THE SYNTHESES AND SPECTRAL PROPERTIES OF DIETHYL α-AMINOALKYLPHOSPHONATES, DIETHYL α-AMINOALKYL-PHOSPHONATE HYDROCHLORIDES AND α-AMINOALKYL-PHOSPHONIC ACIDS. THE ALUMINUM-AMALGAM REDUCTION AND SPECTRAL PROPERTIES OF OXIMES OF DIETHYL ACYLPHOSPHONATES

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to my wife

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INTRODUCTION

The α-aminoalkylphosphonic acids and their corresponding dialkyl esters are not well documented in chemical literature even though they show an analogous structure to α-amino acids. This situation has existed largely because good synthetic methods from readily available materials have not been developed for the phosphorus analogs. It is the purpose of the present study to develop a direct synthetic route to these useful and intriguing compounds.

The present methods for the preparation of dialkyl α-aminoalkylphosphonates have certain inherent limitations. Among these limitations are low yields, by-products which are difficult to separate, by-products which are highly colored, starting materials which are difficult or impossible to obtain and synthetic procedures which cleave the alkoxy linkages and thus render the preparation of the dialkyl α-aminoalkylphosphonates impossible.

Infrared (IR) and nuclear magnetic resonance (NMR) spectral data are essentially unknown for diethyl α-aminoalkylphosphonates and α-aminoalkylphosphonic acids. Consequently, an objective of the present study is to establish the structures for all dialkyl α-aminophosphonates prepared. In addition it seems possible to correlate IR and NMR data so as to provide useful diagnostic information regarding the identification of members of these families of organophosphorus compounds.

CHAPTER I

HISTORICAL

Occurrence and Biochemical Properties of Naturally Occurring Aminoalkylphosphonic Acids

α-Aminoalkylphosphonic acids are interesting compounds chiefly because they are like α-aminocarboxylic acids in structure and, consequently, in potential biological activity. Although no α-aminoalkylphosphonic acids have yet been found in living organisms, they have been found to possess biological activity.

Ryzhkov and coworkers[75] have found that at very high concentrations these compounds are toxic. α-Amino-β-phenylethylphosphonic acid was found to kill chicken embryos, to retard the development of silkworms, to retard the propagation of tobacco mosaic virus and to repress the growth of tobacco rootlets. These workers further found through similar studies with a series of compounds having the structure $RR'C(NH_2)$-$P(O)(OH)_2$ (where R=R'=H; R=R'=CH_3; R=H, R'=isopropyl; R=H, R'=isobutyl; R=H, R'=isoamyl; and R=H, R'=phenyl) that these compounds are not true biological analogs of α-aminocarboxylic acids. That the α-aminoalkylphosphonic acids do not compete with amino acids in metabolism was established through nutrition studies with silkworms; no phosphorus was found to be incorporated in the silk produced. Liver, kidney and plant tissues failed to transform the C-P linked phosphorus into inorganic phosphate. Staib[78] has investigated the inotropic effects of

aminomethylphosphonic acid and some of its derivatives (acetyl,benzoyl, nicotinoyl, p-methoxybenzoyl, o-chlorobenzoyl, and p-chlorobenzoyl) on the hypodynamic frog heart. He found these compounds were without influence on hypodynamia caused either by aconitine nitrate or by reduced calcium content of the perfusion liquid.

Compounds containing a C-P bond are rarely found in nature. While no α-aminoalkylphosphonic acids have been found in living tissues, a related compound, 2-aminoethylphosphonic acid, may have wide distribution in nature. This compound occurs in protozoa, in coelenterata of several phyla, in some fresh-water mollusks, in bovine brain and in goat liver. It has not yet been demonstrated whether the 2-aminoethylphosphonic acid found in the two ruminants mentioned is a natural constituent of these animals or is a product of rumen protozoa. It is not known whether or not compounds containing C-P linkages exist in the plant kingdom. In 1964, Kittredge and Hughes[47] found a compound related to 1-amino-2-phosphonopropionic acid in Tetrahymena and a zoanthid. Also in 1964 Hori and coworkers[36] isolated a sphingolipid containing 2-aminoethylphosphonic acid from shellfish.

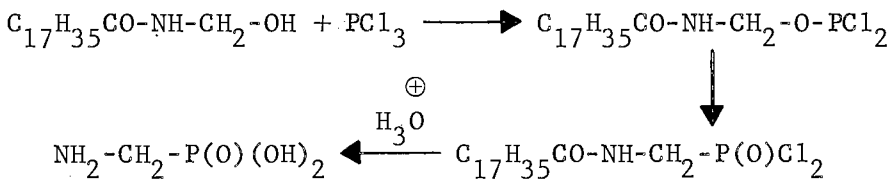
The existence in nature of compounds possessing a C-P bond has only recently been discovered. The questions of the method of biosynthesis of the carbon-phosphorus bond, and of why nature has included compounds of this type in living systems, remain to be answered.

Syntheses of α-Aminoalkylphosphonic Acids and Dialkyl α-Aminoalkylphosphonates

A number of methods for the preparation of α-aminoalkylphosphonic acids have been reported. Each of these methods, however, has certain

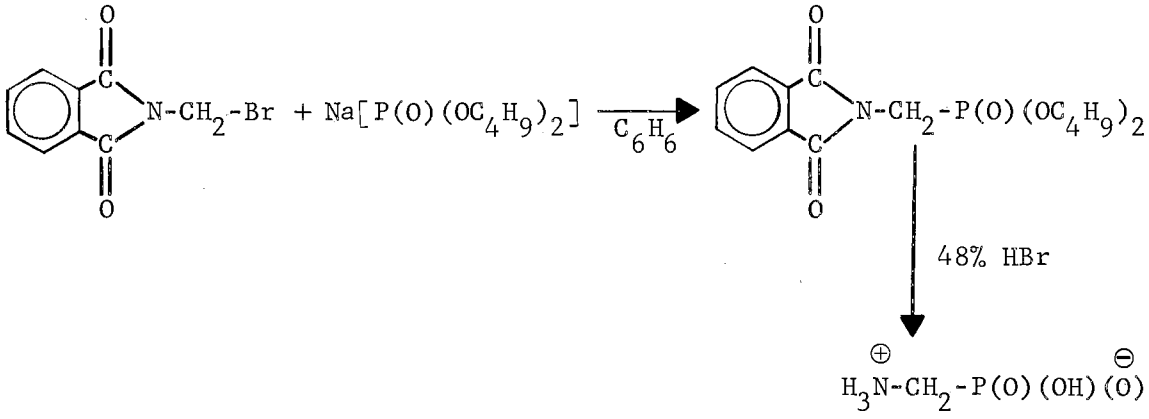
intrinsic limitations.

Engelmann and Pikl[28,68] were the first to synthesize an α-aminoalkylphosphonic acid. They prepared aminomethylphosphonic acid from hydroxymethyl derivatives of stearamide.



This synthesis involves prolonged reaction times (12 hours to 7 days are necessary to complete the reaction). Also it seems to be limited to the preparation of amino derivatives of methylphosphonic acid.

During the early 1940's, V. Chavane began a study of aminoalkylphosphonic acids in which he synthesized a number of amino acid analogs, including those of glycine, β-alanine, and aspartic acid. His work, however was not made known until it was published posthumously (in 1947-1949).[19-21] He has prepared aminomethylphosphonic acid from N-bromomethylphthalimide and sodium dibutyl phosphite with subsequent hydrolysis of the phthalimide derivative with hydrobromic acid.



The yield of aminomethylphosphonic acid was 35-40%. This author found values of ionization constants as follows: $pK_1[(H_3\overset{\oplus}{N}\text{-}CH_2\text{-}P(O)(OH_2)) \rightleftarrows H_3\overset{\oplus}{N}\text{-}CH_2\text{-}P(O)(\overset{\ominus}{O})(OH) + H)] = 1.85$; $pK_2[(H_3\overset{\oplus}{N}\text{-}CH_2\text{-}PO_3H \rightleftarrows H_3\overset{\oplus}{N}\text{-}CH_2\text{-}P(O)(\overset{\ominus}{O})_2 +$

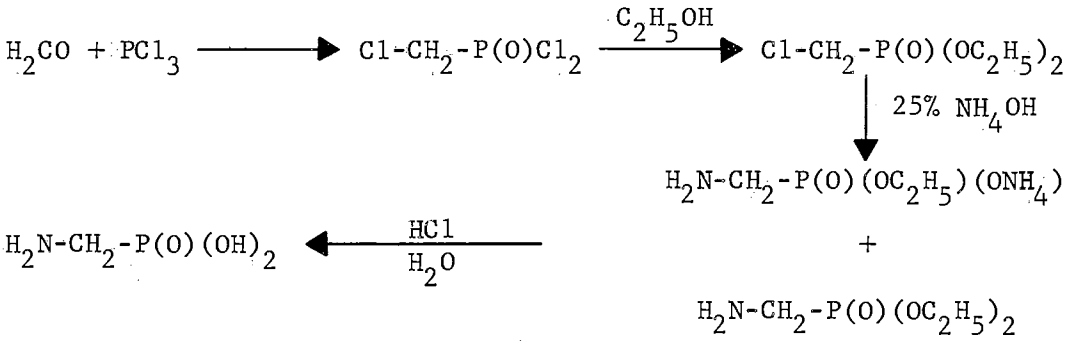
$\overset{\oplus}{H})] = 5.35$; and $pK_3[(\overset{\oplus}{H_3}N\text{-}CH_2\text{-}P(O)(\overset{\ominus}{O})_2 \rightleftarrows H_2N\text{-}CH_2\text{-}P(O)(\overset{\ominus}{O})_2 + \overset{\oplus}{H})] = 10.0$. The constant K_3 was shown to be due to the ammonium ionization by a titration in the presence of HCHO. These ionization constants in comparison to constants of related compounds indicated α-aminomethylphosphonic acid to exist as a zwitterion. Chavane also prepared a series of aminoalkylphosphonic acids, $H_2N\text{-}(CH_2)_n\text{-}P(O)(OH)_2$ (where n = 2, 4, 5, 10), from the phthalimide derivative. Chavane's method depends on the availability of the various phthalimide derivatives. Inasmuch as N-vinylphthalimide is readily available it may be possible to prepare dialkyl 1-aminoethylphosphonates through addition of sodium dialkyl phosphites as well as 1-aminomethylphosphonic acid. Aside from the preparation of these two α-aminophosphonic acids Chavane's method is not general.

Kosolapoff has obtained α-aminoalkylphosphonic acids by several methods. In 1947[50] he reported the preparation of 1-amino-1-phenylethylphosphonic acid through ammonolysis of 1-chloro-1-phenylethylphosphonic acid. The reaction time was two weeks and resulted in a 12% yield. At the same time he prepared α-aminobenzylphosphonic acid[50] by reducing diethyl benzoylphosphonate p-nitrophenylhydrazone with hydrogen in the presence of 2% palladium-charcoal catalyst. Hydrolysis of the diethyl α-aminobenzylphosphonate with concentrated hydrochloric acid provided the crude α-aminobenzylphosphonic acid (68% yield). However, the product was contaminated with the aniline salt and no method was found for purification. In 1948 Kosolapoff[51] reduced diethyl benzoylphosphonate p-nitrophenylhydrazone with aluminum-amalgam. He did not attempt to isolate the diethyl α-aminobenzylphosphonate but hydrolyzed the product of reduction directly to the acid with hydrochloric acid. A 43% yield (based upon diethyl benzoylphosphonate) of the acid was realized. The

aromatic amines produced in the reduction were oxidized to colored materials and caused difficulty in obtaining a pure, colorless product.

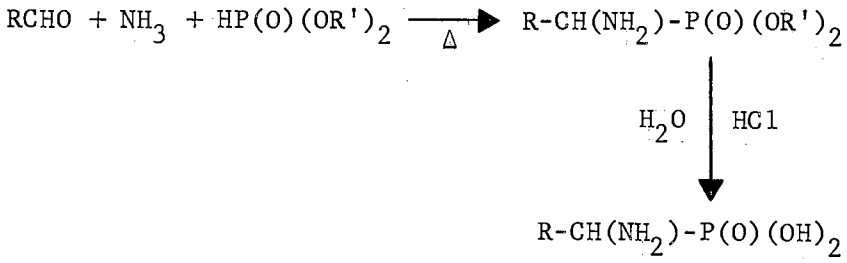
Schiffner and Langes[76] have reported the preparation of diammonium aminomethylphosphonate by heating chloromethylphosphonic acid with urea at 130°.

In the early 1950's Kabachnik and Medved published several methods for preparing α-aminoalkylphosphonic acids and the corresponding esters.[39-42] These workers prepared aminomethylphosphonic acid from diethyl chloromethylphosphonate by heating it with 25% aqueous ammonia in a sealed tube at 150° for 2 hr.[41] Hydrolysis with hydrochloric acid



provided the acid. Considerable difficulty was encountered in separating the aminomethylphosphonic acid from the reaction mixture. The yields ranged from 3.2 to 23.5% (based on diethyl chloromethylphosphonate).

In 1953[41] Kabachnik and Medved reported a general method for preparing α-aminoalkylphosphonic acids from ammonia, an aldehyde and a dialkyl hydrogenphosphonate. This Strecker-like approach to



α-aminoalkylphosphonic acids employed such starting materials as benzaldehyde, p-tolualdehyde, p-isopropylbenzaldehyde, p-anisaldehyde, piperonal and vanillin. Diethyl and dibutyl hydrogenphosphonates were employed. The reaction was carried out by heating equimolar amounts of an aldehyde and a dialkyl hydrogenphosphonate with a small excess of a 10% alcoholic solution of ammonia in a sealed tube in a water bath. The amino esters were isolated as the hydrochlorides or picrates. Hydrolysis with hydrochloric acid provided the α-aminoalkylphosphonic acids. Overall yields of 6.5 to 43% (based on the aldehyde) was achieved. It was found that the half ammonium salt-half alkyl esters of α-aminoalkylphosphonic acids were preferentially formed if the temperature was raised to 130-140°. At room temperature an insignificant amount of a dialkyl α-aminoalkylphosphonate formed while the chief product was a dialkyl α-hydroxyalkylphosphonate.

In light of some work by Abramov[1] (the reaction of aldehydes with dialkyl hydrogenphosphonates in the presence of catalytic amounts of sodium alkoxides, gives, in high yield, dialkyl α-hydroxyalkylphosphonates), Kabachnik and Medved proposed a mechanism for their synthetic procedure for dialkyl α-aminoalkylphosphonates in which the dialkyl α-hydroxyalkylphosphonate occurs as an intermediate. They reported the preparation (in low yields) of dialkyl α-aminoalkylphosphonates from a reaction of ammonia with dialkyl α-hydroxyalkylphosphonates. Fields[29] studied the reaction of amines with aldehydes and dialkyl hydrogenphosphonates and reported that dialkyl α-hydroxylalkylphosphonates do not react with amines at or below 56° and that at 175° the mixture gave a dark resinous mass in which the odor of phosphine was evident.

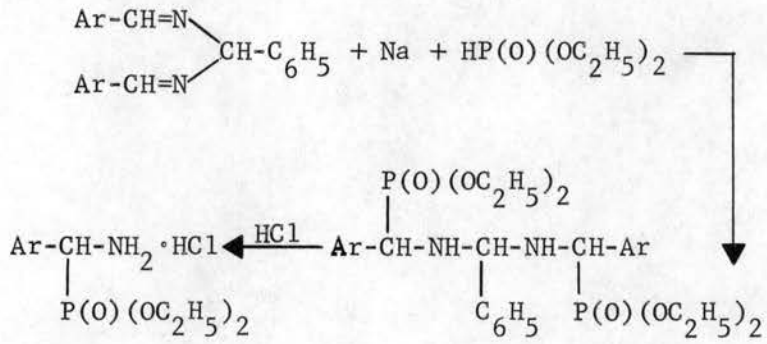
Kabachnik and Medved[38] have also reported the similar synthesis of α-aminoalkylphosphonic acids and dialkyl esters using ketones with ammonia and a dialkyl hydrogenphosphonates and realized overall yields of 12 to 43%. The ketones used and the yields of the corresponding acids were as follows: acetone (43%), butanone (20%), 2-pentanone (18%), 4-heptanone (less than 33%), cyclohexanone (17%), acetophenone (27%) and benzophenone (12%).

In 1953 Chalmers and Kosolapoff[17] repeated the synthesis of α-aminoalkylphosphonic acids from aldehydes by Kabachnik and Medved.[39] They were able to improve the yields somewhat by premixing the aldehyde and ammonia (anhydrous) in alcohol. Chalmers and Kosolapoff prepared α-aminobenzylphosphonic acid (20%), 1-aminopropylphosphonic acid (41%), 1-aminoethylphosphonic acid (31%), α-amino-p-methoxybenzylphosphonic acid (29%), α-amino-p-hydroxybenzylphosphonic acid (24%), α-amino-o-hydroxybenzylphosphonic acid (22%) and 1-amino-2-phenylethylphosphonic acid (26%).

Several problems appear when the method of Kabachnik and Medved is used for the preparation of α-aminoalkylphosphonic acids and esters. There is a dependence upon the availability of the necessary aldehydes and ketones which may be difficult to obtain. The separation of the dialkyl α-aminoalkylphosphonates from the dialkyl α-hydroxyalkylphosphonates and the half-ammonium salts of both types of compounds is difficult. The α-aminoalkylphosphonic acids, likewise, must be separated from their α-hydroxy cognomers. The yields are low and the conditions of the reaction must be maintained within certain limits to facilitate the formation of desired products.

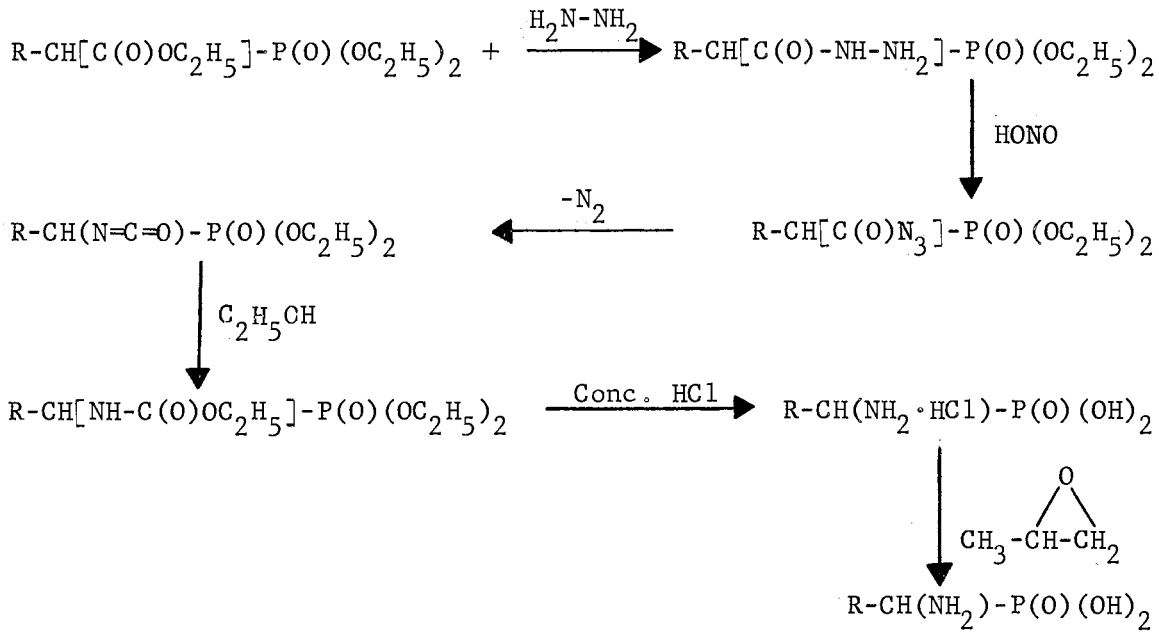
In 1959 Kreutzkamp and Cordes[52] reported the synthesis of diethyl

α-aminobenzylphosphonate hydrochloride and diethyl α-aminobenzylphosphonate hydrochloride and diethyl α-amino-p-methoxybenzylphosphonate hydrochloride and the subsequent acid hydrolysis to the respective α-aminoalkylphosphonic acids. These workers achieved an overall yield



(based on the diimine) of 46% for α-aminobenzylphosphonic acid and 66% for α-amino-p-methoxybenzylphosphonic acid. Although the yields are an improvement over those of other methods, this method is limited to the synthesis of α-aminoalkylphosphonates and α-aminoalkylphosphonic acids from the diimines prepared from available aromatic aldehydes.

In 1962 Chambers and Isbell[18] reported the use of the Curtius reaction for the preparation of 1-aminoalkylphosphonic acids utilizing substituted diethyl phosphonoacetylhydrazides. These workers prepared three α-aminoalkylphosphonic acids via this route and reported overall yields from the α-halocarboxylate of 21% for aminomethylphosphonic acid; 66% for 1-aminoethylphosphonic acid and less than 56% for 1-amino-2-phenyl-ethylphosphonic acid. None of the intermediate compounds were isolated. This method apparently cannot be used to prepare esters of α-aminoalkylphosphonic acids inasmuch as the reaction sequence calls for boiling the urethane derivative of the dialkyl α-aminoalkylphosphonates in concentrated conc. hydrochloric acid for two days which would remove the alkyl groups of the phosphorus esters. Also, the method utilizes



α-halocarboxylates, which are not as readily available as certain other starting materials (i.e., aldehydes, ketones or acid halides).

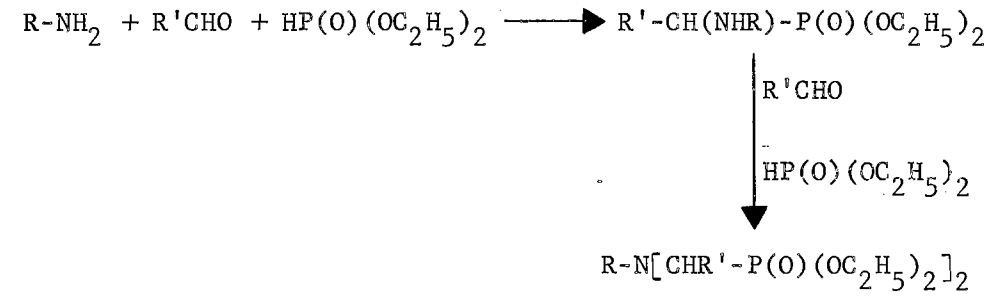
Okamoto and Sakurai,[63] in 1967, published the synthesis of long chain 1-aminoalkylphosphonic acids using the same method for preparation of these compounds as Isbell and Chambers.[18]

Syntheses of N-Substituted α-Aminoalkylphosphonic Acids and N-Substituted Dialkyl α-Aminoalkylphosphonates

While the primary groups of compounds with which this thesis is concerned, are the diethyl acylphosphonate oximes, the diethyl α-aminoalkylphosphonates and the α-aminoalkylphosphonic acids, it seems appropriate briefly to mention some of those compounds containing alkyl substituents of the nitrogen atom. Only the more recent and leading references will be cited.

Fields[29] has prepared a series of dialkyl N,N-dialkyl-1-aminoalkylphosphonates using a primary or a secondary amine, an aldehyde or a ketone, and a dialkyl hydrogenphosphonate. The primary amines gave much

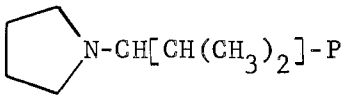
lower yields of pure products than did the secondary amines. This was believed to be due to further reaction of the primary reaction product.

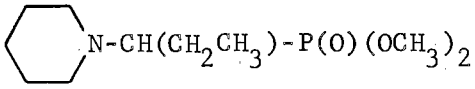


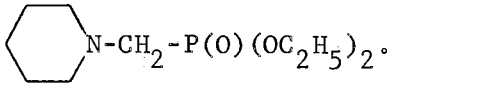
Considerable amounts of undistillable residues were obtained using primary amines.

Probably the first α-aminoalkylphosphonic acid prepared was N,N-diphenyl-1-amino-chloroethylphosphonic acid, which was reported by Claus in 1881.[22] The yield was quite low.

Schiff bases have been found to condense with dialkyl hydrogenphosphonates to give the dialkyl N-alkyl-α-aminoalkylphosphonates by Zimmer and Bercz.[84]

Opitz, Griesinger and Schubert,[64] in 1963, reported the preparation of the dialkyl α-aminoalkylphosphonates: 

$(OC_2H_5)_2$, 

and 
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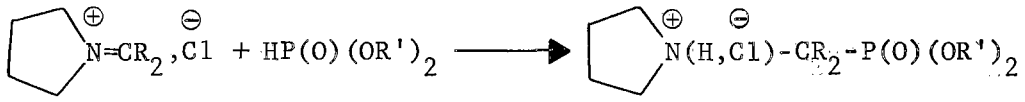
The addition of a dialkyl hydrogenphosphonate to an N-alkylidene immonium salt furnished the dialkyl α-aminoalkylphosphonate hydrochlorides.



Inner Salts of α-Aminoalkylphosphonates and α-Aminoalkylphosphonic Acids

Exhaustive methylation of 1-aminophosphonic acids and their esters was achieved by Medved and Kabachnik[55] using dimethyl sulfate in a basic solution. $(CH_3)_2C[P(O)(OH)(\overset{\ominus}{O})]\overset{\oplus}{N}(CH_3)_3 \cdot H_2O$ was obtained through methylation of 1-amino-1-methylethylphosphonic acid. Using CH_3I as the methylating agent, these individuals were able to synthesize the mono- and dimethyl derivatives.

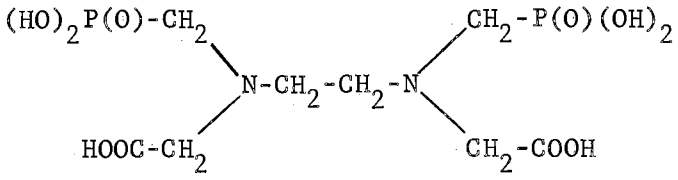
Myers and Jibril[62] made a series of N,N,N-trimethylammoniumalkylphosphonic acids, $(CH_3)_3\overset{\oplus}{N}-(CH_2)_n-P(O)(\overset{\ominus}{O})(OH)$ (where n = 1, 2 and 3), and diethyl N,N,N-trimethylammonium alkylphosphonate iodides, $(CH_3)_3\overset{\oplus}{N}-(CH_2)_n-P(O)(OC_2H_5)_2,\overset{\ominus}{I}$ (where n = 1, 2 and 3). Others[16] have prepared the similar compounds $(CH_3)_2CH-CH[\overset{\oplus}{N}(CH_3)_3]-P(O)(\overset{\ominus}{O})(OCH_3)$, $(CH_3)_2CH-CH[\overset{\oplus}{N}H_2(CH_2)_3CH_3]-P(O)(\overset{\ominus}{O})(OCH_3)$ and $(CH_3)_2CH-CH[\overset{\oplus}{N}H(CH_3)(CH_2)_3CH_3]-P(O)(\overset{\ominus}{O})(OCH_3)$.

Phosphorus Analogs of Ethylenediaminetetraacetic Acid and Other Multidentate Chelating Agents

Since the discovery of the extraordinary chelating properties of compounds containing in the molecule one or more "nitrilodiacetate" groups, $-N(CH_2-COOH)_2$, such as ethylenediaminetetraacetate acid and nitrilotriacetic acid, $N(CH_2-COOH)_3$, efforts have been made to synthesize phosphorus analogs of these compounds. Bersworth,[13] as well as Banks and Yerick,[6] prepared compounds with $-N[CH_2-P(O)(OH)_2]_2$ moieties. Moedritzer and Irani[59] have reported a preparation of a class of aminomethylphosphonic acids by a Mannich-type reaction using orthophosphorous

acid, formaldehyde (other aldehydes and ketones will also react[60]), and ammonia or amines according to $R_{3-n}NH_n + nCH_2O + nHP(O)(OH)_2 \longrightarrow R_{3-n}N[CH_2P(O)(OH)_2]_n$ where n = 1, 2 or 3. The amines employed were ammonia, primary or secondary amines, polyamines and functionally substituted amines.

Dyatlova, Kabachnik, Medved, Rudomino and Belugin[22] have investigated the phosphorylated polyamines: ethylenediamine-N,N'-bis(methylphosphonic acid), $(HO)_2P(O)-CH_2-NH-CH_2-CH_2-NH-CH_2-P(O)(OH)_2$; ethylenediamine-N,N'-bis(isopropylphosphonic acid), $(HO)_2P(O)-C(CH_3)_2-NH-CH_2-CH_2-NH-C(CH_3)_2-P(O)(OH)_2$; and ethylenediamine-N,N'-bis(methylphosphonic acid)-N,N'-bis(acetic acid). Uhlig and Achilles[82] have also prepared



ethylenediamine-N,N'-bis(methylphosphonic acid), ethylenediamine-N,N,N'-tris(methylphosphonic acid) and ethylenediamine-N,N,N',N'-tetrakis (methylphosphonic acid).

These polydentate phosphorus chelating agents have been found to form coordination compounds with a large variety of metal ions, namely, Group IIA and IIB metals, transition metals and lanthanides. Even beryllium(II) forms chelates with these complexing agents. Westerback, Rajan and Martell[83] report that ligands of the type described above may have exceptionally high affinities for metal ions possessing a +4 charge. The excellent coordinating ability of these complex-forming compounds seems to stem from the increased dentation, the unique stereochemistry, and the bond strengths of the P-O-M linkage. The stability constants for a variety of the phosphorus ligands and various metals

have been determined[27,83] by both potentiometric titration and polarographic methods. Large differences exist between the values for the stability constants of the organophosphorus chelating agents and for their "nitriloacetic" acid analogs. The phosphorus compounds were found to form appreciably stronger chelates with a variety of metal ions.

Synthesis of Dialkyl α-Aminoalkylphosphonothioates

Reaction of $(RO)_2P(S)H$ with carbonyl compounds in the presence of ammonia gives dialkyl α-aminoalkylphosphonothioates.[42] Hydrolysis of $(CH_3)_2\ C(NH_2)\text{-}P(S)(OC_2H_5)_2$ with 1:1 hydrochloric acid in a sealed tube gave $(CH_3)_2C(NH_2)\text{-}P(O)(OH)_2$. Kabachnik and coworkers[42] prepared $(CH_3)_2\ C(NH_2)\text{-}P(S)(OC_2H_5)_2$, $(CH_3)_2C(NH_2)\text{-}P(S)[(OCH(CH_3)_2)]_2$, $(CH_3)_2C(NH_2)\text{-}P(S)(OCH_2CH_2CH_2CH_3)_2$, $CH_3(CH_2)_3C\text{-}(CH_3)(NH_2)\text{-}P(S)(OC_2H_5)_2$, $CH_3(CH_2)_3\text{-}C(CH_3)(NH_2)\text{-}P(S)[(O\text{-}CH(CH_3)_2)]_2$, $C_6H_5\text{-}CH[(NH_2\cdot HOC_6H_2(NO_2)_3\text{-}2,4,6)]\text{-}P(S)(OC_2H_5)_2$ and $C_6H_5\text{-}C(CH_3)[(NH_2\cdot HOC_6H_5(NO_2)_3\text{-}2,4,6)]\text{-}P(S)(OC_2H_5)_2$. Pudovik[71,73] prepared dialkyl N-aryl-α-aminoalkylphosphonothioates by reaction of aromatic imines with $(RO)_2P(S)H$.

Some Reactions of α-Aminoalkylphosphonic Acids and Dialkyl α-Aminoalkylphosphonates

The amino group on α-aminoalkylphosphonic acids and dialkyl α-aminoalkylphosphonates undergoes many of the reactions of simple amines. For example, salts from hydrobromic, hydrochloric, or picric acid are easily formed with dialkyl α-aminoalkylphosphonates.

Medved and Kabachnik[54] prepared the N-acetyl and N-benzoyl derivatives of diethyl α-aminoalkylphosphonates, α-aminoalkylphosphonic acids and dialkyl α-aminoalkylphosphonothioates with acetic anhydride and

benzoyl chloride. It was observed that tosyl chloride reacts similarly with the amino compounds. Staib[78] has also prepared N-aryl and N-aroyl derivatives of aminomethylphosphonic acid.

Pudovik, Gozman, and Nikitina[72] passed excess ketene into a benzene solution of $(CH_3)_2$-C(NH_2)-P(O)(OC_2H_5)$_2$ in the presence of water and were able to isolate CH_3-C(O)NH-C(CH_3)$_2$-P(O)(OC_2H_5)$_2$. Other α-aminoalkylphosphonates were also acetylated by ketene.

Diethyl α-aminoalkylphosphonates have been found by Kabachnik and Medved[38] to form ureas through reaction with phenyl isocyanate and thioureas through reaction with phenyl isothiocyanate. The dialkyl α-aminophosphonothioates, NH_2-CR_2-P(S)(OR')$_2$, reacted with the same reagents to form the analogous sulfur compounds.

Kabachnik and Medved[57] have added phosgene to diethyl 1-amino-1-methylethylphosphonate and were able to isolate the isocyanate, which is only slowly decomposed by water. Similarly prepared was $(C_2H_5O)_2$P(S)-C(CH_3)$_2$N=C=O which is rapidly decomposed with water. Ammonia reacted with these isocyanates to give the corresponding ureas. Dialkyl α-aminoalkylphosphonates were found to give thioureas through reaction of the amines with CS_2. The isocyanates reacted with alcohols as expected to give the corresponding urethanes. Medved and Kabachnik[56] also synthesized urethanes by adding CH_3O-C(O)Cl to dialkyl α-aminoalkylphosphonates and dialkyl α-aminoalkylphosphonothioates in benzene-pyridine solutions.

Reduction of Oximes to Amines

A variety of reagents has been found to reduce oximes to amines. An excellent review of these reduction methods and their references

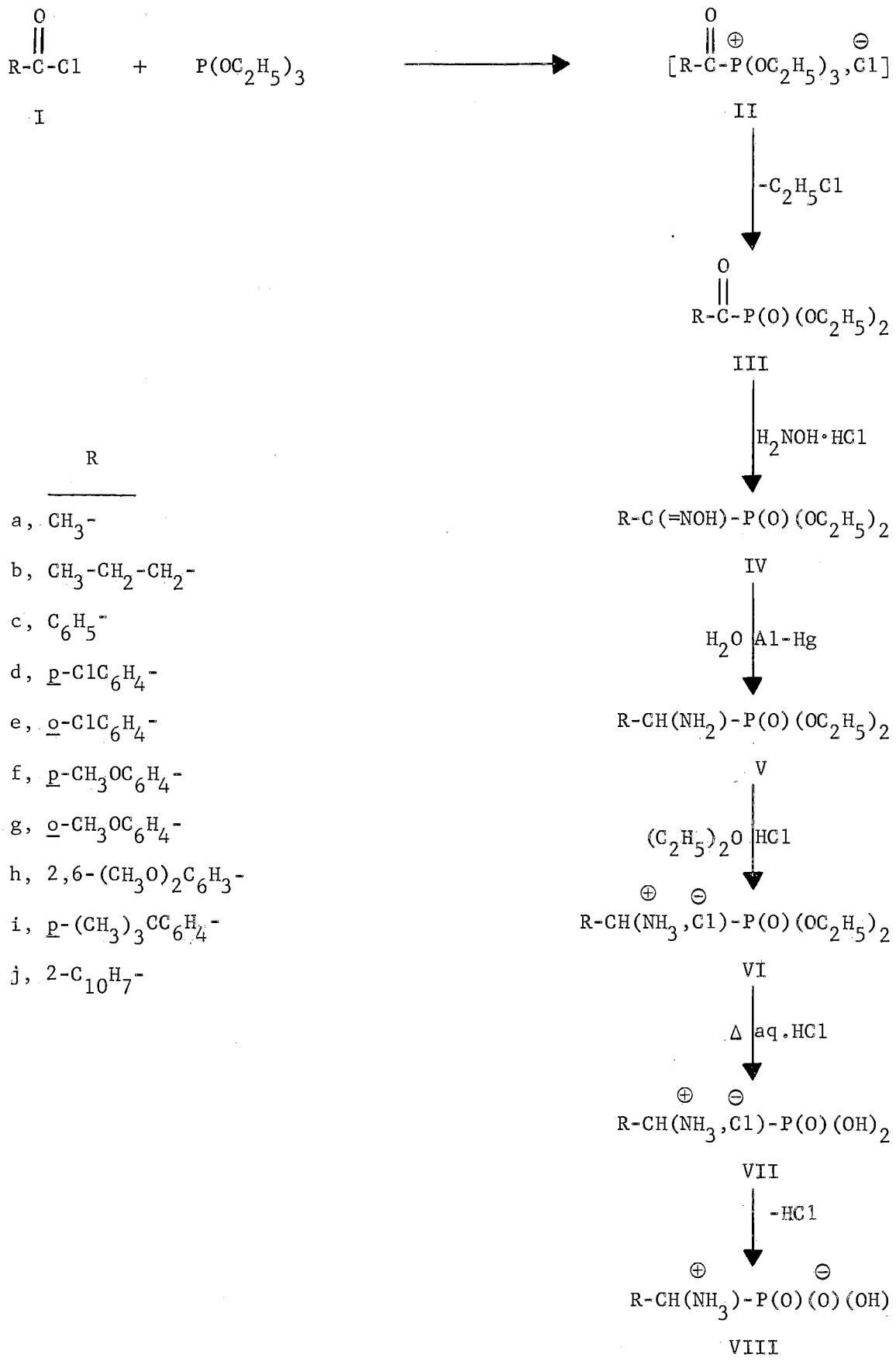
through 1956 has been provided by Muller.[61] Oximes have been reduced by zinc in acid or alkali,[34] diborane,[15] sodium in liquid ammonia,[80] lithium aluminum hydride,[61] aluminum-amalgam,[61] tin or stannous chloride[61] in hydrochloric acid, hydrogen with metal catalysts,[61] sodium amalgam in acid solution[61] and sodium in various alcohols.[61] Electrolytic reduction of oximes to amines has also been reported.[30]

CHAPTER II

DISCUSSION AND RESULTS

A new family of compounds, the oximes of dialkyl acylphosphonates, has been synthesized. New methods are reported for the syntheses of α-aminoalkylphosphonic acids, diethyl α-aminoalkylphosphonates, and diethyl α-aminoalkylphosphonate hydrochlorides in good yields by aluminum-amalgam reduction of diethyl acylphosphonate oximes. IR and NMR spectra of diethyl acylphosphonate oximes, diethyl α-aminoalkylphosphonates, diethyl α-aminoalkylphosphonate hydrochlorides and α-aminoalkylphosphonic acids were studied for the first time. Unique intramolecularly hydrogen-bonded structures, as indicated by the IR spectra, were found to exist in the oximes of diethyl acylphosphonates and the diethyl α-aminoalkylphosphonate hydrochlorides. NMR analyses of the diethyl α-aminoalkylphosphonate hydrochlorides and the diethyl α-aminoalkylphosphonates indicated the existence of magnetically nonequivalent alkoxy groups as expected from the presence of an asymmetric center.

This present synthetic route began with acid halides I and led to diethyl acylphosphonates III, diethyl acylphosphonate oximes IV, diethyl α-aminoalkylphosphonates V, diethyl α-aminoalkylphosphonate hydrochlorides VI and diethyl α-aminoalkylphosphonates V, diethyl α-aminoalkylphosphonate hydrochlorides VI and α-aminoalkylphosphonic acids VIII. With the exceptions of the quasiphosphonium salts II and the α-aminoalkylphosphonic acid hydrochlorides VII, members of each family of



R

a, CH_3-

b, CH_3-CH_2-CH_2-

c, C_6H_5-

d, p-ClC_6H_4-

e, o-ClC_6H_4-

f, p-$CH_3OC_6H_4$-

g, o-$CH_3OC_6H_4$-

h, 2,6-$(CH_3O)_2C_6H_3$-

i, p-$(CH_3)_3CC_6H_4$-

j, 2-$C_{10}H_7$-

in the sequence have been isolated and characterized. From the diethyl acylphosphonates III, the free acids VIII were prepared in good yields (45-71%) when the intermediates were isolated. In an experiment in which α-amino-p-chlorobenzylphosphonic acid (VIIId) was prepared directly from diethyl p-chlorobenzoylphosphonate (IIId), an overall yield of 66.5% was obtained for VIIId.

Diethyl Acylphosphonates III

The diethyl acylphosphonates III were prepared from triethyl phosphite and acid chlorides I utilizing the classical Michaelis-Arbuzov rearrangement as described by Berlin and others.[19-21] The reaction mechanism is not fully understood.[33] It apparently involves an initial nucleophilic displacement of chloride by the electron pair on phosphorus, resulting in the formation of an intermediate quasiphosphonium salt II. The quasiphosphonium salt, whose existence has not been confirmed for those having an acyl function, seem to rapidly decompose giving chloroethane and a diethyl acylphosphonate.

The IR spectral data for the diethyl acylphosphonates III listed in Table I (Plates I-X are reductions of the actual spectra obtained) correlate well with data described elsewhere. Two general reviews covering the IR analysis of organophosphorus compounds have appeared recently.[24,70] The IR spectra of dialkyl acylphosphonates III have been discussed by Berlin and coworkers.[11,12]

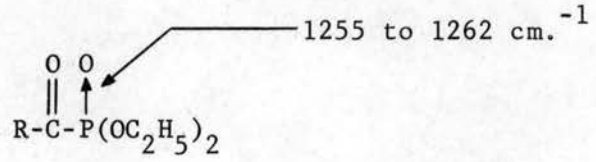
The phosphoryl frequency in organophosphorus compounds is influenced by the total electronegativity of the substituents on the phosphorus atom.[70] As the total electronegativity of the substituent groups increases, the phosphoryl linkage becomes stronger and absorption occurs

at a shorter wavelength.[23]

Normally, when the P→O group is incorporated in a phosphorus ester, it absorbs in the range 1250-1300 cm.$^{-1}$. However, hydrogen bonding will weaken the bond and thus shift the absorption to longer wavelengths with an attendant increase in intensity.[23] Daasch and Smith[26] noted that the maxima for the phosphoryl moiety in phosphonic and phosphinic acids differ by 50-80 cm.$^{-1}$ in the direction of lower frequencies compared with maxima found for P→O in the corresponding esters of these acids. These effects were attributed to hydrogen bonding. Shift variations for the P→O frequency as high as 45 cm.$^{-1}$ have resulted in solvents containing hydroxyl or amino groups.[70] Generally, compounds containing the P-O-C (aliphatic) linkage exhibit a strong absorption in the 970-1050 cm.$^{-1}$ region,[23] with the majority of compounds absorbing at 1030 cm.$^{-1}$. An ethoxy group bonded to phosphorus exhibits absorptions near 2900 (CH_3 asymmetric stretch),[23] 1485 (O-CH_2 deformation),[23] 1450 (CH_3 asymmetric deformation),[23] 1395 (O-CH_2 wag),[23] 1375 (CH_3 symmetric deformation)[23] and 1170-1150 cm.$^{-1}$ (CH_3 rock).[67] Berlin and Taylor[12] observed carbonyl absorptions for dialkyl aroylphosphonates in the 1639-1672 cm.$^{-1}$ region.

The IR spectral data for the diethyl acylphosphonates listed in Table I (Plates I-X) correlate well with the data just described. The diethyl aroylphosphonates show peaks in their IR spectra characteristic for conjugated carbonyl in the range 1649-1669 cm.$^{-1}$. The IR spectra for the diethyl acylphosphonates IIIa (Plate I) and IIIb (Plate II) show C=O frequencies at 1696 and 1692 cm.$^{-1}$, respectively. The carbonyl absorptions for IIIa and IIIb would be expected to be lower than the carbonyl frequency in diethyl aroylphosphonates since the former

molecules do not contain conjugation with an aromatic ring. The phosphoryl frequencies for III listed in Table I range from 1255 to 1262 $cm.^{-1}$. Methyl rocking frequencies of 1162-1168 $cm.^{-1}$ for the $P\text{-}O\text{-}CH_2$-

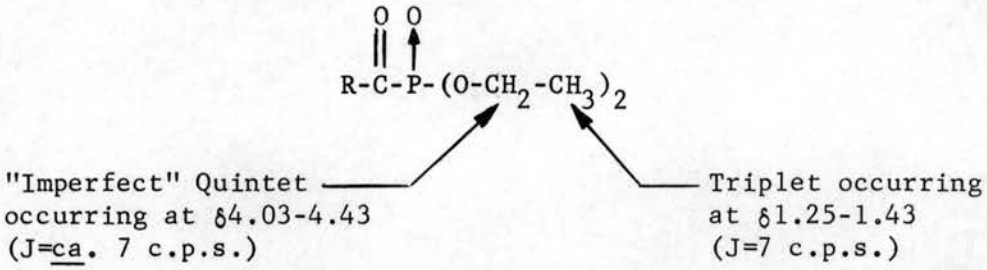


CH_3 linkage are observed for III. These CH_3 rocking absorptions are easily recognized since no other absorptions appear in the near vicinity in the spectra. Absorptions for P-O-C appear in the 1010-1050 $cm.^{-1}$ region for all of the diethyl acylphosphonates III.

The NMR spectral data for diethyl acylphosphonates III are listed in Table V. Plates XXXVI-XLV are reductions of the actual NMR spectra for IIIa-IIIj. The NMR spectral data for diethyl acylphosphonates III correlate well with that found elsewhere for similar compounds.

Gordon[31] has written an extensive review on the NMR spectra of organophosphorus compounds. Hellwege[35] has studied the NMR spectra of substituted phosphonates and has reported $J_{P\text{-}O\text{-}C\text{-}H}$ coupling constants of 1.8 to 15.5 c.p.s. and $J_{P\text{-}O\text{-}C\text{-}C\text{-}H}$ coupling constants of 1.1 c.p.s. or less for various organophosphorus compounds. Vicinal $J_{P\text{-}C\text{-}C\text{-}H}$ coupling constants of 1 to 42.3 c.p.s. have been observed while geminal $J_{P\text{-}C\text{-}H}$ constants range from 0.5 to 30.1 c.p.s.[31]

The identification of diethyl acylphosphonates III through examination of their NMR spectra is straightforward. A triplet is observed for the methyl moiety of the alkoxy group bonded to phosphorus which occurs in the region of δ1.25-1.43. A coupling constant of J=7 c.p.s. is observed for each of these triplets.

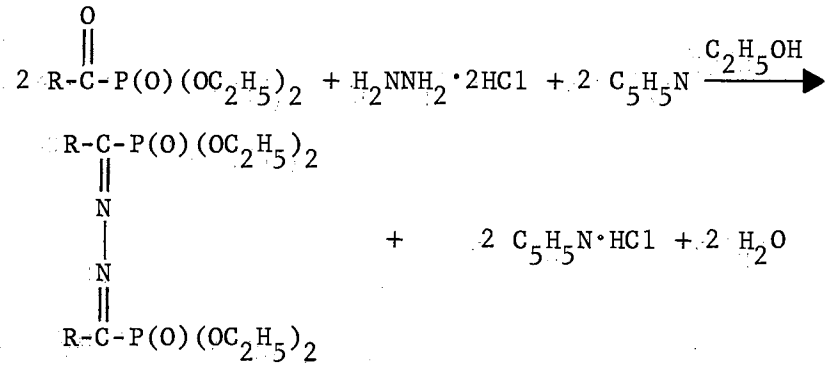


The methylene moiety of the alkoxy group appears as an imperfect quintet in the NMR spectra of III due to P^{31}-H^1 splitting in the P-O-C group. A coupling constant of J=7 c.p.s. has generally been reported for these signals.[12] However, upon more careful examination of these peaks it appears that these quintets result from two quartets whose centers are separated by about 7.5 c.p.s. The P-O-C-H splitting constant in these ethyl esters of phosphorus cannot be determined accurately until an experiment in which decoupling of the methyl protons is accomplished. Gordon[31] has listed a $J_{P\text{-}O\text{-}C\text{-}H}$ value of 7.90 c.p.s. for triethyl phosphite and values of 6.84, 8.38, and 8.4 c.p.s. for triethyl phosphate which closely approximate the 7.5 c.p.s. values observed in this study. The imperfect quintets seen in the NMR spectra for the ethyl esters of phosphorus acids often appear in 1:4:6:4:1 patterns in those cases where the value for the P^{31}-H^1 coupling constant for the P-O-C-H linkage approaches the value for the H^1-H^1 coupling constant for the H-C-C-H linkage. The NMR spectra of diethyl acetylphosphonate (IIIa, Plate XXXVI) exhibits a doublet centered at δ2.37 ($J_{P\text{-}C(O)\text{-}C\text{-}H}$ = 5 c.p.s.). This agrees with the value reported and discussed elsewhere.[35] Diethyl butyrylphosphonate (IIIb) exhibits a triplet (3H, J=7 c.p.s.) at δ0.99, a triplet (2H, J=7 c.p.s.) at δ2.96 and a multiplet (2H) at δ1.6 in addition to the usual imperfect quintet and triplet observed for the ethoxy moiety. Aromatic proton signals in the NMR spectra for III are listed in Table V and have been adequately discussed elsewhere.[12,79]

Diethyl Acylphosphonate Oximes IV

The dialkyl acylphosphonates III readily undergo condensation reactions with a variety of nucleophilic reagents. Derivatives of these esters have been prepared such as 2,4-dinitrophenylhydrazones,[11,12] p-nitrophenylhydrazones,[50] cyanohydrins[46] and phenylhydrazones.[46] 2,4,6-Trinitrophenylhydrazones have been synthesized by Arbuzov and Azanovskaya[3] and an addition compound with sodium bisulfite has been obtained by Kabachnik and coworkers.[46]

Attempts to reduce any of the phenylhydrazones have led to various aromatic amines which readily oxidize in air to colored products difficult to separate from the desired α-aminoalkylphosphonic acids or esters. Consequently the various phenylhydrazones are not desirable precursors to dialkyl α-aminoalkylphosphonates and α-aminoalkylphosphonic acids. Semicarbazones, azines and oximes have not been prepared from dialkyl acylphosphonates. The azines and oximes, since they can be prepared in good yields, are better subjects for reduction to the corresponding amines since the by-products of reduction present fewer purification problems. Preliminary experiments indicated that both the oximes and azines form in high yields with diethyl acylphosphonates. Only a few studies were conducted with the azines inasmuch as the oximes were of primary interest in this investigation.



The diethyl acylphosphonates III formed oximes in high yields through reaction with hydroxylamine hydrochloride in pyridine-ethanol solution at room temperature. The reaction was only slightly exo-

$$R\text{-}\overset{\overset{O}{\|}}{C}\text{-}P(O)(OC_2H_5)_2 + H_2NOH\cdot HCl + C_5H_5N \xrightarrow{C_2H_5OH} H_2O + C_5H_5N\cdot HCl + R\text{-}C(=NOH)\text{-}P(O)(OC_2H_5)_2$$

thermic. In the case of the diethyl aroylphosphonates the reaction could be followed by a color change (yellow to colorless) which accompanied the condensation reaction. If dialkyl acylphosphonates other than diethyl are desired the alcohol corresponding to the alkyl groups in the phosphorus ester must be used to prevent transesterification. Yields of the crude oximes are generally nearly quantitative and the crude oxime can be used directly in the aluminum-amalgam reduction. Table VII lists the oximes IV along with some of their physical properties. The oximes of the acylphosphonates were liquids. Diethyl benzoylphosphonate oxime (IVc) was also a liquid (attempted distillation of this oxime resulted in a violent decomposition; the odor of benzonitrile was noticed in the effluent gases). The substituted aroylphosphonate oximes, on the other hand, were white, crystalline solids.

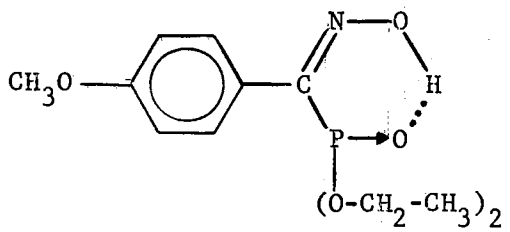
The hydroxyl proton in diethyl acetylphosphonate oxime (IVa) is acidic. A 0.01 M solution of IVa shows a pH of approximately 3.

The IR spectral data for the oximes IV are listed in Table II (Plates XI-XX). The IR frequencies found for IV correlate well with the absorptions for the same linkages in similar compounds.[23] Simple oximes in general (including aliphatic, aromatic and amide oximes) absorb broadly at 3300-3150 $cm.^{-1}$ owing to bonded O-H stretching and

near 930 cm.$^{-1}$ owing to the stretching of the N-O linkage.[23]

The oximes IV of diethyl acylphosphonates exhibited O-H stretching frequencies of 3104-3208 cm.$^{-1}$, phosphoryl absorptions at 1214-1251 cm.$^{-1}$, N-O stretching frequencies at 927-933 cm.$^{-1}$ and P-O-CH_2-CH_3 (CH_3 rock) absorptions at 1163-1171 cm.$^{-1}$. In all cases the phosphoryl absorption in the oximes IV occurred at a longer wavelength than did the phosphoryl absorption for the corresponding diethyl acylphosphonate. The differences ranged from 11 to 45 cm.$^{-1}$. No correlation of the shift of the phosphoryl absorption with the structure of the compounds was obvious.

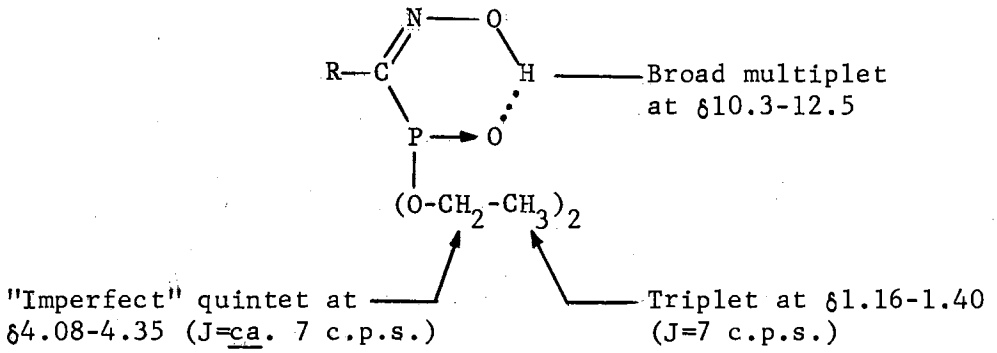
The IR spectra of diethyl p-methoxybenzoylphosphonate oxime (IVf) were obtained both in a potassium bromide pellet (Plate XVI) and in chloroform solution in order to determine whether the O-H and P→O frequencies were primarily due to intramolecular of intermolecular hydrogen bonding. The potassium bromide pellet (Plate XVI) exhibits frequencies at 3208 cm.$^{-1}$ (O-H) and 1240 cm.$^{-1}$ (P→O). A 10% solution of the oxime in chloroform shows absorptions of 3225 cm.$^{-1}$ for O-H and 1250 cm.$^{-1}$ for P→O. A 1.3% solution in chloroform shows 3195 cm.$^{-1}$ for O-H and 1250 cm.$^{-1}$ for P→O. The slight shifts of both the O-H and P→O in going from the crystalline state to a chloroform solution (as well as the dilution studies) indicates that hydrogen bonding in IVf is primarily intramolecular as shown by structure IX.



IX

Miller and coworkers[58] have studied the IR spectra of dialkyl 1-hydroxyalkylphosphonates in the crystalline state (mineral oil mull) and in carbon disulfide solution. The P→O and O-H frequencies of the crystalline dialkyl 1-hydroxyalkylphosphonates occurred in the regions 1190-1220 $cm.^{-1}$ and 3180-3250 $cm.^{-1}$, respectively. When dissolved in carbon disulfide these compounds exhibited a P→O absorptions of 1230-1232 $cm.^{-1}$ and O-H stretching frequencies of 3180-3285 $cm.^{-1}$. The low values of the frequencies found for dialkyl α-hydroxyalkylphosphonates as mulls in mineral oil and the negligible shifts from these frequencies when the compounds dissolved in carbon disulfide were ascribed by the authors to intramolecular hydrogen bonding.

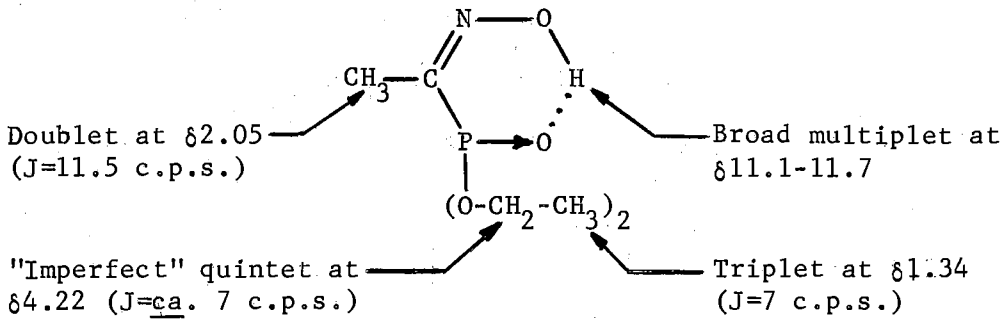
The NMR spectral data for diethyl acylphosphonate oximes IV are listed in Table V. Plates XLVI-LV are reductions of the actual NMR spectra for IVa-IVj. The NMR spectra for the oximes IV are quite similar to those for the diethyl acylphosphonates. The ethoxy groups exhibit a triplet at δ1.16-1.40 (J=7 c.p.s., CH_3) and a quintet at δ4.08-4.35 (J=ca. 7 c.p.s., CH_2).



The quintet, upon closer examination, appears to result from the overlapping of two quartets whose centers are separated by approximately 7.5 c.p.s. as similarly found for the dialkyl acylphosphonates (page 21). These quartets closely resemble the corresponding pattern

observed for these methylene protons in diethyl acylphosphonates.

Diethyl acetylphosphonate oxime (IVa) in addition to the usual ethoxy signals, shows a doublet (3H, J=11.5 c.p.s.) at δ2.05 which represents the methyl function in the acetyl group of the oxime. This in-



crease in the P-C-C-H coupling constant from the value of 5 c.p.s. observed for diethyl acetylphosphonate (IIIa) is striking. Vicinal P-C-C-H couplings have been less extensively studied than those involving geminal P-C-H couplings primarily because of the scarcity of compounds showing interpretable patterns for the β-protons. Values for P-C-C-H coupling constants are believed to depend upon the electron-withdrawing ability of the groups bonded to phosphorus, and the s character of the phosphorus-carbon bond (J increases as the s character increases).[31] Insufficiency of NMR data for organophosphorus compounds substituted at the α-carbon which also exhibit a P-C-C-H linkage prevents easy interpretation of this difference in the coupling constants for IIIa and IVa. The s character of the carbon and phosphorus orbitals making the C-P bond in the oxime or the acylphosphonate would be expected to be essentially the same. The best explanation seems to lie in the fact that the phosphoryl group is nonidentical in the two compounds inasmuch as the oxime is found to contain an intramolecularly hydrogen-bonded structure. Thus the polarity of the phosphoryl group of the oxime differs from that

found in diethyl acetylphosphonate (IIIa). This change in the polarity results in the weakening of the bond and is reflected in the lowering of the P→O absorption in the IR spectrum. Substituents on the α-carbon atom of these cognomers influence the value for $J_{P\text{-}C\text{-}C\text{-}H}$, but the mechanism of interaction cannot be ascertained until additional models are available. Other derivatives (2,4-dinitrophenylhydrazones, p-nitrophenylhydrazones, etc.) generally are not soluble in suitable solvents and thus useful NMR data is not available for these compounds. A crude sample of the azine of diethyl acetylphosphonate (prepared in the same manner as IVa only using 3 moles of pyridine and 1.3 moles of hydrazine dihydrochloride) exhibits a doublet for the CH_3 group having a $J_{P\text{-}C\text{-}C\text{-}H}$ value of about 11-13 c.p.s. This seems to indicate that the primary factor determining the coupling constant for the P-C-C-H linkage is the nature of the substituent on the α-carbon rather than the change in the electron density of the phosphoryl group as a result of intramolecular hydrogen bonding. However, the s character of the carbon and phosphorus orbitals comprising the C-P bond may be particularly important.

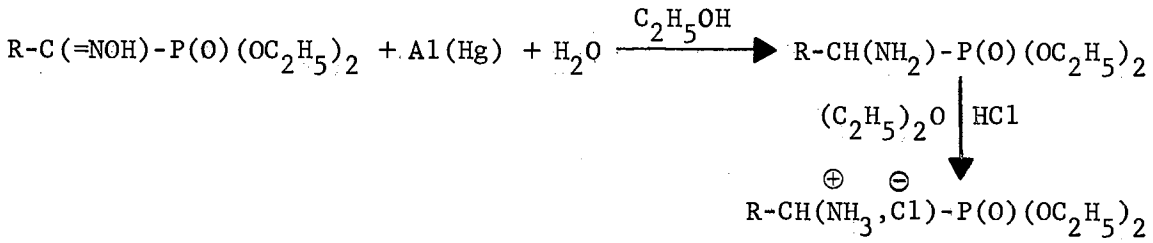
In addition to the NMR peaks already discussed, a broad multiplet (1H) was observed at δ10.3-12.5 for the hydroxyl protons in these oximes IV. The chemical shifts for the hydroxyl proton in oximes have been recently studied by Kleinspehn, Jung and Studniarz.[49] These workers observed proton signals at δ8.6-13.3. The observation of two peaks in the NMR spectra for the hydroxyl proton of certain oximes was taken to signify either the presence of a mixture of syn and anti isomers or the existence in the molecule of two or more nonequivalent groupings. These investigators found that oximino ketones generally exhibit signals in the range of δ11.7-12.5 (glyoximes exhibited signals in the

range of δ11.0-11.9 and α-oximinoacetoacetate showed a very broad peak centered at ca. δ13.1). In the case of glyoximes the number of hydroxyl proton signals observed was reported to be equal to the number of non-equivalent oxime groupings present in the molecule.

A single, broad absorption in the NMR spectrum by the hydroxyl proton in diethyl acylphosphonate oximes IV indicates, in light of the preceding discussion, the presence of a single structure for these compounds. The absence of two peaks precludes syn- and anti-oxime formation by the unsymmetrical acylphosphonates. The best explanation for this phenomena is found in the formation of the intramolecularly hydrogen-bonded structure IX suggested by the IR data for the diethyl acylphosphonate oximes IV.

Aluminum-Amalgam Reduction of Diethyl Acylphosphonate Oximes IV to Diethyl α-Aminoalkylphosphonates V. Subsequent Hydrochloride Salt VI Formation

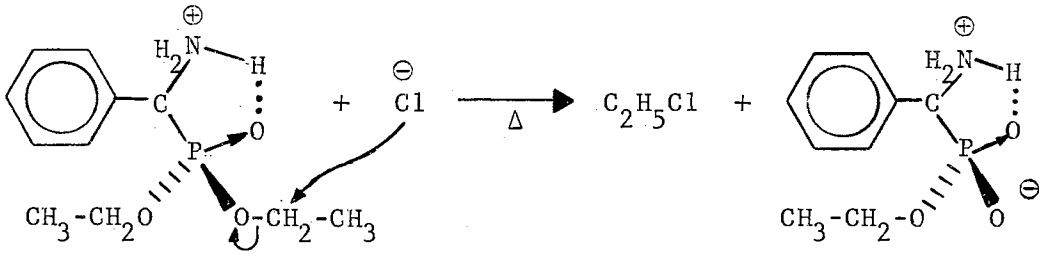
Aluminum-amalgam in a mixture of ethanol and water will easily reduce either the crude, vacuum-dried or the pure oximes of diethyl aroylphosphonates directly to diethyl α-aminoarylmethylphosphonates V under very mild conditions. The ester is not hydrolyzed to any appreciable



extent. After removal of the gray solids by filtration and evaporation of the solvents, the crude diethyl α-aminoarylmethylphosphonates V obtained can be either distilled or precipitated as the hydrochloride VI

through treatment with anhydrous hydrogen chloride in dry ether. The hydrochlorides VI of the diethyl α-aminoarylmethylphosphonates were obtained in yields of 38-85% based on the crude oximes IV. Table VIII lists the diethyl α-aminoarylmethylphosphonate hydrochlorides VI along with some of their physical properties.

The diethyl α-aminoarylmethylphosphonate hydrochlorides VI included in this study melt from 126° to 183°. At the melting point, the hydrochlorides decompose with the production of a gas. In the cases of para-substituted or unsubstituted diethyl α-aminoarylmethylphosphonate hydrochlorides the compounds resolidify and melt again at a higher temperature. For example VIc was found to melt (with frothing) at 162.2-163.4° and then to resolidify and melt again at 240-241°. Evidently the loss of a simple molecule by VIc occurs inasmuch as the second melting point is fairly sharp. α-Aminobenzylphosphonic acid monoethyl ester has been reported to have a melting point of 247°.[52] Evidently, diethyl α-aminobenzylphosphonate hydrochloride (VIc) suffers an attack by a chloride ion resulting in the loss of chloroethane and in the formation of the monoethyl ester of the corresponding acid. If hydrogen chloride were lost (as might be suspected) by VIc in the



decomposition, rather than chloroethane, the resulting product would be diethyl α-aminobenzylphosphonate (Vc) which has a melting point of 83-84°,[53] and would not melt at 240-241°.

This hypothesis was tested through a pyrolysis experiment in which

diethyl α-aminobenzylphosphonate hydrochloride VIc was kept at 225° for 1 hr. The solid became gummy and evolved a gas, but never resolidified. Attempted separation and purification of the pyrolysis products were unsuccessful. Exclusion of air by running the pyrolysis under deoxygenated nitrogen should give better results.

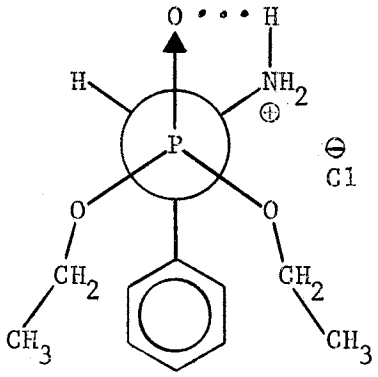
The IR spectral data for diethyl α-aminoalkylphosphonate hydrochlorides VI are listed in Table III. Plates XXIV-XXXI are reductions of the actual spectra for VIc-VIj.

The hydrochlorides VI exhibit a peak in the 1971-2035 $cm.^{-1}$ region which is believed to be a combination bond of the $-\overset{\oplus}{N}H_3$ group. α-Aminocarboxylic acids, which are known to exist as zwitterions, show an absorption between 2000 and 2200 $cm.^{-1}$ which has been assigned as a combination bond of $-\overset{\oplus}{N}H_3$ asymmetric deformation and $-\overset{\oplus}{N}H_3$ hindered rotation.[23] Primary amine salts also exhibit a band near 2000 $cm.^{-1}$ which is believed to be a combination band of $-\overset{\oplus}{N}H_3$ torsional oscillation and asymmetric deformation.[23] The diethyl α-aminoalkylphosphonate hydrochlorides VI show phosphoryl absorption between 1221 and 1258 $cm.^{-1}$ indicating hydrogen-bonding. In all cases the phosphoryl absorption is lower than that of the corresponding acyl cognomer. Differences in the P→O absorptions for acyl and α-aminoalkylphosphonate range from 4 to 37 $cm.^{-1}$. Inasmuch as the phosphoryl frequency is influenced both by hydrogen bonding and by the total electronegativity of the substituents on the phosphorus atom the lowering of the phosphoryl absorption cannot easily be correlated with hydrogen-bonding effects alone.

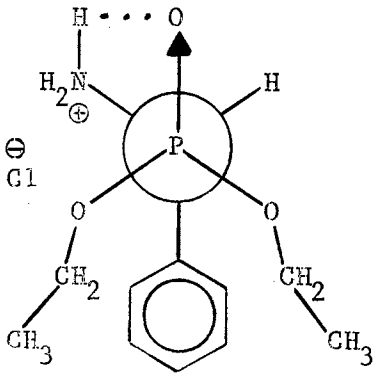
That the hydrochlorides of diethyl α-aminoalkylphosphonates are intramolecularly hydrogen-bonded structures can be shown by comparison of IR spectra of the solid and a solution of the compound. A study of

the IR spectra of diethyl α-amino-p-methoxybenzylphosphonate (VIf) showed only insignificant changes in the N-H and P→O absorptions. Frequencies of 2900 and 1244 $cm.^{-1}$ are observed for the N-H stretch and P→O absorptions, respectively, if solid VIf is in a potassium bromide pellet (Plate XXVII). A 1.3% solution of VIf in chloroform shows absorptions of 2950 $cm.^{-1}$ for N-H and 1250 $cm.^{-1}$ for P→O whereas a 0.93% solution of VIf in chloroform exhibits peaks at 2965 $cm.^{-1}$ and 1244 $cm.^{-1}$ for the two moieties. The ammonium group is expected to form intramolecular hydrogen bonds with the phosphoryl function more easily than the hydroxyl group in α-hydroxyalkylphosphonates inasmuch as the nitrogen atoms in the hydrochlorides VI are positively charged. That dialkyl α-hydroxylalkylphosphonates exist as intramolecularly hydrogen-bonded entities has been discussed previously.[58] This hydrogen bonding would be expected severely to restrict rotation around the C-P bond in these molecules. Consequently, the diethyl α-aminoalkylphosphonate hydrochlorides VI are believed to exist as the intramolecularly hydrogen-bonded structures represented by Newman projections XII [(R) diethyl α-aminobenzylphosphonate hydrochloride] and XIII [(S) diethyl α-aminobenzylphosphonate hydrochloride]. Conformations X, XI, XIV and XV are higher-energy forms which are not favored.

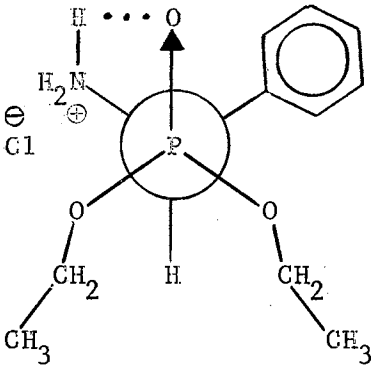
The intramolecularly hydrogen-bonded Newman projections for (RS) diethyl α-aminobenzoylphosphonate hydrochloride (VIc) conformations shown by XII [(S) diethyl α-aminobenzylphosphonate hydrochloride] and XIII [(S) diethyl α-aminobenzylphosphonate hydrochloride] are the least-hindered conformations among the six possibilities (X-XV). In XII and XIII the aromatic ring may lie between the oxygen of the phosphoryl group and an ethoxy group (the least-hindered position) and still is



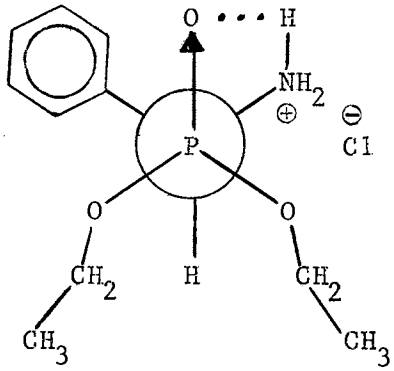
X



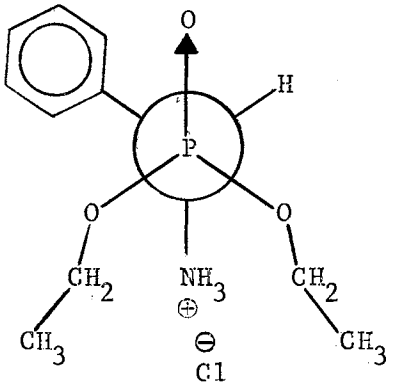
XI



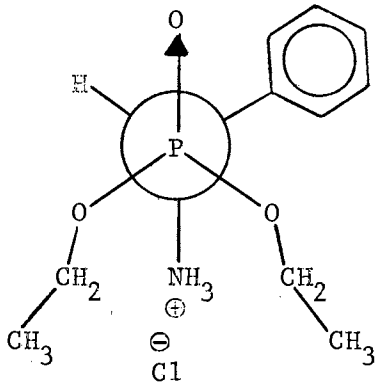
XII



XIII



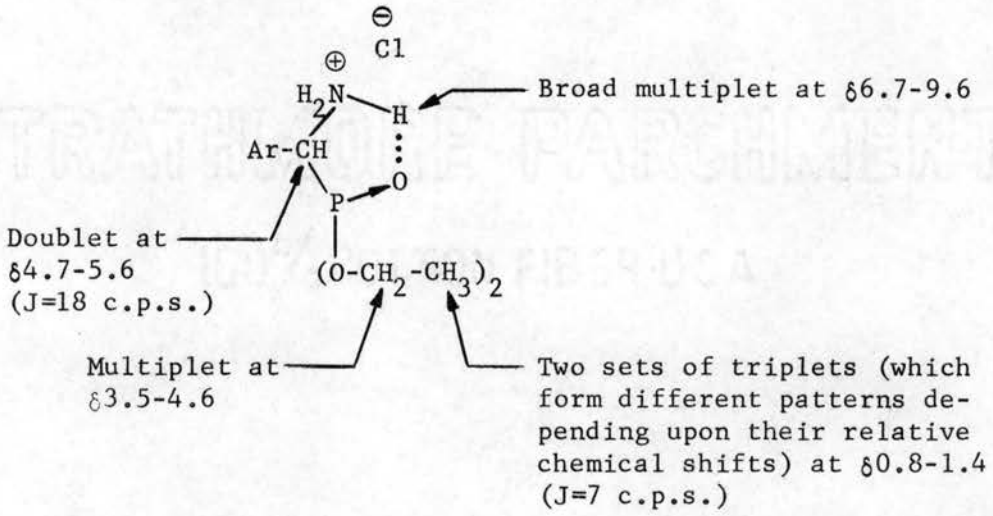
XIV



XV

intramolecularly hydrogen bonded. Structures X and XI, although hydrogen-bonded, force the aromatic ring to lie between two ethoxy groups and thus are higher-energy conformations. In structures XIV and XV, although the aromatic group lies between the phosphoryl oxygen and an ethoxy group, intramolecular hydrogen bonding is not possible and thus these conformations are not as likely to occur.

The NMR speectral data for diethyl α-aminoalkylphosphonate hydrochlorides are listed in Table V. Plates LVIII-LXIV are reductions in size of the actual NMR spectra recorded for VIc-VIj. These spectra are not as simple as those for families III and IV and exhibit several interesting features.



The benzyl proton in the diethyl α-aminobenzylphosphonate hydrochlorides VI occurs as a doublet and is seen at δ4.7-5.6. The geminal P^{31}-C-H^{1} splitting generally results in a coupling constant of 18 c.p.s. (a value of 17 c.p.s. is observed for diethyl α-amino-p-methoxybenzylphosphonate hydrochloride). The NMR spectra of dialkyl α-hydroxybenzylphosphonates exhibit a $J_{P\text{-}C\text{-}H}$ coupling constant of 13.5 c.p.s. for diethyl and dimethyl α-hydroxybenzylphosphonate.[10] (The α-hydroxyalkylphosphonic esters have been shown to be intramolecularly hydrogen-bonded

entities).[58] Geminal P-C-H coupling reportedly is related to the electron densities in both the P-C and C-H bonds (and thus dependent upon the substituents on both phosphorus and carbon)[69] and the P-C-H angle[31] (however, very little bond angle data is available). Inasmuch as the P-C-H angle would be expected to be essentially the same for α-aminoalkyl- and α-hydroxyalkylphosphonates, the electron-withdrawing character of the $-\overset{\oplus}{N}H_3$ group versus that of the -OH may be part of the explanation for the difference in the J_{P-C-H} values for the two families of compounds. The nitrogen atom carries a full positive charge and the oxygen atom is essentially neutral. Therefore the nitrogen atom would be expected to be a better electron acceptor than the oxygen atom and the electron density for the C-O bond would be expected to be greater than for the C-N bond. Thus as the electron-withdrawing ability of a substituent on the α-carbon atom in substituted benzylphosphonates increases, J_{P-C-H} will decrease in value. Geminal P-C-H coupling constants of 2.6 to 30.1 c.p.s. have been reported.[31]

It is interesting to note that diethyl α-aminobenzylphosphonate (Vc) exhibits a doublet at δ-4.31 (J=18 c.p.s.) for the benzyl proton. This data seems to contradict the conclusion that the electron-withdrawing ability of a substituent determines the J_{P-C-H} since the electron withdrawing ability of a NH_2 group would differ from that of positively charged $\overset{\oplus}{N}H_3$.

A second possible explanation for the variation in the values for the geminal P-C-H coupling constants for the benzyl proton in diethyl α-substituted benzylphosphonates comes to mind. The hydrogen bonding in α-aminobenzylphosphonates, α-hydroxybenzylphosphonates and α-aminobenzylphosphonate hydrochlorides may differ in the strength of the O···H bond.

This difference could give rise to changes in the s character of the phosphorus orbital which forms the P-C bond. Thus, since the coupling constant is known to vary with the s character of both the carbon and phosphorus bonding orbitals, the J_{P-C-H} variance is not unexpected.

The $-\overset{\oplus}{N}H_3$ protons were found to give a signal between δ6.7 and δ9.6 in the NMR spectra of diethyl α-aminoalkylphosphonate hydrochlorides VI. This signal appeared as a broad multiplet. That this peak represented the ammonium hydrogen atoms was evident from the NMR spectra of VId and VIj (Plates LIX and LXV, respectively), which were obtained from deuterium oxide solutions. The ammonium protons exchange with D_2O and, instead of the $-\overset{\oplus}{N}H_3$ multiplet, there appears a DOH singlet at δ4.84 for VId and at δ4.74 for VIj.

The NMR spectra also exhibit the expected aromatic hydrogen signals and other proton absorptions. These are predictable and do not merit further comment.

The NMR spectra for diethyl α-aminobenzylphosphonate hydrochlorides VI have a second interesting feature in that they exhibit magnetic nonequivalent ethoxy moieties. The two methyl groups of the ethoxy functions give rise to two triplets in the spectra of family VI. These two triplets may give the appearance of a quartet (as in the cases of VIc, VIg and VIh, Plates LVIII, LXII and LXIII, respectively) when their centers are separated by about 7 c.p.s., a sextet (as in the case of VIj, Plate LXV), when their centers are separated by about 3.5 c.p.s., or as a multiplet when separations other than 3.5 or 7 c.p.s. are realized. The methyl absorptions appear at δ0.8-1.4. Likewise, magnetic nonequivalence is seen in the methylene groups. However, since these protons normally exist as imperfect quintets, the two overlapping

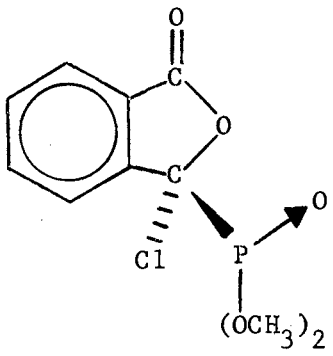
quintets appear as nondescript multiplets and appear in the range of δ3.5 to δ4.6 and defy easy interpretation.

The intramolecularly hydrogen-bonded Newman projections for (RS) diethyl α-aminobenzylphosphonate hydrochloride (VIc) conformations shown previously by XII and XIII are the least-hindered conformations which also allow for hydrogen bonding. As discussed previously, in XII and XIII the aromatic ring may lie between the oxygen of the phosphoryl and one of the ethoxy groups thus placing this ethoxy group nearer the magnetically anistropic benzene ring than the second ethoxy group. Thus the two ethoxy moieties experience different magnetic environments. NMR spectra of these compounds taken at higher temperatures should confirm these conclusions by determining whether the two magnetically-nonequivalent methyl groups of the ethoxy moieties coalesce into a single triplet.

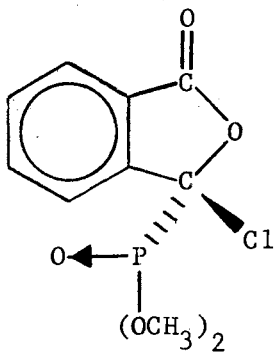
Another explanation for the magnetic nonequivalence observed, although not likely, would be "long range" P^{31}-O-C-C-H^{1} splitting. This type of splitting, however, generally does not exceed 1.1 c.p.s.[35] and is not obvious in the NMR spectra of the similar diethyl acylphosphonate III and diethyl acylphosphonate oxime IV cognomers.

Magnetic nonequivalence has been reported for alkoxy groups in phosphorus esters previously, but not for α-aminoalkylphosphonate esters nor salts. Siddell[77] has listed the conditions for protons (or groups or radicals) to be magnetically nonequivalent. Siddell has also reported that the alkoxy groups on certain carbamylmethylenephosphonates which have an asymmetric α-carbon atom exhibit magnetic nonequivalence. Berlin and others[9] have recently found magnetically nonequivalent methyl groups in (RS) dimethyl α-chlorophthalidylphosphonate (drawings XVI and

XVII). Certain similarities exist between (RS) dimethyl chlorophthal-

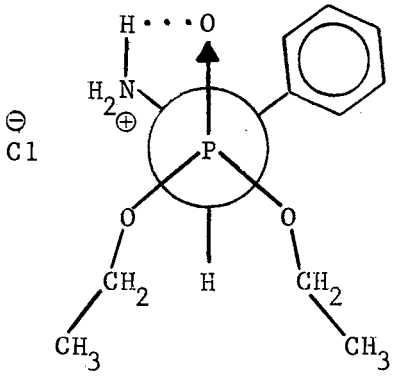


XVI

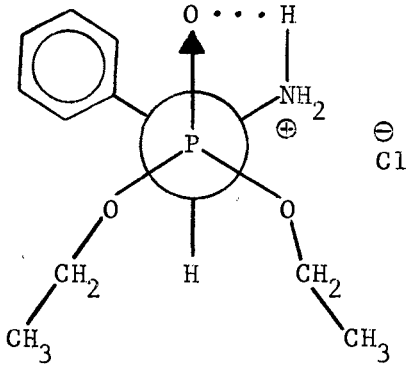


XVII

idylphosphonate and the diethyl α-aminobenzylphosphonates VI. First, an asymmetric center exists at the α-carbon. Second, this asymmetric center creates nonequivalent magnetic environments for the two alkoxy groups by causing one of them to lie nearer the place of a magnetically anisotropic benzene ring which occurs in both sets of compounds. It can be seen from Newman projections XVIII and XIX [which represent the (R)



XVIII

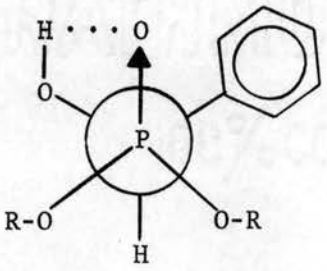


XIX

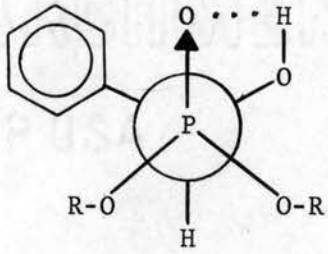
and (S) conformations best depicting racemic diethyl α-aminobenzylphosphonate hydrochloride (VIc)] that the asymmetric α-carbon atom of both (R) and (S) diethyl α-aminobenzylphosphonate hydrochloride (VIc) causes one of the ethoxy groups to lie nearer the plane of the magnetically anisotropic benzene ring than the second. The same arguments

can be applied to the other (RS) diethyl α-aminoarylmethylphosphonate hydrochlorides (Plates LVIII-LXV) are composed of molecules whose conformations could be projected in similar fashion. The intramolecularly hydrogen-bonded structures represented by drawings of conformers XVIII and XIX [for the (R) and (S) configurations of VIc and by subsequent extension to the other members of family VI] seem to best represent those properties suggested by the NMR and IR spectra of the diethyl α-aminoarylmethylphosphonate hydrochlorides.

Magnetic nonequivalent alkoxy groups have also been seen in the NMR spectra of racemic α-hydroxybenzylphosphonic esters.[10] Newman projections (please refer to drawings XX and XXI) of the lower-energy conformations for the dialkyl α-hydroxybenzylphosphonates show similar-



XX



XXI

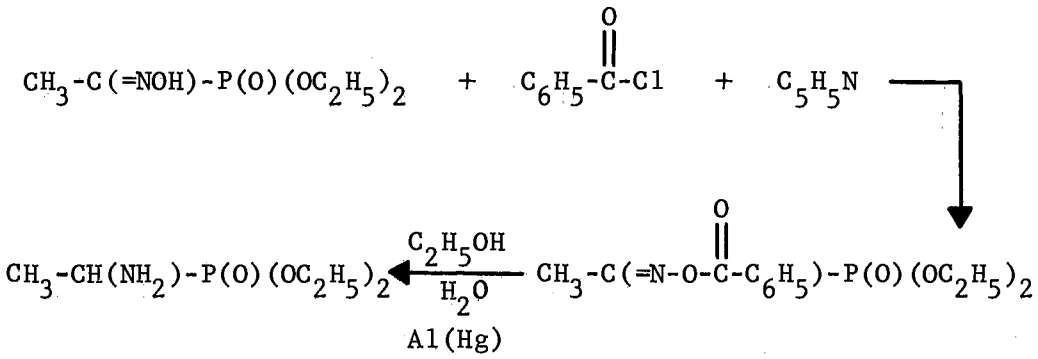
ities to those of the (RS) diethyl α-aminobenzylphosphonates VI.

The NMR spectral data for diethyl 1-aminoethylphosphonate (Va) are listed in Table V. Plate LVI is a reduction of the actual NMR spectra recorded for Va. A triplet occurs at δ1.33 which is assigned to the methyl in the ethoxy group. The methylene protons give a quintet at δ4.19. At δ1.53 a singlet appears which upon treatment with deuterium oxide shifts to the position for DOH absorption; thus assignment of this peak to NH_2 seems justified. A multiplet appearing in the region δ1.1-1.6 is assigned to the methyl group bonded to the methine carbon atom. The methine proton shows a multiplet at δ2.7-3.4. Magnetic

nonequivalence is not observed in Va (diethyl 1-aminoethylphosphonate) but is observed for diethyl α-aminobenzylphosphonate, (Plate LVII). The NMR spectrum of Va does not provide clean P-C-H and P-C-C-H splitting constants since considerable overlapping of peaks occur where the methyl group β to phosphorus absorbs and since the methine absorption occurs as a multiplet.

Reduction of Diethyl Acylphosphonate Oximes

Although diethyl 1-aminoethylphosphonate (Va) was not obtained through aluminum-amalgam reduction of diethyl acetylphosphonate oxime (IVa), amalgamated aluminum was found to reduce the benzoylated IVa.



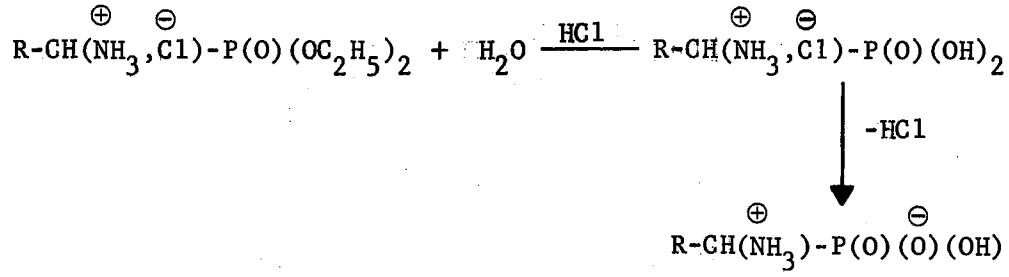
The yield for the expected α-amino compound Va was 20.6% based on this benzoylated oxime. An attempted aluminum-amalgam reduction of acetylated diethyl propionylphosphonate oxime gave a highly stable lyophilic gel which could not be separated from the solution either through filtration or by centrifuging at 1800 r.p.m. for 45 min. Several other reduction procedures were tried and found to be unsatisfactory. Shaking IVa for 60 hr. with W-6 Raney nickel using a hydrogen pressure of 3.5 atm. did not provide diethyl 1-aminoethylphosphonate (Va). Experiments using PtO_2 (in an ethanol solution with a hydrogen pressure of 3.5 atm.) or 5% palladium on charcoal (in an absolute ethanol solution)

catalysts gave no reaction--starting material was recovered from the reaction mixture in high yield (80-90 percent). A mixture of diethyl acetylphosphonate oxime (IVa) and lithium aluminum hydride in an ether solution rapidly evolved a gas which had the odor of a phosphine. Sodium borohydride and the p-nitrophenylhydrazone of diethyl benzoylphosphonate did not give Vc. With zinc and acetic acid in an attempted reduction of IVa, an insignificant amount of a syrup having the odor of Va was obtained. Infrared analysis indicated that the product was a mixture of IVa and Va. Va may also be coordinated to the Zn(II) resulting from the reaction since α-aminoalkylphosphonic acids are known to form chelates with transition metals.[7] Sodium in absolute ethanol was found to reduce IVb but low yields resulted.

IR analysis of diethyl 1-aminoethylphosphonate (Va, Plate XXII) gives absorptions of 3366 and 3290 $cm.^{-1}$ for N-H, of 1236 $cm.^{-1}$ for P→O and 1166 $cm.^{-1}$ for P-O-C_2H_5. The frequency for the P→O bond is appreciably lower than for the same bond in the acetylphosphonate ester IIIa (1257 $cm.^{-1}$) but of the same order of absorption as found in the corresponding oxime IVa (1239 $cm.^{-1}$). Also the amino group absorbs at a lower frequency than would be expected for a free amino group. These considerations indicates that hydrogen bonding exists in Va.

α-Aminoalkylphosphonic Acids VIII

The α-aminoalkylphosphonic acid hydrochlorides VII were obtained through hydrolysis of the diethyl α-aminoalkylphosphonate hydrochlorides VI using hydrochloric acid. The solution was evaporated to dryness *in vacuo* and the resulting solid was dissolved in a minimum of cold water and boiled until the free white acid began to crystallize out. High



yields (73-88 percent) of the acids were realized (based on the diethyl α-aminoalkylphosphonate hydrochlorides VI). The new α-aminoalkylphosphonic acids along with some of their physical properties are listed in Table IX.

Phosphinic and phosphonic acids, in general, exhibit a strong band at 910-1040 cm.$^{-1}$ which probably involves the stretching of the P-O(H) bond.[23] The O-H stretching vibration gives rise to broad medium intensity bands at 2500-2700 cm.$^{-1}$ and 2100-2300 cm.$^{-1}$ in organic phosphorus acids.[23] Acid salts containing the P-O-H group show broad bands at 2560-2700 cm.$^{-1}$ and 1600-2500 cm.$^{-1}$.[23] Salts of $R_2P(O)(\overset{\ominus}{O})$ and $R(H)P(O)(\overset{\ominus}{O})$ show two strong bands at 1100-1190 cm.$^{-1}$ and 1000-1075 cm.$^{-1}$; these are believed to be due to symmetric and asymmetric stretch of $-P(O)(\overset{\ominus}{O})$.[23] It is difficult to make specific assignments for absorptions in the 970-1300 cm.$^{-1}$ region for α-aminoalkylphosphonic acids, inasmuch as the phosphoryl stretching frequency at 1200-1300 cm.$^{-1}$ is accompanied by two absorptions for the $\overset{\ominus}{PO_2}$ group (1150-1300 cm.$^{-1}$ and 970-1300 cm.$^{-1}$).[24] The IR spectrum of 2-aminoethylphosphonic acid has been published,[37,48] but no discussion of the details of the spectrum was included.

The diffuse nature of the P→O, $\overset{\ominus}{PO_2}$, O-H and P-O-H bands in phosphorus acids has been taken as evidence for extensive intermolecular hydrogen bonding.[70] The formation of dimers by alkyl alkylphosphonothioic acids and dialkyl phosphonic acids has been confirmed by

cryoscopic studies.[26,58] Inasmuch as the dialkyl α-aminoalkylphosphonate hydrochlorides VI have been found to be intramolecularly hydrogen-bonded compounds, α-aminoalkylphosphonic acids VIII might be expected to possess this same tendency to form dimers or higher polymers. This may explain the extreme broadness in the IR spectra of α-aminoalkylphosphonic acids.

Table IV gives the IR spectral data for the α-aminoalkylphosphonic acids. Infrared spectra are recorded for VIIIc (Plate XXXII), VIIId (Plate XXXIII), VIIIf (Plate XXXIV) and VIIIj (Plate XXXV). These spectra are characterized by broad diffuse absorptions at 1800-3700 $cm.^{-1}$. These broad diffuse bands are anticipated in light of the spectra observed for similar compounds. However, it is difficult to make definitive assignments for the various peaks which occur in these regions.

Inasmuch as α-aminomethylphosphonic acid has been shown to exist as the zwitterion $H_3\overset{\oplus}{N}-CH_2-P(O)(\overset{\ominus}{O})(OH)$,[20] other α-aminoalkylphosphonic acids are expected to also exist as zwitterions.

The NMR spectral data for α-aminoalkylphosphonic acids are listed in Table V. Plates LXVI and LXVII are reductions of the actual NMR spectra for VIIId and VIIIf. Generally, these acids are insoluble in most solvents. Trifluoroacetic acid was used as the solvent in obtaining the NMR spectra of these acids but the acidic protons of the phosphorus compound are rapidly exchanged and are not individually defined.

The benzyl proton in VIIId and VIIIf occurs as a doublet near δ5.0 and is quite broad and the coupling constant is estimated to be about 16±2 c.p.s..

The ammonium group shows an absorption between δ7.2 and 8.4 and

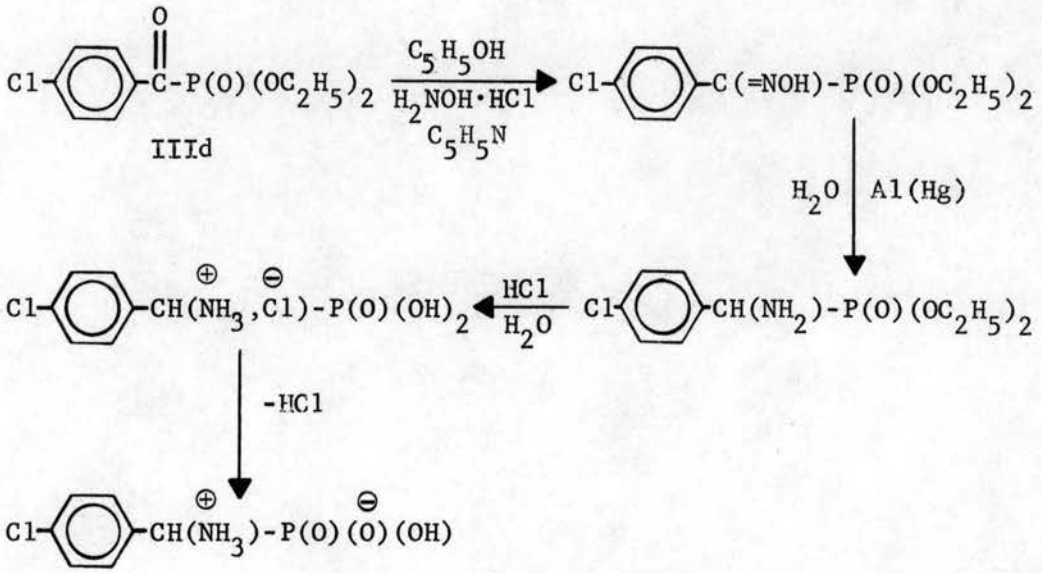
integrated for three protons. That these compounds exist as zwitterions cannot be ascertained from the NMR spectra inasmuch as the acid solvent will protonate the amino group if R-CH(NH_2)-P(O)(OH)$_2$ is the prevailing structure or will protonate the oxide ion if R-CH($\overset{\oplus}{N}H_3$)-P(O)($\overset{\ominus}{O}$)(OH)$_2$ is the actual formula. In either event an ammonium group will result which will show three protons in the NMR spectra.

The aromatic proton signals occur in the expected region of δ6.7-7.3. The protons of the P-O-H linkage are not seen and are assumed to be included in the large trifluoroacetic acid peak at δ10.7.

The Direct Preparation of α-Amino-p-chlorobenzylphosphonic Acid (VIIId) From Diethyl p-Chlorobenzoylphosphonate (IIId)

The synthesis of α-aminoalkylphosphonic acids VIII from dialkyl acylphosphonates III, directly (i.e., without isolating or purifying the intermediate oximes IV or α-aminophosphonates V) was accomplished.

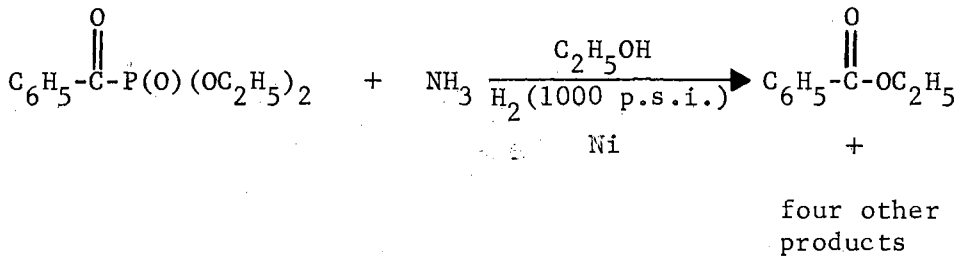
Diethyl p-chlorobenzoylphosphonate (IIId) was added to hydroxylamine hydrochloride in a solution of pyridine and ethanol and stirred



at room temperature for 72 hr. The workup is reported in the Experimental section. The resulting crude oxime IVd was stirred for 40 hr. with amalgamated aluminum in ethanol and water to effect the reduction to diethyl α-amino-p-chlorobenzylphosphonate (Vd). The workup afforded a crude syrup (diethyl α-amino-p-chlorobenzylphosphonate) which was boiled with hydrochloric acid for 14 hr. Removal of the volatile components of the resulting solution gave the crude α-amino-p-chlorobenzylphosphonic acid hydrochloride (VIId). This crude material formed a solid mass upon standing in water. Purification by precipitation from cold water gave the white, crystalline acid (66.5% based on diethyl p-chlorobenzoylphosphonate).

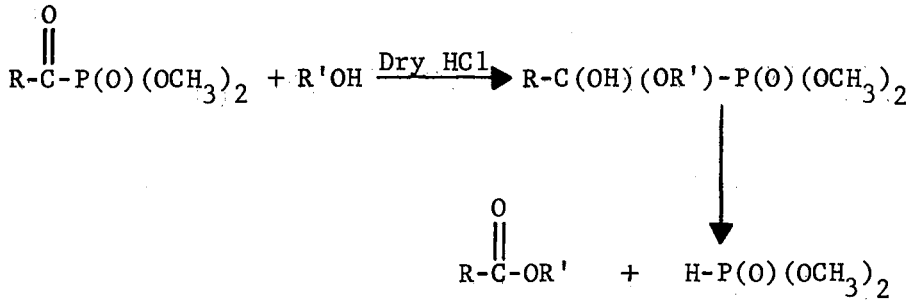
Attempted Reductive Amination of Diethyl Benzoylphosphonate (IIIc)

An attempt to produce diethyl α-aminobenzylphosphonate (Vc) through reductive amination of IIIc failed. W-6 Raney nickel was added to an absolute ethanol solution of IIIc and anhydrous ammonia. The mixture was shaken at room temperature under a hydrogen pressure of 1000 p.s.i. for 19 hr. GLC analysis of the syrup (injected neat) exhibited five peaks, one having the same retention time as ethyl benzoate. This indicated the cleavage of the C-P bond.

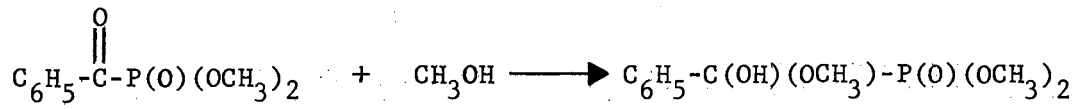


Although the carbon-phosphorus bonds in dialkyl alkylphosphonates

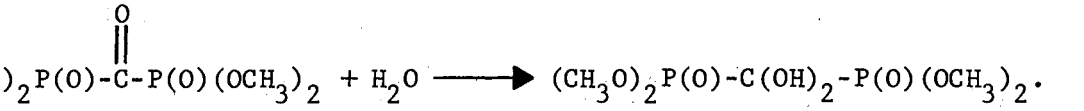
in general are quite resistant to cleavage,[23] the C-P bond in dialkyl acylphosphonates III has been cleaved by alcoholic sodium hydroxide (under mild conditions),[44] by water in dioxane,[2] and by alcohols (reaction acid-catalyzed).[53] In experiments[43] using methanol, ethanol and propanol with dimethyl acetylphosphonate and dimethyl benzoylphosphonate (anhydrous hydrogen chloride was used as the catalyst) the following mechanism was believed to operate. In the absence of hydrogen chloride



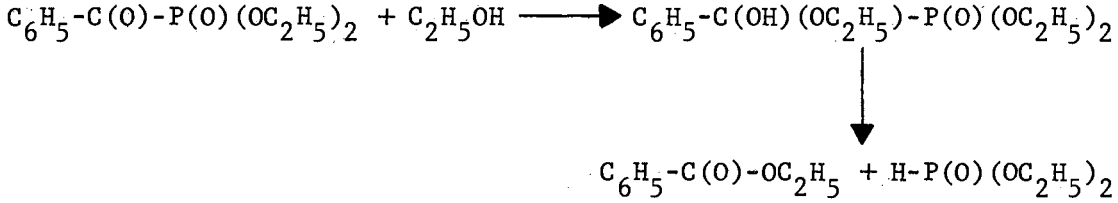
these workers found that dimethyl benzoylphosphonate formed an addition compound of hemiacetal type with methanol. Also Kabachnik and Rossii-



skaya[45] reported the quantitative addition with water:



As stated previously, attempted reductive amination of diethyl benzoylphosphonate (IIIc) the C-P bond was cleaved and ethyl benzoate was one of at least five products according to GLC evidence. A possible mechanism is illustrated which is similar to that postulated by



others.[43] No diethyl α-aminobenzylphosphonate hydrochloride could be isolated upon treating the crude product of the attempted reductive amination of the ester salt with anhydrous hydrogen chloride. Inasmuch as water in dioxane has been found to cleave the C-P linkage in acylphosphonates,[2] ammonia, a better Bronsted base than water, would also be expected to cleave this bond.

Summary

It is now possible to prepare dialkyl α-aminoalkylphosphonates, dialkyl α-aminoalkylphosphonate hydrochlorides and α-aminoalkylphosphonic acids from the easily prepared oximes of dialkyl acylphosphonates. These preparations may be accomplished with little difficulty under relatively mild conditions and result in high yields.

Several interesting and novel physical features in the oximes and phosphonates were observed for the first time. Both diethyl acylphosphonate oximes and diethyl α-aminoalkylphosphonate hydrochlorides have been found for the first time to exist as intramolecularly hydrogen-bonded molecules in which the labile proton of the hydroxyl or ammonium group is hydrogen-bonded to the phosphoryl oxygen.

Magnetic nonequivalence in the alkoxy groups of diethyl α-aminoarylmethylphosphonates and diethyl α-aminoarylmethylphosphonate hydrochlorides was observed for the first time in the NMR spectra for these compounds. This nonequivalence is believed to arise from the asymmetric center present which causes one of the ethoxy groups to lie closer to the planar anisotropic aromatic ring and thus experience a different magnetic environment than the other ethoxy group.

The NMR and IR spectra for the diethyl acylphosphonate oximes, for

the diethyl α-aminoalkylphosphonates, for the diethyl α-aminoalkylphosphonate hydrochlorides and for the α-aminoalkylphosphonic acids were recorded and are discussed for the first time.

TABLE I

IR SPECTRAL DATA FOR DIETHYL ACYLPHOSPHONATES, R-CO-P(O)$(OC_2H_5)_2$

Cpd.[a]	Plate	C=O	P→O	P-O-C_2H_5
IIIa	I	1696	1257	1162
IIIb	II	1692	1257	1163
IIIc	III	1659	1255	1164
IIId	IV	1656	1258	1165
IIIe	V	1669	1258	1163
IIIf	VI	1649	1260	1168
IIIg	VII	1651	1262	1167
IIIh	VIII	1669	1258	1164
IIIi	IX	1653	1259	1165
IIIj	X	1651	1256	1165

[a] Liquid samples, determined neat as a film on NaCl plates.

TABLE II

IR SPECTRAL DATA FOR OXIMES OF DIETHYL ACYLPHOSPHONATES, R-C(=NOH)-P(O)$(OC_2H_5)_2$

Cpd.	Plate	O-H	P→O	N-O	P-O-C_2H_5
IVa[a]	XI	3166	1239	927	1166
IVb[a]	XII	3153	1223	928	1168
IVc[a,b]	XIII	3124	1219	- -	1165
IVd[c]	XIV	3104	1244	928	1163
IVe[c]	XV	3108	1218	928	1165
IVf[c]	XVI	3208	1240	933	1166
IVg[c]	XVII	3127	1251	927	1171
IVh[c]	XVIII	3132	1228	931	1166
IVi[c]	XIX	3142	1214	- -	1168
IVj[b,c]	XX	3116	1228	932	1166

[a] Liquid sample; determined as a film on NaCl plates.

[b] Crude sample.

[c] Solid sample; determined in a KBr pellet.

TABLE III

IR SPECTRAL DATA FOR DIETHYL α-AMINOALKYLPHOSPHONATE HYDROCHLORIDES, Ar-CH($\overset{\oplus}{N}H_3$,$\overset{\ominus}{C}l$)-P(O)(OC_2H_5)$_2$

Cpd.[a]	Plate	$-\overset{\oplus}{N}H_3$	P-O-C_2H_5	P→O
VIc	XXIV	2025	1162	1241
VId	XXV	2020	1163	1221
VIe	XXVI	2062	1162	1230
VIf	XXVII	2035	1163	1244
VIg	XXVIII	1971	1163	1258
VIh	XXIX	1947	1172	1233
VIi	XXX	2024	1163	1228
VIj	XXXI	2035	1163	1221

[a] All infrared spectra of diethyl α-aminoalkylphosphonate hydrochlorides were obtained in KBr pellets.

TABLE IV

IR SPECTRAL DATA FOR α-AMINOALKYLPHOSPHONIC ACIDS, $Ar\text{-}CH(\overset{\oplus}{N}H_3)\text{-}P(O)(\overset{\ominus}{O})(OH)$

Cpd.[a]	Plate	-POH -O-H $-NH_3^{\oplus}$	P→O $PO_2^{\ominus}$	P-O-H
VIIIc	XXXII	1850-3550 3125 2918 2310 2128	1270 1257 1213 1197	1082
VIIId	XXXIII	1900-3700 3135 2917 2842 2617 2325	1273 1250 1214 1201	1082
VIIIf	XXXIV	1800-3600 3544 3356 3247 3040 2984 2881 2884 2837 2598	1252 1239 1227 1193	1085

TABLE IV (CONTINUED)

Cpd.[a]	Plate	-POH -O-H $-NH_3^{\oplus}$	P→O $PO_2^{\ominus}$	P-O-H
VIIIj	XXXV	1800-3300 3125 3059 2613 2545 2280	1261 1203	1077

[a] All infrared spectra of α-aminoalkylphosphonic acids were obtained in potassium bromide pellets.

TABLE V

NMR COUPLING CONSTANTS AND CHEMICAL SHIFTS OF PRODUCTS

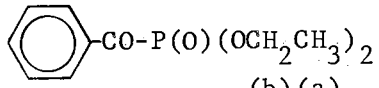
Cpd.	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Integ.	Assignment
CH_3-CO-P(O)$(OCH_2CH_3)_2$ (c) (b)(a)	XXXVI	CCl_4	1.33 t	7.0	6	CH_3 (a)
			2.37 d	5.0	3	CH_3 (c)
IIIa			4.11 qt	7.0	4	CH_2 (b)
CH_3-CH_2-CH_2-CO-P(O)$(OCH_2CH_3)_2$ (e) (d) (c) (b)(a)	XXXVII	$CDCl_3$	0.99 t	7.0	3	CH_3 (e)
			1.43 t	7.0	6	CH_3 (a)
IIIb			1.6 m	- -	2	CH_2 (c)
			2.96 t	7.0	2	CH_2 (d)
			4.43 qt	7.0	4	CH_2 (b)
 (b)(a)	XXXVIII	CCl_4	1.37 t	7.0	6	CH_3 (a)
			4.20 qt	7.0	4	CH_2 (b)
IIIc			7.3-7.7 m	- -	3	Ar-H
			8.1-8.4 m	- -	2	Ar-H

TABLE V (CONTINUED)

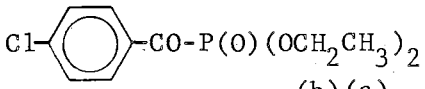
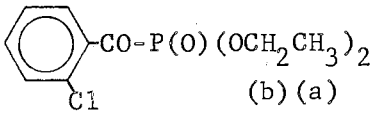
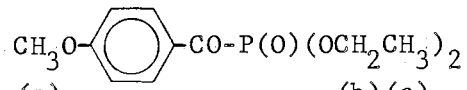
Cpd.	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Integ.	Assignment
 (b)(a)	XXXIX	CCl_4	1.38 t	7.0	6	CH_3 (a)
			4.20 qt	7.0	4	CH_2 (b)
IIId			7.46 d	8.0	2	Ar-H
			8.21 d	8.5	2	Ar-H
 (b)(a)	XL	CCl_4	1.31 t	7.0	6	CH_3 (a)
			4.17 qt	7.0	4	CH_2 (b)
IIIe			7.1-7.5 m	- -	3	Ar-H
			7.9-8.3 m	- -	1	Ar-H
 (c) (b)(a)	XLI	CCl_4	1.36 t	7.0	6	CH_3 (a)
			3.84 s	- -	3	CH_3 (c)
IIIf			4.18 qt	7.0	4	CH_2 (b)
			6.90 d	8.5	2	Ar-H
			8.19 d	9.0	2	Ar-H

TABLE V (CONTINUED)

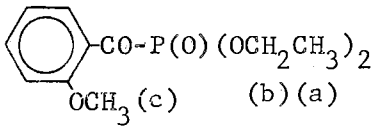
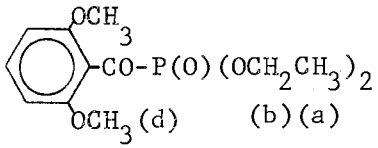
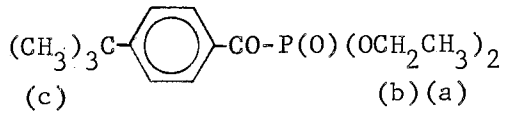
Cpd.	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Integ.	Assignment
 IIIg	XLII	CCl_4	1.28 t	7.0	6	CH_3 (a)
			3.83 s	- -	3	CH_3 (c)
			4.12 qt	7.0	4	CH_2 (b)
			6.7-7.8 m	- -	4	Ar-H
 IIIh	XLIII	CCl_4	1.25 t	7.0	6	CH_3 (a)
			3.70 s	- -	6	CH_3 (c)
			4.03 qt	7.0	4	CH_2 (b)
			6.3-6.6 m	- -	2	Ar-H
			7.0-7.4 m	- -	1	Ar-H
 IIIi	XLIV	CCl_4	1.38 t	7.0	6	CH_3 (a)
			1.36 s	- -	9	CH_3 (c)
			4.19 qt	7.0	4	CH_2 (b)
			7.46 d	8.5	2	Ar-H
			8.16 d	8.5	2	Ar-H

TABLE V (CONTINUED)

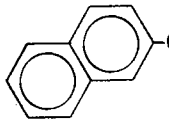
Cpd.	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Integ.	Assignment
 $-CO-P(O)(OCH_2CH_3)_2$ (b)(a)	XLV	$CDCl_3$	1.36 t	7.0	6	CH_3 (a)
			4.35 qt	7.0	4	CH_2 (b)
IIIj			7.4-9.3 m	- -	7	Ar-H
$CH_3-C(=NOH)-P(O)(OCH_2CH_3)_2$ (d) (c) (b)(a)	XLVI	$CDCl_3$	1.34 t	7.0	6	CH_3 (a)
			2.05 d	11.5	3	CH_3 (d)
IVa			4.22 qt	7.0	4	CH_2 (b)
			11.1-11.7 m	- -	1	NOH (c)
$CH_3-CH_2-CH_2-C(=NOH)-P(O)(OCH_2CH_3)_2$ (f) (e) (d) (c) (b)(a)	XLVII	$CDCl_3$	1.00 t	7.0	3	CH_3 (f)
			1.40 t	7.0	6	CH_3 (a)
IVb			1.2-2.0 m	- -	2	CH_2 (d & e)
			2.3-3.0 m	- -	2	
			4.35 qt	7.0	4	CH_2 (b)
			10.7-11.8 m	- -	1	NOH (c)

TABLE V (CONTINUED)

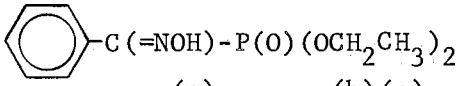
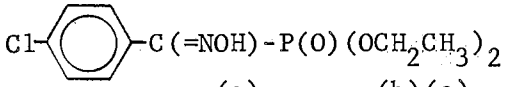
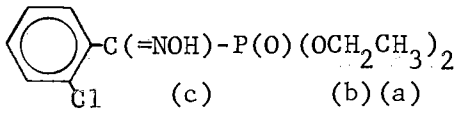
Cpd.	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Integ.	Assignment
 (c) (b)(a) IVc	XLVIII	pyridine-d_5	1.20 t	7.0	6	CH_3 (a)
			3.9-4.6 m	- -	4	CH_2 (b)
			7.1-8.1 m	- -	5	Ar-H
			14.2-14.6 m	- -	1	NOH (c)
 (c) (b)(a) IVd	XLIX	$CDCl_3$	1.28 t	7.0	6	CH_3 (a)
			4.22 qt	7.0	4	CH_2 (b)
			7.41 d	9.0	2	Ar-H
			7.66 d	8.0	2	Ar-H
			11.0-12.3 m	- -	1	NOH (c)
 (c) (b)(a) IVe	L	$CDCl_3$	1.23 t	7.0	6	CH_3 (a)
			4.13 qt	7.0	4	CH_2 (b)
			7.1-7.4 m	- -	4	Ar-H
			11.3-11.6 m	- -	1	NOH (c)

TABLE V (CONTINUED)

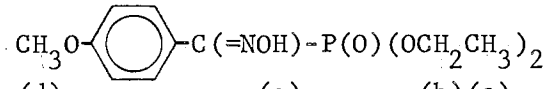
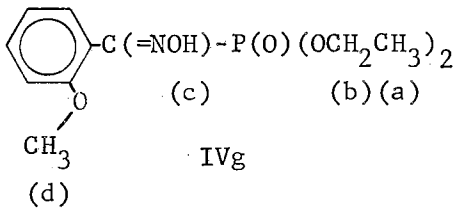
Cpd.	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Integ.	Assignment
 (d) (c) (b)(a) IVf	LI	$CDCl_3$	1.27 t	7.0	6	CH_3 (a)
			3.82 s	- -	3	CH_3 (d)
			4.18 qt	7.0	4	CH_2 (b)
			6.94 d	9.0	2	Ar-H
			7.73 d	9.0	2	Ar-H
			10.3-11.0 m	- -	1	NOH (c)
 (d) IVg	LII	$CDCl_3$	1.23 t	7.0	6	CH_3 (a)
			3.76 s	- -	3	CH_3 (d)
			4.13 qt	7.0	4	CH_2 (b)
			6.7-7.5 m	- -	4	Ar-H
			10.3-10.8 m	- -	1	NOH (c)

TABLE V (CONTINUED)

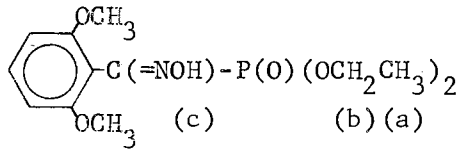
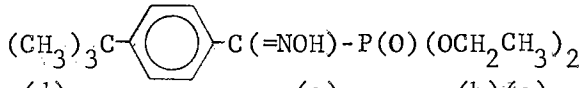
Cpd.	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Integ.	Assignment
 (d) (c) (b)(a) IVh	LIII	$CDCl_3$	1.17 t	7.0	6	CH_3 (a)
			1.23 t	7.0		
			3.70 s	- -	6	CH_3 (d)
			3.8-4.4 m	- -	4	CH_2 (b)
			6.3-6.6 m	- -	2	Ar-H
			7.0-7.4 m	- -	1	Ar-H
			10.8-11.1 m	- -	1	NOH (c)
 (d) (c) (b)(a) IVi	LIV	$CDCl_3$	1.30 t	7.0	6	CH_3 (a)
			1.37 s	- -	9	CH_3 (d)
			4.34 qt	7.0	4	CH_2 (b)
			7.70 d	9.0	9	Ar-H
			7.96 d	9.0	9	Ar-H
			12.2-12.5 m	- -	1	NOH (c)

TABLE V (CONTINUED)

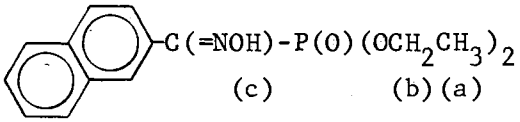
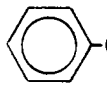
Cpd.	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Integ.	Assignment
 C(=NOH)-P(O)(OCH_2CH_3)$_2$ (c) (b)(a) IVj	LV	$CDCl_3$	1.16 t	7.0	6	CH_3 (a)
			4.08 qt	7.0	4	CH_2 (b)
			7.2-8.2 m	- -	7	Ar-H
			11.8-12.3 m	- -	1	NOH (c)
CH_3-CH(NH_2)-P(O)(OCH_2CH_3)$_2$ (e) (c)(d) (b)(a) Va	LVI	$CDCl_3$	1.33 t	7.0	6	CH_3 (a)
			1.53 s	- -	2	NH_2[b] (d)
			1.1-1.6 m	- -	3	CH_3 (e)
			2.7-3.4 m	- -	1	CH (c)
			4.19 qt	7.0	4	CH_2 (b)
 -CH(NH_2)-P(O)(OCH_2CH_3)$_2$ (c)(d) (b)(a) Vc	LVII	pyridine-d_5	1.08 q	7.0	6	CH_3 (a)
			2.72 s	- -	2	NH_2[b] (d)
			3.6-4.3 m	- -	4	CH_2 (b)
			4.31 d	18.0	1	CH (c)
			7.1-7.8 m	- -	5	Ar-H

TABLE V (CONTINUED)

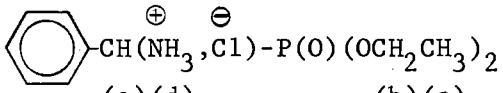
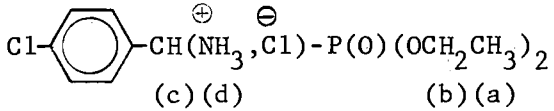
Cpd.	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Integ.	Assignment
 (c)(d) (b)(a) VIc	LVIII	CF_3COOH	1.30 q	7.0	- -	CH_3[c] (a)
			4.0-4.6 m	- -	- -	CH_2 (b)
			5.05 d	18.0[d]	- -	CH (c)
			7.51 s	- -	- -	Ar-H
			7.8-8.5 m	- -	- -	NH_3[b] (d)
 (c)(d) (b)(a) VId	LIX	D_2O	1.34 t	7.0	6	CH_3[c] (a)
			1.37 t	7.0		
			4.27 qt	7.0	4	CH_2 (b)
			4.84 s	- -	3	DOH (ND_3,d)
			5.08 d	18.0	1	CH (c)
			7.64 s	- -	4	Ar-H

TABLE V (CONTINUED)

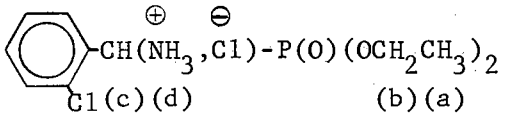
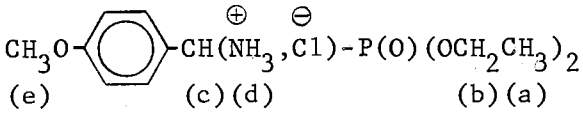
Cpd.	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Integ.	Assignment
 VIe	LX	$CDCl_3$	0.8-1.4 m	- -	6	CH_3[e] (a)
			3.5-4.3 m	- -	4	CH_2 (b)
			5.48 d	18.0	1	CH (c)
			7.1-8.2 m	- -	4	Ar-H
			7.8-8.5 m	- -	3	NH_3 (d)
 VIf	LXI	$CDCl_3$	1.18 t 1.25 t	7.0 7.0	- -	CH_3[e] (a)
			3.80 s	- -	- -	CH_3 (e)
			3.6-4.4 m	- -	- -	CH_2 (b)
			4.77 d	17.0	- -	CH (c)
			6.7-7.7 m	- -	- -	Ar-H
			10.6-11.2 m	- -	- -	NH_3[b] (d)

TABLE V (CONTINUED)

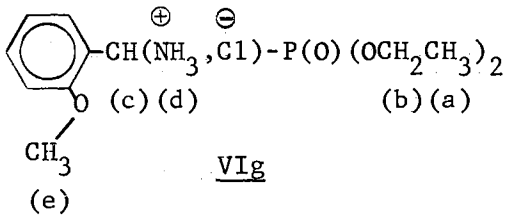
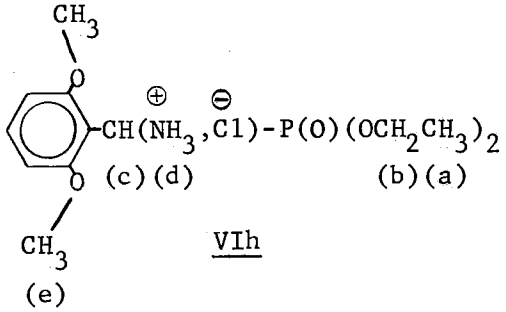
Cpd.	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Integ.	Assignment
 VIg	LXII	$CDCl_3$	1.22 q	7.0	6	CH_3[e] (a)
			3.84 s	- -	3	CH_3 (e)
			3.7-4.3 m	- -	4	CH_2 (b)
			5.17 d	18.0	1	CH (c)
			6.7-7.8 m	- -	4	Ar-H
			8.8-9.6 m	- -	3	NH_3 (d)
 VIh	LXIII	$CDCl_3$	1.20 q	7.0	6	CH_3[e] (a)
			3.83 s	- -	3	CH_3 (e)
			3.6-4.3 m	- -	4	CH_2 (b)
			5.0-5.6 d	- -	1	CH (c)
			6.3-6.7 m	- -	2	Ar-H
			7.0-7.4 m	- -	1	Ar-H
			8.6-9.4 m	- -	3	NH_3 (d)

TABLE V (CONTINUED)

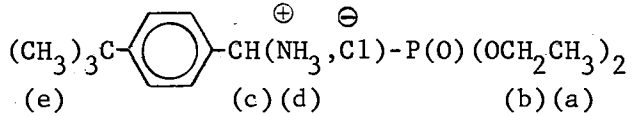
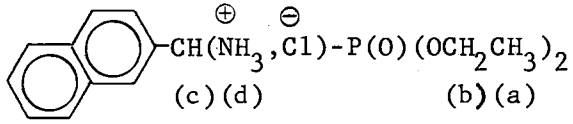
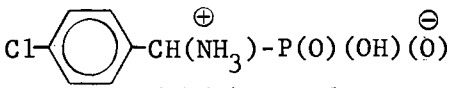
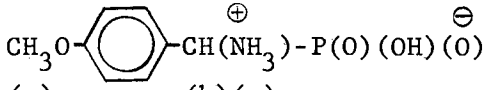
Cpd.	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Integ.	Assignment
 (e) (c)(d) (b)(a) VIi	LXIV	$CDCl_3$	1.0-1.4 m	- -	- -	CH_3[e] (a)
			1.30 s	- -	- -	CH_3 (e)
			3.7-4.3 m	- -	- -	CH_2 (b)
			4.88 d	18.0	- -	CH (c)
			7.2-7.8 m	- -	- -	Ar-H
			9.2-9.6 m	- -	- -	NH_3 (d)
 (c)(d) (b)(a) VIj	LXV	D_2O	1.19 t	7.0	6	CH_3[e] (a)
			1.25 t	7.0		
			3.8-4.4 m	- -	4	CH_2 (b)
			4.74 s	- -	3	DOH (ND_3,d)
			5.12 d	18.0	1	CH (c)
			7.3-8.2 m	- -	7	Ar-H
 (b)(a) VIIId	LXVI	CF_3COOH	5.0 d	ca.15±2	1	CH (b)
			7.47 s	- -	4	Ar-H

TABLE V (CONTINUED)

Cpd.	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Integ.	Assignment
 (c) (b)(a) VIIIf	LXVII	CF_3COOH	7.2-8.4 m	- -	3	NH_3 (a)
			3.94 s	- -	3	CH_3 (c)
			4.95 d	ca.16±2	1	CH (b)
			6.84 d	8.5	2	Ar-H
			7.28 d	8.5	2	Ar-H
			7.2-7.9 m	- -	3	NH_3 (a)

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

[b] This absorption shifts to DOH (singlet) position when D_2O is used as solvent.

[c] Magnetic nonequivalence of the alkoxy groups causes two triplets to appear for the two methyl groups of the alkoxy moiety. The separations of these triplets vary and they thus may appear as a quartet, heptet, etc. depending on the chemical shifts.

[d] Using D_2O as the solvent a splitting constant of 18 is evident.

[e] Magnetic nonequivalence of the alkoxy groups is observed; please refer to Chapter II.

TABLE VI

SYNTHESIS AND PROPERTIES OF DIETHYL ACYLPHOSPHONATES, R-CO-P(O)$(OC_2H_5)_2$

Cpd.	Moles of Acid Chloride	Moles of Triethyl Phosphite	B.p., °C(mm.)	n_D^T	Yield %	Analysis, % C Calcd.	C Found	H Calcd.	H Found	P Calcd.	P Found
IIIa	0.482	0.432	73-78(1.2)[a]	1.4199^{27}	78.4						
IIIb	0.189	0.193	98-103(2.3-3.2)[b]	1.4265^{26}[b]	62.0						
IIIc	0.287	0.288	136-137(1.4-1.5)[c]	1.5084^{25}[c]	84.0						
IIId	0.683	0.694	192-197(.4-.6)	1.5203^{28}	33.6	47.74	47.81	5.10	5.17	11.20	11.10
IIIe	0.400	0.410	158-160(2.3)	1.5070^{23}	80.4	47.76	46.71	5.10	5.25		
IIIf	0.224	0.227	175-179(1.5)[d]	1.5313^{25}	75.9						
IIIg	0.162	0.174	170-171(2.2)	1.5098^{24}	89.7	52.94	52.16	6.29	6.31		
IIIh	0.0875	0.0927	186-189(.6-.8)	1.5155^{23}	69.6	51.66	52.22	6.34	6.48		

TABLE VI (CONTINUED)

Cpd.	Moles of Acid Chloride	Moles of Triethyl Phosphite	B.p., °C(mm.)	n_D^T	Yield %	Analysis, %					
						C		H		P	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
IIIi	0.150	0.161	153-155(3.0)	1.5091^{24}	88.4	60.39	60.20	7.77	7.83	10.38	10.52
IIIj	0.147	0.168	188-191(1.2)	1.5754^{26}	70.2	61.64	61.88	5.86	5.87	10.60	10.00

[a] See McConnell, R. L. and Coover, Jr., H. W., J. Am. Chem. Soc., 78, 4450 (1956): IIIa, b.p. 62-65°(1.5 mm.).

[b] See Ackerman, B., Jordan, T. A., Eddy, C. R., and Swern D., J. Am. Chem. Soc., 78, 4444 (1956): IIIb, b.p. 124-125°(4); n_D^{20} 1.4418.

[c] See Kabachnik, M. I. and Rossiiskaya, P. A., Bull. Akad. Sci. S.S.S.R., Classe Sci. Chim., 364 (1945); Chem. Abstr., 40, 4688 (1946): IIIc, b.p. 141°(2.5); n_D^{20} 1.5065.

[d] See Berlin, K. D. and Taylor, H. A., J. Am. Chem. Soc., 86, 3862 (1964): IIIf, b.p. 158°(0.4).

TABLE VII

SYNTHESIS AND PROPERTIES OF DIETHYL ACYLPHOSPHONATE OXIMES, R-C(=NOH)-P(O)$(OC_2H_5)_2$

Cpd.	Moles of Diethyl Acylphos-phonate	Recryst. Solvent	M.p., °C	Yield %	Analysis, %							
					C		H		N		P	
					Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
IVa	0.121[a]			93.0[b]	36.92	37.11	7.23	7.44	7.18	6.51	15.87	15.70
IVb	0.0601[c]			95.5[b]	43.05	43.97	8.13	8.32			13.88	13.90
IVc	0.108[d]			98.4[b]								
IVd	0.104	ether	93.0-95.0	82.6	45.30	44.99	5.18	5.08	4.80	5.01	10.62	10.75
IVe	0.170	CCl_4-$CHCl_3$	123.3-123.8	66.7					4.80	4.82	10.62	10.77
IVf	0.0985	ether-alcohol	83.6-84.9	99.0[b]	50.18	49.98	6.32	6.25	4.88	5.08	10.78	11.00
IVg	0.104	ethylene glycol monoethyl ether	113.4-114.6	89.5					4.88	5.12	10.78	10.82
IVh	0.0875	ether-CH_2Cl_2	137.5-138.7	64.8[b]								

TABLE VII (CONTINUED)

Cpd.	Moles of Diethyl Acylphos-phonate	Recryst. Solvent	M.p., °C	Yield %	Analysis, %							
					C		H		N		P	
					Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
IVi	0.111	$CHCl_3$	117.9-119.1	76.3	57.50	57.56	7.72	7.76	4.47	4.61	9.88	9.77
IVj[f]	0.0598	CCl_4		101[b]								

[a] Liquid sample having a boiling point of 130-132°(0.3 mm.) was obtained for IVa.

[b] These yields are for the vacuum-dried, crude oxime. This was the material used for the aluminum-amalgam reduction.

[c] Liquid sample; IVb was purified by molecular distillation (details are given in the Experimental discussion).

[d] Liquid sample; IVe could not be crystallized using a variety of solvents and violently decomposed upon attempted distillation.

[e] Elemental analysis for chlorine in IVd was obtained: Calcd.: Cl, 12.15; Found: Cl, 11.99.

[f] Repeated attempts to purify oxime IVj from a variety of solvents failed. A crude sample (m.p. 86-92°) was used for IR and NMR spectra.

TABLE VIII

SYNTHESIS AND PROPERTIES OF DIETHYL α-AMINOALKYLPHOSPHONATE HYDROCHLORIDES, $R\text{-}CH(\overset{\oplus}{N}H_3,\overset{\ominus}{C}l)\text{-}P(O)(OC_2H_5)_2$

Cpd.	Moles of Oximes	M.p., °C[a]	Yield %	Analysis, %									
				C		H		Cl		N		P	
				Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
VIc[b]	0.0312	162.2-163.4	74.5	47.23	47.56	6.84	6.81			5.01	5.10	11.07	11.30
VId[b]	0.0162	173.3-173.8	48.5	42.06	40.93	5.78	5.92	22.57	22.45			9.86	9.83
VIf[c]	0.0203	169.3-169.7	82.0	46.53	46.54	6.83	6.96	11.45	11.23	4.52	4.51	10.00	9.79
VIg[d]	0.0346	126.7-127.1	37.9							4.52	4.73	10.00	10.45
VIh[e]	0.0063	143.7-144.2	85.2					10.43	10.59			9.12	9.39
VIi[b]	0.0160	168.5-169.7	77.9	53.65	53.78	8.10	8.13					9.22	10.33
VIj[b]	0.0189	181.3-183.1	58.7	52.11	54.19	6.12	6.51	10.25	10.77	4.05	4.18	8.96	9.17

[a] The hydrochlorides melted with the evolution of bubbles, giving the appearance of frothing.

[b] Recrystallized from a mixture of ether and alcohol.

[c] Recrystallized from a mixture of benzene and ligroin.

[d] Recrystallized from a mixture of ether and ligroin.

[e] Recrystallized from a mixture of ether and methylene chloride.

TABLE IX

SYNTHESIS AND PROPERTIES OF α-AMINOALKYLPHOSPHONIC ACIDS, $R\text{-}CH(\overset{\oplus}{N}H_3)\text{-}P(O)(\overset{\ominus}{O})(OH)$

Cpd.	Recryst. Solvent	Moles of Hydrochloride	M.p., °C	Yield, %	Analysis, %			
					N		P	
					Calcd.	Found	Calcd.	Found
VIIId	H_2O	0.00579	291.3-292.5	72.7	6.32	6.39	13.98	14.16
VIIIf	H_2O	0.00592	277.8-278.3	87.5	6.45	5.81	14.26	13.18
VIIIj	H_2O	0.00306	307.3-308.4	75.9	5.90	6.01	13.06	13.28

CHAPTER III

EXPERIMENTAL[a-f]

Preparation of Diethyl Acylphosphonates III. This synthesis utilized the classical Michaelis-Arbuzov rearrangement studied by Berlin and Taylor.[8,11,12] The general procedure is described. A slight excess of triethyl phosphite (Matheson, Coleman and Bell, b.p. 62-64°/24 mm.) was added dropwise to an acid chloride (commercially available materials or

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[a] The nuclear magnetic resonance (NMR) spectra were determined on a Varian Associates Model A-60 Analytical NMR Spectrometer with a field-sensing stabilizer ("Super-Stabilizer"). Tetramethylsilane (TMS) was used as an internal standard.

[b] All melting points were corrected and determined with a Thomas-Hoover capillary melting point apparatus (Arthur H. Thomas Co., Philadelphia, Pa.).

[c] The infrared (IR) spectra were obtained using a Beckman IR-5A recording spectrometer as films on sodium chloride cells for liquid samples or in potassium bromide pellets for solids. The IR spectra of solutions were obtained using a rock salt cell having a film thickness of 0.1 mm. The solvent absorptions were balanced in the spectra of IVf and VIf by adjustment of a variable-path wedge rock salt cell which opposed the second solution- (or solvent-) containing cell. Both cells were obtained from the Barnes Engineering Company, Stamford, Conn.

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

[e] High-pressure hydrogenations were performed at 100 (or higher) p.s.i. with an Aminco Hydrogenation Apparatus (American Instrument Co., Silver Spring, Maryland) having a glass-lined reaction chamber and at 50 p.s.i. (or lower) with a Paar Hydrogenation Apparatus (Paar Instrument Co., Moline, Illinois).

[f] Gas chromatographic analyses were performed on a Varian-Aerograph Model 1520 instrument having a hydrogen flame ionization detector.

synthesized from commercially available acid by standard methods) under deoxygenated, anhydrous nitrogen[4] and at such a rate that the temperature of the reaction mixture did not exceed 40°. When necessary, an ice-water bath was provided to control the temperature. The solutions became yellow while being stirred for 4 hr. Chloroethane was evolved during the course of the reaction. The products were purified by vacuum distillation. Elemental analyses and physical properties (Table VI) and spectral data (Tables I and V) were used to confirm the structures of new diethyl acylphosphonates III. Where the acylphosphonates were known, the comparison of spectral and physical properties with those of authentic samples confirmed their identities.

Deviations from the above general procedure were employed with 2-naphthoyl chloride and 2,6-dimethoxybenzoyl chloride (both were solids). These aroyl chlorides were heated (48° for β-naphthoyl chloride and 66° for 2,6-dimethoxybenzoyl chloride, i.e., to temperatures just above their melting points) prior to the addition of triethyl phosphite. The general procedure was then followed.

Preparation of Oximes of Diethyl Aroylphosphonates IV. A diethyl aroylphosphonate[g] was slowly added (dropwise at such a rate so as to maintain the temperature of the reaction mixture below 30°) to 200 ml. of ethanol (absolute) containing hydroxylamine hydrochloride[g] (J. T. Baker Chemical Co., analytical reagent grade) and pyridine[g] (J. T. Baker Chemical Co., analytical reagent grade). The yellow color of the

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[g] The quantities of diethyl aroylphosphonates were varied (they are listed in Table VII) from 0.05 mole to 0.2 mole and the quantities of hydroxylamine hydrochloride and pyridine were correspondingly varied so as to maintain a 0.100:0.133:0.150 molar ratio of aroylphosphonate, hydroxylamine hydrochloride and pyridine.

diethyl aroylphosphonate slowly disappeared [except in the case of diethyl 2,6-dimethoxybenzoylphosphonate (IIIh)] in the course of oxime formation. The mixtures were stirred at room temperature for 72 hr. Evaporation of the ethanol in vacuo gave a syrup which was mixed with 75 ml. of distilled water. This aqueous mixture was extracted with three 75-ml. portions of methylene chloride (purified grade). The organic layers were combined and dried ($MgSO_4$). The solvent was removed in vacuo, and the resulting syrup was dried (1 to 5 mm., room temperature) for 1 to 3 hr. Table VII lists the diethyl aroylphosphonate III used recrystallizing solvents, melting points, results of elemental analyses, and yields of crude solid oximes. IR spectra (Table II) and NMR spectra (Table V) are also recorded.

Deviations from the above general procedure are now described. Efforts to purify the crude diethyl benzoylphosphonate oxime (IVc) through crystallization from a variety of solvents failed. Attempted distillation of this oxime resulted in a violent decomposition as the temperature at the head of the 10-cm. Vigreux column approached $60^{\circ}/0.7$ mm. The vacuum-dried diethyl benzoylphosphonate oxime (IVc), therefore, was used without further purification.

In addition to stirring at room temperature for 72 hr., the reaction mixture for the preparation of diethyl 2,6-dimethoxybenzoylphosphonate oxime (IVh) required boiling for 2 hr. at the end of the stirring period to complete the reaction.

Preparation of Oximes of Diethyl Acylphosphonates IVa and IVb. The diethyl acylphosphonate oximes IVa and IVb were prepared in the manner described previously for the aroylphosphonate oximes. However, the oximes were liquids which could generally not be purified by

vacuum distillation. Diethyl acetylphosphonate oxime (IVa) was vacuum distilled b.p. 130-132/0.3 mm.) in one experiment. An attempted repetition of this distillation resulted in a violent decomposition when the pot temperature reached 160°/2 mm. A Kontes Falling Film Molecular Still Apparatus at a temperature of 111° (toluene) and a pressure of 0.3 mm. provided a small analytical sample of pure, clear, colorless diethyl butyrylphosphonate oxime (IVb). Spectral data for the diethyl acylphosphonate oximes are listed in Tables II and V. Table VI lists the physical properties for these oximes.

Preparation of Aluminum-Amalgam. This procedure is a modification of that used by Hartman and Phillips.[32] Approximately 100 ml. of aqueous 5% mercuric chloride (Baker and Adamson, reagent grade) solution was added to 10.0 g. (3.70 g. atom) of aluminum foil (6 in. x 6 in. x 0.001 in., purified grade metal, J. T. Baker Chemical Co.) which had been cut into approximately 2-cm. squares. The metal remained in contact with the $HgCl_2$ solutions for 5 min. to effect amalgamation. Three 1-liter portions of distilled water were used to wash the amalgam. The amalgamated-aluminum foil was used immediately since it reacts rapidly with moisture.

Aluminum-Amalgam Reduction of Oximes IV of Diethyl Aroylphosphonates and Subsequent Salt Formation. Aluminum-amalgam reduction could be performed either on the pure aroylphosphonate oximes or on the crude aroylphosphonate oximes which had been vacuum-dried. Attempted aluminum-amalgam reduction of diethyl acetylphosphonate oxime (IVa) failed to produce diethyl 1-aminoethylphosphonate (Va).

To aluminum-amalgam (freshly prepared from 5.0 g. of aluminum foil) was added 500 ml. of ethanol (absolute). The oximes (0.01 to 0.05 mole;

actual quantities are listed in Table VIII) in 200 ml. ethanol (absolute) were added to the aluminum-amalgam mixture. Approximately 200 ml. of distilled water was added and the mixture was stirred for 24 hr. The gray gelatinous solids that formed were filtered out and washed with two 100-ml. portions of ethanol (absolute). All washings were combined with the mother liquor. The solvents were stripped in vacuo from the crude diethyl α-aminoalkylphosphonates which were subsequently dissolved in approximately 100 ml. of anhydrous ether. Hydrogen chloride (anhydrous, The Matheson Co., Inc.) was slowly bubbled through the ether solution for 5 min. The hydrochlorides VI of the diethyl α-aminoalkylphosphonates separated either as oils or white, crystalline solids. The oily materials were crystallized using various solvents (the solvents and physical properties are listed in Table VIII). IR spectra (Table III) and NMR spectra (Table V) were recorded.

Aluminum-Amalgam Reduction of Benzoylated Diethyl Acetylphosphonate Oxime. Crude diethyl acetylphosphonate oxime (12.20 g., 0.063 mole) and 5.62 g. (0.071 mole, J. T. Baker Chemical Co., purified grade) of pyridine were dissolved in 20 ml. of ether (anhydrous) and added dropwise to a solution of 9.49 g. (0.067 mole, Baker and Adamson, purified grade) of benzoyl chloride in 20 ml. of ether (anhydrous). The solution of the oxime was added slowly over a 15-min. period and the mixture stirred for 1 hr. The reaction was slightly exothermic and a white precipitate slowly formed. The mixture was filtered and freed from ether in vacuo; the resulting syrup was subjected to a vacuum of 2 mm. for 2 hr. The yield of crude CH_3-C(=N-O-CO-C_6H_5)-P(O)(OC_2H_5)$_2$ was 13.80 g. (73.2%). The IR spectrum of the crude benzoylated oxime (Plate XXI) exhibited peaks for C=O (1752 $cm.^{-1}$), P→O (1249 $cm.^{-1}$), P-O-C_2H_5

(1164 cm.$^{-1}$) and monosubstituted benzene (704 and 1604 cm.$^{-1}$). NMR analysis showed a triplet at δ1.43 (J=7 c.p.s.), a doublet at δ2.36 (J=11 c.p.s.), a quintet at δ4.36 (J=7 c.p.s.) and a multiplet δ7.5 to 8.3).

Crude CH_3-C(=N-O-CO-C_6H_5)-P(O)(OC_2H_5)$_2$ (12.92 g., 0.0432 mole) was reduced by the same aluminum-amalgam procedure as used for the aroylphosphonate oximes. The syrup obtained from removal (in vacuo) of the solvents from the filtrate of the reduction mixture was distilled through a 10-cm. Vigreux column. The yield of diethyl 1-aminoethylphosphonate (Va) was 1.39 g. (20.6%) based on the crude benzoylated oxime. A refractive index of 1.4394_D^{28} (lit.,[51] 1.4150_D^{20}) was observed for the pure amine. The structure of the diethyl 1-aminoethylphosphonate (Va) was indicated by NMR and IR analyses in addition to the elemental analysis.

Anal. Calcd. for $C_6H_{16}O_3NP$: C, 39.78; H, 8.91; N, 7.73; P, 17.10.
Found: C, 40.94; H, 8.90; N, 7.94; P, 17.08.

The IR spectrum (Plate XXII) for diethyl 1-aminoethylphosphonate (Va) shows no absorption for a phenyl or carbonyl group. Peaks for N-H (3366, 3290 cm.$^{-1}$), P→O (1236 cm.$^{-1}$) and P-O-C_2H_5 (1166 cm.$^{-1}$) were observed. NMR data (Plate LVI) is described in Table V.

An attempted aluminum-amalgam reduction of acetylated diethyl propionylphosphonate oxime gave a highly stable lyophilic colloid which could not be separated from the solution either by filtration or by centrifuging at speeds up to 1800 r.p.m. for 45 min.

Hydrolysis of the Hydrochlorides VI of Diethyl α-Aminoalkylphosphonates to α-Aminoalkylphosphonic Acids VIII. The free α-aminoalkylphosphonic acids VIII were obtained by boiling the hydrochlorides VI of diethyl α-aminoalkylphosphonates in 9M hydrochloric acid for 4 to 12 hr.

The water was removed in vacuo giving the crude hydrochloride VII of the α-aminoalkylphosphonic acids. These salts were dissolved in a minimum of cold water and heated to boiling. The less soluble free acid precipitated as a white, crystalline solid which was collected after cooling. The acids along with some of them physical properties are listed in Table IX. Infrared and NMR spectral data for the free acids are listed in Tables IV and V.

The Direct Preparation of α-Amino-p-chlorobenzylphosphonic Acid From Diethyl p-Chlorobenzoylphosphonate. A total of 23.12 g. (0.0761 mole, b.p. 164-166/.4-.6 mm.) of diethyl p-chlorobenzoylphosphonate (IIId) was added dropwise to a mixture of 7.05 g. (0.101 mole, J. T. Baker Chemical Co., analytical reagent grade) of hydroxylamine hydrochloride, 13.11 g. (0.166 mole, J. T. Baker Chemical Co., reagent grade) of pyridine and 100 ml. of ethanol (absolute) at such a rate that the temperature of the mixture did not exceed 30°. The mixture was stirred for 72 hr. The solvent was removed in vacuo and 100 ml. of water was added to the syrup. Four 100-ml. portions of CH_2Cl_2 were used to extract the aqueous mixture. The CH_2Cl_2 layers were dried ($MgSO_4$) and the solvent removed in vacuo. The crude diethyl p-chlorobenzylphosphonate oxime was dissolved in 100 ml. of ethanol and added to a mixture of aluminum-amalgam [prepared as described previously from 20 g. of aluminum foil, 1 liter of ethanol (absolute) and 400 ml. of water]. These materials were stirred for 40 hr. The solids were filtered off and washed with absolute ethanol. The washings and filtrate were combined. The solvents were removed in vacuo and the resultant syrup was boiled with 130 ml. of conc. hydrochloric acid and 100 ml. of water for 14 hr.

Removal of the volatile components in vacuo left an amber syrup. This syrup was mixed with 30 ml. of water and 40 ml. of conc. hydrochloric acid and decolorized. The solution was filtered and the solvent removed in vacuo. A syrup resulted which was mixed with 30 ml. of water; this solidified upon standing. The mixture was filtered and the solid obtained was dissolved in a minimum of cold water and boiled. The less soluble free acid precipitated as a white crystalline solid which was collected after cooling. The yield of α-amino-p-chlorobenzylphosphonic acid was 11.16 g. (66.5%) based on diethyl-p-chlorobenzoylphosphonate. The IR and NMR spectra were identical to those for VIIId (Plates XXXIII and LXVI). A melting point of 288.5-289.2° [a mixture melting point determination with authentic VIIId (m.p. 291.3-292.5°) sample was 290.4-291.8°].

Preparation and Reduction of the p-Nitrophenylhydrazone of Diethyl α-Aminobenzylphosphonate With Aluminum-Amalgam. Synthesis of α-Aminobenzylphosphonic Acid. Exactly 4.67 g. (0.0305 mole, Eastman, White Label grade) of p-nitrophenylhydrazine, 6.52 g. (0.0269 mole, b.p. 120-124°/0.43-0.47 mm.) of diethyl benzoylphosphonate (IIIc), 1 liter of ether (anhydrous, reagent grade and 0.52 g. (0.00865 mole, analytical reagent grade, J. T. Baker Chemical Co.) of glacial acetic acid were stirred together at room temperature for 24 hr. The ether was removed in vacuo until about 100 ml. of solution remained. A total of 3.57 g. (35.2%) of diethyl benzoylphosphonate p-nitrophenylhydrazone crystallized and gave a melting point of 125.9-126.6° (lit.,[50] 126°). An IR spectrum showed absorptions at 1164 (P-O-C_2H_5), 1181 (P→O) and 1329 $cm.^{-1}$ (NO_2).

Diethyl benzoylphosphonate p-nitrophenylhydrazone (4.16 g., 0.011 mole) was added to aluminum-amalgam [freshly prepared from 10.2 g. (0.378 g. atom) of aluminum foil using the procedure described previously] in 1 liter of ethanol (95%, denatured) and 200 ml. distilled water. The mixture was allowed to stand for 24 hr. The solids were filtered out and washed with 500 ml. of 95% ethanol (denatured) and the combined filtrates were treated with 300 ml. of conc. hydrochloric acid. The solution was slowly distilled over a 6-hr. period until the volume amounted to 500 ml. The resulting solution was further concentrated to 50 ml. in vacuo, cooled overnight, and filtered. The filtrate was evaporated to dryness and dissolved in 200 ml. ethanol (95%, denatured). The solution when neutralized to a pH of 5.0 through the addition of aniline gave the crude product. This crude solid was isolated by filtration and dissolved in 30 ml. of warm water, and the pH was adjusted to 12 by the addition of 10% NaOH. The alkaline solution was extracted with two 50-ml. portions of benzene. The aqueous layer was made acid to pH 3.5 using 1:1 hydrochloric acid. The acid solution was concentrated on a hot plate until crystallization started. After cooling, the precipitate was filtered out and washed with 5 ml. ice water. The colored product was dissolved in 50 ml. water and decolorized with charcoal after which the solution was concentrated to 10 ml. and cooled to produce the white crystalline acid. A yield of 0.653 g. (31.7%) of α-aminobenzylphosphonic acid was obtained and a melting point of 269-270° (lit.,[51] m.p. 272-273°) observed. The IR spectrum (Plate XXXII) has its major absorptions listed in Table IV.

Reduction of Diethyl Benzoylphosphonate p-Nitrophenylhydrazone With Hydrogen and Palladium-Carbon Catalyst. This reduction was a repetition

of the procedure of Kosolapoff, who reported the palladium-carbon reduction of diethyl benzoylphosphonate p-nitrophenylhydrazone and subsequent hydrolysis to α-aminobenzylphosphonic acid in 68% yield.[50] Kosolapoff was unable to purify the product and reported the following analysis:

Anal. Calcd. for $C_7H_{10}O_3NP$: N, 10.05.
Found: N, 9.72, 9.65.

Diethyl benzoylphosphonate p-nitrophenylhydrazone (3.69 g., 0.00977 mole), 175 ml. of ethanol (absolute) and 5.5 g. of 5% Pd/C (Engelhard Industries) were placed in a thick-walled glass container of 200 ml. capacity, mounted on a Paar Hydrogenation Apparatus, and purged three times with hydrogen gas. The p-nitrophenylhydrazone was reduced over 18 hr. with constant shaking under a beginning hydrogen pressure of 54 p.s.i. The final pressure of the system was 49 p.s.i. The mixture was filtered giving a yellow solution which turned red upon standing. Approximately 50 ml. of water and 100 ml. of conc. hydrochloric acid were added to the filtrate and the mixture was boiled for 4 hr. at 92°. The solution was concentrated to 50 ml. and cooled to yield rose-colored crystals. The solids were filtered out, the filtrate evaporated to dryness in vacuo, and the residue dissolved in 200 ml. of ethanol (absolute). Aniline was added until the pH was 5.0 (pHydrion indicator paper). The solution was evaporated to dryness and the residue dissolved in 30 ml. of warm water. The pH of the solution was adjusted to 12 using 10% NaOH and the solution was extracted twice with benzene. The pH of the aqueous layer was adjusted to 3.5 using 1:1 hydrochloric acid. The brown solution was decolorized with charcoal and concentrated to 5 ml. Upon cooling 0.356 g. (19.5%) of α-aminobenzylphosphonic acid

was collected, m.p. 267-268 (lit.,[51] m.p. 272-273°). The elemental analysis was unsatisfactory.

Anal. Calcd. for $C_7H_{10}O_3NP$: C, 44.93; H_5 5.39; P, 16.56.
Found: C, 47.54; H, 6.01; P, 13.77.

The IR spectrum was identical to that described by Plate XXXII.

Reduction of Diethyl Benzoylphosphonate Oxime (IVc) With Hydrogen and W-6 Raney Nickel. Exactly 27.0 g. (0.104 mole) of crude, vacuum-dried diethyl benzoylphosphonate oxime (IVc), 150 ml. of ethanol (absolute) and a teaspoonful of W-6 Raney nickel[14] were placed in a thick-walled 200 ml. glass vessel and mounted on a Paar Hydrogenation Apparatus. After purging the apparatus three times with hydrogen, it was filled with this gas to a pressure of 50 p.s.i. The mixture was shaken for 6 days. The metal was filtered out and the filtrate concentrated in vacuo to a pale yellow oil which was dissolved in 60 ml. of ethanol (absolute) and 60 ml. ether (anhydrous). Hydrogen chloride (anhydrous, The Matheson Co., Inc.) was bubbled through the solution for 20 min. Fine white needles were collected and washed with two 50-ml. portions of ether. A total of 18.65 g. (74.5%) of diethyl α-aminobenzylphosphonate hydrochloride (VIc) was obtained, m.p. 162.2-163.4 (with frothing).

Anal. Calcd. for $C_{11}H_{19}O_3NPCl$: C, 47.23; H, 6.84; N, 5.01; P, 11.07.
Found: C, 47.56; H, 6.81; N, 5.10; P, 11.30.

The IR and NMR spectra for this compound are identical to those obtained through aluminum-amalgam reduction (Tables III and V).

An attempted reduction of crude diethyl p-methoxybenzoylphosphonate oxime (IVf) in the glass-lined Aminco Hydrogenation Apparatus ($P_{(H_2)}$ = 250 p.s.i.) failed. The metal had lost its activity (i.e., would not

spontaneously ignite in air) and the residual syrup crystallized (m.p. 85.0-86.2°). IR analysis showed the material to be unreacted diethyl p-methoxybenzoylphosphonate oxime (IVf).

Attempted Reductive Amination of Diethyl Benzoylphosphonate (III). Approximately 75 ml. ethanol (absolute) and 17.2 g. (0.071 mole) of diethyl benzoylphosphonate (IIIc, b.p. 142-151°/3.0 mm.) were placed in the glass-liner of the reaction vessel for the Aminco Hydrogenation Apparatus and cooled to -80° (acetone-dry ice). Approximately 1.7 g. (0.10 mole) of ammonia (anhydrous liquid condensed from gas, the Matheson Co., Inc.) and ½ teaspoonful of W-6 Raney nickel[14] were added. The hydrogenation apparatus was assembled and flushed five times with hydrogen and finally filled with hydrogen at 1000 p.s.i. The system was shaken at this pressure for 19 hr. The metal was removed from the mixture by filtration and found to have retained its activity (the metal catalyst was considered to be active if it spontaneously ignited in air). The ethanol was removed from the solution in vacuo leaving a syrup having the odor of ethyl benzoate. GLC of the syrup (injected neat) exhibited five peaks, one having the same retention time as ethyl benzoate (injected neat under the same conditions). Approximately 5 ml. of the syrup was dissolved in 20 ml. of ether. Dry hydrogen chloride was bubbled through the solution for 10 min. A white solid formed. The solid was filtered out and remained solid below 320° [diethyl α-aminobenzylphosphonate hydrochloride (VIc) melts at 162.2-163.4°]. The reaction was not studied further.

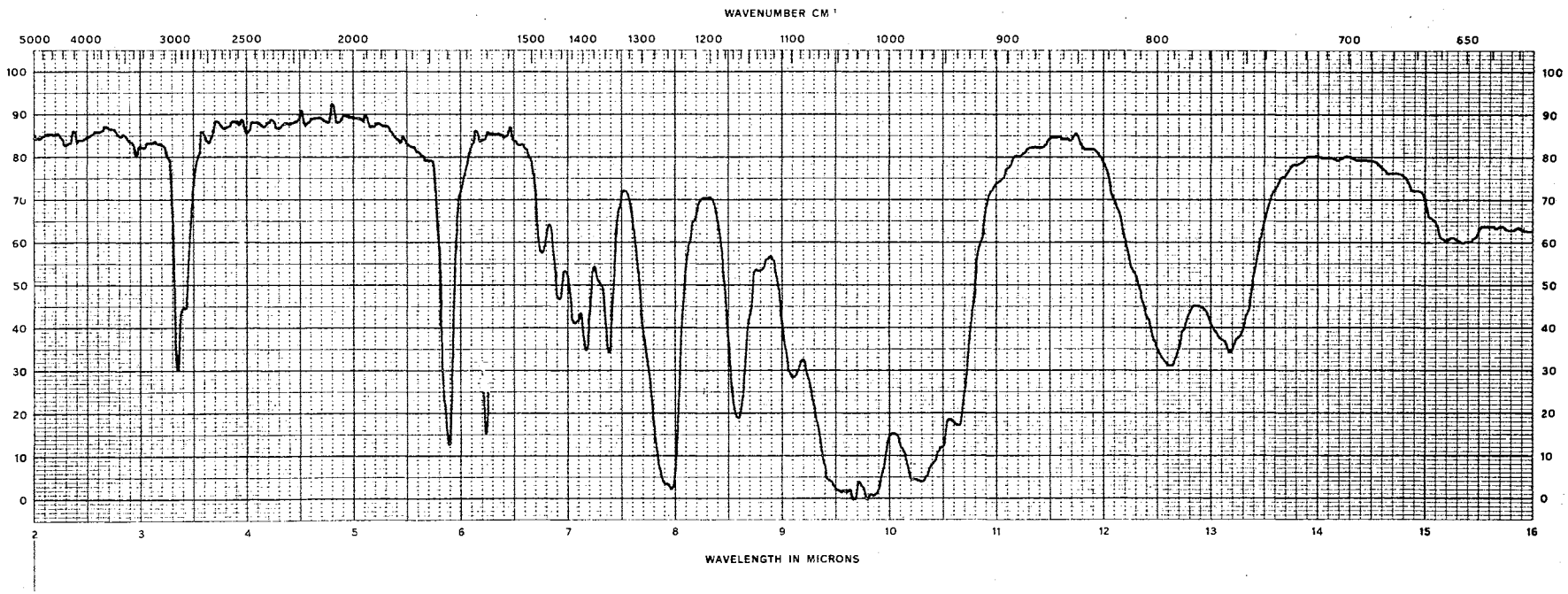
Dilution Studies by IR Analysis of Diethyl p-Methoxybenzoylphosphonate Oxime (IVf) and Diethyl α-Amino-p-methoxybenzylphosphonate Hydrochloride (VIf). IR spectra of IVf and VIf in chloroform

(spectro-quality grade, Matheson, Coleman and Bell) solution were determined using the cells previously described. After balancing the cells until a flat baseline was obtained for the chloroform, solutions of IVf and VIf at several concentrations were analyzed.

Concentrations and absorptions for chloroform solution of oxime IVf were found as follows: 10%; O-H (3225 $cm.^{-1}$), P→O (1250 $cm.^{-1}$); 2.9%, O-H (3245 $cm.^{-1}$), P→O (1250 $cm.^{-1}$); and 1.3%; O-H (3195 $cm.^{-1}$), P→O (1250 $cm.^{-1}$). Plate XVI shows the IR spectrum of the pure, solid oxime taken as a KBr pellet, XVI shows the IR spectrum of the pure, solid oxime taken as a KBr pellet, with an O-H absorption at 3208 $cm.^{-1}$ and a P→O absorption at 1240 $cm.^{-1}$.

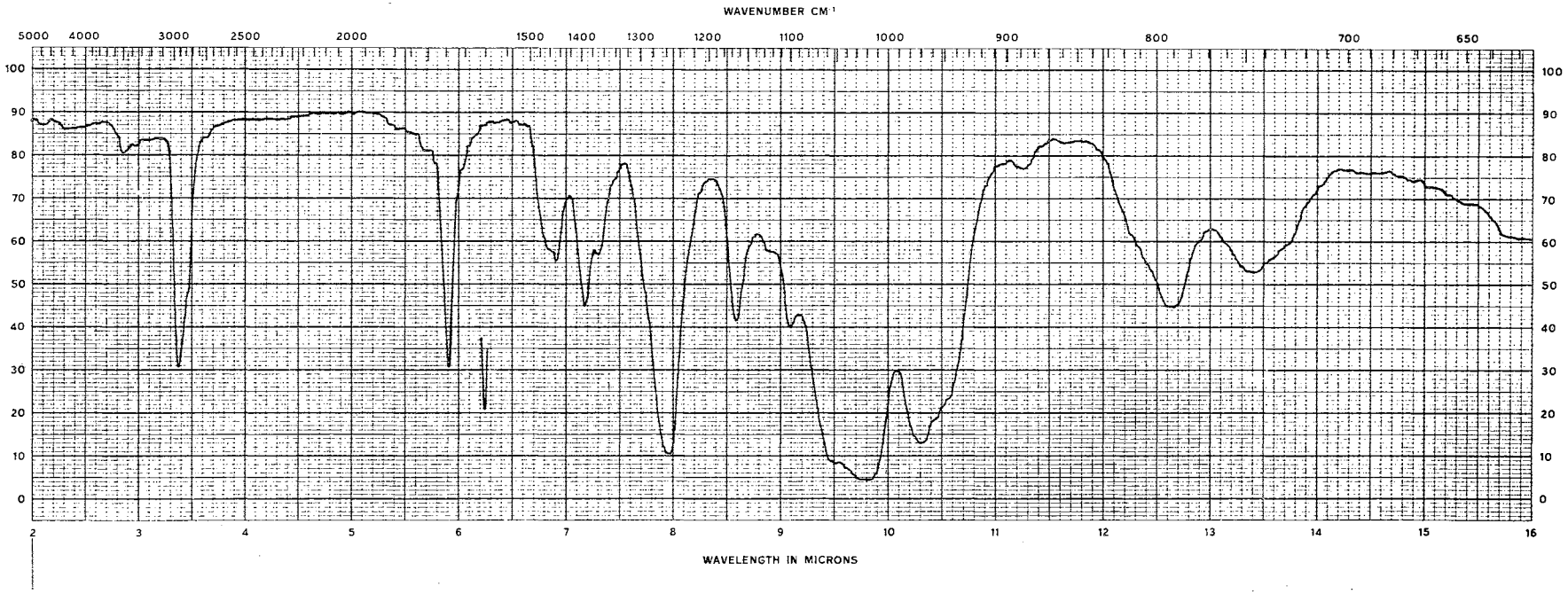
After the baseline for chloroform was balanced, the IR spectra for solutions of diethyl α-amino-p-methoxybenzylphosphonate hydrochloride (VIf) were obtained. A 1.3% solution of the salt exhibited an N-H frequency at 2950 $cm.^{-1}$ and a P→O frequency at 1250 $cm.^{-1}$. When a 0.937 solution of the hydrochloride VIf was examined, N-H absorption at 2965 $cm.^{-1}$ and P→O absorption at 1244 $cm.^{-1}$ were observed. A KBr pellet of diethyl α-amino-p-methoxybenzylphosphonate hydrochloride (VIf, Plate XXVII) exhibited a N-H peak at 2970 $cm.^{-1}$ and a P→O absorption at 1244 $cm.^{-1}$.

Plate I



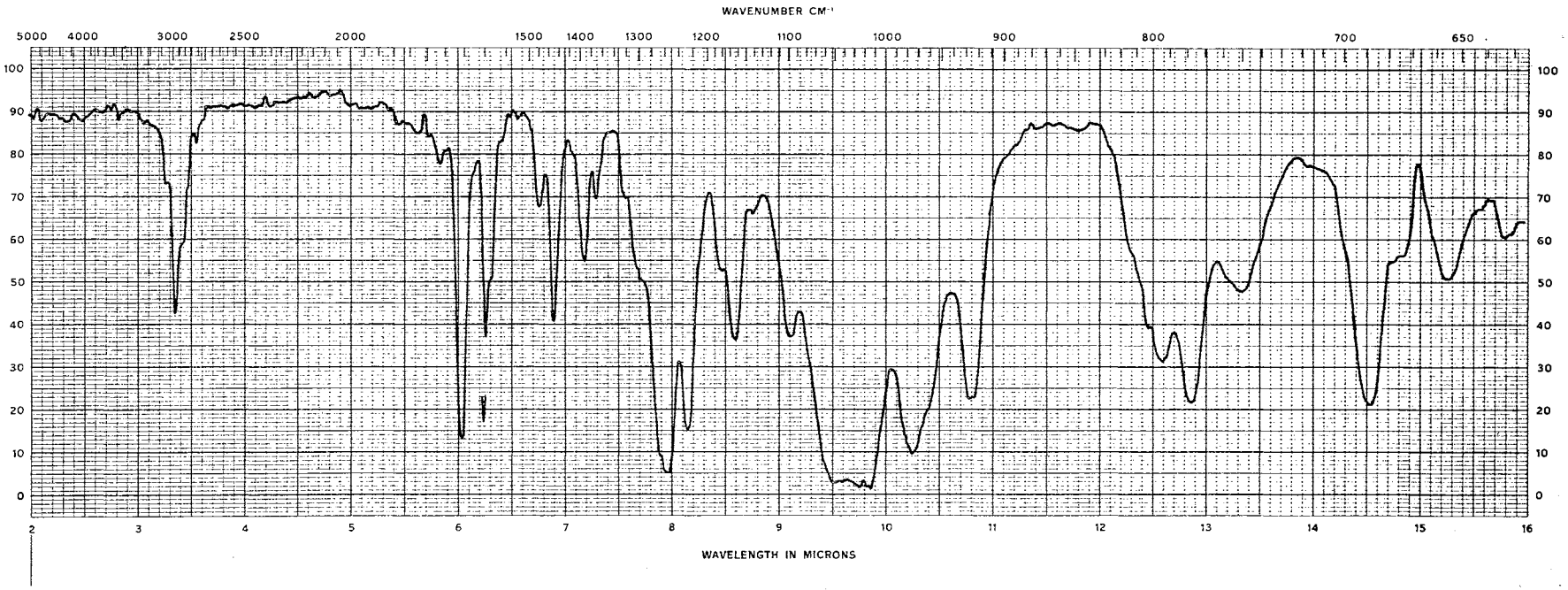
Diethyl Acetylphosphonate (IIIa), Film on NaCl Plates

Plate II



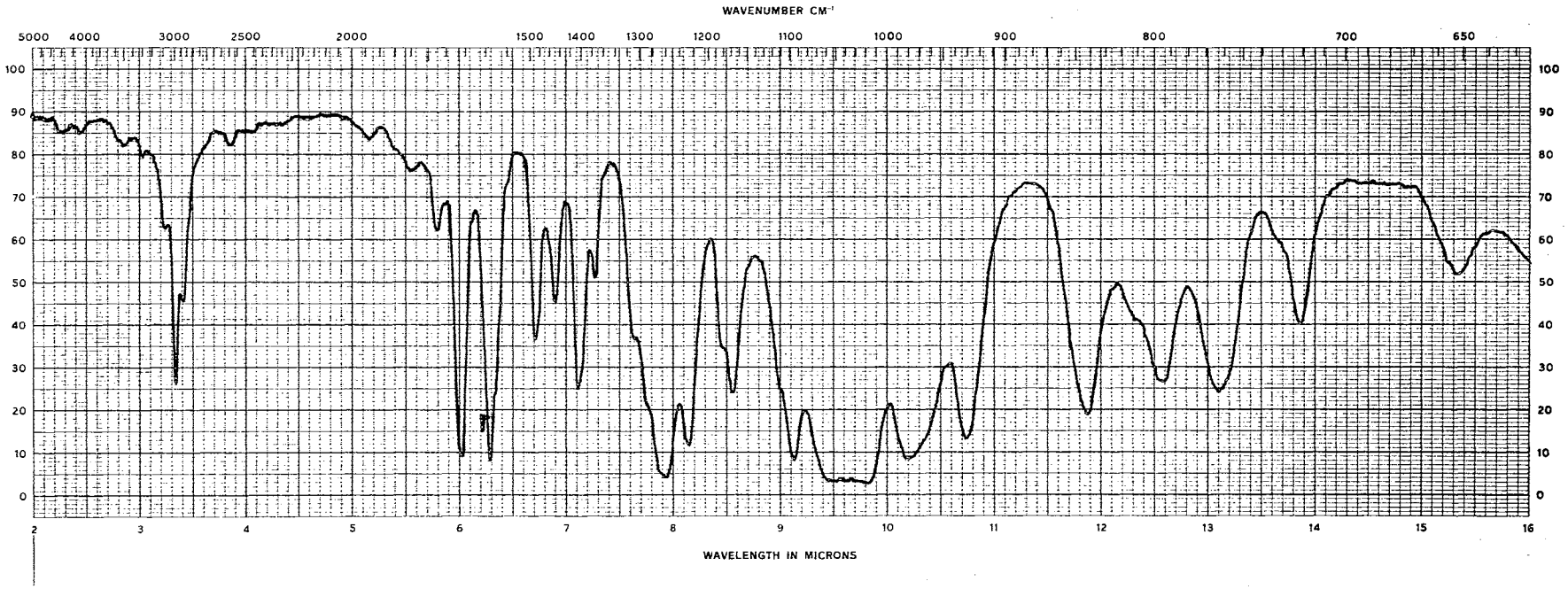
Diethyl Butyrylphosphonate (IIIb), Film on NaCl Plates

Plate III



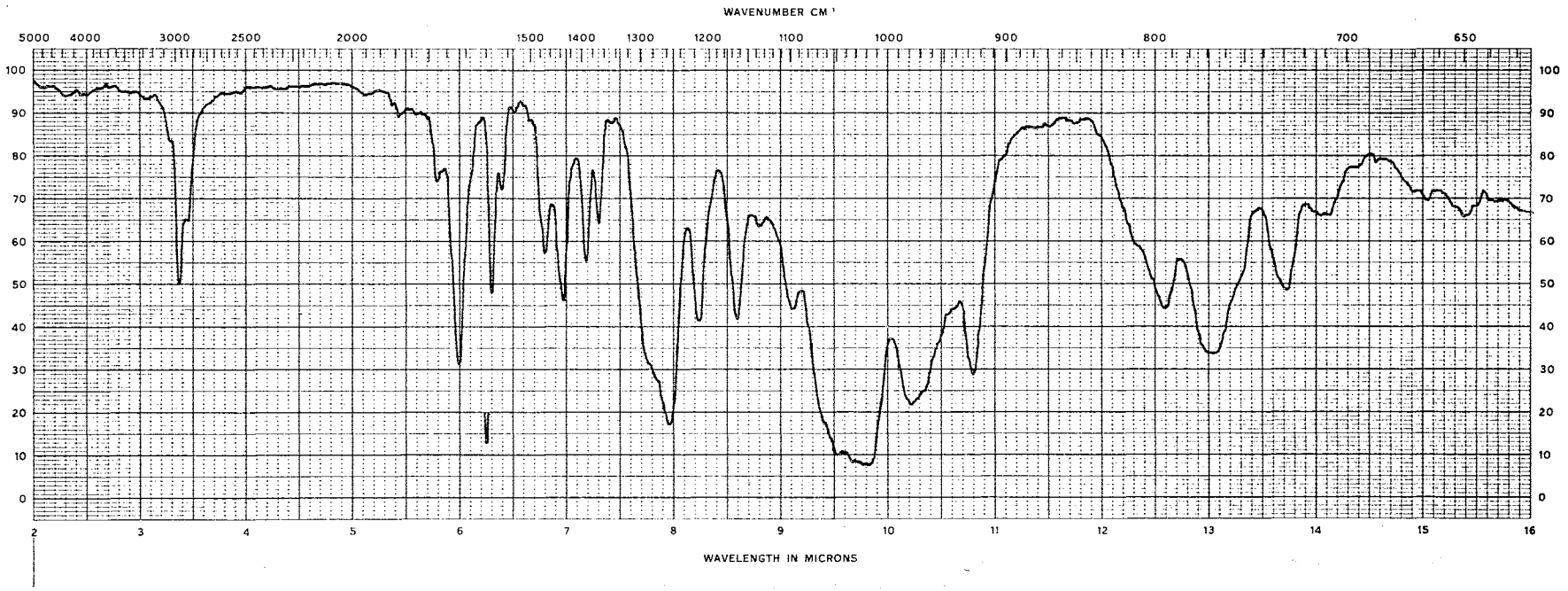
Diethyl Benzoylphosphonate (IIIc), Film on NaCl Plates

Plate IV



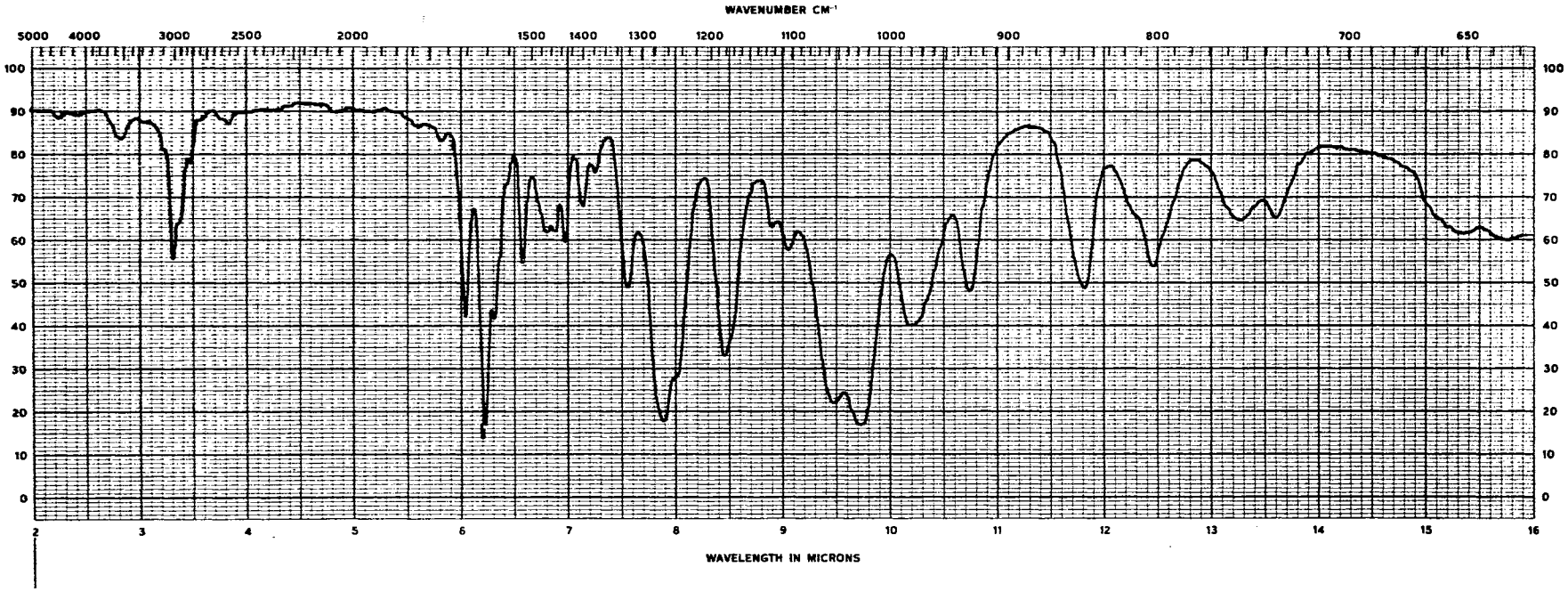
Diethyl p-Chlorobenzoylphosphonate (IIId), Film on NaCl Plates

Plate V



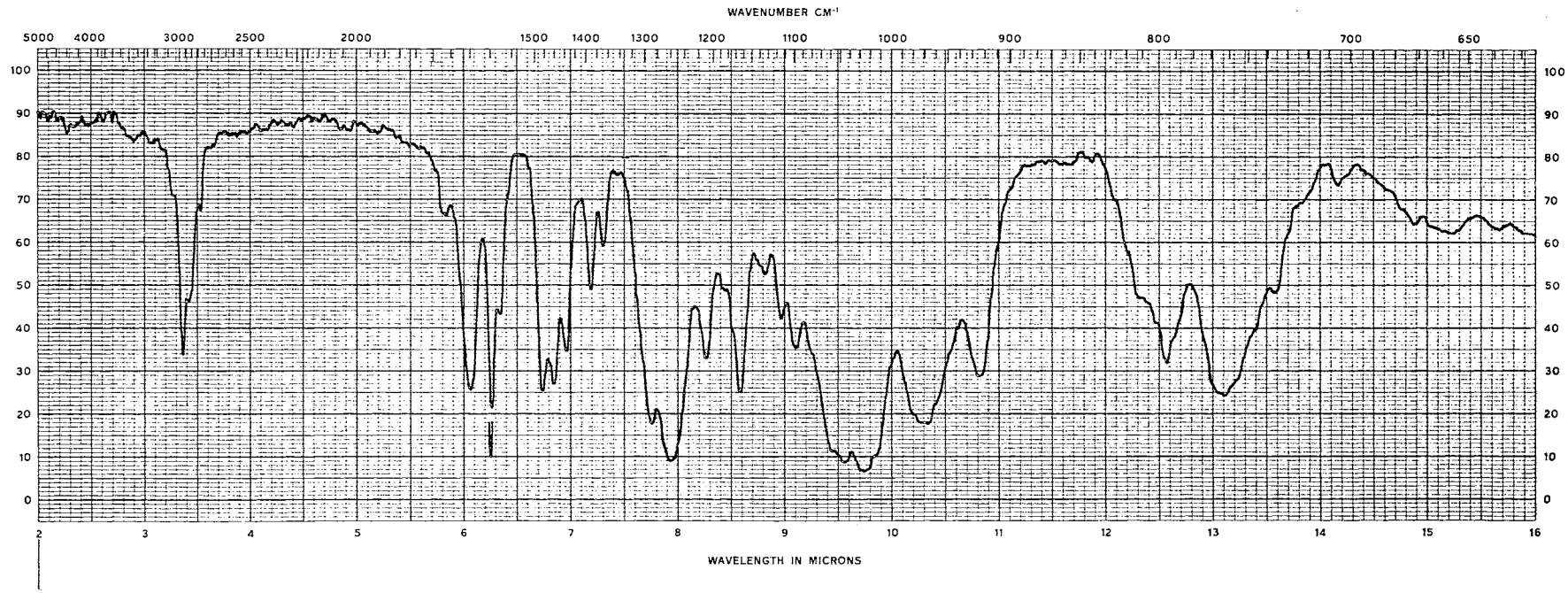
Diethyl o-Chlorobenzoylphosphonate (IIIe), Film on NaCl Plates

Plate VI



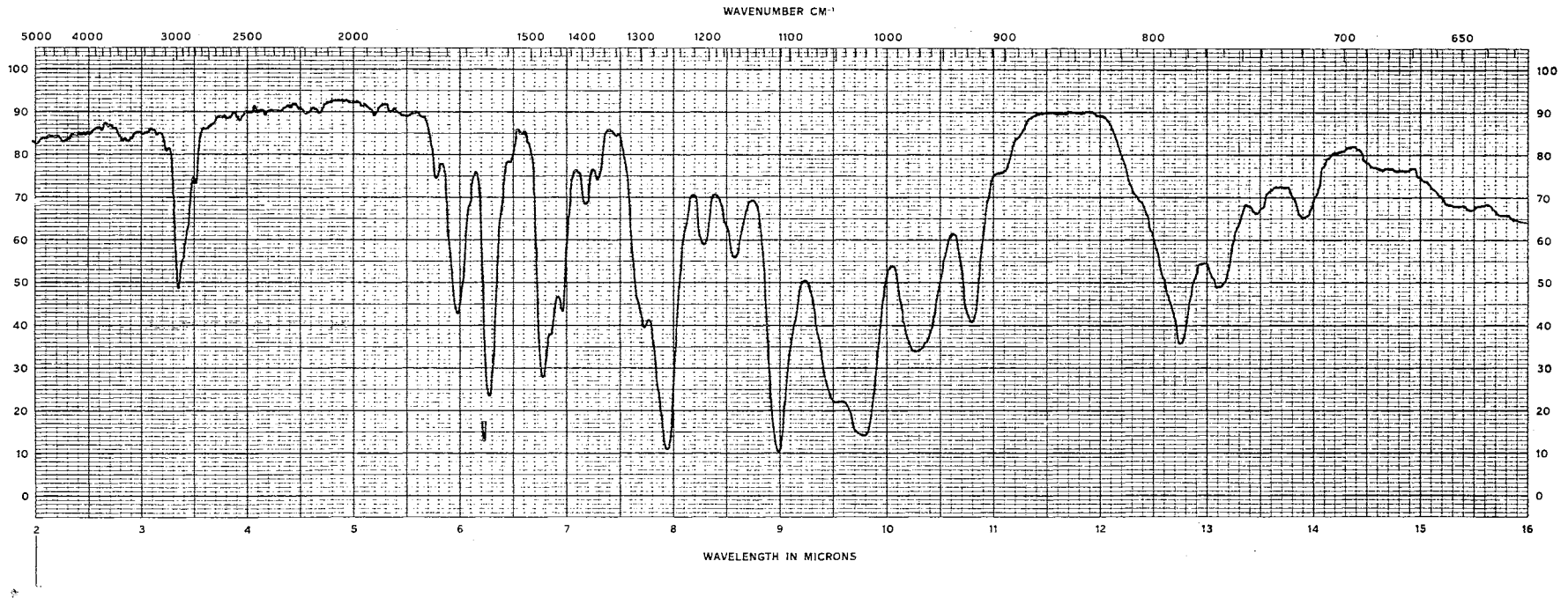
Diethyl p-Methoxybenzoylphosphonate (IIIf), Film on NaCl Plates

Plate VII



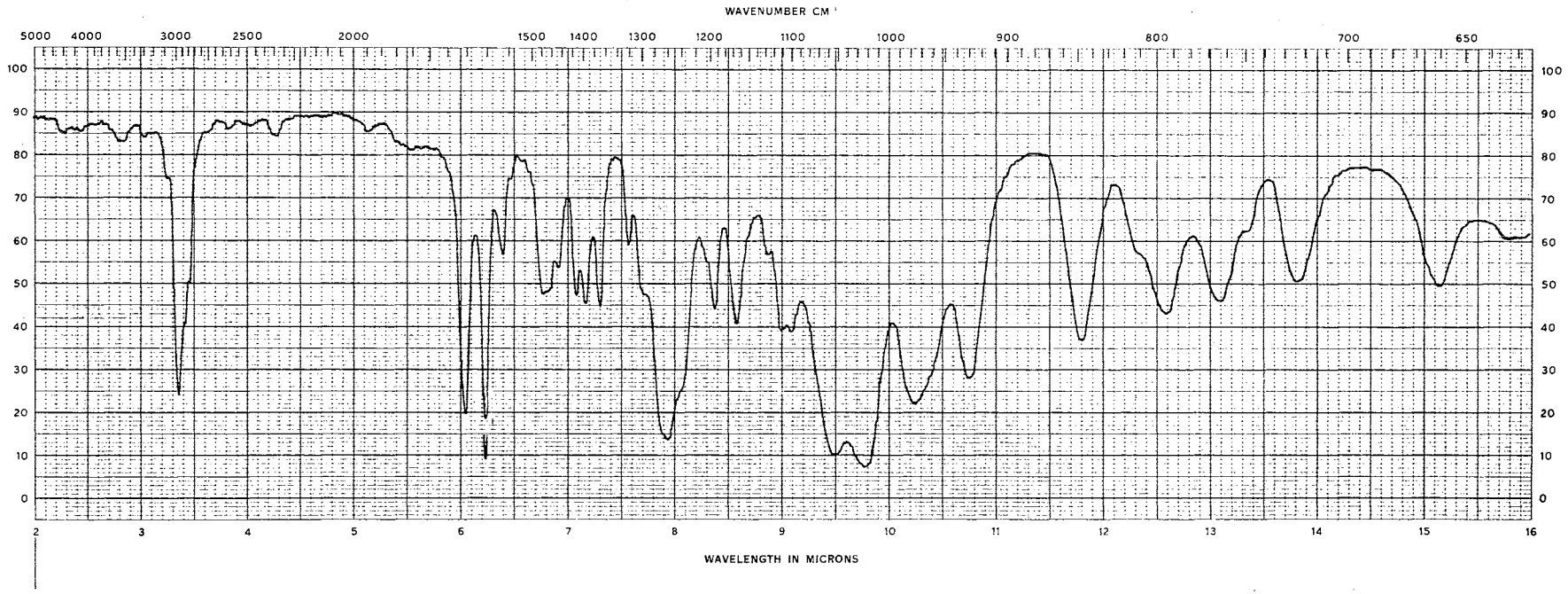
Diethyl o-Methoxybenzoylphosphonate (IIIg), Film on NaCl Plates

Plate VIII



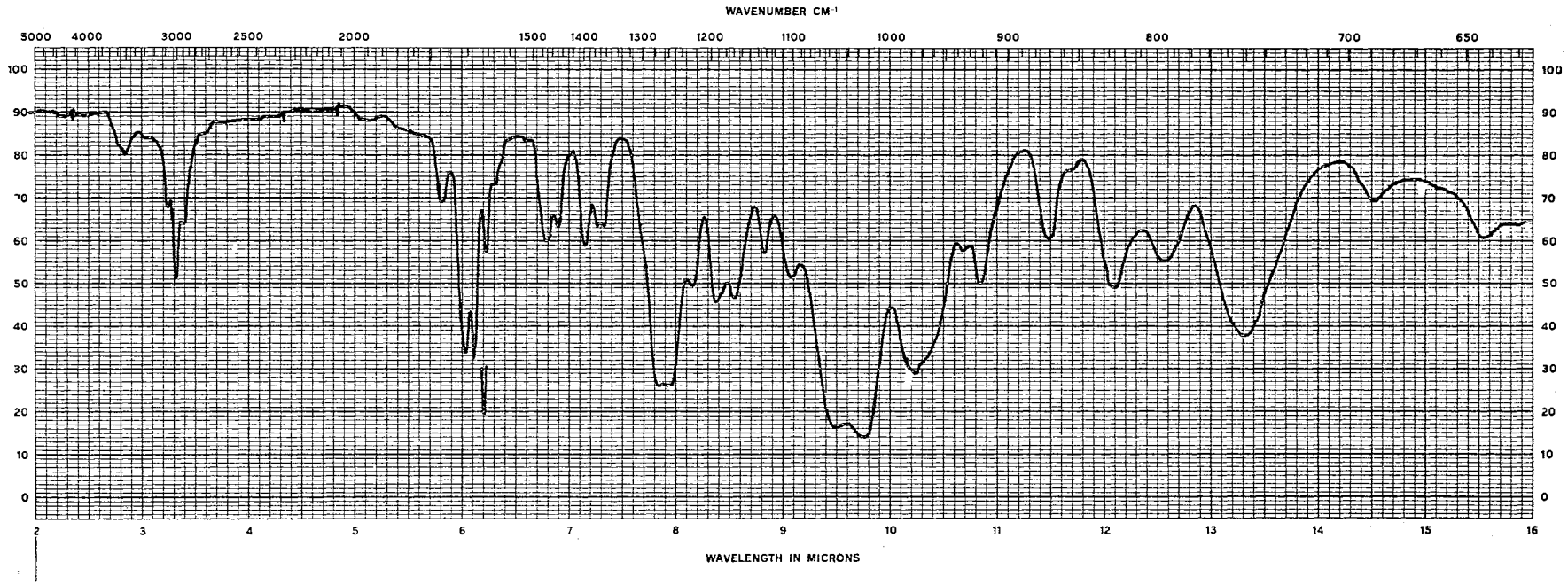
Diethyl 2,6-Dimethoxybenzoylphosphonate (IIIh), Film on NaCl Plates

Plate IX



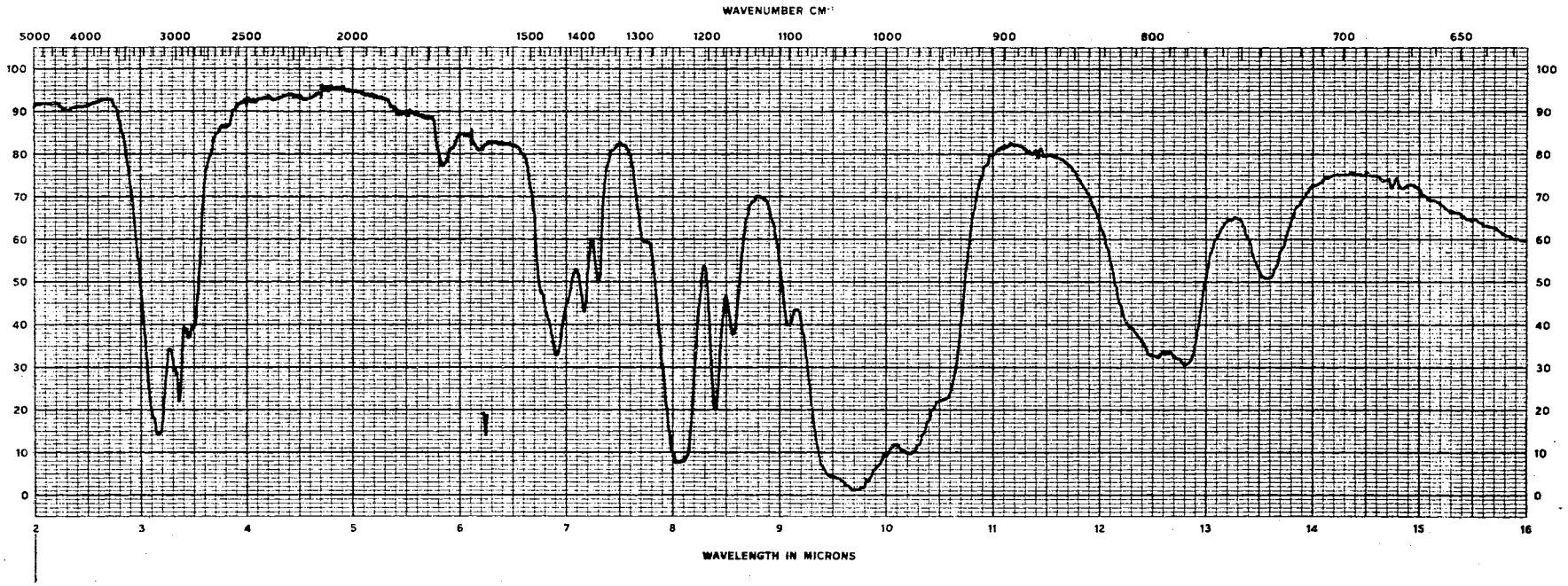
Diethyl p-t-Butylbenzoylphosphonate (IIIi), Film on NaCl Plates

Plate X



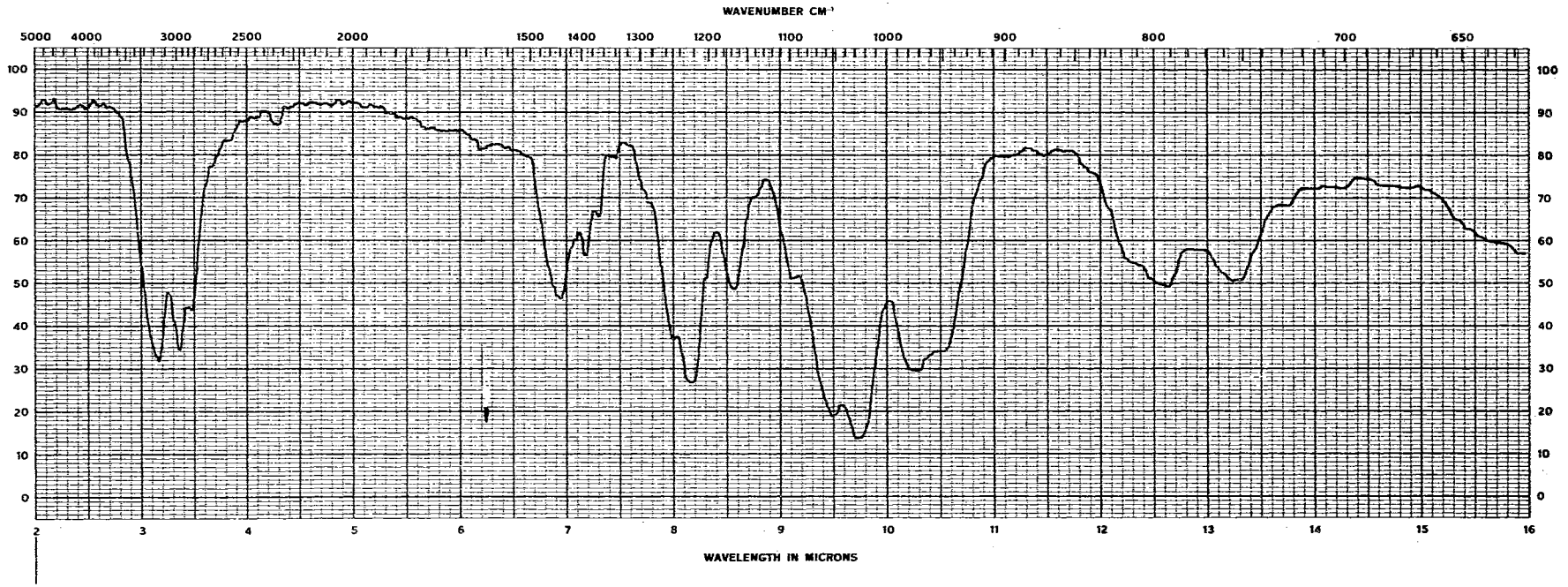
Diethyl 2-Naphthoylphosphonate (IIIj), Film on NaCl Plates

Plate XI



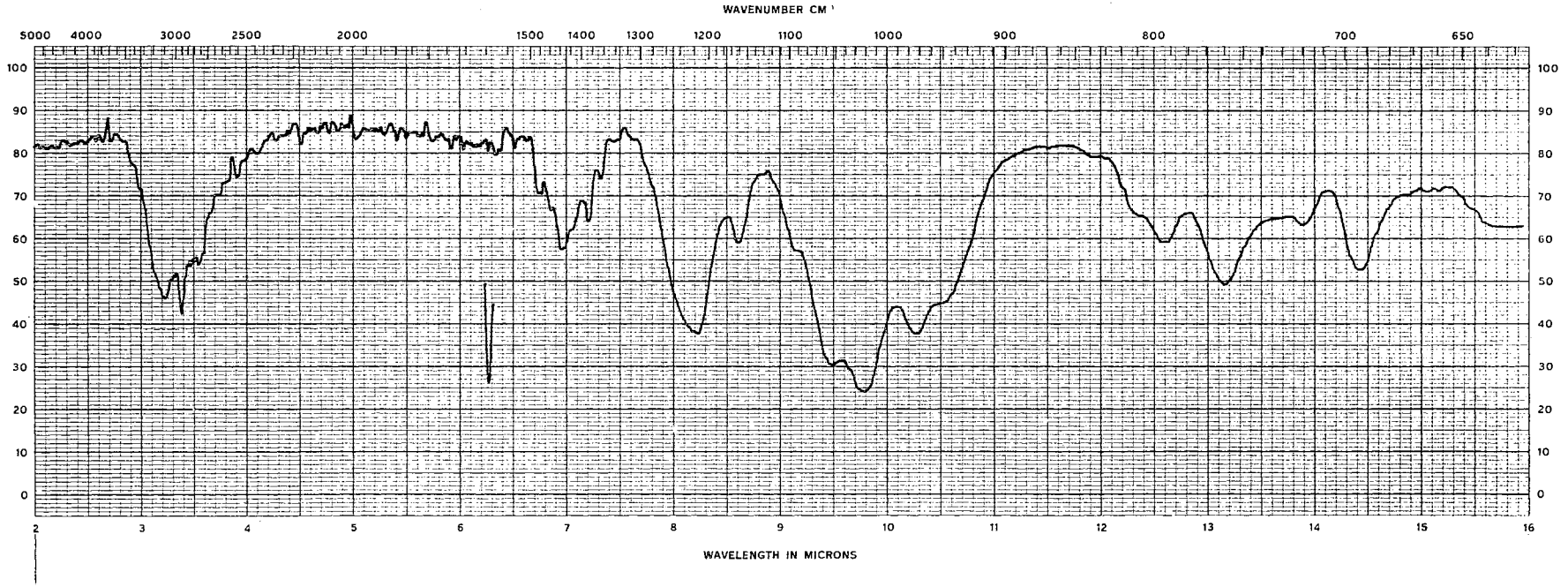
Diethyl Acetylphosphonate Oxime (IVa), Film on NaCl Plates

Plate XII



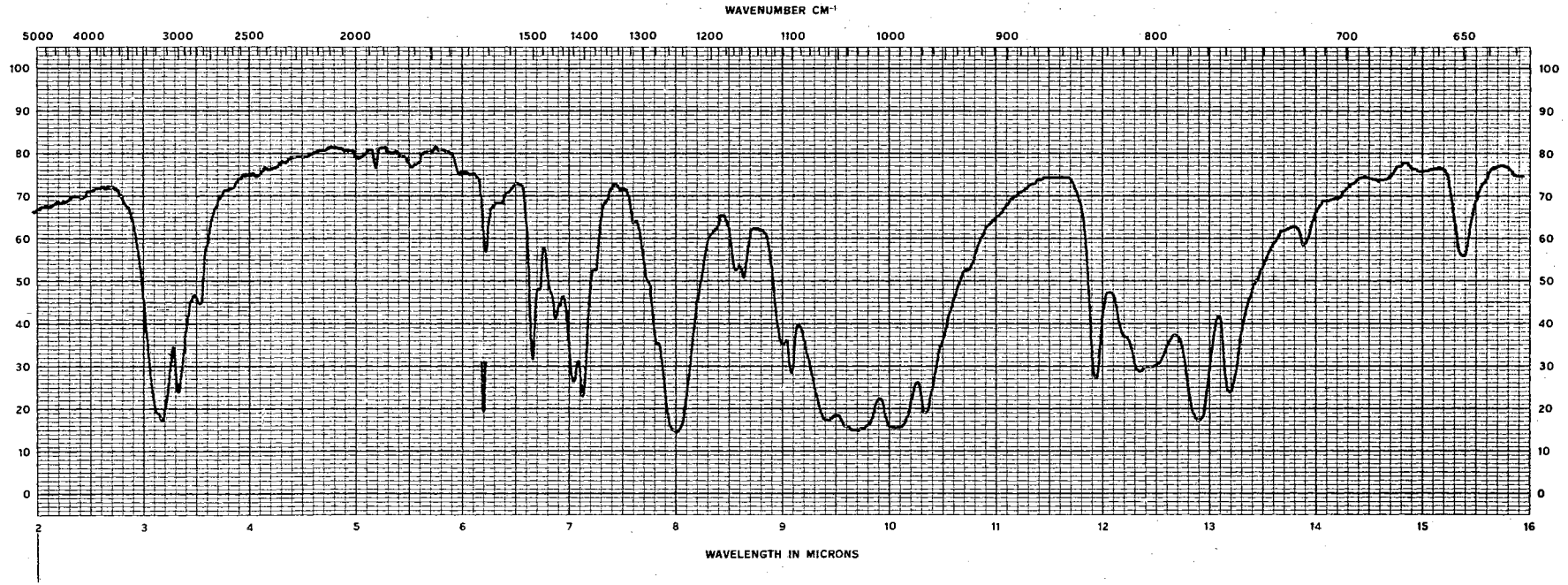
Diethyl Butyrylphosphonate Oxime (IVb), Film on NaCl Plates

Plate XIII



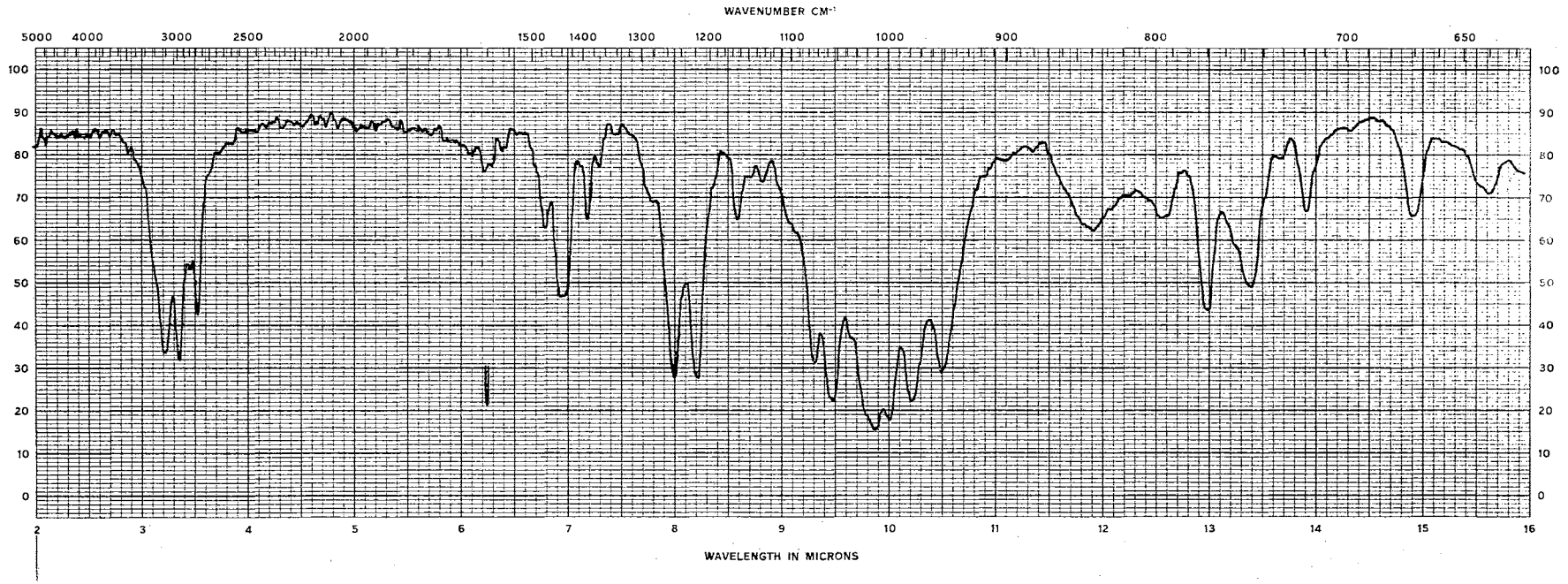
Diethyl Benzoylphosphonate Oxime (IVc, Crude), Film on NaCl Plates

Plate XIV



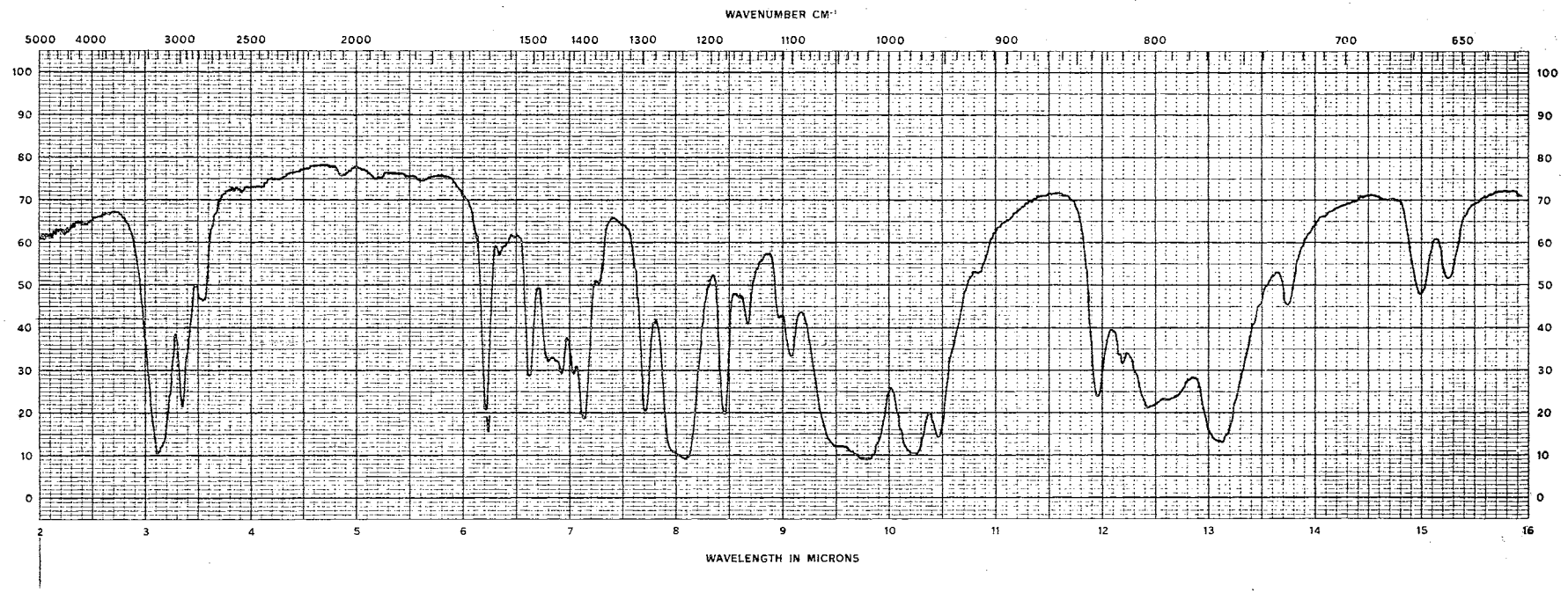
Diethyl p-Chlorobenzoylphosphonate Oxime (IVd), KBr Pellet

Plate XV



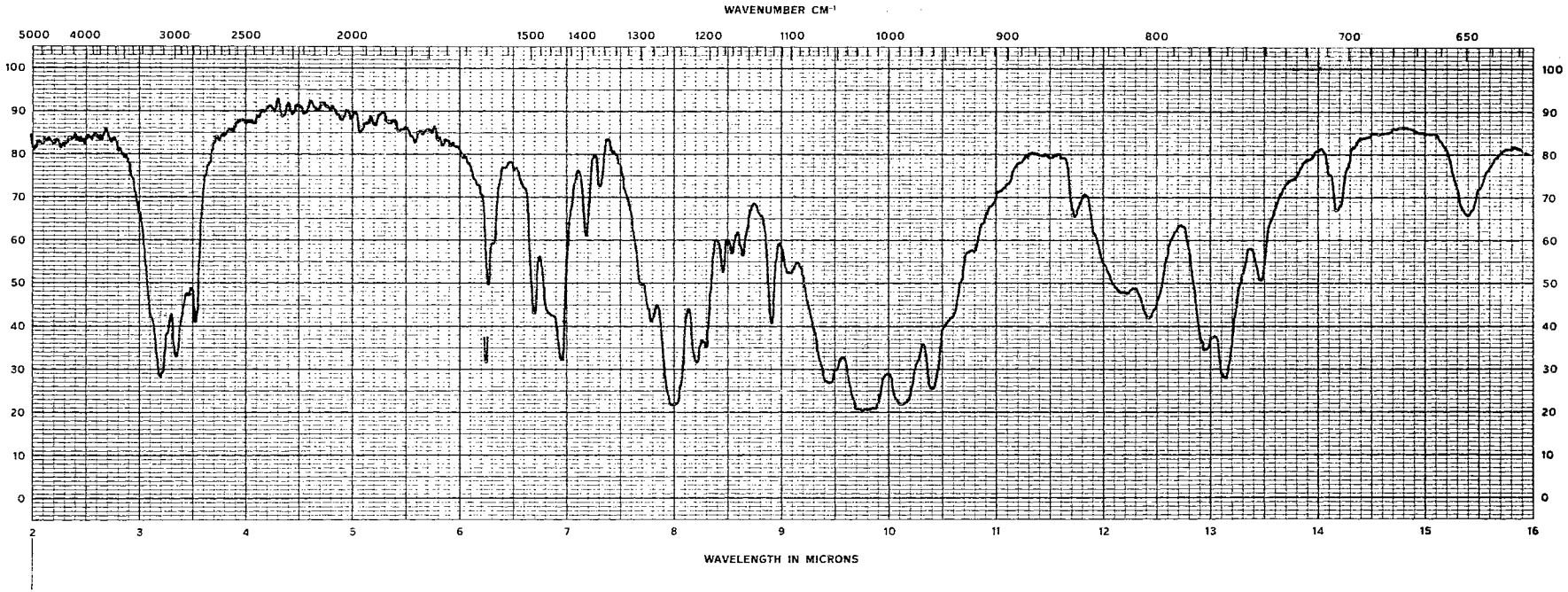
Diethyl o-Chlorobenzoylphosphonate Oxime (IVe), KBr Pellet

Plate XVI



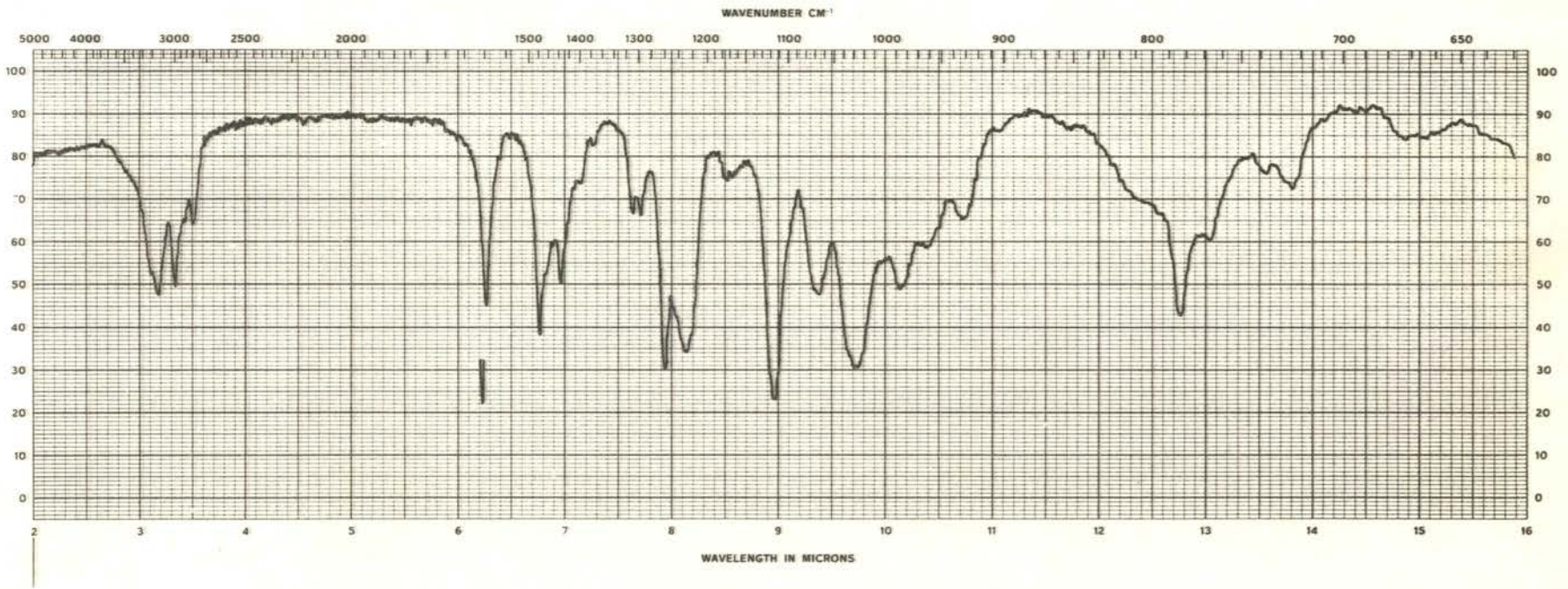
Diethyl p-Methoxybenzoylphosphonate Oxime (IVf), KBr Pellet

Plate XVII



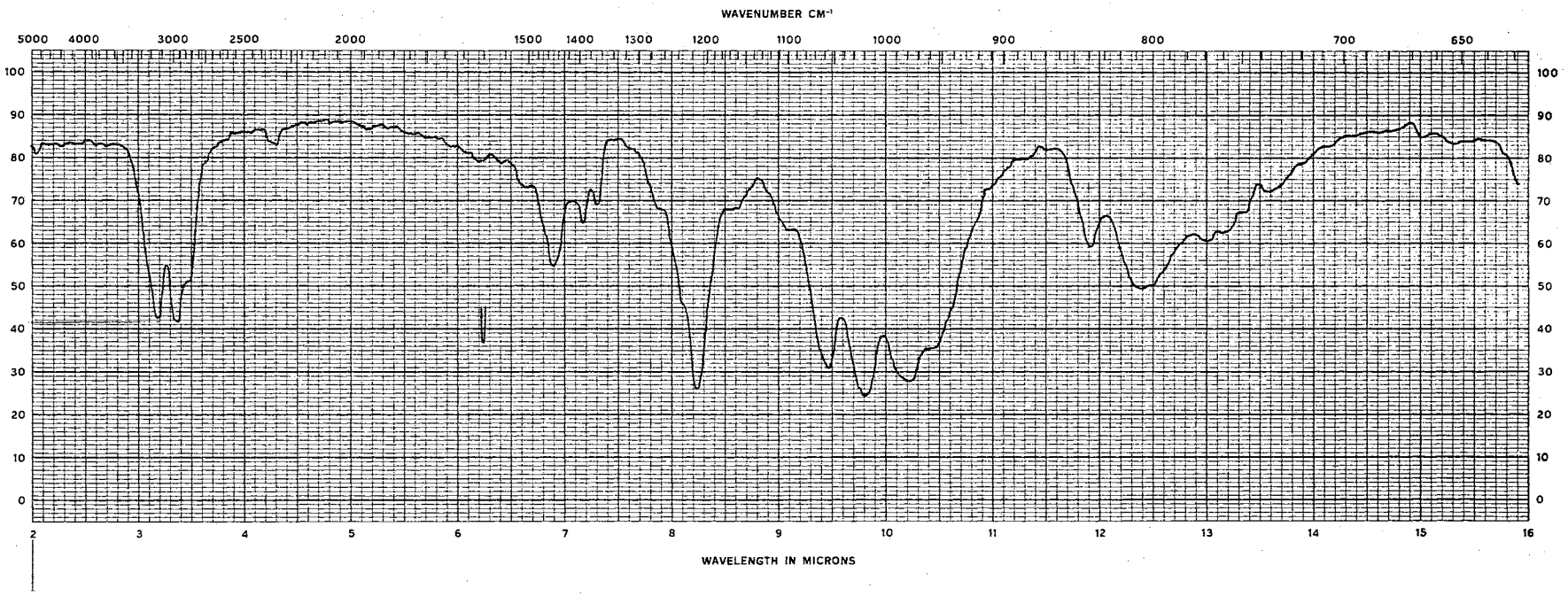
Diethyl o-Methoxybenzoylphosphonate Oxime (IVg), KBr Pellet

Plate XVIII



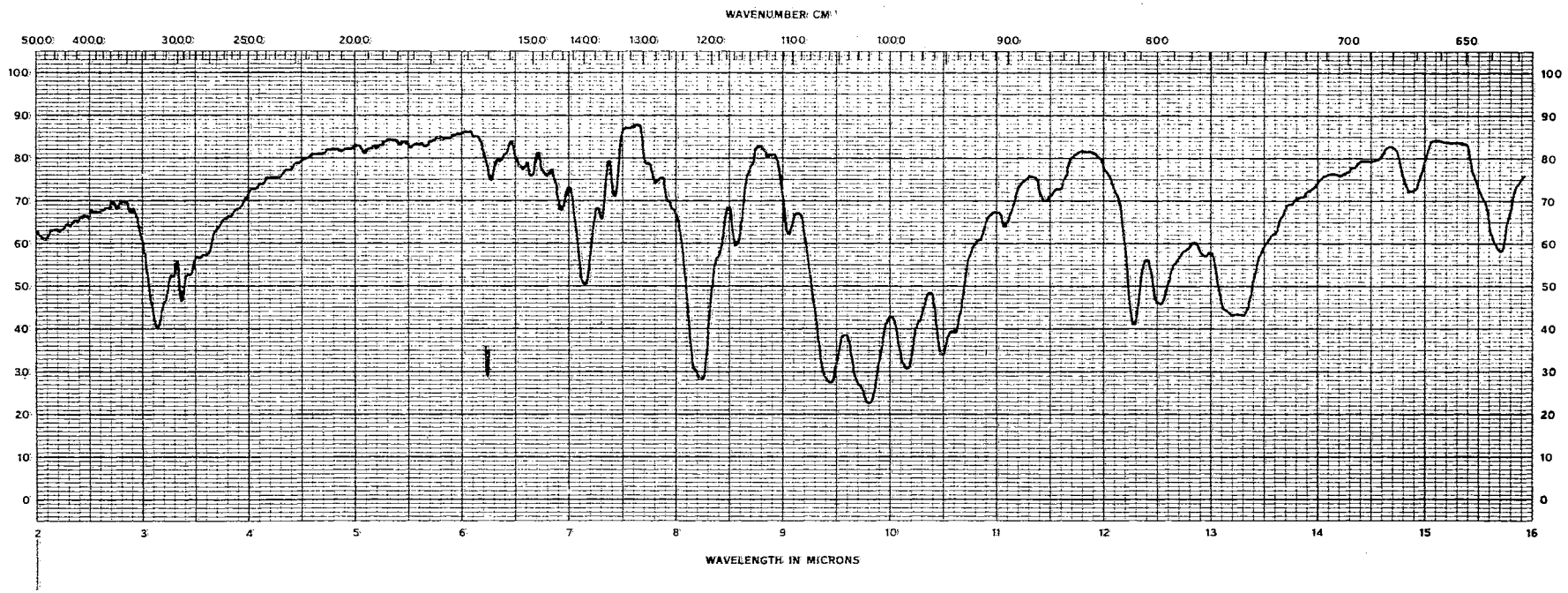
Diethyl 2,6-Dimethoxybenzoylphosphonate Oxime (IVh), KBr Pellet

Plate XIX



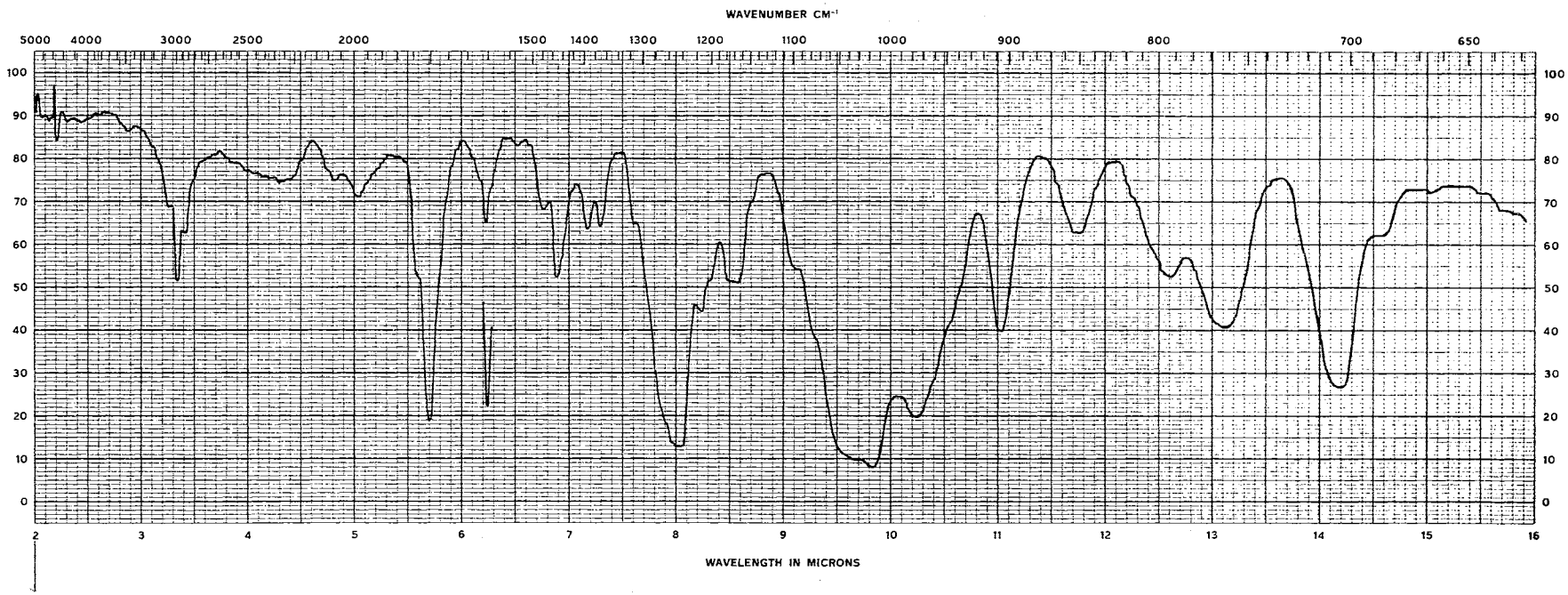
Diethyl p-t-Butylbenzoylphosphonate Oxime (IVi), KBr Pellet

Plate XX



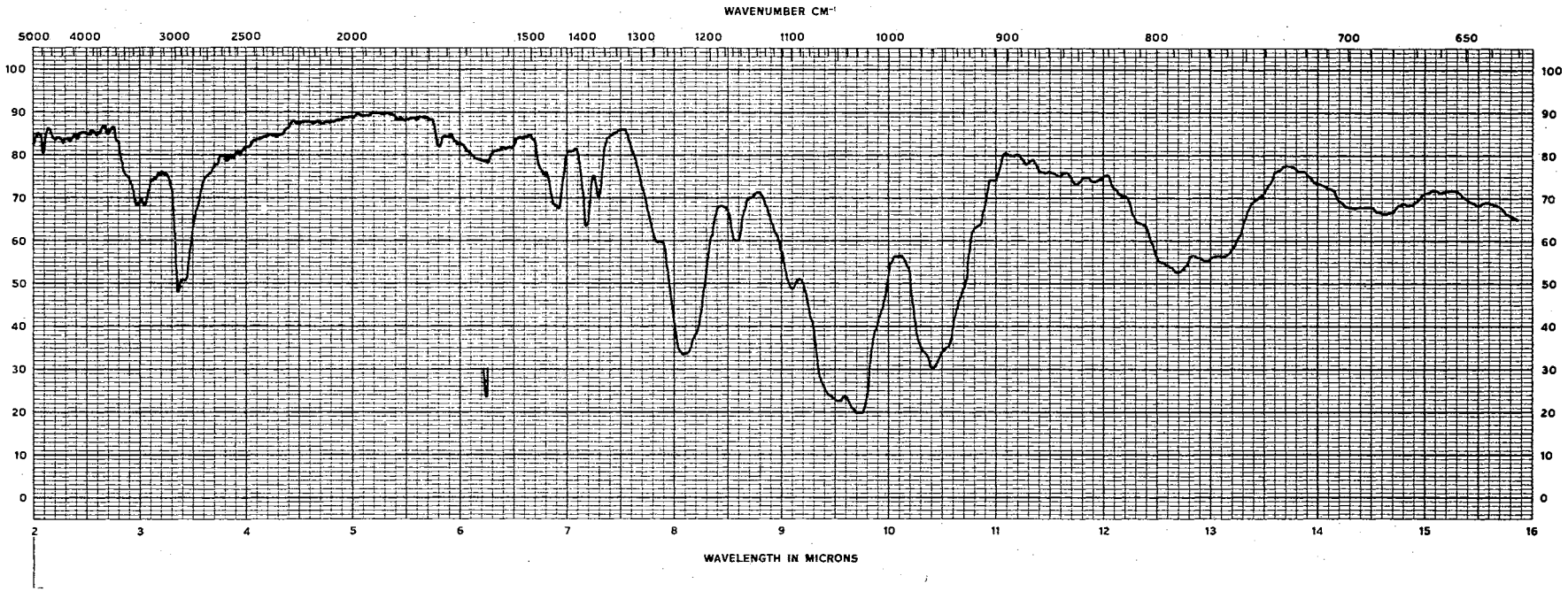
Diethyl 2-Naphthoylphosphonate Oxime (IVj), KBr Pellet

Plate XXI



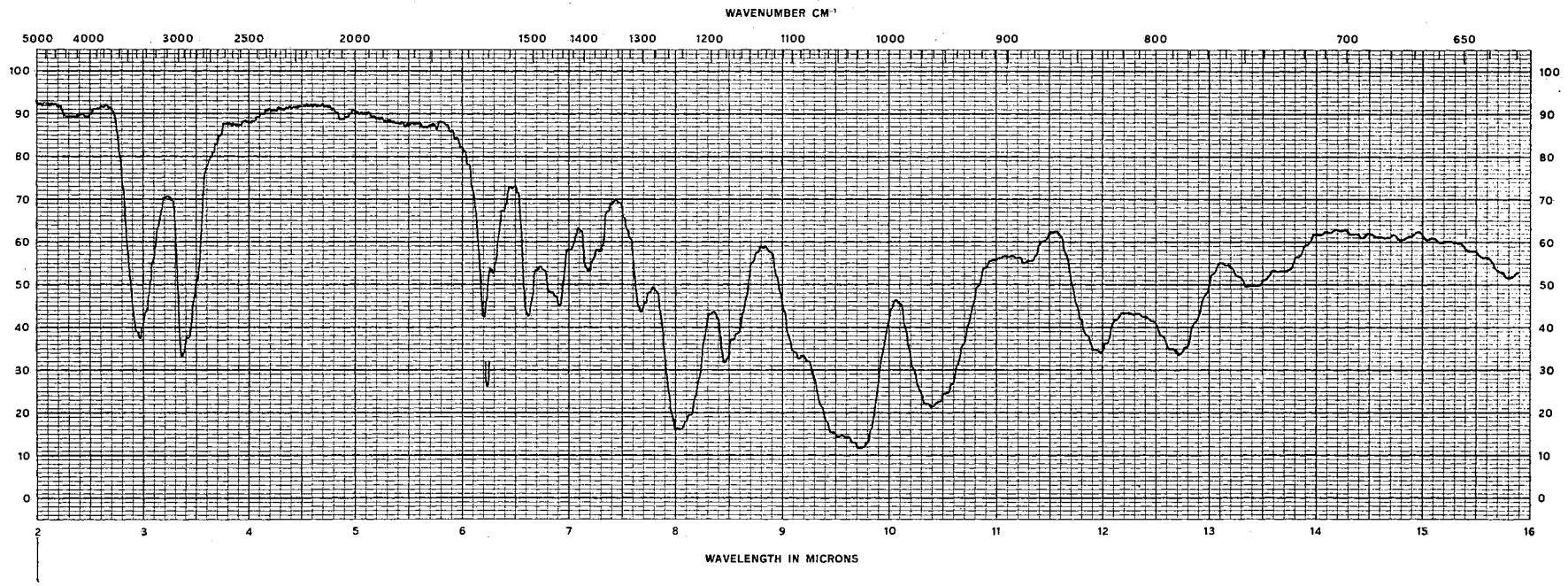
Benzoyl Derivative of Diethyl Acetylphosphonate Oxime (Crude), Film on NaCl Plates

Plate XXII



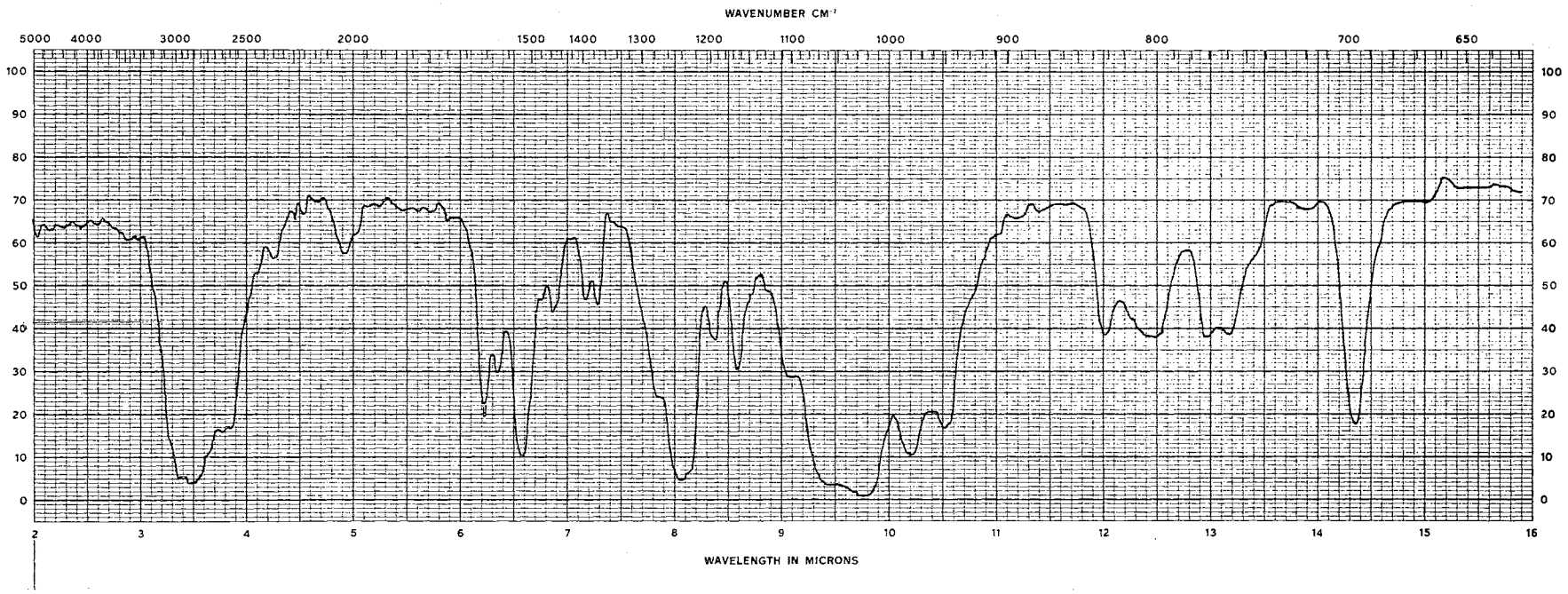
(RS) Diethyl 1-Aminoethylphosphonate (Va), Film on NaCl Plates

Plate XXIII



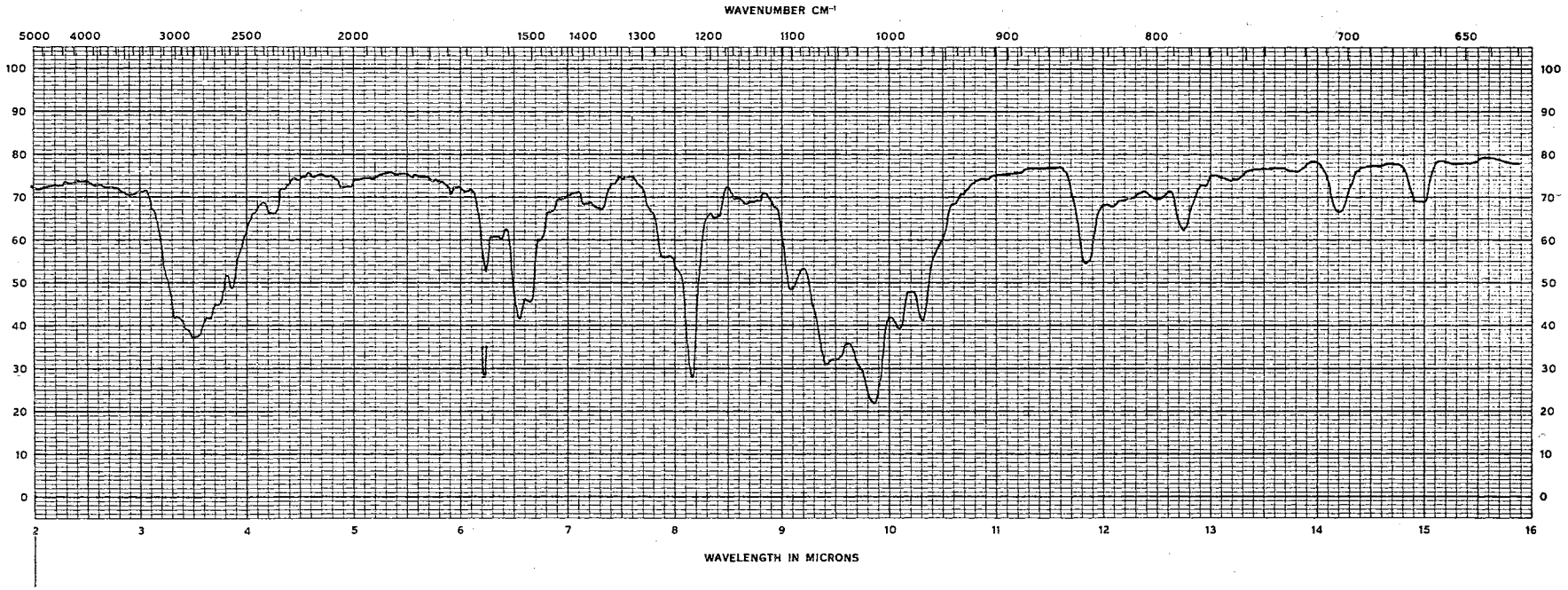
(RS) Diethyl α-Amino-p-methoxybenzylphosphonate (Vf, Crude), Film on NaCl Plates

Plate XXIV



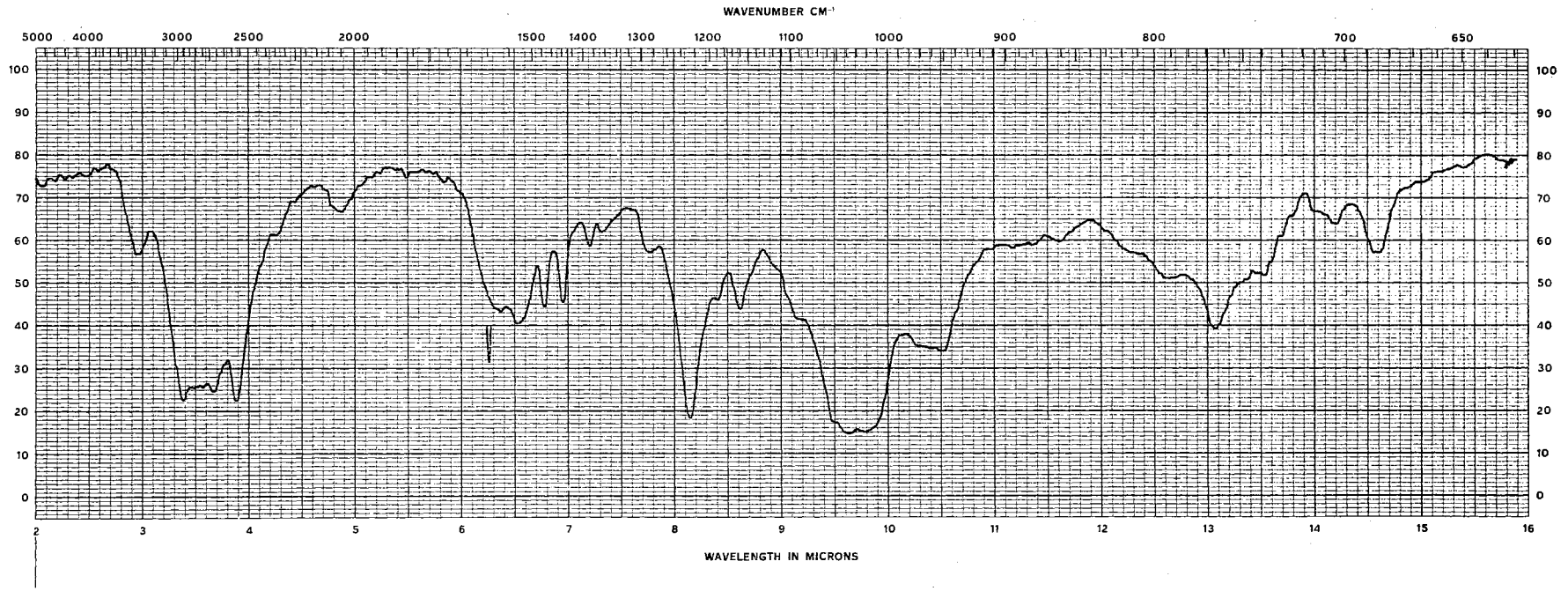
(RS) Diethyl α-Aminobenzylphosphonate Hydrochloride (VIc), KBr Pellet

Plate XXV



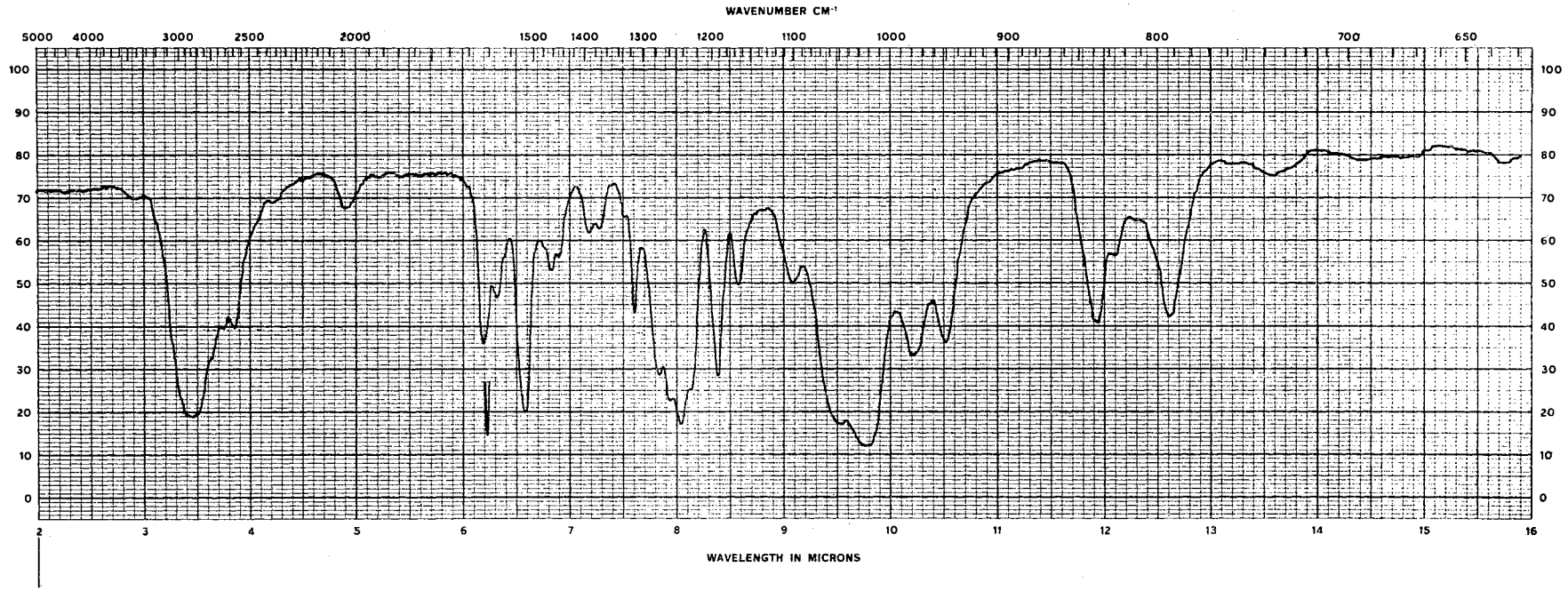
(RS) Diethyl α-Amino-p-chlorobenzylphosphonate Hydrochloride (VId), KBr Pellet

Plate XXVI



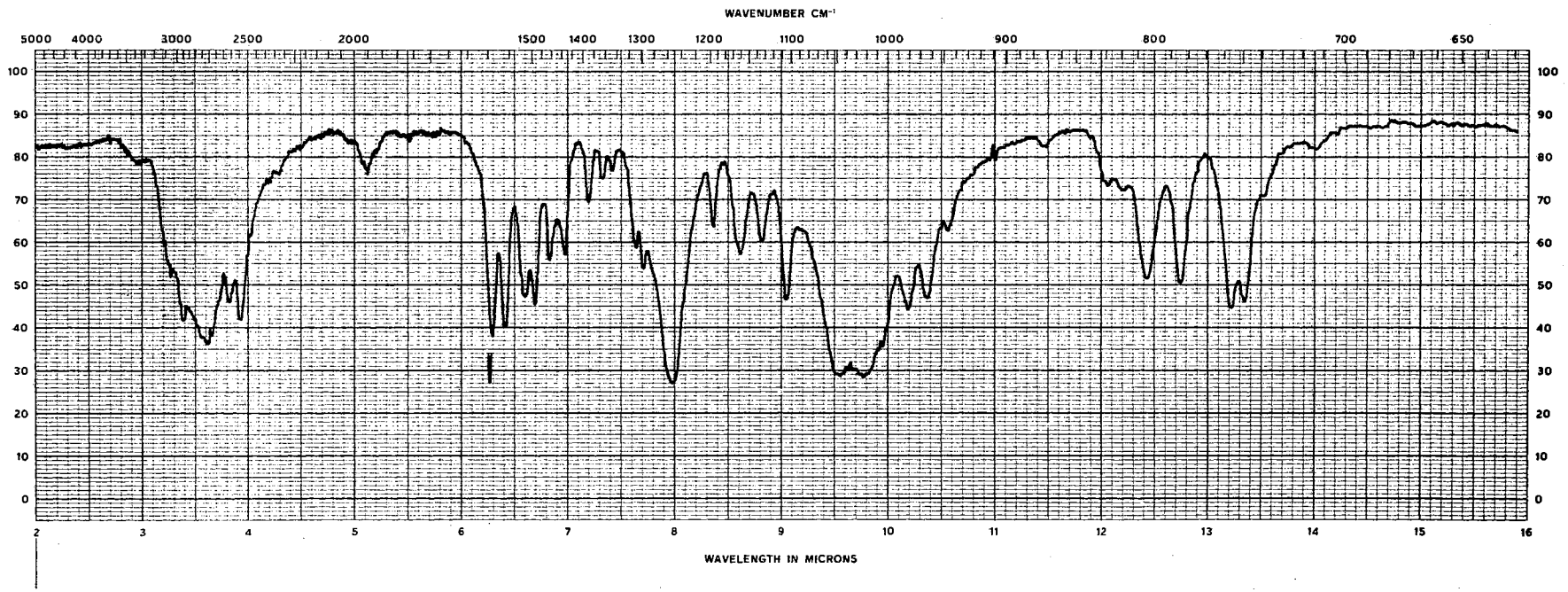
(RS) Diethyl α-Amino-o-chlorobenzylphosphonate Hydrochloride (VIe), KBr Pellet

Plate XXVII



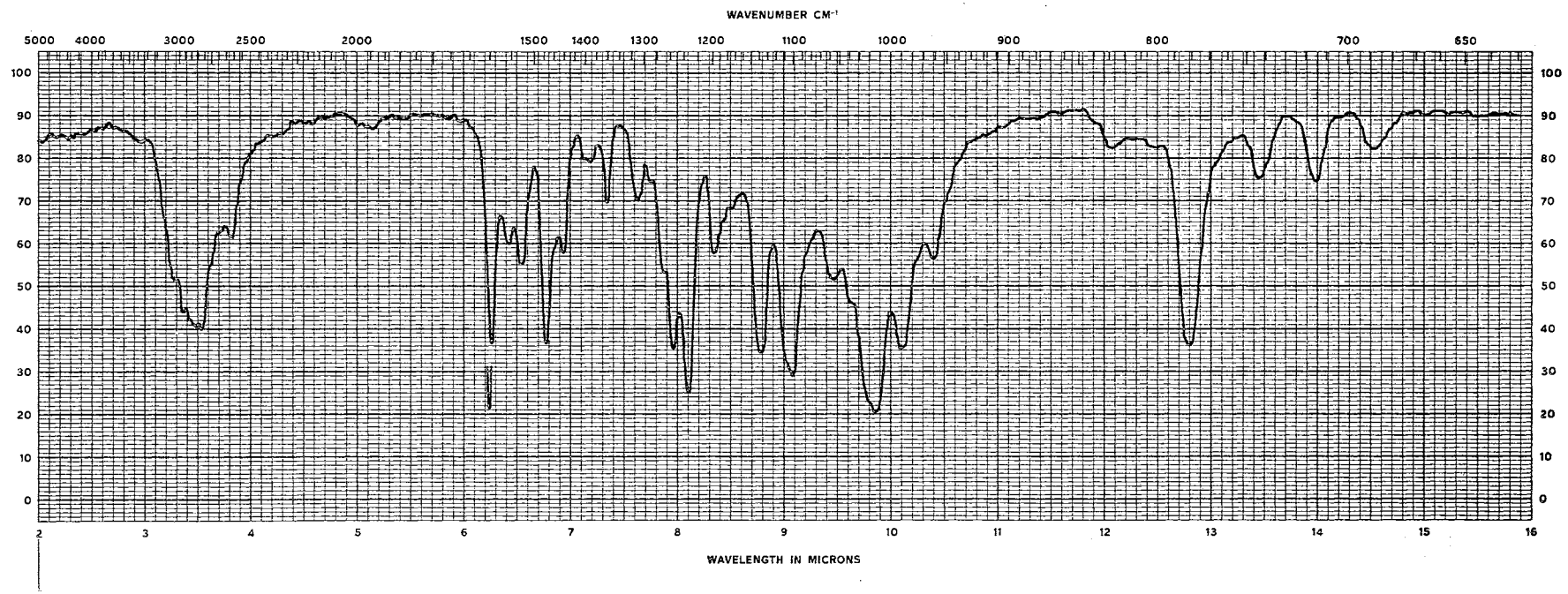
(RS) Diethyl α-Amino-p-methoxybenzylphosphonate Hydrochloride (VIf), KBr Pellet

Plate XXVIII



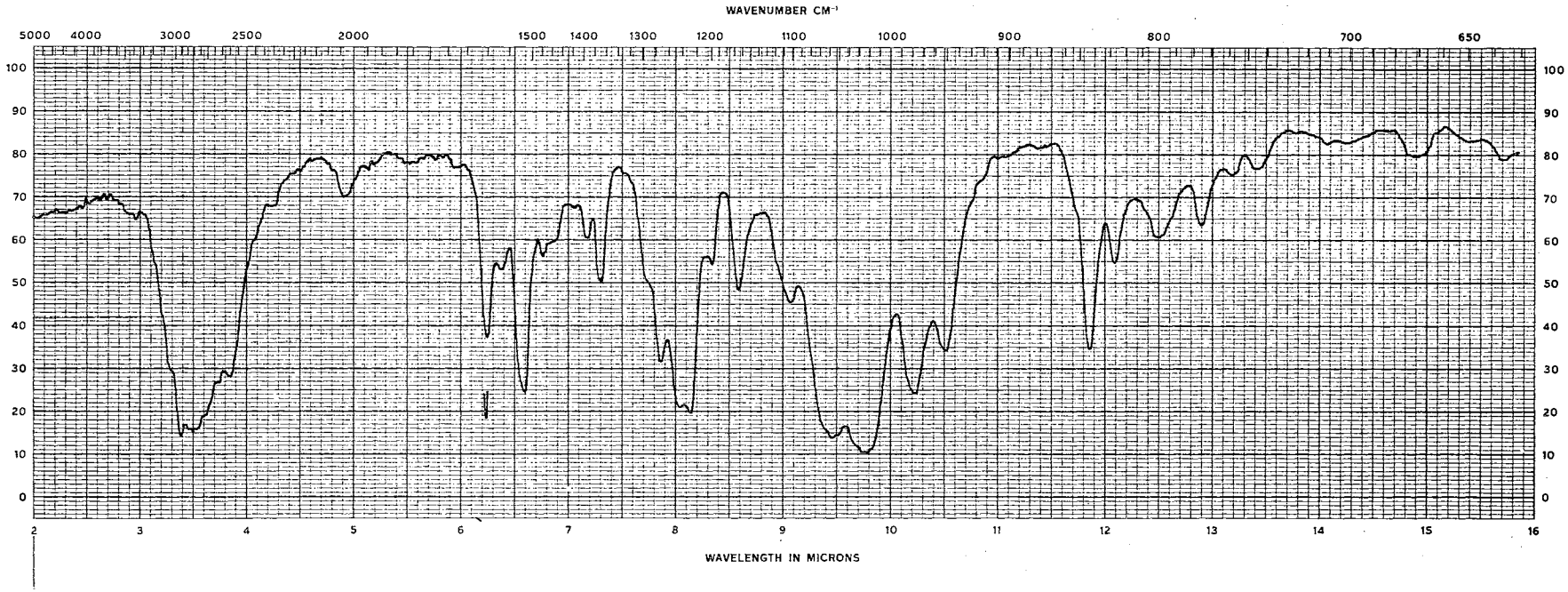
(RS) Diethyl α-Amino-o-methoxybenzylphosphonate Hydrochloride (VIg), KBr Pellet

Plate XXIX



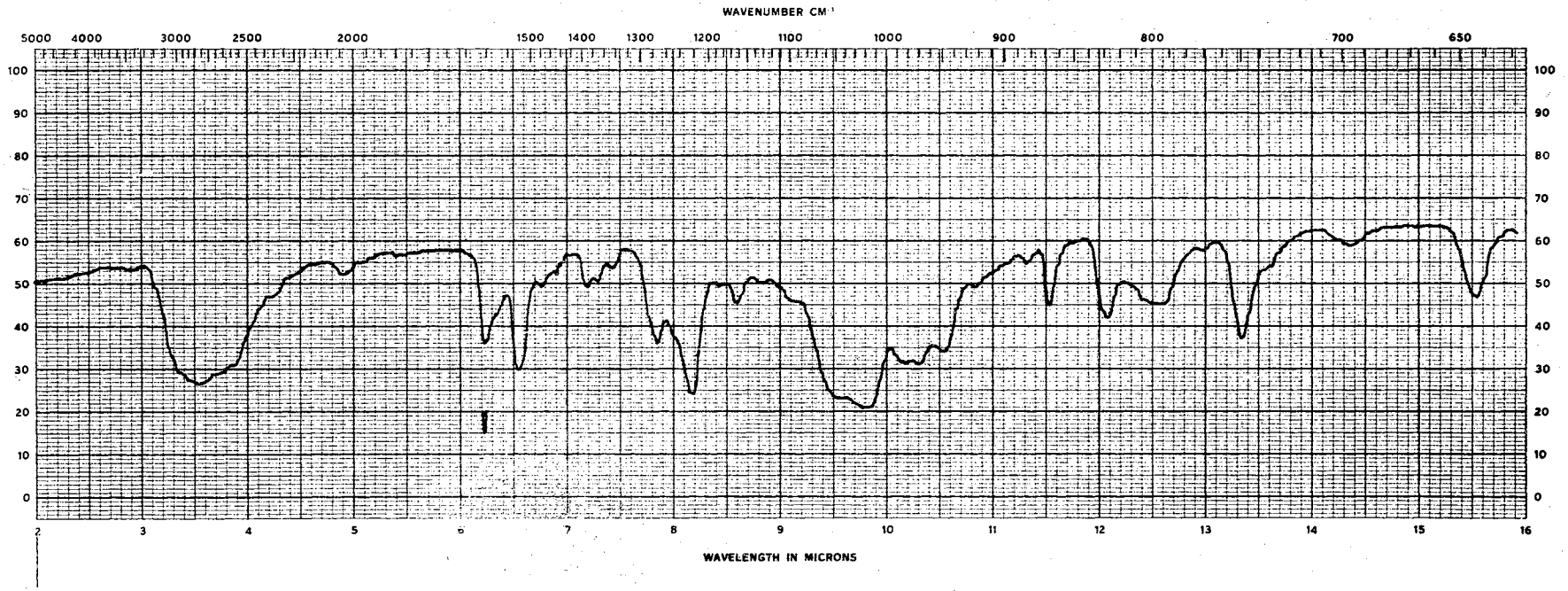
(RS) Diethyl α-Amino-2,6-dimethoxybenzylphosphonate Hydrochloride (VIh), KBr Pellet

Plate XXX



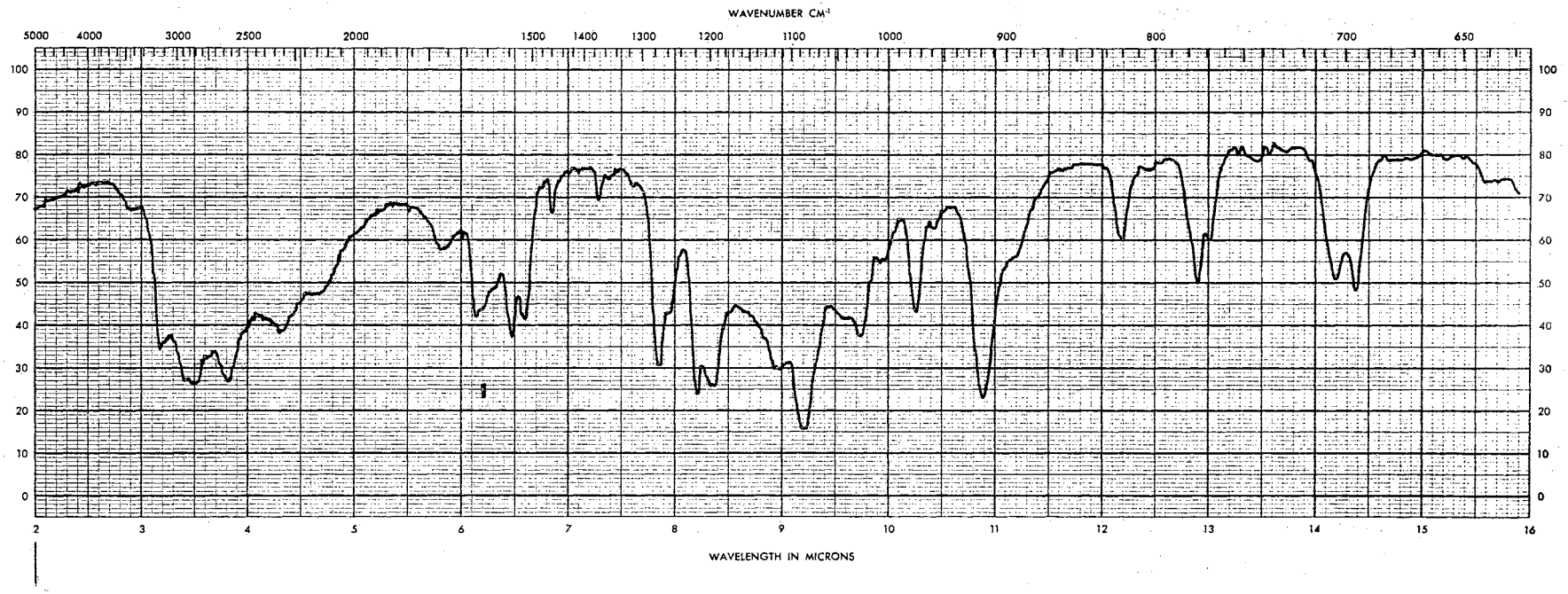
(RS) Diethyl α-Amino-p-t-butylbenzylphosphonate Hydrochloride (VIi), KBr Pellet

Plate XXXI



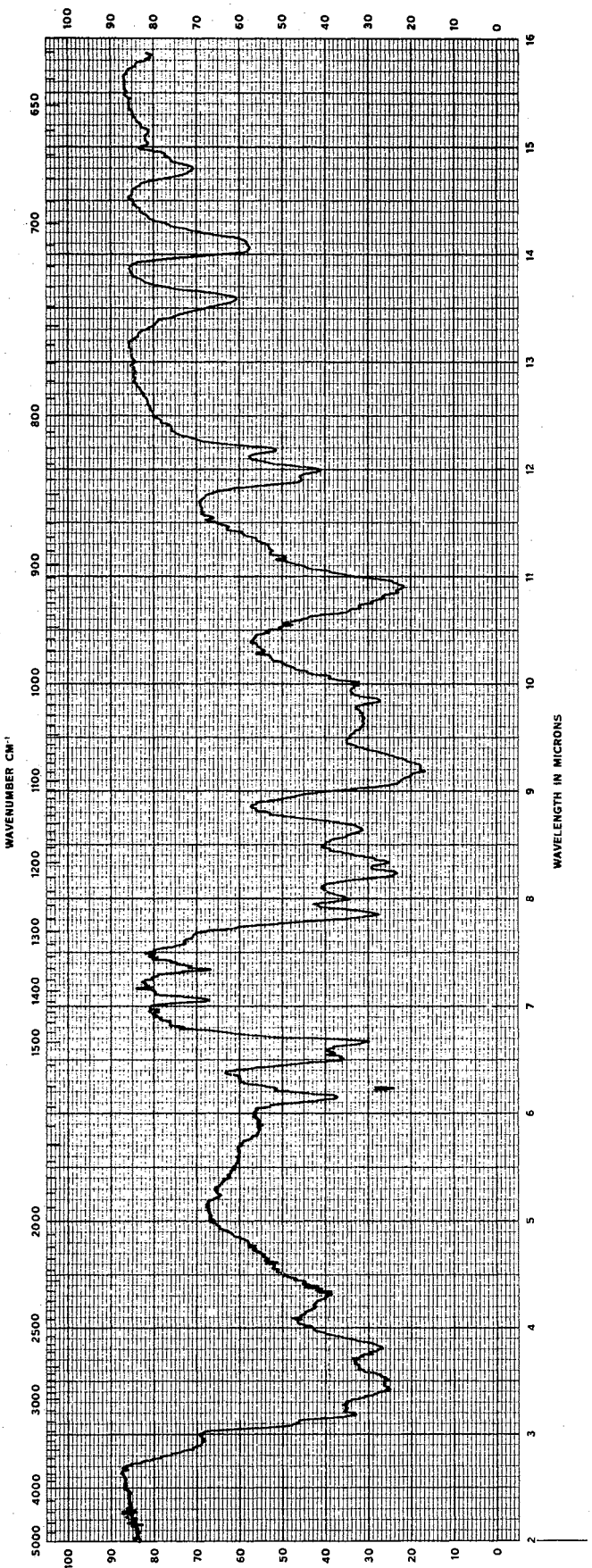
(RS) Diethyl α-Amino-2-naphthylmethylphosphonate Hydrochloride (VIj), KBr Pellet

Plate XXXII



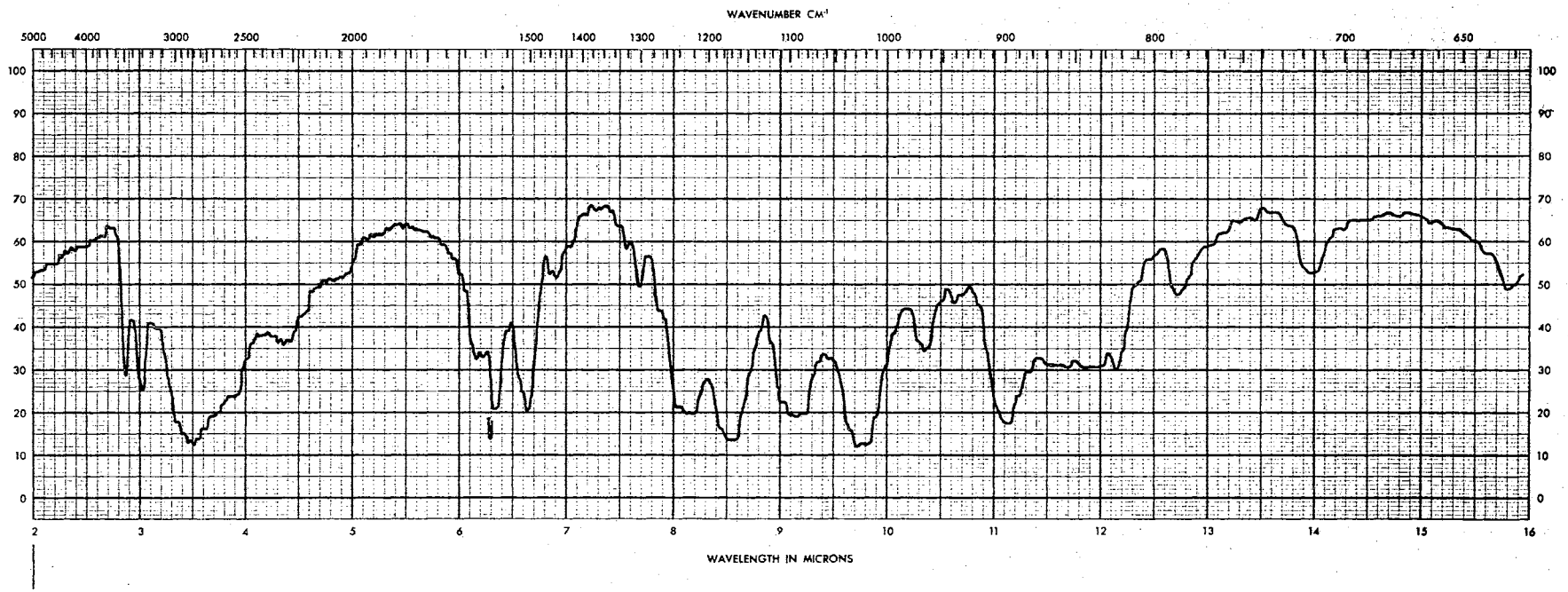
(RS) α-Aminobenzylphosphonic Acid (VIIIc), KBr Pellet

Plate XXXIII



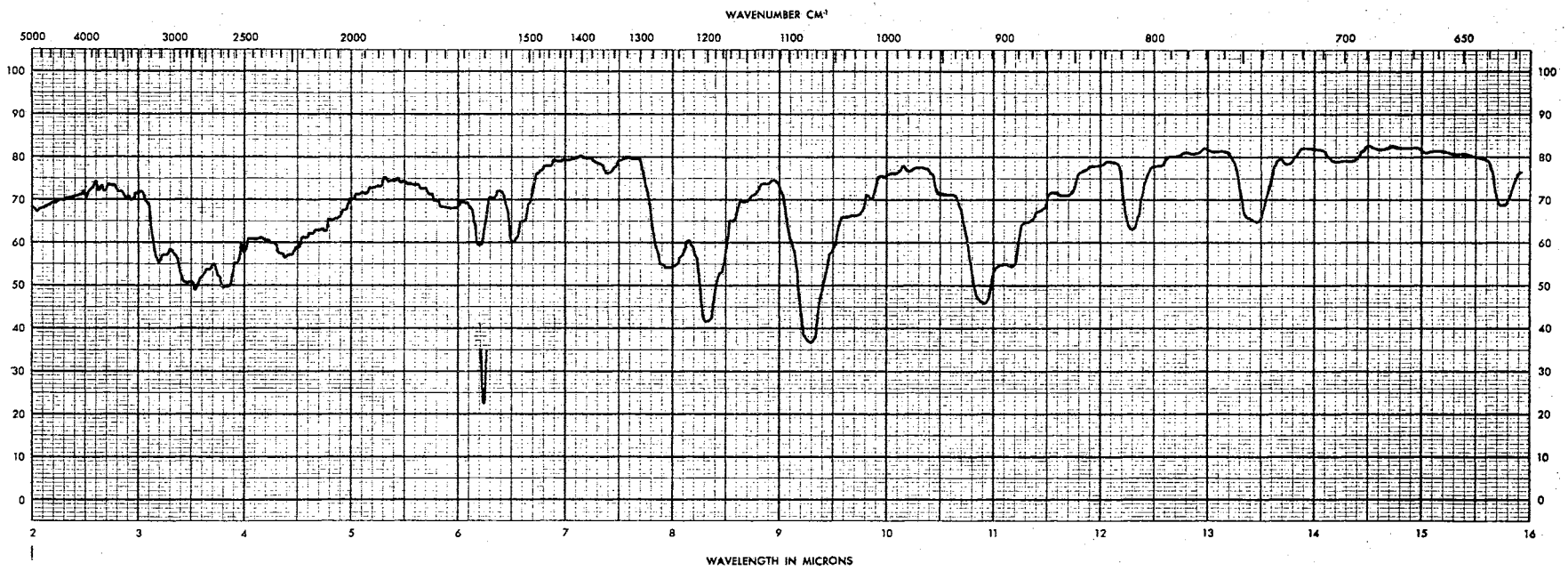
(RS) α-Amino-p-chlorobenzylphosphonic Acid (VIIId), KBr Pellet

Plate XXXIV



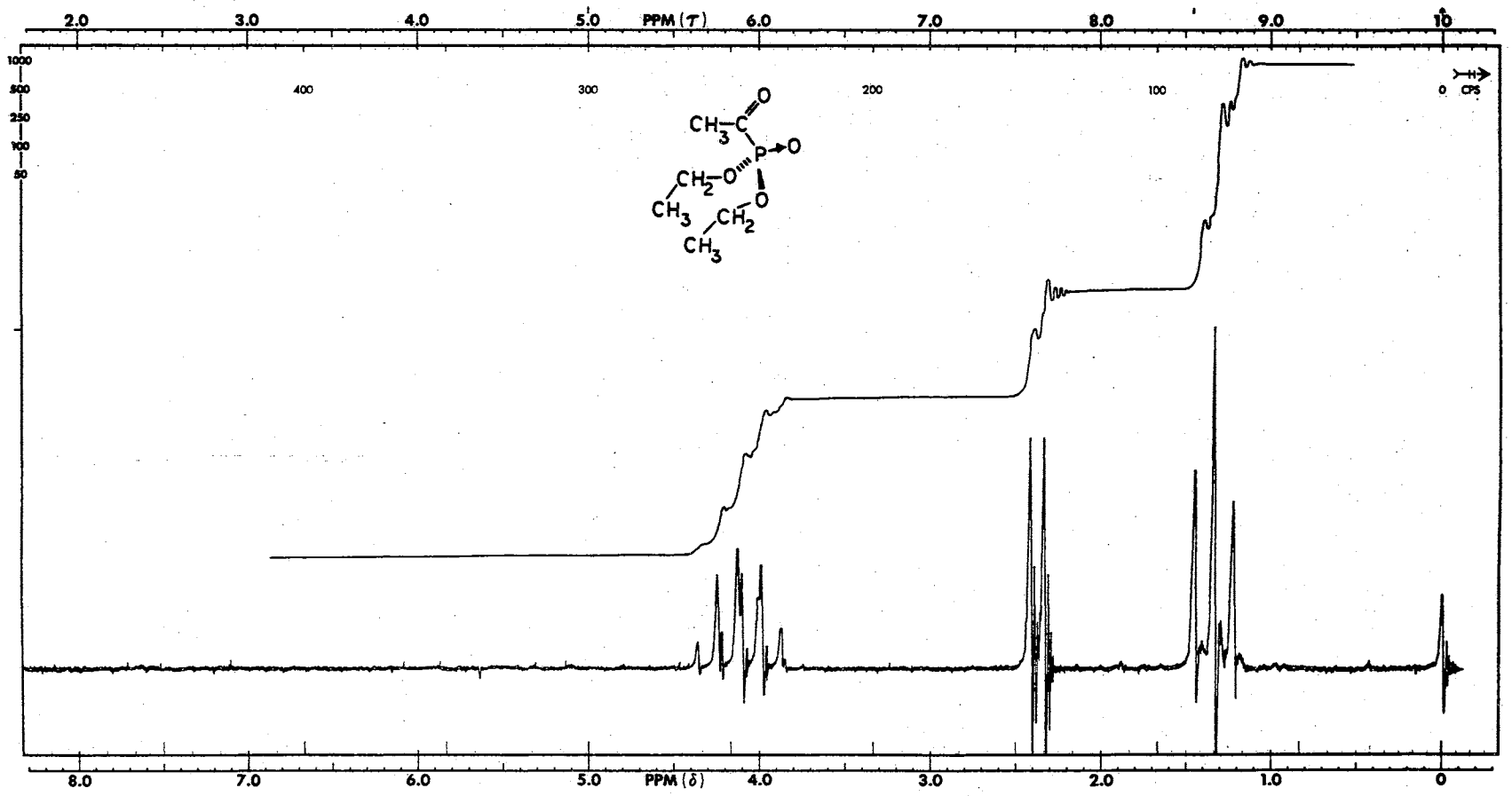
(RS) α-Amino-p-methoxybenzylphosphonic Acid (VIIIf), KBr Pellet

Plate XXXV



(RS) α-Amino-2-naphthylmethylphosphonic Acid (VIIIj), KBr Pellet

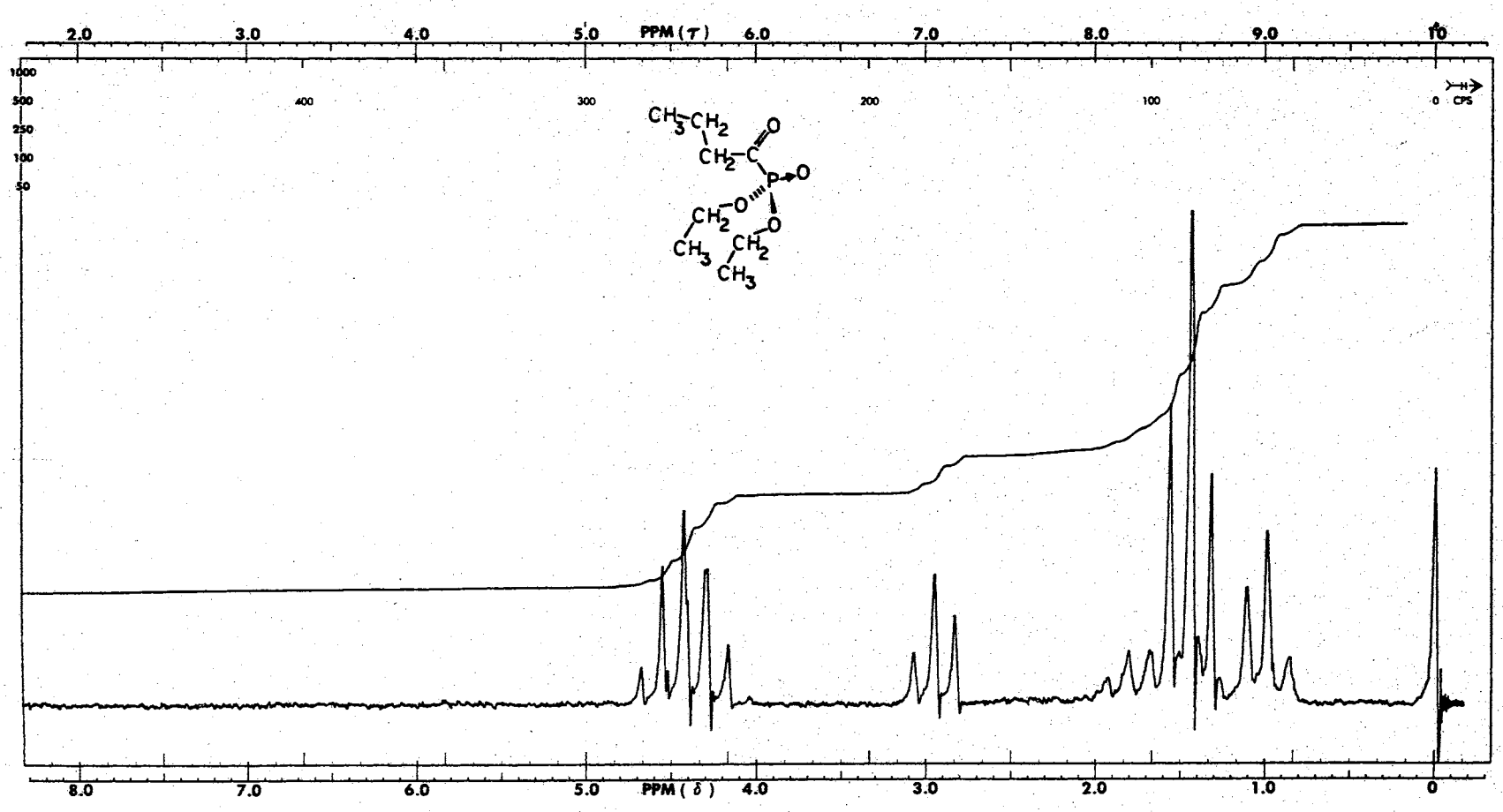
Plate XXXVI



Diethyl Acetylphosphonate (IIIa)

Solvent ..... CCl_4 F. B. ..... 4 cps S. W. ..... 500 cps S. A. 1.6
R. F. Field .... 0.05 mG S. T. ..... 250 sec S. O. ..... 0 cps I. A. 63

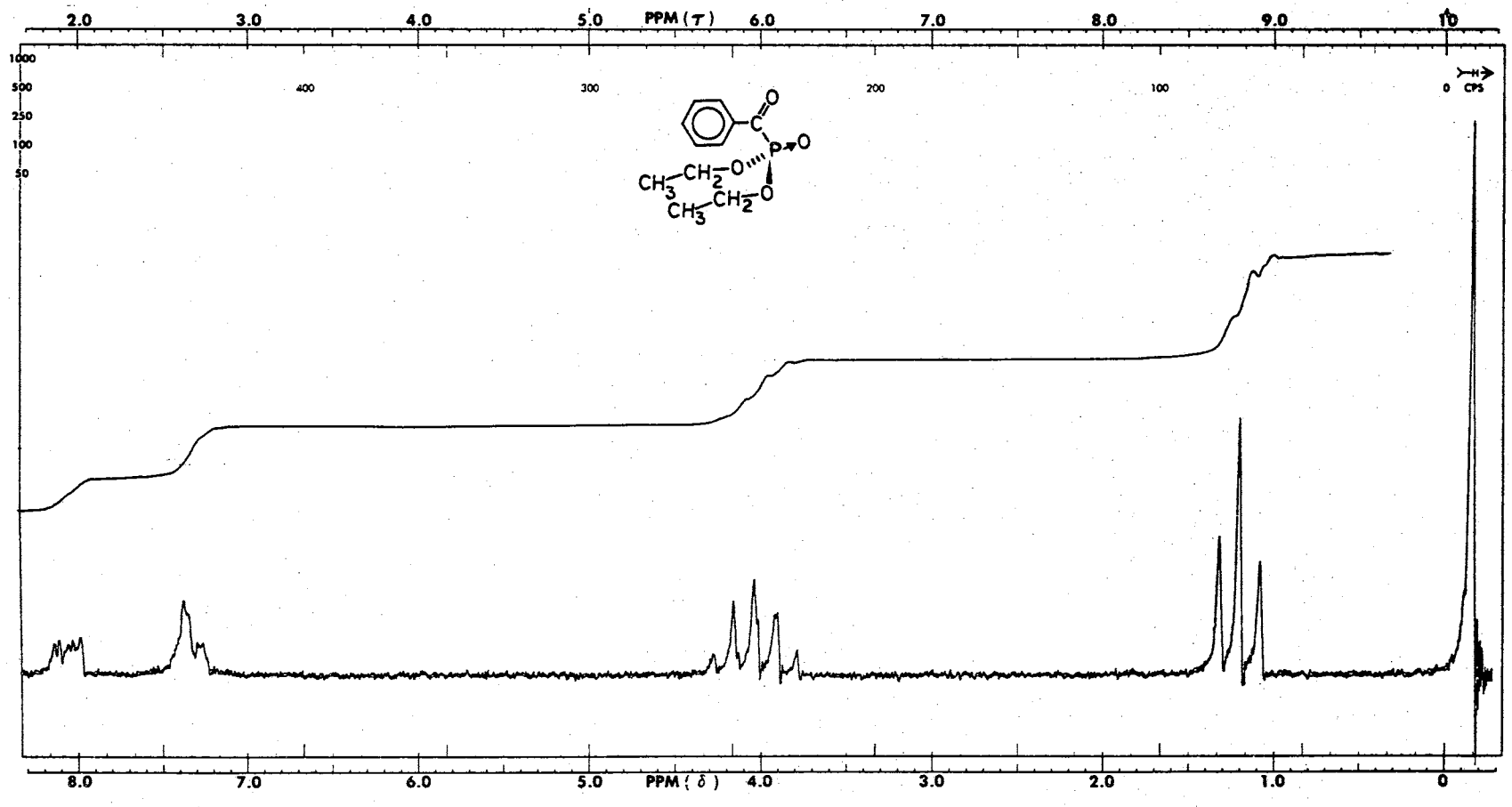
Plate XXXVII



Diethyl Butyrylphosphonate (IIIb)

Solvent ..... $CDCl_3$	F. B. ..... 4 cps	S. W. ..... 500 cps	S. A. 2.0
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0 cps	I. A. 25

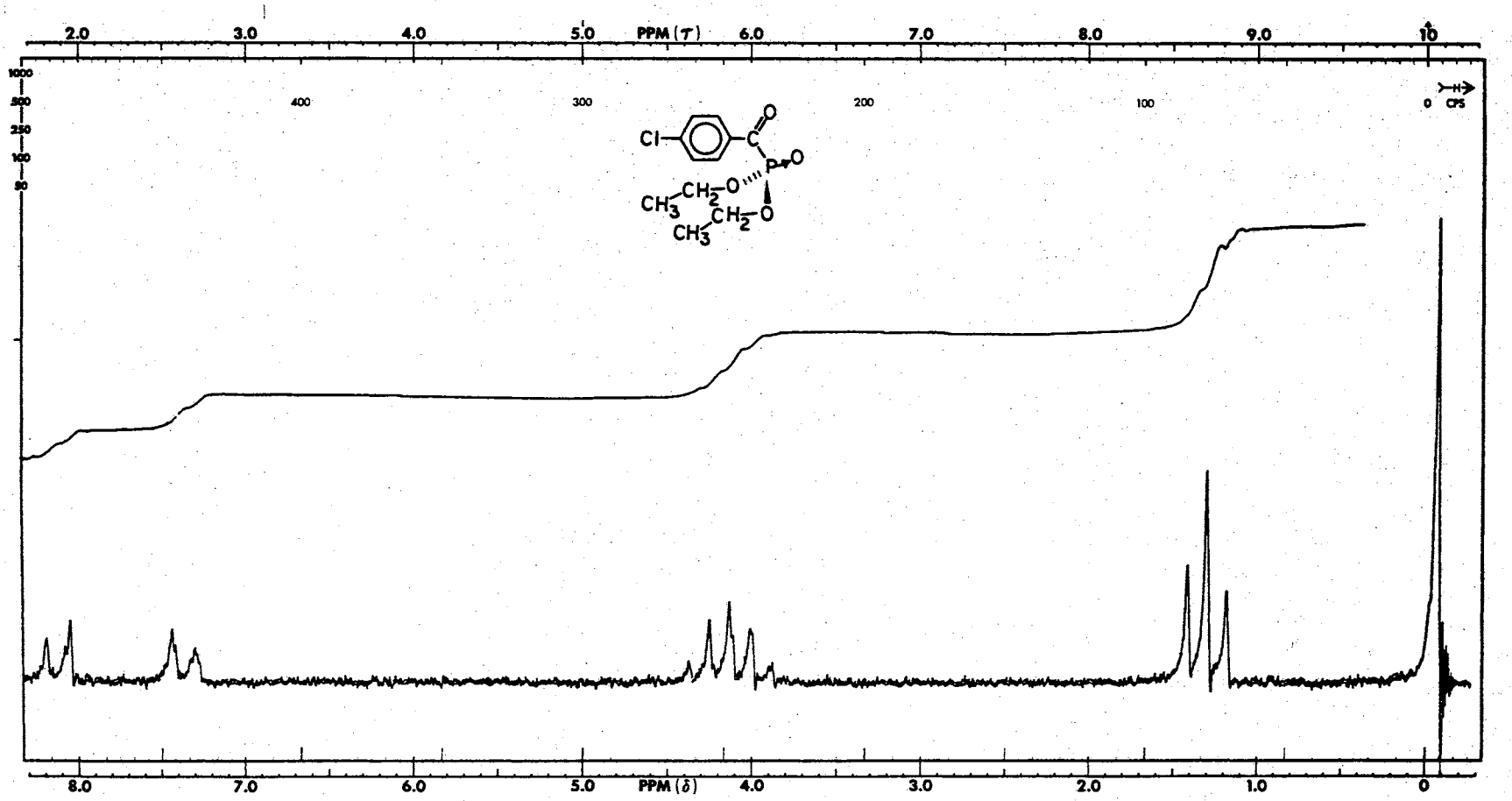
Plate XXXVIII



Diethyl Benzoylphosphonate (IIIc)

Solvent ..... CCl_4	F. B. ..... 2 cps	S. W. ..... 500 cps	S. A. 6.3
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 10 cps	I. A. 63

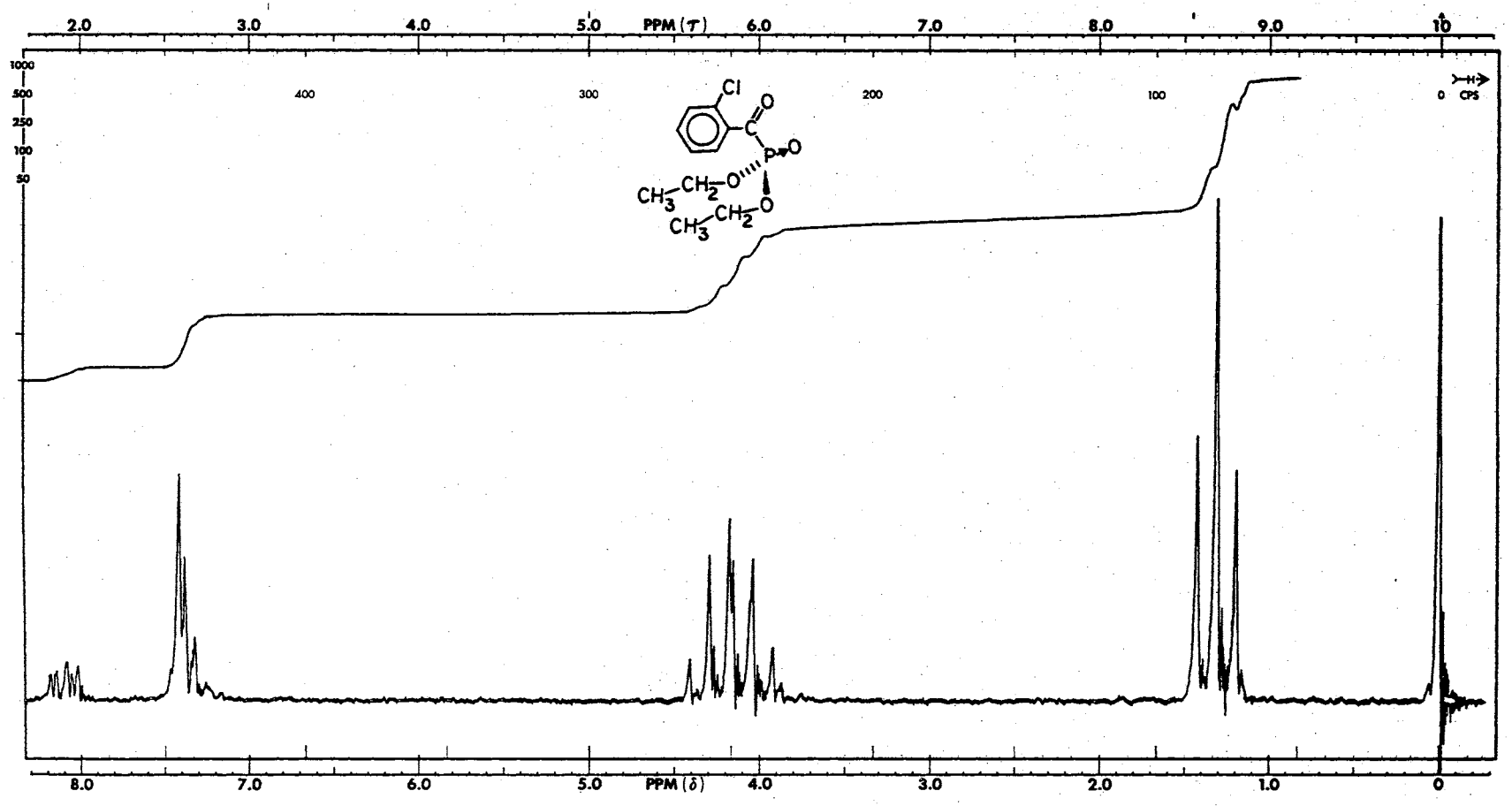
Plate XXXIX



Diethyl p-Chlorobenzoylphosphonate (IIId)

Solvent ..... CCl_4	F. B. ..... 2 cps	S. W. ..... 500 cps	S. A. 8.0
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0 cps	I. A. 63

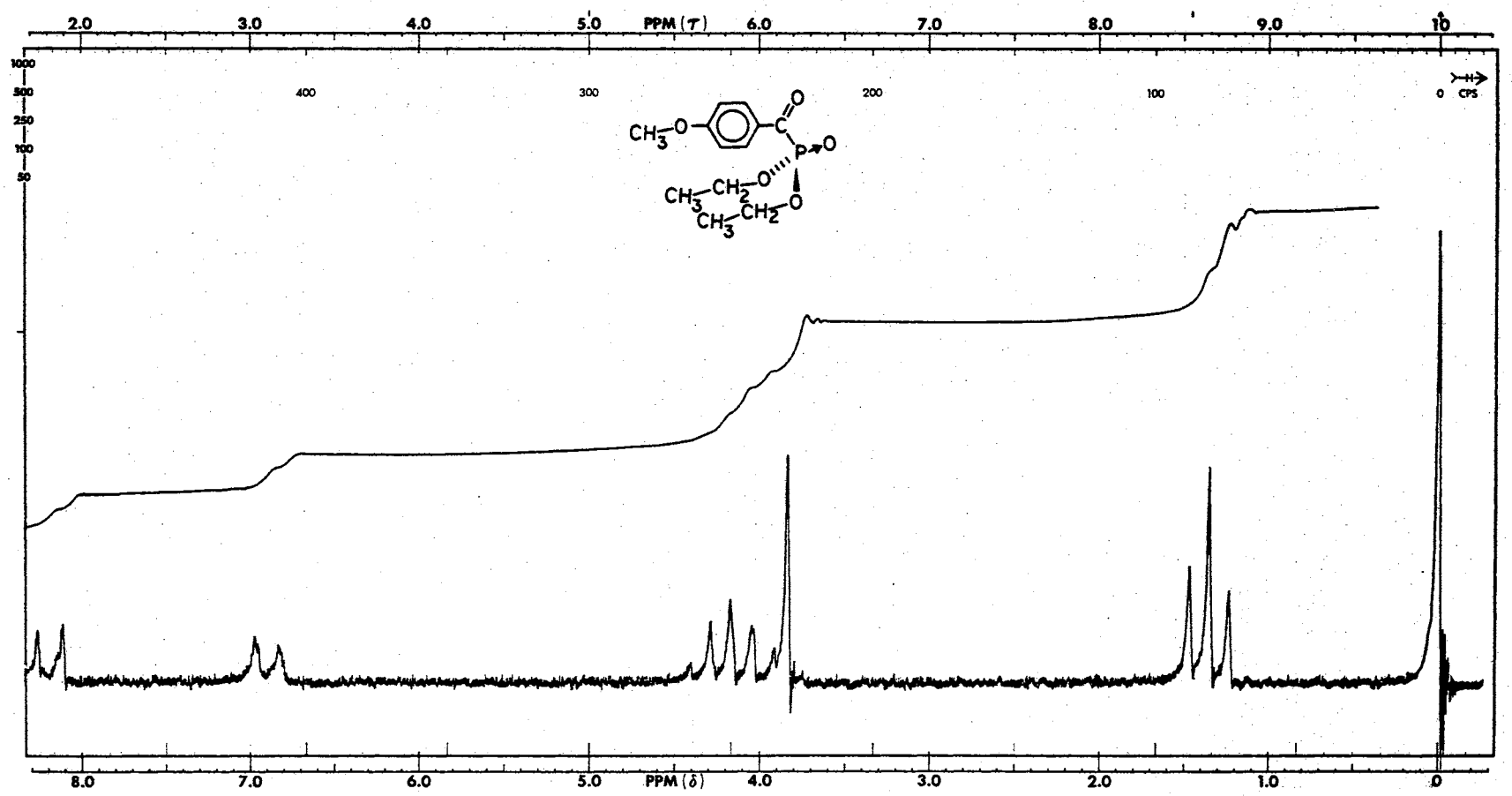
Plate XL



Diethyl o-Chlorobenzoylphosphonate (IIIe)

Solvent ..... CCl_4	F. B. ..... 2 cps	S. W. ..... 500 cps	S. A. 2.5
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0 cps	I. A. 40

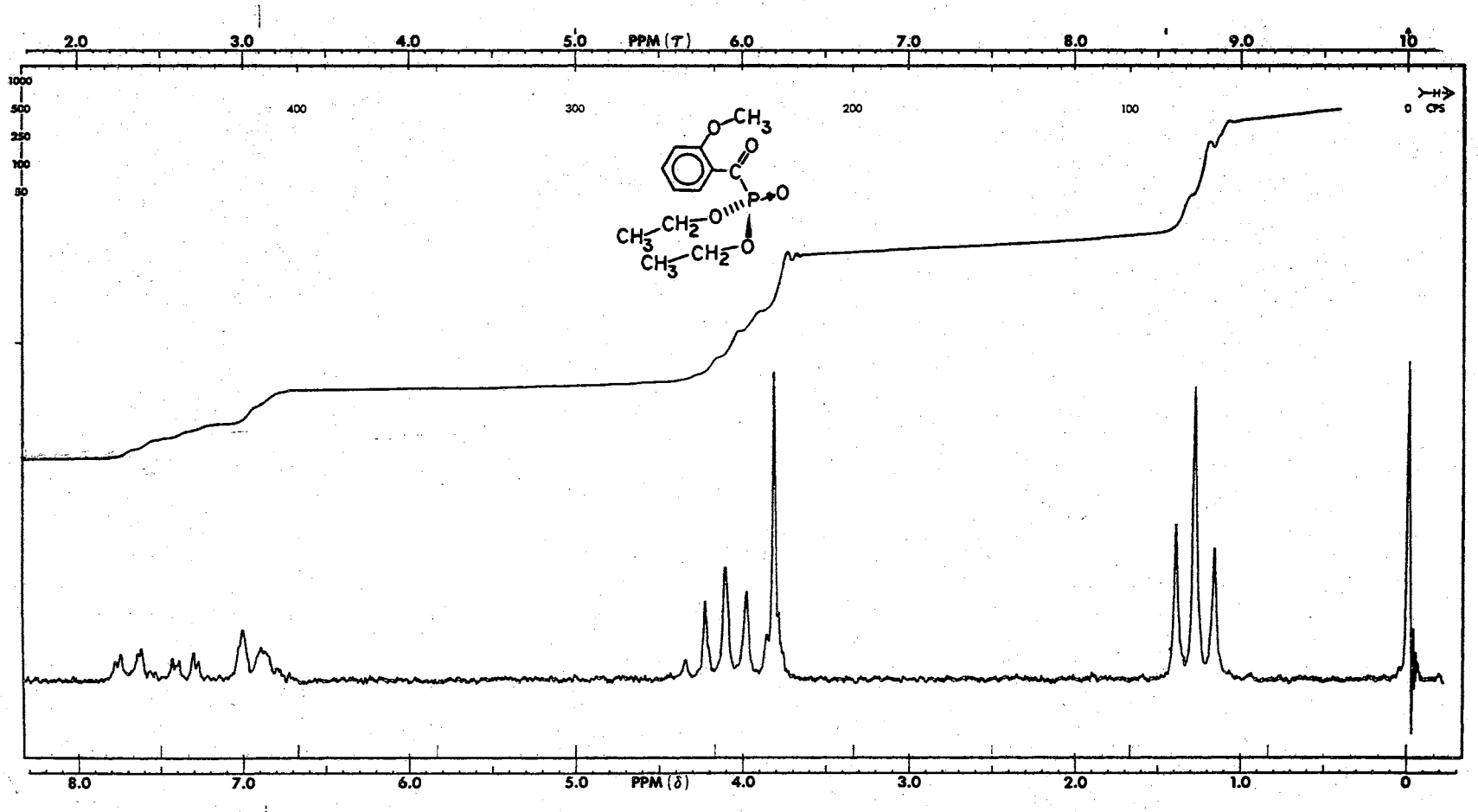
Plate XLI



Diethyl p-Methoxybenzoylphosphonate (IIIf)

Solvent ..... CCl_4	F. B. ..... 4 cps	S. W. ..... 500 cps	S. A. 6.3
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0 cps	I. A. 63

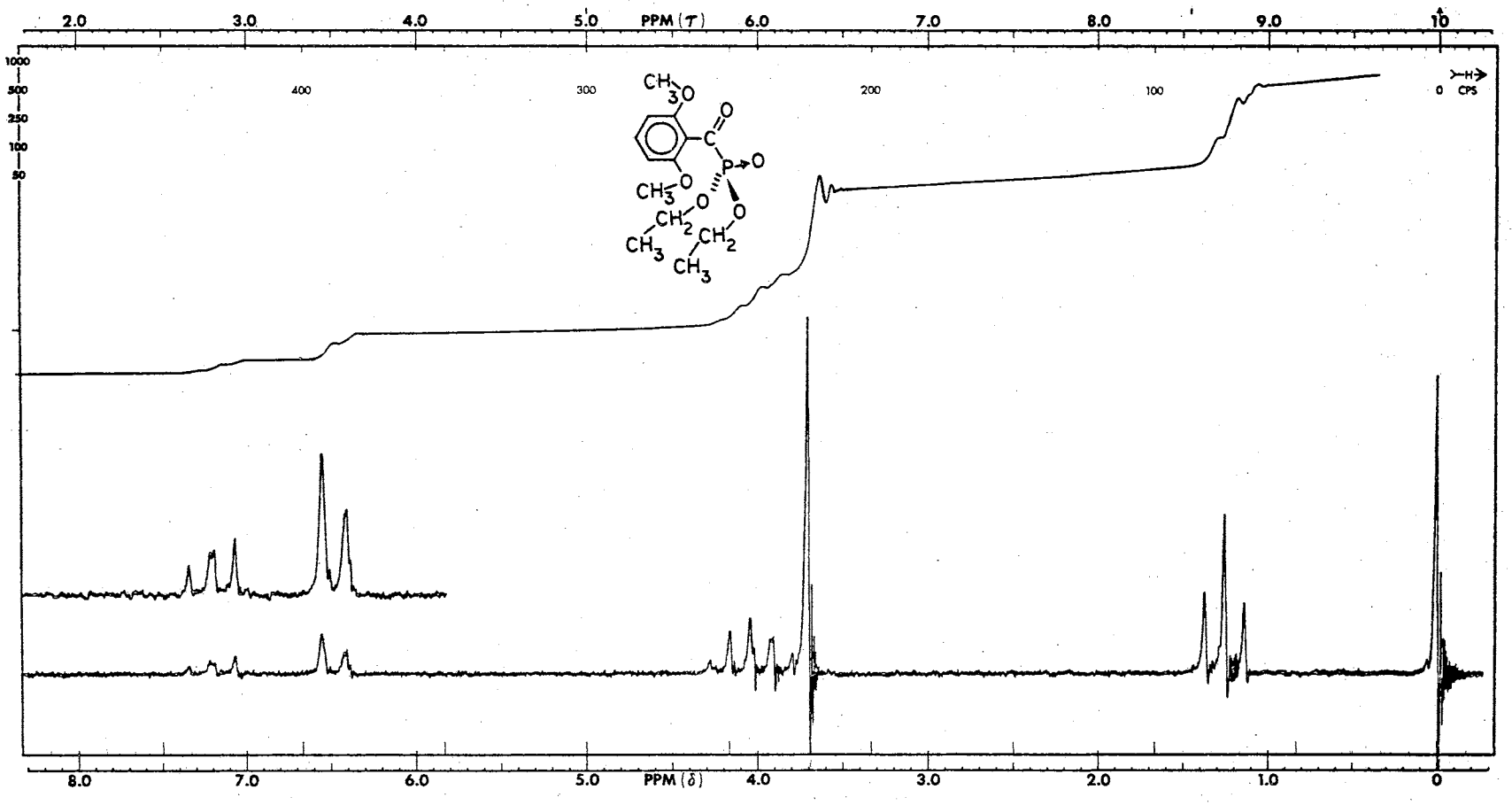
Plate XLII



Diethyl o-Methoxybenzoylphosphonate (IIIg)

Solvent ..... CCl_4	F. B. ..... 1 cps	S. W. ..... 500 cps	S. A. 3.2
R. F. Field .... 0.02 mG	S. T. ..... 250 sec	S. O. ..... 0 cps	I. A. 63

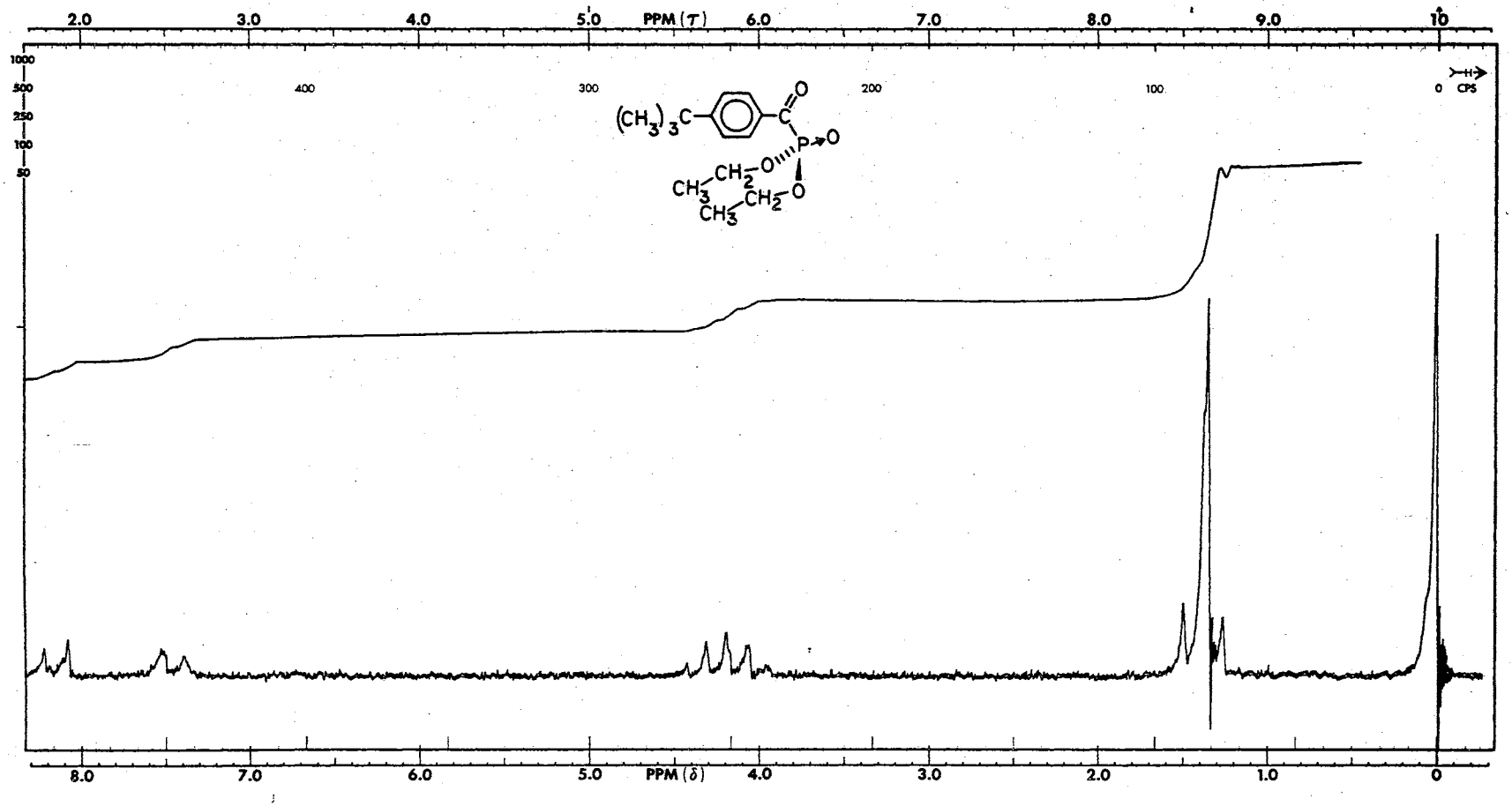
Plate XLIII



Diethyl 2,6-Dimethoxybenzoylphosphonate (IIIh)

Solvent ..... CCl_4	F. B. ..... 4 cps	S. W. ..... 500 cps	S. A. 1.6
R. F. Field .... 0.02 mG	S. T. ..... 250 sec	S. O. ..... 0 cps	I. A. 63

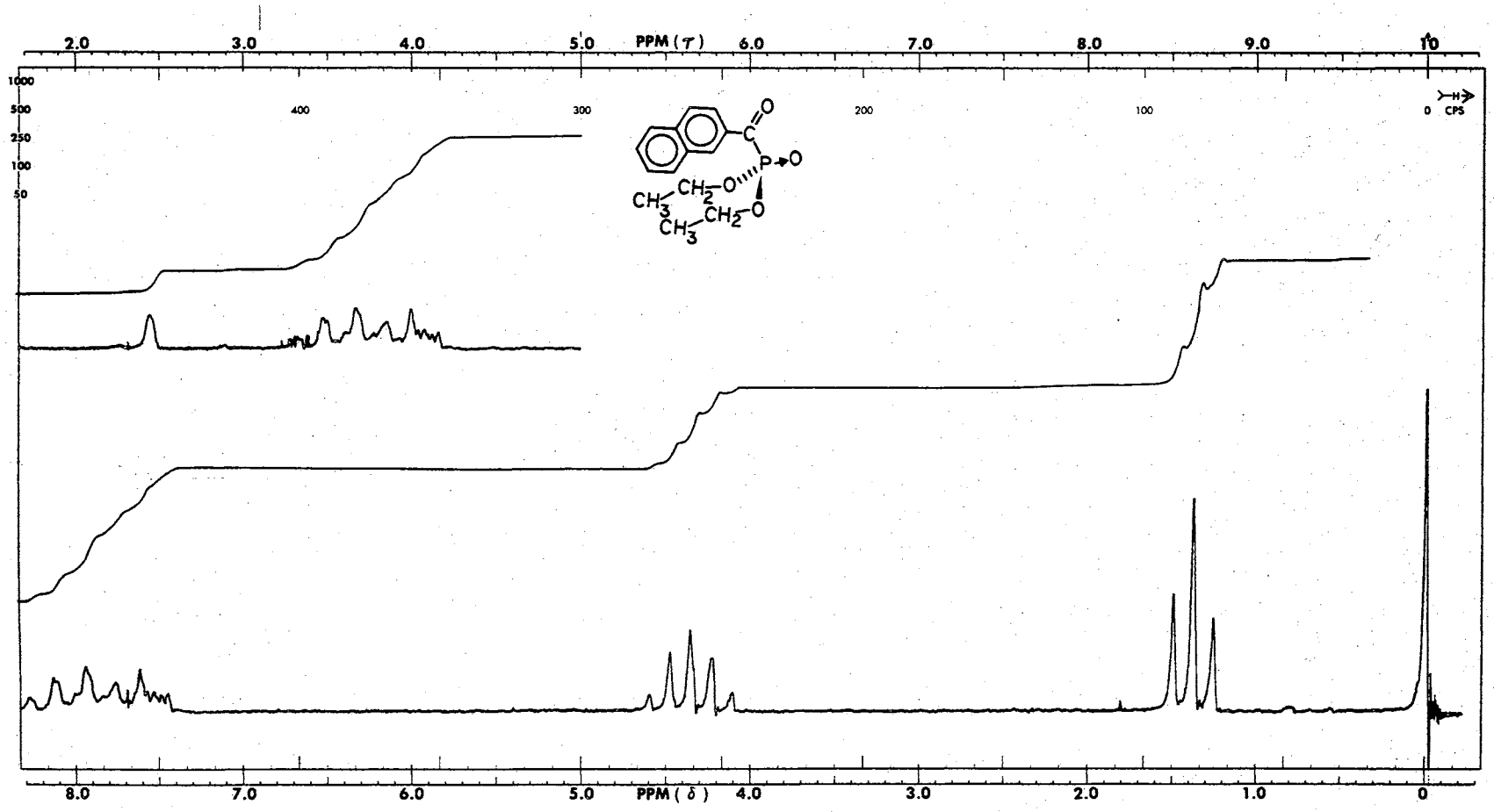
Plate XLIV



Diethyl p-t-Butylbenzoylphosphonate (IIIi)

Solvent ..... CCl_4	F. B. ..... 2 cps	S. W. ..... 500 cps	S. A. 6.3
R. F. Field ....0.075 mG	S. T. ..... 250 sec	S. O. ..... 0 cps	I. A. 63

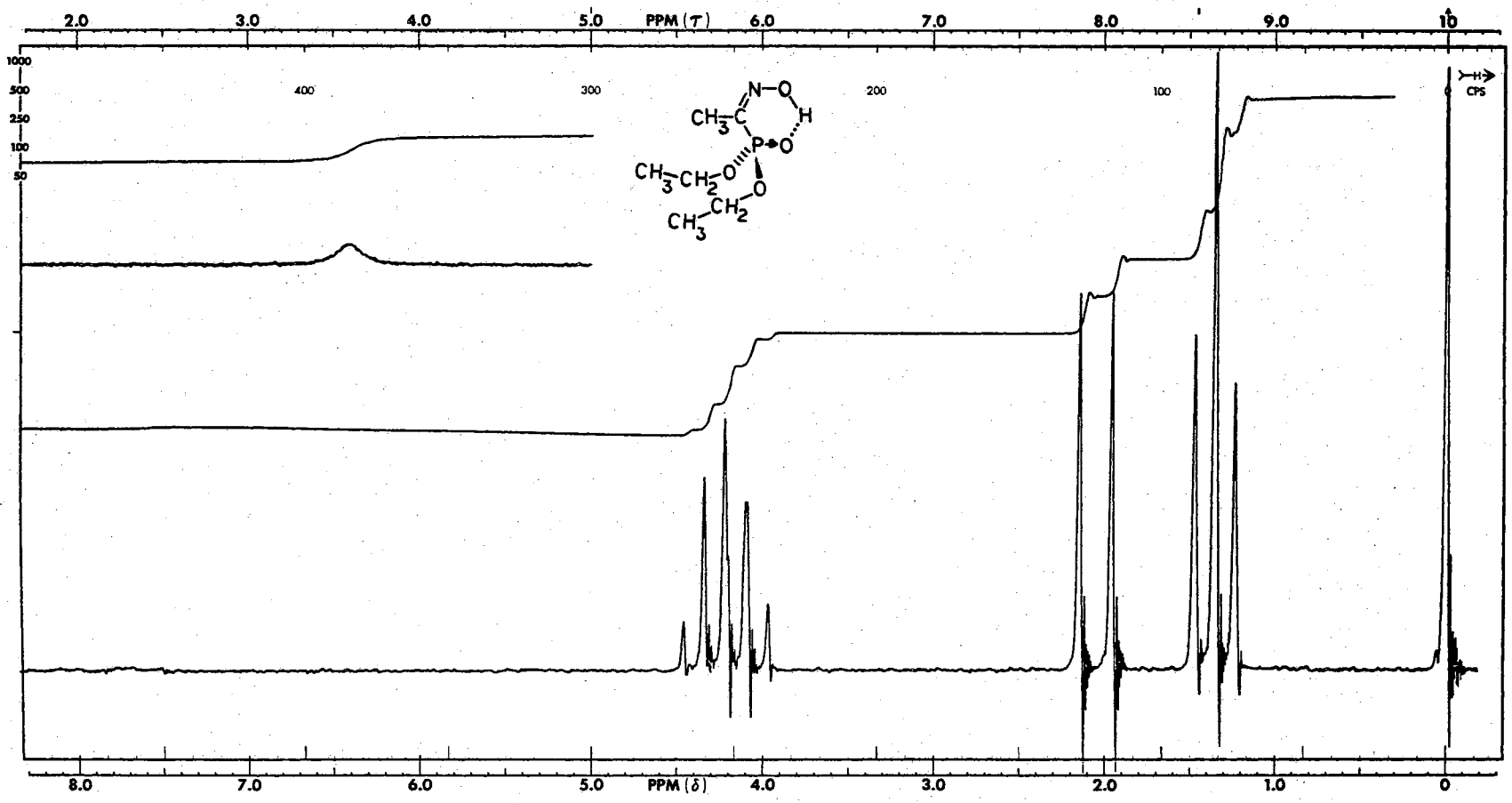
Plate XLV



Diethyl 2-Naphthoylphosphonate (IIIj)

Solvent ..... $CDCl_3$	F. B. ..... 4 cps	S. W. ..... 500 cps	S. A. 8.0
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0,100 cps	I. A. 32

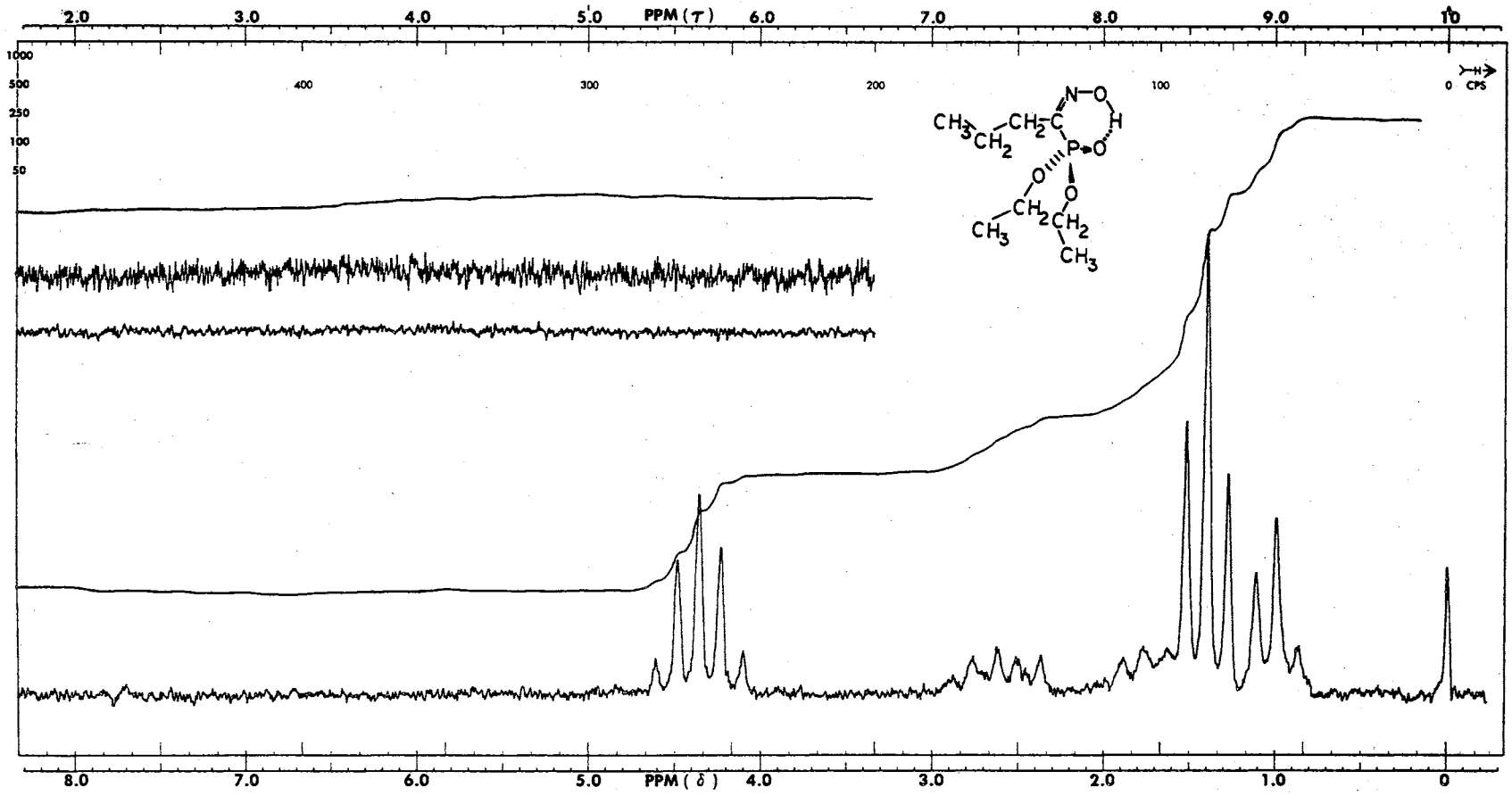
Plate XLVI



Diethyl Acetylphosphonate Oxime (IVa)

Solvent ..... $CDCl_3$	F. B. ..... 4 cps	S. W. ..... 500 cps	S. A. 4.0
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0,300 cps	I. A. 25

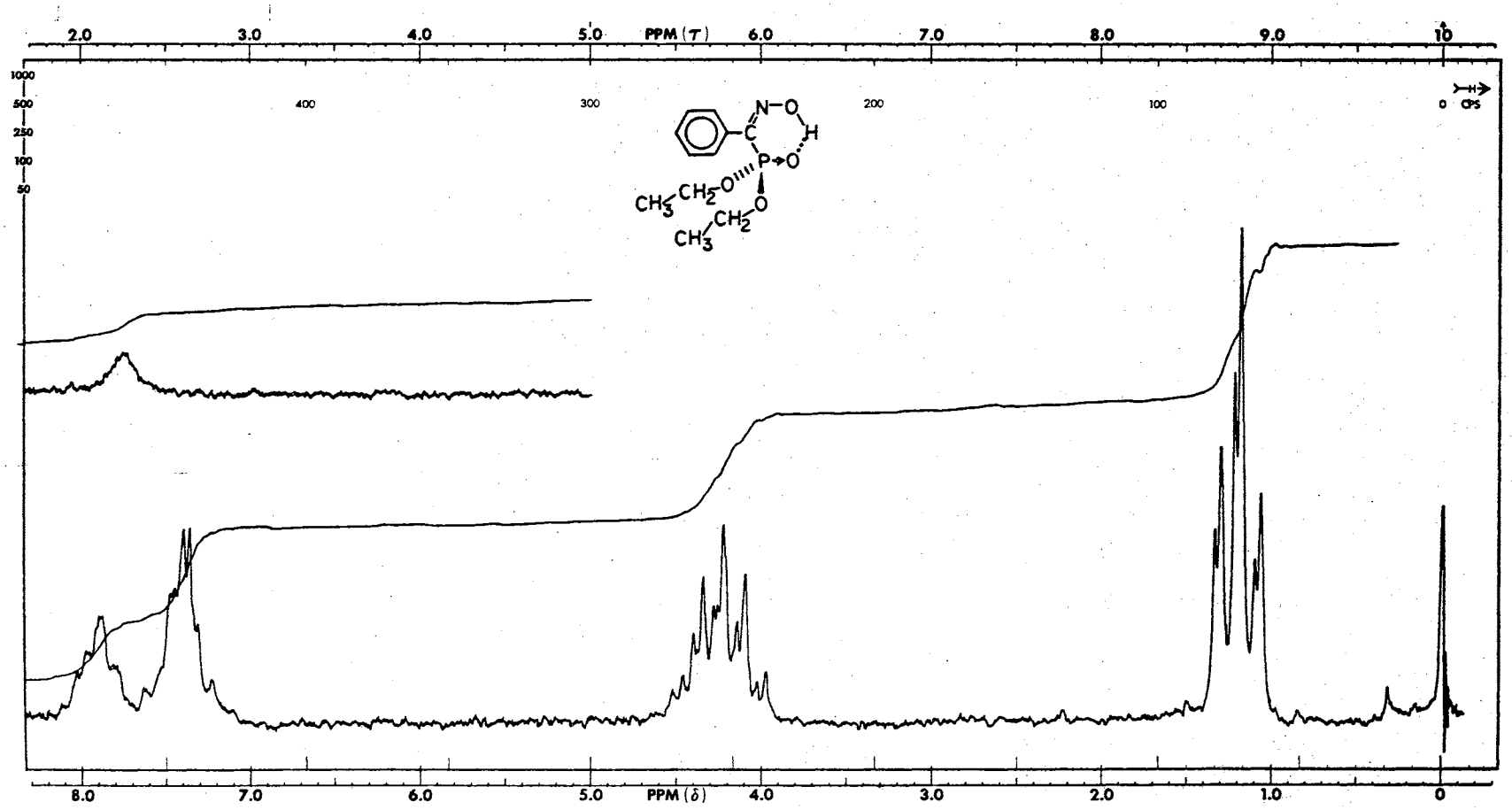
Plate XLVII



Diethyl Butyrylphosphonate Oxime (IVb)

Solvent ..... $CDCl_3$	F. B. ..... 2 cps	S. W. ..... 500 cps	S. A. 5,10,10
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ... 0,300,300 cps	I. A. 5.0

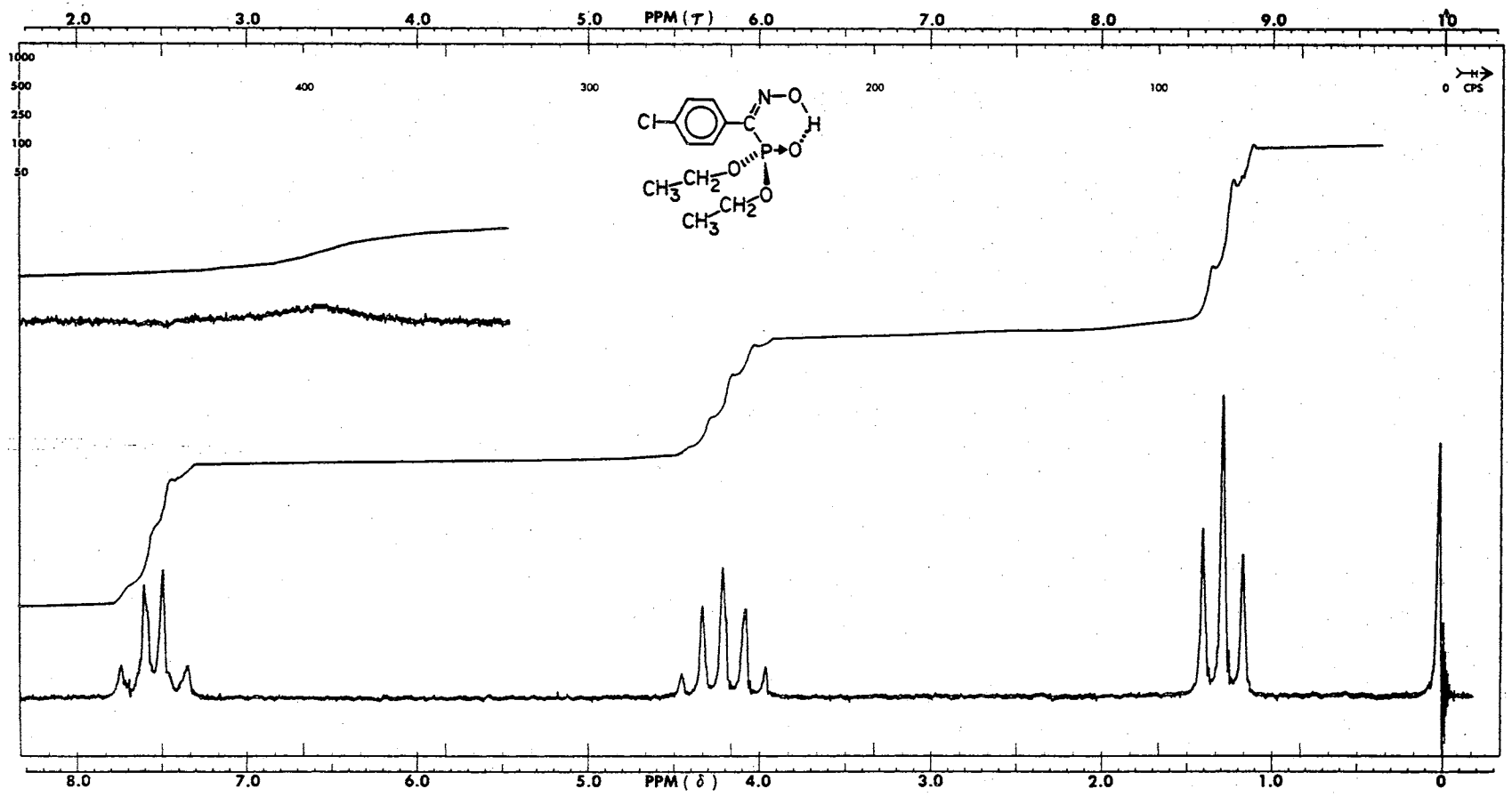
Plate XLVIII



Diethyl Benzoylphosphonate Oxime (IVe, Crude)

Solvent ... Satd., C_5D_5N	F. B. ..... 0.4 cps	S. W. ..... 250 cps	S. A. 8.0
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0,400 cps	I. A. 80

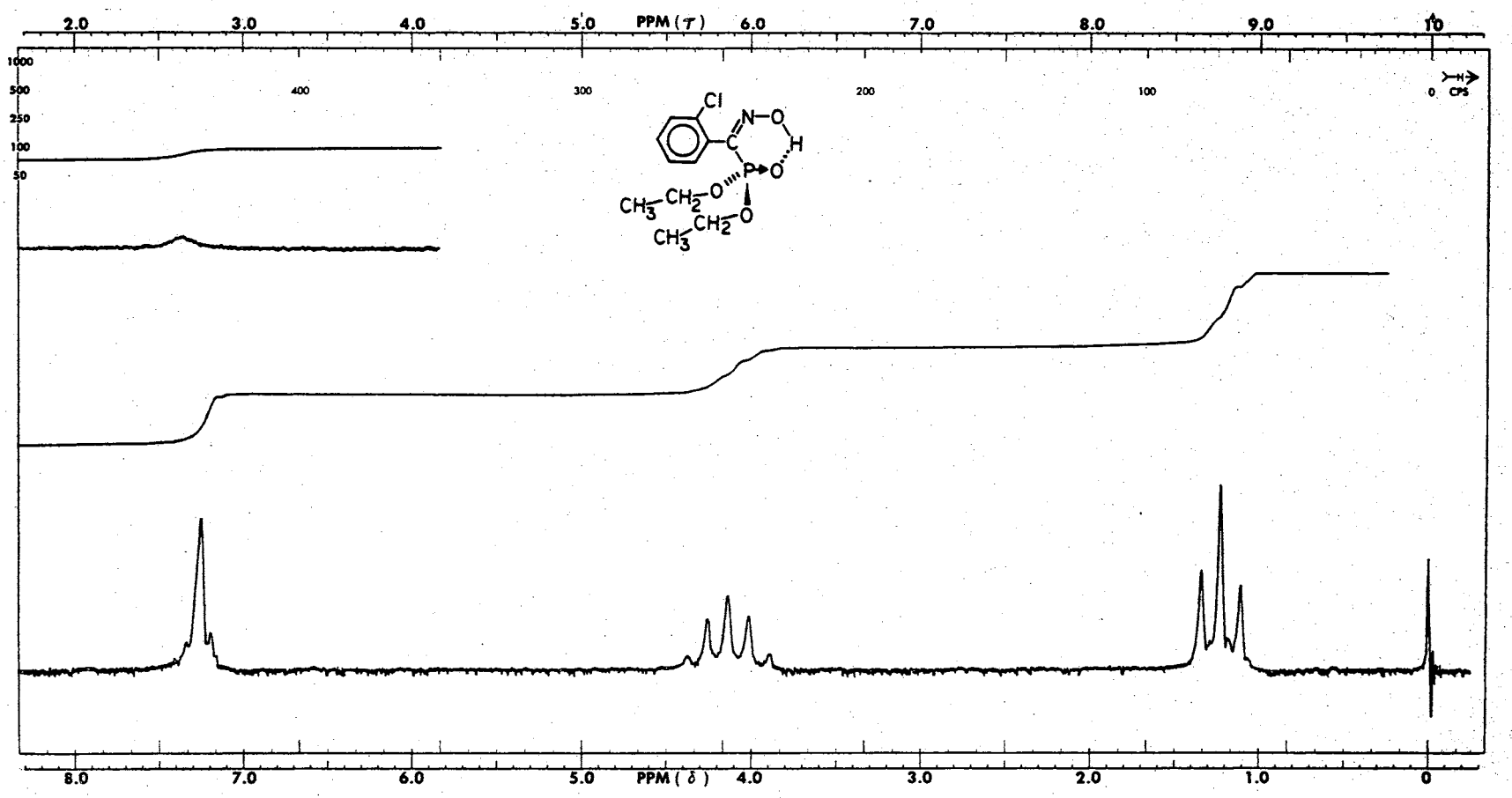
Plate XLIX



Diethyl p-Chlorobenzoylphosphonate Oxime (IVd)

Solvent ..... $CDCl_3$	F. B. ..... 4 cps	S. W. ..... 500 cps	S. A. 4,10
R. F. Field .... 0.20 mG	S. T. ..... 250 sec	S. O. .....0,300 cps	I. A. 80

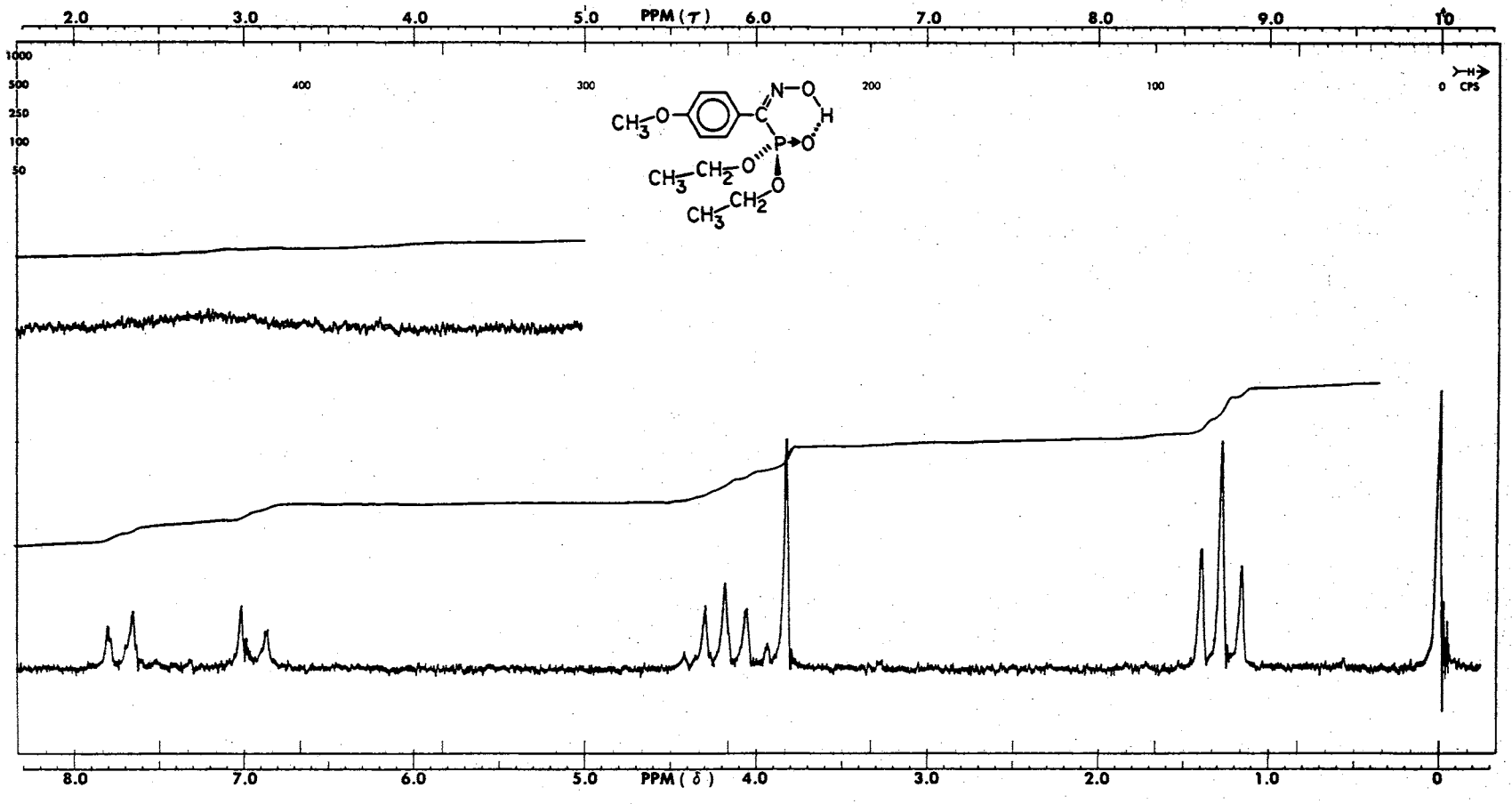
Plate L



Diethyl o-Chlorobenzoylphosphonate Oxime (IVe)

Solvent ..... $CDCl_3$	F. B. ..... 2 cps	S. W. ..... 500 cps	S. A. 2.5
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0,250 cps	I. A. 4.0

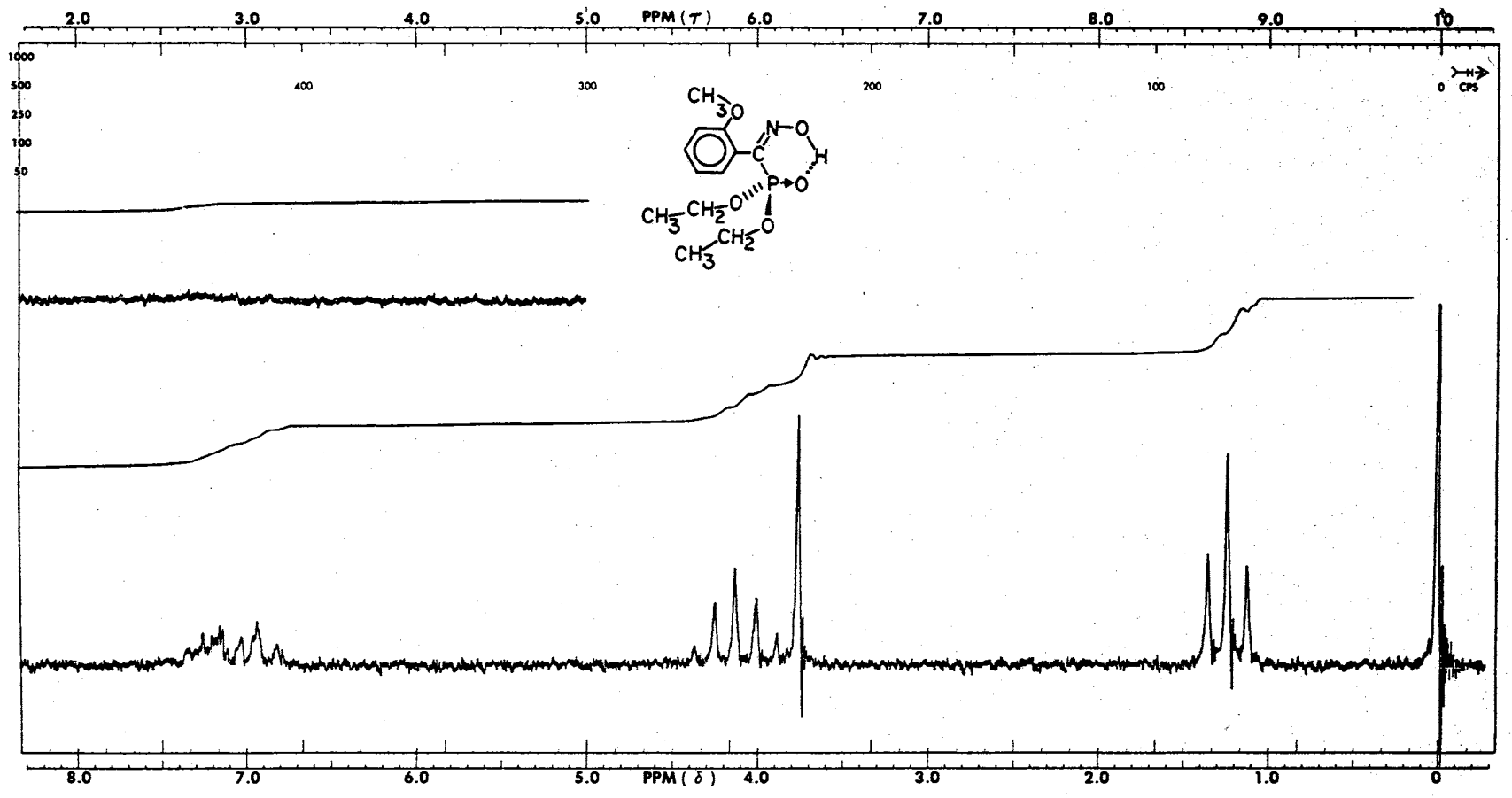
Plate LI



Diethyl p-Methoxybenzoylphosphonate Oxime (IVf)

Solvent ..... $CDCl_3$	F. B. ..... 2 cps	S. W. ..... 500 cps	S. A. 5.0,32
R. F. Field .... 0.10 mG	S. T. ..... 250 sec	S. O. ..... 0,200 cps	I. A. 50

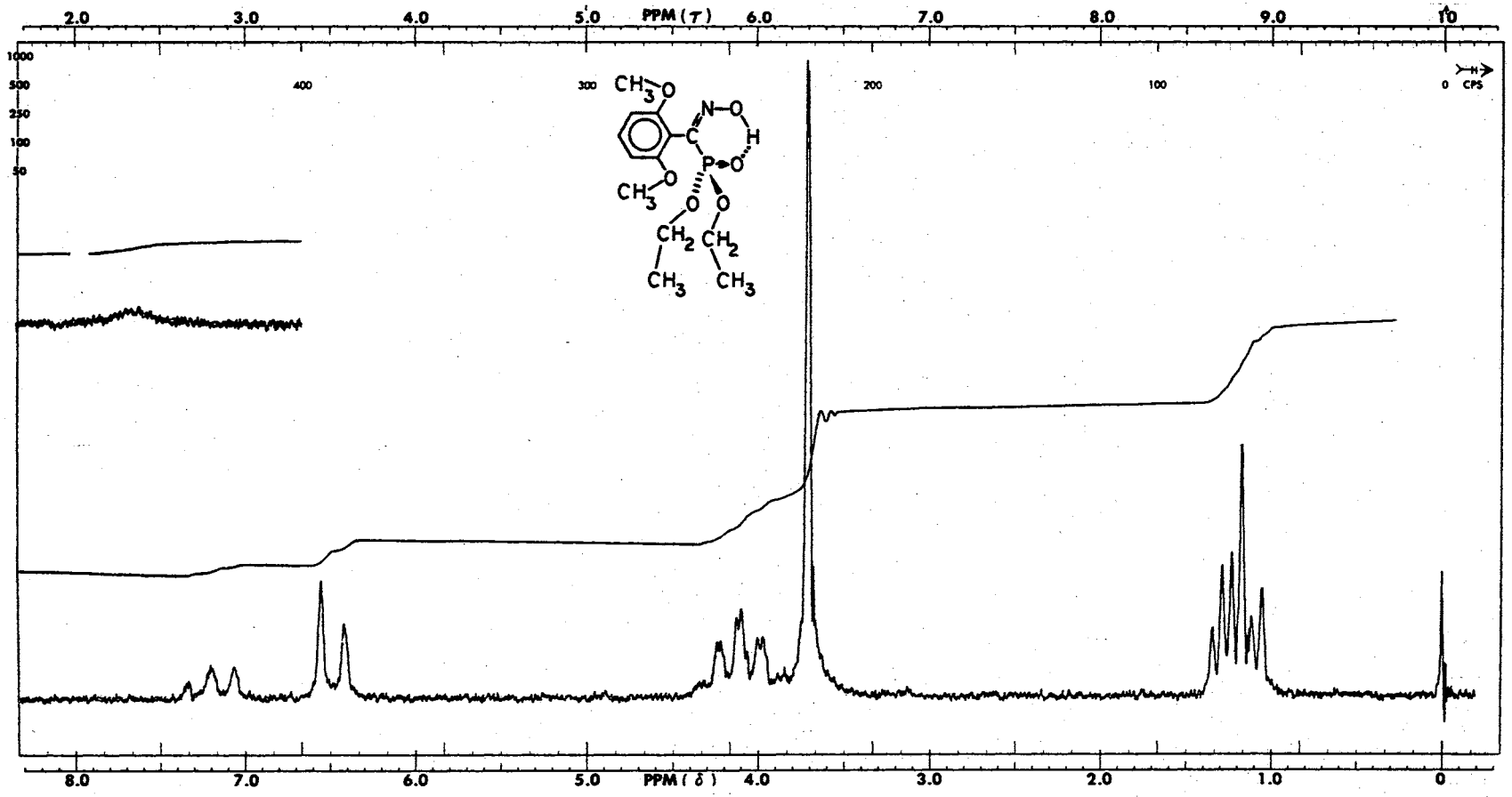
Plate LII



Diethyl o-Methoxybenzoylphosphonate Oxime (IVg)

Solvent ..... $CDCl_3$	F. B. ..... 2 cps	S. W. ..... 500 cps	S. A. 6.3
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0,200 cps	I. A. 50

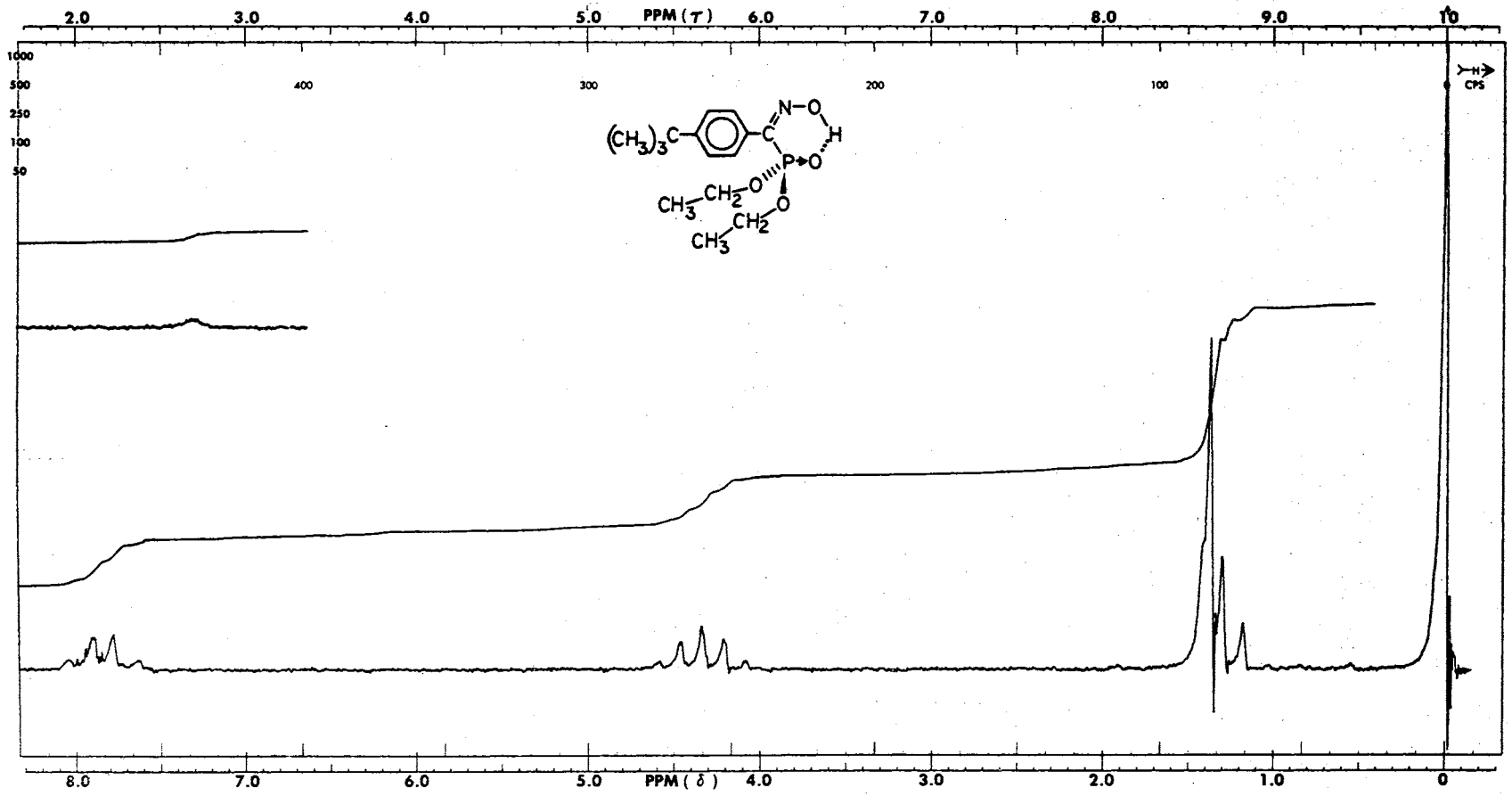
Plate LIII



Diethyl 2,6-Dimethoxybenzoylphosphonate Oxime (IVh)

Solvent ... Satd., $CDCl_3$	F. B. ..... 2 cps	S. W. ..... 500 cps	S. A. 5.0
R. F. Field .... 0.50 mG	S. T. ..... 250 sec	S. O. ..... 0,200 cps	I. A. 63

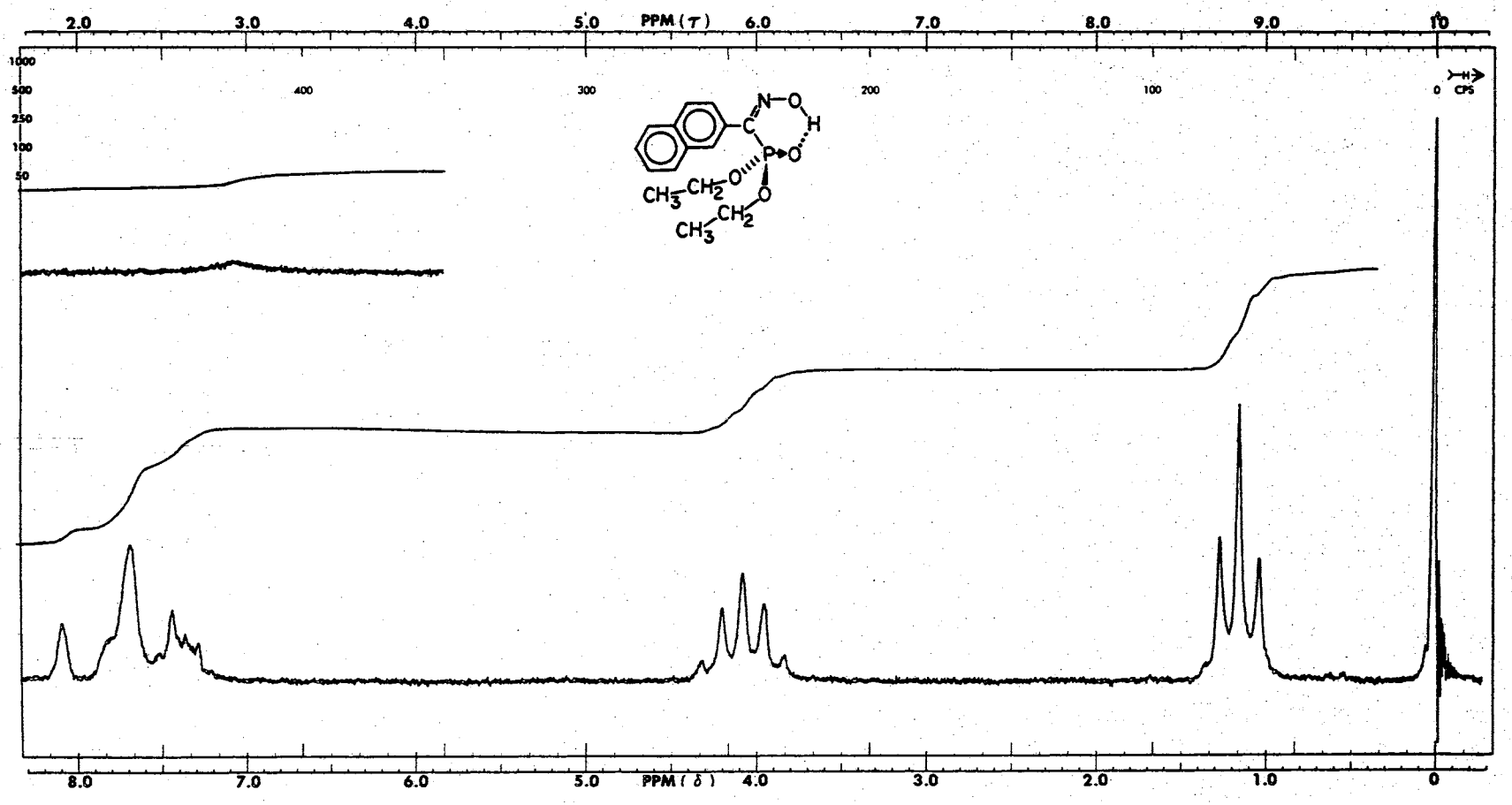
Plate LIV



Diethyl p-t-Butylbenzoylphosphonate Oxime (IVi)

Solvent ... Satd., $CDCl_3$	F. B. ..... 4 cps	S. W. ..... 500 cps	S. A. 1.6
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0,300 cps	I. A. 40

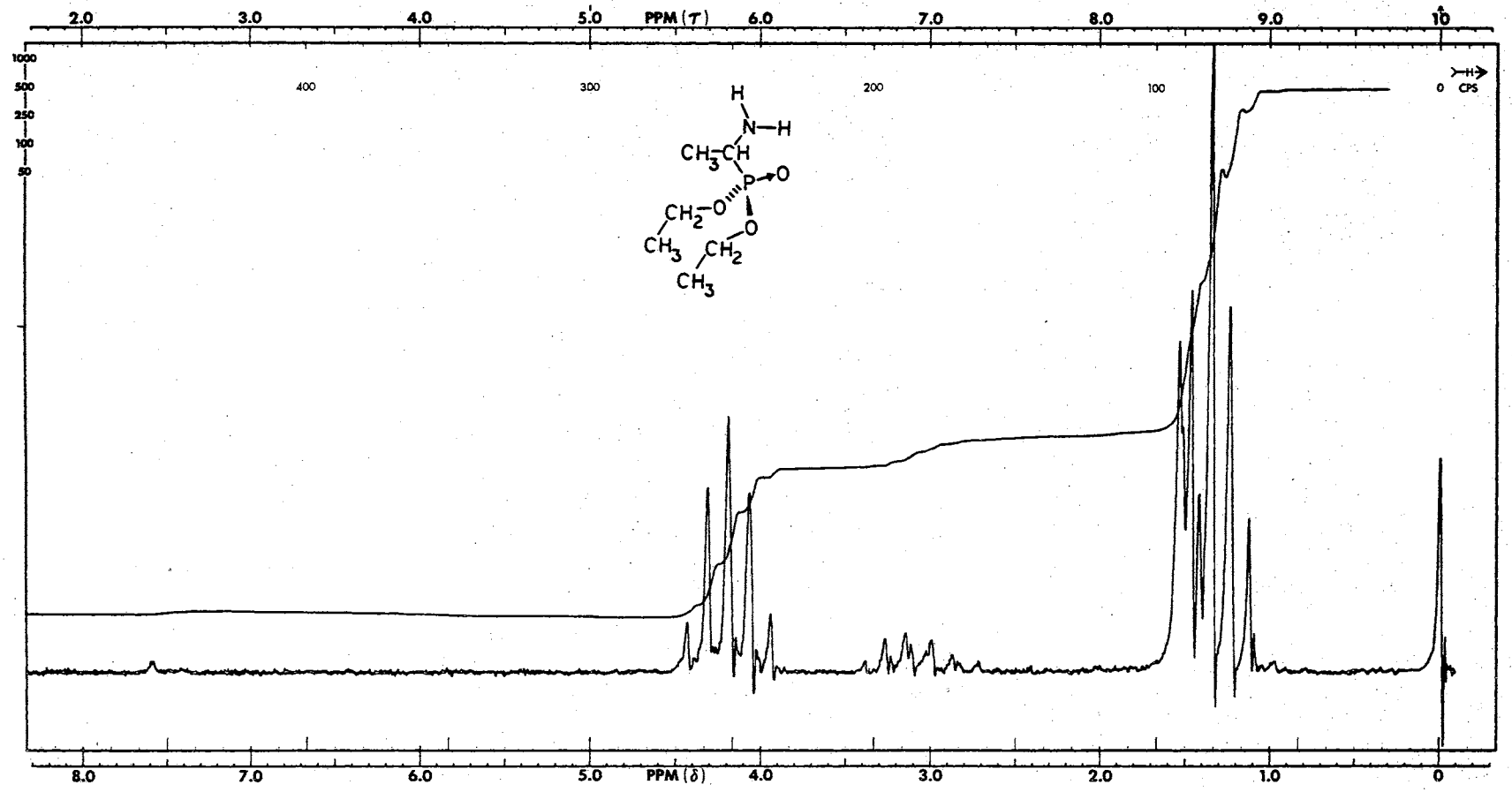
Plate LV



Diethyl 2-Naphthoylphosphonate Oxime (IVj)

Solvent ... Satd., $CDCl_3$	F. B. ..... 4 cps	S. W. ..... 500 cps	S. A. 3.2
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0,300 cps	I. A. 63

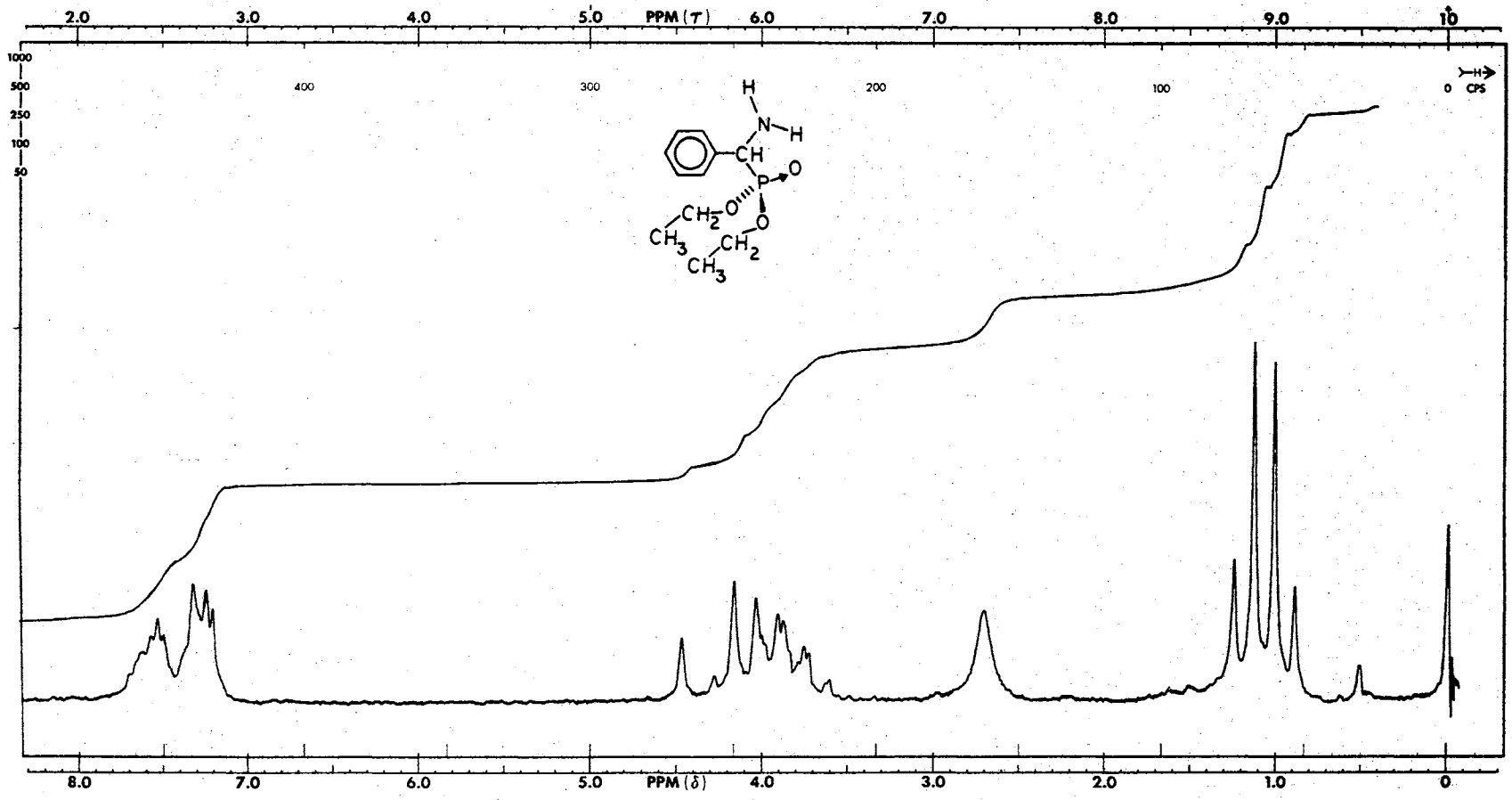
Plate LVI



(RS) Diethyl 1-Aminoethylphosphonate (Va)

Solvent ..... $CDCl_3$	F. B. ..... 4 cps	S. W. ..... 500 cps	S. A. 6.3
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0 cps	I. A. 25

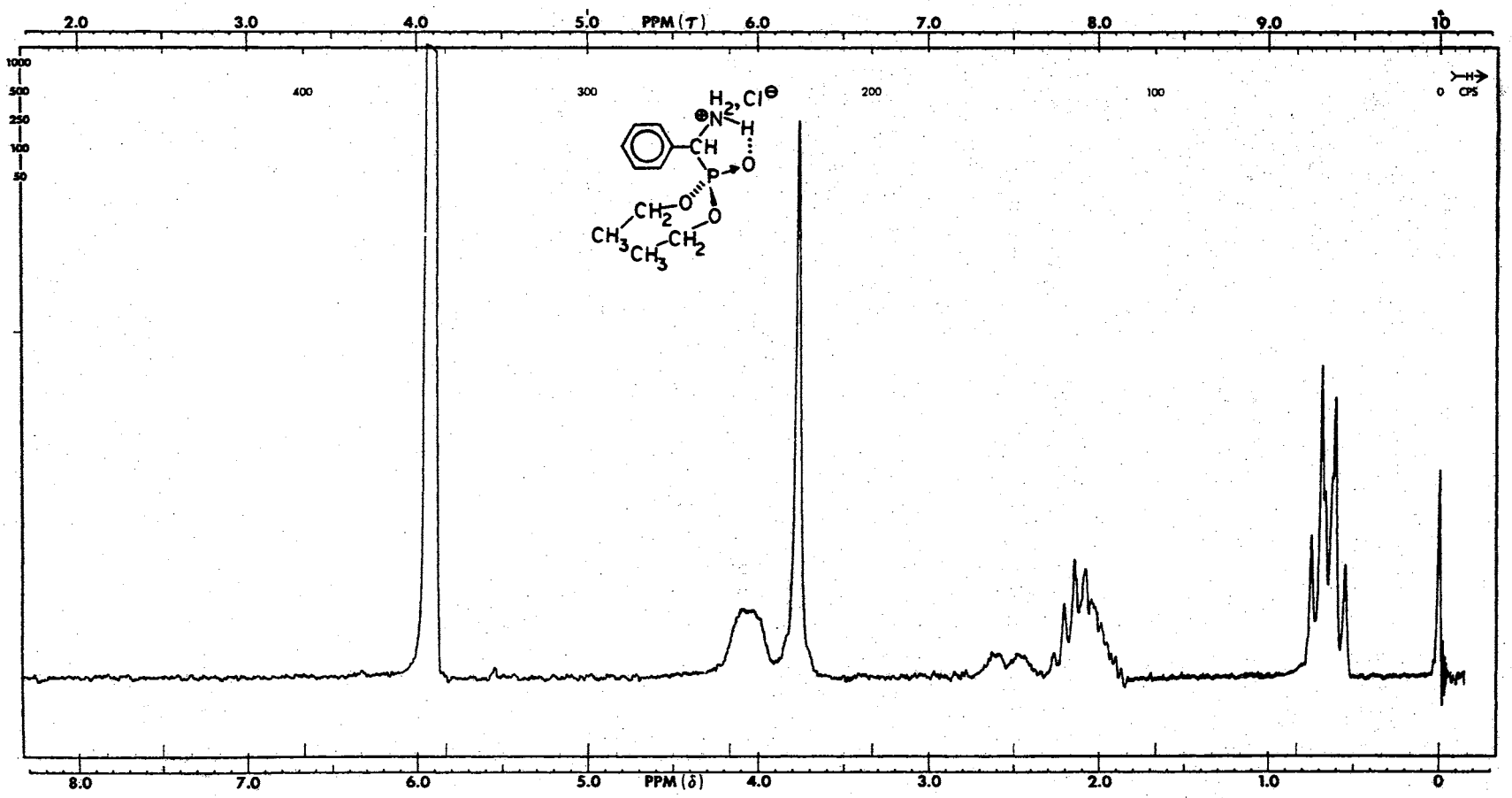
Plate LVII



(RS) Diethyl α-Aminobenzylphosphonate (Vc, Crude)

Solvent ..... C_5D_5N	F. B. ..... 1 cps	S. W. ..... 500 cps	S. A. 2.0
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0 cps	I. A. 20

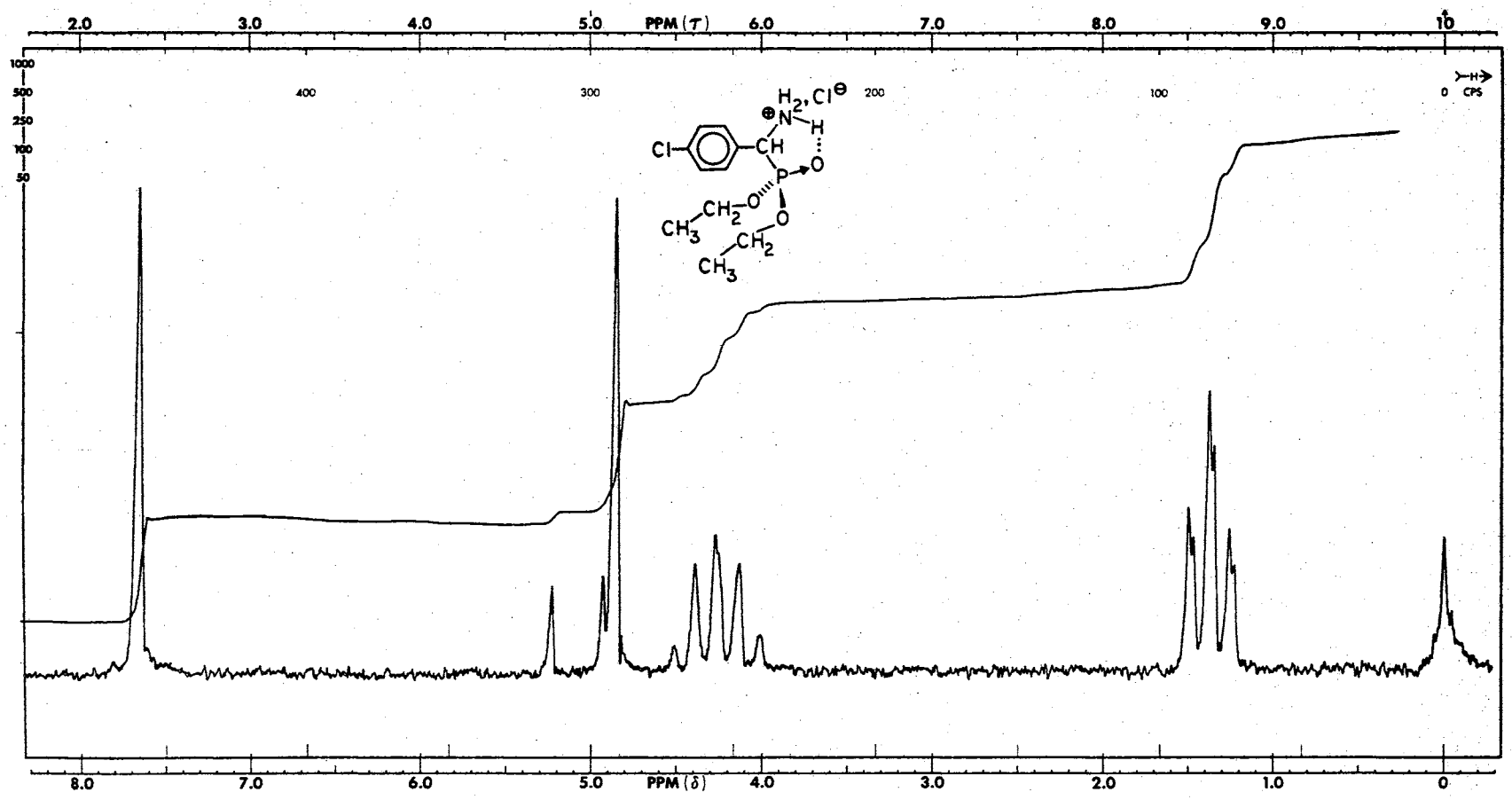
Plate LVIII



(RS) Diethyl α-Aminobenzylphosphonate Hydrochloride (VIc)

Solvent ..... CF_3COOH	F. B. ..... 2 cps	S. W. ..... 1000 cps	S. A. 8.0
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0 cps	I. A. ..... off

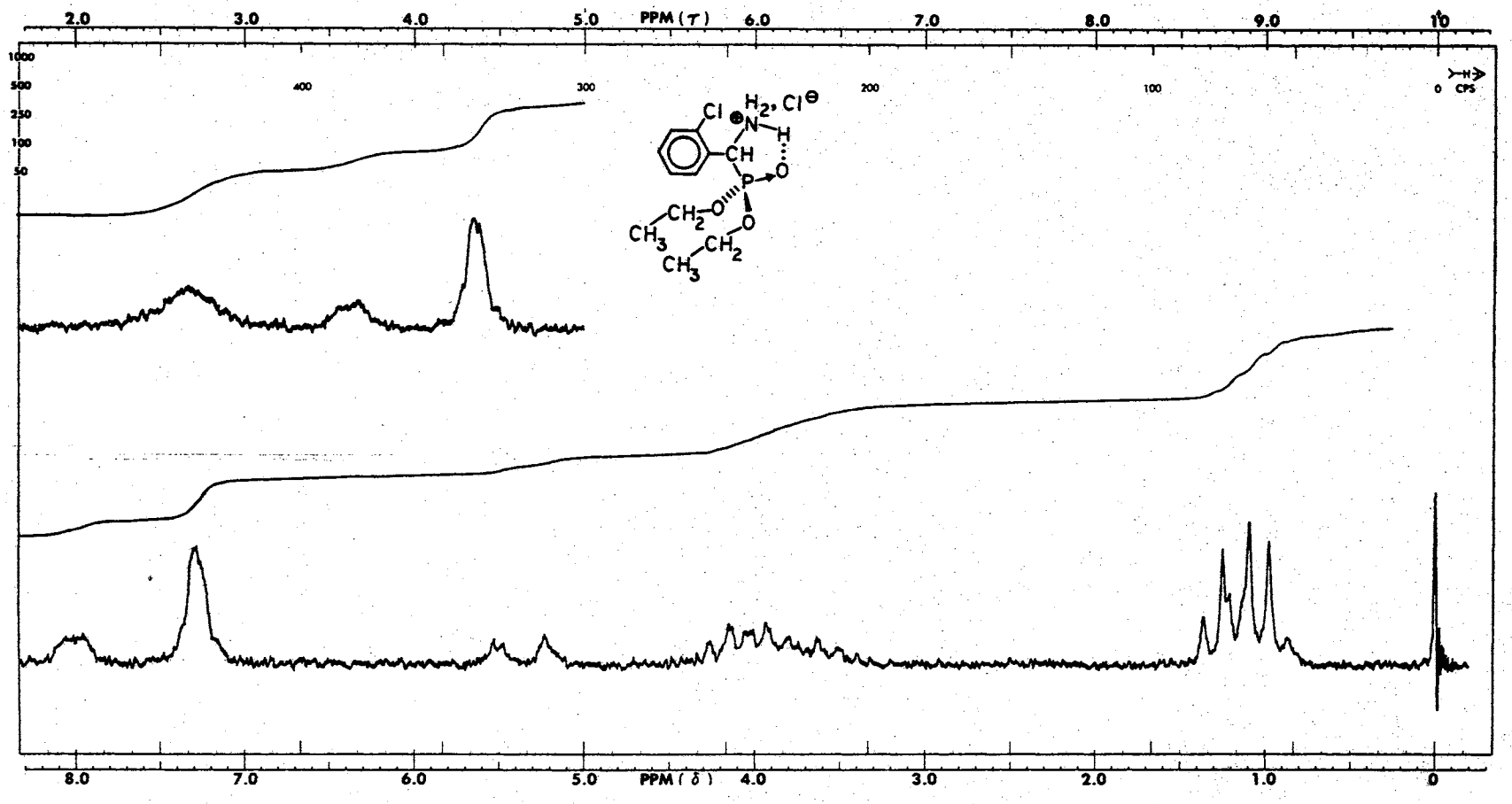
Plate LIX



(RS) Diethyl α-Amino-p-chlorobenzylphosphonate Hydrochloride (VId)

Solvent ..... D_2O	F. B. ..... 2 cps	S. W. ..... 500 cps	S. A. 25
R. F. Field .... 0.13 mG	S. T. ..... 250 sec	S. O. ..... 0 cps	I. A. 20

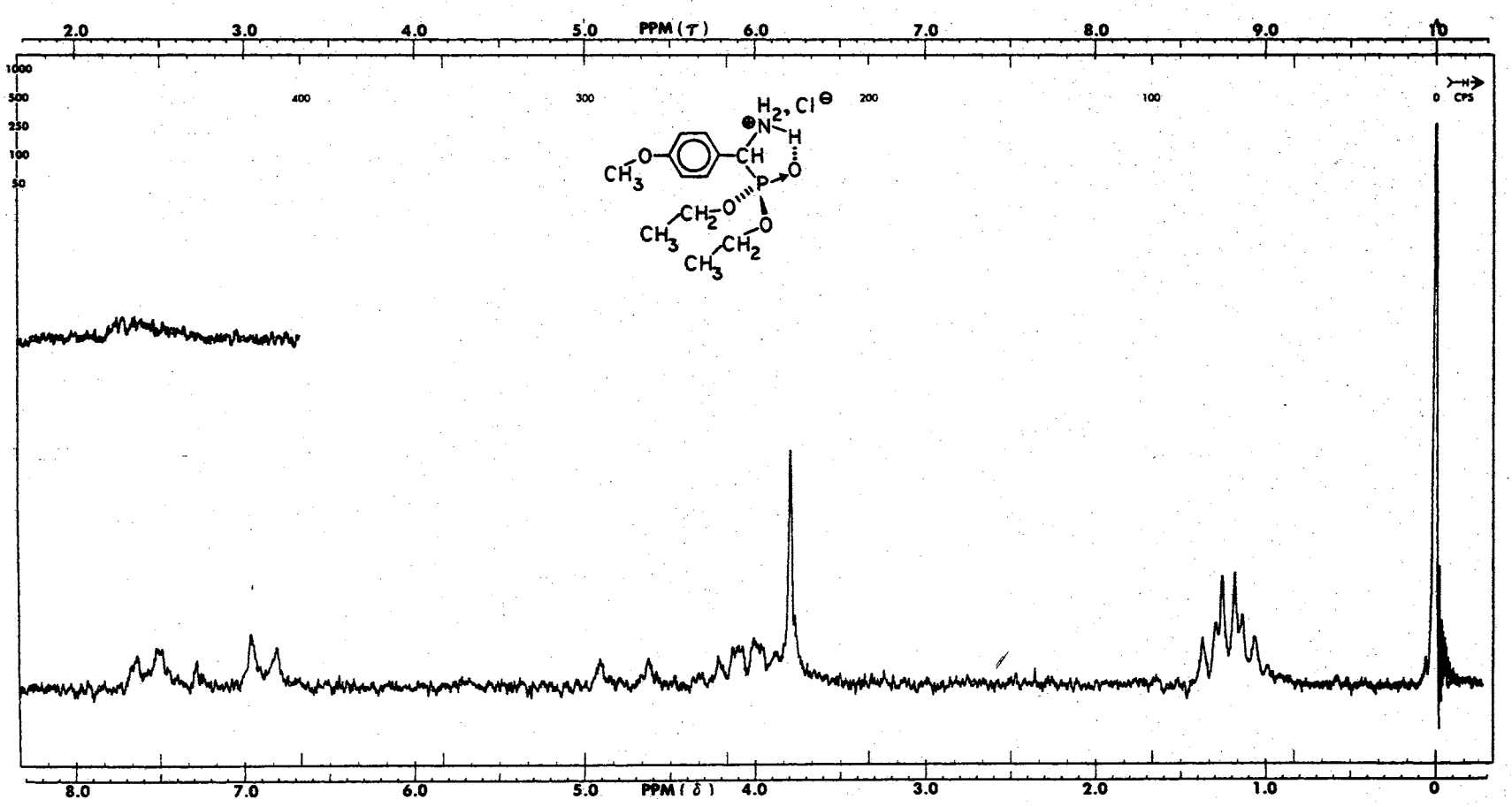
Plate LX



(RS) Diethyl α-Amino-o-chlorobenzylphosphonate Hydrochloride (IVe, Crude)

Solvent ... Satd., $CDCl_3$	F. B. ..... 1 cps	S. W. ..... 500 cps	S. A. 10
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0,100 cps	I. A. 50

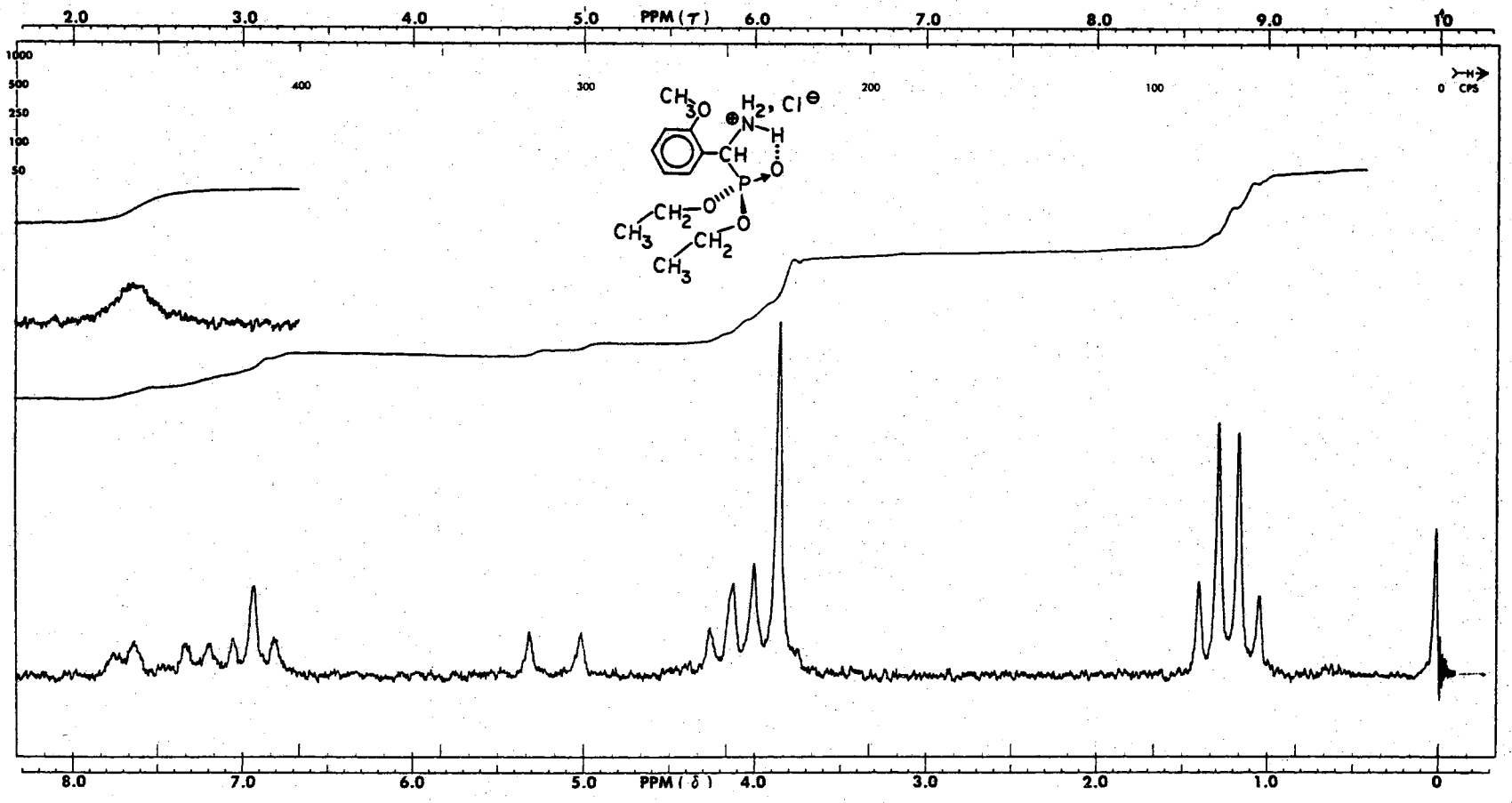
Plate LXI



(RS) Diethyl α-Amino-p-methoxybenzylphosphonate Hydrochloride (VIf)

Solvent .... Satd., $CDCl_3$	F. B. ..... 1 cps	S. W. ..... 500 cps	S. A. 50
R. F. Field .... 0.25 mG	S. T. ..... 250 sec	S. O. ..... 0,100 cps	I. A. .....off

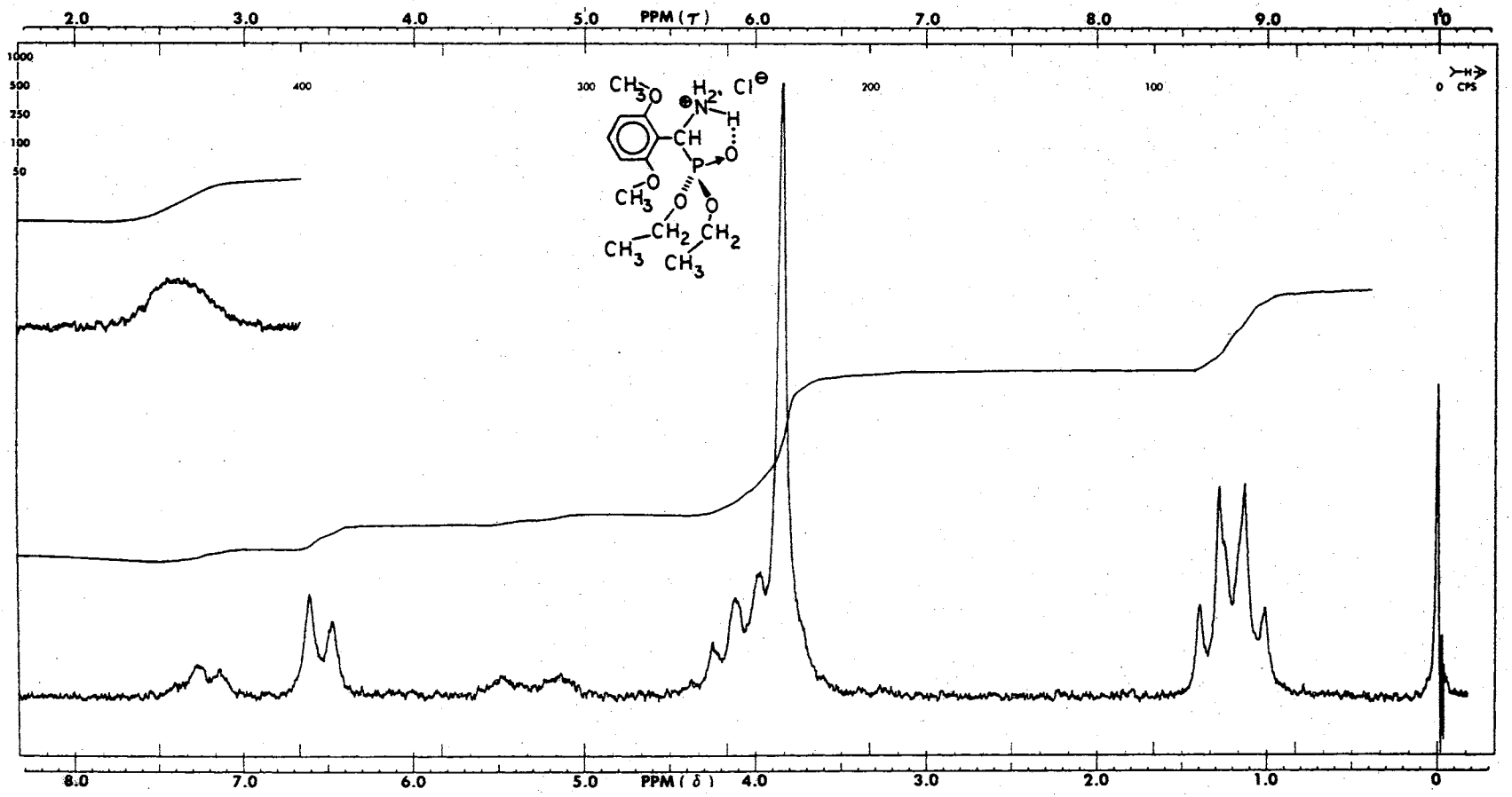
Plate LXII



(RS) Diethyl α-Amino-o-methoxybenzylphosphonate Hydrochloride (VIg)

Solvent ... Satd., $CDCl_3$	F. B. ..... 1 cps	S. W. ..... 500 cps	S. A. 8.0
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0,100 cps	I. A. 50

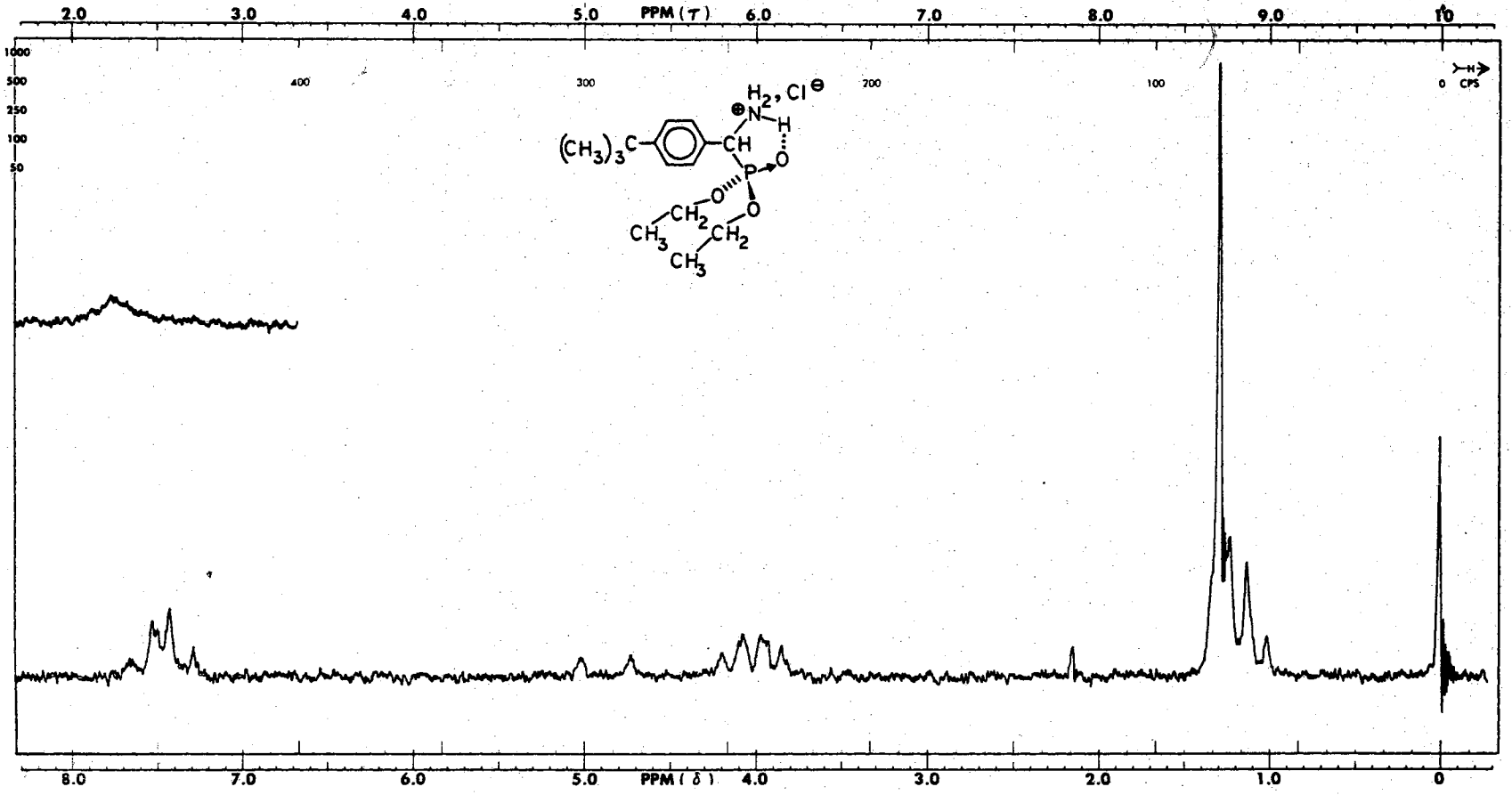
Plate LXIII



(RS) Diethyl α-Amino-2,6-dimethoxybenzylphosphonate Hydrochloride (VIh)

Solvent ... Satd., $CDCl_3$	F. B. ..... 1 cps	S. W. ..... 500 cps	S. A. 10
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0,100 cps	I. A. 63

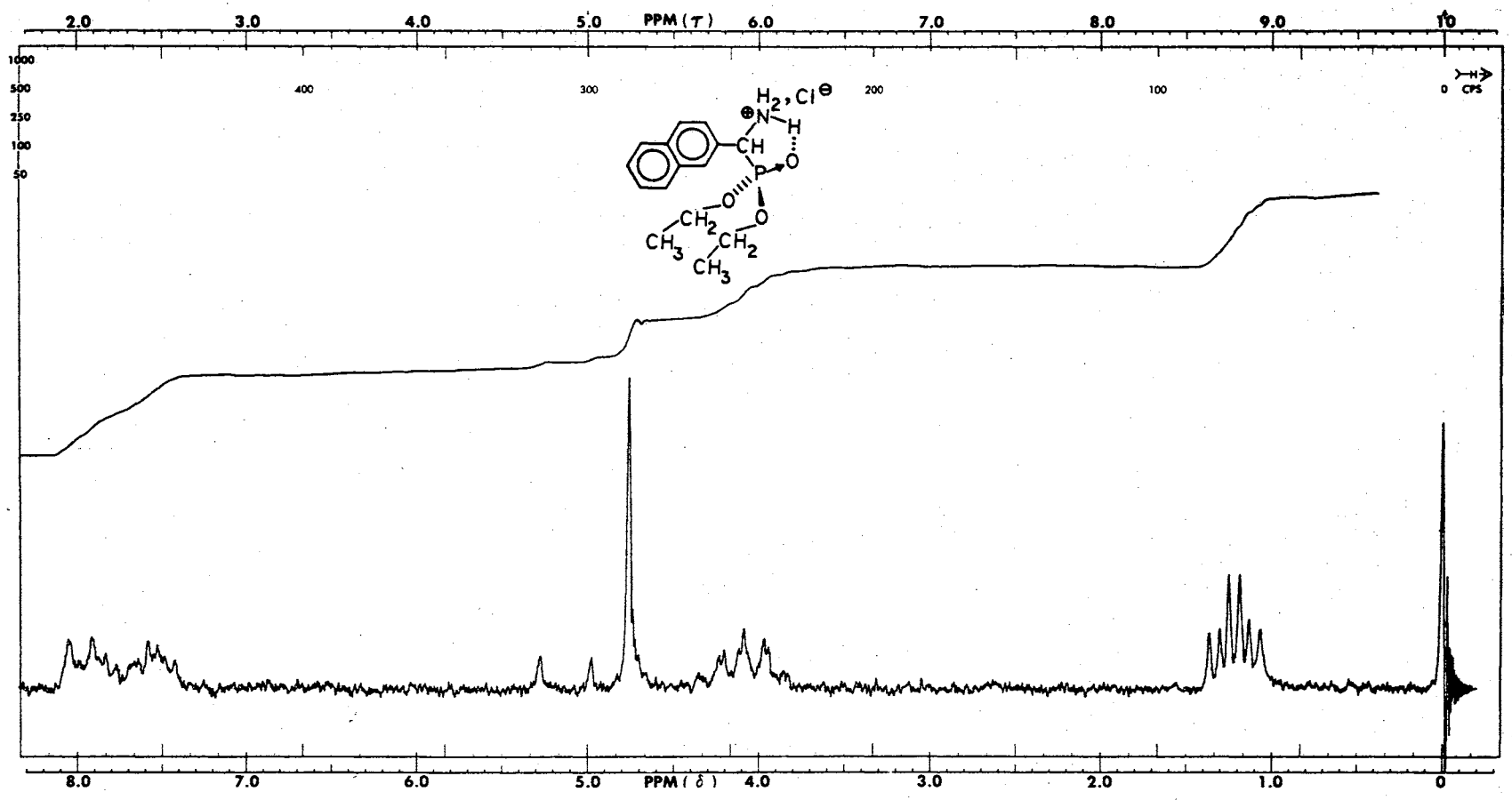
Plate LXIV



(RS) Diethyl α-Amino-p-t-butylbenzylphosphonate Hydrochloride (VIi)

Solvent ... Satd., $CDCl_3$	F. B. ..... 1 cps	S. W. ..... 500 cps	S. A. 10
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. .....0,100 cps	I. A. ..... off

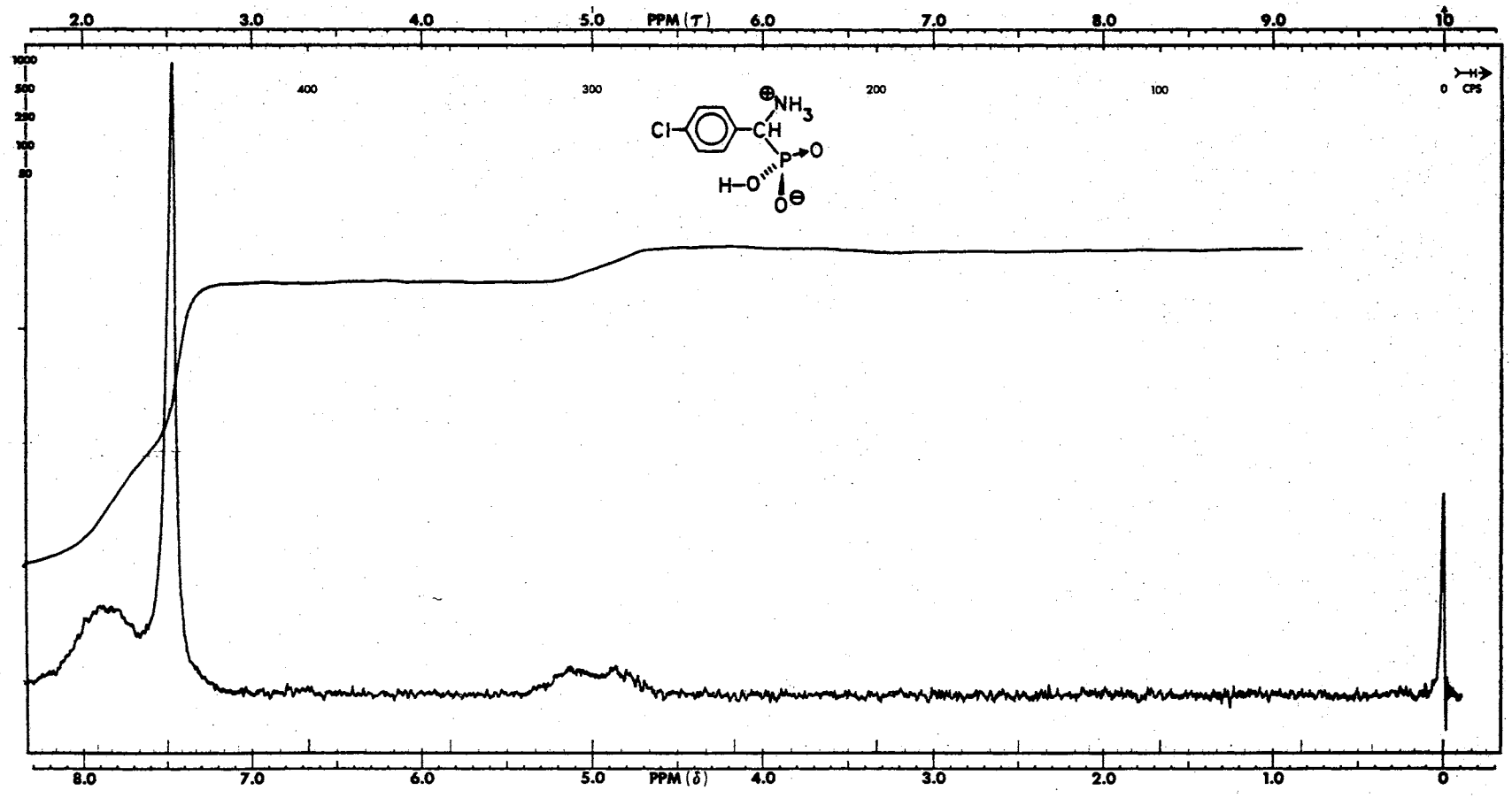
Plate LXV



(RS) Diethyl α-Amino-2-naphthylmethylphosphonate Hydrochloride (VIj)

Solvent ..... Satd., D_2O	F. B. ..... 1 cps	S. W. ..... 500 cps	S. A. 12
R. F. Field ... 0.075 mG	S. T. ..... 250 sec	S. O. ..... 0 cps	I. A. 80

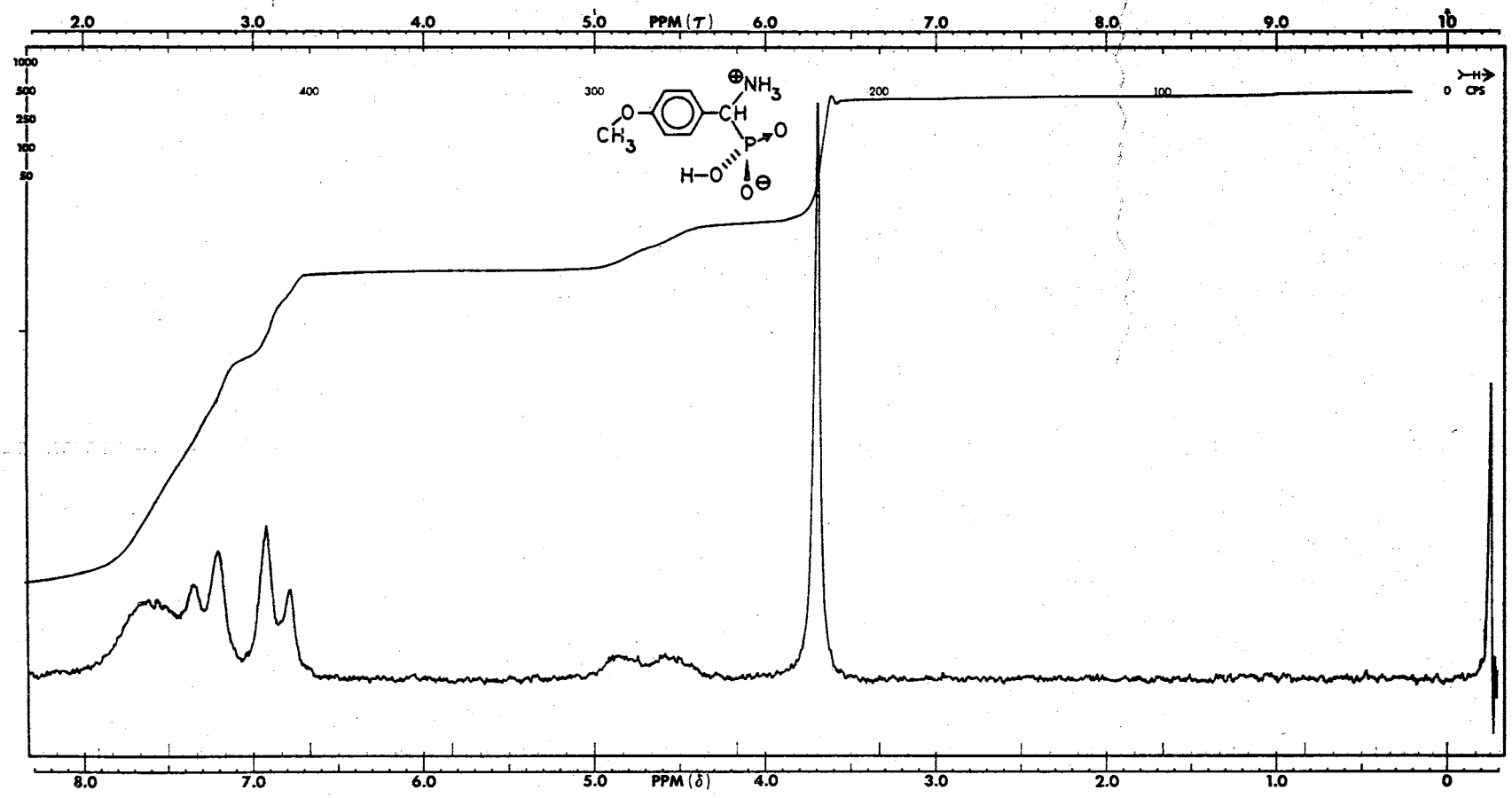
Plate LXVI



(RS) α-Amino-p-chlorobenzylphosphonic Acid (VIIId)

Solvent .. Satd., CF_3COOH	F. B. ..... 2 cps	S. W. ..... 500 cps	S. A. 12
R. F. Field .... 0.05 mG	S. T. ..... 250 sec	S. O. ..... 0 cps	I. A. 40

Plate LXVII



(RS) α-Amino-p-methoxybenzylphosphonic Acid (VIIIf)

Solvent . Satd., CF_3COOH	F. B. ..... 1 cps	S. W. ..... 500 cps	S. A. 10
R. F. Field .....0.05 mG	S. T. ..... 250 sec	S. O. ..... 15 cps	I. A. 40

BIBLIOGRAPHY

1. Abramov, V. S., Zh. Obshch. Khim., 22, 647 (1952); Chem. Abstr., 47, 5351 (1953).

2. Ackerman, B., Jordan, T. A., Eddy, C. R., and Swern, D., J. Am. Chem. Soc., 78, 4444 (1956).

3. Arbuzov, A. E. and Azansovskaya, M. M., Izvest. Akad. Nauk S.S.S.R., Otdel Khim. Nauk, 473 (1949); Chem. Abstr., 44, 1905 (1950).

4. Arthur, P., Anal. Chem., 36, 701 (1964).

5. Axtmann, R. C., Shuler, W. E., and Eberly, J. H., J. Chem. Phys., 31, 850 (1959).

6. Banks, C. V. and Yerick, R. E., Anal. Chim. Acta, 20, 301 (1959).

7. Baxter, C. F. and Roberts, E., J. Biol. Chem., 233, 1135 (1958).

8. Berlin, K. D. and Burpo, D. H., J. Org. Chem., 31, 1304 (1966).

9. Berlin, K. D., Burpo, D. H., Pagilagan, R. U., and Bude, D., to be published.

10. Berlin, K. D. and Hellwege, D. M., Private Communication.

11. Berlin, K. D., Hellwege, D. M., and Nagabushanam, M., J. Org. Chem., 30, 1265 (1965).

12. Berlin, K. D. and Taylor, H. A., J. Am. Chem. Soc., 86, 3862 (1964).

13. Bersworth, F. C., U.S. Patent 2,599,807 (June 10, 1952); Chem. Abstr., 47, 4360 (1953).

14. Billica, H. R. and Adkins, H., "Organic Syntheses," Coll. Vol. III, E. C. Horning, Ed., John Wiley and Sons, Inc., New York, N. Y., 1955, p. 176.

15. Brown, H. C., Feuer, H., Vincent, Jr., B. F., and Bartlett, R. S., J. Org. Chem., 30, 2877 (1965).

16. Burpitt, R. D. and Goodlett, V. W., J. Org. Chem., 30, 4307 (1965).

17. Chalmers, M. E. and Kosolapoff, G. M., J. Am. Chem. Soc., 75, 5278 (1953).

18. Chambers, J. R. and Isbell, A. F., J. Org. Chem., 29, 832 (1964).

19. Chavane, V., Ann. Chim., 4, 383 (1949).

20. Chavane, V., Bull. Soc. Chim., 27, 774 (1948).

21. Chavane, V., Compt. rend., 224, 406 (1947).

22. Claus, A., Ber., 14, 2356 (1881).

23. Colthrup, N. B., Daly, L. H., and Wiberley, S. E., "Introduction to Infrared and Raman Spectroscopy," Academic Press, New York, N. Y., 1964.

24. Corbridge, D. E. C., J. Appl. Chem., 6, 456 (1956).

25. Crofts, P. C., Quart. Rev. (London), 12, 624 (1960).

26. Daasch, L. W. and Smith, D. C., Anal. Chem., 23, 853 (1951).

27. Dyatlova, N. M., Kabachnik, M. I., Medved, T. Ya., Rudomino, M. V., and Belugin, Y. F., Dokl. Akad. Nauk S.S.S.R., 161, 607 (1965); Proc. Akad. Sci. U.S.S.R., Chem. Sect., 160-162, 307 (1965).

28. Engelmann, M. and Pikl, J., U.S. Patent 2,304,156 (Dec. 8, 1943); Chem. Abstr., 37, 3261 (1943).

29. Fields, E. K., J. Am. Chem. Soc., 74, 1528 (1952).

30. Gelb, R. I. and Meites, L., J. Phys. Chem., 68, 630 (1964).

31. Gordon, M., "Proton Magnetic Resonance Spectra of Organophosphorus Compounds." (Ph.D. dissertation, University of Pittsburgh, 1965).

32. Hartmann, W. W. and Phillips, R., "Organic Syntheses," Coll. Vol. II, A. H. Blatt, Ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p. 232.

33. Harvey, R. G. and DeSombre, E. R., "Topics in Phosphorus Chemistry," Vol. 1, M. Grayson and E. J. Griffith, Ed., Interscience Publishers, New York, N. Y., 1964, pp. 57-111.

34. Hassner, A. and Coulter, A. W., Steroids, 4, 281 (1964).

35. Hellwege, M., "NMR Analysis of Substituted Phosphonates." (Ph.D. dissertation, Oklahoma State University, 1966).

36. Hori, T., Itasaka, O., Inoue, H., and Yamada, K., J. Biochem., 56, 477 (1964).

37. Horiguchi, M. and Kandatsu, M., Bull. Agr. Chem. Soc., Japan, 24, 565 (1960); Nature, 184, 901 (1959); Chem. Abstr., 54, 16530 (1960).

38. Kabachnik, M. I. and Medved, T. Ya., Dokl. Akad. Nauk S.S.S.R., 99, 765 (1954); Chem. Abstr., 49, 14664 (1955).

39. Kabachnik, M. I. and Medved, T. Ya., Izvest. Akad. Nauk S.S.S.R., Otdel, Khim. Nauk, 635 (1950); Chem. Abstr., 45, 8444 (1951).

40. Kabachnik, M. I. and Medved, T. Ya., Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, 314 (1953); Bull. Acad. Sci. U.S.S.R., 255 (1954); Chem. Abstr., 48, 10541 (1954).

41. Kabachnik, M. I. and Medved, T. Ya., Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, 868 (1953); Bull, Acad. Sci., U.S.S.R., Div. Chem. Sci., 769 (1953); Chem. Abstr., 49, 840 (1955).

42. Kabachnik, M. I. and Medved, T. Ya., Dokl. Akad. Nauk S.S.S.R., 92, 959 (1953); Chem. Abstr., 49, 839 (1955).

43. Kabachnik, M. I. and Rossiiskaya, P. A., Bull. Acad. Sci. U.S.S.R., Classe Sci. Chim., 597 (1945); Chem. Abstr., 41, 88 (1947).

44. Kabachnik, M. I. and Rossiskaya, P. A., Bull. Acad. Sci. U.S.S.R., Classe Sci. Chim., 364 (1945); Chem. Abstr., 40, 4688 (1946).

45. Kabachnik, M. I. and Rossiiskaya, P. A., Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, 48 (1957); Chem. Abstr., 51, 10366 (1957).

46. Kabachnik, M. I., Rossiiskaya, P. A., and Shepeleva, E. S., Bull. Acad. Sci. U.S.S.R., Classe Sci. Chim., 163 (1947); Chem. Abstr., 42, 4132 (1948).

47. Kittredge, J. S. and Hughes, R. R., Biochem., 3, 991 (1964).

48. Kittredge, J. S., Roberts, E., and Simonsen, D. G., Biochem., 1, 624 (1962).

49. Kleinspehn, G. C., Jung, J. A., and Studniarz, S. A., J. Org. Chem., 32, 460 (1967).

50. Kosolapoff, G. M., J. Am. Chem. Soc., 69, 2112 (1947).

51. Kosolapoff, G. M., J. Am. Chem. Soc., 70, 1283 (1948).

52. Kreutzkamp, N. and Cordes, G., Ann., 623, 103 (1959).

53. Medved, T. Ya. and Kabachnik, M. I., Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, 868 (1953); Chem. Abstr., 49, 840 (1955).

54. Medved, T. Ya. and Kabachnik, M. I., Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, 1043 (1955); Chem. Abstr., 50, 11231 (1956).

55. Medved, T. Ya. and Kabachnik, M. I., Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, 1048 (1955); Chem. Abstr., 50, 11231 (1956).

56. Medved, T. Ya. and Kabachnik, M. I., Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, 327 (1956); Chem. Abstr., 50, 15450 (1956).

57. Medved, T. Ya. and Kabachnik, M. I., Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, 684 (1956); Bull. Acad. Sci. U.S.S.R., Div. Chem. Sci., 695 (1956); Chem. Abstr., 51, 1818 (1957).

58. Miller, C. D., Miller, R. C., and Rogers, W. R., J. Am. Chem. Soc., 80, 1562 (1958).

59. Moedritzer, K. and Irani, R. R., J. Org. Chem., 31, 1603 (1966).

60. Moedritzer, K. and Irani, R. R., U.S. Patent 3,269,812 (Aug. 30, 1966); Chem. Abstr., 66, 76151 (1967).

61. Muller, E., "Methoden der Organischen Chemie," Vol. XI, Part I, Georg Thieme Verlog, Stuttgart, 1957, pp. 495-514.

62. Myers, T. C. and Jibril, A. O., J. Org. Chem., 22, 180 (1957).

63. Okamoto, Y. and Sakurai, H., J. Chem. Soc. Japan, Ind. Chem. Sect., 70, 52 (1967).

64. Opitz, G., Griesinger, A., and Schubert, H. W., Ann., 665, 91 (1963).

65. Peppard, D. F., Terraro, J. R., and Mason, G. W., J. Inorg. Nucl. Chem., 4, 371 (1957).

66. Peppard, D. F., Terraro, J. R., and Mason, G. W., J. Inorg. Nucl. Chem., 7, 231 (1958).

67. Phillips, J. P., "Spectra-Structure Correlation," Academic Press, New York, N. Y., 1964, pp. 134ff.

68. Pikl, J., U.S. Patent 2,328,358 (Aug. 31, 1944); Chem. Abstr., 38, 754 (1944).

69. Pople, J. A., Schneider, W. G., and Bernstein, H. J., "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, Chap. 8.

70. Popov, E. M., Kabachnik, M. I., and Mayants, L. S., Uspekhi Khim., 30, 846 (1961); Russian Chem. Rev., 30, 362 (1961).

71. Pudovik, A. N., Dokl. Akad. Nauk S.S.S.R., 92, 773 (1953); Chem. Abstr., 49, 3049 (1955).

72. Pudovik, A. N., Gozman, I. P., and Nikitina, V. I., Zh. Obshch. Khim., 33, 3201 (1963); J. Gen. Chem. U.S.S.R., 33, 3128 (1963); Chem. Abstr., 60, 4178 (1964).

73. Pudovik, A. N. and Sergeeva, M. K., Zh. Obshch. Khim., 25, 1759 (1959); Chem. Abstr., 50, 7073 (1956).

74. Quin. L. D., "Topics in Phosphorus Chemistry," Vol. 4, M. Grayson and E. J. Griffith, Ed., John Wiley and Sons, New York, N. Y., 1967, pp. 23-48.

75. Ryzhkov, V. L., et.al., Dokl. Akad. Nauk S.S.S.R., 98, 849 (1954); Chem. Abstr., 49, 3403 (1955).

76. Schiffner, R. and Lange, G., Faserforsch. u. Textiltech., 8, 435 (1957); Chem. Abstr., 52, 8568 (1958).

77. Siddall, T. H., J. Phys. Chem., 70, 2249 (1966).

78. Staib, I., Arzneimittel-Forsch., 9, 696 (1959); Chem. Abstr., 54, 5954 (1960).

79. Taylor, H. A., "The Synthesis and Properties of Dialkyl Aroylphosphonates," (M.S. thesis, Oklahoma State University, 1964).

80. Terent'ev, A. P. and Gusar, N. I., Zh. Obshch. Khim., 35, 124 (1965); Chem. Abstr., 62, 13068 (1965).

81. Toth, J. and Janyso, G., Acta Univ. Szegediensis, Acta Phys. et. Chem. [N. S.], 3, 125 (1957); Chem. Abstr., 53, 2084 (1959).

82. Uhlig, E. and Achilles, W., Z. Chem., 5, 109 (1965).

83. Westerback, S., Rajan, K. S., and Martell, A. E., J. Am. Chem. Soc., 87, 2567 (1965).

84. Zimmer, H. and Bercz, J. P., Ann., 686, 107 (1965).

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