SYNTHETIC APPROACHES TO PHOSPHASTEROIDS AND RELATED C-P HETEROCYCLES. RESOLUTION OF CYCLIC PHOSPHONIUM SALTS

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in the memory of

my father

...

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CHAPTER I

HISTORICAL

To date, the most comprehensive review about the chemistry of carbon-phosphorus heterocycles in the literature was published in late 1969.[15] An extensive survey *via* Chemical Abstracts was made through December 31, 1966, with most of the papers published in early 1967 also included.

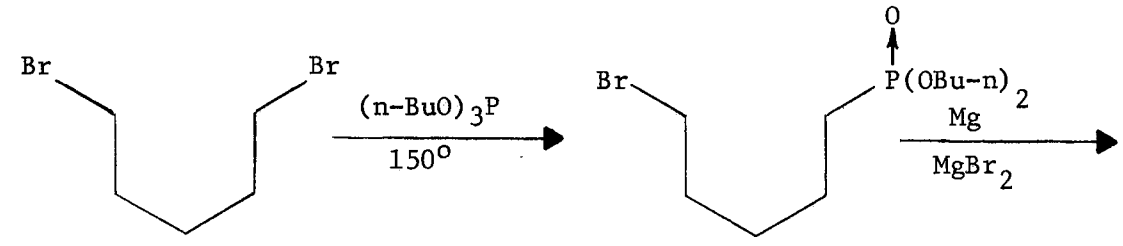
The present historical review will treat recent literature concerning C-P heterocycles since January of 1967. Chemical Abstracts has been searched through July 6, 1970, and most of the current publications through July 31, 1970 have also been surveyed. The rapid progress in this field has been tremendous and most fascinating, as revealed by the appearance of nearly 190 articles and patents about C-P heterocycles throughout the world within the last 3 years. Since a comprehensive review of all the recent literatures (since 1967) concerning C-P heterocyclic chemistry is beyond the scope of this thesis, discussion will be primarily focused on the recent developments in syntheses, reactions, and structure determinations of six-membered C-P heterocycles containing only one phosphorus atom in the ring system. A list of all articles concerning C-P heterocycles which have been published since 1967 (through July 31, 1970) is incorporated at the end of this chapter, except the references which were published in the review of Berlin and Hellwege.[15]

The last part of this chapter will be devoted to the history and development of the resolution of quaternary phosphonium salts, with special attention given to the resolving agents that have been successfully used in the literature in effecting the resolutions.

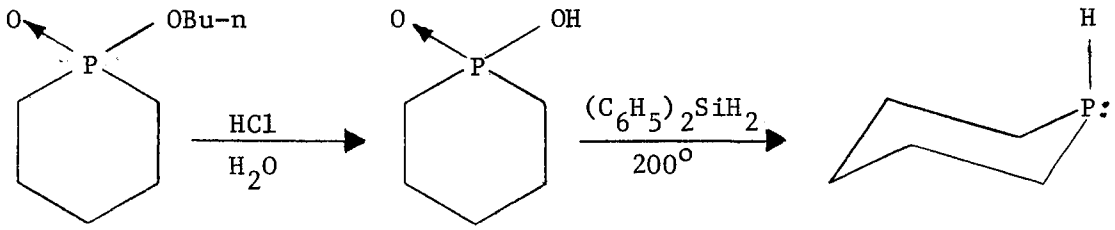
I. Recent Developments in The Syntheses and Chemistry of Six-membered C-P Heterocycles.

A. Derivatives of Simple Phosphorinanes.

The simplest phosphorinane (phosphacyclohexane) (3) was prepared by a known procedure.[15] The method involved an intramolecular Grignard reaction of 1 as the crucial cyclization step, followed by reductions of 2 with diphenylsilane to the desired product 3. The conformation preference of the proton on phosphorus in 3 was determined to be almost



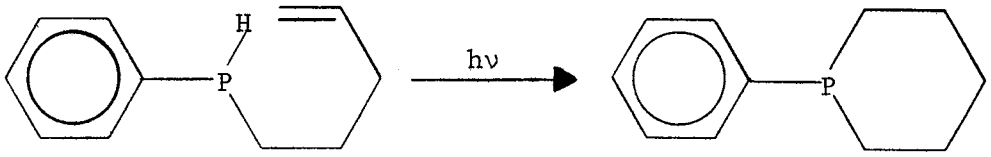
1



2 3

entirely axial[77] by analysis of its NMR coupling pattern and ^{31}P decoupling experiment ($J_{^{31}P-H}$ = 200 ± 10 Hz and J_{ae} = 2.5 Hz) at -50°. It was concluded that no more than 10% of the equatorial isomer could have been present but not detected. However, it should be noted that the phosphorus atom is assumed to be nearly p hybridized, so the nonbonding electron pair resides in an orbital of very high s charactor. The lone pair must therefore have little or no directionality and the properties and interactions of the proton alone must determine its comformational preference.[138] This assumption is based on measurements of the C-P-H and H-P-H bond angles in CH_3PH_2 and thus must be viewed with caution for a C-P heterocycle.

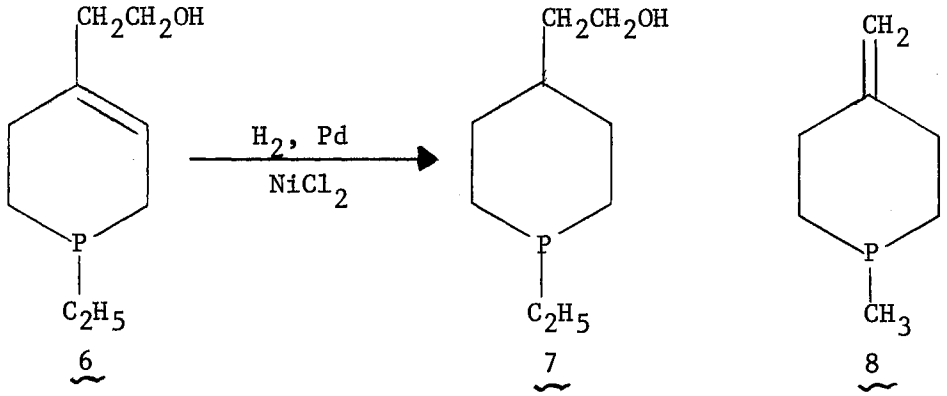
Cyclic phosphines were prepared by UV irradiation of secondary alkenylphosphines in which the double bond of the alkenyl group is either a terminal double bond separated from the P atom by 2-4 carbon atoms or a nonterminal double bond separated from the P atom by 3 carbon atoms.[15] 1-Phenylphosphorinane (5) was synthesized, according to a recent patent,[123] by irradiating (4-pentenyl)phenylphosphine (4)



4 5

in boiling petroleum ether with 3600-Å light for 80 hr. However, no detailed experimental data as to the yield and the purity of the product were recorded.

Hydrogenation of 1-ethyl-4-(2-hydroxyethyl)-1,2,5,6-tetrahydrophosphorin (6) to the corresponding phosphorinane 7 has recently been achieved by Quin and coworders *via* its nickel chloride complex.[116] The hydrogen uptake proceeded slowly and was completed in about 7 days

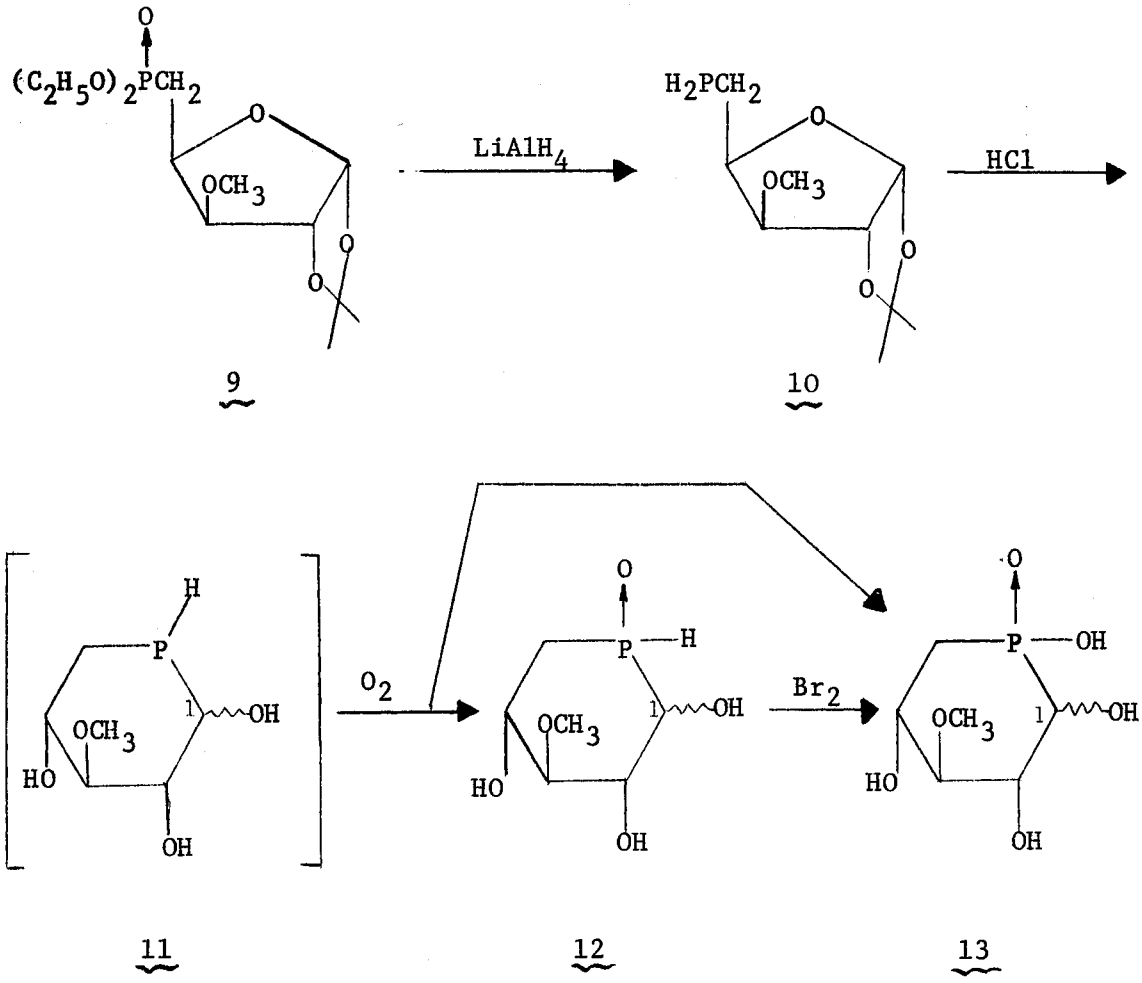


6 7 8

to give a 59% crude yield of 1-ethyl-4-(2-hydroxyethyl)phosphorinane (7) (b.p. 83-5°/0.15 mm). No stereochemical assignment of the product was reported. A related phosphorinane derivative 8, however, failed to undergo the reduction.

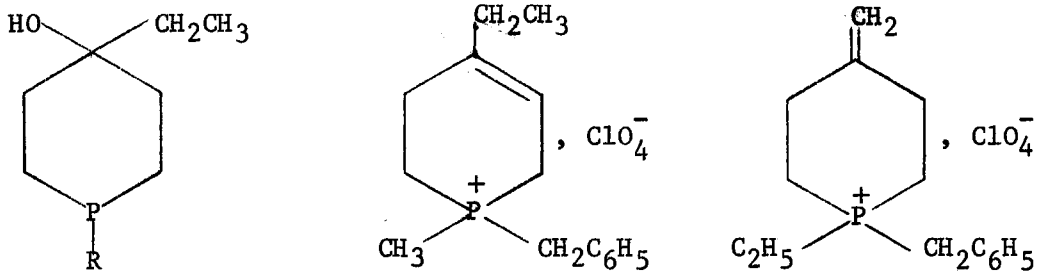
Synthesis of sugar analogs with phosphorus as the heteroatom,[137] 5-deoxy-3-O-methyl-5-(phosphine oxide)-D-xylopyranose (12) and the corresponding phosphinic acid 13, was claimed in yields of 15% and 3.5%, respectively, by a unique reaction involving acid treatment of the intermediate 10, followed by air oxidation. The phosphonate 9 was obtained *via* the usual Arbuzov reaction from the corresponding bromide (or tosylate) and triethyl phosphite. The phosphine oxide 12 could also be converted into 13 by mild oxidation with bromine. The cyclic structures of 12 and 13 were ascertained by NMR analyses. However, the configuration of the anomeric carbon (C-1) was not established. Further structure proof of 13 was provided by its titration curve and neutralization equivalent, which were consistent with

a monobasic acid. Its pKa is calculated to be 1.61. Since compound 11



was not isolated and characterized, the assignment of the structure shown can only be taken as tentative.

The fact that unsaturated phosphines were isolated (identified as benzyl perchlorates 15 and 16, respectively) from reaction of 62%

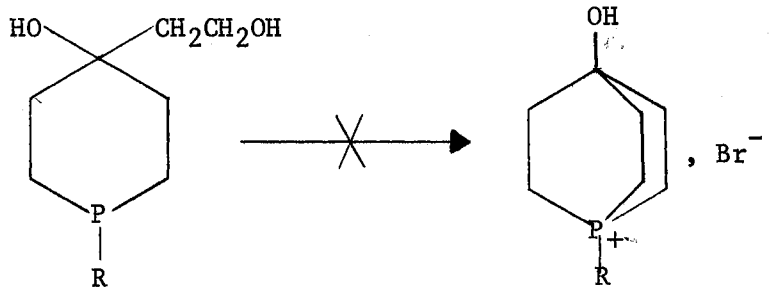


14a R = CH_3
14b R = C_2H_5

15

16

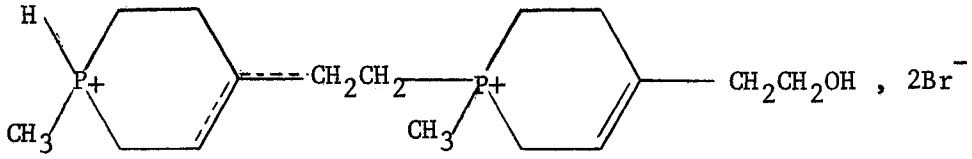
aqueous HBr with a mixture of cis and trans isomers of substituted 4-ethyl-4-phosphorinanol derivatives (14a, R = CH_3; 14b, R = C_2H_5) led Quin and Shook[116] to reinvestigate a previous communication concerning the conversion of 1-alkyl-4-(2-hydroxyethyl)-4-phosphorinanols (17a, R = CH_3; 17b, R = C_2H_5) into bicyclic phosphonium salts by a quinuclidine synthesis.[115] It was found, by NMR and IR spectral analyses, that



17a R = CH_3
17b R = C_2H_5

18a R = CH_3
18b R = C_2H_5

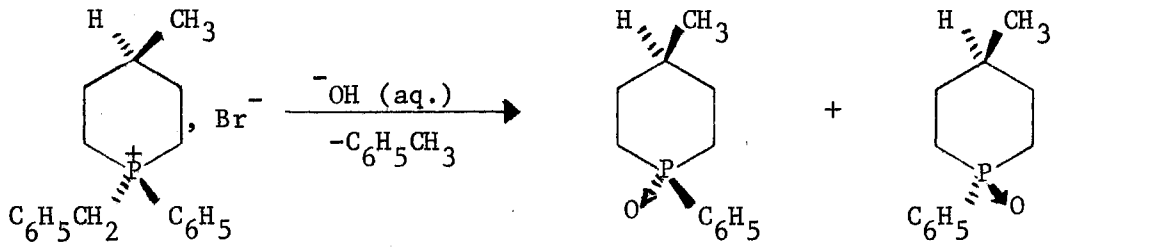
clearly the expected bicyclic phosphonium bromides 18a or 18b were not formed. A dimeric alkylation product 19 has been proposed on account of



19

the acidity and spectral and solubility data of the product from the reaction. However, a satisfactory elemental analysis was not obtained and the entire reaction is wholely unexplained.

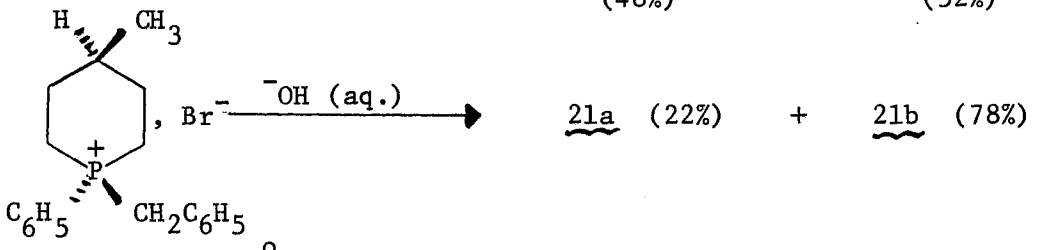
The stereochemistry of alkaline cleavage of cis- and trans-1-benzyl-4-methyl-1-phenylphosphorinanium bromide (20a) and (20b) was investigated recently by Marsi and Clark.[100] Under identical conditions (with 1N NaOH), mixtures of different proportions of cis- and trans-4-methyl-1-phenylphosphorinane 1-oxide (21a) and (21b) resulted from the



20a m.p. 161-3°

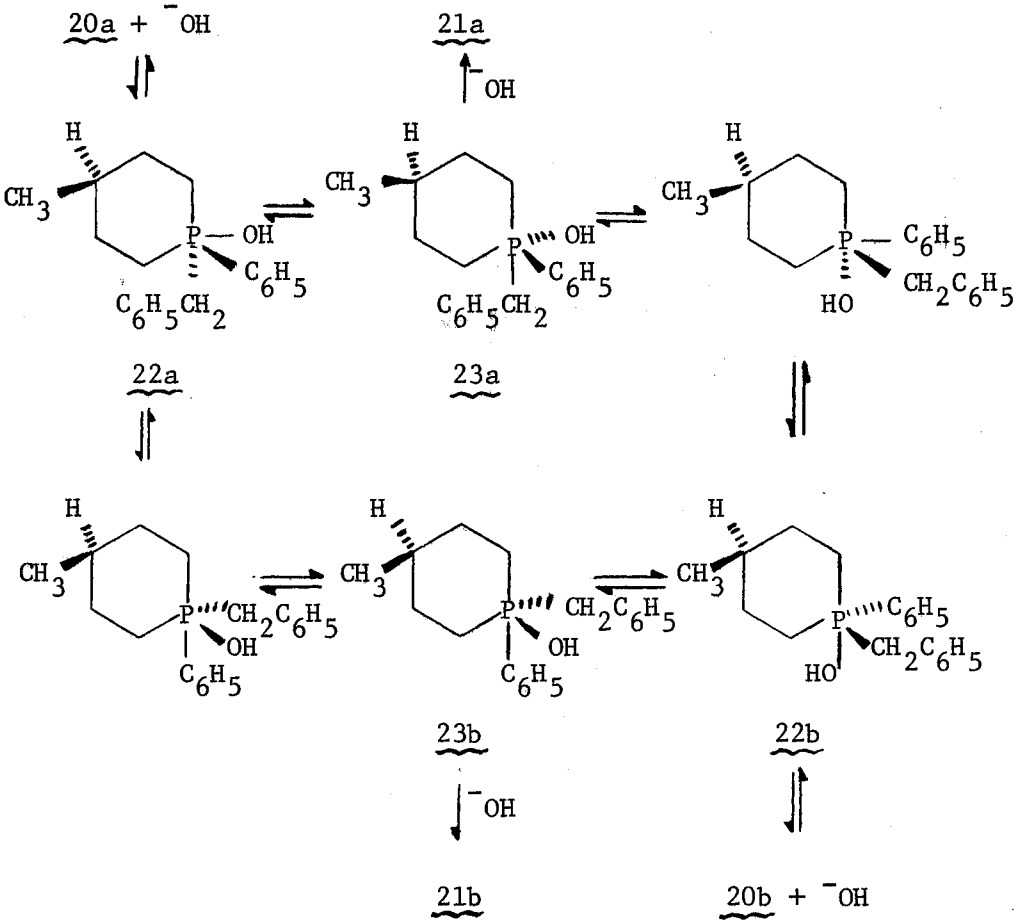
21a m.p. 60-1° (48%)

21b m.p. 148-9° (52%)



20b m.p. 196-7°

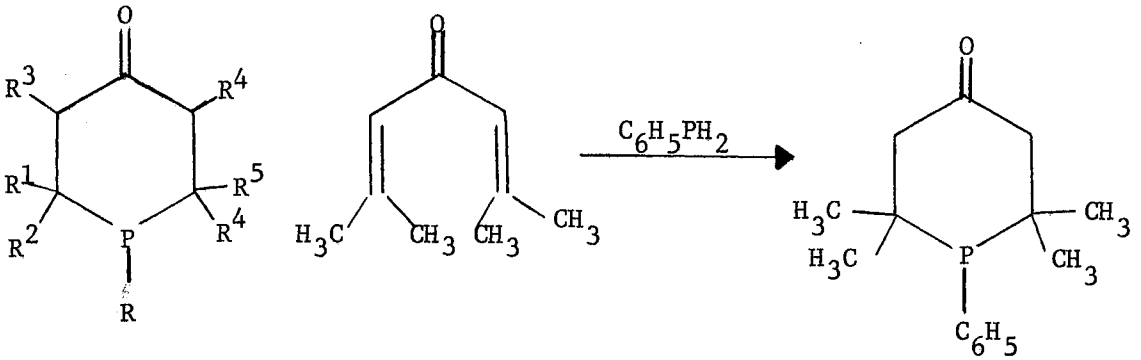
individual salts. Mechanistic interpretations of the data include steric control (methyl and -OH in a trans arrangement) and the involvement



of a pseudorotation process in forming the intermediate phosphoranes (22a and 22b); pseudorotation places the benzyl group in an apical position (presumed to be the preferred orientation for expulsion of the benzyl leaving group, 22a → 23a and 22b → 23b).

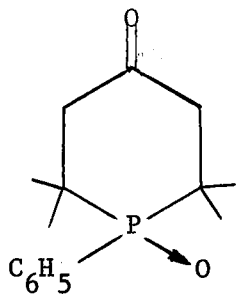
B. Derivatives of Phosphorinanone.

A recent patent by Welcher[136] reported the syntheses of some 35 various substituted phosphorinanones, 24, by heating equimolar amounts of a suitable divinyl ketone and an alkyl- or arylphosphine at temperatures varying from 110-200° depending on the compounds used. These compounds 24, which are oily or waxy solids, are useful as gasoline additives to give protection against misfiring and surface ignition.[136] A typical example was the synthesis of 2,2,6,6-tetramethyl-1-phenyl-4-phosphorinanone (26) obtained by heating a mixture of 2,2,6,6-tetramethyl-2,5-heptadien-4-one (25) and $C_6H_5PH_2$ at 115-30° for 6 hrs. under N_2. Compound 26 was also prepared in good yield by Asinger and Michael[70] via a modification of the above method. The phosphorinanone 26 reacted with oxygen and sulfur to give the corresponding oxide 27 and sulfide 28. Although both 27 and 28 reacted as ketones, their reaction with sulfur and NH_3 failed in each case to give the corresponding



24 25 26

Δ^3-thiazolines. The reaction of 27 with bis(1-phenyl-2,2,6,6-tetramethyl-1-oxaphosphorinan-4-on-3-yl)disulfide, H_2S, and NH_3 reportedly gave 6-oxido-6-phenyl-5,5,7,7-tetramethylphosphorinano[4,3-d]-Δ^3-thiazolin-2-spiro-4'-(1'-phenyl-2',2',6',6'-tetramethylphosphorinane 1'-oxide) (29).[7]



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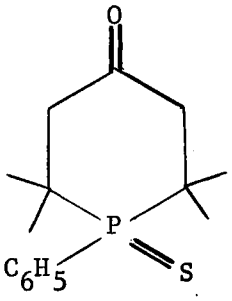

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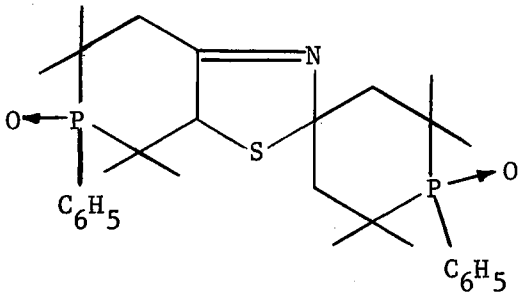
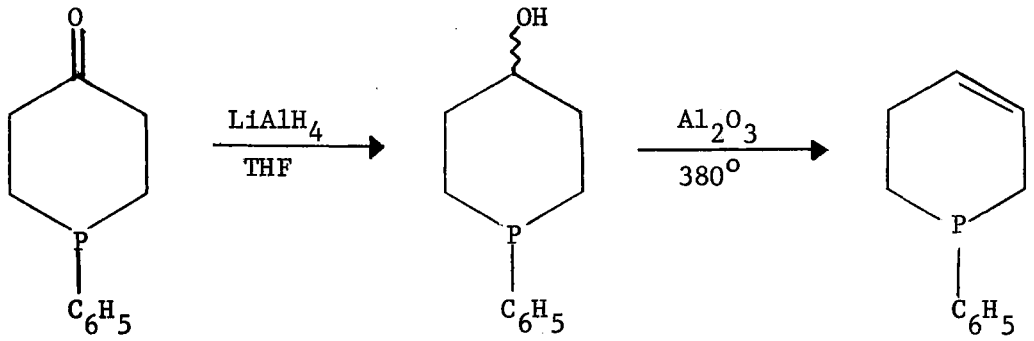


29

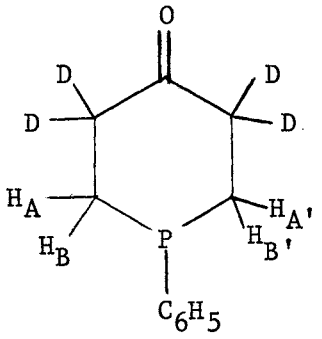
1-phenylphosphorinan-4-one (30), prepared by cyclization of bis-(2-cyanoethyl)phenylphosphine followed by hydrolysis (50% HCl), was readily reduced by $LiAlH_4$ in THF to the corresponding alcohol 31.[124] 1-Phenylphosphorinan-4-ol (31) was found thermally quite stable. Although the dehydration of 31 by use of the conventional methods (i.e. H_2SO_4, $KHSO_4$, PPA, and $SOCl_2$-pyridine) failed to give 1-phenylphosphorin-3-ene (32) in good yield, compound 32 can be realized (in max. 98% yield) by passing 31 (in gas phase at 380°) through an activated alumina



30 31 32

column.[102] Short contact time apparently was essential to the dehydration procedure.

1-Phenyl-3,3,5,5-tetradeuterio-4-phosphorinanone (33) was synthesized in 98% yield by deuterium exchange of 30 in basic medium (Na_2CO_3, pH = 13, D_2O-dioxane 1:1) solution at room temperature.[4] An analysis of the NMR spectrum of the ring protons (AA'BB'X) gave: $^2J_{PH_A} = {}^2J_{PH_{A'}} = \pm 10$ Hz (up field) and $^2J_{PH_B} = {}^2J_{PH_{B'}} = \mp 1$ Hz (down field).[4,5]



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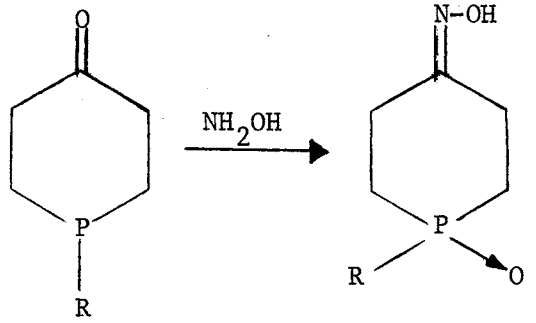


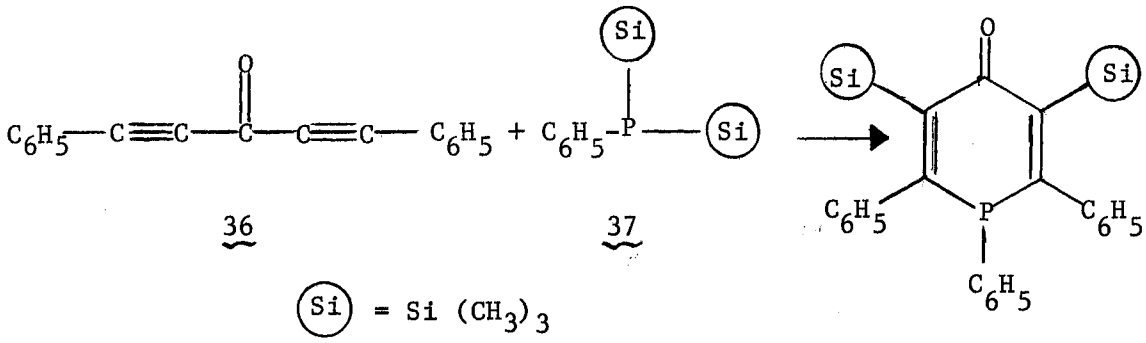
34a R = CH_3 35a R = CH_3

34b R = C_2H_5 35b R = C_2H_5

An unusual oxidation reaction of 1-methyl- and 1-ethyl-4-phosphorinanone (34a and 34b) with hydroxylamine was recently reported to give the oximes of 1-methyl- and 1-ethyl-4-phosphorinanone 1-oxide (35a and 35b) in yield of 25% and 65%, respectively.[101] The transfer of oxygen from a system of general structure N-O-R to trivalent phosphorus is not common. Presumably the hydroxylamine is reduced to ammonia, although no effort was made to detect this product.

The cycloaddition of bis(trimethylsilyl)phenylphosphine (37) to 36 in the presence of 2,2'-azobisisobutyronitrile proceeded smoothly with the product (70%) the lemon-yellow, crystalline 1,2,6-triphenyl-3,5-bis(trimethylsilyl)phospha-2,5-cyclohexadien-4-one (38), m.p. 170-1°.[91] Oxidation of 38 with H_2O_2 in acetone yielded oxide 39 (77%),

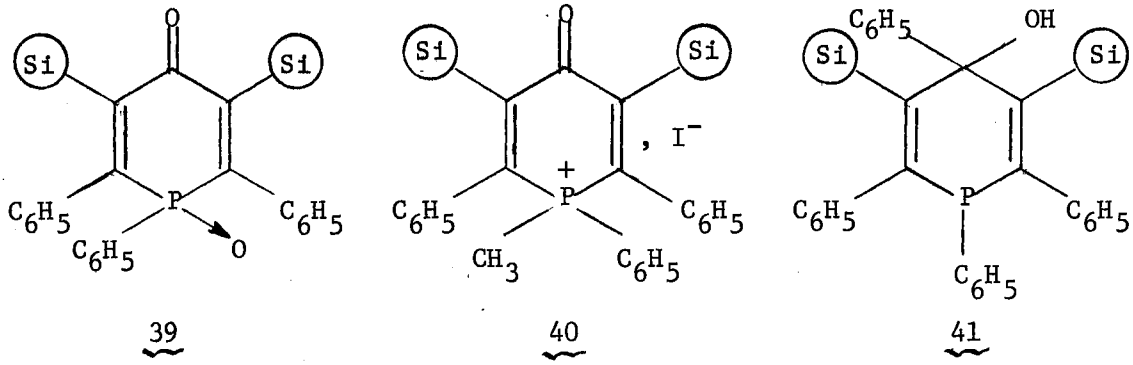
m.p. 215.5-217.5°. Treatment of 38 with methyl iodide gave a 90%



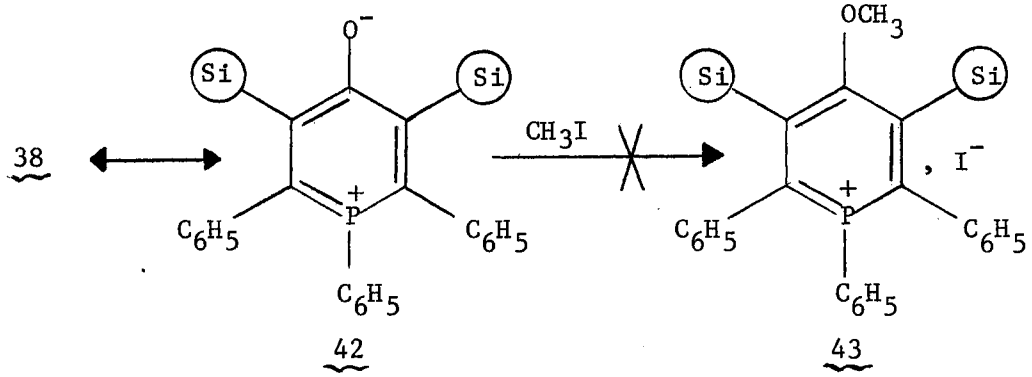
36 37 38

Si = Si $(CH_3)_3$

yield of the methylphosphonium salt 40, m.p. 220-3° dec. Comparison of the UV spectra and the position of C=O stretching in IR in 38, 39, and 40 showed that dipolar valence bond structure 42 of 38 was not excluded. However, alkylation of the compound with CH_3I gave only 40 and no evidence for a reversible, kinetically-controlled O-alkylation to a phosphapyrylium salt 43. Compound 38 reacted smoothly with C_6H_5Li and provided methanol 41 (78%), m.p. 156-7°.[91]

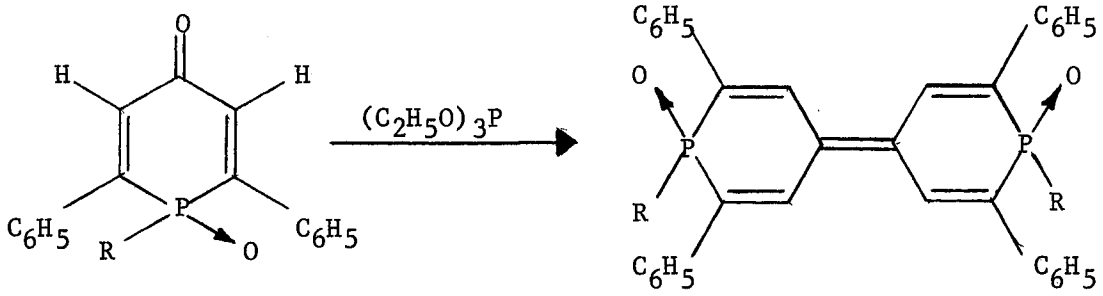


39 40 41



38 42 43

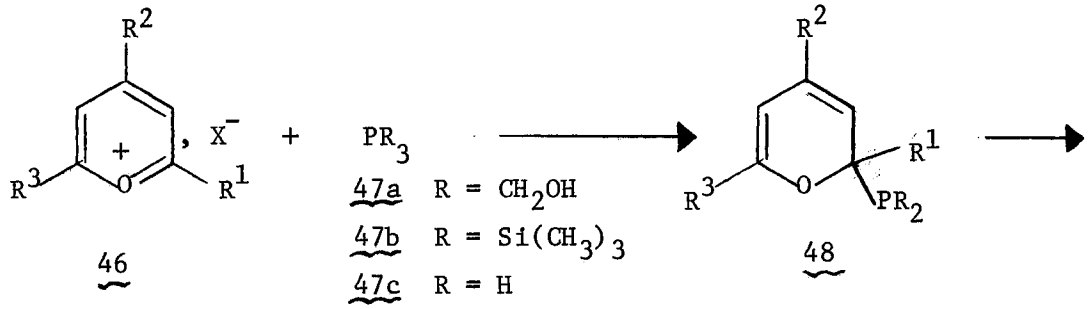
One of the unique reactions of the 1-phospha-2,5-cyclohexadien-4-one 1-oxide (44) (R = $CH_2C_6H_5$) is its tendency to dimerize to 2,2',6,6'-tetraphenyl-4,4'-diphosphapyrylene (45) (R = $CH_2C_6H_5$) upon treatment with triethyl phosphite.[85]

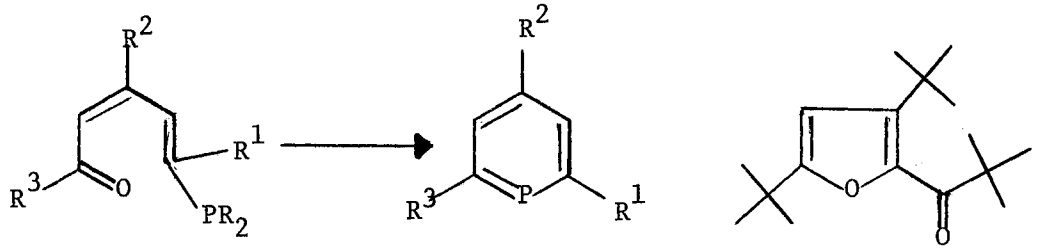


44 45

C. Derivatives of Phosphabenzene.

One of the novel reactions in the synthesis of phosphabenzenes (or phosphorins) 50 ($R^1=R^2=R^3=$ t-Butyl,[38] or Aryl[131]) was the treatment of the corresponding pyrylium salts 46 (X = ClO_4^- or BF_4^-, $R^1=R^2=R^3=$ t-Butyl, or Aryl) with tris(hydroxymethyl)phosphine (47a) in boiling





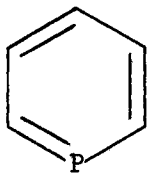
pyridine. Oxidation of 50 with H_2O_2 in ethanol (R^1=R^2=R^3= t-Butyl) was reported[38] to give t-butyl 3,5-di-t-butyl-2-furyl ketone (51), which can also be obtained from 50 by the use of hydroxylammonium chloride.

The introduction of tris(trimethylsilyl)phosphine (47b) into the reaction has made possible the syntheses of a variety of phosphabenzene derivatives without the use of a basic solvent or the formation of H_2O as a reaction by-product.[87] The yields were definitely higher than that of the tris(hydroxymethyl)phosphine synthesis. Because of the low nucleophilicity of the fluoroborate and perchlorate anions, pyrylium iodides (X = I) have to be used in the reaction of 46 with 47b.

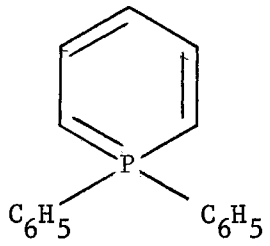
For steric reasons, the synthesis of phosphabenzenes from pyrylium salts 46 and 47a (or 47b) is limited to the 2,4,6-triaryl and tri-t-butyl derivatives.[88] Nucleophilic attack by 47a (or 47b), which could occur at either C-2 or C-4 of 46, is rendered irreversible by the loss of formaldehyde or X-Si$(CH_3)_3$; α-pyrans 48 or their γ-isomers are formed. The introduction of the use of PH_3 (47c, R = H) in the reaction[88] has enlarged the scope of the syntheses. Nucleophilic attack on 46 is reversible, and the smaller steric requirements of PH_3 favors the opening of the α-pyran ring 48 (R = H) to give 49 (R = H), which is required for ring closure. Proton catalysis was found essential for reaction of the primary phosphine with the carbonyl group in the cyclization of the intermediate 49 (R = H). In fact, the pyrylium salts 46 (R^1=R^2=R^3= C_6H_5) reacted smoothly with PH_3 in 1-butanol at 120-130° within 48 hr to yield 2,4,6-triphenylphosphorin without side reactions. Thus, 2- and 4-methylphosphorins 50 (R^1= CH_3, R^2=R^3= C_2H_5;

and $R^1 = CH_3$, $R^2 = R^3 = C_6H_5$) could be prepared for the first time[88] and phosphabenzenes substituted by alkyl groups were thus accessible.

Huckel Molecular Orbital (HMO) calculations on the parent phosphabenzene (52) and 1,1-diphenylphosphabenzene (53) have been discussed by Vilceanu and coworkers.[134] Models of Fukui and Dewar were found to give results which are in accordance with the experimental data concerning electronic spectra, reactivity, and basicity for 1,1-diphenylphosphabenzene (53).



52



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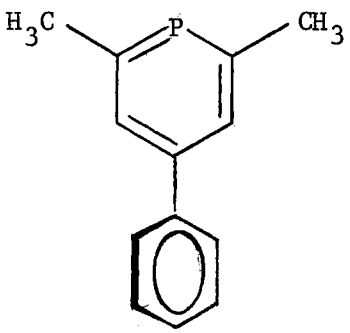
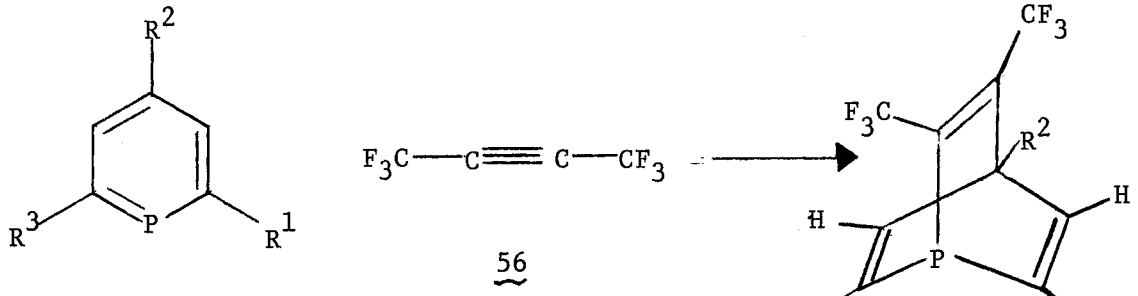


54

The structure of 2,6-dimethyl-4-phenylphosphorin (54) has been determined by single-crystal X-ray methods.[11,13] The molecule possesses an approximate two-fold symmetry axis and the two planar six-membered rings have a dihedral angle of 38.6° in the solid compound. Supporting the concept of a delocalized aromatic nucleus, the planar C-P ring in 53 has two equal P-C bond-lengths of 1.743 Å, and four equal C-C bond-lengths (mean 1.388 Å). The C-P-C angle is 102.4°.

2,4,6-Trisubstituted phosphorins 55 (a-c) have only slight diene reactivity. However, the highly reactive dienophile hexafluoro-2-butyne (56) reacts readily with 55 (a-c) to give the substituted 1-phosphabarrelenes[86] (1-phospha[2.2.2]octa-2,5,7-trienes) 57 (a-c).



56

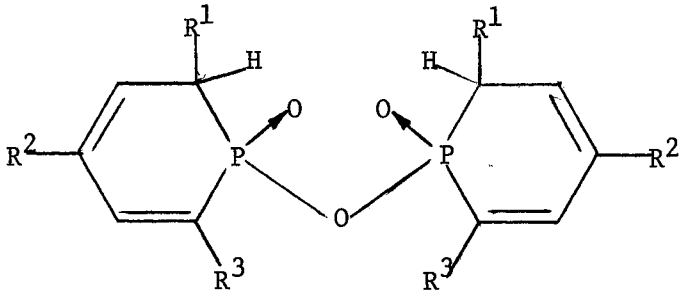
55a $R^1 = R^2 = R^3 = C_2H_5$

b $R^1 = R^3 = t\text{-Bu}$, $R^2 = CH_3$

c $R^1 = R^3 = CH_3$, $R^2 = C_6H_5$

57a-c

2,4,6-Trisubstituted phosphorins 55 were slowly oxidized by air to give the corresponding dimers 58 (a-c).[39]



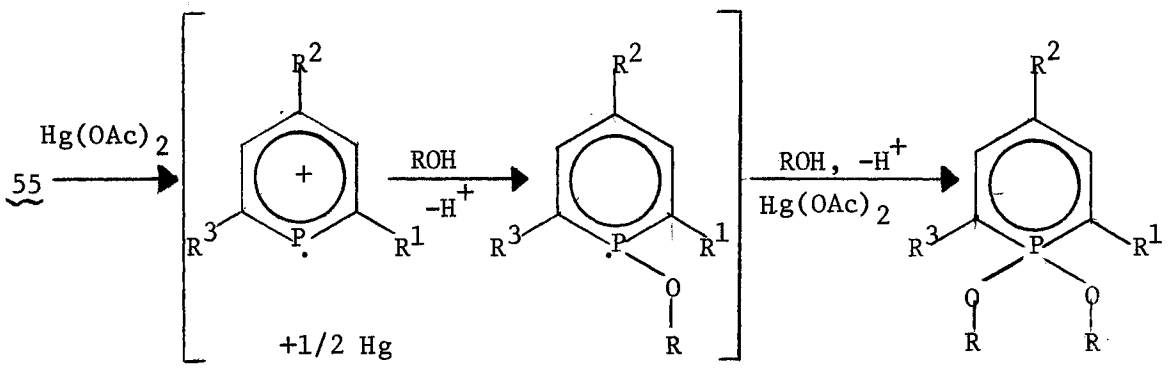
58a-c

a, $R^1 = R^2 = R^3 = C_6H_5$

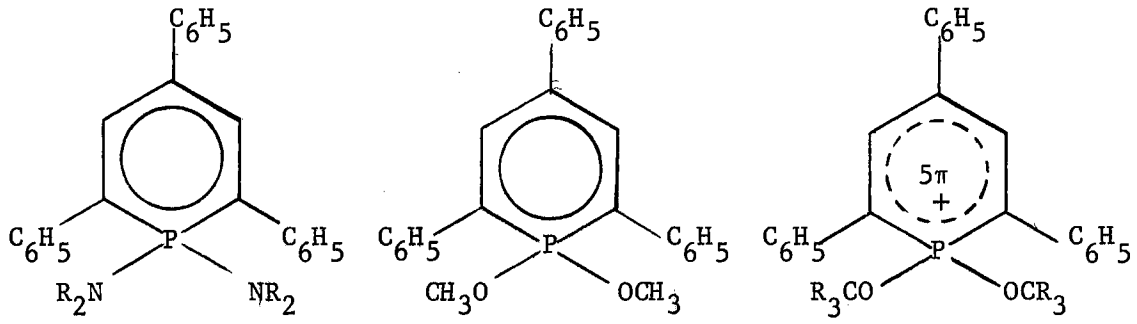
b, $R^1 = R^2 = R^3 = t\text{-Bu}$

c, $R^1 = R^3 = p\text{-}CH_3O\text{-}C_6H_4$, $R^2 = C_6H_5$

Dimroth and Stade[41] were able to obtain 1,1-dialkoxy- and 1,1-diaryloxyphosphorins 60 by oxidation of 2,4,6-trisubstituted phosphorins 55 with mercury(II) acetate in the presence of alcohols or phenols. It was proposed that this reaction proceeded in the first step via the phosphorin radical cation 59. When 2,4,6-triphenylphosphorin (55a) was allowed to react with diphenylamino radical formed on heating tetraphenylhydrazine, the first representative of a new class of compounds, namely, 1,1-bis(diphenylamino)-2,4,6-triphenylphosphorin (61, R = C_6H_5), was formed.[40]



X-ray analysis of the crystal and molecular structure of 1,1-dimethoxy-2,4,6-triphenylphosphorin (62)[129] showed that the C-P heterocyclic ring was aromatic with spd hydridization at the tetrasubstituted



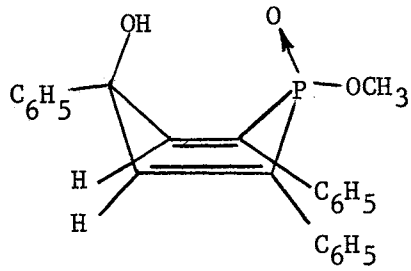
61 62 63a R = H

b R = D

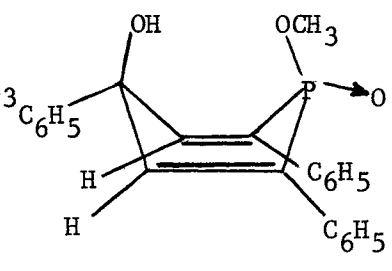
phosphorus. Compounds represented by 60 can be both oxidized to novel stable phosphorus radical cations and reduced to radical anions.[41] The ESR spectrum of 1,1-dimethoxy-2,4,6-triphenylphosphorin radical cation (63a) ($|a_p|$ = 18.4 gauss) was reported.[40] The fact that the radical cation of 1,1-bis(trideuteriomethoxy)-2,4,6-triphenylphosphorin (63b) gave exactly the same spectrum indicated that the delocalization of the unpaired electrons was mainly limited to the aromatic system.

Treatment of 63a in dimethoxyethane with LiBr, acetic anhydride,

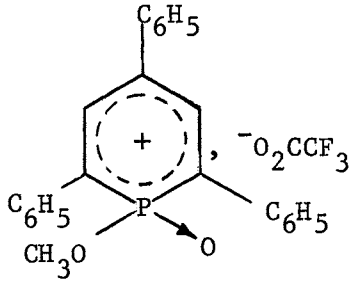
and H_2O_2 was reported[41] to yield two isomeric forms (64 and 65) of 1-methoxy-2,4,6-triphenyl-4-hydroxy-1-phospha-2,5-cyclohexadienone (m.p. 198-200° and 194-198°). However, no proof of their stereochemistry was given. Their OH groups could be acylated without isomerization



64

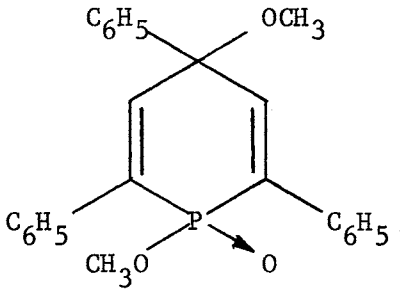


65

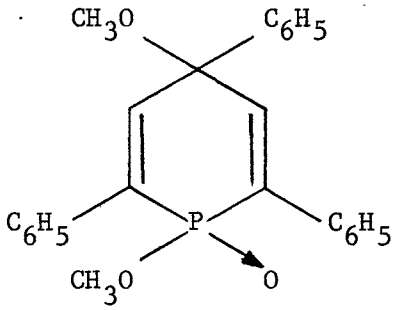


66

with acetic anhydride in pyridine. However, with trifluoroacetic acid, 64 and 65 gave the same deep blue salt 66 which, when treated with alcohols, afforded a mixture of isomeric forms of 1,4-dimethoxy-2,4,6-triphenyl-1-phospha-2,5-cyclohexadien-1-one, (67) and (68), in the approximate ratio of 1:1 and melting over a range of 98-101°. Compound 66 was converted back to 64 and 65 with aqueous acetic acid.

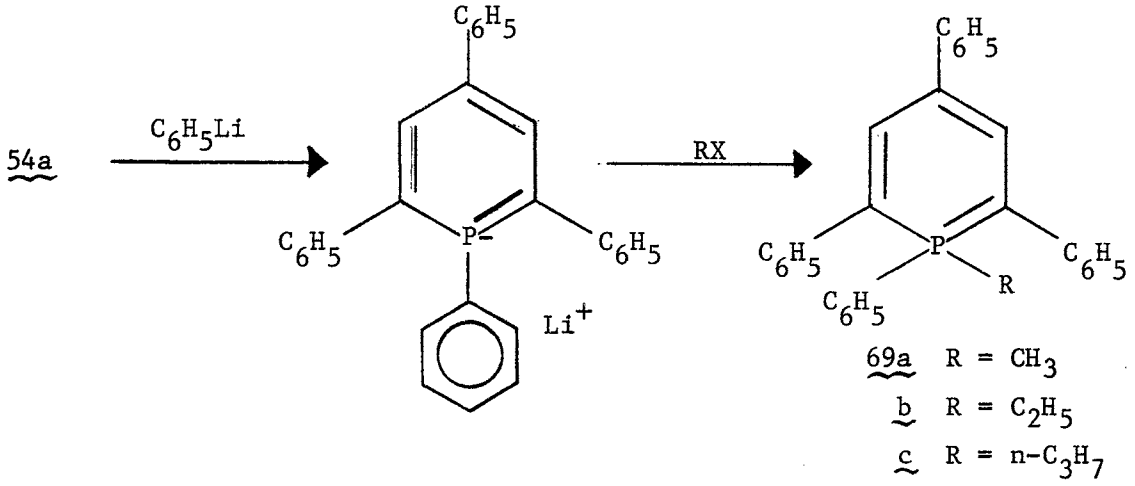


67

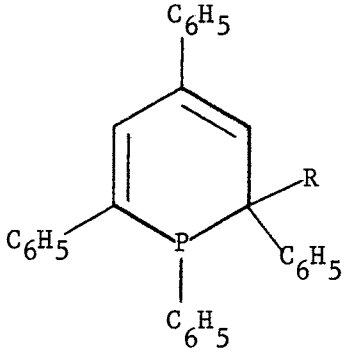


68

Several crystalline phosphabenzenes [such as 69 (a-c)] containing pentavalent phosphorus are available by treating 2,4,6-triphenyl-1-phosphabenzene (54a) with C_6H_5Li and the corresponding halogenated alkane in THF or dimethoxyethane.[89] When benzene was used as the

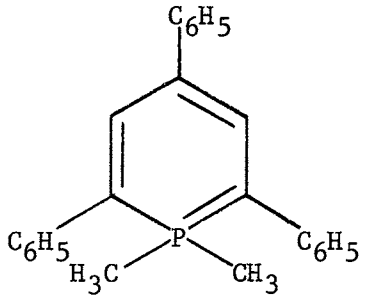


solvent, the reaction products were 2-substituted 1,2,4,6-tetraphenyl-1,2-dihydro-1-phosphabenzene 70 (a-c) which containing trivalent phosphorus (with the exception of CH_3I which gave only 69a).



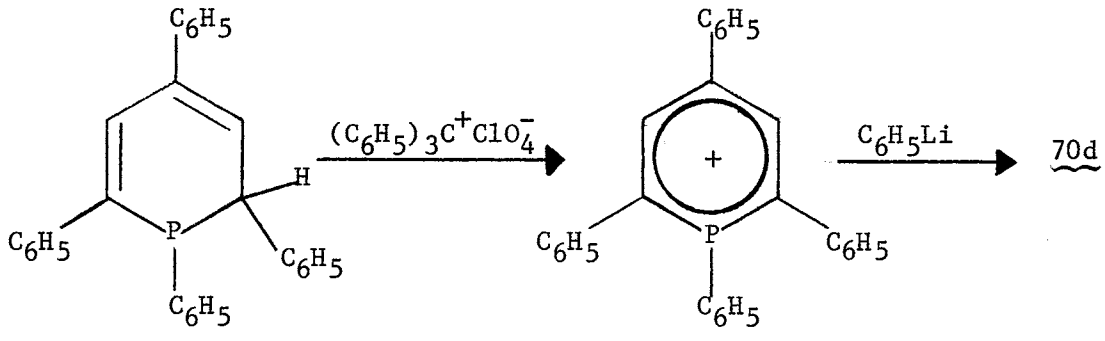
a, R = C_2H_5
b, R = $CH_2C_6H_5$
c, R = CH_2-CH=CH_2
d, R = C_6H_5

70a-d



71

1,1-Diarylphosphabenzole 70d (R = C_6H_5) was synthesized[90] in 80% yield by treating 1,2,4,6-tetraphenyl-1,2-dihydrophosphabenzene (72)



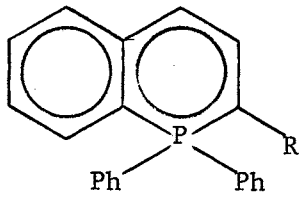
72 73

with $(C_6H_5)_3C^+ClO_4^-$ to give the intermediate cation 73 which reacted with C_6H_5Li.

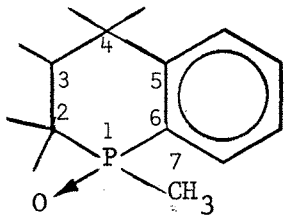
The structure of 1,1-dimethyl-2,4,6-triphenylphosphorin (71) has just recently been determined by single crystal X-ray diffraction methods.[34] The phosphorin ring is almost planar; in it only two different bond lengths were observed, P-C (average 1.749 Å) and C-C (average 1.393 Å). The P-C bond length lies between the mean single-bond length (1.823 Å) for P-C (C_6H_5) and the double-bond length (1.661 Å) of P=C (sp^2) found[12] in $(C_6H_5)_3P{=}CH_2$.

D. Derivatives of Phosphanaphthalene and Phosphinoline.

HMO calculations on derivatives of 1,1-diphenylphosphanaphthalene (74) (R = H or C_6H_5)[84] was discussed by Vilceanu and his coworkers.[133]



74



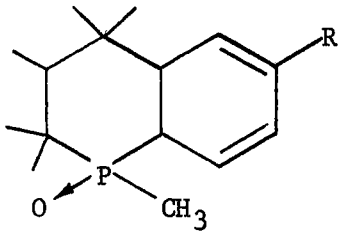
75

Good agreement was obtained with the existent experimental data concerning general stability, basicity, and reactivity of 74 (R = H or C_6H_5), but the arguments were not supported by spectral data.

The first crystal structure of a phosphinoline derivative, 1,2,3,4-tetrahydro-1,2,2,3,4,4-hexamethylphosphinoline 1-oxide (75) was determined by X-ray diffraction techniques with diffractometer data.[104] The conformation of the molecule is similar, but not identical to, that of tetralin in that both the alicyclic ring in tetralin and the phosphorus heterocycle resemble cyclohexene. The P-C distances

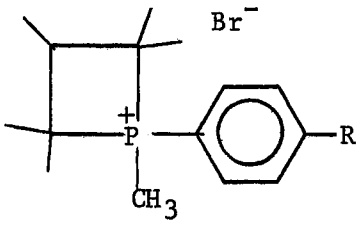
vary from 1.762, 1.786, to 1.864 Å for P(1)-C(6), P(1)-C(2), and P(1)-C(7), respectively. The shortened P(1)-C(6) bond can be explained by partial double-bond character. However, there is no obvious explanation for the shortening of P(1)-C(2) from a normal single-bond length.[105] The angles around phosphorus and the saturated carbon atoms are close to tetrahedral as expected.

Compound 75 was first synthesized by a rearrangement reaction from the methylphosphonium salt of 2,2,3,4,4-pentamethyl-1-phenylphosphetane (77a) (in aqueous NaOH) followed by dehydrogenation. Cremer and Chorvat suggested the structure based on chemical and NMR studies.[31,32]



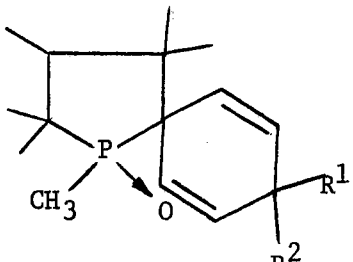
76 a, R = H

b, R = D



77 a, R = H

b, R = D



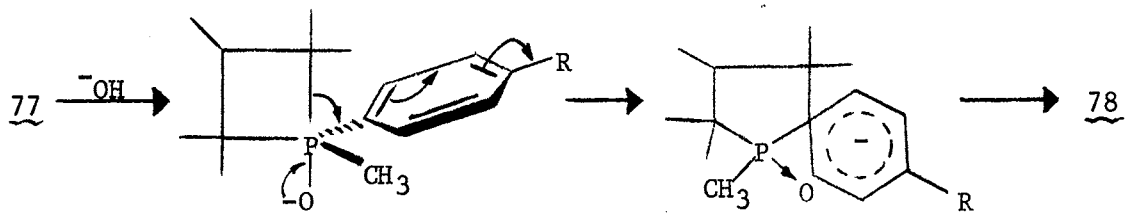
78 a, $R^1 = R^2 = H$

b, $R^1 = H$; $R^2 = D$

c, $R^1 = R^2 = D$

Hexahydrophosphanaphthalene 76a was originally believed to be the alkaline hydrolysis product from 77a before dehydrogenation.[31] The structure 76a was supported by: (a) conversion into 75 (m.p. 157-9°) with 30% Pd/C in boiling decalin; (b) the ^1H NMR and associated ^{31}P-H decoupled spectra. However, Trippett and his coworkers in an independent study[132] have assigned structure 78a to this product. It was found that the absence of UV absorption for a cyclohex-1,3-dienyl chromophore is inconsistent with 76a but is accommodated by 78a. Structure 76 was finally excluded by the evidence provided by a labelling experiment.[32,132] Hydrolysis ($NaOH-H_2O$) of 77b gave a

compound whose NMR spectrum was in accord with 78b (vinyl:allyl proton ratio of 4:1); similar treatment of 77b with NaOD-D_2O produced 78c.

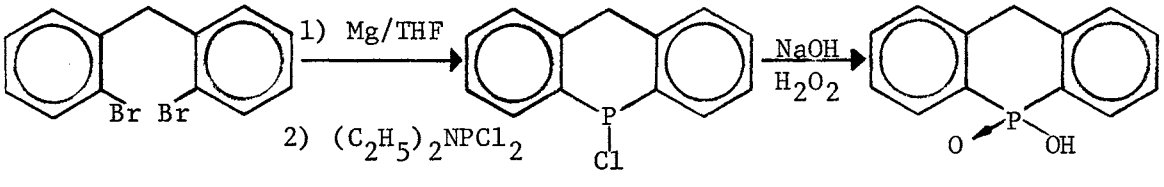


79

An intermediate trigonal bipyramid 79 in which the four-menbered ring is constrained to occupy an apical-equatorial arrangement was proposed.[132] The expected loss of phenyl anion from the apical position opposite to the oxygen cannot therefore occur, and ring expansion results.

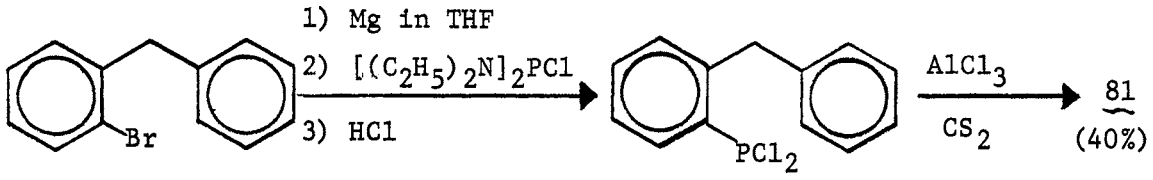
E. Derivatives of Phosphaanthracene.

5-Chloro-5,10-dihydrobenzo[b,e]phosphorin (81), b.p. 142-3°/ 0.01 mm, n_D^{20} 1.6298, was prepared successfully by two different routes by Koe and Bickelhaupt.[72] These were: (1) via the di-Grignard reagent from bis(o-bromophenyl)methane (80) with dichlorodiethylaminophosphine, and followed by treatment of anhydrous HCl; (2) via the Friedel-Crafts cyclodehydrohalogenation ($AlCl_3/CS_2$) of the corresponding



80 81 (47%) 82

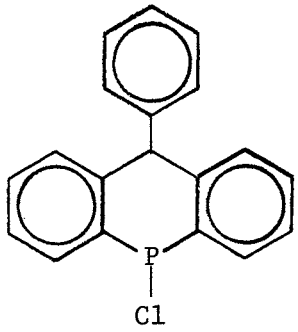
phosphonous dichloride 84, prepared from the Grignard reagent of 83 with chlorobis(diethylamino)phosphine in THF, followed by treatment with



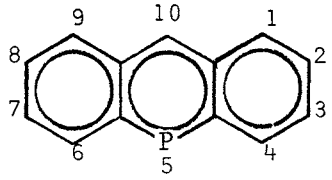
83 84 (68%)

anhydrous HCl in cyclohexane. The structure of 81 was confirmed by oxidizing it in NaOH solution to 82 with H_2O_2.

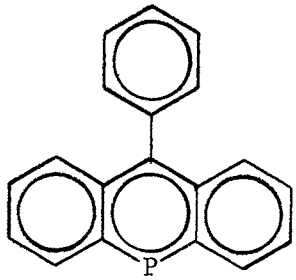
Dibenzo[b,e]phosphorin (86) (9-phosphaanthracene), the phosphorus analogue of acridine, was synthesized by removal of HCl from 81. It



85



86

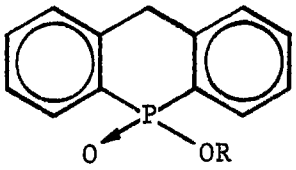


87

was found that a slight excess of 1,5-diazabicyclo[4.3.0]non-5-ene in toluene (or DMF) gave the best result in effecting the dehydrochlorination. The parent 9-phosphaanthracene (86) was unstable, so that its occurrence in solution has only been surmised on the basis of spectroscopic data.[72] However, in contrast to 86, 10-phenyldibenzo[b,e]-phosphorin (87),[73] being stabilized by the phenyl substituent, was found to be isolable and could be purified by vacuum sublimation to give yellow crystals of m.p. 173-6°. Compound 87 was similarly prepared from the corresponding 5-chloro-5,10-dihydro-10-phenyldibenzo-

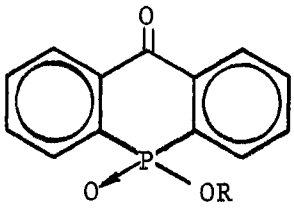
[b,e]phosphorin (85) by dehydrohalogenation in high vacuum.[73] The structure of 87 was supported by elemental analysis, the mass spectrum (molecular ion at m/e 272, 100%), the ^{1}H-NMR spectrum [in CS_2 with TMS as external standard: multiplets at δ7.7-8.5 (11 H) and δ8.72-9.25 (2 H), presumably protons on C-4 and C-6], and the UV spectrum which is largely similar to that of the unsubstituted parent 86.

Recently, an improved synthesis for 9,10-dihydroanthracene-9-phosphinic acid (88) was briefly described.[49] The route involves ring



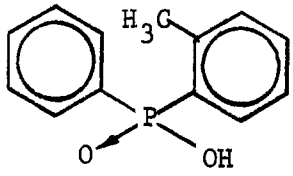
88 R = H

89 R = CH_3



90 R = H

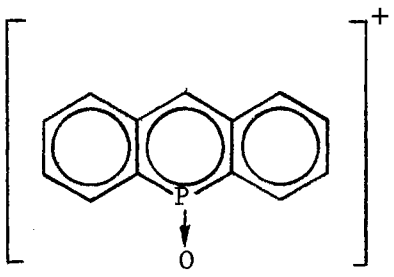
91 R = CH_3



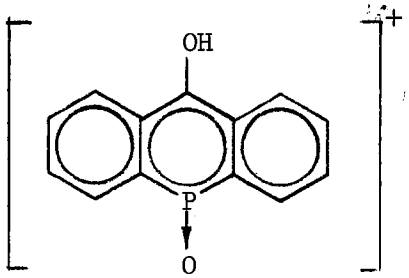
92

closure of the carboxylic acid obtained by oxidation of phenyl-o-tolyl-phosphinic acid (92) and reduction of the resulting oxo compound 90. However, no detailed experimental was given.

The mass spectra of the cyclic acids and methyl esters 88-91 were recently reported and discussed in details by Haake and his coworkers.[50]



93 m/e 212

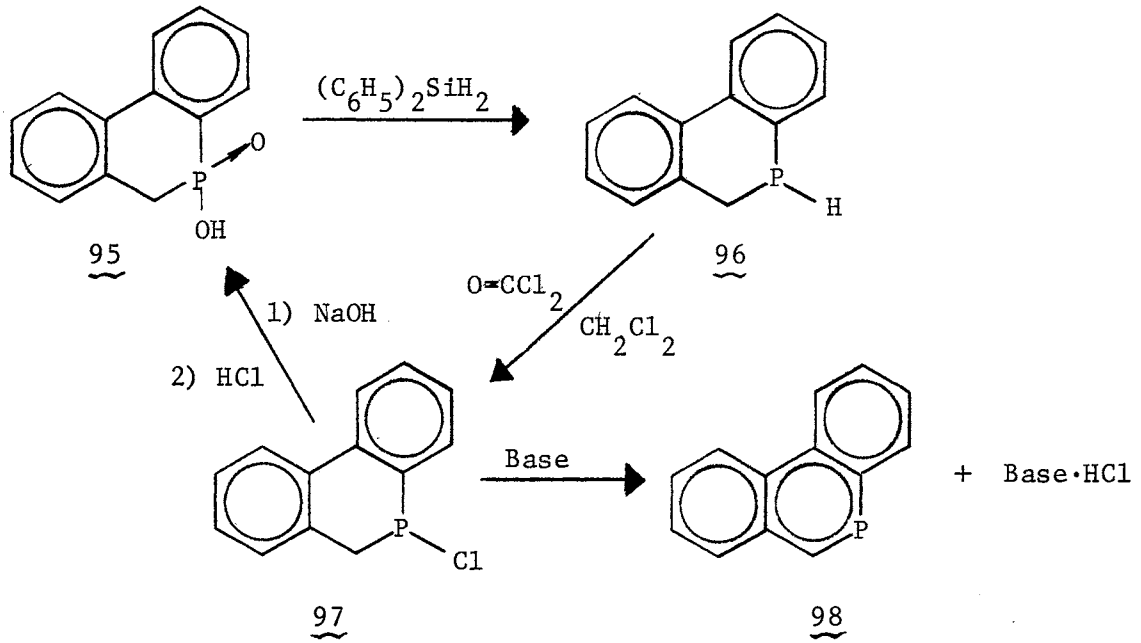


94 m/e 228

Mass spectra were determined with an A.E.I. MS-9 mass spectrometer, using direct insertion technique, at a source temperature of 160° and electron beam energy of 70 eV. Ionic species of structure 93 and 94 were proposed to account for the base peaks at m/e 212 (observed in both the spectra of 88 and 89) and m/e 228 (in the spectrum of 91), respectively, on the basis of their corresponding metastable transitions. The intensities of peaks of 93 and 94 suggest that these heteroaromatic systems may have considerable stability.[50]

F. Derivatives of Phosphaphenanthrene.

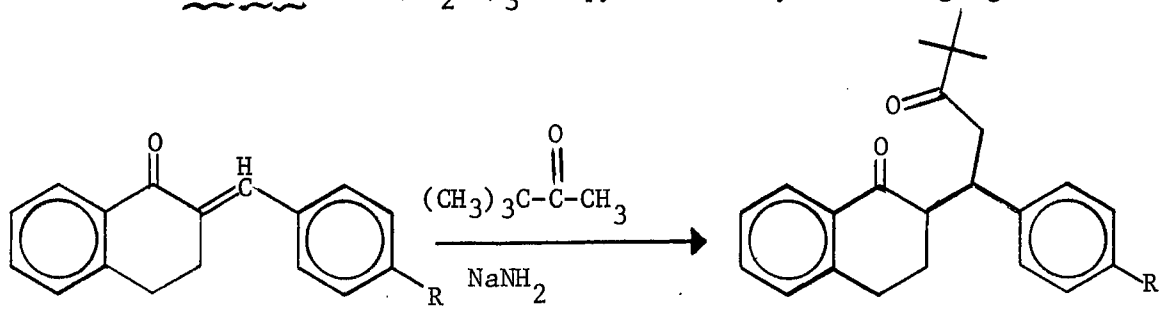
Dibenzo[b,d]phosphorin (or 9-phosphaphenanthrene) (98) in solution was prepared by Koe and coworders[74] from 9,10-dihydro-9-phosphaphenanthrene 9-oxide (95).[82] The cyclic phosphinic acid 95 was reduced to



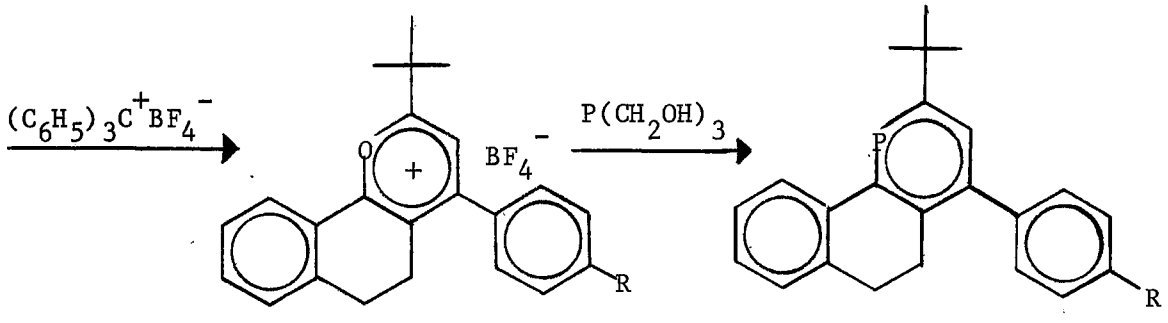
5,6-dihydrodibenzo[b,d]phosphorin (96) in 92% yield by diphenylsilane, which, upon reacting with phosgene in methylene chloride under N_2, gave 5-chloro-5,6-dihydrodibenzo[b,d]phosphorin (97) in a yield of 35%.

Dehydrohalogenation was achieved in a sealed vacuum tube by treating 97 with excess 1,5-diazabicyclo[5.4.0]undec-5-ene in anhydrous, degassed ether at -196°, and subsequently warming the mixture to room temperature. However, owing to its labile nature, compound 98 was not isolated in pure form. A UV maximum at λ = 372 mμ (ε = 0.45) was recorded for the crude 98 in ether. The structure 98 was further supported by a prominent molecular ion at m/e 232 (relative intensity 28%) in its mass spectrum.

2-Tert-butyl-4-aryl-5,6-dihydronaphtho[1,2-b]phosphorin derivatives (101 a-d) were successfully synthesized from the corresponding pyrylium fluoborate 100 a-d and $P(CH_2OH)_3$ in pyridine in yields ranging from



99a-d



100a-d 101a-d

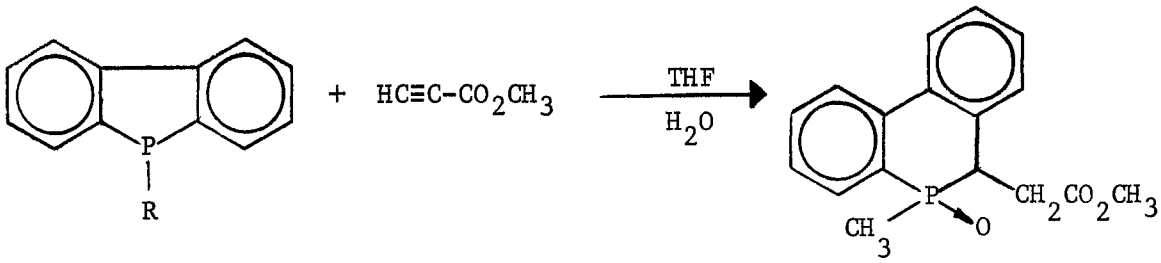
a, R = H; b, R = OCH_3

c, R = Cl; d, R = CH_3

66-81%.[43] The syntheses of cyclic phosphonium salts via their corresponding pyrylium salts have been discussed in the synthesis of phosphabenzene (p. 12). The unique approach to the synthesis of the precursor cyclic carboxonium salts 100 a-d from the ketones 99 a-d deserves further attention.

The crystal structure of 101 b (R = OCH_3) was determined,[43] and is in character with an aromatic ring. Planarity of the phosphorin ring is achieved by expansion of the P-C-C and C-C-C angles to 122-126° in order to accommodate the C-P-C bond angles of 103°.

Ring expansion reactions have been proved in certain cases to be of value in the syntheses of derivatives of phosphaphenanthrene.[6,118] 9-Methyl-9-phosphafluorene (102, R = CH_3), methyl propiolate, and H_2O in

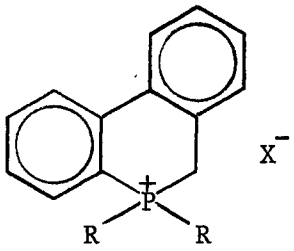


102 R = CH_3 103

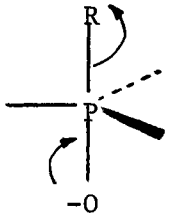
THF gave 9-methyl-10-(methoxycarbonylmethyl)-9,10-dihydro-9-phosphaphenanthrene 9-oxide (103), m.p. 145-8°. The structure was established by NMR, UV and elemental analyses.[118] The chromophoric nature of 103 in its UV spectrum resembles that of the 9-phosphoniaphenanthrene 104 (R = Ph, X = Br).[27]

Haeves and Trippett[51] have pointed out that in alkaline hydrolysis of strained cyclic phosphonium salts competing reactions between ring

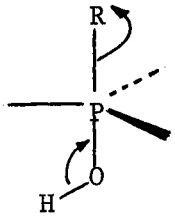
opening and ring expansion depend upon the nature of the substituents attached to phosphorus. The difference in bond angles between apical



104

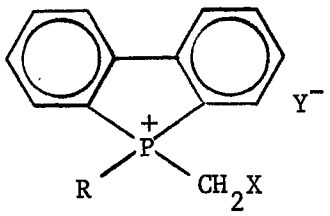


105a

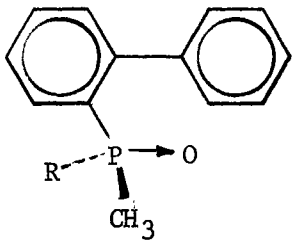


105b

and equatorial (90^{o}) and diequatorial (120^{o}) positions could lead to constraints on the conformation of the intermediate (formulated as 105a and b), such that the ring system spans the apical-equatorial positions,



106

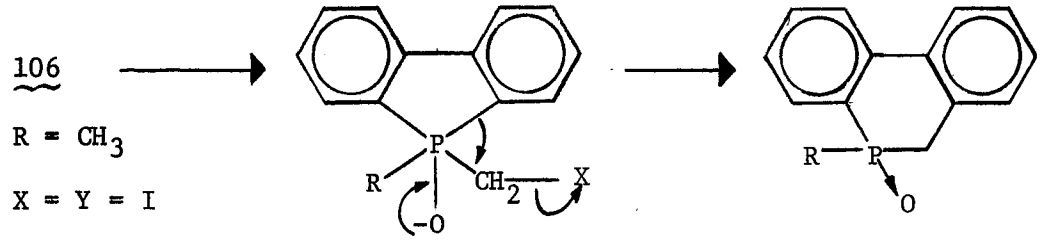


107

leading eventually to ring opening or ring expansion. Thus, alkaline hydrolysis of the salt 106 (R = CH_3, X = OCH_3, Y = Cl) proceeded exclusively with ring opening to furnish biphenyl-2-yl(methoxymethyl)-methylphosphine oxide (107, R = CH_2OCH_3); ring expansion does not occur, presumably because the methoxide ion is an inadequate leaving group. But, alkalin hydrolysis of the salt 106 (R = CH_3, X = I, Y = I) proceeded readily to give the ring-expanded product 108 (R = CH_3) in high yield.[6]

The structure of 9-methyl-9,10-dihydro-9-phosphaphenanthrene

9-oxide (108, R = CH_3) was supported by elemental analysis and NMR and IR (ν_{max} 1150-1200 cm^{-1}, P→ O) spectra. Its characteristic UV spectrum,

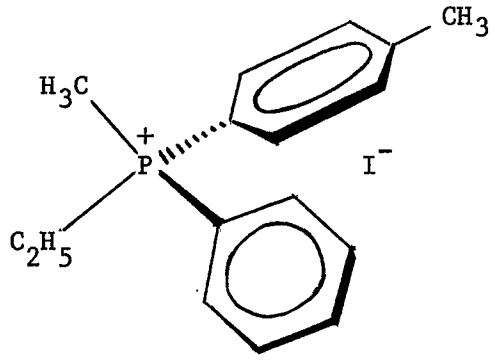


108 R = CH_3

which is very different from that of the ring-opened product 107 (R = CH_2OCH_3), is very similar to those of the structually similar salt, 9,9-diphenyl-9,10-dihydro-9-phosphoniaphenanthrene bromide 104 (R = C_6H_5, X = Br) and the cyclic phosphinic acid, 9,10-dihydro-9-phosphaphenanthrene 9-oxide (95).

II. Resolution of Quaternary Phosphonium Salts.

There are several review articles[67,95,105,110] which deal with the stereochemistry of the derivatives of optically active organophosphorus compounds. The first attempt at resolution of a quaternary phosphonium salt reported in the literature dates back to 1901 and Michaelis.[109] He synthesized and tried to resolve ethylmethylphenyl-



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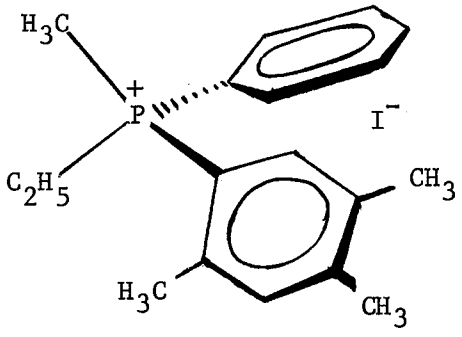
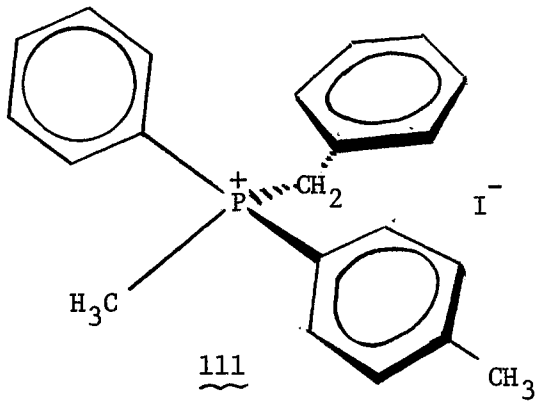


110

p-tolylphosphonium iodide (109) and ethylmethylphenyl-2,4,5-trimethylphenylphosphonium iodide (110) but no positive results were obtained. Later, Wedekind[135] again tried unsuccessfully to resolve 109 and benzylmethylphenyl-p-tolylphosphonium iodide (111). Neither did the endeavors



111

of Radcliffe and Brindley,[117] Meisenheimer and his coworkers,[107] or Kamai[62] lead to positive results.

Meisenheimer and coworkers[107] considered that all the failures to resolve dissymmetric phosphonium salts of the type $[abcdP^+]X^-$ into optical antipodes were due merely to experimental difficulties, since certain salts $[P^+abc(OH)\ X^-$ -- resulted from resolution of asymmetric phosphine oxides via (+)-bromocamphorsulphonic acid] were obtained in an optically active form.[107,108]

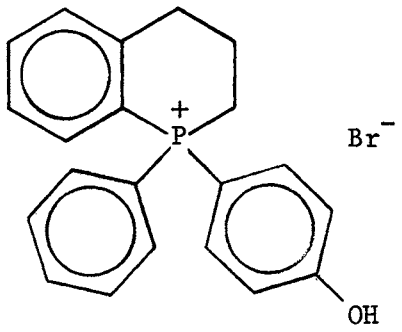
The suggestion was made by Mann[94] that the numerous failures in attempts at resolution of such salts were attributable to the operation

$$RR^1R^2R^3P^+,\ X^- \rightleftharpoons RX + R^1R^2R^3P$$

of a dissociation-equilibrium mechanism, although Wedekind[135] had shown long before that ethylmethylphenyl-p-tolylphosphonium iodide does not dissociate into an alkyl or an aryl halide and a tertiary phosphine in chloroform solution at room temperature or at the boiling point of chloroform. Of course, this proposal by Mann was based on the assump-

tion that the tertiary phosphine, $R^1R^2R^3P$, formed by the dissociation reaction would undergo rapid racemization by a vibration mechanism, in analogy with the known behavior of tertiary amines. It is now clear that this assumption was an incorrect one, for various optically stable, dissymmetric tertiary phosphines and acyclic phosphonium salts have since been successfully resolved.[105]

The earliest successful resolution of quaternary phosphonium salts in the literature was reported by Holliman and Mann[53] in 1947. They attempted to resolve two phosphonium salts -- 1,2,3,4-tetrahydro-2-p-hydroxyphenyl-2-phenylphosphinolinium bromide (112) and the corresponding isophosphinolinium bromide (113) -- into optical antipodes.



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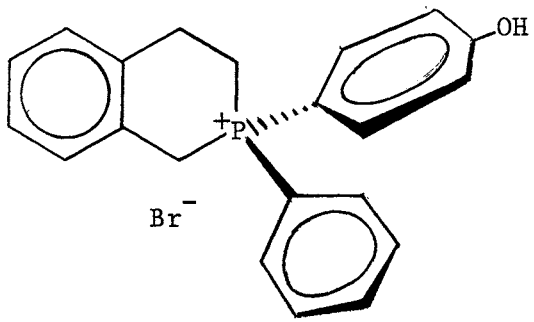
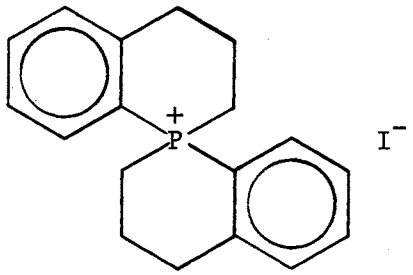


113

Although attempts at the resolution of the former compound were unsuccessful, a dextrorotatory form of the pure crystalline isophosphinolinium bromide 113, having a molecular rotation of $[M]_D$ +32.9° (in aqueous ethanol) was isolated through its (+)-camphorsulfonate. However, unfortunately, later attempts to repeat its separation were unsuccessful.

More recently, Hart and Mann[52] synthesized and successfully effected the resolution of P-spiro-bis-1,2,3,4-tetrahydrophosphinolinium

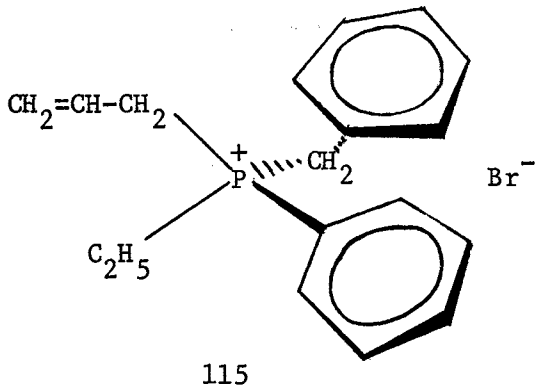
iodide (114) into its dextro and levo isomers ($[M]_D$ +66° and -65° in $HCCl_3$) via the (+)- and (-)-phosphonium (-)-menthoxyacetate. The re-



114

solution of this salt disproved the planar configuration of the phosphonium cation.

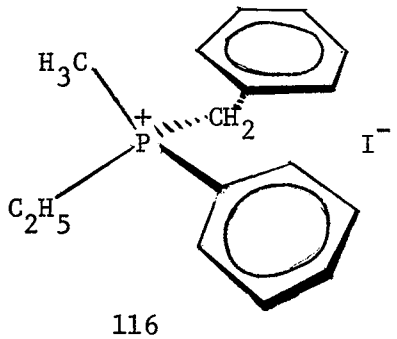
Kamai and Khismatullina[63-65] were able to isolate the crystalline (+)-bromocamphorsulfonate of allylbenzylbutylphenylphosphonium bromide (115). Two diastereoisomeric (+)-bromocamphorsulfonates were obtained from 115, but attempts to prepare the enantiomorphic optically active bromides by metathesis with potassium bromide failed.



115

The first completely successful resolution of a quaternary phosphonium salt in which the phosphorus was not a member of a heterocyclic ring was reported by Kumli, McEwen and VanderWerf[76] in 1959. Both enantiomorphs of benzylethylmethylphenylphosphonium iodide (116) ($[\alpha]_D^{25}$ +24.0° and -23.8° in methanol) were obtained by way of the

hydrogen D(-)-dibenzoyltartrate and L(+)-dibenzoyltartrate salts. The



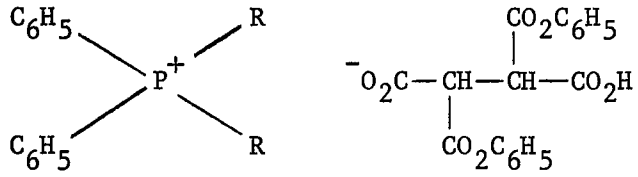
116

iodide was found to be optically stable even in solution, and this fact disposed unequivocally the previously suggested mechanism by Mann for racemization.[94] Various optically active acyclic dissymmetric phosphonium hydrogen D(-)-dibenzoyltartrates were synthesized, separated, characterized by Kamai and Usacheva[66] recently, and their specific rotations were reported (Tables I and II). These phosphonium hydrogen D(-)-dibenzoyltartrates were subjected to metathesis with ammonium chloride, bromide, or iodide in methanol. Only in two cases was definite rotation observed in the corresponding phosphonium salts isolated (namely, the benzylethylmethylphenylphosphonium and benzylethylmethyl-p-tolylphosphonium salts). The dextrorotatory benzylethylmethyl-p-tolylphosphonium chloride, bromide, and iodide isolated were found to be optically stable. The iodide did not change in rotation when heated in chloroform solution at 35° for four hours; the bromide did not change when its chloroform solution was boiled for three hours; and the corresponding (+)-chloride did not change when boiled in chloroform solution for six hours.

Other quaternary non-heterocyclic phosphonium halides resolved, by way of the diastereoisomeric hydrogen dibenzoyltartrate salts, were ethylmethylphenyl-p-tolylphosphonium iodide,[106] benzylmethyl-

TABLE I

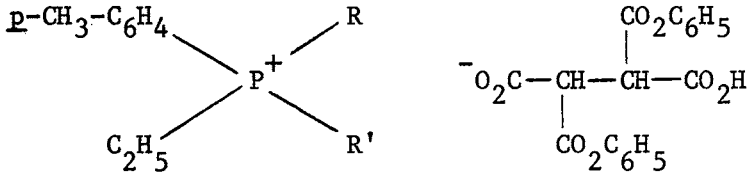
DISSYMMETRIC PHOSPHONIUM HYDROGEN D(-)-DIBENZOYLTARTRATES OF GENERAL FORMULA[66]



R	R'	M.P. °C	$[\alpha]_D^{20}$ (Conc. in CH_3OH)
CH_3	C_3H_5 (allyl)	130-2	-71.82 (1.017)
CH_3	$CH_2CO_2C_2H_5$	122-4	-88.84 (1.622)
n-C_3H_7	C_3H_5 (allyl)	125-7	-75.14 (1.363)
CH_3	$CH_2CH_2C_6H_5$	130-1	-63.29 (1.573)
C_4H_9	$CH_2C_6H_5$	134-5.5	-65.52 (0.926)
C_5H_{11}	$CH_2C_6H_5$	131-2.5	-68.10 (1.078)
C_6H_{13}	$CH_2C_6H_5$	131-2	-79.93 (1.570)
C_7H_{15}	$CH_2C_6H_5$	127-9	-62.59 (1.203)
n-C_3H_7	$CH_2C_6H_5$	122-4	-69.61 (1.492)

TABLE II

DISSYMMETRIC PHOSPHONIUM HYDROGEN D(-)-DIBENZOYLTARTRATES OF GENERAL FORMULA [66]

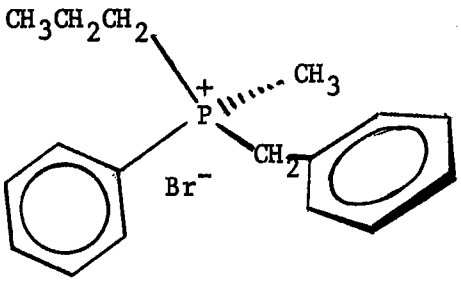


R	R'	M.P. °C	$[\alpha]_D^{20}$ (Conc. in CH_3OH)
CH_3	C_3H_5 (allyl)	124-6	-66.44 (1.128)
CH_3	$CH_2C_6H_5$	149-150	-57.90 (1.375)
C_4H_9	$CH_2C_6H_5$	139-141	-65.65 (0.973)

phenyl-n-propylphosphonium bromide,[56] benzyl-n-butyl-2-cyanoethylmethylphosphonium iodide,[139] allylbenzylmethylphenylphosphonium bromide,[56] benzyl-p-methoxyphenyl-1-naphthylphenylphosphonium bromide, and the corresponding chloride.[54]

Absolute configuration and crystal structure of (+)-benzylmethylphenyl-n-propylphosphonium bromide (117) were determined by Peerdeman and his coworkers;[112] the compound proved to have a S-configurations. It provides a reference substance for the unequivocal assignments of absolute configuration of related compounds.

The first successful resolution of a di-phosphonium salt was reported by Horner and his coworkers in 1966.[55] Meso-, (+,+)-, and (-,-)-1,2-ethylenebis(benzylmethylphenylphosphonium) dibromide (118, X = Br) were all successfully separated. The (+,+) and (-,-)-118



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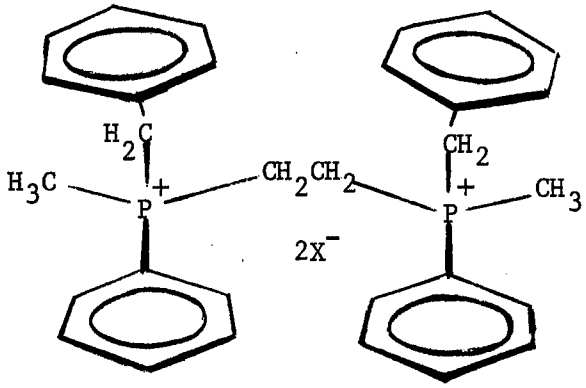

118

(X = Br) were isolated from the racemic mixture via the use of silver hydrogen D(-)-dibenzoyltartrate. The pure enantiomers were characterized as their perchlorates and methyl sulfates. The (+,+)- and (-,-)-methyl sulfates 118 (X = OSO_2OCH_3), m.p. 139° and 175°, had specific rotations of $[\alpha]_D$ +64.05° and -65.4°, respectively.

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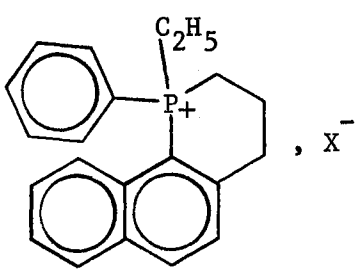
CHAPTER II

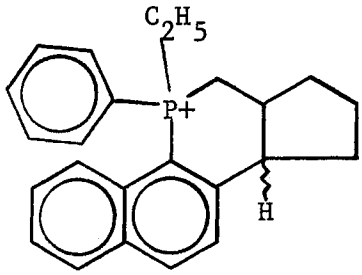
RESULTS AND DISCUSSION

Although various azasteroids,[3,19] oxasteroids,[58,61,68,79,140] thiasteroids,[33,59,125,130] azathiasteroids[69] and azaoxasteroids[68] have been synthesized and known for many years, none of the phosphorus analogs -- phosphasteroids (where phosphorus is incorporated in the basic steroidal ring system) -- has ever been reported. The object of this research was to devise a general approach toward the total synthesis of the previously unknown phosphasteroids and other related C-P heterocycles. Of particular interest is the potential chemotherapeutic value of these compounds, in view of the biological activities observed in many compounds of the azasteroidal family.[3] It is hoped that the novel structures and synthetic approach reported in this thesis will arouse enthusiasm and open an entirely new field of interest in the study of C-P heterocyclic chemistry.

Model compounds of a 4-phosphaphenanthrene derivative -- 1-ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium salts (119a - c) -- were synthesized (Scheme I) with the intention of evaluating the general synthetic approach, of optimizing certain experimental conditions, and especially. of testing the feasibility of the crucial cyclization step in the synthesis. Total synthesis and characterization of the first phosphasteroid (where P is incorporated at the 11-position of the steroid nucleus) -- 5-ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo



, X^-



, X^-

119a X = Br

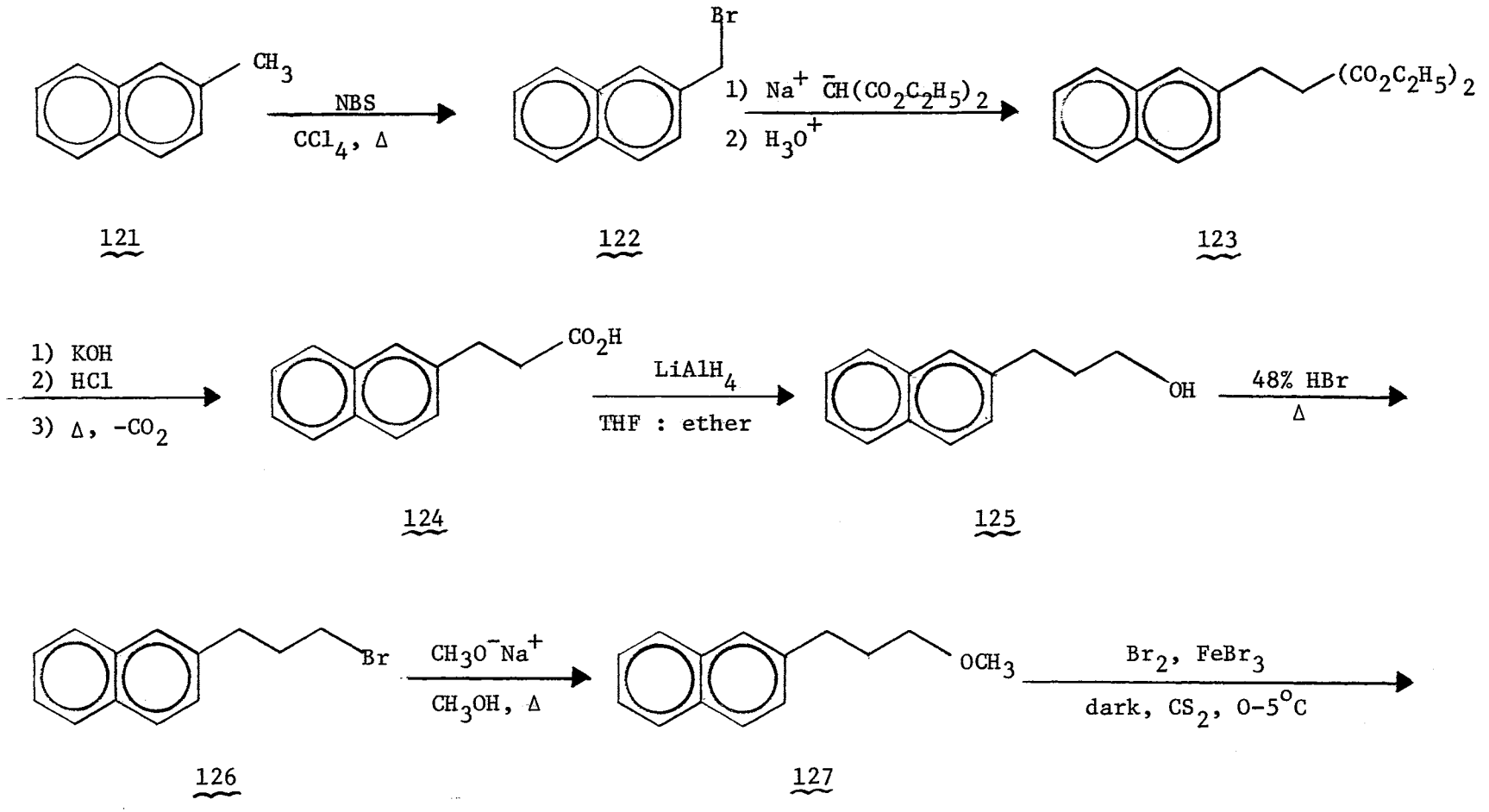
119b X = ClO_4

119c X = Picrate

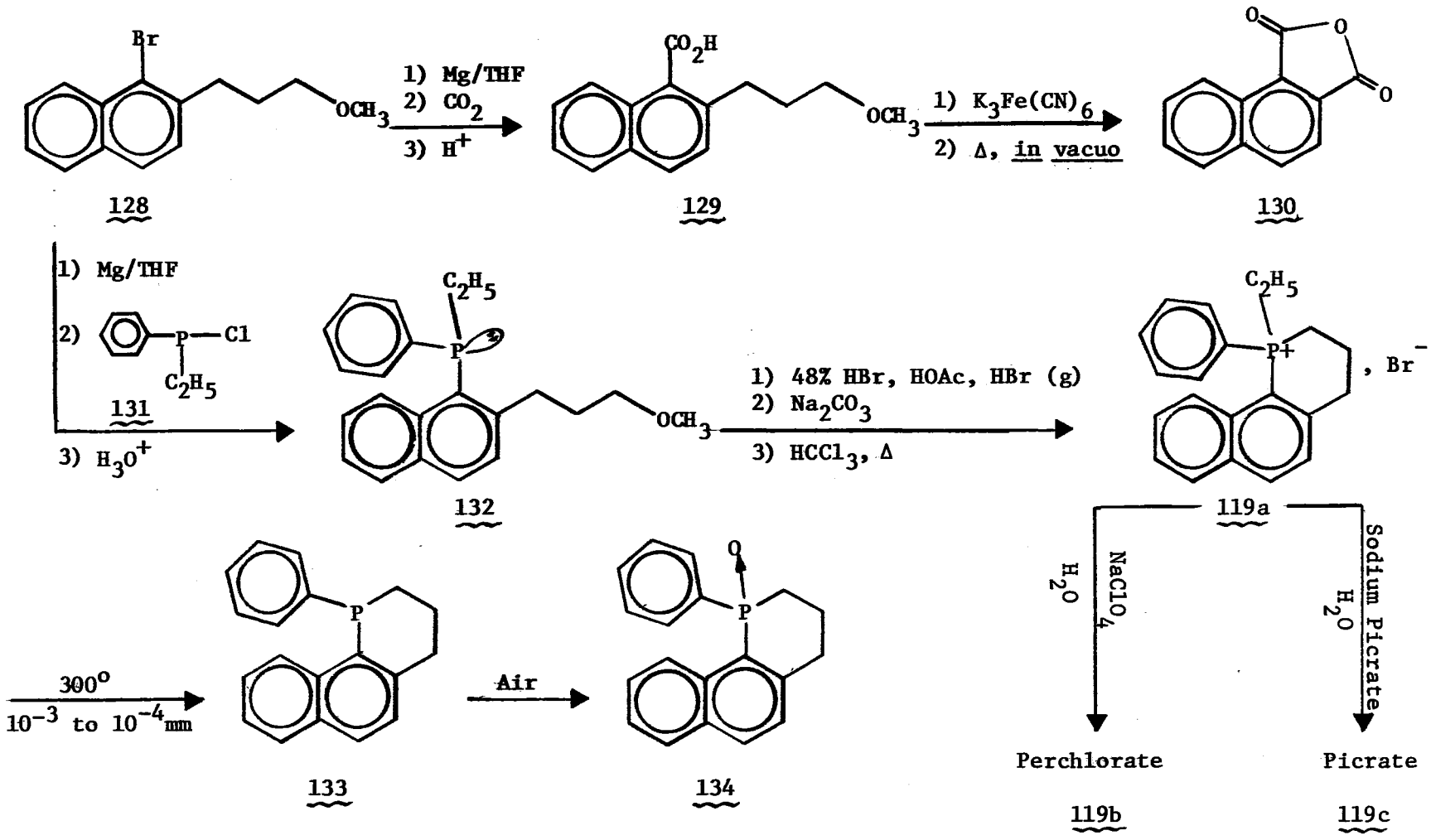
120a X = Br

120b X = ClO_4

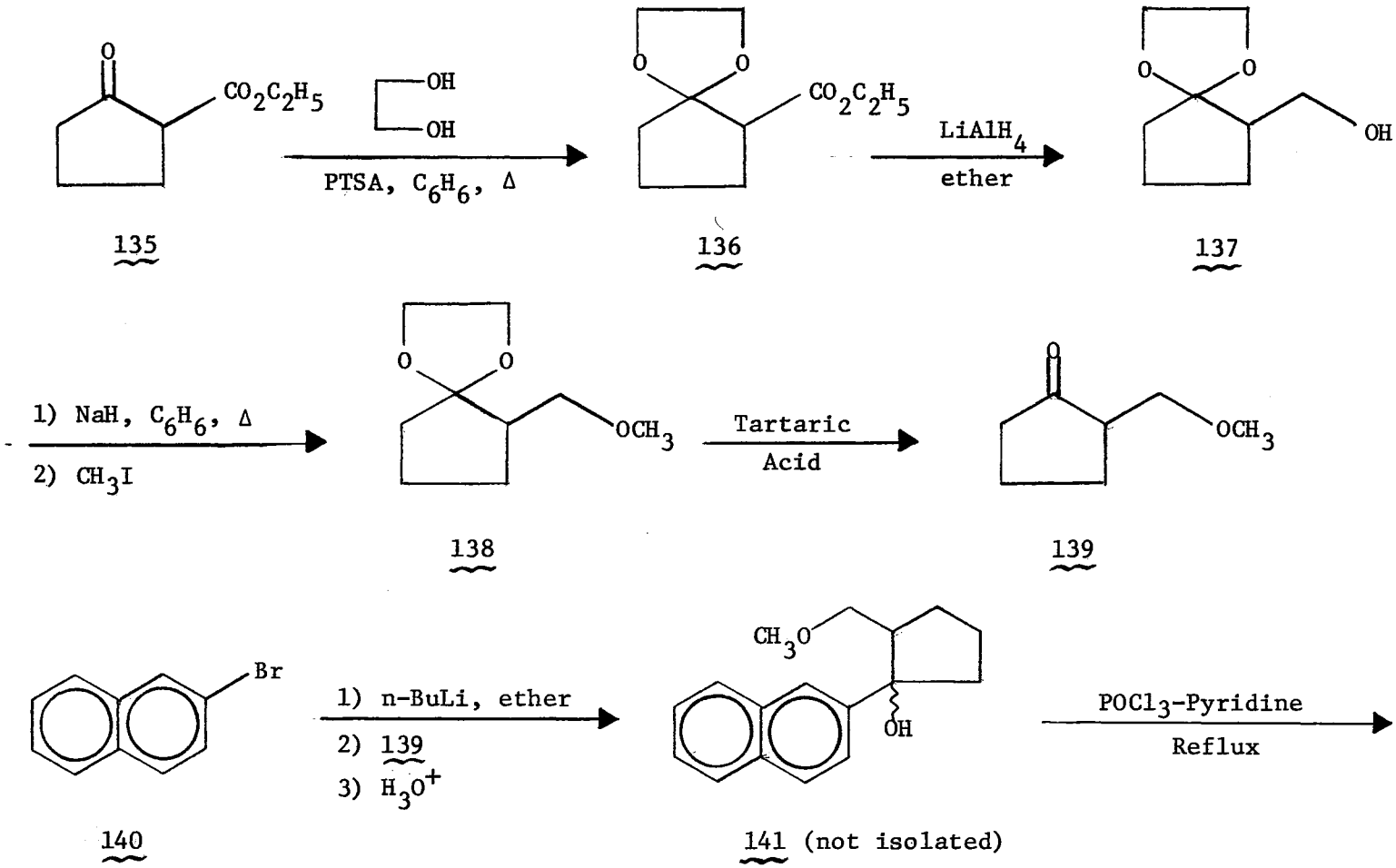
[h]cyclopenta[c]phosphinolinium perchlorate (120b, X = ClO_4) -- was achieved (the stepwise synthesis is outlined in Scheme II). Compounds 119 (a-c) and 120b were characterized by their spectroscopic properties (IR, NMR and mass spectra) and elemental analyses. Intramolecular quaternization proved to be successful for the cyclization. The introduction of the bromine specifically at the C-1 position of the naphthalene ring was achieved by treating the corresponding ethers 127 and 143 with Br_2 in the presence of anhydrous $FeBr_3$ in an inert solvent with ice cooling and exclusion of light. The C-1 positions for the bromine in 128 and 144 were verified by NMR spectral analyses. In the case of model compound 128, it was further proved by convertion to the carboxylic acid 129 and subsequent degradation to the known 1,2-naphthalenedicarboxylic anhydride (130). It should be noted that, only if the bromine was specifically introduced at the C-1 position of the naphthalene ring is it possible to properly attach a phosphorus group for the subsequent cyclization via the intramolecular quaternization to the final products 119a and 120a. The use of ethylphenylphosphinous



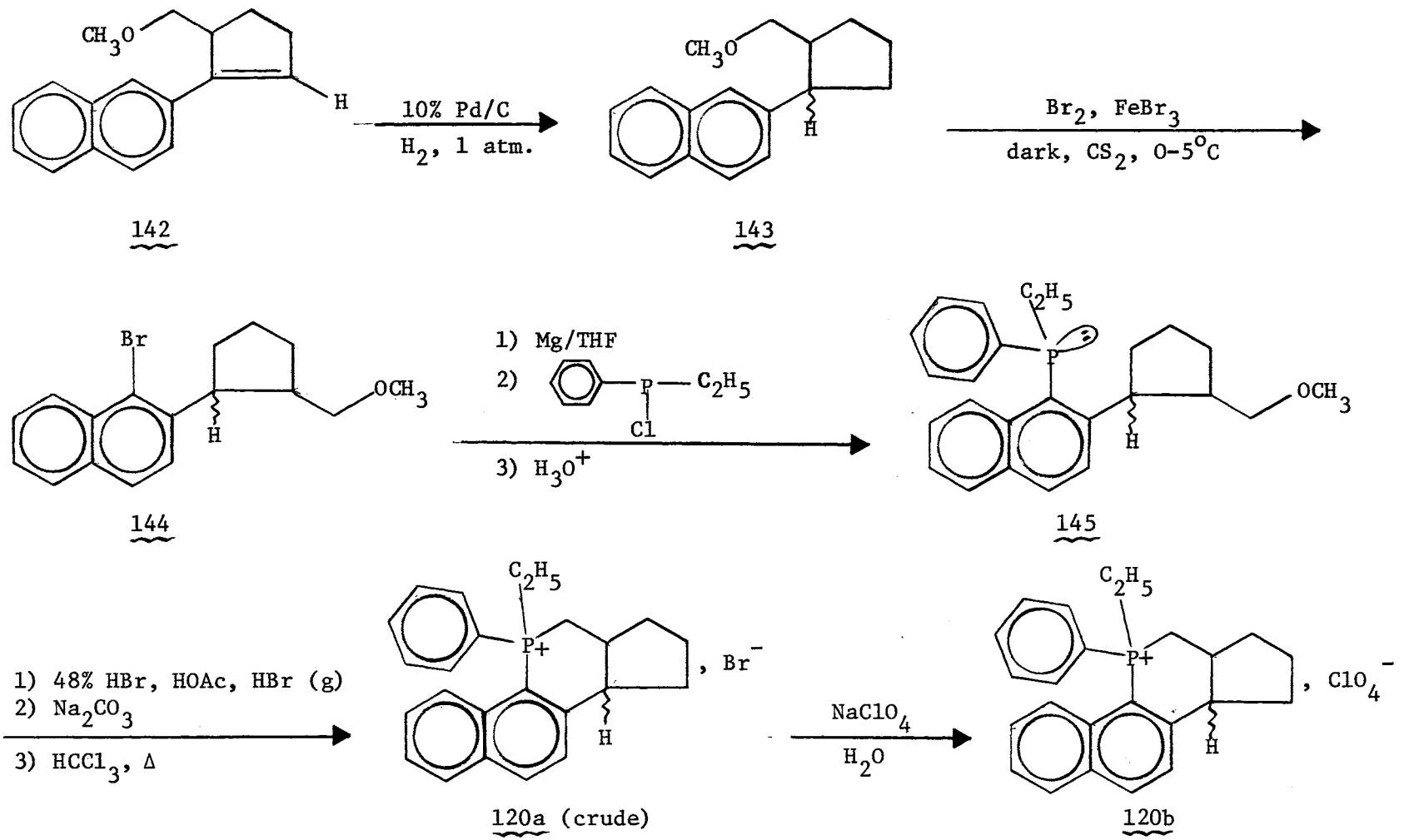
Scheme I. Total Synthesis of a Model Compound -- 1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Bromide (119a)



Scheme I (continued)



Scheme II. Total Synthesis of a Phosphasteroid -- 5-Ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo[h]cyclopenta[c]phosphinolinium Perchlorate (120b)



Scheme II (continued)

chloride (131) is significant in that it not only provided a strong nucleophile for the cyclization by intramolecular quaternization but also provided the system for an asymmetric phosphorus center in 119a and 120a. The latter compounds could potentially be resolved into optically active antipodes. Specific cleavage of the P-C (C_2H_5) bond of 119a to the corresponding cyclic phosphine 133 was achieved by pyrolysis under high vacuum. Further proof of the structure of 133 was also obtained through isolation and characterization of the phosphine oxide 134.

Although optically active acyclic phosphonium salts were well known since Kumli and his coworkers[76] introduced the resolving agents silver hydrogen D(-)- and L(+)-dibenzoyltartrates, very little work has been reported on the resolution of dissymmetric cyclic quaternary phosphonium salts. In fact, only two cyclic quaternary phosphonium salts were reported to be successfully resolved in the literature. Holliman and Mann[53] discussed the resolution of 2-phenyl-2-p-hydroxyphenyl-1,2,-3,4-tetrahydroisophosphinolinium bromide (113) in 1947 via silver (+)-bromocamphorsulfonate. However, the data can only be considered preliminary, for it was later found that these authors could not duplicate their previous results. Recently, P-spiro-bis-1,2,3,4-tetrahydrophosphinolinium iodide (114) was successfully resolved via silver (-)-menthoxyacetate.[52] But, it is to be noted that, in this case, the optical activity was attributed to the molecular dissymmetry of the P-Spiro geometry rather than to a truly asymmetric phosphorus atom of the type $[abcdP^+]\ X^-$.

Efforts were made in the last part of this research to resolve the

new dissymmetric C-P heterocycle -- 1-ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium bromide (119a). Partial resolution was attained by using silver hydrogen D(-)- and L(+)-dibenzoyltartrates (HDBT) as the resolving agents. Interestingly, a stoichiometric inclusion of 1 mole of dibenzoyltartaric acid (DBTA) was found (as revealed by elemental analysis) in the crystalline phosphonium L(+)-HDBT 154 formed by treating silver L(+)-HDBT (153) and the racemic phosphonium bromide 119a in the presence of H_2O. The pure dextrorotatory 1-ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium L(+)-HDBT-L(+)-DBTA (154) has a m.p. of 150° dec and a specific rotation of $[\alpha]_D^{24.5}$ +83° (c 0.0134, CH_3OH). Following the same procedure, the pure levorotatory 1-ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium D(-)-HDBT-D(-)-DBTA (155) was isolated which has a m.p. of 149-149.5° dec and $[\alpha]_D^{25}$ of -83° (c 0.0196, CH_3OH).

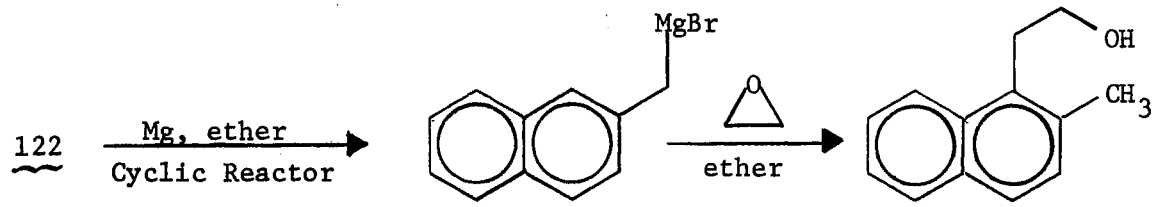
The dextrorotatory 1-ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]-phosphinolinium bromide (119a), $[\alpha]_D^{25}$ + 28°(c 0.0175, $HCCl_3$), m.p. 259° dec (the racemic 119a has m.p. 227.5-228.5°) was obtained by metathesis of the pure dextro-154 with NH_4Br. Further characterization of (+)-119a by conversion to the corresponding optically active perchlorate 119b was also attempted. The perchlorate 119b (probably optically active) obtained has a m.p. of 171.5-172.5° (the corresponding racemic 119b has a m.p. of 159-159.5°). However, owing to the limited quantity of the sample available, no optical rotation was measured for the perchlorate 119b.

The following is a list of new compounds that have been synthesized in this work. Their structures can be found elsewhere in the discussion corresponding to their assigned numbers.

1. 1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium bromide (119a), perchlorate (119b), and picrate (119c).
2. 5-Ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo[h]cyclopenta[c]-phosphinolinium bromide (crude) (120a), and perchlorate (120b).
3. 2-(3-Methoxypropyl)naphthalene (127).
4. 1-Bromo-2-(3-methoxypropyl)naphthalene (128).
5. 2-(3-Methoxypropyl)-1-naphthoic acid (129).
6. Ethyl[2-(3-methoxypropyl)-1-naphthyl]phenylphosphine (crude) (132).
7. 1,2,3,4-Tetrahydro-1-phenylbenzo[h]phosphinoline (133).
8. 1,2,3,4-Tetrahydro-1-phenylbenzo[h]phosphinoline 1-oxide (134).
9. 2-(Methoxymethyl)cyclopentanone cyclic ethylene ketal (138).
10. 2-(Methoxymethyl)cyclopentanone (139).
11. 2-(Methoxymethyl)-1-(2-naphthyl)cyclopentanol (crude) (141).
12. 2-[5-(Methoxymethyl)-1-cyclopenten-1-yl]naphthalene (142).
13. 2-[2-(Methoxymethyl)cyclopentyl]naphthalene (143).
14. 1-Bromo-2-[2-(methoxymethyl)cyclopentyl]naphthalene (144).
15. Ethyl[2-[2-(methoxymethyl)cyclopentyl]-1-naphthyl]phenylphosphine (crude) (145).
16. Diethyl 3-(2-naphthyl)propylphosphonate (147).
17. [3-(2-Naphthyl)propyl]phosphonic acid (148).
18. [3-(2-Naphthyl)propyl]phosphonic dichloride (149).
19. [3-(2-Naphthyl)propyl]phosphonous dichloride (150).
20. 1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium L(+)-HDBT-L(+)-DBTA (154).
21. 1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium D(-)-HDBT-D(-)-DBTA (155).

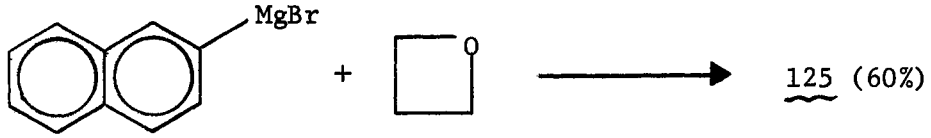
Preparation of 3-(2-Naphthyl)propanol (125) and 2-(3-bromopropyl)naphthalene (126)

One can devise several methods to synthesize 125 from commercially available starting materials. Benzylic bromination of 2-methylnaphthalene (121), followed by the classical lengthening of the carbon chain via reaction of the corresponding Grignard reagent of 133 with ethylene oxide would undoubtedly be the first choice. However, it is reported that, instead of the desired 3-(2-naphthyl)propanol (125), an interesting rearrangement product 2-(2-methyl-1-naphthyl)ethanol (146) is obtained from the reaction.[78]



146

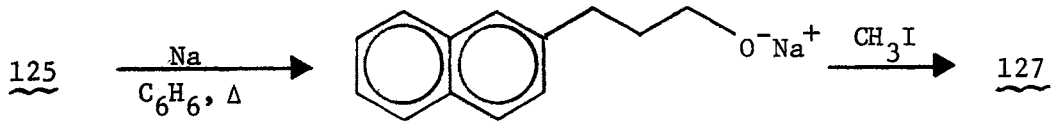
One method which appeared in the literature was the Grignard reaction of 2-bromonaphthalene with oxetane.[122] Although a relatively good yield (60%) of 125 was obtained, the availability of the starting materials economically in large quantities was a limitation.



Thus, it was decided to follow the procedure of Campaign and Heaton[23] (Scheme I -- 121→126). A nearly quantitative yield of crude 2-bromomethylnaphthalene (122) was reported by benzylic bromination of 2-methylnaphthalene (121) with N-bromosuccinimide.[25] However, it was found that upon purification by vacuum distillation, a 30% loss of the product 122 was recorded. Therefore, the crude 2-bromomethylnaphthalene (122) obtained was used immediately in the malonate synthesis (122→123) without further purification, where an overall yield of 40% for 123 based on 2-methylnaphthalene (121) resulted. It is to be noted that the conversions of 124→125 and 125→126 in Scheme I were essentially quantitative. Instead of recrystallizing 126 from hexanes [the crude 2-(3-bromopropyl)naphthalene (126) was found quite soluble in reagent hexanes and slowly turned yellow on standing], purification by chromatography through a silica gel column was found to give the best result.

Syntheses and Bromination of 2-(3-methoxypropyl)naphthalene (127)

Methyl ether 127 was synthesized smoothly from the bromide 126 and sodium methylate in methanol (Scheme I). It can also be prepared by making the alkoxide 147 directly from the corresponding alcohol 125 followed by treatment with excess CH_3I, but in a lower yield. Since

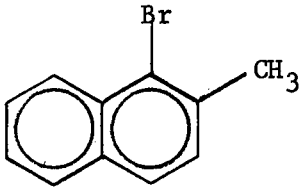


147

the alcohol 125 can be converted quantitatively to the corresponding

bromide 126, the choice of the former procedure (reaction of 126 with $CH_3O^-Na^+/CH_3OH$) is obvious.

Electrophilic substitution in 2-substituted derivatives of naphthalene is known to be favored at the C-1 position for o,p-directing and activating substituents, since this is activated both by the substituent and by the other ring.[36] For example, bromination of 2-methylnaphthalene (148)[1] and bromination of 2-methoxynaphthalene in acetic acid gave 1-bromo-2-methoxynaphthalene (149).[36] Exclusion of light, low



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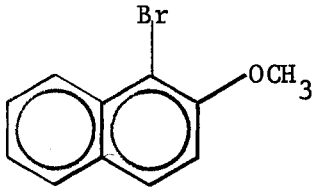


149

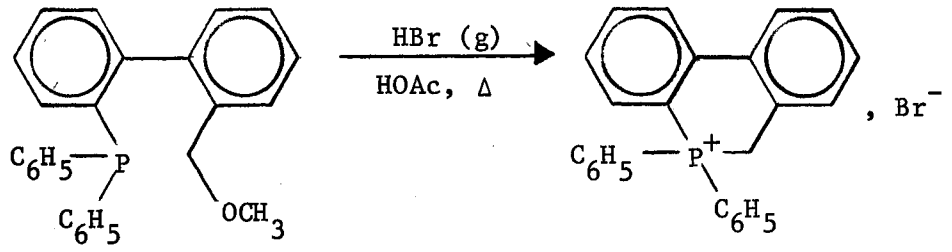
reaction temperature, and the presence of Fe powder seem to be essential in carrying out these reactions to ensure an ionic mechanism. It was found that bromination of 2-(3-methoxypropyl)naphthalene (127) under similar conditions was not successful. Although some reaction did occur after prolonged heating, the low yield of the desired 128 was not of synthetic value. The difficulty of nuclear bromination of methyl ether 127 suggested that some steric hindrance is imposed by the 3-methoxypropyl group at the C-2 position of the naphthalene ring. A more forcing condition than heating (which may enhance undesirable radical side reactions) was evidently demanded. Anhydrous ferric bromide, a much stronger Lewis acid, was found to work very well for this purpose. Thus, bromination of 2-(3-methoxypropyl)naphthalene (127) in CS_2 with bromine in the presence of anhydrous $FeBr_3$ (in the dark and with ice

cooling -- 0-5°) proceeded smoothly to give the desired product, 1-bromo-2-(3-methoxypropyl)naphthalene (128) in good yield. The mono-bromine substitution was confirmed by elemental analysis. Evidence for the C-1 bromine are provided by the NMR spectral analysis and by chemical degradation. The NMR spectra of certain substituted 1-bromonaphthalene derivatives reported in the literature[120] seem to have a characteristic feature in that their C-8 protons (presumably influenced by the adjacent electronegative Br at C-1) usually resonate further down field and are distinctly separated from the rest of the aromatic proton absoptions. This spectroscopic feature, which is also found in 1-bromo-2-(3-methoxypropyl)naphthalene (128) (Plate XXII) (δ8.12-8.35 -- m, 1H; δ7.07-7.78 --m, 5H) is sufficiently distinguishing to permit one to differentiate Br at C-1 from other mono bromo-substituted naphthalene derivatives. The structure was further confirmed by the synthesis of 2-(3-methoxypropyl)-1-naphthoic acid (129) from 128 via carbonation of the corresponding Grignard reagent, followed by oxidative degradation with potassium ferricyanide to 1,2-naphthalenedicarboxylic acid and subsequent dehydration by vacuum sublimation to the known 1,2-naphthalenedicarboxylic anhydride (130) (see Scheme I). It was observed that the Grignard reagent of 128 could not be made in ether and also that attempts to oxidize 129 with $KMnO_4$ gave no positive result.

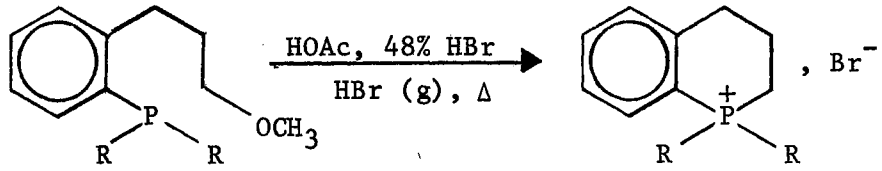
Cyclization by Intramolecular Quaternization

Holliman and Mann were the first to use intramolecular quaternization to effect cyclization in the syntheses of C-P heterocycles.[53] The reaction is so valuable that many C-P heterocycles which were difficult to cyclize by other means were successfully prepared by this reaction.

The following equations show some of the C-P heterocycles which have been obtained by this method.

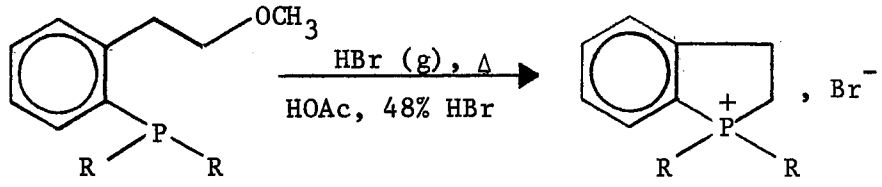


(97%) (Ref. 27)

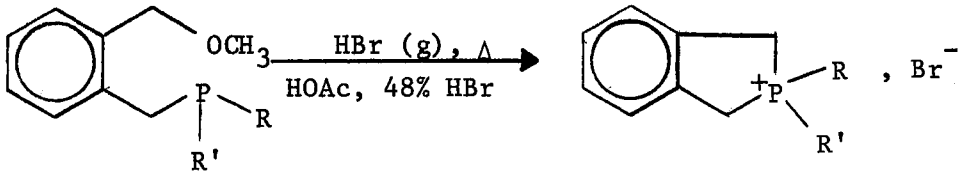


$R = C_2H_5$ (90%) as Picrate (Ref. 14)

$R = C_6H_5$ as BF_4^- (Ref. 84)



$R = C_2H_5$ (29%) as Picrate (Ref. 96)

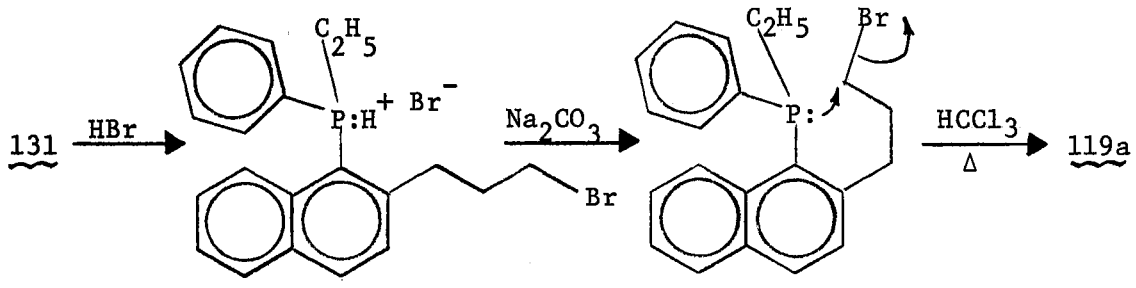


$R = C_6H_5$, $R' = C_2H_5$ (80%) (monohydrate) (Ref. 99)

$R = R' = C_6H_5$ (Ref. 98)

Two other interesting compounds, which have been mentioned briefly in the historical section, 2-phenyl-2-p-hydroxyphenyl-1,2,3,4-tetrahydroisophosphinolinium bromide (113) and P-spiro-bis-1,2,3,4-tetrahydrophosphinolinium iodide (114), were also prepared by this method.[52,53]

The usual procedure in the internal quaternizations with methyl ethers and phosphines involves passing of gaseous HBr into a boiling solution of the corresponding phosphine in glacial acetic acid and constant boiling hydrobromic acid followed by neutralization of the acid with Na_2CO_3. The bromo compound, generated in situ by the cleavage of the methoxy functional group by HBr, is immediately extracted with $HCCl_3$. Intramolecular quaternization (attack of the bromide by the phosphine) to give the cyclized phosphonium bromide usually occurs readily by warming the chloroform solution. Thus, ethyl[2-(3-methoxypropyl)-1-naphthyl]phenylphosphine (132) was smoothly cyclized to the cyclic phosphonium bromide 119a by such a procedure, described in the Experimental part. The cyclization presumably involves the intermediate 150 resulting from the displacement of the methoxy group in 132 and simultaneous protonation of the phosphine moiety by HBr.



150 151

The phosphine 151, which was generated *in situ* by neutralizing 150 with base, cyclized to 119a by intramolecular displacement of the adjacent bromide by the ethylphenylphosphinous group. The evidence for the cyclization and the characterization of 119a are presented in the Experimental section. It is interesting to note that upon recrystallization of 119a from $HCCl_3$-ether, a nonstoichiometric amount of $HCCl_3$ (which could not all be removed even on heating at 100-2°/1.5-2μ for 90 hrs.) was incorporated in the crystalline salt. Thus, although the spectroscopic data were appropriate, the elemental analysis of the phosphonium bromide 119a did not yield the theoretical results. However, excellent elemental analyses were obtained for the derivatives, the phosphonium perchlorate 119b and picrate 119c.

All the workups in the synthesis of the phosphine 132 and the subsequent cyclization were performed under N_2. A special apparatus was designed (shown in Fig. 1, p.98) so that drying the organic extract ($MgSO_4$), filtration, washing the $MgSO_4$ with solvent, boiling and evaporating the solvent ($HCCl_3$) were accomplished smoothly in one operation .

Decomposition of the Cyclized Phosphonium Bromide 119a

Alkaline hydrolysis of phosphonium salts is known to be useful in cleavage of C-P bonds and leads to the formation of phosphine oxides.[71] The ease of elimination of various groups has been noted to be in the same order as the stability of the displaced anions, as follows:[105]

benzyl > α-,or β-naphthyl > phenyl > methyl >

β-phenethyl > ethyl > high alkyls.

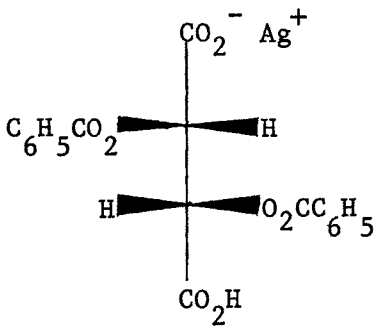
Reaction of 119a with NaOH in several attempts, however, was found to yield complex mixtures of products; at least 4 spots were detected by TLC (silica gel PF_{254}, Brinkmann Instrument Co.). Neither did the reaction of 119a with Ag_2O in H_2O give any major product that was of synthetic use. No effort was made to isolate and characterize the various products from the above reactions.

Pyrolyses of phosphonium bromides (or chlorides) bearing ethyl substituents are known to be useful in the syntheses of certain cyclic phosphines.[14,93,96,99] Upon decomposition, ethylene and HBr (or HCl) are given off and the residual phosphine, partly in the form of the HBr (or HCl) salt and partly in free form, when fully liberated with alkali, can be worked up in the usual way. It was found that the phosphonium bromide 119a was decomposed smoothly at around 300° under high vacuum (10^{-3} to 10^{-4} mm) to yield the 1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinoline (133), which was purified by chromatography through a silica gel (Baker Analyzed Reagent, 80 - 200 mesh) column; recrystallization from hexanes gave rhombic crystals, m.p. 120.5-121.5°.

The isolation of 1,2,3,4-tetrahydro-1-phenybenzo[h]phosphinoline 1-oxide (134) was rather fortuitous. Apparently, it resulted from partial oxidation of phosphine 133 by air during the workups. The successful syntheses and characterizations of the cyclic phosphine 133 and its oxide 134 serve to add further proof for the structure of the precursor -- 1-ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium bromide (119a). The structures of 133 and 134 rest on their IR, NMR, and mass spectrometric data as well as their respective excellent elemental analyses (Experimental -- p.104).

Resolution of 1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h] phosphinolinium Bromide (119a) and Perchlorate (119b)

Some success in the resolution of a cyclic quaternary phosphonium bromide 119a via silver D(-) and L(+)-HDBT was attained. Silver D(-) and L(+)-HDBT, 152 and 153, have been used to effect resolutions of



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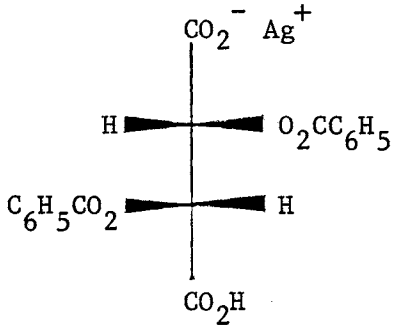
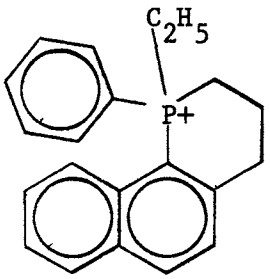


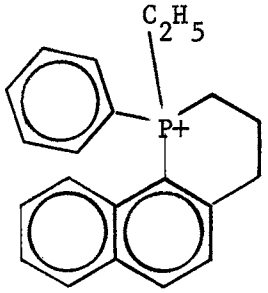
153

acyclic quaternary phosphonium salts (see Historical). However, no one has ever attempted to utilize the optically active hydrogen dibenzoyl-tartrates to resolve a cyclic phosphonium salt. In fact, there have been only 2 papers published in the last 23 years concerning the resolution of cyclic phosphonium salts [the resolving agents used were silver (+)-bromocamphorsulfonate and silver (-)-menthoxyacetate].[52,53]

Two diastereoisomeric salts 154 [m.p. 150° dec, $[\alpha]_D^{24.5}$+83° (c 0.0134, CH_3OH)] and 155 [m.p. 149-149.5° dec, $[\alpha]_D^{25}$-83° (c 0.0196, CH_3OH)] were synthesized and separated by treatment of the (±)-phosphonium bromide 119a with excess Ag L(+)-HDBT (153) and Ag D(-)-HDBT (152) in water, respectively. The identical m.p. and opposite specific rotations of 154 and 155 strongly indicate their enantiomeric nature. The stoichiometric inclusion of one equivalent of L(+)-DBTA found in the crystal of 154, as revealed by its elemental analysis, was most



, L(+)-HDBT - L(+)-DBTA



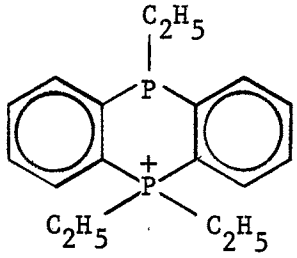
, D(-)-HDBT - D(-)-DBTA

154 155

HDBT = Hydrogen Dibenzoyltartrate

DBTA = Dibenzoyltartaric Acid

interesting. A similar phenomenon was encountered by Davis and Mann[35] in the synthesis of 9,9,10-triethyl-9,10-dihydrophosphanthrene picrate (156a and b), in which one equivalent of picric acid was found included in 156a and one equivalent of sodium picrate was found in 156b. Apparently, the synthesis of 154 and 155 in the presence of H_2O was respon-



, X^-

156a, X = Picrate - Picric Acid; m.p. 120-1°.

156b. X = Picrate - Sodium Picrate; m.p. 209-210°.

sible for the formation and inclusion of the respective dibenzoyltartaric acids.

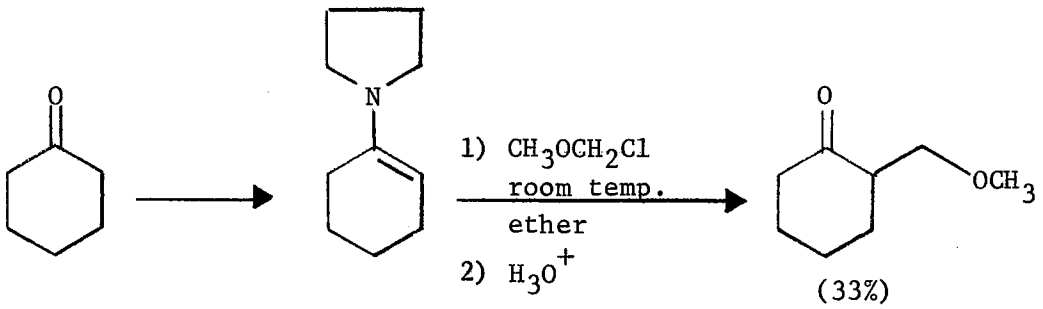
While metathesis of 154 directly to the optically active phosphonium perchlorate 119b (with NH_4ClO_4 in methanol) was unsuccessful (starting material 154 was quantitatively recovered), the metathesis to the dextrorotatory phosphonium bromide 119a with NH_4Br in methanol did give positive results. After repeated recrystallization from chloroform and ether the (+)-119a isolated had a constant m.p. of 259° dec and a specific rotation of $[\alpha]_D^{25}$ +28° (c 0.0175, $HCCl_3$). Although there was no direct proof available (NMR and elemental analysis) of the structure of the resolved dextrorotatory phosphonium bromide 119a, it was supported by its IR spectrum, which was found virtually superimposable on that of the authentic racemic 119a. It is to be noted that the m.p. of the resolved (+)-119a (259° dec) is different from that of the racemic 119a (m.p. 227.5°-228.5°) as expected.

Further proof of the structure of the (+)-119a was provided by its conversion to the corresponding (optically active) perchlorate 119b (m.p. 171.5-172.5°), which again has essentially the same IR spectrum as that of the authentic racemic 119b (m.p. 159-159.5°). The perchlorate derived from metathesis of the dextrorotatory phosphonium bromide 119a is expected to be optically active as demonstrated by the difference in its m.p. and that of the racemic compound. However, because of the extremely small amount of the (optically active) phosphonium perchlorate 119b available no specific rotation was obtained.

Introduction of the D-ring and Total Synthesis of the Phosphasteroid 120b

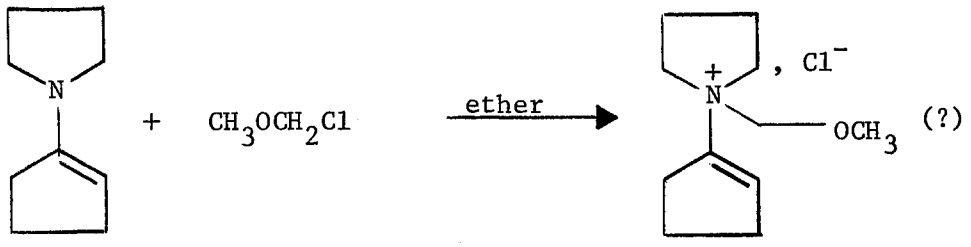
With the general synthetic approach worked out for the model com-

pound 119a as in Scheme I, the planning of the total synthesis of the phosphasteroid -- 5-ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo[h] cyclopenta[c]phosphinolinium perchlorate (120b) -- seemed to be relatively straightforward. The synthetic approach to 120a and 120b is outlined in Scheme II. One of the key compounds in this synthesis is 2-(methoxymethyl)cyclopentanone (139), a precursor of the D-ring in the phosphasteroid 120b. It is interesting to note that, although the homolog of 139, 2-(methoxymethyl)cyclohexanone (158), is known[127] and



157 158

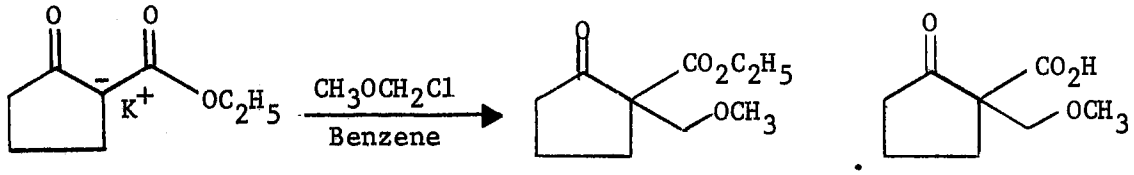
can be readily synthesized by alkylation of the enamine 157 with chloromethyl methyl ether, the same reaction in the case of cyclopentanone was found to give only quantitative N-alkylation instead of the desired C-alkylation. Only cyclopentanone was detected in the organic extract from the hydrolysis of the reaction mixture of the enamine 159 with



159

CH_3OCH_2Cl.

Compound 161 is known and can be synthesized by alkylation of 160 with CH_3OCH_2Cl in benzene.[17] Compound 161, after acid hydrolysis (base would lead to ring opening), should give 162, which, being a β-keto acid, would be expected to yield the desired 2-(methoxymethyl)cyclopentanone (139) upon decarboxylation by heating. However, upon acid (25% HCl) hydrolysis of 161 and subsequent decarboxylation, none of the ex-

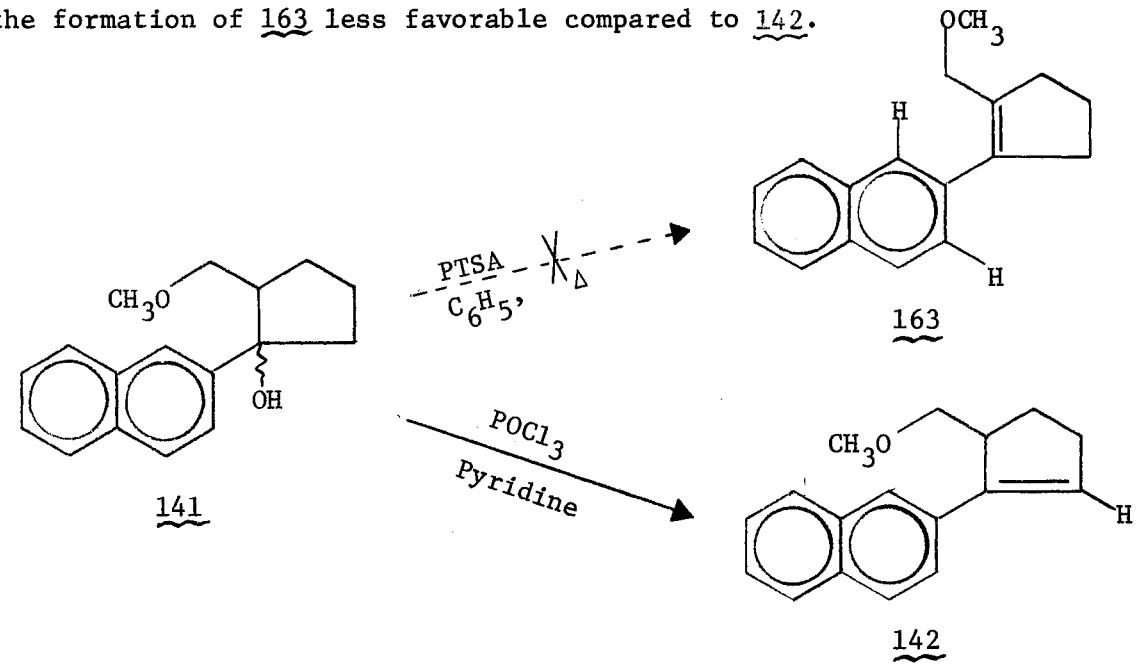


160 161 162

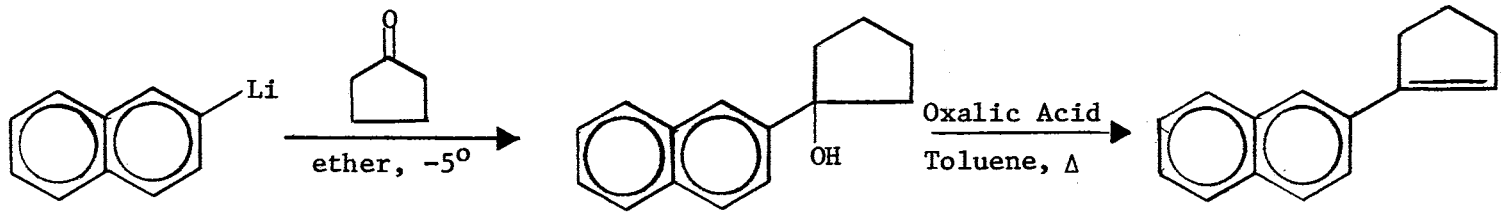
pected 2-(methoxymethyl)cyclopentanone (139) was detected; instead, a product of unknown structure [NMR: δ1.65 (q, 3H), δ2.15-2.7 (m, 4H) and δ7.37 (m, 1H -- a vinyl proton); IR: 1700 cm^{-1} (C=O)] was isolated. Apparently, an interesting rearrangement had occurred in the acid medium upon decarboxylation of 162, but no further effort was made to study the reaction.

2-(Methoxymethyl)cyclopentanone (139) was finally obtained by the method presented in Scheme II. It is to be noted that the reaction of NaH with 2-(hydroxymethyl)cyclopentanone ethylene ketal (137) (to make the corresponding sodium alkoxide for subsequent alkylation with CH_3I) in benzene was very sluggish. Prolonged heating and the use of excess NaH were apparently essential to effect a quantitative conversion.

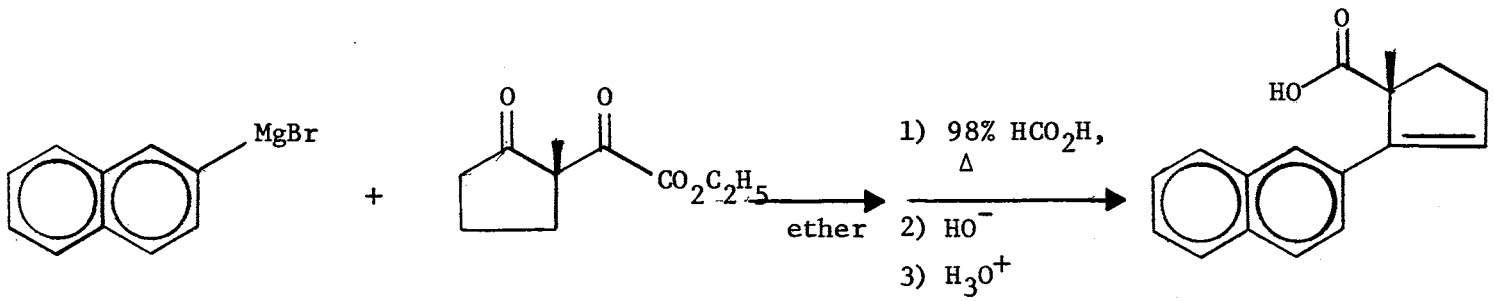
Both the Grignard reagent and the lithium reagent derived from 2-bromonaphthalene (140) were found applicable in reaction with 139, although the latter seemed to yield a better result. The intermediate alcohol 2-(methoxymethyl)-1-(2-naphthyl)cyclopentanol (141) was not isolated. After being separated from its major impurities (naphthalene and 2,2'-binaphthyl), the crude 141 was dehydrated immediately with $POCl_3$-pyridine to the corresponding alkene 2-[5-(methoxymethyl)-1-cyclopenten-1-yl]naphthalene (142). It is interesting to note that attempts to dehydrate 141 in acidic medium (PTSA/benzene), which would be expected to give the most substituted alkene 163, were not successful. The steric hindrance as imposed by cis arrangement in 163 (the presence of the double bond in this position would force two bulky groups -- 2-naphthyl and methoxymethyl -- into one plane) may render the formation of 163 less favorable compared to 142.



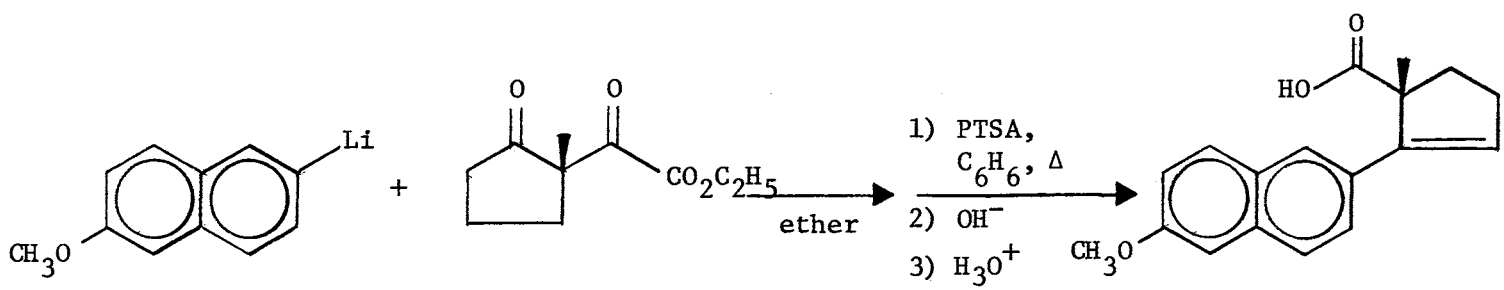
Other similar systems which have been described in the literature are listed below.



(Ref. 10)



(Ref. 60)

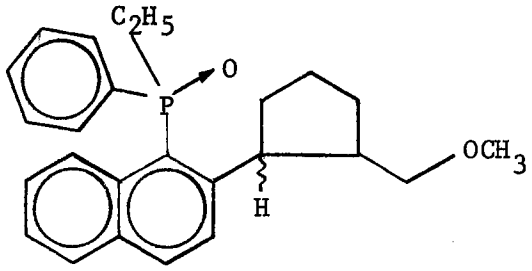


(Ref. 42)

The hydrogenation of 142 to the corresponding saturated hydrocarbon went smoothly in the presence of 10% Pd/C at atmospheric pressure in desulfurized C_2H_5OH. Although the GLC analyses of the product from the hydrogenation of 142 showed the mixture to be isomerically homogeneous, the stereochemistry of 143 (which will be discussed further in the next section) could not be established. Subsequent bromination of 143 under the same conditions as that of the model compound 127 again yielded only one major product, which was characterized as 1-bromo-2-[2-(methoxymethyl)cyclopentyl]naphthalene (144). The position of the bromine at C-1 is supported by the characteristic aromatic proton absorptions [δ8.35, m, 1H (C-8); δ7.11-7.9, m, 5H] observed in the NMR spectrum of 144 (Plate XXXV).

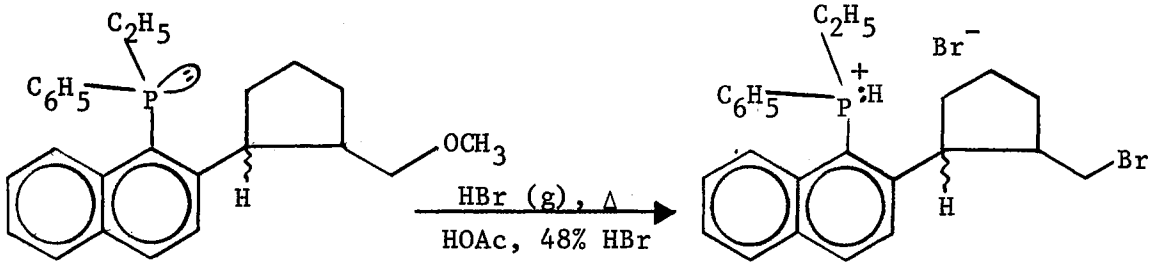
The introduction of an ethylphenylphosphinous group on 144 via the the corresponding Grignard reagent of 144 is outlined in Scheme II. The reaction is similar to that discussed for the model compound 132 (Scheme I), although it should be pointed out that the "entrainment" method seems to be essential in preparing the Grignard reagent (THF) from 144, especially in a small scale run; otherwise, the reaction was found sluggish and the yield was rather poor.

The ethyl[2-[2-(methoxymethyl)cyclopentyl]-1-naphthyl]-phenylphosphine (145) was not obtained in pure form. The product obtained was extremely viscous and high-boiling (b.p. 210-215°/7μ). Even under very high vacuum (diffusion-pump system) and using a Bantam-ware short-path still, it was distilled with difficulty. The crude 145, which was shown by mass spectral analysis to contain a considerable amount of the phosphine oxide 164 (m/e 392), was used directly in the cyclization without further purification.

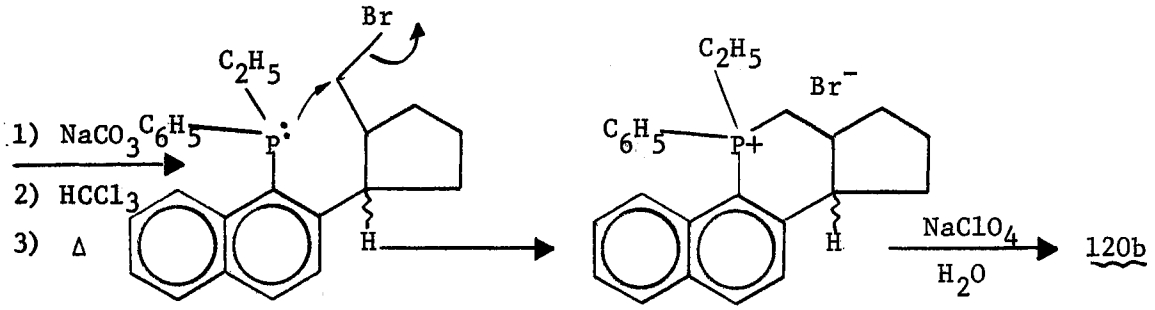


164

The cyclization of 145 (similar to that of the model compound 132) by intramolecular quaternization is described in detail in the Experimental. Various attempts to purify the crude bromide 120a were unsuc-



145



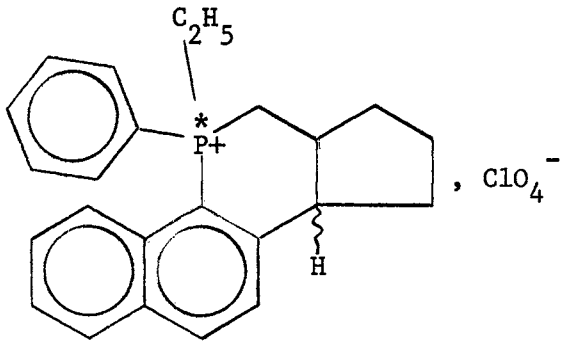
120a

cessful. Characterization was made through the perchlorate 120b (m.p. 183.5-187°) by elemental analysis, and by IR and NMR spectrometry (Plate XVI and XXXVIII). The IR spectrum showed the characteristic very strong and broad band[26] for ClO_4^- at 1090 cm^{-1}. The NMR spectrum

showed the expected proton absorptions at δ7.3-8.5 (ArH -- m, 11H), complexed methylene and methine absorptions at δ1.5-4.0 (m), and the methyl proton absorptions for $PCH_2\underline{CH}_3$ at δ0.6-1.5 (m) (partially overlapping with the former); one sees a total of 15H for alkyl protons. The low yield of 120a (20% based on 144) may be attributed to impurity of the precursor phosphine 145. The major impurity, phosphine oxide 164, apparently could not be cyclized by the intramolecular quaternization mechanism under the experimental conditions, which is understandable.

Stereochemistry of the Phosphasteroid 120b and Related Compounds

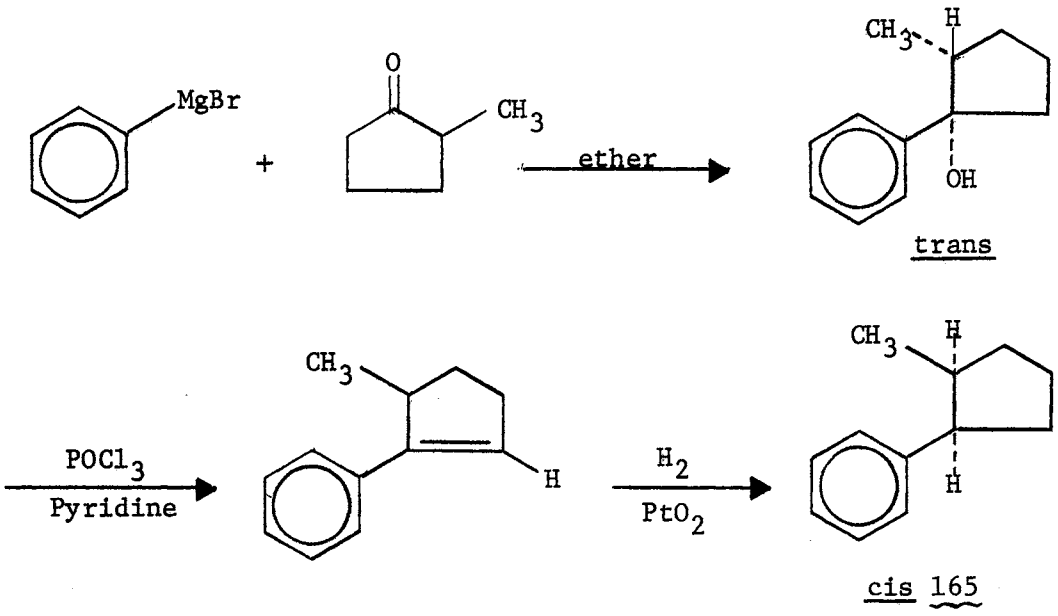
It is to be pointed out that the stereochemistry of C/D ring junction in the phosphasteroid 120b is not fully established, although evidence was accumulated which suggests a cis or trans isomer but not a mixture of both. During the cyclization, a new asymmetric center was



120b

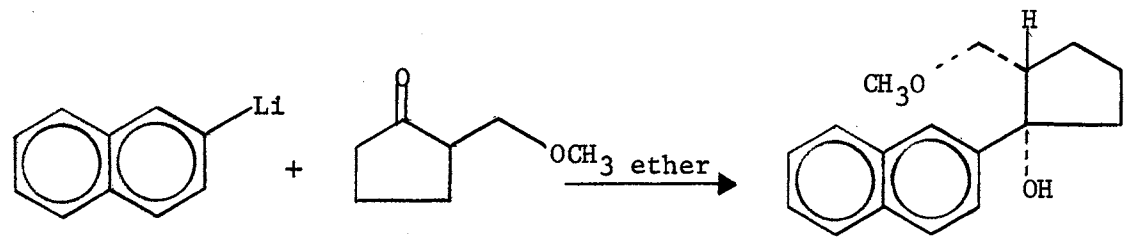
generated by the ethylphenylphosphinous moiety, which will give rise to two diastereoisomers in the cyclized product. This is reflected by the rather wide range of m.p. of 120b (m.p. 183.5°-187°) and its complicated NMR spectra (Plate XXXVIII and XXXIX).

As stated before, the hydrogenation of the alkene 142 was found to give stereospecifically one isomer (isomerically homogeneous as shown by GLC analyses -- checked on 4 separate columns). The stereospecificity was further supported by the subsequent bromination of 143, which was also shown to yield only one isomer 144. Although the NMR spectra of 143 and 144 were too complicated to allow one to identify which isomer (cis or trans C/D) was actually obtained from the hydrogenation of 142, the configuration of 143 might be surmised to be cis following the argument provided by Pines and coworkers[113] in the synthesis of a similar system -- 1-methyl-2-phenylcyclopentane (165). The preferential formation of cis-165 was achieved by a similar procedure from a Grignard reaction followed by dehydration ($POCl_3$ - pyridine) and catalytic hydrogenation as shown.

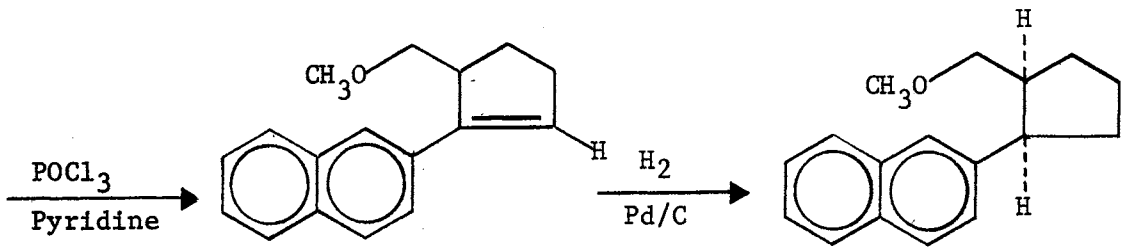


According to Cram's rule,[30] the major product from the reaction of 2-(methoxymethyl)cyclopentanone (139) with 2-naphthyllithium should be a trans isomer. The preferential cis dehydration[113] of this alcohol by $POCl_3$ - pyridine to the alkene 142 and subsequent catalytic hydro-

genation (cis addition of hydrogen to the double bond from the less hindered side[20]) should then result in the preferential formation of the cis-2-[2-(methoxymethyl)cyclopentyl]naphthalene (143).



139 trans 141

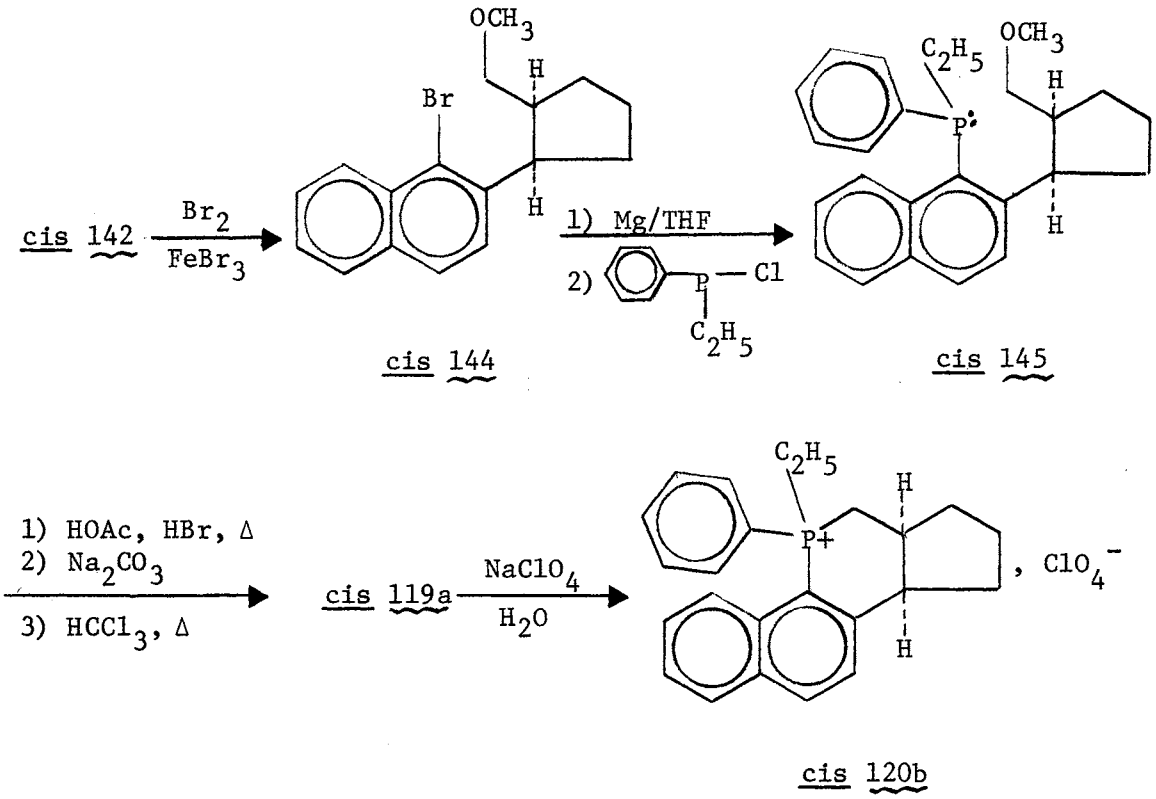


142 cis 143

Nuclear bromination of 143 would then be expected to give the cis-144, which after introduction of the ethylphenylphosphinous group and cyclization, should provide the C/D cis ring junction of the phospha-steroid -- 5-ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo[h]cyclopenta[c]phosphinolinium perchlorate (120b).

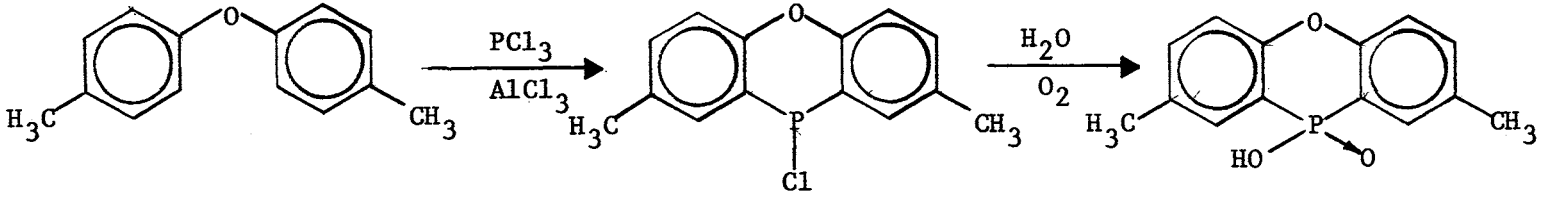
Although stereospecific catalytic hydrogenation by cis addition of hydrogen from the less hindered side is well documented, different stereochemical consequences have been reported for different experi-

mental conditions.[9] Hence, without further evidence, this assignment for 120b can only be taken as tentative.

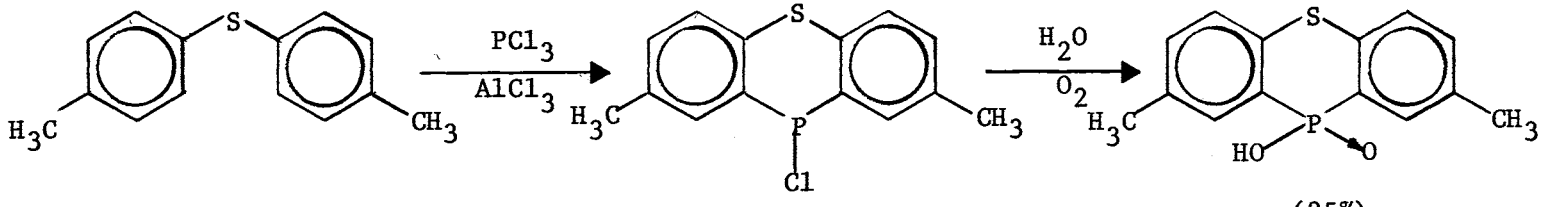


Other Attempted Cyclizations

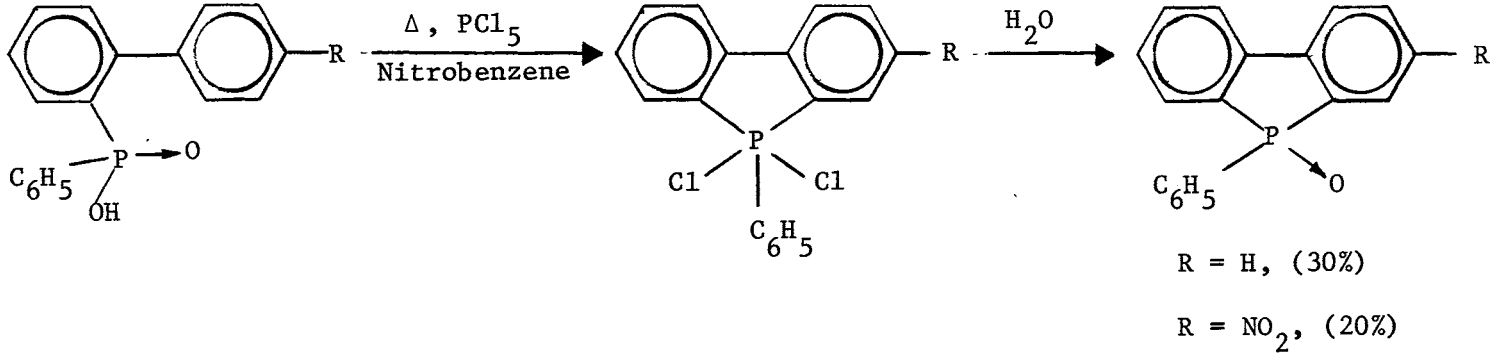
Several pieces of published data suggested originally other approaches to our C-P heterocycles. Cyclodehydration and cyclodehydrohalogenation (Friedel-Crafts reaction) have been shown in many cases to be usable in the syntheses of phenanthrene, anthracene, or fluorene type C-P heterocycles.[15] The following reactions are some typical examples reported in the literature. Other recent examples[72,73] are presented in the historical section of this thesis.



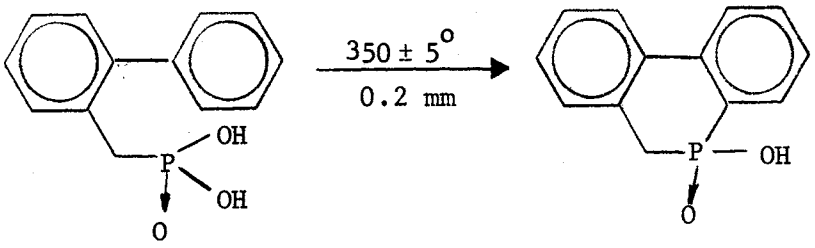
(Ref. 80)



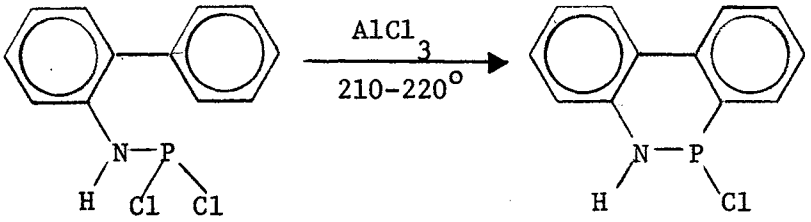
(Ref. 48)



(Ref. 24)



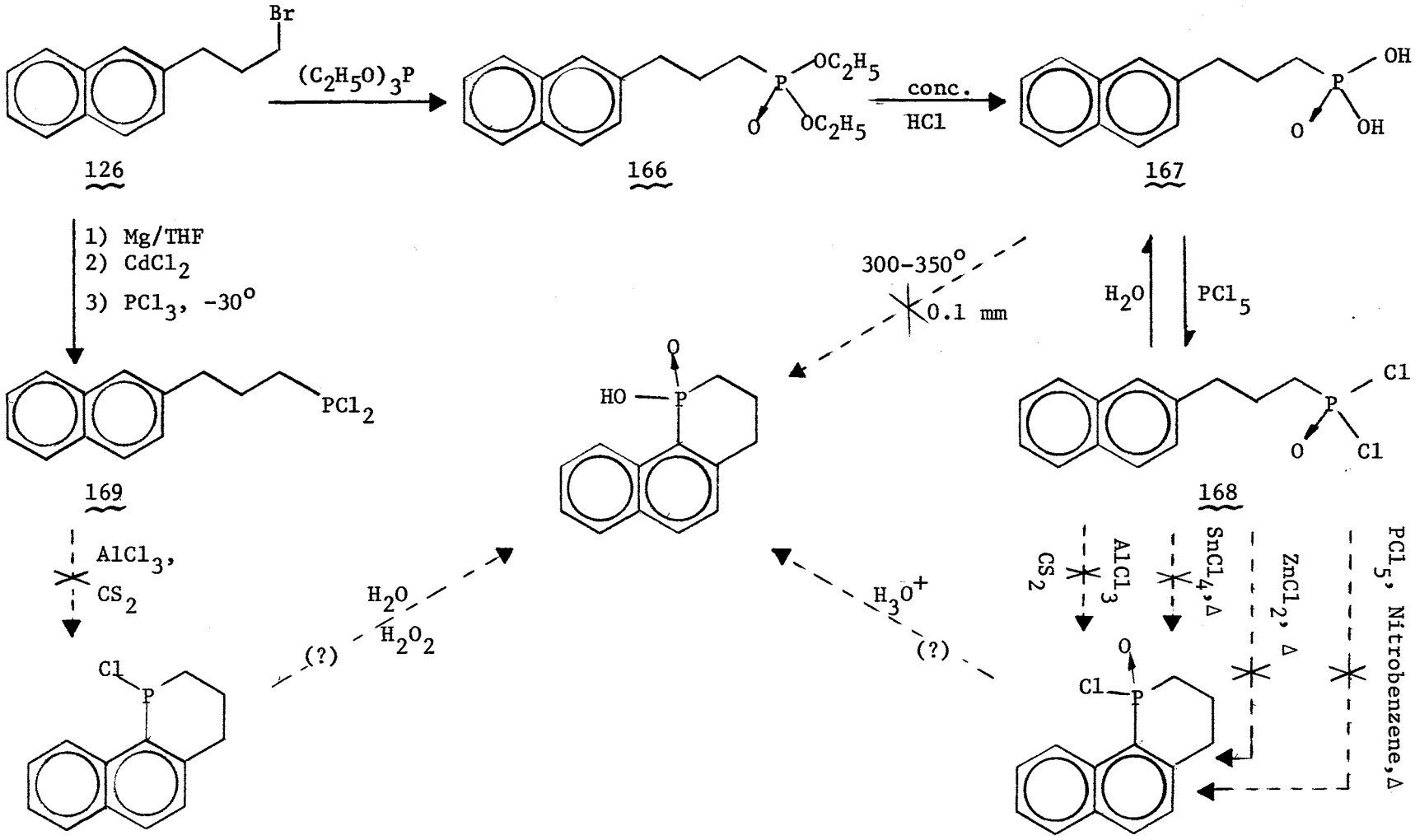
(60%) (Ref. 82)



(42%) (Ref. 37)

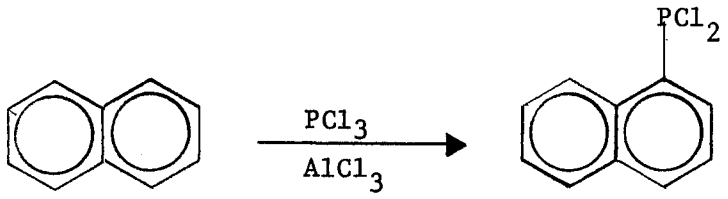
Friedel-Crafts reactions have been known to be a good method for producing organophosphorus compounds from aromatic hydrocarbons. A review was published by Kosolapoff[75] on the Friedel-Crafts reactions of phosphorus compounds. However, the detailed mechanisms involved are still virtually unexplored.

Several potential precursors, diethyl [3-(2-naphthyl)propyl]phosphonate (166), [3-(2-naphthyl)propyl]phosphonic acid (167), [3-(2-naphthyl)propyl]phosphonic dichloride (168), and [3-(2-naphthyl)propyl]phosphonous dichloride (169), were successfully synthesized and characterized for the first time. Their syntheses from 2-(3-bromopropyl)naphthalene (126) are displayed in Scheme III. However, their subsequent cyclizations (dashed-line arrow in Scheme III) via analogous cyclodehydration[82] and cyclodehalogenation[24,37,48,72,73,80] procedures were not



Scheme III. Syntheses of Precursors of Related C-P Heterocycles and Attempted Cyclizations

successful. Attempted cyclization of 167 by pyrolysis *in vacuo* gave only mixtures of polymeric phosphonic anhydrides. Friedel-Crafts reaction of naphthalene with PCl_3 in the presence of aluminum chloride has been reported[81] to yield 1-naphthylphosphonous dichloride (170).



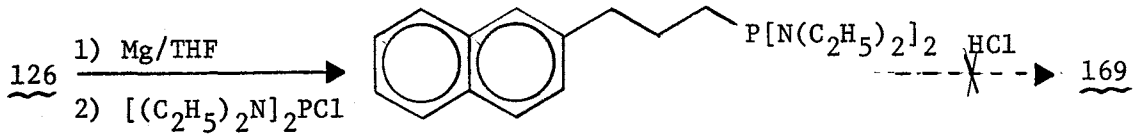
170

However, cyclization of the phosphonic dichloride 168 in the presence of $AlCl_3$ (in CS_2), or in anhydrous $SnCl_4$ gave, after hydrolysis, only traces of unidentified materials. When 168 was directly heated with $ZnCl_2$, extensive polymerization was observed. Attempted cyclization by boiling 168 with PCl_5 in nitrobenzene, and subsequent hydrolysis, resulted in the starting phosphonic acid 167. The attempted cyclization of the phosphonous dichloride 169 in the presence of $AlCl_3$ in CS_2 also gave only negative results.

Apparently, the difficulty for the functional groups at the end of the side chain to curl around to the proximity of the C-1 position (perhaps because of the large P atom) of the naphthalene ring for the ring closure (which thus must compete with intermolecular polymerization) may be the reason for the failure. Usually the C-1 position of naphthalene is highly reactive toward electrophilic substitution.

It is to be noted that the preparation of phosphonous dichloride 169 by the procedure of Koe and Bickelhaupt[72] *via* the intermediate

N,N,N',N'-tetraethyl-p-[3-(2-naphthyl)propyl]phosphonous diamide (171) was not entirely successful. The organocadmium reagent was found far

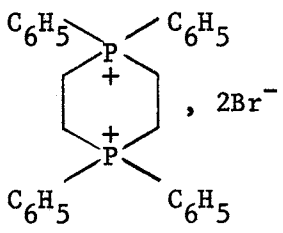


171

superior to the Grignard reagent for the synthesis of [3-(2-naphthyl)-propyl]phosphonous dichloride (169) (see Scheme III).

Mass Spectra of Phosphonium Salts

Very little is known about the mass spectra of phosphonium salts, which may be obtained by direct evaporation in the probe at elevated temperature. In fact, the only paper published is a brief communication by Aguiar and his coworkers[2] who reported that, when a sample of 1,1,4,-4-tetraphenyl-1,4-diphosphoniacyclohexane dibromide (172) was directly evaporated into the ionization chamber of a high-resolution mass spec-



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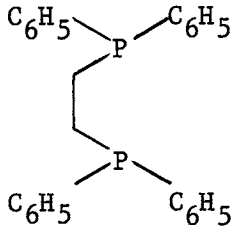

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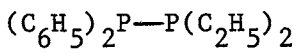

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trometer from a small tube at 310°, a mass spectrum (in which the highest m/e 586 corresponding to the molecular weight of 172), was obtained. Large peaks were observed also at m/e 398 and 370. They were attributed to ethylenebis(diphenylphosphine) (173) and tetraphenylbiphosphine (174), respectively, which are undoubtedly major decomposition products. However, a detailed analysis of the mass spectrum is lacking. It is interesting to note that all the bromine in 172 has been shown chemically to be ionic.[2] It is not easily conceived that an ionic, high molecular weight phosphonium salt 172 can be evaporated at such an elevated temperature (310°) without noticeable decomposition.

Mass spectra of four new cyclic phosphonium salts -- 1-ethyl-1,2,-3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium bromide (119a), the corresponding perchlorate (119b), the corresponding picrate (119c), and 5-ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo[h]cyclopenta[c]phosphinolinium perchlorate (120b) -- are now reported and displayed in Plate XLV, XLVI, XLVII and LI, respectively. They were obtained on a LKB-9000 prototype, magnetic sector, GLC-mass spectrometer by direct evaporation of the salts at the following conditions:

Probe temperature = ca. 200° (at 10^{-7}mm).

Ion source temperature = 310°.

Electron voltage = 70 eV.

Intense ions of each of the spectrum obtained for 119a, 119b, 119c, and 120b are tabulated in Table III. Since 119a, 119b, and 119c have the same phosphonium cation, some similarity among their spectra is to be noted. Of particular interest is that no molecular ions are observed for 119a, 119b, 119c, and 120b. Instead, appreciable intensities for peaks at m/e 302 for 119a, 119b, and 119c, and at m/e 342 for 120b are

TABLE III

INTENSE IONS IN THE MASS SPECTRA OF PHOSPHONIUM SALTS 119a, 119b, 119c, AND 120b[a]

119a (Mol. wt. = 385)		119b (Mol. wt. = 404)	
m/e	% RI	m/e	% RI
108	8	18	87
110	8	36	68
165	12	77	36
183	16.5	141	43
215	8	142	42
261	21	273	100
273	9	276	9.5
276	100	291	38
277	23.5	302	57
302	5		

119c (Mol. wt. = 533)		120b (Mol. wt. = 444)	
m/e	% RI	m/e	% RI
18	100	18	100
28	79	28	59
44	60	44	67
78	13.5	233	7.5
165	8	313	35
207	18	314	15
273	32	316	12
302	15.5	342	17

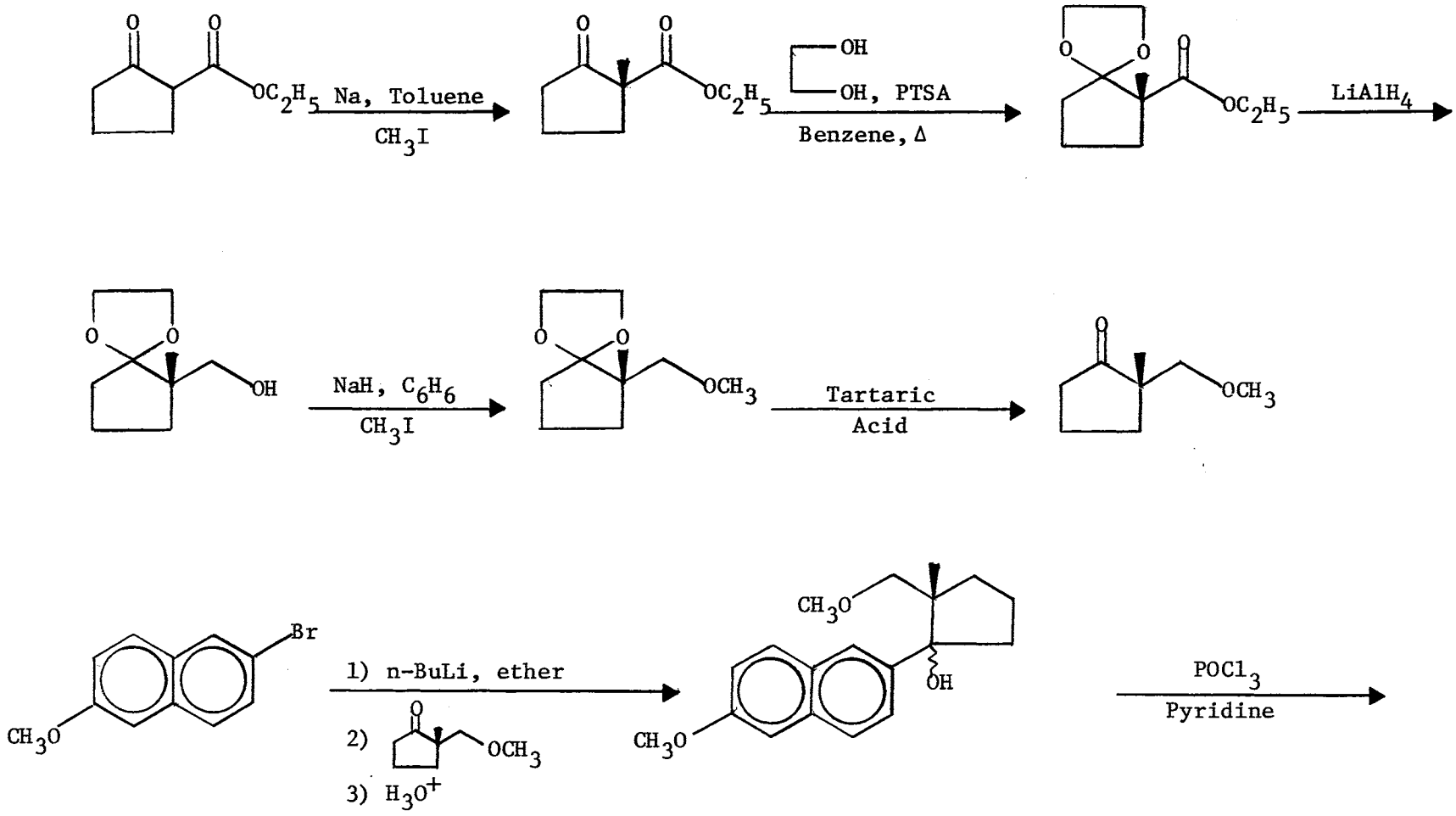
[a]The molecular ions for 119a, 119b, 119c, and 120b are not cleanly observed in any of these examples. There is peak for the corresponding phosphine [corresponding to loss of C_2H_5Br, m/e 108 (^{79}Br) and 110 (^{81}Br)] from 119a. The spectra of 119b, 119c, and 120b are likewise very complex and appear to be results of partial thermal decompositions.

observed. The base peak at m/e 276 in the spectrum of the phosphonium bromide 119a may be attributed to the cyclic phosphine 133 (mol. wt. = 276), which is known to be produced by pyrolysis of 119a under high vacuum (presumably, by loss of ethylene and HBr).[14,93,96,99] Interestingly, intense peaks at m/e 273 are observed in the spectra of both perchlorate 119b and picrate 119c. However, their detailed fragmentation patterns have not been analyzed.

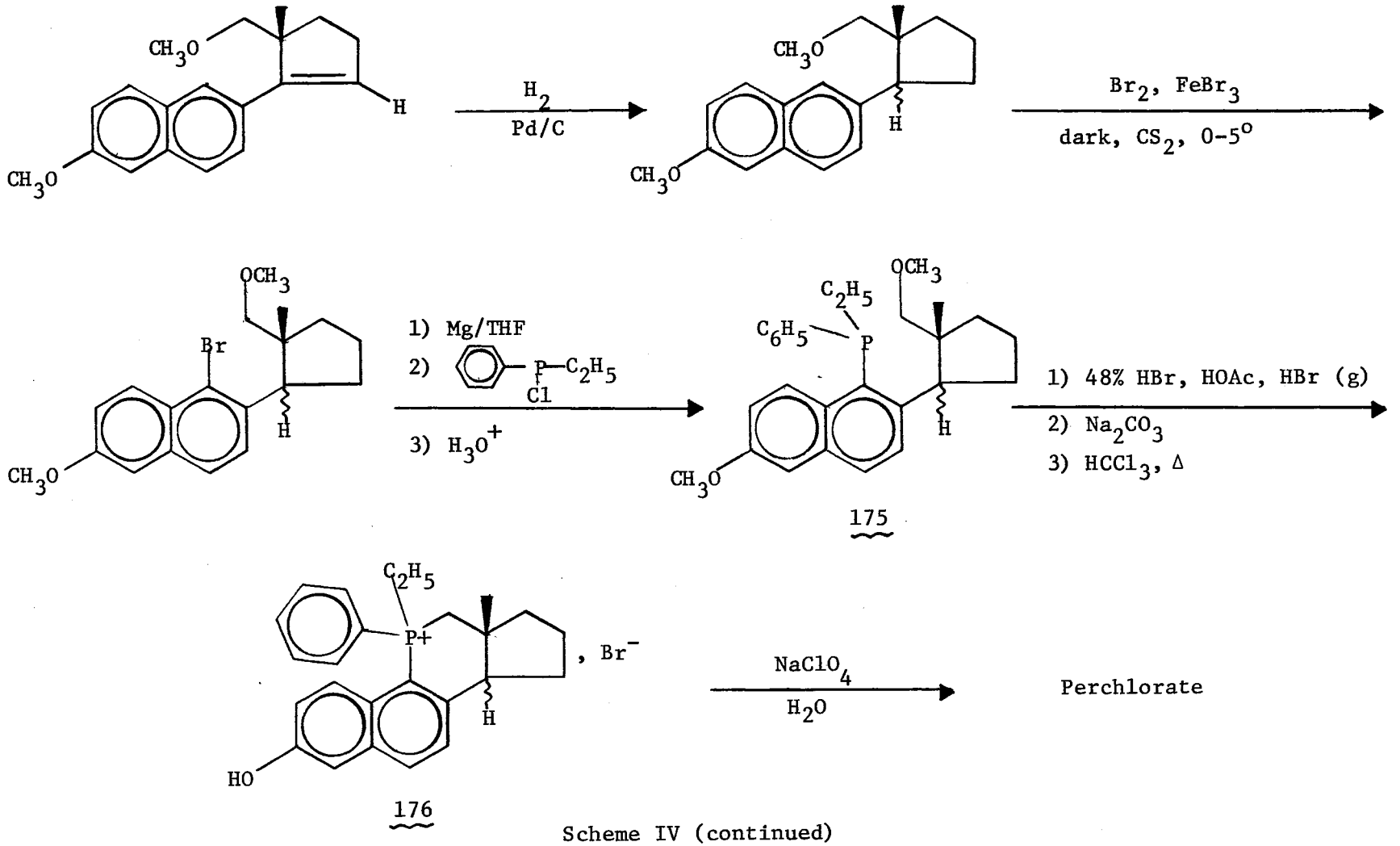
There are indications that these phosphonium salts might have already been decomposed (or thermally "excited") at the evaporation temperature before electron impact actually takes place. This is particularly true for the perchlorates (119b and 120b) and the picrate (119c), in which extremely abundant peaks of low m/e at 18,28,44 and 36 are observed. Apparently, more detailed study is needed to analyze these interesting spectra before any conclusion can be reached [For instance, by lowering the ion source temperature or the electron voltage, one might expect fewer major peaks (including M^+) which could perhaps be more easily rationalized].

Suggestions for Further Work

The successful development of the total synthesis of the hitherto unknown phosphasteroid -- 5-ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo[h]cyclopenta[c]phosphinolinium perchlorate (120b) -- reported in this thesis can be extended to the synthesis of the 11-phosphaequilenane series, a closer analog of the naturally occurring steroid equilenin. The proposed synthesis is outlined in Scheme IV. The presence of the angular methyl would help provide more direct evidence for assigning the stereochemistry of the C/D ring junction of the final product 176



Scheme IV. Proposed Total Synthesis of 11-Phosphaequilenane



Scheme IV (continued)

by analysis of its NMR spectrum (the methyl signal would appear as a distinctive singlet upfield from the rest of the methylene envelop).[16] Because of difference in geometry, the chemical shift of the cis angular methyl group would be expected to be different from that of the trans group in their NMR spectra.[126]

Of special interest in the total synthesis presented in Scheme IV is the one-step combination of demethylation, bromination and ring closure of the phosphine 175 to yield the 11-phosphaequilenane 176 directly upon treatment with HBr in glacial acetic acid. Aromatic methyl ethers are known to react with hot hydrobromic acid to give the corresponding phenols, which are usually stable toward further reaction with HBr.[21] Similar reaction has been reported by Holliman and Mann[53] in the synthesis of 2-phenyl-2-(p-hydroxyphenyl)-1,2,3,4-tetrahydroisophosphinolinium bromide (113) from phenyl-p-anisyl-2-(o-methoxymethylphenyl)-ethylphosphine.

CHAPTER III

EXPERIMENTAL[a-i]

Preparation of Crude 2-Bromomethylnaphthalene (122). The procedure was essentially that of Chapman and Williams.[25] The reagents used were 2-methylnaphthalene (121) (381.3 g., 2.68 mole, Eastman reagent grade) and N-bromosuccinimide (477 g., 2.68 mole, Eastman

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[a]Melting points were obtained on a Thomas-Hoover Capillary melting point apparatus and are uncorrected.

[b]Proton magnetic resonance spectra were taken on a Varian A-60 high resolution spectrometer unless otherwise specified. Tetramethylsilane was used as internal standard and unless otherwise noted, chloroform-d was used as the solvent. Abbreviations used for NMR spectral data are: s, singlet; t, triplet; q, quartet; and m, multiplet.

[c]Infrared spectra were taken on a Beckman IR-5A spectrophotometer with samples as films on sodium chloride or in potassium bromide pellets. Abbreviations used for IR spectral data are: s, strong; vs, very strong; w, weak; m, medium; vw, very weak; sh, shoulder; br, broad; and v. br, very broad.

[d]Mass spectra were obtained on a LKB-9000 prototype, magnetic sector, GLC-mass spectrometer, Biochemistry Department, Oklahoma State University.

[e]Elemental microanalyses were performed by Galbraith Laboratories, Knoxville, Tennessee, and Midwest Microlabs, Inc., Indianapolis, Ind.

[f]Rotations of optically active compounds were taken on a Rudolph polarimeter (O. C. Rudolph & Sons, Inc., Model 80, No. 722) with a circular scale reading to 0.001°, via a micro polariscope tube (W. H. Curtin & Co., bore ca. 1.6 mm., length 100 mm., and capacity 0.2 ml., with black rubber mantle and screw caps).

[g]Gas-liquid chromatographic analyses were performed with a Varian-Aerograph 1520 instrument equipped with a hydrogen ionization and a thermocouple detectors. The column packing used was 5% SE-30 on 60/80, A-W, DMCS-treated Chromosorb G (5 ft. x 1/8 in.) unless otherwise noted.

practical grade, dried in vacuo in the presence of P_2O_5 for 12 hr. before use) in reagent grade CCl_4 (2 l.). The crude bromide 122 obtained upon evaporation of solvent was used immediately in the next step without further purification. It was found that heavy loss of material resulted when a fractional distillation of crude 122 was performed. The IR spectrum of a sample of pure 2-bromomethylnaphthalene (122) [obtained by distillation (b.p. 112-150°/3.5-4.5 mm.) and recrystallization from C_2H_5OH], m.p. 53.5-55° (lit.,[1] m.p. 54°), showed major bands at 1600(vw), 1360(w), 1270(vw), 1205(m), 1125(w), 953(vw), 910 (vw), 889(m), 863(m), 854(m), 825(s), 767(sh), 750(s), 715(w), and 658(m) cm^{-1}. The NMR spectrum showed the expected proton absorptions at δ4.55 (s--CH_2, 2H) and δ7.20-7.91 (m--ArH, 7H).

Preparation of Diethyl 2-Naphthylmethylmalonate (123). According to the procedure described by Campaign and Heaton,[23] the desired ester 123 [327.9 g., b.p. 160-170°/0.2-0.5 mm. (lit.,[57] b.p. 170-4°/2 mm.)] was obtained in a yield of 40% [based on the amount of 2-methylnaphthalene (121) used in the previous step]. The IR spectrum showed major bands at 2970(m), 1730(vs) (C=O), 1450(m), 1370(m), 1270(br), 1230(br), 1150(br), 1080(w), 1037(m), 859(m), 818(m), and 756(m) cm^{-1}. The NMR spectrum showed characteristic proton absorptions for the structure

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[h]Micro thin-layer chromatographic (TLC) plates were prepared with Merck silica gel PF_{254} (purchased from Brinkmann Instruments, Inc., 10-40 mesh size) on 3 in. by 1 in. micro slides. The solvent systems for TLC are listed where used.

[i]Commercial anhydrous ether and benzene were dried over sodium and anhydrous THF was obtained by distilling the commercial reagent over $LiAlH_4$ immediately before use. Unless otherwise specified, commercial reagent grade chemicals and solvents were used without further purification.

$C_{10}H_7CH_2CH(CO_2CH_2CH_3)_2$ at δ1.17 [t--$(-CH_2\underline{CH}_3)_2$, 6H], δ4.71 [q--$(-\underline{CH}_2CH_3)_2$, 4H], δ3.27-3.92 [m($A_2B$)--Ar$\underline{CH}_2\underline{CH}$-, 3H], and δ7.23-8.05 (m--Ar$\underline{H}$, 7H).

Preparation of 3-(2-Naphthyl)propanoic Acid (124). The method of Mayer and Seiglitz[103] was followed. The reagents used were diethyl (2-naphthylmethyl)malonate (123) (148.9 g., 0.496 mole) and 20% methanolic KOH (420 ml.). Purification of the product gave, after recrystallizing from benzene, 3-(2-naphthyl)propanoic acid (124), 75.6 g., m.p. 133-5° (lit.,[103] m.p. 134-5°) [76.5% based on diethyl (2-naphthylmethyl)malonate (123)]. The IR spectrum showed major bands at 2950(v.br) (C(=O)-O-H), 1670(br) (C=O), 1430(m), 1340(w), 1305(m), 1280 (m), 1225(m), 950(sh), 905(br), 864(m), 820(s), 743(br), and 666(br) cm^{-1}. The NMR spectrum showed the expected proton absorptions for structure 2-$C_{10}H_7CH_2CH_2COOH$ at δ2.85 (A_2B_2 doublets--Ar$\underline{CH}_2\underline{CH}_2$-, 4H), δ7.20-7.96 (m--Ar$\underline{H}$, 7H), and δ10.2 (broad s--COO$\underline{H}$, 1H). The presence of the acid proton was confirmed by adding 1 drop of D_2O to the sample. The NMR spectrum showed a new peak for DOH at δ5.10 (s) and the original absorption at δ10.2 was completely wiped out.

Preparation of 3-(2-Naphthyl)propanol (125). The alcohol was prepared by the method of Campaign and Heaton.[23] From 103.7 g. (0.517 mole) of 3-(2-naphthyl)propanoic acid (124) and excess $LiAlH_4$ (44.8 g., 1.18 mole -- 10-mesh size, Ventron, Metal Hydrides Division) in anhydrous THF, the alcohol 125 was obtained (97 g.) in quantitative yield [based on 3-(2-naphthyl)propanoic acid (124)], m.p. 37.5-39.5°, (lit.,[23] m.p. 36.5-38.5°). The IR spectrum showed major bands at 3300(br) (O-H), 3020(sh), 1925(s), 2850(s) (C-H), 1625(w), 1590(w), 1500(w), 1430(br), 1370(br), 1265(w), 1110(br), 1050(br), 893(m),

850(br), 815(s), and 744(s) cm^{-1}. The NMR spectrum showed the expected proton absorptions for the structure 2-$C_{10}H_7CH_2CH_2CH_2OH$ at δ1.90 (quintet--$CH_2\underline{CH_2}CH_2$-, 2H), δ2.80 (t--$\underline{CH_2}OH$, 2H), δ2.92 (broad s--$O\underline{H}$, 1H), δ3.61 (t--$ArC\underline{H_2}CH_2$-, 2H), and δ7.14-7.90 (m--$Ar\underline{H}$, 7H). The presence of the alcoholic proton was confirmed by adding 1 drop of D_2O to the sample tube. The NMR spectrum showed a new peak for DOH at δ4.77 (s) and the original broad absorption buried under the triplet of -$C\underline{H_2}OH$ at δ2.92 was not observed.

Preparation of 2-(3-Bromopropyl)naphthalene (126). The bromide 126 was prepared by the method of Campaign and Heaton[23] with slight modification. 3-(2-Naphthyl)propanol (125) (13.1 g., 0.0705 mole) was boiled with 100 ml. of 48% HBr for 5 hr. by means of an oil bath at 126-130°. After being stirred overnight at room temperature, the dark brown bromide solidified in the aqueous medium, which was then diluted with 200 ml. of ice water. The mixture obtained was extracted with ether. The extracts were washed with dil. $NaHCO_3$ followed by H_2O and dried ($MgSO_4$) overnight. The clear solution, after filtration, was evaporated at 30° and further concentrated under vacuum at 1.5 mm. at room temperature. The dark-brown residual oil was practically pure 126 as shown by TLC analysis using reagent grade hexanes as the developing solvent. Instead of recrystallizing from n-hexane (as described in the literature[2]), purification was achieved by chromatographing the crude product [dissolved in a small amount of benzene], on a 18-in. by 1 1/16-in. column (200 g., 100-200 mesh size) of silica gel, (Grace Davison Chemical), wet-packed in reagent grade hexanes, and eluting with benzene-hexanes (1:4 -- 1.5 l. total volume) solution. Dark-colored impurities were adsorbed at the top of the column, and the

clear eluate, after evaporation, gave a light yellowish oil. The bromide 126 crystallized out in the form of a creamy powder from the chilled (dry ice bath) oil. Vacuum drying at 1 mm. at room temperature for 1 hr. gave pure 2-(3-bromopropyl)naphthalene (126) [17.3 g., 98.7% based on 3-(2-naphthyl)propanol (125)], m.p. 42-43.5° (lit.,[23] m.p. 43.5-44.5°). The IR spectrum showed major bands at 2940(vw), 1600(vw), 1505(vw), 1445(sh), 1425(w), 1365(w), 1279(m), 1245(m), 960(m), 950(sh), 900(m), 863(m), 814(s), 762(vw), and 751(s) cm^{-1}. The NMR spectrum showed the expected proton absorptions for the structure of 2-$C_{10}H_7$-$CH_2CH_2CH_2Br$ δ2.00 (quintet--$CH_2\underline{CH_2}CH_2$-, 2H), δ2.75 (t--$C\underline{H_2}Br$, 2H), δ3.29 (t--$ArC\underline{H_2}$-, 2H), and δ7.07-7.88 (m--$Ar\underline{H}$, 7H). The spectra of certain model compounds (e.g., 3-phenyl-1-propanol and 1-bromo-3-phenylpropane)[121] have been recorded in the literature and are similar.

Synthesis of 2-(3-Methoxypropyl)naphthalene (127). 2-(3-Bromopropyl)naphthalene (126) (10.3 g., 0.0414 mole) in 25 ml. of CH_3OH (not completely soluble) and 25 ml. of benzene was added dropwise via an addition funnel (125 ml.) at room temperature under N_2 to 3.0 g. (0.055 mole) of sodium methylate (Fisher purified reagent) dissolved in 120 ml. of CH_3OH in a 300-ml. 3-neck, r.b. flask (fitted with a mechanical stirrer, N_2 inlet, condenser and $CaCl_2$ tube). During the 20-min. addition period, no exothermic process was detected. The reaction could be followed very nicely by hydrolyzing (ca. 1 ml. of H_2O) a sample (2 or 3 drops) taken from the reaction mixture intermittently and analyzing the organic mixture (in ether) by GLC. It took a total of 25 hr. of heating in a sand bath at 95-100° to bring the reaction to completion. The white suspension was decomposed with cooling (ice) by addition of H_2O (100 ml.). The decomposed mixture

was saturated with NaCl and the aqueous layer was separated and extracted with ether; the combined extracts were washed with 10% NH_4Cl and brine until neutral. The separated aqueous layer was evaporated to remove CH_3OH and re-extracted with ether. The combined ethereal extracts, after being dried ($MgSO_4$), were filtered and evaporated to remove ether. A brownish residual liquid was vacuum distilled via a 3-in. vigreux, vacuum-jacketed column. The desired product, 2-(3-methoxypropyl)naphthalene (127) (b.p. 112-3°/0.8 mm., $n_D^{28.5}$ 1.5751), was collected in a yield of 83.5% (based on 126). The IR spectrum (Plate I) showed the characteristic strong absorption for C-O-C at 1120 cm^{-1}. The NMR spectrum (Plate XXI) showed the typical proton absorptions for the end-substituted propyl side chain attached to an aryl group (e.g., 3-phenyl-1-propanol and 1-bromo-3-phenylpropane)[121] at δ1.90 (m--$CH_2\underline{CH_2}CH_2$-, 2H), δ2.75 (t--$\underline{CH_2}OCH_3$, 2H), and δ3.24 (t--Ar$\underline{CH_2}CH_2$-, 2H) for the structure 2-$C_{10}H_7CH_2CH_2CH_2OCH_3$. The proton absorptions for the methoxy and the aryl groups are at δ3.18 (s--3H) and δ7.05-7.85 (m--7H), respectively.

Anal. Calcd. for $C_{14}H_{16}O$: C, 84.00; H, 8.00.

Found: C, 83.96; H, 7.99.

Bromination of 2-(3-Methoxypropyl)naphthalene (127). Synthesis of 1-Bromo-2-(3-methoxypropyl)naphthalene (128). Light was carefully excluded during the experiment by covering the reaction vessels with black tape. Bromine (4.6 g., 0.029 mole) in 12 ml. of CS_2 was added dropwise with stirring and ice cooling to a 50-ml. 3-neck, r.b. flask (fitted with a mechanical stirrer, addition funnel, N_2 inlet, condenser and $CaCl_2$ tube) containing 5.3 g. (0.0265 mole) of 127 and 0.2 g. of anhydrous $FeBr_3$ (K&K Chemical Co.) in 15 ml. of CS_2 under N_2.

During the period of slow addition (1.25 hr.), the temperature was kept below 5° and HBr evolution was observed. The reaction was essentially complete after being stirred at the ice bath for 5 hr.; it could be followed nicely by hydrolyzing (with ca. 1 ml. of H_2O) a sample (2 or 3 drops) taken from the reaction mixture and analyzing the organic product mixture (in ether) by GLC. The main reaction mixture was decomposed with ice cooling by dropwise addition of 10% NaOH (15 ml.) under N_2. After being stirred for 30 min., the reddish-brown oily mixture was extracted with ether and the extract washed with H_2O (until neutral) and finally dried ($MgSO_4$). A pink oil (ca. 7.5 g.) was left after evaporating the ethereal solution at 40°. This pink oil was distilled *in vacuo* through a 3-in. vigreux vacuum-jacketed column. The main fraction distilled at 130-1°/0.15 mm. to give 5.6 g. of an almost colorless oil (n_D^{26} 1.6057), which proved to be the desired 1-bromo-2-(3-methoxypropyl)naphthalene (128) by IR and NMR analyses (Plate II and XXII). A slightly impure fraction (greenish oil, containing 87% of 128, as shown by GLC analysis) was also collected with the help of a heat gun at the final stage of the distillation. Thus, a yield of 76% of pure 128 or 98% of crude 128, was obtained based on 2-(3-methoxypropyl)-naphthalene (127). Bromination occurred at the 1-position of the naphthalene ring was ascertained by the characteristic proton absorption of the hydrogen at C-8 (as in 1-bromo-2-methylnaphthalene);[119] a peak at δ8.12-8.35 (m--1H) is visible. The corresponding proton is sufficiently deshielded by the adjacent bromine to cause its signal to be separate from those of the rest of the protons of the naphthalene ring (δ7.07-7.78, m--5H). Further evidence was provided chemically in the next two experiments. The compound 128 was found to turn yellow slowly

upon prolonged storage. An analytical sample of 1-bromo-2-(3-methoxypropyl)naphthalene (128) was obtained by refractionation and sealed in vacuum.

Anal. Calcd. for $C_{14}H_{15}BrO$: C, 60.21; H, 5.37; Br, 28.69.
Found: C, 60.49; H, 5.39; Br, 28.65.

Carbonation of the Grignard Reagent of 1-Bromo-2-(3-methoxypropyl)-naphthalene (128). Synthesis of 2-(3-Methoxypropyl)-1-naphthoic Acid (129). The Grignard reagent was prepared by the usual method[70] from 1.7 g. (0.0061 mole) of 128, 0.149 g. (0.0061 g-atom) of Mg turning, and a trace of I_2 in 25 ml. of anhydrous THF. Dry gaseous CO_2 (commercial cylinder from The Matheson Co., passed through conc. H_2SO_4) was passed over the dark brown Grignard solution which was vigorously stirred and maintained at about 0-5° (ice bath). A slight positive pressure of CO_2 was maintained throughout the reaction, which was practically complete within an hour as a distinctive color change from dark brown to dark green was noted. After being stirred for an additional 30 min. under CO_2 (while the temperature rose to 10°), the reaction mixture was decomposed by adding dropwise 25 ml. of 10% H_2SO_4 with ice cooling. The aqueous layer was extracted twice with 150 ml. of ether, and the combined ethereal extracts (slightly yellowish) was washed with brine until neutral. Without drying, the ethereal solution was extracted 4 times with 35 ml. of satd. aqueous Na_2CO_3 solution. The base extracts, after being washed (50 ml. x two) with ether (to remove any neutral organics that might have been left over), were acidified carefully with 20% H_2SO_4 (with ice cooling). The resulting white oily suspension was again extracted with ether and dried ($MgSO_4$). After being completely depleted of ether under vacuum, a pale greenish oil

(1.35 g.), which was shown to pure by TLC analysis (using chloroform as developing solvent), was left as the desired product, 2-(3-methoxypropyl)-1-naphthoic acid (129); yield 87% [based on 1-bromo-2-(3-methoxypropyl)naphthalene (128)]. The IR spectrum (Plate III) showed a characteristic broad band for the carboxylic acid group at 2500-3500 cm^{-1}. The NMR spectrum is displayed in Plate XXIII. A short-path distillation gave a very viscous greenish yellow oil boiling at b.p. 168-172°/0.35 mm. (n_D^{30} 1.5888).

Anal. Calcd. for $C_{15}H_{16}O_3$: C, 73.77; H, 6.56.

Found: C, 73.66; H, 6.47.

Oxidative Degradation of 2-(3-Methoxypropyl)-1-naphthoic Acid (129). Preparation of 1,2-Naphthalenedicarboxylic Anhydride (130). The procedure was essentially that of Cope.[28] The acid 129 (0.135 g., 0.00055 mole), 7.1 g., of $K_3Fe(CN)_6$ (Baker analyzed reagent), and 1.26 g. of KOH (pellet) were dissolved in 26 ml. of distilled H_2O in a 50-ml., r.b. flask (fitted with a magnetic stirrer and a condenser). The solution was warmed at an oil bath of 70-5° for 66 hr. The turbid dark orange reaction mixture was filtered. The clear filtrate, after being acidified carefully (conc. HCl), was extracted with two 25-ml. portions of ether. Without drying, the ethereal solution was evaporated and the residue (a milky greenish mass) was carefully transferred into a micro-sublimation tube (4 in. x 1/2 in.) by dissolving in a little chloroform. Yellowish-white crude 1,2-naphthalenedicarboxylic anhydride (130) (100 mg., m.p. 153-160°) was sublimed at a sand bath temperature of 140-180° and 0.1 mm. The sublimate was recrystallized from ethaol to give light yellowish fine needles of pure 130, m.p. 167-8° (lit.,[18] m.p. 168-9°).

The IR spectrum showed characteristic carbonyl absorptions at 1830(s) (C=O) and 1770(vs) (C=O) for a typical conjugated 5-membered ring carboxylic anhydride.[111] Other major bands were at 1565(w), 1459(w), 1282(s), 1185(s), 1160(sh), 1135(s), 929(s), 905(sh), 900(s), 835(s), 769(s), 746(m), and 728(m) cm^{-1}.

Preparation of Ethylphenylphosphinous Chloride (131). The procedure of Maier[92] was followed. The reagents used were $(C_2H_5)_4Pb$ (32.3 g., 0.3 mole; Ethyl Corporation), dichlorophenylphosphine (53.7 g., 0.3 mole; Aldrich Chemical), and 1.3 g. (0.01 mole) of anhydrous $AlCl_3$ (reagent powder, Mallinckrodt Chem. Co.). Vacuum fractional distillation at 73.5-74°/2.1-2.2 mm. (lit.,[10] b.p. 73-5°/2 mm.) gave 37.9 g. (0.22 mole; 73.5% based on dichlorophenylphosphine) of ethylphenylphosphinous chloride (131) as a colorless liquid extremely sensitive to moisture and air. The NMR spectrum (Plate XXIV) showed the characteristic proton absorptions for the ethyl group attached to phosphorus (--$PCH_2\underline{C}H_3$) at δ0.85 and δ1.12 as 2 triplets ($J_{P-C-C-H}$= 16.5 Hz; $J_{H-C-C-H}$= 7 Hz; 3H--total for both triplets) and δ1.94 (m--$PC\underline{H}_2CH_3$, 2H). The aryl protons appeared at δ7.14-8.0 as a multiplet. A slightly higher integration in the aromatic region than that of theoretical seemed to indicate the presence of traces of unreacted $C_6H_5PCl_2$ in the sample. As was also found by Mann and coworkers,[97] the impurity was difficult to separate by refractionation.

Synthesis of Crude Ethyl[2-(3-methoxypropyl)-1-naphthyl]phenylphosphine (132). All the reactions and workups described in this experiment were performed under N_2. The Grignard reagent was prepared by the general method[70] from 1-bromo-2-(3-methoxypropyl)naphthalene (128) (6.7 g., 0.024 mole), 0.61 g. (0.0025 g-atom) of Mg turnings and a few

crystals of I_2 in 45 ml. of anhydrous THF in a 100-ml. 3-neck, r.b. flask (fitted with a condenser and $CaCl_2$ tube, a magnetic stirrer, addition funnel and a N_2 inlet). After being heated for 2.5 hr. at an oil bath of 75-80°, the dark brown Grignard solution was cooled to about 20° with a cold-water bath. Ethylphenylphosphinous chloride (131) (4.15 g., 0.024 mole) in 25 ml. of anhydrous benzene was added dropwise to the Grignard reagent with ice cooling in 30 min. A slight exothermic reaction was observed and the light brown homogeneous reaction mixture was stirred at room temperature overnight after the addition. Distillation was used to remove THF at an oil bath (kept below 100°) in ca. 1.5 hr. (the flask contents must not be taken to dryness). After the residue was cooled, 50 ml. of ether and 20 ml. of benzene were added to the grayish, yellow residue. With ice cooling, it was decomposed slowly with 30 ml. of satd. aqueous NH_4Cl and stirred for at least 40 min. The reaction mixture was transferred through a goose neck into a separatory funnel and washed out with more ether (250 ml.) under N_2. The light brown organic solution was separated carefully from the colorless aqueous layer, and washed with satd. Na_2CO_3 and dil. $NaHCO_3$ followed by brine; the organic solution was then dried ($MgSO_4$) overnight in a special apparatus shown in Figure 1. The filtration was performed smoothly by replacing the $CaCl_2$ tube on the top with a stopper so that a positive N_2 pressure could be maintained over the organic solution. The clear yellow filtrate collected in the lower flask through the glass wool plug was concentrated and the solvent was distilled out continuously under N_2 at the same time (the oil bath temperature was kept below 100°). After being washed twice with 20 ml. of benzene, the upper flask containing the $MgSO_4$ was removed, and the filtrate in the lower

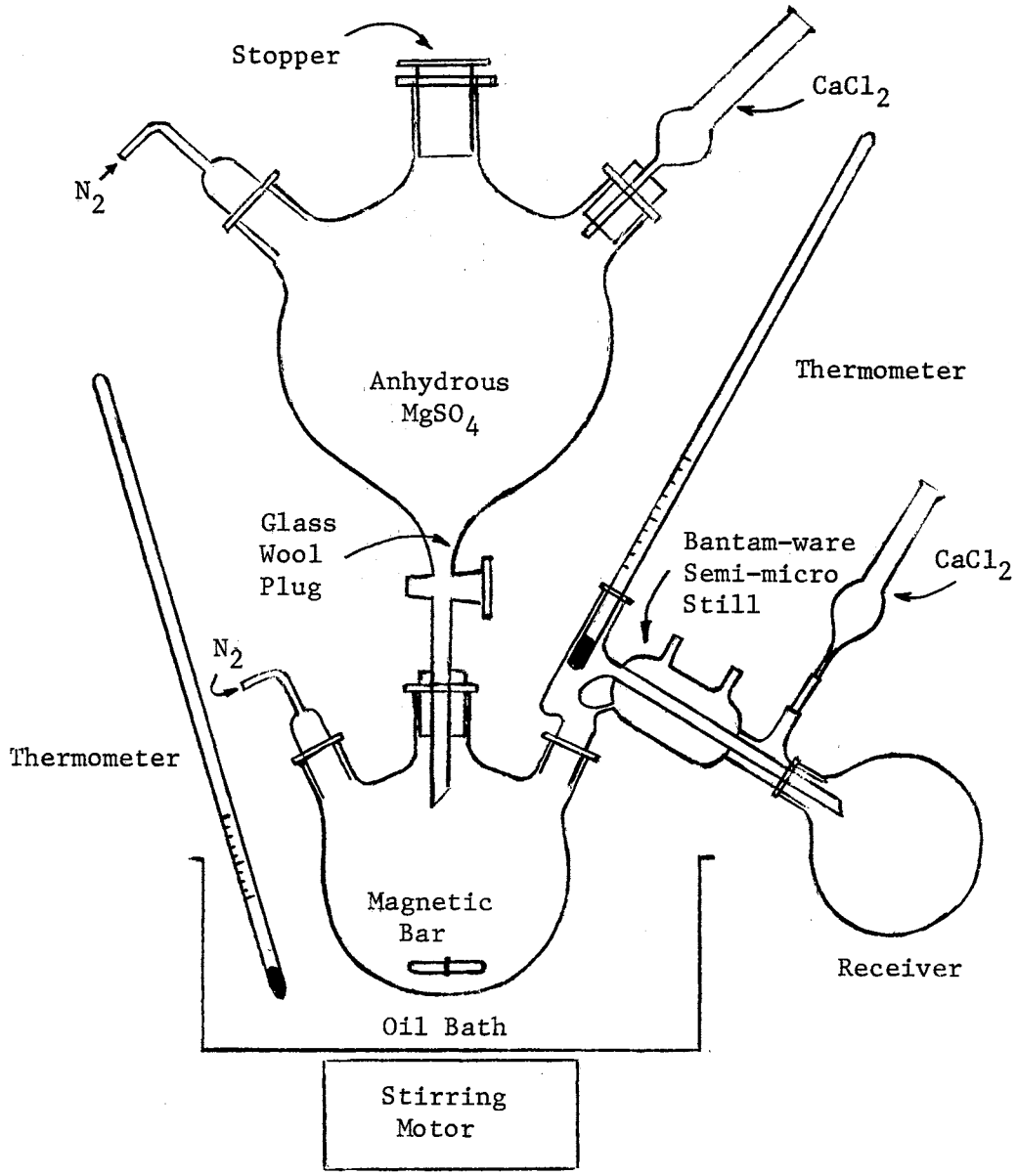

Figure 1. Apparatus for Preparation of Phosphines and Cyclization

flask was concentrated to ca. 10 ml. The yellow viscous residue was transferred quickly into a 15 ml., r.b. flask and distilled immediately by using a short-path, Bantam-ware semi-micro still with a variable receiver under diffusion-pump vacuum. After a forerun (1.11 g.) of low-boiling material at b.p. 96-187°/0.063 mm., the crude ethyl[2-(3-methoxypropyl)-1-naphthyl]phenylphosphine (132) (5.14 g., b.p. 194-7°/0.063 mm.), an extremely viscous greenish liquid (a condenser at steam temperature was necessary to allow free flowing), was collected as the main fraction in a yield of 63.7% (based on 128). The trivalent state of the P atom in the compound 132 was supported by the IR spectrum (Plate IV), which showed the absence of any discernible characteristic band for P→O at region 1150-1300 cm^{-1}. The NMR spectrum (Plate XXV) showed all the chracteristic proton absorptions for the proposed structure at δ0.86, 1.17 [t,t--$PCH_2\underline{CH}_3$ ($J_{P-C-C-H}$= 18.7 Hz, $J_{H-C-C-H}$= 7.5 Hz), 3H], δ1.96 (m--$CH_2\underline{CH}_2CH_2$-, 2H), δ2.35 (t--$\underline{CH}_2OCH_3$, 2H), δ3.27 (s--$O\underline{CH}_3$, 3H), δ3.39 (t--$Ar\underline{CH}_2CH_2$-, 2H), δ(ca.) 3.30 (m--$P\underline{CH}_2CH_3$, 2H), and δ6.95-8.00 (m--Ar<u>H</u>, 11H). While an analytical sample was difficult to get by fractionation, further proof of the structure was provided by mass spectral analysis (Plate XLIV), which showed an intense molecular ion at m/e 336 for the phosphine 132, and only a trace of a peak at m/e 352 (the corresponding phosphine oxide) was detected. The crude 132 was found suitably pure for the next experiment.

Cyclization of the Crude Phosphine 132. Synthesis of 1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Bromide (119a). All reactions described herein were performed under N_2. Crude ethyl-[2-(3-methoxypropyl)-1-naphthyl]phenylphosphine (132) (1.75 g., 0.0052 mole) in 10 ml. of glacial acetic acid was heated (at an oil bath of

120°) with 50 ml. of 48% HBr (Fisher reagent grade) in a 300-ml., 3-neck, r.b. flask fitted with a magnetic stirring bar, N_2 inlet, a condenser, $CaCl_2$ tube, and a sintered glass gas inlet (half immersed in the reaction mixture). A gentle stream of anhydrous HBr (The Matheson Co.) was passed into the reaction mixture during the 2.5-hr. period of reflux. Gaseous HBr was then removed and the slightly yellow, turbid reaction mixture was stirred at room temperature overnight. Excess aqueous HBr and acetic acid were distilled out at 48°/35 mm. (the oil bath was kept below 71°). The concentrated reaction mixture (ca. 20 ml.) was chilled with ice, taken up in $HCCl_3$ (50 ml.) and neutralized carefully by adding dil. aqueous $NaHCO_3$ and solid $Na_2CO_3 \cdot H_2O$. Stirring was continued at room temperature for at least an hour as more $HCCl_3$ and H_2O were added. The colorless $HCCl_3$ extracts (ca. 200 ml.) were carefully separated and dried ($MgSO_4$) overnight in the special apparatus shown in Fig. 1 (p. 98). The entire operation of filtration, reflux (oil bath at 75-80°) and concentration of the $HCCl_3$ solution was performed under N_2 as described in the synthesis of the precursor phosphine 132. After being washed twice (200 ml. of $HCCl_3$), the upper flask containing the $MgSO_4$ was removed and the $HCCl_3$ extracts and washings were concentrated to a milky oil. The residue, after the $HCCl_3$ had been removed under vacuum (0.1 mm.) at room temperature, was a white solid, which was extremely hygroscopic (it became sticky as soon as it was was removed from the N_2 atmosphere). Recrystallization was achieved by carefully dissolving the crude solid in a small amount of $HCCl_3$, filtering out insoluble material, and adding anhydrous ether dropwise until cloudy. Beautiful colorless needles crystallized out overnight at room temperature. Collection on a sintered glass funnel and drying

immediately in a vacuum oven in the presence of P_2O_5 and wax chips gave 1-ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium bromide (119a), m.p. 227.5-228.5° (melted to a brown liquid), in a yield of 1 g. (50%, based on the crude phosphine 132). The m.p. was unchanged by further recrystallization. The bromide 119a was soluble in H_2O, CH_3OH, C_2H_5OH, and only sparingly soluble in ethyl acetate and insoluble in ether. It gave a positive halogen test ($AgNO_3$). The NMR spectrum (Plate XXVI) was most informative in confirming the cyclized structure. The general pattern of the substituted propyl group[121] (2 triplets and 1 multiplet at region δ 2.0-4.5) and a sharp singlet for the methoxy group at around δ 3.27, which showed so vividly in all the precursors, are absent. Due to the rigidity of the cyclic system, the 6 nonequivalent protons of the methylene groups (2 protons are adjacent to phosphorus) display a very complex splitting pattern as expected over the region δ 1.5-4.7. Other distinguishable characteristic proton absorptions are two triplets at δ 1.00 and 1.32 (--$PCH_2C\underline{H}_3$, 3H), which probably resulting from splitting by phosphorus ($J_{P-C-C-H}$ = 20.5 Hz; $J_{H-C-C-H}$ = 7.5 Hz), and δ 7.35-8.45 (m--Ar$\underline{H}$, 11H). A 100-MHz NMR spectrum (Plate XXVII) (courtesy of JEOL Co., on a PS-100 unit) of 119a also has been recorded. The IR spectrum is seen in Plate V. The medium band showed at 3430 cm^{-1} for O-H may account for the hygroscopic nature of the compound. A satisfactory elemental analysis, however, was not obtained.

Anal. Calcd. for $C_{21}H_{22}BrP$: C, 65.45; H, 5.71; Br, 20.79; P, 8.06.
Found: C, 58.57; H, 5.43; Br, 23.27; P, 3.60; Cl, 8.80.

It was found by mass spectral analysis (direct evaporation of the

salt 119a in the probe at 175-220° with electron voltage of 70 eV and ion source temperature of 310°) that a trace of $HCCl_3$ (m/e 118, lost at ca. $97°/10^{-7}$ mm. in the probe) was present in the recrystallized product ($HCCl_3$ - ether). However, the $HCCl_3$ (which was nonstoichiometrically included in the crystal, as shown by simple calculation from the analysis data) was not removed by heating the bromide 119a at 100-102°/1.5-2 μ for 90 hr. The mass spectrum (Plate XLV) of 119a was most interesting in that no molecular ion at m/e 385 (cation + Br^-) was detected; instead, the highest mass was observed at m/e 302. Other characteristic peaks were found at m/e 276 (100%) and m/e 108, 110 (C_2H_5Br). Compound 119a could also be recrystallized from CH_3OH and ether. Two kinds of crystals were obtained (predominantly soft short needles, m.p. 221.5-222°, and some long needles, m.p. 225.5-226°). Although their IR spectra were identical with that in Plate V and there was no $HCCl_3$ included in the crystals (as shown by mass spectral analysis), a good separate elemental analysis for phosphorus, unfortunately, was not obtained.

Anal. Calcd. for $C_{21}H_{22}BrP$: C, 65.45; H, 5.71; P, 8.06.

Found: C, 64.94; H, 6.02; P, 5.25.

Elemental analysis of large phosphorus molecules is difficult, as indicated by both Galbraith and Midwest laboratories. The phosphonium bromide 119a was used in the next experiment.

Synthesis of 1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Perchlorate (119b). Excess satd. aqueous $NaClO_4$ was added dropwise to the crude bromide 119a (250 mg., 0.64 mmole) in ca. 5 ml. of H_2O at room temperature with stirring. White solid immediately precipitated. The crude perchlorate 119b (205 mg., m.p. 156.5-158.5°)

was collected by filtration and washed carefully and thoroughly with distilled H_2O (to remove any excess $NaClO_4$ and unreacted bromide 119a). The solid was dried in an vacuum oven in the presence of P_2O_5 at 55° for 27 hr., yield 75% based on 119a. After two consecutive recrystallizations (slowly) from isopropyl alcohol, 151 mg. of pure 119b, m.p. 159-159.5°, was obtained. The m.p. was found unchanged by further recrystallization. The compound 119b was found soluble in $HCCl_3$ and CH_3OH but not in benzene, ethyl acetate, H_2O or 95% C_2H_5OH. The IR spectrum (Plate VI) showed a very strong and broad band at 1095 cm^{-1} for the characteristic ClO_4^- group.[26] The NMR spectrum (Plate XXVIII) is essentially identical with that of the bromide 119a. The mass spectrum of 119b (Plate XLVI) (obtained under the same conditions as for the bromide 119a) is similar to that of the bromide 119a in that no molecular ion at m/e 404 (cation + ClO_4^-) was detected; instead, an abundant m/e 302 was observed. Excellent elemental analytical results were obtained for P and Cl as well as C, H.

Anal. Calcd. for $C_{21}H_{22}ClO_4P$: C, 62.30; H, 5.44; Cl, 8.78; P, 7.66.

Found: C, 62.41; H, 5.23; Cl, 9.01; P, 7.42.

Synthesis of 1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Picrate (119c). The following experiment was performed in micro quantities and qualitatively. The picrate 119c was made by treating the crude bromide 119b in H_2O with excess aqueous sodium picrate. Yellow precipitate was immediately formed. The gummy solid, after being washed thoroughly with H_2O (to remove any excess sodium picrate and some unreacted bromide) via decantation, was dried in a vacuum oven in the

presence of P_2O_5 at room temperature overnight. Attempted recrystallization of the gummy material from a variety of solvents was unsuccessful. However, when the crude picrate 119c was dissolved in a small amount of abs. C_2H_5OH, anhydrous ether was added dropwise until a very slight cloudiness appeared, and the mixture was then refrigerated, yellow rhombic crystals of the pure picrate 119c, m.p. 109.5-110.5°, were found to crystallize beautifully and very slowly over several weeks. Repeated recrystallization did not improve the m.p. The IR spectrum was recorded in Plate VII. The mass spectrum, which is interestingly similar to that of the perchlorate 119b, is displayed in Plate XLVII. A good elemental analysis for phosphorus was obtained for 119c.

Anal. Calcd. for $C_{27}H_{24}N_3O_3P$: P, 5.81.

Found: P, 5.61.

Thermal Decomposition of 1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Bromide (119a). Synthesis of 1,2,3,4-Tetrahydro-1-phenylbenzo[h]phosphinoline (133) and 1,2,3,4-Tetrahydro-1-phenylbenzo[h]phosphinoline 1-Oxide (134). The phosphonium bromide 119a (0.3994 g., 1.03 mmole) in a 10-ml. r.b. flask (fitted with vacuum outlet and a magnetic stirrer) was heated in a sand bath (250-300°) for 30 min. under a diffusion-pump vacuum of 1.5×10^{-4} mm. Decomposition occurred quite smoothly under these conditions; a colorless liquid was observed to reflux in the flask and gas evolution was also detected as soon as the solid began to melt. The decomposition was essentially complete within 30 min.; it could be followed conveniently by observing the rise in pressure (to ca. 0.2 mm. while the reaction was taking place) which finally returned to 7.5×10^{-4} mm. as decomposition practically ceased. The reaction mixture was kept in a sand bath (290-308°) for another 25

min. before heating was terminated. The mixture taken up immediately in chloroform and transferred quickly into a 100-ml. 3-neck, r.b. flask (fitted with a N_2 inlet, magnetic stirring bar and a condenser) and neutralized with 15 ml. of satd. aqueous $NaHCO_3$ under N_2. Some effervescence was observed (both phosphine 133 and its HBr salt seemed to be present). The chloroform extract went through a series of color changes (from yellow to reddish pink, to orange, and finally back to yellow) while being stirred under N_2 at room temperature in a period of 15 min. The mixture was carefully separated and the aqueous solution, after being extracted twice with 30-ml. portions of $HCCl_3$, was discarded. The combined chloroform extracts were dried ($MgSO_4$), filtered, concentrated and analyzed by TLC using chloroform as the developing solvent. Two major spots were detected; one (principal product) had a very high R_f value of 0.8 and one was not moved by chloroform (minor product). The latter (60 mg., m.p. 215-220°; appeared to be the starting material 119a, as they have similar IR spectra) could be removed from the original reaction product quite nicely by crystallizing it out from chloroform-ether (like the bromide 119a described in the previous experiment, p. 99). Vacuum distillation was not entirely satisfactory for purifying the phosphine 133 left in the chloroform-ether mother liquor; purification by column chromatography was successful. The crude product, after being freed of solvent, was taken up in a small amount of chloroform, introduced on a 9-in. by 5/16-in. column (containing 7 g. of 80-200 mesh silica gel, Baker analyzed reagent, wet-packed in reagent grade hexanes), and eluted with reagent hexanes. Aliquots of 50 ml. each were collected. The phosphine 133 was found completely eluted in 250 ml. of reagent hexanes, as shown by TLC ($HCCl_3$)

analysis. Removal of solvent gave 80.6 mg. (0.29 mmole) of the phosphine 133, m.p. 120-2°, 28% based on 119a. The crude phosphine 133 appeared to be thermally stable as it could be analyzed by GLC at 200° and shown to be practically pure. An anlytical sample, m.p. 120.5-121.5°, was obtained via recrystallization several times from reagent grade hexanes (some insoluble solid was removed by decantation and saved for later investigation). The IR spectrum (Plate VIII) showed no distinctive band in region 1150-1300 cm^{-1} for P→O and the NMR spectrum (Plate XXIX) was in agreement with the expected structure. The mass spectrum (Plate XLVIII) shows a molecular ion at m/e 276.

Anal. Calcd. for $C_{19}H_{17}P$: C, 82.61; H, 6.16; P, 11.23.

Found: C, 82.79; H, 6.31; P, 10.98.

The insoluble solid (8 mg.) obtained during the recrystallization of the phosphine 133 in hot hexanes, could be purified from reagent grade heptanes in the form of soft, fine crystals, m.p. 147.5-148.5°. The IR spectrum (Plate IX) showed a strong band for P→O at 1180 cm^{-1} [and 1160 cm^{-1} (sh)] and the NMR spectrum (Plate XXX) was very much like that of the phosphine 133. A molecular ion of m/e 292 in the mass spectrum (Plate XLIX) confirmed, beyond doubt, the compound to be the phosphine oxide 134, which apparently resulted from the air oxidation of the corresponding phosphine 133 during the work up.

Anal. Calcd. for $C_{19}H_{17}OP$: P, 10.61.

Found: P, 10.62.

Preparation of 2-(Hydroxymethyl)cyclopentanone Cyclic Ethylene Ketal (137). The procedures used in this experiment were essentially those of Takahashi and coworkers,[128] but without isolation of the intermediate 2-carbethoxycyclopentanone cyclic ethylene ketal (136).

Commercial, crude 2-carbethoxycyclopentanone (135) (121.4 g., Columbia Chemical C-380, containing 55% ethyl ester, 41% methyl ester and *ca.* 4% low boiling material, as shown by GLC analysis) was used without further purification. Other reagents used were ethylene glycol (52 g., Fisher Certified reagent) and *p*-toluenesulfonic acid monohydrate (0.1 g.) in 300 ml. of reagent benzene. Azeotropic distillation of water was complete in 8.5 hr. at a sand bath temperature of 120-1° (*ca.* 19 ml. of water was collected). The product formed was evaporated to remove benzene. Crude 136 was taken up in ether (*ca.* 150 ml.) and added immediately dropwise under nitrogen to a suspension of 30.9 g. (0.79 mole) of $LiAlH_4$ (Ventron Metal Hydrides Corp., 10-mesh) in 1 liter of anhydrous ether in a 3-l. 3-neck, r.b. flask (fitted with mechanical stirrer, condenser, $CaCl_2$ tube, addition funnel and a N_2 inlet). The reaction was very vigorous and external ice cooling was necessary. The rate of addition was adjusted so that a gentle reflux of ether was maintained (a total of 4.5 hr.). The light-gray reaction mixture, after being stirred at room temperature for 1 more hr., was decomposed by slow addition of 150 ml. of ethyl acetate (N.F. grade) with ice cooling under N_2. The resulting mixture was stirred overnight and further decomposed (cautiously) with 700 ml. more of ice water with vigorous stirring and cooling (much white complex-like material was found insoluble in the medium and was not decomposed even by adding potassium sodium tartrate). The reaction mixture was thoroughly extracted with ether, and the conbined ethereal extracts were washed with brine (until neutral), dried ($MgSO_4$), filtered, and evaporated to remove ether. The residue was fractionated *via* a 1-ft. silver-coated, vacuum-jacketed vigreux column fitted with a variable receiver. After a forerun of low

boiling material, a main fraction (72.6 g., n_D^{26} 1.4716) of 2-(hydroxymethyl)cyclopentanone cyclic ethylene ketal (137) was collected; b.p. 83-6°/2-2.1 mm. (lit.,[12] b.p. 88°/0.7 mm.), yield 59% based on 121.4 g., 0.77 mole (0.35 mole of methyl ester and 0.42 mole of ethyl ester) of crude 2-carbethoxycyclopentanone (135). The IR spectrum showed major bands at 3400(br) (O-H), 2940(s), 2860(s), 1320(m), 1230(sh), 1205(m), 1155(sh), 1110(br), 1025(br), 960(sh), 950(m), and 835(w) cm^{-1}. The NMR spectrum displayed the expected proton absorptions at δ1.50-2.40 (broad s and m -- 7H) for the protons of the cyclopentane ring, δ3.32 (s--O<u>H</u>, 1H), δ3.57 (d--C<u>H</u>$_2$OH, 2H) and δ3.88 (s--4H) for the ethylene protons of the cyclic ethylene ketal.

Synthesis of 2-(Methoxymethyl)cyclopentanone Cyclic Ethylene Ketal (138). 2-(Hydroxymethyl)cyclopentanone cyclic ethylene ketal (137) (72.5 g., 0.459 mole) in 125 ml. of reagent benzene was added dropwise to a suspension of 25 g. (0.58 mole) of NaH (55.6% dispersion in mineral oil, Metal Hydrides Inc.; washed with benzene before use) in 300 ml. of reagent benzene in a 1-liter, 3-neck, r.b. flask (fitted with a mechanical stirrer, condenser, $CaCl_2$ tube, 250 ml. addition funnel and a N_2 inlet) at room temperature and under N_2. The rate of addition was adjusted so that gentle reflux of the benzene was maintained (a total of 1 hr.). The reaction micture turned from dark gray to a light brown suspension and it was kept at reflux for 60 hr. More fresh NaH (3 g., 55.6% dispersion) was added and the dark-brown reaction mixture was boiled for an additional 25 hr. The mixture was cooled and 70 g. (0.493 mole) of methyl iodide was added dropwise at room temperature under N_2. The reaction mixture was cooled by a cold water bath to keep the exothermic reaction under control. After being stirred over-

night at room temperature, the reaction mixture was again charged with 50 g. of CH_3I and gently boiled under N_2 for 6 more hr. before it was worked up. The light-brown suspension was filtered (by mixing with Celite, analytical filter-aid) and the filtrate was concentrated at 55-60° to give 90 g. of yellow-brownish oil. Distillation *via* a 3-in. vacuum-jacketed vigreux column gave as the main fraction 71.25 g. (0.414 mole) of 2-(methoxymethyl)cyclopentanone cyclic ethylene ketal (138) (b.p. 83-4°/7 mm, n_D^{27} 1.4524), in a yield of 90.2% (based on the alcohol 137). The NMR spectrum (Plate XXXI) showed the characteristic proton absorption for the methoxy group at δ3.31 (s). The IR spectrum is recorded in Plate X.

Anal. Calcd. for $C_9H_{16}O_3$: C, 62.79; H, 9.31.

Found: C, 62.90; H, 9.44.

Synthesis of 2-(Methoxymethyl)cyclopentanone (139). The procedure used in the following was essentially that of Takahashi and coworker.[128] 2-(Methoxymethyl)cyclopentanone cyclic ethylene ketal (138) (22.1 g., 0.128 mole) was mixed with 20 ml. of satd. aqueous tartaric acid and 10 drops of conc. HCl in 30 ml. of abs. alcohol in a 500-ml., r.b. flask fitted with a magnetic stirring bar and a stopper. The solution was stirred and warmed at 50-2° (oil bath) for 50-60 min., followed by stirring at room temperature for 2 more hr. After being neutralized carefully with dil. $NaHCO_3$ and saturated with NaCl, the reaction mixture was extracted with ether (250 ml. x 2). The combined ethereal extracts were washed with brine, dried ($MgSO_4$), filtered and carefully concentrated at 25-30° to give a colorless liquid (*ca.* 35 g.). This was fractionated *via* a 3-in. vacuum-jacketed vigreux column to give, after a forerun of low-boiling material, 13.3 g. of 2-(methoxymethyl)-

cyclopentanone (139) (b.p. 104-105°/59 mm, n_D^{23} 1.4441), in a yield of 81% based on the ketal 138. The IR spectrum (Plate XI) showed the characteristic band for C=O at 1735 cm^{-1}. The NMR spectrum is displayed in Plate XXXII.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.62; H, 9.38.

Found: C, 65.68; H, 9.40.

Synthesis of 2-[5-(Methoxymethyl)-1-cyclopenten-1-yl]naphthalene (142). 2-Naphthyllithium was prepared from 19.8 g. (0.0955 mole) of 2-bromonaphthalene (140) (Eastman Chemical) and a titrated ethereal solution of 0.197 M n-butyllithium[44,46] (485 ml.) in anhydrous ether at 0-5° under N_2 in a 1-liter, 3-neck, r.b. flask (fitted with a mechanical stirrer, a condenser, $CaCl_2$ tube, addition funnel and a N_2 inlet) according to the method described by Gilman and coworker.[45,47] 2-(Methoxymethyl)cyclopentanone (139) (6.72 g., 0.0525 mole) in 100 ml. of anhydrous ether was added dropwise (with ice cooling and vigorous stirring) to the greenish-yellow 2-naphthyllithium solution under N_2. The light-brown but clear reaction mixture, after being stirred at room temperature overnight, was boiled gently for 1.5 hr. It was cooled by ice and decomposed slowly by dropwise addition of 300 ml. of 10% NH_4Cl. The yellowish ethereal solution was separated from the aqueous layer, which was extracted further with benzene (100 ml. x 2). The combined organic extracts were washed with brine (until neutral), dried ($MgSO_4$), filtered and concentrated at 50° to give, after solvent was completely removed under vacuum, 26.1 g. of a yellow oil. The oil was taken up in methanol and the undesired coupling product, 2,2'-binaphthyl (1.6 g.), which was insoluble in methanol, was nicely separated by filtration. The solvent (CH_3OH) was evaporated to

give a brown oil. Naphthalene, which was the remaining major impurity in the oil could easily be removed by sublimation at 60-70°/0.1 mm. The residual 2-(methoxymethyl)-1-(2-naphthyl)cyclopentanol (141) was dehydrated immediately, without further purification, by the following reaction with $POCl_3$ and pyridine.

The crude alcohol 141 (19.6 g.) was mixed with 20 g. (0.131 mole) of reagent $POCl_3$ (Allied Chemical) in 200 ml. of anhydrous pyridine (dried by distillation over CaH_2) in a 500-ml., r.b. flask (fitted with a magnetic stirrer, N_2 inlet, condenser and $CaCl_2$ tube). The mixture was heated to reflux in an oil bath at 128° for 3 hr. and then stirred overnight under N_2 at room temperature. The dark-brown reaction mixture was decomposed by pouring it into 500 ml. of 2N HCl and ice. The resulting dark aqueous solution was thoroughly extracted with ether (considerable black complex-like material was found in the aqueous medium during the extraction, and filtration was necessary to bring about a clean phase separation). The light-brown ethereal extract (a total volume of ca. 1 liter) was washed with dil. $NaHCO_3$, and then brine (until neutral) and dried ($MgSO_4$). GLC analysis at 180° revealed only one major product in the ethereal solution. After the latter was filtered (by mixing with Celite analytical filter-aid), and then evaporated at 50°, 13 g. (after solvent was completely removed at 0.2 mm.) of a dark-brown oil resulted. The latter was distilled via a 3-in. vacuum-jacketed vigreux column (with a variable receiver) to give, after a forerun of low-boiling material, 5 g. (0.021 mole) of 2-[5-(methoxymethyl)-1-cyclopenten-1-yl]naphthalene (142) (b.p. 130-130.5°/0.2 mm., $n_D^{27.5}$ 1.6191) in a yield of 40% based on 2-(methoxymethyl)-cyclopentanone (139). The IR spectrum (Plate XII) showed a strong

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band for C-O-C at 1112 cm^{-1}. An olefinic proton absorption downfield at δ6.19 (t--1H) and a sharp singlet for the methoxy group at δ3.23 (3H) are the characteristic features of its NMR spectrum (Plate XXXIII). An analytical sample was obtained by redistillation.

Anal. Calcd. for $C_{17}H_{18}O$: C, 85.71; H, 7.56.

Found: C, 85.84; H, 7.78.

Synthesis of 2-[2-(Methoxymethyl)cyclopentyl]naphthalene (143).

The catalytic hydrogenation was performed in a standard atmospheric hydrogenation appratus in the usual manner.[8] 2-[5-(Methoxymethyl)-1-cyclopenten-1-yl]naphthalene (142) (4.45 g., 0.0187 mole) was hydrogenated at room temperature over 0.6 g. of 10% Pd/C (Matheson Coleman & Bell Co.) in ca. 100 ml. of abs. ethanol (freshly distilled over W-6 Raney Ni) in a 250-ml. hydrogenation flask fitted with a magnetic stirrer. The reaction (slightly exothermic) could be followed nicely by the rate of H_2 intake. Reduction was essentially complete in a period of 1 hr. with the total volume of H_2 consumed about 490 ml. (theor. 456 ml.). After being stirred for 2 more hr. in the hydrogenation appratus at room temperature, the reaction mixture was worked up by filtering it carefully through a sintered glass funnel. The solid (catalyst) in the funnel was washed thoroughly with methanol. The combined clear filtrate was shown to contain only one major product by GLC analysis at 185°, and concentrated at 45° to give a pale oil (4.55 g.). The oil was distilled through a short-path, Bantamware semi-micro still to give 4.1 g. (0.0171 mole) of colorless 2-[2-(methoxymethyl)cyclopentyl]naphthalene (143) (b.p. 119-121°/0.1 mm; $n_D^{20.5}$ 1.5882); yield 91% (based on the alkene 142). The ether 143 appeared to contain only one isomer as shown by GLC analysis on a

variety of columns (namely: 5% SE-30 on 60/80, A-W, DMCS-treated Chromosorb W, 5 ft. x 1/8 in.; 10% PMPA on 80/100, A-W Chromosorb W, 5 ft. x 1/4 in.; 10% Carbowax 20M on 80/100, A-W, DMCS-treated Chromosorb W, 6 ft. x 1/8 in.; and 15% DMGS on 80/100, A-W, DMCS-treated Chromosorb G, 6 ft. x 1/8 in.). IR and NMR spectra are recorded on Plate XIII and Plate XXXIV, respectively. No olefinic proton absorption is visible in the regions between δ4.50-6.50 in the NMR spectrum. A redistilled sample gave the following elemental analysis.

Anal. Calcd. for $C_{17}H_{20}O$: C, 85.00; H, 8.33.

Found: C, 84.67; H, 8.37.

Bromination of 2-[2-(Methoxymethyl)cyclopentyl]naphthalene (143). Synthesis of 1-Bromo-2-[2-(methoxymethyl)cyclopentyl]naphthalene (144). The ether 143 (4 g., 0.0166 mole) was brominated in the dark at 0-5° with 2.85 g. (0.017 mole) of reagent bromine in the presence of 0.35 g. of anhydrous $FeBr_3$ (K&K Chemical) in 40 ml. of CS_2 by the same procedure described in the synthesis of 1-bromo-2-(3-methoxypropyl)naphthalene (128) (p. 92). After the workup, 6.2 g. of a brown oil was collected. It was shown to contain only one major product by GLC analysis at 210°. The crude product was purified by distillation in vacuo through a 3-in. vacuum-jacketed vigreux column to give, after a forerun of low-boiling material, 4.49 g. (0.0141 mole) of the desired bromo ether (144) (a greenish-yellow viscous oil, b.p. 158.5-160.5°/0.35-0.4 mm; n_D^{20} 1.6158); yield 85% based on 143. The mass spectral analysis showed the expected peaks for the molecular ion at m/e 318 and 320. By virtue of the characteristic isotopic composition of natural bromine, the equal intensities of the two parent peaks separated by 2 mass units confirmed that the compound 144 contained only one bromine atom. The

substitution at C-1 of the naphthalene ring was ascertained by the NMR spectrum (Plate XXXV), which showed the characteristic absorption for the proton at C-8 on the ring at δ8.35 (m--1H). The deshielding effect imposed by the adjacent Br at C-1 caused this proton at C-8 to resonate downfield from the rest of the aromatic protons. Model compounds[119,120] of this nature have been described in the synthesis of the bromo compound 128 (p. 92). Although the peak for the tertiary benzylic proton at δ3.82 (m--1H) appeared to be separated sharply from the absorptions of the methylene envelop of the methoxymethyl and cyclopentyl ring protons, the extreme complexity of the splitting pattern (AA'BC) prohibited a detailed analysis (via decoupling) of the spectrum. Thus, exact assignment of the stereochemistry of the structure are not yet possible. A 220-MHz NMR spectrum of compound 144 (courtesy of Varian Associates) is displayed in Plate XXXVI. The IR spectrum is recorded in Plate XIV. An analytical sample was obtained by redistillation.

Anal. Calcd. for $C_{17}H_{19}BrO$: C, 63.97; H, 5.96.
Found: C, 63.97; H, 6.01.

Synthesis of Crude Ethyl[2-[2-(methoxymethyl)cyclopentyl]-1-naphthyl]phenylphosphine (145). The reaction described herein were all performed under N_2. The Grignard reagent of 1-bromo-2-[2-(methoxymethyl)cyclopentyl]naphthalene (144) was prepared by the "entrainment method"[70] from 3.58 g. (0.0112 mole) of the bromide 144, 0.57 g. (0.023 g-atoms) of Mg turnings, and 2.11 g. (0.0112 mole) of ethylene dibromide (Baker certified reagent) in ca. 40 ml. of anhydrous THF. The equipment used was a 100-ml., 3-neck, r.b. flask fitted with a N_2 inlet, condenser, $CaCl_2$ tube, magnetic stirrer and addition funnel. After being heated in an oil bath (80-5°) for a total of 3 hr., the dark-brown

Grignard solution was cooled (ice) and used immediately in the following reaction.

Ethylphenylphosphinous chloride (131) (1.94 g., 0.0112 mole) in 15 ml. of anhydrous ether was added dropwise over a period of 1 hr. to the Grignard solution with ice cooling. After being stirred at room temperature overnight, the greenish-yellow reaction mixture was worked up in the same manner as that described in the synthesis of the crude phosphine 132 (p. 96). Vacuum distillation of the oily product was performed through a short-path, Bantamware semi-micro still (with the aid of an IR lamp and a hot-water condenser) under diffusion-pump vacuum. After a forerun of low-boiling materials, the main fraction distilled at 210-215°/7 μ to give 2.82 g. (0.0075 mole) of the crude phosphine 145 (an extremely viscous, light-brown oil); yield 32.6% based on 144. The IR spectrum (Plate XV) showed the absence of a strong band for P→O in the region 1150-1300 cm^{-1}. The mass spectral analysis (Plate L) showed the expected molecular ion at m/e 376 for the desired phosphine 145. Nevertheless, a considerable amount of phosphine oxide 164 (which apparently resulted from air oxidation) was also found in the crude sample (as revealed by the presence of peak at m/e 392, 16 mass units higher than that of the phosphine 145). The fact that the ratio of peak intensities of m/e 376 to m/e 392 in the mass spectrum varied during scans taken at different sample pressures confirmed that the latter peak (m/e 392) was indeed an impurity rather than part of the main spectrum. The NMR spectrum (Plate XXXVII) supported the proposed structure for 145. The crude phosphine 145 was used in the cyclization reaction to give 120a without further purification.

Cyclization of Ethyl[2-[2-(methoxymethyl)cyclopentyl]-1-naphthyl]-phenylphosphine (145). Synthesis of 5-Ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo[h]cyclopenta[c]phosphinolinium Perchlorate (120b). The crude phosphine 145 (1.28 g., 3.4 mmole) in 10 ml. of glacial acetic acid was mixed with 50 ml. of 48% hydrobromic acid (Fisher certified reagent) under N_2 in a 200-ml., 3-neck, r.b. flask fitted with a sintered-glass gas inlet (immersed in the reaction mixture, for introducing gaseous HBr), magnetic stirrer, condenser, $CaCl_2$ tube and N_2 inlet. The solution was heated in an oil bath (120-125°) for 2.5 hr. while a gentle stream of anhydrous HBr (The Matheson Co. Inc.) was continuously passed into the reaction mixture. After being stirred at room temperature under N_2 for 4 more hr., the cloudy, almost colorless, reaction mixture was worked up in the same manner as described in a previous experiment (p. 99; synthesis of 119a). The crude 5-ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo[h]cyclopenta[c]phosphinolinium bromide (120a) was obtained in the form of a heavy oil [after chloroform was removed under vacuum (0.1 mm)] and did not solidify at room temperature. Various attempts made to induce crystallization of the bromide 120a were unsuccessful. Consequently, the heavy oil was treated with 80 ml. of anhydrous ether in a 100-ml., 3-neck, r.b. flask (fitted with a condenser, $CaCl_2$ tube, magnetic stirrer, and N_2 inlet), and boiled gently for 10 hr. under N_2. The creamy fine solid that formed was collected by filtration, washed thoroughly (anhydrous ether), and dried immediately in a vacuum oven (in the presence of P_2O_5 at 30° for 12 hr.) to give 0.395 g. (0.69 mmole) of crude phosphonium bromide 120a (m.p. 95-120°); yield 20% based on crude 145. As purification by recrystallization from a variety of solvent systems was again unsuccessful,

conversion of 120a to the perchlorate 120b was undertaken.

The crude bromide 120a (75.7 mg.) was taken up a 5 ml. of distilled water in a 10-ml. Erlenmeyer flask. After being stirred and warmed in an water bath (50-55°) for ca. 10 min., the aqueous mixture was cooled back to room temperature and filtered to remove an insoluble brown gummy material. The latter was washed with 3 more ml. of water, and to the clear combined H_2O solution, 4 ml. of satd. aqueous $NaClO_4$ was added dropwise with stirring at room temperature. White solid immediately precipitated from the aqueous solution. The solid was washed carefully and thoroughly with distilled water (to remove any excess $NaClO_4$ and unreacted bromide 120a) and dried in a vacuum oven (in the presence of P_2O_5 at 35-40° for 10 hr.) to give 37.2 mg. of the crude phosphonium perchlorate 120b. Recrystallization could be achieved (very slowly) at room temperature by dissolving the crude 120b in a small amount of 2-propanol (ca. 2 ml.) on a hot water bath (75-80°) (a trace of insoluble gummy material was carefully removed by use of a spatula) and cooling. A light brown oily gum was formed initially. It gradually crystallized in a period of more than a week to a brown solid. After 3 consecutive recrystallizations from 2-propanol, an analytical sample (13 mg.) of 5-ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo[h]cyclopenta[c]phosphinolinium perchlorate (120b) (m.p. 183.5-187°) was obtained.

Anal. Calcd. for $C_{24}H_{26}ClO_4P$: C, 64.68; H, 5.85; P, 6.98.

Found: C, 64.71; H, 5.69; P, 7.03.

The rather wide melting range of the perchlorate 120b is understandable in view of the probable existence of two diastereoisomers due to the asymmetric phosphorus and cis (or trans) C/D ring junction

in the crystalline product. The IR spectrum (Plate XVI) showed the characteristic very strong and broad band[26] for ClO_4^- at 1090 cm^{-1}. The NMR spectrum is displayed in Plate XXXVIII. A 100-MHz NMR (courtesy of JEOL Co. on a PS-100 unit) of the crude perchlorate 120b (before recrystallization) is also displayed in Plate XXXIX. The nonequivalent proton absorptions for $--PCH_2\underline{CH}_3$ at region around δ0.20-0.80 may indicate the presence of more than one diastereoisomer in the reaction product. The mass spectrum, taken by direct evaporation of the perchlorate 120b into the probe at about 200° (with electron voltage of 70 eV and ion source temperature at 310°), is recorded in Plate LI. It was most interesting in that there were no peaks for the molecular ion at m/e 444; instead what appeared to be the cation part of the molecule was represented by a peak at m/e 342. Other intense ions were found at m/e 18, 28, 44, 207, 233, 313, and 314.

Preparation of D(-)-Dibenzoyltartaric Acid Monohydrate and L(+)-Dibenzoyltartaric Acid Monohydrate. The D(-)-enantiomorph was prepared from d-tartaric acid (75 g., 0.5 mole; Aldrich Chemical) and 2.25 g. (1.6 mole) of benzoyl chloride (Baker reagent grade) by the method of Butler and Cretch[22] to give 148 g. (0.394 mole, m.p. 85-8°; 79% based on d-tartaric acid) of the crude D(-)-dibenzoyltartaric acid monohydrate. Since recrystallization from benzene (as reported in the literature) was unsuccessful, purification was finally achieved by repeated washing with distilled water and benzene to give (after drying) pure D(-)-dibenzoyltartaric acid monohydrate, m.p. 86.5-89°, $[\alpha]_D^{23}$ -111° (c 0.03086 g/ml, acetone) (lit.,[141] m.p. 88.0-90°, $[\alpha]_D^{18}$ -115.78° in C_2H_5OH).

The L(+)-enantiomorph was prepared in the same manner from l-tar-

taric acid (30 g., 0.2 mole; Aldrich Chemical) and 90 g. (0.64 mole) of benzoyl chloride to give 60 g. (0.16 mole, m.p. 85-89.5°; 80% based on the l-tartaric acid) of the crude L(+)-dibenzoyltartaric acid monohydrate. Purification by the same method gave the pure L(+)-dibenzoyltartaric acid monohydrate, m.p. 86-9°, $[\alpha]_D^{23.5}$ +108.8° (c 0.02996 g/ml, acetone) (lit.,[22] m.p. 84.0-86.0°, $[\alpha]_D^{25}$ +109°).

Preparation of Silver Hydrogen D(-)-Dibenzoyltartrate (152) and Silver Hydrogen L(+)-Dibenzoyltartrate (153). The silver salt 152 was prepared from 8.0 g. (0.0213 mole) of D(-)-dibenzoyltartaric acid monohydrate and 21.1 ml. of 1.063 N NH_4OH in 240 ml. of distilled water by the method of Coyne, McEwen and VanderWerf.[29] It was possible to obtain (after drying) 5.95 g. (0.0128 mole; 60% of theoretical) of silver hydrogen D(-)-dibenzoyltartrate (152).

Silver hydrogen L(+)-dibenzoyltartrate (153) (6.4 g., 0.0137 mole) was similarly prepared in 64% yield from L(+)-dibenzoyltartaric acid monohydrate (8.0 g., 0.0213 mole) and 21.1 ml. of 1.063 N NH_4OH in 240 ml. of distilled water.

Resolution of (±)-1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Bromide (119a) with Silver Hydrogen L(+)-Dibenzoyltartrate (153). Synthesis and Separation of (+)-1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Hydrogen L(+)-Dibenzoyltartrate - L(+)-Dibenzoyltartaric Acid (154). The phosphonium bromide 119a (297 mg., 0.772 mmole) in 3 ml. of distilled water was added dropwise to 800 mg. (1.72 mmole) of Ag L(+)-HDBT (153) in 140 ml. of distilled water in a 250-ml. Erlenmeyer flask (fitted with a magnetic stirrer) at room temperature. A white solid immediately precipitated, and the reaction mixture was stirred for about 5 min. before working up by filtration.

The creamy white solid collected was carefully washed with 50 ml. more of distilled water [to remove any unreacted 119a and Ag L(+)-HDBT (153)] and dried in the presence of P_2O_5 and $CaCl_2$ in a vacuum oven at 35° for 20 hr. It was quickly dissolved in 50 ml. of reagent methanol, and the resulting solution was filtered to remove insoluble AgBr in the form of a dark gray powder (120.3 mg., 0.64 mmole; 83% of theoretical). The methanol-soluble portion was evaporated and the last traces of methanol were removed under high vacuum (0.2 mm.) to give a white solid (with some gummy material). Several recrystallizations performed (slowly at room temperature) from reagent 1-propanol were required to produce a constant m.p. and specific rotation. The following data were recorded during the recrystallizations.

No. of Recrystallizations	Vol. of 1-Propanol Used	Wt. of Product	M.P. °C	Specific Rotation (Conc. in CH_3OH)
1.	17 ml.	269 mg.	148-9° dec 145° browned	$[\alpha]_D^{24}$ +96.2° (0.0259 g/ml)
2.	11 ml.	187 mg.	149-150° dec 148.5° browned	-
3.	8 ml.	132.4 mg.	150° dec	$[\alpha]_D^{24.5}$ +83° (0.0134 g/ml)
4. (on 17.6 mg. of crystals from 3rd. recryst'n)	2.5 ml.	9.1 mg.	149.5-150° dec	$[\alpha]_D^{25}$ +83° (0.0229 g/ml)

The constancy of the melting point [m.p. 150° dec] and specific rotation ($[\alpha]_D^{25}$ +83°) of the crystalline compound 154 following two consecutive recrystallizations strongly indicated the achievement of separation of one diastereoisomer from the diastereomeric mixture. The IR spectrum of the crystals from the third recrystallization product

is recorded in Plate XVII. The elemental analysis shows the stoichiometric inclusion of the monoanion of L(+)-dibenzoyltartaric acid and one equivalent of the acid in the crystal of compound 154.

Anal. Calcd. for $C_{39}H_{35}O_8P \cdot C_{18}H_{14}O_8$: C, 66.82; H, 4.81; P, 3.04.
Found: C, 66.87; H, 4.85; P, 3.10.

This behavior is similar to that reported by Davis and Mann[35] for 9,9,10-triethyl-9,10-dihydrophosphanthrene picrate (156a) which contained one equivalent of picric acid.

Resolution of (±)-1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Bromide (119a) by Silver Hydrogen D(-)-Dibenzoyltartrate (152). Synthesis and Separation of (-)-1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Hydrogen D(-)-Dibenzoyltartrate - D(-)-Dibenzoyltartaric Acid (155). The (-)-isomer 155 was prepared in the same manner as the (+)-isomer 154 (p. 120) from 49.0 mg. (0.127 mmole) of the phosphonium bromide 119a in 2 ml. of distilled water and 140.7 mg. (0.31 mmole) of Ag D(-)-HDBT (152) in 24 ml. of distilled water. Silver bromide (21.5 mg., 0.117 mmole; 92% of theoretical) was collected by filtration of the methanol solution. The methanol-soluble portion, after removal of CH_3OH, gave a white solid and some colorless gummy material. The latter was purified by repeated recrystallization (slowly) from reagent 1-propanol, and the following data were collected.

No. of Recrystallizations	Vol. of 1-Propanol Used	Wt. of Product	M.P. °C	Specific Rotation (Conc. in CH_3OH)
1.	5 ml.	27.5 mg.	151.5-152.5° dec 148° browned	$[\alpha]_D^{25}$ -84.9° (0.0244 g/ml)
2.	2 ml.	-	148.5-149.5° dec	-
3.	2 ml.	6 mg.	149-149.5° dec	$[\alpha]_D^{23.5}$ -83° (0.0196 g/ml)

4.	1 ml.	1 mg.	147-149° dec		-

The structure of 155 was confirmed by its IR spectrum, which is superimposable with that of the (+)- isomer 154.

Metathesis of (+)-1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Hydrogen L(+)-Dibenzoyltartrate - L(+)-Dibenzoyltartaric Acid (154). Synthesis and Separation of (+)-1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Bromide (119a). The (+)-isomer of 154 (100 mg., 0.098 mmole) dissolved in ca. 8 ml. of reagent methanol was mixed with excess NH_4Br (89.8 mg., 0.915 mmole; Mallinckrodt Chemical, analytical reagent) in a 50-ml., r.b. flask (fitted with a magnetic bar, condenser and $CaCl_2$ tube). The homogeneous reaction mixture was stirred at room temperature for 15 hr., followed by a period at reflux via an oil bath (70°) for 4 hr.; the mixture was then stirred at room temperature overnight. Methanol was completely stripped off under vacuum and replaced with about 30 ml. of reagent $HCCl_3$. The resulting suspension was gently boiled at 70° for 6.5 hr., and the white, chloroform-insoluble solid (147.4 mg.), which contained mainly the excess NH_4Br and ammonium hydrogen L(+)-dibenzoyltartrate, was removed by filtration. The clear filtrate was concentrated to ca. 5 ml. on a rotary evaporator at 35°. After being cooled to room temperature, the solution was carefully filtered through a disposable pipette (plugged with glass wool, to remove any insoluble material) into a 25-ml. Erlenmeyer flask. Anhydrous ether was added dropwise to the solution until it turned distinctively cloudy. Colorless, fine needles were observed to crystallize out gradually at room temperature. The needle-like material was collected by filtration and was immediately dried in a

vacuum oven in the presence of P_2O_5 at 35-40° for 5 hr. to give 20.6 mg. (0.0535 mmole, 55% of theoretical) of (+)-1-ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium bromide (119a). Further purification was achieved by repeated recrystallization from $HCCl_3$-ether in the same manner as described previously. The following data were recorded:

No. of Recrystallizations	Wt. of Product	M.P. °C	Specific Rotation (Conc. in $HCCl_3$)
1.	20.6 mg.	253-5° dec 172° browned	$[\alpha]_D^{25}$ +30.7° (0.02003 g/ml)
2.	13.2 mg.	259° dec 250° browned	$[\alpha]_D^{25}$ +28° (0.01745 g/ml)
3.	2.1 mg.	259-259.5° dec 250° browned	-

The 2.1 mg. sample (from the third recrystallization) was too small for an accurate determination of rotation via the micro polariscope tube on the Rudolph polarimeter (Model 80). The IR spectrum of the (+)-1-ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium bromide (119a) (m.p. 259° dec, $[\alpha]_D^{25}$ +28°, from the second recrystallization) was found virtually superimposable on that of its racemic precursor 119a (see Plate V).

A small amount (1.7 mg.) of perchlorate 119b [m.p. 171.5-172.5° (2-propanol)] was also prepared (by the method described on p. 102, from the optically active (+)- phosphonium bromide 119a). However, owing to the extremely small amount of sample available, the specific rotation and an elemental analysis of 119b were not obtained. Evidence for the structure of the (optically active) phosphonium perchlorate 119b, is provided by its IR spectrum, which again essentially coincides with that of its racemic precursor (see Plate VI).

Synthesis of Diethyl [3-(2-Naphthyl)propyl]phosphonate (166).

2-(3-Bromopropyl)naphthalene (126) (17 g., 0.0683 mole) was heated with 17 g. (0.1 mole) of redistilled $(C_2H_5O)_3P$ in a 50-ml., 3-neck, r.b. flask (fitted with an immersed thermometer, magnetic stirrer, nitrogen inlet, and a short-path, Bantamware semi-micro still and a receiver) at a sand bath temperature of 165-180° for 1.5 hr. Effervescence was immediately observed as the solution temperature reached 128°, and evolution of gas became very vigorous at 152-4° as $(C_2H_5O)_3P$ smoothly distilled out. At the end of the reaction (effervescence practically ceased), the sand bath temperature was raised to and kept at 190-5° for 3 min. before heat was terminated. After cooling, excess $(C_2H_5O)_3P$ was evaporated off at 40°/0.2 mm. during 45 min. The light brown residue was transferred into a 25-ml., r.b. flask fitted with a short-path semi-micro still and subjected to distillation under diffusion pump vacuum with the help of an IR lamp. A forerun of a low-boiling fraction was discarded. The main fraction weighed 19.6 g. (90.8% based on the bromide 126) and was a viscous liquid, which distilled smoothly at 178-183°/0.0036-0.00085 mm., n_D^{21} 1.5444. The structure of the phosphonate 166 is defined clearly by NMR and IR spectra, which are recorded in Plate XL and Plate XVIII, respectively. An analytical sample was obtained by redistillation via a 3-in. vacuum-jacketed vigreux column at 155-160°/0.3-0.4 μ. An almost colorless center cut was collected.

Anal. Calcd. for $C_{17}H_{23}O_3P$: P, 10.13.

Found: P, 9.91.

Synthesis of [3-(2-Naphthyl)propyl]phosphonic Acid (167). Diethyl [3-(2-naphthyl)propyl]phosphonate (166) (17.7 g., 0.056 mole) was boiled

with 90 ml. of conc. HCl at a sand bath temperature of 136-140° for 6 hr. in a 200-ml., r.b. flask fitted with a condenser and a magnetic stirrer. White solid, which crystallized out immediately after cooling, was collected by filtration and washed thoroughly with H_2O until neutral. After drying in a vacuum oven at 35-37° for 3 hr. in the presence of P_2O_5, 17.7 g. of a white solid was on hand. Recrystallizing from 500 ml. of ethyl acetate (containing 20 ml. of CH_3OH) gave, after drying, 13.7 g. of [3-(2-naphthyl)propyl]phosphonic acid (167) (94.5% based on the phosphonate 166), m.p. 181-2°. The NMR and IR spectra are displayed in Plate XLI and Plate XIX, respectively.

Anal. Calcd. for $C_{13}H_{15}O_3P$: P, 12.40.
Found: P, 12.27.

Synthesis of [3-(2-Naphthyl)propyl]phosphonic Dichloride (168).

[3-(2-Naphthyl)propyl]phosphonic acid (167) (4 g., 0.016 mole) was heated in a sand bath at 100-110° with 6.7 g. (0.035 mole) of PCl_5 for 6 hr. in a 50-ml., r.b. flask fitted with N_2 inlet, a condenser and $CaCl_2$ tube, and a magnetic stirrer. Generated $POCl_3$ was observed boiling out of the dark brown reaction mixture. At the end of heating, $POCl_3$ was distilled at 101°. The residue was transferred carefully under N_2 into a 5-ml., r.b. flask fitted with a Bantam-ware, short-path, semi-micro still. Solidification of the residue to a tan-colored solid occurred as the last traces of $POCl_3$ were carefully removed at 0.1 mm. (room temperature). Vacuum distillation was performed via the use of a diffusion pump system (using an air condenser) and with the help of an IR lamp. An almost colorless and very viscous distillate was collected, b.p. 177.5-180°/6 μ, which solidified gradually at room temperature and comprised 3 g. (65% based on 167) of 168. The product,

m.p. 64-7°, was extremely hygroscopic, and HCl evolution was visible when the compound was exposed to air. It is soluble in benzene and chloroform but not in hexanes. The NMR spectrum is recorded in Plate XLII (because of the sensitivity to atmospheric moisture, the spectrum is likely not that of the pure compound). While the extremely labile nature of the compound prohibited an elemental analysis, further proof of the structure was obtained by mass spectral analysis (Plate LII), which reveals the molecular ion at m/e 286 and only a trace of an ion at m/e 250, which may be the hydrolyzed product. The latter probably resulted during transport of the compound to the probe before taking the spectrum.

Synthesis of [3-(2-Naphthyl)propyl]phosphonous Dichloride (169).

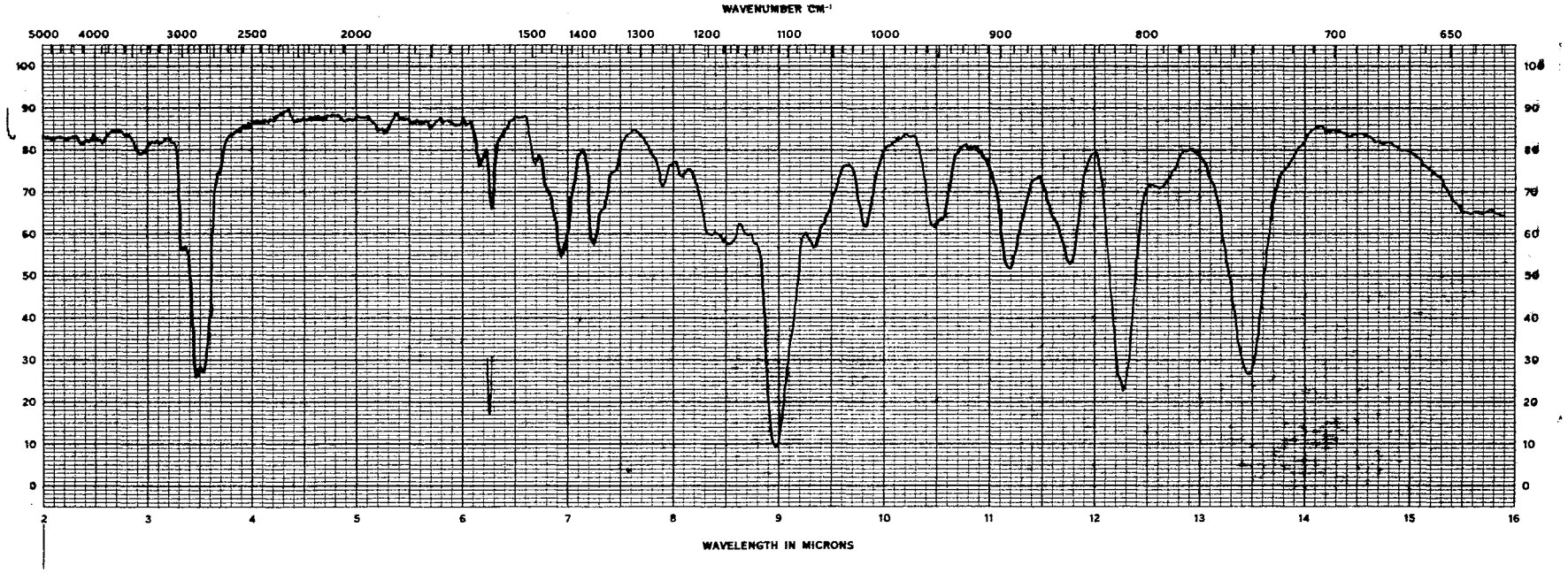
The reactions and workups described in this experiment were all performed under N_2. The Grignard reagent was prepared by the usual procedure.[70] 2-(3-Bromopropyl)naphthalene (126) (9.75 g., 0.0391 mole) in 85 ml. of anhydrous THF was added to 0.96 g. (0.0395 g-atom) of Mg turnings in 25 ml. of anhydrous THF containing a trace of I_2 in a 500-ml., 3-neck, r.b. flask (fitted with a magnetic stirrer, condenser and $CaCl_2$ tube, an addition funnel, and N_2 inlet). After the addition, the reaction mixture was boiled for 5 more hr. Anhydrous $CdCl_2$ (3.6 g., 0.0195 mole; Fisher certified reagent -- dried at 110-120° for 8 hr. before use) was added to the dark brown Grignard solution with vigorous stirring and external ice cooling. After being stirred at room temperature for 12 hr., the organocadmium reagent (a dark-gray suspension) in THF was forced out by N_2 through a glass delivery tube into a clean 500-ml., 3-neck, r.b. flask (fitted with a N_2 inlet, condenser and $CaCl_2$ tube) containing 7 g. (0.05 mole) of PCl_3 (Baker analyzed reagent) in

anhydrous ether (200 ml.) prechilled (-30° to -40°) with an external acetone-dry ice bath. A white precipitate was immediately formed. After being stirred at room temperature for 24 hr., the reaction mixture was worked up *via* filtration and washing the solid with more anhydrous ether. The clear filtrate, after being carefully concentrated at 38-40°, gave a greenish, pungent oil, which was vacuum distilled immediately by using a short-path, Bantam-ware semi-micro still. The compound 169 (a colorless, viscous oil, n_D^{25} 1.6282) was distilled at b.p. 161.5-163°/0.05 mm. as the main fraction [6.3 g., 0.0233 mole; 59.5% based on 2-(3-bromopropyl)naphthalene (126)]. The IR spectrum (Plate XX) (due to its sensitivity to air, it may not be that of the pure compound) showed no distinctive absorption for P→O at region 1150-1300 cm^{-1}. The NMR spectrum is recorded in Plate XLIII. The compound was very sensitive to moisture and air and gradually turned slightly yellow upon prolonged storage. An analytical sample was obtained by redistillation (short-path) and sealed immediately in vacuum.

Anal. Calcd. for $C_{13}H_{13}Cl_2P$: P, 11.44.

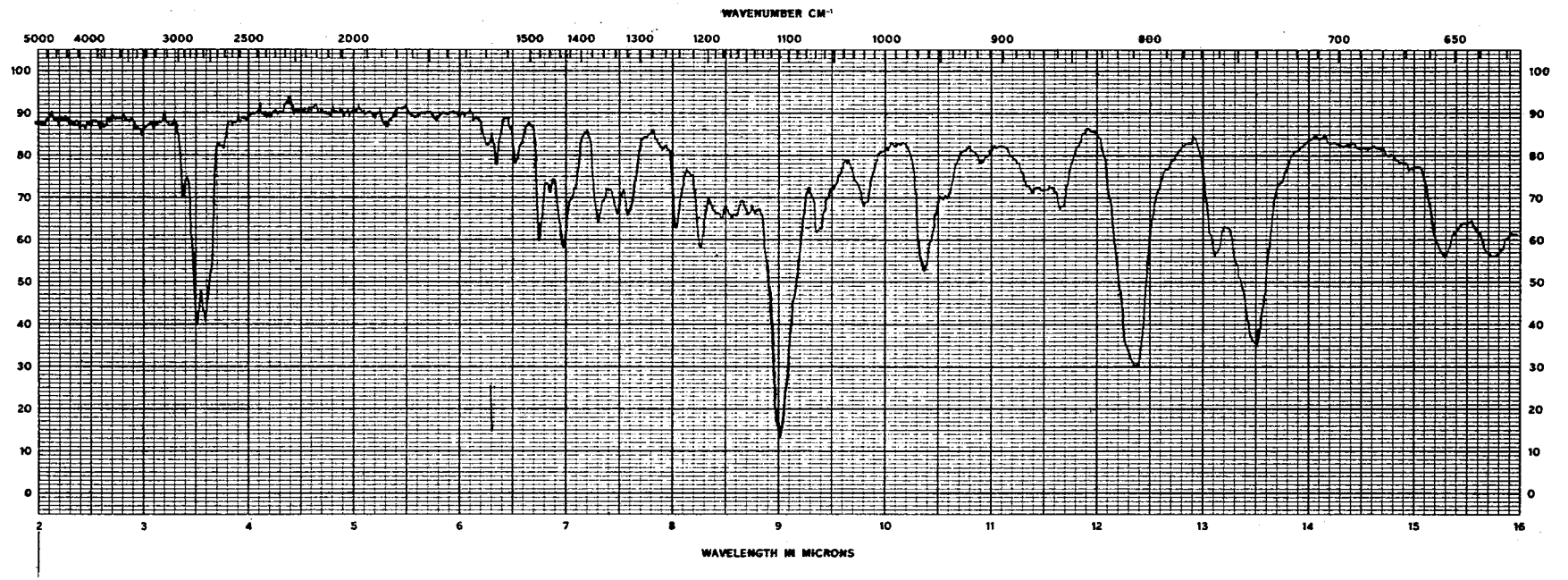
Found: P, 11.28.

Plate I



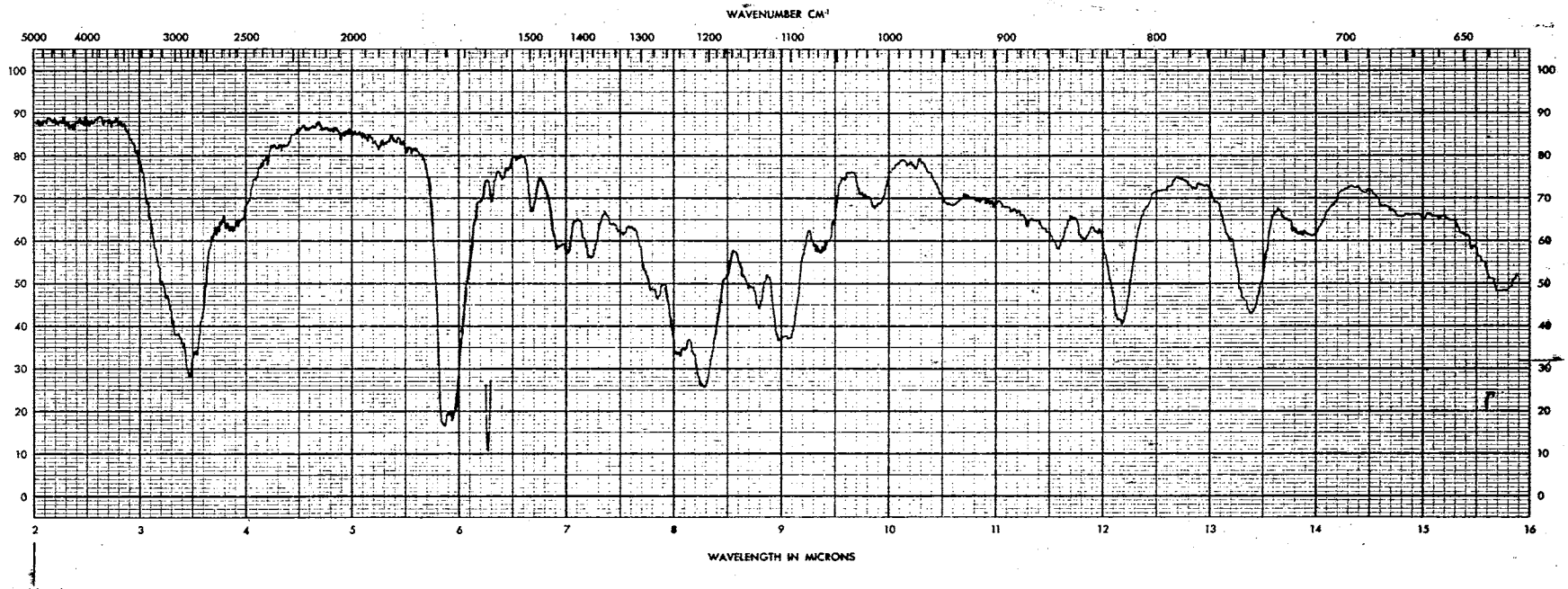
2-(3-Methoxypropyl)naphthalene (127), Film on NaCl Plates

Plate II



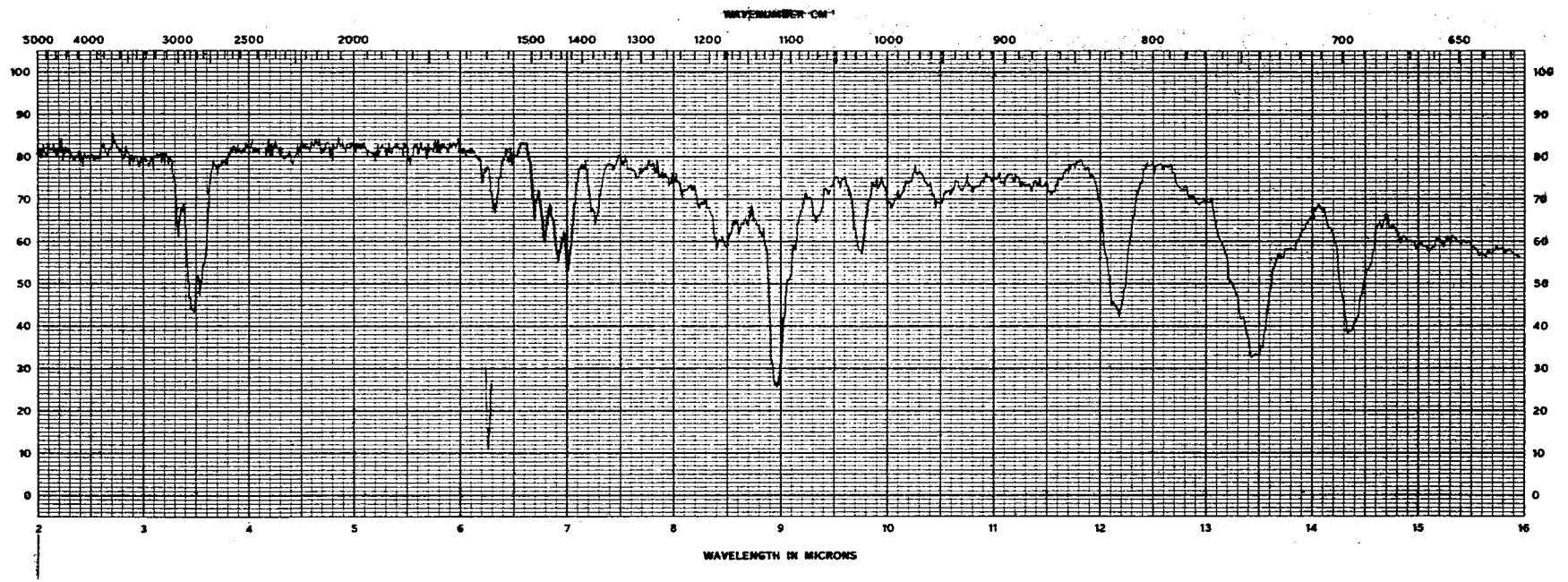
1-Bromo-2-(3-methoxypropyl)naphthalene (128), Film on NaCl Plates

Plate III



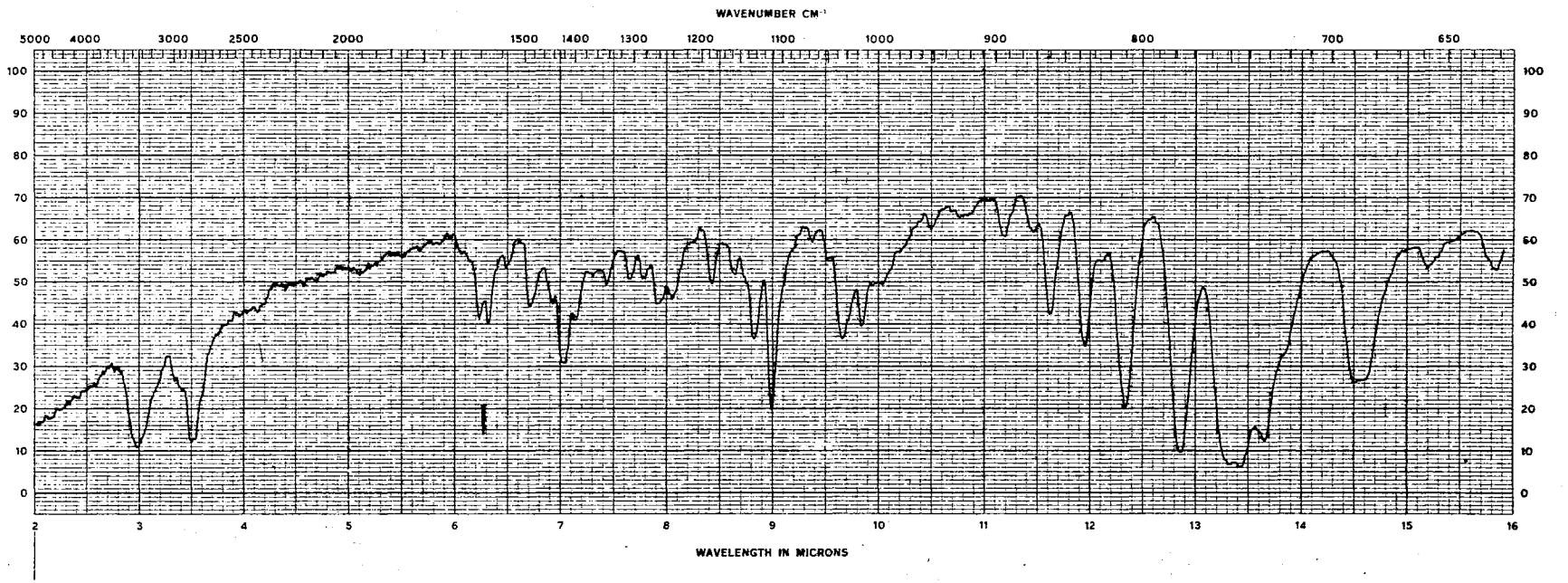
2-(3-Methoxypropyl)-1-naphthoic Acid (129), Film on NaCl Plates

Plate IV



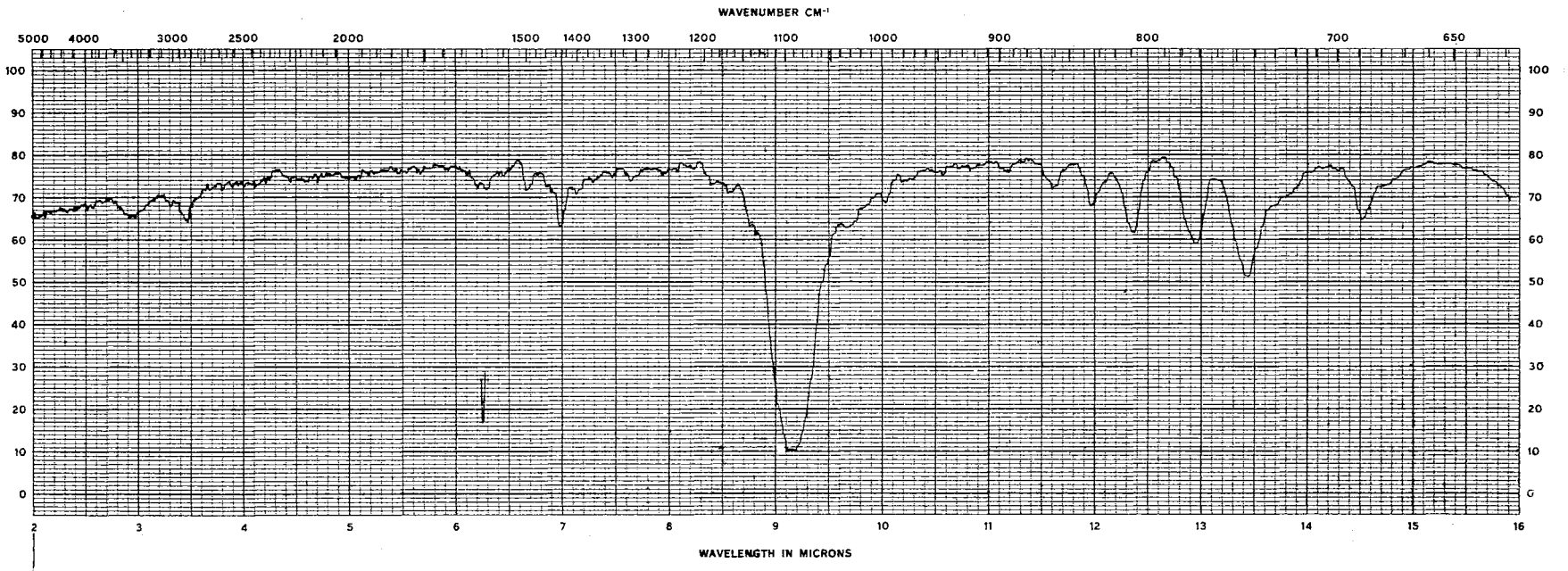
Crude Ethyl[2-(3-methoxypropyl)-1-naphthyl]phenylphosphine (132), Film on NaCl Plates

Plate V



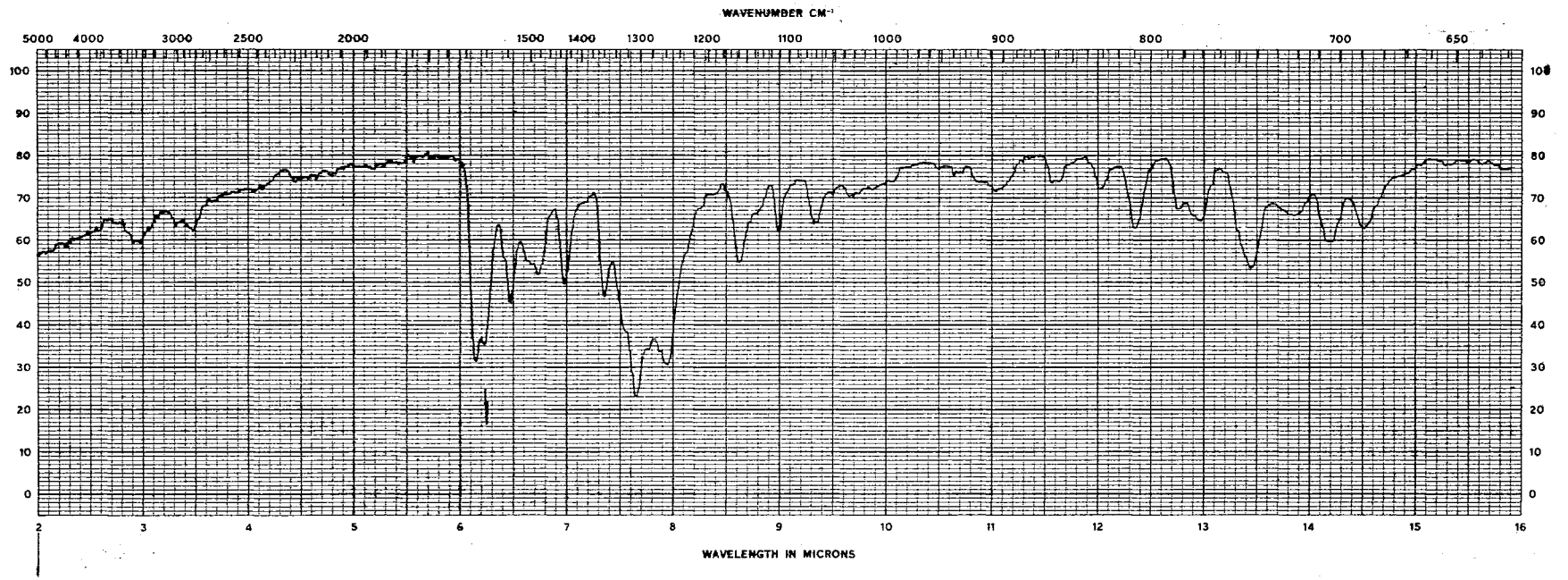
1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Bromide (119a), KBr Pellet

Plate VI



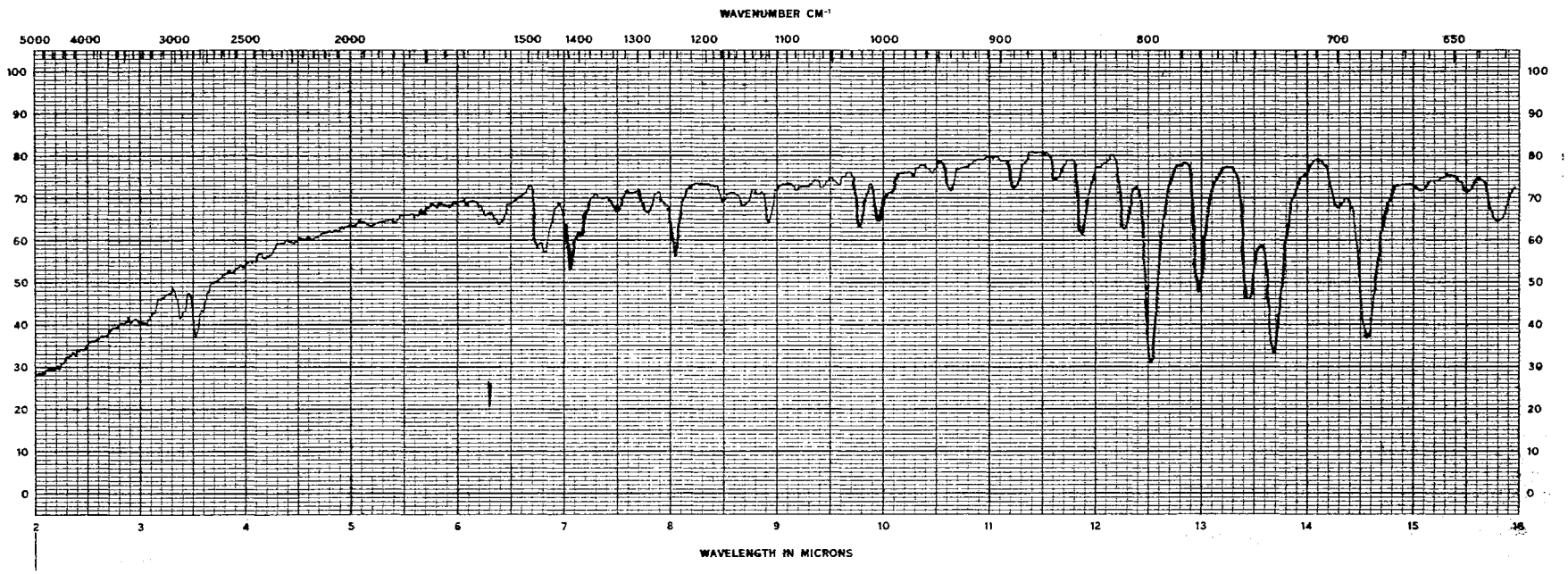
1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Perchlorate (119b), KBr Pellet

Plate VII



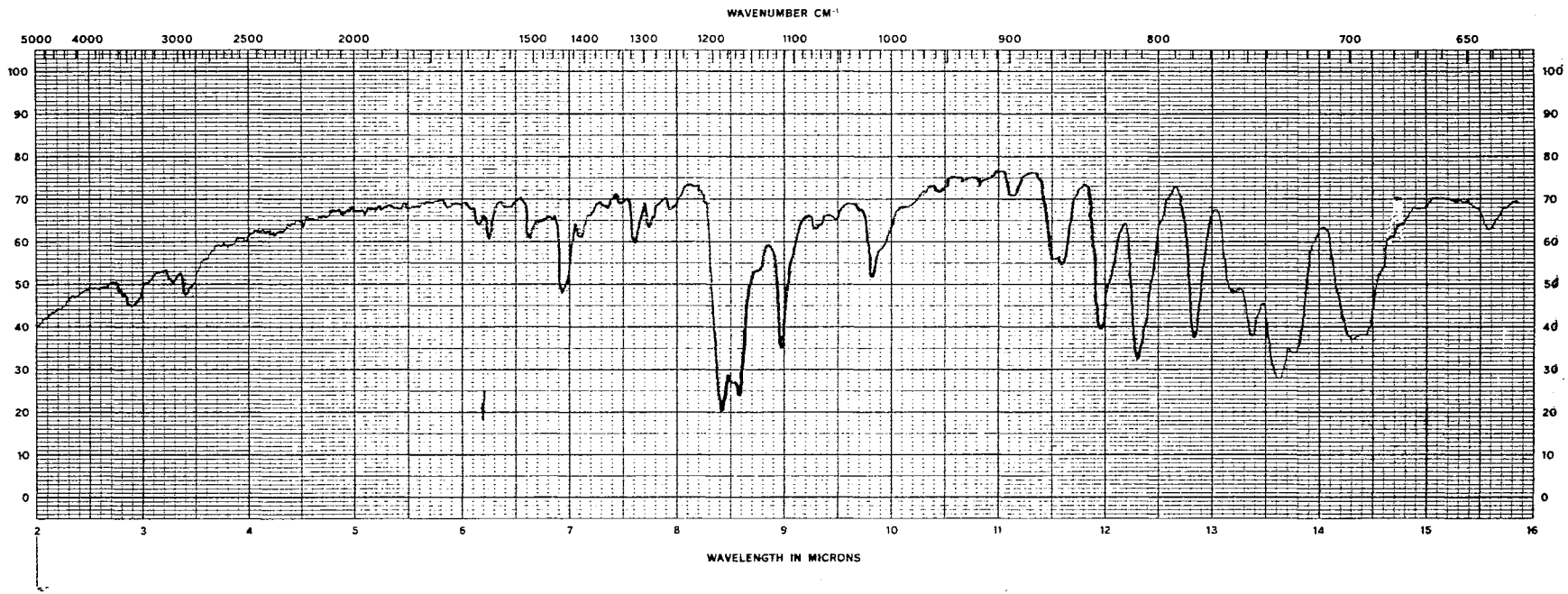
1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Picrate (119c), KBr Pellet

Plate VIII



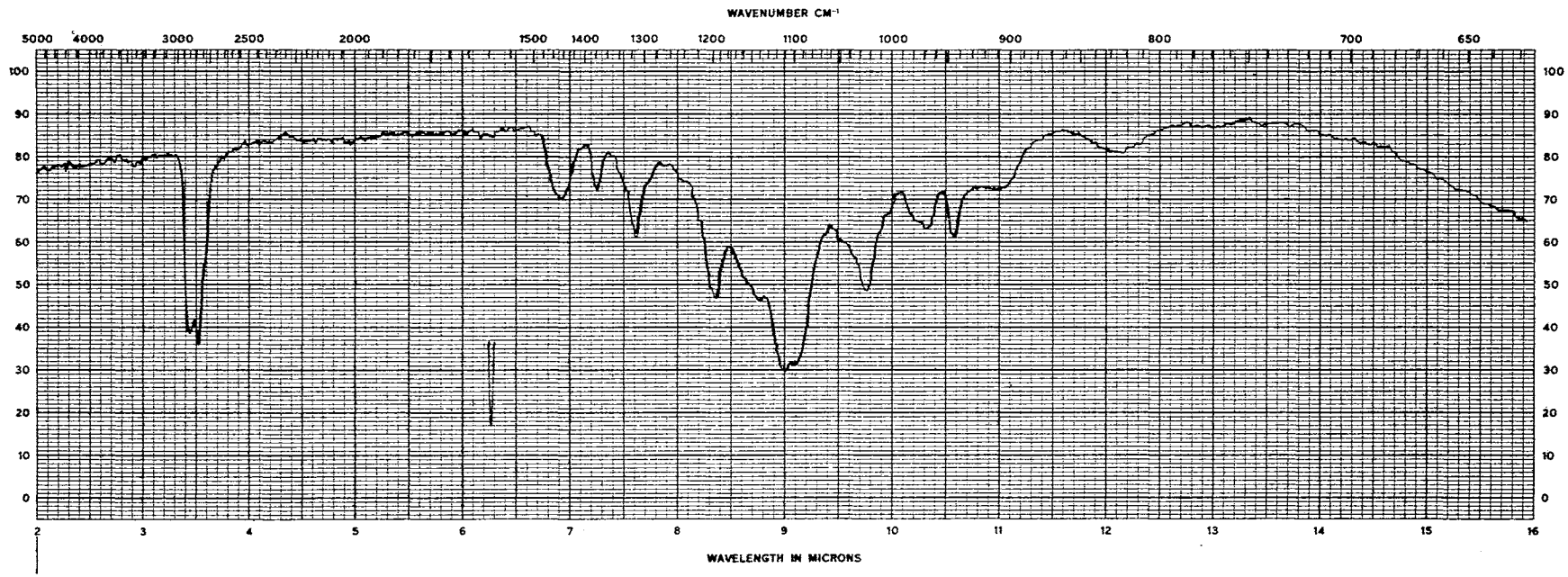
1,2,3,4-Tetrahydro-1-phenylbenzo[h]phosphinoline (133), KBr Pellet

Plate IX



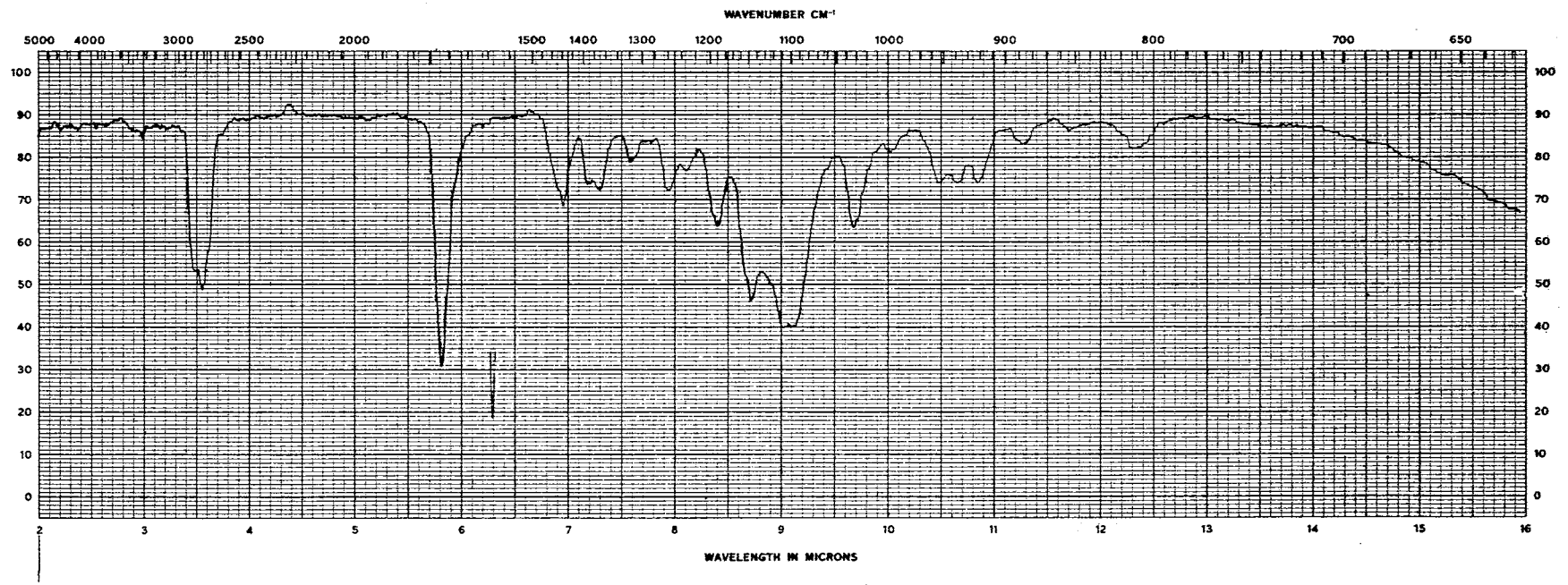
1,2,3,4-Tetrahydro-1-phenylbenzo[h]phosphinoline 1-Oxide (134), KBr Pellet

Plate X



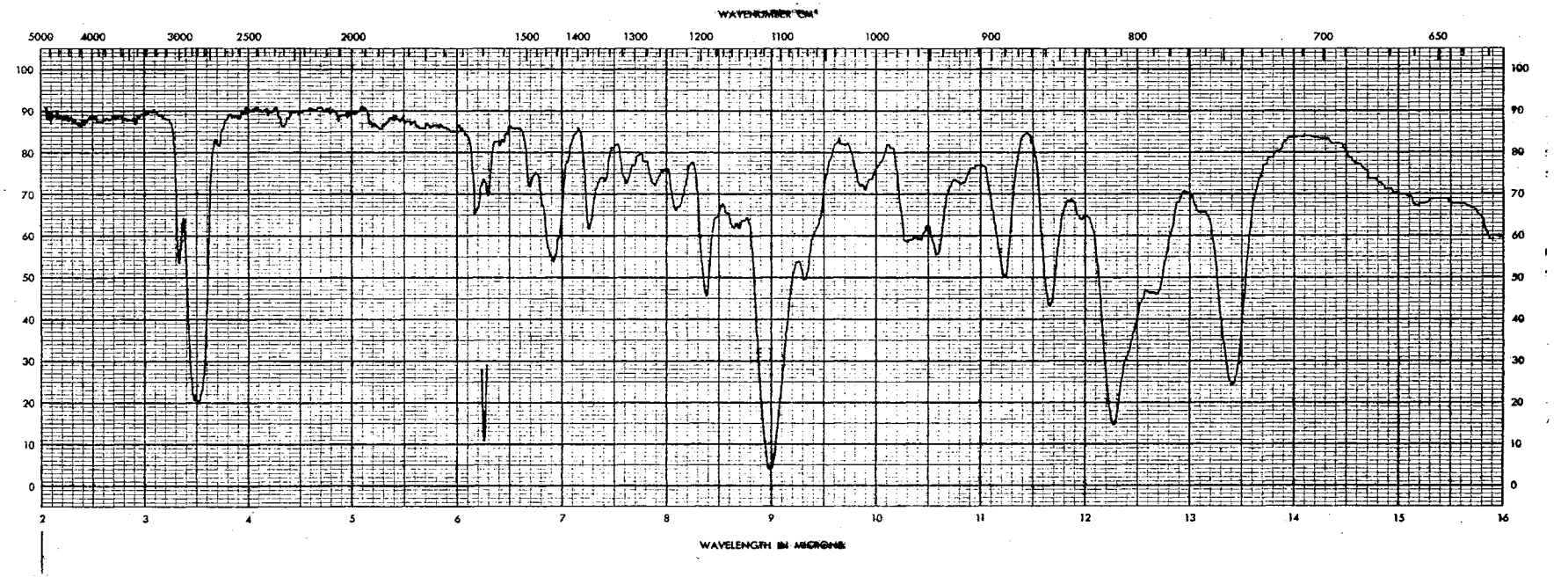
2-(Methoxymethyl)cyclopentanone Cyclic Ethylene Ketal (138), Film on NaCl Plates

Plate XI



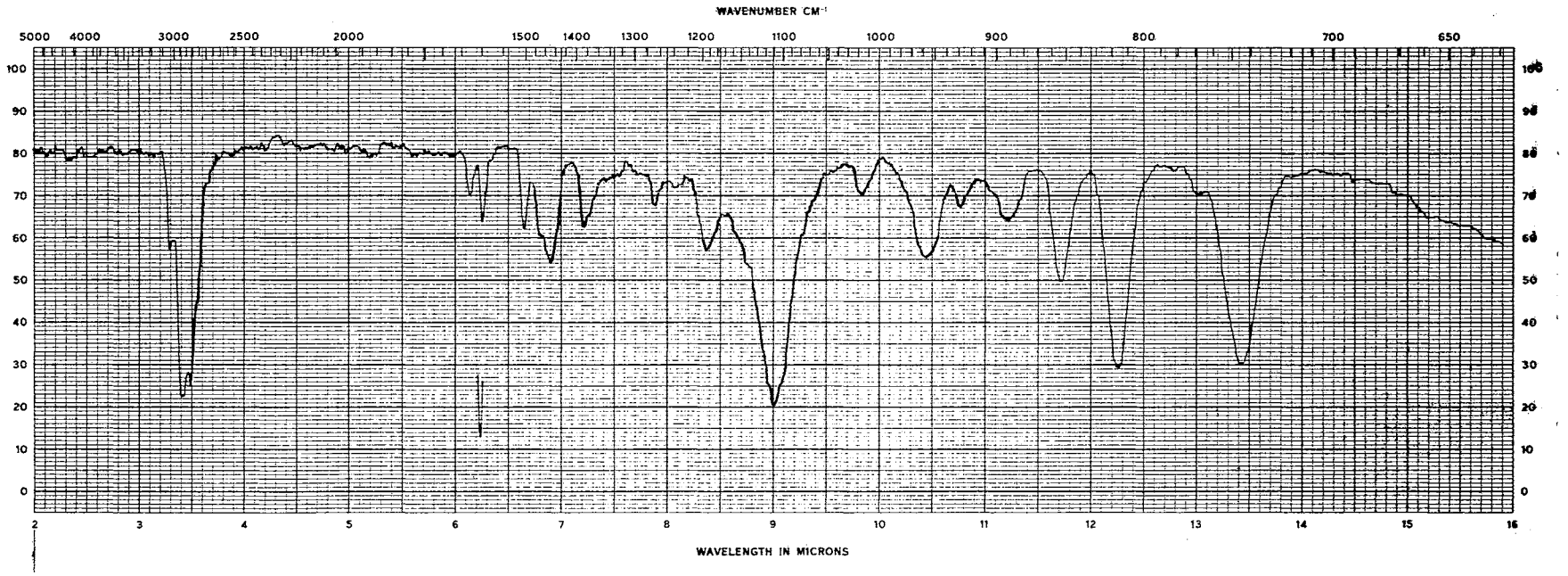
2-(Methoxymethyl)cyclopentanone (139), Film on NaCl Plates

Plate XII



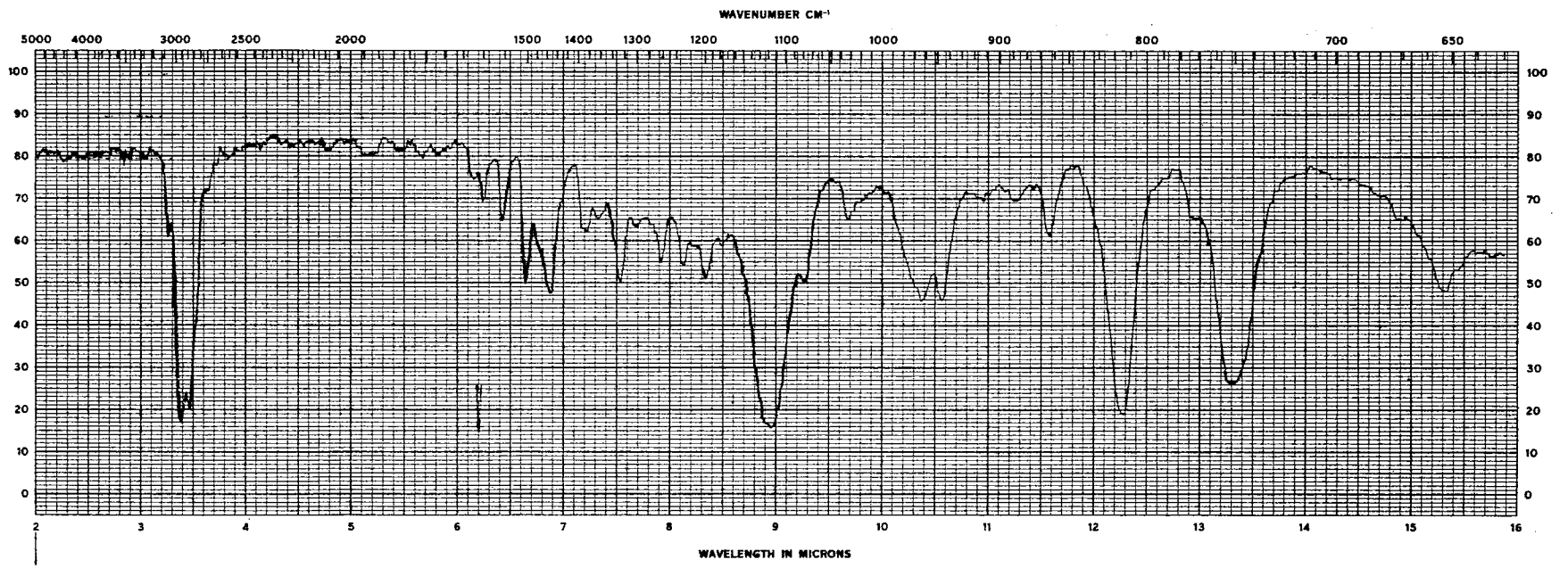
2-[5-(Methoxymethyl)-1-cyclopenten-1-yl]naphthalene (142), Film on NaCl Plates

Plate XIII



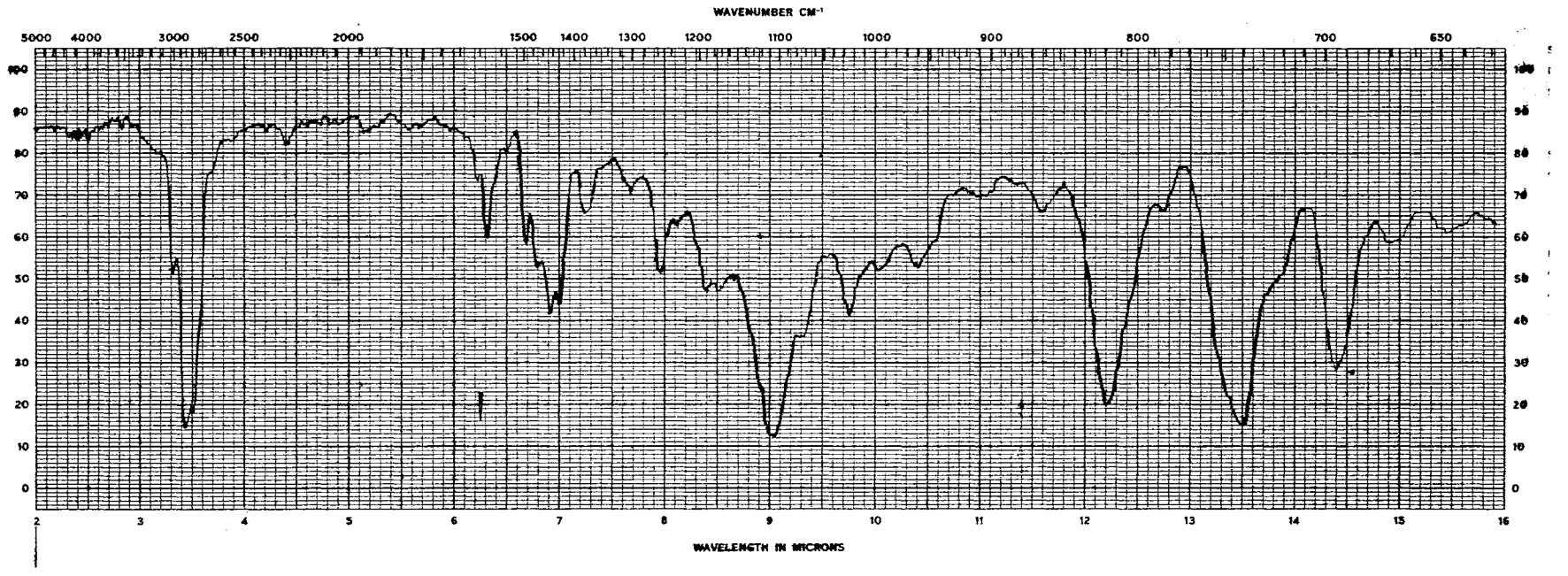
2-[2-(Methoxymethyl)cyclopentyl]naphthalene (143), Film on NaCl Plates

Plate XIV



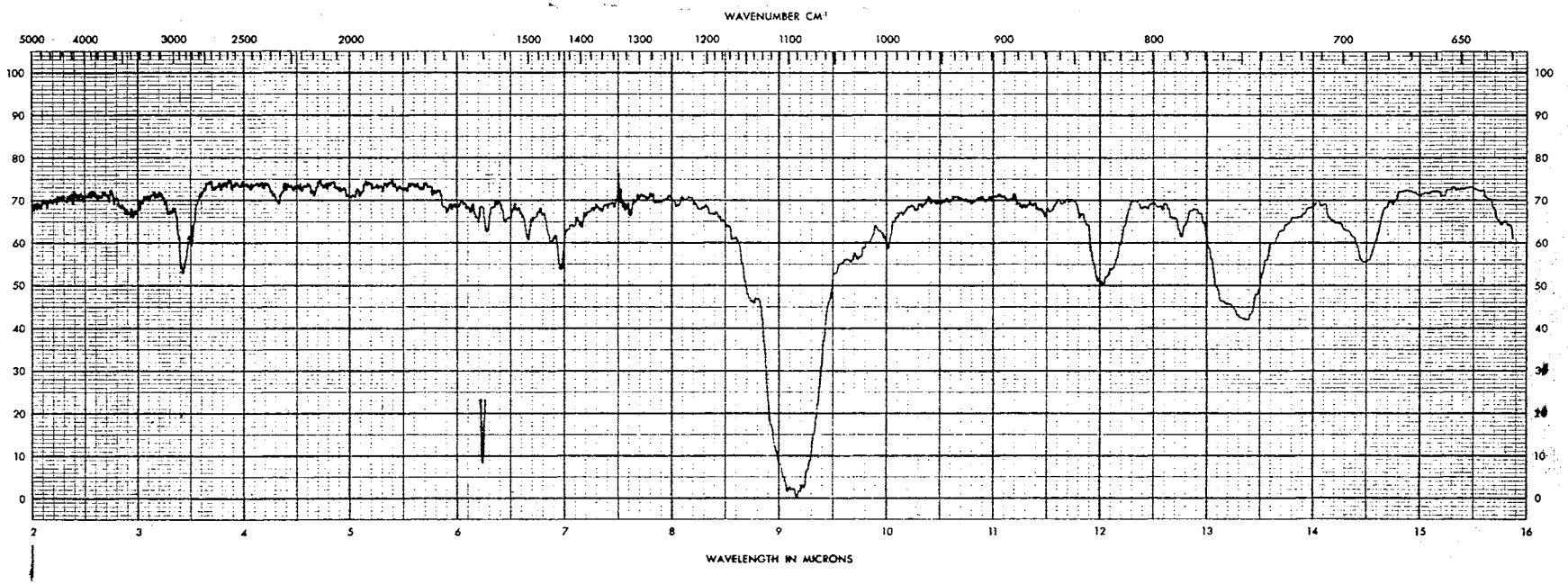
1-Bromo-2-[2-(methoxymethyl)cyclopentyl]naphthalene (144), Film on NaCl Plates

Plate XV



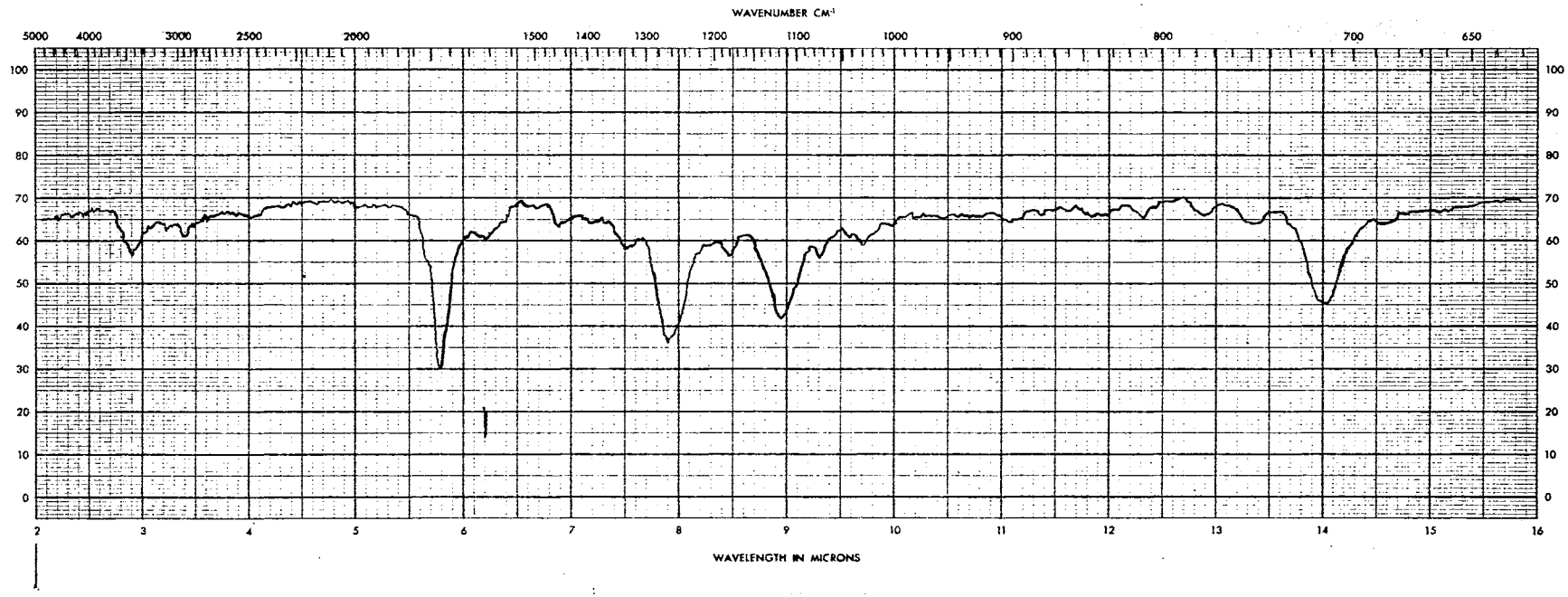
Crude Ethyl[2-[2-(methoxymethyl)cyclopentyl]-1-naphthyl]phenylphosphine (145), Film on NaCl Plates

Plate XVI



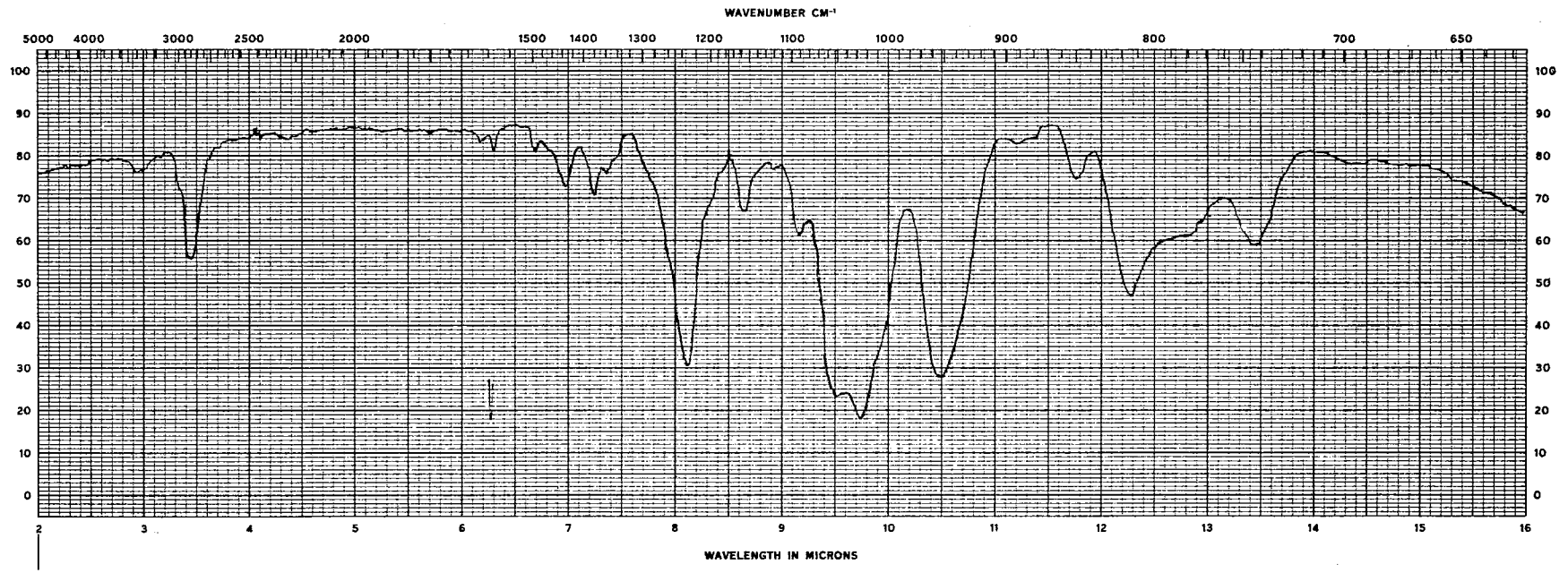
5-Ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo[h]cyclopenta[c]-phosphinolinium Perchlorate (120b), KBr Pellet

Plate XVII



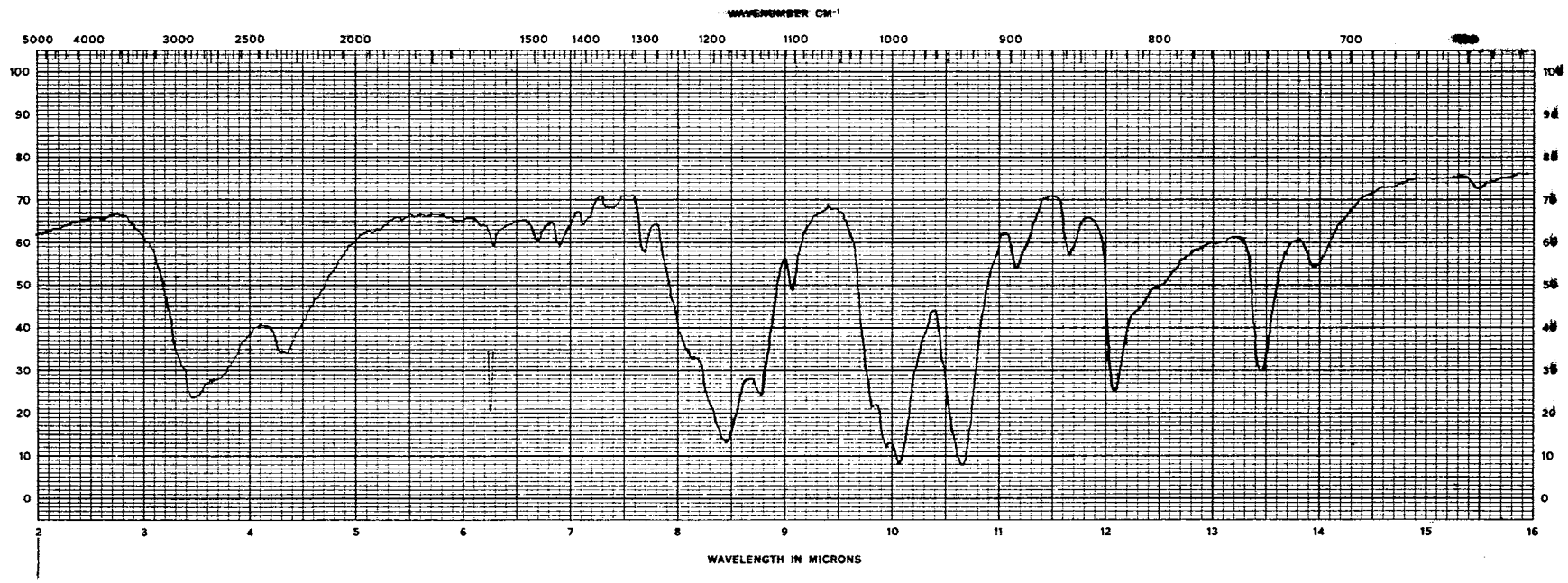
(+)-1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Hydrogen L(+)-Dibenzoyl-tartrate - L(+)-Dibenzoyltartaric Acid (155), KBr Pellet

Plate XVIII



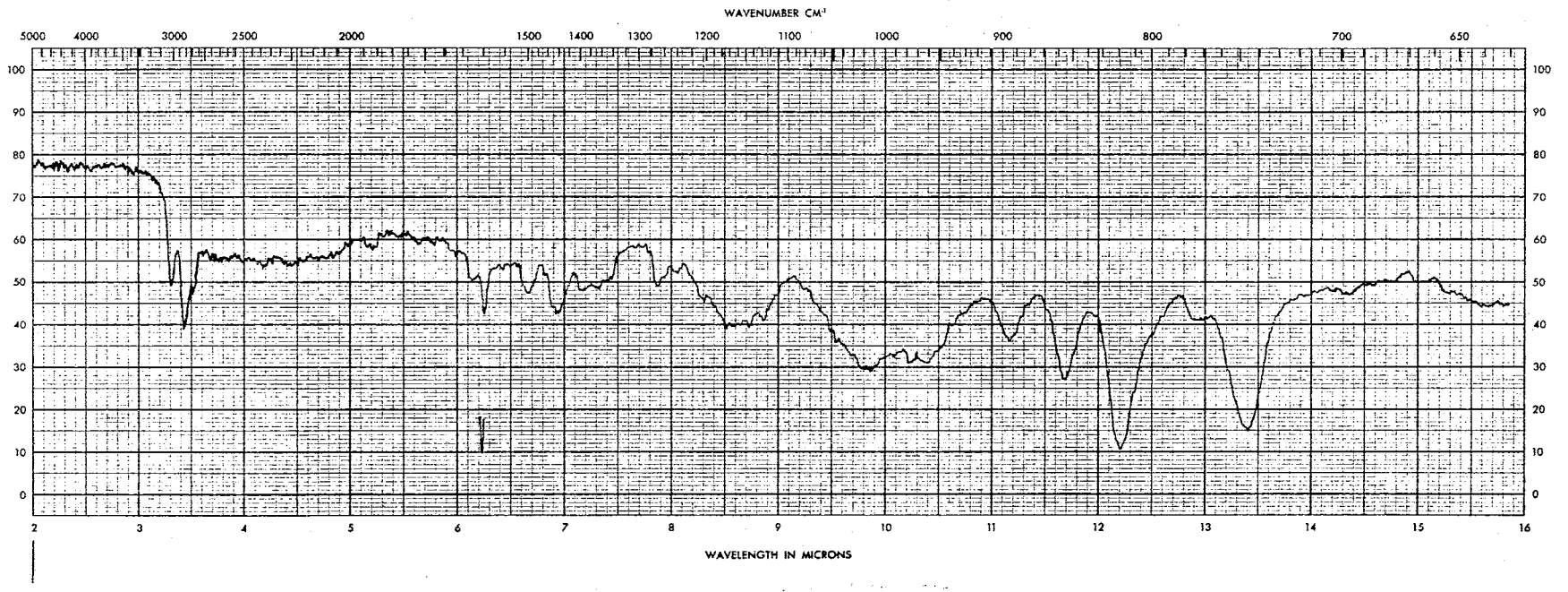
Diethyl [3-(2-naphthyl)propyl]phosphonate (166), Film on NaCl Plates

Plate XIX



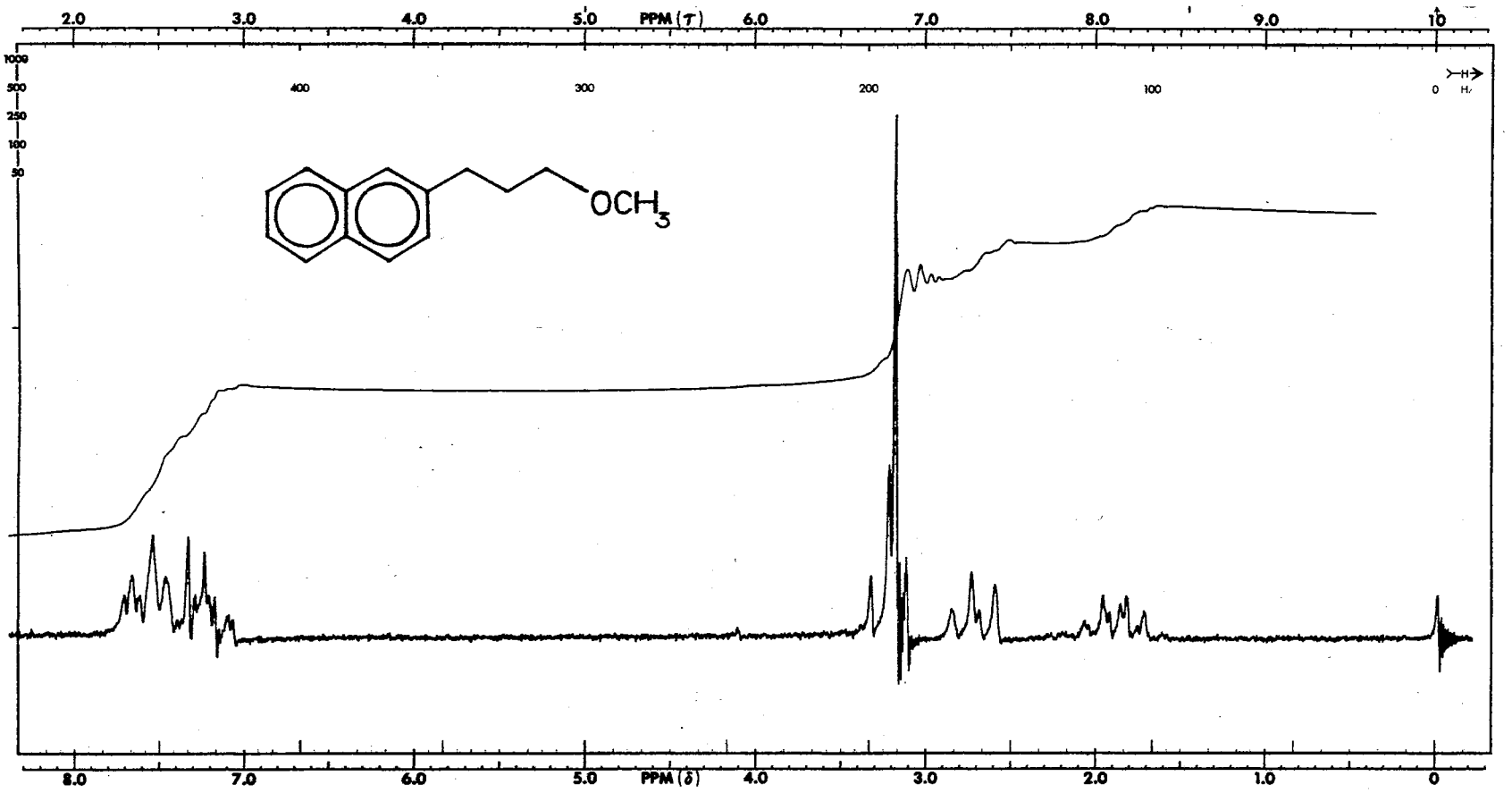
[3-(2-Naphthyl)propyl]phosphonic Acid (167), KBr Pellet

Plate XX



[3-(2-Naphthyl)propyl]phosphonous Dichloride (169), Film on NaCl Plates

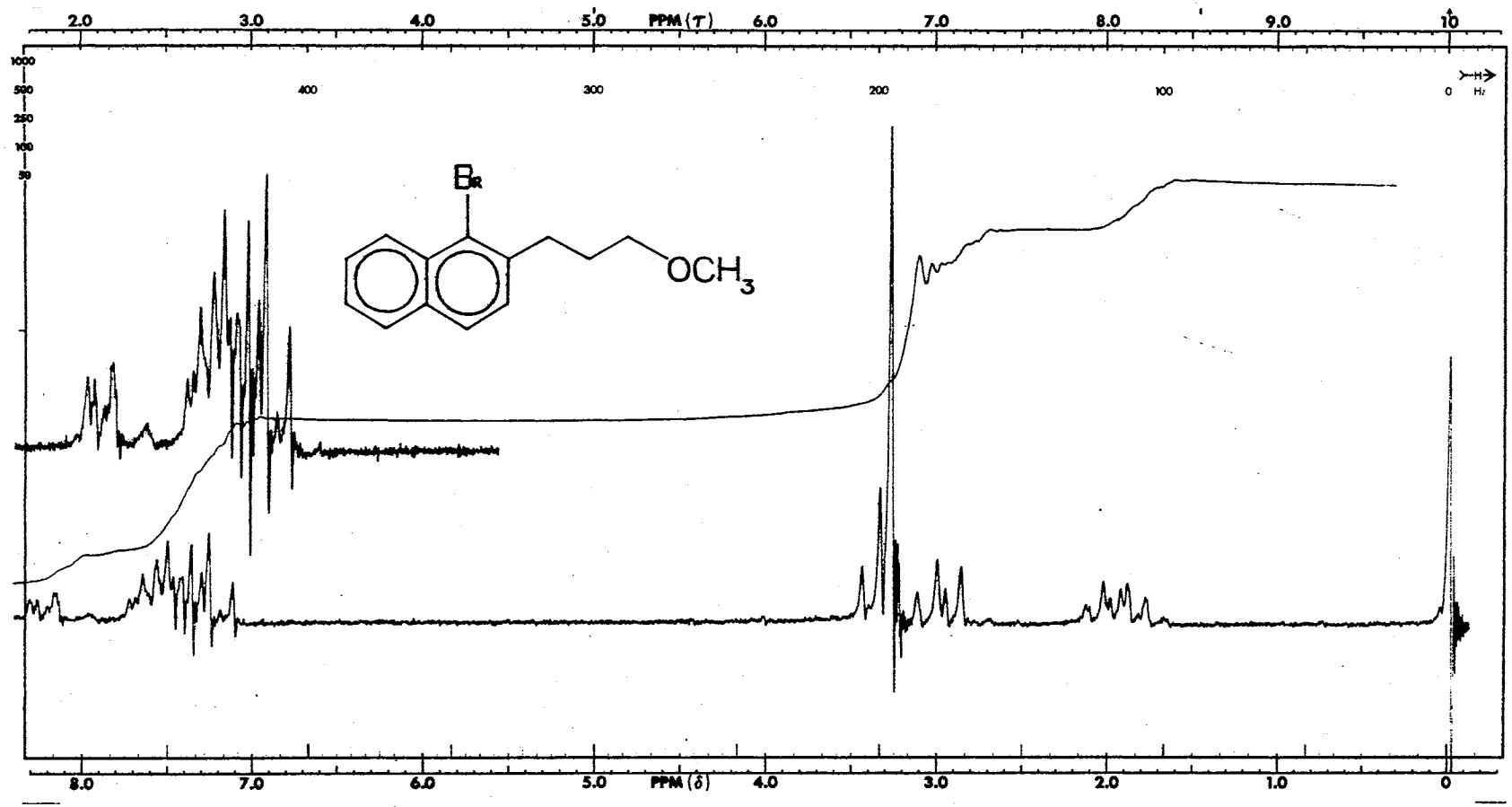
Plate XXI



2-(3-Methoxypropyl)naphthalene (127)

Solvent. . . . . $DCCl_3$	R.F. . . . . 0.01 mG	S.W. . . . . 500 Hz	S.A. 1.0
F.B. . . . . 4.0 Hz	S.T. . . . . 250 sec	S.O. . . . . 0.0 Hz	I.A. 40

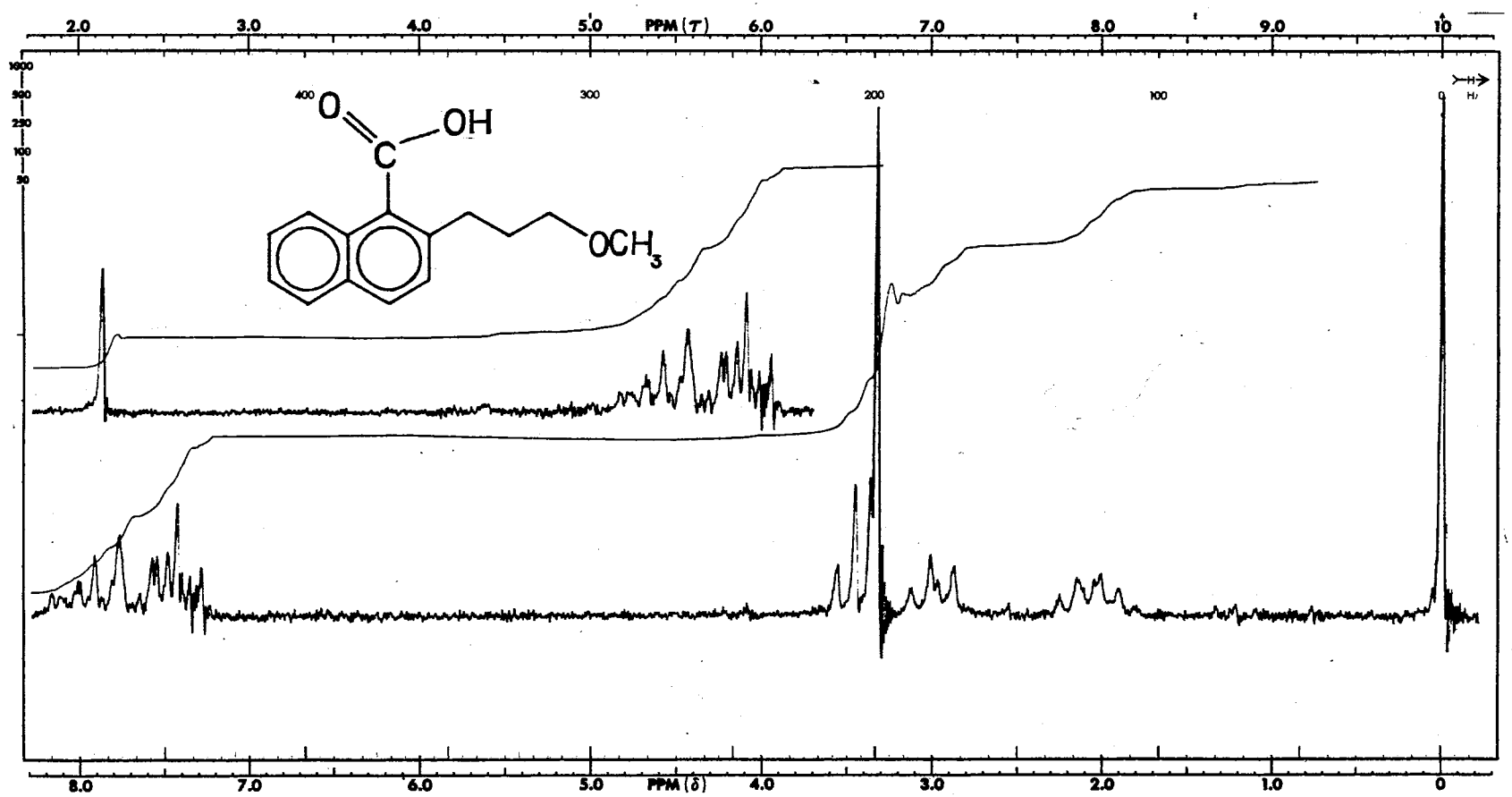
Plate XXII



1-Bromo-2-(3-methoxypropyl)naphthalene (128)

Solvent.	$DCCl_3$	R.F.	0.02 mG	S.W.	500 Hz	S.A.	1.6,5
F.B.	4.0 Hz	S.T.	250 sec	S.O.	0,20 Hz	I.A.	63

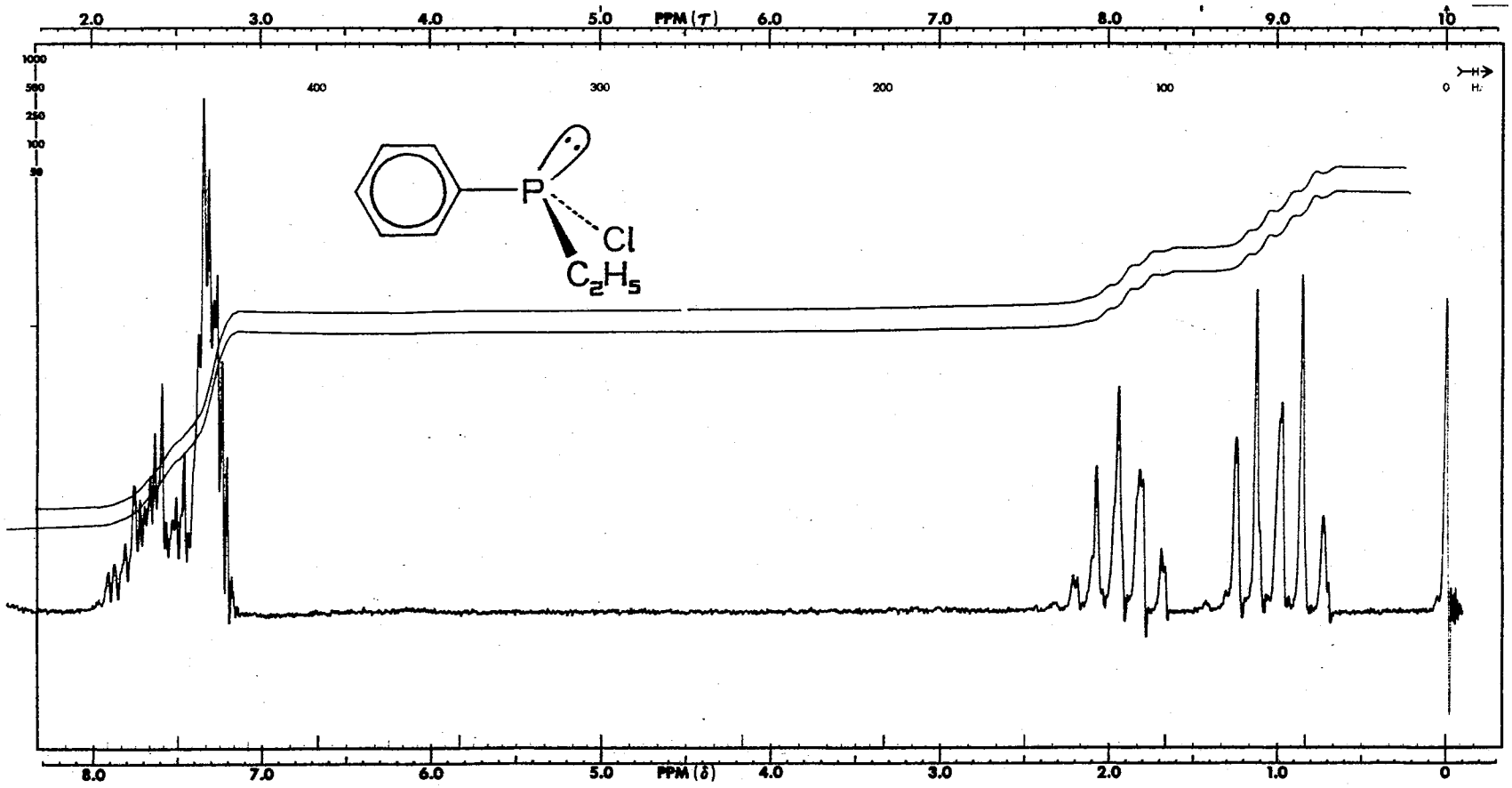
Plate XXIII



2-(3-Methoxypropyl)-1-naphthoic Acid (129)

Solvent.	$DCCl_3$	R.F.	0.03 mG	S.W.	500 Hz	S.A.	2.5
F.B.	4.0 Hz	S.T.	250 sec	S.O. . . .	0.0,200 Hz	I.A.	63

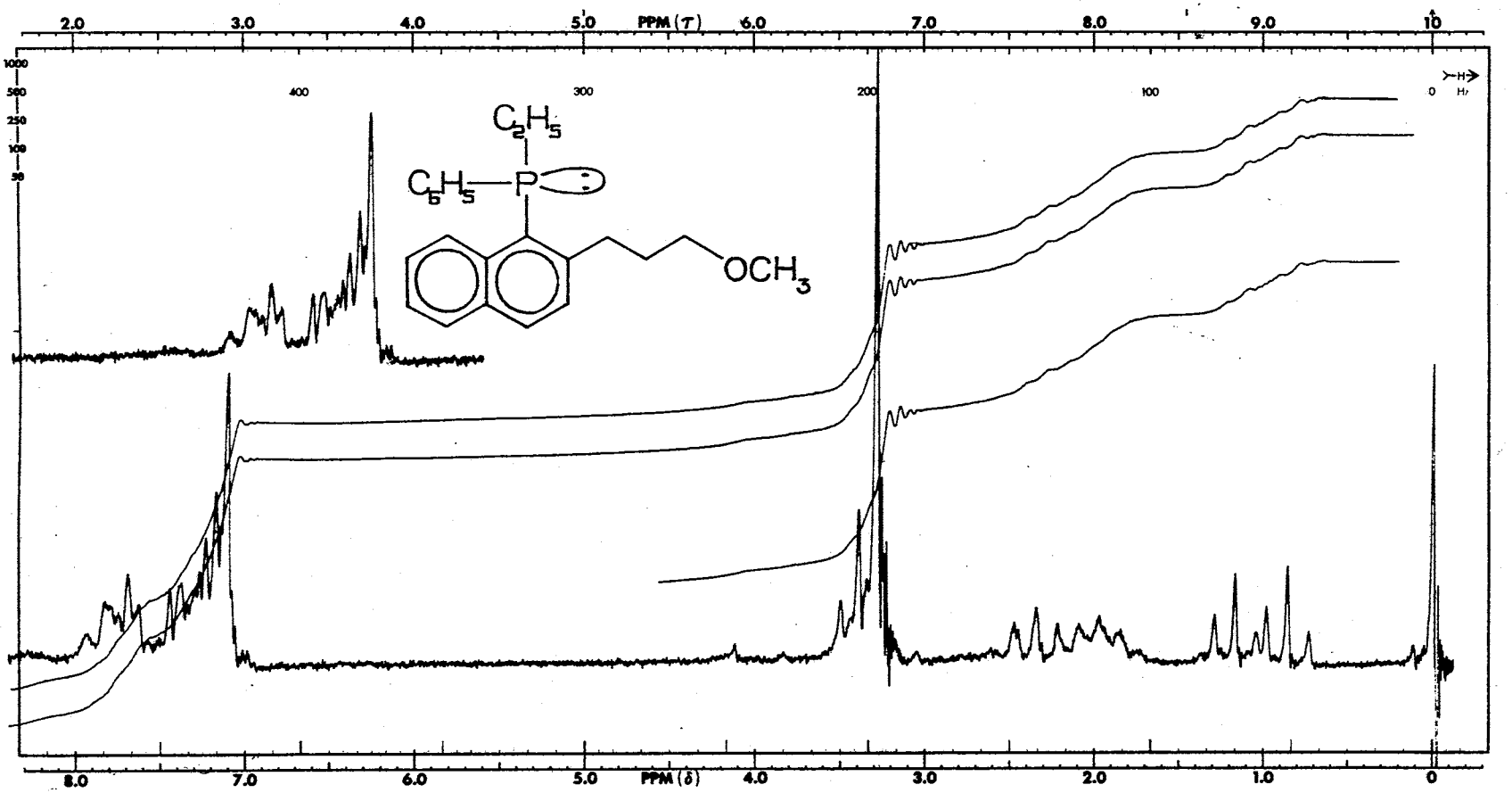
Plate XXIV



Ethylphenylphosphinous Chloride (131)

Solvent. . . . . $DCCl_3$	R.F. . . . . 0.015 mG	S.W. . . . . 500 Hz	S.A. 2
F.B. . . . . 4.0 Hz	S.T. . . . . 250 sec	S.O. . . . . 0.0 Hz	I.A. 20

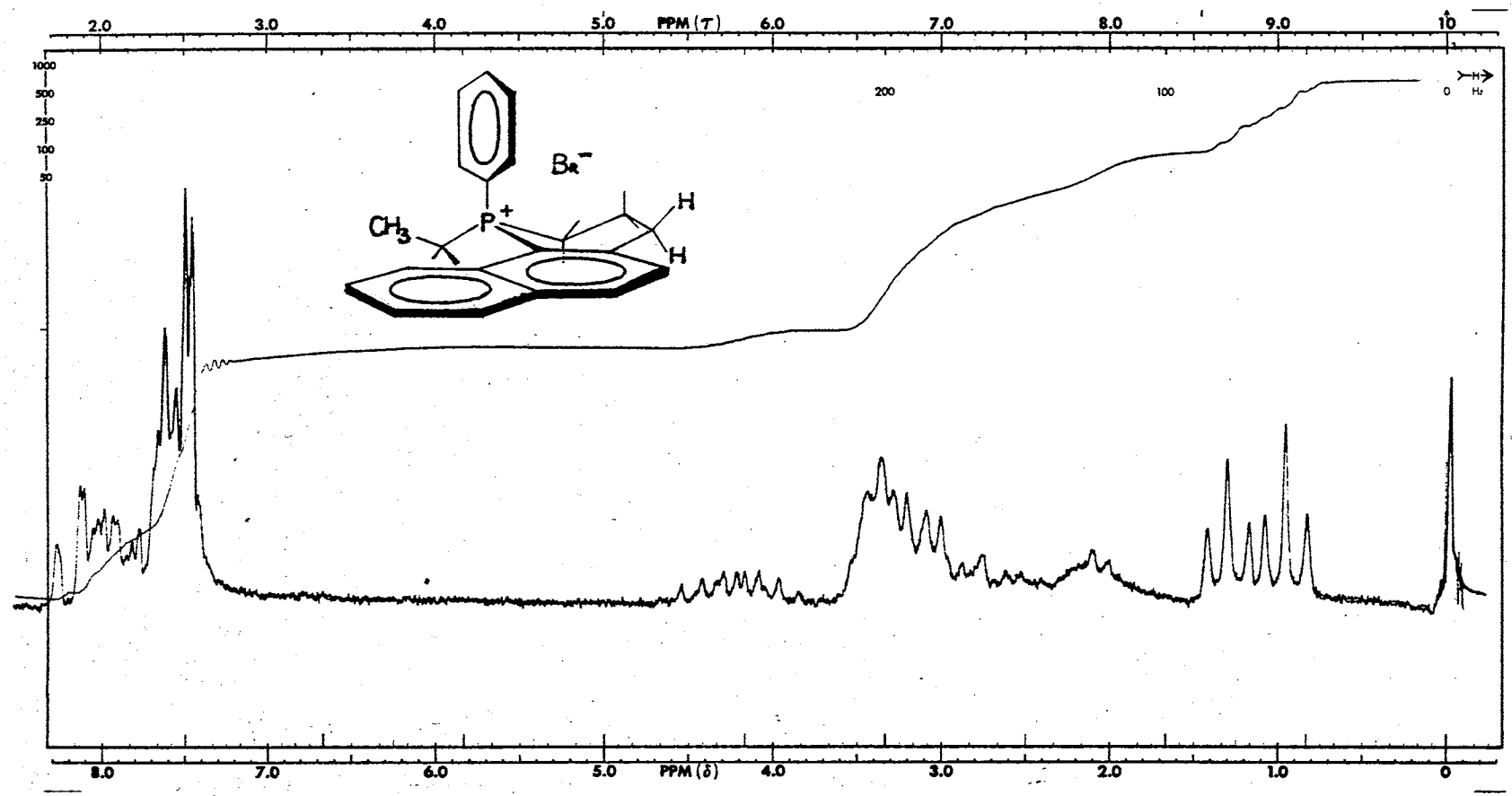
Plate XXV



Crude Ethyl[2-(3-methoxypropyl)-1-naphthyl]phenylphosphine (132)

Solvent.	$DCCl_3$	R.F.	0.05 mG	S.W.	500 Hz	S.A.	5.0
F.B.	4.0 Hz	S.T.	250 sec	S.O.	0.0 Hz	I.A.	50

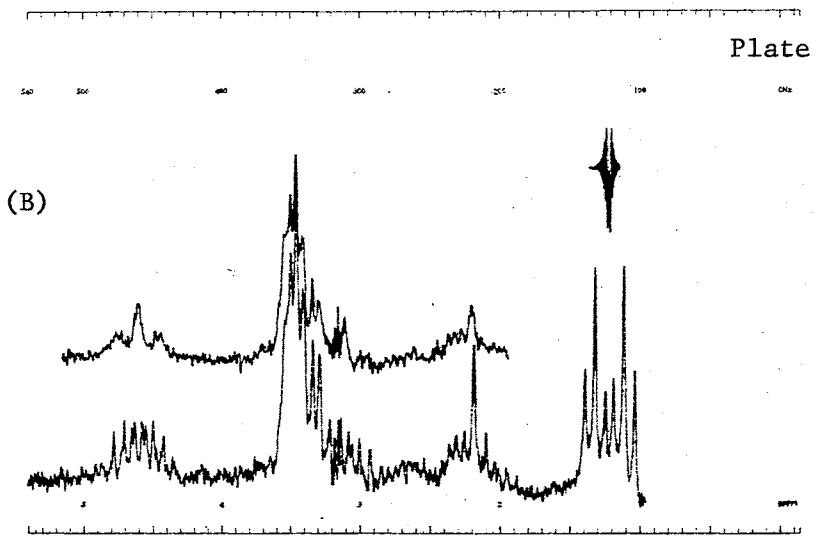
Plate XXVI

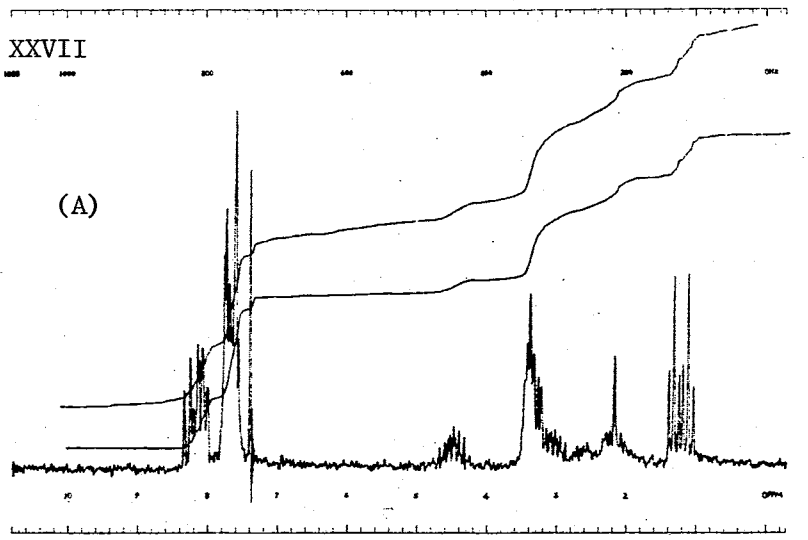


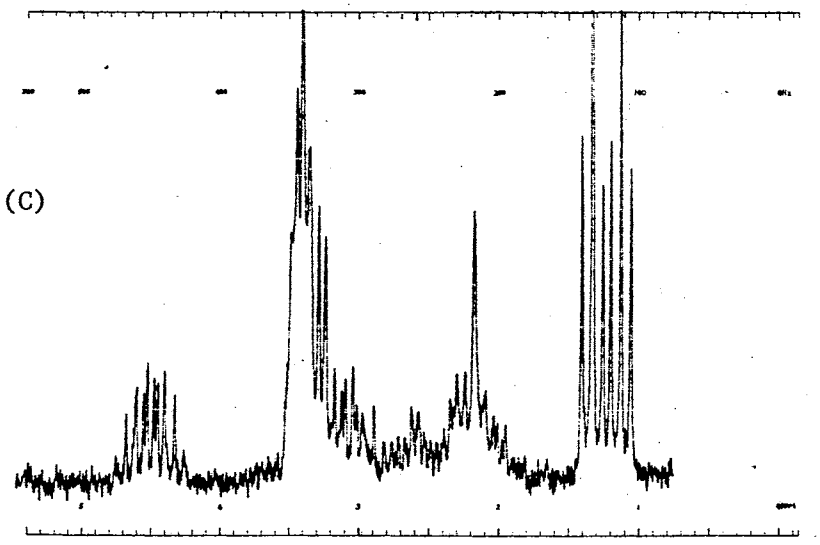
1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Bromide (119a)

Solvent.	$DCCl_3$	R.F.	0.1 mG	S.W.	500 Hz	S.A.	16
F.B.	2.0 Hz	S.T.	250 sec	S.O.	0.0 Hz	I.A.	40

Plate XXVII







1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Bromide (119a) -- 100 MHz

Solvent. . . . $DCCl_3$ Lock. . . . . Ext. TMS

S.W. (Hz). . . . (A) -- 1080; (B) -- 540; (C) -- 540

R.F. (mG). . . . (A) -- 30; (B) -- 50; (C) -- 30

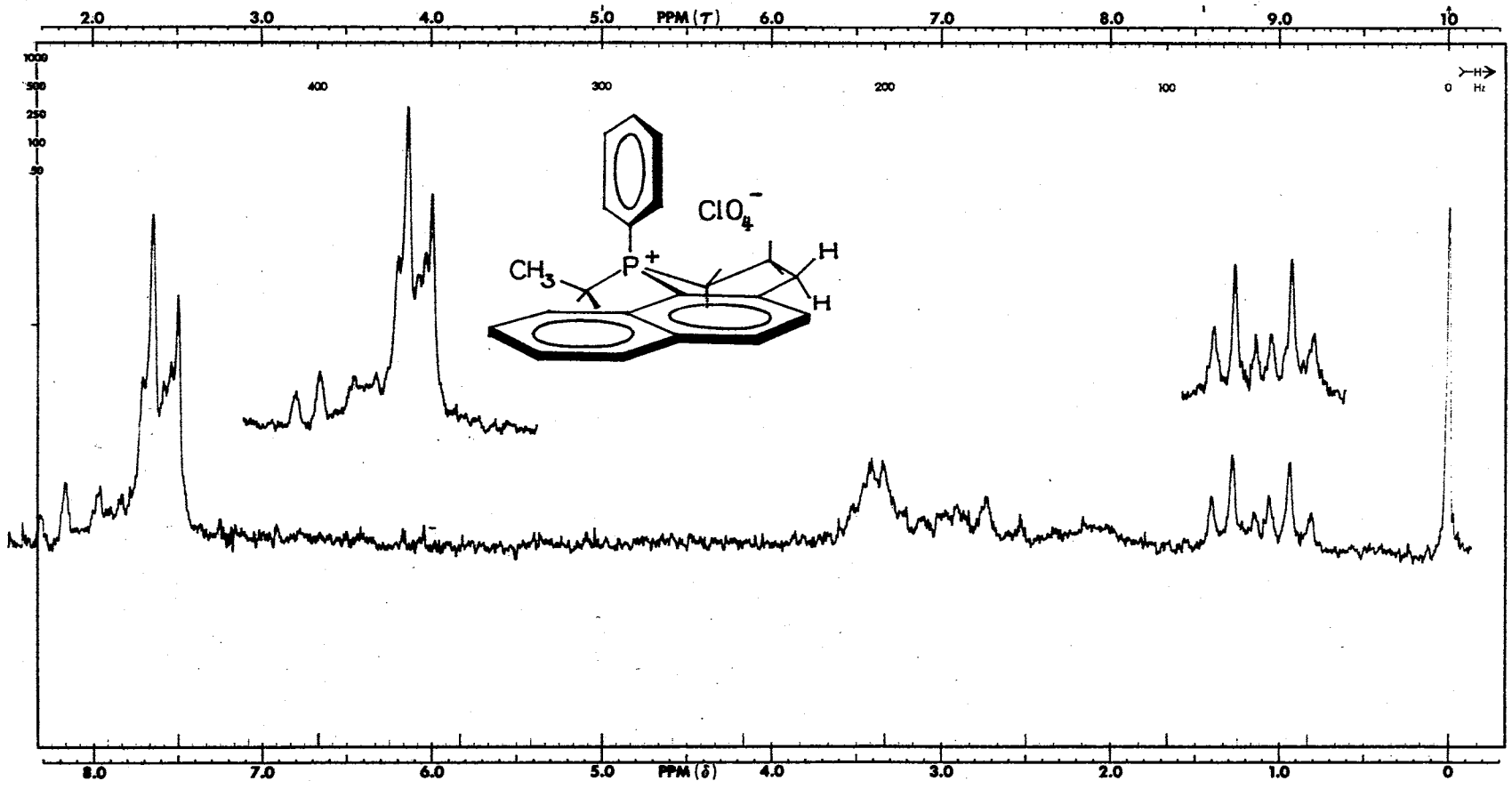
S.A. . . . . (A) -- 20; (B) -- 40; (C) -- 150

S.T. (sec) . . . (A) -- 250; (B) -- 250; (C) -- 500

Integrator . . . (A) -- 6

(Courtesy of JEOL Co.)

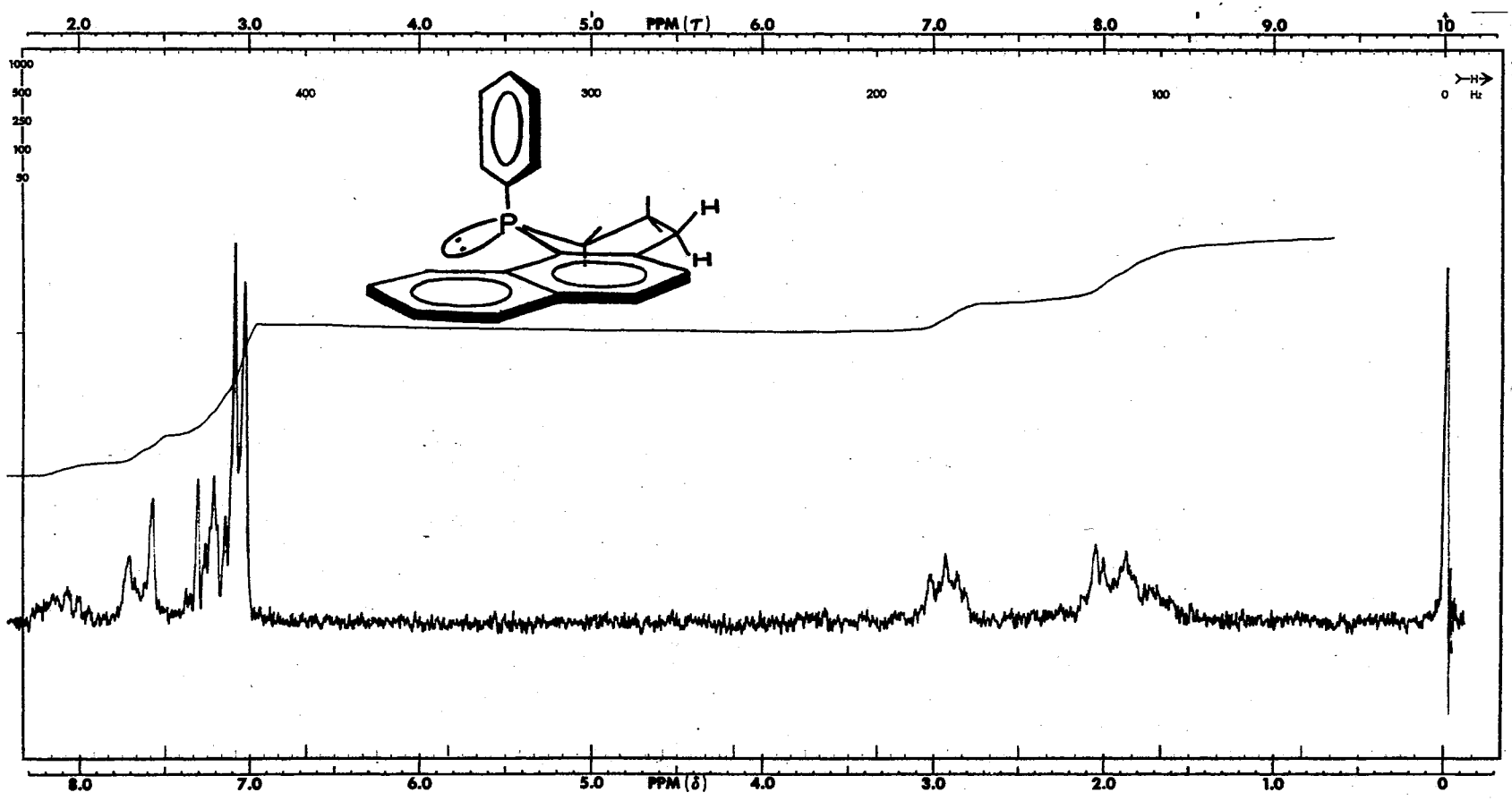
Plate XXVIII



1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Perchlorate (119b)

Solvent. . . . . $DCCl_3$	R.F. . . . . 0.05 mG	S.W. . . . . 500 Hz	S.A. 25,32
F.B. . . . . 1.0 Hz	S.T. . . . . 250 sec	S.O. . . . . 0.0 Hz	I.A. . . . . off

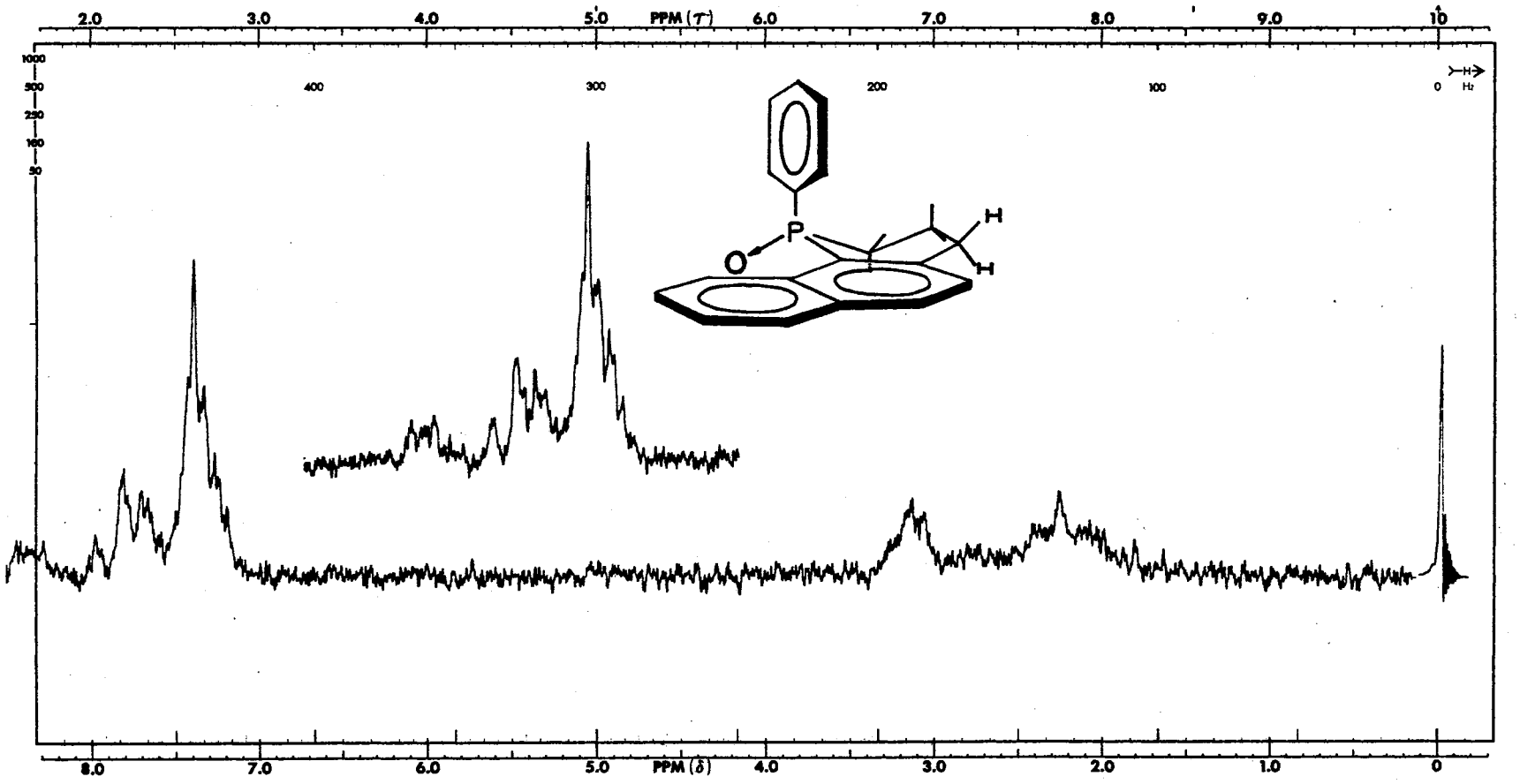
Plate XXIX



1,2,3,4-Tetrahydro-1-phenylbenzo[h]phosphinoline (133)

Solvent.	$DCCl_3$	R.F.	0.05 mG	S.W.	500 Hz	S.A.	20
F.B.	2.0 Hz	S.T.	250 sec	S.O.	0.0 Hz	I.A.	50

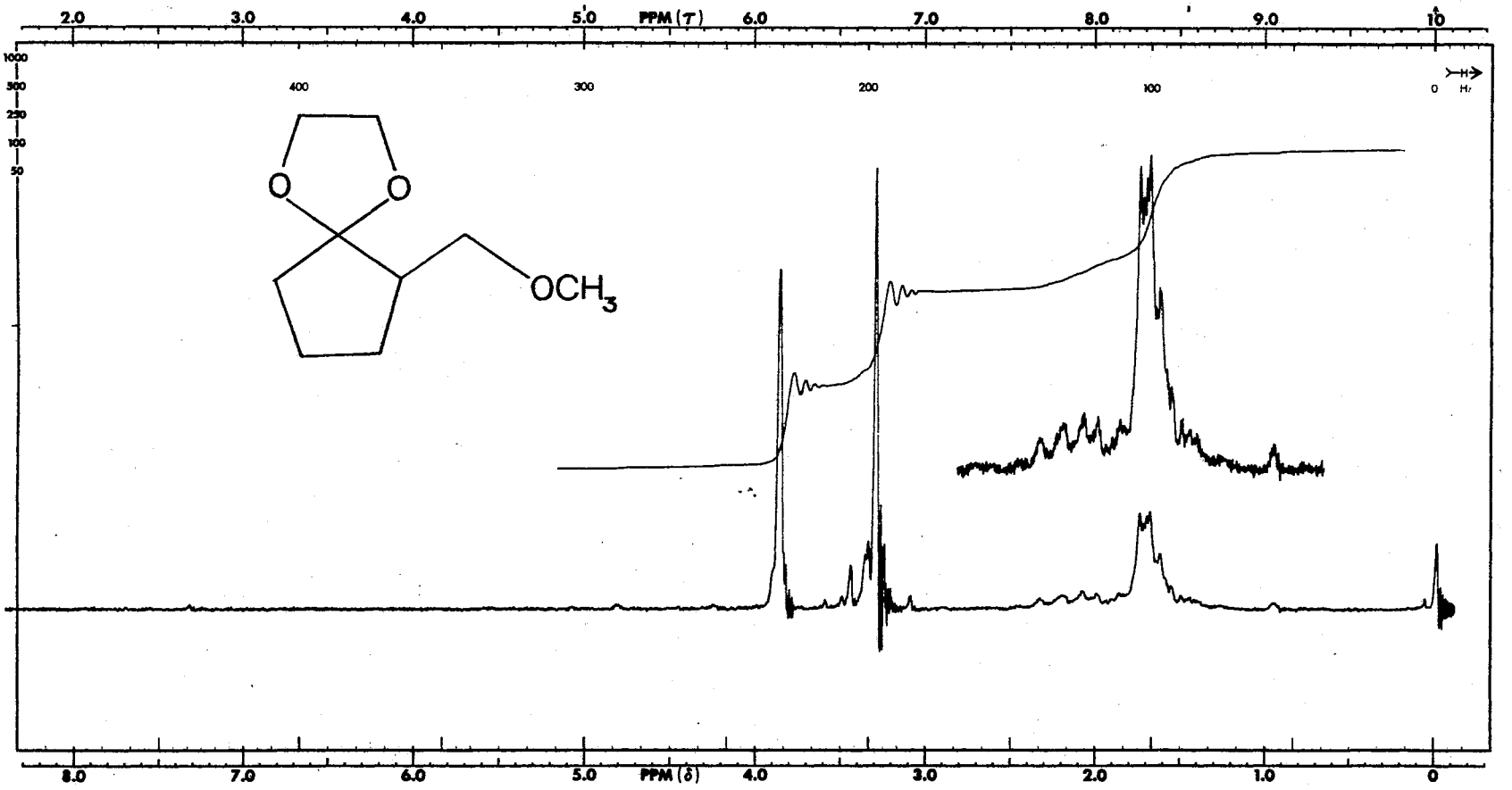
Plate XXX



1,2,3,4-Tetrahydro-1-phenylbenzo[h]phosphinoline 1-Oxide (134)

Solvent.	$DCCl_3$	R.F.	0.05 mG	S.W.	500 Hz	S.A.	50
F.B.	1.0 Hz	S.T.	250 sec	S.O. . . .	0.0,130 Hz	I.A.	off

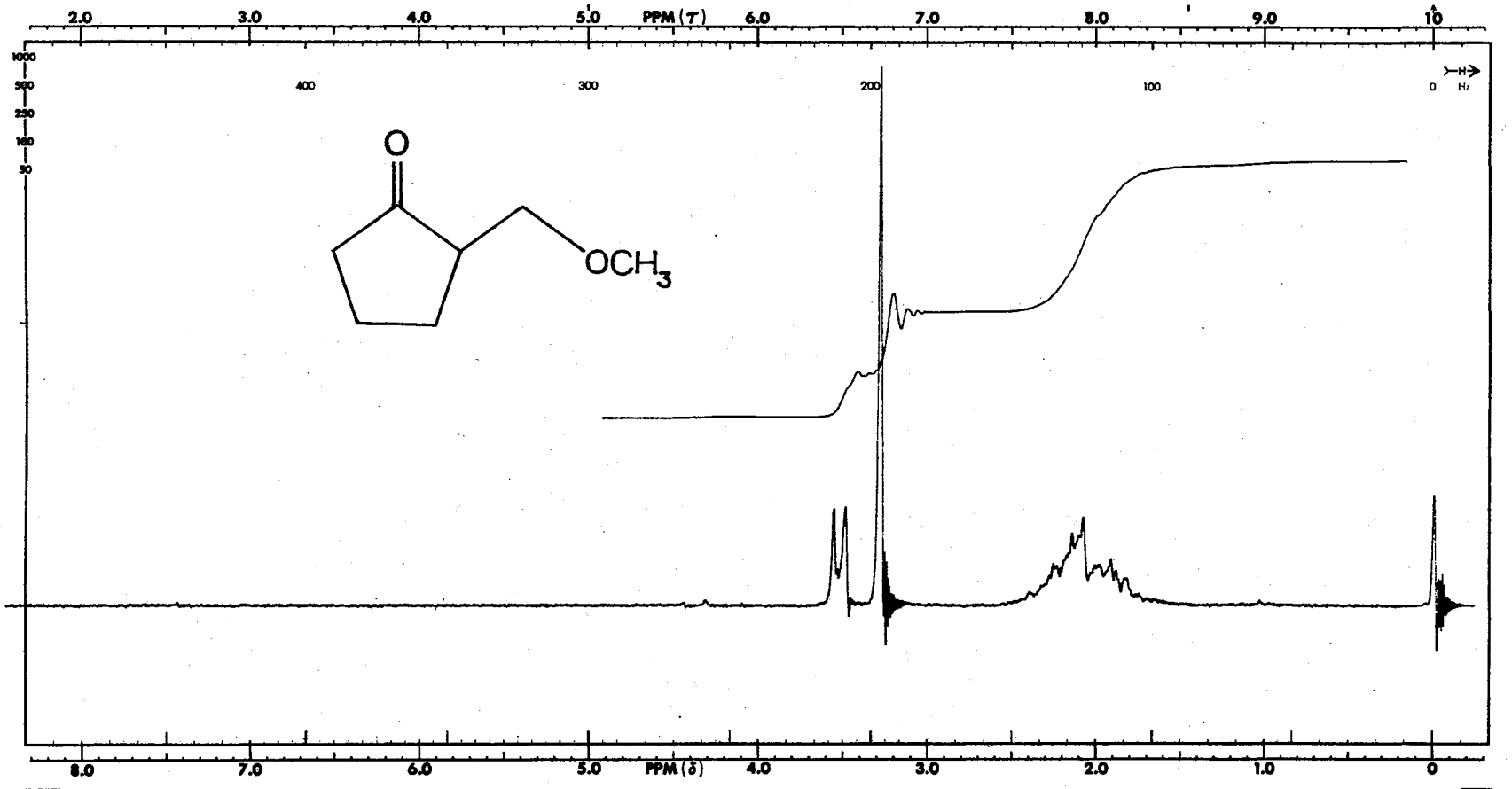
Plate XXXI



2-(Methoxymethyl)cyclopentanone Cyclic Ethylene Ketal (138)

Solvent. . . . . $DCCl_3$	R.F. . . . . 0.03 mG	S.W. . . . . 500 Hz	S.A. 1.2
F.B. . . . . 4.0 Hz	S.T. . . . . 250 sec	S.O. . . . . 0.0 Hz	I.A. 50

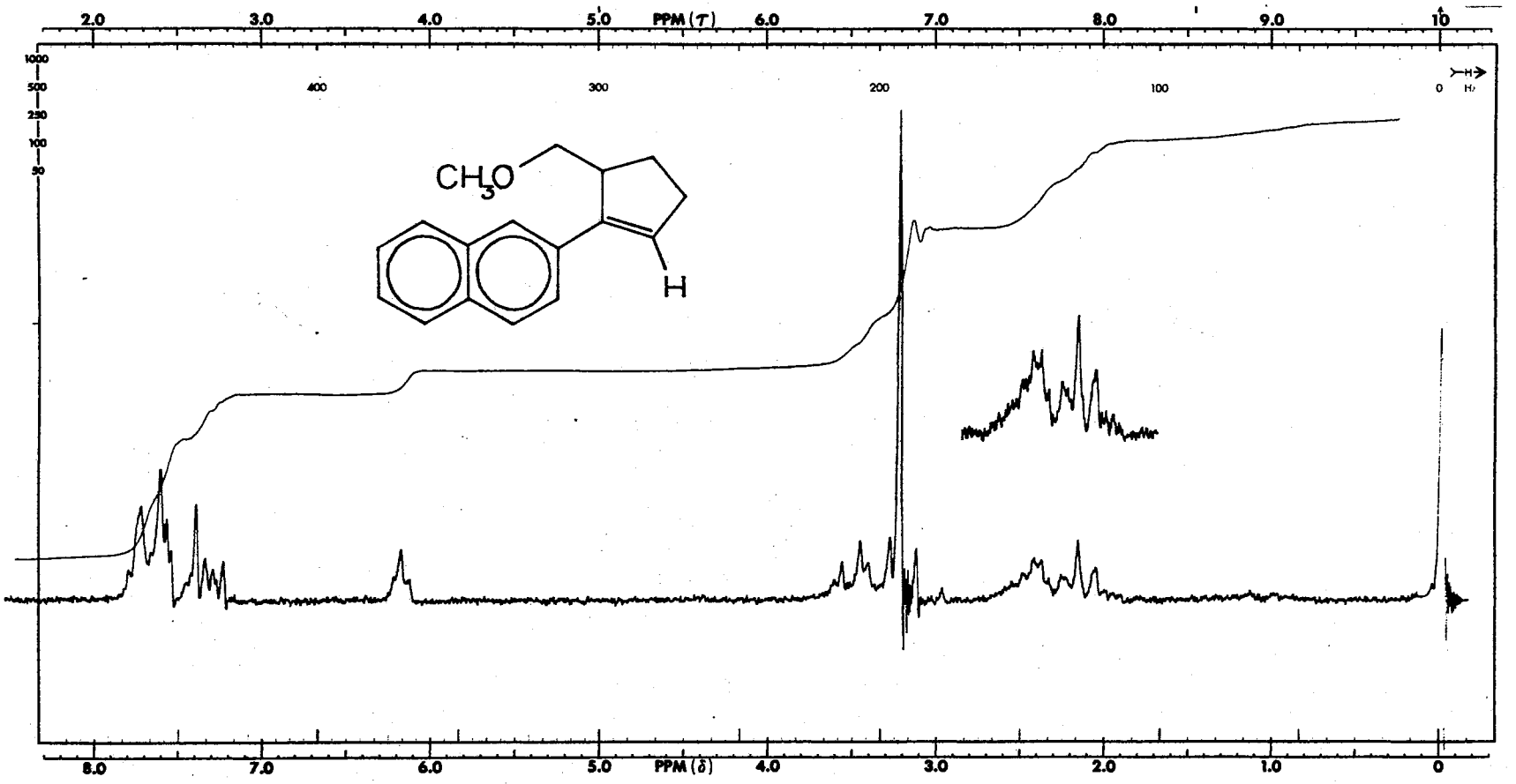
Plate XXXII



2-(Methoxymethyl)cyclopentanone (139)

Solvent. . . . . $DCCl_3$	R.F. . . . . 0.02 mG	S.W. . . . . -500 Hz	S.A. 0.8
F.B. . . . . 4.0 Hz	S.T. . . . . 250 sec	S.O. . . . . 468 Hz	I.A. 63

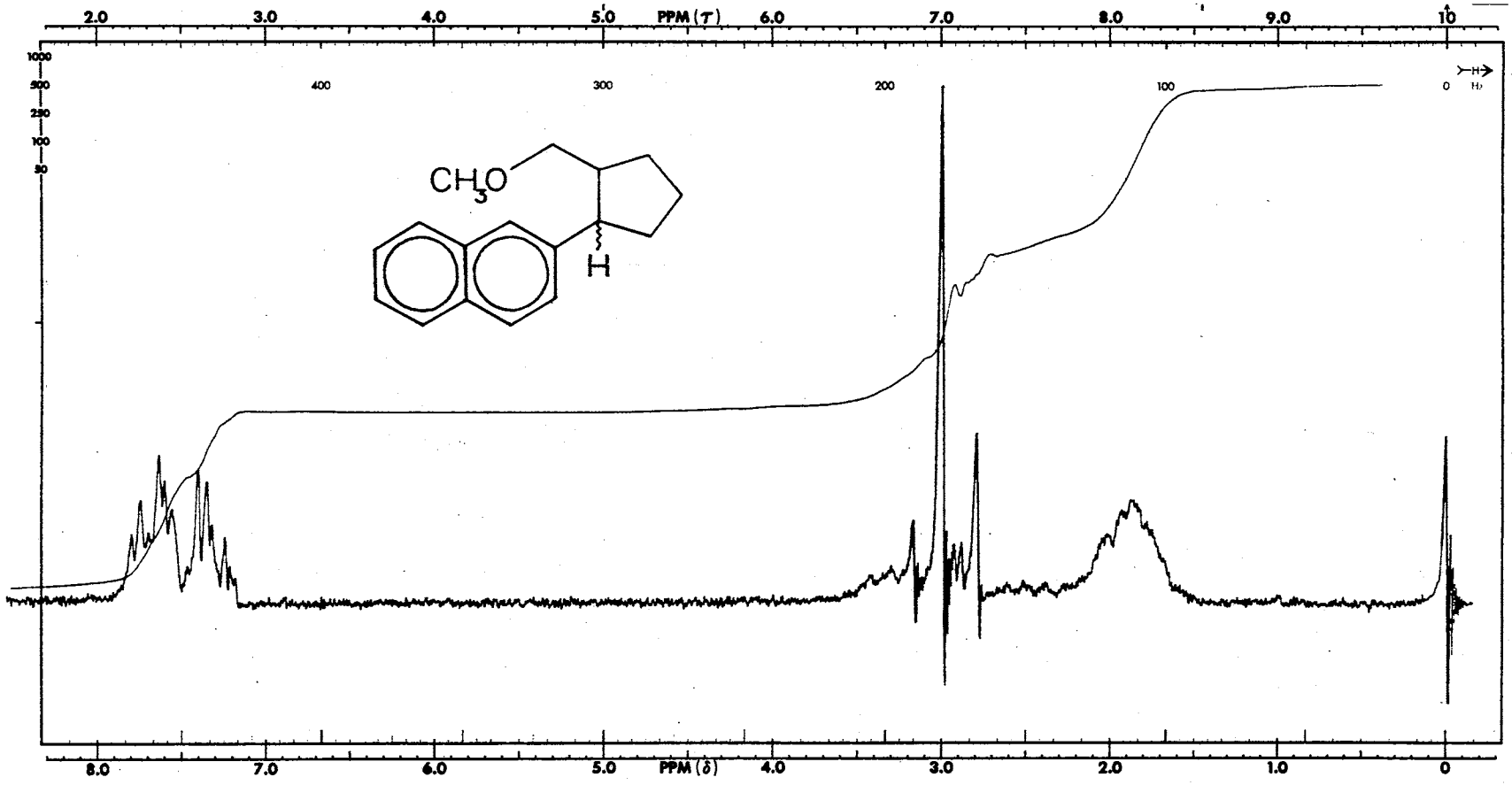
Plate XXXIII



2-[5-(Methoxymethyl)-1-cyclopenten-1-yl]naphthalene (142)

Solvent.	$DCCl_3$	R.F.	0.03 mG	S.W.	-500 Hz	S.A.	5,10
F.B.	4.0 Hz	S.T.	250 sec	S.O.	462 Hz	I.A.	63

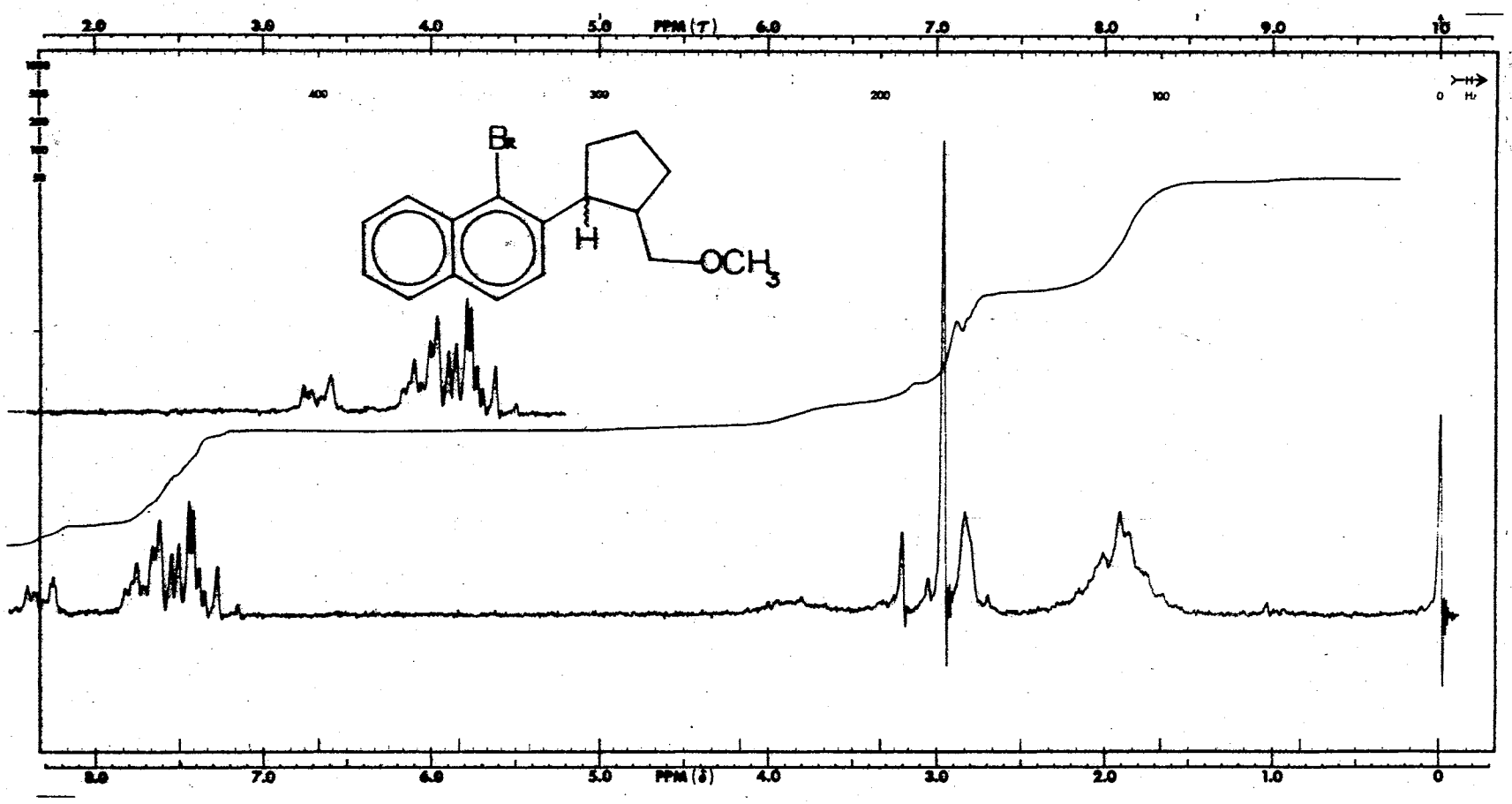
Plate XXXIV



2-[2-(Methoxymethyl)cyclopentyl]naphthalene (143)

Solvent.	$DCCl_3$	R.F.	0.03 mG	S.W.	-500 Hz	S.A.	6.3
F.B.	4.0 Hz	S.T.	250 sec	S.O.	416 Hz	I.A.	40

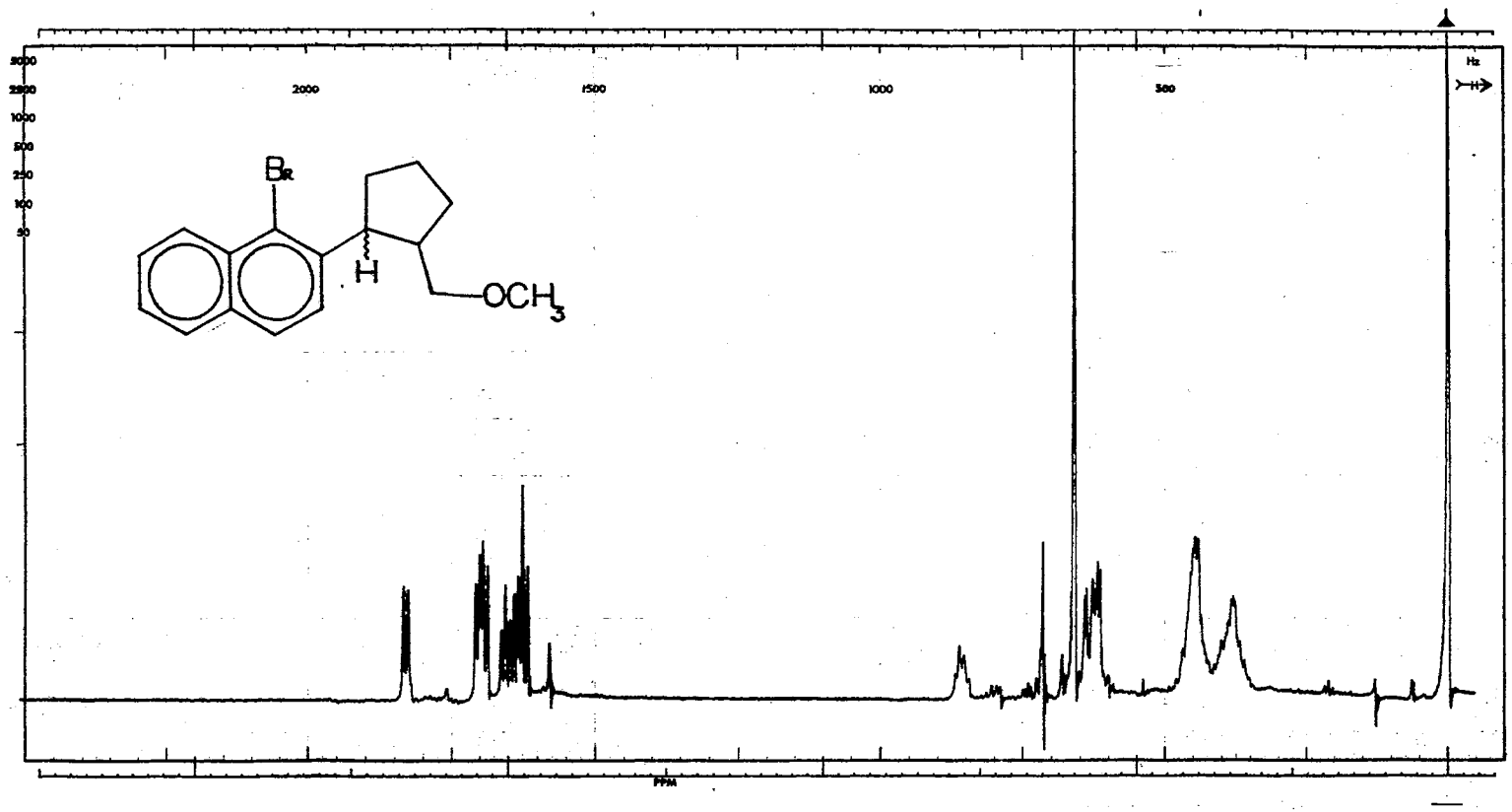
Plate XXXV



1-Bromo-2-[2-(methoxymethyl)cyclopentyl]naphthalene (144)

Solvent.	$DCCl_3$	R.F.	0.025 mG	S.W.	500 Hz	S.A.	3.2
F.B.	4.0 Hz	S.T.	250 sec	S.O.	1,100 Hz	I.A.	40

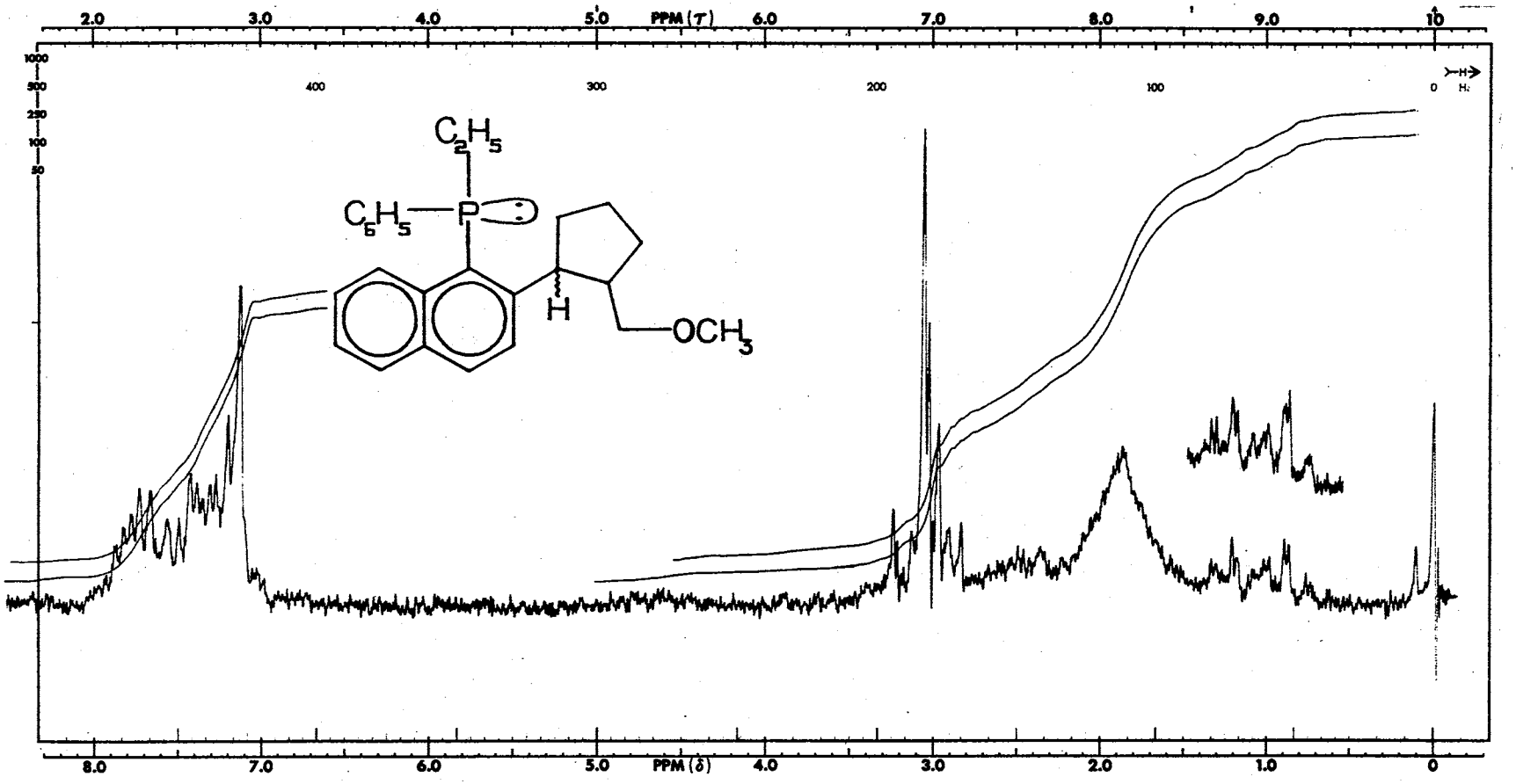
Plate XXXVI



1-Bromo-2-[2-(methoxymethyl)cyclopentyl]naphthalene (144) -- 220 MHz

Solvent.	$DCCl_3$	R.F.	25 db	S.W.	2500 Hz
S.T.	500 sec	S.O.	0.0 Hz	S.A.	16

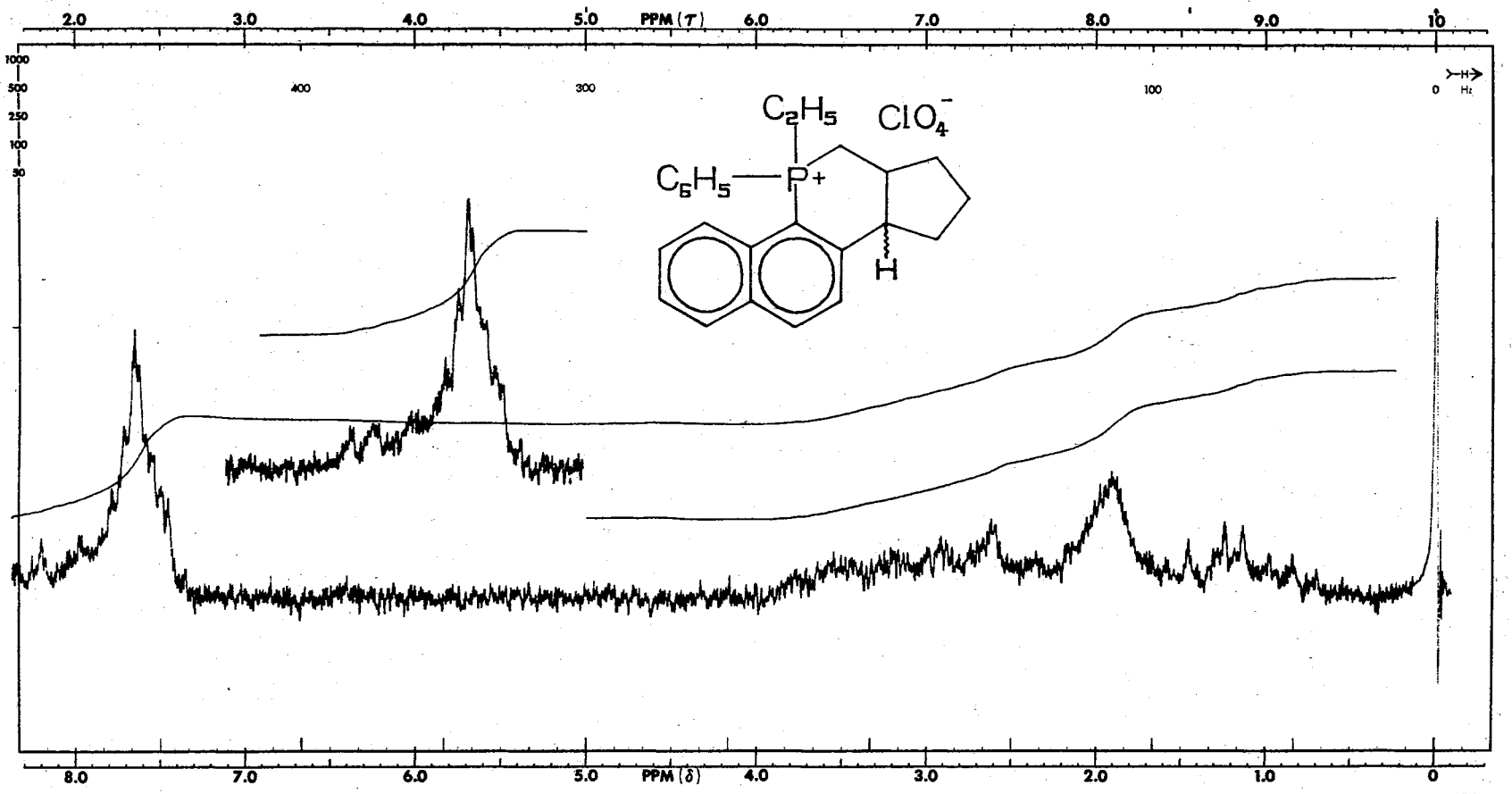
Plate XXXVII



Crude Ethyl[2-[2-(methoxymethyl)cyclopentyl]-1-naphthyl]phenylphosphine (145)

Solvent.	$DCCl_3$	R.F. . . .	0.055,0.1 mG	S.W.	500 Hz	S.A.	32,63
F.B.	2.0 Hz	S.T.	250 sec	S.O.	0.0 Hz	I.A.	50

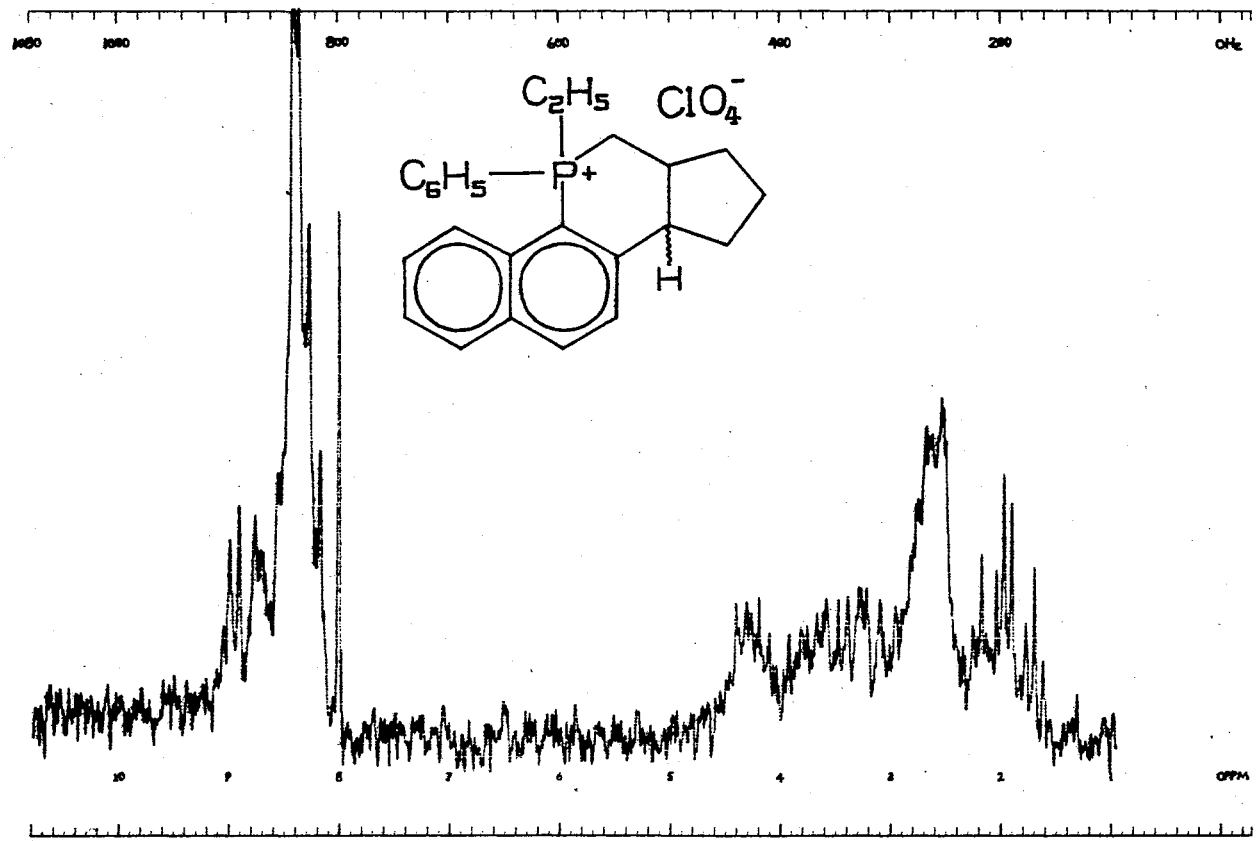
Plate XXXVIII



5-Ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo[h]cyclopenta[c]phosphinolinium Perchlorate (120b)

Solvent.	$DCCl_3$	R.F.	0.05 mG	S.W.	-500 Hz	S.A.	40
F.B.	2.0 Hz	S.T.	250 sec	S.O. . . .	452,570 Hz	I.A.	80

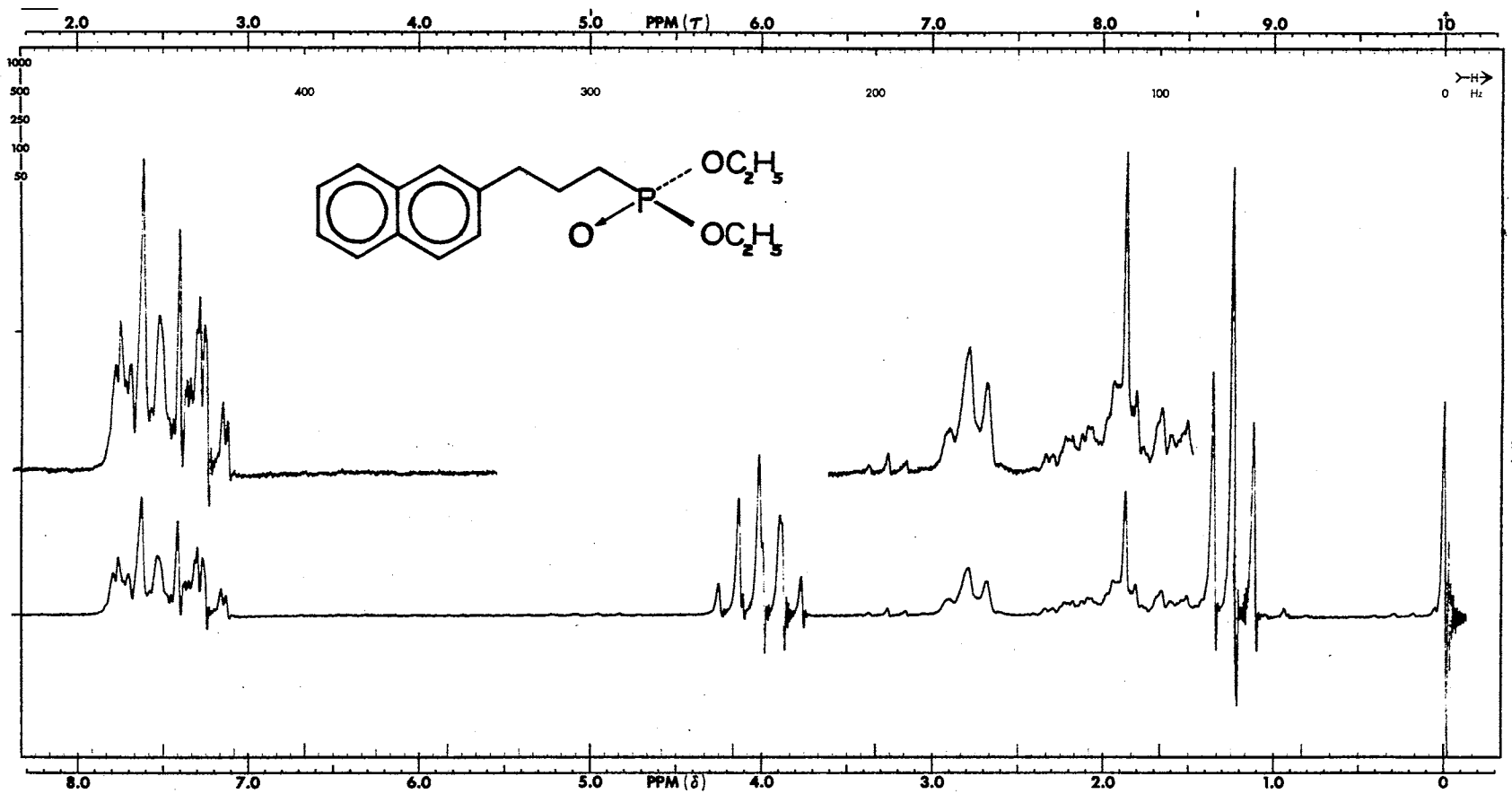
Plate XXXIX



Crude 5-Ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo[h]cyclopenta[c]phosphinolinium Perchlorate (120b) -- 100 MHz

Solvent.	$DCCl_3$	R.F.	30 mG	S.W.	1080 Hz
Filter	5 Hz	S.T.	500 sec	S.A.	150

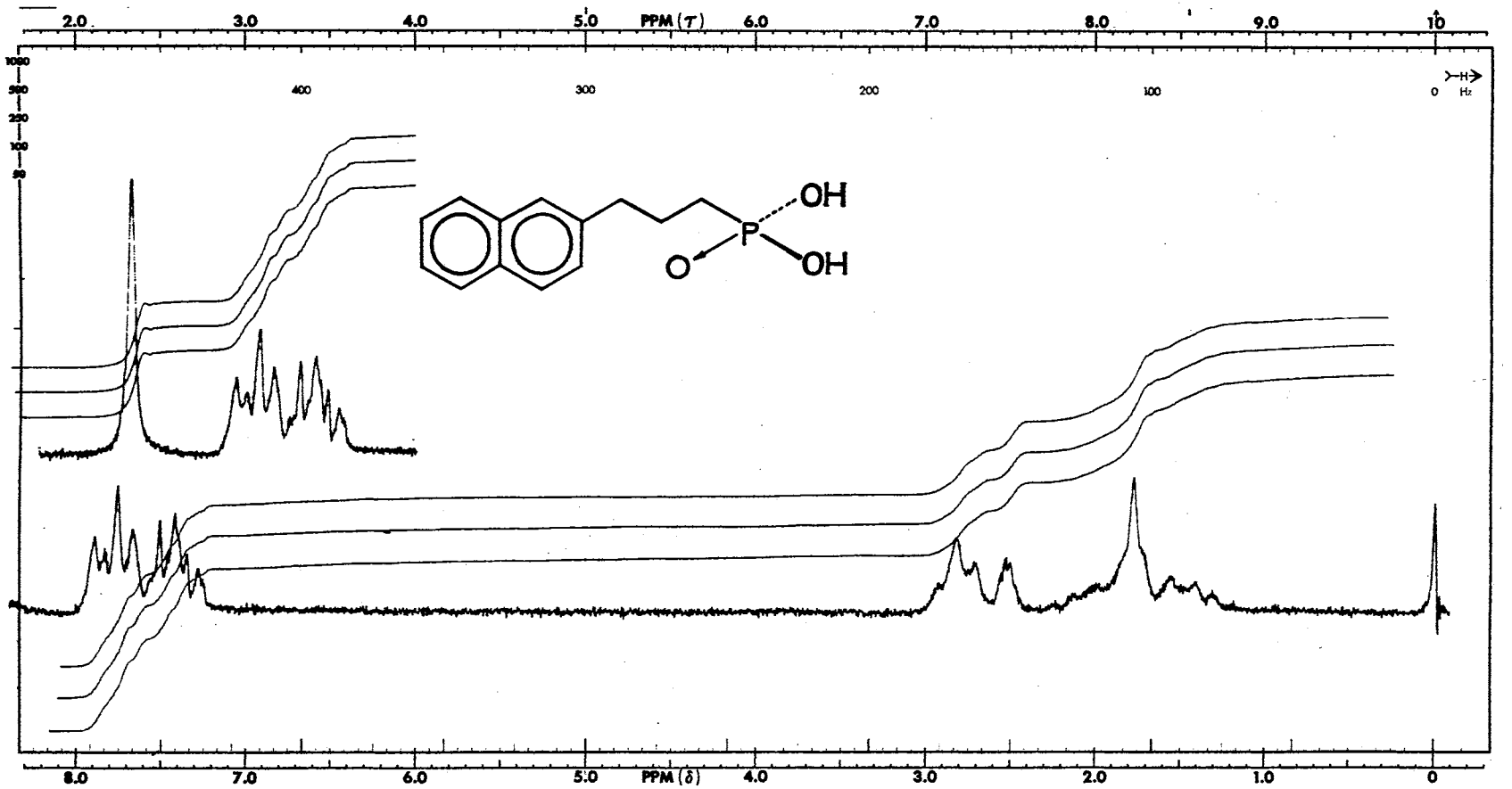
Plate XL



Diethyl [3-(2-naphthyl)propyl]phosphonate (166)

Solvent.	$DCCl_3$	R.F.	0.03 mG	S.W.	500 Hz	S.A.	2.5,6.3
F.B.	4.0 Hz	S.T.	250 sec	S.O.	0.0 Hz	I.A.	off

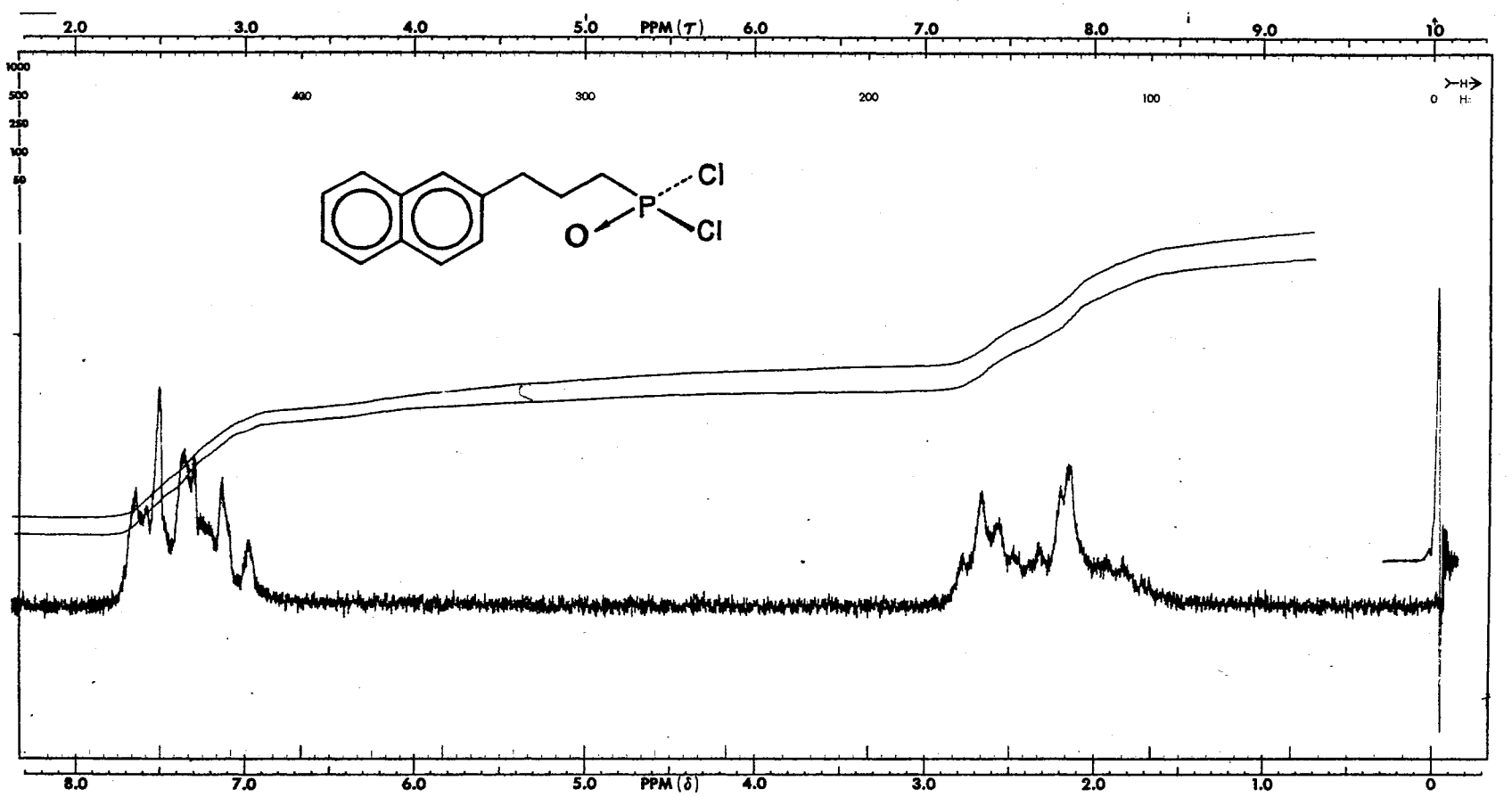
Plate XLI



[3-(2-Naphthyl)propyl]phosphonic Acid (167)

Solvent.	$DCCl_3$	R.F.	0.05 mG	S.W.	500 Hz	S.A.	16
F.B.	4.0 Hz	S.T.	250 sec	S.O. . . .	0.0,50 Hz	I.A.	50

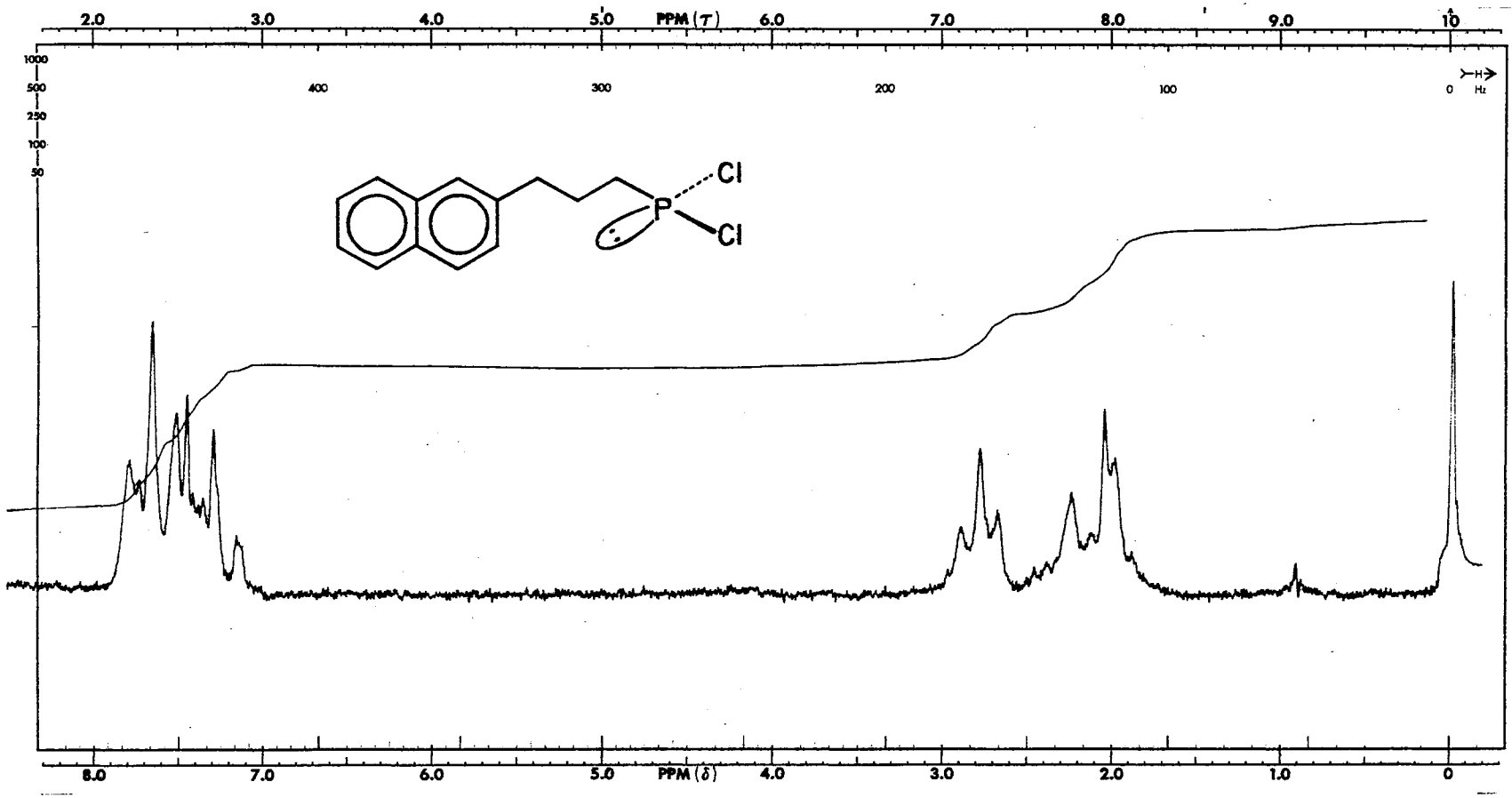
Plate XLII



[3-(2-Naphthyl)propyl]phosphonic Dichloride (168)

Solvent. $DCCl_3$ (ext. TMS)	R.F. . . . . 0.04 mG	S.W. . . . . 500 Hz	S.A. 25
F.B. . . . . 4.0 Hz	S.T. . . . . 250 sec	S.O. . . . . 20 Hz	I.A. 50

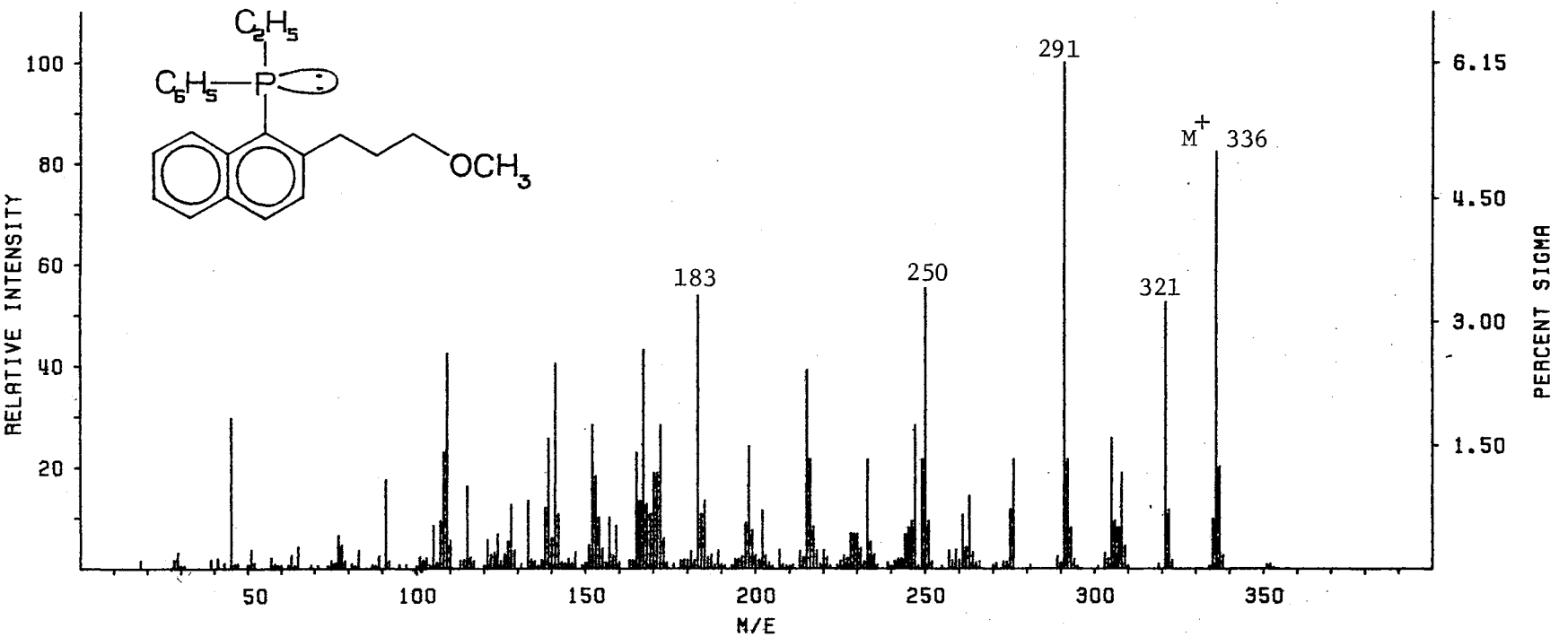
Plate XLIII



[3-(2-Naphthyl)propyl]phosphonous Dichloride (169)

Solvent. . . . . $DCCl_3$	R.F. . . . . 0.03 mG	S.W. . . . . 500 Hz	S.A. 6.3
F.B. . . . . 4.0 Hz	S.T. . . . . 250 sec	S.O. . . . . 0.0 Hz	I.A. 50

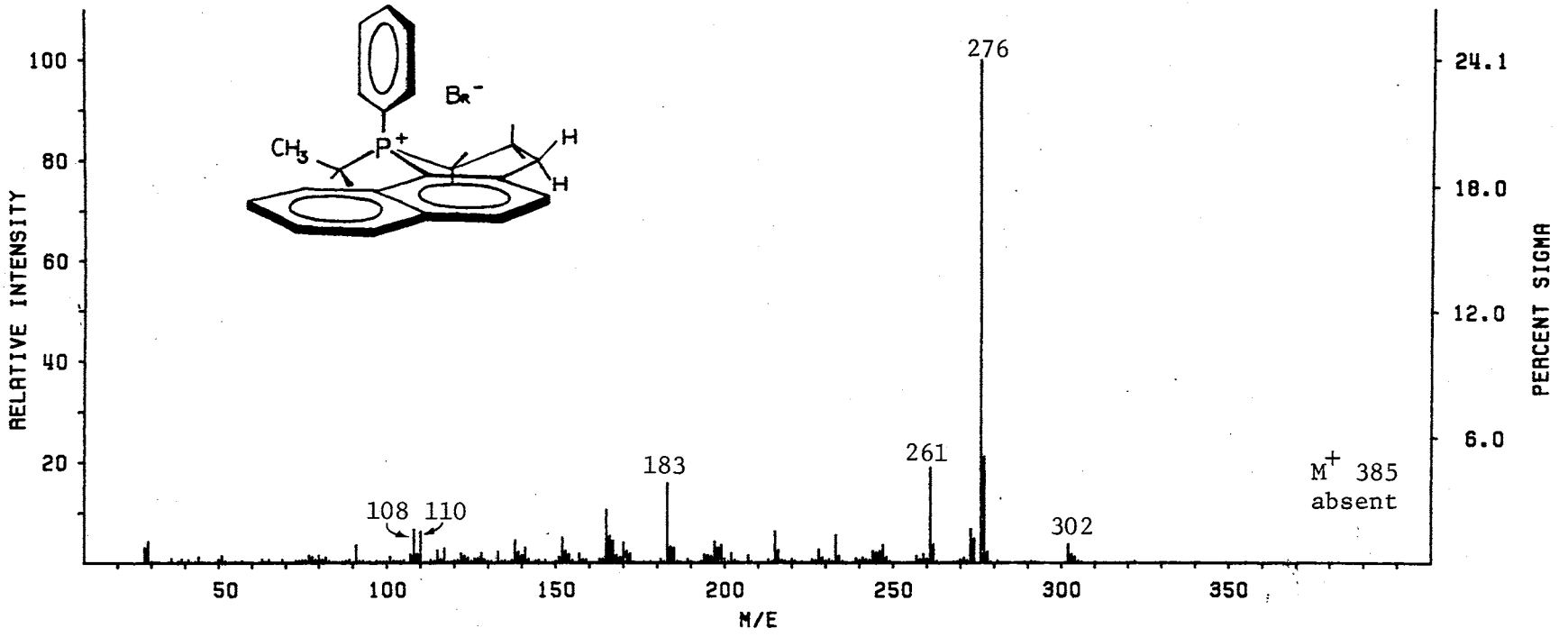
Plate XLIV



Crude Ethyl[2-(3-methoxypropyl)-1-naphthyl]phenylphosphine (132)

Inlet. . . Direct Probe Ionizing Voltage. . . 70 eV Source °C. . . 310° Probe °C. . . ca. 40°

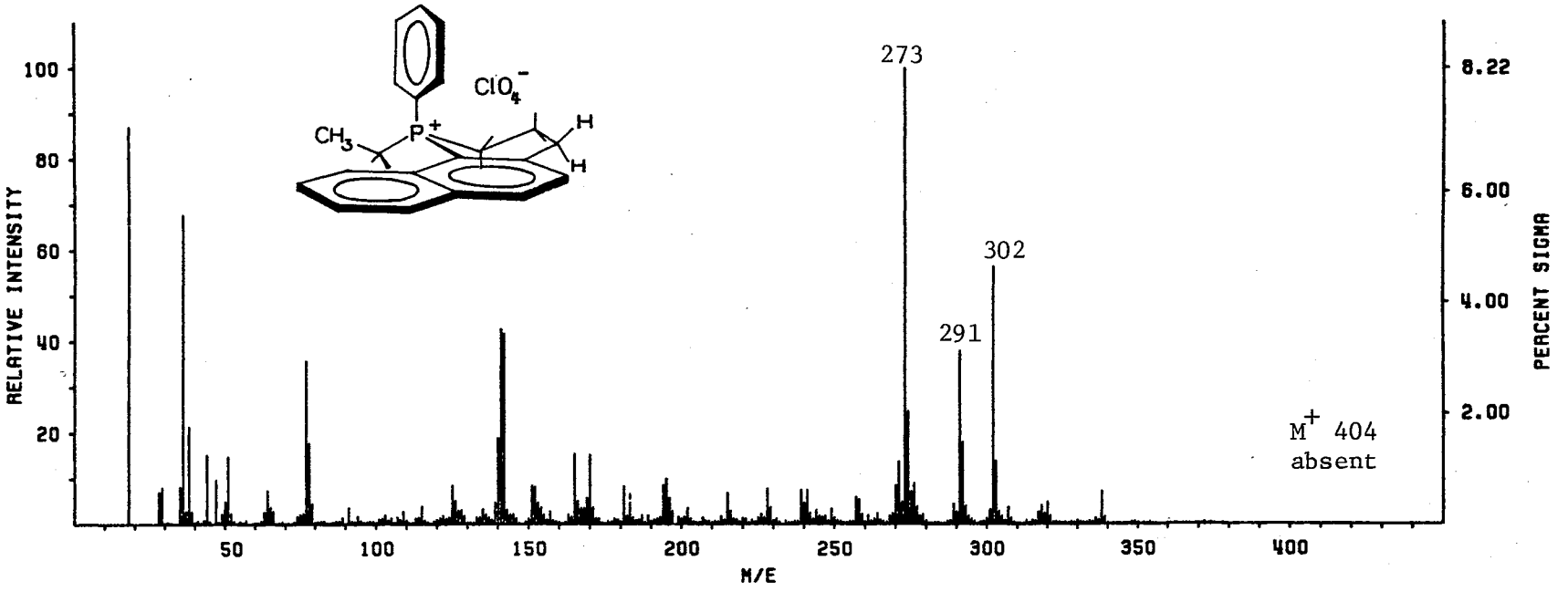
Plate XLV



1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Bromide (119a)

Inlet. . . . Direct Probe Ionizing Voltage. . . 70 eV Source °C. . 310° Probe °C. . ca. 200°

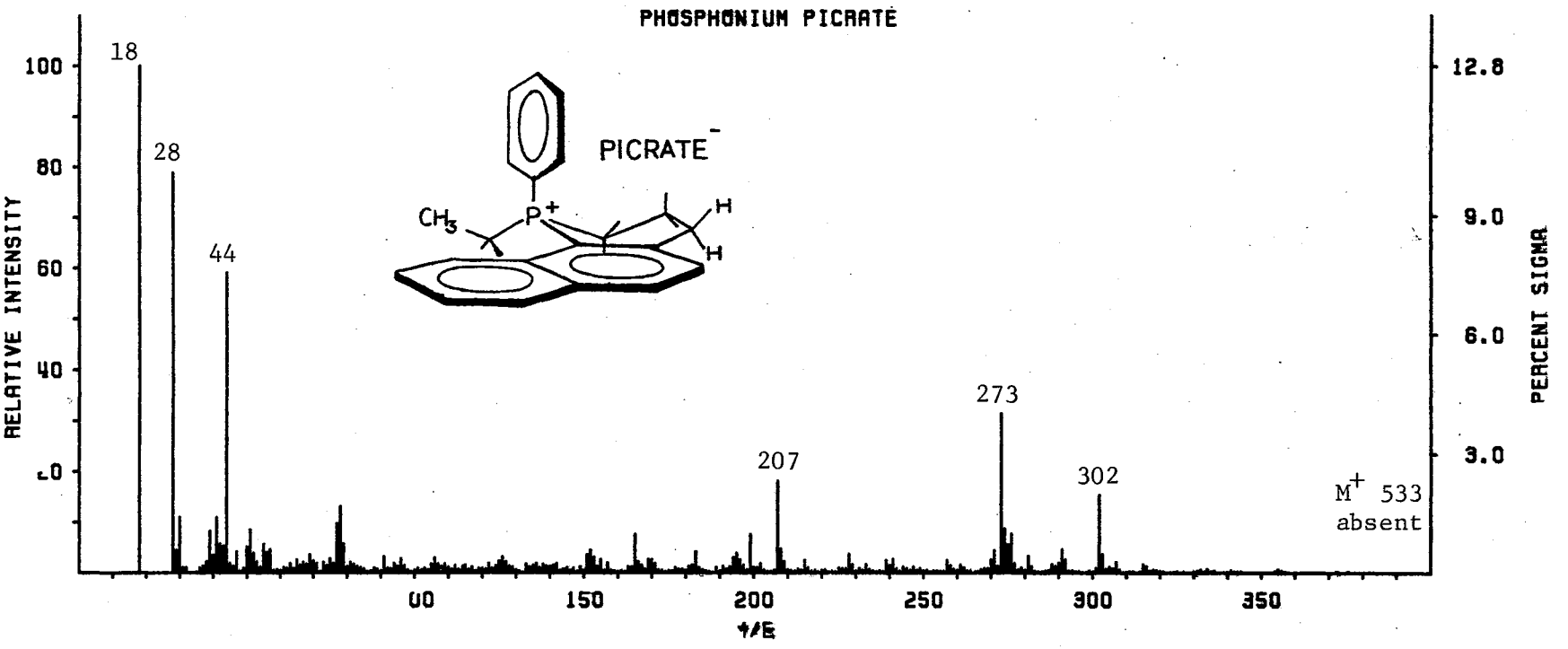
Plate XLVI



1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Perchlorate (119b)

Inlet. . . . Direct Probe Ionizing Voltage. . . 70 eV Source °C. . 310° Probe °C. . ca. 200°

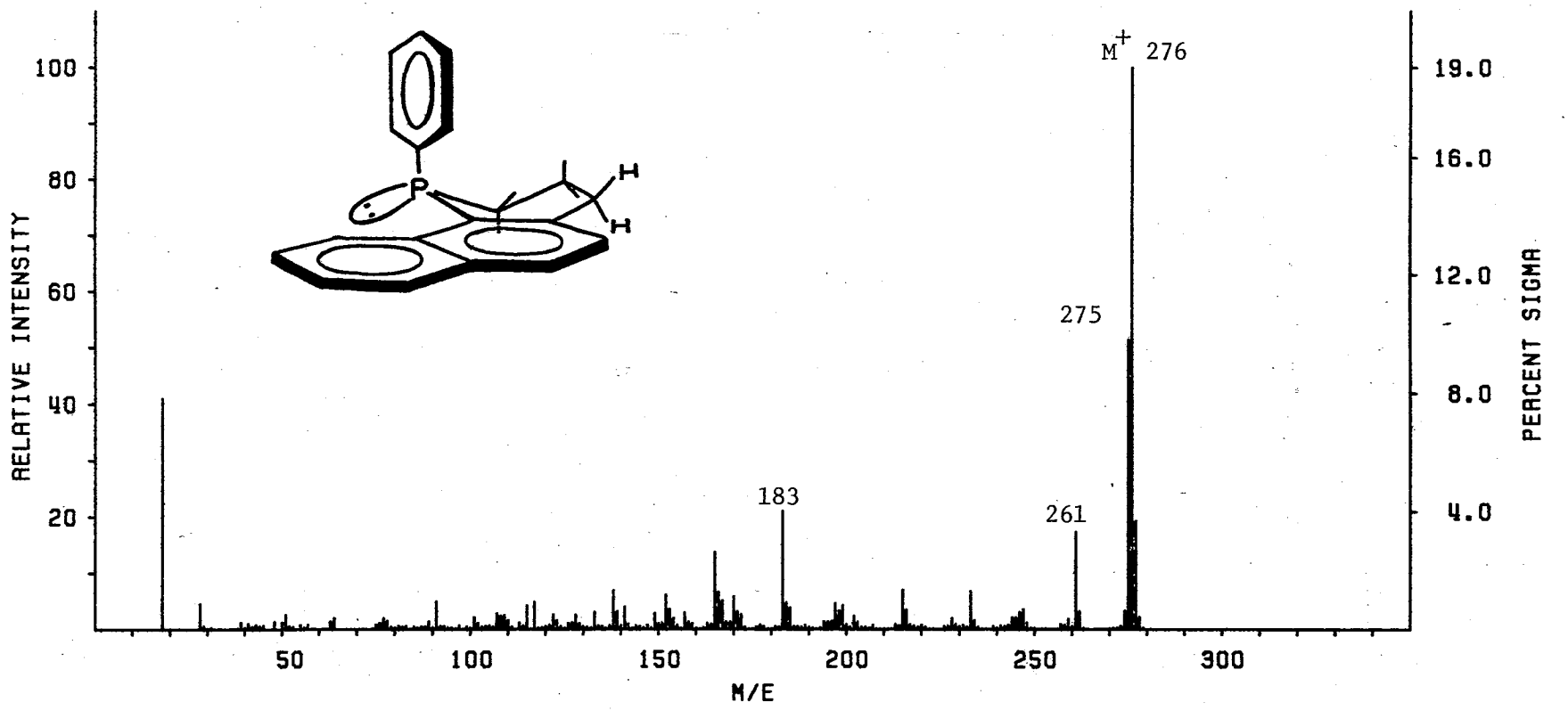
Plate XLVII



1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium Picrate (119c)

Inlet. . . Direct Probe Ionizing Voltage. . . 70 eV Source °C. . . 310° Probe °C. . . ca. 190°

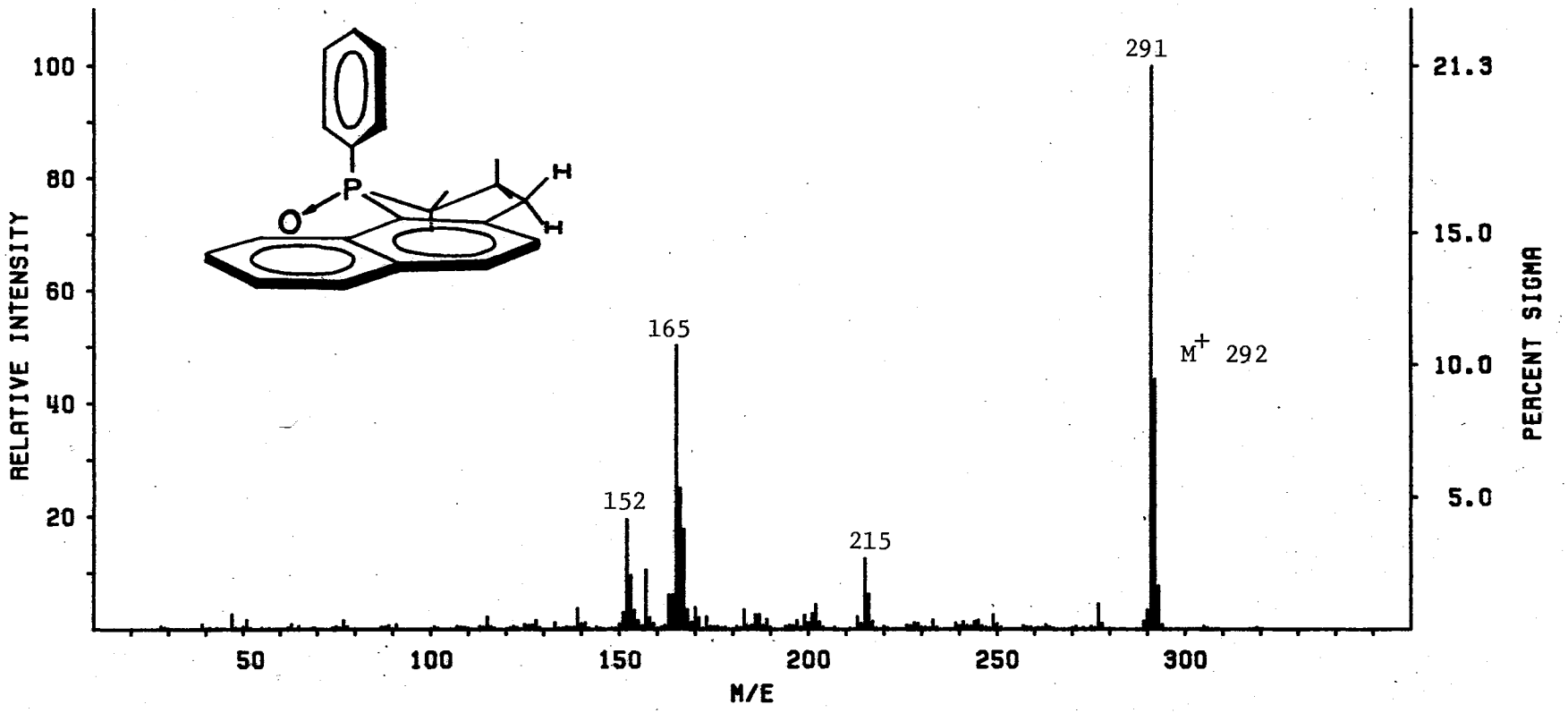
Plate XLVIII



1,2,3,4-Tetrahydro-1-phenylbenzo[h]phosphinoline (133)

Inlet. . . Direct Probe Ionizing Voltage. . . 70 eV Source °C. . . 310° Probe °C. . . ca. 30°

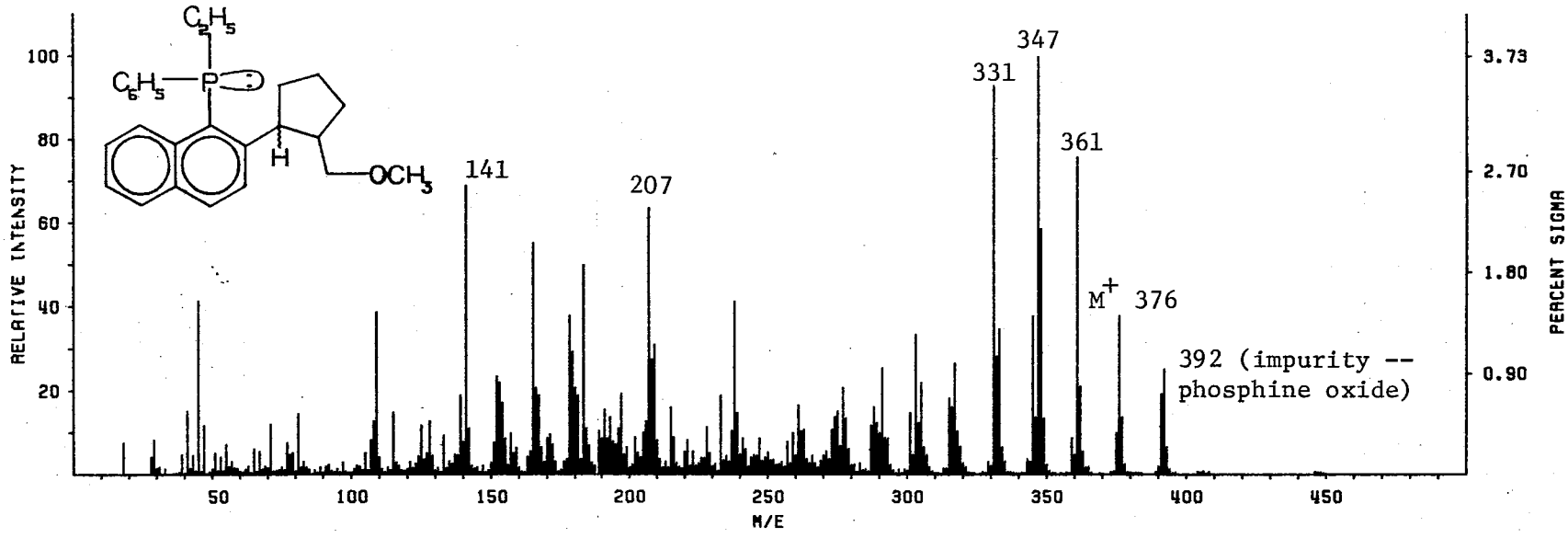
Plate XVIX



1,2,3,4-Tetrahydro-1-phenylbenzo[h]phosphinoline 1-Oxide (134)

Inlet. . . Direct Probe Ionizing Voltage. . . 70 eV Source °C. . . 310° Probe °C. . . ca. 40°

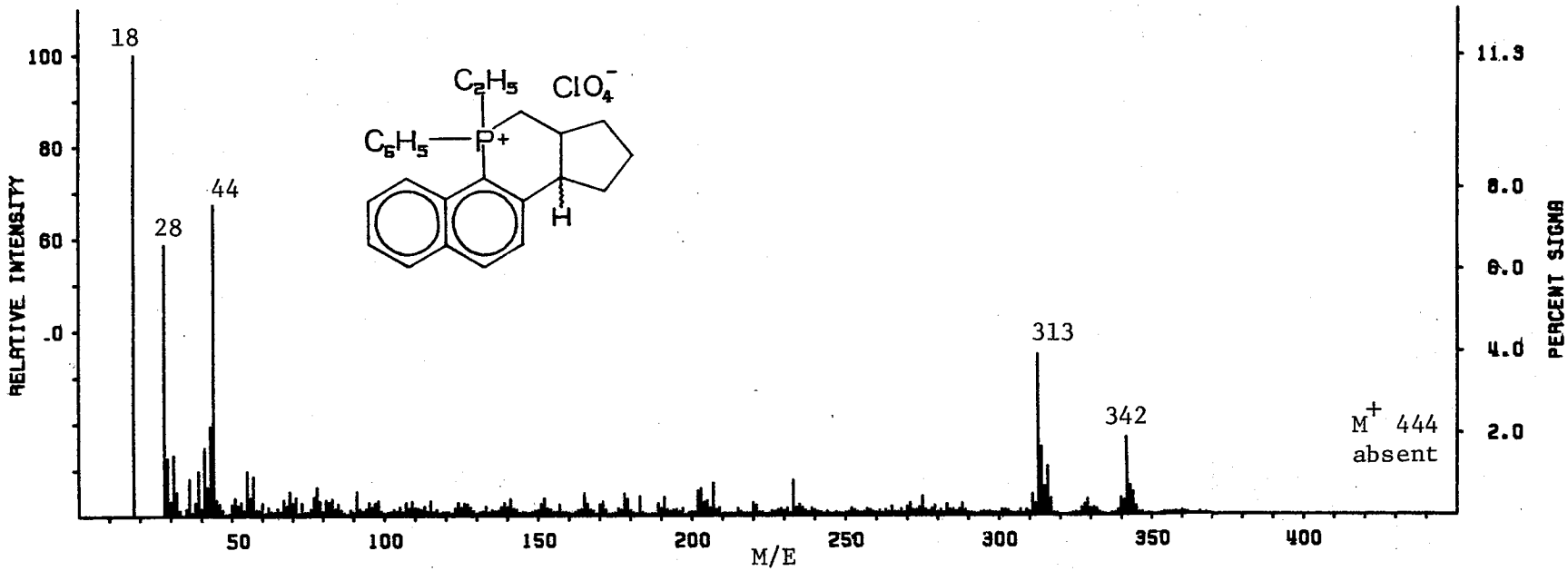
Plate L



Crude Ethyl[2-[2-(methoxymethyl)cyclopentyl]-1-naphthyl]phenylphosphine (145)

Inlet. . . Direct Probe Ionizing Voltage. . . 70 eV Source °C. . . 310° Probe °C. . . ca. 50°

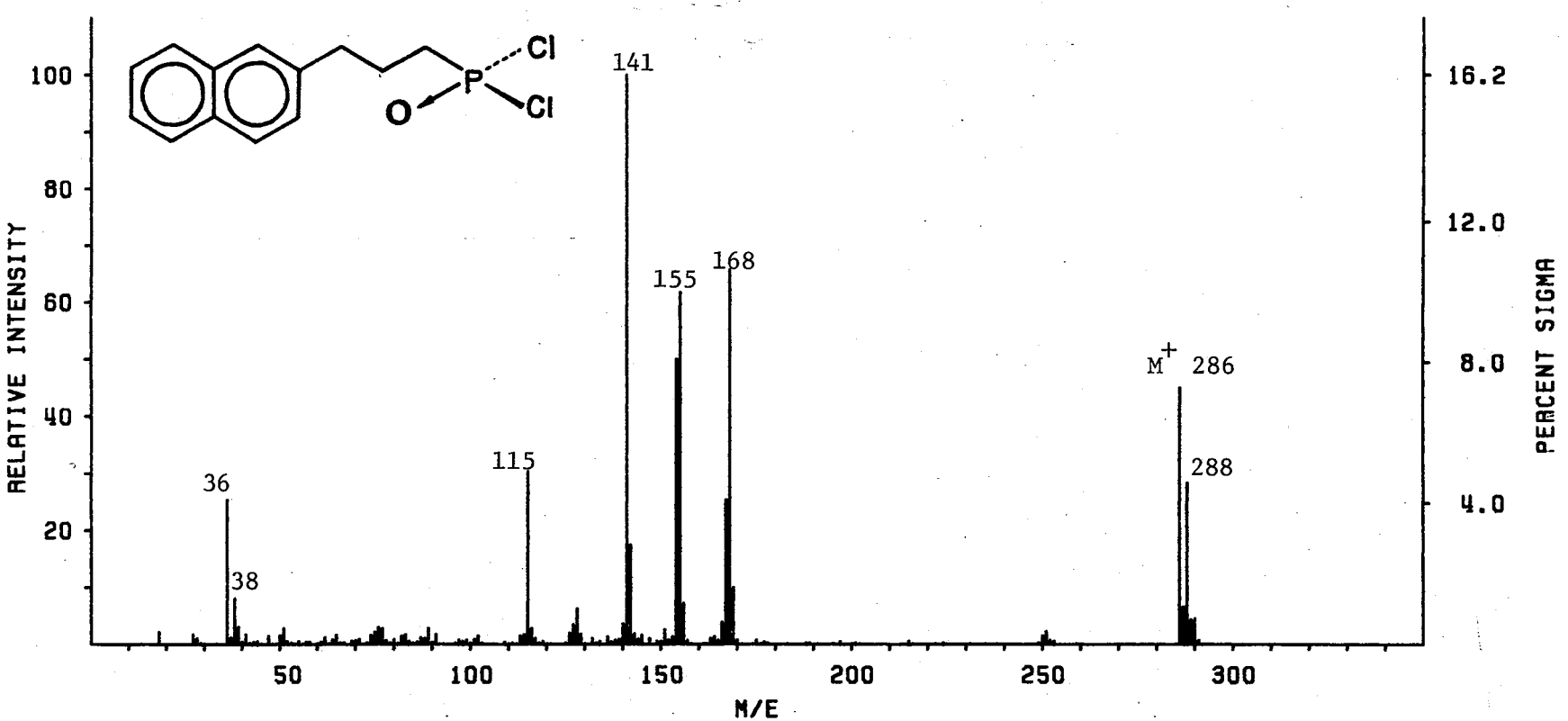
Plate LI



5-Ethyl-6,6a,7,8,9,9a-hexahydro-5-phenyl-5H-benzo[h]cyclopenta[c]phosphinolinium Perchlorate (120b)

Inlet. . . Direct Probe Ionizing Voltage. . . 70 eV Source °C. . . 310° Probe °C. . . ca. 200°

Plate LII



[3-(2-Naphthyl)propyl]phosphonic Dichloride (168)

Inlet. . . Direct Probe Ionizing Voltage. . . 70 eV Source °C. . . 310° Probe °C. . . ca. 30°

BIBLIOGRAPHY

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