A STUDY OF THE MICHAELIS-ARBUZOV REARRANGEMENT WITH 1-PHOSPHA-2,8,9-TRIOXAADAMANTANE

By

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CHAPTER I

INTRODUCTION

In the last sixty years, the reaction and mechanism of the Michaelis-Arbuzov rearrangement has been well documented for the process with acyclic, cyclic, and more recently the bicyclic phosphites. Thus the application of the Michaelis-Arbuzov rearrangement to the tervalent phosphorus atom in a tricyclic phosphite, such as 1-phospha-2,8,9-trioxaadamantane, seems a logical extension of this useful reaction. Also the resulting bicyclic phosphonates are quite interesting in their own right, in view of the many possible stereochemical considerations. The relationship of bicyclic phosphonates to cyclic phosphorylated sugars was apparent. It was anticipated that useful correlations of reactivity and structural orientation might be obtained from a study of the stereochemistry of the ring-opening process in tricyclic phosphites and in bicyclic phosphonates.

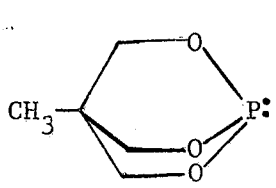
CHAPTER II

HISTORICAL

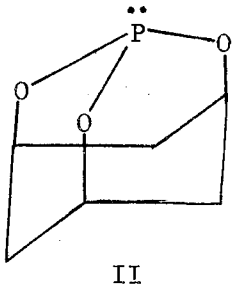
The synthesis of phosphites have been reported via a number of methods. The most common procedure has involved the reaction of phosphorous trihalides with an appropriate alcohol using the high dilution technique and an acid acceptor (60,81,98,103). Also phosphorous trihalides may be reacted with a metallic derivative of the alcohol to prepare certain phosphites (60). When trimethylolethane and phosphorous trichloride were heated in the absence of solvent, Barnes and Hoffman (17) were able to prepare 1-methyl-4-phospha-3,5,8-trioxabicyclo-[2.2.2]octane (I).

The simplicity and ease of preparation and the resulting high yields seemingly make the two procedures developed by Wadsworth and Emmons (104) the methods of choice for the preparations of acyclic and cyclic phosphites. One process consisted of the addition of phosphorous trichloride to the alcohol at 0° followed by slow warming of the mixture to 50-60° under a stream of nitrogen which removed the hydrogen chloride formed. The second procedure is based on simple transesterification of a trialkyl phosphite with an alcohol. The lower-boiling alcohol produced is distilled slowly. The yields of phosphites from both methods are comparable, an 80 per cent to nearly quantitative amount being realized. Either method furnished the bicyclic phosphite I in 90 per cent of theory (104).

Recently, phosphite I was synthesized in 40 percent yield from phosphorous trichloride, trimethylolethane and pyridine under high dilution



I



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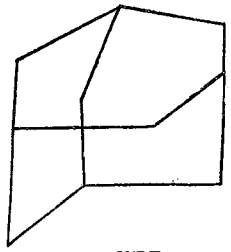


III

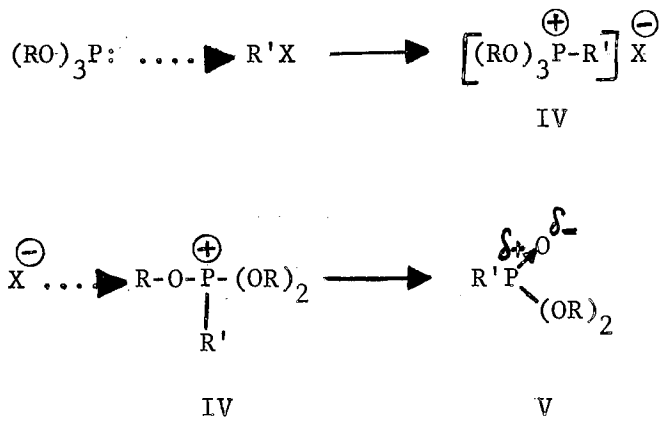
conditions (103). Increased returns (50-55 per cent) were possible when phosphorus trichloride and trimethylolethane were heated in the absence of a solvent (17).

We have applied the transesterification method to the formation of tricyclic phosphites, obtaining an 82 per cent yield of 1-phospha-2,8,9-trioxaadamantane (II), from cis-1,3,5-cyclohexanetriol and trimethyl phosphite. Stetter and Steinacker (98) prepared the tricyclic phosphite II in a 20 per cent yield using high dilution conditions and pyridine as an acid-binding agent with phosphorous trichloride.

Structurally, the tricyclic phosphite II is a member of the adamantane family, a group of compounds whose name is derived from the highly symmetrical, parent hydrocarbon, adamantane (III)(71). First isolated from crude petroleum by Landa and Machacek (64) in 1933, adamantane was assigned the structure of tricyclo$\left[3.3.1.1^{3,7}\right]$decane. Although it is an aliphatic hydrocarbon containing only ten carbon atoms, adamantane melts at 267° (sealed tube), while normal decane melts at -31°. That the molecule III is quite spherical is shown by its ease of sublimation.

X-ray (82) and nuclear magnetic resonance (94) studies show the high symmetry of III. Like adamantane, the tricyclic phosphite II is high melting (208°, sealed tube) and readily sublimes. The adamantane-type compounds have been reviewed by Stetter (96), Fredga (37), and most recently by Stetter (97).

Discovered by Michaelis and Kahne (77) in 1898, the Michaelis-Arbuzov reaction is one of the most widely used methods for the preparation of carbon-phosphorus bonds. The scope of the reaction was rather well explored by Arbuzov (5). Basically it involves the condensation of trialkyl phosphites and related trivalent phosphorus esters with simple alkyl halides. Subsequent decomposition and rearrangement of the quasiphosphonium halide intermediate result in the formation of pentavalent phosphorus compounds. The formation of a dialkyl alkylphosphonate from a trialkyl phosphite and the alkyl halide is the simplest form of this rearrangement.



The mechanism (27,39) proposed for the Michaelis-Arbuzov rearrangement is illustrated by the above two equations. The following experimental observations are the basis for the postulation:

a. Evidence for the nucleophilic displacement of halogen by

phosphorous in the primary step of the Michaelis-Arbuzov reaction is presented by Myers, Preis, and Jensen (80). In agreement with the low reactivity of cyclohexyl halides in S_N2 reactions is the low reactivity found for cyclohexyl tosylate with triethyl phosphite. This data coupled with the well known nucleophilicity of phosphites, would support an initial S_N2 displacement in the Michaelis-Arbuzov reaction.

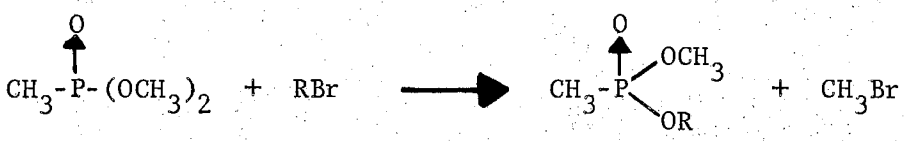
b. The formation of a quasiphosphonium salt IV is supported by the isolation of a salt-like intermediate by Michaelis and Kahne (77) from triphenyl phosphite and methyl iodide. Similarly, crystalline intermediates have recently been isolated by Arbuzov and Sazonova (8) from triaryl phosphites and various alkyl iodides.

c. The nucleophilic attack by halide ion on the alkyl carbon of the ester to eliminate alkyl halide and to form the phosphonate V has been experimentally substantiated. For example, when the intermediate triphenyl phosphite methiodide was treated with optically active 2-octanol, inverted, active 2-iodooctane was isolated (65). Gerrard and Jeacocke (42) similarly obtained the inverted 2-bromooctane from optically active tri-2-octyl phosphite and bromine.

The overall mechanism of the Michaelis-Arbuzov rearrangement can be stated as a nucleophilic displacement of halogen by phosphite to form a quasiphosphonium intermediate. When decomposed, the intermediate eliminates alkyl halide with the subsequent formation of a phosphonate.

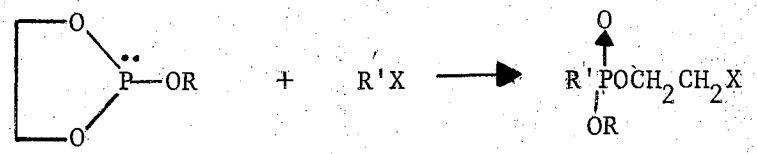
It should be mentioned that the dialkyl alkylphosphonates and phosphates are not inert to alkylation (48,67,86). Laughlin (67) has shown that alkylating agents can react with pentavalent organophosphorus esters. Mechanistically, this alkyl exchange process can be related to the

Michaelis-Arbuzov reaction. The oxygen atom in the phosphoryl group or the sulfur atom in the thiophosphoryl group represents the nucleophilic center that initiates the rearrangement which is reminiscent of an initial, S_N2 displacement. By this process, an ester alkyl group is exchanged with the incoming alkyl group.

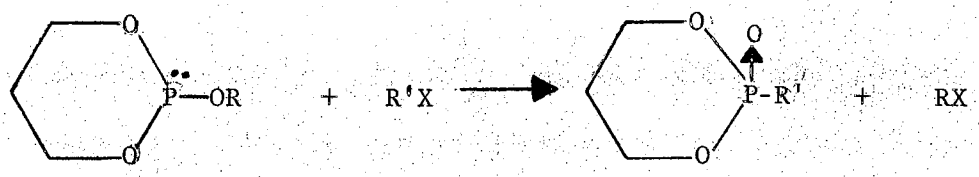


(R = dodecyl)

The application of the Michaelis-Arbuzov rearrangement to cyclic (9,11,60,88), and bicyclic (11,104) phosphite systems has received only



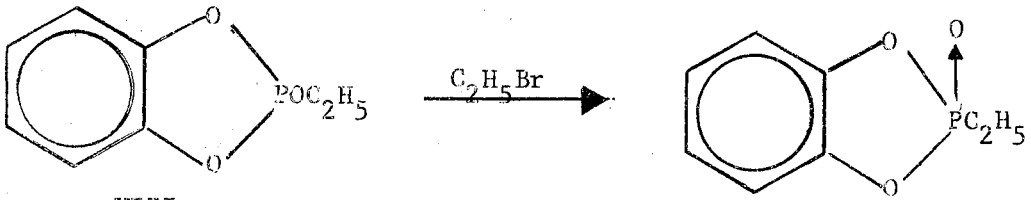
VI



VII

limited consideration while a survey of the literature revealed no applications to tricyclic phosphites. Simple cyclic ethylene phosphites (VI, R = alkyl or aryl) are decomposed by alkyl halide with rupture of the five-membered ring to form the 2-haloethyl ester of the alkyl phosphonate. Substitution usually stabilizes the glycol ring toward ring opening, the acyclic radical departing as alkyl halide (9,60,88). The 1,3,2-dioxaphosphorinane ring-containing phosphites VII undergo reaction with alkyl halides with nearly exclusive ring preservation (11).

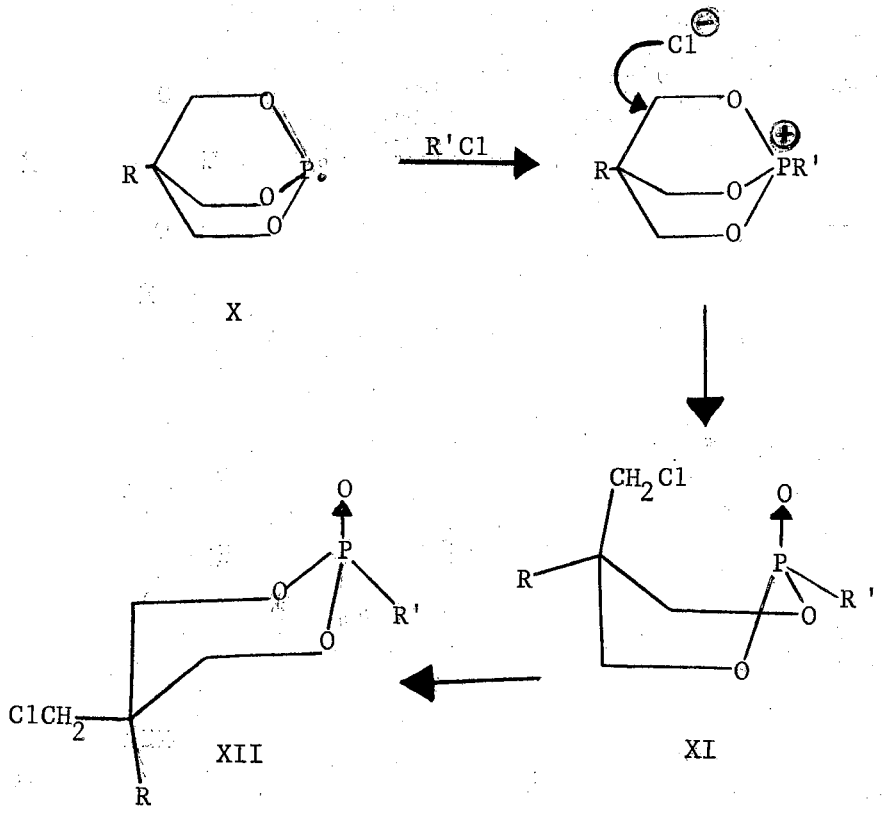
Treatment of 2-ethoxy-1,3,2-benzodioxaphosphole (VIII) with ethyl



VIII IX

bromide has been reported to yield o-phenylene ethylphosphonate (IX)(11). The identification of product IX necessitates halide ion attack on the alkyl carbon atom rather than attack on the aromatic nucleus which might be expected to initiate ring opening. It would be of interest to attempt the rearrangement of a similar trivalent phosphorus compound in which only aromatic carbon atoms were available for nucleophilic attack by the halide ion.

While a number of 1-alkyl-4-phospha-3,5,8-trioxabicyclo [2.2.2]-octanes (X) have been prepared (50,81,103,104), the only study of the Michaelis-Arbuzov rearrangement with this class of bicyclic phosphites has been done by Wadsworth and Emmons (104). They found the bicyclic



phosphites X undergo a stereospecific reaction when treated with alkyl halide to yield the cis-isomer XII. The inherently, unstable boat conformer XI is presumably converted to the thermodynamically more stable chair form XII.

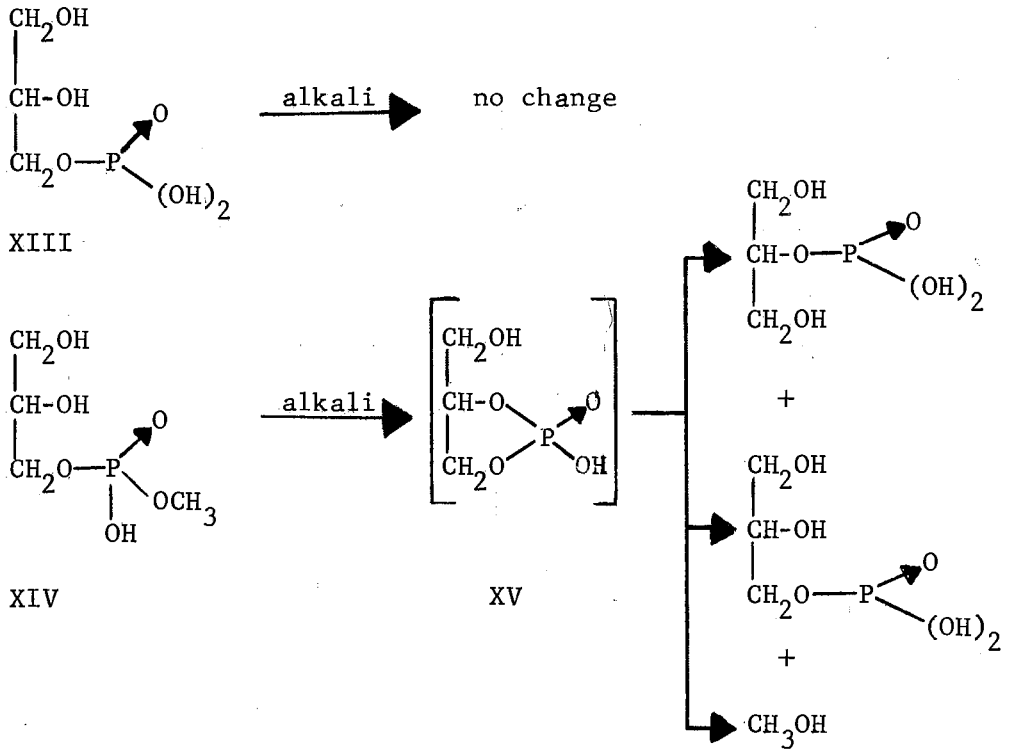
The only cyclic phosphonates produced to date by means of the Michaelis-Arbuzov rearrangement have been the 2-alkyl-2-halomethyl-1, 3-propanediol cyclic phosphonates, XII. Analogous to the formation of phosphites, the substituted phosphonyl halides have been used with acid accepters, i.e. triethylamine, and various glycols in dilute solutions to form cyclic phosphonates (59,75). Korshak, Gribova, and Andreeva (59) reported evidence of initial formation of polymeric esters which were converted to cyclic monomers only through destructive distillation. When heated extensively, the esters polymerized for the most part to

very low molecular weight, viscous oils. Moreover, sodium, water, sodium hydroxide, hydrochloric acid, and phosphoric acid were found to catalyze this polymerization.

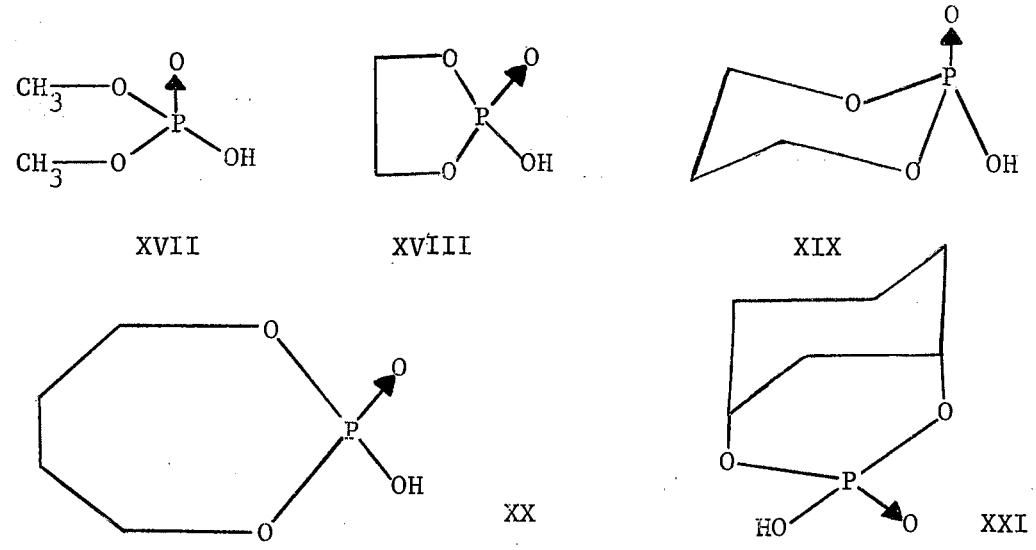
In relation to our own work with bicyclic phosphonates, the similarity with the phosphorylated sugars and related products of natural origin became apparent. While cyclic phosphate esters are the major constituents in these phosphorylated intermediates, the cyclic phosphonates should be similar in their properties and reactions. With the first isolation of a sugar phosphate from natural sources, the importance of phosphorylated intermediates in biological processes was recognized (57). Cyclic phosphate esters and cyclic phosphate intermediates have been found to play significant roles not only in sugar chemistry but also in the chemistry of lipids (47) and nucleotides (25).

The phenomenon of phosphate migration, which gives rise to the cyclic phosphate intermediates encountered in natural products, was first observed by Bailly and Gaume (15). In experiments with the alkaline hydrolysis of alkyl esters of glycerophosphate, they noted that α-glycerophosphate (XIII), was stable to alkaline hydrolysis while methyl α-glycerophosphate (XIV) was altered considerably. Methanol and some of the α-glycerophosphate (XIII) were recovered, as well as some of the β-glycerophosphate (XVI) which could only be explained adequately by assuming phosphate migration through the cyclic intermediate XV.

A definitive explanation of the phosphate migration necessitates an understanding of phosphate hydrolysis and phosphate ring stability. Simple tertiary phosphates have been shown to undergo hydrolysis with carbon-oxygen bond fission in neutral or acidic solutions by Barnard and co-workers (16). Acid catalyzed degradation was not observed. On the



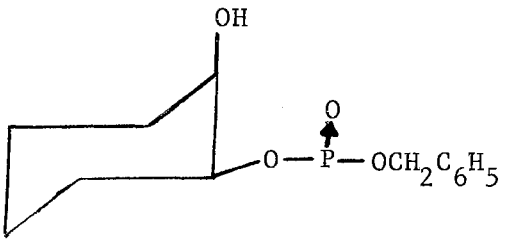
other hand, they found that basic hydrolysis proceeded with phosphorus-oxygen bond fission. The isotopic data obtained from the oxygen-18 enriched water used in these studies indicated that no appreciable isotopic exchange at the phosphoryl oxygen atom was associated with the hydrolytic reactions of these phosphates. The stability of cyclic phosphates appears to be a direct function of ring size. In this respect a



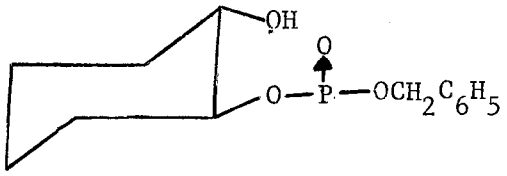
comparison of the simple five-, six-, and seven-membered ring systems and their behavior toward acids and bases was instructive. The cyclic ester XVIII composed of a five-membered ring hydrolyzed in a basic medium about 10^7 times as fast as dimethyl hydrogen phosphate (XVII)(63). Use of oxygen-18 has shown exclusive phosphorus-oxygen bond cleavage in the ethylene glycol cyclic phosphate XVIII (46). The cause of rapid hydrolysis of five-membered cyclic phosphate esters may well lie with the ring strain in the ester itself. The heat of hydrolysis of the methyl derivative of XVIII was seven to nine kilocalories per mole greater than 2-hydroxyethyl dimethyl phosphate (30). The six-membered cyclic phosphate XIX, being much more stable, hydrolyzes only a few times more rapidly than dimethyl hydrogen phosphate (XVII) (58). Cis-cyclohexylidene hydrogen phosphate XXI is very stable toward acid or alkali. The bicyclic phosphorus ester XXI was unaffected by thirty per cent sodium hydroxide at 100° and only slowly hydrolyzed by 3N hydrocholoric acid at 100° with liberation of inorganic phosphate (23). The seven-membered ring compound XX is the most stable of the cyclic phosphates considered (58). With acidic hydrolysis, these cyclic phosphates follow approximately the same order.

The phosphate migration in naturally occurring substances proceeds largely through a five-membered intermediate with very few examples reported of an intermediate composed of a six-membered (14,58,101) or seven-membered ring. Apparently, due to the rapid cyclication and rate of cleavage, five-membered cyclic phosphates predominate in biological processes involving cyclic phosphorus esters. This intramolecular formation, migration, and cleavage is facilitated by vicinal hydroxyl functions as is illustrated by the rate of hydrolysis of cis-and trans-2-hydroxycyclohexyl benzyl hydrogen phosphate (23). The cis-isomer XXII,

with the hydroxyl function in closer proximity to the phosphate group, hydrolyzed faster than the trans-isomer XXIII in either an acidic or basic medium by a factor of six.



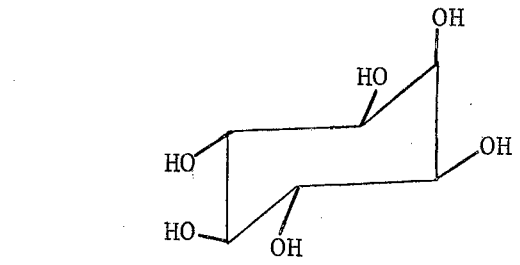
XXII



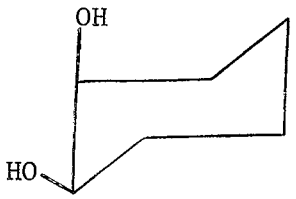
XXIII

Brown and Todd (25) have discussed the nucleic acid structure in relationship to the nucleotide sequence and cyclic phosphate intermediates. Nucleotides containing such phosphorus esters have been identified as products of incomplete ribonuclease digestion of ribonucleic acids (21,24,73). Certain of these nucleotides with cyclic phosphate esters have been synthesized independently (24,36).

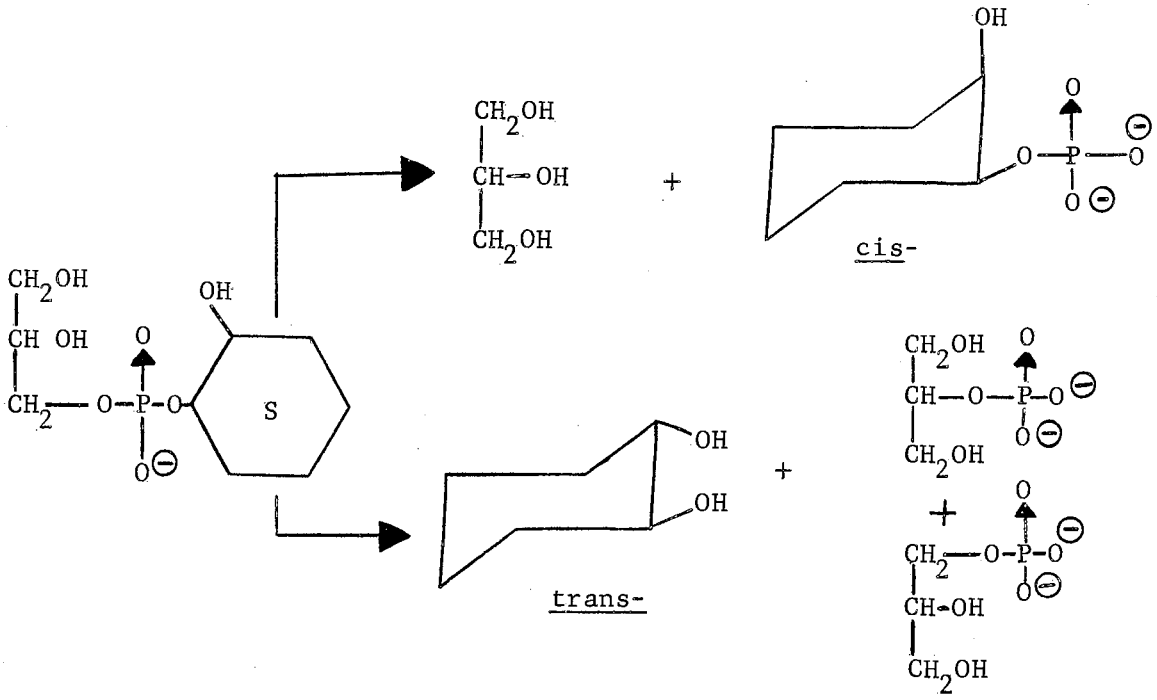
Phospholipids compose another important area of cyclic phosphates (47). On occasion they have been noted as phosphoinositides due to the lipid constituent myo-inositol (XXIV). In relation to the phospholipids, the hydrolysis of both mono and cyclic phosphate esters of cis-1,2-cyclohexanediol (XXV) and its trans-isomer were studied. When the cyclohexanediol was mono-esterified with phosphoric acid in the presence of glycerol, preferential retention of phosphate group was displayed by the cis-isomer while the trans-isomer largely lost the phosphate moiety to the acyclic substituent in either acidic or basic hydrolysis (22). A



XXIV



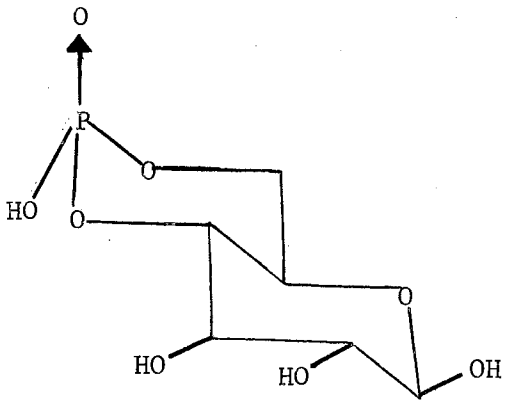
XXV



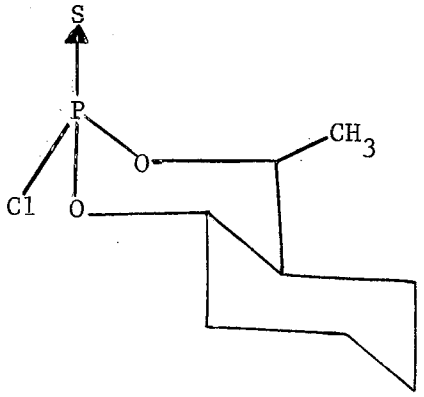
recent review of phospholipids was reported by Hawthorne (49).

While five-membered cyclic phosphates are the most important in sugar chemistry (57), it is here we find examples of a six-membered bicyclic phosphate. An example is D-glucose-4,6-cyclic phosphate (XXVI), whose structure is depicted as shown by virtue of the equatorial conformation of the hydroxyl and hydroxymethyl groups at positions 4 and 5 in the glucopyranoside (14,58). Other six-membered bicyclic phosphates in sugars have been produced (101).

Directly related in biological importance is a large group of synthetic cyclic phosphorus compounds. These compounds derive their importance from their toxic properties. It is only within the last thirty



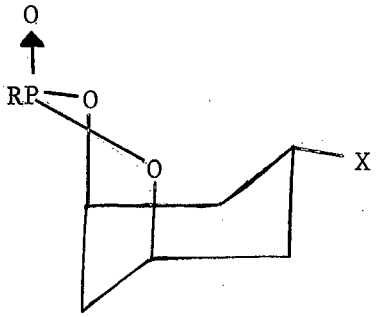
XXVI



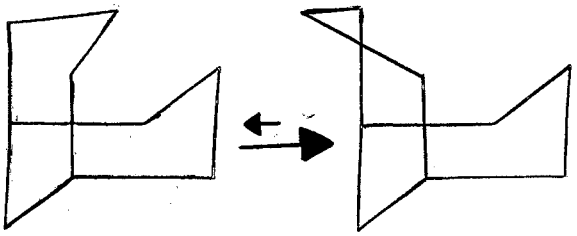
XXVII

years that the poisonous nature of certain organic phosphorus compounds (52,83) has been realized although organophosphorus chemistry is over one hundred and forty years old (60). Perhaps the patent literature best reflects the application of cyclic organophosphorus compounds in this area (66). The bicyclic thiophosphorochloriate XXVII and related compounds have potent insecticidal properties (66).

In the light of their proximity to these biologically important cyclic phosphates, an extensive hydrolysis study of the bicyclic phosphonates XXVIII would be a very useful extension of our work. In a bicyclic bridged system, of which the bicyclic phosphonates XXVIII are members, the stereochemistry of such molecules have often been neglected. These phosphonates XXVIII have the bicyclo[3.3.1]nonane ring system of which XXIX is the hydrocarbon analog. This ring structure might be viewed as two cyclohexane rings with three common atoms as illustrated in the scheme. No stereochemical study has been made of this bicyclic ring system, however, but the stereochemistry of cyclohexane derivatives (4,18,34,84) and fused ring systems containing cyclohexane are well known. In a stereochemical study, spectrometric methods often prove helpful.



XXVIII



XXIX

Bellamy (19) in his comprehensive work, covers the application of infrared spectroscopy to organophosphorus compounds and cyclohexane derivatives as well as most organic materials. The infrared spectra of organophosphorus compounds have lately been reviewed by Popov and Kabachnik (87). Some band correlations for the five-membered 1,3,2-dioxaphospholane ring XVIII at 924-922 $cm.^{-1}$ and the six-membered 1,3,2-dioxaphosphorinane ring XIX at 936-934 $cm.^{-1}$ have been advanced (29). However, later workers (55) have advised caution in their use since only partial correlation for the proposed bands was found with examination of a series of cyclic phosphorus compounds. In a study of several five- and six-membered phosphorus containing rings, Jones and Katritzky (55) report seven medium to weak bands characteristic for the 1,3,2-dioxaphosphorinane rings XIX. As they show, these bands are likely due to the dioxatrimethylene portion of the ring since cyclic trimethylene sulfite (72) has six peaks similar to the bands for the phosphorus compound. Some hydrogen bonding of phosphorus compounds have been studied by infrared

spectroscopy (40,78). Intramolecular as well as intermolecular association of phosphoryl-containing species have been considered (78). Aksnes and Gramstad (1,2) have studied intermolecular hydrogen bonding between phenol and eighteen organophosphorus compounds.

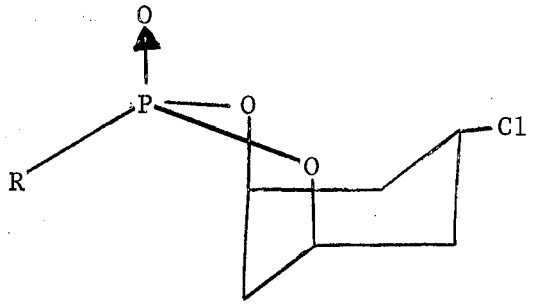
While very little proton magnetic resonance work has been recorded for cyclic phosphorus compounds, such standard references in the field as Jackman (54) have proven beneficial in interpreting their spectra. The only proton magnetic resonance spectrum noted for these cyclic compounds is that of the 1,3,2-dioxaphospholane ring XVIII (46,74,92). This spectrum shows the double splitting characteristic of the phosphorus-31, hydrogen-1 spin-spin coupling (12,33). The coupling constant is 10 cycles per second at 40 megacycles. The proton magnetic resonance spectra of a number of acyclic phosphorus compounds have also been recorded (92,93). Beside the hydrogen-1 nuclei, the phosphorus-31 nuclei may also be studied by means of nuclear magnetic resonance as evidenced by extensive published work (35,56,100). A small group of five- and six-membered phosphorus containing rings were examined by phosphorus-31 nuclear magnetic resonance (56).

Dipole moment measurements (95) have also been used advantageously in the study of organophosphorus compounds. Kosolapoff (61,62), as well as, Arbuzov and Shavska-Tolkacheva (10), have studied a succession of acyclic phosphorus compounds in relation to their dipole moment. An indication of the high dipole moment often encountered in phosphorus compounds may be seen in values obtained for 1-phospha-2,8,9-trioxa-adamantane (II), 4.7 Debye; 1-methyl-4-phospha-3,5,8-trioxabicyclo[2.2.2]-octane (I), 4.15 Debye; and the 1-methyl-4-phospha-3,5,8-trioxabicyclo-[2.2.2]octane, 4-oxide (oxide of I), 7.10 Debye (26).

CHAPTER III

DISCUSSION OF RESULTS AND CONCLUSIONS

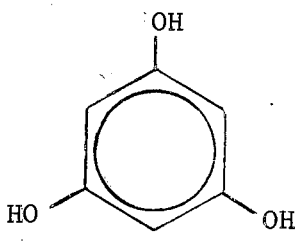
Most alkyl halides react readily with phosphites by way of the Michaelis-Arbuzov rearrangement to yield the corresponding phosphonates (39). We have investigated this reaction with the tricyclic phosphite II as the principal substrate. Of the alkyl halides studied, benzyl chloride, 1-naphthlmethyl chloride, and benzhydryl chloride converted the ester II to the bicyclic phosphonates XXX, XXXI, and XXXII, respectively. Benzyl bromide reacted with II to give an intractable oil while an unidentified solid was isolated from the highly exothermic condensation of trityl chloride with II. All of the phosphonates isolated were high-melting, white, crystalline solids.



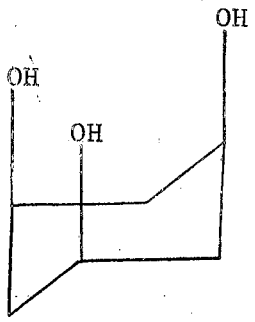
XXX, R = $C_6H_5CH_2$
XXXI, R = 1-$C_{10}H_7CH_2$
XXXII, R = $(C_6H_5)_2CH$

Elementary to the preparation of the bicyclic phosphonates, is the initial starting material required for synthesis of the ester II. Conversion of phloroglucinol (XXXIII) to cis-phloroglucitol (XXXIV) by

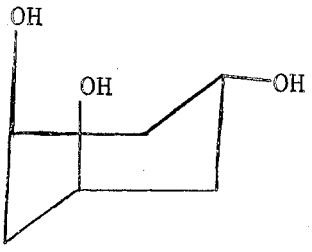
reduction with hydrogen over Raney nickel resulted in the formation of a mixture of isomers. Stetter (98) has reported a 60 per cent yield of the cis-isomer XXXIV at atmospheric pressure. However, repetition of his conditions in several experiments afforded the cis-compound in only 40 per cent of theory. Several exploratory runs with various concentrations of solute and reaction temperatures revealed that both parameters were important. For example, the maximum yield of desired isomer XXXIV was obtained from the reduction performed at 50°. Chief contaminents in the mixture were the trans-isomer XXXV and several cleavage products. To be sure the synthesis deserves further attention with respect to type and quantity of catalyst and well as the nature of the solvent. In addition analysis of the products prior to preliminary workup, by means of a suitable gas chromatography column would be of significant value in arriving at the optimum conditions needed.



XXXIII



XXXIV

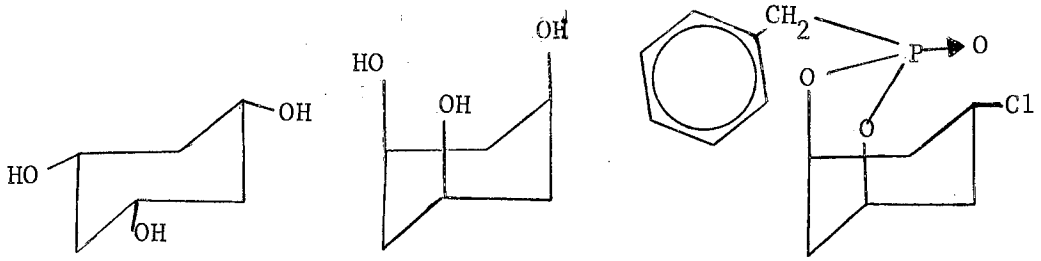


XXXV

Transesterification of the anhydrous cis-phloroglucitol (XXXIV) with trimethyl phosphite gave 1-phospha-2,8,9-trioxaadamantane in yield greater than previously reported (26). It has been shown by x-ray analysis that the dihydrate of XXXIV exists with each hydroxyl group in the equatorial conformation as illustrated in XXXIVa. Formation of the

phosphite II necessitates inversion of XXXIVa to the thermodynamically unfavored XXXIVb where all hydroxyl groups are in the axial conformations. By modifications developed during the course of this study average yields greater than 80 per cent were realized for II. This method may be applicable with related compounds, such as trimethyl borate, in the synthesis of tricyclic esters containing other elements.

Provided the rearrangement of II with the alkyl halides proceeds through the known mechanism for the Michaelis-Arbuzov reaction (39), the isomer XXX would be predicted. Evidence for the structure of this

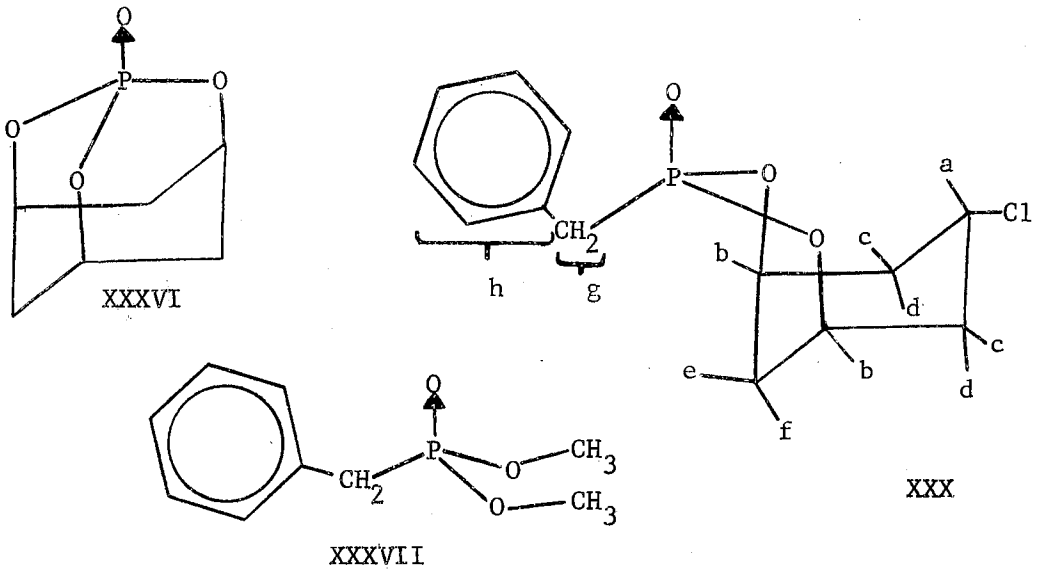


XXXIVa XXXIVb XXXa

compound was provided by nuclear magnetic resonance and infrared spectra, dipole moment measurements, and molecular weight determinations by the Rast method. The experimentally determined molecular weight of 289 (43) agreed with the calculated value of 286 reasonably well. Infrared analysis (Plate VI) of XXX revealed strong absorption at 747 $cm.^{-1}$ which is near the band at 742 $cm.^{-1}$ assigned previously to an equatorial chlorine atom in cyclohexane derivatives (19,68). In contrast only very weak bands appeared in the region below 700 $cm.^{-1}$ while a strong band normally is present near 688 $cm.^{-1}$ for axial chlorine atoms in cyclohexane compounds. Noteworthy is the similar weak bands below 700 $cm.^{-1}$ in the naphthylmethyl derivative XXXI and the near absence of bands in the benzhydryl analog, XXXII. In all examples peaks assignable to the phosphoryl group, the P-O-alkyl linkage, and aromatic hydrogen are available.

While it does eliminate a number of the sixteen possible isomers of XXX, the dipole moment value of 5.9 Debye as measured in dioxane does not allow complete differentiation between a boat-chair or chair-chair arrangement in XXX and XXXa, respectively. Calculations of the dipole moments obligates a selection of vector directions for the individual components. It was discovered that if the vector for the methylene-phosphorus group was directed toward carbon, values of 4.11 Debye and 4.13 Debye were found for XXX and XXXa, respectively. However, if the assumption of vector direction was reversed for this single component, values of 5.6 Debye and 4.64 Debye were calculable. As yet no definite vector assignments have been made with organophosphorus compounds (10,61), but the present work suggests the direction of a vector between a carbon atom and a phosphoryl group is toward phosphorus.

Nuclear magnetic resonance studies of XXX were more instructive. It is here we find a separation of the hydrogen atoms in the compound according to their resonance frequencies which are influenced by the molecular environment and resolved by an induced magnetic field. The spectra determined at 60 Mc. (Plates XV and XVI) show peaks which can be ascribed to hydrogens at locations b, c, d, g, and h. Assignments for hydrogen at a, e, and f are more difficult due to poor resolution at this frequency. A good indication of the field position and coupling constant for the b hydrogens in XXX can be obtained from the model compound XXXVI. Tertiary hydrogens geminal to the oxygen atoms in the phosphate XXXVI (Plate XIV) exhibit a doublet centered at 4.78 tau units with J = 19.5 c.p.s.. Hydrogen arising from b in XXX (Plate XVI) display a doublet with a coupling constant of 17.5 c.p.s. and a chemical shift of 5.22 tau units. Excellent agreement is obtained with respect to g and h hydrogen atoms in XXX



(Plate XV) and the corresponding hydrogens in XXXVII (Plate XII). A doublet (J = 22 c.p.s.) for g hydrogens with a chemical shift of 6.83 tau units appears while h (aromatic hydrogen) has a chemical shift of 2.77 tau units in XXX. Similarly, hydrogen in XXXVII also display a doublet with J = 21.7 c.p.s. and chemical shift of 6.75 tau units for the methylene group and a singlet at 2.72 tau units for aromatic hydrogen. Hydrogen-1, phosphorus-31 spin-spin coupling produces the splitting of the benzyl methylene hydrogens into a doublet (12,33). A complex structure is displayed by the a hydrogen gem to the chlorine atom located in the region of 5.3 tau units (44). Poor resolution plus overlap with the b hydrogens obscures this hydrogen in all but the 1-naphthylmethyl phosphonate XXXI spectrum at 60 Mc. (Plate XVII). Here the true nature of the spin-spin splitting of the a hydrogen is indicated by a nine-line spectra. In the isomer, XXX, most favored mechanistically, the a hydrogen is axial and has as four neighbors, two identical axial and two identical equatorial hydrogens. In theory one hydrogen adjacent to a second hydrogen, A, should be split into $n_A + 1$ peaks where n_A is

the number of identical A hydrogens. The same hydrogen adjacent to two non-identical hydrogens, A and B, should be split into $(n_A + 1)(n_B + 1)$ peaks (53,54). The equation as applied to the a hydrogen in XXX has $n_A = 2$ and $n_B = 2$; thus the signal should be split into $(2 + 1)(2 + 1)$ or 9 peaks. Relative intensities of these peaks should be approximately 1:2:1:2:4:2:1:2:1 (53,54). This splitting and relative intensity is most clearly observable in both the 60 Mc. spectrum of XXXI (Plate XVII) and the 100 Mc. spectrum of XXX (Plate XXI).

The interaction of the various hydrogens within the molecule XXX was clarified further by decoupling the 100 Mc. nuclear magnetic resonance spectrum of XXX using the double resonance technique (91). This 100 Mc. decoupling facilitated complete assignment of hydrogen locations within the molecule XXX. Decoupling involves the determination of the nuclear magnetic resonance spectrum of a proton within a molecule while subjecting an interacting proton (most often vicinal) to a frequency equal to its resonance frequency. Thus the observed spectrum of the former proton is simplified due to the removal of the second proton's magnetic influence.

Plate XXII illustrates the decoupling of a from neighboring hydrogens. From the 100 Mc. spectra (Plate XXI), the a hydrogen is seen to be split into three triplets. Upon observing a while irradiating c, 205 c.p.s. up field, a collapse of the center triplet of a to a singlet was noted. Going from 205 c.p.s. to 209 c.p.s. up field from a by irradiation produced little change in the observed spectrum. However, irradiation at 220 c.p.s. up field shows only one triplet being uneffected. Decoupling of a from d, 306 c.p.s. up field (Plate XXII), resulted in near complete disappearance of the two outside triplets of a with marked reinforcement

of the central triplet. The two spectra shown for the decoupling of a from d illustrate the effect of varying the irradiation. From this it can be surmised that a is coupled with c and d. That c and d are in turn coupled with a can be seen from Plate XXIII, where c is decoupled from a, 221 c.p.s. down field, and d is decoupled from a, 325 or 307 c.p.s. down field. The conversion of f from a doublet to a singlet was produced by decoupling it from e, 51 c.p.s. down field (Plate XXIII). The interaction of c and d was displayed by the decoupling of the first hydrogen from the second hydrogen, 100 c.p.s. up field. Plate XXIII also shows the decoupling of e from b, 325 or 307 c.p.s. down field, as a sharpening of the doublet peaks. It will be noted that the observed effect of decoupling varied between different hydrogens. However, to show that two hydrogens are coupled, the decoupling technique can be of significant value even in complex systems.

While the complete stereochemistry of the phosphonate XXX cannot be stated due to inadequate knowledge of the position of the phosphoryl group, much evidence is presented for the isomer XXX. Dipole moments, infrared spectra, and decoupling of nuclear magnetic resonance spectra lends support to this postulation. Isomer XXXa, the next most likely candidate, appears less favorable because of interaction between the phosphoryl group and the a hydrogen geminal to the chlorine as indicated by Fisher-Taylor-Hirschfelder models. Molecular models of XXX isomer do indicate interaction between the e hydrogen to hinder somewhat the free rotation of the methylene h hydrogens. Attempted preparation of model compounds in which either the benzyl group was replaced with a phenoxy group or the chlorine atom was replaced by a hydroxyl group were unsuccessful (See Experimental, page 62). It is not possible to determine

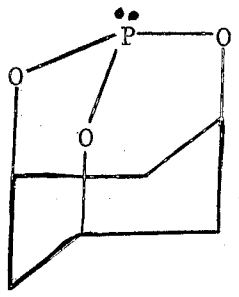
hydrogen bonding in XXX by nuclear resonance without suitable model compounds (32,69,91). It might be noted in passing that molecular association by hydrogen bond formation often results in a shift of the proton line involved toward lower fields (69). The ester and its analogs show a field position near 5.3 tau units for a. It has been recorded that 4-tertiary butyl cyclohexyl chloride exhibits a field position of 6.36 tau units for the axial hydrogen geminal to chlorine (44). Although it is attractive to postulate that intramolecular hydrogen bonding may cause the hydrogen a to resonate at low field, subtle long range shielding effects by the large phosphoryl group may be influential. Similar to the carbonyl group the phosphoryl function might be expected to deshield nearby protons (54). The possibility of hydrogen bonding between the phosphoryl group and the axial hydrogen a in XXX deserves further study. Assignment of the absolute configuration of XXX perhaps best awaits an x-ray examination which is now in progress (76).

The 1-naphthylmethyl, XXXI, and benzhydryl, XXXII, analogs appear to have the same structural relationship as XXX as evidenced by their similar nuclear magnetic resonance and infrared spectra. The lower yields of these analogs may be due to steric hindrance although an extensive search for optimum conditions was not performed.

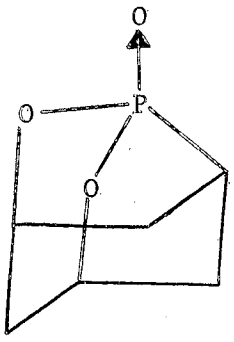
The product isolated from the trityl chloride reaction is evidently not a bicyclic phosphonate since the empirical formula is $C_{42}H_{45}P_2O_9$. Ground state steric repulsion between the trityl group and the cyclohexane ring may prohibit formation of the bicyclic phosphonate as implied by models. Whether the bromine atom presents an additional steric factor compared to the chlorine atom awaits a more effective workup of the intractable oil produced in the benzyl bromide condensation with II.

Acid hydrolysis of XXX was somewhat inconclusive since it appeared to yield a mixture of chlorinated and unchlorinated mono-substituted esters which may be convertable to benzylphosphonic acid by strenuous hydrolysis conditions. Fractional precipitation may offer a means of purifying this product since preliminary experiments with liquid chromatography on alumina were unsatisfactory. Basic hydrolysis may produce a polymeric material, although similar bicyclo[3.3.1]nonane heterocyclics have been found to be relatively inert to a variety of initiators (99). An orange-colored material melting above 300° was obtained from an attempted basic hydrolysis of XXX with 20 per cent sodium hydroxide. In light of the similarity to biologically important substances, hydrolysis of the bicyclic phosphonates deserves additional study. Perhaps vapor phase chromatography would be useful in following the stepwise hydrolysis.

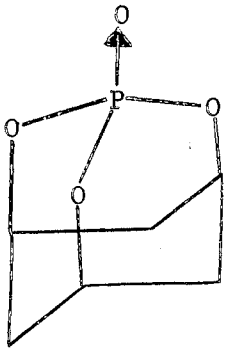
Attempts to effect an intramolecular Michaelis-Arbuzov rearrangement of II with iodine to the tricyclic phosphonate XXXVIII were unsuccessful. Likewise efforts to chlorinate II resulted in the isolation



II



XXXVIII



XXXVI

of the phosphate XXXVI which attests to the increased stability of the ring. The phosphate probably forms a chlorine complex (60) with II which is in contrast with the data published on bicyclic phosphites (104).

No attempt was made to isolate an intermediate quasiphosphonium salt from the Michaelis-Arbuzov rearrangements investigated. Future work along these lines should be profitable.

In summary, a new class of bicyclo[3.3.1]nonane derivatives containing phosphorus has been synthesized. The mechanism and stereochemistry of the reaction and the products have been examined. Useful information on dipole moments, proton magnetic resonance frequencies, and infrared absorption bands have been recorded for all phosphorus compounds obtained.

CHAPTER IV

EXPERIMENTAL[1,2,3,4,5,6,7]

Preparation of cis-Phloroglucitol (XXXIV). A modified form of Stetter's (98) procedure was used. Raney nickel W-7 (20) was prepared from 66.7 g. of nickel-aluminum alloy and 85.3 g. of sodium hydroxide. The sodium hydroxide was dissolved in 333 ml of distilled water contained in a 1-liter Erlynmeyer flask. The alloy was added with stirring

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[1]All melting points are corrected; all boiling points are uncorrected.

[2]The infrared spectra were determined on a Beckman IR-5 and IR-7 with sodium chloride cells.

[3]The microanalyses were performed by Mid West Laboratories, Indianapolis, Indiana.

[4]The molecular weights were performed by C. F. Geiger, Ontario, California.

[5]The 60 Mc. proton magnetic resonance spectra were determined by Professor Melbert Peterson, Augustana College, with a Varian Model A-60 high-resolution spectrometer fitted with a field-sensing stabilizer ("Super Stabilizer"). The concentration and solvent are indicated on the spectra. Tetramethylsilane was used as an internal standard. The author is grateful to Dr. John Verkade, Iowa State University for preliminary nuclear magnetic studies.

[6]The 100 Mc. proton magnetic resonance spectrum and double-resonance (decoupling) spectra were determined by Dr. James N. Shoolery, Eugene A. Pier, and Leroy F. Johnson of Varian Associates.

[7]Dipole moments measurements were determined by Dr. Max T. Rogers, Michigan State University and Dr. John G. Verkade, Iowa State University.

to the caustic solution during thirty minutes at such a rate as to maintain the temperature at 50 ± 2° and then cooled to room temperature. The Raney nickel W-7 was washed three times with 667 ml portions of distilled water and three times with 100 ml portions of 95 per cent ethanol. The nickel catalyst (ca. 33 g.) was washed into a 2-liter, three-necked, round-bottom flask with a small amount of 95 per cent ethanol and covered with one liter of the solvent. The flask was equipped with a mechanical stirrer, reflux condenser, and fritted gas bubbler. Saturation of the catalyst with hydrogen required two hours with rapid stirring (1200 r.p.m.) at room temperature. The flow of hydrogen through the mixture and the stirrer was stopped, and the finely divided nickel was allowed to settle for forty minutes while nitrogen was passed over the mixture. Approximately 500 ml of ethanol was decanted from the flask and used to dissolve 100.0 g. (0.617 moles) of the dihydrate of phloroglucinol (XXXIII) (Fisher Reagent Grade, m.p. 217-219°). The phloroglucinol solution was added dropwise during twenty minutes to the rapidly-stirred reduction catalyst. Hydrogen was passed through the mixture during the addition. When this addition was complete, the mixture was heated at 50 ± 2° for forty-eight hours. After approximately forty hours, the flow of hydrogen appeared to have a cooling effect on the solution since the temperature dropped about 10°. After forty-eight hours, the hydrogen flow was stopped, and the solvent was heated to boiling and rapidly filtered by suction from the nickel. The solution upon standing in an ice bath for twenty-four hours precipitated 23.687 g. of the dihydrate of cis-phloroglucitol (XXXIV), melting at 184-186° after losing water of hydration at 110-130°. The crystals were washed with cold 95 per cent ethanol. The filtrate was

concentrated to one-half the original volume on the rotary evaporator and then cooled for twenty-four hours in an ice bath. Filtration produced 9.436 g. of the dihydrate of XXXIV of a lower purity. Further concentration of the mother liquid to 200 ml furnished 12.402 g of the impure dihydrate of XXXIV when cooled for twelve hours at 0°. As the clear solution was concentrated it took on a yellowish color. The second and third crop of crystals were repeatedly recrystallized from dioxane to yield 17.775 g. of material melting at 184-186° after loss of water of hydration. The total amount of the dihydrate of XXXIV was 41.463 g. (0.247 moles) for a 39.97 per cent yield. Additional recrystallizations from dioxane gives material of melting point 186-187°.

Further concentration of the reaction solution, which was then chilled, produced 11.887 g. of the dihydrate of trans-phloroglucitol (XXXV) contaminated with starting material and hydrogenation by-products. Three recrystallizations from dioxane provided 9.531 g. (0.0567 moles) of the trans-isomer (m.p. 144.0-145.5°) for a 9.19 per cent yield. Starting material XXXIII could be recovered from the mother liquor by removal of the solvent and recrystallization of the yellowish-orange residue with distilled water. Two to four filtrations of the hot solution from activated charcoal followed by repeated recrystallizations from water were necessary to purify the material.

The method described above provided the highest yield of cis-phloroglucitol (XXXIV) obtained under various reaction conditions. Runs with Raney nickel W-5 (20) were unfruitful due to extensive cleavage and the production of intractable yellow oils. A temperature of 40° was not as favorable as 50°, while absolute and 98 per cent ethanol were inferior to 95 per cent ethanol. Combinations of these factors along

with the length of the runs were studied but none improved the yield of the cis-isomer.

Preparation of 1-Phospha-2,8,9-trioxaadamantane (II). The procedure was similar to that described by Wadsworth and Emmons (104). A three-neck, round-bottom, 100-ml flask equipped with an air condenser fitted with a calcium chloride drying tube, a nitrogen inlet tube, and a liquid immersion thermometer, was charged with 2.999 g. (0.023 moles) of cis-phloroglucitol (XXXIV) (m.p. 186-187°) and 15.78 g. (0.127 moles) of trimethyl phosphite (b.p. 109°/ 740 mm.). As the temperature of the reactants was raised cautiously, the solid XXXIV slowly dissolved. The mixture was heated to reflux for one hour to completely dissolve the solid, and the solution was boiled for an additional one-half hour. The solution was allowed to cool and the condenser was replaced by a simple distillation setup. As throughout the entire reaction period, nitrogen was passed through the system during the distillation. The initial vapor stayed at 58-63° for a short time while methanol was recovered in approximately 90 per cent yield. The excess trimethyl phosphite distilled at 107-109° while the pot temperature rose to 150°. The residue was allowed to cool and the nitrogen flow rate was increased over the solid residue remaining in the pot to remove trace amounts of trimethyl phosphite and to protect the unoxidized phosphorous products. Skelly Solvent F (40-50 ml) was added to the cold reaction flask while a rapid stream of nitrogen was passed through the system. The solid residue was then washed with the cold petroleum ether and the supernatant liquid was quickly decanted into a flask which was flushed with nitrogen and stoppered. The initial washing with cold Skelly Solvent F removes most

of the remaining trimethyl phosphite impurity in the residue and consequently is worked up separately. A similar portion (40-50 ml) of Skelly Solvent F was added to the reaction flask which was maintained under a nitrogen atmosphere. The light petroleum ether was boiled with the white, solid, residue for a few minutes by means of a water bath, and the hot solvent was decanted into a flask. Crystallization occurred immediately in the decanted liquid, and the flask was flushed with nitrogen and stoppered. Due to the low solubility of the tricyclic phosphite II in petroleum ether, the sequence had to be repeated about fifteen times. A large volume of solvent could be avoided by decantation of the liquid from the crystalline solid and utilization of this liquid for additional recrystallizations from the reaction flask. The two possible solid impurities in the product are cis-phloroglucitol (XXXIV) and the oxide of the phosphite II, 1-phospha-2,8,9-trioxaadamantane, 1-oxide (XXXVI). The alcohol XXXIV was insoluble in Skelly Solvent F and the tricyclic phosphate XXXVI was only very slightly soluble in the hot petroleum ether. By this method the ester II was obtained in 82.4 per cent yield, (2.993 g.; 0.019 mole), melting point 205.5-207.0°.

The infrared spectrum of the tricyclic phosphite II (Plate IV) shows a strong band at 1105 $cm.^{-1}$ which could possibly be assigned to the P-O-C (alkyl) group (31). Other major peaks are shown at 936, 900, 835, and 712 $cm.^{-1}$. The infrared spectrum of the oxidation product, XXXVI, is shown in Plate V.

A nuclear magnetic resonance spectrum (Plate XIII) of this compound II shows a single peak at 5.67 tau units assignable to a tertiary hydrogen atom attached to the same carbon atom as a oxygen atom (three hydrogen). The methylene group displays two doublets, at 6.94

tau units (total three hydrogen, J = 13.5 c.p.s.; equatorial) and at 8.10 tau units (total three hydrogen, J = 13.0 c.p.s.; axial). The NMR spectrum of the phosphate XXXVI (Plate XIV) displays three similar doublets; 4.80 tau units (J = 19.5 c.p.s.) assigned to the single hydrogens adjacent to the three oxygen atoms; 7.22 tau units (J = 15.5 c.p.s.) and 7.91 tau units (J = 15.5 c.p.s.) assigned to the three methylene groups (102).

Attempted Internal Ring Closure with 1-Phospha-2,8,9-trioxaadamantane (II). To a 2.5 cm. by 10 cm. pyrex tube containing a small magnetic stirrer and fitted with a reflux condenser, was added 0.988 g. (0.00617 moles) of the phosphite II. A small crystal of iodine along with 14 ml of toluene were added. The hetergeneous mixture was refluxed under a nitrogen atmosphere for four hours. A second crystal of iodine was added after one hour. A large part of the phosphite II had dissolved in the toluene by the end of the heating period. Most of the toluene was distilled, and 10 ml of anhydrous methanol was added to the reaction tube to azeotrope out the remaining toluene. When the methanol was removed, two portions of 10 ml each of Skelly Solvent F were added and used to azeotrope out any methanol. The methanol and Skelly Solvent F distillates had a distinct phosphite odor. Boiling Skelly Solvent F was used to extract the mixture, the unreacted phosphite II being soluble. The recovered phosphite II was identified by its melting point, 205-207°, and mixed melting point with a known sample. Some material remained in the tube after the extraction. This material melted at 176-179° and gave a mixed melting point of 178-181° with cis-phloroglucitol (XXXIV). The infrared spectrum also agreed with cis-phoroglucitol (XXXIV). No evidence for internal ring closure initiated by iodine was found.

Preparation of 3-Benzyl-7-chloro-2,4-dioxa-3-phospha-bicyclo[3.3.1]-nonane, 3-Oxide (XXX). In a 1.5 cm. by 7.5 cm. pyrex tube fitted with a 24-40 ground-glass joint, were placed 4.000 g. (0.0250 moles) of 1-phospha-2,8,9-trioxaadamantane (II) (m.p. 205-207°) and 3.957 g. (0.0313 moles) benzyl chloride (b.p. 78-80°/ 26 mm.). The reaction tube was equipped with a nitrogen inlet tube and a condenser to which a calcium chloride drying tube was attached. Upon mixing the two reactants, the benzyl chloride dissolved approximately one-half of the solid phosphite II without a noticeable reaction or temperature change. The reactants were heated under a nitrogen atmosphere by means of a constant temperature bath composed of boiling toluene at 110°. After a short time, a clear, colorless solution resulted. Toward the end of the twenty-four hour heating period, formation of a white solid was noted in the bottom of the reaction tube. Upon cooling, the remaining solution solidified to a white, crystalline mass. The material was dissolved with a minimum of methylene chloride. To this solution was slowly added Skelly Solvent F with intimate mixing until about a twenty-fold excess of the added solvent resulted. The clear solution was allowed to stand, and plates slowly formed after a few hours. The supernatant liquid was decanted, and the crystals were washed with Skelly Solvent F. Recrystallization from this solvent system gave 4.684 g. (0.0163 moles) of product corresponding to a 65.40 per cent yield. This material melted at 197.5-199.0°. Recrystallization from methanol yielded plates which melted at 199.0-200.5° and did not depress the melting point of the material recrystallized from methylene chloride-Skelly Solvent F.

Anal. Calcd. for $C_{13}H_{16}PO_3Cl$:

C, 54.46; H, 5.63; P, 10.80; Cl, 12.37.

Found: C, 53.68; H, 5.70; P, 10.84; Cl, 12.20.

C, 53.79; H, 5.57.

The infrared spectrum of the bicyclic phosphonate XXX (Plate VI) exhibits bands characteristic of hydrogen-bonded phosphoryl group (1248 and 1228 $cm.^{-1}$) (31,45), equatorial chlorine on a cyclohexane ring (747 $cm.^{-1}$) (19,68), mono-substituted benzene (699 $cm.^{-1}$) (89), and the P-O-C (alkyl) linkage (1016 $cm.^{-1}$) (31). A number of other well-defined peaks are also present at 1116, 954, 897, 836, and 796 $cm.^{-1}$. Both the infrared spectrum and the analysis correspond to the expected bicyclic phosphonate XXX.

The nuclear magnetic resonance spectrum of this compound (Plate XV) shows absorption at 2.76 tau units for benzene hydrogen, and a doublet at 6.72 tau units (J = 22 c.p.s.) for methylene hydrogen attached to a benzene ring. The relative area under these curves was 5:1:1, respectively. Similarly in the model compound, dimethyl benzylphosphonate (XXXVII), absorption occurred at 2.73 tau units and at 6.84 tau units (J = 21.7 c.p.s.) for benzene hydrogen and methylene hydrogen, respectively (Plate XII). The spectrum of XXX also shows fine structure at 4.96 to 5.55 tau units (three hydrogen) and doublets at 5.50 tau units (J = 17.5 c.p.s.; two hydrogen), 7.27 tau units (J = 15 c.p.s.; two hydrogen), 8.75 tau units (J = 15 c.p.s.; one hydrogen), and 9.29 tau units (J = 15 c.p.s.; one hydrogen). A triplet with J = 13 c.p.s. appears at 8.32 tau units.

Molecular weights of XXX were determined by the Rast method using camphor as a solvent (43). The experimentally determined molecular weights, 289.3 and 291.3, agree well with the theoretical molecular weight of XXX which is 286.7.

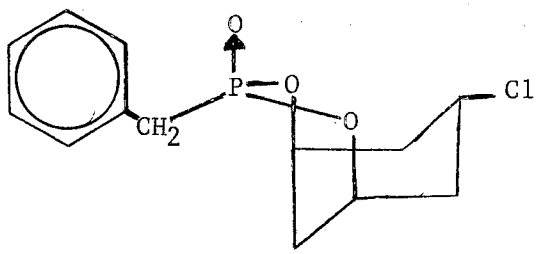
Dipole Moment Calculations for the Possible Isomers of the Bicyclic Benzylphosphonate XXX. Careful consideration of the structure of the bicyclic benzylphosphonate XXX shows that this compound and its analogs could possibly exist in the form of one or more of sixteen different isomers. These sixteen possible isomers arise from the following considerations. In the bicyclo[3.3.1]nonane ring system, there are two six-membered rings fused at the 1,3-positions. In our compound XXX, these two rings are different, one being a cyclohexane ring while the other is a 1,3,2-dioxaphosphorinane ring. Each of these six-membered rings can exist in either a chair or a boat form independent of the other. Also independent of other factors are both the position of the chlorine atom on the cyclohexane ring, either axial or equatorial, and the location of the benzyl group attached to the phosphorus atom which can be located above either the cyclohexane ring or the dioxaphosphorinane ring. The possible isomers are illustrated on the following page.

The following assumptions were used in calculation of the angles and distances within the molecule and the subsequent calculation of dipole moments.

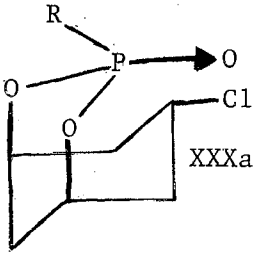
Assumed:

(1) The atoms, see XXX, C_7, P, O_3; H_4, C_4, H_3; and H_1, C_1, Cl, all lie in a common plane which is hereafter referred to as the Major Plane in these calculations.

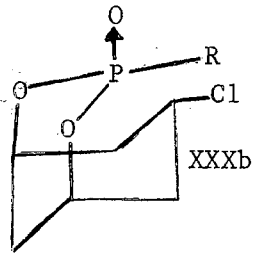
Possible Isomers of XXX



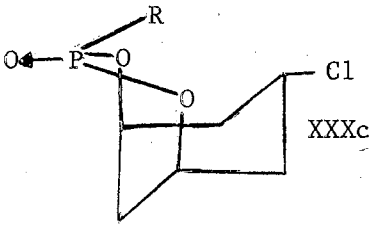
(R = Benzyl)



XXXa



XXXb



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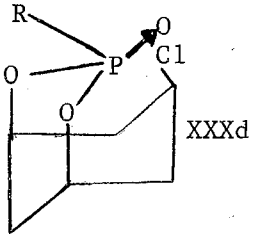

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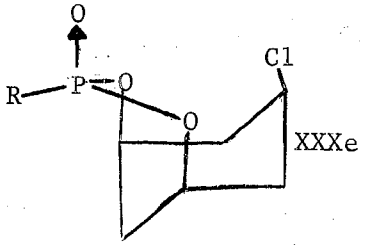

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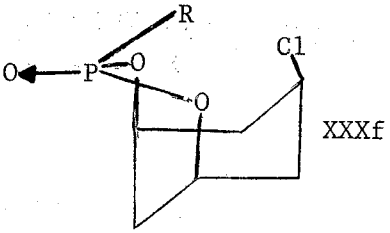

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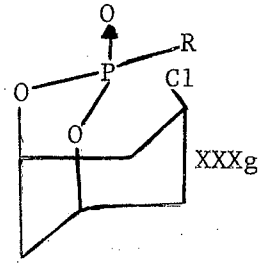

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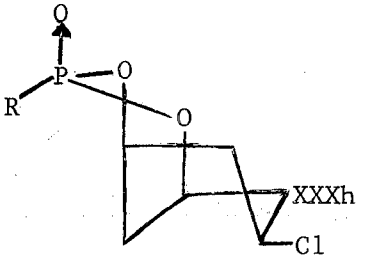

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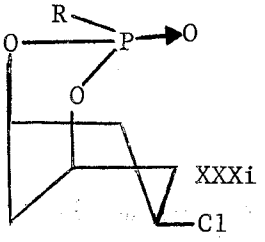
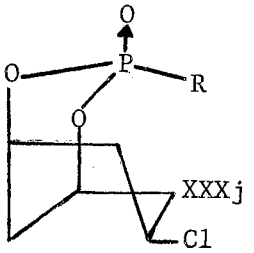


XXXi



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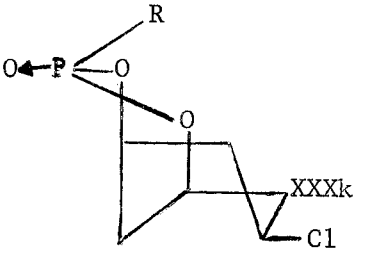

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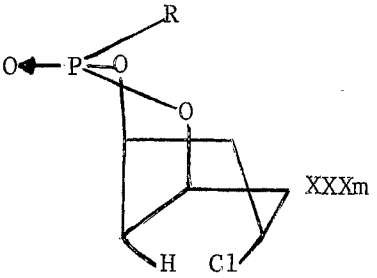

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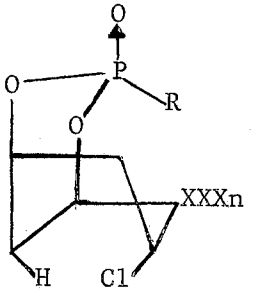

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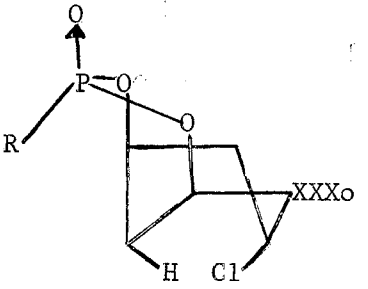
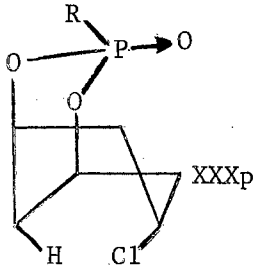
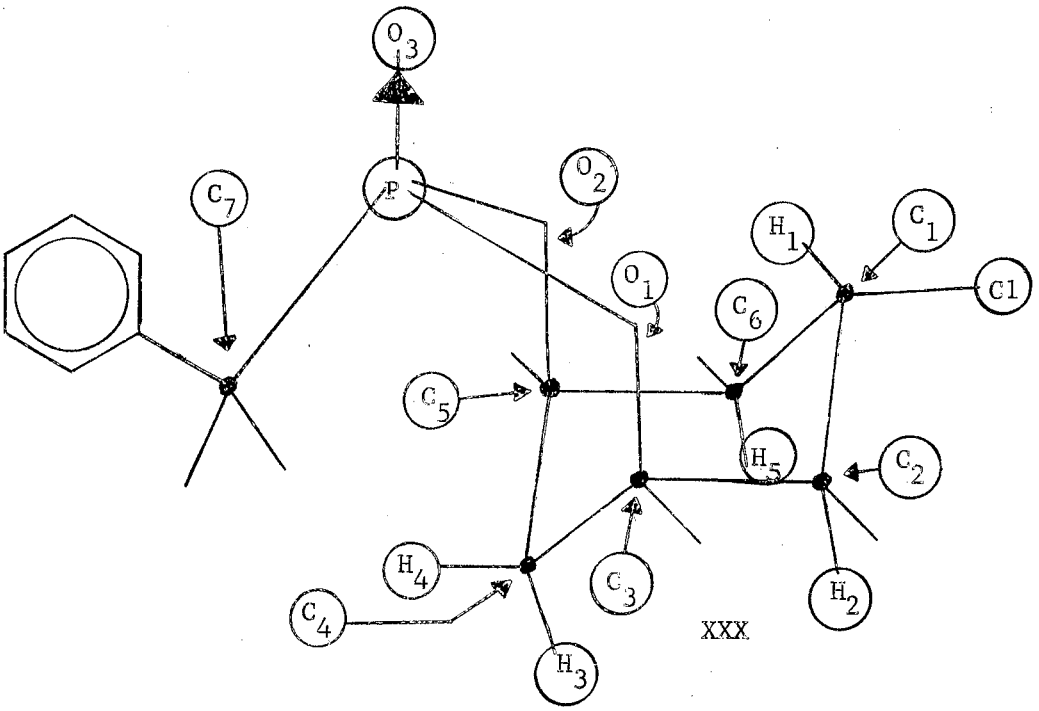


XXXo



XXXp



XXX

(2) The atoms O_1, C_3, C_2, H_2, all lie in a common plane.

(3) The atoms O_2, C_5, C_6, H_5, all lie in a common plane.

(4) All three planes are parallel to each other.

(5) Angles (38,89):

CCC = 109.5°	CCO = 112.5°	CP(=O) = 116.5°
CCH = 109.5°	CPO = 101.5°	OP(=O) = 116.5°
HCH = 109.5°	OPO = 101.5°	COP = 113°

(6) Bond lengths (38,89):

C-C = 1.54 Å	C-O = 1.43 Å	P-O = 1.62 Å
C-H = 1.10 Å	C-Cl = 1.76 Å	P-O = 1.39 Å
	C-P = 1.87 Å	

(7) Dipoles (91,92):

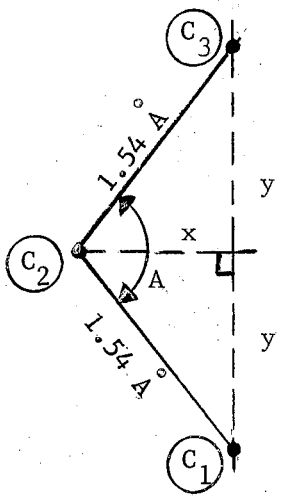
C-Cl = 2.2 D (90)	P-(=O) = 3.5 D	P-O = 1.2 D
C-O = 1.12 D		P-C = 0.8 D

(8) The vectors for individual components are:

$\overrightarrow{C\text{-}Cl}$	$\overrightarrow{P\text{-}(=O)}$	$\overrightarrow{P\text{-}O}$
$\overrightarrow{C\text{-}O}$		$\overrightarrow{P\text{-}C}$

Before the dipole moments can be computed, angles and distances within the molecule must be known. These values were determined from the known bond distances and angles. The computation is shown in the following paragraphs.

Calculation of 1 to 3 Carbon Distance and the Distance $C_2 - C_1$ Projected on the Major Plane.



$C_1 - C_3$ distance.

$A = 109.5°$ $\quad \frac{A}{2} = 54.75°$

$$\frac{1.54 \text{ Å}}{\sin 90°} = \frac{y}{\sin 54.75°}$$

$y = 1.54 \sin 54.75°$

$y = 1.257$

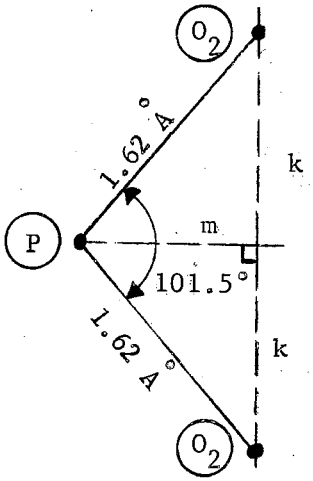
$2y = 2.515$ Å $= C_1 - C_3$ distance.

$C_2 - C_1$ projected on Major Plane.

$x^2 + (1.257)^2 = (1.54)^2$

$x = 0.890$ Å

Calculation of $O_1 - O_2$ Distance and the Distance P - O_1 (or O_2) Projected on the Major Plane.



$101.5 \div 2 = 50.75°$

$90° - 50.75° = 39.25°$

$$\frac{1.62}{\sin 90°} = \frac{k}{\sin 50.75°} = \frac{m}{\sin 39.25°}$$

$O_1 - O_2$ distance $= 2k$

$k = 1.62 \sin 50.75°$

$k = 1.255$ Å

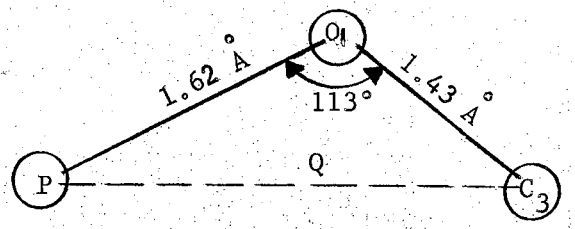
$2k = 2.510$ Å

Projected P - O_1 (or O_2) distance

$m = 1.62 \sin 39.25°$

$m = 1.025$ Å

Calculation of P - C_3 (or C_5) Distance and the P - C_3 (or C_5) Distance Projected on the Major Plane. Calculation of the Angle PO_1C_3 Projected on the Major Plane.



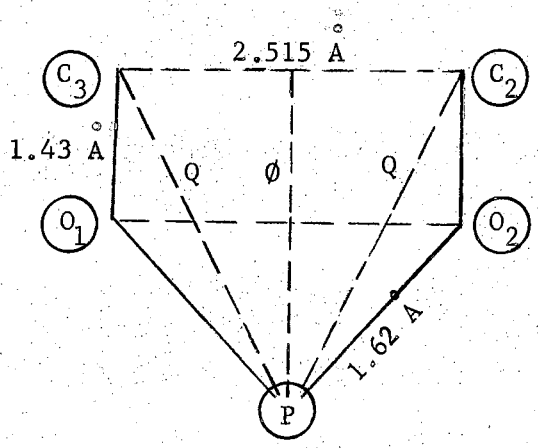
P - C_3 (or C_5) distance

$a^2 = b^2 + c^2 - 2\,bc \cos A$

$Q^2 = (1.62)^2 + (1.43)^2 - 2(1.62)(1.43) \cos 113°$

$Q^2 = 2.546$ Å

Projected P - C_3 (or C_5) distance.



$\phi^2 = Q^2 - (1.257)^2$

$\phi^2 = 6.4796 - 1.5800 = 4.8996$

$\phi = 2.214$ Å

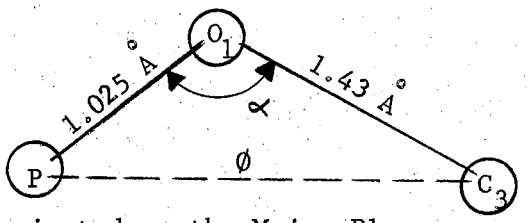
Projected PO_1C_3 angle.

$$\cos \alpha = \frac{b^2 + c^2 - a^2}{2\,bc}$$

$$\cos \alpha = \frac{(1.025)^2 + (1.43)^2 - (2.214)^2}{2\,(1.025)\,(1.43)}$$

$\cos \alpha = 0.6154$

$\alpha = 128°$



Calculation of the Angle O_3PO_1 Projected on the Major Plane.

$$\frac{y'}{\sin 63.5°} = \frac{1.62}{\sin 90°} = \frac{k'}{\sin 26.5°}$$

$y' = 1.62 \sin 63.5°$

$y' = 1.450$ Å

$k' = 1.62 \sin 26.5°$

$k' = 0.723$ Å

$$\frac{1.025}{\sin 90°} = \frac{0.723 \text{ Å}}{\sin \beta} = \frac{x'}{\sin \alpha'}$$

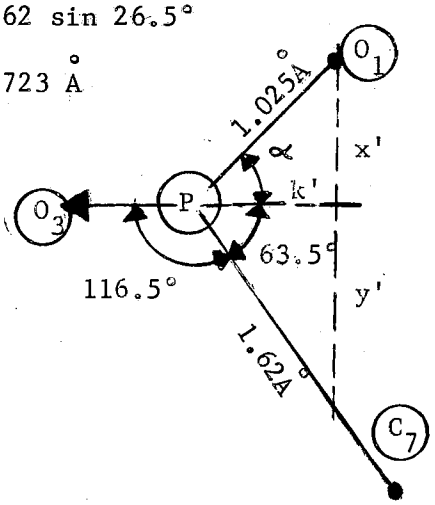
$$\sin \beta = \frac{0.723}{1.025} = 0.7052$$

$$\beta = 44.85°$$

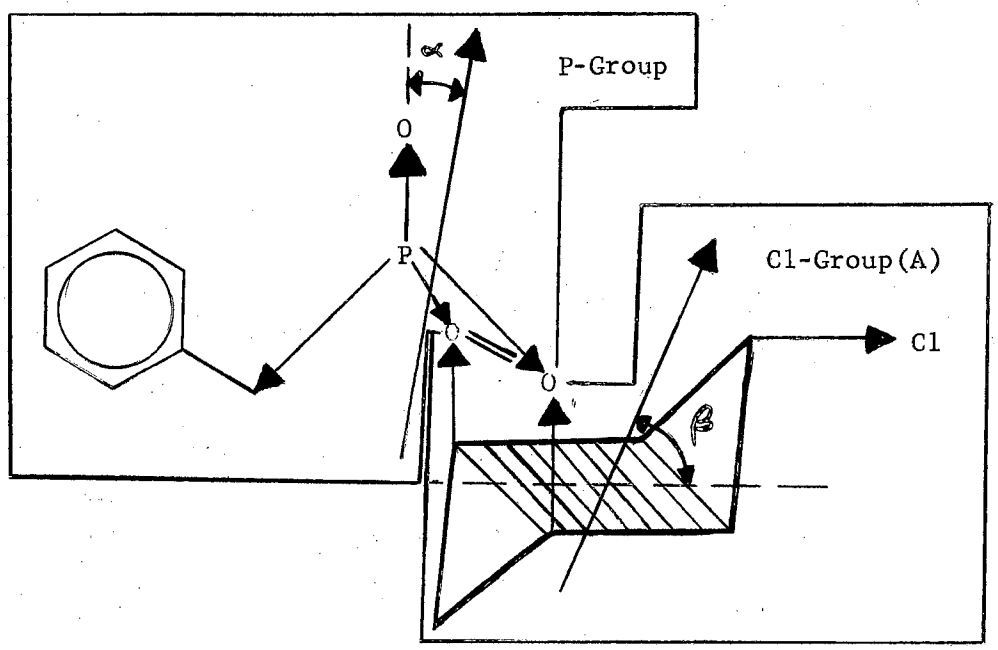
$$\alpha' = 90° - 44.85° = 45.15°$$

$x' = 1.025 \sin \alpha'$

$x' = 0.727$ Å

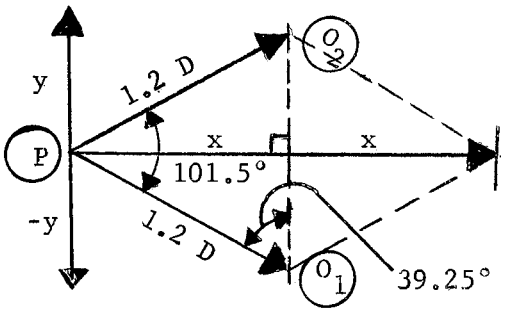


To facilitate calculation of the dipole moments for the sixteen isomers, the various dipoles within the molecule were resolved into two major dipoles. The two major dipoles with the angle between them were then used to calculate the dipole moments.



The P-Group dipole with its angle remains constant from isomer to isomer, however, the Cl-Group dipole and angle changes with the cyclohexane ring shape (chair or boat) and the chlorine position (axial or equatorial).

Calculation of the P-Group Dipole. The magnitude of the two P-O vectors projected on the Major Plane:

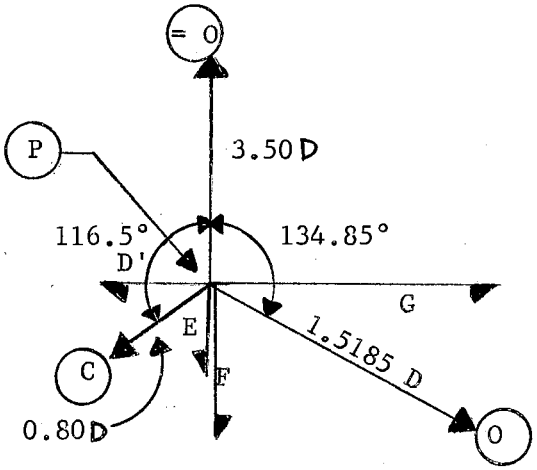


$$\frac{2(1.2)}{\sin 90°} = \frac{2x}{\sin 39.25°}$$

$$2x = 2.4 \sin 39.25°$$

$$2x = 1.5185 \text{ D}$$

Resolution of individual dipoles within the P-Group into x and y vectors and calculation of the P-Group dipole:



Resolution of P-C dipole into vectors D' and E:

$D' = 0.8 \cos 26.5°$

$D' = 0.716$ D

$E = 0.8 \cos 63.5°$

$E = 0.357$ D

Resolution of the projected P-O vectors into F and G vectors:

$F = 1.5185 \cos 45.15°$

$F = 1.071$ D

$G = 1.5185 \cos 44.85°$

$G = 1.077$ D

The x and y vectors of the P-Group dipole:

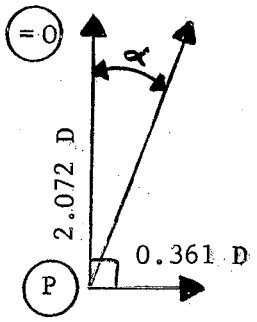
x vector is vector G-minus vector D.

$G - D = 1.077 - 0.716 = 0.361$ D

y vector is (P=O) vector minus vectors E and F.

$(P=O) - E - F = 3.5 - 1.071 - 0.357 = 2.072$ D

Magnitude and angle of P-Group dipole:



$(\text{dipole})^2 = (0.361)^2 + (2.072)^2$

dipole = 2.103 D

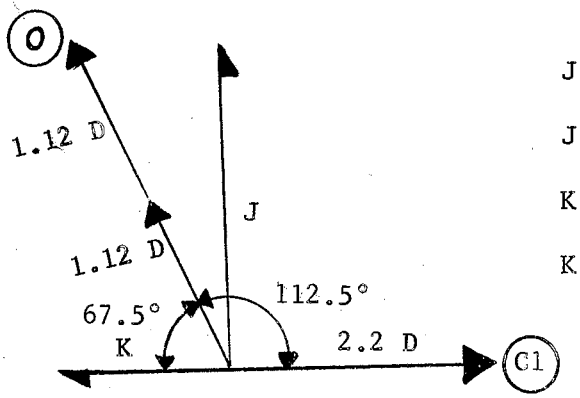
$\tan \alpha = \frac{0.361}{2.072} = 0.1742$

$\alpha = 9.9°$ from the P(=O)

vector, opposite the P-C bond.

Calculation of the Cl-Group (A) Dipole. In the Cl-Group (A) dipole, the cyclohexane ring is in a chair form and the chlorine atom is situated equatorially on the ring.

Resolution of the two C-O dipoles into vectors J and K:



J = 2.24 sin 67.5°

J = 2.070 D

K = 2.24 cos 67.5°

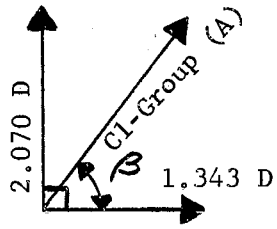
K = 0.857 D

The x vector of the Cl-Group (A) dipole:

(C-Cl) - K = 2.2 - 0.857 = 1.343 D

The y vector of the Cl-Group (A) dipole is merely J which is 2.070 D.

The Cl-Group (A) dipole and angle:



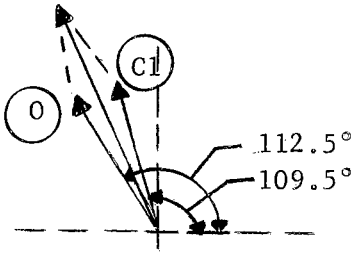
$(\text{dipole})^2 = (2.070)^2 + (1.343)^2$

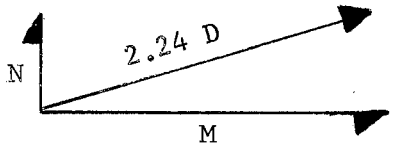
dipole = 2.476 D

$\tan \beta = \frac{2.070}{1.343} = 1.577$

$\beta = 57°$ from the C-Cl vector, between the phosphorus and chlorine atoms.

Calculation of the Cl-Group (B) Dipole. In the Cl-Group (B) dipole, the cyclohexane ring has the chair form while the chlorine atom is located in an axial position.





Resolution of the two P-O vectors into vectors M and N:

$N = 2.24 \sin 3°$ $\qquad$ $M = 2.24 \cos 3°$

$N = 0.117$ D $\qquad$ $M = 2.237$ D

The y vector of the Cl-Group (B) dipole is N which is 0.117 D.

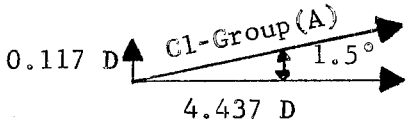
The x vector of the Cl-Group (B) dipole:

$(C\text{-}Cl) + M = 2.2 + 2.237 + 4.437$ D

The Cl-Group (B) dipole and angle:

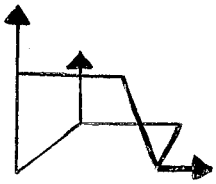
$(\text{dipole})^2 = (0.117)^2 + (4.437)^2$

dipole = 4.439 D



The angle is 1.5° less than that of the C-O vectors or 111° above the plane composed of the central four carbon atoms of the cyclohexane ring.

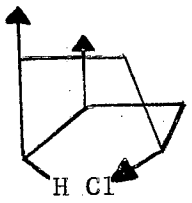
The Cl-Group (C) Dipole.



This group is composed of a cyclohexane ring in a boat form with the chlorine atom occupying an equatorial position. The direction of an equatorial bond at the position where the chlorine atom is located remains essentially the same in going from a chair form to a boat form of the cyclohexane ring. Therefore, the dipole

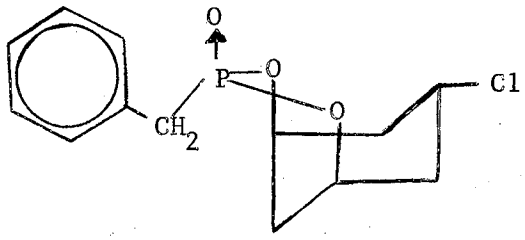
of the Cl-Group (C) would be basically the same as the Cl-Group (A) dipole.

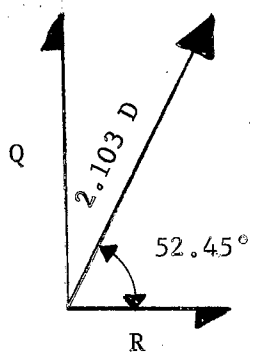
The Cl-Group (D) Dipole.



The Cl-Group (D) dipole contains the boat form of the cyclohexane ring and the chlorine atom located in an axial position on the ring. Due to the great interaction that would exist between the chlorine atom and the hydrogen atom opposite it, it is highly unlikely that this situation would exist. Thus, any isomers which can be vicualized containing this grouping can be disregarded as possible isomers of XXX.

Calculation of the Dipole Moment of Isomer XXX. The isomer XXX is composed of a P-Group dipole and a Cl-Group (A) dipole with an angle of 52.45° between the two.





Resolution of the P-Group dipole into vectors Q and R:

Q = 2.103 cos 37.55° R = 2.103 sin 37.55°

Q = 1.668 D R = 1.282 D

The y vector of the dipole moment is Q or 1.668 D.

The x vector of the dipole moment:

R + Cl-Group (A) = 1.282 + 2.476 = 3.758 D

The dipole moment of isomer XXX:

$\mu = (1.668)^2 + (3.758)^2$

$\mu = 4.111$ D for isomer XXX.

Assuming the phosphorus-carbon dipole vector is directed in the opposite direction, that is from carbon to phosphorus, calculation of a new dipole for the P-Group gives a value of 3.313 D with an angle of 32.77° from the phosphoryl group located between the oxygen atoms. The angle between the new P-Group dipole (P'-Group) and the Cl-Group (A) for the isomer XXX gives a value of 29.58°.

Resolution of the P'-Group dipole into vectors Q and R:

$Q = 3.313 \sin 29.58°$ $\qquad$ $R = 3.313 \cos 29.58°$

$Q = 1.636$ D $\qquad$ $R = 2.881$ D

The y vector of the dipole moment is Q or 1.636 D.

The x vector of the dipole moment:

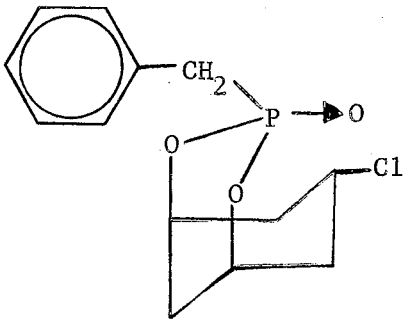
R + Cl-Group (A) = 2.881 + 2.476 = 5.357 D

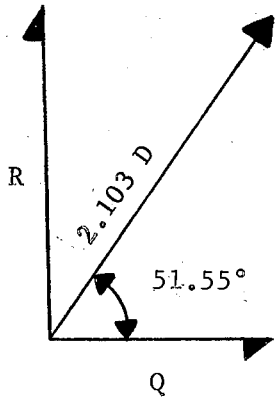
The dipole moment of isomer XXX:

$\mu^2 = (1.636)^2 + (5.357)^2$

$\mu = 5.601$ D for isomer XXX.

Calculation of the Dipole Moment of the Isomer XXXa. The isomer XXXa is comprised of a P-Group dipole with a Cl-Group (A) dipole at an angle of 51.55° from the first dipole.





Resolution of the P-Group dipole into vectors Q and R:

$Q = 2.103 \sin 51.55°$ $\qquad$ $R = 2.103 \cos 51.55°$

$Q = 1.308$ D $\qquad$ $R = 1.647$ D

The y vector of the dipole moment is R or 1.647 D

The x vector of the dipole moment:

Cl-Group (A) + Q = 2.476 + 1.308 = 3.784 D

The dipole moment of isomer XXXa:

$$\mu^2 = (3.784)^2 + (1.647)^2$$

$$\mu = 4.127 \text{ D}$$

Assuming the phosphorus-carbon vector is directed now from carbon to phosphorus, an angle of 74.25° is calculated between the P'-Group and the Cl-Group (A).

Resolution of the P'-Group dipole into vectors Q and R:

$Q = 3.313 \sin 74.25°$ $\qquad$ $R = 3.313 \cos 74.25°$

$Q = 3.191$ D $\qquad$ $R = 0.890$ D

The y vector of the dipole moment is Q or 3.191 D.

The x vector of the dipole moment:

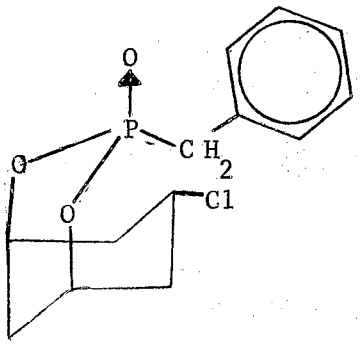
R + Cl-Group (A) = 0.890 + 2.476 = 3.366 D.

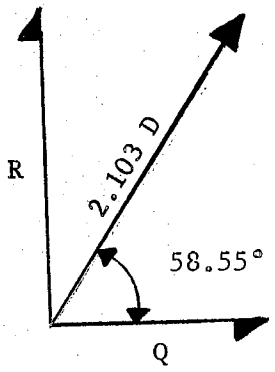
The dipole moment of isomer XXXa:

$\mu^2 = (3.191)^2 + (3.366)^2$

μ = 4.638 D for isomer XXXa.

Calculation of the Dipole Moment of the Isomer XXXb. The isomer XXXb consists of a P-Group dipole and a Cl-Group (A) dipole separated by an angle of 58.55°





Resolution of P-Group dipole into vectors Q and R:

Q = 2.103 cos 58.55° R = 2.103 sin 58.55°

Q = 1.097 D R = 1.794 D

The y vector of the dipole moment is R or 1.794 D.

The x vector of the dipole moment:

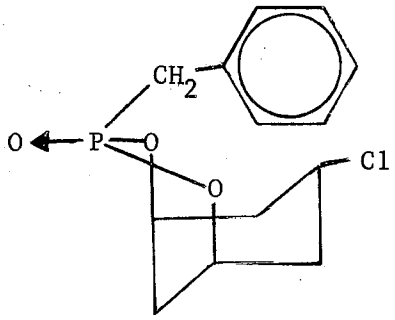
Cl-Group (A) + Q = 2.476 + 1.097 = 3.573 D

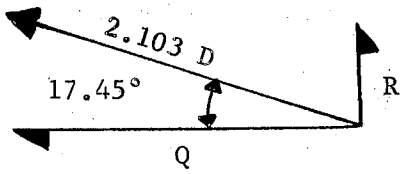
The dipole moment of isomer XXXb:

$$\mu^2 = (3.573)^2 + (1.794)^2$$

$$\mu = 3.998 \text{ D}$$

Calculation of the Dipole Moment of the Isomer XXXc. 62.55° separates the P-Group dipole and the Cl-Group (A) dipole in the isomer XXXc.





Resolution of P-Group dipole into vectors Q and R:

$Q = 2.103 \cos 17.45°$ $\qquad$ $R = 2.103 \sin 17.45°$

$Q = 2.006$ D $\qquad$ $R = 0.631$ D

The y vector of the dipole moment is R or 0.631 D.

The x vector of the dipole moment:

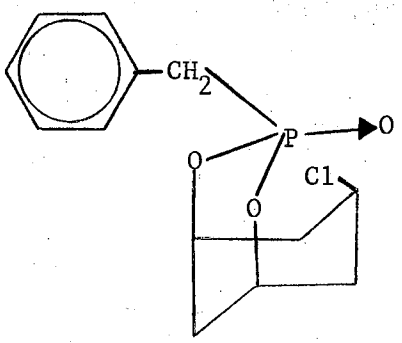
Cl-Group (A) - Q = 2.476 - 2.006 = 0.470 D

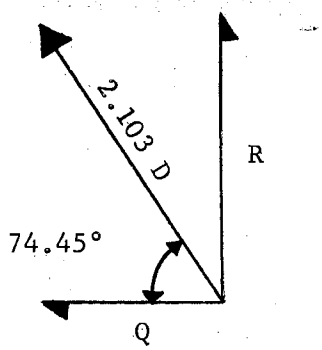
The dipole moment of isomer XXXc:

$$\mu^2 = (0.470)^2 + (0.631)^2$$

$$\mu = 0.787 \text{ D}$$

Calculation of the Dipole Moment of the Isomer XXXd. A P-Group dipole 105.55° from a Cl-Group (B) dipole constitutes the isomer XXXd.





Resolution of P-Group dipole into vectors Q and R:

$Q = 2.103 \cos 74.45°$ $\qquad$ $R = 2.103 \sin 74.45°$

$Q = 0.546$ D $\qquad$ $R = 2.026$ D

The y vector of the dipole moment is R or 2.026 D.

The x vector of the dipole moment:

Cl-Group (B) - Q = 4.439 - 0.564 = 3.875 D

The dipole moment of isomer XXXd:

$$\mu^2 = (2.026)^2 + (3.875)^2$$

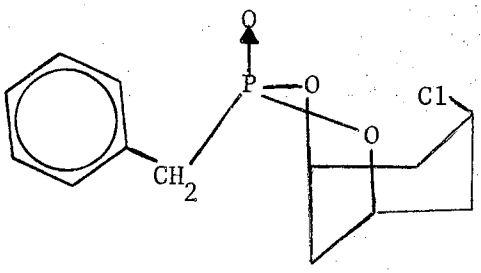
$$\mu = 4.373 \text{ D}$$

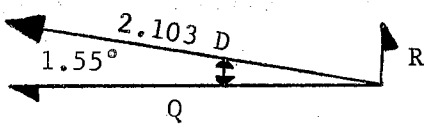
Calculation of the Dipole Moment of the Isomer XXXe. The isomer XXXe is made up of a P-Group dipole located 1.55° from a Cl-Group (B) dipole.

Resolution of the P-Group dipole into vectors Q and R:

$Q = 2.103 \cos 1.55°$ $\qquad$ $R = 2103 \sin 1.55°$

$Q = 2.101$ D $\qquad$ $R = 0.0936$ D





The y vector of the dipole moment is R or 0.0936 D.

The x vector of the dipole moment:

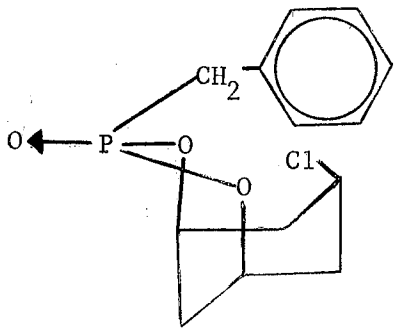
Cl-Group (B) + Q = 4.439 + 2.101 = 6.540 D

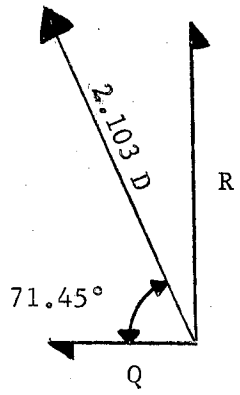
The dipole moment of isomer XXXe:

$$\mu^2 = (6.540)^2 + (0.0936)^2$$

$$\mu = 6.540 \text{ D}$$

Calculation of the Dipole Moment of the Isomer XXXf. The isomer XXXf contains a P-Group dipole located 108.55° from a Cl-Group (B) dipole.





Resolution of P-Group dipole into vectors Q and R:

Q = 2.103 cos 71.45° R = 2.103 sin 71.45°

Q = 0.669 D R = 1.994 D

The y vector of the dipole moment is R or 1.994 D.

The x vector of the dipole moment:

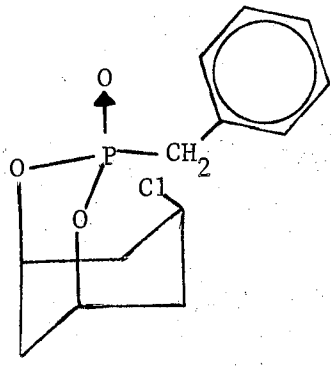
Cl-Group (B) - Q = 4.439 - 0.669 = 3.770 D

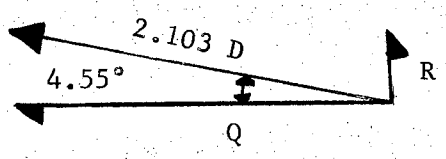
The dipole moment of isomer XXXf:

$$\mu^2 = (3.770)^2 + (1.994)^2$$

$$\mu = 4.265 \text{ D}$$

Calculation of the Dipole Moment of the Isomer XXXg. A P-Group dipole at an angle of 4.55° to a Cl-Group (B) dipole composes the isomer XXXg.





Resolution of the P-Group dipole into vectors Q and R:

Q = 2.103 cos 4.55° R = 2.103 sin 4.55°

Q = 2.097 D R = 0.167 D

The y vector of the dipole moment is R or 0.167 D

The x vector of the dipole moment:

Cl-Group (B) + Q = 4.439 + 2.097 = 6.536 D

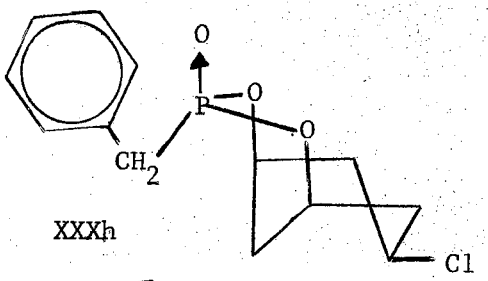
The dipole moment of isomer XXXg:

$$\mu^2 = (6.536)^2 + (0.167)^2$$

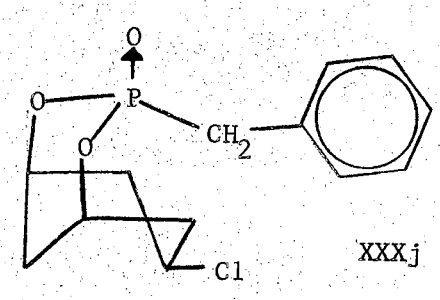
$$\mu = 6.537 \text{ D}$$

The Dipole Moments for the Isomers XXXh, XXXi, XXXj, and XXXk.

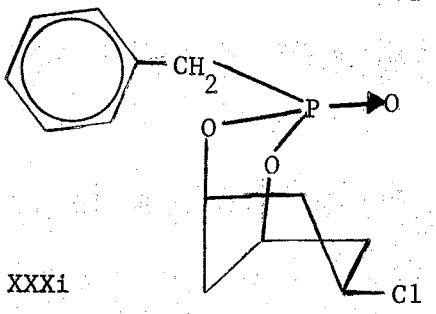
These four isomers each contain the Cl-Group (C) dipole which is identical to the Cl-Group (A) dipole. Therefore, they will have dipole moments of the same magnitude as isomers XXX, XXXa, XXXb, and XXXc.



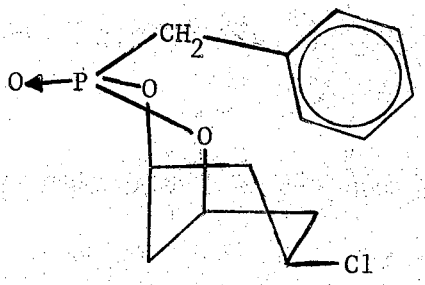
XXXh



XXXj



XXXi



XXXk

Due to the fact that isomers XXXm, XXXn, XXXo, and XXXp each contain a Cl-Group (D) dipole, no dipole moments were calculated for these isomers.

The Experimentally Determined Dipole Moment of the Benzyl Bicyclic Phosphonate XXX. The dipole moment of XXX was determined by Dr. Max T. Rogers, Michigan State University (90). Using carbon tetrachloride as a solvent at 25°, a value of 5.16 Debye was found for benzyl bicyclic phosphonate XXX. Due to the somewhat limited solubility of the phosphonate XXX in carbon tetrachloride, an error in the electric moment is

probable but surely not more than a few tenths of a Debye at most. A more precise determination was obtained in dioxane giving a value of 5.9 Debye at 25°.

Preparation of Dimethyl Benzylphosphonate (XXXVII). To a reaction system similar to that described previously were added 4 ml of benzyl chloride (4.4 g.; 0.0348 moles), b.p. 78-80°/ 26 mm., and 10 ml of trimethyl phosphite (10.5 g.; 0.0848 moles), b.p. 109°/ 740 mm. One drop of triethylamine was added as a catalyst. The reaction vessel was heated twenty-four hours at 110° and was then allowed to cool. Vacuum distillation yielded a sample boiling at 100°/ 0.7 mm.; 3.5 g., 50 per cent. The infrared spectrum shows bands characteristic of the phosphoryl group (1255 $cm.^{-1}$), the P-O-methyl group (1187 $cm.^{-1}$), the P-O-alkyl linkage (1030, 1055 $cm.^{-1}$), and mono-substituted benzene (698, 756 $cm.^{-1}$) (31,89). Nuclear magnetic resonance analysis of dimethyl benzylphosphonate (Plate XII) has absorption at 7.07 and 6.70 tau units corresponding to methylene hydrogen attached to a benzene ring (J = 22 c.p.s.). Peaks at 6.47 and 6.30 tau units are due to methyl groups attached to oxygen (J = 10 c.p.s.), and a single band at 2.72 tau units is due to benzene hydrogen. The ratio of areas under these curves was 1:1:3:3:5. Elemental analysis was also in agreement with the formula.

Anal. Calcd. for $C_9H_{13}PO_3$:

C, 54.00; H, 6.55; P, 15.47.

Found: C, 53.70; H, 6.64; P, 14.72.

Attempted Hydrolysis of 3-Benzyl-7-chloro-2,4-dioxa-3-phosphabicyclo-[3.3.1]nonane, 3-Oxide (XXX). To a 50-ml, round-bottom flask fitted with a reflux condenser were added 2.000 g. (0.00698 moles) of the benzyl bicyclic phosphonate (XXX) and 3.5 ml of concentrated hydrochloric acid. The heterogeneous mixture was boiled twelve hours. An additional 3.5 ml of concentrated acid was added to the flask and heating was continued overnight as some solid with the appearance of starting material was still suspended in the yellowish liquid. In an effort to dissolve the solid, 10 ml of 95 per cent ethanol and 5 ml of concentrated hydrochloric acid were added to the mixture. Since this appeared to have little effect on the solid, the mixture was held at reflux over the weekend. A white solid still remained after this period, however, its shape had changed from the flaky white starting material to a crystalline mass with a few needles protruding. When cooled, most of the liquid solidified. This material was washed into a 150-ml separatory funnel with 10 ml of 95 per cent ethanol and distilled water. The solution was made basic to litmus paper with additions of small portions of sodium bicarbonate. The 100-ml water layer was extracted six times with 10 ml portions of chloroform. Evaporation of the chloroform produced only about 100 mg. of a brownish solid. Attempts to recrystallize it were unsuccessful. The water layer was placed in a 250-ml Erlynmeyer flask and acidified with 3N hydrochloric acid. A white precipitate formed immediately on addition of the acid. This was filtered to yield 1.173 g. of dried material which had a melting point 146-148°+, with some small particles still visible above 160°. Benzylphosphonic acid reportedly melts at 169-170° (60). A small fraction was dissolved in methylene chloride, and a twenty-fold excess of Skelly Solvent F added. Clusters of two and

three needles slowly formed. The recrystallized material melted at 147-148° with residual traces of the higher melting component still visible. The solid is acidic, being able to liberate carbon dioxide from sodium bicarbonate solution. Use of this fact was made in recrystallizing the hydrolysis product. An analytical sample was purified by dissolving it in sodium bicarbonate solution and reprecipitating with acid. In addition it was dissolved in methylene chloride and precipitated by adding an excess of Skelly Solvent F, melting point 147.5-148.5°.

Anal. Found: C, 47.51; H, 5.31; P, 5.03; Cl, 21.90.

This analysis corresponds to none of the calculated values for expected products. The empirical formula is $C_{24}H_{32}PO_8Cl_4$. A molecular weight was determined by adding a known excess of sodium hydroxide to a weighed sample of the crude hydrolysis product and back titrating with hydrochloric acid. Values of 300.4 and 312.4 were obtained for an average value of 306.4.

The infrared spectrum of the hydrolysis product (Plate XI) shows a peak at 699 $cm.^{-1}$ for mono-substituted benzene (96) as the only identifiable band. There is a broad and shallow area from 2950 to 1700 $cm.^{-1}$ which may be due to P-OH.

In an effort to purify the hydrolysis product, it was chromatographed on 200.0 g. of neutral alumia (Merck Reagent). The alumina occupied an area 3 cm. by 24.5 cm. with a 3 cm. layer of sand above and below it. The sample (1.17 g.) was dissolved in 10 ml of methylene chloride and introduced onto the column containing Skelly Solvent F. During elution, 25 ml cuts were collected at fifteen minute intervals. The chromatograph was eluted by 100-ml portions of the following solvent ratios of Skelly

F to ethyl ether: 100:0, 29:1; 19:1; 9:1; 4:1; 2:1; 1:1; 1:2; 1:3; 0:100. Evaporation of the collected fractions produced no products. The column was stripped with 100 ml portions of methanol, ethyl acetate, methylene chloride, 5 per cent acetic acid in methanol, and methylene chloride. No product was isolated upon evaporation of these fractions. To be sure additional experiments and an NMR study of the hydrolysis product are necessary.

Basic hydrolysis of 1.000 g. (0.00349 moles) of the benzyl bicyclic phosphonate (XXX) with 20 ml of boiling 20 per cent sodium hydroxide was attempted over a thirty-six hour period. The solution turned yellow in color, and the solid was converted to an orange mass. Extraction from a basic, neutral, and acidic reaction solution with methylene chloride and ethyl ether failed to yield a product. The brownish-orange solid was filtered from a neutral solution following the attempted extraction. The orange solid, contaminated with silica, was insoluble in common organic solvents, water, and concentrated hydrochloric acid. The solid melted over a range above 300°, and burned only in a direct flame, leaving no residue. Attempts to purify the material were unfruitful. Attempted transesterification of the phosphonate XXX by solvolysis with methanol yielded only starting materials.

Attempted Preparation of 3-Benzyl-7-bromo-2,4-dioxa-3-phosphabicyclo-[3.3.1]-nonane, 3-Oxide. Using the previously described reaction system, 1.868 g. (0.0109 moles) of benzyl bromide was added to 1.749 g. (0.01909 moles) of the phosphite II and heated at a constant temperature of 110° for forty-eight hours. The reactants upon mixing formed a clear solution. When cooled, a semi-solid resulted. This was leached by methylene chloride.

Attempted recrystallizations from chloroform, methanol, cyclohexane, and other organic solvents were unsuccessful, only oils being recovered. Trituration of the viscous oil with such solvents as ethyl acetate, Skelly Solvent F, or methyl ethyl ketone did not induce crystallization.

Preparation of 3-(1-Naphthylmethyl)-7-chloro-2,4-dioxa-3-phospha-bicyclo[3.3.1.] nonane, 3-Oxide (XXXI). 1-(Chloromethyl) naphthalene (b.p. 88-92°/10.2 mm.; $n_D^{25°}$ 1.6357) in the amount of 3.101 g. (0.0176 moles) was added to 2.765 g. (0.0176 moles) of 1-phospha-2,8,9-trioxa-adamantane (III) in an apparatus similar to that described for the benzyl derivative. The solid phosphite III was partially soluble in the 1-(chloromethyl)naphthalene and completely dissolved when heated about two hours. A nitrogen atmosphere was maintained over the solution, as the reactants were first heated for sixteen hours by means of a 110° constant-temperature bath composed of boiling toluene. The heating bath was then changed to xylene, and the solution was heated at 140° for an additional twelve hours. Upon cooling, the melt solidified to a yellowish mass. Recrystallization of the reaction material was attempted without success, although it was soluble in benzene, methanol, chloroform, and methylene chloride while being insoluble in ethyl ether, iso-propyl ether, and normal hexane. Various combinations of mixed solvents failed to yield the pure phosphonate XXXI.

Chromatography on alumina (Merck reagent grade) of a benzene solution of the reaction mixture was successful in separating the components. The column was eluted with 600 ml. of benzene, 300 ml. of 1:1 benzene: ethyl ether, 200 ml. of ethyl ether, 200 ml. of 9:1 ethyl ether: methanol, 200 ml. of 3:1 ethyl ether: methanol, 200 ml. of 1:1 ethyl ether: methanol, and finally stripped with 250 ml. of methanol. Cuts were taken

every 50 ml. Evaporation of the solvent from the first three fractions yielded a small amount of a yellow oil which proved to be 1-(chloromethyl)-naphthalene. The only other residual material found after solvent evaporation from the remaining fractions was a yellow oil which was eluded by the 9:1 ethyl ether: methanol system. This oil slowly solidified to an oily, yellow solid. Attempts to recrystallize the solid from methanol, chloroform, and methyl ethyl ketone were unsuccessful. Similarly trituration of the solid with carbon tetrachloride, Skelly Solvent F, and cyclohexane were not fruitful. The solid could be purified by dissolving it in methylene chloride, adding a fifteen to twenty-fold excess of carbon tetrachloride, and removing the methylene chloride from the clear solution by means of a rotary evaporator. A white, crystalline ester obtained was filtered from the excess carbon tetrachloride. Recrystallization a second time by this method gave fine, white needles, 1.181 g. (0.00351 moles) which corresponded to 20.3 per cent yield of the bicyclic phosphonate XXXI, melting point 179-180°. An analytical sample was obtained when the ester was dissolved in a small amount of acetone and a twenty-fold excess of cyclohexane was added. When allowed to stand four hours, the clear solution yielded fine white needles of the 1-naphthylmethyl bicyclic phosphonate XXXI which melted at 179.5-180.5°.

Anal. Calcd. for $C_{17}H_{18}PO_3Cl$:

C, 60.63; H, 5.40; P, 9.21; Cl, 10.55.

Found: C, 60.88; H, 5.54; P, 8.96; Cl, 10.47.

The infrared spectrum (Plate VII) exhibits an absorption band at

1256 $cm.^{-1}$ for the phosphoryl group, a band at 1017 $cm.^{-1}$ for the P-O-C (alkyl) group (31), two bands at 779 and 759 $cm.^{-1}$ for the naphthene ring (19), and a band at 742 $cm.^{-1}$ for equatorial chlorine on a cyclohexane ring (68). Other strong absorption bands show up at 1108, 955 and 836 $cm.^{-1}$ with medium bands at 1324, 1222, 1076, 907, and 814 $cm.^{-1}$.

The nuclear magnetic resonance spectrum (Plate XVII) of the 1-naphthylmethyl phosphonate XXXI in $CDCl_3$ shows absorption in the region of 1.92 to 2.67 tau units for the seven naphthalene hydrogens. The single hydrogen gem to the chlorine atom is split into three triplets, centered at 5.33 tau units. The coupling constant is 5.0 c.p.s. within each triplet and J = 12 c.p.s. between each triplet. The two hydrogens gem to oxygen have a tau value of 5.83 and are composed of a doublet with J = 16 c.p.s.

Preparation of 3-Benzhydryl-7-chloro-2,4-dioxa-3-phosphabicyclo-[3.3.1]nonane, 3-Oxide (XXXII). 1-phospha-2,8,9-trioxaadamantane II in the amount of 1.592 g. (0.00994 moles) was added to a 1.5 cm. by 7.5 cm. pyrex tube fitted with a 24-40 ground-glass joint, along with 2.025 g. (0.00999 moles) of chlorodiphenylmethane (b.p. 104-105°/ 0.5 mm.). A nitrogen inlet tube and a condenser equipped with a calcium chloride drying tube were attached to the reaction tube. The benzhydryl chloride completely dissolved the tricyclic phosphite II when the two reactants were mixed. The clear solution was heated at 110° under a nitrogen atmosphere for forty-eight hours. At the end of this period, a colorless, clear melt remained. When cooled, the reaction material was found to be a hard, transparent solid. Purification by the same technique as described for the benzyl phosphonate XXX using a 15:1 ratio of Skelly F: methylene chloride, gave a gelatinous solid upon standing.

Suction filtration, with removal of solvent by pressing the material on the filter paper, produced a chalky, white solid. A second purification by this method provided 2.277 g. (0.00628 moles) of the benzhydryl bicyclic phosphonate XXXII (m.p. 211-213°; yield 63.1 per cent). In preparation of an analytical sample, the phosphonate XXXII was found to retain some solvent. Recrystallization from iso-propyl alcohol provided a material somewhat less gelatinous than from the mixed solvents. After being air dried, the solid XXXII was placed under a vacuum of 1 mm. in the presence of paraffin and phosphorus pentoxide. The anhydrous material was found to melt only partially at 212-214° and then resolidified to a white solid which melted sharply at 219.5-220.5°. It was found that sublimation was required to provide an analytical sample of XXXII. The bottom of a 4 cm. by 16 cm. sublimation gun was covered with the phosphonate XXXII. The distance from the solid to the condenser surface was 2.5 cm. Initially, the compound was heated gradually to 100° during two and a half hours while a vacuum of 0.1 mm. was maintained. The temperature was maintained at 100° with ca. 0.3 mm. pressure for three hours. This was followed with one and a half hours at 155-160° and 0.1 mm. Only a few milligrams of material sublimed. The melting point of the material in the bottom of the sublimation gun was found to be unaffected by this treatment. The analytical sample was taken from this material.

Anal. Calcd. for $C_{19}H_{20}PO_3Cl$:

C, 62.90; H, 5.56; P, 8.54; Cl, 9.77.

Found: C, 62.60; H, 5.77; P, 8.68; Cl, 9.42.

The infrared spectrum of the benzhydryl bicyclic phosphonate XXXII (Plate VIII) displays adsorption bands at 703 $cm.^{-1}$ for mono-substituted benzene (89), at 1257 $cm.^{-1}$ for the phosphoryl group, at 1014 $cm.^{-1}$ for P-O-C linkage (31), and at 734 $cm.^{-1}$ for equatorial chlorine on a cyclohexane ring (68). Other strong bands are at 1107 and 960 $cm.^{-1}$ while medium bands are at 1078 and 902 $cm.^{-1}$.

The nuclear magnetic resonance spectrum (Plate XIX) of this phosphonate XXXII in deuterated chloroform shows the ten aromatic hydrogens in the area of 2.48 to 2.90 tau units. The single hydrogen gem to the chlorine appears in the area of 4.90 to 5.46 tau units. The two hydrogens gem to the oxygen atoms display a doublet at 5.50 tau units with J = 17 c.p.s. Apparently, phosphorus-31 coupling (J = 25.5 c.p.s.) causes the single methine hydrogen to be split into a doublet at 5.45 tau units. The two equatorial hydrogens next to the chlorine atom provide a doublet at 7.26 tau units and have J = 15 c.p.s. A triplet (J = 13 c.p.s.) is exhibited by the two axial hydrogen adjacent to the chlorine atom at 8.32 tau units. The equatorial component of the methylene group between the two single oxygen atoms displays a doublet at 8.78 tau units while the axial hydrogen appears as a doublet at 9.00 tau units (J = 15 c.p.s.).

Attempted Preparation of 3-Trityl-7-chloro-2,4-dioxa-3-phosphabicyclo-[3.3.1]nonane, 3-Oxide. To insure complete mixing, 2.000 g. (0.0125 moles) of the phosphite II and 3.475 g. (0.0125 moles) of trityl chloride (m.p. 112.0-112.5°) were mixed and grounded in a mortar and pestle under a nitrogen atmosphere. The mixture was heated in the system previously described by means of xylene at 140°. Preliminary softening of the mixture occurred after forty-five minutes and a partial, pale yellow color

developed which intensified during the three and one-half hour heating period at 140°. When the heating bath temperature was raised to 163° by addition of p-dichlorobenzene to the xylene, the mixture again did not melt. Elevating the temperature to 194° by use of a ethylene glycol bath produced a rubbery mass. Bubbles formed at the base of this viscous fluid and a slow effervesence was observed throughout the twelve-hour reaction period. Upon cooling, the solid was removed as a suspension in methylene chloride. Crystallization from methanol gave 2.278 g. of fine, white needles which melted at 279-282° (sintering at 276°). A second recrystallization gave a value of 281-282°, and was used for the analysis. Trityl phosphonic acid melts at 283° by one source (60).

Anal. Found: C, 66.03; H, 6.27; P, 8.15.

This analysis does not correspond to any expected product. If chlorine is assumed to be absent (no conclusive test was obtained for it), the analysis provides an empirical formula of $C_{42}H_{45}P_2O_9$. Plate X shows this product's infrared spectrum. In a second experiment the reaction became violently exothermic, decomposition being evident from the darkened reaction mixture.

Attempted Preparation of 3-Phenoxy-7-chloro-2,4-dioxa-3-phospha-bicyclo[3.3.1]nonane, 3-Oxide. Chlorine gas was bubbled for fifteen minutes through a solution of 0.400 g. (0.00250 moles) of the phosphite II dissolved in 25 ml of methylene chloride at 0° (104). The resulting yellow solution was boiled until colorless and then evaporated to dryness. Phenol, 0.235 g. (0.00250 moles), dissolved in 10.5 ml of 0.476 N sodium hydroxide, was added to the residual solid. Solution occurred slowly and upon standing a new precipitate formed. The color of the

mixture changed from yellow to brown. The solid was brought into solution by warming the mixture on a water bath. When cooled, the solution was extracted twice (40 and 25 ml) with methylene chloride to yield 0.518 g. of crude material. Acidification of the reaction mixture with dilute hydrochloric acid and extraction of the solution yielded only 92 mg. of a brown oil from the concentrated extracts. Recrystallization of the solid from methanol and from iso-propyl alcohol provided material of melting point 249-250.5°. Nuclear magnetic resonance studies revealed this product to be the impure tricyclic phosphate, XXXVI.

Attempted Preparation of 3-Benzyl-7-hydroxy-2,4-dioxa-3-phosphabicyclo-[3.3.1]nonane, 3-Oxide. To 1.000 g. (0.00757 moles) of trans-phloroglucitol (XXXV), m.p. 144.0-144.5°, was added 1.516 g. (0.00757 moles) of dimethyl benzylphosphonate (XXXVII), b.p. 100°/ 0.7 mm., in a simple distillation apparatus. The receiver was immersed in an ice bath. After being heated two hours at 65-70° and one hour at 140-145°, the mixture released no major distillate, but only traces of the phosphonate, XXXVII. Removal of XXXVII from the reaction flask produced a residue melting at 140-142.5°, which when admixed with starting material, XXXV, showed no depression of melting point.

A second attempt to prepare the compound by an alternate route was undertaken. To 1.000 g. (0.00757 moles) of XXXVII was added 1.113 g. (0.00897 moles) of trimethyl phosphite in a similar reaction apparatus, the receiver of which was immersed in a dry ice-acetone bath. Nitrogen was passed over the mixture as it was heated for two and a half hours at 80-90°, two hours at 100-118°, and two hours at 140-145°. The crude intermediate methyl trans-5-hydroxy-1,3-cyclohexylidene phosphite was obtained in an apparently high yield (1.451 g.; 99 per cent). Some liquid

was found in the dry ice-acetone trap. No further characterization except its refractive index, $n_D^{28.5°}$ 1.3367 (methanol, ca. $n_D^{28.5°}$ 1.326), was recorded for this substance. The crude bicyclic phosphite was heated with 0.932 g. (0.00736 moles) of benzyl chloride for twenty-four hours at 110° (104). The resulting semi-solid was dissolved in methylene chloride, but attempts at recrystallization from various organic solvents produced only an intractable oil.

Plate I

Phloroglucinol (XXXIII), Nujol mull.

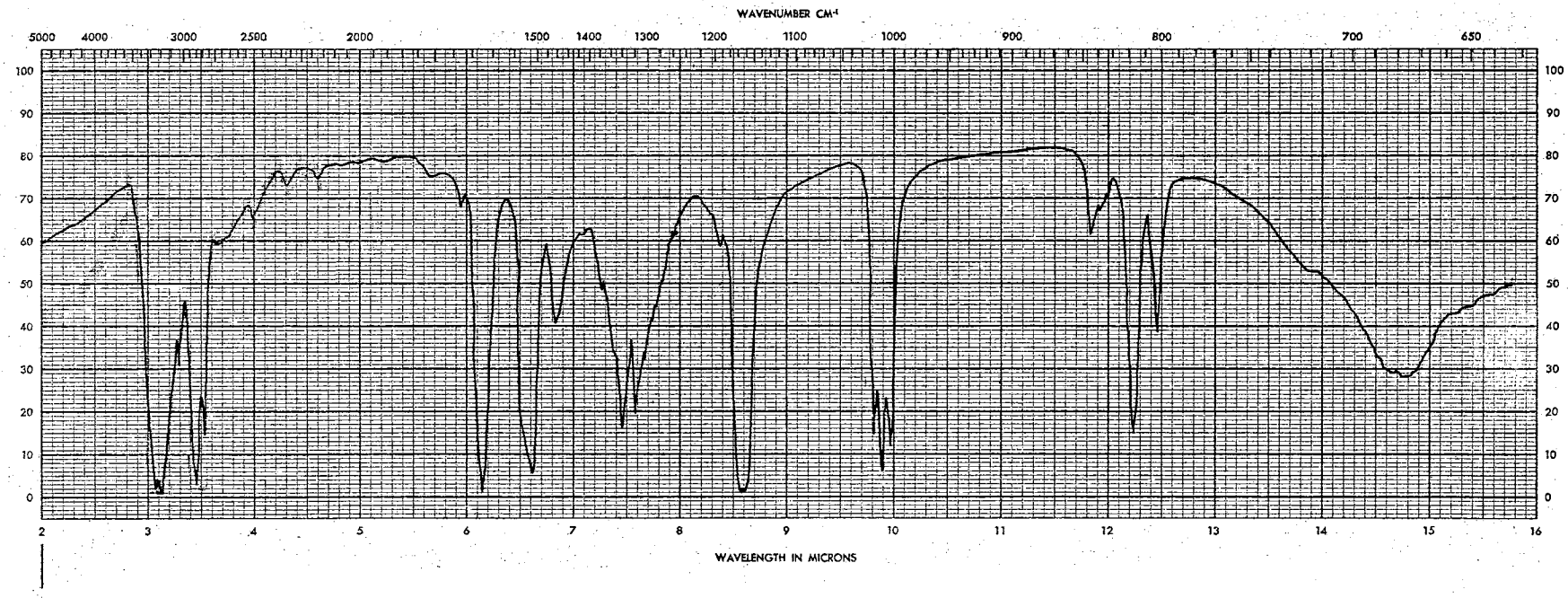


Plate II

<u>cis</u>-Phloroglucitol (XXXIV), 1 mg. in 502.4 mg. KBr.

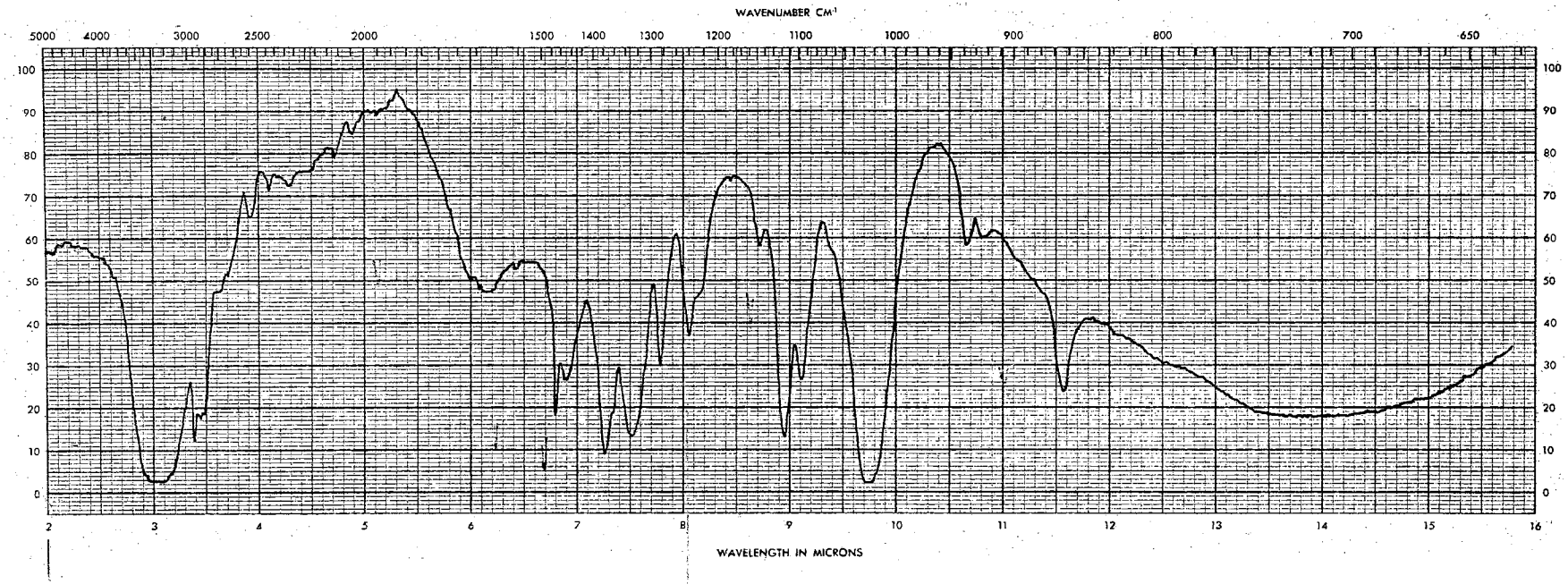


Plate III

trans-Phloroglucitol (XXXV), 1 mg. in 300 mg. KBr.

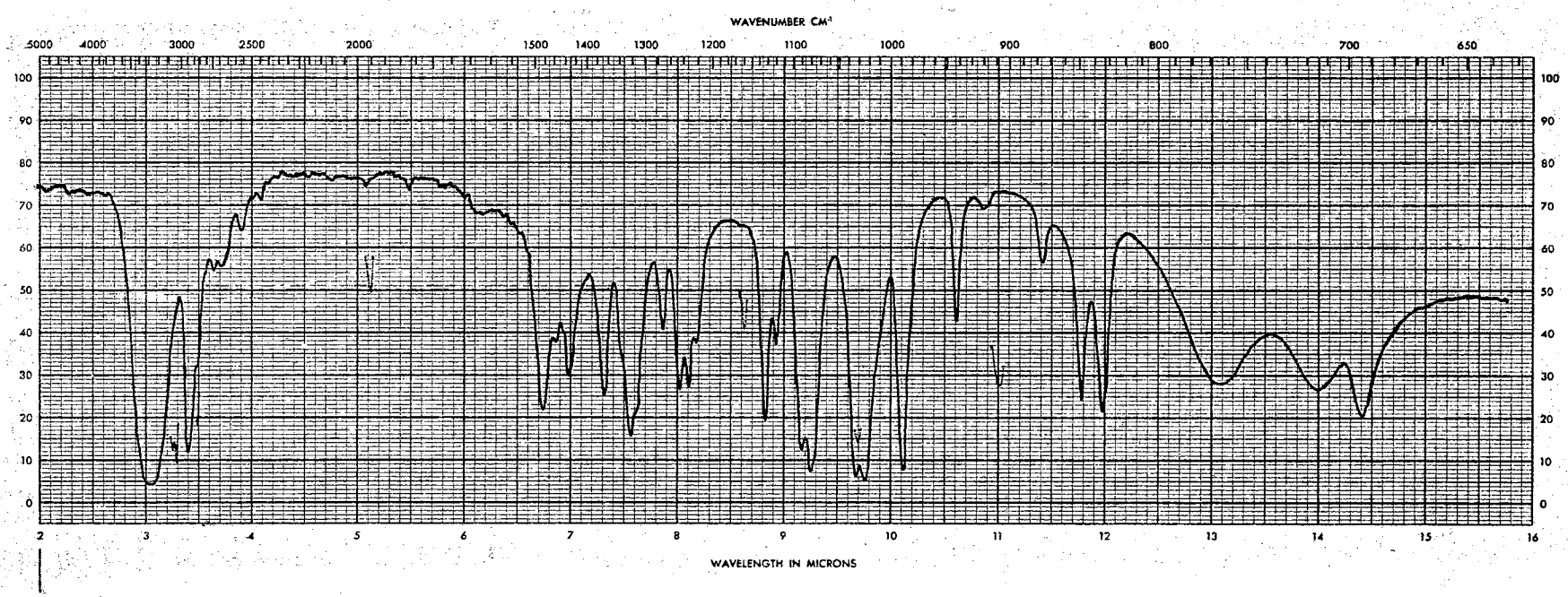


Plate IV

1-Phospha-2,8,9-trioxaadamantane (II), 1 mg. in 302.5 mg. KBr.

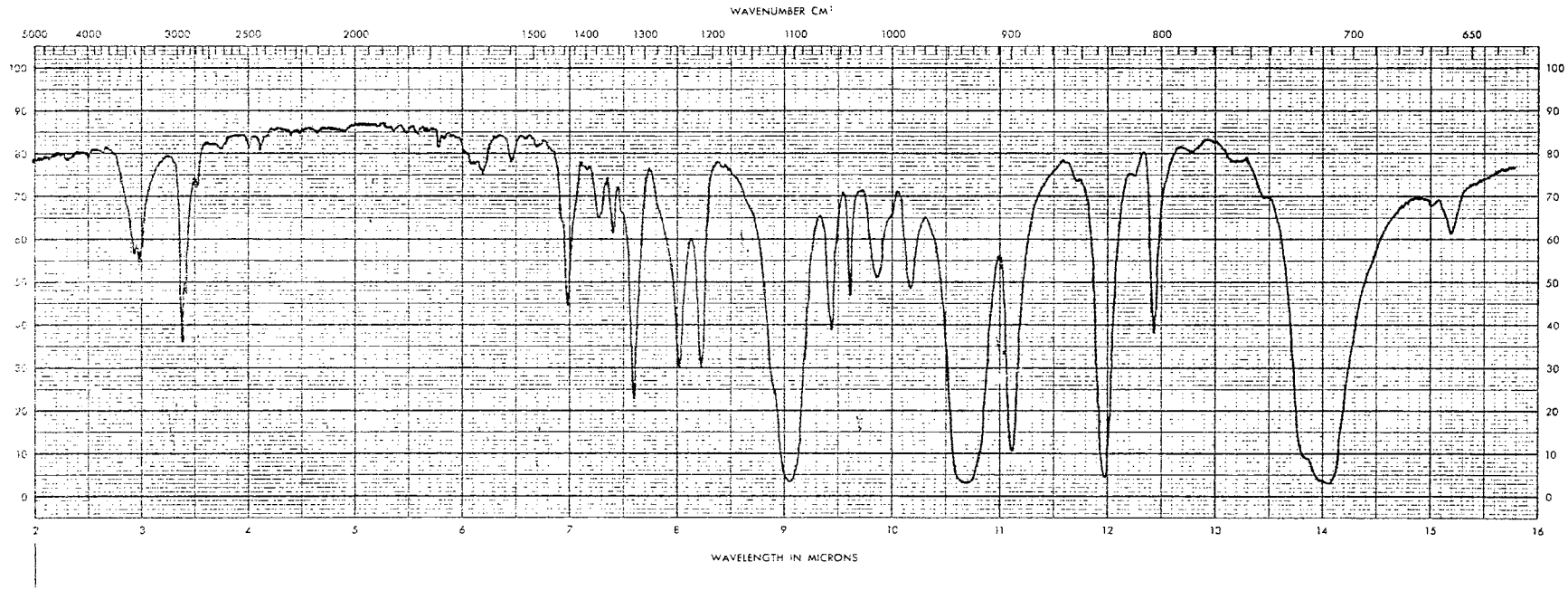


Plate V

1-Phospha-2,8,9-trioxaadamantane, 1-Oxide (XXXVI), 1 mg. in 300 mg. KBr.

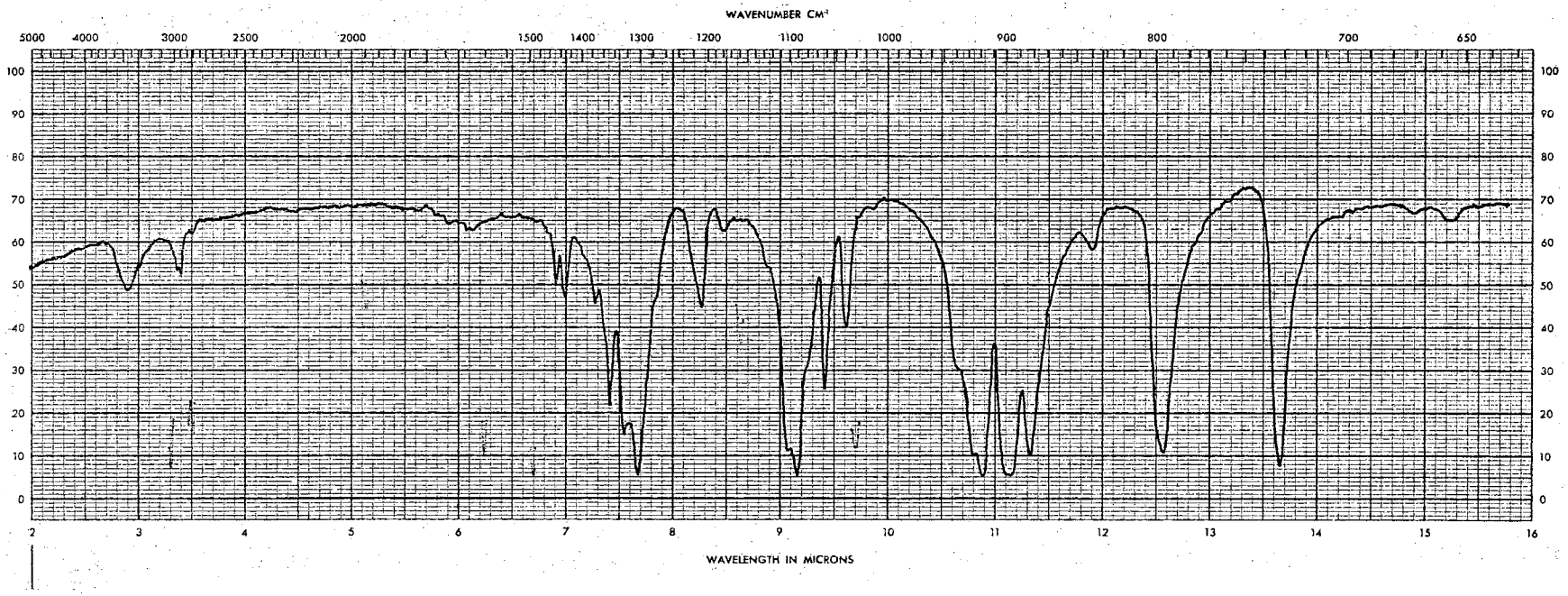


Plate VI

3-Benzyl-7-chloro-2,4-dioxa-3-phosphabicyclo [3.3.1] nonane, 3-Oxide (XXX),
1 mg. in 301.2 mg. KBr.

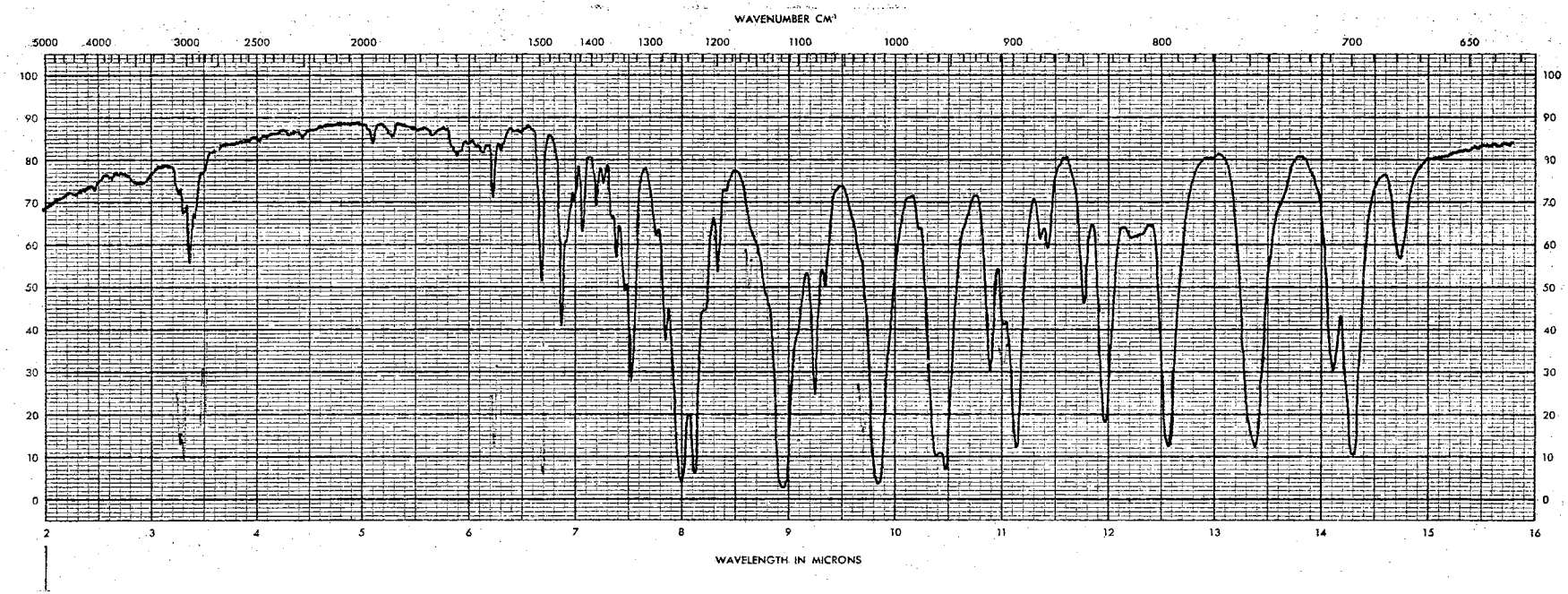


Plate VII

3-(1-Naphthylmethyl)-7-chloro-2,4-dioxa-3-phosphabicyclo [3.3.1.] nonane, 3-Oxide (XXXI), 1.3 mg. in 302.2 mg. KBr.

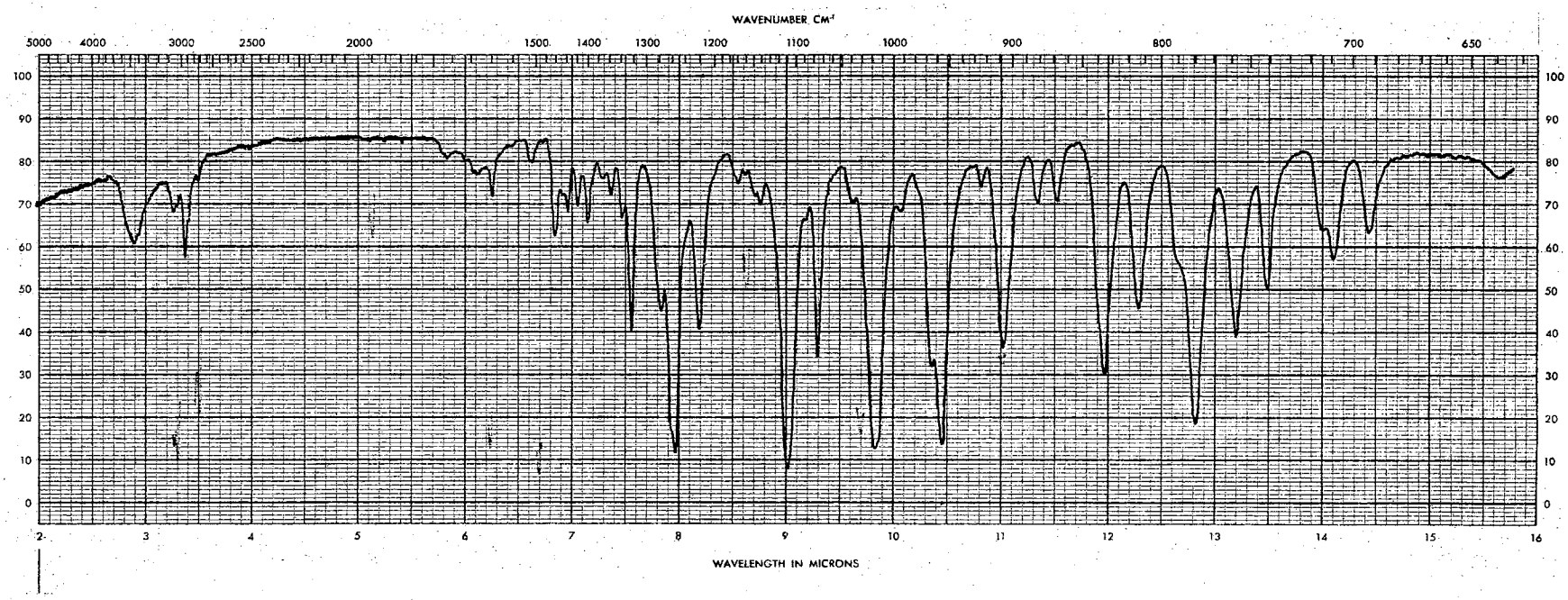


Plate VIII

3-Benzhydryl-7-chloro-2,4-dioxa-3-phosphabicyclo[3.3.1] nonane, 3-Oxide (XXX),
1 mg. in 299.5 mg. KBr.

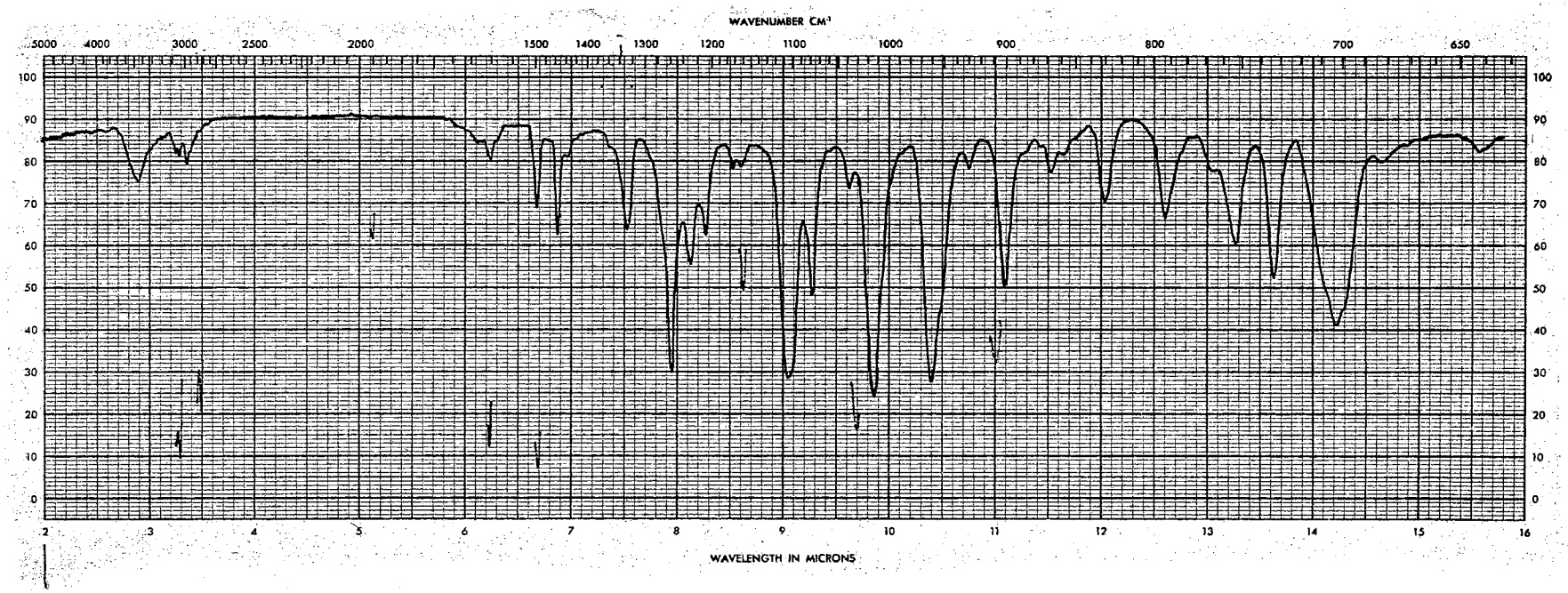


Plate IX

Dimethyl Benzylphosphonate (XXXVII), Film on NaCl cells.

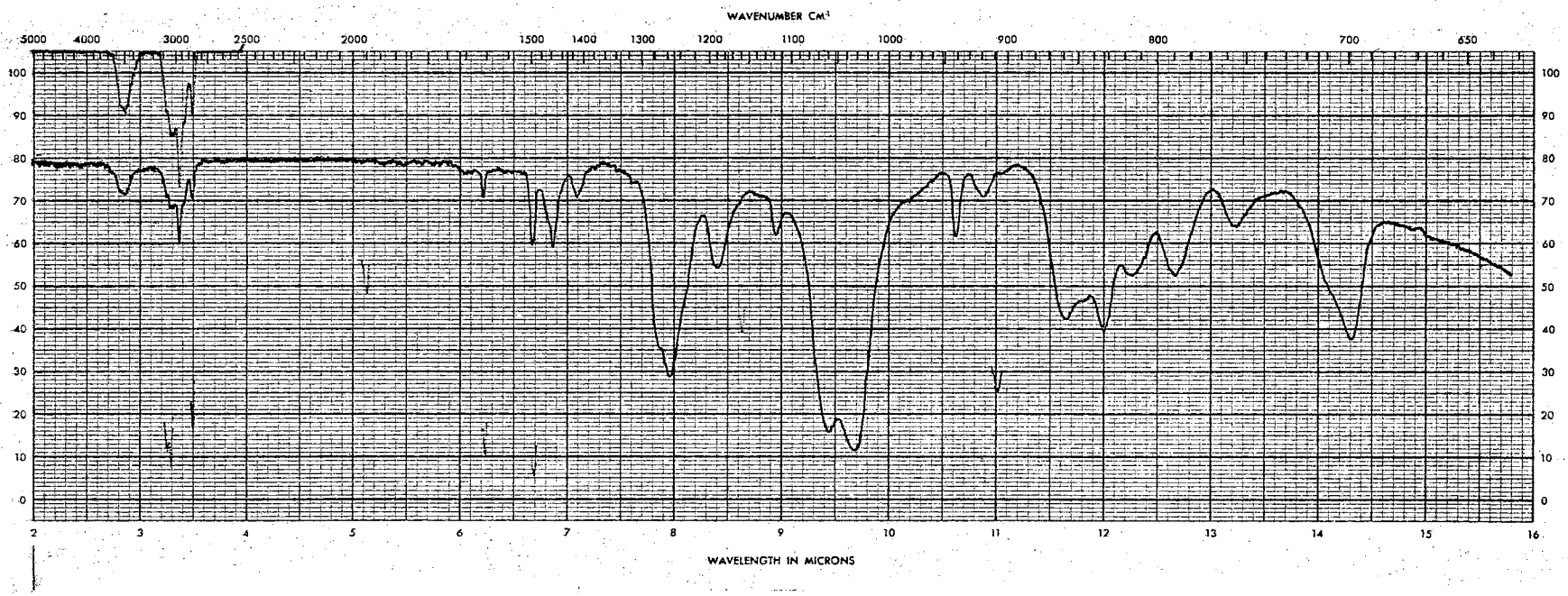


Plate X

Trityl Chloride Reaction Product, 1.5 mg. in 302 mg. KBr.

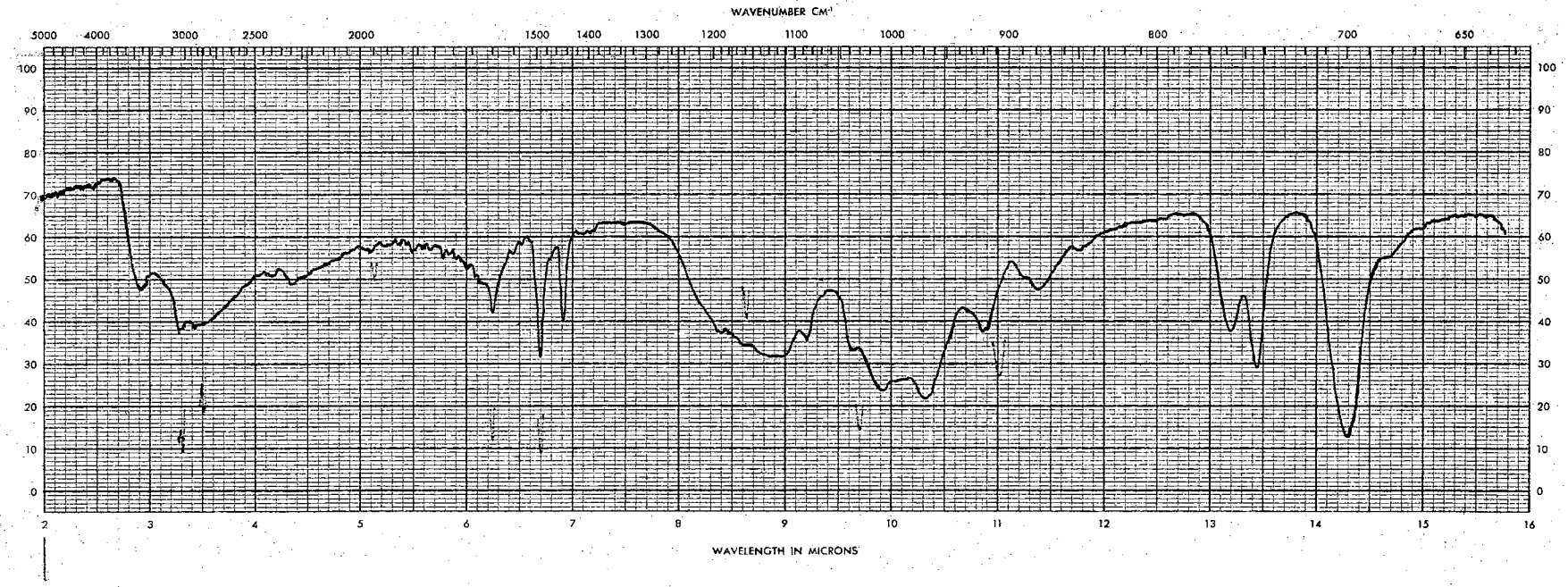


Plate XI

Acidic Hydrolysis Product, 1 mg. in 298.3 mg. KBr.

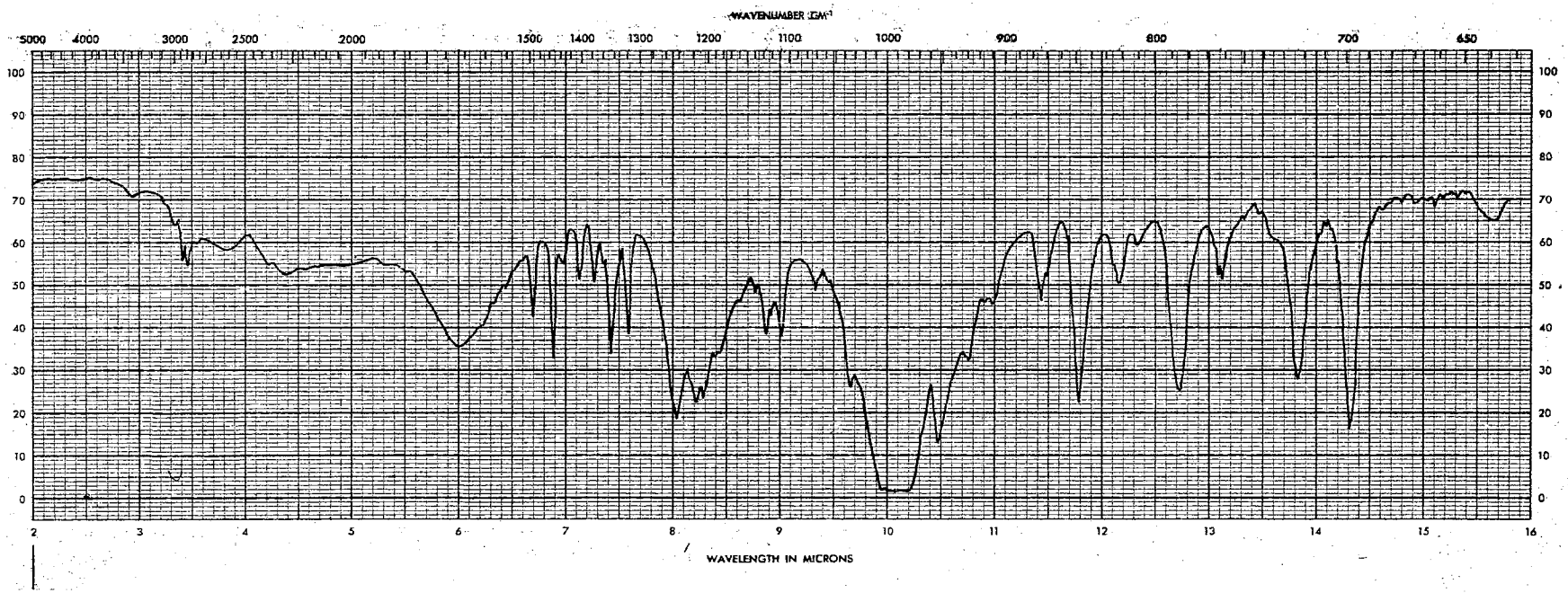


Plate XII

Dimethyl Benzylphosphonate (XXXVII).

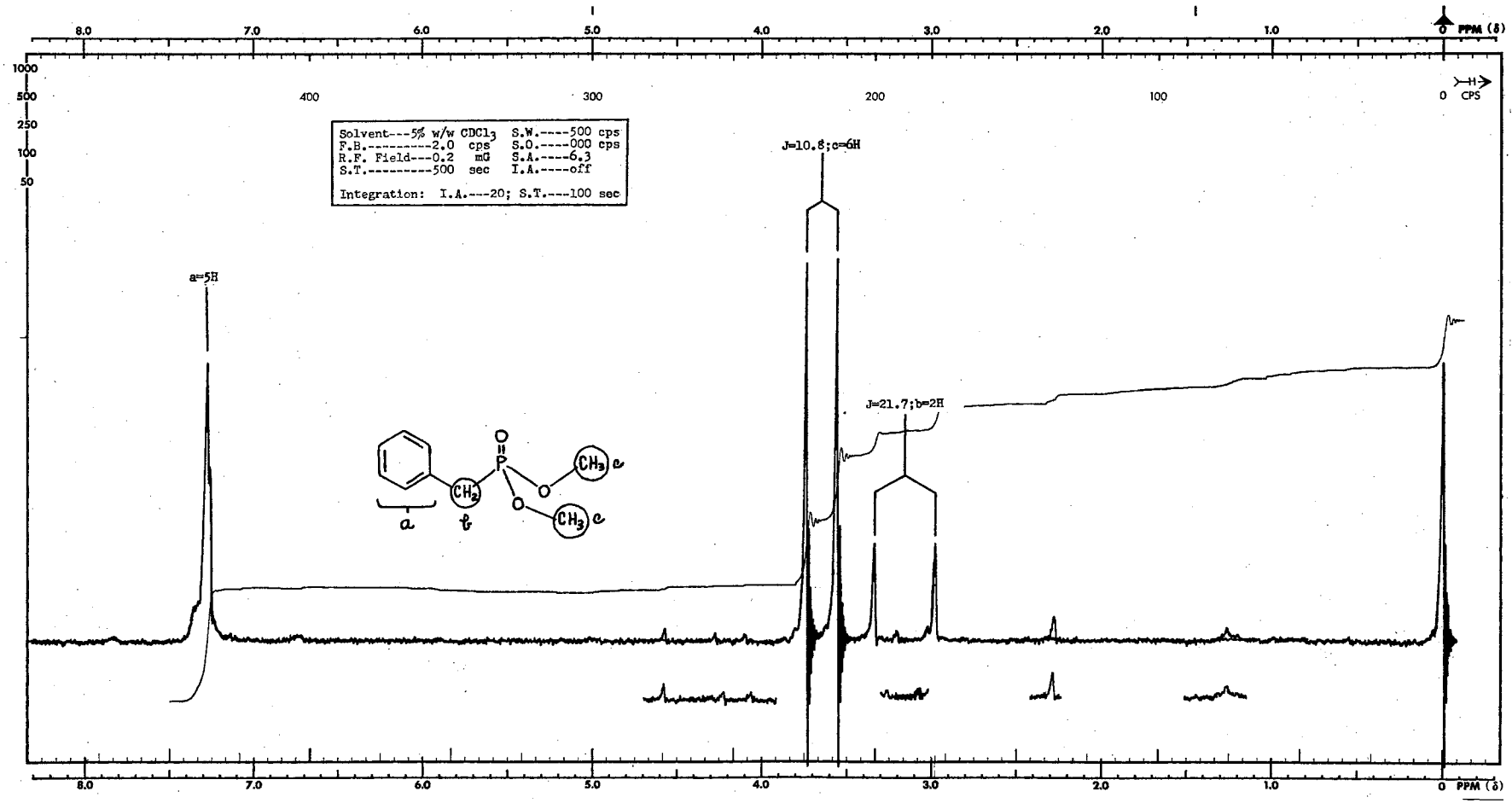


Plate XIII

1-Phospha-2,8,9-trioxaadamantane (II).

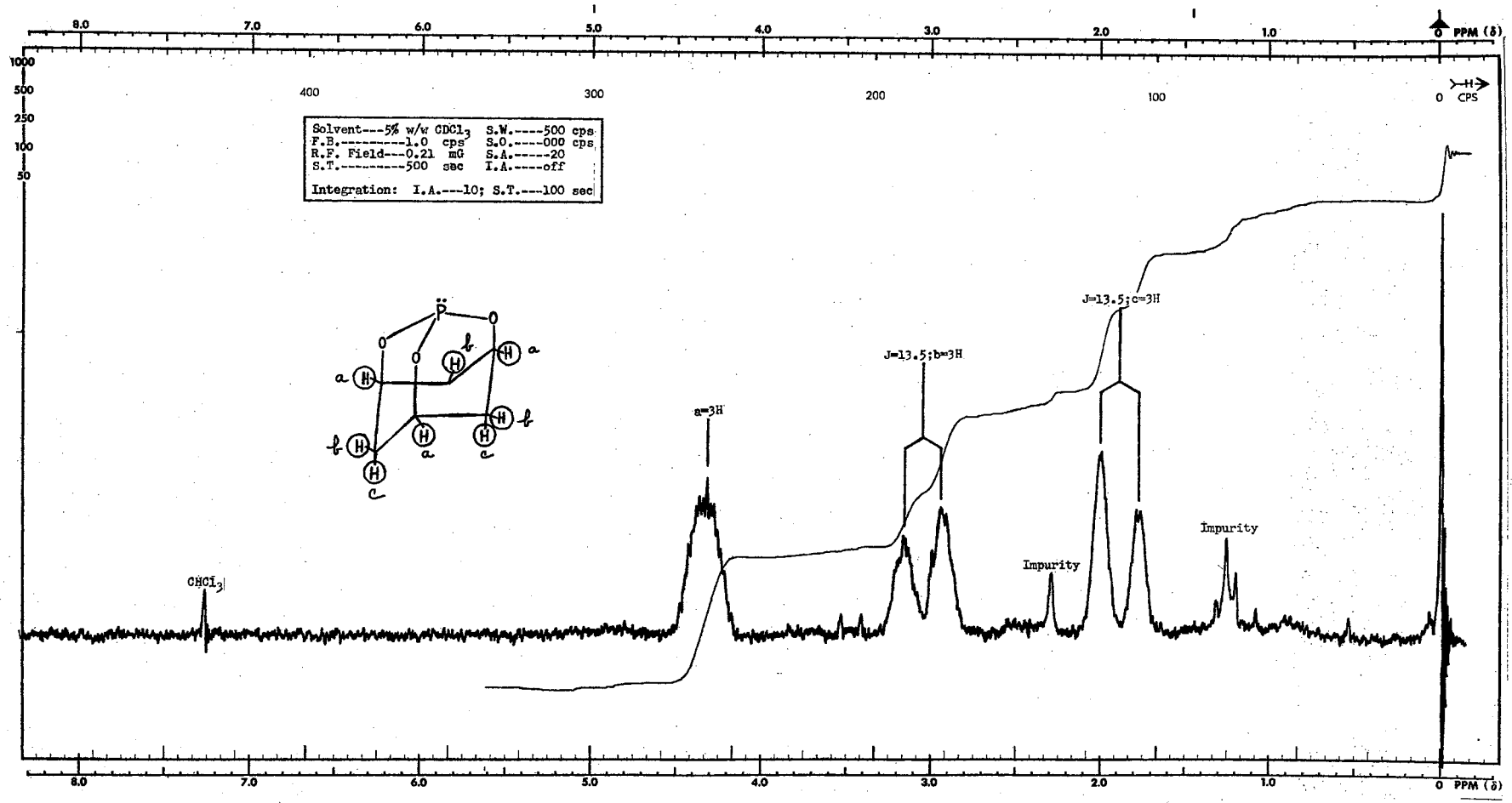


Plate XIV

1-Phospha-2,8,9-trioxaadamantane, 1-Oxide (XXXVI).

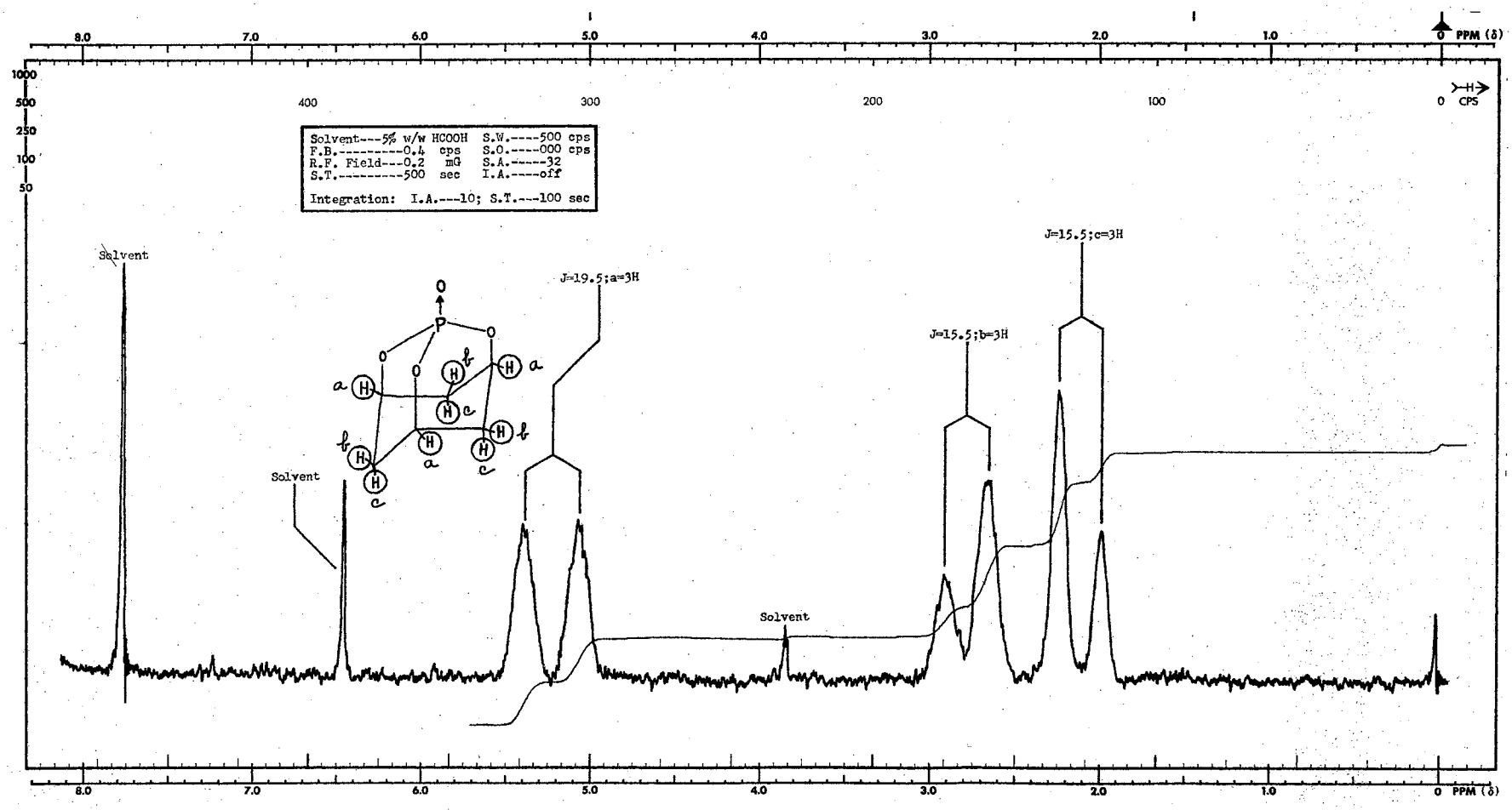


Plate XV

3-Benzyl-7-chloro-2,4-dioxa-3-phosphabicyclo [3.3.1] nonane, 3-Oxide (XXX).

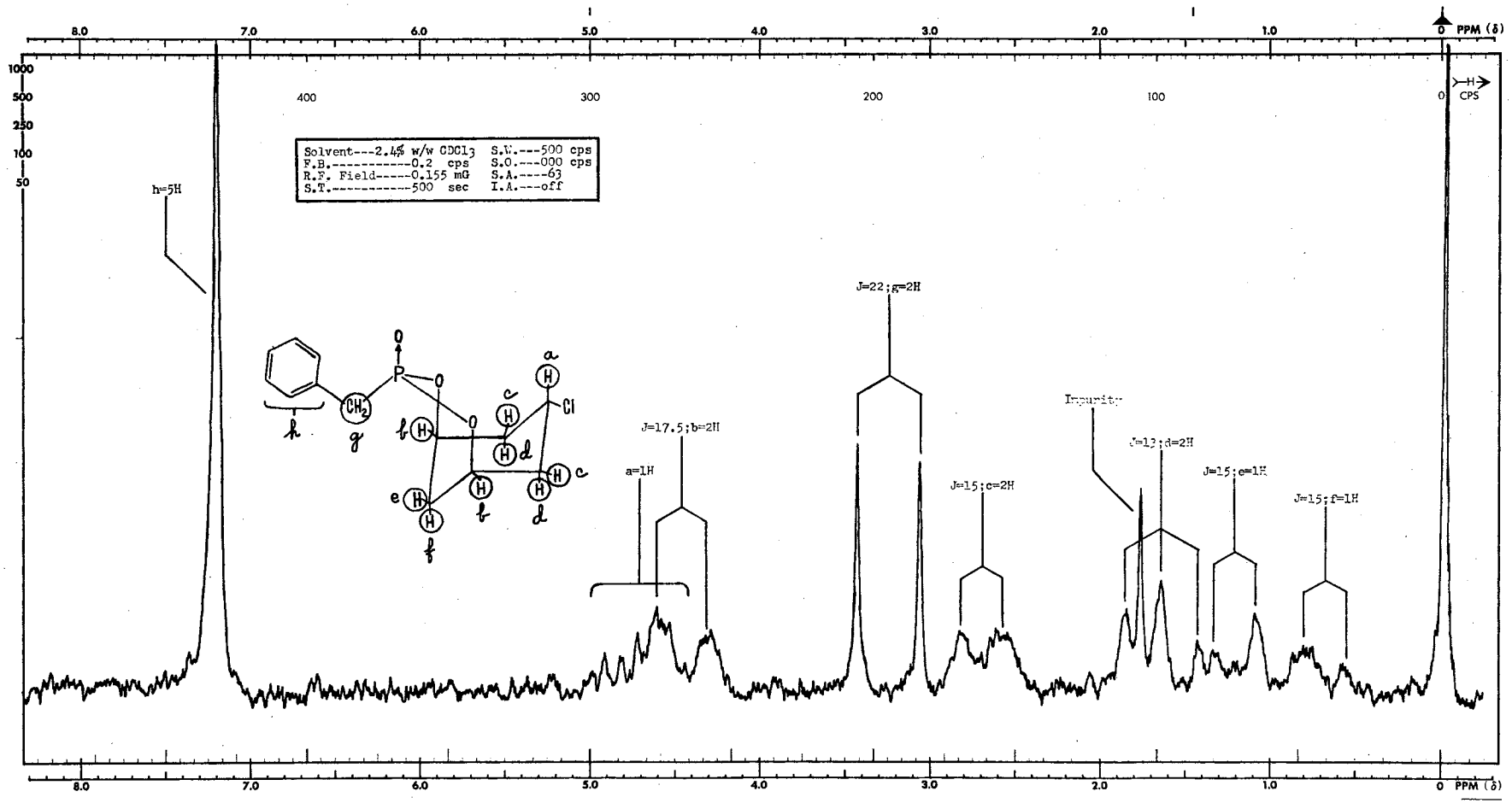


Plate XVI

3-Benzyl-7-chloro-2,4-dioxa-3-phosphabicyclo [3.3.1] nonane, 3-Oxide (XXX).

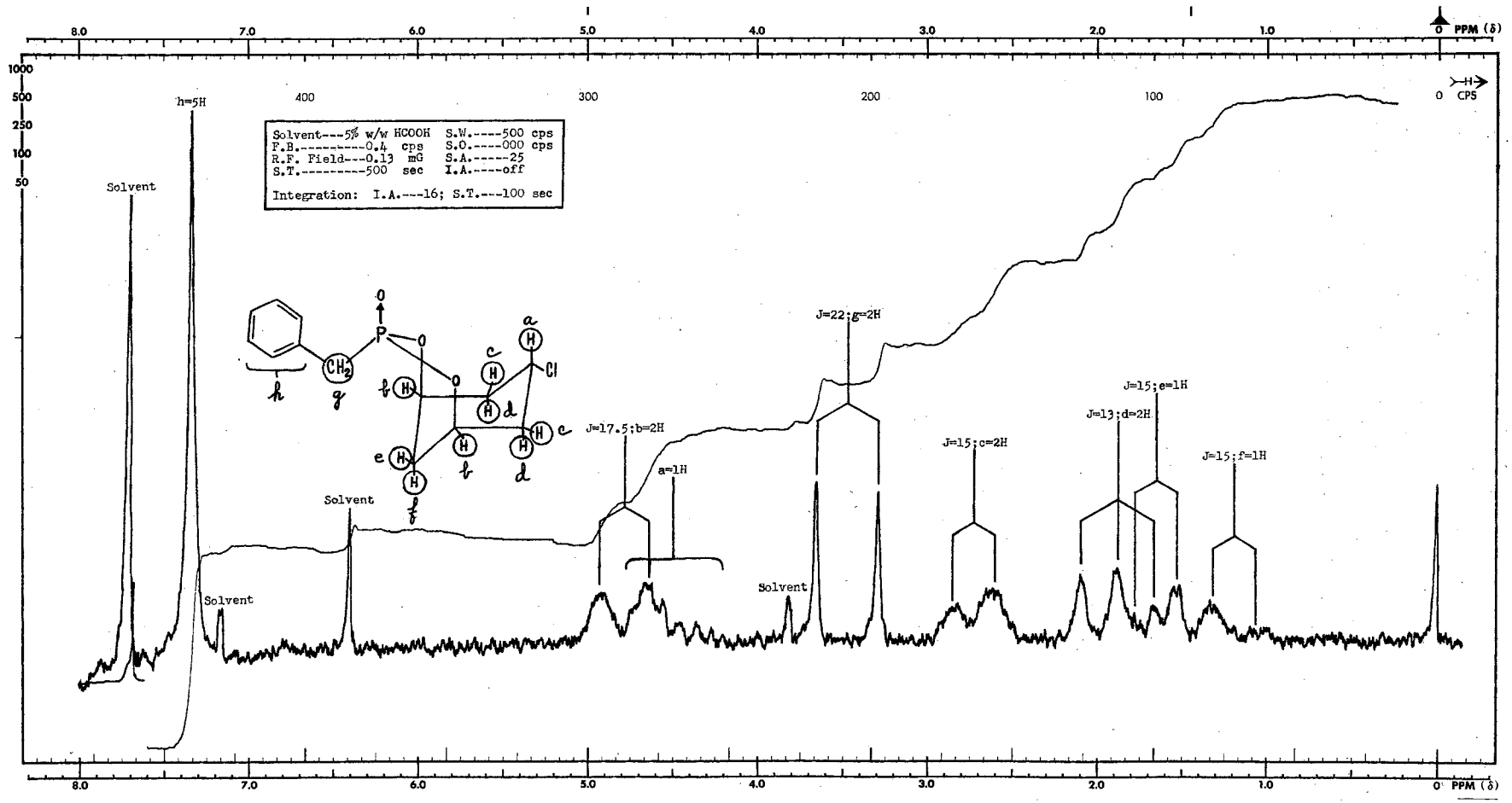


Plate XVII

3-(1-Naphthylmethyl)-7-chloro-2,4-dioxa-3-phosphabicyclo [3.3.1] nonane, 3-Oxide (XXXI).

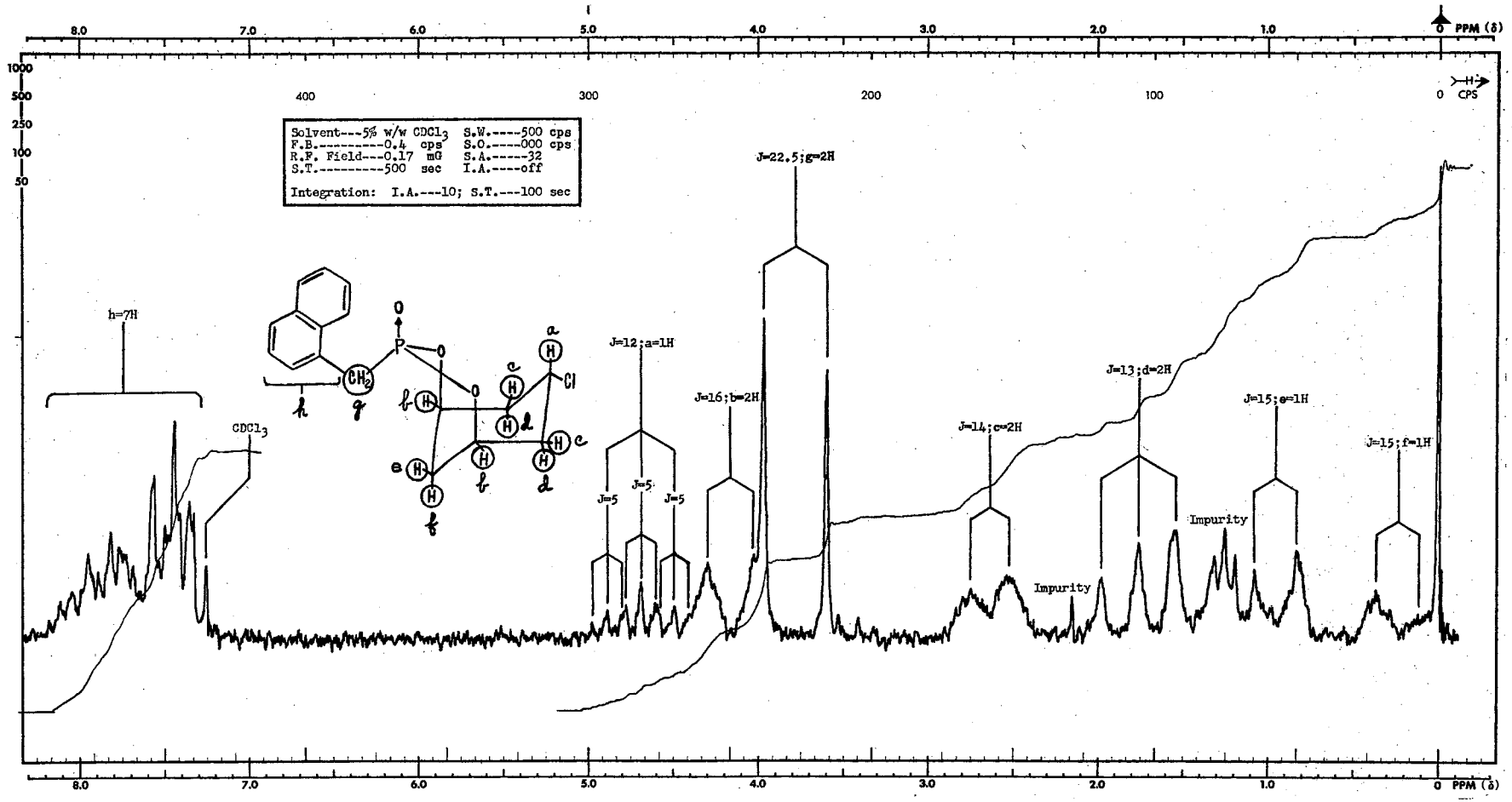


Plate XVIII

3-(1-Naphthylmetyl)-7-chloro-2,4-dioxa-3-phosphabicyclo [3.3.1] nonane, 3-Oxide (XXXI).

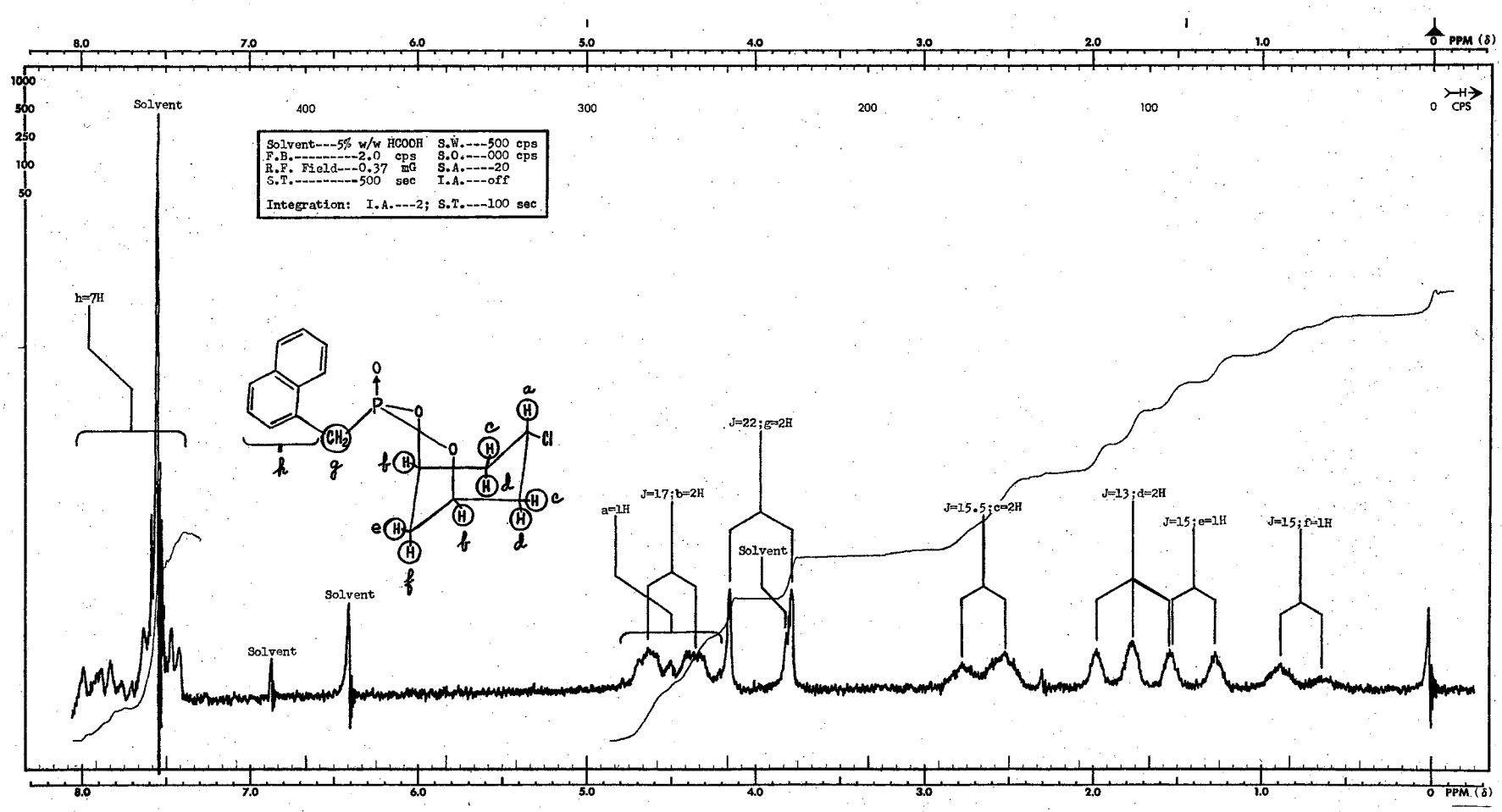


Plate XIX

3-Benzhydryl-7-chloro-2,4-dioxa-3-phosphabicyclo [3.3.1] nonane, 3-Oxide (XXXII).

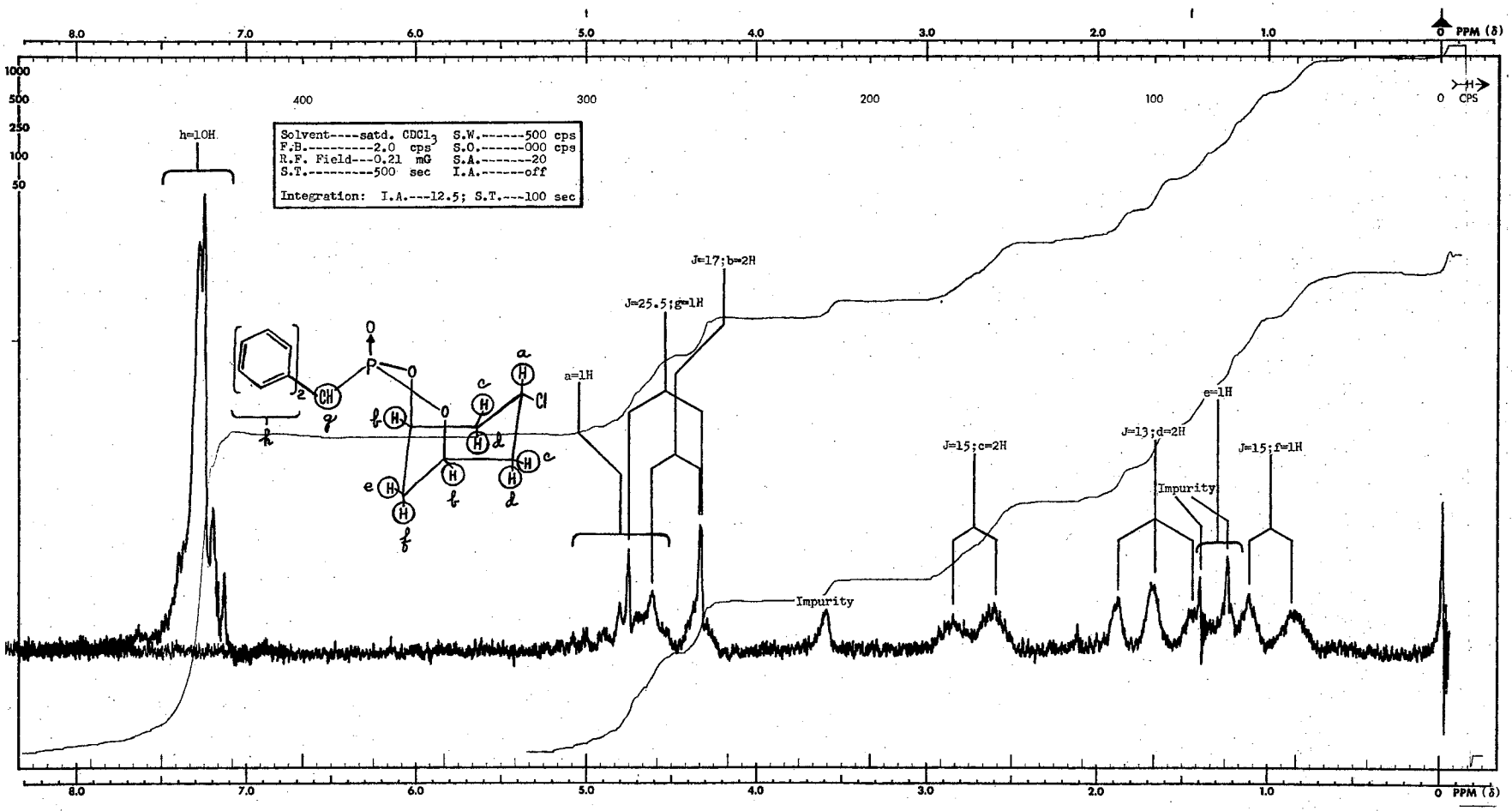


Plate XX

3-Benzhydryl-7-chloro-2,4-dioxa-3-phosphabicyclo [3.3.1] nonane, 3-Oxide (XXXII).

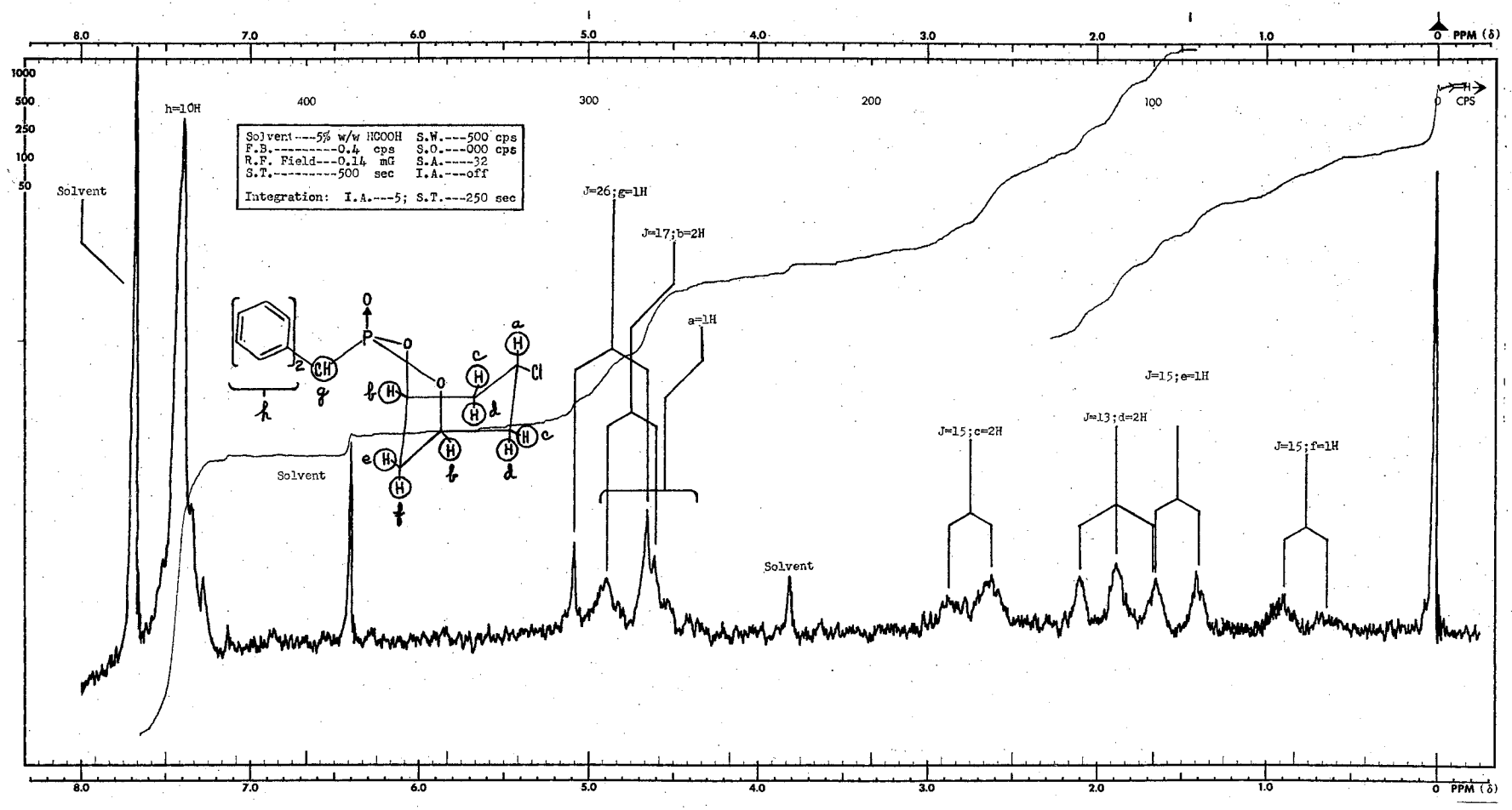


Plate XXI

Nuclear Magnetic Resonance of XXX at 100 Mc.

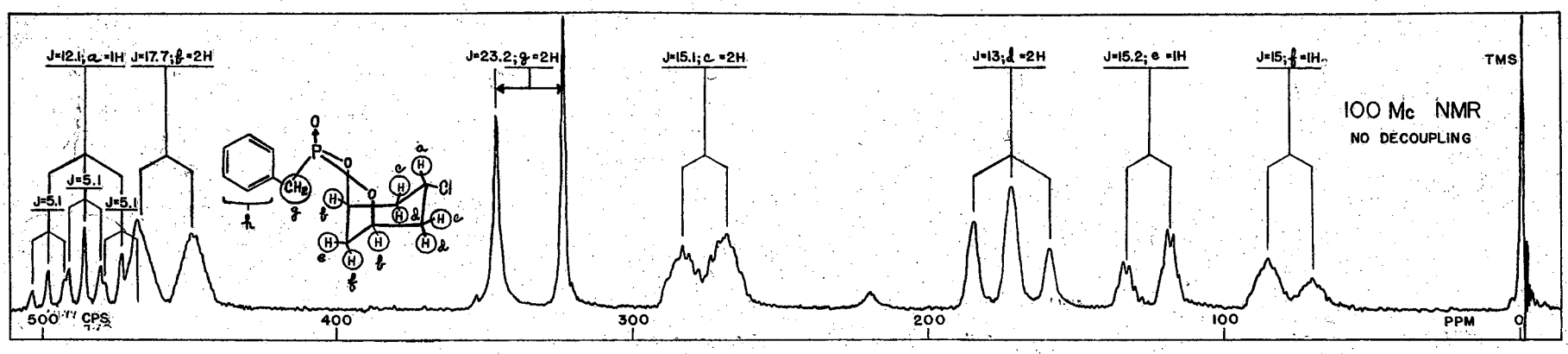
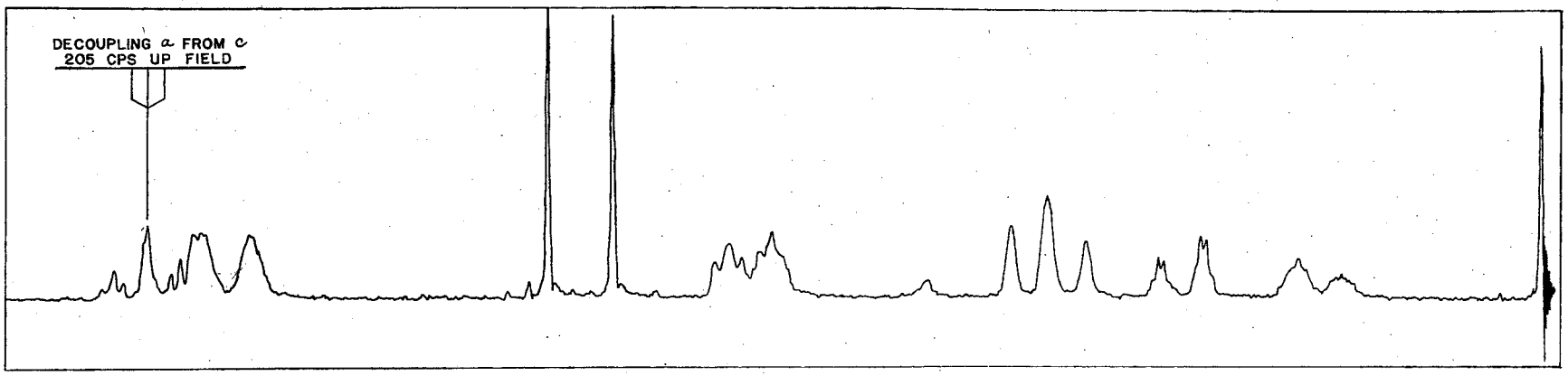
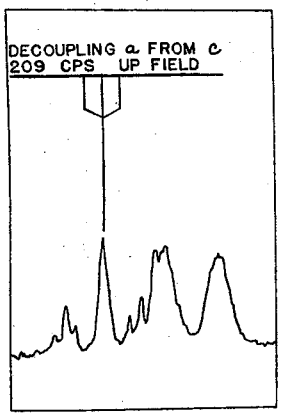
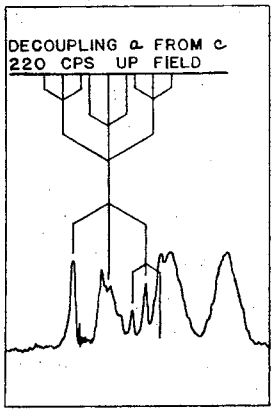


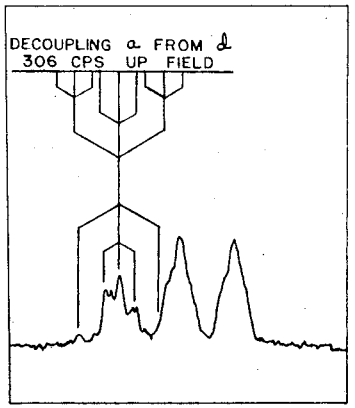
Plate XXII

Decoupling Spectra of XXX at 100 Mc.









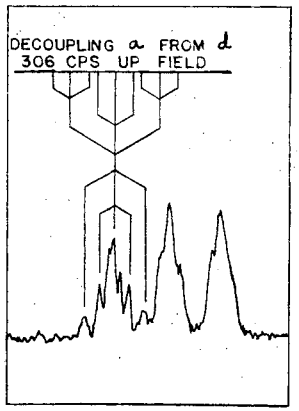
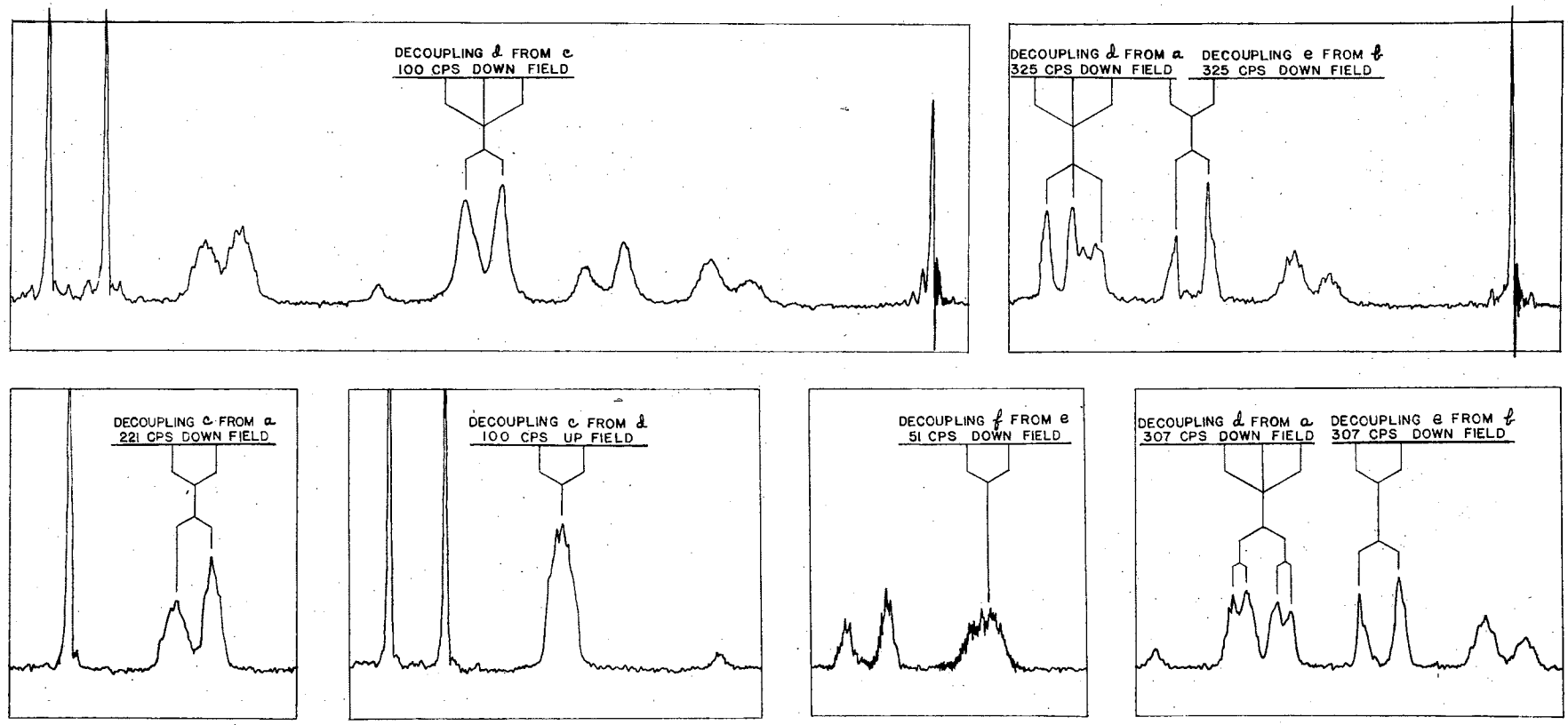


Plate XXIII

Decoupling Spectra of XXX at 100 Mc.



BIBLIOGRAPHY

1. Aksnes, G., Acta Chem. Scand., 14, 1475 (1960).

2. Aksnes, G. and Gramstad, T., Acta. Chem. Scand., 14, 1485 (1960).

3. Anderson, P. and Hassel, O., Acta. Chem. Scand., 2, 527 (1948).

4. Angyal, S. J. and Mills, J. A., Rev. Pure Appl. Chem., 2, 185 (1952).

5. Arbuzov, A. E., J. Russ. Phys. Chem. Soc., 38, 687 (1906); Chem. Zentr., 77, II, 1639 (1906).

6. Arbuzov, A. E. and Nesterov, L. V., Doklady Akad. Nauk S.S.S.R., 92, 57 (1953); C. A. 48, 10538b (1954).

7. Arbuzov, A. E. and Nesterov, L. V., Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, 1954, 427; C. A. 49, 9541b (1955).

8. Arbuzov, A. E. and Sazonova, N. N., Doklady Akad. Nauk S.S.S.R., 115, 1119 (1957); C. A. 52, 6239f (1958).

9. Arbuzov, A. E., Zoroastrova, V. M., and Rizpolozhenskii, N. I., Bull. acad. Sci. U.S.S.R., classe sci. chim., 1948, 208; C. A. 42, 4932g (1948).

10. Arbuzov, B. A., and Shavska-Tolkacheva, T. G., Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, 1954, 812; C. A. 49, 4352d (1955).

11. Arbuzov, B. A., Zoroastrova, V. M., and Saikina, M. K., Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, 1959, 1579; C. A., 54, 8619i (1960).

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

13. Ayres, D. C. and Rydon, H. N., J. Chem. Soc., 1957, 1109.

14. Baddiley, J., Buchanan, J. G., and Szabo, L., J. Chem. Soc., 1954, 3826.

15. Bailly, O. and Gaume, J., Bull. Soc., Chim. France, 2, 254 (1935); 3, 1396 (1936); Compt. Rend., 199, 793 (1934).

16. Barnard, P. W. C., Bunton, C. C., Llewellyn, D. R., Vernon, C. A., and Welch, V. A., J. Chem. Soc., 1961, 2670.

17. Barnes, R. A. and Hoffmann, F. W., Unpublished results, quoted by Wadsworth, W. S. and Emmons, W. D., J. Am. Chem. Soc., 84, 610 (1962).

18. Barton, D. H. R., J. Chem. Soc., 1953, 1027.

19. Bellamy, L. J., "Infrared Spectra of Complex Molecules", J. Wiley and Sons, Inc., New York, 1958.

20. Billica, H. R. and Adkins, H., Org. Syn., Coll. Vol. III, J. Wiley and Sons, Inc., New York, 1955, 179.

21. Brown, D. M., Dekker, C. A., and Todd, A. R., J. Chem. Soc., 1952, 2715.

22. Brown, D. M., Hall, G. E., and Higson, H. M., J. Chem. Soc., 1958, 1360.

23. Brown, D. M. and Higson, H. M., J. Chem. Soc., 1957, 2034.

24. Brown, D. M., Magrath, D. I., and Todd, A. R., J. Chem. Soc., 1952, 2708.

25. Brown, D. M. and Todd, A. R., J. Chem. Soc., 1952, 52.

26. Brown, T. L., Verkade, J. G., and Piper, T. S., J. Phys. Chem., 65, 2051 (1961).

27. Cadogen, J. I. G., Quart. Revs. (London), 16, 208 (1962).

28. Cason, J. and Baxter, W. N., J. Org. Chem., 23, 1302 (1958).

29. Cason, J., Baxter, W. N., and DeAcetis, W., J. Org. Chem., 24, 2479 (1959).

30. Cox, Jr., J. R., Wall, R. E., and Westheimer, F. H., Chem. & Ind. (London), 929 (1959).

31. Daasch, L. W. and Smith, D. C., Anal. Chem., 23, 853 (1951); N.R.L. Report 3657.

32. Dkarmatti, S. S., Govil, G., Kanekar, C. R., and Virmani, Y. P., Arch. Sci. (Geneva), 13, Spec. No., 479 (1960).

33. Dudek, G. O., J. Chem. Phys., 33, 624 (1960).

34. Eliel, E. L., "Stereochemistry of Carbon Compounds", McGraw-Hill Co., Inc., New York, 1962.

35. Finegold, H., Ann. New York Acad. Sci., 70, 875 (1958).

36. Forrest, H. S., Mason, H. S., and Todd, A. R., J. Chem. Soc., 1952, 2530.

37. Fredga, A., Svensk Kem. Tidskr., 72, 151 (1960).

38. Furberg, S., Acta. Chem. Scand., 9, 1557 (1955).

39. Garner, A. Y., Chapin, E. C., and Scanlon, P. M., J. Org. Chem., 24, 532 (1959).

40. Geddes, A. L., J. Chem. Phys., 58, 1062 (1954).

41. Gerrard, W. and Green, W. J., J. Chem. Soc., 1957, 2550.

42. Gerrard, W. and Jeacocke, G. J., J. Chem. Soc., 1954, 3647.

43. Gieger, C. F., Private Communication, Ontario, California, 1962.

44. Greene, F. D., Chu, C. C., and Walia, J., J. Am. Chem. Soc., 84, 2463 (1962).

45. Griffin, C., E, Chem. & Ind., (London), 1058 (1960).

46. Haake, P. C. and Westheimer, F. H., J. Am. Chem. Soc., 83, 1102 (1961).

47. Hanahan, D. J., "Lipide Chemistry", J. Wiley Sons, Inc., New York, 1960.

48. Harwood, H. J. and Grisley, D. W., J. Am. Chem. Soc., 82, 423 (1960).

49. Hawthorne, J. N., J. Lipid Res., 1, 255 (1960).

50. Heitsch, C. W. and Verkade, J. G., J. Inorg. Chem., 1, 392 (1962).

51. Hoffmann, F. W., Ess, R. J., and Usinger, R. P., J. Am. Chem. Soc., 78, 5817 (1956).

52. Holmstedt, B., Pharmacol. Rev., 11, 567 (1959).

53. Huitric, A. C. and Trager, W. F., J. Org. Chem., 27, 1926 (1962).

54. Jackman, L. M., "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", Pergamon Press, New York, 1959.

55. Jones, R. A. Y. and Katritzky, A. R., J. Chem. Soc., 1960, 4376.

56. Jones, R. A. Y. and Katritzky, A. R., Angew. Chem. (Internat. Edit.), 1, 32 (1962).

57. Khorana, H. G., "Some Recent Developments in the Chemistry of Phosphate Esters of Biological Interest", J. Wiley and Sons, Inc., 1961, chap. 3.

58. Khorana, H. G., Tener, G. M., Wright, R. S., and Moffatt, J. G., J. Am. Chem. Soc., 79, 430 (1957).

59. Korshak, V. V., Gribova, I. A., and Andreeva, M. A., Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk, 1957, 631; C. A. 51, 14621g (1957).

60. Kosolapoff, G. M., "Organophosphorus Compounds", J. Wiley and Sons, Inc., New York, 1950.

61. Kosolapoff, G. M., J. Chem. Soc., 1954, 3222.

62. Kosolapoff, G. M., J. Chem. Soc., 1955, 3092.

63. Kumanoto, J., Cox, jr., J. R., and Westheimer, F. H., J. Am. Chem. Soc., 78, 4858 (1956).

64. Landa, S. and Machacek, V., Coll. Cz. Chem. Comm., 5, 1 (1933).

65. Landauer, S. R. and Ryson, H. N., Chem. & Ind. (London), 313 (1951).

66. Lanham, W. M., U. S. Patent 2,910,499 (1959); Brit. Patent 819,424 (1959); C. A., 54, 13149d (1960).

67. Laughlin, R. G., J. Org. Chem., 27, 1005 (1962).

68. Larnandie, M., Compt. Rend., 235, 154 (1952); 236, 909 (1953).

69. Lemanceau, B., Lussan, C., and Souty, N., J. Chem. Phys., 59, 148 (1962).

70. Lucas, H. J., Mitchell, F. W., and Scully, C. N., J. Am. Chem. Soc., 72, 5491 (1950).

71. Mair, B. J., Shamaiengar, M., Krouskop, N. C., and Rossini, F. D., Anal. Chem., 31, 2082 (1954).

72. de la Mare, P. B. D., Klyne, W., Miller, D. J., Pritchard, J. G., and Watson, D., J. Chem. Soc., 1956, 1813.

73. Markham, R. and Smith, J. D., Biochem. J., 52, 552 (1952).

74. Mavel, G. and Martin, G., Compt. Rend., 252, 110 (1961).

75. McConnell, R. L. and Coover, H. W., J. Org. Chem., 24, 630 (1959).

76. McKinney, C., Private Communication, Continental Oil Co., Ponca City, Oklahoma, 1962.

77. Michaelis, A. and Kahne, R., Chem. Ber., 31, 1048 (1898).

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

79. Milobenzki, T. and Szulgin, K., Chemik Polski, 15, 66 (1917); C. A. 13, 2867 (1919).

80. Myers, T. C., Preis, S., and Jensen, E. V., J. Am. Chem. Soc., 76, 4172 (1954).

81. Neunhoeffer, O. and Maiwald, W., Chem. Ber., 95, 108 (1962).

82. Nowacki, W., Helv. Chim. Acta., 28, 1233 (1945).

83. O'Brien, R. D., "Toxic Phosphorus Esters, Chemistry, Metabolism, and Biological Effects", Academic Press, New York, 1960.

84. Orloff, H. D., Chem. Revs., 54, 347 (1954).

85. Oswald, A. A., Can. J. Chem., 37, 1498 (1959).

86. Pischimulka, P., Chem. Ber., 41, 3854 (1908); J. Russ. Phys. Chem. Soc., 44, 1406 (1912); C. A. 7, 987 (1913).

87. Popov, E. M., Kabachnik, M. I., and Mayants, L. S., Russ. Chem. Revs. (English Transl.), 1961, 362.

88. Pudovick, A. N., Medvedeva, G. P., and Kochetkova, V. I., Zh. Obshch. Khim., 31, 2650 (1961); C. A. 56, 12722i (1962).

89. Randall, M. M., Fowler, R. G., Fuson, N., and Dangal, J. R., "The Infrared Determination of Organic Structures", D. Van Nostrand Co., Inc., New York, 1949.

90. Rogers, M. T., Private Communication, Michigan State University, East Lansing, Michigan, 1962.

91. Shoolery, J. N., Pier, E., and Johnson, L., Private Communication, Varian Associates, Palo Alto, California, 1962.

92. Shuler, W. E. and Axtmann, R. C., AEC Research and Development Report, DP-474, 1960.

93. Siddall, T. H. and Prohaska, C. A., J. Am. Chem. Soc., 84, 2502 (1962).

94. Smith, G. W., J. Chem. Phys., 35, 1134 (1961).

95. Smyth, C. P., "Dielectric Behavior and Structure", McGraw-Hill Co., Inc., New York, 1955.

96. Stetter, H., Angew. Chem., 66, 217 (1954).

97. Stetter, H., Angew. Chem. (Internat. Edit.), 1, 286 (1962).

98. Stetter, H., and Steinacker, K. H., Chem. Ber., 85, 451 (1952).

99. Stille, J. K., "Introduction to Polymer Chemistry", J. Wiley and Sons, Inc., New York, 1962, chap. 7.

100. Sutton, L. E., Scientific Editor, "Tables of Interatomic Distances and Configuration in Molecules and Ions", Chem. Soc. Spec. Publ. No. 11 (London), 1958.

101. Szabo, P. and Szabo, L., J. Chem. Soc., 1961, 448.

102. Verkade, J. G., Private Communication, Department of Chemistry, Iowa State University, Ames, Iowa, 1962.

103. Verkade, J. G. and Reynolds, L. T., J. Org. Chem., 25, 663 (1960).

104. Wadsworth, W. S. and Emmons, W. D., J. Am. Chem. Soc., 84, 610 (1962).

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