# Reactions Of Alpha-haloketones And Cyclopentadienones With Tricovalent Phosphorus Compounds.

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# REACTIONS OF ALPHA-HALOKETONES AND CYCLOPENTADIENONES WITH TRICOVALENT PHOSPHORUS COMPOUNDS

by

Morris Anschel

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1967

This dissertation is respectfully submitted to the Graduate Faculty of Lehigh University, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

Morris Anschel

# CERTIFICATE OF APPROVAL

Approved and recommended for acceptance as a dissertation in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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Date

Professor in Charge

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# ABSTRACT

## Part I

The reactions of certain phenacyl halides and α-halocyclohexanones with triethyl phosphite do not proceed by initial attack of phosphorus on halogen. No meaningful dehalogenation is observed in the presence of prototropic reagents. Instead, evidence is found which strongly suggests that the Perkow reaction most likely involves an initial rate-determining attack of triethyl phosphite on carbonyl carbon followed by a rearrangement to oxygen to form enol phosphates.

It is postulated that in the Arbusov reaction the formation of ketophosphonates occurs via $SN_2$ displacement of halide ion. Thus, it is found that the ratio of ketophosphonate to enol phosphate decreases with increasing substitution at the carbon-halogen bond.

Competition experiments between bromo- and chlorocyclohexanone indicate that the rate-determining step in enol phosphate formation cannot involve the loss of halide ion. Phenacyl bromides give enol phosphates to the exclusion of ketophosphonates in reaction with triethyl phosphite in the presence of acetic acid.

The possible mechanistic pathways for the acetic acid reactions are presented and their relationship to the Perkow reaction is discussed.

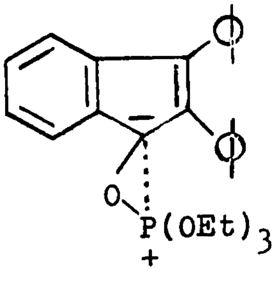
## Part II

The reactions of tertiary phosphites and phosphines with cyclopentadienone systems, i.e. substituted fluorenones, 2,3-diphenyl-1-indenone and tetracyclone, are discussed.

Triethyl phosphite reacts with fluorenones to give 9-diphenylenephenanthrones and small amounts of di-phenyleneethene. Chemical evidence is presented which indicates that the transformation of substituted fluorenones to 9-diphenylenephenanthrones proceeds via isolable cyclic oxyphosphorane intermediates.

The infrared, $P^{31}$ n.m.r. and $H^1$ n.m.r. spectra suggest that the 2:1 adducts have a structure in which the five oxygen atoms are covalently bound to phosphorus.

The reaction of triethyl phosphite with 2,3-diphenyl-1-indenone gave in small amounts a compound whose structure is postulated to be the novel phenyl substituted cyclopentadienate phosphonium zwitterion as shown below. Analytical and infrared data are presented as supporting evidence for this structure.



Tributylphosphine reacts with substituted fluorenones to give high yields of the corresponding fulvalenes. Tetracyclone reacts with tributylphosphine to yield 1,1'-dihydro-

2,3,4,5,2',3',4',5'-octaphenylfulvalene, the structure of which is supported by analytical, chemical, infrared, $H^1$ n.m.r., ultra-violet, and mass spectral data.

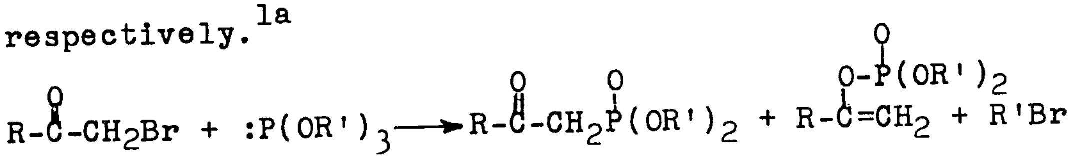
The utility and possible course of the reactions shown are discussed from a mechanistic point of view.

# INTRODUCTION I

Among the many known nucleophiles, those that are derived from trivalent phosphorus are among the most interesting in that they can undergo several possible modes of reaction. Therefore, it is only natural that the reactions of α-haloketones and other activated carbonyl compounds with various phosphorus nucleophiles is of current interest.

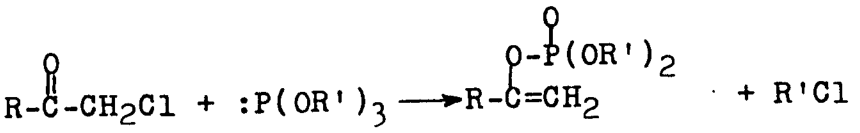
In an excellent review by Lichtenthaler[1b] it was clearly demonstrated that the product composition obtained from the reaction of α-haloketones and trialkyl phosphites depends upon the nature of the nucleophile, the structure of the α-haloketone and the reaction conditions.

The reactions of α-haloketones with trialkyl phosphites lead to the formation of ketophosphonates (I) and enol (vinyl) phosphates (II); the Michaelis-Arbusov and Perkow reactions, respectively.[1a]



$$R-\overset{O}{\overset{\|}{C}}-CH_2Br + :P(OR')_3 \longrightarrow R-\overset{O}{\overset{\|}{C}}-CH_2\overset{O}{\overset{|}{P}}(OR')_2 + R-\overset{O-\overset{O}{\overset{|}{P}}(OR')_2}{\overset{|}{C}}=CH_2 + R'Br \quad (1)$$

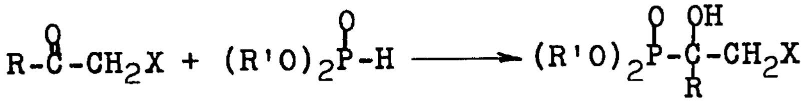
(I) (II)



$$R-\overset{O}{\overset{\|}{C}}-CH_2Cl + :P(OR')_3 \longrightarrow R-\overset{O-\overset{O}{\overset{|}{P}}(OR')_2}{\overset{|}{C}}=CH_2 + R'Cl \quad (2)$$

(II)

Dialkyl hydrogenphosphonates are claimed to react *via* attack on the carbonyl carbon to give α-hydroxy and epoxy phosphonate esters, (III) and (IV),[2,3] respectively, which is in agreement with the mode of attack of other known nucleophiles (e.g., $^-OH$, $^-OR$, $RNH_2$).[4]



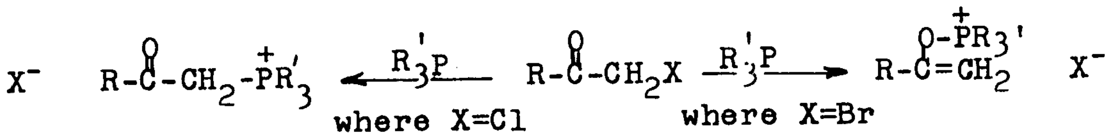
$$R-\overset{O}{\overset{\|}{C}}-CH_2X + (R'O)_2\overset{O}{\overset{\|}{P}}-H \longrightarrow (R'O)_2\overset{O}{\overset{\|}{P}}-\underset{R}{\overset{OH}{C}}-CH_2X \qquad (3)$$

(III)

(4)

(IV)

Tertiary phosphines give products similar in structure to those derived from the tertiary phosphites (e.g., structures V and VI).[5,6] Consequently, many workers[7,8] have assumed for a long time that phosphines and phosphites react with α-haloketones via similar reaction mechanisms.



$$X^- \quad R-\overset{O}{\overset{\|}{C}}-CH_2-\overset{+}{P}R'_3 \xleftarrow[\text{where X=Cl}]{R'_3P} R-\overset{O}{\overset{\|}{C}}-CH_2X \xrightarrow[\text{where X=Br}]{R'_3P} R-\overset{O-\overset{+}{P}R_3'}{C}=CH_2 \quad X^- \qquad (5)$$

(V) (VI)

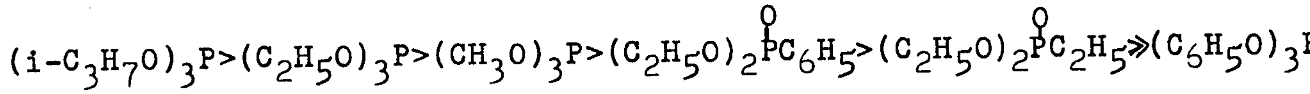
Allen and Johnson[9] found that triaryl phosphites fail to undergo reaction with chloral while monoalkyl diarylphosphonates readily give enol phosphates. It was postulated that the nucleophile must contain at least one alkoxy group to facilitate the elimination of the halide ion.

As is expected phosphites are more reactive towards aldehydes than towards ketones to give enol (vinyl) phosphates II. α-Haloesters are unreactive, while halomalonic[10] and trichloroacetic[11] acid derivatives give enol (vinyl) phosphates. Electron withdrawing substituents (e.g., halogen and carbonyl groups) located at the α-carbon atom enhance the yield of the Perkow reaction product and decrease the Michaelis-Arbusov product. As indicated by Table I[12] an increase in reaction temperature favors the Michaelis-Arbusov reaction product, i.e., ketophosphonate. The reactivities of the α-haloketones with phosphites were found by Pudovik to be in the usual order of I>Br>Cl.[12]

Table I. Ratios of Enol Phosphate to Ketophosponate Derived from Haloacetones

|  | Chloro-acetone | Yield | Bromo-acetone | Yield | Iodo-acetone | Yield |
|---|---|---|---|---|---|---|
| At ca. 155° | 88:12 | 76% | 21:79 | 60% |  |  |
| Refluxing ether |  |  | 80:20 | 63% | 10:90 | 83% |

Kamai and Kharrasova[13] found that the reactivities of substituted phosphites increased with increasing electron donating power of the substituents, in the order,

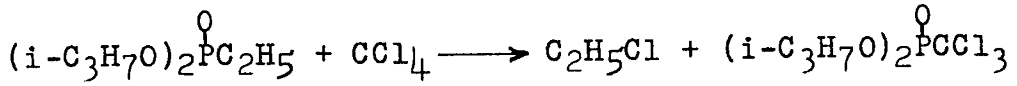


$$(i\text{-}C_3H_7O)_3P > (C_2H_5O)_3P > (CH_3O)_3P > (C_2H_5O)_2\overset{O}{P}C_6H_5 > (C_2H_5O)_2\overset{O}{P}C_2H_5 \gg (C_6H_5O)_3$$

toward carbon tetrachloride,[14,15] giving dialkyl trichloromethylphosphonates in high yield. The ease with which the alkyl groups are cleaved from the mixed trialkyl phosphites depends on the bulkiness of the leaving alkyl group; the smaller group being preferentially cleaved, viz.

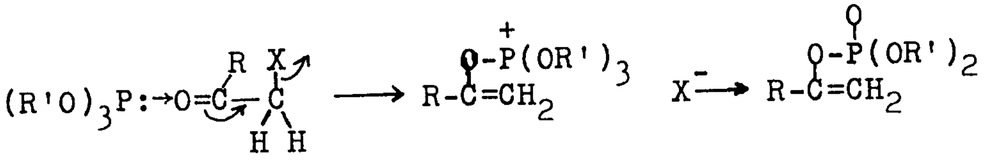
$$CH_3 > C_2H_5 > i\text{-}C_3H_7,$$

as would be anticipated for an $SN_2$ attack by halide ion.[16]

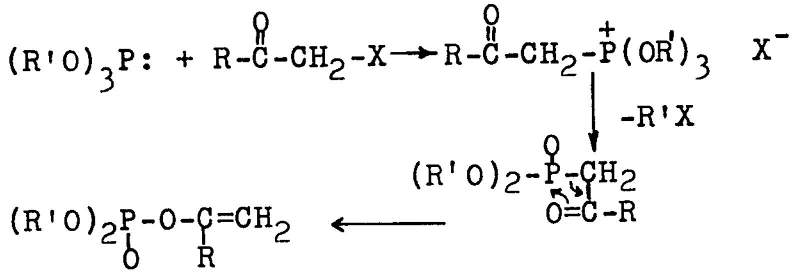


$$(i\text{-}C_3H_7O)_2\overset{O}{P}C_2H_5 + CCl_4 \longrightarrow C_2H_5Cl + (i\text{-}C_3H_7O)_2\overset{O}{P}CCl_3 \qquad (6)$$

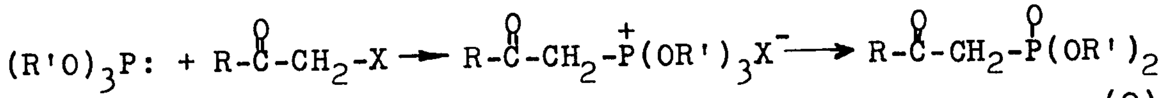
Various mechanistic pathways have been postulated for reactions of trialkyl phosphites with α-haloketones[1b] including initial attack on carbonyl oxygen by the phosphite[17-21] (eqn. 7), initial attack at the α-carbon atom with subsequent rearrangement[22-25] (eqn. 8,9), nucleophilic attack on halogen[5] (eqn. 10), or initial attack on carbonyl carbon[9,11] with subsequent rearrangement to oxygen (eqn. 11).



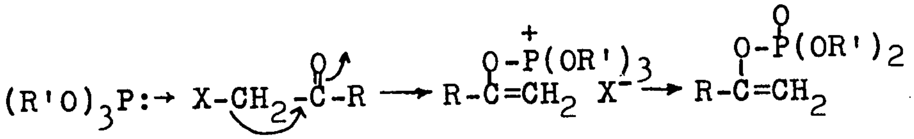
$$(R'O)_3P{:}\rightarrow O{=}C(R)-CH_2X \longrightarrow R-C(O-\overset{+}{P}(OR')_3){=}CH_2\ X^- \longrightarrow R-C(O-P(O)(OR')_2){=}CH_2 \quad (7)$$



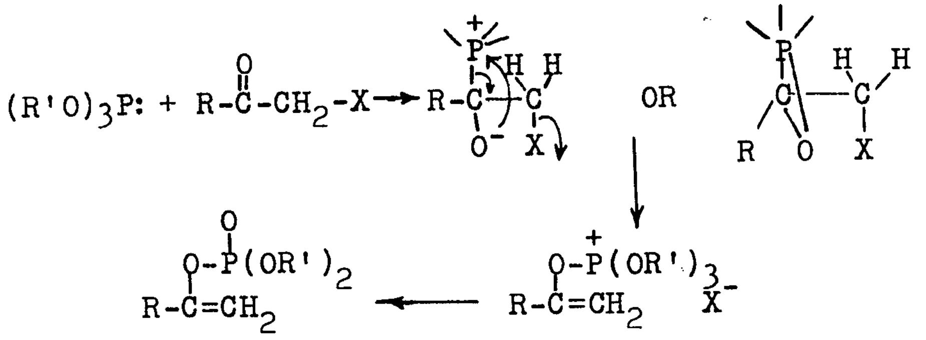
$$(R'O)_3P{:} + R-C(O)-CH_2-X \longrightarrow R-C(O)-CH_2-\overset{+}{P}(OR')_3\ X^- \xrightarrow{-R'X} (R'O)_2-P(O)-CH_2-C(O)-R \longrightarrow (R'O)_2P(O)-O-C(R){=}CH_2 \quad (8)$$



$$(R'O)_3P{:} + R-C(O)-CH_2-X \longrightarrow R-C(O)-CH_2-\overset{+}{P}(OR')_3X^- \longrightarrow R-C(O)-CH_2-P(O)(OR')_2 \quad (9)$$

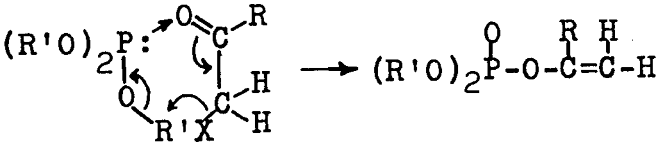


$$(R'O)_3P{:}\rightarrow X-CH_2-C(O)-R \longrightarrow R-C(O-\overset{+}{P}(OR')_3){=}CH_2\ X^- \longrightarrow R-C(O-P(O)(OR')_2){=}CH_2 \quad (10)$$



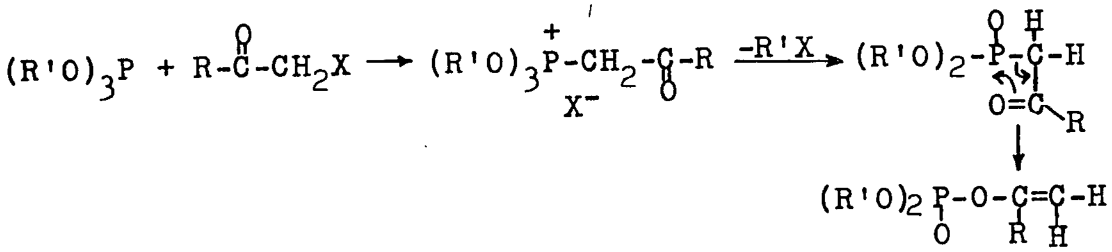
(11)

Pudovik[20,21] proposed that the Perkow reaction was likely to proceed *via* a concerted cyclic mechanism; the initial attack by the nucleophilic phosphorus being on the carbonyl oxygen, *viz.*

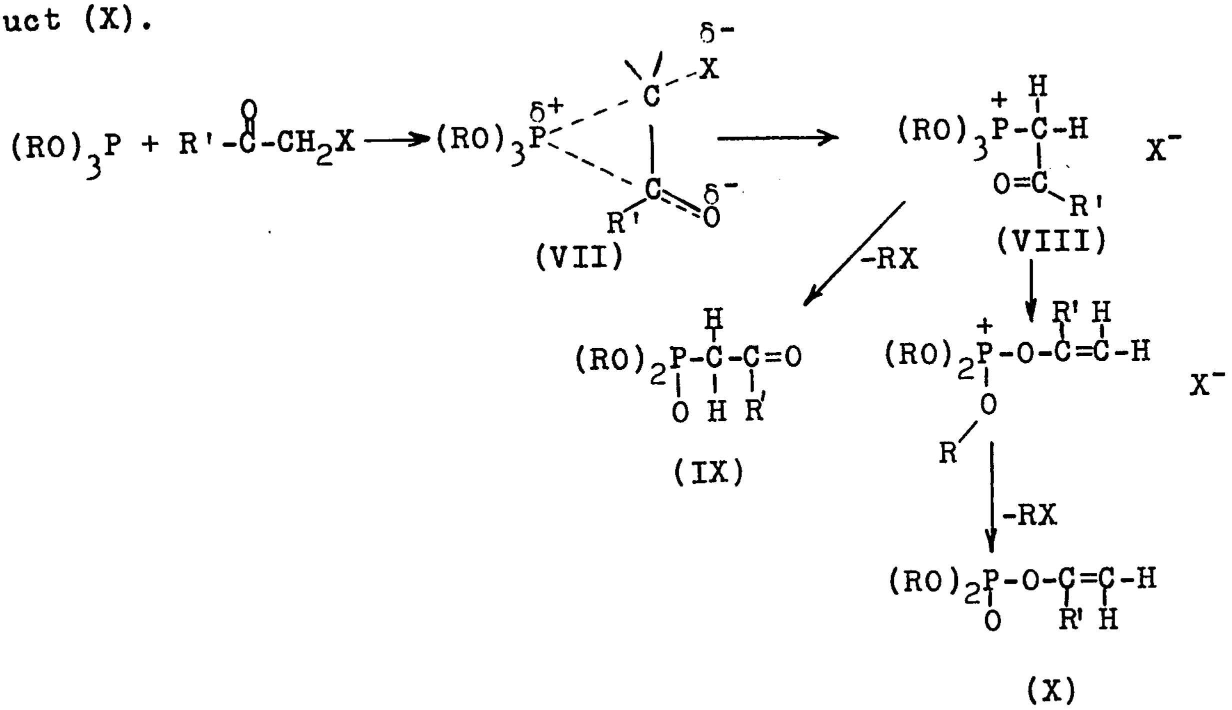

(12)

Direct attack on oxygen was further advocated by Trippett[17,18] and others,[19] although the only support advanced for this mechanism was that it offered the advantage of being the simplest route to enol phosphate formation.

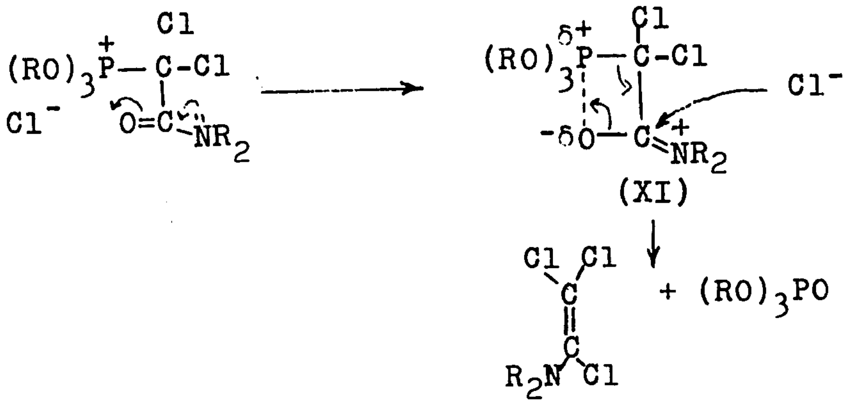
The attack at the α-carbon atom was originally proposed by Perkow,[22,23] modified by Spencer, Todd and Webb[24] and further developed by Cramer.[25] The Spencer-Todd-Webb mechanism postulates that the ketophosphonate-enol phosphate rearrangement is formed by way of an initial Michaelis-Arbusov reaction:


(13)

Cramer envisioned the mechanism as involving an initial attack by the nucleophilic phosphorus on the α-carbon by way of transition state (VII) to give a phosphonium salt intermediate (VIII). This latter intermediate loses alkyl halide directly to form the alkylated product (Michaelis-Arbusov reaction product, IX). VIII can also undergo a ketophosphonate-enol phosphate rearrangement to yield the Perkow reaction product (X).



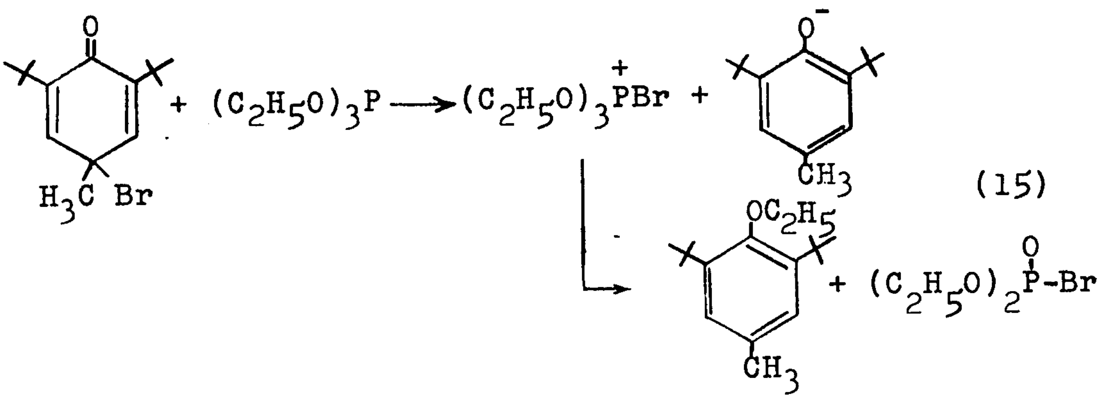
Precedence for this type of rearrangement is deduced from its comparability with the Wittig reaction.[26,27] Furthermore, this mechanism is in agreement with the favored Michaelis-Arbusov reaction order of I>Br>Cl. The increase of the nucleophilic reactivity of the halogen will favor direct elimination of alkyl halide to give the alkylated product (VIII→IX). The reactions of trichloroacetamides with trialkyl phosphites (eqn. 14) are explained by the Wittig reaction (XI). The electron donating power of the amino group enhances nucleophilic attack of chloride ion on the carbonyl carbon atom to yield trichlorovinylamines.



(14)

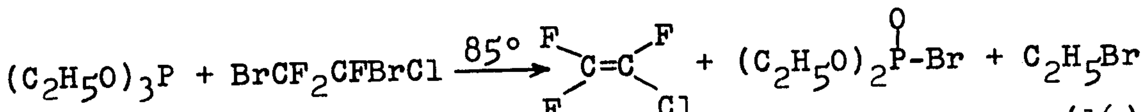
By anology with phosphines the mechanism of the reaction of α-haloketones with phosphites was first proposed by Speziale and Smith[7] to proceed by way of attack on the halogen atom. Many workers, at one time or another, favored attack on halogen on the basis of the conclusive evidence available on the reactions of trivalent phosphines with halogen carbon bonds. It is noteworthy that the topic of attack on halogen by phosphines is well documented and has been reviewed by B. Miller.[28] Examples of nucleophilic attack by phosphites on positive halogen are also well known:

1. Reaction of sterically hindered 4-bromocyclohexadienones[8,29,30] (vinylogs of α-bromoketones), <u>viz</u>.



(15)

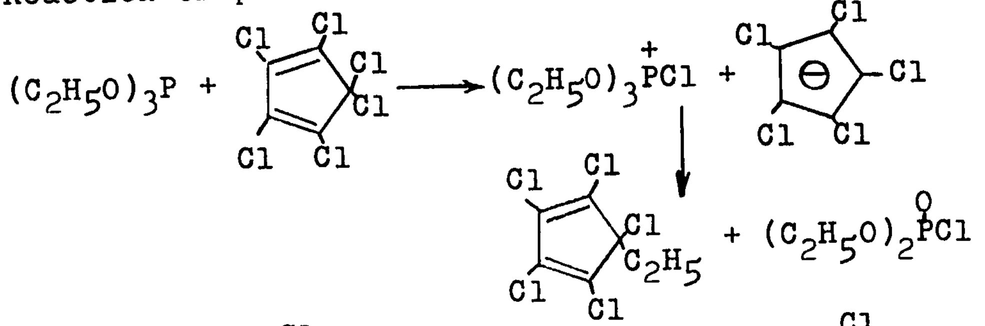
2. Preparation of phosphorohalidates,[31,32] viz.



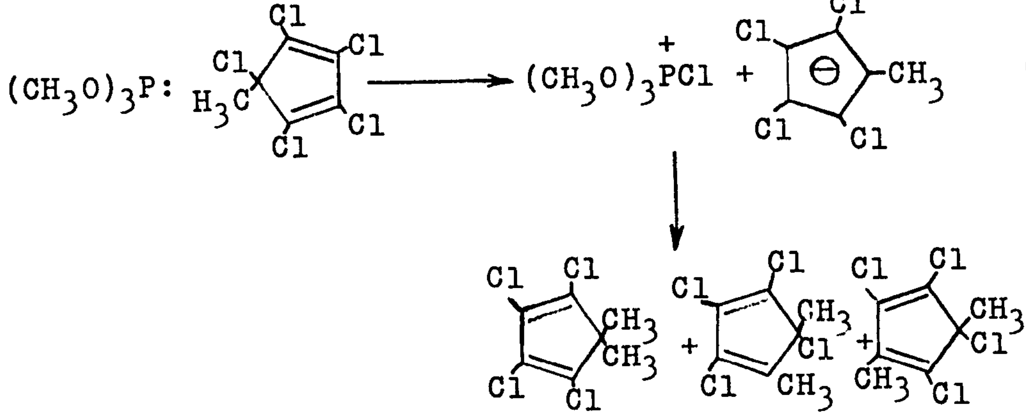
$$(C_2H_5O)_3P + BrCF_2CFBrCl \xrightarrow{85°} F_2C{=}CFCl + (C_2H_5O)_2\overset{O}{P}\text{-}Br + C_2H_5Br$$

(16)

3. Reaction of penta- and hexachlorocyclopentadiene,[33] viz.

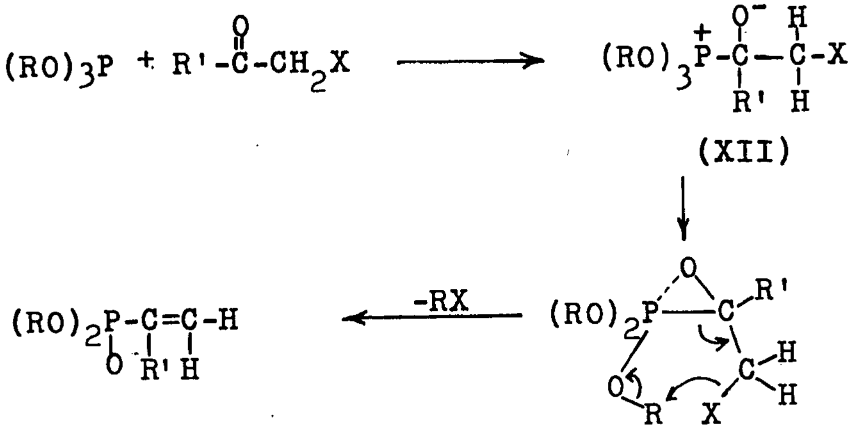


(17)



(18)

As shown previously the carbon of the carbonyl group has been reported as the site of attack at which dialkyl hydrogenphosphonates and their anions react to give α-hydroxyphosphonates and epoxy-phosphonates, respectively.[2,3] By analogy Allen and Johnson[9] and Kharasch and Bengelsdorff[11] have proposed that trialkyl phosphites react to give adduct (XII) in a similar manner.

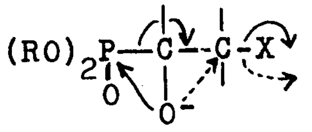


(XII)

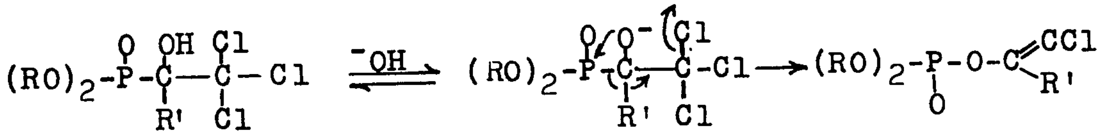
(XIII)

(19)

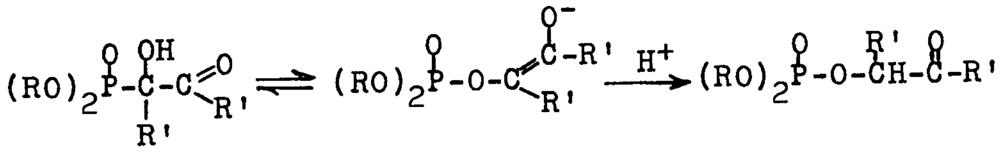
This mechanism has several analogies (eqn. 20,21) wherein a similar intermediate is the precursor of the vinyl phosphate (XIV) or the epoxy-alkylphosphonate (XIV, dotted arrows),[34-36] viz.



(XIV)

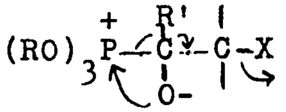


(20)



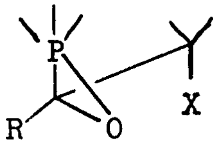
(21)

The lack of formation of epoxides in the Perkow reaction is attributed[37] to the highly electrophilic phosphonium cation (XV), which greatly favors Perkow rearrangement rather than reaction at the adjacent saturated carbon atom. The rearrangement may occur via a phosphorane intermediate.



or

(XV)



R. F. Hudson et al.[37] has recently reported highly convincing evidence for the attack on the carbonyl carbon atom. It was found that the reactions of chloro- and bromoacetone with trialkyl phosphites in highly dilute solutions of a prototropic source (e.g., methanol, acetic acid) yielded α-hydroxyphosphonates (see Table II).

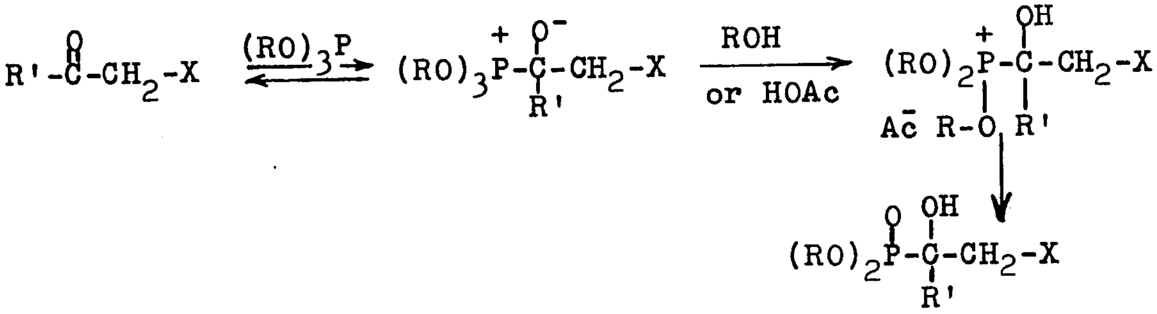
Table II.[37] The Reaction of $CH_3$-CO-$CH_2$X and Trialkyl Phosphites in Hydroxylic Solvents at 25°

| Solvent | Phosphite | Halogen X | Products |
|---|---|---|---|
| Ethanol | $(EtO)_3P$ | Chloride* | 66% A |
| Methanol | $(MeO)_3P$ | Bromide | 65% A<br>55% A; 28% C<br>(at 60°C) |
| Methanol | $(MeO)_3P$ | Chloride | 15% A; 46% B |
| Acetic Acid | $(MeO)_3P$ | Bromide | 30% A; 27% B |

*phenacyl chloride

A=enol phosphate
B=α-hydroxyphosphonate
C=ketophosphonate

Thus evidence for the existence of intermediate (XV) has been substantiated by its interception with hydroxylic solvents, viz.



The synthetic aspects and practical utility of the Perkow and Michaelis-Arbusov reaction products have been thoroughly reviewed by Lichtenthaler[1b] and will not be reported here.

## References

1a. W. Perkow, K. Ullerich and F. Meyer, Naturwiss., 39, 353 (1952).

1b. F. W. Lichtenthaler, Chem. Rev., 61, 607 (1961).

2. V. S. Abramov and A. S. Kapustina, Zh. Obsh. Khim., 27, 1012 (1957); Chem. Abstr. 52, 3667 (1958).

3. A. N. Pudovik and L. G. Biktimirova, Zh. Obsh. Khim., 27, 1708 (1957); Chem. Abstr., 52, 3714 (1958).

4. B. A. Arbuzov, V. S. Vinogradova and N. A. Polezhaeva, Dokl. Akad. Nauk SSSR, 121, 641 (1958); Chem. Abstr., 53, 1180 (1959).

5. H. Hoffmann and H. J. Diehr, Tetrahedron Letters, 583 (1962).

6. I. J. Borowitz and R. Virkhaus, J. Am. Chem. Soc., 85, 2183 (1963).

7. A. J. Speziale and L. R. Smith, J. Am. Chem. Soc., 84, 1868 (1962).

8. B. Miller, J. Org. Chem., 28, 345 (1963).

9. J. F. Allen and O. H. Johnson, J. Am. Chem. Soc., 77, 2871 (1955).

10. F. Cramer and K. G. Gärtner, Chem. Ber., 91, 704 (1959).

11. M. S. Kharasch and I. S. Bengelsdorf, J. Org. Chem., 20, 1356 (1955).

12. A. N. Pudovik and V. P. Avery'anova, Zhur. Obsh. Khim., 26, 1426 (1956); Chem. Abstr., 50, 14512 (1956).

13. G. Kamai and F. M. Kharrasova, Izv. Vysskikh Uchebn. Zavedenii, Khim. i Khim. Tekhnol., 4, 229 (1961); Chem. Abstr., 55, 21762 (1961).

14. G. Kamai and L. P. Egorova, Zh. Obsh. Khim., 16, 1521 (1946).

15. G. M. Kosolapoff, J. Am. Chem. Soc., 69, 1002 (1947).

16. G. Kamai and F. M. Kharrasova, Zh. Obsh. Khim., 27, 953 (1957).

17. S. Trippett, J. Chem. Soc., 2337 (1962).

18. S. Trippett, Proc. Chem. Soc., 106 (1962).

19. G. Kamai and V. A. Kukhtin, Dokl. Akad. Nauk. SSSR 112, 868 (1957); Chem. Abstr., 51, 13742 (1957).

20. A. N. Pudovik, Zh. Obsh. Khim, 25, 2173 (1955); Chem. Abstr., 50, 8486 (1956).

21. V. A. Kukhtin and A. N. Pudovik, Uspekhi Khim, 28, 101 (1959); Chem. Abstr., 53, 9025 (1959).

22. W. Perkow, Chem. Ber., 87, 755 (1954).

23. W. Perkow, E. W. Krockow and K. Knoevenagel, ibid., 88, 662 (1955).

24. E. Y. Spencer, A. R. Todd and R. F. Webb, J. Chem. Soc., 2968 (1958).

25. F. Cramer, Angew. Chem., 72, 236 (1960).

26. U. Schöllkopf, Angew. Chem., 71, 260 (1959).

27. G. Wittig, Angew. Chem., 68, 505 (1956).

28. B. Miller, "Topics in Phosphorus Chemistry," Vol. 2, M. Grayson and E. J. Griffiths, Ed., John Wiley and Sons Inc., New York, N. Y. 1965, pp. 133-199.

29. B. Miller, J. Org. Chem., 26, 4781 (1961).

30. B. Miller, Tetrahedron Letters, 47, 3527 (1964).

31. G. Kamai, Izv. Akod. Nauk SSSR Otd. Khim. Nauk, 923 (1952).

32. H. R. Davis, U. S. Pat. 2,742,510 (1957).

33. V. Mark, Tetrahedron Letters No. 9, 295 (1961).

34. W. F. Barthel, B. H. Alexander, P. A. Giaug, S. A. Hall, J. Am. Chem. Soc., 77, 2424 (1955).

35. R. Muhlmann and G. Schrader, Z. Naturforsch, 12b, 196 (1957).

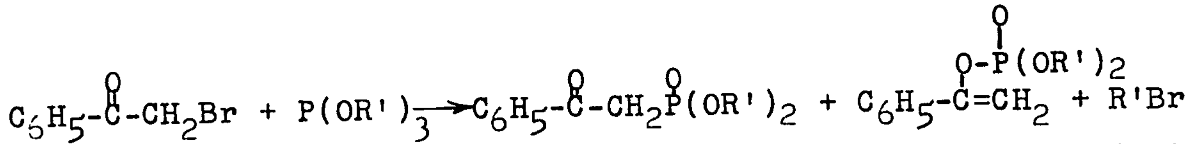
36. V. A. Kukhtin, V. S. Abramov and K. M. Orekhova, Dokl. Akad. Nauk SSSR 128, 1198 (1959); Chem. Abstr., 54, 7536 (1960).

37. P. A. Chopard, V. M. Clark, R. F. Hudson, and A. J. Kirby, Tetrahedron, 21, 1961 (1965).

## RESULTS AND DISCUSSION I

In order to better understand the possible mode of nucleophilic displacement reactions which phosphites undergo, it was decided to study the reactions of phenacyl halides with tertiary phosphites under a variety of reaction conditions. It is readily recognized that α-haloketones contain a number of sites which are available for nucleophilic attack by trialkyl phosphites to give a variety of products. The objective of this work is the elucidation of the actual pathway(s) used by several α-haloketones in reaction with phosphites.

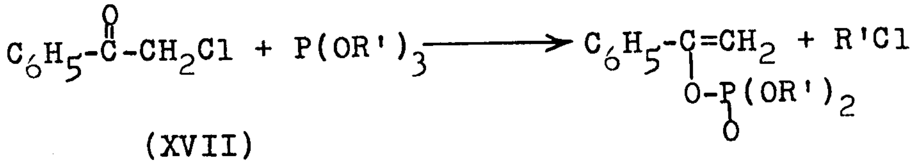
α-Haloketones are known to react (eqn. 23, 24) with trialkyl phosphites to give ketophosphonates (I) and enol phosphates (II) according to the Michaelis-Arbusov and Perkow reactions, respectively.[1]



$$C_6H_5\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_2Br + P(OR')_3 \rightarrow C_6H_5\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_2\overset{O}{\overset{\|}{P}}(OR')_2 + C_6H_5\text{-}\overset{O\text{-}\overset{O}{\overset{\|}{P}}(OR')_2}{\overset{|}{C}}{=}CH_2 + R'Br \qquad (23)$$

(XVI) Ia $R'=C_2H_5$ IIa $R'=C_2H_5$

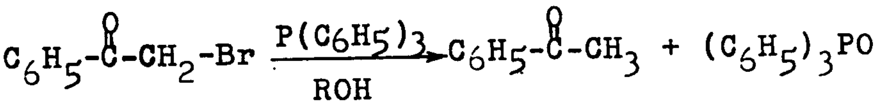
Ib $R'=CH_3$ IIb $R'=CH_3$



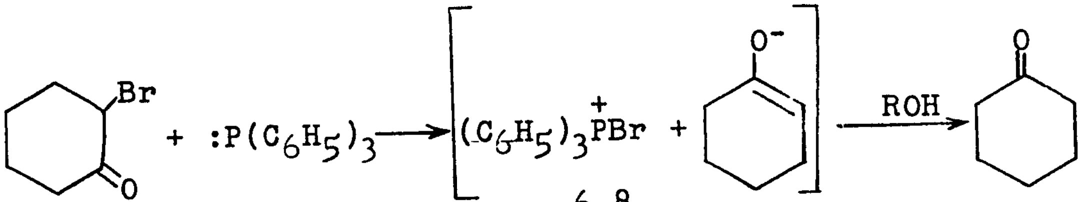
$$C_6H_5\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_2Cl + P(OR')_3 \longrightarrow C_6H_5\text{-}\underset{O\text{-}\underset{O}{\underset{\|}{P}}(OR')_2}{\underset{|}{C}}{=}CH_2 + R'Cl \qquad (24)$$

(XVII)

Work in this laboratory by Borowitz _et al._, has clearly demonstrated that tertiary phosphines react with α-haloketones _via_ direct initial attack at halogen by the phosphorus of the phosphine. Thus, phenacyl bromide, α-bromocyclohexanone and numerous other α-haloketones were found to give high yields of dehalogenated ketones in the presence of hydroxylic proton sources[2-8] (eqn. 25, 26).



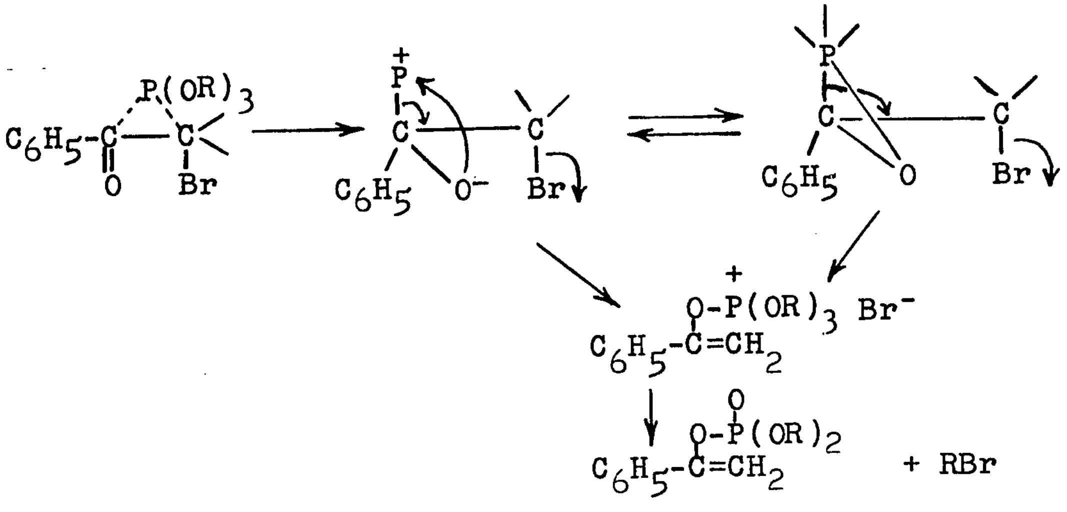
$$C_6H_5-\overset{O}{\overset{\|}{C}}-CH_2-Br \xrightarrow[ROH]{P(C_6H_5)_3} C_6H_5-\overset{O}{\overset{\|}{C}}-CH_3 + (C_6H_5)_3PO \qquad (25)$$



(26)

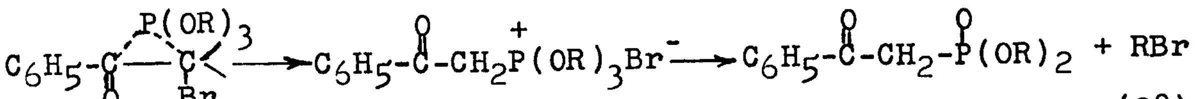
It was clearly demonstrated[6-8] that the reactive intermediate enolate anion formed is readily intercepted by the methanol, acetic acid and other proton sources.

In our work evidence is presented which indicates that attack on the halogen atom by the phosphorus of the phosphite does not take place. Instead, initial attack at the carbonyl carbon followed by rearrangement to carbonyl oxygen is proposed for enol phosphate formation as shown in eqn. 27.



(27)

In a competing process ketophosphonate formation is postulated to occur <u>via</u> an $SN_2$ displacement reaction, <u>viz</u>.



(28)

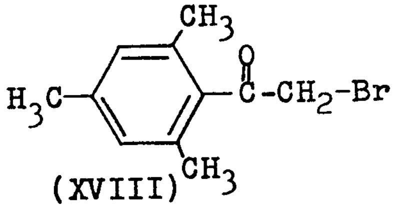
Evidence for the proposed $SN_2$ displacement of halide ion to give ketophosphonate is found by increasing the substitution at the carbon-bromine bond of the α-haloketone (Table III).

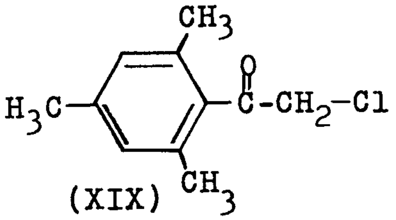
Table III. Ratios of Ketophosphonate/Enol Phosphate Obtained from Reaction of Phenacyl Halides with Triethyl Phosphite

| Haloketone | Ketophosphonate/ Enol Phosphate | % Yield |
|---|---|---|
| Bromoacetophenone (XVI) | 2.8/1 | 88 |
| Bromopropiophenone[11] | 1/4 | 87 |
| Desyl bromide[11] | 0/100 | 68 |
| Bromoisobutyrophenone[11] | 0/100 | 84 |

The above table dramatically shows that a decreasing amount of ketophosphonate is formed as one proceeds down the table towards more sterically hindered α-haloketones, which would be expected for an $SN_2$ process. Furthermore, ketophosphonate formation <u>via</u> an $SN_2$ displacement mechanism has the advantage of being the simplest and most direct route for ketophosphonate formation.

In striking opposition to the reactions of bromoketones with triphenylphosphine in the presence of a proton source, triethyl phosphite in reaction with α-bromo or chloroketones in the presence of ethanol, butanol or acetic acid did not give dehalogenation as the principal process (Table V, VII). While α-bromocyclohexanone reacts rapidly with triphenylphosphine, α-chlorocyclohexanone is completely inert. The great disparity in reactivity between chloro- and bromocyclohexanone suggests that triphenylphosphine is unreactive towards the carbonyl group when compared to trialkyl phosphite. This result indicates that the bromine atom is much more electrophilic than is chlorine.[9] Furthermore, Hudson has shown that 2,4,6-trimethylphenacyl bromide (XVIII) reacts rapidly with triphenylphosphine whereas the corresponding phenacyl chloride (XIX) is inert.[10]


(XVIII)


(XIX)

In contrast tertiary phosphites show comparable reactivities with these haloketones. Since in the Perkow reaction good yields of enol phosphates are obtained from both chloro- and bromoketones when they are reacted with phosphites in the presence of hydroxylic solvents (Table VII), it may be safely concluded that the attack on the halogen is an unlikely mechanism. Thus alterations in the nucleophilicity of the phosphorus atom modifies its mode of reaction with α-haloketones.

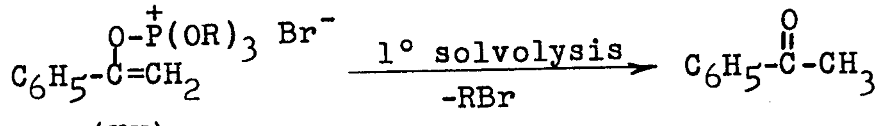
α-Chloroketones in reaction with triethyl phosphite give only enol phosphates. Table IV indicates the yields obtained from these reactions.

Table IV. Reactions of Chloroacetophenones with Triethyl Phosphite

| Chloroketone | Enol Phosphate Yield % |
|---|---|
| Chloroacetophenone (XVII) | 85 |
| Chloropropiophenone[11] | 85 |
| Chloroisobutyrophenone[11] | 62 |

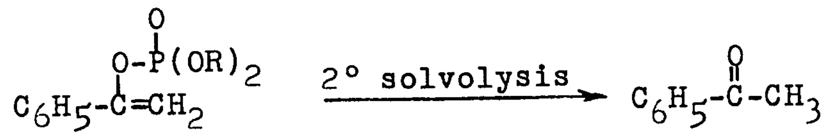
The above results as shown in Table IV indicate that in the chloroketone reactions there is no $SN_2$ displacement of chloride ion to give ketophosphonate but instead the formation of enol phosphate wins out in the competition; thus $SN_2$ displacement of chloride ion is too slow to compete with vinyl phosphate formation.

Reactions in the presence of a prototropic source which led to enol phosphate formation (see Table VII) as the primary product also yielded small to moderate (in the phenacyl bromide case) amounts of dehalogenated ketone. This could arise from primary solvolysis of enol phosphonium salts and secondary solvolysis of enol phosphates as illustrated below.



$$C_6H_5\text{-}\overset{O\text{-}\overset{+}{P}(OR)_3\ Br^-}{\overset{|}{C}}{=}CH_2 \xrightarrow[-RBr]{1^\circ\ \text{solvolysis}} C_6H_5\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_3 \qquad (29)$$

(XX)



$$C_6H_5\text{-}\overset{O\text{-}\overset{O}{\overset{|}{P}}(OR)_2}{\overset{|}{C}}{=}CH_2 \xrightarrow{2^\circ\ \text{solvolysis}} C_6H_5\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_3 \qquad (30)$$

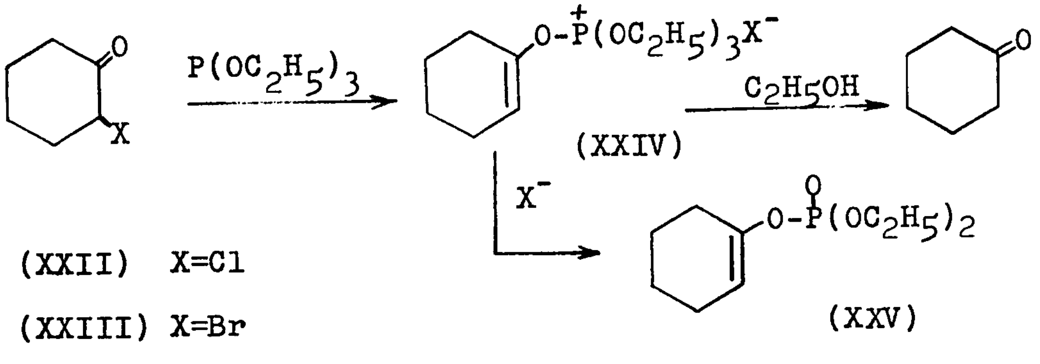
(XXI)

It is noted that the ketone yield gradually increases on storage of the reaction mixture products and on distillation of these reaction mixtures. All reaction mixtures were analyzed by standard vapor phase chromatography and n.m.r. monitoring techniques (for details see Experimental Section).

The reactions of 2-halocyclohexanones with triethyl phosphite in excess ethanol give enol phosphates as the principal product, small to moderate yields of dehalogenated ketone, and no ketophosphonate (Table V).

Evidence is presented in Table V which indicates that attack on the halogen atom of α-halocyclohexanones by the phosphorus of the phosphite does not occur.

The moderate yields (19-33%) of cyclohexanone formation in the reactions conducted at 120° (bath temperature) were dramatically reduced (0-2%) by carrying out the reaction at room-temperature. This temperature phenomena can perhaps be accounted for by the partial solvolysis of the enol phosphate at the higher temperature conditions. Also, the intermediate enol phosphonium salt (XXIV) that is initially formed could possibly more easily give cyclohexanone at the higher temperature and less of the enol phosphate (XXV) than it (XXIV) can allow at the lower temperature.



(31)

(32)

Table V. Reactions of 2-Halocyclohexanones with Triethyl Phosphite

| Haloketone | Reaction Conditions | Keto-phosphonate | Enol Phosphate | Ketone | Unreacted Haloketone |
|---|---|---|---|---|---|
| α-chlorocyclohexanone | 1,3 | 0 | 82 | 20 | |
| α-chlorocyclohexanone | 2,3 | 0 | 52 | 2 | |
| α-bromocyclohexanone | 1,3 | 0 | 49 | 33 | 13 |
| α-bromocyclohexanone | 2,3 | 0 | 73 | 0 | 24 |
| 2-methyl-2-chlorocyclohexanone | Neat, 3 | 0 | 66 | | |
| 2-methyl-2-chlorocyclohexanone | 1,3 | 0 | 40 | 32 | |
| 2-methyl-2-bromocyclohexanone | 1,3 | 0 | 70 | 19 | |

1. Triethyl Phosphite, excess ethanol, 120° (bath temperature) 6 hrs.
2. Triethyl Phosphite, excess ethanol, room temperature.
3. Products by vapor phase chromatography quantitative analysis.

Data on the reactions of aryl-substituted phenacyl bromides with triethyl phosphite is illustrated in the following Table VI.

Table VI. Ratios of Ketophosphonate/Enol Phosphate Obtained from Reaction of Aryl-Substituted Haloacetophenones With Triethyl Phosphite

| Haloketone | Ketophosphonate/Enol Phosphate Ratios |
|---|---|
| p-Methoxy-α-bromoacetophenone (XXVI) | 100/0 |
| Bromoacetophenone (XVI) | 2.8/1 |
| m-Methoxy-α-bromoacetophenone (XXVII) | 2.2/1 |
| p-Nitro-α-bromoacetophenone (XXVIII) | (0.28/1) |

The above Table VI shows that the ketophosphonate to enol phosphate ratio decreases as the electron withdrawing capability of the substituent group is enhanced. As one proceeds down the table, the carbonyl site is increasingly activated for nucleophilic attack by the phosphite at a greater rate than the $SN_2$ displacement of halide anion to give ketophosphonate.[12] Thus, the p-nitro substituent is found to give 3.5 times as much enol phosphate as the corresponding ketophosphonate. On the other hand, in the p-methoxy case where deactivation of the carbonyl site takes place, ketophosphonate (i.e., the $SN_2$ product) formation wins out in the competition over enol phosphate formation. That is, no enol phosphate is formed.

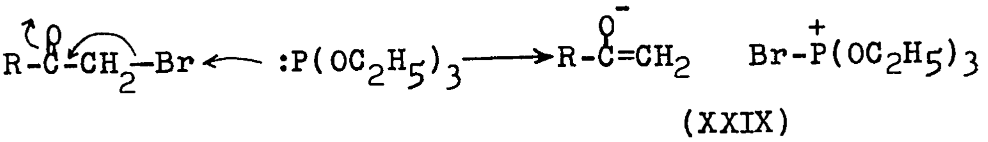
Table VII below summarizes the data obtained from reaction of haloacetophenones with tertiary phosphites.

Table VII. Reactions of Haloacetophenones with Tertiary Phosphites

| Haloketone | Reactions Conditions | Keto-phosphonate | Enol Phosphate | Ketone | Haloketone |
|---|---|---|---|---|---|
| Bromoacetophenone A | 3 (24 hr.), 5, 6 | 65 | 23 | 1 | |
| " " | 4 (20 min.), 8 | 60 | 21 | 0 | 19 |
| " " | 1, 5 | 19 | 16 | 30 | |
| " " | BuOH, 6 hr., 120°, 5 | 42 | 8 | 30 | |
| " " | $(MeO)_3P$-Glyme, 87°, 24 hr., 6 | 52 | 14 | 3 | 0[7] |
| Chloroacetophenone B | 3 (6 hr.), 5 | 0[7] | 85 | 0[7] | |
| " " | 1, 5 | 0 | 69 | 17 | |
| p-MeO-A | 3 (24 hr.), 6 | 60 | 0 | 0 | 7 |
| m-MeO-A | 3 (24 hr.), 8 | 62 | 28 | 0 | 10 |
| p-$NO_2$-A | 4 (24 hr.), 8 | 19 | 68 | 0 | 12.5 |
| p-$NO_2$-A | 2 (23 hr.), 8 | 10 | 71.5 | 3 | 15 |

1. Triethyl phosphite, excess ethanol, 120° (bath temperature) 6 hrs.
2. " " " " , room temperature.
3. " " , in glyme, at reflux.
4. " " , neat, room temperature.
5. Products by v.p.c. analysis.
6. Products by n.m.r. ratios on distillate.
7. Trace present by t.l.c.
8. From n.m.r. ratios on undistilled reaction mixture; ratios, not yields.

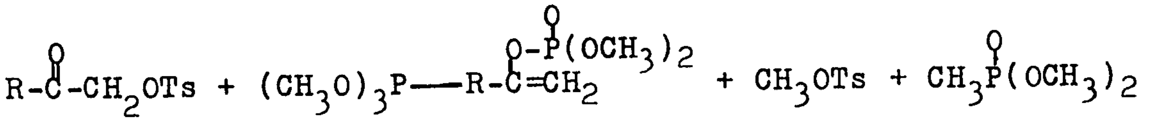
Table VII, which has been previously referred to and analyzed, further indicates that in the p-nitro-α-bromoacetophenone case similar n.m.r. product ratios are obtained whether the reaction is run in the neat or with ethanol present. If attack by phosphite on halogen did occur this case would be most favored because of the resulting resonance stabilization of carbanion (XXIX) which would be formed from the loss of positive bromine.



$$R-\overset{O}{\overset{\|}{C}}-CH_2-Br \longleftarrow :P(OC_2H_5)_3 \longrightarrow \underset{(XXIX)}{R-\overset{O^-}{\overset{|}{C}}=CH_2} \quad Br-\overset{+}{P}(OC_2H_5)_3 \tag{33}$$

$R=p\text{-}NO_2C_6H_5$

Denney and co-workers[13] recently showed that the reactions of α-substituted keto p-toluenesulfonates with tertiary phosphites lead to the formation of vinyl (enol) phosphates, the Perkow reaction product (eqn. 34).



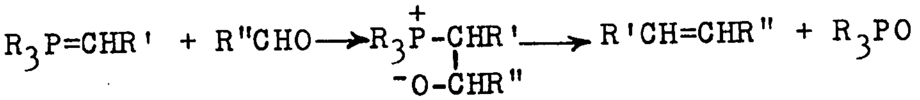
$$R-\overset{O}{\overset{\|}{C}}-CH_2OTs + (CH_3O)_3P \longrightarrow R-\overset{O-\overset{O}{\overset{\|}{P}}(OCH_3)_2}{\overset{|}{C}}=CH_2 + CH_3OTs + CH_3\overset{O}{\overset{\|}{P}}(OCH_3)_2 \tag{34}$$

$R=C_6H_5,\ CH_3$

p-Toluenesulfonate was selected as the leaving group since it behaves similarly to halogen in displacement reactions. Thus far, examples of displacement reactions on the oxygen of the sulfonate group have not been reported; however, nucleophilic displacement on halogen has gained wide acceptance.[14,15] The above dramatically shows that an α-halogen atom is not essential to give enol phosphates in the Perkow reaction.

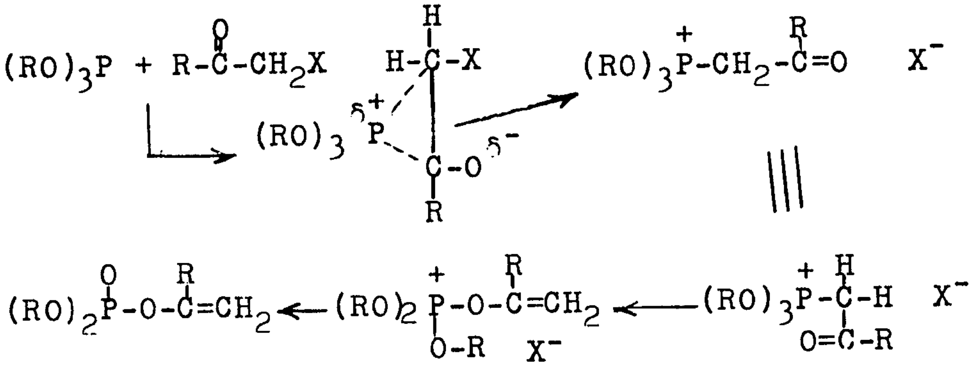
Pudovik[16,17] proposed that the Perkow product formation goes by way of a concerted cyclic mechanism. Such suggested initial nucleophilic attack by the phosphorus atom on the usually nucleophilic carbonyl oxygen atom with subsequent electron shift has the advantage of being the simplest route. The justification of forcing the carbonyl oxygen atom to behave as an electrophile, however, can hardly be attributed to the inductive effect of a lone halogen atom. Moreover, a concerted cyclic mechanism would have to proceed by way of a sterically unfavored seven-membered ring.

The advocates[18,21] for attack at the α-carbon atom have based their support on the rearrangement step being analogous to that occurring in the Wittig reaction.[22,23] The similarity, which on the surface may seem real, is however misleading. The betaine intermediate of the Wittig reaction is not a carbonyl oxygen atom but a nucleophilic negative oxygen atom as illustrated below.



$$R_3P{=}CHR' + R''CHO \longrightarrow \begin{array}{l} R_3\overset{+}{P}\text{-}CHR' \\ \quad {}^{-}O\text{-}CHR'' \end{array} \longrightarrow R'CH{=}CHR'' + R_3PO \qquad (35)$$

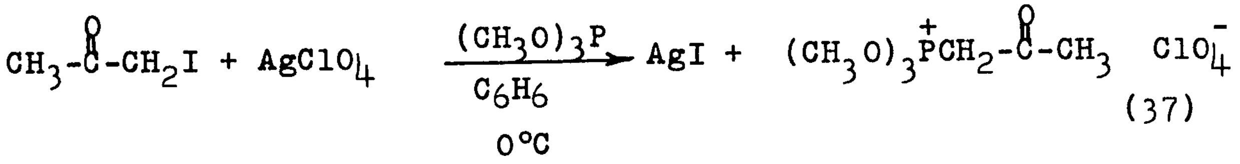
Wittig Betaine
Intermediate



(36)

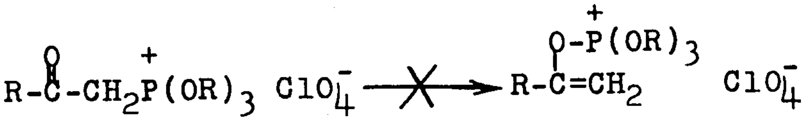
Rearrangement Step

The assumption that the ketophosphonate is a precursor to the vinyl (enol) phosphate is very unlikely, since none of the stable ketophosphonium salts that have been prepared failed to undergo any isomerization.[24-26] Hudson and co-workers[27] have recently synthesized stable ketophosphonium compounds as their perchlorates in benzene solution (eqn. 37).



$$CH_3-\overset{O}{\overset{\|}{C}}-CH_2I + AgClO_4 \xrightarrow[C_6H_6,\ 0^\circ C]{(CH_3O)_3P} AgI + (CH_3O)_3\overset{+}{P}CH_2-\overset{O}{\overset{\|}{C}}-CH_3\ ClO_4^- \qquad (37)$$

These workers then proceeded to demonstrate the absence of "phosphonate-phosphate rearrangement" under the conditions of the Perkow reaction (eqn. 38).



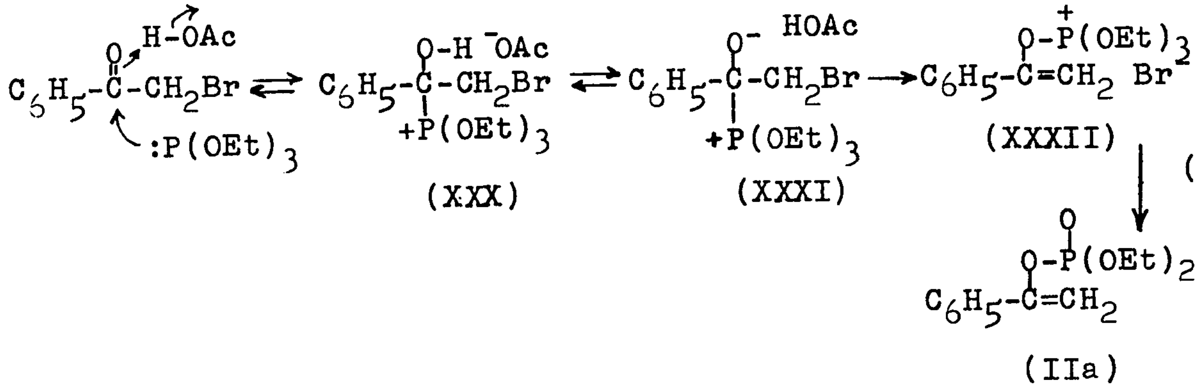
$$R-\overset{O}{\overset{\|}{C}}-CH_2\overset{+}{P}(OR)_3\ ClO_4^- \not\longrightarrow R-\overset{O-\overset{+}{P}(OR)_3}{\overset{|}{C}}=CH_2\ ClO_4^- \qquad (38)$$

Proponents for the initial attack by phosphite at the α-carbon atom must further account for the fact that p-nitrophenacyl bromide (XXVIII) in reaction with triethyl phosphite yielded three times the amount of enol phosphate as did the reaction of phenacyl bromide with triethyl phosphite (Table VII). These results, however, can be explained by initial attack of phosphite at the carbonyl site.

Since trialkyl phosphites in reaction with α-haloketones in the presence of alcohol did not lead to dehalogenation, it was decided to proceed to a stronger proton source such as acetic acid. The Table below indicates the data obtained from the reactions of haloacetophenones with trialkyl phosphites in the presence of acetic acid.

Examination of Table VIII dramatically indicates that α-haloacetophenones in the presence of acetic acid yield enol phosphates with total exclusion of ketophosphonates even in cases where ketophosphonates are usually the major products. For example, p-methoxy-α-bromoacetophenone (XXVI) yields enol phosphate and no ketophosphonate in the presence of acetic acid. In contrast, (XXVI) in the presence of glyme gives ketophosphonate and no enol phosphate. Thus, a general reaction is developed for exclusive enol phosphate formation.

It is postulated that in these reactions attack at the carbonyl carbon of the haloketone is promoted by protonation at oxygen of the carbonyl group (eqn. 39). Attack by tertiary phosphite at the oxygen of the carbonyl for enol phosphate formation is thus hindered.



$$\underset{:P(OEt)_3}{C_6H_5-\overset{\overset{O\ H-OAc}{\|}}{C}-CH_2Br} \rightleftarrows \underset{(XXX)}{C_6H_5-\overset{O-H\ ^{-}OAc}{\underset{+P(OEt)_3}{C}}-CH_2Br} \rightleftarrows \underset{(XXXI)}{C_6H_5-\overset{O^{-}\quad HOAc}{\underset{+P(OEt)_3}{C}}-CH_2Br} \longrightarrow \underset{(XXXII)}{C_6H_5-\overset{O-\overset{+}{P}(OEt)_3}{C}=CH_2\ Br^{-}}$$

$$\downarrow \qquad (39)$$

$$\underset{(IIa)}{C_6H_5-\overset{O-\overset{O}{\overset{\|}{P}}(OEt)_2}{C}=CH_2}$$

The above postulated mechanism is characterized by the reversible formation of structure (XXXI) which is also the intermediate postulated for in the aprotic reaction mechanism to give (XXXII). Enol phosphonium salt (XXXII) then proceeds

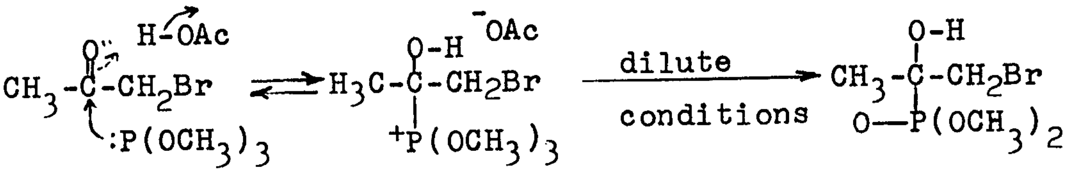
Table VIII. Reactions of Haloacetophenones with Trialkyl Phosphites and Acetic Acid

| Haloketone | Reaction Conditions | Keto-phosphonate | Enol Phosphate | Ketone | Haloketone |
|---|---|---|---|---|---|
| Bromoacetophenone A | $(EtO)_3P$, r.t.<br>46 hr., (1) | 0 | 63 | 4 | 0 |
| Bromoacetophenone A | $(MeO)_3P$, r.t.<br>22 hr., (1) | 0 | 77.5 | 0[2] | 0[2] |
| P-MeO A | $(EtO)_3P$, r.t.<br>20 min., (3) | 0 | 63 | 12 | 25 |
| P-$NO_2$ A | $(EtO)_3P$, r.t.<br>24 hr., (3) | 0 | 60 | 15 | 20 |

1. Products by n.m.r. ratios on distillate.
2. Trace present by t.l.c.
3. From n.m.r. ratios on undistilled reaction mixture; ratios, not yields.

via an Arbusov cleavage to give enol phosphate IIa.

Hudson and co-workers[27] have found that the reaction of bromoacetone with trimethyl phosphite in the presence of a large excess of acetic acid gives some α-hydroxyphosphonate (XXXIII), while reaction at high concentrations of reactants (i.e., small amount of acetic acid) gives enol phosphate almost exclusively, as observed in this laboratory.

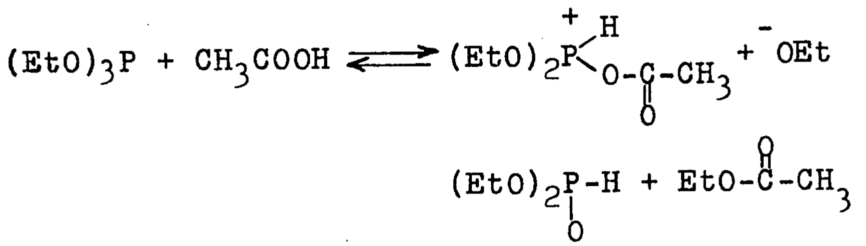


$$CH_3-\overset{O}{\overset{\|}{C}}-CH_2Br \;\; H-OAc \;\; :P(OCH_3)_3 \rightleftharpoons H_3C-\underset{+P(OCH_3)_3}{\overset{O-H}{C}}-CH_2Br \;\; {}^-OAc \xrightarrow[\text{conditions}]{\text{dilute}} CH_3-\underset{O-P(OCH_3)_2}{\overset{O-H}{C}}-CH_2Br \qquad (40)$$

(XXX) (XXXIII)

It is postulated that in the presence of a small amount of acetic acid solution the zwitterion intermediate XXXI is able to undergo a rapid rearrangement to yield XXXII . In the presence of a large excess of acetic acid as demonstrated by Hudson, sturcture XXX is favored to undergo the Arbusov cleavage by the efforts of the acetate ion on the ethoxyl group.

The reaction of triethyl phosphite with acetic acid at room temperature gives diethyl phosphite in a 40% yield,[28] as illustrated below.

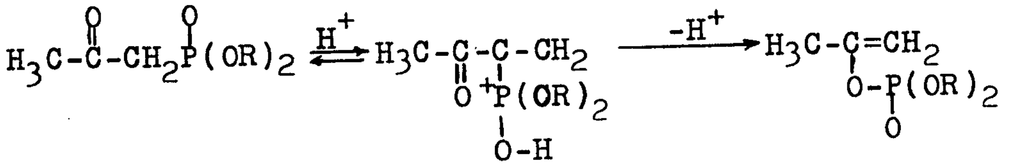


$$(EtO)_3P + CH_3COOH \rightleftharpoons (EtO)_2\overset{+}{P}\genfrac{}{}{0pt}{}{H}{O-\underset{O}{\underset{\|}{C}}-CH_3} + {}^-OEt \qquad (41)$$

$$(EtO)_2\underset{O}{\underset{|}{P}}-H + EtO-\overset{O}{\overset{\|}{C}}-CH_3$$

As a result the following control experiment was carried out. Phenacyl bromide was reacted with diethyl phosphite in acetic acid under the same conditions as carried out previously in the haloketone, phosphite, acetic acid runs. After 29 hours no reaction is observed between the diethyl phosphite and phenacyl bromide as monitored by n.m.r. Thus, it can be safely concluded that if any diethyl phosphite were formed in the α-haloketone-triethyl phosphite-acetic acid reactions there would be no interference by any of the diethyl phosphite with the more reactive triethyl phosphite.[11] Furthermore, a high material balance is shown by Table VIII in the haloacetophenone-acetic acid runs, indicating that triethyl phosphite was the lone reactant with the α-haloketones.

Machleidt and Strehlke[30] have reported that the ketophosphonate (XXXIV) rearranges to the enol phosphate (XXXV) in the presence of phosphoric acid at 170°C. (eqn. 42). It was therefore necessary to run another control reaction on Ia with acetic acid to see if IIa is formed to any appreciable extent. To a diethylphenacylphosphonate (IA) and diethyl 1-phenylvinylphosphate (IIa) mixture was added, at either room temperature or at 110°, a small amount of acetic acid. No appreciable amount of "phosphonate-phosphate rearrangement" occurred under the control conditions.

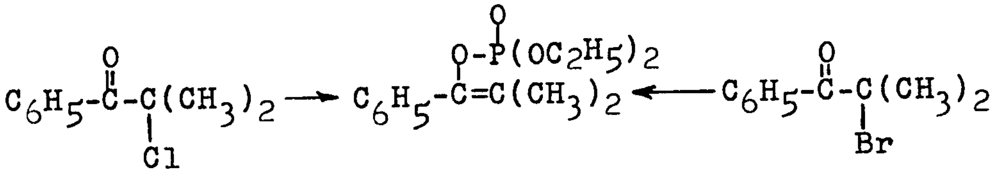


$$H_3C-\overset{O}{\overset{\|}{C}}-CH_2\overset{O}{\overset{\|}{P}}(OR)_2 \xrightleftharpoons{H^+} H_3C-\underset{O}{\underset{\|}{C}}-\underset{\substack{+P(OR)_2\\ |\\ O-H}}{\underset{|}{C}}-CH_2 \xrightarrow{-H^+} H_3C-\underset{\substack{O-P(OR)_2\\ |\\ O}}{\underset{|}{C}}=CH_2 \qquad (42)$$

(XXXIV) (XXXV)

Recent experiments in this laboratory have provided evidence so that attack at the carbon or oxygen of the carbonyl could be further defined. Strong support for enol phosphate formation via initial attack at carbonyl carbon followed by rearrangement to oxygen and dealkylation was obtained.

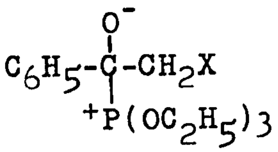
Thus, chloro- and bromocyclohexanone were found to react at equal rates with one equivalent of triethyl phosphite in a competition run to give cyclohexanone enol phosphate. Vapor phase chromatography was used to advantage in followed the reaction to 57% of completion; see Experimental Section for greater detail. Moreover, the competition reaction of bromo- versus chloroisobutyrophenone with triethyl phosphite as monitored by n.m.r. at 34.9° indicated that the chloro compound (XXXVI) reacts faster than does bromoisobutyrophenone (XXXVII) to give enol phosphate (XXXVIII).[11]



$$C_6H_5-\overset{\overset{O}{\|}}{C}-\underset{\underset{Cl}{|}}{C}(CH_3)_2 \longrightarrow C_6H_5-\overset{O-\overset{\overset{O}{\|}}{P}(OC_2H_5)_2}{\overset{|}{C}}=C(CH_3)_2 \longleftarrow C_6H_5-\overset{\overset{O}{\|}}{C}-\underset{\underset{Br}{|}}{C}(CH_3)_2 \qquad (43)$$

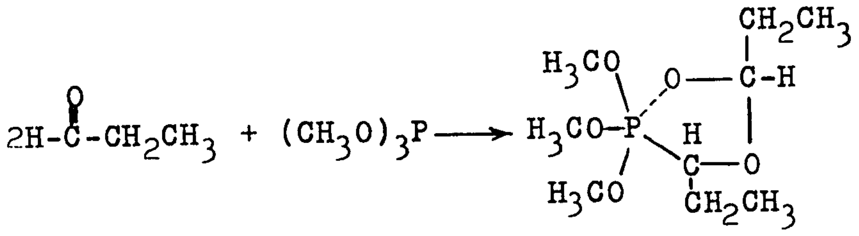
(XXXVI) (XXXVIII) (XXXVII)

The above results indicate that in the Perkow reaction the rate determining step does not involve the loss of halide ion. If enol phosphate formation was dependent on the loss of halide ion (i.e., the slow step in the reaction) bromide anion should depart at a greater rate than does chloride anion.[31] Furthermore, if the rearrangement step were rate determining the intermediate zwitterion (XXXIX) might be expected to add to another carbonyl group to form cyclic phosphoranes as in addition of phosphites to aldehydes,[32] viz.



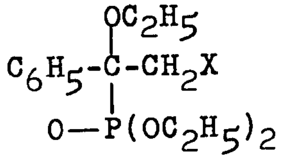
$C_6H_5-\overset{O^-}{\underset{^+P(OC_2H_5)_3}{C}}-CH_2X$

(XXXIX)



(44)

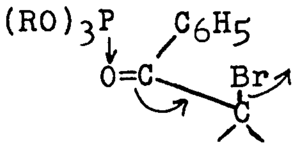
XXXIX might also undergo transfer of an alkyl group to oxygen to give XL in an Arbusov rearrangement.



$C_6H_5-\overset{OC_2H_5}{\underset{O-P(OC_2H_5)_2}{C}}-CH_2X$

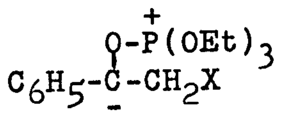
(XL)

The $SN_2^1$ mechanism involving initial attack on oxygen with concomittant loss of halide ion is unreasonable.



It may still be argued that a non-concerted rate-determining initial attack on carbonyl oxygen by phosphite followed by a rapid loss of halide ion is admissible. This mechanism is not likely since it would involve the formation of a carbanion

XLI stabilized only by phenyl. In any case contributions from



$$C_6H_5-\underset{-}{\overset{O-\overset{+}{P}(OEt)_3}{C}}-CH_2X$$

(XLI)

the intermediate betaine XLI if formed should have yielded a cyclic phosphorane by forming a condensation product by adding to another carbonyl group, as observed in addition of phosphites to fluorenones; see secton on Results and Discussion II. Thus the mechanism involving initial attack on oxygen as stated previously seems to be unreasonable and the results are probably best explained by a rate-determining addition of phosphite to carbonyl carbon followed by a rapid rearrangement to oxygen and loss of halide ion.

As a point of interest, this work is being continued by Mr. Steven Firstenberg and Mr. Howard Parnes who are conducting chemical and kinetic studies on the mechanism and further synthetic utility of the reactions of α-haloketones with tertiary phosphites and phosphines.

## References

1. F. W. Lichtenthaler, Chem. Rev., 61, 607 (1961).
2. I. J. Borowitz and L. I. Grossman, Tetrahedron Letters, 471 (1962).
3. H. Hoffman and H. J. Diehr, Tetrahedron Letters, 583 (1962)
4. S. Trippett, J. Chem. Soc., 2337 (1962).
5. P. A. Chopard, R. F. Hudson and G. Klopman, J. Chem. Soc., 1379 (1965).
6. I. J. Borowitz and R. Virkhaus, J. Am. Chem. Soc., 85, 2183 (1963).
7. I. J. Borowitz, K. Kirby and R. Virkhaus, J. Org. Chem., 31, 4031 (1966).
8. P. A. Chopard and R. F. Hudson, J. Chem. Soc., 1089 (1966).
9. R. F. Hudson, Chem. Soc. Special Publ. No. 19, 93 (1965).
10. R. F. Hudson and G. Salvadori, Helv. Chim. Acta., 49, 96 (1966).
11. S. Firstenberg, unpublished results.
12. The reaction of triethyl phosphite with XXXIII is qualitatively faster than the reaction with XXIV.
13. D. B. Denney, N. Gershman and J. Giacin, J. Org. Chem., 31, 2833 (1966).
14. R. N. Hazeldine and B. O. West, J. Chem. Soc., 3631 (1956).
15. D. W. Grisley, Jr., Tetrahedron Letters, 435 (1963).
16. A. N. Pudovik, Zh. Obsh. Khim, 25, 2173 (1955); Chem. Abstr., 50, 8486 (1956).
17. V. A. Kukhtin and A. N. Pudovik, Uspekhi Khim, 28, 101 (1959); Chem. Abstr., 53, 9025 (1959).
18. W. Perkow, Chem. Ber., 87, 755 (1954).
19. W. Perkow, E. W. Krockow and K. Knoevenagel, ibid., 88, 662 (1955).

20. E. Y. Spencer, A. R. Todd and R. F. Webb, J. Chem. Soc., 2968 (1958).

21. F. Cramer, Angew. Chem., 72, 236 (1960).

22. U. Schöllkopf, Angew. Chem., 71, 260 (1959).

23. G. Wittig, Angew. Chem., 68. 505 (1956).

24. A. Michaelis and E. Kohler, Ber., 32, 1566 (1899).

25. F. Ramirez and S. Dershowitz, J. Org. Chem., 22, 41 (1957).

26. W. Caldwell, J. Chem. Soc., 109, 282 (1916).

27. P. A. Chopard, V. M. Clark, R. F. Hudson and A. J. Kirby, Tetrahedron, 21, 1961 (1965).

28. The conversion of trialkyl phosphites to dialkyl phosphites with acids is well known. cf. B. Iselin, W. Rittel, P. Sieber and R. Schwyzer, Helv. Chim. Acta, 42, 373 (1957).

29. R. F. Hudson, "Structure and Mechanism in Organophosphorus Chemistry", Academic Press, Inc., New York, N. Y., 1965, p. 124.

30. H. Machleidt and G. U. Strehlke, Angew. Chem. (Int. Ed.), 3, 443 (1964).

31. Although there is apparently no data on $SN_2'$ reactions involving phosphorus nucleophiles, the $SN_2$ reactions of di-n-butyl phosphite or tributylphosphine go faster with propyl bromide than with propyl chloride by factors of 246:1 and 125:1. respectively. See R. F. Hudson, "Structure and Mechanism in Organophosphorus Chemistry". Academic Press, N. Y., Ch. 5 (1965).

32. F. Ramirez, A. V. Patwardhan and S. R. Heller, J. Am. Chem. Soc., 86, 516 (1964).

## SUMMARY I

A mechanistic study of the Perkow reaction and similar displacement processes are presented in this thesis. The results of a preliminary survey of the reactions of alpha-haloketones with trialkyl phosphites are reported. Such reactions yield ketophosphonates and enol phosphates as general products. The formation of these products is not extensively altered by the initial presence of ethanol although acetic acid causes exclusive enol phosphate formation in several cases where normally both products are obtained. Thus, enol phosphate formation from haloketones cannot start with initial attack on halogen. Phosphites, in contrast to phosphines, probably attack the carbonyl carbon or less likely the carbonyl oxygen. In the presence of acetic acid, protonation on oxygen ensures attack by phosphite on carbonyl carbon. Rearrangement then occurs from carbon to oxygen to give enol phosphonium salts which are rapidly dealkylated to the final product: enol phosphate.

The relative rates at which several sets of bromo- and chloroketones, including bromo- and chlorocyclohexanone, react with triethyl phosphite are about the same. These data eliminates a concerted $SN_2^{\prime}$ mechanism for enol phosphate formation since the bromo species should be much faster than the chloro compound. It therefore seems reasonable to conclude that the best mechanistic pathway for the reaction of trialkyl phosphites with alpha-haloketones proceeds by a rate determining addition to the carbonyl carbon followed by a fast loss of halide ion.

## EXPERIMENTAL I

Microanalyses were performed by Professor V. B. Fish of the Department of Chemistry, Lehigh University, Galbraith Laboratories Inc., Knoxville, Tennessee, and Schwartzkopf Microanalytical Laboratories, Woodside, New York.

Infrared spectra were recorded either on a Perkin-Elmer Model 21 or on a Beckman IR-8 infrared spectrophotometer.

Ultraviolet spectra were recorded on a Beckman DK-2A spectrophotometer. The solvents are specified with the recorded spectra.

Nuclear magnetic resonance spectra were recorded on a Varian A-60 spectrometer with tetramethylsilane, 0 p.p.m., as an internal standard, $P^{31}$ n.m.r. spectra were carried out by Dr. J. Lancaster of the American Cyanamid Co., Stamford, Connecticut using 85% phosphoric acid as an external reference.

Melting points were determined in Kimax capillary tubes using a "Mel-Temp" apparatus (Laboratory Devices, Box 68, Cambridge, Mass.) and are uncorrected. Boiling points are also uncorrected.

Vapor phase chromatograms were recorded on a Varian Aerograph A-700 gas chromatograph. The best results were obtained using glass injection ports with glass columns packed with 3-5% SE-30 on chromosorb W although Carbowax 20M columns were also used. Peak areas were determined by planimeter measurement, cutting out the paper under the peak and weighing it, or by some form of triangulation calculation, such as height times width at half height. The choice varies with the situation. Cutting out peaks is tedious and humidity affects the weight of the paper. A planimeter will give good results after some practice. Height times width at one-half height is the most common method used. Known amounts were injected and calibration curves constructed. The known reaction of the phosphites with alpha-haloketones were employed to obtain standard samples for calibration work. Helium was used as the carrier gas with a flow rate of ca. 60 ml/minute. The accuracy of yields as so determined is estimated to be to 1-5%.

Thin layer chromatography was carried out by using E. Merck Silica Gel $HF_{254}$ (Brinkmann Instruments, Inc., U. S. distributor) as the substrate, unless specified otherwise, activated at 110-120°. The thickness of the adsorbent layer was adjusted to 0.25 mm. using "Desaga" equipment supplied by the Brinkmann Co., Inc., Great Neck, Long Island, New York. The most frequently used developing solution was 5% (by volume) ethyl acetate in benzene. Other solvent systems used were:

a) 5% (by volume) methanol in benzene
b) 15% (by volume) methanol in benzene
c) 25% (by volume) methanol in benzene

The spots were located with ultraviolet light, exposure to iodine vapor or 2,4-dinitrophenylhydrazine spray. The $R_f$ values were then compared with those of purified (by distillation or recrystallization) authentic compounds spotted on the same plate.

Reactions of alpha-haloketones with trivalent phosphorus compounds were carried out under an atmosphere of pre-purified nitrogen (Matheson) with constant magnetic stirring of the reaction mixture. All manipulations were performed in an atmosphere of pre-purified nitrogen unless otherwise stated. Mechanical transfers and other operations in open vessels were continuously flushed with a rapid stream of pre-purified nitrogen prior to distillation. The liquid alpha-haloketones which were synthesized were stored at 0° in brown bottles under an atmosphere of pre-purified nitrogen. Prior to each use all liquids were distilled and checked by V.P.C. Solid alpha-haloketones were recrystallized several times before use, dried, checked by t.l.c. and stored in a vacuum desiccator over calcium chloride. Solvents were stored over the appropriate drying agent, refluxed and distilled prior to use.

Materials

Triethyl phosphite was purchased from Hooker Chemical Corporation, Niagara Falls, New York. The phosphite was dried and distilled from calcium hydride just before use. A large forerun was obtained distilling over the range of 70-155°, the forerun was discarded and the main cut distilled over at 156-157° (lit., 157.9°). The residual liquid was discarded.

Triphenylphosphine was obtained from Mand T. Chemicals, Inc., and was recrystallized from diethyl ether. After drying at a pressure of 0.15 mm over phosphorus pentoxide, the triphenylphosphine, m.p. 80-81° (lit. m.p. 80°). was stored in a vacuum desiccator over calcium chloride.

Phenacyl chloride and phenacyl bromide were purchased from Matheson Coleman and Bell, East Rutherford, New Jersey, and were recrystallized three times from petroleum ether (30-60°), m.p.'s 55.56° (lit., m.p. 55-56°) and 49-50° (lit. m.p. 49.5-51°), respectively.

2-Chlorocyclohexanone (Aldrich Chemical Co.) was redistilled before use, b.p. 90-91° (15 mm) (lit. b.p. 90-91°/14/15 mm).

Reaction of Phenacyl Bromide with Triethyl Phosphite

A. In 1,2-Dimethoxyethane

A solution of phenacyl bromide (3.98 g., 0.020 mole) in 1,2-dimethoxyethane (4 ml) was added dropwise with constant stirring to triethyl phosphite (3.32 g., 0.020 mole) at 120°. The resultant mixture was refluxed under nitrogen for 24 hours. After the solvent was removed in vacuo the residual liquid was distilled to give a mixture of diethyl phenacylphosphonate (Ia) and diethyl 1-phenylvinylphosphate (IIa) (4.50 g., 88% yield; b.p. 100-140°, 0.15 mm). The mixture consisted of the isomeric ratio ca. 74:26 Ia to IIa and ca. 1 part of acetophenone as determined by n.m.r. values and v.p.c. retention times. The actual yields calculated were 65% of Ia, 23% of IIa and 1% of acetophenone. Analysis of thin layer chromatography and v.p.c. revealed the same components.

Infrared Data

The mixture of Ia and IIa exhibited infrared peaks ($CHCl_3$) at 5.95 μ (carbonyl) and 6.10 μ (double bond of IVa). The remaining peaks in the spectrum are common to both IIIa and IVa.

The infrared spectrum was in agreement with the isomeric structures Ia and IIa.

Nuclear Magnetic Resonance Data

The n.m.r. spectrum ($CDCl_3$) of the mixture exhibited a doublet centered at 6.4 tau ($J_{p}31_{H}$=22.5 c.p.s.) for the methylene of Ia situated between the carbonyl and phosphoryl groups. The enol phosphate was identified by a multiplet centered at 4.75 tau for the olefinic protons of IIA. Both isomers exhibited common peaks with multiplets centered at 2.0 tau and 2.5 tau (5H multiplets; aromatic protons), a 4H doublet of quartets centered at 5.95 tau (J=7 c.p.s., methylene of ethyl) and a 6H doublet of triplets centered at 8.80 tau (J=7 c.p.s.; methyl of ethyl).

B. In Ethanol or Butanol

A solution of phenacyl bromide (3.98 g., 0.020 mole in absolute ethanol (5 ml.) was added dropwise to triethyl phosphite (3.32 g., 0.020 mole) with constant stirring at ca. 120° (bath temperature). The mixture was refluxed under pre-purified nitrogen for six hours. Examination of the resultant mixture by v.p.c. (by relative peak area comparison and the use of a calibration curve for IIa) gave results shown in Table VII (p. 25). Reaction in butanol was similarly done at a bath temperature of 135°.

C. No Solvent

Triethyl phosphite (3.32 g., 0.020 mole) was added dropwise to phenacyl bromide (3.98 g., 0.020 mole). The mixture was kept at room temperature under pre-purified nitrogen for 20 min., with constant stirring. After twenty minutes an aliquot was examined by n.m.r. and found to be Ia (60%), IIa (21%) and unreacted bromoacetophenone (19%). The numbers are n.m.r. ratios and should be reasonably related to the actual yields since no extraneous peaks were observed and the loss of material was minimal.

### D. In Acetic Acid

A solution of phenacyl bromide (3.98 g., 0.020 mole) in acetic acid (4.80 g., 0.080 mole) was added dropwise with constant stirring to triethyl phosphite (3.32 g., 0.020 mole). The mixture was kept at room temperature under an atomosphere of nitrogen for 46 hours. After removal of acetic acid and unreacted phosphite in vacuo the residual liquid was distilled to give 3.30 g., b.p. 115-122° (0.15 mm.) of a liquid. Nuclear magnetic resonance ($CDCl_3$) data indicated enol phosphate IIa and acetophenone XLII in 97:3 ratio or yield of 63% of IIa and 4% of XLII. Examination of the liquid by thin layer chromatography gave only these two components.

## Reaction of Phenacyl Bromide with Trimethyl Phosphite

### A. In 1,2-Dimethoxyethane

Reaction of phenacyl bromide (3.98 g., 0.020 mole) in 1,2-dimethoxyethane (4 ml.) with trimethyl phosphite (2.48 g., 0.020 mole) at 87° for 24 hours as in Section A above gave 3.11 g. of distilled liquid, b.p. 110-142° (0.15 mm.). Examination of the liquid (t.l.c., n.m.r.) indicated the presence of Ib and IIb in 3.7:1 ratio or yields of 52% of

Ib, 14% of IIb: 3% of unreacted phenacyl bromide was also found.

B. In Acetic Acid

Reaction of phenacyl bromide (3.98 g., 0.020 mole) with trimethyl phosphite as in Section D gave 3.54 g., b.p. 140-144° (0.6-0.8 mm.) of a liquid; n.m.r. revealed it to be only IIb (77.5% yield). Traces of phenacyl bromide and acetophenone were found by thin layer chromatography.

### Reaction of Phenacyl Chloride with Triethyl Phosphite

A. No Solvent

Phenacyl chloride (3.09 g., 0.020 mole) was added to triethyl phosphite (3.3 g., 0.020 mole) at 120° (bath temperature) and the mixture was refluxed for six hours. Distillation gave IIa, b.p. 110-118° (0.15 mm.), 4.35 g., 0.0169 mole 85% yield; pure by n.m.r., and v.p.c. analysis by thin layer chromatography showed the presence of a trace of diethylphenacylphosphonate and of acetophenone.

B. In Ethanol

Phenacyl chloride (3.09 g., 0.020 mole) in absolute ethanol (5 ml.) was added dropwise to triethyl phosphite (3.32 g., 0.020 mole) at 120° (bath temperature). The mixture was refluxed for six hours, under an atmosphere of prepurified nitrogen with constant stirring. The solvent was removed in vacuo, and the residual liquid was distilled to give a forerun, 3.37 g., which contained 8.5% of acetophenone (v.p.c.) and a main fraction, b.p. 80-161° (3.5-5.0 mm.), of 5.015 g. which contained 2.5% of acetophenone and 70.5% of IIa;

actual yields of acetophenone (0.41 g., 0.0034 mole, 17%) and IIa (3.52 g., 0.0138 mole, 69%) were thus calculated.

## Reaction of p-Nitrophenacyl Bromide with Triethyl Phosphite

### A. No Solvent

Triethyl phosphite (3.32 g., 0.020 mole) was added at once to p-nitrophenacyl bromide (XXVIII) (4.88 g., 0.020 mole) to give an exothermic reaction during which XXVIII went into solution. The resulting solution was cooled to room temperature and stirred under an atmosphere of nitrogen for 23 hours. Analysis by n.m.r. revealed the presence of XXVIII, the ketophosphonate Ia (R=p-$NO_2C_6H_5$) and the enol phosphate IIa (R=p-$NO_2C_6H_5$) in a ratio of 1.00:1.53:5.47. Assuming that these were the only products, as detected by n.m.r. at least, the ratio given corresponds to yields of 0.0025 mole (12.5%) of unreacted XXVIII, 0.0038 mole (19%) of ketophosphonate and 0.0137 mole (68%) of enol phosphate. A trace of p-nitroacetophenone was found by thin layer chromatography but was not detected by n.m.r. This ratio was based on the integrated areas of the methylene protons for the products which absorbed as a singlet at 5.15 tau for XXVIII, a doublet ($J_{p^{31}H^1} = 18$ c.p.s.) centered at 6.20 tau for the ketophosphonate and a doublet of triplets ($J_{p^{31}H^1} = 2$ c.p.s.) at 4.30 tau and 4.55 tau for the enol phosphate. As a check the total integrated area of the three different methylenes was found to be exactly 0.5 that of the 4H aromatic proton area.

### B. In Ethanol

Triethyl phosphite (3.32 g., 0.020 mole) was added dropwise to p-nitrophenacyl bromide (XXVIII) (4.88 g., 0.020 mole) suspended in absolute ethanol (6 ml.). The reaction was exothermic and the mixture stirred under nitrogen for 24 hours at room temperature. After 24 hours the solvent and unreacted phosphite were removed in vacuo and the residual solution was examined by n.m.r. as above. The analysis revealed the presence of p-nitroketophosphonate (10%), p-nitroenol phosphate (71.5%), p-nitroacetophenone (3%; singlet methyl group of 7.32 tau) and unreacted p-nitrophenacyl bromide (15%). Qualitative results by t.l.c. were in agreement with the n.m.r. data.

### C. In Acetic Acid

In a similar experiment involving acetic acid (4.80 g., 0.080 mole), n.m.r. analysis indicated the presence of p-nitroenol phosphate (60%), p-nitroacetophenone (15%) and unreacted p-nitrophenacyl bromide (20%). Qualitative results by thin layer chromatography were in agreement with the n.m.r. data.

## Preparation of p-Methoxyphenacyl Bromide

A solution of bromine (21 g., 0.268 mole) in chloroform (55 ml.) was added dropwise with stirring to a chloroform (70 ml.) solution of p-methoxyacetophenone (20 g., 0.134 mole). The mixture was slowly warmed to 40° and kept at that temperature for twenty minutes with constant stirring. The mixture was kept at room temperature for an additional fourteen hours, filtered, washed several times with $NaHSO_3$ solution, and dried with anhydrous magnesium sulfate. Most of the solvent was removed in vacuo; the dark viscous solid left behind was taken up in absolute methanol, cooled and filtered. Three recrystallizations from methanol gave 13.05 g. of pure crystalline p-methoxyphenacyl bromide, m.p. 70-71°C (lit. m.p. 72). Thin layer chromatography and n.m.r. data were in agreement with the proposed product.

## Reaction of p-Methoxyphenacyl Bromide with Triethyl Phosphite

### A. In 1,2-Dimethoxyethane

Reaction of triethyl phosphite (1.66 g., 0.010 mole) with p-methoxyphenacyl bromide (XXVI) (2.29 g., 0.010 mole) in 1,2-dimethoxyethane (5 ml.) at reflux for 24 hours followed by removal of volatile material *in vacuo* with aliquots removed for n.m.r. analysis. The residual liquid (2.35 g.) was distilled giving 1.89 g., b.p. 168-172° (0.05 mm.) of a liquid which was indicated by n.m.r. to be 91:9 ketophosphonate Ia ($R=p\text{-}MeOC_6H_5$) and unreacted XXVI. A trace of the corresponding enol phosphate was found by thin layer chromatography. *Anal*. Calc'd. for $C_9H_9O_2Br$: Br, 34.93. Found: Br, 3.11. This corresponds to 8.90% of XXVI in the above liquid in excellent agreement with the n.m.r. data. On the basis of the above ratio, the yields of distilled products are 0.0060 mole (60%) of ketophosphonate (75% maximum before distillation) and 0.00074 mole (7.4%) of XXVI (9% maximum before distillation).

### B. In Acetic Acid

p-Methoxyphenacyl bromide (XXVI) (2.29 g., 0.010 mole) in acetic acid (2.40 g., 0.040 mole) was added dropwise to triethyl phosphite (1.66 g., 0.010 mole) with constant stirring. The mixture was stirred for *ca*. 10 minutes under an atmosphere of nitrogen and an aliquot removed. N.m.r. analysis on the aliquot indicated the mixture consisted of the enol phosphate IIa (R=p-MeOC$_6$H$_5$) (63%), XXVI (25%) and p-methoxyacetophenone (12%). No other compounds were present. After one hour the mixture had turned a dark brown and was not further examined.

Reaction of m-Methoxyphenacyl Bromide with Triethyl Phosphite

A. In 1,2-Dimethoxyethane

Triethyl phosphite (3.32 g., 0.020 mole) was added dropwise to a solution of m-methoxyphenacyl bromide (XXVII) (4.58 g., 0.020 mole) in 1,2-dimethoxyethane (5 ml.) at reflux temperature. After 24 hours at reflux the solution was concentrated *in vacuo* and an aliquot removed for n.m.r. analysis. A mixture of ketophosphonate Ia (R=m-MeOC$_6$H$_5$) (62%), enol phosphate IIa (R=m-MeOC$_6$H$_5$) (28%) and XXVII (10%) was indicated. Distillation gave 3.66 g., b.p. 175-185° (0.75 mm.), of ketophosphonate, enol phosphate, XXVII, and m-methoxyacetophenone in the ratio 54:34:7:5. The corresponding yields were: ketophosphonate (34.5%), enol phosphate (21.6%), XXVII (6%) and m-methoxyacetophenone (6%).

Reaction of 2-Chlorocyclohexanone with Triethyl Phosphite

A solution of 2-chlorocyclohexanone (XXII) (2.64 g., 0.020 mole) in absolute ethanol (5 ml.) was added dropwise to triethyl phosphite (3.32 g., 0.020 mole) and the resultant solution was refluxed for 6 hours with stirring. Analysis by v.p.c. indicated enol phosphate XXV (82%) and cyclohexanone (20%). A genuine sample of XXV, used to establish a v.p.c. calibration curve, was obtained from the known reaction of XXII with triethyl phosphite. Similar reaction at room temperature for four hours gave XXV (52%) and cyclohexanone (2%) Although the yield of XXV varied in repetition of the room temperature reaction, the yield of cyclohexanone was always small.

### Reaction of 2-Bromocyclohexanone with Triethyl Phosphite

A solution of 2-bromocyclohexanone (XXIII) (3.54 g., 0.020 mole) in absolute ethanol (5 ml.) was added dropwise to triethyl phosphite (3.32 g., 0.020 mole) and the resultant solution was refluxed for 6 hours. After removal of the solvent *in vacuo*, the residual liquid was distilled to give: (1) 4.34 g., b.p. 37-38° (0.6 mm.) and (2) 3.98 g., b.p. 108-109° (0.2 mm.). Analysis by v.p.c. indicated enol phosphate (49% yield), cyclohexanone (33% yield) and unreacted haloketone XXIII (13% yield). A similar experiment performed at room temperature for 6 hours indicated enol phosphate (73% yield) and unreacted haloketone XXIII (24% yield).

### Preparation of 2-Methyl-2-chlorocyclohexanone

Following the method of E. W. Warnhoff and W. S. Johnson, J. Am. Chem. Soc., 75, 494 (1953), a solution of previously distilled (69-70°) sulfuryl chloride (18.5 g., 0.137 mole) in dry carbon tetrachloride (25 ml.) was added to α-methyl cyclohexanone (15 g., 0.134 mole), in 80 ml. of dry carbon tetrachloride during one hour with stirring. After 48 hours of constant stirring the yellow reaction mixture was washed with three 50 ml. portions of water, two 50 ml. portions of saturated sodium bicarbonate solution, one 50 ml. portion of saturated sodium chloride solution and dried with anhydrous magnesium sulfate. The solution was filtered and the solvent removed.

The residual liquid was distilled, yielding 14.11 g. of a clear, colorless liquid, b.p. 30-32° (0.05 mm.). The product was confirmed by comparison with known XLIII by use of t.l.c., v.p.c. and IR.

### Preparation of 2-Methyl-2-Bromo Cyclohexanone

To a solution of 2-methylcyclohexanone (15 g., 0.134 mole) in 50 ml. of dry carbon tetrachloride was added dropwise a solution of bromine (22 g., 0.137 mole) (containing 0.5 ml. acetic acid) and carbon tetrachloride (15 ml.). The bromine was taken up at once. After 30 hours of constant stirring, the yellow-brown solution was washed with three 50 ml. portions of water, followed by three 50 ml. portions of saturated sodium bicarbonate. The organic layer was dried with anhydrous magnesium sulfate, filtered, and the solvent removed. The residual liquid was distilled from magnesium oxide, yielding 14.73 g. (58%) of a colorless liquid, b.p. 43-45° (0.15 mm.). The product was confirmed by comparison with genuine XLIV by use of t.l.c., v.p.c. and IR.

### Reaction of 2-Chloro-2-Methyl Cyclohexanone and 2-Bromo-2-Methyl Cyclohexanone with Triethyl Phosphite

#### A. Reaction of 2-Chloro-2-Methyl Cyclohexanone (XLIII) (Neat)

Addition of XLIII (2.13 g., 0.0146 mole) dropwise to triethyl phosphite (2.42 g., 0.0146 mole) at a bath temperature of 120° followed by heating for six hours gave 2.396 g.

of 2-methylcyclohexenyl diethyl phosphate (XLV), b.p. 91-92° (0.1 mm), 0.0096 mole, 66% yield. The n.m.r. ($CCl_4$) of XLV exhibited a 3H doublet at 8.37 $\tau$ ($J_{P^{31}H}$=1.5 c.p.s.) for the olefinic methyl and peaks for alicyclic and ethyl group protons.

B. Reactions of XLIII and XLIV in Ethanol

Reaction of either XLIII or XLIV and triethyl phosphite (0.020 mole each) in absolute ethanol (5 ml.) followed by a six hour reflux period gave mixtures which were analyzed by v.p.c. See Table V (p. 23).

Treatment of Ia and IIa with Acetic Acid

A mixture of 76.3:23.7 Ia and IIa was placed in an n.m.r. tube under nitrogen and acetic acid (3 drops) was added. After six hours at room temperature the ratio was 70.8:29.2. No further change occurred after 24 hours. The mixture was heated (90-100°C) with an additional 0.8 ml. of acetic acid for 4 hours to give no further change in the ratio of Ia and IIa.

Reaction of 2-Chlorocyclohexanone (XXII) and 2-Bromocyclohexanone (XXIII) in Competition with Triethyl Phosphite

A mixture of XXII and XXIII (0.020 mole each) in 1,2-dimethoxyethane (5 ml.) was added dropwise to triethyl phosphite (3.32 g., 0.020 mole) at a bath temperature of 85° with stirring. Aliquots were taken at intervals of 1, 2, 3.3 and 4.5 hours and analyzed by v.p.c. to show remaining XXII and XXIII in ratios of 1:1, 1.06:1, 1.12:1, and 1.05:1. Known mixtures of XXII and XXIII were similarly analyzed to an accuracy of ± 5%. After 4.5 hr. reaction had proceeded to give

57% of XXV, as determined with a calibration curve for XXV.

## Reaction of Triethyl Phosphite with Acetic Acid

Triethyl phosphite (3.32 g., 0.020 mole) was treated with acetic acid (4.80 g., 0.080 mole) at room temperature for 25 hours to give diethyl hydrogenphosphonate (40% by v.p.c. analysis using a calibration curve made with genuine diethyl hydrogenphosphonate and starting compounds.

## Attempted Reaction of Phenylacyl Bromide with Diethyl Hydrogenphosphonate

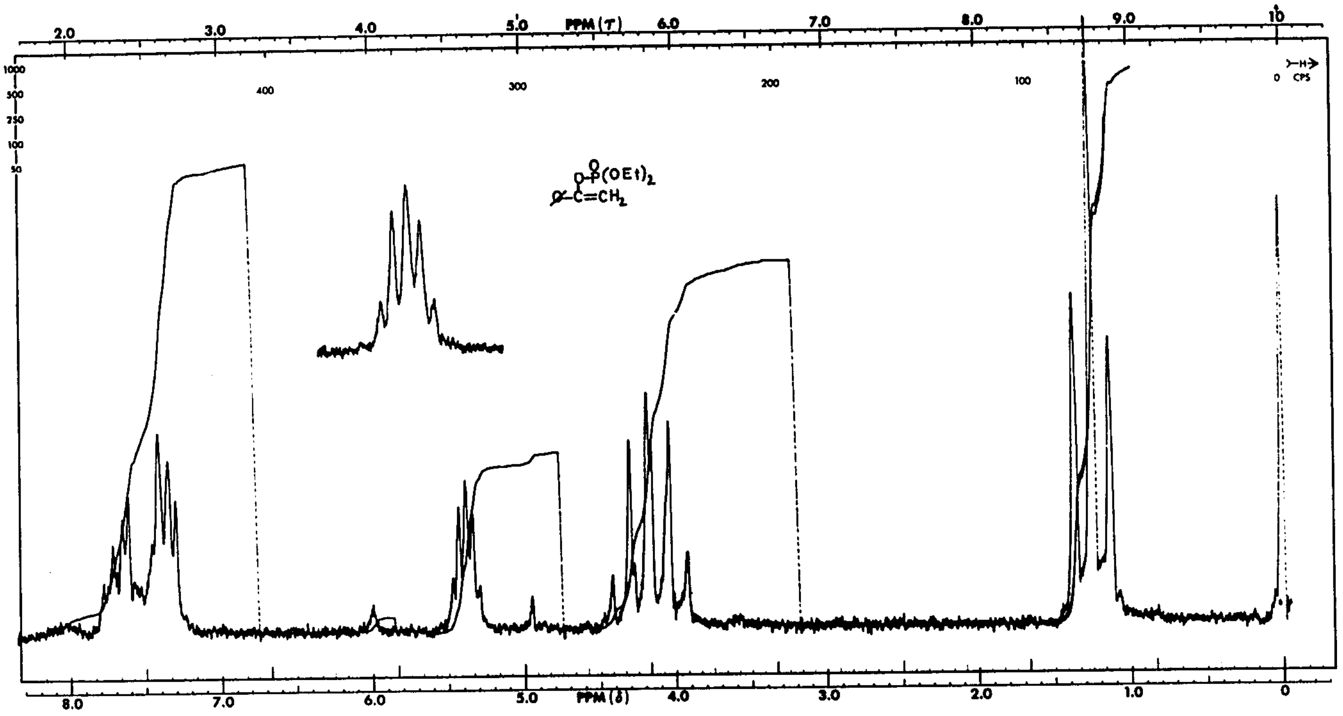
Treatment of phenacyl bromide (2.63 g., 0.0132 mole) with diethyl hydrogenphosphonate (1.82 g., 0.0132 mole) in acetic acid (0.053 mole) at room temperature for 28.8 hr. led to no reaction as indicated by n.m.r. examination.

## Reaction of Phenacyl Bromide and Phenacyl Chloride in Competition with Triethyl Phosphite

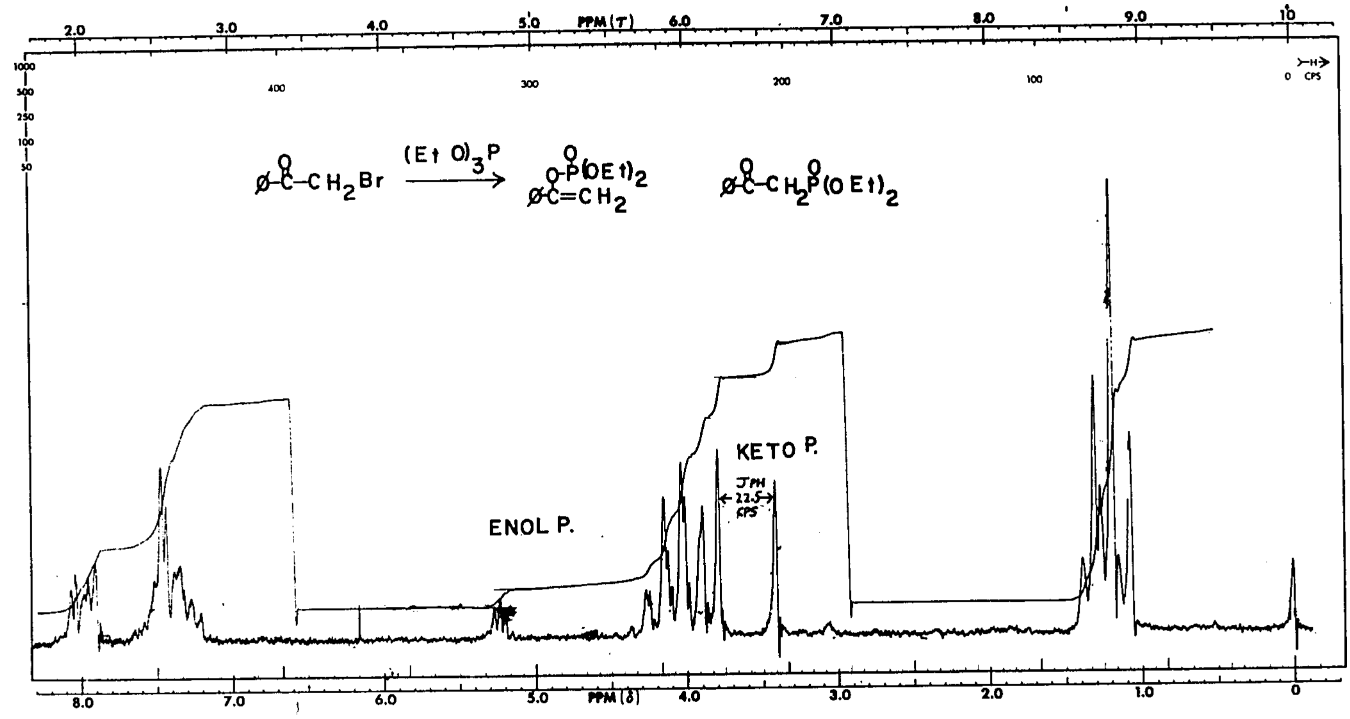
Triethyl phosphite (3.32 g., 0.020 mole) was added dropwise with stirring to a melt (oil bath temperature 61°) consisting of phenacyl bromide (3.98 g., 0.020 mole) and phenacyl chloride (3.09 g., 0.020 mole). The mixture was stirred for one hour (bath temperature 55°C) followed by vigorous stirring at room temperature for 48 hours under pre-purified nitrogen. Aliquots were taken at various intervals and analyzed by n.m.r. to show remaining phenacyl chloride and phenacyl bromide in ratios of 4.08:1, 4.16:1, 4.17:1 and 4.10:1. Known mixtures of chloro and phenacyl bromide were similarly analyzed to an accuracy of 1%.

## Preparation of α-Bromocyclohexanone

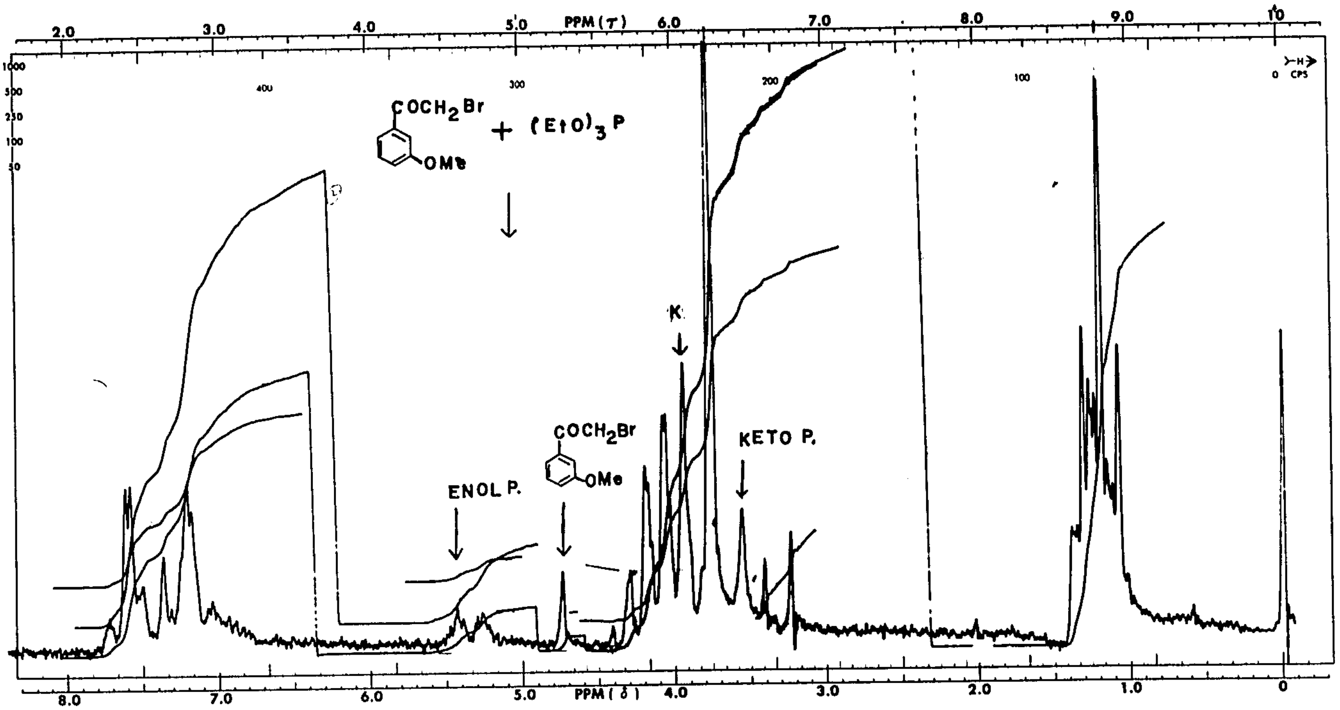
According to the procedure of J. Allinger and N. L. Allinger, Tetrahedron Letters, No. 2, 64 (1958), to freshly distilled cyclohexanone (30.0 g., 0.306 mole) mixed with 75 ml. water was added bromine (48.3 g., 0.305 mole) to yield 31 g. (56%) of a clear liquid, b.p. 73-74° (2 mm.).


PPM (τ)
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10
1000
500
250
100
50
400
300
200
100
0 CPS
O-P(OEt)2
ø-C=CH2
PPM (δ)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

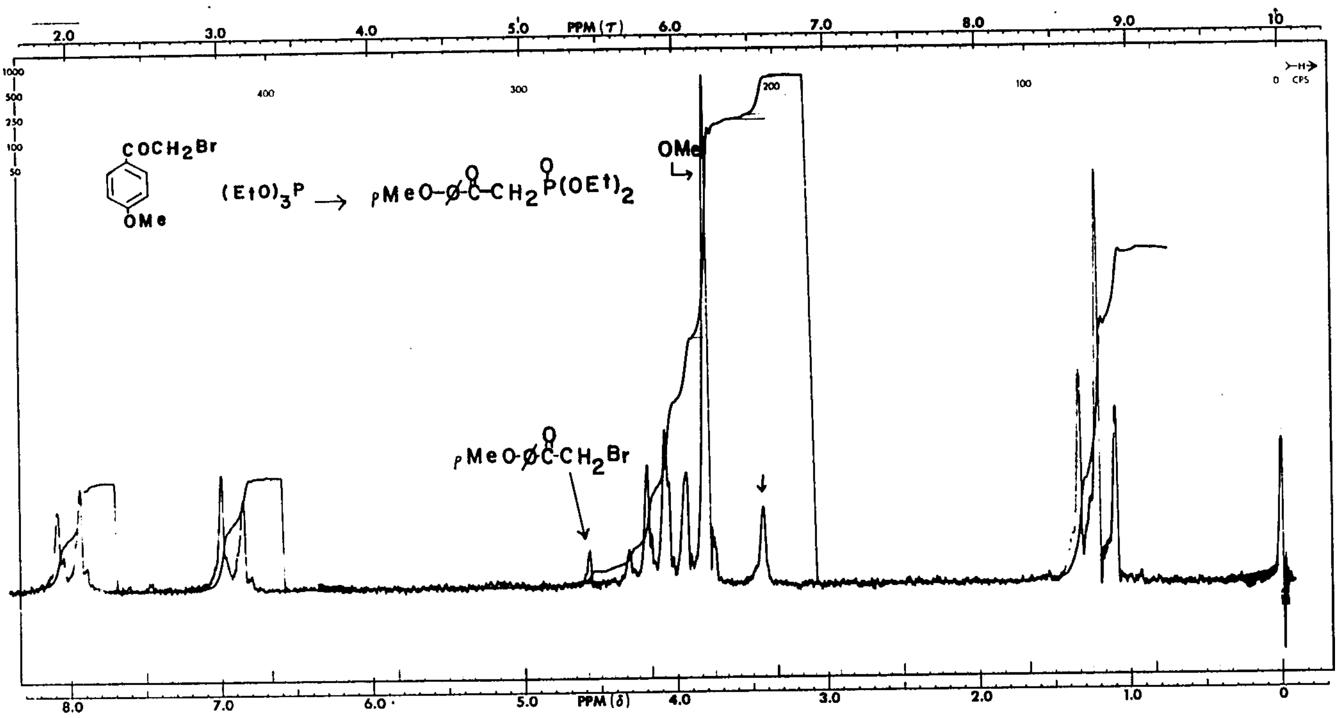
Neat


PPM (τ)
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10
1000
500
250
100
50
400
300
200
100
0 CPS
ø-C(O)-CH2Br
(Et O)3P
O-P(O)(OEt)2
ø-C=CH2
ø-C(O)-CH2P(O)(OEt)2
ENOL P.
KETO P.
JPH
22.5 CPS
PPM (δ)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

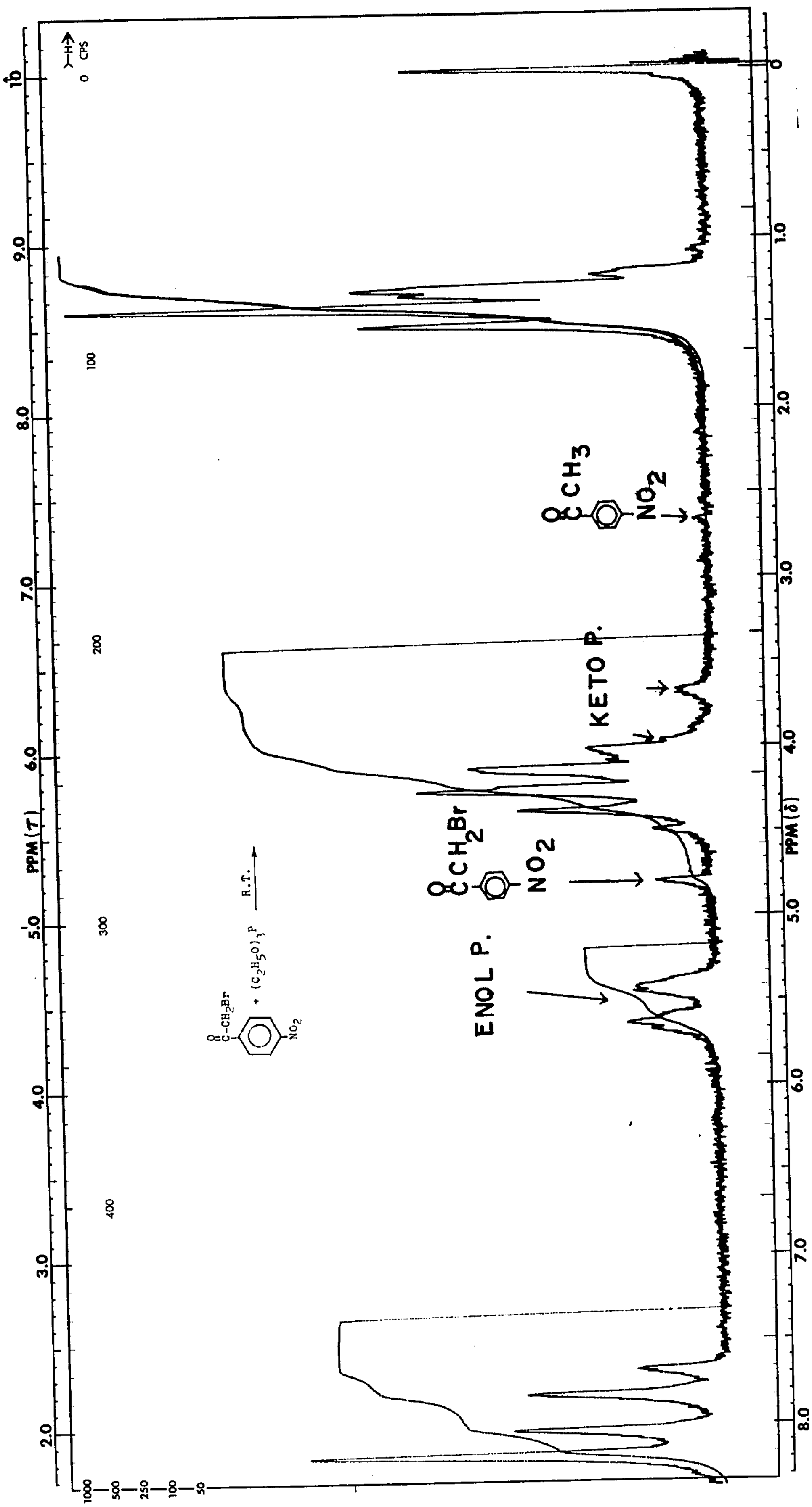
CDCl3


PPM (τ)
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10
400
300
200
100
0 CPS
COCH2Br
OMe
+ (EtO)3P
K
COCH2Br
OMe
KETO P.
ENOL P.
8.0
7.0
6.0
5.0
PPM (δ)
4.0
3.0
2.0
1.0
0

Neat


PPM (τ)
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10
400
300
200
100
0 CPS
COCH2Br
OMe
(EtO)3P → pMeO-ø-C(O)-CH2-P(O)(OEt)2
OMe
pMeO-ø-C(O)-CH2Br
8.0
7.0
6.0
5.0
PPM (δ)
4.0
3.0
2.0
1.0
0

Neat



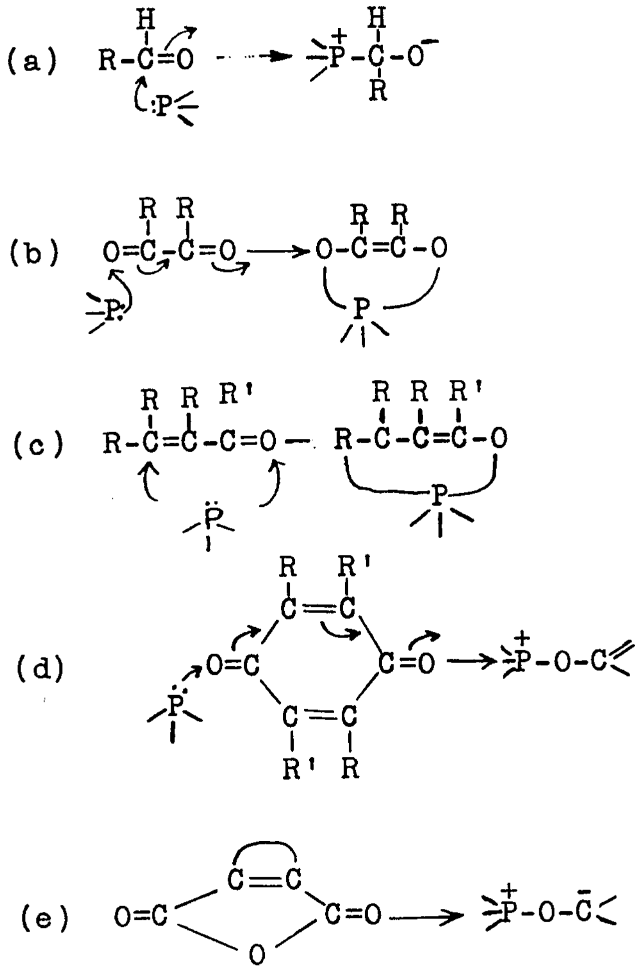
10
9.0
8.0
7.0
6.0
PPM (τ)
5.0
4.0
3.0
2.0
0 CPS
100
200
300
400
0
1.0
2.0
3.0
4.0
PPM (δ)
5.0
6.0
7.0
8.0
1000
500
250
100
50
C-CH2Br
NO2
+ (C2H5O)3P
R.T.
CCH3
NO2
KETO P.
CCH2Br
NO2
ENOL P.

Neat

# INTRODUCTION II

Trivalent phosphite esters are of interest because of their ability to utilize the unshared electron pair on phosphorus to form condensation products with carbonyl compounds.

Trialkyl phosphites were found by various investigators to react with simple aldehydes (a), α-diketones (b), α-keto-esters (b), ortho-quinones (b), α,β-unsaturated ketones (c), para-quinones (d), and cyclic aromatic anhydrides (e) in the following manner.[28]



R=alkyl, aryl or substituted aryls

R=permutations of alkyl, alkoxy, aryl and substituted aryls

R'=alkyl, aryl, or substituted aryls

R=permutations of H, alkyl, aryl, substituted aryls.

$R=R'=H$, Cl or $CH_3$

$R'=Cl$ or $CH_3$; $R=H$

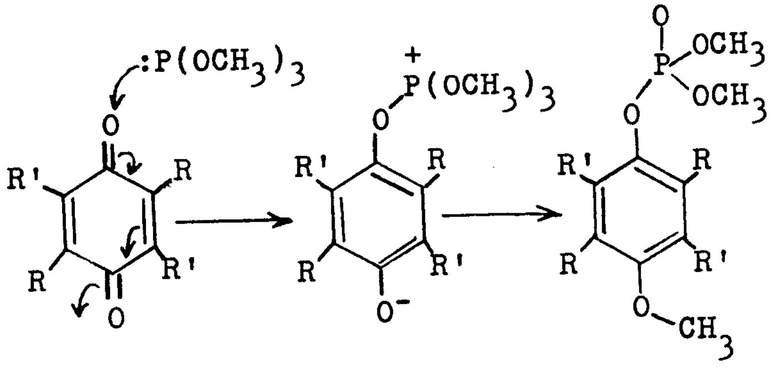
Figure 1.[28] Reactions of Phosphites with Carbonyl Compounds

Various mechanistic pathways are possible for the foregoing reactions.

1. Initial attack by the phosphite on carbonyl oxygen.
2. Initial attack on carbonyl carbon with subsequent rearrangement to oxygen.
3. Attack by the phosphite on carbon of the carbonyl function with no rearrangement.

In such reactions the formation of open dipolar adducts (i.e., 1,3 dipoles and ylids), gives rise to fulvalenes and five-membered cyclic oxyphosphoranes in which the phosphorus is pentavalent.

Ramirez has postulated that trimethyl phosphite reacts with a number of para-quinones via attack on oxygen, giving rise to alkyl ethers of para-quinol phosphates (XLVII).[1-3]

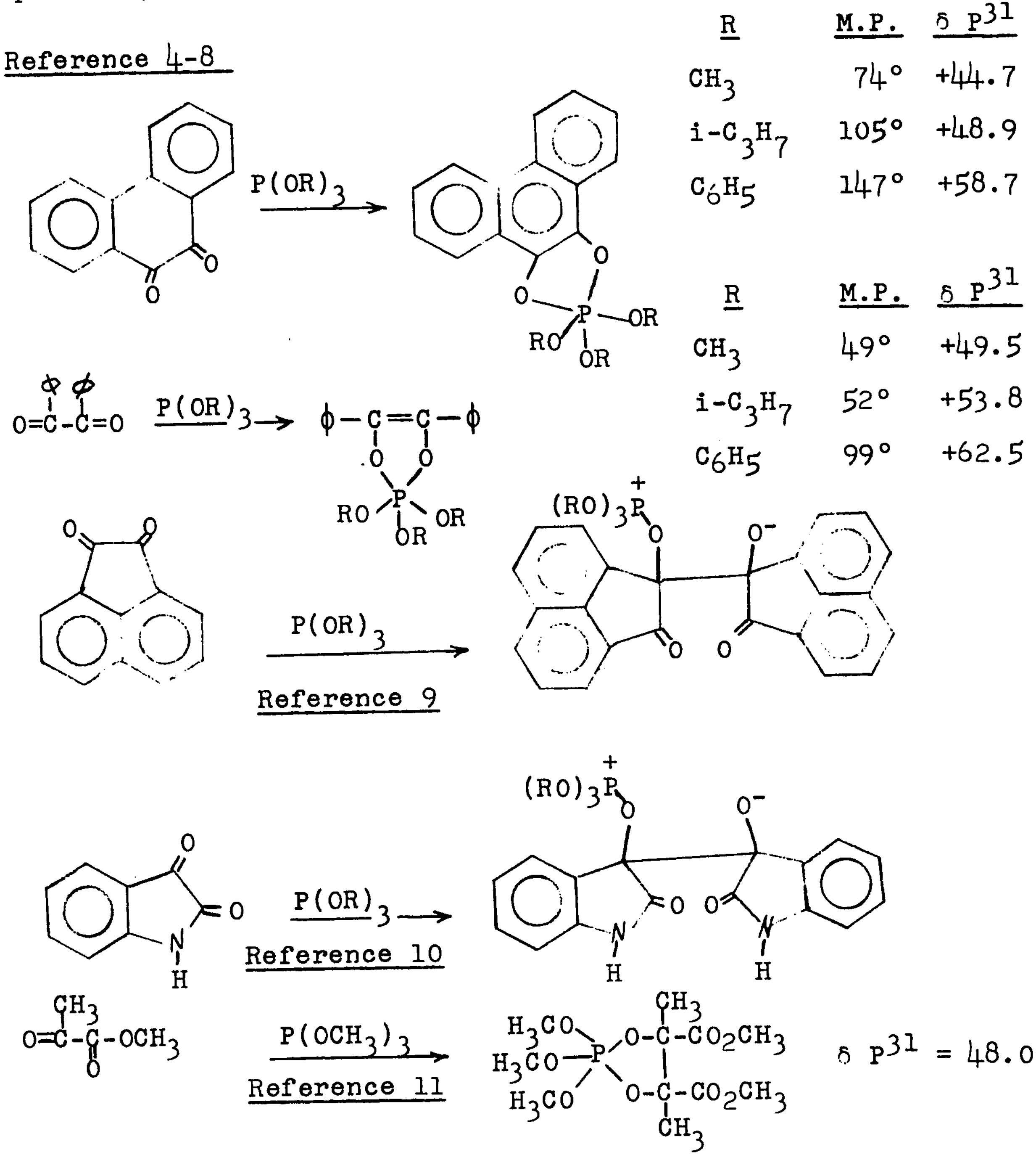


(XLVI) (XLVII)

R=R'=H, Cl or $CH_3$

R=Cl or $CH_3$; R'=H

Generalization of this type of reaction necessitated the examination of other dicarbonyl systems such as ortho-quinones, α-diketones and α-ketoesters with phosphites.



Reference 4-8

| R | M.P. | δ $P^{31}$ |
|---|---|---|
| $CH_3$ | 74° | +44.7 |
| i-$C_3H_7$ | 105° | +48.9 |
| $C_6H_5$ | 147° | +58.7 |

| R | M.P. | δ $P^{31}$ |
|---|---|---|
| $CH_3$ | 49° | +49.5 |
| i-$C_3H_7$ | 52° | +53.8 |
| $C_6H_5$ | 99° | +62.5 |

Reference 9

Reference 10

Reference 11

δ $P^{31}$ = 48.0

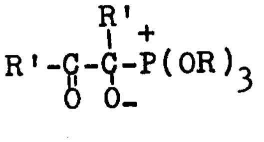
Figure 2. Examples of 1:1 and 2:1 Adducts

(δ $P^{31}$ in p.p.m. vs. 85% $H_3PO_4$)

The 1:1 and 2:1 adducts formed in the reaction of tertiary phosphite esters with ortho-quinones, α-diketones and α-halo-esters led Ramirez to ask the following structural questions:

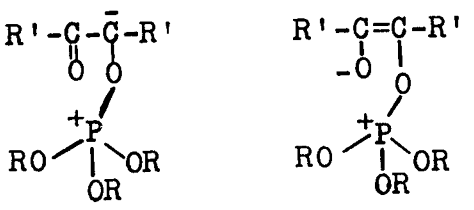
1. Is the initial step in the reaction mechanism a formation of a phosphorus-carbon bond or the formation of a phosphorus-oxygen bond?
2. Is the structure of the adducts an open dipolar form where phosphorus is tetravalent or is it the corresponding cyclic oxyphosphorane form where phosphorus is pentavalent?
3. Is the structural configuration of the cyclic oxyphosphorane formed, in a trigonal bipyramid or another type of configuration?

After considering questions 1 and 2, Ramirez directed an analysis of the following four possible structures for the adduct, as illustrated below:

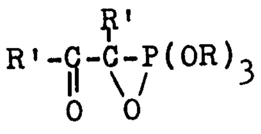


$R'-\underset{\underset{O}{\|}}{C}-\overset{\overset{R'}{|}}{\underset{\underset{O^-}{|}}{C}}-\overset{+}{P}(OR)_3$

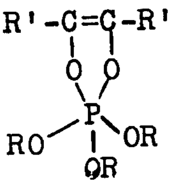
(XLVIII)



(XLIX)

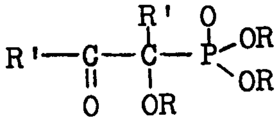


(L)

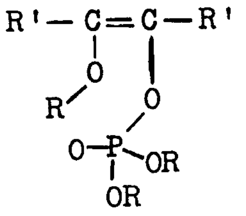


(LI)

The isomeric phosphate ester structures, LII and LIII, were also considered, since it has been shown previously that the occurrence of translocation[1-3] of alkyl groups in the reaction of trialkyl phosphites with para-quinones (XLVI-XLVII) is a common pathway,



(LII)



(LIII)

The adducts derived from the above systems, however, were characterized by the non-existence of translocation of alkyl groups as encountered in the para-quinone case.

After a thorough study of the infrared and Raman spectra, and of the proton and $P^{31}$ nuclear magnetic resonance spectra, Ramirez was led to the conclusion that the ortho-quinones, α-diketones, α-ketoesters and α,β-unsaturated ketone adducts have the structure of cyclic pentaoxyphosphoranes (i.e., the phosphorus is covalently bound to five oxygen atoms).

The signal given by the $P^{31}$ nucleus in the nuclear magnetic resonance (n.m.r.) spectrum appears at a much higher magnetic field in the adducts than in the reference compound (85 per cent phosphoric acid). The large positive chemical shifts in the phosphorane adducts has been attributed to the more effective shielding of the phosphorus nucleus in the adducts than in the reference compound. Table IX summarizes the chemical shifts of various phosphorus compounds.

Table IX.[27] General $P^{31}$ N.M.R. Shifts in P.P.M. V. 85% $H_3PO_4$ of Various Phosphorus Compounds

| | | | | |
|---|---|---|---|---|
| $(CH_3O)_3P$ | $(CH_3O)_3PO$ | $Cl_3P$ | $Cl_3PO$ | |
| -140.0 | +2.4 | -219 | -3 | |
| $(C_2H_5O)_3P$ | $(C_2H_5O)_3PO$ | $Cl_4P^+$ | $Cl_5P$ | $Cl_6P^-$ |
| -138 | +1.0 | -91 | +80 | +300 |

The proton n.m.r. spectrum of the biacetyl-trimethyl phosphite adduct[8] (a representative member of a cyclic oxyphosphorane) showed a doublet at 6.56 $\tau$ ($J_{HP}$ = 13.0 c/s) for the methoxyl protons due to coupling with the phosphorus nucleus (*i.e.*, since the $P^{31}$ nucleus has a magnetic moment with a spin number I=1/2). The two equivalent methyl groups attached to an olefinic carbon gave a single peak at 8.25 $\tau$. Only eight of the ten peaks were observed by Ramirez for the 1:1 biacetyl-trimethyl phosphite adduct. This was an unexpected result, since the phosphorus nucleus is coupled to the nine methoxyl-protons.

The absence of a strong carbonyl band in the infrared spectrum of 1:1 biacetyl-trimethyl phosphite adduct excludes structures XLVIII, L, and LII from further consideration. These structures have been proposed by Kukhtin and his Russian co-workers[12-14] in their earlier papers. However, it appears that these investigators now favor the five-membered cyclic oxyphosphorane structure.[15-18]

The phosphoryl (P-O) stretching vibration in phosphate esters gives rise to a strong band in the infrared region between 7.42-8.00 μ (1350-1250 $cm^{-1}$). Although the 1:1 biacetyl adduct shows bands in this region, their shape and intensity are not of a typical phosphate ester. It was reported that the $P\text{-}O\text{-}CH_3$ group of trimethyl phosphate has a strong absorption in the infrared in the region of 9.55 μ (1045 $cm^{-1}$). The strongest bands of the 1:1 biacetyl adduct are at 9.18 μ (1090 $cm^{-1}$) and 9.30 μ (1075 $cm^{-1}$), significantly lower than the band of trimethyl phosphate. Structure LIII, which is a methyl phosphate ester, is inconsistent with the infrared spectrum of the 1:1 biacetyl adduct. Kukhtin and co-workers have advocated structure LIII in some of their publications.[12-14] The weak olefinic peak (C=C) in the infrared gave rise to a relatively strong and polarized Raman line spectrum as expected[19] for the 1:1 adduct LI.

The molecular structure of the phenanthrenequinone-triisopropyl phosphite adduct has recently been determined by X-ray analysis.[20] The molecule in the crystal form was found to be a nearly perfect trigonal bipyramid with the phosphorus atom at its center, the phenanthrene ring attached to one basal ($O_5$) and one apical ($O_2$) oxygen atom, and the isopropyl groups attached to the remaining two basal and one apical oxygens.

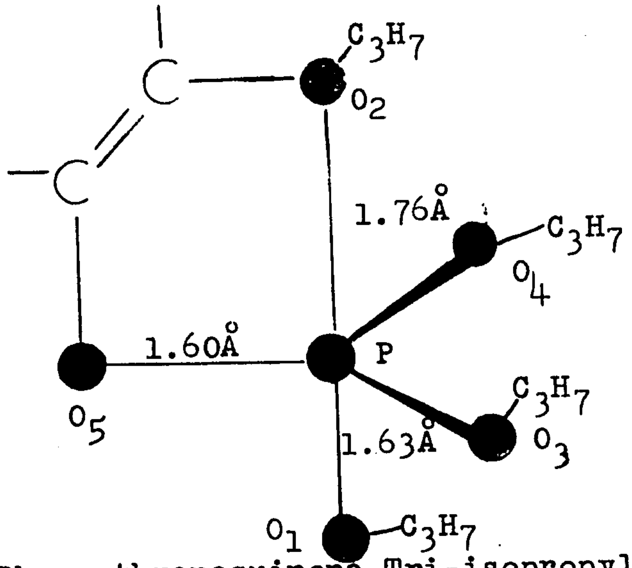
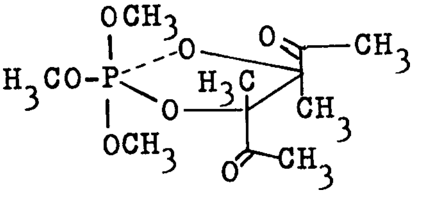
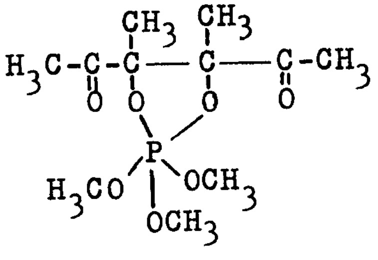


Figure 3. Phenanthrenequinone Tri-isopropyl Phosphite Pentaoxyphosphorane

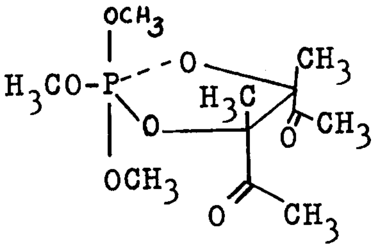
A new type of reductive carbon-carbon condensation was obtained when the 1:1 biacetyl-triethyl phosphite adduct was further reacted with a second molecule of biacetyl.[21] The 2:1 biacetyl-trimethyl phosphite adduct (LIV) has the structure of a cyclic saturated pentaoxyphosphorane.



racemic

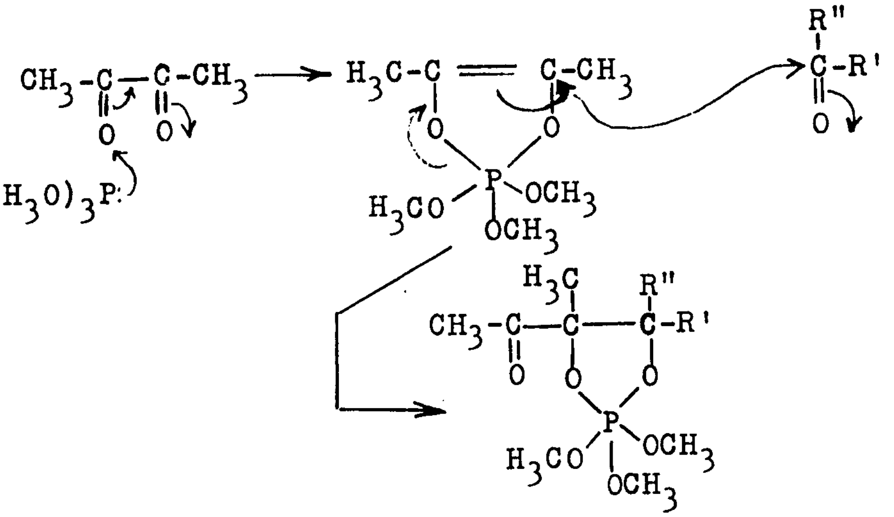


(LIV)

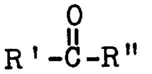


meso

The meso form was obtained in 80 per cent yield and the racemic form in 20 per cent yield. This stereoselective, reductive, carbon-carbon condensation of carbonyl compounds was extended to a number of systems. Ramirez postulated that the mechanism of reaction involves an attack of phosphorus on oxygen. The driving force is the formation of a cyclic unsaturated pentaoxyphosphorane, followed by a nucleophilic addition of carbon to a carbonyl function. The net result is the conversion of an unsaturated into a saturated oxyphosphorane (eqn. 46).

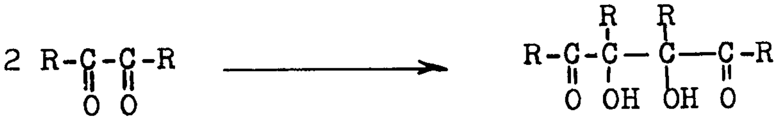


(46)

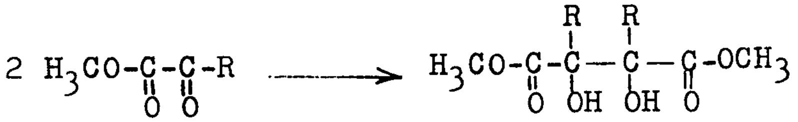


$R'-\overset{\overset{O}{\|}}{C}-R''$ = hexafluoracetone, trifluoroacetone, cyclohexanone, cyclobutanone, acetophenone, p-nitroacetophenone[29]

A significant result of this investigation is the formation of a diketol from an α-diketone and a trialkyl phosphite after hydrolysis.[21]



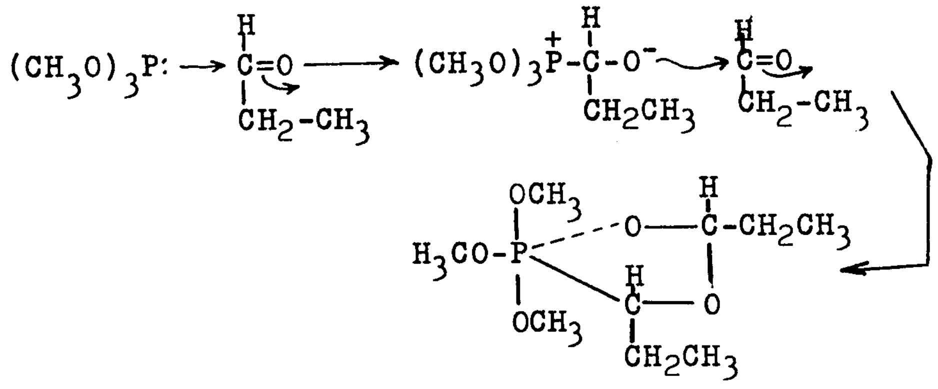
$$2\ R-\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}-R \longrightarrow R-\underset{\underset{O}{\|}}{C}-\overset{R}{\underset{OH}{C}}-\overset{R}{\underset{OH}{C}}-\underset{\underset{O}{\|}}{C}-R \qquad (47)$$



$$2\ H_3CO-\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}-R \longrightarrow H_3CO-\underset{\underset{O}{\|}}{C}-\overset{R}{\underset{OH}{C}}-\overset{R}{\underset{OH}{C}}-\underset{\underset{O}{\|}}{C}-OCH_3 \qquad (48)$$

The proposed attack by phosphorus of the phosphite on the oxygen of the carbonyl group occurs whenever a negative charge on the carbonyl carbon may be stabilized by resonance as in para-quinones, ortho-quinones, α-diketones and α-keto-esters.

Simple aliphatic aldehydes were thought to react with phosphites via attack on the carbon of the aldehyde by phosphorus to form a 1:1 adduct. The 1:1 adduct, however, was not isolated, since it readily combines with a second molecule of the aldehyde to form a 2:1 adduct. The 2:1 adduct gives a cyclic tetraoxyalkylphosphorane, which is a new example of a pentacovalent phosphorus compound[22] (eqn. 49).

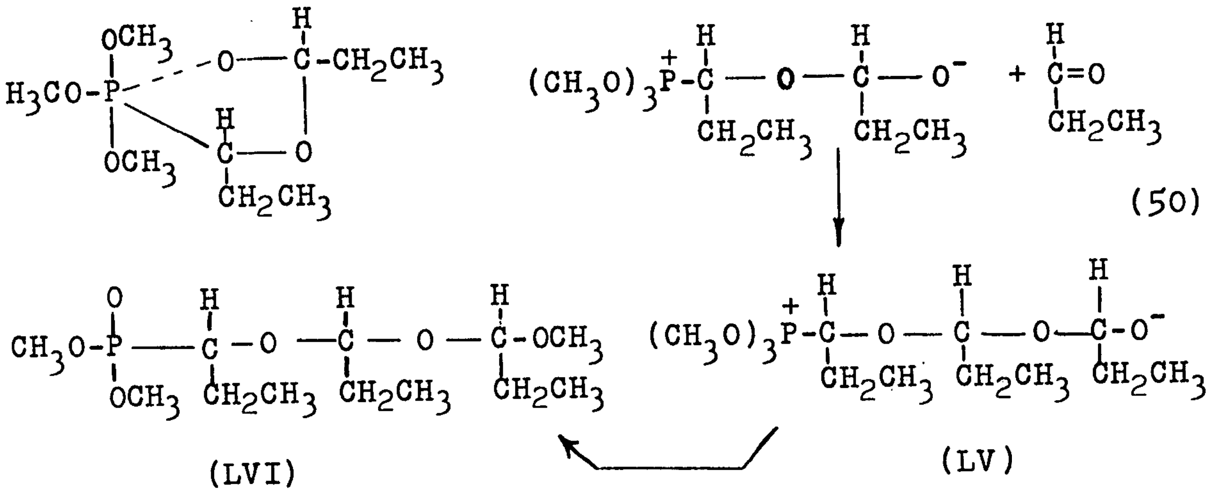


(49)

2 isomers

The 2:1 adduct undergoes an extremely slow reaction with a third molecule of aldehyde to yield an open chain 3:1 adduct (LV). The 3:1 dipolar adduct is further subjected to an

Arbusov cleavage to yield a 3:1 acetal phosphonate (LVI).[22]

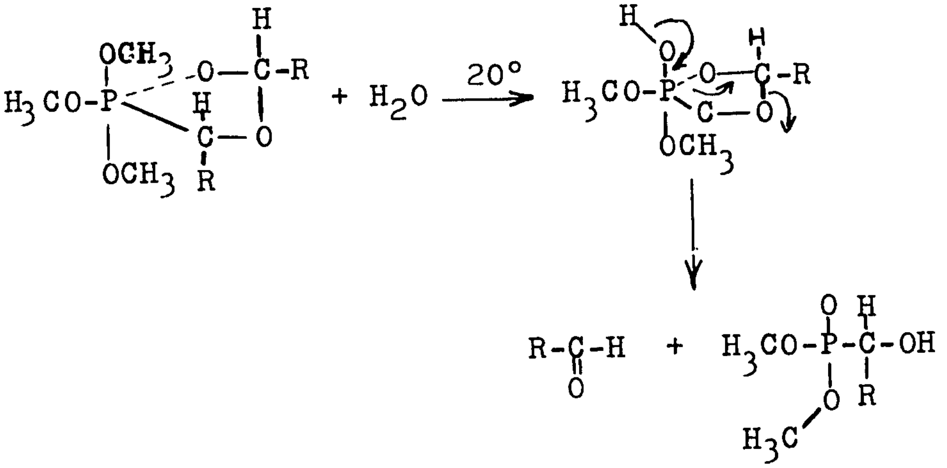


(50)

(LVI)

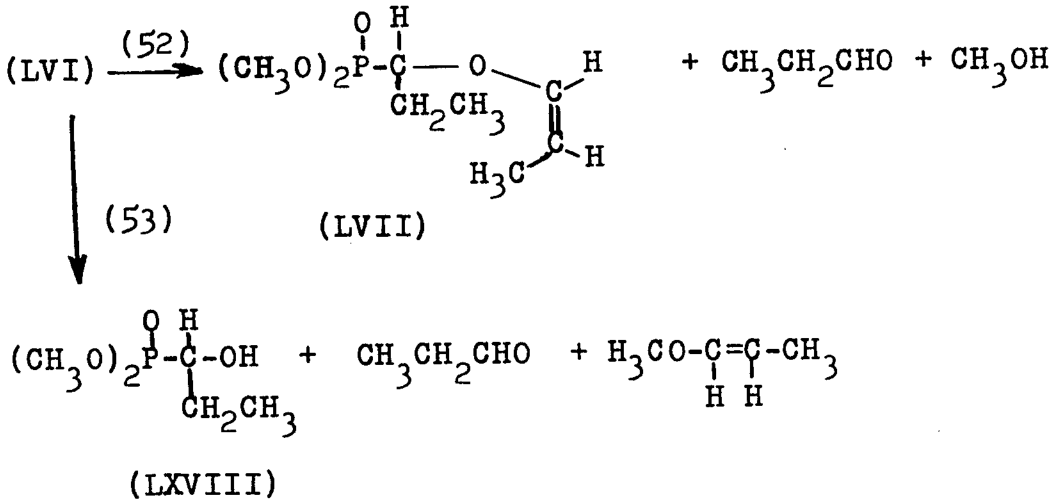
(LV)

The tetraoxyalkylphosphorane is sensitive to hydrolysis by water to yield the parent aldehyde and an α-hydroxyphosphonate.



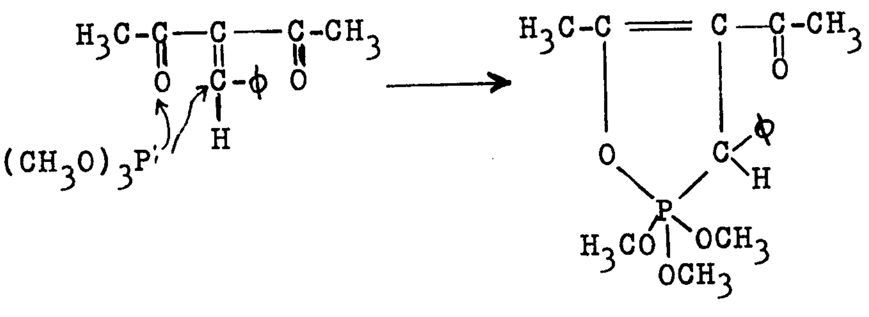
The 3:1 acetal phosphonate (LVI) is capable of thermal decomposition. This decomposition yield a complex mixture of products.[22,23] For this reason it is best to carry out phosphite-carbonyl condensation reactions under mild conditions. Some of the decomposition products were found to be a propenyl ether of the 1:1 α-hydroxyphosphonate (LVII), propionaldehyde,

1:1 α-hydroxyphosphonate (LVIII), methyl propenyl ether and products thereof.



Examples of trialkyl phosphites with aromatic aldehydes have also been reported.[24,25] It is interesting to note that aliphatic aldehydes on reaction with phosphites did not involve deoxygenation or alkyl group translocation at the 1:1 and the 2:1 stages.

In the case of α,β-unsaturated ketones the phosphorus is capable of forming a cyclic oxyphosphorane by either initial attack on oxygen or on the carbon of the ethylenic function. Trimethyl phosphite reacts with 3-benzylidene-2,4-pentanedione at room temperature to yield a tetraoxyalkylphosphorane (LIX).[22]

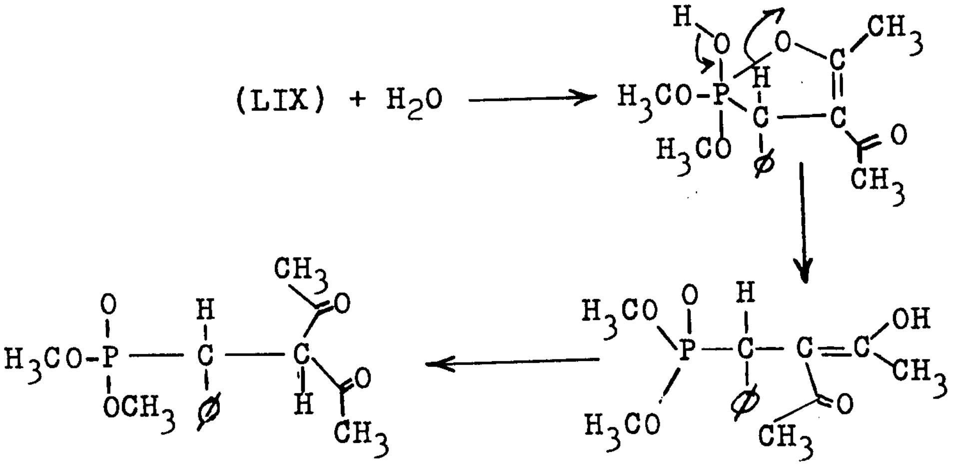


(LIX)

(54)

$\delta$ $P^{31}$ = 27.89 p.p.m. vs. 85% $H_3PO_4$

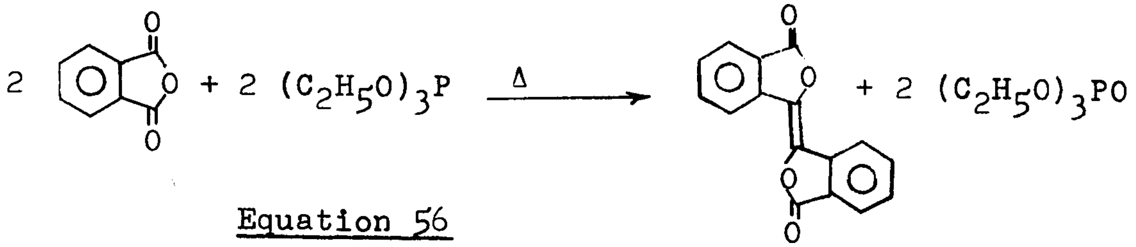
The 1:1 adduct (LIX) is readily hydrolyzed to give an isolable labile enol-phosphonate (LX) and a diketo-phosphonate (LXI).



(LXI) (LX)

(55)

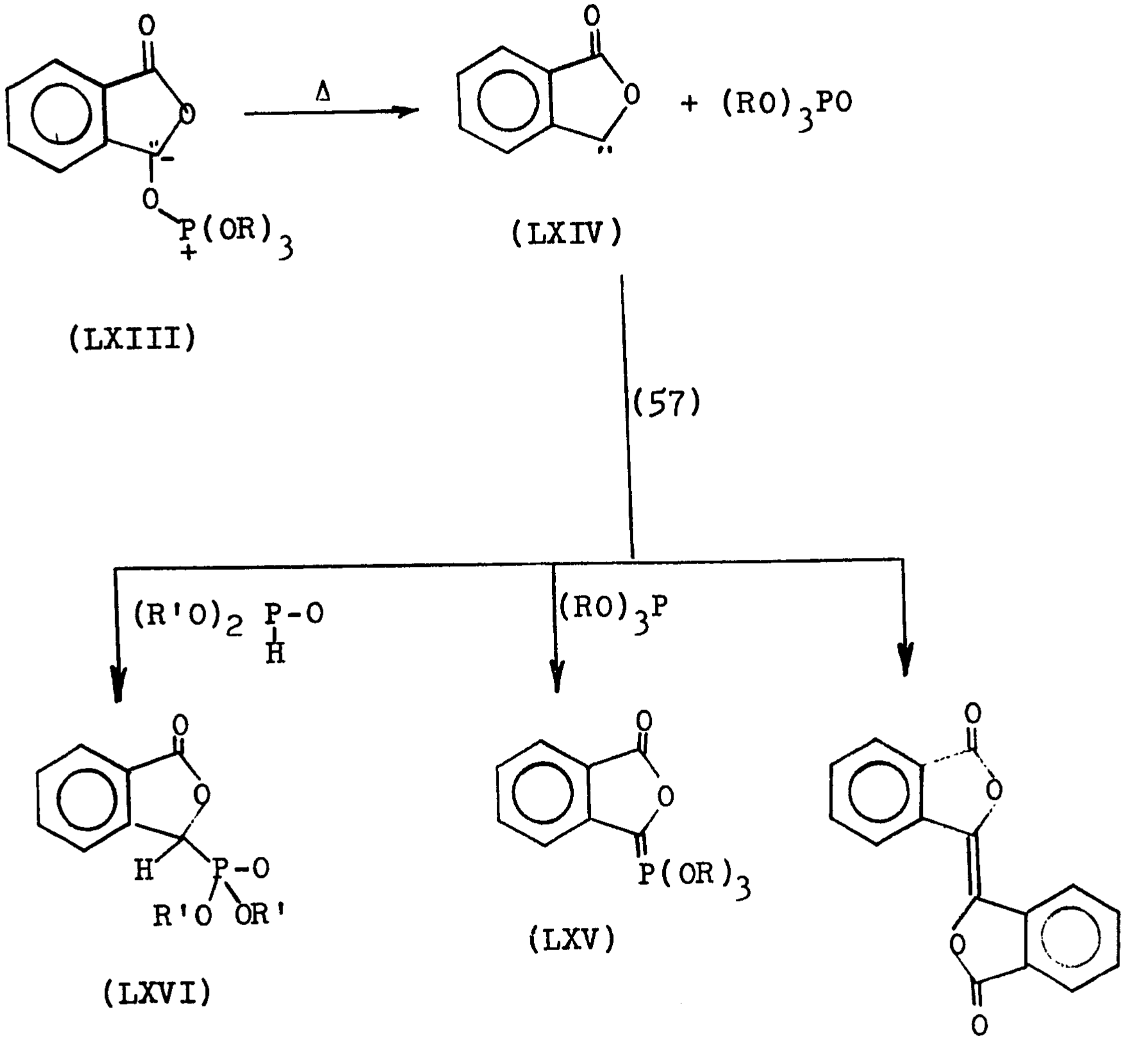
Cyclic aromatic anhydrides react with triethyl phosphite to yield biphthalyls.[26]



Equation 56

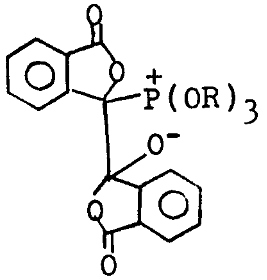
(LXII)

Ramirez originally proposed a possible mechanism for the formation of biphthalyl (LXII). The proposed mechanism involves an attack on the oxygen by phosphorus to produce the 1,3 dipole, 1:1 adduct (LXIII). The 1:1 adduct then loses trialkyl phosphate to give a carbene LXIV.



(LXIII) (LXIV) (LXVI) (LXV) (LXII)

The carbene is then able to dimerize to yield biphthalyl (LXII), or be trapped by excess phosphite to give a phosphite-methylene (LXV). The reaction of phthalic anhydride with dialkyl phosphites has led to phthalide phosphonates (LXVI) as products rather than biphthalyl. The phosphitemethylene (LXV) can react with another mole of anhydride to give biphthalyl (LXII) *via* the Wittig intermediate (LXVII).



(LXVII)

It is worth noting that the workers were unsuccessful in their attempts to trap the carbene by conventional methods (*e.g.*, olefins and secondary amines).

# References

1. F. Ramirez and S. Dershowitz, J. Org. Chem., 22, 856 (1957).

2. F. Ramirez and S. Dershowitz, J. Am. Chem. Soc., 81, 587 (1959).

3. F. Ramirez, E. H. Chen, and S. Dershowitz, ibid., 81, 4338 (1959).

4. F. Ramirez, R. B. Mitra, and N. B. Desai, ibid., 82, 2651 (1960).

5. F. Ramirez, N. B. Desai, J. Am. Chem. Soc., 82, 2652 (1960).

6. F. Ramirez, R. B. Mitra, and N. B. Desai, ibid., 82, 5763 (1960).

7. F. Ramirez, N. B. Desai, and R. B. Mitra, ibid., 83, 492 (1961).

8. F. Ramirez and N. B. Desai, ibid., 85, 3252 (1963).

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

10. A. Mustafa, M. M. Sidky and F. M. Soliman, Tetrahedron, 22, 393 (1966).

11. A. N. Pudovik and I. V. Konovalova, Zh. Obsh. Khim., 33, 3100 (1963).

12. V. A. Kukhtin, Kokl. Akad. Nauk. USSR, 121, 466 (1958); 53, 1105b (1959).

13. V. A. Kukhtin and J. Orekova, Zh. Obsh. Khim., 30, 1208 (1960), J. Gen. Chem., USSR, 30, 1229 (1960); Chem. Abstr., 55, 358i (1961).

14. V. A. Kukhtin, K. M. Kirillova, and R. R. Shagidullin, Zh. Obsh. Khim., 32, 649 (1962); Chem. Abstr., 58, 546h (1963).

15. V. A. Kukhtin, K. M. Kirillova, R. R. Shagidullin, Yu. Yu. Samitov, N. A. Lyazima, and N. F. Rahova, Zh. Obsh. Khim., 32, 2039 (1962); Chem. Abstr., 58, 4543a (1963).

16. V. A. Kukhtin, T. N. Voskoboeva, and K. M. Kirillova, J. Gen. Chem., USSR, 32, 2300 (1962).

17. K. M. Kirillova and V. A. Kukhtin, J. Gen. Chem., USSR, 32, 2305 (1962).

18. V. A. Kukhtin and K. M. Kirillova, J. Gen. Chem., USSR, 32, 2755 (1962).

19. R. C. Gore and E. S. Waight in "Determination of Organic Structures by Physical Methods," Vol. 1; Academic Press. Inc., New York, N. Y., 1955, ch. 6.

20. W. C. Hamilton, S. LaPlaca, and F. Ramirez, J. Am. Chem. Soc., 87, 127 (1965).

21. F. Ramirez, N. Ramanathan, and N. B. Desai, J. Am. Chem. Soc., 85, 3465 (1963).

22. F. Ramirez, A. V. Patwardhan, and S. R. Heller, J. Am. Chem. Soc., 86, 514 (1964).

23. V. A. Ginsburg and A. Ya. Yakubovich, J. Gen. Chem., USSR, 30, 3936 (1960).

24. A. Arbuzov and V. M. Zoroastrova, Izv. Akad. Nauk., USSR, Otd. Khim. Nauk. 1030 (1960).

25. V. A. Kukhtin and K. M. Kirillova, J. Gen. Chem., USSR, 31, 2078 (1961), Zh. Obsh. Khim., 31, 2226 (1961).

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

27. R. A. Y. Jones and A. R. Katritzky, Angew. Chem. Internat. Edit. 1, 32 (1962).

28. F. Ramirez, Pure and Applied Chemistry, 9, 337 (1964).

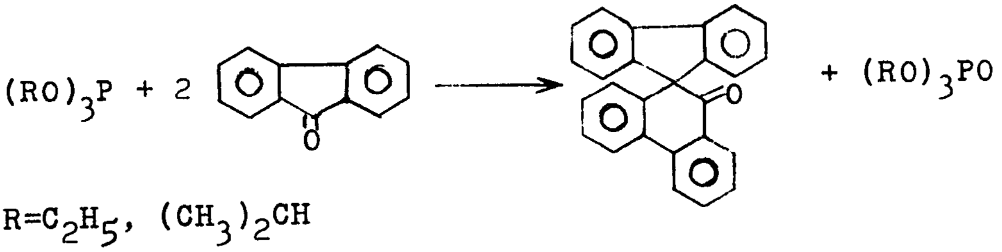
29. F. Ramirez, A. V. Patwardhan, and C. P. Smith, J. Org. Chem., 31, 3159 (1966).

## RESULTS AND DISCUSSION II

Related to the preceding research program (Part I) is a project involving the study of the reactions of trivalent phosphorus compounds with cyclopentadienone derivatives under a variety of conditions. Research dealing with the chemistry of the reactions of mono-ketones with tertiary phosphites and phosphines was the next natural area to be investigated, so that the necessary conditions for nucleophilic attack of trivalent organophosphorus compounds at the carbonyl site could be further defined. It was readily apparent that various interesting mechanistic pathways can be utilized by phosphorus to form condensation products with carbonyl compounds. The objective of the work in this part is to link the information obtained from the preceding research project in order to shed light on the mechanistic course of general nucleophilic phosphorus reactions.

The reactions of cyclopentadienones with trivalent phosphorus has led to the discovery of novel pentacovalent phosphorus compounds: the oxyphosphoranes. Since in cyclopentadienone systems nucleophilic attack by phosphorus on oxygen is feasible the highly exciting chemistry of ylids, 1,3-dipoles, carbenes and fulvalenes promised to receive our attention.

Trialkyl phosphites react with fluorenones to give appreciable quantities of 9-diphenylenephenanthrones and small amounts of di-biphenyleneethenes. Thus, triisopropyl phosphite[1] (as does triethyl phosphite on reaction with fluorenone) gives 9-diphenylenephenanthrone (LXVIII) in 44% and 62% yields, respectively.

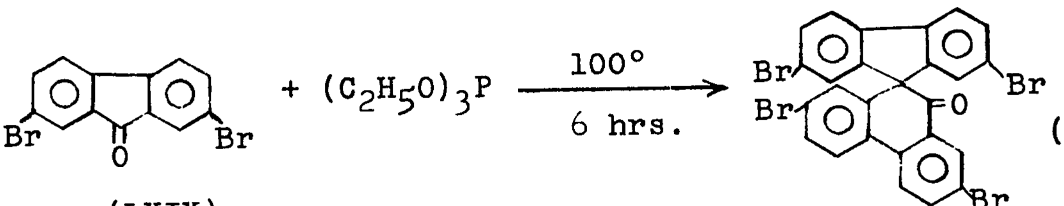


(LXVIII)

(58)

Evidence is now presented which indicates that the formation of 9-diphenylenephenanthrone occurs by way of a novel closed cyclic oxyphosphorane intermediate. Furthermore, it is postulated that cyclic oxyphosphorane formation most likely proceeds by initial phosphite attack at carbonyl oxygen followed by condensation at the carbonyl carbon with another fluorenone molecule.

2,7-Dibromofluorenone (LXIX) reacts with triethyl phosphite without solvent at 100° for 6 hours to give 2,7,2',7'-tetrabromo-9-diphenylenephenanthrone (LXX) in a 58% yield.

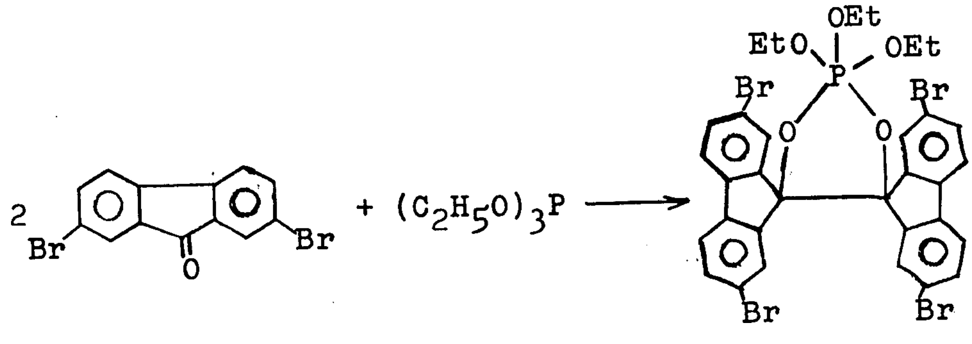


(LXIX)

(LXX)

(59)

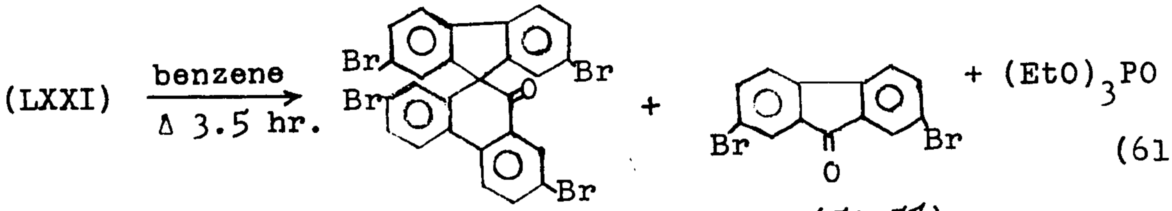
The neat reaction of 2,7-dibromofluorenone (LXIX) with triethyl phosphite at just above room temperature (25-50°) leads to the formation of the corresponding 2:1 adduct LXXI in a 90% yield. The reaction is clean, rapid, and gives high yields provided the phosphite is pure and there is no moisture, oxygen or light present.



(60)

(LXXI)

The 2,7-dibromofluorenone-triethyl phosphite adduct LXXI on refluxing in benzene (dielectric constant 2.28)[2] readily gives 2,7,2',7'-tetrabromo-9-diphenylenephenanthrone (LXX), 2,7-dibromofluorenone and triethyl phosphate.



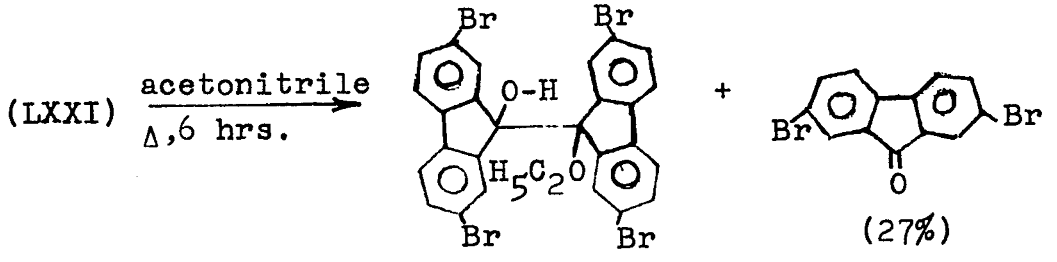
(61)

(42%)

(LXX)

(50.5%)

Refluxing LXXI in the presence of a more polar solvent such as acetonitrile (dielectric constant 37.5)[2] yields the postulated 9-hydroxy-9'-ethoxydifluorene (LXXII) and 2,7-dibromofluorenone.



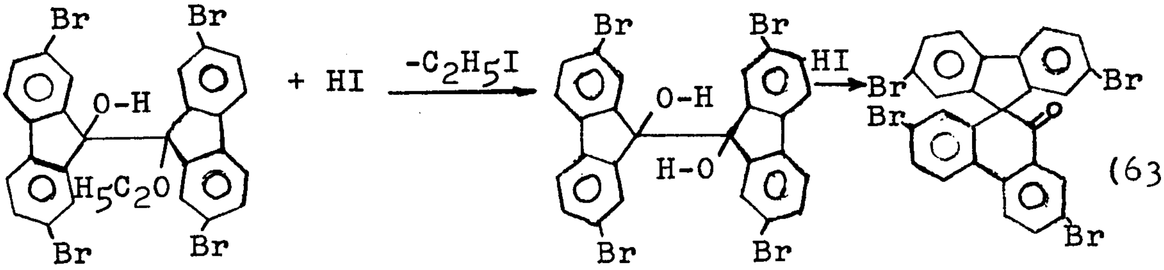
(32%)

(LXXII)

(27%)

(62)

The postulated structure LXXII is found to be slowly converted quantitatively into 2,7,2',7'-tetrabromo-9-diphenylenephanthrone (LXX) in refluxing hydriodic acid.

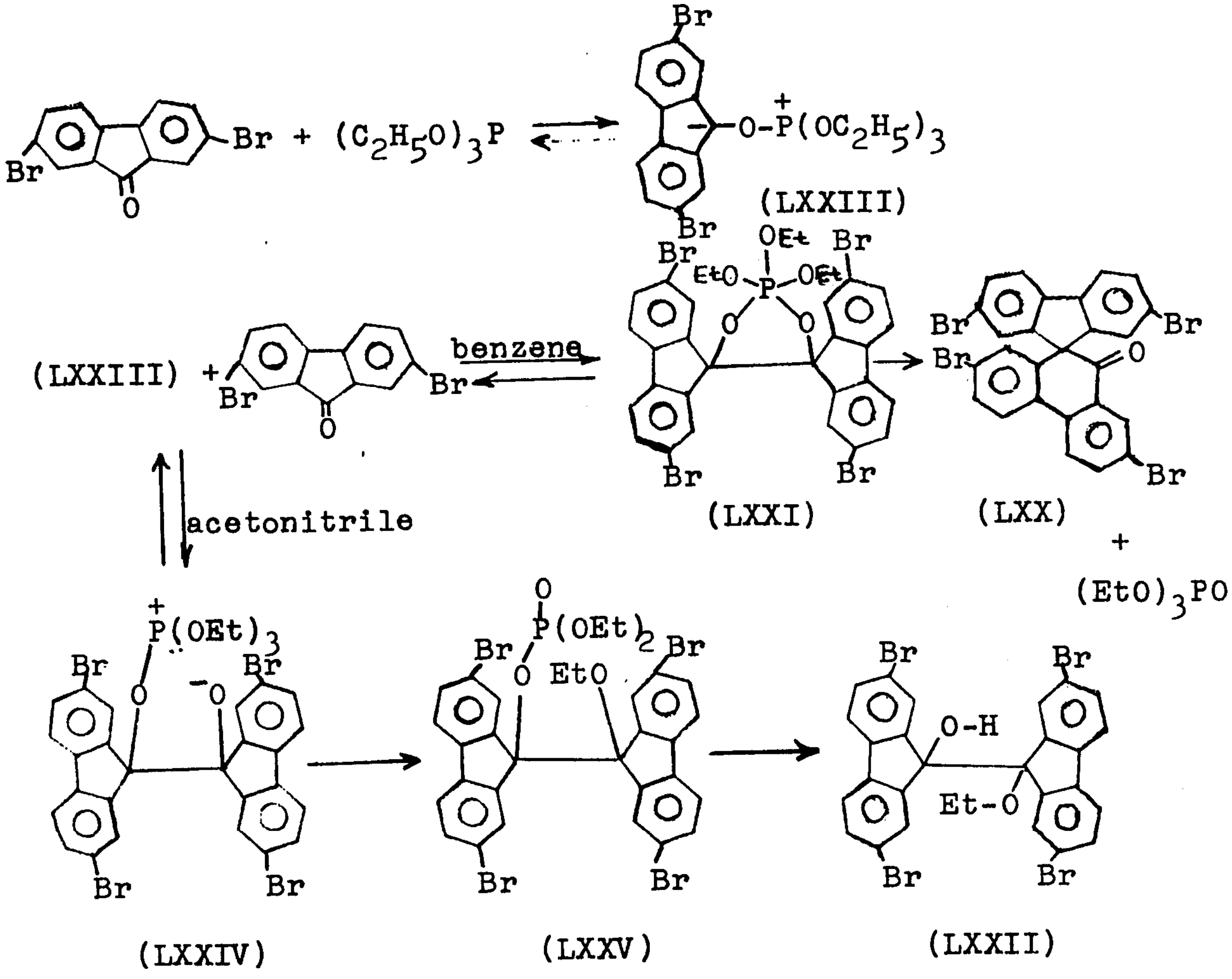


(63)

(LXXII)

(LXX)

The following mechanistic pathway is presented to explain the observations in the foregoing reactions.

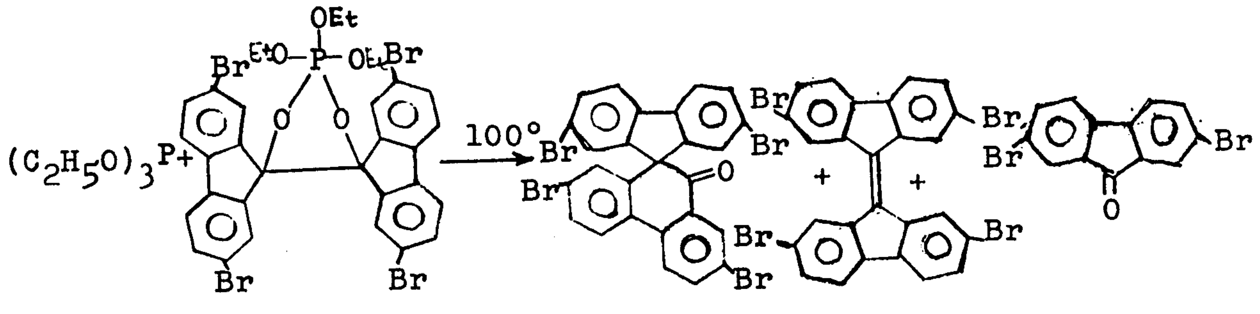


The formation of an intramolecular 1,3-dipolar phosphonium salt LXXIII is suggested as an initial step. Ramirez and others[3] have similarly proposed an analogous intermediate in the synthesis of cyclic oxyphosphoranes derived from reaction of trialkyl phosphites with α-diketones, α-ketoesters, ortho-quinones, α, β-unsaturated ketones, para-quinones, and cyclic aromatic anhydrides.[4]

Isolable adducts of 1,2-diketones and quinones with phosphorus covalently bonded to oxygen have been reported. The reactions of simple monoketones with tricovalent phosphites and phosphines have not been reported.[5]

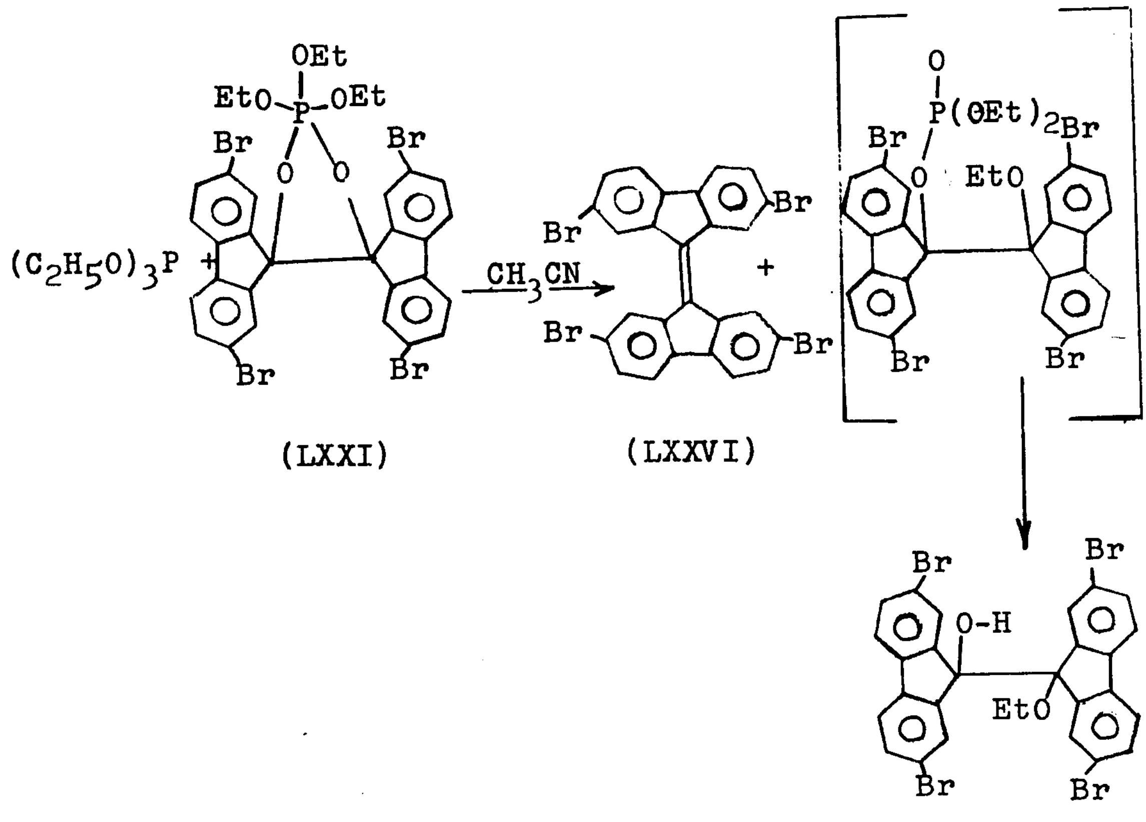
The intramolecular formation of the isolable closed cyclic oxyphosphorane most likely forms in the second step of the reaction. The final cyclic pinacolone LXX is simply obtained _via_ an intermediate intermolecular ring expansion in a non-polar medium such as benzene or triethyl phosphite. Structure LXXII is interpreted to come about _via_ the "open" dipolar form LXXIV which undergoes an alkyl group migration to give the phosphate ether LXXV prior to the postulated formation of LXXII. The formation of the postulated phosphonium alkoxide (LXXIV) should be promoted in a polar medium such as acetonitrile. Further experimental evidence consistent with the above interpretations is found in the reaction of oxyphosphorane (LXXI) with neat triethyl phosphite and in another reaction of LXXI with triethyl phosphite in the presence of acetonitrile.

Thus, the reaction of the 2:1 adduct LXXI with neat triethyl phosphite at 100° for six hours yields phenanthrone (LXX) (20%), di-biphenyleneethene (LXXVI) (14%) and 2,7-dibromofluorenone (3%), while the reaction of the adduct LXXI with triethyl phosphite in the presence of refluxing acetonitrile gives di-biphenyleneethene (LXXVI) (32%) and the postulated 9-hydroxy-9'-ethoxy difluorene (LXXII) (11%).



(LXXI) (LXX) (LXXVI)

Equation 64



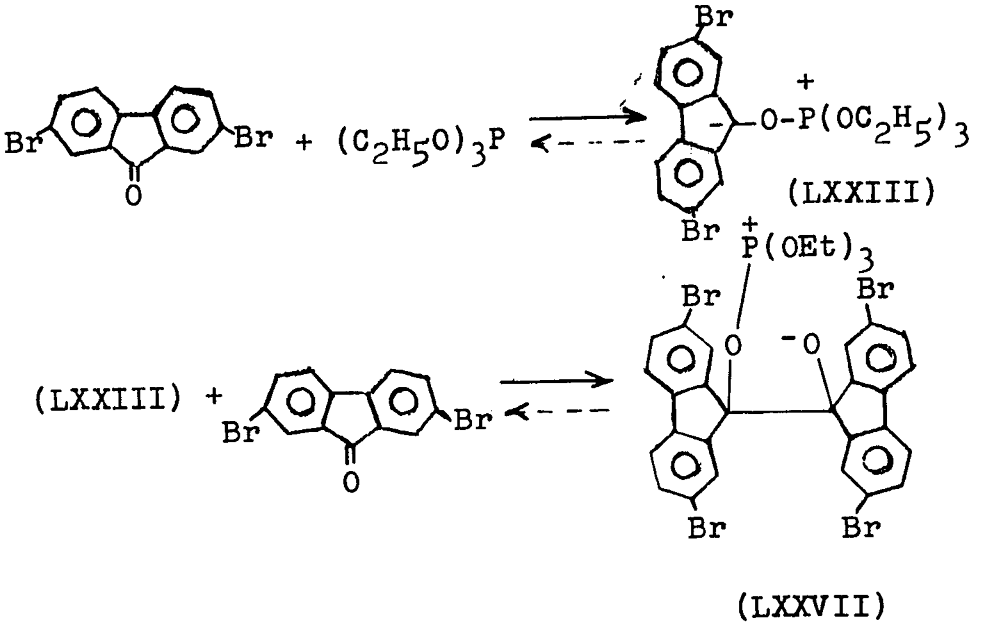
(LXXI) (LXXVI)

(LXXII)

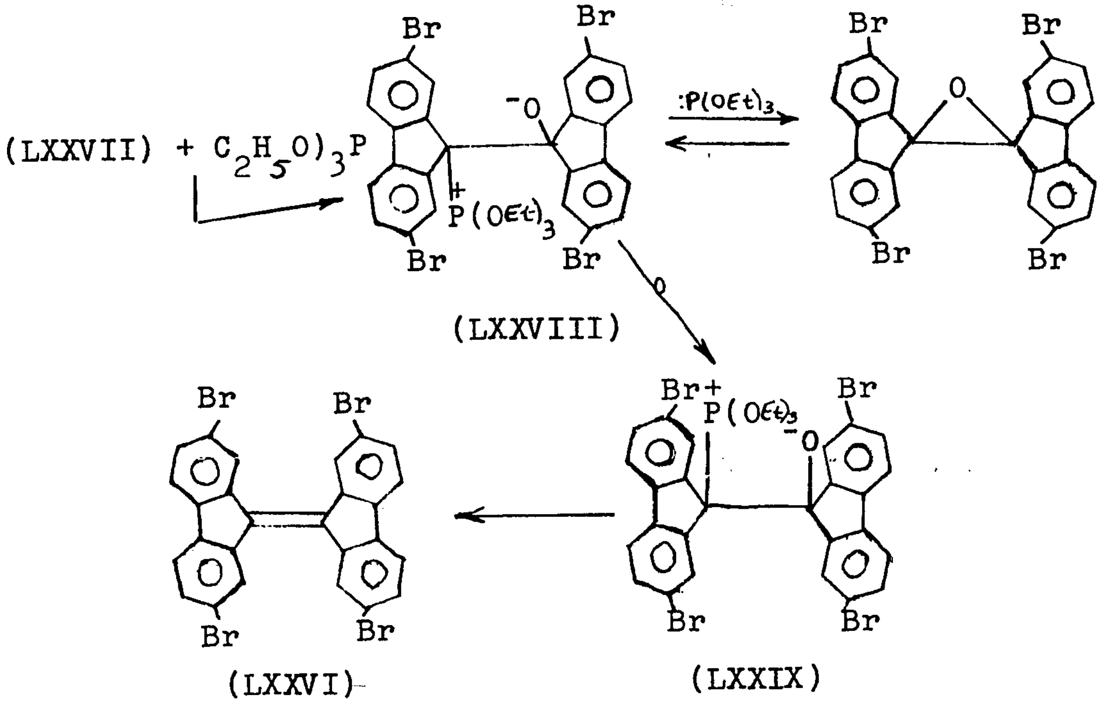
Equation 65

Several possible mechanistic pathways explaining the observed fulvalene formation in the above phosphite runs is presented, viz.,

Pathway 1:

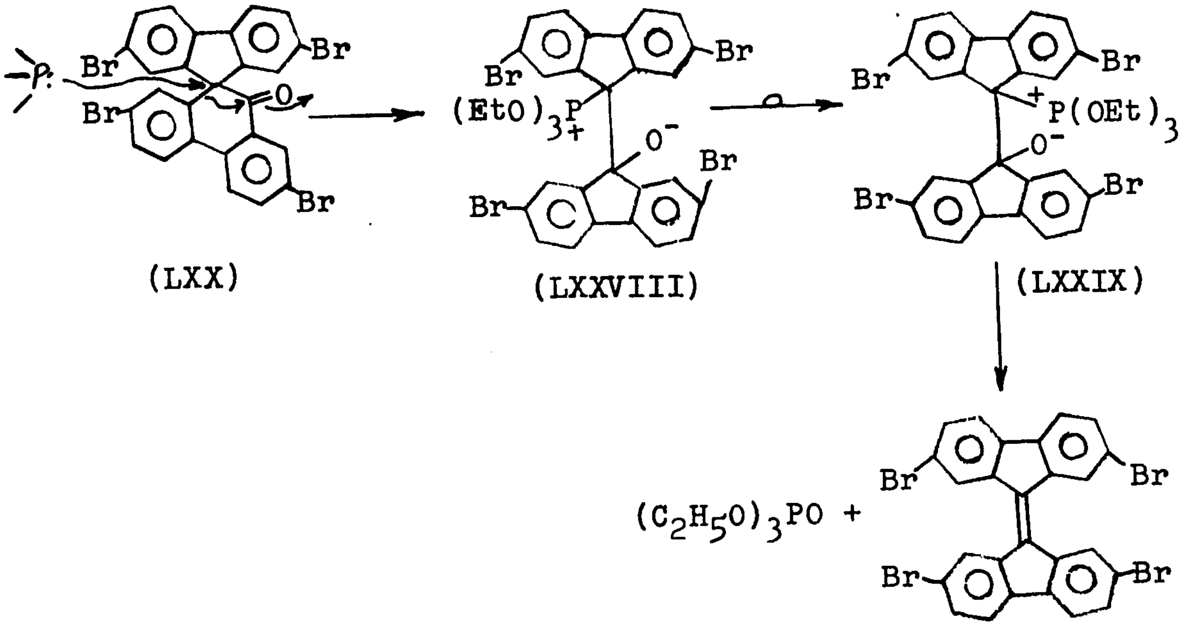


Equation 66



Equation 67

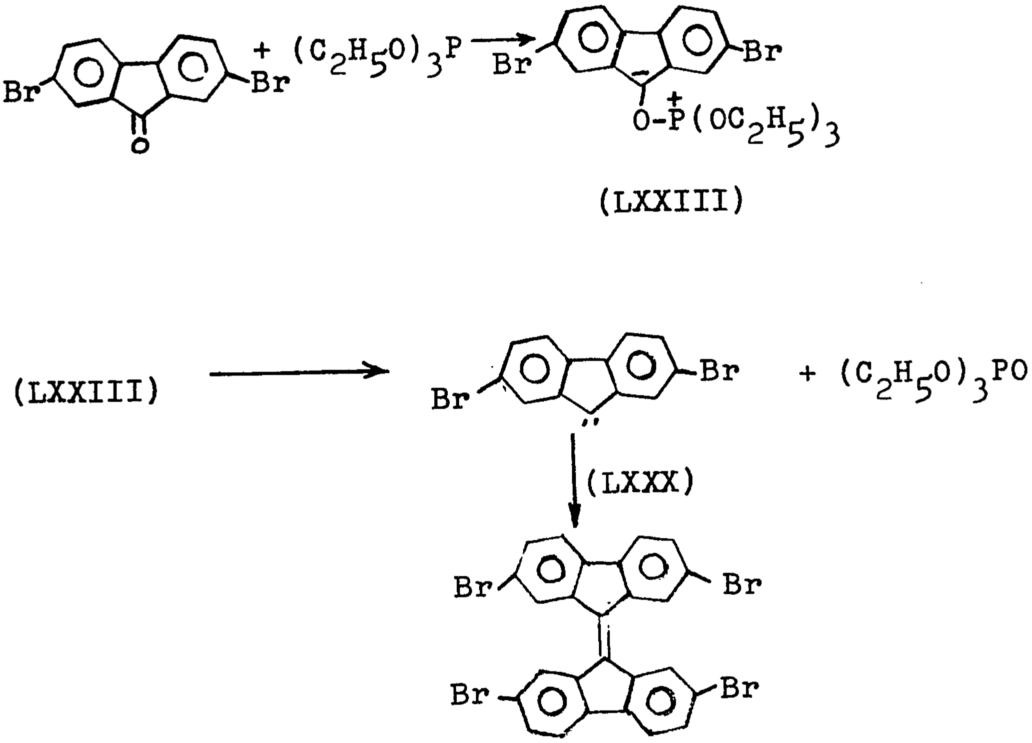
Pathway 2:



(LXXVI)

Equation 68

Pathway 3:



Equation 69

(LXXVI)

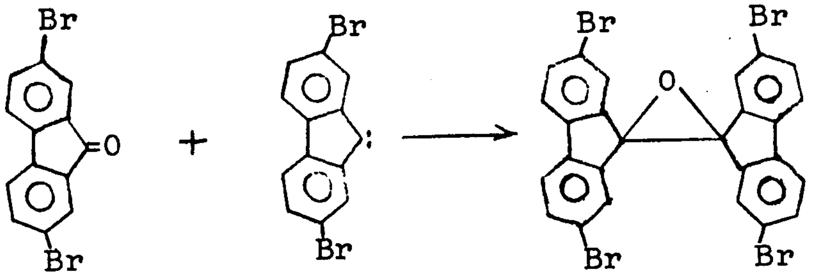
In pathway 1 the suggested phosphonium salt LXXIII reacts with another molecule of ketone to give the phosphonium alkoxide LXXVII. Triethyl phosphite then acts upon the speculated open dipolar species LXXVII, yielding a new carbon-phosphorus bonded species LXXVIII by ejection of triethyl phosphate. The Wittig intermediate LXXVIII thus formed undergoes rearrangement into LXXIX which then deoxygenates by way of a four-centered cyclic mechanism as in the terminating step of the Wittig reaction, yielding a fulvalene.

The reaction of 2,7,2',7'-tetrabromo-9-diphenylenephenanthrone with triethyl phosphite at 100° for 24 hours gives back quantitatively unreacted starting materials. Thus, this result eliminates pathway 2 (i.e., the mechanism involving cleavage at the spiro junction) from further consideration.

Pathway 3 proposes a mechanism involving the initial formation of the 1,3 dipole, 1:1 adduct LXXIII which then loses trialkyl phosphate to give carbene LXXX. The carbene is then able to dimerize to yield the appropriate fulvalene. As a consequence of the results obtained by the investigations carried out by Poshkus, Ramirez and in this laboratory, it is unlikely that carbenes are intermediates in phosphite-ketone reactions. Arguments against carbene formation are as follows:

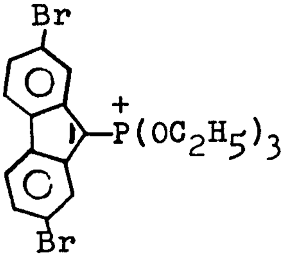
1. Other workers have been unsuccessful in their attempts to trap the carbene intermediates by conventional methods (e.g., olefins, secondary amines and phosphites).

2. Epoxide formation is not observed, even when an excess of the ketone is present.



(70)

3. Reactions carried out in excess phosphite did not yield the methylene trialkoxyphosphorane ylid, which would



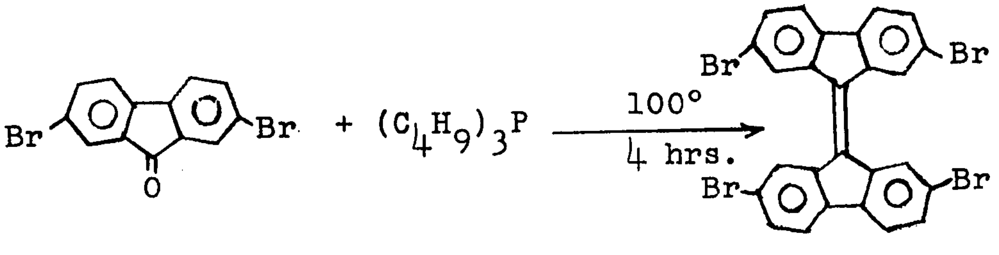
come about by combination of the carbene with the phosphite. This is, however, an unlikely product to isolate.

4. Poshkus[1] observed that the relative amount of fulvalene formed is unchanged whatever the mole ratio of reactants that are used.

The above reasonable expectations are not supported by experimental data, and thus pathway 3 is probably not operative. Pathway 1 is suggested as the most likely mechanism to accommodate the observed experimental data.

The lack of literature on oxyphosphoranes derived from phosphines prompted the investigation of the reaction of tributylphosphine with fluorenones. As a consequence of this investigation, a one-step fulvalene synthesis was developed.

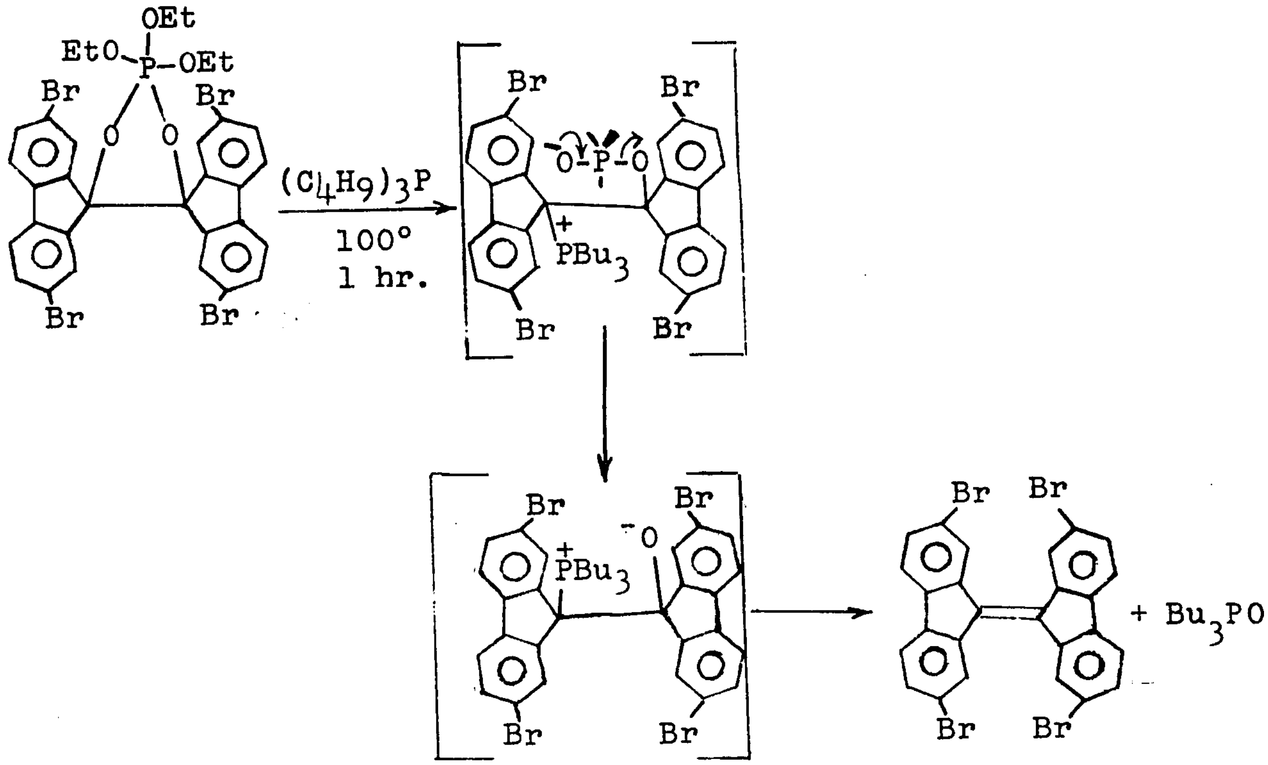
Thus, 9-fluorenone gave di-biphenyleneethene (40%) and unreacted 9-fluorenone (42%), while the more reactive 2,7-dibromofluorenone yielded 2,7,2',7'-tetrabromo-di-biphenyleneethene (LXXVI) in a 64% yield.



(71)

(LXXVI)

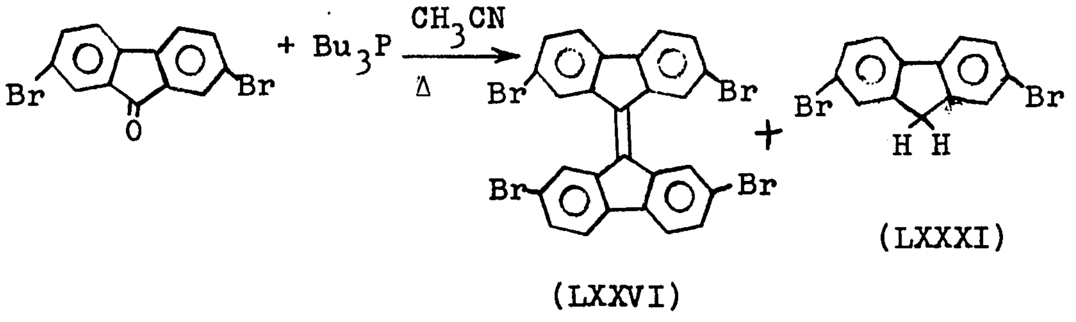
The advantage of the great nucleophilic power of tributylphosphine was utilized by converting the 2:1 oxyphosphorane adduct LXXI into the corresponding fulvalene (70%), viz.



Equation 72

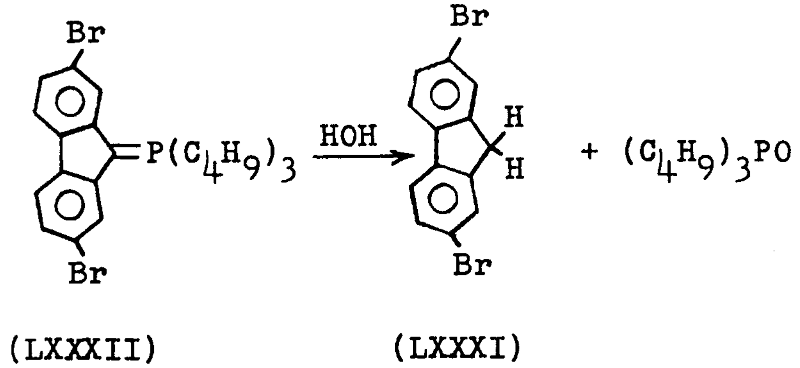
(LXXVI)

Reaction of the phosphine with 2,7-dibromofluorenone in a more polar medium, such as refluxing acetonitrile, yielded the corresponding fulvalene LXXVI (35%) and the unexpected 2,7-dibromofluorene (LXXXI) (43%).



(73)

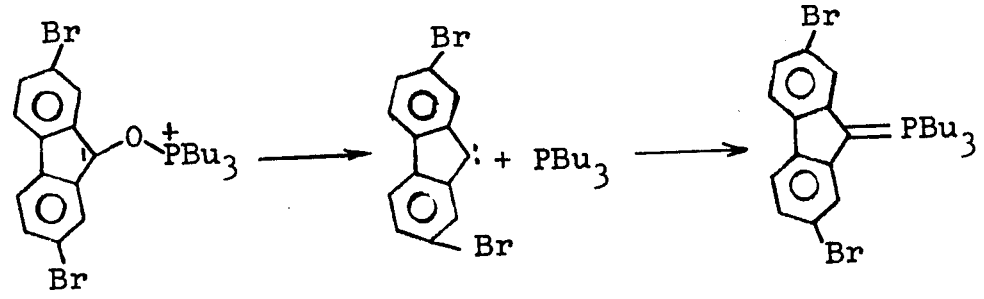
Compound LXXXI may arise <u>via</u> hydrolysis of ylid LXXXII.



(74)

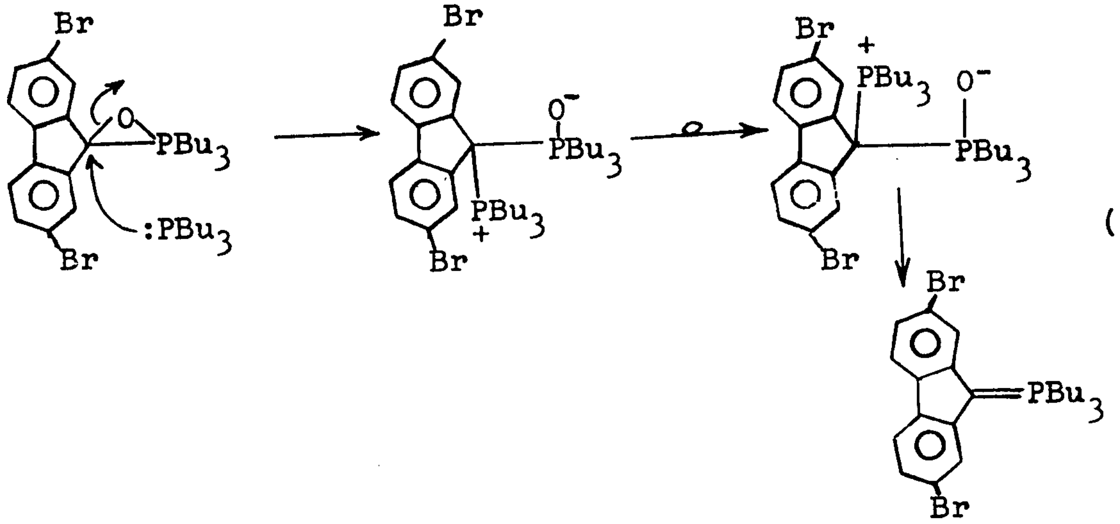
Various possible mechanistic pathways are indicated below for the observed ylid formation (eqn. 75, 76).

Pathway 1:



(75)

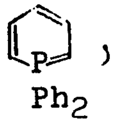
Pathway 2:

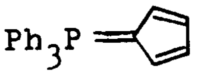


(76)

The formation of 2,7-dibromofluorene is thus indicative of the possibility of the existence of a carbene intermediate in the tributylphosphine-ketone reactions.

Phosphite oxyphosphoranes 2:1 adducts are most likely stabilized by electromeric release from the alkoxy groups. This degree of stabilization cannot be provided by the butyl groups in the phosphine runs, and thus phosphine phosphorane 2:1 adducts are not observed. Phosphinemethylenes such as

$Ph_3P{=}CPh_2$, $Ph_3P{=}CHR'$,  ,  $Ph_3P{=}CH{-}\overset{O}{\overset{\|}{C}}{-}R$,

$Ph_3P{=}CPh_2$, 

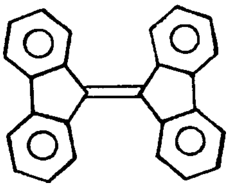
are stabilized by conjugation. The reaction of some of the above with ketones and aldehydes in the Wittig reaction,[6] viz.

$$Ph_3P{=}CHR' + R_2CO \longrightarrow Ph_3PO + R_2C{=}CHR'$$

is promoted by the formation of the highly stabilized phosphoryl group.

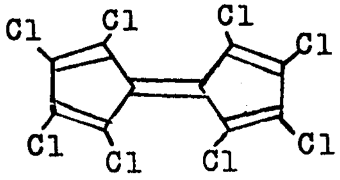
As in the phosphite run, tributylphosphine also did not react with 2,7,2',7'-tetrabromo-9-diphenylenephenanthrone.

Several unsuccessful attempts (see Experimental Section) at epoxidation of bis-diphenyleneethene may be accounted for by the "fulvenic" nature of the central double bond. It is well known that the hydrogen atoms in positions 1, 1', 8, 8' sterically interfere with one another,[7] preventing the planar structure which a normal central double bond demands. The low double bond order of the central linkage is further confirmed by the lack of stereoisomers in suitably substituted derivatives of bis-diphenyleneethene.[8]

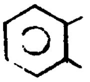


(LXXXIII)

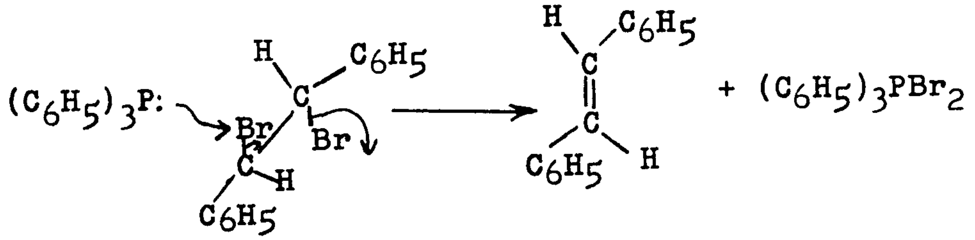
Bergmann[7] in a recent paper concludes that the exact spatial structure of bis-diphenyleneethene LXXXIII cannot be determined from existing available data. X-ray studies by Wheatley[9] on perchlorofulvalene LXXXIV has shown that the molecule is nonplanar with the rings twisted at an angle of 41° with respect to one another, with the central bond length being 1.49Å.



(LXXXIV)

Although the aforementioned X-ray study is by no means an adequate analogy (i.e., Cl-vs.  ) it does stress the unlikelihood of LXXXIII or LXXVI being planar molecules.

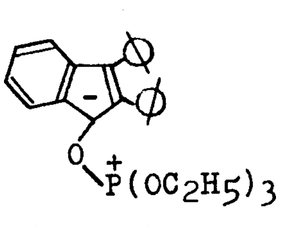
9-Fluorenone and 2,7-dinitrofluorenone failed to react with triphenylphosphine under a variety of conditions. In all cases unreacted starting materials were quantitatively recovered. It thus appears that triethyl phosphite and tributylphosphine are more reactive towards carbonyl groups than is triphenylphosphine, while in the α-haloketone (Part I) reactions the Borowitz group found that triphenylphosphine is much more reactive than is triethyl phosphite towards "positive halogen". Weiss and Thames[10] have found a similar reactivity difference in the 1,2-debromination of meso-stilbene dibromide which reacts with triphenylphosphine in boiling benzene for 24 hours to give stilbene (99%) and triphenylphosphine dibromide (isolated as triphenylphosphine oxide, 95% yield). Triethyl phosphite gives no reaction under these conditions. This elimination most likely involves attack on bromine.



(77)

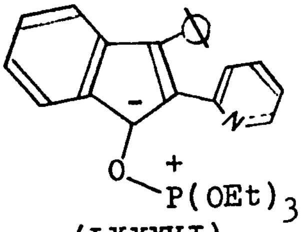
2,3-Diphenyl-1-indenone was the next cyclopentadienone derivative selected for investigation with tertiary phosphites and phosphines under a variety of reaction conditions.

The reaction of triethylphosphite with 2,3-diphenyl-1-indenone is of interest in that a compound which may be the novel stabilized 1,3-dipole LXXXV is isolated.



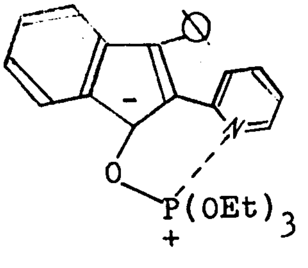
(LXXXV)

For an analysis of structure LXXXV, see section on Discussion of Spectra II. Tributylphosphine and triphenylphosphine react with 2,3-diphenyl-1-indenone to give an unknown compound or compounds[11] whose n.m.r. and IR spectra indicate the absence of aliphatic structure. Inconclusive evidence for the formation of LXXXVI (trace amounts) was obtained from the reaction of 3-phenyl-2(2'-pyridyl) indenone with triethyl phosphite.



(LXXXVI)

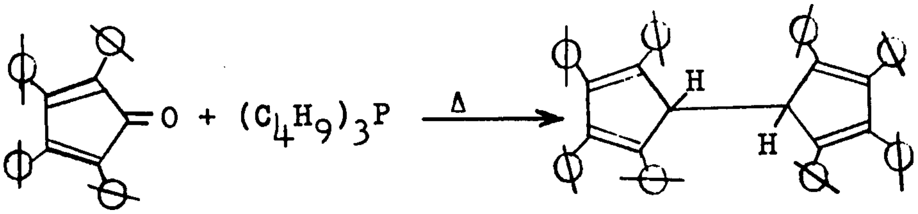
It was hoped that structure LXXXVI would be stabilized in the manner shown below, resulting in a high yield of product.



(LXXXVII)

It is conceivable that the 2,3-substituted pi-electron systems are parallel to one another and perpendicular to the attached ring as in the case of 1,8 phenyl-substituted naphthacenes.[12,13] If this be the case, stabilization through nitrogen-phosphorus bonding would not take place.

Reaction of tetracyclone with tributylphosphine which perhaps contained a prototropic source afforded the novel 1,1'-dihydro-2,3,4,5,2',3',4',5'-octaphenylfulvalene (LXXXVIII). Structure LXXXVIII was characterized by n.m.r., infrared, ultra-violet, mass spectrum, and elemental analysis. Structure LXXXVIII was in complete agreement with the product derived from reaction of 5-bromo-1,2,3,4-tetraphenyl-cyclopentadiene with zinc.



(78)

(LXXXVIII)

Triphenylphosphine reacted with tetracyclone to give an unknown hydrocarbon $C_{58}H_{40}$ (54% yield) and triphenylphosphine oxide. For spectral and physical data concerning this hydrocarbon, see section on Discussion of Spectra. Bromination with excess N-bromosuccinimide gave the $C_{58}H_{39}Br$ derivative. The very oxygen-sensitive $C_{58}H_{40}$ unknown hydrocarbon gave a plethora of products upon preliminary oxidation attempts with potassium permanganate, the bubbling of oxygen through a chloroform solution, 50% nitric acid oxidation and ozonolysis.

The reactivity of fluorenones, 2,3-diphenyl-1-indenone, and tetracyclone towards trivalent phosphorus nucleophiles may be attributed to the resonance stabilization which would be present in the initial cyclopentadienyl anion formation.

Consequently it was not surprising to find benzophenone inert towards tributylphosphine as well as towards trimethyl[1] and triphenyl phosphite[1] or triphenylphosphine.[1] Similarly benzanthrone and xanthone were found to be inert towards tributylphosphine and triethyl phosphite.

For the investigator interested in the reactions of cyclopentadienones with various phosphorus derivatives a fascinating and unexplored territory full of surprises and rewards lies before him.

# References

1. A. C. Poshkus and J. E. Herweh, J. Org. Chem., 29, 2567 (1964).
2. J. Hine in "Physical Organic Chemistry," McGraw-Hill Book Company, Inc., New York, N. Y., 1956, p. 43.
3. R. Ramirez, N. Ramanathan, and N. B. Desai, J. Am. Chem. Soc., 85, 3465 (1963).
4. See section titled Introduction II.
5. A. C. Poshkus and J. E. Herweh proposed and reported a similar pathway but our work had begun some time before publication of this paper.[1] In any case, the work reported in this thesis is based on systems not studied by these authors.
6. G. Wittig and U. Schöllkopf, Ber., 87, 1318 (1954).
7. M. Rabinovitz, I. Agranat, E. D. Bergmann, Tetrahedron Letters No. 18, 1265 (1965).
8. E. D. Bergmann, et al., Bull Soc. Chem. Fr., 19, 78 (1952).
9. P. J. Wheatley, J. Chem. Soc., 4936 (1961).
10. D. Weiss and M. Thames, Lehigh University, unpublished results.
11. F. W. Billmeyer, Jr. in "Textbook of Polymer Science," Interscience Publishers - John Wiley and Sons, 1965, p. 418.
12. H. H. Jaffé and O. Chalvet, J. Am. Chem. Soc., 85, 1561 (1963).
13. V. Balasubramaniyan, Chem. Rev., 66, 567 (1966).

# SUMMARY II

A mechanistic study of the reactions of trivalent phosphorus nucleophiles with cyclopentadienone derivatives are presented. Results of the reactions of fluorenones with triethyl phosphite either neat or with the presence of a solvent of low dielectric constant indicate that the formation of 9-diphenylenephenanthrone may occur by way of an isolable cyclic oxyphosphorane intermediate. It is postulated that cyclic oxyphosphorane formation proceeds by initial attack at the carbonyl oxygen followed by condensation at the carbonyl carbon with another fluorenone molecule. In a high dielectric constant medium such as acetonitrile a derivative of the internal Michaelis-Arbusov rearrangement product is believed to have been isolated.

Tributylphosphine is shown to give high yields of fulvalenes corresponding to the fluorenones reacted. It is concluded that fulvalene formation cannot come about <u>via</u> a carbene mechanism or by way of the further reaction of phosphine with the appropriate 9-diphenylenephenanthrone.

The reactions of triethyl phosphite with 2,3-diphenyl-1-indenone and tributylphosphine with tetracyclone led to highly interesting and novel reaction products, namely a 1:1 triethyl phosphite-2,3-diphenyl-1-indenone adduct and 1,1'-dihydro-2,3,4,5,2',3',4',5'-octaphenylfulvalene, respectively.

The reactivity of trivalent phosphorus nucleophiles towards the cyclopentadienone system is attributed to the

formation of the resonance stabilized cyclopentadienyl anion.

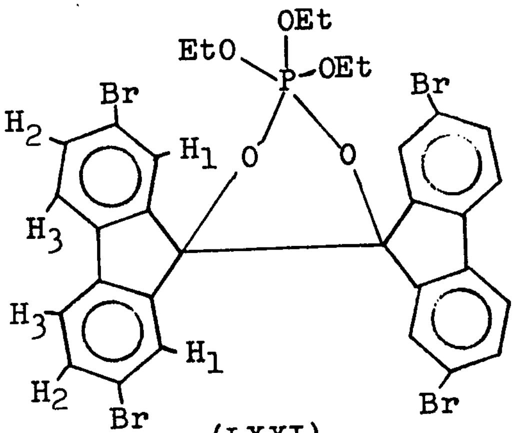
The limitations and possible course of the novel reactions presented are discussed from a mechanistic point of view.

# DISCUSSION OF SPECTRA

## Structure Proof of the 2,7-Dibromofluorenone-Triethyl Phosphite 2:1 Adduct (LXXI)

### Infrared Data

The infrared spectrum of the crystalline adduct LXXI in potassium bromide disc form is reproduced in Figure 4.



(LXXI)

The spectrum represented by Figure 4 is characterized by the following:

1. C-H stretching absorption vibrations occurring at about 2900-3030 cm$^{-1}$.
2. Olefinic C=C stretching vibrations of the aromatic ring which are located near 6.25 μ (1600 cm$^{-1}$.
3. The absence of carbonyl absorption.
4. The absence of strong P-O absorption vibrations.
5. The presence of very intense absorption bands occurring below 1100 cm$^{-1}$ which are due to P-O-C (alkyl) stretching vibrations.[1,2]

The absorption band occurring at 1160 $cm^{-1}$ is assigned[1] to $P-O-C_2H_5$ vibration, in agreement with structure LXXI. Cotton,[1] Bellamy[2] and others have reported that the intense absorption bands occurring below 1100 $cm^{-1}$ are characteristic of organophosphorus compounds containing P-O-alkyl groups; however, the precise assignment of these bands is uncertain.

## Proton Nuclear Magnetic Resonance Data

The n.m.r. spectrum of the crystalline adduct LXXI in deuterobenzene solution is reproduced in Figure 5. There are no impurities present other than the benzene present in deuterobenzene, which gives a singlet at 7.2 $\delta$ (2.8 $\tau$).

The spectrum is in general agreement with the oxyphosphorane structure. However, one cannot distinguish between the closed cyclic saturated or the open dipolar form of the oxyphosphorane from the proton n.m.r. data alone. More cogent in this respect, however, are the $P^{31}$ chemical shift data, given on pp. 100, 101.

The three distinct multiplets observed at 6.5-8.1, 4.2 and 1.25 $\delta$ are assigned to the aromatic, methylene and methyl protons, respectively. Integration affords the ratio 4:2:3 (*i.e.*, 12:6:9) in excellent accordance with these assignments. The twelve aromatic proton assignments are based upon a comparison to the aromatic protons of 2,7-dibromofluorenone.

Table X. Proton N.M.R. Spectrum of Oxyphosphorane LXXI

| $\delta$, p.p.m.[a] | Multiplicity | No. of Protons | Assignment |
|---|---|---|---|
| 1.25 | doublet of triplets ($J_{HH}$=7 c.p.s. $J_{P^{31}H}$=2 c.p.s.) | 9 | methyl protons of the ethyl ester groups |
| 4.2 | multiplet | 6 | methylene protons of the ethoxyl groups |
| 6.5 | doublet ($J_{H_1H_2}$=8 c.p.s.) | 4 | $H_1$ aromatic protons |
| 7.1 | multiplet (masked by $C_6H_6$ absorption, probably quartet) | 4 | $H_2$ aromatic protons |
| 8.1 | doublet ($J_{H_2H_3}$=2 c.p.s.) | 4 | $H_3$ aromatic protons |

[a] $\delta = \frac{\text{H sample - H reference}}{\text{H reference}} \times 10^6$ relative to tetramethyl silane as internal standard

$P^{31}$ Nuclear Magnetic Resonance Data

Figure 6 gives the $P^{31}$ n.m.r. spectrum of the crystalline adduct in deuterochloroform-1% tetramethyl-silane solution at 16.2 Mc./sec. The chemical shift is in p.p.m. ±2, relative to 85% aqueous phosphoric acid, the external primary standard.

The 2,7-dibromofluorenone-triethyl phosphite 2:1 adduct gave a large positive chemical shift value of +48 p.p.m., which is in excellent agreement for structure LXXI existing in the closed cyclic saturated oxyphosphorane form as shown. Table XI summarizes the chemical shifts of various closed cyclic oxyphosphoranes.

Table XI. $P^{31}$ N.M.R. Shifts[3,4] in P.P.M., V., 85% $H_3PO_4$ of Cyclic Oxyphosphoranes

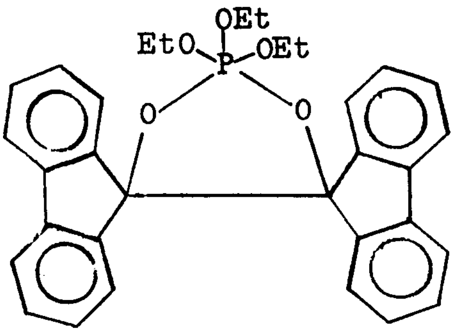
| Carbonyl Compound | R in $(RO)_3P$ | Mol. Formula | $P^{31}$ N.M.R. |
|---|---|---|---|
| Phenanthrenequinone | $C_2H_5$ | $C_{20}H_{23}O_5P$ | +47.1 |
| Benzil | $CH_3$ | $C_{17}H_{19}O_5P$ | +49.5 |
| 2,3-Pentanedione | $CH_3$ | $C_8H_{17}O_5P$ | +46 |

By comparison triphenylphosphate [$(C_6H_5O)_3PO$, $\delta$ = +17 p.p.m.] is observed[5-7] to have the largest positive chemical shift among compounds containing four oxygen atoms bonded to phosphorus. Triphenylphosphite, however, gives a negative shift of $\delta$ = -137 p.p.m.

The large positive chemical shifts in the phosphorane adducts indicated by Table XI have been attributed to the more effective shielding of the phosphorus nucleus in the adducts than in the reference compound.

9-Fluorenone-Triethyl Phosphite 2:1 Adduct LXXXIX

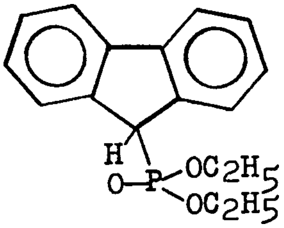
The infrared and proton n.m.r. spectra of LXXXIX are shown in Figures 7 and 8 , respectively. Using similar considerations in structure elucidation as previously (i.e., analysis of LXXI, 2:1 adduct LXXXIX is postulated to have the structure indicated below.



(LXXXIX)

## Nuclear Magnetic Resonance Spectra of Diethyl Fluorenylphosphonate Proton N.M.R. Data

Figure 9 shows a reproduction of the proton n.m.r. spectrum of diethyl fluorenylphosphonate XC in deuterochloroform-1% tetramethylsilane solution.



(XC)

The n.m.r. spectrum of XC fully confirms the above structure as written. The signals at 7.2-8.0, 4.4, 3.8 and 1.0 $\delta$ are assigned to the aromatic, fluorenyl methylene, methylene and methyl protons, respectively. Integration affords the ratio 8:1:4:6 in accordance with these assignments.

Table XII. Proton N.M.R. Spectrum of Diethyl Fluorenylphosphonate (XC)

| $\delta$, p.p.m. | Multiplicity | No. of Protons | Assignment |
|---|---|---|---|
| 1.0 | triplet | 6 | Methyl protons of the ethyl ester groups. |
| 3.8 | multiplet | 4 | Methylene protons of the ethoxyl groups. |
| 4.4 | doublet<br>($J_{HP}$=30 c.p.s.) | 1 | Fluorenyl methylene proton. |
| 7.2-8.0 | multiplet | 8 | Aromatic protons. |

Since the $P^{31}$ nucleus has a magnetic moment with a spin number I=1/2 the signal due to the fluorenyl methylene proton is split into a doublet.

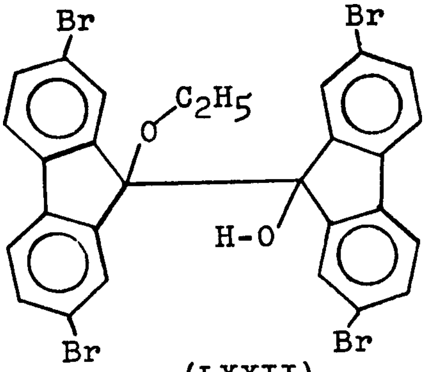
## $P^{31}$ Nuclear Magnetic Resonance Data

The $P^{31}$ spectrum of XC in deuterochloroform-1% tetramethyl silane solution at 16.2 Mc./sec. relative to 85% aqueous phosphoric acid (i.e., the external standard) is reproduced in Figure 10. Structure XC gave a doublet ($J_{PH}$=30 c.p.s.) with a large negative chemical shift of -25.6 p.p.m. as expected for a phosphoryl compound. H. Finegold[8] in a review on $P^{31}$ n.m.r. spectroscopy reports several examples of phosphoryl compounds with ligands OR, OR', and $CH_3$ giving similar negative chemical shifts of -28.4 p.p.m.

## The Postulated 9-Hydroxy-9'-Ethoxy Difluorene LXXII

### Infrared Data

The infrared spectrum of LXXII was determined in potassium bromide and is displayed in Figure 11.



(LXXII)

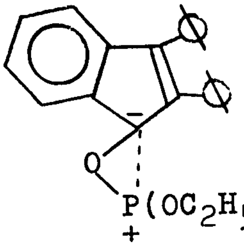
The IR spectrum of LXXII shows bands at 3260 $cm^{-1}$ (OH, hydrogen bonded); 3060 $cm^{-1}$ (Ar-H band); 1650 $cm^{-1}$ (C=C, stretching vibration of the aromatic ring); 1450 and 1375 $cm^{-1}$ (C-$CH_3$) and 1150-1060 $cm^{-1}$ (aliphatic, $CH_2$-O-$CH_2$).

Attempts at obtaining proton n.m.r. signals of LXXII were unsuccessful due to insufficient solubility.

### 2,3-Diphenyl-1-Indenone-Triethyl Phosphite 1:1 Adduct (LXXXV)

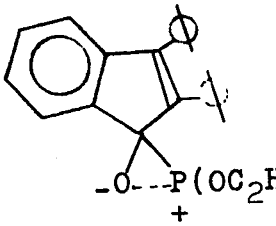
### Infrared Data

The infrared spectrum of LXXXV in Nujol is reproduced in Figure 12.



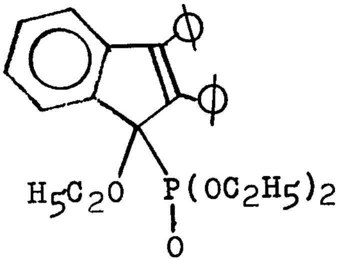
(LXXXVa)

vs.



(LXXXVb)

vs.



(LXXXVc)

The spectrum represented by structure LXXXV is characterized by the following:

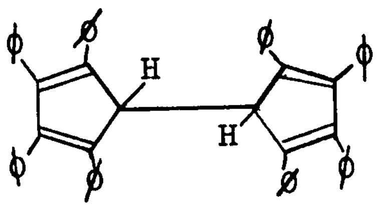
1. C-H stretching absorption vibrations.
2. Olefinic Ar-C=C-Ar stretching vibrations located at 1615 $cm^{-1}$.
3. The absence of carbonyl absorption.
4. The absence of strong P-O absorption vibrations in the region 1180-1250 $cm^{-1}$.[9]
5. The absence of aliphatic C-O stretching vibrations ($C-O-CH_2$) in the region 1060-1150 $cm^{-1}$.
6. The presence of very intense absorption bands occurring below 1100 $cm^{-1}$ which are due to P-O-C (alkyl) stretching vibrations.[1,2]

Structure LXXXVb, which would form as a result of an initial phosphite nucleophilic attack at the carbonyl carbon atom, is expected to undergo a rapid intramolecular Michaelis-Arbusov rearrangement to form LXXXVc or more likely lead to the energetically favored LXXXVa. The latter rearrangement (i.e., formation of LXXXVa) is expected to be rapid, the driving force being the formation of the phosphorus-oxygen single bond by the oxaphilic phosphorus atom. The lack of ether and phosphoryl (P—O) absorption stretching vibrations eliminates structure LXXXVc. Structure LXXXVb, if formed, is expected to be short lived. In any case, the spectrum indicated by Figure 12 is believed to represent structure LXXXVa.

## Structure Proof of 1,1'-Dihydro-2,3,4,5,2',3',4',5'-Octaphenyl fulvalene LXXXVIII

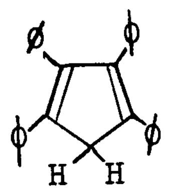
### Infrared Data

The infrared spectra of structure LXXXVIII and known 1,2,3,4-tetraphenyl-1,3-cyclopentadiene XCI in chloroform solution are displayed in Figures 13 and 14.



(m.p. 153°)

(LXXXVIII)



(m.p. 180°)

(XCI)

The superimposable spectra of LXXXVIII and XCI are characterized by the following:

1. C-H stretching absorption vibrations occurring at about 2920-3120 $cm^{-1}$.
2. Olefinic C=C stretching vibrations of the aromatic ring and the carbon-carbon double bond, in conjugation with it, located at 1580-1625 $cm^{-1}$.
3. The absence of carbonyl absorption.
4. Figure 15 is a reproduced spectrum of the product (in chloroform) derived from the reaction of 5-bromo-1,2,3,4-tetraphenyl-1,3-cyclopentadiene with zinc. The spectrum is identical with the spectrum indicated by structure LXXXVIII, Figure 13.

Ultraviolet Data

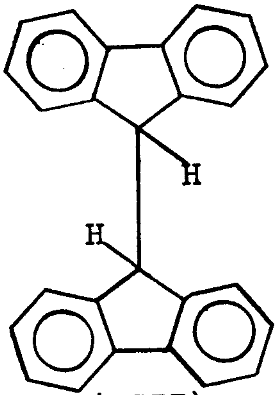
Structure LXXXVIII is confirmed by its characteristic ultraviolet spectrum which is indicated by its similar absorption values and higher molar extinction coefficients, in comparison to that of 1,2,3,4-tetraphenyl-1,3-cyclopentadiene XCI.

Structure LXXXVIII: $\tau_{max}^{95\% \text{ EtOH}}$ in mμ (log ε): 245 (4.68)
346 (4.39)

Structure XCI: $\tau_{max}^{10}$ in mμ (log ε): 245 (2.44)
269 (2.09)
346 (1.40)

Nuclear Magnetic Resonance Data

The n.m.r. spectrum shown in Figure 16 provides further evidence for confirmation of structure LXXXVIII. The signals at 6.85-7.6 (multiplet) and 5.0 δ (singlet) obtained in deuterochloroform as solvent are assigned to the aromatic and allylic protons, respectively. Integration affords the ratio 20:1 in accordance with these assignments. Similarly, di-biphenyleneethane (XCII)[11] gives an allylic singlet at 4.71 δ, while tetraphenylcyclopentadiene gives a more highly shielded allylic singlet at 4.02 δ.



(XCII)

## Spectral Data on Unknown Hydrocarbon $C_{58}H_{40}$

### Infrared Data

The infrared spectrum reproduced in Figure 17 displays the IR data of the $C_{58}H_{40}$ hydrocarbon derived from the reaction of triphenylphosphine with tetracyclone. The spectrum is typical of an aromatic hydrocarbon. On standing in solution ($CCl_4$) for a period of time (3 weeks) the infrared spectrum gave carbonyl absorptions at 5.72 μ (w) and 5.95 μ (s), Figures 18 and 19.

## Ultraviolet Data

The ultraviolet spectrum using spectro grade acetonitrile as solvent:

$\tau_{max}$ in mμ (log ε); 235 (br. sh.) (4.65)
255 (4.59)
363.5 (4.16)

The mass spectrum gives a M/E 736 and indicates the loss of at least six phenyl groups.

## Nuclear Magnetic Resonance Data

The n.m.r. spectrum (HA-100) in deuterochloroform shows aromatic absorption between 6 and 7 δ, weaker absorption between 5 and 6 δ and a single allylic proton peak at 4.5 δ.

Table XIII. Proton N.M.R. Spectrum of $C_{58}H_{40}$ Adduct

| p.p.m. | No. of Protons | Assignments |
|---|---|---|
| 7.3-7.7 | 10 | Two phenyls |
| 7.1-7.2 | 5 | One phenyl |
| 7.03 | 5 | One phenyl |
| 6.95 | 5 | One phenyl |
| 6.83 | 5 | One phenyl |
| 6.72 | 2 | |
| 6.65 | 1 | |
| 6.60 | 1 | |
| 6.40 | 1 doublet | |
| 6.35 | 1 doublet | |
| 6.25 | 1 | |
| 6.18 | 1 triplet | |
| 6.10 | 1 | |
| 5.21 | 1 | Allylic proton |

## References

1. F. A. Cotton and R. A. Schunn, J. Am. Chem. Soc., 85, 2394 (1963).
2. L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen, New York, N. Y., (1958), pp. 315-317.
3. F. Ramirez and N. B. Desai, J. Am. Chem. Soc., 85, 3252 (1963).
4. F. Ramirez, C. P. Smith, A. S. Gulati and A. V. Patwardhan, Tetrahedron Letters, 2151 (1966).
5. J. R. Van Wazer, "Phosphorus and its Compounds," Interscience Publishers, Inc., New York, N. Y., (1938), p. 43.
6. J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, ch. 12, cf. p. 346.
7. J. R. Van Wazer, C. F. Callis, J. N. Shoolery, and R. C. Jones, J. Am. Chem. Soc., 78, 5715 (1956).
8. Finegold, Ann. New York Acad. Sci., 70, 875 (1958).
9. G. Aksnes and D. Aksnes, Acta Chem. Scand., 18, 38 (1964).
10. E. Becker, J. Am. Chem. Soc., 75, 2283 (1953).
11. M. Rabinovitz, I. Agranat and E. D. Bergmann, Tetrahedron Letters, 1265 (1965).

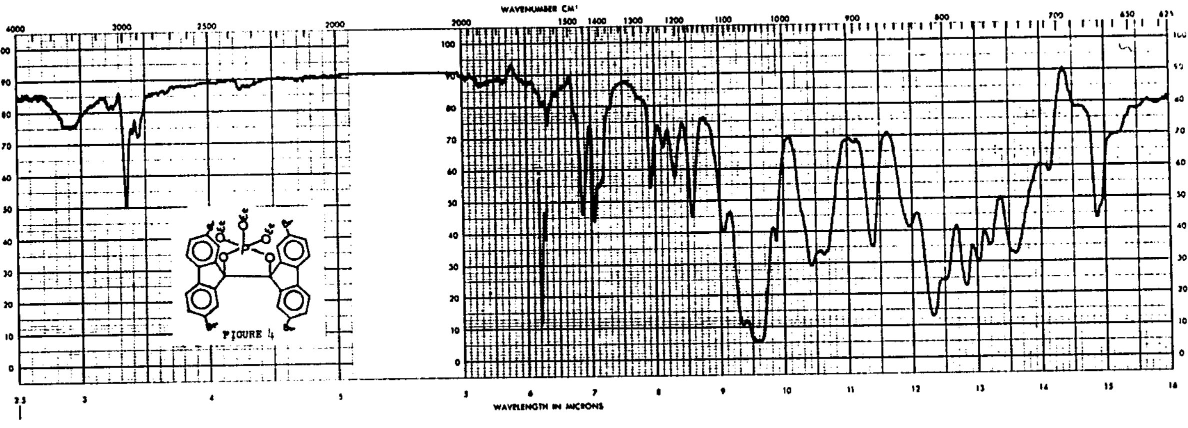


FIGURE 4

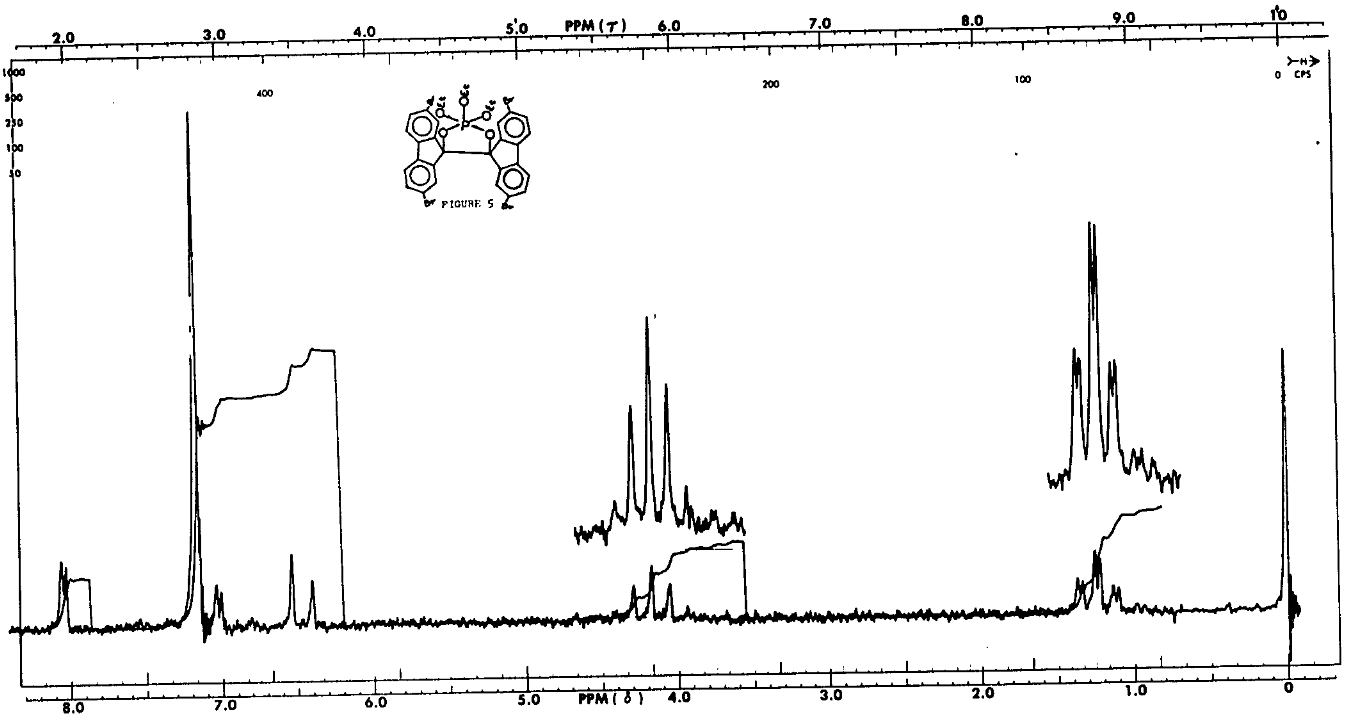


FIGURE 5

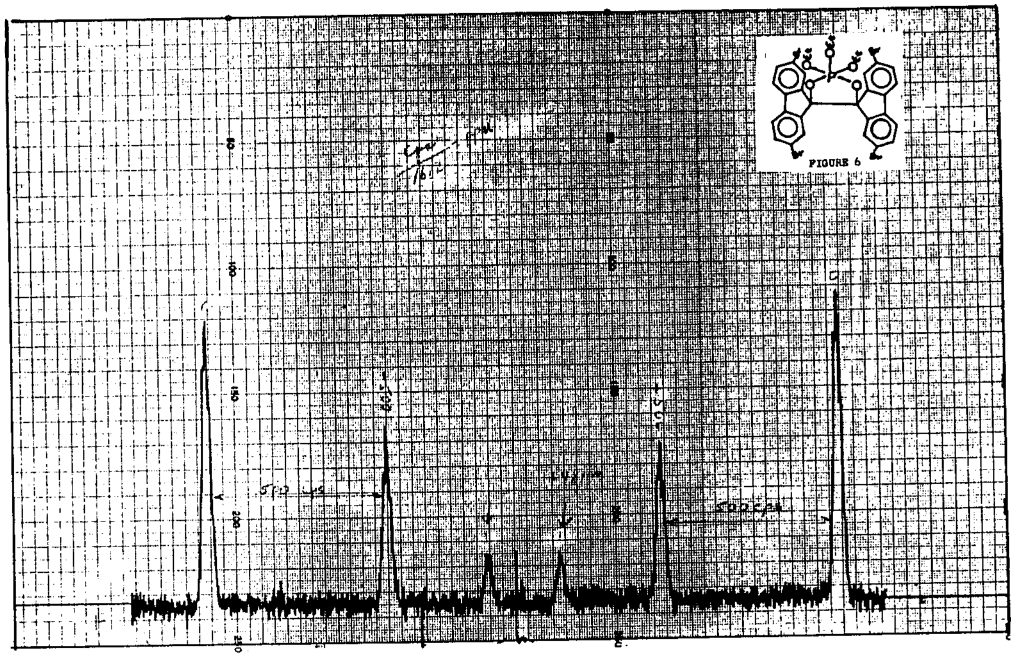


FIGURE 6

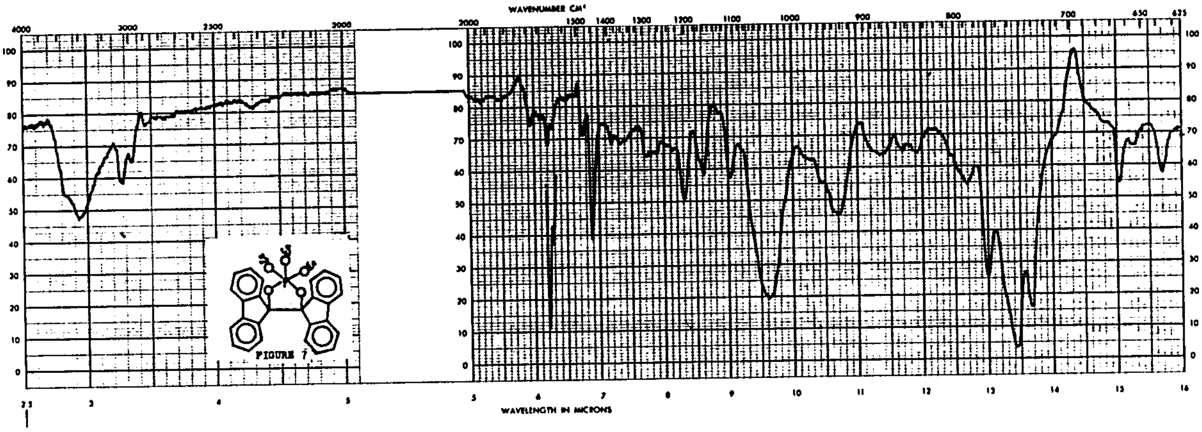


FIGURE 7

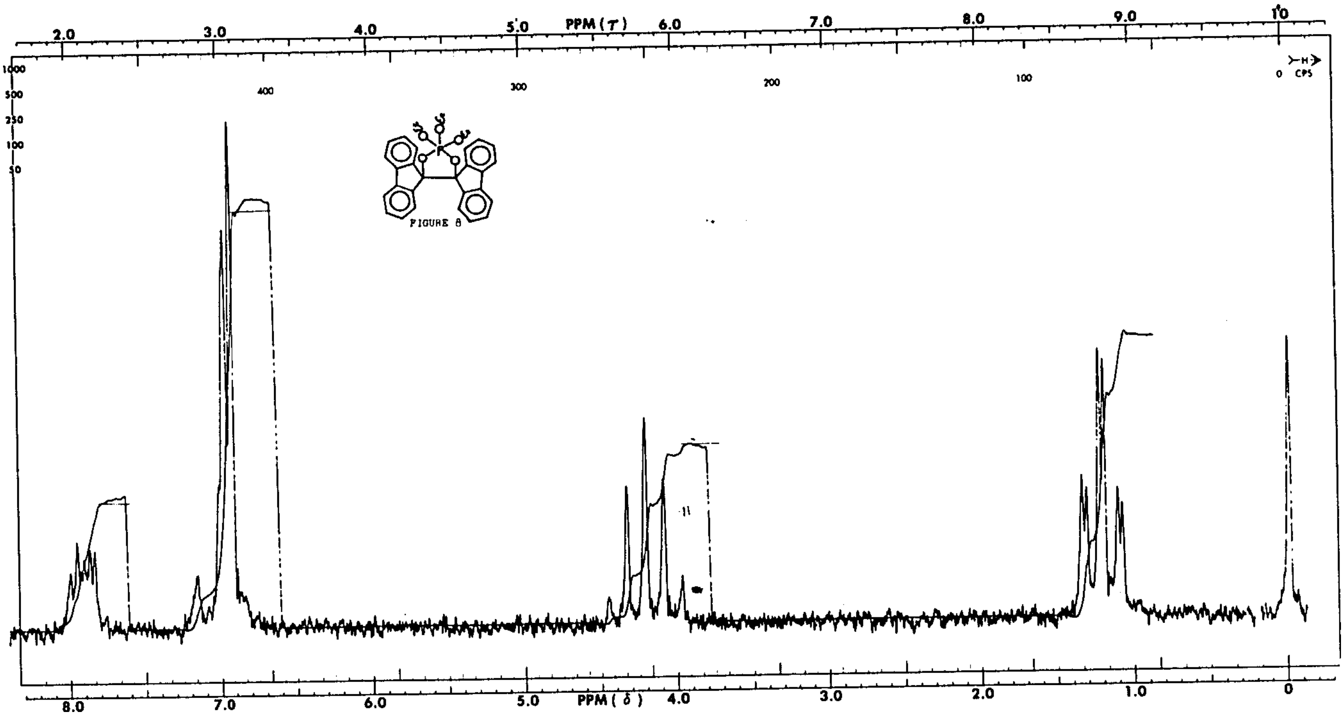


FIGURE 8

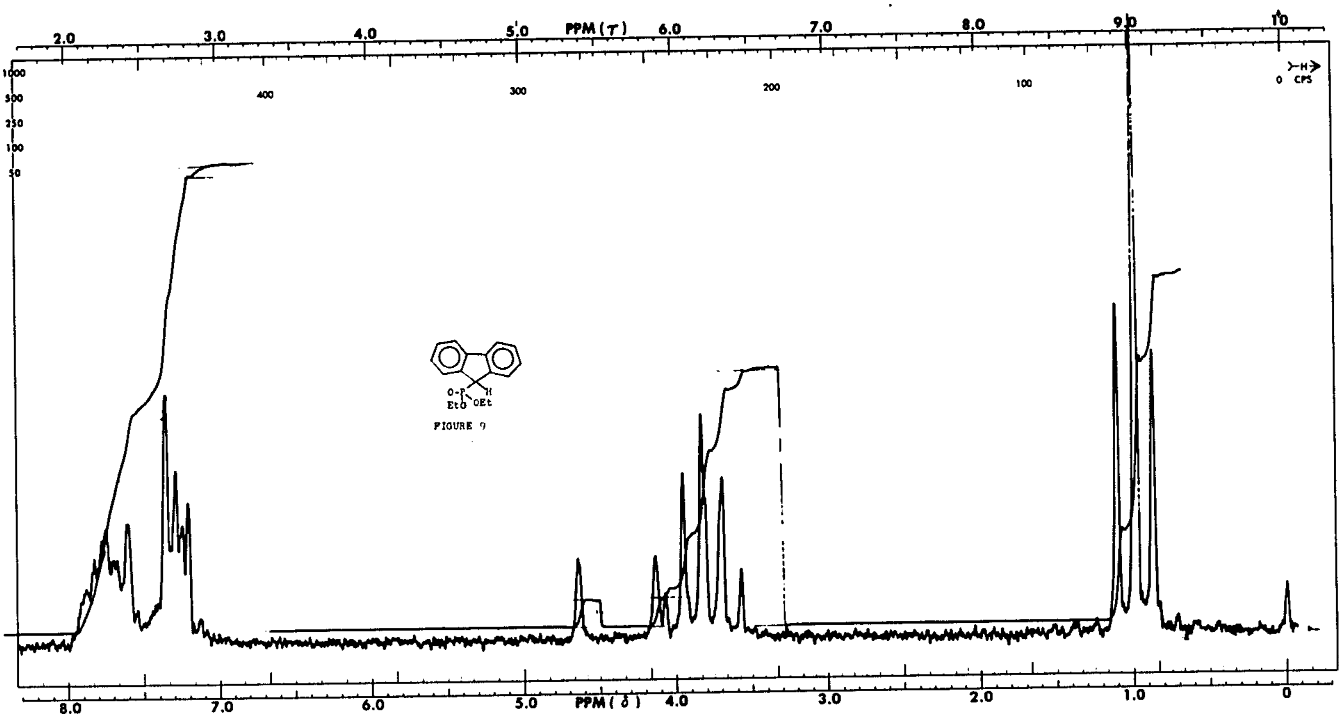


FIGURE 9

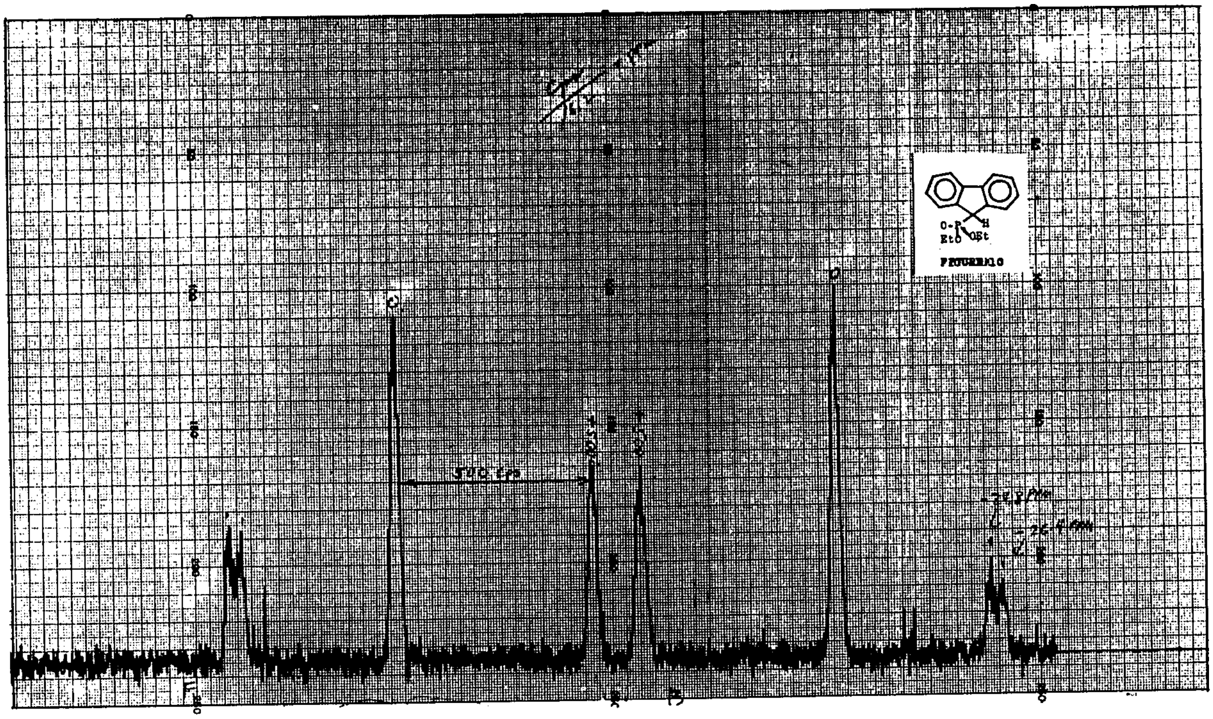
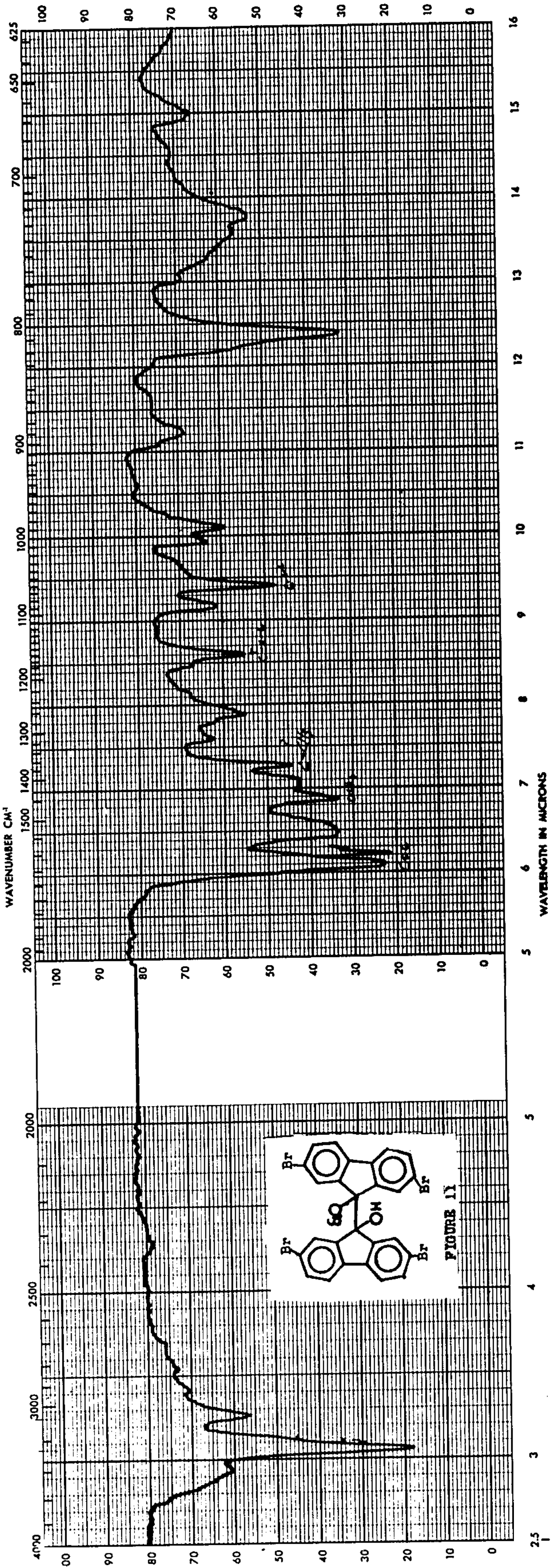


FIGURE 10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3000
2500
2000
1500
1400
1300
1200
1100
1000
900
800
700
650
625
WAVELENGTH IN MICRONS
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3
4
5
6
7
8
9
10
11
12
13
14
15
16
100
90
80
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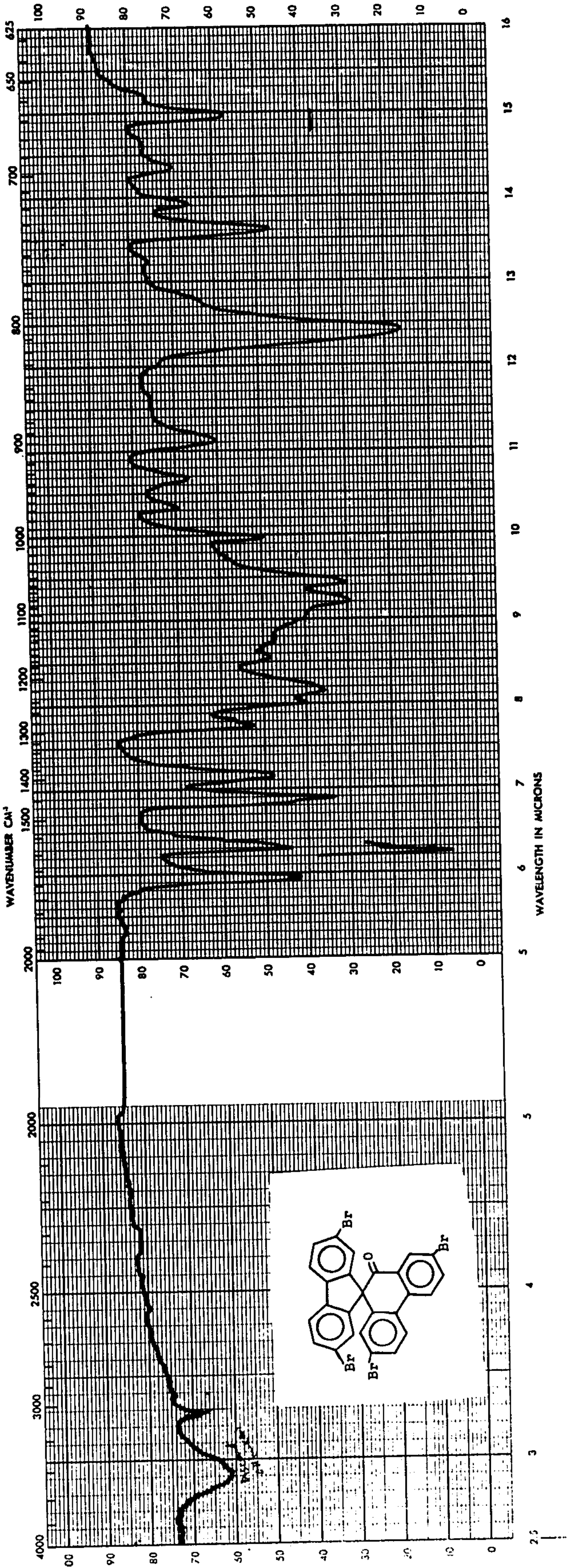
30
20
10
0
Br
Br
Br
Br
OH
HO

FIGURE 11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WAVELENGTH IN MICRONS
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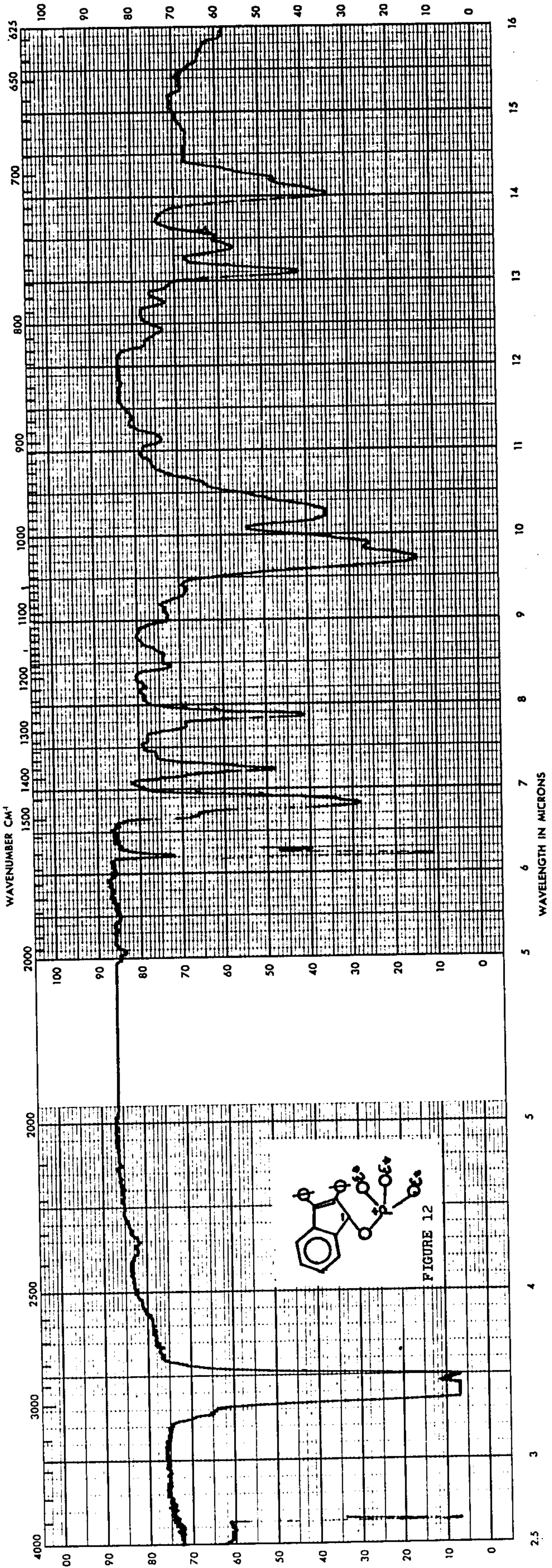
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700
650
625
WAVELENGTH IN MICRONS
2.5
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10
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FIGURE 12

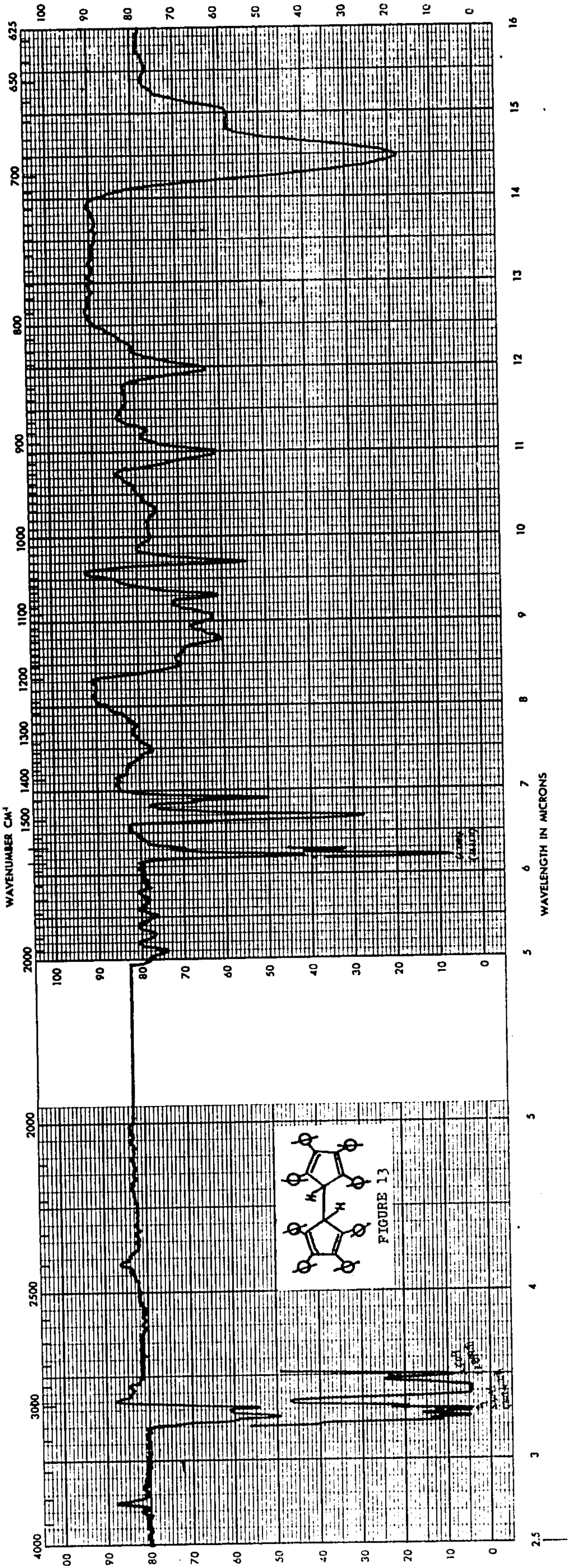


FIGURE 13

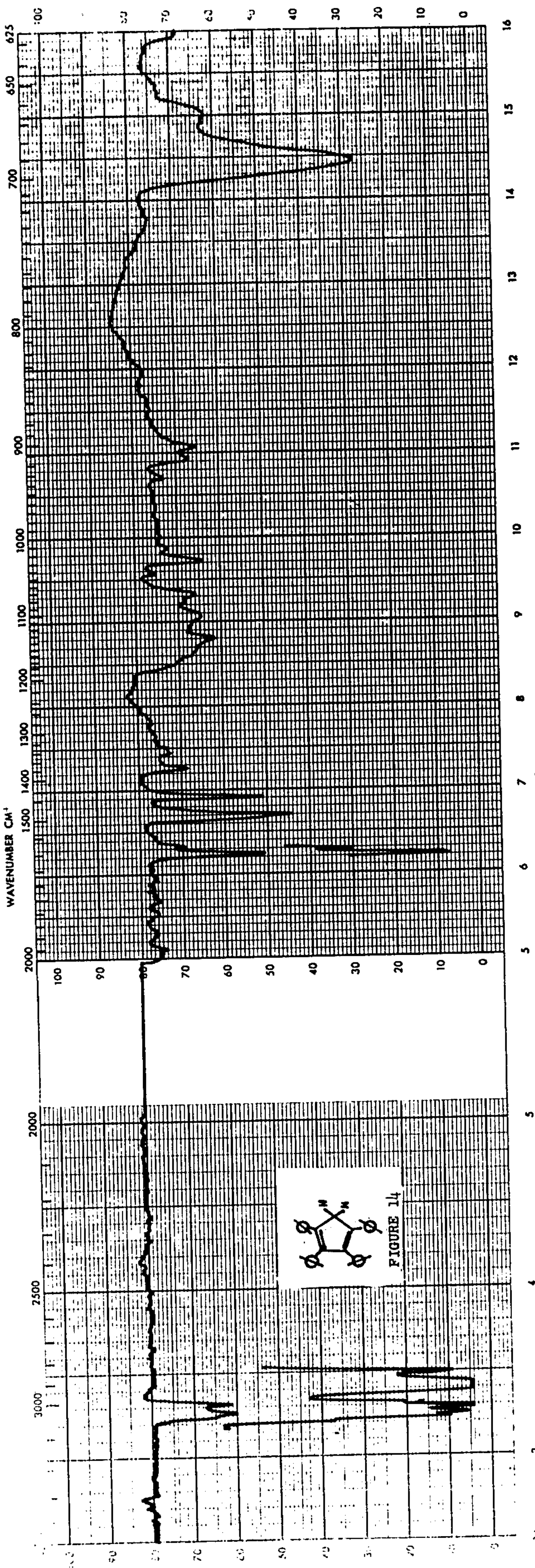


FIGURE 14

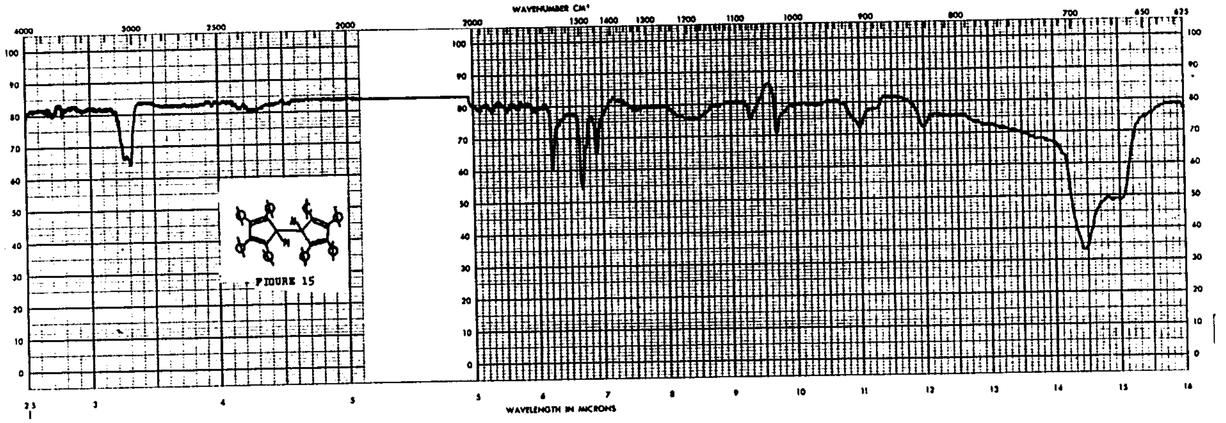


FIGURE 15

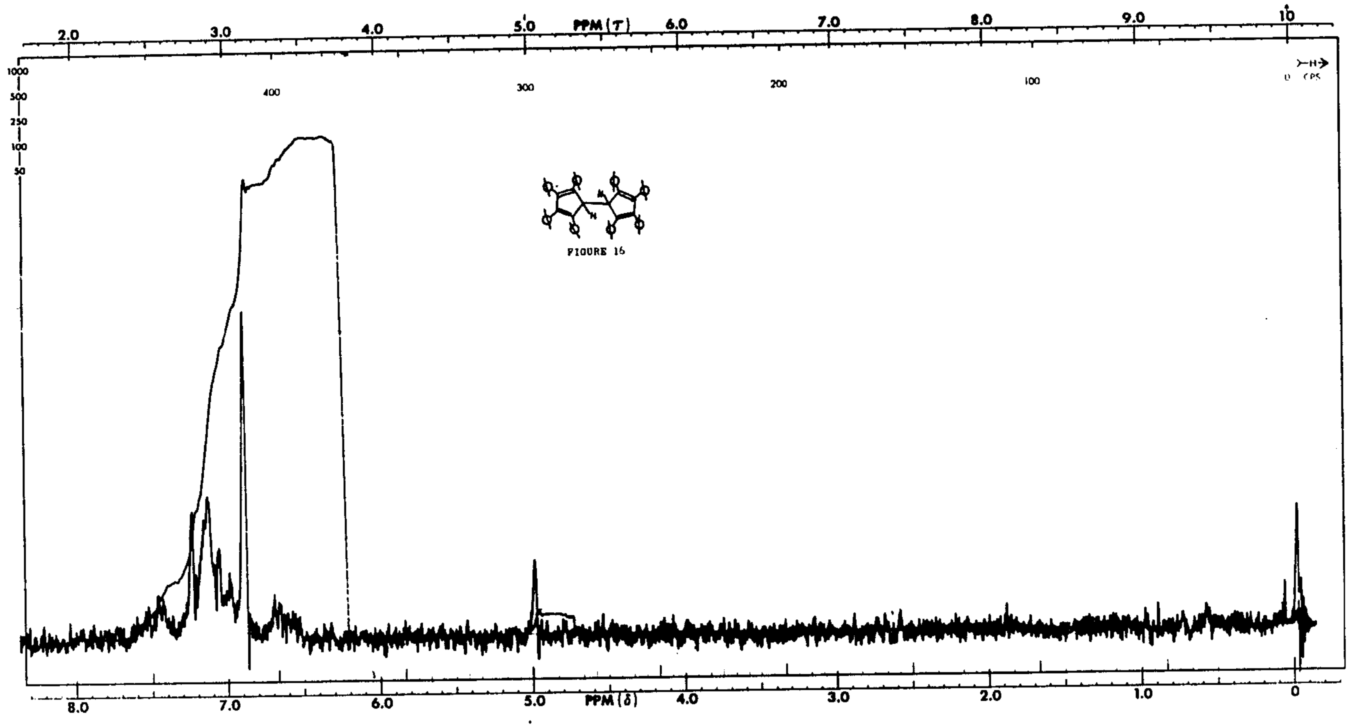
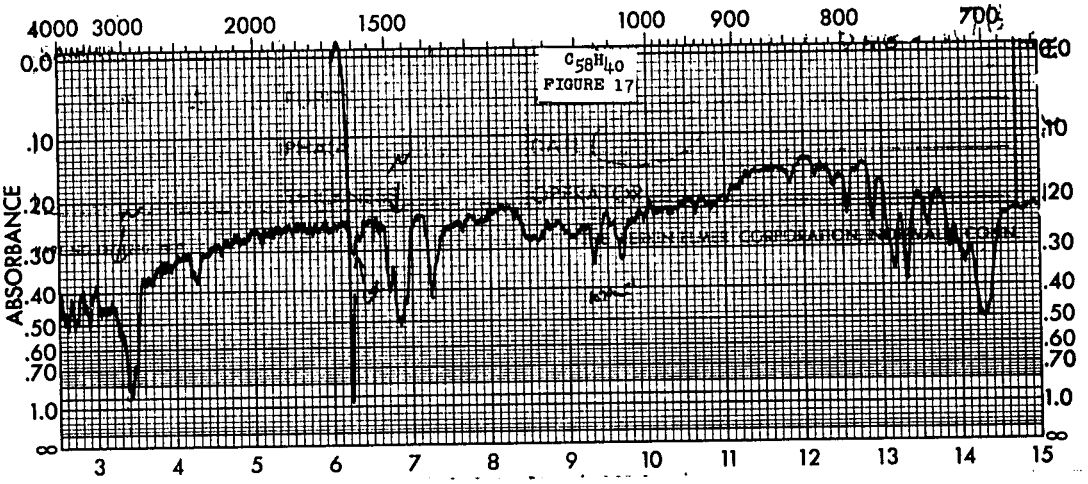
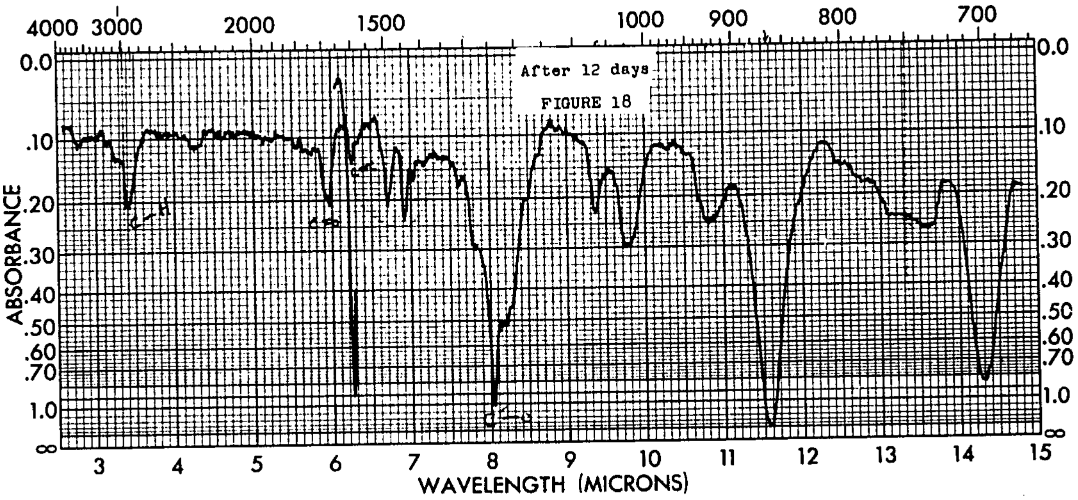


FIGURE 16



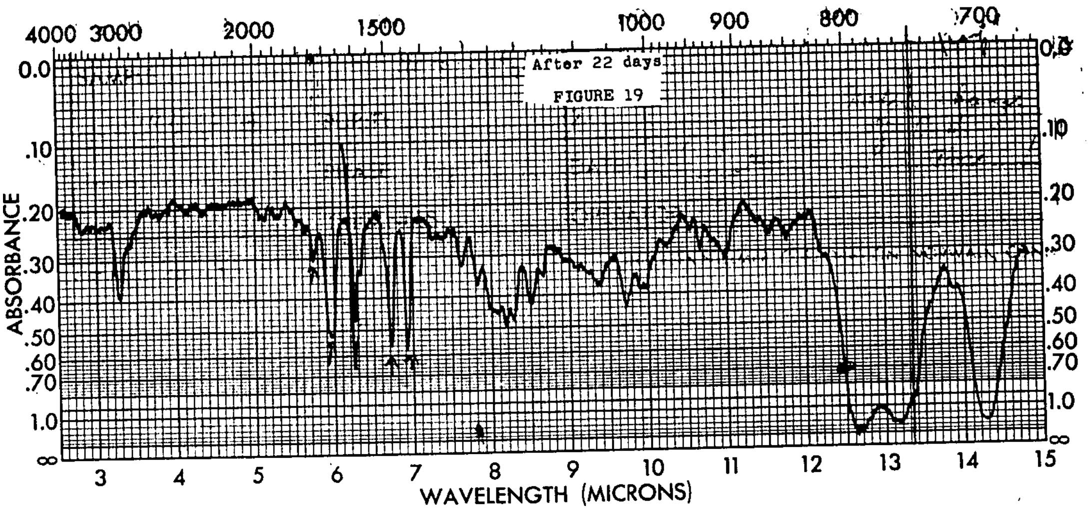
$C_{58}H_{40}$

FIGURE 17



After 12 days

FIGURE 18



After 22 days

FIGURE 19

## EXPERIMENTAL II

Microanalyses were performed by Professor V. B. Fish of the Department of Chemistry, Lehigh University, Galbraith Laboratories Inc., Knoxville, Tennessee, and Schwartzkopf Microanalytical Laboratories, Woodside, New York.

Infrared spectra were recorded either on a Perkin-Elmer Model 21 or on a Beckman IR-8 infrared spectrophotometer.

Ultraviolet spectra were recorded on a Beckman DK-2A spectrophotometer. The solvents are specified with the recorded spectra.

Nuclear magnetic resonance spectra were recorded on a Varian A-60 spectrometer with tetramethylsilane, 0 p.p.m., as an internal standard. $P^{31}$ n.m.r. spectra were carried out by Dr. J. Lancaster of the American Cyanamid Co., Stamford, Connecticut using 85% phosphoric acid as an external reference.

The high resolution mass measurements were made with an Associated Electrical Industries Limited (AEI) MS-9 mass spectrometer. The spectra were carried out at the request of Dr. K. G. Untch of the Mellon Institute, Pittsburgh, Pennsylvania.

Melting points were determined in Kimax capillary tubes using a "Mel-Temp" apparatus (Laboratory Devices, Box 68, Cambridge, Mass.) and are uncorrected. Boiling points are uncorrected.

Thin layer chromatography was carried out by using E. Merck Silica Gel $HF_{254}$ or Alumina $HF_{254}$ (Brinkmann Instruments, Inc., U. S. distributor) as the substrates, unless specified otherwise, activated at 110-120°. The thickness of the adsorbent layer was adjusted to 0.25 mm. using "Desaga" equipment supplied by the Brinkmann Co., Inc., Great Neck, Long Island, N. Y. The most frequently used developing solution was 5% (by volume) ethyl acetate in benzene.

Other solvent systems used were:

a) 5% (by volume) methanol in benzene
b) 15% (by volume) methanol in benzene
c) 25% (by volume) methanol in benzene

The spots were located with ultraviolet light, exposure to iodine vapor or 2,4-dinitrophenyl hydrazine spray. The $R_f$ values were then compared with those of purified (by distillation or recrystallization) authentic compounds spotted on the same plate.

Reactions of cyclopentadienones with trivalent phosphorus compounds were carried out under an atmosphere of pre-purified nitrogen (Matheson) with constant magnetic stirring of the reaction mixture. All manipulations were performed in an atmosphere of pre-purified nitrogen unless otherwise stated. Mechanical transfers and other operations in open vessels were continuously flushed with a rapid stream of pre-purified nitrogen.

All solid samples were recrystallized several times before use, dried, checked by t.l.c., and stored in a vacuum desiccator over calcium chloride. Solvents were stored over the appropriate drying agent, refluxed and distilled prior to use.

## Materials

Triethyl phosphite was purchased from Hooker Chemical Corporation, Niagara Falls, New York. The phosphite was dried and distilled from calcium hydride just before use. A large forerun was obtained distilling over the range of 70-155°. The forerun was discarded and the main cut distilled over at 156-157°. The residual liquid was discarded.

Triphenylphosphine was obtained from M and T Chemicals, Inc., and was recrystallized from diethyl ether. After drying at a pressure of 0.15 mm. over phosphorus pentoxide, the triphenylphosphine, m.p. 80-81° (lit. m.p. 80°), was stored in a vacuum desiccator over calcium chloride. 9-Fluorenone (m.p. 83-84°; lit. m.p. 83-83.5°), 2,7-dinitrofluorenone (m.p. 290°; lit. m.p. 290°), 2,3-diphenyl-1-indenone (m.p. 150-152°; lit. m.p. 150-151°) and tetracyclone (m.p. 218-220°; lit. m.p. 220°) were purchased from Aldrich Chemical Co., Milwaukee, Wisconsin.

Peracid reactions were carried out using m-chloroperbenzoic acid (MCPBA), obtained from FMC Chemical Company, which was 85% pure and contained 15% m-chlorobenzoic acid.

## Reaction of 9-Fluorenone with Triphenylphosphine

### A. In Xylene

The combined reactants of 9-fluorenone (2.464 g., 0.0136 mole) and triphenylphosphine (7.344 g., 0.028 mole) in xylene (25 ml., refluxed over calcium hydride for 6 hrs.) were refluxed for 38 hrs. under pre-purified nitrogen. The solvent was removed *in vacuo* and the residue taken up in a minimum amount of dry benzene. Thin layer chromatography of the benzene solution showed it to contain mostly triphenylphosphine and 9-fluorenone with a trace of triphenylphosphine oxide. The benzene solution was chromatographed over a column packed with 600 g. of acid washed aluminum oxide (Will Corp.) to give triphenylphosphine (7.138 g., 97.20%; elutant benzene), 9-fluorenone (2.420 g., 98.21%; elutant benzene), and a solid mixture (0.185 g.; elutant 95% ethanol) consisting of triphenylphosphine oxide, a trace of fluorenone and three unidentified spots indicated by t.l.c. Fluorenone and triphenylphosphine were recrystallized from petroleum ether (60-110°) and 95% ethanol, respectively. These compounds were characterized by their m.p., mixed m.p. and thin layer chromatogram.

B. No Solvent

Fluorenone (1.08 g., 0.006 mole) and triphenylphosphine (3.18 g., 0.012 mole) were fused (150-160° wood's metal bath temperature) for 38 hours. Chromatography over acid washed aluminum (240 g.) using benzene as elutant yielded unreacted 9-fluorenone (0.97 g., 90% yield; m.p. 83-84°) recrystallized from petroleum ether (60-110°), triphenylphosphine (2.89 g., 91% yield) and di-biphenylene ethene (0.010 g., as identified by t.l.c.).

Reaction of 9-Fluorenone with Tributylphosphine

A. Neat (90-100°)

9-Fluorenone (2.464 g., 0.0136 mole) and tributylphosphine (5.665 g., 0.028 mole) were heated (90-100°) under prepurified nitrogen with stirring for 38 hours. Chromatography of the reddish amber solution over Brinkmann Silica Gel (100 g., 0.2-0.5 mm.) yielded unreacted 9-fluorenone (2.1185 g., 86% yield). Thin layer chromatography indicated the presence of tributylphosphine oxide and two unidentified spots.

B. Neat (155-165°)

9-Fluorenone (2.464 g., 0.0136 mole) and tributylphosphine (5.665 g., 0.028 mole) were heated (155-165°) under pre-purified nitrogen with stirring for 76 hours. Chromatography of the dark red solution on acid washed alumina (205 g.) yielded di-biphenylene ethene (0.883 g., 38% yield: identified by t.l.c. and infrared spectrum which were in agreement with known sample provided by Professor Ernst D. Bergmann). This layer chromatography indicated the presence of tributylphosphine oxide, unreacted 9-fluorenone and a trace of two other unidentified oils. Di-biphenylene ethene was the first to come off the column (benzene as the elutant) as an oil which was triturated with petroleum ether (30-60°) leading to an orange-red solid.

## Reaction of 9-Fluorenone with Triethyl Phosphite

A. In Xylene

9-Fluorenone (2.464 g., 0.0136 mole) and triethyl phosphite (4.65 g., 0.028 mole) in dry xylene were refluxed for 38 hours with stirring under pre-purified nitrogen. Most of the solvent was removed *in vacuo* and the orange solution filtered, yielding 9-diphenylenephenanthrone (0.273 g.). Chromatography of the orange solution over Brinkmann Silica Gel

(70 g.; 0.2-0.5 mm.) gave 9-fluorenone (0.900 g.; 36.5% yield), diphenylene ethene (0.1486 g.; 6.6% yield) and 9-diphenylenephenanthrone (0.561 g., 24% yield; m.p. 262-263°). 9-Diphenylenephenanthrone was identified by its mixed melting point and infrared spectrum. Unidentified yellow oils were obtained by eluting the column with 25% ether-benzene, and 95% ethanol solutions. The oils were found to give at least five spots by t.l.c.

B. Neat (148-155°)

The combined reactants of 9-fluorenone (2.464 g., 0.0136 mole) and triethyl phosphite (4.65 g., 0.028 mole) were heated (148-155° oil bath temperature) under pre-purified nitrogen with stirring for 38 hours. The reaction mixture was cooled and filtered. The white solid collected was recrystallized from benzene yielding 9-diphenylenephenanthrone (1.435 g., 61.5% yield; m.p. 262-263°). The red filtrate was chromatographed over 163 g. acid washed alumina column (32 mm. x 2.5 mm., id.), giving di-biphenylene ethene (0.196 g., 8.8% yield; m.p. 183-185°).

C. Neat (Room Temperature)

9-Fluorenone (4.928 g., 0.0272 mole) and triethyl phosphite (9.30 g., 0.056 mole) were combined and vigorously stirred at room temperature under an atmosphere of pre-purified nitrogen for 24 hours. The reaction was carried out in the dark with the flask covered by aluminum foil. The solid precipitating out of solution was quickly filtered and dried by applying pre-purified nitrogen pressure with slight water aspirator suction. One recrystallization from a hexane-benzene mixture gave a 1,3-dioxaphospholane 3.56 g., of m.p. (in sealed capillary) 132-133° in 50% yield.

Anal. Calc'd for $C_{32}H_{31}O_5P$: C, 72.99; H, 5.93; P, 5.88

Found: C, 72.77; H, 5.82; P, 5.64

For the $P^{31}$, $H^1$ n.m.r. shifts and infrared data, see section on Discussion of Spectra. The 2:1 adduct (pentaoxyphosphorane) was found to be sensitive to light, heat, moisture and oxygen. A second recrystallization of the oxyphosphorane from a hexane-benzene mixture without use of a nitrogen atmosphere converted the 2:1 adduct to the known 9-diphenylenephenanthrone (m.p. 262-263°).

Anal. Calc'd for $C_{26}H_{16}O_1$: C, 90.67; H, 4.69; mol. wt. 344

Found: C, 90.56; H, 4.79; mol. wt. 337

## Preparation of 2,7-Dibromofluorenone

Following the procedure of J. Schmidt and K. Bauer, Ber., 38, 3767 (1905), to recrystallized 9-fluorenone (6 g.) mixed with 50 ml. of water was added bromine (13.4 g.). The reaction mixture was heated at 120-125°C for 19 hours followed by several washings with sodium hydrogen sulfite; the product was dried and recrystallized twice from acetic acid. Mixed melting point (200-202°C), t.l.c. and infrared spectrum were in agreement with authentic 2,7-dibromofluorenone.

## Reaction of 2,7-Dibromofluorenone with Tributylphosphine

### A. No Solvent

2,7-Dibromofluorenone (3.237 g., 0.0096 mole) and tributylphosphine (5.665 g., 0.028 mole) was heated at 100°

(bath temperature) for 4 hours with stirring under pre-purified nitrogen. The yellow solid (2,7-dibromofluorenone, which is insoluble in the phosphine) was converted to a dark red insoluble solid, which was filtered and the dark green filtrate discarded (at least 7 spots by t.l.c.). The red solid was leached with two portions of boiling benzene followed by one portion of boiling 95% ethanol and dried. Thin layer chromatography and infrared data indicated the red amorphous solid to be $2,2^1,7,7^1$-tetrabromodiphenylenethylene (1.3564 g., 63.5% yield). The sample was further purified by recrystallizing two times from mono-bromobenzene, yielding red needles melting at 454-455°.

Anal. Calc'd. for $C_{26}H_{12}Br_4$: C, 48.46; H, 1.86; Br, 49.68[a]

Found: C, 48.23; H, 1.75; Br, 49.45

[a] According to the literature (L. A. Pinck and G. E. Hilbert, J. Am. Chem. Soc., 68, 2014 (1946), $2,2^1,7,7^1$-tetrabromodiphenyleneethylene has never been analyzed correctly (lit., Found: C, 50.59; 49.10; H, 2.12, 2.22; Br, 48.82; m.p. >370°).

In another run the reaction mixture was heated (150-160°) for 67.5 hours with stirring. The black tar formed was discarded.

B. In Acetonitrile (Excess Tributylphosphine)

The combined reactants of 2,7-dibromofluorenone (1.6185 g., 0.0048 mole) and tributylphosphine (2.883 g., 0.014 mole) in dry acetonitrile (15.5 ml., distilled and refluxed over calcium hydride followed by distillation from phosphorous pentoxide) were refluxed for two hours under pre-purified nitrogen with stirring. The red insoluble solid formed was then filtered and dried. Thin layer chromatography and infrared data showed the sample to be 2,2$^1$,7,7$^1$-tetrabromodiphenyleneethylene (0.371 g., 35% yield). The solvent was removed <u>in vacuo</u> and the residual green oil was examined by thin layer chromatography and infrared, which indicated the completion of the reaction by the absence of 2,7-dibromofluorenone. The green oil was exposed to laboratory atmospheric conditions for three weeks and the white solid formed was filtered and dried, m,p. 161.5-162.5°. The product 2,7-dibromofluorene was purified by recrystallization from benzene, m.p. 165.5-166.5° (0.667 g., 43% yield).

<u>Anal</u>. Calc'd for $C_{13}H_8Br_2$: C, 48.19; H, 2.49; Br, 49.32

Found: C, 48.12; H, 2.47; Br, 49.13

2,7-Dibromofluorene was further confirmed by its mixed melting point, t.l.c., infrared (Sadtler spectrum No. 25066) and n.m.r. spectra (methylene protons located at 3.03 δ; $C_6D_6$).

C. <u>In Acetonitrile (Excess 2,7-Dibromofluorenone)</u>

Using the same conditions as before with 0.0048 mole of 2,7-dibromofluorenone and 0.0020 mole of tributylphosphine as reactants with the reaction run for 26 hours led to a recovery of 1.40 g. (86% yield) of 2,7-dibromofluorenone. The same green residual oil yielded 0.050 g. (8% yield) of recrystallized 2,7-dibromofluorene.

<u>Reaction of 2,7-Dibromofluorenone with Triethyl Phosphite</u>

A. <u>Neat (Run No. 1)</u>

2,7-Dibromofluorenone (3.237 g., 0.0096 mole) and triethyl phosphite (4.65 g., 0.028 mole) were heated at 100° (bath temperature) for 5.8 hours with stirring under prepurified nitrogen. The yellow solid (2,7-dibromofluorenone, which is insoluble in phosphite) was converted to an orange colored solid and filtered (2.2076 g. was collected). The orange solid was washed several times with hot benzene and recrystallized from monobromobenzene yielding a colorless amorphous pure (t.lc.) sample, m.p. 391-392° (with decomposition). The latter was identified as the tetrabromo-9-diphenylenephenanthrone by its infrared spectrum (KBr) (carbonyl absorption at 5.95 μ) and analysis.

Anal. Calc'd for $C_{26}H_{12}Br_4O$: C, 47.34; H, 1.83; Br, 48.46

Found: C, 47.17; H, 2.05; Br, 48.55

A few milligrams of 1,3-dioxaphospholane (i.e., 2:1 2,7-dibromofluorenone-triethyl phosphite adduct) was fortunately isolated under the rather extreme thermal conditions under which this reaction was run. The 2:1 adduct was purified by recrystallization from benzene, m.p. 204-205° (opaque orange melt).

Anal. Calc'd for $C_{32}H_{27}Br_4O_5P$: C, 45.64; H, 3.23; Br, 37.96; P, 3.68

Found: C, 45.45; H, 3.27; Br, 37.86; P, 3.53

B. Neat (Run No. 2)

Using the same conditions as before (but this time the orange solid obtained on filtration was washed several times with hot benzene, cold acetonitrile and cold ethylacetate), pure tetrabromo-9-diphenylenephenanthrone (1.84 g., 58% yield; m.p. 391-392° with decomposition) was thereby obtained. The washings gave 0.135 g. of an orange solid which was not identified in this run. The tetrabromo-9-diphenylenephenanthrone was identified by its infrared analysis and mixed melting point. It was found to be insoluble in benzene, acetonitrile, acetone, carbon tetrachloride, chloroform, methanol, ethanol, ethyl acetate, tetrahydrofuran and N,N-dimethylformamide.

Anal. Calc'd for $C_{26}H_{12}Br_4O$: C, 47.34: H, 1.83; Br, 48.46

Found: C, 47.18; H, 1.88; Br, 49.03

C. Neat (Run No. 3)

The same conditions as before were used but this time the reaction mixture was heated (100-110° bath temperature) for 24 hours. The red-orange solid (1.6624 g.) obtained by filtration was fractionally recrystallized many times with monobromobenzene yielding 2,7,2$^1$,7$^1$-tetrabromo-diphenylene-ethene (0.180 g.; 8.5% yield), as identified by t.l.c., m.p., mixed m.p. and infrared spectrum.

D. Neat (Run No. 4)

Triethyl phosphite (2.900 g., 0.0174 mole) was mixed with solid 2,7-dibromofluorenone (3.2370 g., 0.0096 mole) under pre-purified nitrogen with stirring. The mixture was heated (60° bath temperature) for 4.5 hours followed by an additional 30 hours of vigorous stirring at room temperature under nitrogen. A white viscous slurry was obtained which was quickly filtered, washed with acetonitrile and dried by applying pre-purified nitrogen pressure with slight water aspirator suction.

Two recrystallizations from dry benzene yielded a pentaoxyphosphorane (3.6283 g., m.p. 204-205°) in 90% yield. For the $P^{31}$, $H^1$ n.m.r. shifts and infrared data, see section on Discussion of Spectra. The 1:1 adduct is sensitive to light, heat, moisture and oxygen.

Anal. Calc'd for $C_{32}H_{27}Br_4O_5P$: mol. wt., 842

Found: mol. wt., 836

For C, H, Br and P analysis, see Run No. 1.

### Reaction of 9-Bromofluorene with Triethyl Phosphite

Triethyl Phosphite (4.650 g., 0.028 mole) was mixed with solid 9-bromofluorene (4.902 g., 0.02 mole) under pre-purified nitrogen with stirring. The mixture was heated (110° bath temperature) for six hours followed by the removal of the unchanged triethylphosphite in vacuo. The residual liquid was distilled to give 3.75 g., b.p. 162° (0.20 mm.) of a clear highly viscous liquid; $H^1$ and $P^{31}$ n.m.r. revealed it to be diethyl fluorenylphosphonate (62% yield). Examination of the liquid by t.l.c. gave only one component.

### Reaction of Tetrabromo-9-Diphenylenephenanthrone with Triethyl Phosphite

A suspension of tetrabromo-9-diphenylenephenanthrone (1.00 g., 0.0015 mole) in triethyl phosphite (4.65 g., 0.028 mole) was kept 24 hours at 100° (bath temperature), under nitrogen with stirring. The colorless solution was cooled and filtered. The colorless insoluble unreacted tetrabromo-9-diphenylenephenanthrone (0.94 g., m.p. 391-392° with decomposition) was recovered. No trace of tetrabromo-di-biphenyleneethene was detected.

### Reaction of Tetrabromo-9-Diphenylenephenanthrone with Tributylphosphine

Tributylphosphine (2.833 g., 0.014 mole) was mixed with solid tetrabromo-9-diphenylenephenanthrone (0.500 g., 0.00075 mole) under nitrogen. The reaction mixture was kept 5.5 hours at 105-110° (bath temperature) under nitrogen with stirring. The colorless solution was cooled and filtered. The white insoluble tetrabromo-9-diphenylenephenanthrone (0.500 g., 100%; m.p. 391-392° with decomposition) was recovered unchanged. Tetrabromo-di-biphenyleneethene was not detected.

### Reaction of Di-Biphenyleneethene with m-Chloroperbenzoic Acid

To a solution of di-biphenyleneethene (6 g., 0.0182 mole) in chloroform (40 ml.) was added dropwise a solution of 85% m-chloroperbenzoic acid (3.70 g., 0.0182 mole) in chloroform (40 ml.). An exothermic reaction did not ensue. The mixture was then kept at reflux temperature for one week with stirring. After this time, the m-chloroperbenzoic acid was filtered off and the chloroform layer washed with 10% sodium sulfite solution until a negative test was obtained with starch-potassium iodide paper. Residual acid was removed by extraction with saturated sodium bicarbonate solution and the organic layer dried over magnesium sulfate. Removal of the chloroform *in vacuo* left a red oil which became a solid on trituration with cyclohexane. Di-biphenyleneethene (5.8 g.) was recovered unchanged.

### Reaction of 9-Bromofluorene with 9-Fluorenone in Presence of a Methanolic Solution of Potassium Carbonate

According to the method of Bergmann and Hervey, Ber., 62, 908 (1929), 9-bromofluorene (12.4 g., 0.0498 mole) and

9-fluorenone (9.2 g., 0.0510 mole) were mixed together with potassium carbonate (10 g., 0.0498 mole) in methyl alcohol (60 ml.). After refluxing for 4.8 hours the reaction gave di-biphenyleneethene and starting materials. No trace of 9,9'-difluorenyloxide was detected.

## Reaction of 2,7-Dibromofluorenone-Triethyl Phosphite Adduct with Triethyl Phosphite

### A. No Solvent

Triethyl phosphite (2.33 g., 0.014 mole) was mixed with the solid 2:1 adduct (1.564 g., 0.00186 mole) under nitrogen. The reaction mixture was kept 6 hours at 100° (bath temperature) with stirring. The orange solid formed was filtered, washed several times with hot benzene, and fractionally recrystallized from mono-bromobenzene. Di-biphenyleneethene bromo derivative was the first crop to precipitate, followed by tetrabromo-9-diphenylenephenanthrone (0.24 g., 0.000364 mole; 20% yield) as confirmed by m.p., microanalysis, t.l.c., and its infrared spectrum.

Anal. Calc'd for $C_{26}H_{12}Br_4O$: C, 47.34; H, 1.83; Br, 48.46

Found: C, 47.08; H, 1.88; Br, 48.27

The filtrates were combined, concentrated and chromatographed over acid washed alumina (benzene used as elutant) into $2,7,2^1,7^1$-tetrabromo-di-biphenyleneethene and 2,7-dibromofluorenone (0.075 g., 0.00022 mole; 3%). The pure di-biphenyleneethene derivative was obtained in 14% yield (0.116 g., 0.00026 mole).

B. In Acetonitrile

To a suspension of the bromo-pentaxoyphosphorane (0.400 g., 0.000475 mole) in dry acetonitrile (8 ml.) was added triethyl phosphite (0.1665 g., 0.001 mole) at once under pre-purified nitrogen with stirring. The mixture was refluxed for 46.2 hours, cooled and filtered. The di-biphenyleneethene bromo derivative (0.0668 g., 0.00015 mole; 32% yield) collected was identified in the usual manner. Removal of the acetonitrile *in vacuo* left a white solid which was washed with ether and recrystallized from chloroform. The resulting 9-hydroxy-9'-ethoxydifluorene (0.037 g., 0.000052 mole; m.p. 316° was obtained in 11 % yield. Thin layer chromatography indicated that the filtrate contained at least seven components.

### Reaction of 2,7-Dibromofluorenone-Triethyl Phosphite Adduct in Benzene

A solution of the 2:1 adduct (0.4801 g., 0.00057 mole) in dry benzene (8 ml.) was refluxed for 3.5 hours under pre-purified nitrogen with stirring. The white solid precipitating out of solution was filtered and dried. Tetrabromo-9-diphenylenephenanthrone (0.158 g., 0.00024 mole; 42% yield; m.p. 391-392° with decomposition) collected was further identified by its t.l.c. and infrared data. The filtrate was stripped *in vacuo* of benzene to give 2,7-dibromofluorenone (0.195 g., 0.000576 mole; 50.5% yield) as shown by m.p., t.l.c. and its infrared spectrum.

### Reaction of 2,7-Dibromofluorenone-Triethyl Phosphite Adduct in Acetonitrile

A suspension of the bromo-pentaoxyphosphorane 2:1 adduct (0.5910 g., 0.00070 mole) in dry acetonitrile (25 ml.)

was refluxed for 6 hours under nitrogen with stirring. The mixture was cooled, filtered, and the white solid collected was washed with hot benzene. The postulated 9-hydroxy-9'-ethoxy difluorene (0.1591 g. crude; 0.00025 mole; 32% yield was recrystallized from chloroform (m.p. 316°). See section on Discussion of Spectra for infrared data. Due to insufficient solubility an n.m.r. spectrum could not be carried out.

Anal. Calc'd for $C_{28}H_{18}Br_4O_2$: C, 47.63; H, 2.57; Br, 45.27

Found: C, 47.83; H, 3.19; Br, 44.44

The filtrate was stripped *in vacuo* of the acetonitrile-benzene mixture to give 2,7-dibromofluorenone (0.1246 g., 0.000369 mole; 26.4% yield) which was recrystallized from acetic acid (m.p. 201-202°, mixed m.p. 201-202°). Thin layer chromatography and infrared data were in agreement with authentic sample.

NOTE: In order to insure the formation of the postulated 9-hydroxy-9'-ethoxydifluorene a fresh batch of the bromo-pentaxoyphosphorane 1:1 adduct must be prepared for its immediate use in refluxing ultra-dry acetonitrile.

## Reaction of the Proposed 9-Hydroxy-9'-Ethoxydifluorene with Hydriodic Acid

Hydriodic acid (47-50%; 3 ml.) was added to the postulated 9-hydroxy-9'-ethoxydifluorene (0.051 g.). The mixture was kept 12 hours at 110° with stirring. The suspension was cooled, filtered, washed several times with water and dried. Formation of some tetrabromo-9-diphenylenephenanthrone was indicated by infrared data. To the mixture of the phenanthrone and difluorenyl hydroxy ether was added hydriodic acid (47-50%; 10 ml.) with stirring. The mixture was then kept at 120° (bath temperature) for 41 hours. The suspension was worked up in the same manner as before but this time infrared and melting point data indicated the complete conversion of the hydroxyether to the phenanthrone.

## Reaction of 2,7-Dibromofluorenone-Triethyl Phosphite Adduct with Tributylphosphine

The combined reactants of the 2:1 adduct (0.400 g., 0.000475 mole) and tributylphosphine (0.202 g., 0.001 mole) were heated (100° bath temperature) for one hour under nitrogen with stirring. The resulting mixture was cooled and filtered to give crude 2,2',7,7'-tetrabromo-di-biphenyleneethene (0.146 g., 0.000329 mole; 69% yield). The product was purified by recrystallization from mono-bromobenzene to yield the pure fulvalene (0.085 g., 0.000191 mole; 40% yield). Thin layer chromatography of the filtrate revealed the presence of at least seven components, three of which are 2,7-dibromofluorene, 2,7-dibromofluorenone and tributylphosphine oxide.

## Reaction of 2,7-Dinitrofluorenone with Triphenylphosphine

### A. No Solvent

2,7-Dinitrofluorenone (1.89 g., 0.007 mole) and triphenylphosphine (1.92 g., 0.0073 mole) were fused under nitrogen. The mixture was then kept at 85° for 1.25 hr. with stirring. Triphenylphosphine (1.9 g.) and 2,7-dinitrofluorenone (1.8 g.) were recovered unchanged; the former was soluble in ether while the latter was found to be insoluble. Thin layer chromatography confirmed the absence of reaction.

B. In Ether

Triphenylphosphine (1.92 g., 0.0073 mole) and 2,7-dinitrofluorenone (1.89 g., 0.007 mole) were combined and refluxed in ether (25 ml.) for 10 days under nitrogen with stirring. The reaction mixture was cooled, and the unreacted 2,7-dinitrofluorenone filtered (1.89 g., quantitative recovery). The ether was removed *in vacuo* leaving triphenylphosphine (1.9 g.) behind. Thin layer chromatography and melting point data confirmed the above results.

### Reaction of Benzophenone with Tributylphosphine

Benzophenone (2.478 g., 0.0136 mole) and tributylphosphine (5.665 g., 0.028 mole) were heated (150-160° bath temperature) for 197 hours under nitrogen. Thin layer chromatography indicated that benzophenone is relatively inert toward tributylphosphine. Only traces of tetraphenylethylene and tributylphosphine oxide were detected. A. C. Poshkus and J. E. Herweh, J. Org. Chem., 29, 2567 (1964) have reported that benzophenone is inert toward trimethyl and triphenyl phosphite or triphenylphosphine. The reactants were recovered almost quantitatively after heating them for several days at about 160°. Triisopropyl phosphite on reaction with benzophenone was reported to give tetraphenylethylene in only 4% yield.

## Reaction of Benzanthrone with Tributylphosphine

Benzanthrone (3.132 g., 0.0136 mole) suspended in tributylphosphine (11.330 g., 0.056 mole) was heated (145-150° bath temperature) for 39.3 hours under pre-purified nitrogen. The mixture was filtered (yielding unreacted benzanthrone, 1.67 g.) followed by chromatography over acid washed alumina of the filtrate. An additional 0.75 g. of benzanthrone was thereby isolated. Benzanthrone was thus recovered in a 77.3% yield (2.42 g.). Thin layer chromatography indicated the presence of tributylphosphine oxide and at least three other components.

## Reaction of Xanthone with Tributylphosphine

Freshly distilled tributylphosphine (5.665 g., 0.028 mole) was mixed with solid xanthone (2.668 g., 0.0136 mole) under nitrogen. The mixture was then kept at 150-160° (bath temperature) for 133 hours with stirring. Unreacted xanthone (2.605 g.) was recovered quantitatively after the mixture was cooled and filtered. The reactant xanthone was purified by recrystallization from absolute ethanol (m.p. 174°).

## Reaction of Xanthone with Triethyl Phosphite

Using the same conditions as before but with 0.028 mole (4.65 g.) of triethyl phosphite and 0.0136 mole (2.668 g.) of xanthone as reactants led to a quantitative recovery of unreacted xanthone. The reaction was run at 145-155° (bath temperature) for 36 hours.

## Reaction of 2,3-Diphenyl-1-Indenone with Triethyl Phosphite

Triethyl phosphite (4.65 g., 0.028 mole) was mixed with solid 2,3-diphenyl-1-indenone (3.840 g., 0.0136 mole) under nitrogen. The mixture was then kept at 123° (bath temperature) for 30.5 hours with stirring and let stand 1.5 months under nitrogen at room temperature. The black semi-liquid mixture was filtered, the filtrate cooled in a dry ice-acetone bath, treated with petroleum ether (60-110°), re-cooled and re-filtered. Two recrystallizations from benzene gave the colorless indenone-phosphite 1:1 adduct (0.030 g.), m.p. 230-230.5°. See section titled Discussion of Spectra for infrared data.

Anal. Calc'd for $C_{27}H_{29}O_4P$: C, 72.29; H, 6.54; P, 6.91

Found: C, 72.56; H, 5.97; P, 6.84

Removal of the petroleum ether *in vacuo* left a viscous brown-black oil; chromatography over acid washed alumina (using benzene as elutant) gave a brown oil which solidified on standing (0.243 g.). Thin layer chromatography indicated the product to have an identical $R_f$ value as that of the product isolated from the indenone-triphenylphosphine run. Unreacted 2,3-diphenyl-1-indenone (0.224 g.) was next isolated and identified by t.l.c., m.p. and mixed m.p. The final fraction (using 50:50 ethanol/benzene followed by 100% ethanol as elutant) collected (3 g.) was an oil which contained at least six components as revealed by t.l.c.

### Reaction of 2,3-Diphenyl-1-Indenone with Triphenylphosphine

The combined reactants of 2,3-diphenyl-1-indenone (3.840 g., 0.0136 mole) and triphenylphosphine (7.336 g., 0.028 mole) were mixed and heated (160° bath temperature) under nitrogen. After 144 hours t.l.c. indicated the mixture to consist of mostly starting materials. The mixture was then kept at 220-240° for an additional 118 hours. The fused solid was triturated with acetonitrile and filtered. The crude product (3.8624 g.) thus obtained was dissolved in a minimum amount of benzene and chromatographed over acid washed alumina using benzene as the elutant. Removal of the benzene in vacuo left a brown solid which was further subjected to a soxhlet extraction for a period of 139 hours using acetonitrile. The resulting product (3.2275 g., 89% yield; m.p. 280-282° with decomposition) revealed one spot on t.l.c. and analyzed for 2,2',3,3'-tetraphenyl-$\Delta^{1,1'}$-biindene (lit. m.p. 278°).

Anal. Calc'd for $C_{42}H_{28}$: C, 94.70; H, 5.30
$C_{42}H_{30}$: C, 94.34; H, 5.66
Found: C, 93.89; H, 5.85

The above product was rechromatographed two more times over acid washed alumina into a brown solid (m.p. 280-282° with decomposition).

Anal. Calc'd for $C_{42}H_{28}$: C, 94.70; H, 5.30
Found: C, 94.46; H, 5.54

The n.m.r. spectrum in deuterobenzene shows the presence of aromatic protons as a multiplet at 6.65-7.45 δ and no other absorptions. The IR (KBr) spectrum exhibited a peak at ca. 1610 $cm^{-1}$ (C=C), and typical aromatic hydrocarbon absorption peaks.

## Reaction of 2,3-Diphenyl-1-Indenone with Tributylphosphine

Freshly distilled tributylphosphine (5.665 g., 0.028 mole) was mixed with solid 2,3-diphenyl-1-indenone (3.84 g., 0.0136 mole) under nitrogen with stirring. The mixture was then kept at 97° for 22 hours. The resulting black viscous product was treated with acetonitrile cooled in a liquid nitrogen bath and filtered. The dark brown solid (1.75 g.) collected was worked up as before giving IR and n.m.r. spectra which were in agreement with the triphenylphosphine reaction product. The product could not be satisfactorily recrystallized. Thin layer chromatography gave one spot with an $R_f$ value matching that of the triphenylphosphine-indenone product.

## Preparation of 3-Phenyl-2-(2'-Pyridyl)Indenone

According to the method of E. D. Amstutz *et al.*, J. Org. Chem., 23, 373 (1958), 3-phenyl-2-(2'-pyridyl)indenone was synthesized by the reaction of pyrophthalone with phenyllithium followed by hydrolysis and dehydration of the resulting carbinol. The molar ratio of lithium to bromobenzene to phthalone used was 4:2:1. The lithium was cut into small pieces and added to 35 times its weight of absolute ether. A 0.5M solution of bromobenzene in absolute ether was added to the lithium-ether mixture with stirring, at such a rate as to maintain gentle reflux of the ether. Afther the lithium had reacted completely, the phthalone was added as a powder at such a rate as to maintain gentle reflux. After complete addition of the phthalone, the mixture was stirred with gentle reflux for three hours. A yellow solid precipitated during the course of the reaction. The reaction vessel was surrounded by an ice bath and an equal volume of dilute solution of ammonium chloride was slowly added to the reaction mixture with stirring. The solid present dissolved and a new solid precipitated as more ammonium chloride solution was added. Stirring was continued for 0.5 hour after addition of the hydrolysis solution. The solution was filtered, and the solid carbinol was washed with water and dried. The dried carbinol was dissolved in concentrated hydrochloric acid. A great deal of effervescence occurred and the solution became a deep red. The solution was stirred for 30 minutes, cooled with an ice bath, and neutralized with sodium hydroxide solution. The solid which separated was the dehydrated carbinol, which was filtered, washed with 10% sodium bicarbonate solution and dried. The product was purified by recrystallization from an ethanol-water solution; t.l.c., mixed m.p. (130-131°), and infrared spectrum were in agreement with the authentic sample supplied by Professor Amstutz.

### Reaction of 3-Phenyl-2-(2'-Pyridyl)Indenone with Triethyl Phosphite

The combined reactants of the substituted indenone (0.1294 g., 0.00045 mole) and triethyl phosphite (0.83 g., 0.005 mole) were vigorously stirred at room temperature under nitrogen for three days. Thin layer chromatography indicated the mixture to consist of mostly starting material. The mixture was then heated (100° bath temperature) an additional 20 hours, treated with acetonitrile, cooled and filtered. Infrared and ultra-violet spectra (both proved to be inconclusive) of the colorless oil (0.033 g.) clinging to the flask were taken. The red-brown filtrate was concentrated by removal of acetonitrile and excess phosphite in vacuo, yielding an unidentified (0.1839 g.) complex oil (t.l.c. gave at least four components, one of which may possibly be unreacted indenone).

### Reaction of Tetracyclone with Tributylphosphine

Tributylphosphine (5.660 g., 0.028 mole) was mixed with solid tetracyclone (5.229 g., 0.0136 mole) under nitrogen. The mixture was then kept at 97° (bath temperature) for 28.75 hours. The resulting black viscous syrup was taken up in acetonitrile, cooled in an acetone dry ice bath and filtered. The product, 1,1'-dihydro-2,3,4,5,2',3',4',5'-octaphenylfulvalene (2.00 g.; 40%) was purified by recrystallizing two times from acetonitrile. Infrared, ultra-violet, n.m.r. and mass spectral data of the white needle-like solid melting at 153° (yellow-green melt) were recorded. (See section on Discussion of Spectra.)

Anal. Calc'd for $C_{58}H_{42}$: C, 94.28; H, 5.72; mol. wt., 739
Found: C, 94.55; H, 5.63; mol. wt., 726; 739 (mass spectral value)

### Reaction of 5-Bromo-1,2,3,4-Tetraphenylcyclopentadiene with Zinc

5-Bromo-1,2,3,4-tetraphenylcyclopentadiene (0.896 g., 0.0020 mole) and powdered zinc (3.11 g., 0.0475 mole) in benzene (60 ml., freshly distilled over phosphorus pentoxide) were refluxed for 47 hours. The mixture was cooled, filtered and the residue washed with hot benzene. The combined benzene solutions were washed with water, dried over anhydrous magnesium sulfate, and the benzene removed in vacuo yielding a pale yellow solid mixture (0.980 g.). Extraction of this solid with hot acetonitrile gave 1,1'-dihydro-2,3,4,5,2',3',4',5'-octaphenylfulvalene (0.250 g., 34% yield). Thin layer chromatography, m.p., mixed m.p., infrared, and n.m.r. data were in agreement with the tetracyclone-tributylphosphine reaction product.

Anal. Calc'd for $C_{58}H_{42}$: C, 94.28; H, 5.72
Found: C, 94.01; H, 5.85
(another run) C, 94.46; H, 5.75

## Preparation of 5-Bromo-1,2,3,4-Tetraphenylcyclopentadiene

A mixture of 1,2,3,4-tetraphenylcyclopentadiene (2.22 g., 0.0060 mole) and N-bromosuccinimide (1.26 g., 0.0072 mole; recrystallized from water and dried over phosphorus pentoxide) in carbon tetrachloride (50 ml.) was refluxed for 21 hours with stirring. After cooling, the precipitated succinimide was filtered off, and the succinimide washed with hot carbon tetrachloride. The combined carbon tetrachloride solutions were concentrated in vacuo leaving a yellow solid behind (2.25 g.). The solid was taken up in a 50:50 methanol-chloroform solution and cooled. This method of recrystallization was found to be poor. The product, 5-bromo-1,2,3,4-tetraphenylcyclopentadiene (0.896 g.; m.p. 190-191°; lit. m.p. 190-191°) was purified in ethyl acetate yielding an analytically pure compound.

Anal. Calc'd for $C_{29}H_{21}Br$: C, 77.33; H, 4.90; Br, 17.76
Found: C, 77.33; H, 4.65; Br, 17.8

## Reaction of Tetracyclone with Triphenylphosphine

Triphenylphosphine (3.2 g., 0.012 mole) was mixed with tetracyclone (2.0 g., 0.0052 mole) under nitrogen. The mixture was then kept at 220-240° for 98 hours. Droplets forming on the walls of the flask solidified upon scratching the walls. The solid was identified as excess triphenylphosphine. The fused mixture was taken up in a minimum amount of benzene and chromatographed over acid washed alumina (566 g.). Elution with benzene gave an oil (first fraction) which solidified (grayish-white) on workup with acetonitrile. The product, $C_{58}H_{40}$ (1.028 g.; 54% yield) was purified by recrystallization from a huge volume of acetonitrile, m.p. 325-326.5° (dec.). Two dimensional t.l.c. indicated the solid to be pure (one spot). Triphenylphosphine oxide was eluted off the column with absolute ethanol.

| | | |
|---|---|---|
| Anal. | Calc'd for $C_{58}H_{40}$: | C, 94.53; H, 5.47; mol. wt. 736 |
| Foun | Found: | C, 94.59; H, 5.28; mol. wt. M/E 736 (mass spectral value) |
| | | Osmometry: 723, 722, 716 |

Infrared, ultra-violet and n.m.r. data are presented in the section titled Discussion of Spectra.

NOTE: The oxygen-sensitive product ($C_{58}H_{40}$) must be worked up immediately after heating is completed.

## Reaction of $C_{58}H_{40}$ with N-Bromosuccinimide

A mixture of N-bromosuccinimide (0.327 g., 0.0018 mole; recrystallized from water and dried over phosphorus pentoxide) and $C_{58}H_{40}$ (0.368 g., 0.0005 mole) in carbon tetrachloride

(25 ml.) was refluxed for 95.5 hours under nitrogen with stirring. After cooling, the precipitated succinimide was filtered off, and the succinimide washed with hot carbon tetrachloride. The combined carbon tetrachloride solutions were concentrated in vacuo leaving a yellow solid behind. The sample was washed with hot petroleum ether (60-110°), filtered, taken up with freshly distilled mono-bromobenzene, cooled and filtered. The filtrate was stripped of mono-bromobenzene and the resulting solid recrystallized from hot petroleum ether (60-110°). The product was then dissolved in a minimum of benzene and chromatographed over acid washed alumina (2" height) using benzene as an elutant. The benzene was removed in vacuo and the sample was again purified by recrystallization from petroleum ether (60-110°), m.p. 185-187°. Two dimensional t.l.c. (5% ethylacetate-benzene followed by 5% methanol-benzene using silica gel $HF_{254}$ as substrate) gave one spot.

Anal. Calc'd for $C_{58}H_{39}Br$: C, 85.39; H, 4.82; Br, 9.79
Found: C, 85.44; H, 4.94; Br, 9.66

### Oxidation of $C_{58}H_{40}$ Hydrocarbon with Nitric Acid

$C_{58}H_{40}$ (0.5992 g.) derived from the reaction of triphenylphosphine with tetracyclone was suspended in 50% aqueous nitric acid (30 ml.) and refluxed for 24 hours. After the 24 hour reflux period, additional 50% aqueous nitric acid (30 ml.) was added so that no trace of hydrocarbon remained suspended in solution. The reaction mixture was then refluxed for an additional 68 hours resulting in a clear yellow solution.

At the end of the 92 hour period, the mixture was cooled, with a solid precipitating out. The suspension was filtered (0.7422 g. collected). The yellow filtrate was extracted with two 50 ml. and one 22 ml. portions of ether, which in turn were extracted with seven 30 ml. portions of 2N sodium hydroxide solution. Acidification of the alkali layer gave a cloudy solution. The solution was kept in the cold overnight, filtered (0.2252 g.) and identified as p-nitrobenzoic acid (m.p. 237-238°). Mixed m.p., t.l.c. and infrared data were in agreement with the authentic sample. The filtrate of the acidified solution was then extracted with three 50 ml. portions of ether, dried (anhydrous magnesium sulfate) and the solvent removed _in vacuo_, yielding 0.1894 g.

The neutral mixture was taken up in two ml. of acetone and chromatographed over a column packed with 60 grams of acid washed Merck Alumina. Elution with benzene gave a yellow solid (0.060 g.) whose infrared KBr spectrum indicates carbonyl absorption at 5.6μ, 5.75(sh.) and 5.96μ with additional absorptions for typical nitro group absorptions.

## Oxidation of Tetraphenylcylcopentadiene with Nitric Acid

Tetraphenylcyclopentadiene (0.4762 g.) was suspended in 90 ml. of 50% aqueous nitric acid and refluxed for 69 hours at 110° (bath temperature). The resulting clear yellow solution was cooled and extracted with two 50 ml. and one 22 ml. portions of ether, which in turn were extracted with seven 30 ml. portions of 2N sodium hydroxide. The solid precipitating out was filtered, giving 0.220 g. (t.l.c. indicated seven constituents, all of which gave a negative test with bromcresol green). The ether solution was dried with anhydrous magnesium sulfate, the solvent removed to yield an orange solid (0.1098 g.; t.l.c. gave five spots, all of which gave a negative test with bromcresol green). The filtrate was acidified with 2N hydrochloric acid. The acidified solution was extracted with three 50 ml. portions of ether, dried and stripped of solvent *in vacuo*, yielding p-nitrobenzoic acid (0.6195 g.). The acid was recrystallized from water, m.p. 237-238°. Mixed m.p., t.l.c. and infrared data were in agreement by comparison with an authentic sample.

NOTE: $C_{58}H_{40}$ gave a plethora of similar degradation products on oxidation runs with potassium permanganate, ozonolysis, and bubbling of oxygen through a chloroform solution.

## Reaction of Tetracyclone with Triphenylphosphine

### A. In N,N-Dimethylformamide

A mixture of triphenylphosphine (1.59 g., 0.006 mole) and tetracyclone (1.0 g., 0.0026 mole) was refluxed in DMF (30 ml.) for six days under nitrogen with stirring. The solution underwent a color change (purple to yellow). After 10 minutes of cooling the solution took on a red color which could be discharged (to yellow) by refluxing for another 12 hours. The DMF was removed *in vacuo* and the residue then taken up in benzene. The benzene solution was chromatographed over acid washed alumina (679 grams of packing), yielding an oil which was solidified (0.078 g.) by trituration with cyclohexane. Thin layer chromatography gave one fluorescent spot, m.p. 184-186°; % C, 92.76; % H, 7.30; mol. wt., 1,105. Four other components were indicated by t.l.c.

# VITA

Morris Anschel was born on May 27, 1940 in Petach Tikvah, Palestine, the son of Henry and Bina Anschel.

He attended Brooklyn Technical High School in Brooklyn, New York from September, 1955 to June, 1958, when he received his diploma.

In September, 1958, Mr. Anschel entered the City College of New York from which, in June, 1962, he received a Bachelor of Science Degree, having majored in chemistry.

Mr. Anschel entered Lehigh University in February, 1963, as a research fellow to pursue studies for the Doctor of Philosophy degree. Between the years 1963-1966 he has held the Althouse Chemical Company and the Hornor Fellowships.

On November 14, 1966, Mr. Anschel joined the IBM Corporation as a Staff Chemist at their Advanced Process Development Laboratories in Kingston, New York.

Mr. Anschel is a member of the American Chemical Society, the Organic Division of the ACS, the Philadelphia Organic Chemists' Club, and the Society of the Sigma Xi.