Monoketones as Acceptors in the Oxyphosphorane Carbon–Carbon Condensation. Condensation of α Diketones with Monoketones and with Perfluoro Ketones. P^{31} Nuclear Magnetic Resonance Spectra[1,2]

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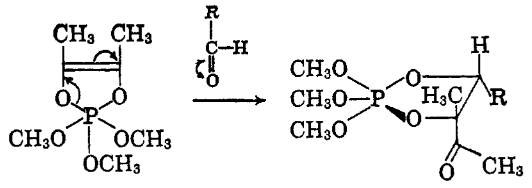
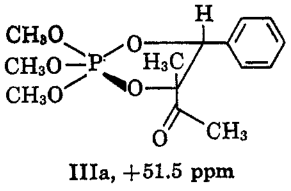
The 2,2,2-trimethoxy-1,3,2-dioxaphospholene made from biacetyl and trimethyl phosphite reacted with cyclohexanone, cyclobutanone, acetophenone, *p*-nitroacetophenone, and *α,α,α*-trifluoroacetophenone, at about 100–120°. The reaction with hexafluoroacetone was rapid even below 10°. These oxyphosphorane condensations proceeded by addition of a carbon atom of the phospholene to the carbonyl carbon of the monoketone, with formation of a 2,2,2-trimethoxy-1,3,2-dioxaphospholane. When the monoketone had different substituents about the carbonyl, two diastereomeric phospholanes were formed. The ratio of diastereomers could be altered by using an excess of the ketone or an excess of the phospholene as the reaction medium. The formation of some *phospholanes* was reversible at elevated temperatures. The pyrolysis of the *phospholene* gave the trialkyl phosphite, the α diketone, trialkyl phosphate, and other products. The following monoketones failed to react with the dioxaphospholene: cyclopentanone, acetone, butanone, 3-hexanone, methyl cyclopropyl ketone, and benzophenone. The P^{31} nmr shifts of the phospholanes were measured at 40.5 Mcps.

A previous paper in this series described the reaction of the 2,2,2-trimethoxy-1,3,2-dioxaphospholene (I) made from biacetyl and trimethyl phosphite, with propionaldehyde and with other aliphatic monoaldehydes.[4] These reactions occurred at 20°, and gave one diastereomer of the 2,2,2-trimethoxy-1,3,2-dioxaphospholane (II).

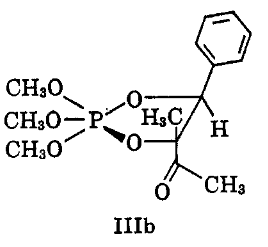


I, $\delta P^{31} = +48.9$ ppm II, $\delta P^{31} = +51.3$ ppm

Configuration II, with the two alkyl groups in *trans* relationship, was based, in part, on the positions of the H^1 nmr signals due to the acetyl and the methyl groups. Considerable information was available on the effect of neighboring groups on the positions of these signals in other related oxyphosphoranes.[2,5] Configuration II was assigned also by analogy with the results of the reaction of the phospholene I with benzaldehyde.[2] In this case, two diastereomers, IIIa and IIIb, were formed in the proportion of 90:10. The H^1 nmr signal due to the acetyl group was at a higher magnetic field in the major isomer (τ 8.40) than in the minor isomer (τ 7.76). This suggested that the acetyl group was *cis* to the phenyl ring in the major isomer, IIIa, and *trans* to the phenyl ring in the minor isomer, IIIb.



IIIa, +51.5 ppm



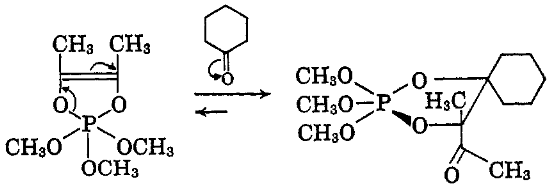
IIIb

The pentaoxyphosphoranes II and III gave positive P^{31} nmr shifts relative to H_3PO_4. In the benzaldehyde case, the minor isomer could not be detected in the P^{31} nmr spectrum. However, in a number of other cases already reported from this laboratory,[5] the P^{31} nmr shifts of the two diastereomeric phospholanes analogous to IIIa and IIIb were easily distinguished at a frequency of 40.5 Mcps. For example, methyl pyruvate reacted with trimethyl phosphite and gave two diastereomeric phospholanes in a 40:60 proportion.[6] The minor isomer, which had two methyl groups in *cis* relationship gave a decet centered at +52.2 ppm; the major isomer (racemic) had its decet displaced 1.8 ppm to lower field.[5]

The present paper extends our studies of the oxyphosphorane carbon–carbon condensation to the case of aliphatic, alicyclic, and aromatic monoketones. Various types of ketones with and without polar substituents were studied in order to ascertain more fully the stereoelectronic factors which influence the condensation, and to delimit its synthetic scope.

Results

Reaction of Alicyclic Monoketones with Dioxaphospholenes.—Cyclohexanone reacted with the dimethyldioxaphospholene I under the conditions given in Table I. The P^{31} and the H^1 nmr shifts of the resulting dioxaphospholane, IV, are listed in Table II. Note,



I IV, +54.3 ppm

in particular, the large positive value of the P nmr shift. These values and the infrared data given in the Experimental Section establish structure IV, as discussed in previous papers of this series.[2,4,5]

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[1] Organic Compounds with Pentavalent Phosphorus. Part XXIII. Supported by Public Health Service Research Grant No. CA-04769-07 from the National Cancer Institute and by the National Science Foundation, GP-3341.

[2] Part XXII: F. Ramirez, A. V. Patwardhan, and C. P. Smith, *J. Org. Chem.*, **31**, 474 (1966).

[3] National Science Foundation Senior Postdoctoral Fellow, 1965–1966.

[4] F. Ramirez, A. V. Patwardhan, N. Ramanathan, N. B. Desai, C. V. Greco, and S. R. Heller, *J. Am. Chem. Soc.*, **87**, 543 (1965).

[5] F. Ramirez, *Pure Appl. Chem.*, **9**, 337 (1964).

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

TABLE I

REACTION OF THE TRIMETHYL BIACETYLPHOSPHITE 1:1 ADDUCT[a] WITH MONOKETONES

Expt	Monoketone	Mole ratio[b]	Temp, °C[c]	Time	Dioxaphospholane,[d] %
1	Cyclohexanone	5	95	7 days	78
2	Cyclohexanone	3	100	40 hr	42
3	Cyclohexanone	3	130	1 hr	25
4	Cyclohexanone	1	155[e]	3 hr	40
5	Cyclohexanone	3	158	3 hr	42
6	Cyclohexanone	3	158	6 hr	45
7	Cyclohexanone	5	20	6 days	0
8	Cyclopentanone	3	135	6 hr	0
9	Cyclobutanone	3	100	40 hr	40
10	Cyclobutanone	3	100	5 days	53
11	Cyclobutanone	3	100	3 hr	15
12	Cyclobutanone	4	20	6 days	0
13	Acetone	5	20	3 months	0
14	Butanone	3	80	48 hr	0
15	3-Hexanone	3	140	40 hr	0
16	Methyl cyclopropyl ketone	3	100	40 hr	0
17	Hexafluoroacetone	f	−70 to +20	3 hr	90
18	Acetophenone	3	125	72 hr	50[g]
19	Acetophenone	1	100	16 hr	*Ca.* 5
20	*p*-Nitroacetophenone	2	100	72 hr	h
21	*p*-Nitroacetophenone	0.5	100	64 hr[i]	65[j]
22	*p*-Nitroacetophenone	0.3	95	24 hr	30[k]
23	α-Trifluoroacetophenone	1	95	20 hr	85[l]
24	α-Trifluoroacetophenone	1	20	4 days	30
25	Benzophenone	1	140	24 hr	0

[a] 2,2,2-Trimethoxy-4,5-dimethyl-1,3,2-dioxaphospholene. [b] Monoketone–adduct (1:1). [c] Internal temperature, ±5°. [d] Distilled or crystallized. [e] Initial reflux temperature; final reflux temperature, *ca.* 170°. [f] An excess of gaseous ketone was condensed into a solution of adduct in hexane at −70°. [g] Only one isomer with the acetyl *trans* to the phenyl could be detected. [h] Product not isolated. H^1 nmr showed mostly the phospholane with acetyl *trans to p*-nitrophenyl. Minor amounts of *cis* isomer and of $(CH_3O)_3PO$ were observed. [i] Little change after 40 hr. [j] Crystalline mixture of *trans* and *cis* isomers (IXa + IXb) in 20:80 proportion. Original crude mixture of IXa + IXb in 35:65 proportion (90% yield). Pure *cis* isomer isolated in 41% yield. [k] Pure *cis* isomer IXb. [l] Liquid mixture of *trans* and *cis* isomers Xa + Xb in 82:18 proportions. All isomer proportions from integration of H^1 nmr signals.

Experiments 1 to 7 of Table I disclosed that the temperature was an important factor in the condensation. Significant reaction was noted only above 90°; however, there was a rather narrow limit to the useful temperature range, because both the phospholene I and the phospholane IV began to decompose, slowly, at about 130°. The best conditions for making the latter, IV, were those of expt 1 and 5.

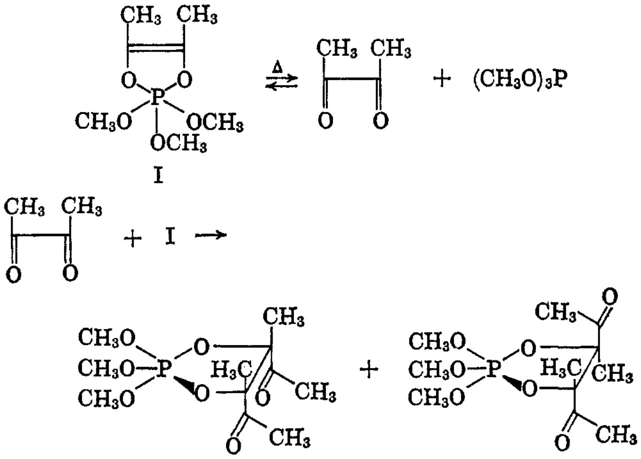
Several products were formed when the phospholene I was kept for 72 hr at 125°: (a) trimethyl phosphate, (b) trimethyl phosphite, and (c) the *meso* and racemic forms of the 2,2,2-trimethoxy-4,5-dimethyl-4,5-diacetyl-1,3,2-dioxaphospholane (Va and Vb). The latter had been previously made from the phospholene I and biacetyl.[7] Therefore, part of the pyrolysis of the 1:1 adduct I proceeded as shown.

TABLE II

P^{31} AND H^1 NMR SHIFTS[a] OF 2,2,2-TRIMETHOXY-1,3,2-DIOXAPHOSPHOLANES[b] FROM THE CONDENSATION OF THE TRIMETHYL BIACETYLPHOSPHITE 1:1 ADDUCT[c] (I) WITH MONOKETONES

Monoketone acceptor	No.	δP^{31}	τ_{Ac}[d]	τ_{Me}[d]	τ_{Me}[e]	τ_{MeO}	J_{HP}[f]
Cyclohexanone	IV	+54.3	7.83	8.85	None[g]	6.44	12.5
Cyclobutanone	VI	+53.1	7.82	8.80	None[h]	6.45	12.6
Hexafluoroacetone	VII	+52.6	7.72[i]	8.51[j]	None	6.38	13.0
Acetophenone	VIII	+54.2	7.70[k]	9.15[l]	8.55	6.40	12.8
p-Nitroacetophenone	IXa	+54.0	7.60[m]	9.12[l]	8.53	6.32	12.6
	IXb	+52.4	8.37[n]	8.50	8.30	6.34	12.5
α-Trifluoroacetophenone	Xa	+52.5	7.60[k]	9.00[l]	None	6.35	12.5
	Xb	+49.6	8.42[o]	8.25[p]	None	...	...

[a] P shifts in parts per million from 85% H_3PO_4 = 0; measured at 40.5 Mcps in CCl_4 or CH_2Cl_2. H shifts in parts per million from TMS = 10 (τ values); measured at 60 Mcps in CCl_4 or $CDCl_3$. [b] Diastereomers at carbon are possible with certain monoketones. [c] 2,2,2-Trimethoxy-4,5-dimethyl-1,3,2-dioxaphospholene. [d] Acetyl and methyl groups derived from biacetyl. [e] Methyl group derived from monoketone. [f] Coupling in cycles per second, between methoxy protons and phosphorus. [g] The ten methylene protons gave a broad signal at *ca.* τ 8.4. [h] The six methylene protons gave a signal at *ca.* τ 7.8. [i] Quartet, J_{HF} = 0.8 cps. [j] Quartet, J_{HF} = 2 cps; see Figure 1. [k] Acetyl *trans* to phenyl. [l] Methyl *cis* to phenyl, hence signal at higher magnetic field. [m] Acetyl *trans* to *p*-nitrophenyl. [n] Acetyl *cis* to *p*-nitrophenyl, hence signal at higher magnetic field. [o] Acetyl *cis* to phenyl. [p] Methyl is broad owing to *cis*-trifluoromethyl.



I

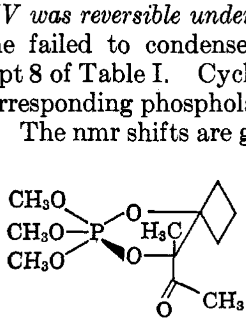
Va, +54.3 ppm

Vb, +52.1 ppm

The origin of the trimethyl phosphate is being investigated further.

The major product of the decomposition of the phospholane IV after 6 hr at 165° was cyclohexanone; *i.e., the formation of IV was reversible under these conditions.*

Cyclopentanone failed to condense with the phospholene I; *cf.* expt 8 of Table I. Cyclobutanone, however, gave the corresponding phospholane VI, as shown in expt 9 and 10. The nmr shifts are given in Table II.



VI, + 53.1 ppm

Reaction of Aliphatic Monoketones with Dioxaphospholenes.—Experiments 13 to 16 disclosed that most of these ketones did not engage in the oxyphosphorane condensation. On the other hand, hexafluoroacetone proved to be the most reactive of all the monoketones studied; this is shown in expt 17.

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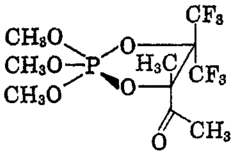
[7] (a) F. Ramirez, N. Ramanathan, and N. B. Desai, *J. Am. Chem. Soc.*, **84**, 1317 (1962); (b) F. Ramirez and N. B. Desai, *ibid.*, **85**, 3252 (1963); (c) F. Ramirez, N. Ramanathan, and N. B. Desai, *ibid.*, **85**, 3465 (1963).

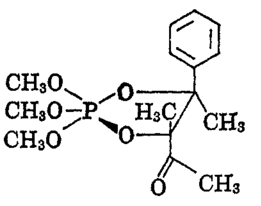
The nmr shifts of the phospholane VII are given in Table II.

The H^1 nmr spectrum of VII is reproduced in Figure 1, to show the long-range coupling of the H^1 and the F^{19} nuclei. Long-range H^1–F^{19} couplings have been observed previously in other systems.[8]

Reaction of Aromatic Monoketones with Dioxaphospholenes.—Acetophenone reacted with the dimethyldioxaphospholene I as shown by expt 18 of Table I. Only one of the two possible diastereomeric phospholanes could be isolated in the case. This isomer is thought to have the acetyl group in *trans* relationship to the phenyl ring as in formula VIII.



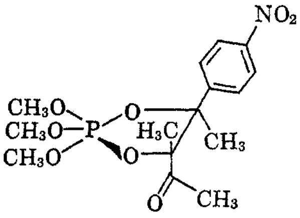
VII, +52.6 ppm



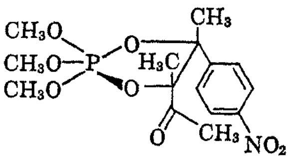
VIII, +54.2 ppm

The basis for this configurational assignment is the position of the signal due to the protons of one of the methyl groups in the molecule. As shown in Table II, this signal is at a relatively high magnetic field (τ 9.15); this is understandable if the methyl is *cis* to the phenyl ring.[2,4,5]

p-Nitroacetophenone was an excellent acceptor in the oxyphosphorane condensation. Preliminary experiments were carried out with an excess of the ketone, as shown in Table I, expt 20. Under these conditions, the major product was the phospholane IXa with the acetyl group *trans* to the *p*-nitrophenyl ring. This configurational assignment followed also from the nmr data shown in Table II. Note the relatively high position (τ 9.12) of the methyl group *cis* to the *p*-nitrophenyl ring. The crude reaction mixture contained small amounts of the isomer IXb with *cis*-acetyl *p*-nitrophenyl groups. In addition, some trimethyl phosphate had been produced.



IXa, +54.0 ppm



IXb, +52.4 ppm

Since *p*-nitrophenylacetophenone is a solid, and since it was difficult to remove from the product, subsequent experiments were carried out with an excess of the liquid phospholene I, as shown in expt 21 and 22 of Table I. *Under these conditions, the major product was the phospholane IXb with the acetyl group cis to the p-nitrophenyl group.* The isomers IXa + IXb were formed in the proportion of 35:65 and in 90% yield. One crystallization from hexane gave a mixture of IXa + IXb in a 20:80 proportion and in 65% yield. One crystallization from benzene–hexane gave the major isomer, IXb, in pure form (40% yield).

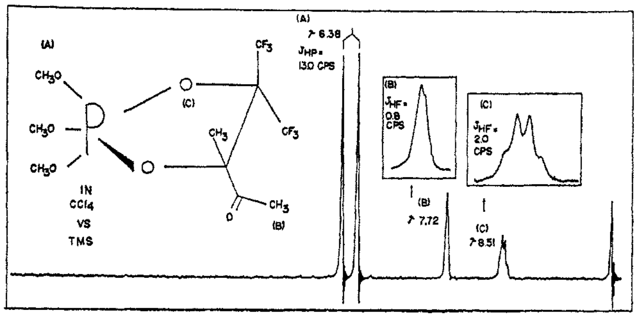


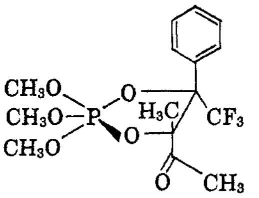
Figure 1.

Note the high position, τ 8.37, of the H^1 nmr signal due to the acetyl group *cis* to a *p*-nitrophenyl ring.

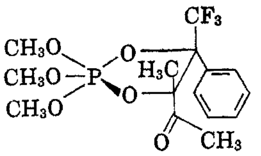
The different isomer ratio obtained under different experimental conditions seemed to indicate that the phospholanes IXa and IXb were formed reversibly at elevated temperatures. Indeed, the pure *cis* isomer (IXb) lost *p*-nitroacetophenone and regenerated the phospholene I at 120°, although rather slowly. The pyrolysis gave also small amounts of the *trans* isomer IXa. In addition, trimethyl phosphate and a fifth substance were produced; the latter had a H^1 nmr signal at τ 7.82, but it was not further characterized at this time.

The pyrolysis of these, and of other phospholanes, is under investigation.

α,α,α-Trifluoroacetophenone was an excellent acceptor in the oxyphosphorane condensation, as shown by expt 23 of Table I. This monoketone was a rather volatile liquid and could be used as the reaction medium and then recovered. Under these conditions the diastereomers Xa and Xb were formed in the proportion of 82:18 and in 90% yield or better. Table II lists the corresponding nmr shifts. The minor isomer Xb exhibited a small H^1–F^{19} long-range coupling which is consistent with the *cis* relationship of the CH_3 and the CF_3 groups.



Xa, + 52.5 ppm



Xb, + 49.6 ppm

Discussion

This investigation showed that monoketones are, in general, much less reactive than monoaldehydes toward dioxaphospholenes. However, electron-withdrawing substituents greatly enhanced the reactivity of the ketones; thus, hexafluoroacetone[9] and trifluoroacetophenone were among the most reactive acceptors so far encountered in the oxyphosphorane condensation.

The thermal decomposition of the phospholenes and of the phospholanes imposed certain limitations on the scope of the oxyphosphorane condensations with the

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[8] (a) A. H. Lewin, *J. Am. Chem. Soc.*, **86**, 2303 (1964); (b) A. D. Cross and P. W. Landis, *ibid.*, **86**, 4005 (1964); (c) A. D. Cross, *ibid.*, **86**, 4011 (1964).

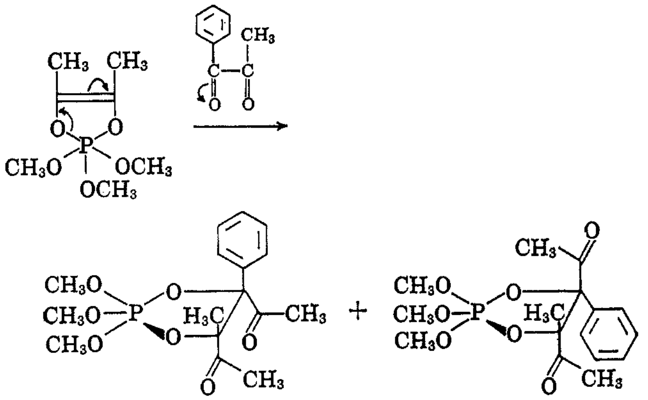
[9] Fluorine activation of carbon–carbon double bond toward nucleophiles has been discussed by W. T. Miller, Jr., J. H. Fried, and H. Goldwhite, *ibid.*, **82**, 3091 (1960), and previous papers; A. L. Henne and M. Nager, *ibid.*, **74**, 650 (1952); D. C. England, R. V. Lindsey, Jr., and L. R. Melby, *ibid.*, **80**, 6442 (1958).

less reactive ketones. These decompositions became significant above 130° and were quite destructive at about 170°.

The oxyphosphorane condensation can be pictured as a concerted process in which a P–O bond breaks as the new C–C bond forms.[2,10] This is shown in transition states XI and XII. Little or no charge separation is required, since the new phospholane ring can be formed as the existing phospholene ring is being broken. These reactions occurred best in solvents of low polarity. The available data[2,4–7,10,11] suggest that the interplay of steric[12] and electronic factors associated with the four groups, R', R'', R''', and R'''', in the transition states XI and XII will determine (1) the degree of reactivity of the carbonyl compound, (2) the direction of the condensation when the nature of the groups R permits the formation of structural isomers, and (3) the proportion of the two diastereomers, *trans* and *cis* of a given structure.

The relative reactivity of the cyclic ketones seemed to conform with the general behavior of these compounds toward nucleophiles.[13]

The most surprising effect is, perhaps, the greater reactivity of acetophenone over the simple aliphatic monoketones like 3-hexanone. In this connection, it should be noted that 1-phenylpropanedione was a more reactive acceptor than benzil in the oxyphosphorane condensation; yet, the *benzoyl carbon rather than the acetyl carbon was involved in the condensation.* Isomers XIIIa (*cis*) and XIIIb (*trans*) were formed in the proportion 70:30.[2] These results were attributed partly to the stronger attraction between two acetyl groups when compared with the attraction between an acetyl and a benzoyl group in the transition state of the condensation. This should lead to attack at the benzoyl rather than at the acetyl group. Moreover, it was pointed out that steric factors, in the form of methyl–phenyl and methyl–methyl repulsions, might be contributing also to the direction of the condensation, *i.e.*, to the nature of the preferred structural isomer.

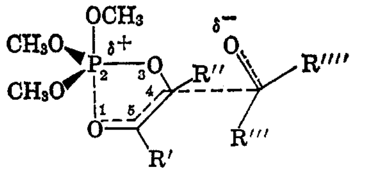


XIIIa, +54.7 ppm XIIIb, +52.4 ppm

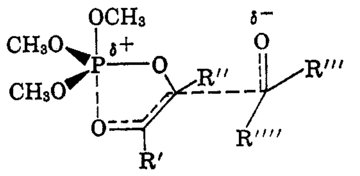
The predominance of the *cis* isomer XIIIa over the *trans* isomer XIIIb was in agreement with the hypothesis of a significant dipole–dipole interaction involving the two carbonyl groups in the transition state.[14] The isomer ratio, again, suggested a relatively small repulsion between a methyl and a phenyl in the transition state.[15]

When the role of acceptor in these condensations is taken by a *monocarbonyl* compound, the main, if not the only factor involved is likely to be the relative steric repulsions[12,15] of the four groups, R', R'', R''', and R'''', in XI and XII. The lack of reactivity of the purely aliphatic ketones may simply reflect strong repulsions among the alkyl groups in the transition state. The greater reactivity of acetophenone is understandable if the methyl–phenyl repulsion is smaller than the methyl–alkyl repulsion.[15]

As to the stereochemical results observed in this work, the evidence tentatively suggests that the kinetically favored diastereomer has the acetyl group *trans* to the phenyl ring. This is consistent with the relatively small *cis* methyl–phenyl repulsion. In the *p*-nitroacetophenone case, the thermodynamically favored diastereomer appeared to have the acetyl group *cis* to the *p*-nitrophenyl ring. This could be due, in part, to a dipole–dipole attraction between the carbonyl and the nitro group. However, a second factor could be related to the shape of the group $R'''' = C_6H_4 \cdot NO_2$-*p* and to the steric requirements of a trigonal bipyramid. The latter is assumed to represent the geometry of the dioxaphospholane in solution. X-Ray analysis of a dioxaphospholene disclosed that the molecule in the crystal is a trigonal bipyramid with the five-membered ring in an apicalequatorial plane.[16] Models show that there is considerable crowding involving group R'''' and the other groups attached to the phosphorus in a configuration like XI (*trans*-acetyl/R''''). It seems quite possible that the crowding due to group R'''' in the *trans* configuration is



XI, *trans*-$R'CO/R''''$, *trans*-R''/R'''



XII, *cis*-$R'CO/R''''$, *cis*-R''/R'''

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[10] F. Ramirez, A. V. Patwardhan, and C. P. Smith, *J. Org. Chem.*, **30**, 2575 (1965).

[11] (a) F. Ramirez, H. J. Kugler, and C. P. Smith, *Tetrahedron Letters*, **No. 4**, 261 (1965); (b) F. Ramirez and N. Ramanathan, *J. Org. Chem.*, **26**, 3041 (1961); (c) F. Ramirez, A. V. Patwardhan, N. B. Desai, N. Ramanathan, and C. V. Greco, *J. Am. Chem. Soc.*, **85**, 3056 (1963).

[12] For a recent discussion of the differences between "steric requirements" of groups, and group sizes measured by van der Waals radii, see (a) H. C. Brown and R. L. Khimisch, *ibid.*, **88**, 1425 (1966); (b) H. C. Brown, *J. Chem. Educ.*, **36**, 424 (1959).

[13] (a) H. C. Brown, J. H. Brewster, and H. Shechter, *J. Am. Chem. Soc.*, **76**, 467 (1954); (b) M. S. Newman, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p 237.

[14] All previous oxyphosphoranes condensations were carried out at 20° or below. It was shown that, under those conditions, the condensations were irreversible. There was no detectable equilibration among diastereomers, once they were formed. See ref 2, 4, 6, 7, 10, and 11.

[15] The van der Waals radius ("size") of the methyl group is said to be 2.0 A, while the half-thickness of the aromatic ring has been estimated as 1.85 A; *cf.* L. Pauling, "The Nature of the Chemical Bond," 3rd ed, Cornell University Press, Ithaca, N. Y., 1960. However, see footnote 9 for difficulties in estimating steric requirements of groups from their "sizes."

[16] W. C. Hamilton, S. J. LaPlaca, and F. Ramirez, *J. Am. Chem. Soc.* **87**, 127 (1965).

more significant in the product IX than in the corresponding transition state because the former might be closer than the latter to being a pure trigonal bipyramid.

It is becoming apparent that the formation of carbon–carbon bonds *via* oxyphosphoranes is a rather general reaction. The dioxaphospholanes can be hydrolyzed to cyclic and open-chain phosphate esters and to phosphorus-free polyhydroxycarbonyl compounds. This paper constitutes a significant extension of the synthetic scope of this new reaction.

Experimental Section

P^{31} nmr shifts are given in parts per million *vs.* 85% H_3PO_4, taken at 40.5 Mcps.[4] H^1 nmr shifts are given in parts per million from tetramethylsilane = 10 (τ values), taken in a Varian A-60 instrument.[4] Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

Reaction of the Trimethyl Biacetylphosphite 1:1 Adduct (I)[4] with Cyclohexanone. Preparation of 2,2,2-Trimethoxy-4-acetyl-4-methyl-5-spiropentamethylene-1,3,2-dioxaphospholane (IV).—A mixture of 1:1 adduct I[4] (10.5 g, 50 mmoles) and freshly distilled cyclohexanone (25 g, 250 mmoles) was kept at 95–100°, under N_2. Analysis of the mixture by H^1 nmr spectrometry showed about 60% reaction after 4 days and *ca.* 75% reaction after 7 days. Some trimethylphosphate began to appear at the longer reaction time. Unreacted I and the excess cyclohexanone were removed at 45–50° (20 mm; bath at 100°). **The cyclohexanonetrimethyl biacetylphosphite adduct IV** (12.1 g, 78% yield) was collected at 90–92° (0.05 mm; bath at 135–140°) using a 6-in. Vigreux column: $n^{25}\mathrm{D}$ 1.4641.

Anal. Calcd for $C_{13}H_{25}O_6P$: C, 50.6; H, 8.1; P, 10.1; mol wt, 308. Found: C, 50.4; H, 8.0; P, 9.9; mol wt, 261 (cryoscopic in benzene).

The P^{31} (in CCl_4) and the H^1 (in CCl_4) nmr shifts are listed in Table II. The infrared spectrum (CCl_4) had a C═O band at 5.84, and the strong and broad absorption at 9.3 μ due to the oxyphosphorane $POCH_3$ groups.

Effect of Temperature, Time, and Mole Ratio in the Reaction of I with Cyclohexanone.—These results are given in Table I. The following procedure (expt 5) provided 42–45% of the dioxaphospholane IV consistently. A mixture of I (21.0 g, 0.1 mole) and cyclohexanone (31 ml, 0.3 mole) was kept for 3 hr at reflux temperature (internal temperature 155–159°). The unreacted ketone was removed below 60° (18 mm, bath at 90°) and the residue was separated into three fractions by means of a 6-in. Vigreux column: (1) 4.6 g, bp 35–50° (0.04 mm); (2) 4.11 g, bp 50–86° (0.04 mm); (3) 13.0 g, 42% yield of IV, bp 86–92° (0.04 mm), $n^{25}\mathrm{D}$ 1.4641.

Behavior of the Trimethyl Biacetylphosphite 1:1 Adduct (I) at Elevated Temperatures. A.—Pure I was kept 72 hr at 125°. The P^{31} nmr spectrum of the resulting liquid had the signals due to: (1) recovered 1:1 adduct I, (2) *meso-* and *rac*-trimethylbiacetylphosphite 2:1 adduct, 2,2,2-trimethoxy-4,5-diacetyl-4,5-dimethyl-1,3,2-dioxaphospholane, Va and Vb; (3) trimethyl phosphate, $(CH_3O)_3PO$; (4) trimethyl phosphite, $(CH_3O)_3P$. The H^1 nmr spectrum confirmed the presence of these substances in the pyrolysis mixture.

B.—Sufficient *meso* and racemic 2:1 adducts (Va and Vb) had been produced after 6 hr at 160°, for detection in the H^1 nmr spectrum of the pyrolysis mixture.

Behavior of the Trimethyl Biacetylcyclohexanonephosphite Adduct (IV) at Elevated Temperature.—The dioxaphospholane IV underwent significant decomposition after 6 hr at 165°. The formation of some cyclohexanone was verified, but the mixture was not investigated further.

Reaction of the Trimethyl Biacetylphosphite 1:1 Adduct (I) with Cyclobutanone. Preparation of 2,2,2-Trimethoxy-4-acetyl-4-methyl-5-spirotrimethylene-1,3,2-dioxaphospholane (IV).—A mixture of 1:1 adduct I (9.4 g) and cyclobutanone (9.4 g, 3 mole equiv) was kept for 40 hr at reflux temperature. The internal temperature ranged from 99 to 105°. The excess cyclobutanone was recovered at 96–105° (760 mm) and the residue was distilled using a 6-in. Vigreux column: (1) about 50% of the 1:1 adduct I was recovered at 30–45° (0.05 mm); (2) 1.1 g of dioxaphospholane VI, $n^{25}\mathrm{D}$ 1.4474, was collected at 60–62° (0.05 mm); (3) the main portion of VI, 2.1 g, $n^{25}\mathrm{D}$ 1.4486, was collected at 62–65° (0.05 mm). The combined yield of VI was 40%.

Anal. Calcd for $C_{11}H_{21}O_6P$: C, 47.2; H, 7.5; mol wt, 280. Found: C, 46.5; H, 7.3; mol wt, 256 (cryoscopic in benzene).

The P^{31} (CH_2Cl_2) and the H^1 (CCl_4) nmr shifts are given in Table II. The infrared spectrum (CCl_4) had a C═O band at 5.84 and the strong band at 9.3 μ due to the $POCH_3$ group.

Reaction of the 1:1 Adduct (I) with Hexafluoroacetone. Preparation of 2,2,2-Trimethoxy-4-acetyl-4-methyl-5,5-bistrifluoromethyl-1,3,2-dioxaphospholane (VII).—The gaseous hexafluoroacetone was introduced into a solution of 1:1 adduct I (8.4 g) in hexane (80 ml), cooled in a Dry Ice–acetone bath. After 40 min, the mixture was removed from the bath and was allowed to reach 20° (3 hr). The solvent was removed at 20°, first at 20, then at 1 mm. The residue (14.9 g; theoretical yield, 15.0 g) was distilled through a 6-in. Vigreux column: (1) 0.8 g collected at 34–59° (0.1 mm; bath at 85°); (2) 4.47 g of dioxaphospholane VII, $n^{25}\mathrm{D}$ 1.3911, bp 60–62° (0.05 mm; bath at 100°). The yield of VII was 90%.

Anal. Calcd for $C_{10}H_{15}F_6O_6P$: C, 31.9; H, 4.0; P, 8.2. Found: C, 33.8; H, 4.1; P, 8.5.

The P^{31} (in CH_2Cl_2) and the H^1 (in CCl_4) nmr shifts are given in Table II. The infrared spectrum (in CCl_4) had a C═O band at 5.78 and a broad and strong band at 9.3 μ due to the $POCH_3$ group. There was a very strong band at 8.20 μ.

Reaction of the 1:1 Adduct (I) with Acetophenone. Preparation of 2,2,2-Trimethoxy-4α-acetyl-4β,5α-dimethyl-5β-phenyl-1,3,2-dioxaphospholane (VIII).—A mixture of 1:1 adduct I (21.0 g, 0.1 mole) and acetophenone (36.0 g, 0.3 mole) was kept for a total of 72 hr at 125°. The H^1 nmr spectra of aliquots were examined after 24 and 48 hr in CCl_4. The signal of the acetyl group of the product VIII was seen to appear at τ 7.70 next to the acetyl of acetophenone at 7.52. The methyl groups of the product VIII appeared at τ 9.15 and at 8.55.

The excess of monoketone and unreacted I were collected at 38–44° (0.05 mm), using an 8-in. Vigreux column. The dioxaphospholane VIII (17 g, 50%) was collected at 90–105° (0.07 mm; bath at 140–150°). Infrared and H^1 nmr spectra showed contamination with small amounts of acetophenone and of 1:1 adduct I. Pure VIII, bp 110° (0.07 mm; bath at 150°), $n^{25}\mathrm{D}$ 1.4936, was obtained in *ca.* 40% yield after an additional distillation through a 1-in. column.

Anal. Calcd for $C_{15}H_{23}O_6P$: C, 54.5; H, 7.0; P, 9.4. Found: C, 54.8; H, 7.2; P, 9.4.

The P^{31} (CH_2Cl_2) and the H^1 (CCl_4) nmr shifts are listed in Table II. The infrared (CCl_4) spectrum showed a C═O band at 5.84 and the $POCH_3$ absorption as a strong, broad, and split band at 9.25 and 9.32 μ.

Reaction of the 1:1 Adduct (I) with *p*-Nitroacetophenone. Preparation of 2,2,2-Trimethoxy-4α-acetyl-4β,5α-dimethyl-5β-*p*-nitrophenyl-1,3,2-dioxaphospholane (IXa) and of the Diastereomer, 5β-Methyl-5α-*p*-nitrophenyl-1,3,2-dioxaphospholane (IXb).—A mixture of I (42.0 g, 200 mmoles) and *p*-nitroacetophenone (16.5 g, 100 mmoles) was kept for 64 hr at 100°. The H^1 nmr spectra of aliquots taken after 40 and 60 hr showed little change. The signals due to the diastereomeric phospholanes, IXa and IXb, with *trans-* and *cis*-$CH_3\cdot CO/C_6H_4$-NO_2-*p*, respectively, are listed in Table II. The proportion of isomer was 35:65, *trans/cis*. About 5% of unreacted *p*-nitroacetophenone was present also.

The above mixture was heated to 100° (0.1 mm) to remove the excess phospholene (I) which boiled in the range 40 to 60°. The residue was kept for 20 hr at −10 under 30 ml of hexane. The crystalline mixture of isomers IXa and IXb (24 g, 65%) was collected by filtration. The H^1 nmr spectrum showed the *trans/cis* isomers in the proportion of *ca.* 20:80 (the *trans* isomer is more soluble in hexane). The hexane filtrate (12 g after evaporation) contained the balance of IXa + IXb. The H^1 nmr showed also the presence of some *meso-* and *rac*-trimethyl biacetylphosphite 2:1 adducts (*meso*, τ 7.80 and 8.68; racemic, τ 7.70 and 8.76). Some phospholene I was present (τ 8.23).

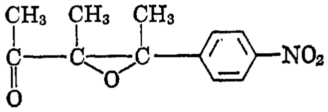
The crystalline mixture of IXa + IXb (23 g) was recrystallized from 20 ml of benzene and 30 ml of hexane (16 hr at 10°). The major *cis* isomer IXb, mp 91–92°, was isolated in 41% yield (14 g).

Anal. Calcd for $C_{15}H_{22}NO_8P$: C, 48.0; H, 5.9; N, 3.7; P, 8.3. Found: C, 48.3; H, 6.1; N, 3.9; P, 8.3.

The nmr data is given in Table II. The infrared spectrum (CCl_4) had strong bands at 5.85 (CO), 6.58 and 7.45, and 9.32 μ (phosphorane $POCH_3$).

The benzene–hexane filtrate, from which 41% of *cis* isomer (IXb) had been removed, was evaporated. The residue (9 g) consisted of IXa + IXb in about 60:40 proportion, with some *p*-nitroacetophenone as impurity.

Pyrolysis of the Trimethyl Biacetyl-*p*-nitrophenylphosphite Adduct (IXb), *cis*-$CH_3CO/C_6H_4 \cdot NO_2$-*p*.—The phospholane IXb (2.0 g) was kept for 16 hr at 120°, under N_2. The resulting brown mixture was dissolved in CCl_4. The H^1 nmr spectrum of this solution showed the three signals of some unreacted adduct IXb at τ 8.37, 8.50, and 8.30. The signals of a small amount of the *trans* isomer (IXa) were present at τ 7.60, 9.12, and 8.53. There were considerable amounts of *p*-nitroacetophenone recognized by the acetyl signal at τ 7.33. The corresponding dissociation product, the biacetyltrimethylphosphite 1:1 adduct (I), was recognized by its singlet at τ 8.20 ($CH_3C{=}C$) and by its doublet at 6.50 (CH_3O), J_{HP} = 13.0 cps. There were relatively large amounts of trimethylphosphate (doublet at τ 6.26, J_{HP} = 11.0 cps). A set of signals at τ 7.82, 8.10, and 7.78 could be due to an epoxide.



Reaction of the 1:1 Adduct (I) with α,α,α-Trifluoroacetophenone. Preparation of 2,2,2-Trimethoxy-4α-acetyl-4β-methyl-5α-trifluoromethyl-5β-phenyl-1,3,2-dioxaphospholane (Xa) and of the Diastereomer, 5β-Trifluoromethyl-5α-phenyl-1,3,2-dioxaphospholane (Xb).—A mixture of 1:1 adduct I (21.0 g, 100 mmoles) and α,α,α-trifluoroacetophenone (17.4 g, 100 mmoles) was kept for 20 hr at 95°. The course of the reaction was followed by H^1 nmr spectroscopy. The mixture was distilled through a 3-in. Vigreux column: (1) forerun, bp 35 to 116° (0.1 mm), 2.5 g; (2) main portion of the two diastereomers Xa + Xb, bp 116–118° (0.15 mm, bath at 165°), $n^{25}D$ 1.4664, yield 25 g, 85%. A second distillation of Xa + Xb at 0.1 mm (bath at 150–155°) afforded little separation of stereoisomers; the mixture had bp 110–112° (0.1 mm), $n^{25}D$ 1.4673.

Anal. Calcd for $C_{15}H_{20}F_3O_6P$: C, 46.9; H, 5.2; F, 14.8; P, 8.1. Found: C, 47.9; H, 5.4; F, 15.2; P, 8.5.

The H^1 nmr spectrum (in CCl_4) gave the signals listed in Table II; integration showed a proportion of 82:18 for the *trans*: *cis*-$CH_3 \cdot CO/C_6H_5$ isomers. The P^{31} nmr signals (in CH_2Cl_2) are listed in Table II. The infrared spectrum (in CCl_4) had a C=O band at 5.84 and the strong, split band at 9.22 and 9.40 μ due to the $POCH_3$ group. A strong characteristic double band was present at 8.40 and 8.60 μ.

Acid-Catalyzed Decomposition of Peroxydienones Derived from Hindered Phenols[1]

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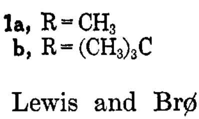
Decompositions of 4-*t*-butylperoxy-4-methyl-2,6-di-*t*-butyl-2,5-cyclohexadien-1-one (**1a**) and 4-*t*-butylperoxy-2,4,6-tri-*t*-butyl-2,5-cyclohexadien-1-one (**1b**) by a variety of Lewis and Brønsted acids have been carried out at ambient temperature in dilute solution. With sulfuric acid in acetic anhydride **1a** gives 3,5-di-*t*-butyl-4-acetoxybenzyl acetate (**2**) in excellent yield, whereas the major product resulting from the reaction of **1a** with boron trifluoride etherate in benzene is 3,5-di-*t*-butyl-4-hydroxybenzaldehyde (**7**). Evidence is presented for the intermediacy of quinone methide **3** in these reactions. In contrast, decomposition of **1a** with hydrogen chloride in benzene gives mostly 2-*t*-butyl-6-chloro-*p*-cresol (**20**). Approximately 90% of **20** is formed by a mechanism that does not require the presence of a chlorinating agent which is able to attack aromatic nuclei. The remaining 10% of **20** results from chlorodealkylation of 2,6-di-*t*-butyl-*p*-cresol (**10**) by a chlorinating species generated *in situ* from hydrogen chloride and *t*-butyl hydroperoxide. Hydrogen chloride catalyzed conversion of chlorodienone **22** to **20** occurs in high yield and proceeds by a mechanism which is entirely different from that involved in the hydrogen halide catalyzed conversion of bromodienone **23** to 2-*t*-butyl-6-bromo-*p*-cresol (**24**). Decomposition of **1b** gave high yields of 2,6-di-*t*-butylquinone (**8**) under all of the conditions studied.

It is now generally agreed that inhibition of the low-temperature liquid phase autoxidation of hydrocarbons by hindered phenols[2] involves the formation of peroxycyclohexadienones.[3] Mechanistic studies of inhibited autoxidation have frequently been carried out on the assumption that these peroxides were stable under the reaction conditions, and there seems to be no reason to doubt the validity of this postulate in most of the cases where it has been put forth. On the other hand, it is clear that there are many systems encountered in practical stabilization work where reactions of peroxycyclohexadienones are likely to occur.[4] Drastic changes in over-all inhibition mechanisms might easily come about as a consequence of these reactions, and for this reason the chemistry of peroxycyclohexadienones is of potential practical interest.

The present paper is concerned with the acid-catalyzed[5] decompositions of these peroxides, a topic which heretofore has not been subjected to systematic scrutiny. Two representative compounds, **1a** and **b**, were selected for study, and the objectives of the work were twofold: first, to determine what products are formed from these substances when they are decomposed by common Lewis and Brønsted acids; and second, to arrive at qualitative descriptions of the



1a, R = CH_3
b, R = $(CH_3)_3C$

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(1) Presented at the Southeast-Southwest Regional Meeting of the American Chemical Society, Memphis, Tenn., Dec 2, 1965. This paper constitutes part III of a series on oxidation inhibitors. Parts I and II are (a) N. P. Neureiter and D. E. Bown, *Ind. Eng. Chem., Prod. Res. Develop.*, **1**, 236 (1962); (b) N. P. Neureiter, *J. Org. Chem.*, **28**, 3486 (1963).

(2) The literature through 1960 relating to this subject has been reviewed by K. U. Ingold, *Chem. Rev.*, **61**, 563 (1961).

(3) For examples of the preparation of alkylperoxycyclohexadienones and discussions of their role in inhibition, see (a) T. W. Campbell and G. M. Coppinger, *J. Am. Chem. Soc.*, **74**, 1469 (1952); (b) A. F. Bickel, E. C. Kooyman, and C. la Lau, *J. Chem. Soc.*, 3211 (1953); (c) C. E. Boozer, G. S. Hammond, C. E. Hamilton, and J. N. Sen, *J. Am. Chem. Soc.*, **77**, 3233 (1955); (d) E. C. Horswill and K. U. Ingold, *Can. J. Chem.*, **44**, 263,269 (1966).

(4) See ref 1a for a discussion of some systems of this type.

(5) The term "acid-catalyzed" is used here merely for convenience, since there is no guarantee that all of the acids employed in this work functioned as true catalysts (*i.e.*, were not destroyed during reaction).