THE CHEMISTRY OF BENZOPHOSPHOLE DERIVATIVES

by

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Ph.D Chemistry

The Chemistry of Benzophosphole Derivatives

Abstract

The synthesis of 1-ethoxybenzo[b]phosphole 1-oxide, starting from the Diels-Alder reaction of E,E-1,4-diacetoxy butadiene and 1-ethoxy-2-phospholene 1-oxide is described. Reduction of this benzo[b]phosphole oxide with different silanes and lithium aluminium hydride was attempted.

2-Phenylisophosphindoline 2-oxide was prepared in one step, by the reaction of o-xylylene dibromide and diethyl phenylphosphonate in the presence of sodium bis(2-methoxyethoxy)aluminium hydride.

2-Phenylisophosphindole 2-oxide, the first example of the least substituted compound in the benzo[c]phosphole series was generated by base-promoted dehydrobromination of r-1-bromo-t-2-phenylisophosphindoline 2-oxide. 2-Phenylisophosphindole 2-oxide was found to be unstable and dimerized rapidly. Its existence was confirmed by trapping with various dienophiles as the Diels-Alder adducts.

The synthesis of 2-phenylisophosphindole was also attempted.

The chemistry of benzophosphole derivatives is discussed.

Ph.D. Chimie

La chimie des dérivés de benzophosphol

Résumé

La synthèse de l'éthoxy-1 oxo-1 benzo[b]phosphol par la réaction de Diels-Alder entre E,E-diacétoxy-1,4 butadiène et éthoxy-1 oxo-1 phospholène-2 a été décrite.

La réduction de cet oxyde de benzo[b]phosphol par différents silanes et par l'hydrure de lithium-aluminium a été essayée.

Phényl-2 oxo-2 isophosphindoline a été préparée en une seule étape par la réaction du dibromure de o-xylylène sur le phényl phosphonate de diéthyle en présence de l'hydrure de sodium bis(méthoxy-2 éthoxy)aluminium.

Phényl-2 oxo-2 isophosphindol, le premier exemple de la série des benzo[c]phosphols les moins substituées, a été généré par la déshydrobromination basique de r-bromo-1 oxo-2 t-phényl-2 isophosphindoline. Oxo-2 phényl-2 isophosphindol s'avère très instable et dimérise rapidement; son existence a été confirmée par la formation de ses produits d'addition avec différents diénophiles.

La synthèse de phényl-2 isophosphindol a été aussi essayée.

La chimie des dérivés de benzophosphol a été discutée.

TO MY PARENTS

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ABBREVIATIONS

The following abbreviations have been used in this thesis:

Ac	acetyl, CH_3CO-
Et	ethyl
Me	methyl
Ph	phenyl, C_6H_5-
$PhCH_2$	benzyl, $C_6H_5CH_2$-
m.p.	melting point
b.p.	boiling point
i.r.	infrared
n.m.r.	nuclear magnetic resonance
u.v.	ultraviolet
ppm	parts per million (chemical shift δ)
Hz	hertz
MHz	megahertz
nm	nanometer
ε	molar extinction coefficient
λ_{max}	wavelength of the absorption peak
ν_{max}	wavenumber of the absorption band

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INTRODUCTION

At the present time organophosphorus compounds are being intensively studied in view of their chemical importance and their applications in industry and agriculture. Many of the applications of phosphorus compounds depend on their biological activities and these applications range from fertilizers to pesticides. Organophosphorus compounds are also widely used as medical preparations. They have been used as plasticisers, flotation agents and oil and gasoline additives. In recent years, they have been widely used for chemical crop protection. Being considerably more effective than previously known insecticides, various phosphorothioates have proven particularly valuable.

The phosphorus compounds play an important role in living processes and the phosphate esters are of importance in nucleic acid synthesis. Phosphate esters are also believed to be involved in terpene and steroid biosyntheses. Since the discovery of Wittig reaction, a wide range of organic synthetic applications has been found for tervalent phosphorus compounds and for phosphonium salts. These important factors have led to the increase activity in the field of organophosphorus chemistry.

CHAPTER 1

THE CHEMISTRY OF PHOSPHOLE DERIVATIVES

Some Aspects of Organophosphorus Chemistry

Electronic Structure

Since nitrogen and phosphorus are both members of Group V of the periodic table and have similar electronic configuration, one might therefore expect some resemblances in the organic chemistry of these two elements. In reality, however, there are some striking differences between these two elements. These differences are due mainly to the larger size of phosphorus atom and the lower 3s-3d promotional energy[1] for phosphorus (17 ev) compared to that of nitrogen (23 ev).

1) Phosphorus is less electronegative than nitrogen:

Table I shows the electronegativity values of some of the elements. The lower electronegativity of phosphorus in comparison with nitrogen is due to the larger size of second-row element phosphorus.

2) Unshared pair of electrons in phosphorus are better nucleophiles:

The better nucleophilicity of phosphorus is also due to its larger size, which allows the greater polarizability of

TABLE I

ELECTRONEGATIVITIES*

Element	Electronegativity
Silicon	1.8
Hydrogen	2.1
Carbon	2.5
Oxygen	3.5
Nitrogen	3.0
Phosphorus	2.1
Chlorine	3.0

*Ref. 2 and 4

the outermost electrons. These electrons, which are farther from the nucleus are less attracted to the nucleus and can be more freely moved towards the external positive centers. Unshared pair of electrons can accommodate better to the stereoelectronic requirements of a reaction, such as nucleophilic displacement.

The better nucleophilicity of phosphorus is evident on comparing tertiary phosphine with the corresponding amine. Tertiary phosphines are more powerful nucleophiles than the corresponding amines, as measured by the second-order rate constants for reaction with a given alkyl halide. Thus, quaternisation of Me_2P-NMe_2 with methyl iodide occurs at phosphorus

rather than at nitrogen[3].

3) Phosphorus is reluctant to form P_π-P_π double bonds:

The sideway overlap of parallel p-orbitals necessary to form a stable π-bond is much less extensive in the case of second-row element phosphorus. This is attributed to its greater size and longer bond length. The single-bond covalent radius of phosphorus is 1.1 Å which is 0.4 Å larger than that of nitrogen. The bond lengths of P-P and N-N are 2.2 Å and 1.4 Å respectively[4]. There is no known example of compound with phosphorus forming double bonds, either with itself ($3_{p\pi}$-$3_{p\pi}$) or with other elements ($3_{p\pi}$-$2_{p\pi}$)[1]. In its reluctance to form the p_π-p_π type of double bond, phosphorus resembles other second-row elements such as silicon and sulfur.

4) Availability of phosphorus d orbitals:

The electronic configurations (only the outer valence shell is considered) of nitrogen and phosphorus is $2s^2\ 2p^3$ and $3s^2\ 3p^3$ respectively. Phosphorus contains not only the s and p orbitals which dominate bonding by seeking the full octet, but also empty d orbitals into which covalent electrons can be accommodated. For second-row element phosphorus, the energy separation between the 3s to 3d orbital is much smaller and hence d orbitals play an important role for bonding. Phosphorus can expand its valence shell to accommodate 10 or 12 electrons by utilizing its empty 3d orbitals. This expectation is in

agreement with the existence of compounds such as $(C_6H_5)_5P$, PX_5, PX_6^- and $[PX_4]^+$ $[PX_6]^-$ where phosphorus has a coordination number of 5 or 6. Formation of analogous pentacovalent nitrogen compounds is considered unlikely, because of the high energy of nitrogen 3d orbitals relative to 2s and 2p orbitals and indeed, no such compounds have been found.

p_π - d_π Bonding

Although phosphorus is reluctant to form p_π-p_π type of double bonds, it has a tendency to form a different type of double bond involving d orbitals, with elements X having unshared pair of p electrons. This type of bonding arises from the donation of non-bonding p electrons of the elements X into the vacant d orbitals of phosphorus and is called "p_π-d_π bonding". It is sometimes referred to as "backbonding".

The consequences of vacant d orbitals are also evident on comparing amine oxide R_3NO with phosphine oxide R_3PO. The electronic structure of N-Oxide can be represented by the single canonical structure $R_3\overset{+}{N}\text{-}\bar{O}$, whereas for R_3PO, the bond to oxygen have multiple character and are represented by the following resonance structures.

$$R_3\overset{+}{P} - \bar{O} \longleftrightarrow R_3P = O$$

The high dissociation energies, small bond lengths and bond moments of P=O bonds suggest that p_π-d_π bonding is involved in contrast to the coordinate bonding in amine oxides. The P=O bond energies lie in the range of 120 to 150 k cal/mole[5], whilst

N→O bond energy is in 50 to 70 k cal/mole range. Moreover, the P=O bond length is shorter than expected on the basis of ordinary single bond whereas the N→O bond length is approximately equal to the calculated single bond length. The bond moment of P=O bond is less than calculated for the dipolar form, $\geq \overset{+}{P} - \bar{O}$. Bond length and dipole moment data of phosphine oxide give the evidence for the double bond character of P=O bond.

One important feature of the delocalization of adjacent electron pairs by back donation is the relative stability of carbanions. The Wittig reagents[6] are carbanions stabilized alpha to phosphorus.

$$\geq \overset{+}{P}\text{-}\overset{-}{C}HR \longleftrightarrow \geq P{=}CHR$$

Wittig reagents

The high P=O bond energy is the fundamental of some of the most important reactions in organophosphorus chemistry.

Thus the tautomerism such as

$$\geq P\text{-}OH \rightleftharpoons \geq P(H)=O$$

indicates the strong tendency for P=O formation.

More evidence in support of p_π-d_π bonding has been obtained from the study of ultraviolet, infrared, nuclear quadrupole resonance and nuclear magnetic resonance spectroscopy[1].

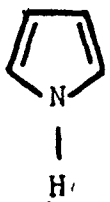
Phosphole Derivatives

There has been a fluorish of research activity in the field of organophosphorus chemistry in the past two decades. The chemistry

of heterocyclic compounds containing phosphorus has been a subject of much interest and the possibilities for aromatic character in these compounds provide some incentive for investigation. Particular attention is also paid to the question whether the heterocyclic system of phosphorus would exhibit the same properties as that of nitrogen.

Furan, thiophene and pyrrole (1) have been known for many decades and have been investigated extensively. However, the related phosphole (2) system has been little explored[7-10] and no phosphorus analog of an aromatic monocyclic nitrogen compound had been prepared until 1959.

Similarly, the chemistry of indole (benzo[b]pyrrole) (3) has been explored much more thoroughly than that of phosphindole (benzo[b]phosphole) (4). However, both the isoindole (benzo[c]pyrrole) (5) and isophosphindole (benzo[c]phosphole) (6) systems have been rarely investigated.



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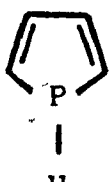

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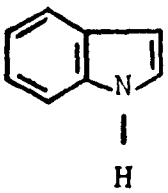

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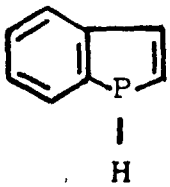

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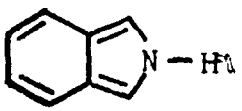

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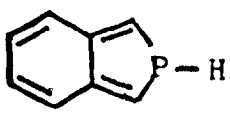


(6)

The inherent interest of the phosphole system can be attributed to two factors, namely (a) the possible aromatic character as compared with the common heterocyclopentadienes, especially the pyrrole system and (b) the behaviour of phosphole as secondary or tertiary phosphines.

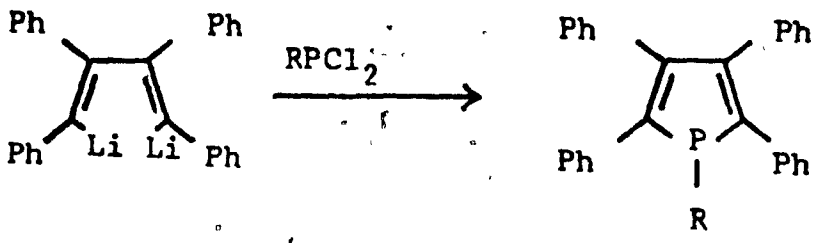
Several reviews[7,8,9] on the chemistry of phosphole derivatives have appeared, the last one[10] is by Mann in 1970. The review on the same subject with the literatures covering up to December, 1973 will be presented in this chapter.

The field of phosphole chemistry can be generally divided into (1) Simple phosphole (2) Dibenzophosphole and (3) Benzophosphole.

Synthesis of simple phosphole

Phosphole (2) itself has not yet been synthesized and all phospholes thus far reported carried at least one substituent.

Hubel and Braye[11,12] and Leavitt et al[13,14] reported independently that 1,4-dilithio-1,2,3,4-tetraphenylbuta-1,3-diene (7), obtained by the dimerization of diphenylacetylene with lithium is a very useful starting material for the synthesis of phospholes. It reacted with alkyl or aryl dichlorophosphine to give P-alkyl or P-aryl-2,3,4,5-tetraphenylphosphole (8) (Eq. 1).



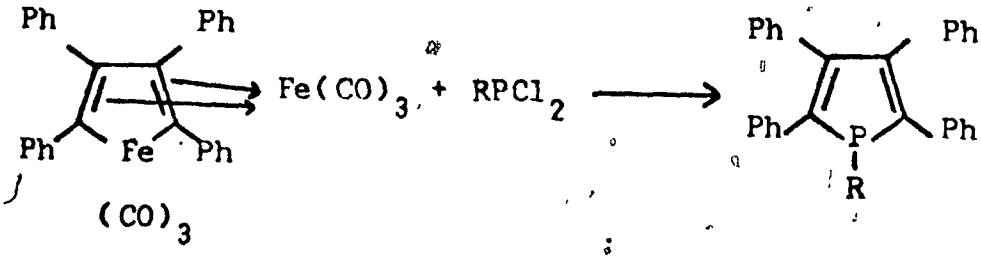
(1)

(7)

(8)

R = Ph, CH_3, $PhCH_2$

In a related synthesis, Hubel et al[11,12] used iron carbonyl-diphenylacetylene complex (9) in place of dilithio compound. 9 was obtained by the reaction of $[Fe(CO)_4]_3$ with diphenylacetylene. The iron carbonyl-tolan complex contains a cisoid system bonded to an iron atom and reacts in a similar manner as 7 with phenyl or benzyldichlorophosphine (Eq. 2).



(2)

(9)

(8)

R = Ph, $PhCH_2$

Campbell et al[15] prepared 1,2,5-triphenylphosphole (TPP)* (11) by heating phenyldichlorophosphine with diphenylbutadiene. Presumably, the process initially involved the normal McCormack

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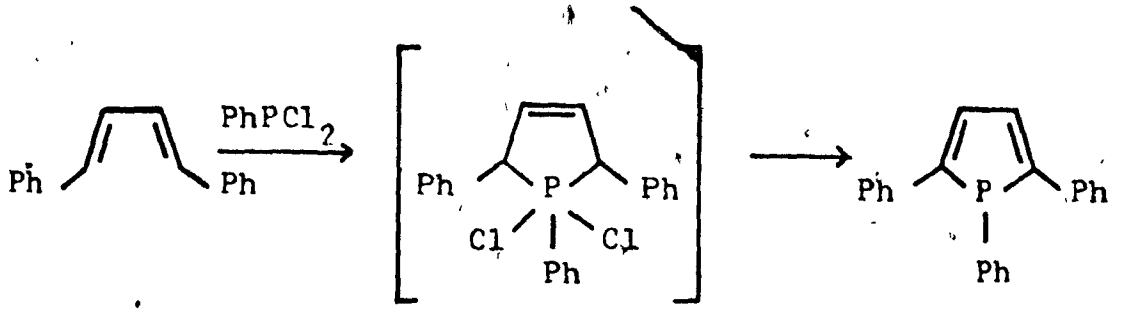
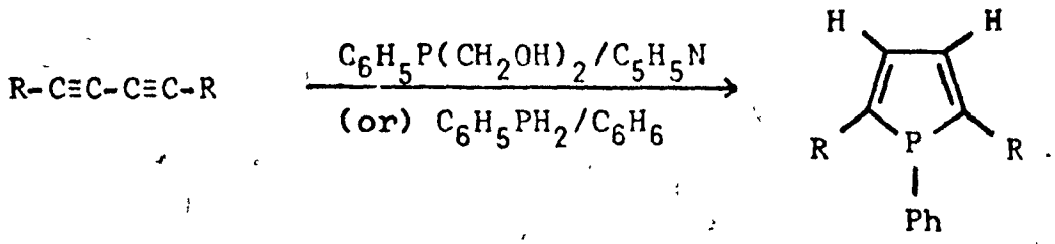
*Throughout this thesis TPP will be used to denote 1,2,5-triphenylphosphole.

reaction[16] to give the adduct 10, which then dehydrohalogenated under the conditions of the reaction to give the phosphole 11 (Eq. 3).



(10) (11) (3)

The most general approach to simple phosphole synthesis was reported by Markl and Potthast[17] and was closely related to pyrrole[18] and thiophene[19] syntheses from conjugated diynes. Bis(hydroxymethyl)phenylphosphine in pyridine and phenylphosphine in benzene both reacted readily with 1,3-butadiynes (12) in the presence of a catalytic amount of phenyl lithium to give the corresponding phospholes 13 (Eq. 4).

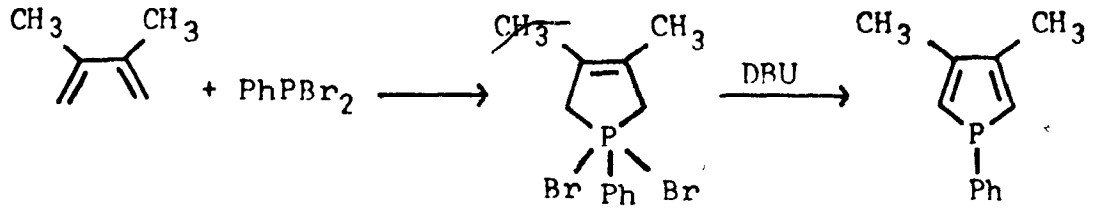


(12) (13) (4)

R = alkyl, aryl

Recently, Mathey[20] has reported a simple synthesis of phosphole which involved the reaction of 2,3-dimethylbutadiene with

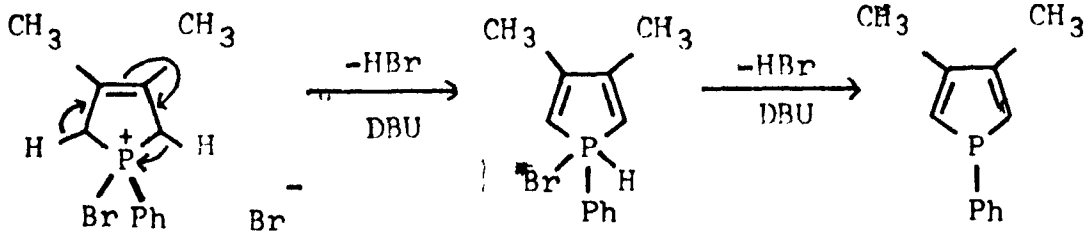
phenyldibromophosphine in the presence of 1,5-diazabicyclo (5.4.0) undecene-5 (DBU) to afford 1-phenyl-3,4-dimethylphosphole (14) (Eq. 5).



(5)

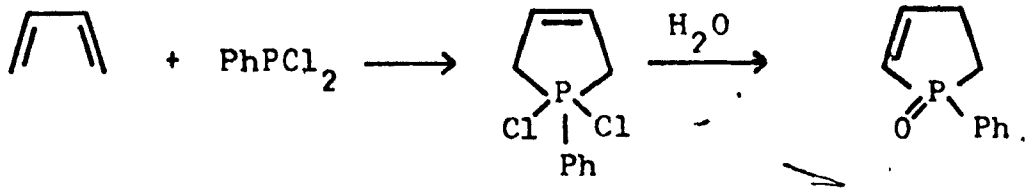
(14)

The initial reaction is the normal McCormack reaction[16] followed by the dehydrobromination with the strong base DBU. The mechanism was proposed as follows: -



The above are the several routes to various highly substituted phospholes. The synthetic approach to the less substituted phospholes involves the dehydrohalogenation of phospholene intermediates. Thus, the synthetic approach of Donadio and Howard[21] was via the addition of bromine to 1-phenyl-2-phospholene 1-oxide (15) followed by dehydrobromination of the dibromophospholane 16 to give the corresponding phosphole oxide 17 (Eq. 6). 15 was

prepared by the McCormack's method by the addition of phenyldichlorophosphine to butadiene, followed by the hydrolysis of the adduct.



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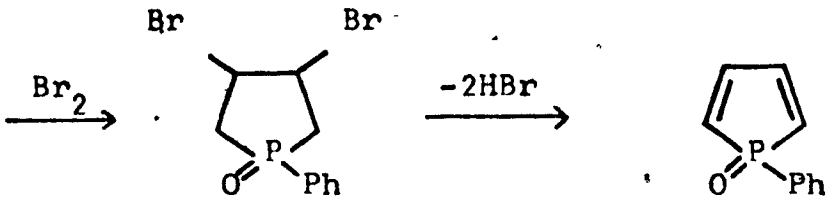
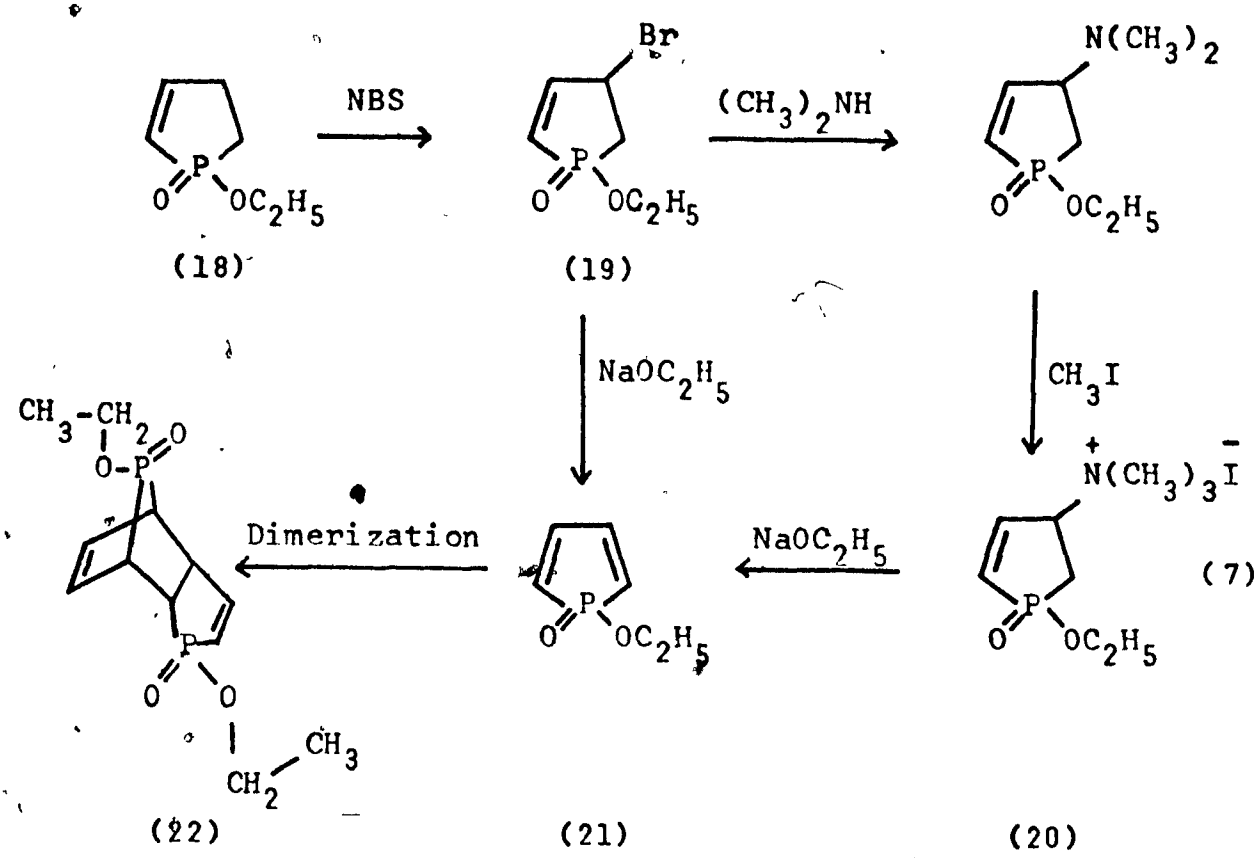


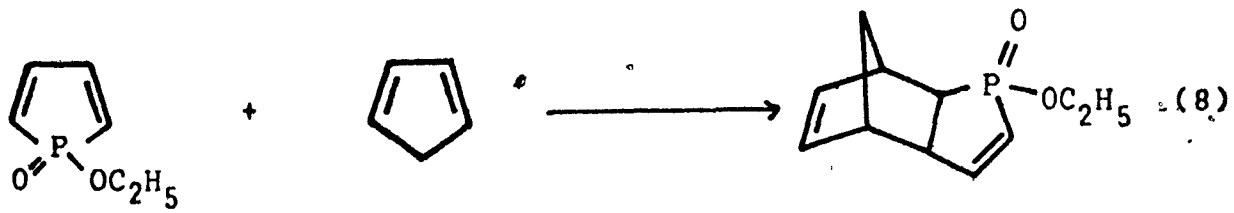
(16) (17) (6)

1-phenylphosphole oxide (17) undergoes dimerization at room temperature[21,25].

Westheimer et al[22] used similar approach for the synthesis of 1-ethoxyphosphole 1-oxide (21) in which bromophospholene 19, prepared by the N-bromosuccinimide bromination of phospholene oxide 18, was dehydrobrominated with base or by converting into the quaternary ammonium iodide 20, followed by Hofmann elimination (Eq. 7).



Rapid dimerization of 21 prevented its isolation, but it could be trapped by reacting with cyclopentadiene (Eq. 8). Recently, Chiu and Lipscomb[23] have reported the molecular and crystal structure of the dimer 22. It shows a tricyclic system and the ring juncture is shown to be endo. The stereochemistry of O atoms and O-C_2H_5 units at the P-atoms was established as shown in 22.

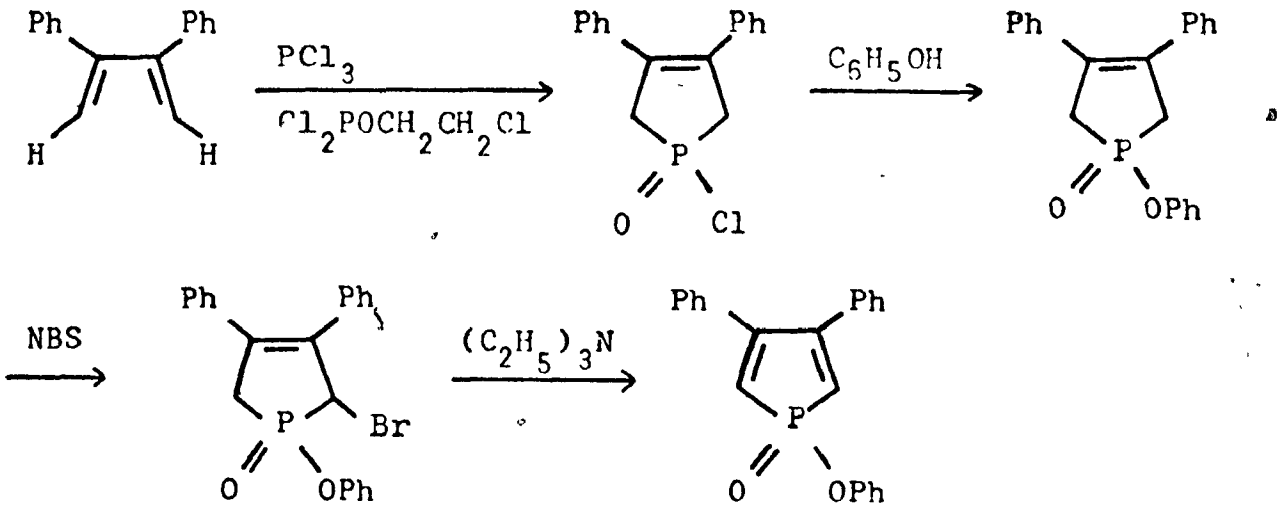


(21)

Recently, Westheimer et al[24] have reported the preparation of 1-phenoxy-3,4-diphenylphosphole 1-oxide (23) which is the first phosphole oxide that can be isolated. Previously reported 1-ethoxyphosphole 1-oxide[22] and 1-phenylphosphole 1-oxide[21,25] undergo rapid dimerization. Although 1-ethoxy-3,4-dimethylphosphole[26] is more stable in solution and dimerizes less rapidly, it has not yet been isolated.

Their synthetic approach is analogous to those previously employed[22,26] and it is illustrated in scheme I.

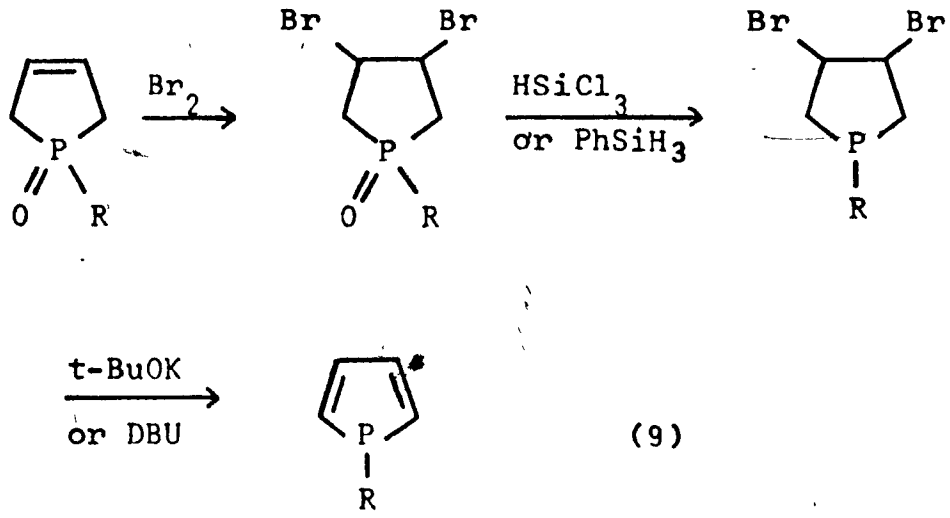
Scheme I



(23)

The simplest phospholes such as 1-methylphosphole (24a) and 1-phenylphosphole (24b) were prepared by Quin[27,28] and Markl[25] respectively. In each case, appropriate 3-phospholene oxide[16] was brominated to give the corresponding dibromophospholane, which was then reduced with trichlorosilane or phenylsilane, followed

by dehydrobromination with strong base like potassium tert-butoxide or 1,5-diazabicyclo (5.4.0) undecene-5 (DBU) (Eq. 9).

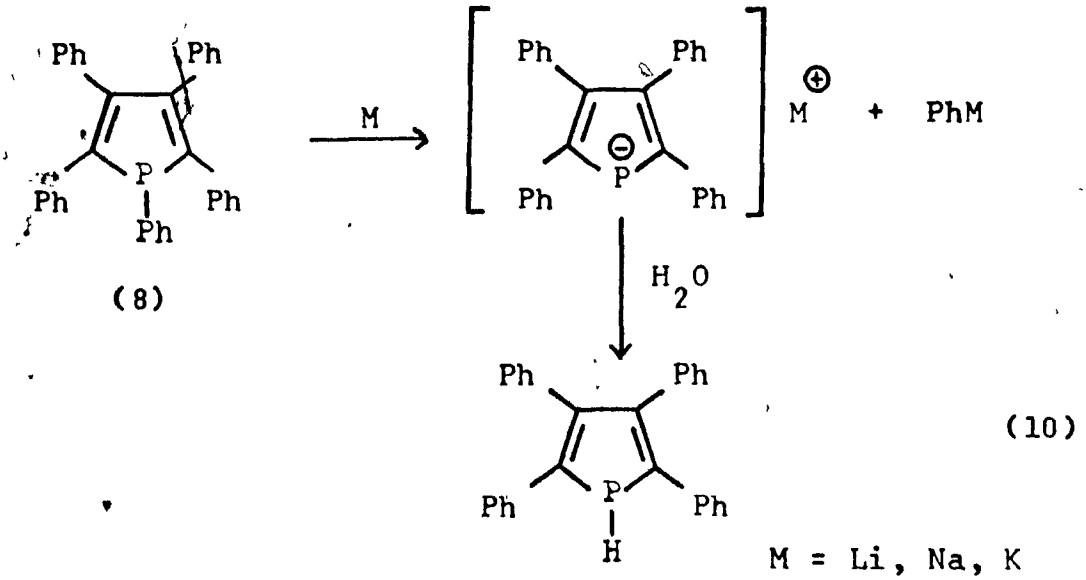


(9)

(24)

(24a) R = CH_3, (24b) R = Ph,

Braye et al[29,30] have reported the synthesis of the first P-unsubstituted phosphole 25 which was based on the reaction of pentaphenylphosphole (8) with an alkali metal such as lithium, potassium and sodium, followed by hydrolysis (Eq. 10).



(8)

(10)

(25)

Since, 1-phenylphosphole[25] is now known, this method might prove to be the possible route to the hitherto unknown parent phosphole (2).

Properties of simple phosphole

As mentioned earlier, the main interest of the phosphole system lies in its potentially aromatic character as compared with common heterocyclopentadienes and its behaviour as secondary or tertiary phosphines. Obviously, the normal tertiary phosphine reactions like the formation of oxides, sulfides, selenides, quaternary salts, phosphonium ylids, phosphine dihalides and inorganic complexes would be expected to occur at phosphorus atom of the phosphole system, thus showing the availability of non-bonding electron pair for reaction. The diminution of the phosphine-like character might indicate the possible delocalization of lone

electron pair on phosphorus into the phosphole ring.

In order to elucidate the degree of aromaticity in phospholes, several studies on X-ray, ^{1}H, ^{31}p and ^{13}C n.m.r., u.v., semi-emperical calculations, dipole moment and chemical behaviour have been investigated.

Oxidation

Like tertiary phosphines, simple phospholes readily form oxides[12,15,25,31], sulfides[12,15,25,31], selenides[12,31], P-dibromides[27,31] and quaternary salts[27,28,31,32]. Phosphole oxides can be readily obtained by treating phospholes with hydrogen peroxide. However, solutions of phospholes having aryl substituents on the ring carbon atom and alkyl substituents like methyl or benzyl on the phosphorus atom can be oxidised in air spontaneously[12,39]. By heating with sulfur or selenium, phospholes usually give the corresponding sulfides and selenides. Sulfide can also be prepared by heating the phosphole with sodium polysulfide[11,12].

The ease of oxidation is also obvious in the reaction with halogens. Phosphole P-dibromides[27,31] are prepared by treating phospholes with bromine. The reaction occurs at phosphorus rather than at the ring carbon atoms. Iodine also combines with the phosphorus of 1-methylphosphole, but in slower rate than it does with 1-methyl-3-phospholene[27].

1-methylphosphole can also be oxidised by mercuric acetate, where upon metallic mercury was formed[27]. This behaviour may be contrasted to that of thiophene, where electrophilic substitution

by the acetoxymercuri group takes place[33].

The above reactions of phosphole might reveal that it retains the reactivity of the tertiary phosphine. However, reduced reactivity towards oxidation by iodine, relative to a tertiary phosphine might indicate the diminution of phosphine character beyond that attributable to divinyl substitution.

Quaternization

Phosphole readily reacts with methyl iodide or benzyl bromide to form quaternary salts[28,31,32,39]. The reaction of 1-methylphosphole with methyl iodide[27,28] can be contrasted with that of N-methylpyrrole where reaction occurs at the α-position rather than at the nitrogen atom[34].

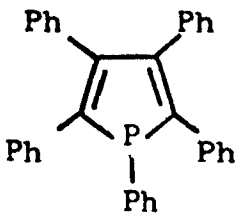
As in the case of oxidation, quaternization also destroys the 6π electron system and it appears that phosphole possesses phosphine character.

Complexation

The possession of a reactive lone electron pair on phosphorus in phosphole is supported by the formation of phosphole complexes of metal carbonyls[11,12,35] and metal halides[36,37].

Pentaphenylphosphole (8; R=Ph) on treatment with iron pentacarbonyl ($Fe(CO)_5$) gives pentaphenylphosphole-iron tetracarbonyl (26c). However, with $Fe_3(CO)_{12}$ it gives in addition to 26c, the other complexes 27 and 28[12]. In 27, the four π -electrons of the conjugated double bonds are donated to the iron atom. Thus,

phospholes resemble non-aromatic conjugated dienes which react very easily with iron carbonyls[38] and show characteristics of tertiary phosphines.



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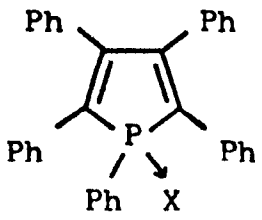
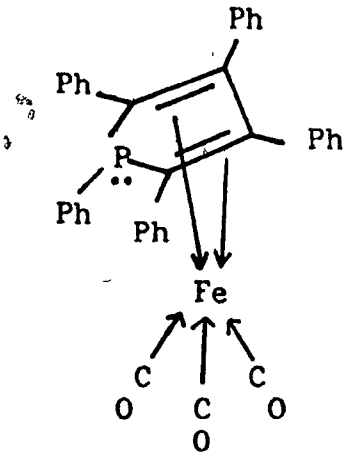


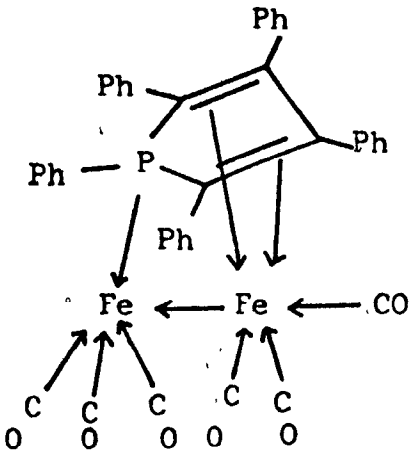
(26) (a) X = O

(b) X = S

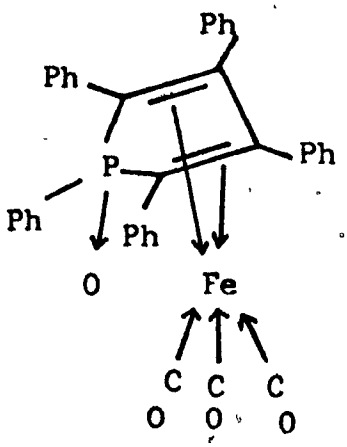
(c) X = $Fe(CO)_4$



(27)



(28)

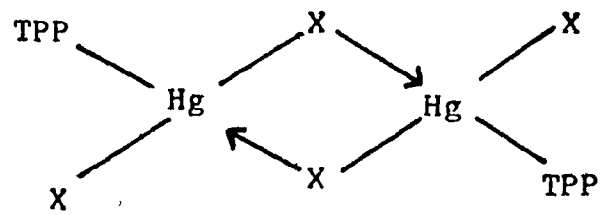


(29)

Pentaphenylphosphole oxide (26a) also undergoes complexation with $Fe(CO)_5$ to give the complex 29. However, the same reaction with the corresponding sulfide 26b results in the cleavage of P=S bond and gives only the complex 26c[12].

The reactions of TPP (11) and its oxide with different metal carbonyls such as $Fe(CO)_5$, $Fe_2(CO)_9$, $Ni(CO)_4$, $Cr(CO)_6$, $Mo(CO)_6$ and $W(CO)_6$ were investigated by Cookson and co-workers[35]. TPP and its oxide both give the π-complexes analogous to 27 and 29, on treatment with $Fe(CO)_5$ whereas a normal phosphine complex analogous to 26c was obtained in the case of the reaction with $Fe_2(CO)_9$.

TPP reacts with $M(CO)_6$ (M=Cr, Mo and W) to form $TPP.M(CO)_5$ complex. It also gives $TPP.Ni(CO)_3$ complex with $Ni(CO)_4$. Walton[36] has reported that TPP also reacts with metal halides of Pd, Pt, Hg and Rh to form complexes of the type $MX_2.2TPP$(M=Pd, Pt; X=Cl or Br); $HgX_2.TPP$ (X=Cl or Br) and $RhCl_3.TPP$. The stoichiometry of the complexes $MX_2.2TPP$ suggests that the ligand is phosphorus-bonded. Similarly $HgX_2.TPP$ (X=Cl or Br) are probably halogen bridged dimers 30 with phosphorus-bonded TPP.



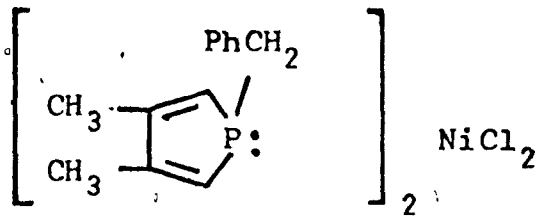
(30)

Recently, the reactions of TPP, its oxide, sulfide and selenide with some transition metal halides have been studied by Hughes and co-workers[37]. The reactivity of these ligands is found to be a function of the oxidation states of the metal, with the order being M(II) < M(III) < M(IV) < M(V). The ligands fail to react with the halides of the metal (II) such as Mn, Fe and Ni, whereas they react rapidly with Nb(V) and Ta(V). TPP also reduces both Fe(III) and Cu(II). These complexes are simple adducts of the metal halides. These adducts are easily hydrolysed on exposure to air and the phosphole is displaced by coordinating solvents like acetonitrile and even, ether. These facts reveal the weakness of the metal-phosphorus bond.

Hughes[37] concluded that TPP and its oxide, sulfide and selenide are weak donors, especially with lower valent metal halides. They closely follow the behaviour of their triphenylphosphine analogs in the reactions with Nb(V) and Ta(V) halides. The weakness of metal-phosphorus bond in the phosphole complexes might indicate the possible delocalization of lone pair of electrons on phosphorus atom into the ring, although steric effects may also be involved.

Quin[27] also suggested that 1-methylphosphole has reduced phosphine character since it fails to form the typical coloured complexes with ethanolic nickel chloride and with carbon bisulfide. 1-Benzylphosphole[39,40] also does not form a complex with nickel chloride. Quin[40] has reported very recently that 1-benzyl-3, 4-dimethylphosphole readily forms a complex 31 with nickel chloride, where the phosphole ligand is bound to the metal through σ-bonds.

The phosphine-character of this phosphole is also evident from the ready quaternization with alkyl halides.



(31)

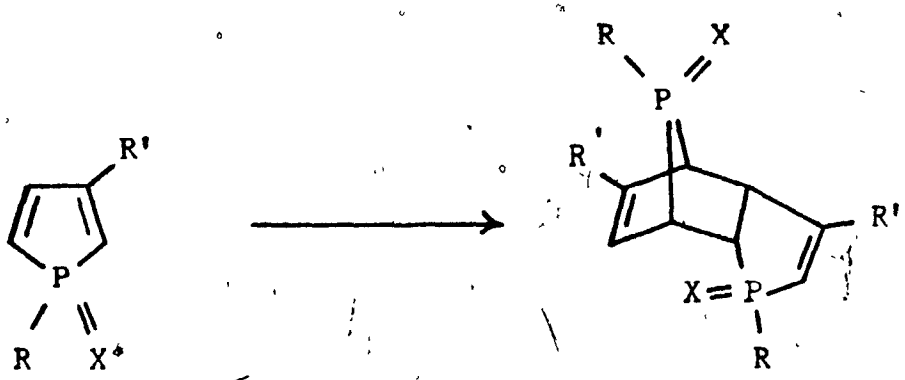
Basicity

1-methylphosphole[27], unlike 1-methyl-3-phospholene is not extracted from pentane even by 2N hydrochloric acid. This shows that 1-methylphosphole is less basic than phospholene. The behaviour of this phosphole in the formation of a polymeric material on treatment with 6N hydrochloric acid is similar to that of pyrrole, in being unstable in acid. 1-Methylphosphole has a very low pk_a value of 0.5 compared with a value of 5.2 estimated for the model compound, divinylphosphine. The lower pk_a value of 1-methylphosphole has been attributed to the delocalization of the phosphole ring system as in the pyrrole system.

The site of protonation in phosphole derivatives has been established by Hughes et al[41], very recently. It was found that for TPP, the site of protonation is at the phosphorus atom. This should be contrasted to that of pyrrole, where α or β ring carbon atoms are protonated, depending upon the substitution pattern[42].

Dimerization

Phosphole oxides and sulfides without aryl substituents on the ring dimerize very rapidly to give a Diels-Alder dimer 32[21,22,25] (Eq. 11).



(11)

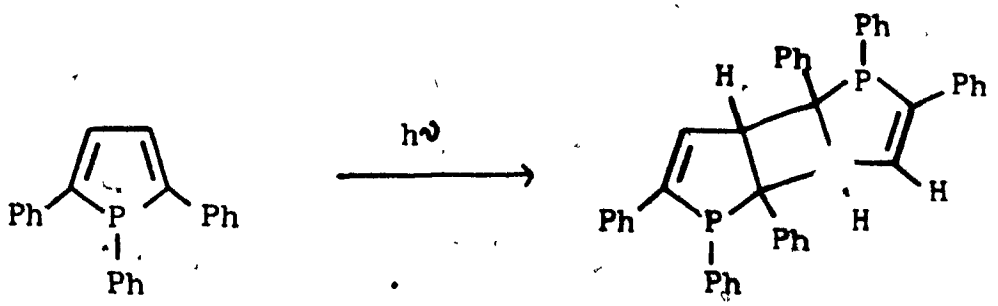
(32)

R = Ph, OEt; R' = H, CH_3; X = O, S

1-Ethoxyphosphole 1-oxide (21)[22] dimerizes too rapidly to allow its isolation, but its existence has been demonstrated by its ultraviolet spectrum and by trapping it as a Diels-Alder adduct with cyclopentadiene (Eq. 8). Highly substituted phosphole oxide such as pentaphenylphosphole is quite stable under normal conditions, whereas TPP oxide undergoes photodimerization[31] and the corresponding sulfide tends to dimerize[31] on exposure to daylight. This chemical behaviour is not surprising, since cyclopentadiene and thiophene 1, 1-dioxide[43] undergo similar dimerization.

Barton et al[44] have reported that TPP (11) forms a photodimer 33 (Eq. 12), on irradiation with a medium pressure 450 watt mercury lamp. The behaviour of the photodimerization would

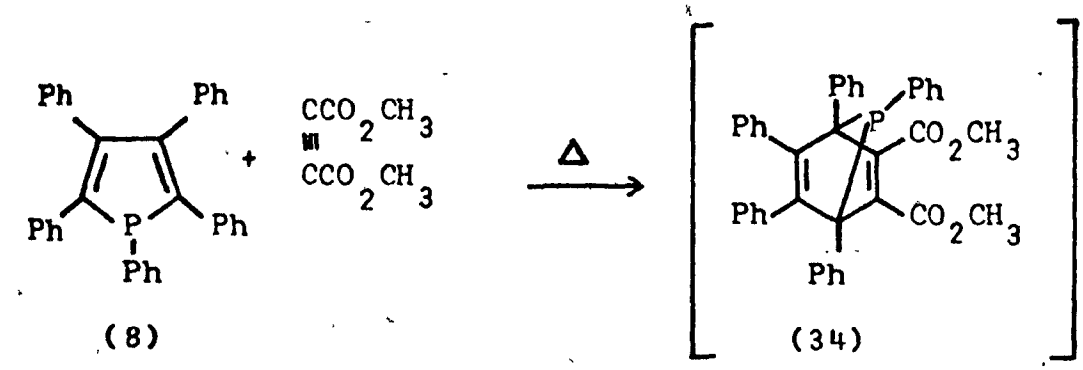
seem to cast doubt upon the possible aromatic character of the phosphole system, in view of the fact that thiophene fails to undergo photodimerization. This behaviour of TPP (11) should also be contrasted to that of 1,2,5-triphenylpyrrole[19] which remained unchanged on irradiation under the same condition.



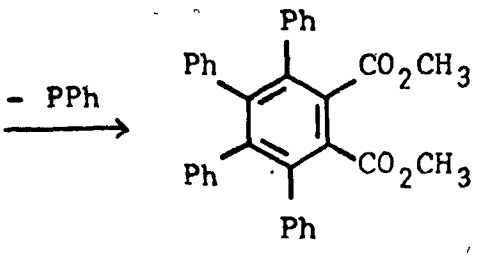
(11) (33) (12)

Diels-Alder Reaction

Pentaphenylphosphole (8) reacts with dimethyl acetylenedicarboxylate in a Diels-Alder reaction[12] to yield dimethyl tetraphenylphthalate (35) which must have resulted from the intermediate compound 34 by the extrusion of P-Ph group. (Eq. 13).



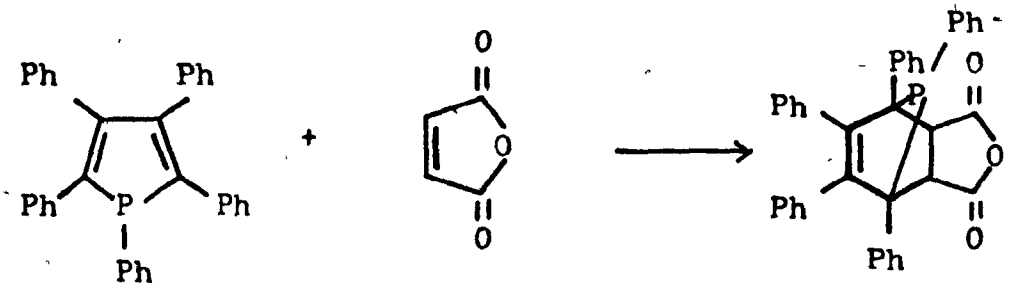
(8) (34)



(35)

(13)

However, 8 gives normal Diels-Alder adduct 36 with maleic anhydride[12]. (Eq. 14).

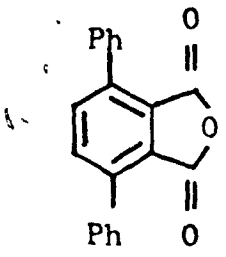


(8) (36)

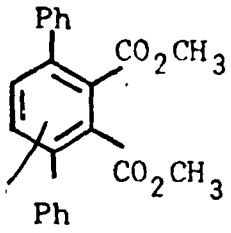
(14)

TPP also undergoes similar reactions[31], but with maleic anhydride, the extrusion of the phosphorus fragment also occurs to form the aromatized compound 37.

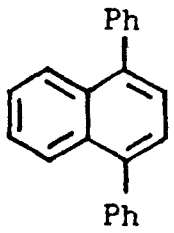
Pentaphenylphosphole oxide reacts more readily with maleic anhydride whereas the corresponding sulfide has the same reactivity as the parent phosphole[12]. TPP oxide forms the normal adduct with maleic anhydride[31] and acrylonitrile[31,35]. However, with dimethyl acetylenedicarboxylate in hot benzene[31] and with benzyne[45], the phosphorus fragment is again lost in each case to give the product 38 and 39 respectively.



(37)



(38)



(39)

1-Ethoxyphosphole 1-oxide[22] (21) undergoes Diels-Alder reaction as shown by the reaction with cyclopentadiene (Eq. 8).

Whereas phosphole and derivatives behave as typical dienes in the Diels-Alder reaction, pyrrole undergoes such reaction with considerable difficulty and it only gives the product of substitution[46]. Thiophene does not enter into reactions with dienophiles[47].

Aromatic Character of simple phospholes

During the past decade, a great deal of work has been done in an attempt to gauge the extent of delocalization of phosphorus electron pair in the phosphole system. However, this question

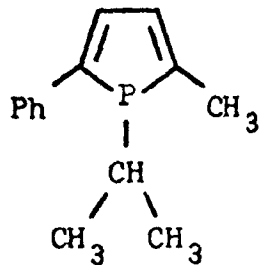
remains a subject of discussion and arguments.

The chemical behaviours of pentaphenylphosphole led Braye[12] to conclude that "phospholes behave as tertiary phosphines having a conjugated diene system and possess little or no aromatic character".

Quin[27], on the other hand suggested that the phosphine-like character of 1-methylphosphole does not necessarily show that delocalization is absent in phosphole. His argument is that the delocalization is expected to be accompanied only by a diminished, but not the absence of phosphine-like character.

Perhaps, this apparent non-aromatic behaviour in the chemical sense can be misleading. Brown[48] has pointed out that the formation of oxides and quaternary salts for pyrrole and phosphole systems would involve the arrangements of a planar configuration to a tetrahedral one about the hetero-atom. The difference in energy between these two arrangements for nitrogen is very much greater than for phosphorus atom, thus phosphole readily undergoes these reactions. Moreover, Brown[48] has calculated that the planar configuration of phosphole has a substantial conjugation energy of 1.49β, close to that of pyrrole (1.37β). The argument made by Brown is not valid in view of Mislow's work[50], which has shown that the energy barrier to inversion about the phosphorus atom in 1-isopropyl-2-methyl-5-phenylphosphole (40) has the unusually low value of 16 k cal/mole compared with the values of 29-36 k cal/mole for various alkyl and aryl phosphines. This has been interpreted as a manifestation of cyclic (3p-2p)π conjugation, which is maximum in the planar transition state, relative to

pyramidal ground state.



(40)

From the thermochemical measurements, Mortimer[49] found that the dissociation energy for P=O bond of pentaphenylphosphole oxide is very much less than those of other phosphine oxides (Table II), and has suggested that the decrease in dissociation energy might be a measure of the conjugation energy of the phosphole system relative to its oxide.

TABLE II

Dissociation Energies of P=O bonds in Some Phosphine Oxides[7]

Phosphine Oxide	$D_{P=O}$ (k cal/mole)
Pentaphenylphosphole Oxide	100.4 ± 9.5
9-Phenyl-9-phosphafluorene Oxide	126.0 ± 9.0
Triphenylphosphine Oxide	128.4 ± 5.5
Trimethylphosphine Oxide	139.3 ± 3.0

NMR measurements provide some supporting evidences for the possible aromatic character of phosphole system. Quin[27] has pointed out that the downfield position of the ring protons in the n.m.r. spectrum of 1-methylphosphole is in accord with that of related heteroaromatics and this results from the anisotropic magnetic susceptibility of the ring i.e. "ring current" effect. The low-field shift of phosphorus in ^{31}P n.m.r. spectrum of 1-methylphosphole relative to noncyclic divinyl compounds can also be attributed to the delocalization of the lone pair of electrons on phosphorus into the cyclic π system. Quin[27] also noted that u.v. and mass spectra of 1-methylphosphole are similar to those of N-methylphosphole. Markl[17] has also stated that since the chemical shifts of the ring protons and of the methyl groups in 2,5-dimethyl-1-phenylphosphole are very similar to those of related furan, pyrrole and thiophene derivatives, the phosphole ring might possess some aromatic character. Markl[25] also found that the chemical shifts of the ring protons in 1-phenylphosphole are in the normal aromatic region and that the spectrum is similar to that of N-phenylpyrrole.

From the ^{13}C NMR spectral parameters of 1-phenylphosphole, Jakobsen[51] has pointed out that there is some degree of delocalization of phosphorus electron pair into the ring.

From an X-ray crystallographic study of TPP, Clardy[52] has concluded that the phosphole shows little if any electron delocalization. Quin[39] has recently reported from an X-ray analysis of 1-benzylphosphole that there is a slight puckering of the phosphole ring and retention of pyramidal configuration at phosphorus,

which is in agreement with the conclusion made by Mislow[50] who studied the barrier to pyramidal inversion at phosphorus in phospholes.

Very recently, Mislow[53] has studied the kinetics of the cleavage of phosphonium hexafluoro-antimonates by sodium methoxide (Eq. 15).

$$R_3\overset{+}{P}CH_2CH_2CN + \overset{-}{O}CH_3 \rightleftharpoons R_3\overset{+}{P}CH_2\overset{-}{C}HCN + CH_3OH$$

$$R_3\overset{+}{P}\text{-}CH_2\text{-}\overset{-}{C}H\text{-}CN \longrightarrow R_3P + CH_2{=}CHCN \qquad (15)$$

Mislow made the assumption that because the P-C σ bonding electrons in cyanoethylphospholium ion become part of the cyclic 6π electron system in the phosphole formed, there should be an acceleration effect if there is any delocalization of lone pair on phosphorus. Mislow found that phospholium ion of TPP is cleaved at a faster rate than those of other comparable phospholium ions, and this has been attributed to the delocalization of the lone pair of electrons on phosphorus in phospholes.

Dipole moment studies on TPP by Hughes[9] gives results of 1.4D and 1.08D in p-xylene and dioxan respectively. However, these values are very close to that of triphenylphosphine[54] which has a value of 1.4D in benzene.

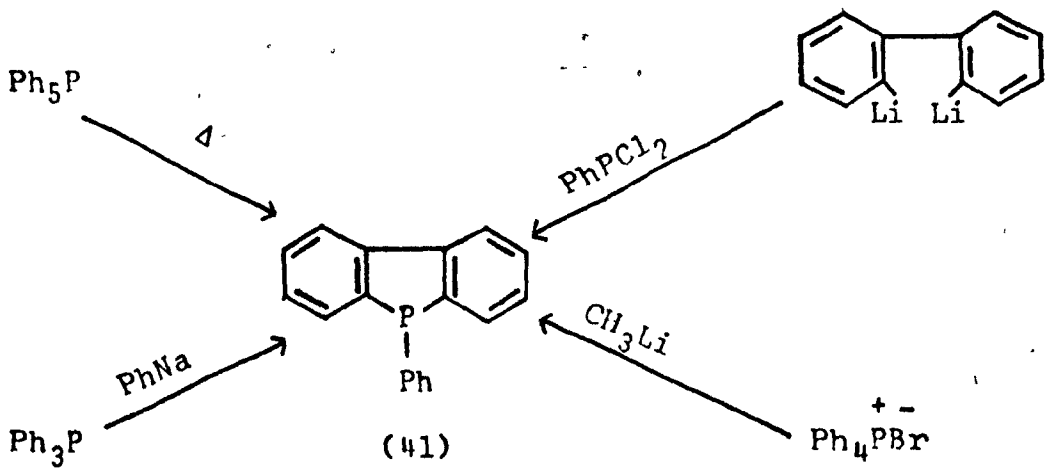
In view of the behaviour of phospholes in complexation reaction, formation of oxides, sulfides, selenides, quaternary salts and P-dibromides, it is evident that phosphorus in phospholes possesses reactive lone pair of electrons. These behaviours cast

doubt upon the notion of significant delocalization of lone pair of electrons into the phosphole ring. However, thermochemical measurements, semiempirical calculations, n.m.r., u.v. and mass spectral data suggested the possible aromatic character of phospholes. From the above evidences, it may be concluded that phospholes might possess some aromatic character, although they behave like tertiary phosphines.

Synthesis of Dibenzophosphole

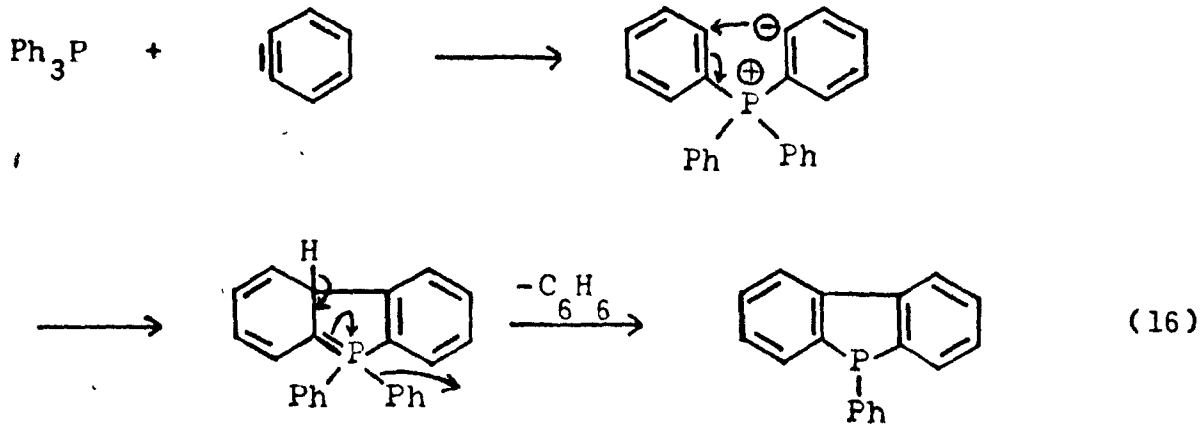
The first dibenzophosphole, 9-phenyl-9-phosphafluorene (41) was prepared by Wittig[55] in 1953 and this isolation was the impetus for the preparation of other phosphole derivatives. The four different methods are summarized in Scheme II. However, in all cases the yields were poor.

Scheme II



Several modified routes[49,56] were later employed for the preparation of higher yields of 41 and its derivatives with substituents such as $-CH_3$ and $-N(CH_3)_2$ on the rings.

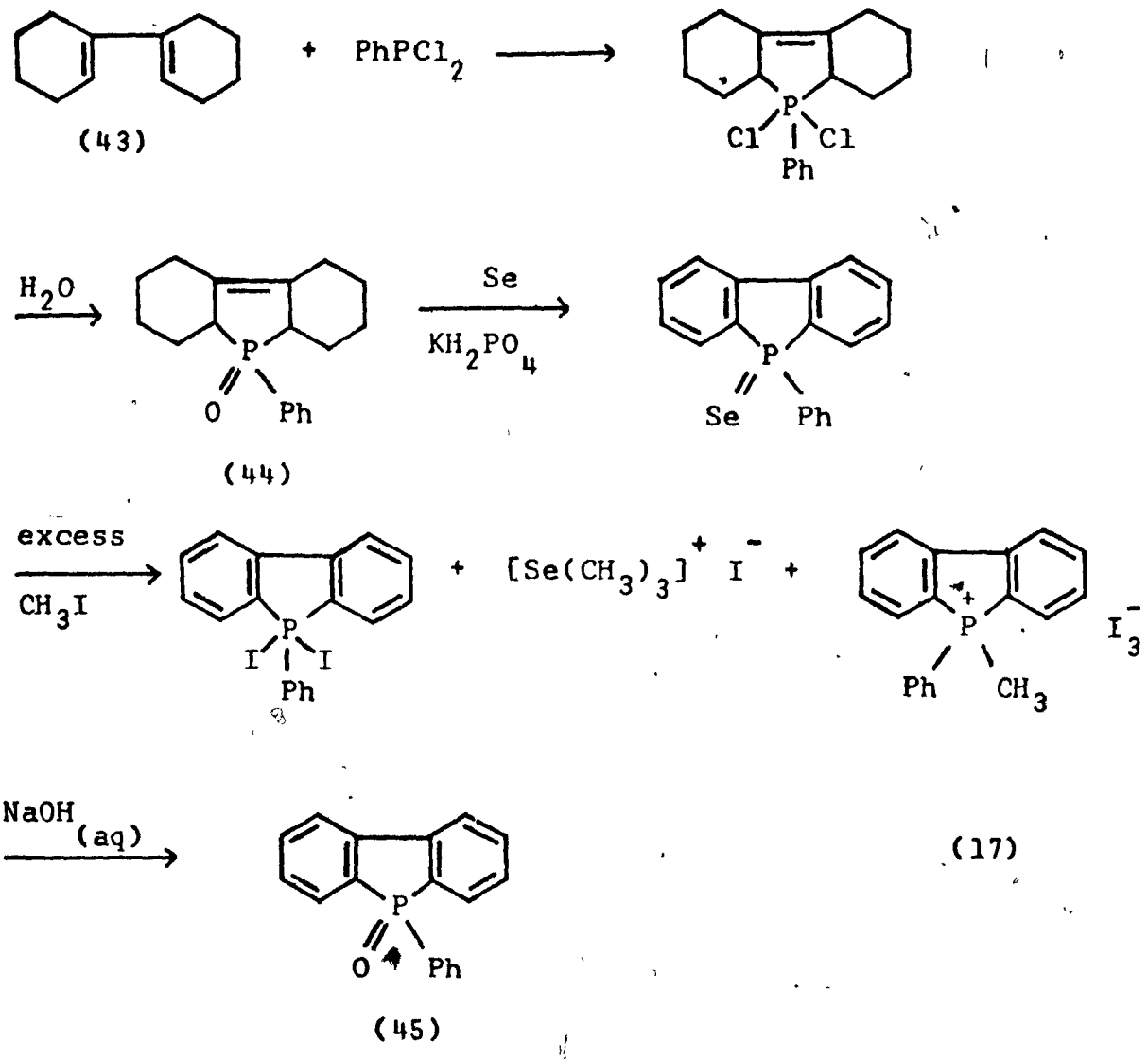
Wittig[57] and Zbiral[58] used the same approach which involved the reaction of benzyne with triphenylphosphine to give initially 42 followed by elimination of benzene. (Eq. 16).



(16)

(42) (41)

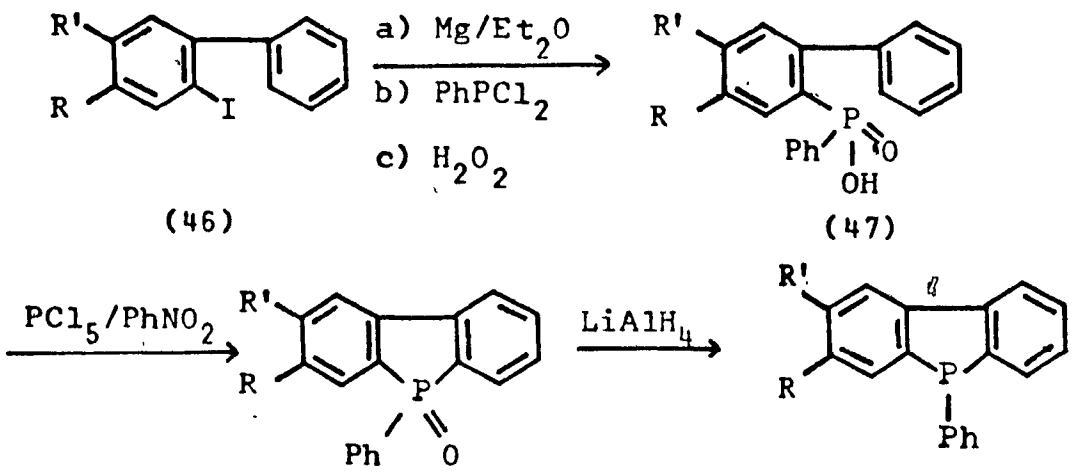
Campbell[31] used a more conventional approach for the synthesis of dibenzophosphole and this was based on McCormack's synthesis[16] of 3-phospholene oxides. 1,1'-biscyclohexenyl (43) was treated with phenyldichlorophosphine, followed by hydrolysis to afford the phosphole oxide 44. Dehydrogenation with selenium and potassium dihydrogen phosphate gave the corresponding selenide. Methylation removed the selenium and the quaternary salt was decomposed by aqueous base to yield dibenzophosphole oxide 45. (Eq. 17).



(17)

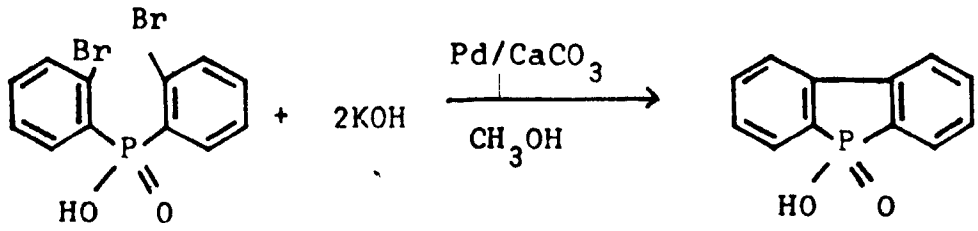
Campbell's second approach[59] was the cyclization of 2-biphenylylphenylphosphinic acid (47) according to Scheme III. The starting phosphinic acid was obtained by the Grignard reaction of appropriate iodobiphenyl (46) with phenyldichlorophosphine.

Scheme III



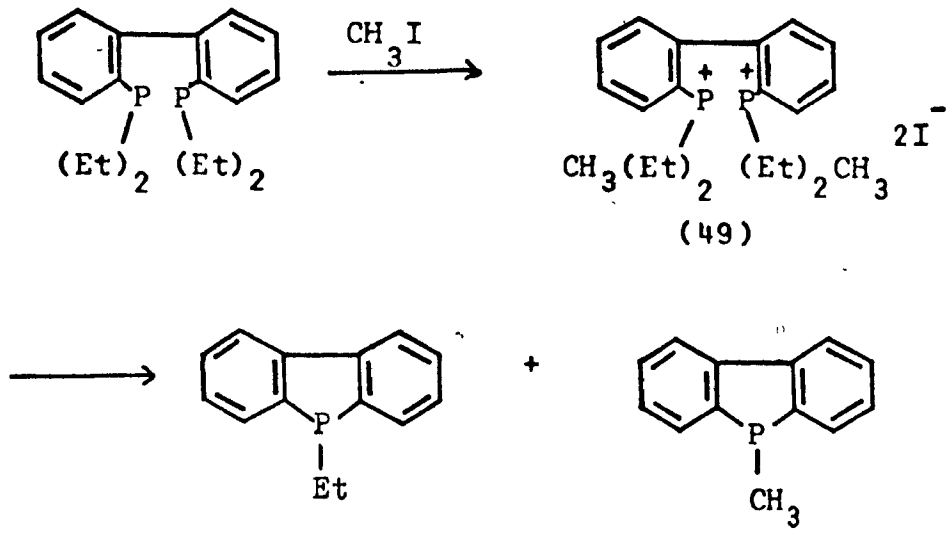
R = H or Me, R' = H or Br

A synthesis of 9-hydroxyphosphafluorene 9-oxide (48) was developed by Freedman and Dodk[60] (Eq. 18).



$$+ 2KBr + H_2O + CH_2O \qquad (18)$$

A novel synthesis of dibenzophosphole was reported by Millar[61] which involved the pyrolysis of diphosphonium salts 49 (Eq. 19). The mechanism of this reaction is still unknown.



(19)

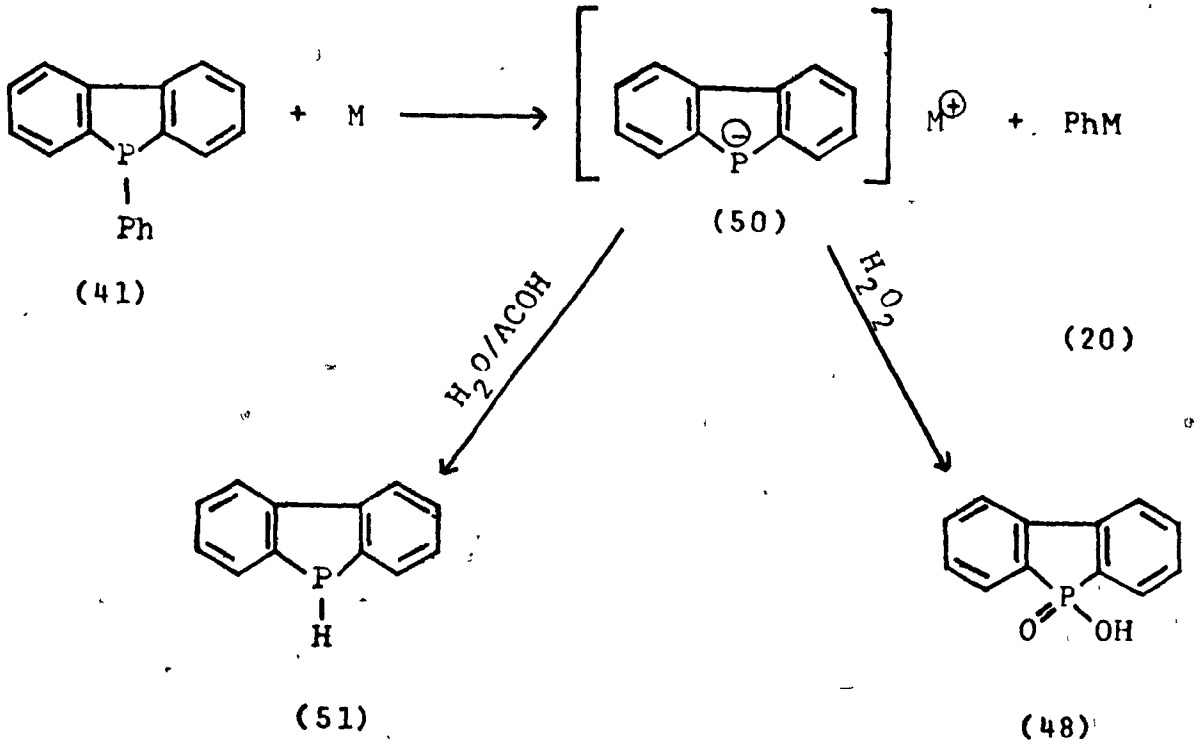
Properties of Dibenzophosphole

In general, all the reported reactions of dibenzophosphole occur at the phosphorus atom. Thus, like simple phospholes, dibenzophospholes undergo the normal tertiary phosphine reactions such as the formation of oxides, sulfides, selenides and quaternary salts. These reactions reveal the availability of lone pair of electrons on phosphorus for combination.

From thermochemical measurements, Millar[49] has found that dibenzophosphole possesses a slightly lower P=O bond dissociation energy than for normal phosphine oxides. The $D_{P=O}$ value is 126 ± 9 k cal/mole which is comparable with that of triphenylphosphine oxide, but it is lower than that of trimethylphosphine oxide (Table II). Since this value is higher than that of pentaphenylphosphole, it appears that the extent of delocalization of phosphorus lone electron pairs is small.

Alkali metals such as lithium, sodium, potassium and cesium cleave the P-Ph bond of 9-phenyl-9-phosphafluorene (41) to give

the metal phosphide 50, which can be trapped by treating with hydrogen peroxide to form 9-hydroxy-phosphafluorene 9-oxide (48). 50, on hydrolysis with H_2O/AcOH gives the P-unsubstituted dibenzophosphole 51[29,30] (Eq. 20).



M = Li, Na, K, Cs

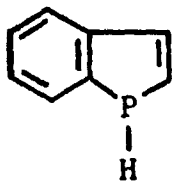
Dibenzophosphole also forms a complex with Cu(I) and Cu(II) chlorides[37].

Benzophospholes

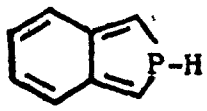
The field of benzophosphole chemistry may be divided into two, namely (a) benzo[b]phosphole or phosphindole (4) and (b) benzo[c]phosphole or isophosphindole (6).

In phosphindole, the benzene ring is fused to the 2- and

3- positions of the phosphole ring. Fusion at 3- and 4- positions gives isophosphindole.



(4)



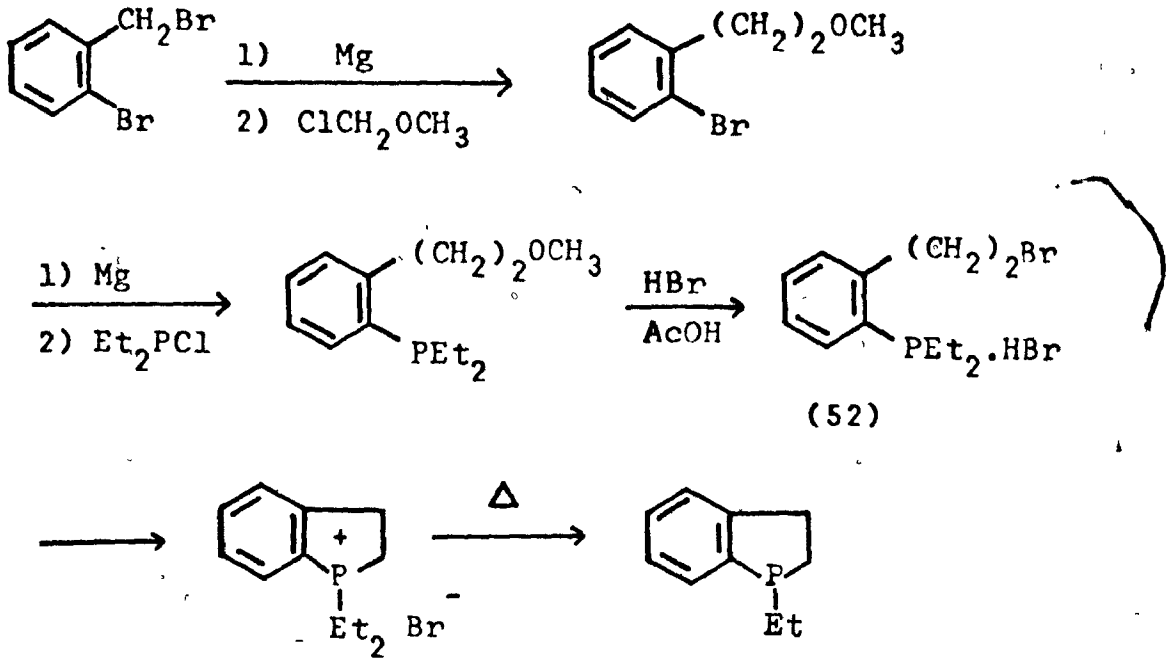
(6)

Synthesis of Benzo[b]phosphole or Phosphindole

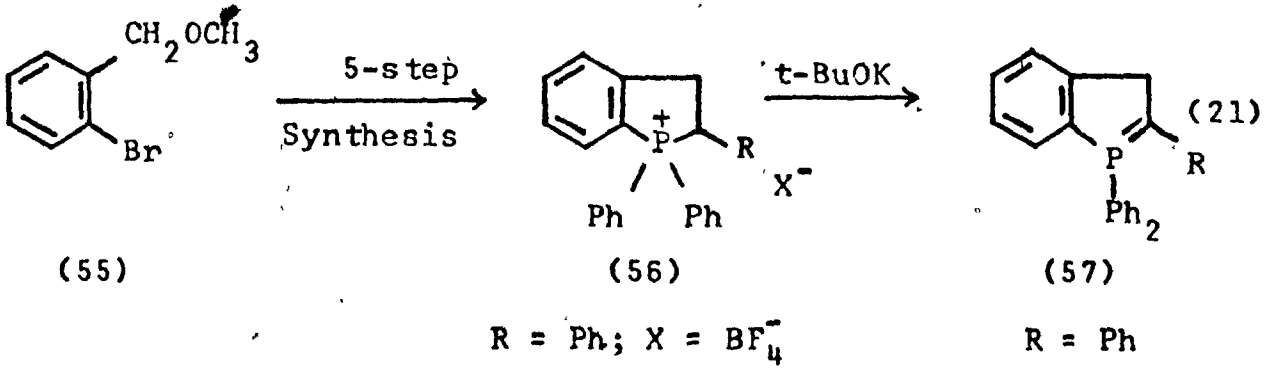
There has been no report on the synthesis of 4 itself. Benzo[b]phosphole derivatives have been reported, but are rare in contrast to other phospholes.

A 2,3-dihydrobenzo[b]phosphole derivative 54 was first synthesized by Mann and Millar[62], according to Scheme IV. The key step was the intramolecular cyclization of 52 to 53. The final step involved the thermal decomposition of the phosphindolinium salt 53 to give 2,3-dihydro-1-ethylbenzo[b]phosphole (54).

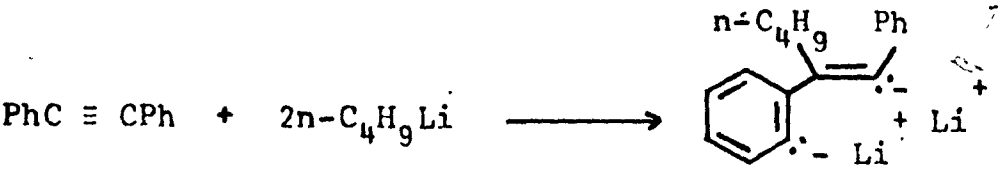
Scheme IV



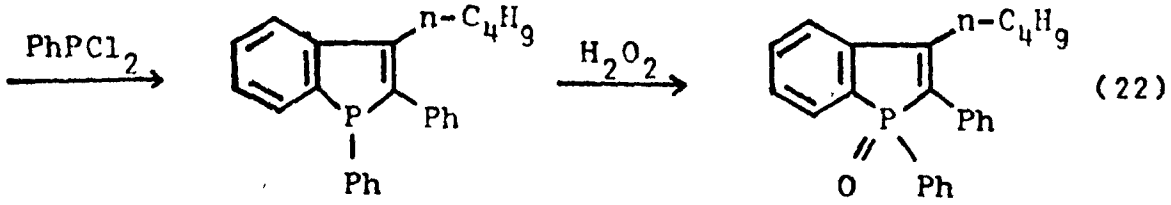
Another reported benzo[b]phosphole derivative is the cyclic ylid[63] 57. It was obtained via a 6-step synthesis, starting from o-bromobenzyl methyl ether (55). The final step involved the dehydrohalogenation of the cyclic phosphindolinium salt 56 ($X=BF_4^-$) with potassium tert-butoxide (Eq. 21).



The synthesis of highly substituted benzo[b]phosphole was reported by Rausch and Klemann[64]. Their synthetic approach involved the reaction of diphenylacetylene with n-butyllithium to produce a dilithium derivative 58, which on treatment with phenyldichlorophosphine gave 3-n-butyl-1,2,-diphenylbenzo[b]-phosphole (59) (Eq. 22). The corresponding oxide 60 was prepared by peroxide oxidation.

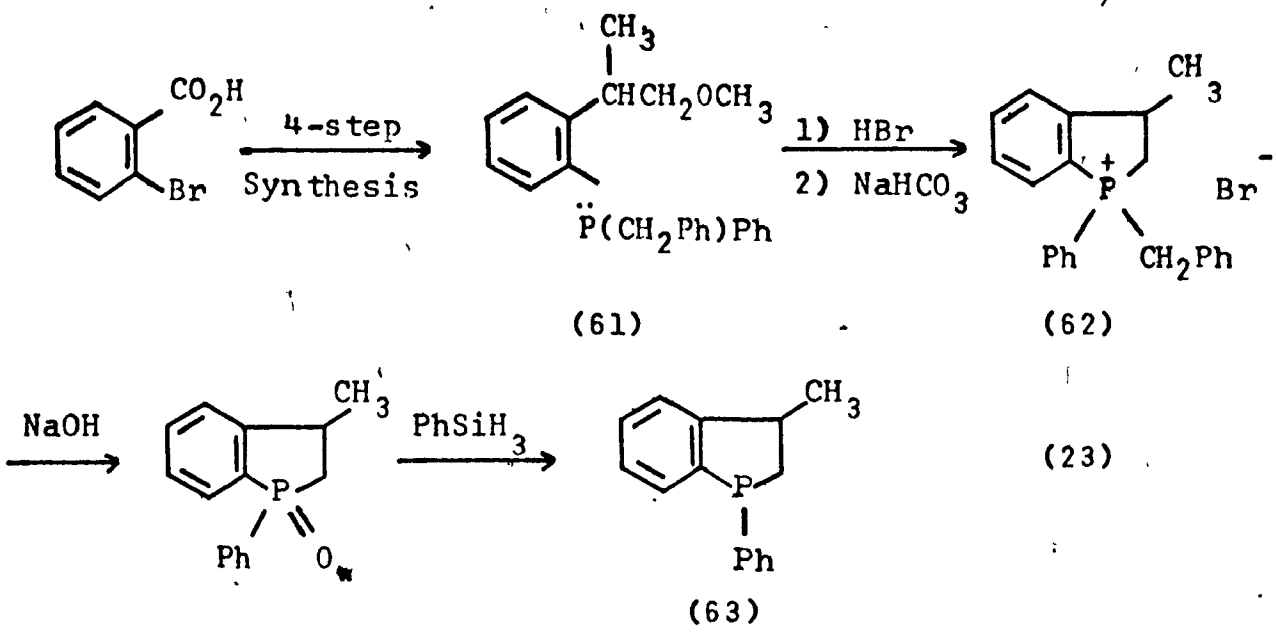


(58)



(59) (60) (22)

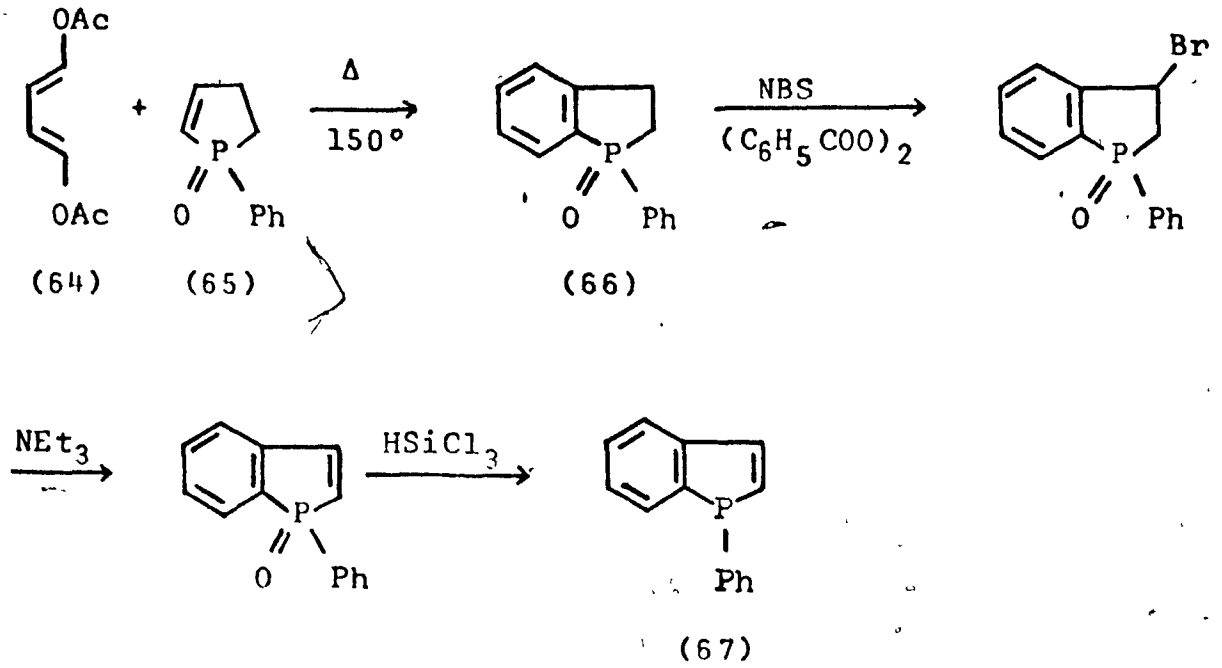
Recently, Mislow and co-workers[50] have reported the synthesis of 2,3-dihydro-3-methyl-1-phenylbenzo[b]phosphole (63) which involved a 7-step synthesis and the key step was the cyclization of 61 to 62, analogous to that used by Mann and Millar[62] (Eq. 23).



(61) (62) (23) (63)

Other than the above syntheses, there has been few reports on the benzo[b]phosphole system. More recently, Chan and Wong[65] have developed a synthesis of the first simple benzo[b]phosphole derivative, 1-phenylbenzo[b]phosphole (67). The synthetic route is shown in Scheme V. The benzene ring was constructed by the method of Hill and Carlson[67]. By heating E,E-1,4-diacetoxybutadiene (64) with 1-phenyl-2-phospholene oxide (65) furnished the adduct 66. N-bromosuccinimide bromination, followed by dehydrobromination and reduction gave 1-phenylbenzo[b]phosphole (67).

Scheme V



Properties of Benzo[b]phosphole

Like tertiary phosphines, 1-phenylbenzo[b]phosphole is easily oxidised by air to the oxide and it quaternizes with benzyl bromide[65,66].

2, 3-Dihydro-1-ethylbenzo[b]phosphole (54) forms a complex with palladous bromide[62].

Supporting evidence for the possible aromatic character in benzo[b]phosphole is provided by the u.v. and the n.m.r. spectra of 1-phenylbenzo[b]phosphole[65,66]. Its u.v. spectrum closely resembles that of 1-phenylindole. The phenyl and vinylic protons are well separated in the 220 MHz n.m.r. spectrum. The P-CH_α and P-CH_β coupling constants are in agreement with those reported for 1-methylphosphole[27]. The chemical shifts of the vinylic protons are in the normal aromatic region. These observations have been

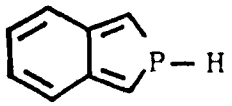
attributed to the delocalization of lone pair of electrons on phosphorus and thereby imposing aromatic character on the phosphole ring.

Mislow and co-workers[50] have measured the pyramidal inversion barriers of substituted benzo[b]phosphole and dibenzophosphole and compared with those of model compounds. They have found the unusually low barrier to pyramidal inversion (15-16 k cal/mole) at phosphorus in phosphole system. But in benzo[b]phosphole and dibenzophosphole, a significant increase in barrier height (8 and 10 k cal/mole respectively) was observed, relative to the parent system. The abnormally low barrier to inversion at phosphorus in phosphole system is interpreted as a manifestation of cyclic (3p-2p)π conjugation, which is maximum in the planar transition state, relative to pyramidal ground state. The increase in barrier height in benzo[b]phosphole and dibenzophosphole has been attributed to a virtual disruption of the possible delocalization in phosphole system, upon annulation.

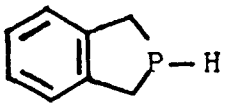
Although the properties of phospholes and dibenzophospholes have been studied widely, the chemistry of benzo[b]phosphole has been less explored. More evidences from the X-ray analysis, dipole moment measurements, thermochemical measurements and the other chemical behaviours will be necessary in order to solve the problem concerning the degree of aromaticity in benzo[b]phosphole system.

Synthesis of Benzo[c]phosphole or Isophosphindole*

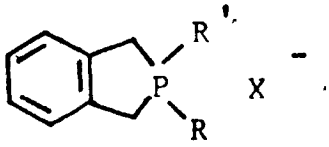
The chemistry of isophosphindole (6) itself is still unknown and its derivatives are also very rare. However, isophosphindoline (68) and isophosphindolinium (69) systems have been reported.



(6)

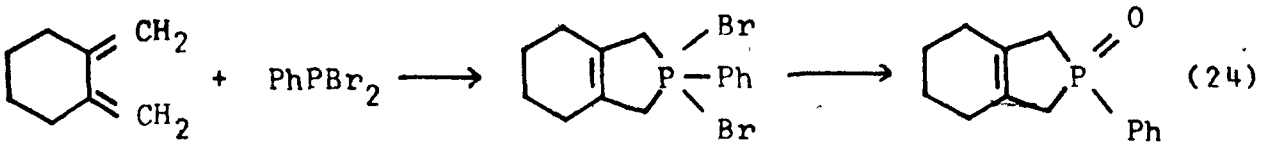


(68)



(69)

The isophosphindoline system was first synthesized by McCormack[16] who treated 1,2-dimethylenecyclohexane (70) with phenyldibromophosphine to produce isophosphindolinium salt 71, which on hydrolysis gave 4,5,6,7-tetrahydro-2-phenylisophosphindoline 2-oxide (72) (Eq. 24).



(70) (71) (72) (24)

Mann et al[68,69] investigated several syntheses of 2-phenylisophosphindoline (74). In their first attempt, o-xylylene dibromide

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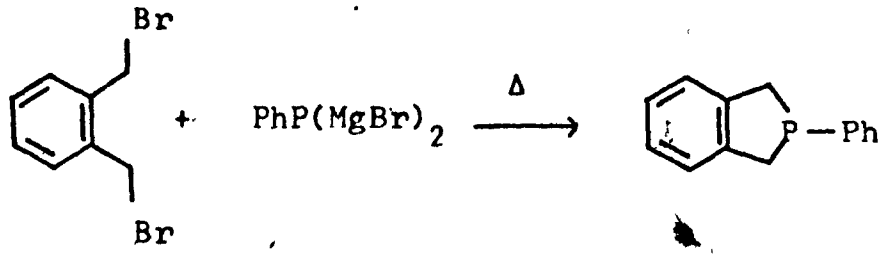
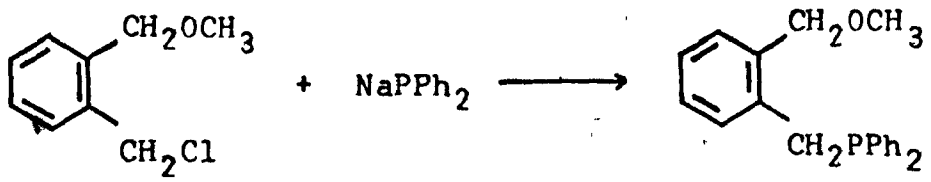
* Isophosphindole is the trivial name for benzo[c]phosphole according to Ring Index and this term will be used frequently throughout this thesis.

(73) was treated with the Grignard reagent $C_6H_5P(MgBr)_2$ to form an amorphous powder which was then thermally decomposed to give 74 in very low yield (Eq. 25).

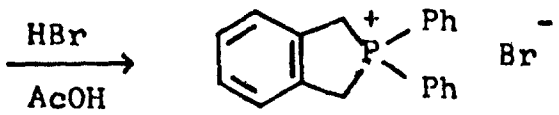


(73) (74) (25)

An improved procedure was achieved by treating o-methoxymethylbenzyl chloride (75) with $(C_6H_5)_2PNa$ to afford the phosphine 76. This phosphine in acetic acid-hydrobromic acid gave 2,2-diphenylisophosphindolinium bromide (77) (Eq. 26).

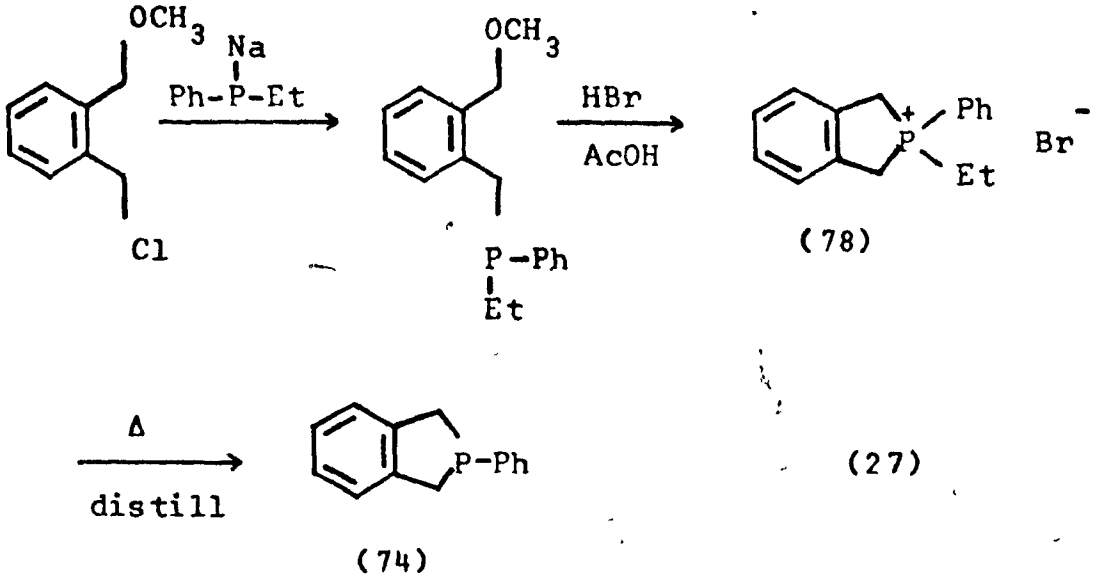


(75) (76)

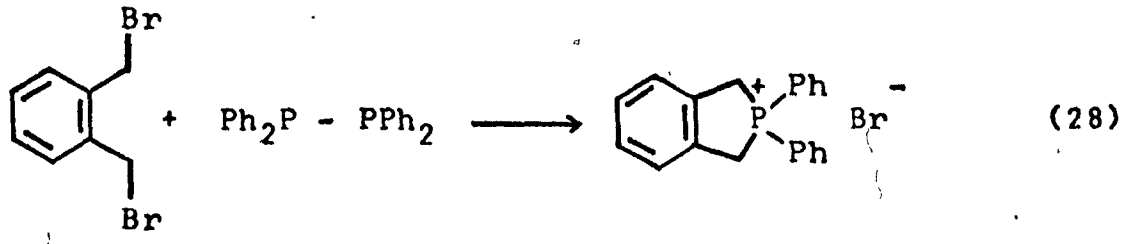


(77) (26)

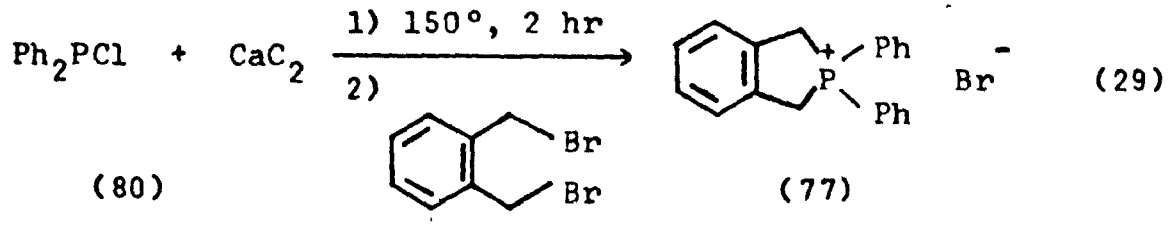
A modified synthesis of 74 was developed by the same group[69], as illustrated in Eq. 27. The final step involved the thermal decomposition of the isophosphindolinium bromide 78 to yield 74.



Markl[70] and more recently Snider and Berlin[71] have reported facile synthetic entries to the isophosphindolinium system 69. The synthetic approach of Markl was the treatment of o-xylylene dibromide (73) with tetraphenyldiphosphine (79) to produce the isophosphindolinium bromide 77 (Eq. 28).



While our work was in progress, the report on the synthesis of 77, by Snider and Berlin[71] appeared. They heated diphenyl phosphonous chloride (80) and CaC_2 in the presence of o-xylylene dibromide (73) to afford 77 (Eq. 29).

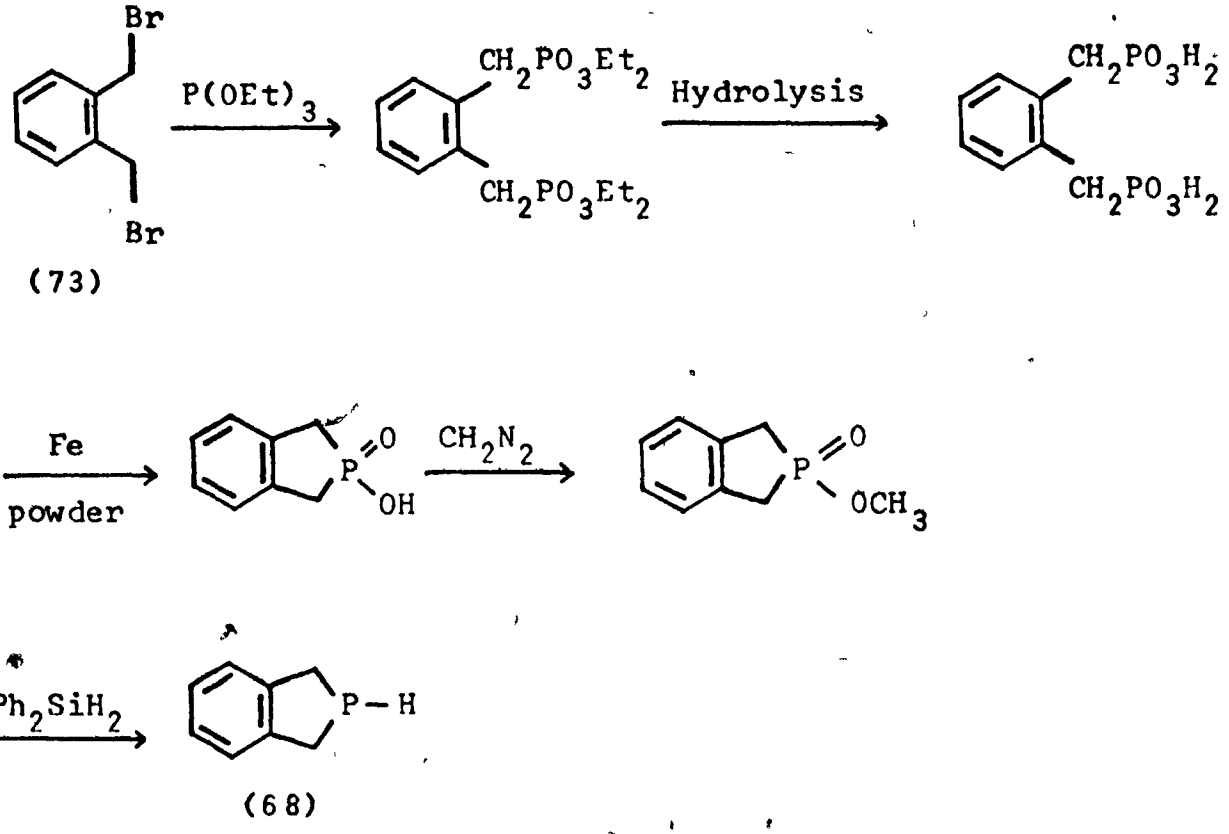


(80) (77) (29)

Two reports on the syntheses of isophosphindoline[72] and isophosphindole[73] derivatives appeared, at the time of the completion of our work.

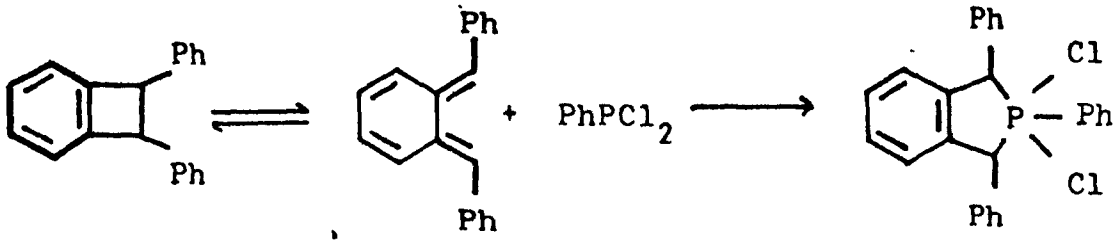
One report was by Robinson and Lewis[72] who prepared isophosphindoline (68), starting from o-xylylene dibromide (73), according to Scheme VI.

Scheme VI

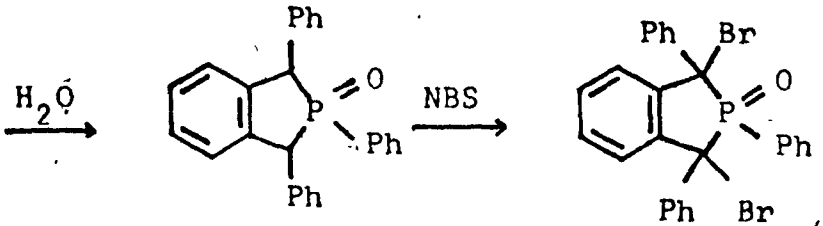


The mechanism of the reaction with iron powder has not yet been determined.

The other report was by Holland and Jones[73] who prepared the substituted isophosphindole derivative. This method was based on the McCormack's reaction between the o-quinonoid tautomer 81 of diphenylbenzocyclobutene and phenyldichlorophosphine to form an adduct, which on hydrolysis afforded the phospholene oxide 82. N-bromosuccinimide bromination, followed by reduction with copper powder furnished 1,2,3-triphenylisophosphindole 2-oxide (83), which dimerized spontaneously to give 84 (Eq. 30).



(81)



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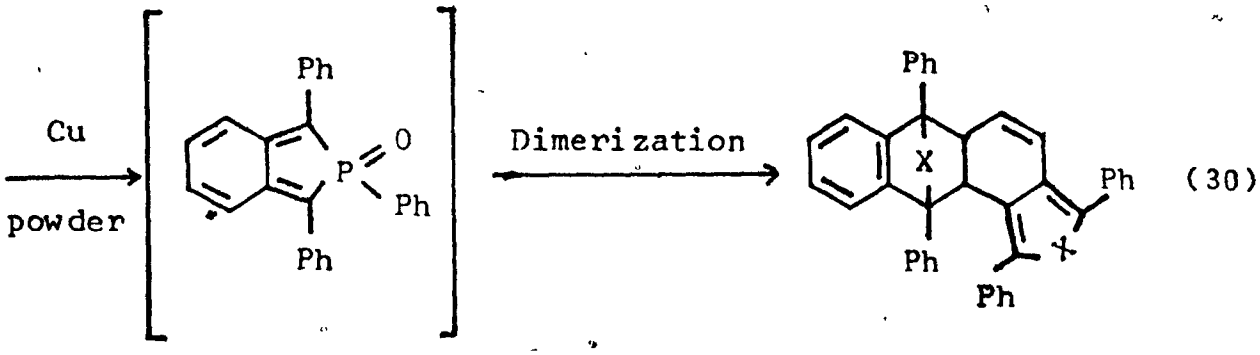


(83) (84), X = P(O)Ph

Properties of Benzo[c]phosphole

The synthesis and properties of isophosphindole (6) have not yet been reported. However, some properties of 2-phenylisophosphindoline (74) have been studied by Mann and Millar[68,69].

2-Phenylisophosphindoline has the normal properties of tertiary phosphines. It readily quaternizes with methyl iodide. It forms normal stable covalent complexes of composition

$(C_{14}H_{13}P)_2Pd\ X_2$, where X=Cl, Br and I and $C_{14}H_{13}P$=2-phenyliso-phosphindoline, with dihalogenopalladium (II). It gives compounds with certain metallic halides in which the metal shows an usual coordination number[74,75,76].

With the dihalogenopalladiums, it gives complexes of the type 85, which are covalent in crystalline state and in non-polar solvents. However, they are in equilibrium with the ionic form 86 in polar solvents[74]. It also forms similar type of compounds with dihalides of platinum, nickel and cobalt, but the cobalt compounds do not give the ionic form 86[75].

$$(C_{14}H_{13}P)_3PdX_2 \rightleftharpoons [(C_{14}H_{13}P)_3PdX^+]X^-$$

(85) (86)

Mann et al[76] also investigated the coordinated derivatives of 2-phenylisophosphindole with copper (I), silver (I) and gold (I) halides. With cuprous and silver iodides it gives tetrameric 1:1 complex 87, whereas with aurous iodide, it forms monomeric 1:1 complex 88. The three-co-ordinate covalent complexes 89 are obtained when it combines with the above mentioned iodides. On further combination, produces the four-co-ordinate covalent complexes 90. The ionic salt 91 where X=NO_3 and ClO_4 is given only by cuprous iodide[76].

$[C_{14}H_{13}P,\ Cu\ I]_4$ $[C_{14}H_{13}P,\ AuX]$

(87) (88)

$[(C_{14}H_{13}P)_2MX]$ (89) $[(C_{14}H_{13}P)_3MX]$ (90) $[(C_{14}H_{13}P)_4Cu]X$ (91)

The reaction of 2-phenylisophosphindoline with palladous halides[68] is of considerable interest. The complexes of composition $[(C_{14}H_{13}P)_2PdX]$ where X=Br, Cl are obtained on reacting with potassium palladohalides. These compounds undergo association in solution. However, they are stable coordinated derivatives of univalent palladium, thus representing a new type of coordinated metallic compound.

Isophosphindoline (68) readily forms isophosphindolinium salt with o-xylylene dibromide[72].

The substituted isophosphindole oxide (83) tends to dimerize so rapidly that its isolation is not possible. But its existence is confirmed by its u.v. spectrum and by trapping it with cyclopentadiene and N-phenylmaleimide[73].

Since the chemistry of benzophosphole is incomplete, the exploration in this field would provide some more informations for the series of phosphole chemistry and it will be of considerable interest to make a comparison between the chemistry of phosphindole and the isoconjugated isomer isophosphindole.

Very recently, Mislow et al[77] have calculated the pyramidal inversion barriers in 1-methylisophosphindole and they predicted a substantial decrease in barrier height (6.9 k cal/mole), relative to a model compound. They further predicted that the delocalization of lone pair of electrons on phosphorus may be favour-

able in the transition state to inversion, resulting from the increased benzenoid character for the carbocyclic portion of the bicyclic structure. Hence, this decrease in barrier height can be experimentally verified, if isophosphindole system can indeed be synthesized.

In this thesis, the chemistry of benzophosphole derivatives will be discussed.

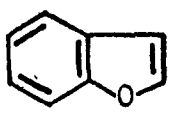
CHAPTER 2

RESULTS AND DISCUSSION

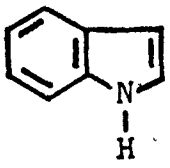
1-Ethoxybenzo[b]phosphole 1-Oxide

General Synthetic Route to 1-Heteroindene

1-Heteroindenes like benzofuran (92), indole (3) and benzothiophene (93) have been known for many decades. Amongst these three systems, indole and its derivatives hold an important place in organic chemistry, since the indole ring system is found in many naturally occuring compounds of great chemical and biochemical interest.



(92)



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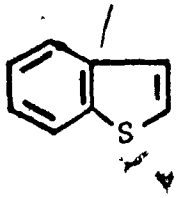
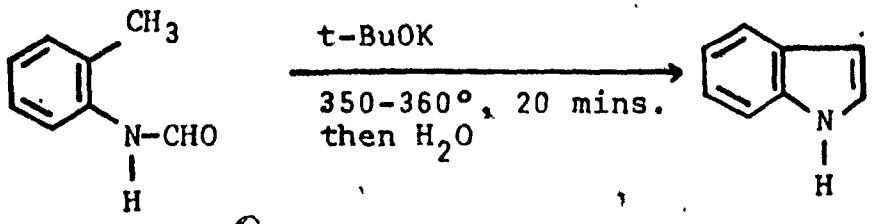
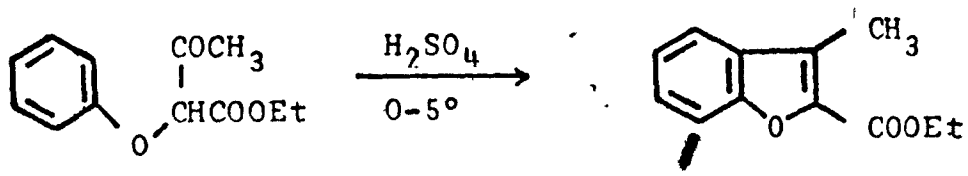


(93)

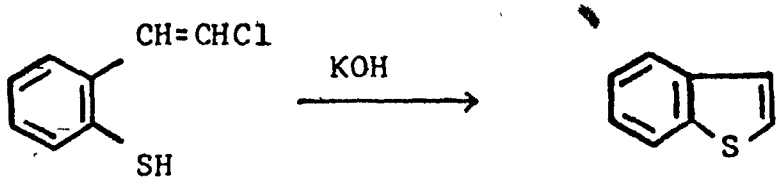
The majority of the general synthetic route to 1-heteroindenes start from mono substituted or ortho disubstituted benzenes and form the five-membered ring. Some of the synthetic approaches[78,79] are illustrated in Eqs. 31-33.



(31)

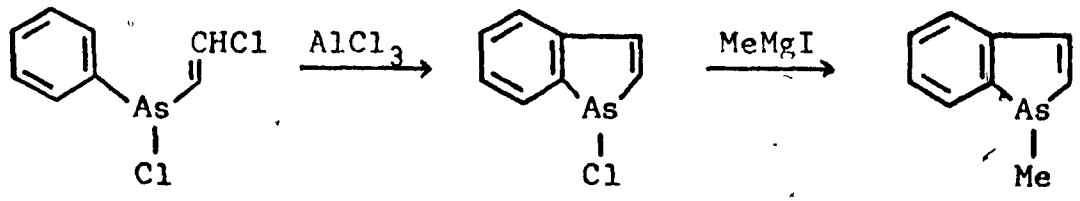


(32)



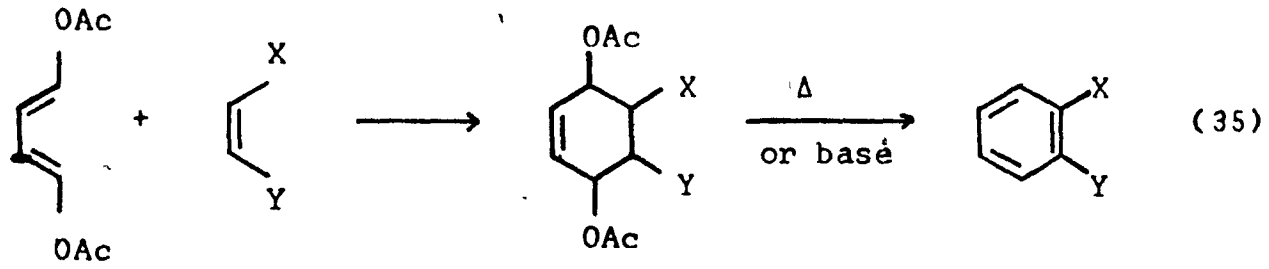
(33)

Similar synthetic approaches were used for the analogous compounds like arsindole[80,81] (Eq. 34) and phosphindole[64] derivatives (Eq. 22).



(34)

An alternative approach, involving the construction of benzene ring, instead of forming the heterocyclic ring at the critical step might serve as a new approach to the synthesis of 1-heteroindenes. A simple and direct method for forming benzene ring has been developed by Hill and Carlson[67], which is based on the cycloaddition of E, E-1, 4-diacetoxybutadiene (64) with dienophiles. The Diels-Alder adduct 94 was found to eliminate acetic acid thermally or when treated with base to yield the corresponding aromatized compound 95 (Eq. 35).

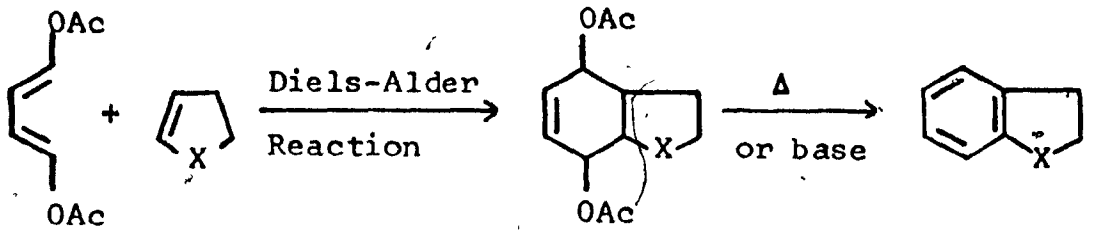


(35)

(64) (94) (95)

This method of forming aromatic ring appears to be general for many dienophiles[82]. It has been successfully applied for the construction of benzene ring in the syntheses of 1-hetero-

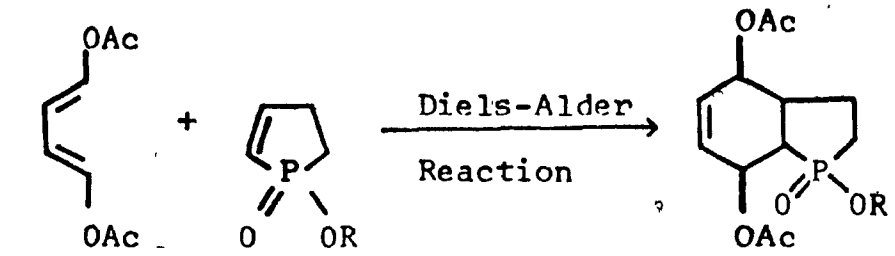
indenes such as 1-phenylbenzo[b]phosphole and benzo[b]thiophene 1, 1-dioxide in our laboratory[65,66] (Eq. 36).



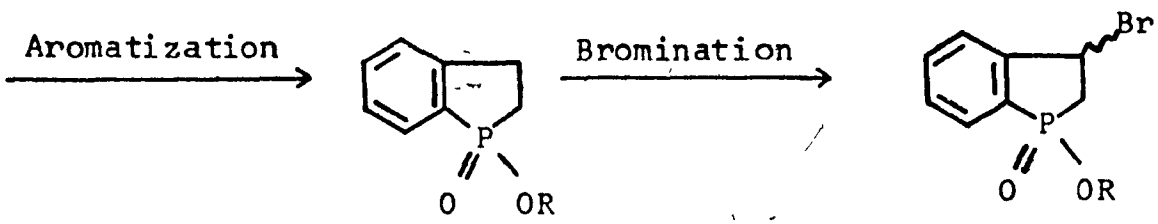
(36)

X = SO_2, P(O)Ph

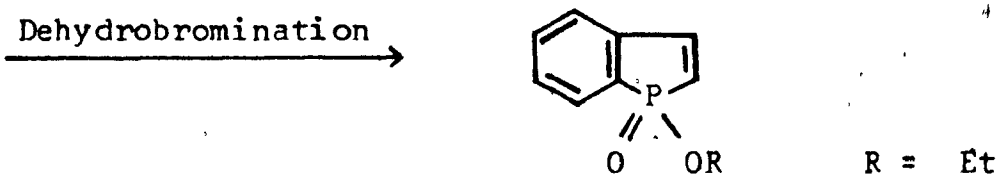
The synthesis of benzo[b]phosphole appears to be particularly attractive, since benzo[b]phosphole, being unsymmetrical, cannot be prepared by the general synthetic pathways used for the symmetrical phospholes and dibenzophospholes. However, this approach has so far been applied to one simple compound (i.e. X=P(O)Ph, Eq. 36). It seems to us that it is necessary to explore the generality of the reaction. Furthermore, there has been relatively few reports on the benzo[b]phosphole system in the literature. Therefore, it is one of the objectives of this research project to examine the following synthetic route.



(64) (18) (98)



(99) (100)



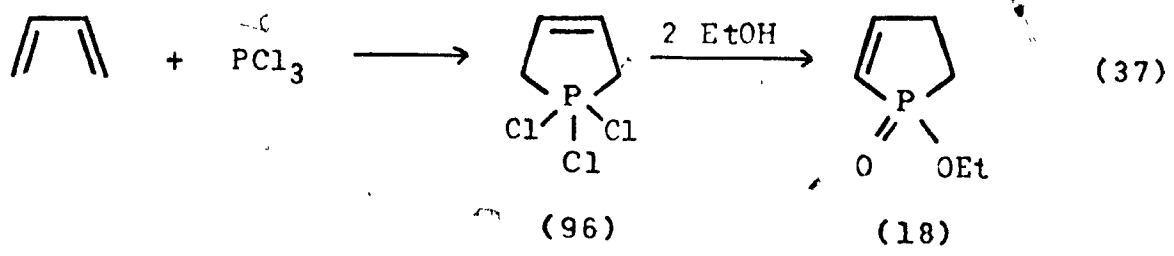
(101)

It is felt that the ethoxy group on phosphorus would present quite a different case from the phenyl substitution. The final product, 1-ethoxybenzo[b]phosphole 1-oxide will represent the first example of benzophosphole, where phosphorus is functionalized.

1-Ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide

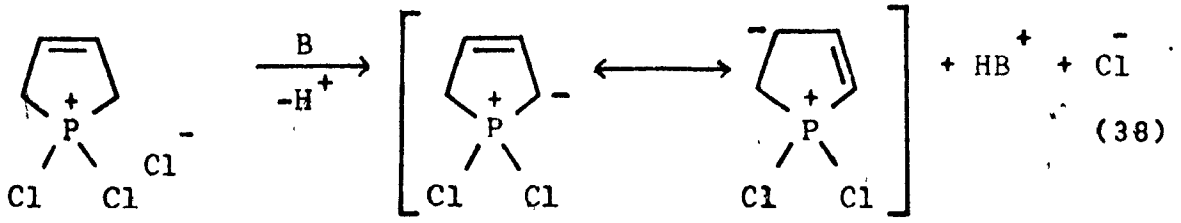
In the synthesis of 1-ethoxy-2,3-dihydrobenzo[b]phosphole

1-oxide, the most suitable dienophile to be treated with E, E-1,4-diacetoxybutadiene (64) was chosen to be 1-ethoxy-2-phospholene 1-oxide. The dienophile required was prepared according to the method of Hasserodt and co-workers[83]. This method involved the initial addition of phosphorus trichloride to 1,3-butadiene to form the corresponding adduct 96, which on treatment with excess ethanol afforded 1-ethoxy-2-phospholene 1-oxide (18) (Eq. 37).



(96) (18) (37)

The mechanism of the double bond migration is still uncertain, due to the lack of adequate evidence. Hunger et al[84] have suggested that the adduct undergoes proton abstraction so readily that even alcohol is a sufficiently strong base to accomplish this. A resonating dipolar ion 97 was pictured as the intermediate, which on protonation, followed by hydrolysis then gave either the 2- or the 3- isomer (Eq. 38).



(97) (38)

A mixture of equal molar quantities of E, E-1,4-diacetoxybutadiene (64) and 1-ethoxy-2-phospholene 1-oxide (18) was heated in a sealed tube at 135° for 7 to 14 days. A new compound was isolated by preparative thin layer chromatography. Mass spectrum showed that it was the Diels-Alder adduct 98. Infrared spectrum also confirmed the presence of the acetate groups. Similar adduct was also formed in the reaction of 2, 3-dihydrothiophene 1, 1-dioxide with E, E-1,4-diacetoxybutadiene[65,66]. On the contrary, the Diels-Alder adduct of 1-phenyl-2-phospholene 1-oxide eliminated acetic acid thermally during the reaction conditions to give the aromatized product[65,66]. In the present case, the elimination of acetic acid from the diacetoxy adduct 98 was achieved by directly treating the reaction mixture with base, without isolating the intermediate adduct. Thus, the reaction mixture was refluxed in alcoholic sodium hydroxide solution for 12 hours. A new compound was isolated in 25% yield (based on reacted 1-ethoxy-2-phospholene 1-oxide) by column chromatography on silica gel, eluting with ethyl acetate. It was identified as 1-ethoxy-2, 3-dihydrobenzo[b]phosphole 1-oxide (99) by its spectroscopic data and elemental analysis.

The infrared spectrum of the diacetoxy adduct 98 is quite simple and it shows a strong C=O stretching band at 1740 cm^{-1}, a sharp C-O stretching band at 1370 cm^{-1}, a weak C=C stretching band at 1600 cm^{-1} and a characteristic strong P=O stretching band at 1260 cm^{-1}.

The infrared spectrum of 1-ethoxy-2, 3-dihydrobenzo[b]-phosphole 1-oxide (fig. 1) exhibits a strong band at 1260 cm^{-1},

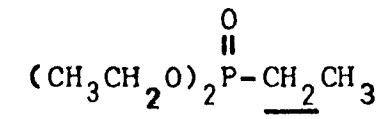
attributable to P=O stretching and a sharp band at 1600 cm^{-1}, associated with C=C stretching.

The u.v. spectrum of 1-ethoxy-2, 3-dihydrobenzo[b]phosphole 1-oxide (fig. 8) consists of a high intensity primary band at 217 nm and a low intensity secondary band with vibrational fine structure, maximum at 269 nm. The spectrum greatly resembles those of triphenylphosphine oxide[85], diphenylphosphinic acid[86] and 1-phenyl-2, 3-dihydrobenzo[b]phosphole 1-oxide[65,66] (Table IV). The high intensity band at 217 nm is assigned to correspond to the primary E-band of benzene at 203 nm, displaced by substitutions. The low intensity band at 269 nm corresponds to the B-band of benzene at 256 nm. It has been observed[87] that alkyl substitution intensifies and also shifts the secondary band of benzene to longer wavelengths. This has been attributed to the predominant C-H hyperconjugation. In ethyl benzene, the ethyl group shifts the 256 nm band of benzene to 260 nm[88]. In 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide, it may be considered that the benzene ring is substituted with a $-CH_2-CH_2-$ group. Hence, the shift of 256 nm band of benzene to the longer wavelength 269 nm may be associated with the alkyl substitution of benzene ring.

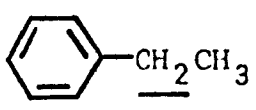
Sklar[89] has stated that a benzene derivative with considerable resonance interaction between the substituent and the ring will have an u.v. spectrum which differs markedly from that of the parent compound. In view of the general similarity between the spectra of benzene and 1-ethoxy-2,3-dihydrobenzo-[b]phosphole 1-oxide and the presence of the vibrational fine structure, the conclusion may be drawn that no resonance exists

between the benzene ring and the -P(O)OEt group. The same kind of conclusion has been drawn for diarylphosphinic acid and arylphosphonic acid[86].

The proton n.m.r. spectrum of 1-ethoxy-2,3-dihydrobenzo-[b]phosphole 1-oxide (fig. 3) consists of a 4-H multiplet at 7.5 δ for the aromatic protons, a 2-H quintet at 4.2 δ for the methylene protons attached to oxygen, two 2-H multiplets at 3.1 δ and 2.2 δ for the two methylene groups on the ring and a 3-H triplet at 1,3 δ for the ester methyl protons. The complexity of the spectrum is in part associated with the coupling of protons with the phosphorus atom. It is not easy to make an assignment on the two methylene groups. However, it seems probable that the benzylic proton might resonate at a lower field than does the methylene proton attached to -P(O)OEt group. Supporting evidence for the above consideration can be obtained by comparing the chemical shift values of methylene protons in diethyl ethylphosphonate (102)[90] and ethyl benzene (103). It has been observed that the benzylic protons in 103 resonate at 2.62 δ[94], whereas the methylene protons attached to -P(O)$(OEt)_2$ group in 102 give signals at 1.88 δ[90]. Thus, the multiplet at 3.1 δ may be assigned to the benzylic protons and the one at 2.2 δ to the methylene groups adjacent to -P(O)OEt group.



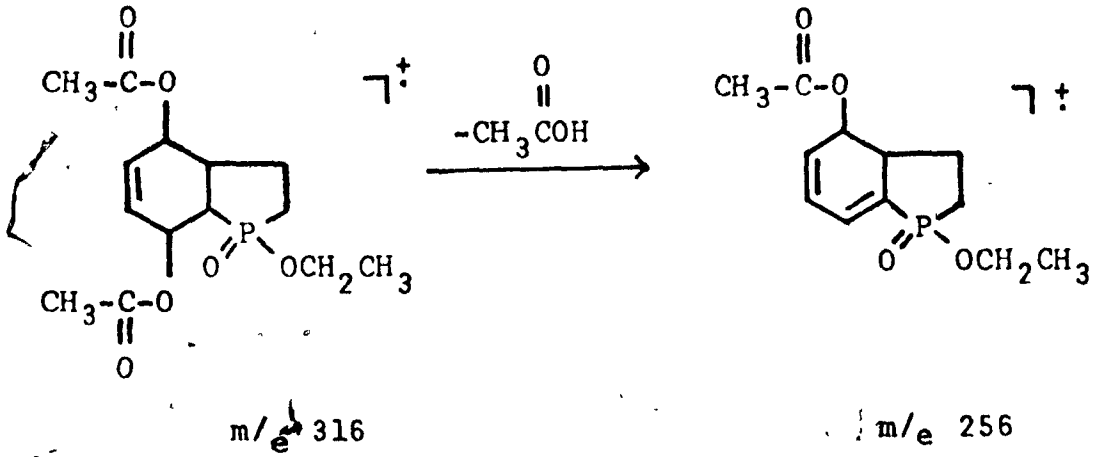
(102)



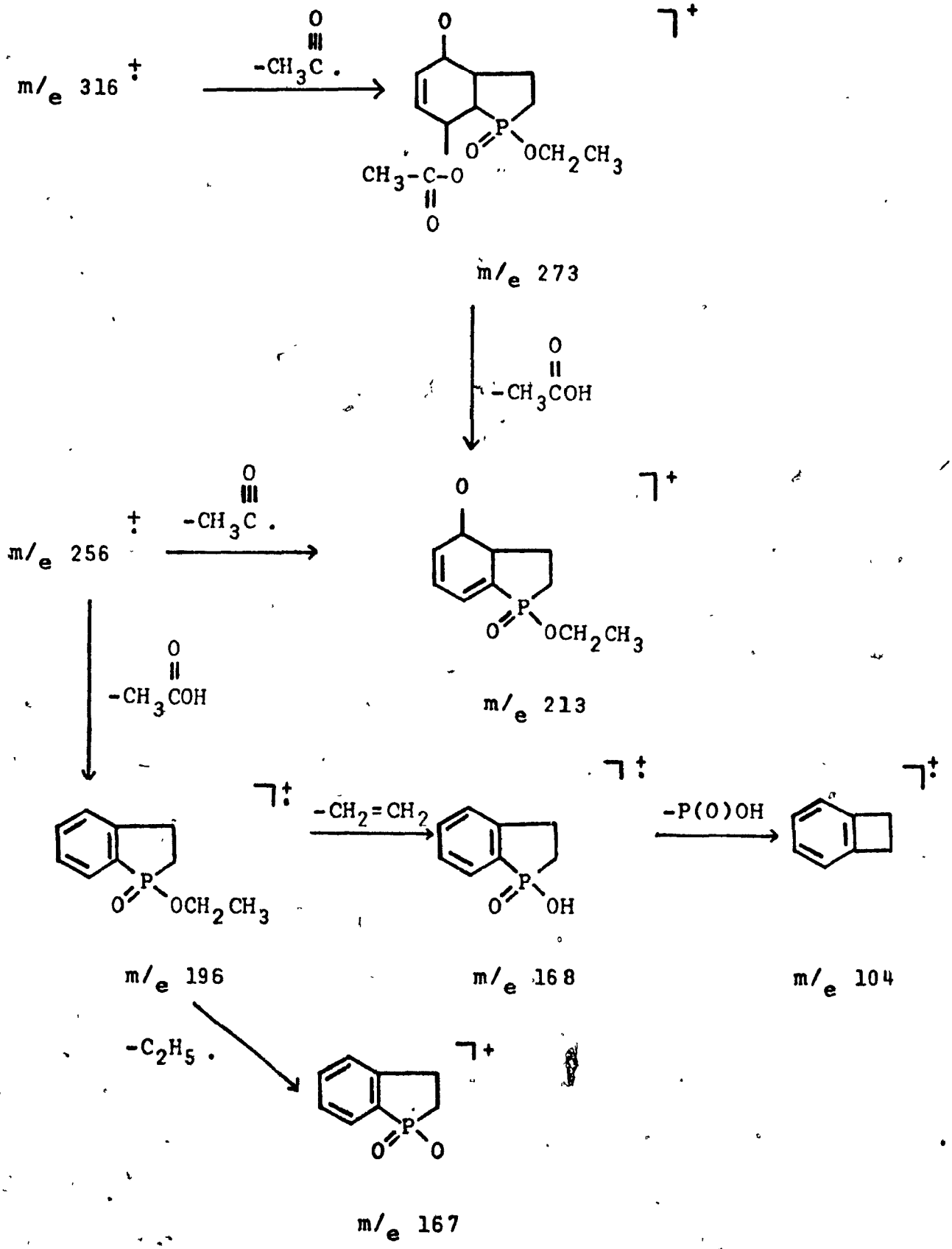
(103)

The mass spectrum of the diacetoxy adduct 98 shows a weak molecular ion (M^+) at $m/_e$ 316. The base peak is at $m/_e$ 213 and the other prominent peaks are at $m/_e$ 273, 256, 196, 168, 167 and 104. The ion at $m/_e$ 273 arises from the loss of $CH_3C{\equiv}O$ radical, a process which is characteristic of acetate esters. Another interesting feature is the successive elimination of acetic acid from the molecular ion to give the ions at $m/_e$ 256 and 196. Loss of ethylene molecule by the McLafferty rearrangement from the ion at $m/_e$ 196 provides the ion at $m/_e$ 168. This kind of fragmentation is observed in triethyl phosphate[91]. The ion at $m/_e$ 168 further loses the -P(O)OH moiety to afford the ion at $m/_e$ 104. The fragmentation pattern is illustrated in Scheme VII.

Scheme VII

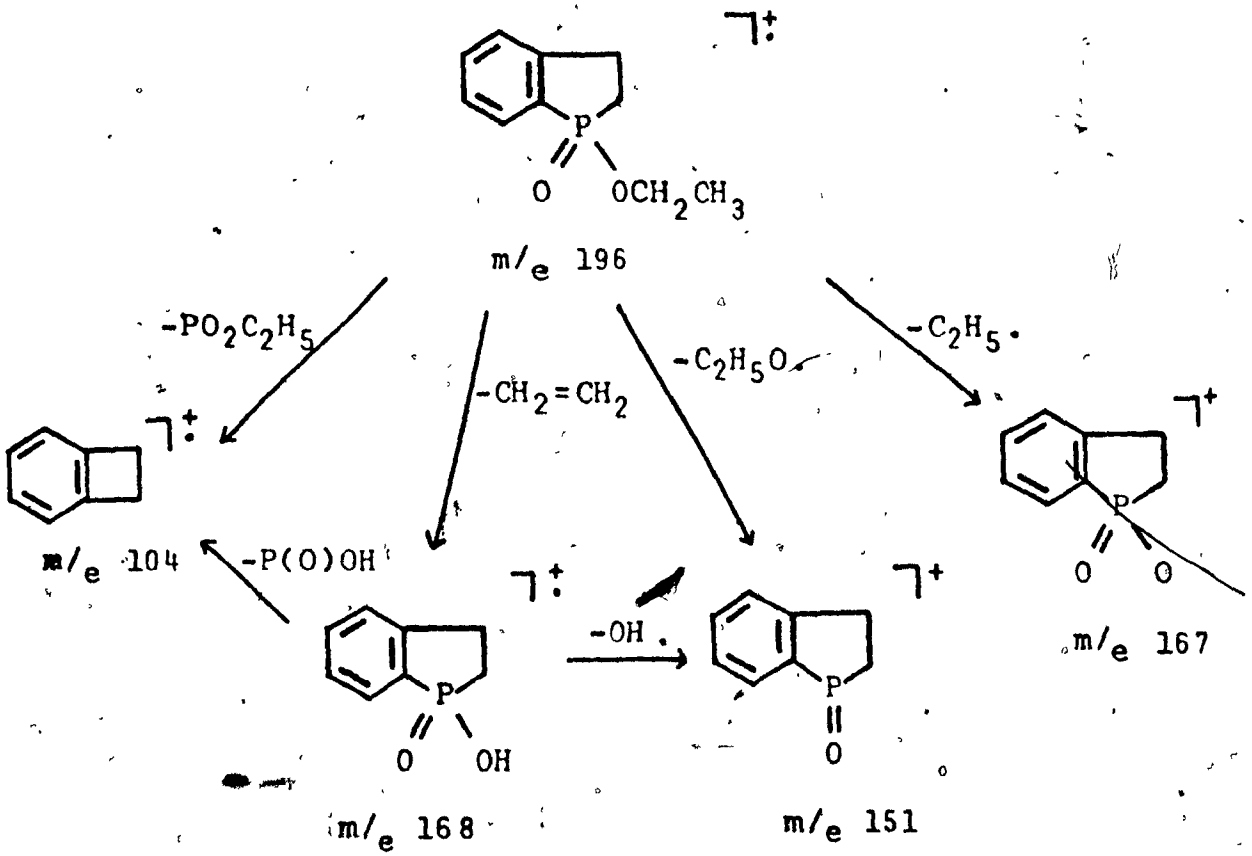


Scheme VII (cont'd)



The mass spectrum of 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide (fig. 5) is of considerable interest. It exhibits a rather intense molecular ion (M^+) at $m/_e$ 196. The base peak at $m/_e$ 168 may arise from the loss of ethylene molecule by the McLafferty rearrangement from the molecular ion. This kind of elimination has similarly been observed in 1-ethoxy-2-phospholene 1-oxide (fig. 7). The other prominent peaks are at $m/_e$ 167, 151 and 104, which arise from the loss of C_2H_5, C_2H_5O radicals and the $-PO_2C_2H_5$ group respectively from the molecular ion. The fragmentation pattern is shown in Scheme VIII.

Scheme VIII



Reaction Conditions

The Diels-Alder reaction between E, E-1, 4-diacetoxybutadiene with 1-ethoxy-2-phospholene 1-oxide did not occur when the reaction was carried out in refluxing solvents such as benzene, toluene or xylene. The reaction seemed to proceed very slowly below 120° in a sealed tube. At higher temperature (150° or higher), polymerization occurred. Therefore, the optimum reaction temperature was in the range of 130 - 140°. Thus, the reaction mixture was heated in a sealed tube at 135° for 7 to 14 days. Further heating for over three weeks failed to improve the yield.

Various bases, such as alcoholic sodium hydroxide, sodium ethoxide in ethanol, triethylamine in benzene and toluene, potassium tert-butoxide in tert-butanol and dimethyl sulfoxide and 1, 5-diazabicyclo (3.4.0) nonene-5 (DBN) in benzene and toluene, all in refluxed condition, were attempted for the elimination of acetic acid from the diacetoxy adduct 98. Amongst these bases, triethylamine was found to be too weak to effect the elimination. With DBN in benzene or toluene, the elimination seemed to be incomplete, even after refluxing for 2 days. In the case of potassium tert-butoxide, some of the materials were lost during work-up. Either sodium hydroxide or sodium ethoxide in refluxing ethanol gave good yield. Sodium hydroxide was finally chosen, because of its simplicity in operation. The elimination process was carried out for 10 to 12 hours. The yield was not changed when the refluxing time was increased.

In this reaction, some polymer was also formed and its formation could not be prevented.

Variation of the Stoichiometry of the Diene

Since the Diels-Alder reaction is reversible, using excess of one of the reactants might drive the reaction to the side of the product. However, the yield of the product was not improved by using 1, 2 or 3 molar excess of the diene under the same reaction conditions.

Other Dienes

Hoping that some other dienes might be more effective in the Diels-Alder reaction, several attempts were made by using butadiene, isoprene and 1-acetoxybutadiene[92]. It was found that none of the above mentioned dienes were as effective as E, E-1, 4-diacetoxybutadiene. In all cases, the starting materials were recovered. It is not surprising that E, E-1, 4-diacetoxybutadiene is the most reactive, since the electron-donating acetoxy group is known to facilitate the Diels-Alder reaction.

Bromination of 1-Ethoxy-2, 3-dihydrobenzo[b]phosphole 1-Oxide

1-Ethoxy-2, 3-dihydrobenzo[b]phosphole 1-oxide (99) was

brominated with equal mole of recrystallized N-bromosuccinimide[93] in the presence of a catalytic amount of benzoyl peroxide in refluxing benzene for 12 hours. A new compound was isolated in 30% yield by preparative thin layer chromatography. It was identified as the monobromo derivative 100 by n.m.r., i.r. and mass spectra. It is probable that it is the 3-position of the benzophosphole ring which is brominated, since radical reaction is more likely to take place at the benzylic position. It has been suggested that the allylic position was brominated in 1-ethoxy-2-phospholene 1-oxide[22] (Eq. 7).

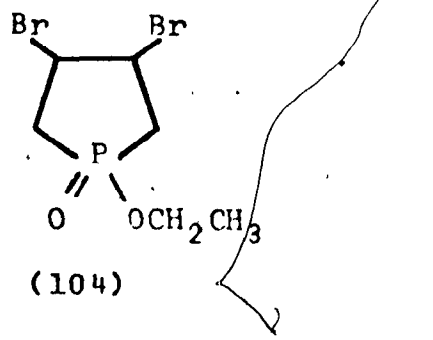
In addition to the monobromo derivative, some dibromo derivatives were also formed as revealed by the mass spectrum of the reaction mixture. But their purification were not attempted.

The use of pure recrystallized N-bromosuccinimide[93] gave a better yield of the product. Attempts to prevent the formation of dibromo derivatives by decreasing either the reaction time or the reaction temperature were unsuccessful.

The infrared spectrum of 1-ethoxy-3-bromo-2,3-dihydrobenzo-[b]phosphole 1-oxide (100) shows a strong characteristic P=O stretching at 1270 cm^{-1} and a sharp C=C stretching band at 1601 cm^{-1}.

The n.m.r. spectrum of 1-ethoxy-3-bromo-2,3-dihydrobenzo-[b]phosphole 1-oxide shows a 4-H multiplet at 7.6 δ for the aromatic protons, a 1-H multiplet at 5.6 δ for the benzylic proton, a 2-H multiplet at 2.7 δ for the ring methylene protons, a 2-H multiplet at 4.3 δ for the ester methylene protons and a 3-H triplet at 1.3 δ for the ester methyl protons.

Due to the lack of reports on the n.m.r. spectral data of the monobromo derivatives of 1-ethoxy-2-phospholene 1-oxide[22] and 1-phenyl-2,3-dihybrobenzo[b]phosphole 1-oxide[65,66], it is not possible to make a comparison between those compounds and 1-ethoxy-3-bromo-2,3-dihydrobenzo[b]phosphole 1-oxide. However, there is one report on the n.m.r. of the dibromo derivative 104 of 1-ethoxy-3-phospholene 1-oxide[26]. In its n.m.r. spectrum, the ring methylene protons adjacent to -P(O)OEt group give signals as a multiplet, centred at 2.6 δ. In view of this chemical shift value, it is reasonable to assign that a multiplet centred at 2.7 δ in the n.m.r. spectrum of 1-ethoxy-3-bromo-2,3-dihydrobenzo[b]phosphole 1-oxide should correspond to the ring methylene protons adjacent to -P(O)OEt group. Thus the remaining signal at 5.6 δ should correspond to the benzylic protons, attached to -Br.



(104)

Furthermore, in the n.m.r. spectrum of 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide, the multiplets centred at 3.1 δ and 2.2 δ have been already assigned to benzylic protons and ring methylene protons, adjacent to P(O)OEt group, respectively.

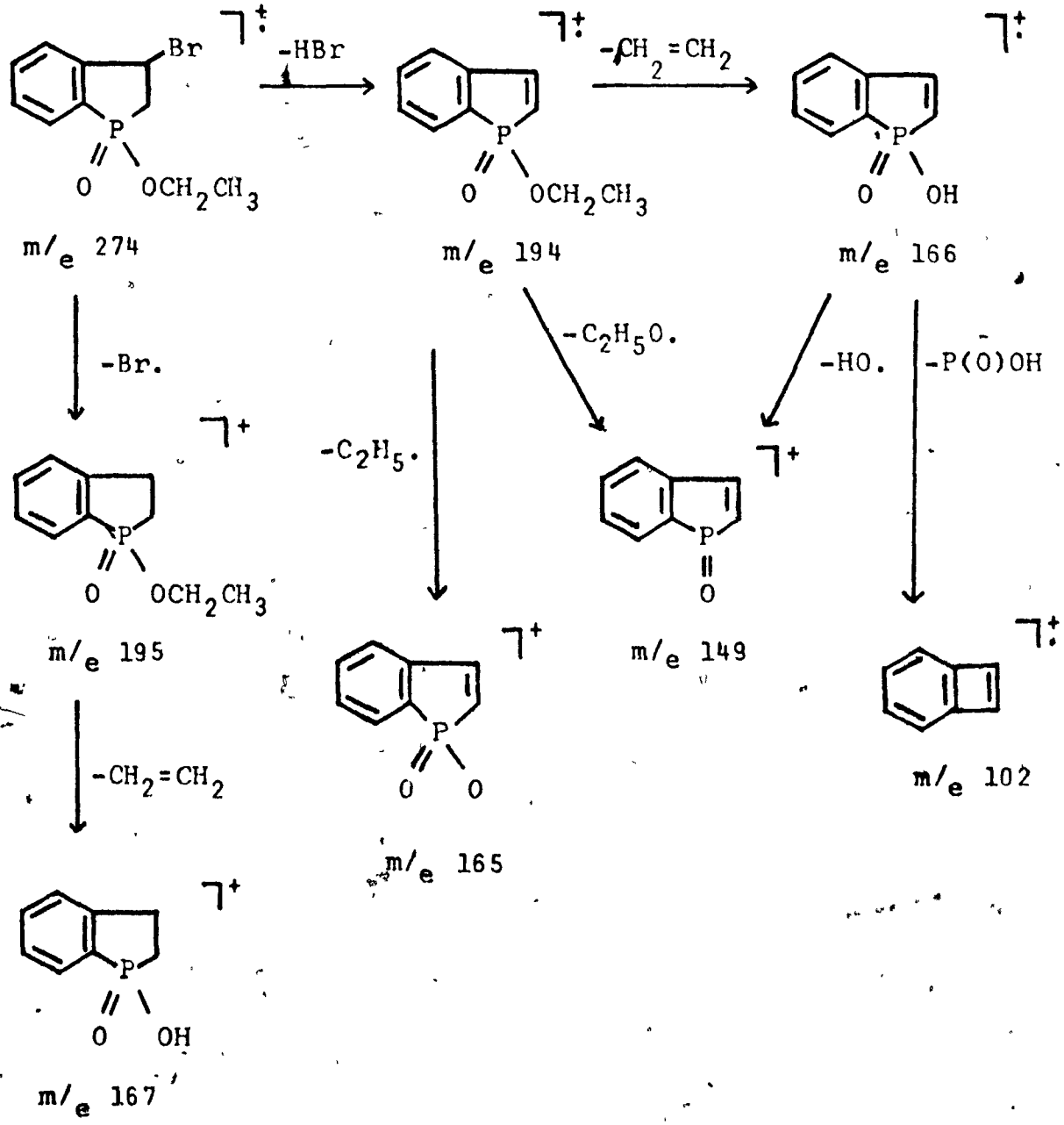
Thus, a multiplet centred at 2.7 δ in the n.m.r. spectrum of 1-ethoxy-3-bromo-2,3-dihydrobenzo[b]phosphole 1-oxide may not be due to the benzylic protons. A multiplet centred at 5.6 δ should therefore correspond to benzylic protons. It is also known that the benzylic protons which usually resonate at 2.7 δ shift to a lower field 4.4 δ, when brominated[94]. Hence, it is reasonable that the benzylic protons which resonate at 3.1 δ in 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide shift to a lower field 5.6 δ, when brominated. In light of all these considerations, it is probable that the benzylic position is brominated rather than the 2-position adjacent to -P(O)OEt group, in the benzoyl peroxide catalysed N-bromosuccinimide bromination of 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide.

The assignment of stereochemistry of -Br with respect to -P=O and -OEt group in 1-ethoxy-3-bromo-2,3-dihydrobenzo[b]-phosphole 1-oxide might be greatly facilitated by n.m.r. spectroscopy. It can be considered that the magnitude of $^{3}J(PCCH)$ coupling constant might depend on the orientation of the phosphoryl group as in the same manner as its dependence on phosphorus lone pair orientation[95]. However, $^{3}J(PCCH)$ value cannot be easily obtained since the benzylic proton gives a complex multiplet.

The mass spectrum of 1-ethoxy-3-bromo-2,3-dihydrobenzo[b]-phosphole 1-oxide exhibits P($m/_e$ 274) and P+2($m/_e$ 276) peaks in 1:1 intensity ratio, characteristic of a monobromo compound. The peaks at $m/_e$ 195 and 194, arising from the loss of -Br. and HBr respectively from the molecular ion are important fragments.

The base peak at $m/_e$ 149, may arise from the loss of C_2H_5O radical from the peak at $m/_e$ 194. The other prominent peaks are at $m/_e$ 167, 166, 165 and 102. The fragmentation pattern is illustrated in Scheme IX.

Scheme IX



1-Ethoxybenzo[b]phosphole 1-Oxide

Dehydrobromination of 1-ethoxy-3-bromo-2,3-dihydrobenzo-[b]phosphole 1-oxide (100) was carried out by stirring with excess triethylamine in benzene. A new compound was isolated by preparative thin layer chromatography in 45% yield and it was identified as 1-ethoxybenzo[b]phosphole 1-oxide (101) by its spectroscopic data.

It was found that better yield of the product was obtained by using 2 to 3 molar excess of the base. Triethylaminehydrobromide salt was isolated as the other product.

The infrared spectrum of 1-ethoxybenzo[b]phosphole 1-oxide (fig. 2) shows two sharp bands at 1601 cm^{-1} and 1590 cm^{-1} attributable to C=C stretching, which is conjugated. The characteristic strong P=O band is observed at 1300 cm^{-1}.

The P=O absorption bands of 1-ethoxybenzo[b]phosphole 1-oxide and its derivatives should be compared with that of 1-ethoxy-2-phospholene 1-oxide[84] which is observed at 1250 cm^{-1}. Since all the spectra were taken in chloroform solution the bands due to P-O-C stretching were obscured by the absorption of the solvent.

The u.v. spectrum of 1-ethoxybenzo[b]phosphole 1-oxide (fig. 9) shows the high intensity bands at 221 nm and 227 nm. It also shows an additional band centering at 312 nm as in the case of 1-phenylbenzo[b]phosphole 1-oxide[65,66].

The u.v. spectra of heteroindenes like benzofuran, benzothiophene and indole show the general resemblance to each other

and to the corresponding fused-ring hydrocarbon naphthalene. However, the u.v. spectrum of indene[96] is quite different from that of either indole or benzofuran, which are similar to one another (Table III).

TABLE III

U.V. Spectral Data of Indene and Heteroindenes

Compounds	λ_{max} in n.m.	log ε	Ref.
Indene	220, 249, 280	3.97, 3.97, 2.68	96
	285, 290	2.38, 2.14	
Indole	219, 288	4.5, 3.9	97
Benzofuran	281, 244	3.5, 4.0	97
Benzothiophene	227, 257, 288	4.45, 3.74, 3.31	97

The disappearance of the fine vibrational structure and increase in intensity of the absorption maximum (Table IV) in the u.v. spectrum of 1-ethoxybenzo[b]phosphole 1-oxide indicates that the benzene ring [λ_{max}(log ε) at 203 (3.87) and 256 n.m. (2.31)] is conjugated with Π-bonded system, thus showing an increase in the extent of the chromophore. It also shows the effect of added conjugation by absorbing at longer wavelength than the monocyclic heterocycle, 1-ethoxy-2-phospholene 1-oxide[84].

TABLE IV

U.V. Spectral Data of Some Phosphorus Compounds

Compounds	λ_{max} in n.m.	log ε	Ref.
Triphenylphosphine Oxide	224.5, 265.5	4.33, 3.38	85
Diphenylphosphinic Acid	224, 265	4.12, 3.08	86
1-Phenyl-2,3-dihydrobenzo-[b]phosphole 1-oxide	225, 272		65, 66
1-Ethoxy-2,3-dihydrobenzo-[b]phosphole 1-oxide	217, 269	3.91, 3.26	This work
1-Phenylbenzo[b]phosphole 1-oxide	228, 285, 313		65, 66
1-Ethoxybenzo[b]phosphole 1-oxide	221, 227, 283, 312	4.12, 4.09 3.07, 3.13	This work
1-Ethoxy-2-phospholene 1-oxide	199	3.66	84

In the n.m.r. spectrum of 1-ethoxybenzo[b]phosphole 1-oxide (fig. 4) the signal due to the four aromatic protons appears as a multiplet centred at 7.4 δ. The spectrum also shows 6 lines centred at 6.6 δ due to the two vinylic protons. Actually 8 lines should be observed, if it is considered as AMX system ($X=^{31}P$). Thus, it is probable that the 2 missing lines are obstructed by the aromatic protons. This spectrum should be

compared with that of 1-phenylbenzo[b]phosphole 1-oxide[65,66] where the vinylic protons show similar chemical shifts and multiplicities. However, in the n.m.r. spectrum of 1-phenylbenzo[b]phosphole[65,66], the vinylic protons are well separated from the aromatic protons and their splitting give 8 lines.

The n.m.r. spectrum of 1-ethoxybenzo[b]phosphole 1-oxide also exhibits a 2-H quintet at 4.2 δ for the ester methylene protons and a 3-H triplet at 1.3 δ for the methyl protons.

The chemical shift values of 1-ethoxybenzo[b]phosphole 1-oxide and its derivatives should be compared with those of 2-phospholene oxides and 1-phenylbenzo[b]phosphole 1-oxide (Table V).

TABLE V

N.M.R. Spectral Data of Some 2-Phospholene Oxides and Benzo[b]-phosphole Oxides[a]

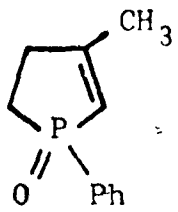
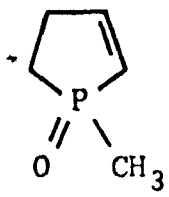
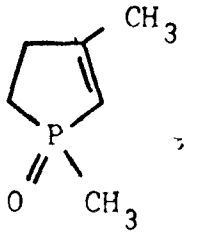
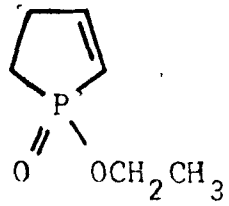
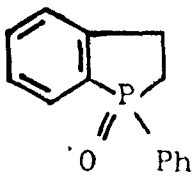
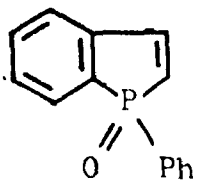
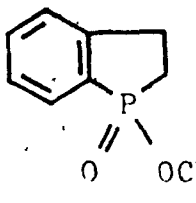
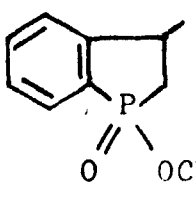
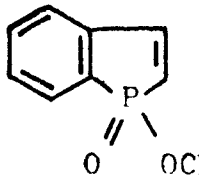
Compounds	CH_2	=CH	$-O-CH_2$	$-CH_3$	Ref.
	1.8-3.1	5.97	-	-	98
	2.2-3.3	6.1-7.8	-	-	98

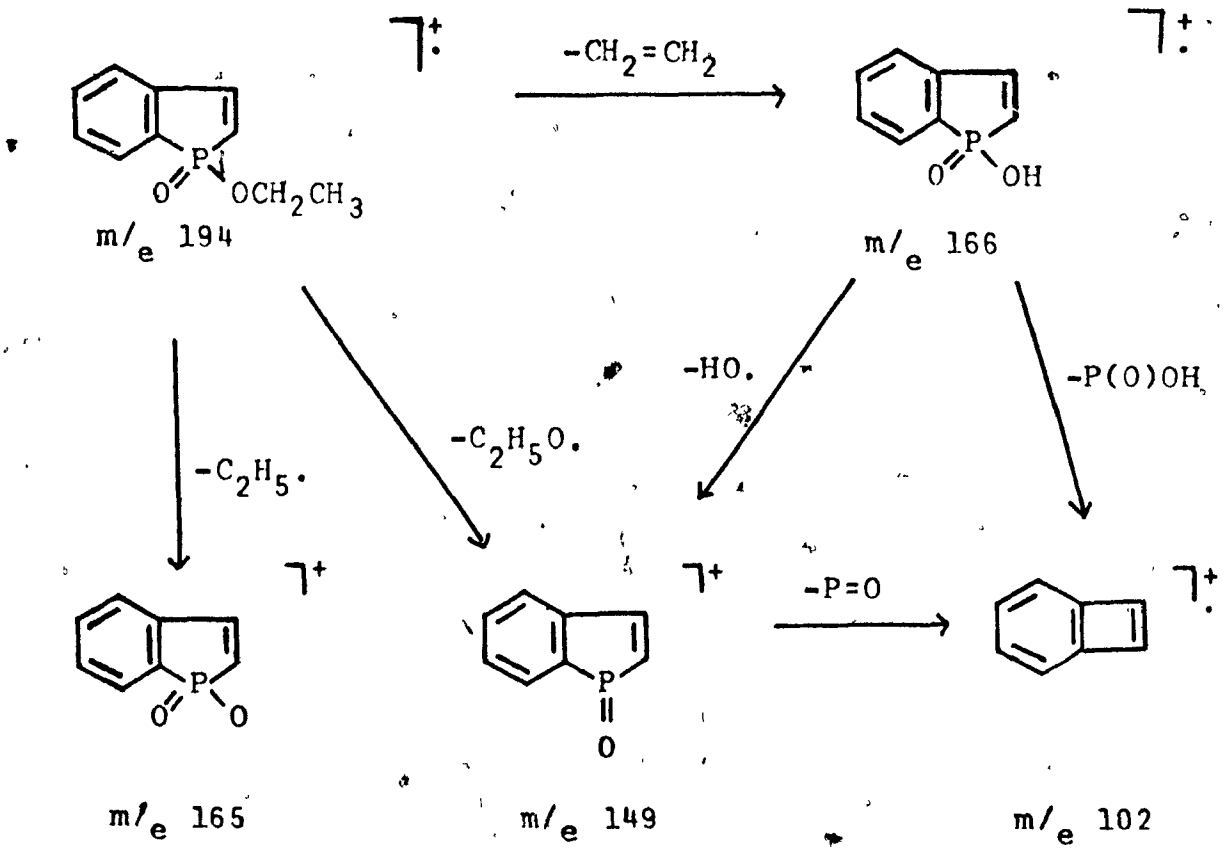
TABLE V (cont'd)

Compounds	CH_2	=CH	$-O-CH_2$	$-CH_3$	Ref.
	2.1-3.2	6.29	-	-	98
	1.9-2.7	6.0-7.8	4.2	1.2	84,106
	2.4,3.3	-	-	-	65,66
	-	7.4	-	-	65,66
	2.2,3.1	-	4.2	1.3	This work
	2.7	-	4.3	1.3	This work
	-	6.6	4.2	1.3	This work

a - Data given in δ(ppm)

The mass spectrum of 1-ethoxybenzo[b]phosphole 1-oxide (fig. 6) shows a strong molecular ion at $m/_e$ 194. The base peak at $m/_e$ 166 is due to the elimination of ethylene from the molecular ion, by the McLafferty rearrangement. The other prominent peaks are at $m/_e$ 165, 149 and 102. The fragmentation pattern is quite similar to that of its dihydro derivative and is depicted in Scheme X.

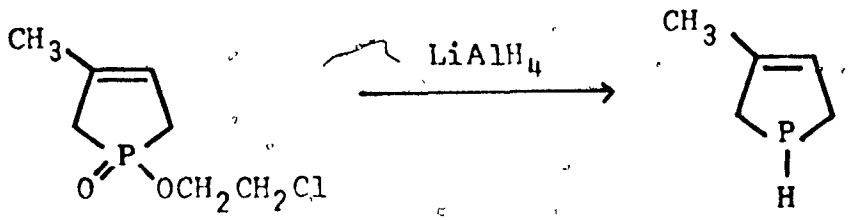
Scheme X



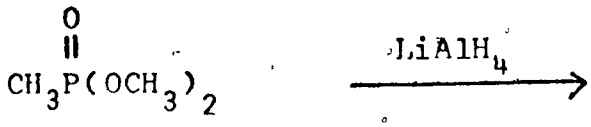
Attempted Reduction of 1-Ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide

In view of the successful reduction of phosphinic acids and their esters by aryl silanes[99], attempt was made to reduce 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide (99) by phenylsilane ($PhSiH_3$). Excess phenylsilane in benzene was refluxed with 99 for 20 hours. Thin layer chromatography and i.r. spectrum of the reaction mixture, after working up, indicated that no new compound was formed. There was no evidence of the presence of the P-H stretching in the i.r. spectrum. Only starting material was recovered. Either by extended period of refluxing or using higher boiling solvent like toluene, failed to give a new product.

Attempted reductions with other silanes such as diphenylsilane (Ph_2SiH_2) and trichlorosilane ($HSiCl_3$) in either benzene or toluene were also unsuccessful. Lithium aluminium hydride which was found to be an effective reducing agent for phosphinic acid chloride[100] (Eq. 39) and phosphonate[101] (Eq. 40) was ineffective in this particular example.



(39)



(40)

Attempted reduction with lithium aluminium hydride in anhydrous ether at room temperature or in refluxed condition also met with failure. Starting material was recovered as shown by i.r., n.m.r. spectra and thin layer chromatography.

It is not clear why 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide resists reduction in contrast to 1-ethoxy-2-phospholene 1-oxide[99]. In view of the unsuccessful reduction of 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide, the reduction of 1-ethoxybenzo[b]phosphole 1-oxide has not been attempted.

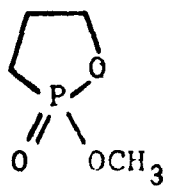
The Chemistry of 1-Ethoxybenzo[b]phosphole 1-Oxide

The successful synthesis of 1-ethoxybenzo[b]phosphole 1-oxide represents the first compound in the benzo[b]phosphole series, where phosphorus is functionalized.

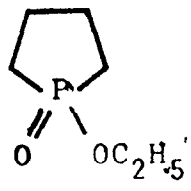
1-ethoxybenzo[b]phosphole 1-oxide was isolated as a stable liquid. Its stability should be contrasted to that of 1-ethoxyphosphole 1-oxide[22] which dimerized so rapidly that its isolation

was not possible. We can conclude that in general, benzo[b]-phosphole oxides are more stable than phosphole oxides. For example it has been observed that 1-phenylbenzo[b]phosphole 1-oxide[65,66] is a stable solid, whereas 1-phenylphosphole 1-oxide[21,25] dimerizes even at room temperature. Thus, the stability of phosphole ring is enhanced by the mono annulation (with a benzene ring).

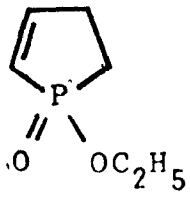
There are several reports[102] on the hydrolysis of five-membered cyclic esters such as phosphinates[103,104] and phostonate[105]. It has been observed that the five-membered phostonate ester 105 undergoes hydrolysis of the ester group external to the ring. Furthermore, the rate of hydrolysis of simple cyclic phosphinates 18, 106 and 107 is found to be lowered than those of their acyclic analogs[103,104].



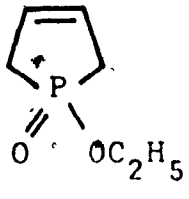
(105)



(106)



(18)

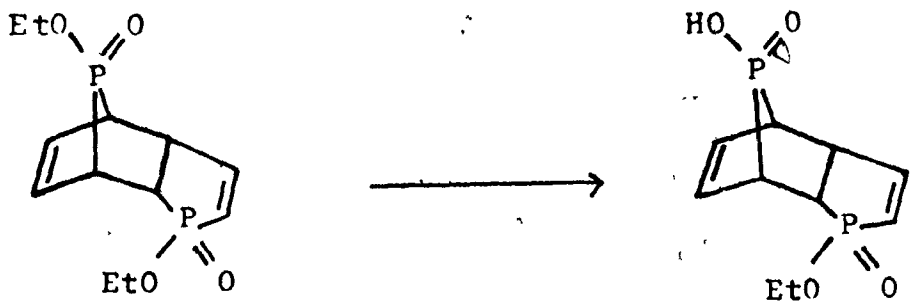


(107)

Westheimer[103] explained that this is presumably due to the energetically unfavourable configuration of the trigonal-bipyramidal phosphorane intermediates, which would have the alkyl group placed in the apical position.

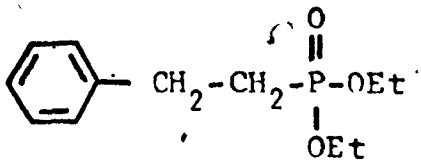
Westheimer[26] also studied the hydrolysis of the dimer of

1-ethoxyphosphole 1-oxide (Eq. 41) and its hydrogenated derivative. It was observed that the first ester groups of both of these compounds undergo hydrolysis at a faster rate than the second ester group in the same molecule. Westheimer[26,102] suggested that presumably, the relief of strain in the trigonal-bipyramidal intermediate involving the phosphorus of the [2,2,1] system is sufficient to overcome the demand of having an alkyl group in an apical position. Thus, hydrolysis in here is faster.



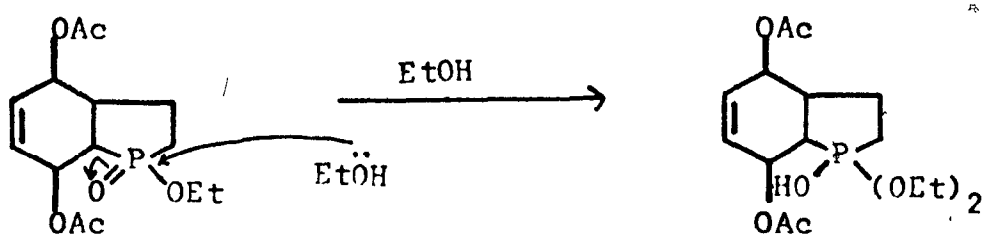
(41)

In this connection, it is interesting to mention that column chromatography of the crude mixture obtained from the reaction of the diacetoxy adduct 98 with ethanolic sodium hydroxide afforded, in addition to 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide, another compound, the spectroscopic data of which indicated that it may be the ring opened product 108.

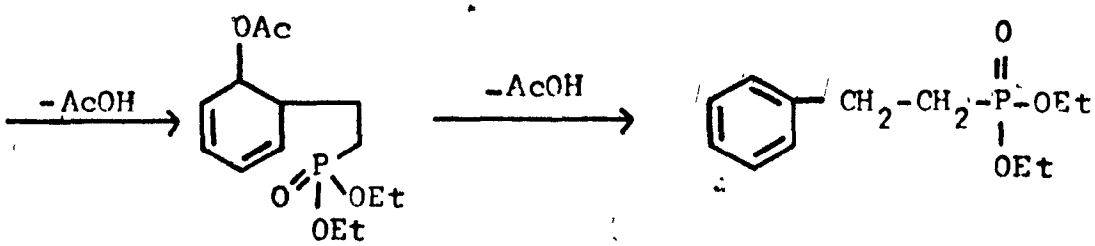


(108)

In view of Westheimer's work, it is therefore of considerable interest to study on the hydrolysis of the benzo[b]phosphole system. Thus, 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide was refluxed in ethanolic sodium hydroxide solution for 12 hours. Polymerization occurred and thin layer chromatography revealed that 108 was not formed. The formation of 108 would therefore have to be derived from the diacetoxy adduct 98, presumably first by a ring opening step, followed by aromatization as follows: -



(98)

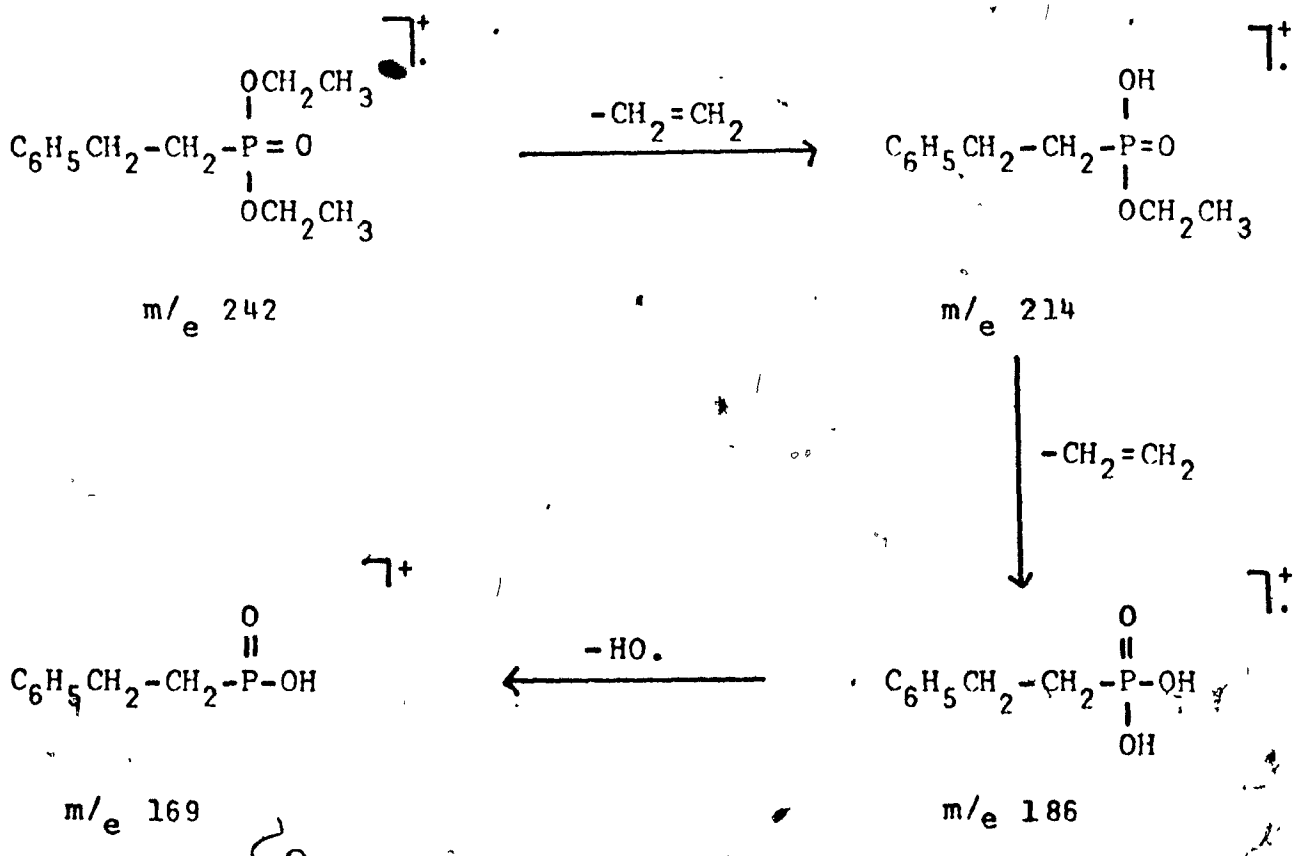


(108)

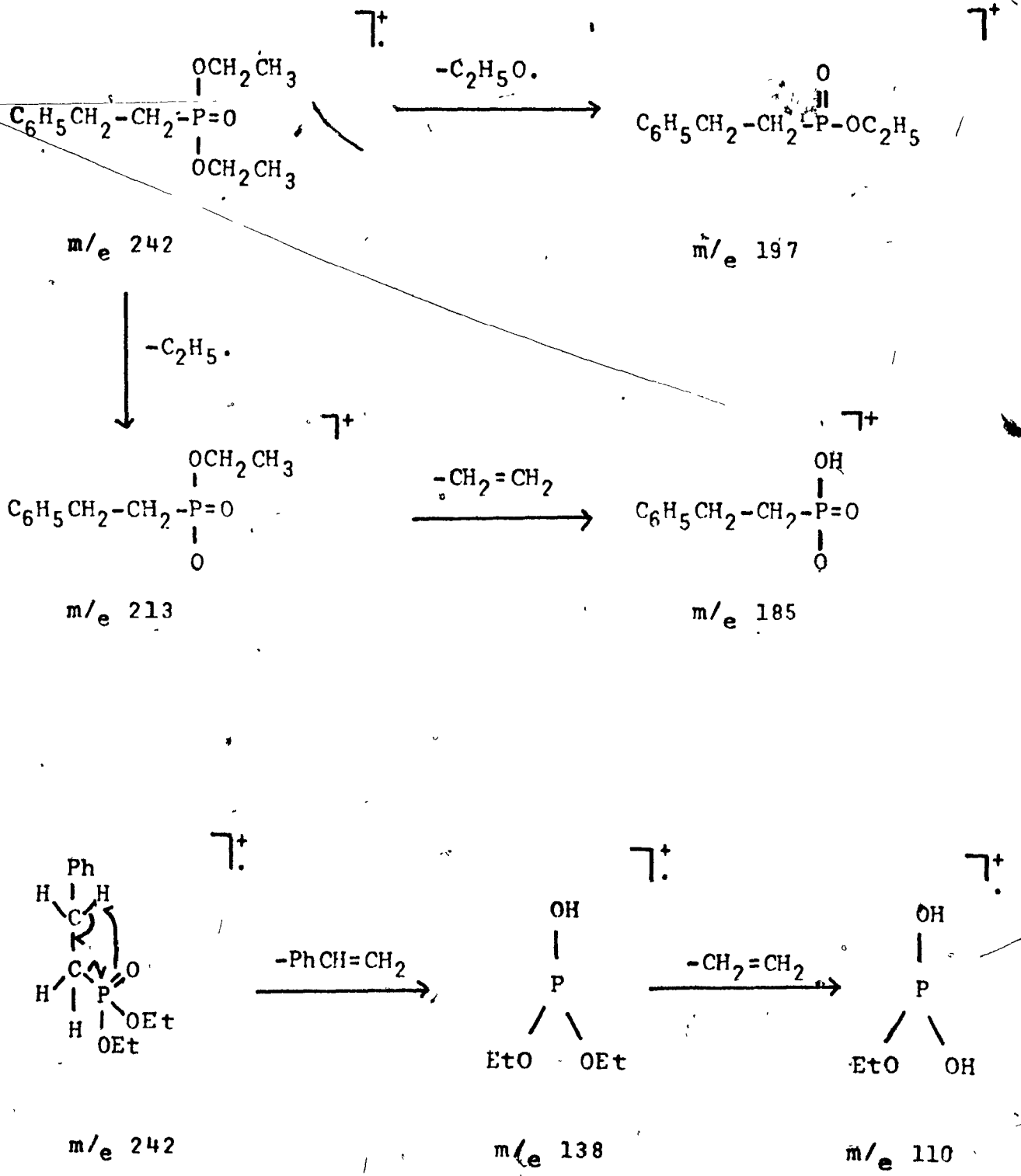
The n.m.r. spectrum of 108 exhibits a 5-H singlet at 7.4 δ for the aromatic protons, a 4-H quintet at 4.3 δ for ester methylene protons, a 2-H multiplet at 3.1 δ for methylene protons, a 2-H multiplet at 2.4 δ for methylene protons and a 6-H triplet at 1.5 δ for ester methyl protons. The multiplet at 3.1 δ can be assigned to the benzylic protons and the multiplet at 2.4 δ to the methylene protons adjacent to $-P(O)(OEt)_2$, as in the case of 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide.

The mass spectrum of 108 exhibits a strong molecular ion at $m/_e$ 242. A base peak at $m/_e$ 138 may arise from the loss of $PhCH=CH_2$ from the molecular ion. The other prominent peaks are at $m/_e$ 214, 213, 197, 186, 185, 169 and 110. The fragmentation pattern is shown in Scheme XI.

Scheme XI



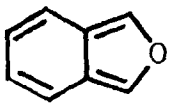
Scheme XI (cont'd)



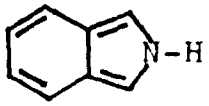
Benzo[c]phosphole and Derivatives

General Synthetic Route to 2-Heteroisoindene

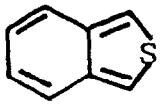
Isobenzofuran (109)[107] and isoindole (5)[108] have been known as transient reaction intermediates for a decade, whereas isothianaphthene (isobenzothiophene) (110) has proved sufficiently stable for isolation[109, 110]. However, the recent pioneering works of Warrener[111], Wege[112] and Bonnett[113] have shown that the isolations of isobenzofuran and isoindole are possible.



(109)

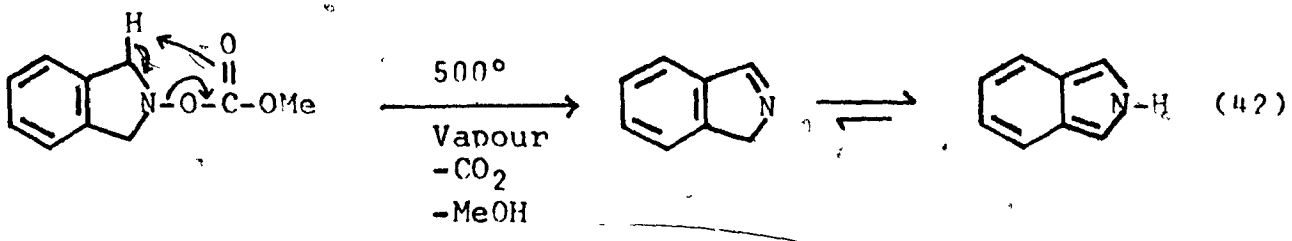


(5)



(110)

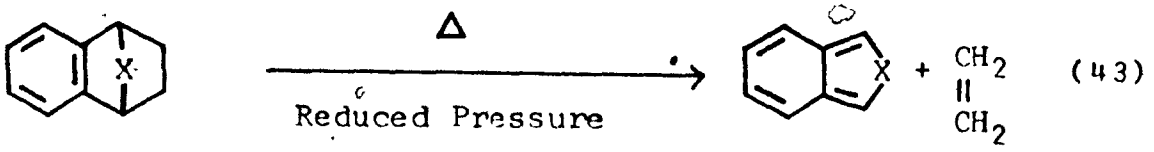
Bonnett and Brown[113] have successfully isolated isoindole (5), from the pyrolysis of 2-(methoxycarbonyloxy) isoindoline (111) at 500° and 0.1 mm Hg pressure (Eq. 42).



(42)

(111) (5)

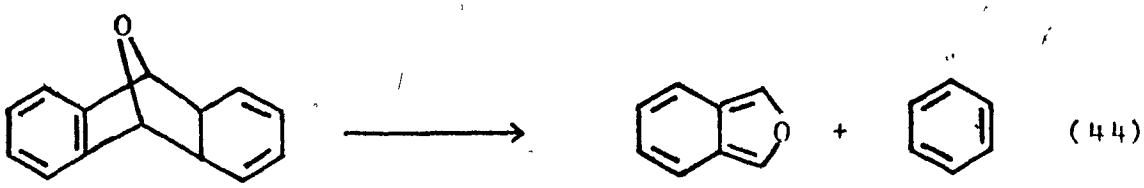
The alternative approaches to both isoindole[114] and isobenzofuran[112,115] involved the Retro-Diels-Alder reaction as illustrated in Eqs. 43 and 44.



(43)

(5); X=N-H

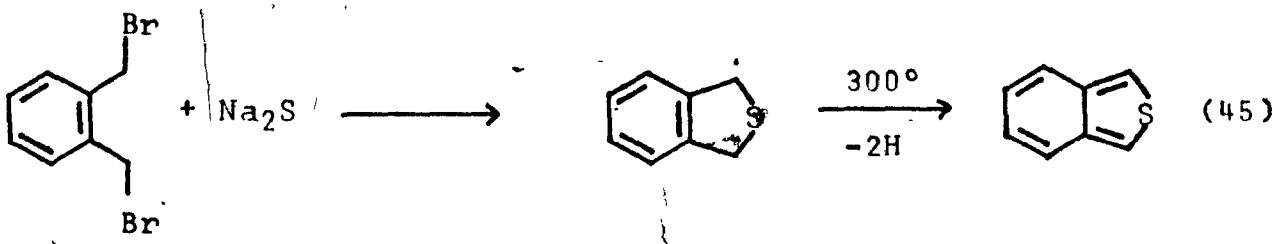
(109); X=O



(44)

(109)

Isobenzothiophene (110) is the first compound that has been successfully isolated in the heteroisoindene series, by Mayer et al[109] and their synthetic route started from o-xylylene dibromide (73) as shown in Eq. 45.

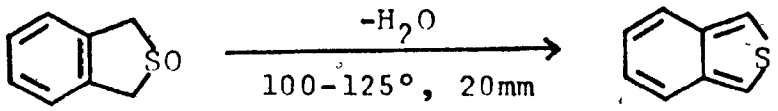


(45)

(73)

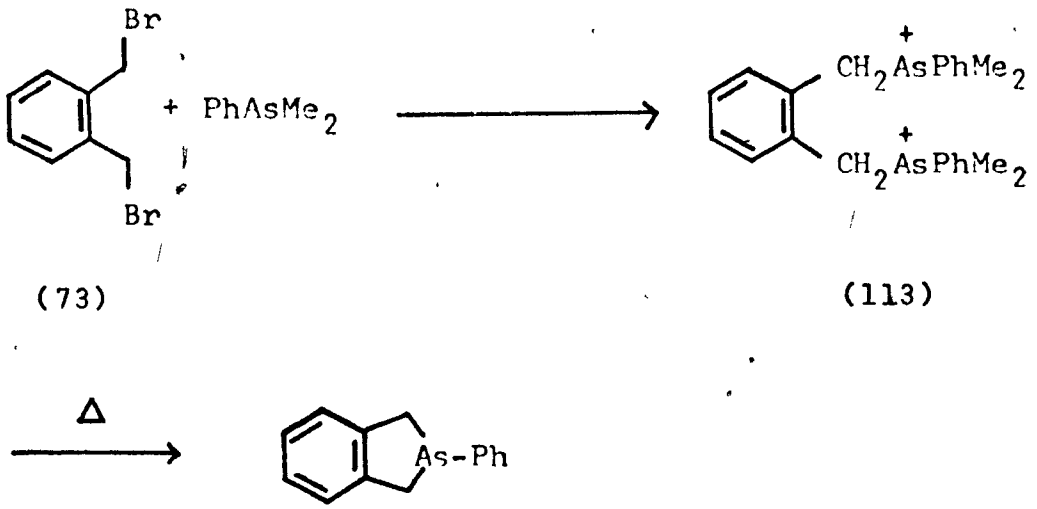
(110)

Later report by Cava[110] involved the dehydration of 1,3-dihydrobenzo[c]thiophene 2-oxide (112) (Eq. 46).



(112) (110) (46)

Mann et al[116] have prepared 2-phenylisoarsindoline (114) by two methods, the best one being the interaction of o-xylylene dibromide (73) and phenyldimethylarsine to give the diquaternary bromide 113, which on thermal decomposition afforded 114 (Eq. 47).



(73) (113)

(114) (47)

Mann and co-workers[68,69] have also investigated several synthetic routes to 2-phenylisophosphindoline (74). The best method has been previously mentioned (Eq. 27).

After our work was complete, Robinson et al[72] and Holland et al[73] also reported the preparation of isophosphindoline (68) (Scheme VI) and 1,2,3-triphenylisophosphindole 2-oxide (83) (Eq. 30).

Theoretical studies[117,118] predicted that isobenzofuran and isoindole are much less stable than furan and indole. Isobenzofuran is predicted to be devoid of aromatic character, whereas isoindole may be aromatic.

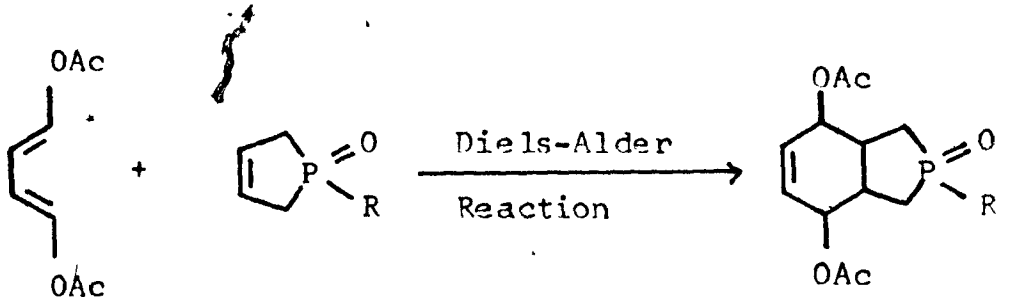
Theoretical and experimental works on the aforementioned systems led us to expect benzo[c]phosphole (6) system to be extremely reactive, if it can indeed be synthesized. A comparison between benzo[b]phosphole with its isoconjugated isomer benzo[c]phosphole will be of considerable interest.

Mislow has predicted[77] a substantial decrease in barrier height to the pyramidal inversion of phosphorus (6.9 k cal/mole) in 1-methylisophosphindole, relative to a model compound which has a value of 16.7 k cal/mole, based on a semiempirical calculation. He further predicted that delocalization will be favourable in the transition state to inversion, since the benzenoid character for the carbocyclic portion of the bicyclic structure is increased. If this prediction were true, the isophosphindole system would have the lowest barrier to inversion. It is the aim of this research project to make investigation on the synthesis and chemistry of benzo[c]phosphole system and its derivatives.

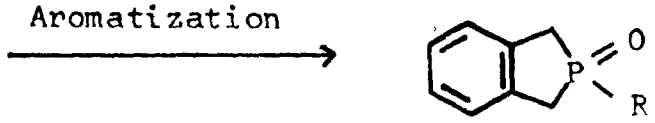
Isophosphindoline Oxide and Isophosphindoline

Attempted Diels-Alder Reaction of 1-Methyl-3-phospholene 1-Oxide with various dienes

The construction of the benzene ring by the method of Hill and Carlson[67] appears to be a convenient route for the synthesis of benzo[c]phosphole system.



(64) (115)

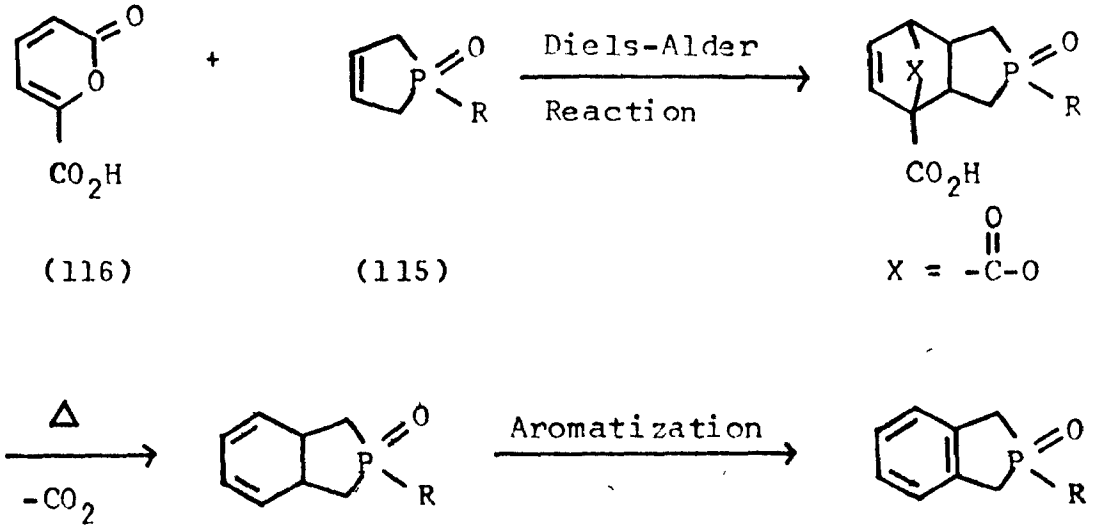


The most appropriate dienophile was chosen to be 1-methyl-3-phospholene 1-oxide, which could be easily prepared by the method of Quin and co-workers[95]. A mixture of equal molar quantities of E,E-1,4-diacetoxybutadiene[67] (64) and 1-methyl-3-phospholene 1-oxide (115, R = CH_3) was heated in a sealed tube at

125° for 7 to 14 days. Thin layer chromatography and i.r. spectrum revealed that no reaction took place. It is not surprising that 3-phospholene oxide, in contrast to the 2-phospholene isomer does not undergo Diels-Alder reaction. It is known that the electron-withdrawing phosphoryl group on conjugation with dienophile facilitates the reaction.

The Diels-Alder reaction of 115 (R = CH_3) with other dienes such as 1,3-butadiene, isoprene and 1-acetoxybutadiene[92] also failed.

In view of the report of Zimmermann[119] who used α-pyrone as the diene in the Diels-Alder reaction, α-pyrone-5-carboxylic acid (116) with the 3-phospholene oxide 115 (R = CH_3) might offer a method for the construction of benzene ring.



(116) (115)

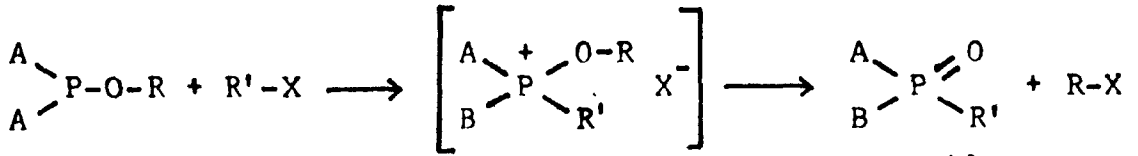
However, even at 130°, 116 and 115 failed to give any of the

adduct.

An alternative approach may involve the construction of the heterocyclic ring through ring closure, starting from mono or disubstituted benzene. The disubstituted benzene can be conveniently obtained from the Michaelis - Arbuzov reaction[120] of o-xylylene dibromide and the appropriate phosphorus ester.

Ethyl(2'-bromomethyl-benzyl)phenylphosphinate

Michaelis - Arbuzov[121,122] reaction is one of the most versatile methods for the formation of carbon-phosphorus bonds, involving the reaction of an alkyl halide with an ester of trivalent phosphorus. This reaction has been postulated to proceed via an ionic phosphonium intermediate, which then decomposes by the expansion of phosphorus valency. The overall process can be depicted as follows: -

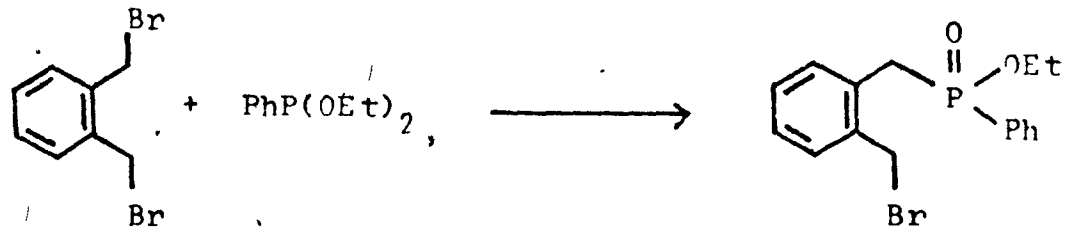


A, B = alkoxy, aryloxy, aryl, alkyl

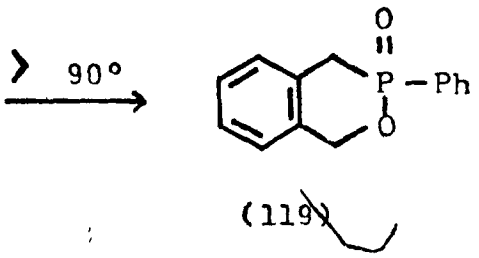
R, R' = alkyl

The competition between the reactant alkyl halide and the by-product halide can generally be minimized by the removal of the latter, during the course of the reaction. The normal reactivity sequence is acyl > primary alkyl > secondary alkyl and iodide > bromide > chloride.

Ethyl(2'-bromomethyl-benzyl)phenylphosphinate (118) was prepared by the Michaelis - Arbuzov reaction of equal molar quantities of o-xylylene dibromide (73) and diethyl phenylphosphonite (117) at 90° for 2 hours. Ethyl bromide was distilled off during the course of the reaction. Column chromatography of the reaction mixture on silica gel, eluting with ethyl acetate furnished 45% yield of the product as white crystals. It was identified as ethyl(2'-bromomethyl-benzyl)phenylphosphinate (118) (Eq. 48) by its spectroscopic properties and elemental analysis.



(73) (117) (118)



(119) (48)

Under higher temperature, 118 underwent intramolecular cyclization to give the cyclic phosphinate ester 2-phenyl-3-oxa-1,2,3,4-tetrahydroisophosphinoline 2-oxide (119). This kind

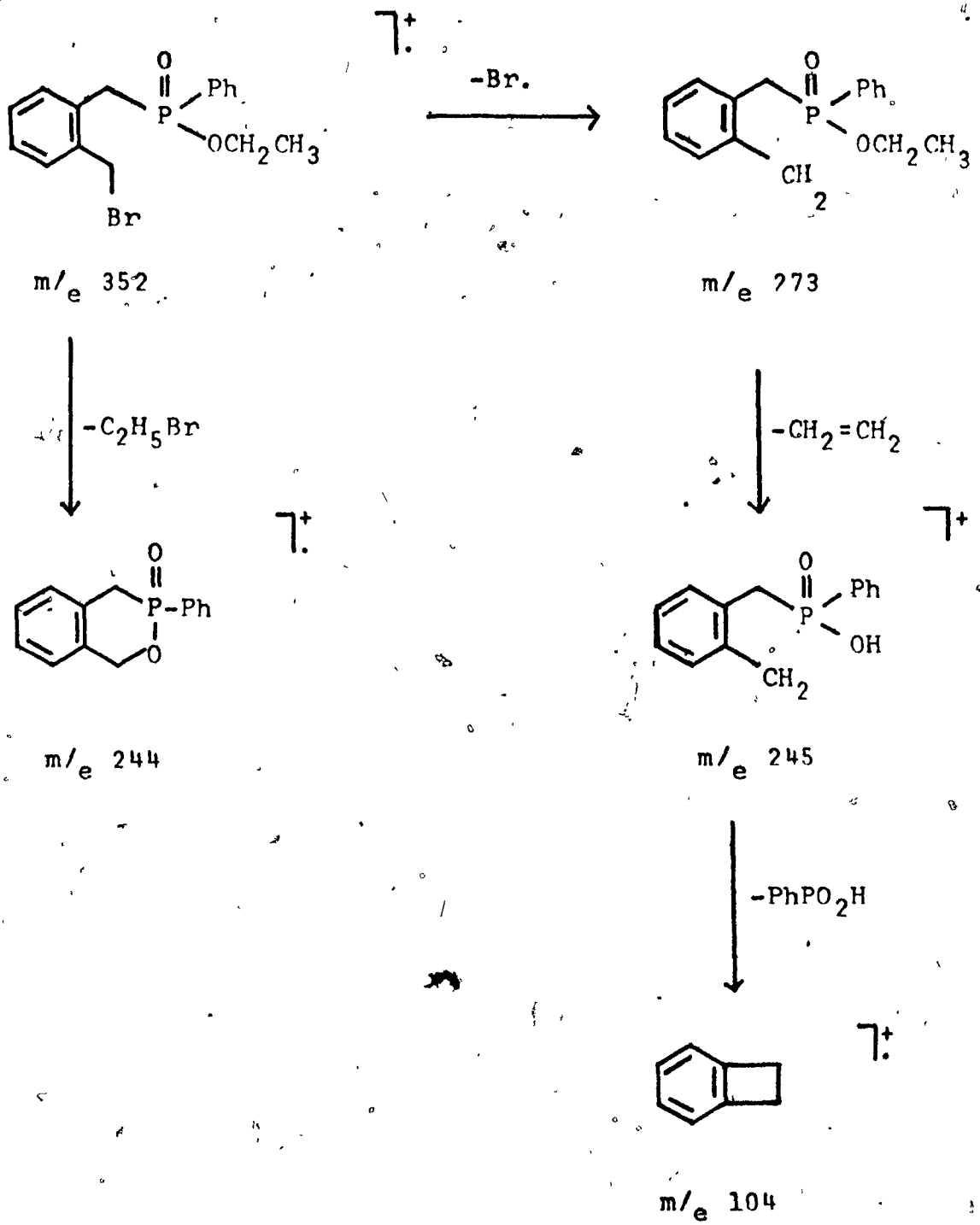
of cyclization has been previously reported[123,124].

The infrared spectrum of ethyl(2'-bromomethyl-benzyl)phenylphosphinate (118) exhibits a strong band at 1220 cm^{-1}, attributable to P = O absorption, and a broad band at 1040 cm^{-1} and medium intensity band at 1160 cm^{-1} associated with P-O-C_2H_5 absorption. It also shows the strong phenyl bands at 1440 cm^{-1} and 700 - 800 cm^{-1}.

The proton n.m.r. (p.m.r.) spectrum of ethyl(2'-bromomethyl-benzyl)phenylphosphinate consists of a 9-H multiplet at 7.4 δ for the aromatic protons, a 2-H singlet at 4.5 δ for the benzylic protons attached to -Br, a 2-H quintet at 3.8 δ for the ester methylene protons, a 2-H two overlapped doublets (J_{P-CH} = 20 Hz, 18 Hz) at 3.3 - 3.7 δ for the nonequivalent benzylic protons adjacent to the P = O group and a 3-H triplet at 1.2 δ for the ester methyl protons.

The mass spectrum of 118 shows the P ($m/_e$ 352) and P+2 ($m/_e$ 354) peaks in 1:1 intensity ratio, which is indicative of a monobromo compound. It also exhibits an intensive (P-Br.) peak at $m/_e$ 273, which further eliminates ethylene molecule to give rise to the peak at $m/_e$ 245. Further loss of the $PhPO_2H$ group provides the base peak at $m/_e$ 104. The fragmentation pattern is illustrated in Scheme XII.

Scheme XII



The cyclic phosphinate ester 119 has a simple n.m.r. spectrum featuring a 9-H multiplet at 7.0 - 7.8 δ for the aromatic protons, a 2-H doublet at 5.3 δ for the methylene protons adjacent to oxygen (J_{POCH} = 16 Hz) and a 2-H doublet at 3.3 δ for the methylene protons adjacent to P = O (J_{P-CH} = 18 Hz).

Reaction of Ethyl(2'-bromomethyl-benzyl)phenylphosphinate with Vitride Reagent

A useful and general method for the formation of the carbon-phosphorus bonds has recently been discovered by Wetzel and Kenyon[125]. This method involves the reaction of phosphorus ester such as phosphonate, phosphinate or phosphate with an alkyl halide, in the presence of sodium bis(2-methoxyethoxy) aluminium hydride[126] (commercially known as Vitride or Red-Al; for simplicity the former term will be used throughout this thesis) (Eq. 49).

$$(RO)_n\overset{O}{\overset{\|}{P}}R'_{(3-n)} \xrightarrow[nR''X]{nNaAlH_2(OCH_2CH_2OCH_3)_2} R''_n\overset{O}{\overset{\|}{P}}R'_{(3-n)} \qquad (49)$$

R' = alkyl, aryl,

R = primary or secondary alkyl.

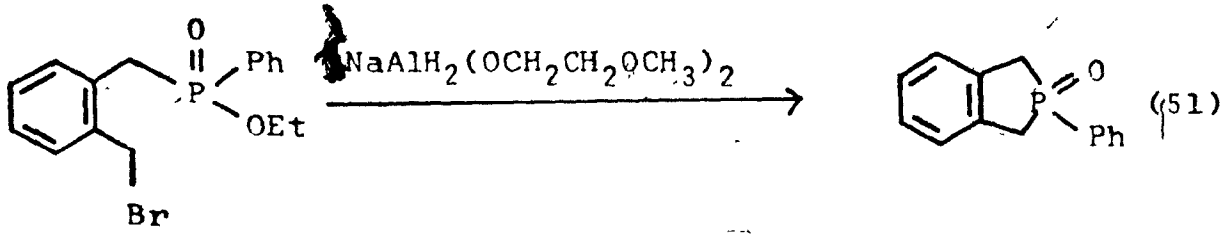
It is suggested that the reaction proceeds via an intermediate sodium salt of phosphorus anion 120, which is derived from the action of hydride on the phosphorus ester. The anion 120 is alkylated by the alkyl halide in a nucleophilic substitution,

furnishing the phosphine oxide and sodium halide (Eq. 50).

$$H^- + R_2P(=O)-OR \longrightarrow R_2PH(=O) \xrightarrow{H^-} R_2P(=O)^- \xrightarrow{R''X} R_2PR''(=O) + X^- \quad (50)$$

(120)

It is expected that the above P-C bond formation reaction might probably offer a straightforward method for the cyclization of ethyl(2'-bromomethyl-benzyl)phenylphosphinate to the isophosphindoline system. Thus 118 was treated with an excess of Vitride reagent in refluxing benzene for 48 hrs. After working up, the resulting reaction mixture was chromatographed on silica gel, eluting with ethyl acetate to give 13% yield of a product, which was identified as 2-phenylisophosphindoline 2-oxide (121) (Eq. 51) by its spectroscopic properties and elemental analysis.



(51)

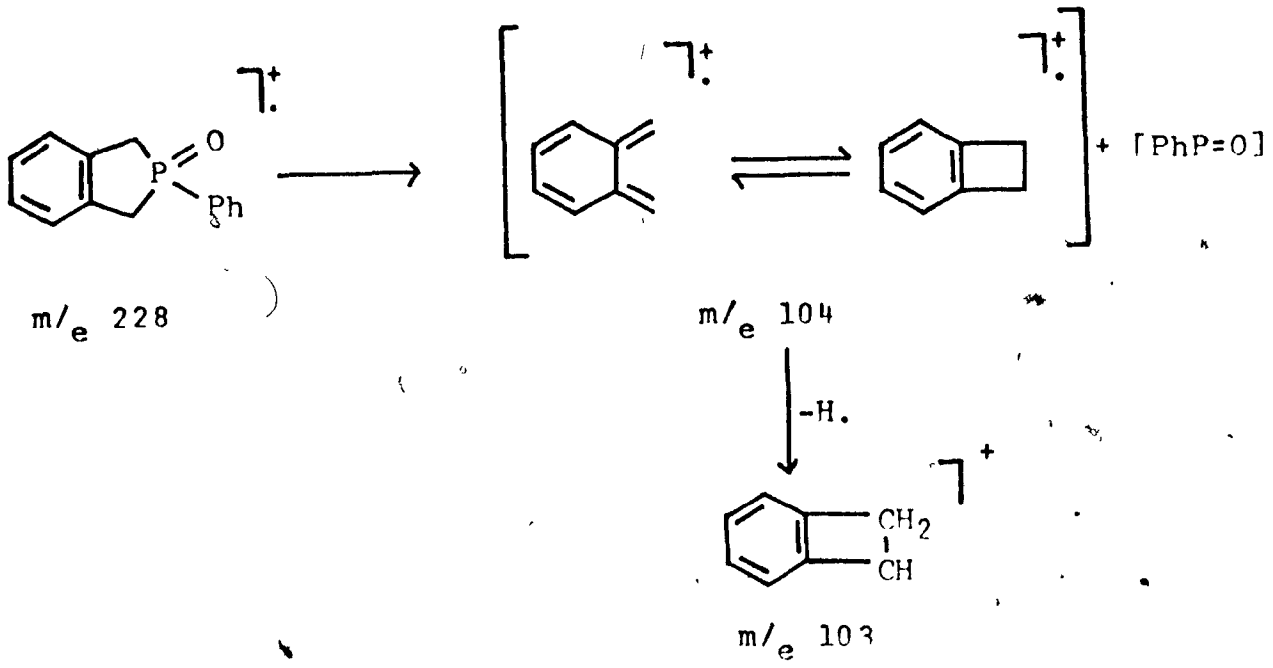
(118) (121)

2-Phenylisophosphindoline 2-oxide (121) (fig. 19) has a simple infrared spectrum consisting of a strong characteristic P=O stretching at 1210 cm^{-1} and strong phenyl bands at 1440 cm^{-1} 1100 cm^{-1} and 700 - 800 cm^{-1}. The band at 1100 cm^{-1} is probably

associated with aromatic vibration involving some P-C stretching[127].

The 100 MHz proton n.m.r. spectrum of 2-phenylisophosphindoline 2-oxide (121) (fig. 24) revealed that the methylene protons are nonequivalent and could be considered as part of an ABX ($X = {}^{31}P$) system, with the following spectral parameters, $J_{AB} = 17$, $J_{AX} = 16$, $J_{BX} = 9$ Hz, $\delta_A = 3.51$ and $\delta_B = 3.35$ ppm. The aromatic protons appear at 7.5 - 8.0 δ as 5-H multiplet, which may be probably due to the P-phenyl protons and at 7.4 δ as a 4-H singlet, attributable to the protons of the fused benzene ring. In the n.m.r. spectrum of o-xylylene dibromide, a 4-H singlet is also observed for the aromatic protons.

The mass spectrum of 2-phenylisophosphindoline 2-oxide (121) (fig. 29) is very simple. A strong molecular ion appears at $m/_e$ 228. The other prominent peak at $m/_e$ 104 may arise from the loss of PhPO moiety from the molecular ion, a process which finds parallel in the corresponding heterocycles[128,129]. Loss of -H radical from this peak provides the peak at $m/_e$ 103. The other peaks are very weak. The fragmentation pattern is as follows: -



The u.v. spectrum of 2-phenylisophosphindoline 2-oxide (121) (fig. 34) shows a high intensity primary band at 222 nm and a low intensity secondary band featuring vibrational fine structure with a maximum at 266 nm. The spectrum bears resemblance to those of triphenylphosphine oxide[85], 1-phenyl-[65,66] and 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxides. Similar assignment can be made as in the benzo[b]phosphole oxides. The high intensity band at 222 nm (log ε 3.66) is assigned to correspond to the primary E band of benzene at 203 nm, displaced by substitution. The low intensity band at 266 nm (log ε 2.81) may correspond to the B band of benzene at 256 nm. Since increasing alkyl substitution causes displacement of the B band of benzene, the shift of 256 nm band of benzene to the longer wavelength 266 nm is associated with the alkyl substitutions of the benzene ring. This absorption should be compared with those of indane[130] (λ_{max} 273 nm, log ε 3.20) and o-xylene[130] (λ_{max} 262 nm, log ε 2.48).

In view of the general similarity of the spectrum to that of triphenylphosphine oxide[85] and the presence of the fine structure, the conclusion may be drawn that 2-phenylisophosphindoline 2-oxide has unperturbed or weakly perturbed benzene rings.

Diethyl phenylphosphonate

The successful synthesis of 2-phenylisophosphindoline 2-oxide led us to attempt an alternative one-step synthesis by treating o-xylylene dibromide with diethyl phenylphosphonate in the presence of Vitride reagent.

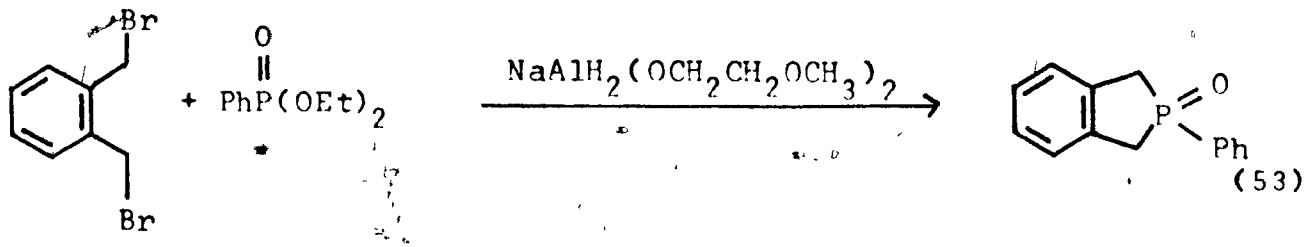
Diethyl phenylphosphonate was prepared by the slightly modified method of Siddall et al[131] from phenylphosphonic dichloride (122) and excess absolute ethanol, in the presence of triethylamine (Eq. 52). Distillation of the crude mixture, after working up, gave 68% yield of diethyl phenylphosphonate (123) as colourless liquid.

$$\underset{(122)}{PhPCl_2(=O)} + 2\ EtOH \xrightarrow{NEt_3} \underset{(123)}{PhP(=O)(OEt)_2} \qquad (52)$$

2-Phenylisophosphindoline 2-Oxide

2-Phenylisophosphindoline 2-oxide (121) was prepared from o-xylylene dibromide (73) and diethyl phenylphosphonate (123) in the presence of excess Vitride reagent (Eq. 53). The reaction was carried out in dry benzene at 70° for 48 hrs. On working

up, the crude product (55%) showed n.m.r. spectrum identical to the expected 2-phenylisophosphindoline 2-oxide. Column chromatography of the crude mixture on silica gel, eluting with ethyl acetate afforded (15% - 20%) of pure 2-phenylisophosphindoline 2-oxide, the spectroscopic properties of which were identical in all respects with the compound obtained in the previous experiment.



(53)

(73) (123) (121)

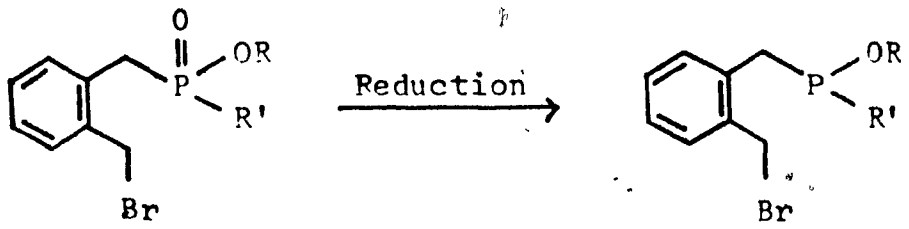
Attempts to improve the yield of the product by decreasing or increasing the reaction time or temperature were unsuccessful.

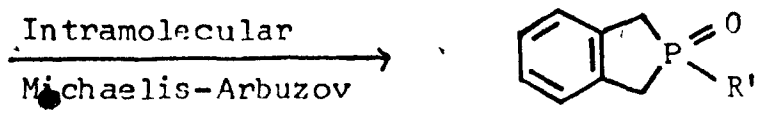
Although the yield is only moderate, this method offers a convenient one-step synthesis of 2-phenylisophosphindoline 2-oxide and is preferable to the rather long pathways that have been reported[8,10].

Reaction of Ethyl(2'-bromomethyl-benzyl)phenylphosphinate with Trichlorosilane

An alternative approach for the cyclization reaction is to reduce the phosphonate or phosphinate ester to the corresponding

phosphine, which may then undergo intramolecular Michaelis-Arbuzov reaction to produce the desired compound (Eq. 54).

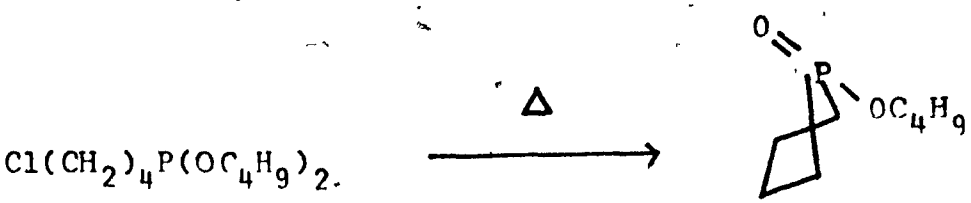




(54)

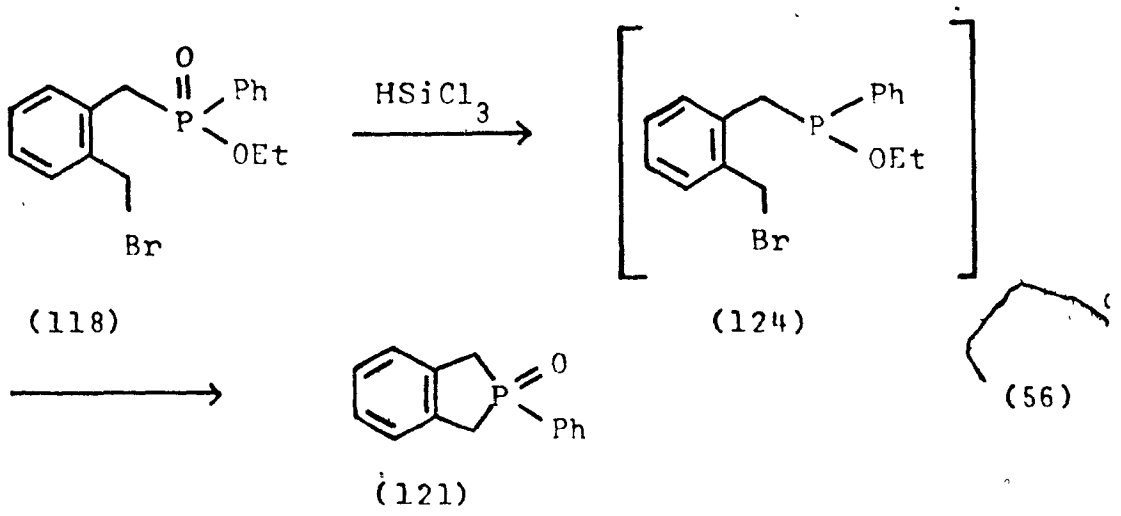
R' = alkyl, aryl, alkoxy (OR)

Silanes appear to be the suitable reducing agents for this purpose. Intramolecular Michaelis-Arbuzov reaction is quite probable, since this kind of reaction has been demonstrated[132] (Eq. 55).



(55)

Ethyl(2'-bromomethyl-benzyl)phenylphosphinate (118) was treated with two molar excess of trichlorosilane in refluxing benzene, under nitrogen for 48 hours. The reaction after hydrolysis and removal of solvent gave on preparative thin layer chromatography, 12% yield of 2-phenylisophosphindoline 2-oxide (Eq. 56).

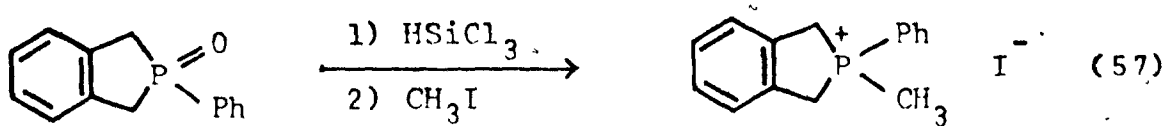


The isolation of 121 indicates that in this reaction, the P=O bond was reduced[99] first to give the corresponding phosphinite ester 124, which then underwent intramolecular Michaelis - Arbuzov reaction to form the product (Eq. 56).

Reduction of 2-Phenylisophosphindoline 2-Oxide with Trichlorosilane and Quaternization with Methyl Iodide

2-Phenylisophosphindoline 2-oxide was treated with two molar excess of trichlorosilane in refluxing benzene, under nitrogen, for 48 hours. To the reaction mixture, 30% NaOH solution was added to hydrolyse the silane. Without isolation of the iso-

phosphindoline, methyl iodide was added and the reaction mixture was kept stirring overnight. 2-Methyl-2-phenylisophosphindolinium iodide (125) (Eq. 57) was obtained in 25% yield as white solid. m.p. 205 - 207° (Lit.[68] m.p. 207 - 209°).



(121) (125) (57)

The infrared spectrum of 125 shows strong phenyl bands at 1440 cm^{-1}, 1120 cm^{-1} and 700 - 800 cm^{-1}. A sharp medium band at 1320 cm^{-1} is attributable to P-CH_3 stretching[133].

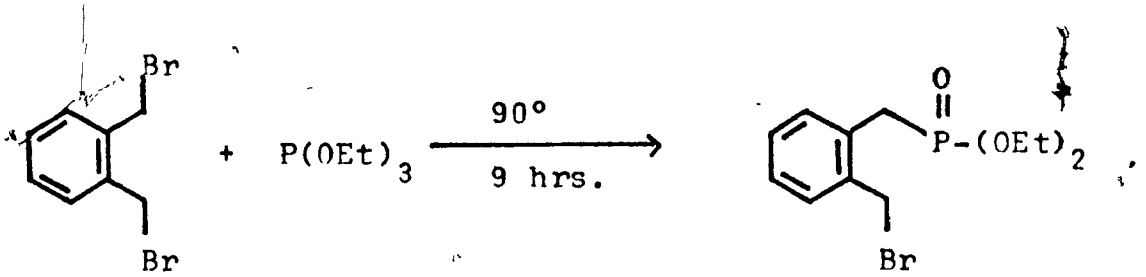
Dialkyl(2'-bromomethyl)benzylphosphonates and their Chemical Transformations

Following the successful synthesis of 2-phenylisophosphindoline 2-oxide by the above methods, it seems reasonable to expect that isophosphindoline systems with functional groups attached to phosphorus can be similarly prepared. We therefore explored the chemistry of dialkyl(2'-bromomethyl)benzylphosphonates and found to our surprise rather different results.

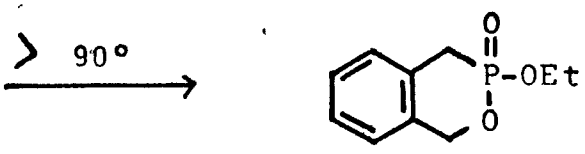
Diethyl(2'-bromomethyl)benzylphosphonate

By heating a mixture of equal molar quantities of o-xylylene dibromide (73) and freshly distilled triethyl phosphite (126) at 90° for 9 hours, 50% yield of diethyl(2'-bromomethyl)benzylphosphonate (127) was obtained after separation by column chromatography on silica gel, eluting with ethyl acetate. A low boiling liquid ethyl bromide was distilled off, during the course of the reaction. Diethyl(2'-bromomethyl)benzylphosphonate was identified by its spectroscopic properties and elemental analysis.

Under higher reaction temperature, the product underwent intramolecular cyclisation, to yield the cyclic phosphonate ester 2-ethoxy-3-oxa-1,2,3,4-tetrahydroisophosphinoline 2-oxide (128) (Eq. 58).



(73) (126) (127)



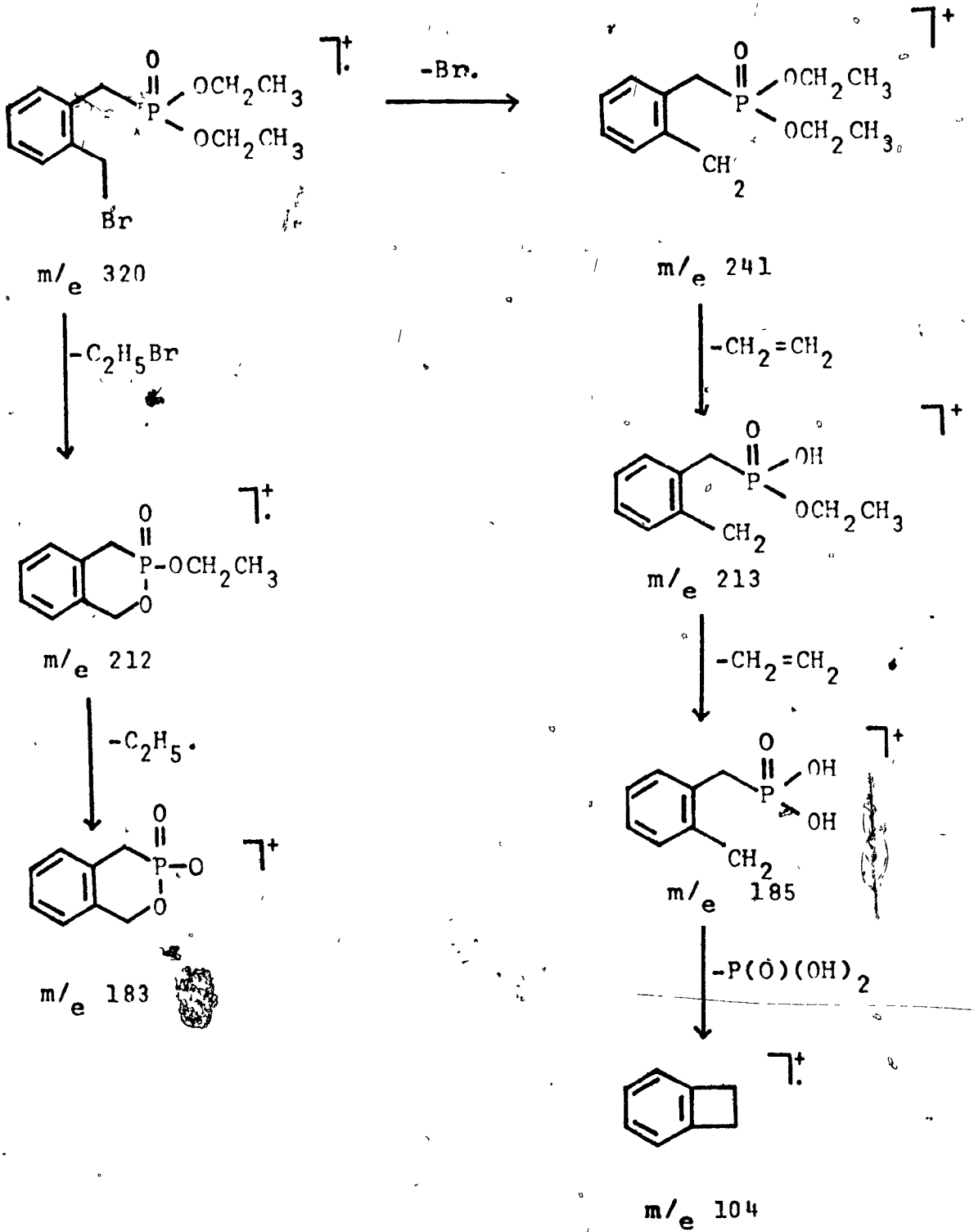
(128) (58)

The infrared spectrum of diethyl(2'-bromomethyl)benzylphosphonate (127) features a strong band at 1250 cm^{-1}, characteristic of the P=O absorption, a broad band at 1020 cm^{-1} and a medium intensity band at 1160 cm^{-1} associated with P-O-C_2H_5 absorption.

The n.m.r. spectrum of diethyl(2'-bromomethyl)benzylphosphonate consists of a 4-H multiplet at 7.5 δ for the aromatic protons, a 2-H singlet at 4.9 δ for the benzylic protons adjacent to -Br, a 4-H quintet at 4.3 δ for the ester methylene protons, a 2-H doublet (J_{P-CH} = 24 Hz) at 3.5 δ for the benzylic protons adjacent to P=O, and a 6-H triplet at 1.4 δ for the ester methyl protons.

The mass spectrum of 127 exhibits P($m/_e$ 320) and P+2($m/_e$ 322) peaks in 1:1 intensity ratio. An important fragment is (P-Br.) ion at $m/_e$ 241. The base peak is at $m/_e$ 185, which may arise from the successive loss of two ethylene molecules by McLafferty rearrangement from the (P-Br.) ion. The fragmentation pattern is shown in Scheme XIII.

Scheme XIII


-Br.
m/e 320
m/e 241
-C2H5Br
-CH2=CH2
m/e 212
m/e 213
-C2H5·
-CH2=CH2
m/e 183
m/e 185
-P(O)(OH)2
m/e 104

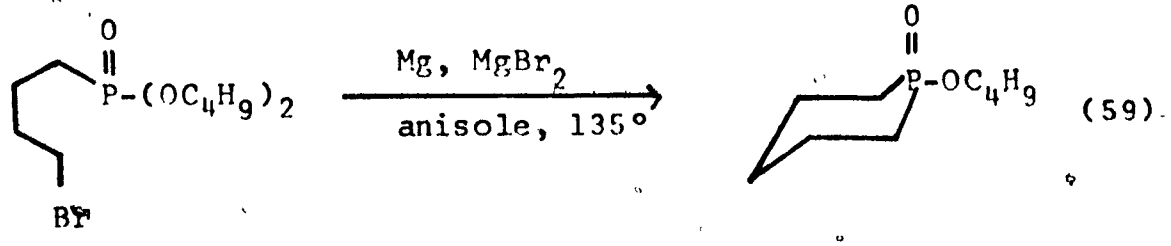
A peak at $m/_e$ 212 may be formed by the loss of C_2H_5Br from the molecular ion. The peak at $m/_e$ 212 further loses C_2H_5 radical to give the peak at $m/_e$ 183. The elimination of $-P(O)(OH)_2$ from the base peak at $m/_e$ 185 provides the peak at $m/_e$ 104.

The peak associated with the loss of ethylene molecule from the (P-Br.) ion is also observed in analogy to the other compounds containing the -P(O)OEt moiety e.g. Scheme IX.

The n.m.r. spectrum of the cyclic phosphonate ester 128 exhibits a 4-H multiplet at 7.5 δ for the aromatic protons, a 2-H doublet (J_{POCH} = 16 Hz) at 5.5 δ for the methylene protons adjacent to oxygen, a 2-H quintet at 4.4 δ for the ester methylene protons, a 2-H doublet (J_{P-CH} = 20 Hz) at 3.3 δ for the methylene protons adjacent to P=O group and a 3-H triplet at 1.4 δ for the ester methyl protons.

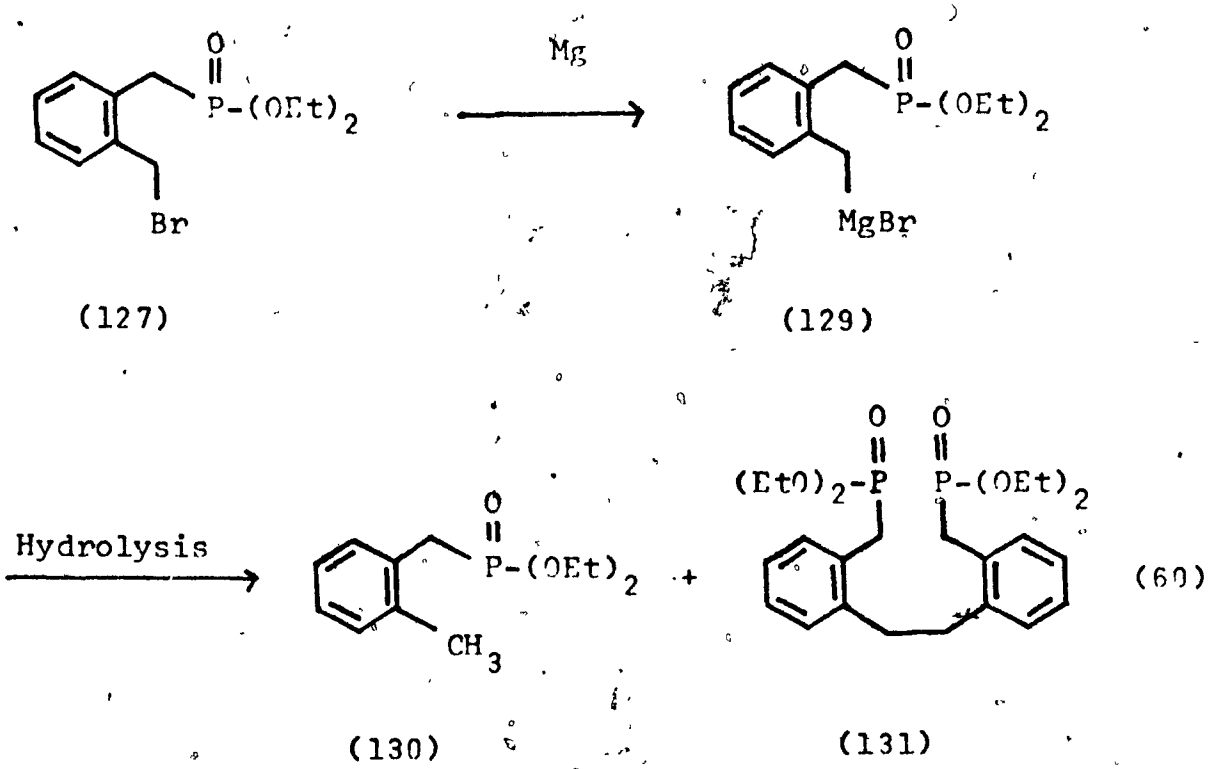
Attempted Cyclization of Diethyl(2'-bromomethyl)benzylphosphonate with Magnesium and Lithium

In view of the report by Howard[134] who achieved the ring closure of the phosphonate ester by Grignard reaction (Eq. 59), it is felt that the Grignard reagent of dialkyl(2'-bromomethyl)-benzylphosphonate might cyclize to give isophosphindoline.



(59)

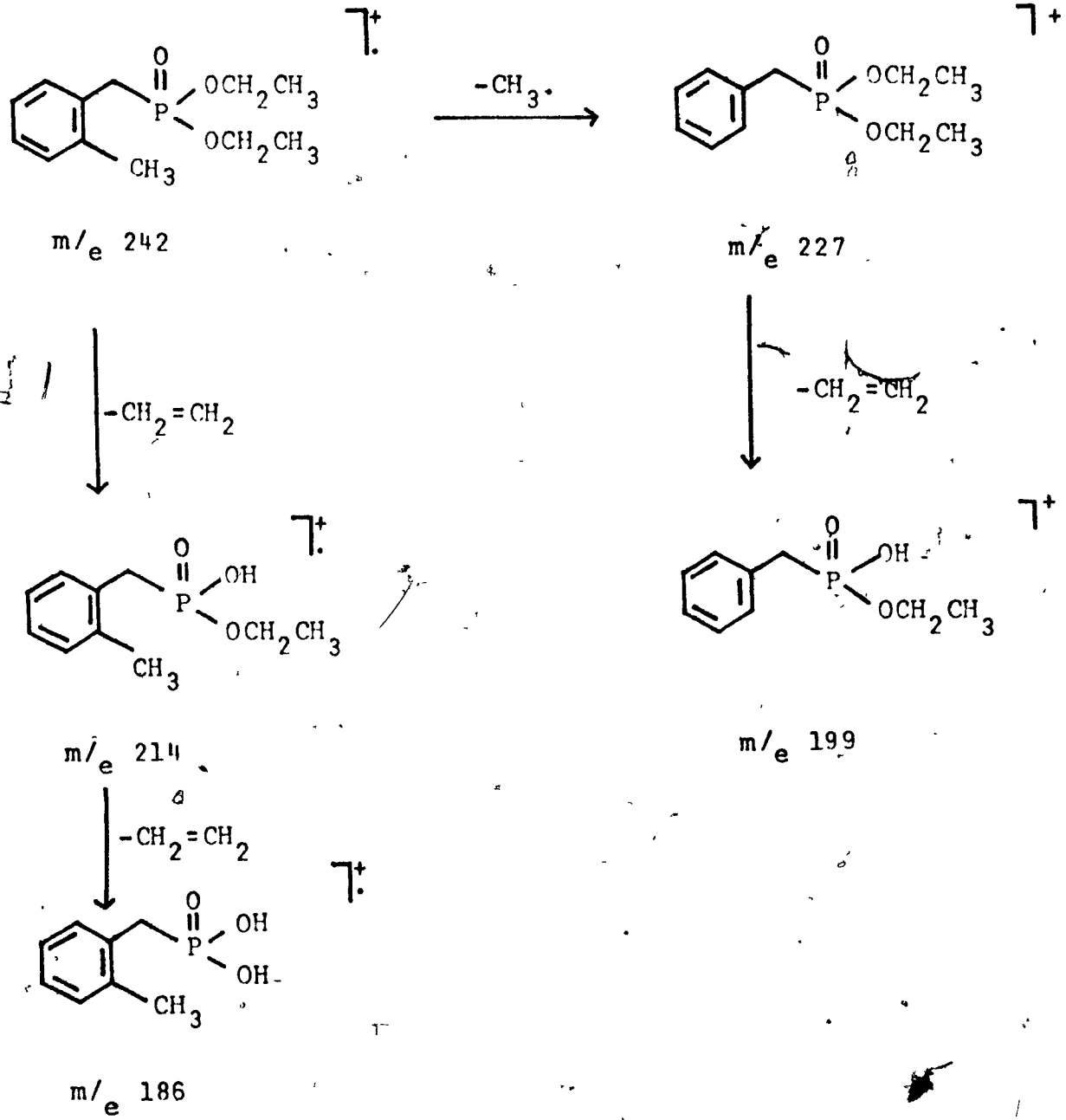
Thus, the Grignard reagent was prepared from diethyl(2'-bromomethyl)benzylphosphonate (127) and excess magnesium powder in refluxing benzene for 24 hours. After hydrolysis, the reaction mixture, on separation by preparative thin layer chromatography, afforded two products. They were identified by mass, n.m.r. and i.r. spectra as diethyl(2'-methyl)benzylphosphonate 130 and 1,2-di[o-(diethylphosphonato-methyl)phenyl]ethane 131 (Eq. 60).



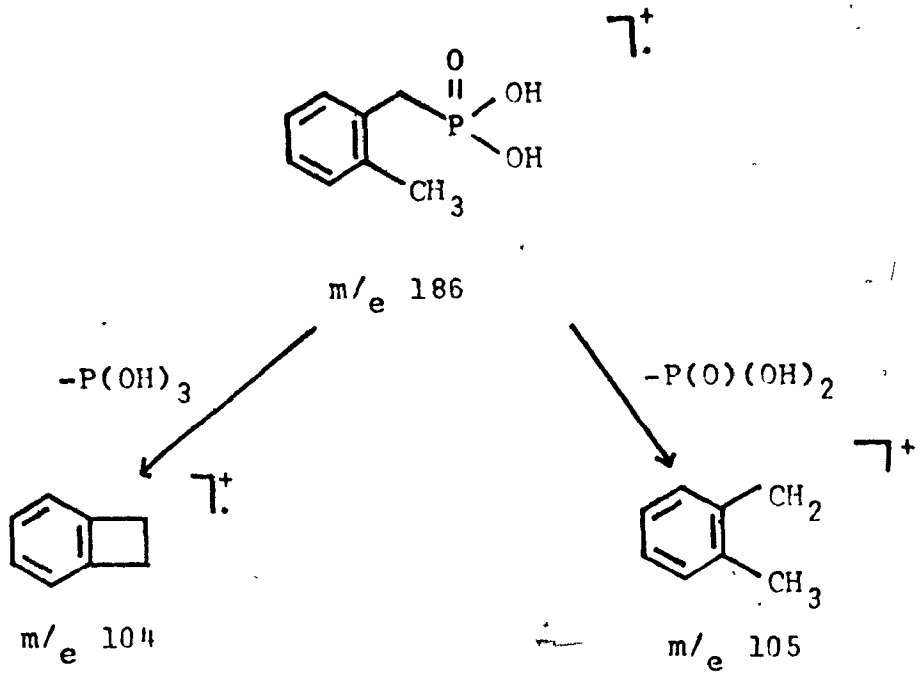
The n.m.r. spectrum of 130 exhibits a 4-H multiplet at 7.4 δ for the aromatic protons, a 4-H quintet at 4.1 δ for the ester methylene protons, a 2-H doublet at 3.3 δ for the benzylic protons; J_{P-CH} = 22 Hz), a 3-H singlet at 2.5 δ for the methyl protons and a 6-H triplet at 1.3 δ for ester methyl protons.

The mass spectrum of 130 shows a strong molecular ion at $m/_e$ 242. Loss of methyl radical and ethylene molecule provide the peaks at $m/_e$ 227 and 214 respectively. The peak at $m/_e$ 214 again loses ethylene molecule to give the peak at $m/_e$ 186, which further eliminates $-P(O)(OH)_2$ moiety to provide the base peak at $m/_e$ 105. The fragmentation pattern is illustrated in Scheme XIV.

Scheme XIV



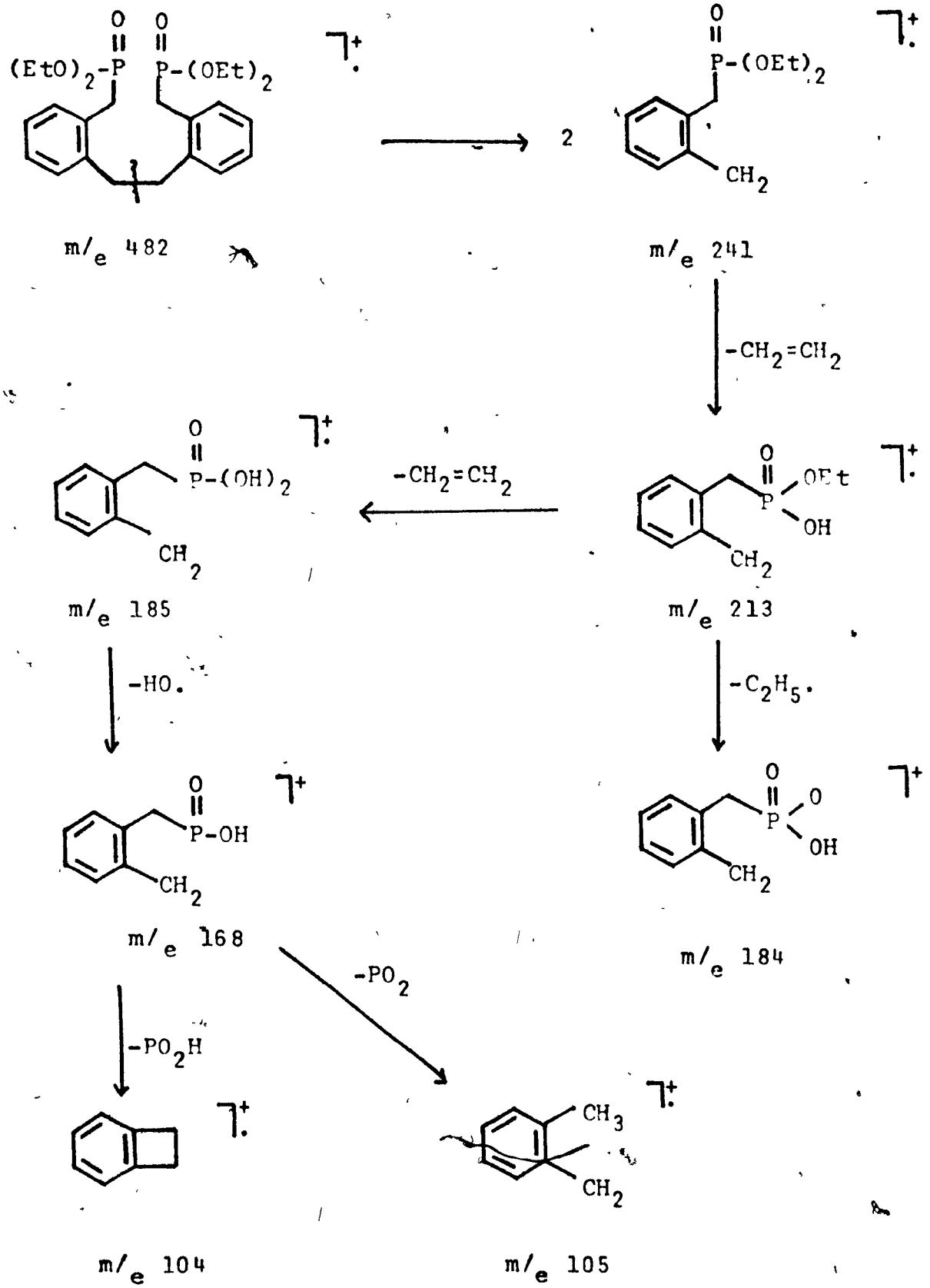
Scheme XIV (cont'd)



The n.m.r. spectrum of 131 features a 8-H multiplet at 7.4 δ for the aromatic protons, a 8-H quintet at 4.1 δ for the ester methylene protons, a 4-H doublet at 3.2 δ for the benzylic protons adjacent to P=O,(J_{P-CH} = 24 Hz), a 4-H singlet at 3.1 δ for the benzylic protons and a 12-H triplet at 1.2 δ for the ester methyl protons.

The mass spectrum of 131 consists of a base peak at m/e 482 (M^+). The (M^+-241) peak at m/e 241 loses ethylene molecule to give the peak at m/e 213. This peak again loses ethylene molecule and ethyl radical to provide the peaks at m/e 185 and 184 respectively. The other peaks are at m/e 168, 105 and 104. The fragmentations involved are depicted in Scheme XV.

Scheme XV


(EtO)2-P
P-(OEt)2
m/e 482
2
P-(OEt)2
CH2
m/e 241
-CH2=CH2
P-(OH)2
CH2
m/e 185
-CH2=CH2
OEt
OH
CH2
m/e 213
-HO.
-C2H5.
P-OH
CH2
m/e 168
P
O
OH
CH2
m/e 184
-PO2
-PO2H
CH3
CH2
m/e 104
m/e 105

It seemed that the Grignard reagent 129 was apparently generated. However, it failed to undergo intramolecular nucleophilic displacement reaction to furnish the expected isophosphindoline oxide.

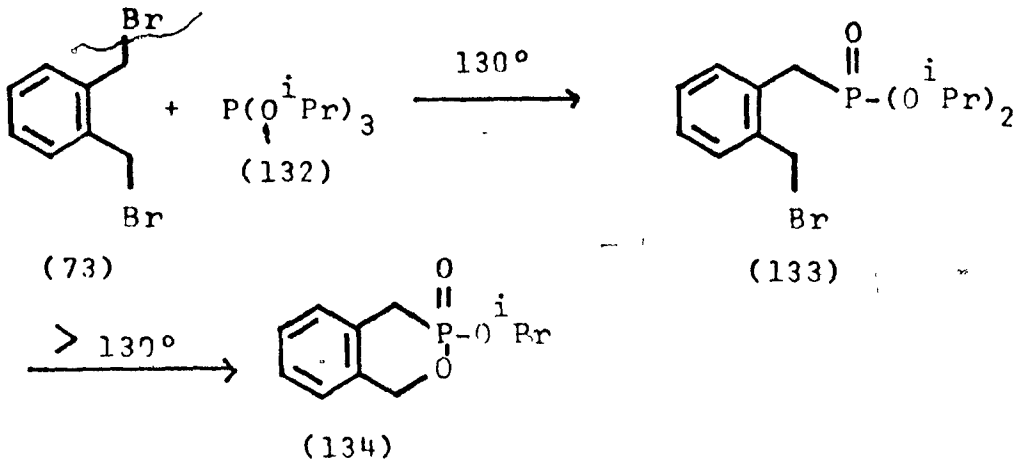
It is generally accepted that organo-lithium compounds are more reactive as nucleophiles than the corresponding magnesium Grignard reagents. Therefore, the lithium reagent was prepared from diethyl(2'-bromomethyl)benzylphosphonate and excess lithium powder. Even in this case, the intramolecular cyclization failed to occur. The reaction mixture on working up, gave the same products 130 and 131.

The occurrence of the coupling product 131 is not unexpected. It is generally known that coupling reaction takes place readily between the Grignard reagent and active halides.

Diisopropyl(2'-bromomethyl)benzylphosphonate

Diisopropyl(2'-bromomethyl)benzylphosphonate was prepared by the Michaelis - Arbuzov reaction of o-xylylene dibromide (73) and freshly distilled triisopropyl phosphite (132) at 130° for 2 hours. During the course of the reaction, a low-boiling liquid isopropyl bromide was distilled off. Column chromatography of the reaction mixture on silica gel, eluting with ethyl acetate, afforded 40% yield of a product, the spectroscopic properties of which, were in accord with the structure of diisopropyl(2'-bromomethyl)benzylphosphonate (133) (Eq. 61). In analogy to the diethyl ester, it also transformed to a cyclic

phosphonate ester 134 at higher temperature (Eq. 61).



(61)

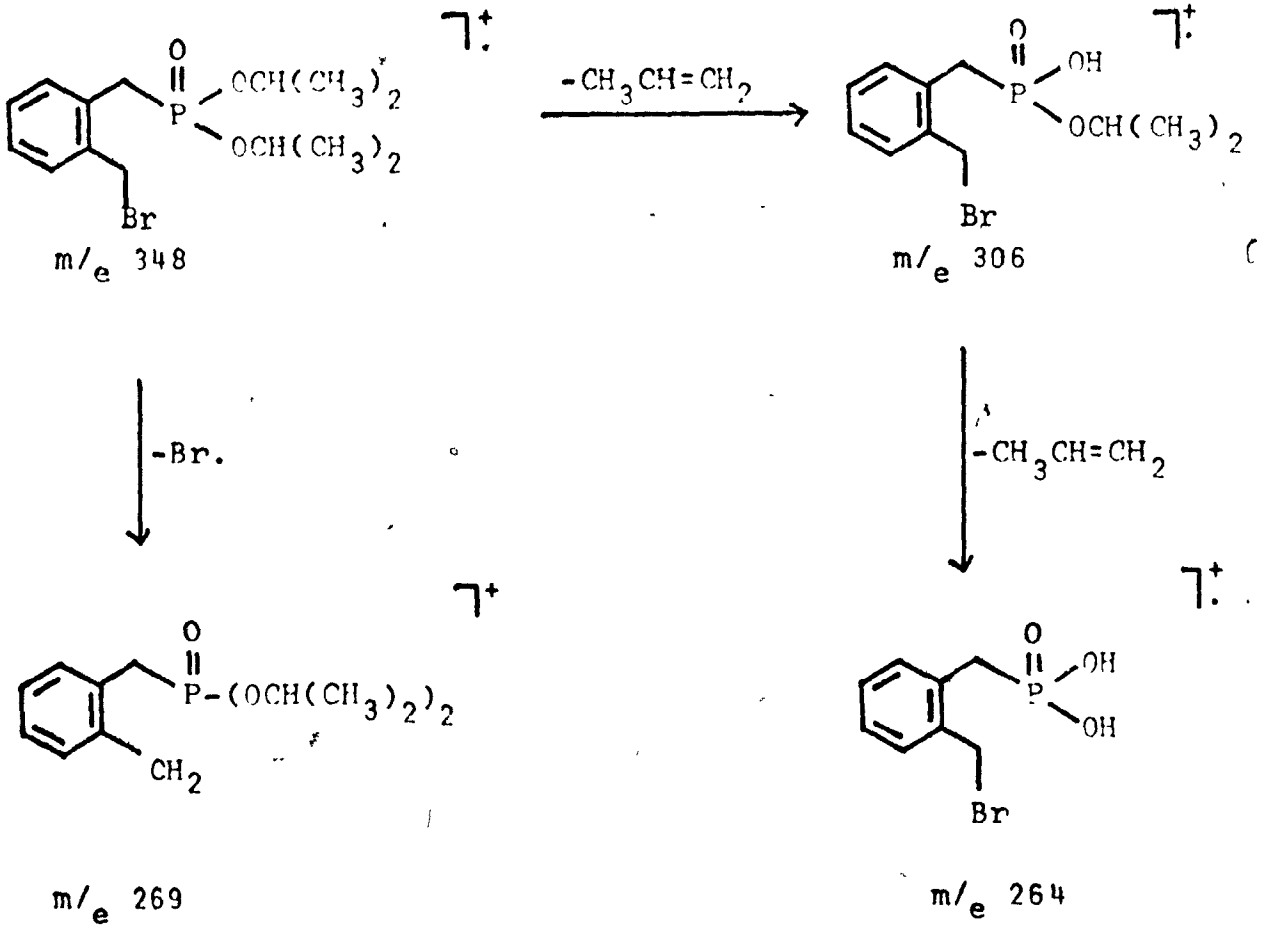
The infrared spectrum of diisopropyl(2'-bromomethyl)benzylphosphonate (133) features a characteristic strong P=O stretching at 1260 cm^{-1}, a broad band at 1020 cm^{-1} and a medium intensity band at 1150 cm^{-1}, attributable to P-O-C absorption. It also exhibits a strong doublet at 1390 cm^{-1} and 1395 cm^{-1} which is indicative of the isopropyl group.

The n.m.r. spectrum of 133 shows a 4-H multiplet at 7.4 δ for the aromatic protons, a 2-H singlet at 4.9 δ for the benzylic protons adjacent to -Br, a 2-H multiplet centred at 4.7 δ for the isopropyl methine protons and a 2-H doublet (J_{P-CH} = 24 Hz) corresponds to the benzylic protons adjacent to P=O group. In addition, a 12-H two doublets appear at 1.1 - 1.4 δ for the non-equivalent two methyl groups of isopropyl moiety. This kind of resonance doubling has been observed by Siddall et al[131].

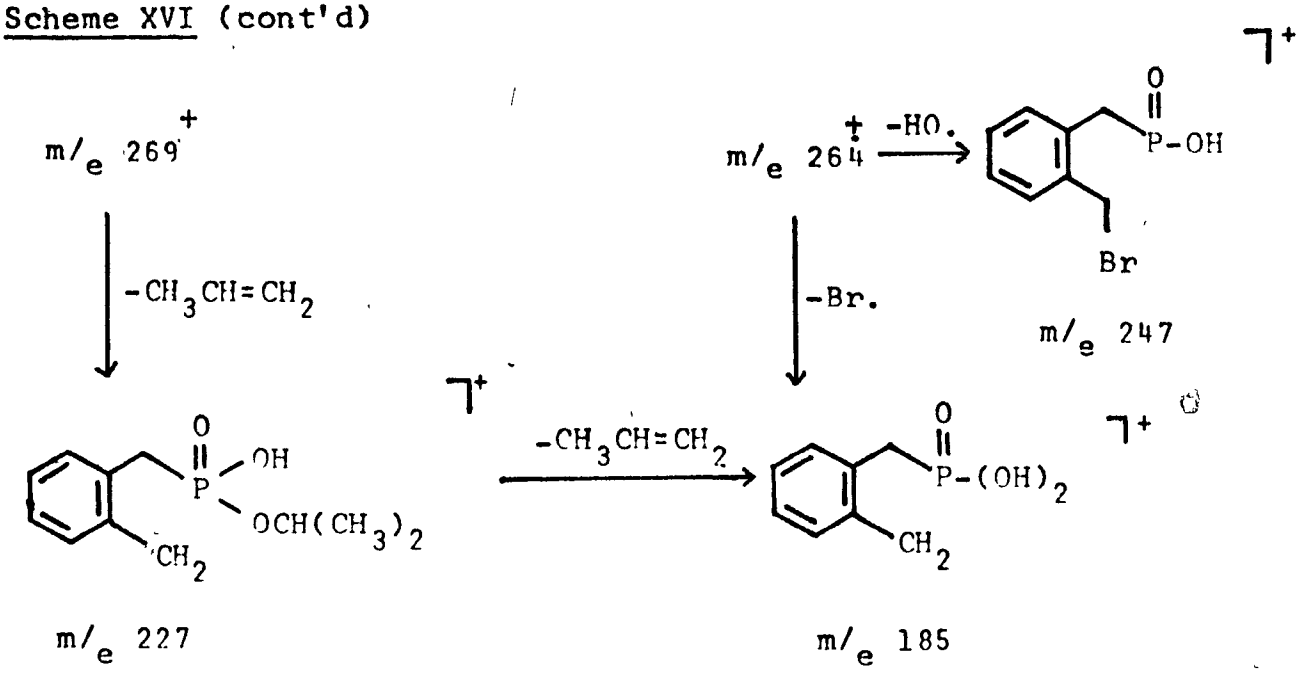
The mass spectrum of 133 exhibits P($m/_e$ 348) and P+2($m/_e$ 350) peaks in 1:1 intensity ratio. It also shows a (P-Br.) peak at $m/_e$ 269. Loss of $CH_3CH = CH_2$ ($m/_e$ 42) molecule by McLafferty rearrangement from the molecular ion provides the peaks at $m/_e$ 306

and 308 in 1:1 intensity ratio. Further loss of $CH_3CH = CH_2$ gives rise to the peaks at $m/_e$ 264 and 266 in 1:1 intensity ratio. The base peak is at $m/_e$ 185, arising from the loss of -Br radical from the (P-42-42) peak. Alternatively, the base peak may be derived from the successive loss of two molecules of $CH_3CH = CH_2$ by McLafferty rearrangement from the (P-Br.) peak. Loss of -OH radical from the (P-42-42) peak gives rise to the peaks at $m/_e$ 247 and 249 in 1:1 intensity ratio. The fragmentation pattern is illustrated in Scheme XVI.

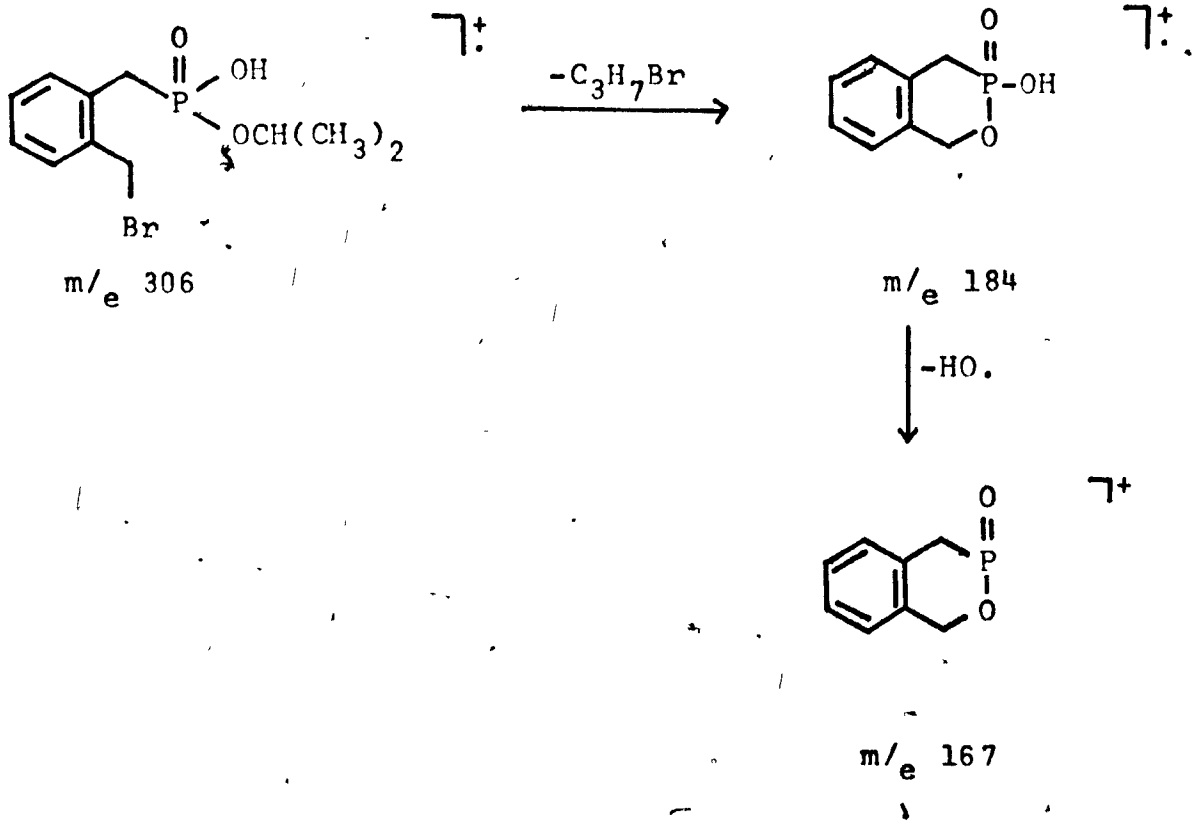
Scheme XVI

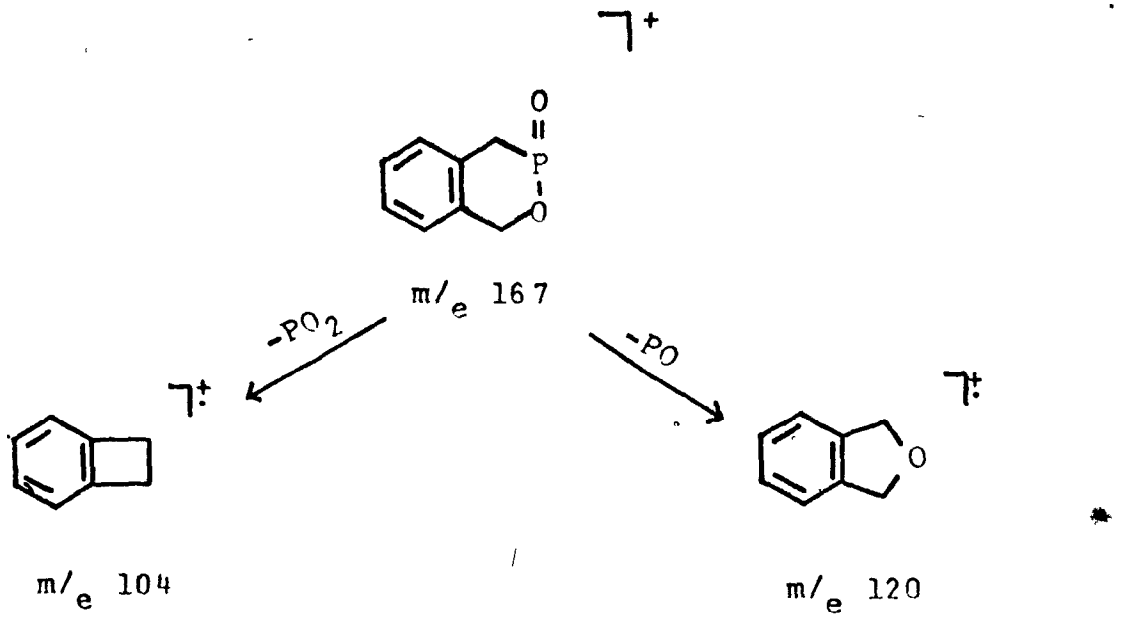


Scheme XVI (cont'd)



Other peaks in the mass spectrum of 133 may be accounted for by the following fragmentation.



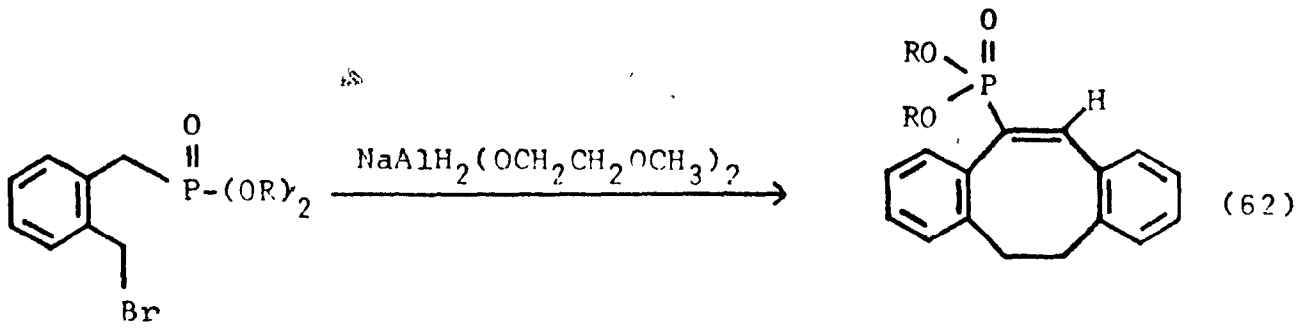


The n.m.r. spectrum of the cyclic phosphonate ester 134 shows a 4-H multiplet at 7.4 δ for the aromatic protons, a 2-H doublet (J_{POCH} = 16 Hz) at 5.4 δ for the methylene protons adjacent to oxygen, a 1-H multiplet at 4.8 δ for the isopropyl methine proton, a 2-H doublet (J_{P-CH} = 20 Hz) at 3.3 δ for the methylene protons adjacent to P=O group and a 6-H doublet at 1.4 δ for the methyl protons.

Reaction of Dialkyl(2'-bromomethyl)benzylphosphonate with Vitride Reagent

Diisopropyl(2'-bromomethyl)benzylphosphonate (133) was treated with excess Vitride reagent in dry diglyme, under nitrogen at 135° for 48 hours. The resulting mixture, after working up, was separated by preparative thin layer chromatography to give 54% yield of a new compound. It was assigned to the structure 135 (b) (Eq. 62) on the basis of its spectroscopic data.

Similarly the reaction of diethyl(2'-bromomethyl)benzylphosphonate (127) with excess Vitride reagent in dry diglyme at 135° for 24 hours, afforded 40% yield of a new compound, the spectroscopic properties of which were consistent with the structure 135 (a) (Eq. 62).



(62)

(127); R = C_2H_5
(133); R = $^iC_3H_7$

135 (a); R = C_2H_5
(b); R = $^iC_3H_7$

The infrared spectrum of 3-[diisopropylphosphonato]-7,8-dihydro-1,2,5,6-dibenzocyclooctatetraene (135 b) (fig. 10) features a strong band at 1240 cm^{-1} attributable to P=O absorption and a broad band at 1000 cm^{-1}, associated with P-O-C absorption. The characteristic isopropyl splitting is observed at 1375 cm^{-1} and 1385 cm^{-1}.

The diethyl analog 135 (a) has a similar infrared spectrum (fig. 11), featuring a strong characteristic P=O stretching band at 1230 cm^{-1} and a broad P-O-C stretching band at 1100 cm^{-1}.

The conspicuous feature of the n.m.r. spectrum of (135 b) (fig. 13) includes a 1-H doublet ($J_{PC=CH}$ = 24 Hz) centred at

8.0 δ for the vinylic proton, a 8-H multiplet at 7.2 δ for the aromatic protons, a 2-H multiplet at 4.8 δ for the isopropyl methine protons, a 4-H singlet at 3.2 δ for the benzylic protons and a 12-H overlapped doublet at 1.3 δ for the nonequivalent two methyl groups of isopropyl moiety. The trans -PC=CH and cis -PC=CH coupling constants for tetra-coordinated phosphorus derivatives of ethylene have been reported[135] as (28 - 51 Hz) and (10 - 20 Hz) respectively. Thus PC=CH coupling constant found in 135 (b) is more consistent with a cis structure.

The n.m.r. spectrum of 3-[diethylphosphonato]-7,8-dihydro-1,2,5,6-dibenzocyclooctatetraene (135 a) (fig. 14) is similar to the diisopropyl analog. It shows a 1-H doublet ($J_{PC=CH}$ = 24 Hz) centred at 8.0 δ for the vinylic proton, a 8-H multiplet at 7.3 δ for the aromatic protons, a 4-H quintet at 4.3 δ for the ester methylene protons, a 4-H singlet for the benzylic protons and a 6-H triplet for the methyl protons of the ethyl group.

The $J_{PC=CH}$ values of dialkylphosphonatodihydrodibenzocyclo-octatetraene (135) should be compared with those of vinylphos-phonic acids and ester (Table VI).

TABLE VI

NMR Spectral Parameters of Vinylphosphonic Acids and Esters

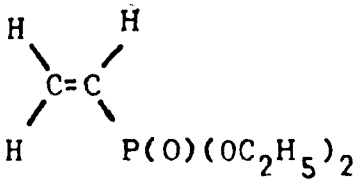
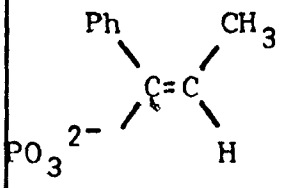
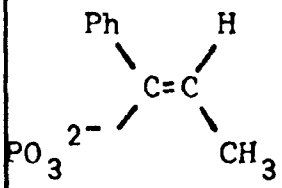
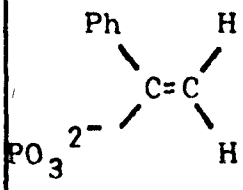
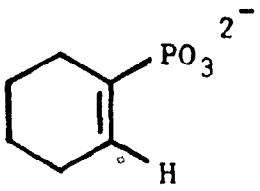
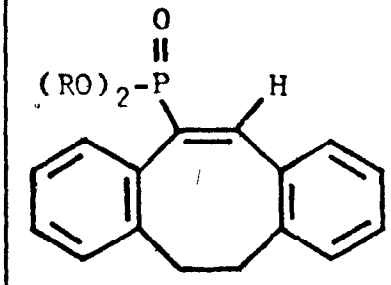
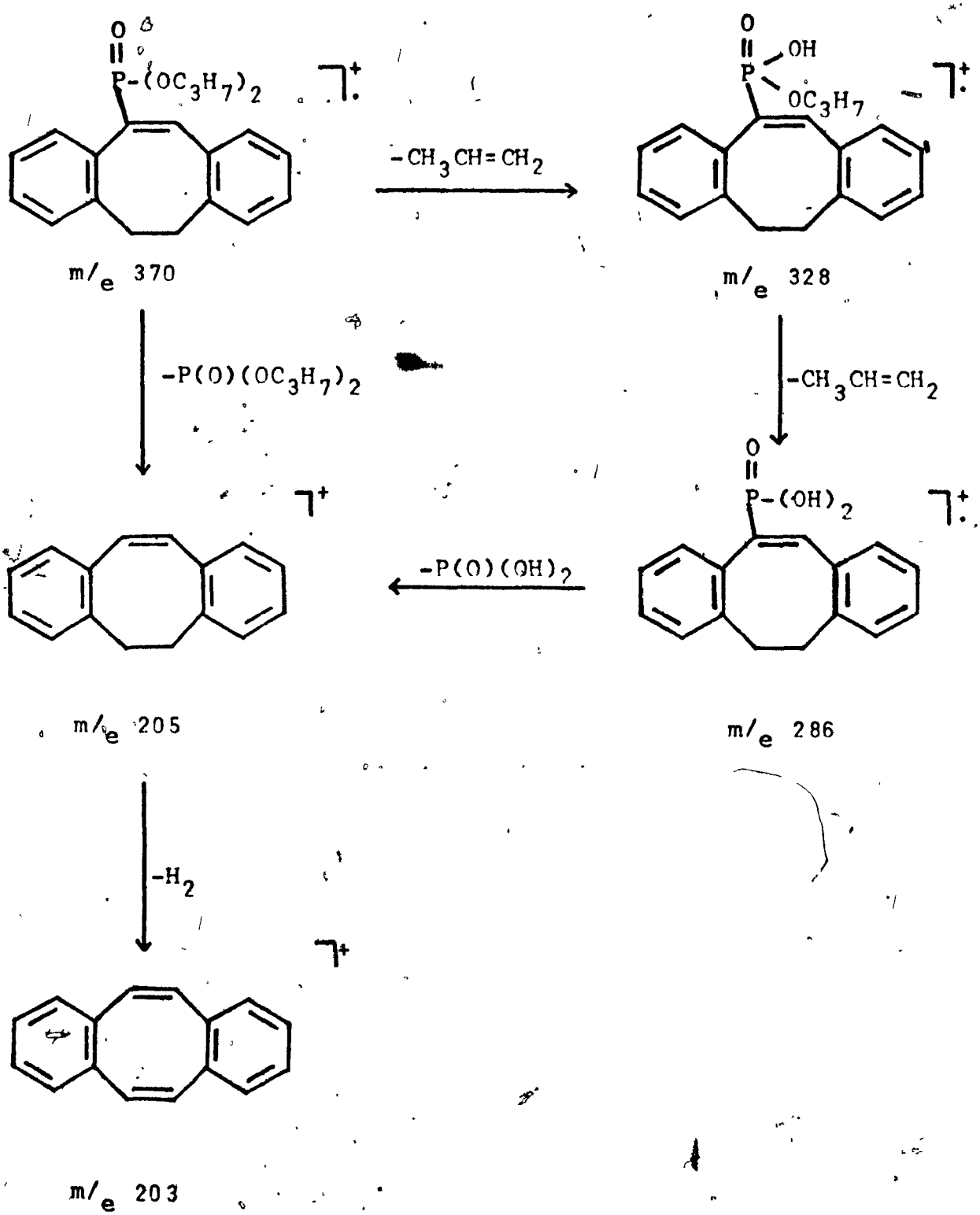
Compounds	$J_{PC=CH}$ in Hz	Ref.
	24 (cis), 50 (trans)	136
	20 (cis)	137
	38 (trans)	137
	22 (cis), 45 (trans)	137

TABLE VI (cont'd)

Compounds	$J_{PC=CH}$ in Hz	Ref.
	19 (cis)	137
 ($R = C_2H_5$, $^{i}C_3H_7$)	24	This work

The mass spectrum of 135 (b) (fig. 16) is quite simple. The molecular ion ($m/_e$ 370) is of medium intensity. It loses two molecules of $CH_3CH = CH_2$ by McLafferty rearrangement, successively to give a peak at $m/_e$ 328 and a base peak at $m/_e$ 286. The molecular ion can eliminate the $-P(O)(OC_3H_7)_2$ group to provide a peak at $m/_e$ 205. Loss of hydrogen molecule from the peak at $m/_e$ 205 provides the peak at $m/_e$ 203. The fragmentation pattern is illustrated in Scheme XVII.

Scheme XVII



m/e 370

m/e 328

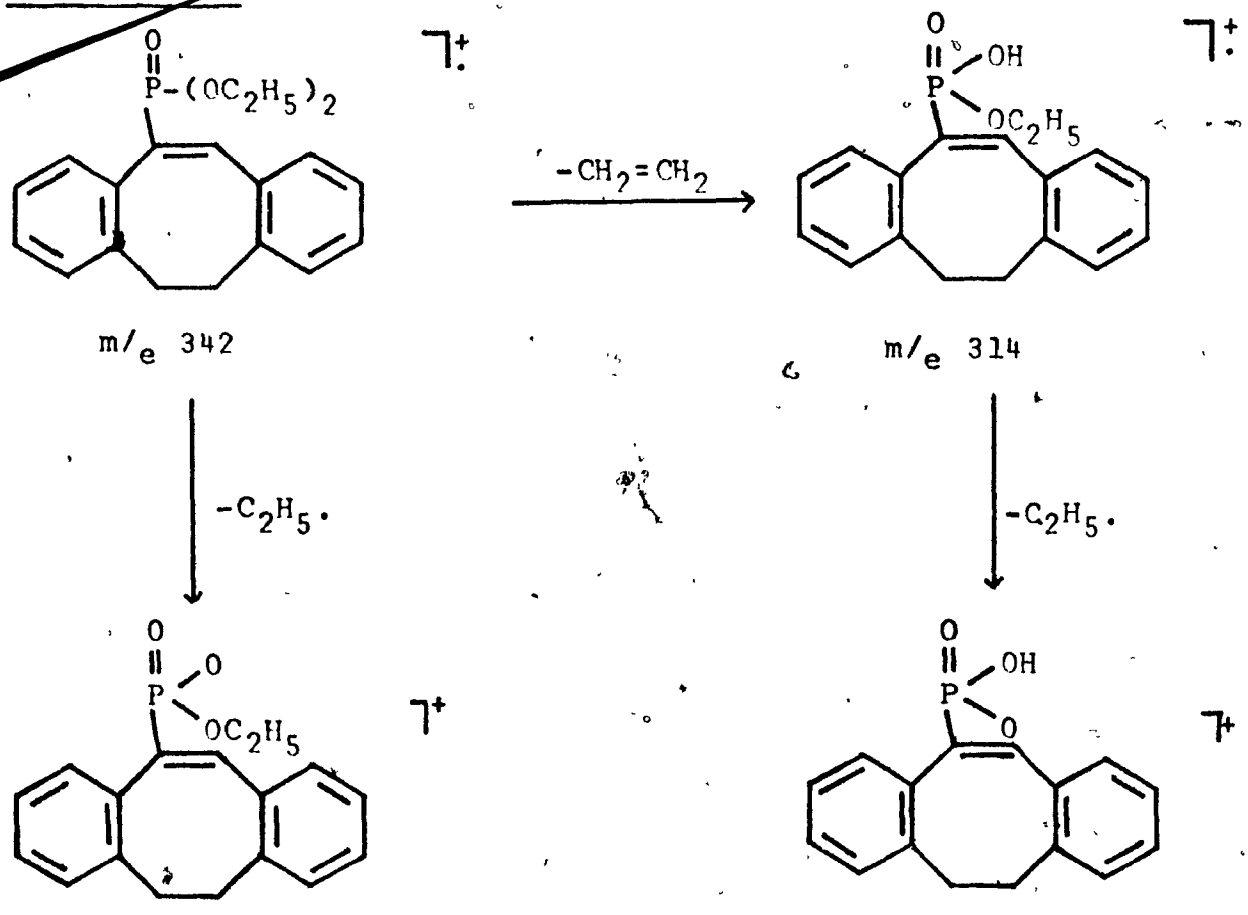
m/e 286

m/e 205

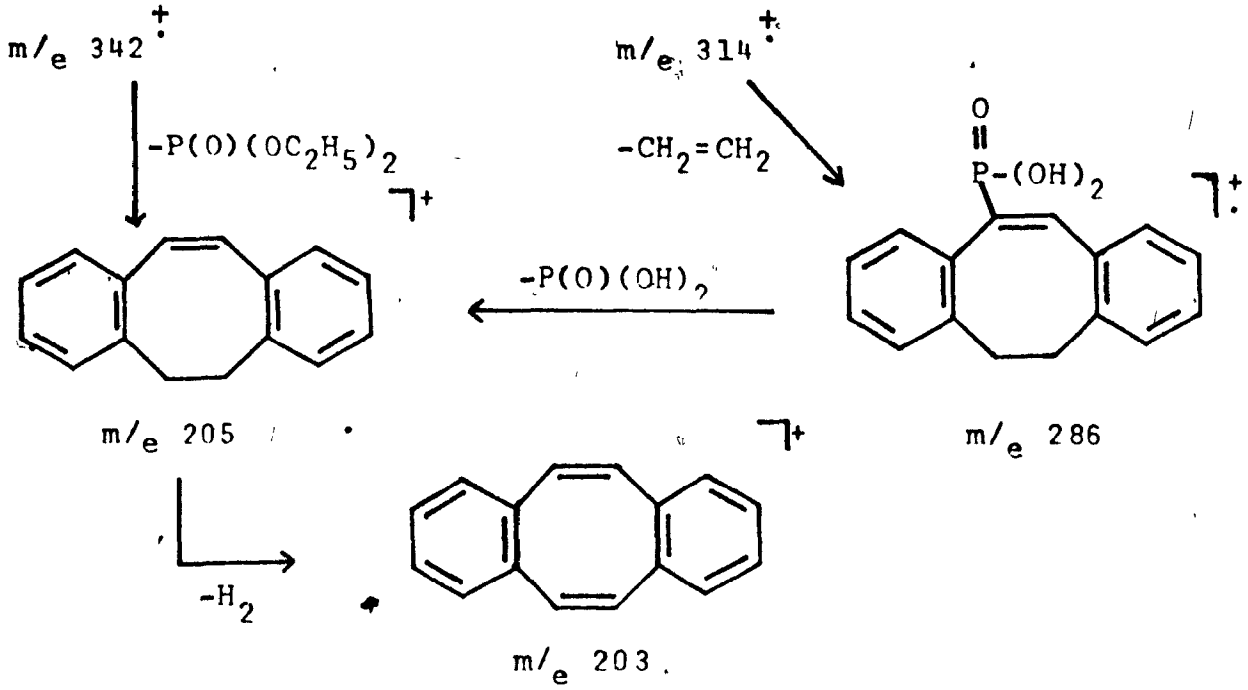
m/e 203

The mass spectrum of 135 (a) (fig. 17) is quite similar to that of the isopropyl analog. Its molecular ion ($m/_e$ 342) is the base peak. It loses two molecules of ethylene successively by McLafferty rearrangement to give rise to the peaks at $m/_e$ 314 and 286. The peak at $m/_e$ 205 may arise either from the loss of $-P(O)(OEt)_2$ moiety from the molecular ion or from the loss of $-P(O)(OH)_2$ moiety from the peak at $m/_e$ 286. Further loss of hydrogen from this peak provides the ion at $m/_e$ 203. The fragmentation pattern is shown in Scheme XVIII.

Scheme XVIII

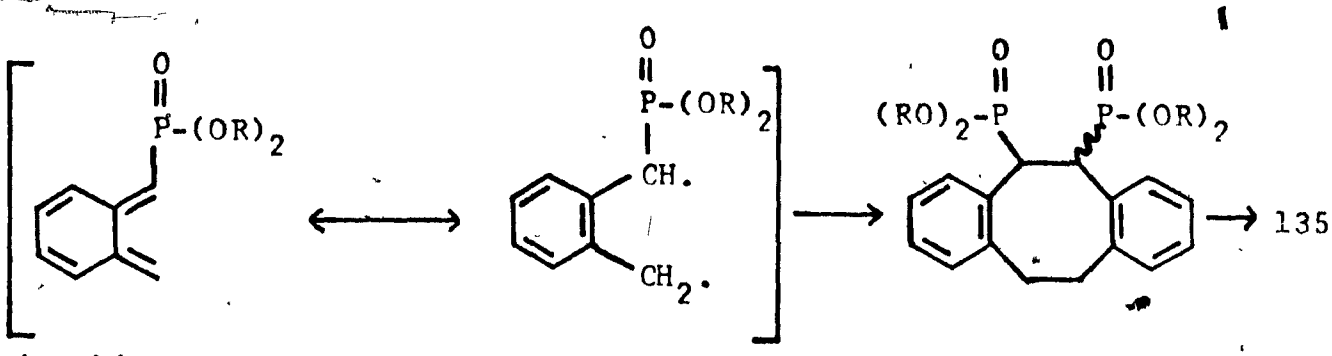


Scheme XVIII (cont'd)



With the foregoing interpretation of the spectroscopic data, the structures assigned to 135 (a) and (b) appear to be secure. It seems that the replacement of a phenyl group on phosphorus by an alkoxy group has altered dramatically the course of the reaction. It is interesting to speculate on the mechanism for the formation of 135.

A possibility is that the formation of dialkylphosphonato-dihydrodibenzocyclooctatetraene (135) may result from the dimerization of an unstable o-quinonoid intermediate 136 to give di[dialkylphosphonato]dibenzocyclooctadiene (137), followed by β-elimination of one of the dialkyl phosphono [$-P(O)(OR)_2$] groups (Eq. 63).

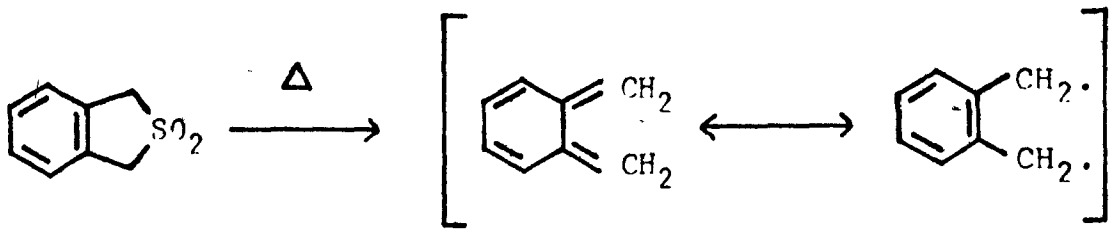


(136)(a); R = C_2H_5
(b); R = $^iC_3H_7$

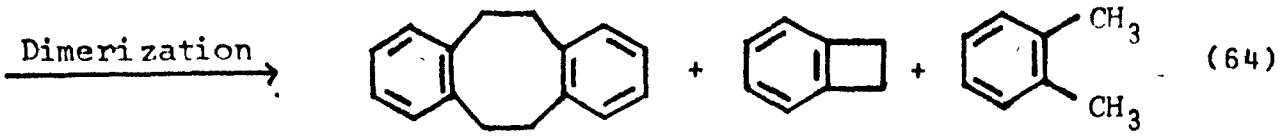
(137)(a); R = C_2H_5
(b); R = $^iC_3H_7$

(63)

The formation of dibenzocyclooctadiene via a very reactive o-quinonoid intermediate is not without precedent. Indeed, this kind of reaction has been invoked by Cava et al (Eq. 64)[128] and Errede (Eq. 65)[138].

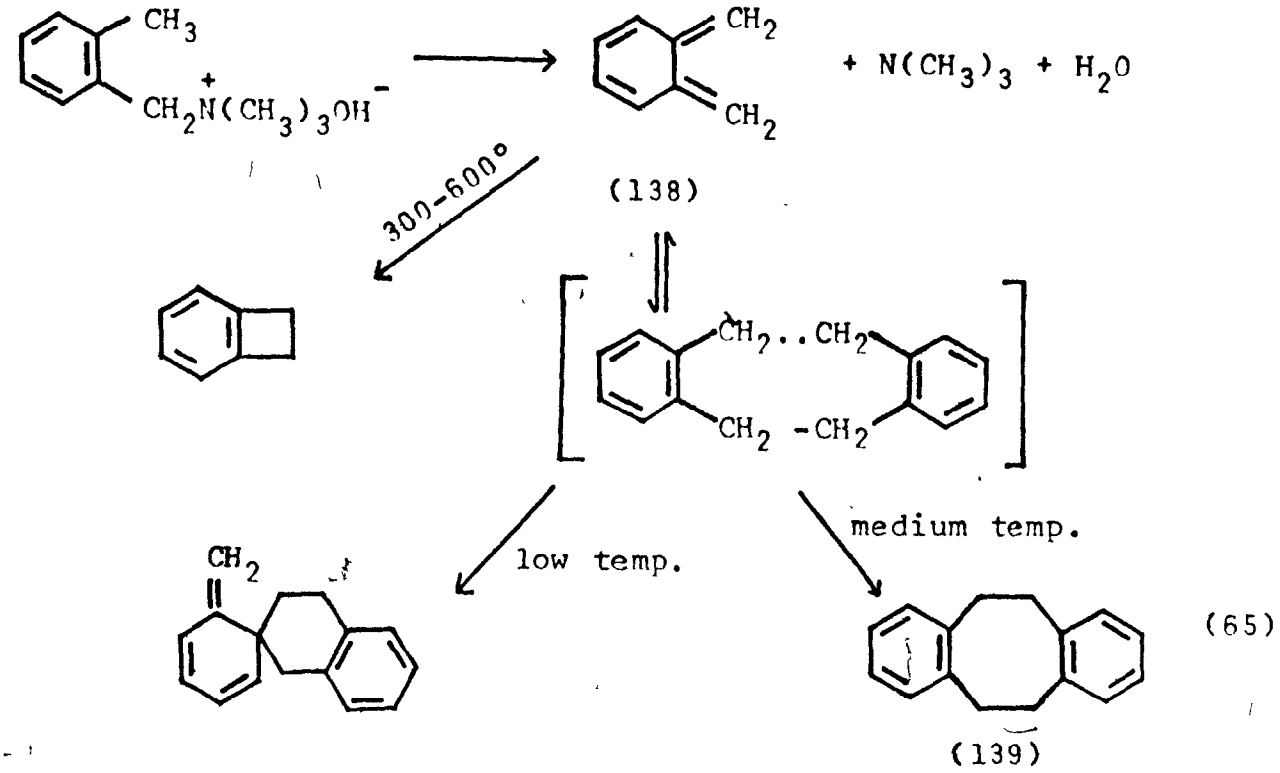


(138)



(64)

(139)



(65)

It has been mentioned in both reports[128,138] that the formation of the products depend greatly on the reaction temperature. The work of Errede[138] showed that 1,2,5,6-dibenzocyclooctadiene (139) was the main product at the medium reaction temperature range of 0 - 200°. Cava[128] also reported that the yield of 139 was increased when the reaction was carried out in a solution of diethyl phthalate at 300°.

The intermediate 136 postulated for the present reaction is expected to have chemical behaviour not unlike that of the o-quinodimethane 138. Hence, the formation of the dimer 137 in the temperature range of 135° would be quite reasonable in view of the above reports.

Support for the intermediacy of 137b was gained by carrying

out the reaction of diisopropyl(2'-bromomethyl)benzylphosphonate (133) with excess Vitride reagent at a lower temperature 125° for 30 hours, in toluene or diglyme. Under these conditions, a new compound was isolated, instead of 135 (b), in 33% yield by preparative thin layer chromatography. Its spectroscopic data were in accord with the structure 137 (b).

The infrared spectrum of 3,4-di[diisopropylphosphonato]-1,2,5,6-dibenzocyclooctadiene (137 b) (fig. 12) consists of a strong characteristic P=O absorption band at 1240 cm^{-1} and a strong isopropyl doublet at 1370 cm^{-1} and 1380 cm^{-1}. A strong broad band at 1000 cm^{-1} due to P-O-C absorption is also observed.

The infrared spectral data of dialkyl(2'-bromomethyl)benzyl-phosphonates and the related compounds are summarized in Table VII.

TABLE VII

I.R. Spectral Data of Some Phosphorus Esters

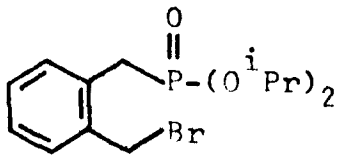
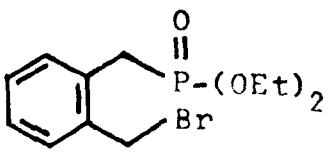
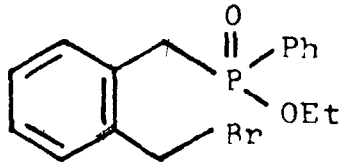
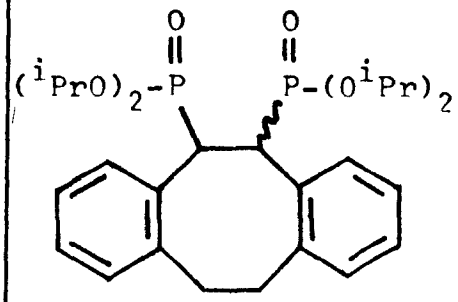
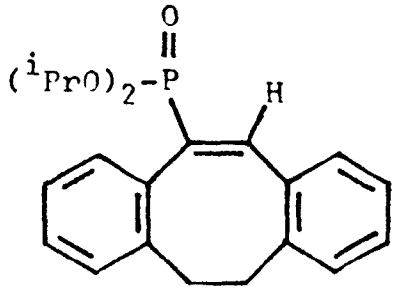
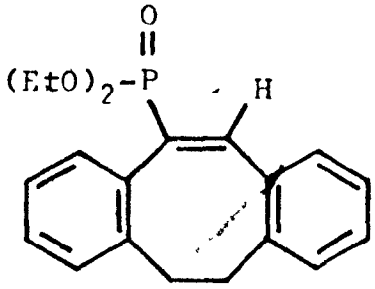
Compounds	$\nu_{P=O}$ in cm^{-1}	ν_{P-O-C} in cm^{-1}	Medium
	1260	1020, 1150	Film
	1250	1020, 1160	Film

TABLE VII (cont'd)

Compounds	$\nu_{P=O}$ in cm^{-1}	ν_{P-O-C} in cm^{-1}	Medium
	1220	1040, 1160	KBr
	1240	1000	$CHCl_3$
	1240	1000	CCl_4
	1230	1100	$CHCl_3$

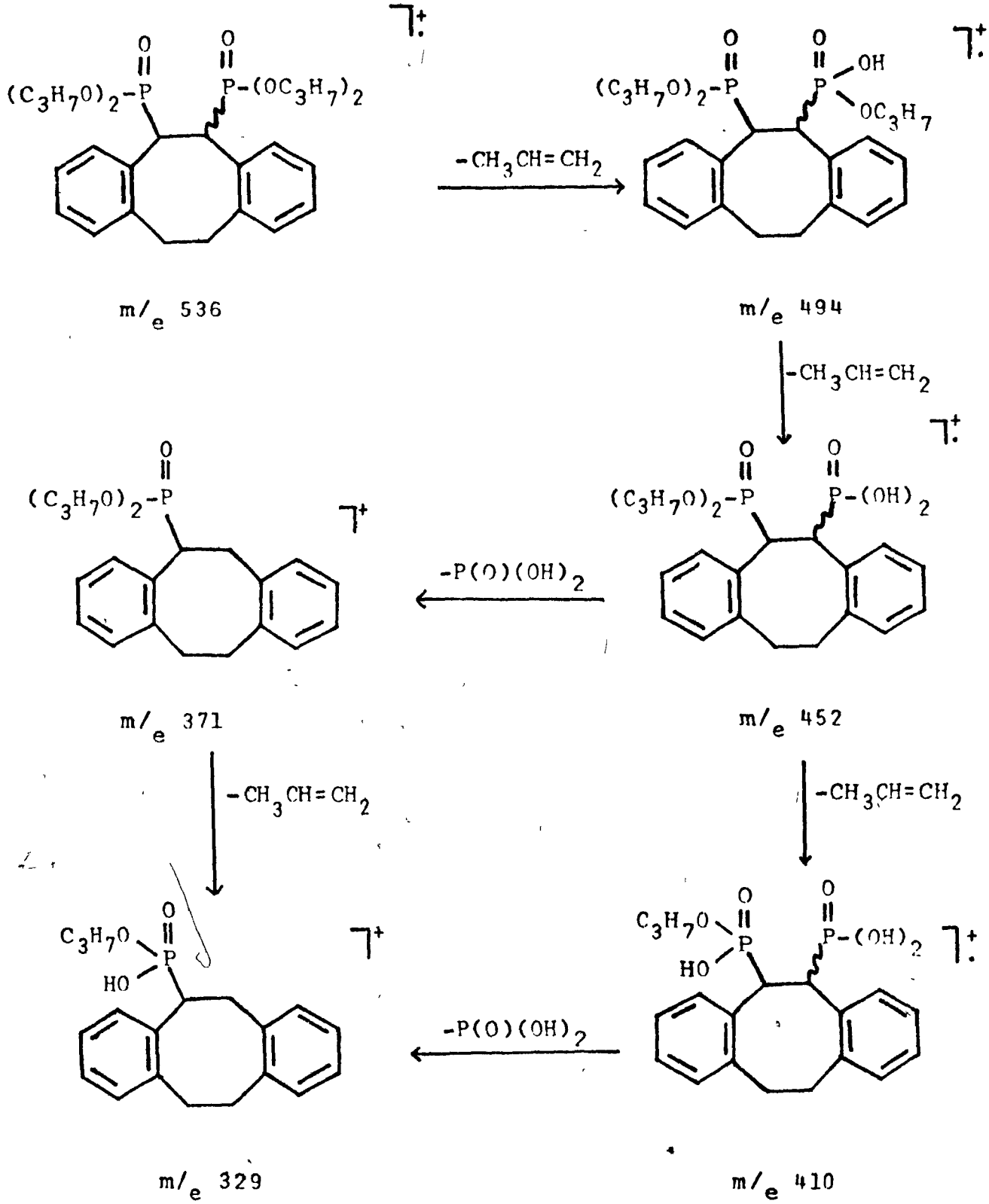
The $\nu_{P=O}$ values of dialkyl(2'-bromomethyl)benzylphosphonate should be compared to that of o-xylylenediphosphonic acid[72] which shows the characteristic P=O absorption at 1260 cm^{-1}.

The 220 MHz n.m.r. spectrum of 3,4-di[diisopropylphosphonato]-1,2,5,6-dibenzocyclooctadiene (137 b) (fig. 15) is in agreement with a head-to-head dimeric structure. It gives a 8-H multiplet at 7.3 δ for the aromatic protons, a 4-H multiplet at 4.6 δ for the isopropyl methine protons, a 2-H A_2B_2 pattern at 3.7 δ for the benzylic protons[#], a 2-H doublet (J_{P-CH} = 20 Hz) at 3.3 δ for the methine protons adjacent to the P=O group and 24-H two separate doublets at 1.0 - 1.3 δ for the nonequivalent methyl groups of the isopropyl moiety. Thus 137 (b) is an equal mixture of cis- and trans-isomers. The absence of coupling between the benzylic methylene protons and phosphorus atom ruled out the head-to-tail dimeric structure.

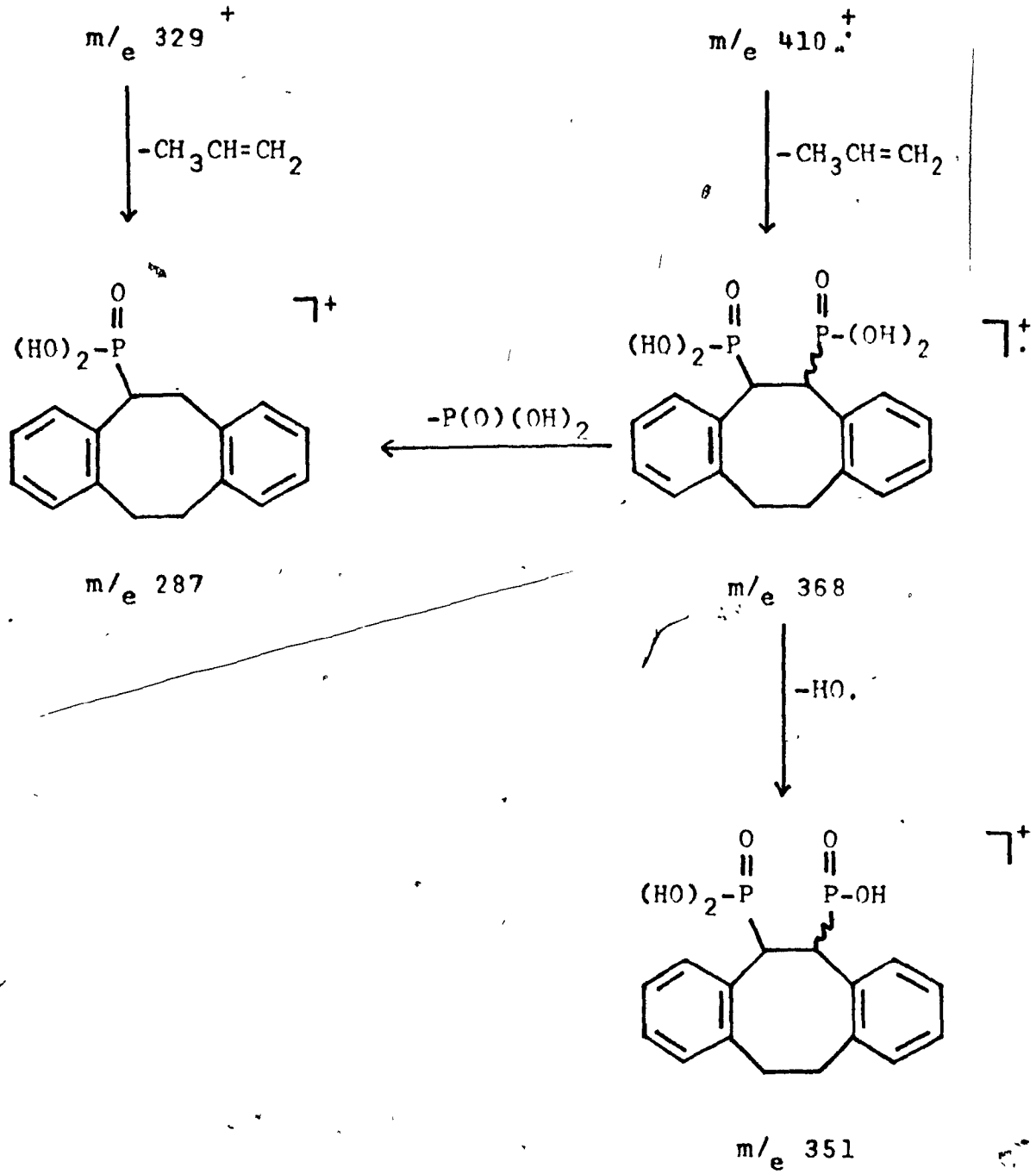
The mass spectrum of 137 (b) (fig. 18) features a medium intensity molecular ion at $m/_e$ 536. The peaks at $m/_e$ 494, 452, 410 and 368 may arise from the successive loss of four molecules of $CH_3CH = CH_2$ by McLafferty rearrangement from the molecular ion. Elimination of $-P(O)(OH)_2$ moiety from each of the peaks at $m/_e$ 452, 410 and 368 provide the peaks at $m/_e$ 371, 329 and 287 respectively. The fragmentation pattern is shown in Scheme XIX. Exact mass measurement: - Calcd. for $C_{28}H_{42}P_2O_6$ - 536.2446, Found - 536.2457.

[#] a 2-H singlet is also observed at 3.4 δ for the benzylic protons.

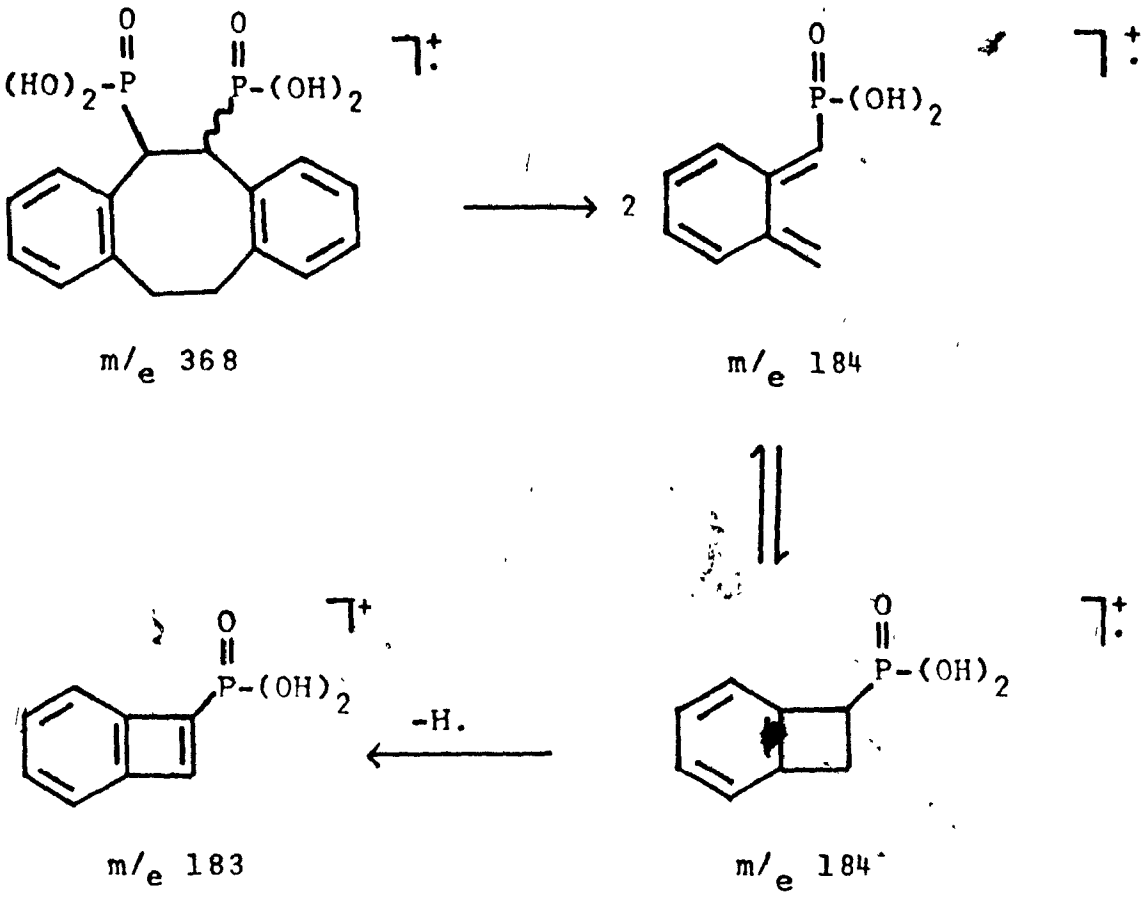
Scheme XIX


m/e 536
-CH3CH=CH2
m/e 494
-CH3CH=CH2
m/e 452
-P(O)(OH)2
m/e 371
-CH3CH=CH2
m/e 410
-P(O)(OH)2
m/e 329

Scheme XIX (cont'd)



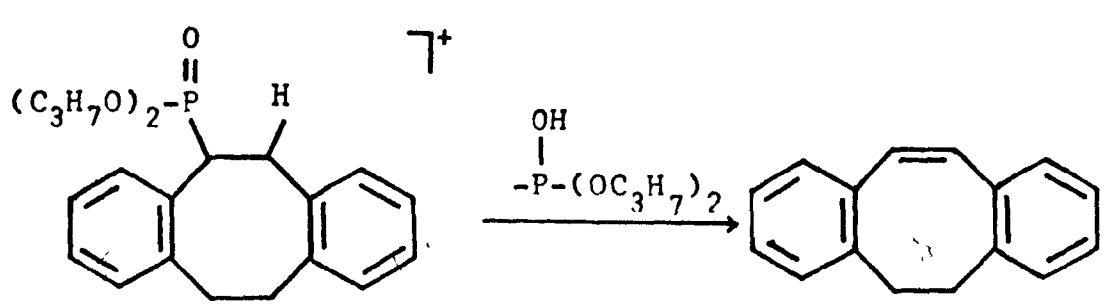
A peak at $m/_e$ 368 may decompose to give the peak at $m/_e$ 184. The base peak at $m/_e$ 183 may arise from the loss of -H radical from the peak at $m/_e$ 184.



m/e 368 m/e 184

m/e 183 m/e 184

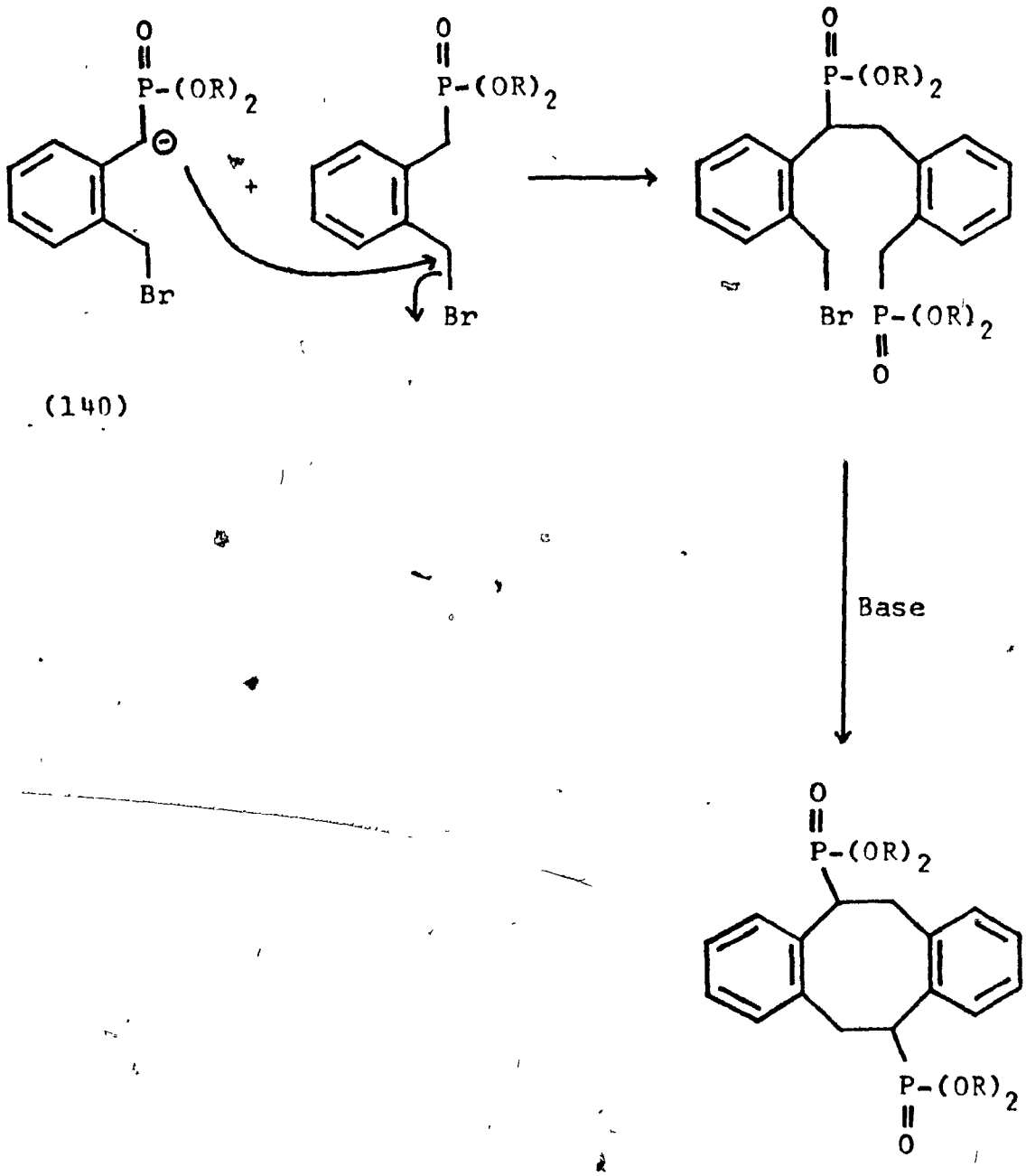
A peak at m/e 371 can also eliminate $-P(OH)(OC_3H_7)_2$ moiety to form the peak at m/e 205.



m/e 371 m/e 205

That 137 (b) is indeed the intermediate in the formation of 135 (b) can be proved by the following experiment. The reaction of diisopropyl(2'-bromomethyl)benzylphosphonate (133) with Vitride reagent was carried out to give 137 (b) at 125° for 30 hours as ascertained by nmr spectroscopy. The reaction mixture was then heated further at 135° for 48 hours. Under these conditions 137 (b) disappeared and 135 (b) was formed.

One may speculate on the mechanism for the formation of 137 (b). An intermolecular S_N2 reaction involving carbanion such as 140 can be ruled out, because it will lead to the head-to-tail dimer 141.

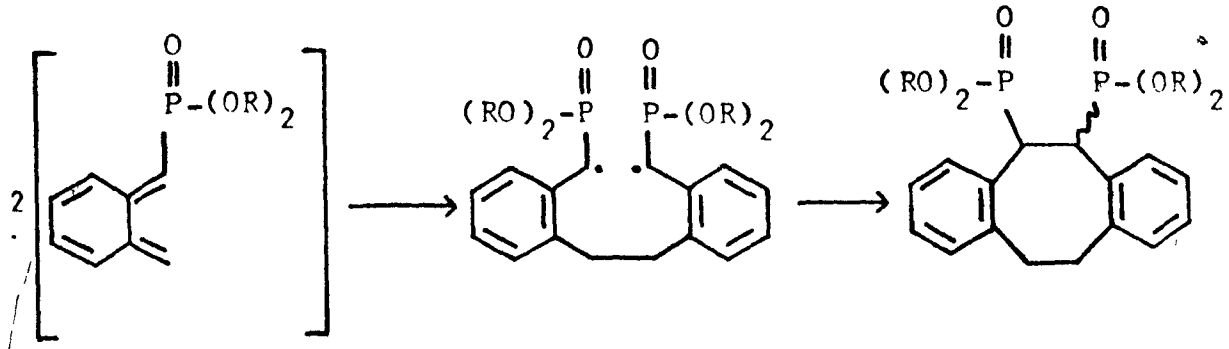


(140)

(141)

The o-quinonoid intermediate appears to be reasonable. The dimerization can proceed either by a concerted ($_{\pi}4_{S}$ + $_{\pi}4_{S}$) cycloaddition. This pathway, according to the principle of the con-

servation of orbital symmetry as formulated by Woodward and Hoffmann, is however considered forbidden under thermal condition[139]. This is also in agreement with the observation that no head-to-tail dimer was formed, since it is difficult to see how a cycloaddition would have favoured only one mode of addition. On the other hand, the reaction may proceed by a two-step pathway involving, perhaps a diradical intermediate.



If this were the case, then a head-to-head dimerization will be favoured since the diradical can be stabilized by the phosphoryl group. This is indeed observed experimentally.

There remains the question on the formation of the intermediate 136. A reasonable assumption is that 136 is derived from the base-promoted elimination of HBr from the starting material.

Thus, in the reaction of dialkyl(2'-bromomethyl)benzylphosphonate with Vitride reagent, the hydride reagent served as a base to cause the elimination of hydrogen bromide from the phosphonate ester to generate the o-quinonoid intermediate.

One may expect the other strong base might also effect the same transformation. Indeed, when diisopropyl(2'-bromomethyl)-benzylphosphonate was treated with freshly sublimed potassium tert-butoxide in diglyme at 110° for 24 hours, 137 (b) was formed, albeit in lower yield.

Support for the formation of o-quinodimethane (138) has been confirmed by trapping it with dienophiles such as N-phenylmaleimide[128] and anthracene[140].

We hope therefore to implicate the o-quinonoid intermediate 136 by trapping it with various dienophiles. Thus, diisopropyl-(2'-bromomethyl)benzylphosphonate was treated with excess Vitride reagent in diglyme at 130°, in the presence of dimethyl acetylene dicarboxylate for 24 hours. Thin layer chromatography and n.m.r. spectrum of the reaction mixture, after working up indicated the formation of the dimer 137 (b) only. The attempted trapping reactions with anthracene and dimethyl maleate under the same reaction conditions were also unsuccessful.

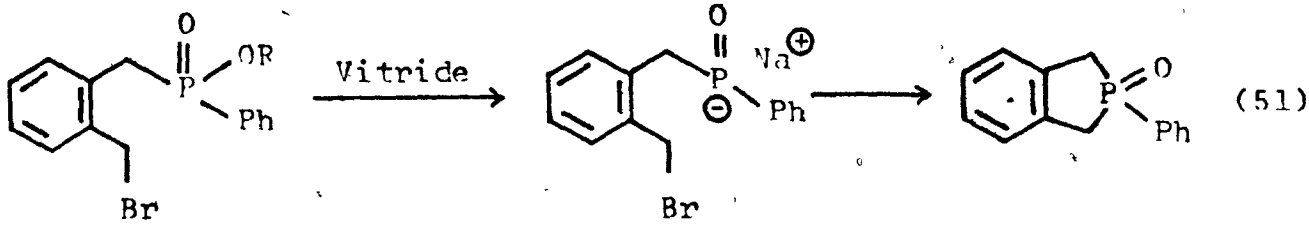
The attempted reaction of the same phosphonate ester with potassium tert-butoxide in diglyme at 130°, in the presence of the above mentioned dienophiles, also failed to give any adduct.

The failure of the trapping reactions may probably be due to the complicated side reactions of dienophiles with Vitride reagent or potassium tert-butoxide.

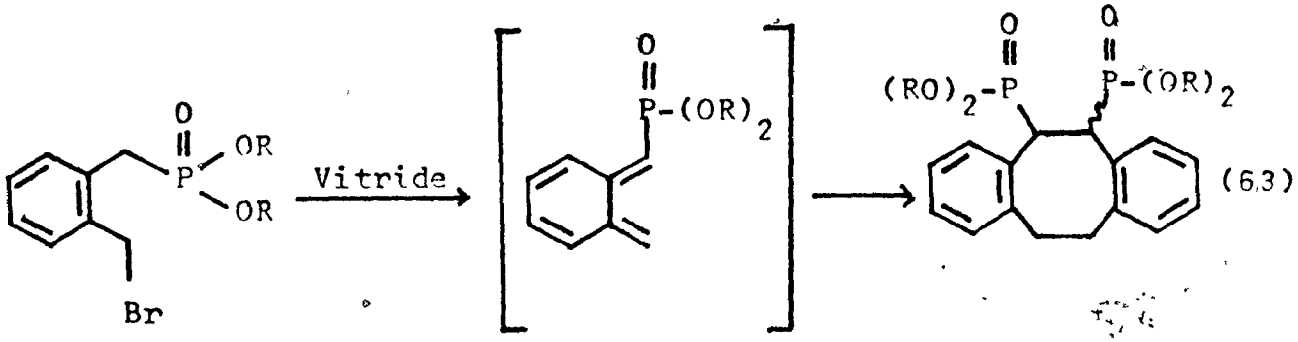
As stated earlier, the formation of dialkylphosphonatodihydrodibenzocyclooctatetraene (135) may be postulated as resulting from the dimer 137 followed by the β-elimination of one of the dialkyl phosphono groups. Similar kind of β-elimination in phos-

phinate esters has been observed by Haake and Diebert[141]. Three mechanisms have been advanced for the elimination reaction namely (a) a free radical mechanism (b) a cyclic elimination mechanism and (c) carbonium ion mechanism.

In conclusion, the reaction of dialkyl(2'-bromomethyl)benzylphosphonates with Vitride reagent provides an interesting anomaly from the carbon-phosphorus bond formation reaction. It demonstrates that the course of this reaction is subject to the influence of subtle structural change. In one case (Eq. 51), Vitride behaves as a nucleophile but, in the other case, it acts as a base (Eq. 63).



(51)



(63)

Halogenation of 2-Phenylisophosphindoline 2-Oxide

With the ready availability of 2-phenylisophosphindoline 2-oxide by one-step synthesis, we began to explore the chemistry of the isophosphindole system.

We have described in the previous section the reduction of the phosphine oxide to the phosphine and its subsequent quaternization. In the following sections, we shall describe the halogenation of 2-phenylisophosphindoline 2-oxide with various reagents.

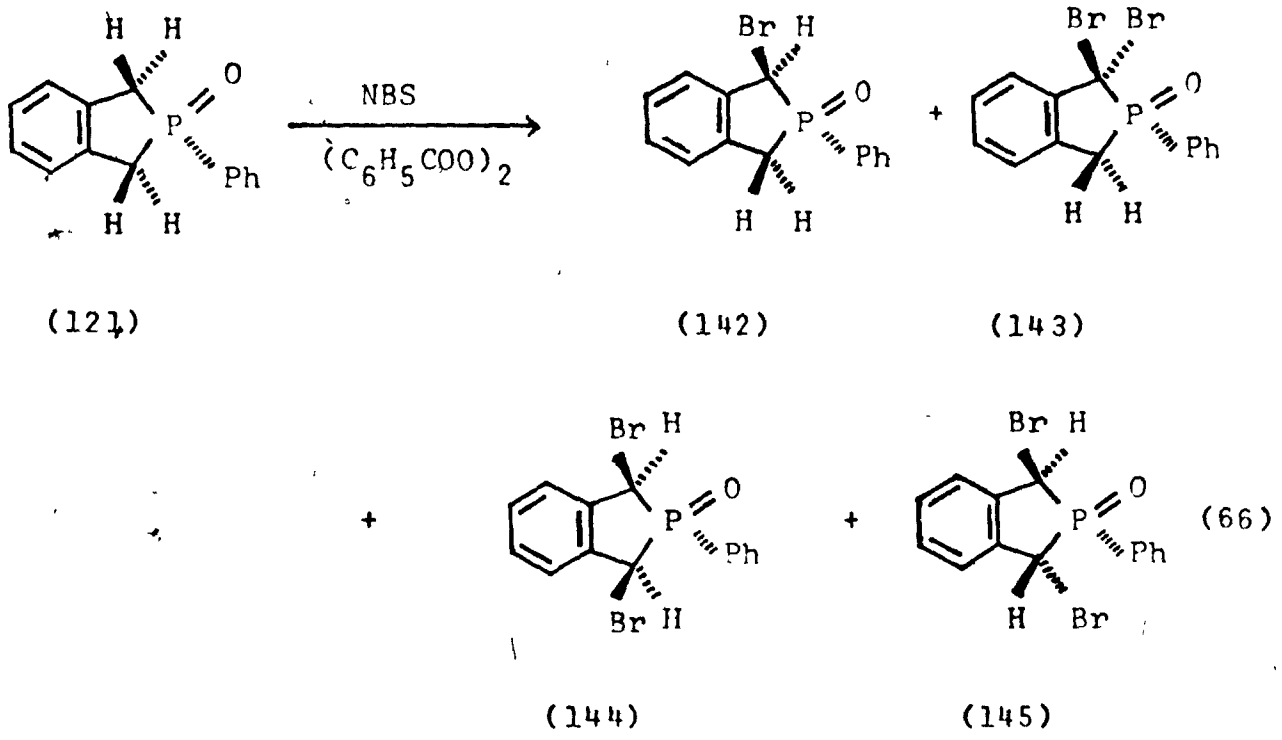
With N-Bromosuccinimide

2-Phenylisophosphindoline 2-oxide was brominated with equal molar quantity of recrystallized N-bromosuccinimide[93], in the presence of a catalytic amount of benzoyl peroxide, in refluxing benzene for 12 hours. After removal of succinimide and the solvent, the reaction mixture was separated by preparative thin layer chromatography to furnish 50% yield of one major product. The spectroscopic data and elemental analysis of this compound were in accord with the structure of r-1-bromo-t-2-phenylisophosphindoline 2-oxide (142) (Eq. 66).

Also isolated as minor products were 10% yield of 1,1-dibromo-2-phenylisophosphindoline 2-oxide (143), 8% yield of r-1-c-3-dibromo-t-2-phenylisophosphindoline 2-oxide (144) and 5% yield of trans-1,3-dibromo-2-phenylisophosphindoline 2-oxide (145) (Eq. 66).

It is of interest to find out whether r-1-bromo-c-2-phenyl-isophosphindoline 2-oxide (146) was formed (see later section). Careful examination of the reaction mixture by thin layer chromatography showed that there was only a trace of this compound. The yield of this compound was therefore extremely low (<5%).

The formation of the dibromo compounds could not be minimized by decreasing either the reaction temperature or time.



(121) (142) (143) (144) (145) (66)

Structural determination of these products was achieved by n.m.r. spectroscopy and mass spectrometry.

All the bromo derivatives of 2-phenylisophosphindoline 2-oxide feature strong characteristic P=O stretching and these absorptions are summarized in Table VIII. They all show strong phenyl bands at 1440 cm^{-1}, 1120 - 1100 cm^{-1} and 700 - 800 cm^{-1}.

TABLE VIII

P=O Absorption in the i.r. spectra of Bromo Derivatives of 2-Phenylisophosphindoline 2-Oxide

Name of Compounds	$\nu_{P=O}$ in cm^{-1}
r-1-bromo-t-2-phenylisophosphindoline 2-oxide*	1230
r-1-bromo-c-2-phenylisophosphindoline 2-oxide	1220
1,1-dibromo-2-phenylisophosphindoline 2-oxide	1240
trans-1,3-dibromo-2-phenylisophosphindoline 2-oxide	1230
r-1,c-3-dibromo-t-2-phenylisophosphindoline 2-oxide	1240

* See fig. 20

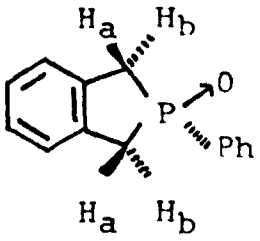
In the n.m.r. spectra of all the above bromo compounds, the aromatic protons appear as multiplet in the region 7.2 - 7.8 δ, the benzylic protons attached to -Br give doublet and the other benzylic protons appear as part of an ABX pattern (X = ^{31}P).

By careful examination of the n.m.r. spectra of these compounds, it is possible to deduce the relative stereochemistry of the various isomers.

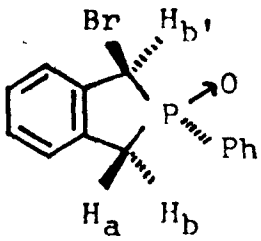
The assignment of the stereochemistry is based on two considerations. First, there is the sheilding effect of the phenyl ring[95]. Secondly, the magnitude of the geminal $^{2}J(P-CH)$ coupling constants depends on the orientation of the phosphoryl group[142,143].

TABLE IX

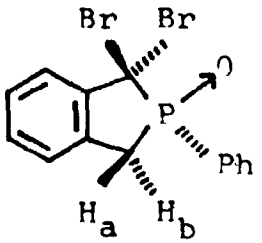
The Chemical Shifts (δ in p.p.m.) and Geminal Coupling Constants (in Hz) of Benzylic Protons of Some Isophosphindolines



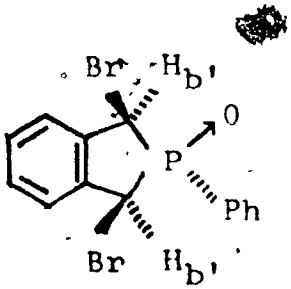
(121)



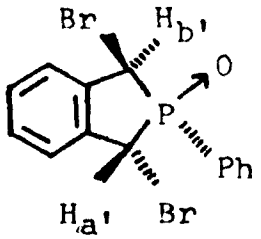
(142)



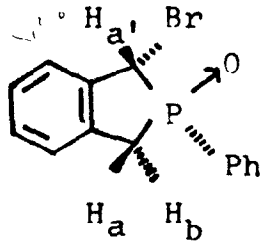
(143)



(144)



(145)

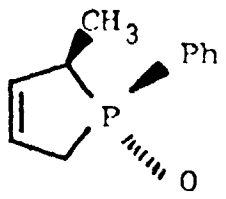


(146)

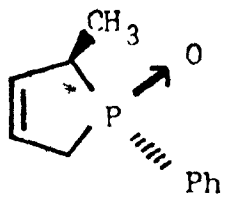
	121	143	142*	144	145	146
$\delta_{H_a}(^2J(PCH_a))$	3.51(16)	3.59(17)	3.59(17)			3.59(17)
$\delta_{H_b}(^2J(PCH_b))$	3.35(9)	3.36(9)	3.36(9)			3.36(9)
$\delta_{H_a'}(^2J(PCH_a'))$					5.6(10)	5.6(10)
$\delta_{H_b'}(^2J(PCH)_b')$			5.2(2)	5.2(2)	5.3(2.5)	

* See fig. 25

The shielding effect of phenyl ring in modifying the chemical shift of adjacent spin system is well documented. Within the field of organophosphorus compounds, this shielding effect has been used for stereochemical assignment. For example, Quin[95] assigned the structures of the two isomeric phospholene oxides 147 (a) and (b) by noting that the methyl signal of the cis-isomer 147 (a) appears at a higher field by 0.45 p.p.m. than that of the trans-isomer 147 (b).



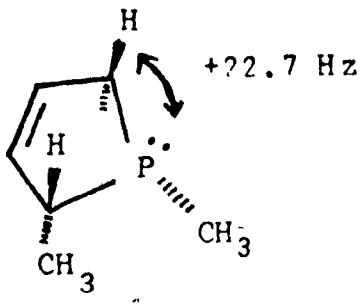
(147a)



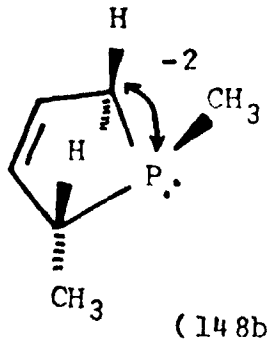
(147b)

Examination of molecular models of the various isomers of the bromo-derivatives of 2-phenylisophosphindoline 2-oxide suggests that the benzylic protons cis to the phenyl ring should be similarly shielded, i.e. they should appear at a higher field.

The dependence of the geminal coupling constant $^{2}J(P\text{-}C\text{-}H)$ on the phosphorus lone pair orientation has been observed[142] in 1,2,5-trimethyl-3-phospholene (148 a and b). The larger $^{2}J(P\text{-}C\text{-}H)$ coupling constant (+22.7 Hz) is attributed to the isomer 148 (a) in which the C-H bond cis to the phosphorus lone pair and the smaller $^{2}J(P\text{-}C\text{-}H)$ coupling constant (-2 Hz) to the trans-isomer 148 b.



(148a)



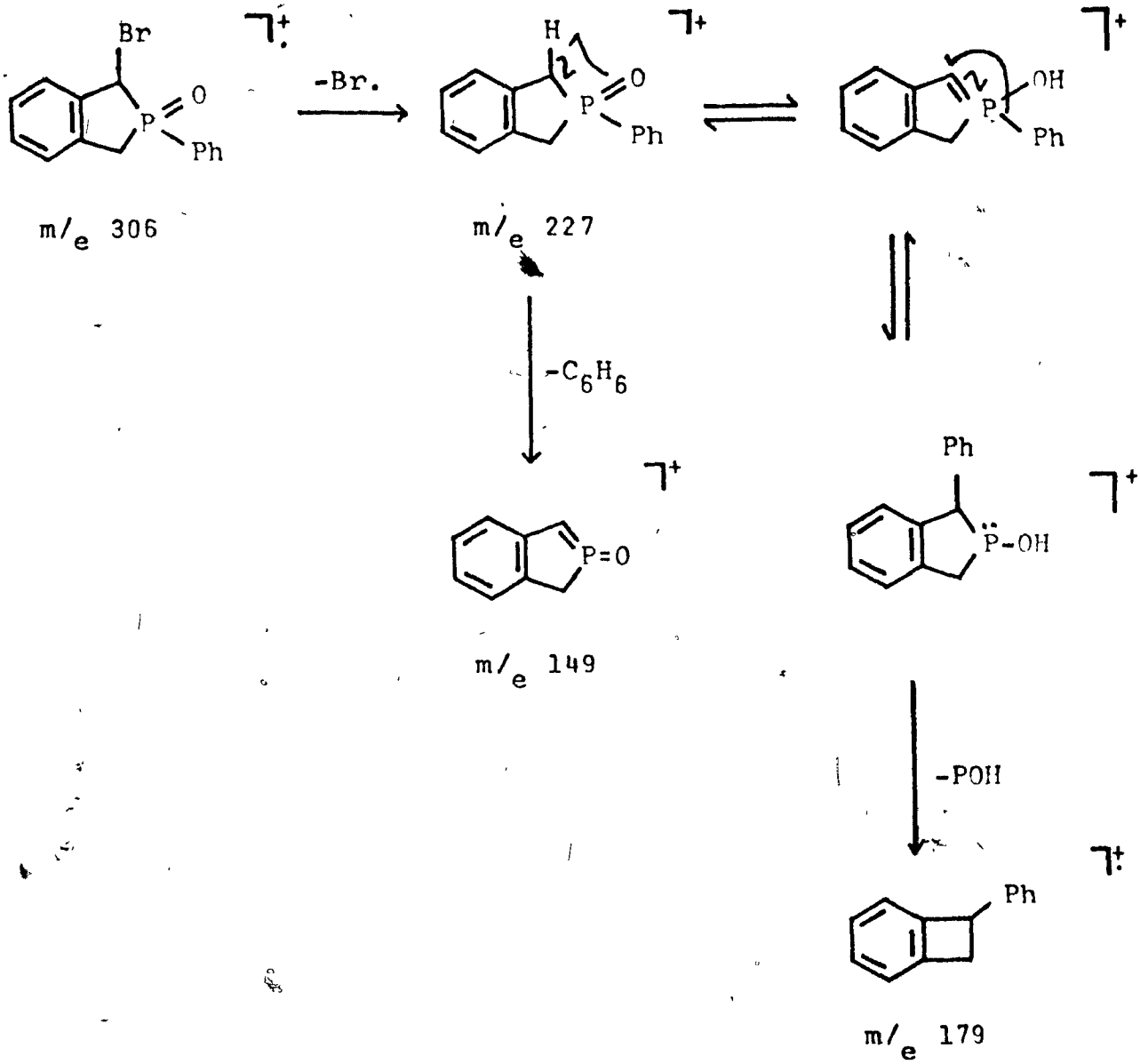
(148b)

If one argues that the magnitude of the $^{2}J_{(P-C-H)}$ coupling constant depends not so much on the orientation of the lone pair, but rather on the orientation of the polar group, then one may predict that in the isophosphindoline P-oxide systems, the magnitude of the geminal $^{2}J_{(P-C-H)}$ coupling constant is a function of the orientation of the phosphoryl group. If one further argues that the dependence is in the same direction, then the proton trans to the phosphoryl group (i.e. cis to the phenyl group) should have the smaller coupling constant as shown in Table IX.

The argument appears to be consistent with the data in Table IX. Similar dependence of geminal $^{2}J_{(C-C-H)}$ coupling constants on the orientation of a polar group on carbon has been observed[144].

The mass spectrum of r-1-bromo-t-2-phenylisophosphindoline 2-oxide (142) (fig. 30) shows P($m/_e$ 306) and P+2($m/_e$ 308) in 1:1 intensity ratio. The base peak is at $m/_e$ 227, which arises from the loss of -Br radical from the molecular ion. The other prominent peak at $m/_e$ 179 may arise from the rearranged ion of $m/_e$ 227 as shown in Scheme XX. Loss of C_6H_6 from the peak at $m/_e$ 227 also provides the peak at $m/_e$ 149.

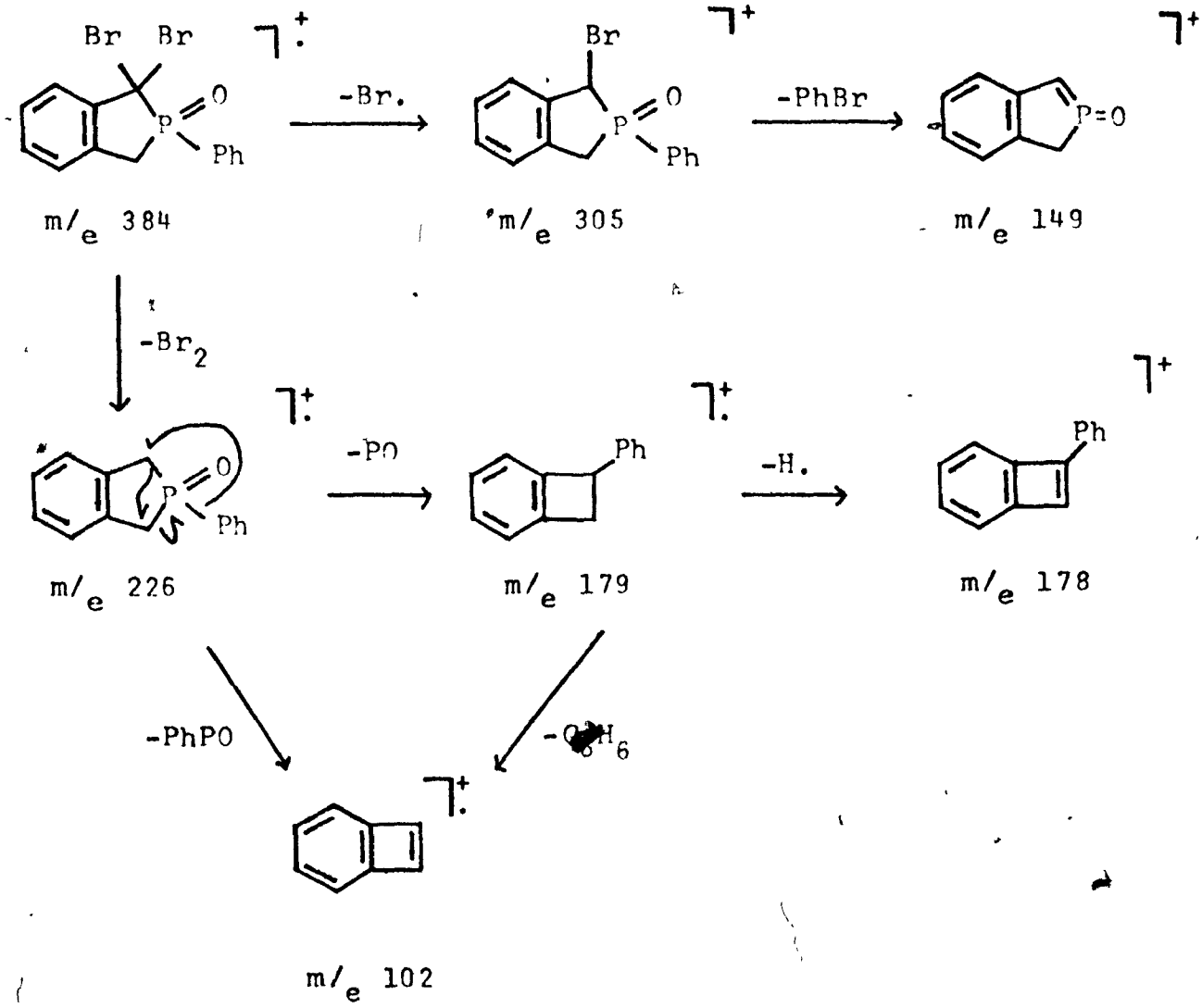
Scheme XX



The mass spectrum of 1,1-dibromo-2-phenylisophosphindoline 2-oxide (143) shows P($m/_e$ 384), P+2($m/_e$ 386) and P+4($m/_e$ 388) in 1:2:1 intensity ratio. The other feature includes (P-Br.) ion at $m/_e$ 305 and 307 in 1:1 intensity ratio. The base peak

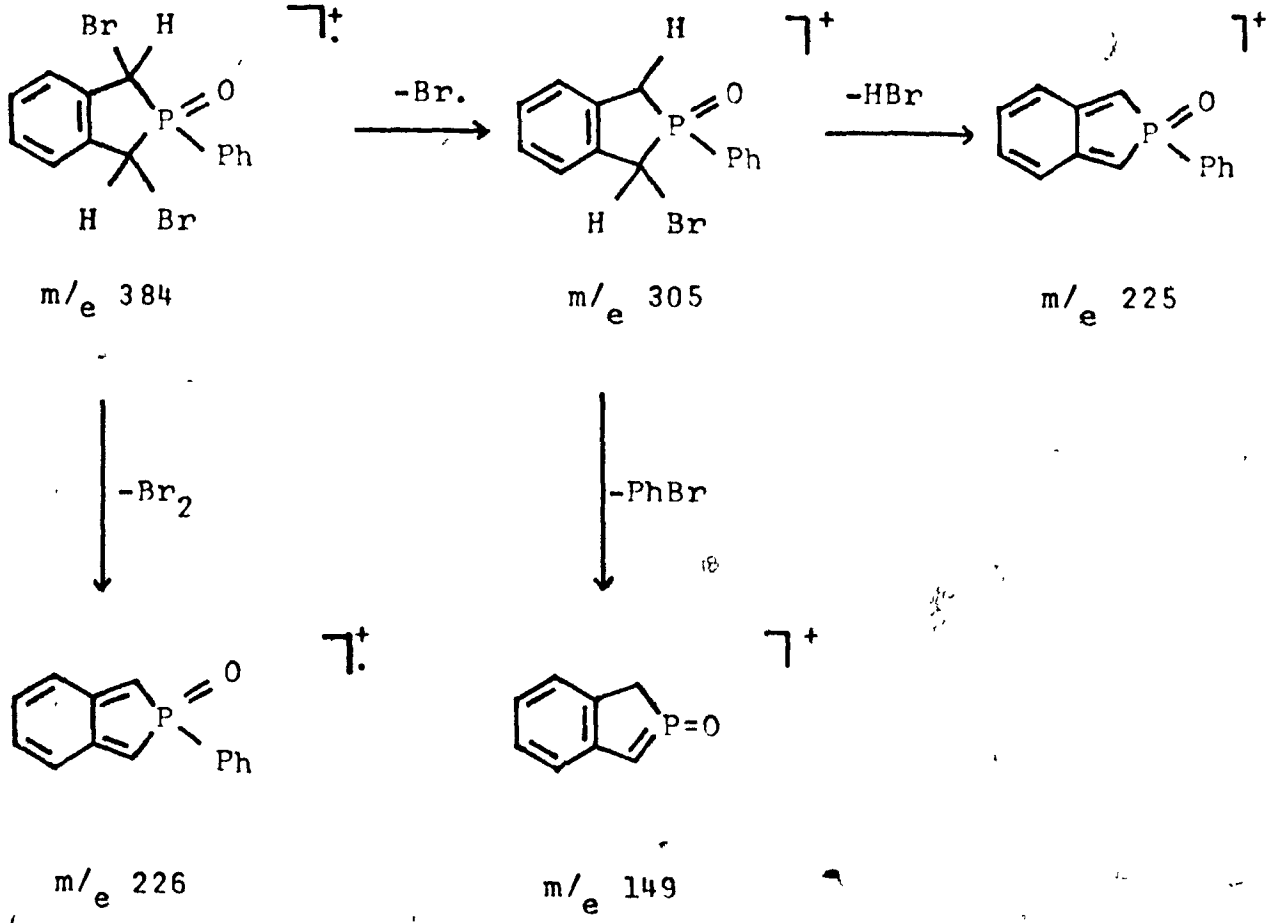
at $m/_e$ 149 may be formed by the elimination of PhBr from the (P-Br.) ion. Loss of Br_2 molecule from the molecular ion provides the peak at $m/_e$ 226. The other peaks at $m/_e$ 179, 178 and 102 may be accounted for by the fragmentation pattern as shown in Scheme XXI.

Scheme XXI



The mass spectrum of trans-1,3-dibromo-2-phenylisophosphindoline 2-oxide (145) also exhibits P($m/_e$ 384), P+2($m/_e$ 386), and P+4($m/_e$ 388) in 1:2:1 intensity ratio. Loss of -Br radical and Br_2 from the molecular ion gives rise to the peaks at $m/_e$ 305, 307 in 1:1 intensity ratio and at $m/_e$ 226 respectively. The base peak at $m/_e$ 149 may arise from the loss of PhBr from (P-Br.) peak. Loss of HBr from (P-Br.) peak also provides the peak at $m/_e$ 225. The fragmentations involved are depicted in Scheme XXII.

Scheme XXII



$m/_e$ 384 $m/_e$ 305 $m/_e$ 225

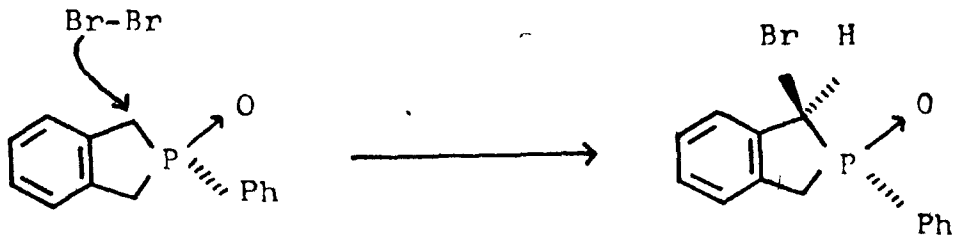
$m/_e$ 226 $m/_e$ 149

The other 1,3-dibromo isomer (144) exhibits all the prominent peaks observed in the mass spectrum of the trans-isomer. The fragmentation pattern may indeed be the same as in Scheme XXII.

The mass spectrum of r-1-bromo-c-2-phenylisophosphindoline 2-oxide (146) shows all the prominent peaks observed in that of the other isomer 142, and the fragmentation pattern is same as in Scheme XX.

With the stereochemistry of the various bromo compounds properly assigned, it is interesting to note that the trans-isomer 142 is formed in greater than 10 fold excess of the cis-isomer 146. This stereoselectivity is rather unexpected because free radical bromination is not known to be so selective[145].

It may be that in the present case, with the constraint imposed by the bicyclic system, in the product formation step, the approach of the reagent bromine may come preferentially from the side opposite to the more bulky phenyl group.



An alternative explanation may be the "Gauche Effect" proposed by Wolfe[146]. In many reaction involving carbanions adjacent to polar bond, the stereospecificity is explained to be due to the preference of the carbanion electron pair to be gauche

to the adjacent polar bond. Whether such an explanation is applicable to the present reaction involving free radical intermediate is a question which requires much further work.

With N-Chlorosuccinimide

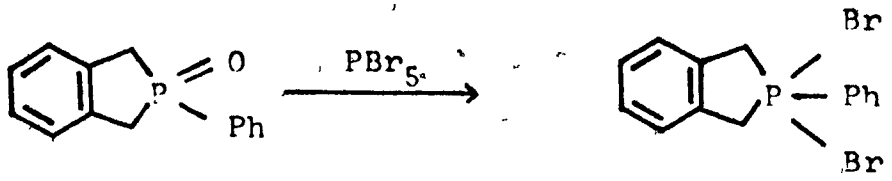
If it is the steric effect which is controlling the stereospecificity, then one may expect that the free radical chlorination of 2-phenylisophosphindoline 2-oxide (121) might be less stereoselective, since chlorine atom is smaller in size than bromine.

Thus, 121 was chlorinated with equal molar quantity of recrystallized N-chlorosuccinimide[93], in the presence of a catalytic amount of benzoyl peroxide in refluxing benzene for 12 hours. The n.m.r. spectrum of the reaction mixture revealed that monochlorinated compound, analogous to 142 was formed stereoselectively as in the case of N-bromosuccinimide. The isolation of the products was however not attempted.

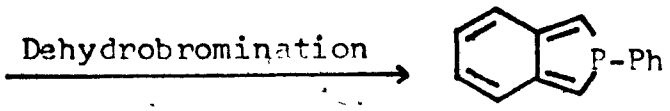
With Phosphorus Pentabromide

It is expected that if 2-bromo-2-phenylisophosphindolinium bromide (149) can indeed be synthesized, dehydrobromination of this will lead to 2-phenylisophosphindole (150). Similar kind of dehydrobromination has been reported by Mathey[20] (Eq. 5) and Quin[147]. The possible method to prepare 149 is the treatment of 2-phenylisophosphindoline 2-oxide (121) with phosphorus penta-

bromide in analogy to the reaction of ketone with the same reagent to give dibromo compound.



(121) (149)



(150)

Thus, treatment of 2-phenylisophosphindoline 2-oxide with phosphorus pentabromide in refluxing benzene for 24 hours led to the formation of 15% yield of r-1-bromo-t-2-phenylisophosphindoline 2-oxide (142), rather than the expected product. Most of the starting material was recovered. It seems that phosphorus pentabromide behaves as a brominating agent and the same stereoselectivity is observed.

Other Reactions of 2-Phenylisophosphindoline 2-Oxide

Thermal Decomposition

In view of the report by Cava et al[110] on the synthesis of isobenzothiophene (110) (Eq. 46), it is hoped that 2-phenylisophosphindoline 2-oxide (121) might also undergo thermal decomposition to form the corresponding isophosphindole.

Thus, when a 1:2 mixture of 113 and neutral alumina was heated under 12 mm Hg pressure at 120° in a sublimer, a white crystalline solid was collected on the cold finger. It was identified as the starting material by its spectroscopic properties and by thin layer chromatography.

Attempted Dehydration of 2-Phenylisophosphindoline 2-Oxide

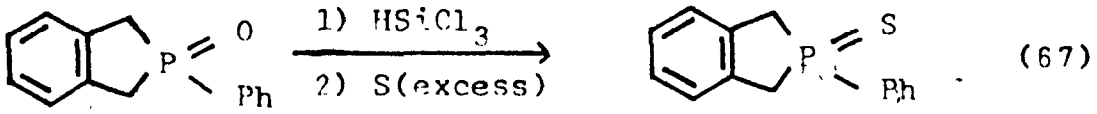
In analogy to 1,3-dihydrobenzothiophene 2-oxide (112)[110], 2-phenylisophosphindoline 2-oxide (121) might undergo dehydration by chemical means. Thus, 121 was treated with excess acetic anhydride in refluxing benzene for 48 hours. However, no new compound was formed as shown by thin layer chromatography and n.m.r. spectroscopy.

The attempted reaction of 121, either with p-toluenesulfonyl chloride alone, or with the same reagent in the presence of pyridine also failed to give any new compound.

2-Phenylisophosphindoline 2-Sulfide

Expecting that phosphine sulfide might undergo decomposition, 2-phenylisophosphindoline 2-sulfide was prepared as follows: -

2-Phenylisophosphindoline 2-oxide was reduced with excess trichlorosilane in refluxing benzene for 48 hours. After hydrolysis, the reaction mixture was treated with excess sulfur at room temperature. A new compound was obtained as yellow solid in 60% yield. The spectroscopic properties were in accord with 2-phenylisophosphindoline 2-sulfide (151) (Eq. 67).



(121) (151) (67)

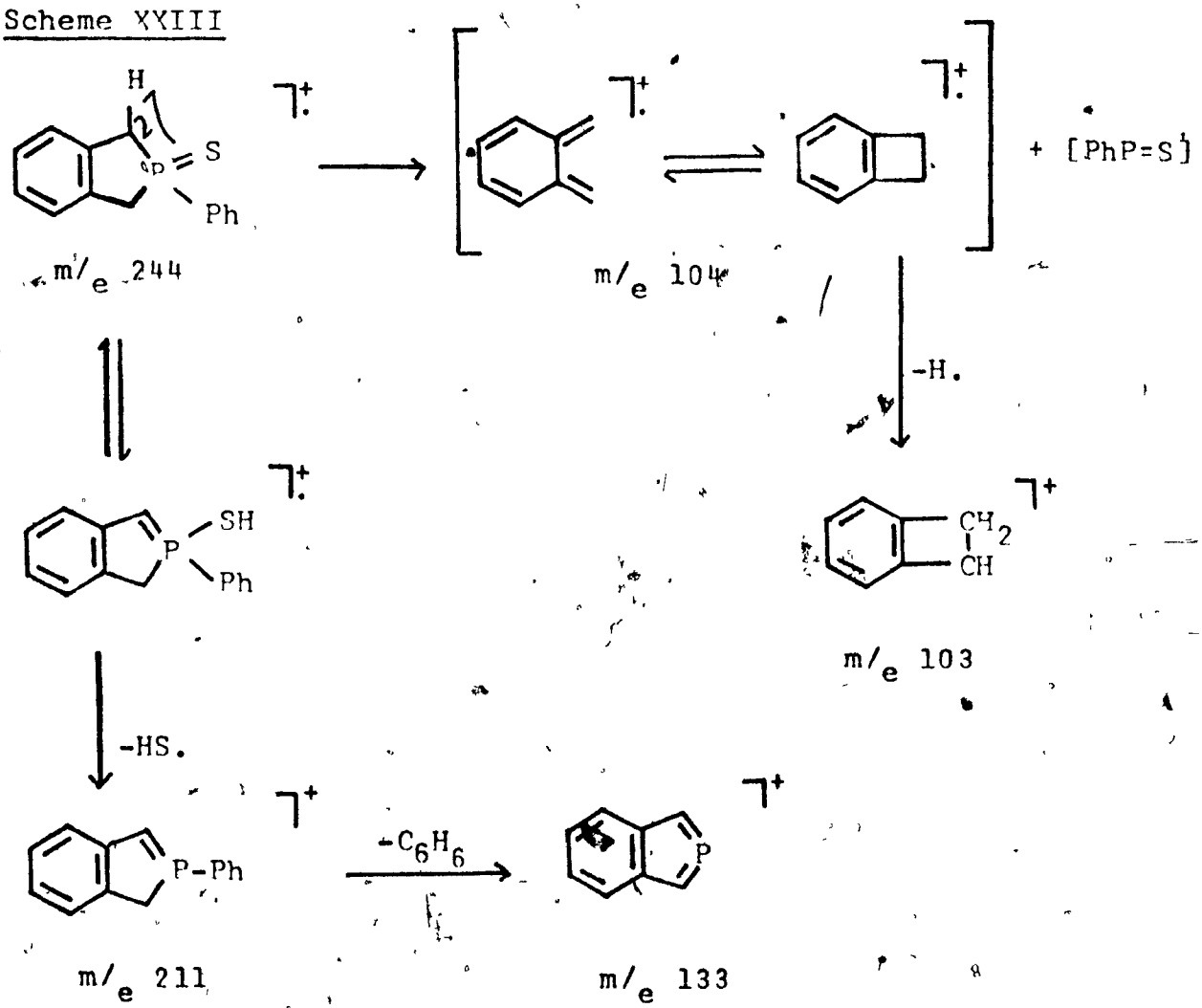
The infrared spectrum of 2-phenylisophosphindoline 2-sulfide (151) shows strong phenyl bands at 1440 cm^{-1}, 1100 cm^{-1} and 700 - 800 cm^{-1}. A weak band at 650 cm^{-1} is attributable to the P=S stretching.

The 60 MHz n.m.r. spectrum of 2-phenylisophosphindoline 2-sulfide is of considerable interest. The methylene signals appear as a doublet at 3.7 δ (J_{P-CH} = 12 Hz) in $CDCl_3$ solution. However, in benzene solution, the pattern of the methylene protons is the same as those in 2-phenylisophosphindoline 2-oxide, i.e. as part of an ABX system at 3.8 δ. A 5-H multiplet at 7.5 - 8.0 δ

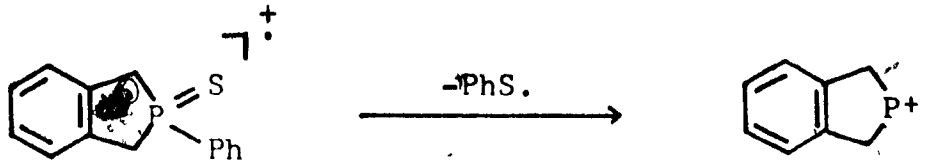
and a 4-H singlet at 7.3 δ are observed for the aromatic protons.

The mass spectrum of 2-phenylisophosphindoline 2-sulfide shows a molecular ion P at $m/_e$ 244 as the base peak. There is the characteristic P+2 ($m/_e$ 246) peak for sulfur compound. A peak at $m/_e$ 104 is also observed as in the case of its oxygen analog 121. An interesting fragment is at $m/_e$ 135, which may arise from the loss of PhS radical from the molecular ion, a process which has been reported[148]. The fragmentation pattern is illustrated in Scheme XXIII. Exact mass measurement: - Calcd. for $C_{14}H_{13}PS$ - 244.0467, Found - 244.0476.

Scheme XXIII



Scheme XXIII (cont'd)



m/e 244 m/e 135

Attempted Decomposition of 2-Phenylisophosphindoline 2-Sulfide

Treatment of 2-phenylisophosphindoline 2-sulfide (151) with excess acetic anhydride in refluxing benzene for 48 hours failed to lead to the formation of any new product. On the other hand, by refluxing 151 in acetic anhydride alone for 36 hours, 2-phenylisophosphindoline 2-oxide was obtained (Eq. 68).

(68)

(151) (121)

This reaction may proceed by an oxa-thia exchange reaction as indicated in Eq. 68. Similar kind of reaction involving epoxides and phosphine sulfides has been reported[149].

The attempted reaction of 151 either with p-toluenesulfonyl chloride or with the same reagent in the presence of pyridine also met with failure.

The fact that 2-phenylisophosphindoline 2-oxide (121) and its sulfur analog 151 fail to undergo dehydration, in contrast to 1,3-dihydrobenzothiophene 2-oxide (112), may probably be due to the greater polarity of the S=O bond compared to that of P=O or P=S bond.

2-Phenylisophosphindole 2-Oxide

Dehydrobromination of r-1-bromo-t-2-phenylisophosphindoline 2-Oxide with 1,5-Diazabicyclo[3.4.0.]nonene-5 (DBN) or Triethylamine

An easy entry into the isophosphindole system can be achieved by dehydrobromination of r-1-bromo-t-2-phenylisophosphindole 2-oxide with base.

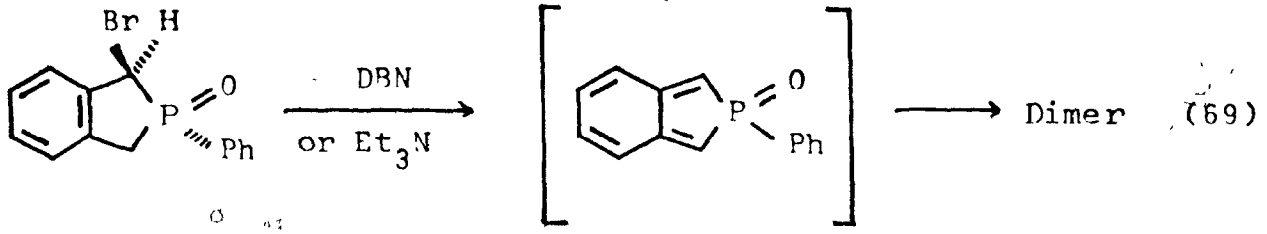
r-1-bromo-t-2-phenylisophosphindoline 2-oxide (142) was dehydrobrominated with excess DBN in refluxing benzene for 8 hours. After working up, the resulting reaction mixture, on separation by preparative thin layer chromatography afforded 62% yield of a new compound (Eq. 69). Its mass spectrum and elemental analysis were consistent with the dimer of 2-phenylisophosphindole 2-oxide (152).

Dehydrobromination of 142 with excess triethylamine in refluxing benzene for 12 hours gave 50% yield of the same product.

The formation of DBN.HBr and NEt_3.HBr salts in both reaction

indicated that dehydrobromination has indeed taken place.

The isolation of the dimer indicates that 152, if formed must be unstable and it dimerizes too rapidly to allow its isolation. The reactivity of 152 should be compared with that of 1,2,3-triphenylisophosphindole 2-oxide (83) which underwent dimerization, as well (Eq. 30).



(69)

(142) (152)

The dimerization of 2-phenylisophosphindole 2-oxide is not unexpected, in view of the strong tendency of unstable o-quinonoid system to undergo dimerization[128,138].

The infrared spectrum of the dimer (fig. 21) exhibits a strong band at 1210 cm^{-1}, attributable to phosphoryl stretching and strong bands at 1440 cm^{-1}, 1120 cm^{-1} and 700 - 800 cm^{-1}, all associated with phenyl absorption.

The 60 MHz, 100 MHz and 220 MHz n.m.r. spectra (fig. 26) shows a 14-H multiplet at 7.0 - 7.8 δ for aromatic protons, a 4-H multiplet at 6.3 δ for olefinic protons, a 1-H doublet of doublet at 5.3 δ for another olefinic proton (J_{P-CH} = 22 Hz), two 1-H multiplet at 4.2 δ and 3.9 δ for two nonequivalent methine protons and a 1-H multiplet at 3.4 δ for another methine protons.

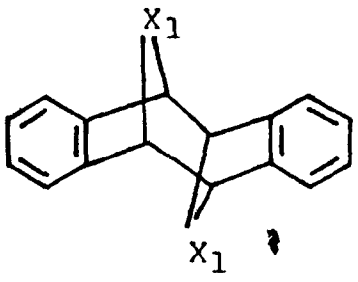
The mass spectrum (fig. 31) of the dimer features a molecular ion at $m/_e$ 452. The other prominent peaks are at $m/_e$ 226, 150 and 149. Since the structure is not certain, the fragmentation pattern is not interpreted at this point.

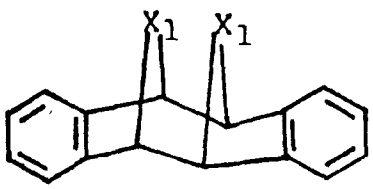
Structure of the Dimer

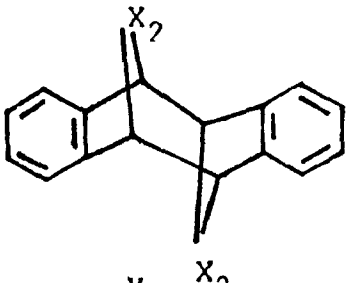
The exact structure and stereochemistry of the dimer is still inconclusive. The elucidation of the structure is not an easy task.

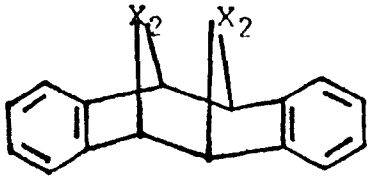
If one considers that the dimer arises from two molecules of 2-phenylisophosphindole 2-oxide, there are altogether 36 possible structures.

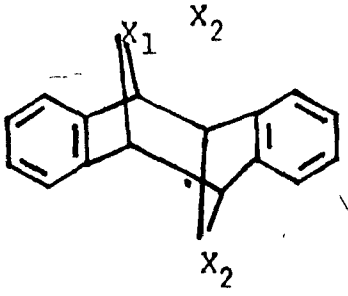
i to vi $\quad X_1 = {}^{O}\!\!=\!\!P\text{-}Ph \quad ; \quad X_2 = Ph\text{-}P\!\!=\!\!O$

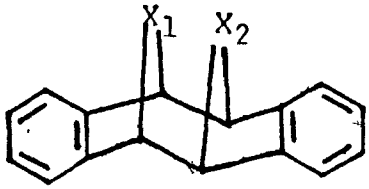




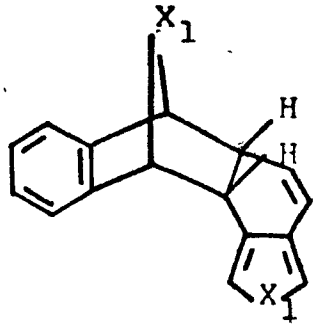


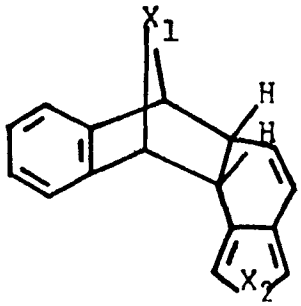


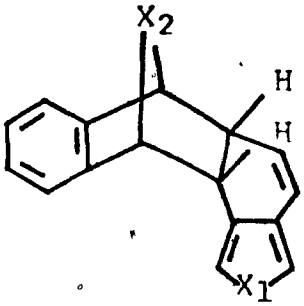


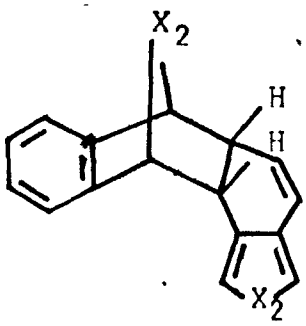


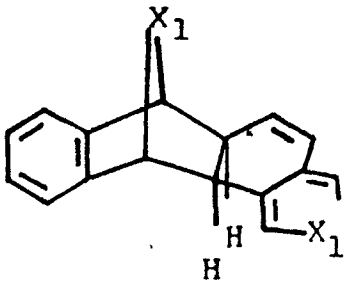
vii to xiv

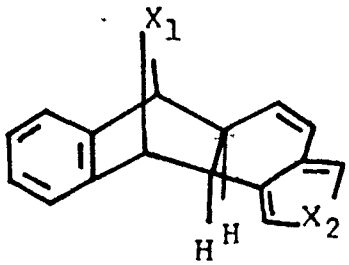


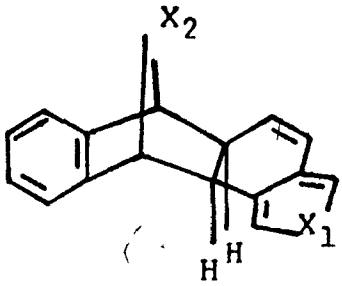


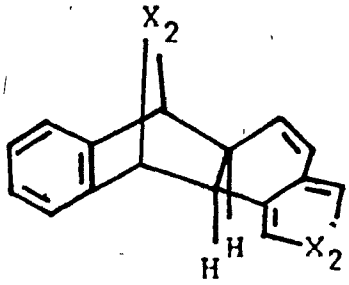




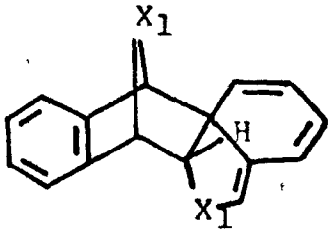


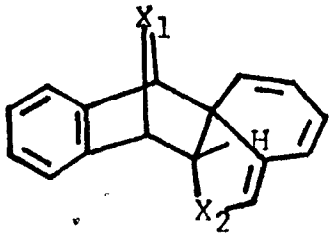


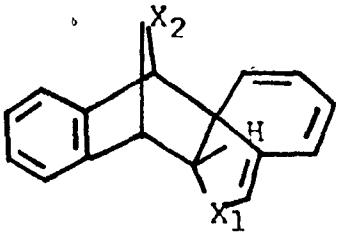


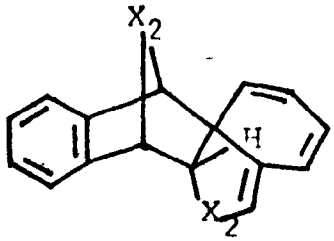


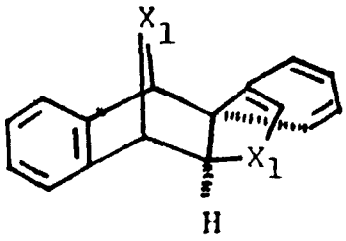
xv to xxii

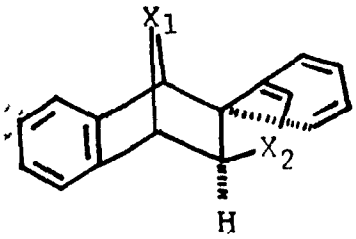


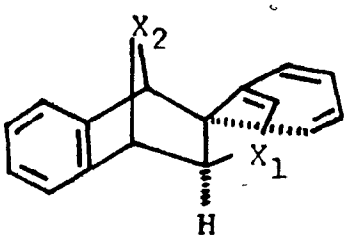


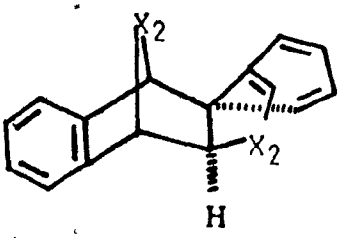




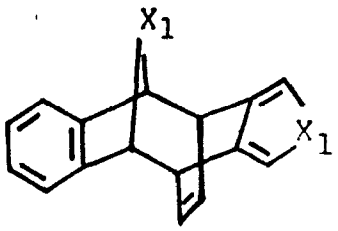


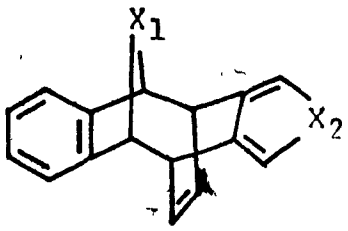


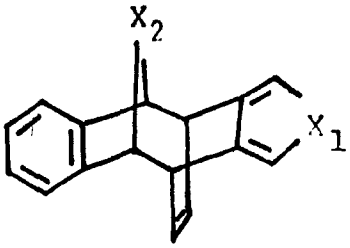


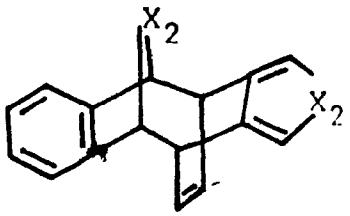


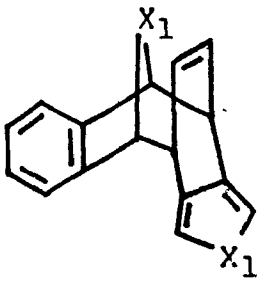
xxiii to xxx

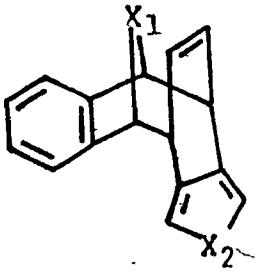


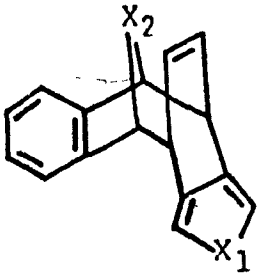


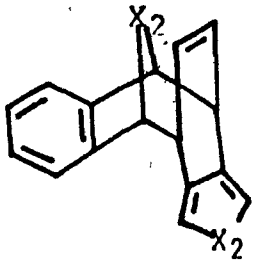




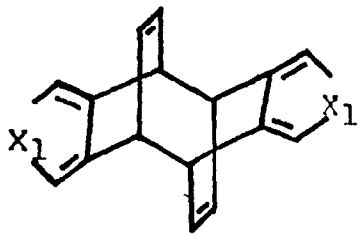


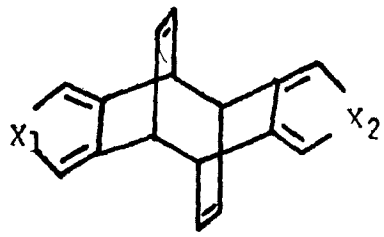


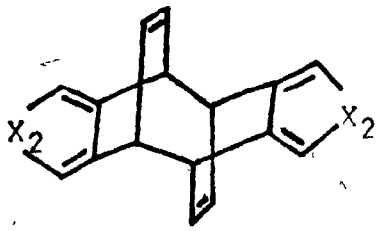


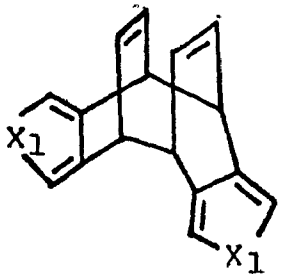


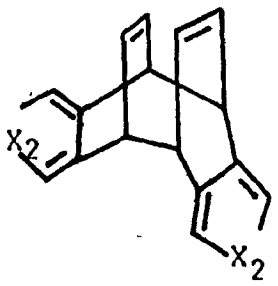
xxxi to xxxvi

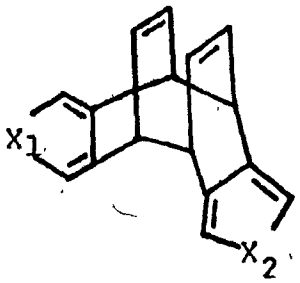






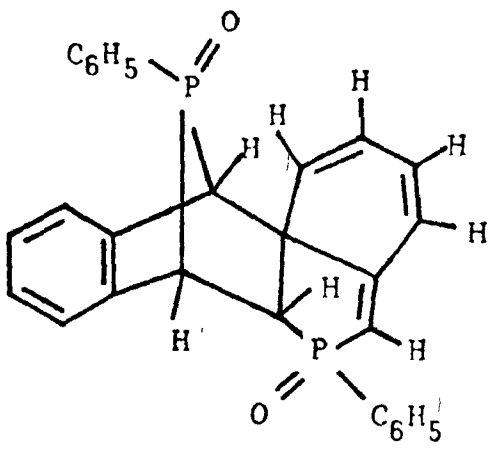






Some of these structures can be eliminated. Structures i to vi are not likely, because of the absence of olefinic protons. Structures xxxi to xxxvi, being symmetry, are predicted to have simple n.m.r. spectra. The complexity of the observed n.m.r. spectrum of the dimer rules out these structures.

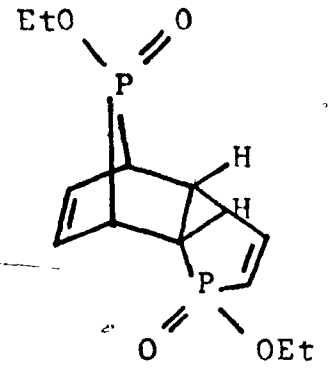
The observation of one olefinic proton with large J_{P-CH} coupling constant would favour the structures x v to xxii. The other features of the n.m.r. spectrum also favour these structures. It is difficult to differentiate between these structures from the n.m.r. spectrum alone. At the moment, we favour structure 153 as the structure of the dimer.



(153)

From reactions which will be discussed in later part of this thesis, Diels-Alder reaction of 2-phenylisophosphindole 2-oxide with another dienophile involves endo addition. This is also the case for the Diels-Alder adducts of separate isophosphindole P-oxides. Thus we feel quite confident that the exo structures

can be eliminated from consideration. The stereochemistry at phosphorus is uncertain. We favour 153, because it places the more bulky phenyl group away from the approaching diene during cycloaddition. In the dimerization of 1-ethoxyphosphole 1-oxide, the stereochemistry has been deduced by X-ray and found to be:



Thus, one can assign the n.m.r. spectrum to structure 153 accordingly.

The integration ratio in the n.m.r. spectrum of the dimer is consistent with the structure 153. If the structure 153 is assumed to be the correct one, one may expect that it may possess some diene character. Moreover, hydrogenation would be expected to yield some useful informations in structure elucidation.

Attempted Reaction of 2-Phenylisophosphindole 2-Oxide Dimer with Dienophiles

Treatment of 2-phenylisophosphindole 2-oxide dimer with excess dimethyl acetylenedicarboxylate in refluxing benzene for

48 hours, only led to the recovery of the starting material, as revealed by thin layer chromatography and n.m.r. spectrum of the reaction mixture.

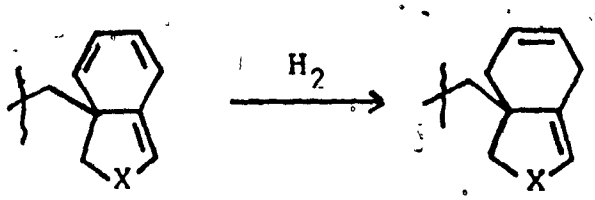
The dimer was also treated with excess tetracyanoethylene in refluxing methylene chloride for 48 hours. Again, no new compound other than the starting material was detected by thin layer chromatography and n.m.r. spectroscopy.

Hydrogenation of 2-Phenylisophosphindole 2-Oxide Dimer

The dimer was hydrogenated at 1 atmosphere pressure at 65° in the presence of 10% palladium on charcoal. Absolute ethanol was used as the solvent. The reaction mixture was agitated overnight. After removal of catalyst and solvent, a white solid was obtained. Its mass spectrum showed that one molecule of hydrogen has been absorbed.

In the expectation that the dimer 153 would absorb more than one molecule of hydrogen, hydrogenation was repeated at 50 atmosphere pressure at 80°, in the presence of 10% palladium on charcoal for 3 hours. However, the mass spectrum of the product showed that further addition of hydrogen did not take place.

Thus, the chemical evidence does not give any conclusive results. It is probable that hydrogenation of 153 led to the 1,4-addition product.



(153)

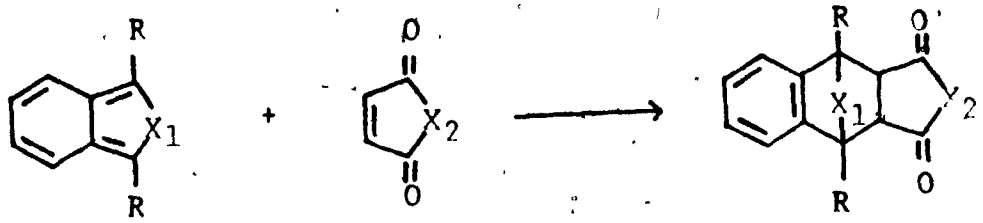
X = P(O)Ph

It is our hope that with the use of ^{13}C n.m.r. spectroscopy, it may be possible to deduce conclusively the structure of the dimer in the future.

Recently, the generation of 1,2,3-triphenylisophosphindole 2-oxide[73] has been achieved by a similar scheme. Similarly, the formation of dimer was observed. The structure 84 (Eq. 30) was proposed for this dimer. However, the stereochemistry of the structure has not been considered.

2-Phenylisophosphindole 2-Oxide as Diels-Alder Diene with Dimethyl Acetylenedicarboxylate

The existence of many transient o-quinonoid intermediates has been confirmed by trapping with various dienophiles[107,108, 128,138]. Before the successful isolation of isoindole (5)[113] and isobenzofuran (109)[111,112], their transient existence has been trapped as Diels-Alder adducts[107,108] (Eq. 70; X_1=N-H; X_2=O, N-Ph; R=H and Eq. 71).

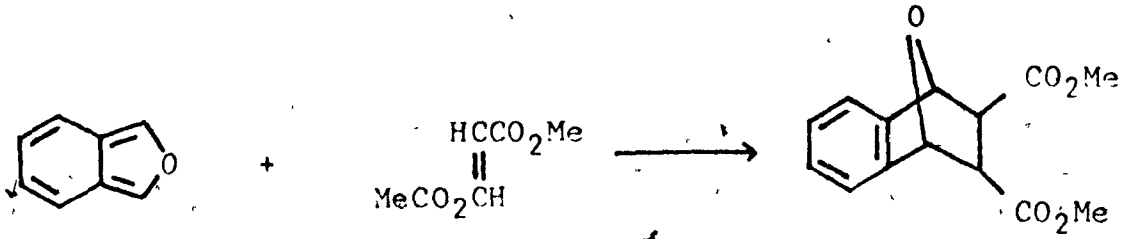


(70)

X_1 = N-H

X_2 = O, N-Ph

R = H, Ph



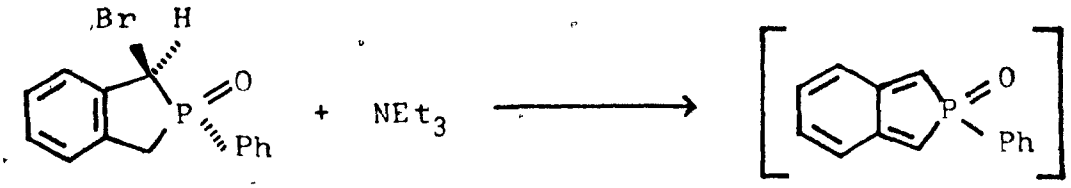
(71)

Isoindene has been also postulated as a reactive intermediate and has been trapped with maleic anhydride[150] (Eq. 70, X_1=CH_2; X_2=O, R=H), whereas evidence has been found for the formation of the chlorosubstituted isoindene by Mackenzie et al[151].

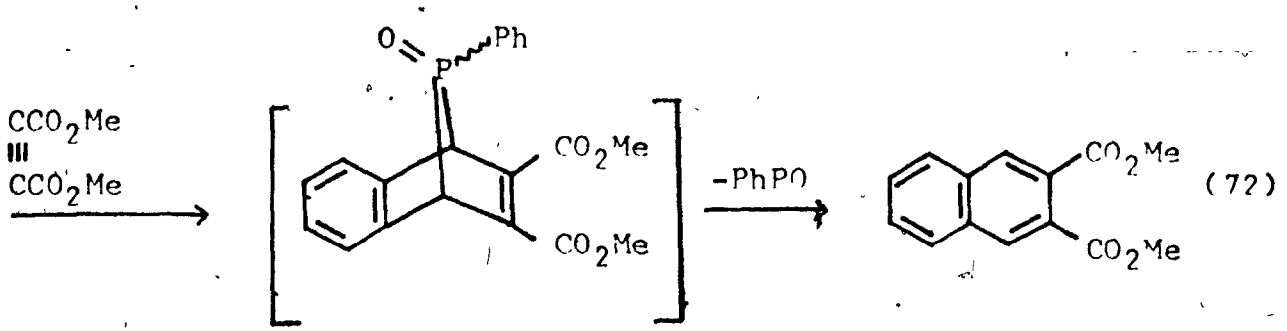
The existence of 1,2,3-triphenylisophosphindole 2-oxide[73] has also been proved by trapping with N-phenylmaleimide (Eq. 70; X_1=P(O)Ph; X_2=N-Ph; R=Ph).

In order to demonstrate that 2-phenylisophosphindoline 2-oxide is indeed the reaction intermediate, we sought to trap it in the form of the Diels-Alder adduct. Thus, treatment of r-1-bromo-t-2-phenylisophosphindoline 2-oxide (142) with excess triethylamine in the presence of dimethyl acetylenedicarboxylate,

in refluxing benzene for 48 hours, led to the isolation of 28% yield of a new compound by preparative thin layer chromatography. It was identified as dimethyl 2,3-naphthalene dicarboxylate (155) (Eq. 72) on the basis of its spectroscopic properties and m.p. 45 - 46 (Lit.[152] m.p. 47). The spectroscopic data of the isolated compound were identical to those of an authentic sample, prepared from the esterification of 2,3-naphthalene dicarboxylic acid.



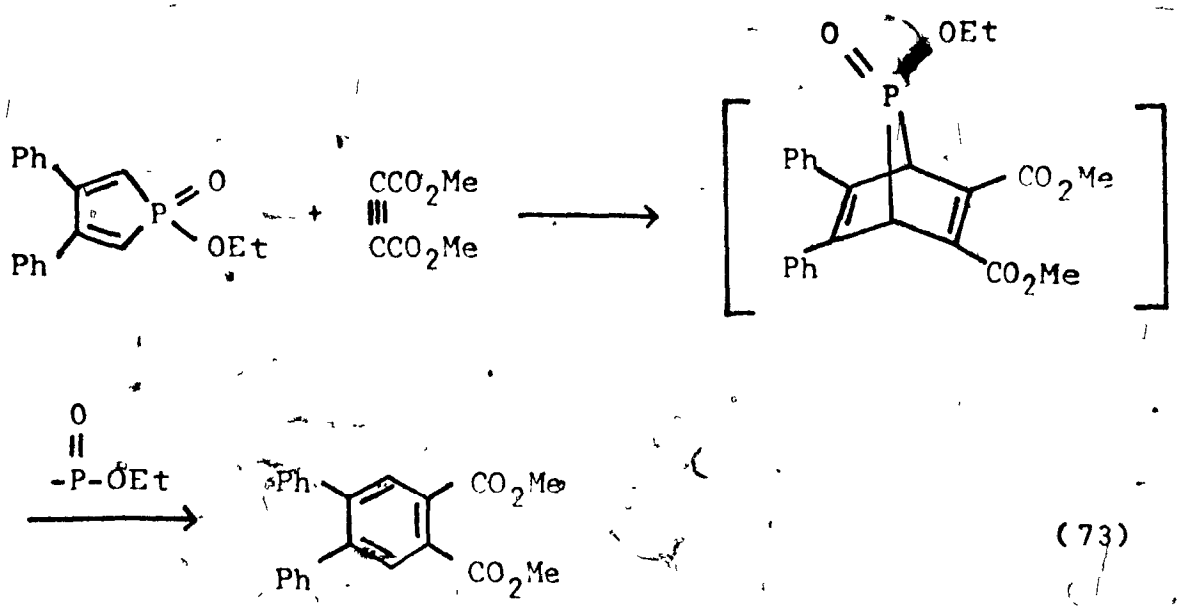
(142) (152)



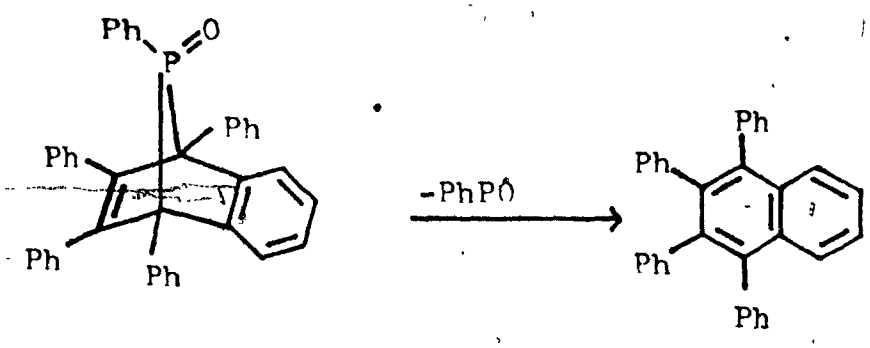
(72)

(154) (155)

The formation of the ester 155 can only arise from the Diels-Alder adduct 154 by the extrusion of the PhPO moiety. Similar kind of extrusion has been well documented[12,24,31,153] (Eqs. 13, 73, 74).

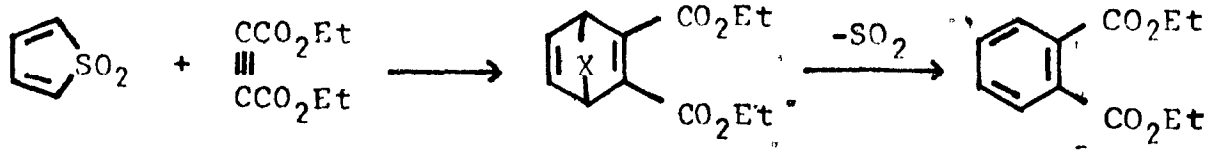


(73)



(74)

Analogous extrusion has also been observed in sulfur heterocycles[154] (Eq. 75).



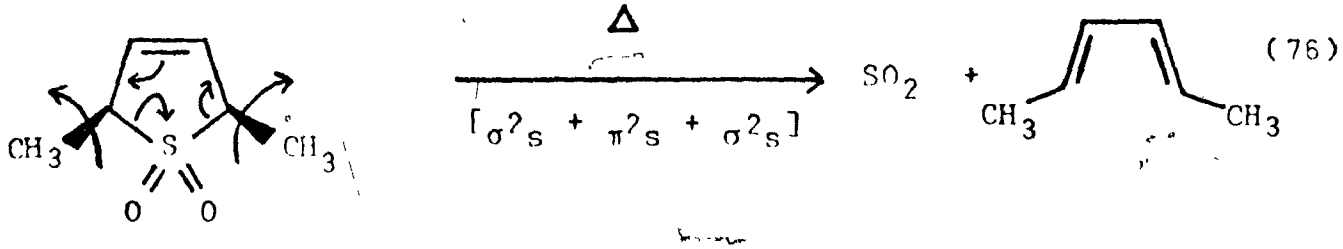
(75)

X = SO_2

The infrared spectrum of dimethyl 2,3-naphthalene dicarboxylate (155) consists of a very strong C=O stretching band at 1720 cm^{-1} and characteristic C-O-C stretching bands at 1280 cm^{-1}.

The n.m.r. spectrum of 155 consists of a 2-H singlet at 8.2 δ for the aromatic protons at 1 and 4 positions, a 2-H multiplet at 7.7 - 8.0 δ for the aromatic protons at 5 and 8 positions, a 2-H multiplet at 7.4 - 7.7 δ for those at 6 and 7 positions and a 6-H singlet at 3.98 δ for the methyl protons.

The extrusion of PhPO moiety from the adduct 154 may be considered as a six electron ($\sigma^2_s + \pi^2_s + \sigma^2_s$), linear, cheletropic cycloreversion process. A cheletropic process is one- "in which two σ-bonds which terminate at a single atom are made, or broken, in concert".[139] The extrusion of PhPO group might accompany by the disrotatory motion as in the case of extrusion of SO_2 from the sulfolene 156[155] (Eq. 76).

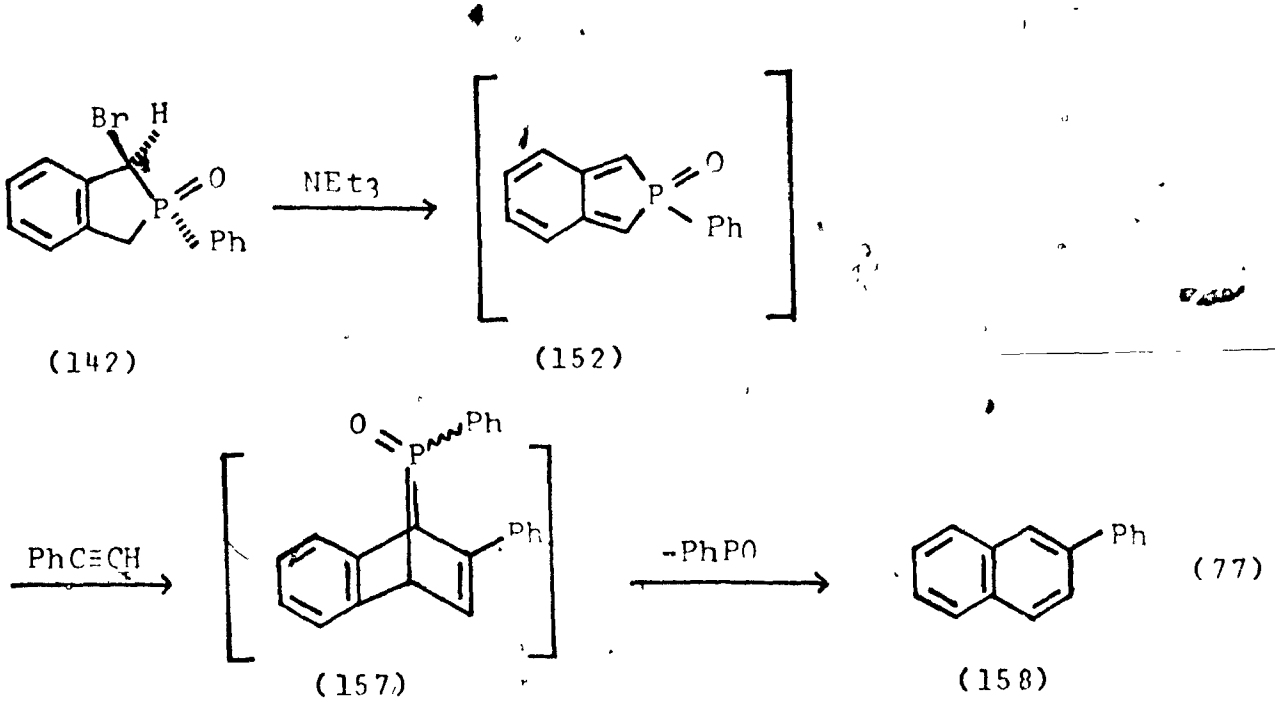


(156) (76)

With Phenylacetylene

Dehydrobromination of r-1-bromo-t-2-phenylisophosphindoline 2-oxide (142) with excess triethylamine in the presence of phenylacetylene in refluxing benzene for 48 hours, afforded 2-phenyl-

naphthalene (158) in 15% yield. 2-Phenylisophosphindole 2-oxide dimer was also isolated in 25% yield. In this reaction the PhPO moiety was extruded from the adduct 157 (Eq. 77).



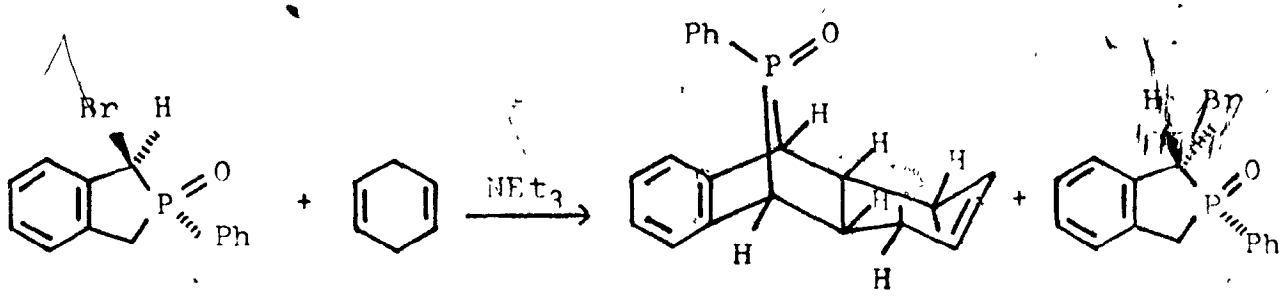
Hence, the dehydrobromination reaction of r-1-bromo-t-2-phenylisophosphindoline 2-oxide (142) in the presence of various acetylenes, seems to offer a general method for the preparation of naphthalene derivatives.

Trapping experiments were also carried out by using DBN as a base, in the presence of various dienophiles such as dimethyl maleate, dimethyl fumarate and dimethyl acetylenedicarboxylate. However, the reaction seems to give complex mixture of products. This may be due to the reactions between DBN and the dienophiles.

With 1,4-Cyclohexadiene

r-1-Bromo-t-2-phenylisophosphindoline 2-oxide (142) was dehydrobrominated with triethylamine in the presence of 1,4-cyclohexadiene. The expected adduct was isolated by preparative thin layer chromatography in 34% yield. Its spectroscopic properties and elemental analysis were consistent with the structure 159 (Eq. 78).

Interestingly, from this reaction was also isolated r-1-bromo-c-2-phenylisophosphindoline 2-oxide (146). Presumably, it arose from a base-catalysed isomerization reaction.



(142) (159) (146)

(78)

The infrared spectrum of (159) (fig. 22) is quite simple, featuring a strong P=O absorption at 1210 cm^{-1} and strong phenyl bands at 1440 cm^{-1}, 1100 cm^{-1} and 700 - 800 cm^{-1}.

The adduct 159 has a rather complicated n.m.r. spectrum (fig. 27) featuring a 9-H multiplet at 7.2 δ for the aromatic protons, a 2-H multiplet at 5.7 δ for the olefinic protons, a 2-H doublet at 3.5 δ for the methine protons adjacent to P=O group (J_{P-CH} = 10 Hz), a 2-H multiplet at 3.2 δ for the methine

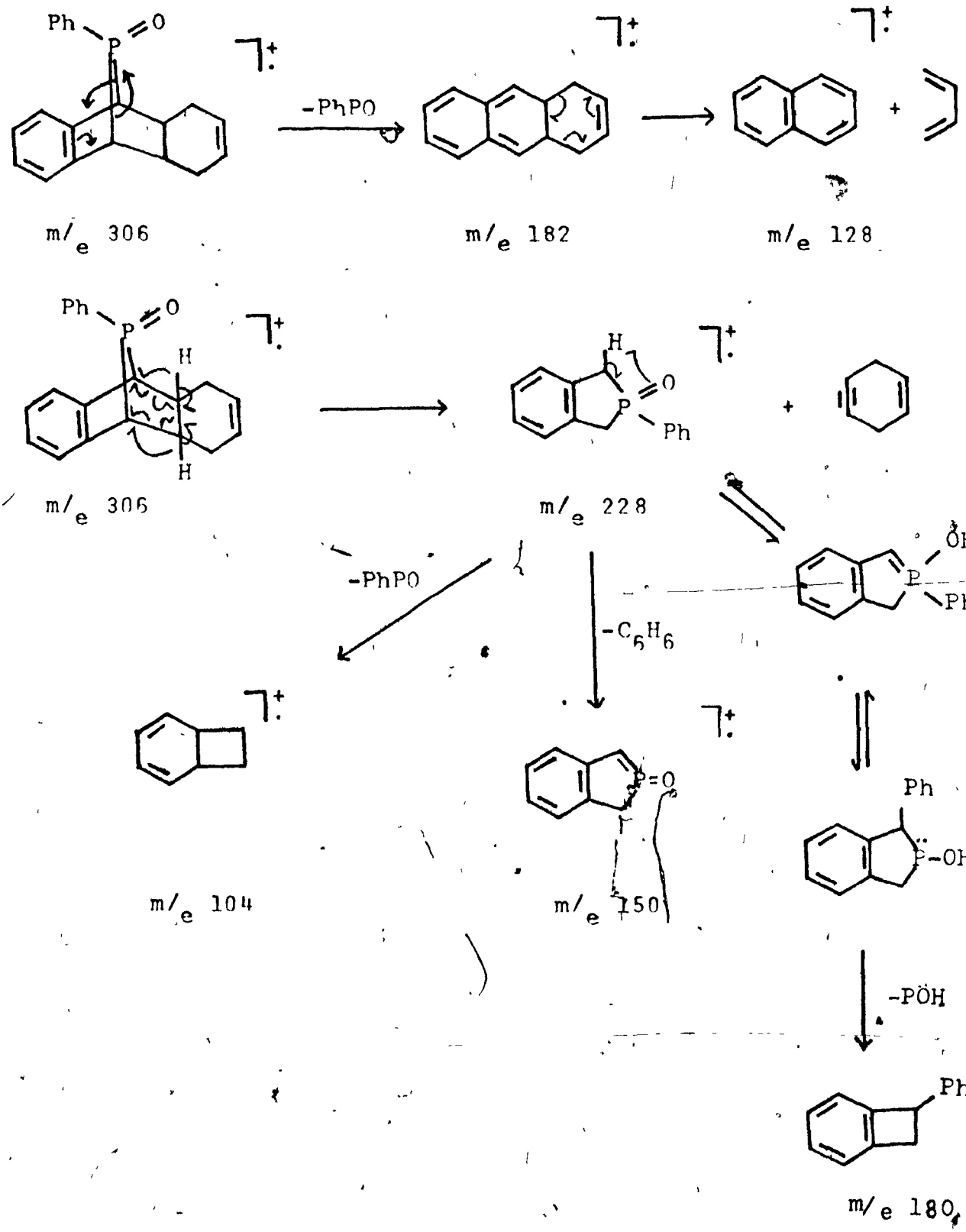
protons at the ring junction (J_{CH-CH} = 10, $^3J_{PCCH}$ = 0 Hz), a 2-H multiplet at 2.2 δ for the equatorial allylic protons (J_{HCH} = 15 Hz), a 2-H doublet of doublet at 1.3 δ for the axial allylic protons (J_{HCH} = 15 Hz, J_{CH-CH} = 10 Hz).

From the coupling constant of phosphorus with the methine protons at the ring junction, it is possible to assign the stereochemistry of the Diels-Alder adduct to be endo. Recently, Benezra[156] has reported the variation of vicinal $^{31}P-C-C-H$ couplings with dihedral angle and found a Karplus type relationship (fig. 35).

It can be seen that in 159 the endo isomer would be expected to have a dihedral angle of ~90°, thus a $^3J_{P-C-C-H}$ value of 0 Hz is within the experimental value.

The mass spectrum of the adduct 159 (fig. 32) features a molecular ion at $m/_e$ 306. Elimination of PhPO from the molecular ion gives the peak at $m/_e$ 182. Further elimination of butadiene provides the peak at $m/_e$ 128. The fragmentations involved are depicted in Scheme XXIV.

Scheme XXIV


Ph
P
O
-PhPO
m/e 306
m/e 182
m/e 128
H
H
m/e 306
m/e 228
Ph
-PhPO
-C6H6
OH
P
Ph
m/e 104
m/e 150
Ph
P-OH
-POH
Ph
m/e 180

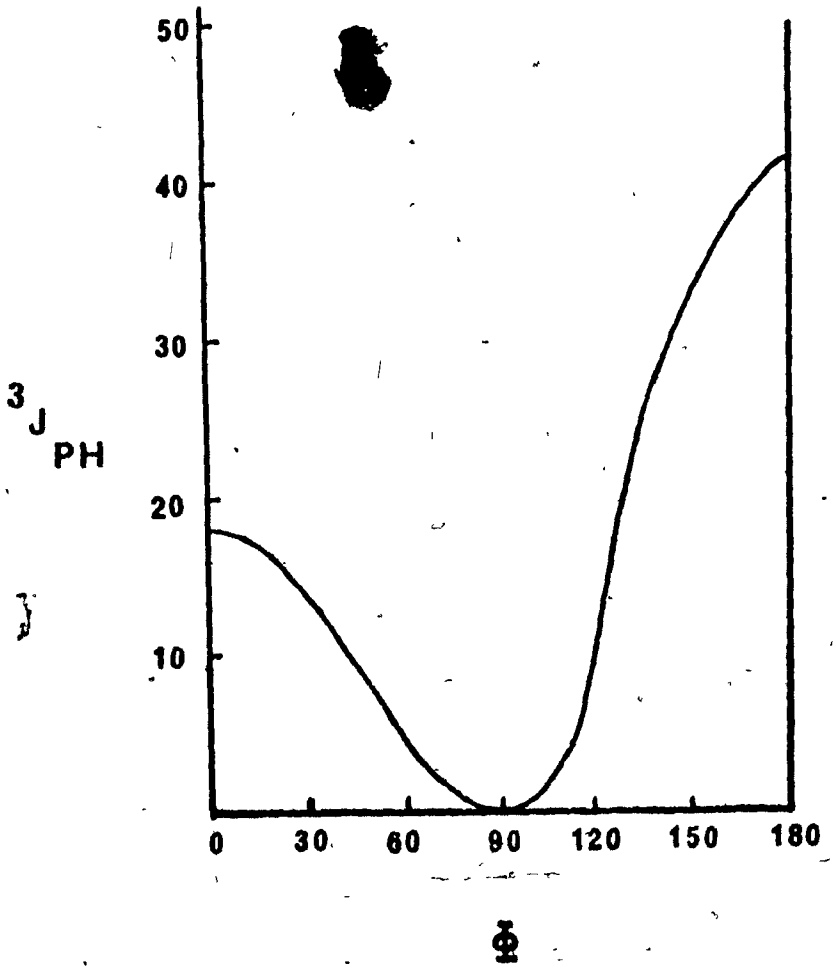


Fig. 35 - Curve representing the variation of vicinal P,H coupling as a function of dihedral angle.

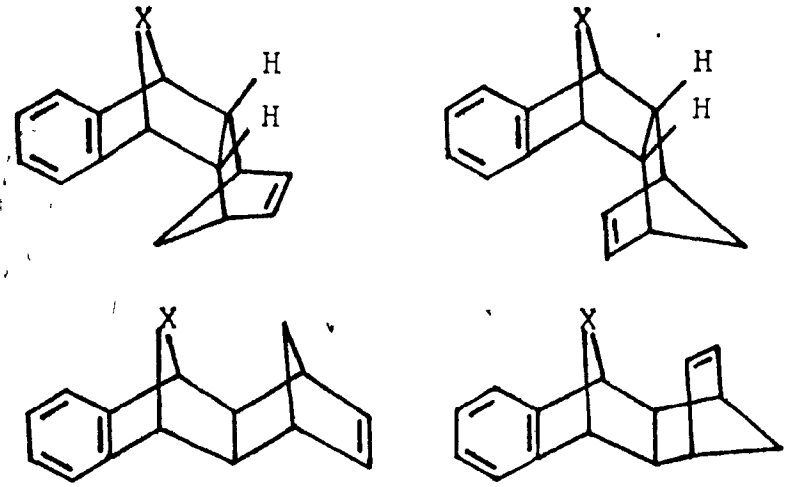
With 2,5-Norbornadiene

It will be of considerable interest to investigate the Diels-Alder reaction of 2-phenylisophosphindole 2-oxide and 2,5-norbonadiene.

In general, the principles which seem to govern the stereochemistry of Diels-Alder addition may be summarized as follows: -

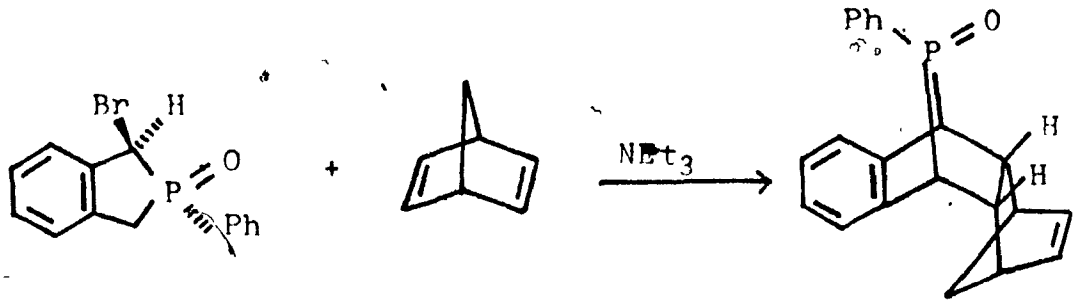
1. The diene must be oriented in the "cisoid" conformation before addition.
2. With respect to the dienophile, the addition is always cis. No exceptions are known. Thus the addition is stereospecific.
3. Substituents in the dienophile prefer to lie above the unsaturated system of the diene, leading to endo addition.
4. The diene and dienophile tend to approach each other from the less hindered side of each.

One can ask the question whether 2-phenylisophosphindole 2-oxide would show a similar stereochemistry in its Diels-Alder reaction as a diene. The cycloaddition with norbornadiene is particularly interesting because an additional element of stereochemistry is introduced, the syn- and anti- orientation of the methylene group of the norbornadiene moiety. Thus in principle, eight products could be obtained.



X = Ph–P(=O)– ; –(O=)P–Ph

It was found that on treatment of r-1-bromo-t-2-phenylisophosphindoline 2-oxide (142) with excess triethylamine in the presence of excess 2,5-norbornadiene in refluxing benzene for 48 hours, there was obtained the adduct 160 in 25% yield (Eq. 79). In addition, r-1-bromo-c-2-phenylisophosphindoline 2-oxide (10% yield), the dimer of 2-phenylisophosphindole 2-oxide (20% yield) and the starting material (30%) were isolated. The adduct was assigned to the structure 160 on the basis of its spectroscopic data and elemental analysis.



(79)

(142) (160)

The reaction is therefore stereospecific and is in agreement with the stereochemistry expected from the other Diels-Alder reactions.

The infrared spectrum of 2-phenylisophosphindole 2-oxide-norbornadiene adduct (160) (fig. 23) shows a strong characteristic P=O stretching at 1200 cm^{-1} and strong phenyl bands at 1450 cm^{-1} and 700 - 800 cm^{-1}.

The 220 MHz n.m.r. spectrum of 160 (fig. 28) exhibits a 9-H multiplet at 7.2 δ for the aromatic protons, a 2-H singlet* at 6.2 δ for the olefinic protons, a 2-H doublet at 3.7 δ for the methine protons adjacent to P=O (J_{P-CH} = 10 Hz), a 2-H singlet* at 3.1 δ for the allylic methine protons, a 2-H singlet* at 2.6 δ for the methine protons at the ring junction and two 1-H doublets at 0.8 δ and -0.3 δ for the two nonequivalent bridgehead methylene protons (J_{AB} = 10 Hz). A J_{AB} value of 9 Hz has been observed for dichloronorbornadiene[157].

The endo stereochemistry of the adduct is assigned on the basis of the vicinal P-C-C-H coupling ($^3J_{PCCH}$ = 0 Hz). It was observed by Benezra[156] that J_{PCCH} is a function of the dihedral angle in agreement with Karplus relationship. Molecular model shows that for the exo adduct the dihedral angle of P-C-C-H would be close to 180° and therefore a $^3J_{PCCH}$ of 40 Hz would be observed.

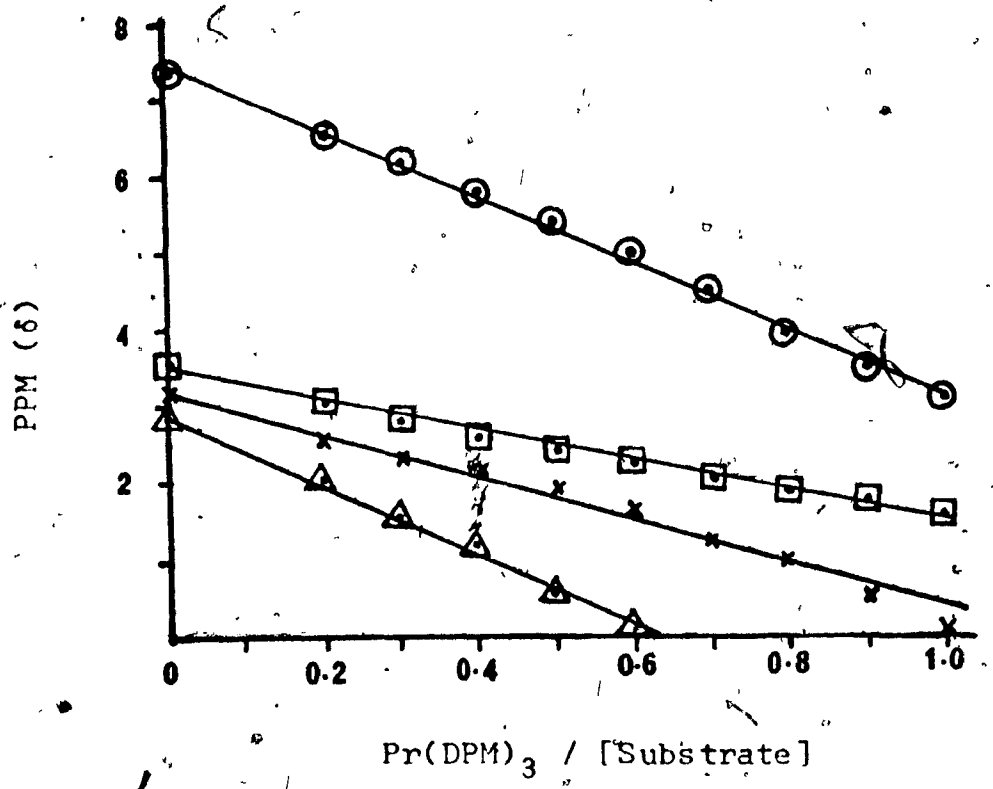
---

* The 100 MHz n.m.r. spectrum shows a multiplet.

The assignment of the orientation of the methylene bridge is based on two factors. The rather large difference in chemical shifts of the two protons indicates that one of the proton must be strongly shielded (-0.3 δ) by the benzene ring. Also the absence of vicinal H-C-C-H coupling between the ring junction protons and the bridgehead protons shows that they are 90° with respect to each other. From inspection of molecular models, this is more likely for the structure proposed.

It is more difficult to deduce the stereochemistry at phosphorus. Normally, in the Diels-Alder reaction, the more bulky group is away from the approaching diene. In the dimerization of 1-ethoxyphosphole 1-oxide[22], the structure of the dimer 22 has been determined by X-ray[23] and found to be with the more bulky ethoxy group away (Eq. 7).

In order to confirm the stereochemistry of the adduct 160, the shift reagent tris(dipivalo-methano-praseodymium (III) [$Pr(DPM)_3$] was added in varying amounts to a $CDCl_3$ solution of 160. A plot of chemical shift vs. [$Pr(DPM)_3$]/[Substrate] ratio for various peaks in the n.m.r. spectrum of 160 in $CDCl_3$ measured at 60 MHz, is shown in fig. 36. It was observed that the shift was in the decreasing order of phenyl ring protons attached to P=O > methine protons at the ring junction > allylic methine protons > methine protons adjacent to P=O. Using the assumption that the multiplets corresponding to protons closest to the complexed Pr atom should display the greatest slope[158,159] in a plot, we can conclude that the P=O group is on the side of the ring junction whereas the phenyl group is away from it, as shown in the structure 160.



⊙ - Aromatic protons

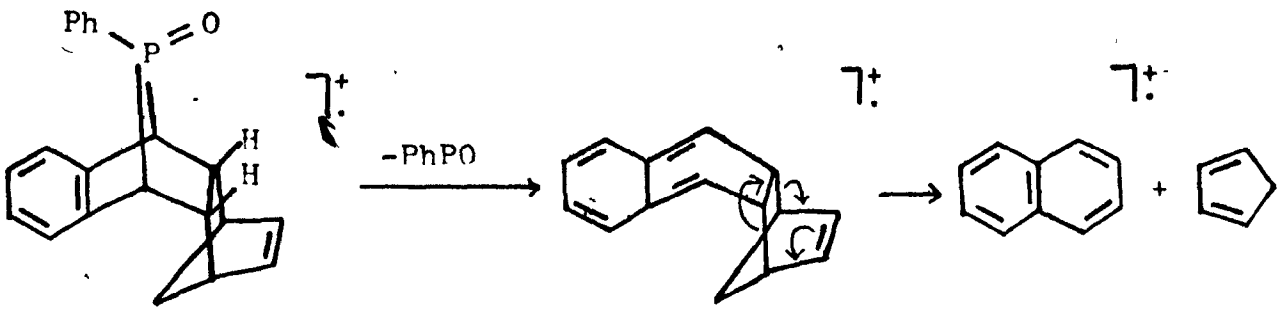
⊡ - Methine protons adjacent to P=O

× - Allylic methine protons

△ - Methine protons at the ring junction

Fig. 36 - A plot of Chemical Shift vs $Pr(DPM)_3$ / [Substrate]

The prominent peaks in the mass spectrum of 2-phenylisophosphindole 2-oxide-norbonadiene adduct (160) (fig. 33) are at $m/_e$ 194 and $m/_e$ 128, arising from the successive loss of PhPO and cyclopentadiene from the molecular ion ($m/_e$ 318). The other peaks are very weak compared to the peak at $m/_e$ 128. The fragmentation pattern can be illustrated as follows: -



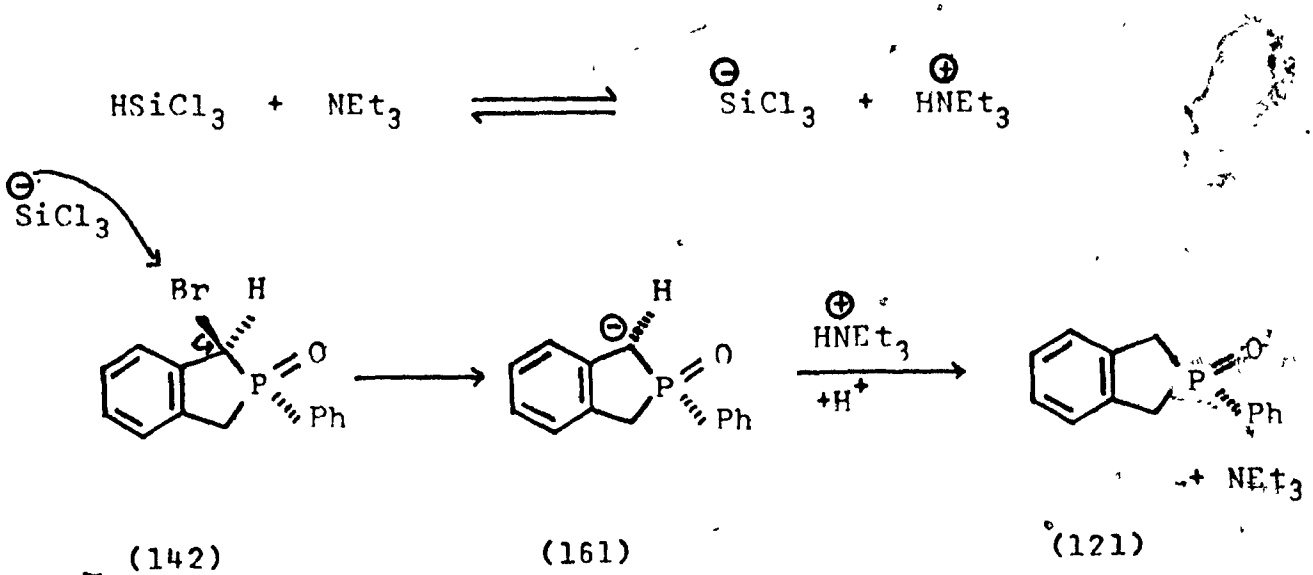
$m/_e$ 318 $m/_e$ 194 $m/_e$ 128

Attempted Generation of 2-Phenylisophosphindole

The ready availability of 2-phenylisophosphindoline 2-oxide has led us to investigate the isophosphindole system. However, 2-phenylisophosphindole 2-oxide (152) dimerizes too rapidly to allow its isolation. Thus, reduction reaction of 152 to form 2-phenylisophosphindole cannot be carried out. On the other hand, one may expect that simultaneous dehydrobromination and reduction of the precursor lead to the expected product. Trichlorosilane-triethylamine system seems to be appropriate for this purpose, so that triethylamine may serve as the dehydrobrominating reagent as well as a catalyst[160] for the reduction reaction with trichlorosilane.

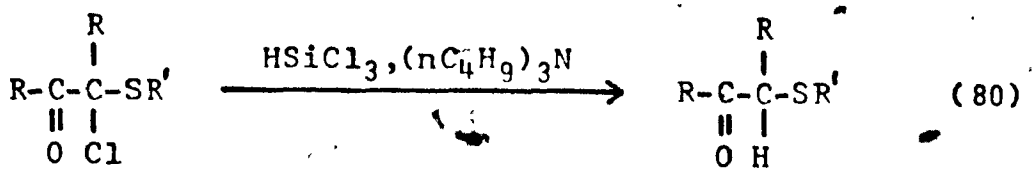
Reduction of r-1-Bromo-t-2-phenylisophosphindoline 2-Oxide with Trichlorosilane-Triethylamine

r-1-Bromo-t-2-phenylisophosphindoline 2-oxide was reduced with excess trichlorosilane in the presence of excess triethylamine. The reaction was carried out in refluxing benzene for 36 hours. The reaction mixture, after working up, was separated by preparative thin layer chromatography to afford 41% yield of a compound, the spectroscopic properties of which were in agreement with 2-phenylisophosphindoline 2-oxide (121). Thus, it is likely that in this reaction, the reduction of -C-Br, rather than P=O has taken place. The formation of the product 121 may be postulated as to proceed by way of the carbanion ion 161 as follows: -



(142) (161) (121)

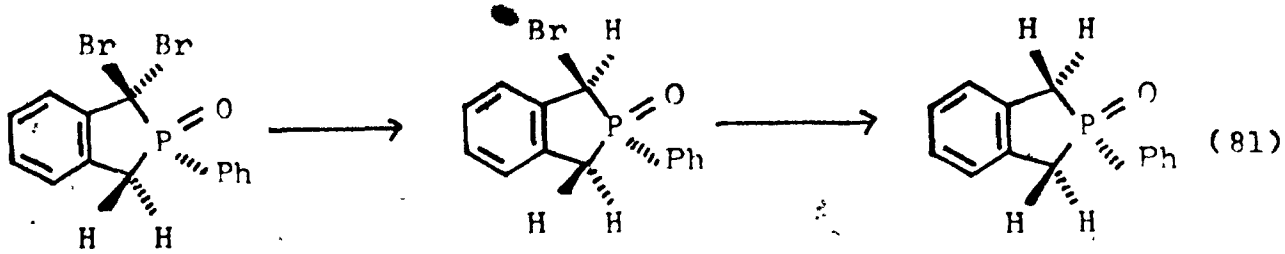
This reaction is not surprising, in view of the report[161] on a similar kind of reduction in carbonyl compounds (Eq. 80).



(80)

The reduction reaction of r-1-bromo-t-2-phenylisophosphindoline 2-oxide (142), where the -Br is substituted at the α-position of the P=O group should be contrasted with those of dibromophospholanes[21,23,27] 24 (Eq. 9), where -Br substitution is at the β-position.

The reduction of 1,1-dibromo-2-phenylisophosphindoline 2-oxide (143) with trichlorosilane-triethylamine system also led to the isolation of 2-phenylisophosphindoline 2-oxide (121) (Eq. 81). It is likely that the dibromo compound was reduced first to the monobromo compound which was further reduced to 2-phenylisophosphindoline 2-oxide.



(81)

(143) (142) (121)

2-Bromo-2-phenylisophosphindolinium Bromide

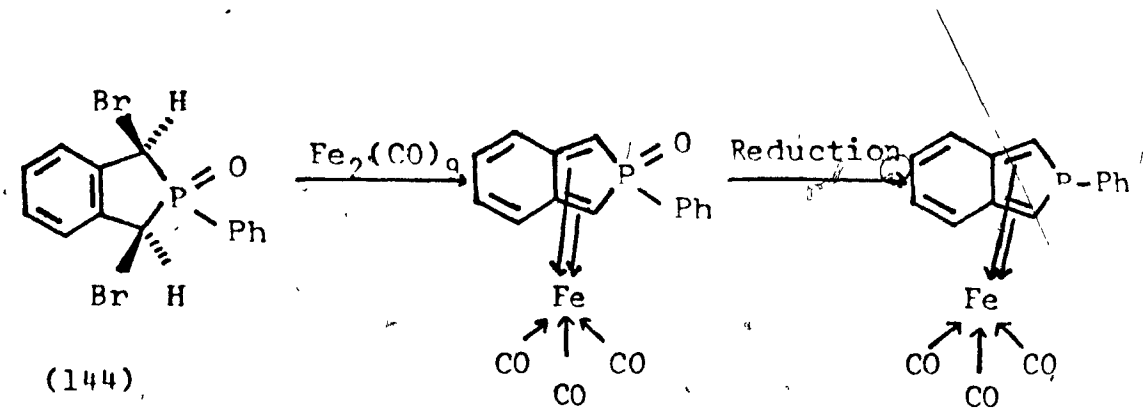
It has been mentioned that if 2-bromo-2-phenylisophosphindolinium bromide (149) can be synthesized, dehydrobromination

of this may lead to 2-phenylisophosphindole. The reduction of 2-phenylisophosphindoline 2-oxide to the corresponding phosphine, followed by bromine addition seems to be a reasonable method for the preparation of 149.

Thus, the reduction of 2-phenylisophosphindoline 2-oxide (121) was carried out with an excess of trichlorosilane, under nitrogen in refluxing benzene for 36 hours. After the hydrolysis of excess silane, the corresponding phosphine, without isolation was treated with bromine and the reaction mixture was stirred overnight. The yellow solid was isolated, the mass spectrum of which showed a peak at $m/_e$ 228 and at $m/_e$ 158, 160, 162 in 1:2:1 intensity ratio. It is likely that 149 was formed and it decomposed to bromine and 2-phenylisophosphindoline which was oxidised by air to the phosphine oxide. The peaks at $m/_e$ 158, 160, 162 is due to molecular bromine and the peak at $m/_e$ 228 may correspond to 2-phenylisophosphindoline 2-oxide. Thus, it is likely that either 149 or 2-phenylisophosphindoline 2-oxide-bromine complex was formed. However, the yield was very low.

Attempted Reaction of r-1-c-3-Dibromo-t-2-phenylisophosphindoline 2-Oxide with Ironnonacarbonyl

The reports[162,163] on the properties of ironnonacarbonyl as dehalogenating and complexing reagent, led us to investigate the use of this reagent, in achieving our aim, as in the following proposed scheme.



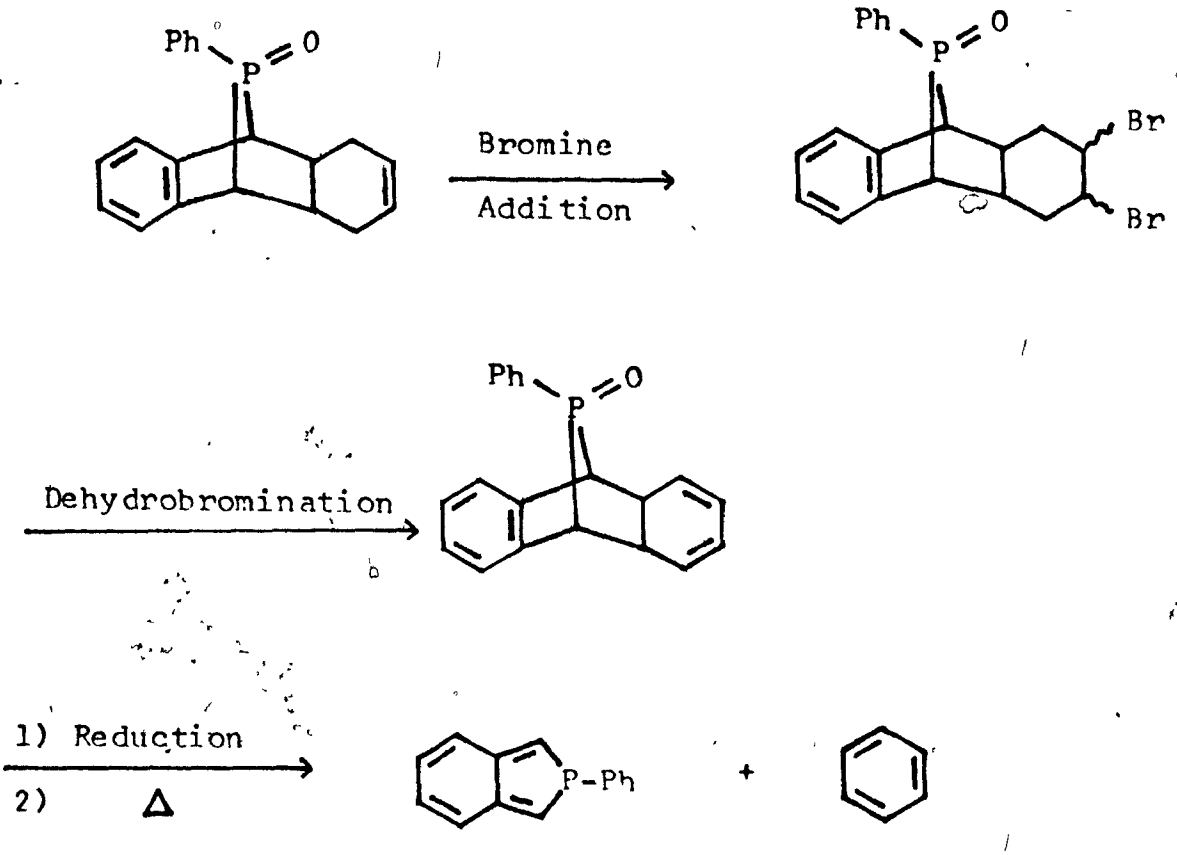
(144)

Thus, r-1,c-3-dibromo-t-2-phenylisophosphindoline 2-oxide (144) was treated with excess ironnonacarbonyl in benzene at room temperature for 15 hours. After filtration of excess ironnonacarbonyl and removal of solvent, there was obtained a residue which showed two bands at 2100 cm^{-1} and 2040 cm^{-1} in its i.r. spectrum. This was different from that of the starting material ironnonacarbonyl[164], which exhibited three bands at 2080 cm^{-1}, 2034 cm^{-1} and 1828 cm^{-1}. The n.m.r. spectrum was also different from that of the starting material and it showed two multiplets at 7.5 δ and 2.9 δ respectively. However, the mass spectrum showed only the starting material. Hence, the product could not be positively identified.

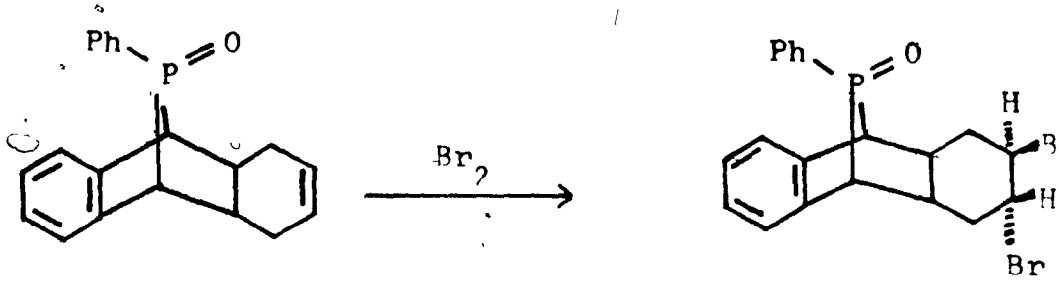
Bromination of 2-Phenylisophosphindole 2-Oxide-1,4-Cyclohexadiene adduct

Isoindole (5)[114] and isobenzofuran (109)[112,115] have been prepared by Retro-Diels-Alder reaction (Eq. 43 and 44).

It is felt that isophosphindole may also be synthesized in an analogous manner by the following proposed scheme.



Thus, 2-phenylisophosphindole 2-oxide-1,4-cyclohexadiene adduct was brominated at room temperature in chloroform for 20 hours. After removal of excess bromine and solvent, there was obtained 85% yield of a new compound as a light yellow crystal. It was assigned to the structure 162 (Eq. 82) on the basis of its spectroscopic properties.



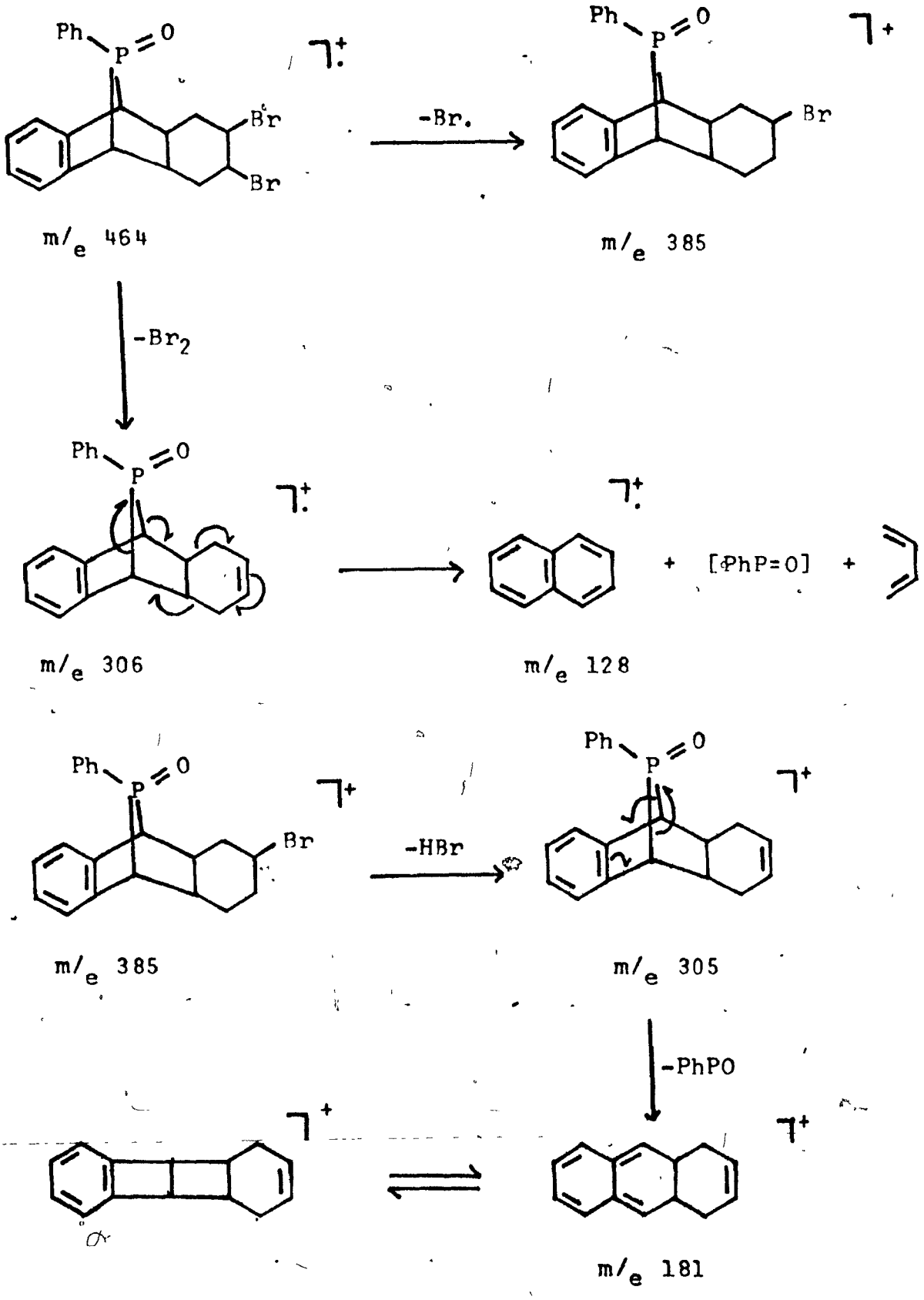
(159) (162) (82)

The infrared spectrum of dibromo compound 162 shows a strong P=O stretching at 1210 cm^{-1} and strong phenyl bands at 1450 cm^{-1}, 1100 cm^{-1} and 700 - 800 cm^{-1}.

The 220 MHz spectrum of 162 exhibits a 9-H multiplet at 7.2 δ for the aromatic proton, two multiplets at 4.5 δ and 4.3 δ for the two methine protons attached to -Br, a 2-H multiplet at 3.6 δ for the methine protons adjacent to P=O group, a 2-H multiplet at 3.5 δ for the methine protons at the ring junction, a 2-H multiplet at 2.0 δ for the equatorial methylene protons and a 2-H multiplet at 1.3 δ for the axial methylene protons.

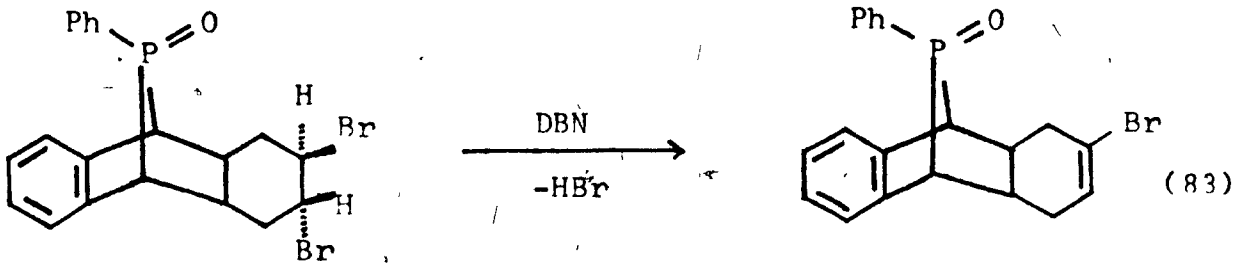
The mass spectrum of 162 features P($m/_e$ 464), P+2($m/_e$ 466) and P+4($m/_e$ 468) in 1:2:1 intensity ratio. Loss of Br radical from the molecular ion provides the peaks at $m/_e$ 385 and 387 in 1:1 intensity ratio. The molecular ion also loses Br_2 to give rise to a peak at $m/_e$ 306, which further eliminates CH_2=CH-CH=CH_2 and PhPO to provide the base peak at $m/_e$ 128. The other peaks are at $m/_e$ 305, and 181. The fragmentation pattern is illustrated in Scheme XXV.

Scheme XXV


Ph
P
O
Br
Br
-Br.
-Br2
-HBr
-PhPO
[ΦPhP=O]
m/e 464
m/e 385
m/e 306
m/e 128
m/e 385
m/e 305
m/e 181

Dehydrobromination of the Dibromo derivative of 2-Phenylisophosphindole 2-Oxide-1,4-Cyclohexadiene adduct

The dibromo compound 162 was dehydrobrominated with excess DBN in refluxing benzene for 20 hours. Thin layer chromatography of the reaction mixture, after working up, revealed that a new compound was formed. However, the mass and n.m.r. spectra showed that the new compound was likely to be 163 (Eq. 83), rather than the diene.



(83)

(162) (163)

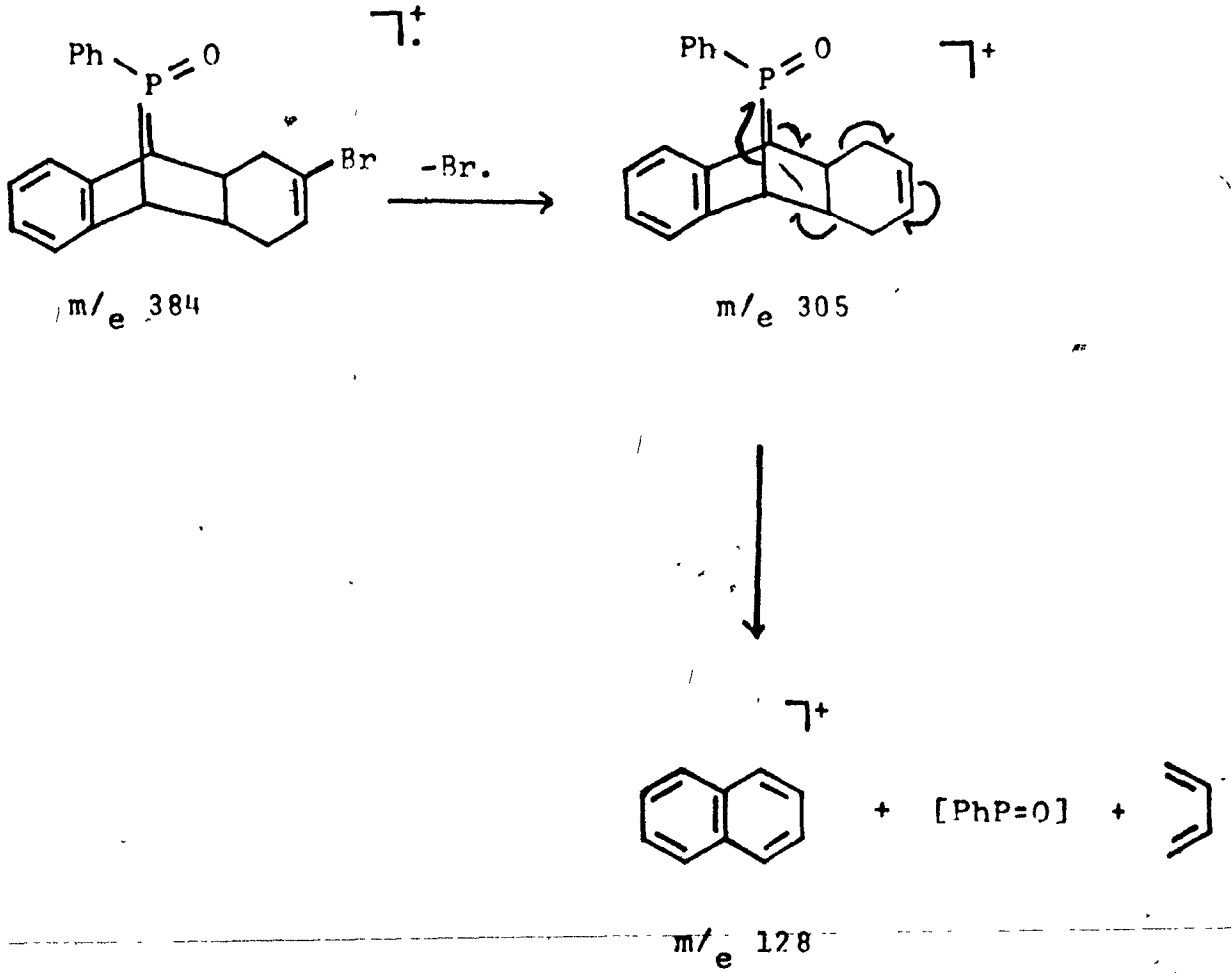
It is probable that because of the stereochemistry of the dibromo compound 162, the base attached preferentially at 2- or 3- position rather than at 1- and 4- positions.

The n.m.r. spectrum of 163 shows a 9-H multiplet at 7.3 δ for the aromatic protons, a 1-H multiplet at 5.9 δ for the olefinic proton, a 2-H multiplet at 3.5 δ for the methine protons adjacent to P=O, a 2-H multiplet at 3.2 δ for the methine protons at the ring junction, a 2-H multiplet at 2.5 δ for the equatorial

allylic protons, and a 2-H multiplet at 1.3 δ for the axial allylic protons.

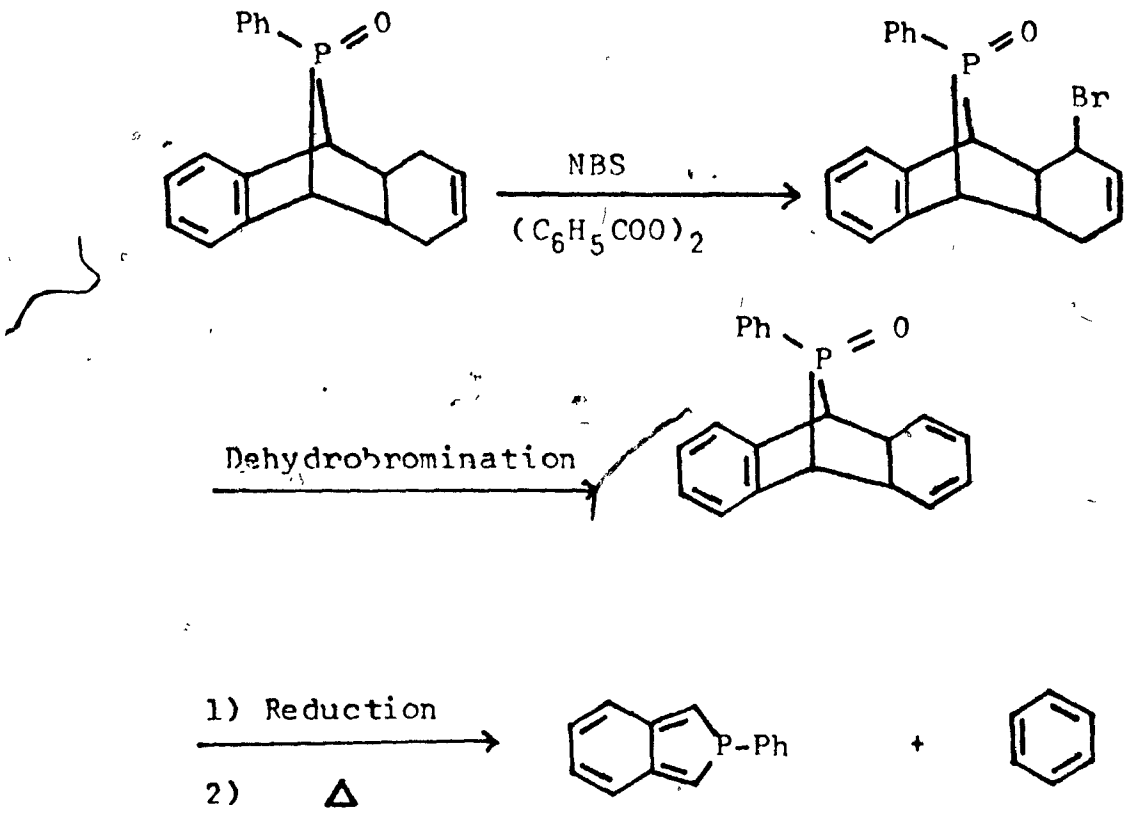
The mass spectrum of 163 exhibits P($m/_e$ 384) and P+2($m/_e$ 386) in 1:1 intensity ratio. Loss of -Br radical from the molecular ion provides the peak at $m/_e$ 305. The base peak at $m/_e$ 128 may arise from the loss of PhPO and C_4H_5 moieties from the peak at $m/_e$ 305. The fragmentation pattern is depicted in Scheme XXVI.

Scheme XXVI



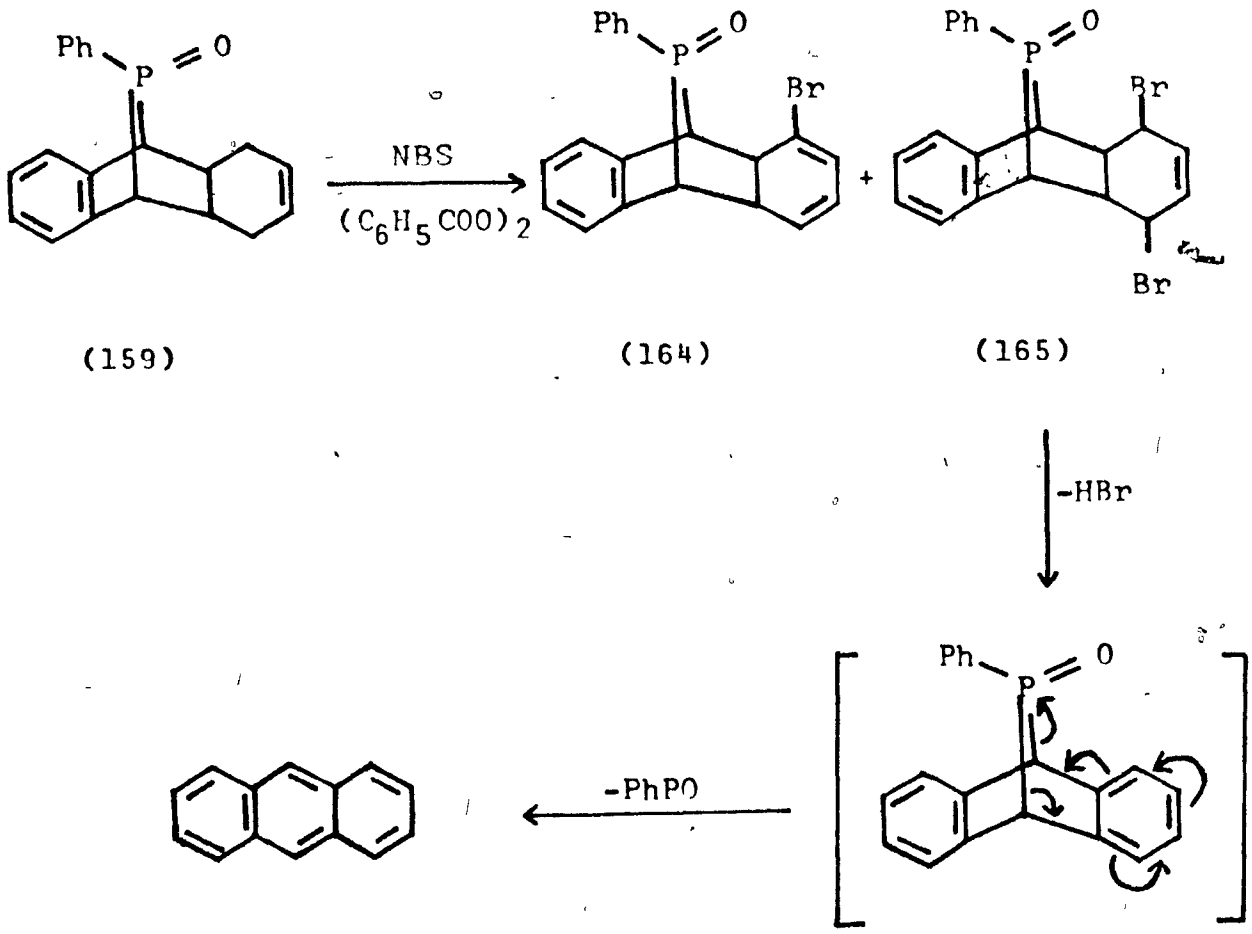
Free Radical Bromination of 2-Phenylisophosphindole 2-Oxide-1,4-Cyclohexadiene adduct

Since the attempted dehydrobromination of dibromo compound 162 was unsuccessful, we considered an alternative route to achieve the Retro-Diels-Alder reaction.



Thus, 2-phenylisophosphindole 2-oxide-1,4-cyclohexadiene adduct was brominated with equal molar quantity of recrystallized N-bromosuccinimide[93], in the presence of a catalytic amount of benzoyl peroxide, in refluxing benzene for 48 hours. The residue,

after working up was separated by thin layer chromatography to give anthracene (40% yield) as major product. It was identical in all respects with authentic sample. Also isolated as minor products were 164, 165 which were identified by mass spectrometry. The formation of anthracene can be derived by the following route.



The present approach to the diene is therefore not a profitable one. It is interesting to note however, that 2-phenyl-isophosphindole 2-oxide may serve as a useful synthetic intermediate to yield anthracene and its derivatives.

CHAPTER 3

EXPERIMENTAL SECTION

1) All melting points are uncorrected.

2) Nuclear magnetic resonance (n.m.r.) spectrum were recorded on Varian T-60 and Varian HA-100 spectrometers. The 220 MHz spectra were run by the 220 MHz laboratory, Sheridan Park, Ontario. Unless otherwise mentioned, all the n.m.r. spectra were taken in deuteriochloroform ($CDCl_3$). Tetramethylsilane (TMS) was generally used as either an external or internal standard. All proton spectra are reported in δ units relative to tetramethylsilane (TMS). Abbreviations used in reporting of n.m.r. spectra are: s, singlet; d, doublet; t, triplet; q, quintet; m, multiplet.

3) Infrared (i.r.) spectra were recorded on a Perkin-Elmer Model 257 spectrophotometer and a Unicam SP 1000 spectrophotometer with polystyrene calibration. Solid samples were taken as KBr pellets, and liquid samples either as thin film (neat) or in chloroform or carbontetrachloride.

4) Mass spectra were recorded on AEI MS-902 mass spectrometer at a temperature of 100-150°. The operating conditions were a 70 ev electron energy, resolution of 1000 and 8 KV accelerating voltage.

5) Ultraviolet (u.v.) spectra were recorded on an Unicam SP

800 A UV spectrophotometer.

6) Organic Microanalyses were performed by Scandanavian Microanalytical Laboratories, Herlev, Denmark and Organic Microanalyses (Dr. C. Daessle), Montreal, Canada.

7) Benzene and toluene were dried and distilled over sodium wire.

8) Thin layer chromatograms were run on silica gel sheets with fluorescent indicator made by Eastman Organic Chemicals.

9) Preparative thin layer chromatography was performed on silica gel (HF 254 + 366 according to Stahl, made by E.M. Damsterdt Company, Germany) plates and were developed in ethyl acetate unless otherwise stated.

10) Column chromatography was performed on silica gel (mesh size 100-200), Grade 923, made by Davison Chemicals.

E,E-1,4-Diacetoxybutadiene

This compound was prepared by the method of Hill and Carlson[67]. It had m.p. 103-104° (Lit.[67] m.p. 103-104°).

1,1,1-Trichlorophospholene

The above compound was prepared according to the method of Hasserodt, Hunger and Korte[83] as follows:

A mixture of 13.5g (0.25 mole) of butadiene and 34.4g (0.25 mole) of phosphorus trichloride were kept in the pressure bottle together with 0.4g of copper stearate as polymerization inhibitor, at room temperature for 45 days.

The bottle was opened in a glove bag and the unreacted phosphorus trichloride was removed by repeated decantation with dried petroleum ether (b.p. 30-60°). The yellowish brown product was then dried *in vacuo*. Yield: 28g, (58%).

1-Ethoxy-2-phospholene 1-Oxide

This compound was prepared by the method of Hasserodt, Hunger and Korte[83]. To a suspension of 24g (0.125 mole) of 1,1,1-trichlorophospholene in 150 ml of dry methylene chloride at -10° (dry ice/acetone bath) was added slowly 17.2 g (0.375 mole) of absolute ethanol. After the addition, the reaction mixture was warmed to room temperature and stirred for 2 hrs. The solvent was evaporated and the residue was dried *in vacuo* for 1 hr. to

give a dark brown oil, which on vacuum distillation gave 5.4 g (30%) of 1-ethoxy-2-phospholene 1-oxide, b.p. 110°/0.75 mm; (Lit.[83] b.p. 75°-78°/0.1 mm).

Reaction of E,E-1,4-diacetoxybutadiene with 1-Ethoxy-2-phospholene 1-Oxide

A mixture of 1 g (0.006 mole) of E,E-1,4-diacetoxybutadiene, 0.86 g (0.006 mole) of 1-ethoxy-2-phospholene 1-oxide and a pinch of hydroquinone was heated in a sealed tube at 135° for 7 days. The sealed tube was opened and the dark residue was dissolved in 20 ml of 95% ethanol. A quantity of 0.6 g of sodium hydroxide was added and the reaction mixture was refluxed for 12 hrs. The flask was cooled in an ice-bath and excess sodium hydroxide was neutralized with 5% hydrochloric acid solution. The precipitate formed was filtered and the filtrate was extracted with chloroform. The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. Column chromatography of the reaction mixture on silica gel, eluting with ethyl acetate afforded 0.16 g. (25% based on the reacted 1-ethoxy-2-phospholene 1-oxide) of 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide as liquid. A quantity of 0.34 g (40%) of 1-ethoxy-2-phospholene 1-oxide was recovered.

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.5 (m, 4H, Ar-H); 4.2 (q, 2H, $-O-CH_2-$); 3.1 (m, 2H, $ArCH_2$); 2.2 (m, 2H, $-CH_2$); 1.3 (t, 3H, $-CH_3$).

i.r. spectrum ν_{max} ($CHCl_3$): 1260 cm^{-1} (P=O); 1600 cm^{-1} (C=C).

mass spectrum: $m/_e$ 196 (79.5%); $m/_e$ 168 (100%); $m/_e$ 167 (74%); $m/_e$ 151 (50%); $m/_e$ 104 (28%).

Anal. Calcd. for $C_{10}H_{13}PO_2$: C, 61.22%; H, 6.68%; P, 15.79%;
Found: C, 61.07%; H, 6.81%; P, 15.85%;

Bromination of 1-Ethoxy-2,3-dihydrobenzo[b]phosphole 1-Oxide

To a solution of 0.1 g (0.5 m mole) of 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide in 20 ml of dry benzene was added 0.09 g (0.5 m mole) of N-bromosuccinimide (recrystallized from water as described by Dauben and McCoy[93]) and a few grains of benzoyl peroxide. The reaction mixture was refluxed for 12 hrs. and cooled. Benzene was evaporated and after the addition of anhydrous ether, the insoluble succinimide was filtered. The solvent was then evaporated to give a dark residue, which on separation by preparative thin layer chromatography afforded 0.04 g (30%) of 1-ethoxy-3-bromo-2,3-dihydrobenzo[b]phosphole 1-oxide as a colourless oil.

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.6 (m, 4-H, Ar-H); 5.6 (m, 1-H, ArCH-); 2.7 (m, 2-H, $-CH_2$); 4.3 (m, 2-H, $-CH_2-O-$); 1.3 (t, 3-H, $-CH_3$).

i.r. spectrum $\nu_{max.}$ ($CHCl_3$): 1270 cm^{-1} (P=O); 1601 cm^{-1} (C=C).

mass spectrum: $m/_e$ 276 (3.3%); $m/_e$ 274 (3.3%); $m/_e$ 195 (40%); $m/_e$ 194 (26.7%); $m/_e$ 167 (33.3%); $m/_e$ 166 (66.6%); $m/_e$ 165 (10.6%); $m/_e$ 149 (100%); $m/_e$ 102 (13.4%).

1-Ethoxybenzo[b]phosphole 1-oxide

To a solution of 0.14 g (0.5 m mole) of 1-ethoxy-3-bromo-2,3-dihydrobenzo[b]phosphole 1-oxide in 15 ml of dry benzene was added 0.2 g (2 m moles) of triethylamine and the reaction mixture was stirred overnight. The triethylaminehydrobromide salt was filtered and the solvent was removed from the filtrate. The residue was separated by preparative thin layer chromatography to give 0.043 g (45%) of 1-ethoxybenzo[b]phosphole 1-oxide as an oil.

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.4 (m, 4-H, Ar-H); 6.6 (6 lines, 2-H, vinylic protons); 4.2 (q, 2-H, $-CH_2-O-$); 1.3 (t, 3-H, $-CH_3$).

i.r. spectrum ν_{max} ($CHCl_3$): 1300 cm^{-1} (P=O); 1601 cm^{-1} and 1590 cm^{-1} (C=C).

mass spectrum: $m/_e$ 194 (66.8%); $m/_e$ 166 (100%); $m/_e$ 165 (16.7%); $m/_e$ 149 (77.8%); $m/_e$ 102 (33.3%).

Anal. Calcd. for $C_{10}H_{11}PO_2$: C, 61.86%; H, 5.71%;
Found: C, 62.02%; H, 5.81%;

Attempted Reduction of 1-Ethoxy-2,3-dihydrobenzo[b]phosphole 1-Oxide with Trichlorosilane

To a solution of 0.05 g (0.25 m mole) of 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide in 10 ml of dry benzene was added a solution of 0.1 g (0.75 m mole) of trichlorosilane in 10 ml of

dry benzene, under nitrogen. The reaction mixture was refluxed for 10 hrs., cooled in an ice-bath and hydrolysed with 30% NaOH solution. The organic layer was washed twice with water, dried over anhydrous $MgSO_4$, filtered and the solvent removed. Starting material was recovered almost quantitatively. Thin layer chromatography and i.r. spectrum of the residue revealed that no reaction had taken place. There was no evidence of the P-H stretching band in the i.r. spectrum.

Attempted Reduction of 1-Ethoxy-2,3-dihydrobenzo[b]phosphole 1-Oxide with Phenylsilane

A solution of 0.05 g (0.5 m mole) of phenylsilane in 10 ml of dry toluene was added to a solution of 0.05 g (0.25 m mole) of 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide in 10 ml of toluene, under nitrogen. The reaction mixture was refluxed for 20 hrs. and the solvent removed. Thin layer chromatography and i.r. spectrum of the residue showed that no reaction had occurred.

Attempted Reduction of 1-Ethoxy-2,3-dihydrobenzo[b]phosphole 1-Oxide with Diphenylsilane

To a solution of 0.05 g (0.25 m mole) of 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide in 10 ml of dry benzene was added a solution of 0.09 g (0.5 m mole) of diphenylsilane in 10 ml of dry benzene, under nitrogen. The solvent was removed after

refluxing for 12 hrs. Neither thin layer chromatography nor i.r. spectrum of the residue showed the formation of any new product.

Attempted Reduction of 1-Ethoxy-2,3-dihydrobenzo[b]phosphole 1-Oxide with Lithium Aluminium Hydride

To a suspension of 0.004 g (1 m mole) of lithium aluminium hydride in 10 ml of sodium dried ether was added a solution of 0.05 g (0.25 m mole) of 1-ethoxy-2,3-dihydrobenzo[b]phosphole 1-oxide in 10 ml of sodium dried ether, under nitrogen. After the addition, the reaction mixture was refluxed for 24 hrs. and cooled in an ice-bath. Excess lithium aluminium hydride was destroyed by adding ethyl acetate, the precipitate formed was filtered and the solvent removed from the filtrate. Thin layer chromatography, i.r. and n.m.r. spectra of the residue showed only the starting material. The starting material was recovered almost quantitatively.

Ethyl (2'-bromomethyl-benzyl) phenylphosphinate

A quantity of 3.96 g (0.02 mole) diethyl phenylphosphonite was added dropwise to 5.26 g (0.02 mole) of o-xylylene dibromide at 90°. Ethyl bromide as formed was distilled from the reaction mixture and collected in a trap, cooled in a dry-ice bath. After the addition, the reaction mixture was heated at 90° for another 2 hrs. Column chromatography of the reaction mixture

on silica gel, eluting with ethyl acetate gave 3.2 g (45%) of ethyl (2'-bromomethyl-benzyl)phenylphosphinate as white crystals. m.p. 93-95° (hexane/chloroform).

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.4 (m, 9-H, Ar-H); 4.5 (s, 2-H, $ArCH_2$-); 3.8 (q, 2-H, $-CH_2$-O); 3.3-3.7 (2 overlapped d, 2-H, J_{P-CH} = 20Hz and 18Hz; $ArCH_2$-PO); 1.2 (t, 3-H, $-CH_3$).

i.r. spectrum ν_{max} (KBr): 1220 cm^{-1} (P=O); 1040 cm^{-1} and 1160 cm^{-1} (P-O-C_2H_5); 1440 cm^{-1}, 700-800 cm^{-1} (Ph).

mass spectrum: $m/_e$ 354 (27.8%); $m/_e$ 352 (27.8%); $m/_e$ 273 (44.5%); $m/_e$ 245 (11%); $m/_e$ 244 (16.5%); $m/_e$ 181 (44.5%); $m/_e$ 179 (11%); $m/_e$ 104 (100%).

Anal. Calcd. for $C_{16}H_{18}PO_2Br$: C, 54.42%; H, 5.14%; Br, 22.62%;
Found: C, 54.28%; H, 5.25%; Br, 22.98%;

Reaction of Ethyl (2'-bromomethyl-benzyl)phenylphosphinate with Vitride Reagent[126]

To a stirred solution of 1.76 g (5 m mole) of ethyl (2'-bromomethyl-benzyl)phenylphosphinate in 200 ml of dry benzene at room temperature, under nitrogen, was added dropwise a solution of 1.21 g (6 m mole) of Vitride reagent in 200 ml of dry benzene. After the addition, the reaction mixture was refluxed for 48 hrs. The solution became cloudy with the formation of sodium bromide after several minutes. The reaction mixture was hydrolysed with 8 ml of water and filtered. The filtrate was dried over

anhydrous $MgSO_4$, filtered and the solvent removed. The residue, when chromatographed on silica gel, eluting with ethyl acetate afforded 0.15 g (13%) of 2-phenylisophosphindoline 2-oxide as white crystals. m.p. 85-87°. Analytical sample was obtained by sublimation at $100°/_{12\ mm}$, m.p. 89-91° (after drying over P_2O_5 at $60°/_{0.1\ mm}$, Lit.[69] 98-100° for monohydrate)

n.m.r. spectrum (100 MHz) δ_{TMS} ($CDCl_3$): 7.5-8.0 (m, 5-H, -Ph-P); 7.4 (s, 4-H, Ar-H); 3.5-3.3 (Part of ABX, 4-H, $-CH_2$, J_{AB}=17, J_{AX}=16, J_{BX}=9 Hz).

i.r. spectrum ν_{max} (KBr): 1210 cm^{-1} (P=O); 1440 cm^{-1}, 1100 cm^{-1} and 700-800 cm^{-1} (Ph).

mass spectrum: $m/_e$ 228 (100%); $m/_e$ 104 (60%); $m/_e$ 103 (20%); $m/_e$ 78 (22.5%); $m/_e$ 77 (20%).

Anal. Calcd. for $C_{14}H_{13}PO.1/2H_2O$: C, 70.91%; H, 5.95%;
Found: C, 71.19%; H, 5.87%;

Diethyl Phenylphosphonate

Diethyl phenylphosphonate was prepared by the slightly modified method of Siddall, III and Prohaska[131].

To a well stirred mixture of 6.9 g (0.15 mole) of absolute ethanol and 12.6 g (0.125 mole) of triethylamine in 100 ml of dry benzene was added dropwise a solution of 9.8 g (0.05 mole) of phenyl phosphonicdichloride in 50 ml of dry benzene, while the flask was cooled in an ice-bath. The solution turned milky

during the addition. After the addition, the reaction mixture was stirred overnight at room temperature.

The triethylaminehydrochloride salt was filtered off and the filtrate was washed twice with water. The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent removed. Vacuum distillation of the crude mixture afforded 7.3 g (68%) of diethyl phenylphosphonate as colourless liquid. b.p. 100°/0.5mm (Lit.[131] b.p. 121-123°/2 mm).

Reaction of Diethyl phenylphosphonate with Vitride Reagent

To a well stirred solution of 6.42 g (0.03 mole) of diethyl phenylphosphonate in 250 ml of dry benzene at room temperature was added dropwise 15.15 g (0.075 mole) of Vitride reagent in 300 ml of dry benzene. The solution turned yellow during the addition. A solution of 7.89 g (0.03 mole) of o-xylylene dibromide in 250 ml of dry benzene was then added dropwise. During the addition the yellow colour discharged and the solution became cloudy with the formation of sodium bromide. After the addition, the reaction mixture was heated at 70° for 48 hrs. The mixture was cooled, hydrolysed with 15 ml of water and filtered. The filtrate was dried over anhydrous $MgSO_4$, filtered and the solvent was removed to give 8 g of residue of crude 2-phenylisophosphindoline 2-oxide as shown by n.m.r. Column chromatography of the residue on silica gel, eluting with ethyl acetate, afforded 1.03 g - 1.3 g (15%-20%) of the crystalline sample. m.p. 89-91°. The spectroscopic data of the product are identical in all respects

with 2-phenylisophosphindoline 2-oxide obtained by the previous experiment.

Reaction of Ethyl(2'-bromomethyl-benzyl)phenylphosphinate with Trichlorosilane

To a stirred solution of 0.35 g (1 m mole) of ethyl(2'-bromomethyl-benzyl)phenylphosphinate in 30 ml of dry benzene at room temperature, under nitrogen was added dropwise a solution of 0.41 g (3 m mole) of trichlorosilane in 10 ml of dry benzene. After the addition, the reaction mixture was refluxed for 48 hrs., then cooled, and hydrolysed with 30% NaOH solution. The silica was filtered and the filtrate was washed twice with water. The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was removed. Preparative thin layer chromatography of the residue gave 0.03 g (12%) of 2-phenylisophosphindoline 2-oxide as white crystals. m.p. 89-91°.

Reduction of 2-Phenylisophosphindoline 2-Oxide and Quaternization with Methyl Iodide

To a stirred solution of 0.23 g (1 m mole) of 2-phenylisophosphindoline 2-oxide in 20 ml of dry benzene was added dropwise a solution of 0.41 g (3 m mole) of trichlorosilane in 20 ml of dry benzene, under nitrogen. The reaction mixture was refluxed for 48 hrs., after the addition. After cooling and hydrolysis with 30% NaOH solution, the reaction mixture was filtered and

the filtrate was washed twice with water. The organic layer was dried over anhydrous $MgSO_4$ and filtered into a three-necked flask equipped with nitrogen inlet, a reflux condenser and a dropping funnel. A quantity of 0.57 g (4 m mole) of methyl iodide was added dropwise under nitrogen and the reaction mixture was stirred overnight at room temperature. The white solid (2-methyl-2-phenylisophosphindolinium iodide) was filtered and recrystallized from absolute ethanol. Yield - 0.09 g (25%) m.p. 205-207° (Lit.[68] m.p. 207-209°).

i.r. spectrum ν_{max} (KBr): 1320 cm^{-1} ($P-CH_3$), 1440 cm^{-1}, 1120 cm^{-1} and 700-800 cm^{-1} (Ph).

Diethyl(2'-bromomethyl)benzylphosphonate

To 2.63 g (0.01 mole) of o-xylylene dibromide at 90°, 1.7 g (0.01 mole) of freshly distilled triethyl phosphite was added dropwise. Ethyl bromide was distilled as formed from the reaction mixture and collected in a trap, cooled in a dry-ice bath. After the addition, the reaction mixture was heated at 90° for another 9 hrs. and cooled. It was chromatographed on silica gel, eluting with ethyl acetate to give 1.6 g (50%) of diethyl(2'-bromomethyl)-benzylphosphonate as yellow oil.

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.3 - 7.8 (m, 4-H, Ar-H); 4.9 (s, 2-H, $ArCH_2-$); 4.3 (q, 4-H, $-CH_2O-$); 3.5 (d, 2-H, $ArCH_2PO$, J_{P-CH} = 24 Hz); 1.4 (t, 6-H, $-CH_3$).

i.r. spectrum ν_{max} (Film): 1250 cm^{-1} (P=O); 1020 cm^{-1} and

1160 cm^{-1} (P-O-C_2H_5).

mass spectrum: $m/_e$ 322 (37.5%); $m/_e$ 320 (37.5%); $m/_e$ 241 (62.5%); $m/_e$ 213 (25%); $m/_e$ 212 (12.5%); $m/_e$ 185 (100%); $m/_e$ 104 (87.5%).

Anal. Calcd. for $C_{12}H_{18}PO_3Br$: C, 44.86%; H, 5.64%; Br, 24.84%;
Found: C, 44.34%; H, 5.83%; Br, 24.72%;

Thermal Cyclization of Diethyl(2'-brompmethyl)benzylphosphonate

When the above experiment was carried out at a temperature higher than 90°, diethyl(2'-bromomethyl)benzylphosphonate underwent thermal cyclization to give 2-ethoxy-3-oxa-1,2,3,4-tetrahydroisophosphinoline 2-oxide in 25% yield.

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.5 (m, 4-H, Ar-H); 5.5 (d, 2-H, $ArCH_2$-O, J_{P-CH} = 16 Hz); 4.4 (q, 2-H, $-CH_2$-O); 3.3 (d, 2-H, $ArCH_2$-, J_{P-CH} = 20 Hz); 1.4 (t, 3-H, $-CH_3$).

Reaction of Diethyl(2'-bromomethyl)benzylphosphonate with Magnesium

A suspension of 0.03 g (1 m mole) of magnesium powder (mesh size - 50) in 5 ml of dry benzene was stirred magnetically in a 25 ml three-necked flask, equipped with nitrogen inlet, a reflux condenser and a dropping funnel. A solution of 0.32 g (1 m mole) of diethyl(2'-bromomethyl)benzylphosphonate in 10 ml of dry benzene was added dropwise. A few crystal of iodine was added and the flask was warmed with a small flame to initiate the reaction. When the addition was complete, the reaction

mixture was refluxed for 24 hrs. The flask was cooled and the contents in the flask were poured onto the crushed ice containing 2 ml of 5% sulfuric acid solution. Saturated ammonium chloride solution was also added to hydrolyse the magnesium salt. The organic layer was separated and the aqueous layer was extracted with ether. The extracts were combined, dried over anhydrous $MgSO_4$, filtered and the solvent removed. The residue was separated by preparative thin layer chromatography to afford two compounds. They were identified as the hydrolysed product (R_f value = 0.47) and the coupled product (R_f value = 0.38) of the Grignard reagent of the starting material. 0.05 g (20% yield) of hydrolysed product and 0.07 g (30% yield) of coupled product were obtained.

Attempt of the same reaction on higher dilution also gave the same products.

Diethyl(2'-methyl)benzylphosphonate (Hydrolysed product)

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.4 (m, 4-H, Ar-H); 4.1 (q, 4-H, $-CH_2-O$); 3.3 (d, 2-H, $ArCH_2-$, J_{P-CH} = 22 Hz); 2.5 (s, 3-H, $ArCH_3$); 1.3 (t, 6-H, $-CH_3$).

mass spectrum: $m/_e$ 242 (75%); $m/_e$ 227 (8.3%); $m/_e$ 214 (25%); $m/_e$ 199 (8.3%); $m/_e$ 186 (50%); $m/_e$ 105 (100%); $m/_e$ 104 (80%).

1,2-di[o-(diethylphosphonato-methyl)phenyl]ethane (Coupled product)

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.4 (m, 8-H, Ar-H); 4.1 (q, 8-H,

$-CH_2-O$); 3.2 (d, 4-H, $ArCH_2PO-$, J_{P-CH} = 24 Hz); 3.1 (s, 4-H, $ArCH_2-$); 1.2 (t, 12-H, $-CH_3$).

mass spectrum: $m/_e$ 482 (100%); $m/_e$ 241 (16.6%); $m/_e$ 213 (8.3%); $m/_e$ 196 (16.6%); $m/_e$ 185 (50%); $m/_e$ 184 (16.6%); $m/_e$ 168 (8.3%); $m/_e$ 167 (8.3%); $m/_e$ 105 (16.6%); $m/_e$ 104 (83%).

Reaction of Diethyl(2'-bromomethyl)benzylphosphonate with Lithium

To a suspension of 0.04 g (6 m mole) of lithium powder in 30 ml of sodium dried ether under nitrogen, was added dropwise a solution of 0.32 g (1 m mole) of diethyl(2'-bromomethyl)benzylphosphonate in 35 ml of sodium dried ether. After the addition, the reaction mixture was stirred at room temperature for 12 hrs. Excess lithium and lithium bromide were filtered. The filtrate was concentrated by distilling off ether, under nitrogen and 75 ml of dry benzene was added. The reaction mixture was refluxed for 24 hrs., cooled, and poured onto crushed ice containing 5% sulfuric acid solution. Saturated ammonium chloride solution was also added. The organic layer was separated and the aqueous layer was extracted with benzene. The combined organic phase was then dried over anhydrous $MgSO_4$, filtered and the solvent removed. Separation of the reaction mixture by preparative thin layer chromatography afforded the same products in about the same yield as in the case of the reaction with magnesium.

Diisopropyl(2'-bromomethyl)benzylphosphonate

A quantity of 2.08 g (0.01 mole) of freshly distilled triisopropyl phosphite was added dropwise to 2.63 g (0.01 mole) of o-xylylene dibromide at 130°. Isopropyl bromide as formed was distilled from the reaction mixture and collected in a cold trap. After the addition, the reaction mixture was heated at 130° for another 2 hrs. Column chromatography of the reaction mixture on silica gel, eluting with ethyl acetate afforded 1.4 g (40%) of diisopropyl(2'-bromomethyl)benzylphosphonate as yellow oil.

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.2 - 7.7 (m, 4-H, Ar-H); 4.9 (s, 2-H, $ArCH_2$-); 4.7 (m, 2-H, -CH<); 3.4 (d, 2-H, $ArCH_2PO$, J_{P-CH} = 24 Hz); 1.3 (2d, 12-H, $-CH_3$).

i.r. spectrum ν_{max} (Film): 1260 cm^{-1} (P=O); 1020 cm^{-1} and 1150 cm^{-1} (P-O-C); 1390 cm^{-1}, 1395 cm^{-1} (isopropyl).

mass spectrum: $m/_e$ 350 (10%); $m/_e$ 348 (10%); $m/_e$ 308 (5%); $m/_e$ 306 (5%); $m/_e$ 269 (10%); $m/_e$ 264 (10%); $m/_e$ 247 (10%); $m/_e$ 185 (100%); $m/_e$ 184 (10%); $m/_e$ 104 (60%).

Anal. Calcd. for $C_{14}H_{22}PO_3Br$: C, 48.16%; H, 6.35%, Br, 22.89%;
Found: C, 48.09%; H, 6.40%; Br, 22.57%;

Thermal Cyclization of Diisopropyl(2'-bromomethyl)benzylphosphonate

When the above experiment was carried out at the temperature

higher than 130°, diisopropyl(2'-bromomethyl)benzylphosphonate underwent thermal cyclization to give 2-isopropoxy-3-oxa-1,2,3,-4-tetrahydroisophosphinoline 2-oxide in 30% yield.

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.4 (m, 4-H, Ar-H); 5.4 (d, 2-H, $ArCH_2$-O, J_{P-CH} = 16 Hz); 4.8 (m, 1-H, -CH<); 3.3 (d, 2-H, $ArCH_2$-, J_{P-CH} = 20 Hz); 1.4 (d, 6-H, CH_3).

Reaction of Diisopropyl(2'-bromomethyl)benzylphosphonate with Vitride Reagent

(1) To a stirred solution of 0.35 g (1 m mole) of diisopropyl-(2'-bromomethyl)benzylphosphonate in 35 ml of dry toluene at room temperature under nitrogen, was added dropwise a solution of 0.4 g (2 m mole) of Vitride reagent in 40 ml of dry toluene. The reaction mixture became cloudy with the formation of sodium bromide. After the addition, the reaction mixture was heated at 125° for 30 hrs. The mixture was cooled, hydrolysed with 0.6 ml of water and filtered. The filtrate was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The residue, on separation by thin layer chromatography afforded 0.09 g (33%) of 3,4-di[diisopropylphosphonato]-1,2,5,6-dibenzocyclooctadiene.

n.m.r. spectrum (220 MHz) δ_{TMS} ($CDCl_3$): 7.1 - 7.4 (m, 8-H, Ar-H); 4.5 - 4.8 (m, 4-H, -CH<); 3.7 (A_2 B_2, 2-H, $ArCH_2$-); 3.4 (s, 2-H, $ArCH_2$-); 3.3 (d, 2-H, -CH-PO-, J_{P-CH} = 20 Hz); 1.0 - 1.3 (2d, 24-H, $-CH_3$).

i.r. spectrum ν_{max} ($CHCl_3$): 1240 cm^{-1} (P=O); 1370 cm^{-1} and 1380 cm^{-1} (isopropyl).

mass spectrum: $m/_e$ 536 (25%); $m/_e$ 494 (33.3%); $m/_e$ 452 (5%); $m/_e$ 410 (5%); $m/_e$ 371 (58.5%); $m/_e$ 368 (8.5%); $m/_e$ 329 (13.6%); $m/_e$ 287 (92%); $m/_e$ 183 (100%); $m/_e$ 104 (58.5%). Exact mass measurement:- Calcd. for $C_{28}H_{42}P_2O_6$ - 536.2446, Found - 536.2457.

(2) The same procedure was done in dry diglyme and heated at 135° for 48 hrs. (Diglyme was dried by first stirring with Vitride and distilled under reduced pressure.) Preparative thin layer chromatographic separation of the reaction mixture afforded 0.1 g (54%) of 3-[diisopropylphosphonato]-7,8-dihydro-1,2,5,6-dibenzocyclooctatetraene.

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 8.0.(d, 1-H, vinyl proton, $J_{PC=CH}$ = 24 Hz); 7.1 - 7.5 (m, 8-H, Ar-H); 4.8 (m, 2-H, -CH<); 3.2 (s, 4-H, $ArCH_2$-); 1.1 - 1.5 (2d, 12-H, $-CH_3$).

i.r. spectrum ν_{max} (CCl_4): 1240 cm^{-1} (P=O); 1375 cm^{-1} and 1385 cm^{-1} (isopropyl).

mass spectrum: $m/_e$ 370 (29%); $m/_e$ 328 (10%); $m/_e$ 286 (100%); $m/_e$ 205 (54%); $m/_e$ 204 (84.5%); $m/_e$ 203 (57.5%).

Anal. Calcd. for $C_{22}H_{27}PO_3.H_2O$: C, 68.01%, H, 7.53%;

Found: C, 68.4%; H, 7.67%;

(3) When the reaction was carried out in dry diglyme at 125° for 30 hrs., 3,4-di[diisopropylphosphonato]-1,2,5,6,-dibenzocyclooctadiene was formed according to the n.m.r. spectrum of

the reaction mixture after hydrolysis and removal of the solvent. The same reaction mixture was then heated in dry diglyme at 135° for another 48 hrs. The n.m.r. spectrum of the reaction mixture, after working up, showed the formation of 3-[diisopropylphosphonato]-7,8-dihydro-1,2,5,6-dibenzocyclooctatetraene.

Attempted Reaction of Diisopropyl(2'-bromomethyl)benzylphosphonate with Vitride Reagent in the presence of Dienophiles

To a suspension of 0.18 g (1 m mole) of anthracene in 10 ml of dry diglyme, under nitrogen was added dropwise a solution of 0.35 g (1 m mole) of diisopropyl(2'-bromomethyl)benzylphosphonate in 25 ml of dry diglyme, followed by a solution of 0.40 g (2 m mole) of Vitride reagent in 40 ml of dry diglyme. After the addition, the reaction mixture was heated at 130° for 24 hrs. After cooling, the reaction mixture was hydrolysed with 0.8 ml of water and stirred for 15 mins. and filtered. The filtrate was dried over anhydrous $MgSO_4$, filtered and the solvent was removed by distillation at reduced pressure. The white crystals which appeared after removal of the solvent, was filtered after adding absolute ethanol. It was identified as anthracene by its spectroscopic data. The solvent was evaporated from the filtrate and the resulting residue showed the presence of 3,4-di[diisopropylphosphonato]-1,2,5,6-dibenzocyclooctadiene. Anthracene was recovered quantitatively.

The same procedure was carried out in the presence of other dienophiles such as dimethyl acetylenedicarboxylate and dimethyl

maleate. Neither of these reactions gave any of the expected adduct and only 3,4-di[diisopropylphosphonato]-1,2,5,6-dibenzocyclooctadiene was formed in both cases.

Reaction of Diisopropyl(2'-bromomethyl)benzylphosphonate with Potassium tert-butoxide

To a solution of 0.23 g (2 m mole) of t-BuOK (purified by sublimation) in 40 ml of dry diglyme was added dropwise, a solution of 0.35 g (1 m mole) of diisopropyl(2'-bromomethyl)benzylphosphonate in 40 ml of dry diglyme, under nitrogen. After the addition, the reaction mixture was heated at 120° for 24 hrs. The flask was cooled, and the reaction mixture was neutralized with dilute sulfuric acid solution and filtered. The filtrate was dried over anhydrous $MgSO_4$, filtered and the solvent was removed by distillation at reduced pressure. Preparative thin layer chromatography of the reaction mixture resulted in the isolation of 0.03 g (10%) of 3,4-di[diisopropylphosphonato]-1,2,5,6-dibenzocyclooctadiene.

The same procedure was carried out in the presence of dienophiles such as dimethyl maleate and dimethyl acetylenedicarboxylate. Only 3,4-di[diisopropylphosphonato)-1,2,5,6-dibenzocyclooctadiene was isolated in both cases.

Attempted Reaction of Diisopropyl(2'-bromomethyl)benzylphosphonate with Diphenylsilane

A mixture of 0.35 g (1 m mole) of diisopropyl(2'-bromomethyl)-benzylphosphonate and 0.37 g (2 m mole) of diphenylsilane was heated under nitrogen, at 120° for 24 hrs. Diphenylsilane was removed under reduced pressure. Preparative thin layer chromatography of the crude mixture gave 2-isopropoxy-3-oxa-1,2,3,4-tetrahydroisophosphinoline 2-oxide in 30% yield.

Reaction of the same phosphonate ester with trichlorosilane also gave only the same cyclized ester.

Reaction of Diethyl(2'-bromomethyl)benzylphosphonate with Vitride Reagent

To a solution of 0.32 g (1 m mole) of diethyl(2'-bromomethyl)-benzylphosphonate in 40 ml of dry diglyme was added dropwise a solution of 0.40 g (2 m mole) of Vitride reagent in 40 ml of dry diglyme under nitrogen. The reaction mixture was stirred at 135° for 24 hrs., cooled and hydrolysed with 0.6 ml of water and filtered. The filtrate was dried over anhydrous $MgSO_4$, filtered and the solvent was removed by distillation under reduced pressure. Preparative thin layer chromatography of the crude residue on silica gel afforded 0.07 g (40%) of 3-[diethylphosphonato]-7,8-dihydro-1,2,5,6-dibenzocyclooctatetraene.

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 8.0 (d, 1-H, vinyl proton, $J_{PC=CH}$ = 24 Hz); 7.1 - 7.5 (m, 8-H, Ar-H); 4.3 (q, 4-H, $-CH_2-O$);

3.2 (s, 4-H, $ArCH_2$-); 1.3 (t, 6-H, $-CH_3$).

i.r. spectrum ν_{max} ($CHCl_3$): 1230 cm^{-1} (P=O)

mass spectrum: $m/_e$ 342 (100%); $m/_e$ 314 (8%); $m/_e$ 313 (8%); $m/_e$ 286 (8%); $m/_e$ 285 (12.2%); $m/_e$ 205 (51.5%); $m/_e$ 204 (97%); $m/_e$ 203 (94%).

Reaction of 2-Phenylisophosphindoline 2-Oxide with N-bromosuccinimide

A mixture of 0.23 g (1 m mole) of 2-phenylisophosphindoline 2-oxide and 0.18 g (1 m mole) of N-bromosuccinimide (recrystallized from water as described by Dauben and McCoy[93]) were refluxed in 40 ml of dry benzene, in the presence of a catalytic amount of benzoyl peroxide for 12 hrs. The reaction mixture was cooled and washed twice with water to remove succinimide and the organic layer was dried over anhydrous $MgSO_4$ and filtered. On evaporation of the solvent, followed by preparative thin layer chromatography of the residue, there was obtained 0.15 g (50%) of r-1-bromo-t-2-phenylisophosphindoline 2-oxide. m.p. 90-92° (ether). R_f value = 0.45.

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.5 (m, 4-H, Ar-H); 5.2 (d, 1-H, -CH); 3.3 - 4.0 (part of ABX, 2-H, $-CH_2$, $^2J_{P-CH_a}$ = 17, $^2J_{P-CH_b}$ = 9 Hz).

i.r. spectrum ν_{max} (KBr): 1230 cm^{-1} (P=O); 1440 cm^{-1}, 1120 - 1100 cm^{-1} and 700 - 800 cm^{-1} (Ph).

mass spectrum: $m/_e$ 308 (10%); $m/_e$ 306 (10%); $m/_e$ 227 (100%); $m/_e$ 179 (30%); $m/_e$ 149 (20%)

Anal. Calcd for $C_{14}H_{12}POBr$: C, 54.75%; H, 3.94%; Br, 26.02%;
Found: C, 54.91%; H, 4.13%; Br, 25.5%;

Also isolated as minor products were 0.03 g (10%) of 1, 1-dibromo-2-phenylisophosphindoline 2-oxide, m.p. 107 - 110° (chloroform/hexane), R_f value = 0.48, 0.025 g (8%) of r-1, c-3-dibromo-t-2-phenylisophosphindoline 2-oxide, m.p. 186 - 188° (ether), R_f value = 0.53, 0.015 g (5%) of trans-1,3-dibromo-2-phenylisophosphindoline 2-oxide, m.p. 95 - 98° (chloroform/hexane), R_f value = 0.57, and a trace of r-1-bromo-c-2-phenylisophosphindoline 2-oxide. m.p. 140 - 142° (ether), R_f value = 0.4.

Spectral data of Dibromo derivatives

1,1-dibromo-2-phenylisophosphindoline 2-oxide

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.3 (m, 4-H, Ar-H); 3.1 - 4.0 (part of ABX, 2-H, $-CH_2$, $^2J_{P-CH_a}$ = 17, $^2J_{P-CH_b}$ = 9 Hz);

i.r. spectrum ν_{max} (KBr): 1240 cm^{-1} (P=O); 1440 cm^{-1}, 1120 - 1100 cm^{-1} and 700 - 800 cm^{-1} (Ph).

mass spectrum: $m/_e$ 388 (5%); $m/_e$ 386 (10%); $m/_e$ 384 (5%); $m/_e$ 307 (20%); $m/_e$ 305 (20%); $m/_e$ 226 (50%); $m/_e$ 179 (20%); $m/_e$ 178 (30%); $m/_e$ 149 (100%); $m/_e$ 102 (10%).

r-1-c-3-dibromo-t-2-phenylisophosphindoline 2-Oxide

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.4 (m, 4-H, Ar-H); 5.3 (d, 1-H, -CH, $^2J_{P-CH_b}$ = 2.5 Hz); 5.6 (d, 1-H, -CH, $^2J_{P-CH_a}$ = 10 Hz).

i.r. spectrum ν_{max} (KBr): 1240 cm^{-1} (P=O), 1440 cm^{-1}, 1120 - 1100 cm^{-1} and 700 - 800 cm^{-1} (Ph).

mass spectrum: $m/_e$ 388 (5%); $m/_e$ 386 (10%); $m/_e$ 384 (5%); $m/_e$ 307 (20%); $m/_e$ 305 (20%); $m/_e$ 226 (25%); $m/_e$ 225 (20%); $m/_e$ 179 (100%); $m/_e$ 178 (90%); $m/_e$ 149 (80%); $m/_e$ 102 (10%).

trans-1,3-dibromo-2-phenylisophosphindoline 2-Oxide

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.3 (m, 4-H, Ar-H); 5.2 (d, 1-H, -CH, $^2J_{P-CH_b}$ = 2 Hz).

i.r. spectrum ν_{max} (KBr): 1230 cm^{-1} (P=O); 1440 cm^{-1}, 1120 - 1100 cm^{-1} and 700 - 800 cm^{-1} (Ph).

mass spectrum: $m/_e$ 388 (2%); 386 (4%); 384 (2%); $m/_e$ 307 (21.3%); $m/_e$ 305 (21.3%); $m/_e$ 226 (5%); $m/_e$ 225 (8%); $m/_e$ 179 (100%); $m/_e$ 178 (97%); $m/_e$ 149 (31%); $m/_e$ 102 (34%).

Reaction of 2-Phenylisophosphindoline 2-Oxide with Phosphorus Pentabromide

A solution of 0.43 g (1 m mole) of phosphorus pentabromide in 35 ml of dry benzene was added dropwise to a solution of

0.23 g (1 m mole) of 2-phenylisophosphindoline 2-oxide in 30 ml of dry benzene under nitrogen. The reaction mixture was refluxed for 24 hrs. and the solvent was evaporated. The crude mixture was separated by preparative thin layer chromatography to give 0.045 g (15%) of r-1-bromo-t-2-phenylisophosphindoline 2-oxide, identical in all respects with the product obtained by bromination of 2-phenylisophosphindoline 2-oxide with N-bromosuccinimide. Starting material was also recovered (75%).

Thermal Decomposition of 2-Phenylisophosphindoline 2-Oxide

A 1:2 mixture of 2-phenylisophosphindoline 2-oxide (0.23 g) and neutral alumina (0.2 g) was heated under 20 mm. pressure at 100 - 125° in a sublimer. A white crystalline solid condensed on the cold finger. m.p. 89 - 91°. It was identified as the starting material by its spectroscopic data.

Attempted Reaction of 2-Phenylisophosphindoline 2-Oxide with Acetic Anhydride

To a solution of 0.11 g (0.5 m mole) of 2-phenylisophosphindoline 2-oxide in 20 ml of dry benzene was added a solution of 0.10 g (1 m mole) of acetic anhydride in 20 ml of dry benzene and the reaction mixture was refluxed for 8 hrs. The flask was cooled and the reaction mixture was poured into 25 ml of water. The organic layer was washed twice with water, dried over anhydrous $MgSO_4$, filtered and the solvent was removed. Thin layer

chromatography and n.m.r. spectrum of the residue showed that no reaction had taken place.

The reaction of 2-phenylisophosphindoline 2-oxide either with p-toluenesulfonyl chloride alone or with the same reagent in the presence of pyridine failed to give any new product.

2-Phenylisophosphindoline 2-Sulfide

A solution of 0.41 g (3 m mole) of trichlorosilane in 30 ml of dry benzene was added dropwise to a solution of 0.23 g (1 m mole) of 2-phenylisophosphindoline 2-oxide in 30 ml of dry benzene, under nitrogen. The reaction mixture was refluxed for 48 hrs., cooled and filtered into a three-necked flask containing 0.06 g (2 m mole) of sulfur flowers. The mixture was stirred at room temperature overnight, under nitrogen and then hydrolysed with 5 ml of water. The aqueous layer was extracted with ether. The combined organic phase was dried over anhydrous $MgSO_4$ and the solvent was removed. Ether was added to the residue and the undissolved sulfur was filtered. Addition of ether and filtration were repeated until no more sulfur remained in the residue. Evaporation of the solvent gave 0.15 g (60%) of 2-phenylisophosphindoline 2-sulfide as yellow solid. m.p. 80 - 82° ($CHCl_3$/hexane).

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.5 - 8.0 (m, 5-H, ArH); 7.3 (s, 4-H, -P-Ph); 3.7 (d, 4-H, $-CH_2$, J_{P-CH} = 12 Hz).

i.r. spectrum ν_{max} (KBr): 1440 cm^{-1}, 1100 cm^{-1} and 700 - 800 cm^{-1}

(-Ph); 650 cm^{-1} (P=S).

mass spectrum: $m/_e$ 246 (13%); $m/_e$ 245 (20%); $m/_e$ 244 (100%); $m/_e$ 211 (60%); $m/_e$ 135 (13%); $m/_e$ 133 (52.8%); $m/_e$ 104 (26%); $m/_e$ 103 (20%). Exact mass measurement:- Calcd. for $C_{14}H_{13}PS$ - 244.0467, Found - 244.0476.

Reaction of 2-Phenylisophosphindoline 2-Sulfide with Acetic Anhydride

To a solution of 0.12 g (0.5 m mole) of 2-phenylisophosphindoline 2-sulfide in 20 ml of dry benzene was added dropwise a solution of 0.10 g (1 m mole) of acetic anhydride in 20 ml of dry benzene and the reaction mixture was refluxed for 48 hrs., and poured into 25 ml of water. The organic layer was dried over anhydrous $MgSO_4$, filtered, and the solvent was removed. The n.m.r. spectrum and thin layer chromatography of the residue revealed that no reaction had occurred.

The reaction was repeated by refluxing 0.12 g (0.5 m mole) of 2-phenylisophosphindoline 2-sulfide in 25 ml of acetic anhydride for 36 hrs. The reaction mixture, after working up gave a residue, the n.m.r. spectrum of which was identified to 2-phenylisophosphindoline 2-oxide. Its formation was also shown by thin layer chromatography. Preparative thin layer chromatography of the residue gave (40%) of 2-phenylisophosphindoline 2-oxide. m.p. 89 - 91°.

Attempted Reaction of 2-Phenylisophosphindoline 2-Sulfide with p-Toluenesulfonyl Chloride

A solution of 0.2 g (1 m mole) of p-toluenesulfonyl chloride in 20 ml of dry benzene was added to a solution of 0.12 g (0.5 m mole) of 2-phenylisophosphindoline 2-sulfide in 20 ml of dry benzene, and the reaction mixture was refluxed for 48 hrs. The reaction mixture, after removal of the solvent gave only the starting material, as shown by n.m.r.

The same reaction was repeated in the presence of pyridine and the reaction mixture was refluxed for 48 hrs. The n.m.r. spectrum and thin layer chromatography of the reaction mixture revealed that no new product was formed.

Dehydrobromination of r-1-Bromo-t-2-phenylisophosphindoline 2-Oxide with 1, 5-Diazabicyclo[3.4.0]nonene-5 (DBN)

To a solution of 0.31 g (1 m mole) of r-1-bromo-t-2-phenylisophosphindoline 2-oxide in 40 ml of dry benzene was added 0.20 g (1.5 m mole) of DBN and the reaction mixture was refluxed for 8 hrs. The reaction mixture became cloudy with formation of DBN.HBr salt after 20 mins. The reaction mixture was cooled and filtered, and excess DBN was neutralized with 5% sulfuric acid solution. The organic layer was washed twice with water, dried over anhydrous $MgSO_4$, filtered and the solvent was removed. Preparative thin layer chromatographic separation of the residue afforded 0.14 g (62%) of 2-phenylisophosphindole 2-oxide dimer.

It was recrystallized from chloroform/haxane to give hygroscopic white solid. m.p. 216 - 220° (decomposed).

n.m.r. spectrum (220 MHz) δ_{TMS} ($CDCl_3$): 7.0 - 7.8 (m, 14-H, Ar-H); 6.3 (m, 4-H, =CH); 5.3 (d of d, 1-H, =CH, J_{P-CH} = 22 Hz); 4.2 (m, 1-H, -CH); 3.9 (m, 1-H, -CH); 3.4 (m, 1-H, -CH).

i.r. spectrum ν_{max} (KBr): 1210 cm^{-1} (P=O); 1440 cm^{-1}, 1120 cm^{-1} and 700 - 800 cm^{-1} (Ph).

mass spectrum: $m/_e$ 452 (10%); $m/_e$ 228 (25%); $m/_e$ 150 (25%); $m/_e$ 149 (100%).

Anal. Calcd. for $C_{28}H_{22}P_2O_2.H_2O$: C, 71.48%; H, 5.14%;
Found: C, 70.87%; H, 5.12%;

Dehydrobromination of r-1-Bromo-t-2-phenylisophosphindoline 2-Oxide with Triethylamine

To a solution of 0.31 g (1 m mole) of r-1-bromo-t-2-phenylisophosphindoline 2-oxide in 40 ml of dry benzene was added 0.40 g (4 m mole) of triethylamine and the reaction mixture was refluxed for 12 hrs. After cooling, the reaction mixture was filtered and the solvent was evaporated. Preparative thin layer chromatographic separation of the residue resulted in the isolation of 0.12 g (50%) of 2-phenylisophosphindole 2-oxide dimer. m.p. 216 - 220° (decomposed) (chloroform/hexane).

Hydrogenation of 2-Phenylisophosphindole 2-Oxide Dimer

A mixture of 0.08 g of 2-phenylisophosphindole 2-oxide dimer, 50 ml of absolute ethanol and palladium on charcoal (10%, 10 mg) was placed under a hydrogen atmosphere (Pressure 1 atmosphere, temperature 65°). The system was agitated overnight. The catalyst was then filtered over celite. Evaporation of the solvent from the filtrate yielded a white solid, the mass spectrum of which revealed that one molecule of hydrogen was absorbed.

Attempted further hydrogenation using 10% palladium on charcoal at 50° atmosphere pressure at 80° for 3 hrs. gave a white solid, the mass spectrum of which showed no further uptake of hydrogen as deduced from the molecular ion.

Attempted Reaction of 2-Phenylisophosphindole 2-Oxide Dimer with Dimethyl Acetylenedicarboxylate

To a solution of 0.05 g (0.1 m mole) of 2-phenylisophosphindole 2-oxide dimer in 10 ml of dry benzene was added dropwise a solution of 0.03 g (0.2 m mole) of dimethyl acetylenedicarboxylate in 10 ml of dry benzene. The reaction mixture was refluxed for 48 hrs. Evaporation of the solvent gave a white solid, the n.m.r. spectrum of which was the same as that of the starting material. Thin layer chromatography also showed that no reaction had occurred.

Attempted Reaction of 2-Phenylisophosphindole 2-Oxide Dimer with Tetracyanoethylene

To a solution of 0.05 g (0.01 m mole) of 2-phenylisophosphindole 2-oxide dimer in 10 ml of dry methylene chloride was added dropwise a solution of 0.03 g (0.02 m mole) of tetracyanoethylene in 10 ml of dry methylene chloride. When the addition was complete, the reaction mixture was refluxed for 48 hrs. and the solvent removed. Thin layer chromatography and n.m.r. spectrum of the reaction mixture revealed that no new product was formed.

Trapping of 2-Phenylisophosphindole 2-Oxide with Dimethyl Acetylenedicarboxylate

To a mixture of 0.30 g (3 m mole) of triethylamine and 0.28 g (2 m mole) of dimethyl acetylenedicarboxylate in 20 ml of dry benzene was added dropwise a solution of 0.31 g (1 m mole) of r-1-bromo-t-2-phenylisophosphindoline 2-oxide in 20 ml of dry benzene at room temperature. After the addition, the reaction mixture was refluxed for 48 hrs. and then cooled. It was then filtered to remove triethylaminehydrobromide salt. The filtrate was evaporated and the residue was separated by preparative thin layer chromatography (solvent - chloroform) to give 0.07 g (28%) of dimethyl 2,3-naphthalene dicarboxylate m.p. 45 - 46° (ether/petroleum ether), (Lit.[152] m.p. 47°), identical in all respects with authentic sample prepared below.

Dimethyl 2,3-Naphthalenedicarboxylate

A mixture of 4.32 g (0.2 mole) of 2,3-naphthalenedicarboxylic acid, 3.2 g (0.1 mole) (4 ml) of methyl alcohol and 0.5 ml of concentrated sulfuric acid were refluxed for 10 hrs. Methyl alcohol was evaporated and the residue was dissolved in chloroform and washed twice with water to remove sulfuric acid. The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was removed to give 4.6 g (95%) dimethyl 2,3-naphthalenedicarboxylate. Recrystallization from ether-petroleum ether gave analytical sample. m.p. 46° (Lit.[152] m.p. 47°)

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 8.2 (s, 2-H), 7.7 - 8.0 (m, 2-H); 7.4 - 7.7 (m, 2-H); 3.98 (s, 6-H, $-CH_3$).

i.r. spectrum ($CHCl_3$): 1720 cm^{-1} (C=O).

Dehydrobromination of r-1-Bromo-t-2-phenylisophosphindoline 2-Oxide in the presence of Phenylacetylene

To a mixture of 0.3 g (3 m mole) of triethylamine and 0.2 g (2 m mole) of phenylacetylene in 20 ml of dry benzene was added dropwise a solution of 0.3 g (1 m mole) of r-1-bromo-t-2-phenylisophosphindoline 2-oxide in 20 ml of dry benzene, under nitrogen, at room temperature. The reaction mixture was refluxed for 48 hrs., after the addition. It was cooled and the solvent was evaporated. The crude residue was separated by preparative thin layer chromatography to give 0.03 g (15%) of 2-phenyl naphthalene.

m.p. 101 - 102° (Ethanol). (Lit.[152] m.p. 103 - 104°).

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 8.3 (m, 1-H); 8.0 (m, 2-H); 7.4 - 8.0 (m, 9-H).

mass spectrum: $m/_e$ 204 (100%).

Also isolated was 0.06 g (25%) of 2-phenylisophosphindole 2-oxide dimer.

Dehydrobromination of r-1-Bromo-t-2-phenylisophosphindoline 2-Oxide in the presence of 1,4-Cyclohexadiene

To a mixture of 0.3 g (3 m mole) of triethylamine and 3 ml of 1,4-cyclohexadiene in 25 ml of dry benzene was added dropwise a solution of 0.3 g (1 m mole) of r-1-bromo-t-2-phenylisophosphindoline 2-oxide in 15 ml of dry benzene under nitrogen, and the reaction mixture was refluxed for 48 hrs. After removal of the solvent, the crude mixture was separated by preparative thin layer chromatography to give 0.11 g (34%) of 2-phenylisophosphindole 2-oxide -1,4-cyclohexadiene adduct as white crystals. m.p. 185 - 187° (chloroform/hexane).

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.2 (m, 9-H, Ar-H); 5.7 (m, 2-H, CH = CH); 3.5 (d, 2-H, -CHP = O); 3.2 (m, 2-H, C-H); 2.2 (m, 2-H, equatorial allylic); 1.3 (d of d, 2-H, axial allylic).

i.r. spectrum ν_{max} (KBr): 1210 cm^{-1} (P=O)

mass spectrum: $m/_e$ 306 (9.4%); $m/_e$ 228 (27.2%); $m/_e$ 182 (22.8%);

$m/_e$ 180 (100%); $m/_e$ 150 (9.4%); $m/_e$ 128 (74%); $m/_e$ 104 (22.8%); $m/_e$ 91 (13.6%); $m/_e$ 77 (27.2%).

Anal. Calcd. for $C_{20}H_{19}PO$: C, 78.42%; H, 6.25%;
Found: C, 77.72%; H, 6.39%;

Also isolated as minor product was 0.03 g (10%) of r-1-bromo-c-2-phenylisophosphindoline 2-oxide as white crystals. m.p. 140 - 142° (ether).

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.5 (m, 4-H, Ar-H); 5.6 (d, 1-H, -C-H, J_{P-CH} = 10 Hz); 3.3 - 3.9(part of ABX, 2-H, $-CH_2$, J_{P-CH_a} = 17, J_{P-CH_b} = 9 Hz).

i.r. spectrum ν_{max} (KBr): 1240 cm^{-1} (P=O)

mass spectrum: $m/_e$ 308 (6.6%); $m/_e$ 306 (6.6%); $m/_e$ 227 (100%); $m/_e$ 179 (26.6%); $m/_e$ 149 (26.6%).

Anal. Calcd. for $C_{14}H_{12}POBr$: C, 54.75%; H, 3.94%; Br, 26.02%;
Found: C, 55.35%; H, 4.14%, Br, 26.09%.

Dehydrobromination of r-1-Bromo-t-2-phenylisophosphindoline 2-Oxide in the presence of 2,5-Norbornadiene

To 0.1 g (1 m mole) of triethylamine and 2 ml of norbornadiene in 15 ml of dry benzene was added a solution of 0.1 g (0.03 m mole) r-1-bromo-t-2-phenylisophosphindoline 2-oxide in 15 ml of dry benzene, under nitrogen. After the addition, the reaction mixture was refluxed for 48 hrs. and cooled. It was

then filtered to remove triethylaminehydrobromide salt. The filtrate was evaporated and preparative thin layer chromatography of the crude residue afforded 0.03 g (25%) of 2-phenylisophosphindole 2-oxide-norbornadiene adduct as white crystals. m.p. 156 - 158° (chloroform/hexane).

n.m.r. spectrum (220 MHz) δ_{TMS} ($CDCl_3$): 7.2 (m, 9-H, Ar-H; 6.2 (m, 2-H, -CH = CH); 3.7 - 3.6 (m, 2-H, -CHP = O); 3.1 (m, 2-H, -CH); 2.6 (m, 2-H, -CH); 0.8 (d, 1-H, -CH);-0.3 (d, 1-H, -CH);

i.r. spectrum ν_{max} (KBr): 1200 cm^{-1} (P=O); 1450 cm^{-1}, 1100 cm^{-1} and 700 - 800 cm^{-1} (Ph).

mass spectrum: $m/_e$ 318 (6%); $m/_e$ 252 (5%); $m/_e$ 228 (5%); $m/_e$ 227 (5%); $m/_e$ 179 (5%); $m/_e$ 178 (8%); $m/_e$ 128 (100%).

Anal. Calcd. for $C_{21}H_{19}PO.3/4H_2O$; C, 76.07%, H, 6.22%;
Found: C, 76.24%; H, 6.04%

0.01 g (10%) of r-1-bromo-c-2-phenylisophosphindoline 2-oxide was also isolated.

Reduction of r-1-Bromo-t-2-phenylisophosphindoline 2-Oxide with Trichlorosilane

To a mixture of 0.3 g (1 m mole) of r-1-bromo-t-2-phenylisophosphindoline 2-oxide and 0.6 g (6 m mole) of triethylamine in 50 ml of dry benzene was added dropwise a solution of 0.4 g (3 m mole) of trichlorosilane in 25 ml of dry benzene under

nitrogen. The reaction mixture was refluxed for 36 hrs., cooled and hydrolysed with 30% NaOH solution. The silica was filtered and the filtrate was washed twice with water. The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was removed. On separation of the residue by preparative thin layer chromatography, there was obtained 0.094 g (41%) of 2-phenylisophosphindoline 2-oxide.

Reduction of 1,1-Dibromo-2-phenylisophosphindoline 2-Oxide with Trichlorosilane

Reduction of 0.04 g (0.1 m mole) of 1,1-dibromo-2-phenylisophosphindoline 2-oxide with 0.04 g (0.3 m mole) of trichlorosilane in the presence of 0.02 g (0.2 m mole) of triethylamine in dry benzene at refluxing temperature for 24 hrs., gave 0.007 g (30%) of 2-phenylisophosphindoline 2-oxide.

Attempted Preparation of 2-Bromo-2-phenylisophosphindolinium Bromide

To a solution of 0.23 g (1 m mole) of 2-phenylisophosphindoline 2-oxide in 35 ml of dry benzene was added dropwise a solution of 0.34 g (2.5 m mole) of trichlorosilane in 30 ml dry benzene under nitrogen. The reaction mixture was refluxed for 36 hrs., cooled and hydrolysed with 30% NaOH solution. The silica was filtered and the filtrate was washed twice with water.

The organic layer was dried over anhydrous $MgSO_4$, and filtered into a three-necked flask, equipped with a nitrogen inlet, a condenser and a dropping funnel. A quantity of 0.2 g (2 m mole) of bromine was added under nitrogen, while the flask was cooled in an ice-bath, and the reaction mixture was stirred overnight at room temperature. The yellow solid formed was filtered and the mass spectrum was recorded. It showed a base peak at $m/_e$ 228 and the other peaks are at $m/_e$ 158, 160, 162 in the intensity ratio of 1:2:1. It was likely that 2-bromo-2-phenylisophosphindolinium bromide was formed and it decomposed into bromine and 2-phenylisophosphindoline which was then oxidized to the corresponding phosphine oxide. Thus, the peak at $m/_e$ 228 may be due to 2-phenylisophosphindoline 2-oxide and the peaks at $m/_e$ 158, 160, 162 may correspond to bromine. It was likely that either 2-phenylisophosphindoline 2-oxide-bromide complex or 2-bromo-2-phenylisophosphindolinium bromide was formed. But the yield was low.

Reaction of r-1-c-3-Dibromo-t-2-phenylisophosphindoline 2-Oxide with Ironnonacarbonyl

To a suspension of 0.22 g (0.6 m mole) of ironnonacarbonyl in 20 ml of dry benzene was added dropwise a solution of 0.08 g (0.2 m mole) of r-1,c-3-dibromo-t-2-phenylisophosphindoline 2-oxide in 15 ml of dry benzene and the reaction mixture was kept stirring overnight at room temperature.

The yellow solid was filtered off and the solvent was removed from the filtrate. The i.r. ($CHCl_3$) spectrum of the residue showed two bands at 2100 cm^{-1} and 2040 cm^{-1}. The n.m.r. spectrum was also different from the starting material and it showed two multiplets at 7.5 δ and 2.9 δ respectively. However, the mass spectrum showed only the starting material.

Bromination of 2-Phenylisophosphindole 2-Oxide-1,4-Cyclohexadiene adduct

Bromination was done as in the same manner as the method described by Quin[27].

A solution of 0.1 g (0.6 m mole) of bromine in 20 ml of chloroform was added to a solution of 0.09 g (0.3 m mole) of 2-phenylisophosphindole 2-oxide-1,4-hexadiene adduct in 20 ml of chloroform and the reaction mixture was stirred at room temperature for 24 hrs. Then the reaction mixture was worked up by adding some ice, neutralizing with 5% $NaHCO_3$ solution and destroying excess bromine with saturated sodium thiosulfate solution. The mixture was filtered and the filtrate was extracted with chloroform. The combined organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent removed. The residue, dibromo derivative was obtained as yellow solid. m.p. 153 - 155°.

n.m.r. spectrum (220 MHz) δ_{TMS} ($CDCl_3$): 7.2 (m, 9-H, Ar-H); 4.5 (m, 1-H, -CHBr); 4.3 (m, 1-H, -CHBr); 3.6 (m, 2-H, -CHP=O); 3.5 (m, 2-H, -CH); 2.0 (m, 2H, equatorial -CH); 1.3 (m, 2H, axial -CH).

i.r. spectrum ν_{max} (KBr): 1210 cm^{-1} (P=O);

mass spectrum: $m/_e$ 468 (1%); $m/_e$ 466 (2%); $m/_e$ 464 (1%); $m/_e$ 385 (5%); $m/_e$ 340 (10%); $m/_e$ 306 (5%); $m/_e$ 305 (5%); $m/_e$ 181 (92%); $m/_e$ 180 (80%); $m/_e$ 128 (100%).

Dehydrobromination of the Dibromo derivative of 2-Phenylisophosphindole 2-Oxide-1,4-Cyclohexadiene adduct

To a solution of 0.05 g (0.1 m mole) of dibromo compound in 15 ml of dry benzene was added dropwise a solution of 0.03 g (0.2 m mole) of DBN in 15 ml of dry benzene. The reaction mixture was refluxed for 48 hrs. and cooled. Excess DBN was neutralized with 5% sulfuric acid solution. The organic layer was washed twice with water, dried over anhydrous $MgSO_4$, filtered and the solvent removed. Preparative thin layer chromatography of the residue gave 0.008 g (20%) of a monobromo derivative of 2-phenylisophosphindole 2-oxide-1,4-cyclohexadiene adduct, rather than the expected diene product. Most of the starting material (70%) was recovered. The product has the following spectroscopic data.

n.m.r. spectrum δ_{TMS} ($CDCl_3$): 7.3 (m, 9-H, Ar-H); 5.9 (m, 1-H, =CH); 3.5 (m, 2-H, -CHP=O); 3.2 (m, 2-H, -CH); 2.5 (m, 2-H, equatorial allylic); 1.3 (m, 2-H, axial allylic).

mass spectrum: $m/_e$ 386 (10%); $m/_e$ 384 (10%); $m/_e$ 305 (20%); $m/_e$ 128 (100%).

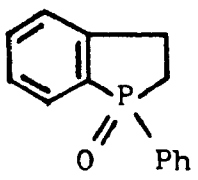
CHAPTER 4

CONCLUSION AND SUGGESTION FOR FURTHER WORK

A brief comparison between the phosphindole and isophosphindole systems

With the results reported in this investigation it is possible to make certain comparison between the phosphindole and isophosphindole systems.

The dihydro compounds 66 and 121 can now be synthesized readily in essentially one-step processes in moderate yields.



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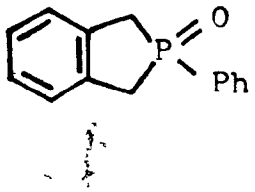
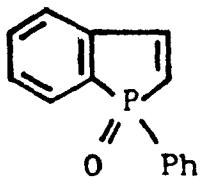
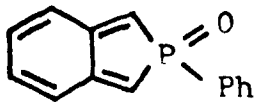


(121)

They behave as normal phosphine oxides in their chemistry. They can be reduced to the corresponding phosphine by silanes. They are stable thermally up to 250°.

The introduction of another double bond into the system drastically changes the chemical reactivity of the two compounds. While 1-phenylphosphindole 1-oxide[65,66] is a stable solid, 2-phenylisophosphindole is an extremely reactive compound and its existence has only been demonstrated by trapping it with a dienophile.





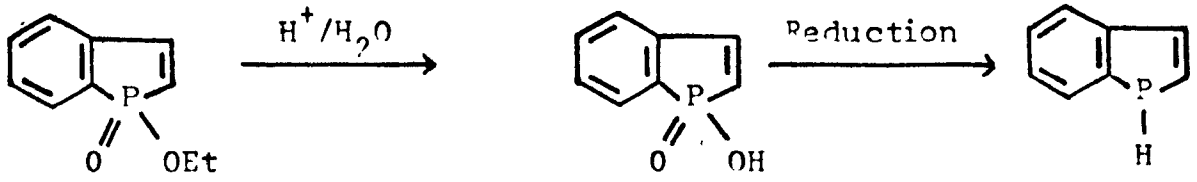
(152)

The pattern of chemical reactivities is in qualitative agreement with other heterocyclic systems. For example, indole, benzofuran and benzothiophene are stable compounds, whereas isoindole[113], isobenzofuran[111,112] and isobenzothiophene[109] are reactive and can undergo cycloaddition with dienophiles. Similarly, isoindene[150,151] is also believed to be extremely reactive. It rearranges readily to indene. Its existence has been demonstrated by trapping it with dienophile[150]. The reactivity is associated with the quinodimethane structure. In the case of 152, the phosphorus does not possess lone electron pair to allow for any extent of possible aromaticity.

The phosphindole[65,66] system has been prepared and found to possess reasonable stability. It is believed to have some aromatic character on the basis of its spectroscopic properties. Unfortunately, the isophosphindole system cannot be prepared by our various attempts. If one were to draw any analogy from the heteroisoindene system, one would expect isophosphindole to be reactive, but perhaps isolable.

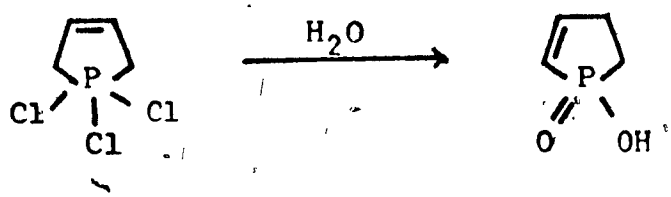
Suggestion for further work

It has been mentioned that the attempted reduction of 1-ethoxybenzo[b]phosphole 1-oxide to benzo[b]phosphole (4) is not successful. An alternative method of preparing 4 may involve the hydrolysis of 1-ethoxybenzo[b]phosphole 1-oxide to the corresponding phosphinic acid 166, followed by reduction with silanes or lithium aluminium hydride as follows: -



(166) (4)

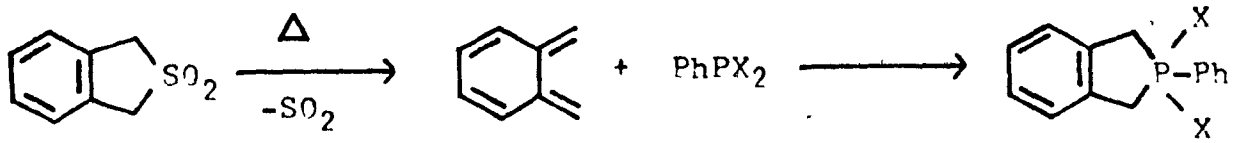
In view of the successful reduction[99], of phosphinic acid to the corresponding phosphine, it seems probable that the reduction of 166 might give the expected product. Furthermore, 166 can be alternatively prepared by the Diels-Alder reaction of E,E-1,4-diacetoxybutadiene with the appropriate dienophile, 1-hydroxy-2-phospholene 1-oxide (167) which can be easily obtained by the hydrolysis of 1,1,1-trichlorophospholene[83,84] (Eq. 84).



(167) (84)

It has been mentioned that 2-phenylisophosphindole 2-oxide has been detected as transient reaction intermediate and has been trapped as Diels-Alder adducts. Further work can be extended for the synthesis of the isophosphindole system, according to the following synthetic route:

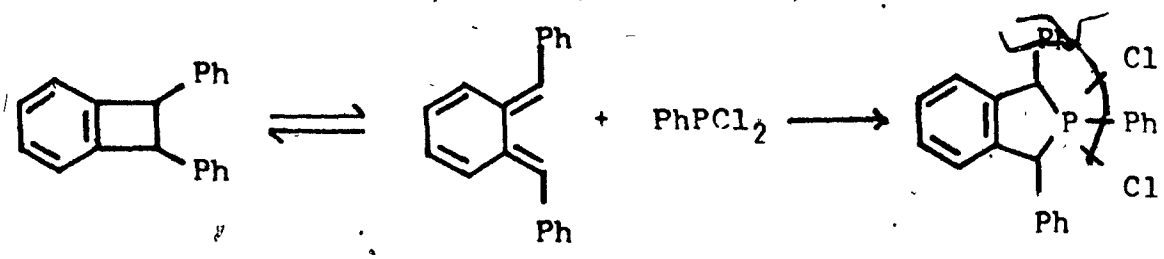
McCormack[16] reaction of phenyldihalogenophosphine with o-quinodimethane, which can be produced by the thermal decomposition of 1,3-dihydrobenzo[c]thiophene 2,2-dioxide[128], followed by the dehydrohalogenation of the adduct with DBU. Similar kind of dehydrohalogenation reactions to give phospholes have been reported[20,147].



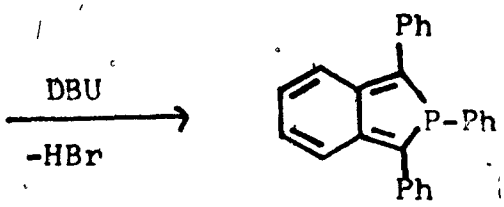
(150)

One may expect that highly substituted isophosphindole may be sufficiently stable for isolation and the same method may be used for its preparation. In fact, 82 has recently been prepared by Holland and Jones[73]. The subsequent transformation remains

to be investigated.



(82)



CONTRIBUTION TO ORIGINAL KNOWLEDGE

1-Ethoxybenzo[b]phosphole 1-oxide, the first example of benzo[b]phosphole, where phosphorus is functionalized has been synthesized.

2-Phenylisophosphindoline 2-oxide was prepared by a new synthetic route in one step by the reaction of o-xylylene dibromide and diethyl phenylphosphonate in the presence of sodium bis(2-methoxyethoxy)aluminium hydride.

Free radical halogenation of 2-phenylisophosphindoline 2-oxide was found to occur stereospecifically to give r-1-bromo-t-2-phenylisophosphindoline 2-oxide.

Dehydrobromination of r-1-bromo-t-2-phenylisophosphindoline 2-oxide by base gave 2-phenylisophosphindole 2-oxide as a transient intermediate. Its existence has been confirmed by trapping with various dienophiles as the Diels-Alder adducts. This is the first time that isophosphindole system is generated. The stereochemistry of the Diels-Alder adduct was also examined.

The use of sodium bis(2-methoxyethoxy)aluminium hydride as a reagent for the formation of carbon-phosphorus bond in the isophosphindole system was studied. Anomaly was found to occur in the case of dialkyl(2'-bromomethyl)benzylphosphonate which gave compounds of dibenzocyclooctadiene ring, substituted with dialkyl phosphono group.

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SPECTRA

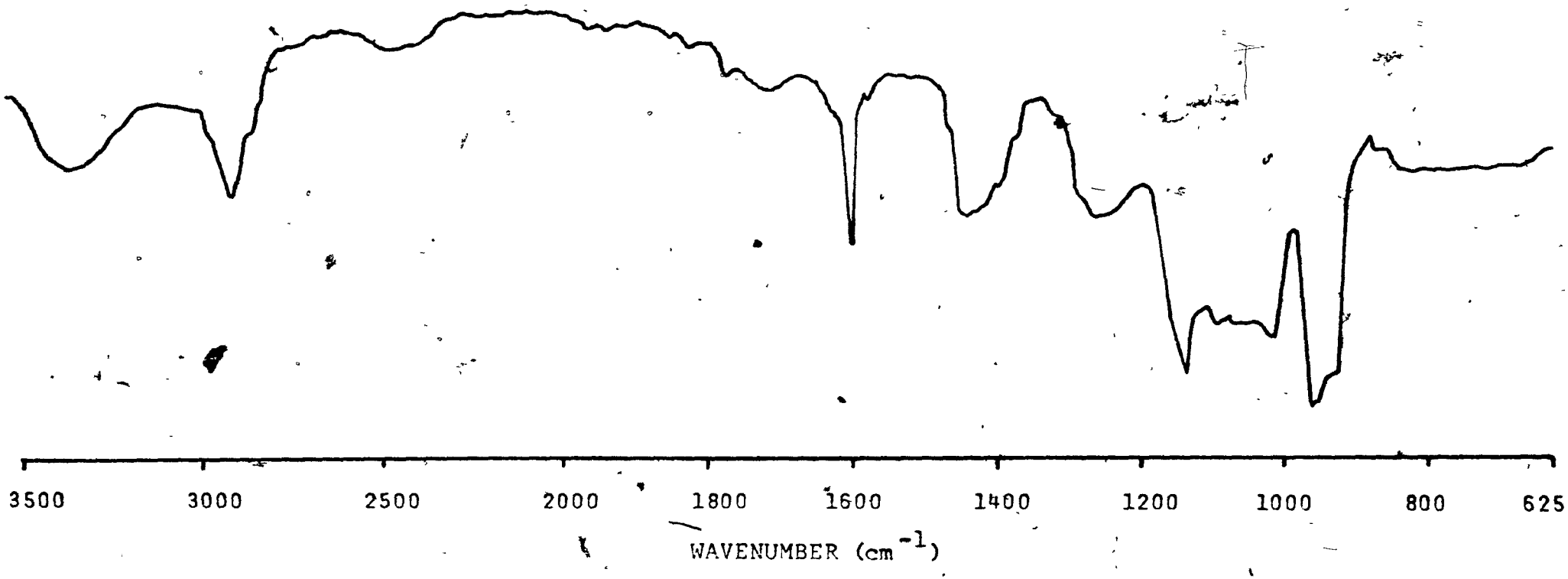


Fig. 1 - Infrared Spectrum ($CHCl_3$) of 1-Ethoxy-2,3-dihydro-benzo[b]phosphole 1-Oxide

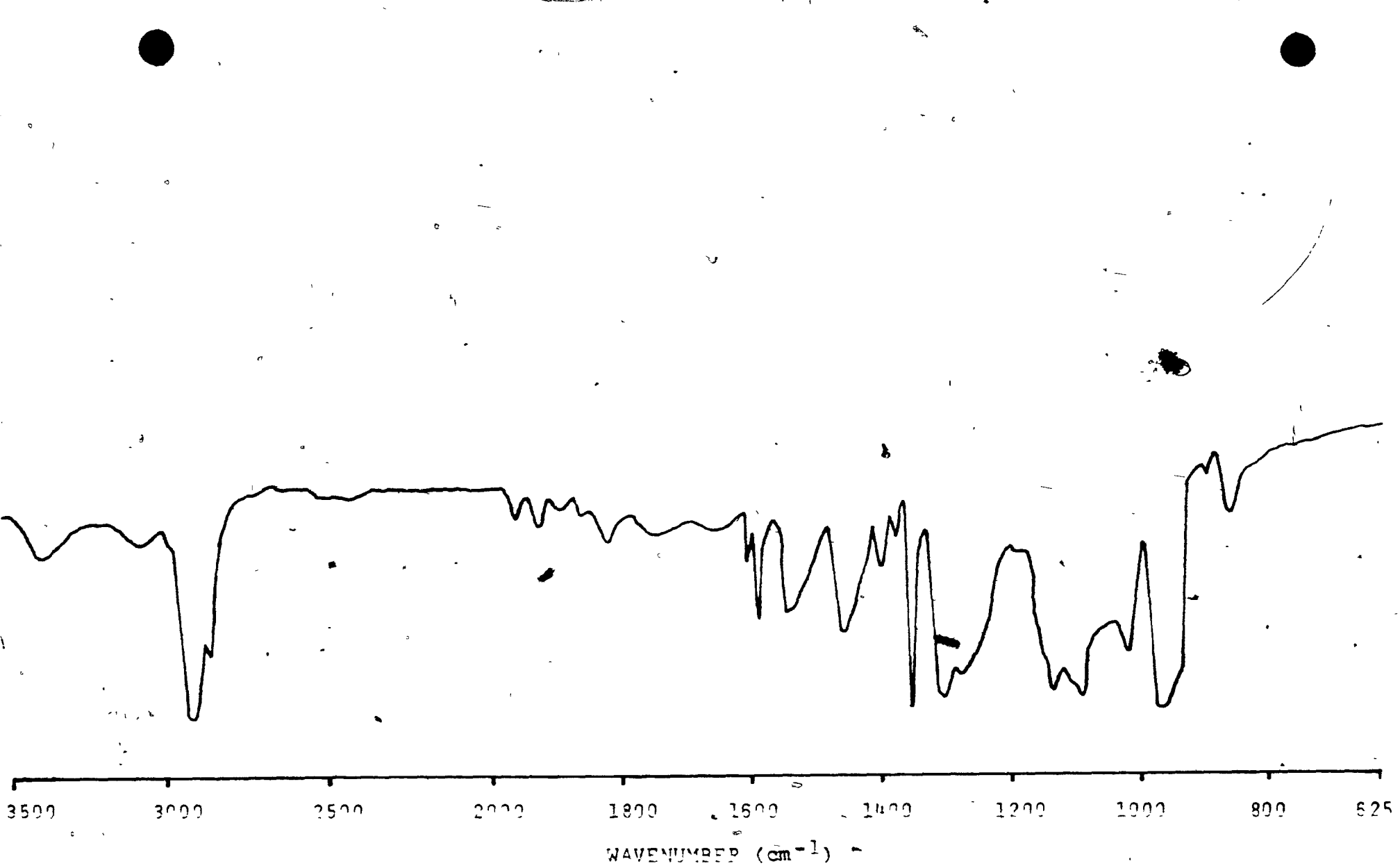


Fig. 2 - Infrared Spectrum ($CHCl_3$) of 1-Ethoxybenzo-[b]phosphole 1-Oxide

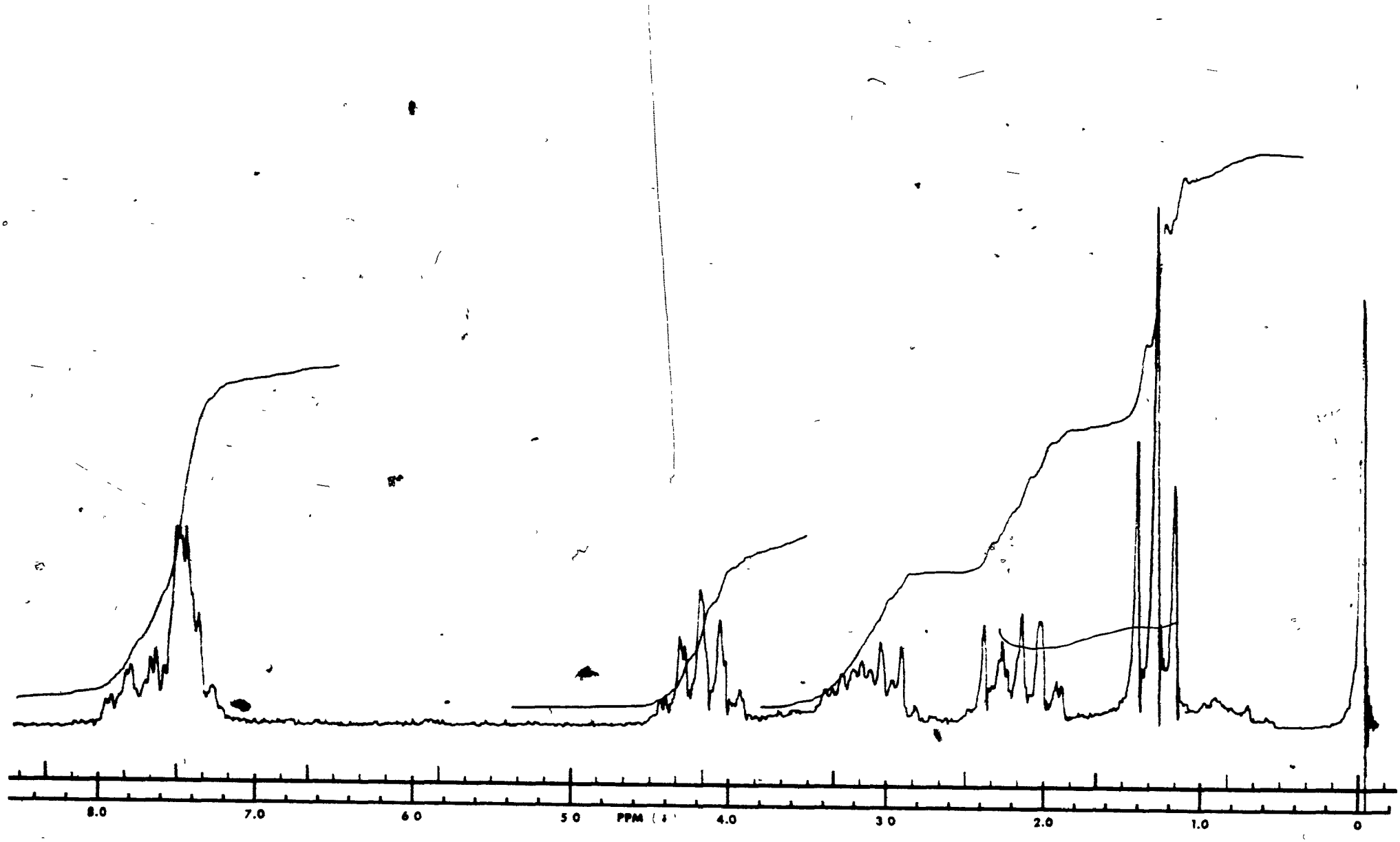
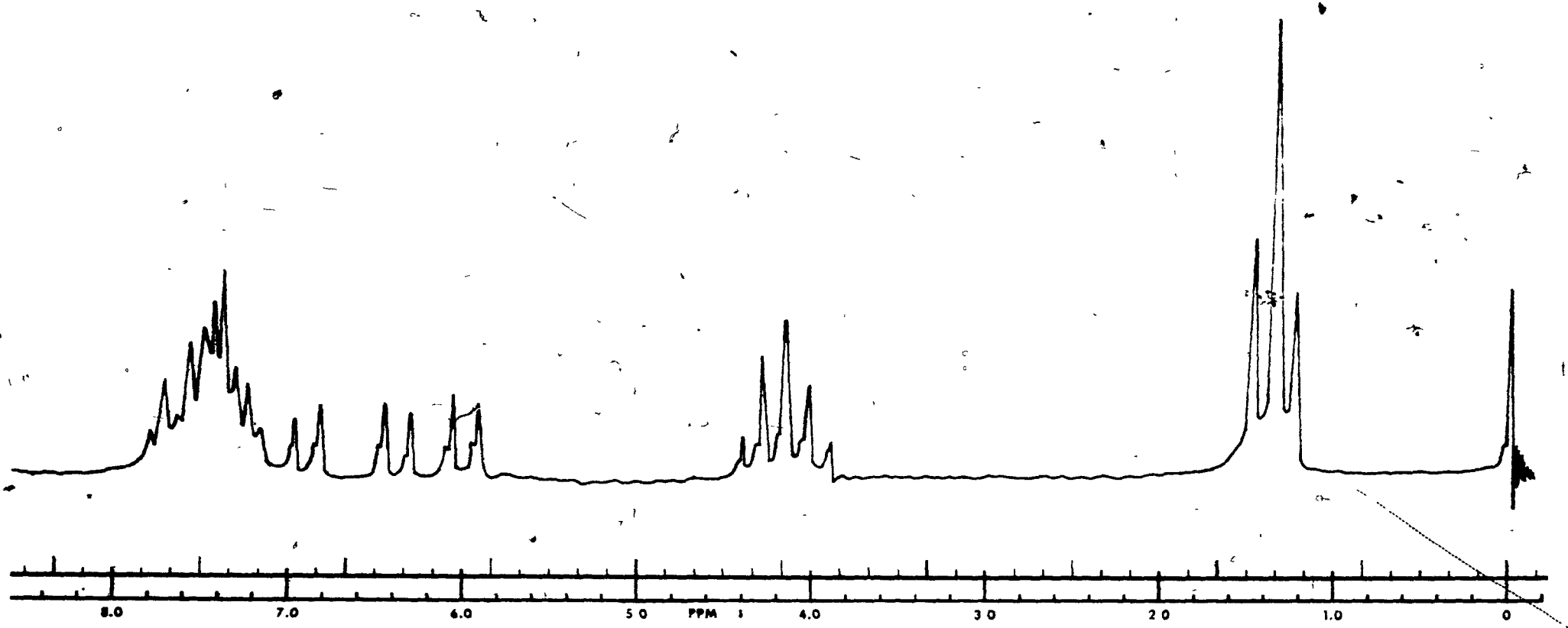


Fig. 3 - N.M.R. Spectrum of 1-Ethoxy-2,3-dihydrobenzo-[b]phosphole 1-Oxide



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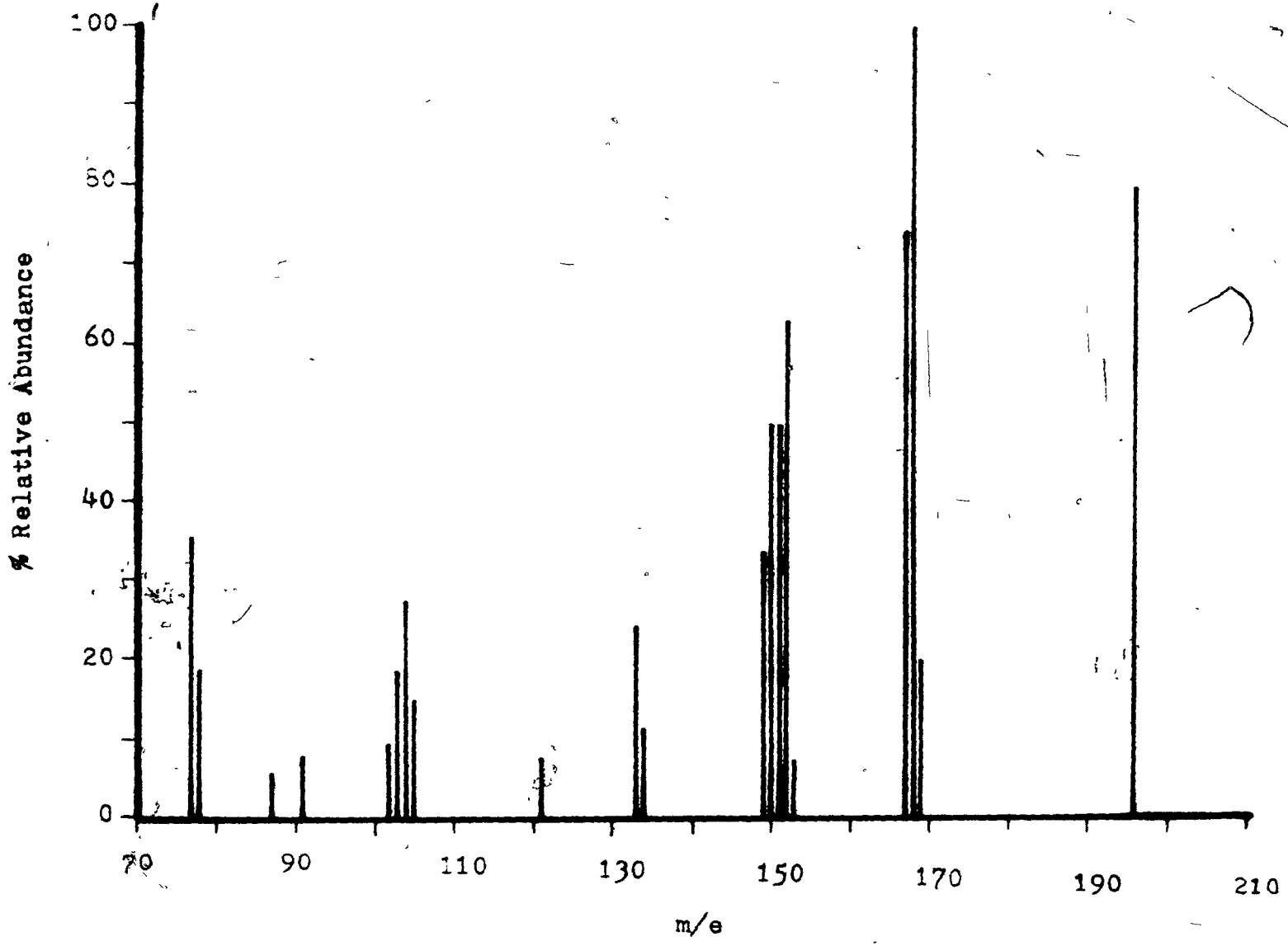


Fig. 5 - Mass Spectrum of 1-Ethoxy-2,3-dihydrobenzo[b]phosphole 1-Oxide

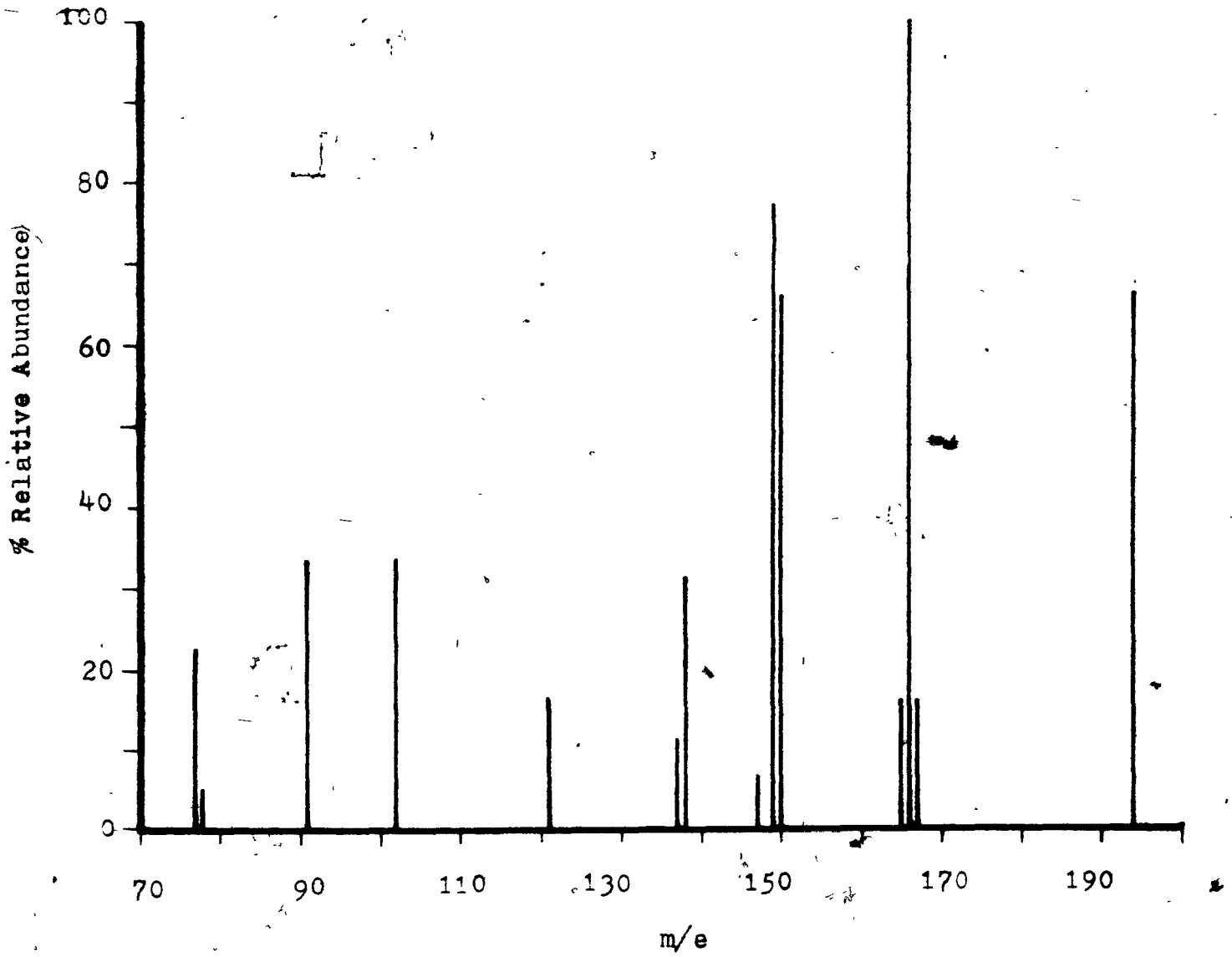


Fig. 6 - Mass Spectrum of 1-Ethoxybenzo[b]phosphole 1-Oxide

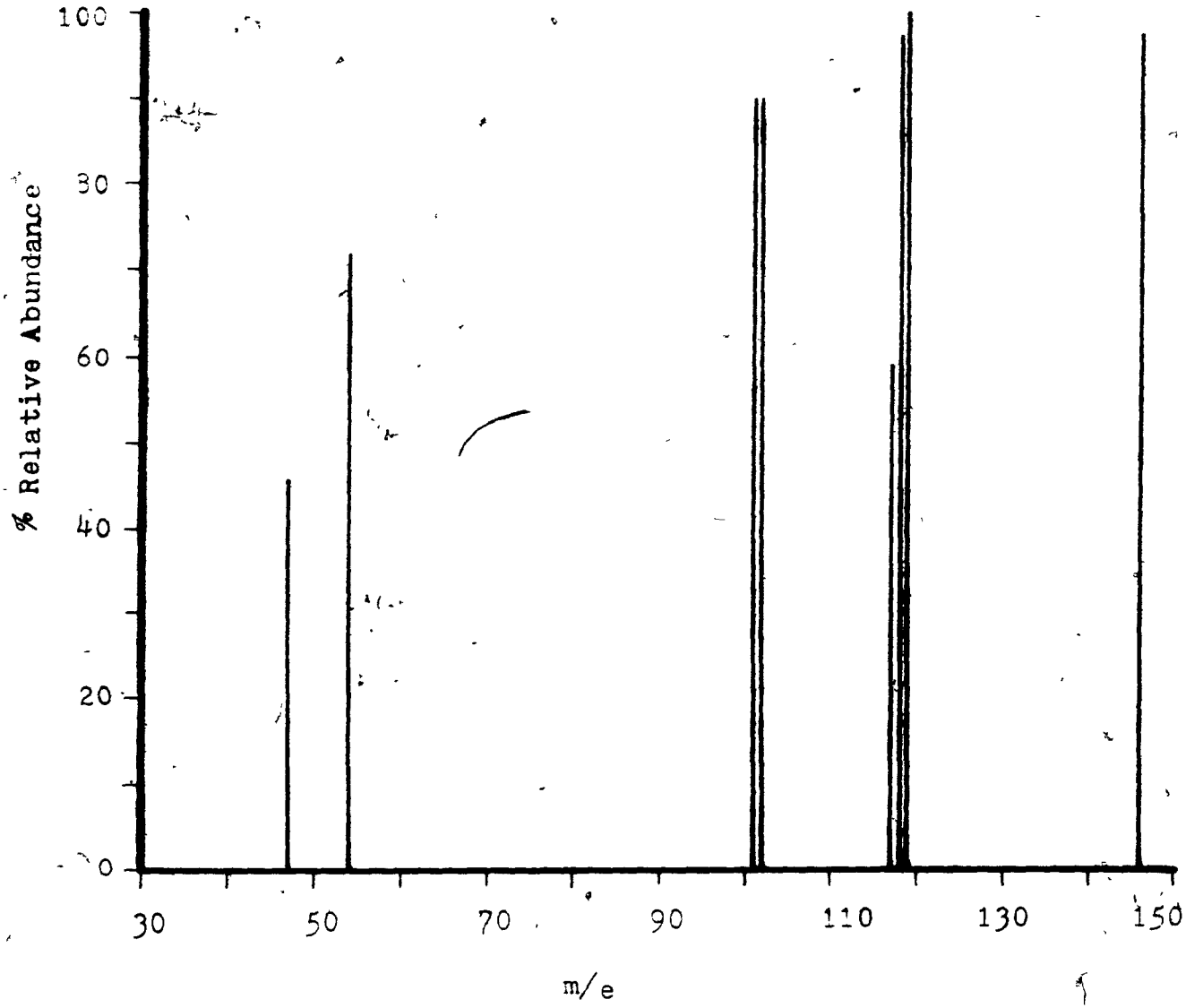


Fig.7 - Mass Spectrum of 1-Ethoxy-2-phospholene 1-Oxide

Fig. 8 - Ultraviolet Spectrum of 1-Ethoxy-2,3-dihydrobenzo[b]phosphole 1-Oxide

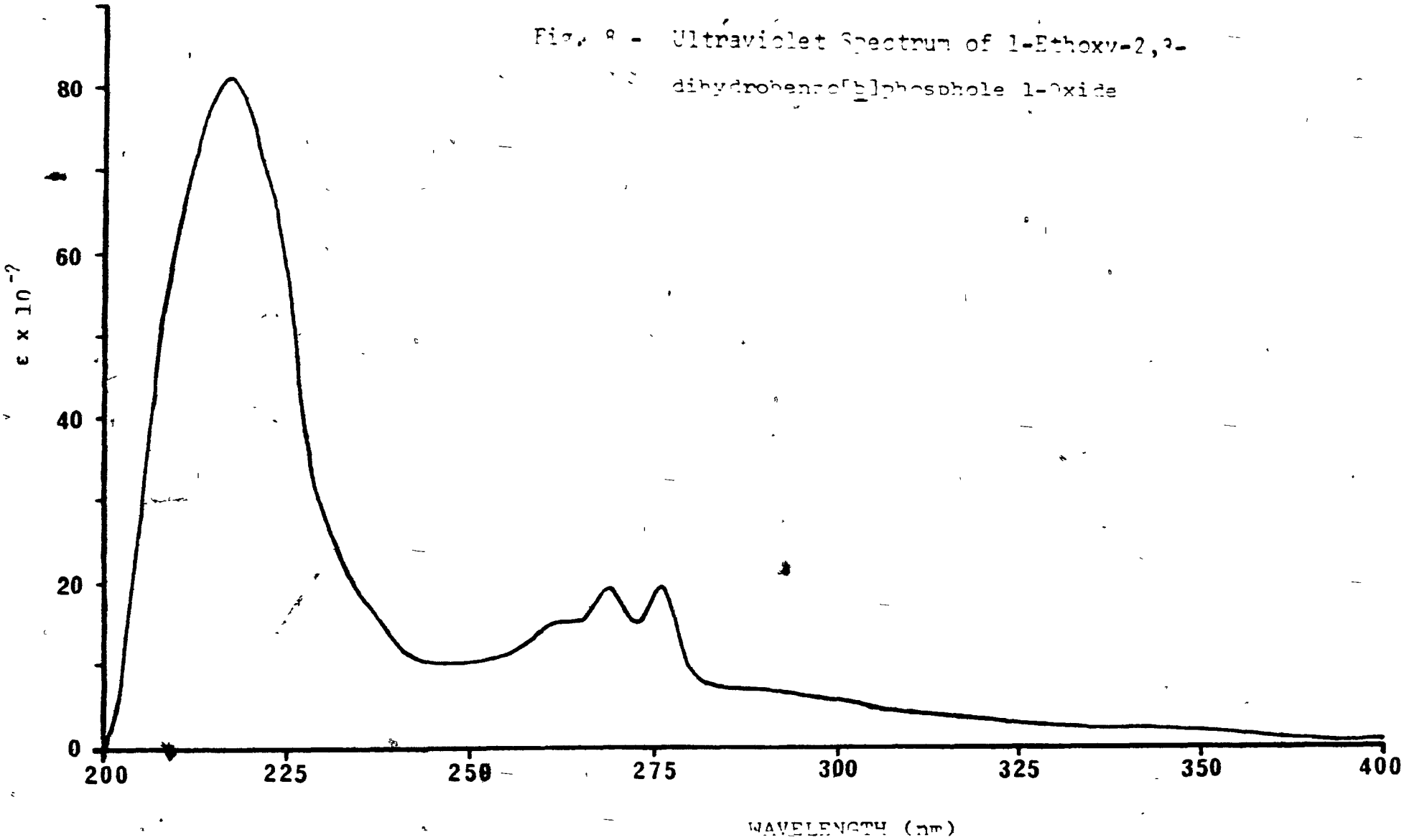
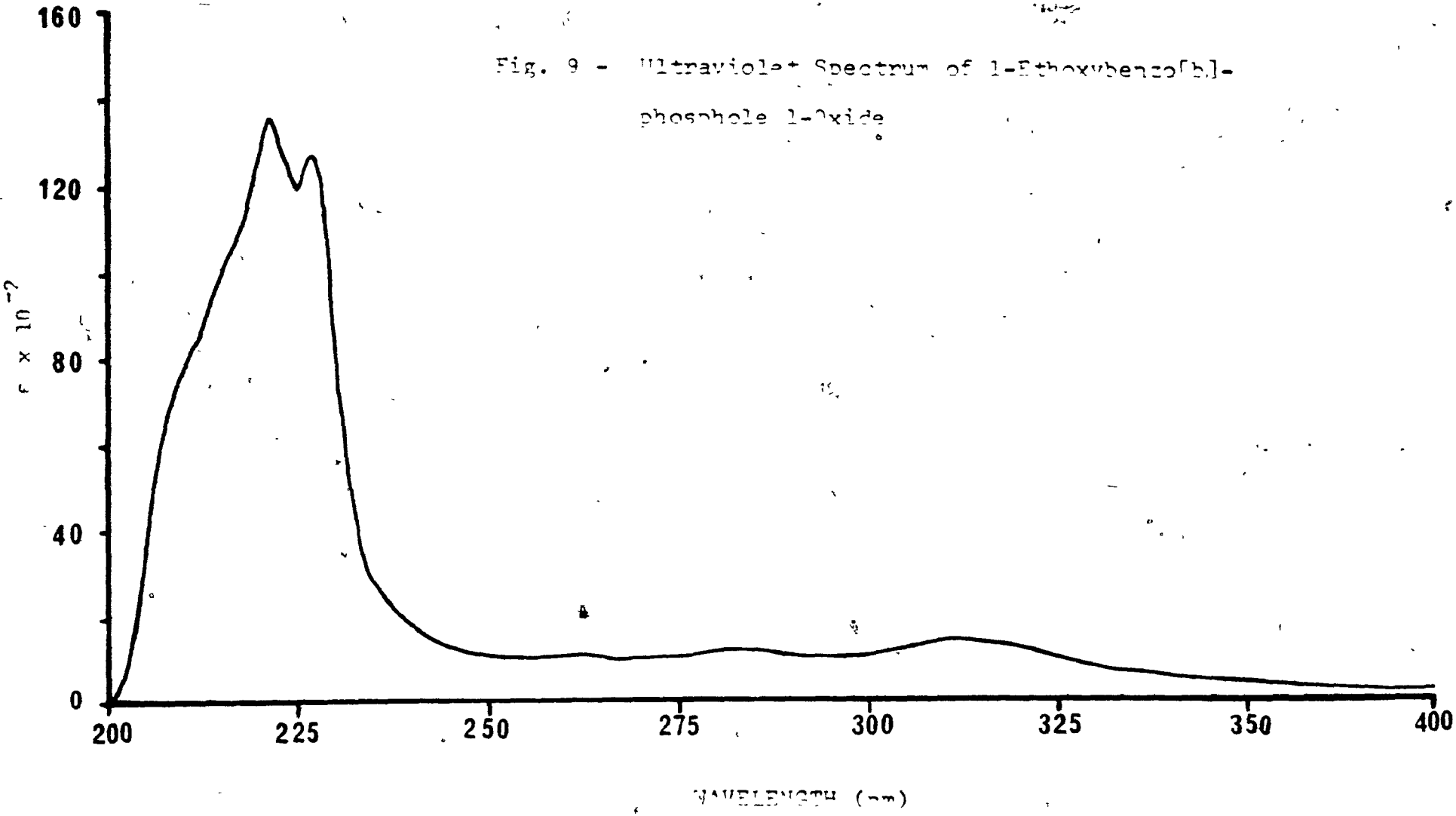


Fig. 9 - Ultraviolet Spectrum of 1-Ethoxybenzo[b]-phosphole 1-Oxide



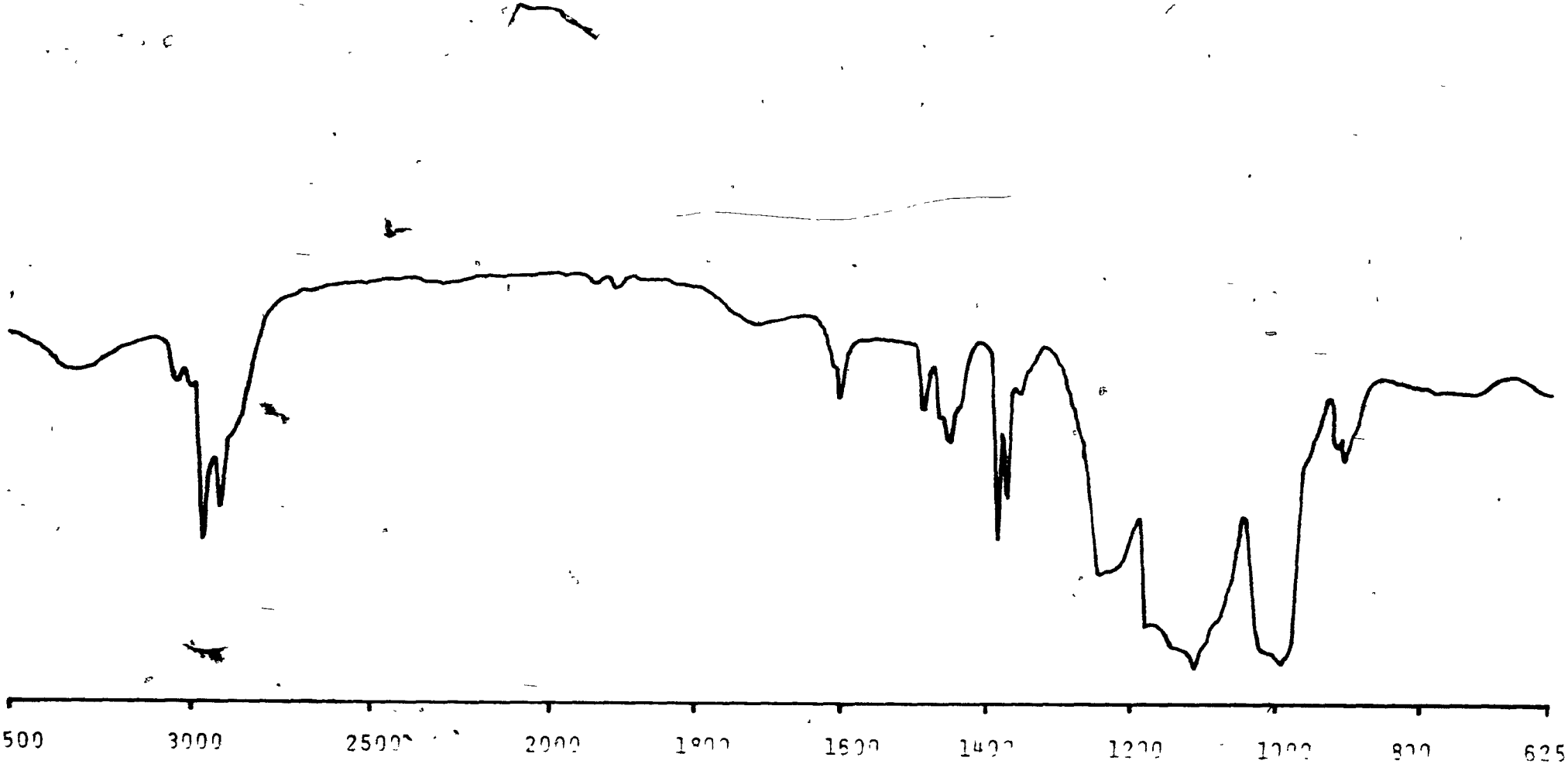


Fig. 10 - Infrared Spectrum (CCl_4) of 3-(Diisopropylphosphonato)-7,8-dihydro-1,2,5,6-dibenzocyclooctatetraene

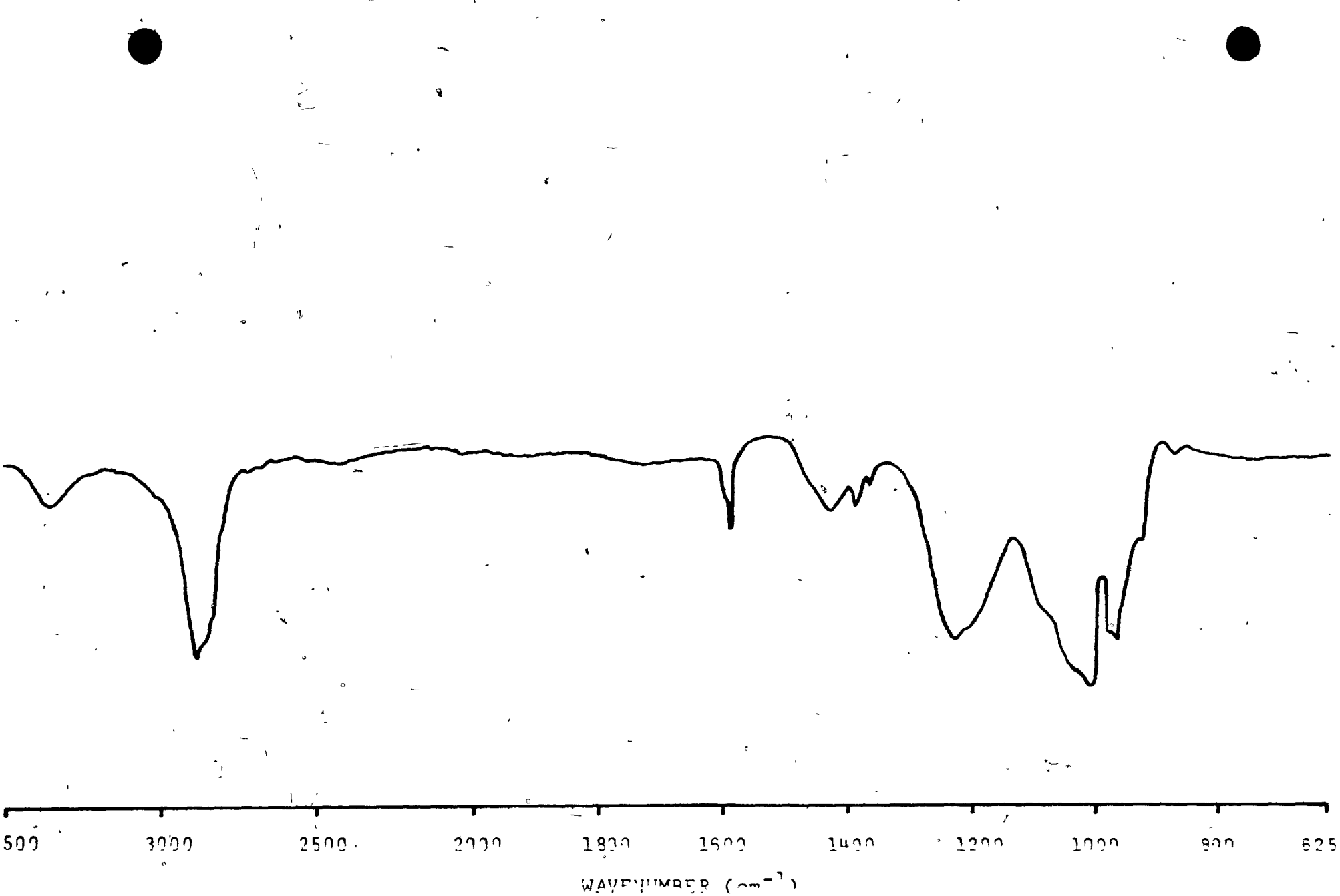


Fig. 11 - Infrared Spectrum ($CHCl_3$) of 3-(Diethylphosphonato)-7,8-dihydro-1,2,5,6-dibenzocyclooctatetraene

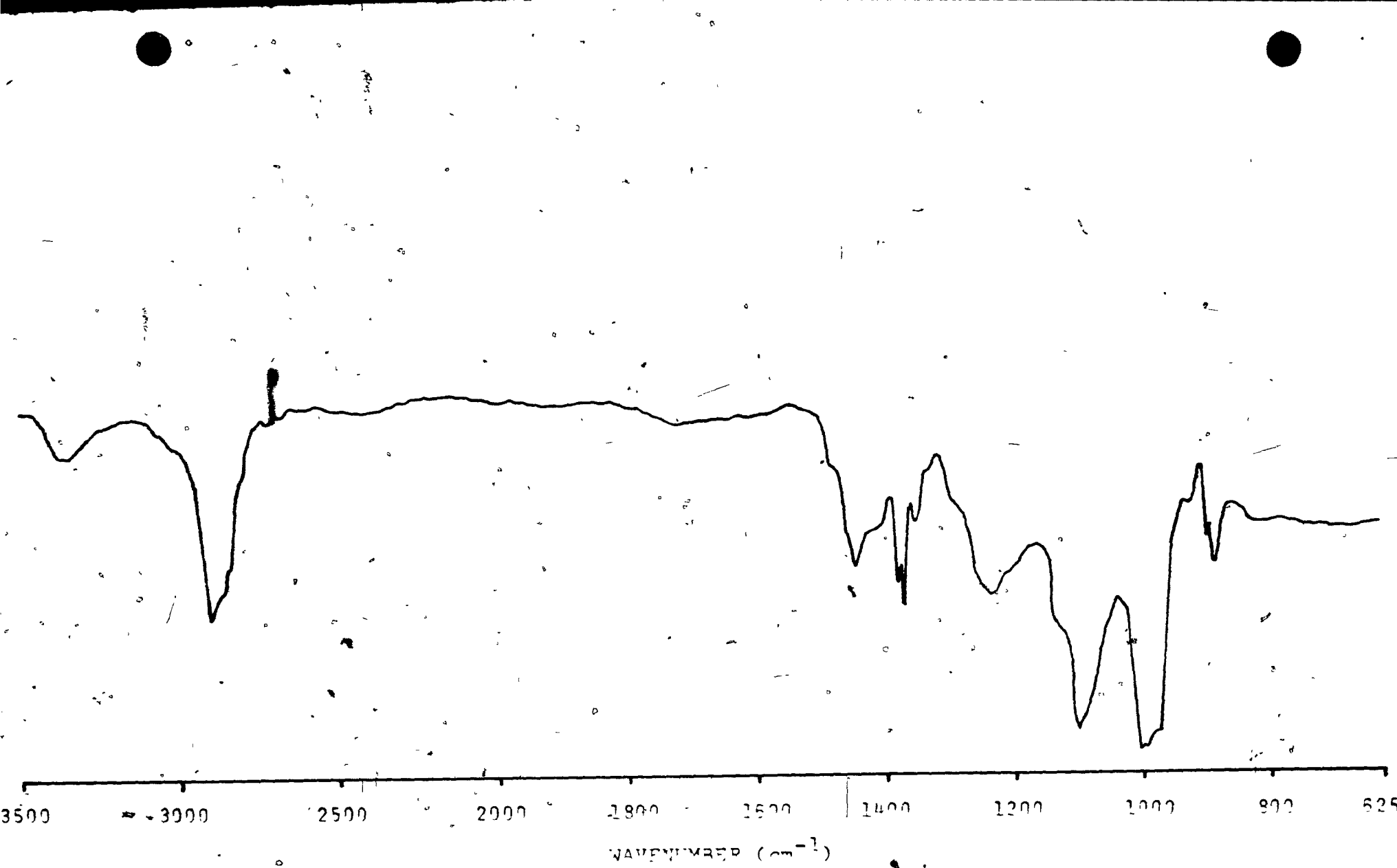


Fig. 12 - Infrared Spectrum ($CHCl_3$) of 3,4-Di(diisopropyl-phosphonato)-1,2,5,6-dibenzocyclooctadiene

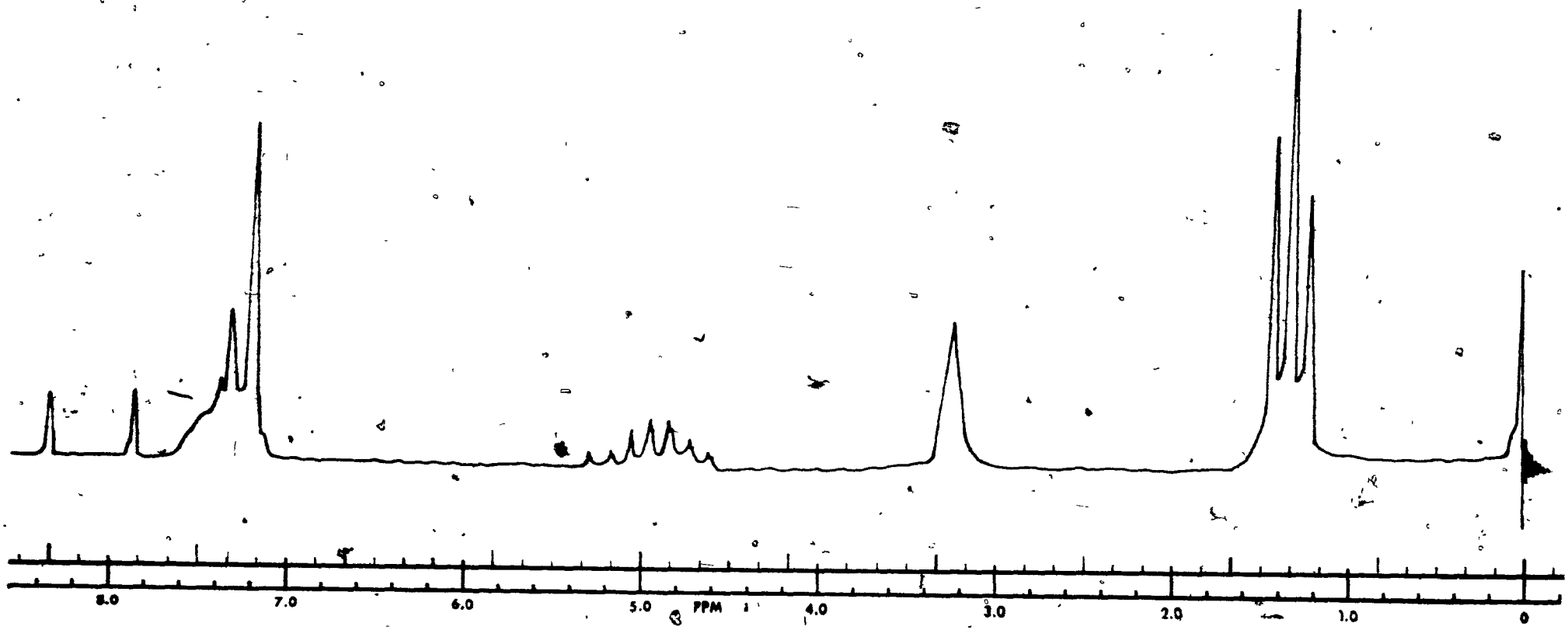


Fig. 1a - N.M.R. Spectrum of 3-(Diisopropylphosphonato)-7,8-dihydro-1,2,5,6-dibenzocyclooctatetraene

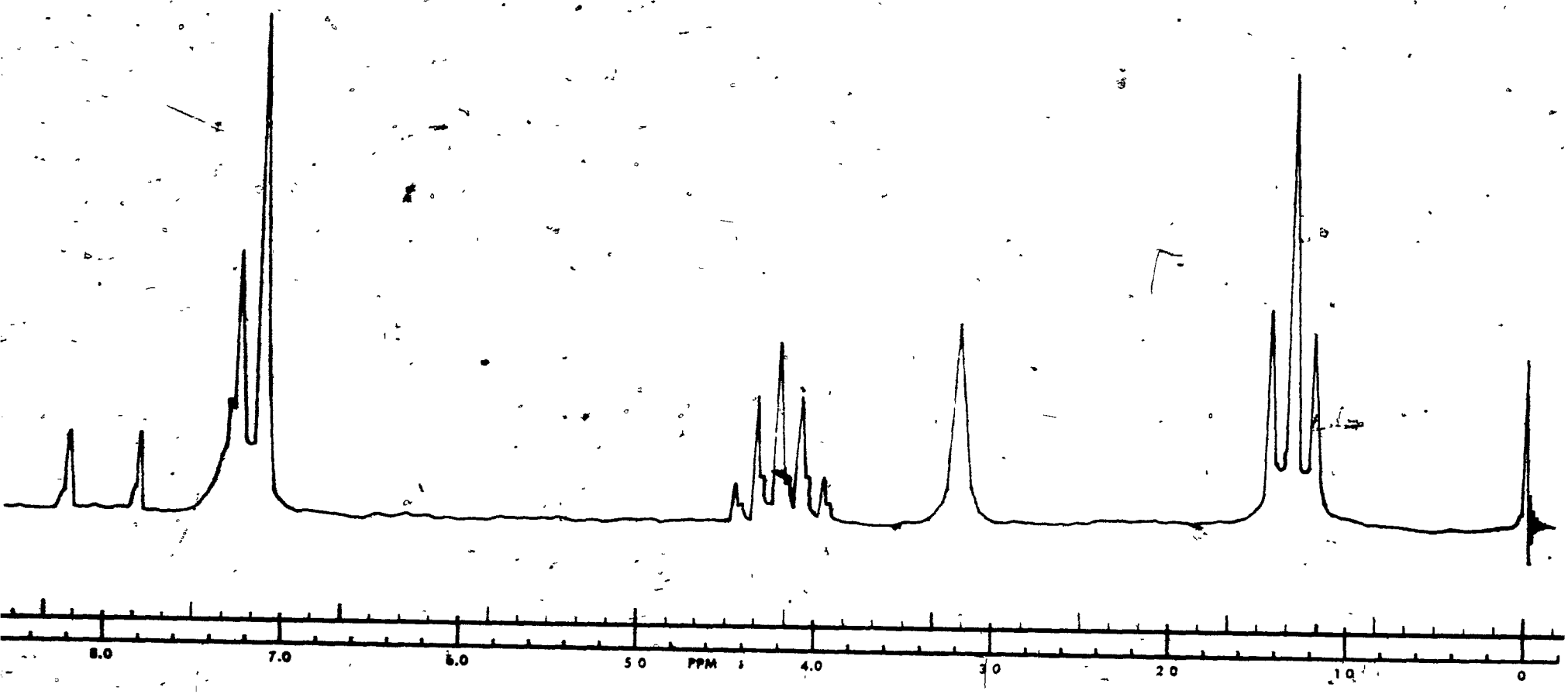


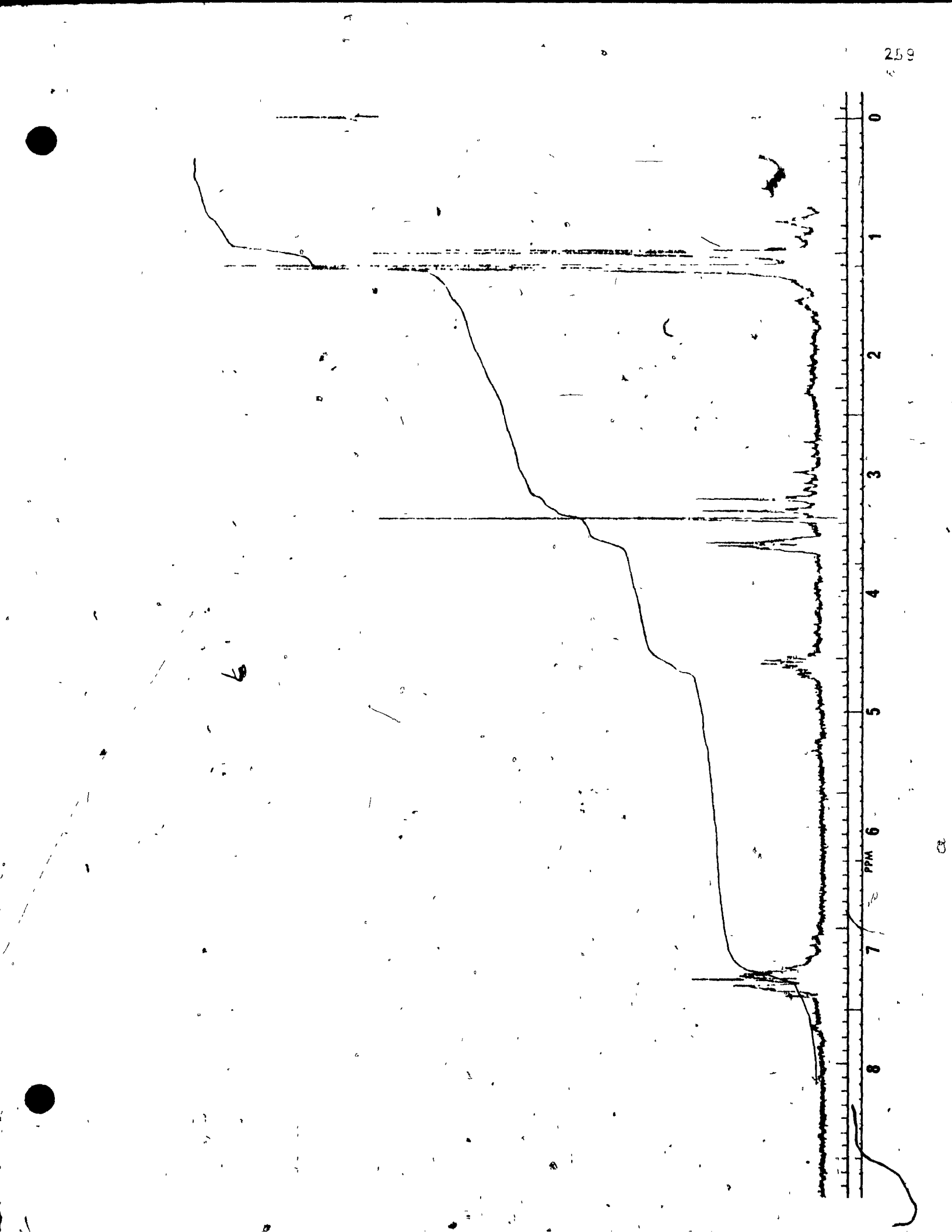
Fig. 14 - N.M.R. Spectrum of 3-(Diethylphosphonato)-7,8-dihydro-1,2,5,6-dibenzocyclooctatetraene

Fig. 15

220 MHz N.M.R. Spectrum of

3,4-di(diisopropylphosphonato)-

1,2,5,6-dibenzocyclooctadiene


0
1
2
3
4
5
6
PPM
7
8

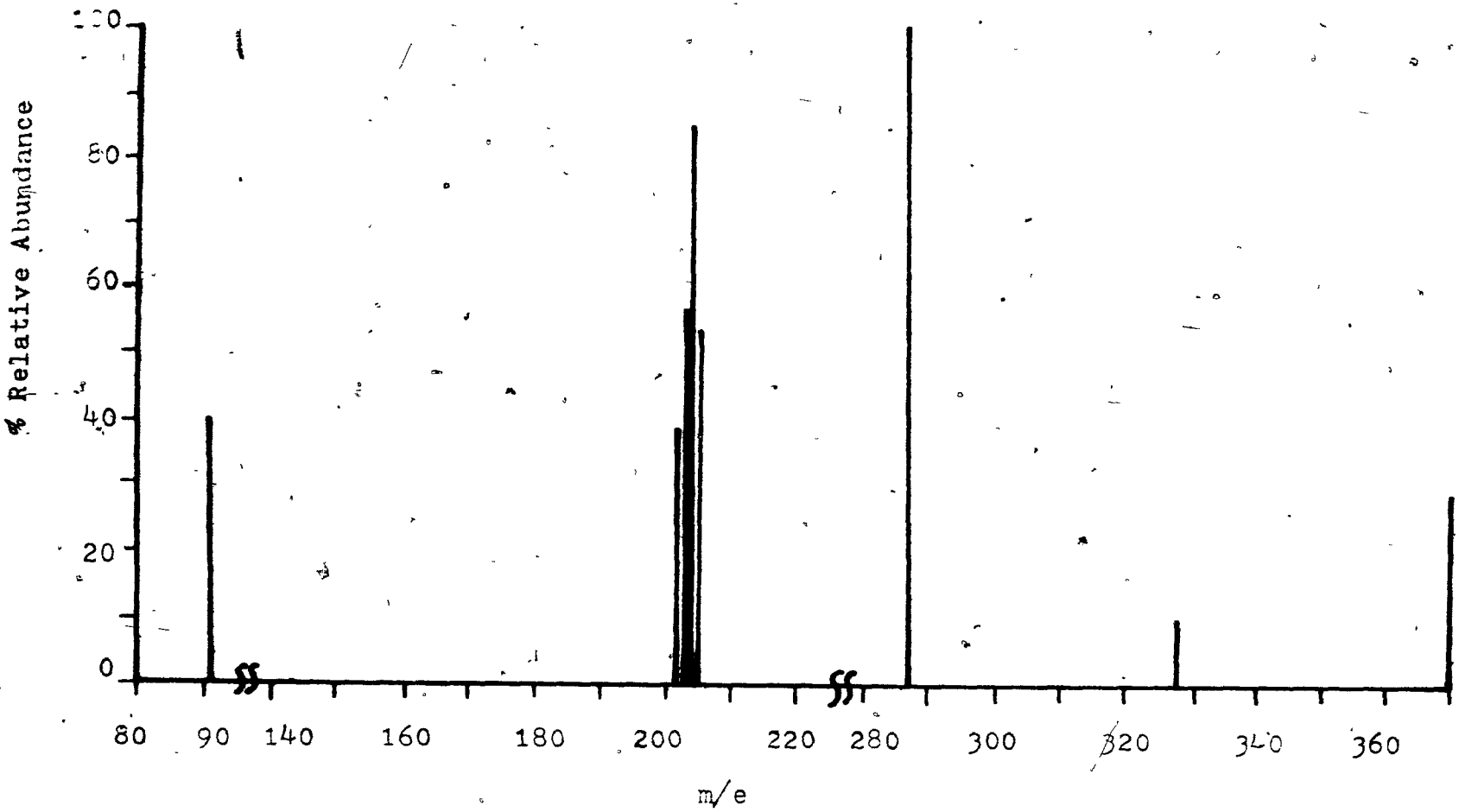


Fig. 16 - Mass Spectrum of 3-(diisopropylphosphonato)-7,8-dihydro-1,2,5,6-dibenzocyclooctatetraene

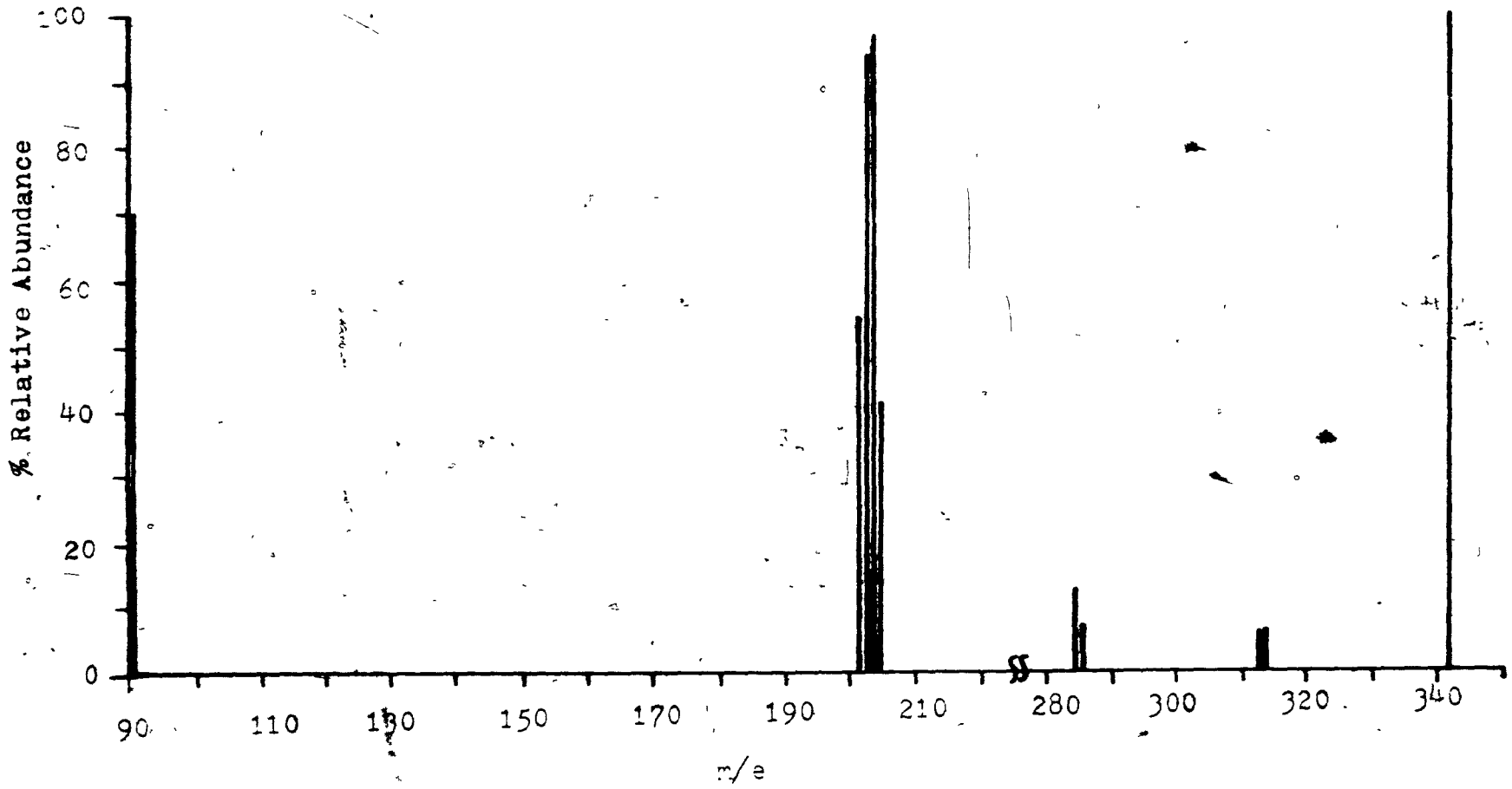


Fig. 17 - Mass Spectrum of 3-(diethylphosphonato)-7,8-dihydro-1,2,5,6-dibenzocyclooctatetraene

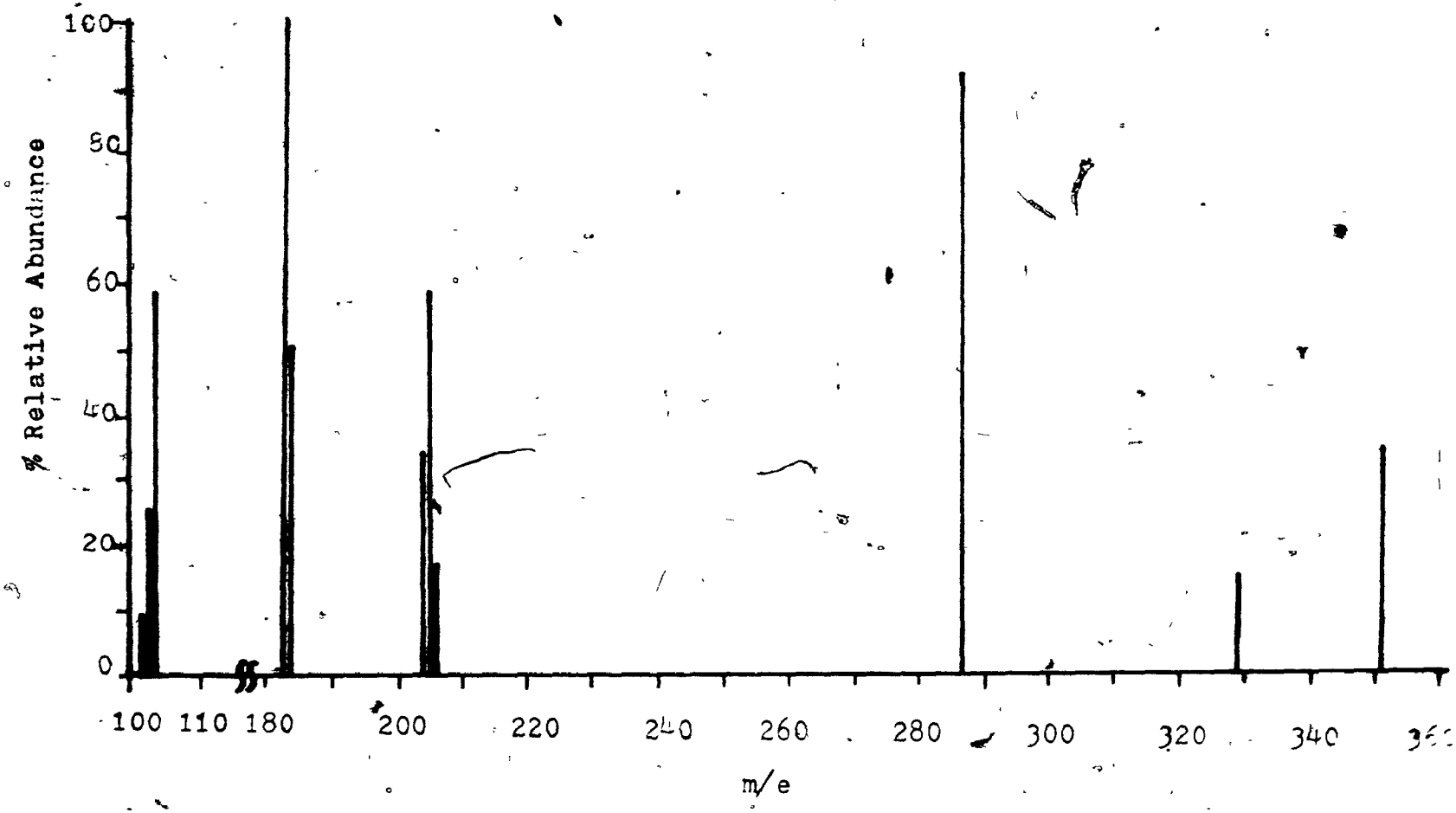


Fig. 18 - Mass Spectrum of 3,4-di(diisopropylphosphonato)-1,2,5,6-dibenzocyclooctadiene

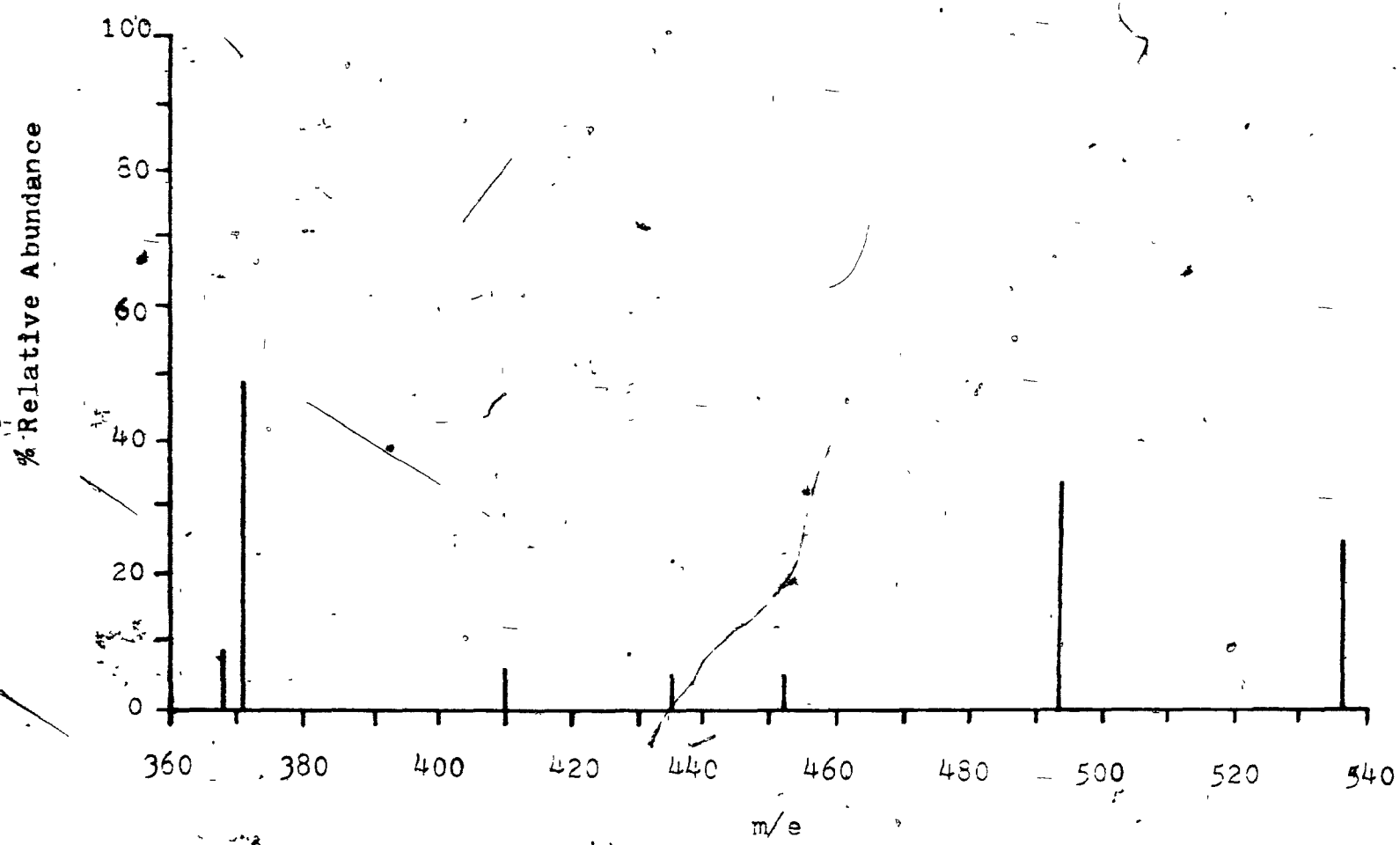

% Relative Abundance
100
80
60
40
20
0
360
380
400
420
440
460
480
500
520
540
m/e

Fig. 18 (con'd)

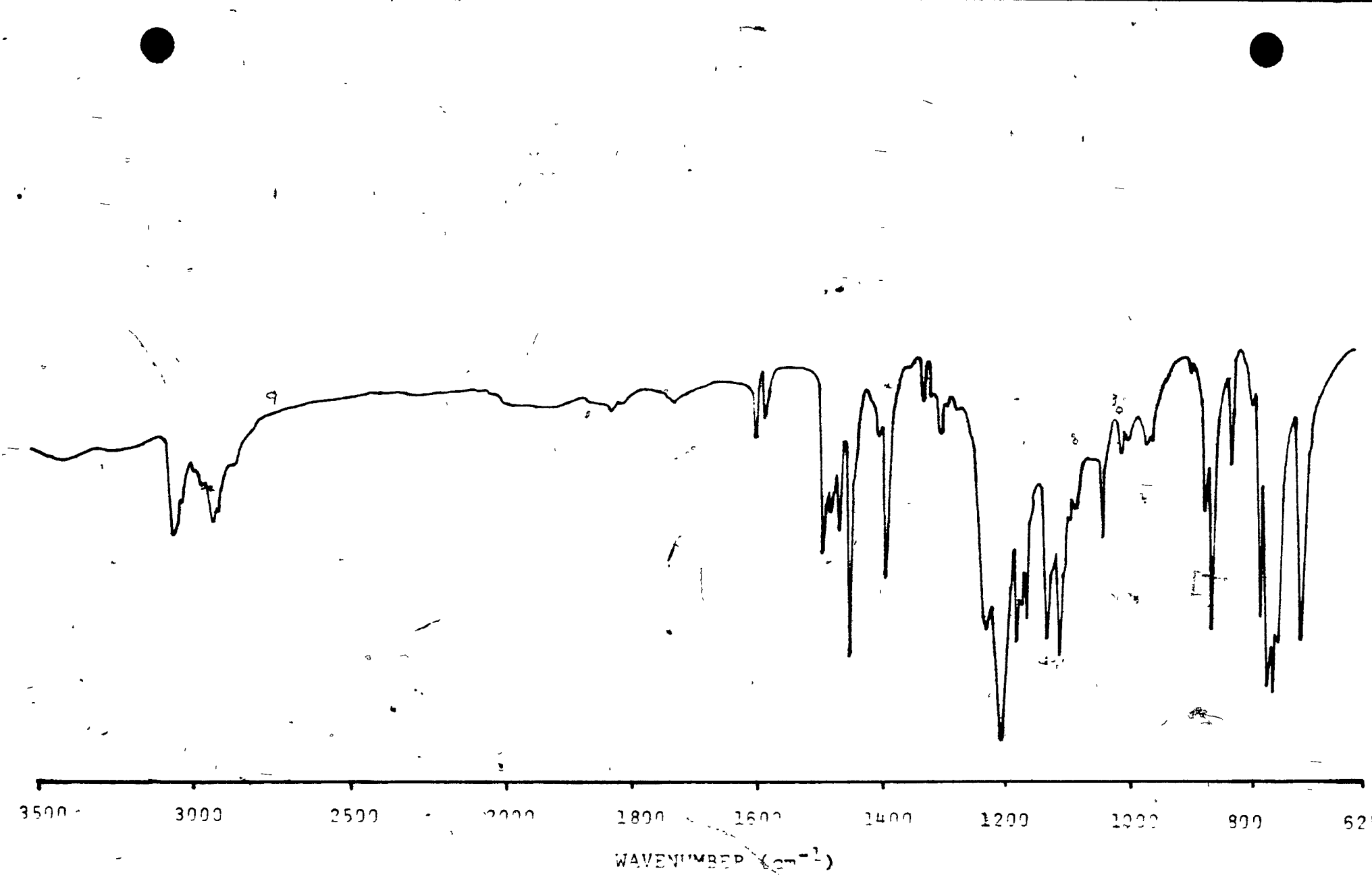


Fig. 19 - Infrared Spectrum (KBr) of 2-Phenylisophosphindoline 2-Oxide

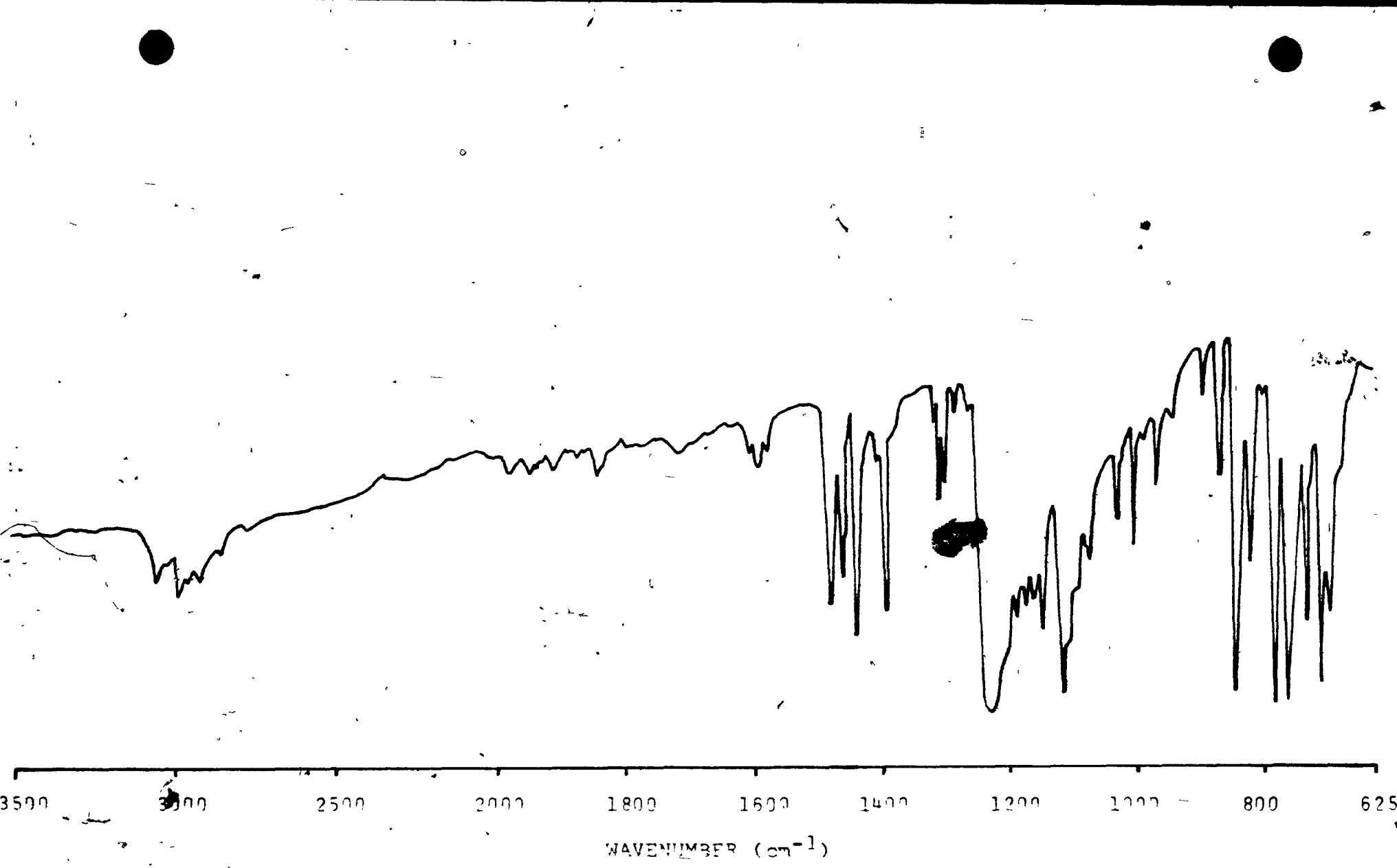


Fig. 20 - Infrared Spectrum (KBr) of n-1-Bromo-t-2-phenylisophosphindoline 2-Oxide

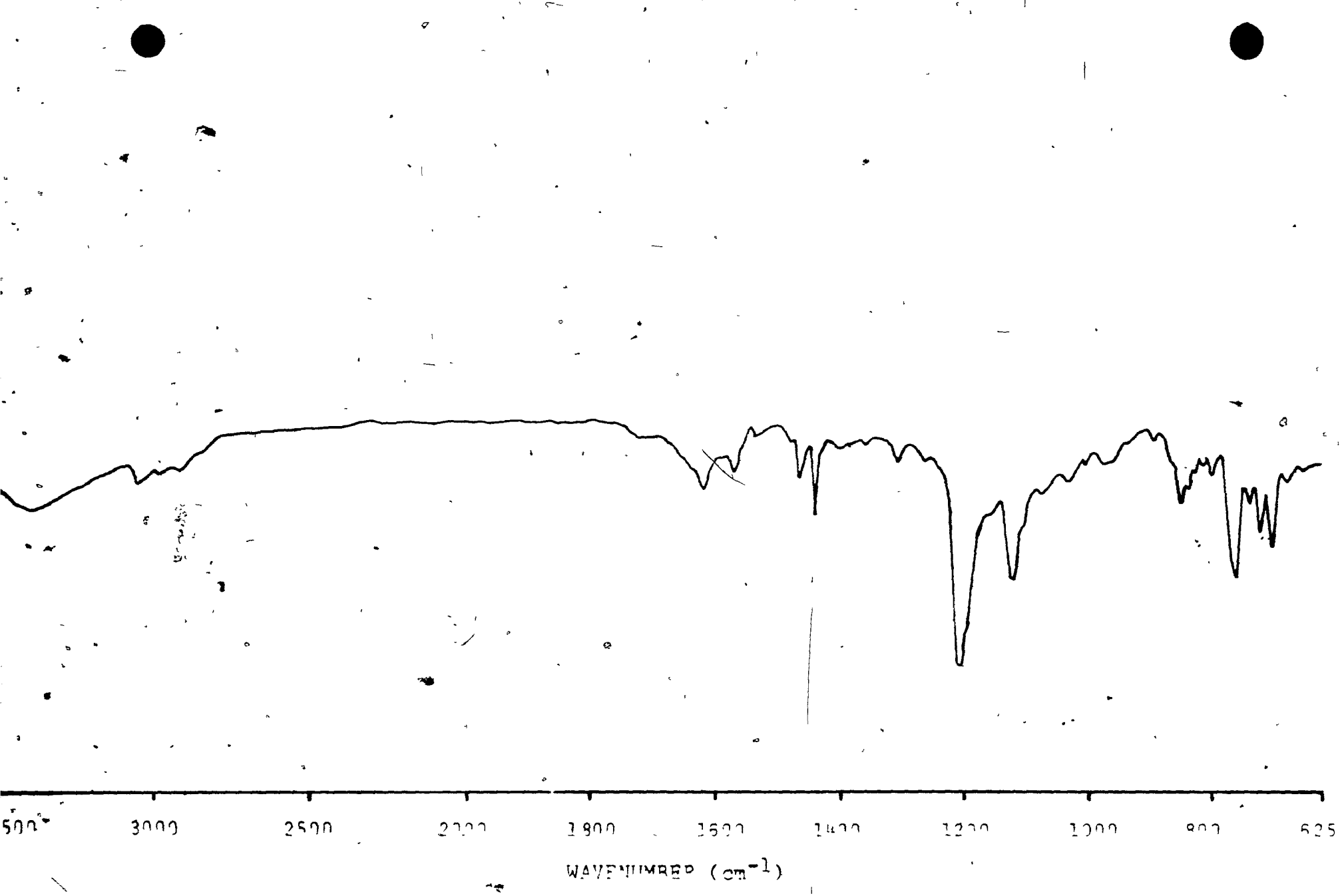


Fig. 21 -- Infrared Spectrum (KBr) of 3-Phenylisophosphindole 2-Oxide Dimer

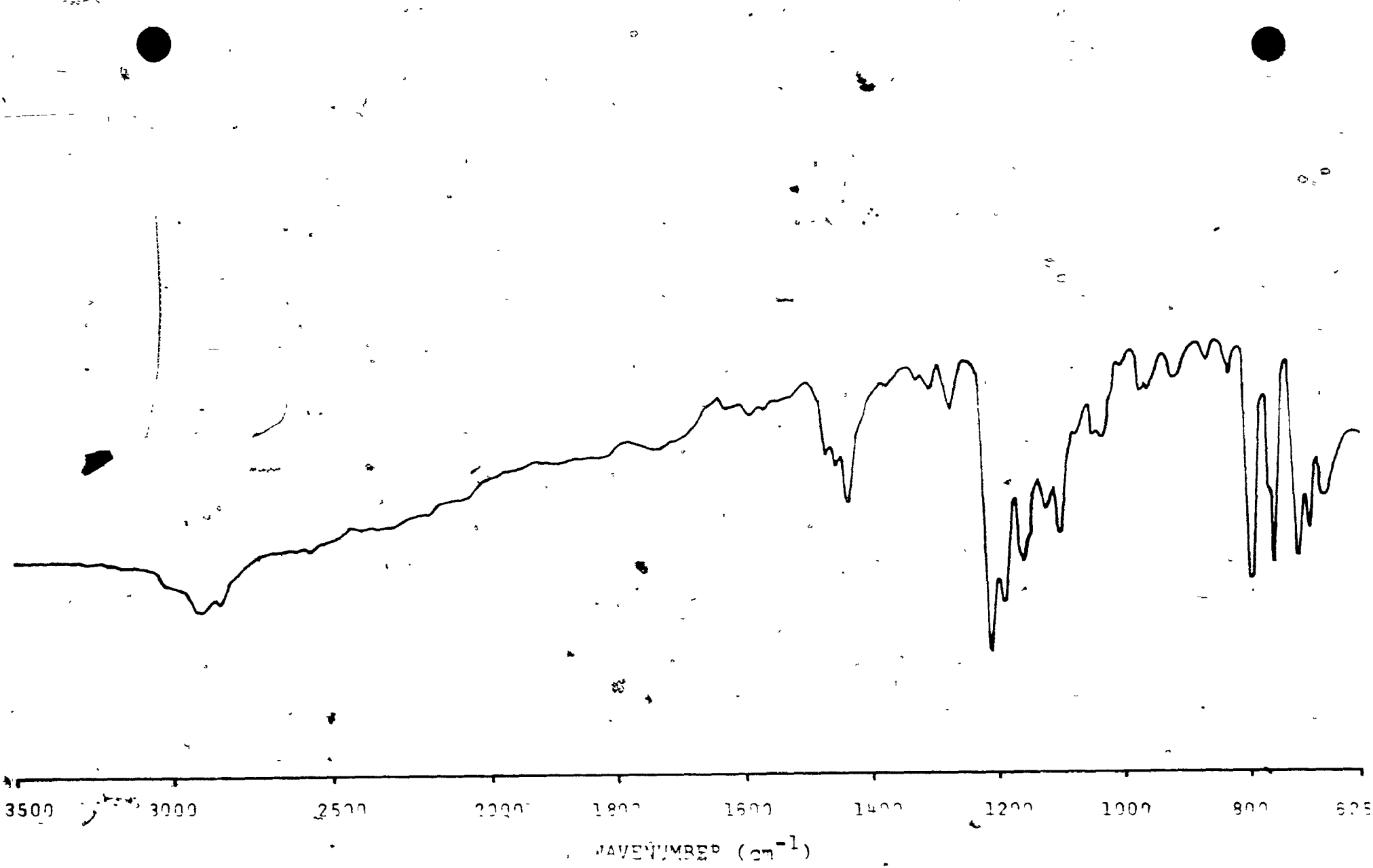


Fig. 22 - Infrared Spectrum (KBr) of 2-Phenylisophosphindole 2-Oxide-1,4-Cyclohexadiene Adduct

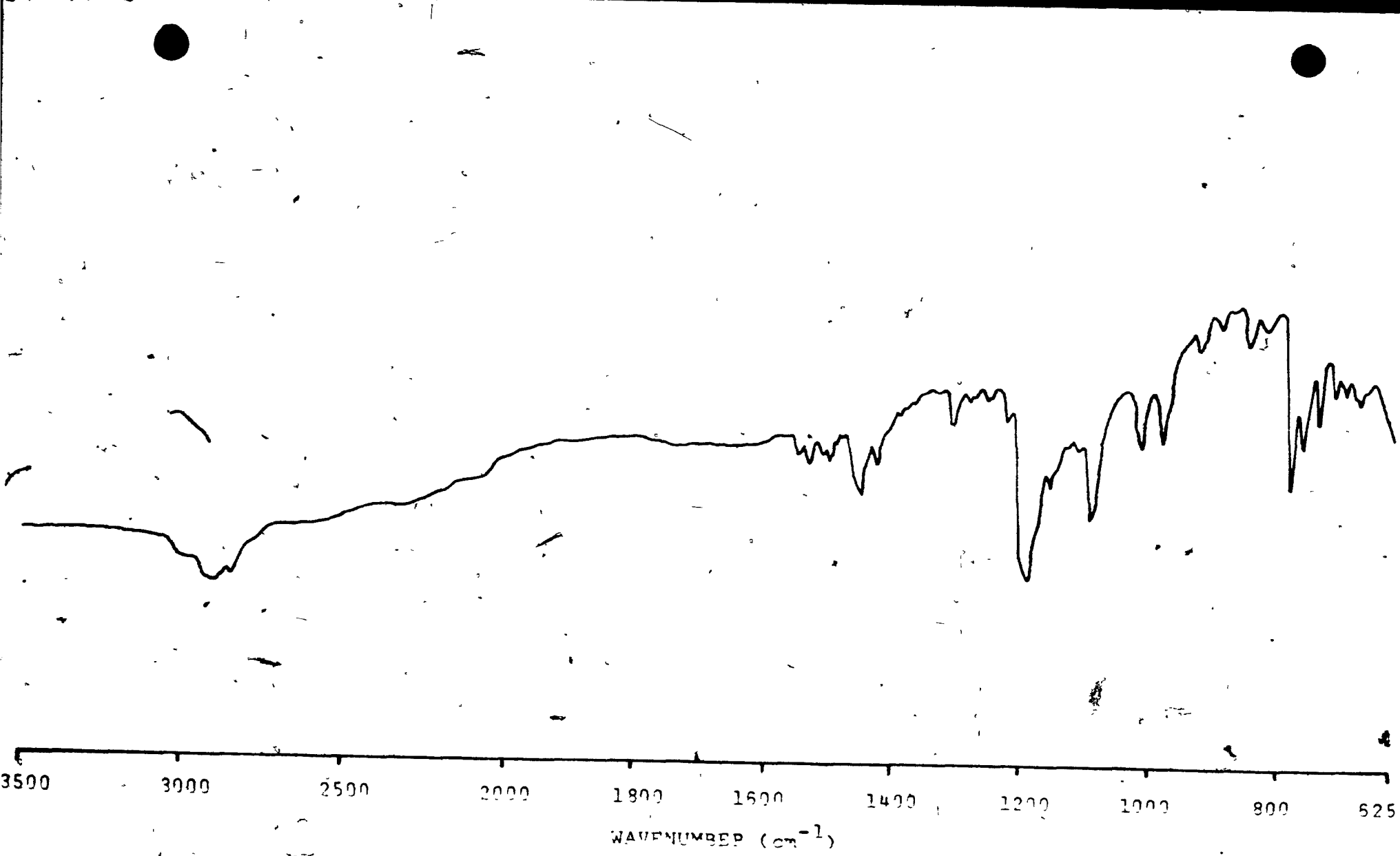


Fig. 23 - Infrared Spectrum (KBr) of 2-Phenylisophosphindole ^{2}-Oxide-2,5-Norbornadiene Adduct

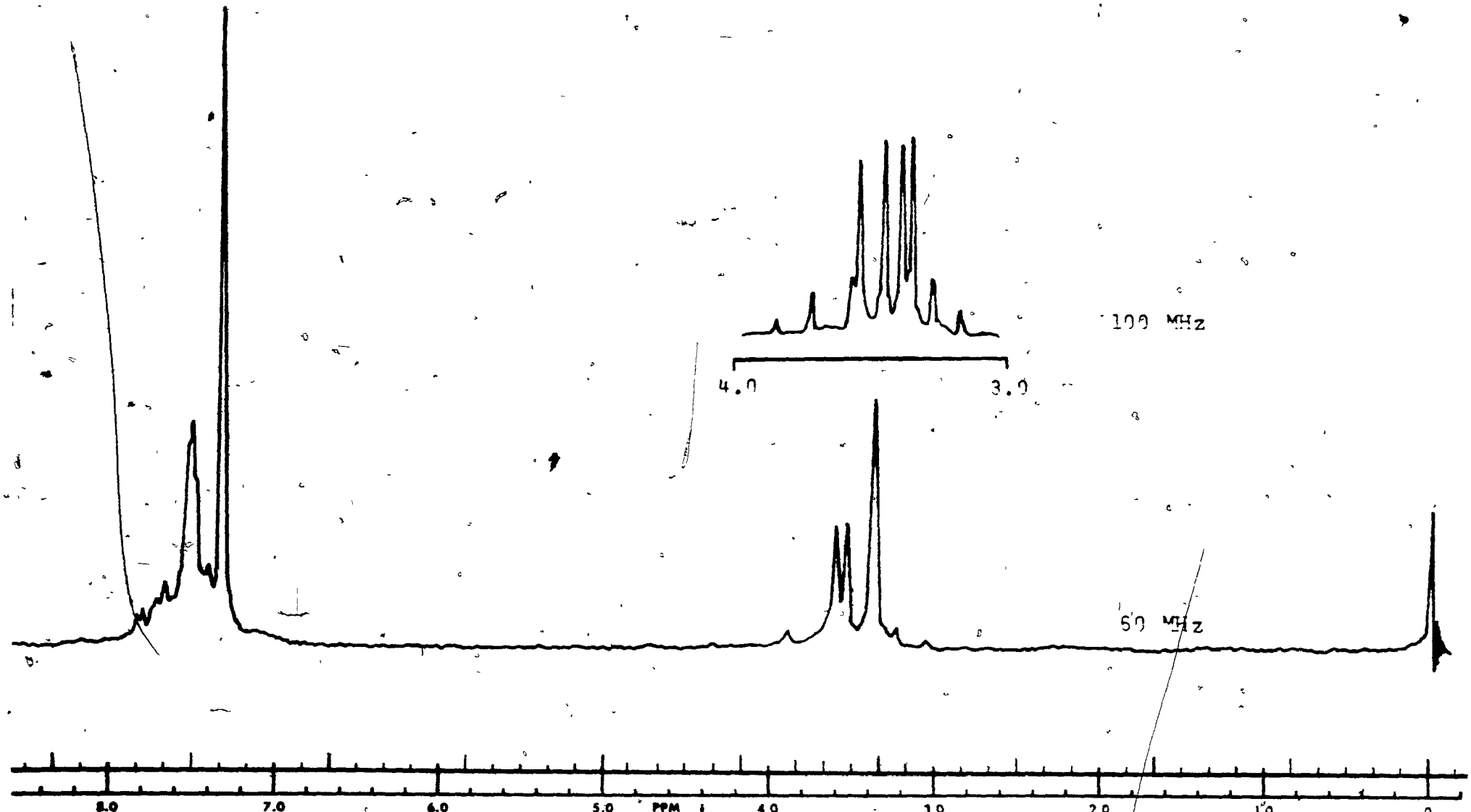


Fig. 2 - 60 MHz and 100 MHz N.M.R. spectra of 2-Phenylisophosphindoline 2-Oxide

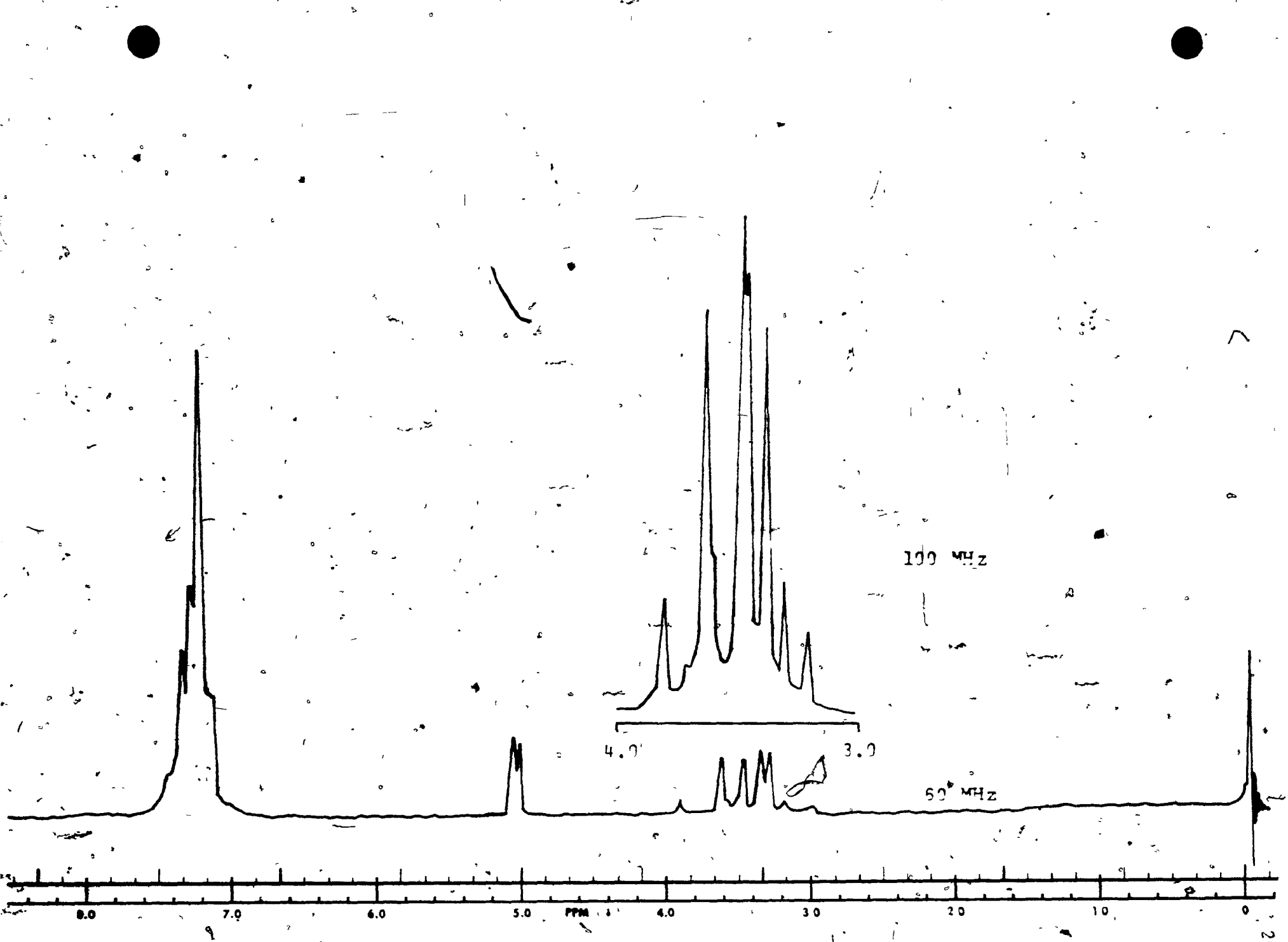


Fig. 25 - 60 MHz and 100 MHz N.M.R. spectra of

<u>D</u>-1-Bromo-<u>t</u>-2-phenylisophosphindoline 2-oxide

Fig. 26

220 MHz N.M.R. Spectrum of

2-Phenylisophosphindole 2-Oxide Dimer

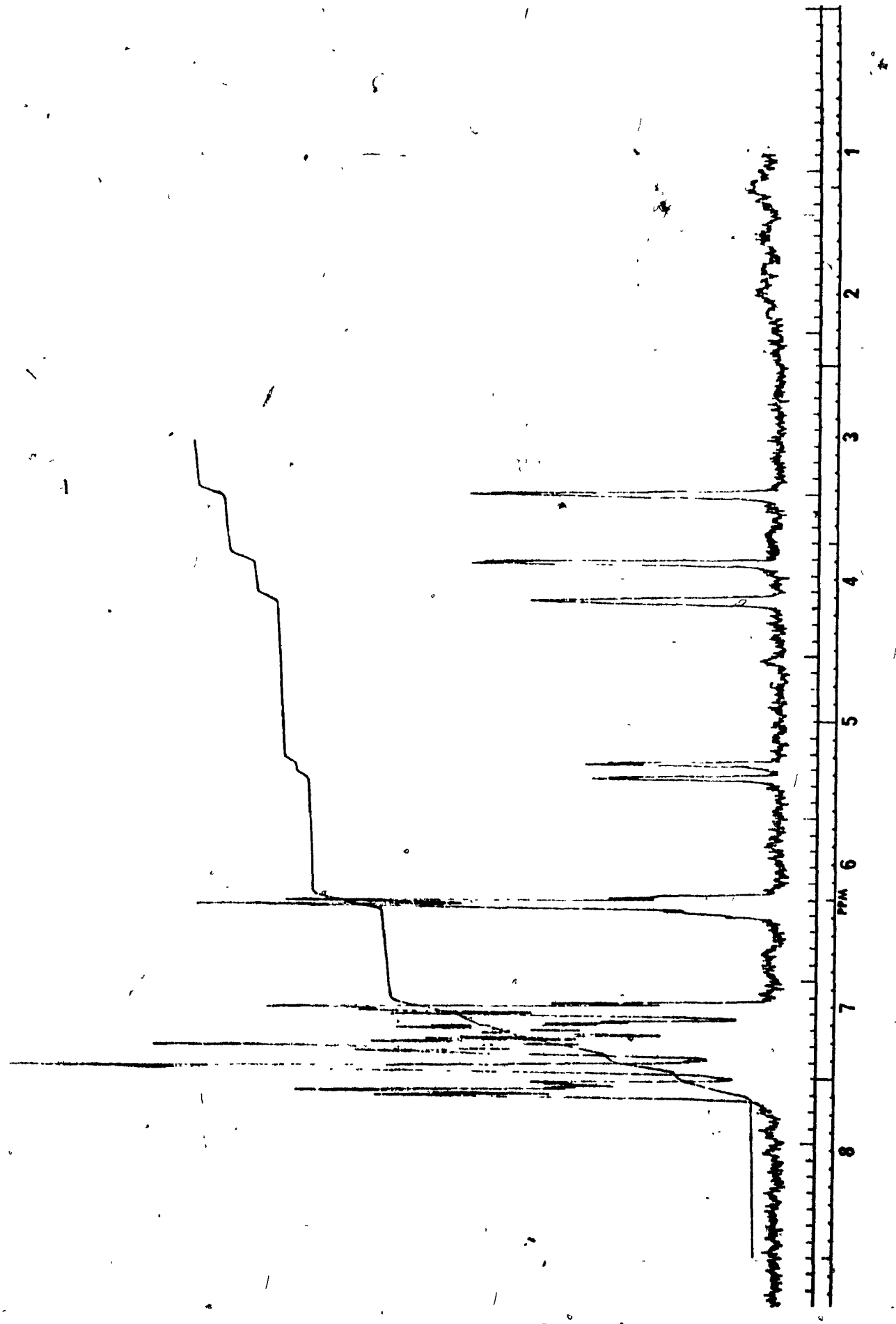
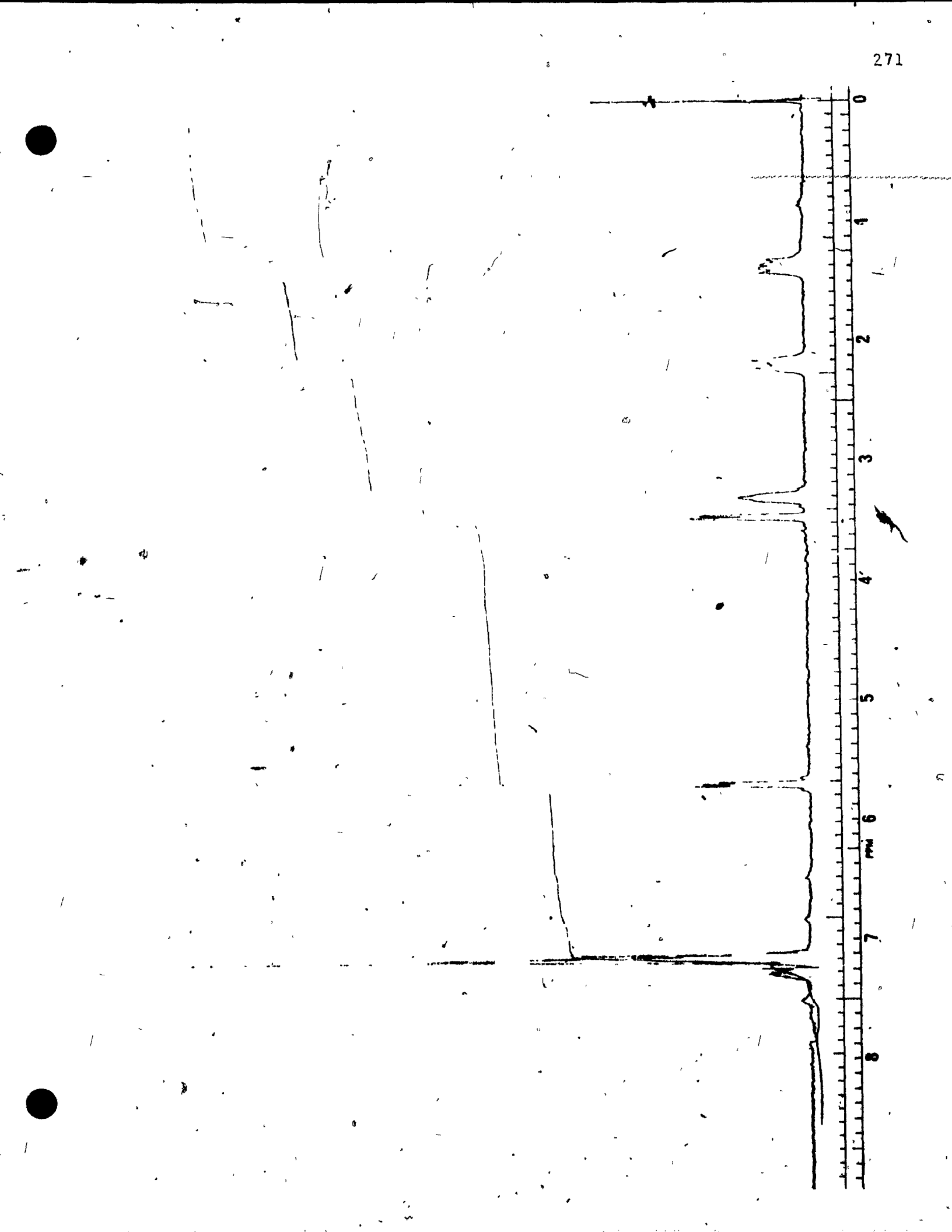

1
2
3
4
5
6
PPM
7
8

Fig. 27

220 MHz N.M.R. Spectrum of 2-Phenyliso-phosphindole 2-Oxide-1,4-Cyclohexadiene Adduct


0
1
2
3
4
5
6
7
8
PPM

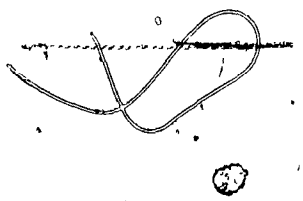
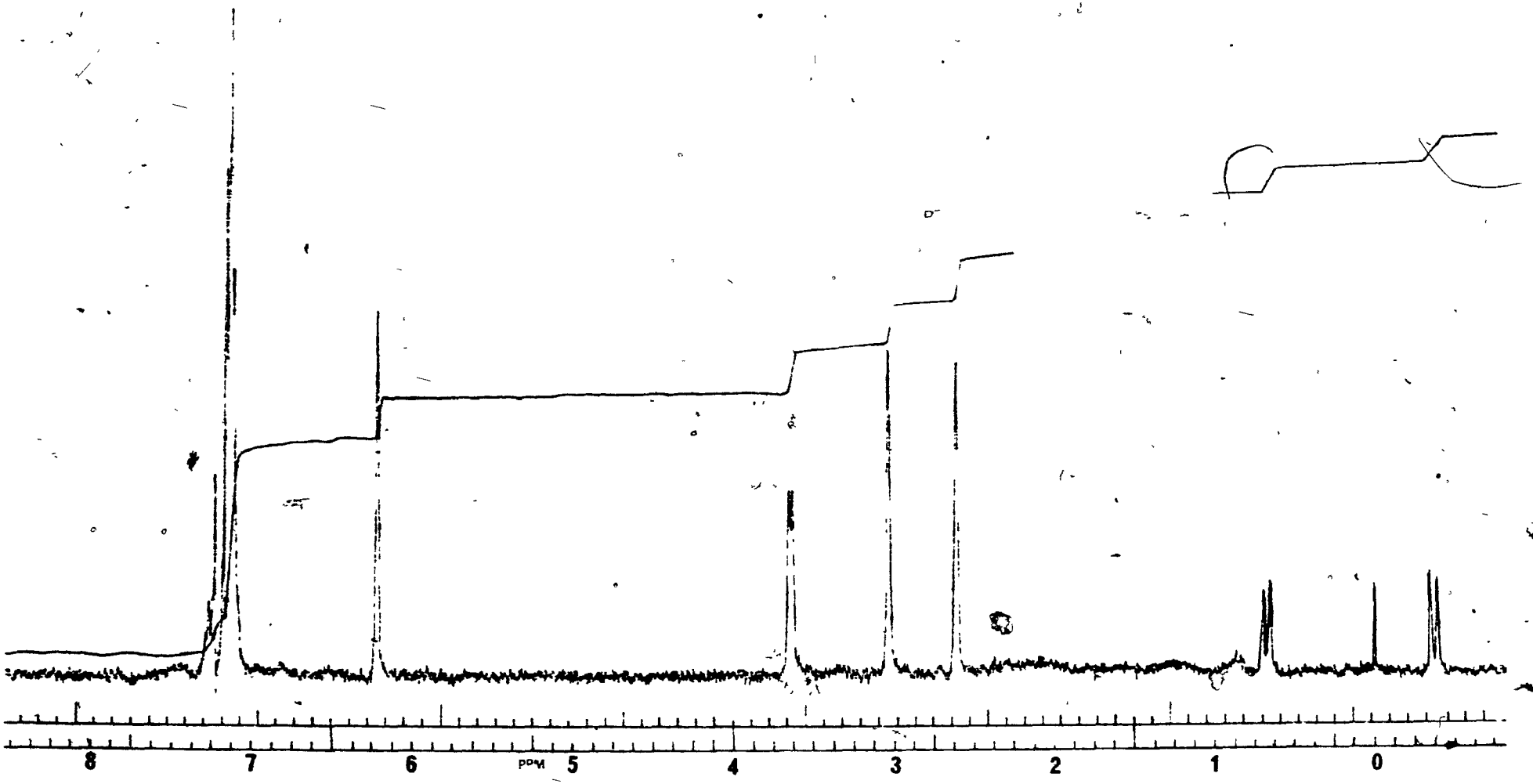


Fig. 28

220 MHz N.M.R. Spectrum

of 2-Phenylisophosphindole

2-Oxide-2,5-Norbornadiene Adduct


8
7
6
ppm
5
4
3
2
1
0

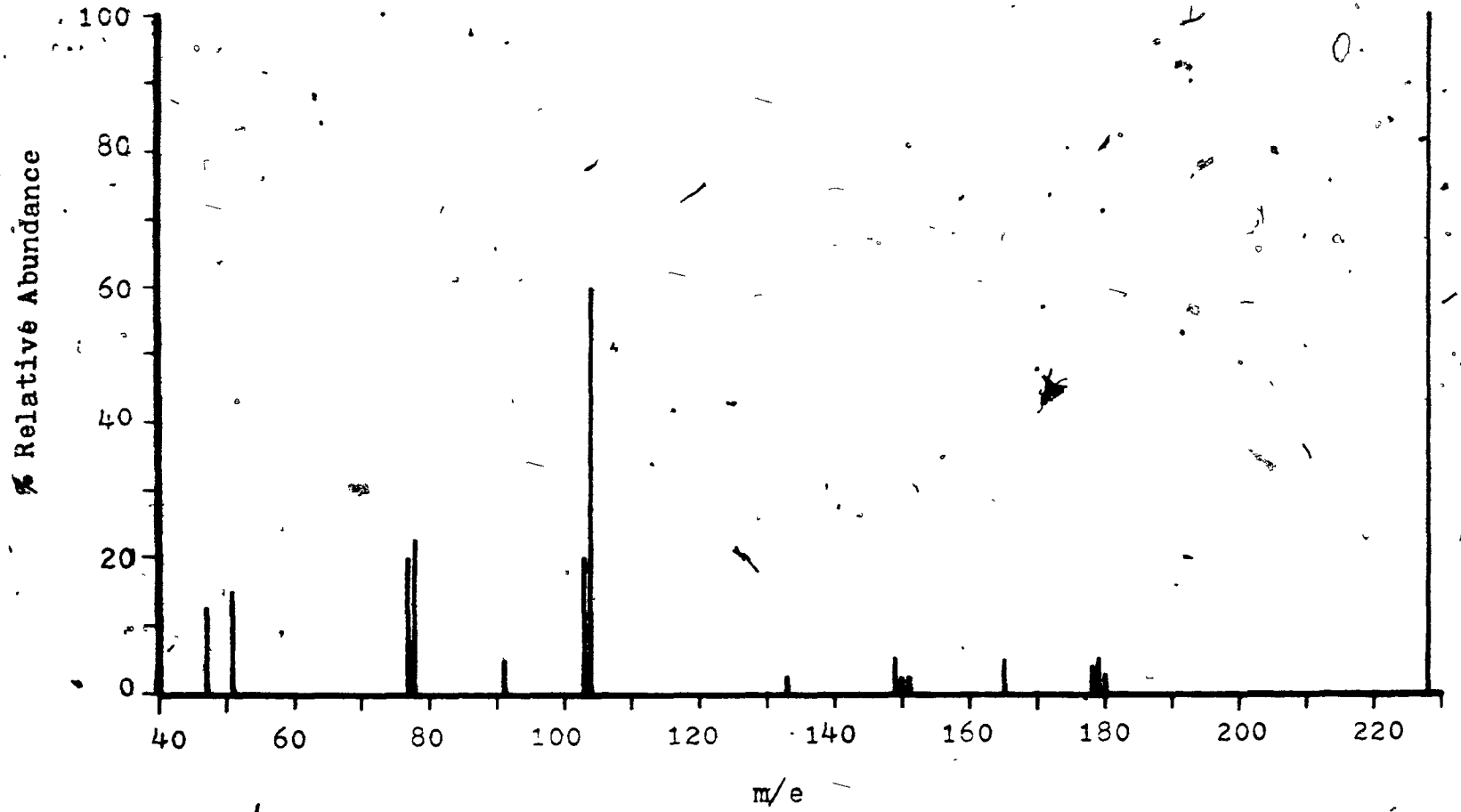


Fig. 29 - Mass Spectrum of 2-Phenylisophosphindoline 2-Oxide

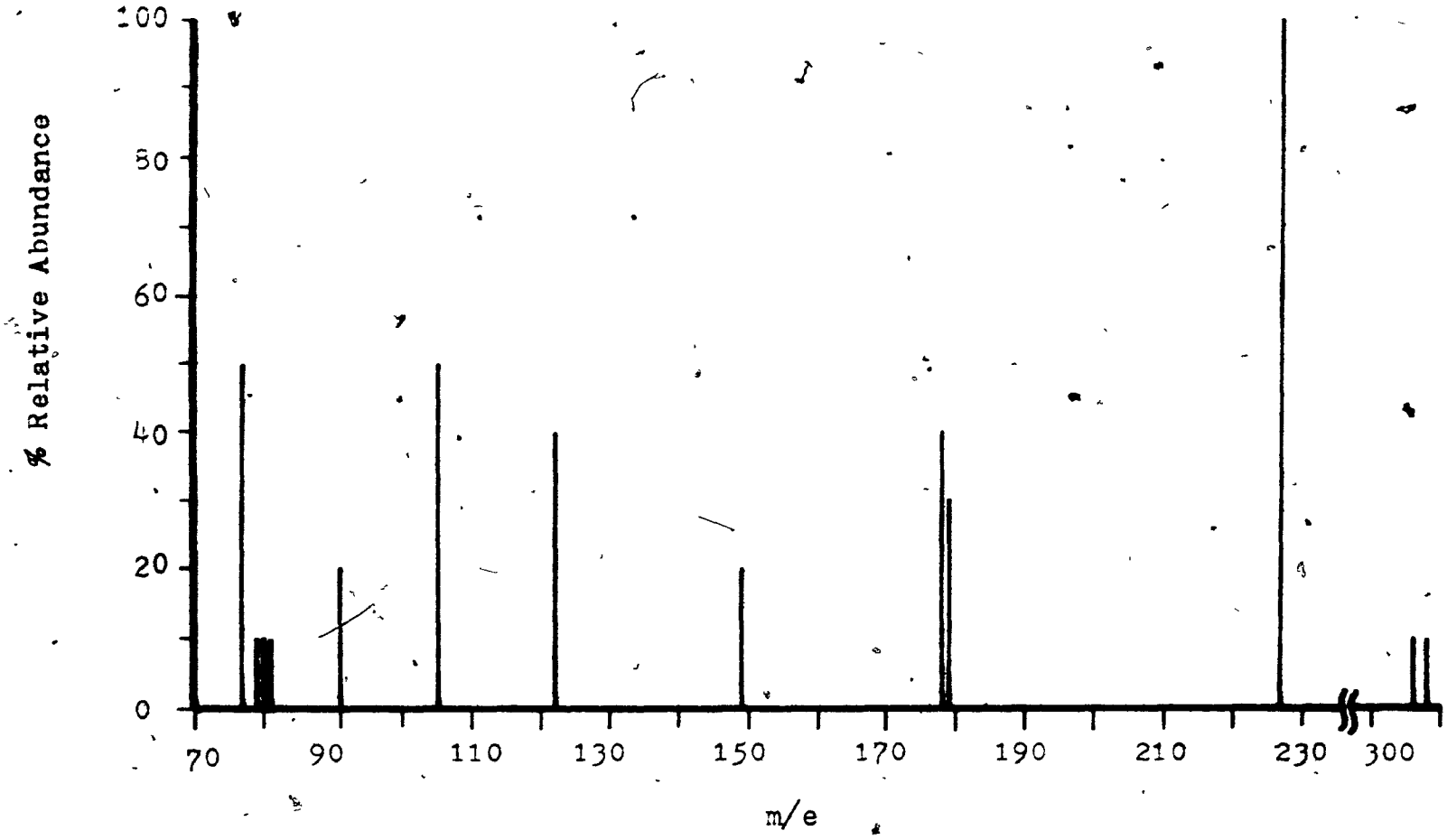


Fig. 30 - Mass Spectrum of r-1-Bromo-t-2-phenyl-isophosphindoline 2-Oxide

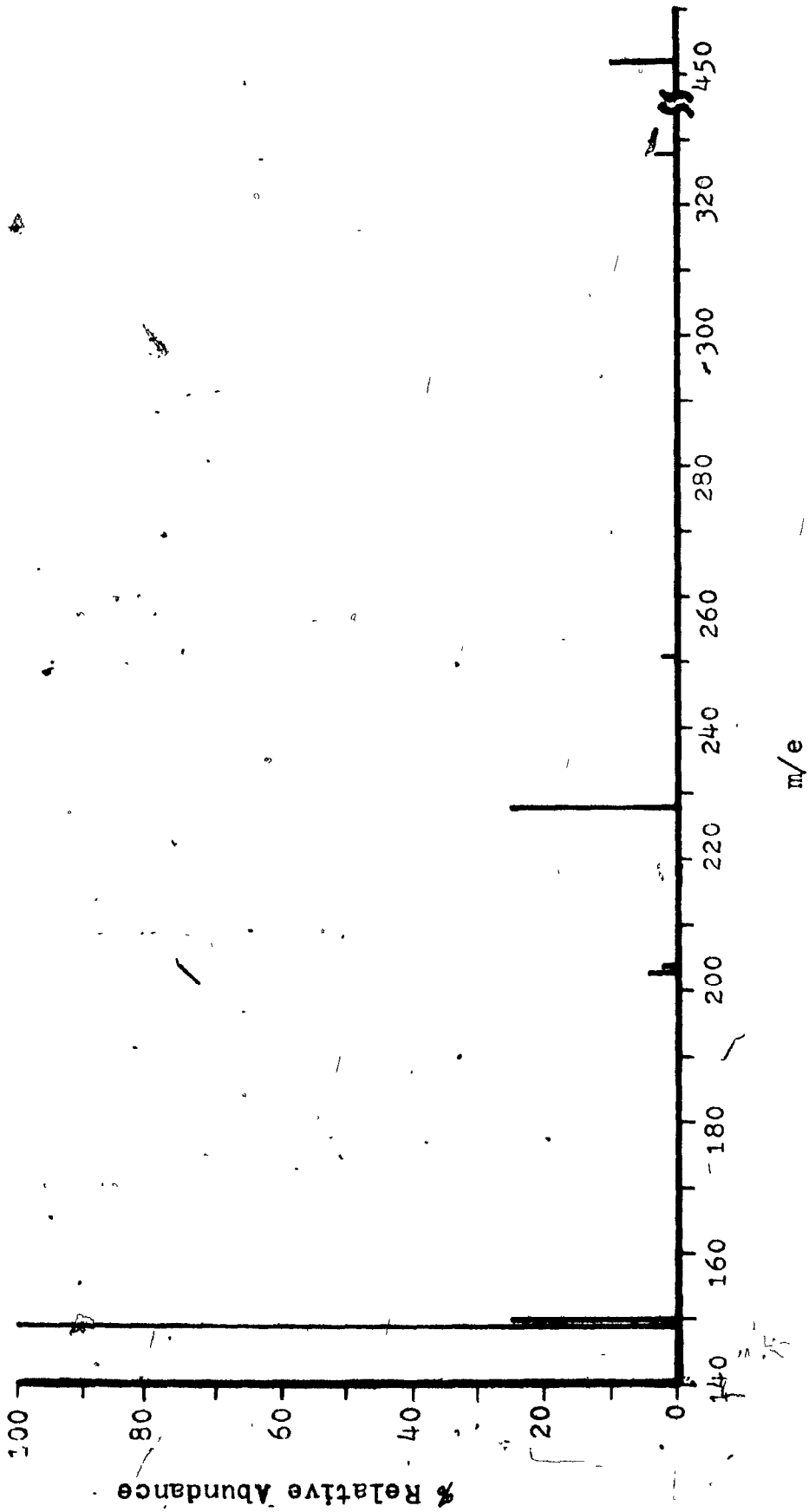


Fig. 31 - Mass Spectrum of 2-Phenylisophosphindole 2-Oxide Dimer

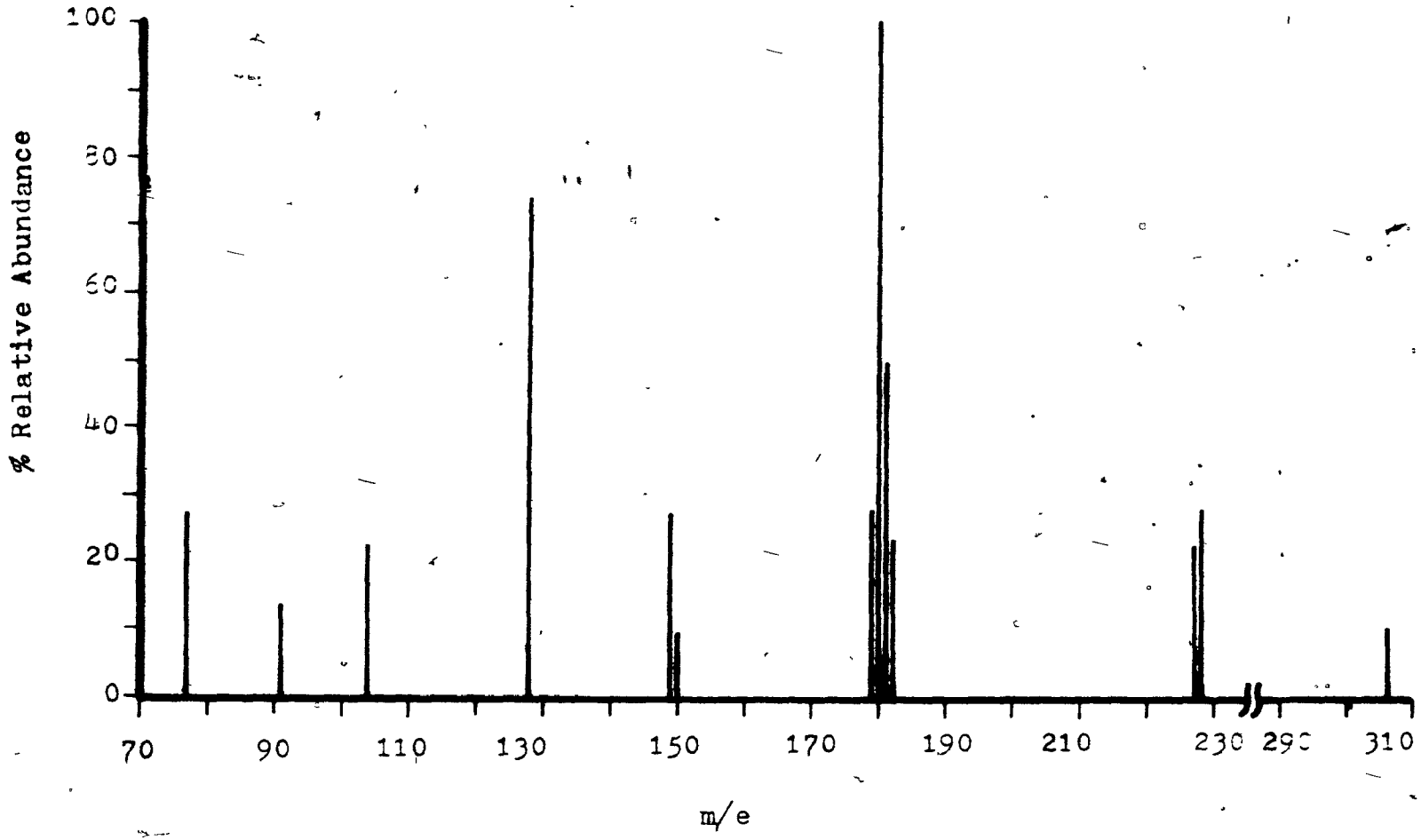


Fig. 32 - Mass Spectrum of 2-Phenylisophosphindole 2-Oxide-1;4-Cyclohexadiene Adduct

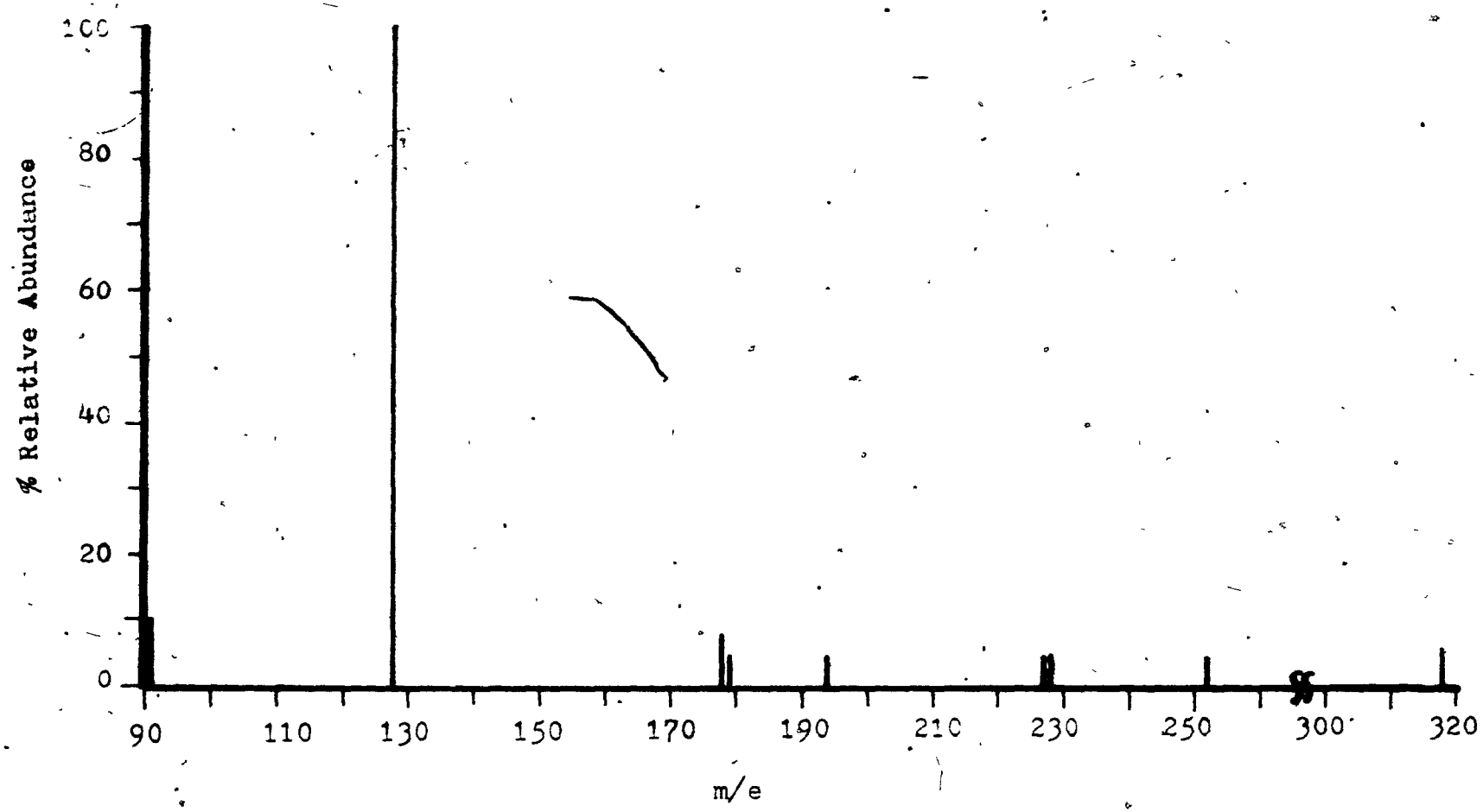


Fig. 33 - Mass Spectrum of 2-Phenylisophosphindole 2-Oxide-2,5- Norbornadiene Adduct

Fig. 34 - Ultraviolet Spectrum of 2-Phenylisophosphindoline 2-Oxide