

A New Synthesis of α,β -Dihydroxy Ketones via Oxyphosphoranes. Condensation of Aliphatic α -Diketones with Aldehydes by means of Trialkyl Phosphites. P^{31} and H^1 Nuclear Magnetic Resonance Spectra^{1,2}

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The biacetyl-trimethyl phosphite 1:1 adduct reacts with aliphatic and aromatic aldehydes to form one diastereomeric form of a cyclic saturated oxyphosphorane structure with the 1,3-dioxaphospholane ring system. The pentavalent phosphorus structures are based on P^{31} n.m.r., H^1 n.m.r., and infrared spectra. The oxyphosphoranes from aliphatic aldehydes give α,β -dihydroxy ketones in boiling water at pH 5. The biacetyl-benzaldehyde-phosphite adduct loses trimethyl phosphate and forms the enol form of 3-methyl-4-phenyl-2,4-butanedione in methanol solution.

Trimethyl phosphite reacts rapidly with the α -diketone biacetyl and gives a 1:1 adduct⁴⁻⁶ with the structure of a cyclic unsaturated pentaoxyphosphorane I, a derivative of the 1,3-dioxaphospholene ring system. The 1:1 adduct reacts slowly with a second molecule of biacetyl and yields two diastereomeric forms of a 2:1 adduct,⁷ meso-II and racemic III, in an 80:20 proportion.

The phosphorus can be removed from the 2:1 adducts by treatment with water in benzene solution.⁷ This constitutes a new synthesis of α -diketols IV and V of known configuration.

This paper reports the reaction of the biacetyl-trimethyl phosphite 1:1 adduct I with propionaldehyde, *n*-butyraldehyde, heptanal, and benzaldehyde, in order to extend this new carbon-carbon condensation reaction to the synthesis of α,β -dihydroxy ketones.

Results

The biacetyl-phosphite adduct I reacted slowly with anhydrous propionaldehyde (VI) and gave a distillable oil, $C_{10}H_{21}O_6P$, in ca. 85% yield. The data discussed below show that this oil is one of the two diastereomers

(1) (a) Organic Compounds with Pentavalent Phosphorus, Part XIV. (b) Part XIII: F. Ramirez, S. B. Bhatia, R. B. Mitra, Z. Hamlet, and N. B. Desai, *J. Am. Chem. Soc.*, **86**, 4394 (1964).

(2) Preliminary report: F. Ramirez, A. V. Patwardhan, N. B. Desai, N. Ramanathan, and C. V. Greco, *ibid.*, **85**, 3056 (1963).

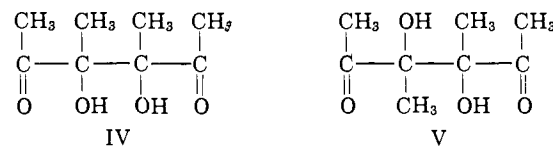
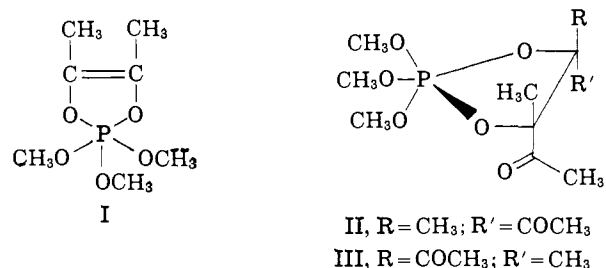
(3) This investigation was supported by Public Health Service Research Grant No. CA-04769-05 from the National Cancer Institute, and by the National Science Foundation (G 19509).

(4) (a) F. Ramirez and N. B. Desai, *J. Am. Chem. Soc.*, **82**, 2652 (1960); (b) *ibid.*, **85**, 3252 (1963).

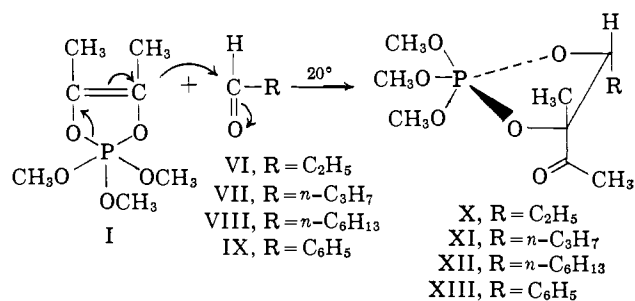
(5) (a) G. H. Birum and J. L. Dever, Abstracts, Division of Organic Chemistry, 135th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1958, p. 101P; (b) G. H. Birum and J. L. Dever, U. S. Patents 2,961,455 (1960) and 3,014,949 (1961).

(6) (a) V. A. Kukhtin, *Dokl. Akad. Nauk. SSSR*, **121**, 466 (1958); (b) V. A. Kukhtin and K. M. Orekhova, *J. Gen. Chem. USSR*, **30**, 1229 (1960); (c) V. A. Kukhtin and K. M. Kirillova, *ibid.*, **32**, 2755 (1962).

(7) (a) F. Ramirez, N. Ramanathan, and N. B. Desai, *J. Am. Chem. Soc.*, **84**, 1317 (1962); (b) *ibid.*, **85**, 3465 (1963).



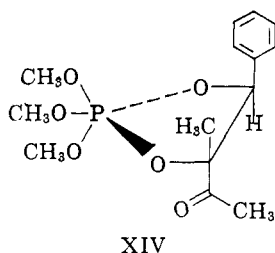
X which are possible for a cyclic oxyphosphorane structure. The reaction proceeded smoothly with



other aliphatic aldehydes. One diastereomer was formed in each case: XI from *n*-butyraldehyde (VII) and XII from heptanal (VIII).

Benzaldehyde (IX) reacted with the 1:1 adduct I and afforded mostly one oxyphosphorane XIII. In this case, however, small amounts of the second isomer, XIV, were detectable by means of H^1 n.m.r. spectroscopy. The isomers were produced in about 90:10 proportion. Since both isomers were available, and since the effect exerted by the phenyl ring on the chemical shifts of adjacent protons is relatively large, an assignment of configuration was possible. It was assumed that the oxyphosphoranes isolated in the aliphatic series X, XI, and XII had the same configuration as the major isomer XIII formed in the benzaldehyde case. (a) The infrared spectra of the aldehyde adducts showed the very strong band(s) in the region 9.2-9.4 μ which are due to POCH₃ stretching vibrations in oxyphosphoranes. The C=O stretching vibrations were at 5.85 μ . (b) The P^{31} n.m.r. signal⁸ of the pro-

(8) Documentation in ref. 4b, footnotes 13-16, and R. A. Y. Jones and A. R. Katritzky, *Angew. Chem. Intern. Ed. Engl.*, **1**, 32 (1962).



propionaldehyde adduct, X is shown in curve 1 of Figure 1; this is a 20-line signal, of which 16 lines are detectable above the noise. Curve 2 is the 10-line signal (8 lines visible) of a side band from the trimethyl phosphite used for calibration. The 20 lines of curve 1 correspond to a phosphorus signal split into 10 lines, $J_{PH} = 12.6$ c.p.s., by the 9 methoxyl protons. Each of these 10 lines is split into two lines, $J_{PH} = 6.3$ c.p.s., by the lone proton on the ring carbon.

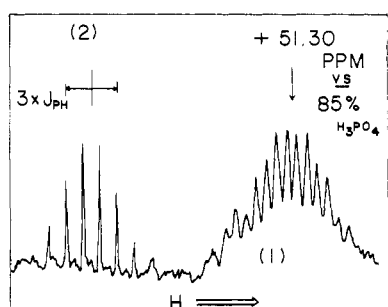


Figure 1. Calibration of the P^{31} n.m.r. spectra. (1) Signal due to the biacetyl-propionaldehyde-trimethyl phosphite adduct (X) as neat liquid. (2) Side band of reference, $(CH_3O)_3P$, contained in a sealed capillary tube immersed in the liquid adduct, X. The side band 2 was $+7621.5 \pm 0.1$ c.p.s. to high field from the phosphite, measured by a frequency counter. The coupling constant of trimethyl phosphite was found to be $J_{HP} = 10.48$ c.p.s.; from it, the separation between 1 and 2 was 124.8 c.p.s. The chemical shift of adduct vs. phosphite was $+191.26$ p.p.m. Similar measurements of the chemical shift of trimethyl phosphite vs. 85% H_3PO_4 , with the latter in the capillary tube, gave $\delta_{P^{31}} = -140.00$ p.p.m. for $(CH_3O)_3P$. Therefore, $\delta_{P^{31}} = +51.26$ p.p.m. vs. 85% H_3PO_4 . A duplicate calibration gave $+51.34$ p.p.m. For previous measurements on trimethyl phosphite see: H. Finegold, *Ann. N. Y. Acad. Sci.*, **70**, 875 (1958); J. R. Van Wazer, C. F. Callis, J. N. Shooley, and R. C. Jones, *J. Am. Chem. Soc.*, **78**, 5715 (1956).

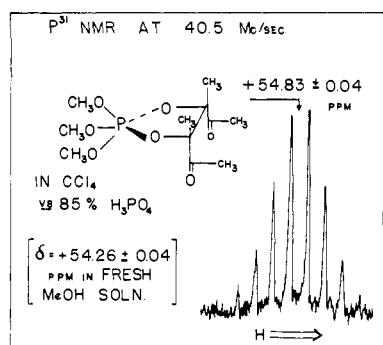


Figure 2

The P^{31} n.m.r. spectrum of the *meso* 2:1 biacetyl-trimethyl phosphite adduct⁷ II is shown in Figure 2. In this spectrum, the phosphorus signal is split into 10 lines only, since the 1,3-dioxaphospholane ring does

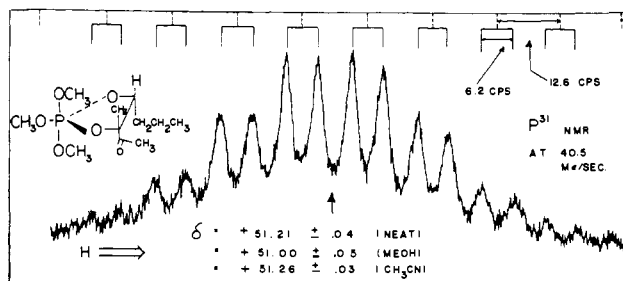


Figure 3.

not carry hydrogen atoms. The large positive chemical shifts vs. 85% H_3PO_4 in the spectra of the biacetyl-propionaldehyde adduct X, $\delta_{P^{31}} = +51.30$ p.p.m. and of the 2:1 biacetyl adduct⁷ II, $\delta_{P^{31}} = +54.83$ p.p.m., suggest pentacovalent phosphorus⁴⁻⁶ in both adducts.

The P^{31} n.m.r. spectra of the butyraldehyde, heptanal, and benzaldehyde adducts XI, XII, and XIII gave large positive chemical shifts also: $\delta_{P^{31}} = +51.2$, $+51.3$, and $+51.5$ p.p.m., respectively. The spectrum of the butyraldehyde adduct XI is reproduced in Figure 3 to show the optimum resolution which was obtained in these measurements. No significant changes were noted in acetonitrile or even in a *freshly prepared* methanol solution. (c) The H^1 n.m.r. spectra of the oxyphosphoranes X, XI, and XII are consistent with the structures shown. The nine methoxy protons gave one doublet, $J_{HP} = 12.7$ c.p.s. at 6.4 p.p.m. in the τ -scale⁹; therefore, the three methoxy groups are equivalent^{4,7,10} under the conditions of the measurements. The doublet due to the ring proton was hidden under the methoxy doublet, as shown by the integration value. The acetyl and the ring methyl protons gave singlets at τ 7.8 and 8.7, respectively.

The symmetry of the P^{31} signals (Figures 1 and 3), the H^1 n.m.r. data, and the results of the hydrolysis experiments (*vide infra*) show that the distilled oxyphosphoranes X, XI, and XII are stereochemically pure.

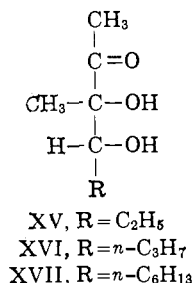
The H^1 n.m.r. spectrum of the benzaldehyde adduct XIII showed the ring proton at τ 5.45, split by the phosphorus, $J_{HP} = 5.6$ c.p.s., in agreement with the value found in the P^{31} spectrum. The methoxy doublet was at τ 6.42, $J_{HP} = 12.5$ c.p.s.; a second, much weaker doublet displaced 1.7 c.p.s. to higher field is attributed to a diastereomer, XIV. The acetyl protons of the *major isomer* and the ring methyl protons of the *minor isomer* were at abnormally high fields (τ 8.40 and 9.18, respectively). The acetyl protons of the *minor isomer* and the ring methyl protons of the *major isomer* were normal (τ 7.76 and 8.52, respectively). This probably reflects the shielding of protons by the phenyl ring in the isomers: major XIII and minor XIV.

The oxyphosphoranes X, XI, and XII derived from *aliphatic* aldehydes were converted into α,β -dihydroxy ketones in boiling water at pH 5. The yields were about 50%. In neutral or in alkaline solutions, de-

(9) See, for example, L. M. Jackman, "Applications of N.M.R. Spectroscopy in Organic Chemistry," Pergamon Press Inc., New York, N. Y., 1959, pp. 47, 77.

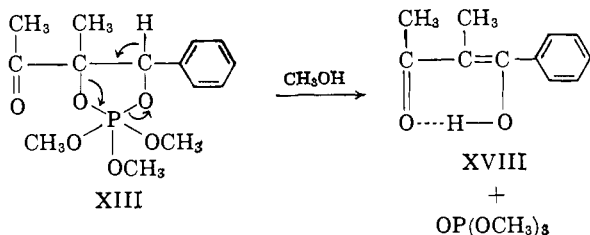
(10) E. L. Muttarties, W. Mahler, and R. Schmutzler, *Inorg. Chem.*, **2**, 613 (1963), discussed the equivalence of the three fluorine atoms in $(CH_2)_3PF_3$.

aldolization was the predominant reaction. The *erythro* configuration, XV¹¹, XVI, and XVII, is assigned to the dihydroxy ketones, since no epimerization was detected during the hydrolysis. For example, the H¹ n.m.r. of DL-*erythro*-3-methylhexane-3,4-diol-2-one¹¹ (XV), which is reproduced in Figure 4, shows the signals to be expected from one diastereomer only. The



structure of the dihydroxy ketones is based on H¹ n.m.r. and infrared spectra.

No α,β -dihydroxy ketone could be isolated from the hydrolysis of the benzaldehyde adduct XIII. Apparently, this type of oxyphosphorane is quite unstable in hydroxylic solvents. When a solution of XIII in methanol was heated, ejection of trimethyl phosphate from the molecule was observed. This reaction produced the enol form (XVIII) of 3-methyl-4-phenyl-2,4-butanedione, a fragrant, crystalline substance having a relatively high vapor pressure. The infrared



and the H¹ n.m.r. spectra (see Experimental) support the enol structure XVIII. The compound gave an instantaneous purple color with FeCl₃ and reacted with 2,4-dinitrophenylhydrazine in the manner expected from a β -diketone.

The oxyphosphoranes derived from aliphatic aldehydes did not lose trimethyl phosphate in methanol solution.

Discussion

These investigations show that trialkyl phosphites are capable of effecting the condensation of: (1) an aliphatic α -diketone with (a) a simple aliphatic or aromatic aldehyde, (b) another aliphatic⁷ or aromatic^{7a} α -diketone, and (c) an α -keto ester²; (2) two molecules of an aromatic α -diketone¹², *i.e.*, acenaphthenequinone; (3) two molecules of an α -keto ester¹³; and (4) two molecules of a cyclic aromatic anhydride.¹⁴ In cases 1, 2, and 3, the condensations involve cyclic oxyphosphoranes as intermediates and/or final products. The reaction of a cyclic *unsaturated* oxyphos-

(11) Formula VIIa of ref. 2, which shows a *threo* configuration for this dihydroxy ketone, is in error, and should be replaced by formula XV of the present paper, which shows the *erythro* configuration.

(12) F. Ramirez and N. Ramanathan, *J. Org. Chem.*, **26**, 3041 (1961).

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

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

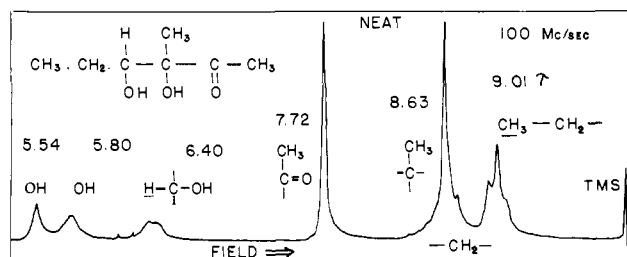
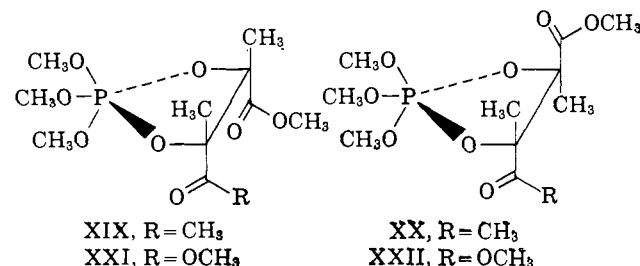


Figure 4.

phorane like I with a carbonyl function can be pictured as a concerted rupture of a phosphorus-oxygen bond in I, and a nucleophilic addition of carbon to the carbonyl function (VI-IX). However, the intervention of undetectably small amounts of an open-chain dipolar form of the adduct I cannot be ruled out.

The reaction of the biacetyl-phosphite 1:1 adduct I with monoaldehydes gave exclusively or predominantly one diastereomeric oxyphosphorane X-XIII with a *trans* CH₃-alkyl configuration. However, the reaction of I with biacetyl⁷ produced about 80% *meso*-II with *cis* CH₃-CH₃, and 20% racemic III. The reaction of I with methyl pyruvate² gave a minor isomer with *cis* CH₃-CH₃ XIX and a major isomer with *trans* CH₃-CH₃ XX. When two molecules of methyl pyruvate were condensed by means of trimethyl phosphite,¹³ the minor isomer (*ca.* 40%) had the *meso* configuration XXI and the major isomer (60%) had the racemic configuration XXII. Possibly, steric repulsion between alkyl groups in the transition state



favors a *trans* alkyl-alkyl configuration in the 2:1 oxyphosphorane, while dipole-dipole attraction between carbonyls tends to give oxyphosphoranes with the *cis* alkyl-alkyl configuration. If this is so, the results imply a stronger attraction between two acetyl groups (II > III) than between two carbomethoxy groups (XXI < XXII) or an acetyl and a carbomethoxy (XIX < XX). Stereoelectronic factors in the reaction of phosphorus ylids with carbonyl compounds (Wittig reaction) have been extensively discussed.¹⁵

There are significant differences in the magnitude of the P³¹-H¹ spin-spin splitting in the system POCH when the proton is part of the ring or of the methoxy group in the oxyphosphoranes X-XIII, possibly due to differences in the dihedral angles between the planes P-O-C and H-C-O.¹⁶

The formation of α,β -dihydroxy ketones XV-XVII is not as easy as the formation of α -diketols⁷ IV and V from the corresponding oxyphosphoranes.

The difference in the stability of oxyphosphoranes derived from aliphatic aldehydes X-XII and aromatic

(15) See S. Trippett, *Quart. Rev.* (London), **17**, 406 (1963); pp. 416-420.

(16) J. G. Verkade and R. W. King, *Inorg. Chem.*, **1**, 948 (1962).

aldehydes XIII in hydroxylic solvents is probably due to the enhanced acidity of the benzylic hydrogen in XIII, and to the additional driving force which is provided by conjugation of the olefinic double bond with the benzene ring in the transition state of the decomposition into phosphate ester and enol XVIII. Drastic molecular rearrangements have been observed in the methanolysis of the 2:1 acenaphthenequinone-phosphite adduct¹² and the biacetyl-acenaphthenequinone-phosphite adduct.^{7a}

Experimental

The infrared spectra were determined on a Perkin-Elmer 21 spectrometer. The H^1 n.m.r. were taken in a Varian A60 or in a Varian HR-100 instrument, as indicated, using tetramethylsilane (TMS) as internal reference. The analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

Calibration of P^{31} N.m.r. Spectra. The P^{31} spectra were determined in a Varian HR-100 instrument at 40.5 Mc./sec. The spectra were calibrated against trimethyl phosphite; the chemical shift of the latter was measured against 85% H_3PO_4 . The procedure is given in Figure 1. All chemical shifts are referred to 85% H_3PO_4 .

Biacetyl-Trimethyl Phosphite 1:1 Adduct (2,2,2-Trimethoxy-4,5-dimethyl-1,3-dioxaphospholene) (I). Freshly distilled biacetyl was added, dropwise, under N_2 , to 1.1 mole equiv. of dry trimethyl phosphite held at 0–5°. The mixture was allowed to come to 20°, kept there overnight, and then distilled. The yield of colorless adduct, n^{25}_D 1.4385 (b.p. in the range 45 to 55° at 0.2 to 0.5 mm.) was 95%. The adduct must be protected against moisture and oxygen. Repeated exposures to oxygen produce yellow biacetyl which reacts further with the 1:1 adduct to yield colorless 2:1 adduct.⁷

Reaction of the Biacetyl-Trimethyl Phosphite 1:1 Adduct (I) with Propionaldehyde. Preparation of 2,2,2-Trimethoxy-4 β -methyl-4 α -acetyl-5 α -ethyl-1,3-dioxaphospholane (X). Propionaldehyde was shaken with Drierite for several hours and then distilled.

The biacetyl-phosphite adduct I (52.5 g.) and the propionaldehyde (43.5 g., 1:3 mole ratio) were allowed to react at 20° for 8 days under N_2 with stirring. The H^1 n.m.r. of this material exhibited only traces of the signal at τ 8.23 which is due to I. The excess propionaldehyde was removed at 15 mm. and the residue was distilled using a 12-in. spinning band column: (1) 0.9 g. of forerun below 70° (0.5 mm.); (2) 57.3 g. (87%) of biacetyl-aldehyde-phosphite adduct (IX), n^{25}_D 1.4351, collected at 69–71° (0.4 mm.); (3) 5.2 g. (9%) of a cyclic phospho triester,² n^{25}_D 1.4360, collected at 83–90° (0.4 mm.); (4) ca. 3 g. of residue shown to be mostly phosphate by infrared.

Fraction 2 was separated into three arbitrary fractions by means of a 12-in. spinning band column. Fraction 2-1 was colorless liquid (6 g., ca. 10%), n^{25}_D 1.4320, collected at 36–63° (0.2 mm.). This was shown by H^1 n.m.r. to be mostly adduct IX contaminated with traces of adduct I and an unidentified component of lower refractive index. Fractions 2-2 (25 g., n^{25}_D 1.4360) and 2-3 (23 g., n^{25}_D 1.4361) were collected at 63–64° and 64–66° (0.2 mm.), respectively.

These constituted a 72% yield of 2,2,2-trimethoxy-4 β -methyl-4 α -acetyl-5 α -ethyl-1,3-dioxaphospholane (X).

Anal. Calcd. for $C_{10}H_{21}O_6P$: C, 44.8; H, 7.8; P, 11.6. Found: C, 44.5; H, 7.9; P, 12.2.

The P^{31} n.m.r. spectrum of the neat liquid adduct X had 16 detectable lines centered at $+51.27 \pm 0.03$ p.p.m. vs. 85% H_3PO_4 as external reference. The spectrum corresponded to a P-signal which is split into 10 lines with $J_{PH} = 12.6$ c.p.s., each line being split into two lines with $J_{PH} = 6.3$ c.p.s.

The infrared spectrum (in CCl_4) had bands at 5.85 (1705 cm^{-1} , strong carbonyl) and 9.22 μ (1085 cm^{-1} , very strong $POCH_3$).

The H^1 n.m.r. spectrum (neat, 60 Mc./sec.) had a doublet at 6.46 ($J_{HP} = 12.7$ c.p.s.), which integrated as $10H^1$ since the lone methine proton and the nine methoxyl protons coincide; there was a $3H^1$ singlet at 7.83 (acetyl) and another at 8.73 (methyl attached to quaternary carbon); there was a multiplet at 9.0 (methyl of ethyl group); the latter two signals integrated as $8H^1$ since the two methylene protons fall in the same region.

The adduct X was very sensitive to moisture. Other experiments in which the 1:1 biacetyl-phosphite adduct I and propionaldehyde were kept, in a 1:3 mole ratio, for 64 and 88 hr. gave lower yields (50–55%) of X. A 136-hr. experiment gave 3.5% of forerun (b.p. 50–54° at 0.5 mm., n^{25}_D 1.4318); 82% of adduct X (b.p. 62–68° at 0.2 mm., n^{25}_D 1.4360).

Attempt to Detect Further Reaction of the 1:1 Biacetyl-Propionaldehyde-Trimethyl Phosphite Adduct (X) with Propionaldehyde. The adduct X and propionaldehyde (5 mole equiv.) were kept for 10 days at 20° under N_2 . The infrared spectrum showed no significant change except the appearance of bands due to a small amount of phosphate produced by hydrolysis. At least 75% of original adduct was recovered by distillation. No biacetyl was formed (v.p.c.).

Hydrolysis of the Biacetyl-Propionaldehyde-Trimethyl Phosphite Adduct (X) with an Excess of Water. Preparation of DL-erythro-3-Methylhexane-3,4-diol-2-one (XV). Adduct X (8.9 g.) was mixed with 10 ml. of water and treated with 16.7 ml. of 2 N NaOH (1 equiv.). This solution was kept for 2 hr. at the boiling point, cooled, saturated with NaCl, and extracted with chloroform. Distillation gave 2.2 g. (45%) of liquid DL-erythro-3-methylhexane-3,4-diol-2-one (XV), b.p. 48–50° (0.2 mm., bath at 95°), n^{25}_D 1.4490.

Anal. Calcd. for $C_7H_{14}O_3$: C, 57.5; H, 9.6. Found: C, 57.4; H, 10.0.

The infrared spectrum (in CCl_4) had bands at 2.90 (shoulder), 2.94 (m), 5.90 (strong), 7.40 (ms), and 8.60 (m) μ .

The H^1 n.m.r. spectrum (neat liquid) at 100 Mc./sec. had singlets at τ 5.54 and 5.80, multiplet at 6.40, singlets at 7.72 and 8.63, and a multiplet at 9.0. At 60 Mc./sec. (neat) there were signals at τ 5.60, 5.87, and 6.42 which integrated as $3H^1$, a $3H^1$ singlet at τ 7.74, a singlet at 8.63, and a multiplet at 9.0, $J_{HH} = 5.5$ c.p.s.; the latter two integrated as $8H^1$ since they included the two methylene protons. The spectrum in CCl_4 showed no significant differences.

Reaction of the 1:1 Biacetyl-Trimethyl Phosphite Adduct (I) with Butyraldehyde. Preparation of 2,2,2-Trimethoxy-4 β -methyl-4 α -acetyl-5 α -n-propyl-1,3-dioxaphospholane (XI). Adduct I (42.0 g.) and *n*-butyraldehyde (43.2 g., 1:3 mole ratio, Eastman Kodak Co., used as received) were allowed to react at 20° for 8 days under N₂ with stirring. The excess butyraldehyde was removed at 40° and 15 mm. The residue was fractionated using a 12-in. spinning band column: (1) 3.1 g. of forerun, below 75° (0.7–0.4 mm.); (2) 27.8 g. of colorless liquid, *n*^{25D} 1.4381, b.p. 72–78° (0.4–0.2 mm.); (3) 17.3 g., *n*^{25D} 1.4381, b.p. 72–73° (0.2 mm.); (4) 3.4 g., *n*^{25D} 1.4382, b.p. 72–73° (0.2 mm.). Fractions 2, 3, and 4 gave identical infrared and H¹ n.m.r. spectra and constituted an 86% yield of 2,2,2-trimethoxy-4 β -methyl-4 α -acetyl-5 α -*n*-propyl-1,3-dioxaphospholane (XI).

Anal. Calcd. for C₁₁H₂₃O₆P: C, 46.8; H, 8.2; P, 11.0. Found: C, 46.3; H, 8.1; P, 11.3.

The P³¹ n.m.r. spectrum of the neat liquid adduct XI had 16 detectable lines centered at +51.21 \pm 0.04 p.p.m. vs. 85% H₃PO₄. The P-signal was split into 10 lines, *J*_{PH} = 12.6 c.p.s.; each line was split into two lines, *J*_{PH} = 6.2 c.p.s. The spectrum was also examined in a freshly prepared methanol solution ($\delta_{P^{31}}$ = +51.00 \pm 0.05 p.p.m.) and acetonitrile solution ($\delta_{P^{31}}$ = +51.26 \pm 0.03 p.p.m.).

The infrared spectrum (CCl₄) had bands at 5.86 (1705 cm.⁻¹ strong carbonyl) and split band at 9.22 (1085 cm.⁻¹) and 9.35 μ (1070 cm.⁻¹, very strong POCH₃).

The H¹ n.m.r. spectrum (neat, 60 Mc./sec.) had a 10H¹ doublet at τ 6.47, *J*_{HP} = 12.8 c.p.s., for the three methoxyl groups and the methine proton; a 3H¹ singlet at τ 7.83 (acetyl); a singlet at τ 8.73 (methyl attached to quaternary C plus methylenes); and a multiplet at τ 9.1 (methyl of *n*-propyl group); the latter two signals integrated as 10H¹. The spectrum was examined also at 100 Mc./sec.; the coupling constants were 12.5 and 6.2 c.p.s., respectively.

Hydrolysis of the Biacetyl-Butyraldehyde-Trimethyl Phosphite Adduct (XI) with an Excess of Water. Preparation of DL-erythro-3-Methylheptane-3,4-diol-2-one (XVI). Adduct (XI, 41.5 g.) was mixed with 70 ml. of water. A solution of 6 g. of sodium hydroxide in 30 ml. of water was added. The mixture (pH ca. 5.0) was kept for 2 hr. at the boiling point, cooled, saturated with sodium chloride, and extracted with chloroform. Distillation gave 13 g. (55%) of the liquid DL-erythro-3-methylheptane-3,4-diol-2-one (XVI), b.p. 76–78° (0.2 mm., bath at 110°), *n*^{25D} 1.4491.

Anal. Calcd. for C₈H₁₆O₃: C, 60.0; H, 10.0. Found: C, 59.9; H, 9.8.

The infrared spectrum (in CCl₄) had bands at 2.84 (mw), 2.91 (m), 5.88 (s), 6.90 (mw), 7.40 (m), 8.61 (m), 9.1 (w), and 9.3 (w) μ .

The H¹ n.m.r. spectrum (in CCl₄) had a 2H¹ signal at τ 5.92 (OH); a 1H¹ multiplet at τ 6.3 (methine); a 3H¹ singlet at 7.80 (acetyl); a singlet at 8.70 and a multiplet at 9.1, which integrated as 10H¹ since the four methylene protons fell in this region also.

*Reaction of the Biacetyl-Trimethyl Phosphite 1:1 Adduct (I) with Heptanal. Preparation of 2,2,2-Trimethoxy-4 β -methyl-4 α -acetyl-5 α -*n*-hexyl-1,3-dioxaphospholane (XII).* Adduct I (21 g.) and heptanal (34

g., 3 mole equiv., Eastman Kodak Co., used as received) were allowed to react at 20° under N₂. The reaction was followed by means of infrared spectra; no changes were detectable after 10 days. The heptanal was removed at 95° (15 mm.). The residue was fractionated through a 12-in. spinning band column: (1) g. of forerun below 80° (0.3 mm.); (2) 32 g. of colorless liquid, *n*^{25D} 1.4418, b.p. 96–101° (0.2 mm.), bath temperature 150–155°; this represented a nearly quantitative yield of 2,2,2-trimethoxy-4 β -methyl-4 α -acetyl-5 α -*n*-hexyl-1,3-dioxaphospholane (XII).

Anal. Calcd. for C₁₄H₂₉O₆P: C, 51.9; H, 8.9; P, 9.6. Found: C, 52.1; H, 9.0; P, 9.8.

The P³¹ n.m.r. spectrum of the neat liquid had a 20-line multiplet at +51.35 \pm 0.04 p.p.m. vs. 85% H₃PO₄.

The infrared spectrum had a band at 5.81 (1720 cm.⁻¹, C=O), a very strong broad band at 9.17 (1090 cm.⁻¹), and a shoulder at 9.01 μ (1110 cm.⁻¹, POCH₃).

The H¹ n.m.r. spectrum (CCl₄) had a 10H¹ doublet at τ 6.45, *J*_{HP} = 13 c.p.s. (methoxy plus methine protons), a 3H¹ singlet at 7.82 (acetyl), a broad signal at 8.70, and a multiplet at 9.1; these two signals integrated as 16H¹.

Hydrolysis of the Biacetyl-Heptanal-Trimethyl Phosphite Adduct (XII) with an Excess of Water. Preparation of DL-erythro-3-Methyldecane-3,4-diol-2-one (XVII). The adduct XII (10.21 g., 31.5 mmoles) was added to water (25 ml.) and the two-phase system was stirred at 20°. An exothermic reaction occurred within 8 min.; the pH of the clear solution was 1.2. This solution was titrated with 2 *N* aqueous NaOH to pH 5.0, consuming 12.3 ml. (78% of the theory for one acidic function). The solution was kept for 3 hr. at reflux, cooled, and extracted with chloroform (without addition of NaCl). The chloroform extracts were combined, dried over MgSO₄, and evaporated. The residue was taken up in benzene, filtered, and evaporated at 20° (18 mm., last traces at 0.2 mm.). The thick oil was analyzed without further purification. Yield of α,β -dihydroxy ketone XVII was ca. 50%.

Anal. Calcd. for C₁₁H₂₂O₃: C, 65.3; H, 10.9. Found: C, 65.1; H, 10.8.

The infrared spectrum (CCl₄) had bands at 2.90 and 5.85 μ . The proton n.m.r. spectrum (CCl₄) had a 2H¹ signal at τ 5.5, a 1H¹ multiplet at τ 6.3, a 3H¹ singlet at τ 7.76, a multiplet at τ 8.70, and a multiplet at τ 9.1; the last two signals integrate as 16H¹.

When the aqueous layer from which the dihydroxy ketone XVII had been removed was salted out with NaCl and the mixture was re-extracted with chloroform, a waxy material, turning to an amorphous powder on drying at 30° (0.1 mm.), was obtained. The spectral data suggest that this material may result from polymerization of dihydroxy ketone.

Reaction of the Biacetyl-Trimethyl Phosphite 1:1 Adduct (I) with Benzaldehyde. Preparation of 2,2,2-Trimethoxy-4 β -methyl-4 α -acetyl-5 α -phenyl-1,3-dioxaphospholane (XIII) and 5 β -Phenyl Isomer (XIV). A mixture of 1:1 adduct I (10.5 g.) and benzaldehyde (15.9 g., 3 mole equiv., dried and freshly distilled) was stirred for 120 hr., at 20° under N₂. The excess benzaldehyde was removed at 0.3 mm. in a bath at 40–60° (ca. 10 g. recovered). The viscous residue

was distilled in an oil-jacketed, short-path distillation flask. The first 10% of material which distilled below ca. 100° (0.1 mm., bath at ca. 110°) was discarded. The 2,2,2-trimethoxy-4 β -methyl-4 α -acetyl-5 α - and -5 β -phenyl-1,3-dioxaphospholane (XIII and XIV) distilled as a colorless, viscous oil, n_D^{25} 1.4940, b.p. 110–112° (0.1 mm., bath 120°); the yield was 80%.

Anal. Calcd. for C₁₄H₂₁O₆P: C, 53.1; H, 6.6; P, 9.8. Found: C, 52.7; H, 6.7; P, 10.1.

The P^{31} n.m.r. spectrum (neat) had a signal at +51.5 \pm 0.1 p.p.m. vs. 85% H₃PO₄. This signal corresponded to a P-line split into 10 lines with $J_{PH} = 12.5$ c.p.s., each one of them being split into two lines with $J_{PH^1} = 5$ c.p.s. Only one diastereomer was detectable; the second was present in amounts too small for detection.

The infrared spectrum (in CCl₄) had a strong, sharp band at 5.85 (1707 cm.⁻¹, C=O) and a very strong split band at 9.26 and 9.40 μ (1080 and 1065 cm.⁻¹, POCH₃).

The H^1 n.m.r. spectrum (in CCl₄) had five aromatic protons at 2.84; a one-proton doublet at τ 5.45, $J_{HP} = 5.6$ c.p.s.; a major 9H¹ doublet at τ 6.42, $J_{HP} = 12.5$ c.p.s.; a minor doublet 1.7 c.p.s. toward high field (CH₃OP of two diastereoisomers, roughly 90:10); the acetyl of the major isomer gave a 3H¹ singlet at τ 8.40, that of the minor isomer was at 7.76; the methyl of the major isomer was at τ 8.52, that of the minor isomer at 9.18.

Failure to remove excess benzaldehyde can be recognized by the appearance of bands at 6.2 and 8.3 μ in the contaminated product. If the 1:1 adduct is not completely consumed, it will contaminate the 2:1 adduct; this is recognized by the presence of the doublet at τ 6.52 (7 c.p.s. toward high field of XIII) and the singlet at 8.25 due to I.

Samples of the 2:1 adduct, XIII, which were heated to ca. 170° at 0.5–0.2 during attempts to effect fractional distillation, became contaminated with a material having a signal at τ 8.2 in the H^1 n.m.r.; possibly this is due to decomposition into 1:1 biacetyl adduct I and/or enol XVIII.

Decomposition of the Biacetyl-Benzaldehyde-Tri-methyl Phosphite Adduct (XIII) in Methanol Solution.

Preparation of 3-Methyl-4-phenyl-3-buten-4-ol-2-one (XVIII). A solution of the adduct XIII (24.5 g.) in anhydrous methanol (50 ml.) was kept for 1 hr. at reflux temperature and for 16 hr. at 20°. The methanol was removed at 760 mm. The infrared spectrum of the residue showed the presence of a very weak carbonyl band at 5.8 and of a strong, broad band at 6.2 μ , in addition to the bands of trimethyl phosphate. The latter was collected at 27–30° (0.1 mm.) (ca. 90% of the theory). The residue was submitted to short-path distillation at 0.2 mm. in a bath at 100–105°; the distillate, b.p. ca. 65–75° (0.2 mm.) solidified to colorless crystals, m.p. 51–53°. The yield of 3-methyl-4-phenyl-3-buten-4-ol-2-one (XVIII) was 11.2 g. (82%), m.p. 53–54° (hexane).

Anal. Calcd. for C₁₁H₁₂O₂: C, 75.0; H, 6.8; mol. wt., 176. Found: C, 75.1; H, 6.9; mol. wt., 186 (isothermal distillation).

The infrared spectrum (CCl₄) had a very broad and strong band from 5.9 to 6.6 (1675 to 1515 cm.⁻¹) with a minimum at 6.25 μ (1600 cm.⁻¹); it had bands at 7.14 and 7.55 ($m\mu$).

The H^1 n.m.r. spectrum (CCl₄) at 60 Mc./sec. showed a 1H¹ signal at τ -7.17, a 5H¹ signal at τ 2.5 (aromatic), and a 6H¹ signal at τ 8.20. The spectrum was similar in CDCl₃ and in benzene. In CCl₄ solution at 100 Mc./sec., the τ 8.20 signal could not be resolved.

The enol form (XVIII) of 3-methyl-4-phenyl-2,4-butanedione reacted in methanol solution with 2,4-dinitrophenylhydrazinium sulfate and gave an orange compound (m.p. 152–153° (ethanol), showing bands at 6.25 (strong, single) and 6.5 and 7.5 μ) which is assumed to be 1-(2,4-dinitrophenyl)-3,4-dimethyl-5-phenylpyrazole.

Anal. Calcd. for C₁₇H₁₄N₄O₄: C, 60.3; H, 4.2; N, 16.6. Found: C, 60.1; H, 4.2; N, 16.4.

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