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TRIALKYL PHOSPHITES AS REAGENTS IN THE CARBON–CARBON CONDENSATIONS OF α-DIKETONES WITH α,β-UNSATURATED ALDEHYDES

THE HYDROLYSES OF 5-MEMBERED CYCLIC PENTAOXYPHOSPHORANES AND PHOSPHATE ESTERS*

F. Ramirez, H. J. Kugler and C. P. Smith
Department of Chemistry of the State University of New York,
Stony Brook, N.Y., 11790

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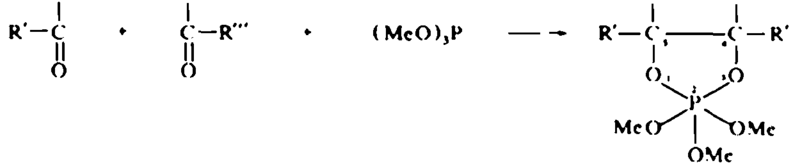
Abstract—2,2,2-Trimethoxy-4,5-dimethyl-2,2-dihydro-1,3,2-dioxaphospholene, made from trimethyl phosphite and biacetyl, reacted with crotonaldehyde and gave 2,2,2-trimethoxy-4β-methyl-4α-acetyl-5α-(*trans*-1-propenyl) 2,2-dihydro-1,3,2-dioxaphospholane. The hydrolyses of the phospholane by one mole equivalent of water in aprotic solvents and by an excess of water were studied. Two hydrolytic pathways were observed at 20°. (1) A substitution of the OMe groups on phosphorus by OH groups. This led to 5-methyl-2-heptene-4,5-diol-6-one-(5-dihydrogen phosphate), which underwent a relatively slow isomerization to the corresponding 4-dihydrogen phosphate. (2) An attack by water on the allylic carbon, with C—O bond fission. This led to the formation of trimethyl phosphate and 5-methyl-2-heptene-4,5-diol-6-one. At 100°, the dihydrogen phosphate ester lost phosphoric acid and gave an unsaturated dihydroxyketone. Methanolysis of the phospholane produced trimethyl phosphate and 4-methoxy-5-methyl-2-heptene-5-ol-6-one by C—O bond fisson.

INTRODUCTION

This paper describes the condensation of biacetyl, Me.CO.CO.Me, with crotonaldehyde, Me—CH=CH—CHO, by means of trimethyl phosphite, $(MeO)_3P$, and the hydrolysis and methanolysis of the product of that condensation.

The reductive C—C condensation of two molecules of a CO compound by one molecule of a trialkyl phosphite to form a derivative of the 2,2-dihydro-1,3,2-dioxaphospholane ring system, I, was first reported in 1961.[1]



I

These condensations involved an attack of the phosphite on C=O to form 1:1 adducts. In some cases, these 1:1 adducts, with structures like II or III, were only fleeting intermediates that could not be isolated because they reacted rapidly with a second molecule of the CO compound to form the corresponding 2:1 adducts, I.

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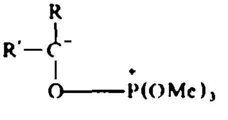
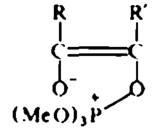
This happened with certain monocarbonyl compounds like *p*-nitro- and *o*-nitrobenzaldehydes,[2] *o*-phthalaldehyde,[3] hexafluoroacetone,[4] and fluorenone,[5] and with some α-dicarbonyl compounds like acenaphthenequinone[1] and methyl pyruvate.[6]

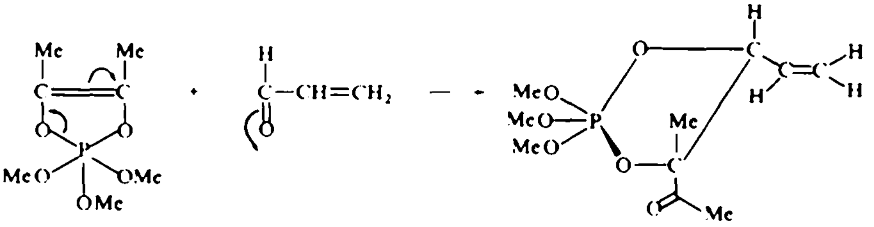


II



III

Sometimes the 1 : 1 adducts were relatively stable derivatives of the 2,2-dihydro-1,3,2-dioxaphospholene ring system,[7]* IV. Adducts of this type could be isolated and allowed to react with a second molecule of the same or of a different CO compound.[8–10] An example is the condensation of biacetyl with acrolein by means of trimethyl phosphite,[8] where the phospholene IV was reacted with acrolein to give the phospholane V.



IV: δP^{31} = +48·9 ppm *vs* H_3PO_4

V: δ^{31} = +50·9 ppm

The phospholane V underwent a very rapid hydrolysis when treated with one mole equivalent of water in aprotic solvents. The product was a 5-membered cyclic phosphotriester, which was obtained as two diastereomers at phosphorus, VIa and VIb. The cyclic triester was converted by methanol into an open chain phosphotriester, VII, with the phosphate group at the α-position of an α,β-dihydroxy ketone. The α-phosphate VII rearranged to the β-phosphate VIII very rapidly.[8]

The hydrolysis of phospholane V by an excess of water gave mainly the open-chain α-phosphomonoester, IX, which isomerized to the corresponding β-monoester, X. A minor product of this hydrolysis with an excess of water was the open triester

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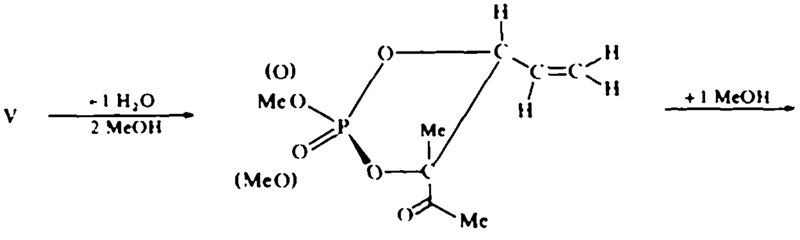
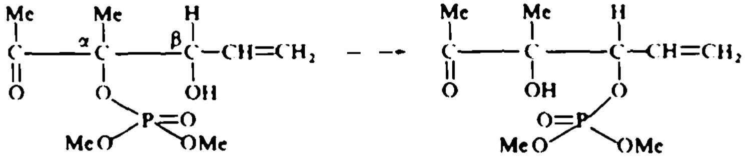
* An investigation of these compounds was initiated in our Laboratory in 1957, when it was found that the reaction of trialkyl phosphites with p-quinones resulted in an attack by the phosphorus on *carbonyl-oxygen*; see Ref. 7a and 7b. This reaction was then applied to the o-quinones. Our first publication of these results was in 1960; see Ref. 7c, and 7d. The demonstration that these substances had pentacovalent phosphorus and that the phosphorus was situated at the center of a regular trigonal bipyramid was based on X-ray analysis published in 1964; see Ref. 7e, 7f and 7g. Two reports on the reaction of trialkyl phosphites with α-diketones appeared in 1958; see Ref. 7h and 7i. Birum and Dever assigned to their compounds structures with pentavalent phosphorus from ^{31}P NMR data; although their original report gave no data for individual compounds, they were able to report a range of +47 to +68 ppm *vs* H_3PO_4 for their compounds; see also Ref. 7j. Kukhtin *et al.* have, at various times, assigned to their compounds structures with P—C bonds and with P—O bonds, having phosphonate and phosphate structures and phosphorane structures; see also Ref. 7k and 7l. For a review on this question see Ref. 7m and 7n.



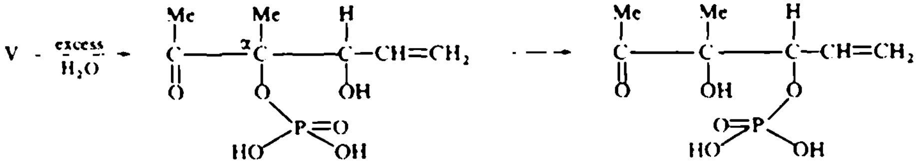
VIa, VIb: δP^{31} = −14·7, −15·7 ppm



VII

VIII: δP^{31} = −0·5 ppm

VIII. The latter was stable under the conditions of the hydrolysis and hence was not the precursor of the monoesters IX and X.



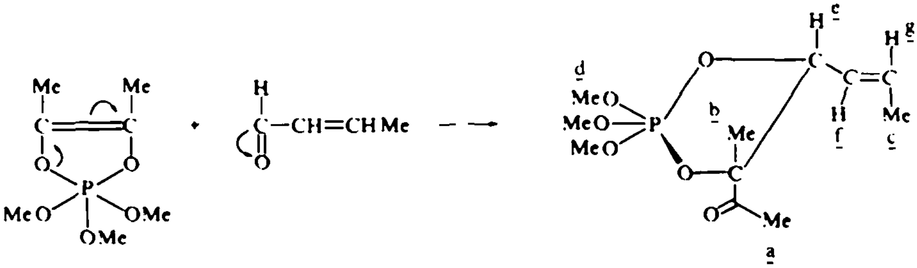
IX: δP^{31} = +4·1 ppm

X: δP^{31} = +1·5 ppm

The phospholane V and the phosphate esters VI–X derived from acrolein, have allylic carbons with a C–O bond. The purpose of the present investigation was to compare the hydrolytic behavior of these compounds with those derived from crotonaldehyde.

RESULTS

Reaction of the biacetyl-trimethyl phosphite adduct with crotonaldehyde. The biacetyl-trimethyl phosphite adduct, IV, reacted with crotonaldehyde at 30° and gave one of the two possible diastereomers of the phospholane XI.



IV

XI: δP^{31} = +51·0 ppm

The structure of the phospholane XI was based on the large positive value of the ^{31}P NMR shift.[11] Other spectral properties in support of structure XI are listed in Table 1. The *cis*-relationship of the Me and the H on the phospholane ring was assigned by analogy with related compounds.[11b] The *trans* relationship of the two hydrogens on the propenyl side-chain was based on the relatively large coupling constant of the two vinyl protons, $J_{H^gH^f}$ = 18·0 c/s in the ^1H NMR spectrum. As in all previous cases, the three OMe groups of the cyclic pentaoxyphosphorane were magnetically equivalent, due to rapid positional exchange in the trigonal bipyramid under the conditions of the ^1H NMR measurements.[11, 12]*†

Table 1. Spectral properties[a] of the products derived from the condensation of biacetyl with crotonaldehyde by means of trimethyl phosphite[b]

	Pentaoxyphosphorane[c] XI	Unsat. Ketodiol[d,e] XV
τ H^a	7·86	7·81
τ H^b	8·68	8·60
τ H^c	8·32	8·80
τ H^d	6·43	none
τ H^e	6·07	5·71
τ H^f	4·46	ca. 4·2
τ H^g	4·51	ca. 4·2
$J_{H^cH^g}$	6·0	6·4
$J_{H^gH^f}$	18·0	..[f]
$J_{H^eH^f}$	4·6	6·6
J_{H^dP}	12·5	none
J_{H^eP}	7·0	none
λ_{CO}	5·83[g]	5·88[h]

[a] ^1H NMR at 60 Mc/s in ppm *vs* TMS = 10 (τ values). J in c/s. λ(infrared) in μ. Solvents: $CDCl_3$ for ^1H NMR and CH_2Cl_2 for infrared.

[b] Protons: a, acetyl; b, Me on ring; c, Me of 1-propenyl; d, Me of MeO; e, proton on ring; f and g, protons on positions 1 and 2 of 1-propenyl, respectively.

[c] 4β-Methyl-4α-acetyl-5α-(*trans*-1-propenyl)-2,2,2-trimethoxy-2,2-dihydro-1,3,2-dioxaphospholane (XI).

[d] 5-Methyl-2-heptene-4,5-diol-6-one (XV).

[e] The protons of the two OH groups were at τ 5·51

[f] The two vinyl protons gave unresolved signals.

[g] 9·32 μ due to $POCH_3$.

[h] 6·17 and 7·39 μ due to CH=CH.

Reaction of the biacetylcrotonaldehyde-trimethyl phosphite adduct with one and with two mole equivalents of water. The hydrolysis with *one mole equivalent of water* was carried out in $CHCl_3$ solution, and the course of the reaction was followed by

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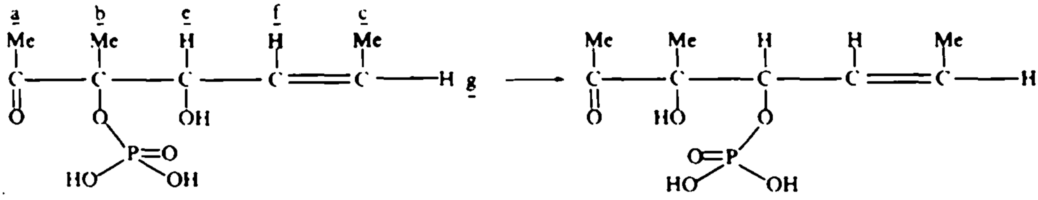
* For a discussion of positional exchange in other compounds with pentavalent phosphorus, see Ref. 12a and 12b.

† The three methoxy groups of a related cyclic tetraoxyalkylphosphorane, which was made from trimethyl phosphite and 3-benzylidene-2,4-pentanedione by Ramirez *et al.* (cf. Ref. 13a) exhibited also magnetic equivalence at 20°. However, a recent preliminary Communication by Gorenstein and Westheimer reported that the three groups became magnetically non-equivalent at −67° (cf., Ref. 13). Our continuing studies on this system (Ref. 13*a*, *c*) will be published elsewhere

means of ^{31}P and ^{1}H NMR spectrometry. It was found that at least 50% of the original phospholane XI was unaffected by the water. This was unexpected since previous work[10,11a,14] had shown that pentaoxyphosphoranes are extremely sensitive to water. A possible interpretation of this phenomenon is given in the discussion section.

Four hydrolysis products were identified. Two of these were the structurally isomeric α- and β-phosphomonoesters, XII and XIII, derived from a γ-unsaturated α,β-dihydroxyketone. The formation of these monoesters required three moles of water per mole of phospholane. The combined monoesters, XII and XIII, were formed in about 20% yield based on the phospholane XI. The spectral properties of these compounds are listed in Table 2. The phosphorus signal of the α-isomer XII was a singlet, while the corresponding signal of the β-isomer XIII was a doublet, due to the coupling of the phosphorus nucleus with the methine β-proton.

The α-phosphomonoester XII underwent a relatively slow isomerization into the β-phosphomonoester XIII in solution.

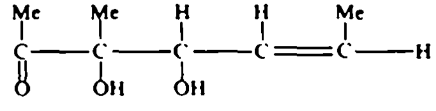


XII: δP^{31} = +4·0 ppm
(singlet)

XIII: δP^{31} = +1·3 ppm
(doublet)

The other two products of the hydrolysis were trimethyl phosphate (XIV) and the phosphorus-free γ-unsaturated α,β-dihydroxyketone XV. The formation of these products required one mole equivalent of water. XIV and XV were formed in roughly equivalent amounts, and their yields were about 15% based on the phospholane XI. The phosphomonoesters, XII and XIII, were not converted into the dihydroxyketone XV under the conditions of these experiments.

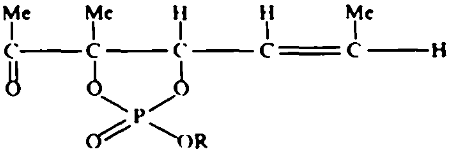
$(MeO)_3PO$
XIV: δP^{31} = −2·5 ppm



$MeC(=O){-}C(Me)(OH){-}CH(OH){-}CH{=}C(Me){-}H$

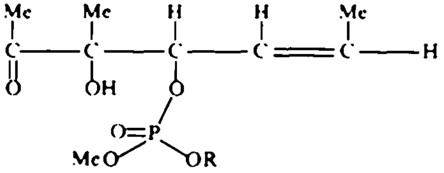
XV

In the early stages of the hydrolysis, two very weak ^{31}P NMR signals were observed, whose values corresponded to the 5-membered cyclic phosphotriester XVI and the corresponding cyclic diester,[14b,15,16] XVII. However, these compounds were formed in very small amounts and were not fully characterized.



XVI: R = Me; δP^{31} = −15 ppm
XVII: R = H; δP^{31} = −14 ppm

The hydrolysis also produced small amounts (ca. 5%) of a substance that could be phosphoric acid or the open-chain esters, XVIII or XIX, or a mixture of all three.



XVIII; R = Me
XIX: R = H

TABLE 2. PARTIAL H NMR SPECTRA[a] OF PHOSPHOMONOESTERS DERIVED FROM THE HYDROLYSIS OF THE BIACETYLCROTONALDEHYDE-TRIMETHYL PHOSPHITE ADDUCT[b]

	α-Phosphomonoester, XII	β-Phosphomonoester, XIII
τ H^a	7·75	7·80
τ H^b	8·45	8·60
τ H^c	[c]	8·26
τ H^e	[c]	5·10
$J_{H^cH^g}$	–[c]	4·6
J_{H^eP}	None	8·1
$J_{H^eH^f}$	[c]	6·0

[a] ^{1}H NMR in ppm *vs* TMS = 10 (τ values), *J* in c/s.

[b] Protons: a, acetyl; b, Me on carbon α to CO; c, Me of 1-propenyl; e, proton on carbon β to CO; f and g, protons on positions 1 and 2, respectively, of 1-propenyl.

[c] Multiplet not resolved.

The reaction of the phospholane XI with *two mole equivalents of water* was analogous except that now a correspondingly smaller amount of unreacted phospholane XI remained at the end of the hydrolysis. These results suggested that the hydrolysis of the phospholane XI involved several processes which varied in their stoichiometry with respect to water.

Reaction of the biacetylcrotonaldehyde-trimethyl phosphite adduct with an excess of water. The oxyphosphorane was added to *an excess of water* at 20°, and the resulting solution was analyzed by ^{31}P NMR spectrometry at various time intervals. The results are given in Table 3. Note that in the early stages of the reaction, the α-monoester XII and trimethyl phosphate (XIV) predominanted. After 4 hr, the main products were the β-monoester XIII and trimethyl phosphate. In other words, the α-monoester XII was slowly converted into the β-monoester XIII, but the amount of trimethyl phosphate remained essentially constant.

The monoester XIII lost phosphoric acid when the solution was heated to 100°.

The phosphorus-free dihydroxyketone XV was isolated in about 83% yield from the complete hydrolysis of the phospholane XI, first at 0° and then at 100°.

Reaction of the biacetylcrotonaldehyde-trimethyl phosphite adduct with methanol. The phospholane XI lost trimethyl phosphate when treated with methanol at 20°.

TABLE 3. ^{31}P NMR SPECTRUM[a] OF SOLUTIONS OF THE BIACETYLCROTONALDEHYDE-TRIMETHYL PHOSPHITE ADDUCT IN AN EXCESS OF WATER AT 20°

Time	$\delta^{31}P^b$	%	$\delta^{31}P^c$	%	$\delta^{31}P^d$	%	$\delta^{31}P^e$	%
5 min	+4·0	35	+1·3	10	−2·5	50	0	5
30 min	+4·0	30	+1·3	15	2·5	50	0	5
1·5 hr	+4·0	20	+1·3	25	2·5	50	0	7
4 hr	+4·0	5	+1·3	40	2·5	50	0	10
4 hr[f]	+4·0	0	+1·3	0	2·5	50	0	50

[a] $\delta^{31}P$ in pp, *vs* H_3PO_4 as zero.

[b] Singlet due to 5-methyl-2-heptene-4,5-diol-6-one-5-dihydrogen phosphate (XII).

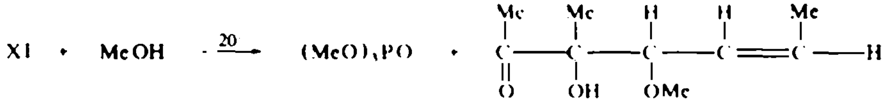
[c] Doublet due to the 4-hydrogen phosphate isomer, XIII.

[d] $(MeO)_3PO$ (XIV).

[e] Probably H_3PO_4 and open-chain phosphotriester XVI or phosphodiester XVII.

[f] The solution was kept 3 min at 100°.

The phosphorus-free material was assigned the tentative structure of 4-methoxy-5-methyl-2-heptene-5-ol-6-one (XX) on the basis of its ^{1}H NMR spectrum, which had a singlet at τ 7·79 (CH_3CO), a singlet at τ 8·60 (CH_3C), a doublet at τ 8·80, J_{HH} = 6·4 c/s, (CH_3CH), a singlet at τ 6·77 (CH_3O), a doublet at τ 6·19 (methine), a broad signal at τ 5·46 (OH), and a multiplet at τ 4·16 (vinyl protons).



$$XI + MeOH \xrightarrow{20°} (MeO)_3PO + MeC(=O)\text{—}C(Me)(OH)\text{—}CH(OMe)\text{—}CH{=}C(Me)\text{—}H$$

XX

DISCUSSION

The dioxaphospholanes XI and V, made from the reaction of the biacetyl-trimethyl phosphite adduct IV with crotonaldehyde and with acrolein[8] respectively, had very similar spectral properties. However, their reactions with methanol and with water gave significantly different results. Methanolysis of the crotonaldehyde adduct XI gave trimethyl phosphate and the monomethyl ether of an α-β-dihydroxyketone XX. *Under comparable conditions, methanol did not significantly affect the acrolein adduct V.* When the conditions of the latter reaction were forced, complex transformations occurred which are now being investigated. A possible explanation of this difference is that the C—O bond fission involving the allylic carbon was easier when the latter was part of a 1-propenylcarbinyl than a vinylcarbinyl system. In other words, the energy of the transition state associated with the C—O bond fission should be lower in the crotonaldehyde case due to increased resonance stabilization of the incipient positive charge on the allylic carbon. This is shown in terms of the two resonance structures* XXI and XXII.

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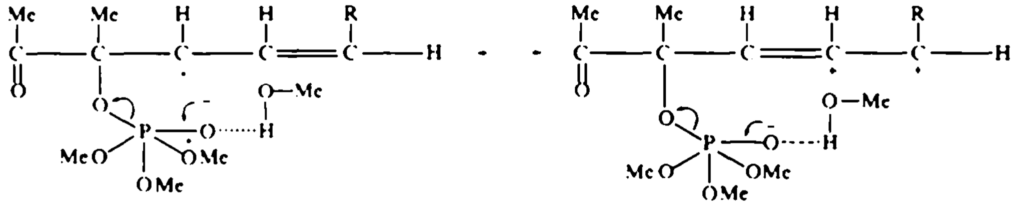
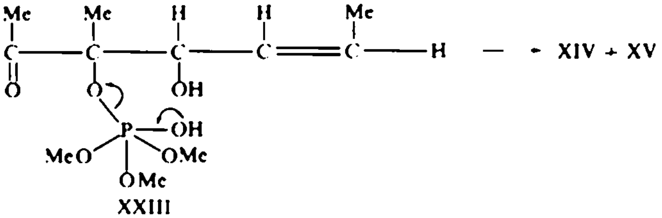
* The same argument can be developed whether the transition state for the methanolysis has a great deal of carbonium ion character or very little of it; see Ref. 17. Note that the resulting ether could have the methoxy group at either one of the two positions of the allylic system. Only one methanolysis product was detected, and it was formulated as the 4-methoxy-derivative XX from the similarities of its ^{1}H NMR spectrum with those of the dihydroxyketone XV and its phosphomonoesters XII and XIII. This point was not established conclusively, however.



XXI: R = Me
XXII: R = H

This difference between phospholanes XI and V was reflected also in the results of the hydrolysis. The crotonaldehyde adduct XI gave considerable amounts of trimethyl phosphate (XIV) and of the dihydroxyketone XV, when the hydrolysis was carried out with one mole equivalent of water or with an excess of water. *This type of behavior was not observed in the case of the acrolein adduct V.* We suggest that one of the hydrolytic pathways open to the crotonaldehyde adduct XI but not to the acrolein adduct V-under comparable experimental conditions—involves C—O bond fission at the allylic position with formation of the intermediate open hydroxytetraalkoxyphosphorane XXIII. It is possible that both hydrolytic pathways are actually available to both adducts, XI and V, but that they will be observable only at certain temperatures.

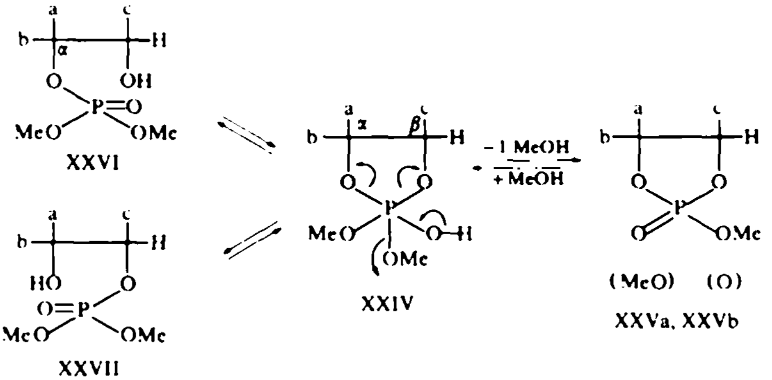
An intermediate of type XXIII should collapse to the observed products, ie., trimethyl phosphate (XIV), and the dihydroxyketone XV. The alternate collapse of the phosphorane XXIII to the open triester (an isomer of structure XVIII) should be less favorable because it involves the ejection of a methoxide ion. Since methanol should be a weaker acid than the dihydroxyketone XV, the methoxide ion should be a poorer leaving group than the conjugate base of the dihydroxyketone.



XXIII

Another difference observed during the hydrolyses of the crotonaldehyde and the acrolein derivatives pertains to the stability of the corresponding β-phosphomonoesters, XIII and X. The monoester XIII lost phosphoric acid and gave the intact dihydroxyketone XV, in water at 100°. *This was not observed in the case of the acrolein monophosphate X, where no hydrolysis occurred under mild conditions and where forcing conditions led to decomposition of the sensitive unsaturated dihydroxyketone.* This again suggests a facile C—O bond fission in the hydrolysis of β-phosphomonoester XIII.

A second hydrolytic pathway which is available to both the crotonaldehyde and the acrolein adducts, XI and V, involves the nucleophilic substitution of a OMe group by a hydroxy group with retention of the 5-membered ring,[11,14]* XI or V → XXIV. The cyclic hydroxytetraalkoxyphosphorane XXIV can collapse to a cyclic phosphotriester, XXVa and XXVb, by ejection of methoxide and retention of the ring. Both diastereomers at phosphorus, XXVa and XXVb, of the cyclic triesters are sometimes observable[8,11,14], and they are readily interconvertible by addition of methanol to the phosphoryl group to form the common intermediate XXIV. The cyclic intermediate XXIV can collapse also with rupture of the ring to form both the α- and the β-phosphotriesters, XXVI and XXVII, respectively. There is evidence that the α-triester XXVI forms first and then rearranges very rapidly to the β-triester XXVII. This rearrangement can easily occur through the cyclic intermediate XXIV.†



The substitution of one OMe group of XXIV by a OH group results in the formation of a cyclic dihydroxytrialkoxyphosphorane, XXVIII, which is identical with the product of the addition of one molecule of water to the cyclic phosphotriesters XXVa and XXVb. As before, the collapse of the cyclic intermediate XXVIII can occur with ring retention to form the cyclic phosphodiester XXIX. The cyclic intermediate XXVIII can also collapse to form the α- and the β-phosphodiesters, XXX and XXXI.

The replacement of the remaining OMe group of XXVIII gives the cyclic trihydroxydialkoxyphosphorane, XXXII. The latter is identical with the product of the addition of one mole equivalent of water to the cyclic phosphodiester XXIX. *Evidently,* XXXII *could result directly upon treatment of the crotonaldehyde adduct* XI *or the acrolein adduct* V *with an excess of water.* The collapse of XXXII with ring retention provides simply a mechanism for the exchange of oxygen from solvent water in the cyclic diester XXIX. On the other hand, the collapse of XXXII with

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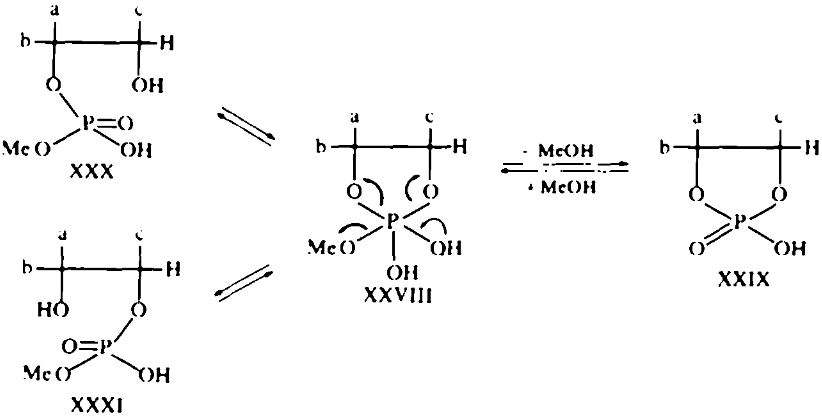
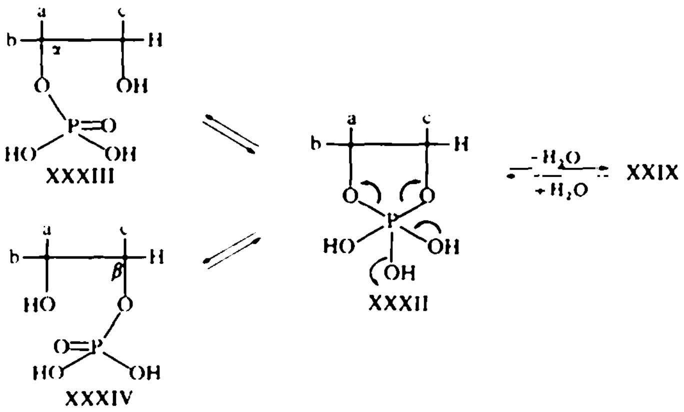
* The X-ray analysis of a cyclic pentaoxyphosphorane (Ref. 7c, f, g) showed that the phosphorus was at the center of a regular trigonal bipyramid and that the apical P—O bonds were longer than the corresponding equatorial bonds. If this reflects a relative weakness of the apical P—O bonds, then the substitution may commence at the apical position. There is ample evidence that rapid positional exchange occurs among the groups attached to the phosphorus. This point has been discussed recently in connection with the mechanism of hydrolysis of cyclic pentaoxyphosphoranes (see Ref. 15 and 20) and of cyclic phosphate esters (see Ref. 15 and 20 and Ref. 18a, 18b and 18c).

† The mechanism of the isomerization of glycol phosphates whereby a phosphoryl group, $P(O)(OR)_2$, moves from one oxygen to another has attracted a great deal of attention due to its significance in the chemistry of glycerol and of sugar phosphates and nucleic acids. Prior to the recognition of the relative stability of *cyclic* pentaoxyphosphoranes (cf. Ref. 7) this isomerization was discussed in terms of cyclic transition states rather than in terms of cyclic intermediates like XXIV. (cf. Ref. 19).



ring opening produces the α- and the β-phosphomonoesters, XXXIII and XXXIV, respectively. The isomerization of α-XXXIII to β-XXXIV merely involves the reformation of the cyclic intermediate XXXII.



One of the most striking differences between the crotonaldehyde adduct XI and the acrolein adduct V seems to be the relative rates at which the OMe groups on phosphorus are substituted by OH groups, as indicated in the sequence XI or V → XXIV → XXVIII → XXXII. Note that the addition of one mole of water to the crotonaldehyde adduct XI led to the formation of considerable amounts of phosphomonoesters XXXIII and XXXIV and left considerable amounts of unreacted adduct XI. On the other hand, *the addition of one mole equivalent of water to the acrolein adduct* V *gave exclusively the cyclic phosphotriesters*[*] VIa *and* VIb. We noted very little cyclic triester XVI and cyclic diester XVII in the crotonaldehyde case. Again, we observed very little or no open-chain triester XVIII and diester XIX in the crotonaldehyde case. The implication seems to be that the formation of a

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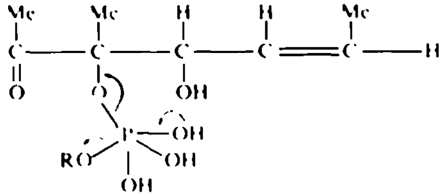
[*] It was shown that most or all of the open phosphotriesters α-VII and β-VIII produced in this hydrolysis resulted from a secondary methanolysis of the cyclic triesters VIa and VIb, probably *via* intermediate XXIV; see Ref. 20.

cyclic trihydroxydialkoxyphosphorane XXXII from the corresponding penta-alkoxyphosphorane was significantly faster in the crotonaldehyde case XI than in the acrolein case V. It is not clear why the substitution of a vinyl group by a 1-propenyl group on a dioxaphospholane ring should lead to this difference, although the stability of pentavalent phosphorus appears to be extremely sensitive to electronic and steric characteristics of the groups attached to the phosphorus.[21]

It is conceivable that the key intermediate in the hydrolysis of the crotonaldehyde adduct XI is the open hydroxytetraalkoxy-phosphorane XXIII. Open-chain penta-alkoxyphosphoranes are known[22] and are much less stable than the 5-membered cyclic pentaoxyphosphoranes. Therefore, very rapid substitutions of alkoxy groups by OH groups in XXIII would be expected. These substitutions lead to open tri-hydroxydialkoxyphosphoranes XXXV and tetrahydroxyphosphoranes XXXVI. The collapse of XXXV and XXXVI with ejection of methoxide and of hydroxide respectively would give the observed α-monoester XXXIII (i.e. XII) and would account for all the observations made in these hydrolyses, including the difference in behavior between acrolein and crotonaldehyde. However, it is not clear why the open phosphoranes XXXV and XXXVI or any precursors of them derived from XXIII should not collapse by loss of dihydroxyketone XV. Therefore, we favor the mechanism XI → XXIV → XXVIII → XXXIII + XXXIV for the formation of the phosphomonoesters XII and XIII.



XXXV: R = Me
XXXVI: R = H

The evidence now available strongly suggests that 5-membered cyclic phosphotriesters and phosphodiesters like XXV and XXIX are capable of adding methanol or water to the phosphoryl group to form oxyphosphoranes like XXIV, XXVIII, and XXXII. There is no evidence, however, for a similar addition of alcohol or of water to the phosphoryl group of open-chain phosphotriesters, diesters, and monoesters like XXVI, XXX, and XXXIII. This difference has been explained[20] as the combined effect of the relative instability of a 5-membered cyclic phosphate due to steric strain[23] and the relative stability of a 5-membered cyclic oxyphosphorane due to a decrease in the intramolecular overcrowding in a trigonal bipyramid.[7e] In the open-chain compounds, the phosphate becomes more stable, and the oxyphosphorane becomes less stable. Consequently, the "phosphoryl-hydration" mechanism[*] is replaced by the usual nucleophilic substitution at the quadruply-connected phosphorus in the case of open-chain phosphate esters.

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[*] Haake and Westheimer (see Ref. 24a) considered the possibility of the involvement of transition states or of intermediates in the hydrolysis of five-membered cyclic phosphates. See also Ref. 24b. More recently, Westheimer *et al.* claimed to have obtained evidence in favor of intermediates rather than of transition states on the basis of arguments related to pseudorotation in the trigonal bipyramidal structure of compounds with pentacoordinated phosphorus (see Ref. 24c). The trigonal bipyramidal configuration of the pentaoxyphosphoranes and of hypothetical intermediates of this type formed in the hydrolyses of phosphates is based on the work of Ref. 7e, f, g).

EXPERIMENTAL

Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N.Y. All ^{31}P NMR data are given in ppm from 85% H_3PO_4 as zero; they were determined at 40·5 Mc/s.

Reaction of the biacetyl-phosphite adduct (IV) *with crotonaldehyde*

Freshly distilled crotonaldehyde (44·1 g, 0·21 moles) was mixed with the adduct[9] IV (44·5 g, 0·064 moles) at 0°. The mixture was stirred 2 hr at 0° and 2 days at 20°. The excess crotonaldehyde was removed at 45° (20 mm), and the residue was distilled to give 2,2,2-*trimethoxy*-4β-*methyl*-4α-*acetyl*-5α-(trans-1-*propenyl*)-2,2-*dihydro*-1,3,2-dioxaphospholane (XI), b.p. 104 (0·2 mm), n_D^{25} 1·4512. The phospholane XI was obtained in 90% yield. (Found: C, 47·3; H, 7·9. $C_{11}H_{21}O_6P$ requires: C, 47·2; H, 7·6%). The spectral data are listed in Table 1.

Reaction of the biacetylcrotonaldehyde-trimethyl phosphite adduct (XI) *with one and with two mole equivalents of water*

(a) A stirred soln containing 11·8 g of XI in 30 ml $CHCl_3$ was treated with one mole equiv water at 20°. The ^{31}P NMR spectrum taken immediately showed the signals of the 5-membered cyclic triester XVI and diester XVII. These had vanished after 30 min when the soln contained the signals due to XII and XIII (20% combined) and XIV (15%). The ^1H NMR spectrum of this soln confirmed these results and showed the presence of XV (15%). An additional weak ^{31}P NMR signal which could be due to H_3PO_4 or to the open phosphates XVIII and XIX was also noted.

(b) A stirred soln containing 15 g of XI in 30 ml $CHCl_3$ was treated with 2 mole equivs water at room temp. ^{31}P and ^1H NMR spectrometry after 1 hr showed XII and XIII, XIV, and XV in approximately equal proportions. A weak signal at $\delta P^{31} = 0$ was also present, but XI was absent.

Reaction of the biacetylcrotonaldehyde-trimethyl phosphite adduct (XI) *with an excess of water*

(a) The phospholane XI was mixed with an equal volume of water at 20°, and the soln was analyzed by ^{31}P NMR spectrometry. The results are given in Table 3.

(b) The phospholane XI (3 g) was added to water (3 ml) at 0°. After 10 min, the soln was extracted with six 20 ml portions of $CHCl_3$ to remove XIV and XV. the ^1H NMR spectrum of the water soln taken afer 15 min showed the signals due to the XII and XIII; they are listed in Table 2. After 3 hr, the signals due to XII had decreased to about 10% of their original intensities, and the signals due to the β-XIII had increased about 90% of their original intensities. These changes were confirmed by the ^{31}P NMR spectra of the aqueous solutions after 15 min and after 3 hr.

(c) The hydrolysis was repeated, and the soln was thoroughly extracted with $CHCl_3$ after 4 hr. The ^{31}P and ^1H NMR spectra of the aqueous solns contained only the signals due to XIII.

(d) The phospholane XI (26 g) was added to water (150 ml) at 0° with stirring. After 10 min at 0°, the soln was heated to 100°, kept there 3 min, and extracted with six 100 ml portions $CHCl_3$. The $CHCl_3$ extract was distilled giving 5-*methyl*-2-*heptene*-4,5-*diol*-6-*one* (XV), b.p. 75° (0·2 mm), in 83% yield. (Found: C, 60·7; H, 8·9. $C_8H_{14}O_3$ requires: C, 60·5; H, 8·8%). The spectral data are given in Table 1.

Trimethyl phosphate (XIV) was obtained in 46% yield from the fractional distillation of the material in the $CHCl_3$ extracts mentioned above.

Reaction of the biacetylcrotonaldehyde-trimethyl phosphite adduct (XI) *with methanol*

A soln of XI in an excess of MeOH was kept 3 hr at 20°. The only ^{31}P NMR signal observed was that of XIV. The ^1H NMR spectrum corresponded to that of 4-*methoxy*-5-*methyl*-2-*heptene*-5-*ol*-6-*one* (XX).

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