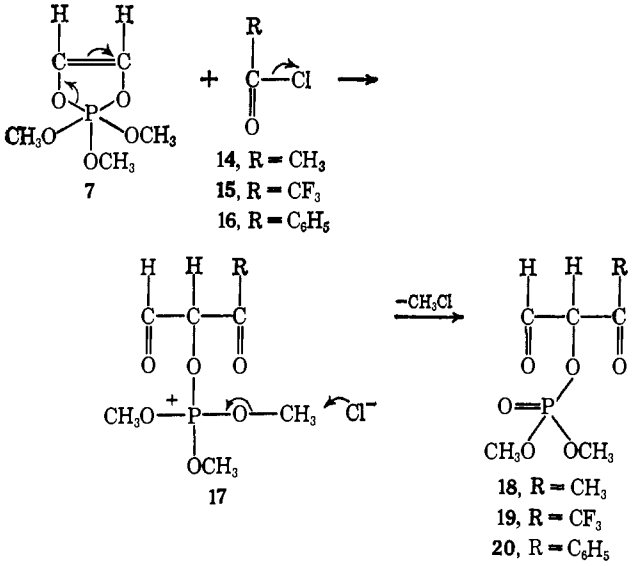
Phosgene (**21**) converted the phospholene **7** into dimethyl phosphohydroxymalonaldehyde chloride (**22**). The spectral data of Table II support structure **22**. The

Table II. Spectral Properties of Phosphate Esters Derived from Glycolaldehyde, α-Hydroxy β-Keto Aldehydes, and α-Hydroxymalonaldehyde Chloride[a]

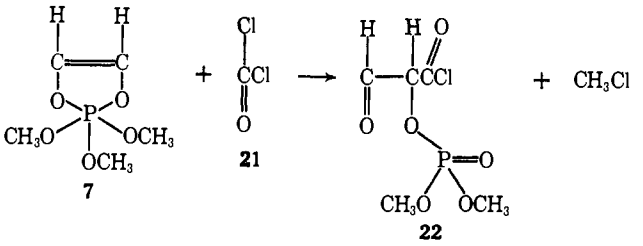


Compd	R	$\delta^{31}P$, ppm	τ_{H_A}	τ_{H_B}	τ_{H_C}	$J_{H_AH_B}$	J_{H_AP}	J_{H_BP}	J_{H_CP}	Ir, cm^{-1} CO	Ir, cm^{-1} PO	Ir, cm^{-1} $POCH_3$
11	H	−1.2	0.39	5.28	6.22	*Ca.* 0	1.3	10.2	11.1	1743	1295 1280	1053
18	$COCH_3$	+2.6	3.15	3.83	6.15[b]	3.6	0.9	5.3	11.5	1765	1305 1286 1260[c]	1055
19	$COCF_3$	+3.2	3.10	3.52	6.15	3.5	1.2	5.9	11.5	1795 1775	1305 1290 1255[d]	1060
20	COC_6H_5	+2.6	2.85	3.69	6.15	3.6	0.9	5.4	11.5	1740	1300 1290 1250	1060
22	COCl	+2.9	3.25	3.65	6.15	3.5	1.2	5.9	11.5	1803 1778	1315 1293 1263	1063

[a] ^{31}P nmr are given in parts per million *vs.* H_3PO_4 in CH_2Cl_2 at 40.5 Mcps. ^1H nmr are given in parts per million *vs.* TMS = 10 in $CDCl_3$ at 60 Mcps; *J* values in cps. Infrared spectra in dilute CCl_4 determined in a Perkin-Elmer 21 spectrometer calibrated *vs.* polystyrene. [b] Singlet at τ 7.80 (CH_3CO). [c] Additional band at 1220 cm^{-1}. [d] Additional band at 1235 cm^{-1}.



chloride **22** could be distilled unchanged under appropriate conditions; however, it underwent decomposition above certain temperatures.



Approximately 10% of trimethyl phosphate was formed as by-product in this reaction, presumably *via* an intermediate analogous to **17**. Some phosphoglycolaldehyde (**11**) was also formed due to traces of HCl in the phosgene. This can be minimized by passing the phosgene through anhydrous $CuSO_4$.

The availability of phosphate **22** opens a route to several derivatives of the hydroxymalonaldehyde system, for example, the dialdehyde obtainable by hydrogenation of the chloride.

Spectral Characteristics of the Hydroxy Aldehyde Phosphates (Table II). The P nucleus of phosphoglycolaldehyde (**11**) was slightly more shielded than that of trimethyl phosphate [$(CH_3O)_3PO$, $\delta^{31}P$ −2.4 ppm in CH_2Cl_2] and about as shielded as that of dimethyl phosphoacetoin (**9**) ($\delta^{31}P$ −0.2 ppm in CH_2Cl_2); *cf.* formula **1**, R = R′ = H and R = R′ = CH_3, respectively.

The introduction of an additional carbonyl function in phosphoglycolaldehyde (**11**) to give the α-hydroxy β-keto aldehyde phosphates **18–20** caused a small increase in the shielding of the P nucleus. This increase was virtually identical with that observed upon introduction of the same carbonyl function in dimethyl phosphoacetoin (**9**) to give the α-hydroxy β-diketone phosphates;[9a] *cf.* formula **2**, R = R′ = H and R = R′ = CH_3, respectively.

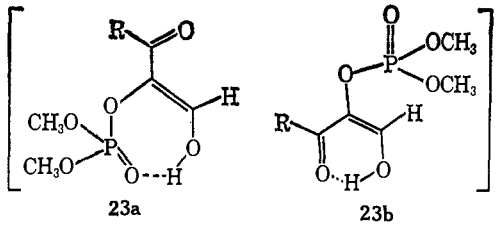
The introduction of an additional carbonyl function in phosphoglycolaldehyde (**11**) resulted in the following changes in the ^1H nmr spectrum. (1) The negligible coupling between the aldehyde proton and the proton on the α-carbon [J_{H_ACCHB}] in **11** was increased significantly. (2) The coupling between the α-proton and the phosphorus [J_{H_BCOP}] decreased. (3) The shielding of the aldehyde proton increased enormously (τ 0.4–3.0). The first effect[15] probably reflects changes in the dihedral angle formed by the planes defined by the set of atoms H_A–C–C and C–C–H_B in formulas **1** and **2** (R = R′ = H); this change can be visualized as a rotation around bond 1 in formulas **1** and **2** resulting from alterations in

(15) For discussion and references see: (a) F. Ramirez, A. V. Patwardhan, N. B. Desai, and S. R. Heller, *J. Am. Chem. Soc.*, 87, 549 (1965); (b) C. Benezra and G. Ourisson, *Bull. Soc. Chim. France*, 1825 (1966); (c) G. Mavel and G. Martin, *J. Chem. Phys.*, **59**, 762 (1962); (d) G. Mavel, *Ibid.*, **59**, 683 (1962).

the dipole interactions among C=O and P=O groups, and from steric effects. The second effect[15] is understandable if the dihedral angle formed by the plane defined by the set of atoms H_B–C–O and C–O–P is altered; this can result from a rotation around bond 2 in formulas **1** and **2**. Rotations around bonds 1 and 2 are affected by rotations around the P–O bond 3. The third effect[15] (shielding) is not independent of the first two (coupling) since the relative positions of the aldehyde proton and the ketone function (and hence the proton shielding) depend on the over-all conformation of the phosphates **1** and **2**; *cf.* rotation about acyl bond 4.

The carbonyl stretching frequency of phosphoglycolaldehyde (**11**) in dilute CCl_4 solution fell within the range which has been observed in normal unconjugated alkyl aldehydes[16a] (1740–1720 cm^{-1}). Both carbonyl frequencies in the acetyl analog (**18**) appeared at about the same frequency, which was somewhat higher than that of the parent compound; the ketone frequency here was definitely higher than that of saturated open-chain ketones (1725–1705 cm^{-1}). As expected, the two carbonyls of the trifluoroacetyl analog **19** were resolved; the lower frequency aldehyde band was relatively weak in intensity. The two carbonyls of the benzoyl analog **20** could not be resolved, which was unexpected in view of the usual relatively low frequency of C=O in aryl ketones (1700–1680 cm^{-1}).

The spectral evidence supports the dicarbonyl tautomers, **18–20** and **22**, as the predominant structures of these polyfunctional phosphates under the conditions of the measurements. The existence of significant amounts of enol tautomers **23a** or **23b** (or the corresponding ones involving the ketone function) was not conclusively established.[17]



23a **23b**

Experimental Section

The analyses were performed by the Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

2,2,2-Trimethoxy-2,2-dihydro-1,3,2-dioxaphospholene (7). a. A 500-ml, round-bottomed flask, having a N_2 inlet tube and a pressure-releasing valve, was connected by 10-mm glass tubing and by short sections of Tygon tubing to a 250-ml, round-bottomed flask fitted with a reflux condenser. *All parts must be scrupulously dry to avoid polymerization of the glyoxal.* The glyoxal trimer dihydrate[10] was dried in a vacuum desiccator over molecular sieves, and was mixed (63 g, 0.3 mol) with P_2O_5 (51 g, 0.36 mol) in the 500-ml flask. This mixture was immersed in a bath at 120°, and the bath temperature was slowly raised—with a stream of dry N_2 over the mixture—until yellow vapors of anhydrous monomeric glyoxal were evolved (*ca.* 135°). The vapors were led by the N_2 below the surface of a solution containing 112 g (0.9 mol) of freshly distilled trimethyl phosphite and 60 ml of anhydrous benzene at 25°. A mildly exothermic reaction occurred in the benzene solution and the yellow color of the glyoxal was discharged. The generation of the glyoxal from the trimer was exothermic after it had been initiated and the bath temperature was regulated accordingly. Under optimum reaction conditions, little or no yellow glyoxal should escape through the condenser, no glyoxal polymer should clog the apparatus, and only little polymerization should be observable in the benzene.

The solvent and the excess of phosphite were removed at 30° (*ca.* 0.5 mm). The residue was distilled through a 4-in. Vigreux column yielding the phospholene **7**, bp 36–37° (0.05 mm), in amounts ranging from 30 to 50 g (20–30%). The infrared spectrum in CCl_4 had bands at (cm^{-1}): 1645 (w), 1453 (w), 1205 (s), 1176 (s), and 1085 (vs). The ^1H and ^{31}P nmr spectra are described in the Results.

Anal. Calcd for $C_5H_{11}O_5P$: C, 32.9; H, 6.1; P, 17.0; mol wt, 182. Found: C, 32.7; H, 5.9; P, 17.1; mol wt, 189 (thermoelectric method in benzene).

In this procedure, formation of small amounts of glyoxal polymer was noted at the end of the inlet tube and in the condenser. This jelly-like film did not interfere with the reaction.

b. The phospholene **7** was also obtained when the monomeric glyoxal vapor was introduced into pure trimethyl phosphite, kept at 10 ± 2° by external cooling. However, the reaction was highly exothermic and difficult to control. When the phosphite was cooled to 0°, the glyoxal in the condensed phase was converted into polymer almost exclusively.

c. A benzene solution of monomeric glyoxal was kept 5 hr at 20° without evident polymerization. However, addition of this solution to a 1:1 phosphite–benzene solution gave only polymer and no phospholene.

d. *Caution! The possible formation of carbon monoxide during the pyrolysis of the trimer and the possible occurrence of violent polymerization of anhydrous monomeric glyoxal must be anticipated.*

Reaction of the Phospholene with Hydrogen Chloride. Anhydrous HCl was bubbled slowly through a stirred solution containing the phospholene **7** (14 g), benzene (55 ml), and a crystal of methyl orange indicator, at 0°. Completion of the reaction (*ca.* 1 hr) was indicated by red color of indicator; the solvent was removed at 30° (25 mm), and the residue was distilled through a 4-in. Vigreux column. The analytical and spectra data for dimethyl 2-oxoethyl phosphate (dimethyl phosphoglycolaldehyde (**11**) are given in Tables I and II.

Reaction of the Phospholene with Carboxylic Acid Chlorides. The acid chlorides were freshly distilled with protection against moisture. Trifluoroacetyl chloride was passed through $CuSO_4$ prior to reaction. The reactions were carried out as indicated in Table I. The reagents were mixed in the presence or in the absence of solvents, depending on the reactivity of the chlorides; the solvent was evaporated and the residue was purified by vacuum distillation. The properties of the phosphates **18–20** are given in Tables I and II.

Reaction of the Phospholene with Phosgene. The phosgene was condensed in a trap at −70°, was then passed through anhydrous $CuSO_4$, and led into a 2 *M* solution of the glyoxal–trimethyl phosphite adduct in CH_2Cl_2 at 0°.[18] The addition of the phosgene was carried out over a 40-min period; the chloride was used in excess (*ca.* 1.7 mol equiv). The solution was kept 1 additional hr at 0° and was evaporated, carefully, at 30° (10 mm) avoiding decomposition of the acid chloride. The product was analyzed by ^1H and ^{31}P nmr spectroscopy. In addition to the phosphohydroxymalonaldehyde chloride (**22**) (*ca.* 80%) there was trimethyl phosphate (*ca.* 10%) and phosphoglycolaldehyde (**11**) (*ca.* 10%, $\delta^{31}P$ −1.0 ppm). The aldehyde chloride **22** was purified by very short-path distillation at *ca.* 0.05 mm and a bath temperature not exceeding 80°. The properties are given in Tables I and II. *The acid chloride should be handled with care since it may be toxic.*

(16) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley & Sons, Inc., New York, N. Y., 1958: (a) Chapter 9; (b) Chapter 18.

(17) NOTE ADDED IN PROOF. The two CH_3O groups attached to the phosphorus in phosphates **18–20** and **22** gave *one doublet* in the ^1H nmr (Table II). No significant differences were noted in the spectra of **20** in CCl_4, $CDCl_3$, and C_6D_6 at 25°, and in CH_2Cl_2 at −77°. Presumably there was rapid keto–enol equilibration (involving small amounts of enol) which resulted in an equivalency of the two CH_3O groups.

(18) NOTE ADDED IN PROOF. It is better to add the phospholene to 2 mol equiv of phosgene in 5 *M* CH_2Cl_2 at 0°. The phospholene reacts with chloride **22**; however, this reaction interferes only at 25°.