Unsymmetrically Substituted α-Diketones in the Oxyphosphorane Condensation. P^{31} and H^1 Nuclear Magnetic Resonance Spectra[1,2]

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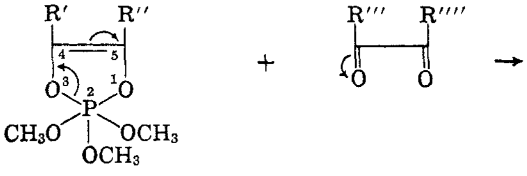
Received September 27, 1965

The *cyclic unsaturated pentaoxyphosphorane* (1,3,2-dioxaphosphol*ene*) made from biacetyl and trimethyl phosphite reacted slowly with benzil and rapidly with 1-phenylpropanedione, with the formation of a carbon–carbon bond. A benzoyl group was attacked exclusively, in preference to an acetyl group. Two diastereomers of the corresponding *cyclic saturated pentaoxyphosphoranes* (1,3,2-dioxaphosphol*anes*) were produced. The phospholene made from 1-phenylpropanedione and trimethyl phosphite reacted slowly with biacetyl and rapidly with phenylglyoxal. In the former case, two *structural isomers* were produced, each in two diastereomeric forms. In the latter case, only one structure (two diastereomers) was formed. The aldehyde group was attacked exclusively. Hydrolyses of the phospholanes to cyclic phosphates and to phosphorous-free diketols are described. The P^{31} and H^1 nmr spectra are given.

4-Phenyl-2,2,2-trimethoxy-1,3,2-dioxaphospholene (I), prepared from phenylglyoxal and trimethyl phosphite (TMP), reacted slowly with biacetyl (III) at 20°. The product was a 60:40 mixture of *cis*- and *trans*-4-benzoyl-5-acetyl-5-methyl-2,2,2-trimethoxy-1,3,2-dioxaphospholane (Va and Vb); *i.e.*, the reactive site of the phospholene I was, exclusively, the carbon atom that carried the hydrogen.[2]

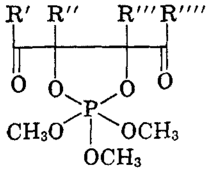


I, R' = C_6H_5; R'' = H

II, R' = R'' = CH_3

III, R''' = R'''' = CH_3

IV, R''' = H; R'''' = C_6H_5



V, R' = C_6H_5; R'' = H; R''' = R'''' = CH_3

VI, R' = R'''' = C_6H_5; R'' = R''' = H

VII, R' = R'' = R''' = R'''' = CH_3

The 4,5-dimethyldioxaphospholene II, made from biacetyl and TMP, reacted very rapidly with phenylglyoxal (IV), even at 0°, and gave an 85:15 mixture of the same *cis* and *trans* isomers Va and Vb; *i.e.*, the reactive site of the "acceptor" carbonyl compound was the aldehyde group.[2]

Probably, the second reaction was faster than the first for at least two reasons: (1) the phospholene II is less stable, and hence, more reactive than I because it lacks groups capable of effective conjugation with the carbon–carbon double bond;[3] (2) the carbonyl group of the aldehyde, IV, is more reactive than that of the ketone, III. The ratios of diastereomers formed in both reactions were different, and there seemed to be no interconversion among the isomers. Therefore, some differences must exist in the energies of the corresponding transitions states.[2] The self-condensation of two molecules of phenylglyoxal[2] to the phospholane VI, and of two molecules of biacetyl[4] to the phospholane VII, could be effected *stepwise*, because the carbonyl compound, in each case, reacted faster with TMP than with the phospholene (I and II, respectively). Therefore, these intermediate 1:1 adducts could be isolated. However, the highly reactive α-diketone acenaphthenequinone[5] gave *directly* a dioxaphospholane (2:1 adduct) when treated with TMP. The same was true for the α-keto ester methyl pyruvate.[6] Presumably, the *1:1 adducts* are very reactive in these cases, and may in fact be open dipolar ions rather than phospholenes.

The condensation of the 4,5-dimethyldioxaphospholene, II, with acenaphthenequinone,[7] *p*-benzoquinone,[8] methyl pyruvate,[9] propionaldehyde,[10] and benzaldehyde[10] has been carried out.

This paper is concerned with the behavior of unsymmetrically substituted α-diketones, for example, 1-phenylpropanedione, $C_6H_5COCOCH_3$, in the oxyphosphorane condensation. The possibility of using less reactive aromatic α-diketones like benzil, $C_6H_5COCOC_6H_5$, in these condensations was also explored.

Results

Reaction of Benzil with Dioxaphospholenes.—Benzil proved to be a rather poor "acceptor" toward the dimethylphospholene II. The product was a mixture of the two diastereomers, IXa and IXb, which are possible for the dioxaphospholane structure. The major isomer (85%) was assigned the *cis*-acetyl/benzoyl configuration. (See Scheme I.)

The structure and the configurations are based on the following data: (1) the presence of infrared bands due to aliphatic and aromatic carbonyl groups; (2) the positive values[2–10] of the P^{31} nmr signals given in Table I. The major signal was at higher magnetic

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(1) Organic Compounds with Pentavalent Phosphorus. Part XXII. Supported by Public Health Service Research Grant No. CA-04769-06 from the National Cancer Institute and by the National Science Foundation, GP3341.

(2) Part XXI: F. Ramirez, A. V. Patwardhan, and C. P. Smith, *J. Org. Chem.*, **30**, 2575 (1965).

(3) The phospholene made from diphenylpropanetrione and TMP is exceptionally stable; the carbon–carbon double bond in it is conjugated with a phenyl and a benzoyl group.

(4) (a) F. Ramirez, N. Ramanathan, and N. B. Desai, *J. Am. Chem. Soc.*, **85**, 3465 (1963); (b) F. Ramirez and N. B. Desai, *ibid.*, **85**, 3252 (1963); (c) *ibid.*, **82**, 2652 (1960).

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

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

(7) F. Ramirez, N. Ramanathan, and N. B. Desai, *J. Am. Chem. Soc.*, **84**, 1317 (1962).

(8) F. Ramirez, H. J. Kugler, and C. P. Smith, *Tetrahedron Letters*, **No. 4**, 261 (1965).

(9) F. Ramirez, A. V. Patwardhan, N. B. Desai, N. Ramanathan, and C. V. Greco, *J. Am. Chem. Soc.*, **85**, 3056 (1963).

(10) F. Ramirez, A. V. Patwardhan, N. Ramanathan, N. B. Desai, G. V. Greco, and S. R. Heller, *ibid.*, **87**, 543 (1965).

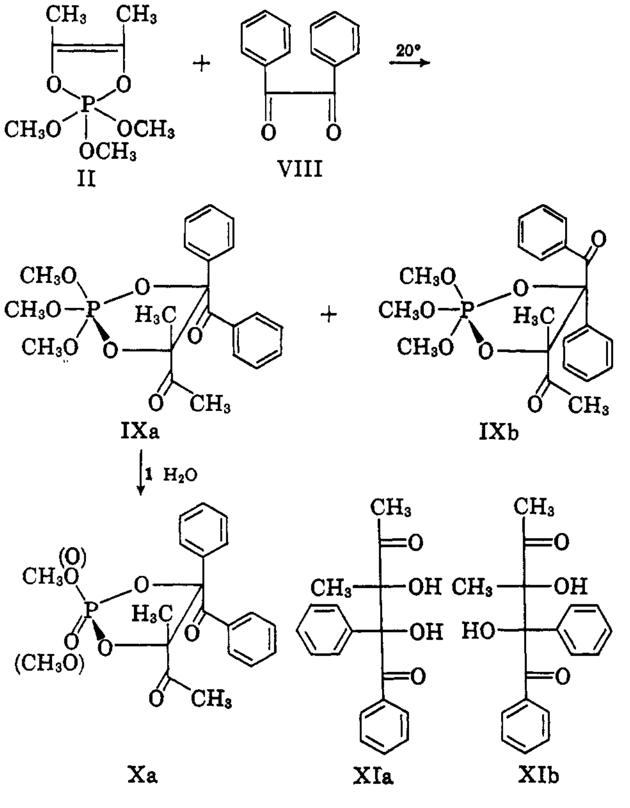
TABLE I

P^{31} AND H^1 NMR SHIFTS[a] OF 2,2,2-TRIMETHOXY-1,3,2-DIOXAPHOSPHOLANES[b] DERIVED FROM THE CONDENSATION OF DIOXAPHOSPHOLENES[c] WITH α-DIKETONES AND α-KETOALDEHYDES

		Dioxaphospholane							
		Major diastereomer				Minor diastereomer			
Dioxaphospholene from	Carbonyl acceptor	No.	δ (P^{31})	τ_{Ac}	τ_{Me}	No.	δ (P^{31})	τ_{Ac}	τ_{Me}
Biacetyl	Biacetyl	VII	+54.8	7.85	8.69	VII	+52.6	7.75	8.83
Biacetyl	Benzil	IXa	+54.7	7.55	9.08	IXb	+52.7	8.70	8.25
1-Phenylpropanedione	Biacetyl	XIVa	+54.7	7.65[d] 8.18[e]	9.14[f]	XIVb	+52.4	7.98[d] 8.68[e]	8.33
		XVa	+54.6	7.70	8.63[g] 8.42[h]	XVb		7.78	8.58[g] 8.32[h]
Biacetyl	Phenylpropanedione	XIVa	+54.7	7.66[d] 8.16[e]	9.13[f]	XIVb	+52.7	7.98[d] 8.68[e]	8.33
Biacetyl	Phenylglyoxal	V	+50.1	7.75	8.54	V	...	7.75	8.95
1-Phenylpropanedione	Phenylglyoxal	XIXa	+49.4	8.27	None	XIXb	...	7.75	None

[a] P^{31} shifts in parts per million from 85% H_3PO_4, determined at 40.5 Mcps in CH_2Cl_2. H^1 shifts in parts per million from TMS = 10 (τ values), determined at 60 Mcps in CCl_4 or $CDCl_3$. [b] *cis* and *trans* relationship of substituents at carbons 4 and 5 gives rise to stereoisomerism. [c] From the reaction of trimethyl phosphite with an α-dicarbonyl compound. [d] *Probably* on carbon carrying a phenyl ring. [e] *Probably* on carbon carrying a methyl group. [f] *cis* to a phenyl ring. [g] *Probably* on carbon carrying an acetyl group. [h] *Probably* on carbon carrying a benzoyl group.

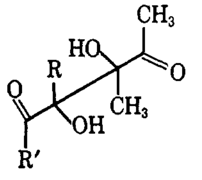
SCHEME I



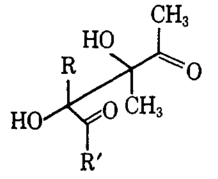
field than the minor signal, which is in agreement with the *cis* configuration for the most abundant diastereomer.[4] (3) The protons of the methyl group in the *major* isomer gave an nmr signal at the highest magnetic field (see Table I); it is, probably, *cis* to a phenyl. The same effect (τ 9.18) was observed in the *minor* isomer of the phospholane made from the biacetyl–TMP adduct II and benzaldehyde,[10] where there was a *cis*-phenyl/methyl relationship. Note that the protons of the acetyl group in the *minor* isomer of the biacetyl–benzil–TMP adduct, IXb, gave a signal at a relatively high field also. (4) The *cis*-phospholane, IXa, was converted into a cyclic phospho triester Xa by 1 mole equiv of water.[4,11]

TABLE II

H^1 NMR SHIFTS[a] OF DIASTEREOMERIC α-DIKETOLS MADE BY THE OXYPHOSPHORANE CONDENSATION[b]



erythro



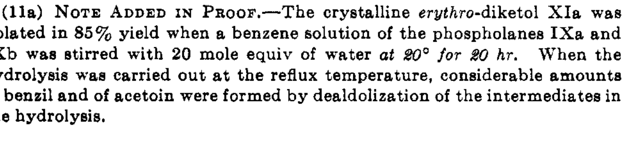
threo

		erythro[c]		*threo*[c]	
R	R′	τ_{CH_3CO}	τ_{CH_3}	τ_{CH_3CO}	τ_{CH_3}
CH_3	CH_3[d]	7.64	8.75	7.77	8.70
C_6H_5	C_6H_5	8.08	8.55	7.98	8.87
C_6H_5	CH_3	7.83, 8.12	8.67	7.70, 8.00	8.98
CH_3	C_6H_5	7.74	8.47, 8.70	...	...

[a] In parts per million from TMS = 10 (τ). [b] From hydrolysis of 1,3,2-dioxaphospholanes with 20 mole equiv. of water in benzene. [c] The configurations based on those of the parent dioxaphospholanes. The *erythro* is related to the *cis*-R′CO/CH_3CO. [d] Reference 4. The configuration of the parent phospholane was independently established by comparison with that of the related cyclic phospho triester.

(5) The mixture of *cis*- and *trans*-phospholanes, IXa + IXb, was hydrolyzed to a mixture of *erythro*- and *threo*-α-diketols, XIa + XIb.[11a] The H^1 nmr signals of the diketols are given in Table II.

The dioxaphospholene, XII, derived from benzil[4] and TMP, failed to react with a second molecule of



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[11] F. Ramirez, A. V. Patwardhan, N. B. Desai, and S. R. Heller, *J. Am. Chem. Soc.*, **87**, 549 (1965).

[11a] NOTE ADDED IN PROOF.—The crystalline *erythro*-diketol XIa was isolated in 85% yield when a benzene solution of the phospholanes IXa and IXb was stirred with 20 mole equiv of water *at 20° for 20 hr.* When the hydrolysis was carried out at the reflux temperature, considerable amounts of benzil and of acetoin were formed by dealdolization of the intermediates in the hydrolysis.

benzil or of the more reactive acceptor, biacetyl. This is attributable to the stability conferred on the phospholene by the "*cis*-stilbene" conjugation.

Behavior of 1-Phenylpropanedione (Methylphenylglyoxal) in the Oxyphosphorane Condensation.— This α-diketone reacted rapidly and exothermally with trimethyl phosphite at 0°; 4-phenyl-5-methyl-2,2,2-trimethoxy-1,3,2-dioxaphospholene (XIII) was obtained in nearly quantitative yield. The P^{31} nmr signal was at +49.5 ppm *vs.* 85% H_3PO_4, as expected.[2] The protons of the methyl group attached to the C–C double bond[4] gave a signal at τ 7.92. Other data given in the Experimental Section also support the cyclic oxyphosphorane structure.[12]

We cannot explain the high temperature (130°) employed by Kirillova and Kukhtin[13] in their recent preparation of XIII in 30–48% yield. Likewise, we did not find in our product the phosphonates mentioned by the Russian investigators, if the trialkyl phosphite was free from dialkyl phosphite and from moisture.

The phenylmethylphospholene was rather unreactive toward the "acceptor" biacetyl. The reaction was nearly complete after 20 days at 20°, using an excess of biacetyl (1:3). *Two structural isomers were produced, each one in two diastereomeric forms.* The major structure, XIVa (60%), resulted from an attack by the carbon that carried the phenyl ring (*path a*, Scheme II); the two acetyl groups are assumed to have the *cis* configuration for reasons discussed below. The diastereomer, XIVb, was formed in small amounts (*ca.* 5%). The minor structure, XVa (30%), resulted from an attack by the carbon that carried the methyl group (*path b*); the *cis*-acetyl/benzoyl configuration is assigned to it. Very little (*ca.* 5%) of the *trans* isomer, XVb, was detected, but not further characterized.

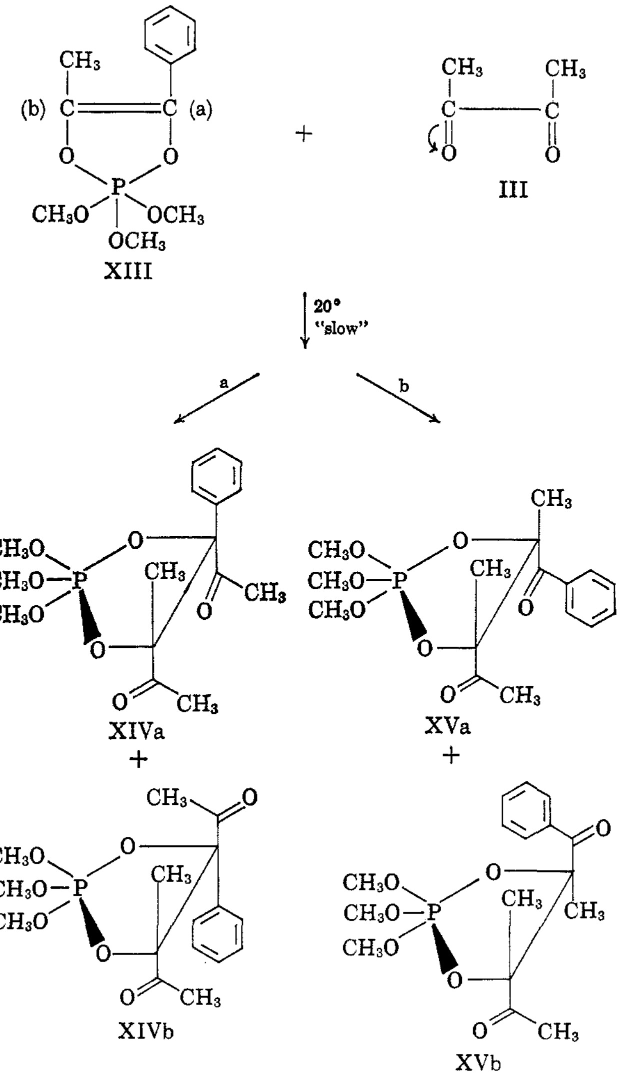
The P^{31} nuclei of the *structural* isomers with the same configuration, XIVa and XVa, gave very similar nmr shifts, as shown in Table I. However, the signal of an isomer with the *cis* configuration, XIVa, was at significantly higher field than that of the *trans* isomer, XIVb. This is one of the bases for the configurational assignment.[4]

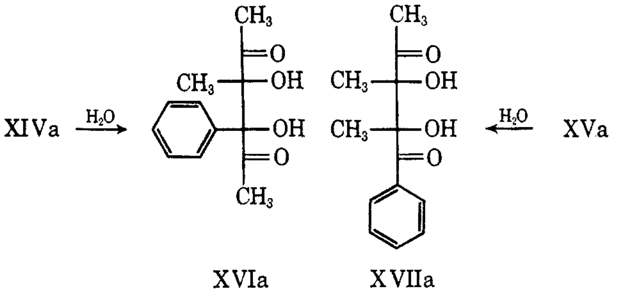
The H^1 nmr signals due to acetyl groups and to ring-methyl groups are listed in Table I. The strong signal at the highest magnetic field was ascribed to a methyl adjacent to a phenyl ring, hence to XIVa; this led to the identification of its two strong acetyl signals. Other model compounds[2,4] aided in the assignment of H^1 signals (Table I).

The infrared spectrum of the mixture showed the aliphatic and the aromatic carbonyl bands with the expected relative intensities. The major *cis* isomer, XIVa, crystallized out of the mixture in 40% yield. However, this is not the best route to this substance (*vide infra*).

Hydrolysis of the mixture of phospholanes which remained after the separation of some XIVa gave two α-diketols, *erythro*-3-methyl-4-phenylhexane-3,4-diol-2,5-dione (XVIa) and *erythro*-3,4-dimethyl-5-phenylpentane-3,4-diol-2,5-dione (XVIIa); *cf.* Table II.

SCHEME II





Kirillova and Kukhtin[13] reported the "formation in 16.9% yield" of a structure like XIVa or XIVb, from the condensation of the phenylmethylphospholene XIII with biacetyl (II). They did not mention stereoisomers or the structural isomer XV.

1-Phenylpropanedione (XVIII) was an excellent "acceptor" for the dimethylphospholene II, derived from biacetyl. *Only one structural isomer, in two diastereomeric forms, was produced.* The major isomer (70%) proved to be the substance, XIVa, with two *cis*-acetyl groups, that had been formed also in the previous, more complex and slower reaction. This phospholane XIVa was obtained in crystalline form in 55% yield. The spectral data are included in Table I.

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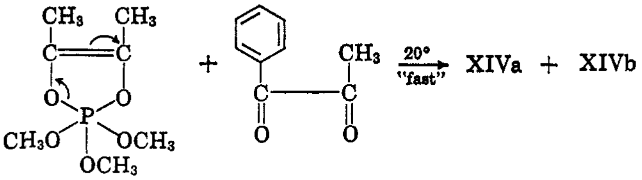
[12] The molecular structure of a dioxaphospholene was determined by X-ray analysis. See W. C. Hamilton, S. J. La Placa, and F. Ramirez, *J. Am. Chem. Soc.*, **87**, 127 (1965).

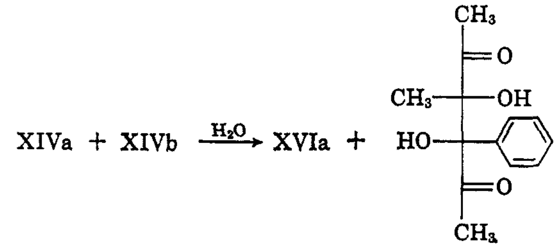
[13] K. M. Kirillova and V. A. Kukhtin, *Zh. Obsch. Khim.*, **35**, 544 (1965); *Chem. Abstr.*, **63**, 5236 (1965). This publication appeared after our work had been completed; see also F. Ramirez, *Pure Appl. Chem.*, **9**, 337 (1964).

The minor isomer (30%) had the *trans*-acetyls configuration XIVb. These products resulted from the addition of a phospholene carbon to the *benzoyl rather than the acetyl group of the diketone*, a rather unusual occurrence in nucleophilic additions.



II XVIII

Hydrolysis of the crystalline phospholane XIVa gave the *erythro*-diketol XVIa as before. Hydrolysis of the mixture of diastereomers, XIVa,b, gave the mixture of *erythro*-XVIa and *threo*-XVIb diketols.[13a]

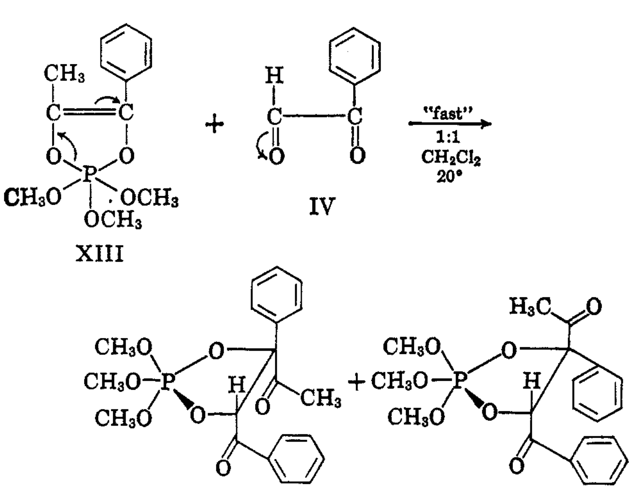


XVIb

Kirillova and Kukhtin[13] did not describe the condensation between the dimethylphospholene II and 1-phenylpropanedione (XVIII).

The self-condensation of two molecules of 1-phenylpropanedione (XVIII) by trimethyl phosphite was impractically slow.

Condensation of 1-Phenylpropanedione (XVIII) with Phenylglyoxal by Means of Trimethyl Phosphite.—This was easily accomplished by first making the dioxaphospholene XIII from 1-phenylpropanedione (XVIII) and then treating it with phenylglyoxal (IV). *Although four structures are possible, only one was produced, in two diastereomeric forms, XIXa and XIXb.*



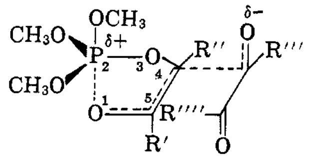
XIII IV

XIXa XIXb

The "conjugate reaction," I + XVIII, was of no preparative value. The dioxaphospholene made from phenylglyoxal, I, is about as reactive as that made from methylphenylglyoxal (XVIII), but the latter α-diketone is much less reactive as an "acceptor" than the α-ketoaldehyde IV.

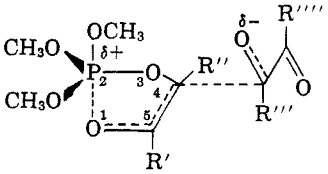
Discussion

The course of the reaction between phospholenes and carbonyl compounds was explained[2] in terms of a concerted transition state, XXa, in which the P–O bond of the phosphol*ene* was broken as the new C–C and P–O bonds of the phosphol*ane*, with *cis*-R''/R''' configuration, were formed. A second transition state, XXb, can be constructed for the *trans*-R''/R''' diastereomer.



cis-R''/R'''; *cis*-$R'CO/R''''CO$

XXa



trans-R''/R'''; *trans*-$R'CO/R''''CO$

XXb

If this picture of the oxyphosphorane condensation is a satisfactory one, it should help explain several observations made in this investigation. (1) The dimethylphospholene, II ($R' = R'' = CH_3$), reacted much faster with 1-phenylpropanedione than with benzil, although the attack was on a *benzoyl carbon* in both cases; $R''' = C_6H_5$, $R'''' = CH_3$ or C_6H_5, respectively. (2) The benzoyl, and not the acetyl, of the "acceptor" 1-phenylpropanedione, was involved in the reaction with the dimethylphospholene; *i.e.*, $R''' = C_6H_5$ not CH_3 in XX. (3) Two structures, XIV and XV, resulted from the "slow" reaction of the methylphenylphospholene, XIII ($R' = CH_3$; $R'' = C_6H_5$ and *vice versa*), with biacetyl. Only one structure, XIV, resulted from the "fast" reaction of the dimethylphospholene, II, with phenylpropanedione ($R''' = C_6H_5$; $R'''' = CH_3$). Yet, both reactions bring into play the same four groups, R', R'', R''', and R''''. (4) The phenylmethylphospholene, XIII, utilizes its two potentially reactive positions, *i.e.*, C-4 and C-5, in the "slow" reaction with biacetyl (II) but only one position, the phenyl-bearing carbon, R'', in the "fast" reaction with phenylglyoxal (IV).

Observation 1 above suggests that the steric and the electronic properties of *both groups* R' *and* R'''' in XX are important in the condensation reaction. Furthermore, this and other examples suggest that the presence of an acetyl group, $R'''' = CH_3$, in the acceptor favors the condensation, relative to the case in which $R'''' = C_6H_5$.

Observation 2 can be understood if the attraction between the "existing" acetyl, R'''', and the "incip-

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[13a] NOTE ADDED IN PROOF.—The liquid *erythro*-diketol XVIa and the crystalline *threo*-diketol XVIb were obtained in good yield when the hydrolyses of the phospholanes, XIVa and XIVb, were carried out in a benzene–water mixture at *20°* for *20 hr*. Higher temperatures in the hydrolyses favored dealdolization of intermediates with formation of phenylpropanedione.

ient" acetyl, $R' = CH_3$, in the transition state, overcome (a) the CH_3–phenyl repulsion, and (b) the lower reactivity of a benzoyl group (*vs.* an acetyl group). The comparison here must be with the attraction between the "existing" benzoyl, $R'''' = C_6H_5$, and the "incipient" acetyl, $R' = CH_3$, which would produce the second structural isomer (not formed). The nature of group R'''' emerges as a rather important factor in these condensations.

Observations 3 and 2, taken together, suggest that an acetyl group is more effective in favoring the condensation when it is present in the acceptor, $R'''' = CH_3$, than when it is being formed in the transition state, $R' = CH_3$. Note that the essential difference in the two reactions is that two structural isomers were produced only when an acetyl group was present as R'''' in the transition state. When a benzoyl group was required as R'''', that product was not obtained.

The greater reactivity of the dimethylphospholene *vs.* the methylphenylphospholene due to conjugation effects was already mentioned.

Observation 4 is understandable since the hydrogen atom of the acceptor, $R''' = H$, does not offer much hindrance to either a phenyl or a methyl group, $R'' = C_6H_5$ or CH_3. However, the attraction between an existing benzoyl, $R'''' = C_6H_5$, should be greater toward an incipient acetyl, $R' = CH_3$, than toward an incipient benzoyl, $R' = C_6H_5$. There is no reason for an involvement of the methyl-bearing carbon when the methylphenylphospholene reacts with phenylglyoxal.

The reaction of the dimethylphospholene, II, with benzil gave the *cis* and the *trans* isomers, IXa and IXb, in the proportion 85:15. The same phospholene with phenylpropanedione gave the corresponding isomers, XIVa and XIVb, in the proportion of 70:30. Note that in both cases there is CH_3–phenyl repulsion in the formation of the *cis* isomer. One must explain the formation of so little *trans* isomer (or of so much *cis* isomer) in the benzil case. Probably, the size of group R'''' must be considered also among the factors which determine the *cis*:*trans* ratio; *i.e.*, *the larger the size of* R'''', *the greater the cis:trans ratio.* We have suggested[2] two other factors: (1) the sizes of R'' and R''' (the larger these groups the smaller the *cis*:*trans* ratio); (2) the attraction between the R'CO and the R''''CO (the greater this attraction, the greater the *cis*:*trans* ratio).

The size of group R'''' may affect the isomer ratio because the "*trans* orientation" of this group in the transition state conflicts with the steric requirements of the trigonal bipyramid (see formula XXb). The X-ray analysis of an oxyphosphorane[12] shows a great deal of crowding in the pertinent sections of the molecule, at least in the crystal.

In comparing reactions between two dioxaphospholenes and two α-dicarbonyl compounds, both carrying unsymmetrical substituents, one must consider (1) the relative stability of the phospholenes; (2) the relative reactivity of all the carbonyl functions involved; (3) the relative sizes of the groups R', R'', R''', and R''''; and (4) the attraction, and even the possible repulsions, of the carbonyl functions which exist in the acceptor and which originate from the phospholene during the reaction.

Experimental Section

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

Reaction of the Biacetyl–Trimethyl Phosphite 1:1 Adduct (II) with Benzil. Preparation of *cis*- and *trans*-2,2,2-Trimethoxy-4-acetyl-5-benzoyl-4-methyl-5-phenyl-1,3,2-dioxaphospholane (IXa and IXb). A.—A mixture of 1:1 adduct II (28 g, 0.13 mole) and benzil (21 g, 0.10 mole) was kept 59 days, under N_2, at 20° with occasional stirring. The course of the reaction was followed by means of infrared spectra of aliquots taken at various intervals. The new aliphatic C=O band in the product appeared at 5.82 μ and finally became equal in intensity to the aromatic C=O at 5.92 μ. The excess of 1:1 adduct was removed at 0.2 mm (bath at 100°, last traces at 130°). The residue was kept 10 hr at 0° under pentane. The crystals were washed twice with fresh pentane (20-ml portions) and dried at 0.5 mm. The yield of crude *cis* and *trans* adducts (IXa and IXb), mp 70–90°, was 31 g (80%). The H^1 nmr spectrum (CCl_4) showed signals at τ 7.56 (major acetyl), 9.08 (major CH_3), 8.70 (minor acetyl next to phenyl ring), and 8.25 (minor CH_3). Integration showed that the proportion of diastereomers was 85:15.

A 10-g sample was suspended in hot hexane (3 ml/g) and diluted with benzene. The pure *cis*-biacetyl–benzil–trimethyl phosphite adduct (IXa) (6 g, mp 108–110°) separated on cooling.

Anal. Calcd for $C_{21}H_{25}O_7P$: C, 60.0; H, 6.0; P, 7.4. Found: C, 60.0; H, 6.1; P, 7.3.

The P^{31} (in CH_2Cl_2) and the H^1 (in $CDCl_3$) nmr shifts are listed in Table I. In addition, the nine protons of the three CH_3O groups gave one doublet, $J_{HP} = 13.3$ cps, at τ 6.50 and the ten protons of the aromatic rings gave signals at τ 2.2 (2H), 2.6 (2H), and 2.8 (6H). The infrared spectrum (CCl_4) *had two C=O bands at 5.82 and 5.92* μ, and strong bands in the P–OCH_3 region at 8.94 and 9.16 μ.

The benzene–hexane mother liquid deposited about 2 g of additional crystalline *cis* isomer IXa contaminated with some *trans* isomer IXb. Finally, the solvent was removed from the mother liquid, leaving a pale yellow noncrystalline isomer mixture, showing the expected H^1 nmr signals and the signal at τ 8.23 due to the methyl groups of a little unreacted 1:1 adduct (II).

B.—In another experiment, 3 moles of the 1:1 adduct II and 1 mole of benzil were kept *20 days at 20°*. The yield of crude *cis*- and *trans*-dioxaphospholane IXa and IXb was 80%. Pure *cis* isomer was obtained in 50% yield by recrystallizations from benzene–pentane.

Hydrolysis of the Biacetyl–Benzil–Trimethyl Phosphite Adduct (IXa) with 1 Mole Equiv of Water. Preparation of DL-*erythro*-Methyl (3-Methyl-4,5-diphenylpentane-3,4-diol-2,5-dione) Cyclic Phosphate (Xa).—A solution of *cis*-phospholane IXa (4.3 g) in benzene (25 ml) was treated with water (0.185 ml, 1 mole equiv) at 20°, with stirring. The solvent was removed after 6 min, first at 15 mm, then at 2 mm, both at 20°. The residue was dissolved in benzene (10 ml) and the solution was diluted with hexane (10 ml) and then cooled. The crystalline phosphate (3.0 g), mp 127–132°, was recrystallized to give the analytical sample, mp 132–134° (benzene–pentane).

Anal. Calcd for $C_{19}H_{19}O_6P$: C, 60.9; H, 5.1; P, 8.3. Found: C, 60.7; H, 5.2; P, 8.5.

The H^1 nmr spectrum (fresh $CDCl_3$ solution) had ten protons at τ 2.2 and 2.6; a three-proton doublet, $J_{HP} = 11.8$ cps, at τ 6.60; three protons each at τ 7.50 (acetyl) and at τ 8.72 (methyl). The infrared spectrum (CH_2Cl_2) had C=O bands at 5.80 and 5.90 μ, P=O band at 7.65 μ, and P–OCH_3 band at 9.50 μ.

Hydrolysis of *cis* and *trans* Biacetyl–Benzil–Trimethyl Phosphite Adduct (IXa and IXb) with an Excess of Water. Preparation of DL-*erythro*-3-Methyl-4,5-diphenylpentane-3,4-diol-2,5-dione (XIa).—A solution of the original mixture of *cis*- and *trans*-phospholanes, IXa and IXb (13 g), in benzene (100 ml) was allowed to react with 20 mole equiv of water (11 ml, which contained a few drops of 85% H_3PO_4) and then the mixture was stirred at 20° for a period of 20 hr. The benzene layer was evaporated and the residue was recrystallized from hexane giving the *erythro*-diketol XIb, mp 119–120°, in 85% yield. The infrared spectrum (CCl_4) showed no bands due to phosphorus compounds, a band at 2.9–3.0 μ (OH), and a broad band at 5.90 to 5.98 μ (CO). The H^1 nmr spectrum ($CDCl_3$) showed strong signals due to aromatic protons at τ 2.2 and 2.7, and the signals listed in Table II.

Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.5; H, 6.0. Found: C, 72.2; H, 6.3.

The *threo*-diketol XIb was not isolated in pure form. Its H^1 nmr signals are given in Table II.

Reaction of II with 1-Phenylpropanedione (XVIII). Preparation of *cis*- and *trans*-2,2,2-Trimethoxy-4,5-diacetyl-4-methyl-5-phenyl-1,3,2-dioxaphospholane (XIVa and XIVb).—A mixture of 1:1 adduct II (28.0 g, 133 mmoles) and 1-phenylpropanedione (XVIII) (19.7 g, 133 mmoles) was kept at 20° under N_2, with stirring. The course of the reaction was followed by examination of the infrared and the H^1 nmr spectra (both in CCl_4) at various intervals: 1 hr, 24 hr, 48 hr, 4 days, and 5 days. The two carbonyl bands of the diketone (5.85 and 5.98 μ) were replaced by a single carbonyl band at 5.82 μ; *therefore, the product contained acetyl groups and lacked benzoyl groups,* due to exclusive attack at the benzoyl function. The H^1 signals due to the acetyl in the diketone (τ 7.50) and the methyl in the 1:1 adduct II (τ 8.23) disappeared and were replaced by two acetyl signals, one methyl signal, and one methoxy doublet due to the *cis* isomer, and the corresponding signals of the *trans* isomer, of the dioxaphospholanes (XIVa and XIVb) (Table I). Most of the reaction had taken place after 48 hr. Integration of the H^1 signals showed a 70:30 proportion of diastereomers.

Benzene (15 ml) was introduced after 5 days, and the solution was allowed to deposit crystals for 4 days at 20°. The first crop (16 g after drying at 20°, 1 mm) had the H^1 nmr signals due to the major isomer (XIVa), and very faint signals due to the minor isomer (XIVb). The second crop (10.0 g) was similar. Total yield of *cis* isomer XIVa was 53%. The H^1 nmr spectra of the mother liquids which remained after the stepwise removal of *cis* isomer showed the signals of both isomers in the corresponding proportions. Removal of solvent (1 mm at 20°) left 20 g of XIVa and XIVb, which were used in hydrolyses experiments.

The analytical sample of *cis*-dioxaphospholane (XIVa) had mp 92–93° (benzene–hexane).

Anal. Calcd for $C_{16}H_{23}O_7P$: C, 53.6; H, 6.4; P, 8.7. Found: C, 54.7; H, 7.0; P, 8.85.

The P^{31} and the H^1 nmr shifts are listed in Table I. In addition, the three CH_3O groups gave *one* doublet, J_{HP} = 13.0 cps, at τ 6.45 and the five protons of the aromatic ring gave signals at τ 2.6 and 2.8. *The infrared spectrum had only one strong C=O band at* 5.82 μ and strong P–OCH_3 bands at 9.10 and 9.30 μ (shoulder at 9.43 μ).

Hydrolysis of the *cis* Biacetyl–Phenylpropanedione–Trimethyl Phosphite Adduct (XIVa) with an Excess of Water. Preparation of DL-*erythro*-3-Methyl-4-phenylhexane-3,4-diol-2,5-dione (XVIa).—A solution of crystalline *cis* adduct XIVa (8.4 mmoles) in benzene (15 ml) was stirred 20 hr at 20° with 3 ml of water containing a few drops of 85% H_3PO_4. The benzene layer was evaporated and the residue was freed from solvent under reduced pressure and submitted to analysis. The liquid *erythro*-diketol XVIa could not be crystallized nor purified by distillation. Its purity was ascertained by infrared spectrum [there were no bands due to phosphorus compounds; there was a band at 3.0 μ (OH) and another at 5.90 μ (hydrogen-bonded CO)] and by the H^1 nmr spectrum given in Table II. Yield was 85%.

Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.1; H, 6.8. Found: C, 65.6; H, 6.7.

Hydrolysis of *cis* and *trans* Biacetyl–Phenylpropanedione–Trimethyl Phosphite Adduct (XIVa and XIVb). Preparation of *erythro*- and *threo*-3-Methyl-4-phenylhexane-3,4-diol-2,5-dione (XVIa + XVIb).—The material used (20 g) was the residue obtained in the previous oxyphosphorane condensation after removal of 53% of *cis*-phospholane, (XIVa). A solution of the *cis* and *trans* XIVa and XIVb (20 g) in benzene (30 ml) was treated with 10 mole equiv of water (10 ml) and kept 6 hr at reflux.[13a] The benzene layer afforded 11.2 g of diketols. The infrared spectrum was similar to that of the previous hydrolysis. The H^1 nmr (CCl_4) had the set of three signals of the *threo*-XVIb (strong) and the set of three signals of the *erythro*-XVIa (weak). This mixture was dissolved in hot benzene (1 ml/g). The pure *threo*-XVIb (4 g, mp 86°) separated on cooling.

Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.1; H, 6.8. Found: C, 66.2; H, 7.2.

The H^1 (in CCl_4) nmr shifts are listed in Table II. In addition the five protons of the aromatic ring gave signals at τ 2.82 and the two protons of –OH groups were at τ 4.55 and 5.83. The infrared spectrum (CCl_4) had bands at 3.0 (–OH) and 5.90 μ (hydrogen-bonded acetyl).

Reaction of Trimethyl Phosphite with 1-Phenylpropanedione (Methylphenylglyoxal). Preparation of 2,2,2-Trimethoxy-4-phenyl-5-methyl-1,3,2-dioxaphospholene (XIII).—The phenylpropanedione was dried over $CaCl_2$ and then distilled. The trimethyl phosphite was treated with Na ribbon and distilled. The diketone XVIII (30 g, 0.203 mole) was added, dropwise over a 30-min period, to the phosphite (27.5 g, 0.220 mole), and kept at 0–5° by external cooling. (The reaction was exothermic, but somewhat less vigorous than the reactions of biacetyl and of phenylglyoxal with trimethyl phosphite.) The mixture was allowed to warm to 20° and was stirred for an additional 2–10 hr (no significant change after 2 hr). The excess phosphite was removed at 30° (1 mm), and the residue was submitted to short-path distillation. The phospholene was collected at 115–118° (0.2 mm, bath at 140°); yield, 50 g (92%); $n^{25}D$ 1.5283. Redistillation gave bp 117–119° (0.2 mm), $n^{25}D$ 1.5286.

Anal. Calcd for $C_{12}H_{17}O_5P$: C, 52.9; H, 6.3; P, 11.4. Found: C, 53.1; H, 6.3; P, 10.6.

The H^1 nmr spectrum (in CCl_4) had five aromatic protons at τ 2.7; a nine-proton doublet, J_{HP} = 13.0 cps, at τ 6.42 (CH_3O); and a three-proton singlet at τ 7.92 (CH_3 on unsaturated carbon); $\delta(P^{31})$ = +49.5 ppm (CH_2Cl_2). The infrared spectrum (CCl_4) had a *weak band* at 5.95 μ (weaker than the C–H band at 3.42 μ) and bands at 6.23 (vw), 6.70 (vw), 6.85 (vw), 6.95 (vw), 7.25 (vw), 7.80 (m), 8.40 (w), 9.20 (vs), and 9.35 (vs) μ.

Reaction of the 1-Phenylpropanedione–Trimethyl Phosphite 1:1 Adduct (XIII) with Biacetyl. Preparation of *cis*- and *trans*-2,2,2-Trimethoxy-4,5-diacetyl-4-methyl-5-phenyl-1,3,2-dioxaphospholane (XIVa and XIVb) and of *cis*- and *trans*-2,2,2-Trimethoxy-4-acetyl-5-benzoyl-4,5-dimethyl-1,3,2-dioxaphospholane (XVa and XVb).—A mixture of phospholene (XIII) (15.7 g. 57.6 mmoles) and biacetyl (15 g. 175 mmoles) was stirred at 20° under N_2. The infrared spectra of aliquots were examined at intervals; no further changes occurred after 30 days. Volatile material was removed at 40° (20 and 1 mm). The infrared spectrum of the residue, in CCl_4, had a very strong band at 5.82 μ, attributed to the acetyl groups of both structural isomers, XIV and XV, and a weak band at 5.93 μ *attributed to the single benzoyl group of the minor structural isomer, XV.* The H^1 nmr spectrum (CCl_4) showed the signals listed in Table I. The assignments were made with the aid of the spectrum of the *cis*- and *trans*-4,5-diacetyl-4-methyl-5-phenyldioxaphospholane previously made. The assignments of the signals due to the *trans* form of the minor structural isomer XVb are uncertain (Table I). The structural isomers were formed in *approximately* 65:35 proportion.

The crude mixture was dissolved in hexane (20 ml) and benzene (5 ml). Crystals appeared after several days at 10° (8.3 g, 40%, mp 91–93°). The crystals had one type of P^{31} nucleus, $\delta(P^{31})$ = +54.7 ppm (CCl_4); they gave the H^1 nmr spectrum previously found for the 4,5-diacetylphospholane XIVa. The solvent was removed from the filtrate. The glassy residue showed at least three P^{31} nuclei in the nmr spectrum at 40.5 Mcps (see Table I for shifts). The H^1 nmr spectrum had the expected signals with the expected relative intensities (Table I). The infrared spectrum had a band at 5.92 μ (benzoyl) only slightly weaker than the band at 5.82 μ (acetyl). This mixture of isomers was submitted to hydrolysis.

Hydrolysis of the Mixture of Products from the Reaction of XIII with Biacetyl. Preparation of *erythro*-3-Methyl-4-phenylhexane-3,4-diol-2,5-dione (XVIa) and of *erythro*-3,4-Dimethyl-5-phenylpentane-3,4-diol-2,5-dione (XVIIa).—The material used was the mixture of structural and diastereomers (XIVa, XIVb, and XVa, XVb) previously described. This (5 g) was dissolved in benzene (15 ml) and treated with 10 mole equiv of water (3 ml). After 6 hr at reflux,[13a] the benzene layer was evaporated, giving 2 g of crude diketols. The infrared spectrum (CCl_4) had bands at 3.0 (OH), 5.90 (strong, hydrogen-bonded acetyl), and 6.0 μ (slightly weaker hydrogen-bonded benzoyl); no phosphorus was present. The H^1 nmr spectrum (CCl_4) had the signals due to *two diastereomers* of one structure (XVIa and XVIb) and one diastereomer of the second structure (XVIIa) with the expected intensities (Table II). The signals of the second diastereomer could not be assigned.

Reaction of XIII with Phenylglyoxal (IV). Preparation of *cis*- and *trans*-2,2,2-Trimethoxy-4-acetyl-5-benzoyl-4-phenyl-1,-3,2-dioxaphospholane (XIXa and XIXb).—The phospholene XIII (4.4 g, 16 mmoles) and the ketoaldehyde IV (2.2 g, 16 mmoles) were dissolved in methylene chloride (16 ml) at 20°, under N_2. The infrared and the H^1 nmr spectra of aliquots were examined after 1, 18, 42, and 54 hr. Two H^1 nmr signals began to appear at τ 7.75 and 8.25 in a 40:60 proportion. Reaction had proceeded to about 70% of completion in 54 hr. In addition to the signals listed in Table I, the H^1 nmr spectrum (CCl_4) of the crude mixture showed signals at τ 2.10 and 2.75 (aromatic protons). The ring proton of the major (XIXa) and the minor (XIXb) isomers each showed a doublet at τ 4.92, J_{HP} = 21 cps, and at τ 4.56, J_{HP} = 24 cps. The two nine-proton doublets, J_{HP} = 12.8 cps, due to the CH_3O- groups attached to the P, were centered at τ 6.63 (major, XIXa) and 6.57 (minor, XIXb). The infrared spectrum (CCl_4) had bands at 5.82 (acetyl) and 5.92 μ (benzoyl).

Attempted Reaction of XIII with 1-Phenylpropanedione.—The reagents were kept at 20° in CH_2Cl_2 solution in a 1:1 mole ratio. The H^1 nmr spectrum after 4 months showed little evidence of formation of the expected dioxaphospholanes. No appreciable reaction was noted after 20 days when the reagents were kept at 20° in a 1:3 mole ratio.

Polymethyleneketene Dimers and Trimers

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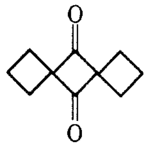
Received August 31, 1965

Polymethyleneketene dimers were converted by a base-catalyzed process to polymethyleneketene trimers. This conversion involves the formation of 1,3,5-cyclohexanetriones from 1,3-cyclobutanediones. The dimers, dispiro[3.1.3.1]decane-5,10-dione (I), dispiro[4.1.4.1]dodecane-6,12-dione (II), and dispiro[5.1.5.1]tetradecane-7,14-dione (III), were converted to the corresponding trimers, trispiro[3.1.3.1.3.1]pentadecane-5,10,15-trione (IV), trispiro[4.1.4.1.4.1]octadecane-6,12,18-trione (V), and trispiro[5.1.5.1.5.1]heneicosane-7,14,21-trione (VI). These diones and triones were completely reduced to diols and triols, respectively. Dodecahydrotriphenylene (XX) was obtained by the dehydration of trispiro[4.1.4.1.4.1]octadecane-6,12,18-triol (XVIII). Alcoholysis of the dimers and trimers gave the corresponding esters (IX–XIV). Alkaline hydrolysis of IV resulted in cleavage followed by decarboxylation to the β-diketone VII. The formation of unsaturated δ-lactone trimers, isomeric with the normal trimers, has been discussed.

In a recent investigation[3] it was shown that dimethylketene and its dimer, tetramethyl-1,3-cyclobutanedione, were converted by a base-catalyzed process to the trimer, hexamethyl-1,3,5-cyclohexanetrione. We now report the conversion of several polymethyleneketene dimers to polymethyleneketene trimers, and some of their reactions. No polymethyleneketene monomers, with the exception of pentamethyleneketene, have been reported, and only two polymethyleneketene dimers, tetramethyleneketene dimer (II) and pentamethyleneketene dimer (III), have been described in the literature, whereas the polymethyleneketene trimers are apparently unknown.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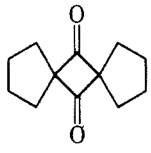
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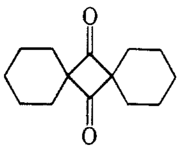
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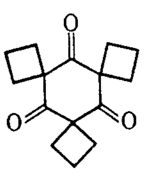
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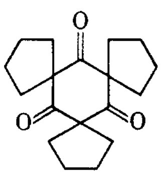
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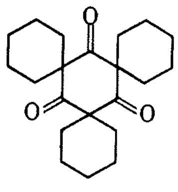
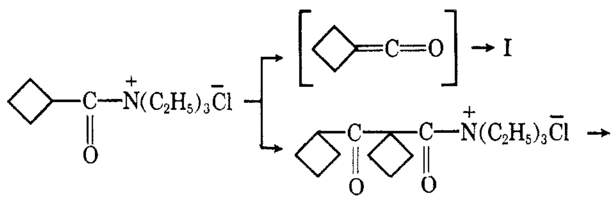

VI

The polymethyleneketene dimers were prepared by a well-known reaction—the dehydrohalogenation of cycloalkanecarbonyl chlorides with triethylamine. In some cases the initial step in the reaction between the acyl halide and a tertiary amine is evidenced by the formation of an insoluble acyl quaternary ammonium halide. Such salts have been obtained by Minunni,[4] Adkins and Thompson,[5] Doering and McEwen,[6] and Baumgarten,[7] from various acyl halides and bases. Walborsky[8] treated cyclopropanecarbonyl chloride with triethylamine and obtained a solid product which was designated as an acyl quaternary ammonium salt, and which acylated aniline to give cyclopropanecarboxanilide. The failure of this salt to yield dimethyleneketene was attributed to I strain. In view of such evidence, it appears that an acyl quaternary ammonium salt is the initial product resulting from the reaction of an acyl halide with a tertiary amine.

The dimer of trimethyleneketene, dispiro[3.1.3.1]decane-5,10-dione (I), was first prepared by Walborsky.[9] We have studied this reaction in greater



detail, and have determined the products obtained under different reaction conditions. This dimer was prepared in 70% yield from the reaction of cyclobutanecarbonyl chloride and triethylamine at 50°. When the reaction was carried out below room temperature, a precipitate was formed, presumably cyclobutanecarbonyltriethylammonium chloride. This high-melting salt, a powerful acylating agent, reacted

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