SYNTHESIS OF SUBSTITUTED 2,3,4,5-TETRAHYDRO-5-OXO-2,2-DIPHENYL-1H-2-BENZOPHOSPHEPINIUM SALTS — INTRAMOLECULAR ACYLATION OF CERTAIN PHOSPHONIUM SALTS VIA 115% POLYPHOSPHORIC ACID CATALYSIS

By

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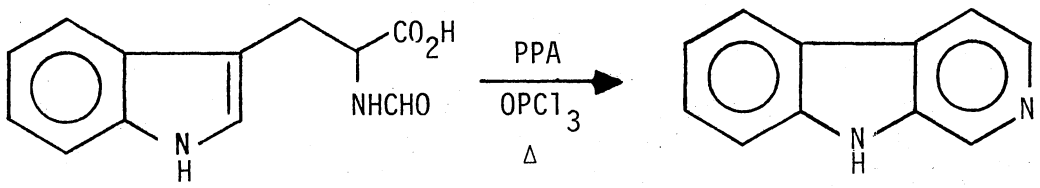
CHAPTER I

HISTORICAL

Syntheses and Chemistry of Heterocyclic Ketones via Polyphosphoric Acid Catalysis

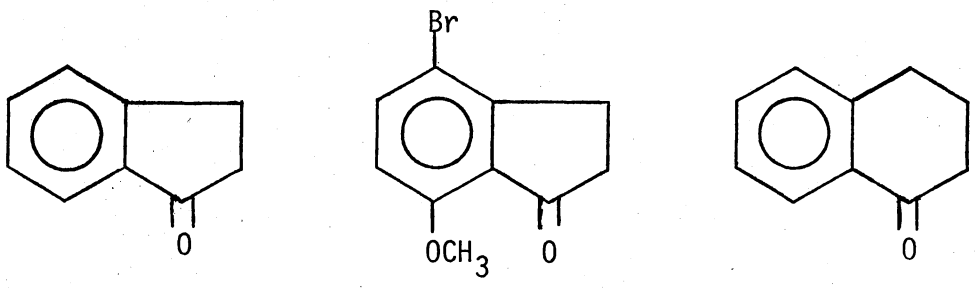
The use of polyphosphoric acid (PPA) as a cyclization agent for heterocyclic synthesis has been known for many years.[40,63,78] One of the first successful preparations[71] employing PPA was that of Snyder and Werber. N-Formyl-*dl*-trytophan (1) heated with PPA and phosphorus oxychloride at 125° (85 minutes) gave norharman (2) in modest yield (36%). Snyder and Werber also recorded[72] the synthesis of α-hydrindone



1 2

(3), 4-bromo-7-methoxy-1-indanone (4), α-tetralone (5), anthraquinone (6), and 1,2-benzanthraquinone (7) by the use of PPA as the cyclizing reagent.

Later work[37] on the preparation of carbocyclic ketones developed an improved general cyclization procedure so that PPA competed favorably in many cases with Friedel-Crafts-type intramolecular



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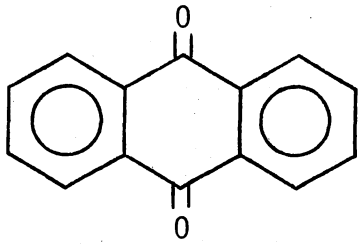

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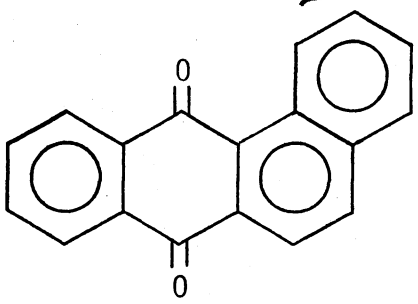
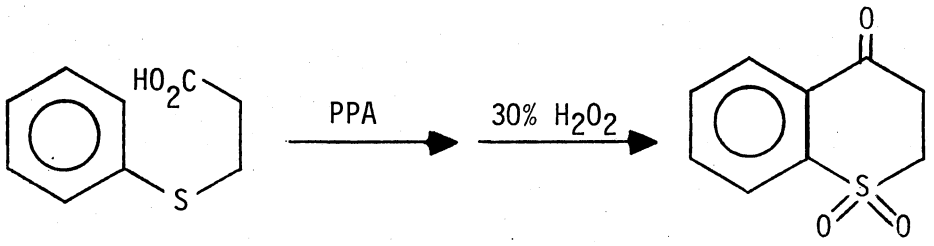


7

acylations, as well as with cyclizations catalyzed by sulfuric acid, hydrogen fluoride, and phosphorus pentoxide. Typically,[40,63,78] a small amount (1-10 g) of the compound is added slowly, with stirring, to approximately 10 times its weight of PPA, heated beforehand to the required temperature. The reaction mixture is maintained at this required temperature, with stirring, for a predetermined time. Cooling the reaction mixture (if at elevated temperature) and then hydrolyzing with ice water gives either the final product or a homogeneous solution to be extracted with suitable solvent.

Interestingly, PPA proved to be an extremely effective reagent for promoting cyclization of 3-phenylmercaptopropionic acid (8) to 4-thiochromanone, converted to the sulfone 9 for ease of isolation. 3-(p-Nitrophenoxy)propionic acid (10) similarly yielded 6-nitro-4-chromanone (11).[33] The nitrogen analog, N,N-diphenyl-β-alanine (12) cyclized to 2,3-dihydro-1-phenyl-4(1H)-quinolone (13).



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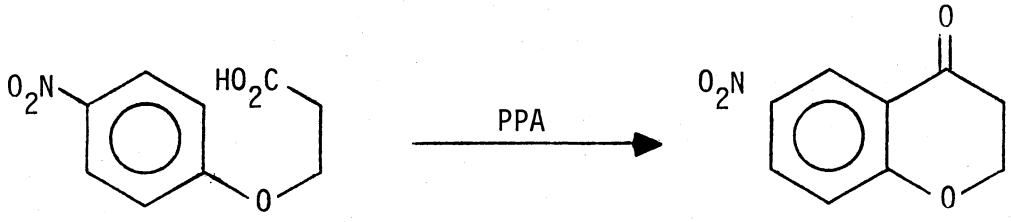

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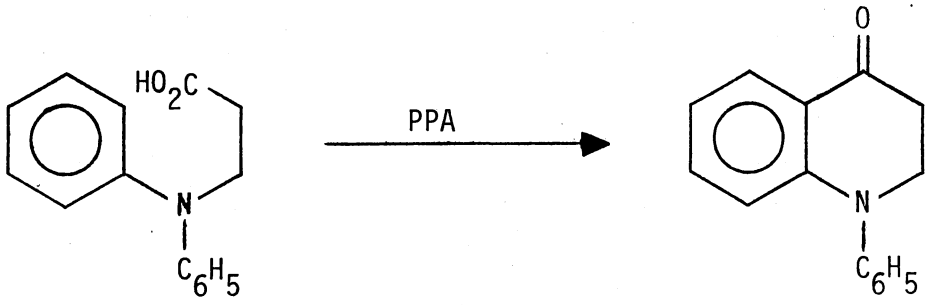
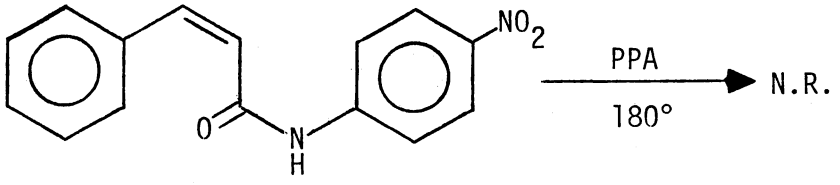


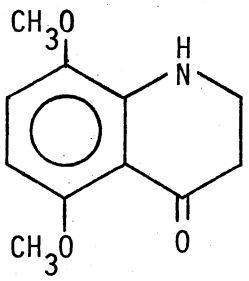
12 13

It is interesting to note[10] that N-(p-nitrophenyl)cinnamamide (14) did not cyclize at reaction temperatures as high as 180°. Starting material was recovered nearly quantitatively.



14

Other nitrogen analogs in the chromone series have been synthesized by this same technique.[38] For example, 5,8-dimethoxy-4-keto-1,2,3,4-tetrahydroquinaldine (15) was obtained by mixing the corresponding acid 16 with PPA and heating the stirred mixture on a



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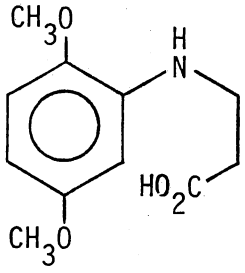
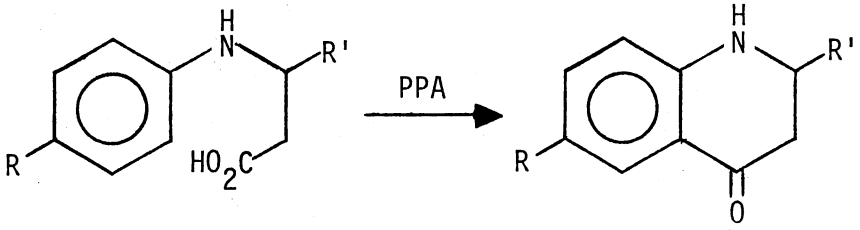


16

steam bath (30 minutes). After the appropriate work-up, the cyclization afforded 16 in moderate yield (36%).

In the preparation of substituted 2,3-dihydro-4(1H)-quinolones 18,[39] cyclization of 3-anilinopropionic acids 17 via PPA catalysis proceeded readily in good yields (55-65%). This cyclization procedure

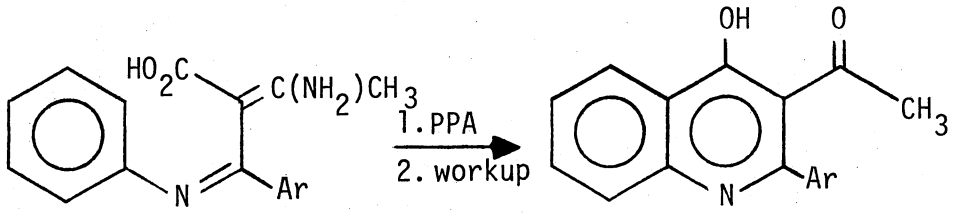


17 18

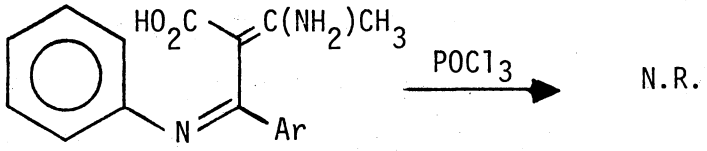
R = Cl, R' = H
R = Cl, R' = CH_3
R = CH_3O, R' = H

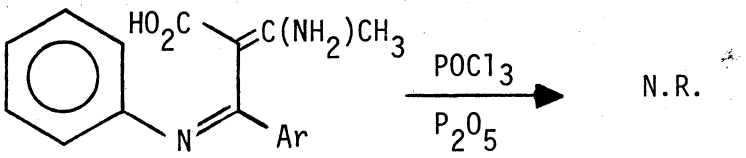
proved fruitful even in the presence of the active hydrogen on the nitrogen atom of the starting acid.

Staskun[74] reported the synthesis of 2-aryl-3-acetyl-4-quinolinols by intramolecular cyclization of the corresponding alkyl β-amino-α(N-arylimidobenzylcrotonates with PPA. The general procedure involved



19 20

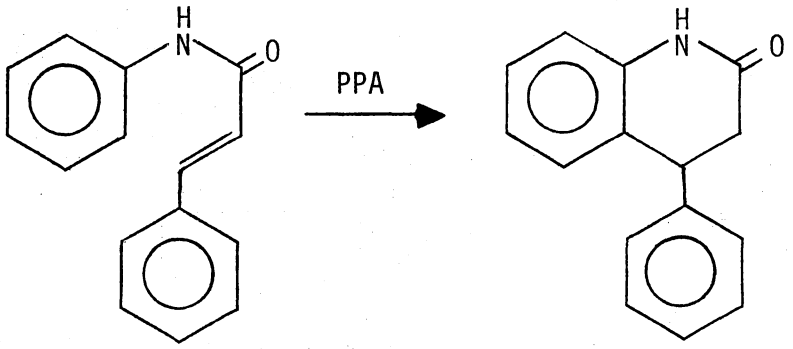




mixing 0.5-1 g of the crotonate 19 with approximately 5-10 g of PPA and heating the solution, with stirring, at 165-175° (15 minutes). Upon cooling, the reaction mixture was hydrolyzed with water, and the resulting solution was made basic with NaOH, filtered, and treated with charcoal. Upon acidification with acetic acid a quinolinol 20 precipitated (60-80%). Recrystallization (ethanol) gave the pure quinolinol 20 . Cyclization was also attempted with phosphorus oxychloride and a mixture of phosphorus oxychloride and phosphorus

pentoxide. However, only starting material was recovered in both cases.

PPA was found likewise to be an extremely useful reagent in the conversion of N-phenylcinnamamides like 21 to 3,4-dihydro-4-phenylcarbostyrils like 22.[10] One gram of N-phenylcinnamamide (21) and



21 22

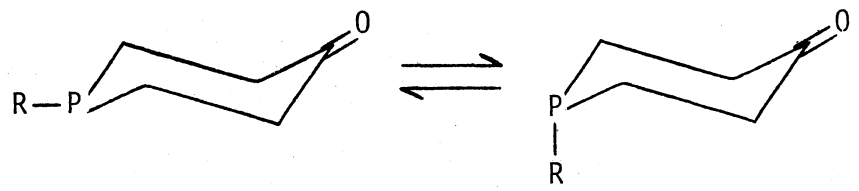
20 g of PPA were heated to 120° (10 minutes). The solution was then cooled, hydrolyzed (ice water), and extracted ($HCCl_3$). The extracts were combined, dried ($MgSO_4$), and evaporated to yield, after recrystallization (ethanol-water), 3,4-dihydro-4-phenylcarbostyril (22) [m.p. 177-178° (94%)].

It is thus apparent that the technique has wide applicability in heterocyclic synthesis. Surprisingly, many functional groups tolerate the action of hot PPA.

Syntheses and Chemistry of Carbon-Phosphorus Heterocyclic Ketones

A. Simple Heterocyclic Systems

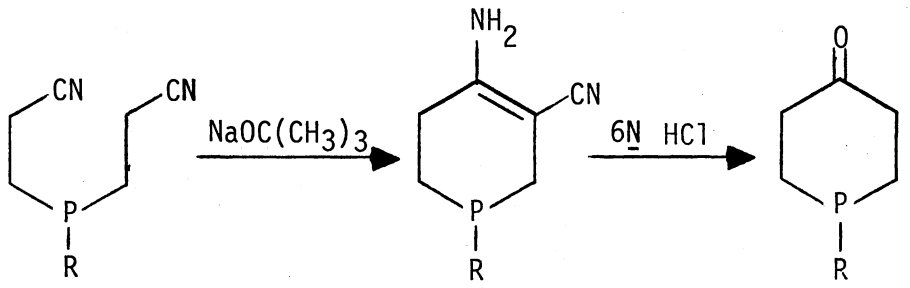
Welcher, Johnson, and Wystrach[80] (1960) reported the synthesis of a new class of carbon-phosphorus (C-P) heterocycles, the 4-phosphorinanones 23 . The general procedure is represented in Scheme I. Bis-(2-cyanoethyl)phosphines 24 were cyclized to



23a 23b

4-amino-1,2,5,6-tetrahydrophosphorin-3-carbonitriles 25 with sodium t-butoxide. Subsequent hydrolysis and decarboxylation with boiling 6 N

SCHEME I



24 25 26

a. R = C_2H_5

b. R = C_6H_5

a. R = C_2H_5 ($\nu_{C=O}^{film}$ 1715 cm^{-1})

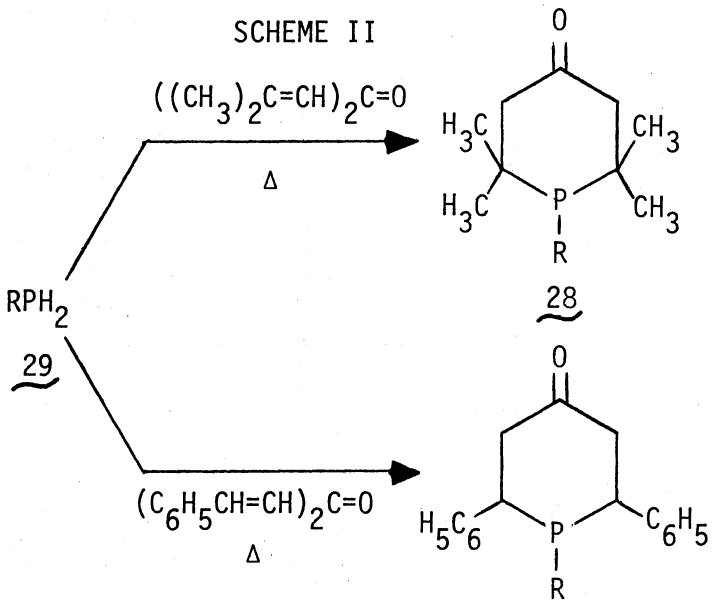
b. R = C_6H_5 ($\nu_{C=O}^{film}$ 1695 cm^{-1})

HCl gave the corresponding 4-phosphorinanones 26 . Characterizations of the 4-phosphorinanones 26 included derivatization via preparation of the semicarbazone and the methiodide.

Another method for synthesis of 4-phosphorinanones involved the addition of a primary phosphine 27 to a conjugated dienone.[79]

Several 4-phosphorinanones, 28 and 29, were obtained in this manner (Scheme II) and were subsequently characterized via semicarbazone, methiodide, and sulfide derivatives.

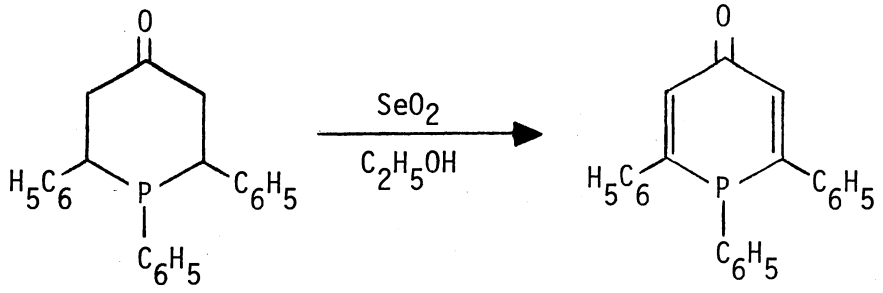
SCHEME II



R = C_6H_5, CH_2CH_2CN,

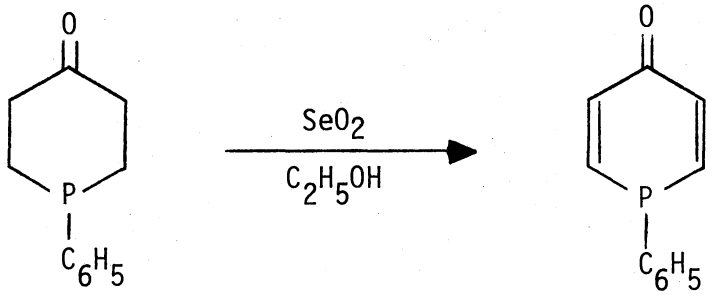
C_6H_{11}, i-C_4H_9, n-C_8H_{17}

Phosphorinanones behave as expected in many reactions. For example, several substituted 4-phosphorinanones have been dehydrogenated with SeO_2 in ethanol.[87] 1,2,5-Triphenyl-4-phosphorinanone (30) gave the corresponding 4-oxo-1-phosphacyclohexadienone 31, m.p. 162° ($\nu_{C=O}$ =



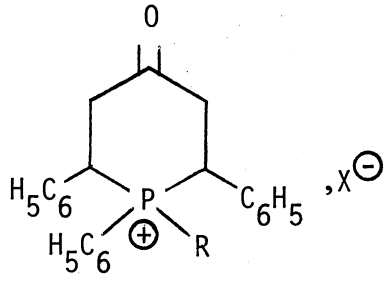
30 31

1627 cm^{-1}). Likewise, 1-phenyl-4-phosphorinanone (32) was converted to the corresponding 1-phenyl-4-oxo-1-phosphacyclohexadienone (33),



32 33

m.p. 130-131° ($\nu_{C=O}$ = 1650 cm^{-1}). Somewhat surprising is that related and stable phosphonium salts 34 gave the corresponding phosphonia-cyclohexadienones 35.



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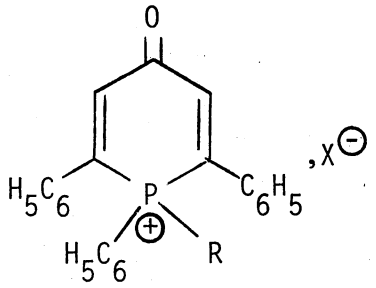


35

R = C_2H_5, $CH_2C_6H_5$

R = C_2H_5 ($\nu_{C=O}$ 1680 cm^{-1})

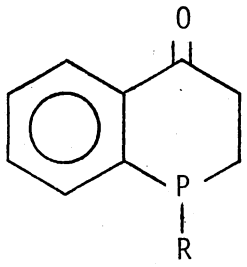
= $CH_2C_6H_5$ ($\nu_{C=O}$ 1650 cm^{-1})

Although this area has been reviewed,[3,45,70] very few examples are recorded. Much work is likely to be forthcoming on phosphorinanones since they are related to the biologically active piperidones.

B. Polycyclic Carbon-Phosphorus Systems

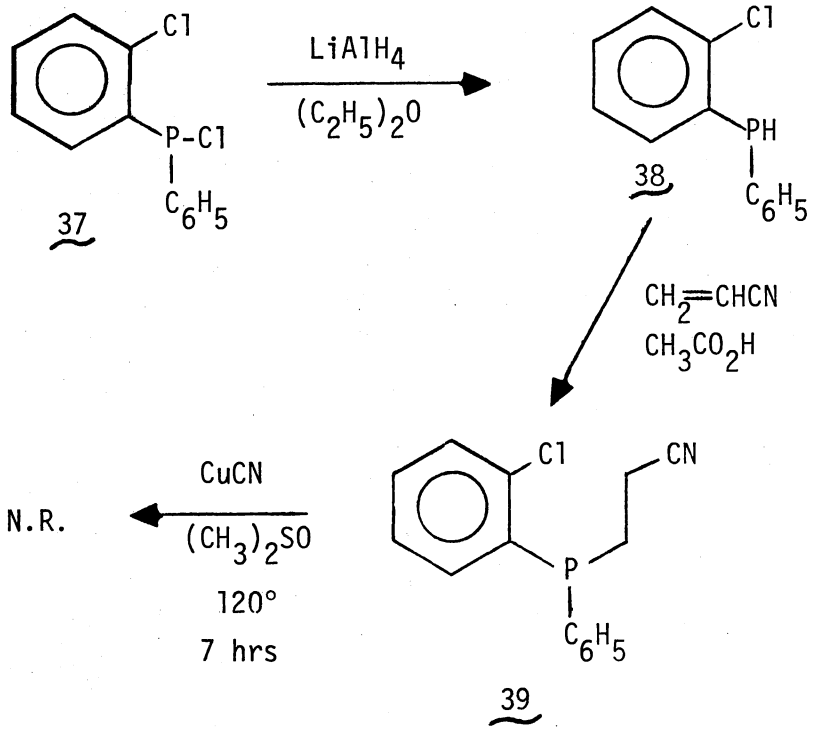
The corresponding phosphorus analogs of 1,2,3,4-tetrahydroquinolines and 1,2,3,4-tetrahydroisoquinolines are very rare. The chemistry of the few examples recorded has not been well elucidated. The phosphorus systems are known as phosphinolines and isophosphinolines.

Gallagher, Kirby, and Mann[21] investigated the synthesis of 1-substituted 1,2,3,4-tetrahydro-4-oxophosphinolines 36 by a number of



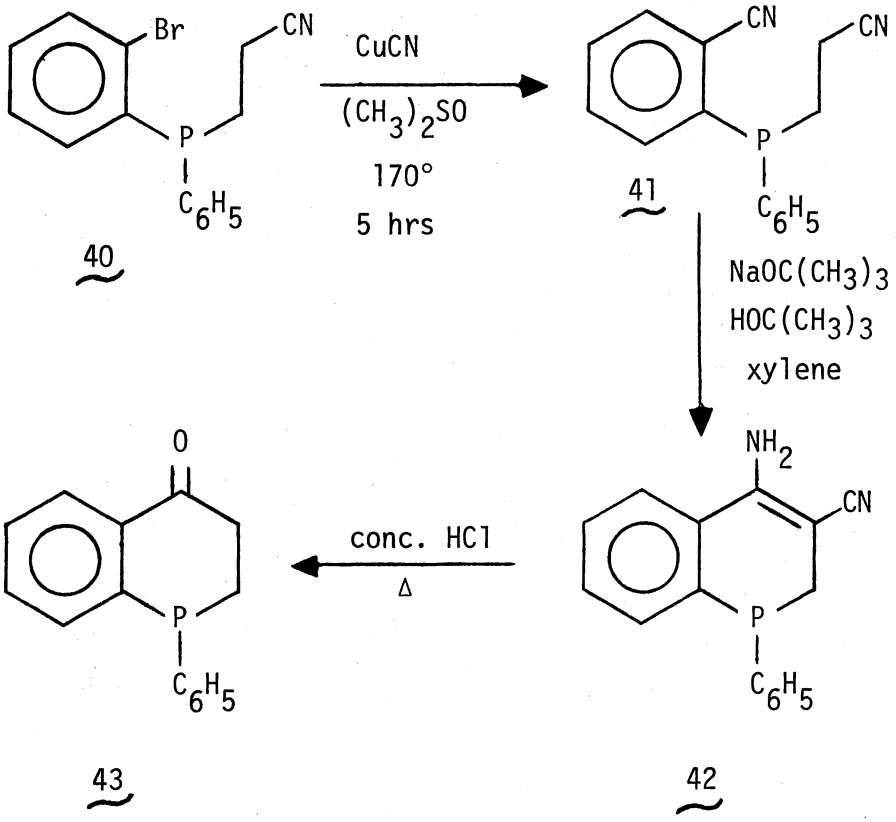
36

routes. (o-Chlorophenyl)phenylphosphinous chloride (37) was reduced to the secondary phosphine 38 with lithium aluminum hydride in an ethereal solution. The phosphine 38 condensed with acrylonitrile in acetic acid, and gave o-chlorophenyl-2-cyanoethylphenylphosphine (39) [b.p. 183-185°/0.005 mm]. Treatment of the phosphine 39 with cuprous cyanide in dimethyl sulfoxide at 120° for 7 hours resulted only in the recovery of starting material. When o-bromophenyl-2-cyanoethylphenylphosphine (40), similarly prepared,[21] was allowed to react with cuprous cyanide in dimethyl sulfoxide at 170° (5 hours), the corresponding 2-cyanoethyl-o-cyanophenylphenylphosphine (41) resulted. Cyclization of the crude dinitrile 42 was achieved with



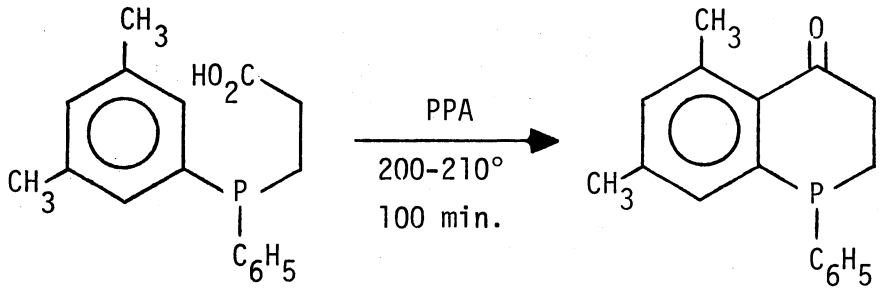
sodium t-butoxide in t-butyl alcohol and xylene. The amino nitrile 42 was hydrolyzed and decarboxylated by boiling in concentrated HCl to give, after workup, 1,2,3,4-tetrahydro-1-phenylphosphinolin-4-one (43), m.p. 46-47° [b.p. 143-145°/0.05 mm (55%)]. The phosphinolinone 43 was characterized as a semicarbazone (m.p. 225-226°), methopicrate [of the phosphine, m.p. 153-154°], and an oxide of the phosphine (m.p. 124-126°).

Another procedure was followed to obtain a 4-phosphinolinone system.[21] [(3,5-Dimethylphenyl)phenylphosphino]propionic acid (44) and



40 41 42 43

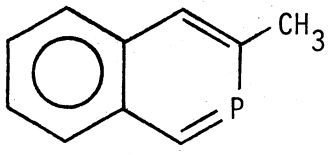
an excess of PPA were heated at 200-210° (100 minutes). The reaction mixture was cooled, hydrolyzed, and neutralized. Extraction of the



44 45

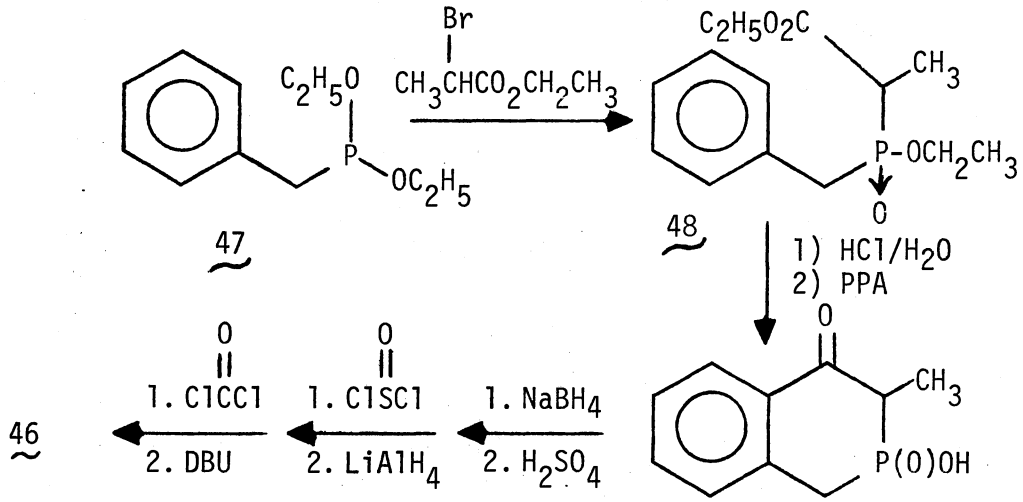
solution with ether gave a new solution which was dried and evaporated to a brown oil. Distillation of the oil (150-152°/0.2 mm) gave the impure phosphine 45 with a carbonyl absorption in the infrared region at 1680 cm^{-1}. A methopicrate of the oil was prepared (m.p. 170-171°). The final cyclization step proceeded in such low yield (actual percent not stated) that the fruitfulness of the synthesis was negated.

H. G. de Graaf and co-workers[13] recently prepared the first derivative of 2-phosphanaphthalene 46. Diethyl benzylphosphonite (47)

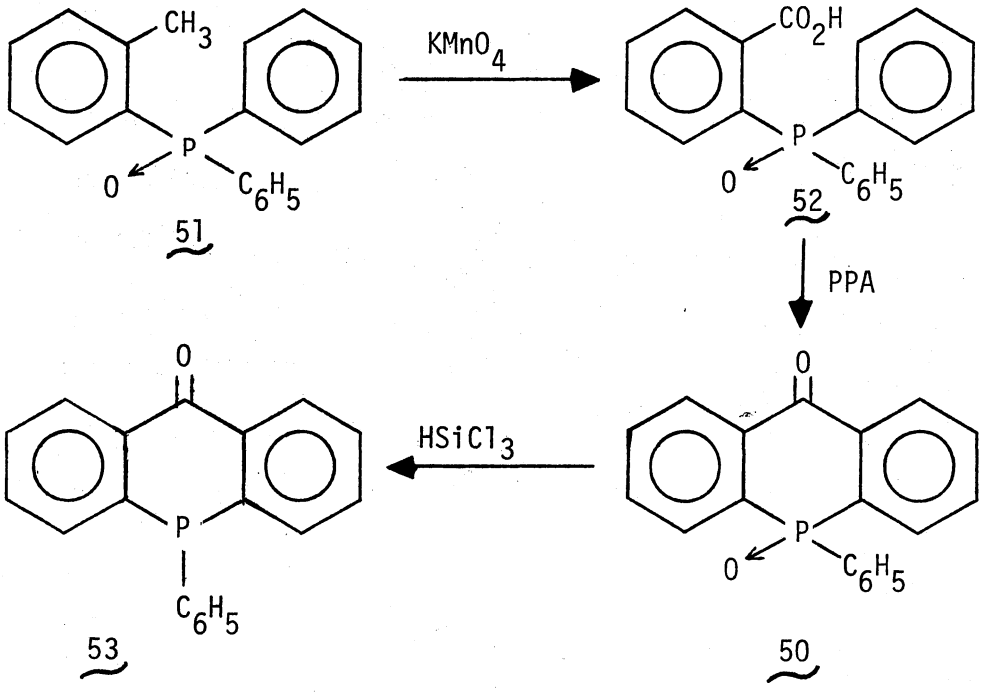


46

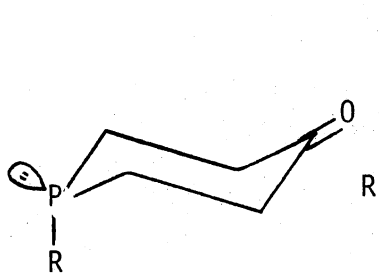
and ethyl-α-bromopropionate gave the Arbuzov product 48. When the diester was hydrolyzed with hydrochloric acid and cyclized with PPA, the oxophosphinic acid 49 (m.p. 204-205°) resulted.



In similar fashion,[68] 4,10-dihydro-5-phenyldibenzo[b,e]phosphorin-10-one 5-oxide (50) has been obtained. Diphenyl(o-tolyl)phosphine oxide (51) was converted via oxidation with $KMnO_4$ to o-(diphenylphosphinyl)-benzoic acid (52). The acid 52 cyclized when heated with PPA at 175° for 3 hours and gave, after hydrolysis, 50 [m.p. 222-223° (50%)].



Reduction of the phosphine oxide 50 with excess trichlorosilane produced oxophosphine 53, m.p. 135°(90%). Almost certainly this phosphine 53 is not flat, but may have a boat form for the phosphorinanone ring. An X-ray analysis is needed to determine the validity of this postulate. Unfortunately, the infrared spectrum of 53 was not recorded. Accordingly, any interaction of the lone pair of electrons on phosphorus with the carbonyl group cannot be compared with that in simple phosphorinanones 54[79,80] and the phosphinolinones



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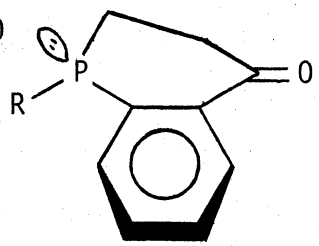

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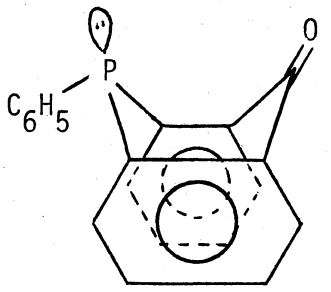
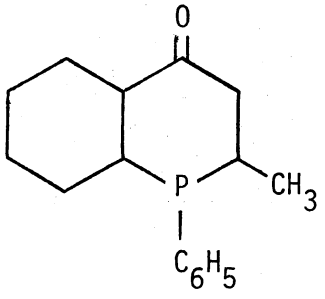


53

55 . The $\nu_{C=O}$ (KBr) for 1-phenyl-4-phosphorinanone 26b occurs at 1695 cm^{-1} while that of the 1-ethyl-4-phosphorinanone (26a) is at 1715 cm^{-1} (liquid film, p. 7).[80] Phosphinoline 45 showed $\nu_{C=O}$ at 1680 cm^{-1}[21] but there is a methyl group in a peri position to the C=O group, the force constant of which could be altered (p. 12).

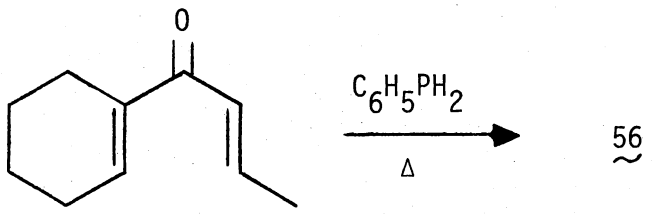
Following a procedure similar to that of Welcher and Day,[79] Kashman and Ronen[36] prepared 3-methyl-2-phenyl-2-phosphabicyclo[4.4.0]-decan-5-one (56). 1-Propenyl-cyclohexenyl ketone (57) and phenyl-



56

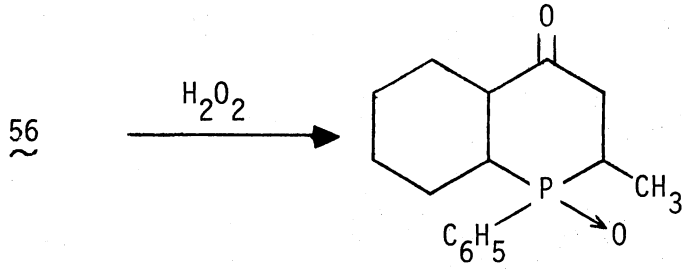
phosphine were heated under N_2 for one hour at 115-120°. The solution was cooled and chromatographed (under N_2) on a silica gel column (Merck 7734). A white, crystalline phosphine 56 was obtained with a $\nu_{C=O}$ (KBr) at 1700 cm^{-1}. This compares with $\nu_{C=O}$ 1710 cm^{-1} for

cyclohexanone[82] and ν_{CO} 1710 cm^{-1} for decalone.[25] Unfortunately, no data were available to determine if the isomer had a cis or trans ring junction. The phosphine 56 was believed to be a mixture of two isomers based on PMR analysis, [$DCCl_3$; dd, δ 0.93, $J_{\underline{P}C\underline{C}H_3}$ = 16.5 Hz and $J_{C\underline{H}C\underline{H}_3}$ = 7 Hz, dd, δ 1.27, $J_{\underline{P}C\underline{C}H_3}$ = 13 Hz and $J_{C\underline{H}C\underline{H}_3}$ = 7 Hz].



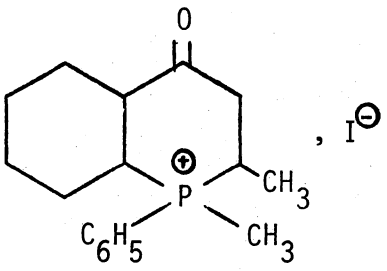
57

Oxidation of 56 with H_2O_2 gave a solid which yielded, upon recrystallization (CH_3CN), one predominate isomer 58, m.p. 178-180° ($\nu^{KBr}_{C=O}$ 1705 cm^{-1}, $\nu^{KBr}_{P=O}$ 1175 cm^{-1}). Further characterization of the



58

phosphine 56 included preparation of a methiodide 59 [m.p. 215-216°, $\nu_{C=O}$ (KBr) 1710 cm^{-1}] and a benzyl chloride quaternary salt 60 [m.p. 262-263°, $\nu_{C=O}$ (KBr) 1720 cm^{-1}].



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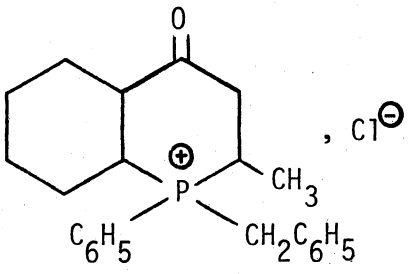
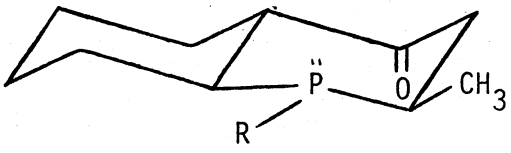
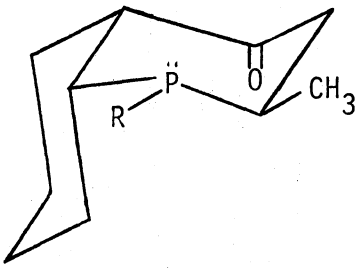


60

Possibly cis,trans isomers result from the Michael addition process, as shown. More likely, oxidation can occur on both invertomers

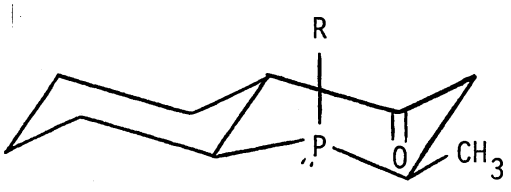


61a

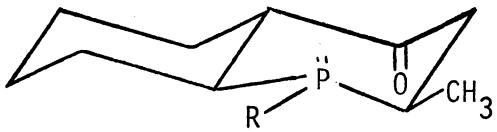


61b

but the suspected more stable 61a with a trans ring junction may be present in larger quantity than 61b. Conceivably, two invertomers with trans ring junctions could exist and give two oxidation products, the amounts dependent upon the initial concentrations of 62a and 62b



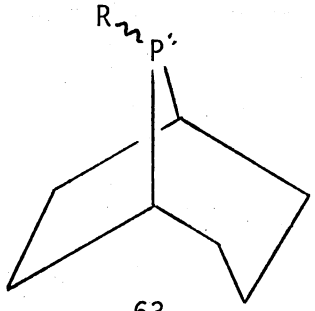
62a



62b

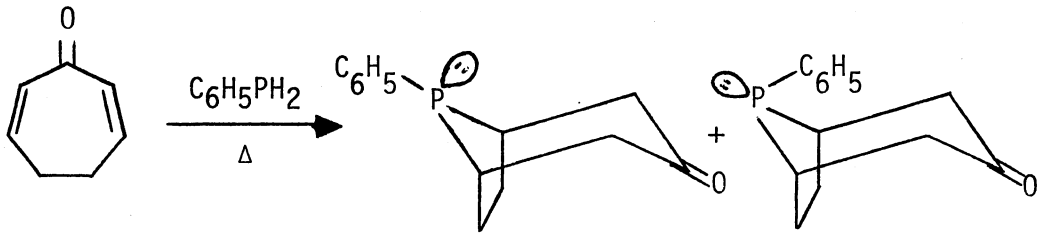
The lengthened C-P bonds[20] and known low inversion rate around phosphorus[41] could easily account for the formation of two invertomers. 1,3-Interactions have been recognized to be of less significance in phosphorinanone systems (compared to cyclohexyl systems) and thus high populations of axial substituents are permitted.[59] Consequently, the greater C-P bond length (compared to C-C distances) reduce steric compressional effects from groups two atoms removed in the ring system.

8-Phosphabicyclo[3.2.1]octanic systems 63 are rare, but have been prepared[34] in view of the configurational and conformational

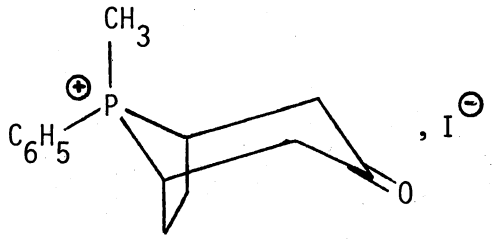


63

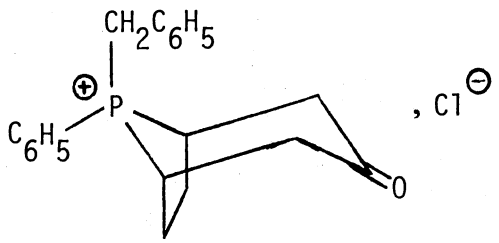
relationships to the tropanic system. Unfortunately, little biological activity has been recorded for this family. Cyclohepta-2,6-dien-1-one (64) and phenylphosphine heated (under N_2) for 12 hours at 140-150° gave, after recrystallization (acetone), predominately 8-phenyl-8-phosphabicyclo[3.2.1]octan-3-one (65) [m.p. 144-146° (47%)]. Ketone



64 65a 65b

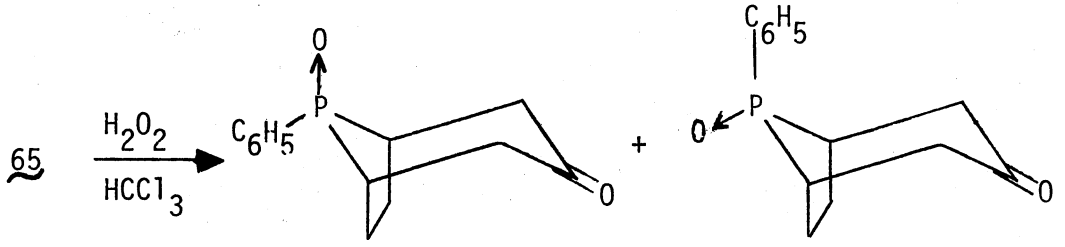


66



67

65 exhibited a $\nu_{C=O}$ (KBr) at 1700 cm^{-1}. The structure of 65 was supported by an acceptable elemental analysis as well as the analysis and PMR spectra of its methiodide 66 and benzyl chloride 67 salts.

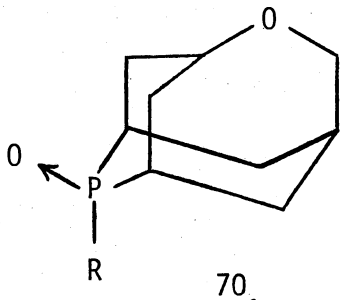


68

69

In the PMR spectra (D_2O) of each of the above only one doublet resulted for 66 [$\underline{P}$-$C\underline{H}_3$ at δ 2.91 (J = 15 Hz)] and for 67 [$\underline{P}$-$C\underline{H}_2$ at δ 4.65 (J = 14 Hz)]. Oxidation (H_2O_2) of the produced phosphine 65 gave two oxides, 68 (m.p. 235-237°) and 69 (m.p. 247-248°), which could be separated since they crystallized in two distinct forms. The slow inversion on phosphorus[41,65] and because the oxidation was performed below room temperature for two hours strongly imply that phosphines 65a and 65b are produced in the original condensation and are precursors of 68 and 69.

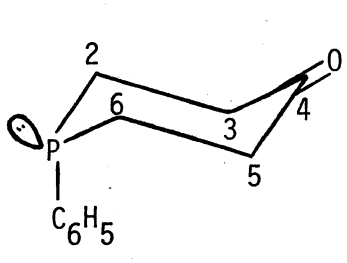
Interestingly,[35] derivatives of 2-phospha-6-oxaadamantan-2-one (70) have been recorded. The procedure (Scheme III) consisted of a



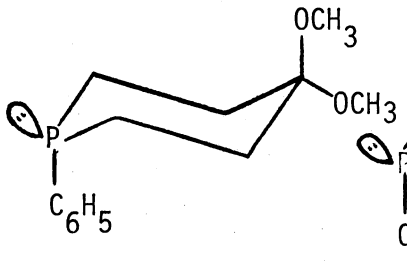
70

double Michael addition of phenylphosphine to 2,7-cyclooctadien-1-one (71). Oxidation of the resulting phosphine 72 with hydrogen peroxide followed by catalytic hydrogenation gave the phosphine oxide 73. Potassium borohydride reducted the carbonyl group to yield the phosphorinanol 74, which was subsequently converted to 70 with $Pb(OAc)_4$.

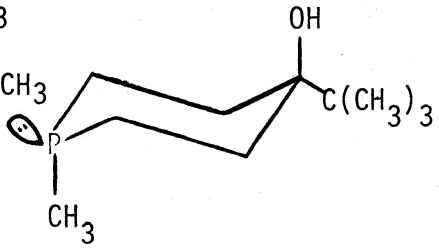
The X-ray analysis of several phosphorinanones and derivatives 26b, 75, and 76 reveal features common also to cyclohexanes and



26b

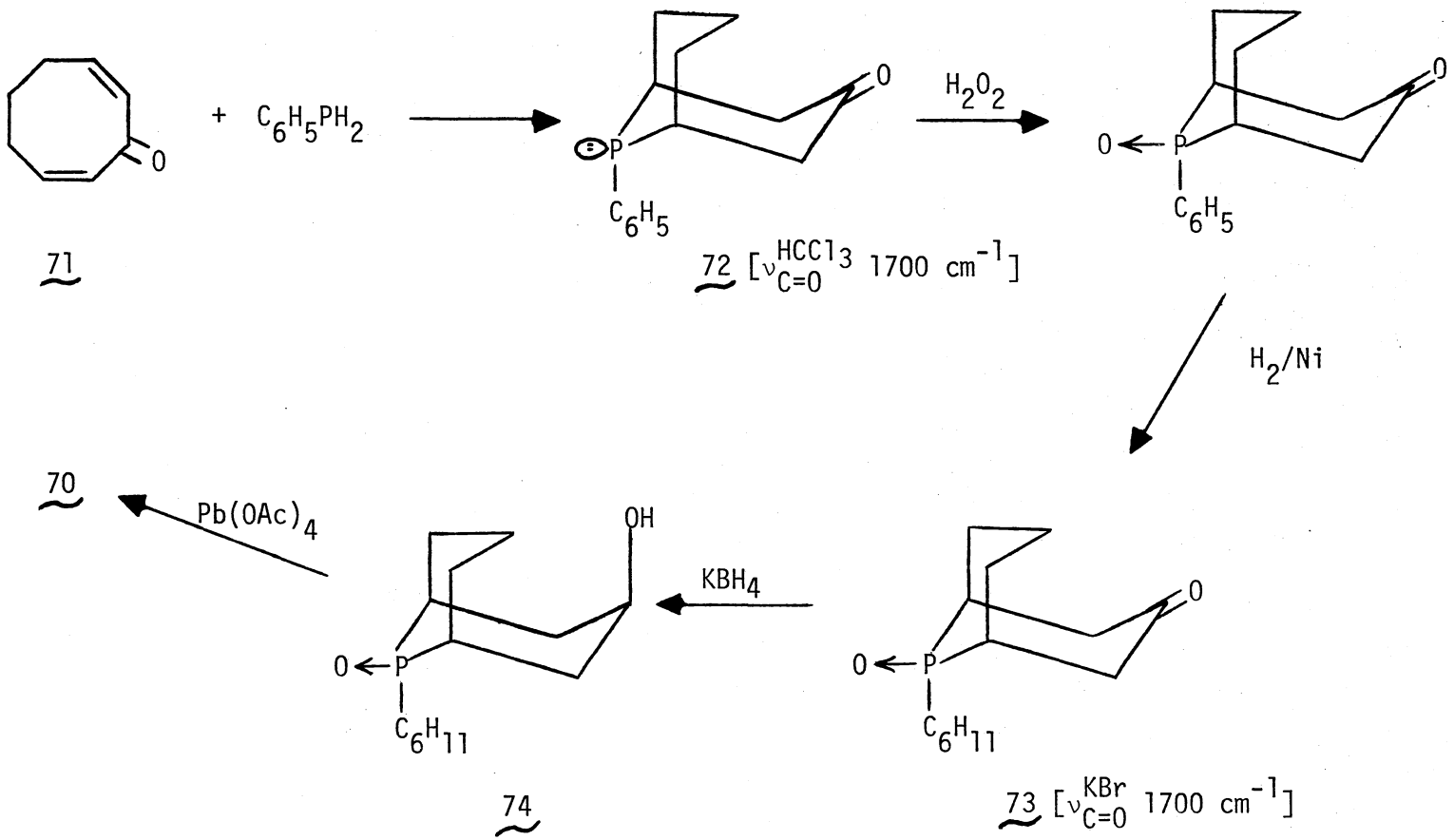


75



76

cyclohexanones.[59,60,61] The most striking difference is that the C-P heterocycles are "flattened". This property is likely conveyed to the bicyclic C-P heterocycles. A C-P bond length of 1.838 Å is recorded



71 72 [$\nu_{C=O}^{HCCl_3}$ 1700 cm^{-1}] 73 [$\nu_{C=O}^{KBr}$ 1700 cm^{-1}] 74 70

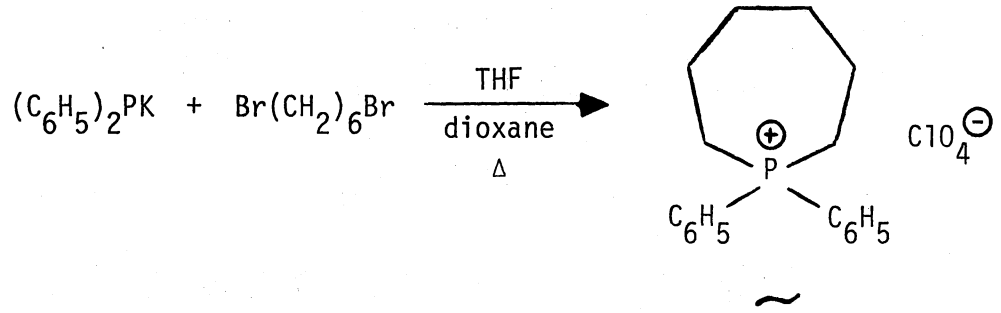
SCHEME III

for 26b and 1.855 Å for 75, and a C-P bond angle (endocyclic) is 98.2° for 26b, 97.7° for 75 and 97.7° for 76. The single crystal data show compounds 26b,[60] 75,[59] and 76[61] to have an axial or pseudo-axial group on phosphorus. This sharp difference from cyclohexyl systems must be due to the size of the P atom as well as C-P bond length.

Synthesis and Chemistry of Selected Seven-Membered Carbon-Phosphorus Heterocycles

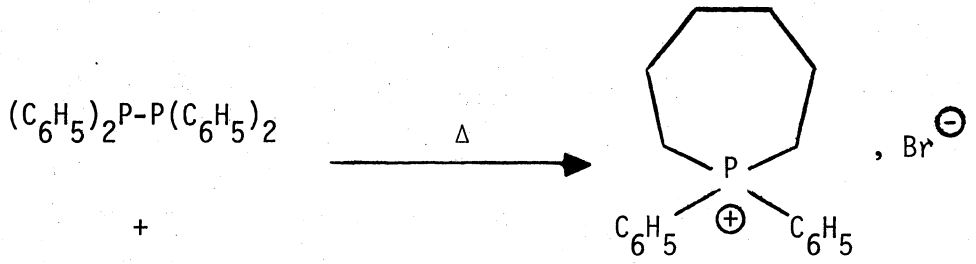
A. Derivatives of Phosphepane

Märkl[47] was the first to prepare 1,1-diphenylphosphepanium perchlorate (77) [m.p. 208° (36%)] by the addition of diphenylphosphinopotassium to a solution of 1,6-dibromohexane. In a later



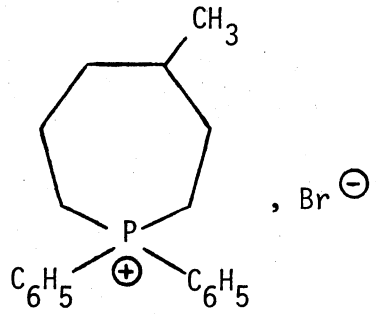
77

communication,[48] the corresponding bromide [m.p. 245-247° (54%)] 78 was synthesized via the cleavage of tetraphenyldiphosphine with 1,6-dibromohexane. In studying the applicability of the above reaction sequence, Marsi and co-workers[54] discovered that C-methylated five-, six-, seven- and eight-membered rings could be prepared in reasonably good yields (26-85%). For example, 4-methyl-1,1-diphenylphosphepanium



78

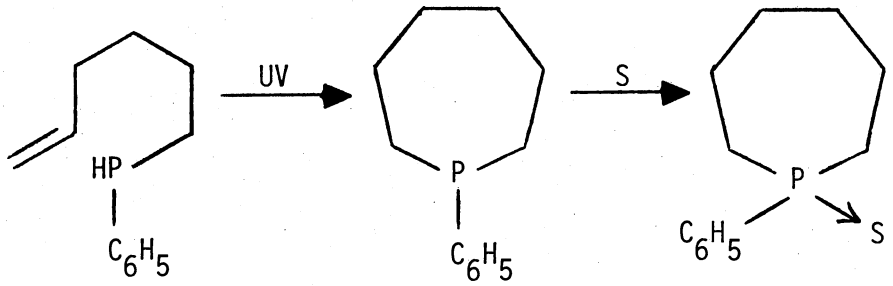
bromide (79) [m.p. 212.5-213.5° (85%)] was obtained from the required dihaloalkane and tetraphenyldiphosphine in boiling o-dichlorobenzene.



79

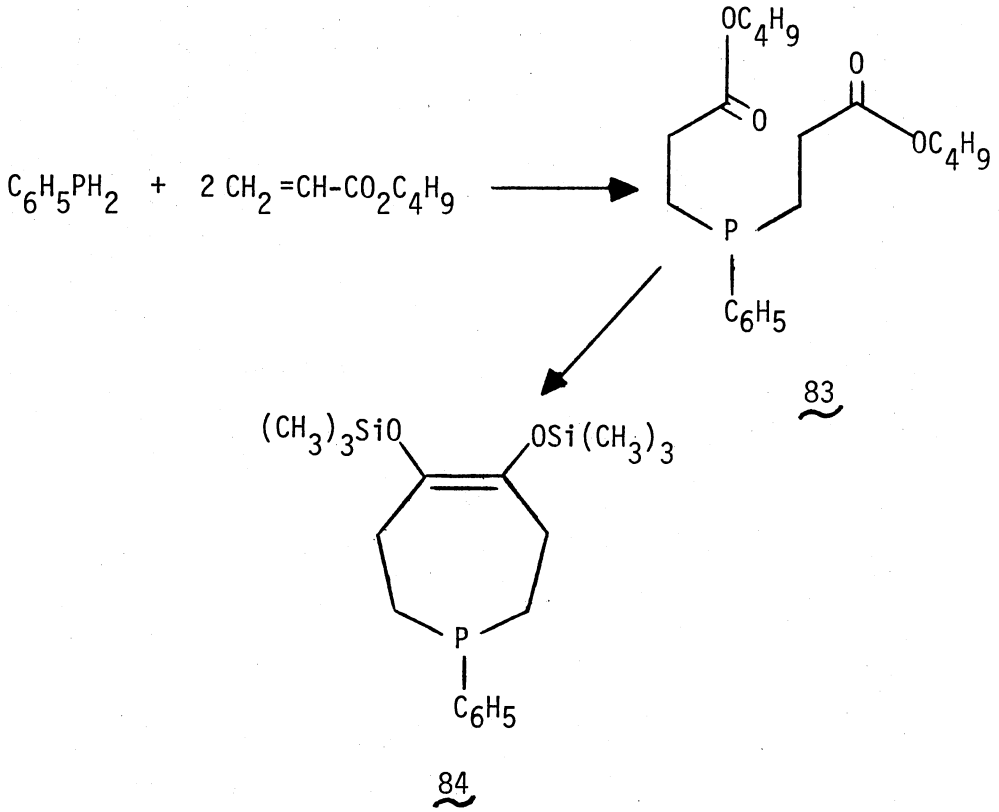
Ultraviolet irradiation of certain terminally unsaturated secondary phosphines yielded cyclic phosphines instead of the expected polymers.[12] 1-Phenylphosphepane (80) [b.p. 106-120°/1.5 mm (41%)] could be obtained from 5-hexenylphenylphosphine (80) upon irradiation. Conversion of phosphepane 81 to the sulfide 82 [m.p. 90.5-91.5° (37%)] was facile. The corresponding five-, six-, and seven-membered rings gave the unexpected cyclic phosphines.

In the development of a synthetic procedure[86] for the preparation of large-ring C-P heterocycles, acyloin condensation of



80 81 82

[(butyloxycarbonyl)alkyl]phenylphosphines gave the corresponding cyclic phosphines in somewhat poor yield. Phenylphosphine was added to butyl acrylate to give tertiary phosphine 83. An acyloin condensa-

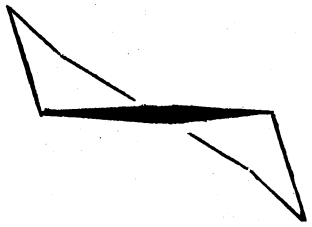


83

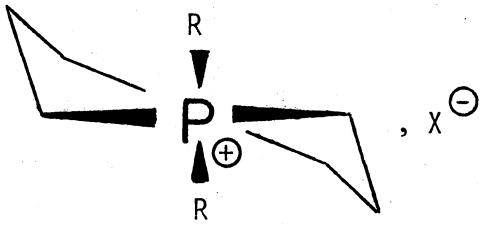
84

tion of 83 with toluene as the solvent (in the presence of trimethylsilyl chloride) yielded bis(trimethylsiloxy)phosphacycloheptene (84) [b.p. 118-128°/0.16 mm (44%)].

Although the exact geometry of the phosphepanium ring is unknown, it is likely to resemble that in cycloheptane 85.[27] Again, an X-ray study of a salt like 86 would be instructive.



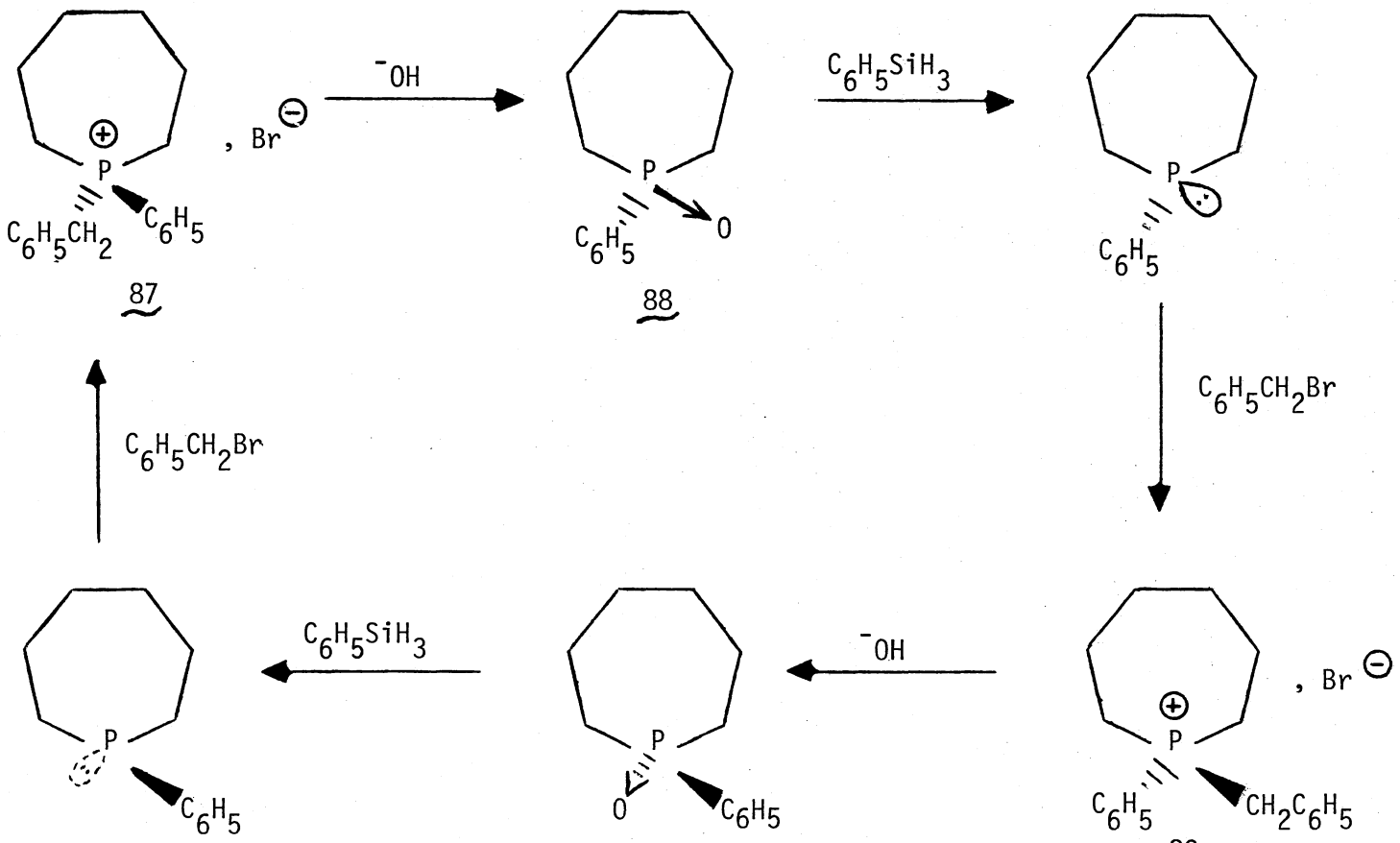
85



86

Relatively few reactions of phosphepanium derivatives have been investigated. An area of active interest in smaller rings is that of C-P cleavage via hydrolysis.[57] Base-mediated debenzylation of cis and trans-1-benzyl-4-methyl-1-phenylphosphepanium salts (Scheme IV) has been shown to proceed with complete inversion of configuration at phosphorus.[57] In Scheme IV the reaction sequence consisted of preparing the salts by the procedure of Märkl.[48] Basic hydrolysis of the salt 87 was followed by reduction of the oxide 88 with phenylsilane, a reagent known to deoxygenate with retention of configuration.[52] Subsequent requaternization to 89 proceeded with retention of configuration. The entire sequence was repeated on the new salt 89 to give a phosphepanium salt with properties identical to those of the starting salt 87.

Since functionalization of the phosphepane ring has not been accomplished easily, additional chemistry is unknown. The next section will treat a few novel, substituted phosphepanes recently reported.

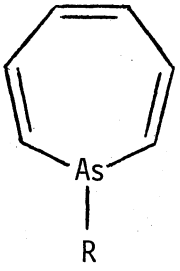


87 88 89

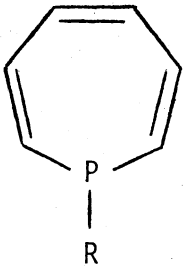
SCHEME IV

B. Derivatives of Phosphepin

Mann and co-workers[46] synthesized derivatives of arsepin (90) and

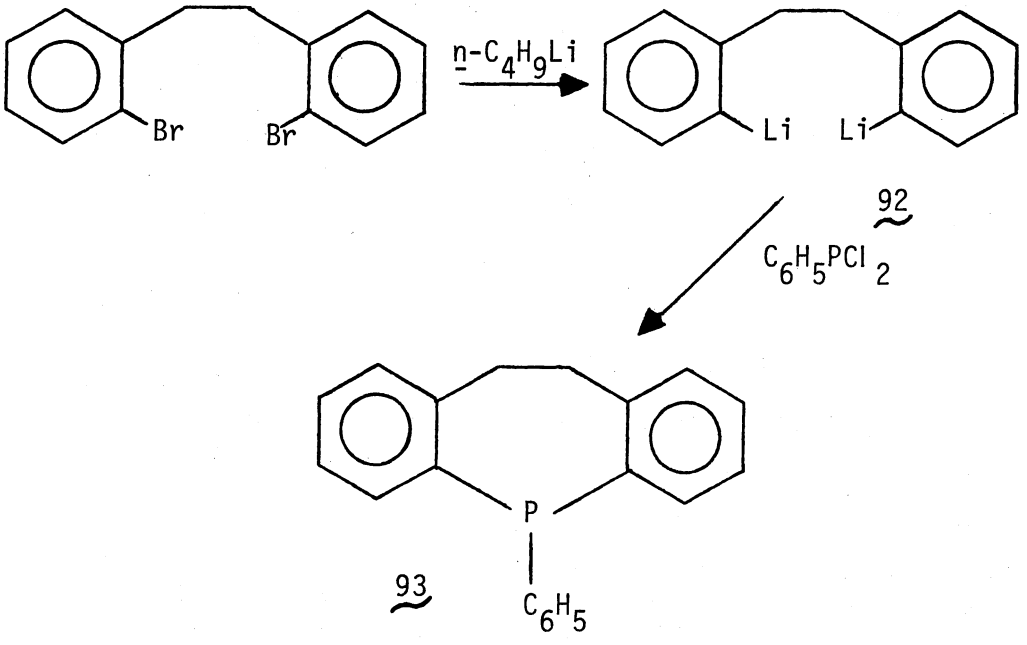


90



91

phosphepin (91) for spectral analysis. The preparative route was identical for both heterocompounds. 1,2-Bis(2-bromophenyl)ethane was caused to react with n-butyllithium to give the dilithium reagent 92

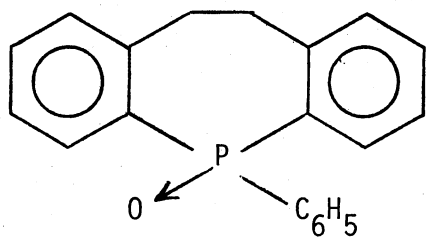


93

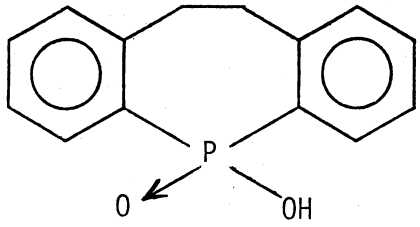
which was treated with phenylphosphonous dichloride in boiling benzene for 3 hours. 10,11-Dihydro-5-phenyl-5H-dibenzo[b,f]phosphepin (93) was

obtained, and characterized via its methiodide [m.p. 251-252°] and phosphine oxide [m.p. 173.5-174.5°] (94).

Later work[75] on the preparation of cyclic phosphinic acid 95

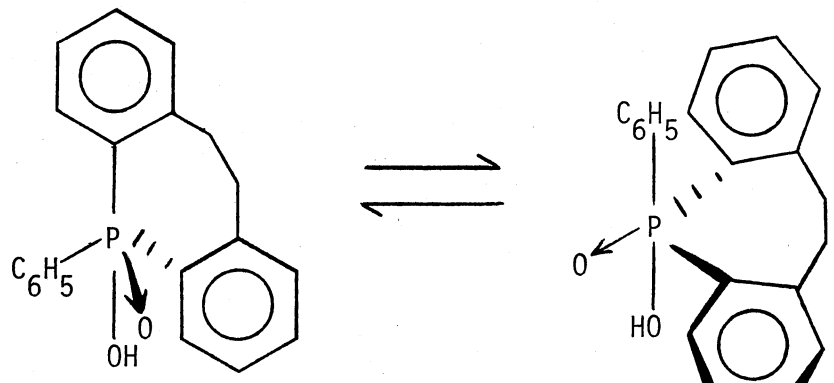


94



95

employed 93 and its oxide 94. Treatment of 94 with molten NaOH and subsequent acidification gave the phosphinic acid 95 [m.p. 246-251° (92%)]. Presumably, the product results from cleavage to remove that aryl group which can form the most stable carbanion. However, since any one of three aryl groups can be cleaved off and usually the departing group is apical[43,58] (assuming a trigonal bipyramidal intermediate[58,65]), bonding of the P atom through two equatorial ligands could place strain on the ring system. Nevertheless it was suggested for six-membered rings that such a rotamer is possible.[53] Thus, it does



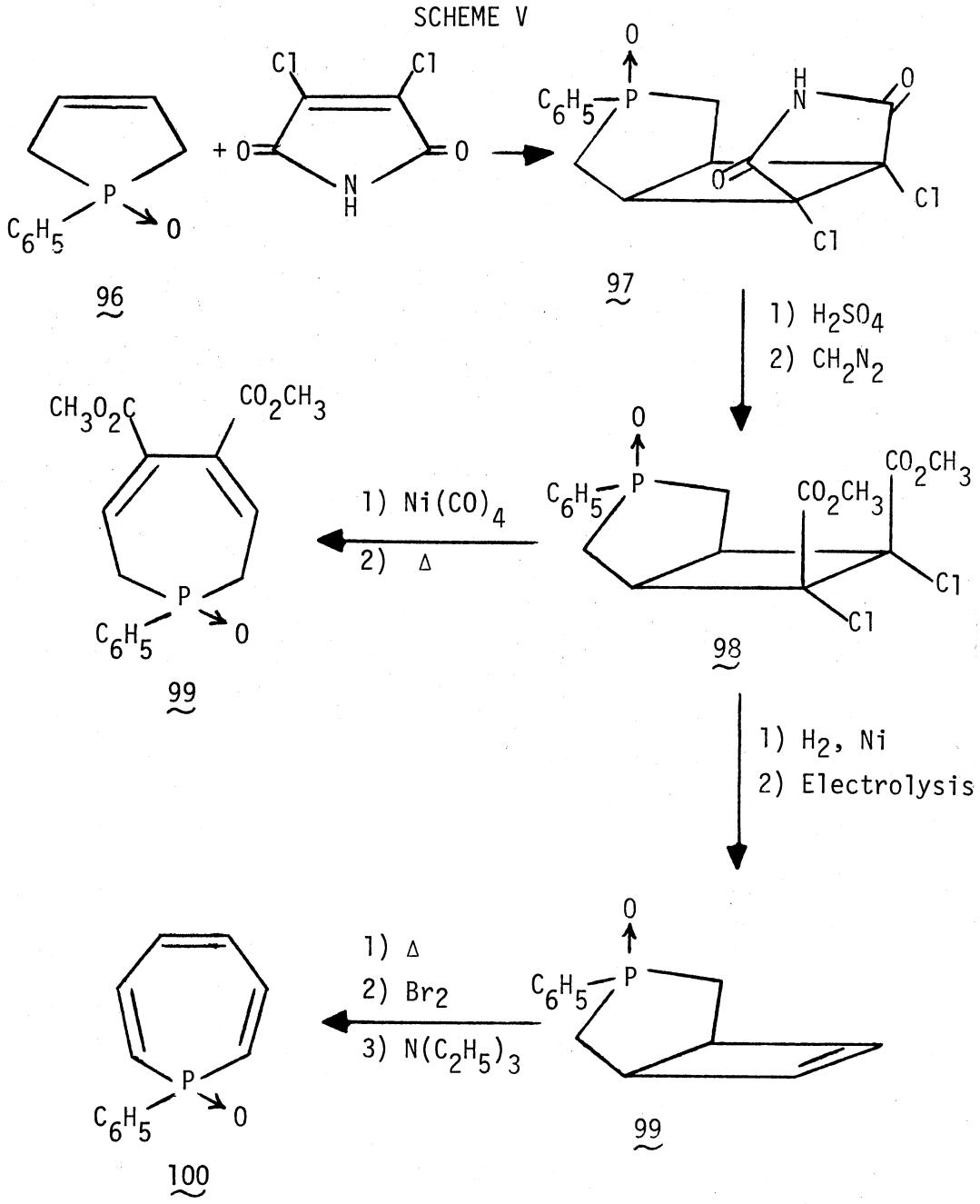
a,e-rotamer

e,e-rotamer

not seem unreasonable that a pseudorotation is possible in the seven-membered ring system also to give an e,e-rotamer.

1-Phenyl-3-phospholene 1-oxide (96) participated in a Diels-Alder reaction (Scheme V) to produce 97 (plus the exo isomer). Acidic

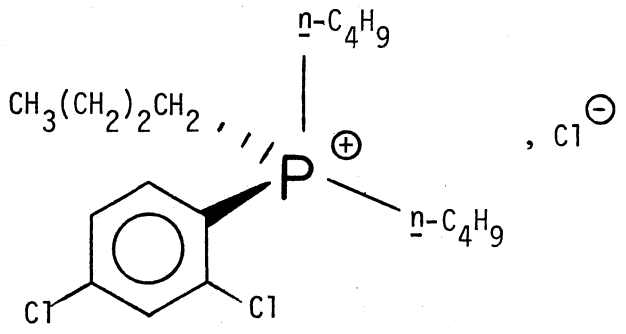
SCHEME V



hydrolysis of the adduct followed by methylation (with diazomethane) gave the diester 98. Treating the diester 98 with $Ni(CO)_4$ and pyrolyzing the product yielded 99 [b.p. 230°/0.1 mm].[50] Hydrogenolysis of 98 followed by electrolysis gave phosphine oxide 99. Subsequent pyrolysis, bromination, and dehydrobromination with triethylamine gave 1-phenyl-phosphepin 1-oxide (100). Interestingly, deoxygenation of 100 could give a completely conjugated C-P heterocyclic phosphine, the aromatic properties of which are unknown.

Biological Activity of Selected Organophosphorus Compounds

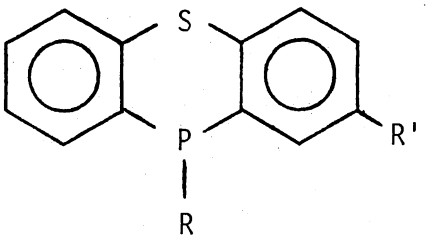
Very few organophosphorus compounds, either open-chain or heterocyclic, have been tested for biological activity. P. Beck[2] in an extensive review of quaternary phosphonium salts cited several applications. Many phosphonium salts have been suggested for the mothproofing of textiles,[44] for plant growth regulation,[64] and in plant protection.[84] One of the most biologically active salts is 2,4-dichlorobenzyltributylphosphonium chloride (101) (phosfon). Recent reviews[17,62]



101

have pointed out the significant contribution of organophosphorus compounds in the area of insecticides and pesticides.

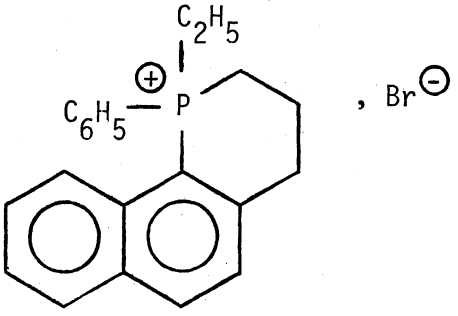
A few heterocyclic phosphorus compounds have shown biological activity recently. Depression of spontaneous activity in mice was caused by 102.[83]



102

R = Cl, SCH_3, OCH_3
R' = $(CH_2)_3N(CH_3)_2$

Preparation[6] and testing of the phosphinolinium system 103 has con-



103 (NCS 145185)

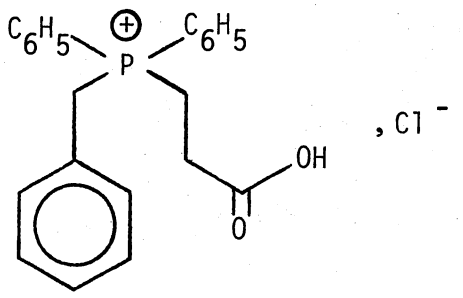
firmed activity against the 3P531[C] system (P388 lymphocytic leukemia cell line). The field appears ripe for development by synthetic and theoretical, as well as, biological chemists.

CHAPTER II

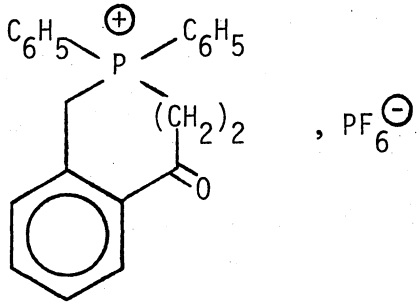
RESULTS AND DISCUSSION

Synthetic methods for the preparation of organophosphorus heterocycles containing a keto function are very rare and laborious.[13,21,34,35,36,68] One objective of this research was to develop an entry into functionalized, bicyclic C-P heterocycles.

A series of substituted-benzyl(2-carboxyethyl)diphenylphosphonium salts 104-108 (Table I) were found to undergo intramolecular acylation



104



109

in the presence of 115% polyphosphoric acid (PPA) to yield substituted 2,3,4,5-tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium hexafluorophosphates 109-113 (Table II). Characterization of these heretofore unknown C-P heterocycles consisted of IR (Table III), PMR (Table IV), ^{31}PMR (Table V), mass spectral (Table VI) and elemental analyses. Chemical degradation of 109 to yield 114 confirmed the basic C-P heterocyclic structure.

TABLE I

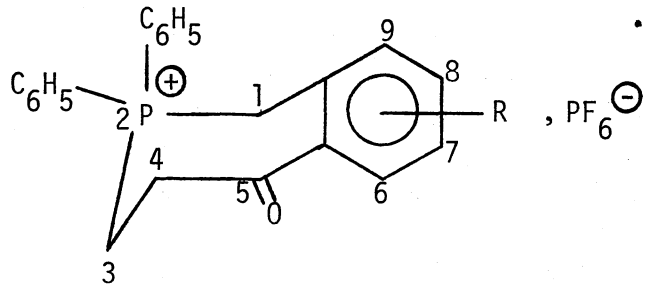
SUBSTITUTED BENZYL(2-CARBOXYETHYL)DIPHENYLPHOSPHONIUM SALTS 104-108

Cpd. Name	Cpd.	m.p., °C	Yield (%)
Benzyl(2-carboxyethyl)diphenylphosphonium Chloride	104	223-225	58
(3-Methylbenzyl)-(2-carboxyethyl)-diphenylphosphonium Chloride	105	187-190	34.5
(3-Chlorobenzyl)-(2-carboxyethyl)-diphenylphosphonium Chloride	106	225-229	40
(4-tert-Butylbenzyl)-(2-carboxyethyl)-diphenylphosphonium Chloride	107	167.5-171	33.4
(2,5-Dimethylbenzyl)-(2-carboxyethyl)-diphenylphosphonium Chloride	108*	----	----

*See Experimental.

TABLE II

2,3,4,5-TETRAHYDRO-5-OXO-2,2-DIPHENYL-1H-2-BENZOPHOSPHEPINIUM HEXAFLUOROPHOSPHATES



Cpd. Name	Cpd.	R	m.p.(°C)	Yield (%)
2,3,4,5-Tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate	109	H	126-129	64
2,3,4,5-Tetrahydro-8-methyl-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate	110	8-CH_3	187-190	37
8-Chloro-2,3,4,5-tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate	111	8-Cl	186-188	58
7-tert-Butyl-2,3,4,5-tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate	112	7-$C(CH_3)_3$	92	44.5
2,3,4,5-Tetrahydro-6,9-dimethyl-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate	113	6,9-CH_3	227	63

TABLE III

INFRARED SPECTRA OF PRODUCTS[a,b]

Cpd.	O-H	C=O	C-O	P-C_6H_5	Miscellaneous Bands
119	2860 (m) 2600 (w)	1740 (s)	1223 (m)	1140 (s), 1115 (s), 996 (w), 726 (s)	1366 (s), 1340 (s), 950 (w), 910 (w), 858 (w), 816 (m), 751 (s), 740 (s), 689 (s)
120	2860 (s) 2620 (s)	1740 (s) 1710 (s)	1222 (s)	1440 (s), 1113 (s), 996 (m), 726 (s)	1580 (m), 1482 (m), 1387 (s), 1346 (s), 1168 (s), 1019 (m), 866 (w), 842 (w), 792 (m), 777 (m), 755 (s), 743 (s), 693 (s)
121	2950 (b)	1710 (s)	1272 (m)	1438 (m), 1115 (m), 732 (m)	1417 (m), 1204 (w), 1162 (w), 1043 (w), 977 (w), 882 (w), 845 (s), 835 (s), 763 (w), 743 (m), 688 (m)

TABLE III (Continued)

Cpd.	O-H	C=O	C-O	P-C_6H_5	Miscellaneous Bands
122	2700 (b)	1700 (s)	1230 (s)	1437 (m), 1115 (s), 996 (w), 722 (m)	1422 (m), 1330 (w), 1174 (s), 1021 (m), 909 (m), 886 (m), 833 (w), 793 (w), 774 (s), 742 (m), 696 (w), 687 (m)
145				1438 (s), 1115 (s), 996 (w), 716 (s)	3340 (s), 2920 (m), 2840 (m), 1620 (w), 1480 (w), 1350 (w), 1190 (w), 1170 (w), 927 (m), 912 (s), 903 (s), 797 (m), 791 (m), 758 (s), 750 (s), 743 (s) 638 (s)
147				1440 (s), 1117 (s) 1003 (w)	2990 (w), 2900 (w), 1580 (w), 1418 (m), 1343 (w), 1320 (m), 1303 (m), 1190 (w), 1167 (w), 958 (s), 926 (s), 873 (s), 840 (b), 776 (w), 763 (w), 748 (s), 742 (s), 690 (s)

TABLE III (Continued)

Cmpd.	O-H	C=O	C-O	P-C_6H_5	Miscellaneous Bands
104	3370 (m) 2820 (s) 2630 (m)	1720 (s)	1233 (s)	1440 (s), 1112 (s)	1496 (m), 1415 (s), 1180 (s), 893 (m), 806 (m), 743 (s), 692 (s)
105	3390 (m) 2790 (s) 2550 (s)	1730 (s)	1234 (s)	1447 (s), 1115 (s) 1002 (m)	1496 (m), 1410 (m), 1390 (m), 1022 (m), 961 (m), 915 (s), 748 (s), 688 (s)
106	3380 (s) 2840 (s)	1720 (s)	1220 (s)	1110 (s), 997 (m)	1630 (m), 1580 (m), 1465 (m), 1417 (s), 1335 (w), 1310 (w), 1170 (s), 1076 (m), 1042 (w), 953 (w), 881 (s), 815 (s), 795 (s), 748 (s), 698 (s), 686 (s)
107	3360 (w) 2790 (s) 2520 (m)	1730 (s)	1235 (m)	1440 (s), 1117 (s)	1390 (s), 1337 (m), 1193 (m), 848 (s), 745 (s), 691 (s)
108	3320 (w) 2940 (m)	1730 (s)	1243 (s)	1443 (s), 1115 (s) 1000 (m)	1580 (w), 1192 (s), 1048 (m), 844 (sb), 747 (sb), 691 (sb)

TABLE III (Continued)

Cmpd.	O-H	C=O	C-O	P-C_6H_5	Miscellaneous Bands
127				1436 (s), 1117 (s) 997 (w)	3420 (m), 2870 (s), 1410 (m), 1330 (w), 1308 (m), 1239 (w), 1188 (w), 1147 (w), 1072 (w), 1030 (w), 928 (m), 902 (s), 851 (m), 795 (m) 749 (s), 706 (s), 693 (s)
109		1670 (m)		1115 (m), 998 (w) 735 (m)	3380 (w), 2880 (w), 2330 (w), 1600 (w), 1460 (m), 1390 (w), 1336 (w), 1255 (m), 1181 (m), 931 (w), 840 (b), 796 (m), 774 (w), 746 (m), 735 (m), 688 (m)
110		1660 (s)		1439 (s), 1112 (s) 730 (m)	3400 (w), 2950 (w), 1610 (m), 1406 (w), 1317 (w), 1265 (s), 1183 (w), 1139 (w), 844 (b), 761 (w), 745 (m), 737 (m), 688 (m)

TABLE III (Continued)

Cmpd.	O-H	C=O	C-O	P-C_6H_5	Miscellaneous Bands
111		1710 (s)		1437 (s), 1114 (s)	2900 (m), 1580 (m), 1470 (m), 1407 (m), 1263 (m), 1193 (m), 840 (b), 740 (s), 687 (s)
112		1680 (s)		1446 (s), 1115 (s)	3400 (m), 2970 (m), 1590 (m), 1410 (m), 1322 (w), 1250 (w), 1002 (w), 843 (s), 743 (m), 690 (m)
113		1680 (s)		1440 (s), 1112 (s) 996 (m)	3360 (m), 2920 (m), 1395 (m), 1322 (w), 1258 (s), 1166 (m), 854 (s), 833 (s), 793 (m), 746 (s), 687 (s)

TABLE III (Continued)

Cmpd.	O-H	C=O	C-O	P-C_6H_5	Miscellaneous Bands
114		1670 (s)		1438 (m), 1120 (s) 728 (s), 717 (s)	3020 (w), 1580 (w), 1555 (w), 1477 (w), 1413 (m), 1338 (m), 1276 (w), 1238 (s), 1192 (s) P=O, 1073 (m), 971 (s), 953 (m), 835 (m), 795 (s), 776 (m), 748 (s), 737 (s), 696 (s)

[a]Samples were as KBr pellets, except for 108 which was taken as a melt and 114 which was taken as a thin film.

[b]Values given are in reciprocal centimeters (cm^{-1}). The intensity of each peak is indicated as follows: (s) - strong, (m) - medium, (w) - weak, (b) - broad.

TABLE IV

PMR COUPLING CONSTANTS AND CHEMICAL SHIFTS OF PRODUCTS

Structure	Cpd.	Plate	Solvent	δ (values) (p.p.m.)[a]	Assignments
$(C_6H_5)_3\overset{\oplus}{P}\underbrace{CH_2CH_2}_{a}CO_2H,\ Cl^{\ominus}$	119		$DCCl_3$ (5 drops of CF_3CO_2H)	2.72-3.06 (m)	CH_2 (a)
				3.32-3.68 (m)	CH_2 (a)
				7.52-8.04 (m)	ArH
$(C_6H_5)_2\overset{CH_3}{\overset{\vert}{\overset{\oplus}{P}}}CH_2CH_2CO_2H,\ PF_6^{\ominus}$	121		$DCCl_3$ (5 drops of CF_3CO_2H)	2.28 (d), J_{PCH} = 14 Hz	CH_3
				2.62-3.38 (m)	CH_2CH_2
				7.50-8.02 (m)	ArH
$(C_6H_5)_3\overset{\oplus}{P}\underbrace{CH_2}_{c}\underbrace{CH_2}_{b}\underbrace{CH_2}_{a}CO_2H,\ Cl^{\ominus}$	120		CF_3CO_2H	2.87 (t), J_{CH-CH} = 7 Hz	CH_2 (a)
				1.98-2.48 (m)	CH_2 (b)
				3.12-3.56 (m)	CH_2 (c)
				7.60-8.08	ArH

TABLE IV (Continued)

Structure	Cpd.	Plate	Solvent	δ (values) (p.p.m.)[a]	Assignments
$(C_6H_5)_2\overset{\oplus}{P}(\overset{CH_3}{|})CH_2CH_2CH_2CO_2H$, $Cl^{\ominus}$ (c b a)	122		CF_3CO_2H	2.45 (d), J_{PCH} = 14 Hz	CH_3
				2.69 (t), J_{HCCH} = 7 Hz	CH_2 (a)
				1.66-2.12 (m)	CH_2 (b)
				2.69-3.08 (m)	CH_2 (c)
				7.42-7.92 (m)	ArH
$(C_6H_5)_3\overset{\oplus}{P}CH_3$, $Cl^{\ominus}$	145		$DCCl_3$	3.28 (d), J_{PCH} = 14 Hz	CH_3
				7.56-7.94 (m)	ArH
$(C_6H_5)_2\overset{\oplus}{P}(CH_3)_2$, $PF_6^{\ominus}$	147		$DCCl_3$ (5 drops of CF_3CO_2H)	2.48 (d), J_{PCH} = 14 Hz	CH_3
				7.64-7.98 (m)	ArH

TABLE IV (Continued)

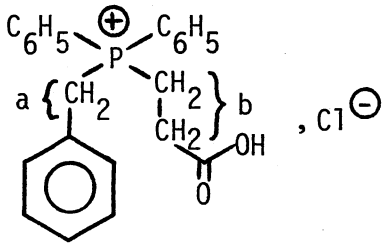
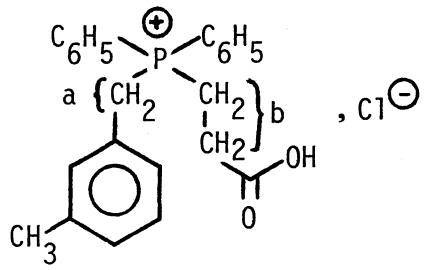
Structure	Cpd.	Plate	Solvent	δ (values) (p.p.m.)[a]	Assignments
	104	I	$DCCl_3$ (5 drops of CF_3CO_2H)	2.50-3.24 (m) 4.20 (d), J_{PCH} = 14 Hz 6.72-6.94 (m) 7.10-7.40 (m) 7.40-7.98 (m)	CH_2CH_2 (b) CH_2 (a) ArH (2) ArH (3) ArH (10)
	105	IV	$DCCl_3$ (5 drops of CF_3CO_2H)	2.14 (s) 2.46-3.24 (m) 4.17 (d), J_{PCH} = 14 Hz 6.46-6.84 (m) 7.00-7.26 (m) 7.40-8.00 (m)	CH_3 CH_2CH_2 (b) CH_2 (a) ArH (2) ArH (2) ArH (10)

TABLE IV (Continued)

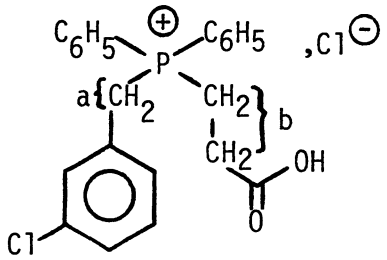
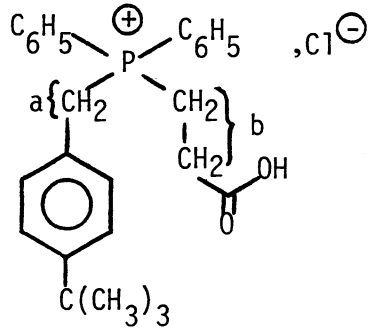
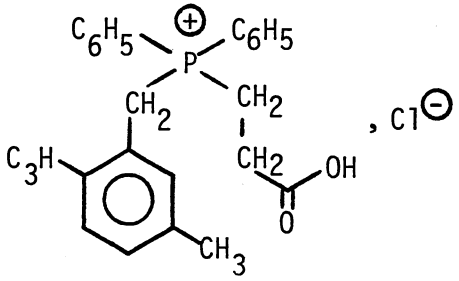
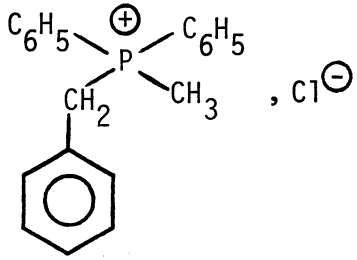
Structure	Cpd.	Plate	Solvent	δ (values) (p.p.m.)[a]	Assignments
	106	VI	$DCCl_3$ (5 drops of CF_3CO_2H)	2.56-3.34 (m) 4.32 (d), J_{PCH} = 14 Hz 6.66-7.00 (m) 7.00-8.04 (m)	CH_2CH_2 (b) CH_2 (a) ArH (2) ArH (12)
	107	IX	D_3CSOCD_3	1.23 (s) 3.00-3.20 (m) 4.82 (d), J_{PCH} = 14 Hz 6.86-7.08 (m) 7.12-7.34 (m) 7.54-8.04 (m)	$C(CH_3)_3$ CH_2CH_2 (b) CH_2 (a) ArH (2) ArH (2) ArH (10)

TABLE IV (Continued)

Structure	Cpd.	Plate	Solvent	δ (values) (p.p.m.)[a]	Assignments
	108	XI	$DCCl_3$ (5 drops of CF_3CO_2H)	No strict assignments made for cpd. 108*	
	127		$DCCl_3$	2.76 (d), J_{PCH} = 14 Hz 4.96 (d), J_{PCH} = 14 Hz 7.00-8.12 (m)	CH_3 CH_2 ArH

*See experimental

TABLE IV (Continued)

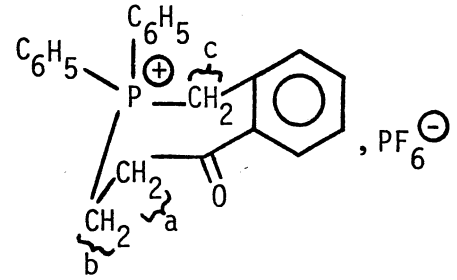
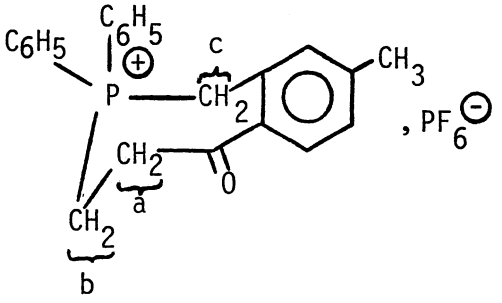
Structure	Cpd.	Plate	Solvent	δ (values) (p.p.m.)[a]	Assignments
	109	XIII	$DCCl_3$ (5 drops of CF_3CO_2H)	3.16 (s) 2.93-3.56 (m) 4.35 (d), J_{PCH} = 14 Hz 6.96-7.02 (m) 7.42-7.98 (m)	CH_2 (a) CH_2 (b) CH_2 (c) ArH (1) ArH (13)
	110	XVI	$DCCl_3$ (5 drops of CF_3CO_2H)	2.35 (s) 3.19 (s) 2.94-3.62 (m) 4.34 (d), J_{PCH} = 14 Hz 6.89 (s) 7.30-8.06 (m)	CH_3 CH_2 (a) CH_2 (b) CH_2 (c) ArH (1) ArH (12)

TABLE IV (Continued)

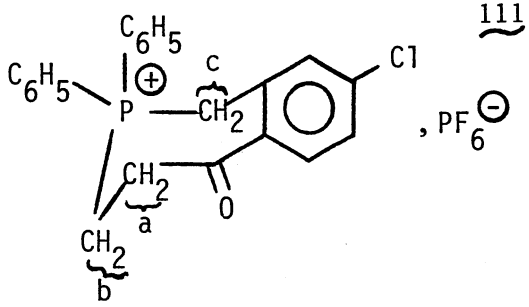
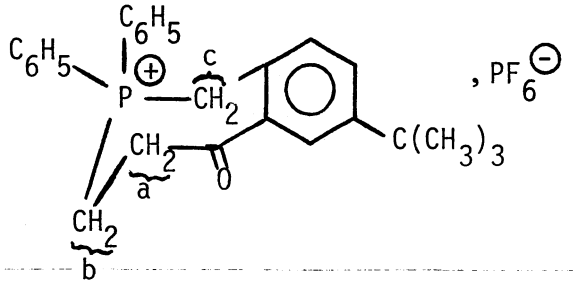
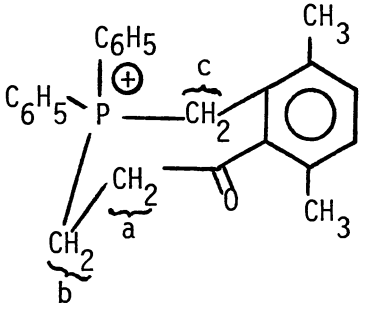
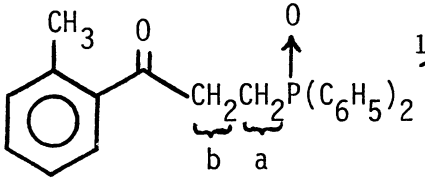
Structure	Cpd.	Plate	Solvent	δ (values) (p.p.m.)[a]	Assignments
	111	XVIII	D_3CSOCD_3	3.45 (s)	CH_2 (a)
				3.00-3.76 (m)	CH_2 (b)
				5.06 (d), J_{PCH} = 14 Hz	CH_2 (c)
				7.08-8.32 (m)	ArH
	112	XX	D_3CSOCD_3 (5 drops of CF_3CO_2H)	1.29 (s)	CH_3
				3.44 (s)	CH_2 (a)
				3.08-3.64 (m)	CH_2 (b)
				5.23 (d), J_{PCH} = 14 Hz	CH_2 (c)
				5.27 (d), J_{PCH} = 14 Hz	CH_2 (c)
				6.12-8.16 (m)	ArH

TABLE IV (Continued)

Structure	Cpd.	Plate	Solvent	δ (values) (p.p.m.)[a]	Assignments
	113	XXII	$DCCl_3/CF_3CO_2H$	1.70 (s)	CH_3
				2.38 (s)	CH_3
				3.12 (s)	CH_2 (a)
				2.94-3.30 (m)	CH_2 (b)
				4.14 (d), J_{PCH} = 14 Hz	CH_2 (c)
				7.20-8.08 (m)	ArH
	114	XXIV	$DCCl_3$	2.45 (s)	CH_3
				2.58-2.92 (m)	CH_2 (a)
				3.06-3.42 (m)	CH_2 (b)
				7.06-7.94 (m)	ArH

[a]The multiplicity of each peak is indicated as follows: singlet, (s); doublet, (d); triplet, (t); multiplet, (m).

TABLE V

^{31}PMR CHEMICAL SHIFTS OF PRODUCTS[a]

Cpd.	Solvent	δ (value) (ppm)
104	$DCCl_3/CF_3CO_2H$ (4:1)	-25.05
105	CH_3SOCH_3/CF_3CO_2H (10:1)	-26.04
106	CH_3SOCH_3/CF_3CO_2H (10:1)	-26-72
107	C_2H_5OH	-25.45
108	$HCCl_3/CF_3CO_2H$ (4:1)	-27.32, -24.60, -20.32
109	$DCCl_3/CF_3CO_2H$ (4:1)	-21.51
110	$HCCl_3/CF_3CO_2H$ (4:1)	-21.48
111	CH_3COCH_3	-21.04
112	$HCCl_3$	-29.13, -21.39
113	$HCCl_3/CF_3CO_2H$ (4:1)	-20.07

[a]Chemical shifts are relative to 85% H_3PO_4 as the external standard.

TABLE VI

INTENSE IONS IN THE MASS SPECTRA OF PRODUCTS[a]

Cpd.	Pressure (mm)	Probe Temp. (°C)	Source Temp. (°C)	M^*-146[b] (RI %)	M^*-122[c] (RI %)	M^*-108[d] (RI %)	m/e (RI %)
119	5.2×10^{-6}	125	190			262 (100)	263 (21), 261 (12), 184 (10), 183 (14), 182 (69), 162 (10), 108 (22), 107 (41), 77 (9), 72 (28), 55 (21), 51 (17)
121	2.5×10^{-5}	150	220			200 (100)	216 (19), 215 (39), 201 (58), 199 (31), 185 (63), 184 (16), 183 (98), 152 (12), 121 (15), 107 (51), 91 (10), 85 (12), 77 (10), 52 (36), 51 (51)
120	6×10^{-6}	150	200		262 (37)		263 (13), 184 (13), 183 (100), 108 (13), 107 (7), 77 (4)

TABLE VI (Continued)

Cpd.	Pressure (mm)	Probe Temp. (°C)	Source Temp. (°C)	M^*-146[b] (RI %)	M^*-122[c] (RI %)	M^*-108[d] (RI %)	m/e (RI %)
122	4×10^{-6}	170	200		200 (100)		286 (46), 216 (24), 215 (64), 202 (15), 201 (36), 199 (18), 185 (35), 184 (10), 183 (57), 108 (6), 107 (9), 77 (11),
145	6×10^{-6}	210	200				263 (25), 262 (100), 261 (13), 185 (13), 184 (16), 183 (76), 115 (5), 108 (23), 107 (17), 77 (10), 51 (16)
147	2.2×10^{-6}	210	200				320 (35), 319 (49), 301 (12), 299 (12), 297 (22), 217 (35), 215 (12), 214 (30), 213 (100), 201 (40), 200 (30), 199 (18), 185 (13), 183 (40), 178 (12), 165 (15), 123 (19), 121 (20), 109 (15), 107 (40), 91 (22), 85 (16), 77 (41), 51 (11)

TABLE VI (Continued)

Cpd.	Pressure (mm)	Probe Temp. (°C)	Source Temp. (°C)	M^*-146[b] (RI %)	M^*-122[c] (RI %)	M^*-108[d] (RI %)	m/e (RI %)
104	6×10^{-6}	135	260			276 (81)	277 (17), 275 (14), 186 (14), 185 (100), 184 (14), 183 (96), 107 (12), 91 (24), 77 (5)
105	2.8×10^{-6}	110	240			290 (25)	202 (30), 201 (100), 185 (19), 183 (22), 124 (14), 105 (18), 91 (15), 86 (39), 84 (76), 78 (17), 77 (40), 51 (18), 48 (75)
106	2.8×10^{-6}	140	240			310 (14)	202 (12), 201 (38), 185 (23), 184 (43), 183 (15), 182 (100), 152 (11), 125 (18), 107 (15), 78 (16), 77 (23), 51 (10)
107	1×10^{-5}	130	200			232 (62)	333 (17), 186 (11), 185 (61), 184 (10), 183 (90), 152 (11), 148 (21), 147 (100), 132 (45), 131 (10), 117 (51), 115 (11), 107 (11), 91 (21), 77 (8)

TABLE VI (Continued)

Cpd.	Pressure (mm)	Probe Temp. (°C)	Source Temp. (°C)	M^*-146[b] (RI %)	M^*-122[c] (RI %)	M^*-108[d] (RI %)	m/e (RI %)
108	1×10^{-5}	40	175				262 (10), 234 (10), 87 (12), 85 (66), 83 (100), 39 (10), 38 (16), 37 (31), 36 (10), 35 (19), 33 (17)
127	3×10^{-6}	160	260				277 (12), 276 (59), 275 (11), 186 (16), 185 (100), 184 (13), 183 (81), 153 (11), 107 (14), 91 (38), 77 (7), 65 (11)
109	2.4×10^{-6}	165	210	330 (100)			332 (23), 329 (15), 302 (20), 301 (74), 183 (49), 167 (13), 128 (15), 115 (20), 107 (33), 91 (8), 77 (7)

TABLE VI (Continued)

Cpd.	Pressure (mm)	Probe Temp. (°C)	Source Temp. (°C)	M^*-146[b] (RI %)	M^*-122[c] (RI %)	M^*-108[d] (RI %)	m/e (RI %)
110	2.4×10^{-6}	160	240	344 (91)			345 (24), 343 (14), 316 (14), 315 (48), 201 (29), 185 (21), 184 (14), 183 (100), 181 (31), 158 (14), 152 (14), 142 (14), 141 (19), 133 (14), 131 (29), 129 (24), 128 (29), 116 (38), 115 (53), 108 (14), 107 (95), 91 (48), 88 (19), 78 (24), 77 (43), 51 (29),
111	3×10^{-6}	160	200	364 (91)			366 (29), 365 (24), 346 (19), 337 (29), 336 (19), 335 (71), 201 (24), 185 (19), 183 (52), 164 (14), 162 (29), 107 (100), 88 (43), 85 (24), 77 (5), 40 (19)

TABLE VI (Continued)

Cpd.	Pressure (mm)	Probe Temp. (^{o}C)	Source Temp. (^{o}C)	$M^{*}-146$[b] (RI %)	$M^{*}-122$[c] (RI %)	$M^{*}-108$[d] (RI %)	m/e (RI %)
112	2.3×10^{-6}	180	180	386 (12)			357 (30), 330 (25), 301 (27), 253 (100), 234 (21), 221 (23), 220 (16), 204 (29), 203 (29), 202 (12), 201 (71), 133 (17), 132 (21), 108 (36), 107 (40), 105 (29), 91 (21), 77 (43), 57 (25), 51 (29)
113	2.5×10^{-5}	150	200	358 (100)			359 (25), 357 (12), 343 (42), 330 (18), 329 (42), 215 (12), 201 (22), 200 (23), 185 (18), 183 (55), 157 (15), 156 (12), 129 (13), 115 (17), 107 (42), 91 (12) 77 (12)

TABLE VI (Continued)

Cpd.	Pressure (mm)	Probe Temp. (°C)	Source Temp. (°C)	M^*-146[b] (RI %)	M^*-122[c] (RI %)	M^*-108[d] (RI %)	m/e (RI %)
114	2.4×10^{-6}	105	280				348 (30), 229 (16), 219 (11), 215 (9), 203 (15), 202 (100), 201 (32), 119 (75), 91 (50), 77 (23), 65 (14), 51 (13)

[a] All spectra were recorded at 70 eV; M^* symbolizes the cation portion of the particular molecule since at 70 eV (ionization potential) the molecular cation M^+ was not observed in either the open-chain or cyclic compounds.

[b] The symbol M^*-146 refers to a m/e corresponding to the loss of hexafluorophosphoric acid (m/e 146).

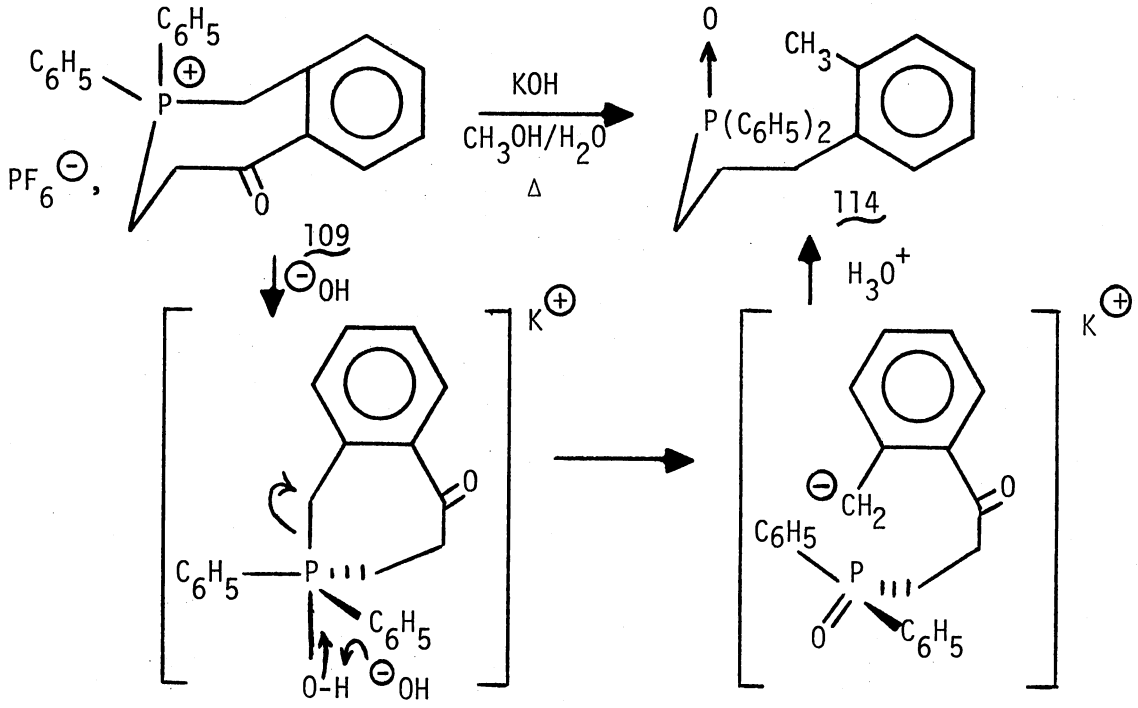
[c] The symbol M^*-122 refers to a m/e corresponding to the loss of 4-chlorobutanoic acid (m/e 122).

[d] The symbol M^*-108 refers to a m/e corresponding to the loss of 3-chloropropanoic acid (m/e 108).

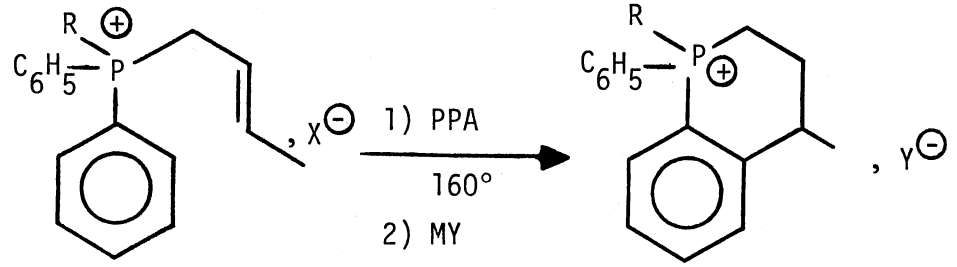
TABLE VII

ELEMENTAL ANALYSIS OF PRODUCTS

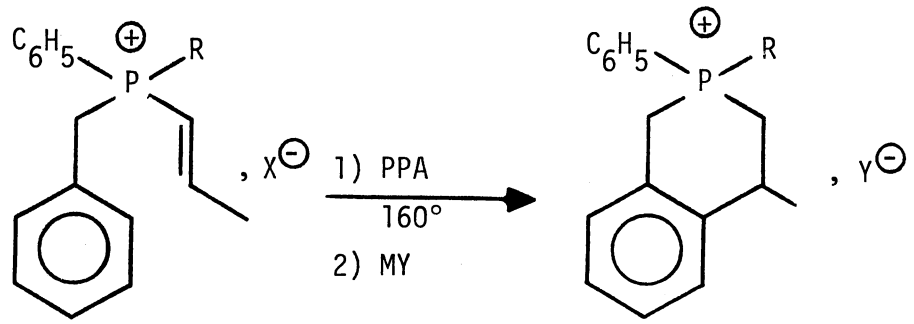
Cpd.	Molecular Formula	% P Calc.	% P Found
121	$C_{16}H_{18}F_6O_2P_2$	14.82	14.87
122	$C_{17}H_{20}ClO_2P$	9.60	9.69
147	$C_{14}H_{16}F_6P_2$	17.15	17.29
104	$C_{22}H_{22}ClO_2P$	8.05	8.04
105	$C_{23}H_{24}ClO_2P \cdot CH_2Cl_2$	6.44	6.20
106	$C_{20}H_{21}Cl_2O_2P \cdot H_2O$	7.08	6.95
107	$C_{26}H_{30}ClO_2P$	7.03	7.25
127	$C_{20}H_{20}ClP$	9.49	9.80



Recent work[15] on the cyclization of alkenyl substituted phosphonium salts 115 and 116, to give the corresponding phosphinolinium 117



115 117



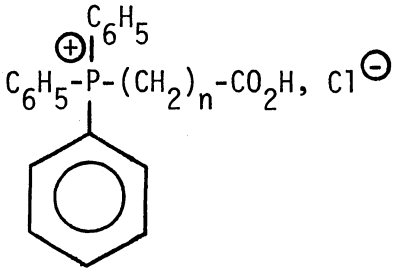
116 118

and isophosphinolinium 118 salts with PPA demonstrated the utility of the technique for cyclization of phosphonium salts with alkenyl side chains. However, the cyclization to the ketones 109-113 required much higher temperatures and longer reaction times.

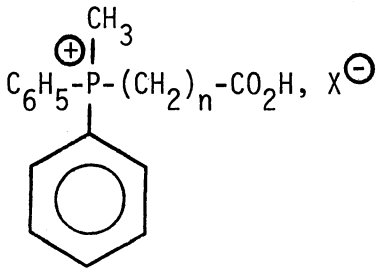
Several reviews[40,63,78] have set forth the versatility of PPA as an acylating agent. Among the more useful specialties of this reagent are the ability to solvate organic compounds at high temperature, the strong dehydrating ability, and the production of relatively few side reactions in many acylations. Utilization of PPA does not require any special equipment and decomposition of the reaction mixture is easily accomplished with ice water. Commercially available 115% PPA from the FMC Corporation[76] was employed in our cyclizations.

Preparation and Attempted Cyclization of ω-Carboxyalkyl-Substituted Phosphonium Salts 104-108 and 119-122

Initially, the ω-carboxyalkylphosphonium chlorides 119-120 and the ω-carboxyalkylmethyldiphenylphosphonium salts 121-122 were prepared



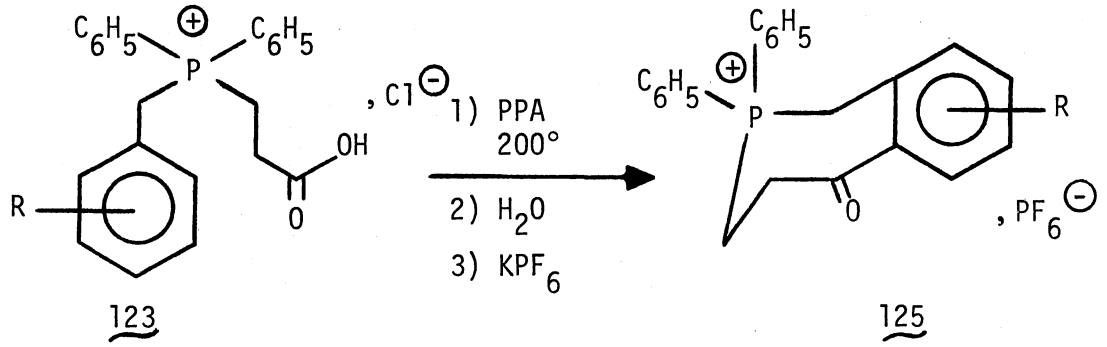
Cpd.	n
119	2
120	3



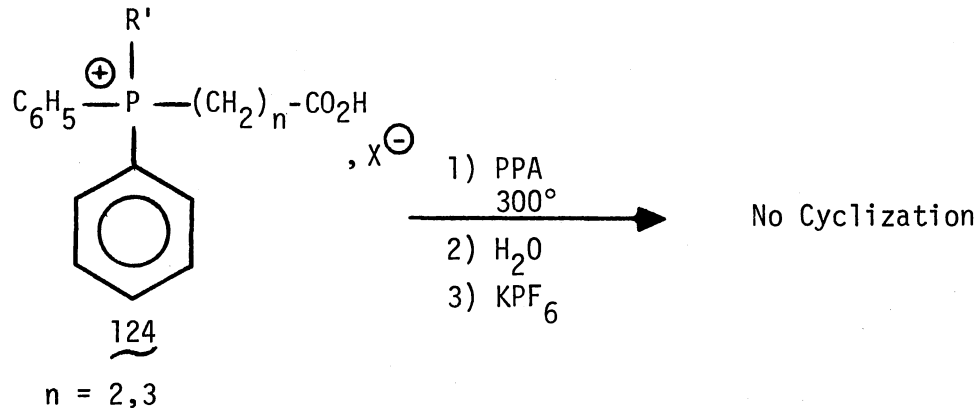
Cpd.	n	X
121	2	PF_6
122	3	Cl

via a modification of a classic alkylation process.[14] Essentially, the phosphine (either triphenylphosphine or methyldiphenylphosphine) with a slight excess of the halo acid (either 3-chloropropanoic or 4-chlorobutanoic) were placed together in a suitable boiling solvent (benzene, toluene, xylene). The crude phosphonium salt precipitated as a solid or formed an oil immiscible with the solvent. Upon cooling, the reaction mixture was evaporated to a solid. The crude salt was then dissolved (H_2CCl_2 or CH_3OH), and the solution was treated with ether, which caused the salt to precipitate. In the case of 121, the crude salt did not reprecipitate immediately, and again the salt was dissolved (CH_3OH). When a massive excess of a saturated aqueous solution of potassium hexafluorophosphate was added, the salt 121 precipitated. No further purification was necessary.

Two phosphonium systems 123 and 124 were examined for their ability



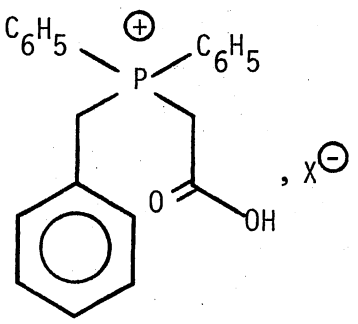
123 125



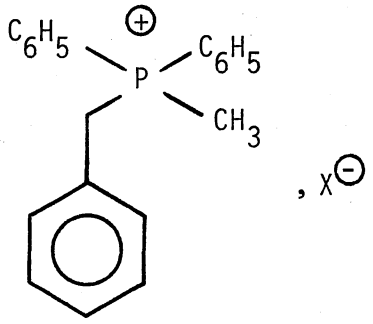
124

n = 2,3

to undergo ring closure to the corresponding keto salts. As stated previously, 123 cyclized smoothly to 125. However, in the attempted preparation of 126, decarboxylation occurred during quaternization and

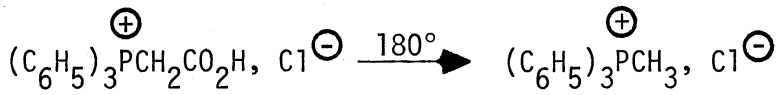


126



127

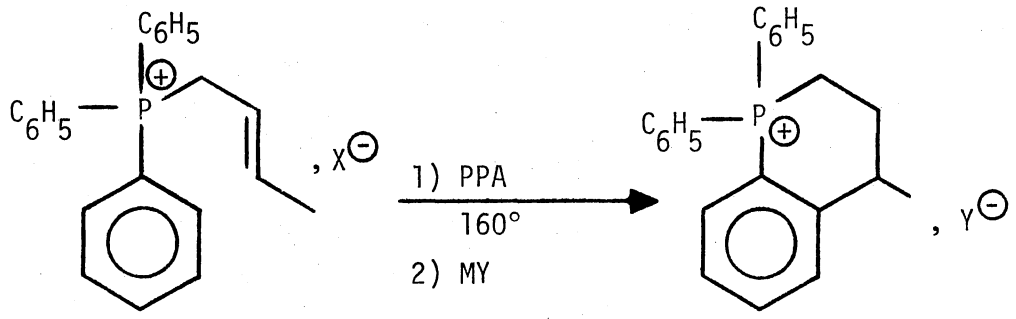
gave the simple salt 127. This observation is reminiscent of the report by Denney and Smith[14] that salt 128 lost carbon dioxide at 180°. It is



128

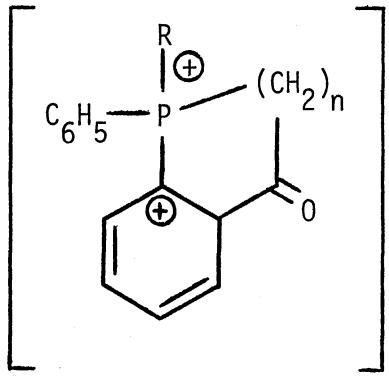
interesting to note that in our case the attempted preparation of 126 was carried out in boiling toluene, way below the temperature used by Denney and Smith. The mechanism for this type of decarboxylation has not been investigated but it may be catalyzed by acid.

Triarylphosphonium salts 119-122 were totally resistant to cyclization under the conditions employed. This was surprising in view of reported[15] success with alkenyl salts 129. However, the mechanism of the attack of PPA on 124 or of the acylation step may be

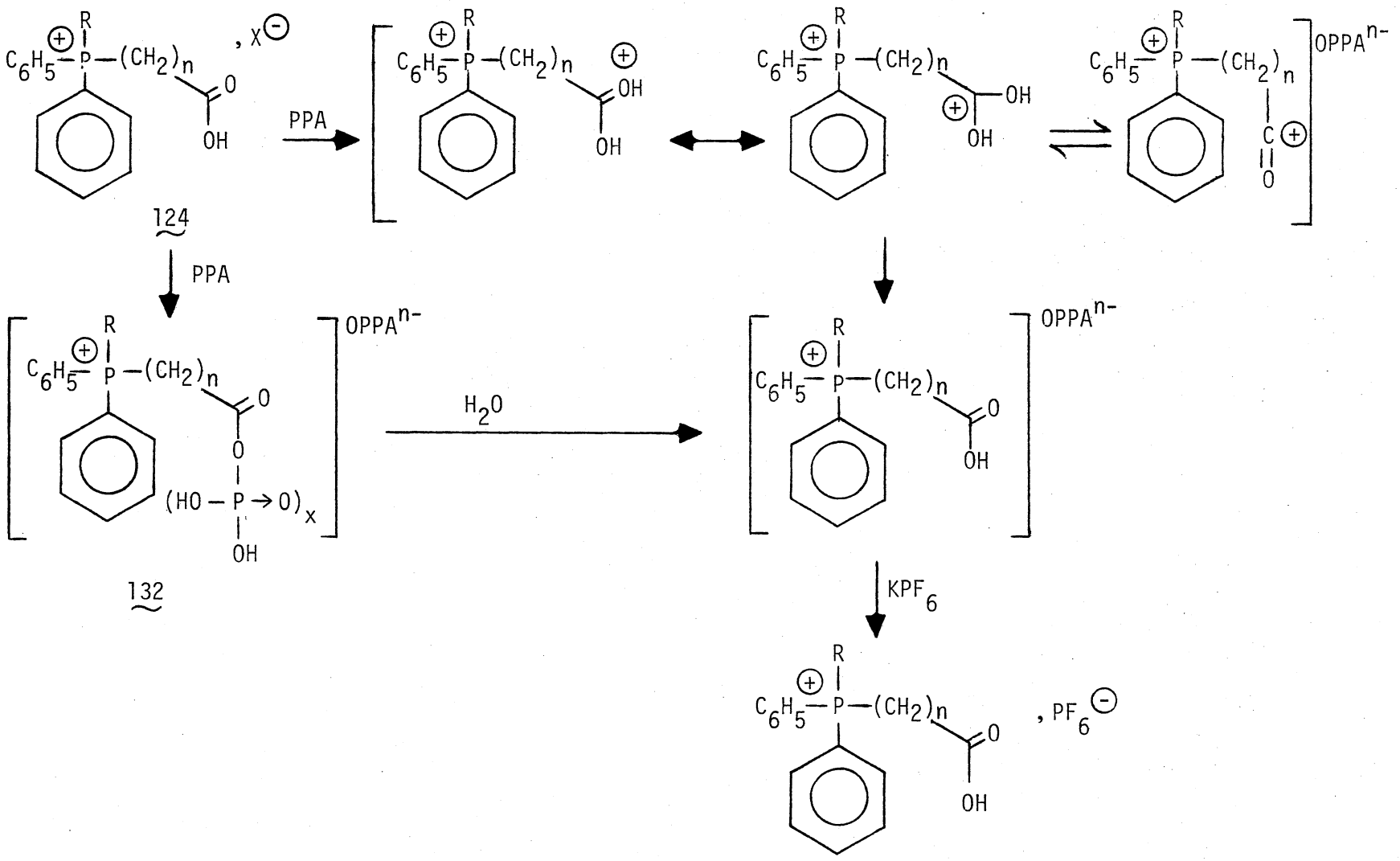


129 130

different from that in 129 to 130. In both cases a gas is evolved immediately upon the addition of the salt to hot PPA; it is presumably HX. Scheme VI presents a tentative mechanism for the possible reaction of 124 with PPA. Production of a mixture of cations is not impossible although one would intuitively expect for one cation to form initially, perhaps stabilized by $\ominus$OPPA. The stabilization of the charge by a bulky $\ominus$OPPA and the high energy requirement to attack the aromatic ring for cyclization are possible reasons for the inability of salts 119-122 to cyclize. If cyclization were to occur, a plausible intermediate 131, with adjacent positive charges would



131



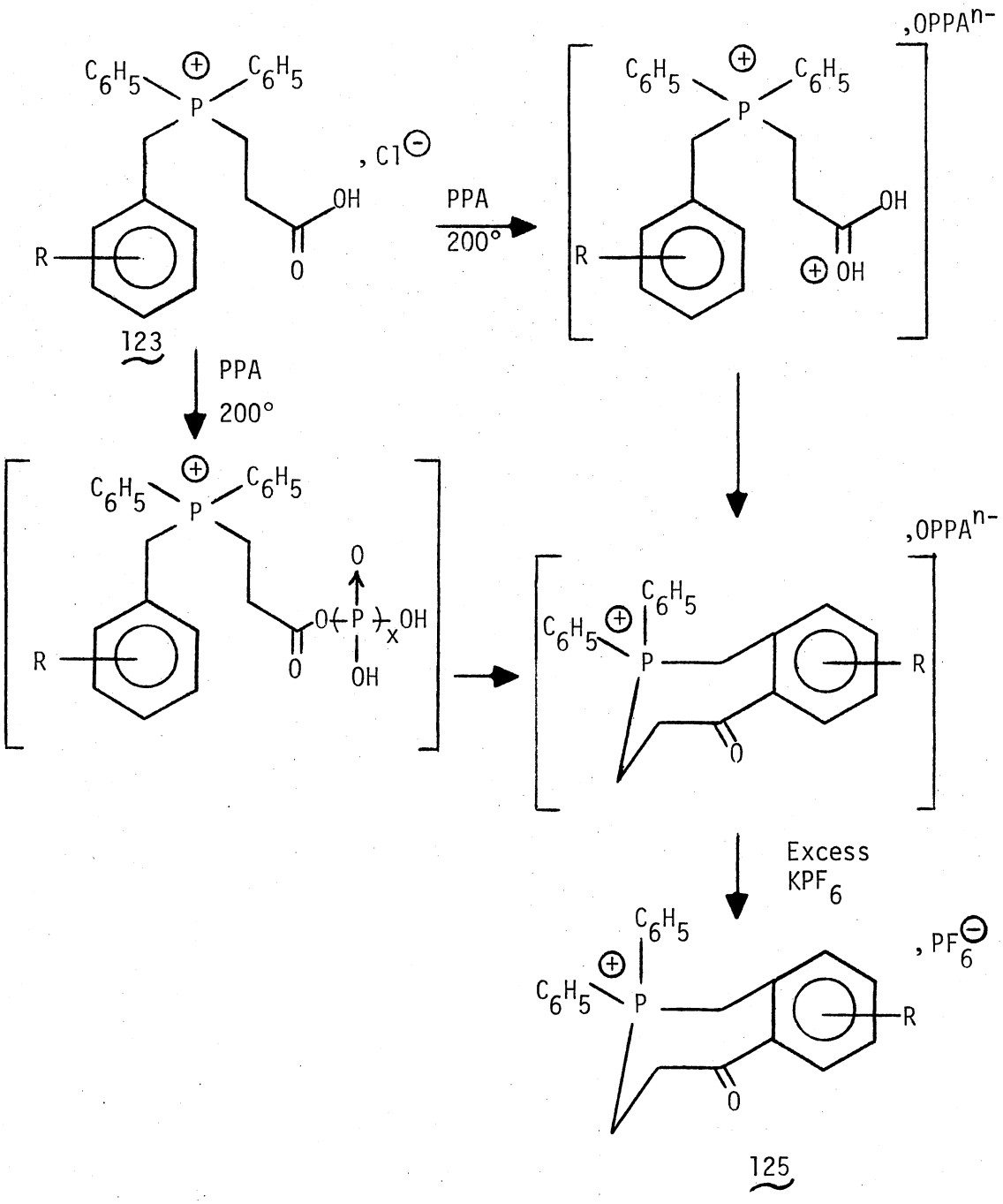
SCHEME VI

expectedly be a highly unstable system. Thus, the reaction might not proceed readily as in acylations of arenes which contain a powerful electron-withdrawing group.[22]

Another conceivable reason for the failure of cyclization of salts 119-122 might involve formation of a mixed anhydride. Although a similar structure with the alkenyl systems 129 is not impossible, formation of a large bulky salt like 132 is not unreasonable from 124, and a steric hindrance to cyclization could result. It is our contention that the energy required to force the cyclization is large enough because of the nature of the intermediate that reaction is very slow and total structural decomposition becomes competitive. This is supported by the observation that as the cyclization temperature was raised from 100° to 300°, the amount of starting material recovered decreased and the amount of decomposition increased markedly. Moreover, when the P atom was removed one carbon further from the benzene ring, as in 123, cyclization could occur below 250°.

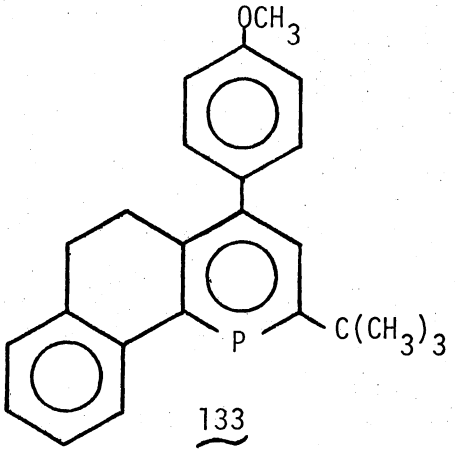
The standard technique discussed previously for the cyclization of β-alkenyl-substituted phosphonium salts[15] was employed in the intramolecular acylation of salts 104-108. The cyclization afforded moderate to good yields of the keto phosphepinium salts. 3-Chlorobenzyl(2-carboxyethyl)diphenylphosphonium chloride (106) required a temperature of 250° to induce ring closure. Again, the more severe conditions necessary to form keto salt 111 support a sluggish reaction.

A generalized mechanism, similar to that of the intramolecular acylation of γ-phenylbutyric acid[1] can be postulated for the ring closure of salts 104-108. Reaction of phosphonium salt 123 with PPA could result in either protonation or the formation of a mixed

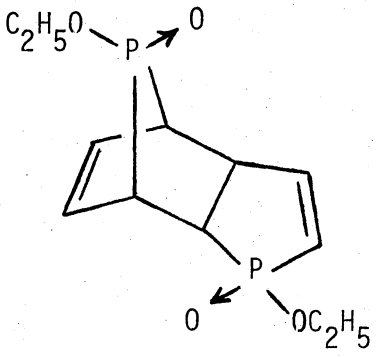


anhydride. Since the yields are not maximum, possibly a steric factor is important in the immediate precursor to the cyclized product. Compared with the alkenyl-substituted systems (yields were 24-88%),[15] one might speculate that the intermediate(s) leading to 125 were more hindered or much less reactive in the acylation process than in alkylation.[15]

To be sure, the structures of salts of the type under discussion have never been analyzed by X-ray or electron diffraction techniques. The few examples 133-138 reported[7,11,19,28,29,81] in the literature are



133



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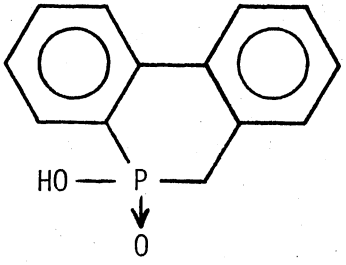

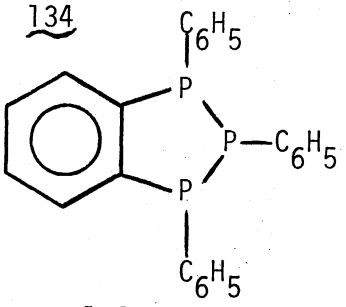

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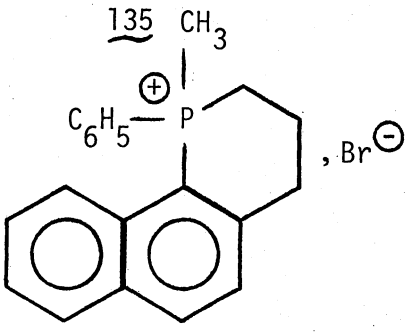
135



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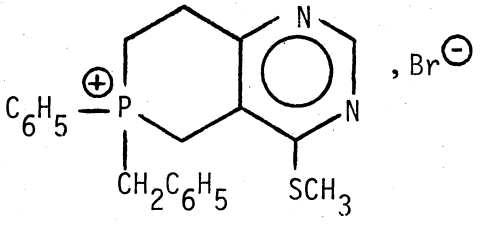
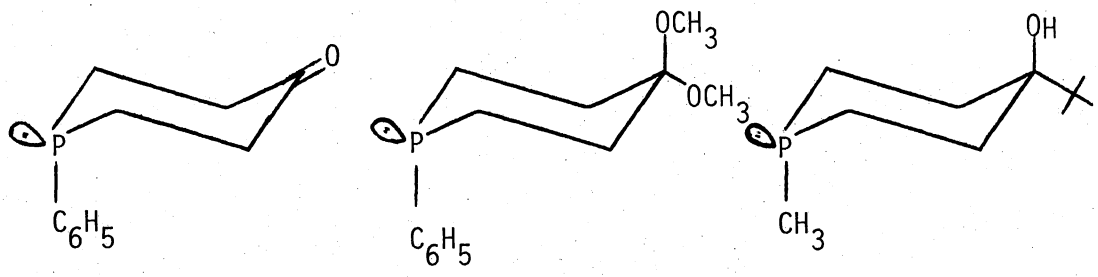


138

phosphole derivatives or systems related to phosphorinane (containing P in a six-membered ring). Very few structural analogies can be drawn due to the absence of a carbonyl function in the above mentioned compounds. Interestingly, it has already been shown that in

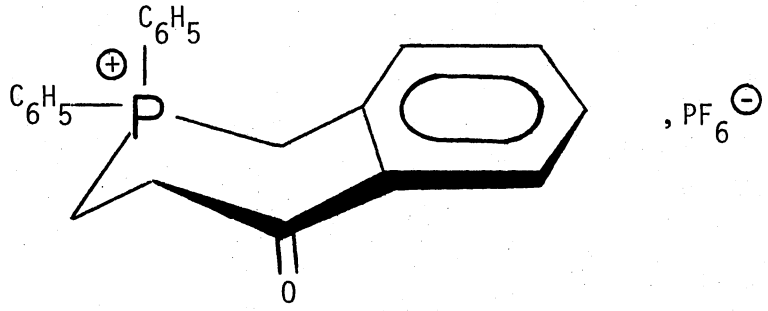
1-phenylphosphorinanone (139),[60] 1-phenyl-4,4-dimethoxyphosphorinane



139 140 141

(140),[59] and trans-1-methyl-4-tert-butyl-4-phosphorinanol (141)[61] the C-P heterocyclic ring is flatter than the cyclohexane counterpart.

Our procedure proved fruitful for only members related to the acid 135 but with a larger ring unit. No physical data are available in the literature on our systems. Almost certainly the P-containing



125

ring is not planar. An X-ray examination is planned if suitable crystals can be grown which is currently being attempted.

In the case of keto-salt 112, the PMR spectrum indicates a mixture of compounds present, based on the observation of two overlapping doublets for the benzylic protons. This fact can be rationalized by either protonation of the open-chain salt, with subsequent loss of isobutene, followed by ring closure to give salt 109 or by initial ring closure to give keto salt 112 followed by protonation and loss of the tert-butyl function to give salt 109. Further proof could be offered by allowing salt 112 to react with PPA at an elevated temperature for an extended time, followed by the appropriate work-up to yield only salt 109. In any case, a mixture resulted and has defied separation to date.

The low-resolution (70 eV) mass spectrum of salt 112 supports this salt as being a mixture of compounds. Fragment ions at m/e 386 and m/e 330 are observed for the loss of HPF_6 from the tert-butyl substituted cyclid salt 112 and the non-substituted cyclic salt 109, respectively. As no metastable transition corresponding to the loss of the tert-butyl function from m/e 386 to yield m/e 330 was observed further support is given to the presence of both components in this mixture.

The structure of the open-chain phosphonium salts 104-108 are supported by IR, PMR, ^{31}PMR and mass spectral analyses (Tables III, IV, V and VI). The infrared spectra of the salts 104-108 show strong, broad hydroxyl absorption at 2500-3400 cm^{-1} and carbonyl absorption at 1720-1730 cm^{-1}. In all cases absorptions were observed at 1430-1440, 1100-1120, 995-1005 and 710-730 cm^{-1}, these are indicative[85] of phenyl-substituted phosphonium salts.

The PMR spectra of the open-chain phosphonium salts are listed in Table IV. A characteristic doublet, J_{PCH} = 14 Hz, was observed for the benzylic protons in all cases. The two methylene groups (one adjacent to phosphorus, the other next to the carboxyl group) exhibit a multiplet due to the HC-CH coupling as well as short- and long-range P-CH coupling.[56] The remaining functions (3-methyl in 105, 4-tert-butyl in 107 and 2,5-dimethyl in 108) exhibit resonance peaks at the appropriate locations relative to similar systems.

The ^{31}PMR spectra of the salts 104-108 are given in Table V. The ^{31}P absorption of the phosphonium function displayed a small chemical shift downfield, relative to 85% H_3PO_4 as the standard. These values compare well with those of other simple phosphonium salts.[15,24,56]

The low-resolution mass spectra (70 eV) of the salts 104-108 (Table VI) support the assigned structures by comparison with related systems.[6,15,69] It is interesting to note that no molecular ion (M^+) was observed for any of the salts at 70 eV. The most abundant, large mass ion observed is that of the open-chain salt minus chloropropanoic acid (m/e 108). This loss of the carboxyalkyl side-chain is analogous to the loss of the alkenyl side-chain in related compounds such as 115 and 116.

The infrared spectra of the substituted 2,3,4,5-tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium hexafluorophosphates 109-113 (Table III and the corresponding Plates) show strong carbonyl absorption in the range of 1660-1680 cm^{-1}, except for keto-salt 111 which exhibits a band at $\nu_{C=O}^{KBr}$ 1710 cm^{-1}. An extremely strong, broad band due to the hexafluorophosphate function is characteristically observed in the range 790-850 cm^{-1}. This band for the PF_6^- function has been observed by other workers.[15]

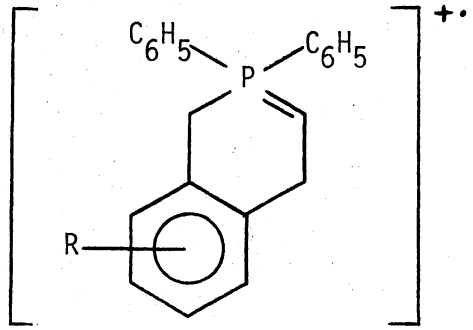
PMR data for the keto-salts 109-113 are given in Table IV and the corresponding Plates. In all cases the benzylic protons exhibit a doublet with J_{PCH} = 14 Hz. The methylene protons adjacent to phosphorus (non-benzylic) show two multiplets due to the $C\underline{H}$-$C\underline{H}$ coupling and PCH coupling. Overlapping these resonances is a broad singlet due to the methylene protons adjacent to the carbonyl group. This broad, single resonance was observed even at 25 Hz (spectral width). Disregarding any structural effects, one might expect a multiplet for $C\underline{H}_2C{=}O$. However, since no model systems were known, it was not possible to make immediate comparisons.

Homonuclear (PMR) decoupling of protons $-\overset{\oplus}{P}C\underline{H}_2C\underline{H}_2C{=}O$ did not prove fruitful because of a low $J/\Delta\nu$ ratio which produced harmonic frequencies overlapping the signals. However, the degradation of 109 to 114 (p. 58) is convincing chemical proof (along with the IR spectrum, mass spectral and elemental analysis) for the correctness of the structural assignments given for 109 and its relatives 110-113. We must conclude that the protons $-C\underline{H}_2-CH_2-C{=}O$ (underscored) must be fortuitously magnetically equivalent due to a peculiar structural geometry placing these protons in very similar environments as constructed models imply. Thus, the signals for $C\underline{H}_2-C{=}O$ should be a triplet from first-order considerations but the H-C-C-H angle may be of such magnitude to minimize coupling so that what appears to be a singlet is revealed. In contrast, protons $-\overset{\oplus}{P}-C\underline{H}_2-CH_2-$ appeared as a doublet with complex fine structure which demonstrates P-C-H ($J_{PCH} \approx 25$ Hz) coupling and the magnetic non-equivalence of protons $C\underline{H}_2-C{=}O$ (which is also suggested from examination of models). This assuredly hints at ring deformation from planarity for the C-P system.

Of course, a low temperature study ($T < -80^{o}$) might reveal a non-equivalence for $-\underline{CH}_2-CH_2-C=O$ but poor solubility of 109 in all solvents investigated did not allow such a study.

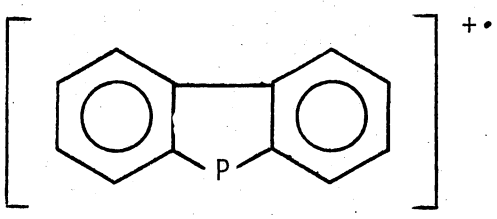
The ^{31}PMR spectra of salts 109-113 are listed in Table V and the spectrum of compound 109 is displayed in Plate XIV. The ^{31}P absorption of the cyclic phosphonium compound 109 is observed approximately 4 ppm upfield relative to the same absorption in the open-chain salts 104-108. This fact corresponds well with that observed by Dilbeck, Morris and Berlin[15] in the isophosphinolinium systems.

The low-resolution (70 eV) mass spectra of cyclic salts 109-113 are listed in Table VI. The most abundant, large-mass ion observed is that of the cyclic salt minus HPF_6 (m/e 146). A tentative structure for this ion is exemplified by structure 142. In all cases, a fragment



142

with m/e 183 was observed. This probably corresponds to the ion 143,



143

which has been observed in the fragmentation of several alkylidenetriphenylphosphoranes[9] and triphenyl- and biphenylene phosphines.[26]

Suggestions for Further Work

The preparation of substituted 2,3,4,5-tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium salts 109-113 could possibly lead to the synthesis of phosphasteroidal systems like 103 via condensations involving the carbonyl group in the phosphepin ring.

As was discussed earlier, cyclization did not occur in phosphonium salts such as 124. The replacement of the carboxyl group by an ester function and the addition of certain electron-donating groups in key positions in one or more of the benzene rings could possibly lead to ring closure. With the increased impetus for the preparation of biologically active compounds, especially in cancer chemotherapy, from rather simple starting materials and through short synthetic routes, the systems prepared in this work certainly aid the biological chemist in this one small area of chemotherapeutic chemistry.

CHAPTER III

EXPERIMENTAL[a-f]

Reagents. All liquids obtained from commercial sources were purified by distillation: From Aldrich Chemical Company - m-methylbenzyl chloride b.p. 197-199°, $n_D^{26.5}$ 1.5310 [lit.[32] 195-196°, n_D^{25} 1.5327]; m-chlorobenzyl chloride b.p. 45°/0.3 mm, $n_D^{26.5}$ 1.5531 [lit.[73] 111-113°/25 mm]; 4-tert-butylbenzyl alcohol b.p. 140°/20 mm, $n_D^{26.5}$ 1.5145 [lit.[30] 96-100°/1 mm, n_D^{27} 1.5150]; 2,5-dimethylbenzyl chloride b.p. 66°/2 mm, $n_D^{26.5}$ 1.5342; diphenylphosphinous chloride b.p. 124-127°/0.8 mm, $n_D^{26.5}$ 1.6331 [lit.[23] 112-113°/0.5 mm, n_D^{20} 1.6358]; 4-chlorobutanoic acid b.p. 90-92°/1 mm, $n_D^{26.5}$ 1.4483 [lit. 107-108°/6 mm,[4] n_D^{20} 1.4512[67]]. From Eastman Kodak Company - benzyl chloride b.p. 88°/15 mm, $n_D^{26.5}$

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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 XL-100(15) high resolution NMR spectrometer operating at 100.1 MHz with tetramethylsilane (TMS) used as the internal standard.

[c] ^{31}P magnetic resonance spectra were taken on a Varian XL-100(15) high resolution NMR spectrometer operating at 40.5 MHz using 85% H_3PO_4 as the external standard.

[d] Infrared spectra were taken on a Beckman-5A spectrometer with samples in thin films and potassium bromide pellets.

[e] Low resolution mass spectra were obtained on a CEC 21-100B double-focusing mass spectrometer.

[f] Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee.

1.5350 [lit.[31] n_D^{25} 1.5363]; triphenylphosphine m.p. 79-80° [lit.[16] 79.5°]; 3-chloropropanoic acid b.p. 118°/30 mm [lit.[18] 120°/30 mm]. From J. T. Baker Chemical Company - 2-chloro-2-methylpropane b.p. 50-52°, $n_D^{26.5}$ 1.3818 [lit.[77] 50.5°, n_D^{20} 1.38786]. From Fisher Scientific Company - chloroacetic acid b.p. 183-185° [lit.[42] 186°]. From FMC Corporation - 115% polyphosphoric acid [82.3% P_2O_5, guaranteed minimum].

Solvents. Diethyl ether, benzene, toluene and xylene (Fisher Scientific Co., A.C.S. Certified) were dried over sodium and filtered prior to use. Tetrahydrofuran was distilled from sodium hydride immediately before use.

General Procedure for the Synthesis of (Carboxyalkyl)triphenylphosphonium Chlorides 119-120 and (Carboxyalkyl)methyldiphenylphosphonium Salts 121-122. Preparation of (2-Carboxyethyl)triphenylphosphonium Chloride (119). In a 250-ml, round-bottom flask under N_2 were placed 5 g (19 mmole) of triphenylphosphine in 25 ml of xylene and 2.5 g (23 mmole) of 3-chloropropanoic acid in 25 ml of xylene. The mixture was then boiled for 18 hrs. and, upon cooling, a white solid precipitated. The solid was collected by vacuum filtration (Buchner), dissolved in a minimum amount (ca. 25 ml) of hot H_2CCl_2, and reprecipitated by the slow addition of anhydrous diethyl ether. A white solid, collected by vacuum filtration, was dried in vacuo (110°/5 mm) to yield 6.25 g (89%) of 119, m.p. 196-198° [lit. m.p. 196-198.5°[14]]. The IR, PMR, and mass spectral results (Tables III, IV, and VI, respectively) support the structure of 119.

Preparation of (3-Carboxypropyl)triphenylphosphonium Chloride (120). Triphenylphosphine (3 g, 0.0115 mole) and 4-chlorobutanoic

acid (1.4 g, 0.0115 mole) were allowed to react in a 25-ml, 1-necked, round-bottom flask under N_2 at 180° for 2 hrs. The resulting transparent solid was dissolved in acetone (ca. 25 ml) and reprecipitated by the slow addition of diethyl ether. The solid, collected by vacuum filtration, was dried in vacuo (110°/5 mm) to yield 2.7 g (61%) of 120, m.p. 235-237° [lit. m.p. 235-237°[14]]. The structure of 120 is supported by IR, PMR, and mass spectral analyses (Tables III, IV and VI, respectively).

Preparation of (2-Carboxyethyl)methyldiphenylphosphonium Hexafluorophosphate (121). Methyldiphenylphosphine (20 g, 0.115 moles) and 3-chloropropanoic acid (14 g 0.129 mole) in 80 ml of anhydrous benzene were boiled for 18 hrs in a 250-ml, 1-necked, round-bottom flask under N_2. After cooling and removal of solvent on a rotary evaporator, the resulting oil in H_2CCl_2 could not be induced to solidify by the addition of anhydrous ether. Again the solvent was removed by evaporation, and the resulting oil was dissolved in a minimum amount (ca. 50 ml) of methanol to which was added an excess (ca. 60 ml) of saturated aqueous KPF_6. A white precipitate formed immediately, was collected by vacuum filtration, and was dried in vacuo (110°/5 mm) to give 19.27 g (43%) of 121, m.p. 210-215°. The IR, PMR, and mass spectral results (Tables III, IV, and VI, respectively) support the structure of 121.

Preparation of (3-Carboxypropyl)methyldiphenylphosphonium Chloride (122). Methyldiphenylphosphine (10 g, 0.05 moles) and 4-chlorobutanoic acid (6.2 g, 0.05 mole) were allowed to react at 180° for 2 hrs in a 25-ml, round-bottom flask under N_2. A resulting transparent solid was reprecipitated from an acetone solution (ca. 25 ml) by the addition of anhydrous ether. The white precipitate, collected by vacuum filtration,

was dried in vacuo (110°/5 mm) to yield 11.82 g (73%) of 122, m.p. 210-212°. The structure of 122 is supported by IR, PMR, and mass spectral analyses (Tables III, IV, and VI, respectively).

Attempted Preparation of (Carboxymethyl)triphenylphosphonium Chloride (144). The previous procedure was used for the attempted preparation of 144. Triphenylphosphine (5 g, 19 mmole) and chloroacetic acid (3.9 g, 21 mmole) were boiled in 50 ml of anhydrous benzene in a 250-ml, round-bottom flask under N_2. The resulting oil, after cooling the reaction mixture, was dissolved in anhydrous methanol (ca. 25 ml) and triturated with ether to give 4.78 g (81%) of methyltriphenylphosphonium chloride, (145) m.p. 218-220° [lit.[8] 221°]. The IR, PMR, and mass spectral results (Tables III, IV, and VI) support the structure of 145.

Attempted Preparation of (Carboxymethyl)methyldiphenylphosphonium Chloride (146). The same general procedure was followed for the attempted preparation of 146. Methyldiphenylphosphine (20 g, 0.1 mole) and chloroacetic acid (12 g, 0.11 mole) in 100 ml of anhydrous benzene were boiled for 12 hrs. in a 250-ml, round-bottom flask under N_2. After cooling and evaporation of the solvent to a total volume of approximately 25 ml, the resulting oil was dissolved in the minimum amount (ca. 50 ml) of methanol. To this solution was added an excess (ca. 100 ml) of saturated aqueous KPF_6. A white solid formed immediately, was collected by vacuum filtration, and was dried in vacuo (110°/5 mm) to give 30.06 g (85%) of dimethyldiphenylphosphonium hexafluorophosphate (147), m.p. 134-136°. The structure of 147 is supported by IR, PMR, and mass spectral analyses (Tables III, IV, and VI).

General Procedure for the Synthesis of Arylmethyl(carboxyalkyl)-diphenylphosphonium Chlorides 104-108. Preparation of

Benzyl(2-carboxyethyl)diphenylphosphonium Chloride (104). In a 500-ml, round-bottom flask under N_2 was placed 1.2 g (0.05 g-atom) of Mg and 10 ml of anhydrous ether. Into an attached 125-ml addition funnel was placed 6.3 g (0.05 mole) of benzyl chloride in 100 ml of anhydrous ether. The reaction flask containing the Mg was charged with approximately 5 ml of the benzyl chloride solution. When the reaction began, the remaining benzyl chloride solution was added dropwise over a 2-hour period, and then the solution was stirred for 4 hours. To the addition funnel was added 11.0 g (0.05 mole) of diphenylphosphinous chloride in 100 ml of anhydrous toluene. This solution was added dropwise over a 1-hour period to the Grignard solution. When the addition was complete, the ether was distilled off (a volume of ca. 20 ml remained) and the remaining heterogeneous mixture was boiled for 12 hrs. After cooling to room temperature, the mixture was hydrolyzed with 2.7 g (0.05 mole) of NH_4Cl in 50 ml of degassed (N_2 bubbled through for one-half hour) H_2O. Two layers then separated under N_2, and the organic layer was dried ($MgSO_4$). The dried organic layer was filtered (under N_2) and delivered to a 500-ml, round-bottom flask (under N_2) containing 6.5 g (0.06 mole) of 3-chloropropanoic acid in 25 ml of anhydrous toluene. The solution was then boiled for 24 hrs., after which cooling caused formation of an oil. Toluene was removed by rotary evaporation to give an extremely viscous white oil. The oil was dissolved in a minimum amount (ca. 25 ml) of hot H_2CCl_2, and the phosphonium salt 104 was precipitated by the dropwise addition of anhydrous ether (ca. 25 ml). After standing 12 hrs, a white solid was collected by vacuum filtration and dried in vacuo (110°/5 mm) to yield 11.05 g (58% based on benzyl chloride) of 104, m.p. 223-225°. The structure of salt 104 is

supported by PMR (Plate I), ^{31}PMR (Plate II), IR (Plate III) and mass spectral analyses (Table VI).

Preparation of (3-Methylbenzyl)-(2-carboxyethyl)diphenylphosphonium Chloride (105). The general procedure discussed previously was used for the preparation of 105. The gram-weight and molar quantities of reactants are as follows: Mg (0.48 g, 0.02 g-atom); 3-methylbenzyl chloride (2.8 g, 0.02 mole); diphenylphosphinous chloride (4.4 g, 0.02 mole); NH_4Cl (1.09 g, 0.02 mole) and, 3-chloropropanoic acid (2.2 g, 0.02 mole). The yield of 105 was 2.75 g, m.p. 187-190° [34.5% based on 3-methylbenzyl chloride]. The structure of salt 105 is supported by PMR, IR (Plates IV and V, respectively), ^{31}PMR and mass spectral analyses (Tables V and VI).

Preparation of (3-Chlorobenzyl)-(2-carboxyethyl)diphenylphosphonium Chloride (106). The general procedure was used for the preparation of 106. The gram-weight and molar quantities are as follows: Mg (0.84 g, 0.035 g-atom); 3-chlorobenzyl chloride (5.6 g, 0.035 mole); diphenylphosphinous chloride (8.8 g, 0.04 mole); NH_4Cl (2.18 g, 0.04 mole) and 3-chloropropanoic acid (4.4 g, 0.04 mole). The yield of salt 106 was 5.77 g (40%, based on 3-chlorobenzyl chloride), m.p. 225-229°. PMR, IR (Plates VI and VII, respectively), ^{31}PMR, and mass spectral results (Tables V and VI, respectively) support the structure of 106.

Synthesis of 4-tert-Butylbenzyl Chloride (148). To 9.6 g (0.059 mole) of 4-tert-butylbenzyl alcohol in a 25-ml reaction flask was added slowly 7.85 g (0.066 mole) $SOCl_2$; vigorous reaction occurred. After the addition was complete the reaction mixture was warmed on an oil bath (100°/24 hrs), cooled, and excess $SOCl_2$ removed at atmospheric pressure. The remaining liquid was distilled under vacuum to yield

8.5 g (79.5%) of 148, b.p. 67°/0.7 mm, n_D^{24} = 1.5195 [lit.[66] 88-89°/3 mm, n_D^{24} = 1.5194]. The structure of 148 is supported by PMR and IR spectral data [Plate VIII].

Preparation of (4-t-Butylbenzyl)-(2-carboxyethyl)diphenylphosphonium Chloride (107). In a 500-ml, 3-necked, round-bottom flask (under N_2) was placed 0.54 g (0.0224 g-atom) of Mg to which was added 10 ml of anhydrous ether. To this was added approximately 5 ml of a solution of 4-t-butylbenzyl chloride (4.1 g, 0.0224 mole) in 100 ml of anhydrous ether. After the reaction started (ca. 30 min.) the remaining 4-t-butylbenzyl chloride solution was added dropwise over a 2-hr. period. The heterogeneous mixture was then stirred 6 more hours. To this mixture was added dropwise a solution of 4.95 g (0.0244 mole) of diphenylphosphinous chloride in 50 ml of anhydrous THF. The mixture was boiled for 3 hours, cooled, and hydrolyzed by the slow addition of 1.22 g (0.0224 mole) of NH_4Cl in 50 ml of degassed H_2O. The organic layer was separated (under N_2), dried ($MgSO_4$), and filtered under N_2. The ether-THF solution of the crude phosphine was placed in a 500-ml reaction flask (under N_2) to which was added 2.43 g (0.0224 mole) of 3-chloropropanoic acid in 100 ml of anhydrous toluene. The reaction mixture was boiled for 48 hrs. and cooled; a white solid precipitated, and was collected by vacuum filtration. Reprecipitation from H_2CCl_2/ether (1:1) gave a solid which when dried in vacuo (110°/5 mm) weighed 3.3 g (33.4%, based on 4-t-butylbenzyl chloride) and was 107, m.p. 167.5-171°. The structure of 107 is supported by PMR (Plate IX) ^{31}PMR (Table V), IR (Plate X), and mass spectral analyses (Table VI).

Preparation of (2,5-Dimethylbenzyl)-(2-carboxyethyl)diphenylphosphonium Hexafluorophosphate (108). In a 300-ml, 3-necked, round-bottom

flask under N_2 was placed 0.535 g (0.0765 g-atom) of Li in 50 ml of anhydrous THF and 10 g (0.0382 mole) of triphenylphosphine in 50 ml of anhydrous THF. The mixture was then stirred mechanically for 5 hrs and gradually became dark red. tert-Butyl chloride (3.54 g, 0.0382 mole) in 25 ml of anhydrous THF was then added dropwise to decompose the unreacted Li and phenyllithium. The reaction mixture was again stirred for 1 hr. 2,5-Dimethylbenzyl chloride (5.9 g, 0.0382 mole) in 50 ml of anhydrous THF was then added to the red solution over a 1-hr. period. After the addition was complete, the reaction mixture was stirred for 3 hours. The solution of crude phosphine thus prepared, was delivered (filtration through glass wool) under N_2 to 4.15 g (0.0382 mole) of 3-chloropropanoic acid in 100 ml of anhydrous toluene (under N_2). The THF was then distilled (ca. 150 ml collected) and the reaction mixture was boiled for 24 hrs. Cooling caused deposition of a light brown oil. The solvents and unreacted starting materials were decanted and the oil was dissolved in 100 ml of 95% ethanol. Carbon black was added to the ethanolic solution with subsequent boiling for one-half hour. Filtration and removal of the ethanol (rotary evaporator) gave approximately 15 ml of an extremely viscous oil. Dissolution of this oil in 50 ml 95% ethanol and addition of saturated aqueous KPF_6 (ca. 60 ml) resulted again in oil formation. Removal of the ethanol-water by rotary evaporation to a volume of approximately 10 ml and placing the residue on a vacuum line (60°/1 mm) for 48 hrs gave 14.45 g of crude 108. The PMR (Plate XI) and IR (Plate XII) indicate that the salt 108 is the major component (with the phosphine oxide as contaminant). Further purification of the crude salt by extraction of a $HCCl_3$ solution with saturated aqueous $NaHCO_3$, reacidification, and re-extraction into chloroform proved unsuccessful.

Attempted Preparation of Benzyl(2-carboxymethyl)diphenylphosphonium Chloride (126). In a 300-ml, inverse Grignard flask under N_2 was placed 2.4 g(0.1 g-atom) of Mg. Benzyl chloride (12.6 g, 0.1 mole) in 100 ml anhydrous ether was placed in an attached 125-ml addition funnel. Approximately 10 ml of the benzyl chloride solution was delivered into the flask to initiate the reaction. After the reaction had begun the remaining benzyl chloride solution was added dropwise (with mechanical stirring) over a one-hour period. Diphenylphosphinous chloride (22.1 g, 0.1 mole) in 100 ml anhydrous toluene was placed in the funnel and added slowly (ca. one hour) to the Grignard solution, followed by boiling the heterogeneous mixture for one hour.

In an attached 500-ml, 3-necked, round-bottom flask (under N_2) was placed 7.6 g (0.08 mole) of chloroacetic acid in 50 ml of anhydrous toluene. The crude phosphine was then delivered into the bottom flask over an 8-hr. period. The upper flask was then removed and replaced by a water-cooled condenser. The reaction mixture was boiled for 24 hours, cooled, and diluted with ether. After standing several hours, some solid had precipitated which was collected by vacuum filtration. Evaporation of the filtrate and trituration of the resulting oil gave a solid. The two solid portions were combined, dissolved in a minimum amount (ca. 25 ml) of hot H_2CCl_2, and reprecipitated with ether (ca. 25 ml). The white solid, collected by vacuum filtration, was dried in vacuo (110°/5 mm) to yield 10.61 g (40.5%) of benzylmethyldiphenylphosphonium chloride (127), m.p. 238-241°. The structure of 127 is supported by IR, PMR, ^{31}PMR, and mass spectral analysis (Tables III, IV, V, and VI).

General Procedure for the Cyclization of Arylmethyl(2-carboxyethyl)diphenylphosphonium Salts 104-108. Preparation of 2,3,4,5-Tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (109). In a 100-ml beaker was placed 60 ml of commercial (FMC) 115% polyphosphoric acid (PPA) which was then heated on a hot plate to 200°. To the hot PPA was slowly added 2 g (5.2 mmole) of 104. After the addition was complete the solution was maintained at 200 ± 10° (with stirring) for 90 minutes. The solution was then cooled to approximately 120° and poured onto 300 ml of ice water. A homogeneous solution was produced by stirring for 5 minutes. Upon the addition of excess saturated aqueous KPF_6 (ca. 60 ml) crude 109 precipitated. The solid, collected by vacuum filtration, was washed with water (ca. 100 ml). The tan solid was then dissolved in 50 ml of 95% ethanol, to which carbon black was added, and the mixture boiled on a steam bath for 15 minutes. Vacuum filtration followed by evaporation gave solid 109. The solid was then stirred in 100 ml of anhydrous ether for 2 hrs., collected by vacuum filtration, and dried in vacuo (110°/5 mm) to yield 1.59 g (64%) of 109, m.p. 126-129°. The PMR and IR spectra of 109 are displayed in Plates XIII and XIV, respectively, while mass spectral results are in Table VI.

The ^{31}P magnetic resonance of 109 (Plate XV) showed ^{31}P absorption of the phosphonium function at δ -21.51 [15% in $DCCl_3/CF_3CO_2H$ (4:1)] relative to 85% H_3PO_4.

Anal. Calcd. for $C_{22}H_{20}F_6OP_2$: P, 13.00.

Found: P, 12.99.

Preparation of 2,3,4,5-Tetrahydro-8-methyl-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (110). The general procedure

was used for the preparation of 110. However, the time allowed for heating the PPA solution was only 15 minutes as the solution turned extremely dark immediately after the addition of 105. The gram-weight and molar quantity of 105 were 2 g and 5 mmole, respectively. The yield of 110 was 0.9 g (37%), m.p. 187-190°. The structure of 110 is supported by PMR and IR spectra (Plates XVI and XVII) along with mass spectral data (Table VI).

The ^{31}P magnetic resonance of 110 showed ^{31}P absorption of the phosphonium function at δ -21.48 [15% $HCCl_3/CF_3CO_2H$ (4:1)] relative to 85% H_3PO_4.

Anal. Calcd. for $C_{23}H_{22}F_6OP_2$: C, 56.33; H, 4.52; P, 12.63.

Found: C, 56.24; H, 4.61; P. 12.67.

Preparation of 8-Chloro-2,3,4,5-tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (111). The same general procedure described previously was employed. The gram-weight and molar quantity of salt 106 were 1.7 g and 4.1 mmole. The reaction temperature was 250 ± 10° and the time allowed for reaction was 2 hours. Initial work-up gave 1.5 g (58%) of 111, m.p. 90° dec. The crude salt 111 was then dissolved in H_2CCl_2 (ca. 10 ml) and reprecipitated with anhydrous ether to yield 111 (m.p. 186-188°) after drying in vacuo (81°/5 mm). The structure of 111 is supported by PMR and IR spectra (Plates XVIII XIX) and mass spectral data (Table VI).

The ^{31}P magnetic resonance of 111 showed ^{31}P absorption at δ -21.04 [15%, acetone] relative to 85% H_3PO_4.

Anal. Calcd. for $C_{22}H_{19}ClF_6OP_2$: P, 12.13.

Found: P, 12.15.

Attempted Preparation of 7-tert-Butyl-2,3,4,5-tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (112). The same general procedure described previously was employed. The gram-weight and molar quantity of open-chain salt 107 were 2.35 g and 5.3 mmole. The reaction temperature was 200 ± 10° and the time allowed for reaction was 2 hours. Initial work-up gave 1.25 g (44.5%) of crude salt. The crude salt was then dissolved in H_2CCl_2 (ca. 50 ml) and carbon black was added. Boiling the mixture for 15 minutes followed by vacuum filtration and reprecipitation with ether again gave a crude salt, m.p. 92° (begins to volatilize). Further attempts at purification proved unsuccessful. The infrared spectrum (Plate XXI) exhibits a broad absorption at 1680 cm^{-1} which could indicate a mixture of cyclic compounds. The PMR spectrum (Plate XX) gives rise to at least two overlapping doublets for the benzylic protons, again possibly indicating a mixture of cyclic compounds.

The ^{31}P magnetic resonance of crude salt 112 showed ^{31}P absorptions at δ -29.13 and δ -21.39 [15%, $HCCl_3$] relative to 85% H_3PO_4.

The mass spectral analyses of crude salt 112 is listed in Table VI.

Preparation of 2,3,4,5-Tetrahydro-6,9-dimethyl-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (113). The same general procedure discussed previously was used in the preparation of 113. The gram-weight of crude 108 was 3.06 g. Hydrolysis of the PPA reaction mixture followed by stirring until homogeneous gave a small amount of insoluble material which was filtered out. To the resulting clear, yellow solution was added 100 ml of a saturated aqueous KPF_6 solution with immediate precipitation of a light yellow solid. Collection of the solid (vacuum filtration) and drying in vacuo (25°/5 mm) gave 1.93 g

(63%) of crude 113. The crude salt was then dissolved in 50 ml H_2CCl_2 to which was added carbon black and $MgSO_4$. The mixture was then boiled for 15 minutes and filtered (hot), and the volume was reduced to ca. 10 ml by vacuum evaporation. Addition of anhydrous ether to the clear solution followed by cooling gave a solid, which after drying in vacuo (60°/5 mm) gave pure 113, m.p. 227 dec. The structure of 113 is supported by PMR and IR spectra (Plates XXII and XXIII) and mass spectral data (Table VI).

The ^{31}P magnetic resonance of 113 showed ^{31}P absorption at δ -20.07 [15%, $HCCl_3$/TFA (4:1)] relative to 85% H_3PO_4.

Anal. Calcd. for $C_{24}H_{24}F_6OP_2$: C, 57.15; H, 4.79; P, 12.28.

Found: C, 57.02; H, 4.87; P, 12.26.

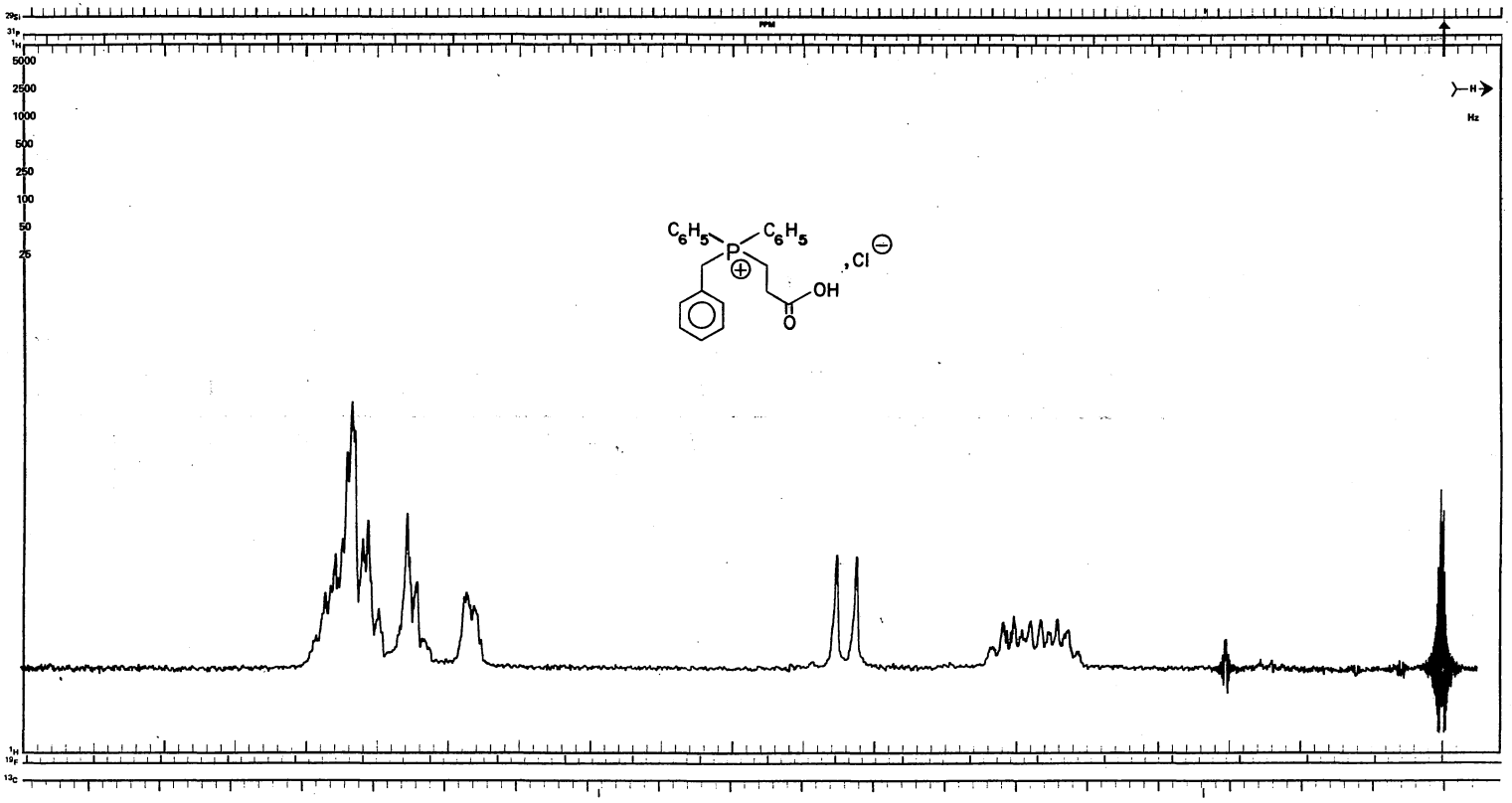
Preparation of (3-Diphenylphosphinyl)-2'-methylpropiophenone (114) via Alkaline Hydrolysis of 2,3,4,5-Tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (109). Ketone 109 (900 mg, 1.9 mmole) was added to 60 ml of CH_3OH/H_2O (4:1) in which 6 g of KOH had been dissolved. The resulting solution was boiled for 12 hours, cooled, and 50 ml of H_2O was added. Extraction with $HCCl_3$ (6 x 25 ml) gave an organic phase which was collected, dried ($MgSO_4$), and filtered. Evaporation gave a light green oil, which after standing for 2 hrs. deposited light green crystals. Recrystallization twice (hexane/H_2CCl_2, 4:1) gave 480 mg (73%) of ketophosphine oxide 114, m.p. 114-116°. The PMR and IR of oxide 114 (Plate XXIV and XXV) along with mass spectral analyses (Table VI) support the structure of 114.

Anal. Calcd. for $C_{22}H_{21}O_2P$: C, 75.85; H, 6.08; P. 8.89.

Found: C, 75.99; H, 6.01; P, 9.02.

Attempted Preparation of (3-Diphenylphosphinyl)-2'-methylpropiophenone (114) via Alkaline Cleavage of 109 in 70% Aqueous Dimethyl Sulfoxide. In the manner prescribed by Marsi[55] hydrolysis of 109 gave a heavy mixture after 5 hrs. The normal work-up, followed by vacuum distillation of the DMSO, produced a dark oil, the IR spectrum of which had a $\nu_{C=O}^{film}$ 1680 cm^{-1} and $\nu_{P=O}^{film}$ 1190 cm^{-1}. Chromatography over neutral alumina (Merck 1077) gave another intractable, dark oil. The IR and PMR spectra reveal the same absorptions found in the pure ketophosphine oxide 114 but also indicate a contamination with other products. Loss of the benzylic doublet signal in the PMR spectrum of the mixture indicates C-P cleavage, however, it seems that other extensive bond cleavages occur under the conditions employed.

PLATE I

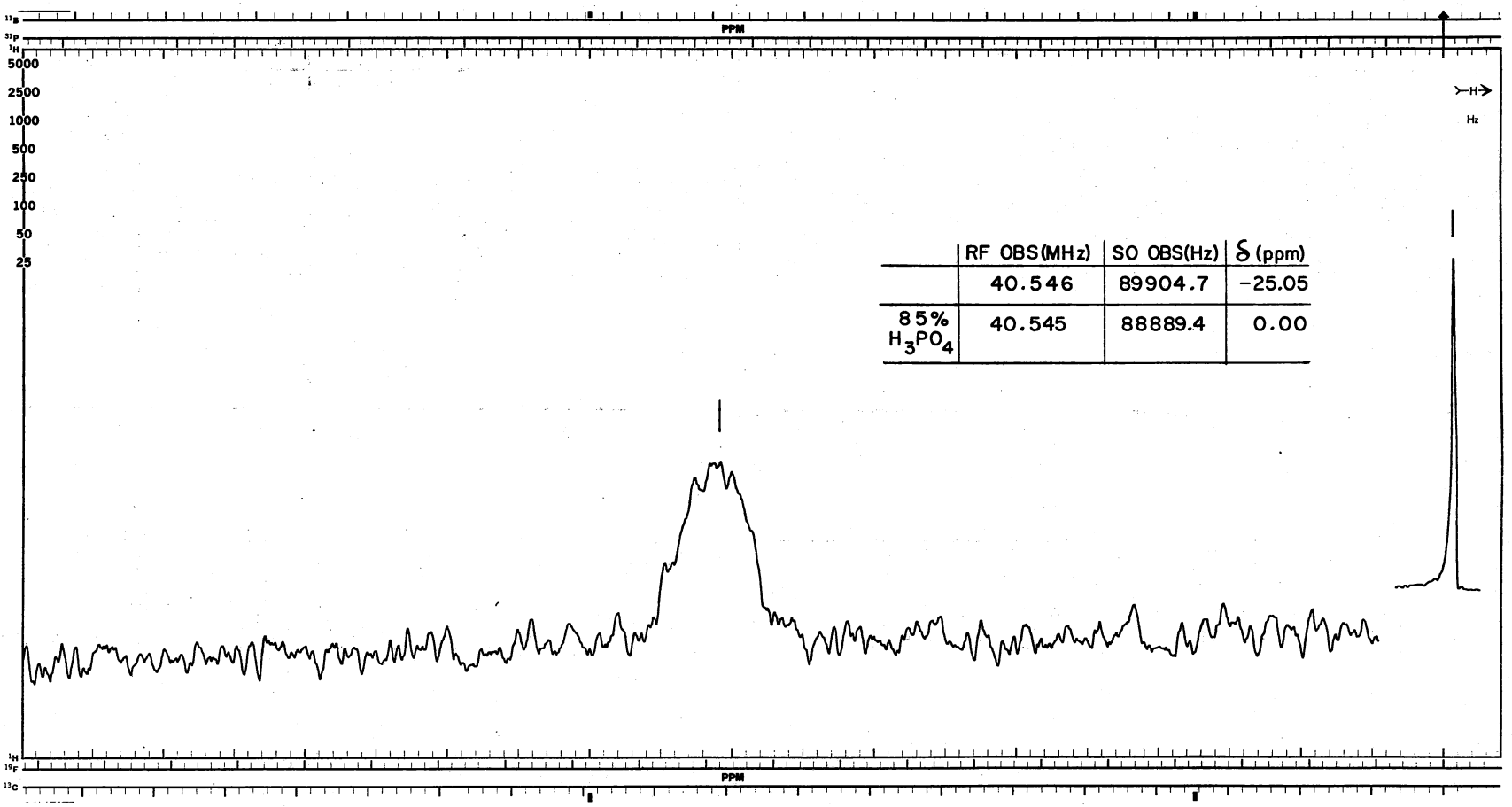


Benzyl(2-Carboxyethyl)diphenylphosphonium Chloride (104)

Solvent. . . $DCCl_3/CF_3CO_2H$ O.F. . . 100.1 MHz F.B. . . . 2.0 Hz R.F. .66 dB

S.W. . . . . 1000 Hz S.T. . . .500 sec. S.O. . . 85701 Hz S.A. . 5.0 Lock . HOMO

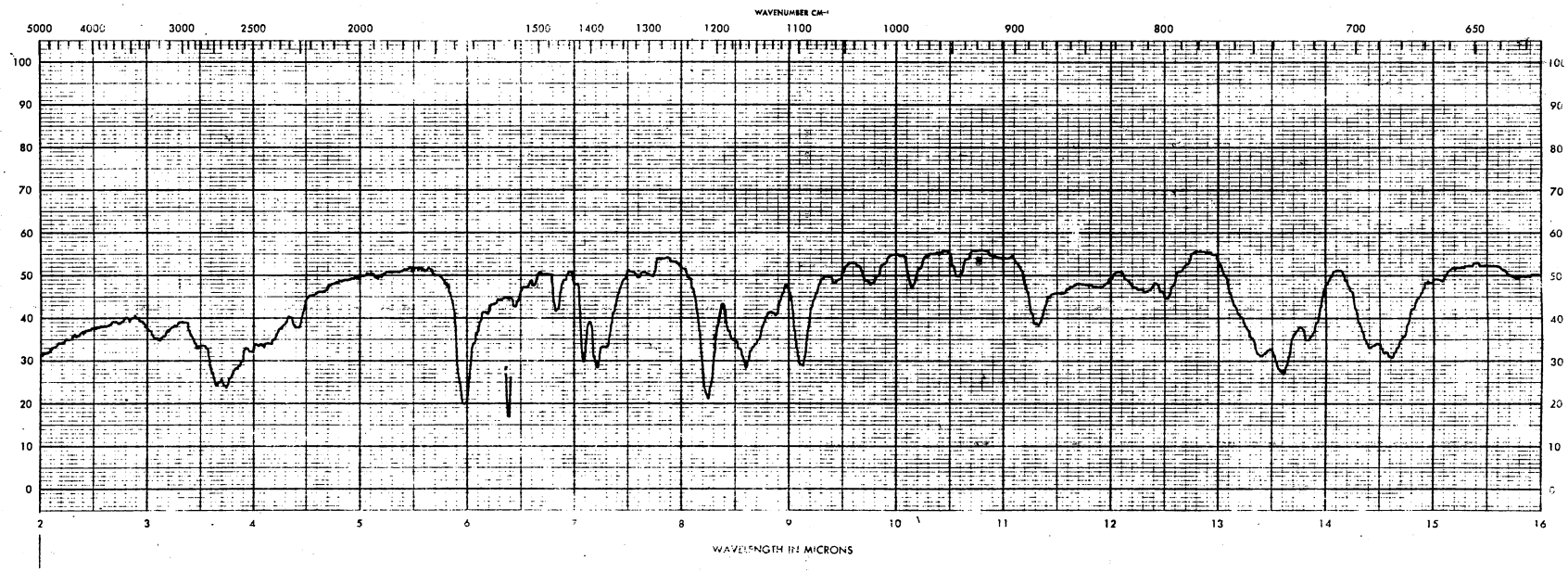
PLATE II



	RF OBS(MHz)	SO OBS(Hz)	δ (ppm)
	40.546	89904.7	-25.05
85% H_3PO_4	40.545	88889.4	0.00

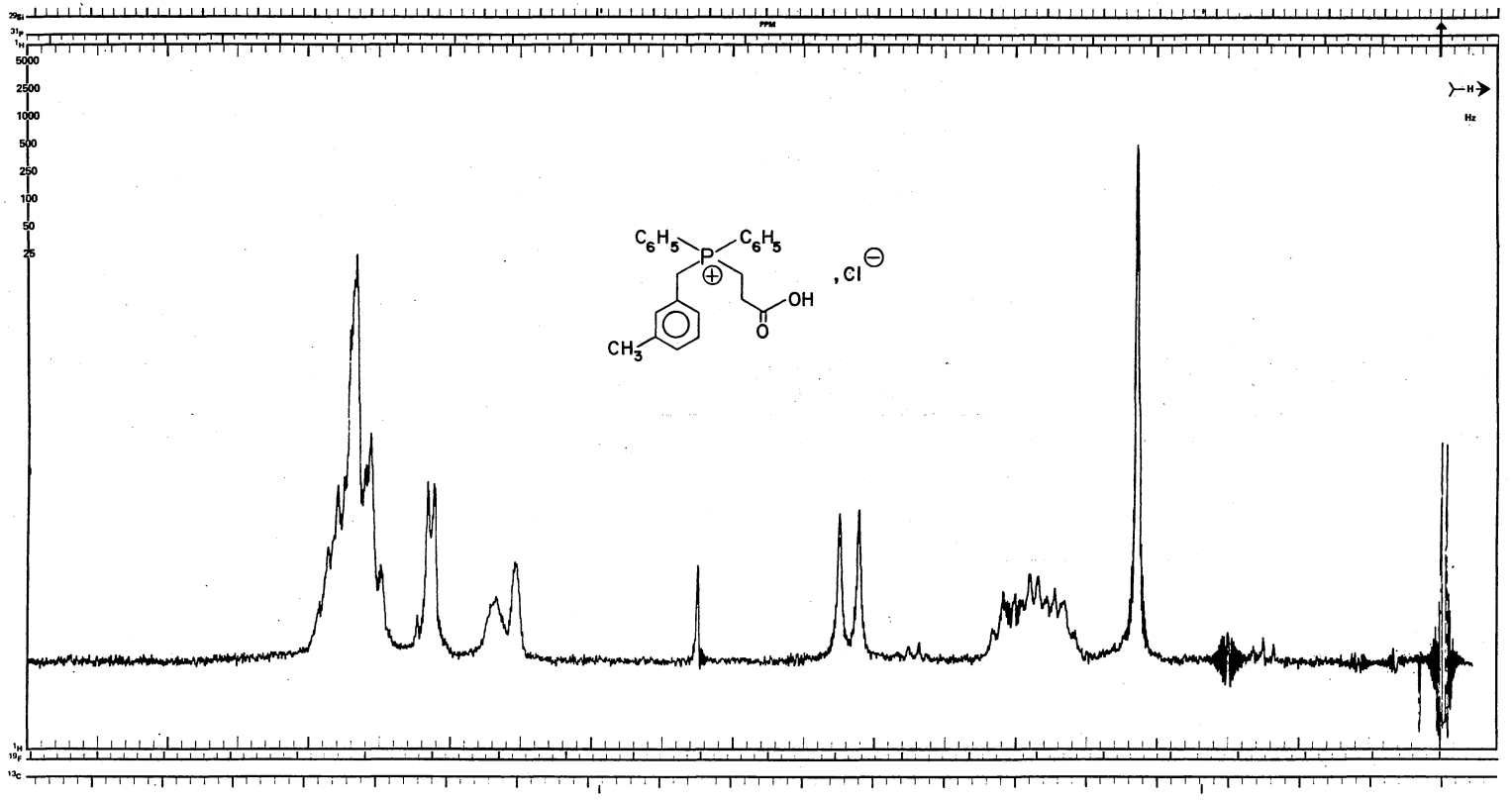
^{31}P Spectrum of Benzyl(2-carboxyethyl)diphenylphosphonium Chloride (104)

PLATE III



Benzyl(2-carboxyethyl)diphenylphosphonium Chloride (104), KBr Pellet

PLATE IV

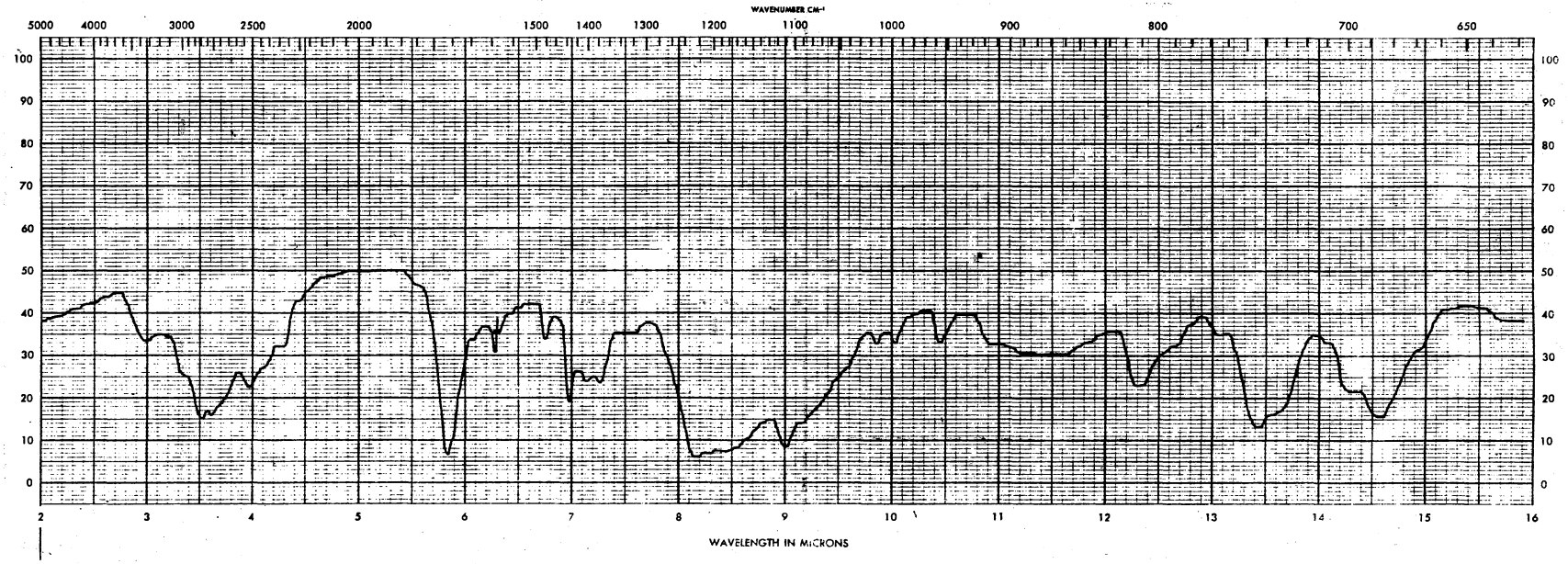


(3-Methylbenzyl)-(2-carboxyethyl)diphenylphosphonium Chloride (105)

Solvent. . .$DCCl_3/CF_3CO_2H$ O.F. . 100.1 MHz F.B. . . 4.0 Hz R.F. . 68 dB

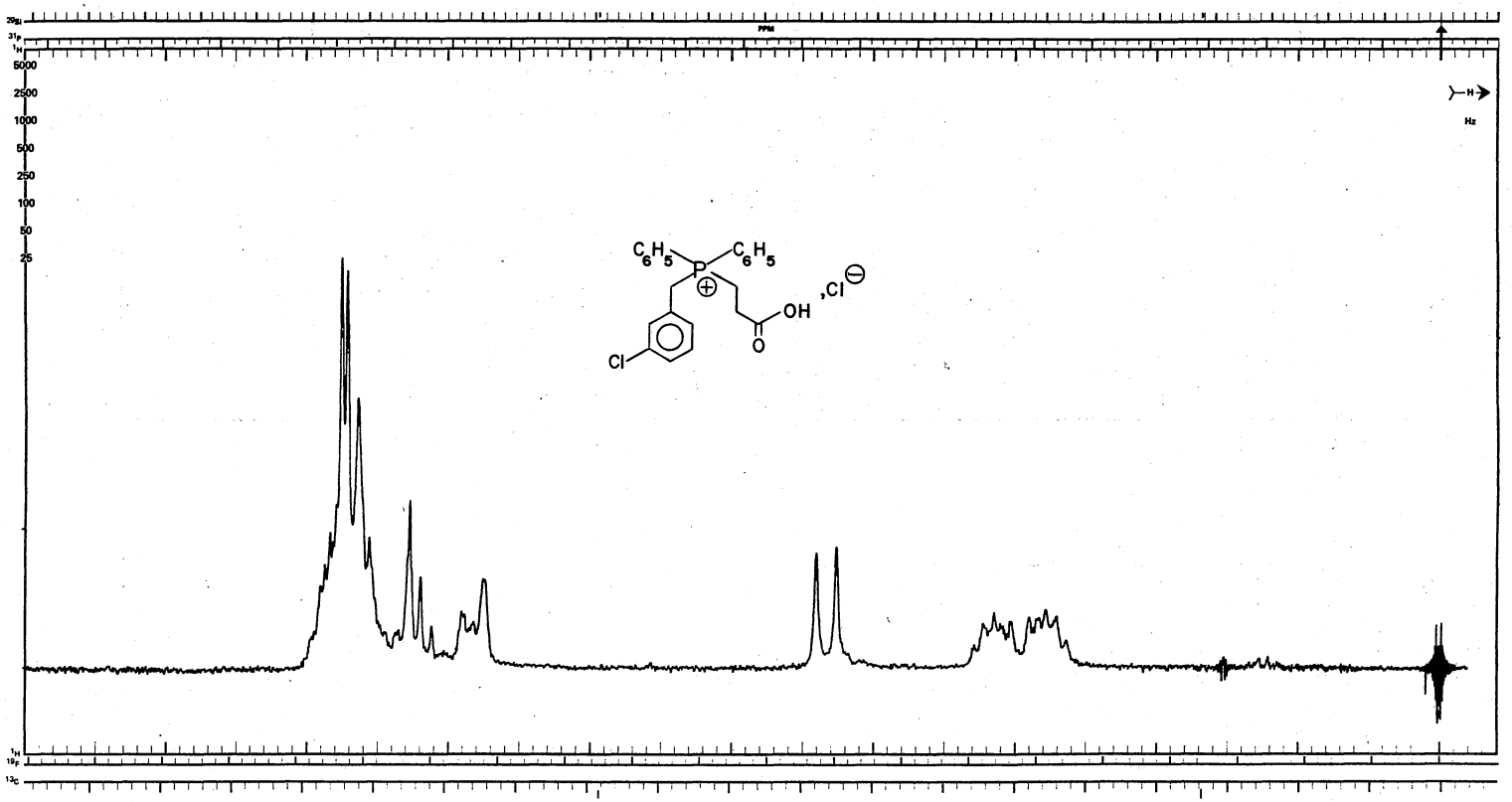
S.W. . . . . .1000 Hz S.T. . .250 sec. S.O. . 85701 Hz S.A. . . 5.0 Lock . .HOMO

PLATE V



(3-Methylbenzyl)-(2-carboxyethyl)diphenylphosphonium Chloride (105), KBr Pellet

PLATE VI

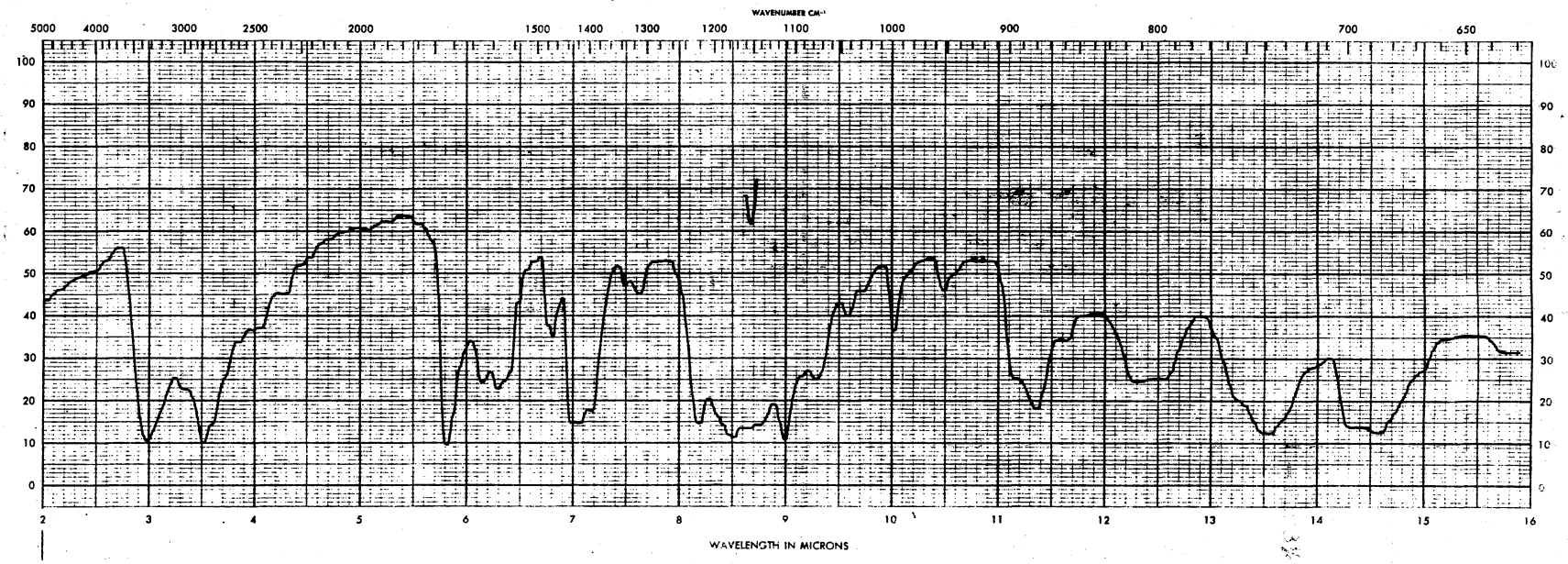


(3-Chlorobenzyl)-(2-carboxyethyl)diphenylphosphonium Chloride (106)

Solvent. . .$DCCl_3/CF_3CO_2H$ O.F. . 100.1 MHz F.B. . . 2.0 Hz R.F. . 65 dB

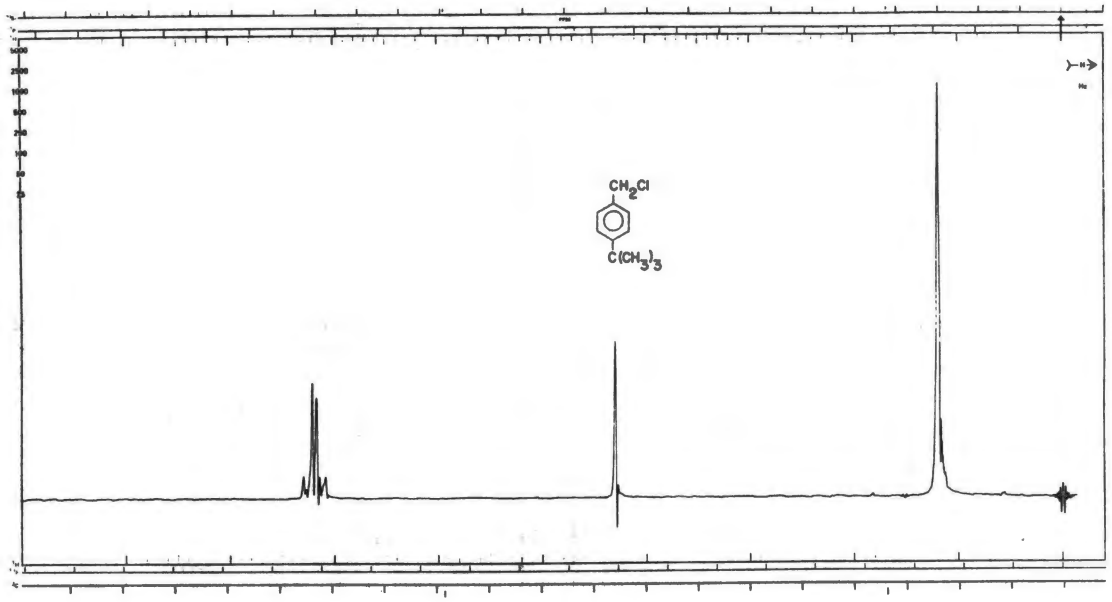
S.W. . . . . .1000 Hz S.T. . .500 sec. S.O. . 85701 Hz S.A. . . 5.0 Lock. .HOMO

PLATE VII

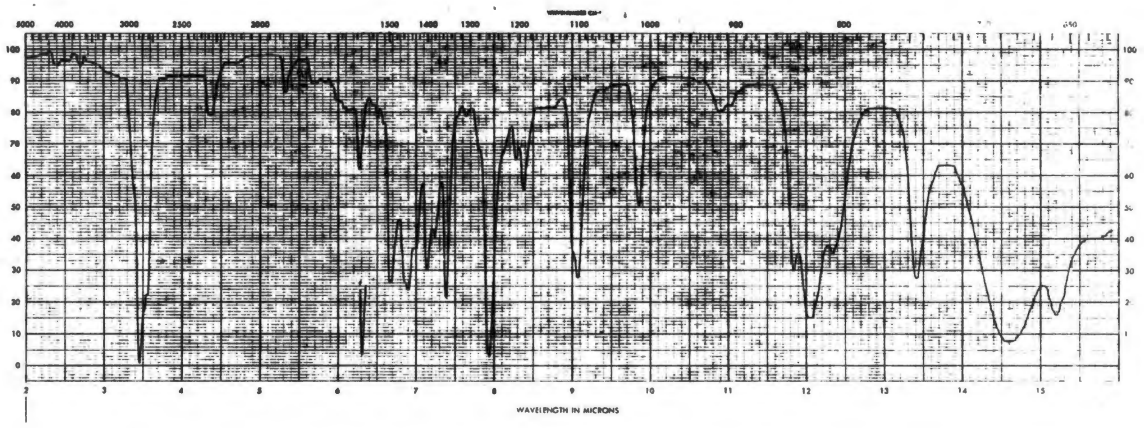


(3-Chlorobenzyl)-(2-carboxyethyl)diphenylphosphonium Chloride (106), KBr Pellet

PLATE VIII

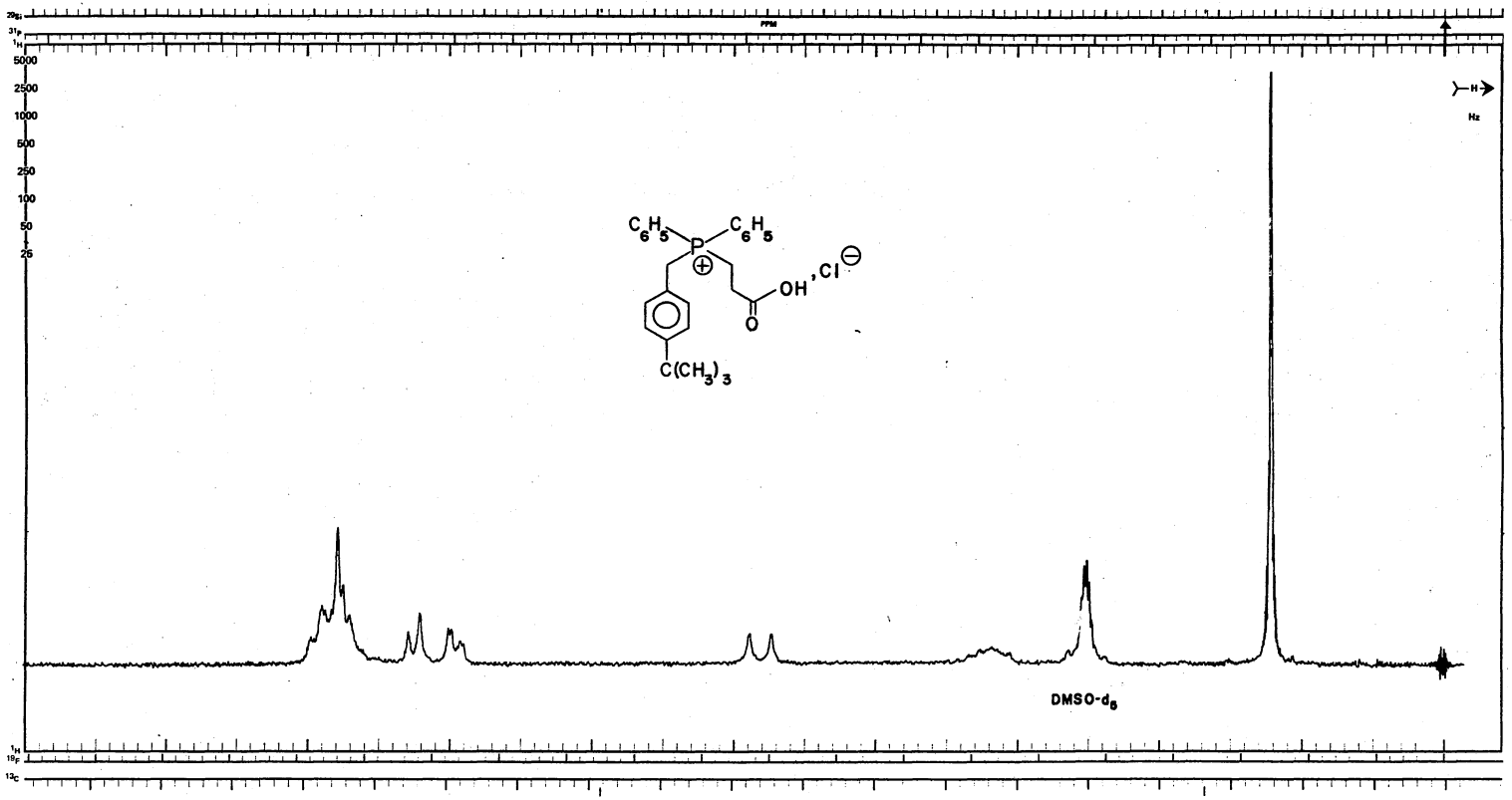


PMR Spectrum of 4-tert-Butylbenzyl Chloride (148)



Infrared Spectrum of 148, Thin Film

PLATE IX

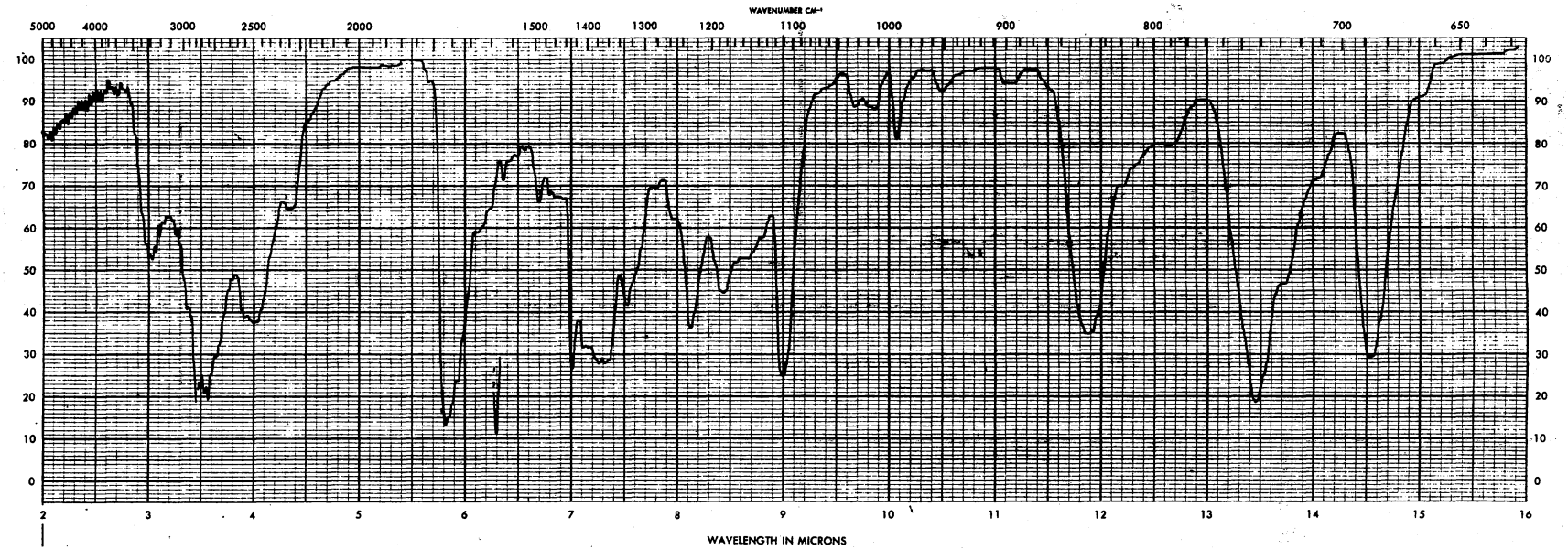


(4-tert-Butylbenzyl)-(2-carboxyethyl)diphenylphosphonium Chloride (107)

Solvent. . . . DMSO-d_6 O.F. . . 100.1 MHz F.B. . . 2.0 Hz R.F. . 66 dB

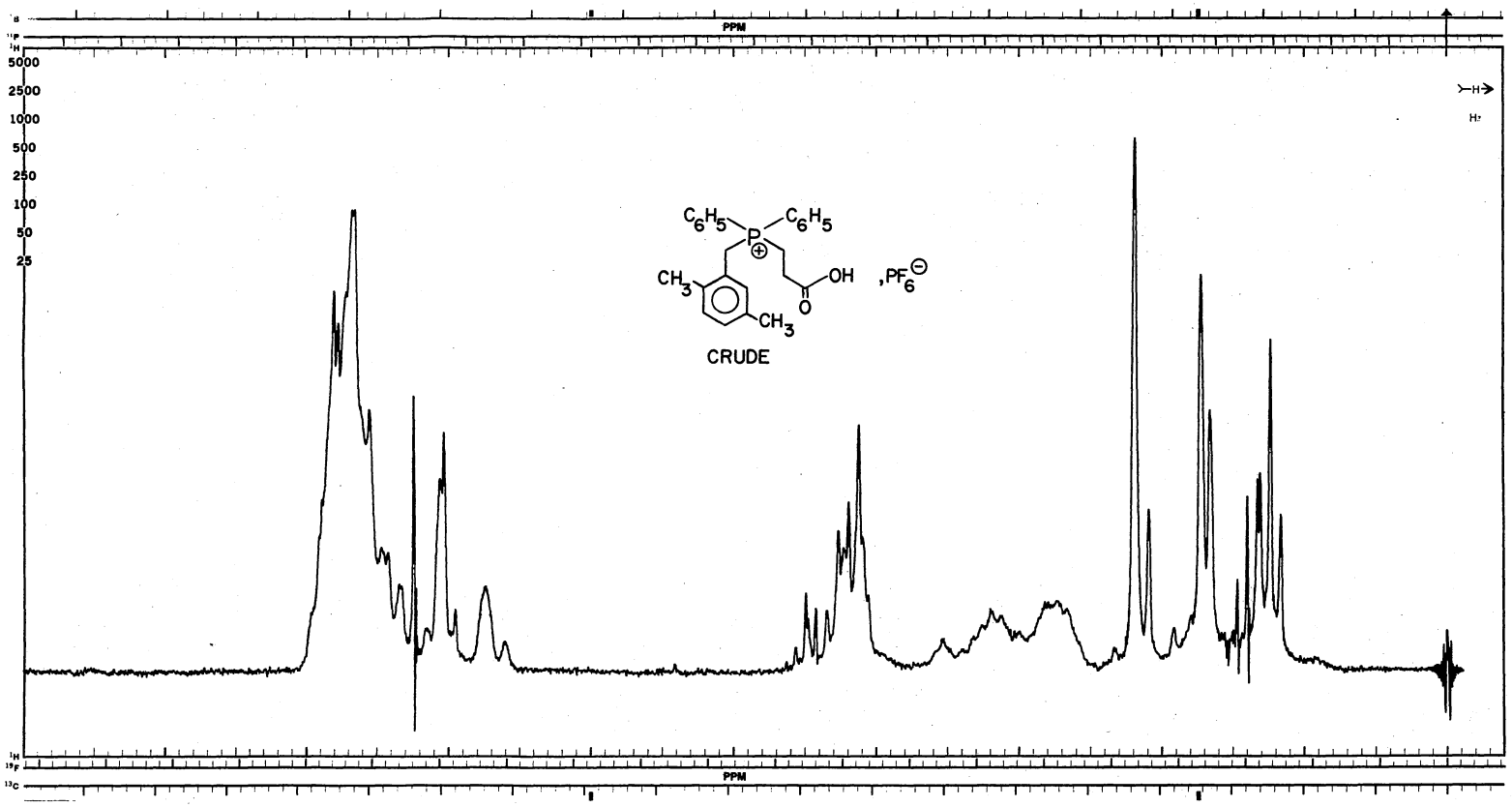
S.W. . . . . 1000 Hz S.T. . . .500 sec. S.O. . 85701 Hz S.A. . . 3.2 Lock. .HOMO

PLATE X



(4-tert-Butylbenzyl)-(2-carboxyethyl)diphenylphosphonium Chloride (107), KBr Pellet

PLATE XI

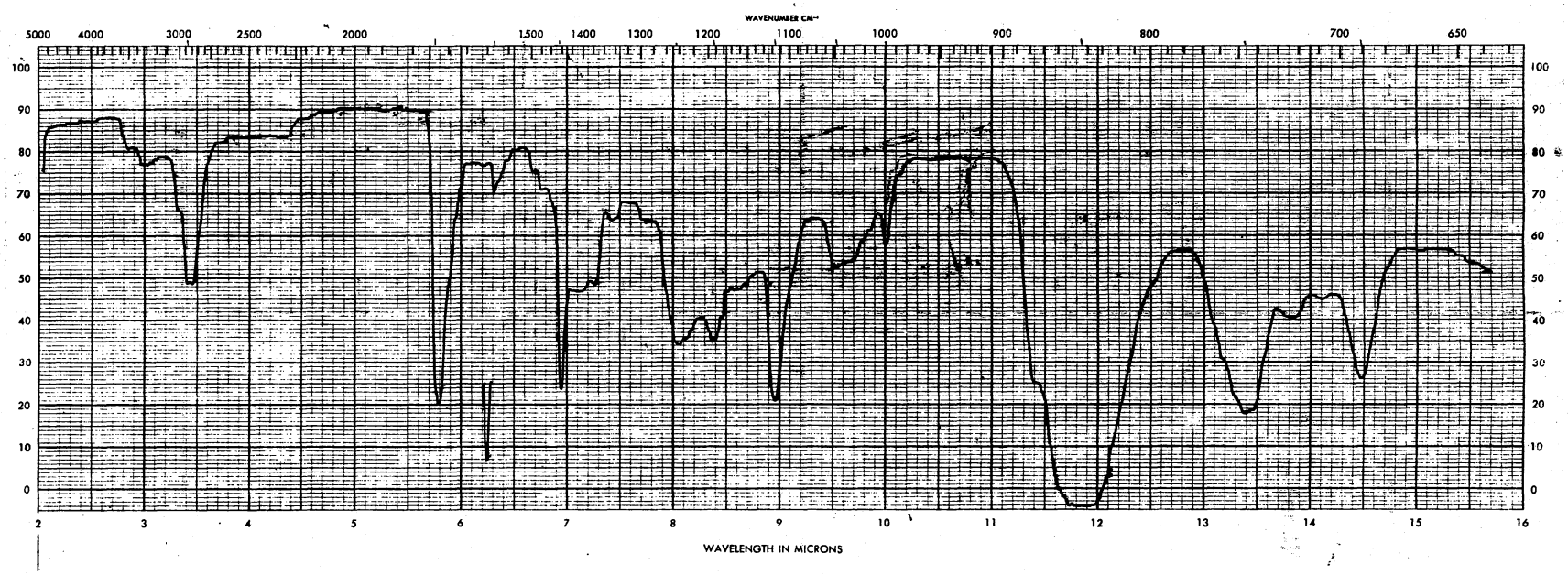


(2,5-Dimethylbenzyl)-(2-carboxyethyl)diphenylphosphonium Hexafluorophosphate (108)

Solvent. . .$DCCl_3/CF_3CO_2H$ O.F. . 100.1 MHz F.B. . . 2.0 Hz R.F. . 68 dB

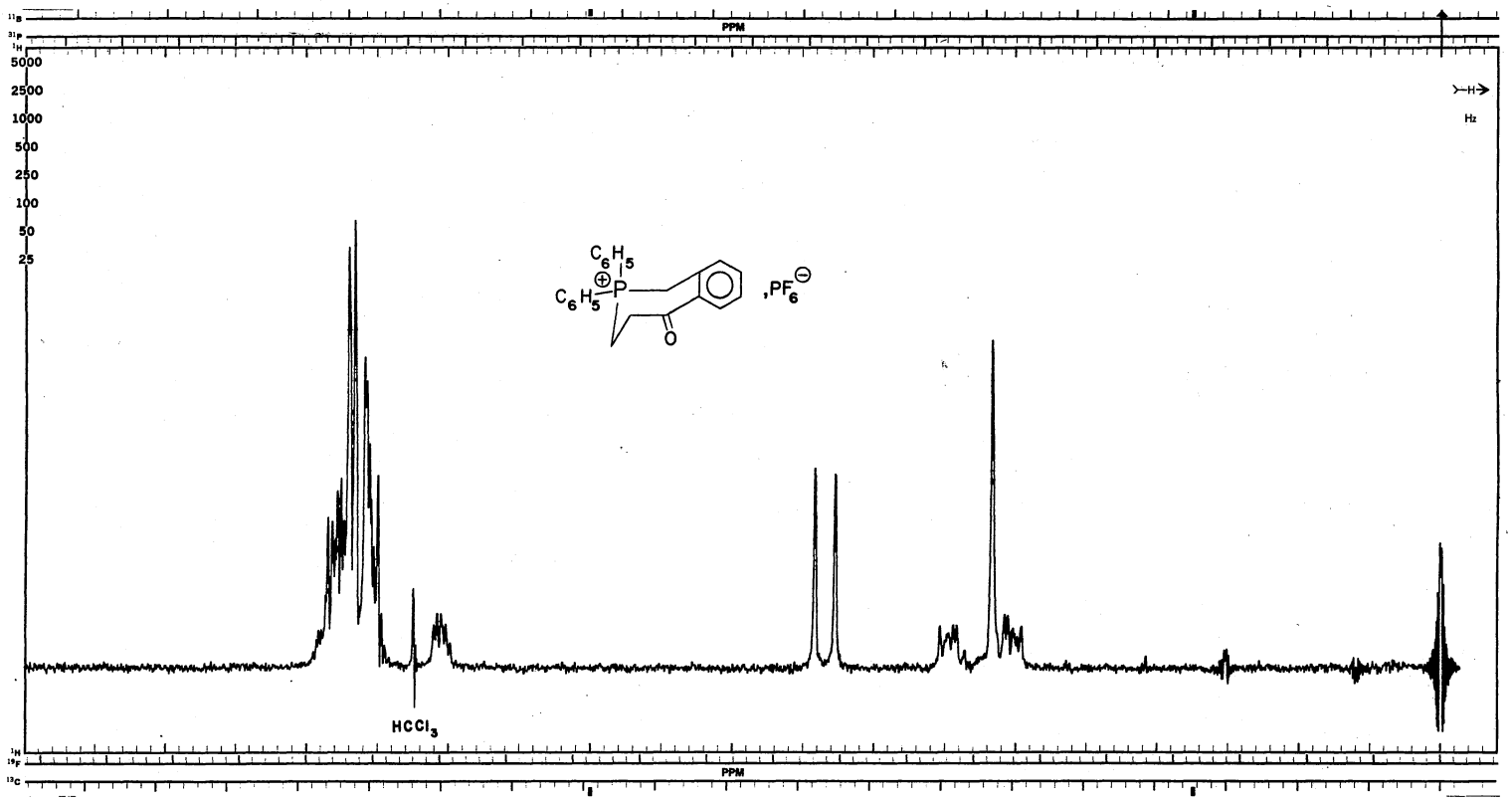
S.W. . . . . .1000 Hz S.T. . .500 sec. S.O. . 83701 Hz S.A. . . 5.0 Lock. . .HOMO

PLATE XII



(2,5-Dimethylbenzyl)-(2-carboxyethyl)diphenylphosphonium Hexafluorophosphate (108), Melt

PLATE XIII

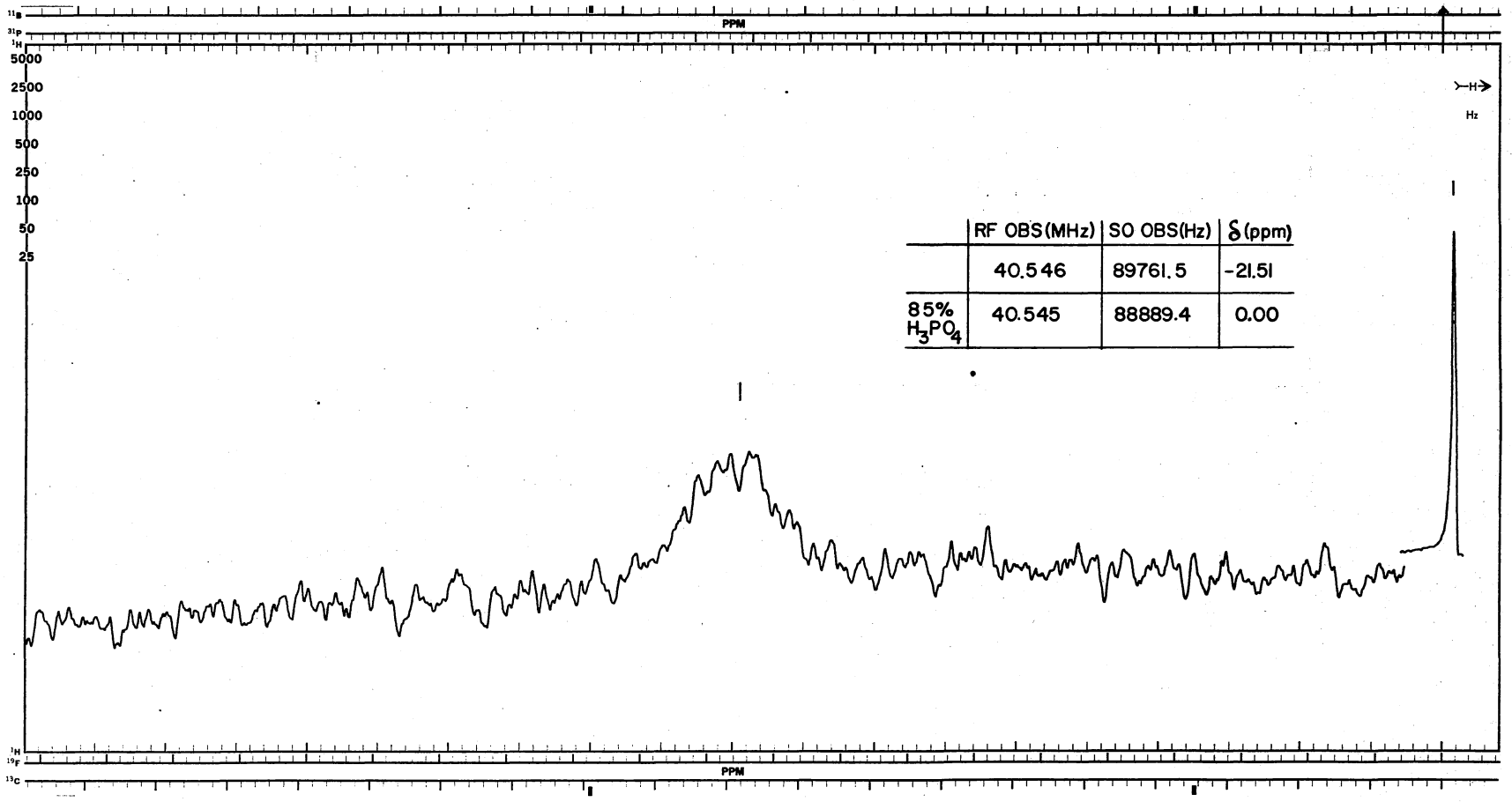


2,3,4,5-Tetrahydro-5-oxo-2,2-dipheny1-1H-2-benzophosphepinium Hexafluorophosphate (109)

Solvent. . .$DCCl_3/CF_3CO_2H$ O.F. . 100.1 MHz F.B. . . 2.0 Hz R.F. . 67 dB

S.W. 1000 Hz S.T. 500 sec. S.O. 85701 Hz S.A. 6.3 Lock. .HOMO

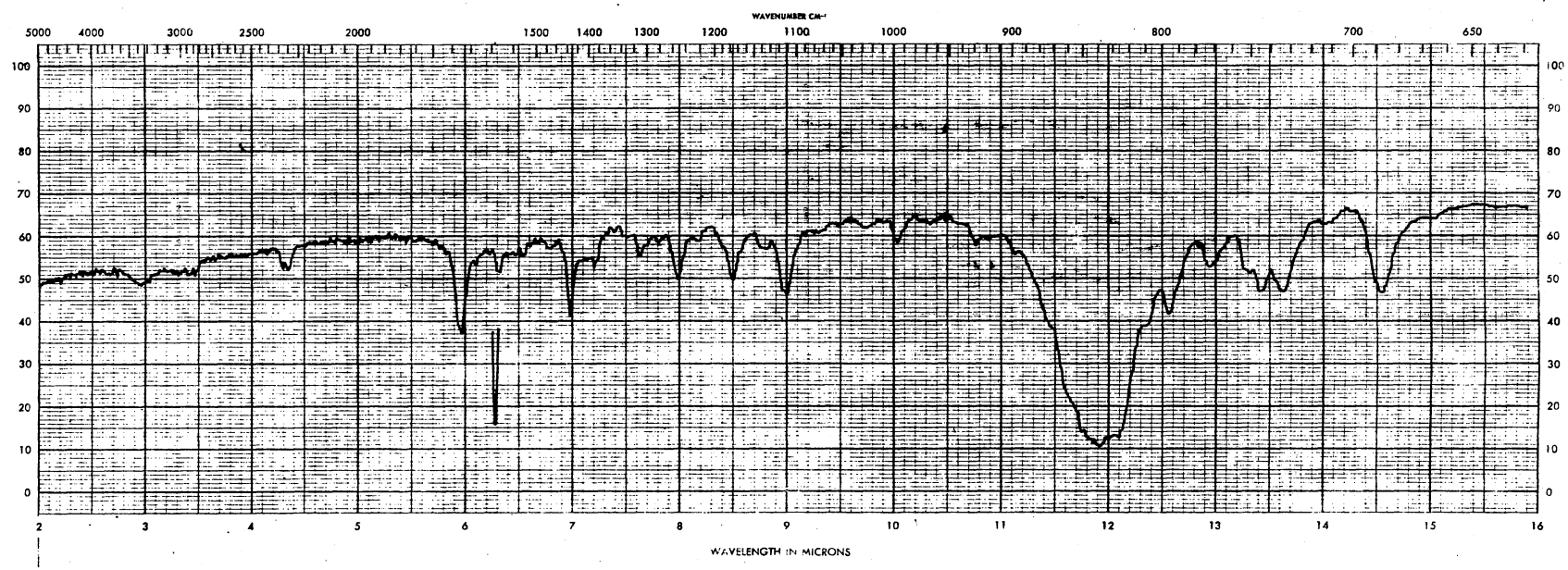
PLATE XIV



	RF OBS(MHz)	SO OBS(Hz)	δ(ppm)
	40.546	89761.5	-21.51
85% H_3PO_4	40.545	88889.4	0.00

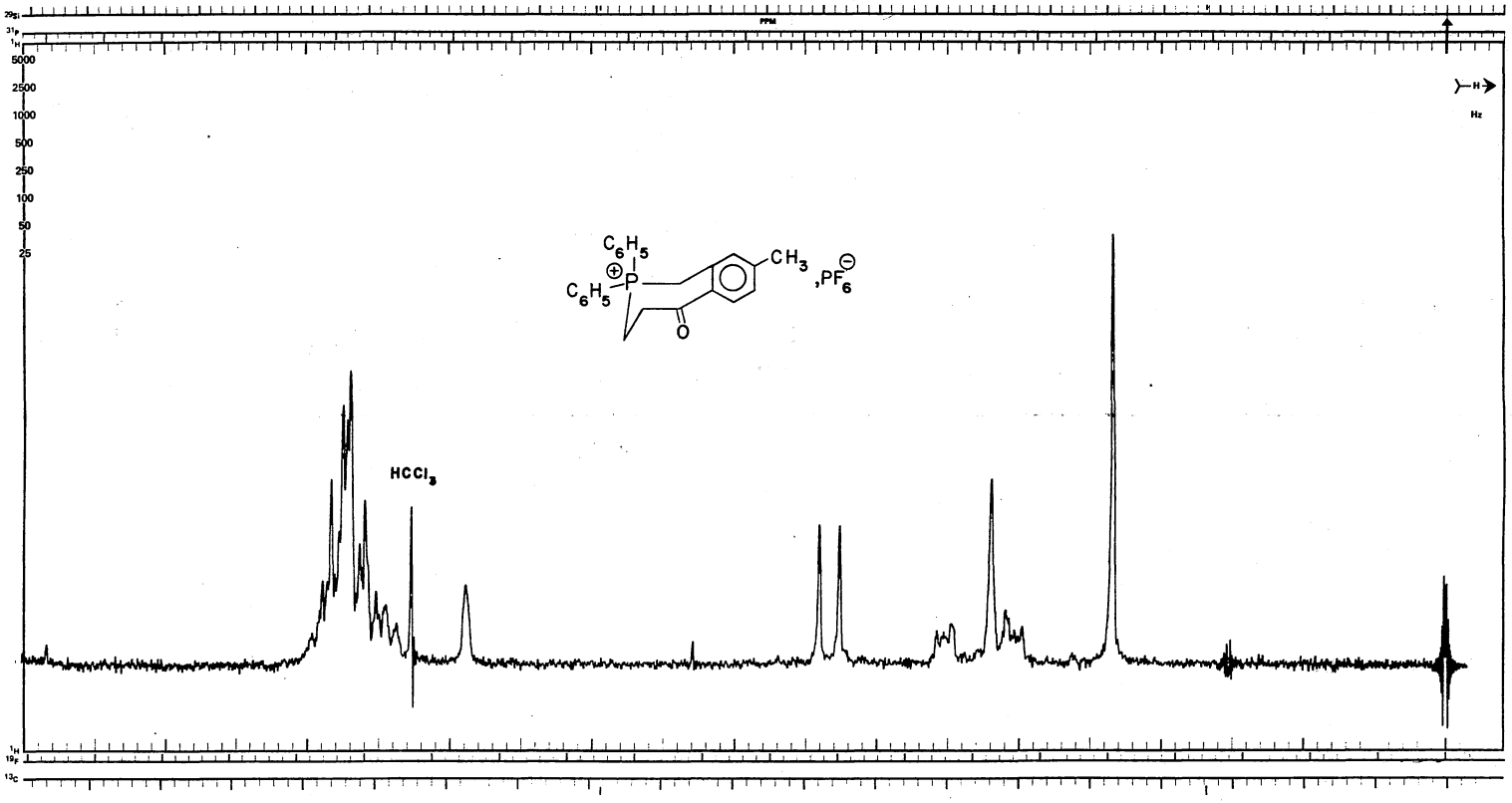
^{31}P Spectrum of 2,3,4,5-Tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (109)

PLATE XV



2,3,4,5-Tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (109), KBr Pellet

PLATE XVI

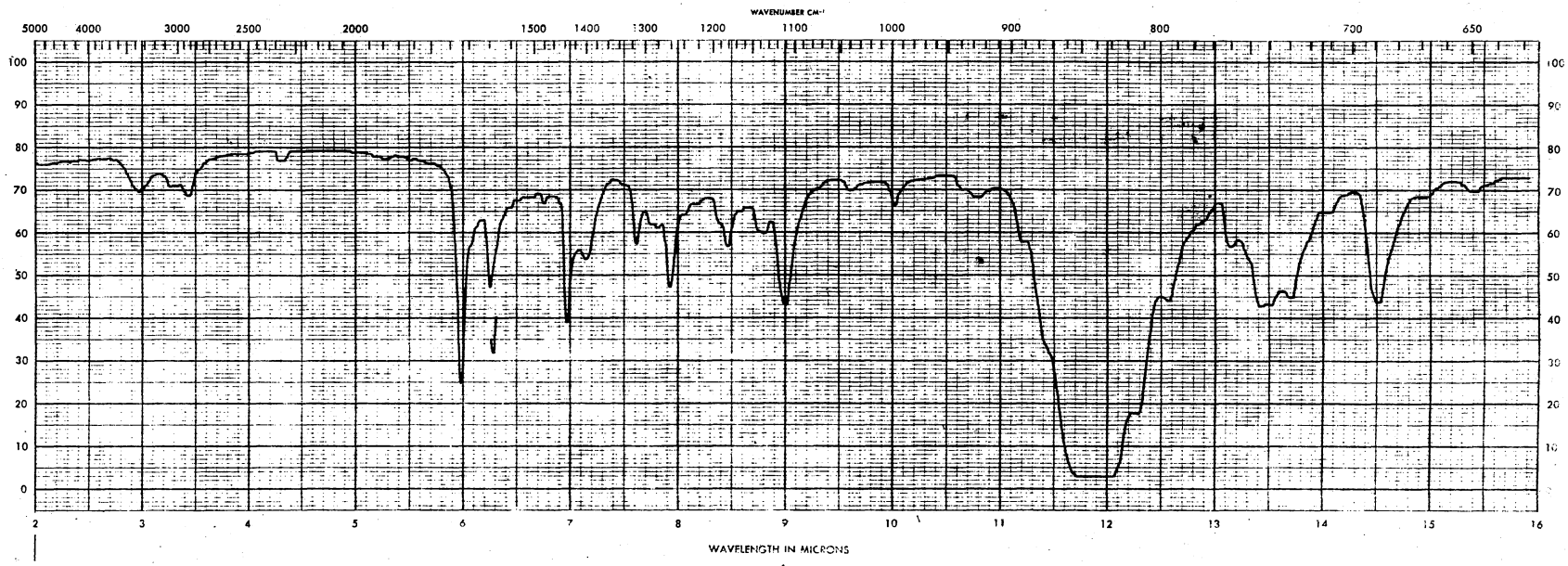


2,3,4,5-Tetrahydro-8-methyl-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (110)

Solvent. . .$DCCl_3/CF_3CO_2H$ O.F. . 100.1 MHz F.B. . . 2.0 Hz R.F. . 70 dB

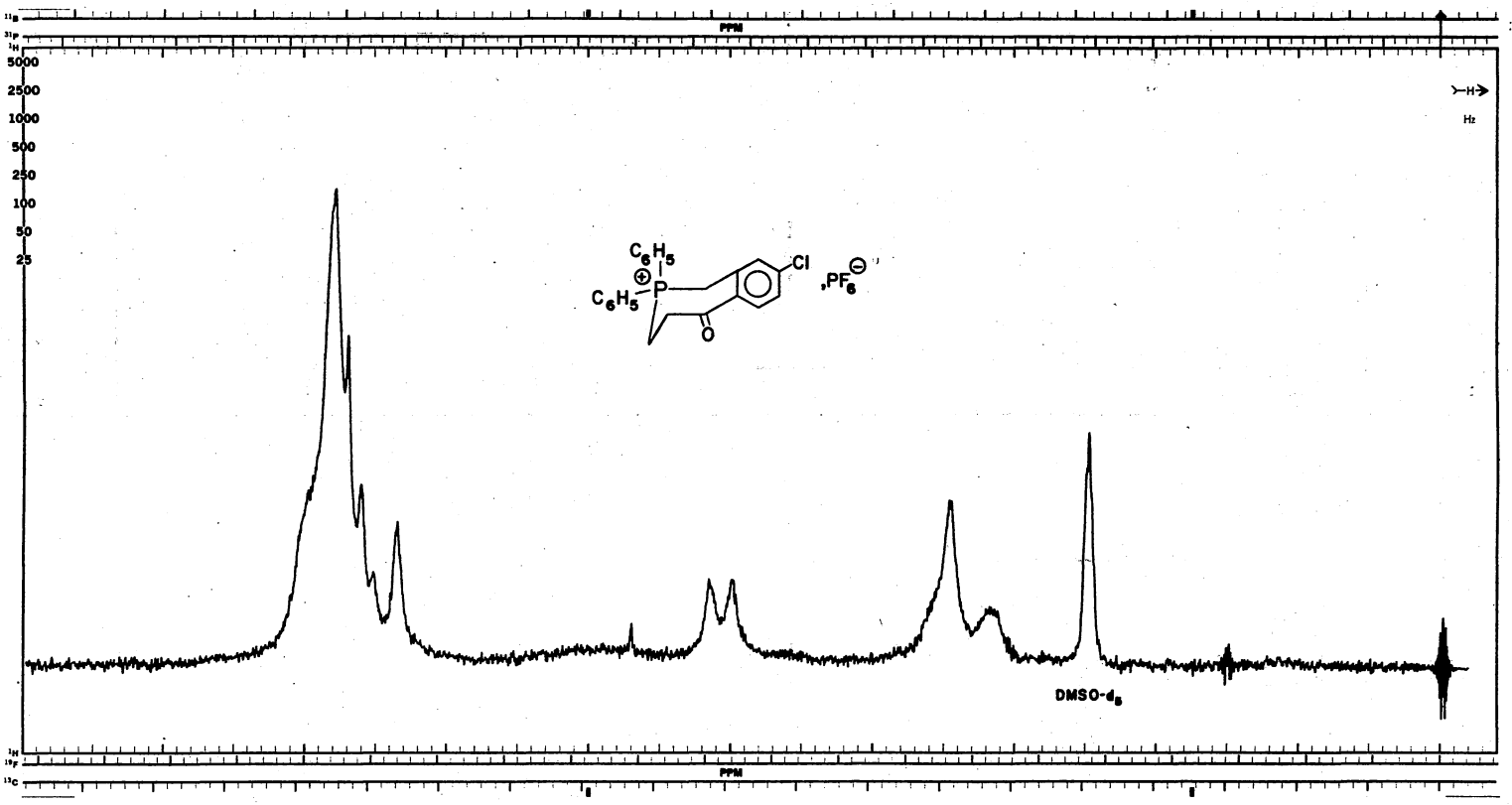
S.W. 1000 Hz S.T. 500 sec. S.O. 85701 Hz S.A. 8.0 Lock. .HOMO

PLATE XVII



2,3,4,5-Tetrahydro-8-methyl-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (110), KBr Pellet

PLATE XVIII

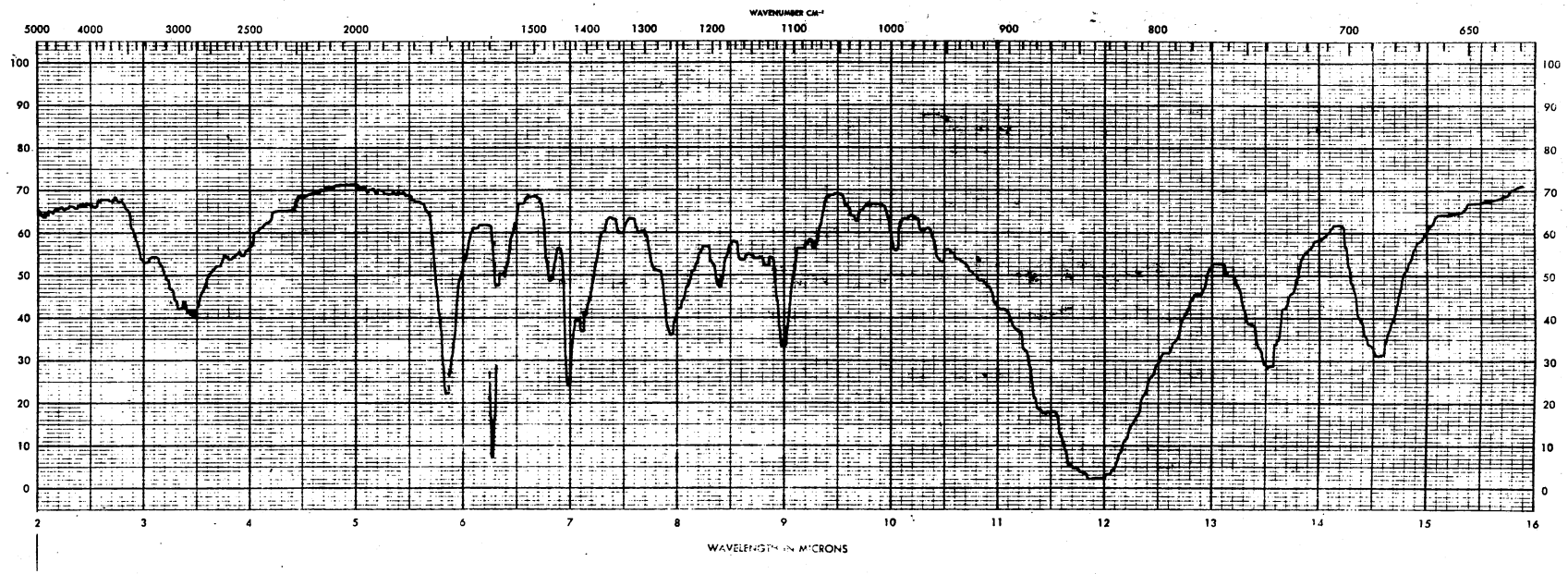


8-Chloro-2,3,4,5-tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (111)

Solvent. . . . DMSO-d_6 O.F. . 100.1 MHz F.B. . . 2.0 Hz R.F. . 70 dB

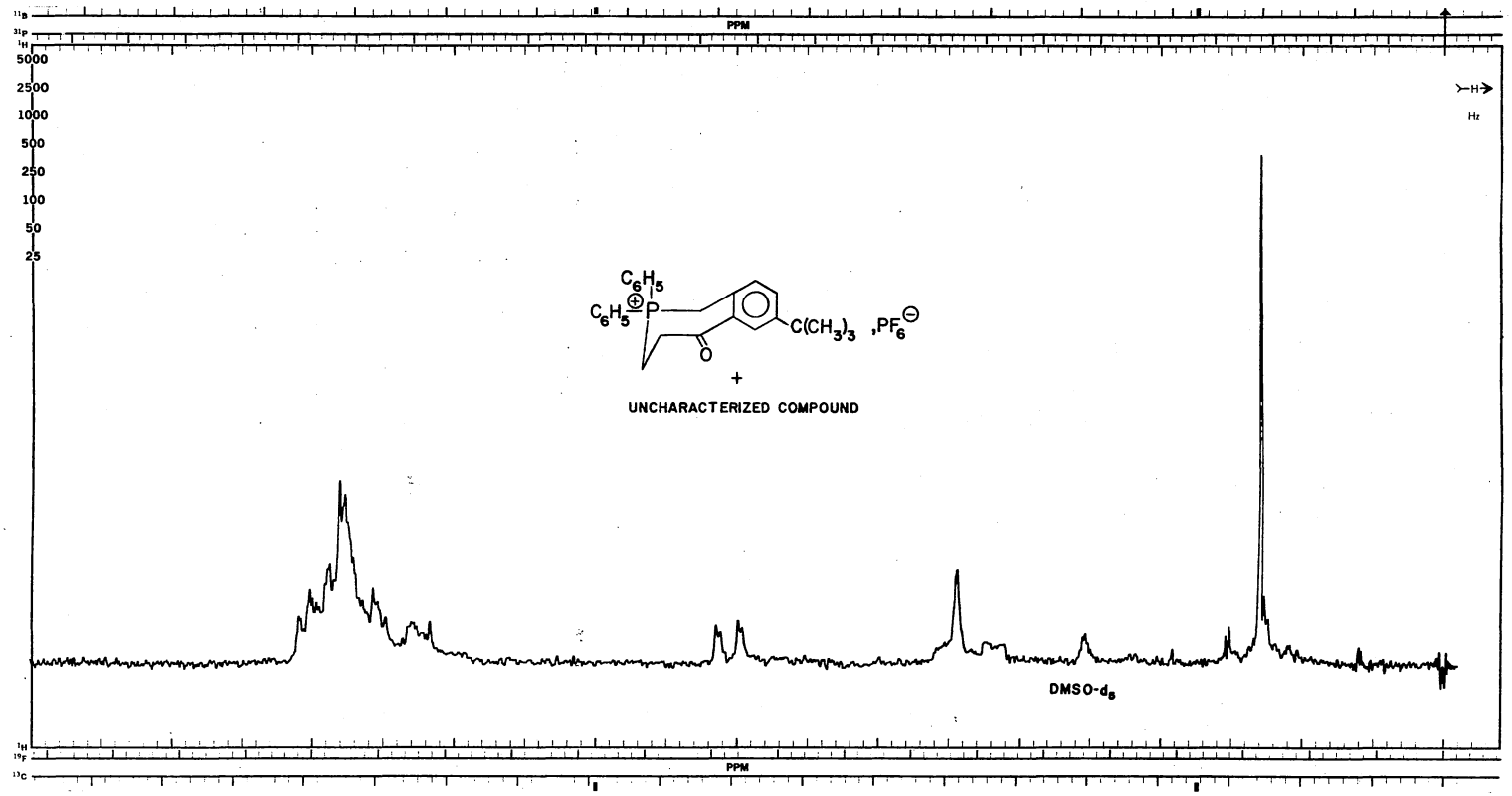
S.W. . . . . 1000 Hz S.T. . .500 sec. S.O. . 85701 Hz S.A. . . .10 Lock. . .HOMO

PLATE XIX



8-Chloro-2,3,4,5-tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (111), KBr Pellet

PLATE XX

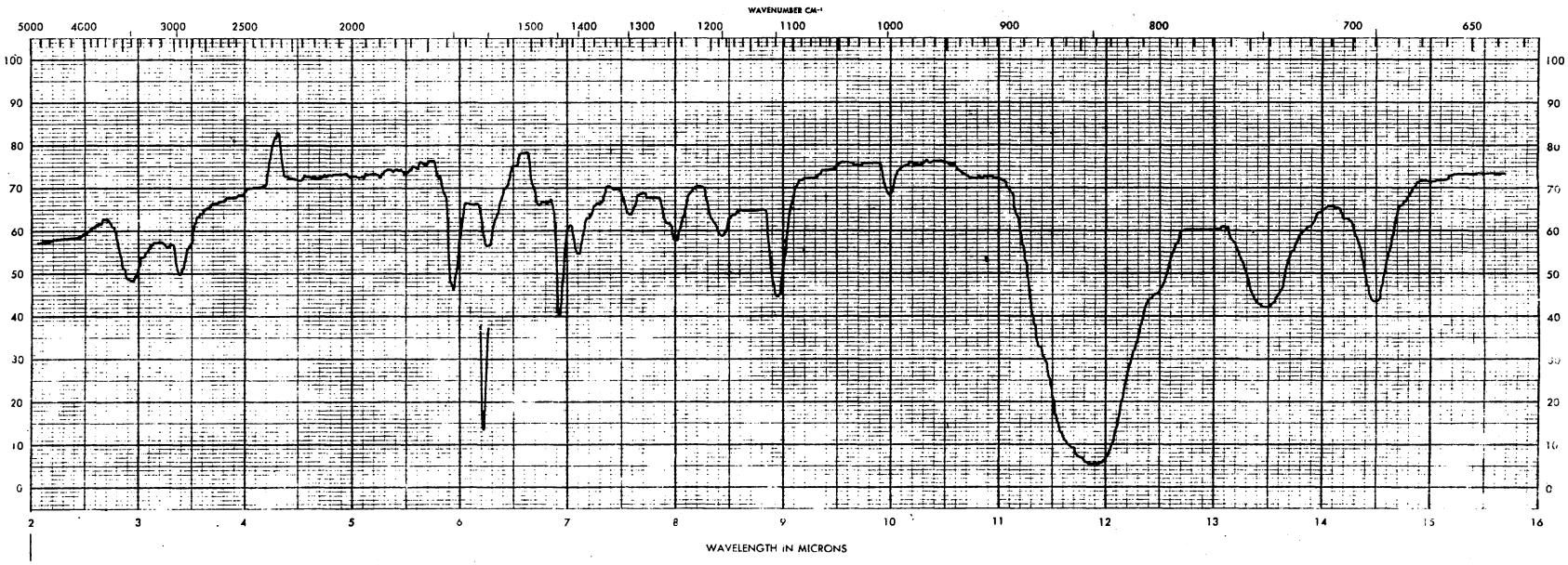


7-tert-Butyl-2,3,4,5-tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (112)

Solvent. . .$DCCl_3/CF_3CO_2H$ O.F. . 100.1 MHz F.B. . . 2.0 Hz R.F. . 70 dB

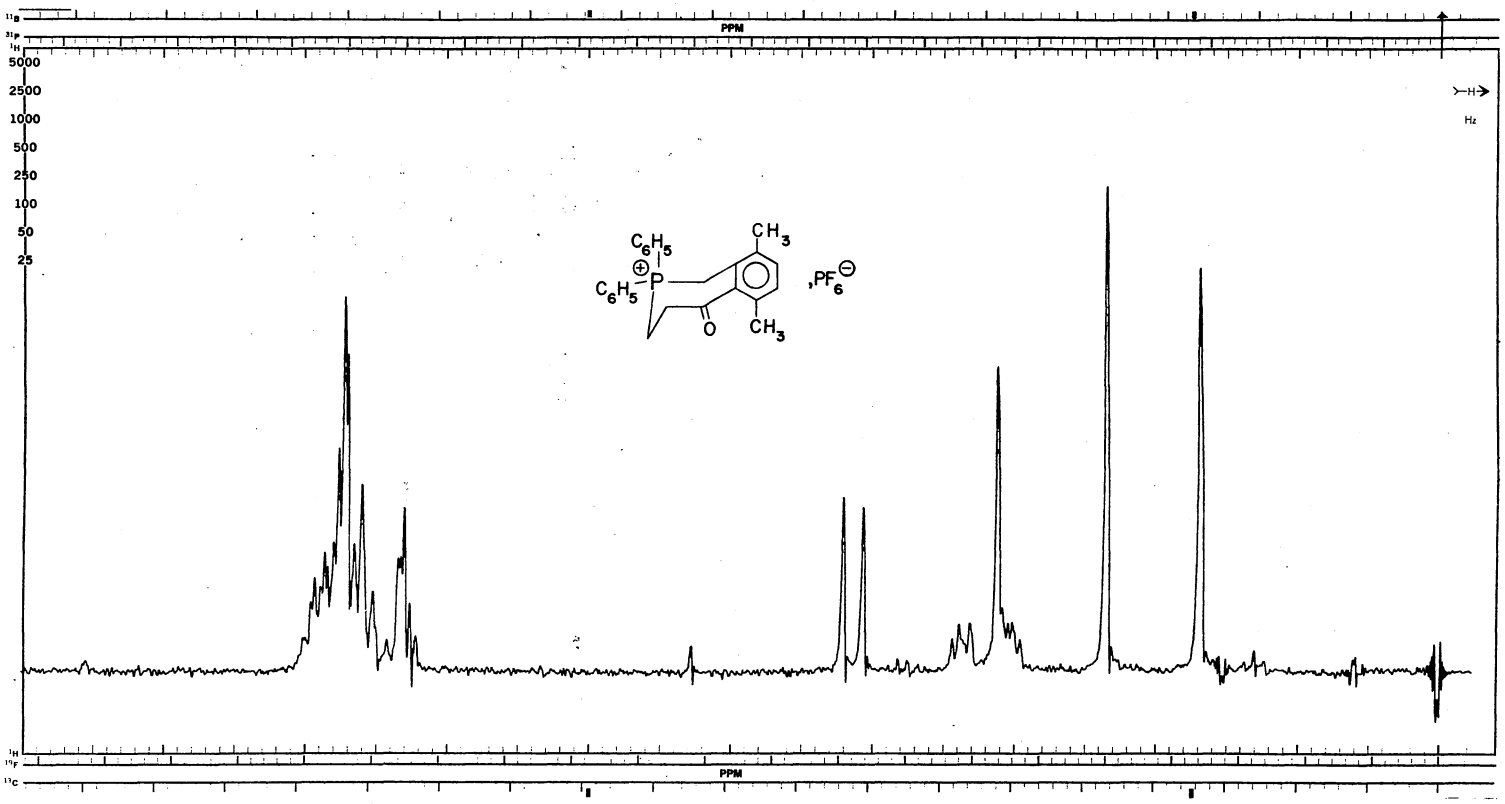
S.W. . . . . .1000 Hz S.T. . .250 sec. S.O. . 85701 Hz S.A. . . 6.3 Lock. .HOMO

PLATE XXI



7-tert-Butyl-2,3,4,5-tetrahydro-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (112), KBr Pellet

PLATE XXII

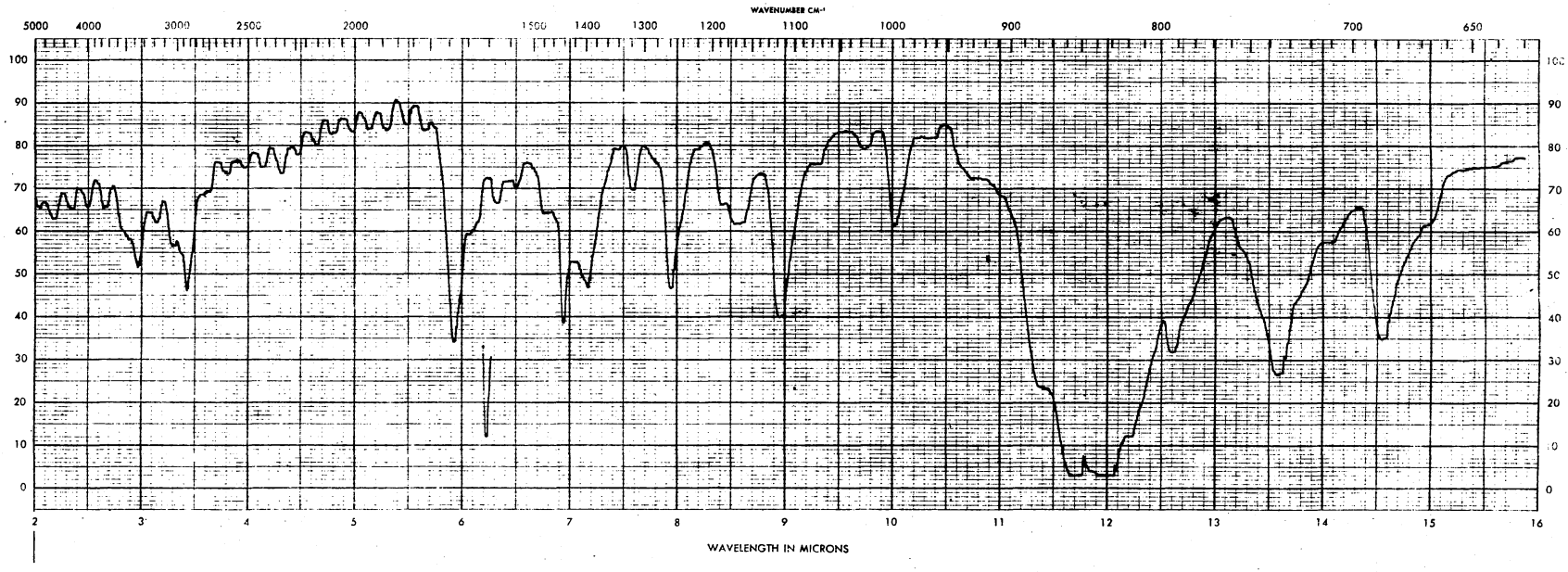


2,3,4,5-Tetrahydro-6,9-dimethyl-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (113)

Solvent. . .$DCCl_3/CF_3CO_2H$ O.F. . 100.1 MHz F.B. . . 2.0 Hz R.F. . 70 dB

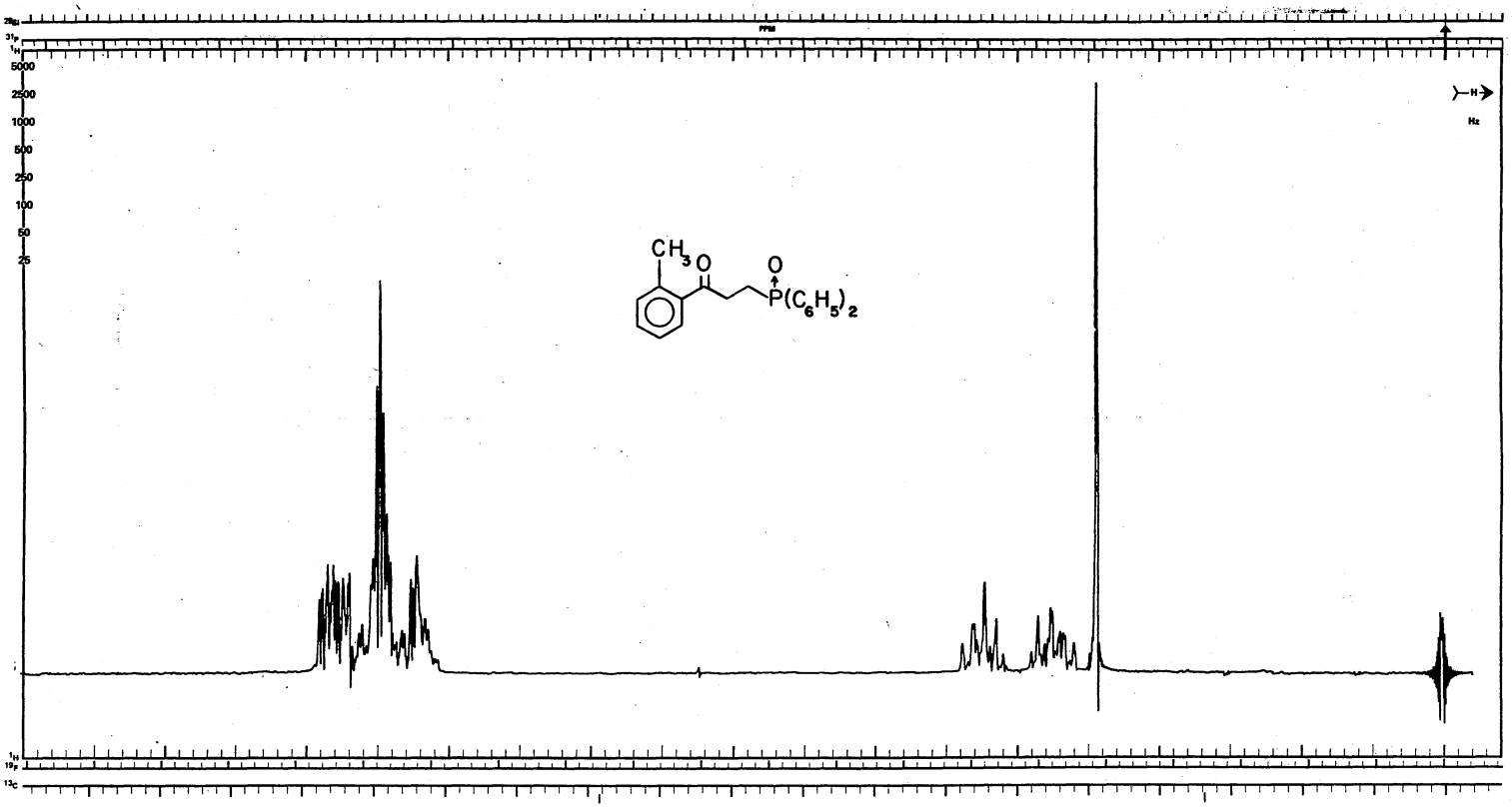
S.W. . . . . .1000 Hz S.T. . .250 sec. S.O. . 85701 Hz S.A. . . 6.3 Lock. .HOMO

PLATE XXIII



2,3,4,5-Tetrahydro-6,9-dimethyl-5-oxo-2,2-diphenyl-1H-2-benzophosphepinium Hexafluorophosphate (113), KBr Pellet

PLATE XXIV

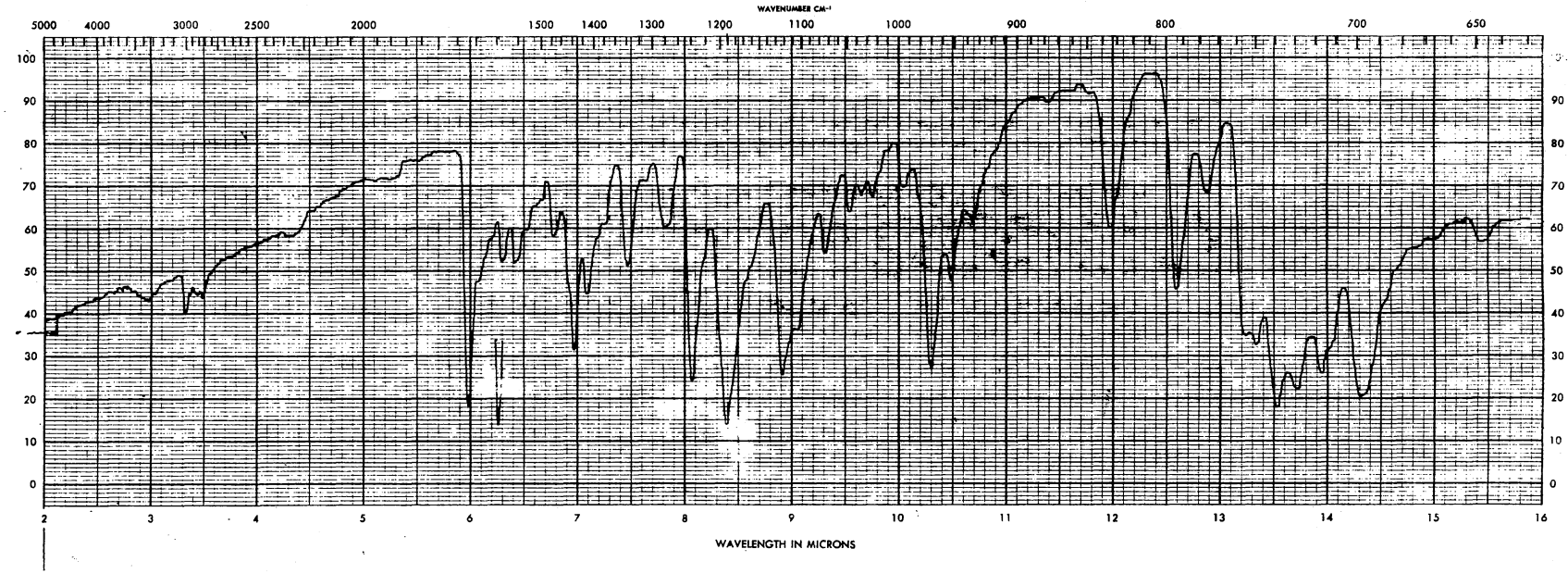


(3-Diphenylphosphinyl)-2'-methylpropiophenone (114)

Solvent. . . . $DCCl_3$ O.F. . 100.1 MHz F.B. . . 2 Hz R.F. . 66 dB

S.W. . . . . 1000 Hz S.T. . .500 sec. S.O. 85701 Hz S.A. . .1.25 Lock. . . . .HOMO

PLATE XXV



(3-Diphenylphosphinyl)-2'-methylpropiophenone (114), Thin Film

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