I. STUDIES ON REACTIONS OF TRIALKYL PHOSPHATES WITH GRIGNARD REAGENTS: C-ALKYLATION VERSUS P-ALKYLATION

II. STEREOCHEMISTRY AND MECHANISM OF PYROLYTIC ELIMINATIONS IN PHOSPHINATES

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PART I

STUDIES ON REACTIONS OF TRIALKYL PHOSPHATES WITH GRIGNARD REAGENTS: C-ALKYLATION VERSUS P-ALKYLATION

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INTRODUCTION

This thesis constitutes a report on two separate investigations. The investigations are discussed separately, each with its own historical introduction, discussion of results and experimental section.

The reaction of trimethyl phosphate with phenyl Grignard reagent has been examined in detail. Evidence regarding the reaction mechanism has been obtained by examining the effect of change in ratio of reactants, temperature and mode of combination of reactants. Data has been found that indicates the occurrence of both C-alkylation and P-alkylation. A mechanism to account for the observations is proposed.

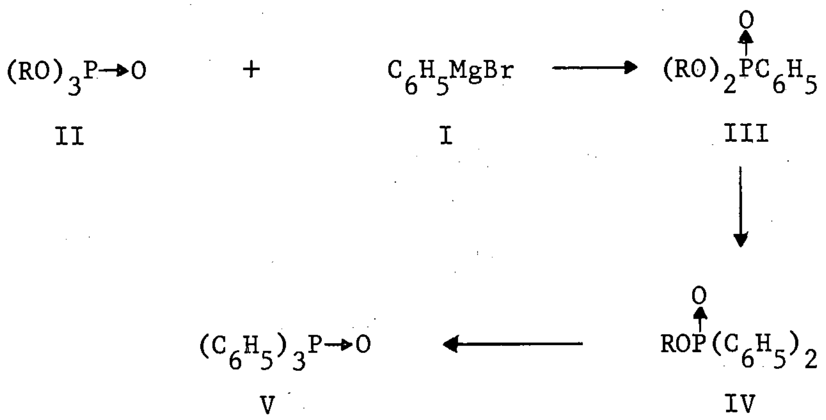
The second part of the thesis involves an investigation of the mechanism and stereochemistry of the pyrolytic decomposition of some alkyl diphenylphosphinates. The esters used possessed structural features which would aid in defining the pyrolysis mechanism. Evidence indicates the decomposition proceeds by a concerted cyclic pathway.

CHAPTER I

HISTORICAL

The Reaction of Esters of Tetravalent Phosphorus With Grignard Reagents

The condensation of Grignard reagents with neutral esters of phosphoric acid has been used rather extensively in the formation of C-P bonds.[55,78] Despite its synthetic utility no systematic investigation of the reaction appears in the literature. One would anticipate that, under appropriate conditions, one or more -OR groups of the ester could be displaced by the Grignard reagent. Reaction of the phenylmagnesium bromide (I) with an alkyl phosphate II would yield successively the corresponding phosphonate III, phosphinate IV and phosphine oxide V. Examination of the literature substantiates this though not all intermediates are found in each case.



$$\underset{\text{II}}{(RO)_3P\rightarrow O} + \underset{\text{I}}{C_6H_5MgBr} \longrightarrow \underset{\text{III}}{(RO)_2\overset{\overset{O}{\uparrow}}{P}C_6H_5}$$

$$\underset{\text{III}}{(RO)_2\overset{\overset{O}{\uparrow}}{P}C_6H_5} \longrightarrow \underset{\text{IV}}{RO\overset{\overset{O}{\uparrow}}{P}(C_6H_5)_2} \longrightarrow \underset{\text{V}}{(C_6H_5)_3P\rightarrow O}$$

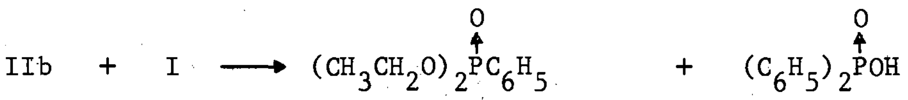
a, $R = CH_3$ b, $R = C_2H_5$ c, $R = C_6H_5$

When a 4:1 excess of I was employed with triphenyl phosphate (IIc), Gilman and Vernon[37] obtained V (less than 20 percent) plus phenol (about 40 percent). The same Grignard reagent was reported to produce V (50 percent) in reaction with tri-p-tolyl phosphate at 105° for 5 hours.[37]

$$(\underline{p}\text{-}CH_3C_6H_4O)_3P\rightarrow O \quad + \quad I \quad \longrightarrow \quad V$$

No report is made of other products, but it is significant that gas-liquid chromatography (GLC) was not employed in any previous work.

Condensation of triethyl phosphate (IIb) with I (at 92°) was reported to give diethyl phenylphosphonate (IIIb) and diphenylphosphinic



$$\text{IIb} \quad + \quad \text{I} \quad \longrightarrow \quad (CH_3CH_2O)_2\overset{\overset{\displaystyle O}{\uparrow}}{P}C_6H_5 \qquad + \quad (C_6H_5)_2\overset{\overset{\displaystyle O}{\uparrow}}{P}OH$$

IIIb VI

acid (VI) in low yields (16 and 17 percent, respectively).[36] The latter compound apparently was formed by hydrolysis of ethyl diphenylphosphinate (IVb).

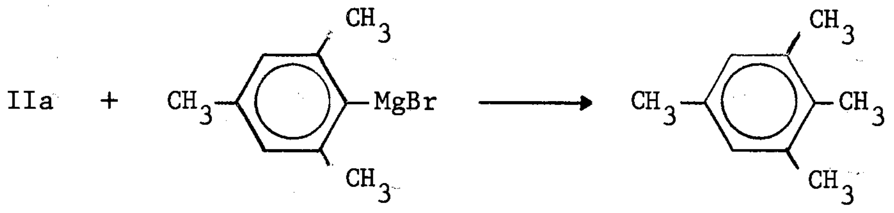
The temperature of the reaction is important for product control as indicated by the observation of Gilman and Vernon.[37] Tri-n-propylphosphine oxide was obtained when n-propylmagnesium bromide was allowed to condense with triphenyl phosphate (IIc) in ether-toluene at 95°.

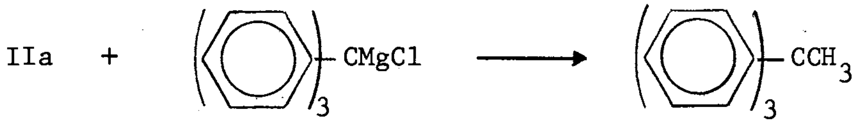
$$\text{IIc} \quad + \quad \underline{n}\text{-}C_3H_7MgBr \quad \longrightarrow \quad (\underline{n}\text{-}C_3H_7)_3P\rightarrow O$$

By contrast, heating the reagents (4:1 mole ratio of Grignard reagent to ester) in boiling ether for 6 hours gave no reaction.

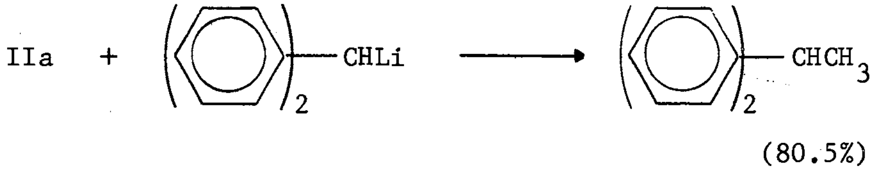
No products resulting from attack on phosphorus were reported[34] from the reaction of trimethyl phosphate (IIa) with mesitylmagnesium bromide. However, C-alkylation was detected since

1,2,3,5-tetramethylbenzene was identified as a product. 1,1,1-Triphenylethane (77 percent) formed when tritylmagnesium chloride was employed. These results have been attributed to the bulkiness of the





Grignard reagent, which apparently retards approach to the phosphorus atom. Further evidence of the steric effect was obtained by noting that the related bulky lithium reagents diphenylmethyllithium[34] and triphenylsilyllithium[35] produced C-alkylation products in major amounts.



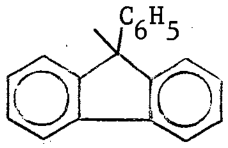
$$(RO)_3P\rightarrow O \quad + \quad (C_6H_5)_3SiLi \longrightarrow (C_6H_5)_3SiR$$

$$R = CH_3,\ \underline{n}\text{-}C_4H_9,\ \text{iso-}C_4H_9$$

In general lithium reagents have proved to be more reactive than the corresponding Grignard reagents. The phosphine oxide V has been obtained in 85 percent yield when phenyllithium was condensed with phosphoric acid esters $(RO)_3P\rightarrow O$.[88] No data was presented to indicate which R groups were used. Whereas tri-n-butyl phosphate and triphenylmethyllithium, 9-phenyl-9-fluorenyllithium or diphenylmentyllithium, gave

$$RLi + (\underline{n}\text{-}C_4H_9O)_3P \rightarrow O \longrightarrow R\text{-}\underline{n}\text{-}C_4H_9$$

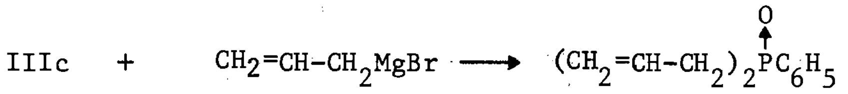
R = $(C_6H_5)_3C$-,



, $(C_6H_5)_2CH$-

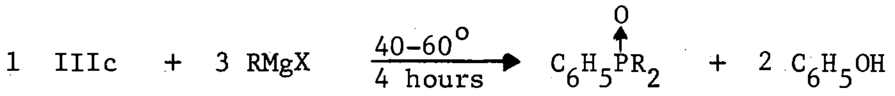
corresponding alkylation products, (77.5, 94 and 74.5 percent, respectively). No C-alkylation occurred with mesitylmagnesium bromide.[34]

A variety of substituted phosphonates have been caused to react with Grignard reagents. Morgan and Herr obtained methyldi(p-tolyl)-phosphine oxide (60 percent) from diphenyl methylphosphonate.[66] The condensation of allyl Grignard reagent with diphenyl phenylphosphonate (IIIc) resulted in the formation of diallylphenylphosphine oxide.[9,10]



$$\text{IIIc} + CH_2{=}CH\text{-}CH_2MgBr \longrightarrow (CH_2{=}CH\text{-}CH_2)_2\overset{O}{\overset{\uparrow}{P}}C_6H_5$$

The same phosphonate IIIc has been used as a source of unsymmetrical

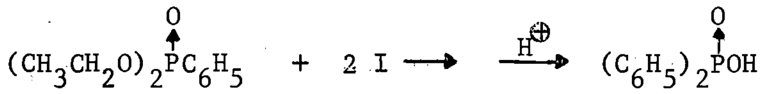


$$1\ \text{IIIc} + 3\ RMgX \xrightarrow[\text{4 hours}]{40\text{-}60^\circ} C_6H_5\overset{O}{\overset{\uparrow}{P}}R_2 + 2\ C_6H_5OH$$

R = C_2H_5, $(CH_3)_2CH$, C_4H_9, $C_6H_5CH_2$, $C_6H_5CH_2CH_2$, C_6H_5,
$\underline{o}\text{-}CH_3C_6H_4$, $1\text{-}C_{10}H_7$

tertiary phosphine oxides. Yields ranged from 78 to 92 percent.[11]

In the above examples of reaction of phosphonates a 1-mole excess of Grignard reagent was always present. In a related experiment Kosolapoff[54] obtained only diphenylphosphinic acid (VI) (32 percent) from

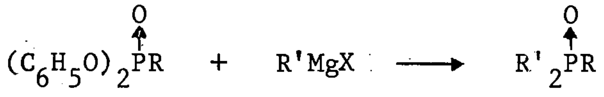


$$(CH_3CH_2O)_2\overset{O}{\overset{\uparrow}{P}}C_6H_5 + 2\ I \longrightarrow \xrightarrow{H^{\oplus}} (C_6H_5)_2\overset{O}{\overset{\uparrow}{P}}OH$$

IIIb VI

IIIb and I under strenuous conditions (85-95°, 8 hours at reflux). Failure to obtain V has been attributed to lack of excess Grignard reagent.[18]

Laughlin[58] has used the condensation of methyl and ethyl Grignard reagents with dialkyl alkylphosphonates to obtain excellent yields of dimethyl- and diethylalkylphosphine oxides (4:1 mole ratio of Grignard

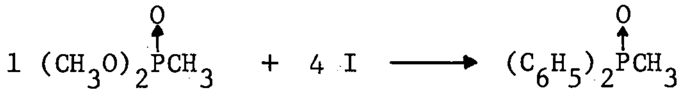


$$(C_6H_5O)_2\overset{O}{\overset{\uparrow}{P}}R \quad + \quad R'MgX \longrightarrow R'_2\overset{O}{\overset{\uparrow}{P}}R$$

$R = C_{12}H_{25}, C_{14}H_{29}, C_{16}H_{33}, C_{18}H_{37}.$ $\quad R' = CH_3$ or $CH_3CH_2.$

reagent to ester) in boiling tetrahydrofuran (THF).

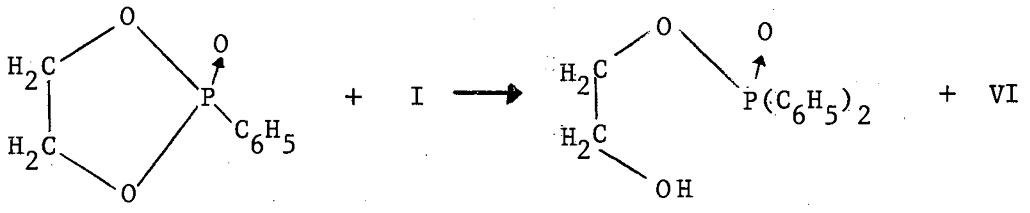
Berlin and co-workers used excess I to obtain a quantitative yield of methyldiphenylphosphine oxide from



$$1\ (CH_3O)_2\overset{O}{\overset{\uparrow}{P}}CH_3 \quad + \quad 4\ I \longrightarrow (C_6H_5)_2\overset{O}{\overset{\uparrow}{P}}CH_3$$

dimethyl methylphosphonate.[7]

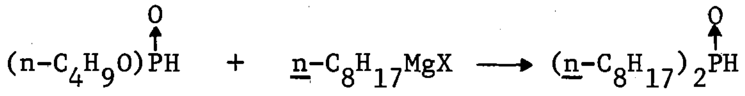
Edmundson and Wrigley have examined the reaction of Grignard reagents with certain cyclic phosphonates.[30] 2-Oxo-2-phenyl-1,3,2-dioxaphospholane (VII) was converted to 2-hydroxyethyl



VII VIII

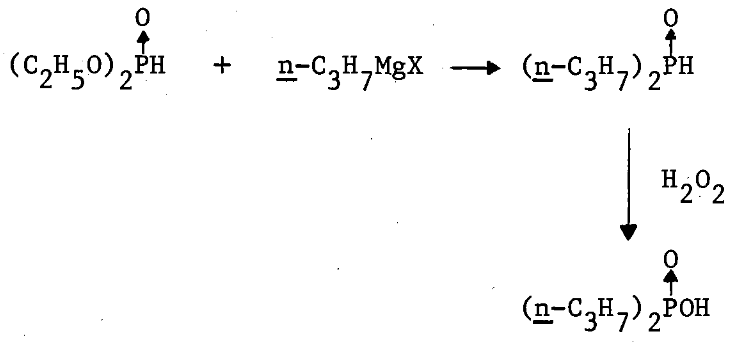
diphenylphosphinate (VIII) and the acid VI when low ratios of I to ester were used. In the presence of excess (3:1) phenylmagnesium bromide, V was detected in small amounts; no VI was evident in this instance.

Displacement of alkoxy groups from dialkyl hydrogenphosphonates by Grignard reagents has been reported to give secondary phosphine oxides.[22,25,48,65,90] Di-n-butyl hydrogenphosphonate gave di-n-octylphosphine oxide (70 percent) when condensed with the appropriate Grignard reagent.[89]

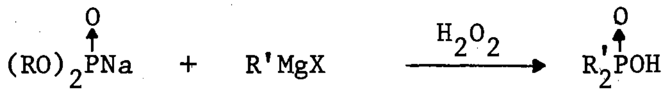


$$(n\text{-}C_4H_9O)\overset{O}{\overset{\uparrow}{P}}H + \underline{n}\text{-}C_8H_{17}MgX \longrightarrow (\underline{n}\text{-}C_8H_{17})_2\overset{O}{\overset{\uparrow}{P}}H$$

The synthetic utility of the above reaction was enhanced by the observation that the secondary phosphine oxide can be readily converted to the corresponding phosphinic acid with hydrogen peroxide. Sodium salts of the dialkyl hydrogenphosphonates undergo displacement of alkoxy groups to give, after hydrolysis and oxidation, phosphinic acids.[74] The secondary phosphine oxide obtained before oxidation has been shown to be in equilibrium with the corresponding phosphinous



$$(C_2H_5O)_2\overset{O}{\overset{\uparrow}{P}}H + \underline{n}\text{-}C_3H_7MgX \longrightarrow (\underline{n}\text{-}C_3H_7)_2\overset{O}{\overset{\uparrow}{P}}H \xrightarrow{H_2O_2} (\underline{n}\text{-}C_3H_7)_2\overset{O}{\overset{\uparrow}{P}}OH$$

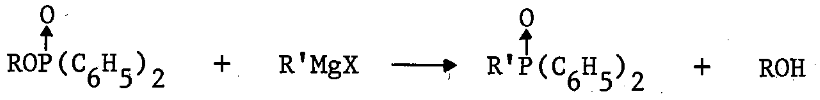


$$(RO)_2\overset{O}{\overset{\uparrow}{P}}Na + R'MgX \xrightarrow{H_2O_2} R'_2\overset{O}{\overset{\uparrow}{P}}OH$$

acid.[48]

$$R'_2\overset{\overset{O}{\uparrow}}{P}H \longrightarrow R'_2POH$$

In our Laboratory a careful mechanistic study has been carried out on the reaction of alkyl Grignard reagents with alkyl diphenylphosphinates.[13] Results indicate the reactivity of the esters to parallel

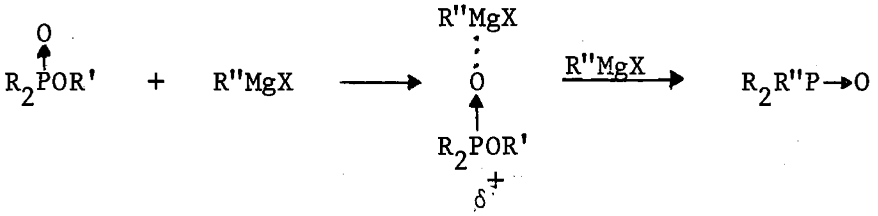


$$RO\overset{\overset{O}{\uparrow}}{P}(C_6H_5)_2 \quad + \quad R'MgX \longrightarrow R'\overset{\overset{O}{\uparrow}}{P}(C_6H_5)_2 \quad + \quad ROH$$

$R = \underline{n}\text{-}C_3H_7,\ \text{iso-}C_4H_9,\ \text{neo-}C_5H_{11},\ \underline{t}\text{-}C_4H_9$

$R' = CH_3$

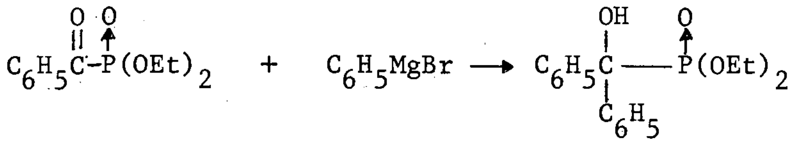
their ability to complex with anhydrous magnesium iodide.[12] Examination of the infrared spectra of these complexes suggests that the ability of these alkyl diphenylphosphinates to complex decreases in the order methyl > n-propyl > isobutyl > isopropyl ~ neopentyl.[75] A mechanism is postulated for displacement of the alkoxy group involving complex



$$R_2\overset{\overset{O}{\uparrow}}{P}OR' \quad + \quad R''MgX \longrightarrow \underset{\underset{\delta+}{R_2POR'}}{\underset{\uparrow}{\overset{\overset{R''MgX}{\vdots}}{O}}} \xrightarrow{R''MgX} R_2R''P\rightarrow O$$

formation between the phosphoryl group and the Grignard reagent.[13]

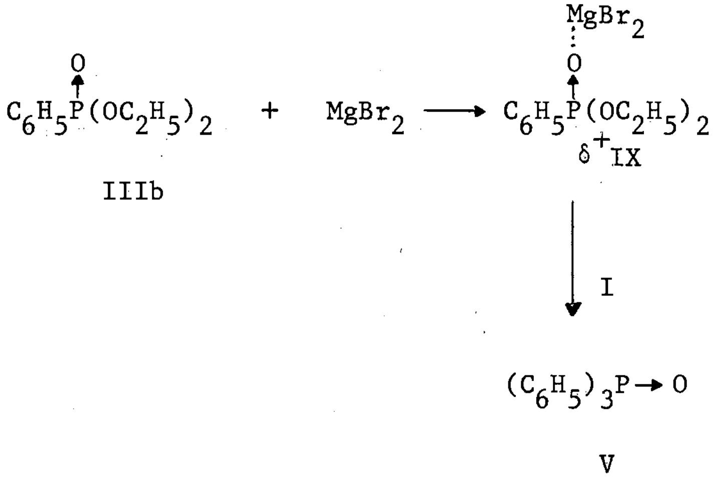
The relative lack of reactivity of the phosphoryl group in comparison to the carbonyl group when reacted with Grignard reagents is evident from the work of Shahak and Bergmann.[81] Treatment of a series of α-ketophosphonates [$RCOP(O)(OEt)_2$] with Grignard reagents(1:1 mole ratio) resulted in attack at the carbonyl group only. A typical example



$$C_6H_5\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\uparrow}{P}}(OEt)_2 + C_6H_5MgBr \longrightarrow C_6H_5\underset{C_6H_5}{\overset{OH}{C}}-\overset{O}{\overset{\uparrow}{P}}(OEt)_2$$

is shown. Alkaline hydrolysis cleaved the α-hydroxyl phosphonate and benzophenone was the only product isolated.

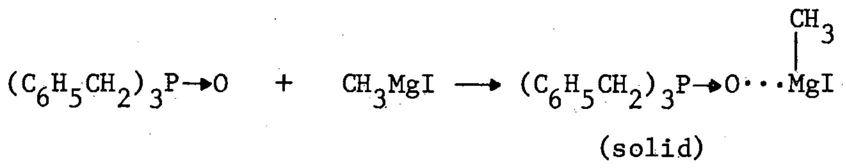
In the foregoing discussion attention was drawn to the effect on product composition of the ratio of Grignard reagent to ester. Failure to obtain V from IIIb and I[54] has been attributed to the absence of excess Grignard reagent.[8] Insight into the need for excess Grignard reagent was first provided by Dawson and Burger.[23] They reported that addition of a magnesium bromide-dimethyl phenylphosphonate (IIb) mixture to I resulted in production of V (55 percent). Coordination of the magnesium bromide with the phosphoryl oxygen to form an activated complex IX was invoked to account for the observation. Presumably, the electropositive character of the phosphorus atom would be enhanced in



$$\underset{\text{IIIb}}{C_6H_5\overset{O}{\overset{\uparrow}{P}}(OC_2H_5)_2} + MgBr_2 \longrightarrow \underset{\delta^+ \;\text{IX}}{C_6H_5\overset{\overset{MgBr_2}{\vdots}}{\overset{O}{\overset{\uparrow}{P}}}(OC_2H_5)_2} \xrightarrow{\text{I}} \underset{\text{V}}{(C_6H_5)_3P\rightarrow O}$$

the complex and the phosphorus thus be more susceptible to nucleophilic attack.[8]

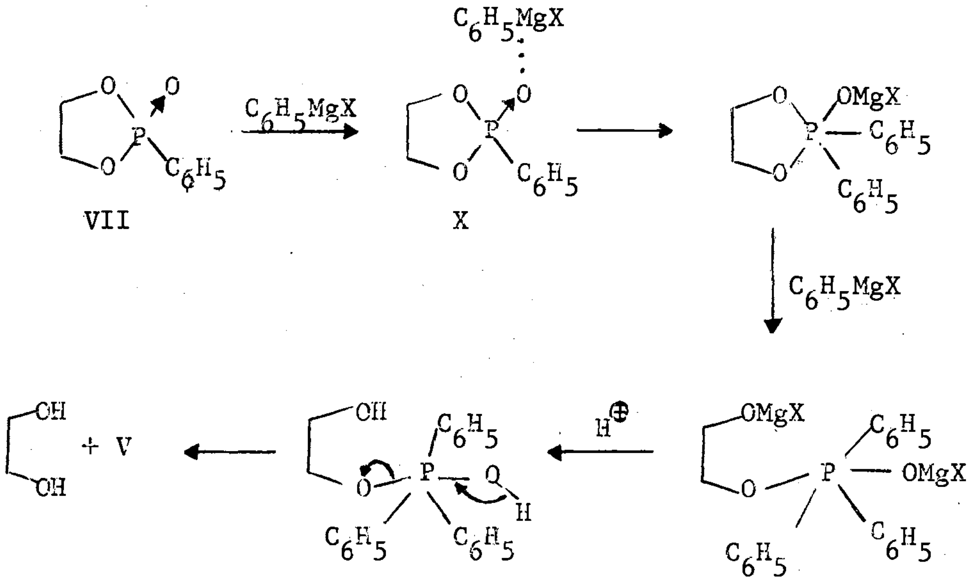
Formation of such a complex between the Grignard reagent and the phosphoryl group may be visualized with the phosphate II, phosphonate III, phosphinate IV and the phosphine oxide V. Isolation of a complex of methylmagnesium iodide and tribenzylphosphine oxide has been

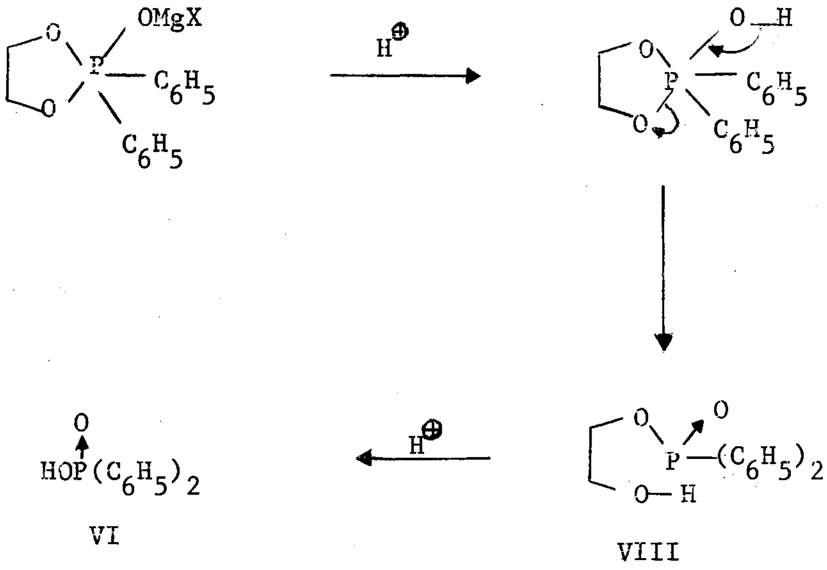


$$(C_6H_5CH_2)_3P\rightarrow O \quad + \quad CH_3MgI \longrightarrow \underset{\text{(solid)}}{(C_6H_5CH_2)_3P\rightarrow O\cdots\overset{CH_3}{\overset{|}{Mg}}I}$$

reported.[75] Formation of an ester-Grignard reagent complex has been used by Berlin and coworkers to explain the observed reaction of trimethyl phosphite and the phenyl Grignard reagent.[7] Indeed, a white precipitate in the reaction mixture was considered to be a complex of esters of tetravalent phosphorus (oxidation during work-up) and the Grignard reagent. In addition, an insoluble complex was obtained when I and V were mixed in ether solution.[7]

The intermediacy of a Grignard reagent-ester complex X has been invoked to explain the conversion of VII to the observed displacement products.





VI

VIII

A decrease in the relative rate of reaction of n-propyl diphenylphosphinate with methylmagnesium iodide in the presence of added methyldiphenylphosphine oxide has been observed.[13] The retardation has been attributed to complexation of the Grignard reagent with the oxide.

As a related observation, Berlin and Austin reported a nearly quantitative yield of triphenylphosphine when I was treated with trimethyl phosphate in ratios greater than three (Grignard reagent to

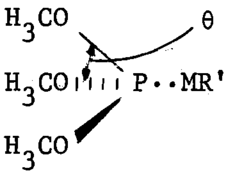
$$(CH_3O)_3P \quad + \quad 4\ \mathrm{I} \longrightarrow (C_6H_5)_3P$$

ester).[7] However, when an exact 3:1 ratio was used a maximum yield of 63 percent was obtained. Failure to achieve higher yield with the 3:1 ratio is attributed to loss of some Grignard reagent in complexed form.

Examples of complex formation between phosphorus and other metals have been reported. Use of tributyl phosphate as a solvent and extractant for metal ions is quite extensive.[30] Phosphonates[32,82] and phosphine oxides[72] have been cited as complexing agents.

A complex of triphenylphosphine oxide (V) with lithium iodide has been examined in detail by X-ray analysis.[92] In the crystal structure (5:1 $(C_6H_5)_3P\rightarrow O/LiI$) one triphenylphosphine oxide moiety is presumably enclosed in a clathrate type complex.

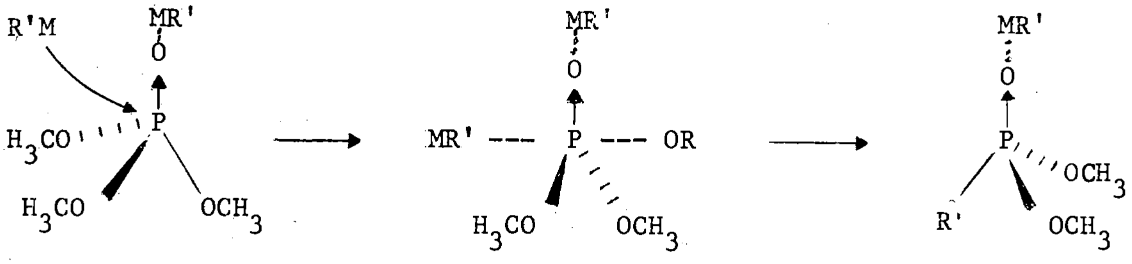
A stepwise mechanism has been proposed for the reaction of Grignard reagents with trimethyl phosphite[7] and trimethyl phosphate.[14] Formation of a Grignard-phosphite complex XI is postulated to involve a



XI

change in bond angle θ from 100° in the ester to 109° in the complex, thus making attack on phosphorus more facile. With the esters of tetravalent phosphorus no such change of bond angle need occur in formation of the complex XI. This may account for the observed decrease reactivity of the phosphate toward I.[14]

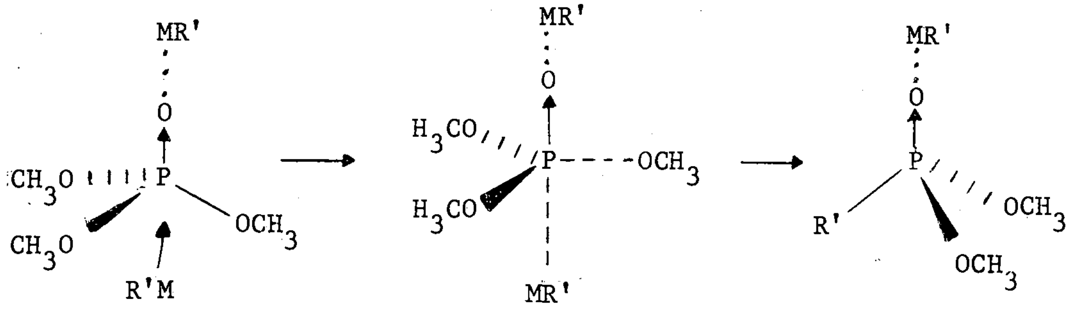
The attack of a second mole of I has been visualized as occurring in one of two different processes. A classical SN2 type of reaction could occur if the nucleophile approached between two of the ester groups. The angle between the attacking group and leaving group would thus be 180°. The transition state XIIa requires the existence of pentacovalent phosphorus. The availability of 3d orbitals in phosphorus would allow the existence of such a species.[38]



XIIa

R'M = Grignard reagent.

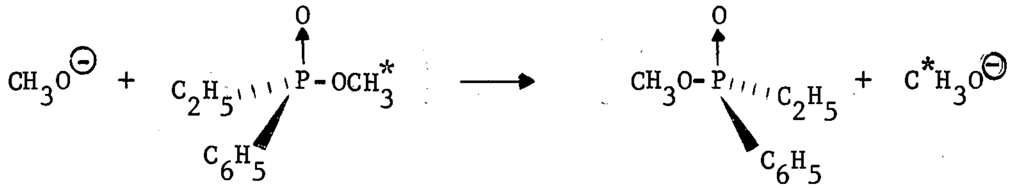
An alternative pathway would involve the approach of the nucleophile from the "underside" of the phosphoryl group. The angle between the attacking and leaving groups in the transition state XIIb would be approximately 90°. Again a transition state involving pentacovalent phosphorus is required.



XI XIIb

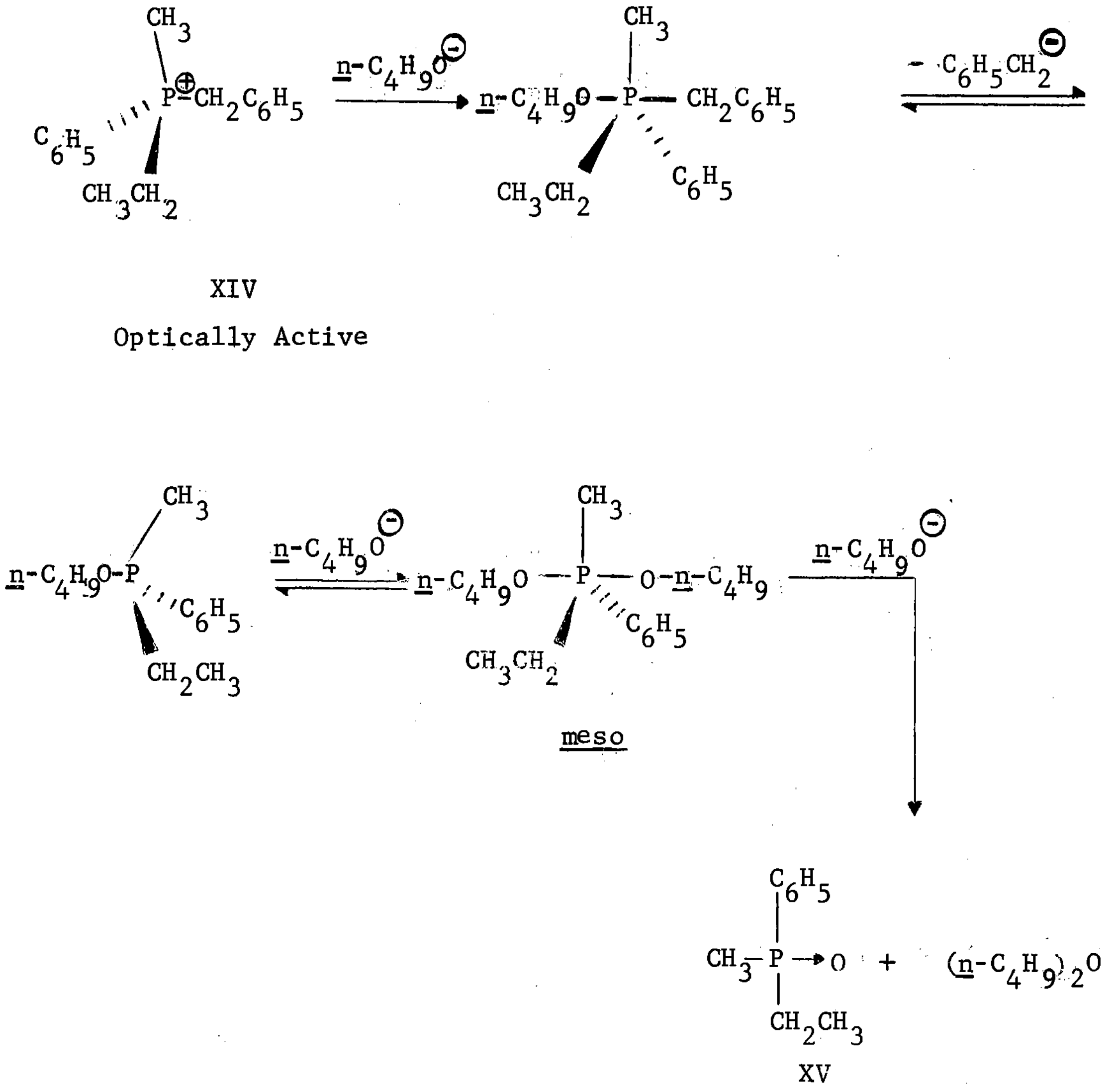
R'M = Grignard reagent

Such an intermediate (a trigonal bipyramid) has been proposed to rationalize the exchange reaction of methoxide ion with the methoxy (isotopically-labeled carbon) group of optically active methyl ethylphenylphosphinate(XIII).[38] The rate of racemization was found to be



exactly twice that of exchange. Each displacement is therefore accompanied by inversion of configuration at the phosphorus atom.

Treatment of optically active benzylethylmethylphenylphosphonium n-butoxide (XIV) with butoxide ion gave racemic ethyl methylphenylphosphine oxide (XV).[70] McEwen and coworkers have resorted to a



XIV

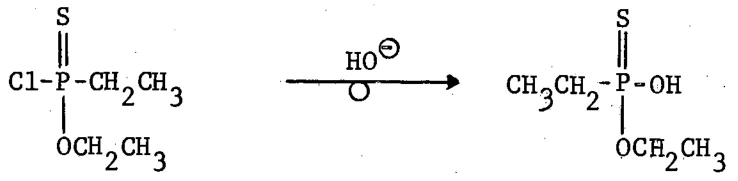
Optically Active

meso

XV

five-bonded transition state to account for the results. Toluene and dibutyl ether are the other products.

The alkaline hydrolysis of optically active O-ethyl ethylphos-



$$\mathrm{Cl{-}\underset{OCH_2CH_3}{\overset{S}{\overset{\|}{P}}}{-}CH_2CH_3 \xrightarrow{HO^{\ominus}} CH_3CH_2{-}\underset{OCH_2CH_3}{\overset{S}{\overset{\|}{P}}}{-}OH}$$

XVI

phonochloridothionate (XVI) was found to go with inversion of configurtion at the thiophosphoryl center.[64] A transition state involving a trigonal bipyramid would account for the results.

The trigonal bipyramid transition state has generally been accepted for nucleophilic substitution in phosphorus esters. Other examples in which the same transition state appears to satisfy experimental evidence are cited in reviews by McEwen[61] and by Hudson and Green.[46] No case appears in the literature in which simple substitution at phosphorus proceeds with retention of configuration.[64]

Reactions of Other Nucleophiles With Phosphorus Esters

Numerous examples of the use of phosphates as agents alkylating atoms other than C and P appear in the literature. Several examples are cited; an exhaustive survey is not intended. O-alkylation of phenols has been observed by Noller and Dutton.[67] Conditions were not

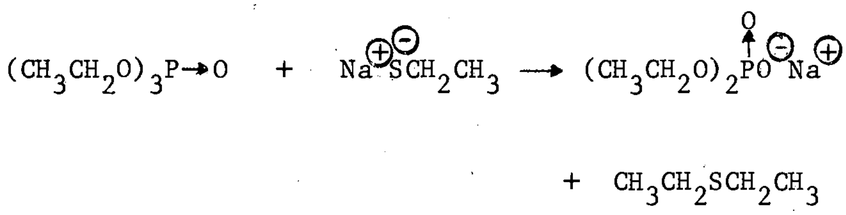
$$\mathrm{(RO)_3P{\rightarrow}O \;+\; C_6H_5OH \longrightarrow C_6H_5OR \;+\; (RO)_2\overset{O}{\overset{\uparrow}{P}}OH}$$

$R = C_2H_5$ 21.6% $R = \underline{sec}\text{-}C_4H_9$ 18.7%

$R = \underline{n}\text{-}C_4H_9$ 39.0% $R = \underline{n}\text{-}C_5H_{11}$ 15.0%

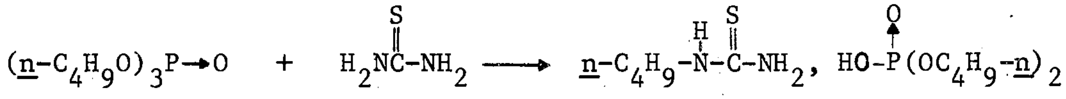
adjusted for maximum yield and yields were based on the amount of alkyl radical available. With aliphatic alcohols the corresponding methyl ethers were obtained in yields ranging from 55 to 70 percent based on the alcohol used.[86] From a practical standpoint the reaction is limited to alcohols boiling above 160°.

During the reaction of esters of phosphoric acid with sodium ethylmercaptide S-alkylation of the mercaptide has been observed.[50]

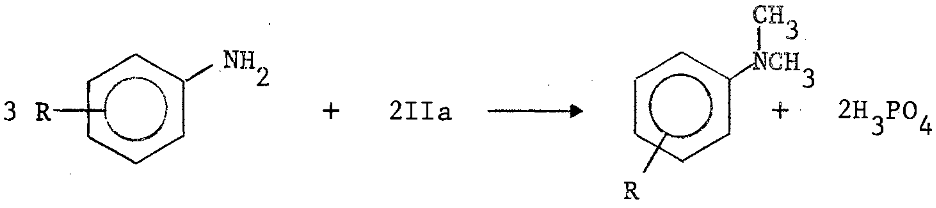


$$(CH_3CH_2O)_3P\rightarrow O \quad + \quad Na^{\oplus}\,{}^{\ominus}SCH_2CH_3 \longrightarrow (CH_3CH_2O)_2\overset{\overset{O}{\uparrow}}{P}O^{\ominus}\,Na^{\oplus} \quad + \quad CH_3CH_2SCH_2CH_3$$

N-Alkylation has been reported in several instances. Parker and Smith[71] prepared N-alkylthiouronioum salts from alkyl phosphates. When isobutyl phosphate was employed as the alkylating agent, the yield dropped from 33 to 12 percent. When trimethyl phosphate (IIa) or triethyl phosphate (IIb) was heated with equimolar amounts of substituted anilines, N,N-dialkylanilines resulted (53-95 percent).[85] An attempt to alkylate p-nitroaniline resulted only in decomposition of the starting material.[28]

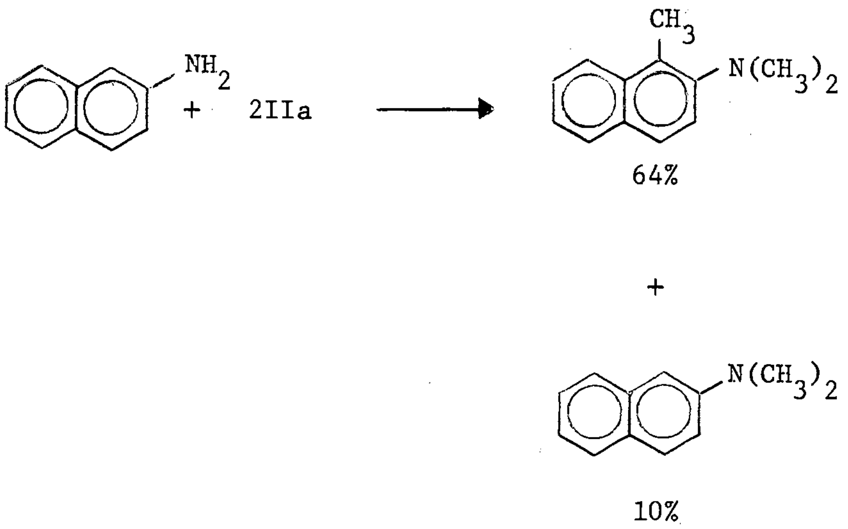


$$(\underline{n}\text{-}C_4H_9O)_3P\rightarrow O \quad + \quad H_2N\overset{\overset{S}{\|}}{C}\text{-}NH_2 \longrightarrow \underline{n}\text{-}C_4H_9\text{-}\overset{H}{\underset{}{N}}\text{-}\overset{\overset{S}{\|}}{C}\text{-}NH_2,\ HO\text{-}\overset{\overset{O}{\uparrow}}{P}(OC_4H_9\text{-}\underline{n})_2$$



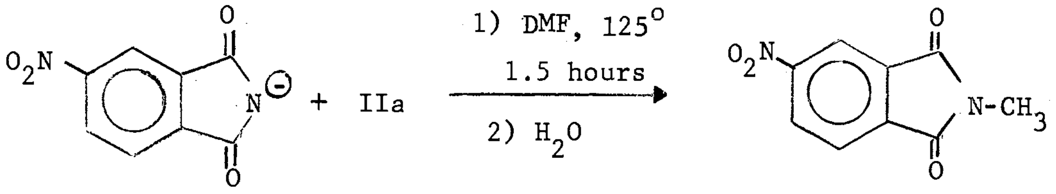
R = Cl, CH_3, CH_3O.

Jones and coworkers observed both C- and N-alkylation when certain naphthylamines were heated (250-275°, 2 hours) with IIa.[50] The nuclear



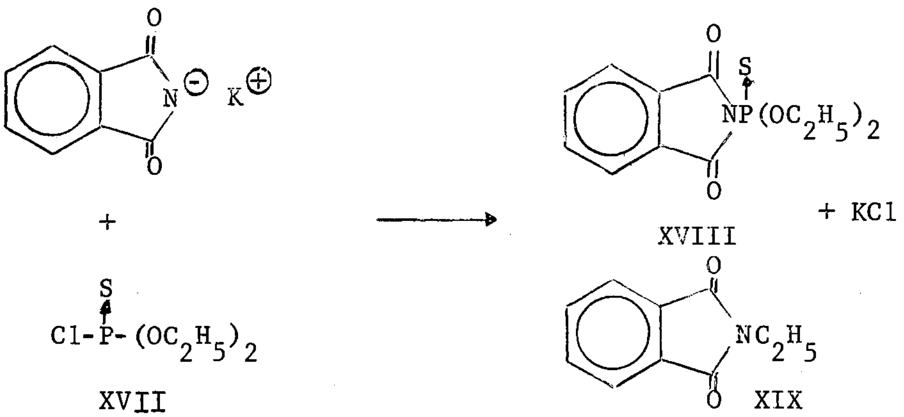
methylation is apparently accompanied by decomposition of the diester anion. Salts of dimethyl hydrogen phosphate have been reported to undergo decomposition near 250°.[18]

Trimethyl phosphate (IIa) can cause N-alkylation as is the case



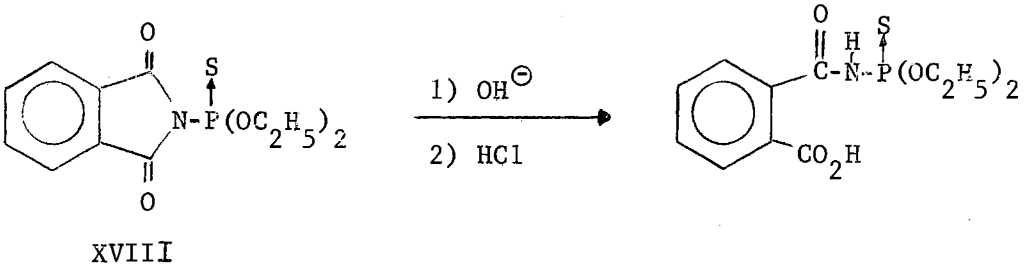
with the 4-nitrophthalimide anion.[15]

In a recent synthesis of dicarboximidophosphonothioates from 0,0-diethyl phosphorochloridothioate (XVII) and potassium phthalimide, evidence of N-alkylation was detected.[69] In addition to a 50 percent

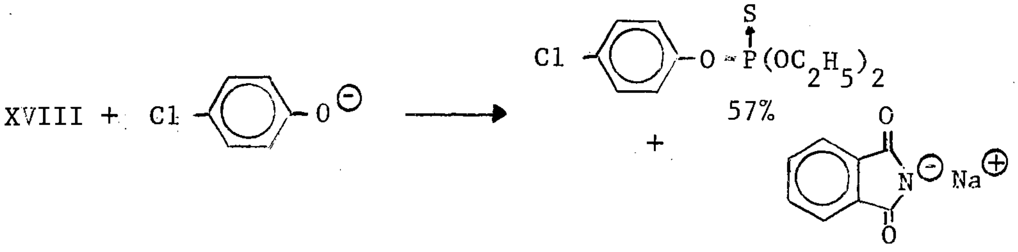


yield of O,O-diethyl phthalimidophosphonothioate (XVIII), yields of 11 and 16 percent of N-ethylphthalimide (XIX) were obtained in two separate experiments. Since XVIII is not a good alkylating agent,[2] XVII is presumed to be the source of the alkyl group. Compound XVIII was identified by its spectral properties and by alternative methods of synthesis.

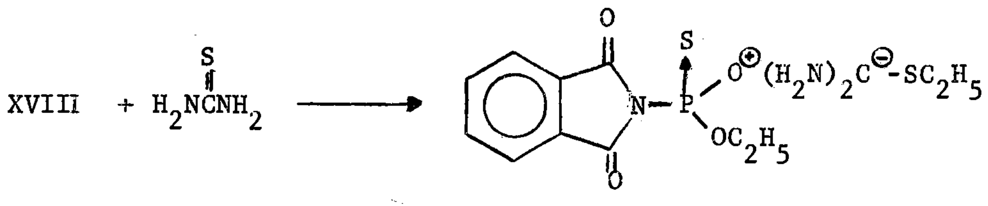
When XVIII and some of its alkyl analogues were treated with various nucleophiles, attack was found to occur primarily at the carbonyl



carbon.[68] The reaction with $OH^{\ominus}$ is illustrative. When p-chlorophenoxide ion was used the main site of attack was on phosphorus.



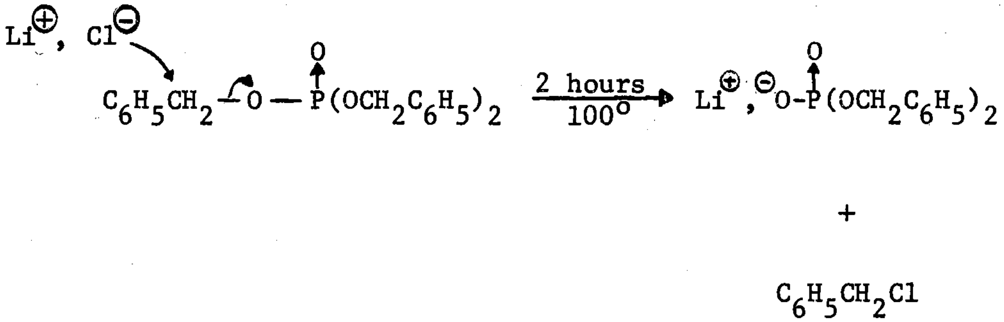
Displacement on carbon occurred when thiourea served as the nucleophile.



XX

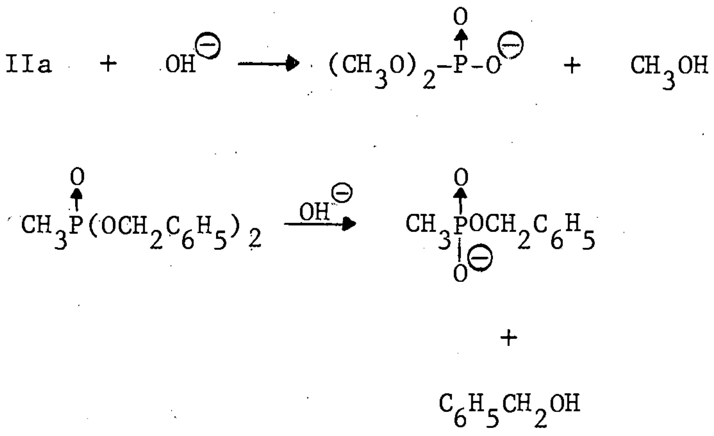
The salt XX was not isolated but S-ethylisothiourea was obtained in 65 percent yield.

Nucleophiles other than Grignard reagents have been shown to exhibit specificity as to position of attack on phosphorus esters. Attack on carbon by the chloride ion was found to occur when tribenzyl phosphate was treated with lithium chloride (1:3 mole ratio) in 2-



ethoxyethanol.[19] The yield was quantitative. Facile removal of the benzyl group from phosphorus-containing esters is of particular interest from a biochemical standpoint. Phenyl dibenzyl phosphate and 2-hydroxycyclohexyl dibenzyl phosphate were converted to the corresponding monobenzyl esters (cyclohexylamine salts). Under essentially identical conditions benzyl hydrogen phosphoramidate (lithium salt) was obtained from the appropriate dibenzyl ester. Triphenyl phosphate (IIc) was unaffected by lithium chloride.

Kinetic data was employed by Hudson and Harper to correlate the basicity of a series of nucleophiles with position of attack.[47] Nucleophiles examined included water, chloride, bromide, thiocyanate, thiosulfate, iodide and hydroxide. Only the hydroxide ion was found to attack at phosphorus in phosphates and phosphonates. It is suggested



$$\text{IIa} + OH^{\ominus} \longrightarrow (CH_3O)_2-\overset{\overset{O}{\uparrow}}{P}-O^{\ominus} + CH_3OH$$

$$CH_3\overset{\overset{O}{\uparrow}}{P}(OCH_2C_6H_5)_2 \xrightarrow{OH^{\ominus}} CH_3\underset{\underset{O^{\ominus}}{|}}{\overset{\overset{O}{\uparrow}}{P}}OCH_2C_6H_5 + C_6H_5CH_2OH$$

that the more basic anions are required to displace alkoxyl groups from phosphorus. Anions of strong acids (e.g. $Cl^{\ominus}$) would be expected to attack at carbon.[19] One would anticipate that the more basic Grignard reagents would thus attack at phosphorus if basicity was the only factor involved.

Reactions of Other Hetero-Atom Containing Esters With Grignard Reagents

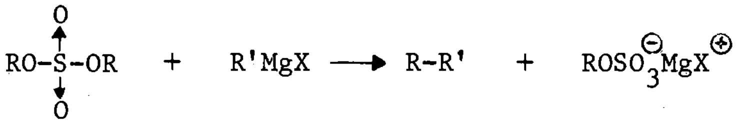
Alkyl esters of other inorganic acids except those of sulfur have been shown to react with organometallic compounds <u>via</u> attack at the central element.[36] Only a few typical examples will be cited. No C-alkylation was observed in the reaction of I with esters of nitrous, nitric, vanadic, arsenous and arsenic acid. The reaction of alkoxy silanes with Grignard reagents has been reviewed.[51] In all cases attack occurred on silicon; no examples of C-alkylation were cited.

In one apparent exception trimethyl borate reportedly gave toluene upon reaction with I.[52] Gilman and Vernon were unable to reproduce

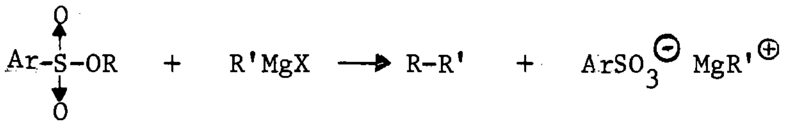
$$(CH_3O)_3B \quad + \quad I \quad \not\longrightarrow \quad CH_3C_6H_5$$

this result.[37] An 86 percent yield of phenylboronic acid was obtained.

Alkyl sulfates and sulfonates are well known as alkylating agents for R-M type compounds (M = metal). The extensive use of alkyl sulfates



$$RO-\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}-OR \quad + \quad R'MgX \longrightarrow R-R' \quad + \quad ROSO_3^{\ominus}MgX^{\oplus}$$



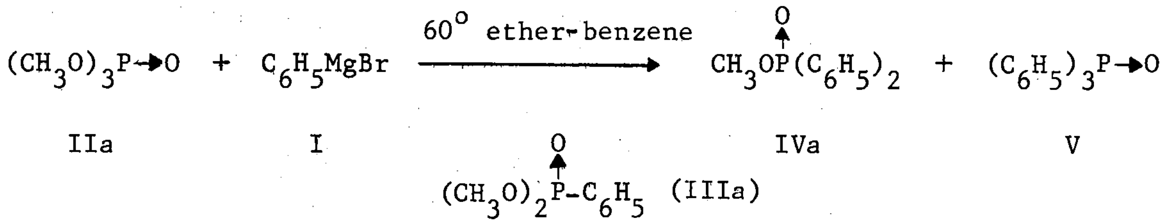
$$Ar-\overset{\overset{O}{\uparrow}}{\underset{\underset{O}{\downarrow}}{S}}-OR \quad + \quad R'MgX \longrightarrow R-R' \quad + \quad ArSO_3^{\ominus}\ MgR'^{\oplus}$$

and sulfonic esters has been well documented[51,84] and will not be discussed further.

CHAPTER II

DISCUSSION OF RESULTS AND CONCLUSIONS

The condensation of trimethyl phosphate (IIa) with phenylmagnesium bromide (I) has been examined under a variety of conditions (see Tables IV-VI). The mole ratio of Grignard reagent to ester has been varied from 1:1, 3:1 and 4:1 at several temperatures, viz. 30°, 60° and 100°. The P-alkylation products methyl diphenylphosphinate (IVa) and triphenylphosphine oxide (V) were detected by GLC in a ratio of 2.6 to 1 with a 1:1 ratio of Grignard reagent to ester at 60°. With a 4:1 ratio of reactants the product ratio changed to 1.47/1.00. Concurrently the yields of IVa and V increased by a factor of 2.29 and 4.10, respectively, when compared to those from the 1:1 reaction. Use of a higher temperature (100°-3:1) resulted in a marked increase in the yield of V; the amount of IVa was not quantitatively determined. Apparently a bulky complex with the Grignard reagent was formed when tetrahydrofuran (THF) was used as a solvent. The yield of oxide was reduced by a factor of 25 when compared with the normal run at 60° (3:1).



$$\underset{\text{IIa}}{(CH_3O)_3P\rightarrow O} + \underset{\text{I}}{C_6H_5MgBr} \xrightarrow[(CH_3O)_2\overset{\overset{O}{\uparrow}}{P}-C_6H_5\ (\text{IIIa})]{60^{o}\ \text{ether-benzene}} \underset{\text{IVa}}{CH_3O\overset{\overset{O}{\uparrow}}{P}(C_6H_5)_2} + \underset{\text{V}}{(C_6H_5)_3P\rightarrow O}$$

Surprisingly, no dimethyl phenylphosphonate (IIIa) was present in detectable amounts in any reaction of I with IIa. It is suspected that

IIIa forms a complex with I which is highly reactive toward a second equivalent of I.

When phenylmagnesium bromide (I) was added to IIa in an inverse addition (0.5 hour) the yields of IVa and V were reduced by factors of 10 and 100, respectively, and the ratio of IVa to V was found to increase (Table V). The ester, always in excess during the addition, apparently ties up the Grignard reagent in complex form, thus limiting further displacement. When the addition time was increased to 1.75 hours, the total yield of IVa and V was equal to that from normal addition. Greater conversion of IVa to V was observed, however. The IVa/V ratio was reduced from 2.6:1.00 to 1.43:1.00.

In separate experiments addition of a 1-mole excess of I to dimethyl phenylphosphonate (IIIa) at 30° resulted in a marked increase in yield of ester IVa and oxide V over that obtained from a 4:1 reaction with the phosphate IIa (Table VI). The condensation also resulted in an increased conversion of the phosphinate IVa to V. Consequently, at 30° the high conversion (~30 percent) of IIIa is indicative of the high reactivity of the complex. The regular runs of I with IIa were performed at 60°.

In similar fashion a 1-mole excess of I with methyl diphenylphosphinate (IVa) resulted in a 26-fold increase in V. These results suggest the availability of a higher concentration of uncomplexed Grignard reagent.

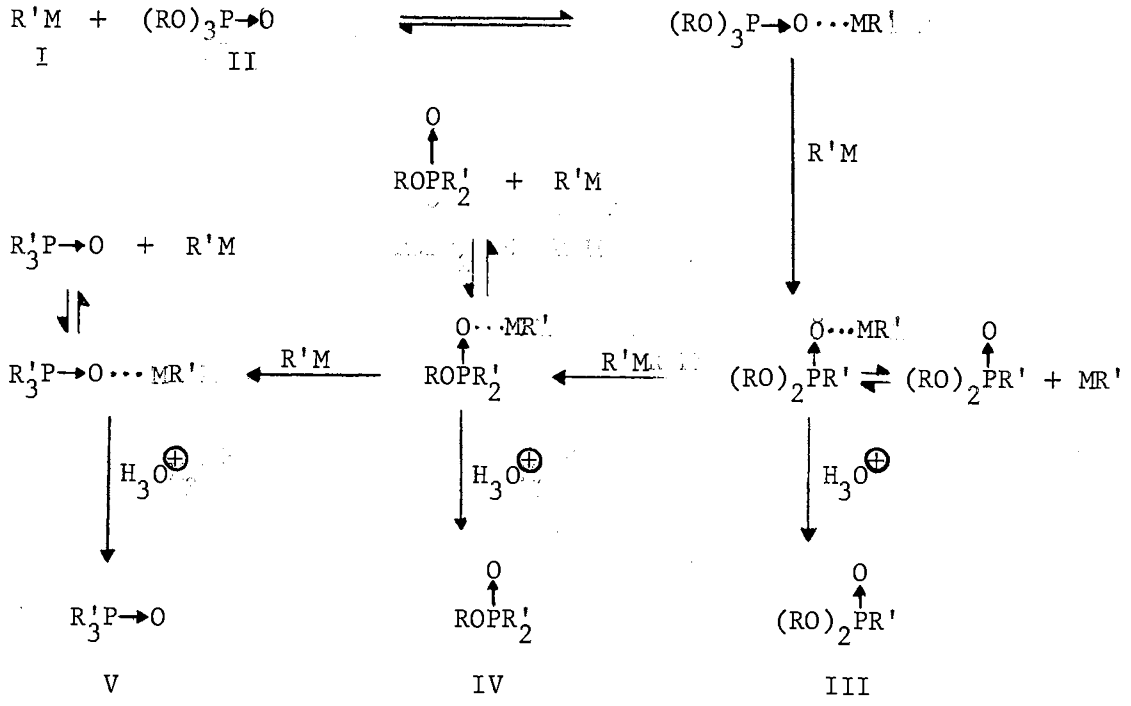
Interestingly, in all cases examined of condensation of I with IIa the C-alkylation product toluene was obtained. The amount of toluene was found to decrease as the ratio of Grignard reagent to IIa increased. The presence of higher concentrations of I certainly result in a greater amount of complexed ester; the complexed species appears therefore to be more susceptible to P- than C-alkylations at higher concentration of Grignard reagent.

Use of the inverse mode of addition resulted in a decrease in C-alkylation. Again, as the Grignard reagent was added it appears to have been tied up in complexed form. Increasing the addition period from 0.5 to 1.75 hours gave a 20 percent increase in the yield of toluene. However, the yield was only half of that obtained in the normal addition.

The reaction of phenyl Grignard reagent with trimethyl phosphate (IIa) has been observed to be a stepwise process. Complexation between IIa, and the intermediates IIIa and IVa occurs with I. Product yields and compositions are highly concentration-dependent. In addition, C-alkylation competes poorly with P-alkylation in reaction of either trimethyl phosphate (IIa) or triethyl phosphate (IIb).

The displacement process may be depicted as follows. The Grignard reagent is visualized as reversibly complexing with the phosphoryl oxygen of the ester (Scheme 1) and thus increasing the positive character of the phosphorus atom and enhancing its susceptibility to attack by the Grignard reagent. Displacement of the alkoxide groups yields successively the phosphonate III, phosphinate IV and the phosphine oxide V. Each of these products is believed to be complexed with the Grignard reagent in solution. Subsequent hydrolysis converts the complex into the corresponding displacement product.[3,7]

In many respects the reaction of IIa with the Grignard reagent



$R = CH_3$ $\qquad R'M = C_6H_5MgBr$ $\qquad R' = C_6H_5$

Scheme 1

was found to be quite different from that of trimethyl phosphite.

$$1\ (CH_3O)_3P: \ +\ 3\ I \longrightarrow (CH_3O)_2\ddot{P}C_6H_5 \ +\ CH_3O\ddot{P}(C_6H_5)_2 \ +\ (C_6H_5)_3P:$$

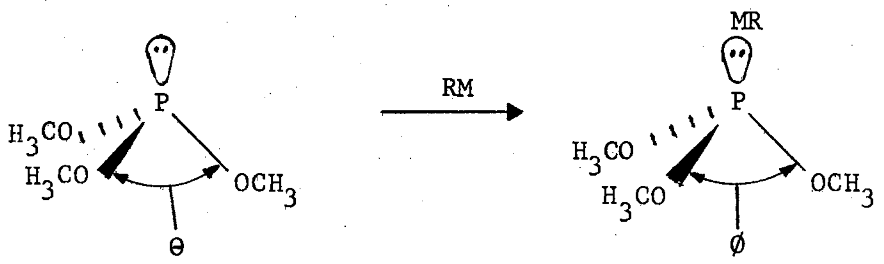
A quantitative yield of triphenylphosphine resulted when the phosphite was added to the Grignard reagent (4:1 ratio of I to ester).[3,7] By way of contrast only 10 to 20 percent yields of triphenylphosphine oxide (V) were obtained from IIc under comparable conditions. It is interesting to point out that a high yield (90-95 percent) of V was obtained when

$$\underset{\text{IIc}}{1\ (C_6H_5O)_3P\rightarrow O} \ +\ 4\ I \longrightarrow \underset{\text{V}}{(C_6H_5)_3P\rightarrow O} \ +\ C_6H_5OH$$

triphenyl phosphate (IIc) was added to I.[14] It is evident that the nature of the leaving group is important in the displacement process.

Whereas trimethyl phosphite immediately gave a fine white precipitate in a vigorous exothermic reaction upon addition to I,[7] regardless of the ratio of I and IIa, only a moderate rise in temperature (1-2°) was recorded. At the completion of the addition of the ester a gummy material was observed on the sides of the reaction vessel.

Two factors may account for the difference in reactivity of the phosphate and phosphite. Low conversion to the complexed form in the phosphate series under investigation would account for lower yields of displacement products observed. It seems likely that formation of such a phosphite complex would be favored because of the greater basicity of the unshared electron pair on phosphorus. In addition complex formation with the phosphate would produce a change of the O-P-O bond angle



$\theta = 100^\circ$ $\phi = 109^\circ$

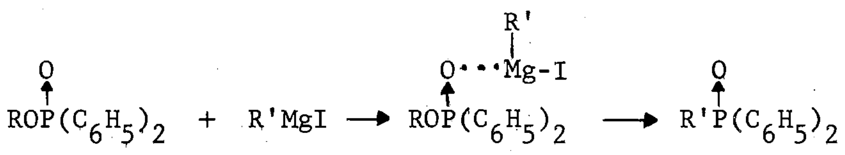
RM = Phenylmagnesium bromide

from 100° to 109° by relief of compressional forces exerted by the nonbonded orbital on the P-O σ-bonds.[7] No such relief of strain can occur in formation of the phosphate complex.

Formation of the complex between the ester phosphoryl oxygen atom and the magnesium of the Grignard reagent has been postulated to account for several observations.[31,42] Kosolapoff was able to obtain only diphenylphosphinic acid (VI) (32 percent) when diethyl phenylphosphonate (IIIb) was treated with two moles of the Grignard reagent I (one mole complexed).[7] In sharp contrast Dawson and Burger[23] were able to obtain V (55% yield) from the ester upon addition of magnesium bromide (solid complex isolated) prior to reaction with I. In a number of preparations of phosphine oxides from alkyl and aryl phosphonates excess Grignard reagent was employed.[3,5,39,56,79]

Not only is the complex formation important in activating the phosphoryl group, the insolubility of complexes of some of the intermediates must markedly affect the yield of displacement product. In the 30°-reactions of I with IIa, IIIa and IVa, a dark oil settled out during the addition. That the oil is a complex mixture is evidenced by the fact that IVa and V were detected in the workups of all of the oily layers.

Complexes of alkyl phosphinates with magnesium iodide have been isolated and characterized by melting point and infrared analysis.[12,13] The relative reactivity of a series of alkyl diphenylphosphinates IV with alkylmagnesium iodides was observed to parallel the ability of the ester to complex with magnesium iodide.[13] A mechanism involving coordination of the Grignard reagent with the phosphinate was proposed.



$$\mathrm{RO}\overset{\overset{\mathrm{O}}{\uparrow}}{\mathrm{P}}(C_6H_5)_2 + \mathrm{R'MgI} \longrightarrow \mathrm{RO}\overset{\overset{\overset{\mathrm{R'}}{|}}{\mathrm{O}\cdots\mathrm{Mg\text{-}I}}}{\overset{\uparrow}{\mathrm{P}}}(C_6H_5)_2 \longrightarrow \mathrm{R'}\overset{\overset{\mathrm{O}}{\uparrow}}{\mathrm{P}}(C_6H_5)_2$$

R = $\underline{n}$-C_3H_7, iso-C_4H_9, neo-C_5H_{11}

R' = CH_3, $\underline{n}$-C_3H_7, $\underline{\text{sec}}$-C_4H_9

Berlin and Pagilagan[13] were able to isolate a syrupy precipitate in the condensation of methylmagnesium iodide and the phosphinates cited above. Both phosphine oxide and phosphinate as well as magnesium ions were found in the precipitate. On the basis of this work it is apparent that some Grignard reagent is tied up with the phosphinate IV and phosphine oxide V in the condensation of Ia and IIa. Indeed, added methyldiphenylphosphine oxide was found to decrease the relative rate of reaction of methylmagnesium iodide with n-propyl diphenylphosphinate.[13]

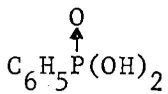
Triphenylphosphine oxide (V) has been reported to undergo attack by alkyl Grignard reagents to produce benzene and a phosphorus-containing

$$(C_6H_5)_3P\rightarrow O + RCH_2MgBr \xrightarrow[\text{reflux}]{\text{THF}} (C_6H_5)_2\overset{\overset{O}{\uparrow}}{P}\underset{\underset{MgBr}{|}}{C}HR + C_6H_5$$

V

organometallic reagent.[80] Absence of an alkyl group containing alpha hydrogen in I precludes such a reaction in this study. A 3:1 complex of tribenzylphosphine oxide and methylmagnesium iodide has been isolated.[75]

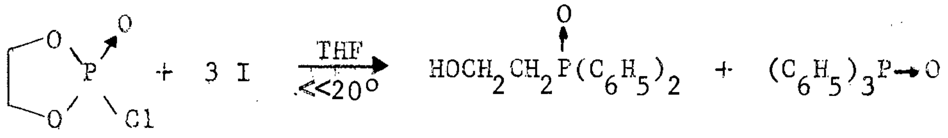
Since no phosphonate was isolated from any reaction mixtures of IIa with I, it appears that the postulated phosphonate complex is highly reactive when formed. Careful examination of the aqueous layer obtained during workup failed to reveal the presence of any phenylphos-



$$C_6H_5\overset{\overset{O}{\uparrow}}{P}(OH)_2$$

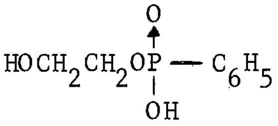
XXIII

phonic acid (XXIII) or the corresponding monomethyl ester. Failure to obtain the phosphonate has been reported in a similar case. When 2-chloro-2-oxo-1,3,2-dioxaphospholane was treated with phenylmagnesium bromide (I) compounds VIII and V were obtained, but the cyclic phosphonate 2-oxa-2-phenyl-1,3,2-dioxaphospholane (VII) could not be iso-



VIII V

lated.[30] The ester VII is known to hydrolyze readily under aqueous conditions to acid XXII.[20,29] However, attempts to obtain VII under



$$\mathrm{HOCH_2CH_2O}\overset{\overset{\displaystyle O}{\uparrow}}{\underset{\displaystyle \overset{|}{OH}}{P}}\mathrm{-C_6H_5}$$

XXII

anhydrous workup procedures were unsuccessful.

The nature of the phosphoryl bond is of prime importance in this work. Base strength of the phosphoryl oxygen in each of the compounds IIa, IIIa, IVa and V will determine the strength of complex formed with the magnesium atom of the Grignard reagent. Dipole moments would be of value in assessing the importance of these points. However, insufficient data is at hand for critical evaluation. Other types of data are available and may give some insight into the nature of the complexes.

That alkoxy groups attached to phosphorus are more electronegative than aryl groups has been established;[4,60] hence, in the series IIa-V the phosphoryl group of trimethyl phosphate (IIa) would be expected to carry the greatest positive charge. Experimental results indicate, however, that the complexed phosphonate IIIa must be more reactive <u>viz.</u> no phosphonate can be isolated. Evidence has shown that pπ-dπ bonding[27,44] between the aromatic ring and the phosphorus atom is operative and enhances the positive character of phosphorus as aromatic groups are added.

In a series comparable to IIa-IVa, the ease of hydrolysis in the pressure of $OH^{\ominus}$ was found to be $(CH_3O)_3P{\rightarrow}O \gg (CH_3O)_2P(O)C_2H_5 \cong CH_3OP(O)(C_2H_5)_2$.[47] This order is also significant since evidence indicates that the reactivity decreases for the complexed phosphinate. In related work it has been observed that replacement of P-O-C bond by P-C in the series PO_4^{-3}, $CH_3PO_3^{-2}$, $(CH_3)_2PO_2^{-1}$ and $(CH_3)_3P{\rightarrow}O$ results in increase of the charge on phosphorus in the order indicated.[33] In the series IIa-IVa the replacement of the methyl group by the phenyl group would be expected further to enhance the charge on phosphorus. Again the order of reactivity would be predicted to be IIa < IIIa < IVa.

In agreement with the above, nuclear quadrupole resonance data[60] and $^{36}Cl^{\ominus}$ exchange data[27] have indicated the phenyl group to have a greater activating influence on the phosphoryl group than methoxy. Examination of the shift in P→O absorption frequency in the infrared in phenolic complexes has shown that replacement of methoxy with phenyl enhances the base or complexing strength of the phosphoryl group.[27]

No kinetic studies were performed on the reaction of ester IIa with I. It was found, however, that rate data for the reaction of alkyl diphenylphosphinates with methylmagnesium iodide did not satisfy linear first, second or third order plots.[13]

The existence of an equilibrium between the free and complexed esters in solution is postulated for the reaction of IIa with I as depicted in Scheme 1. The situation is further complicated by the separation of a syrupy oil when the reagents are mixed. Because of the complicated nature of the equilibria involved it was not feasible to obtain solubility data on the various complexes. The low yield of displacement products obtained must be attributed in part to slight solubility of one or more of the complexed species. When IIa, IIIa and IVa were condensed with I at 30° (Table VI), a dark oily layer appeared.[14] The two layers were separated, worked up and analyzed independently. The hydrolysis of the oily layer was very exothermic; this could result from either hydrolysis of unreacted Grignard reagent or magnesium salts. Analysis of the two layers by GLC proved the presence of IVa and V in all cases. When trimethyl phosphate (IIa) was condensed with I, no IIIa was detected. However, in the case where IIIa was used as starting material unreacted ester was detected in significant amounts.

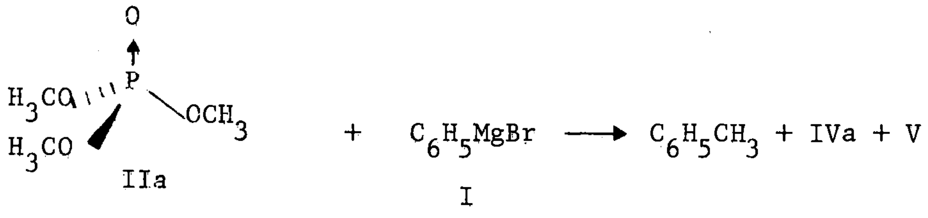
From the foregoing discussion it would seem that the phosphinate complex should be highly reactive with the addition of the second phenyl group. Therefore explanation for the isolation of phosphinate in the reaction mixture appears difficult. Two factors may have a bearing in this instance. The aforementioned solubility question may be important. If the complex has sufficiently low solubility, then this could account for the failure to convert it entirely to V.

Secondly, examination of models reveals that the increased number of phenyl groups may sterically hinder attack at the phosphorus atom by the nucleophile. In addition the effective coordination between the $P \rightarrow O$ group and the Grignard reagent may be reduced.

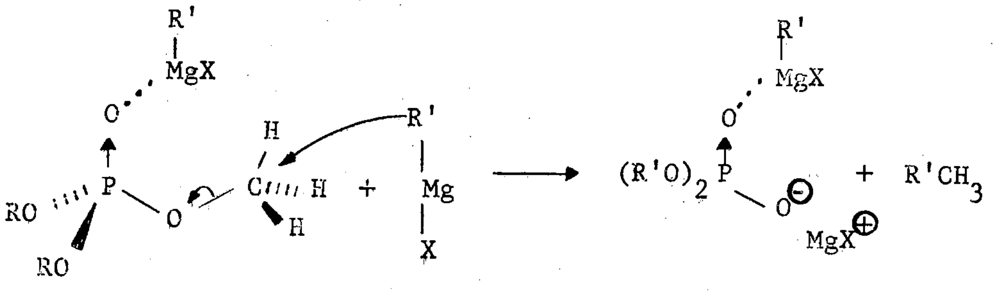
Acidification of each of the aqueous layers to pH 1 resulted in precipitation of diphenylphosphinic acid (VI). The amount of acid has been included in Tables IV-VI as the ester equivalent. Attack of the Grignard reagent on the methyl carbon of the phosphinate ester IVa

(C-alkylation) in the reaction mixtures could conceivably serve as the source of the acid. This seems unlikely, however, in view of the very low yield of toluene from IVa in comparison to that from IIa (see Table VI).

In all cases examined of condensation of I and IIa the C-alkylation product toluene was identified by GLC. Pertinent data are included in Tables IV through VI. It appears C-alkylation is competative with attack on phosphorus. An increase in the Grignard-ester ratio (1:1 to 4:1) was accompanied by a decrease in the yield of toluene. A corresponding increase in yields of phosphorus displacement products was noted. When the inverse mode of addition was used, an increase in the length of addition time from 0.5 to 1.75 hours led to a twofold increase in the C-alkylation product (compare runs 2 and 3, Table V). With an excess of ester present throughout most of the addition period the concentration of the complexed species would be low. Thus the possibility exists for attack on the uncomplexed ester to give C-alkylation, On the other hand the inductive effect of the complexed phosphorus present should have an activating effect on the α-carbon. The decrease in C-alkylation can then be attributed to direct competition with the phosphorus atom at the site of alkylation. It is thus difficult to speculate on the extent of participation of the uncomplexed ester in the reaction.



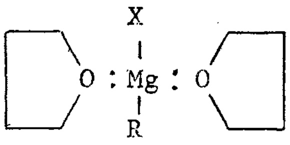
The formation of the C-alkylation product is thought to occur via an SN2 type displacement on carbon. (Scheme 2). That triethyl phosphate (IIb) is less reactive toward I may be rationalized as due to increased steric hindrance at the α-carbon. Furthermore, the electron density at the α-carbon atom of IIa is possibly less than in triethyl phosphate (IIb), based on hyperconjugation considerations.[14] Thus attack by nucleophilic I would be hindered. In the light of the above, the reported inertness of tri-n-butyl phosphate toward mesityl Grignard reagent[34] is understandable.



R'MgX = Phenylmagnesium bromide R = CH_3

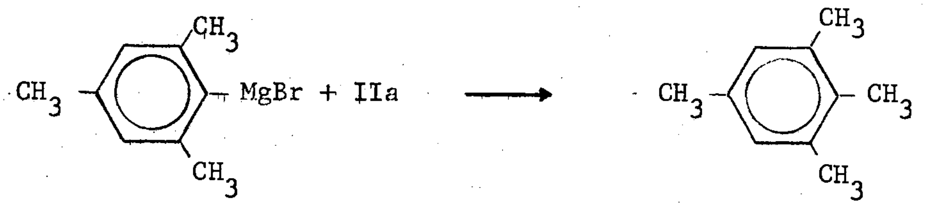
Scheme 2

When THF was used (run 5, Table IV) as the reaction solvent (3:1 Grignard to ester mole ratio), a 75 percent increase in C-alkylation resulted. At the same time a drastic decrease in attack on phosphorus was noted. An important factor for decreased attack on phosphorus may be the bulkiness of the solvated Grignard reagent XXI. Laughlin[58] and Lewis and Wright[59] have examined the effect of solvent basicity on the Grignard reaction. It is significant in our data that both C- and



XXI

P-alkylation have been observed with phenylmagnesium bromide even though it is not generally considered to be a bulky Grignard reagent. Examples of C-alkylation with IIa have appeared in the literature. All have been with so-called bulky or hindered Grignard reagents. Trimethyl phosphate IIa has previously been reported to undergo attack at

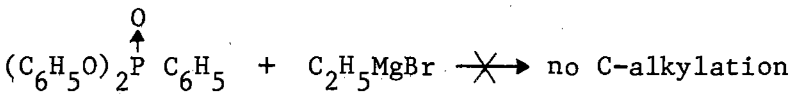


carbon.[34] No data was presented which could be attributed to attack on phosphorus. Similar results were observed with hindered lithium reagents.[34]

Triphenyl phosphate (IIc) and diphenyl phenylphosphonate (IIIc) were condensed with ethyl Grignard reagent (1 mole excess). Only a

$$(C_6H_5O)_3P\rightarrow O \quad + \quad C_2H_5MgBr \quad \longrightarrow \quad C_2H_5C_6H_5 \text{ (trace)}$$

IIc

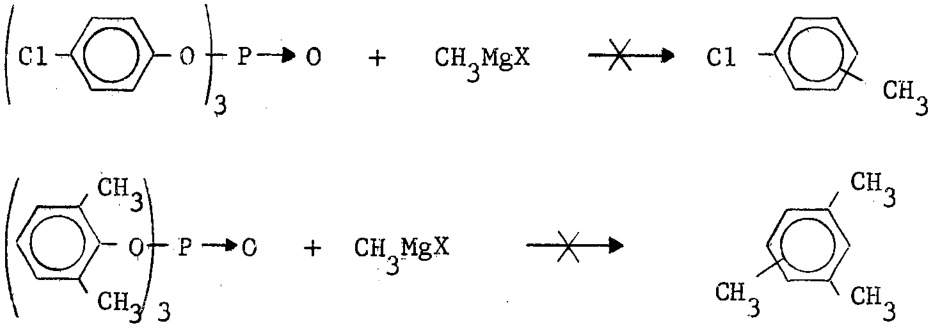


$$(C_6H_5O)_2\overset{\overset{O}{\uparrow}}{P}\,C_6H_5 \quad + \quad C_2H_5MgBr \quad \not\longrightarrow \quad \text{no C-alkylation}$$

IIIc

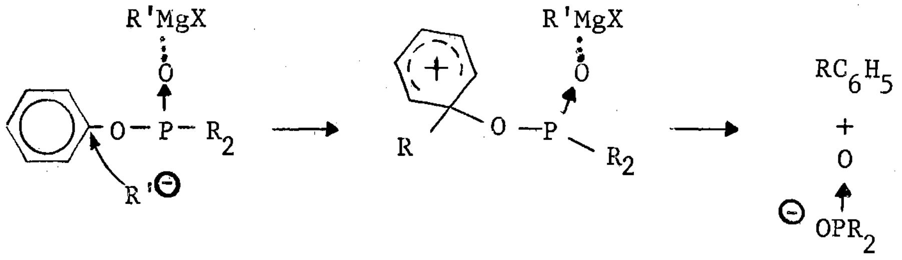
trace of C-alkylation product was detected from the reaction with IIc.

In order to examine the scope of the C-alkylation process further, tris(p-chlorophenyl) phosphate and tris(2,6-dimethylphenyl) phosphate were allowed to react with excess methylmagnesium iodide.

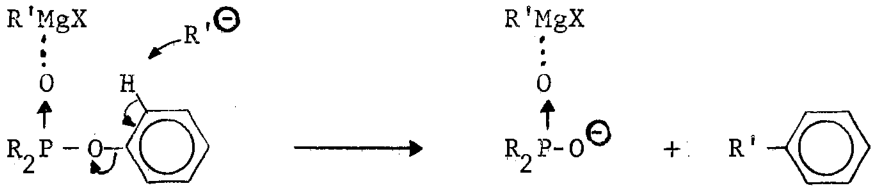


No C-alkylation product (p-chlorotoluene or 1,2,3-trimethylbenzene) was detected by GLC analysis. Nucleophilic attack at the ring carbon (A) or formation of a benzyne-type intermediate (B) had been envisioned as

(A)



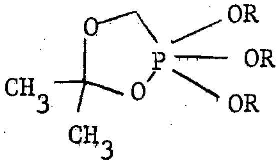
(B)



$R = OC_6H_5$

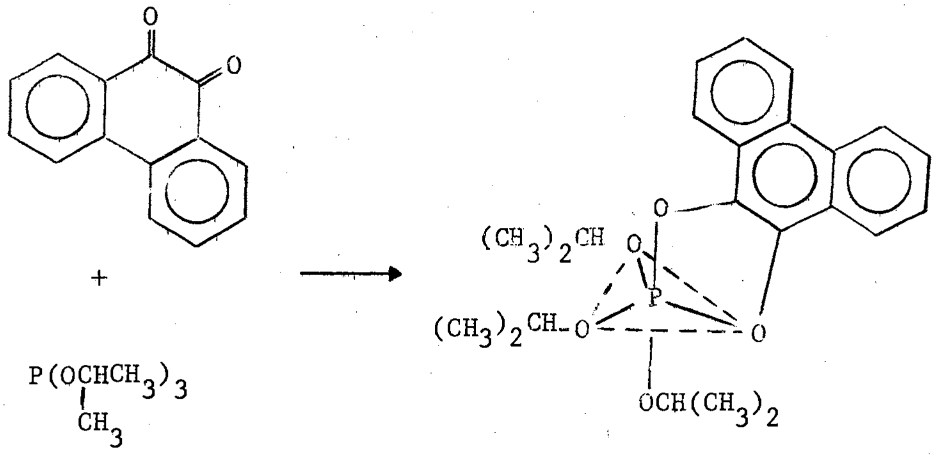
pathways for C-alkylation of the aryl ester.

The attack of the second molecule of anionic Grignard reagent on the ester complex is believed to go through a transition state involving pentacovalent phosphorus. Several compounds in which phosphorus is pentacovalent have been characterized in detail. Representative examples will be cited. PCl_5, PF_5 and PF_3Cl_2 are bipyramidal in the gas phase.[73] PCl_5 has been found to be bipyramidal in benzene solution.[10] Taking advantage of the stabilizing effect of electronegative groups, Ramirez and coworkers[76] have prepared several oxyphosphoranes in which phosphorus is pentacovalent. Compound XXIV is an example.



XXIV

When triisopropyl phosphite was condensed with phenathraquinone, a



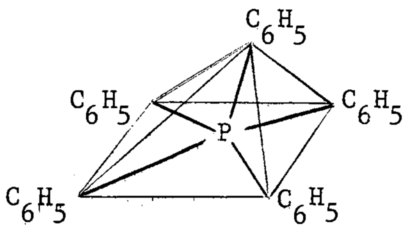
bipyramidal adduct was obtained.[77]

Most interesting is the compound pentaphenylphosphorane (XXIX). X-ray

$(C_6H_5)_5P$

XXIX

diffraction and dipole moment studies have established its structure (solid state) to be of another type.[41,87] The phenyl groups are found at the corners of a square pyramid with

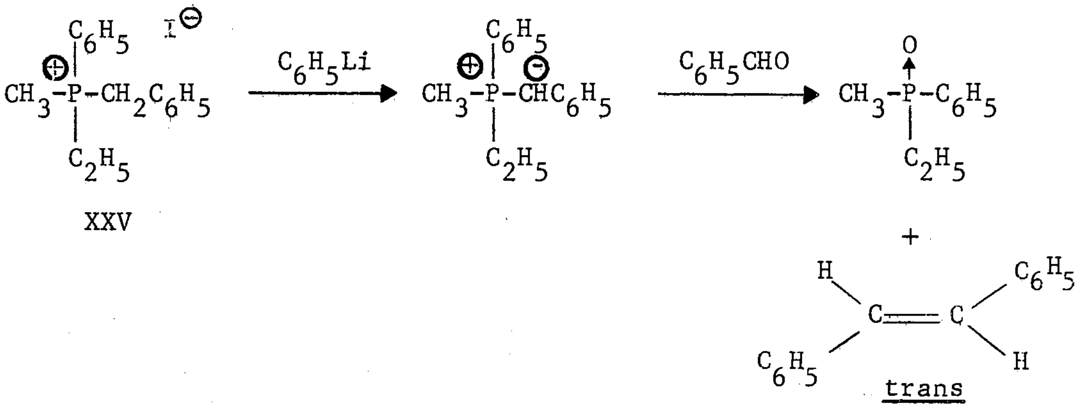


XXIX

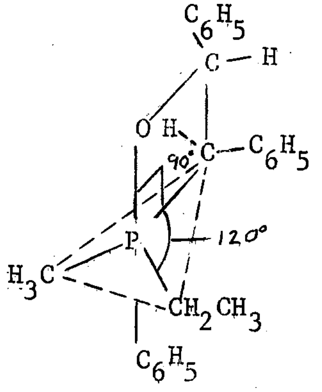
the phosphorus atom located at the center. Earlier reports had indicated a trigonal bipyramid structure.[91] In summary both trigonal bipyramid and square planar compounds of phosphorus are known to exist. In a sense XXIX appears to be of an intermediate type.

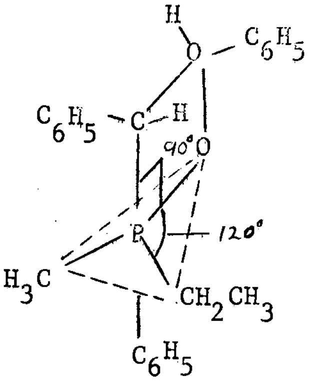
Involvement of a pentacovalent state of phosphorus has been used successfully to account for many experimental observations.[46,61] Two pertinent examples have been cited in the Historical part of this thesis (pages 12 and 13). Two further examples will be discussed.

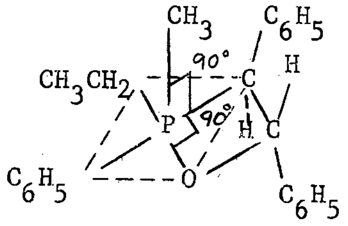
Both product specificity and stereospecificity have been observed in the Wittig reaction of optically active methylethylphenylbenzylphosphonium iodide (XXV).[17,62] Three possible unstable intermediates (two



trigonal bipyramidal and one square planar) have been postulated. In



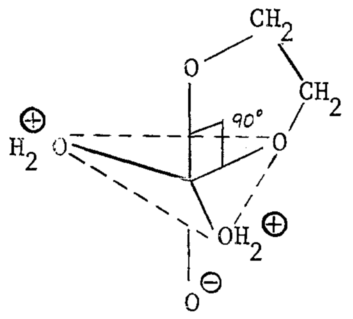




each of the three no unusal angle strain in the transition state or intermediate is involved. Collapse of each would give the optically active phosphine oxide with retention of configuration and the <u>trans</u>-stilbene as observed.

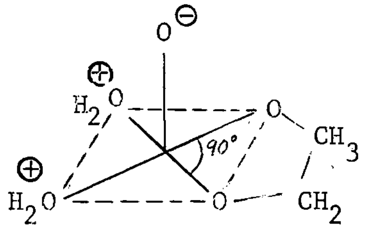
Haake and Westheimer[40] examined the kinetics of the acid-catalyzed hydrolysis of ethylene hydrogen phosphate in oxygen-18 enriched water. The following observations were made. (1) The ester underwent exchange of oxygen with the solvent at a rate one-fifth the rate of hydrolysis. (2) The rate of hydrolysis at the P-O bond was 10^8 times the rate for dimethyl hydrogen phosphate. The observed exchange of oxygen between the ester and solvent requires that there be strain relief in the formation of the activated complex for <u>both</u> hydrolysis and exchange. The following pairs of transition state geometries were proposed for the hydrolysis and exchange processes. It can be readily seen that differentiation between the pairs is experimentally very difficult.

On the basis of these and numerous additional examples cited in references 34 and 35 a transition state (or an intermediate)



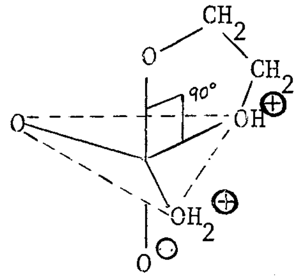
exchange

XXXVIIa



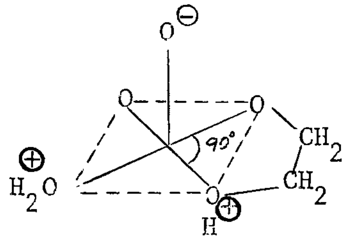
exchange

XXVIIIa



hydrolysis

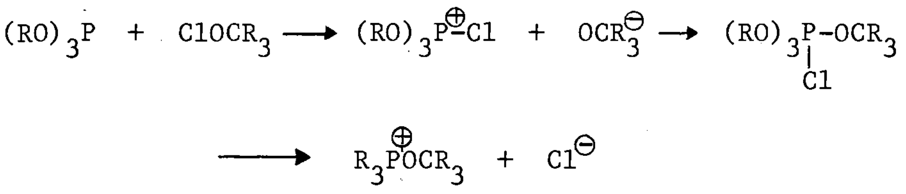
XXVIIb



hydrolysis

XXVIIIb

trigonal bipyramidal structure appears to be logical for the displacement reaction on phosphorus esters. Whether a transition state or an intermediate is involved is a question which cannot be decided on the available evidence. Precedent for an intermediate pentacovalent phosphorus is found in the work of Denney and DiLeone.[24] Such an intermediate was proposed to account for the observed stereochemistry in the

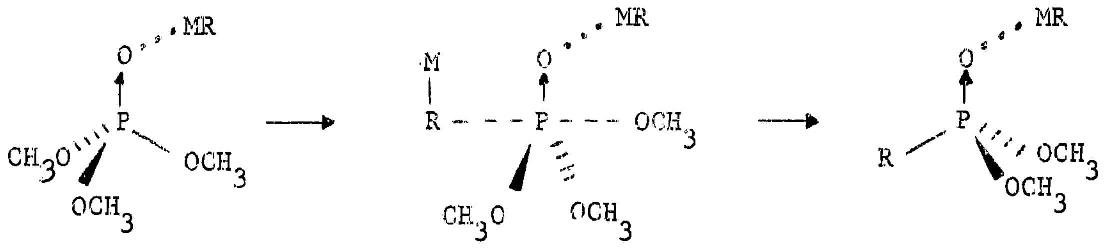


$$(RO)_3P + ClOCR_3 \longrightarrow (RO)_3\overset{\oplus}{P}{-}Cl + OCR_3^{\ominus} \longrightarrow (RO)_3\underset{Cl}{\underset{|}{P}}{-}OCR_3$$

$$\longrightarrow R_3\overset{\oplus}{P}OCR_3 + Cl^{\ominus}$$

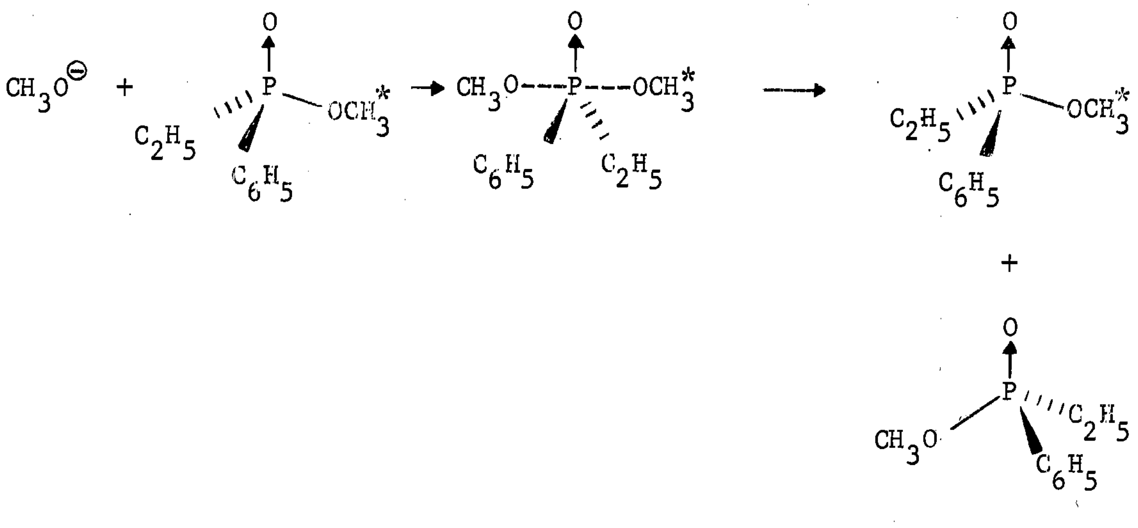
the reaction of tertiary-butyl hypochlorite with triphenyl phosphite.

Assuming such an intermediate to be operative there are three modes of attack available to a nucleophile such as the Grignard reagent in the present work. Attack can occur in a manner analogous to a classical S_N2 mechanism (A) in carbon chemistry. A transition state in which the attacking and leaving groups are at 180° to each other would



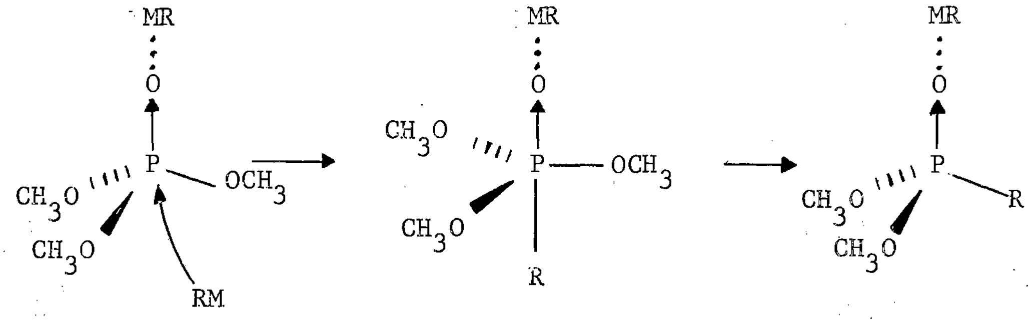
RM = Phenylmagnesium bromide Pathway A

result. Precedent for such a pathway is provided by the work of Hudson and Green with methyl ethylphenylphosphinate.[38] When the carbon-14 labeled ester (methoxy group) was treated with methoxide ion the rate of exchange was found to be exactly one-half the rate of racemization.



Every displacement must thus have caused inversion at the phosphorus atom.

An alternate pathway would be by attack at the base of the pyramid, i.e., from the underside of the phosphorus atom (B), followed by collapse to the product. In pathway B the angle between the attacking

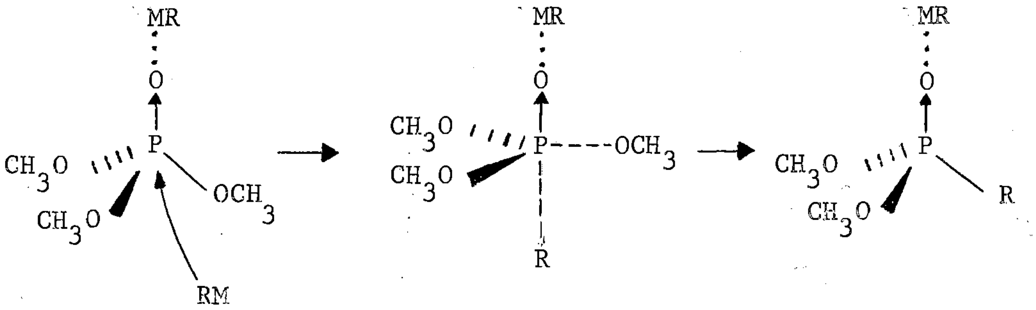


RM = Phenylmagnesium bromide

Pathway B

and leaving groups is 90°. Pathway B requires the existence of at least a short-lived five-bonded intermediate whereas in A bond-making and bond-breaking are concerted.

A third alternative (C) is possible using essentially the same



RM = Phenylmagnesium bromide

Pathway C

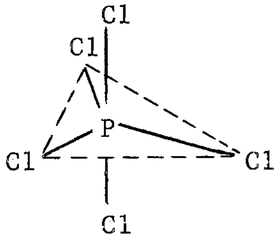
geometry as in (B). In (C) the angle between the two bonds in the bond-making bond-breaking process would be 90°. Lack of precedent would make C seem least likely.

To distinguish between A and B would be difficult. Haake and

Westheimer have made a rather elegant analysis of the stereochemical consequences of the relative position of attacking and leaving groups on an asymmetric phosphorus atom.[40] By examination of the stereochemical results of attack on an asymmetric ester it would be possible to distinguish between the two paths A and B.

In the trigonal bipyramid proposed for the transition state evidence indicates non-equivalence of the bonds. For example three of the

$$PCl_5 + 3\ Cl^{*\ominus} \longrightarrow PCl_3^{*}\ Cl_2 + 3\ Cl^{\ominus}$$



chlorines atoms in PCl_5 (sp^3d hybridized) are readily replaced by radioactive chlorine.[26] In sp^3d hybridization Duffy[28] has assumed the bonds to be of equal length and has calculated the radial bonds (sp^2) to be weaker than the axial bonds. If the bonds are assumed to be equal in energy[21,49] then the axial bonds must be longer than the equitorial bonds.

Other possible transition states may be proposed. For example both attacking and leaving groups may be in the equitorial or basal position. The alternatives discussed above, A-C, appear to require a minimum of reorganization of the relative positions of substituents in passing through the transition state.

On the basis of the experimental data obtained in this investigation it is evident that the nucleophilic displacement of alkoxy and aryloxy groups from IIa is a stepwise process. The use of phosphate esters of the type $(RO)_3P \rightarrow O$ does not appear to be superior to other methods in the synthesis of phosphine oxides. Because of the better leaving properties of aryloxy groups, use of aryl esters may be more effective. Analysis of data obtained on product yield reveals a clear dependence on the relative concentration of reactants. Although the postulated intermediate dimethyl phenylphosphonate was not detected in any reaction mixture of IIa with I sufficient evidence is available to substantiate its participation.[14]

Comparison of yields of displacement products indicates that trimethyl phosphate (IIa) is considerably less reactive than the corresponding phosphite. The comparison is of special value since identical leaving groups are being displaced and the reaction conditions are identical. Whether the complexing ability or the geometric features of the two esters governs the course of the reaction is problematical.[44] The problem of relative solubilities of the complexes and their influence on yield is unsolved. Exploration of other solvent systems certainly might prove fruitful.

Toluene, the product of C-alkylation, was found in all reaction mixtures obtained from I and IIa. Though trimethyl phosphate has been successfully used as an alkylating agent (see Historical, Chapter I) the yields in this work were too low to be of synthetic value. Use of THF as a solvent led to marked increase in the yields of alkylated product. Further exploration in this direction might be warranted.

CHAPTER III

EXPERIMENTAL[a-e]

Starting Materials. The following chemical reagents were purchased: trimethyl phosphate (IIa), b.p. 62-64°/5.5-7.0 mm., $n_D^{24.3}$ 1.3938 [lit.[3] 73°/10 mm., $n_D^{25°}$ 1.3950], Ethyl Corporation; triethyl phosphate (IIb), b.p. 74-76°/1.5-1.7 mm., $n_D^{23.8°}$ 1.4032 [lit.[1] 77-79°/2 mm., n_D^{20} 1.4063], Matheson, Coleman, and Bell; diphenyl phenylphosphonate (IIIc), m.p. 61-63° [lit.[63] 63.5°], and triphenyl phosphate (IIc), m.p. 48.5-50° [lit.[83] 50°], Victor Chemical Company; tris(2,6-dimethylphenyl) phosphate, m.p. 134.5-136° [lit.[42] 136-138°] Aldrich Chemical Company; and phenylmagnesium bromide (I), ethylmagnesium bromide, and methylmagnesium iodide as ~ 3N solutions, Araphoe Chemicals Inc. Methyl diphenylphosphinate (IVa), b.p. 178°/2.4 mm., [lit.[7] 140°/0.34 mm.], and

---

[a] All melting points are corrected; all boiling points are uncorrected.

[b] The infrared spectra were determined on a Beckman IR-5A spectrometer as films on sodium chloride cells or as potassium bromide pellets.

[c] Gas chromatographic analyses were performed using an Aerograph Hy-Fi Model A-550 with a hydrogen flame ionization detector from Wilkens Instrument and Research, Inc., Walnut Creek, California.

[d] The nuclear magnetic resonance spectra were determined on a Varian A-60 high resolution spectrometer with a field sensing stabilizer ("Super-Stabilizer"). Tetramethylsilane was used as an internal standard.

[e] The microanalyses were performed by Galbraith Laboratories, Knoxville, Tennessee.

triphenylphosphine oxide (V), m.p. 152.5-153.5° [lit.[53] 152-153°], were generously supplied by Dr. T. H. Austin. The liquids were distilled and center cuts were taken and examined for purity by GLC on two different columns (see Table I).[5] Only one peak was revealed in each case. After recrystallization, each solid, dissolved in ether-benzene showed a single peak by GLC.

Preparation of Dimethyl Phenylphosphonate (IIIa). A 1-liter three-necked flask was equipped with a mechanical stirrer, a condenser, a thermometer, and a pressure-equalizing addition funnel. After the system had been swept with anhydrous nitrogen, 76.80 g. (0.39 mole) of phenylphosphonic dichloride in 300 ml. of anhydrous ether was added to the flask. A solution of triethylamine (95.75 g., 0.94 mole) in 100 ml. of anhydrous ether was added dropwise with stirring over a 30-minute period. The flask was then immersed in an ice-salt bath and the temperature adjusted to 10°. Methanol (28.85 g., 0.88 mole) was added at such a rate as to maintain the temperature below 16°. It was necessary to add 100 ml. of ether to facilitate stirring of the white slurry which formed at this point. The reaction mixture was then heated under reflux for 45 minutes, cooled and filtered to remove the white inorganic solid. The liquid residue was dried ($MgSO_4$), concentrated to 80-100 ml. of a dark red liquid, and vacuum distilled, b.p. 79-80°/2.0 mm. [lit.[39] 103°/4 mm.]; yield of IIIa, 53.45 g., (72.9%). The IR spectrum was identical with that of an authentic sample.

Preparation of tris(p-Chlorophenyl) Phosphate. A solution of 33.0 g. (0.256 mole) of p-chlorophenol and 29.16 g. (0.29 mole) of triethylamine in 300 ml. of anhydrous ether was placed in a 1-liter three-necked flask equipped as described above. Dry nitrogen was passed through the system. To the solution was added dropwise 12.79 g. (0.083 mole) of phosphorus oxychloride over a 40-minute period. When the oxychloride was first added the temperature rose rapidly to 29°. The reaction was then cooled (ice bath) and the temperature was held between 18° and 25° during the remainder of the addition. During the addition a white precipitate formed. The mixture was vigorously stirred for 1 hour and heated under reflux (39°) for an additional hour and then allowed to stand overnight at room temperature. The solid was collected by filtration, washed with water to remove triethylamine hydrochloride, and dried overnight under vacuum. The reaction solution (A) was saved for further analysis. The solid, m.p. 112-118°, was dissolved in ether-benzene and washed with 10% sodium hydroxide in order to remove bis-(p-chlorophenyl) hydrogen phosphate, m.p. 131-132.5° [lit.[93] 133-135°]. The water layer was washed twice with 100-ml. portions of ether, and the combined organic layers were evaporated on the flash evaporator. After drying in a vacuum dessicator, 16.3 g. of white solid was obtained, m.p. 112.5-113.7°, [lit.[93] 113°].

Anal. Calcd. for $C_{18}H_{12}Cl_3O_4P$: C, 50.32; H, 2.815, Cl, 24.76;
P, 7.20.
Found: Cl, 24.25; P, 6.99.

An additional 6.12 g. of solid was obtained when the original reaction solution (A) was evaporated. Since a phenolic odor was detected, the solid was dissolved in ether-benzene and washed with 100 ml. of 10% sodium carbonate. The two layers were separated and the organic layer was dried ($MgSO_4$). Evaporation of the solvent gave 5.1 g. of white solid, m.p. 135-137°. On the basis of the IR spectrum of this compound (strong absorption at 10.4 μ, P-O-P) it was tentatively identified as tetrakis(p-chlorophenyl) pyrophosphate. It was postulated that this material was formed by the condensation of bis(p-chlorophenyl) chloro phosphate and the corresponding acid (formed by hydrolysis of the acid chloride). No further investigation was conducted on this material.

Reaction of Phenylmagnesium Bromide (I) With Trimethyl Phosphate (IIa) at 60° (3:1). The following procedure is typical of that used for all reactions of trimethyl phosphate (IIa) with I in ratios of 4:1, 3:1, and 1:1. One reaction in which the temperature was at 70° was performed in the same manner. Analytical results are reported in Table IV. A 1-liter three-necked flask (previously calibrated and marked at the 300-ml. level) was equipped with condenser, magnetic stirrer, $CaCl_2$ drying tube, thermometer and pressure-equalizing addition funnel connected to an anhydrous nitrogen supply. After the system was swept with nitrogen 100 ml. of (~ 3N) phenylmagnesium bromide was added to 200 ml. of anhydrous (dried over molecular sieve 5-A) ethyl ether. The concentration of the Grignard reagent was determined by removing three 1.0-ml. aliquots, quenching in 0.1027 N hydrochloric acid, boiling, cooling and back-titrating the excess acid with 0.1028 N sodium hydroxide.[7] The solution was found to contain 0.2941 moles of the Grignard reagent. A solution of IIa (13.73 g., 0.0980 mole) in 50 ml. of anhydrous (molecular sieve 5-A) benzene was then added dropwise with stirring over a 45-minute period. A slight temperature rise (2°) was noted during the addition. As the ester was added a characteristic syrupy solid appeared on the sides of the reaction flask. An additional 150 ml. of dry benzene was added, and the mixture was rapidly heated to 60° and then held under reflux at 60-63° for 1 hour. With the aid of an ice-salt bath the reaction mixture was cooled to 3° and hydrolyzed with 400 ml. of cold 15% NH_4Cl. During addition of the first 25 ml. the reaction was exothermic, necessitating slow controlled addition in order to hold the temperature below 15°C. The remainder was then added rapidly and the mixture brought to room temperature with stirring. Because of slow decomposition of solid in the aqueous layer, stirring was continued for 3 hours. The organic layer was decanted and the aqueous layer was extracted with three 100-ml. quantities of ether. The original organic layer and the extracts were dried ($MgSO_4$), combined and concentrated to 30 ml. The concentrate was diluted to exactly 100.0 ml. with ether for GLC analysis. The method of analysis is discussed in the following section. The water layer, pH ~ 8.0, was acidified to pH 1 with 6N hydrochloric acid to give a small amount of white solid. The precipitate was collected, washed with water and dried, m.p. 192.5-193.5° [lit.[56] 193-194°]. The IR spectrum was identical with that of an authentic sample of diphenylphosphinic acid (VI). Careful examination of the water layer (GLC) failed to reveal any phenylphosphonic acid or monomethyl phenylphosphonate.

Blank Run With Phenylmagnesium Bromide (I) at 60°. A solution (~ 3N) of 100 ml. of commercial I dissolved in 200 ml. dry (molecular sieve-5A) ether was prepared in a 1-liter three-necked flask equipped as described in the previous example. After addition of 300 ml. of dry benzene, the mixture was heated under reflux at 60° for 1 hour. After the customary work-up, the solution was concentrated to 25 ml. and then diluted with ether-benzene to 100.0 ml. for GLC analysis which revealed a number of peaks. Phenol (4%) and biphenyl (3%) were present in significant amounts. Other compounds detected in small amounts were not identified. The presence of phenol, biphenyl and other compounds in hydrolyzed Grignard solutions has been summarized by Kharasch and Reinmuth.[14] The biphenyl presumably arises from coupling of the Grignard reagent. Formation of phenol is attributed to reaction of unreacted I, oxygen and water during the hydrolysis step.[14] Mixed injections with reaction mixtures from I and IIa were used to identify components not resulting from reaction with the phosphate.

Gas Liquid Chromatographic (GLC) Analysis of the Mixture Obtained From Reaction of Organophosphates With Grignard Reagents. In the course of the research presented in this dissertation several reaction mixtures were prepared and analyzed at the same time. The method in general was that outlined by Austin[3] and details will not be herein repeated. Pertinent differences will be discussed. Data for the reactions are presented in Tables I-VI.

Qualitative Analyses. The identity of components of the various mixtures was determined by comparison of retention times with those of known samples and by the technique of mixed injection. During the course of the study several columns were used for the GLC analyses.[5] Those columns which gave most satisfactory results (CA-1, CA-2) are listed in Table I. Typical chromatographs are presented in Plates I-V. Dimethyl phenylphosphonate (IIIa) and biphenyl could not be resolved on CA-1 or CA-2 although a wide range of temperatures and flow rates were examined. As a consequence it was necessary to make use of column CA-3 for both qualitative and quantitative analyses of these compounds. Although phosphorus-containing compounds are characterized by a tendency to tail extensively on the Chromosorb W support, separation of biphenyl and IIIa was adequate for easy analysis (see Plate IV). The

Chromosorb W column (CA-3) did adequately separate the other components of the reaction mixtures, but since the Chromosorb G columns (CA-1,2) provided much cleaner separation, they were chosen for analysis of the remaining mixtures. Retention times and other pertinent data are given in Table II. Optimum conditions for separation of various reaction mixtures occurred at three or four different temperature ranges. Considerable difficulty was experienced in attempting to obtain quantitative information on unreacted IIa in the reaction mixtures. Apparently the ester decomposed on the column (see Plate V), and it was not possible to obtain reproducible results. No IIIa was detected in any reaction mixture in which IIa was used as a starting material.

Quantitative Analysis. Several standard solutions were prepared by dissolving the appropriate compounds in ether-benzene and making up to volume in volumetric flasks. Compositions are reported in Table III. Some preliminary GLC studies were conducted, using an internal standard. However, the complexity of the reaction mixtures obtained made it more feasible to use external standards. In analyzing for a particular component several injections were made of the reaction mixture followed by several injections of the appropriate standard. In most cases it was possible to adjust concentrations so that the injection size and peak areas of the standard and that of the reaction mixture were of similar magnitudes. By comparing the average areas of the standard peaks with those from reaction mixtures the amount of each component was determined.[3] In the early stages of the problem, peak areas were determined by multiplying the height of the peak by the width at half-height height.[79] It was difficult to obtain reproducible values for the peak areas of the phosphorus compounds because of the tailing. Subsequently, peak areas were determined using a compensating planimeter.[f] Each peak was traversed at least three times and an average taken. Results of the analysis of pertinent reactions are presented in Tables IV, V and VI.

Reaction of Phenylmagnesium Bromide (I) With Trimethyl Phosphate (IIa) at 60° (1:1)--Inverse Addition. Into a 1-liter three-necked flask equipped as previously described and swept with dry nitrogen was placed 8.40 g. (0.06 mole) of IIa dissolved in 100 ml. of dry (molecular sieve-5A) benzene. The Grignard reagent, 0.067 moles (diluted to 250 ml.), was placed in the addition funnel. With stirring, the Grignard reagent was added over a period of 0.5 hour during which time the temperature rose 2.0°. An additional 150 ml. benzene was added and the mixture was held under reflux (60-63°) for 1 hour. After cooling to 2°, the mixture was hydrolyzed with 400 ml. of 20% aqueous ammonium chloride. A small amount of inorganic solid was removed by filtration after the two-phase mixture had been stirred overnight. The aqueous layer was extracted with three 100-ml portions of ether. The organic layers were dried ($MgSO_4$), combined and concentrated on the flash evaporator. Dilution with ether-benzene provided 100.0 ml. for GLC analysis. A similar reaction was performed in which the addition time was lengthened to 1.75 hours. Results of both reactions are shown in Table V. The 1:1 normal addition is included for comparison.

Reaction of Phenylmagnesium Bromide (I) With Triethyl Phosphate IIb) at 60° (3:1). To a 1-liter three-necked flask equipped as previously described on page 44 and swept with dry nitrogen was added 100 ml.

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[f] K and E compensating polar planimeter, model 620015.

of ~ 3N (~ 0.28 mole) I and 200 ml. of anhydrous (mole sieve-5A) ether. Since the major objective of the experiment was to ascertain if ethylbenzene was present the exact concentration of the Grignard reagent was not determined. Into the addition funnel was placed 17.38 g. (0.0954 mole) IIb in 50 ml. of dry (molecular sieve-5A) benzene. During the addition period (45 minutes) no precipitate was observed and the temperature did not rise. After an additional 150 ml. of benzene was added the reaction mixture was held under reflux at 60° for 1 hour. Solid material was observed on the surface of the liquid after standing overnight. A 25-ml. portion was removed and worked up in the usual manner for GLC analysis. Though a small peak was observed at approximately the correct retention time for ethylbenzene (oven temperature 50°) the shape of the peak was not characteristic of ethylbenzene. It was concluded that no ethylbenzene was present at this time. To the remaining mixture was added 150 ml. dry benzene and the solution was held at reflux for an additional 3 hours. After the customary work-up, GLC analysis showed a small amount of ethylbenzene (estimated at less than 1% yield). Examination of the mixture (GLC) at higher temperatures revealed the presence of V and IVb (mixed injection of authentic samples). No quantitative analysis was performed on these latter compounds.

<u>Reaction of Ethylmagnesium Bromide With Triphenyl Phosphate (IIc) at 60° (3:1)</u>. In order to investigate further the scope of alkylation the following reaction was performed. To a 1-liter three-necked flask equipped as usual was added 100 ml. of commercial ethylmagnesium bromide (~ 3N) in 200 ml. of anhydrous ether. Analysis of the solution revealed it to contain 0.3115 moles. A solution of IIc (33.87 g., 0.1038

mole) in 100 ml. of benzene was added dropwise over a one-hour period. No precipitate was observed during the addition. A 100-ml portion of dry benzene was added and the dark brown solution was then held under reflux (60-63.5°) for 1 hour. After the usual work-up procedure, a 100.0-ml. ether-benzene solution was prepared for GLC analysis. No ethylbenzene was detected in the reaction mixture. Phenyl diethylphosphinate was identified by GLC but the amount was not determined. A similar reaction of ethylmagnesium bromide with diphenyl phenylphosphonate (IIIc) gave no evidence of C-alkylation on the phosphonate.

Reaction of Methylmagnesium Iodide With tris(2,6-Dimethylphenyl) Phosphate at 60° (4:1). A solution of methylmagnesium iodide (0.15 mole) was placed in a 500-ml. three-necked flask equipped as described on page 44. After the system was swept with dry nitrogen, tris(2,6-dimethylphenyl) phosphate (15.40 g., 0.0375 mole) in 60 ml. of dry benzene was added over a 30-minute period. When addition was completed, a copious solid precipitate was observed. Benzene (75 ml.) was added and the mixture heated under reflux for 1 hour at 60°. A solution was prepared for GLC analysis in the usual manner. Examination of the mixture for the possible C-alkylation products, namely 1,2,3-trimethyl benzene or mesitylene, failed to disclose detectable amounts of either hydrocarbon.

Reaction of Methylmagnesium Iodide With tris(p-Chlorophenyl) Phosphate at 60° (4:1). The ester (0.46 g., 0.015 mole) was allowed to react with 0.06 mole of the Grignard reagent in a procedure identical with that used in the preceding experiment. Careful analysis by GLC failed to reveal the presence of any of the chlorotoluene isomers.

Use of Tetrahydrofuran (THF) as a Solvent for Reaction of Phenylmagnesium Bromide (I) With Trimethyl Phosphate (IIa) at 60° (3:1). THF was used to determine the effect of solvent change on the ratio of C-alkylation to P-alkylation. The ester IIa (6.77 g., 0.048 mole) dissolved in 50 ml. of ether was added dropwise to 50 ml. (0.29 mole) of I in the previously described apparatus. Addition required 35 minutes. THF (100 ml.) was added and the mixture heated under reflux (60°) for 1 hour. At the conclusion of the normal work-up procedure, the organic liquid was concentrated to a thick oil and then diluted to 50.0 ml. for GLC analysis. Results are presented in Table IV.

Reaction of Phenylmagnesium Bromide (I) With Trimethyl Phosphate (IIa) at 30° (3:1). In an attempt to trap dimethyl phenylphosphonate (IIIa) the reaction was performed at 30° in the following manner. Trimethyl phosphate (IIa) (6.77 g., 0.048 mole) in 25 ml. of benzene was added dropwise over 35 minutes to 0.1449 mole of I in 150 ml. of ether. The reaction mixture was stirred (30°) for 1 hour and worked up in the normal fashion. The organic concentrate was diluted to the mark in a 50-ml. volumetric flask for GLC analysis. Results are reported in Table V.

Reaction of Phenylmagnesium Bromide (I) With Dimethyl Phenylphosphonate (IIIa) at 30° (3:1). In order to determine whether C-alkylation occurred on the phosphonate IIIa and phosphinate IVa these esters were reacted with I. A solution of 8.99 g. (0.048 mole) of IIIa dissolved in ether-benzene (15 ml.-35 ml.), was added to 150 ml. of I (0.1449 mole). A white solid appeared immediately. When approximately half the ester had been added, a dark oil settled out. The reaction mixture was stirred for 1 hour (30°). The two layers were separated and worked up independently. The workup of the lower layer was noteworthy in that the hydrolysis was extremely exothermic in contrast to the behavior of the usual reaction mixture. During GLC analysis on the CA-3 column unreacted ester was readily detected. Additional results are presented in Table VI. A similar reaction with IVa was also performed and results are presented in Table VI. Data from the 4:1 reaction with IIa at 30° is included for comparison.

Reaction of Phenylmagnesium Bromide (I) With Trimethyl Phosphate (IIa) at 100° (3:1). In order to determine the effect of temperature change on the yield of displacement products, anisole was used as the solvent. In the usual apparatus (page 44) 11.61 g., (0.0928 mole) of IIa in 30 ml. dry benzene was added to 0.2487 moles of I in 350 ml. of ether. At the completion of addition (20 minutes) 300 ml. of dry anisole was added. After most of the ether was displaced by heating the mixture slowly to 45° (condenser off) the mixture was held under reflux at 100-105° for 1 hour. The mixture was worked up with cold aqueous ammonium chloride (15%) and a 100.0-ml. portion was taken for GLC analysis. Only the yield of V was determined. Results are included in Table IV. The relative amount of phosphinate compared to oxide was considerably less than at lower temperatures. No IIIa was detected.

TABLE I

COLUMNS[a] USED IN ANALYSIS OF REACTION MIXTURES

Substrate	Support[b]	Concentration[d] (W/W%)	Mesh Size	Dimension
CA-1[e] Silicone rubber	Chromosorb G (DMCS)[c]	5%	60-80	6 ft.
CA-2 Silicone 30	Chromosorb G (DMCS)[c]	6%	80-100	6 ft.
CA-3 SE 30	Chromosorb W	5%	60-80	5 ft.

[a] All of the columns were obtained commercially and were of 1/8 in. stainless steel.

[b] The supports were all acid-washed.

[c] The Chromosorb G was pretreated with dimethyldichlorosilane (DMCS) by the supplier.

[d] Flow rates of nitrogen carrier gas and hydrogen were maintained at approximately 30 and 22 ml./minute, respectively.

[e] Column analytical (CA).

TABLE II

GLC ANALYSIS[a] CHARACTERISTIC RETENTION TIMES

Compound	Column[b] and Temperature (°C)		Retention Time (Min.)
$(CH_3O)_3P\rightarrow O$ (IIa)	CA-2	110°	2.2
$C_6H_5P(O)(OCH_3)_2$ (IIIa)	CA-3	180°	3.8
$C_6H_5-C_6H_5$	CA-3	180°	6.2
$(C_6H_5)_2P(O)OCH_3$ (IVa)	CA-2	260°	4.8
$(C_6H_5)_2P(O)OC_6H_5$ (IVc)	CA-2	260°	9.0
$(C_6H_5)_3P\rightarrow O$ (V)	CA-2	260°	10.3

[a] See Plates I-V for typical chromatograms.

[b] See Table I for column specifications.

TABLE III

GLC STANDARD SOLUTIONS

Solution	Component	Conc.	Moles x 10^3
1	$(CH_3O)_3P\rightarrow O$ (IIa)	1.0095 g./100 ml.	7.206
2	$C_6H_5P(O)(OCH_3)_2$ (IIIa)	2.004 g./50 ml.	10.75
3	$C_6H_5CH_3$	0.4958 g./25 ml.	5.38
4	$C_6H_5\text{-}C_6H_5$	1.5073 g./50 ml.	9.78
5	$(C_6H_5)_2P(O)OCH_3$ (IVa)	1.5534 g. /100 ml.	6.689
	$(C_6H_5)_2P(O)OC_6H_5$ (IVc)	1.5139 g.	4.878
	$(C_6H_5)_3P\rightarrow O$ (V)	2.4932 g.	8.958

TABLE IV

DATA ON REACTIONS OF TRIMETHYL PHOSPHATE (IIa) WITH PHENYLMAGNESIUM BROMIDE (I) AT 60°

Exp. No.	I/IIa	Ratio[a] of Products Formed					
		Phosphinate IVa	Phosphine Oxide V	Toluene	Phosphinate IVa	Phosphine Oxide V	Toluene
1	1:1	2.63	1.00[b]	10.2	1.00	1.00[c]	1.00
2	3:1	0.58	1.00	4.84	0.56	2.53	0.59
3	4:1	1.47	1.00	0.75	2.29	4.10	0.30
4	3:1 (70°)	0.16	1.00	1.13	0.40	6.82	0.75
5	3:1 (THF)	1.75	1.00	156.0	0.08	0.11	1.75
6	3:1 (100°)[d]	--	5.9[e]	--	--	14.92	--

[a] The actual per cent yields of methyl diphenylphosphinate (IVa), triphenylphosphine oxide (V) and toluene are based on trimethyl phosphate (IIa). A minimum of two runs was performed at each set of conditions.

[b] These numbers pertain to the ratios of IVa, V and toluene and can be compared horizontally for each run (except 6) with the phosphine oxide as the standard.

[c] These numbers correspond to relative ratios of IVa, V and toluene and can be compared to run 1 as the standard (=1.00).

[d] Anisole used as the solvent.

[e] Based on run 2.

TABLE V

DATA ON 1:1 REACTIONS, NORMAL AND INVERSE ADDITIONS AT 60°

		Ratio[a] of Products Formed					
Run No.	Time (min.) and Mode of Addition	Phosphinate IVa	Phosphine Oxide V	Toluene	Phosphinate IVa	Phosphine Oxide V	Toluene
1	30 Normal	2.63	1.00[b]	10.2	1.00	1.00[c]	1.00
2	30 Inverse	34.0	1.00	4.00	0.12	0.01	0.37
3	105 Inverse	1.43	1.00	5.23	0.71	1.31	0.66

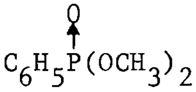
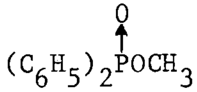
[a] The actual per cent yields of IVa, V and toluene are based on (IIa). A minimum of two runs was performed at each set of conditions.

[b] The numbers in this section pertain to the ratios of phosphinate, phosphine oxide and toluene and can be compared horizontally for each run with the phosphine oxide as the standard.

[c] The numbers in this section correspond to ratios of IVa, V and toluene and can be compared to run 1 as the standard (=1).

TABLE VI

DATA ON REACTIONS OF ESTERS IIa, IIIa and IVa WITH PHENYLMAGNESIUM BROMIDE (I) AT 60°

Ester	I Ester	Relative Ratio[a] of Products					
		Phosphinate IVa	Phosphine Oxide V	Toluene	Phosphinate IVa	Phosphine Oxide V	Toluene
$(CH_3O)_3P \rightarrow O$ IIa	4:1	3.58	1.00	22.9	1.00[c]	1.00	1.00
 $C_6H_5\overset{O\uparrow}{P}(OCH_3)_2$ IIIa	3:1	2.19	1.00	0.55	8.97	14.7	0.35
 $(C_6H_5)_2\overset{O\uparrow}{P}OCH_3$ IVa	2:1	(1.78)[d]	1.00	0.37	(13.05)[d]	26.2	0.042

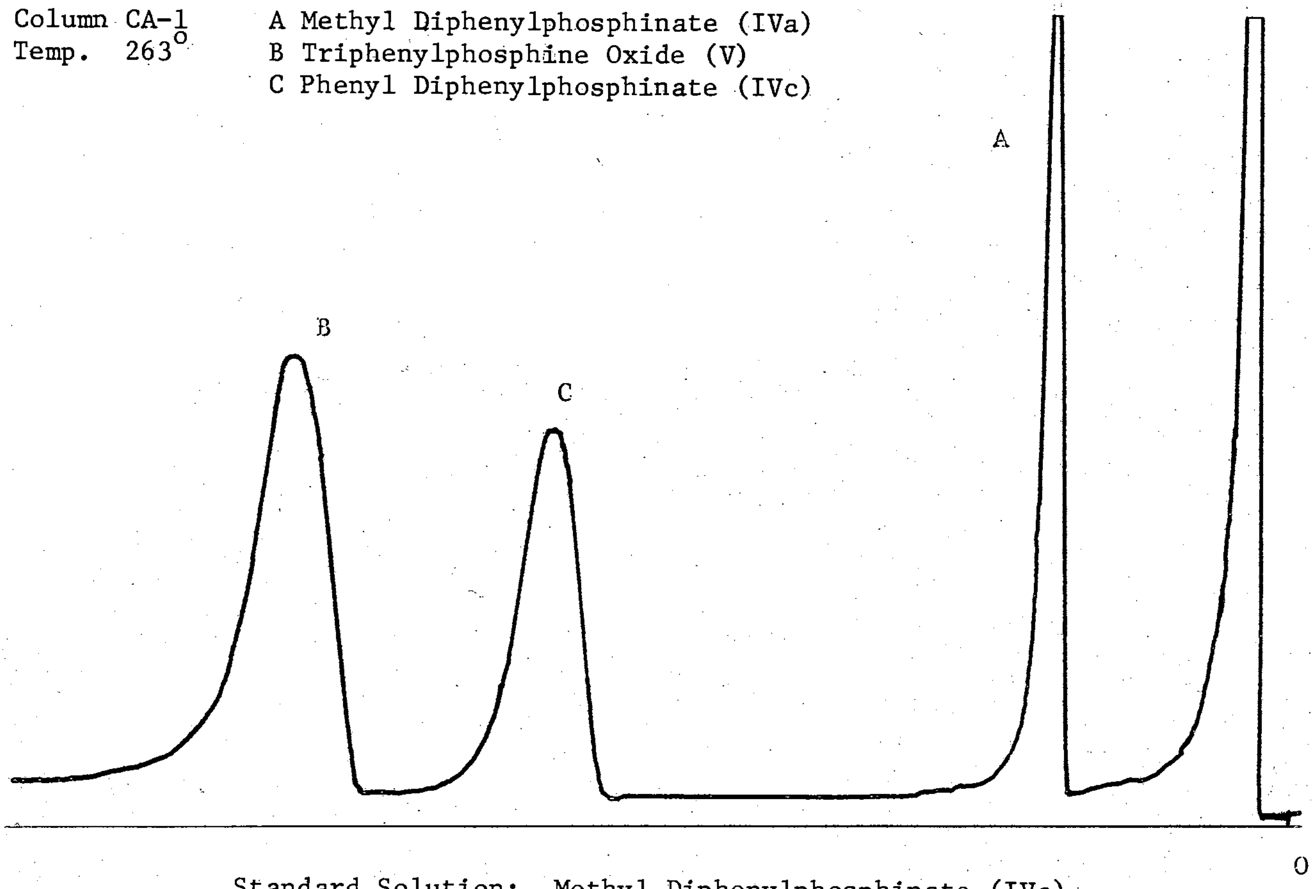
[a] The actual per cent yields are based on amount of ester used. A minimum of two runs was performed for each set of conditions.

[b] These numbers pertain to the ratios of IVa, V and toluene and can be compared horizontally for each run with the V as standard (1.00).

[c] The numbers in this section correspond to ratios of IVa, V and toluene based on yields from IIa standard (1.00).

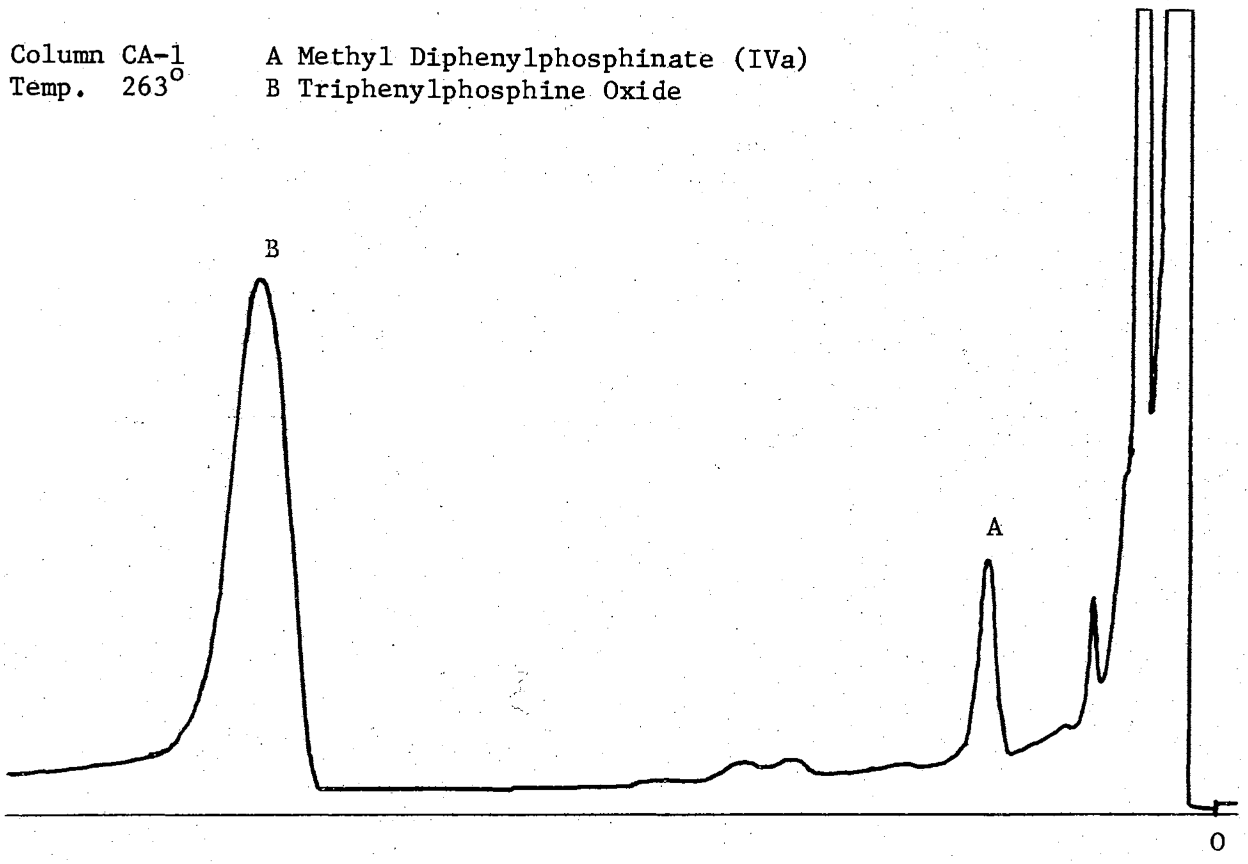
[d] Numbers in parentheses indicate recovered starting material.

Plate I



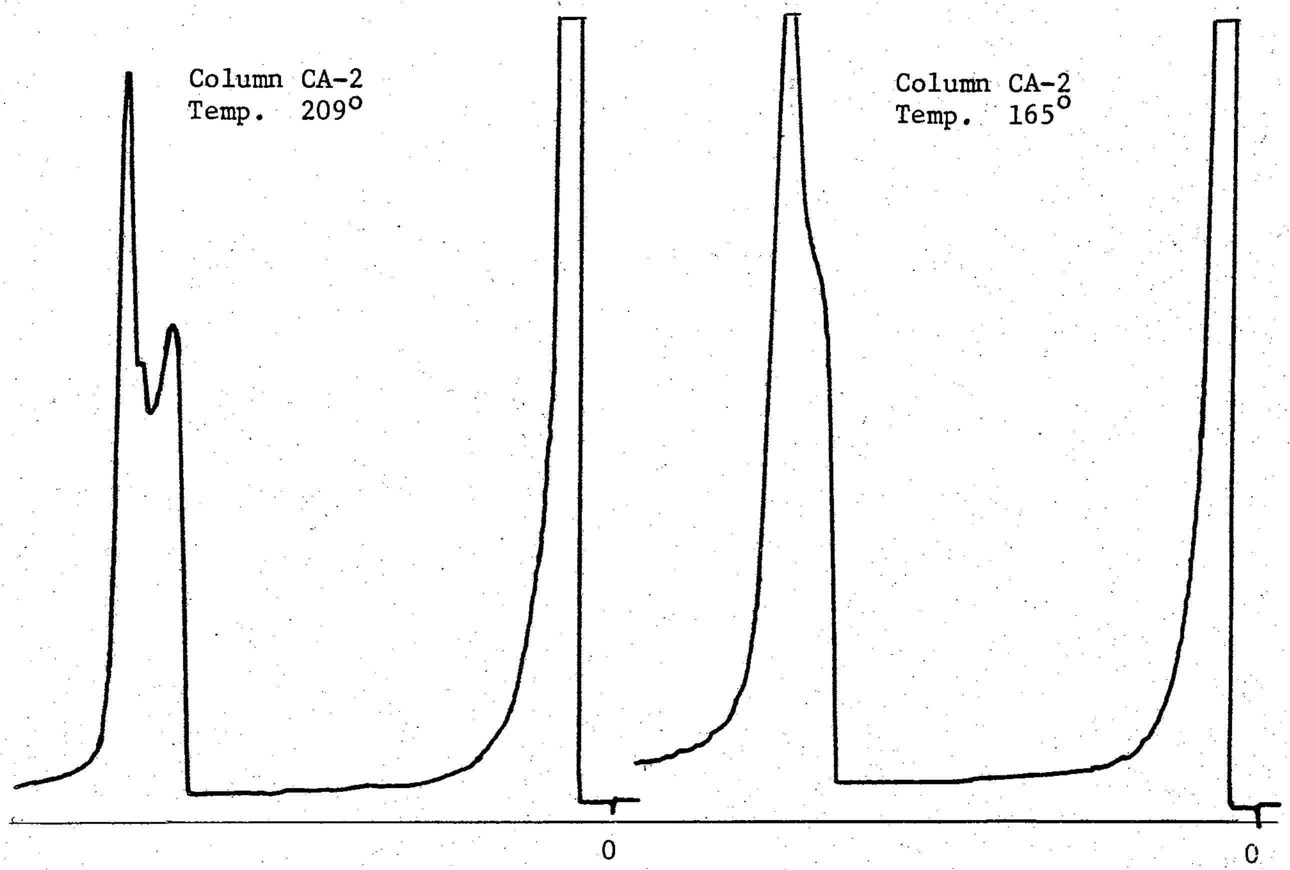
Standard Solution: Methyl Diphenylphosphinate (IVa) and Triphenylphosphine Oxide (V)

Plate II



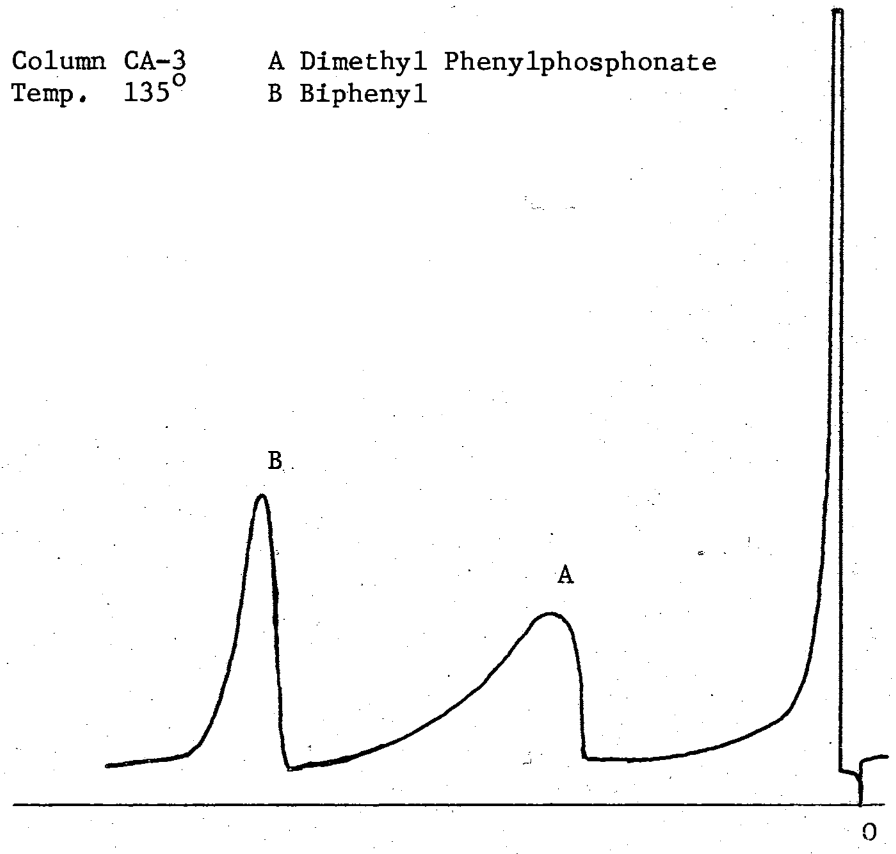
Reaction Mixture 3:1

Plate III



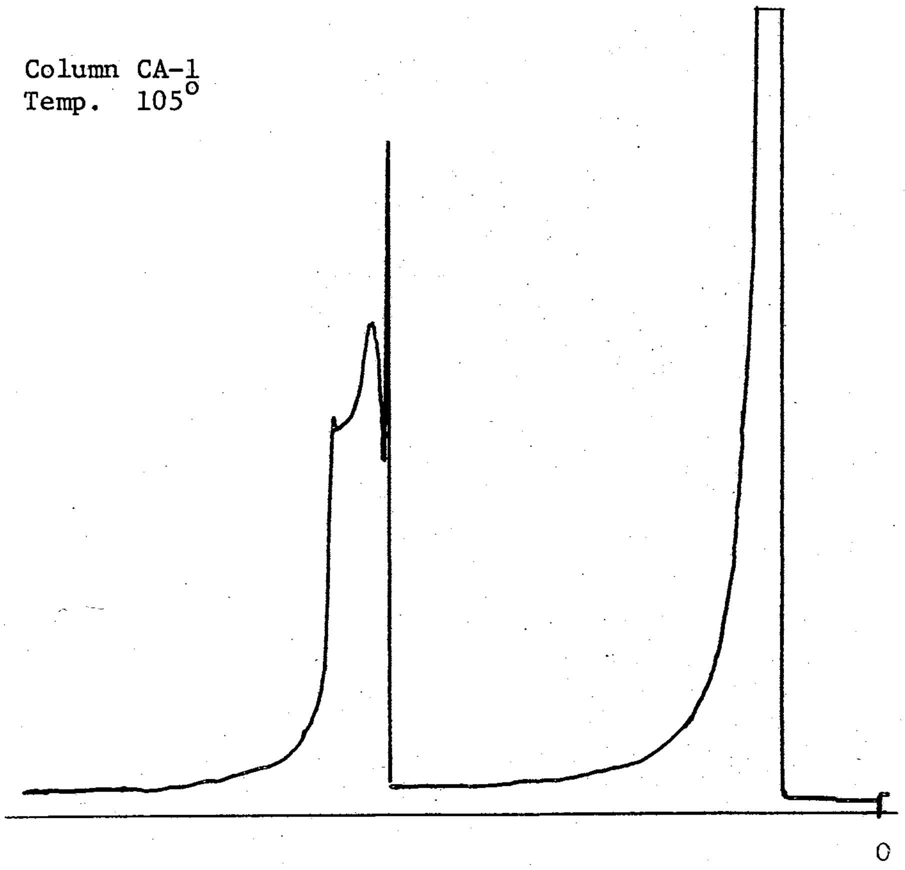
Attenpted Separation of Dimethyl Phenylphosphonate (IIIa) and Biphenyl on Chromosorb W

Plate IV



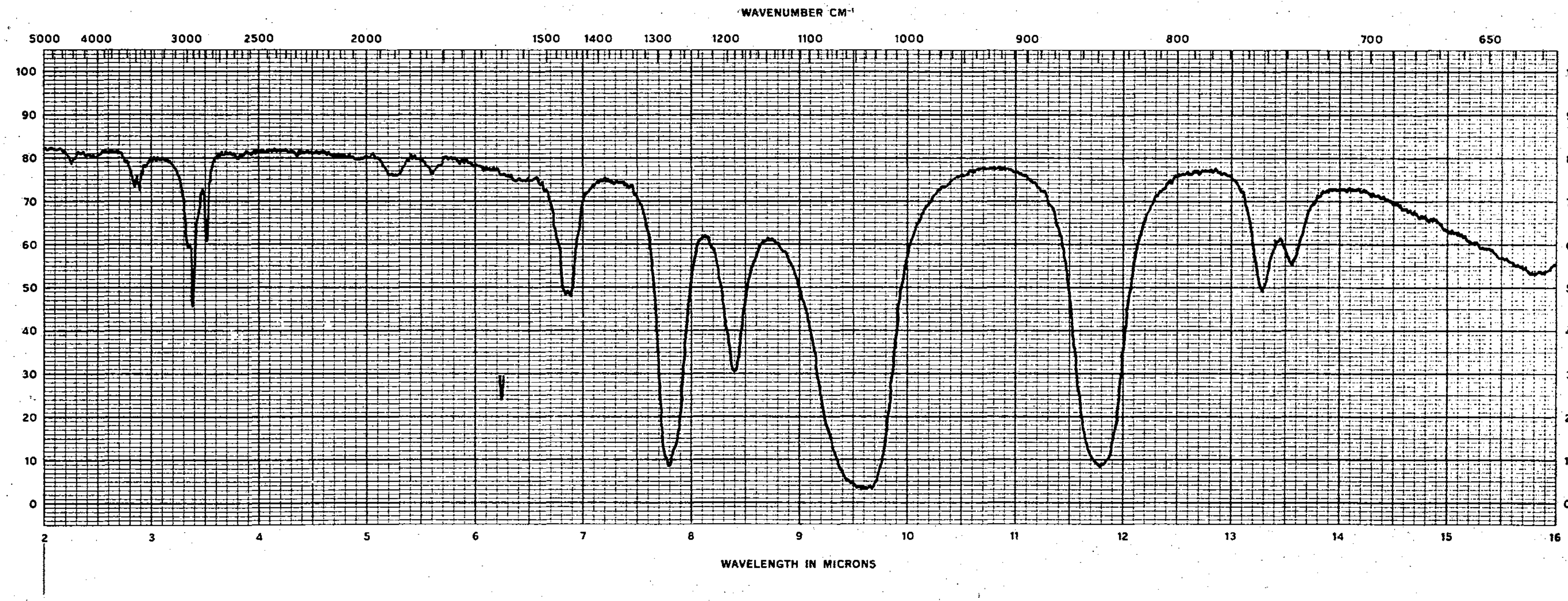
Separation of Dimethyl Phenylphosphonate (IIIa) and Biphenyl on Chromosorb W

Plate V



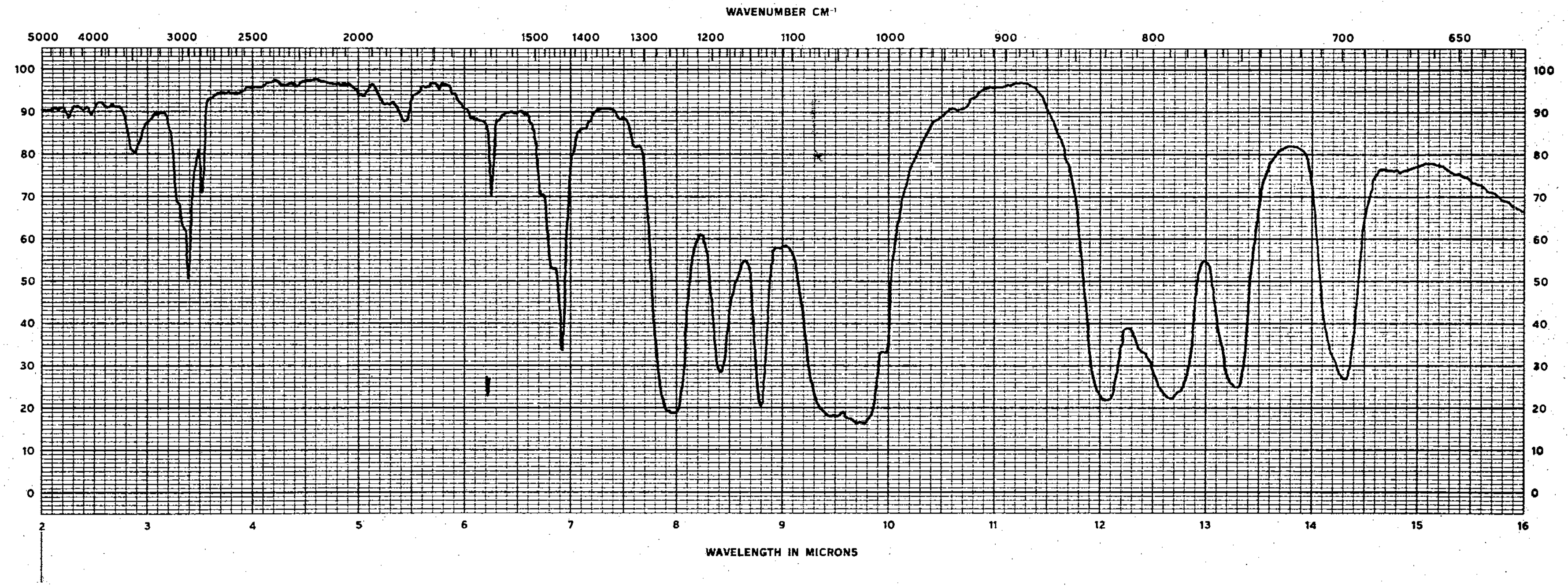
Trimethyl Phosphate IIa

Plate VI



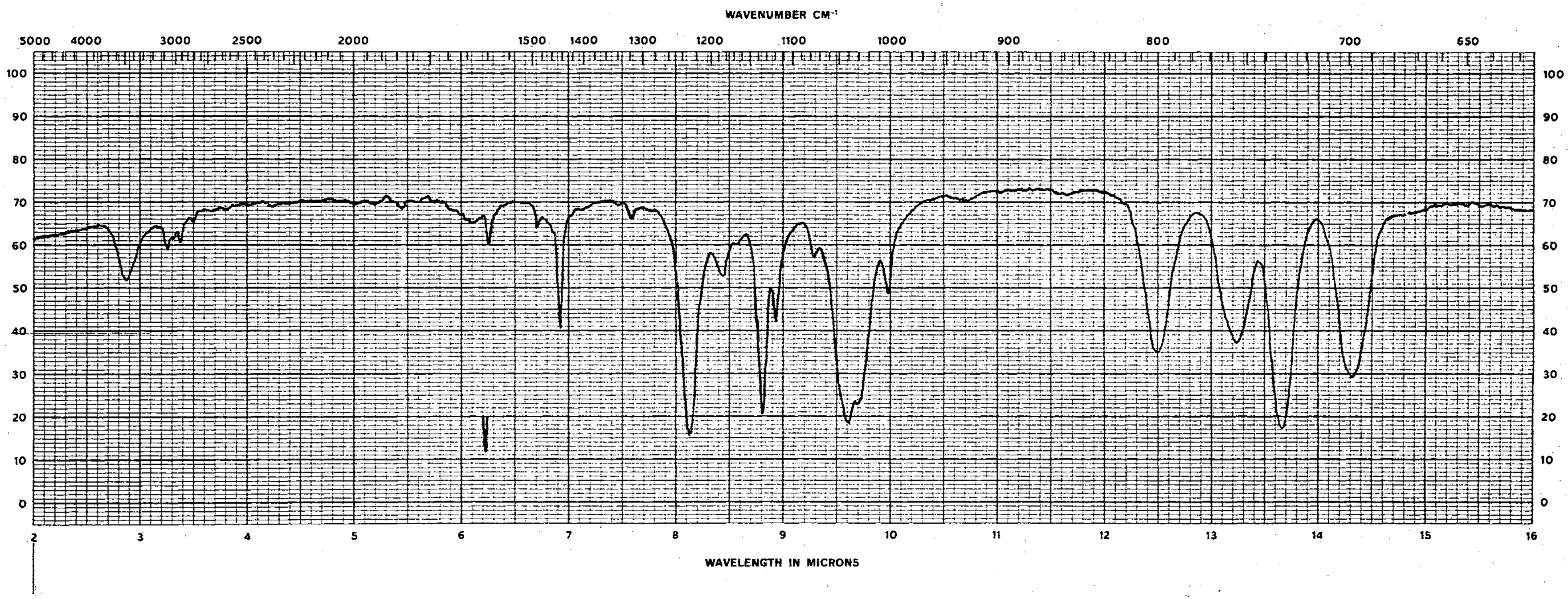
Trimethyl Phosphate (IIa), Film on NaCl Plates

Plate VII



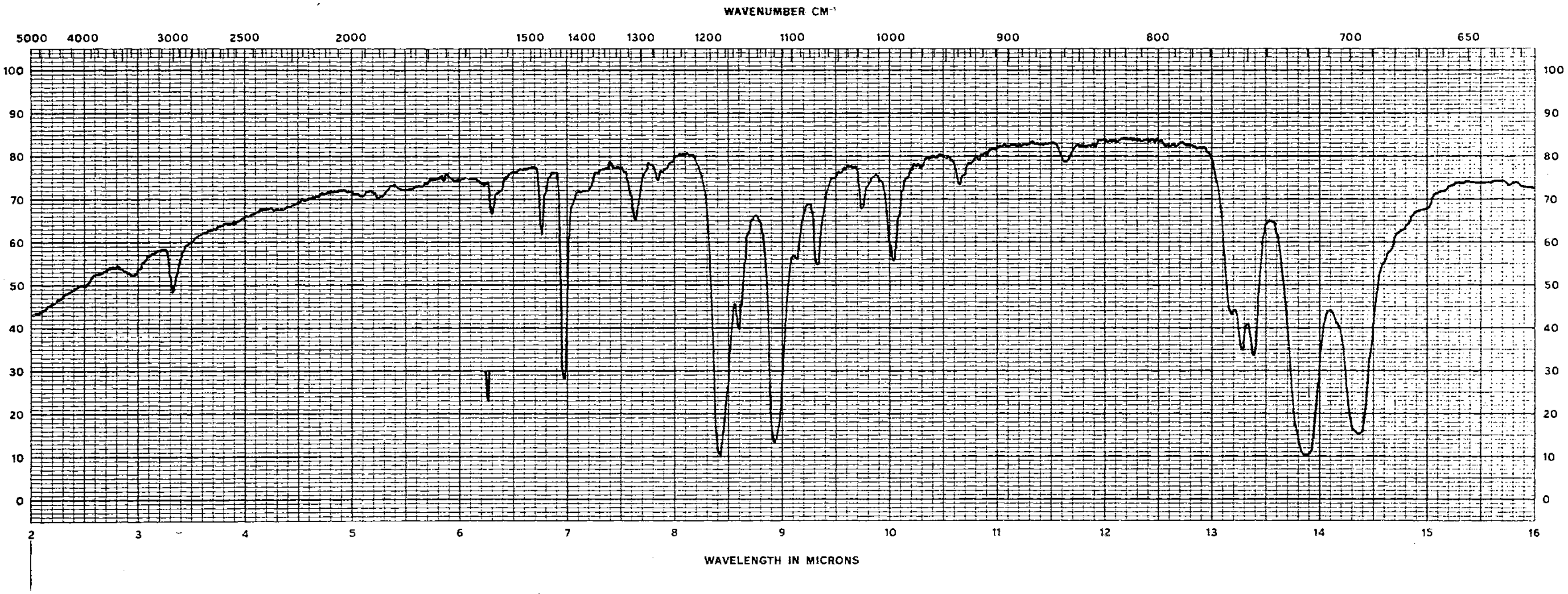
Dimethyl Phenylphosphonate (IIIa), Film on NaCl Plates

Plate VIII



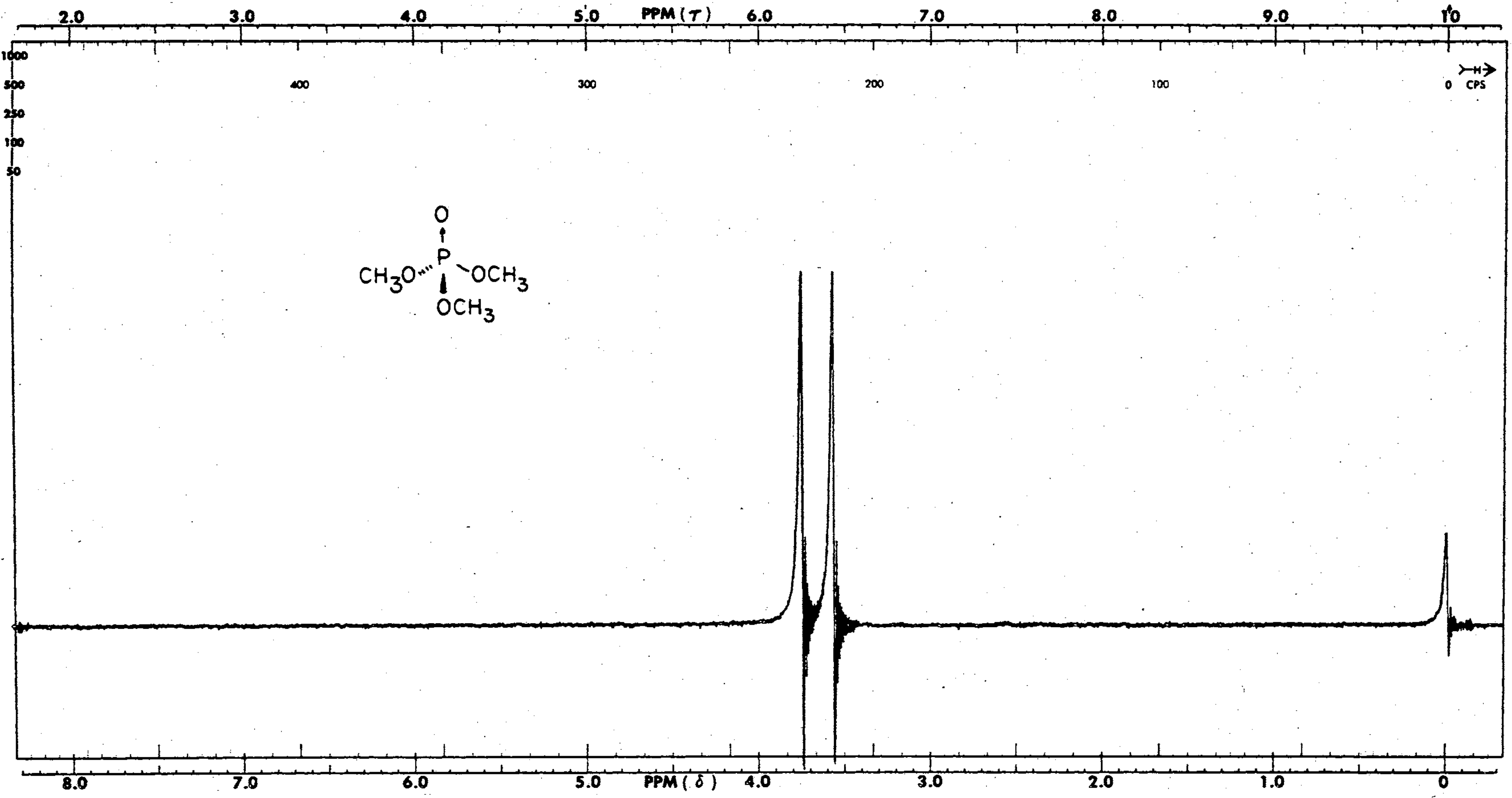
Methyl Diphenylphosphinate (IVa), KBr Pellet

Plate IX



Triphenylphosphine Oxide (V), KBr Pellet

Plate X

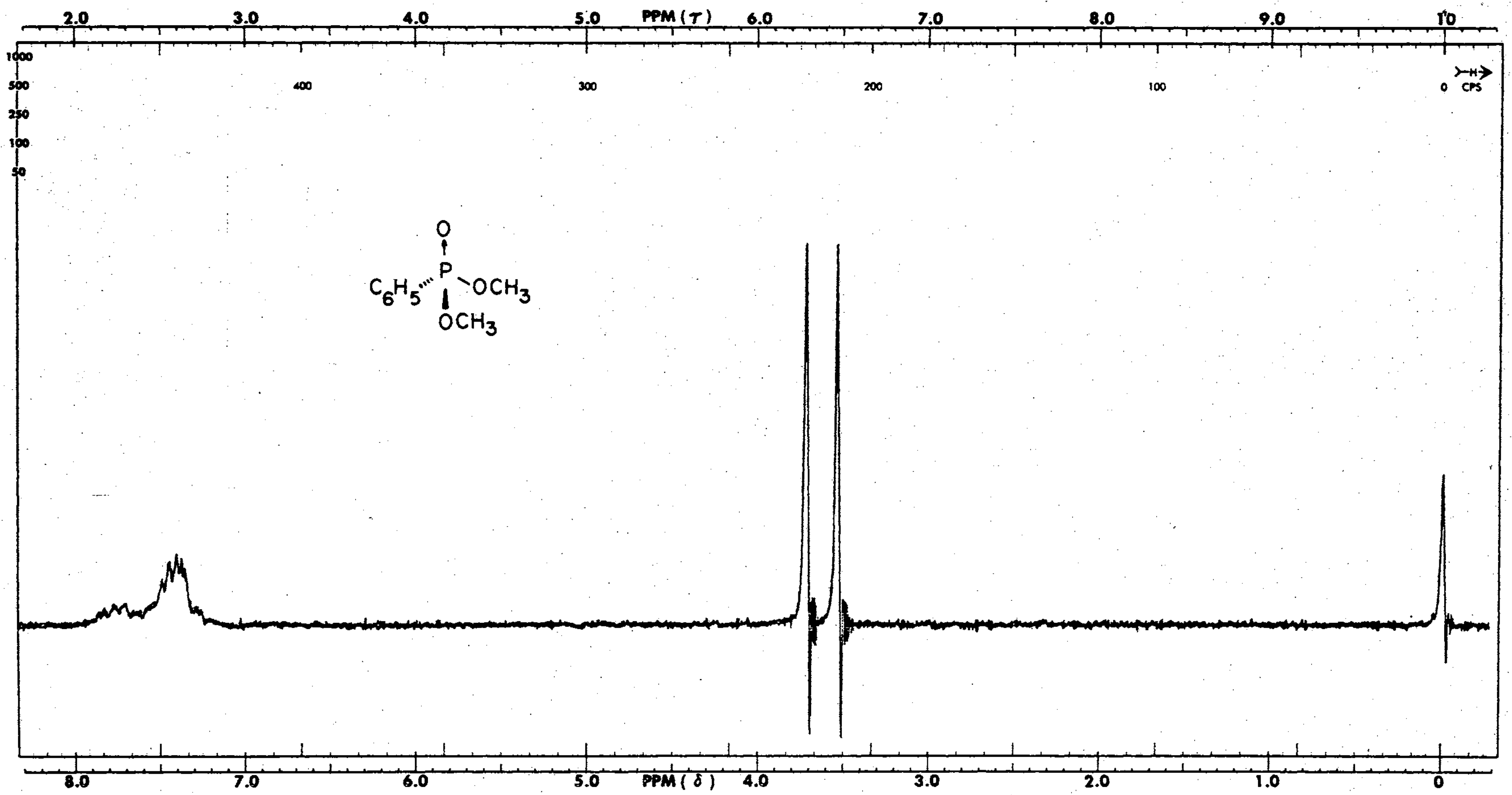


Trimethyl Phosphate (IIa)

Solvent . . . . . CCl_4 R.F. Field . . . . 0.04 mG S.W. . . . . 500 cps S.A. 1.6

F.B. . . . . . . .4.0 cps S.T. . . . . 250 sec S.O. . . . . 000 cps I.A. . . . . . . off

Plate XI

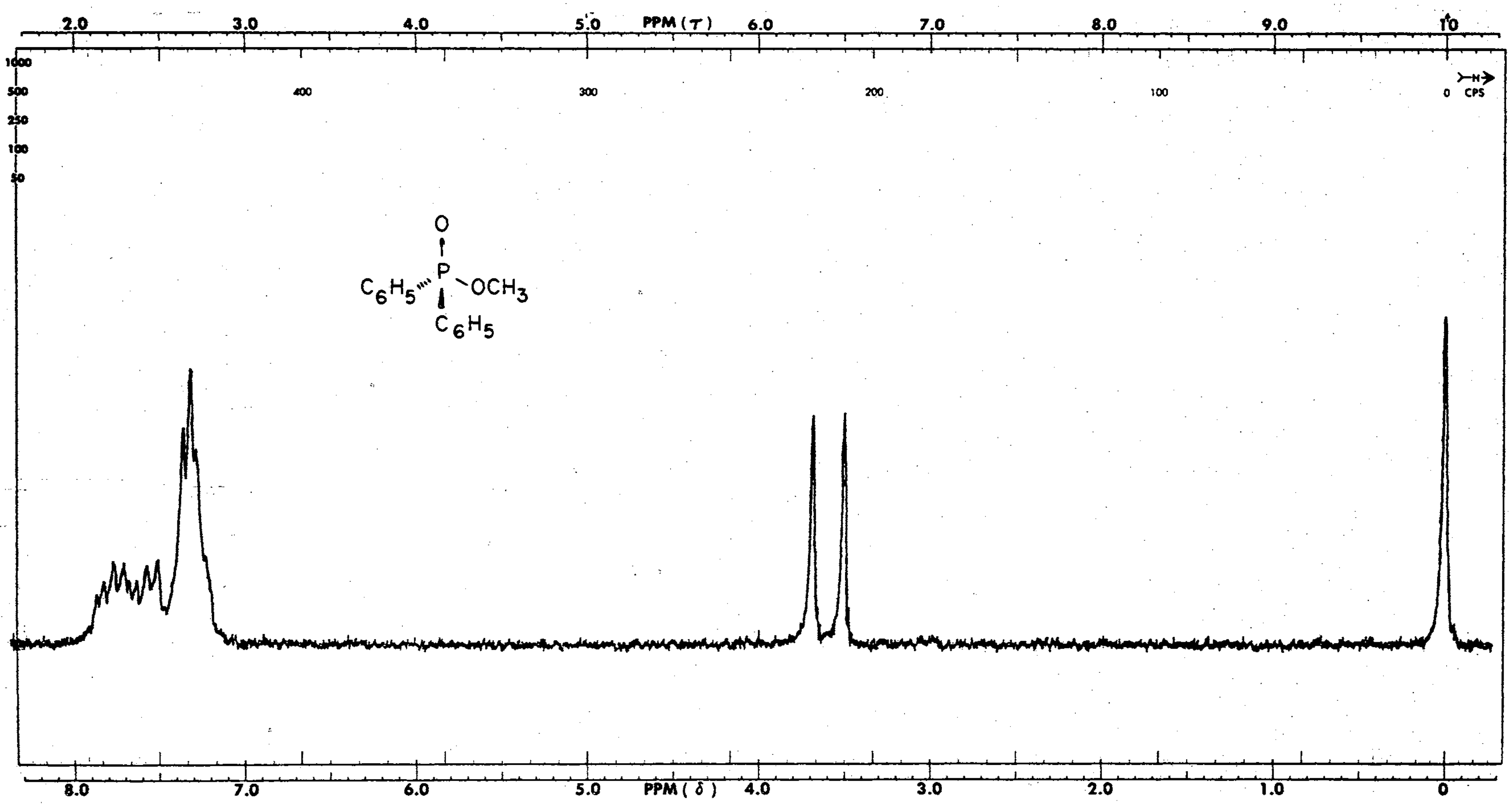


Dimethyl Phenylphosphonate (IIIa)

Solvent . . . . . CCl_4 R.F. Field . . . . 0.04 mG S.W. . . . . 500 cps S.A. 2.5

F.B.. . . . . . .4.0 cps S.T. . . . . 250 sec S.O. . . . . 000 cps I.A. . . . . . . off

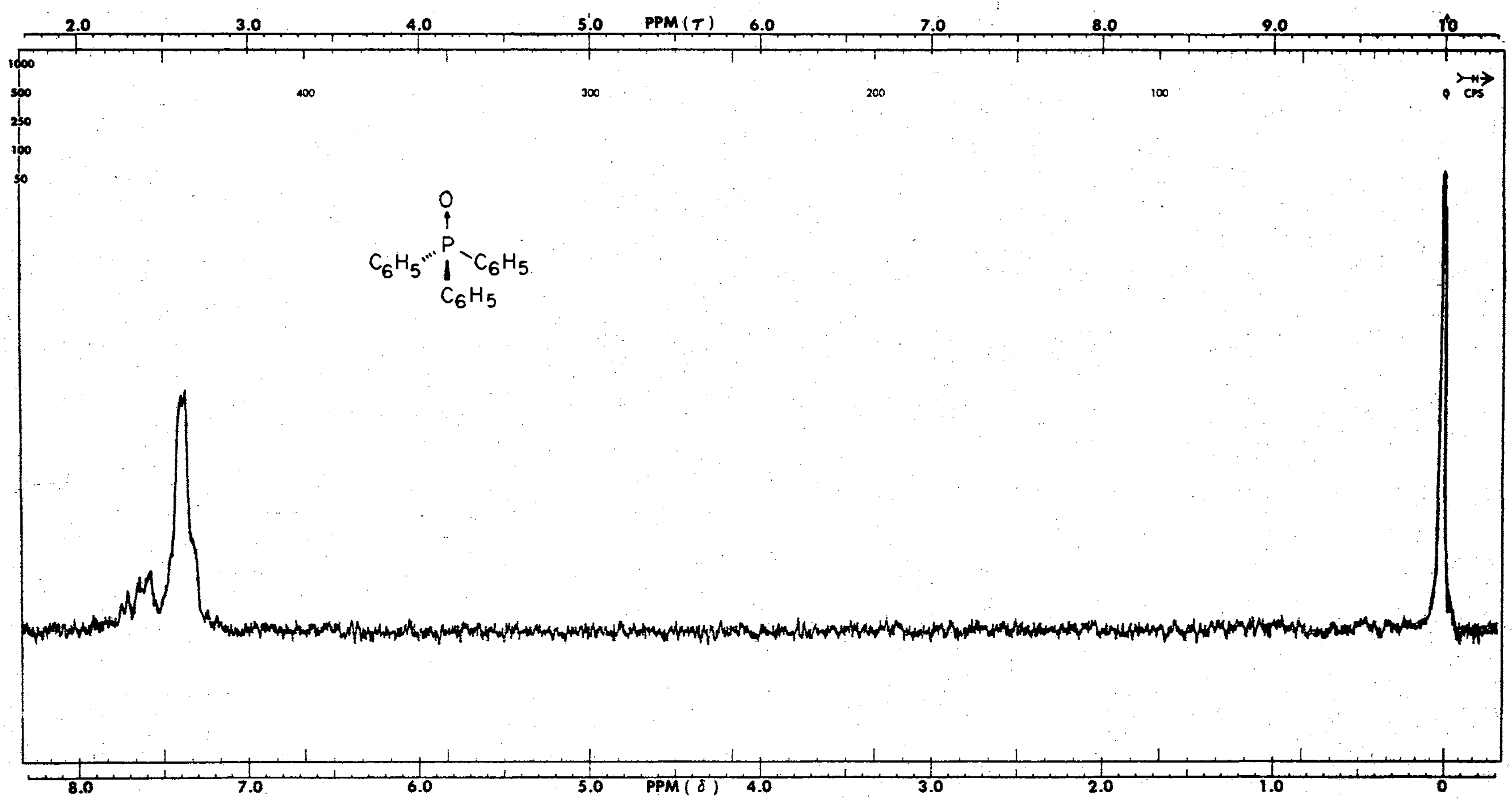
Plate XII



Methyl Diphenylphosphinate (IVa)

Solvent	CCl_4	R.F. Field	0.04 mG	S.W.	500 cps	S.A.	5.0
F.B..	2.0 cps	S.T.	250 sec	S.O.	000 cps	I.A.	off

Plate XIII



Triphenylphosphine Oxide

Solvent . . . . . CCl_4 R.F. Field . . . . 0.04 mG S.W. . . . . 500 cps S.A. 12.0

F.B.. . . . . . .1.0 cps S.T. . . . . 250 sec S.O. . . . . 000 cps I.A. . . . . . . off

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PART II

STEREOCHEMISTRY AND MECHANISMS OF PYROLYTIC ELIMINATIONS IN PHOSPHINATES

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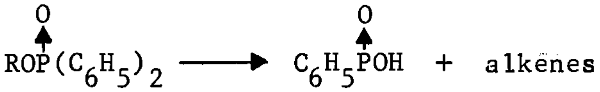
CHAPTER I

HISTORICAL

Although the observation that pyrolysis of carboylic acid esters leads to olefin formation was first made in 1854[33], only recently was a similar observation reported for esters of phosphorus-containing acids. The thermolytic decomposition of esters of diphenylphosphinic acid was found to be an excellent preparation of alkenes.[12] When alkyl diphenylphosphinates of the type Ic-g were heated to about 200 to 250° high



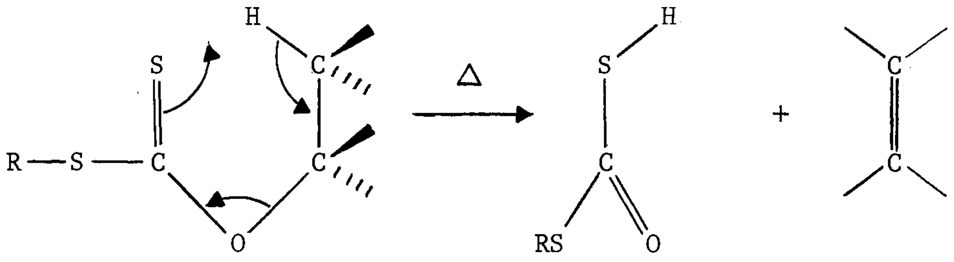
$$RO\overset{O}{\overset{\uparrow}{P}}(C_6H_5)_2 \longrightarrow C_6H_5\overset{O}{\overset{\uparrow}{P}}OH + \text{alkenes}$$

I

I a	R = *trans*-2-Methylcyclohexyl	
b	R = 1,2-Diphenylethyl	$C_6H_5CH_2\overset{\mid}{C}HC_6H_5$
c	R = Cyclohexyl	C_6H_{11}-
d	R = 2-Phenylethyl	$C_6H_5CH_2CH_2$-
e	R = 1-Octyl	*n*-C_8H_{17}-
f	R = 2-Octyl	*n*-$C_6H_{13}\overset{\mid}{C}H(CH_3)$
g	R = Cholesteryl	$C_{27}H_{45}$-
h	R = $C_6H_5CH_2CH_2CH_2$	$C_6H_5CH_2CH_2CH_2$-
i	R = Benzyl	$C_6H_5CH_2$-

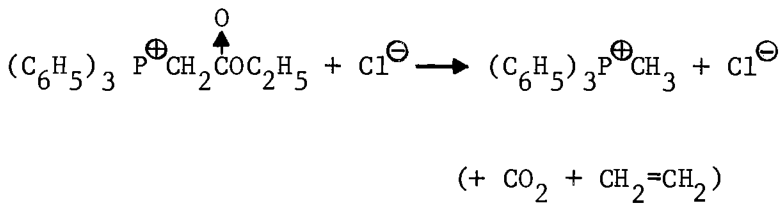
yields of alkenes were obtained with a minimum of rearrangement.

It has been postulated that the elimination mechanism is a cis-concerted process.[12] Thus, the reaction appears to be of the same type as the well known thermal decomposition of esters of carboxylic acids, xanthates and amine oxides. The reaction sequence involves removal of a cis-hydrogen beta to the multiple bond in a cyclic transition state.



The process, depicted for the pyrolysis of xanthate, is thought to be essentially the same for acetates and amine oxides.[25] These pyrolyses have been thoroughly reviewed[3,25] and only those reactions of carboxylic esters having a direct bearing on the work of this thesis will be described. An attempt will be made to review the work done on phosphorus compounds with emphasis on phosphorus esters.

Michaelis and Gimborn[40] apparently were the first to report the pyrolytic decomposition of an organophosphorus compound. When carbothoxymethyl triphenyl phosphonium chloride was heated to 100°, methyltriphenylphosphonium chloride was isolated. Though no identification

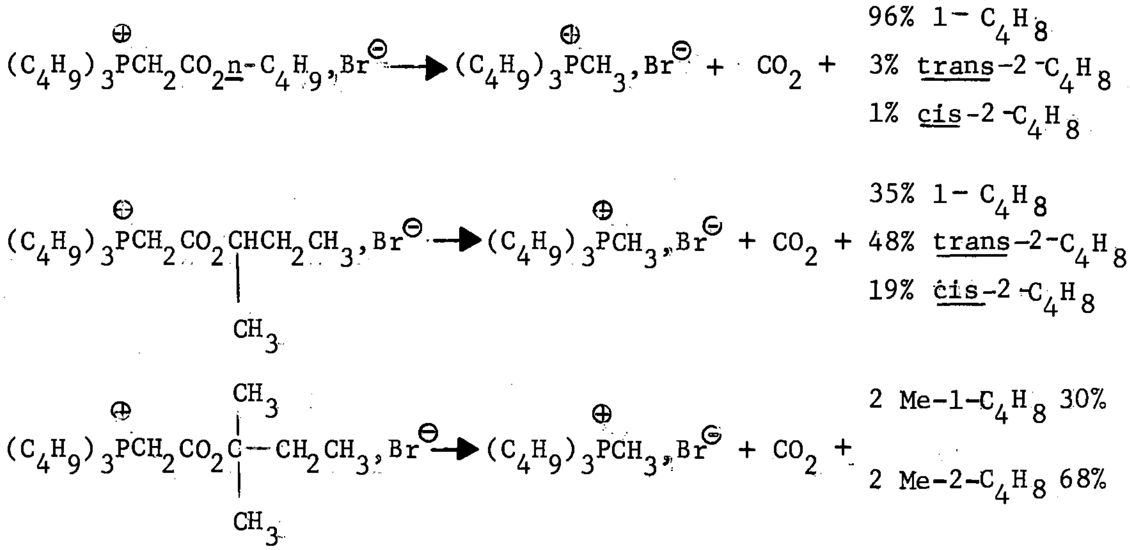


$$(C_6H_5)_3\,P^{\oplus}CH_2\overset{\overset{O}{\uparrow}}{C}OC_2H_5 + Cl^{\ominus} \longrightarrow (C_6H_5)_3P^{\oplus}CH_3 + Cl^{\ominus}$$

$$(+\ CO_2 + CH_2{=}CH_2)$$

was made, the authors speculated on the nature of the other products.

Confirmation for the existence of the olefinic products was obtained by Denney and co-workers.[23,24] Pyrolytic decomposition of several carbalkoxymethyl quaternary phosphonium salts was employed in the investigation. Carbon dioxide and an olefin were obtained in addition to the methylphosphonium salt. The olefin was found to correspond to the alcohol portion of the ester. The versatility of the reaction is illustrated by the following reactions.



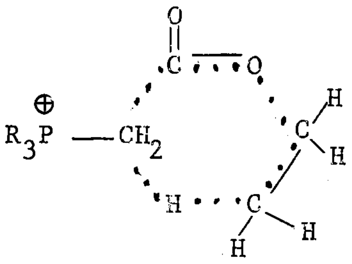
$$(C_4H_9)_3\overset{\oplus}{P}CH_2CO_2\underline{n}\text{-}C_4H_9,Br^{\ominus} \longrightarrow (C_4H_9)_3\overset{\oplus}{P}CH_3,Br^{\ominus} + CO_2 + \begin{array}{l}96\%\ 1\text{-}C_4H_8\\ 3\%\ \underline{trans}\text{-}2\text{-}C_4H_8\\ 1\%\ \underline{cis}\text{-}2\text{-}C_4H_8\end{array}$$

$$(C_4H_9)_3\overset{\ominus}{P}CH_2CO_2\underset{CH_3}{\underset{|}{C}}HCH_2CH_3,Br^{\ominus} \longrightarrow (C_4H_9)_3\overset{\oplus}{P}CH_3,Br^{\ominus} + CO_2 + \begin{array}{l}35\%\ 1\text{-}C_4H_8\\ 48\%\ \underline{trans}\text{-}2\text{-}C_4H_8\\ 19\%\ \underline{cis}\text{-}2\text{-}C_4H_8\end{array}$$

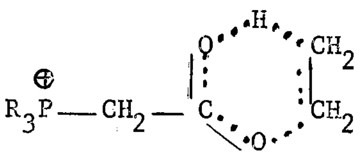
$$(C_4H_9)_3\overset{\oplus}{P}CH_2CO_2\overset{CH_3}{\underset{CH_3}{\overset{|}{\underset{|}{C}}}}-CH_2CH_3,Br^{\ominus} \longrightarrow (C_4H_9)_3\overset{\oplus}{P}CH_3,Br^{\ominus} + CO_2 + \begin{array}{l}2\ Me\text{-}1\text{-}C_4H_8\ 30\%\\ 2\ Me\text{-}2\text{-}C_4H_8\ 68\%\end{array}$$

Total yields of olefins were reported to be better than 70%.

The authors postulated the transition state II for the reaction.[24]

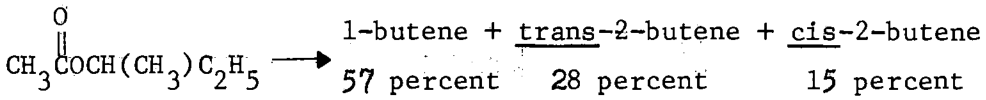


II



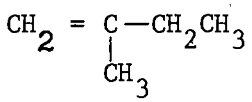
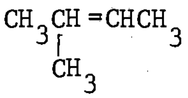
III

This of course differs from the usual transition state pictured for cis-elimination III in that hydrogen is transferred to carbon instead of to oxygen. If III were operative one might expect a close similarity in product distribution to that observed when the corresponding acetate is pyrolyzed. However the product distribution is seen to be

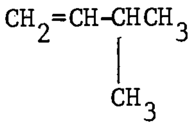


$$CH_3\overset{O}{\overset{\|}{C}}OCH(CH_3)C_2H_5 \longrightarrow \underset{57\text{ percent}}{\text{1-butene}} + \underset{28\text{ percent}}{\underline{\text{trans}}\text{-2-butene}} + \underset{15\text{ percent}}{\underline{\text{cis}}\text{-2-butene}}$$

significantly different.[29] One is tempted to discount III on this basis although temperature effects cannot be disregarded. Bailey and Hale[4] found a marked temperature dependence in the product ratio when they examined the pyrolysis of _t_-amyl acetate at temperatures from 225 to 600°. The change in ratio of 1- and 2-alkene as the temperature was

	Hofmann product	Saytzeff product
	 $CH_2=\underset{CH_3}{\underset{\mid}{C}}-CH_2CH_3$	 $CH_3\underset{CH_3}{\underset{\mid}{C}}H=CHCH_3$
225°	42	58
400°	70	30
600°	55	30[a]

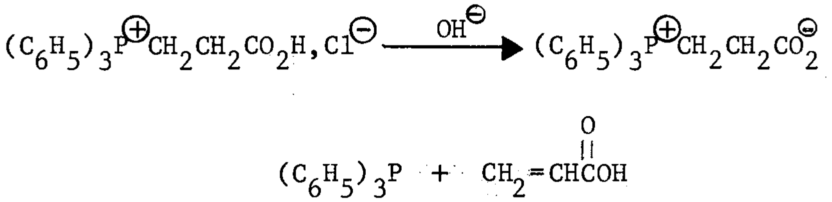
[a] Plus 15%



$CH_2=CH-\underset{CH_3}{\underset{\mid}{C}}HCH_3$

lowered was attributed either to increasing importance of alkene stability or to a change in mechanism from that involving the cyclic intermediate to another pathway.

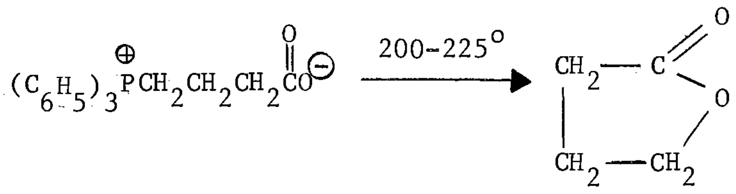
α,β-Unsaturated carboxylic acids have been obtained in a similar process from phosphobetaines.[24] When the betaine obtained by treating



$$(C_6H_5)_3\overset{\oplus}{P}CH_2CH_2CO_2H, Cl^{\ominus} \xrightarrow{OH^{\ominus}} (C_6H_5)_3\overset{\oplus}{P}CH_2CH_2CO_2^{\ominus}$$

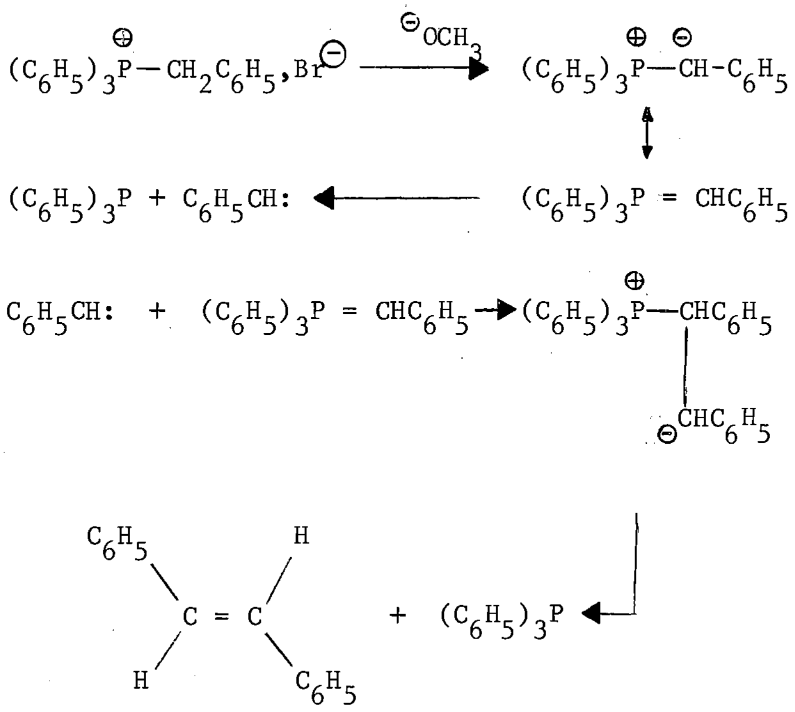
$$(C_6H_5)_3P + CH_2=CH\overset{O}{\overset{\|}{C}}OH$$

carboxypropyl triphenylphosphonium chloride with bases was heated,



γ-butylrolactone was formed.

That the carbonyl group in these phosphonium salts is not necessary for formation of the alkene is shown by the pyrolysis of benzyltriphenylphosphonium bromide in the presence of methoxide ion.[20] A

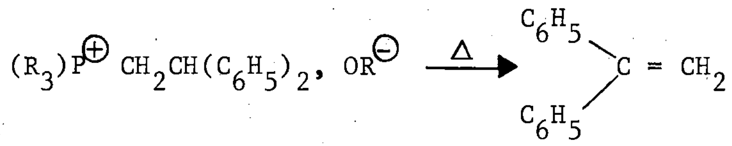


carbene intermediate was postulated.

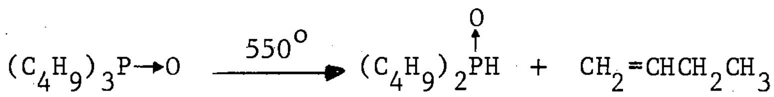
The thermal decomposition of quaternary ammonium hydroxides (Hofmann degradation) has long been used as a diagnostic tool in organic chemistry. The products, an alkene and tertiary amine, can give information about the parent compound. On the other hand the phosphorus analogue, the quaternary phosphonium hydroxides, yield alkenes and phosphine oxides.[25] For example, ethylene and triethylphosphine oxide were obtained from tetraethylphosphonium hydroxide.

$$(C_2H_5)_4P^{\oplus}\ OH^{\ominus} \longrightarrow (C_2H_5)_3P\rightarrow O + C_2H_4$$

When either trialkyl(2,2-diphenylethyl)phosphonium hydroxide or alkoxide was pyrolyzed, good yields (90 percent) of 1,1-diphenylethylene resulted.



Normally, the C-P bond is considered to be quite stable. However, Bailey and coworkers[5] have found that 1-butene is produced when tributylphosphine oxide is heated at 550°. Dibutylphosphine oxide, the



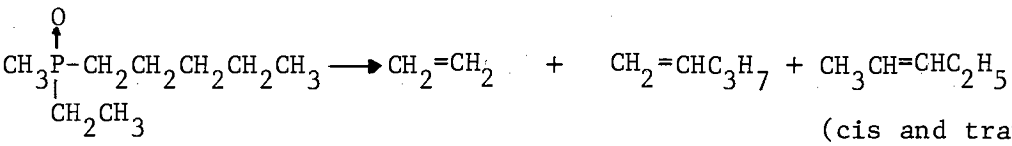
$$(C_4H_9)_3P\rightarrow O \xrightarrow{550^{\circ}} (C_4H_9)_2\overset{\overset{O}{\uparrow}}{P}H + CH_2{=}CHCH_2CH_3$$

other product, could have been formed by a tautomeric rearrangement of dibutylphosphinous acid. Existence of such an equilibrium has been

$$R_2POH \rightleftharpoons R_2\overset{\overset{O}{\uparrow}}{P}{-}H$$

established.[19,37]

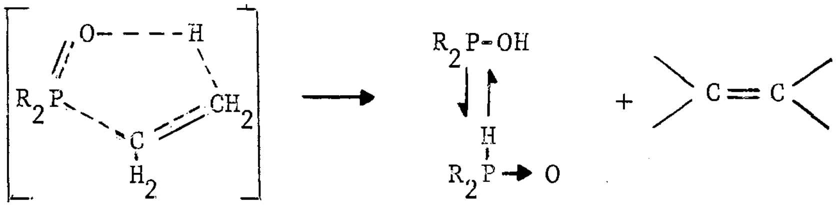
At 550° no alkene isomerization of tributylphosphine oxide was observed. At higher temperatures isomerization did occur.[26] In the pyrolysis of methylethylpentylphosphine oxide (410-565°) both olefin-yield and isomerization increased as higher temperatures were used.[7]



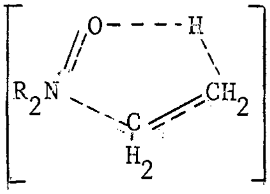
$$CH_3\underset{\underset{CH_2CH_3}{|}}{\overset{\overset{O}{\uparrow}}{P}}{-}CH_2CH_2CH_2CH_2CH_3 \longrightarrow CH_2{=}CH_2 + CH_2{=}CHC_3H_7 + CH_3CH{=}CHC_2H_5$$

(cis and trans)

The absence or near absence of isomerization in the products at lower temperatures makes a cyclic mechanism attractive. In cases where no α-hydrogens are present the oxides show unusual stability. Trimethylphosphine oxide and triphenylphosphine oxide are stable to 700°. Bailey and coworkers[5] have proposed a cyclic mechanism reminiscent of



IV



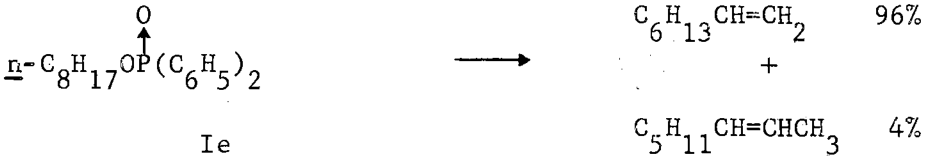
V

the one proposed for amine oxide pyrolysis.[25] The proposed transition states are shown (IV and V).

Berlin and Austin[12] have successfully pyrolyzed a series of alkyl diphenylphosphinate (I). Both primary and secondary alkyl groups were

Ic

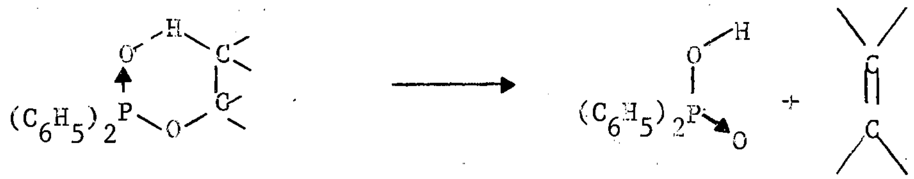
Id



$$\underline{n}\text{-}C_8H_{17}O\overset{O}{\overset{\uparrow}{P}}(C_6H_5)_2 \longrightarrow C_6H_{13}CH{=}CH_2 \quad 96\% \; + \; C_5H_{11}CH{=}CHCH_3 \quad 4\%$$

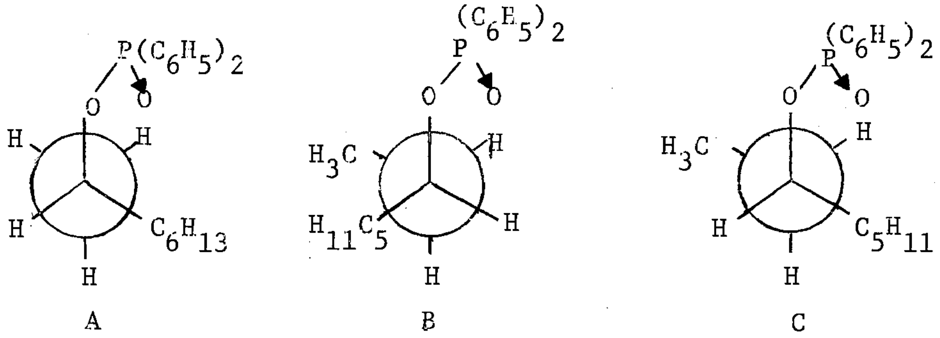
Ie

present in the examples. A concerted cis-elimination was postulated to account for the products and the ratios obtained.



That no polystyrene was obtained from the pyrolysis of Id was interpreted as eliminating a free-radical mechanism. Had a carbonium ion mechanism been operative one would not expect the high yield of 1-octene from the 1-octyl ester; similarly the 2-octyl ester would have certainly formed some of the 3- and 4-alkenes by isomerization. It is significant that no isomerization occurred when the 1- and 2-octenes were heated at the boiling point in the presence of diphenylphosphinic acid.

The alkene distribution obtained from the 2-octyl ester (If) was explained in part by examination of Newman projections of the transition states for each conformer.

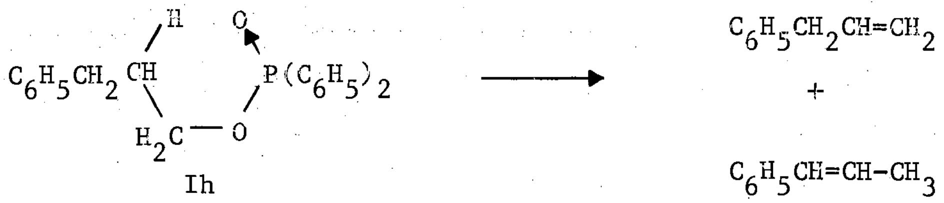


Yields 1-isomer Yields cis-isomer Yields trans-isomer

If

Possible gauche interactions in B may explain the predominance of the trans-isomer (C) over the cis (B). However, A would be expected to be the preferred conformation and thus lead to a high yield of the 1-octene. The reverse was observed; the ratio of internal olefin B and C to external olefin A was 4:1. The predominance of 2-alkenes is similar to that observed by Bailey[4] at low temperatures.

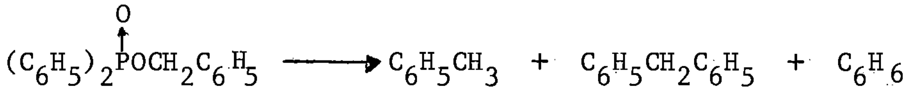
When 3-phenylpropenyl diphenylphosphinate (Ih) was pyrolyzed at 240-260°, allylbenzene (91%) was obtained as the chief product.[44]



Ih

Boiling allylbenzene (156°) did not induce isomerization of the alkene in the presence of diphenylphosphinic acid. Formation of the phenyl-2-propenes was attributed to either thermal isomerization at the higher pyrolysis temperature or to the operation of a second type of mechanism. However, no alternate mechanism was offered.

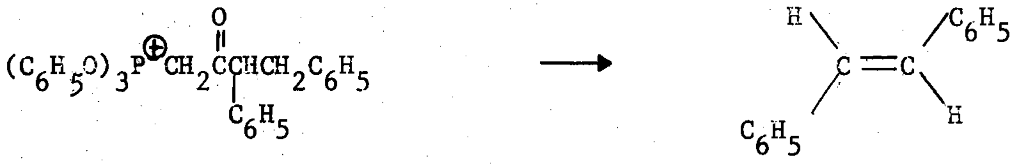
Benzyl diphenylphosphinate (Ii) gave evidence of a different mode of decomposition. Benzene, toluene and diphenylmethane were observed in the pyrolyzate. A free-radical mechanism was postulated to account for the products. It is to be noted that no beta-hydrogen is present in the alkyl group of the ester. Thus a different mechanism could well be operative in this case. No product yields were reported.



$$(C_6H_5)_2\overset{\overset{O}{\uparrow}}{P}OCH_2C_6H_5 \longrightarrow C_6H_5CH_3 + C_6H_5CH_2C_6H_5 + C_6H_6$$

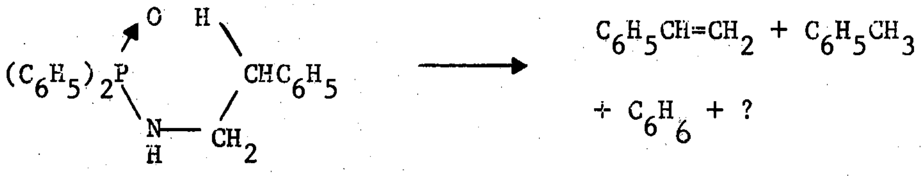
Ii

In a preliminary report Pivonka observed that Ia gave trans-stilbene on heating to 220°.[44] Tentatively cis-stilbene was also identified (GLC) but ratios were not determined. Interestingly enough, Denney[23] observed that the quaternary phosphonium salt of tributyl



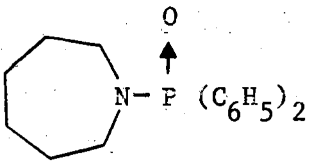
phosphine and 1,2-diphenylethyl bromoacetate gave trans-stilbene (90%).

Pivonka also examined the thermal decomposition of some related amides of diphenylphosphinic acid.[44] Pyrolysis of N-(2-phenylethyl) diphenylphosphinamide (VIa) was found to yield styrene, toluene and benzene plus an unidentified substance with a phosphine-like odor.



Pyrolysis of diphenylphosphinic acid itself proved to be a source of benzene.

Decomposition of N,N-hexamethylene-P,P-diphenylphosphinic amide (VII) led to benzene and an unidentified component.[44] Infrared analysis

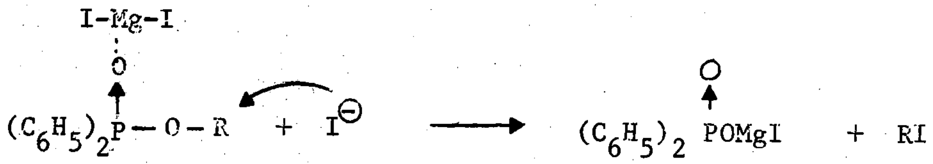


VII

failed to reveal the presence of an olefinic double bond. Surprisingly, both 1,5- and 2,4-hexadiene were found to be absent on the basis of mixed GLC injections.

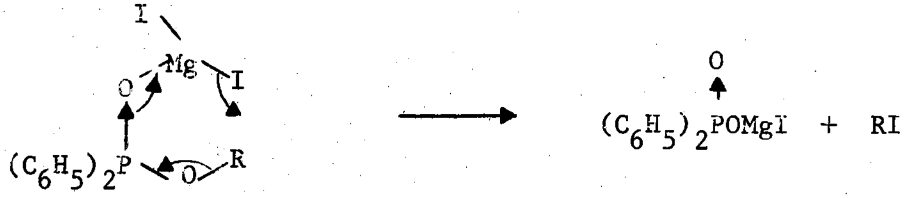
Certain magnesium iodide complexes of alkyl diphenylphosphinates I have been found to decompose when heated at about 5° above their respective melting points.[15] Alkyl iodides (no isomerization) were obtained in 80-85% yield. Both SN2(a) of SNi(b)

(a)



$(C_6H_5)_2\overset{\overset{\text{I-Mg-I}}{\vdots}}{\overset{O}{\uparrow}}{P}-O-R + I^{\ominus} \longrightarrow (C_6H_5)_2\overset{O}{\overset{\uparrow}{P}}OMgI + RI$

(b)

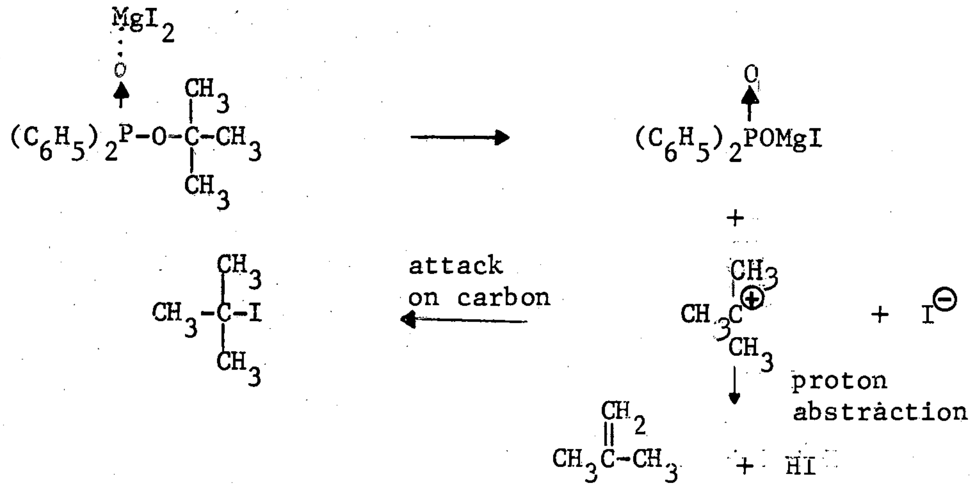


$(C_6H_5)_2\overset{O}{\overset{\uparrow}{P}}-O-R \cdots MgI_2 \longrightarrow (C_6H_5)_2\overset{O}{\overset{\uparrow}{P}}OMgI + RI$

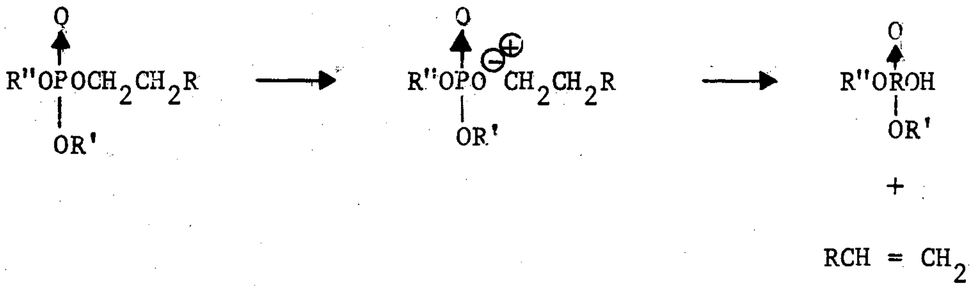
R = CH_3, n-C_3H_7, iso-C_3H_7, iso-C_4H_9 and neo C_5H_{11}

mechanisms were considered as possible pathways. Since a high yield of neopentyl iodide was obtained despite the difficulty of a backside approach, (b) was favored.

An unusual decomposition was observed when an attempt was made to form a complex of t-butyl diphenylphosphinate with magnesium iodide. Isobutylene and t-butyl iodide were obtained. The process was envisoned to involve formation of a tertiary carbonium ion with subsequent collapse to the olefin. Driving force for the reaction was attributed to relief of B-strain in the ester and stability of the carbonium ion.



Alkyl dimethyl phosphates, dialkyl methyl phosphates, and trialkyl phosphates have been pyrolyzed (350°) by Baumgarten and Setterquist.[10] Extensive bond migration was detected by IR analysis. Di-n-octyl methyl phosphate (350°) gave a mixture of alkenes (99 percent). That isomerization had taken place was shown by IR analysis. Both terminal and internal double bonds were indicated. No quantitative analysis of the mixture was obtained. The authors excluded the possibility of a

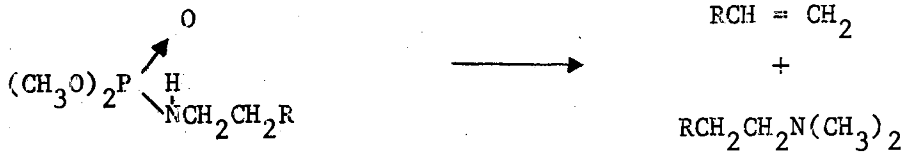


$R' = R'' = CH_3$ or RCH_2CH_2

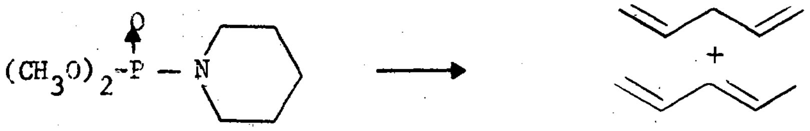
concerted cis-elimination because of the observed isomerization. An ionic mechanism is favored. There exists also the possibility that after a cis-elimination, the strong acids formed caused the observed rearrangement.

No alkene was obtained when N-aryl phosphoramidates were heated to 240-250°. Only the mono N-alkylanilines[30] or the di N,N-dialkylanilines were found.[18]

On the other hand when dimethyl N-alkylphosphoranidates were heated to 350-400° both the olefin and a tertiary amine would be detected.[9]

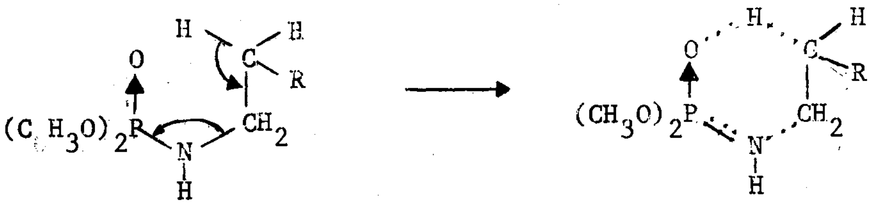


Yields of alkene ranged from 20 to 69 percent. It is of interest in relation to the work of Pivonka[44] that the pyrolysis of dimethyl piperidinophosphonate IX gave both 1,3- and 1,4-pentadiene. From the



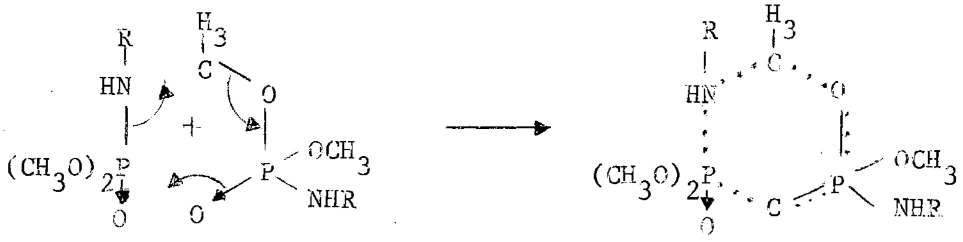
IX

dimethyl N-(*n*-octyl) compound, alkene (isomeric mixture) and amine were obtained in 31 and 33 percent, respectively. A cyclic transition state was offered to account for the formation of alkene. Strong acid in the



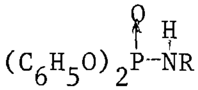
X

pyrolyzate would explain some rearrangement observed. The amine-alkylation process was competitive with alkene production and thus


X

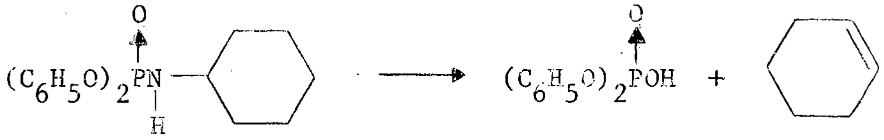
markedly lowered the yield of alkene. A bimolecular quasi six-membered cyclic transition state X was suggested as a possible pathway for the alkylation reaction.

In an effort to improve the yield of olefins from N-alkylphosphoramidates the related N-alkyl diphenyl phosphoramidates were prepared


$$(C_6H_5O)_2\overset{O}{\overset{\uparrow}{P}}-\overset{H}{N}R$$

XI

and pyrolyzed (350°-450°).[11] Since the methoxy group in the previous work was postulated to be involved in the competitive amine formation, the phenoxy group was introduced in order to minimize the side reaction. No tertiary amine was found to be present in the reaction mixtures. Though the yield of alkene was improved (60 to 95 percent) the alkenes still showed considerable rearrangement. Only the N-cyclohexyl compound

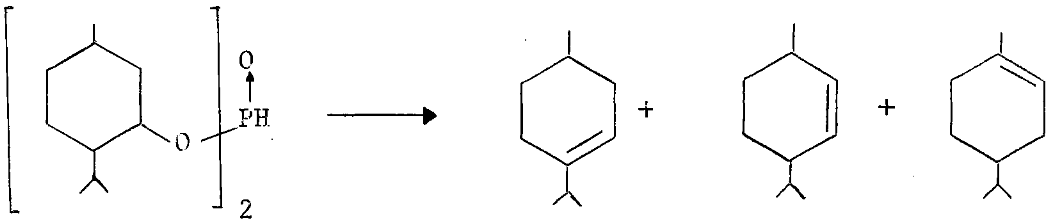


XII

XII was free of isomers.

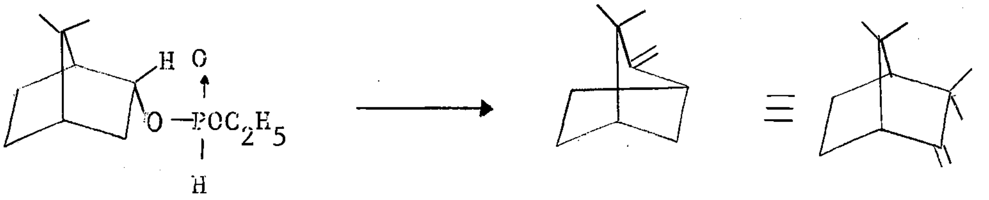
A series of phosphite esters of the type $(RO)_2POH$ have been pyrolyzed to form olefinic hydrocarbons. At 320° bornyl ethyl phosphite (XIII) was found to form a 78 percent yield of camphene (XIV).[27]

Dibornyl phosphite also gave predominantly camphene (XIV) with 6-10 percent of tricyclene (XVI) and traces of bornylene (XV). At 150° di(p-methyl) phosphite (XVII) gave a 90% yield of p-3-methene (XVIIIa). The 2-isomer XVIIIb and a trace of the 1-isomer XVIIIc were also found by



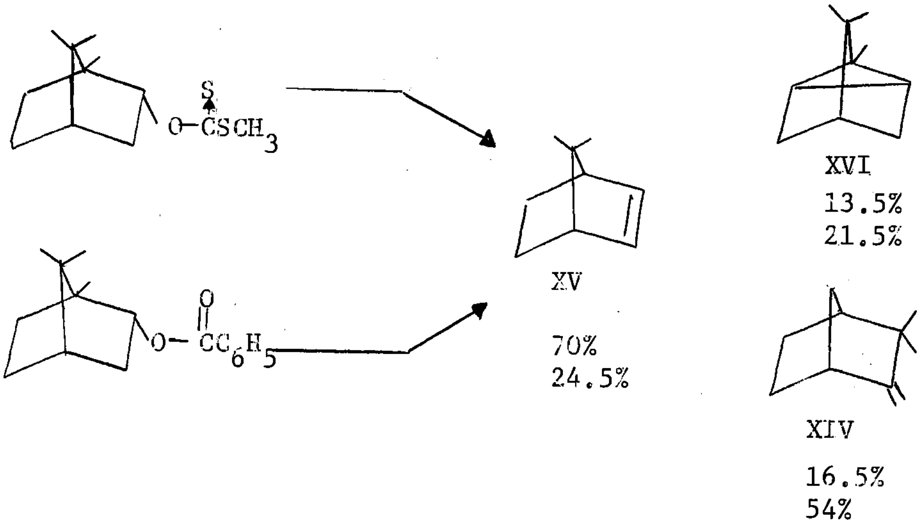
XVII XVIIIa XVIIIb XVIIIc

instrumental analysis.

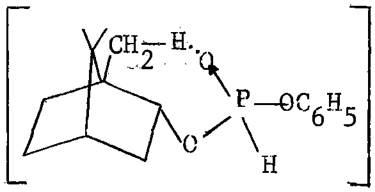


XIII XIV

That a carbonium ion mechanism may be operative here is indicated by examination of results obtained by Bunton and co-workers.[17] Pyrolysis of bornyl benzoate and bornyl methyl xanthate gave bornylene (XV), tricyclene (XVI) and camphene (XIV). Formation of bornylene was attributed to the cis-elimination. Camphene cannot be formed in the same manner.



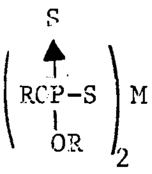
A seven-membered transition state (XIX) would be required.



XIX

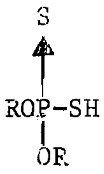
One would expect the benzoate to form carbonium ions more readily than the xanthate and indeed the benzoate gives greater yield of camphene. The implication is that camphene formation occurs through a carbonium-ion process. The same path would appear likely for the bornyl phosphites.

The formation of olefins has been reported when metal O,O-dialkylphosphorodithoates XX were pyrolyzed. Hanneman and Porter[32] had examined the olefins obtained from O,O-diisoamyldithiophosphoric acid (XXI). S-bornyl diisoamyldithiophosphate (XXII) and zinc O,O-diisoamyldithiophosphate (XXa).



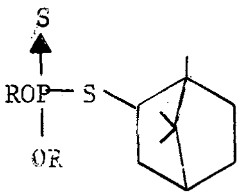
$\left(RO\overset{S}{\overset{\uparrow}{\underset{OR}{P}}}-S\right)_2M$

XX



$RO\overset{S}{\overset{\uparrow}{\underset{OR}{P}}}-SH$

XXI



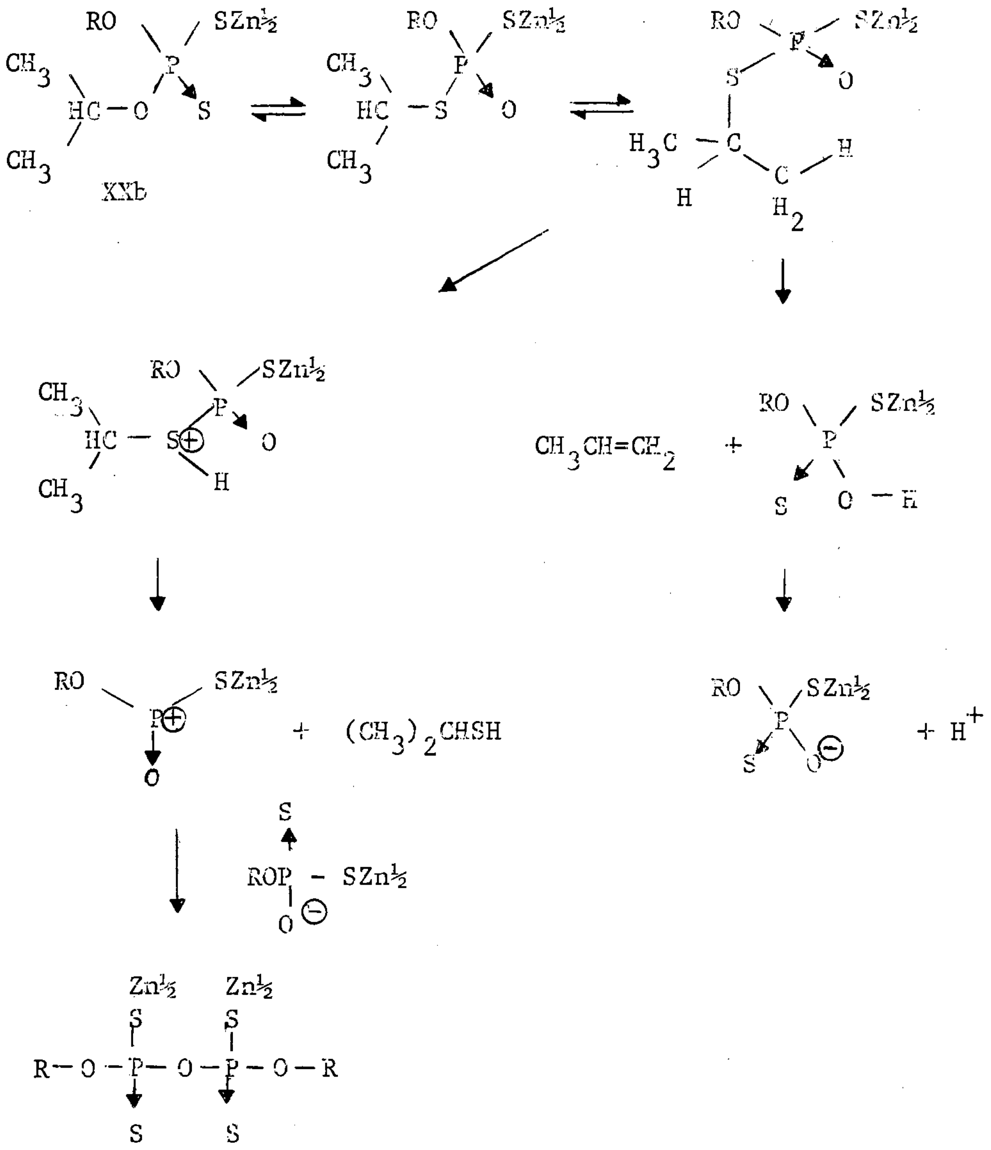
XVII

XXa, R = $CH_3CH_2CH(CH_3)_2$ M = Zn

XXb, R = $(CH_3)_2CH$ M = Zn

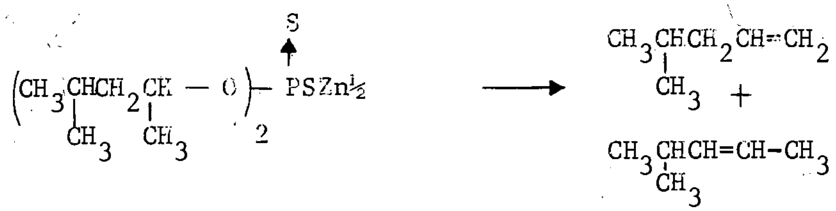
XXc, R = $(CH_3)_2CHCH_2CH_2$ M = Zn

In every case examined the product ratio approached that predicted by assuming a carbonium-ion mechanism. Other studies on XX led to the conclusion that the reaction went by radical mechanism,[39] or that after partial isomerization of XX, decomposition both by free-radical and carbonium-ion pathways occurred.[2] In a very detailed investigation, Dickert and Rowe determined that the rate of thermal decomposition of compounds of type XX (155°) increased with the number of hydrogens on the α-carbon atoms of the alkyl group and with decreasing size of the bivalent metal atom.[26] A mechanism involving an isomerization followed by an intramolecular cis-elimination was proposed to account for the results. The mechanism is pictured for the diisopropyl ester (Scheme 1). The isomerization noted previously[2] was attributed to acid-catalyzed isomerization at elevated temperatures. Further conformation for the cis-elimination was noted in the work of Perry.[43] Zinc O,O-di-(4-methyl-2-pentyl)phosphorodithioate (XXc) gave 96 percent of the cis-elimination products 4-methyl-1-pentene and 4-methyl-2-pentene and



Scheme I

only 4% of the rearrangement products 2-methyl-1-pentene and 2-methyl-2-pentene.

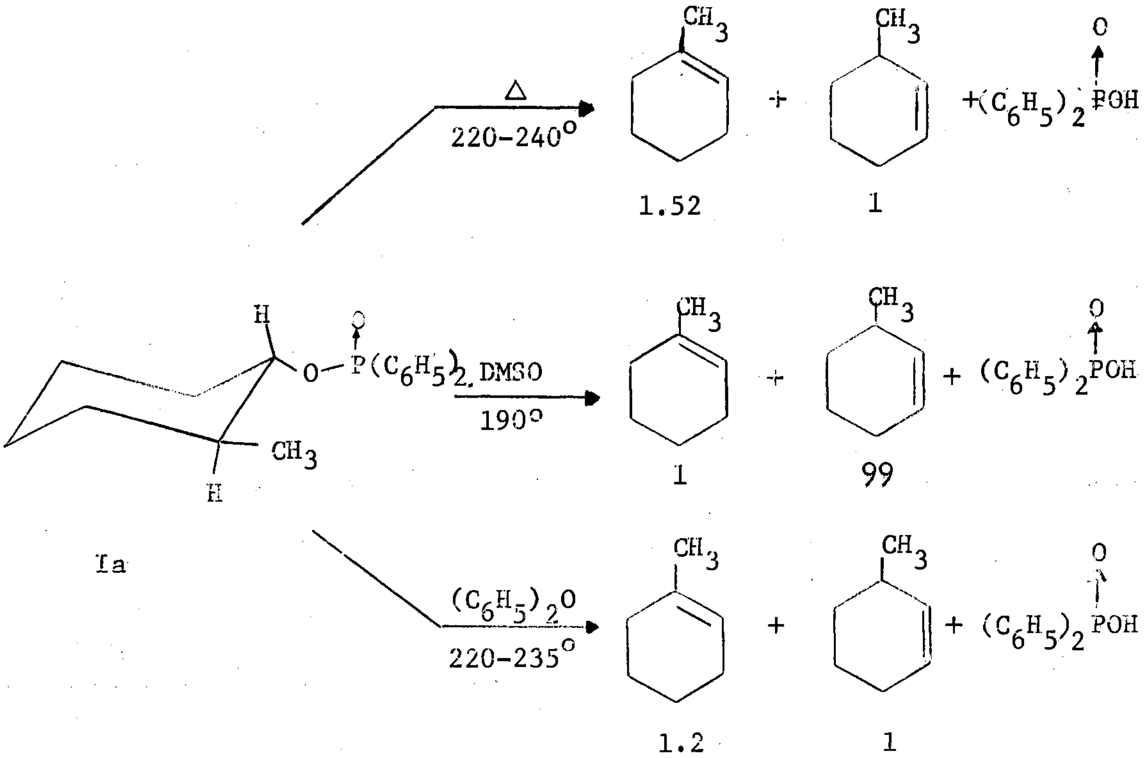


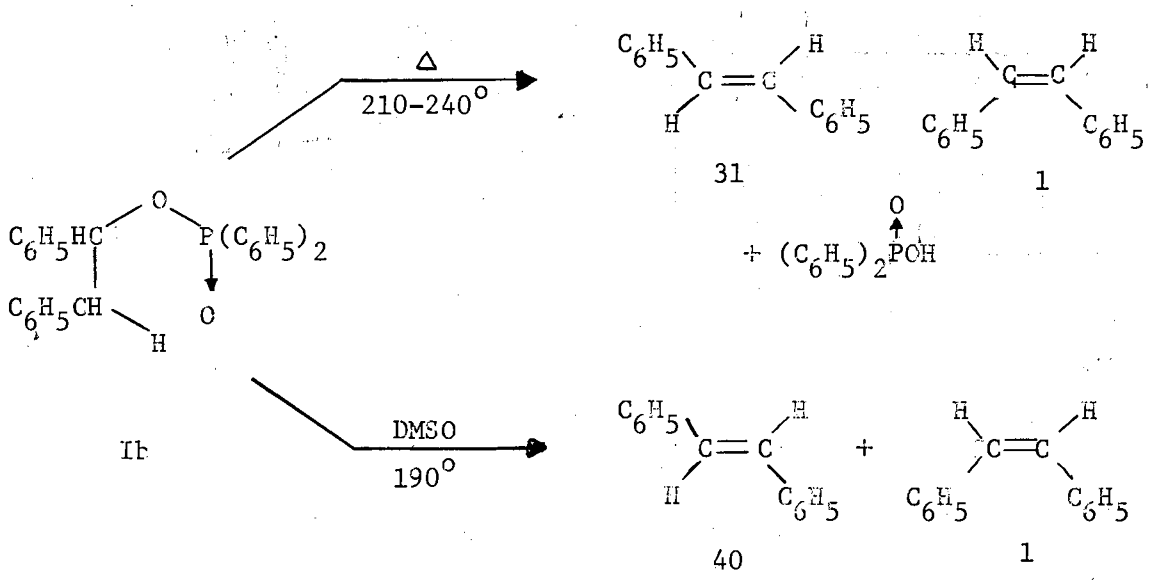
Until recently no work had been done on the pyrolysis of the phosphorus analogues of carboxylic esters. Preliminary data has now appeared[12] which indicates that a concerted cis-elimination may be operative.

CHAPTER II

DISCUSSION OF RESULTS AND CONCLUSIONS

It has been found that trans-2-methylcyclohexyl diphenylphosphinate (Ia) decomposes at 220-240° to give 1-methylcyclohexene and 3-methylcyclohexene in a 1.52:1 ratio. In dimethylsulfoxide (DMSO) a drastic change in the ratio (1:99) was observed while in diphenyl ether the ratio of alkenes was 1.22:1, similar to that found in the static pyrolyses. With 1,2-diphenylethyl diphenylphosphinate (Ib) cis-stilbene and trans-stilbene were detected in the pyrolyzate by GLC analysis. A

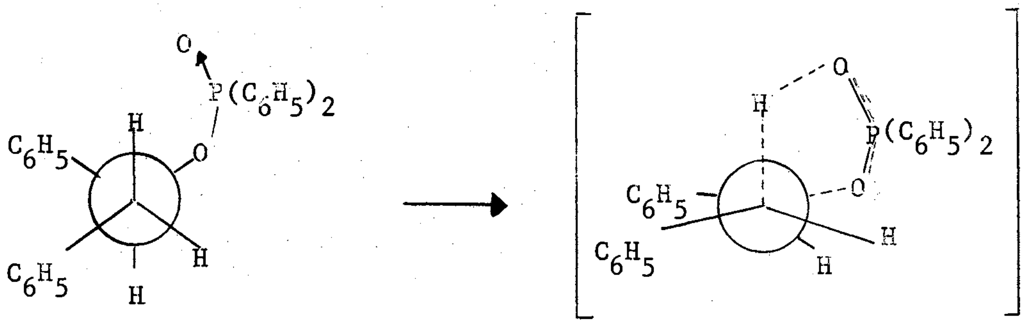




predominance of trans-stilbene over cis-stilbene (36:1) was observed from the static pyrolysis or the decomposition in DMSO. With Ia or Ib, diphenylphosphinic acid was found in quantitative yield in each pyrolysis.

A mixture of 3-methylcyclohexene and diphenylphosphonic acid was heated at 110° for 60 minutes without isomerization of the alkene. No change in composition of the mixture was observed when 1- and 3-methylcyclohexene (1:1.2 mole ratio) were heated with diphenylphosphinic acid in diphenyl ether for 3.5 hours at 100-110°. The anomalous results from the pyrolysis of Ia in DMSO do not support a carbonium ion mechanism as 1-methylcyclohexene would be the expected product rather than 3-methylcyclohexene. In regard to the stereochemistry of the process, a concerted mechanism for the pyrolysis of Ia with a near statistical ratio (1:1) of the alkenes seems reasonably well favored from the results of the static decomposition as well as the experiment performed in diphenyl ether. The possibility exists that DMSO participates in the decomposition of Ia, although when 1-methylcyclohexene and diphenylphosphinic acid (1:1) were heated in DMSO (170-180°) for 1.5 hours, no isomerization was detected.

With Ib the high yield of *trans*-stilbene might be expected on consideration of steric factors in the transition state XXII leading to *cis*-stilbene. However, in DMSO pure *cis*-stilbene rearranged at about

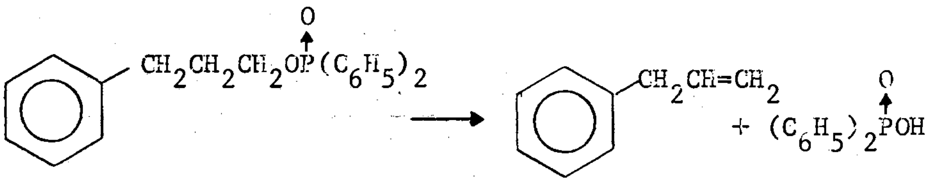


Ib

transition state

XXII

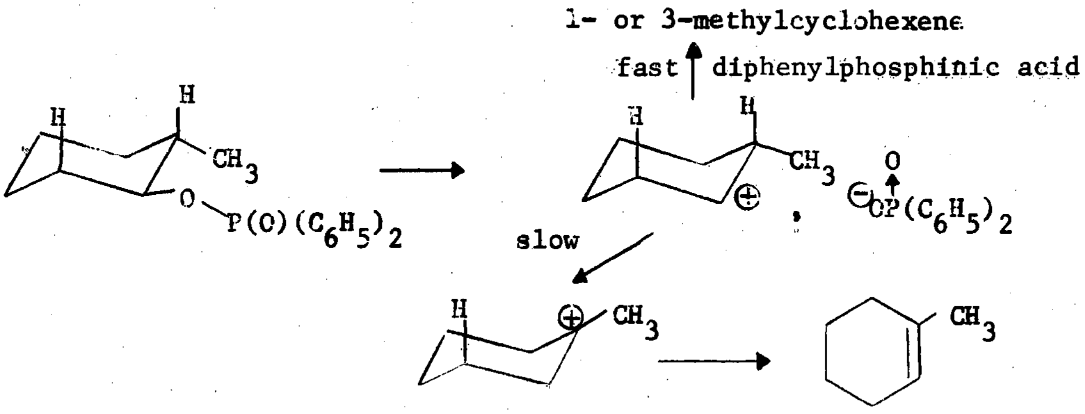
220° in 48 minutes to give a *cis*-stilbene:*trans*-stilbene ratio of approximately 1:1. Consequently, some *cis*-stilbene could have formed from pyrolysis of Ib but would be isomerized to the trans-alkene under the reaction conditions. If a cation is formed by heterolytic C-O bond cleavage, the cation could undergo a structural rearrangement to place the adjacent phenyl groups at maximum distance apart. From the results of both Ia and Ib and from the observation of Dr. Pivonka



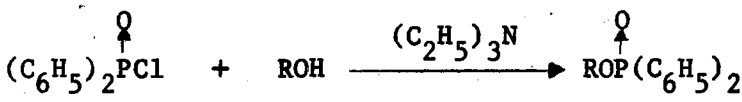
Ih

91%

in this laboratory[44] with Ih (less than 9 percent of 1-phenyl-2-propene was produced), it is tentatively concluded that a concerted mechanism is operative or if ion pairs are formed, proton abstraction by the anion of diphenylphosphinic acid is faster than an elimination process or hydride migration to give a tertiary carbonium ion.



The esters used in the study were prepared by modifications of known methods.[12,13,44] The condensation of the appropriate alcohol and diphenylphosphinic chloride was effected in the presence of triethyl amine.

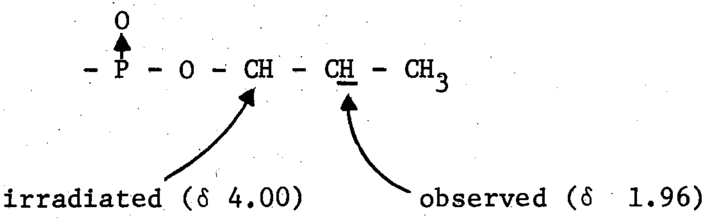


$$(C_6H_5)_2\overset{O}{\uparrow}{P}Cl + ROH \xrightarrow{(C_2H_5)_3N} RO\overset{O}{\uparrow}{P}(C_6H_5)_2$$

I

The identity of the esters was confirmed by elemental analysis and by instrumental methods. IR analysis (Plates I and II) indicated the phosphoryl adsorption at 8.1-8.2 μ and the P-phenyl absorption at 10.0-10.1 μ to be good agreement with that reported for similar esters.[12]

NMR spectra revealed several interesting features. In Ia (Plate VI) the tertiary H-C-O ring proton was evident as a broad weak multiplet at δ 4.00. In addition to the two adjacent cis-hydrogen atoms and the single trans-hydrogen atom, the proton was split by ^{1}H - ^{31}P coupling. Because of the complexity of the signal pattern it was not possible to determine coupling constants. A broad multiplet centered at δ 1.96 was, on the basis of decoupling work, tentatively assigned to the



$$-\overset{O}{\overset{\uparrow}{P}}-O-CH-C\underline{H}-CH_3$$

irradiated (δ 4.00) observed (δ 1.96)

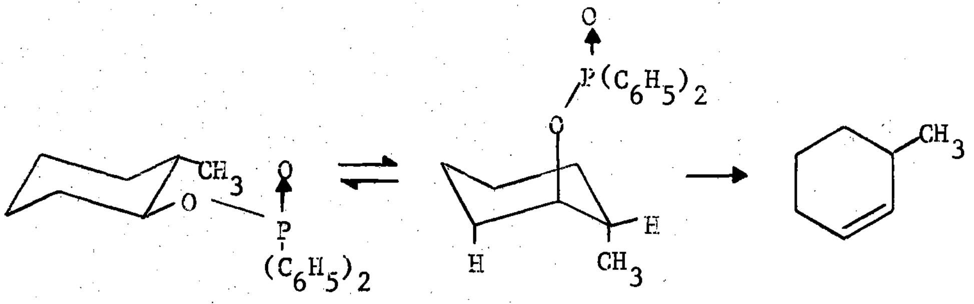
$-C\underline{H}-CH_3$ protons. Again the complex pattern was not resolvable so that any vicinal coupling constants could be obtained accurately. The methyl group appeared as a doublet centered at δ 0.93. The remaining ring protons appeared at δ 0.78-1.90 in a typical cycloalkene pattern. Aromatic protons were evident as a multiplet at δ 7.28 to 8.08.

In Ib (Plate VII) the aliphatic protons appeared as a multiplet at δ 3.15 ($-C\underline{H}_2-$) and a multiplet at δ 5.45 ($-C\underline{H}-O$). The methine proton displayed the characteristic splitting by ^{31}P in addition to the expected splitting by the adjacent methylene protons. A broad multiplet at δ 7.20-8.25 was assigned to the aromatic protons.

All pyrolyses were performed in a nitrogen atmosphere on pure Ia or Ib or on solutions of the esters in DMSO or diphenyl ether. Product analysis was determined by GLC. Though pyrolysis appeared to be complete in 20 to 30 minutes heating was continued in all cases for an sdditional 15 minutes to insure complete decomposition. Results of the pyrolyses are recorded in Table III.

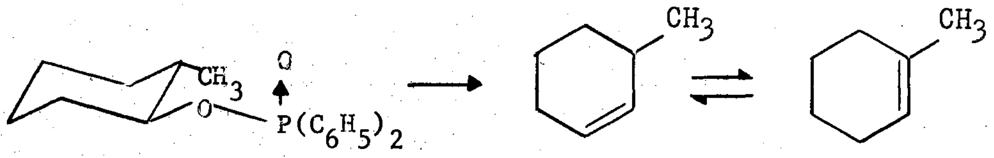
Examination of the results obtained from the static pyrolysis of

Ia reveal some interesting facts. Had an E_2 mechanism been operative one would expect only 3-methylcyclohexene (if only conformer Ia' underwent the elimination) instead of the observed 1- to 3-isomer ratio



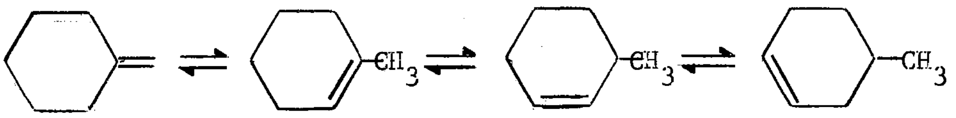
Ia Ia'

of 1.2:1. The possibility does exist that after formation of the 3-isomer, an isomerization to the 1-isomer (possibly acid catalyzed)



could occur. That such an equilibration exists is unlikely, however. All attempts to isomerize 1- and/or 3-methylcyclohexene under simulated reaction conditions were unsuccessful. Support for the absence of isomerization is found in the work of Cope and coworkers.[20] 1-Methylcyclohexene and methylenecyclohexene (XXIII) were equilibrated in the presence of p-toluenesulfonic acid in acetic acid. Only the exo- and endo-isomers were obtained ($k_{endo}/k_{exo} = 240$); no other methylcyclohexenes were detected. The implication is that under the mildly acidic conditions employed in the pyrolysis, no conversion of the 1- to the 3-isomer occurrs.

When stronger acid conditions were employed (methylenecyclohexane and 1-methylcyclohexene heated over activated alumina at 250°) the indicated equilibrium mixture was obtained:[16]



1.8 62.9 16.5 18.8

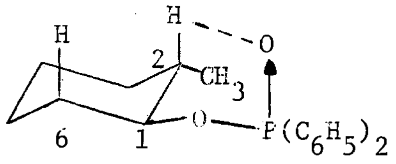
XXIII XXIV

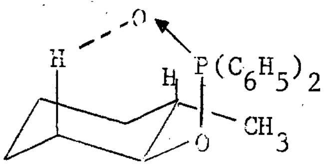
In no case with Ia was methylenecyclohexane (XXIII) or 4-methylcyclohexene detected. Had an equilibrium been established one would anticipate finding these isomers in addition to 1- and 3-methylcyclohexene.

The absence of isomerization with diphenylphosphinic acid has been reported previously. Attempts to isomerize 1-octene or cis-octene by heating to reflux (112-113°) in the presence of diphenylphosphinic acid were unsuccessful.[12]

In this laboratory it has been observed that another terminal alkene, allylbenzene did not isomerize at reflux (112-113°) in the presence of diphenylphosphinic acid.[44] The presence of a small amount (less than 9 percent) of _cis_- and _trans_-1-phenyl-2-propene in the pyrolyzate of 3-phenylpropyl diphenylphosphinate (Ih) was attributed either to thermal isomerization or to a duality of mechanisms in the elimination reaction.

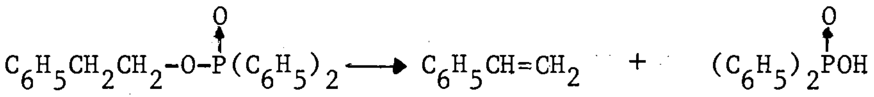
The nearly statistical ratio of 1-methylcyclohexene and 3-methylcyclohexene from the static pyrolysis of Ia suggests a cis-concerted elimination. Both the cis-1- and cis-3-protons are readily accessible to the phosphoryl oxygen in a cyclic transition state. The slight predominance of the 1-isomer over the 3-isomer is difficult to explain.





However, examination of Dreiding models of Ia reveals that, when the P→O group is oriented toward the C-2 hydrogen, the two phenyl groups are at a maximum distance from the methyl group. In the transition state for formation of 3-methylcyclohexene the phenyl groups appear to project closer to the methyl group. This steric factor, if operative, is undoubtedly small in magnitude. A similar effect was offered to explain an observed asymmetric inductive effort in the pyrolysis of optically active 4-methylcyclohexylatropates.[31]

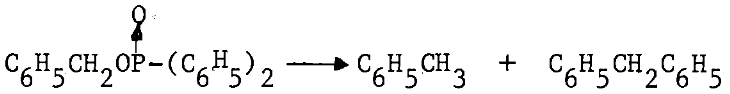
Botteron and Shulman[16] have investigated the pyrolysis of the *cis*- and *trans*-2-methylcyclohexyl methylxanthates. Essentially the same ratio of 1-:3-methylcyclohexene (56:44 percent) was obtained from the trans-isomer as was found with Ia. The increase of the 1-:3-ratio (to 67:33 percent) on addition of benzoyl peroxide to the *trans*-xanthate was suggested to imply the intervention of a free radical mechanism. However, the operation of a free radical mechanism in the pyrolysis of Ia and other phosphinates has been eliminated on the basis of several experiments. For example, when Ia was pyrolyzed in diphenyl ether in the presence of added hydroquinone, a known radical scavanger, no change in the 1-:3-methylcyclohexene ratio was observed (Table III). It had been reported that in the pyrolysis of 2-phenylethyl diphenylphosphinate (Id) no polymerization of styrene was observed.[12] In the



$$C_6H_5CH_2CH_2\text{-O-}\overset{O}{\overset{\uparrow}{P}}(C_6H_5)_2 \longrightarrow C_6H_5CH=CH_2 \quad + \quad (C_6H_5)_2\overset{O}{\overset{\uparrow}{P}}OH$$

Id

example, benzyl diphenylphosphinate (Ii) identification of toluene and



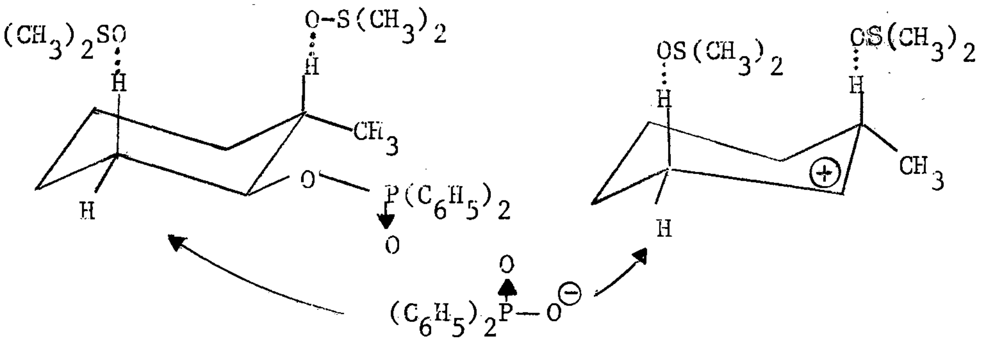
$$C_6H_5CH_2O\overset{O}{\overset{\uparrow}{P}}\text{-}(C_6H_5)_2 \longrightarrow C_6H_5CH_3 \quad + \quad C_6H_5CH_2C_6H_5$$

Ii

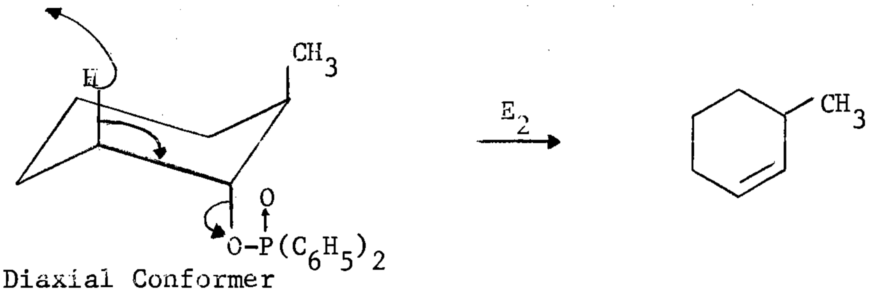
diphenylmethane in the pyrolyzate may result from a free radical process.[44] With this ester, however, no β-hydrogen atom is available for the cis-elimination mechanism.

The pyrolysis of Ia performed in DMSO presents certain interesting features. The low overall yields obtained (45 percent) may be attributed to the lower temperature maintained during the pyrolysis. The high proportion of 3-methylcyclohexene is difficult to explain. Solvent participation in the transition state may be a factor, although the exact nature of such involvement is difficult to visualize.

Solvation may be of such nature as to cause preferential orientation of the phosphoryl group toward the 3-proton.



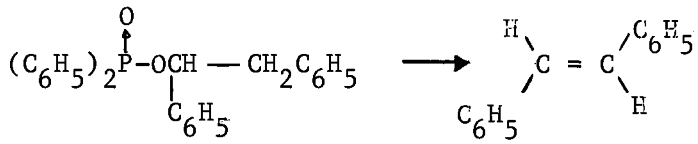
In the strongly polar DMSO ionization could well be an important process. Approach of the solvent molecules from the methyl side of the ester on the carbonium ion may be hindered by the projecting methyl group. Consequently approach of the diphenylphosphinate anion would be from the underside. Such attack would lead exclusively to the 3-alkene. On the other hand if the elimination were proceeding by an ionic pathway, the more stable 1-isomer would be the expected major product. If the ester were in the diaxial conformation, the 3-alkene



Diaxial Conformer

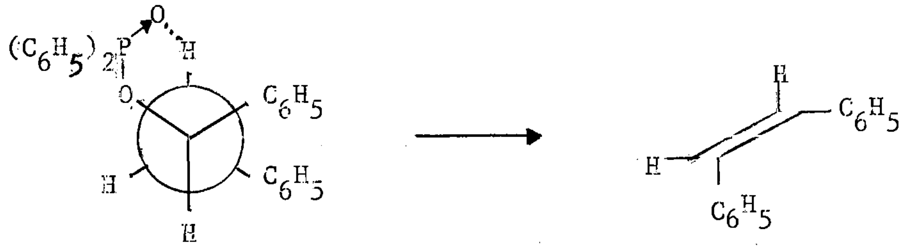
could be readily explained by an E_2 elimination.[12] However, the conformation with both substituents in the equatorial rather than axial would be the preferred one for Ia.

Pyrolysis of Ib resulted in almost complete conversion to <u>trans</u>-stilbene. The percentage of trans-isomer was greater than 97 percent both in a static pyrolysis (220-240°) and in DMSO (190°). Examination

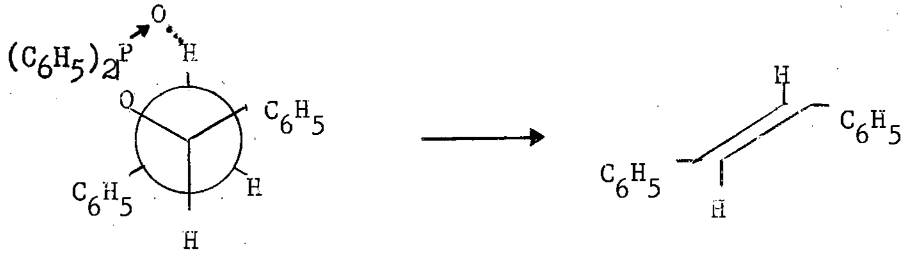

$$(C_6H_5)_2\overset{O}{\overset{\uparrow}{P}}\text{-}O\underset{C_6H_5}{\underset{|}{C}}H - CH_2C_6H_5 \longrightarrow$$

Ib 97%

of Newman projection formulas reveals that steric interactions are at a minimum in conformation (B) thus favoring formation of the trans-isomer. In the transition state (A) gauche interactions between the



A

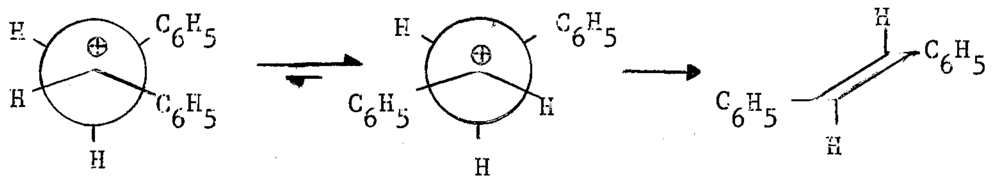


B

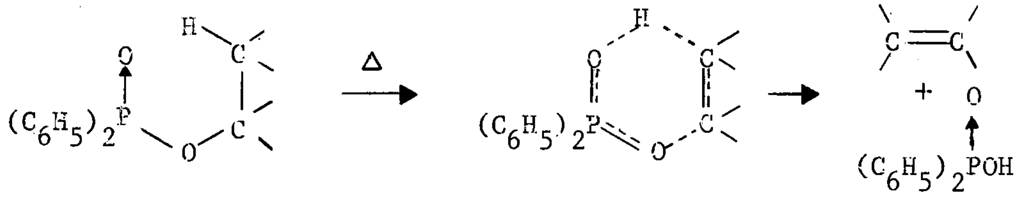
groups would be expected to reduce the stability of the transition state.

Both thermal and acid catalyzed isomerization of cis- to trans-stilbene were found to occur. Heating cis-stilbene (neat) for 40 minutes resulted in a 75:25 ratio of cis- to trans-isomer. When an equivalent amount of diphenylphosphinic acid was added to cis-stilbene under the same conditions, a mixture of the alkenes (55 percent cis-45 percent trans-isomer) was obtained. Assuming such an isomerization in the pyrolysis of Ib, a maximum of 6 to 7 percent of the cis-isomer would have been formed in the reaction. In view of the work reported by Nace,[10] an E_1 elimination must be considered as a possibility.

DMSO was found to be effective in promoting the decomposition of sulfonate esters by an ionic pathway. However, similar results would be expected from Ib by an E_1 or a concerted elimination; that is a predominance of trans-stilbene. It is not possible on the basis of



available evidence to distinguish between the two paths in DMSO. An ionic mechanism would be more feasible in a highly polar solvent such as DMSO. On the basis of evidence presented here and in previous work,[12,44] the results of pyrolytic decomposition of alkyl diphenylphosphinates are best explained by a concerted cis-elimination in much the same fashion as the carboxylic ester and xanthate pyrolyses.[25]



Pyrolysis of <u>cis</u>-2-methylcyclohexyl diphenylphosphinate and either bornyl or isobornyl diphenylphosphinate would be useful in the determination of the stereochemistry of the reaction as well as contributing to knowledge of the overall mechanism.

The decomposition of phosphinates shows promise of being a very useful synthetic reaction. Starting esters are now readily available.[12,13] The products are formed at comparatively low temperatures and are readily isolated.

CHAPTER III

EXPERIMENTAL[a-e]

Reagents. The following chemicals were obtained from commercial sources: From Aldrich Chemical Co. cis-stilbene b.p. 82-84°/0.4 mm., n_D^{20} 1.6215 [lit.[8] 110-110.5/1.2 mm, n_D^{20} 1.6130]; trans-stilbene (scintillation grade) m.p. 122-123.5° [lit.[45] 124°. 5-124.8]; and, 3-methyl-cyclohexene, b.p. 100.5-102°, n_D^{20} 1.4422 [lit.[6] 100-101°, n_D^{25} 1.4424 . From Chemical Samples Co. trans-2-methylcyclohexanol, IR maxima 9.40, 9.50, and 9.63μ [lit.[28] 9.39, 9.50 and 9.63μ] $n_D^{26.5}$ 1.4578 [lit.[16] n_D^{20} 1.4620] and cis -2-methylcyclohexanol, IR maxima at 9.82, 10.23 and 10.58μ [lit.[28] 9.83, 10.23 and 10.60μ] $n_D^{26.5}$ 1.4622 [lit.[16]

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[a] All melting points are corrected; all boiling points are uncorrected.

[b] The infrared spectra were determined using a Beckman IR-5A spectrometer as films on sodium chloride cells or as potassium bromide pellets.

[c] Gas chromatographic analyses were performed using a Varian-Aerograph dual column Model 1520B from Wilkins Instrument and Research Inc., Walnut, California. A hydrogen flame detector was used for qualitative analysis. Quantitative analysis was performed using a thermal conductivity detector.

[d] The nuclear magnetic resonance spectra were determined on a Varian A-60 high resolution spectrometer with a field sensing stabilizer ("Super-Stabilizer"). Tetramethylsilane was used as an internal standard.

[e] The microanalyses were performed by Galbraith Laboratories, Knoxville, Tennessee.

n_D^{20} 1.4640]. 1-Methylcyclohexene, b.p. 109-110.5°, n_D^{27} 1,4519 [lit.[6] 109-109.5, n_D^{20} 1.4503] was generously supplied by Dr. E. J. Eisenbraun. Reference samples of 1,2-diphenylethyl diphenylphosphinate, m.p. 71-72°, and <u>trans</u>-2-methylcyclohexyl diphenylphosphinate, m.p. 142-143°, were provided by Dr. W. C. Pivonka.

<u>Preparation of Diphenylphosphinic Chloride</u>. Commercial diphenylphosphinous chloride, $n_D^{23.3}$ 1.6347, (198.7g, 0.9007 mole) was placed in a 1-liter three-necked flask equipped with fritted glass oxygen inlet tube, magnetic stirrer and thermometer. The solution was heated to 135-140° and dried (H_2SO_4) oxygen was admitted at a moderate rate over a 28-hour period. Oxidation was monitored by observing the decrease in refractive index to a constant value of $n_D^{23.4}$ 1.6080.[18] The dark yellow-orange liquid was distilled <u>in vacuo</u> at 137-138°/0.03-0.06 mm., [lit.[2] 135-136°/ 0.07 mm.], to give 183.1 g. (86.3%) $n_D^{24.3}$ 1.6083 [lit.[2] n_D^{20} 1.6068] of diphenylphosphinic chloride.

<u>Preparation of trans-2-Methylcyclohexyl Diphenylphosphinate (Ia)</u>. Into a 500 ml. three-necked flask equipped with a magnetic stirrer, thermometer, condenser, pressure-equalizing funnel, drying tube ($CaCl_2$) and nitrogen-inlet tube was placed 5.71 g (0.0500 mole) of <u>trans</u>-2-methylcyclohexanol and 7.08 g (0.0700 mole) triethylamine in 100 ml. of anhydrous (dried over sodium) ether. To this solution was added dropwise 9.46 g (0.04 mole) of diphenylphosphinic chloride in 50 ml. of dry ether. The temperature rose 2.3° during the 40-minute addition period. A very light white solid formed in the solution and in the space above the liquid as the chloride was added. The mixture was heated at 39° for 14 hours during which time the solid appeared to become more crystalline. Removal of the solid was effected by suction-

filtration. The solid was found to be completely water soluble and was identified by comparison of m.p. and IR spectrum with those of an authentic sample of triethylamine hydrochloride. The bands at ~3.8μ, 11.75μ, and 12.4μ were useful in distinguishing it from the ester. Additional solid appeared in the filtrate and was removed by filtration. This process was repeated six times. During the last filtration another solid was obtained. After recrystallization from benzene-hexane, IR analysis revealed absorptions for P-O-P (10.35μ), P→O (8.1μ) and P-C_6H_5(6.95μ). No P-O-C (10.1μ for the ester) absorption was observed. The compound was identified by comparison of m.p. 141.5-142.5° [lit.[29] 143°] and IR spectrum of an authentic sample of diphenylphosphinic anhydride.[47] The anhydride presumably was formed from diphenylphosphinic chloride and diphenylphosphinic acid (hydrolysis of the acid chloride) in the presence of triethylamine. After the last filtration the solvent was removed from the filtrate, and the resulting solid was extracted with hot hexane. After chilling overnight a white solid was obtained. The product Ia, m.p. 71-72°, was identified by comparison of the IR and NMR spectra (Plates I and VI) with that of an authentic sample of trans-2-methylcyclohexyl diphenylphosphinate (Ia).

Anal. Calcd. for $C_{19}H_{23}O_2P$: C, 72.59; H, 7.38; P, 9.85.
Found: C, 72.63; H, 7.40; P, 10.04.

A small amount of solid remaining after the hexane extraction was identified as triethylamine hydrochloride (IR).

Preparation of 1,2-Diphenylethyl Diphenylphosphinate (Ib). Into a 500 ml., three-necked flask equipped with a magnetic stirrer, condenser and pressure-equalizing addition funnel was placed a solution of 9.9 g. (0.05 mole) of 1,2-diphenylethanol and 10.1 g. (0.1 mole) of triethylamine dissolved in 75 ml. of anhydrous (dried over sodium) ether. A solution of 11.8 g. (0.05 mole) of diphenylphosphinic chloride in 50 ml. of anhydrous ether was added with stirring over a 20-minute period. During addition the temperature rose so as to cause gentle boiling. Additional ether was added (150 ml.) to break up the heavy slurry and the mixture was heated under reflux for 1.5 hours. The precipitate was collected by filtration, washed with water to remove triethylamine hydrochloride and recrystallized from benzene-hexane to yield 14.4 g. (72.7%) of 1,2-diphenylethyl diphenylphosphinate (Ib). The compound was identified by comparison of its m.p. (142.2-143°) and spectra (IR Plate II and NMR Plate VII) with those of an authentic sample.

Pyrolysis of *trans*-2-Methylcyclohexyl Diphenylphosphinate (Ia). The procedure employed during this pyrolysis study is essentially the same as that of Austin[12] and of Pivonka[44] with some modification. The method for *trans*-2-methylcyclohexyl diphenylphosphinate will be described. The reaction was carried out in a 10 ml. pear-shaped two-necked flask equipped with a thermometer and magnetic stirrer and connected to a pyrolysis train. The train consisted of three traps connected in series, the first being air-cooled and the latter two immersed in Dewar flasks. Each of the three traps was filled with ether to approximately one inch above the lower end of the inlet tube. The outlet of the last trap was connected to a drying tube ($CaCl_2$). The system was swept with dry deoxygenated nitrogen.[1] Nitrogen flow was continued during pyrolysis to insure rapid product removal. The reaction vessel was placed in a sand-bath and the bath temperature was monitored with a thermometer inserted into the sand. The reaction vessel was then charged with 1.200 g. (0.00383 mole) of <u>trans</u>-2-methylcyclohexyl diphenylphosphonate (Ia). Heat was applied slowly until the ester had melted (~75°) and then the temperature (monitored by the thermometer immersed in the liquid) was raised to 300°. At this point liquid droplets were noted in the connecting tube. The temperature was held between 200 and 220° for 40 minutes. At the conclusion of the heating period no further condensate appeared to be forming. The sand bath and the dry-ice traps were removed, the nitrogen flow was discontinued, and the system was slowly restored to room temperature. The slightly discolored solid in the flask was dissolved in 10% NaOH and the yellow alkaline solution was extracted several times with ether. Contents of the three traps were combined with the ether extract, condensed on the flash evaporator to a volume of 15.0 ml., and transferred to a 25 ml. volumetric flask for GLC analysis. The yellow alkaline solution, when acidified with 6N hydrochloric acid, gave a white solid which after drying at 25° <u>in vacuo</u> for 24 hours, melted at 193-194° [lit.[38] 192-193.5°]. The infrared spectrum was identical with that of an authentic sample of diphenylphosphinic acid. GLC analysis of the ether solution revealed the presence of benzene and 1- and 3-methyl-cyclohexene. Pivonka has observed that diphenylphosphinic acid itself gives rise to benzene when subjected to the reaction conditions.[44] The ratio of 3- to 1-methylcyclohexene was found to be 1:1.59 (Table III). A minimum of two runs was made for each ester.

<u>Pyrolysis of trans-2-Methylcyclohexyl Diphenylphosphinate (Ia) in Diphenyl Ether</u>. In order to determine the effect of solvents on the bond-breaking process the pyrolysis was performed in diphenyl ether and dimethyl sulfoxide (DMSO). The procedure used with diphenyl ether

is typical of that followed. To the apparatus described on page 117 (modified to use a 15 ml. two-necked flask) was added 1.0021 g. (3.183 x 10^{-3} mole) of trans-2-methylcyclohexyl diphenylphosphinate (Ia) in 8 ml. (12.63 g.) of diphenyl ether. Since the melting point of the ether is 27-28° it was necessary to warm the ether in a water bath (40°) during the preparation of the sample for pyrolysis. No condensation in the pyrolysis train occurred until the temperature in the pot reached 210°. The flask was held between 210 and 235° for 45 minutes. At the completion of the pyrolysis, as evidenced by the lack of additional condensate in the side arm, the system was restored to room temperature. The solid in the flask, presumably diphenyl ether and diphenylphosphinic acid, was extracted with ether and the remaining solid was removed by filtration. The IR spectra of the white solid, m.p. 191-193°, was identical with that of an authentic sample of diphenylphosphinic acid. The ether solution and the contents of the traps were combined, concentrated until cloudiness appeared and then diluted to mark in a 25 ml. volumetric flask for analysis by GLC. 3-Methylcyclohexene and 1-methylcyclohexene were obtained in a 1:1.2 ratio (Table III). Similar pyrolysis were performed with the trans-2-methylcyclohexyl diphenylphosphinate (Ia) and 1,2-diphenylethyl diphenylphosphinate (Ib) in DMSO. The only difference in the procedures was that the temperature of pyrolysis in DMSO was ~190° because of the lower boiling point of the latter solvent. In DMSO the ratio of 3-methylcyclohexene to 1-methylcyclohexene was 99:1.0. When Ib was pyrolyzed the ratio of cis- to trans-stilbene was 1:40.8.

Attempted Isomerization of 1- and 3-Methylcyclohexenes. A mixture of 0.3580 g. (3.723 x 10^{-3} mole) of 3-methylcyclohexene, 0.3007 g. (3.127×10^{-3} mole) of 1-methylcyclohexene and 0.6900 g. (3.162×10^{-3} mole) of diphenylphosphinic acid were placed in 20.0 ml. (31.5 g.) of diphenyl ether was placed in a 50 ml., three-necked flask equipped with the previously described pyrolysis accessories. The system was swept with dry deoxygenated nitrogen[1] and heated to 80°. The temperature was then slowly raised to 105° during which time samples were periodically removed for GLC analysis. As the temperature rose to near 100° it became evident that the alkene was distilling from the mixture. At the end of the heating period the diphenylphosphinic acid was removed by filtration (quantitative recovery) and the liquid remaining in the flask, plus the ether in the traps, were combined for GLC analysis. No detectable isomerization occurred (Table IV).

The Pyrolysis of *trans*-2-Methylcyclohexyl Diphenylphosphinate (Ia) in the Presence of Hydroquinone.--The ester (1.0014 g., 3.18×10^{-3} mole) and 0.0035 g. (3×10^{-5} mole) of hydroquinone were dissolved in 10 ml. (15.8 g.) of diphenyl ether was placed in a 15 ml., three-necked flask equipped as described on page 117 and previously swept with dry deoxygenated nitrogen.[4] The temperature was held between 210 and 234° for 1 hour. The diphenylphosphinic acid (0.64 g., 92%) was removed by filtration, and the ether solutions from the flasks and the pyrolysis traps were combined in a 25 ml. volumetric flask for GLC analysis. The ratio of 3- and 1-methylcyclohexene was found to be: 1:1.20 (Table III).

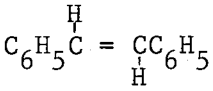
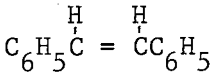
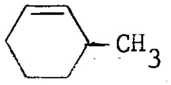
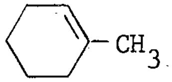
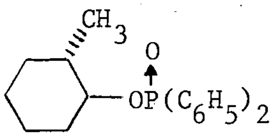
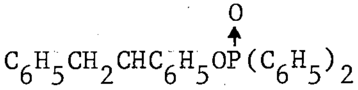
Heat Catalyzed Isomerization of *cis*-Stilbene.--*cis*-Stilbene (0.63 g., 3.5×10^{-3} mole) was heated in the usual apparatus at 225 to 250° for 1 hour. Only slight discoloration was noted at the end of the heating period. A 10.00 ml. solution of the reaction mixture was analyzed by GLC. Results are given in Table IV.

Acid Catalyzed Isomerization of *cis*-Stilbene. *cis*-Stilbene (1.00 g., 5.545 x 10^{-3} mole) and 0.97 g. (4.447 x 10^{-3} mole) of diphenylphosphinic acid were heated for 50 minutes at 225 to 245° in the usual apparatus. The solid which formed on cooling to room temperature was treated with 10% sodium hydroxide. The alkaline solution was acidified with hydrochloric acid to give 0.9455 g. (97.5% recovery) of diphenylphosphinic acid, m.p. 190-193°, unrecrystallized. Solution of the alkali-insoluble material in ether (placed in a 25 ml. volumetric flask) gave a sample for GLC analysis. Results are presented in Table IV.

Gas Chromatographic Analysis (GLC). Qualitative identification of compounds involved in this study were performed by the technique of mixed injection[16] using a hydrogen flame ionization detector. All analyses were performed on a 6' x 1/8" stainless steel column with a 4% silicone 30 substrate on a 80-100 mesh, acid washed, DMCS-treated Chromosorb G column. Quantitative analyses were performed on the same column using a thermal conductivity detector. Standard solutions were prepared of the reaction products (Table II). Multiple injections were made of the standard solution followed by multiple injections of the reaction mixture. The areas under the peaks were measured by a Disc Chart Integrator - Model 224-4 from Disc Instruments, Inc., Santa Ana, California. From the ratio of the area of the peak of a reaction component to that of the standard solution, the concentration was determined.[3] The only difficulty occurred in those reaction mixtures with DMSO as a solvent and in which *trans*-stilbene was a product. In those cases washing the mixture with 10% sodium hydroxide removed the interferring peak (DMSO).

TABLE I

GLC ANALYSIS: CHARACTERISTIC RETENTION TIMES

Compound	Temperature	Time (minutes)	Carrier Gas Gage Pressure	Gas Flow Controls (%)[a]
 $C_6H_5\overset{H}{C} = \underset{H}{C}C_6H_5$	201°	3.75	60#	47.8
 $C_6H_5\overset{H}{C} = \overset{H}{C}C_6H_5$	201°	2.4	60#	47.5
	70°	5.4	60#	16
	70°	6.8	60#	16
	265°	9.6	60#	26
$C_6H_5-C_6H_5$	185°	3.6	60#	50
 $C_6H_5CH_2CHC_6H_5O\overset{O}{\overset{\uparrow}{P}}(C_6H_5)_2$	250°	4.2	60#	45

[a] Indicates relative flow rate of carrier gas through the injector-column-detector flow system as measured on the instrument.

TABLE II

STANDARDS FOR GLC ANALYSIS

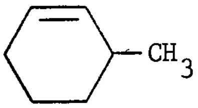
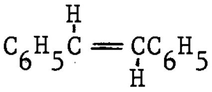
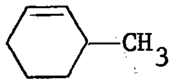
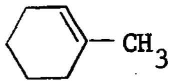
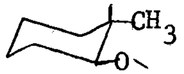
Compound	Concentration	Moles	Moles/ml.
	0.2570g./50 ml.	2.672×10^{-3}	5.344×10^{-8}
 $C_6H_5\overset{H}{C}=\underset{H}{C}C_6H_5$	0.4153g./10 ml.	2.306×10^{-3}	2.306×10^{-7}

TABLE III

PYROLYSIS DATA FOR $(C_6H_5)_2P(O)OR$

R	Solvent	Temperature of Pyrolysis	Yield (%)	Products (%)		Ratio
						
	neat	200-220°	93	39.75	60.25	1.0:1.52
	DMSO	185-192°	48	99	1.0	99:1.0
	$(C_6H_5)_2O$	210-235°	90	45.4	54.6	1.0:1.2
	$(C_6H_5)_2O$ hydroquinone	210-234°	86	46.2	53.8	1.0:1.2
				cis-Stilbene	trans-Stilbene	
$C_6H_5CH_2CHC_6H_5-$	neat	210-240°	88	3.1	96.9	1.0:31.2
	DMSO	184-190	65	2.4	97.6	1.0:40.8
				allylbenzene	other isomers	
$C_6H_5(CH_2)_3-$[a]	neat	240-270	--	91	9	--

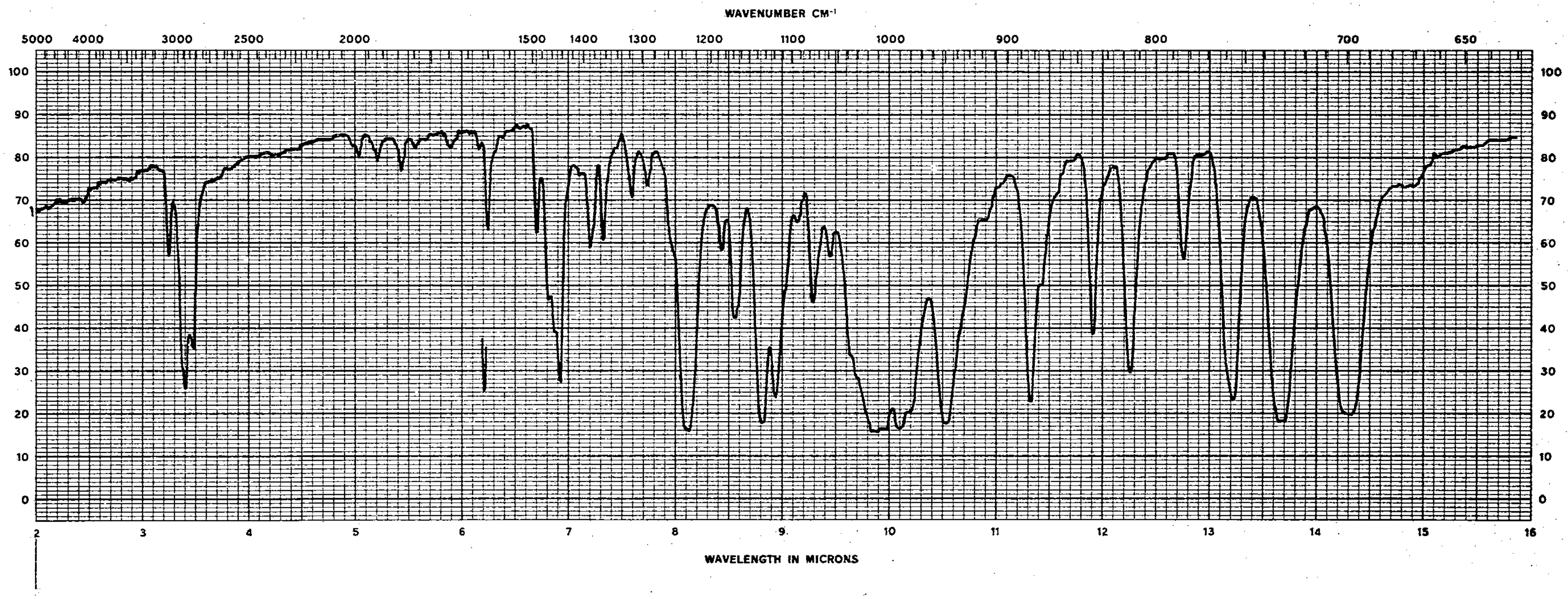
[a] Prepared and pyrolyzed by W. C. Pivonka.[44]

TABLE IV

PRODUCT EQUILIBRATION STUDIES

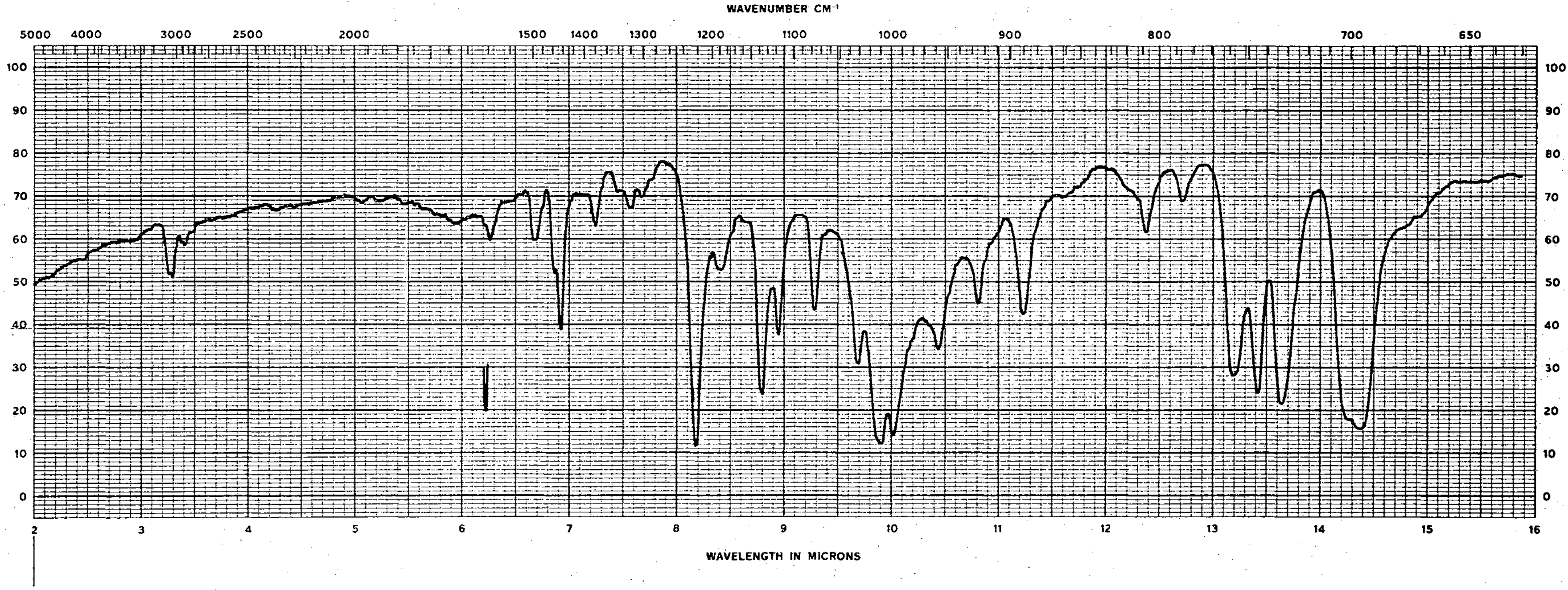
Compound	Catalyst and Solvent	Temperature (°C)	Products (%)		Ratio
Cyclohexene			Cyclohexene 1-Methyl-	3-Methyl-	
1-Methyl-	$(C_6H_5)_2P(O)OH$ in DMSO	175-185	99	1	99:1
3-Methyl-	$(C_6H_5)_2P(O)OH$	102-120	-	100	-
1- and 3-Methyl	$(C_6H_5)_2P(O)OH$ in diphenyl ether	90-105	45.5	54.4	1.0:1.20
			cis-Stilbene	*trans*-Stilbene	
cis-Stilbene	heat	220-245	75.3	24.7	3.05:1.0
	heat + $(C_6H_5)_2P(O)OH$	220-245	55.4	46.5	1.2:1.0
trans-Stilbene	heat + $(C_6H_5)_2P(O)OH$	210-240	2.2	97.8	1.0:44.5

Plate I



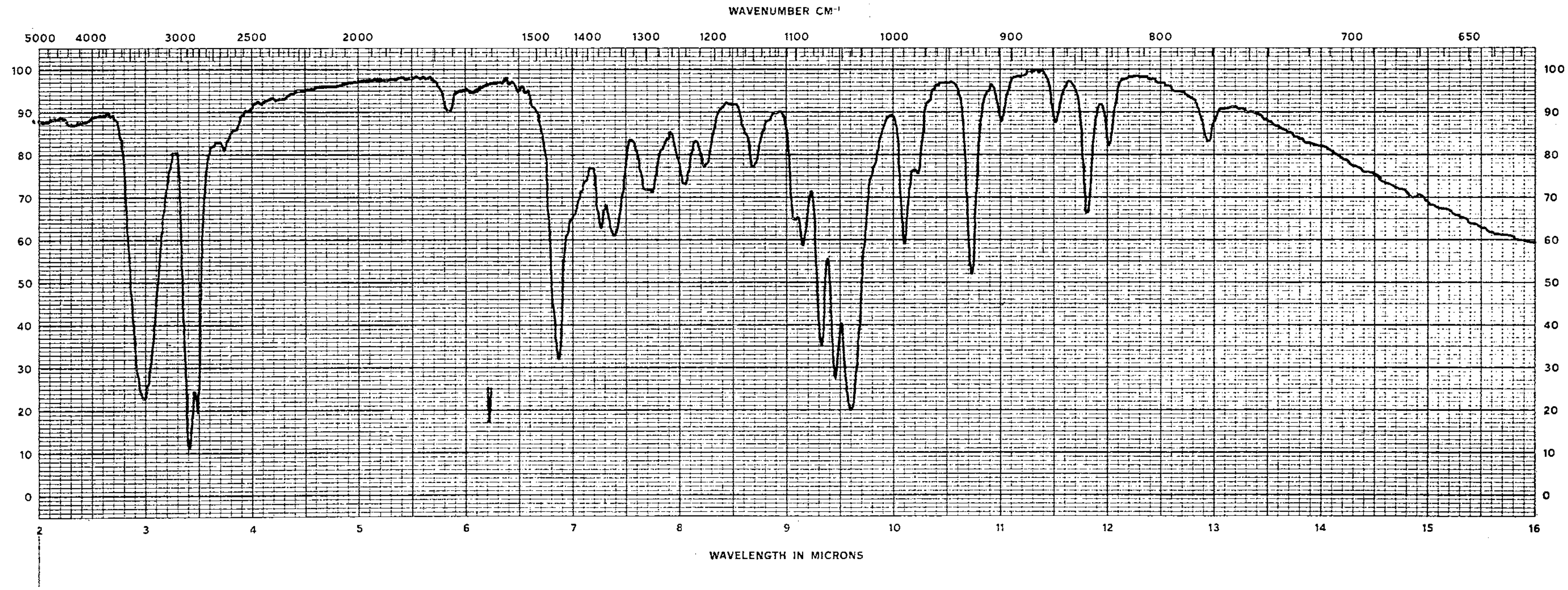
trans-2-Methylcyclohexyl Diphenylphosphinate (Ia), KBr Pellet

Plate II



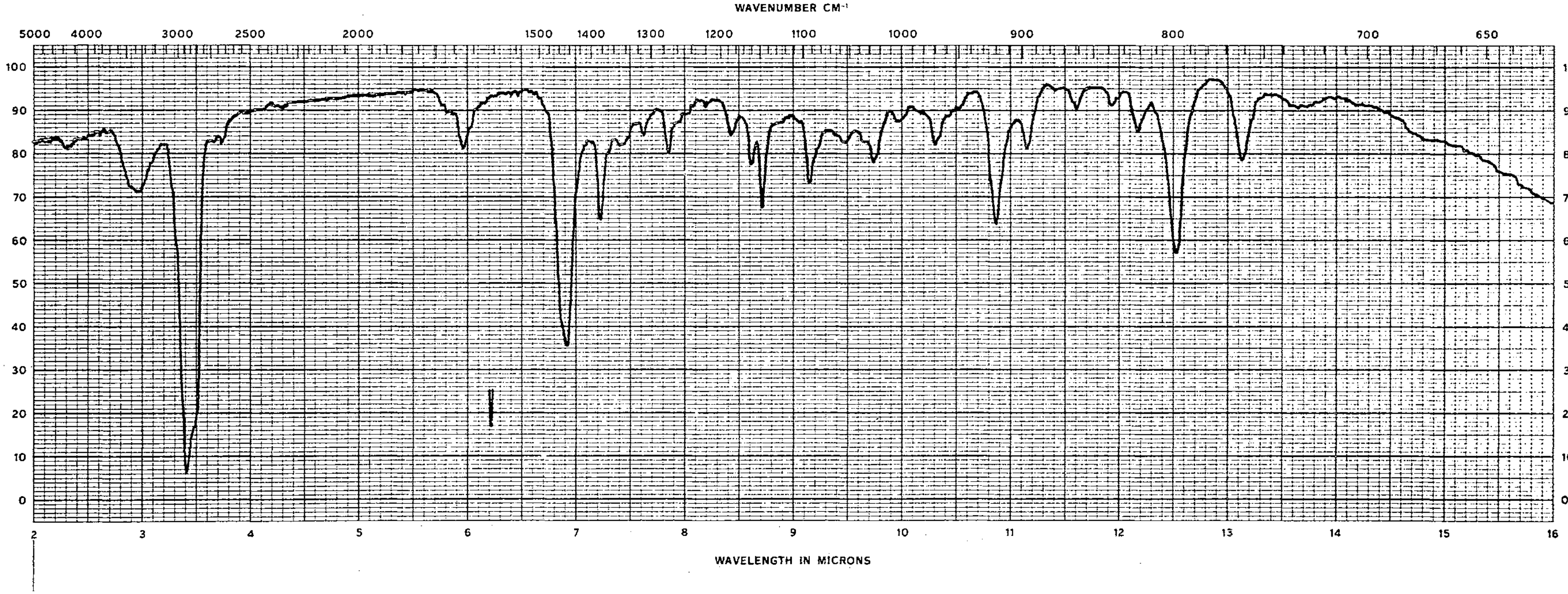
1,2-Diphenylethyl Diphenylphosphinate (Ib), KBr Pellet

Plate III



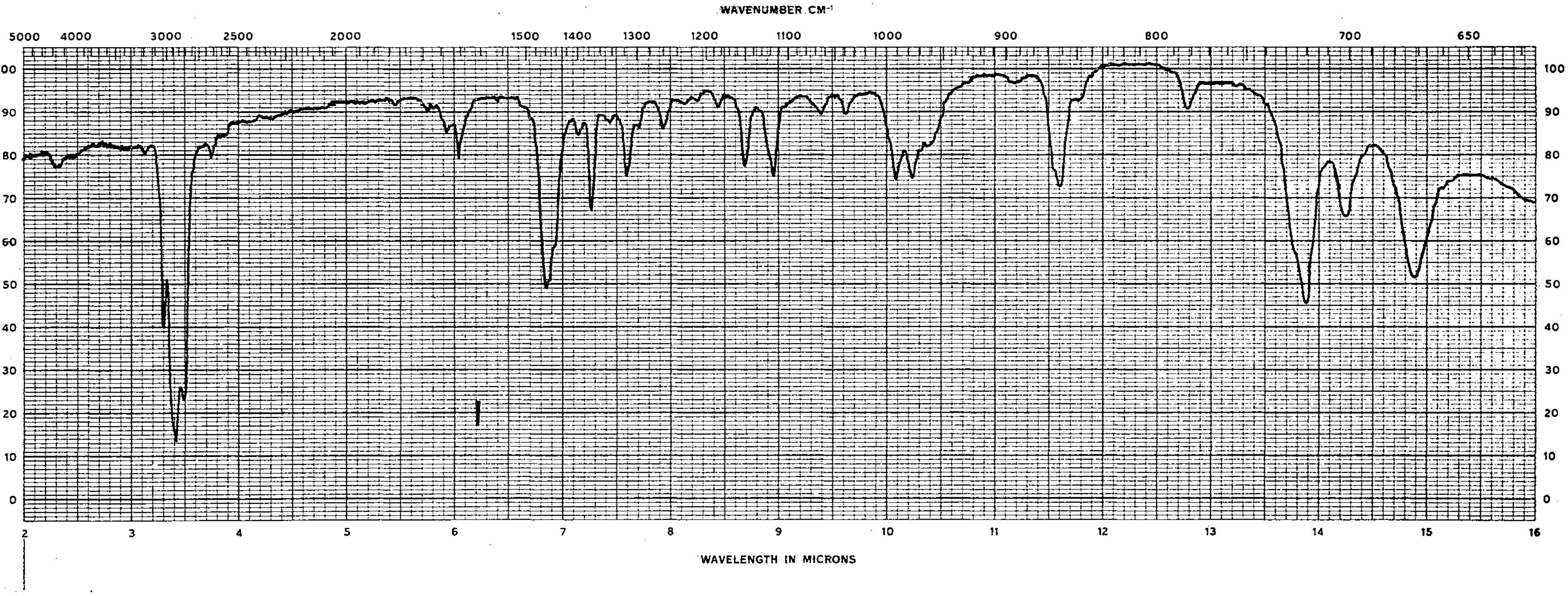
trans-2-Methylcyclohexanol, Film on NaCl Plates

Plate IV



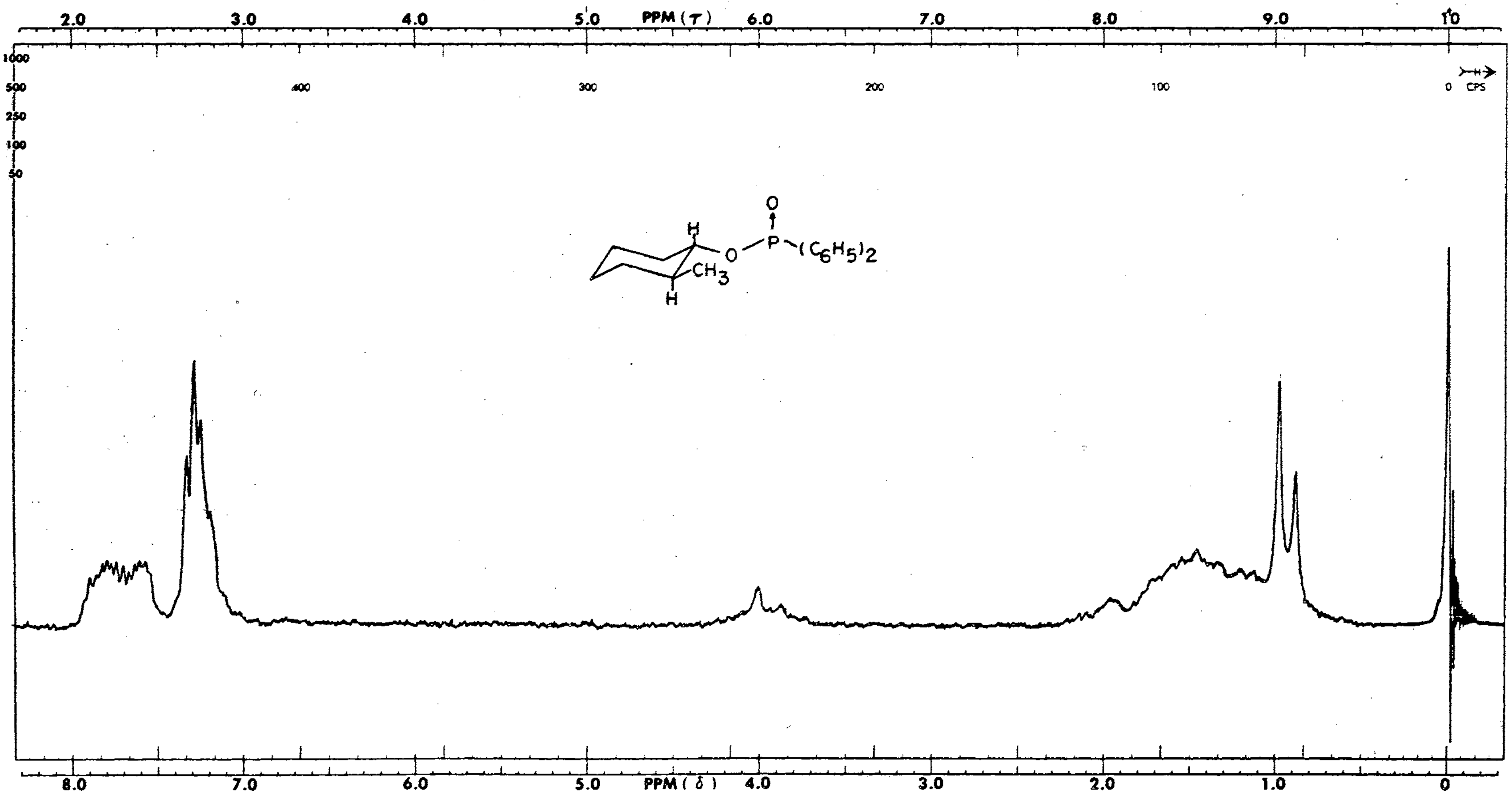
1-Methylcyclohexene, Film on NaCl Plates

Plate V



3-Methylcyclohexene, Film on NaCl Plates

Plate VI



trans-2-Methylcyclohexyl Diphenylphosphinate (Ia)

Solvent . . . . . CCl_4

F.B.. . . . . . .1.0 cps

R.F. Field . . . . 0.05 mG

S.T. . . . . 250 sec

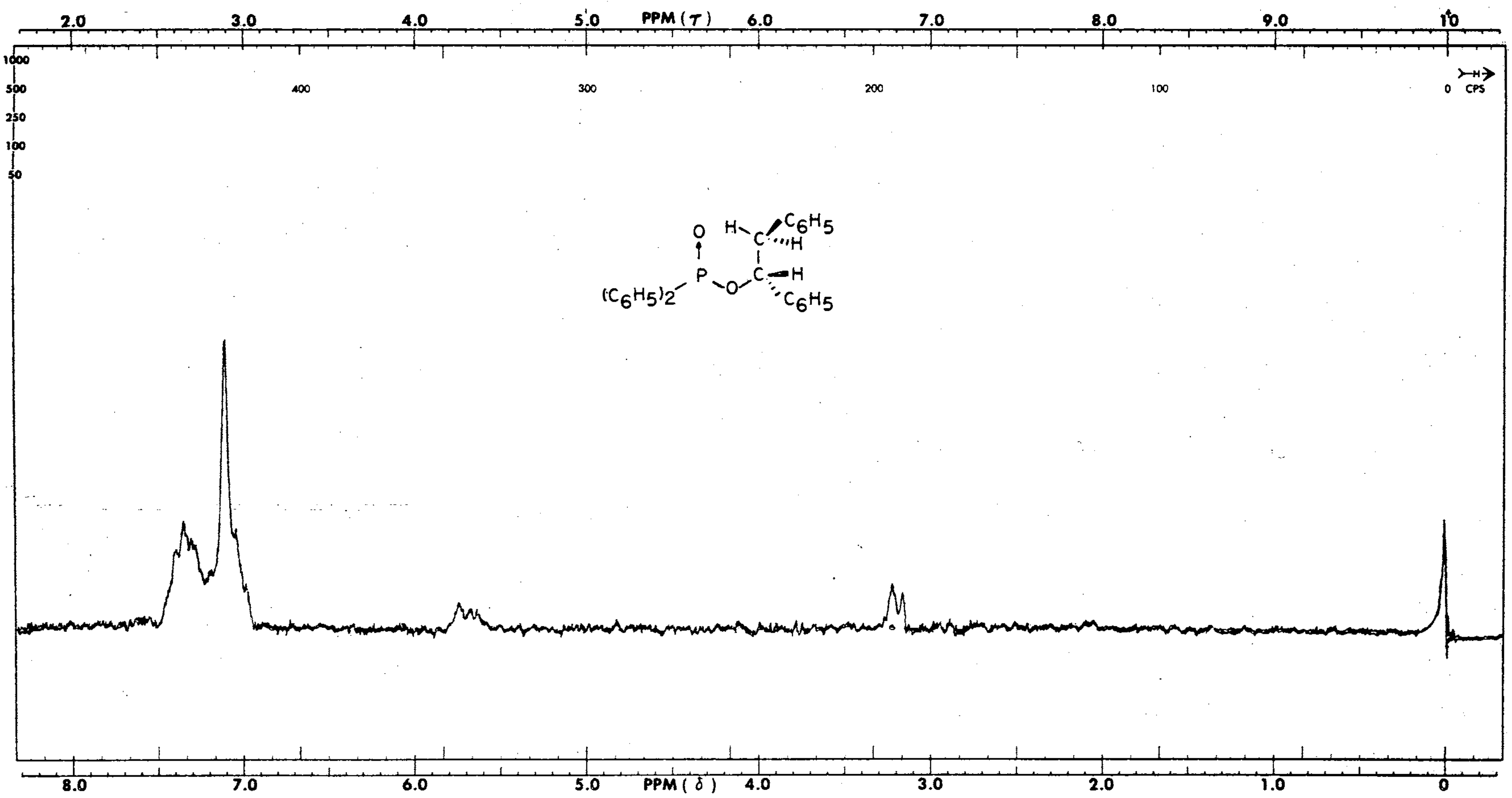
S.W. . . . . 500 cps

S.O. . . . . 000 cps

S.A. 6.3

I.A. . . . . . . off

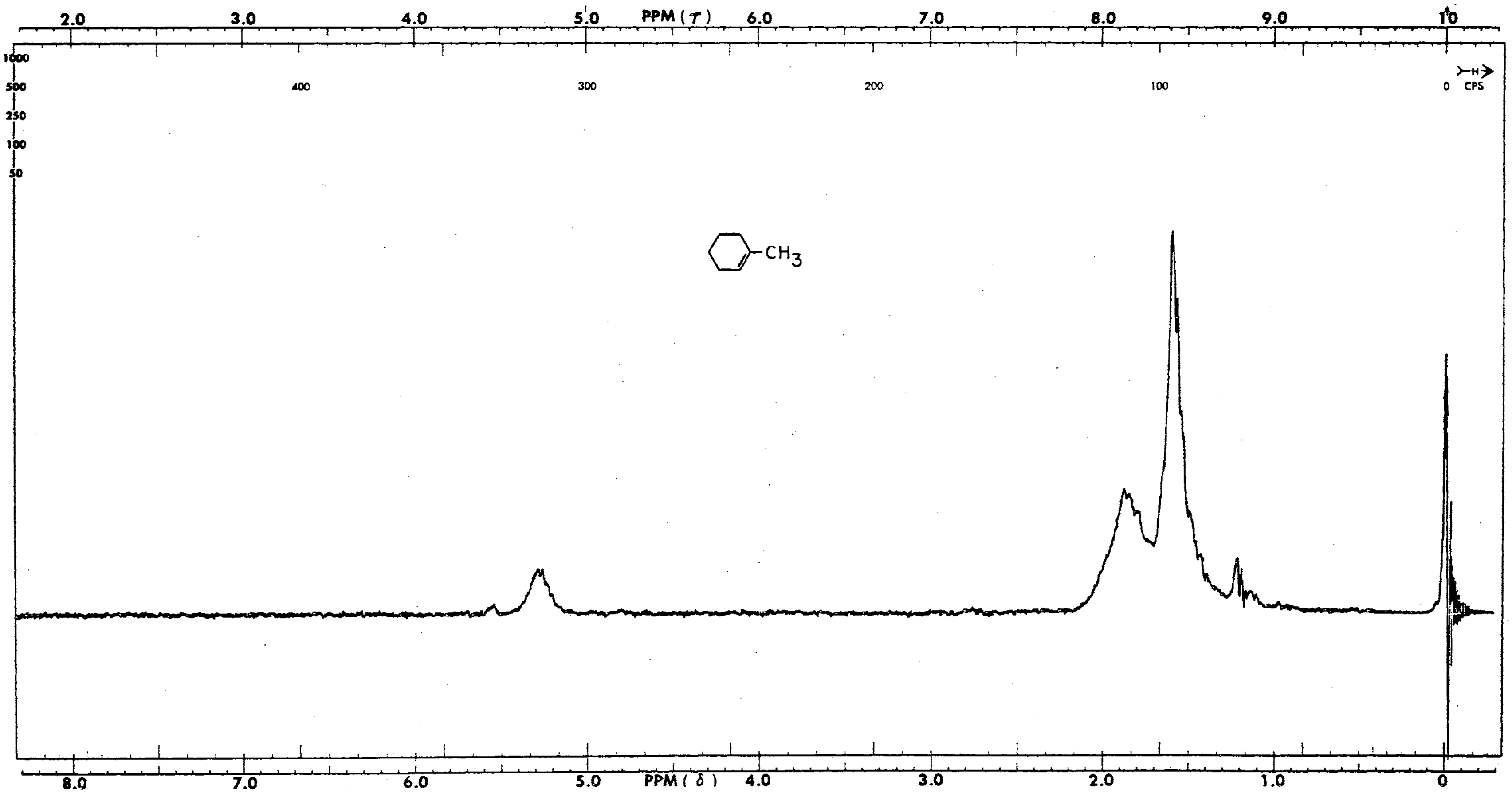
Plate VII



1,2-Diphenylethyl Diphenylphosphinate (Ib)

Solvent	$CDCl_3$	R.F.	0.04 mG	S.W.	500 cps	S.A.	10.0
F.B..	1.0 cps	S.T.	250 sec	S.O.	000 cps	I.A.	off

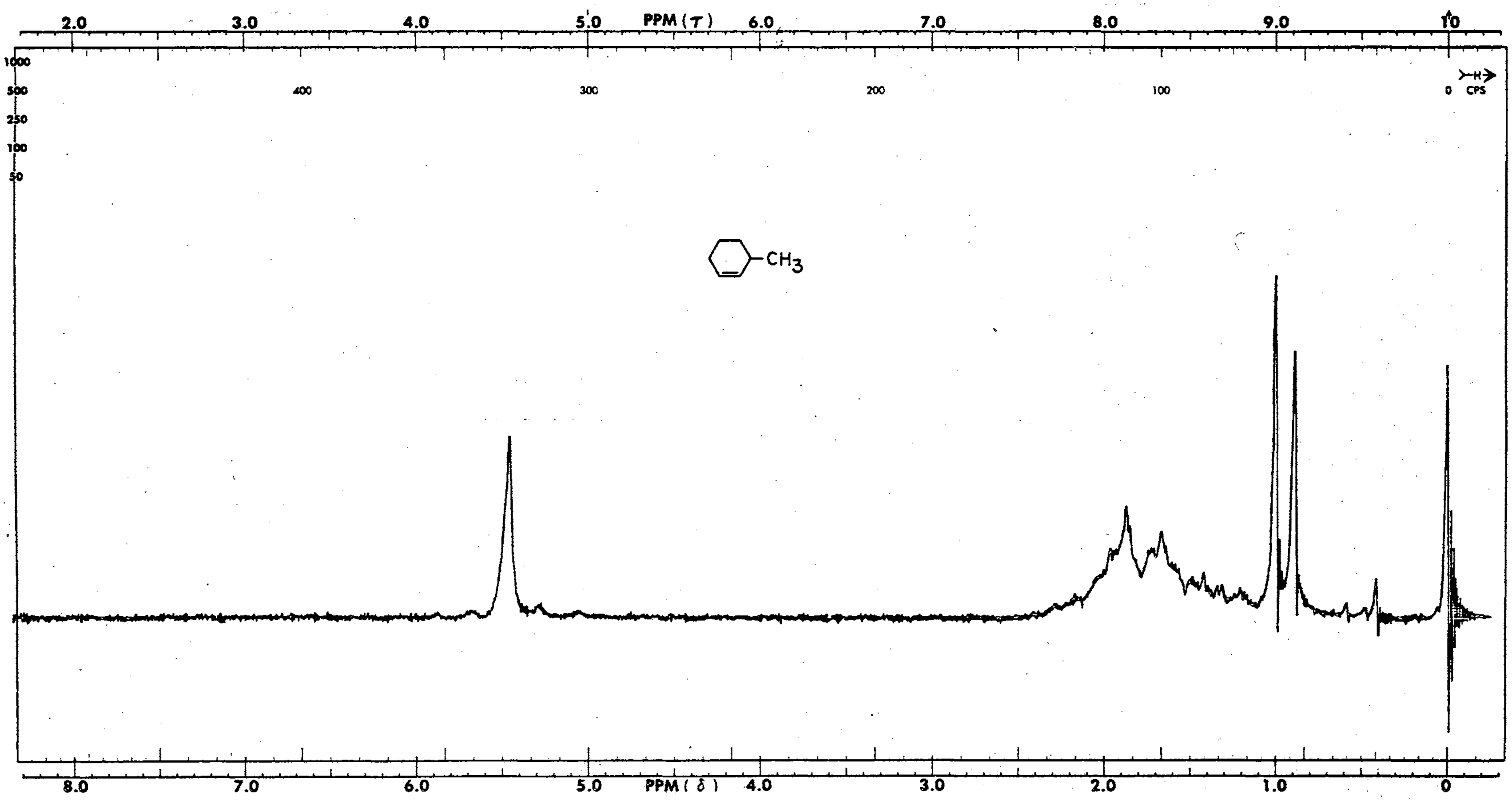
Plate VIII



1-Methylcyclohexene

Solvent	CCl_4	R.F. Field	0.05 mG	S.W.	500 cps	S.A.	3.2
F.B..	2.0 cps	S.T.	250 sec	S.O.	000 cps	I.A.	off

Plate IX



3-Methylcyclohexene

Solvent . . . . . CCl_4 R.F. Field . . . . 0.05 mG S.W. . . . . 500 cps S.A. 2.5

F.B.. . . . . . .4.0 cps S.T. . . . . 250 sec S.O. . . . . 000 cps I.A. . . . . . . off

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VITA

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II. STEREOCHEMISTRY AND MECHANISM OF PYROLYTIC ELIMINATIONS IN PHOSPHINATES

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