I. REACTIONS OF ORTHO-SUBSTITUTED AROYL CHLORIDES WITH TRIALKYL PHOSPHITES

II. SOME SYNTHESES OF OPTICALLY ACTIVE PHOSPHORUS COMPOUNDS

By

DONALD HOWARD BURPO

Bachelor of Science
Bethany Nazarene College
Bethany, Oklahoma
1963

Master of Science
Oklahoma State University
Stillwater, Oklahoma
1965

Submitted to the faculty of the Graduate College
of the Oklahoma State University
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Thesis Approved:

K D Berlin
Thesis Adviser

Ernest M. Hodnett

Tom E. Moore

H. A. Pohl

J. Durham
Dean of the Graduate College

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PART I

REACTIONS OF ORTHO-SUBSTITUTED AROYL CHLORIDES WITH TRIALKYL PHOSPHITES

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INTRODUCTION

The thesis is composed of two distinct sections. Each major part is presented separately with individual subsections and is thus complete within itself.

Acid chlorides and trialkyl phosphites react in a Michaelis-Arbuzov reaction with the formation of compounds containing C-P bonds. Evidence is provided in Part I that phthaloyl chloride and trimethyl phosphite give a new phosphorylated heterocycle in an unusual cyclization process. The mechanism of the reaction and structure determination of the products are discussed.

Several new optically active organophosphorus compounds were synthesized as described in Part II. Synthetic methods outlined include formation of P-O and P-N bonds via nucleophilic displacement reactions on phosphorus by the oxygen and nitrogen atoms of alcohols and amines. In all cases optical activity in the products resulted from an asymmetric center in the alcoholic or amine portion of the molecule rather than an asymmetric phosphorus atom.

CHAPTER I

HISTORICAL

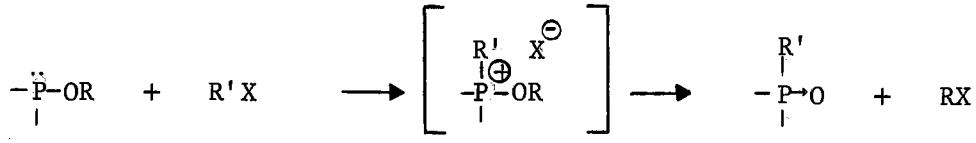
The Michaelis-Arbuzov Rearrangement

Since 1898, when the reaction of trialkyl phosphites with alkyl halides to yield phosphonates was discovered by Michaelis and Kaehne,[67] the Michaelis-Arbuzov rearrangement has been one of the most versatile methods for the formation of carbon-phosphorus bonds. This reaction

$$(RO)_3P + R'X \longrightarrow (RO)_2P(O)R' + RX$$

has been extended to other trivalent-phosphorus esters for the synthesis of phosphinic esters and phosphine oxides. The order of reactivity of trivalent-phosphorus esters in this reaction has been demonstrated to be phosphite < phosphonite < phosphinite.[88] The usual reactivity sequence of the halide is: secondary alkyl < primary alkyl < acyl, and chloride < bromide < iodide.[42] Several reviews on the scope and limitations of this rearrangement and related reactions may be found in the literature.[8,42,47,54,55]

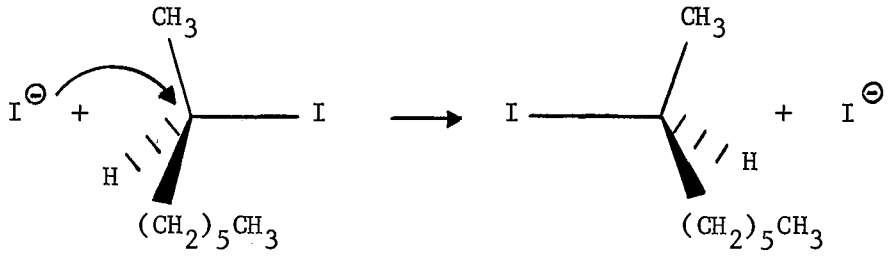
A two-step mechanism was first proposed by Arbuzov.[2] Crystalline



1:1 adducts, which decompose to phosphine oxides upon warming, were isolated from low-temperature reactions of alkyl dialkylphosphinites with alkyl halides.[89] The degree of ionic character in the quasiphosphonium intermediate is uncertain.[42]

In the first step of the rearrangement, an assumed S_N2 mechanism with primary halides has not been established by the existing kinetic and stereochemical data.[42] When some optically active secondary halides were heated with triethyl phosphite, the halides underwent extensive racemization in preference to furnishing the expected phosphonates as shown below.[35] An S_N1 mechanism for the first step has been suggested

$$(CH_3CH_2O)_3P + CH_3(CH_2)_5CH(CH_3)I \longrightarrow CH_3CH_2I + (CH_3CH_2O)_2P(O)CH(CH_3)(CH_2)_5CH_3$$



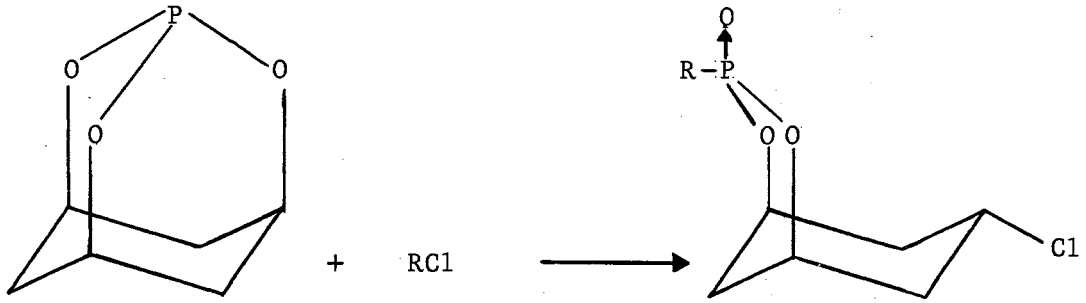
$$(CH_3CH_2O)_3P + CH_3CH_2I \longrightarrow (CH_3CH_2O)_2P(O)CH_2CH_3 + CH_3CH_2I$$

for the fast-reacting benzhydryl and 9-fluorenyl bromides[93] and triarylmethyl halides.[42]

Stereochemical evidence for inversion of configuration in the attack of the halide ion on the alkyl carbon of the ester has been reported by various workers.[15-17,35,57] Gerrard and Green,[35] using tri-2-octyl phosphite prepared from (+)-2-octanol, found that reaction

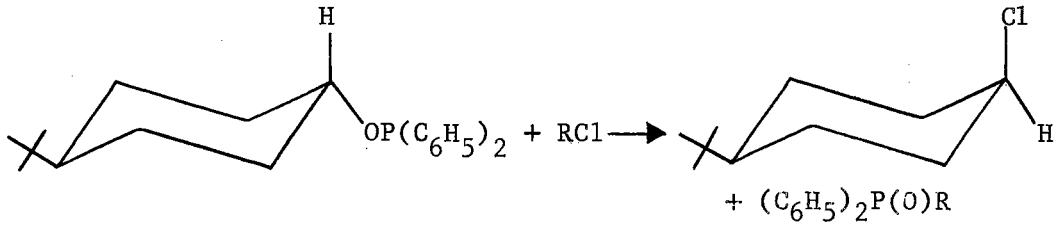
with ethyl iodide proceeded with inversion to yield (-)-2-iodooctane. From treatment of benzyltriphenoxyphosphonium chloride with optically active 2-octanol, Landauer and Rydon[57] obtained 2-chlorooctane of the inverted configuration. Presumably interchange of an octyloxy for a phenoxy group was followed by an inversion step in the decomposition of the quasiphosphonium salt.

A series of bicyclic phosphonates were synthesized by reacting 1-phospha-2,8,9-trioxaadamantane with several alkyl halides.[16,17]



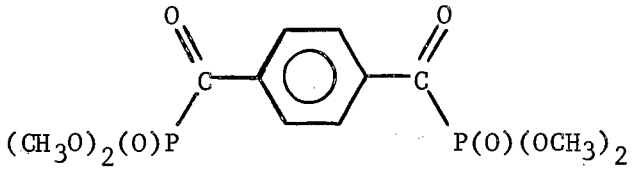
An equatorial chlorine in the bicyclic phosphonates, indicated by IR, NMR, and dipole moment studies, suggested an S_N2 displacement by chloride ion at a bridgehead atom in the quasiphosphonium intermediate.

Recently, Berlin and coworkers[15] reacted trans-4-t-butylcyclohexyl diphenylphosphinite with benzyl chloride and with carbon tetrachloride. In both reactions, cis-4-t-butylcyclohexyl chloride and none of the trans-isomer was produced. This is indicative of a stereospecific inversion at the C-1 position as expected if a Michaelis-Arbuzov

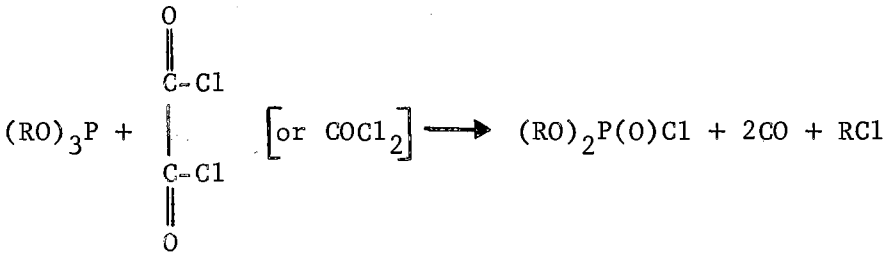


reaction followed an S_N2 mechanism in the last step.

The acid chlorides of a series of long-chain aliphatic dibasic acids and trimethyl phosphite react to give tetramethyl diphosphonates in nearly quantitative yields.[68] When trimethyl phosphite was added to terephthaloyl chloride, the reaction apparently proceeded as expected to form tetramethyl terephthaloyldiphosphonate.[95] However, the product



was not isolated. Only tar was reported[76] for the vigorous reaction of triethyl phosphite with maleoyl chloride. Addition of a trialkyl phosphite to either oxalyl chloride or phosgene yielded not the expected diphosphonate, but instead the phosphorochloridate, carbon monoxide, and alkyl halide.[42]

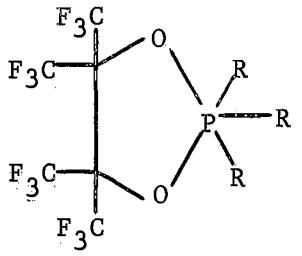


Cyclizations Involving Trivalent Phosphorus Compounds

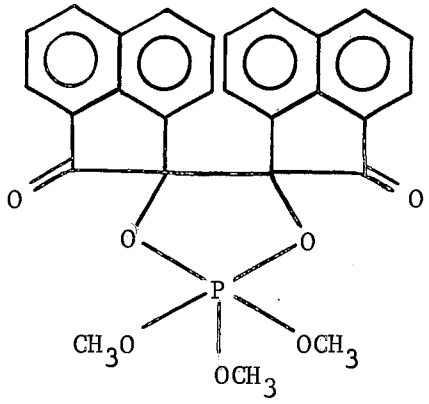
In recent years several reviews[13,30,31,63,73,77,80] of the chemistry of cyclic phosphorus compounds have appeared. These reviews describe the synthesis and reactivity of phosphorus heterocycles containing other hetero atoms,[30] cyclic systems formed from carbonyl

compounds[73,77,80] and systems based on phosphorus and carbon as the only ring atoms.[13,63,77]

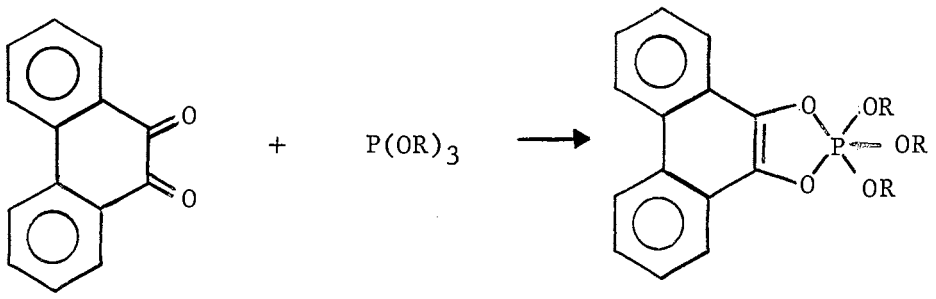
A variety of carbonyl-containing compounds (which possess electron-withdrawing groups adjacent to the carbonyl group) react with trivalent-phosphorus esters. Monocarbonyl compounds of this type,[69,86] such as perfluroacetone,[86] are reported to produce 2:1 adducts (1,3,2-dioxaphospholanes) with phosphines or trivalent-phosphorus esters. A 2:1



adduct[85] formed from reaction of acenaphthenequinone with trimethyl phosphite. Addition of phosphorus esters to <u>ortho</u>-quinones,[81,82]

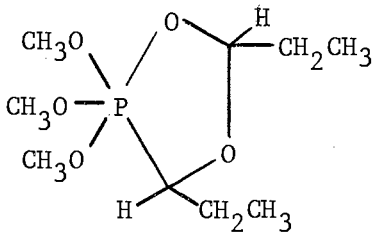


α-diketones,[56,81,82] α-ketoaldehydes,[84] and triketones[84] led to 1,3,2-dioxa-4-phospholenes. An example[80] of this ring system is that produced by reaction of triisopropyl phosphite with phenanthrenequinone. The structure of this compound was confirmed by IR and Raman spectra, proton and ^{31}P NMR spectra, and X-ray analysis. Not only phosphites but also triphenylphosphine, alkyl diphenylphosphinites, and dialkyl

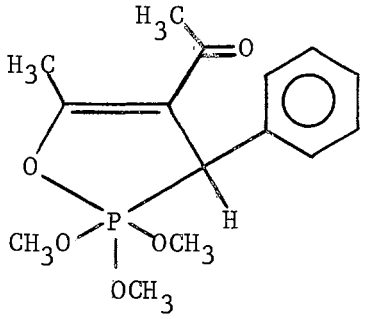


phenylphosphonites[86] added to phenanthrenequinone to give 1,3,2-dioxa-4-phospholenes.

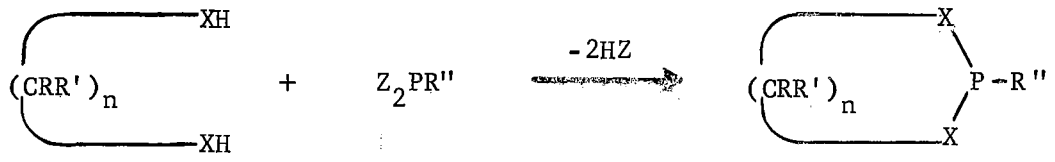
Ramirez[80] noted that a 3:1 mole ratio of propionaldehyde and trimethyl phosphite, when stirred for 14 days at 20°, yielded a 2:1 adduct (a 1,4,2-dioxaphospholane). An α,β-unsaturated ketone, 3-



benzylidene-2,4-pentanedione, and trimethyl phosphite condensed to form the phosphorus heterocycle shown below.[83]

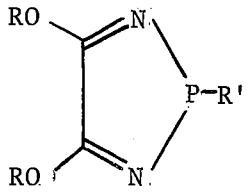


Cyclizations[31] of α,ω-difunctional organic compounds with trivalent-phosphorus halides or esters give rings containing two hetero-atoms. Included in the studies were aliphatic diols, dithiols, diamines, and their aromatic counterparts.

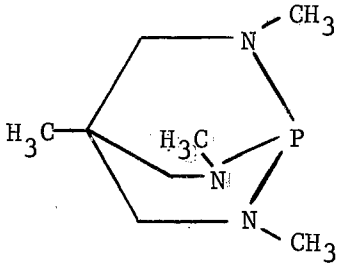


Aliphatic and alicyclic diols react with phosphorus trichloride to produce cyclic phosphorochloridites.[3-6] Most attention[30] has been devoted to 1,2- and 1,3-diols, which give rise to the 1,3,2-dioxaphospholane and 1,3,2-dioxaphosphorinane ring systems, respectively. These same ring systems result from reaction of diols with phosphorodichloridites,[4,7] catechol with phosphorus trichloride,[30] and diols with tertiary phosphites[10,36,71] or dialkyl phosphites.[71] Transesterification has also been applied to the preparation of bicyclic systems[19,25,27,32] from triols and tertiary phosphites.

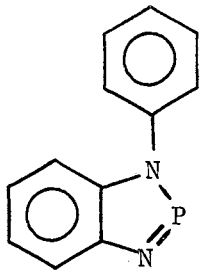
Some unusual ring systems containing phosphorus and nitrogen have been synthesized recently. A cyclic product was formed from dichlorophosphines and esters of oxalodiimidic acid.[28] Cyclization of a



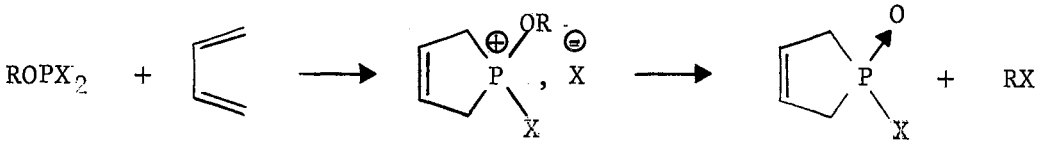
triamine with phosphorus trichloride afforded 2,6,7-trimethyl-4-methyl-2,6,7-triaza-1-phosphabicyclo[2.2.2]octane.[58] An even more unusual



heterocycle results from reaction of an aromatic ortho-diamine with triphenyl phosphite.[74]

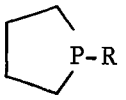


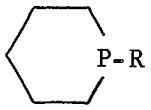
Trivalent-phosphorus halides generally add to dienes producing phospholenes.[13,77] Phosphorodichloridites, phosphorodibromidites, and cyclic phosphorochloridites condense with dienes to give initially what is thought[77] to be an aryloxy-[91] or an alkoxyphosphonium salt. The latter adducts decompose giving an alkyl halide and a 3-phospholene 1-oxide.[1,90] Likewise phosphonous dihalides[64-66] and phosphorus



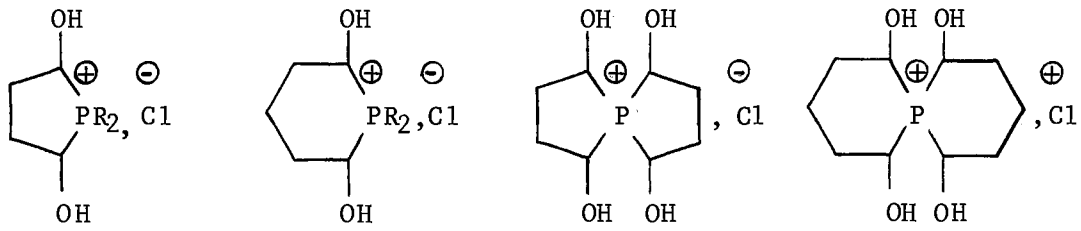
trihalides[9,44] add to dienes yielding phosphonium salts. Both 2- and 3-phospholene structures are reported from this reaction when the halogen is chlorine.[44,78,79]

Carbon-phosphorus heterocycles[13] have also been synthesized by treating α,ω-difunctional compounds, such as dihaloalkanes, di-Grignard reagents, di-lithium reagents, and dialdehydes with an appropriate trivalent-phosphorus compound. Both 1,4- and 1,5-dihaloalkanes react with dilithium salts of phosphonous dihalides to produce phospholanes and phosphorinanes, respectively.[49,50] Di-Grignard reagents[39,40] or

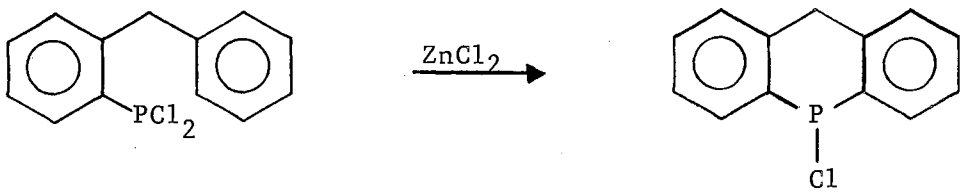




di-lithium reagents[60,61,98] with phosphonous dihalides likewise have provided the above ring systems and even 7-membered rings.[61] Dialdehydes react with secondary phosphines and hydrochloric acid to give phosphonium salts,[20] while phosphine produces spirans.[21]



Intramolecular cyclization is another method for synthesizing phosphorus-carbon heterocycles.[13] Examples obtained include phosphonium salts by an intramolecular cyclization,[51] phosphinic esters by an intramolecular Michaelis-Arbuzov rearrangement,[45] and tertiary phosphines by irradiation of secondary alkenylphosphines.[26] An intramolecular aromatic substitution resulted in formation of a substituted phosphanthracene.[29]



^{31}P Spectra of Related Compounds

A few general reviews[24,33,53,70,75,96] of ^{31}P spectra are available. In phosphoryl compounds, each substituent on phosphorus appears to make a given contribution to the total shift.[96] Shielding by substituents has been shown experimentally[96] to occur in the order: Se < S < aliphatic C ≤ aromatic C ≈ P < N ≈ Cl ≤ H < O ≤ F. With the exception of hydrogen and phosphorus, the above order is that of increasing electronegativity.

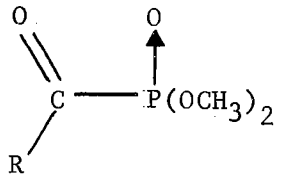
The chemical shifts for a series of phosphonic acids[96] and phosphonates[34,94,96] have been discussed and recorded. These compounds offer a direct way to measure the relative electron-donating ability of organic groups, since carbon is attached directly to phosphorus in these compounds.[96] As with other phosphoryl compounds, the stronger electron-donating groups cause reduced shielding of the phosphorus nucleus.

The above correlation has been demonstrated for a series of 20 or more dialkyl phosphonates.[34,96] The chemical shift (p.p.m.) relative to 85% orthophosphoric acid and the organic group linked to phosphorus are given here for a few diethyl phosphonates: benzoyl (+2±1),[96] acetyl (+2±1),[96] dimethylcarbamyl (0±0.5),[96] trichloromethyl (-6.5±0.5),[96] dichloromethyl (-9.3),[34] chloromethyl (-18),[34] and methyl (-30±1).[96]

CHAPTER II

DISCUSSION OF RESULTS AND CONCLUSIONS

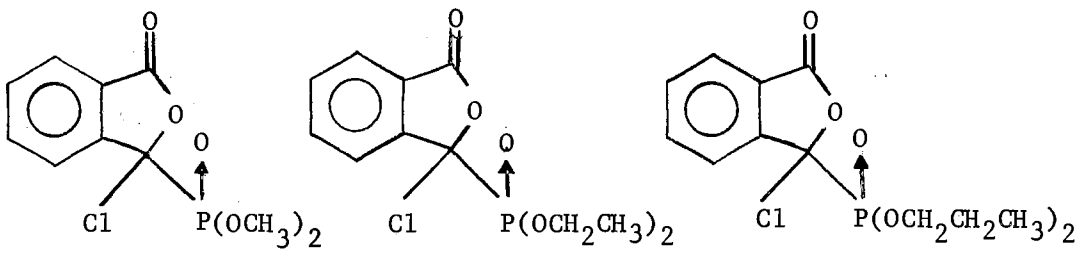
Trialkyl phosphites were allowed to react with ortho-substituted aroyl chlorides with the intention of preparing ortho-substituted dialkyl aroylphosphonates VI-IX. It was thought that rotation around the carbon-phosphorus bond might be hindered sufficiently by the ortho-substituent to create nonequivalent magnetic environments for the two alkyl groups. However, the ortho-substituted aroylphosphonates pre-



R

VI	o-$C_6H_5C_6H_4$-	VIII	2,4,6-$(CH_3)_3C_6H_2$-
VII	1-$C_{10}H_7$-	IX	o-$CH_3OC_6H_4$-

pared did not show a nonequivalency of alkyl groups at room temperature. The products X, XVII, and XVIII from the reactions of phthaloyl chloride with trialkyl phosphites contained nonequivalent alkyl groups in unexpected phosphorylated heterocycles.



X XVII XVIII

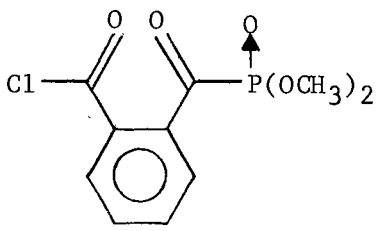
The aroyl chlorides used were as follows: o-phenylbenzoyl chloride (I), α-naphthoyl chloride (II), mesitoyl chloride (III), o-anisoyl chloride (IV), and phthaloyl chloride (V). Compounds I-IV reacted with trimethyl phosphite to produce dimethyl aroylphosphonates as expected for the Michaelis-Arbuzov rearrangement.[11,18,42] The dimethyl aroylphosphonates prepared were: dimethyl o-phenylbenzoylphosphonate (VI), dimethyl α-naphthoylphosphonate (VII), dimethyl mesitoylphosphonate (VIII), and dimethyl o-anisoylphosphonate (IX).

The IR spectral data for the dimethyl aroylphosphonates VI-IX listed in Table I (Plates II-V) correlate well with data described elsewhere. Berlin and Taylor[18] reported that IR spectra of some dimethyl aroylphosphonates showed absorption for conjugated carbonyl (1639-1672 $cm.^{-1}$), phosphoryl (1258-1269 $cm.^{-1}$), and the P-O-C linkage (1031-1036 $cm.^{-1}$). The IR spectra of compounds VI-IX display similar peaks for conjugated carbonyl (1645-1675 $cm.^{-1}$), phosphoryl (1260 $cm.^{-1}$), and the P-O-C linkage (1025-1035 $cm.^{-1}$).

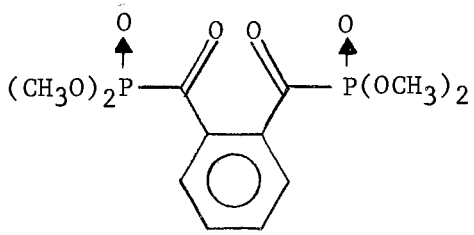
NMR data for compounds VI-IX, listed in Table II (Plates VII-X), lend additional support to the proposed structures. The dimethyl aroylphosphonates prepared by Berlin and Taylor[18] exhibited doublets in the region of δ3.80-3.90 with a $J_{P-O-C-H}$ coupling constant of 11 c.p.s. for the methyl ester protons. Corresponding doublets in the spectra of compounds VI-IX are in the region of δ3.68-3.88 with an identical $J_{P-O-C-H}$ coupling constant of 11 c.p.s.

The magnetic equivalence of the methyl ester groups at room temperature indicates free rotation around the carbon-phosphorus bond. Examination of molecular models suggests a possible slow rotation around the aryl-to-carbonyl bond and a resulting free rotation of the carbon-phosphorus bond. The relatively large upfield chemical shift (δ3.68) for the methyl protons in VI compared to that (δ3.82)[18] in dimethyl benzoylphosphonate suggests a probable shielding component on the methyl protons arising from the magnetically anisotropic ortho-phenyl substituent.[52]

Addition of trimethyl phosphite to V (1:1 mole ratio) and inverse addition of V to trimethyl phosphite (1:2 mole ratio) gave 64% and 40% yields, respectively, of dimethyl 3-chlorophthalidylphosphonate (X). An ortho-substituted dimethyl aroylphosphonate structure XI was originally expected for the former reaction (1:1 mole ratio) and a tetramethyl phthaloyldiphosphonate structure XII was considered possible for the latter reaction (1:2 mole ratio). It seems reasonable that production of X in both reactions followed a similar pathway. A

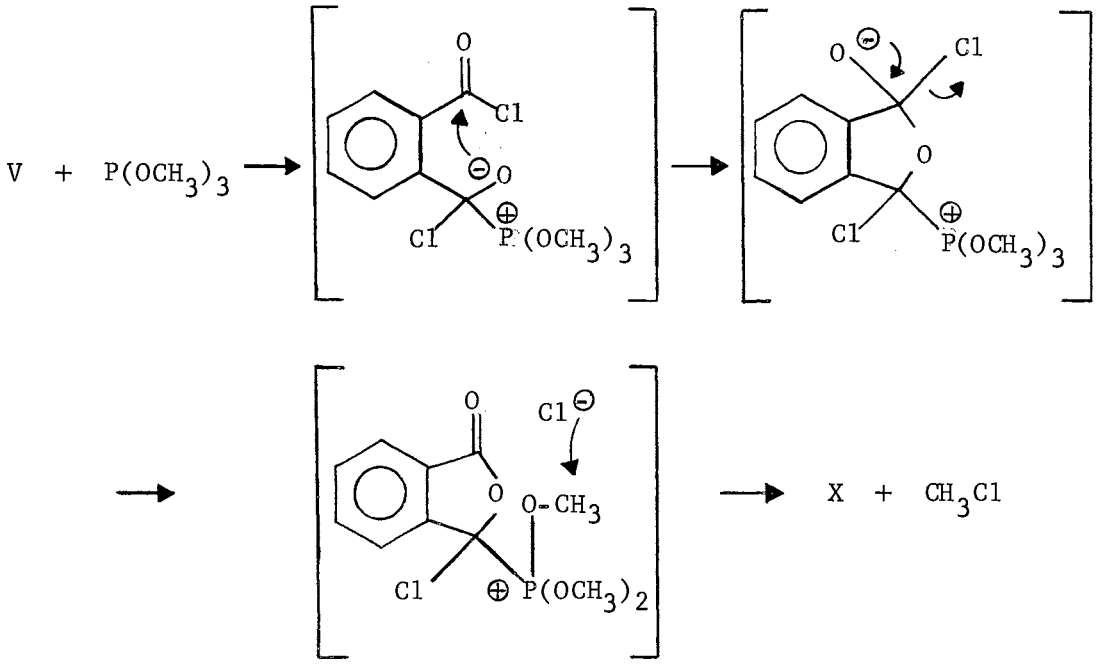


XI

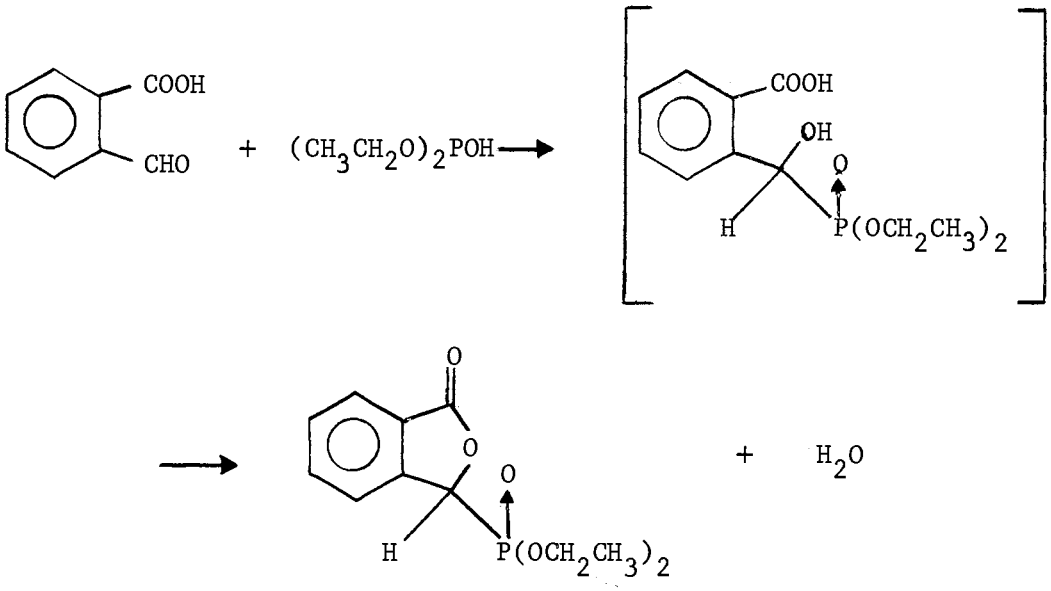


XII

possible mechanism for the formation of X is depicted. It is presumed that the close proximity of the second aroyl chloride group results in a ring closure step prior to loss of chloromethane.

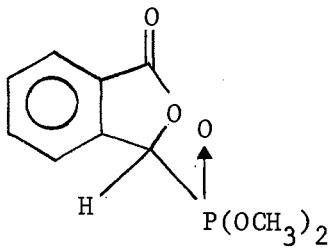


A very similar compound, diethyl phthalidylphosphonate (XIII), also has been prepared by ring closure.[87] Reaction of ortho-phthalaldehydic acid with diethyl phosphite (or diethyl hydrogenphosphonate) is thought to produce a phosphorylated intermediate which then condenses to give XIII.



XIII

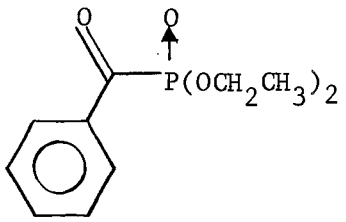
The IR (Plate VI), ^{31}P NMR, and ^{1}H NMR (Plate XI and Table V) spectral data for X support the proposed heterocyclic structure. Rather strong IR absorption was found for C=O (1803 $cm.^{-1}$), P→O (1287 and 1273 $cm.^{-1}$), and P-O-C (1047 $cm.^{-1}$). This absorption is reminiscent for that observed for dimethyl phthalidylphosphonate (XIV): C=O (1787 $cm.^{-1}$), P→O (a doublet peak at 1281 $cm.^{-1}$), and P-O-C (1041 $cm.^{-1}$).[87] Carbonyl group absorptions for the dimethyl aroylphosphonates



XIV

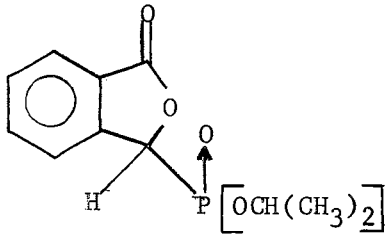
VI-IX occurs in a markedly different range (1645-1675 $cm.^{-1}$); see Table I.

The ^{31}P NMR spectrum (benzene; 20% w./w.) of X displayed a septet at -9.7 p.p.m. relative to 80% phosphoric acid, which approximates that for diethyl dichloromethylphosphonate (neat; -9.3 p.p.m.).[34] It should be noted that both alkylphosphonates contain two electron-withdrawing substituents on the carbon linked to phosphorus. Compound XIII, which contains one electron-withdrawing oxygen atom on the carbon linked to phosphorus, gives a multiplet in the ^{31}P NMR spectrum at -13.2 p.p.m. relative to 85% phosphoric acid.[12] The ^{31}P NMR signal for diethyl benzoylphosphonate (XV) (neat; +2 p.p.m.)[96] is significantly upfield from that for X.



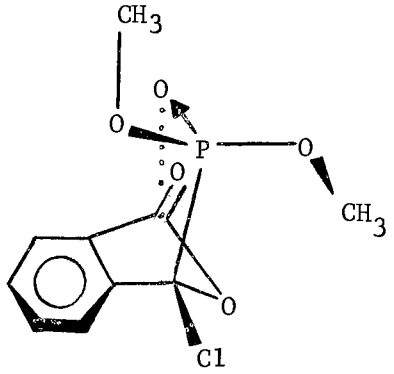
XV

Proton NMR spectra of X revealed a $J_{P-O-C-H}$ coupling constant of 11 c.p.s. in several solvents at 60 or 100 M.c.p.s. (Table III). Siddall and Prohaska[92] observed a similar temperature effect upon the separation, Δ, of the chemical shifts for the methyl group protons in both XIII and diisopropyl phthalidylphosphonate (XVI) when the compounds



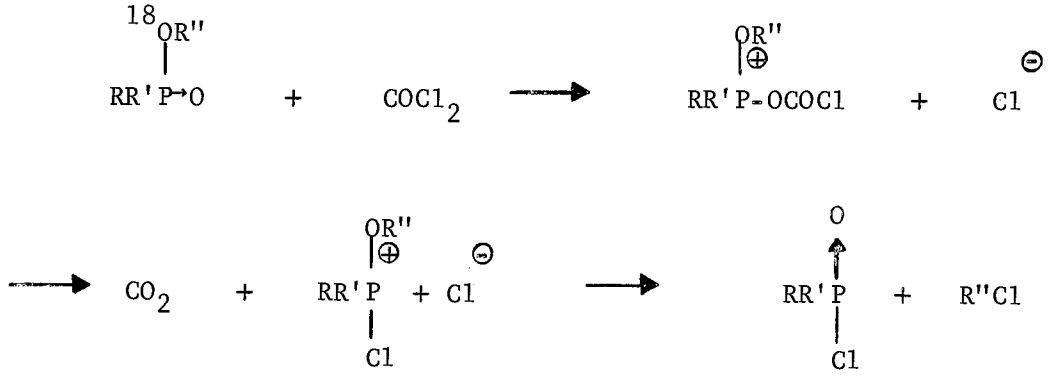
XVI

were examined neat or in deuterochloroform. Inherent asymmetry arising from the asymmetric carbon atom creates nonequivalent environments for the two methyl groups. Presumably a wagging process of the 5-membered ring as well as rotations around the C-P-O-C linkages could be operative at room temperature. However, the magnitudes of Δ (Table III) for carbon tetrachloride and perchloroethylene solutions (near room temperature) were large, 39 and 41 c.p.s., respectively. This suggests a significant population of a molecular conformer having methyl groups with different spatial relationships to the magnetically anisotropic benzene ring.[52] In another report,[97] a similar argument has been made with respect to the nonequivalence of the methylene protons of 1-phenylethyl benzyl ether; fairly large changes in Δ were observed with variation in solvent. From examination of a molecular model of X it is possible to hypothesize the existence of a given preferred conformer. (see below). This conformer conceivably may be stabilized by an



electrostatic attraction between the phosphoryl oxygen and the carbonyl carbon. The nucleophilic nature of phosphoryl oxygen with respect to carbon centers is indicated by several reactions.[22,23,37,43,48,59,62] An example[37] is that of benzyl methylphenylphosphinate with phosgene

to give carbon dioxide, methylphenylphosphinyl chloride, and benzyl chloride. The following mechanism was considered most probable by Green and Hudson.[37]



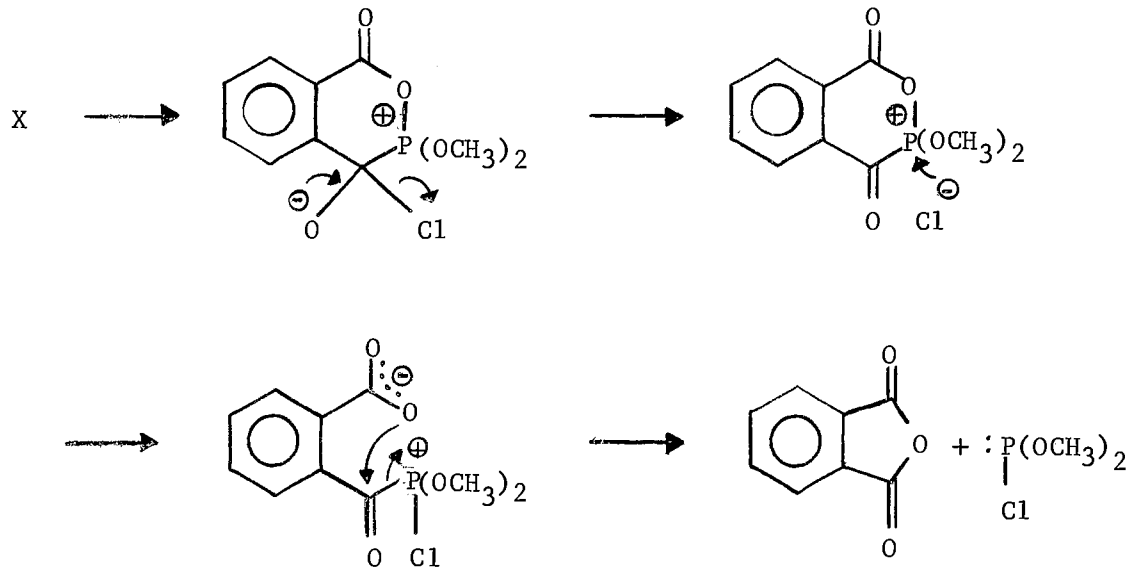
Another example[59] is shown below.

$$(CH_3O)_2(CH_3)P\rightarrow O + C_{12}H_{25}Br \longrightarrow CH_3Br + (CH_3O)(CH_3)(O)POC_{12}H_{25}$$

When the approximate positions of the two methyl groups in the above conformer of X are placed on the plot by Johnson and Bovey[52] for the magnetic anisotropic effect of the benzene ring versus distance from the benzene ring, a Δ value of 41 c.p.s. is obtained. This approximate value agrees well with those found for carbon tetrachloride and perchloroethylene solutions near room temperature (Table III). The Δ value observed when the temperature is raised to 100° suggests a large population of molecules in which free rotation occurs around the P-O-C linkages but the phosphoryl oxygen and the carbonyl carbon remain in a relatively fixed spatial relationship. In dimethylformamide, the existence of solute-solvent electrostatic interactions may destroy the rigid conformation. In addition to intramolecular steric interactions in X, the solute-solvent steric interactions may lead to a new

conformation. This is supported by the relatively large Δ value which indicates a large population of molecules in which the two methyl groups are in different average positions with respect to the benzene ring.

Thermal decomposition of X occurred at 190° with the formation of considerable tar, phthalic anhydride, and dimethyl phosphorochloridite. The phosphorus compound was converted into dimethyl hydrogenphosphonate by the action of moist ether. It is interesting to note that only tar was reported from the vigorous reaction of maleoyl chloride with triethyl phosphite.[42] Decomposition of X to give phthalic anhydride and dimethyl phosphorochloridite may proceed by a pathway similar to that



proposed by Green and Hudson[37] for the reaction of benzyl methylphenylphosphinate with phosgene as discussed previously.

Reaction of V with triethyl phosphite or tri-n-propyl phosphite gave oils which could not be induced to crystallize. IR absorption of the first oil occurred for C=O (1805 $cm.^{-1}$), P→O (1272 and

1248 cm.$^{-1}$), and P-O-C (1024 cm.$^{-1}$). Peaks in the IR spectrum of the second oil were existent for C=O (1800 cm.$^{-1}$), P→O (1270 and 1244 cm.$^{-1}$), and P-O-C (1001 cm.$^{-1}$). NMR signals of the former oil indicated two nonequivalent ethyl groups [triplets at δ1.13 (J = 7 c.p.s.) and δ1.45 (J = 7 c.p.s.) and multiplets at δ4.02 and δ4.42] while those of the latter oil indicated two nonequivalent n-propyl groups [triplets at δ0.77 (J = 7 c.p.s.) and δ0.98 (J = 7 c.p.s.) and multiplets at δ1.43, δ1.71, δ3.89, and δ4.35]. Attempted vacuum distillation of either oil gave phthalic anhydride and the respective dialkyl phosphorochloridite. The obvious similarities of spectral data and decomposition products of the oils to those for X suggest that alkyl homologs (XVII and XVIII) of X were produced.

In summary, a series of ortho-substituted dimethyl aroylphosphonates were synthesized and characterized. Magnetic equivalence of the methyl ester groups indicates free rotation around the carbon-phosphorus bond at room temperature in most of the cases examined. In the exception, reaction of phthaloyl chloride with trimethyl phosphite produced a novel phosphorylated heterocycle which was characterized by elemental analysis and spectral data. Mechanisms for cyclization and decomposition to phthalic anhydride and dimethyl phosphorochloridite are suggested. In dimethylformamide, the magnitude for Δ indicates a large population of molecules in which the two methyl groups are in different average positions with respect to the benzene ring. A given molecular conformer is hypothesized to exist in significant quantity in carbon tetrachloride and perchloroethylene at room temperature. A large population of molecules having a relatively fixed spatial relationship of the phosphoryl oxygen and the carbonyl carbon is suggested to explain

the slight change in the NMR spectrum of the perchloroethylene solution when the temperature is raised to 100°. Formation of alkyl homologs of X is proposed in view of the obvious similarities of spectral data and decomposition products to those for X.

TABLE I

IR ABSORPTION MAXIMA ($cm.^{-1}$) OF DIMETHYL AROYLPHOSPHONATES

$RC(O)P(O)(OCH_3)_2$

Cpd.	R	Plate	C=O	P→O	P-O-C
VI	o-$C_6H_5C_6H_4$-	II	1660	1260	1025
VII	1-$C_{10}H_7$-	III	1645	1260	1035
VIII	2,4,6-$(CH_3)_3C_6H_2$-	IV	1675	1260	1025
IX	o-$CH_3OC_6H_4$-	V	1650	1260	1030

TABLE II

PROTON NMR DATA FOR DIMETHYL AROYLPHOSPHONATES[a]

$RC(O)P(O)(OCH_3)_2$

Cpd.	R	Plate	δ, Ester Protons	δ, Aromatic Protons	δ, Other Protons
VI	o-$C_6H_5C_6H_4$-	VII	3.68d	7.13-8.17	
VII	1-$C_{10}H_7$-	VIII	3.88d	7.40-9.02	
VIII	2,4,6-$(CH_3)_3C_6H_2$-	IX	3.75d	6.83	2.22, 2.27
IX	o-$CH_3OC_6H_4$-	X	3.79d	6.87-7.84	3.85

[a]Spectra were obtained in CCl_4 solutions at 22°; $J_{P-O-C-H}$ for all compounds was 11 c.p.s.; d = doublet.

TABLE III

PROTON NMR DATA FOR DIMETHYL 3-CHLOROPHTHALIDYLPHOSPHONATE[a]

Solvent	Temp., °C.	δ, CH_3		Δ, c.p.s.	δ, Aromatic Protons
$HC(O)N(CH_3)_2$[b]	22	3.85d[c]	4.03d[c]	18[d]	
CCl_4[b]	22	3.68d	4.07d	39[d]	7.60-7.98
C_2Cl_4[e]	27	3.59d	4.00d	41	7.49-7.93
C_2Cl_4[e]	100	3.58d	3.96d	38	7.45-7.98

[a] $J_{P-O-C-H}$ = 11 c.p.s.; Δ = separation of methyl signals; d = doublet.

[b] Spectrum obtained on a Varian A-60 spectrometer.

[c] An apparent triplet resulting from overlapping doublets.

[d] This value was calculated by multiplying 1.67 by the Δ value (c.p.s.) obtained on a Varian A-60 spectrometer.

[e] Spectrum obtained on a Varian HA-100 spectrometer.

TABLE IV

PREPARATION AND PROPERTIES OF AROYL CHLORIDES

RCOCl

Cpd.	R	Moles of Acid	Moles of Thionyl Chloride	Yield, %	B.p., °C. (mm.)	Reference
I	o-$C_6H_5C_6H_4$-	0.050	0.202	75.8	108(0.44)	38
II	1-$C_{10}H_7$-	0.058	0.232	86.7	131-2(2.2)	41
III	2,4,6-$(CH_3)_3C_6H_2$-	0.030	0.120	84.8	57-8(0.40)	41

TABLE V

PREPARATION AND PROPERTIES OF DIMETHYL AROYLPHOSPHONATES, $RC(O)P(O)(OCH_3)_2$

Cpd.	R	Moles of Acid Chloride	Moles of Trimethyl Phosphite	B.p., °C. (mm.)	n_D^t	Yield,[a] %	Analysis, % P	
							Calcd.	Found
VI	o-$C_6H_5C_6H_4$-	0.020	0.024	174-6(0.70)	1.5792^{25}	64	10.68	10.75
VII	1-$C_{10}H_7$-	0.025	0.028	158-61(0.25)	1.5958^{25}	49	11.74	11.74
VIII	2,4,6-$(CH_3)_3C_6H_2$-	0.026	0.030	123-5(0.21)	1.5100^{25}	24	12.11	12.22
IX	o-$CH_3OC_6H_4$-	0.088	0.100	135-6(0.08)	1.5343^{24}	56	12.70	12.55

[a] Yields are based on acid chloride as starting material.

CHAPTER III

EXPERIMENTAL[a-e]

Preparation of o-Phenylbenzoyl Chloride (I).--This compound and other acid chlorides which were not commercially available were synthesized by the following general procedure.[46] The results are summarized in Table IV. A 100-ml., 1-necked flask was fitted with a condenser, a drying tube, and a magnetic stirring bar. A sample (10.0 g., 0.0505 mole) of o-phenylbenzoic acid and 14.5 ml. (24.05 g., 0.202 mole) of thionyl chloride were added to the flask. The mixture was stirred for 41 hours. The excess thionyl chloride was removed by simple

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[a]All melting points are corrected; all boiling points are uncorrected. The Skelly Solvent F used boiled at 30-60°.

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

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

[d]The proton nuclear magnetic resonance spectra were determined on a Varian A-60 high resolution spectrometer with a field-sensing stabilizer ("Super-Stabilizer") unless otherwise specified. Tetramethylsilane was used as an internal standard. Unless otherwise stated, the solvent employed was carbon tetrachloride.

[e]Gas chromatographic analyses were performed using an Aerograph Hy-Fi Model A-550 with a hydrogen flame ionization detector from Wilkens Instrument and Research, Inc., Walnut Creek, California. The column used was a 6'x1/8" stainless steel column with a 6% silicone-30 substrate on a 80/100 mesh, acid washed, DMCS-treated Chromosorb G support.

distillation followed by azeotropic distillation with benzene to remove the last traces of the inorganic halide. The remaining material was distilled to yield 8.3 g. (75.8%) of material boiling at $108^{\circ}/0.44$ mm. [lit.[38] 99.5-$101^{\circ}/0.3$ mm.]. IR absorption (Plate I) supported the structure.

Preparation of Dimethyl Aroylphosphonates (VI-IX).--This synthesis utilized the classical Michaelis-Arbuzov rearrangement studied by Berlin and coworkers.[11,14,18] The general procedure is described for preparation of the esters found in Table II. A 200-ml., 3-necked flask was fitted with a condenser, a drying tube, an immersion thermometer, a pressure-equalizing addition funnel, a nitrogen inlet, and a magnetic stirring bar. A slight excess of trimethyl phosphite was added dropwise to an aroyl chloride under anhydrous nitrogen at such a rate that the temperature of the reaction mixture did not exceed 40°. Effervescence was noted shortly after the addition started, presumably due to expulsion of chloromethane. The resulting mixture was stirred for 12 hours at room temperature. The products were purified by vacuum distillation. Elemental analyses (Table V) and spectral data (Tables I and II) were used to confirm the structures of the unknown dimethyl aroylphosphonates.

Deviation from the above general procedure was employed in the reaction of mesitoyl chloride III. An exothermic process with effervescence was not observed in the system during the addition of trimethyl phosphite to III. Therefore the reaction mixture was immediately heated to reflux (78°) and held there for 2 hours.

Reaction (1:1) of Trimethyl Phosphite with Phthaloyl Chloride (V) - Run 1.[12,72]--All solvents were dried, and all manipulations were

carried out under a nitrogen atmosphere. To 10.0 g. (0.05 mole) of phthaloyl chloride dissolved in 125 ml. of benzene held at 0° was added dropwise 6.2 g. (0.05 mole) of trimethyl phosphite dissolved in 75 ml. of benzene over a period of 1.75 hours. After the mixture was stirred (4 hours) and boiled (1 hour), benzene was removed by distillation. An oil resulted in which a solid formed after standing overnight. Two recrystallizations from benzene-Skelly Solvent F yielded 8.8 g. (64%) of X, m.p. 77.5-78.5°.

Anal. Calcd. for $C_{10}H_{10}O_5ClP$: C, 43.75; H, 3.90; Cl, 12.82; P, 11.40.

Found: C, 43.17; H, 3.73; Cl, 12.75; P, 11.03.

The IR spectrum, ^{31}P NMR spectrum, and ^{1}H NMR spectra (Table III) confirmed the structure of X. Absorption in the IR (Plate VI) occurred for C=O (1803 $cm.^{-1}$), P→O (1287 and 1273 $cm.^{-1}$), and P-O-C (1047 $cm.^{-1}$). A signal in the ^{31}P NMR spectrum (benzene; 20% w./w.) occurred as a septet at -9.7 p.p.m. relative to 80% phosphoric acid.

Reaction (2:1) of Trimethyl Phosphite with Phthaloyl Chloride (V) - Run 2.[12,72]--Anhydrous solvents and a nitrogen atmosphere were used as in Run 1. To 12.4 g. (0.10 mole) of trimethyl phosphite dissolved in 70 ml. of benzene was added dropwise 10.0 g. (0.05 mole) of phthaloyl chloride dissolved in 50 ml. of benzene. After heating (3 hours) the mixture at 60°, benzene was removed by distillation. Upon standing overnight the resulting oil partially solidified. Recrystallization of the solid from benzene-Skelly Solvent F produced 5.5 g. (40%) of X.

Thermal Decomposition of Dimethyl 3-Chlorophthalidylphosphonate (X).[12,72]--When dimethyl 3-chlorophthalidylphosphonate was heated to

190°, decomposition occurred with formation of considerable tar, a low-boiling fraction, and a high-boiling component. The latter was characterized by mixture melting point determination and IR and NMR analyses as phthalic anhydride. The low-boiling fraction gave a positive test for chloride ion (silver nitrate). When this fraction was added to moist ether and subsequently analyzed by GLC, the major component was identified as dimethyl hydrogenphosphonate.

Reaction of Triethyl Phosphite with Phthaloyl Chloride (V).[12,72]--The procedure was essentially the same as that for the reaction (1:1) of trimethyl phosphite with V. Deviations are now described. The addition was carried out at room temperature and boiling was continued for 2 hours. The product was an oil which could not be induced to crystallize with benzene-Skelly Solvent F.

The IR spectrum of the oil exhibited peaks for C=O (1805 $cm.^{-1}$), P→O (1272 and 1248 $cm.^{-1}$), and P-O-C (1024 $cm.^{-1}$). NMR analysis indicated 2 nonequivalent ethyl groups [triplets at δ1.13 (J = 7 c.p.s.) and δ1.45 (J = 7 c.p.s.) and multiplets at δ4.02 and δ4.42].

Attempted vacuum distillation of the oil at 145° resulted in thermal decomposition. Product analysis was analogous to that used for the pyrolysate from thermal decomposition of X. In this case diethyl hydrogenphosphonate was identified by GLC analysis of the moist ether solution. Again the high-boiling component was characterized as phthalic anhydride.

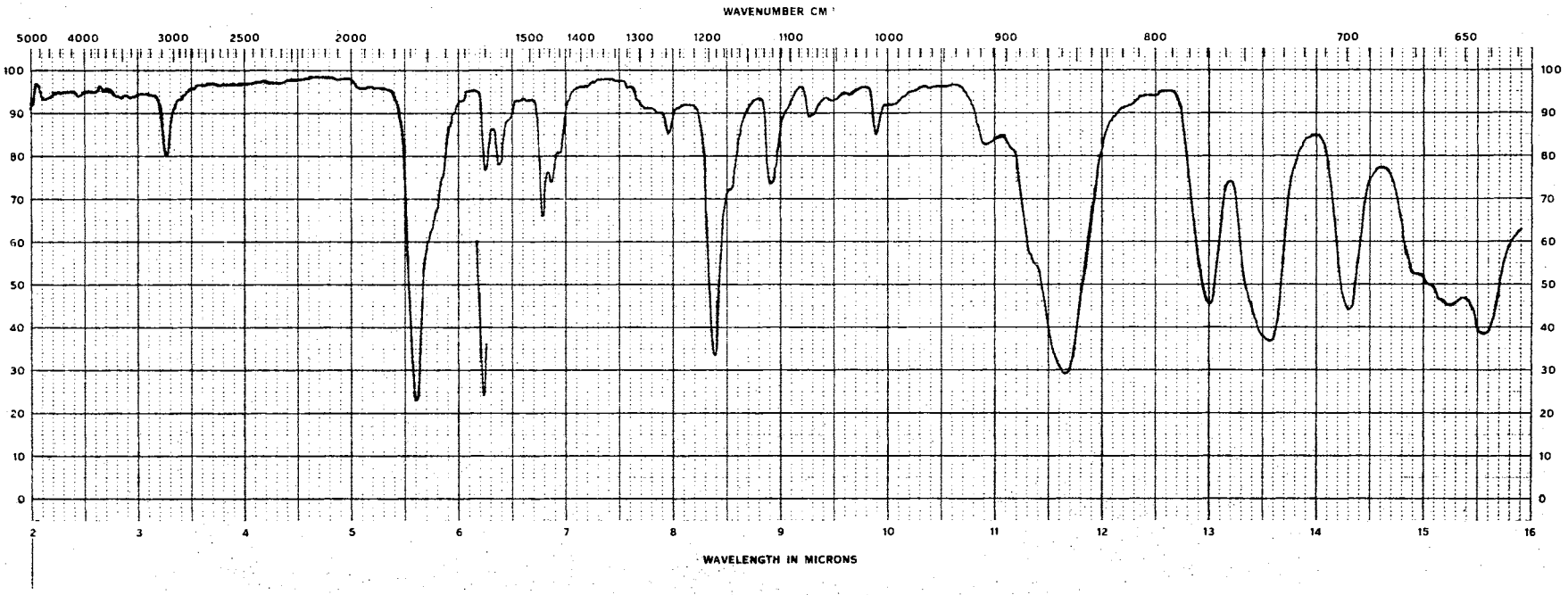
Reaction of Tri-n-propyl Phosphite with Phthaloyl Chloride (V).[12,72]--The procedure was essentially the same as that for the reaction (1:1) of trimethyl phosphite with V. Deviations are now described. The addition was carried out at 55° and heating at 55° was

continued for 7 hours. The product was an oil which could not be induced to crystallize with benzene-Skelly Solvent F.

Peaks in the IR spectrum of the oil were exhibited for C=O (1800 $cm.^{-1}$), P→O (1270 and 1244 $cm.^{-1}$), and P-O-C (1001 $cm.^{-1}$). A complex NMR spectrum indicated 2 nonequivalent n-propyl groups [triplets at δ0.77 (J = 7 c.p.s.) and δ0.98 (J = 7 c.p.s.) and multiplets at δ1.43, δ1.71, δ3.89, and δ4.35].

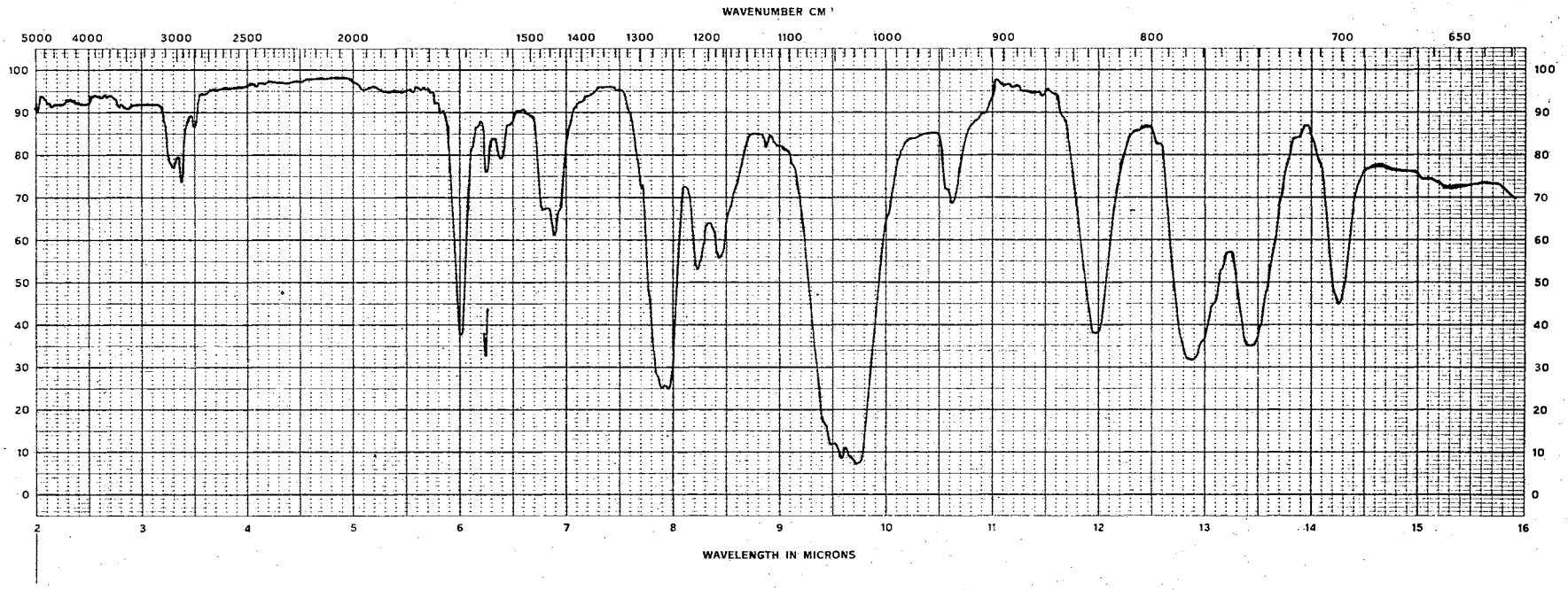
Attempted vacuum distillation of the oil resulted in decomposition producing considerable tar, a low-boiling fraction, and a high-boiling component. The low-boiling fraction gave positive tests for both phosphorus and chlorine. As suspected, the high-boiling component was characterized as phthalic anhydride.

Plate I



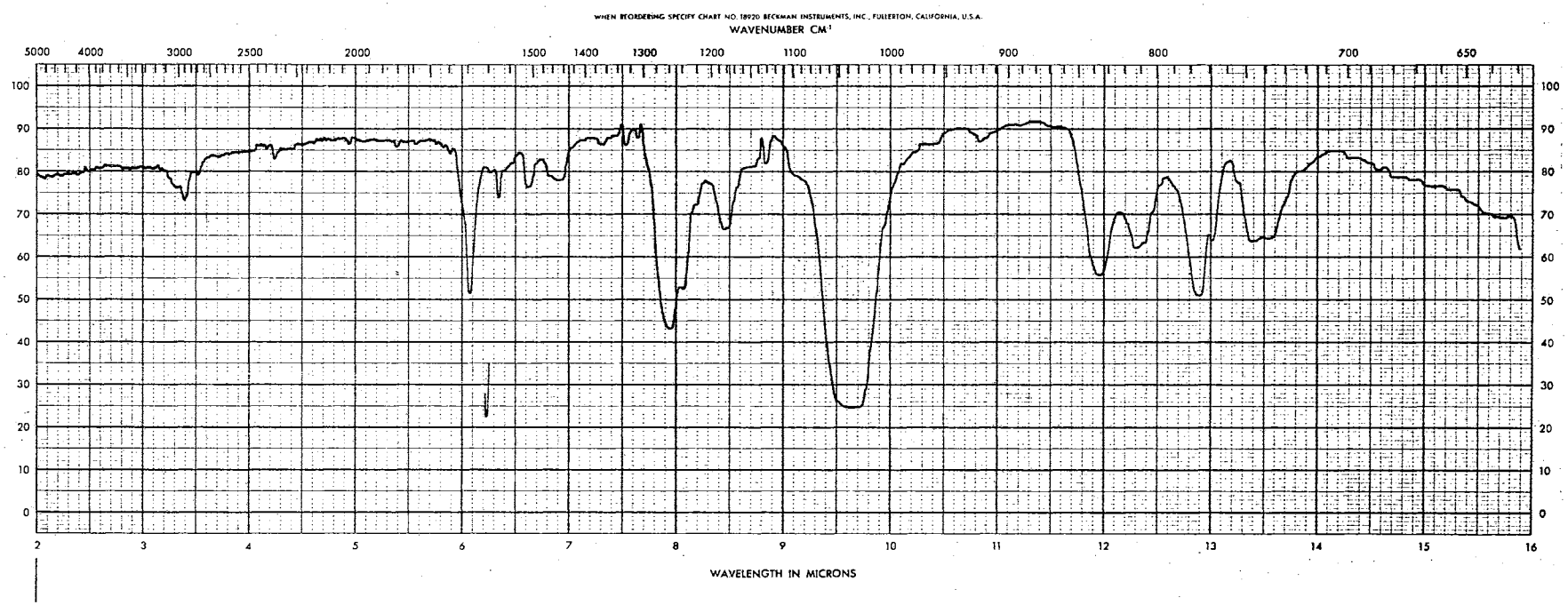
o-Phenylbenzoyl Chloride (I), Film on NaCl Plates

Plate II



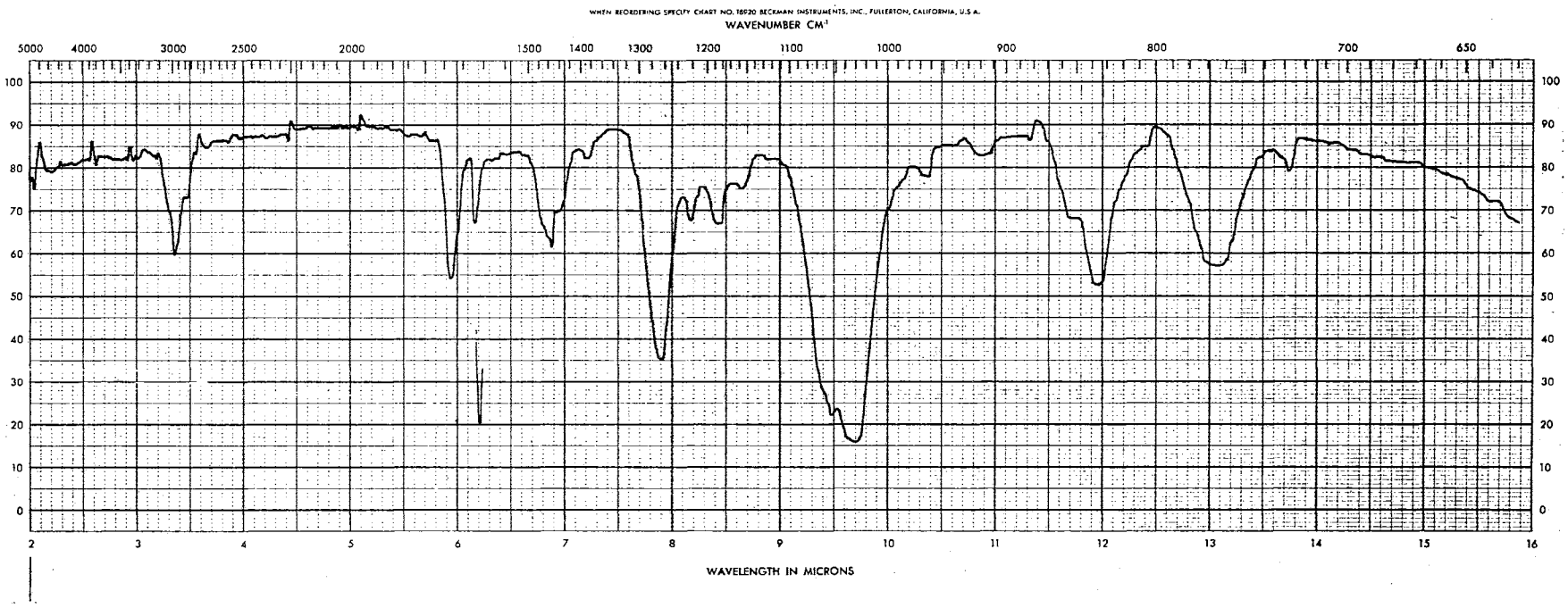
Dimethyl o-Phenylbenzoylphosphonate (VI), Film on NaCl Plates

Plate III



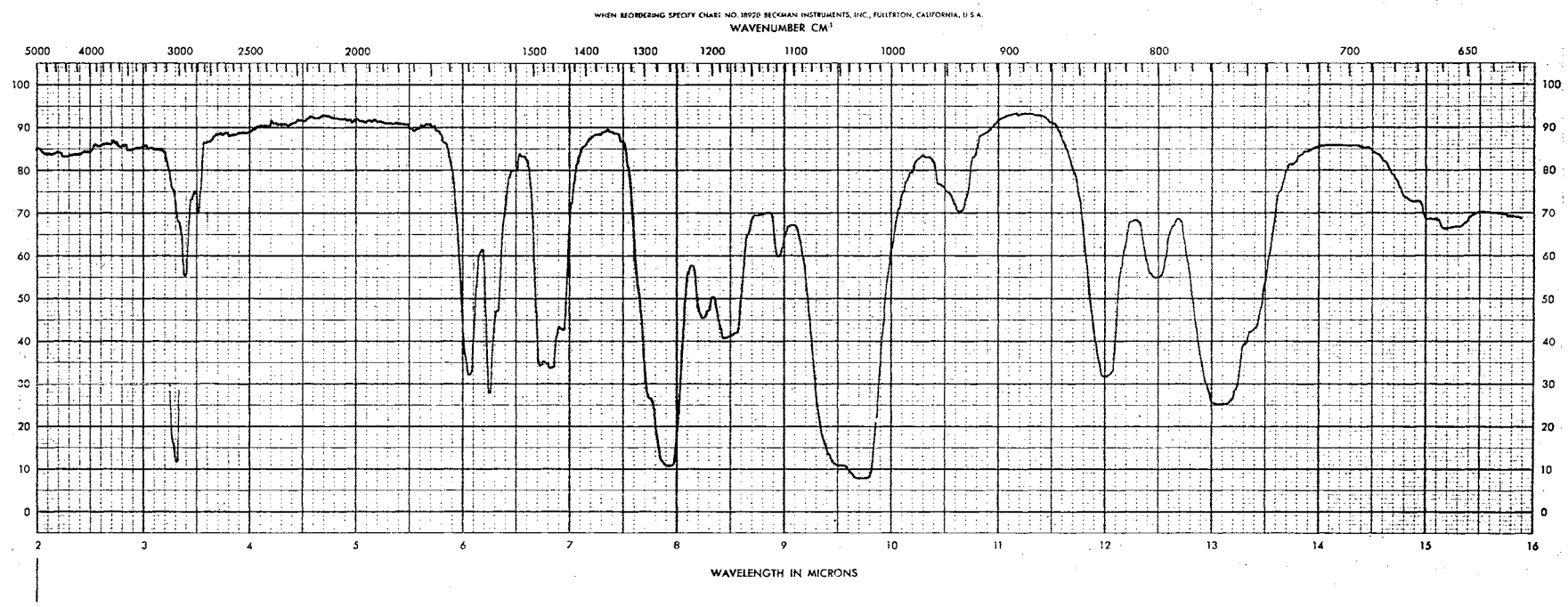
Dimethyl α-Naphthoylphosphonate (VII), Film on NaCl Plates

Plate IV



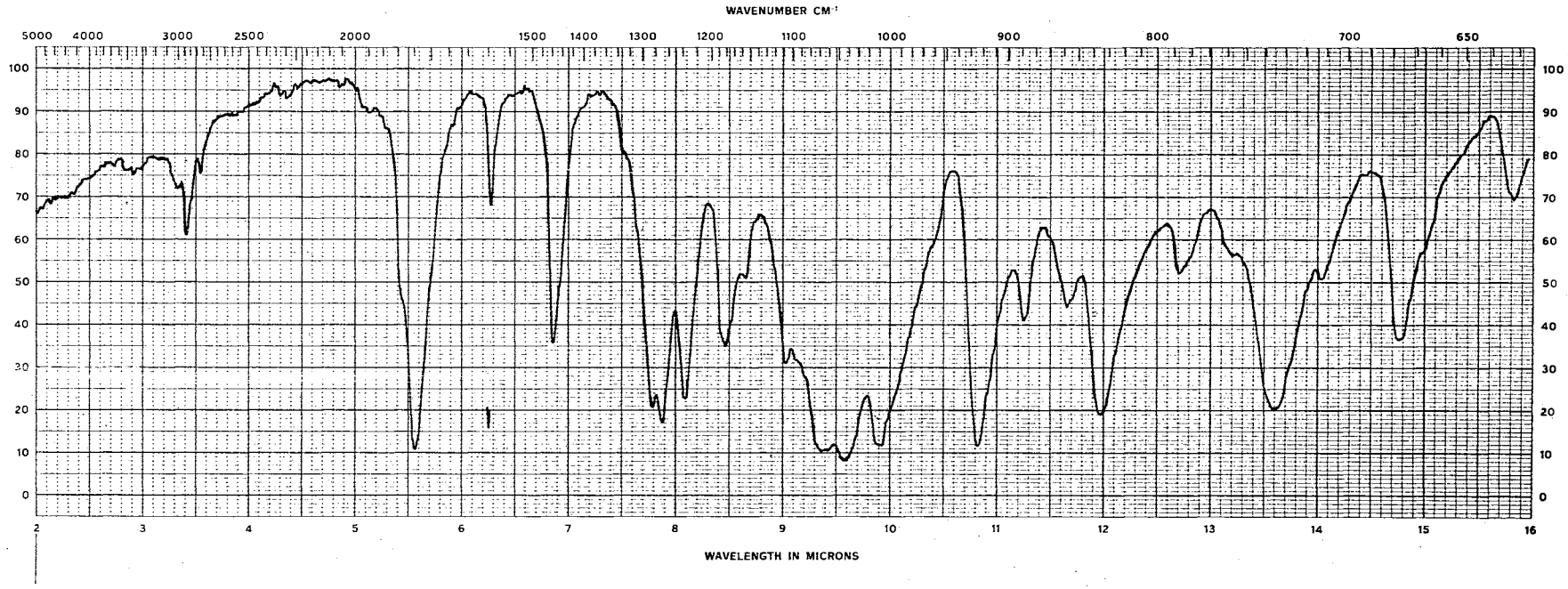
Dimethyl Mesitoylphosphonate (VIII), Film on NaCl Plates

Plate V



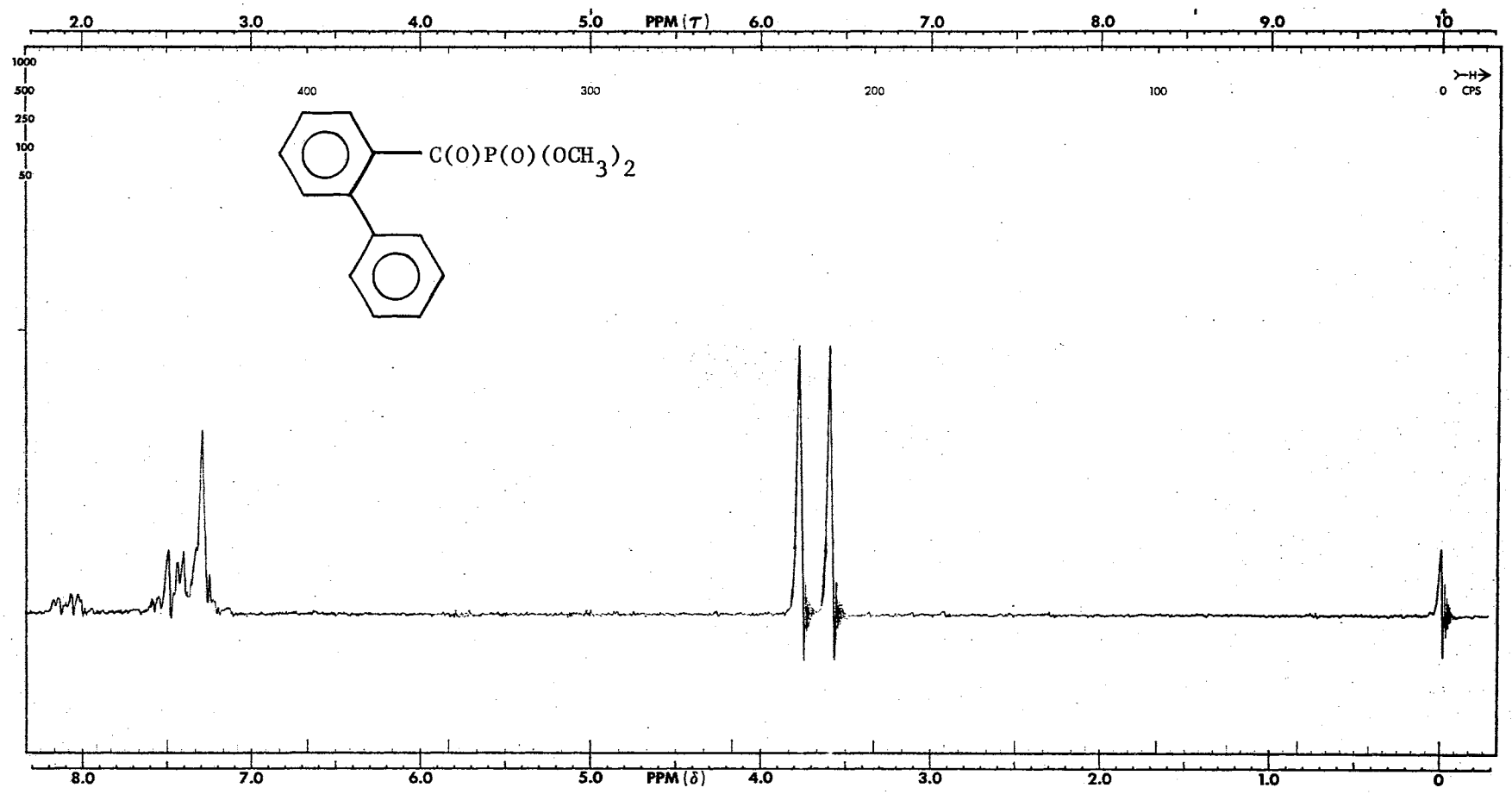
Dimethyl o-Anisoylphosphonate (IX), Film on NaCl Plates

Plate VI



Dimethyl 3-Chlorophthalidylphosphonate (X), KBr Pellet

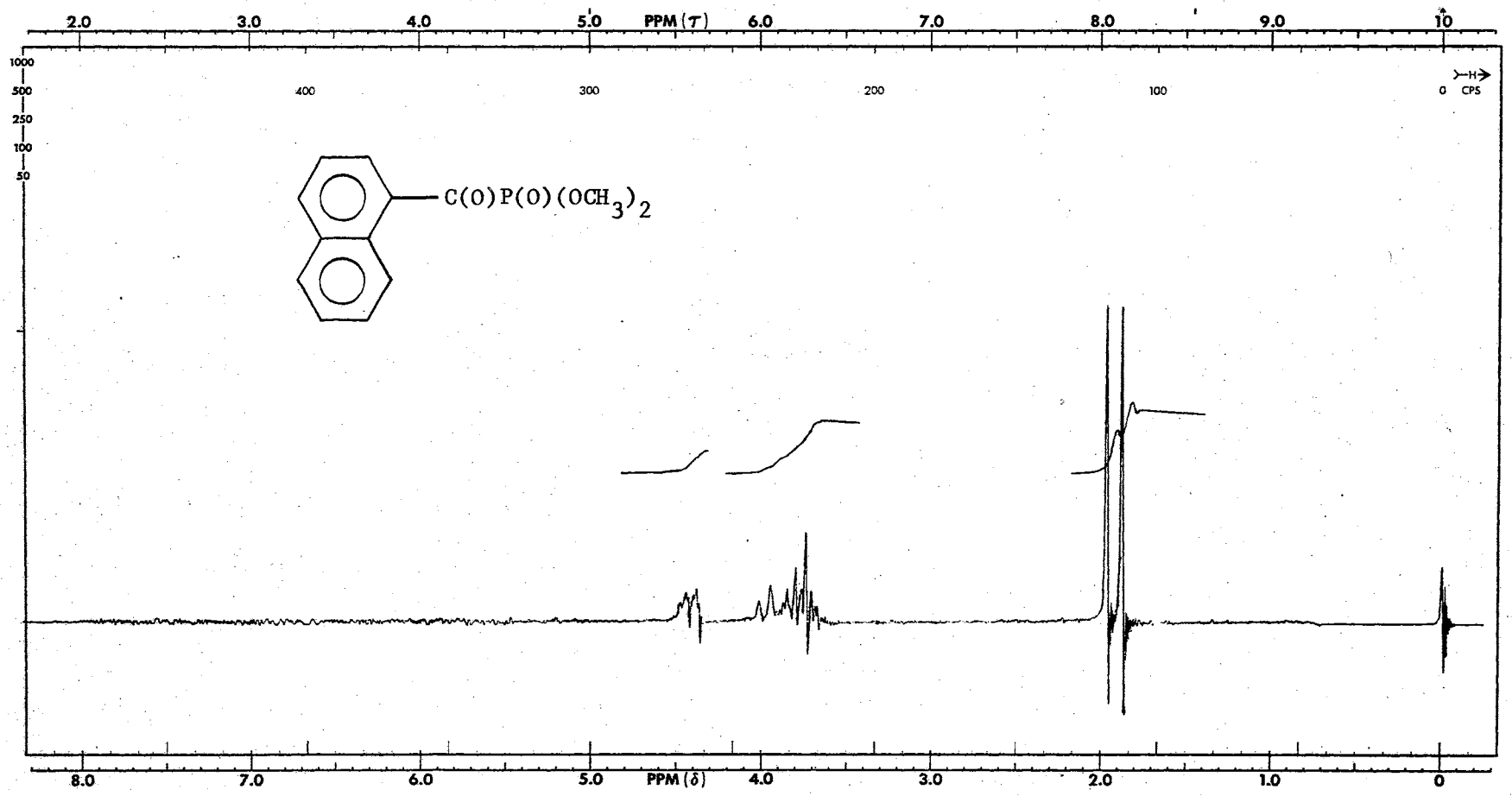
Plate VII



Dimethyl o-Phenylbenzoylphosphonate (VI)

Solvent . . . . . CCl_4	R.F. Field . . . . 0.05 mG.	S.W. . . . . 500 cps	S.A. 2.5
F.B. . . . . 4.0 cps	S.T. . . . . 250 sec	S.O. . . . . 000 cps	I.A. . . . . off

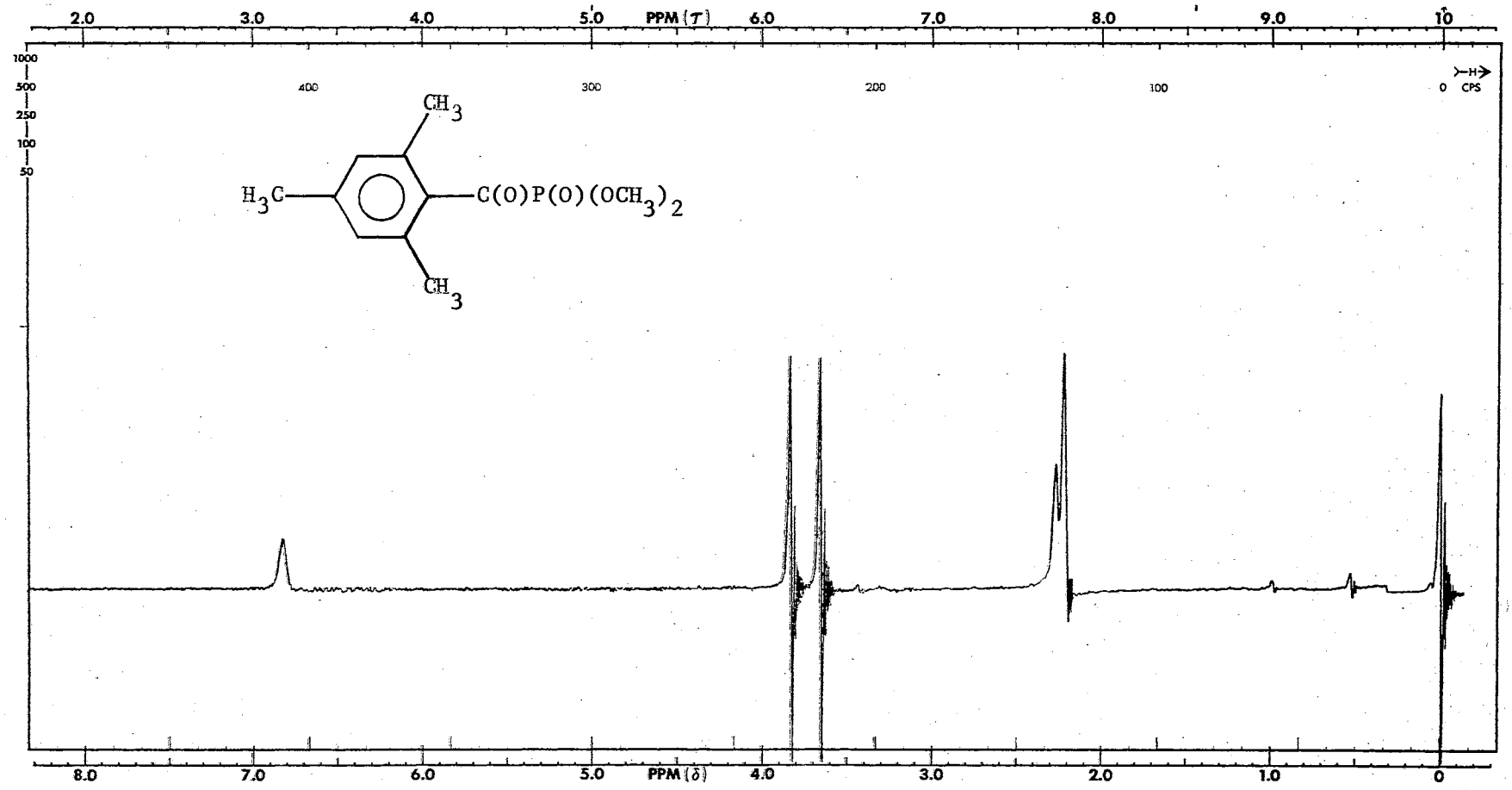
Plate VIII



Dimethyl α-Naphthoylphosphonate (VII)

Solvent	CCl_4	R.F. Field	0.05 mG	S.W.	1000 cps	S.A.	2.0
F.B.	4.0 cps	S.T.	250 sec	S.O.	000 cps	I.A.	.80

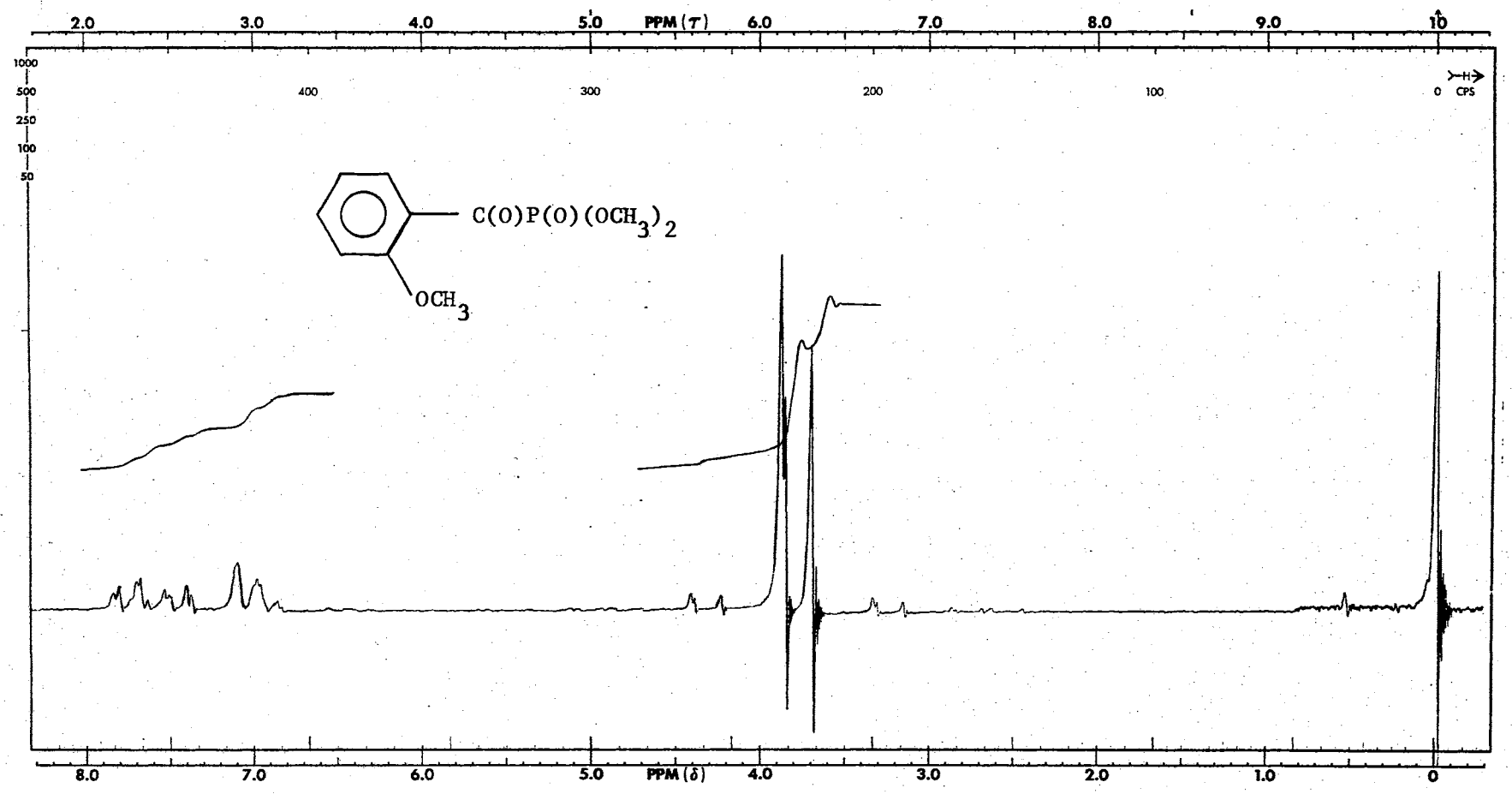
Plate IX



Dimethyl Mesitoylphosphonate (VIII)

Solvent . . . . . CCl_4	R.F. Field . . . . 0.05 mG	S.W. . . . . 500 cps	S.A. 2.0
F.B. . . . . 4.0 cps	S.T. . . . . 250 sec	S.O. . . . . 000 cps	I.A. . . . . off

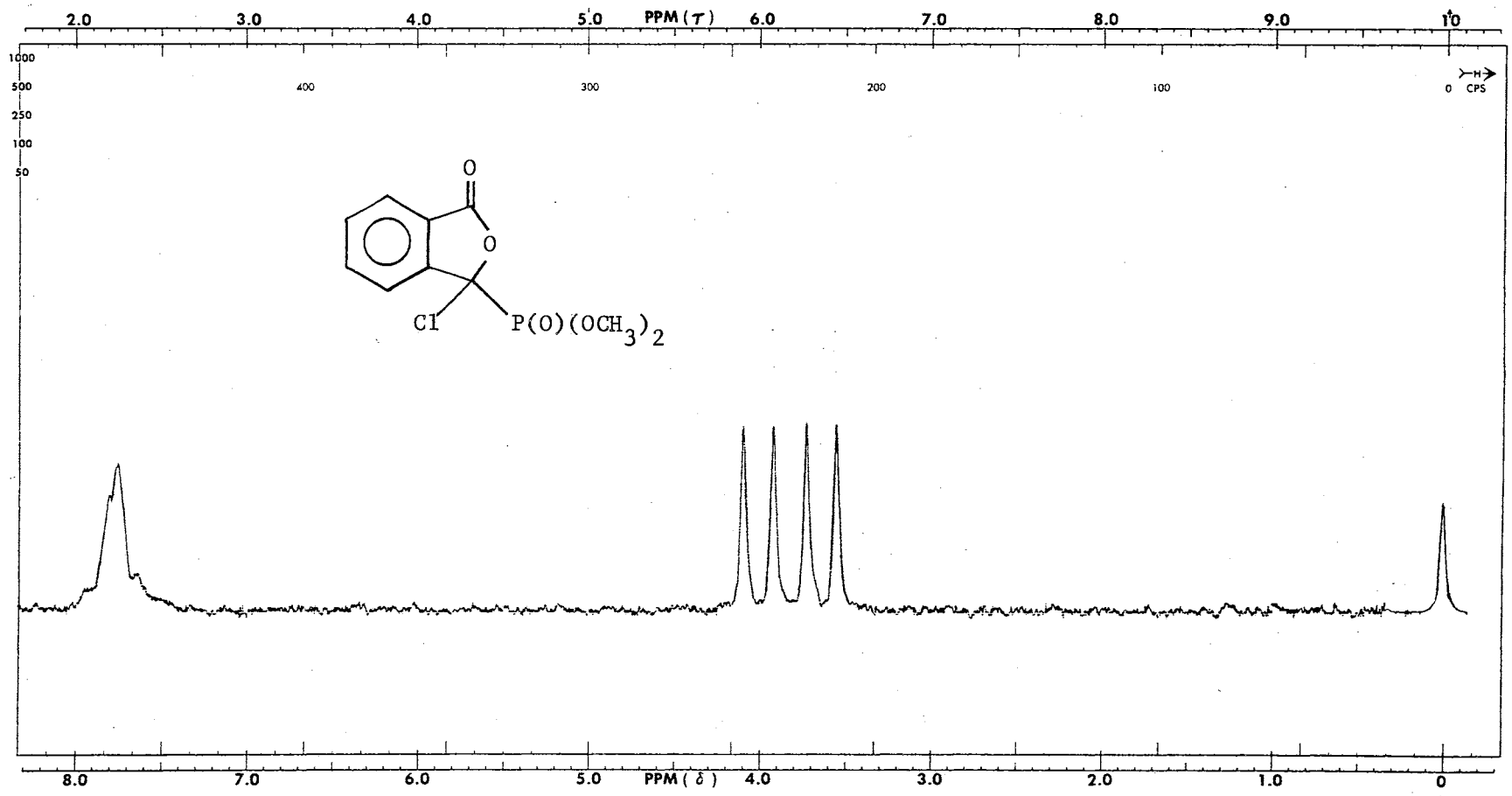
Plate X



Dimethyl o-Anisoylphosphonate (IX)

Solvent . . . . . CCl_4	R.F. . . . . 0.04 mG.	S.W. . . . . 500 cps	S.A. 1.0
F.B. . . . . 4.0 cps	S.T. . . . . 250 sec	S.O. . . . . 000 cps	I.A. 80

Plate XI



Dimethyl 3-Chlorophthalidylphosphonate (X)

Solvent . . . . . CCl_4	R.F. . . . . 0.05 mG	S.W. . . . . 500 cps	S.A. 20.0
F.B. . . . . 4.0 cps	S.T. . . . . 250 sec	S.O. . . . . 045 cps	I.A. . . . . .off

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PART II

SOME SYNTHESES OF OPTICALLY ACTIVE PHOSPHORUS COMPOUNDS

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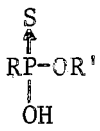
CHAPTER I

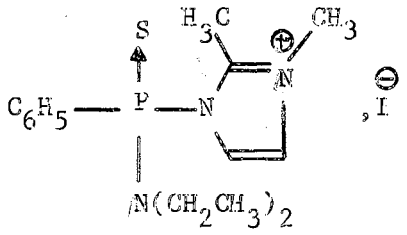
HISTORICAL

The synthesis, resolution, and reactions of optically active organophosphorus compounds in which phosphorus is the asymmetric center have been the subject of a considerable amount of recent interest.[13,23,34,40,44] Optically active phosphoryl and thiophosphoryl compounds have been prepared either by the resolution of suitable derivatives or by synthesis from resolved phosphonium salts.[34,40] In particular, the method of resolution of alkyl alkylphosphonothioic acids developed by



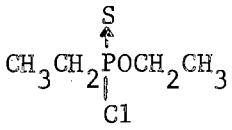
Aaron and co-workers[1] has made available intermediates from which a number of optically active derivatives have been prepared by nucleophilic displacement reactions.[2,8,18,45,46,48] By far the majority of the evidence[2,8,18,34,40,45,46,48] indicates that such displacements occur with inversion of configuration at the phosphoryl and thiophosphoryl centers.

Seiber and Tolkmith[55] reported the preparation and certain stereospecific transformations of (-)-1-[(diethylamino)phenylphosphinothioyl]-2,3-dimethylimidazolium iodide. The imidazolium function was demonstrated[55] to be a facile leaving group in nucleophilic displacements by

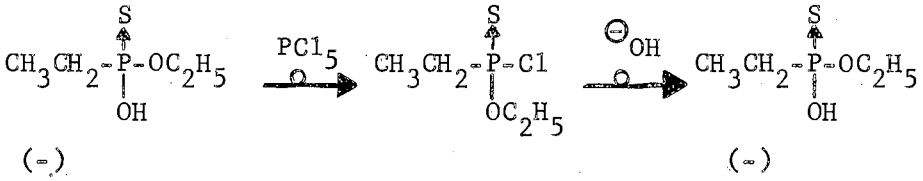


2-methylimidazol-1-yl anion, methoxide ion, and n-butylamine.

Optically active phosphonochloridothionates were recently used to study the stereochemistry at an asymmetric phosphorus atom.[45,47,49] Examples include the ethyl ethylphosphonochloridothionates, $CH_3CH_2P(S)(OCH_2CH_3)Cl$. The readily available ethyl ethylphosphonothioic acids,

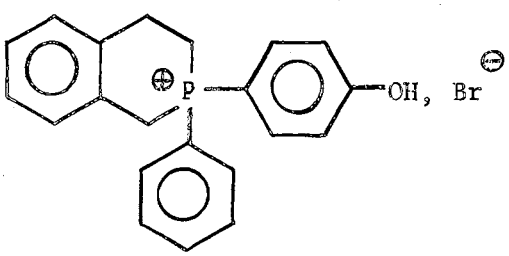


resolved according to Aaron and co-workers,[1] were converted into optically active phosphonochloridothionates with phosphorus pentachloride. The optically active phosphonochloridothionates reacted with a number of nucleophilic reagents yielding optically active esters, amides, and anhydrides.[45] Reaction of ethyl ethylphosphonothioic acids with phosphorus pentachloride and the subsequent reaction of the chloride with potassium hydroxide both proceed with inversion of configuration[49] at the thiophosphoryl center. Together these reactions lead to the acid of the original configuration.

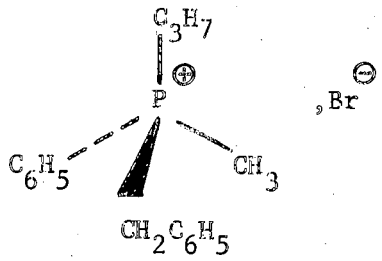


The present revival of interest in phosphorus stereochemistry perhaps began with the resolution of the phosphonium salts[19,22] shown below. The first optically active quaternary phosphorus compound

obtained in which the phosphorus atom was not incorporated in a hetero-



cyclic ring was resolved *via* its hydrogen dibenzoyltartrate salt.[37] A number of phosphonium salts have been resolved more recently by the same method.[27,33,42] The absolute configuration of one of these salts, (+)-benzylmethylphenyl-*n*-propylphosphonium bromide, is now known.[52]



Optically active phosphonium salts containing a 2-cyanoethyl group undergo reaction with sodium ethoxide to give optically active phosphines and 3-ethoxypropionitrile.[42] Reduction of several phosphonium

$$CH_3CH_2O^{\ominus} + RR'R''\overset{\oplus}{P}-CH_2CH_2CN \longrightarrow RR'R''P + CH_2{=}CHCN + C_2H_5OH$$

$$CH_3CH_2OH + CH_2{=}CHCN \xrightarrow{C_2H_5O^{\ominus}} CH_3CH_2O-CH_2CH_2CN$$

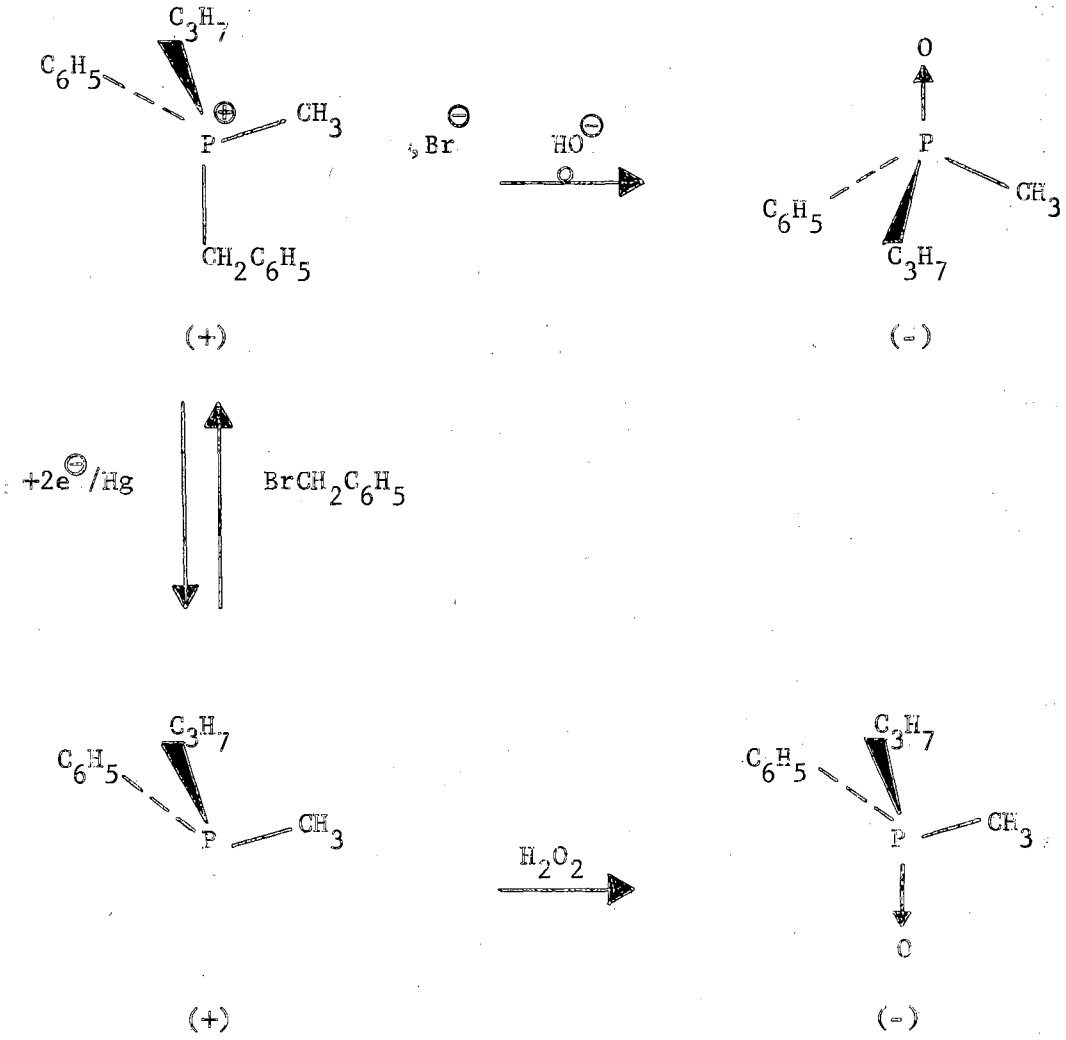
salts has produced the following orders of phosphorus-carbon bond strengths:[25,26]

(in H_2O) $C_6H_5CH_2 < o\text{-}CH_3C_6H_4 < C(CH_3)_3 < C_6H_5 <$ alkyl

(in C_2H_5OH) $C_6H_5CH_2 < CH(CH_3)_2 < C(CH_3)_3 < o\text{-}CH_3C_6H_4$

$$< n\text{-}C_4H_9 < C_6H_5 < C_2H_5 < CH_3$$

Optically active phosphonium salts are reduced by lithium aluminum hydride to give racemic phosphines.[42] Conversely, electrochemical reduction, using a mercury cathode, forms optically active phosphines.[33] That cathodic cleavage and quaternization both proceed with retention has been proven by the following set of reactions:[33]

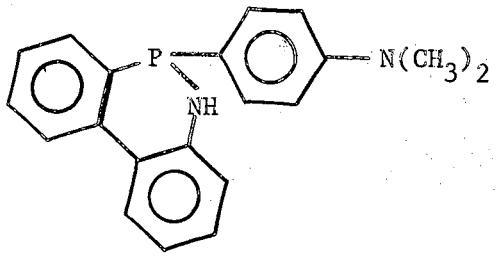


The scheme depends on the known inversion of an optically active phosphonium salt when it reacts with alkali to give an optically active phosphine oxide. Methyl-n-propylphenylphosphine which was synthesized from its benzyl bromide quaternary salt reformed the same optically active quaternary salt upon alkylation with benzyl bromide. Oxidation

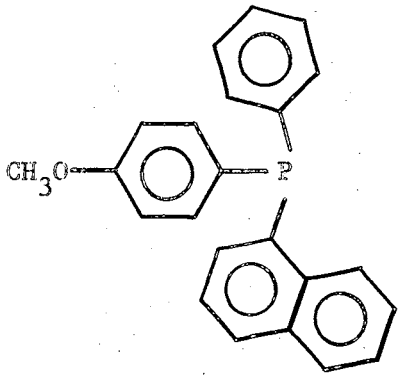
with hydrogen peroxide gave the mirror image of the phosphine oxide that was obtained by reaction of the corresponding phosphonium salt with alkali.

Heating optically active phosphines at atmospheric pressure results in racemization.[33] The kinetics of racemization of (+)-methylphenyl-n-propylphosphine have been measured and the energy of activation for the process determined as being about 30 kcal./mole.[31]

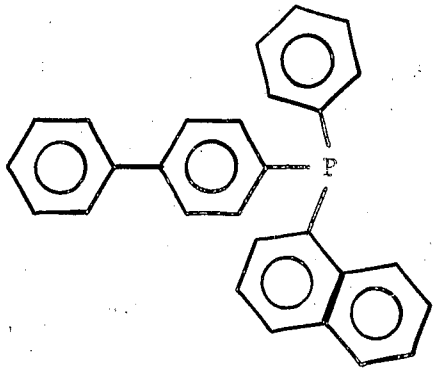
Campbell[14] resolved a cyclic phosphine, (+) and (-) 10-(p-dimethylaminophenyl)-9,10-dihydro-9-aza-10-phosphaphenanthrene.



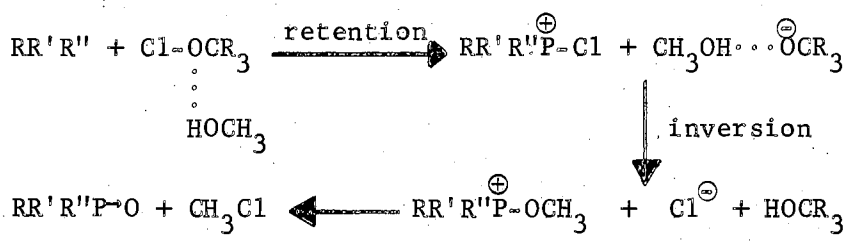
Horner[27] reported the isolation of the first optically active triarylphosphine, phenyl-p-anisyl-α-naphthylphosphine. Another unsymmetrical



triarylphosphine, p-biphenylyl-α-naphthylphenylphosphine, was resolved by Wittig and co-workers.[57] In order to accomplish the resolution, use was made of the fact that phosphines in the presence of acid and paraformaldehyde react to give α-hydroxymethylphosphonium salts.



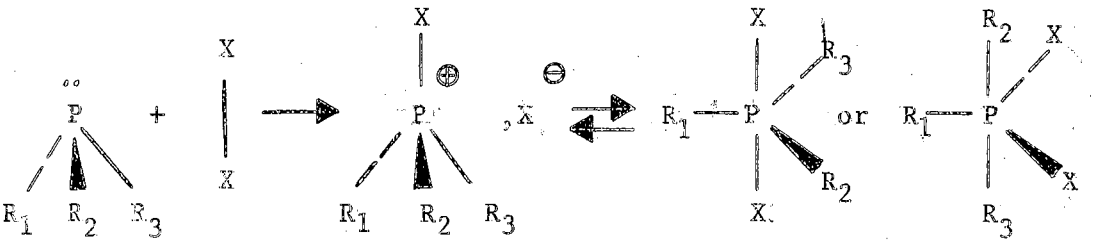
Oxidation of optically active phosphines with hydroperoxides results in retention of configuration,[16,33] but with t-butyl hypochlorite in methanolic methylene chloride, inversion of configuration is noted.[16] In the absence of methanol, t-butyl hypochlorite leads to almost complete racemization. This was construed as supporting the following mechanism:[16]



Reaction of methyl-n-propylphenylphosphine with benzenesulfinic acid gives a partly racemic phosphine oxide.[32] The amount of racemization increases when a more polar solvent is used. Reaction of the same phosphine with benzoyl peroxide also gives increasing racemization as the polarity of the solvent increases.[32]

Reaction of optically active phosphines with halogens, followed by hydrolysis, leads to racemic phosphine oxides.[30] In aqueous acetonitrile, this same reaction sequence produces phosphine oxides of inverted configuration.[30] These results are consistent with a mechanism in which an optically active phosphonium salt, formed initially, is in

equilibrium with a pentacovalent-phosphorus intermediate. The latter is initially in the form of a symmetric trigonal bipyramid. Subsequent to the formation of this trigonal-bipyramidal structure, flipping of group positions could occur.[50] This conclusion appears to be strengthened by the observations that: (a) optically active phosphonium salts react with sodium hydroxide to form phosphine oxides of inverted configuration;[29,38] and (b) optically active phosphine oxides racemize in

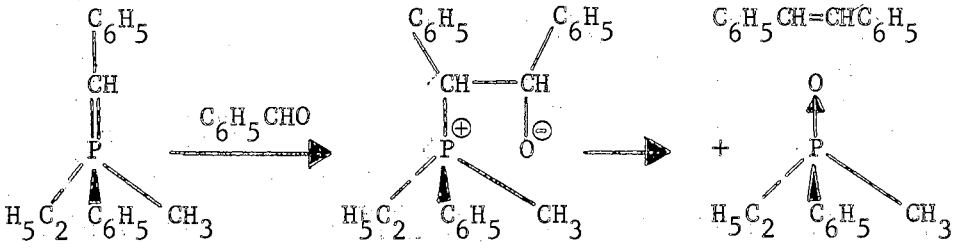


the presence of anhydrous hydrochloric acid.[17] It is interesting to contrast the decomposition of optically active methylethylphenylbenzylphosphonium n-butoxide, which is reported[51] to produce methylethylphenylphosphine oxide with over 90% racemization.

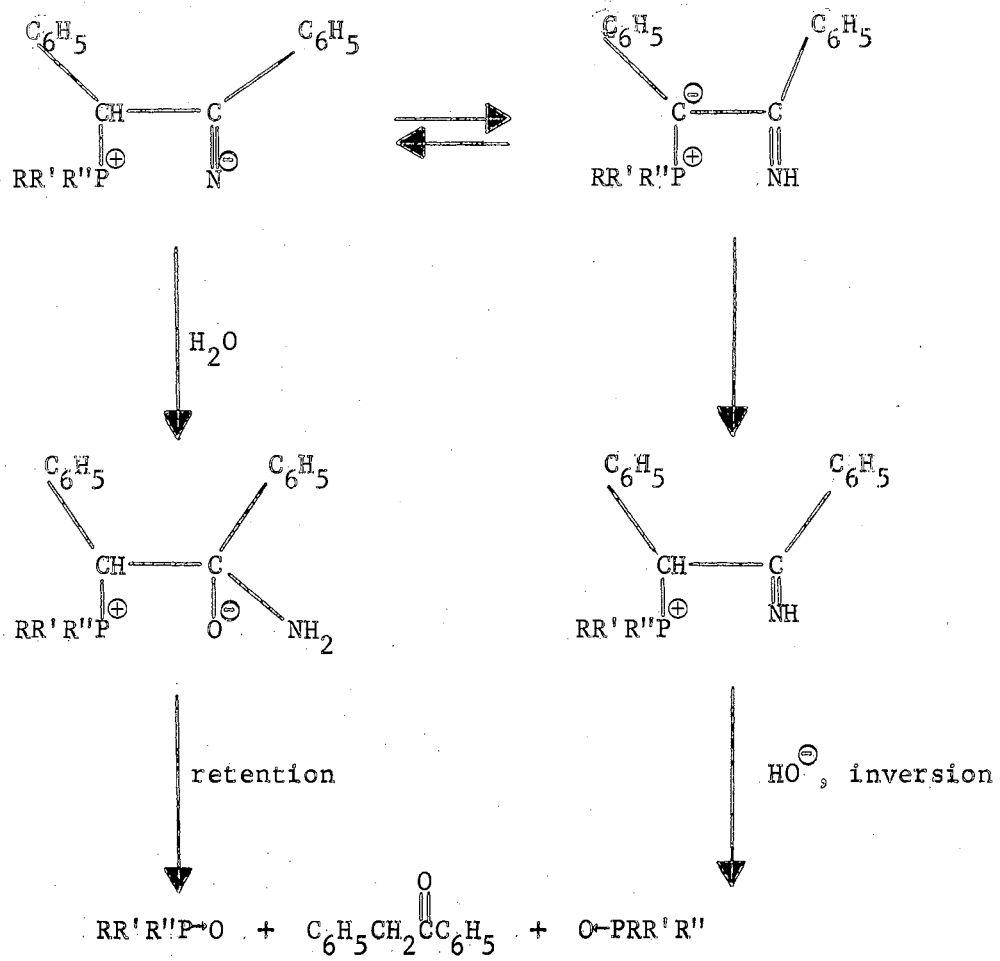
Optically active phosphines retain their configuration on sulfuration.[33] Either cyclohexene episulfide, octatomic sulfur, or monatomic sulfur reacts with optically active methyl-n-butylbenzylphosphine to give the phosphine sulfide with retention of configuration.[28,58]

In the presence of phenyllithium, optically active benzylethylmethylphenylphosphonium iodide affords the corresponding phosphorane with retention of configuration.[6] Reaction of this phosphorane with

benzaldehyde gives phosphine oxide with a high degree of retention of configuration. This supports[6] the existence of a cyclic transition state for the Wittig reaction. Similarly reaction of the phosphorane



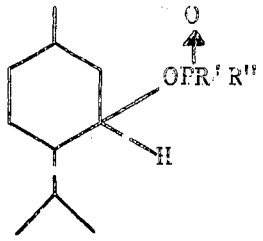
with benzonitrile affords an intermediate, which upon treatment with alkali yields a phosphine oxide with 68% inversion of configuration. This shows that two paths are involved, one proceeding with retention and the other with inversion of configuration.



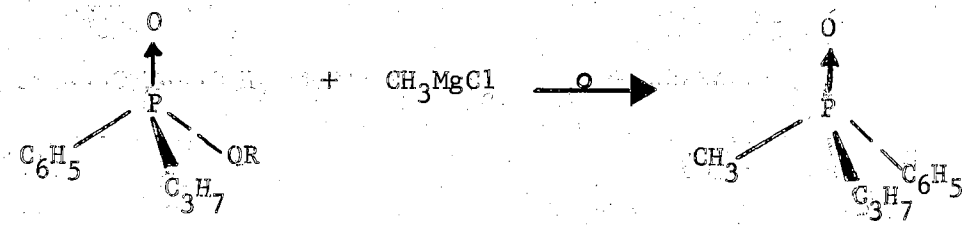
The same phosphorane was shown to react with styrene oxide to form a betaine, which upon pyrolysis at 190-200° yielded, among other products, racemic phosphine and phosphine oxide of 50% net inverted configuration.[41] Racemic phosphine presumably arose as a consequence of the thermal racemization of the optically active phosphine. A concerted, base-assisted decomposition of a pentacovalent-phosphorus intermediate has been suggested to lead to the inverted phosphine oxide.

Optically active phosphine oxides occupy a key position in the stereochemical investigations of phosphorus compounds.[36] Resolution of ethylmethylphenylphosphine oxide provided the first example of an optically active phosphorus compound.[43] Phosphine oxides are precursors to optically active phosphines by reduction with trichlorosilane.[24]

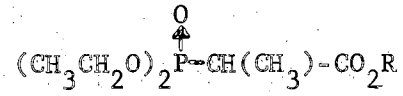
Korpiun and Mislow[36] have developed a synthetic route to the preparation and configurational correlation of optically active phosphine oxides that does not require resolution of phosphine oxides or phosphonium salts. Unsymmetrically substituted menthyl phosphinates were



readily separated into the diastereomeric forms. Reaction of the phosphinates with alkyl or aryl Grignard reagents in benzene at 70° affords phosphine oxides[5] with a high degree of stereospecificity. For example,[36] methylmagnesium chloride and diastereomerically pure (-)-menthyl phenyl-n-propylphosphinate give (+)-methylphenyl-n-propylphosphine oxide. Since the absolute configuration of the above phosphinic ester



had been determined by X-ray analysis, it was concluded that the Grignard reaction proceeded with inversion of configuration. The diastereomerically pure menthyl phosphinates are reported[39] to give NMR and ORD spectra which are characteristic of their configurations. Optical rotations are known for both (-)-menthyl- and (-)-bornyl P,P-diethyl 2-phosphonopropionate.[56] The latter two compounds were synthesized

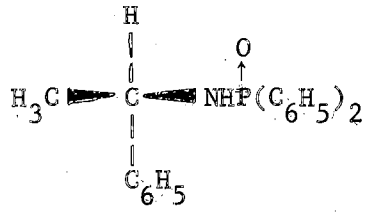


from triethyl phosphite and the corresponding α-bromopropionic ester. Another example of an optically active organophosphosphorus compound is (-)-menthyl diphenylphosphinate.[39]

CHAPTER II

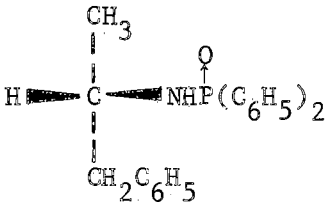
DISCUSSION OF RESULTS AND CONCLUSIONS

Optically active primary amines and optically active alcohols were starting materials in the synthesis of amides and esters of diphenylphosphinic acid. The purpose of this work was to develop good methods for the preparation of some optically active organophosphorus compounds which do not contain an asymmetric phosphorus atom. The products were as follows: (+)-N-(α-methylbenzyl)diphenylphosphinic amide (II), (+)-N-(α-methylphenethyl)diphenylphosphinic amide (III), (-)-N-[α-(1-naphthyl)ethyl]diphenylphosphinic amide (IV), (-)-menthyl diphenylphosphinate (V), (-)-bornyl diphenylphosphinate (VI), and (+)-2-methyl-1-butyl diphenylphosphinate (VII).

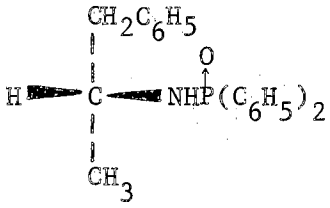


(+)-N-(α-methylbenzyl)diphenylphosphinic amide (II)

$$[\alpha]_D^{23.5} = +33.5^\circ$$

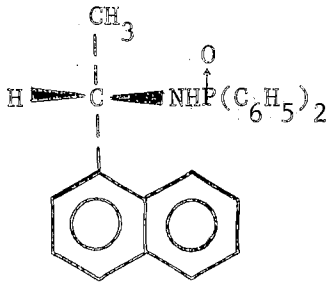


or

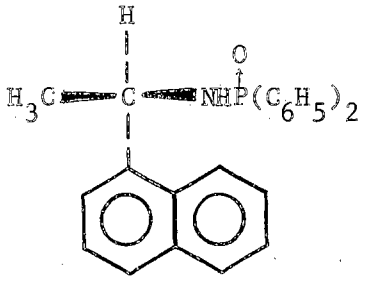


(+)-N-(α-methylphenethyl)diphenylphosphinic amide (III)

$$[\alpha]_D^{24.0} = +19.6^\circ$$

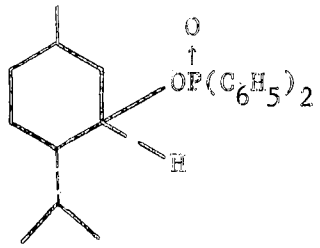


or



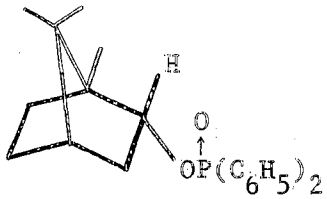
(-)-N-[α-(1-naphthyl)ethyl]diphenylphosphinic amide (IV)

$$[\alpha]_D^{24.5} = -44.8^\circ$$



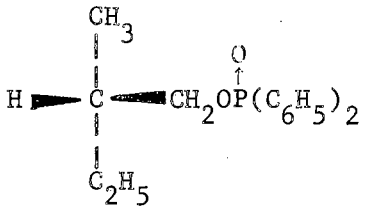
(-)-menthyl diphenylphosphinate (V)

$$[\alpha]_D^{25.5} = -73.0^\circ$$



(-)-bornyl diphenylphosphinate (VI)

$$[\alpha]_D^{25.5} = -14.3^\circ$$



(+)-2-methyl-1-butyl diphenylphosphinate (VII)

$$[\alpha]_D^{24.0} = +4.18^\circ$$

The primary amines were (+)-α-methylbenzylamine, (+)-α-methylphenethylamine, and (+)-α-(1-naphthyl)ethylamine. The alcohols were (-)-menthol, (-)-borneol, and (-)-2-methyl-1-butanol. Two equivalents of amine per one equivalent of diphenylphosphinic chloride (I) were utilized in the preparation of the amides. The second equivalent of amine was used to combine with the hydrochloric acid. The sodium alkoxides of (-)-menthol and (-)-borneol were prepared in order to

$$2RNH_2 + (C_6H_5)_2\overset{O}{\uparrow}PCl \longrightarrow RNH\overset{O}{\uparrow}P(C_6H_5)_2 + \overset{\oplus}{R}NH_3Cl^{\ominus}$$

promote formation of esters from I. Triethylamine was used as an acid

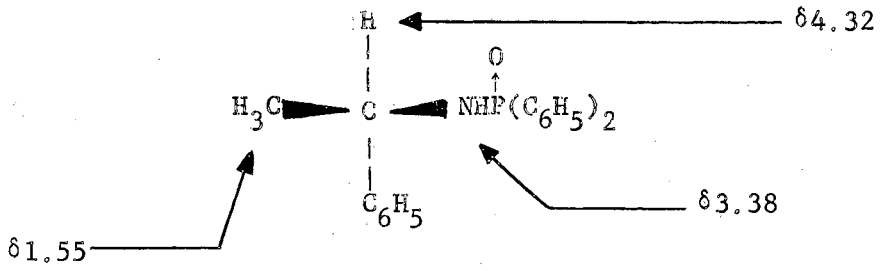
$$ROH + Na \longrightarrow RONa + \tfrac{1}{2}H_2$$

$$RONa + (C_6H_5)_2P(O)Cl \longrightarrow ROP(O)(C_6H_5)_2 + NaCl$$

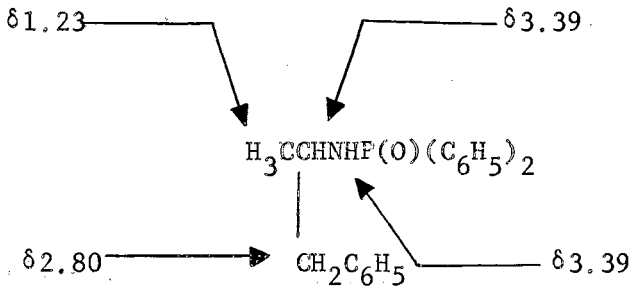
scavenger in the ester synthesis from (-)-2-methyl-1-butanol and I.

$$ROH + (C_6H_5)_2P(O)Cl + (CH_3CH_2)_3N \longrightarrow ROP(O)(C_6H_5)_2 + \overset{\oplus}{(CH_3CH_2)_3}NH\ Cl^{\ominus}$$

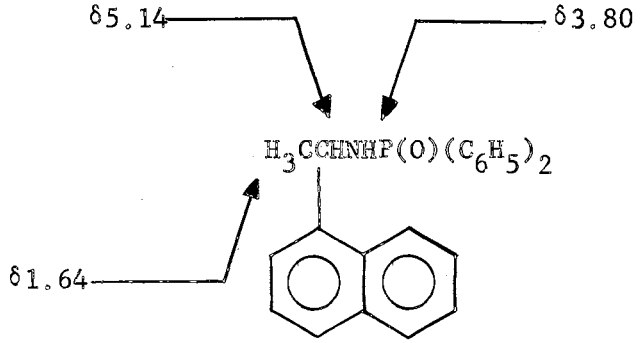
NMR (Table II), IR (Table I), and elemental analyses (Table III) for II-VII are in accord with the proposed structures. Physical properties such as melting point and specific rotation also are recorded in Table III.



II



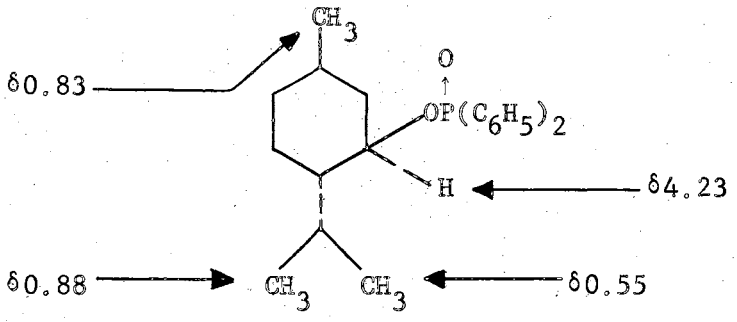
III



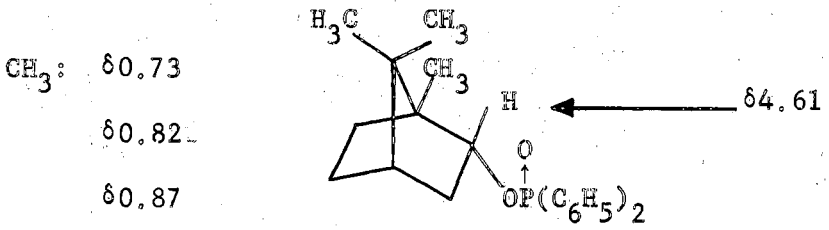
IV

IR spectra of the amides II-IV display hydrogen-bonded N-H absorption maxima at 3090-3160 $cm.^{-1}$. The phosphoryl frequencies are observed at 1182-1197 $cm.^{-1}$. These values approximate the N-H and P=O

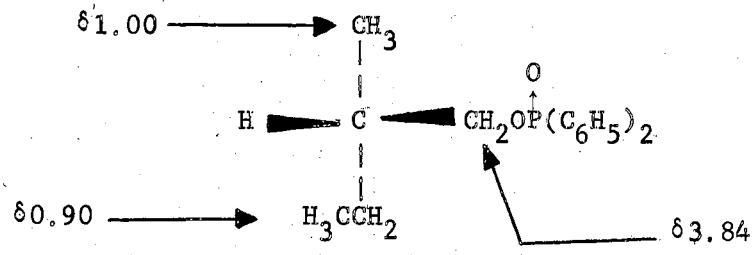
maxima reported by Bellamy.[4] A broad multiplet at ca. δ3.38-3.80 appears in the NMR spectra of II-IV for the NH proton of the amide linkage. Likewise, a multiplet at ca. δ3.39-5.14 is observed for the single methine proton in the amides. Each of the amides also gives doublets in the range of δ1.23-1.64 with coupling constants of ca. 5.2-6.5 c.p.s. for the methyl group. The remaining peaks for II-IV appear at δ values according to the classical predictions.



V



VI



VII

IR spectra of the esters V-VII display P→O and P-O-C absorption maxima in the ranges of 1224-1230 $cm.^{-1}$ and 1014-1023 $cm.^{-1}$, respectively. The above values correlate well with those for a series of alkyl diphenylphosphinates prepared by Austin.[3] Each of compounds V-VII produces a multiplet in the NMR spectrum at δ7.2-8.1 for the aromatic protons. The OCH proton in V and VI gives a multiplet at δ4.23 and δ4.61, respectively. The OCH_2 protons in VII produce a triplet at δ3.84 (J = 5.9). The three methyl groups in V [(a), (b), and (d), respectively] give rise to doublets at δ0.55 (J = 6.8), δ0.88 (J = 7.0), and δ0.83 (J = 5.0) while the three methyl groups in VI yield singlets at δ0.73, δ0.82, and δ0.87. The two methyl groups [(b) and (c)] in VII overlap in the spectrum and appear at ca. δ1.00 and δ0.90 (J = 3.0), respectively. As with the amides, the remaining peaks for the esters appear at δ values consistent with classical predictions.

Compound I was obtained by oxidative chlorination of diphenylphosphinous chloride in the presence of phosphorus pentoxide. The reaction equation is given below. Vacuum distillation was used to

$$3(C_6H_5)_2PCl + P_2O_5 + 3Cl_2 \longrightarrow 3(C_6H_5)_2P(O)Cl + 2POCl_3$$

obtain the pure product.

The reactions involving the optically active amines with I were only slightly exothermic. During addition of I to the amine, the amide and the hydrochloride of the amine immediately began to precipitate. In the workup of the reaction mixtures, the solid precipitate was washed with water to dissolve the ionic salt. The residue was then recrystallized to give pure amide.

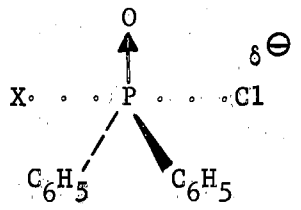
Formation of the sodium derivatives of (-)-menthol and (-)-borneol

required vigorous stirring and heating at 100-105° for 7 hours. After cooling to room temperature, the excess sodium was removed with forceps. The subsequent reaction between the alkoxide and I was highly exothermic but could be controlled by the use of an external ice-water bath. I was removed by extraction with aqueous sodium bicarbonate. Attempts to remove unreacted (-)-menthol by vacuum distillation and (-)-borneol by sublimation were unsuccessful. However, steam distillation proved useful for this purpose. Stability of the phosphinic esters, V and VI, toward aqueous hydrolysis was evident in the fact that the unreacted alcohols could be removed by steam distillation.

The reaction between (-)-2-methyl-1-butanol, I, and triethylamine was only slightly exothermic. Excess I and triethylamine hydrochloride were removed by extraction with aqueous sodium bicarbonate. Again steam distillation was used to remove the unreacted alcohol.

The reactions involving I include the formation of P-N and P-O bonds in nucleophilic displacement on phosphorus by nitrogen and oxygen atoms, respectively. The transition state probably involves a penta-substituted phosphorus atom.[34,40]

X = N or O



Compounds very similar to V and VI have been prepared. They are menthyl and bornyl hydrogen phenylphosphonate[15] (see Chapter I). Optical rotation has been measured[56] for two organophosphosphorus compounds which contain either a menthyl or bornyl group. The compounds are (-)-menthyl and (-)-bornyl P,P-diethyl 2-phosphonopropionate (see Chapter I). Respective specific rotations for these compounds in ethanol are

-50.9° and -32.5°. Temperature was not reported.

Specific rotations of chloroform solutions containing the starting materials leading to compounds II-VII were $+35.6^{\circ}$, $+36.2^{\circ}$, $+41.3^{\circ}$, -44.7°, -20.8°, and -5.33°, respectively. Specific rotations for compounds II-VII in chloroform were $+33.5^{\circ}$, $+19.6^{\circ}$, -44.8°, -73.0°, -14.3°, and $+4.18^{\circ}$, respectively. Of course inherent asymmetry arising from the asymmetric configuration[9-11] in the amine or alcoholic portion of II-VII is a sufficient cause for producing optical activity. In addition, asymmetric conformations[12] of the molecule could contribute to the sign and magnitude of the specific rotation. Knowledge of "allowed" conformations[9,12] and of the rotatory effects[9-12] of dissymmetric molecules and certain molecular conformations conceivably might be useful in explaining the sign and magnitude of the specific rotation for II-VII.

Brewster[9] reported that the known configurations in the "carbinyl" series (HCXRR') and in the "methine" series (HCRR'R") made feasible an attempt to relate sign of rotation to structure, absolute configuration, and conformation. This was done for a few compounds by use of two general rules, a simple method of conformational analysis and a small number of empirical rotation constants. It is interesting to note Brewster's rationalization[9] that the result of opposed atomic and conformational asymmetry effects could be a relatively small rotation of unpredictable sign.

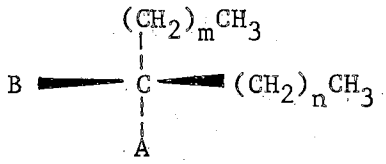
In Brewster's discussion[9,12] of open-chain compounds, optical rotatory effects of asymmetric conformational units are said to be observable only when enantiomeric units exist in unequal amounts.

A' or A ≠ H

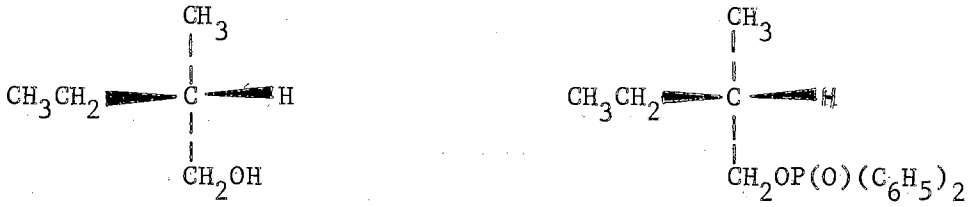
Restraints on rotation about the central bond of the conformational unit is sufficient cause for the above situation. In 3-methylhexane, which contains three such conformational units, all combinations of "allowed" conformations are considered to contribute equally to the specific rotation.

Empirical rotation constants for all the substituent groups bonded to the asymmetric carbon atoms in compounds II-VII are not known. Furthermore, a useful method for predicting the preferred conformations in such compounds has not yet been developed. These limitations make it impossible to explain fully the magnitude or sign of the specific rotation for II-VII. It should be noted that the sign of specific rotation for the organophosphorus product, IV or VII, is opposite to that of the corresponding amine or alcohol. The observed changes are from $+41.3^{\circ}$ to -44.8° and from -5.33° to $+4.18^{\circ}$. The reversals of sign suggest that (in these compounds) some P-N, N-C, P-O, and O-C conformations may be preferred over the corresponding enantiomeric conformations. It appears reasonable that the change in conformational asymmetry effect in going from (+)-α-(1-naphthyl)ethylamine to IV (or from (-)-2-methyl-1-butanol to VII) may account for the change in sign of the specific rotation.

When m>n in the series of compounds below, it has been postulated that: (1) a negative rotation will be observed if A and B have similar



steric requirements; and (2) a positive rotation will be observed if A has larger steric requirements than B. Comparison of the above configuration with those for (-)-2-methyl-1-butanol and VII produces interesting results. In the reaction which gave VII, configuration of the asym-



VII

metric carbon was not changed, but the size of one of the substituents [OH changed to $OP(O)(C_6H_5)_2$] was greatly increased. All substituents remained unchanged except the OH function which was converted to a $OP(O)(C_6H_5)_2$ group. Therefore, a change of sign from negative to positive appears to be logical.

In summary, a series of amides and esters of diphenylphosphinic acid were synthesized. These compounds are among the few optically active organophosphorus compounds which do not contain an asymmetric phosphorus atom. The methods of preparation are discussed and physical constants of the compounds are reported. IR and NMR spectra and specific rotations have been used to characterize the optically active products, II-VII.

TABLE I

IR ABSORPTION MAXIMA($cm.^{-1}$) OF OPTICALLY ACTIVE PHOSPHORUS COMPOUNDS II-VII

Cpd.	Plate	N-H	P→O	P-O-C
II	I	3160	1182	
III	II	3090	1197	
IV	III	3150	1192	
V	IV		1224	1014
VI	V		1230	1023
VII	VI		1224	1016

TABLE II

NMR COUPLING CONSTANTS AND CHEMICAL SHIFTS OF PRODUCTS[a]

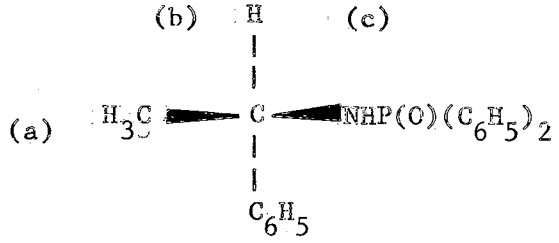
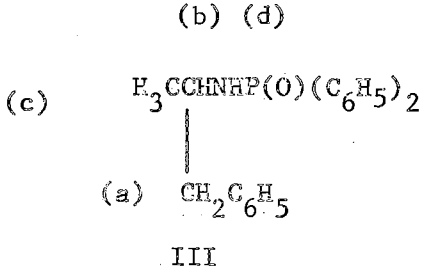
Cpd.	Plate	δ(p.p.m.)[b]	J(c.p.s.)	Integ.	Assignment
 II	VII	1.55 d	6.5	3	CH_3 (a)
		4.32 m	- -	1	CH (b)
		3.38 m	- -	1	NH (c)
		7.1-8.1 m	- -	15	Ar-H
 III	VIII	2.80 m	- -	2	CH_2 (a)
		3.39 m	- -	1	CH (b)
		1.23 d	5.2	3	CH_3 (c)
		3.39 m	- -	1	NH (d)
		6.9-8.0 m	- -	15	Ar-H

TABLE II (CONTINUED)

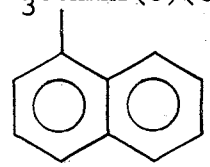
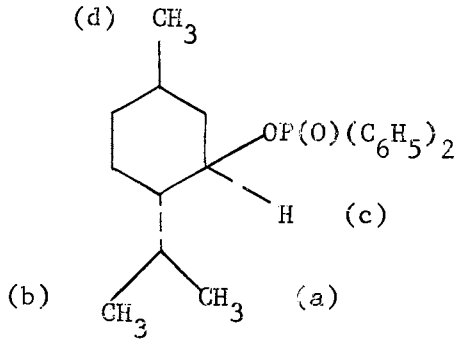
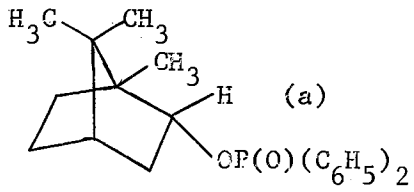
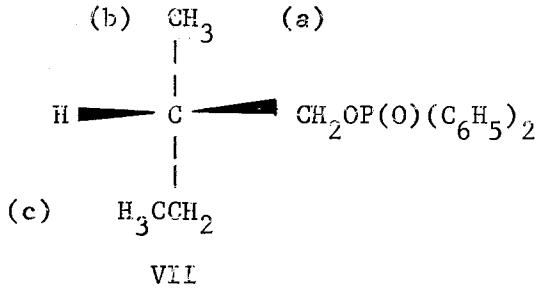
Cpd.	Plate	δ(p.p.m.)[b]	J(c.p.s.)	Integ.	Assignment
(b) (c) (a) $H_3CCHNHP(O)(C_6H_5)_2$  IV	IX	1.64 d	6.5	3	CH_3 (a)
		5.14 m	- -	1	CH (b)
		3.80 m	- -	1	NH (c)
		7.0-8.1 m	- -	17	Ar-H
(d) CH_3 $OP(O)(C_6H_5)_2$ H (c) (b) CH_3 CH_3 (a)  V	X	0.55 d	6.8	3	CH_3 (a)
		0.88 d	7.0	3	CH_3 (b)
		4.23 m	- -	1	OCH (c)
		0.83 d	5.0	3	CH_3 (d)
		7.2-8.1 m	- -	10	Ar-H

TABLE II (CONTINUED)

Cpd.	Plate	δ(p.p.m.)[b]	J(c.p.s.)	Integ	Assignment
 VI	XI	0.73 s	- -	3	CH_3
		0.82 s	- -	3	CH_3
		0.87 s	- -	3	CH_3
		4.61 m	- -	1	OCH (a)
		7.2-8.1 m	- -	10	Ar-H
 VII	XII	3.84 t	5.9	2	CH_2 (a)
		ca. 1.00 d	- -	3	CH_3 (b)
		0.90 t	3.0	3	CH_3 (c)
		7.2-8.1 m	- -	10	Ar-H

[a]The solvent used was deuterochloroform.

[b]The multiplicity of each signal is indicated as follows: singlet, s; doublet, d; triplet, t; multiplet, m.

TABLE III

SYNTHESIS AND PROPERTIES OF OPTICALLY ACTIVE PHOSPHORUS COMPOUNDS II-VII

Cpd.	Yield,[a] %	M.p., °C.	$[\alpha]_D^t$ (c, g./100 ml. in chloroform)	Analysis, %							
				C		H		N		P	
				Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
II	71.7	192-193	$+33.5^{23.5}$ (6.160)					4.36	4.31	9.64	9.57
III	61.3	121.5-122.5	$+19.6^{24.0}$ (5.467)					4.18	4.05	9.24	9.29
IV	60.8	163-164	$-44.8^{24.5}$ (3.261)					3.77	3.70	8.34	8.11
V	51.2	72-73	$-73.0^{25.5}$ (8.280)	74.13	74.17	8.20	8.15			8.69	8.69
VI	53.8	74-75	$-14.3^{25.5}$ (5.892)	74.55	74.61	7.68	7.66			8.74	9.01
VII	43.1	42-43	$+4.18^{24.0}$ (4.658)	70.81	71.04	7.34	7.41			10.74	10.89

[a] Yields are based on optically active amine or alcohol as starting material.

CHAPTER III

EXPERIMENTAL[a-e]

Preparation of Diphenylphosphinic Chloride (I). This compound was synthesized by modification of a known procedure.[3] A cylinder of chlorine was connected through a trap to a 3-l., 3-necked flask equipped with a mechanical stirrer, a condenser with a drying tube, a thermometer, and a fritted glass delivery tube. To the flask was added 761.6 g. (3.45 moles) of diphenylphosphinous chloride (neat). Phosphorus pentoxide (155 g., 1.09 moles) was slowly added to the flask with gentle stirring, and a suspension of the solid in the acid chloride was obtained. With vigorous stirring, chlorine gas was passed into the flask

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[a] All melting points are corrected; all boiling points are uncorrected. The petroleum ether used boiled at 37.4-50.7°.

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

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

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

[e] The optical rotations were obtained using a Model 80 universal high precision polarimeter manufactured by O. C. Rudolph and Sons, Caldwell, New Jersey. The solvent used was Certified A.C.S. chloroform sold by Fisher Scientific Company.

through the fritted glass tube at such a rate that the exothermic reaction produced a slow rise in temperature. When the temperature reached 70° (20 minutes), a water bath was applied and the temperature was held between 70 and 80°. Chlorination of the mixture was continued until a greenish color developed in it (color change occurred abruptly). A slow stream of chlorine gas was maintained while the mixture was heated slowly to 110° at which point the chlorination was terminated. The mixture was then boiled for 1.5 hours (maximum temperature attained was 145°). Distillation of the phosphoryl chloride was accomplished at reduced pressure using a potassium hydroxide-calcium oxide trap between the apparatus and the water aspirator. The mixture was heated (71-76°) until 150 ml. of phosphoryl chloride had been collected and the distillation was terminated. Transfer of the reaction mixture to a 2-l. distillation flask was accomplished under anhydrous conditions. Diphenylphosphinic chloride was distilled in vacuo [142-147°/0.01 mm.; lit.[21] 135-136°/0.07 mm.]; yield 518.1 g. (63.6%)[$n_D^{24.5}$ 1.6076; lit.[21] n_D^{20} 1.6068].

Preparation of Optically Active N-Substituted Diphenylphosphinic Amides II-IV. The general method[54] of preparation is illustrated in detail for (+)-N-(α-methylbenzyl)diphenylphosphinic amide (II). Significant deviations from the general procedure are then stated for the other amides III and IV. Elemental analyses (Table III) and spectral data (Tables I-II) support the proposed structures for II-IV.

A 200-ml., 3-necked flask equipped with a magnetic stirring bar, addition funnel, condenser, and thermometer was charged with a solution of 3.5 g. (0.0289 mole) of (+)-α-methylbenzylamine ($[\alpha]_D^{23}$ = +35.6°) in 160 ml. of anhydrous (dried over Linde 3A molecular sieve) ethyl

ether. Diphenylphosphinic chloride (3.41 g., 0.0144 mole) in 15 ml. of anhydrous ethyl ether was added dropwise at such a rate as to cause gentle boiling of the solvent. The addition required 10 minutes. The reaction mixture was then boiled (34°) for 6 hours. The amide and the hydrochloride of the amine were removed from the ether by filtration. This solid residue was washed with four 125-ml. portions of water. Recrystallization of the remaining solid from ethanol-water (2:1) gave 3.3 g. (71.7%) of II, m.p. 192-193°.

A mechanical stirrer was used in the preparation of (+)-N-(α-methylphenethyl)diphenylphosphinic amide (III) and of (-)-N-[α-(1-naphthyl)ethyl]diphenylphosphinic amide (IV). Diphenylphosphinic chloride (17.5 g.; 0.074 mole) in 50 ml. of anhydrous ethyl ether was added dropwise to 20.0 g. (0.148 mole) of (+)-α-methylphenethylamine ($[\alpha]_D^{23}$ = +36.2°) in 250 ml. of anhydrous ethyl ether. Other reaction conditions and workup were essentially the same as those for II. Recrystallization of the crude product from chloroform-heptane (1:3) gave 15.2 g. (61.3%) of III, m.p. 121.5-122.5°.

Diphenylphosphinic chloride (13.8 g.; 0.0585 mole) in 50 ml. of anhydrous ethyl ether was added dropwise to 20.0 g. (0.117 mole) of (+)-α-(1-naphthyl)ethylamine ($[\alpha]_D^{24}$ = +41.3°) in 350 ml. of anhydrous ethyl ether. Again other reaction conditions and workup were essentially the same as those for II. Recrystallization from benzene-heptane gave 13.2 g. (60.8%) of IV, m.p. 163-164°.

Preparation of (-)-Menthyl Diphenylphosphinate (V). A 500-ml. flask was equipped with an immersion thermometer, nitrogen inlet tube, mechanical stirrer, addition funnel, condenser, and calcium chloride drying tube. An oil bath was placed around the reaction flask. Sodium

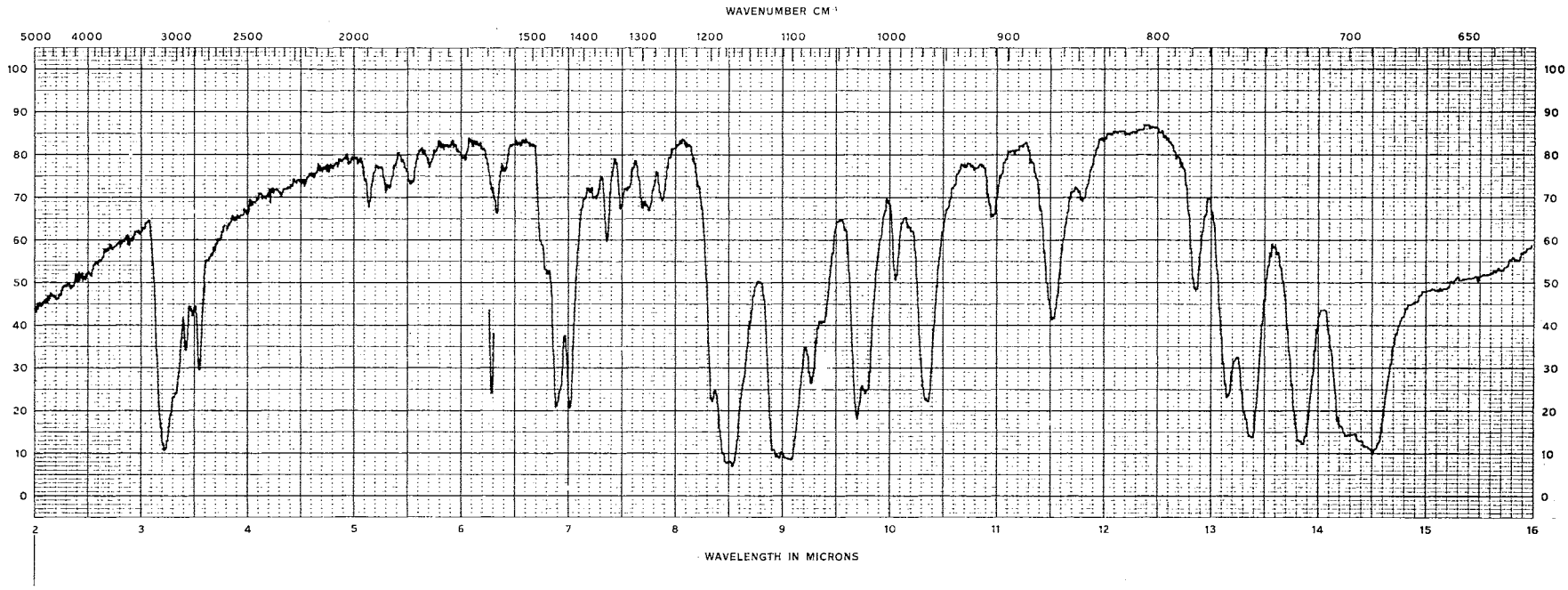
(2.76 g.; 0.12 mole), 15.63 g. (0.10 mole) of (-)-menthol ($[\alpha]_D^{23}$ = -44.7°), and 50 ml. of toluene (dried over sodium) were stirred vigorously for 7 hours while the oil bath temperature was held at 100-105°.[35] After the mixture was allowed to cool to room temperature, the unreacted chunk of sodium was removed mechanically. Next 26.0 g. (0.11 mole) of diphenylphosphinic chloride in 50 ml. of toluene was added dropwise to the sodium alkoxide with external cooling. During addition (15 minutes), the temperature was kept below 40°. The mixture was then boiled at 85° for 4 hours, cooled, extracted with 200 ml. of 5% sodium bicarbonate, and washed with water. Steam distillation of the organic layer was performed until about 1.5 l. of distillate had been collected in order to remove the unreacted menthol. The nonvolatile organic residue was extracted with ethyl ether. The ether solution was dried ($MgSO_4$) and then evaporated. After a small amount of n-hexane was added to the residual oil, cooling in dry ice-acetone bath caused solidification. Recrystallization from n-hexane gave 18.25 g. (51.2%) of V, m.p. 72-73°. Elemental analysis (Table III) and spectral data (Tables I-II) support the proposed structure.

Preparation of (-)-Bornyl Diphenylphosphinate (VI). The reaction conditions and workup were essentially the same as those for V. Amounts of sodium, toluene, and diphenylphosphinic chloride were the same as above. The weight of (-)-borneol ($[\alpha]_D^{23}$ = -20.8°) used was 15.43 g. (0.10 mole). Recrystallization from n-hexane gave 19.1 g. (53.8%) of VI, m.p. 74-75°. Elemental analysis (Table III) and spectral data (Tables I-II) support the proposed structure.

Preparation of (+)-2-Methyl-1-butyl Diphenylphosphinate (VII). The apparatus used was the same as that used for V. Diphenylphosphinic

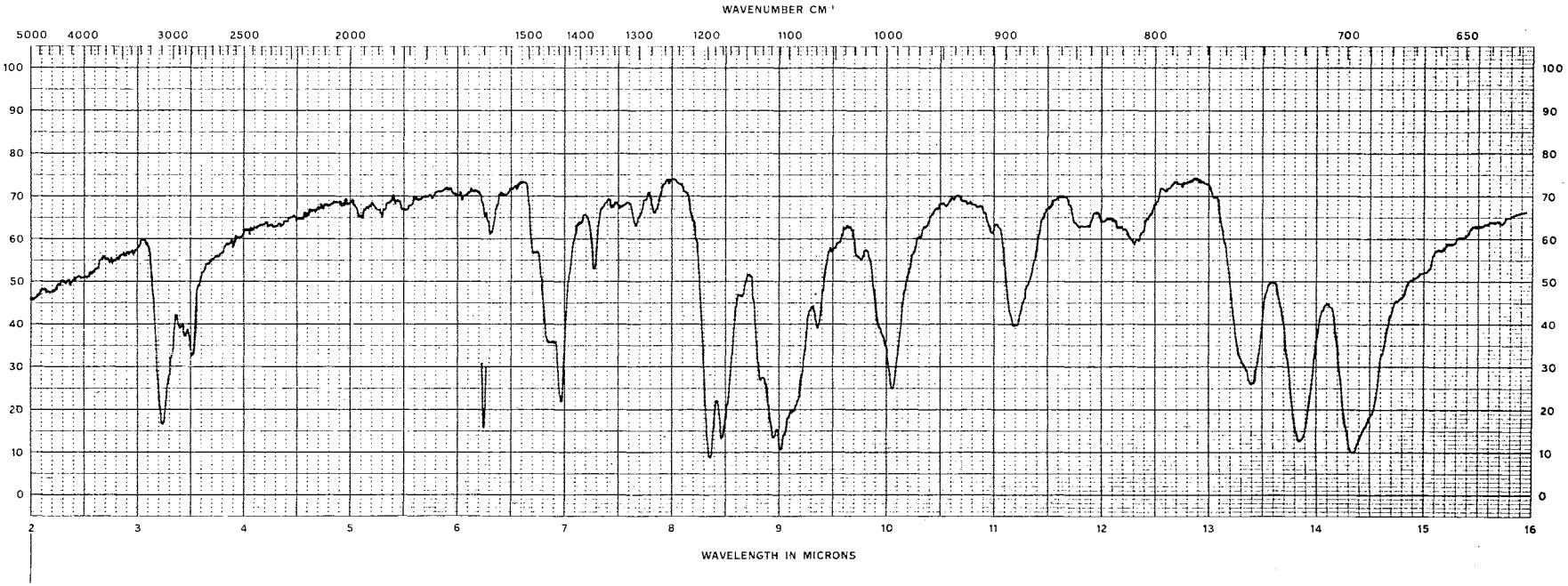
chloride (26.0 g., 0.11 mole) in 50 ml. of anhydrous (Linde 3A molecular sieve) ethyl ether was added dropwise to 12.15 g. (0.12 mole) of triethylamine and 8.8 g. (0.10 mole) of (-)-2-methyl-1-butanol ($[\alpha]_D^{23}$ = -5.33°) in 150 ml. of anhydrous ethyl ether. The temperature rose from 25 to 30° during the 10-minute addition. After the mixture was boiled at 37° for 4 hours, it was stirred at room temperature for 1 hour. The mixture was then extracted with 400 ml. of 5% sodium bicarbonate and washed with water. Steam distillation of the organic layer was performed until 0.5 l. of distillate had been collected in order to remove the unreacted alcohol and amine. The nonvolatile organic residue was extracted with a mixture of benzene and ethyl ether. After drying the organic layer ($MgSO_4$) and evaporation of the solvent, the crude ester VII was mixed with 250 ml. of warm hexane (50°). The resulting, warm mixture was filtered to remove 0.4 g. of diphenylphosphinic acid; then the solvent was evaporated from the filtrate. Cooling of the residual oil to -15° made it solidify. Recrystallization of the solid from n-hexane-ethyl ether (20:1) gave 12.4 g. (43.1%) of VII, m.p. 42-43°. Elemental analysis (Table III) and spectral data (Tables I-II) are in accord with the proposed structure.

Plate I



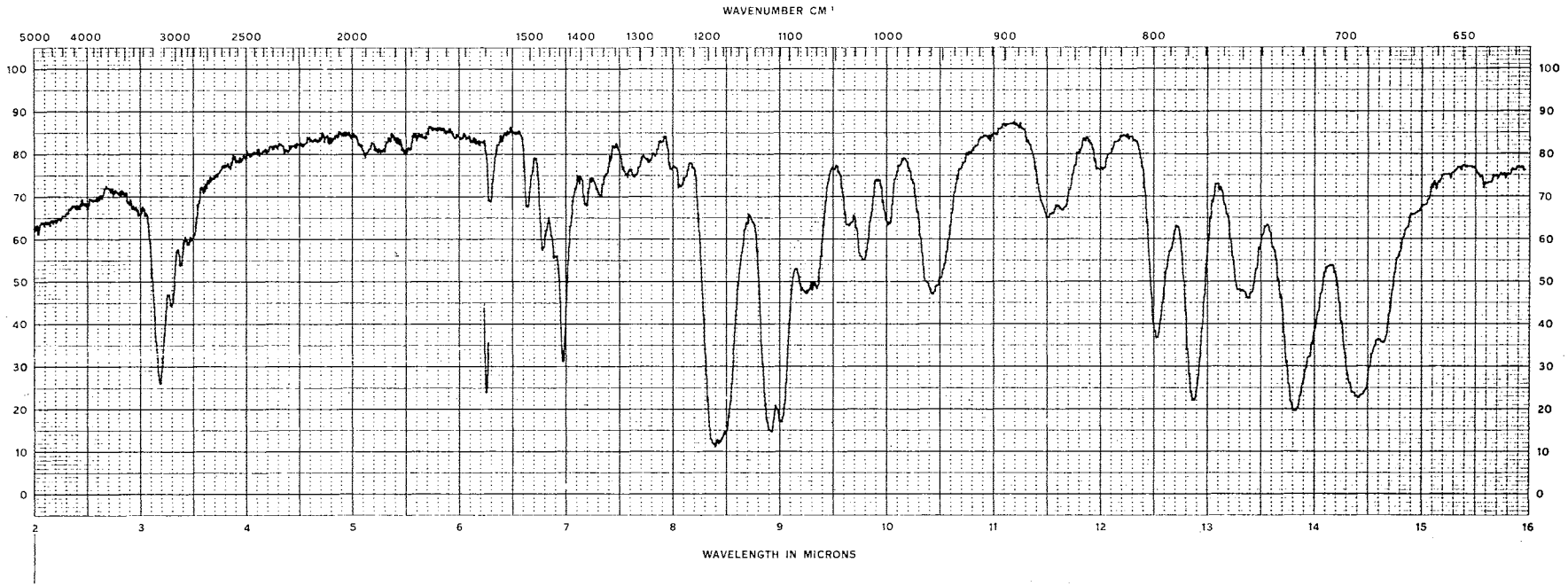
(+)-N-(α-Methylbenzyl)diphenylphosphinic Amide (II), KBr Pellet

Plate II



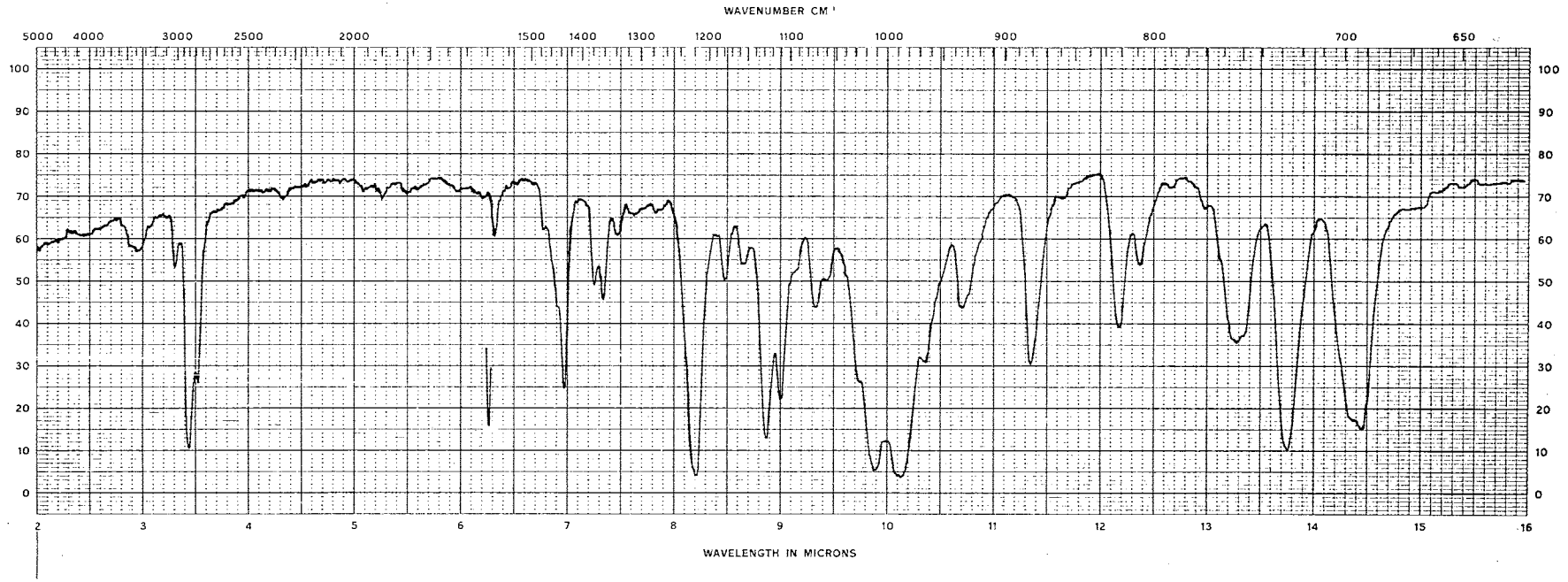
(+)-N-(α-Methylphenethyl)diphenylphosphinic Amide (III), KBr Pellet

Plate III



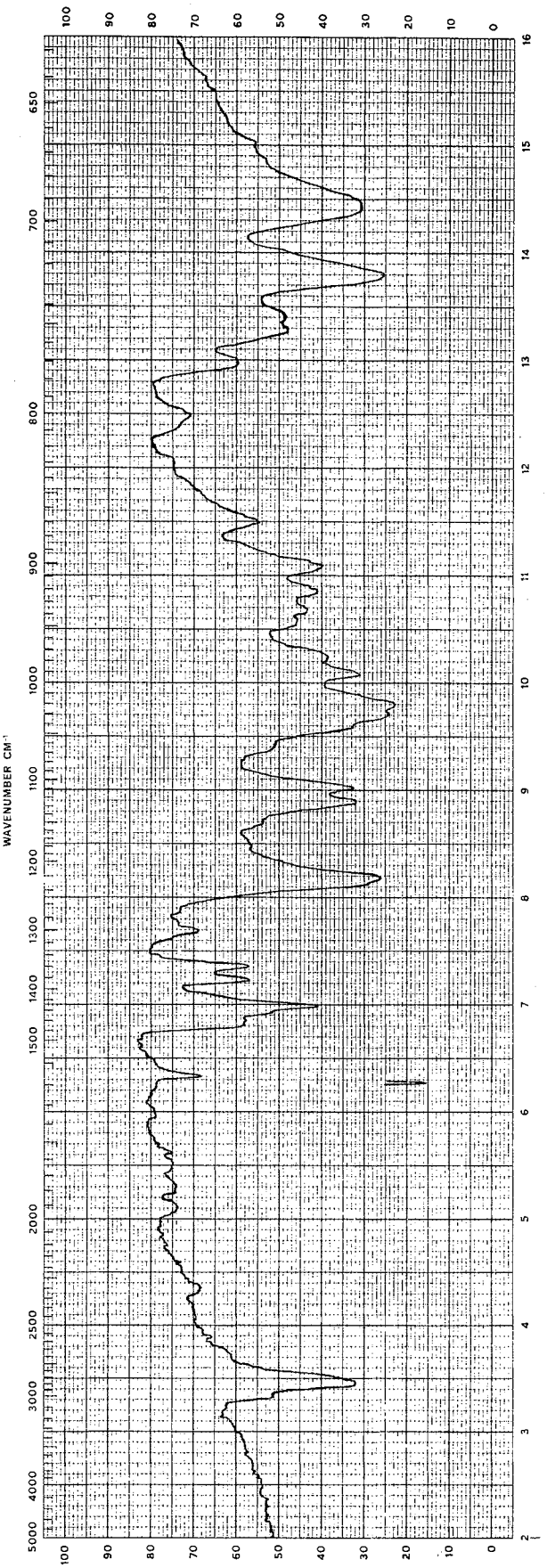
(-)-N-[α-(1-Naphthyl)ethyl]diphenylphosphinic Amide (IV), KBr Pellet

Plate IV



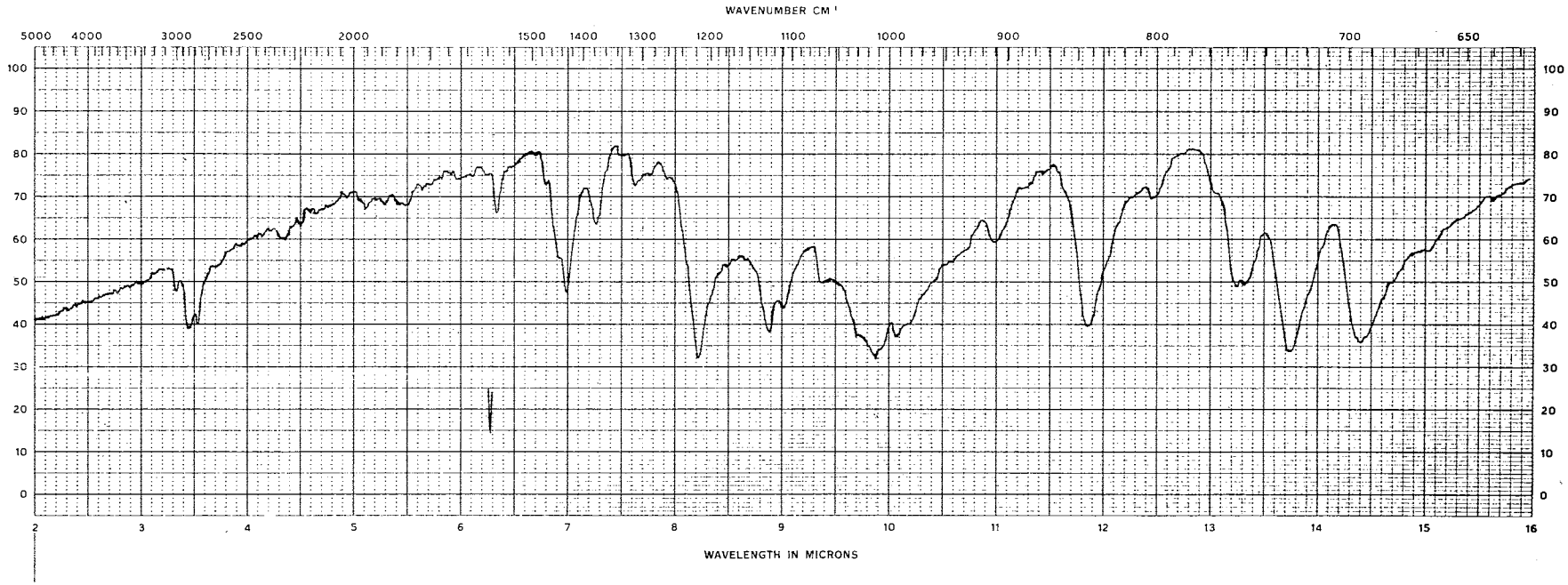
(-)-Menthyl Diphenylphosphinate (V), KBr Pellet

Plate V



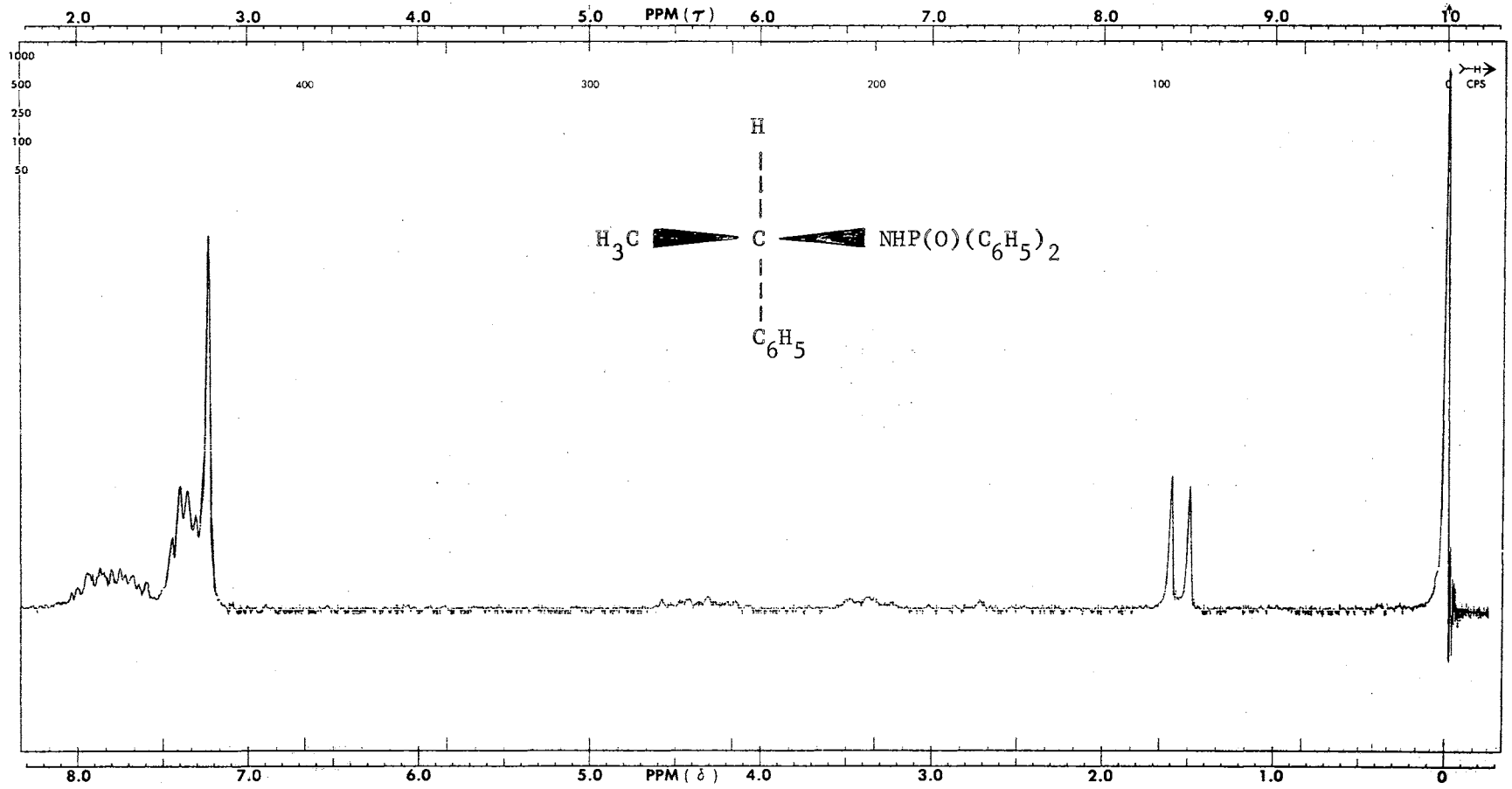
(-)-Bornyl Diphenylphosphinate (VI), KBr Pellet

Plate VI



(+)-2-Methyl-1-butyl Diphenylphosphinate (VII), KBr Pellet

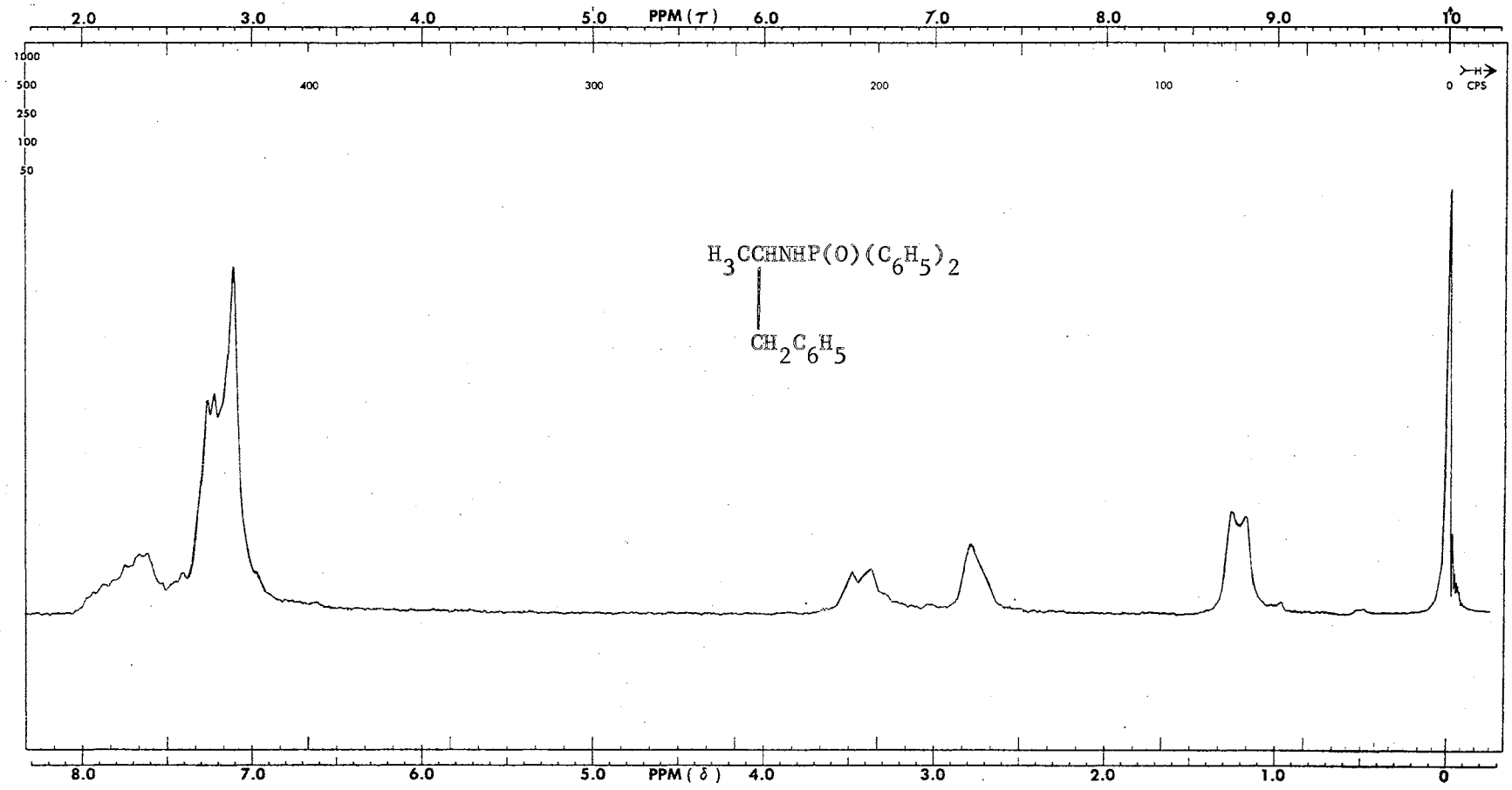
Plate VII



(+)-N-α-Methylbenzyldiphenylphosphinic Amide (II)

Solvent	$CDCl_3$	R.F.	0.05 mG	S.W.	500 cps	S.A.	8.0
F.B.	1.0 cps	S.T.	250 sec	S.O.	004 cps	I.A.	off

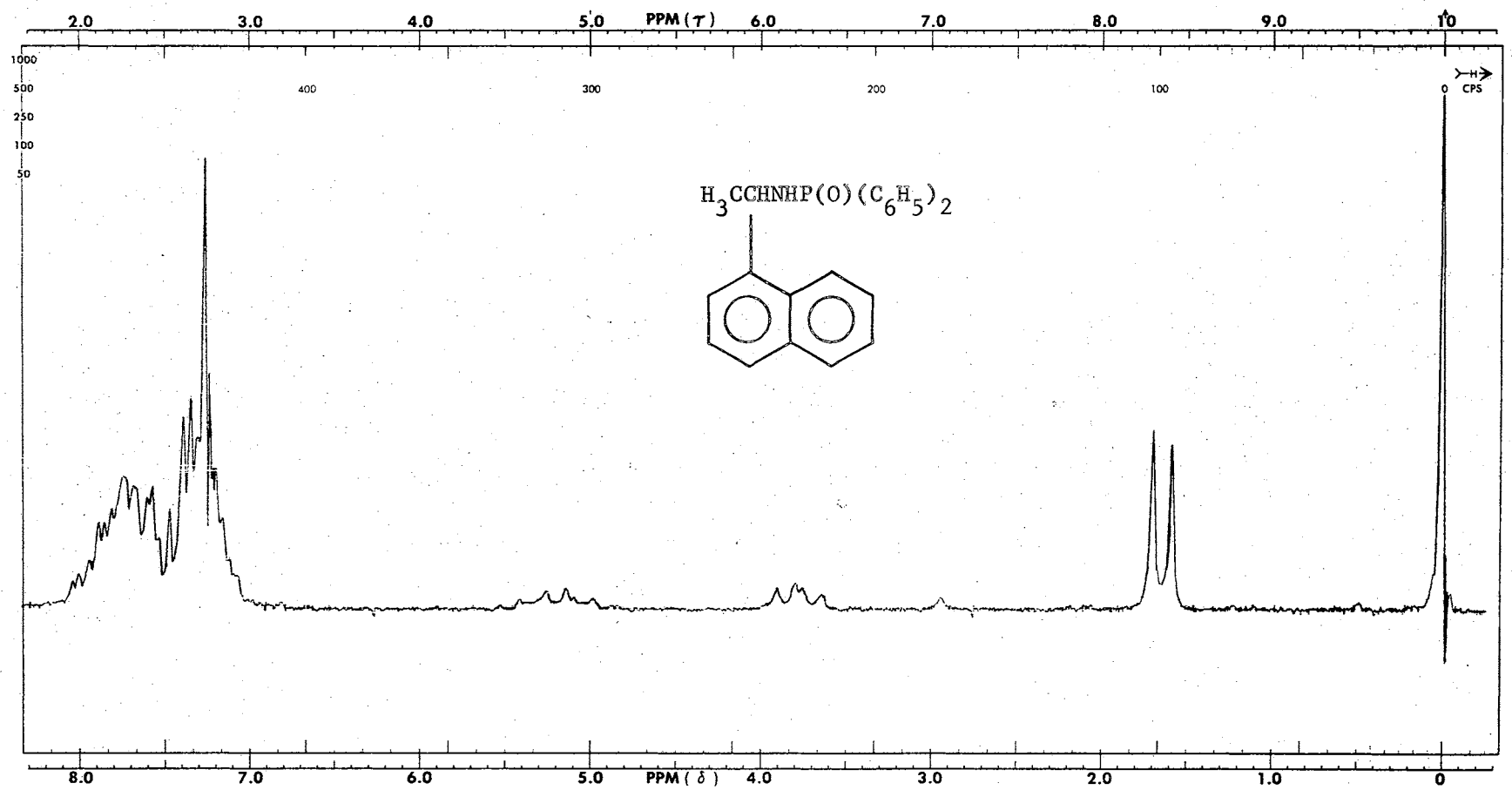
Plate VIII



(+)-N-α-Methylphenethyldiphenylphosphinic Amide (III)

Solvent . . . . . $CDCl_3$	R.F. . . . . 0.05 mG	S.W. . . . . 500 cps	S.A. 4.0
F.B. . . . . 1.0 cps	S.T. . . . . 250 sec	S.O. . . . . 000 cps	I.A. . . . . off

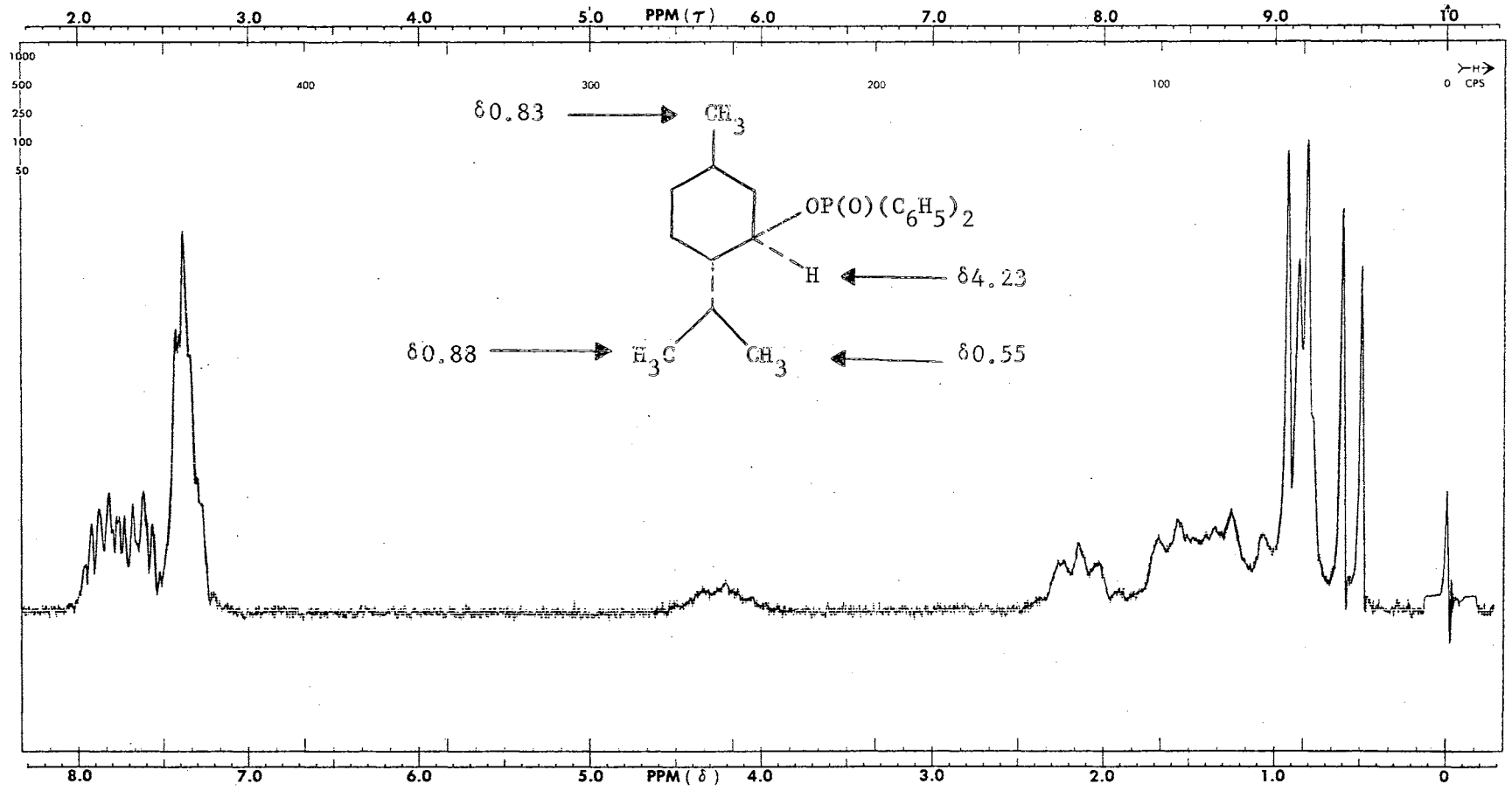
Plate IX



(-)-N-[α-(1-Naphthyl)ethyl]diphenylphosphinic Amide (IV)

Solvent	$CDCl_3$	R.F.	0.05 mG	S.W.	500 cps	S.A.	6.3
F.B.	1.0 cps	S.T.	250 sec	S.O.	001 cps	I.A.	off

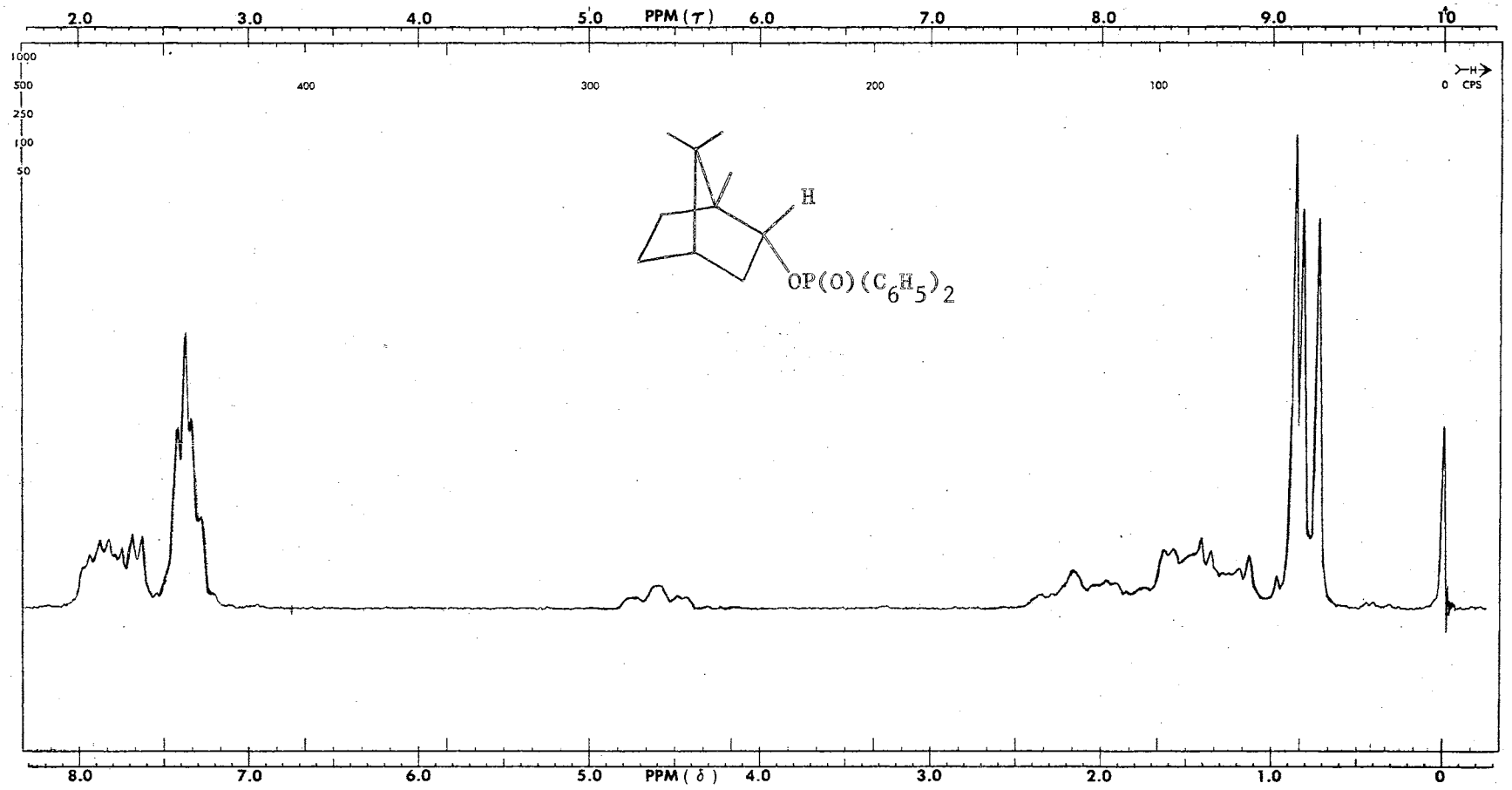
Plate X



(-)-Menthyl Diphenylphosphinate (V)

Solvent . . . . . $CDCl_3$	R.F. . . . . 0.05 mG	S.W. . . . . 500 cps	S.A. 10.0
F.B. . . . . 2.0 cps	S.T. . . . . 250 sec	S.O. . . . . 000 cps	I.A. . . . . off

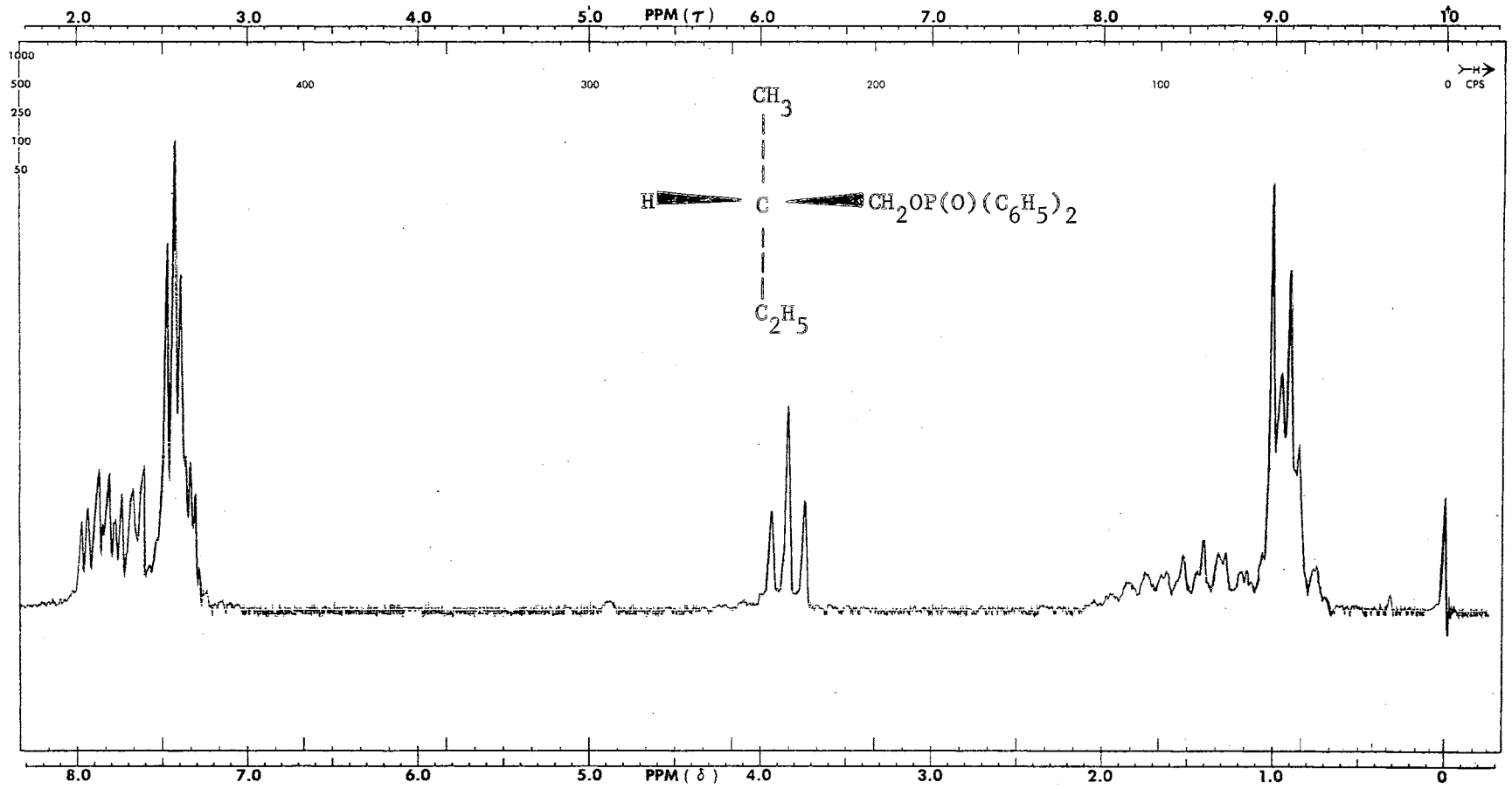
Plate XI



(-)-Bornyl Diphenylphosphinate (VI)

Solvent . . . . . $CDCl_3$	R.F. . . . . 0.05 mG	S.W. . . . . 500 cps	S.A. 4.0
F.B. . . . . 1.0 cps	S.T. . . . . 250 sec	S.O. . . . . 000 cps	I.A. . . . . off

Plate XII



(+)-2-Methyl-1-butyl Diphenylphosphinate (VII)

Solvent . . . . . $CDCl_3$	R.F. . . . . 0.05 mG	S.W. . . . . 500 cps	S.A. 10.0
F.B. . . . . 1.0 cps	S.T. . . . . 250 sec	S.O. . . . . 002 cps	I.A. . . . . .off

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VITA

Donald Howard Burpo

Candidate for the Degree of

Doctor of Philosophy

Thesis: I. REACTIONS OF ORTHO-SUBSTITUTED AROYL CHLORIDES WITH TRIALKYL PHOSPHITES
II. SOME SYNTHESES OF OPTICALLY ACTIVE PHOSPHORUS COMPOUNDS

Major Field: Organic Chemistry

Biographical:

Personal Data: The author was born in Cushing, Oklahoma, on December 17, 1941, the son of Loyd V. and Ruby Burpo.

Education: The author attended the Ponca City Public School System and graduated from Ponca Senior High School in Ponca City, Oklahoma, in 1959. He received the Bachelor of Science degree from Bethany Nazarene College, Bethany, Oklahoma, in 1963. He received a Master of Science degree from Oklahoma State University, Stillwater, Oklahoma, in 1965. At Oklahoma State University he completed the requirements for the Doctor of Philosophy degree in May, 1968.

Professional Experience: The author worked in the chemical divisons of Continental Oil Company and of Halliburton Company during the summers of 1963 and 1964, respectively. He served as a graduate teaching assistant during 1963-1964 and during 1967-1968. He also served as a graduate research assistant from September, 1964, to May, 1967.

Membership in Professional Societies: The author is a member of Phi Lambda Upsilon.