SYNTHESIS AND RESOLUTION OF SELECTED α,ω-ALKANE-DIYLBIS(1,2,3,4-TETRAHYDROPHOSPHINOLINIUM) SALTS. THE USE OF ^{31}P NMR ANALYSIS TO MONITOR THE RESOLUTION

By

NARAYANASAMY GURUSAMY

Bachelor of Science
University of Madras
Madras, India
1968

Master of Science
University of Madras
Madras, India
1970

Submitted to the Faculty of the Graduate College
of the Oklahoma State University
in partial fulfillment of the requirements
for the Degree of
DOCTOR OF PHILOSOPHY
July, 1981

SYNTHESIS AND RESOLUTION OF SELECTED α,ω-ALKANE-DIYLBIS(1,2,3,4-TETRAHYDROPHOSPHINOLINIUM) SALTS. THE USE OF ^{31}P NMR ANALYSIS TO MONITOR THE RESOLUTION

Thesis Approved:

K D Berlin
Thesis Adviser

Horacio A Mottola

Oldon C. Nelson

Warren T. Ford

Norman N Durham
Dean of the Graduate College

ACKNOWLEDGMENTS

With great pleasure and privilege I express my sincere and heartfelt gratitude to Dr. K. D. Berlin for his advice, guidance and encouragement throughout the course of my research, not to mention his invaluable assistance during the preparation of this thesis. I thank the members of my Advisory Committee for having agreed to serve on the Committee. I am indebted to Dr. K. Ramalingam whose help and encouragement made my higher education in this country a dream come true. I express my appreciation to my colleagues in Dr. Berlin's research group (especially Dr. N. Satyamurthy) for their helpful suggestions and companionship.

Thanks are due to the Department of Chemistry at Oklahoma State University and the National Institute of Health for financial support during my graduate tenure.

I thank Professor Dick van der Helm at the University of Oklahoma, for his expertise in obtaining the X-ray data and Mr. Stan Sigle for his help in obtaining the NMR data. A special thank you is due to Mrs. Sue Heil for typing the manuscript.

I am tremendously indebted to my parents, Mr. and Mrs. G. Narayanasamy for their constant love, dedication and spiritual encouragement given so generously to me during these many years. My thanks are due to my paternal uncle, Mr. G. Venugopalsamy Naidu, and all my relatives for all their help. I extend my deepest appreciation

to my wife, Vasantha, for her abiding love, understanding, sacrifices, encouragement and inspiration without which this work would not have been possible. Above all, I wish to dedicate the whole of this work to my beloved sons, Jayakumar and SriHari, for the little things that mean so much to me.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF PLATES

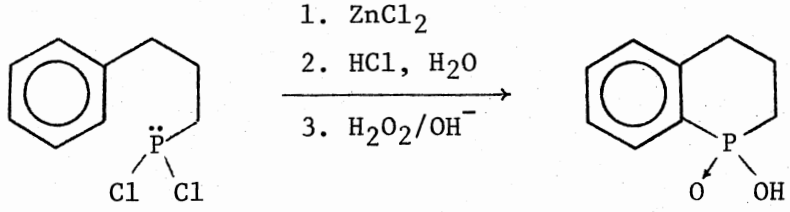
CHAPTER I

HISTORICAL

Recent Developments in the Syntheses and Chemistry of Derivatives of Phosphinolines

The chemistry of polycyclic carbon-phosphorus (C-P) heterocycles is currently an active area under intense development.[112] To date, the most comprehensive review[132] on the chemistry of fused polycyclic C-P heterocycles was published in early 1977 although earlier reviews[9,91,119] had included the very meager data available through 1966. In order to lay a proper foundation for the discussion of our results, a brief survey will be given on recent developments in carbon-phosphorus heterocyclic chemistry.

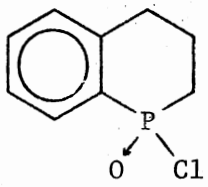
In a recent patent[121] a phosphinoline system was obtained from precursors which underwent phosphorylation on an arene ring. For example, it was shown that 1 treated with a Lewis acid gave a 1,2,3,4-



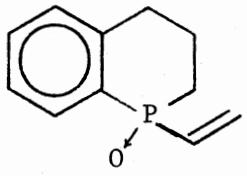
1 2

tetrahydrophosphinoline system 2 (91%). Chlorination of 2 with $SOCl_2$

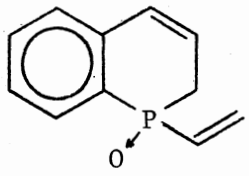
produced the 1-chloro derivative 3 which, upon reaction with vinylmagnesium bromide, led to the P-vinyl derivative 4 (74%), the key



3

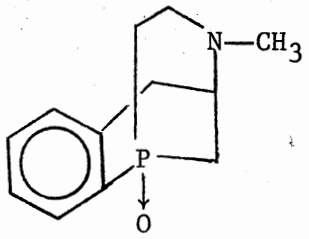


4

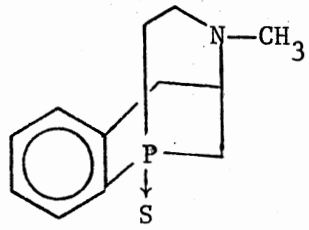


5

precursor to the P-analogs of benzomorphan analgestics. Bromination of 4 with N-bromosuccinimide (NBS) followed by heating the solution in DMF gave 5 (90%) which underwent cyclization with methylamine to give 6 (77%). Reduction of 6 with trichlorosilane followed by



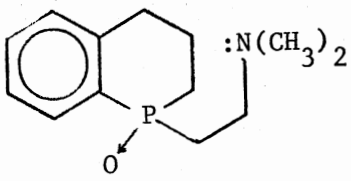
6



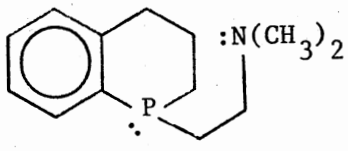
7

addition of sulfur resulted in formation of phosphine sulfide 7 (82%).

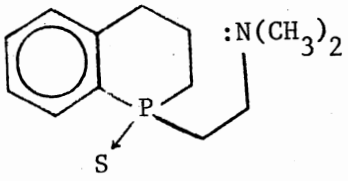
Michael-type addition of dimethylamine to the P-vinyl derivative 4 gave 8 which, upon reduction with trichlorosilane, led to 9. Treat-



8



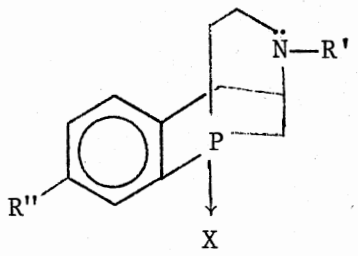
9

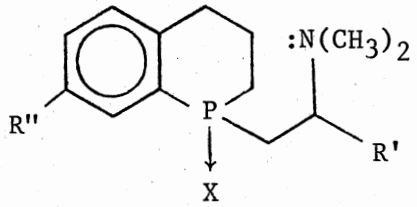


10

ment of 9 with sulfur produced 10 (95%).

Other N-alkyl derivatives reported in this patent were 11, 12, and 13.[121] ^1H NMR, IR and mass spectral data supported all of the structures.



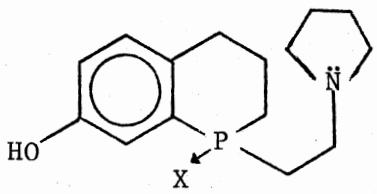


11

	R'	R''	X
11a	H	H	S
11b	H	CH_3O	S
11c	$-CH_2-CH_2-C_6H_5$	OH	S
11d	$-CH_2-CH=C(CH_3)_2$	OH	S
11e	$-CH_2-CH_2-C_6H_5$	OH	O
11f	$-CH_2-CH=C(CH_3)_2$	OH	O
11g	CH_3	H	$=N-CO_2C_2H_5$
11h	CH_3	H	Lone pair

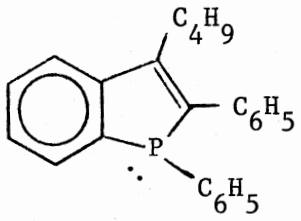
12

	R'	R''	X
12a	H	OH	S
12b	CH_3	H	S

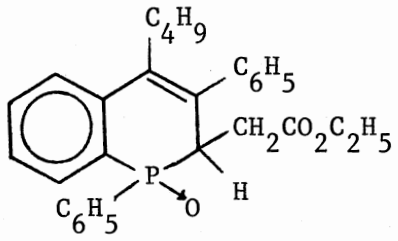


13

Ring expansion reactions proved in certain cases to be of value in the syntheses of derivatives of phosphinoline.[74] The possibility of a one carbon ring expansion of phosphindoles to get a phosphanaphthalene system had been studied.[74] 3-Butyl-1,2-diphenylphosphindole (14), ethyl propiolate and H_2O in THF gave 4-butyl-2-(ethoxylcarbonylmethyl)-1,2-dihydrobenzo[b]phosphin-1-oxide (15) as a glass. The structure was established by IR, NMR and mass spectral analyses. It was also

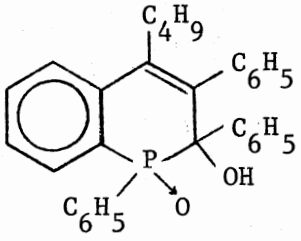


14

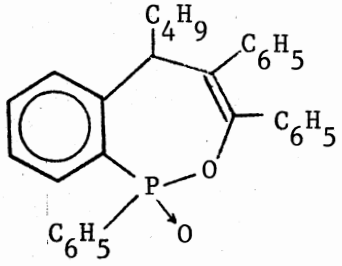


15

demonstrated that reaction of 14 with benzoyl chloride in the presence of triethylamine in dry ether, followed by treatment with water, led to the ring-expanded product 16 (13%), mp 221-224°C. Microanalytical and



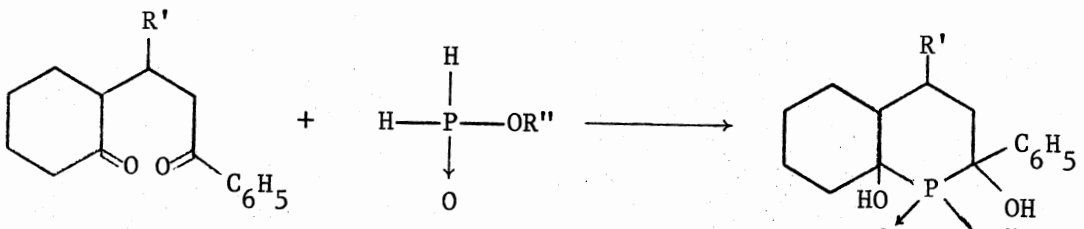
16



17

spectroscopic data were in excellent agreement with this proposed structure. Further expansion of 16 to a seven-numbered ring system 17 (18%) was achieved by treatment of 16 with NaH in DMF.[74]

In several recent developments, some perhydrophosphinoline systems were prepared from the cyclization of semicyclic 1,5-diketones with suitable phosphorus reagents.[133-135] The reaction of 1,5-diketones 18 with alkyl hypophosphites[135] was investigated by Vysotskii and



(R' = H, C_6H_5, p-$CH_3OC_6H_4$)

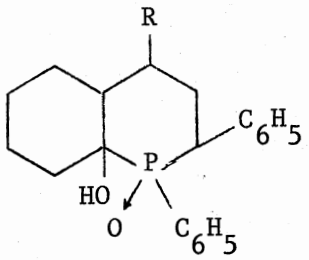
18

(R" = H, CH_3, C_2H_5, C_4H_9, $C_6H_5CH_2$)

19

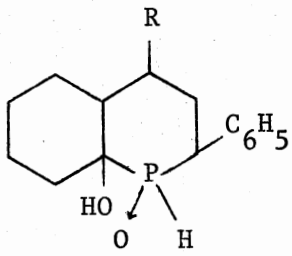
co-workers and led to 8a-hydroxyperhydrophosphinolines 19 (10-40%).

Cyclization of 18 in the presence of phenylphosphine ($C_6H_5PH_2$) gave the perhydrophosphinoline derivative 20 (16-55%)[133] whereas treatment of 18 with phosphine (PH_3) led to 21. The configurations of



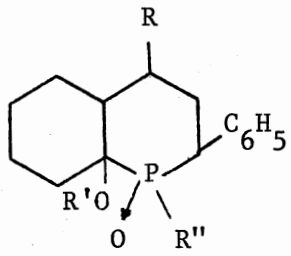
(R = H, C_6H_5)

20



(R = H, C_6H_5)

21

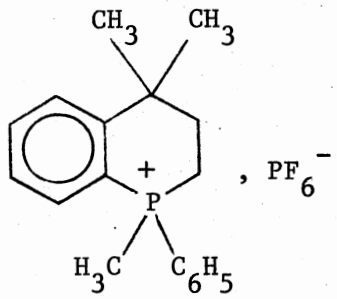


(R = H, C_6H_5, R' = H, CH_3CO), R" = H, CH_3)

22

stereoisomers of 21 were investigated by spectral methods.[134] Treatment of 21 with the appropriate reagents gave derivatives 22.

X-Ray analysis of the crystal structure of 1,2,3,4-tetrahydro-4,4-dimethyl-1-methyl-1-phenylphosphinolinium hexafluorophosphate (23) showed[146] that puckering occurred at the two carbon unit attached to

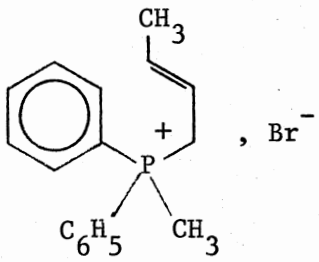


23

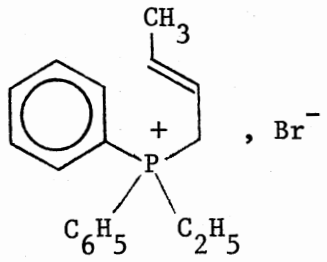
phosphorus. The conformational angles in the phosphorinane ring

demonstrated it to be half-chair. The ionic nature of the structure was reflected in the number of short H---F distances.

As a part of investigation of the mechanism of polyphosphoric acid (PPA) induced cyclization[110] of β-alkenyl-substituted phosphonium salts 24 and 25, an X-ray analysis was performed[50] on crystals of

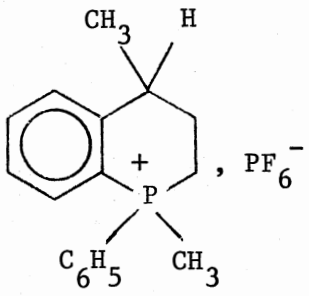


24

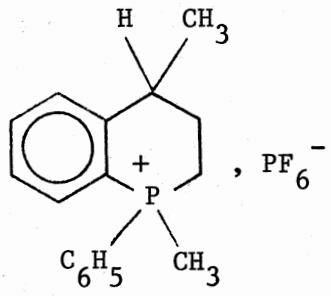


25

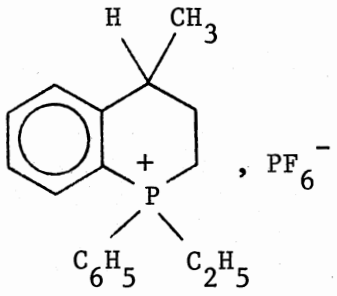
1,2,3,4-tetrahydro-1,4-dimethyl-1-phenylphosphinolinium hexafluorophosphate (26) and 1,2,3,4-tetrahydro-1-ethyl-4-methyl-1-phenylphosphinolinium hexafluorophosphate (27). These data revealed an unusual co-crystallization of the two diastereomers 26a and 26b in the



26a



26b

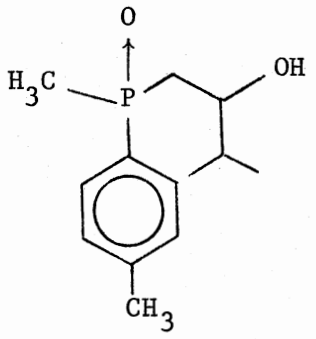


27

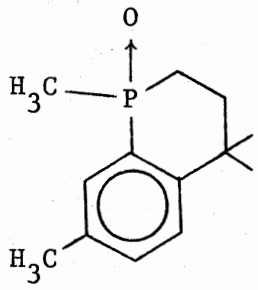
crystalline structure of 26 and thus confirmed the formation of two inseparable diastereomers during cyclization of 24 to 26 in the presence of 115% PPA at 160°C. However, 115% PPA-induced cyclization of 25 gave only one diastereomer 27. An X-ray diffraction analysis

confirmed its structure also.[50] The X-ray analysis of 26 and 27 showed the conformations of the heterocyclic ring in both the compounds to be very similar. The P^+-C (phenyl) distances were rather long (1.792 A^o in 26 versus 1.788 A^o in 27) due to steric hindrance, and the P^+-CH_3 distance (1.783 A^o) was shorter than the P^+-CH_2CH_3 distance (1.792 A^o). In the heterocyclic rings, the aryl-P^+ bond distances (1.788 A^o in 26 versus 1.795 A^o in 27) were different as expected.

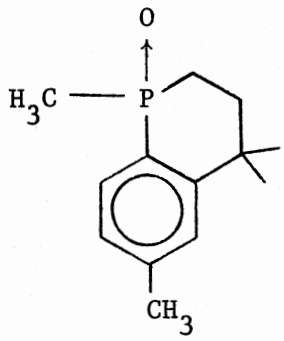
Polyphosphoric acid (PPA) has been extensively used in the annulation of phosphorus heterocycles.[112,132] The cyclization of 1-(methyl-p-tolylphosphinoyl)-3-methyl-butan-2-ol (28) in the presence of PPA[28] at 120°C produced an inseparable isomeric mixture (83%) of 1,4,4,7- and 1,4,4,6-tetramethylphosphinoline oxides 29 and 30 in the



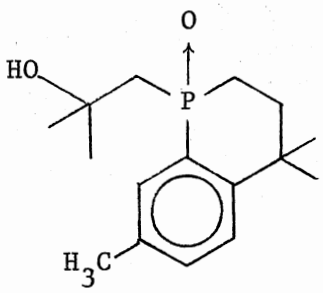
28



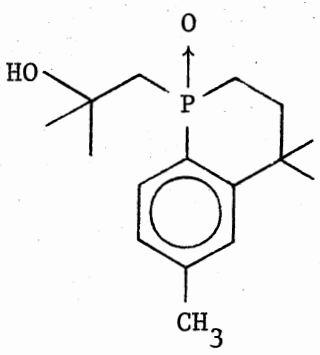
29



30



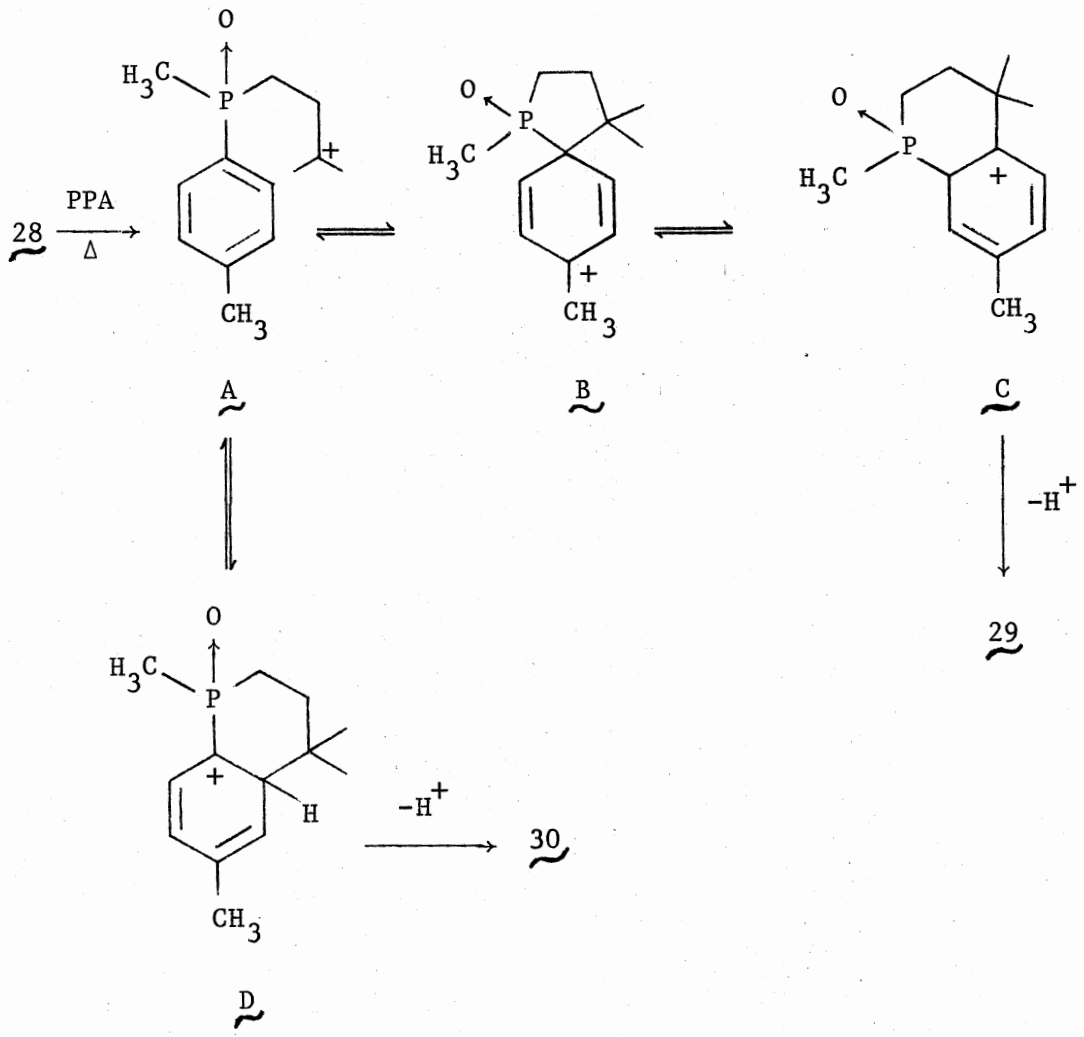
31



32

ratio of ca. 3:1. Further reaction of the mixture containing 29 and 30 with n-C_4H_9Li in THF near 10°C, followed by addition of acetone at -78°C, led to a mixture of isomeric alcohols 31 and 32 (60%) in the ratio of ca. 4:1.

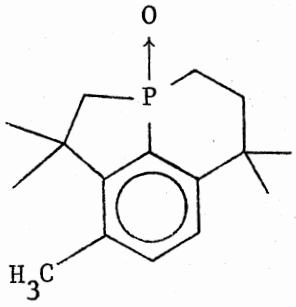
The formation of the tetrahydraphosphinoline oxide 29 during PPA cyclization of 28 was rationalized[28] by a mechanism which involved cationic ipso cyclization followed by migration of the phosphinoyl group. Ipso ring closure of the carbonium ion A formed the spiro-



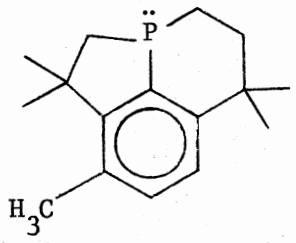
conjugated carbonium ion B. Migration of the phosphinoyl group to produce the new carbonium ion C is favored by the restoration of the

cisoid diene conjugation. Loss of a proton to regain aromaticity could favor the formation of 29. The P-oxide 30 should have as a precursor the carbonium ion D.

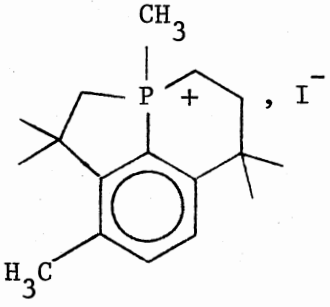
Cyclization of the mixture containing 31 and 32 with PPA at 170-180°C gave the tricyclic product 33 (22%).[28] Reduction of 33 with excess trichlorosilane in benzene at reflux led to 1,1,5,5,8-pentamethylphosphalilodine (34) (82%) which was converted into stable methyl-substituted phosphonium salt 35. Treatment of 29 and 30 with



33

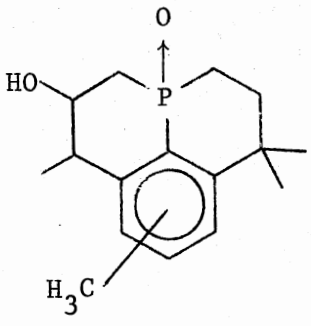


34

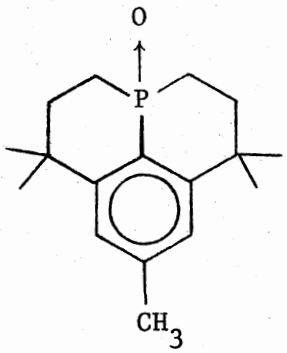


35

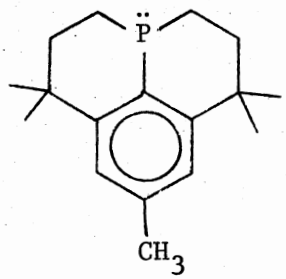
n-C_4H_9Li in THF, followed by addition of excess of isobutyraldehyde at -78°C, gave a diastereomeric mixture of 36 (34%). The cyclization of 36 in the presence of PPA led to 37 which was purified via prepara-



36



37



38

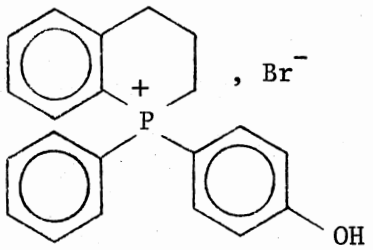
tive TLC analysis. Reduction of 37 with trichlorosilane produced

1,1,6,6,8-pentamethylenephosphajulalidine (38) (85%) as a colorless, viscous oil. Elemental analyses, ^{1}H NMR, ^{31}P NMR and mass spectral analyses supported all of the structures. UV spectroscopic and cyclic voltammetric data suggested that 34 and 38 have essentially no n-Π interaction between the lone pair electrons on the phosphorus and the adjacent aromatic Π system. These selected examples of polycyclic carbon-phosphorus heterocycles are only representative of work done in the field but other cases have been cited in the new reference of Quin.[112]

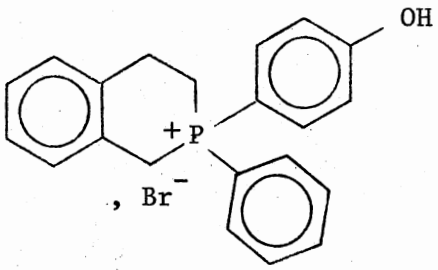
Resolution of Heterocyclic Phosphonium Salts

The stereochemistry of derivatives of optically active organophosphorus compounds has been discussed in several review articles.[30,31,54,63,73,77,89,99-101] Tables of known optically active organophosphorus compounds are also available in literature.[98,140] Methods and reagents applicable for the resolution of all types of the organophosphorus compounds have been discussed by Snider[120] whereas specific resolution of quaternary phosphonium salts has been reviewed by Chen.[29] The methods for the determination of the absolute configurations of quaternary phosphonium salts have been cited by Klyne and Buckingham.[82]

Holliman and Mann[67] pioneered the earliest successful resolution of a heterocyclic phosphonium salt in 1947. They attempted to resolve two heterocyclic phosphonium salts 1,2,3,4-tetrahydro-2-p-hydroxyphenyl-2-phenylphosphinolinium bromide (39) and the corresponding isophosphinolinium bromide 40 into optical antipodes. Although they were unsuccessful with the former compound, the isolation of a dexterorotatory



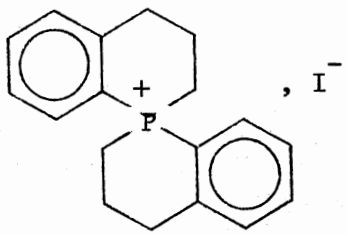
39



40

form of the isophosphinolinium bromide 40 [having a molecular rotation of $[M]_D^{17^\circ} = +32.9^\circ$ (in aqueous ethanol)] was achieved through its (+)-camphorsulfonate ($[M]_D^{17^\circ} = +113.5^\circ$; ethanol). The isolation of the corresponding levorotatory form was not realized and also later attempts to repeat the first successful resolution met with failure.[67] These failures were attributed to the formation of partial racemates of 40.

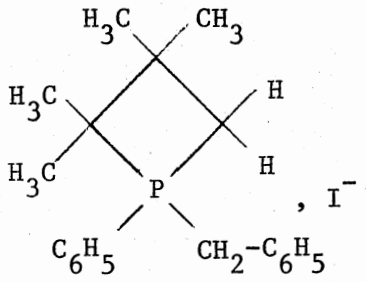
Hartman and Mann[64] recorded the total resolution of P-spiro-bis-1,2,3,4-tetrahydrophosphinolinium iodide (41) into its dextro- and levo-isomers ($[M]_D = +66^\circ$ and -65°, respectively; $HCCl_3$) via the



41

(+)- and (-)-phosphonium (-) menthoxyacetate. The (+)- and (-)-isomers of 41 have high optical stability. However, the spiro-salt 41 owes its optical activity to molecular dissymmetry rather than to the presence of an asymmetric phosphorus atom.[64]

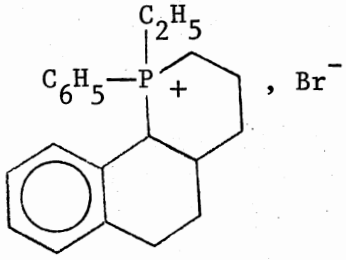
The alkaline hydrolysis of the topically active 2,2,3,3-tetramethylphosphetanium salt 42 has been reported by Trippett and co-



42

workers.[36] The iodide 42 had a specific rotation of $[\alpha]_D = +21.8^o$. However, the details of the resolution of 42 have not yet been disclosed.

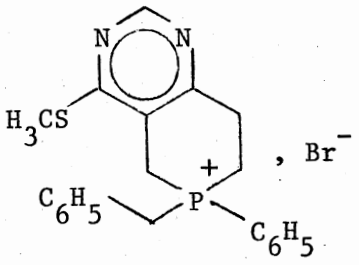
Chen and Berlin[27] were the first to use silver D(-)- and L(+)-hydrogendibenzoyltartrates (HDBT) to resolve a carbon-phosphorus heterocyclic salt. Partial resolution of 1-ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]phosphinolinium bromide (43) was obtained via the use



43

of D(-)- and L(+)-HDBTs. The dextro-isomer of 43 [$[\alpha]_D^{25} = +28^o$ ($HCCl_3$)] was isolated. This was the first reproducible and unambiguous example of the resolution of a polycyclic phosphonium salt reported in literature.

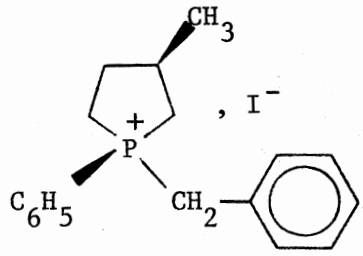
The successful resolution of 5,6,7,8-tetrahydro-4-(methylthio)-6-benzyl-6-phenylphosphornia[4,3-d]pyrimidine bromide (44) with silver



44

D(-)- and L(+)-HDBT as resolving agents was recorded in 1973 by Snider and Berlin.[118] The isolation of both dextro- and levo-forms having reproducible values for optical rotation [$[\alpha]_D^{25}$ = +78° and -77°, respectively; CH_3OH] was achieved.

Marsi and Tuinstra[93] recorded in 1975 the first instance of the complete resolution of a five-membered ring with a quaternary phosphorus atom. Resolution of trans-1-benzyl-3-methyl-1-phenylphospholanium iodide (45) was realized with the aid of silver (+)-10-camphorsulfonate



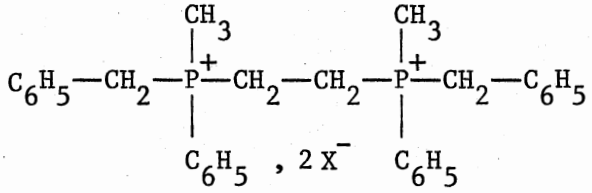
45

into (+)- and (-)-45 [$[\alpha]_D^{22}$ = +2.16 ± 0.09° and -2.14 ± 0.11°, respectively; $DCCl_3$]. A unique triangular scheme of recrystallization employing a minimum amount of hot ethanol and ethyl acetate was successfully utilized to separate the two diastereomeric salts of 45.

Holmes and co-workers[40] were able to assign the absolute configuration to the levorotatory form of solid 45 based on X-ray analysis on an optically pure sample. In agreement with the predictions made from ^{1}H NMR analysis and a reaction of known stereochemistry, the methyl and benzyl groups have a trans arrangement. Guided by the rules[22] governing chiral derivatives, the (-)-45 was designated as (1 R,3 S)-(-)-trans-1-benzyl-3-methyl-1-phenylphospholanium iodide.

Separation and Resolution of Stereoisomers of Bisphosphonium Salts

The first and only previous successful separation of diastereomers and resolution of an open-chain bisphosphonium salt was reported[68] by Horner and co-workers in 1966. Fractional crystallization (using CH_3OH) of 1,2-ethanediylbis(benzylmethylphenylphosphonium) diperchlorate (46, X = ClO_4) derived from the dibromide of 46 (X = Br),

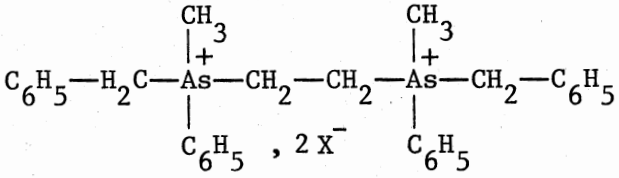


46

gave the pure meso- and racemic-form of the diperchlorates of 46. The latter were converted to the corresponding dibromides [mps 278° and 293°, respectively]. The (+)- and (-)-46 (X = Br) isomers were isolated from the racemic mixture via the use of silver hydrogen D(-)-dibenzoyltartrates. The pure enaniomers were converted to and characterized as perchlorates and methyl sulfates. The (+)- and (-)-46, (X = OSO_2OCH_3), (mps 139° and 175°, respectively) isomers had specific rotations of

$[\alpha]_D$ = +64.05° and -65.4°, respectively, in CH_3OH. The (+)-46 (X = ClO_4) had a specific rotation of $[\alpha]_D$ = 34.1°. This is the only example of a separation and resolution of stereoisomers of a non-heterocyclic bisphosphonium salt reported in literature.

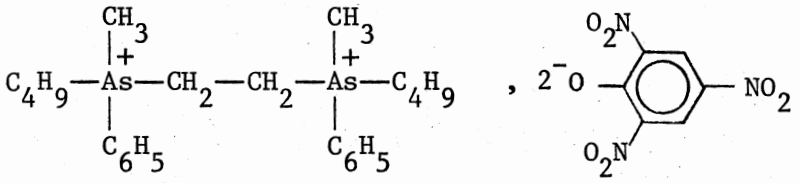
Recently, the resolution of racemic 1,2-ethanediylbis(benzylmethylphenylarsonium) diiodide (47), the arsenic analogue of 46, was



47

recorded[12] via the use of AgD(-)HDBT. The pure enantiomers were characterized as the bis(hexafluorophosphates). The (+)- and (-)-47 (X = PF_6) had specific rotations of $[\alpha]_D^{20}$ = +5.22° and -7.74°, respectively, in acetone.

It is of interest to note that the meso- and racemic-forms of 1,2-ethanediylbis(phenylmethyl-n-butylarsonium) dipicrate (48) were



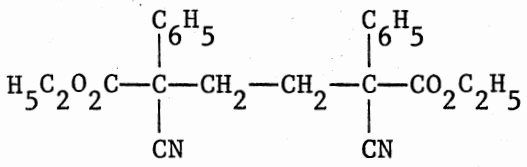
48

isolated by Chatt and Mann[26] some 30 years before the resolution of 47 was achieved. The separation of 48 into two forms was effected by fractional crystallization using ethanol (the α-form had a mp 113-115°C and the β-form had a mp of 139.5-140.5°C). These two forms must

represent meso- and racemic-isomerides and the latter should therefore be resolvable into optically active forms. No attempt to do so has been reported possibly because of the great difficulty in resolving dissymmetric arsonium salts and the comparative inaccessibility of the two pure picrates.

Separation of Diastereomers and Discrimination of Stereochemical Configurations by NMR Spectroscopy

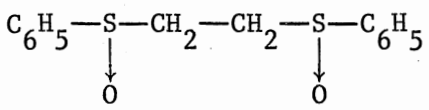
Methods of optical resolution have been summarized and discussed in several reviews.[11,13,34,139,141] The same strategies employed in optical resolutions have also been extended to the separation of meso- and racemic-forms of compounds bearing two equivalent chiral centers. Fractional crystallization continues to be the most widely employed technique to separate the diastereomeric pairs of compounds. For instance, separation of meso- and (±)-49 was accomplished by fractional



49

crystallization using methanol.[24] The first crop of crystals (mp 131-133°C) had the meso configuration whereas the second crop (mp 98-100°C) obtained from the crystallization liquor proved to be the racemic mixture.

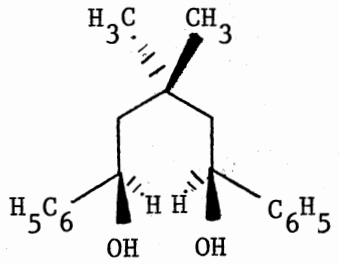
Mechanical separation of the diastereomers was possible in the case of 1,4-diphenyl-1,4-dithiabutane-1,4-dioxide (50). The direct



50

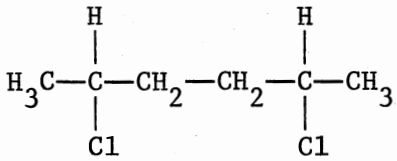
crystallization of 50 from toluene resulted in the formation of meso and racemate crystals which were separated mechanically.[106]

Chromatography has been successfully applied to the separation of some diastereomers.[33,51] Thus, with 51 the meso- and (±)-forms were



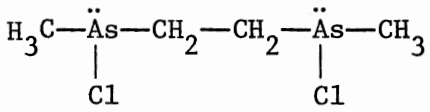
51

obtained by column chromatography (Merck silica gel) using 80:20 hexane-ethyl acetate as the eluant system.[57] Gas chromatography has also been employed for the separation of diastereomeric pairs of a simple molecule like 52.[23]



52

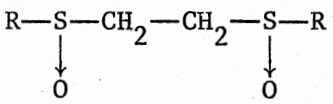
Complex formation[12] has been instituted to obtain individual diastereomers of ethylene-1,2-bis(methylphenylarsine) (Dias) (53). Complexation of 53 with chloropalladate(II) in methanol resulted in the formation of [Pd Dias·Cl_2] which could be separated when chromat-



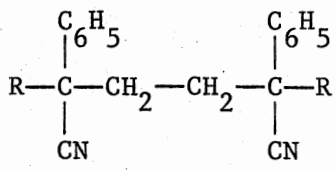
53

ographed on silica gel and eluted with 5% THF-CH_2Cl_2. The first species to be eluted was the (±)-[Pd Dias·Cl_2]. The more slowly moving fraction gave meso-[Pd Dias·Cl_2]. Decomposition of the complexes with NaCN produced the corresponding diastereomers of 53.

The determination of the configuration at an atom by NMR spectroscopy has been extensively discussed in a review[56] published in 1977. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR analyses were employed as tools to discriminate meso- and (±)-forms of molecules which contained symmetrically disposed chiral groups. ^{1}H NMR differentiation and identification of meso- and (±)-forms of acyclic structures with two equivalent chiral centers have also been widely explored in systems in which two asymmetric centers were separated by one carbon atom.[56] The same criterion, based on symmetry principles,[102] such as anisochronism of diastereotopic groups of one of the diastereomers, was also applied to certain molecules which have asymmetric centers separated by two carbon atoms.[24,33,76] In accordance with the findings of Jung and Bothner-By,[76] the (±)-isomers exhibited an AA'BB' quartet while meso-isomers showed a simplified ^{1}H NMR spectra (in some cases, a fortuitous singlet) for the -CH_2—CH_2- groups in γ-disulfoxides 54



54

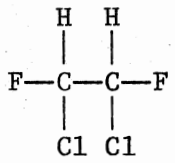


55

(R = C_6H_5 or substituted phenyl)[33,122] and in α,α'-diphenylsubstituted adiponitriles 49.[24] However, the assignment of a singlet to the methylene protons of the meso-isomer was not observed[24] for meso-55 (R = CH_3 or C_2H_5) which exhibited an AA'BB' quartet like the racemic form.

It is known that the mediated effect of an asymmetric center on the anisochronism of diastereotopic groups decreases with distance.[137] Casini and co-workers[57] used geminal probes to examine the effect of distance on the anisochronism of diastereotopic groups from two equivalent chiral centers separated by three carbon atoms such as in 51. Anisochronism of diastereotopic protons was used for assignment of the configurations of asymmetric centers in the diastereomers.

That chiral solvents and chiral shift reagents can be used to distinguish meso- from d- or l-diastereomers has been discussed by Gaudemer.[56] The ^{19}F spectrum of a mixture of meso- and (±)-1,2-difluoro-1,2-dichloroethane (56) in L-bornyl acetate resolved the ^{19}F

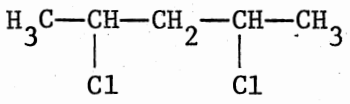


56

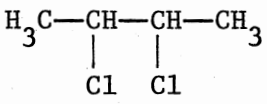
resonances of the separate d- and l-stereoisomers, thus identifying the dl-mixture.[1] However, three other chiral solvents, viz., fenchol, fenchone and carvone, did not induce sufficient resolution in the spectrum of 56 to show two signals for ^{19}F.

The use of ^{13}C NMR spectroscopy for the determination of configurations was predicted[45,86] only after 1970. ^{13}C NMR analysis appears

complementary to ^{1}H NMR spectroscopy in terms of providing evidence on the relative configurations of atoms in acyclic compounds. This is due to the sensitivity of ^{13}C shifts to steric effects[47] and the greater magnitude of these shifts compared with proton chemical shifts.[23] Meso- and (±)-forms of 57 and 58 have markedly different



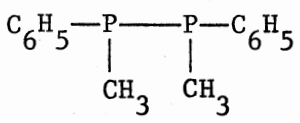
57



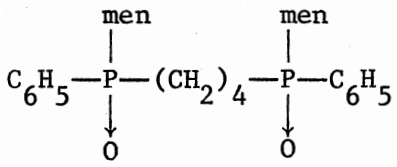
58

^{13}C NMR chemical shifts for each carbon.[23,56] Recently, configurations of atoms in diastereomers with vicinal asymmetric centers in 2,3-disubstituted butanes and 5,6-disubstituted n-decanes have been discussed by Levy, Pehk and Lippmaa[85] in terms of ^{13}C shifts. In some cases, ^{15}N chemical shifts and solvent-lattice relaxation times have also been evaluated. Hasan[65] reported that the meso- and (±)-forms of a number of α,α'-disubstituted succinic acids have different ^{13}C chemical shifts. The significant difference observed between certain chemical shifts $[\delta_{meso}-\delta_{rac}]$ has been rationalized on the basis of non-bonded interactions affecting the asymmetric center in the preferred conformation of each isomer.

The importance of steric effects on ^{31}P chemical shifts is well-known.[111,112] However, the use of ^{31}P NMR spectroscopy for the determination of configurations around P in phosphorus compounds has not been explored to date. In 1962, Maier[88] noted that the ^{31}P NMR spectrum of diphosphine 59 exhibited two peaks corresponding to the meso- and (±)-forms of 59. Recently, Valentine and co-workers[129] observed two signals at 44.8 and 42.53 ppm downfield from external phosphoric acid



59



(men = menthyl)

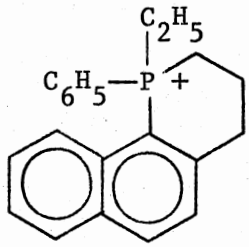
60

in the ^{1}H decoupled ^{31}P NMR spectrum ($DCCl_3$) of meso-60. This area appears ripe for exploration.

Biological Activity of Derivatives of Phosphinoline

The determination of biological potential of carbon-phosphorus heterocycles received renewed attention in the last decade.[112] Several successful applications of phosphonium salts in the biological field were listed in another extensive review.[5]

In the course of studies in collaboration with the National Cancer Institute of the National Institutes of Health, Berlin and co-workers discovered that certain heterocyclic phosphonium salts exhibited carcinostatic activity. 1-Ethyl-1,2,3,4-tetrahydro-1-phenylbenzo[h]-phosphinolinium bromide (43) was prepared by Chen and Berlin.[27] The



NSC-145185

T/C = 142 (6.25 mg/kg)

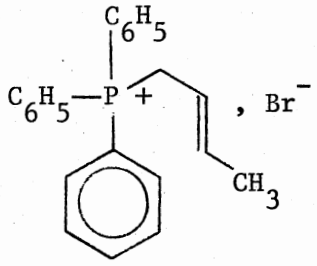
[3 $P531^{c}$ tumor system]

43

National Cancer Institute established and confirmed that phosphonium

bromide 43 had a high level of activity against $3P531^{C}$ system [P-388 lymphocytic leukemia cell line]. Rather striking was the finding that 43 had the highest test/control (T/C) value (survival time of test animals/survival time of control animals) of all the benzophosphinolinium salts tested to date. This small breakthrough accelerated interest in the synthesis and study of biological activity of this class of compounds. The NSC number refers to that number assigned to that compound by National Cancer Institute.

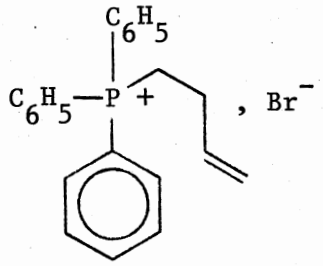
In spite of the difference in the test system employed (L-1210 leukemic line versus P388 leukemic line), it was observed[114] that cyclization of open phosphonium salts generally led to a phosphinoline system with a marked increase in the T/C value. For example, 115% PPA-induced cyclization[43,110] of both the open-chain precursors 61 and



NSC-245392

T/C = 110
(6.25 mg/kg)

61 [L-1210]

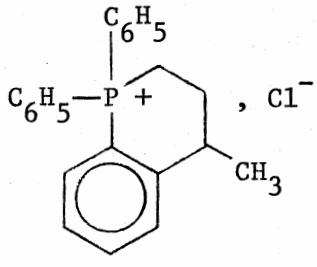


NSC-248535

T/C = 125
(12.5 mg/kg)

62 [L-1210]

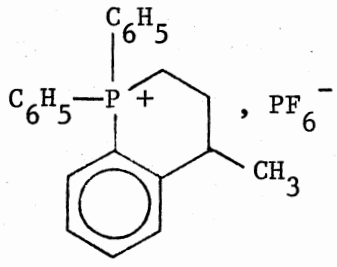
62 produced 63 when NaCl was added in the final step of the workup (or



NSC-273810

T/C = 155
(25 mg/kg)

63 [P-388]

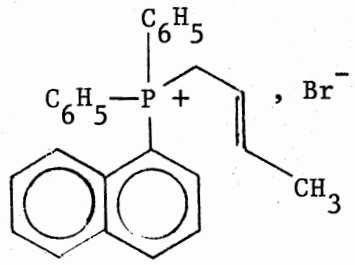


NSC-245397

T/C = 107
(6.25 mg/kg)

64 [L-1210]

64 when KPF_6 was used in the final step). The T/C value increased from 110 for 61 and 125 for 62 to 155 with the cyclic product 63. The low T/C value (107) for 64 was tentatively attributed to an unknown effect of PF_6 anion. The observation that PF_6 salts always had a smaller T/C value compared to the counterpart with a Br or Cl anion was supported via analysis of the products obtained from conversion of open phosphonium salt 65 to benzophosphinolinium salts 66 and 67 as shown below. The chloride 66 had a T/C value of 118 while the PF_6

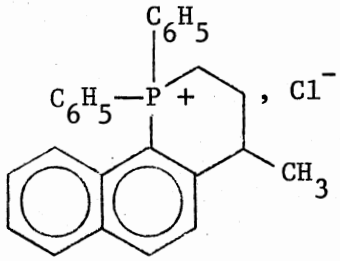


NSC-245394

T/C = 94
(25 mg/kg)

[L-1210]

65

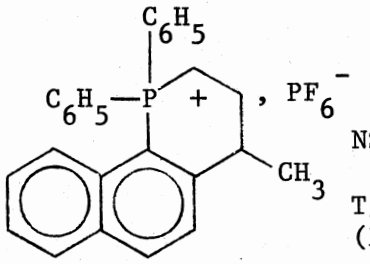


NSC-273808

T/C = 118
(6.25 mg/kg)

[P-388]

66



NSC-245398

T/C = 106
(12.5 mg/kg)

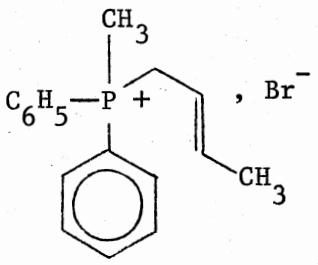
[L-1210]

67

salt 67 had a value of 106.

Besides the nature of the anion, the type of substituent on phosphorus is likely important for maximum activity. Recently, Berlin and co-workers evaluated[50] the screening data furnished by National Cancer Institute in terms of carcinostatic activity of phosphinolinium salts versus the type of substitution on phosphorus. The 115% PPA-

induced cyclization of 24 at 160°C gave a mixture of two diastereomers 26a and 26b (NSC-248536) in the ratio 3:1 and having a T/C value of 107

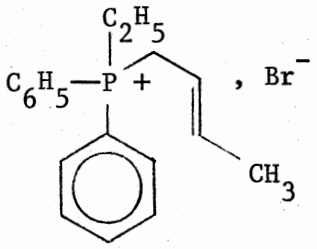


NSC-245853

T/C = 104
(0.8 mg/kg)

[P-388]

24

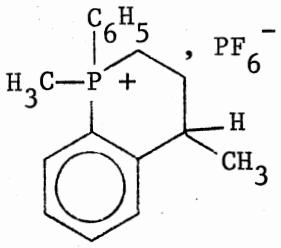


NSC-24393

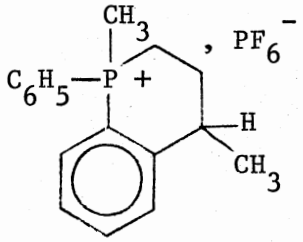
T/C = 112
(3.13 mg/kg)

[P-388]

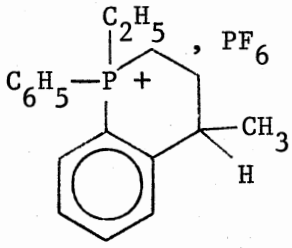
25



26a



26b



27

NSC-245396

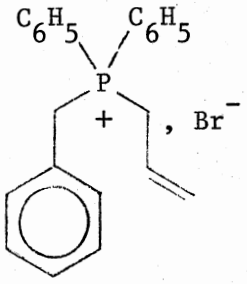
T/C = 121
(6.25 mg/kg)

[L-1210]

(3.13 mg/kg) in the L-1210 leukemic system. However, cyclization of 25 produced 27 with a larger increase in T/C value. Both acyclic and cyclic phosphonium salts 25 and 27 having an ethyl substituent on phosphorus had higher T/C values than the corresponding phosphonium salts with a methyl substituent on phosphorus.

The position of the phosphorus atom in the ring also appears

crucial for maximum biological activity of compounds. It was observed that in certain isophosphinoline systems the T/C values did not change significantly when the open-chain precursors 68 and 69 were compared to

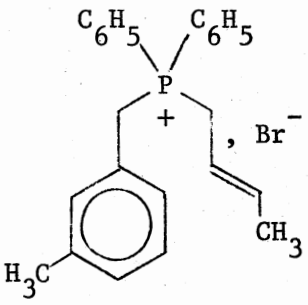


NSC-245383

T/C = 115
(12.5 mg/kg)

[L-1210]

68



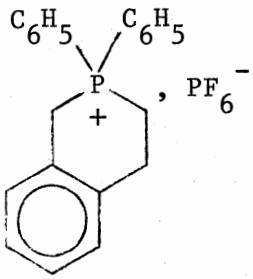
NSC-245386

T/C = 113
(6.25 mg/kg)

[L-1210]

69

the cyclic products 70 and 71. The low T/C values for 70 and 71 might

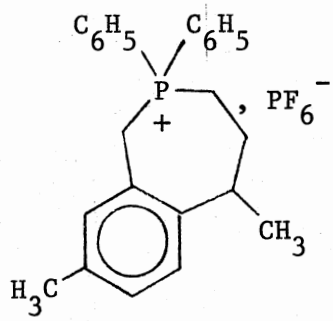


NSC-245388

T/C = 117
(6.25 mg/kg)

[L-1210]

70



NSC-245391

T/C = 102
(100 mg/kg)

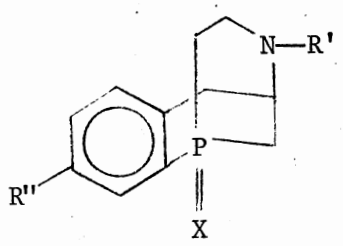
[L-1210]

71

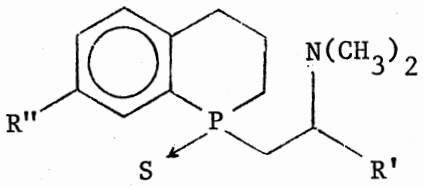
be due to the presence of the PF_6 anions.

At this time, there exists no unequivocal rationale to explain the biological activity in terms of structure of a carbon-phosphorus heterocycle or for many systems in fact. Steric effects and the influence of several conformations of flexible molecules in solution remain parameters difficult to evaluate in predicting biological activity.[20]

Some phosphinoline systems have exhibited other types of biological activity. For example, N-alkyl derivatives of phosphinoline 11 and 12 were prepared[121] and subjected to a Mouse Writhing Test and to the



11



12

McKenzie Beechy Mouse Tail Stimulation Test to determine the analgesic activity present. The compounds in which X = S showed high activity. Phosphine sulfide 12 (X = S; R' = R'' = H) was active at 16 mg/kg in the Tail Stimulation Test which was comparable to morphine in this assay. The toxicity test for 12 showed an LD_{50} of 170 mg/kg.

The high degree of activity exhibited by phosphinolinium salts 43 and 63 has offered encouragement that other phosphinoline derivatives and selected C-P heterocycles may have chemotherapeutic value. Much work remains to be done in this field.

Applications of Bisphosphonium Salts

Several successful applications of quaternary phosphonium salts were listed in an extensive review[5] published in 1972. The appearance of nearly 70 patents and articles about the applications of bisphosphonium salts in the last decade has revealed the potential use of such salts in medicine and industry. Since it is impractical to list all the recent literatures (since 1970) concerning the applications of bisphosphonium salts, the discussion will primarily focus on selected references judged on the basis of potential utility.

Bisphosphonium salts have exhibited high antimicrobial and moderate antifungal activity *in vitro*.[126] Recently, strong anticholenergic

activity of α,ω-alkanediylbis(triphenylphosphonium) salts 72 (n = 2, 3,

$$[(C_6H_5)_3\overset{+}{P}-(CH_2)_n-\overset{+}{P}(C_6H_5)_3] \quad , 2\ X^-$$

72

5, 6; X = Br) has been discovered.[97] 1,10-Decanediylbis(triphenylphosphonium dibromide (72; n = 10; X = Br) has been used as a bactericide[7] in detergents, for example. Bisphosphonium salts 73 are useful as

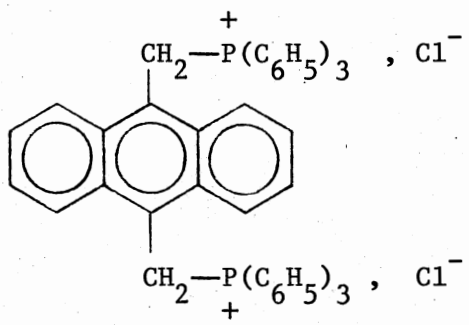
$$[(C_6H_5)_2\overset{+}{P}-\underset{R'}{\underset{|}{C}}HR''-\underset{R'}{\underset{|}{C}}-\overset{+}{P}(C_6H_5)_2] \quad , 2\ X^-$$

73

(R' = C_6H_5 or substituted C_6H_5, R" = C_6H_5, H, X, alkyl, etc. X = halogen)

antiparasitics[55] to control helminths in domestic and farm animals. Methylenebis(triphenylphosphonium)dibromide (73; R' = C_6H_5; R" = H; X = Br) controlled larger number of helminths in sheep at 15-30 mg/kg.

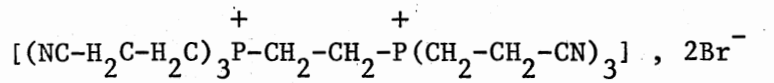
Horner and co-workers discovered[70] that bisphosphonium salts, expecially those with C_{4-10} bridges between the P-centers, were excellent corrosion inhibitors for metals in acid solutions. Certain bis-salts were better corrosion inhibitors than polymers with incorporated "phosphonium" centers. The protective value (Z) of α,ω-alkanediylbis(triphenylphosphonium) salts 72 (n = 2, 4, 5, 6, 10; X = Br, Cl, $FeCl_4$) was found[72] to be higher at low inhibitor concentration for iron specimens. The protection is apparently due to secondary inhibition. Evidence for secondary inhibitors formed on iron boundaries from reductive degradation of 74 has been obtained by UV absorption and fluorescence spectroscopy.[69] Corrosion of aluminum,[58] zinc,[125] iron and steel[115] in different environments was inhibited with the aid of selected



74

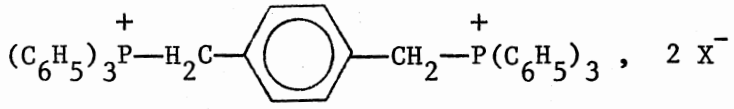
bisphosphonium salts.

The application of bisphosphonium salts in fire-proofing of plastics and textiles is also well known.[5] Many patents deal with 1,2-ethanediylbis[tris(2-cyanoethyl)phosphonium] dibromide (75) as a



75

flame retardant for polypropylene,[103] polystyrene,[138] ABS,[103] poly-(esterethers)[19] and poly(methylmethacrylate).[41] Thermogravimetric[49] and mechanism studies[116] of a flame-retardant system containing 75 and ammonium polyphosphate indicated that the synergistic effect observed by combination of the two components was due to the formation of a P-rich char which forms an insulating layer on the polymer surface with little effect on thermal and mechanical properties of polymers. The bis-salt 75 has been used as fire-retardant-adhesion-promoter for polystyrene based adhesives.[104] Heat-resistant films of vinyl polymers on metals like aluminium are formed[94] by electrolyzing monomers in the presence of bis-salt 76 (X = Br). The bisphosphonium salt 76 (X = Br) is also useful as a non-opaque flame-retardant[48] for polycarbonates and an antistatic agent for nylon fabrics.[117] Use has been made of

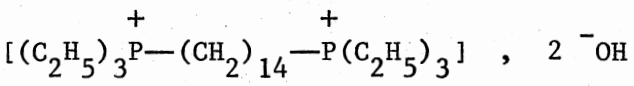


76

several bisphosphonium salts as colorfast agents[53] in textiles against heat, light and laundering.

Many bisphosphonium salts have been employed as catalysts for polymerization reactions. The use of bis-salt 76 [X = $(C_6H_5)_4B$] as a promotor for cross-linking of epoxy resins with anhydrides has been proposed.[107] Bisphosphonium salts have served as catalysts[38] for polymerization of epoxides with isocyanates, thickening accelerators[42] for unsaturated polyester resin solutions by MgO and chiral phase transfer catalyst[80] for $NaBH_4$ reduction of α-keto esters.

Quaternary phosphonium ionomers have been formed by the reaction of α,ω-alkanediylbisphosphonium dihydroxides like 77 with sulfonated



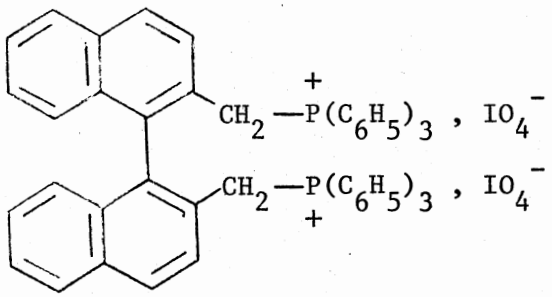
77

rubbers.[16] The ionic polymers formed vary from water-soluble polyelectrolytes useful as thickening agents to thermoplastic rubbers useful as speciality and general purpose rubbers.

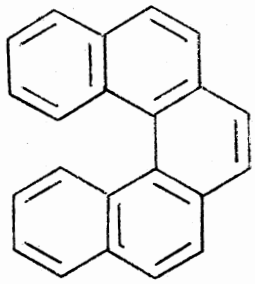
Bisphosphonium salts have found value in waste-water treatment,[52] extraction of uranium[8] and deactivation of glass surfaces and glass capillary columns.[90] In the photographic field, bisphosphonium salts have been used as photographic hardening agents.[142]

In synthetic chemistry, bisphosphonium salts can serve as

precursors for the bis-ylids used in the synthesis of polyenes,[79] macrocyclic compounds,[113] fluorescent whiteners[87] for organic materials and azo dyes[4] to list only a few examples. Cyclization[10] of bis-salt 78 with lithium ethoxide in ethanol gave (+)-pentahelicene (79). 1,2-Ethenediylbis(triphenylphosphonium) dibromide (80) reacted with alcohol

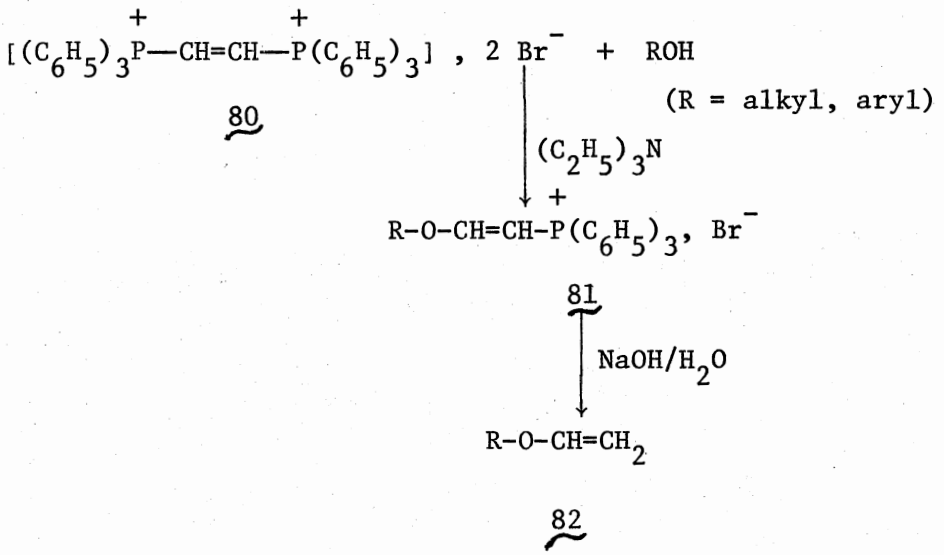


78



79

or phenol[32] in the presence of triethylamine to yield 81 which was hydrolyzed by base to the vinyl ether 82 (overall yield 50-76%). Com-



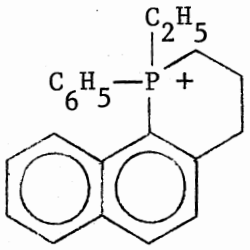
80 81 82

paratively, little use has been made of bisphosphonium salts for organic synthesis as concluded from a literature survey.

CHAPTER II

RESULTS AND DISCUSSION

1,2,3,4-Tetrahydrophosphinolinium salts are of special interest both from a stereochemical point of view[27] as well as for potential biological activity.[50,114] Substituted 1,2,3,4-tetrahydrophosphinolinium salts 43 and 63 are the only C-P heterocycles which have

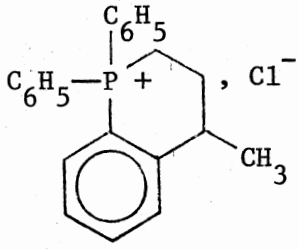


43

NSC-145185

T/C = 142

[P-388 system]



63

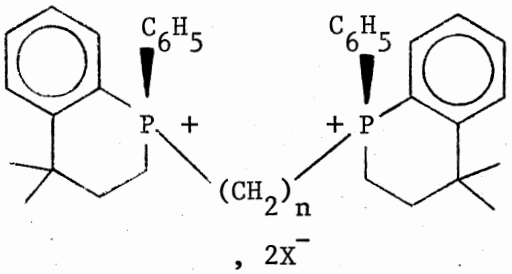
NSC-273810

T/C = 155

[3 P531[c] system]

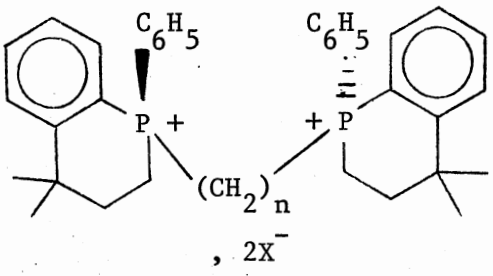
confirmed carcinostatic activity as demonstrated by the National Cancer Institute during the routine screening process. In addition, certain α,ω-alkanediylbisphosphonium salts have exhibited anticholenergic,[97] antimicrobial[7] and antihelminitic[55] activity. They are also valuable in several industrial applications (vide infra).

Although simple 1,2,3,4-tetrahydrophosphinoline systems have been synthesized,[9,112,132] no method has ever been recorded for the preparation of α,ω-alkanediylbis(1,2,3,4-tetrahydrophosphinolinium) salts. The general formula for the family of targeted compounds is illustrated by 83 (meso-form) and 84 (d,l-pair possible). Also, a search of the literature revealed that no attempt has been made to separate such



, $2X^-$

83

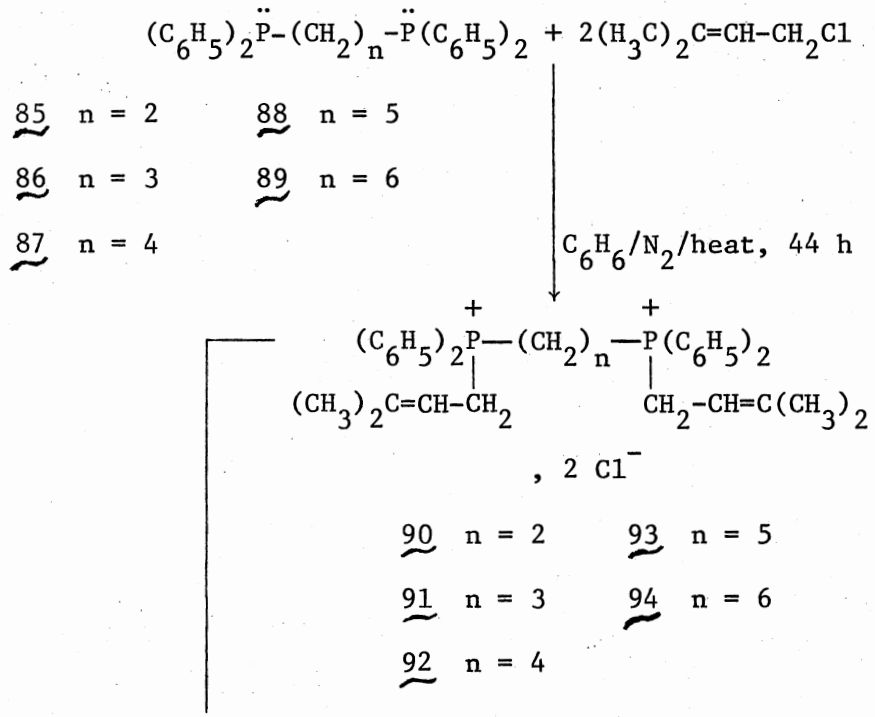


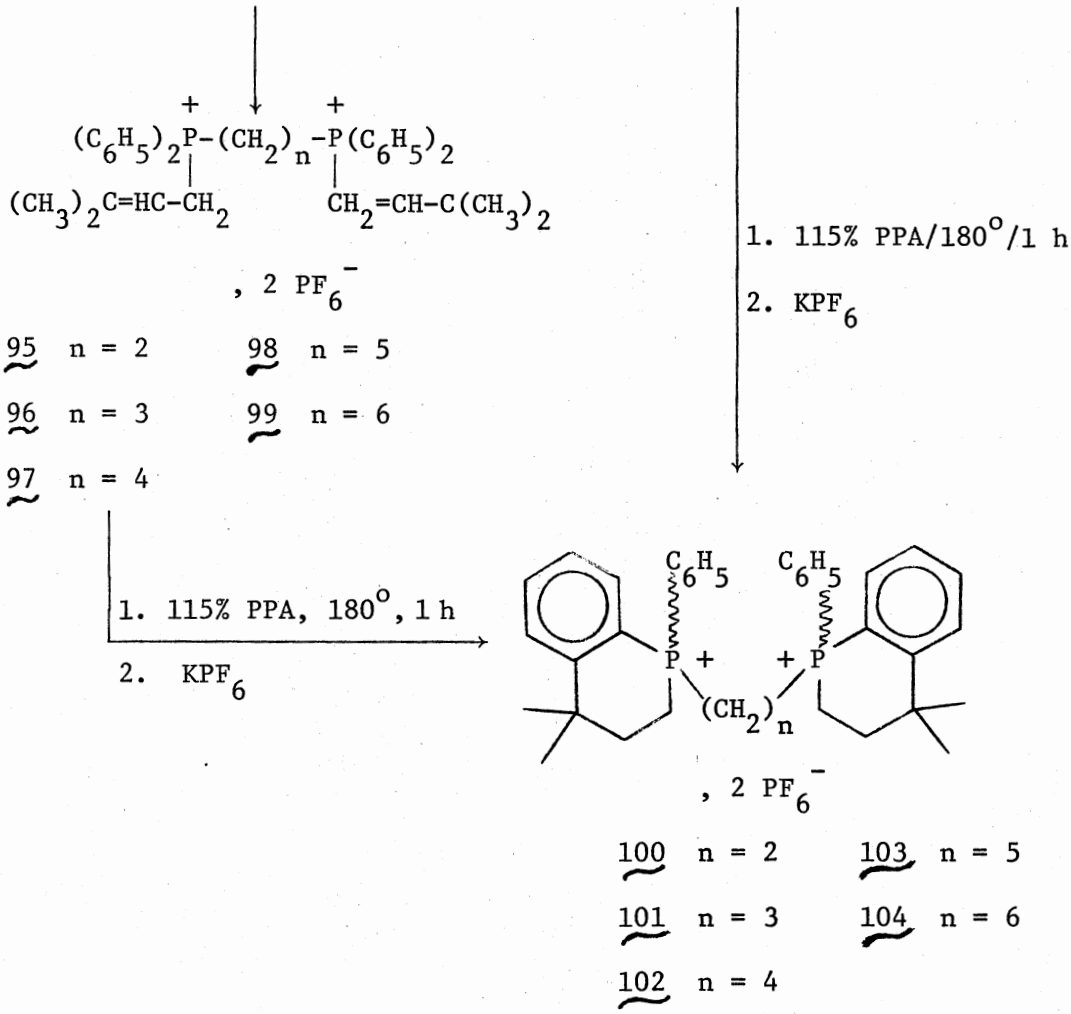
, $2X^-$

84

diastereomers or to resolve the d,l-pair of a C-P heterocycle containing two asymmetric phosphorus atoms in the rings. Stimulated by these observations and an interest to explore the cyclization technique for preparing C-P heterocycles found in our laboratory,[43] we attempted the preparation of certain substituted α,ω-alkanediylbis(1,2,3,4-tetrahydrophosphinolinium) salts which are dissymmetric because of two asymmetric phosphorus atoms. In addition, we anticipated that the bis-salts would possess useful biological activity.

Diquaternization of commercially available bisphosphines (85-89)

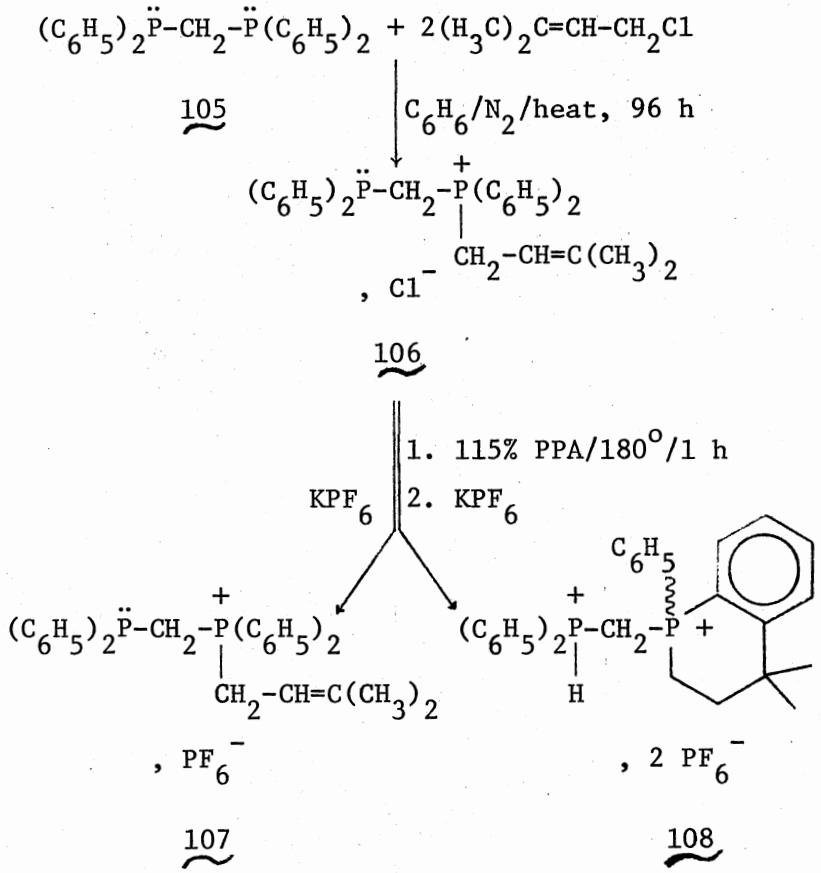




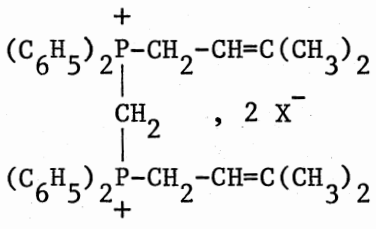
with 1-chloro-3-methyl-2-butene gave β-alkenyl-substituted bisphosphonium dichlorides 90-94 [characterized as bis(hexafluorophosphates) 95-99]. Cyclization of open-chain bisphosphonium salts in presence of 115% PPA produced 100-104 which always displayed two ^{31}P NMR signals arising from the racemic- and meso-forms in solution.

Treatment of bis(diphenylphosphino)methane (105) with 1-chloro-3-methyl-2-butene, following the same procedure as discussed previously, gave only the mono-alkylated product 106, possibly due to steric hindrance of the trigonal phosphorus atom by the quaternized P atom. Even an excess of the reagent, longer reaction periods and using a high boiling solvent like toluene or xylene did not produce the dialkylated

product. The mono-chloride 106 (converted to and characterized as 107) did cyclize, however, to 108. Dialkylation of 105 to 109 was finally

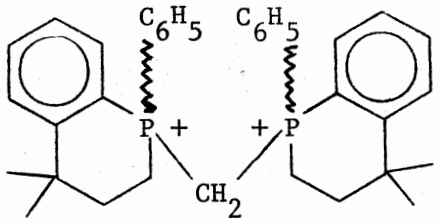


achieved with 1-bromo-3-methyl-2-butene, although the reaction time was long (10 days). Cyclization of the dibromide 109 (characterized as 110) with 115% PPA at 205°C for one hour gave 111.



109 X = Br

110 X = PF_6



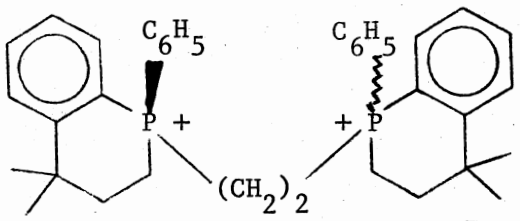
111

Using our general procedure, diquaternization of bisphosphine 85 with allyl bromide led to 112 and, with 5-bromo-1-pentene, produced 113 (characterized as 114). Similarly, diquaternization of 87 with 4-bromo-1-butene gave 115 (characterized as 116). When these compounds were subjected to our general cyclization procedure, several unusual observations were made as a result of the formation of several isomers.

$$\left[(C_6H_5)_2\overset{+}{P}\text{-}(CH_2)_n\text{-}\overset{+}{P}(C_6H_5)_2 \right] , \; 2\ X^-$$

112	n = 2;	R = $-CH_2-CH=CH_2$;	X = Br
113	n = 2;	R = $-CH_2-CH_2-CH_2-CH=CH_2$;	X = Br
114	n = 2;	R = $-CH_2-CH_2-CH_2-CH=CH_2$;	X = PF_6
115	n = 4;	R = $-CH_2-CH_2-CH=CH_2$;	X = Br
116	n = 4;	R = $-CH_2-CH_2-CH=CH_2$;	X = PF_6

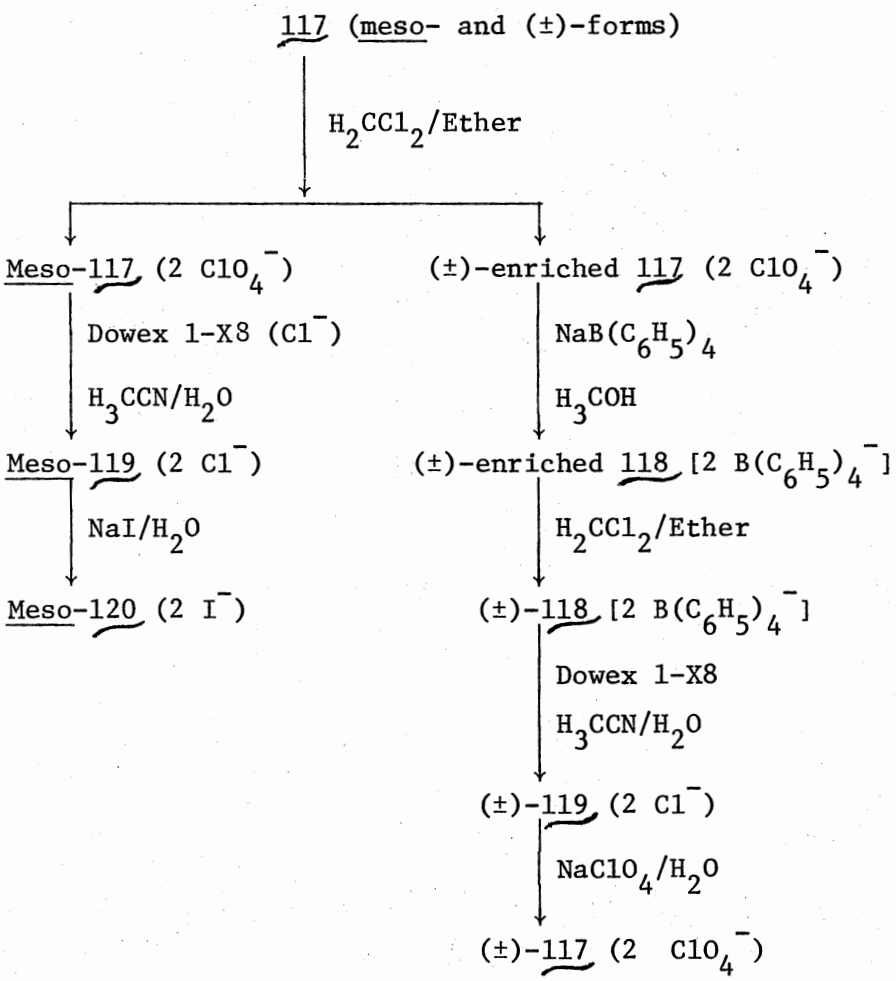
For the separation of diastereomers, it proved beneficial to prepare the diperchlorate 117. Cyclization of 90 in the presence of 115% PPA at 180°C for one hour, followed by treatment with saturated aqueous $NaClO_4$, resulted in the formation of a mixture of racemic- and meso- forms of 117. Fractional crystallization of the mixture of



, 2 X^-

117	X = ClO_4	120	X = I
118	X = $B(C_6H_5)_4$	121	X = L(+)HDBT
119	X = Cl	122	X = D(-)HDBT

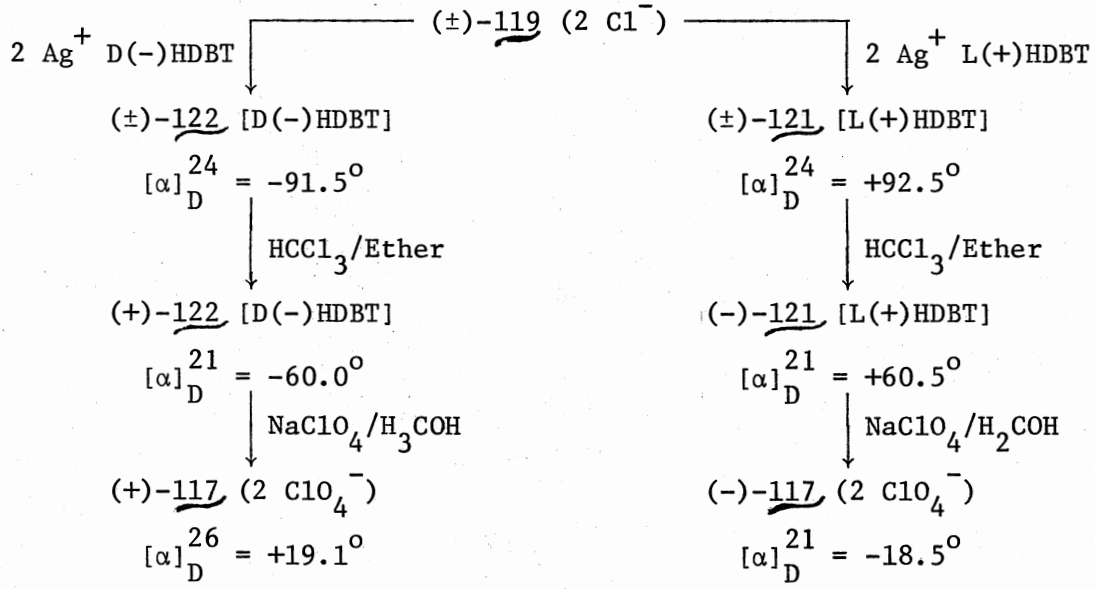
diperchlorates 117 with H_2CCl_2-ether resulted in the separation of the much less soluble meso-117 (outlined below). Treatment of the other fraction, highly enriched with the racemic-117, with a methanol solution of sodium tetraphenylborate gave enriched (±)-118 (tetraphenyl-



borate). Fractional crystallization of the crude racemic-enriched mixture with H_2CCl_2-ether was successful and (±)-118 was separated in pure form. Both meso-117 and (±)-118 were converted into the respective dichlorides, meso-119 and (±)-119, via passage through a column of Dowex 1-X8 (Cl^-). Further proof of the structure for meso-119 was obtained through metathesis and characterization of the diiodide, meso-120, whereas (±)-119 was converted to and characterized as the

diperchlorate, (±)-117. The ^{31}P NMR analysis was advantageously used to monitor the separation of diastereomers.

Efforts were expended to resolve the new dissymmetric C-P enantiomers of (±)-119. Partial resolution was achieved by using silver hydrogen D(-)- and L(+)-dibenzoyltartrates (HDBT) as the resolving agents (outlined below) and monitoring the process via ^{31}P NMR

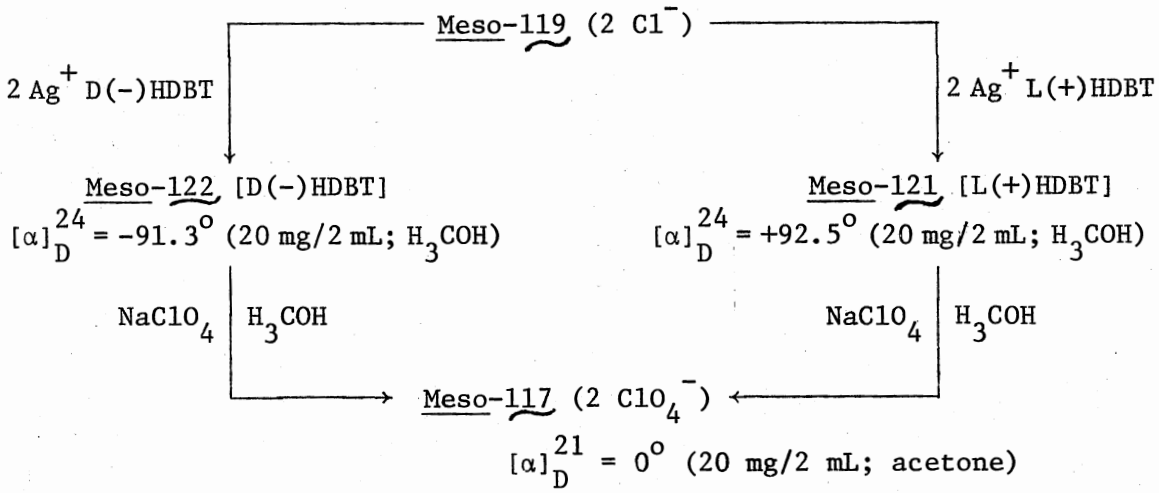


spectroscopy. Metathesis of (±)-119 with Ag L(+)-HDBT in methanol gave a mixture of diastereomers from which it was possible to fractionally crystallize ($HCCl_3$-ether) out in pure form (-)-121 [L(+)HDBT; mp 151-153°C (d); $[\alpha]_D^{21} = +60.5°$ (c = 1.0 g/100 mL; H_3COH)]. Following the same procedure, (+)-122 [D(-)HDBT] was isolated and had a mp 147.5-149°C (d) and $[\alpha]_D^{20} = -60.0°$ (c = 1.0 g/100 mL; H_3COH). The inclusion of 1 equiv. of water was found (as revealed by elemental analysis) in the crystalline (+)-122 [D(-)HDBT].

Metathesis of (+)-122 [D(-)HDBT] with $NaClO_4$ in H_3COH resulted in the formation of the enantiomer (+)-117, mp 263-264.5°C; $[\alpha]_D^{21} = +19.1°$;

(c, 1.0 g/100 mL; acetone). Following the same procedure, the other enantiomer (-)-117 was isolated and had a mp 262.5-264°C and $[\alpha]_D^{21}$ = -18.5° (c = 1.0 g/100 mL; acetone). This is the first example of a resolution of C-P heterocycles involving a bisphosphonium salt.

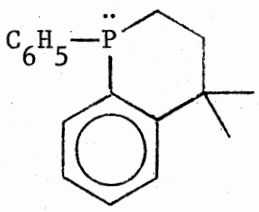
Then meso-119 (2 Cl^-) was subjected to similar experiments as employed in the resolution of (±)-119. The diastereomers meso-121 [L(+)HDBT] and meso-122 [D(-)HDBT] upon metathesis with $NaClO_4$ in



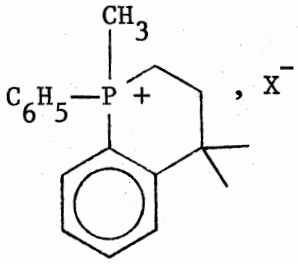
H_3COH, gave the same meso-117 (2 ClO_4^-) with a rotation of 0° as expected. Elemental analysis revealed the inclusion of one mole of water in the crystalline meso-121 [L(+)HDBT] but not in meso-122 [D(-)HDBT].

In view of the lack of work in the area and the scarcity of model systems, chemical degradation of 1,1'-(α,ω-alkanediyl)bis[1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium] salts was investigated via basic hydrolysis studies and a single crystal analysis of one member of the family via X-ray diffraction. Thus, meso-119 (2 Cl^-) in methanol was mixed with aqueous NaOH and boiled. Assuming attack by hydroxide ion on one phosphorus atom, loss of ethylene apparently

occurred with concomitant formation of the phosphine 123 isolated as the methiodide 124 (converted to and identified as 125). In addition

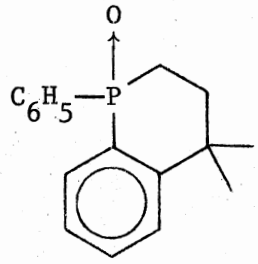


123



124 X = I

125 X = PF_6



126

phosphine oxide 126 was isolated. Moreover, reduction of meso-119 (2 Cl^-) in dry THF with $LiAlH_4$ or NaH gave the phosphine 123 which was converted to salt 124 and characterized as 125, but all in low yields.

An X-ray diffraction examination of meso-117 (2 ClO_4^-) provided unequivocal evidence for its structure and was supportive of our general postulated structures of the 1,1'-(α,ω-alkanediyl)bis[1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium] salts. This work is also the first for this family. Moreover, the structures of all new materials described herein are supported by IR, ^1H NMR and ^{31}P NMR data listed in Tables I-IV in addition to elemental analyses found in the Experimental Section.

Diquaternization of α,ω-Bis(diphenylphosphino)-alkanes (85-89 and 105)

Several synthetic methods have been employed for the preparation of quaternary phosphonium compounds but the most widely used process is the Menshutkin-type reaction of a phosphine with a compound RX (R = H, alkyl

TABLE I

IR AND ^{31}P NMR SPECTRAL DATA FOR OPEN-CHAIN BISPHOSPHONIUM SALTS

Compd	IR Spectra in KBr Pellets[a]		^{31}P NMR Spectra[b]	
	Plate	Selected bands, cm^{-1}	Plate	ppm[c]
95	I	1440(s), 1120(vs), 997(m), 845(br), 730(vs), 690(vs)	LVII	+26.48
96	II	1438(s), 1122(vs), 997(m), 844(br), 735(vs), 688(vs)	LVIII	+23.81
97	III	1442(vs), 1118(vs), 1001(m), 844(br), 743(vs), 692(vs)	LIX	+24.63
98	IV	1442(vs), 1118(vs), 1001(m), 844(br), 743(vs), 690(vs)	LX	+23.76
99	V	1442(vs), 1118(vs), 999(m), 844(br), 742(vs), 689(vs)	LXI	+24.36
107[d]	VI	1440(vs), 1115(vs), 999(m), 844(br), 742(vs), 689(vs)	LXII	+23.80 (d, J_{PCP} = 66.80 Hz); -30.18 (d, J_{PCP} = 66.08 Hz)
110	VII	1439(vs), 1114(vs), 998(m), 844(br), 744(s), 685(vs)	LXIII	+19.97
112	VIII	1440(vs), 1118(vs), 998(m), 738(vs), 691(vs)	LXIV	+26.79
114	IX	1440(vs), 1118(vs), 998(m), 844(br), 741(vs), 689(vs)	LXV	+29.77
116	X	1438(vs), 1118(vs), 997(m), 844(br), 743(vs), 688(vs)	LXVI	+26.56

[a]Abbreviations used for IR spectral data are: s, strong; vs, very strong; w, weak; m, medium; br, broad.

[b]^{31}P NMR Spectra obtained in $DCCl_3$ with 1-2 drops of CF_3CO_2H added, unless otherwise specified.

[c]^{1}H decoupled ^{31}P resonance in ppm relative to 85% H_3PO_4 standard external.

[d]^{31}P NMR Spectrum obtained in DMSO-d_6. The trigonal phosphorus in 107 has a value of -30.18 ppm and the quaternary phosphorus has a value of +23.80 ppm.

TABLE II

^{1}H NMR CHEMICAL SHIFTS AND COUPLING CONSTANTS FOR OPEN-CHAIN BISPHOSPHONIUM SALTS[a]

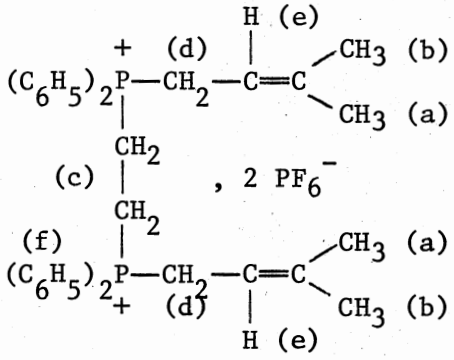
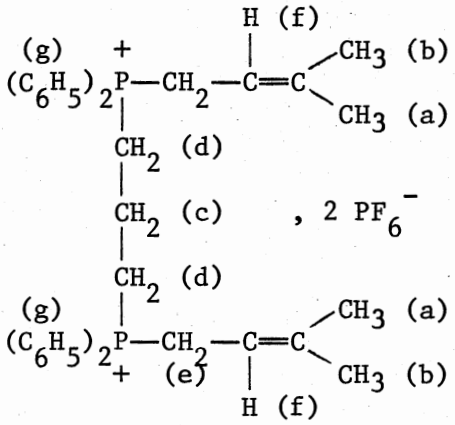
Structure	Compd.	Plate	δ values from TMS[b]	Assignments
	95	XXIX	1.08 (s, 6 H)	CH_3 (a)
			1.60 (s, 6 H)	CH_3 (b)
			2.76-3.26 (m, 4 H)	CH_2-CH_2 (c)
			3.32-3.84 (dd, 4 H, J_{PCH} = 13, J_{HCCH} = 8 Hz)	CH_2 (d)
			4.64-5.02 (m, 2 H)	CH (e)
			7.30-8.04 (m, 20 H)	Ar-H (f)
	96	XXX	1.09 (d, 6 H, J_{PH} = 3.5 Hz)	CH_3 (a)
			1.63 (d, 6 H, J_{PH} = 5.5 Hz)	CH_3 (b)
			1.42-1.92 (m, 2 H), overlapped with CH_3	CH_2 (c)
			2.70-3.16 (m, 4 H)	CH_2 (d)
			3.22-3.62 (dd, 4 H, J_{PCH} = 13, J_{HCCH} = 8 Hz)	CH_2 (e)
			4.68-5.02 (m, 2 H)	CH (f)
			7.32-7.96 (m, 20 H)	Ar-H (g)

TABLE II (Continued)

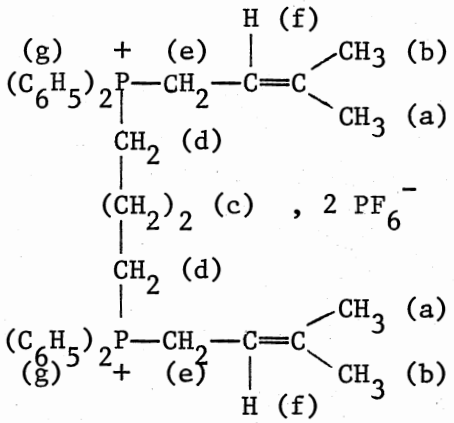
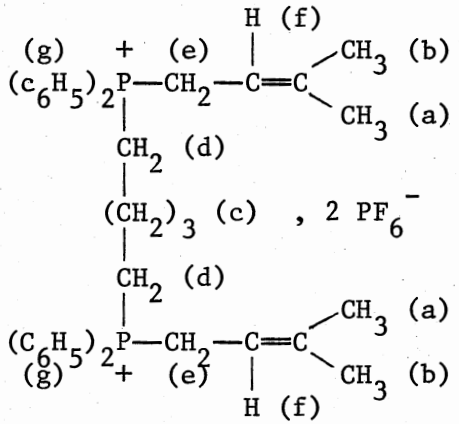
Structure	Compd.	Plate	δ values from TMS[b]	Assignments
	97	XXXI	1.16 (d, 6 H, J_{PH} = 3.5 Hz)	CH_3 (a)
			1.63 (d, 6 H, J_{PH} = 5.5 Hz)	CH_3 (b)
			1.44-1.96 (m, 4 H), overlapped with CH_3	CH_2 (c)
			2.56-3.04 (m, 4 H)	CH_2 (d)
			3.30-3.72 (dd, 4 H) J_{PCH} = 13, J_{HCCH} = 8 Hz)	CH_3 (e)
			4.78-5.06 (m, 2 H)	CH (f)
			7.30-7.94 (m, 20 H)	Ar-H (g)
	98	XXXII	1.16 (d, 6 H, J_{PH} = 3.5 Hz)	CH_3 (a)
			1.65 (d, 6 H, J_{PH} = 5.5 Hz)	CH_3 (b)
			1.25-1.80 (m, 6 H), overlapped with CH_3	CH_2 (c)
			2.44-2.94 (m, 4 H)	CH_2 (d)
			3.26-3.58 (dd, 4 H, J_{PCH} = 13, J_{HCCH} = 8 Hz)	CH_2 (e)
			4.76-5.04 (m, 2 H)	CH (f)
			7.36-7.94 (m, 20 H)	Ar-H (g)

TABLE II (Continued)

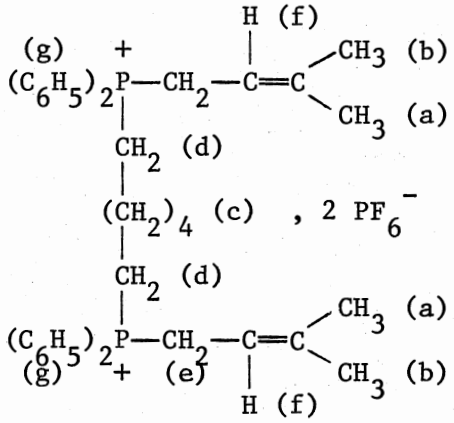
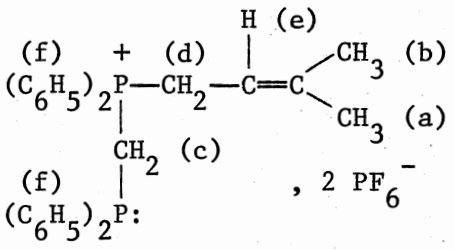
Structure	Compd.	Plate	δ values from TMS[b]	Assignments
	99	XXXIII	1.20 (d, 6 H, J_{PH} = 3.5 Hz)	CH_3 (a)
			1.66 (d, 6 H, J_{PH} = 5.5 Hz)	CH_3 (b)
			1.28-1.58 (m, 8 H), overlapped with CH_3	CH_2 (d)
			2.4-2.88 (m, 4 H)	CH_2 (d)
			3.24-3.63 (dd, 4 H, J_{PCH} = 13, J_{HCCH} = 8 Hz)	CH_2 (e)
			4.76-5.10 (m, 2 H)	CH (f)
			7.43-7.90 (m, 20 H)	Ar-H (g)
	107[c]	XXXIV	1.22 (d, 3 H, J_{PH} = 3.5 Hz)	CH_3 (a)
			1.59 (d, 3 H, J_{PH} = 5.5 Hz)	CH_3 (b)
			3.36-3.62 (d, 2 H, J_{PCH} = 13 Hz)	CH_2 (c)
			3.48-3.78 (dd, 2 H, J_{PCH} = 13, J_{HCCH} = 8 Hz), overlapped with CH_2 (c)	CH_2 (d)
			4.70-5.00 (m, 1 H)	CH (e)
			7.20-7.84 (m, 20 H)	Ar-H (f)

TABLE II (Continued)

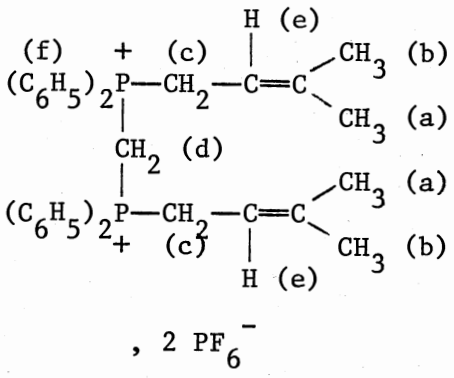
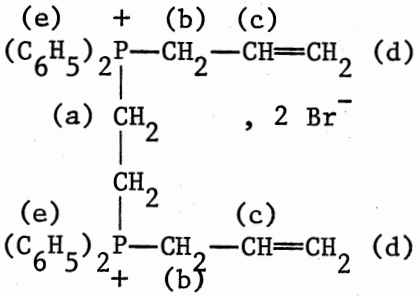
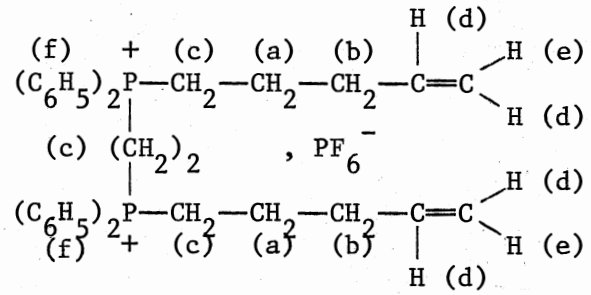
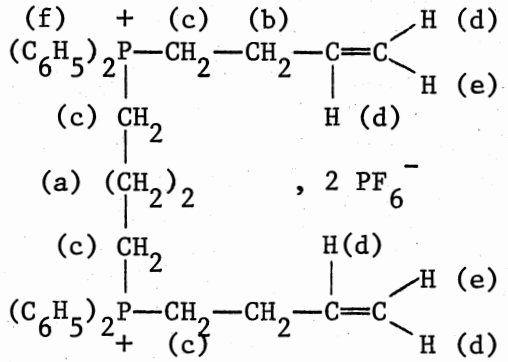
Structure	Compd.	Plate	δ values from TMS[b]	Assignments
	110	XXXV	0.88 (d, 6 H, J_{PH} = 3.5 Hz)	CH_3 (a)
			1.53 (d, 6 H, J_{PH} = 5.5 Hz)	CH_3 (b)
			2.98-3.32 (dd, 4 H, J_{PCH} = 13, J_{HCCH} = 8 Hz)	CH_2 (c)
			4.60-5.01 (t, 2 H, J_{PCH} = 15 Hz)	CH_2 (d)
			4.60-5.01 (m, 2 H), overlapped with CH_2 (d)	CH (e)
			7.48-8.04 (m, 20 H)	Ar-H (f)
	112	XXXVI	3.18-3.58 (m, 4 H)	CH_2CH_2 (a)
			4.02-4.44 (dd, 4 H, J_{PCH} = 13, J_{HCCH} = 8 Hz)	CH_2 (b)
			5.04-5.60 (m, 6 H)	CH (c) CH_2 (d)
			7.44-8.10 (m, 20 H)	Ar-H (e)

TABLE II (Continued)

Structure	Compd.	Plate	δ values ppm from TMS[b]	Assignments
	114	XXXVII	1.16-1.64 (m, 4 H)	CH_2 (a)
			1.94-2.28 (m, 4 H)	CH_2 (b)
			2.62-3.08 (m, 8 H)	CH_2 (c)
			4.82-5.11 (m, 4 H)	CH (d)
			5.22-5.79 (m, 2 H)	CH (e)
			7.46-8.02 (m, 20 H)	Ar-H (f)
	116	XXXVIII	1.50-1.92 (m, 4 H)	CH_2 (a)
			2.02-2.44 (m, 4 H)	CH_2 (b)
			2.58-3.04 (m, 8 H)	CH_2 (c)
			4.92-5.28 (m, 4 H)	CH (d)
			5.42-5.96 (m, 2 H)	CH (e)
			7.48-7.93 (m, 20 H)	Ar-H (f)

[a]Spectra obtained in $DCCl_3$ with 1-2 drops of CF_3CO_2H added unless otherwise specified.

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

[c]Spectra obtained in DMSO-d_6.

TABLE III

IR AND ^{31}P NMR SPECTRAL DATA FOR CYCLIC PRODUCTS

Compd.	IR Spectra in KBr Pellets[a]		^{31}P NMR Spectra[b]	
	Plate	Selected bands, cm^{-1}	Plate	ppm[c]
100	XI	1441(vs), 1114(vs), 1000(m), 844(br), 741(vs), 688(vs)	LXVII	+15.09; +16.03
101	XII	1440(vs), 1116(vs), 998(m), 844(br), 739(vs), 690(vs)	LXVIII	+12.50; +12.92
102	XIII	1440(vs), 1118(vs), 998(m), 844(br), 741(vs), 690(s)	LXIX	+13.28; +13.37
103	XIV	1442(vs), 1119(vs), 1001(m), 844(br), 752(vs), 691(s)	LXX	+13.02; +13.08
104	XV	1442(vs), 1119(vs), 1000(m), 844(br), 752(vs), 692(s)	LXXI	+13.91; +13.96
108[d]	XVI	1438(vs), 1110(vs), 999(s), 844(br), 740(vs), 688(vs)	LXXII	+21.24 (d, J_{PCP} = 10.6 Hz); +30.03 (d, J_{PCP} = 10.6 Hz).
111	XVII	1438(vs), 1110(vs), 994(vs), 844(br), 745(vs), 692(vs)	LXXIII	+10.01; +11.25
meso-117	XIX	1439(vs), 1111(vs), 1085(br), 745(vs), 689(s), 624(s)	LXXV	+14.85
(±)-117	XX	1438(vs), 1085(br), 998(m), 730(s), 688(s), 622(vs)	LXXVI	+15.93
(+)-117	XXI	1439(vs), 1085(br), 998(m), 750(s), 690(s), 622(vs)	LXXVII	+16.04
(-)-117	XXII	1438(vs), 1085(br), 998(m), 730(s), 689(s), 622(vs)	LXXVIII	+16.03
(±)-118	XXIII	1439(s), 1112(s), 998(m), 732(vs), 705(vs), 688(s), 611(vs)	LXXIX	+16.24
meso-120	XXIV	1438(vs), 1115(vs), 744(s), 998(m), 689(vs)	LXXX	+15.13
(-)-121[e]	XXV	1725(vs), 1438(s), 1114(vs), 689(m), 614(vs)	LXXXII	+16.97
meso-121[e]	XXVI	1724(vs), 1439(m), 1112(vs), 998(m), 689(m), 615(vs)	LXXXIII	+15.62 +15.58

TABLE III(Continued)

Compd.	IR Spectra in KBr Pellets[a]		^{31}P NMR Spectra[b]	
	Plate	Selected bands, cm^{-1}	Plate	ppm[c]
(+)-122[e]	XXVI	1724(vs), 1439(m), 1112(vs), 998(w), 689(m), 615(vs)	LXXXIII	+16.90
meso-122[e]	XXVIII	1724(vs), 1440(m), 1112(vs), 998(m), 689(m), 615(vs)	LXXXIV	+15.54 +15.51

[a]Abbreviations used for IR spectral data are: s, strong; vs, very strong; w, weak; m, medium; br, borad.

[b]^{31}P NMR Spectra obtained in $DCCl_3$ with 1-4 drops of CF_3CO_2H added unless otherwise specified.

[c]^{1}H decoupled ^{31}P resonance in ppm relative to 85% H_3PO_4 standard external.

[d]^{31}P NMR Spectrum obtained in DMSO-d_6.

[e]^{31}P NMR Spectra obtained in $DCCl_3$.

TABLE IV

^{1}H NMR CHEMICAL SHIFTS AND COUPLING CONSTANTS FOR CYCLIC PRODUCTS[a]

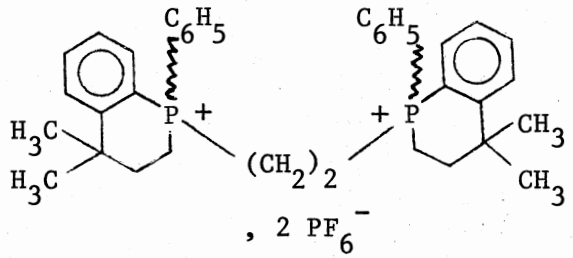
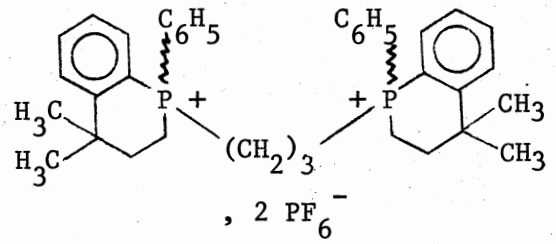
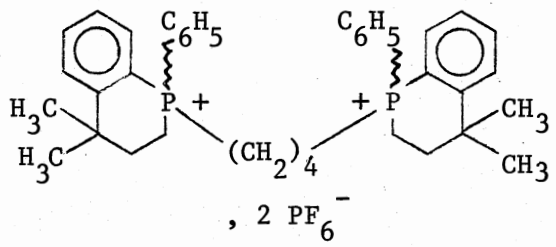
Structure	Compd.	Plate	δ values from TMS[b]	Assignments
	100	XXXIX	1.39 (s, 12 H)	CH_3
			1.82-3.25 (m, 12 H)	CH_2
			7.36-7.96 (m, 18 H)	Ar-H
	101	XL	1.14-1.48 (m, 12 H)	CH_3
			1.66-3.38 (m, 14 H)	CH_2
			7.34-7.98 (m, 18 H)	Ar-H
	102	XLI	1.40 (s, 12 H)	CH_3
			1.50-3.20 (m, 16 H)	CH_2
			7.28-7.92 (m, 18 H)	Ar-H

TABLE IV (Continued)

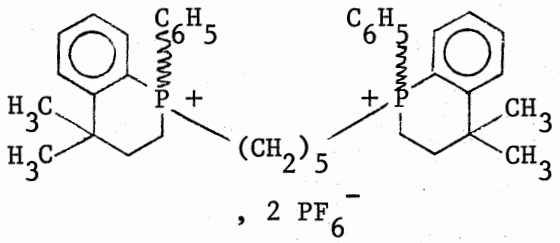
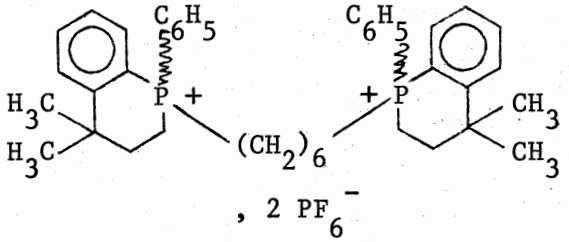
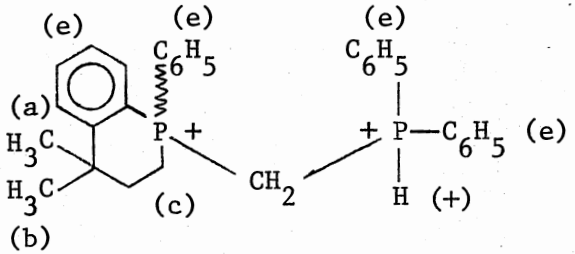
Structure	Compd.	Plate	δ values from TMS[b]	Assignments
	103	XLII	1.14-3.84 (m, 12 H)	CH_3
			1.14-3.84 (m, 18 H), overlapped with CH_3	CH_2
			7.32-7.98 (m, 18 H)	Ar-H
	104	XLIII	1.43 (s, 12 H)	CH_3
			1.14-3.08 (m, 20 H) overlapped with CH_3	CH_2
			7.38-8.06 (m, 18 H)	Ar-H
	108[c,e]	XLIV	1.58 (s, 3 H)	CH_3 (a)
			1.75 (s, 3 H)	CH_3 (b)
			2.8-3.98 (m, 4 H)	CH_2-CH_2 (c)
			4.73 (t, 2 H, J_{PCH} = 13 Hz)	CH_2 (d)
			7.42-8.04 (m, 20 H)	Ar-H (e) P-H (f)

TABLE IV (Continued)

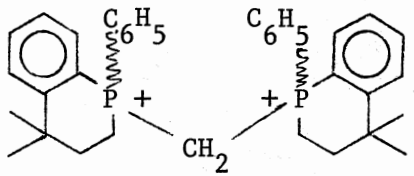
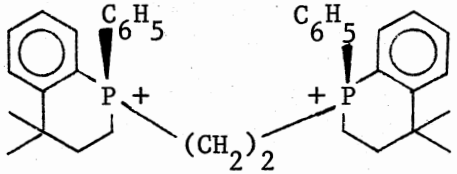
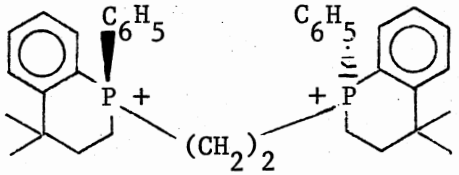
Structure	Compd.	Plate	δ values from TMS[b]	Assignments
 , 2 PF_6^-	111[d]	XLV	0.99-1.40 (m, 12 H)	CH_3
			1.48-3.62 (m, 10 H)	CH_2
			7.12-7.96 (m, 18 H)	Ar-H
 , 2 ClO_4^-	meso-117	XLVII	1.39 (d, 12 H), two singlets overlapped into a doublet	CH_3
			1.62-3.38 (m, 12 H)	CH_2
			7.38-8.04 (m, 18 H)	Ar-H
 , 2 ClO_4^-	(±)-117	XLVIII	1.39 (d, 12 H), two singlets overlapped into a doublet	CH_3
			1.72-3.74 (m, 12 H)	CH_2
			7.30-8.04 (m, 18 H)	Ar-H

TABLE IV (Continued)

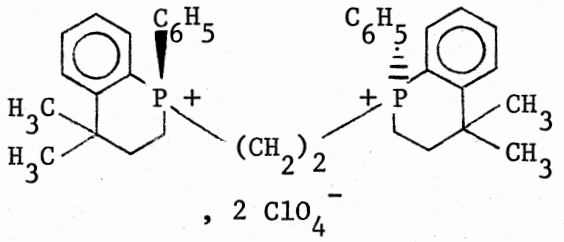
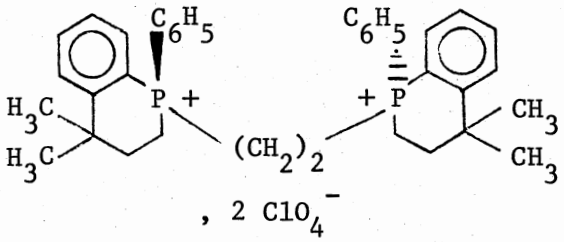
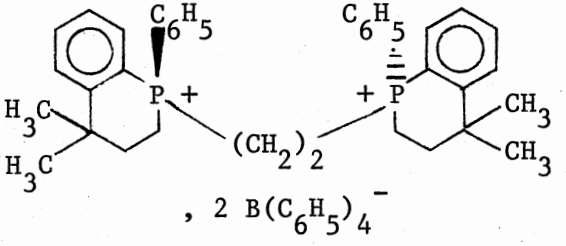
Structure	Compd.	Plate	δ values from TMS[b]	Assignments
	(+)-117	XLIX	1.38 (d, 12 H), two singlets overlapped into a doublet	CH_3
			1.70-3.64 (m, 12 H)	CH_2
			7.44-8.02 (m, 18 H)	Ar-H
	(-)-117	L	1.38 (d, 12 H), two singlets overlapped into a doublet	CH_3
			1.72-3.64 (m, 12 H)	CH_2
			7.44-8.05 (m, 18 H)	Ar-H
	(±)-118	LI	1.39 (s, 12 H)	CH_3
			1.48-3.94 (m, 12 H)	CH_2
			7.26-8.00 (m, 58 H)	Ar-H

TABLE IV (Continued)

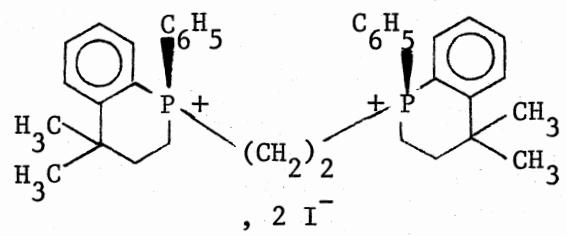
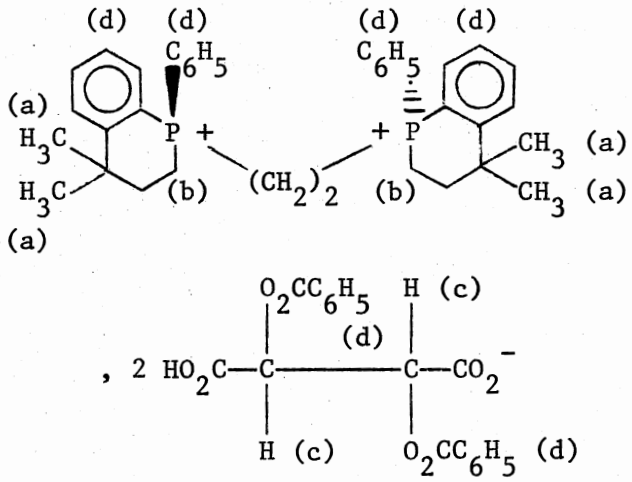
Structure	Compd.	Plate	δ values from TMS[b]	Assignments
	meso-120	LII	1.40 (d, 12 H), two singlets overlapped into a doublet	CH_3
			1.58-3.62 (m, 12 H)	CH_2
			7.42-8.38 (m, 18 H)	Ar-H
	(-)-121[d]	LIII	1.32 (d, 12 H), two singlets overlapped into a doublet	CH_3 (a)
			1.50-4.42 (m, 12 H)	CH_2 (b)
			5.78 (s, 4 H)	CH (c)
			7.02-8.18 (m, 28 H)	Ar-H (d)

TABLE IV (Continued)

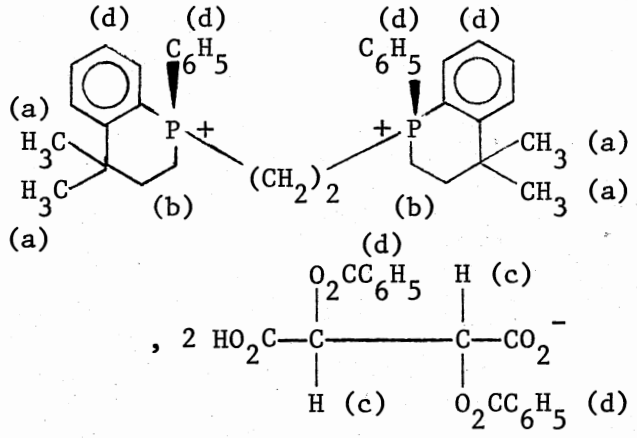
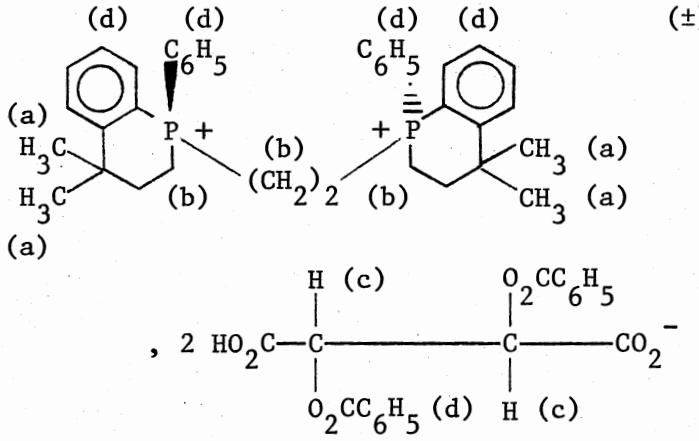
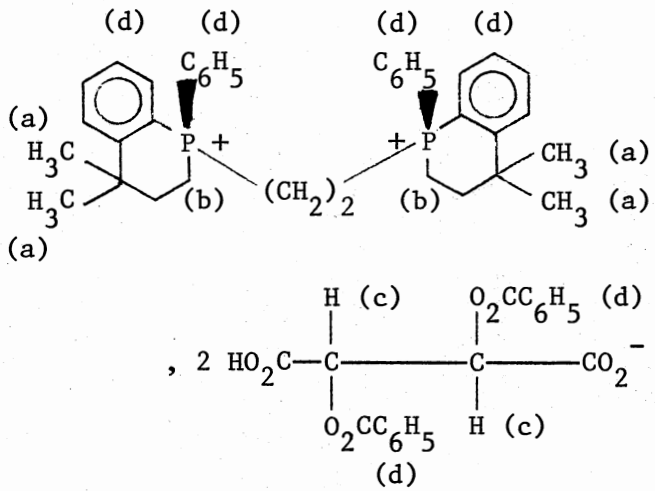
Structure	Compd.	Plate	δ values from TMS[b]	Assignments
	meso-121[d]	LIV	1.22 (s, 12 H)	CH_3 (a)
			1.48-3.88 (m, 12 H)	CH_2 (b)
			5.78 (s, 4 H)	CH (c)
			7.12-8.34 (m, 28 H)	Ar-H (d)
	(±)-122[d]	LV	1.24 (d, 12 H) two singlets overlapped into a doublet	CH_3 (a)
			1.54-4.58 (m, 12 H)	CH_2 (b)
			5.81 (s, 4 H)	CH (c)
			7.10-8.26 (m, 28 H)	A-H (d)

TABLE IV (Continued)

Structure	Compd.	Plate	δ values from TMS[b]	Assignments
	meso-122[d]	LVI	1.23 (s, 12 H)	CH_3 (a)
			1.48-3.84 (m, 12 H)	CH_2 (b)
			5.79 (s, 4 H)	CH (c)
			6.96-8.32 (m, 28 H)	Ar-H (d)

[a] All spectra obtained in $DCCl_3$ with 1-4 drops of CF_3CO_2H added unless otherwise specified.

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

[c] Spectra obtained in DMSO-d_6.

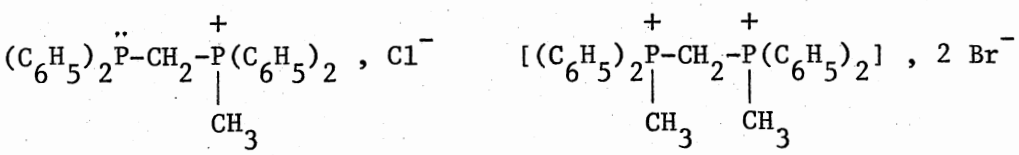
[d] Spectra obtained in $DCCl_3$.

[e] The assignments of CH_3 protons may be interchangeable.

or acyl group; Y = halogen or acyl group).[5] Commercially available bisphosphines 85-89 and 105 were used in direct quaternizations with selectively substituted allylic halides to form the open-chain bisphosphonium salts 90-94 and 109. These bisphosphonium salts possess the capability for conversion into C-P heterocycles via the use of 115% PPA.[43,110]

Reaction of one equivalent of bis(diphenylphosphino)alkane 85-89 with more than two equivalents of 1-chloro-3-methyl-2-butene at 80°C in benzene under N_2 for a period of 44 hours afforded the symmetrically substituted bisphosphonium dichlorides 90-94 (66-98%). The elemental analyses strongly implied the hygroscopic nature of the dichlorides. Therefore, these salts were converted into the corresponding bis(hexafluorophosphates) 95-99 (via metathesis with aqueous KPF_6 at room temperature in H_3COH) for characterization. However, following the same procedure, bis(diphenylphosphino)methane (105) and 1-chloro-3-methyl-2-butene gave only the monoalkylated product 106 (characterized as 107). Attempts to effect dialkylation of 105 using excess 1-chloro-3-methyl-2-butene for longer reaction period (96 h) at the boiling temperature of different solvents (benzene, toluene and xylene) gave no indication of formation of dialkylated product as revealed by ^{31}P NMR analysis. The reluctance of 105 to form a dialkylated product may possibly be due to steric hindrance to the approaching electrophile or to the decreased basicity of phosphino moiety of the monoalkylated product 106. The electron-withdrawing effect of $>\overset{+}{P}<$ which is in close proximity to the phosphino moiety in 106 reduces the effectiveness of the latter to displace a poor leaving group like Cl^- in an S_N2 reaction. Hussian and Schmidbaur[75] reported similarly a type of monoalkylation of

105 with methyl chloride giving 127 even in sealed tube, but they were



127 128

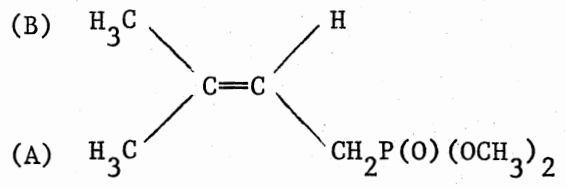
able to prepare the dialkylated product 128 with methyl bromide. Using 1-bromo-3-methyl-2-butene in benzene at 80°C, diquaternization of 105 was attained after 10 days. This reaction was monitored by ^{31}P NMR analysis. Only after 10 days did the reaction product show a lone ^{31}P NMR signal corresponding to the symmetric dibromide 109 (99%).

Numerous solvent systems have been recorded for the purification of phosphonium salts.[5] We found that the most successful method involved dissolution of the bisphosphonium salt in a minimum amount of H_2CCl_2 followed by addition of anhydrous diethyl ether until the solution became cloudy. Reprecipitation of the salt resulted when the solution was allowed to stand at room temperature or by scratching the sides of the flask with a spatula. When H_3CCN or H_3COH was used for purification, great difficulty was encountered in removing the last traces of solvent. Since phosphonium salts tend to be hygroscopic, water was excluded in all solvents employed.

The IR absorptions of all the open-chain bisphosphonium salts in this study listed in Table I are in excellent agreement with data on simple systems tabulated in a survey done by Witchard and Griffin.[143] Characteristic maxima at 1430-1440 and 1110-1120 cm^{-1} have been assigned to the H_5C_6-P bond.[124] It is thought[143] that the absorption in the range 1430-1440 cm^{-1} is due to a vibration arising from the deformation

of planarity of the phenyl ring bonded to a heavy atom (phosphorus). The very strong absorption at 844 cm^{-1} has been assigned to a PF_6 anion.

The ^1H decoupled ^{31}P NMR data and the ^1H NMR shifts for open-chain bisphosphonium salts are condensed in Tables I and II. All 2-butenylphosphonium salts exhibited a doublet of doublets in the ^1H NMR spectrum corresponding to the methylene protons adjacent to phosphorus ($P-C\underline{H}_2-CH=$). This phenomenon was not observed in 114 and 116 containing 4-alkenyl and 3-alkenyl substituents. We would expect to see a doublet for the methyl protons in the ^1H NMR spectrum of 2-butenylphosphonium salts 94-99, 107 and 110. Of course, these compounds exhibited a doublet of doublets for methyl protons due to long range J_{P-H} coupling.[59] In the ^{31}P decoupled ^1H NMR spectra of these compounds, the doublet of doublets collapsed to a lone doublet (Plate



J_{PH}

H_A; 4.2 c.p.s.

H_B; 5.4 c.p.s.

XXXI), confirming the coupling of methyl protons with phosphorus.

Several reviews concerning ^{31}P NMR spectra of organophosphorus compounds have been published.[61,96,112] Each symmetrically substituted bisphosphonium salt in our work showed a single peak as expected for phosphorus nuclei in 95-99. The ^{31}P chemical shift differences for these salts are relatively small and these values compare very well with those of many open-chain bisphosphonium salts such as 1,3-propanediylbis(triphenylphosphonium)dibromide, + 23.2 ppm.[62] An AB spectrum was observed for the unsymmetrical molecule 107 containing two nonidentical P nuclei with $^2J_{PCP}$ = 66.08 Hz. The PF_6 anion has

value at -143.99 ppm and -143.92 ppm in 97 and 107, respectively, compared to KPF_6 in H_2O (all compared to 85% H_3PO_4 standard-external) which has a value of +144.68 ppm.

Synthesis of 1,1'-(α,ω-Alkanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hexafluorophosphates(1-)] (100-104 and 111) and 1-[(Diphenylphosphonio)methyl]-1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium Bis[hexafluorophosphate(1-)] (108)

Polyphosphoric acid (PPA) has been widely used in the annulation of a variety of heterocyclic systems.[83] Several reviews[108,128] have illustrated the broad range of functional groups which can be treated by this reagent to promote cyclization. The versatility of PPA arises from the fact that its mild action seldom causes charring of organic compounds, although it is a strong dehydrating agent. Moreover, PPA does not cause phosphonation of aromatic compounds under many reported conditions and structural rearrangements are at a minimum. In addition, PPA solutions can be heated to over 300°C and are easily decomposed by pouring into ice-water. This reagent is often one of the choices over such reagents as sulfuric acid, hydrogen fluoride, phosphoric anhydride, aluminium chloride and methanesulfonic acid for cyclization reactions.[83]

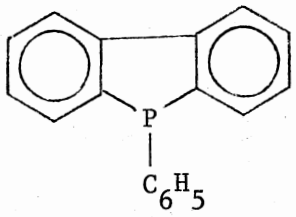
Our cyclizations were performed via the use of a special 115% PPA that was commercially available from the FMC Corporation[123] through the generosity of Mr. J. P. Cassidy. A partial listing of the composition

of the acid is shown below:

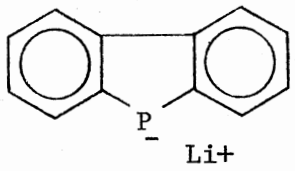
% P_2O_5 in H_3PO_4		Composition of 115% H_3PO_4 from FMC	
% H_3PO_4	% P_2O_5	P_2O_5 %	83.2
115	83.2	P_2O_5 distributed as	
105	76.0	orthophosphoric acid	5%
85	61.5	pyrophosphoric acid	16%
75	54.0	triphosphoric acid	17%
		tetraphosphoric acid	16%
		higher polymer acids	46%

Recent discoveries that β-alkenyl substituted phosphonium salts,[43,110] β-hydroxyalkyl substituted phosphine oxides[28] and ω-carboxyalkylphosphonium salts[130,131] undergo Friedel-Craft's cyclization in PPA have provided new entries to C-P heterocycles. It was found that a preparation of 115% PPA prepared from the addition of P_2O_5 to commercial H_3PO_4 failed to promote a rapid cyclization in all phosphonium salts subjected to a variety of conditions. Thus, the 115% PPA from FMC has properties uniquely required in the synthesis.

Tables of organophosphorus compounds containing two phosphorus atoms have been included in extensive reviews.[5,132] However, very few bisphosphonium salts of the type P-$(CH_2)_n$-P containing two C-P heterocycles have been recorded. For example, alkali metal cleavage of C-P bond in 1-phenyldibenzophospole (129) with an excess of Li in THF at room temperature gave the lithium salt 130. Reaction of 130 with α,ω-dibromoalkanes produced the cyclic bisphosphines 131. Diquaternization

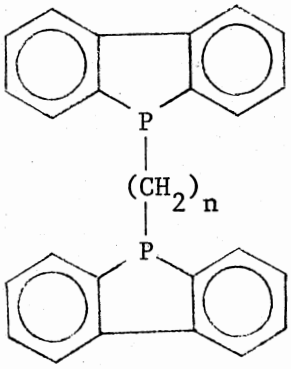


129

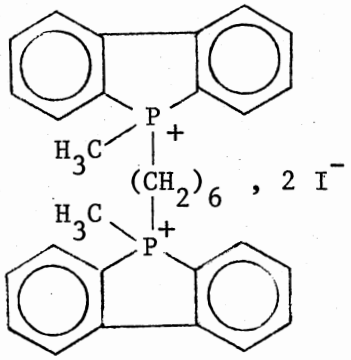


130

of 131 (n = 6) with excess H_3CI in boiling benzene gave 132.[14] The

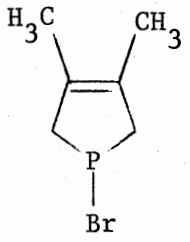


131 (n = 2,6)

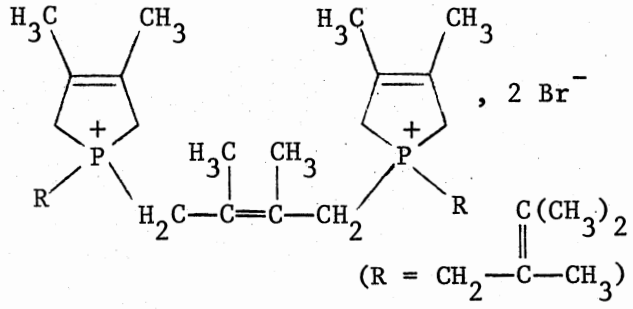


132

bisphosphonium dibromide 134 was obtained as one of the products in the reaction of 1-bromo-3,4-dimethylphosphol-3-ene (133) with the conjugated



133



134

diene 2,3-dimethyl-1,3-butadiene.[95] It is to be noted that in the preparations of 132 and 134 C-P heterocycles are starting materials. However, we elected to extend the scope of the cyclization method

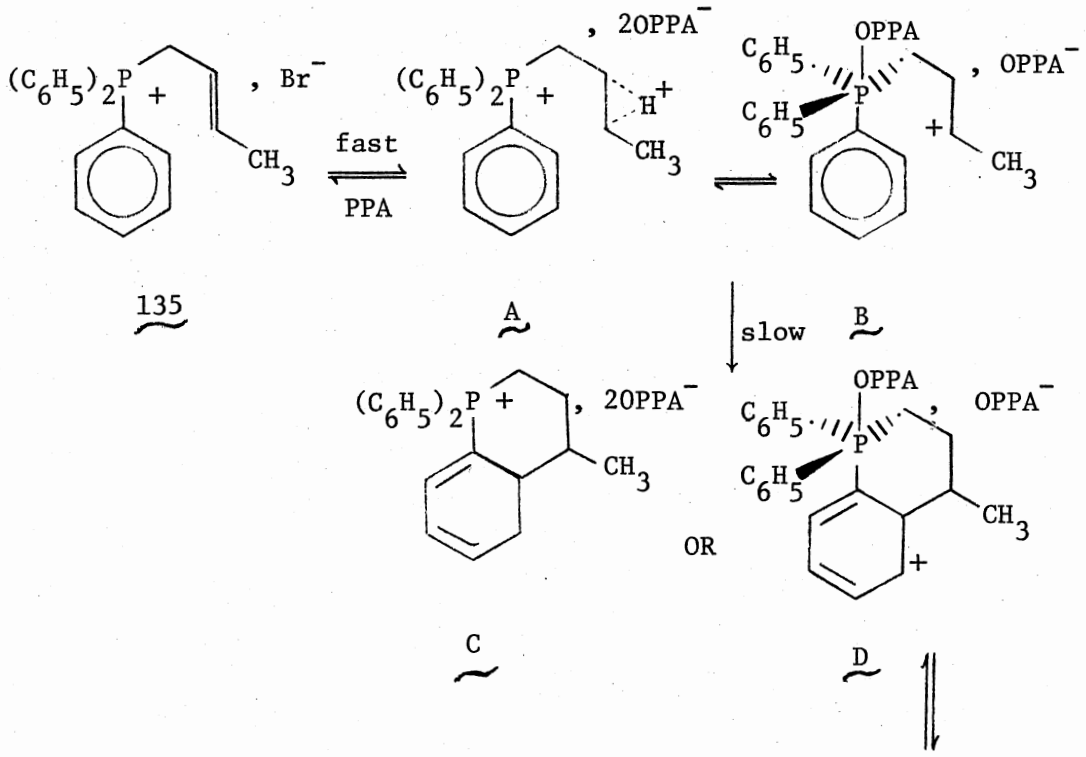
developed in our laboratory[43,110] to prepare the P-$(CH_2)_n$-P systems containing two C-P heterocycles from selectively substituted open-chain bisphosphonium salts because of the difficulty anticipated to obtain other precursors.

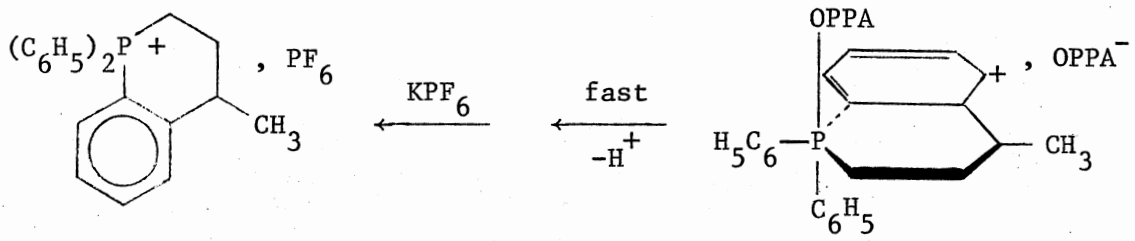
Our general method of cyclization utilized very basic laboratory equipment, moderate reaction conditions and employed a very simple work-up procedure. The standard technique for the cyclization was to add slowly approximately 1 g of β-alkenyl-substituted bisphosphonium salt 90-94 to 115% PPA at 180°C. A gas presumably HCl (dense white fumes with $NH_3 \cdot H_2O$) was given off about 10-15 seconds after the addition of the salt.[43,110] Upon stirring at the same temperature for 1 hour, the reaction mixture turned from colorless to a light green-colored solution. Several authors have noted the formation of intense colors during PPA catalyzed cyclizations and have suggested color development as a means of determining the severity of conditions to be used.[78,127] When the reaction was completed, the golden-colored mixture was cooled to 100-120°C and slowly poured into 200-250 mL of ice-water. Decomposition of the reaction mixture was accomplished by continued stirring which produced a clear homogeneous solution. A precipitation was effected by the addition of a large excess of KPF_6 solution to the reaction mixture. Crude C-P heterocycles 100-104 formed and were purified by the same method employed for the open-chain bisphosphonium salts. Following the same procedure, the chloride 106 was cyclized to give 108 and the dibromide 109 to 111.

The cyclizations of open-chain bisphosphonium salts are not limited to chloride or bromide as the anion of the salt. Other salts with PF_6 anion could be used. The cyclization of bis(hexafluorophosphate) 98 to

103 was achieved by the use of 115% PPA. In earlier work, a variety of reaction temperatures were tested and it was found that at temperatures below 160°C cyclization failed and frequently only a metathesis occurred depending upon the salt added to precipitate the bisphosphonium compound from H_2O. At temperatures above 195°C extensive charring frequently occurred.

Several workers have studied the mechanism of cyclization of β-alkenyl-substituted phosphonium salts in 115% PPA via stereochemical analysis of the products and ^{31}P NMR monitoring of the cyclization process at variable temperatures.[50,110] One postulate has that the reaction was believed to proceed through a mechanism reminiscent of an acid-catalyzed alkylation of an arene in an electrophilic substitution process. An intermediate with a strong ^{31}P NMR signal was observed in the reaction of 135 to give 136. Since a gas (presumably





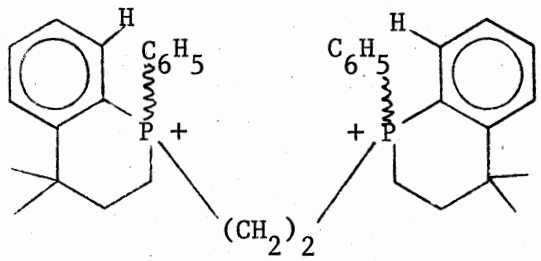
136 E

HBr) was evolved during the cyclization, the only reasonable anion remaining in the solution was that of PPA^{n-}. An initial π complex A was predicted to form between a proton and β-alkenylphosphonium salt, a step not uncommon in most electrophilic substitution processes. The logical second step in an electrophilic attack on an arene ring is to form an electron-deficient system (C or D) attached in our case to a quaternary phosphorus atom and this should be a very high energy process. Conceivably a tight-ion pair involving PPA^- could account for the stability of the dication C but this is not currently favored. This cyclization is remarkable in that the intramolecular alkylation takes place ortho to the phosphonium group which is a strong meta-director. Thus, the more favored mechanism has involved the formation of an intermediate B containing a penta-covalent phosphorus atom. This avoids generation of an intermediate like C but rather favors D (from B). We assume same mechanism is operating in the cyclization of similar β-alkenyl-substituted bisphosphonium salts 90-94.

The IR, ^1H NMR and ^1H decoupled ^{31}P NMR spectral data were recorded in Tables III and IV. ^1H NMR spectra of 100-104 and 108 were very complex due to severe signal overlap of CH_2 protons in the ring with those of methylene protons in the bridge. The methyl protons in 4-position of the rings showed a singlet for compounds 100, 102 and

103 and a doublet for compounds 101, 104 and 108. Since the cyclic salts 100-104, 108 and 111 are a mixture of meso- and (±)-isomers with different conformational preferences, there is no clear rationale at the moment to explain the different signal patterns. In the case of 108, the signal due to P-H proton is found to overlap with those of aromatic protons.[15]

^{1}H decoupled ^{31}P NMR spectra of the cyclic bisphosphonium salts showed expected upfield shifts compared to open chain analogues. Fusion of the benzo group at the b-face of phosphorinane ring as in 100 leads to the installation of a double bond adjacent to P(IV). It



100

is accepted[2,3] that interaction of π electrons on an adjacent double bond with P(IV) can cause upfield ^{31}P NMR chemical shifts. It may be due to the sharing of some of the electron density on the α-carbon. In general, an increase in d-orbital utilization produces shielding. Installation of unsaturation next to phosphorus necessarily changes non-bonded interactions and bond angles and hence a chemical shift is a consequence of several molecular alterations. In addition to the conjugative electronic effect on P(IV), benzannelation brings about a significant modification in the steric environment about phosphorus.

Specifically an eclipsing interaction (also shielding) may develop with the ortho C-H bond in the fused benzene ring.[112]

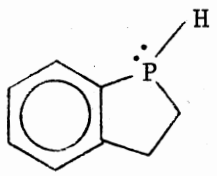
The cyclic bisphosphonium salts 100-104 always exhibited two ^{31}P NMR signals arising from the meso- and racemic-forms in solution. It is reasonable that the phosphorus atom in the chiral center may give different ^{31}P NMR chemical shifts in the meso- and racemic-forms. This is supported by the fact that the carbon atom in the chiral center of the molecules of the meso- and racemic-forms has been proved to exhibit different ^{13}C chemical shifts.[23,65,85,86] The unsymmetrical molecule 108 containing two non-identical quaternary phosphorus nuclei showed an AB spectrum with $^{2}J_{PCP}$ = 10.6 Hz.

We assume a heavy population of anti-rotamer in solution for bisphosphonium salts because the electrostatic repulsion and bulkiness should keep the two phosphorus atoms with like charges at the greatest distance from each other. Single crystal X-ray diffraction analysis of meso-1,1'-(1,2-ethanediyl)bis[1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium] diperchlorate (meso-117) revealed that the molecule indeed assumed an anti-conformation in the solid state. However, the dihedral angle between C-P bonds was found to be 143.6° rather than the expected 180°. The X-ray analysis data will be discussed later as a proof for the stereochemistry of the partially unsaturated ring of fused C-P heterocycle and preferred conformation of meso-117 in the solid state.

Other Attempted Cyclizations

Due to the success of the synthesis of 1,1'-(α,ω-alkanediyl)bis-[1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium] salts with

the use of cyclization procedure, we considered the preparation of other substituted α,ω-alkanediylbis(1,2,3,4-tetrahydrophosphinolinium) salts and bisphosphonium salts containing the phosphorus in 5-membered phosphindole 137 ring systems. Diquaternization of 1,2-bis(diphenyl-



137

phosphino)ethane (85) with allyl bromide, using standard conditions, gave 112 (70%) within 24 hours whereas with 5-bromo-1-pentene, it took 96 hours to form 113 (64%). With 4-bromo-1-butene, 1,4-bis(diphenyl-

$$\left[(C_6H_5)_2\overset{R}{\overset{|}{\overset{+}{P}}}-(CH_2)_n-\overset{R}{\overset{|}{\overset{+}{P}}}(C_6H_5)_2 \right] , \; 2\ X^-$$

112 n = 2; X = Br; R = $-CH_2-CH=CH_2$

113 n = 2; X = Br; R = $-CH_2-CH_2-CH_2-CH=CH_2$

114 n = 2; X = PF_6; R = $-CH_2-CH_2-CH_2-CH=CH_2$

115 n = 4; X = Br; R = $-CH_2-CH_2-CH=CH_2$

116 n = 4; X = PF_6; R = $-CH_2-CH_2-CH=CH_2$

phosphino)butane (87) gave 115 (61%) after 96 hours in benzene as solvent. The salts 113 and 115, being hygroscopic, were converted into 114 and 116, respectively, for characterization. The structures of 112, 114 and 116 were supported by elemental analyses in addition to the IR, ^{1}H NMR and ^{31}P NMR spectra (Tables I and II).

When these compounds were subjected to our general cyclization

procedure, several unusual observations were noted. Using 115% PPA, cyclization of 112 was attempted at different temperatures (160-250°C). Only a metathesis with KPF_6 was observed below 240°C. At 250°C, a solid formed and it showed a lone ^{31}P NMR signal (+20.00 ppm) confirming the presence of a pure single product. However the ^{1}H NMR spectrum was very complicated. It has not been possible to assign a reasonable structure to the product with the data available. It was found that attempts to cyclize simple salts like 138 to get pure cyclic

$$[(C_6H_5)_3\overset{+}{P}—CH_2—CH=CH_2] \ , \ Br^-$$

138

product were unsuccessful with 115% PPA over a temperature range of 160-300°C.[44]

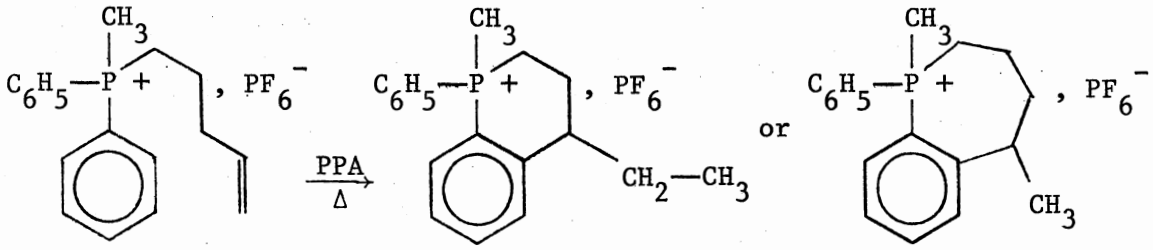
Compounds 113 and 115 appeared to undergo cyclization with 115%

$$[(C_6H_5)_2\overset{R}{\underset{+}{P}}—(CH_2)_n—\overset{R}{\underset{+}{P}}(C_6H_5)_2] \ , \ 2\ Br^-$$

113 n = 2; R = $-CH_2-CH_2-CH_2-CH=CH_2$

115 n = 4; R = $-CH_2-CH_2-CH=CH_2$

PPA at 195°C. The ^{1}H NMR spectra were again very complicated and showed no signal for the corresponding olefinic hydrogen atoms. Several ^{31}P NMR signals observed for products from 113 and 115 may be due to the formation of several possible isomers (*cis*- and *trans*-, *racemic*- and *meso*-) along with structural isomers containing six- and/or seven-membered rings as reported for the cyclization of the simple system such as 139.[110] These isomeric mixtures have resisted all

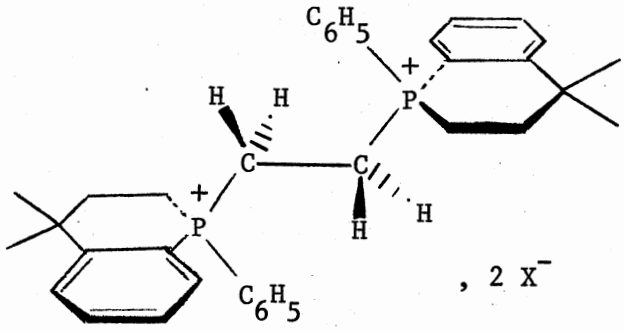


139 140 141

attempts of separation and purification.

Separation of Diastereomers and Resolution of Racemic-form of 1,1'-(1,2-Ethanediyl)bis-(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Diperchlorate (117)

The separation of meso- and (±)-forms from the diastereomeric mixture of 117 was achieved by fractional crystallization using

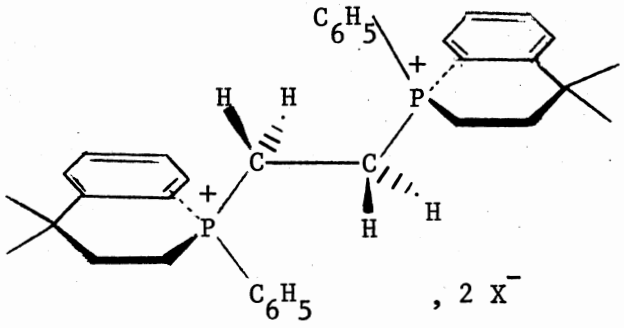


meso-117 X = ClO_4 meso-121 X = L(+)HDBT

meso-119 X = Cl meso-122 X = D(-)HDBT

meso-120 X = I

H_2CCl_2-ether (see page 36). The meso-117 (2 ClO_4^-) was isolated in the pure form and had a mp 291-293°C. Several attempts to separate



, 2 X^-

(±)-117 X = ClO_4

(±)-118 X = $B(C_6H_5)_4$

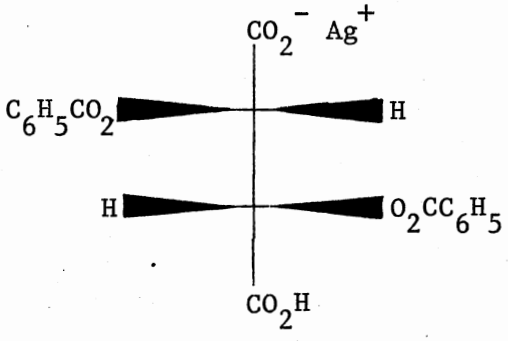
(±)-119 X = Cl

(±)-121 X = L(+)HDBT

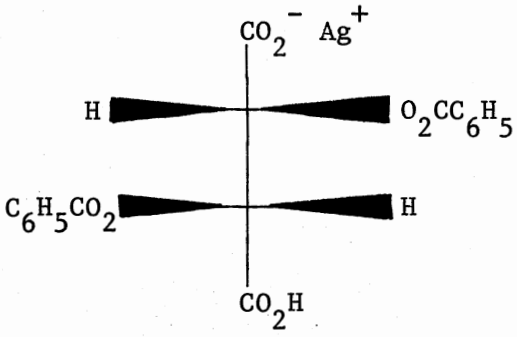
(±)-122 X = D(-)HDBT

pure (±)-117 were unsuccessful. Conversion of (±)-enriched 117 into enriched (±)-118, followed by fractional crystallization using H_2CCl_2 ether, resulted in the isolation of pure (±)-118 [2 $B(C_6H_5)_4^-$].

Silver D(-)- and L(+)-HDBTs (142 and 143) have been used to effect resolutions of a few quaternary phosphonium salts.[27,68,84] It was



142



143

found convenient to employ dihalides (±)-119 (2 Cl^-) as reactants with silver salts 142 and 143. The conversion of (±)-118 [2 $B(C_6H_5)_4^-$] to (±)-119 (2 Cl^-) was effected by passing (±)-118 [2 $B(C_6H_5)_4^-$] through an anion-exchange column packed with Dowex 1-X8 (Cl^-) anion exchange resin. Metathesis of (±)-119 (2 Cl^-) with $NaClO_4$ in H_2O gave (±)-117

(2 ClO_4^-), mp 256-258°C. Since there was no simple experimental method available to distinguish a meso-form from (±)-form of the compound, we subjected both the diastereomers, meso- and (±)-117 (2 ClO_4^-), to reaction with Ag L(+)- and D(-)-HDBTs, respectively. Therefore, meso-117 (2 ClO_4^-) was converted into meso-119 (2 Cl^-) by anion-exchange with Dowex 1-X8 (Cl^-).

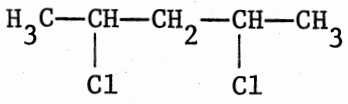
Some success in the resolution of (±)-119 (2 Cl^-) with Ag D(-)-HDBT and L(+)HDBT (142 and 143) was also attained. Two diastereomeric salts, (-)-121 [L(+)HDBT], [mp 151-153°C (d), $[\alpha]_D^{21}$ = +60.5° (c = 1.0 g/100 mL; H_3COH)] and (+)-122 [D(-)HDBT] [mp 147.5-149°C (d), $[\alpha]_D^{20}$ = -60.0° (c = 1.0 g/100 mL; H_3COH)] were obtained by treatment of (±)-119 (2 Cl^-) with Ag L(+)HDBT (143) and Ag D(-)-HDBT (142) in H_3COH, respectively, followed by fractional crystallization using $HCCl_3$-ether. The stoichiometric inclusion of one equivalent of water in the crystal of (+)-122 [D(-)HDBT] was revealed by elemental analysis. Such an inclusion of solvent is not unknown with phosphonium salts.[27,39,105]

Metathesis of (+)-122 [D(-)HDBT] and (-)-121 [L(+)HDBT] with $NaClO_4$ in H_3COH gave the pure enantiomers (+)-117 (2 ClO_4^-) [mp 263-264.5°C, $[\alpha]_D^{21}$ = +19.1° (c = 1.0 g/100 mL; acetone)] and (-)-117 (2 ClO_4^-) [mp 262.5-264°C $[\alpha]_D^{21}$ = -18.5° (c = 1.0 g/100 mL; acetone)], respectively. The structures of (+)- and (-)-117 (2 ClO_4^-) were confirmed by IR, ^1H NMR, ^{31}P NMR and elemental analyses (Tables III and IV).

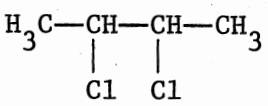
Metathesis of meso-119 (2 Cl^-) with Ag D(-)HDBT (142) and Ag L(+)HDBT (143) resulted in the formation of meso-122 [D(-)HDBT] and meso-121 [L(+)HDBT], respectively, as shown on page 38. Treatment of both meso-117 (2 ClO_4^-) and meso-122 [D(-)HDBT] with $NaClO_4$ in H_3COH gave

the same meso-117 (2 Cl^-) with a rotation of 0^o as expected. Elemental analysis revealed the inclusion of one equivalent of water in the crystalline meso-121 [L(+)HDBT].

The ^1H NMR, ^1H decoupled ^{31}P NMR and IR spectral data are recorded in Tables I and II. ^{31}P NMR spectroscopy was advantageously used to monitor the separation of diastereomers of 117 (2 ClO_4^-) and the resolution of racemic-119 (2 Cl^-). The diastereomeric mixture of 117 gave two ^{31}P NMR signals corresponding to meso-117 (2 ClO_4^-) and (±)-117 (2 ClO_4^-), whereas the diastereomers (meso-117, (±)-117, (±)-118, meso-119, (±)-119 or meso-120) exhibited a lone ^{31}P NMR signal. This is reasonable since the carbon atoms in the chiral centers of meso- and (±)-isomers of compounds such as 57 and 58 are shown to



57



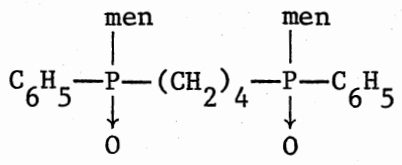
58

exhibit different ^{13}C chemical shifts.[23.56] The meso-isomer of a salt always showed a ^{31}P NMR signal upfield relative to the corresponding (±)-isomer which may be due to differences in non-bonded interactions in the preferred conformation of the diastereomers.[65,85] The stereochemistry of the complex substituents attached to phosphorus could complicate the conformational analysis, and X-ray analysis of the diastereomers would be instructive as to the stereochemistry of the molecule in the solid state.

It is interesting to note that diastereomeric mixtures having chiral anions, (±)-121 [L(+)HDBT] or (±)-122 [D(-)HDBT], showed two ^{31}P NMR signals in $DCCl_3$ corresponding to two diastereomers. One

common interaction between optically active molecules, which is important in resolution procedures, is the dipolar attraction between anions and cations.[25] The dipolar attraction between the chiral anions to the chiral phosphorus centers creates a chiral environment and results in two ^{31}P NMR signals, each signal corresponding to a phosphorus atom with different configuration. It was fortuitously observed that the addition of a drop of trifluoroacetic acid (TFA) to the solution of (±)-121 [L(+)HDBT] [or (±)-122] in $DCCl_3$ made the two ^{31}P NMR signals collapse to one signal (Table V). This may be due to the replacement of chiral anion, L(+)HDBT by trifluoroacetate anion. Each pure diastereomer, (-)-121 [L(+)HDBT] or (+)-122 [D(-)HDBT], as well as each pure enantiomer, (-)-117 (2 ClO_4^-) or (+)-117 (2 ClO_4^-) exhibited a lone ^{31}P NMR signal as expected, either in $DCCl_3$ or in $DCCl_3$ containing a drop of TFA.

Two ^{31}P NMR signals observed for meso-121 [L(+)HDBT] or meso-122 [D(-)HDBT] in $DCCl_3$ (Table V) may also be explained by a similar argument. In the chiral environment created by dipolar attraction of chiral anions to chiral phosphorus centers, the two phosphorus atoms with different configurations in the meso-121 [L(+)HDBT] or meso-122 [D(-)HDBT] may be able to exhibit different ^{31}P chemical shifts. Valentine and co-workers[129] observed two ^{31}P NMR signals for meso-60



(men = menthyl)

60

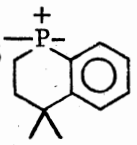
in which a chiral ligand is directly attached to each phosphorus atom

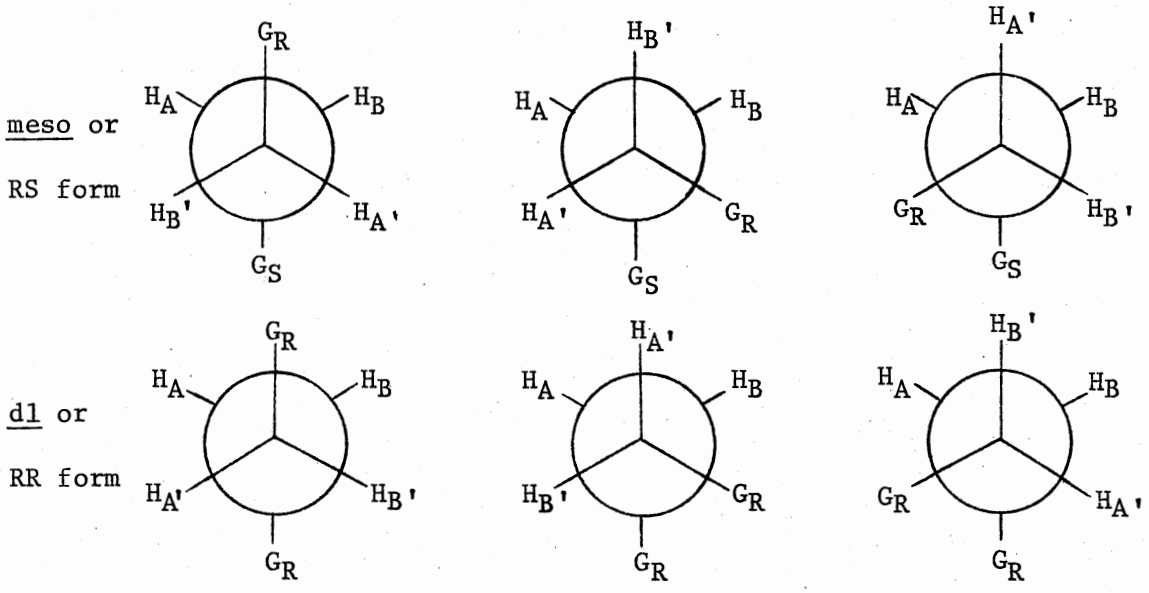
TABLE V

^{31}P NMR SPECTRAL DATA FOR DIASTEREOMERIC MIXTURES
[(±)-121, MESO-121, (±)-122 and MESO-122]

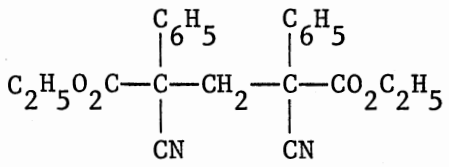
Compound	Anion	^{31}P NMR Data (ppm from 85% H_3PO_4)	
		$DCCl_3$	$DCCl_3$ with a drop of TFA
(±)-121	L(+)HDBT	17.27; 17.03	15.91
(±)-122	D(-)HDBT	17.45; 17.21	15.98
meso-121	L(+)HDBT	15.62; 15.58	15.06
meso-122	D(-)HDBT	15.54; 15.51	15.07

by a covalent bond. In our examples, it was observed that the two ^{31}P NMR signals of meso-121 [L(+)HDBT] or meso-122 [D(-)HDBT] collapsed into one signal by the addition of a drop of TFA to the solution ($DCCl_3$), apparently due to the destruction of chiral environment around each phosphorus atom, as indicated previously.

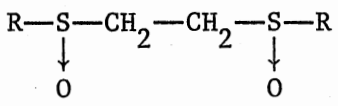
The ^{1}H NMR spectra of the diastereomers and enantiomers were complex due to severe signal overlap of bridge $C\underline{H}_2$ protons with $C\underline{H}_2$ protons in the phosphorinane ring, but there are some interesting features. The ^{31}P decoupled ^{1}H NMR spectrum of meso-117 is distinct from that of (±)-117 (2 ClO_4^-) (Plates XLVII and XLVIII, respectively). The difference in these spectra may be explained on the basis of a preferred conformation. The most reasonable staggered conformations are represented in the following diagram. G_R and G_S refer to the two opposite configurations of the group  Indeed, because of notable steric hindrance and the like charges of the G_R and G_S groups, the anticonformation is probably the most populated



in both meso- and dl-forms. When a methylene group is adjacent to an asymmetric atom, the two methylene protons are diastereotopic and therefore, in principle, anisochronous.[102] Since the J_{HH} trans values are larger than the J_{HH} gauche values, one should obtain a greater value for $J_{AB'}$ in the dl-form and for $J_{AA'}$ in the meso-form due to heavy population of antirotamers. The $-CH_2-CH_2-$ group would be expected to give an AA'BB'-type multiplet pattern both in the meso- and dl-forms. However, it has been observed that a simplified spectrum (in some cases a fortuitious singlet) was detected for the bridge methylene protons in the meso-form and a multiplet for the dl-form. Such examples include the α,α'-diphenyl substituted adiponitrile 49[24] and γ-sulfoxides 54 (R = C_6H_5 or substi-



49



54

tuted phenyl).[33,122] The antirotamer of meso-117 (2 ClO_4^-) is a centrosymmetric molecule in which the H atoms trans to each other in the bridge are in identical environments whereas the trans H atoms in the ethylene bridge of antirotamer (±)-117 (2 ClO_4^-) are in different environments due to lack of symmetry in the molecule. Accordingly, a simplified spectrum (a fortuitous singlet) was observed for the bridge $-C\underline{H}_2-C\underline{H}_2-$ protons in meso-117 (2 ClO_4^-) and, in the case of (±)-117 (2 ClO_4^-), the ethylene group gave a AA'BB'-type multiplet. However, signal overlap of the methylene protons in the phosphorinane ring with bridge $C\underline{H}_2$ protons further complicated the

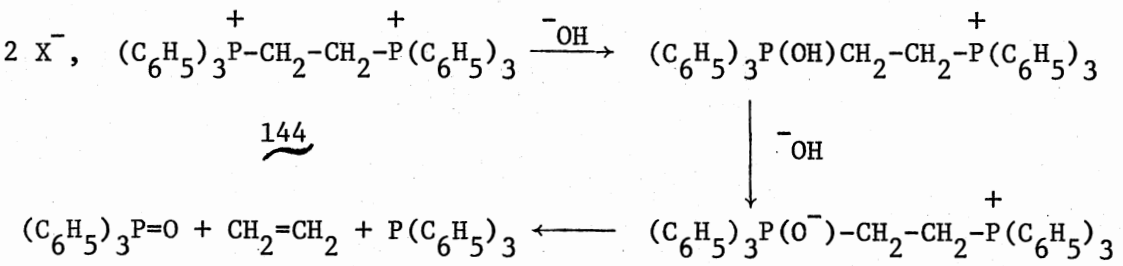
analysis. Thus, this phenomenon of a singlet for $\delta_{\underline{CH_2}-\underline{CH_2}}$ in the meso-isomer with the required structure discussed may well be a distinguishing feature for this type of diastereomer, assuming no extraordinary differences exist in the magnetic shielding for each of the geminal protons on one carbon.

Chemical Degradation of Meso-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Dichloride (Meso-119)

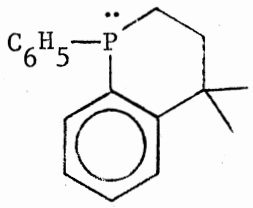
Alkaline hydrolysis of phosphonium salts is known to be useful in cleavage of C-P bonds and leads to the formation of phosphine oxides.[81] The ease of elimination of various groups has been noted in the same order as the stability of the displaced anions as follows:[99]

benzyl > α- or β- naphthal > phenyl > methyl > β-phenethyl > ethyl > high alkyls.

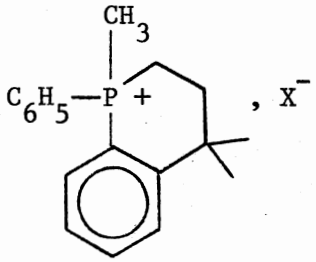
1,2-Ethanediylbisphosphonium salts 144 have been found to underto cleavage by alkali into a phosphine oxide with a loss of the two-



carbon bridge.[17,144] Similar products were isolated (see page 39) from alkaline hydrolysis of meso-119 (2 Cl^-). The phosphine 123 was isolated

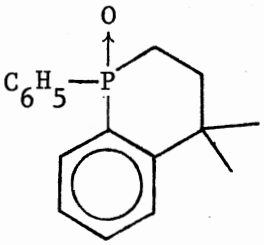


123



124 X = I

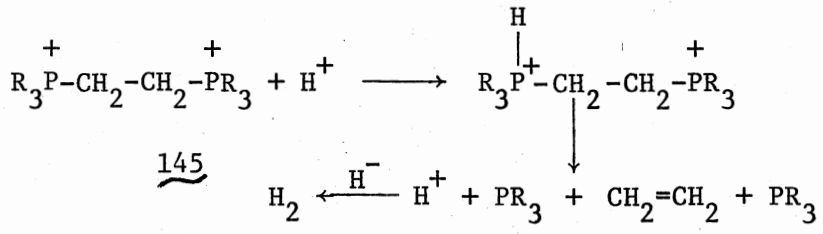
125 X = PF_6



126

as salt 124 which was converted to 125 by metathesis with KPF_6. The properties of compounds 125 and 126 were compared to those in the literature[46,110] and identified by spectroscopic means.

Reduction of 1,2-ethanediylbisphosphonium salts 145 with metal



hydrides gave phosphines with the loss of ethylene bridge. It has been suggested[18] that a monophosphorane is formed which subsequently fragments in a manner analogous to alkaline hydrolysis. Reduction of meso-119 (2 Cl^-) in dry THF and NaH gave the phosphine 123 which was isolated as methiodide 124. Lithium aluminium hydride with meso-119 (2 Cl^-) in dry THF behaved similarly and resulted in the formation of 124. Thus, identification of chemical degradation products of meso-119 (2 Cl^-) provided additional support for its structure. Final confirmation came via an X-ray examination of meso-117 (2 ClO_4^-).

Single Crystal Analysis of Meso-117 (2 ClO_4^-) by X-ray Diffraction

Preliminary reports of single crystal analysis by X-ray diffraction of meso-117 (2 ClO_4^-) are shown in Figure 1 (numbering scheme and bond distance) and Figure 2 (bond angles). The tortional angles are given in Table VI. As can be seen from the torsional angles, meso-117 (2 ClO_4^-) assumes a near anti-conformation in the solid state. The dihedral angle between the C-P bonds, P(1)-C(18)-C(36)-P(2), was found to be the 143.6°. All data including electron densities, bond angles, bond lengths, torsional angles, least-squares refinement and location of H atoms would be instructive to explain the deviation of the C-P dihedral angle from 180°. Moreover, the preliminary data proves the structure of meso-117 (2 ClO_4^-) unequivocally and is supportive of the proposed structures of α,ω-alkanediylbis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) salts 100-104 and 111.

To summarize, syntheses of the novel C-P heterocycles, the dissymmetric 1,1'-(α,ω-alkanediyl)bis(1,2,3,4-tetrahydrophosphinolinium salts 100-104 and 111, have been attained from readily available bisphosphines 85-89. The open-chain precursors were easily prepared by diquaternization of the bisphosphine 85-89, and 105 with alkenyl halides. The acid-induced (115% PPA) intramolecular alkylation of the open-chain precursors 90-94 and 109 at 180°C for one hour furnished the hitherto unknown family of the substituted 1,1'-(α,ω-alkanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) salts 100-104 and 111 which were dissymmetric because of two asummetric phosphorus atoms. With 1-chloro-3-methyl-2-butene, the bis(diphenylphosphino)methane (105)

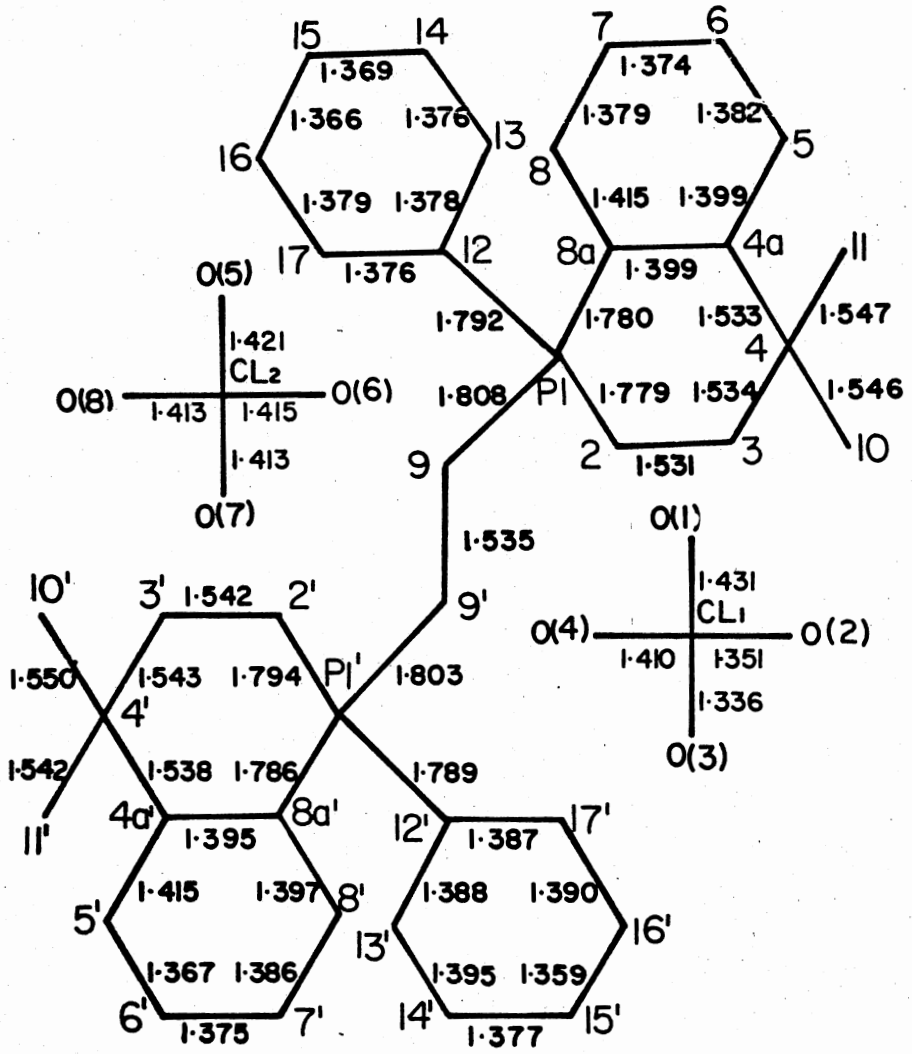


Figure 1. Numbering Scheme and Bond Distance (in $\overset{\circ}{A}$) for Meso-117 (2 ClO_4^-)

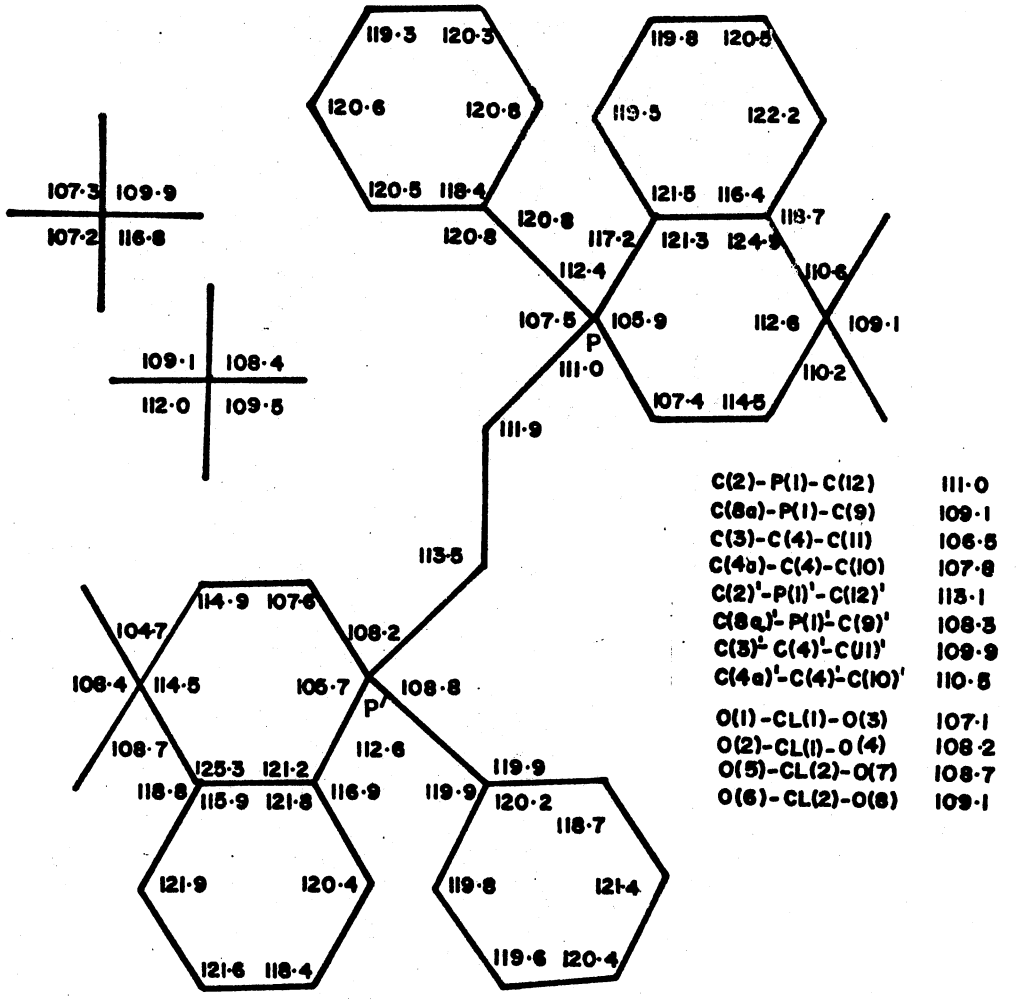


Figure 2. Bond Angles for Meso-117 (2 ClO_4^-)

TABLE VI

COMPARISON OF SOME SELECTIVE TORSION ANGLES IN THE TWO HALVES OF MESO-117 (2 ClO_4^-)

Fragment	Torsional Angle (°)	
	Unprimed	Primed
C(9)-P(1)-C(2)-C(3)	161.0	-70.9
C(9)-P(1)-C(12)-C(13)	97.3	35.8
C(9)'-C(9)-P(1)-C(2)	46.5	-73.6
C(9)'-C(9)-P(1)-C(8a)	162.8	172.3
C(9)'-C(9)-P(1)-C(12)	-75.1	49.6
P(1)-C(9)-C(9)'-P(1)'	143.6	

yielded the monoalkylated product 106 which underwent cyclization with 115% PPA at 180°C to give a mono(1,2,3,4-tetrahydrophosphinolinium) salt 108. The ^{1}H NMR, ^{31}P NMR, IR and elemental analyses supported the structures of all the new compounds.

The ^{31}P NMR analysis was advantageously used to monitor the separation of diastereomers and the resolution of (±)-form of 1,1'-(1,2-ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) diperchlorate (117) by fractional crystallization. This is the first case to be reported in the literature regarding the separation of diastereomers and resolution of (±)-form of a bisphosphonium salt containing two asymmetric phosphorus atoms in two C-P heterocycles.

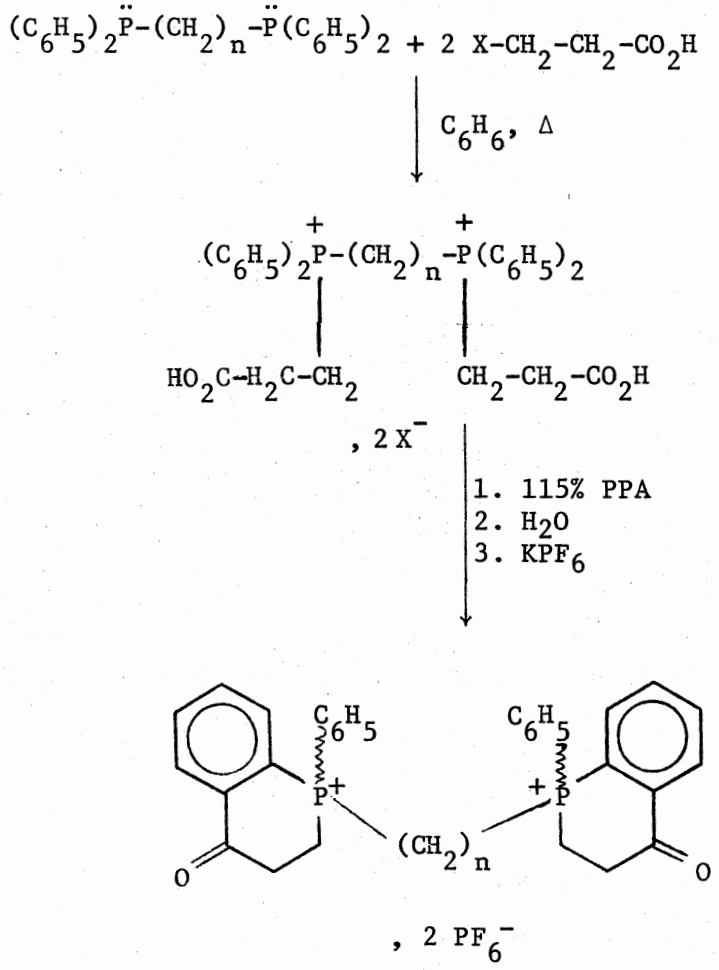
Chemical degradation studies of meso-119 (2 Cl^-) and X-ray analysis of meso-117 (2 ClO_4^-) conclusively supported the proposed structures of 1,1'-(α,ω-alkanediyl)bis(1,2,3,4-tetrahydrophosphinolinium) salts 100-104 and 111. It was also evident from the X-ray analysis that the meso-117 (2 ClO_4^-) assumes a near anticonformation in the solid state. This X-ray analysis is also the first for this family.

The National Cancer Institute is now carrying out the screening tests to evaluate the biological activity of the bisphosphonium salts 90-94 and 100-104. It is anticipated that the future chemistry and biological testing results of these bisphosphonium salts will be both interesting and fruitful.

Suggestions for Future Work

The successful procedure for the preparation of 1,1'-(α,ω-alkane-

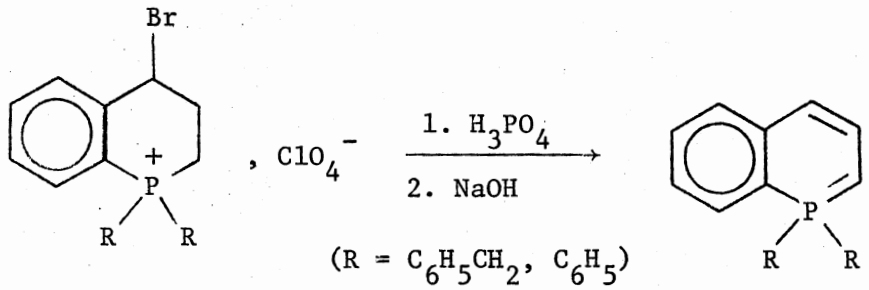
diyl)bis(1,2,3,4-tetrahydrophosphinolinium) salts described herein provide a basic starting point for the preparation of many derivatives of this previously unknown family. These derivatives should have sufficient chemical and structural variation to allow an initial evaluation of the gross overall chemotherapeutic value of this family of heterocycles. For instance, it should be possible to prepare 1,1'-(α,ω-alkanediyl)bis(4-oxo-1,2,3,4-tetrahydrophosphinolinium) salts 146 from commercially available bisphosphines (outlined below). The



146

separation and resolution of the cyclic bisphosphonium salts 146 could be monitored by ^{31}P NMR analysis.

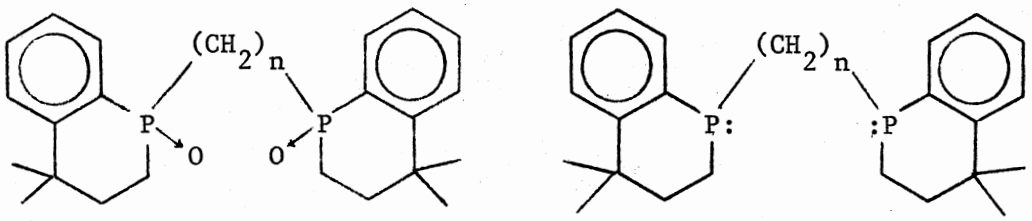
Cyclic 1,2,3,4-tetrahydrophosphinolinium salts 147 have been used as precursors for the phosphanaphthalene derivatives such as 148.[16,92] Using our methods to obtain cyclic phosphinolinium salts, a wide



147 148

variety of systems containing two phosphorin rings could possibly be obtained. The biological activity of these systems is certainly open for investigation.

As an extension of this work, the base-catalyzed hydrolysis of 1,1'-(α,ω-alkanediyl)bis(1,2,3,4-tetrahydrophosphinolinium) salts (n > 3) will probably give the dioxides 149 and reduction of these salts with metal hydrides will lead to the bisphosphines 150. These



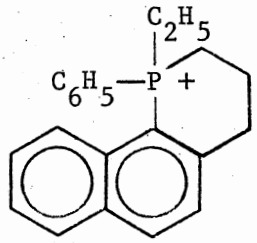
149 150

reactions are of considerable interest from a mechanistic point of view[17,18] and provide two new series of dissymmetric C-P heterocycles

having two asymmetric phosphorus atoms. The bisphosphines 150 may be valuable as chelating agents in organometallic chemistry.

Since the resolution of (+)-117 (2 ClO_4^-) and (-)-117 (2 ClO_4^-) has been achieved, the framework has been laid for a possible investigation of their dynamic stereochemistry. Of particular interest would be whether the base-catalyzed cleavage of (+)-117 or (-)-117 occurred with retention, inversion or racemization. The direction of cathodic reduction will also be of interest, in view of the known stereochemistry, i.e., cleavage with retention.[71] The group eliminated is probably the one which would form the most stable anion.[99]

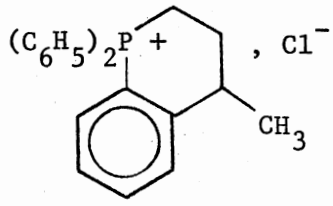
Also of particular interest would be the potential carcinostatic activity of 1,1'-(α,ω-alkanediyl)bis(1,2,3,4-tetrahydrophosphinolinium) salts in view of the biological activities observed in simple systems such as 43 and 63 by the National Cancer Institute (vide infra). This



, Br^-

T/C = 142

43



, Cl^-

T/C = 155

63

small breakthrough may be an indication that interest in this class of compounds will increase not only from the medicinal point of view, but also from a synthetic standpoint.

CHAPTER III

EXPERIMENTAL

General Information

Reactions were carried out under an atmosphere of N_2 wherever necessary. Melting points were obtained on a Thomas-Hoover melting point apparatus and were uncorrected. The ^{1}H and ^{31}P NMR spectra were recorded on a Varian XL-100(15) NMR spectrometer equipped with a Nicolet TT-100 PFT accessory operating at 100.1 MHz for ^{1}H and at 40.5 MHz for ^{31}P signals with $(CH_3)_4Si$ as internal standard for ^{1}H and 85% phosphoric acid as external standard for ^{31}P. Infrared spectral data were collected from a Perkin-Elmer 681 spectrophotometer with samples in potassium bromide pellets. Elemental microanalyses were performed by Galbraith Laboratories, Knoxville, Tennessee. Rotations of optically active compounds were taken on a Rudolph polarimeter (O. C. Rudolph & Sons, Inc., Model 80, No. 722) with a circular scale reading to 0.001^{o} via a 1 dm. polarimeter cell (Rudolph 21). All spectral data are reported in Tables I-V in the Results and Discussion.

Starting Materials

All liquid reagents obtained from commercial sources were purified by distillation prior to use. 1-Chloro-3-methyl-2-butene (Eastman Kodak

Company) bp 108.5°C, $n_D^{23.5}$ = 1.4480 [lit.[136] 109°C, n_D^{20} = 1.4485]; 1-bromo-3-methyl-2-butene (Alfa Products) bp 65-66°C/55 mm, n_D^{23} = 1.4955 [lit.[136] 50-51°C/40 mm. n_D^{15} = 1.4930]; 3-bromopropene (Matheson Coleman & Bell) bp 69.5-70.5°C, $n_D^{23.5}$ = 1.4685 [lit.[136] 70°C, n_D^{20} = 1.4697]; 5-bromo-1-pentene (K & K Rare and Fine Chemicals) bp 121-125°C, n_D^{23} = 1.4634 [lit.[145] 121-126°C]; 4-bromo-1-butene (Aldrich Chemical Company) bp 97.5-98.5°C, n_D^{23} = 1.4635 [lit.[136] 98.5°C, n_D^{20} = 1.4622]; benzoylchloride (Baker Chemical Company) bp 82°C/15 mm, n_D^{24} = 1.5614 [lit.[136] 71°C/9 mm, n_D^{20} = 1.5537]. All solid reagents were used as purchased without further purification. Bis(diphenylphosphino)methane (Pressure Chemical Company) mp 120.5°C [lit.[109] 121°C]; 1,2-bis(diphenylphosphino)ethane (Arapahoe Chemicals) mp 143°C [lit.[109] 144°C]; 1,3-bis(diphenylphosphino)propane (Strem Chemicals) mp 62°C [lit.[109] 62°C]; 1,4-bis(diphenylphosphino)butane (Strem Chemicals) mp 132°C [lit.[109] 133°C]; 1,5-bis(diphenylphosphino)pentane (Strem Chemicals) mp 42°C [lit.[109] 42°C]; 1,6-bis(diphenylphosphino)hexane (Strem Chemicals) mp 127°C [Lit.[109] 127°C]; d-tartaric acid (Aldrich Chemical Co.) mp 170°C(dec), $[\alpha]_D^{24}$ = +12.2° (c = 4.0g/100 mL; H_2O) [lit.[136] 171-4°C, $[\alpha]_D^{20}$ = + 12.7 (c = 17.4 g/100 mL; H_2O)]; l-tartaric acid (Aldrich Chemical Co.) mp 171-174°C, $[\alpha]_D^{24}$ = - 13.8° (c = 2.0 g/100 mL; H_2O) [lit.[66] 168-170°C, $[\alpha]_D^{20}$ = - 14.2° (c = 4.05 g/100 mL; H_2O)]; sodium tetraphenylborate (Aldrich Chemical Co.); KPF_6 (Pennwalt); anhydrous $NaClO_4$ (G. Frederick Smith Chemical Co.); silver nitrate (Goldsmith Bros.); 115% polyphosphoric acid (FMC Corporation, 82.3% P_2O_5 guaranteed minimum]. Dowex 1-X8 (Cl^-) anion exchange resin (Baker Chemical Company) was used for packing in an anion-exchange column.

Organic solvents used were of reagent grade. Benzene (Mallinckrodt) and anhydrous ether (Mallinckrodt) were dried over sodium and filtered prior to use. Tetrahydrofuran (THF) (Fischer Scientific Company) was dried by distillation first from NaH and then from $LiAlH_4$.

General Procedure for Synthesis of α,ω-Alkanediylbis[diphenyl-(3-methyl-2-butenyl)-phosphonium] Bis[hexafluorophosphates(1-)] (95-99)

The synthesis of 1,2-ethanediylbis[diphenyl(3-methyl-2-butenyl)-phosphonium] bis[hexafluorophosphate(1-)] (95) is used as an example to illustrate the general procedure. A solution of 4.59 g (0.0112 mol) of 1,2-ethanediylbis(diphenylphosphine) (85) in 40 mL of benzene was added dropwise over a 3-h period from an addition funnel to a preheated solution of 3.14 g (0.03 mol) of 1-chloro-3-methyl-2-butene in 50 mL of benzene in a 250 mL, 3-necked, round-bottomed flask. The latter was equipped with a mechanical stirrer, condenser and N_2 inlet. The solution was boiled another 40 h with stirring and then was allowed to cool to room temperature. The solid which separated was collected by filtration and was then dissolved in a minimum amount of H_3COH (ca. 20 mL). Reprecipitation was effected by the dropwise addition of anhydrous $(C_2H_5)_2O$ until the solution became cloudy. This mixture was allowed to stand at room temperature for 24 h. A white solid precipitated and was collected by filtration and dried *in vacuo* to yield 6.14 g (88%) of the dichloride 90, mp 293-295°C. Elemental analysis showed that 90 was mildly hygroscopic and hence it was

converted to the corresponding bis(hexafluorophosphate) 95. Thus, 1.00 g (0.0016 mol) of dichloride 90 was dissolved in minimum amount of methanol (ca. 2 mL), and the solution was diluted with an equal volume of water. An equal volume of saturated aqueous KPF_6 solution was added, and the solution was mechanically stirred for a 2-h period. The solid formed was separated by filtration and then dissolved in H_2CCl_2 (ca. 20 mL). This new solution was dried (Na_2SO_4), and the resulting mixture was filtered to give a filtrate which was concentrated to ca. 10 mL on a rotary evaporator. Dry ether (ca. 5 mL) was added, and the solution was allowed to stand for 1 h. The precipitate was collected by filtration and was again dissolved in a minimum amount of H_2CCl_2 (ca. 5 mL). Reprecipitation was effected by the dropwise addition of dry ether until the solution became cloudy. After 1 h, a precipitate was collected by filtration and was recrystallized (H_2CCl_2-ether). This precipitate was dried in vacuo to give 0.80 g (60%) of 95, mp 252-254°C. The ^1H NMR spectrum (Plate XXIX), the ^{31}P NMR spectrum (Plate LVII) and the IR spectrum (Plate I) supported the structure of 95.

Anal. calcd. for $C_{36}H_{42}P_4F_{12}$: C, 52.31; H, 5.12; P, 14.99.
Found: C, 52.18; H, 5.03; P, 15.05.

Preparation of 1,3-Propanediylbis[diphenyl-(3-methyl-2-butenyl)phosphonium] Bis-[hexafluorophosphate(1-)] (96)

Bisphosphine 86 (4.61 g; 0.0112 mol) was diquaternized with 1-chloro-3-methyl-2-butene (3.14 g; 0.03 mol) using the general procedure. The crude dichloride 91 was reprecipitated twice (H_2CCl_2-

ether) to give 5.2 g (74%) of pure 91, mp 190-192°C. Using the general metathetic procedure, 1.00 g (0.0016 mol) of dichloride 91 was converted into bis(hexafluorophosphate) 96. Two reprecipitations (H_2CCl_2-ether) were required to give 1.00 g (74%) of 96, mp 214-215°C. The IR, ^1H NMR and ^{31}P NMR spectra are displayed in Plates II, XXX and LVIII, respectively.

Anal. calcd. for $C_{37}H_{44}P_4F_{12}$: C, 52.87; H, 5.28; P, 14.74.
Found: C, 52.94; H, 5.28; P, 14.56.

Preparation of 1,4-Butanediylbis[diphenyl(3-methyl-2-butenyl)phosphonium] Bis[hexafluorophosphate(1-)] (97)

The diquaternarization of bisphosphine 87 (4.77 g; 0.0112 mol) was successfully performed by the general procedure using 1-chloro-3-methyl-2-butene (3.14 g; 0.03 mol). Crude salt 92 was reprecipitated twice (H_2CCl_2-ether) to yield 7.00 g (98%) of pure 92, mp 190-192°C. The conversion of the dichloride 92 (1.00 g; 0.0016 mol) into bis-(hexafluorophosphate) 97 was effected by the metathetic procedure. Crude salt 97 was purified by two reprecipitations (H_2CCl_2-ether) to produce 0.70 g (52%) of pure 97, mp 174-175°C. The structure is supported by the ^1H NMR, ^{31}P NMR and IR spectra (Plates XXXI, LIX and III).

Anal. calcd. for $C_{38}H_{46}P_4F_{12}$: C, 53.40; H, 5.43; P, 14.50.
Found: C, 53.44; H, 5.38; P, 14.65.

Preparation of 1,5-Pentanediylbis[diphenyl(3-methyl-2-butenyl)phosphonium] Bis[hexafluorophosphate(1-)] (98)

The general method was employed to diquaternize the bisphosphine 88 (4.92 g; 0.0112 mol) using 1-chloro-3-methyl-2-butene (3.14 g; 0.03 mol). Crude dichloride 93 was obtained in the form of semisolid which resisted all attempts at crystallization. This semisolid was dissolved in a minimum amount of methanol (ca. 25 mL), and the solution was diluted to ca. 50 mL by addition of water. Then, 100 mL of saturated aqueous KPF_6 solution was added, and the resulting mixture was stirred for 1 h. The solid formed was extracted (H_2CCl_2; ca. 200 mL), and the aqueous layer was separated. The H_2CCl_2 layer was dried (Na_2SO_4), and the resulting mixture was filtered to give a filtrate which was concentrated to ca. 25 mL. Dry ether (ca. 20 mL) was added dropwise until the solution became cloudy. The precipitate was collected by filtration and was reprecipitated again (H_2CCl_2-ether). This precipitate was dried in vacuo to yield 7.7 g (78%) of pure 98, mp 232-233°C. The proposed structure of 98 is supported by the IR, ^1H NMR and ^{31}P NMR spectra (Plates IV, XXXII and LX).

Anal. calcd. for $C_{39}H_{48}P_4F_{12}$: C, 53.92; H, 5.57; P, 14.26.

Found: C, 54.04; H, 5.71; P, 14.08.

Preparation of 1,6-Hexanediylbis[diphenyl(3-methyl-2-butenyl)phosphonium] Bis[hexafluorophosphate(1-)] (99)

With 1-chloro-3-methyl-2-butene (3.14 g; 0.03 mol), the bisphos-

phine 89 (5.08 g; 0.0112 mol) was diquaternized via the general procedure. Crude dichloride 94 was reprecipitated twice (H_2CCl_2-ether) to produce 7.45 g (65.7%) of pure 94, mp 259-261°C. The conversion of the dichloride 94 (1.00 g; 0.0015 mol) into bis(hexafluorophosphate) 99 was effected in the usual manner. Two reprecipitations of crude salt 99 (H_2CCl_2-ether) were required to acquire 0.8 g (60.4%) of pure 99, mp 181-182°C. Structure identification was supported by the ^1H NMR, ^{31}P NMR and IR spectra (Plates XXXIII, LXI and V).

Anal. calcd. for $C_{40}H_{50}P_4F_{12}$: C, 54.43; H, 5.71; P, 14.03.
Found: C, 54.61; H, 5.76; P, 13.95.

Preparation of [(Diphenylphosphino)methyl]-(3-methyl-2-butenyl)diphenylphosphonium Hexafluorophosphate(1-) (107)

A solution of 4.33 g (0.0112 mol) of diphosphine 105 in 40 mL of benzene was added dropwise over a 3-h period from an addition funnel to a boiling solution of 3.14 g (0.03 mol) of 1-chloro-3-methyl-2-butene in 40 mL of benzene in a 250 mL, 3-necked, round-bottomed flask equipped with a mechanical stirrer, condenser and was then allowed to cool to room temperature. A solid formed was collected by filtration and was then dissolved in H_2CCl_2 (ca. 70 mL). Reprecipitation was effected by the dropwise addition of ether. After 1 h, a solid separated and was collected by filtration and again reprecipitated (H_2CCl_2-ether). The solid was dried *in vacuo* to give 4.67 g (85.68%) of the chloride, 106, mp 217-220°C. Then 1.00 g (0.002 mol) of 106 was dissolved in methanol (ca. 10 mL) which was diluted to 20 mL by the addition of water. Exactly 20 mL of saturated aqueous KPF_6

solution was added, and the resulting mixture was stirred for a period of 1 h. The solid formed was extracted with H_2CCl_2 (4 x 25 mL). The H_2CCl_2 layer was separated, dried (Na_2SO_4) and concentrated to ca. 10 mL on a rotary evaporator. Dry ether was added until the solution became cloudy. The solid formed was collected by filtration and was again reprecipitated from H_2CCl_2-ether. The precipitate was dried in vacuo to give 1.0 g (83.5%) of 107, mp 171-172°C. The structure is supported by the IR, ^1H NMR and ^{31}P NMR spectra (Plates VI, XXXIV and LXII).

Anal. calcd. for $C_{30}H_{31}P_3F_6$: C, 60.21; H, 5.22; P, 15.53.
Found: C, 60.22; H, 5.40; P, 15.62.

Preparation of Methanediylbis[diphenyl(3-methyl-2-butenyl)phosphonium] Bis[hexafluorophosphate(1-)] (110)

The general procedure was employed to diquarternize bis(diphenylphosphino)methane (105) (1.92 g; 0.005 mol) using 1-bromo-3-methyl-2-butene (3.0 g; 0.02 mol). ^{31}P NMR analysis was used to monitor the conversion of 105 into dialkylated product 109. A reaction period of 10 days was required for complete reaction. A lone ^{31}NMR signal at + 21.15 ppm confirmed the formation of 109. Two reprecipitations of crude solid (H_2CCl_2-ether) gave 3.4 g (99%) of pure 109, mp.266-268°C. Then 0.5 g (0.0007 mol) of dibromide 109 was converted into bis(hexafluorophosphate) 110 as usual. Crude salt 110 was purified by two recrystallizations (boiling CH_3OH) and then dried in vacuo to give 0.29 g (49%) of pure 110, mp 207-209°C. The ^1H NMR, ^{31}P NMR and IR spectra (Plates XXXV, LXIII and VII) support the structure.

Anal. calcd. for $C_{35}H_{40}P_4F_{12}$: C, 51.74; H, 4.96; P, 15.25.

Found: C, 51.64; H, 4.98; P, 14.99.

Preparation of 1,2-Ethanediylbis(allyl-diphenylphosphonium) Dibromide (112)

A solution of 8.9 g (0.0225 mol) of 1,2-ethanediylbis(diphenylphosphine) (85) in 100 mL of benzene was heated almost to reflux in a 250 mL, 3-necked, round-bottomed flask fitted with a mechanical stirrer, condenser, N_2 inlet and an additional funnel. A solution of 7.26 g (0.06 mol) of 3-bromopropene in 55 mL of benzene was added from the addition funnel gradually over a 3-h period. The solution was boiled 21 h and was allowed to cool to room temperature. A solid separated was collected by filtration and was then dissolved in a minimum amount of methanol. Reprecipitation was effected by dropwise addition of anhydrous ether until the solution became cloudy. This mixture was allowed to stand at room temperature for 3 h. The white solid separated was filtered and then recrystallized twice (methanol-ether). The solid was dried in vacuo to yield 10.1 g (70%) of pure 112, mp 302-303°C (dec). The IR, ^{1}H NMR and ^{31}P NMR spectra (Plates VIII, XXXVI and LXIV) support the proposed structure of 112.

Anal. calcd. for $C_{32}H_{34}P_2Br_2$: C, 60.02; H, 5.35; P, 9.67; Br, 24.96.

Found: C, 60.22; H, 5.25; P, 9.44; Br, 24.82.

Preparation of 1,2-Ethanediylbis(4-pentenyldiphenylphosphonium) Bis[hexafluorophosphate(1-)] (114)

The general procedure was used to convert bisphosphine 85 (2.39 g; 0.0056 mol) into dibromide 113 using 5-bromo-1-pentene (4.47 g; 0.03 mol) over a period of 90 h. The crude solid was purified by two reprecipitations (H_2CCl_2-ether) to give 2.5 g (64%) of pure 113, mp 244-246°C. Metathesis of 113 (0.5 g; 0.0007 mol) into bis(hexafluorophosphate) 114 was successfully performed using the general procedure. Two reprecipitations of crude 114 (CH_2Cl_2-ether) gave 0.29 g (50%) of pure 114, mp 183-185°C. The ^1H NMR, ^{31}P NMR and IR spectra (Plates XXXVII, LXV, and IX) support the proposed structure of 114.

Anal. calcd. for $C_{36}H_{42}P_4F_{12}$: C, 52.31; H, 5.12; P, 14.99.

Found: C, 52.32; H, 5.13; P, 14.75.

Preparation of 1,4-Butanediylbis(3-butenyldiphenylphosphonium) Bis[hexafluorophosphate(1-)] (116)

Diquaternization of bisphosphine 87 (2.39 g; 0.0056 mol) with 4-bromo-1-butene (4.0 g; 0.03 mol) was successfully performed using the general procedure. A reaction of period of 90 h was required for complete reaction. The crude solid formed was purified by two reprecipitations (H_2CCl_2-ether) to yield 2.4 g (61%) of pure 115, mp 169-171°C. Metathesis of 115 (1.0 g; 0.0014 mol) with 40 mL of saturated aqueous KPF_6 was carried out using the general procedure. Two reprecipitations of crude salt 116 (H_2CCl_2-ether) gave 0.88 g

(76%) of pure 116, mp 167-168°C. Structural characterization of 116 is supported by the IR, ^{1}H NMR and ^{31}P NMR analyses (Plates X, XXXVIII and LXVI).

Anal. calcd. for $C_{36}H_{42}P_4F_{12}$: C, 52.31; H, 5.12; P, 14.99.

Found: C, 52.46; H, 5.24; P, 15.12.

General Procedure for Synthesis of 1,1'-(α,ω-Alkanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis-[hexafluorophosphates(1-)] (100-104)

The synthesis of 1,1'-(1,2-ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) bis[hexafluorophosphate(1-)] (100) is used as an example. In a 100 mL beaker was placed 40 mL of 115% polyphosphoric acid (PPA) which had been heated to 180°C. 1,2-Ethanediylbis[diphenyl-(3-methyl-2-butenyl)phosphonium] dichloride 90 (0.91 g; 0.0015 mol) was added over a 10-min period followed by an additional 1 h of stirring. The solution was allowed to cool in 110°C and was slowly poured into 500 g of crushed ice. This resulted, after stirring for 30 min, in the formation of a homogeneous solution. Upon the addition of 50 mL of saturated aqueous KPF_6 solution, precipitation of a crude compound resulted. The crude, wet solid was collected by filtration and dissolved in a minimum amount of H_2CCl_2 (ca. 50 mL). The water layer was separated and the organic phase was washed with saturated sodium bicarbonate solution (to remove any PPA) followed by washing with water. The organic layer was dried (Na_2SO_4) and treated with charcoal. After filtration, the filtrate was concentrated to ca. 10 mL and reprecipitation was effected by dropwise addition of

ether until the solution became cloudy. A second reprecipitation (H_2CCl_2-ether) followed by drying in vacuo gave 0.50 g (40%) of pure 100, mp 268-270°C. The ^1H NMR, ^{31}P NMR and IR spectra displayed in Plates XXXIX, LXVII and XI support the structure of 100.

Anal. calcd. for $C_{36}H_{42}P_4F_{12}$: C, 52.31; H, 5.12; P, 14.99.
Found: C, 52.19; H, 5.30; P, 14.82.

Preparation of 1,1'-(1,3-Propanediyl)bis-(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hexafluorophosphate(1-)] (101)

The cyclization of 91 (0.9 g, 0.0014 mol) was accomplished by the general procedure. Crude hexafluorophosphate salt 101 was purified by two reprecipitations using H_2CCl_2-ether to give 0.6 g (51%) of pure 101, mp 243-245°C. The proposed structure of 101 is supported by the IR, ^1H NMR and ^{31}P NMR spectra (Plates XII, XL and LXVIII).

Anal. calcd. for $C_{37}H_{44}P_4F_{12}$: C, 52.87; H, 5.28; P, 14.74.
Found: C, 52.69; H, 5.35; P, 14.69.

Preparation of 1,1'-(1,4-Butanediyl)bis-(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hexafluorophosphate(1-)] (102)

The bisphosphinolinium salt 102 was prepared as follows. In a 250 mL beaker was placed 120 mL of 115% polyphosphoric acid (PPA) which had been heated to 180°C. 1,4-Butanediylbis[diphenyl-(3-methyl-2-butenyl)phosphonium] dichloride 92 (2.0 g; 0.0031 mol) was added over a

period of 25 min followed by an additional 1 h of stirring. The solution was then allowed to cool to 110°C and was slowly poured onto 1000 g of crushed ice. This resulted, after stirring for 30 min, in the formation of a homogeneous solution. Upon the addition of 50 mL of saturated aqueous KPF_6 solution, precipitation of a crude compound resulted. The crude, wet solid was collected by filtration and dissolved in a minimum amount of H_2CCl_2 (ca. 50 mL). The water layer was separated and the organic phase was washed with saturated sodium bicarbonate solution (to remove any PPA) followed by washing with water. The organic layer was dried (Na_2SO_4) and treated with charcoal. After filtration, the filtrate was concentrated to ca. 10 mL and reprecipitation was effected by dropwise addition of ether until the solution became cloudy. A second reprecipitation (H_2CCl_2-ether) followed by drying in vacuo gave 1.20 g (45%) of pure 102, mp 214-215°C. The ^1H NMR, ^{31}P NMR and IR spectra displayed in Plates XLI, LXIX and XIII support the structure of 102.

Anal. calcd. for $C_{38}H_{46}P_4F_{12}$: C, 53.40; H, 5.43; P, 14.50.
Found: C, 53.15; H, 5.35; P, 14.26.

Preparation of 1,1'-(1,5-Pentanediyl)bis-(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hexafluorophosphate(1-)] (103)

Cyclization of bisphosphonium salt 93 (0.2 g, 0.00023 mol) was successfully performed at 170°C using the general procedure. Crude bis(hexafluorophosphate) 103 was reprecipitated twice (H_2CCl_2-ether) to yield 0.06 g (30%) of pure 103, mp 148-150°C. Structural identifi-

cation is supported by the IR, ^{1}H NMR and ^{31}P NMR spectra (Plates XIV, XLII and LXX).

Anal. calcd. for $C_{39}H_{48}P_4F_{12}$: C, 53.92; H, 5.57; P, 14.26.
Found: C, 54.06; H, 5.76; P, 14.40.

Preparation of 1,1'-(1,6-Hexanediyl)bis-(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hexafluorophosphate(1-)] (104)

The bisphosphinium salt, 94, (0.5 g; 0.00095 mol) underwent cyclization via the general procedure. The crude bis(hexafluorophosphate) salt 104 was purified by reprecipitations (H_2CCl_2-ether) to give 0.26 g (31%) of pure 104, mp 113-117°C. Structural characterization is supported by the ^{1}H NMR, ^{31}P NMR and IR spectra (Plates XLIII, LXXI and XV).

Anal. calcd. for $C_{40}H_{50}P_4F_{12}$: C, 54.43; H, 5.71; P, 14.03.
Found: C, 54.52; H, 5.84; P, 14.07

Preparation of 1,1'-(Methanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium Bis[hexafluorophosphate(1-)] (111)

The bisphosphonium salt 109 (0.5 g; 0.007 mol) was converted into the crude bis(hexafluorophosphate) 111 by the use of 40 mL of 115% PPA at 205°C following our general procedure. The solution turned golden yellow initially and then dark-brown during cyclization. Four reprecipitations (H_2CCl_2-ether) of crude salt 111 finally gave 0.15 g (26%) of pure 111, mp 165-168°C. The IR, ^{1}H NMR and ^{31}P NMR spectra (Plates

XVII, XLV and LXXIII) support the structure of 111.

Anal. calcd. for $C_{35}H_{40}P_4F_{12}$: C, 51.74; H, 4.96; P, 15.25.

Found: C, 51.53; H, 5.06; P, 15.09.

Preparation of 1-[Diphenylphosphonio)methyl]-1,2,3,4-tetrahydro-4,4-dimethyl-1-phenyl phosphinolinium Bis[hexafluorophosphate(1-)] (108)

In a 100 mL beaker was placed 50 mL of 115% PPA which was preheated to 175°C. Chloride 106 (2.0 g; 0.004 mol) was added over a period of 15 min, followed by an additional 1 h or stirring. The solution was cooled to 120°C and was slowly poured into 500 mL of ice-water. After stirring for 15 min, the solution became homogeneous. Upon the addition of 50 mL of saturated aqueous KPF_6 solution, precipitation of a crude solid resulted. This crude, wet solid was collected by filtration and was dissolved in a minimum amount of H_3CCN (ca. 45 mL). The aqueous layer was separated and the organic phase was dried (Na_2SO_4). The solid was reprecipitated from H_3CCN by the dropwise addition of ether until the solution became cloudy. A second precipitation (H_3CCN-ether) gave 1.55 g (52%) of pure 108, mp 290-292°C. The ^1H NMR, ^{31}P NMR and IR spectra (Plates XLIV, LXXII and XVI) support the proposed structure of 108.

Anal. calcd. for $C_{30}H_{32}P_4F_{12}$: C, 48.40; H, 4.33; P, 16.64.

Found: C, 48.26; H, 4.48; P, 16.47.

Attempted Cyclization of 1,2-Ethanediylbis-(allyldiphenylphosphonium) Dibromide (112)

To 60 mL of 115% PPA at 250°C was slowly added 0.8 g (0.0012 mol) of 112, and the solution was stirred for a period of 1 h. The solution turned golden yellow and was allowed to cool to 120°C and poured slowly into 200 mL of ice water. A solution of KPF_6 (30 mL) was added, and the heavy precipitate formed was filtered out. The solid was dissolved in H_2CCl_2 and reprecipitated with ether three times to obtain 0.5 g of a white solid, mp 212-214°C. ^1H NMR analysis showed some cyclized product but the signal integration was not in agreement with the expected five-membered ring product. The ^1H decoupled ^{31}P NMR spectrum (Plate LXXXVII) showed a single ^{31}P signal confirming the presence of a pure single product. However, it has not been possible to assign a reasonable structure for the product with the data available.

Attempted Cyclization of 1,2-Ethanediylbis-[diphenyl(4-pentenyl)phosphonium] Dibromide (113)

The cyclization of 113 (0.5 g, 0.0007 mol) was carried out by the standard procedure using 30 mL of 115% PPA at 195°C. The crude product was reprecipitated thrice (H_2CCl_2-ether) to give a white solid (0.23 g) which had a very wide range of mp 90-170°C. That cyclization took place was suggested by the complex ^1H NMR spectrum. However, the presence of several ^{31}P NMR signals may be due to the formation of several possible isomers (cis- and trans-, racemic- and meso-isomers)

along with structural isomers containing five and/or six-membered rings. The isomeric mixture has resisted all attempts of separation or purification.

Attempted Cyclization of 1,4-Butanediylbis-[diphenyl(3-butenyl)phosphonium] Dibromide (115)

To 40 mL of 115% PPA at 195°C was added 1.0 g (0.0014 mol) of 115 over 15 min, followed by a 1-h stirring period. The solution was cooled to 120°C and poured into 500 g of ice-water. To the homogeneous aqueous solution was added a saturated KPF_6 solution (40 mL). After 1 h, the solid formed was collected by filtration and dissolved in H_2CCl_2 (20 mL). The latter solution was dried (Na_2SO_4) and concentrated to 10 mL. Dry ether was added until the solution became cloudy and a white solid slowly formed. Three reprecipitations (H_2CCl_2-ether) gave 1.0 g of a white solid, mp 193-196°C. ^1H NMR analysis revealed a complex spectrum but suggested some cyclization product. The ^1H decoupled ^{31}P NMR spectrum (Plate LXXXVIII) showed five signals which may be due to the possible formation of cis- and trans-isomers besides racemic- and meso-forms present in the reaction product. All attempts to separate the isomeric mixture have been unsuccessful to date.

Preparation of 1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Diperchlorate (117) - A Mixture of Racemic-117 (2 ClO_4^-) and Meso-117 (2 ClO_4^-)

Phosphonium salt 90 (3.0 g, 0.0049 mol) was slowly added to 60 g

of 115% PPA at 180°C with stirring for 1 h. The solution was cooled to 120°C and was slowly poured into 500 g of ice-water; continued stirring gave a homogeneous solution. A heavy precipitate separated when the clear solution was treated with 40 mL of aqueous solution containing 15 g of $NaClO_4$. The precipitate was filtered and washed profusely with water. The dissolution of the precipitate in H_2CCl_2 (ca. 25 mL), followed by dropwise treatment with ether, produced crude 117. Reprecipitation (H_2CCl_2-ether) gave 2.5 g (69.4%) of 117, mp 254-258°C.

The rather wide melting range of the diperchlorate 117 is understandable in view of the possible existence of the two diastereoisomers due to the two similar asymmetric phosphorus centers. The existence of the racemic- and meso-forms of 117 in the ratio ca. 5:4 in the mixture was indicated by the two ^{31}P signals at + 15.86 and + 14.83 ppm downfield from 85% phosphoric acid in $DCCl_3$ [a drop of F_3CCO_2H added (Plate LXXIV)]. The IR spectrum (Plate XVIII) showed the characteristic very strong broad band for ClO_4^- at 1090 cm^{-1}. The ^1H NMR spectrum (Plate XLVI) further supported the proposed structure of 117. The separation of meso-117 (2 ClO_4^-) and racemic-117 (2 ClO_4^-) was accomplished as shown on pages 102 and 105, respectively.

Separation of Meso-1,1'-(1,2-Ethanediyl)bis-(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenyl-phosphinolinium) Diperchlorate (Meso-117)

The diperchlorate mixture 117 (24.0 g; 0.30 mol) was dissolved in 350 mL of H_2CCl_2, and dry ether (ca. 50 mL) was added slowly until

the solution became cloudy. The mixture became clear after 2 h, and the solid separated was filtered and dried to give 3 g of the first fraction, mp 286-288°C. The filtrate was made cloudy by the dropwise addition of ether. After 2 h, the solid separated was collected by filtration to give 3.5 g of the second fraction, mp 284-286°C. Reprecipitation of the filtrate (dry ether) was repeated five more times and the successive crops of diperchlorate were collected. Each of the five crops had a mp of: 282-284°C (3.0 g), 258-260°C (2.0 g), 248-250°C (3.0 g), 238-240°C (3.5 g) and 230-234°C (2.5 g), respectively. The meso-117 was conveniently isolated by combining the first three fractions (9.5 g) and recrystallizing from hot methanol (ca. 500 mL) to obtain 8.0 g (75%) of meso-117 (2 ClO_4^-), mp 291-293°C. The ^{31}P NMR spectrum (Plate LXXV) with a lone signal at + 14.85 ppm downfield (85% phosphoric acid; $DCCl_3$ with a drop of F_3CCO_2H) confirmed the separation of the pure meso-form. The proposed structure of meso-117 (2 ClO_4^-) is supported by IR and ^1H NMR spectra (Plates XIX and XLVII).

Anal. calcd. for $C_{36}H_{42}P_2Cl_2O_8$: C, 58.78; H, 5.75; P, 8.42.

Found: C, 58.86; H, 5.81; P, 8.59.

The last four crops (110 g) enriched with the racemic-form were used to isolate racemic-117 (2 ClO_4^-).

Separation of (±)-1,1'-(1,2-Ethanediyl)bis-(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenyl-phosphinolinium) Bis(tetraphenyl-borate) ((±)-118)

The last four fractions of diperchlorate 117 (11.0 g) (from the above experiment) were dissolved in 800 mL of boiling methanol. The

solution was allowed to stand overnight and the solid separated was filtered to give 1.5 g of the diperchlorate 117 enriched with the meso-form. The filtrate was concentrated to 1/2 volume and was then allowed to cool at room temperature; a solid precipitated. Two more crops were obtained by repeating the same procedure. Stripping the mother liquor then gave the fourth crop. The following data were collected for the four crops:

No. of crops	Wt. of product	MP (^{o}C)	(±)-117:meso-117
1	2.5 g	248-250	4:1
2	3.0 g	255-257	10:1
3	2.1 g	244-247	5:2
4	1.2 g	240-246	7:2

The second crop was recrystallized from boiling methanol three times to obtain 1.4 g of the diperchlorate 117 mp 255-257^{o}C. The ^{31}P NMR analysis of this product displayed two signals corresponding to (±)-117 (2 ClO_4^-) and meso-117 (2 ClO_4^-) in the ratio of ca. 11:1 (+ 16.15 and + 14.88 ppm downfield to 85% H_3PO_4, respectively). Further attempts at separation to obtain the pure (±)-117 were unsuccessful and hence the conversion or racemic-enriched diperchlorate into the corresponding bis-tetraphenylborate 118 was undertaken.

The 11:1 racemic-enriched mixture of diperchlorates (1.4 g; 0.0019 mol) was dissolved in 100 mL of boiling methanol, and the solution was filtered into an aqueous solution (20 mL) containing 2.0 g of sodium tetraphenylborate. The resulting mixture was stirred for 30 min. The solid separated was filtered and dissolved in H_2CCl_2 (ca. 150 mL).

Exactly 6 drops of methanol were added to clear the solution which was then dried (Na_2SO_4). Reprecipitation was effected by the dropwise addition of ether until the solution became cloudy. The solid formed was filtered and dried in vacuo to yield 2.1 g (94%) of 118, mp 214-217°C. The IR spectral analysis did not show a strong peak at 1090 cm^{-1} for ClO_4^- anion. The ^{31}P NMR analysis of 118 displayed two signals at + 16.15 and + 15.11 ppm for racemic- and meso-forms of 118, respectively.

Then 2.1 g (0.0018 mol) of racemic-enriched 118 was dissolved in 200 mL of H_2CCl_2, and the solution was filtered to remove the insoluble, floating solid. Exactly 40 mL of dry ether was added dropwise to the clear filtrate until it became cloudy; this mixture was allowed to stand overnight. Crystals separated were filtered off and reprecipitated (H_2CCl_2-ether) to give 0.9 g (4.2%) of shining crystals of (±)-118 (2 $B(C_6H_5)_4^-$), mp 218-220°C. The lone ^{31}P signal (Plate LXXIX) at + 16.32 ppm (relative to 85% H_3PO_4) confirmed the achievement of separation of pure racemic form of 118. The ^1H NMR and IR spectra (Plates LI and XXIII) support the proposed structure of (±)-118 (2 $B(C_6H_5)_4^-$).

Anal. calcd. for $C_{84}H_{82}P_2B_2$: C, 85.86; H, 7.03; P, 5.27.
Found: C, 85.90; H, 7.04; P, 5.33.

Preparation of (±)-1,1'-(1,2-Ethanediyl)bis-(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenyl-phosphinolinium) Diperchlorate [(±)-117]

The anion exchange resin, Dowex 1X-8 (Cl^-) (40.0 g), was packed in a column (50 x 1.5 cm) and washed with 100 mL of solution of H_3CCN

and H_2O (4:1). A solution of 2.0 g (0.0017 mol) of (±)-118 (2 $B(C_6H_5)_4^-$) in 200 mL of a solution of $H_3CCN:H_2O$ (4:1) was passed through the column at a rate of 1 drop per min. This column was eluted with 200 mL of a solution of $H_3CCN:H_2O$ (4:1) (drop rate of 1 drop/min), followed by washing with 100 mL of the same solvent mixture. All the eluates were combined and evaporated on a rotary evaporator to dryness. To the residue was added 30 mL of acetone, and the solution was again evaporated to dryness. This new residue was dissolved in 50 mL of H_2CCl_2 and the solution was then dried (Na_2SO_4). This solution was filtered and the filtrate was concentrated to ca. 30 mL under reduced pressure. Excess ether (ca. 30 mL) was added and the solution was allowed to stand overnight. The solid separated was collected by filtration, reprecipitated from H_2CCl_2-ether and dried in vacuo to give (±)-119 (2 Cl^-) [1.03 g (qt); mp 211-216°C]. The bisphosphinolinium dichloride (±)-119 was soluble in H_2O, H_3COH and C_2H_5OH but it was insoluble in ether. The product gave a positive halogen test ($AgNO_3$). The hygroscopic dichloride was characterized as its diperchlorate derivative (±)-117 (2 ClO_4^-) as described below.

An aqueous solution (5 mL) containing 2.0 g of $NaClO_4$ was added dropwise to bisphosphinolinium dichloride (±)-119 (0.1 g, 0.00016 mol) in 2.0 mL of water at room temperature with stirring for 15 min. A white solid immediately precipitated which was filtered and then carefully washed with distilled water [to remove any excess of $NaClO_4$ and unreacted dichloride (±)-119]. The solid was dissolved in H_2CCl_2 (ca. 10 mL), and the solution was dried (Na_2SO_4). This solution was filtered and the filtrate was concentrated to ca. 4 mL under reduced pressure. Reprecipitation was effected by the dropwise addition of

ether until the solution became cloudy. This mixture was allowed to stand overnight and deposited a solid which was collected by filtration. Reprecipitation (H_2CCl_2-ether) and drying in vacuo gave 0.082 g of (±)-117 (2 ClO_4^-) (67.8%), mp 256-258°C. The IR spectrum (Plate XX) displayed a strong peak at 1095 cm^{-1} for the ClO_4^- anion. The ^{31}P NMR spectrum of (±)-117 (Plate LXXVI) showed a lone signal at + 15.93 ppm (relative to 85% H_3PO_4). The ^1H NMR analysis (Plate XLVIII) supports the structure of (±)-117. The diperchlorate (±)-117 was soluble in $HCCl_3$ and H_3COH but not in H_2O.

Anal. calcd. for $C_{36}H_{42}P_2Cl_2O_8$: C, 58.78; H, 5.75; P, 8.42.

Found: C, 58.78; H, 5.89; P, 8.47.

Preparation of Meso-1,1'-(1,2-Ethanediyl)bis-(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenyl-phosphinolinium) Diiodide [(±)-120]

A solution of 4.0 g (0.0054 mol) of meso-117 (2 ClO_4^-) in 250 mL solution of H_3CCN:H_2O (1:1) was passed through a column packed with 40.0 g of anion-exchange resin, Dowex 1X-8 (Cl^-), which had been previously washed with a 100 mL solution of H_3CCN:H_2O (1:1). The column was eluted (drop rate of 2 drops/min) with 250 mL of H_3CCN:H_2O (1:1), followed by washing with 200 mL of the same solvent mixture. Evaporation of the eluate in a rotary evaporator gave a residue which was dissolved in 30 mL of acetone. This solution was again evaporated to dryness, and the residue was dissolved in H_2CCl_2 (ca. 50 mL). This solution was dried (Na_2SO_4) and filtered. Concentration of this filtrate (ca. 30 mL) was effected at reduced pressure. Ether (30 mL) was added and the solution was allowed to stand overnight. A solid

formed was filtrated, reprecipitated (H_2CCl_2-ether) and dried *in vacuo* to give 3.3 g (qt) of meso-119 (2 Cl^-), mp 257-259°C. The salt meso-119 (2 Cl^-) was soluble in H_2O and C_2H_5OH but not in ether. It gave a positive halogen test ($AgNO_3$) and was characterized via its diiodide derivative meso-120 as shown below.

An aqueous solution (2 mL) containing 0.2 g (0.0003 mol) of meso-119 (2 Cl^-) was added dropwise with stirring to an aqueous solution (5 mL) containing 2.0 g of NaI at room temperature (30 min). The solid formed was filtered and dissolved in H_2CCl_2 (ca. 10 mL). The solution was dried (Na_2SO_4), filtered, and concentrated to ca. 5 mL under reduced pressure. Reprecipitation was effected by the dropwise addition of ether until the solution became cloudy. After standing overnight, a solid formed. This was filtered, reprecipitated twice from methanol-ether and dried *in vacuo* to give 0.2 g (77%) of meso-120 (2 I^-), mp 324°C (dec). It gave a positive halogen test ($AgNO_3$). The ^{31}P NMR analysis of meso-120 (Plate LXXX) displayed a lone signal at + 15.12 ppm. The structure of meso-120 (2 I^-) is supported by ^1H NMR and IR spectra (Plates LII and XXIV).

Anal. calcd. for $C_{36}H_{42}P_2I_2$: C, 54.70; H, 5.35; P, 7.84.
Found: C, 54.81; H, 5.48; P, 7.60.

Preparation of D(-)-Dibenzoyltartaric Acid Monohydrate and L(+)-Dibenzoyltartaric Acid Monohydrate

The D(-)-enantiomorph was prepared from d-tartaric acid (15.0 g, 0.1 mol; Aldrich Chemical), and 45.0 g (0.32 mol) of benzoyl chloride by the method of Butler and Cretch[21] to give 30.2 g (84.4%) of D(-)-

dibenzoyltartaric acid monohydrate, mp 87-89°C, $[\alpha]_D^{23}$ = -110° (c = 0.03 g/mL, acetone) [lit.[147] mp 88-90°C, $[\alpha]_D^{18}$ = -115.78°, C_2H_5OH)].

The L(+)-enantiomorph was prepared in an identical manner from l-tartaric acid (15 g, 0.1 mol; Aldrich Chemical) and 45 g (0.32 mol) of benzoyl chloride. Thus was obtained 30 g (0.08 mol) of L(+)-dibenzoyltartaric acid monohydrate, mp 83-85°C, $[\alpha]_D^{23}$ = + 108° (c = 0.03 g/mL, acetone) [lit.[21] mp 84-86°C; $[\alpha]_D^{25}$ = +109°).

Preparation of Silver Hydrogen D(-)-Dibenzoyltartrate (142) and Silver Hydrogen L(+)-Dibenzoyltartrate (143)

The silver salt 142 was prepared from 5.0 g (0.0133 mol) of D(-)-dibenzoyltartaric acid monohydrate and 14.4 mL of 1 N NH_4OH in 150 mL of distilled water by the method of Coyne, McEwen and Vanderwerf.[37] It was possible to obtain (after drying) 2.75 g (45%) of 142.

Silver hydrogen L(+)-dibenzoyltartrate (143) (3.25 g; 53%) was similarly prepared from L(+)-dibenzoyltartaric acid monohydrate (5.0 g, 0.0133 mol) and 14.4 mL of 1 N NH_4OH in 150 mL of distilled water.

Resolution of (±)-1,1'-(1,2-Ethanediyl)bis-(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Dichloride [(±)-119] by Silver Hydrogen L(+)-Dibenzoyltartrate (143). Synthesis and Separation of (-)-1,1'-(1,2-Ethanediyl)bis-(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis(hydrogen L(+)-dibenzoyltartrate) [(-)-121]

The bisphosphonium dichloride (±)-119 (2 Cl^-) (0.4 g, 0.00066 mol) dissolved in 20 mL of H_3COH was slowly added to a suspension of silver hydrogen L(+)-dibenzoyltartrate, (143) (0.62 g, 0.00133 mol) in boiling H_3COH (20 mL), and the mixture was boiled for a period of 1 h. The white Ag HDBT 143 slowly dissolved during the reaction and AgCl precipitated. The mixture was cooled and silver chloride was filtered. The filtrate was evaporated to dryness on the rotary evaporator, and the residue was dissolved in ca. 20 mL of H_2CCl_2. The solution was treated with activated charcoal and filtered. The filtrate was concentrated to ca. 10 mL and excess dry ether was added. A solid separated was filtered and dried in vacuo to give 0.7 g (84.8%) of (±)-121 [L(+)HDBT], mp 152-154°C (d). $[\alpha]_D^{24}$ = + 92.5° (c = 0.02 g/2 mL methanol). The ^{31}P NMR analysis of (±)-121 (Plate LXXXI) displayed two signals at + 17.26 and + 17.03 ppm (1:1) indicative of the existence of two diastereoisomers in equal amounts.

The diastereoisomers of (±)-121 [L(+)HDBT] were separated from the reaction product by fractional crystallization using $HCCl_3$ and ether. When 0.4 g (0.00032 mol) of (±)-121 [L(+)HDBT] was dissolved in 20 mL of $HCCl_3$, an insoluble product formed and was filtered. The filtrate was concentrated to ca. 10 mL and dry ether was added dropwise until the solution became cloudy. After the mixture had stood for 6 h, it was filtered to yield the first fraction. Two more fractions were obtained from the filtrate by reprecipitation using dry ether. The following data were recorded for the precipitations.

No. of reprecipitations	Wt. of product	MP (^{o}C)	(+)-121:(-)-121 (from ^{31}P NMR)
1	55 mg	149-151(d)	1:5
2	100 mg	150-152(d)	1:7
3	45 mg	149-151(d)	0:1

These three fractions were combined and reprecipitated thrice ($HCCl_3$-ether) to yield 135 mg of (-)-121 [L(+)HDBT], mp = 151-153^{o}C(d); $[\alpha]_D^{21}$ = + 60.5^{o} (0.02 g/2 mL; H_3COH). Further reprecipitation from $HCCl_3$ and ether gave 115 mg of (-)-121 with the same melting point and specific rotation. The constancy of the melting point [mp 151-153^{o}(d)] and specific rotation ($[\alpha]_D^{21}$ = + 60.5^{o}) following successive reprecipitations strongly indicated that the separation of a pure diastereomer had been achieved. The lone ^{31}P signal at + 17.18 ppm (relative to 85% H_3PO_4) (Plate LXXXII) shown by (-)-121 (in $DCCl_3$) further confirmed the separation. The direction in which the rotation had changed (i.e. from positive toward negative) indicated that the diastereomer isolated was (-)-121 [L(+)HDBT]. The IR and ^{1}H NMR analyses (Plates XXV and

LIII) support the proposed diastereomeric structure of (-)-121 [L(+)-HDBT].

Anal. calcd. for $C_{72}H_{68}O_{16}P_2$: C, 69.11, H, 5.48; P, 4.95.
Found: C, 68.98; H, 5.46; P, 5.03.

Metathesis of (-)-1,1'-(1,2-Ethanediyl)bis(1,2,-3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hydrogen L(+)-dibenzoyltartrate] [(-)-121] to (-)-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Diperchlorate, [(-)-117]

A solution of (-)-121 [L(+)HDBT] (0.08 g, 0.000064 mol) in 2 mL of H_3COH was added to an aqueous solution (5 mL) of $NaClO_4$ (2.0 g, 0.016 mol), and the solution was stirred for 30 min. The solid formed was collected by filtration, washed profusely with water and dissolved in ca. 20 mL of H_2CCl_2. This solution was dried (Na_2SO_4) and concentrated to ca. 5 mL on the rotary evaporator. Dry ether was added until the solution became cloudy, and the mixture was allowed to stand overnight. The solid was filtered and reprecipitated twice (H_2CCl_2 and ether) to give 37 mg (78.7% of pure enantiomer (-)-117 (2 ClO_4^-), mp 262.5-264°C; $[\alpha]_D^{21} = -18.5°$ (c = 20 mg/2 mL; acetone). The ^1H decoupled ^{31}P NMR spectrum of (-)-117 (Plate LXXVIII) exhibited a single signal at +15.40 ppm in $DCCl_3$ and at + 16.19 ppm in $DCCl_3$ with a drop of F_3CCO_2H (relative to 85% H_3PO_4). The ^1H NMR and IR spectra of (-)-117 (2 ClO_4^-) (Plates L and XXII) were identical to those of its

racemic precursor, (±)-117.

Anal. calcd. for $C_{36}H_{42}P_2Cl_2O_8$: C, 58.78; H, 5.75; P, 8.42.

Found: C, 58.78; H, 5.92; P, 8.40.

Resolution of (±)-1,1'-(1,2-Ethanediyl)bis(1,2,-3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Dichloride [(±)-119] by Silver Hydrogen D(-)-Dibenzoyltartrate (142). Synthesis and Separation of (+)-1,1'-(1,2-Ethanediyl)bis(1,-2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis(hydrogen D(-)-dibenzoyltartrate) [(+)-122]

A solution of bisphosphonium dichloride (±)-119 (2 Cl^-) (0.4 g, 0.00066 mol) in 20 mL of warm methanol was added slowly to a suspension of silver hydrogen D(-)-dibenzoyltartrate (142) (0.62 g, 0.0013 mol) in boiling H_3COH (20 mL). The mixture was boiled for a period of 1 h. The white Ag HDBT 142 slowly dissolved during the reaction and AgCl precipitated out. The mixture was cooled and AgCl was collected by filtration. Evaporation of the filtrate gave a residue which was dissolved in ca. 20 mL of H_2CCl_2. The solution was treated with charcoal and filtered. The filtrate was concentrated to ca. 10 mL and excess dry ether was added. The solid was filtered and dried in vacuo to give 0.55 g (66.7%) of (±)-122 [D(-)HDBT], mp 151-153°C(d);

$[\alpha]_D^{24} = -91.5^o$ (c = 0.02 g/2 mL; H_3COH). ^{31}P NMR analysis of (±)-122 (Plate LXXXIV) displayed two signals at + 17.21 and + 17.44 ppm (1:1) indicating the existence of two diastereomers in equal amounts.

Fractional crystallization of (±)-122 ($HCCl_3$:ether) resulted in the separation of (+)-122 [D(-)HDBT]. Then 0.4 g (0.0003 mol) of (±)-122 was dissolved in 20 mL of $HCCl_3$, and the insoluble matter was filtered. The filtrate was concentrated to ca. 8 mL and dry ether was added dropwise until the solution became cloudy. After 6 h, the first fraction of crystals formed and was collected by filtration. Two more fractions were obtained from the filtrate by repeating the above procedure. The following data were recorded during the reprecipitations.

No. of fractions	Wt. of product	MP (^oC)	(-)-122:(+)-122 (from ^{31}P NMR)
1	200 mg	148-151(d)	1:3
2	60 mg	147-150(d)	2:1
3	40 mg	148-150(d)	2:1

Two more reprecipitations of first fraction ($HCCl_3$ and ether) gave 100 mg of (+)-122 [D(-)HDBT], $[\alpha]_D^{20} = -60^o$ (c = 0.02 g/2 mL; H_3COH). Further reprecipitation of (+)-122 ($HCCl_3$ and ether) gave 85 mg of (+)-122 [D(-)HDBT] with the same melting point and specific rotation as formed previously. A lone ^{31}P signal at + 16.81 ppm (relative to 85% phosphoric acid) (Plate LXXXV) shown by (+)-122 further confirmed the separation of the pure diastereomer. The IR and ^1H NMR analyses (Plates XXVII and LV) support the proposed structure of (+)-122 [D(-)HDBT].

Anal. calcd. for $C_{72}H_{68}O_{16}P_2 \cdot H_2O$: C, 68.13; H, 5.56; P, 4.88.
Found: C, 68.17; H, 5.50; P, 4.80.

Metathesis of (+)-1,1'-(1,2-Ethanediyl)bis(1,2,-3,4-tetrahydro-4,4-dimethyl-1-phenylphosphino-linium) Bis[hydrogen D(-)-dibenzoyltartrate] [(+)-122] to (+)-1,1'-(1,2-Ethanediyl)bis-(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Diper-chlorate [(+)-117]

A solution of (+)-122 [D(-)HDBT] (0.06 g; 0.00004 mol) in 2 mL H_3COH was added dropwise to an aqueous solution (5 mL) of $NaClO_4$ (2.0 g, 0.016 mol), and the solution was stirred for 30 min. The solid formed was filtered and washed profusely with water and then dissolved in ca. 20 mL of H_2CCl_2. The solution was dried (Na_2SO_4) and concentrated to ca. 5 mL on a rotary evaporator. Dry ether was added until the solution became cloudy and the mixture was allowed to stand overnight. The solid formed was filtered and, after two reprecipitations from H_2CCl_2-ether, there was obtained 26 mg (74%) of enantiomer, (+)-117 (2 ClO_4^-), mp 263-264°C, $[\alpha]_D^{26}$ = + 19.1° [c = 20 mg/2 mL; acetone]. The ^1H decoupled ^{31}P NMR spectrum of (+)-117 (Plate LXXVII) showed single signal at + 15.85 ppm ($DCCl_3$). The ^1H NMR and IR spectra of (+)-117 (2 ClO_4^-) (Plates XLIX, XXI) were identical to those of the (±)-117 (2 ClO_4^-).

Anal. calcd. for $C_{36}H_{42}P_2Cl_2O_8$: C, 58.78; H, 5.75; P, 8.42.
Found: C, 58.73; H, 5.88; P, 8.46.

Preparation of Meso-1,1'-(1,2-Ethanediyl)bis[1,-2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium] Bis(hydrogen L(+)-debenzoyltartrate) (Meso-121)

The bisphosphonium dichloride meso-119 (0.5 g, 0.0008 mol) dissolved in 25 mL of warm H_3COH was slowly added to a suspension of silver hydrogen L(+)-dibenzoyltartrate (143) (0.8 g, 0.0017 mol) in 25 mL of boiling methanol. The mixture was boiled for 1 h with stirring and was then cooled and filtered to give AgCl (0.24 g, 100%). The clear filtrate was evaporated to dryness on a rotary evaporator, and the residue was dissolved in ca. 30 mL of H_2CCl_2. The solution was treated with charcoal and filtered. The filtrate was concentrated to ca. 10 mL and excess dry ether (ca. 10 mL) was added. After 2 h, the solid separated was filtered and dried in vacuo to give 0.95 g of meso-121 [L(+)HDBT] (95%), mp 153-155°C(d), $[\alpha]_D^{24}$ = + 92.5° (c = 0.02 g/2 mL; H_3COH). Elemental analysis strongly implied the inclusion (stoichiometric) of one mole of water. Such inclusion of solvent[19,30,105] is not uncommon with phosphonium salts. The IR, ^1H NMR and ^{31}P NMR spectra (Plates XXVI, LIV and LXXXIII) support the structural identification of meso-121 [L(+)HDBT].

Anal. calcd. for $C_{72}H_{68}O_{16}P_2 \cdot H_2O$: C, 68.13; H, 5.56; P, 4.88.
Found: C, 67.97; H, 5.56; P, 4.80.

Metathesis of Meso-1,1'-(1,2-Ethanediyl)bis(1,-2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hydrogen L(+)-dibenzoyltartrate] (Meso-121) to Meso-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Diperchlorate (Meso-117)

The phosphonium salt meso-121, [L(+)HDBT] (200 mg, 0.16 mmole) dissolved in ca. 5 mL of H_3COH was added slowly to 10 mL of an aqueous solution of $NaClO_4$ (2.0 g, 0.016 mol), and the solution was stirred for 30 min. The solid separated was filtered and washed carefully and thoroughly with distilled H_2O (to remove any excess $NaClO_4$). This solid was then dissolved in 25 mL of H_2CCl_2, and the solution was dried (Na_2SO_4). This solution was concentrated to ca. 5 mL on the rotary evaporator and dry ether was added until the solution became cloudy. The mixture was allowed to stand overnight at room temperature. The solid formed was filtered and reprecipitated twice (H_2CCl_2:ether) to yield 0.095 g of a compound, [mp 289-291°C, $[\alpha]_D^{21} = 0^o$ (c = 20 mg/2 mL; acetone)] which is identical to meso-117 (2 ClO_4^-) separated from the diastereomeric mixture of 117.

Preparation of Meso-1,1'-(1,2-Ethanediyl)bis(1,-2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis(hydrogen D(-)-dibenzoyltartrate) (Meso-122)

The bisphosphonium dichloride Meso-119 (2 Cl^-) (0.5 g, 0.0008 mol)

dissolved in 25 mL of warm H_3COH was added dropwise to a suspension of Ag D(-)HDBT (142) (0.8 g, 0.0017 mol) in 25 mL of boiling H_3COH. The mixture was boiled for 1 h with stirring and then allowed to cool to room temperature. The resulting solution was filtered to give AgCl (0.22 g, 100%). The clear filtrate was evaporated to dryness (rotary evaporator). The residue was dissolved in ca. 15 mL of H_2CCl_2, and the solution was treated with charcoal and filtered. The clear filtrate was concentrated to ca. 10 mL and excess dry ether was added. After 2 h, the solid separated was filtered, reprecipitated (H_2CCl_2:ether) and dried in vacuo to give 0.75 g (75%) of meso-122 [D(-)HDBT], mp 149-151°C(d), $[\alpha]_D^{24^o}$ = - 91.3° (c = 20 mg/2 mL; H_3COH). The proposed structure of meso-122 [D(-)HDBT] is supported by ^1H NMR, ^{31}P NMR and IR spectra (Plates LVI, LXXXVI and XXVII).

Anal. calcd. for $C_{72}H_{68}O_{16}P_2$: C, 69.11; H, 5.48; P, 4.95.

Found: C, 68.96; H, 5.44; P, 4.96.

Metathesis of Meso-1,1'-(1,2-Ethanediyl)bis(1,-2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis(hydrogen D(-)-dibenzoyltartrate) (Meso-122) to Meso-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Diperchlorate (Meso-117)

The phosphonium salt, meso-122 [D(-)HDBT] (200 mg, 0.16 mmole) was dissolved in 5 mL of H_3COH, and the solution was added slowly to 10 mL of aqueous solution containing $NaClO_4$ (2.0 g, 0.016 mole) with stirring at room temperature. A white solid immediately precipitated

from the aqueous solution. This solid was washed carefully and thoroughly with distilled water (to remove any excess $NaClO_4$) and was then dissolved (25 mL of H_2CCl_2). The solution was dried (Na_2SO_4) and concentrated to ca. 5 mL in the rotary evaporator. Dry ether was added until the solution became cloudy, and the solution was allowed to stand overnight at room temperature. The solid separated was filtered, and two reprecipitations (H_2CCl_2-ether) were required to get 0.085 g (72%) of a compound, [mp 289-291°C, $[\alpha]_D = 0^\circ$ (c = 20 mg/2 mL; acetone)] which is identical to meso-117 (2 ClO_4^-) separated from the diastereomeric mixture of 117.

Alkaline Hydrolysis of Meso-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Dichloride (Meso-119)

Aqueous sodium hydroxide (10 mL, 2 N) was added to a solution of the bis-salt meso-119 (2 Cl^-) (2.0 g, 0.0033 mol) in 50 mL of H_3COH, and the mixture was boiled for 3 h with presumably the evolution of ethylene. The cooled reaction mixture was diluted with water (200 mL) and extracted with benzene (3 x 50 mL). The extract was dried (Na_2SO_4) and treated with 3 mL of H_3CI. The mixture was allowed to stand overnight at room temperature. The solid separated was filtered and reprecipitated (H_2CCl_2-ether) to give 0.98 g (75%) of methiodide 124, mp 198-200°C. The methiodide 124 was characterized as the hexafluorophosphate 125 which was prepared by treating 0.5 g (0.00126 mol) of 124 in 20 mL of H_3COH:H_2O (1:1) with 20 mL of saturated aqueous KPF_6. The mixture was stirred for 30 min. The solid formed was collected by

filtration and dissolved in H_2CCl_2 (ca. 15 mL). The solution was dried (Na_2SO_4) and excess ether was added until the solution became cloudy. After a period of 2 h, a solid separated was filtered and reprecipitated twice (H_2CCl_2:ether) to yield 0.43 g (83.7%) of 125, mp 211-213°C (lit.[110] mp 211-213.5°C). The benzene filtrate, after separation of methiodide 124, was evaporated on a rotary evaporator. The yellow oil obtained was chromatographed over silica gel (benzene) and the resulting oil was stored in a refrigerator for a period of 3 days. The waxy solid obtained was recrystallized (hexane) to give 0.4 g (45%) of phosphine oxide 126, mp 103-105°C (lit.[46] mp 99-101°C).

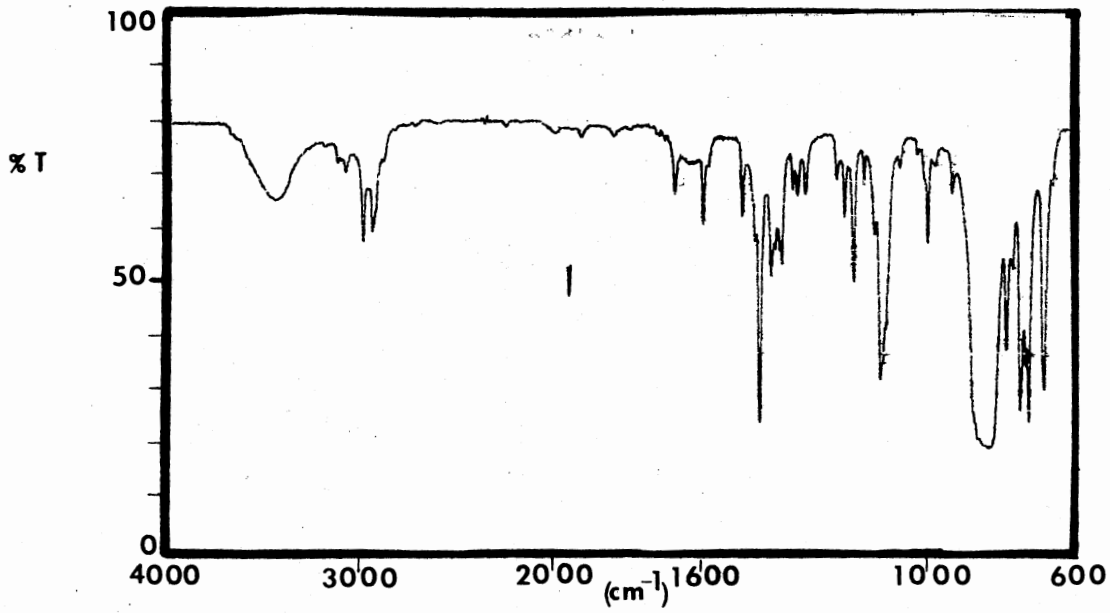
Lithium Aluminium Hydride Reduction of Meso-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Dichloride (Meso-119)

Lithium aluminium hydride (0.125 g; 0.0033 mol) and meso-119 (0.4 g, 0.0006 mol) were stirred under reflux in dry THF (25 mL) for a period of 24 h. The reaction mixture was cooled to room temperature and the excess hydride was destroyed by careful addition of ice-cold water (ca. 0.25 mL). The reaction mixture was extracted with ether (3 x 25 mL). The extract was dried (Na_2SO_4), concentrated to ca. 10 mL and treated with H_3CI (2 mL). The mixture was allowed to stand overnight in refrigerator. The solid separated was filtered and reprecipitated (H_2CCl_2-ether) to give 0.16 g (31%) of 124, mp 198-200°C. A small amount (0.10 g) of the methiodide 124 was converted to the hexafluorophosphate 125, mp 211-213°C (lit.[110] mp 211-213.5°C).

Sodium Hydride Reduction of Meso-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Dichloride (Meso-119)

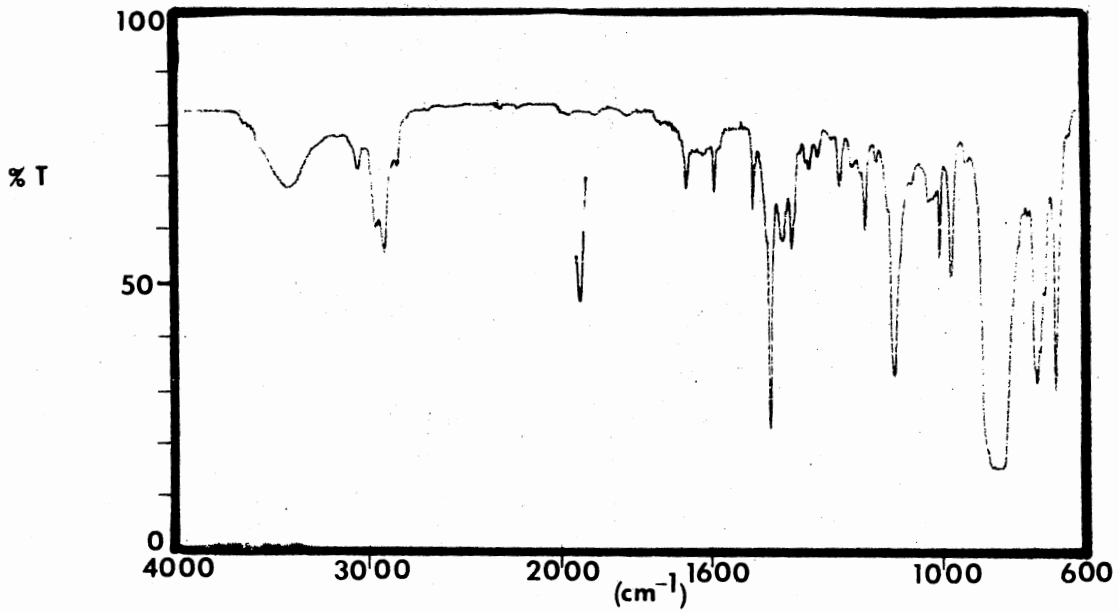
A suspension of meso-119 (2 Cl^-) (0.607 g, 0.001 mol) and sodium hydride (0.048 g, 0.002 mol, 50% dispersion in paraffin; washed with dry ether) in THF (20 mL, distilled from $LiAlH_4$) was stirred at room temperature for a period of 12 h. The reaction mixture was filtered directly into a large excess of H_3CI (5 mL) in ether (20 mL). The mixture was filtered and reprecipitated (H_2CCl_2-ether) to give 0.115 g (15%) of 124, mp 198-200°C. A small amount (0.075 g) of the methiodide 124 was converted into 125, mp 211-213°C (lit.[110] mp 211-213.5°C).

PLATE I



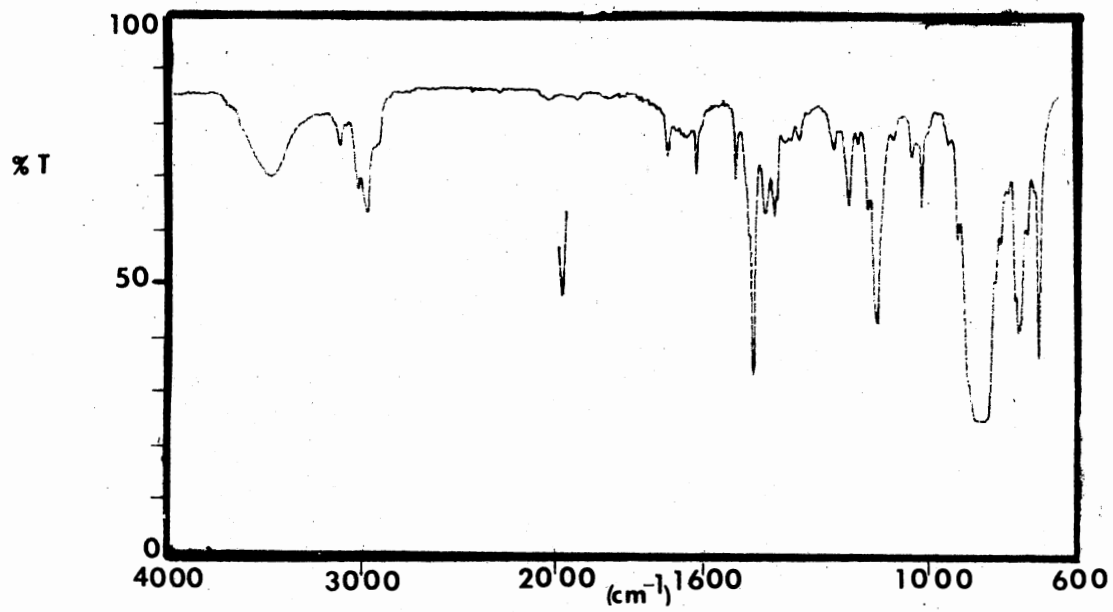
1,2-Ethanediylbis[diphenyl-(3-methyl-2-butenyl)phosphonium] Bis[hexafluorophosphate(1-)] (95), KBr Pellet

PLATE II



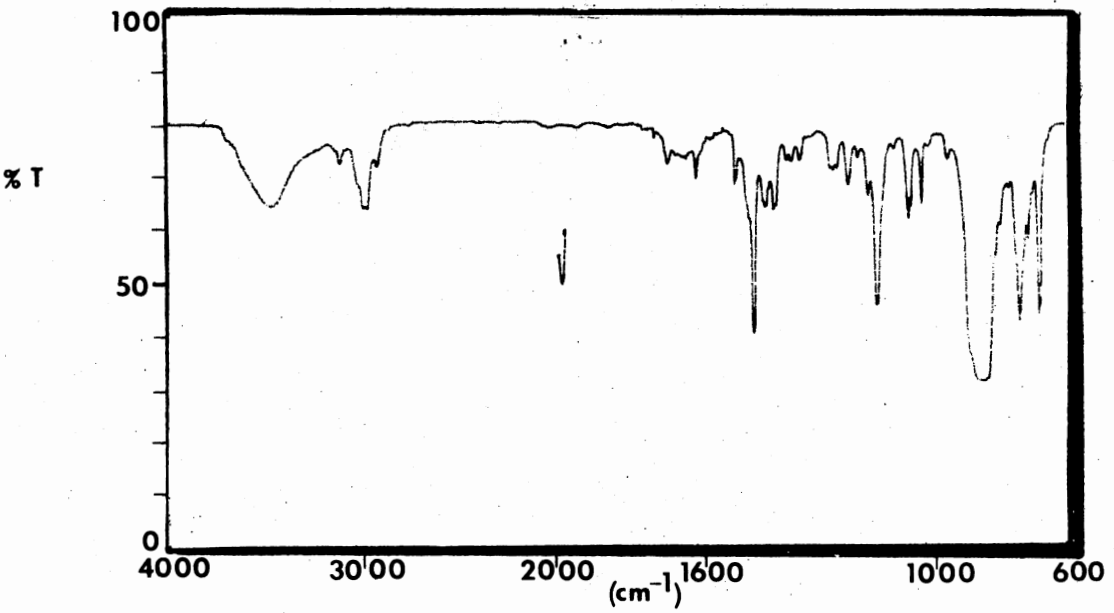
1,3-Propanediylbis[diphenyl-(3-methyl-2-butenyl)phosphonium] Bis[hexafluorophosphate(1-)] (96), KBr Pellet

PLATE III



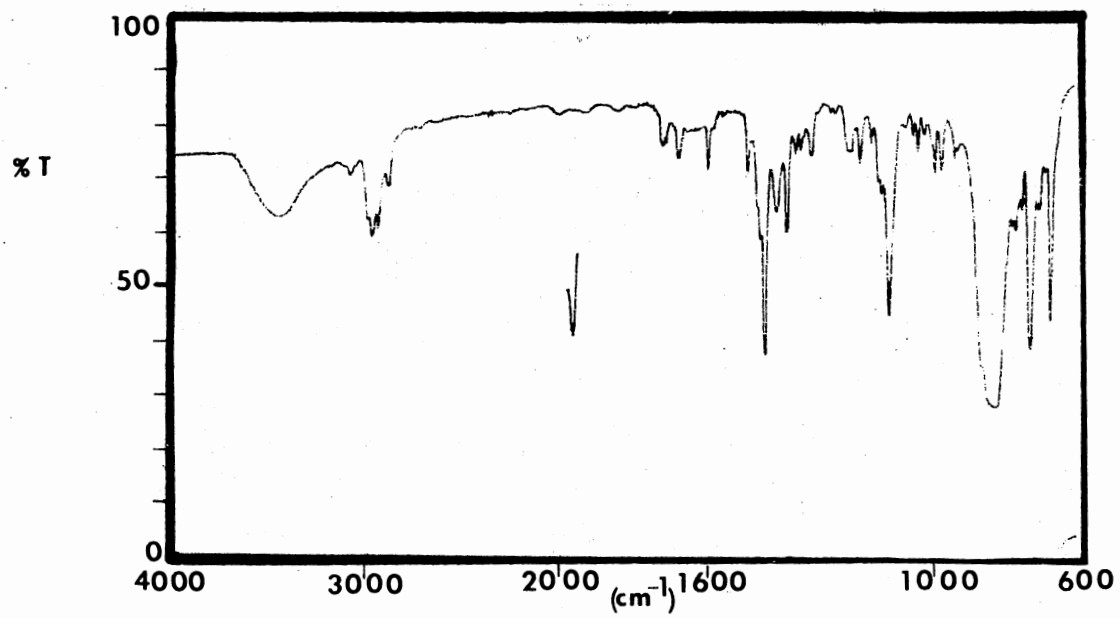
1,4-Butanediylbis[diphenyl-(3-methyl-2-butenyl)phosphonium] Bis[hexafluorophosphate(1-)] (97), KBr Pellet

PLATE IV



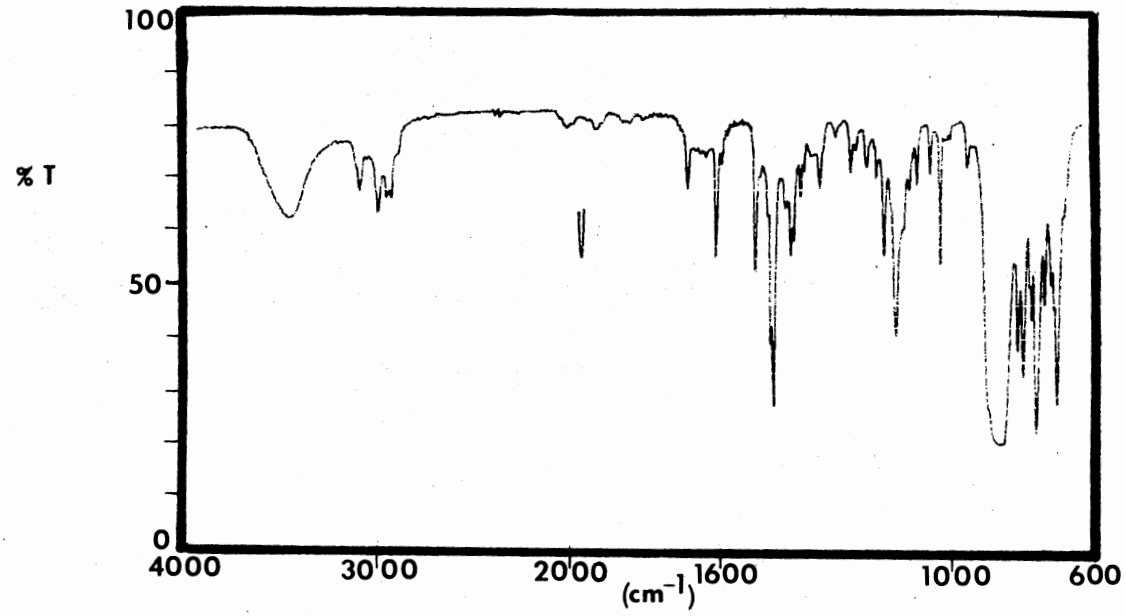
1,5-Pentanediylbis[diphenyl-(3-methyl-2-butenyl)phosphonium] Bis[hexafluorophosphate(1-)] (98), KBr Pellet

PLATE V



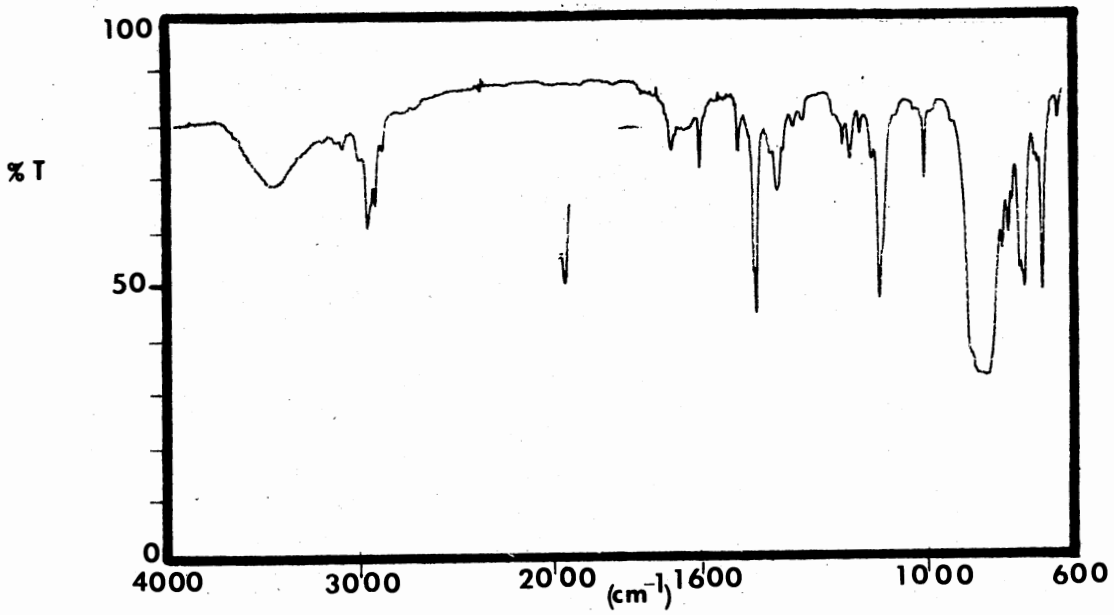
1,6-Hexanediylbis[diphenyl-(3-methyl-2-butenyl)phosphonium] Bis[hexafluorophosphate(1-)] (97), KBr Pellet

PLATE VI



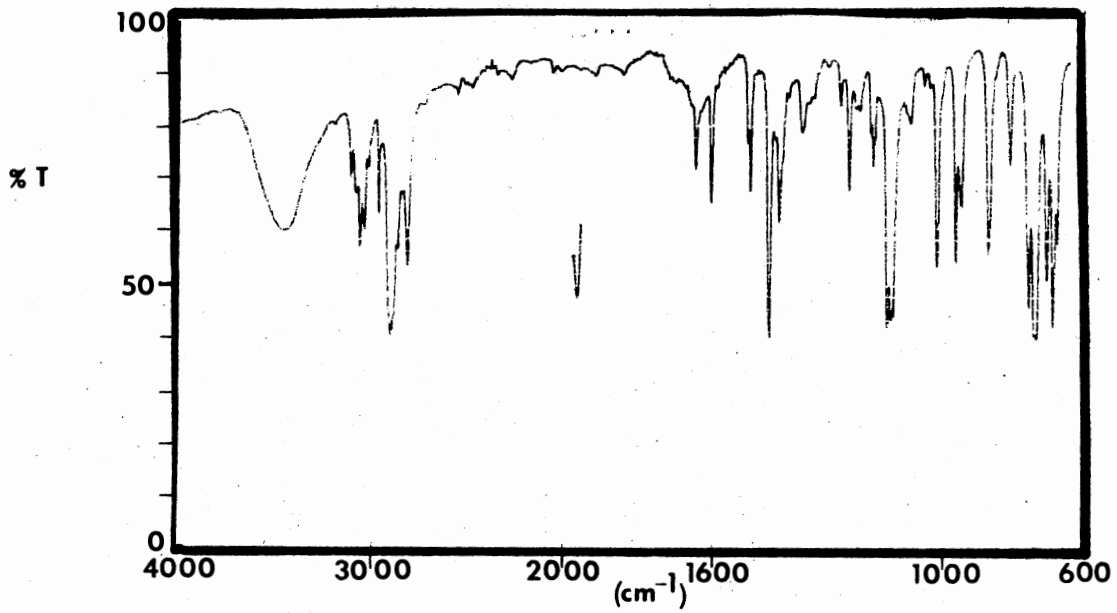
[(Diphenylphosphino)methyl](3-methyl-2-butenyl)diphenylphosphonium Hexafluorophosphate (107), KBr Pellet

PLATE VII



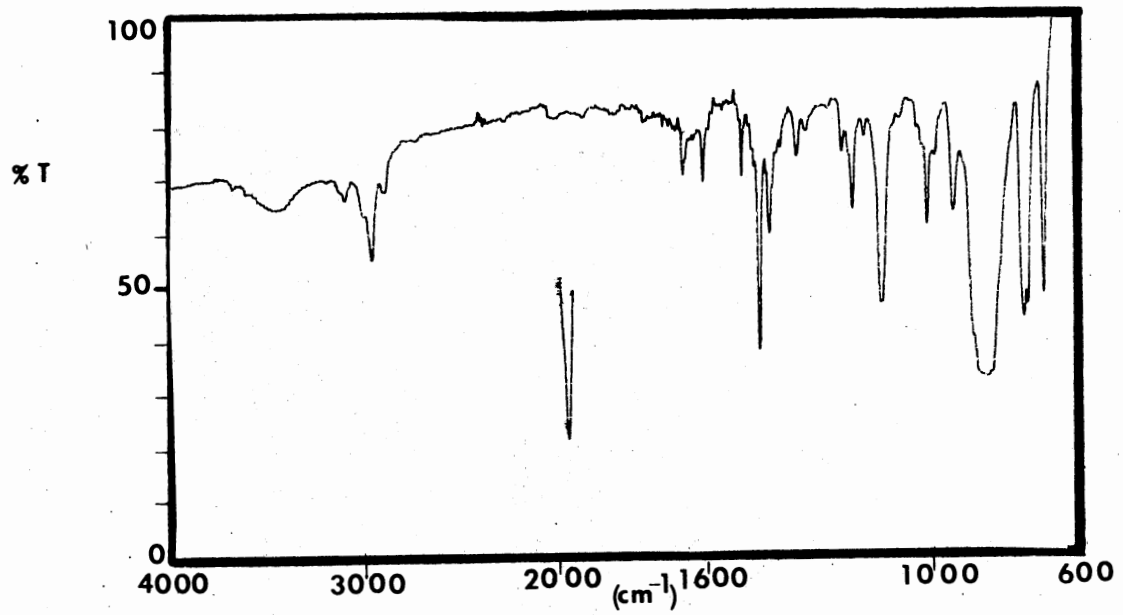
Methanediylbis[diphenyl(3-methyl-2-butenyl)phosphonium] Bis[hexafluorophosphate(1-)] (110), KBr Pellet

PLATE VIII



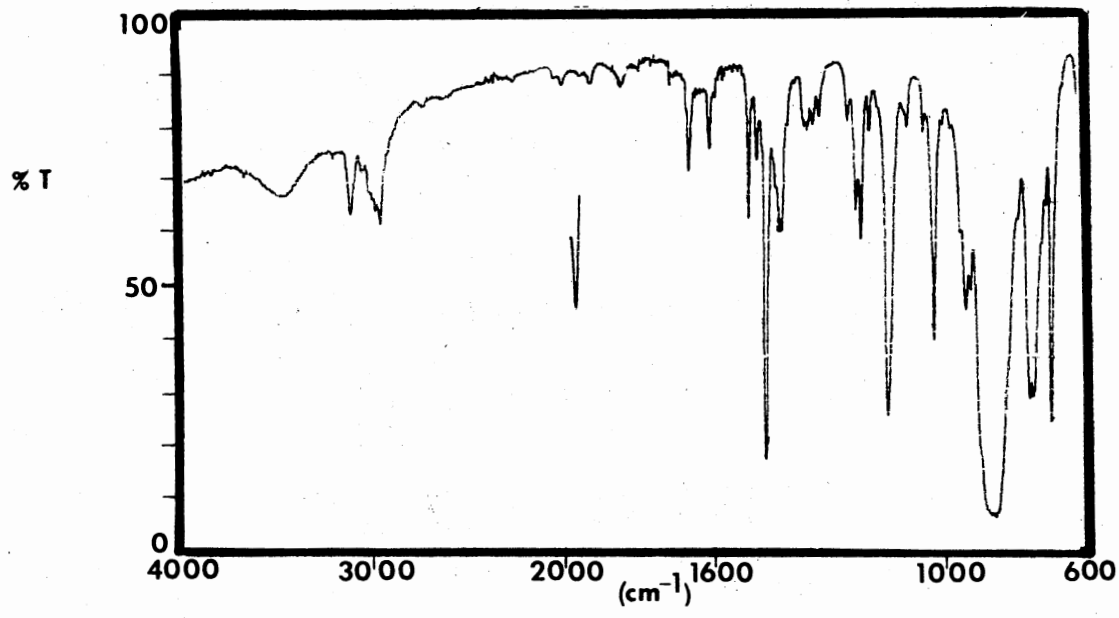
1,2-Ethanediylbis(allyldiphenylphosphonium) Dibromide (112), KBr Pellet

PLATE IX



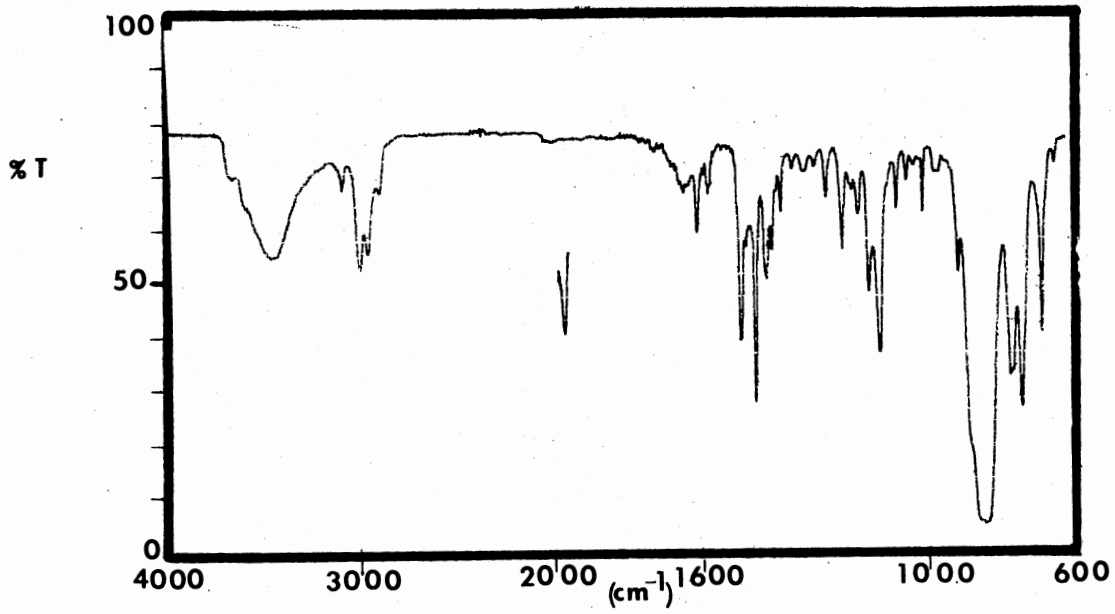
1,2-Ethanediylbis(4-pentenyldiphenylphosphonium) Bis[hexafluorophosphate(1-)] (114), KBr Pellet

PLATE X



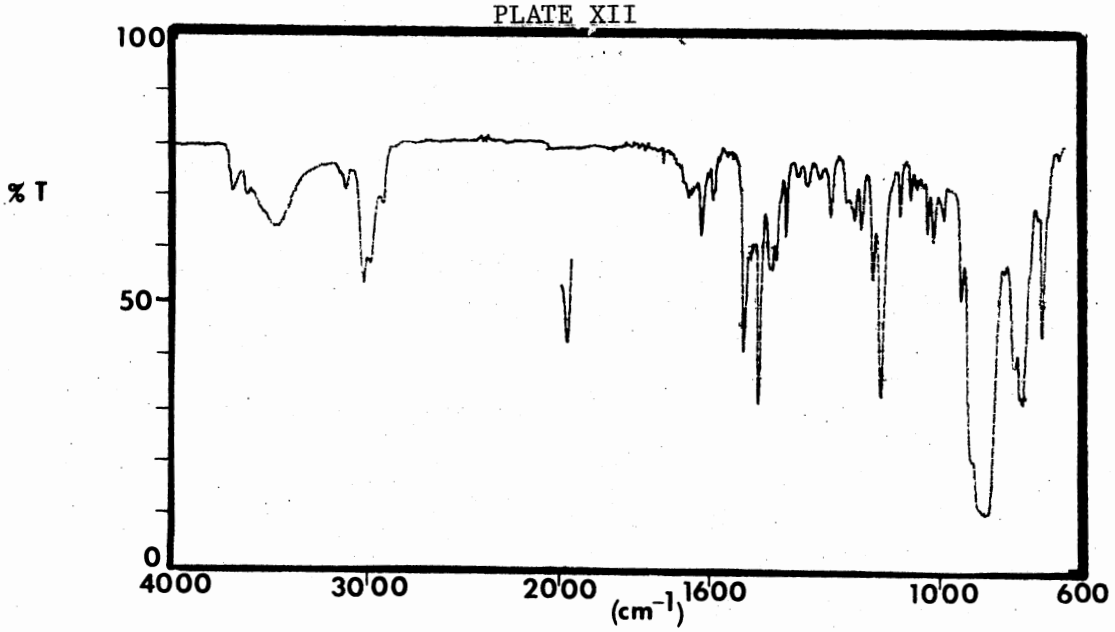
1,4-Butanediylbis(3-butenyldiphenylphosphonium) Bis[hexafluorophosphate(1-)] (116), KBr Pellet

PLATE XI



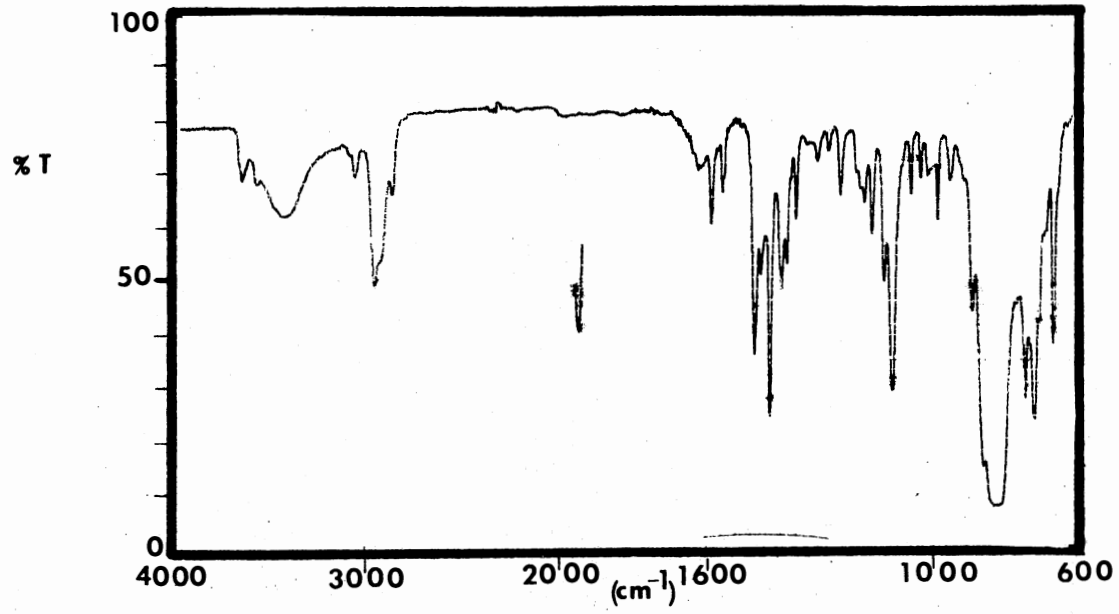
1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hexafluorophosphate(1-)] (100), KBr Pellet

PLATE XII



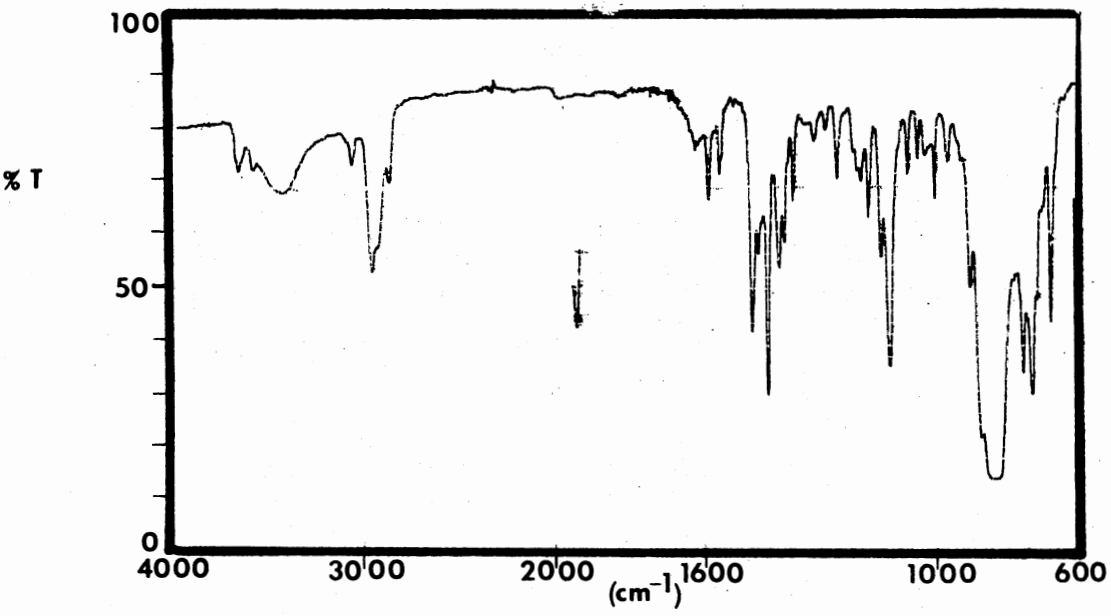
1,1'-(1,3-Propanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hexafluorophosphate(1-)] (101), KBr Pellet

PLATE XIII



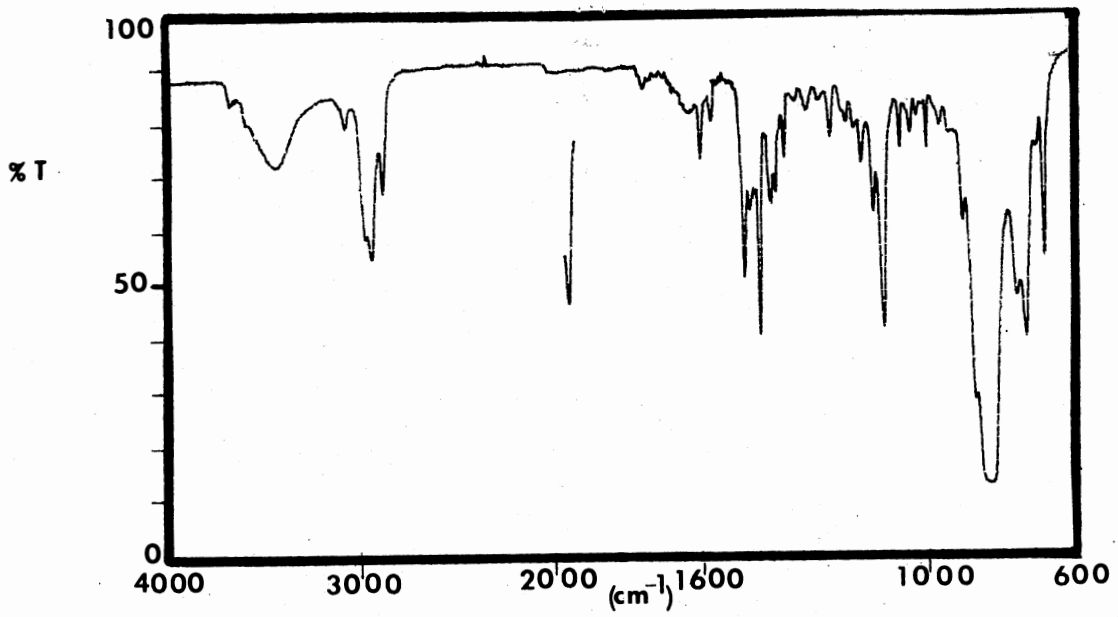
1,1'-(1,4-Butanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hexafluorophosphate(1-)] (102), KBr Pellet

PLATE XIV



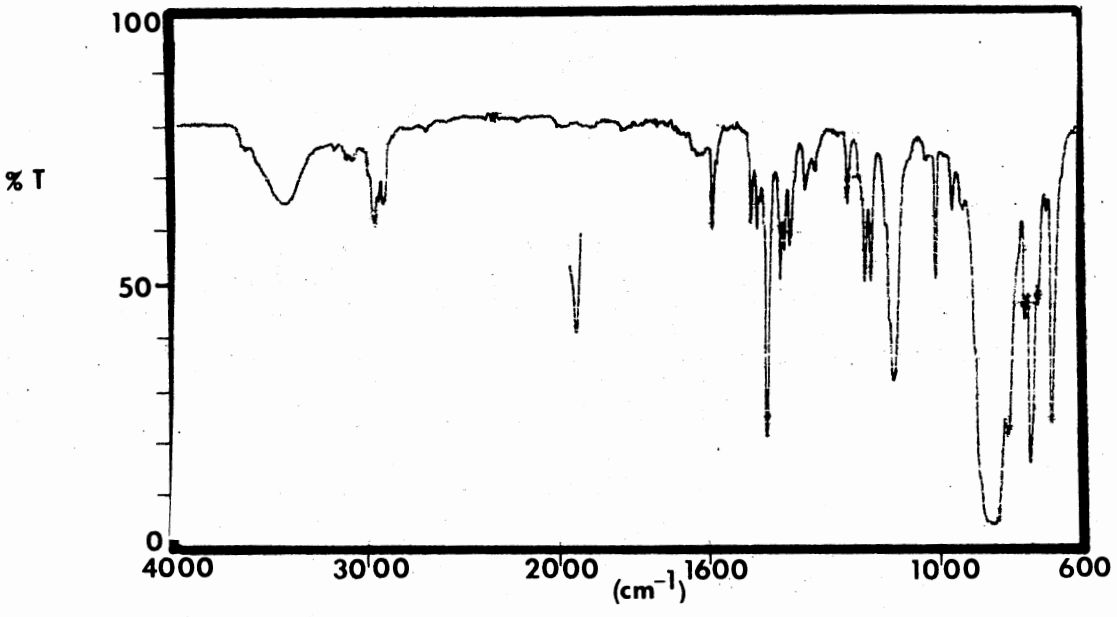
1,1'-(1,5-Pentanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hexafluorophosphate(1-)] (103), KBr Pellet

PLATE XV



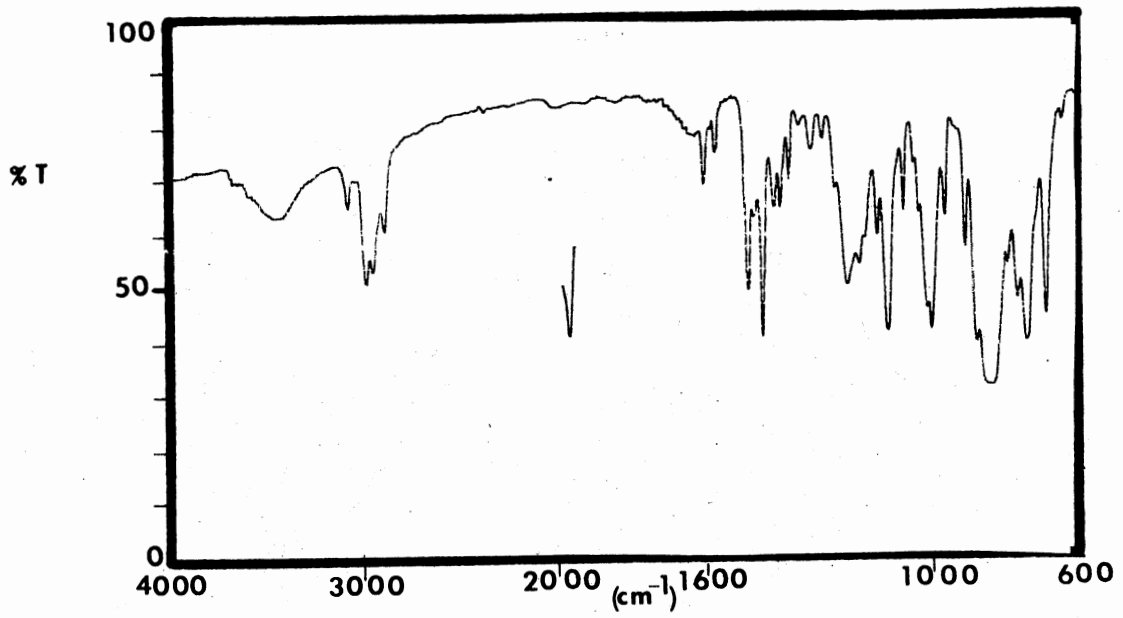
1,1'-(1,6-Hexanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hexafluorophosphate(1-)] (104), KBr Pellet

PLATE XVI



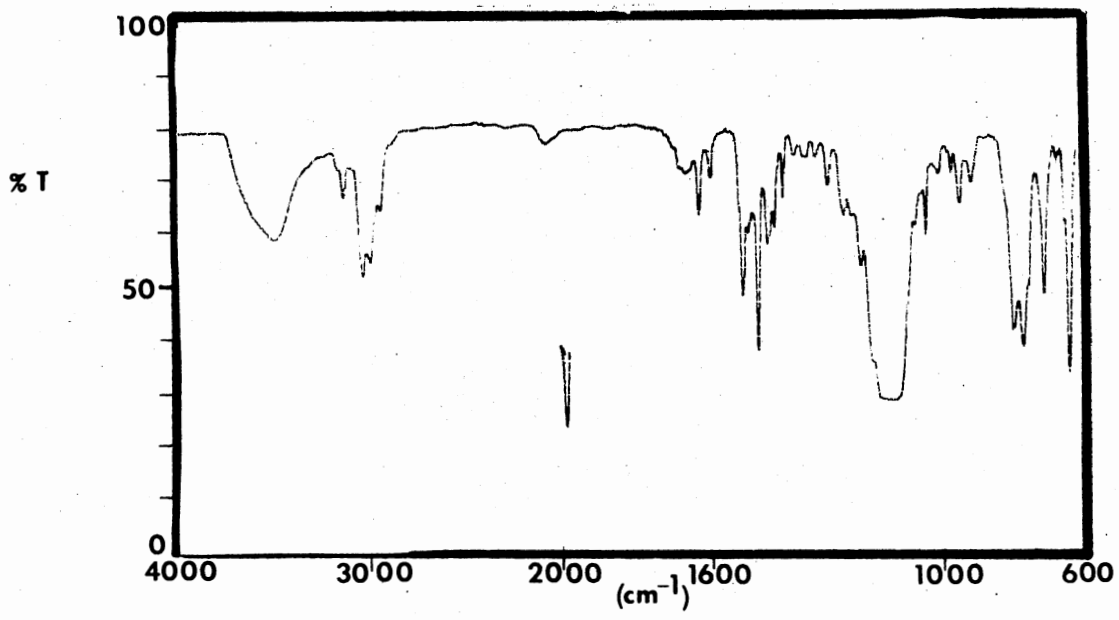
1-[(Diphenylphosphonio)methyl]-1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium Bis[hexafluorophosphate(1-)] (108), KBr Pellet

PLATE XVII



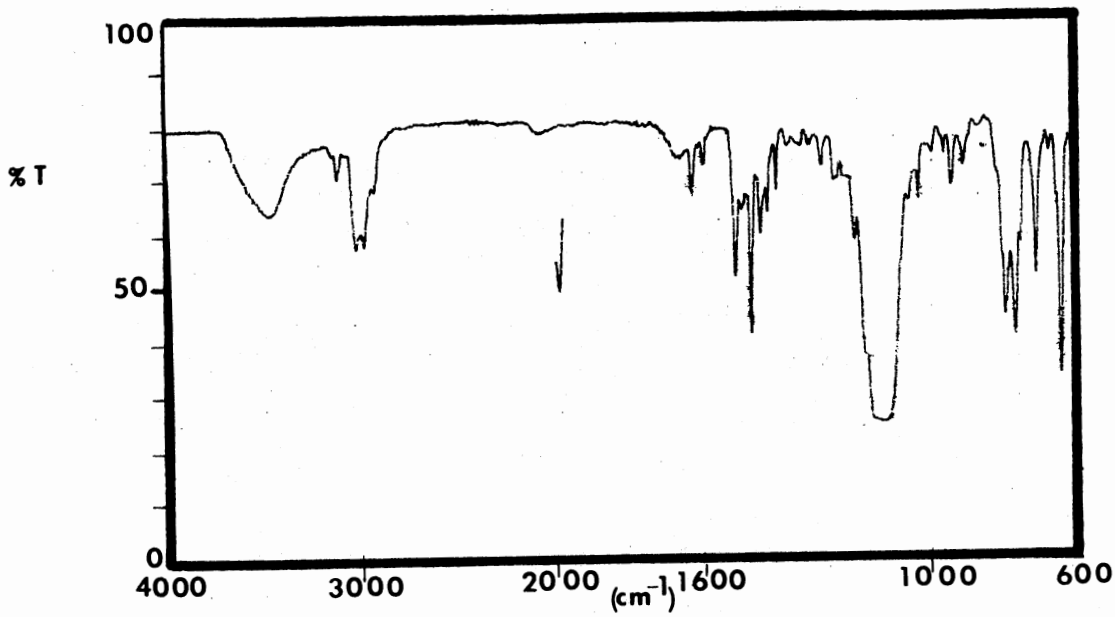
1,1'-(Methanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hexafluorophosphate(1-)] (111), KBr Pellet

PLATE XVIII



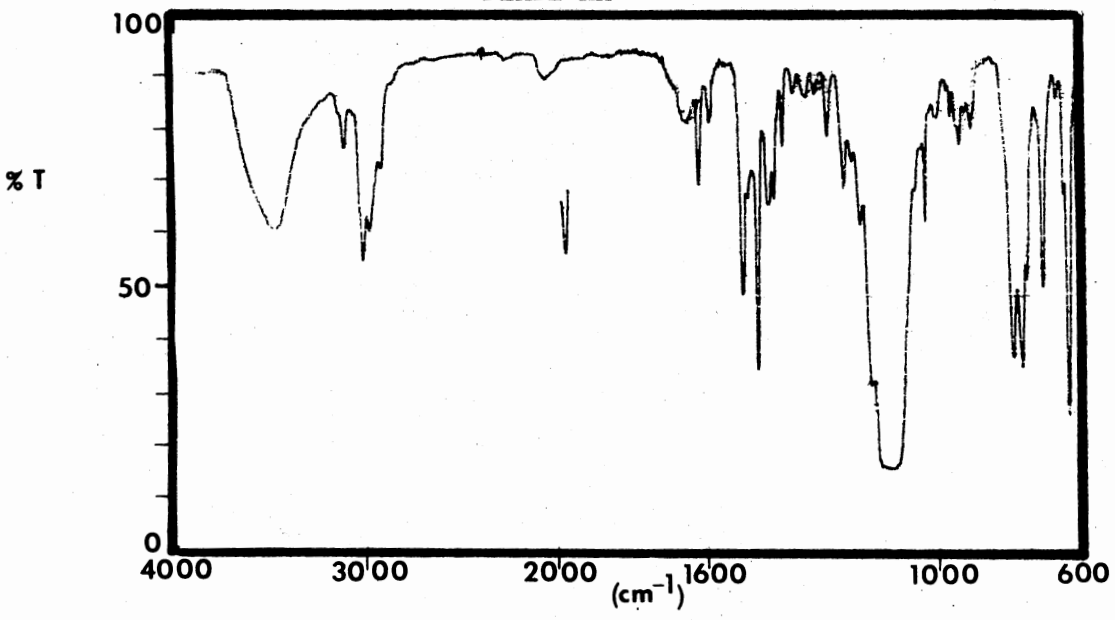
1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Diperchlorate (117), KBr Pellet

PLATE XIX



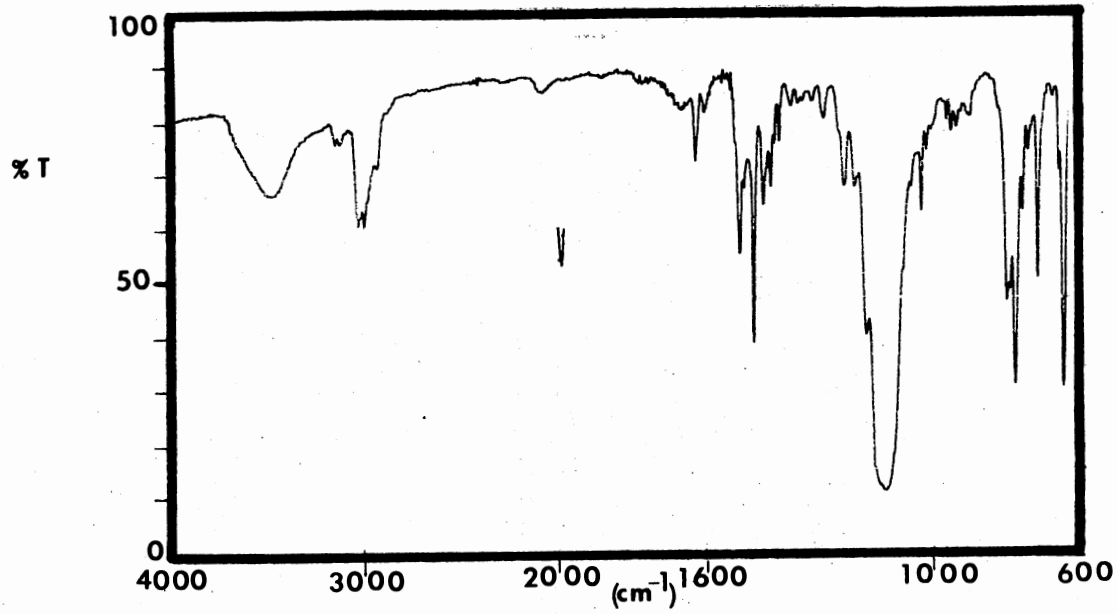
Meso-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Diperchlorate (Meso-117), KBr Pellet

PLATE XX



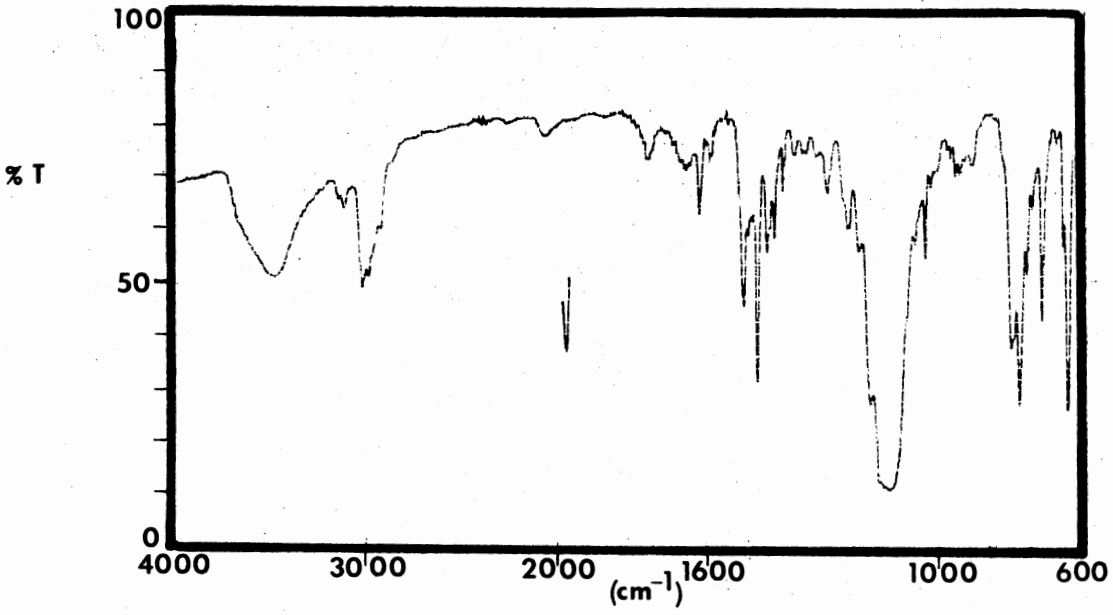
(±)-1,1-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Diperchlorate [(±)-117], KBr Pellet

PLATE XXI



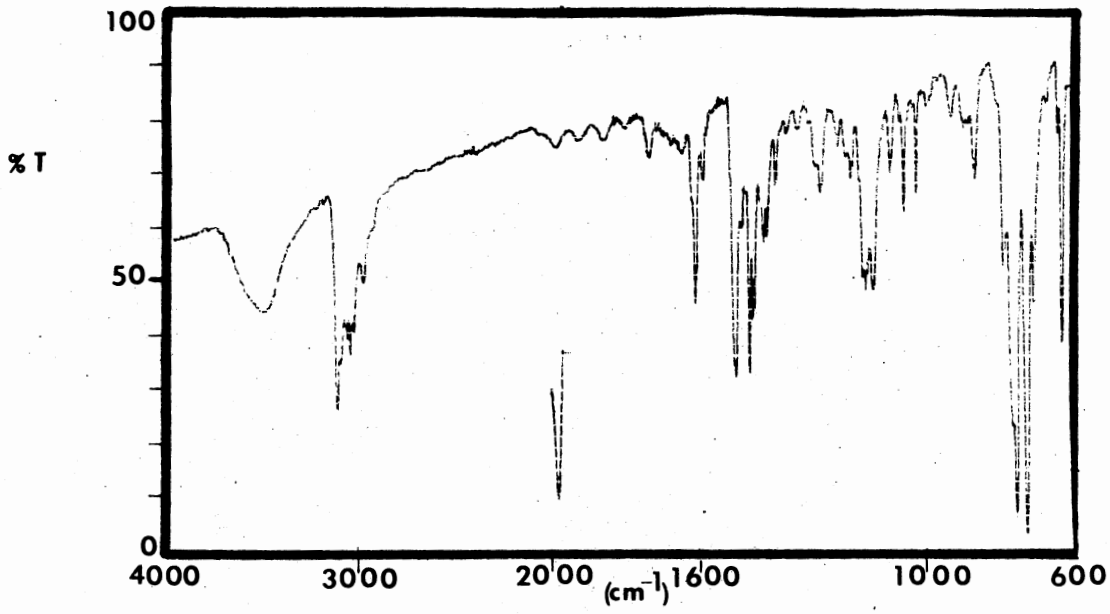
(+)-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Diperchlorate [(+)-117], KBr Pellet

PLATE XXII



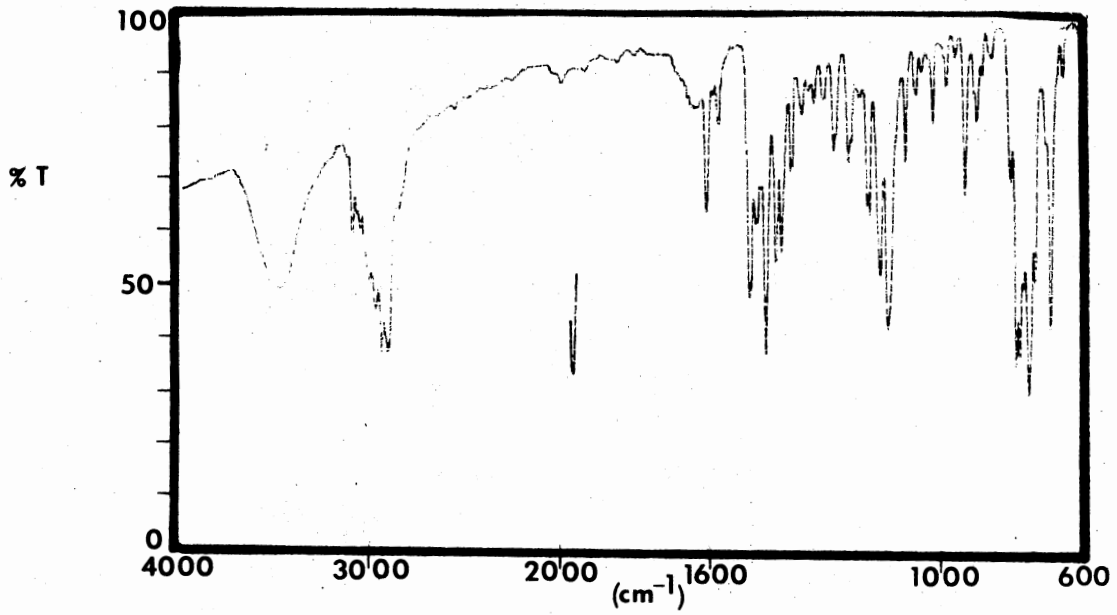
(-)-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Diperchlorate [(-)-117], KBr Pellet

PLATE XXIII



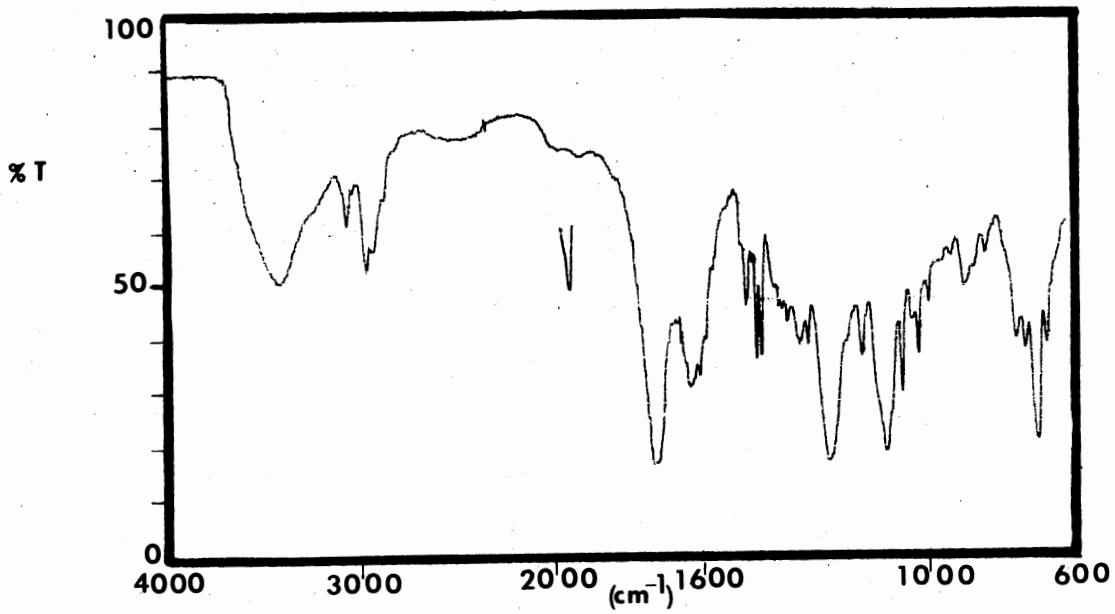
(±)-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis(tetraphenylborate) [(±)-118], KBr Pellet

PLATE XXIV



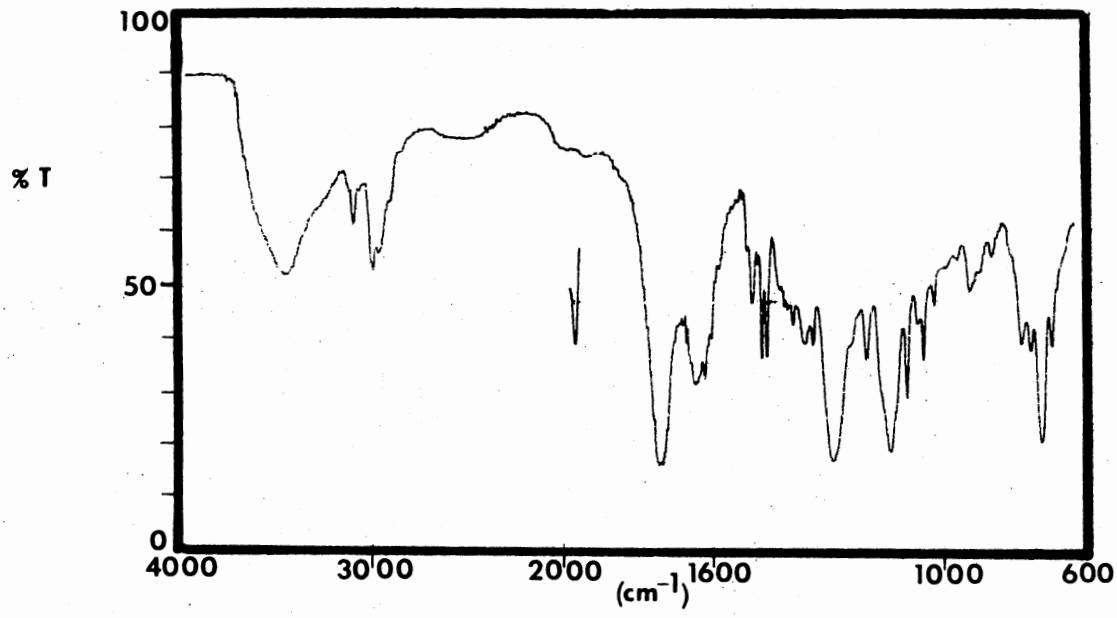
Meso-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Diiodide (Meso-120), KBr Pellet

PLATE XXV



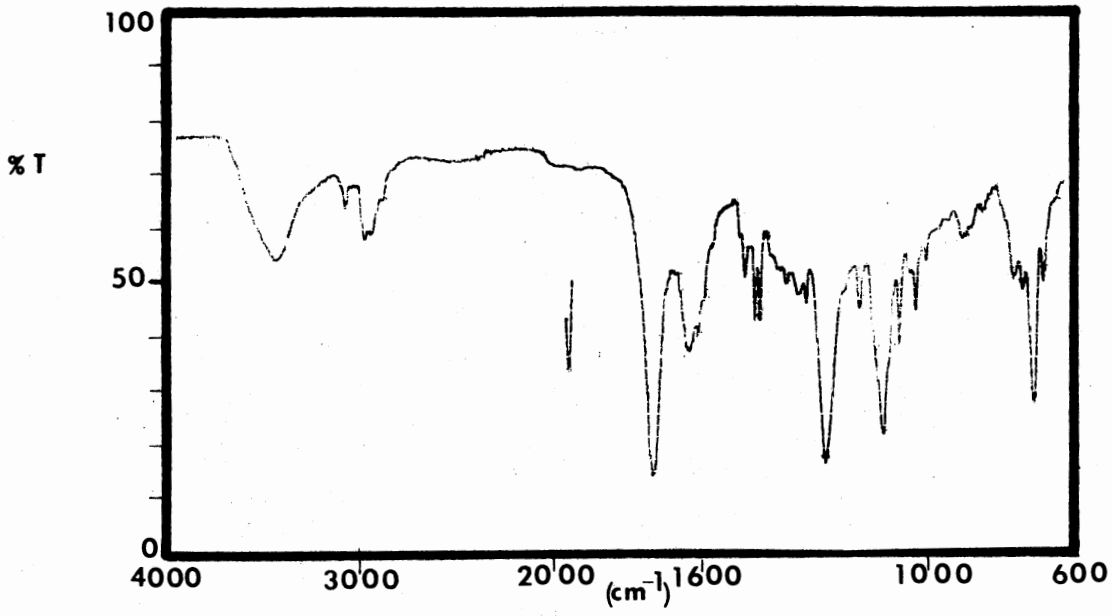
(-)-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hydrogen L(+)-dibenzoyltartrate] [(-)-121], KBr Pellet

PLATE XXVI



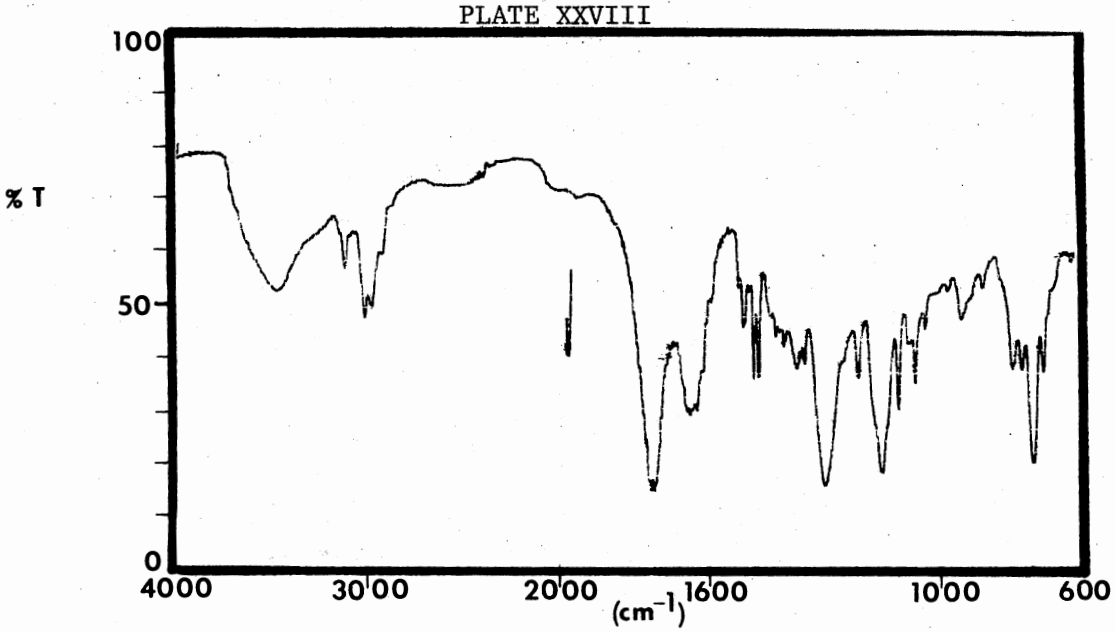
Meso-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hydrogen L(+)-dibenzoyltartrate] (Meso-121), KBr Pellet

PLATE XXVII



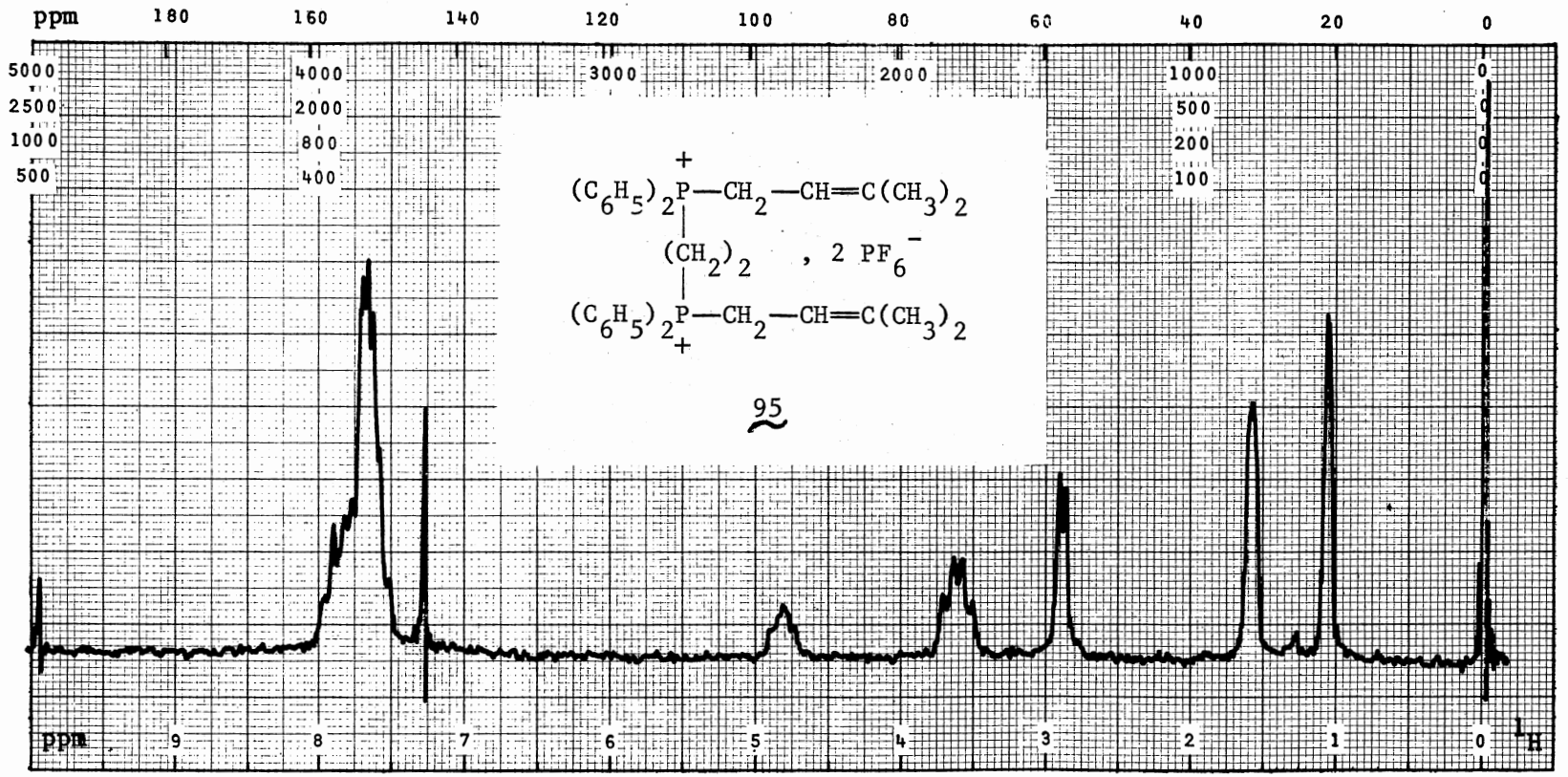
(+)-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hydrogen D(-)-dibenzoyltartrate] [(+)-122], KBr Pellet

PLATE XXVIII



Meso-1,1'-(1,2-Ethanediyl)bis(1,2,3,4-tetrahydro-4,4-dimethyl-1-phenylphosphinolinium) Bis[hydrogen D(-)-dibenzoyltartrate] (Meso-122), KBr Pellet

PLATE XXIX



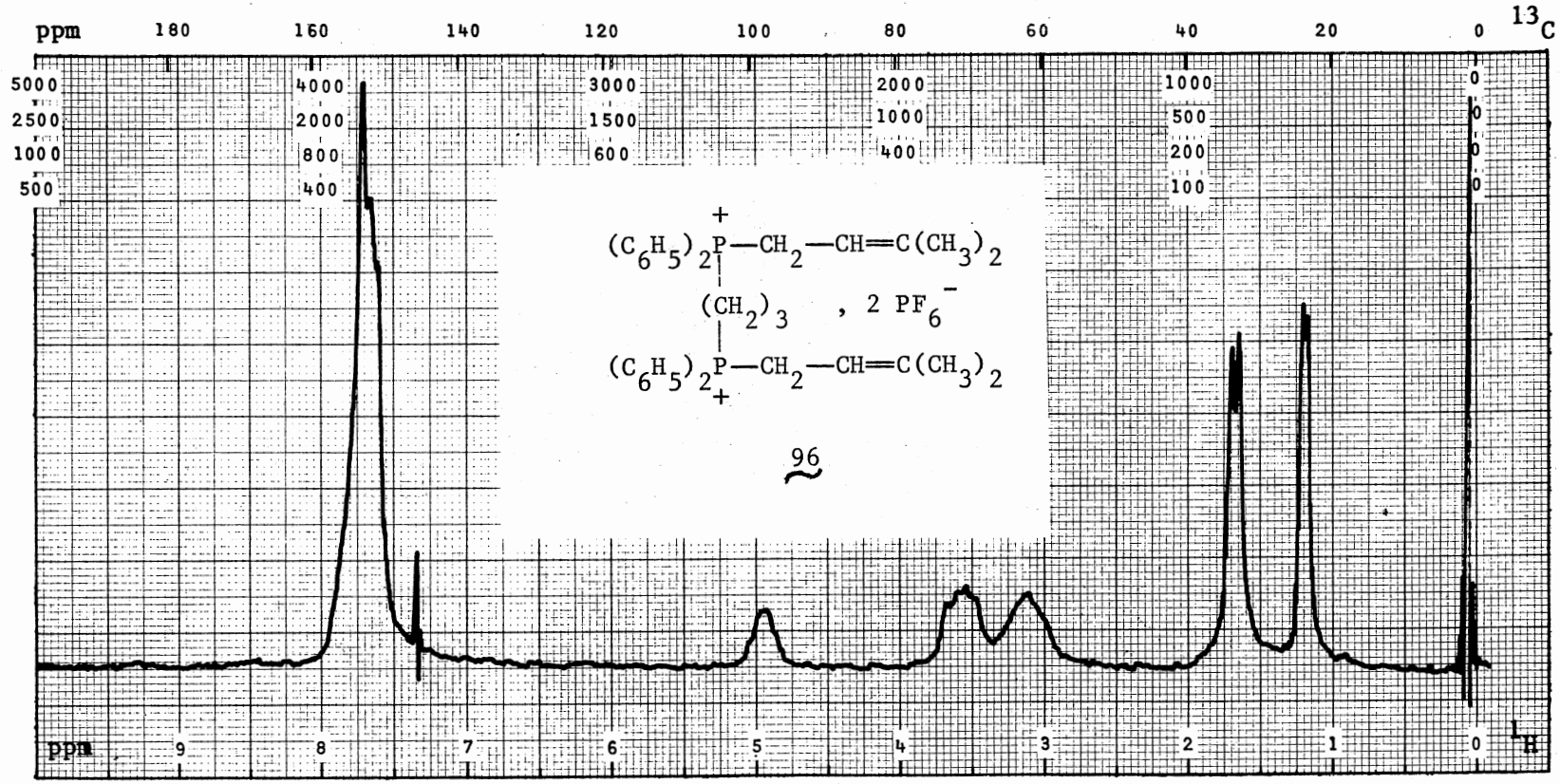
95

^{1}H NMR Spectrum of 95

PFT CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 70 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XXX

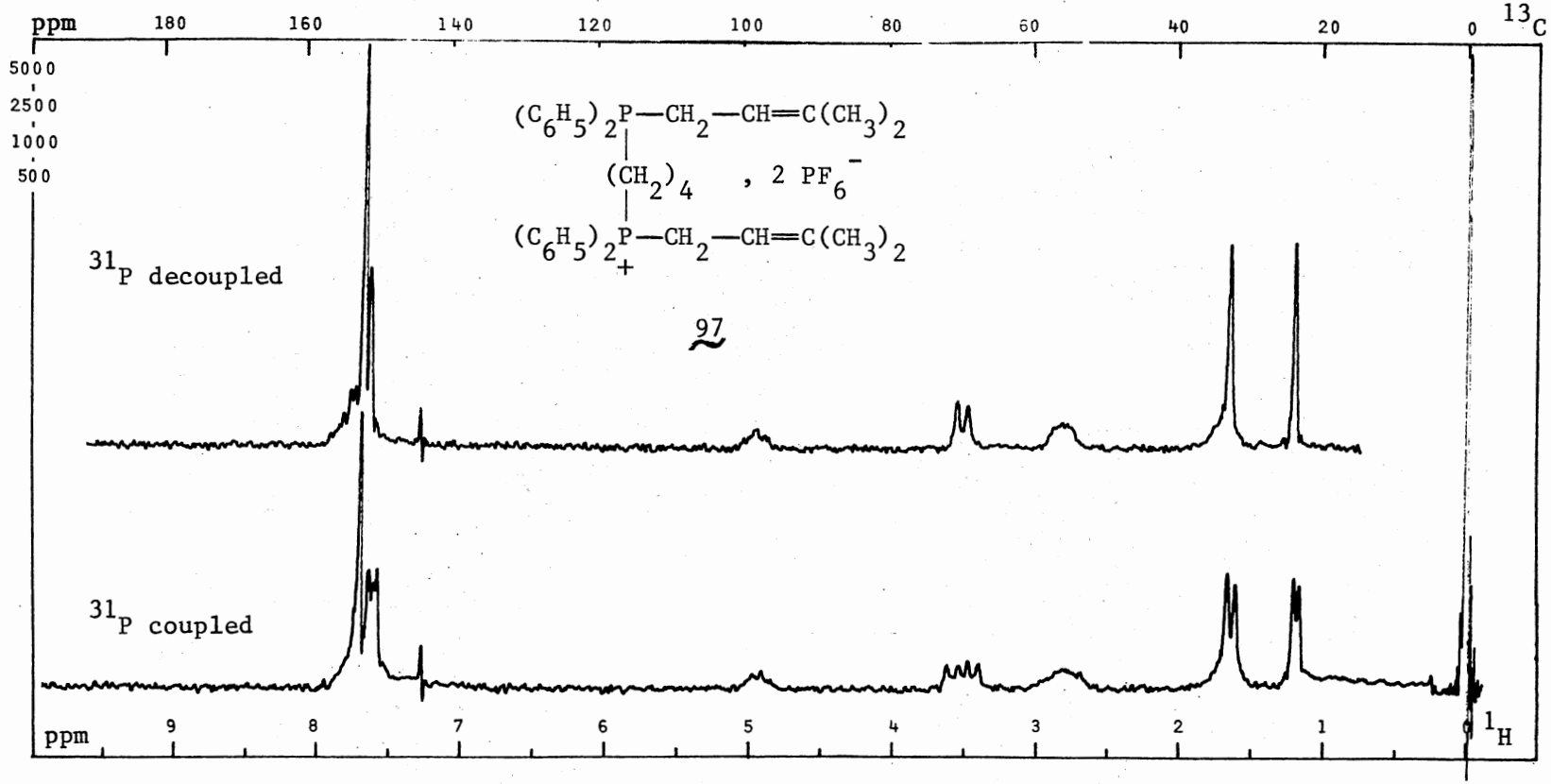


^{1}H NMR Spectrum of 96

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 72 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XXXI



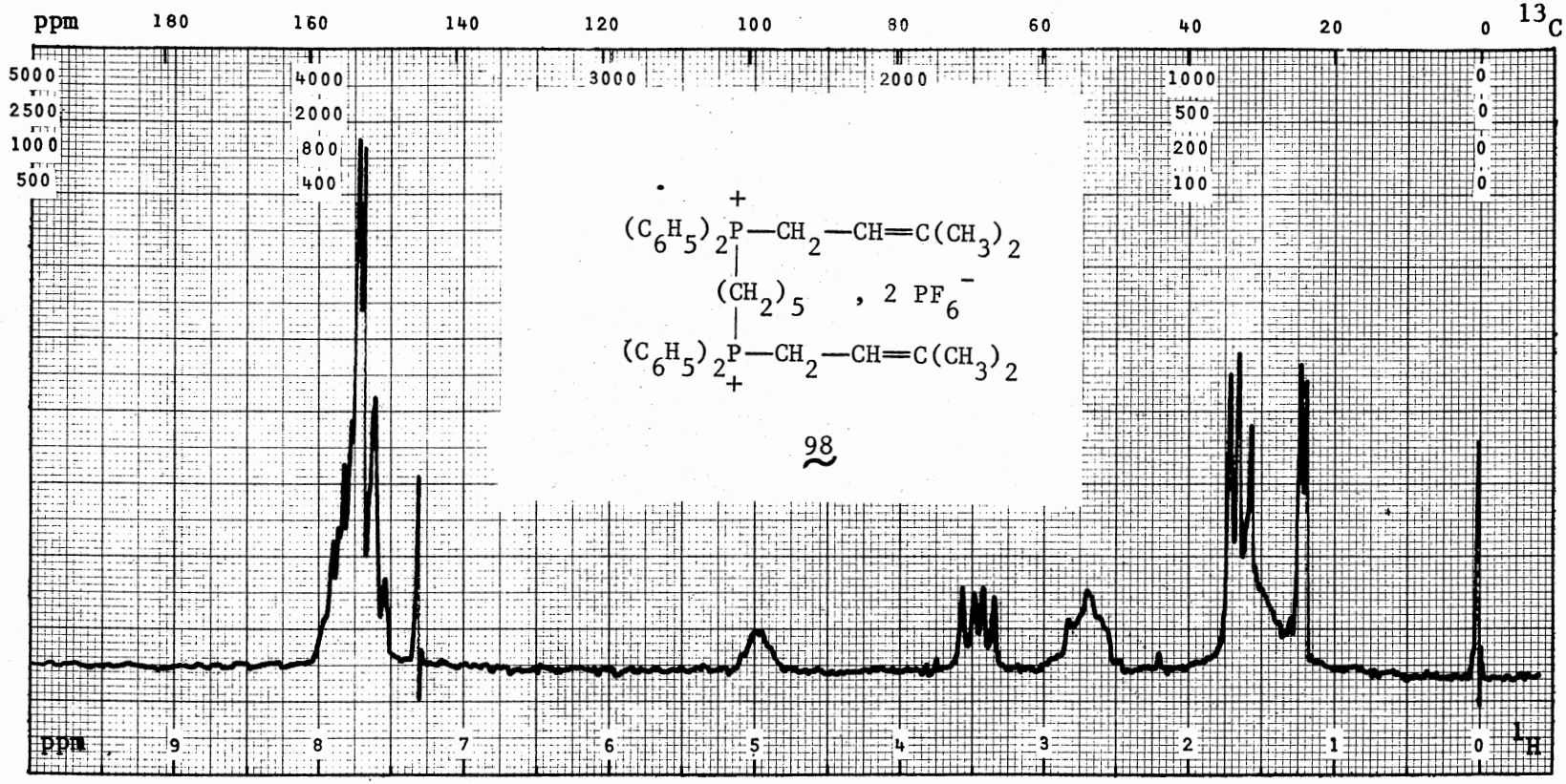
^1H NMR Spectrum of 97

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 26°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 69 µs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^2H; D5/ST . . 250 s.

DC . . . ^{31}P; Gated Off . . ; Offset . 59401 Hz; RF . 1.5 W/dB; NBW . 100 Hz.

PLATE XXXII

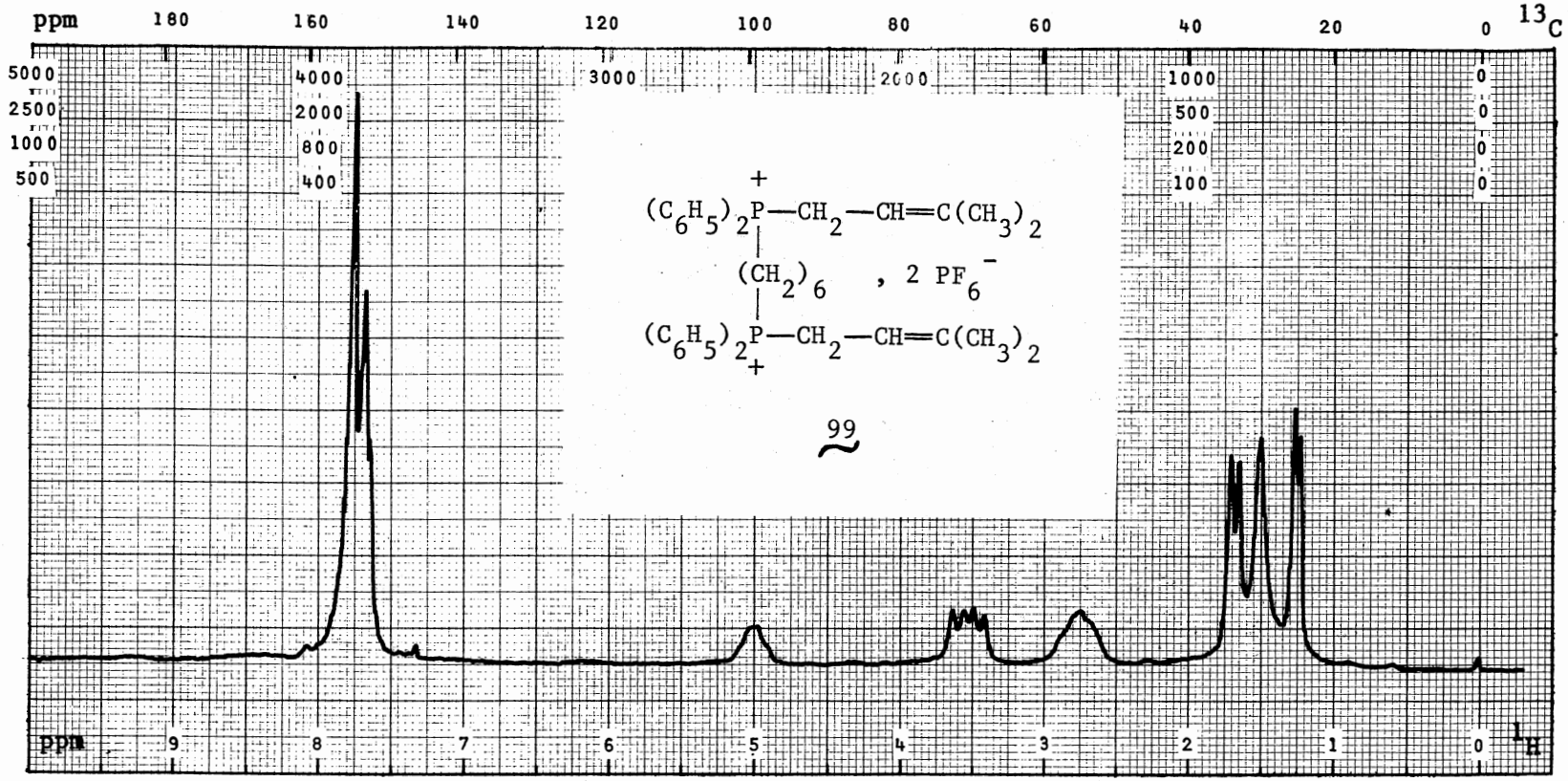


^1H NMR Spectrum of 98

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 70 µs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^2H; D5/ST . . 250 s.

PLATE XXXIII



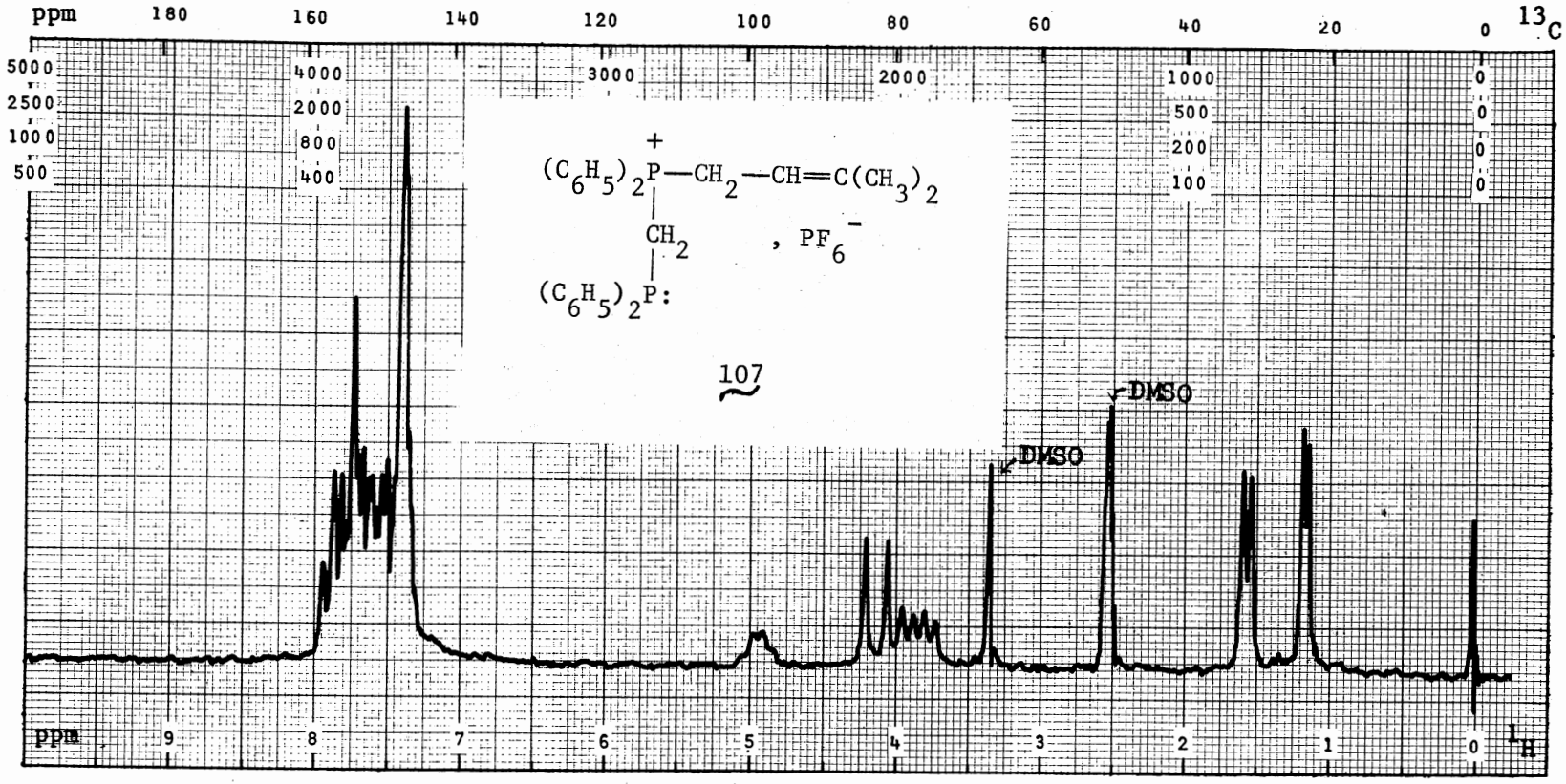
99

^{1}H NMR Spectrum of 99

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 59 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XXXIV



$$(C_6H_5)_2P(CH_2)(CH_2)P(C_6H_5)_2 \cdot 2PF_6^-$$

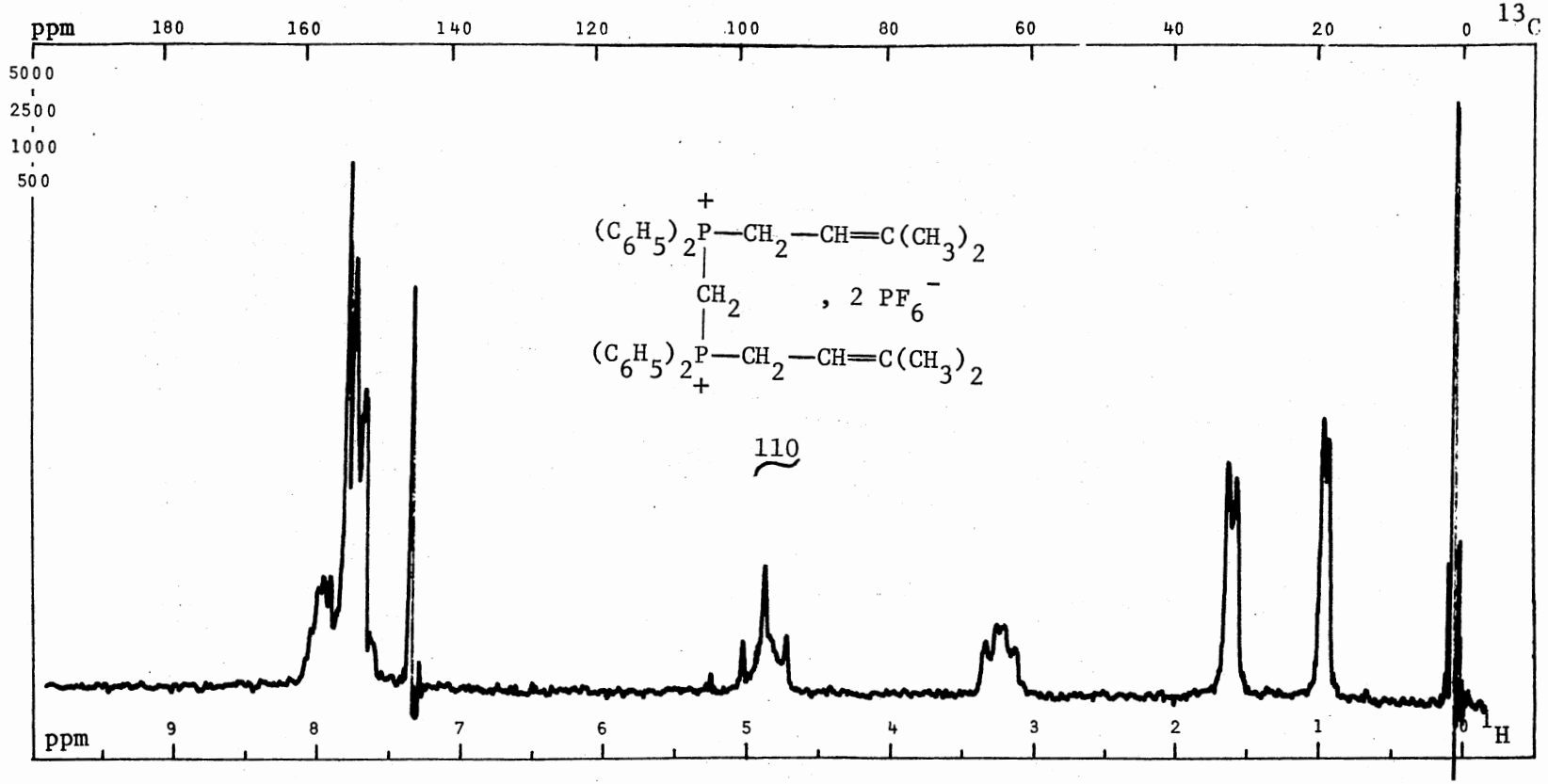
107

^{1}H NMR Spectrum of 107

PFT _ CW X; Solvent . . . . DMSO-d_6; SO . . 86295 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 70 µs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XXXV

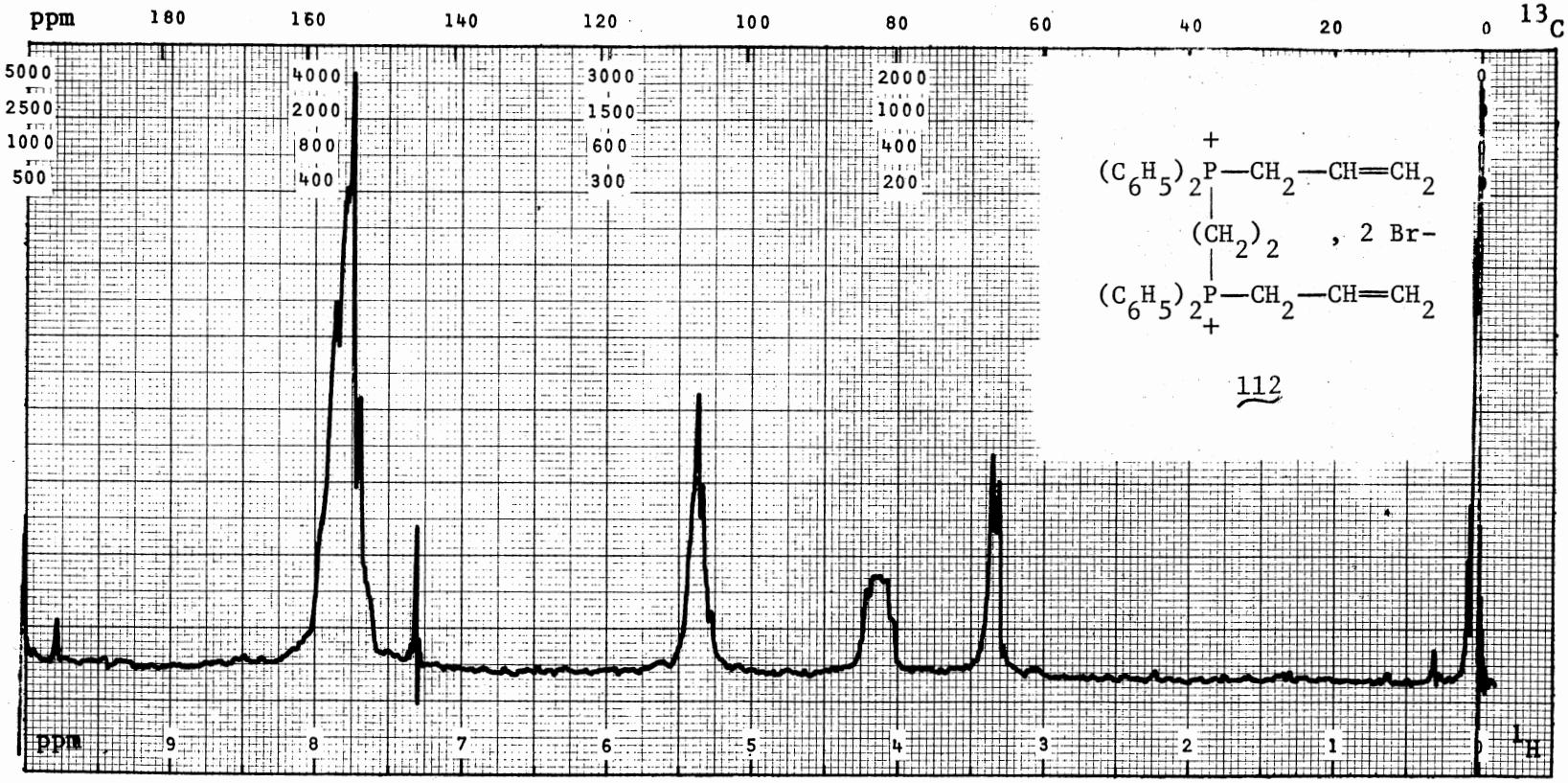


^{1}H NMR Spectrum of 110

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 28°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 71 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XXXVI

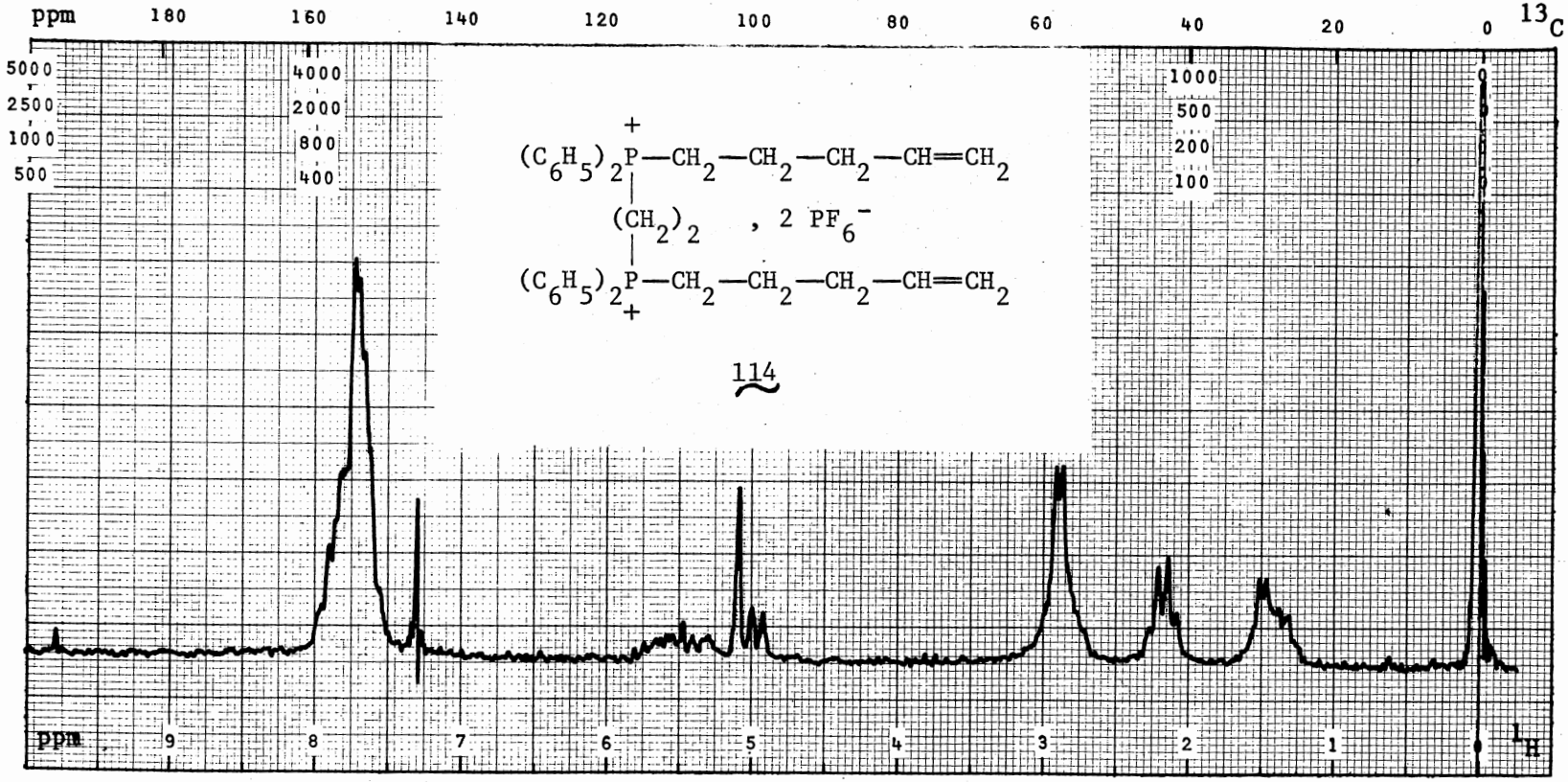


^{1}H NMR Spectrum of 112

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 28°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 69 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XXXVII



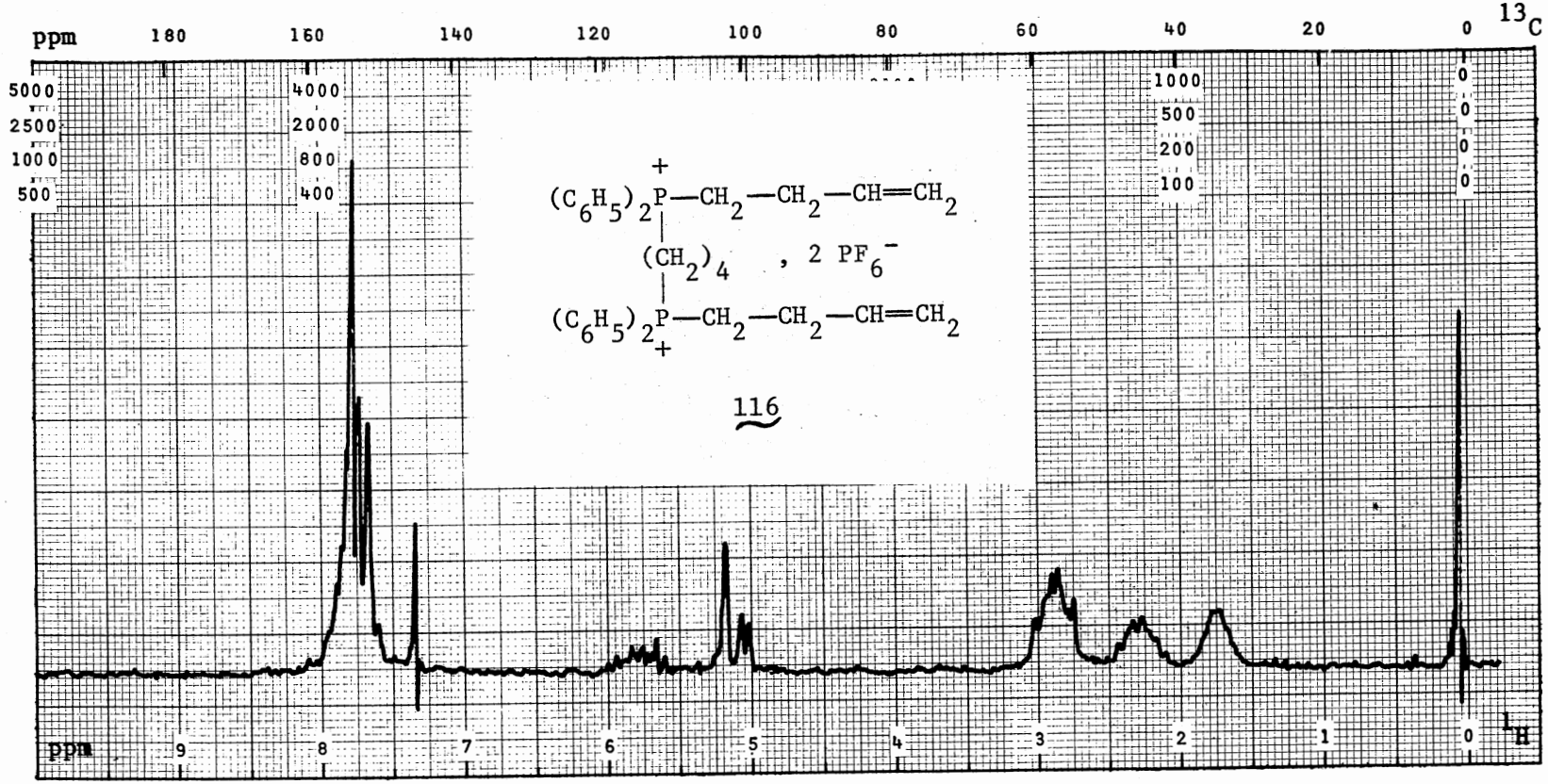
114

^{1}H NMR Spectrum of 114

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 28°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 69 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XXXVIII



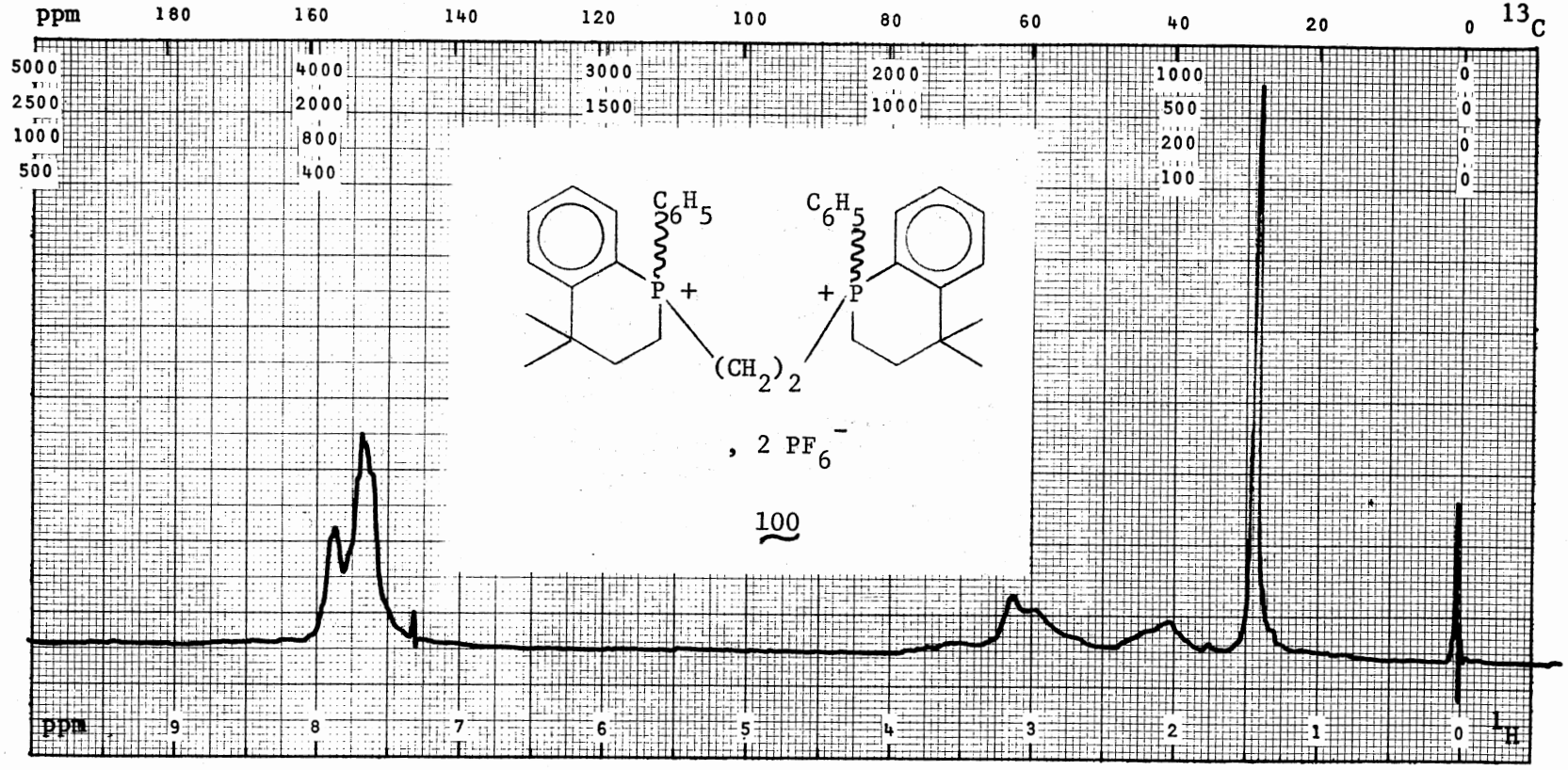
116

^{1}H NMR Spectrum of 116

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 69 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XXXIX

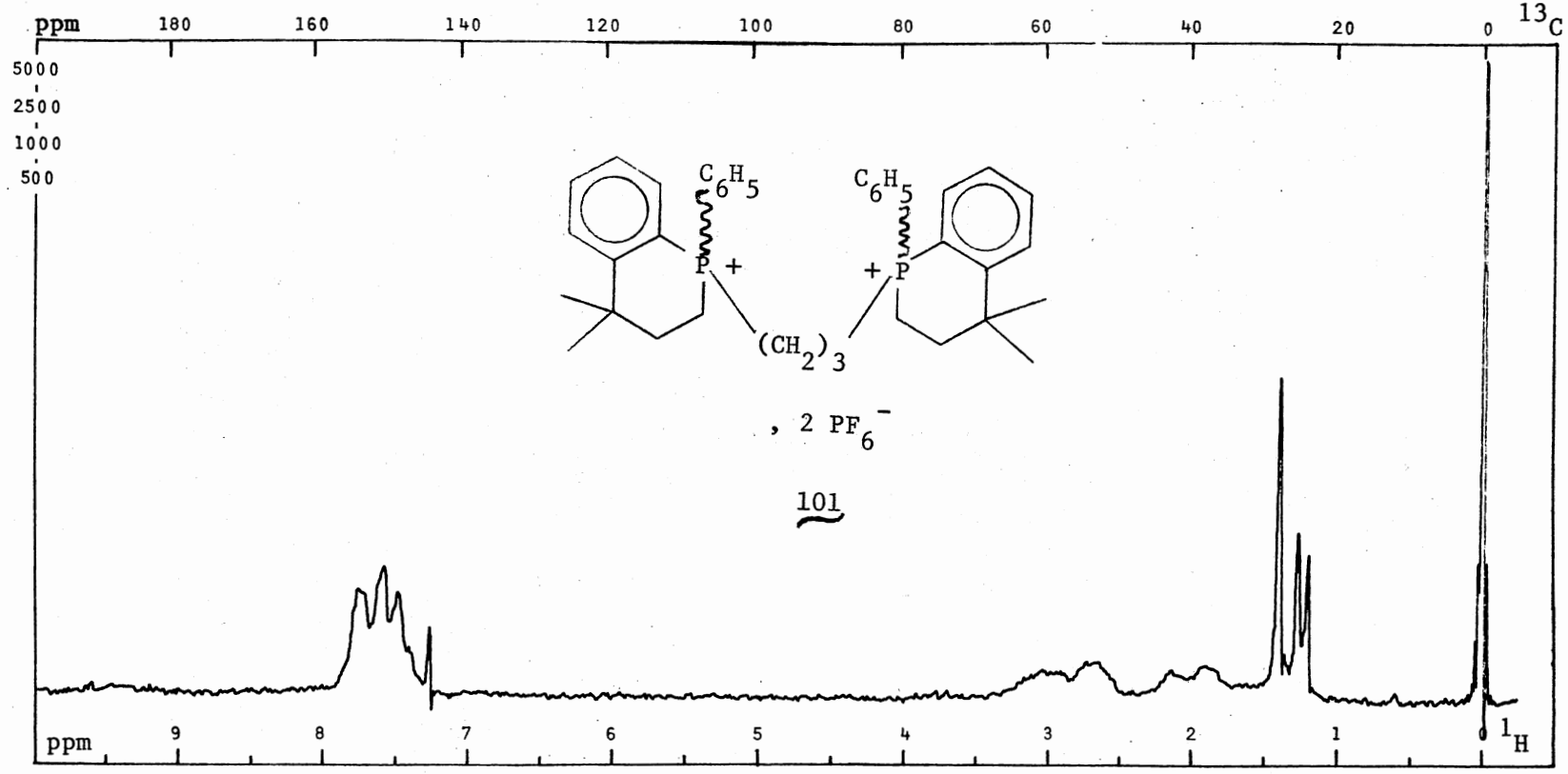


^{1}H NMR Spectrum of 100

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 28°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 61 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XL

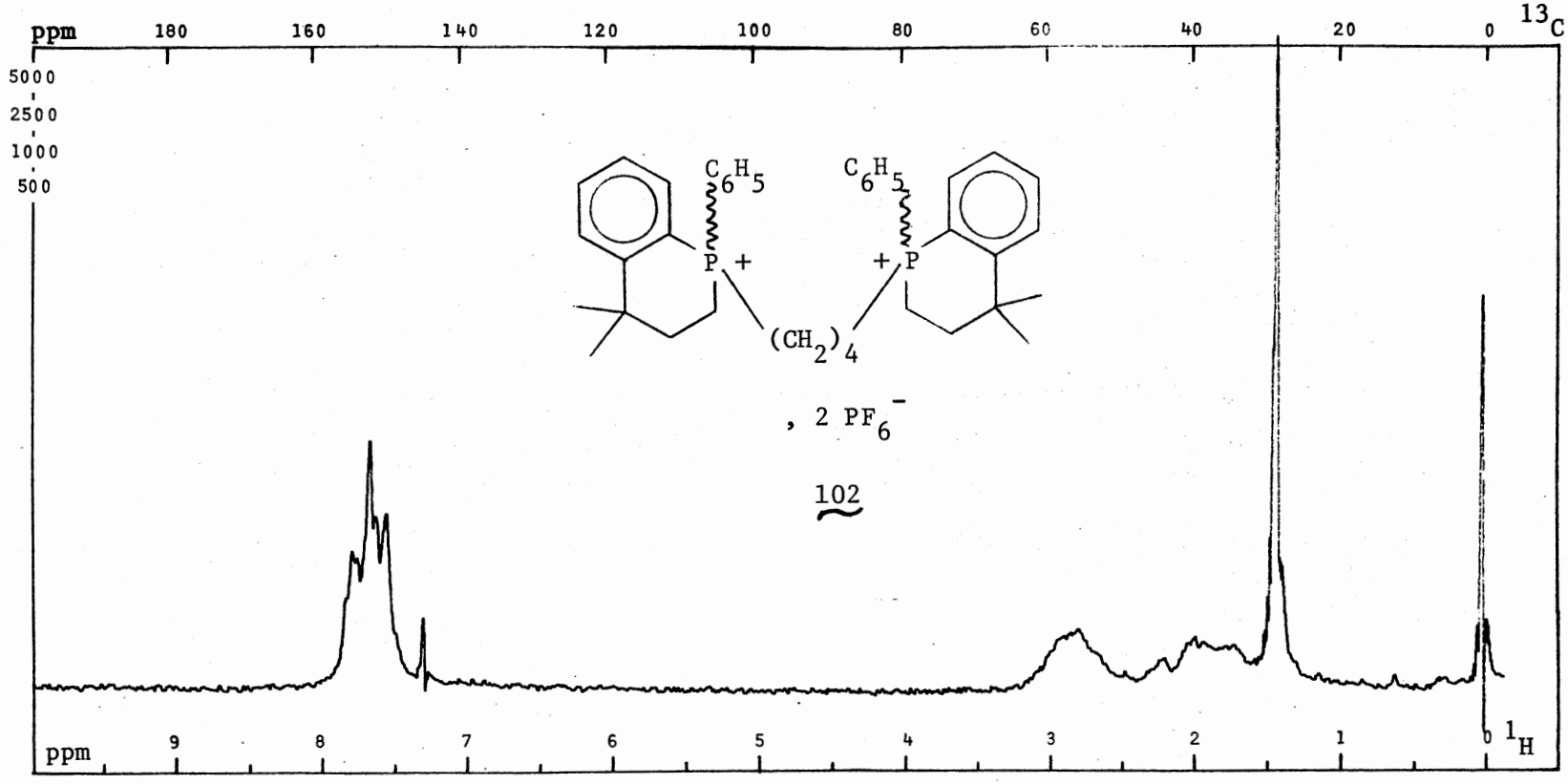


^{1}H NMR Spectrum of 101

PFT _ CW X; Solvent . . $DCCl_3$ + TFA: SO . . 85771 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 71 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XLI

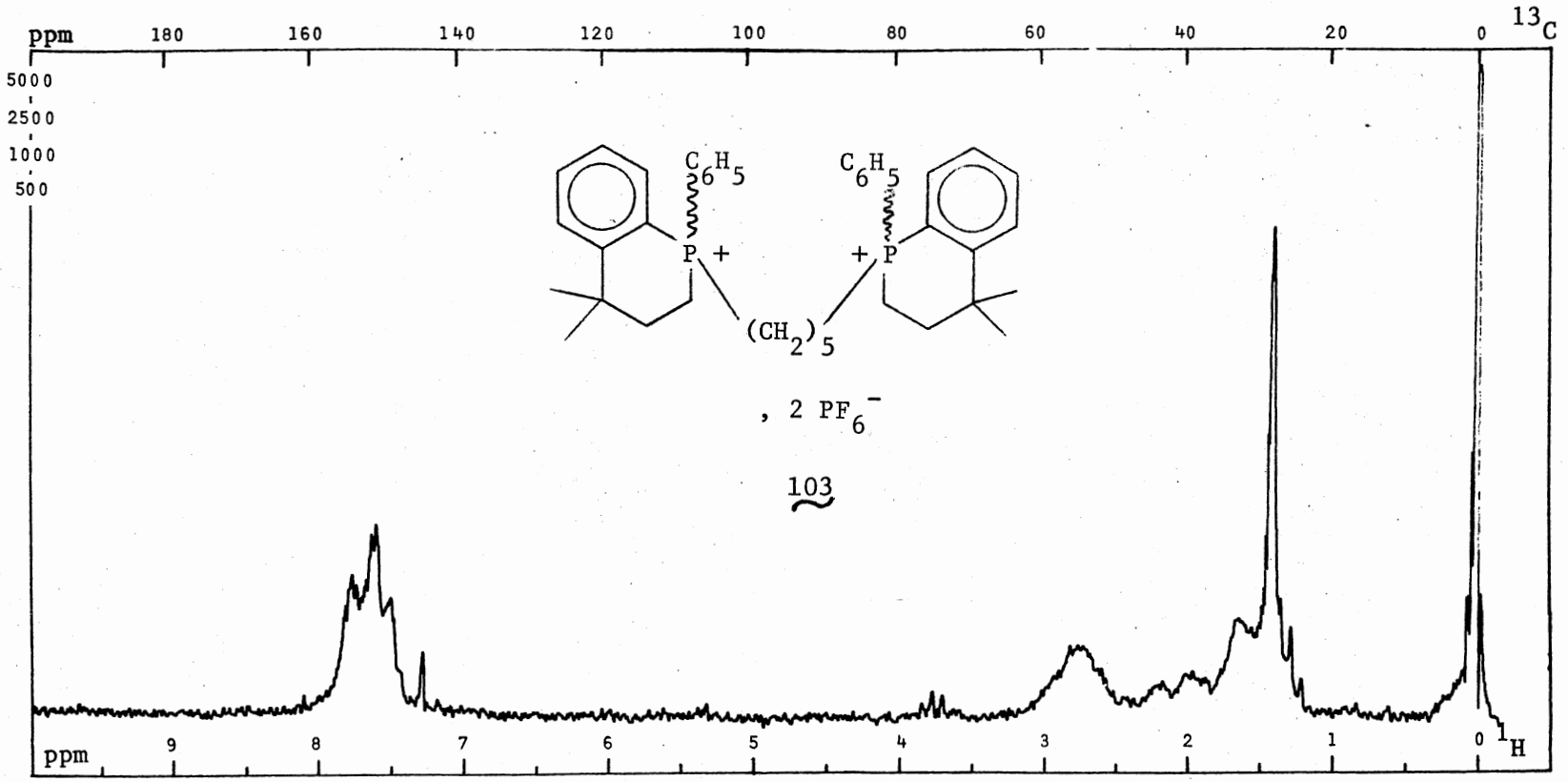


^{1}H NMR Spectrum of 102

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 29°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 69 µs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XLII

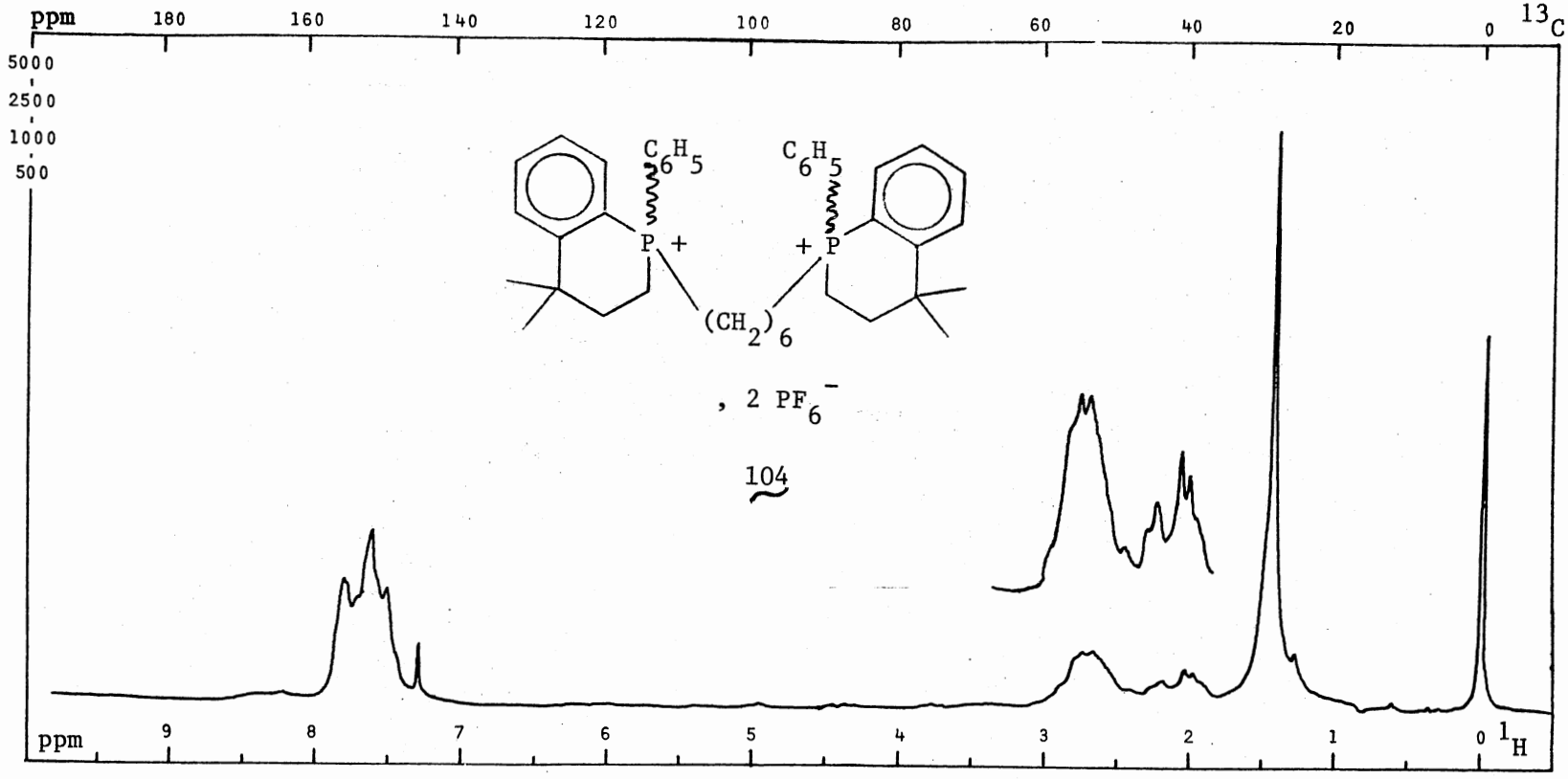


^{1}H NMR Spectrum of 103

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 29°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 72 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XLIII

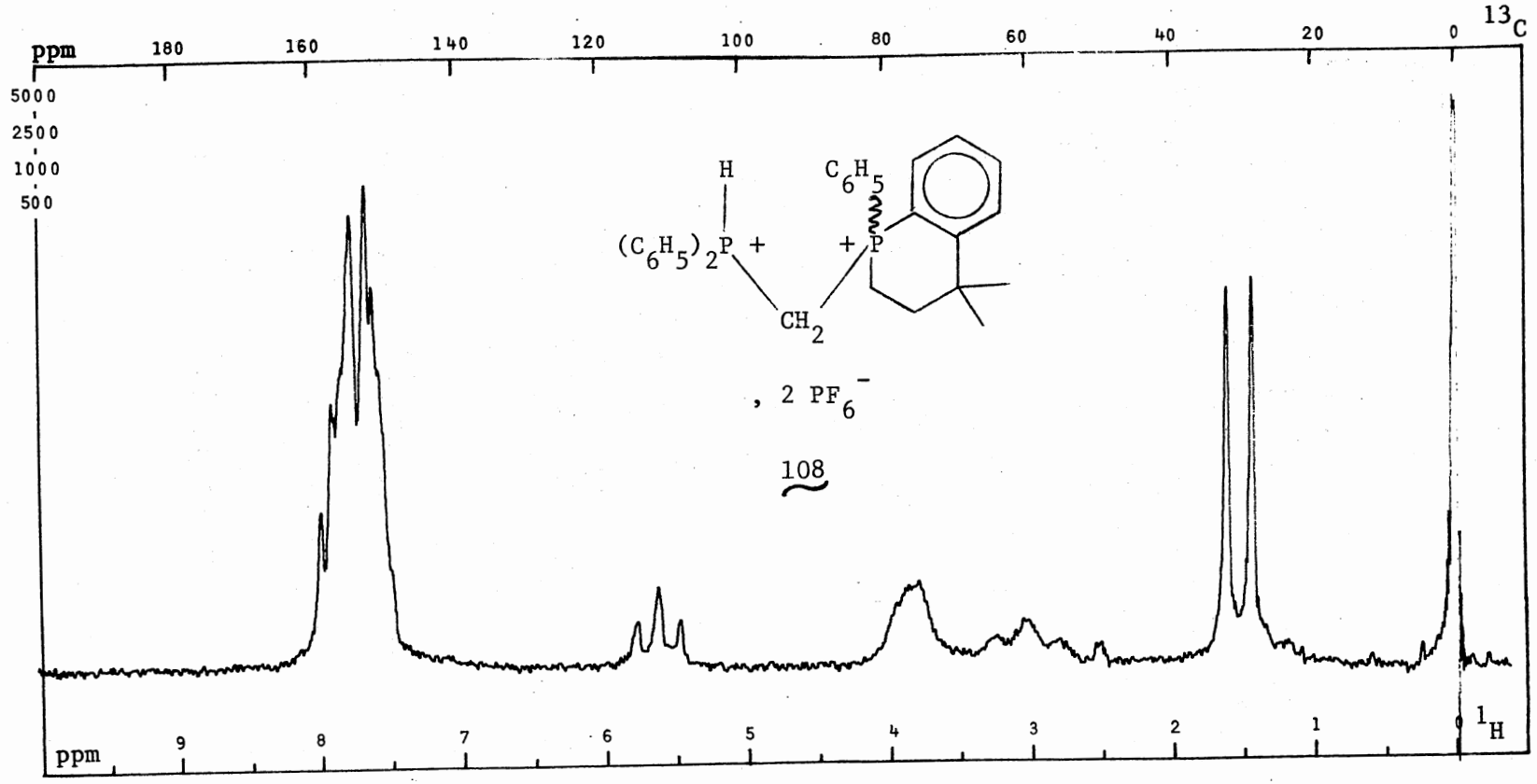


^{1}H NMR Spectrum of 104

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 45251 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . . 5 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XLIV

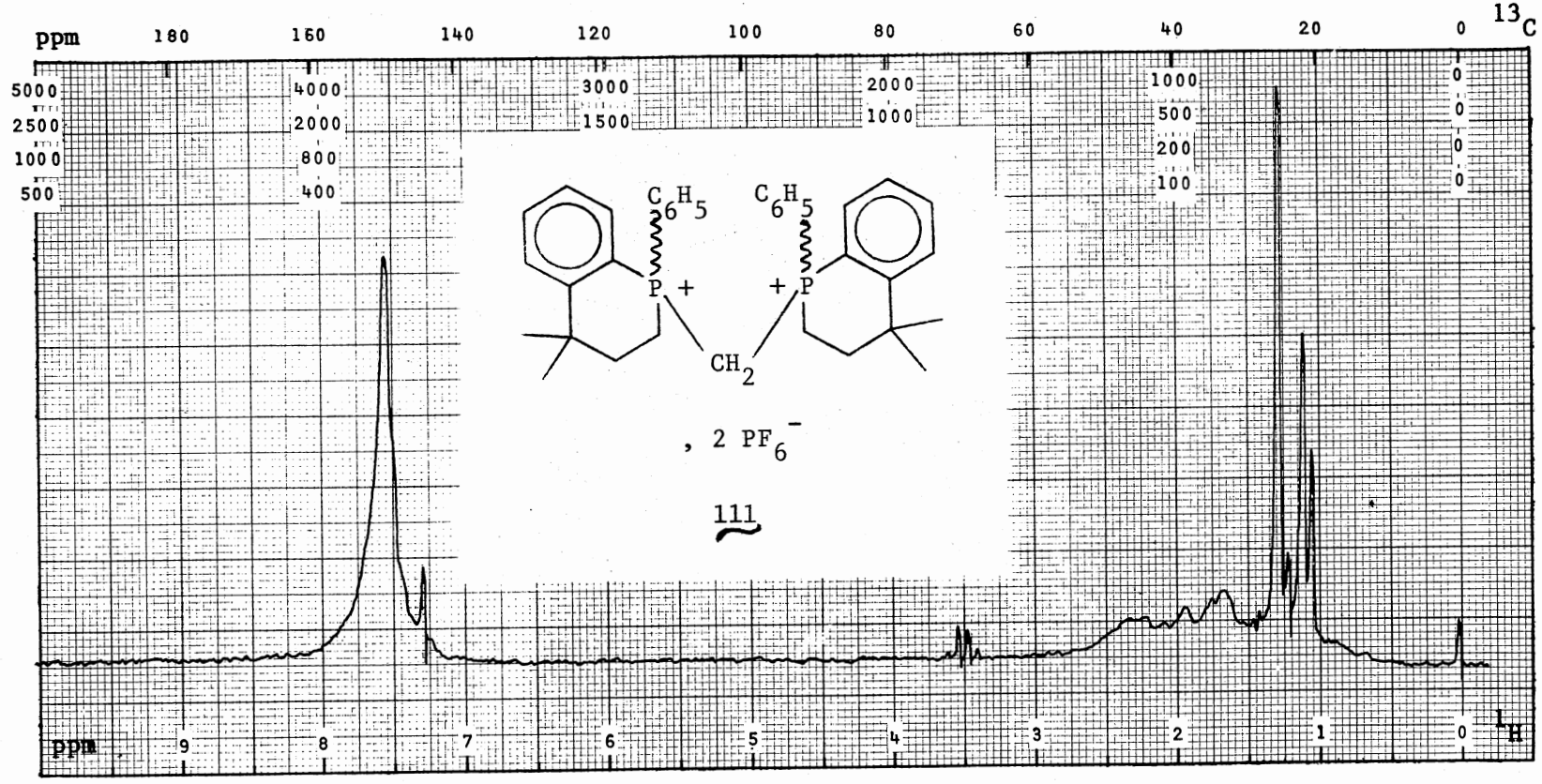


^{1}H NMR Spectrum of 108

PFT _ CW X; Solvent . . . . DMSO-d_6; SO . . 86295 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 70 µs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XLV

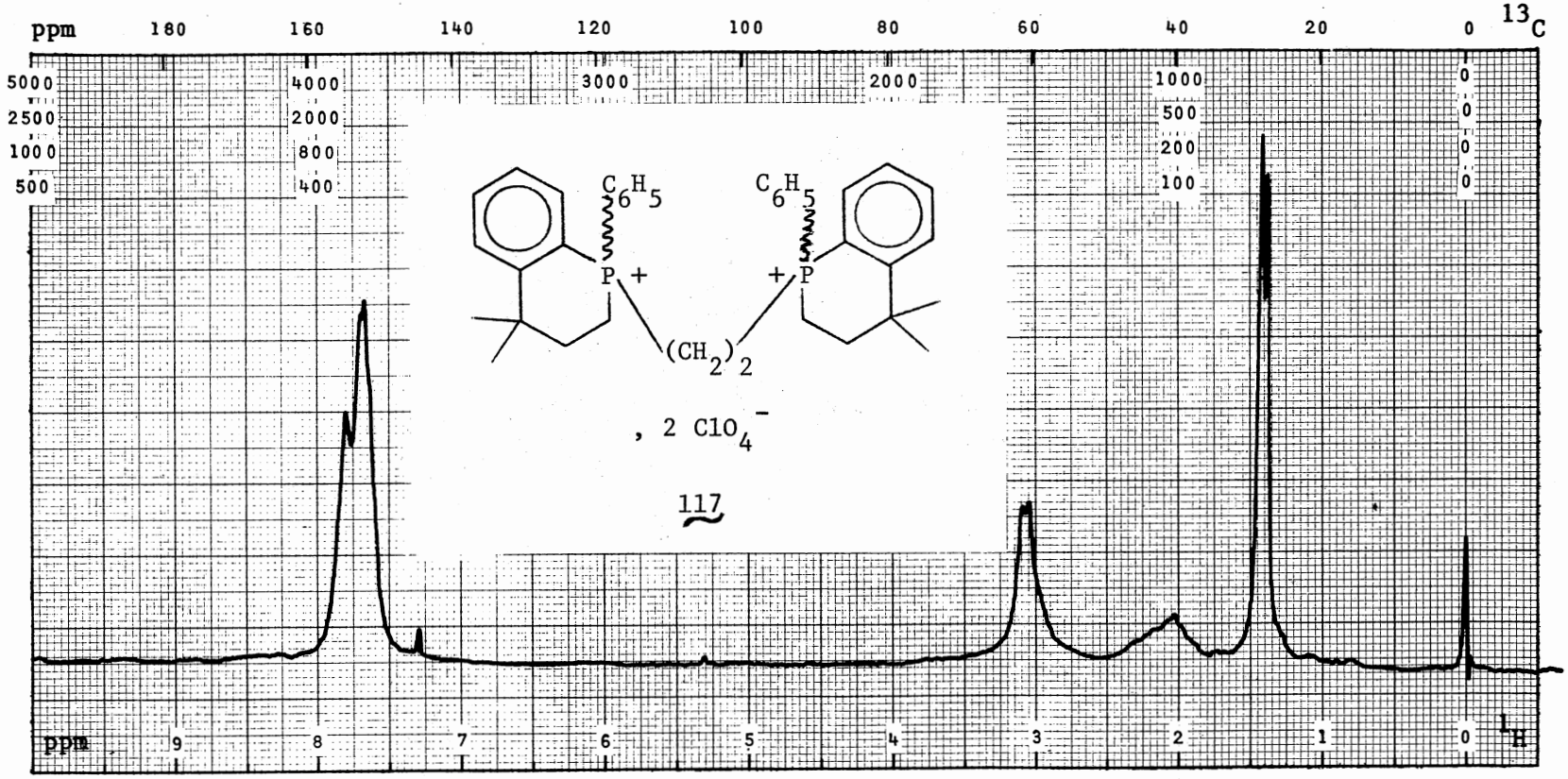


^{1}H NMR Spectrum of 111

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 70 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XLVI

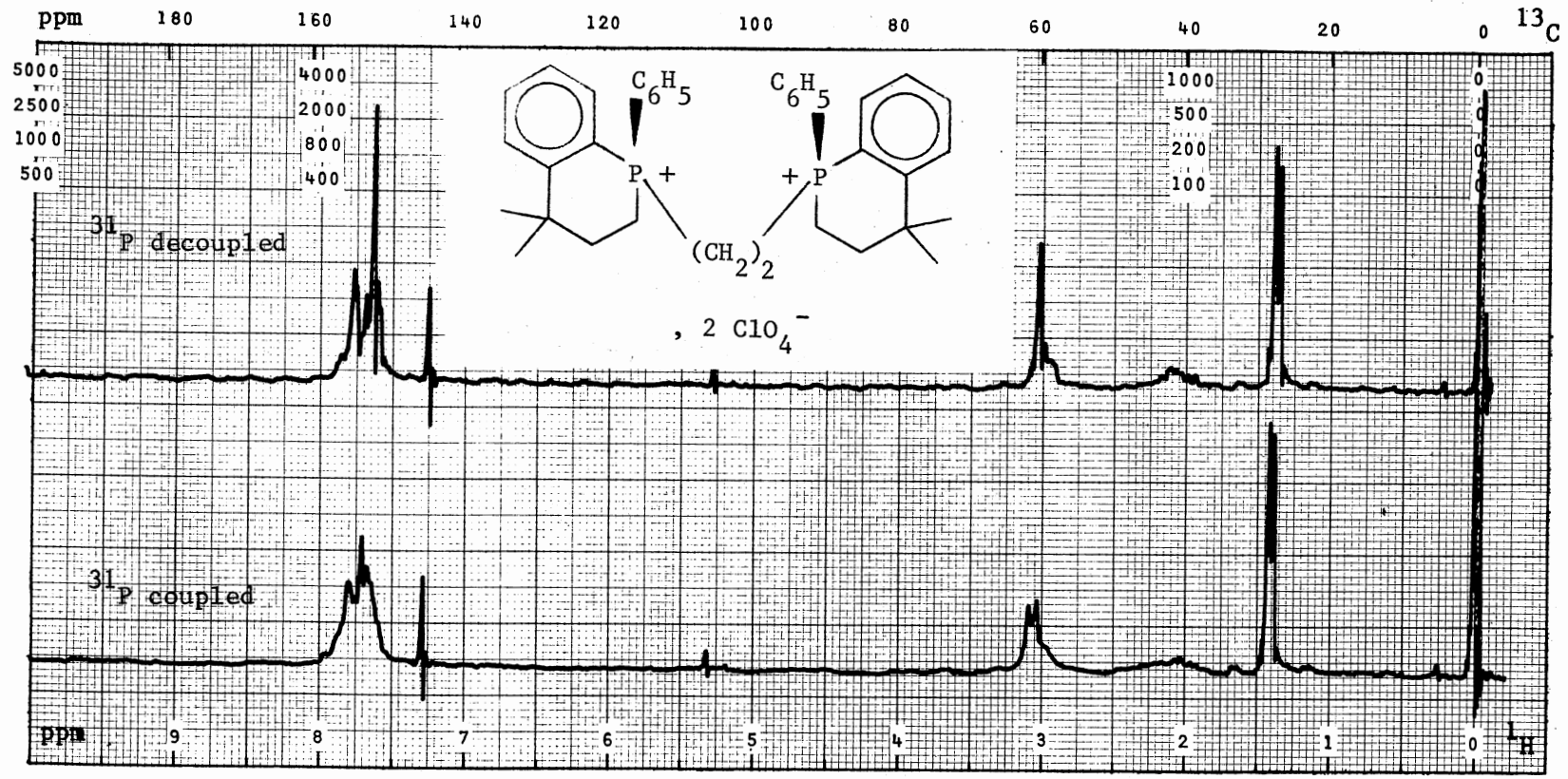


^{1}H NMR Spectrum of 117

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 28°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 69 µs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE XLVII



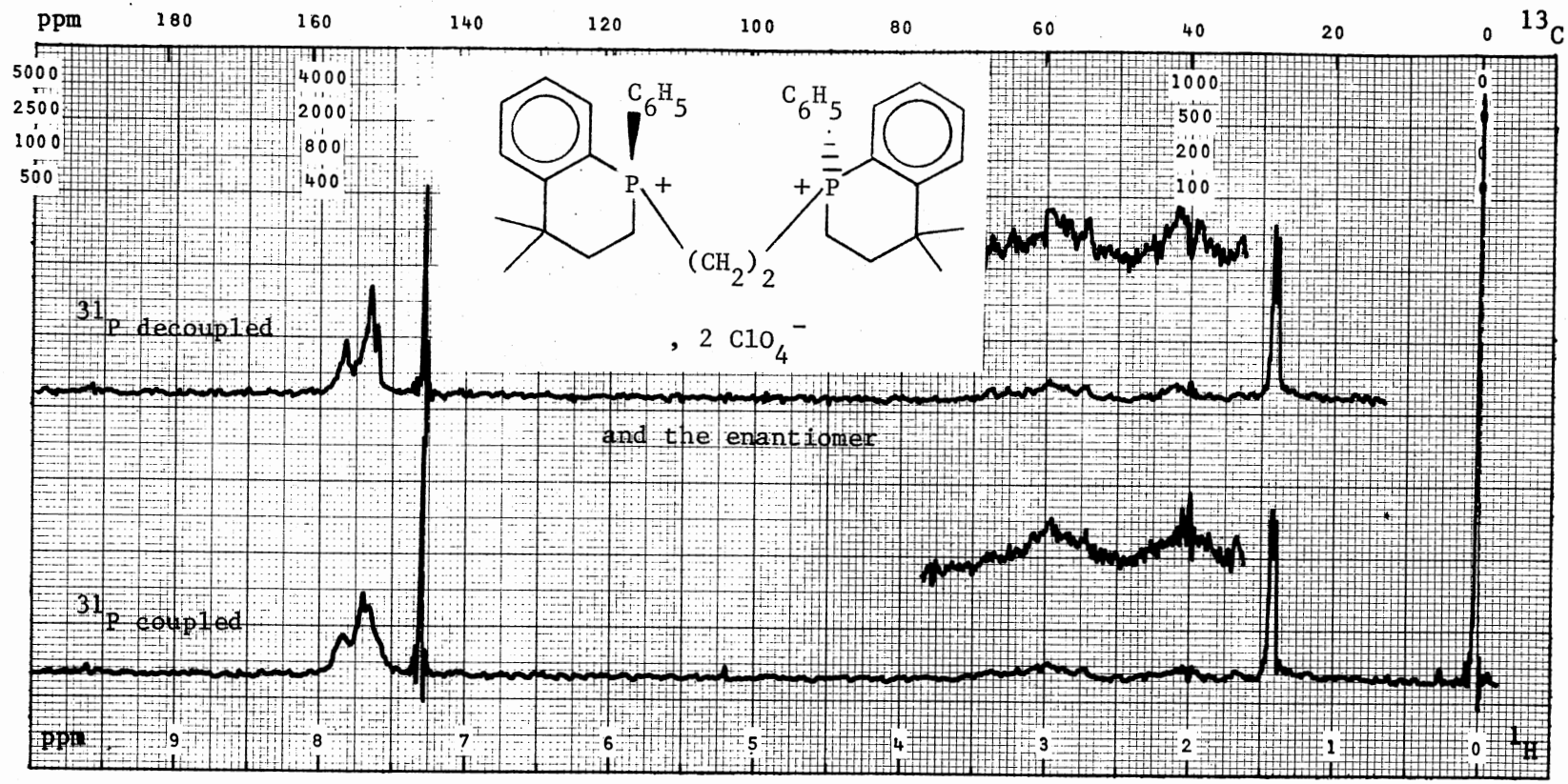
^{1}H NMR Spectrum of Meso-117

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 28°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 69 µs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

DC . . . ^{31}P; Gated Off . . ; Offset . 58655 Hz; RF . 7.5 W/dB; NBW . 100 Hz.

PLATE XLVIII



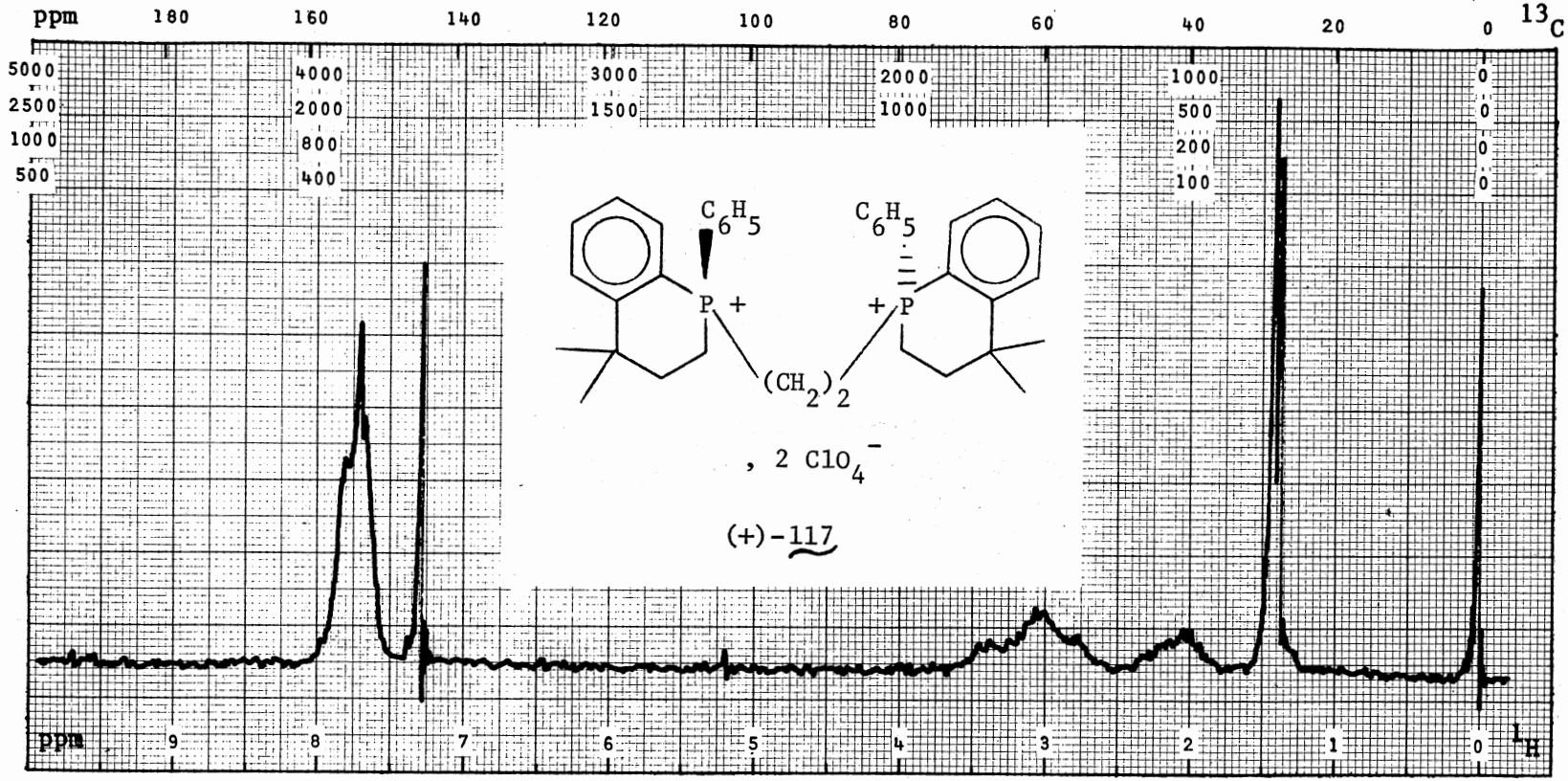
^{1}H NMR Spectrum of (±)-117

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 29°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 72 µs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 500 s.

DC . . . ^{31}P; Gated Off . . ; Offset . 58755 Hz; RF . 7.5 W/dB; NBW . 100 Hz.

PLATE XLIX

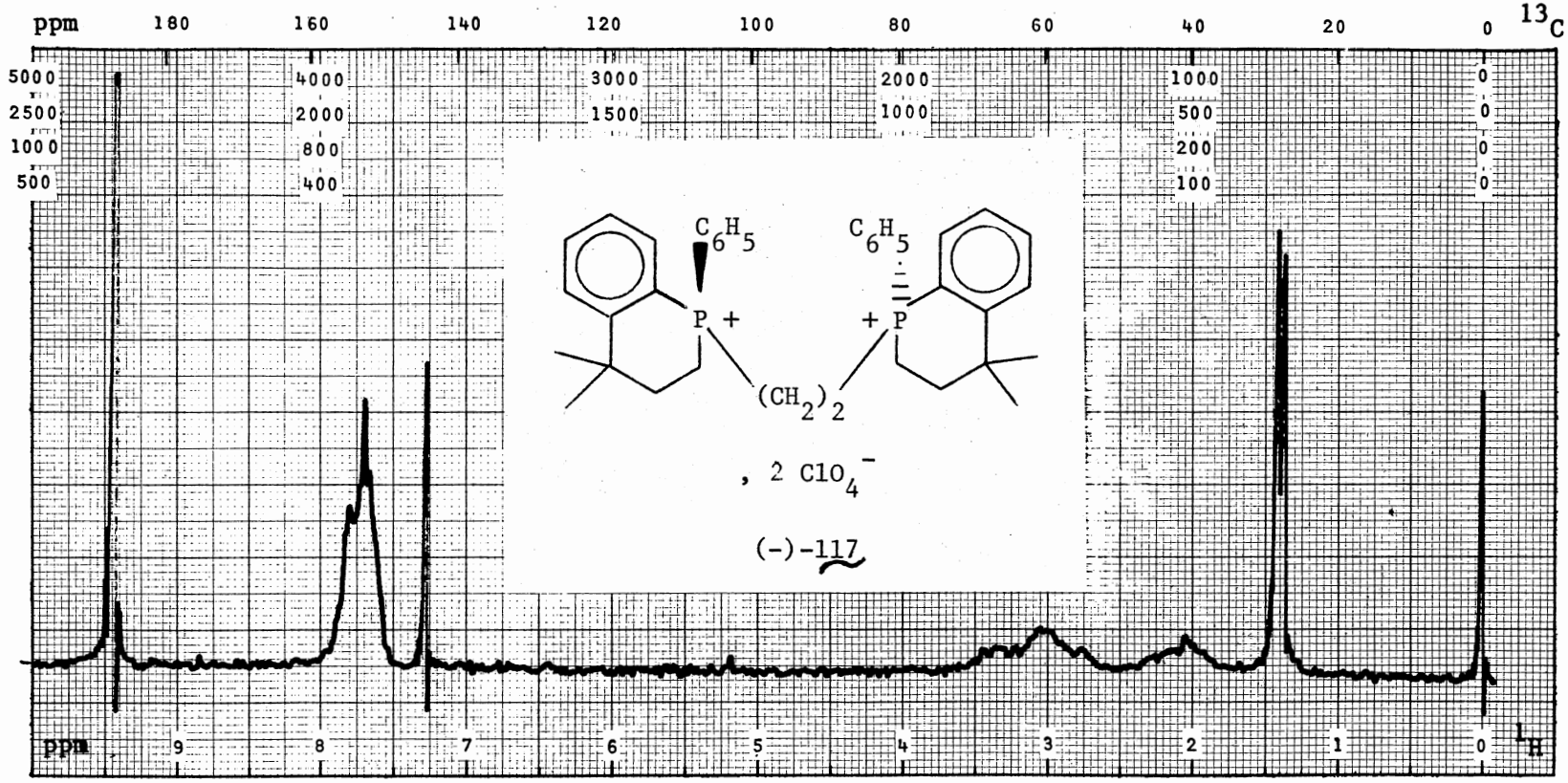


^{1}H NMR Spectrum of (+)-117

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 66 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE L

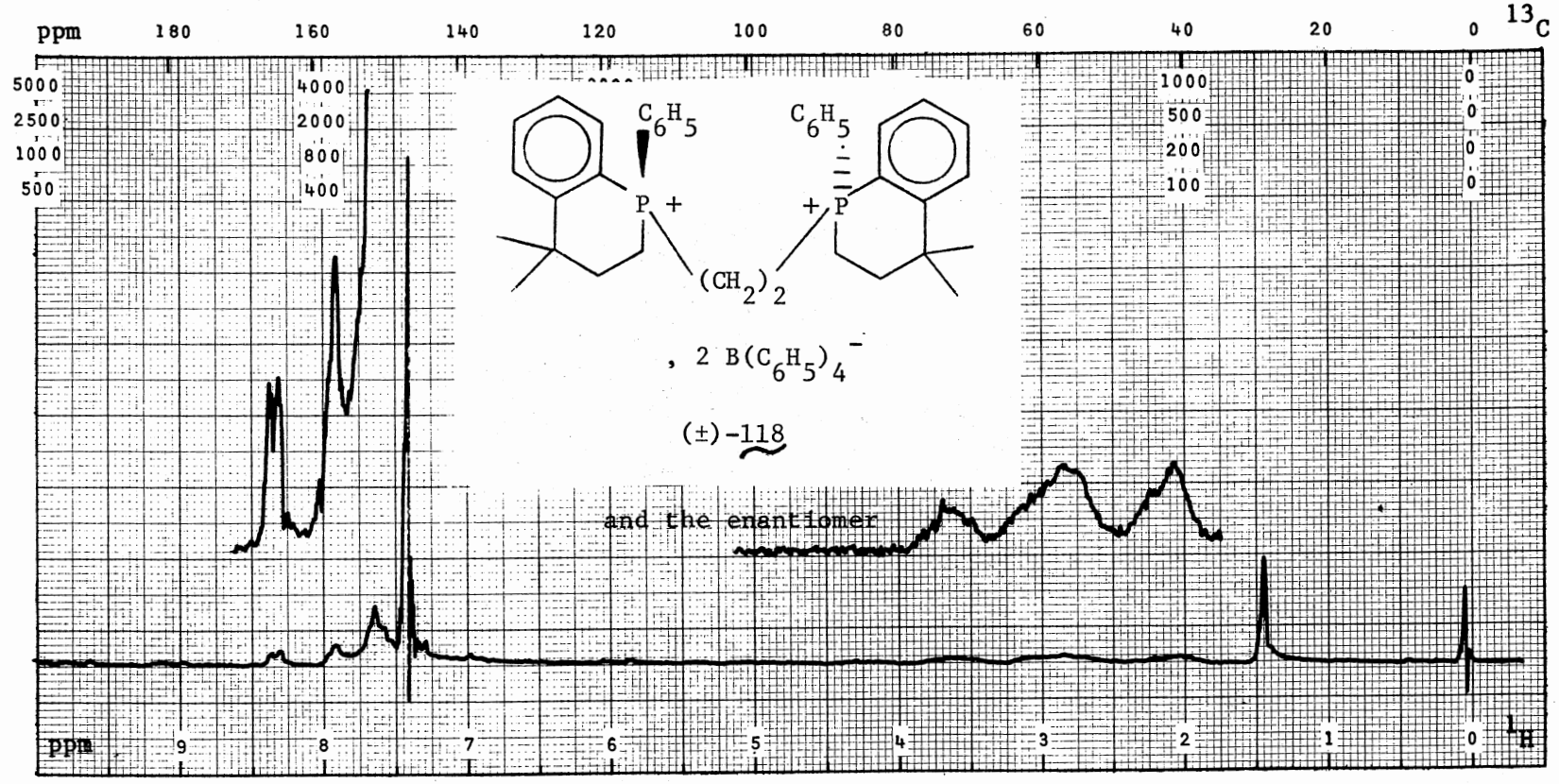


^{1}H NMR Spectrum of (-)-117

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 29°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 59 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE LI

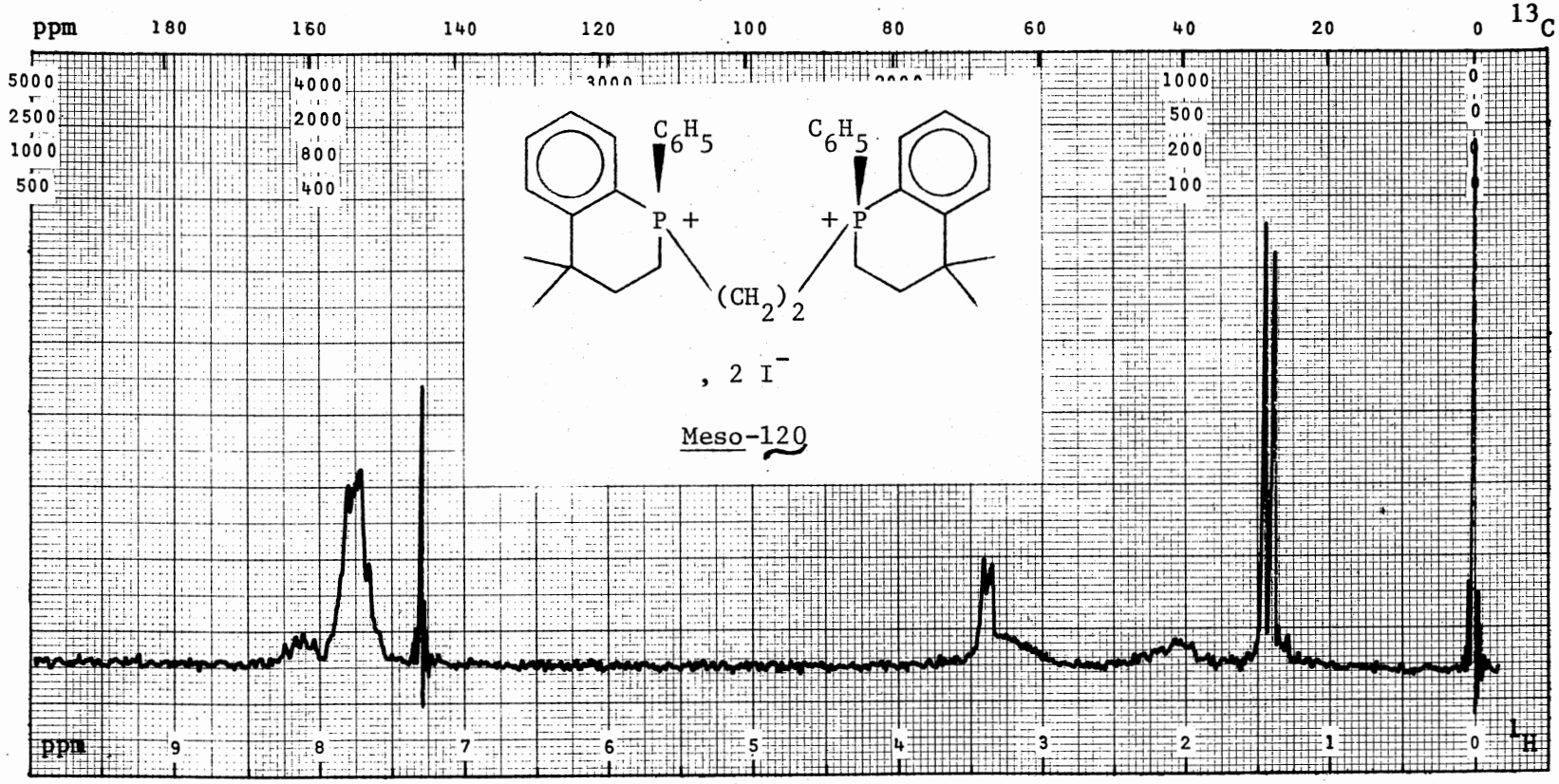


^{1}H NMR Spectrum of (±)-118

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 65 µs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE LII

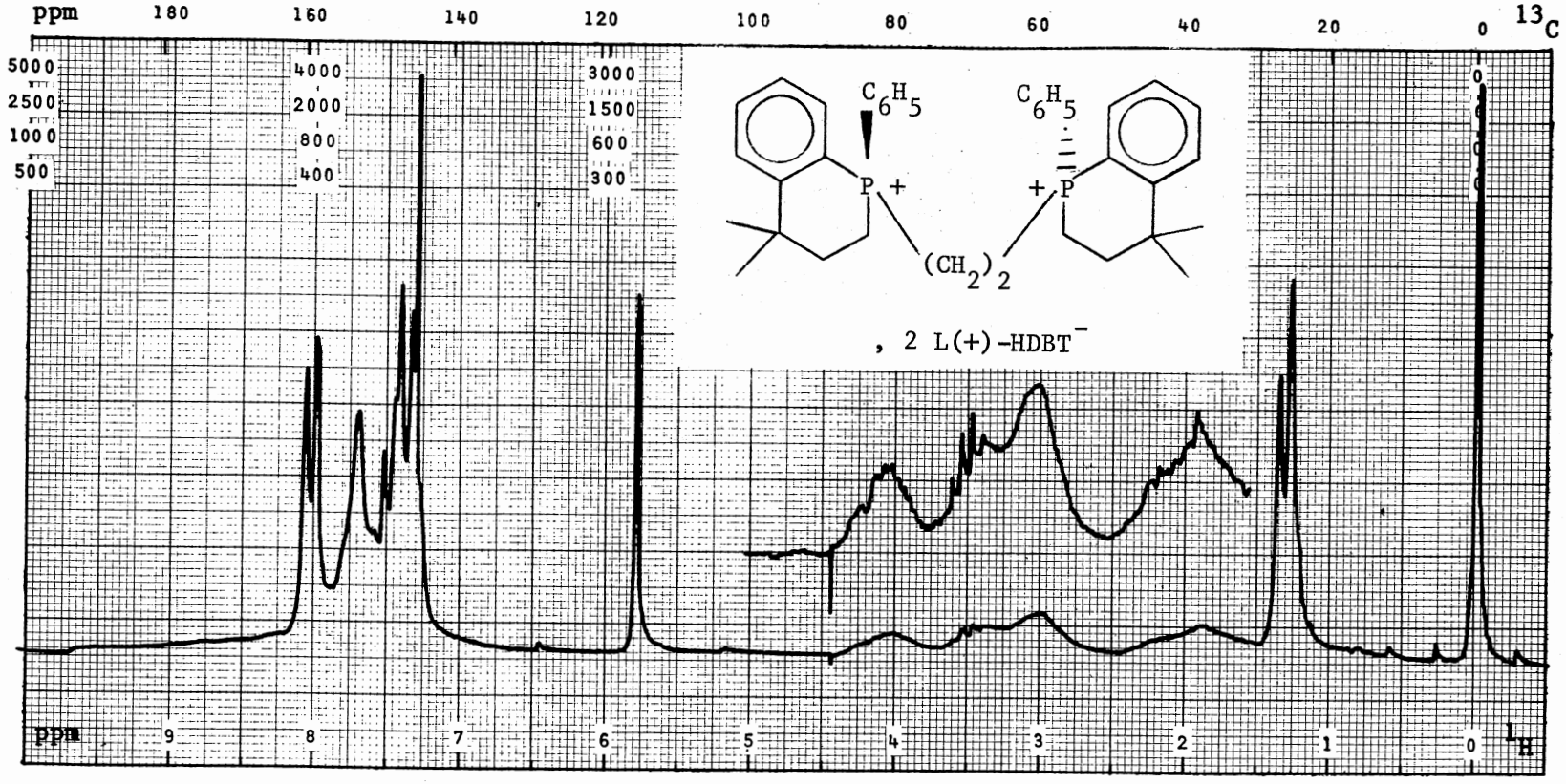


^{1}H NMR Spectrum of Meso-120

PFT _ CW X; Solvent . . $DCCl_3$ + TFA; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 70 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE LIII

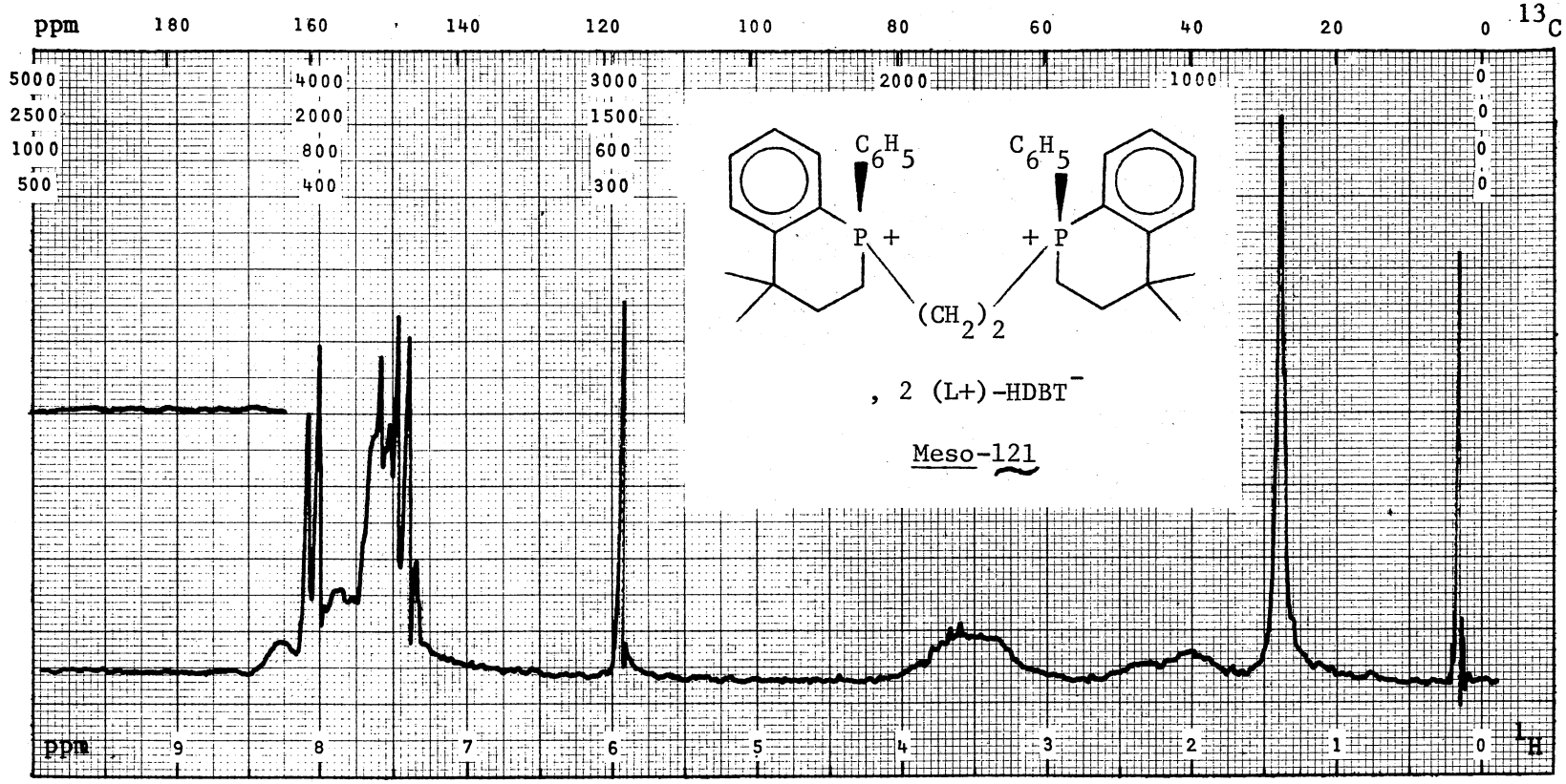


^{1}H NMR Spectrum of (-)-121

PFT X CW _; Solvent . . . . . $DCCl_3$; SO . . 45251 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . . 5 μs/dB; SF . . 100.1 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . . 2 s.

PLATE LIV

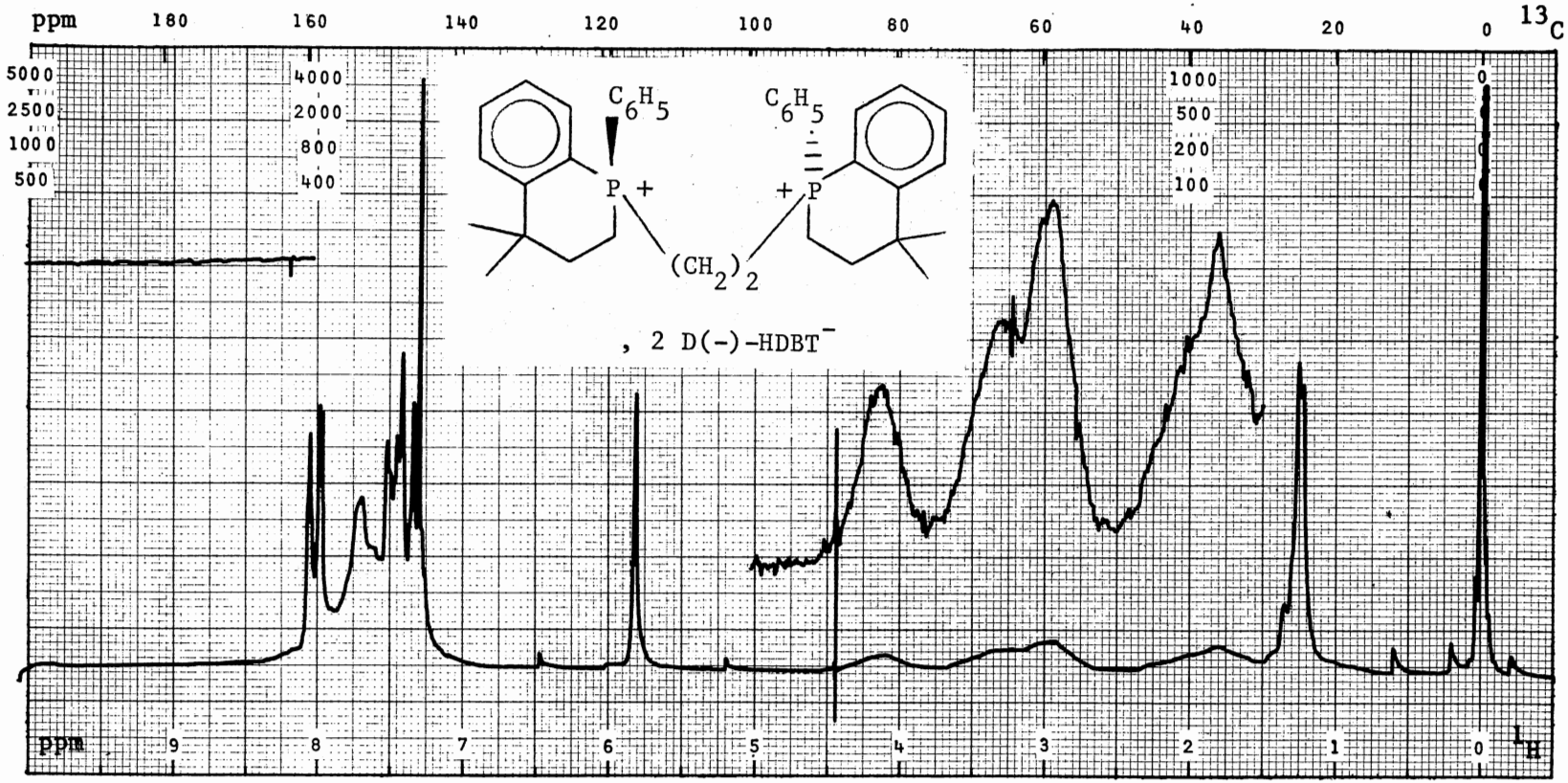


^{1}H NMR Spectrum of Meso-121

PFT _ CW X; Solvent . . . . . $DCCl_3$; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 29°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 69 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE LV

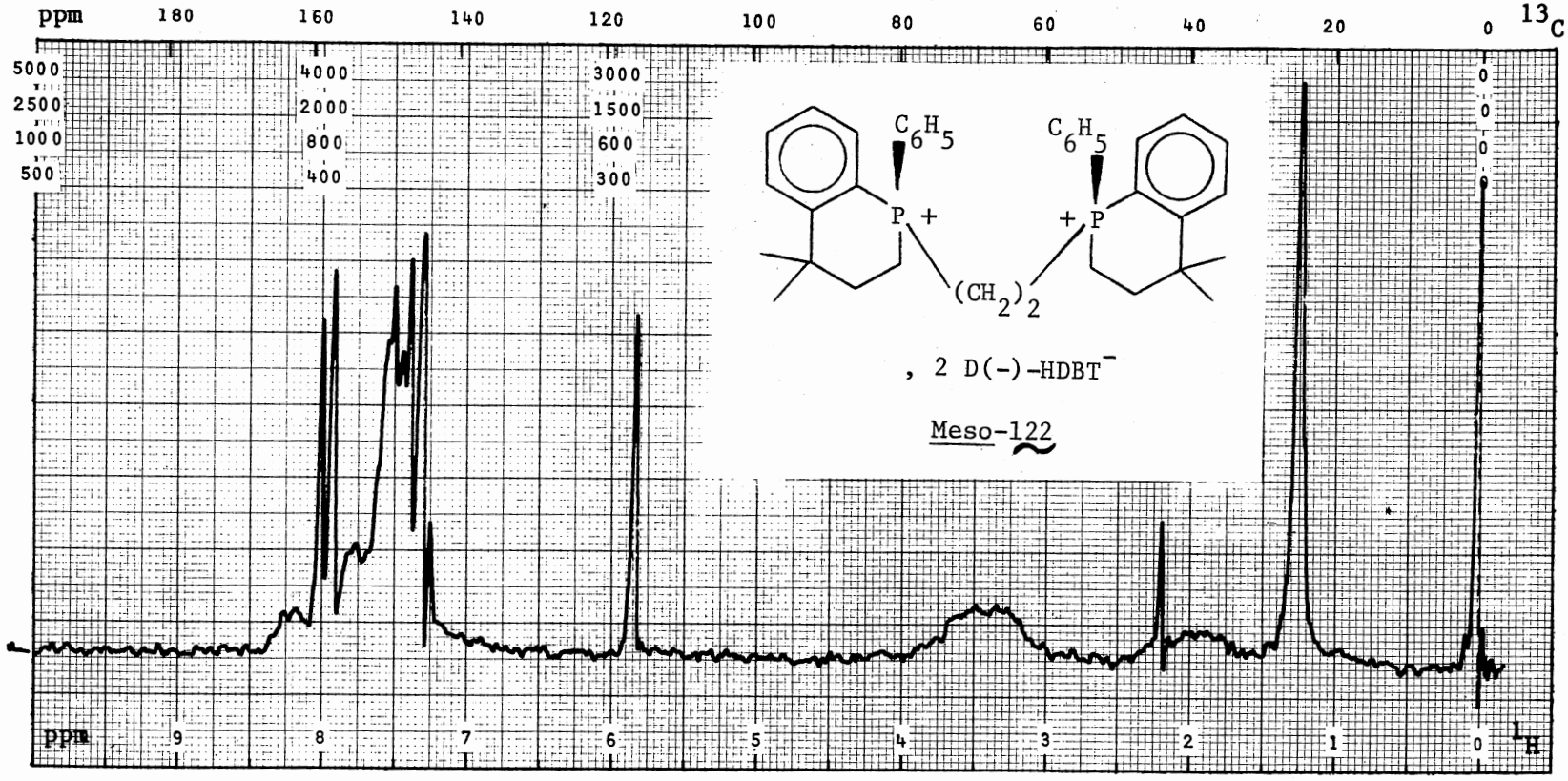


^{1}H NMR Spectrum of (+)-122

PFT X CW _; Solvent . . . . . $DCCl_3$; SO . . 45251 Hz; PW . . 1000 Hz; T. . . 29°C; Acq/SA . . 180.

Size . . 8 K; P2/RF . . . . . 5 μs/dB; SF . . 100.1 MHz; FB . . . 1 Hz; Lock . . ^{2}H; D5/ST . . 10 s.

PLATE LVI

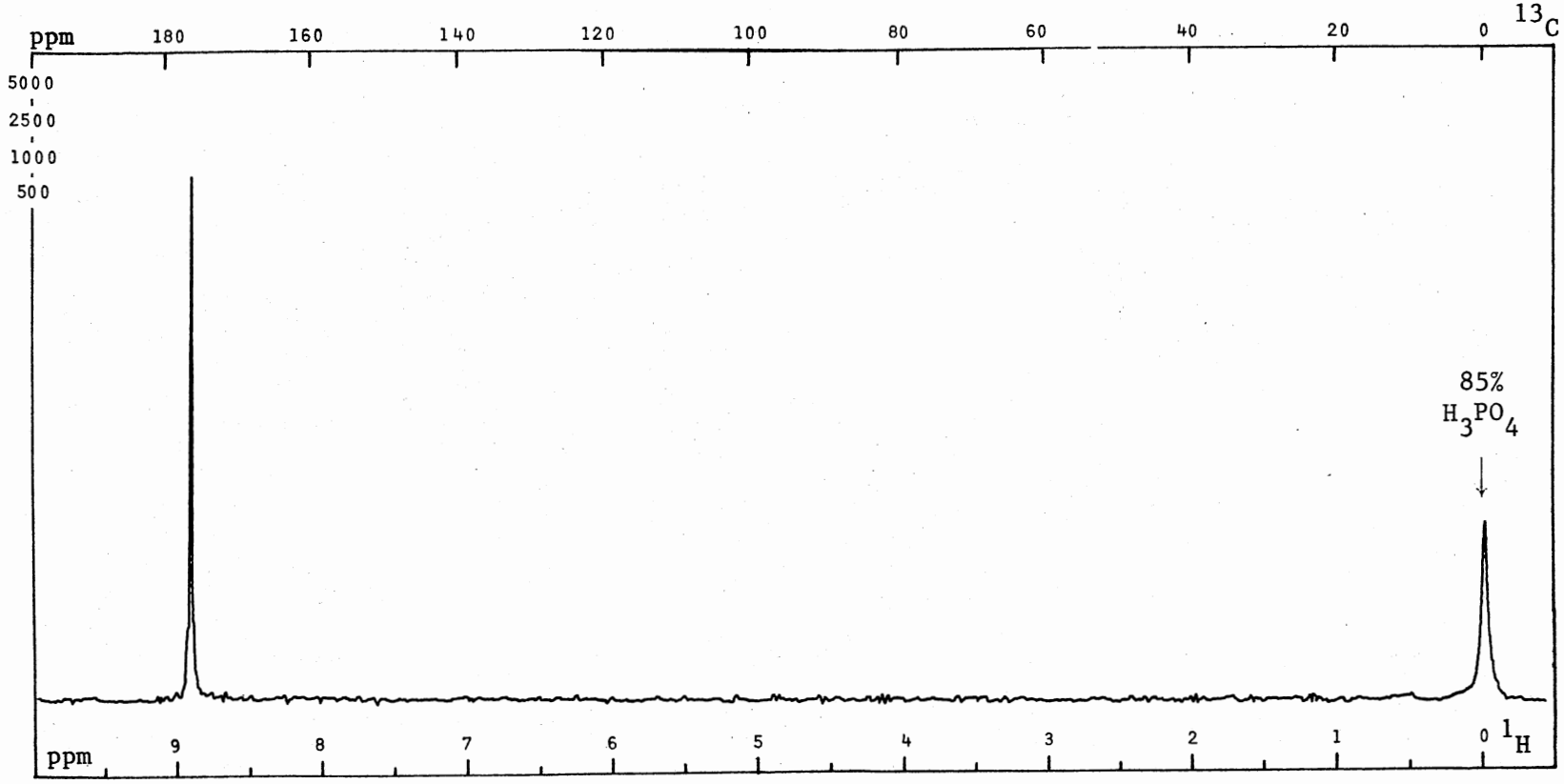


^{1}H NMR Spectrum of Meso-122

PFT _ CW X; Solvent . . . . . $DCCl_3$; SO . . 85771 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . . 1.

Size . . 8 K; P2/RF . . . . 69 μs/dB; SF . . 100.1 MHz; FB . . . 2 Hz; Lock . . ^{2}H; D5/ST . . 250 s.

PLATE LVII



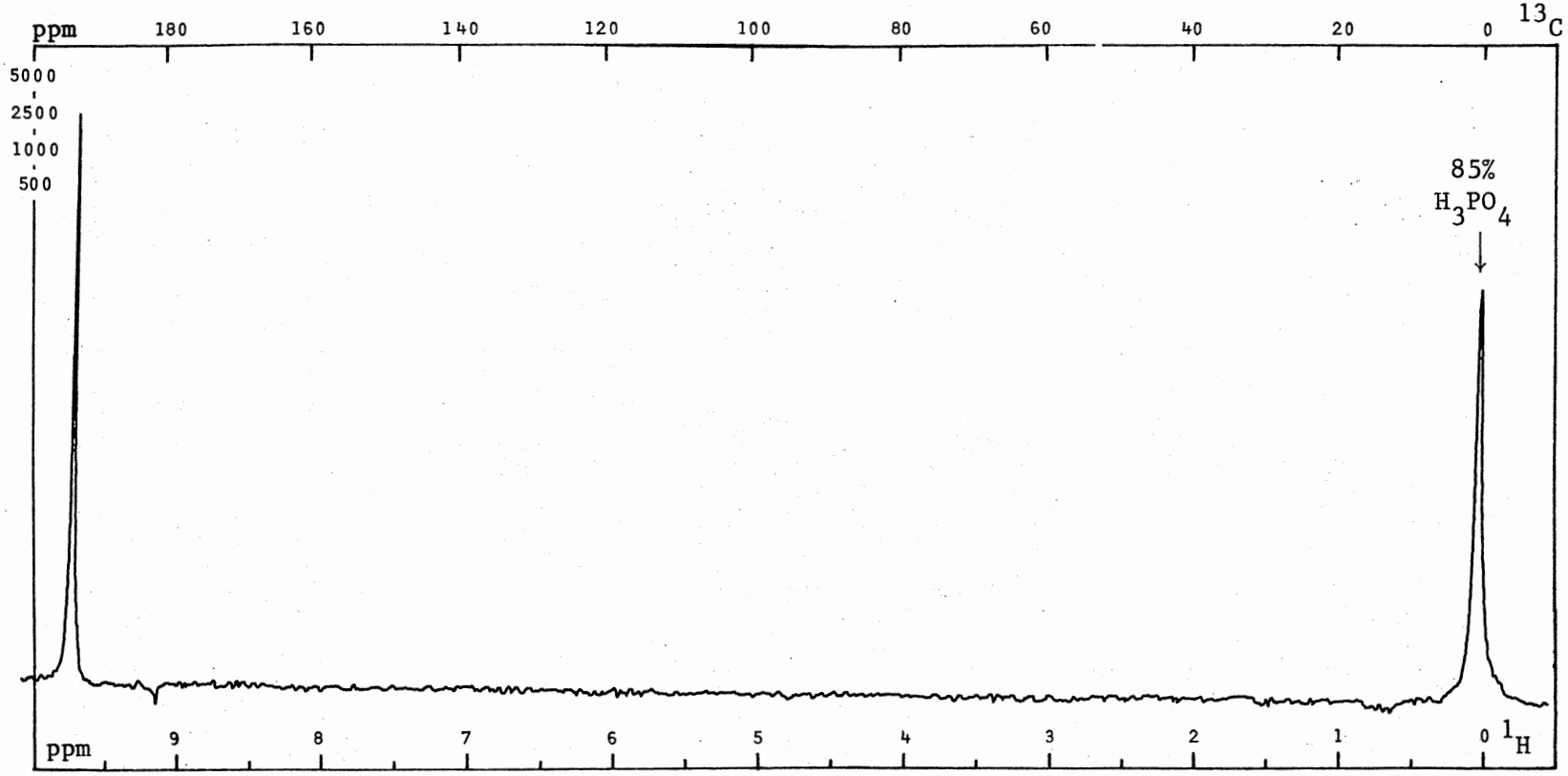
^{31}P NMR Spectrum of 95

PFT X CW _: Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1500 Hz; T. . . 27°C; Acq/SA . . 100.

Size . . 8 K; P2/RF . . . . 10 μs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 47308 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LVIII



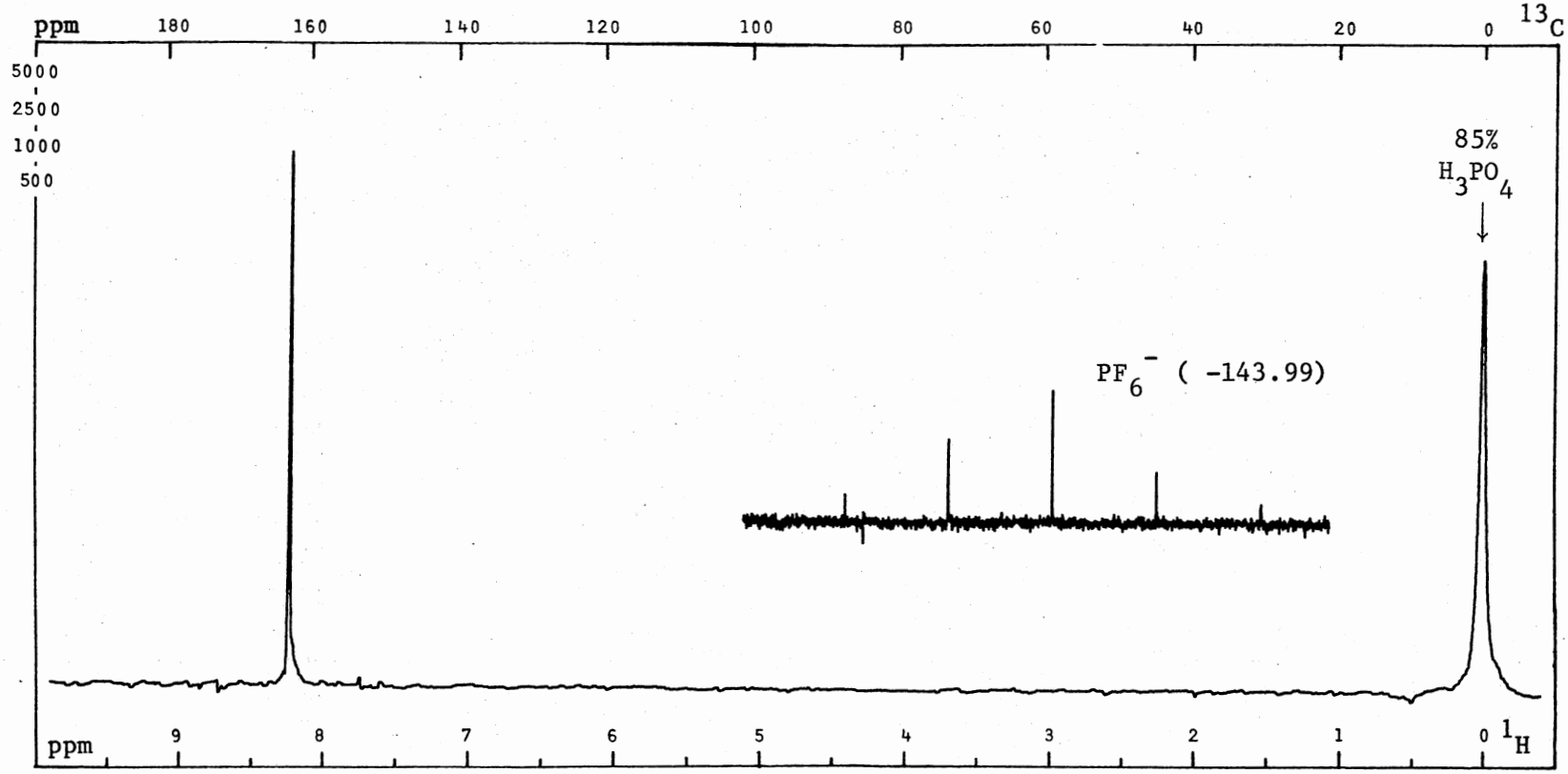
^{31}P NMR Spectrum of 96

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 20.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LIX



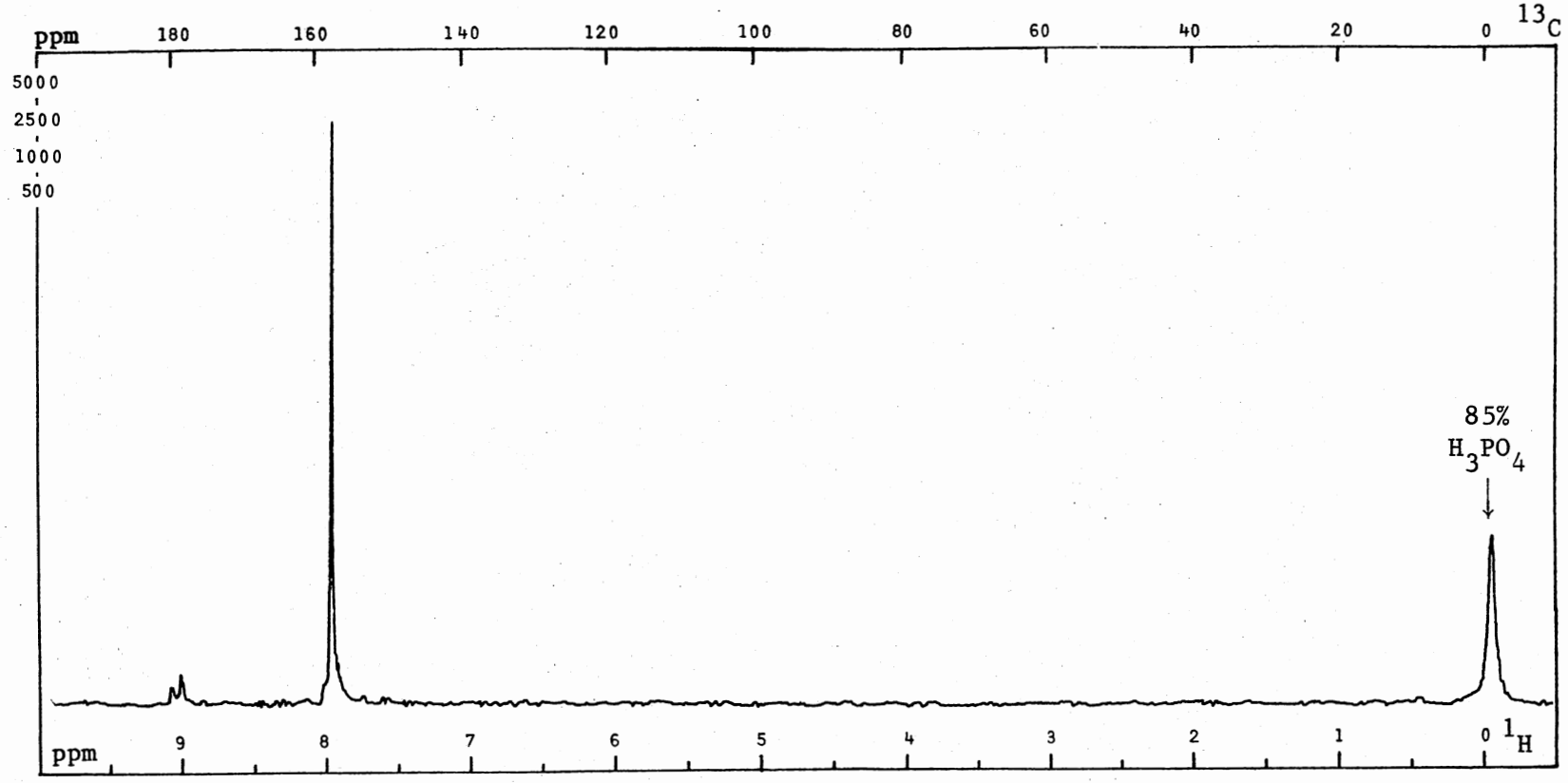
^{31}P NMR Spectrum of 97

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1200 Hz; T. . . 27°C; Acq/SA . . . 4.

Size . . 8 K; P2/RF . . . . 10 μs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LX



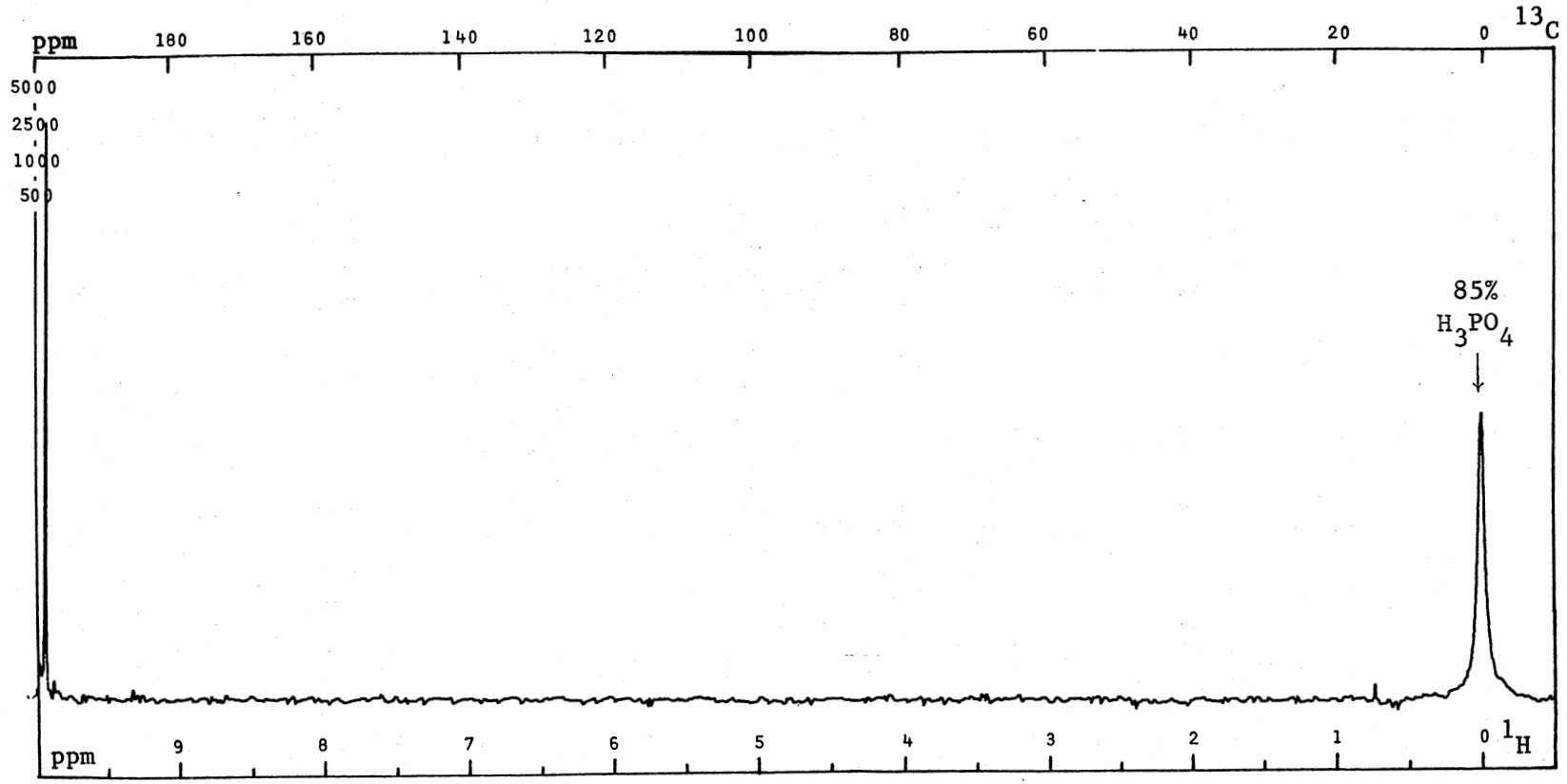
^{31}P NMR Spectrum of 98

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1200 Hz; T. . . 27°C; Acq/SA . . 40.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXI



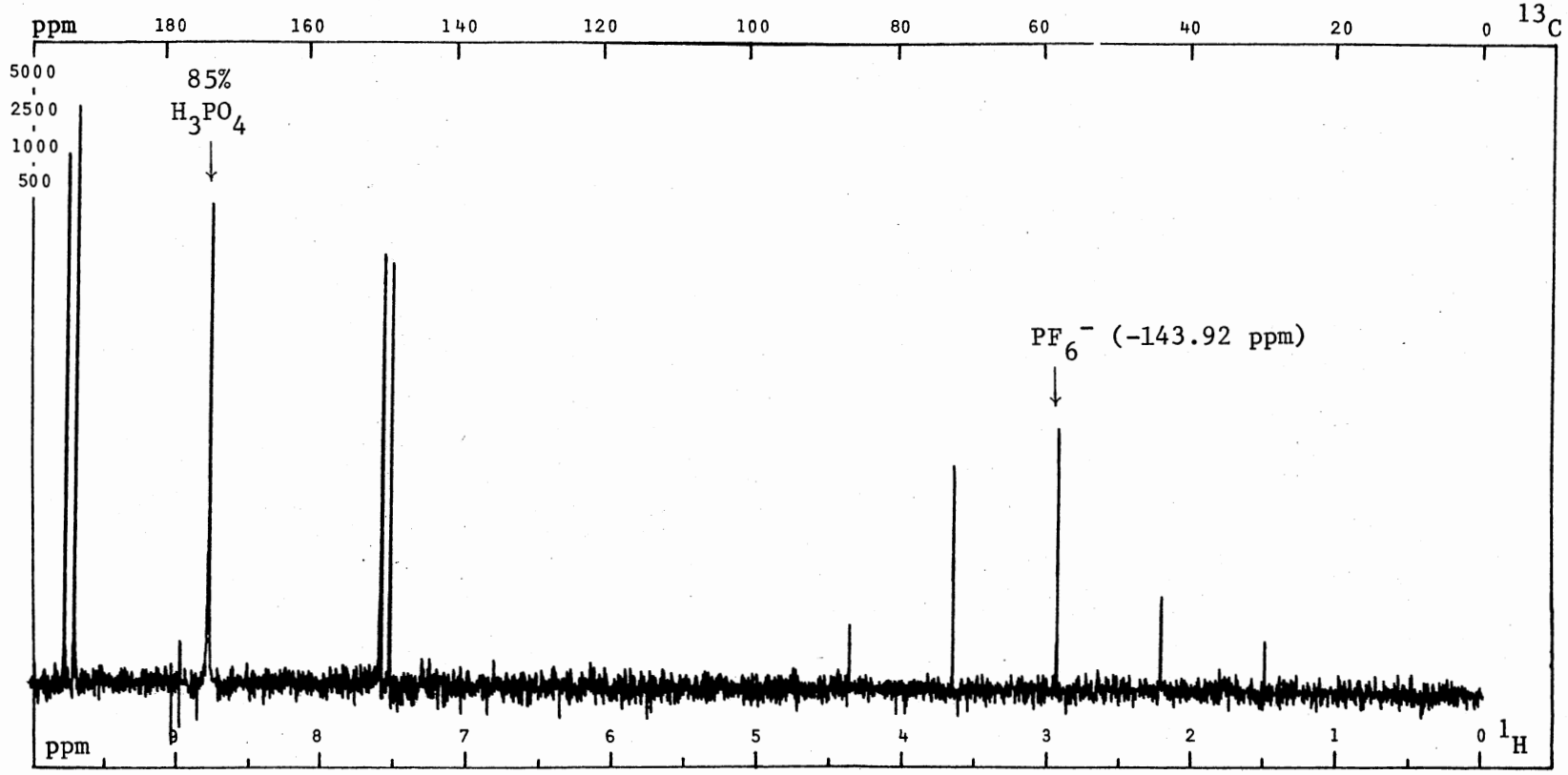
^{31}P NMR Spectrum of 99

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/Sa . . . 4.

Size . . 8 K; P2/RF . . . . 10 μs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXII



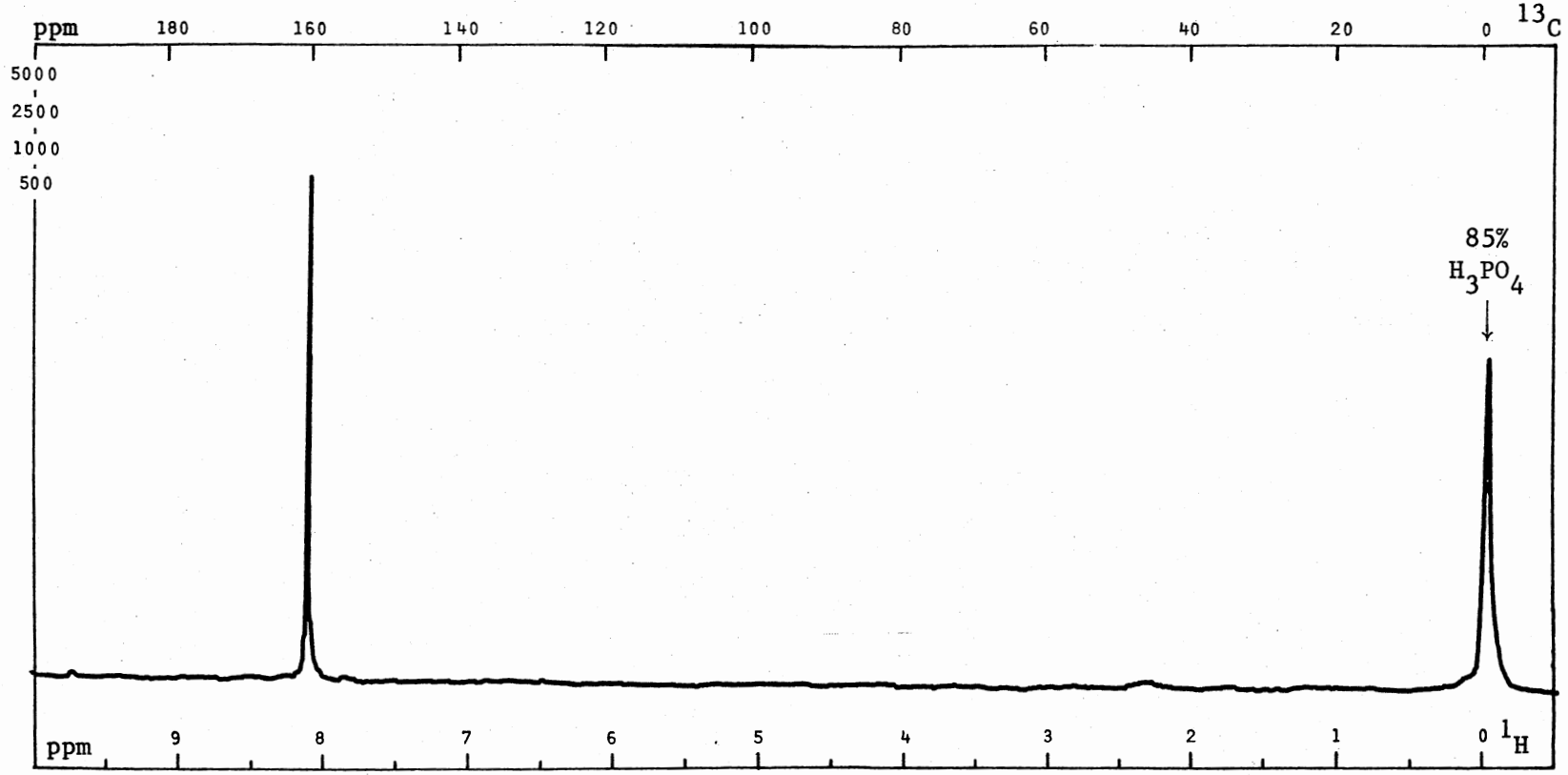
^{31}P NMR Spectrum of 107

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . 10000 Hz; T. . . 27°C; Acq/SA . . 12.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^2H; D5/ST . . 7 s.

DC . . . ^1H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXIII



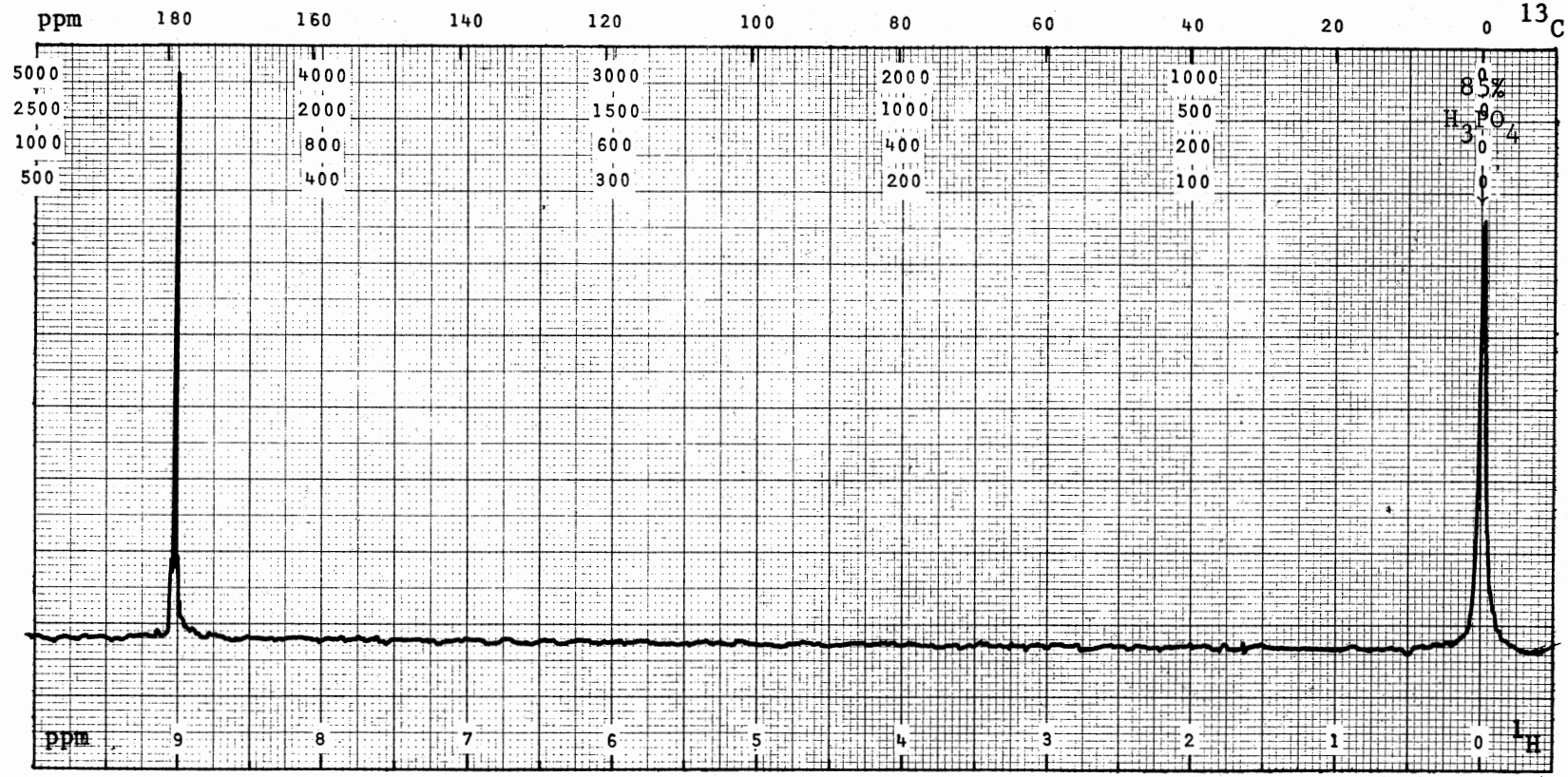
^{31}P NMR Spectrum of 110

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 32.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXIV



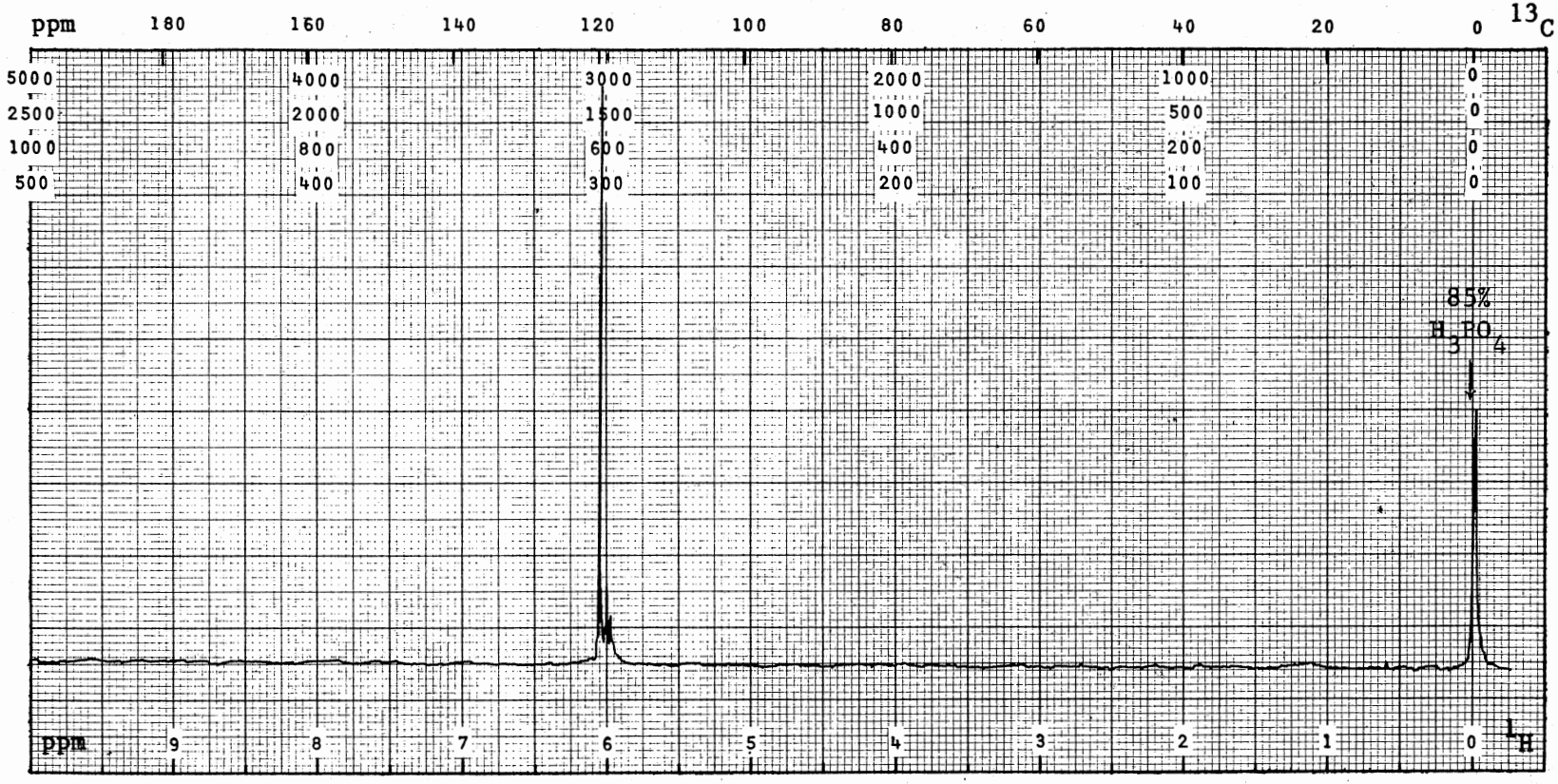
^{31}P NMR Spectrum of 112

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1200 Hz; T. . . 27°C; Acq/SA . . 16.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^2H; D5/ST . . 5 s.

DC . . . ^1H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXV



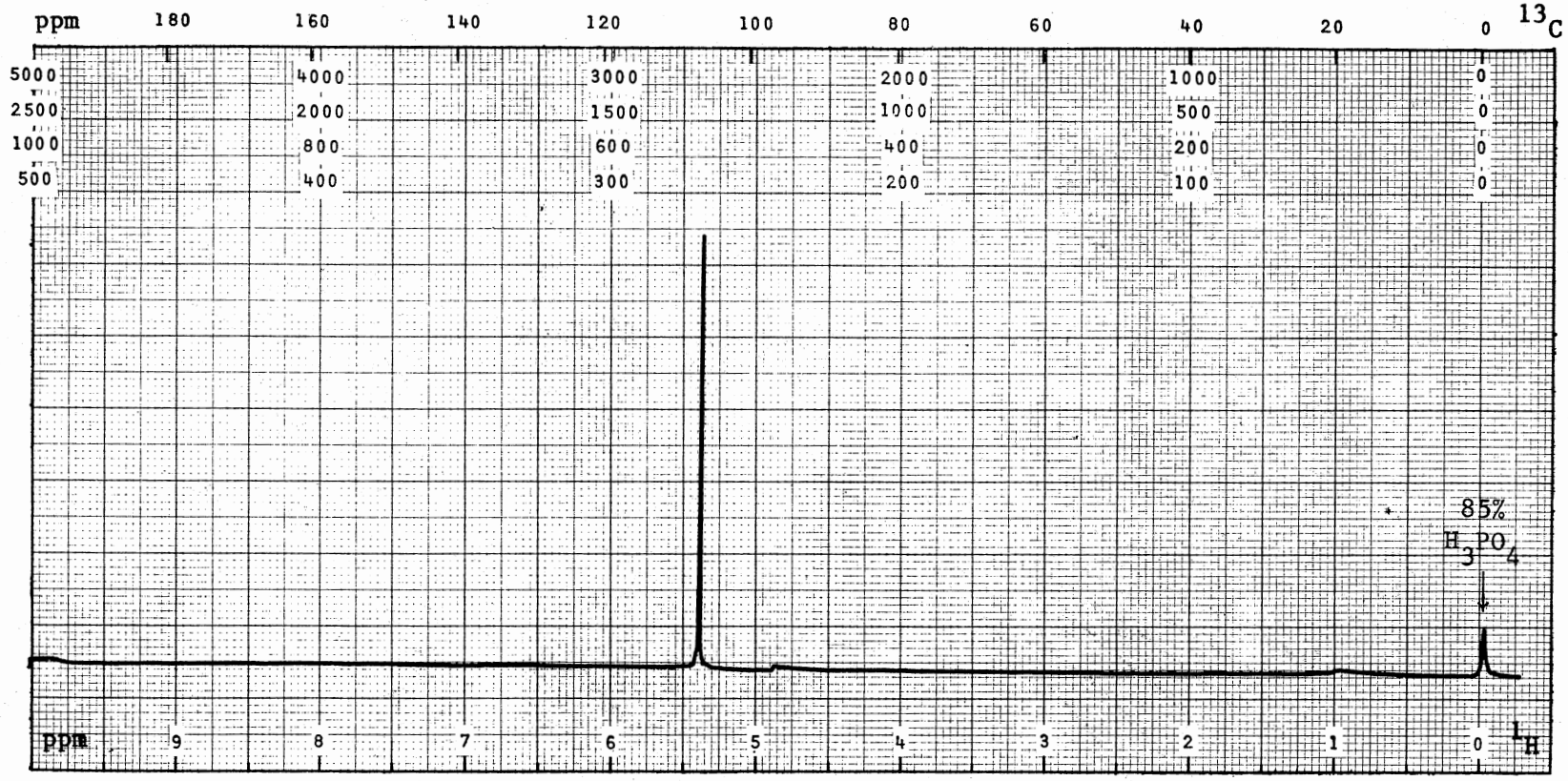
^{31}P NMR Spectrum of 114

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 2000 Hz; T. . . 27°C; Acq/SA . . 40.

Size . . 8 K; P2/RF . . . . 10 μs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^2H; D5/ST . . 5 s.

DC . . . ^1H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXVI



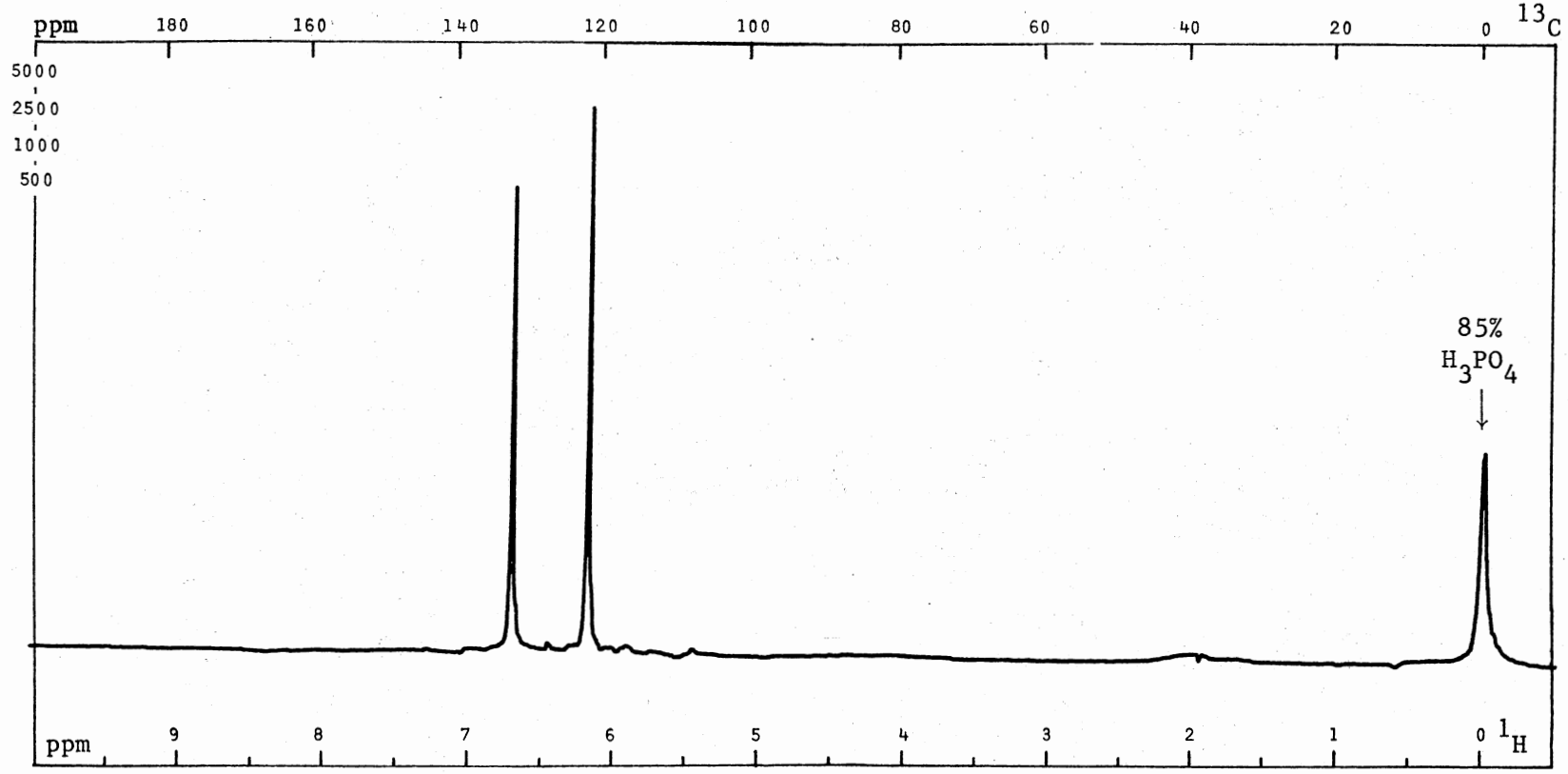
^{31}P NMR Spectrum of 116

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 2000 Hz; T. . . 27°C; Acq/SA . . 20.

Size . . 8 K; P2/RF . . . . 10 μs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^2H; D5/ST . . 5 s.

DC . . . ^1H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXVII



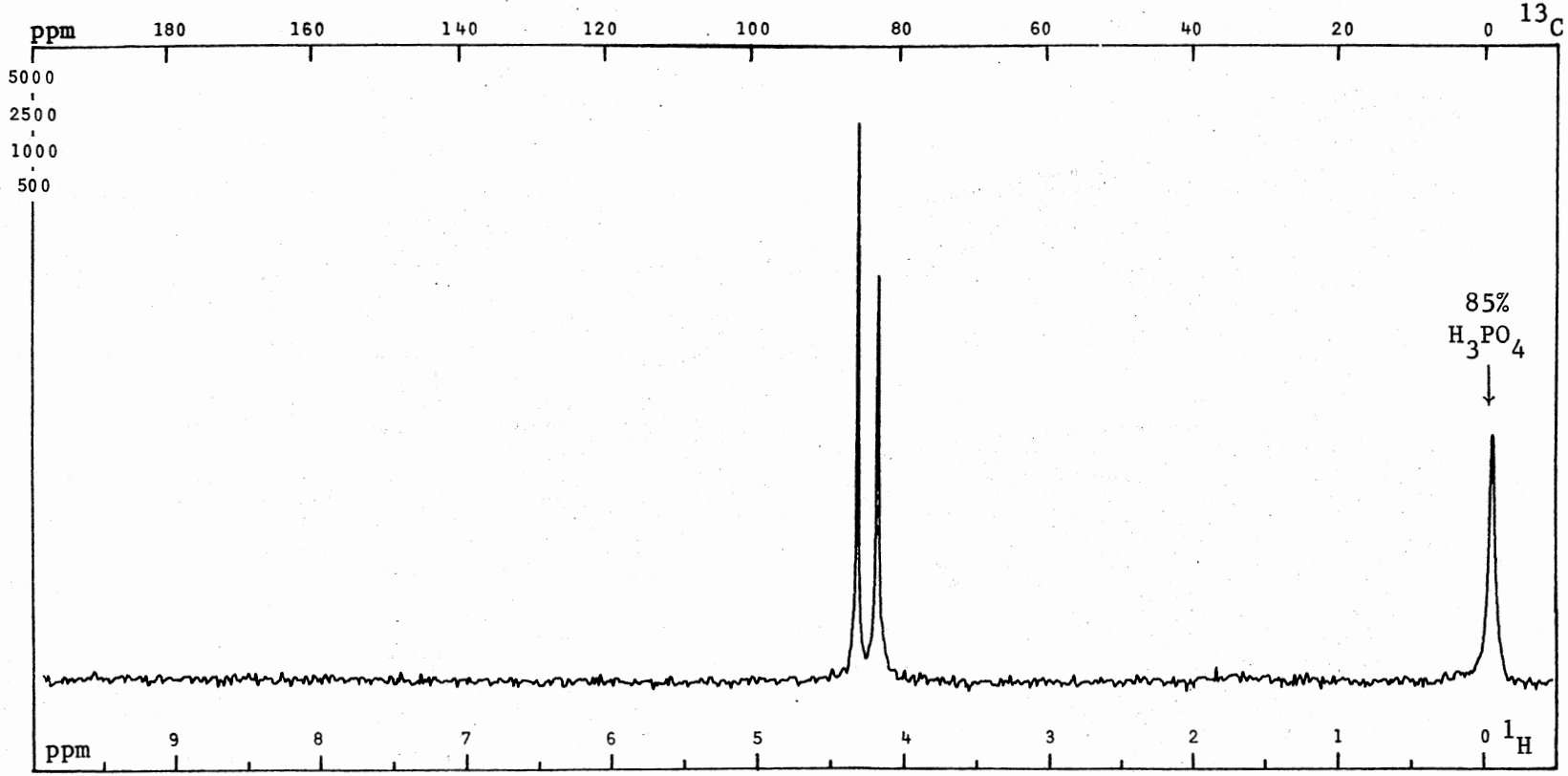
^{31}P NMR Spectrum of ~~100~~ (Meso- + dl-pair)

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 100.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXVIII



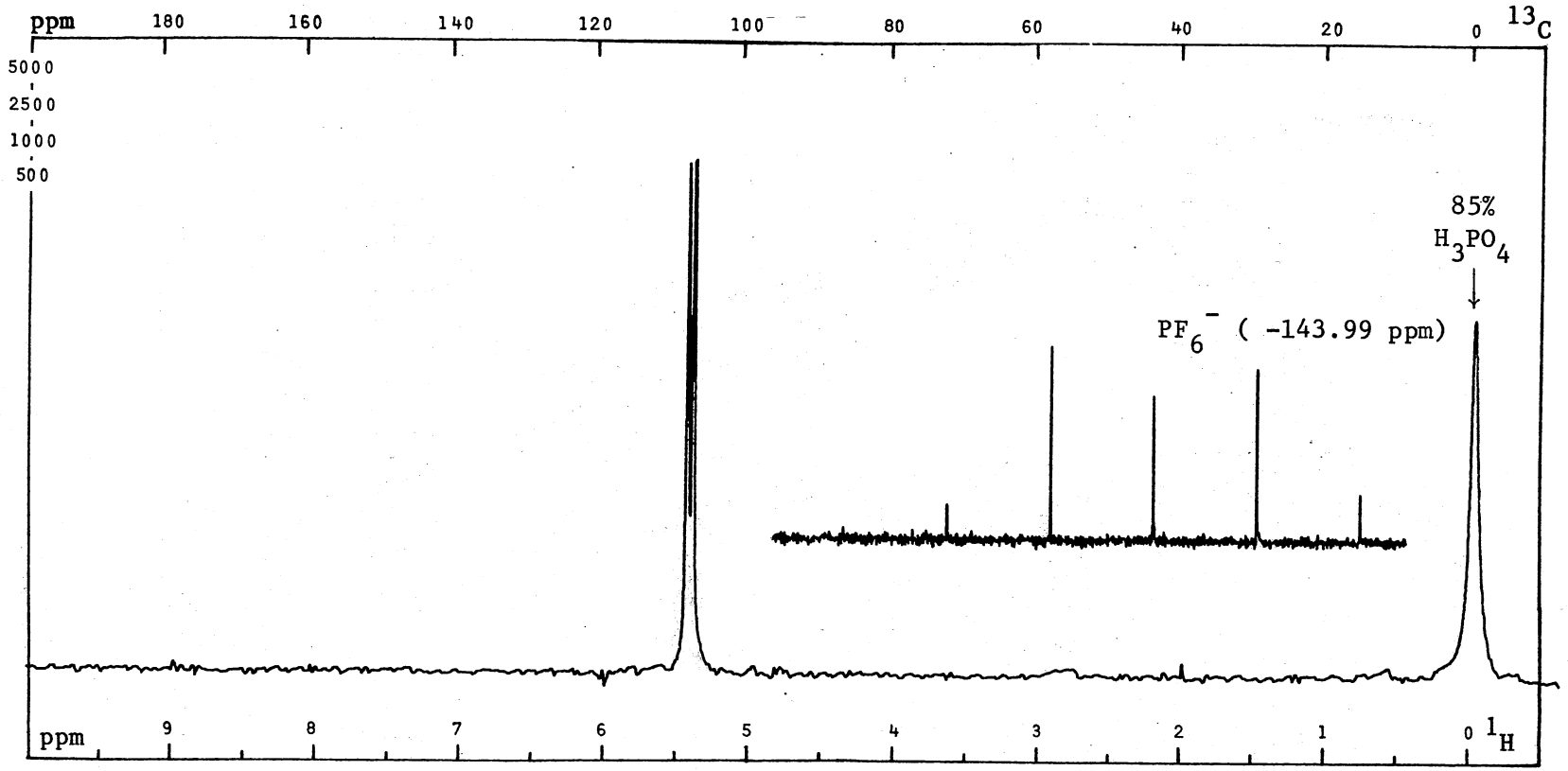
^{31}P NMR Spectrum of 101 (Meso- + dl-pair)

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 120.

Size . . 8 K; P2/RF . . . . 10 μs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXIX



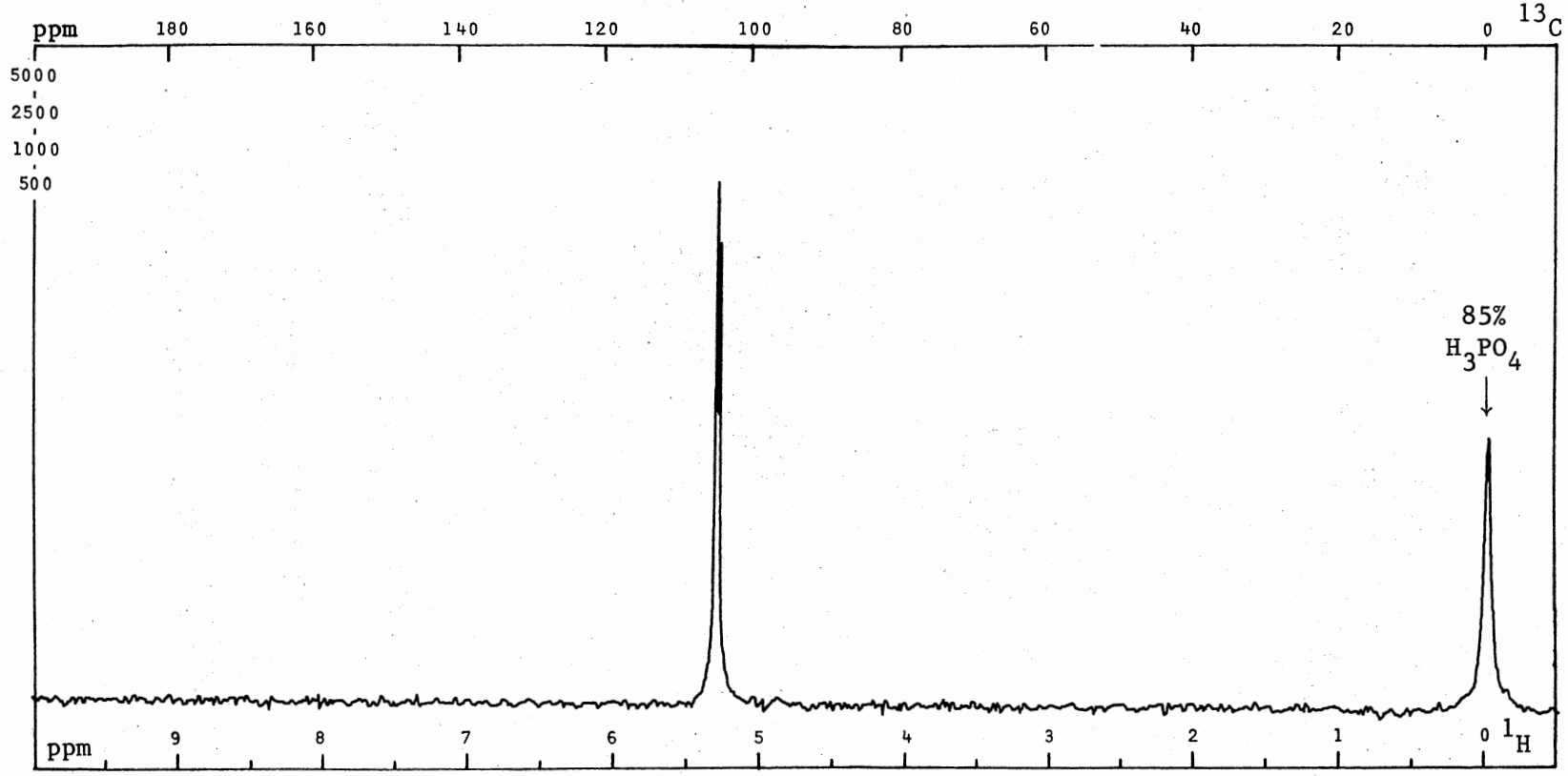
^{31}P NMR Spectrum of 102 (Meso- + dl-pair)

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 30°C; Acq/SA . . 40.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXX



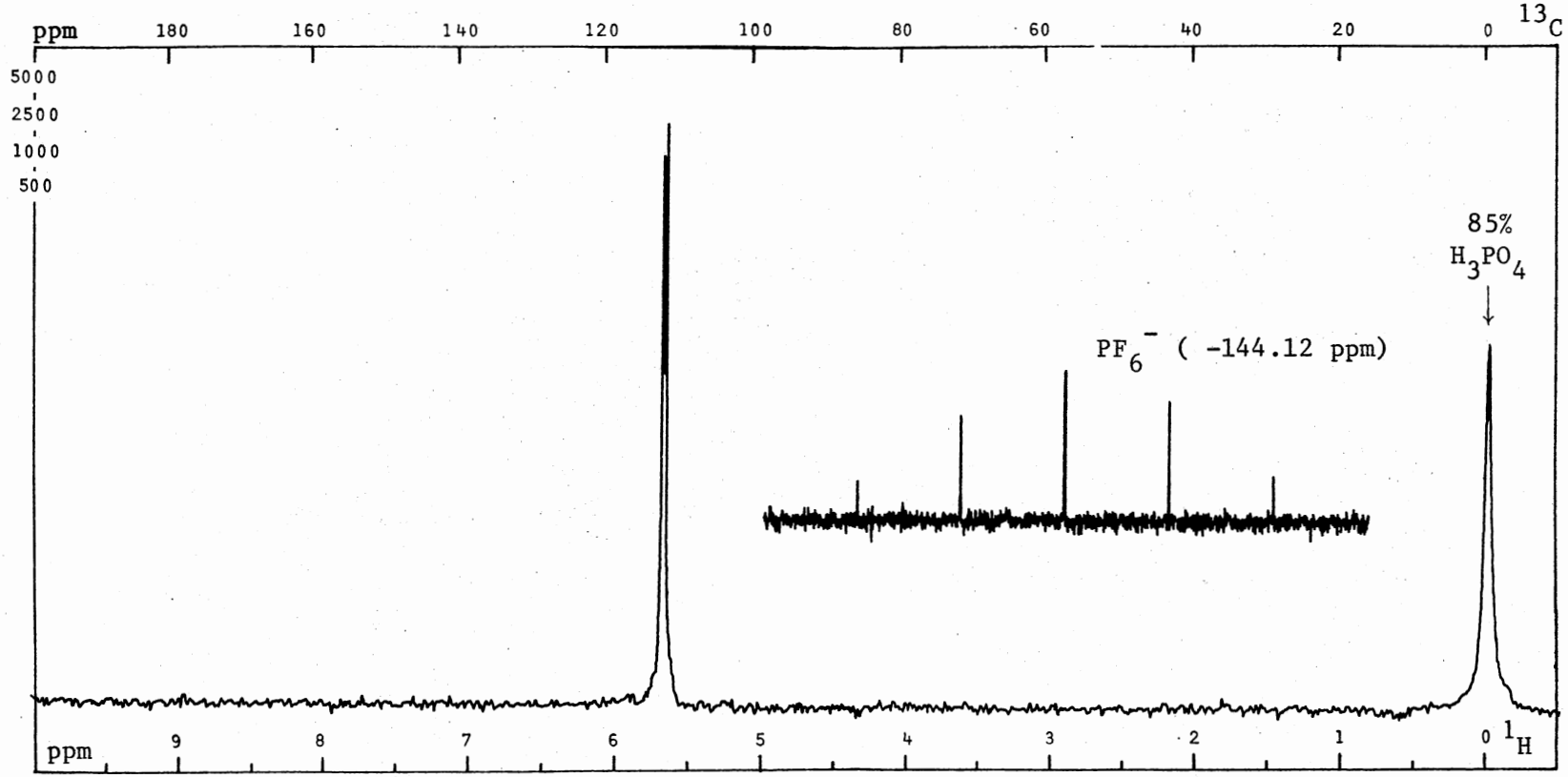
^{31}P NMR Spectrum of ~~103~~ (Meso- + dl-pair)

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 100.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXI



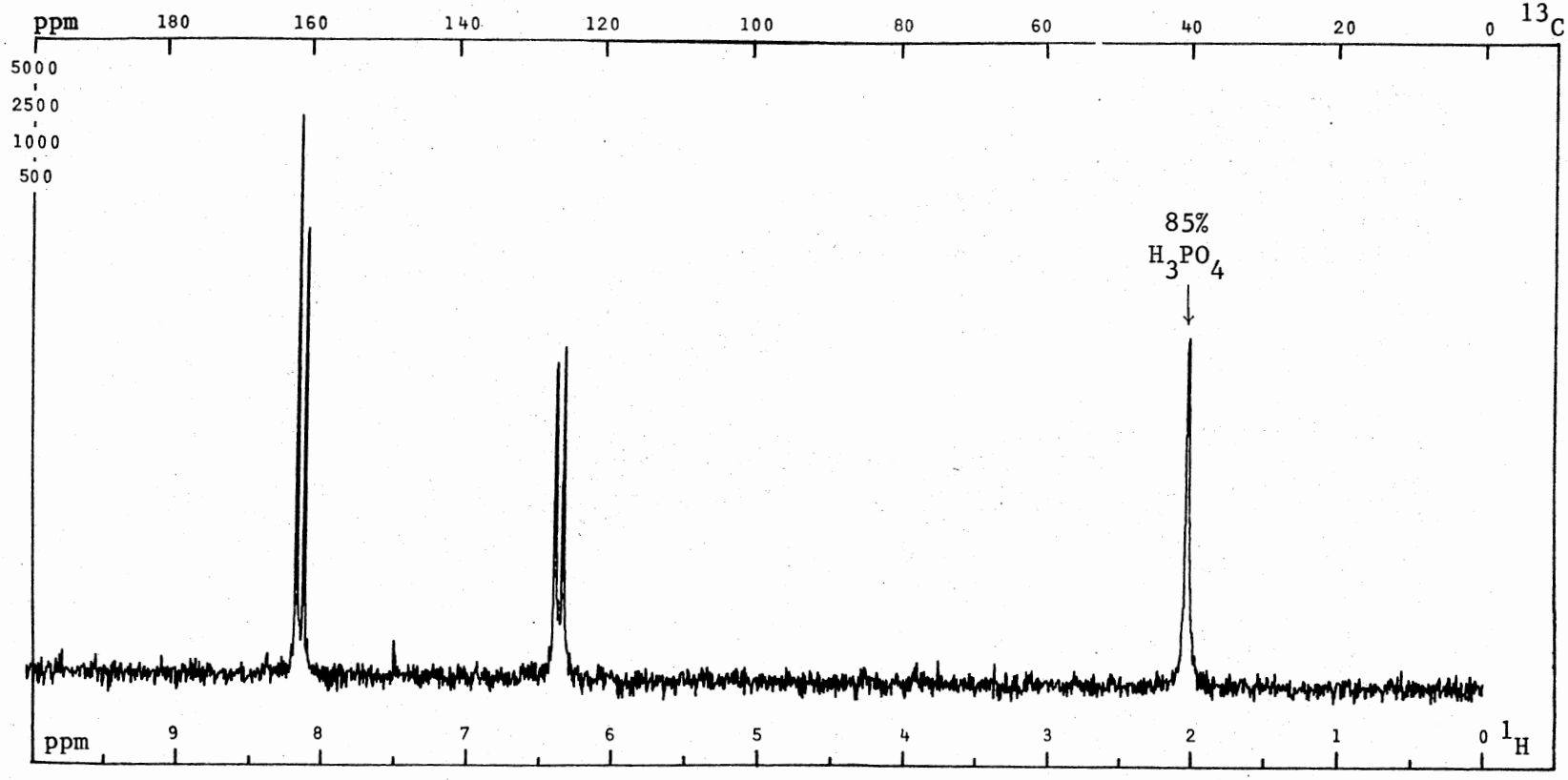
^{31}P NMR Spectrum of 104 (Meso- + dl-pair)

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 20.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^2H; D5/ST . . 5 s.

DC . . . ^1H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXII



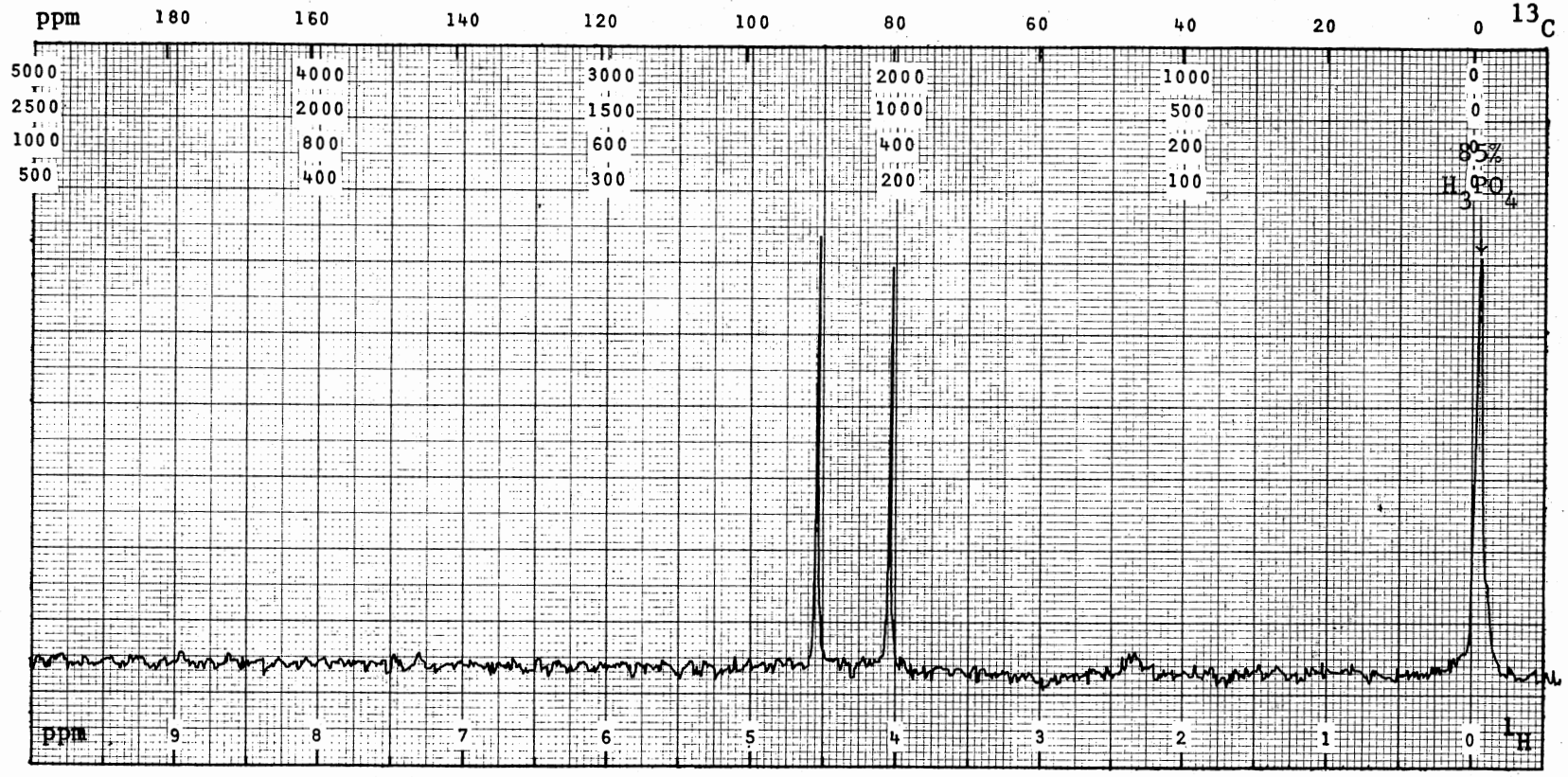
^{31}P NMR Spectrum of 108

PFT X CW _; Solvent . . . . DMSO-d_6; SO . . 49201 Hz; PW . . 2000 Hz; T. . . 27°C; Acq/SA . . 12.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXIII



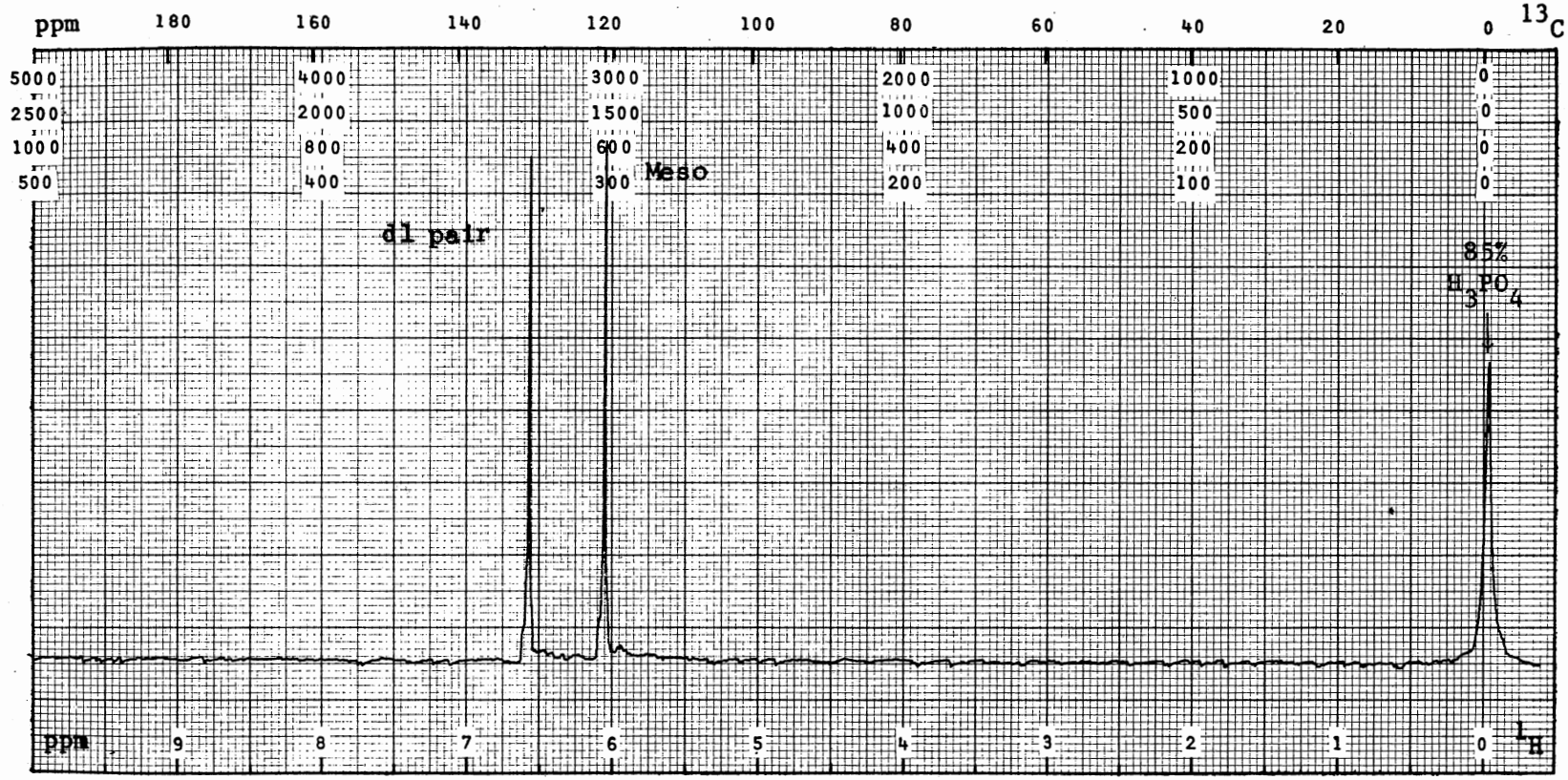
^{31}P NMR Spectrum of 111 (Meso- + dl-pair)

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 40.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; Rf . . 9 W/dB; NBW . 100 Hz.

PLATE LXXIV



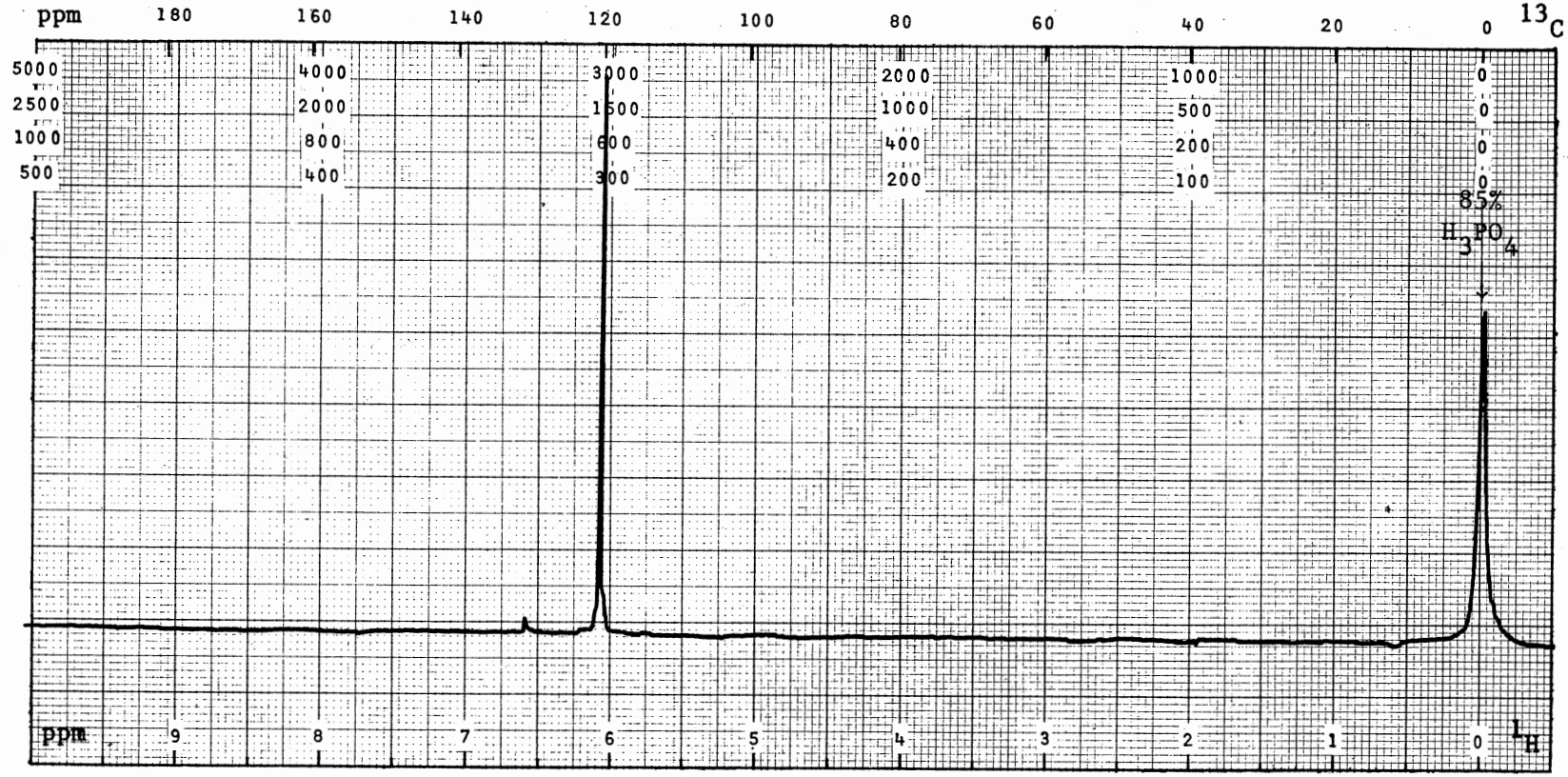
^{31}P NMR Spectrum of 117 (Meso- + dl-pair)

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . . 4.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXV



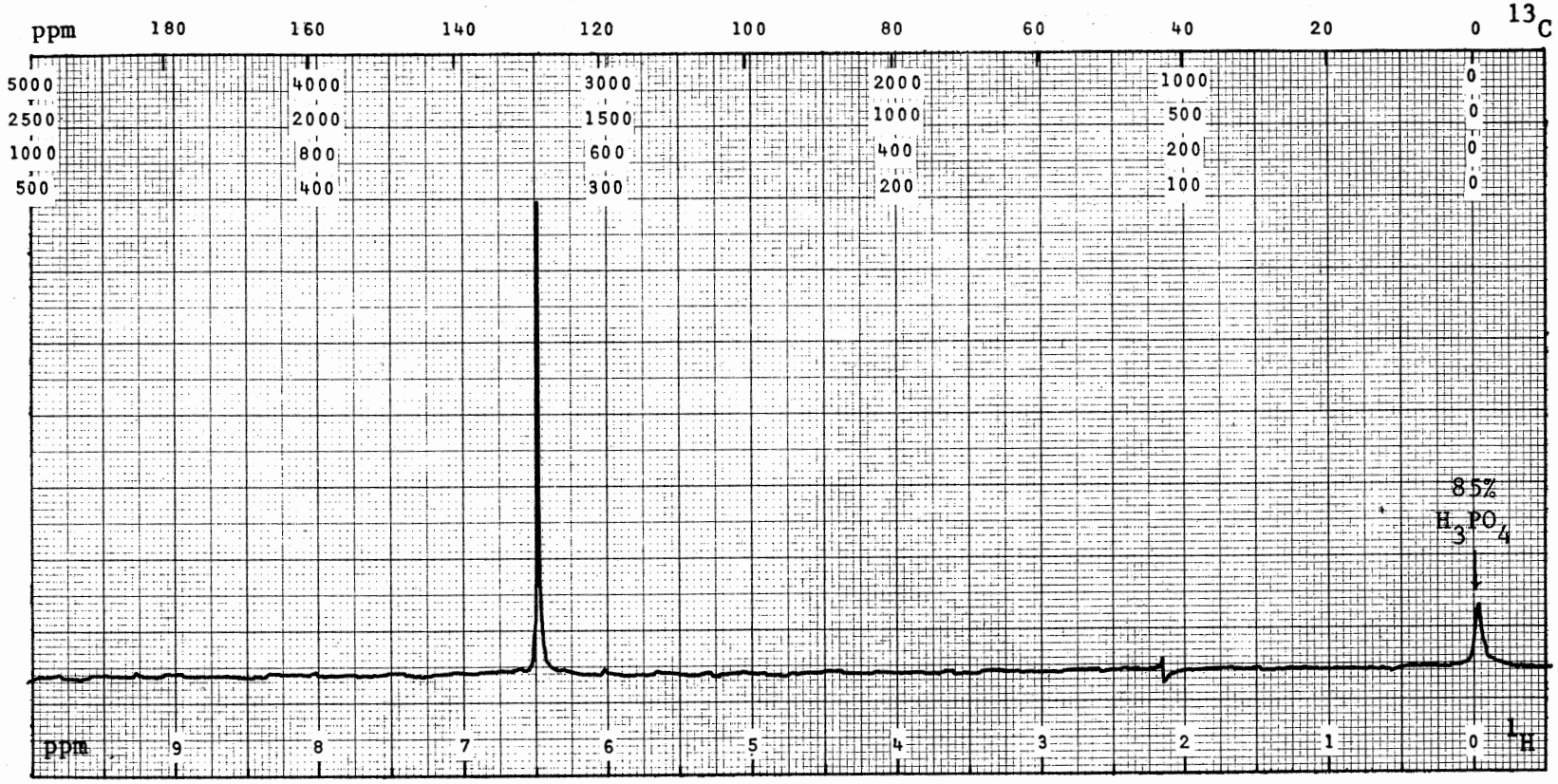
^{31}P NMR Spectrum of Meso-117

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 12.

Size . . 8 K; P2/RF . . . . 10 μs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXVI



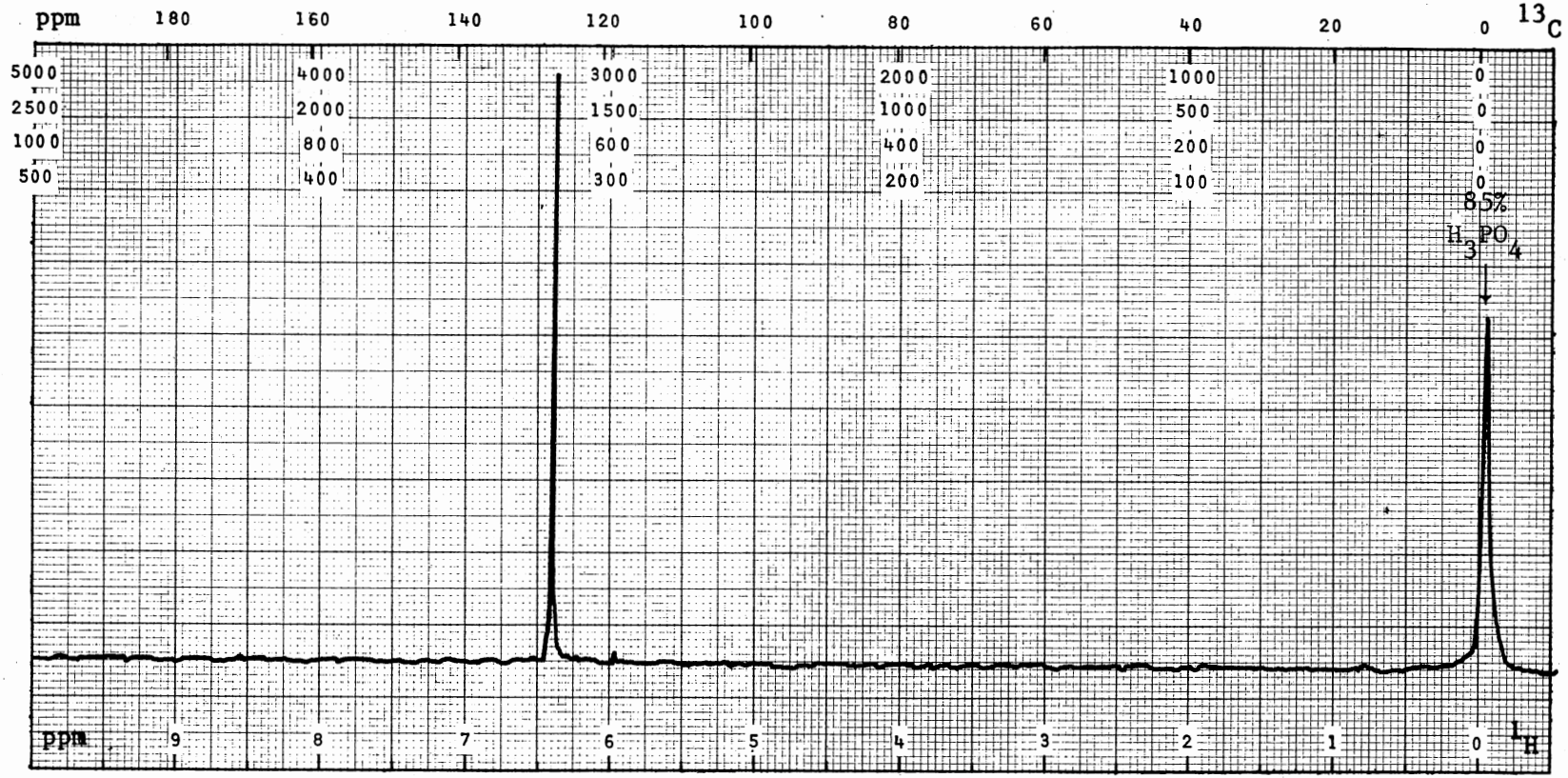
^{31}P NMR Spectrum of (±)-117

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 29°C; Acq/SA . . 20.

Size . . 8 K; P2/RF . . . . 10 μs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXVII



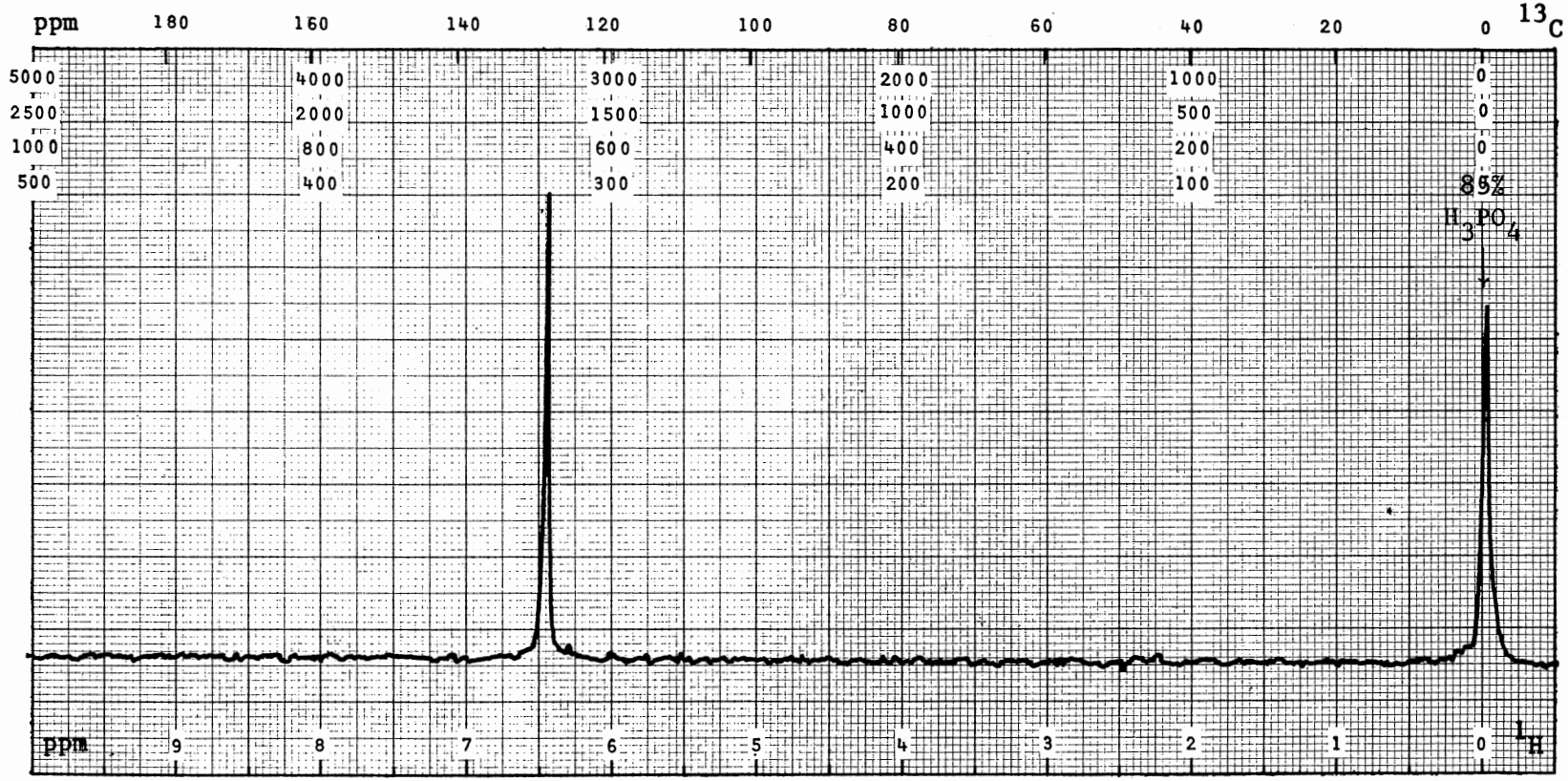
^{31}P NMR Spectrum of (+)-117

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 32.

Size . . 8 K; P2/RF . . . . 10 μs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45041 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXVIII



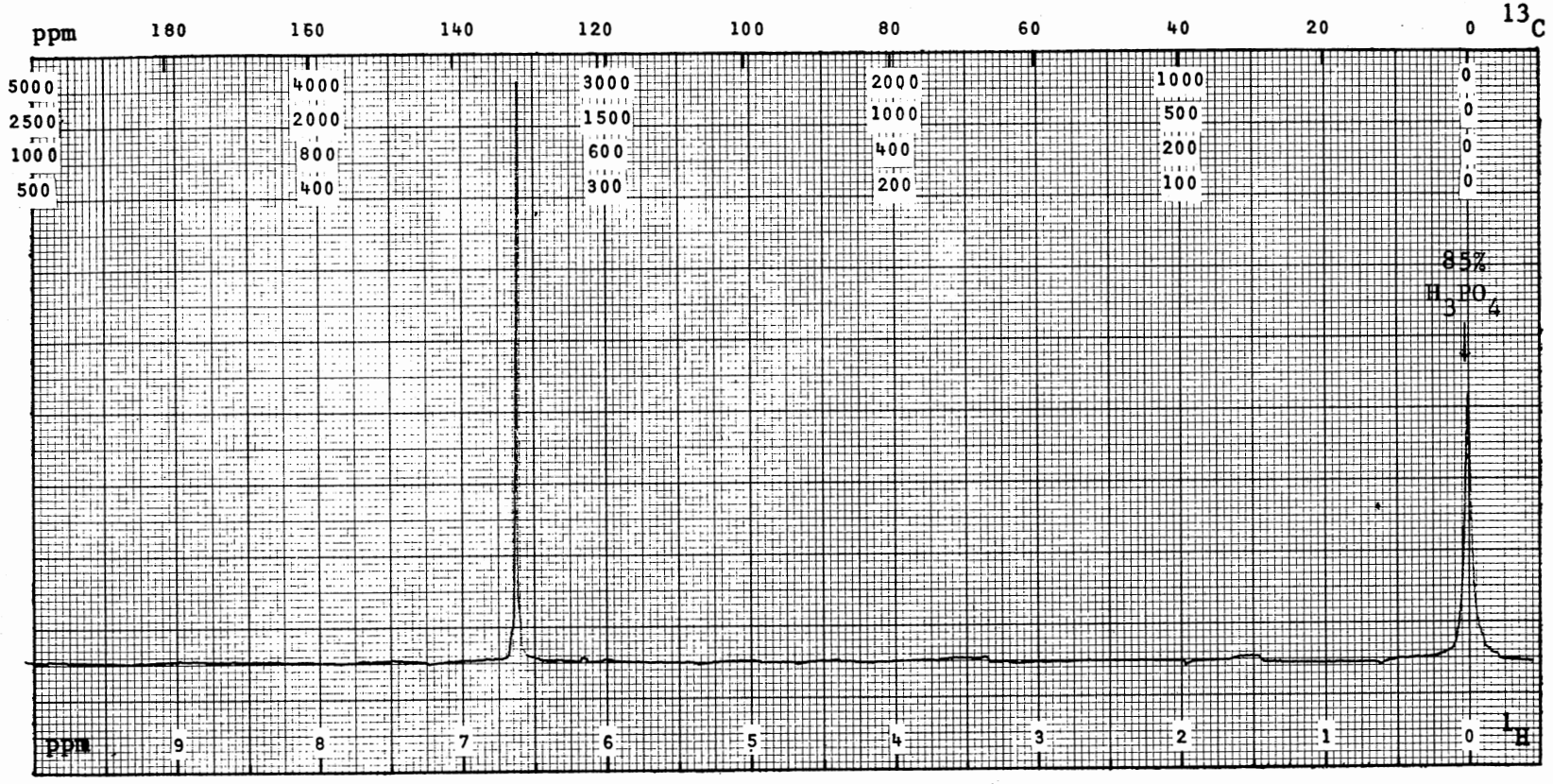
^{31}P NMR Spectrum of (-)-117

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 32.

Size . . 8 K; P2/RF . . . . 10 μs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXIX



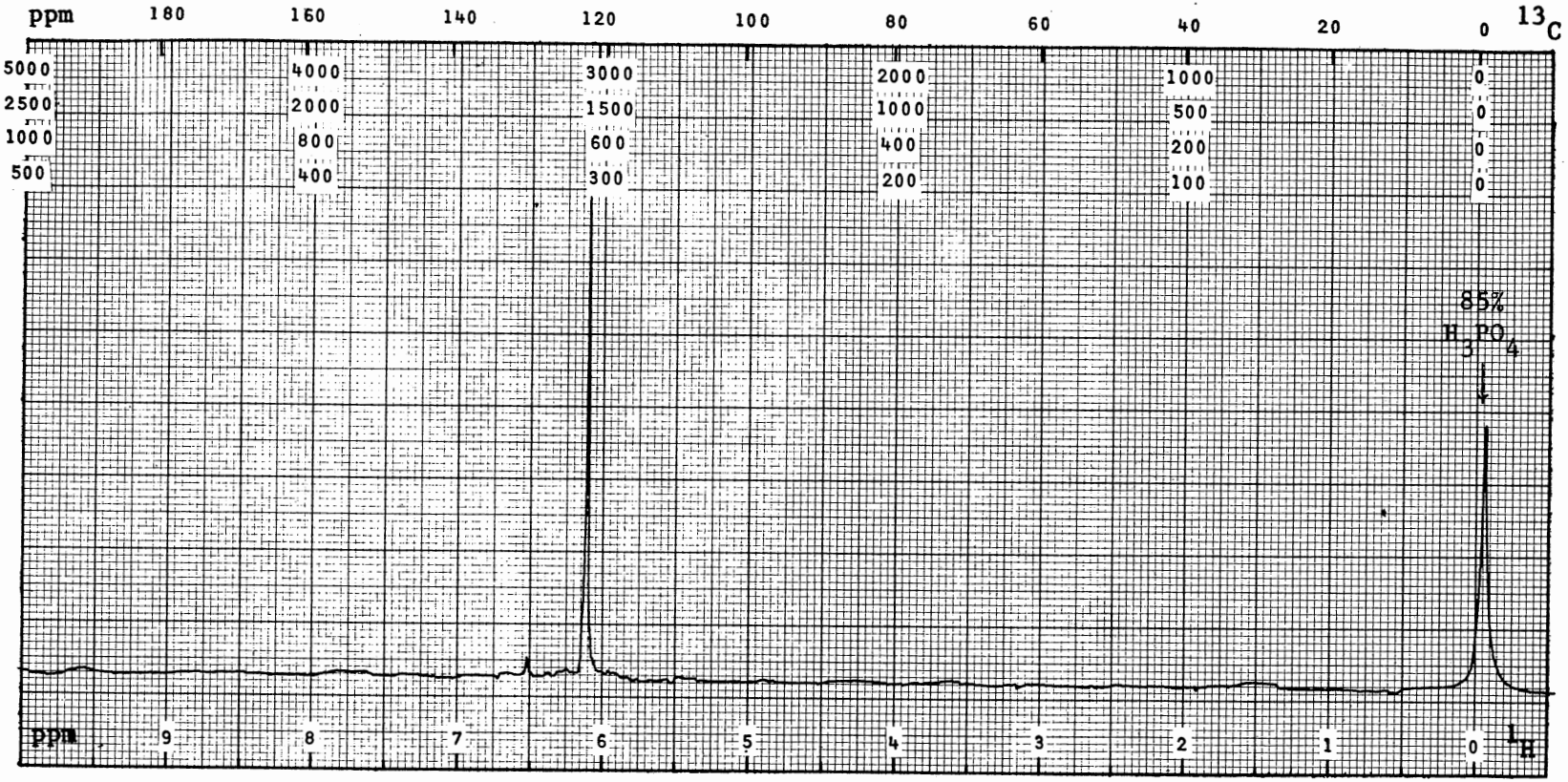
^{31}P NMR Spectrum of (±)-118

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 16.

Size . . 8 K; P2/RF . . . . 10 μs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXX



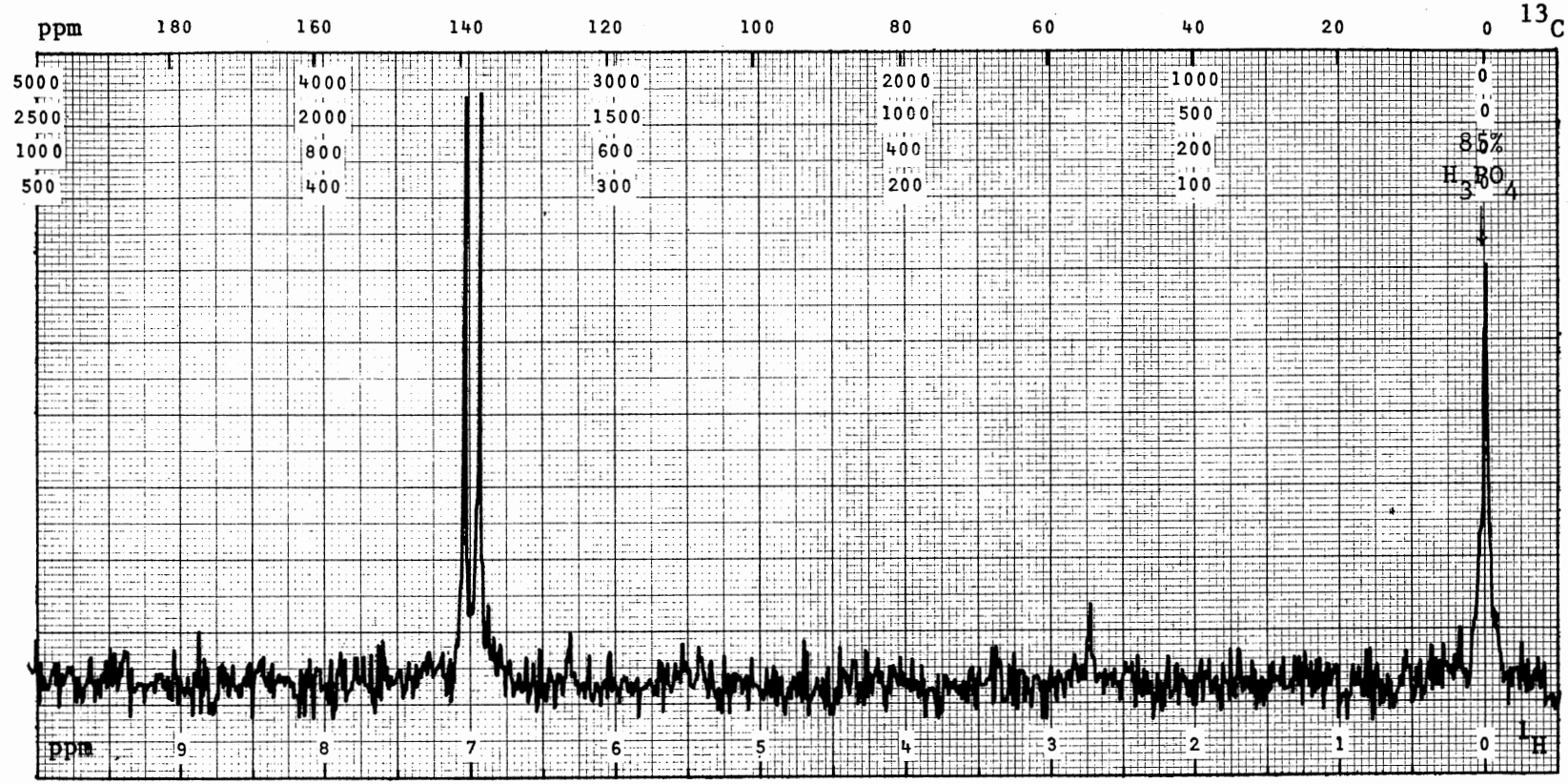
^{31}P NMR Spectrum of Meso-120

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 28°C; Acq/SA . . 20.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXXI



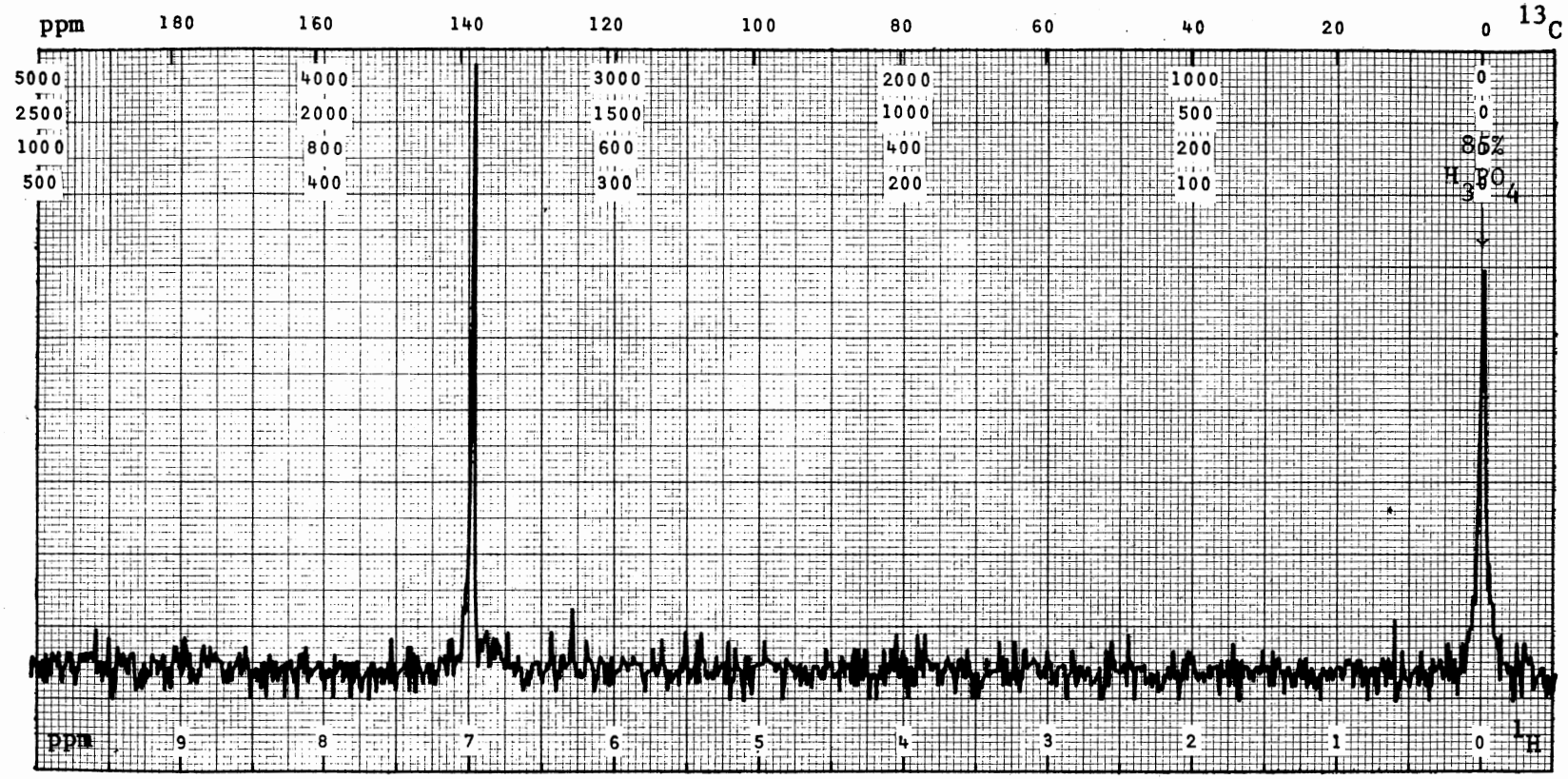
^{31}P NMR Spectrum of (±)-121 [L(+)HDBT]

PFT X CW _; Solvent . . . . . $DCCl_3$; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 20.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXXII



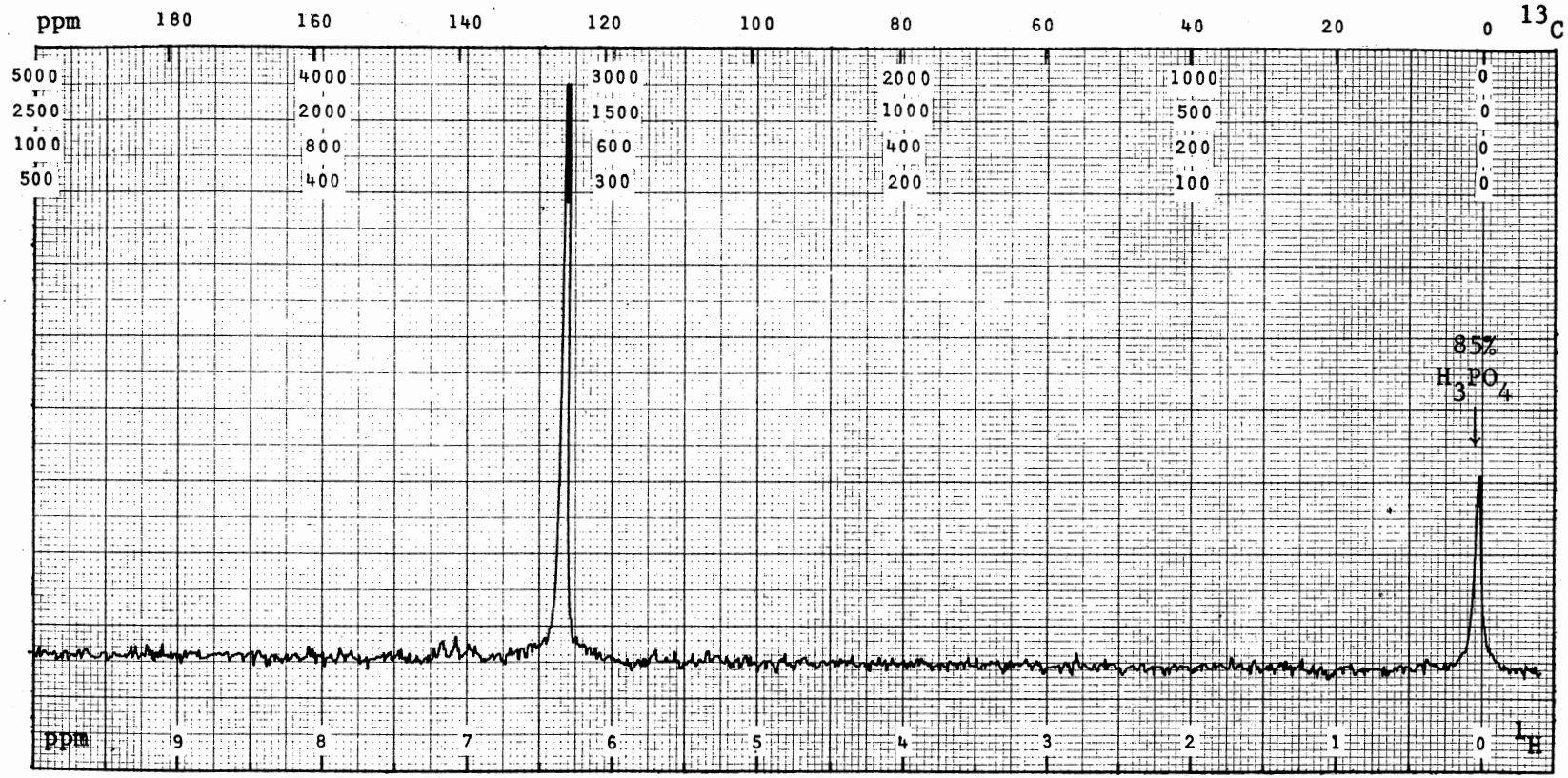
^{31}P NMR Spectrum of (-)-121 [L(+)HDBT]

PFT X CW _; Solvent . . . . . $DCCl_3$; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 20.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXXIII



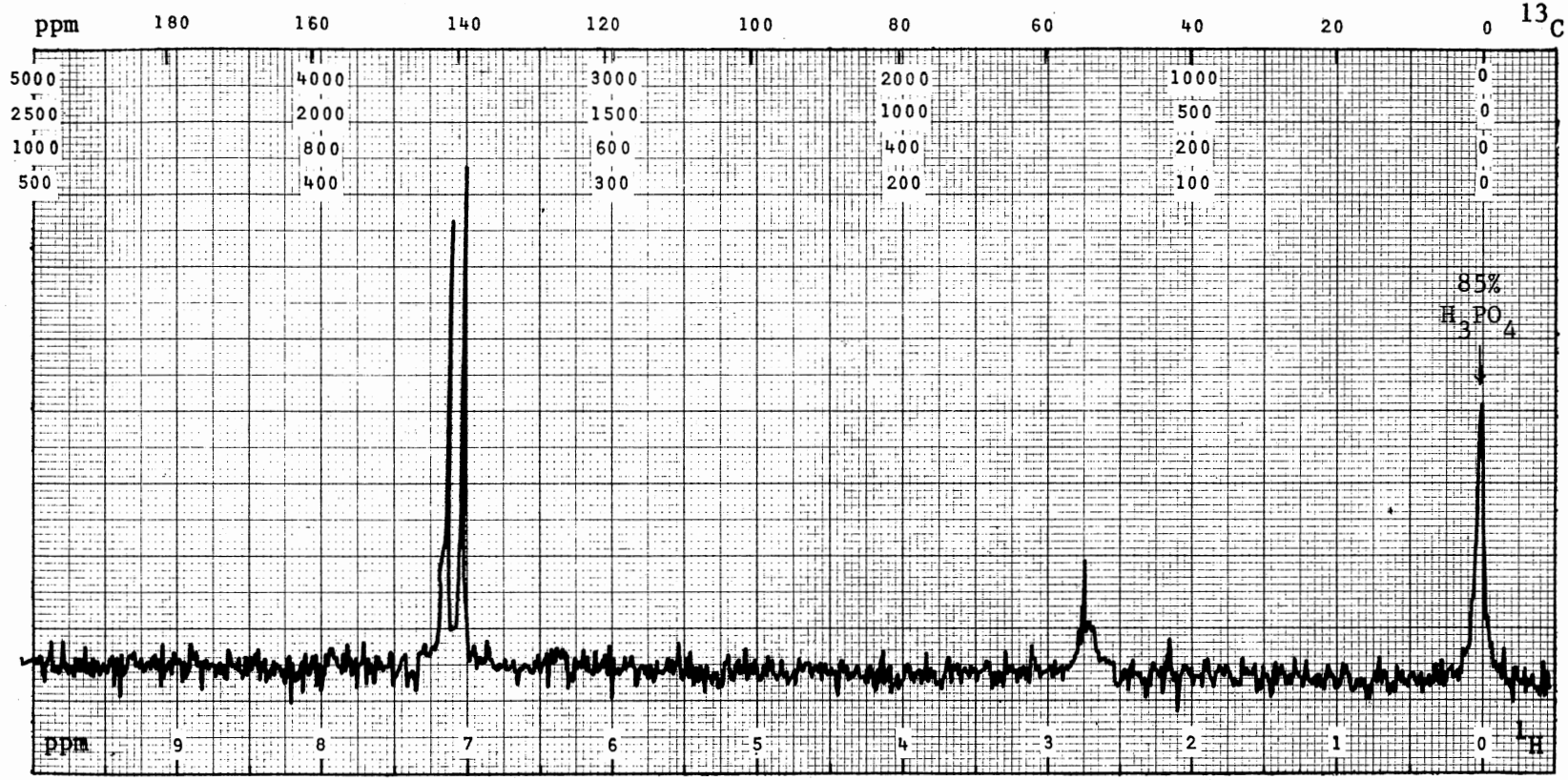
^{31}P NMR Spectrum of Meso-121 [L(+)HDBT]

PFT X CW _; Solvent . . . . . $DCCl_3$; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 20.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXXIV



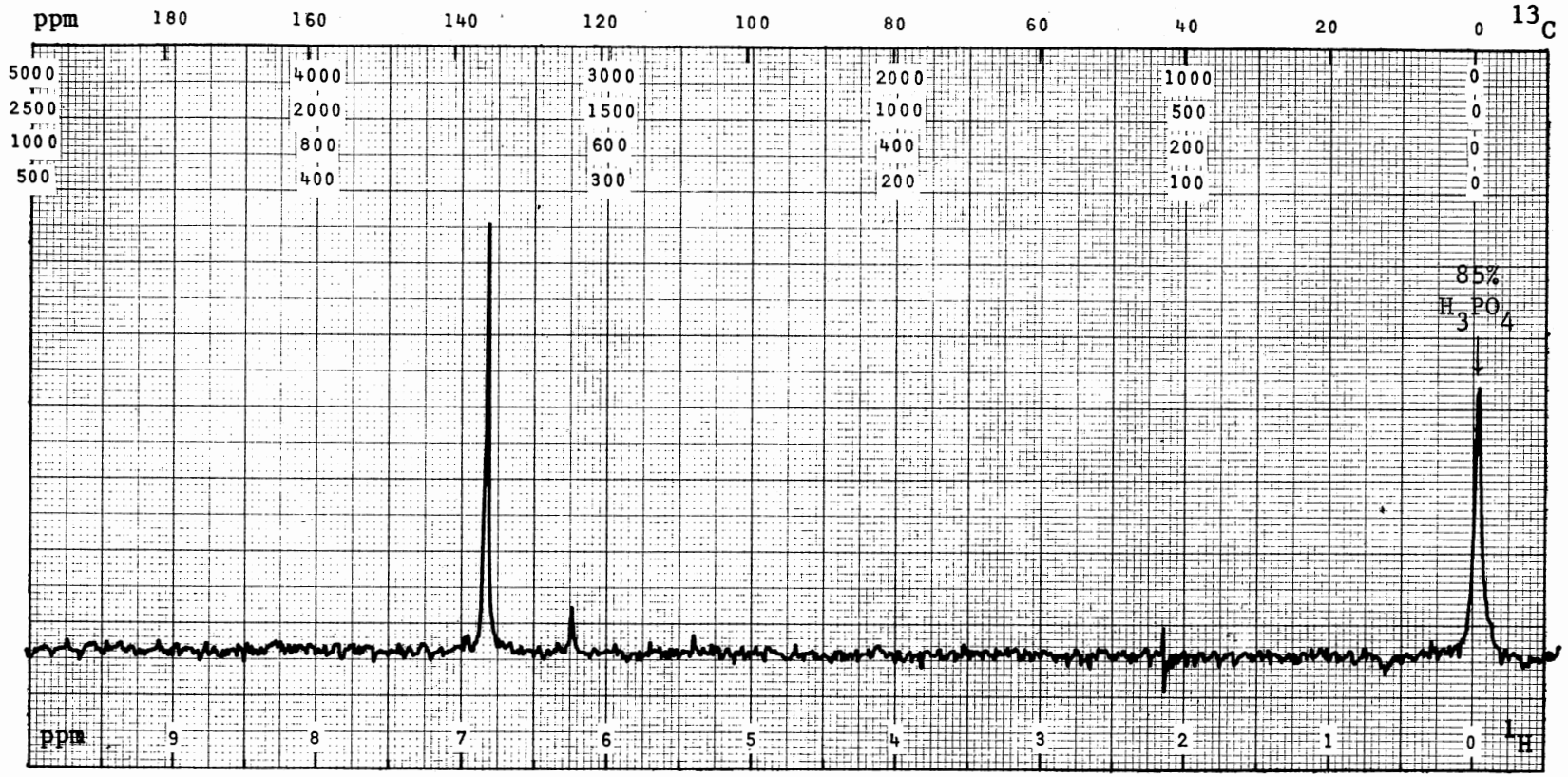
^{31}P NMR Spectrum of (±)-122 [D(-)HDBT]

PFT X CW _; Solvent . . . . . $DCCl_3$; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 20.

Size . . 8 K; P2/RF . . . . 10 µd/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXXV



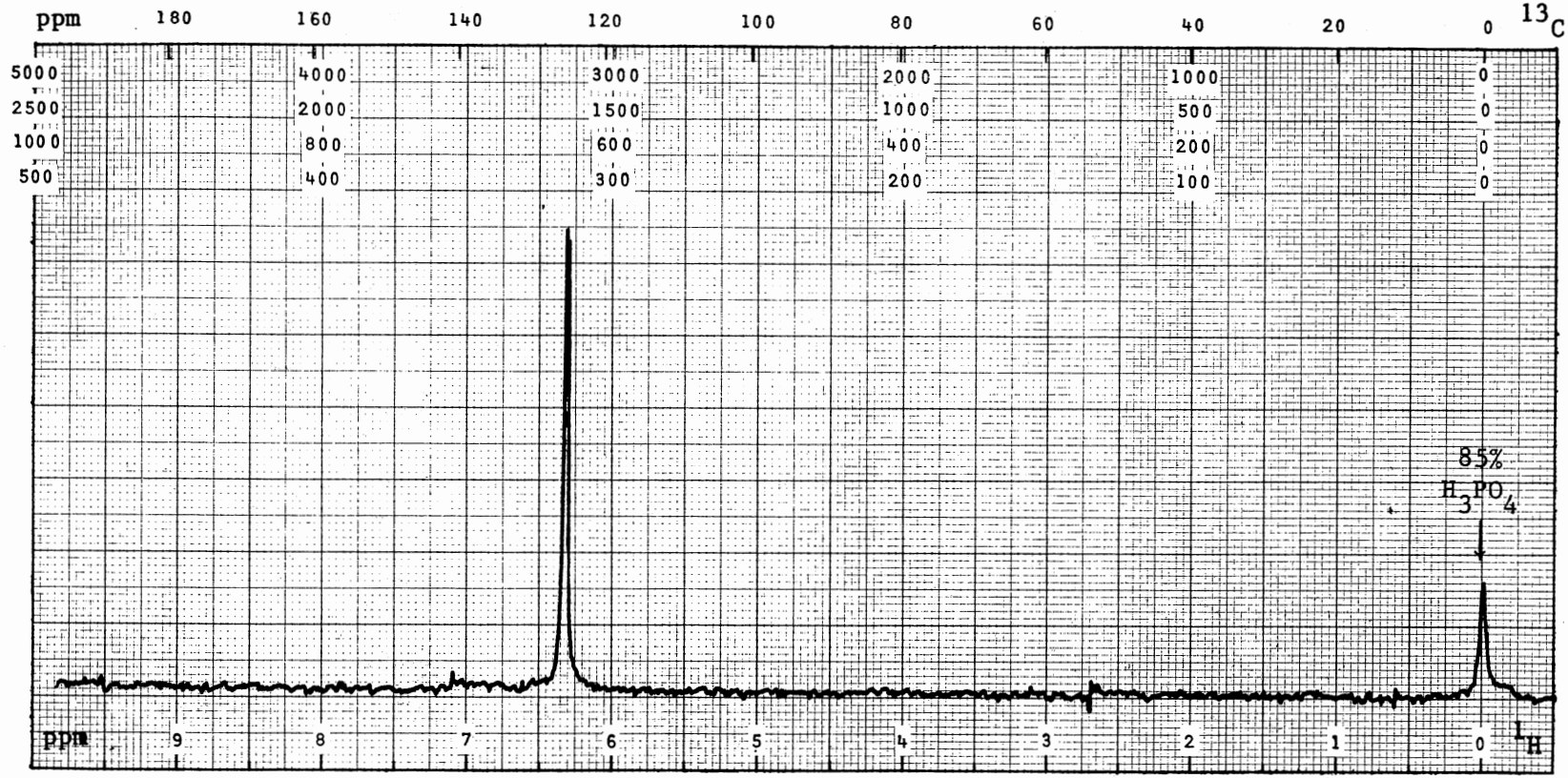
^{31}P NMR Spectrum of (+)-122 [D(-)HDBT]

PFT X CW _; Solvent . . . . . $DCCl_3$; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 60.

Size . . 8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXXVI



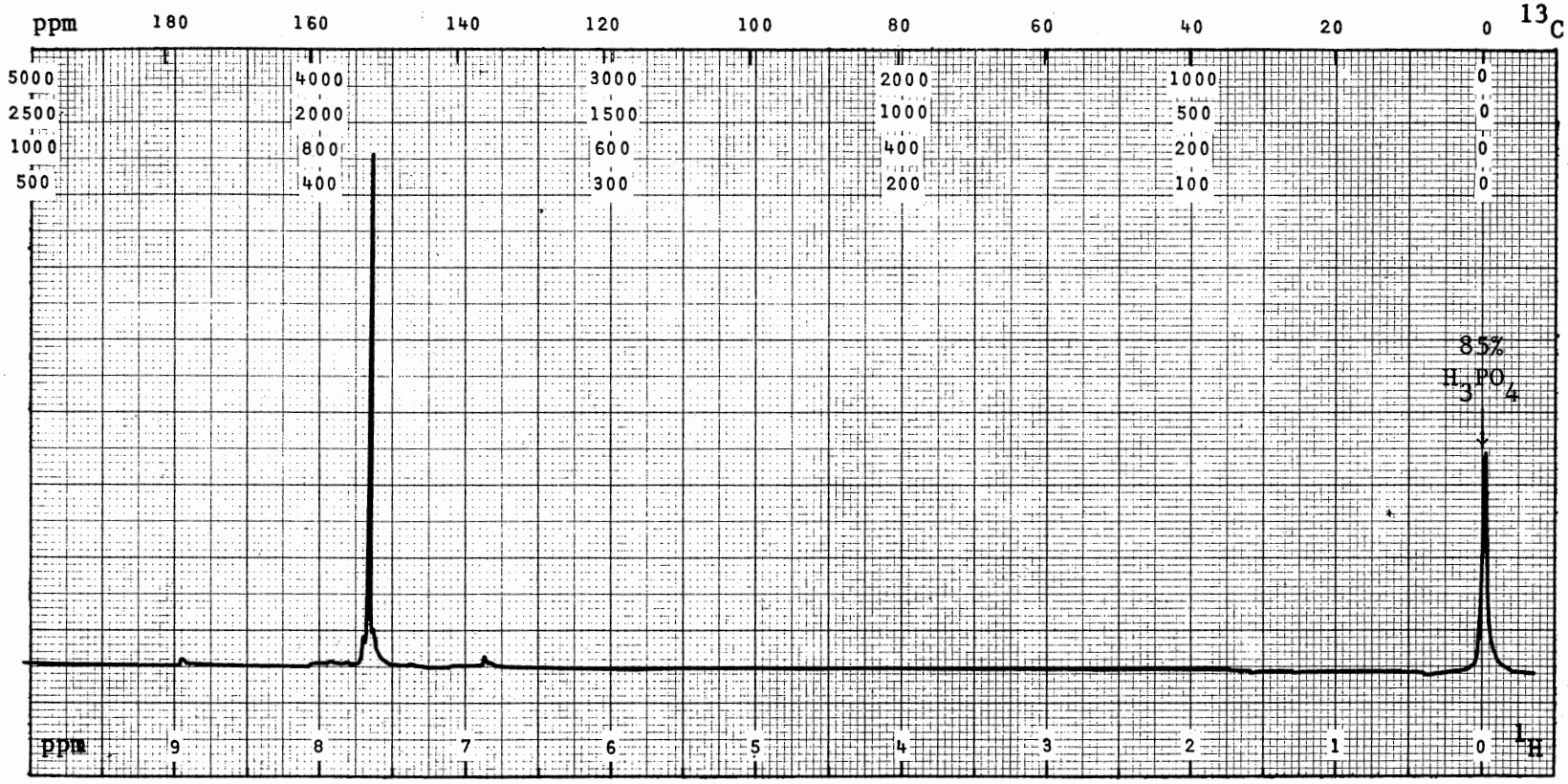
^{31}P NMR Spectrum of Meso-122 [D(-)HDBT]

PFT X CW _; Solvent . . . . . $DCCl_3$; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 16.

Size . .8 K; P2/RF . . . . 10 µs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^{2}H; D5/ST . . 5 s.

DC . . . ^{1}H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXXVII



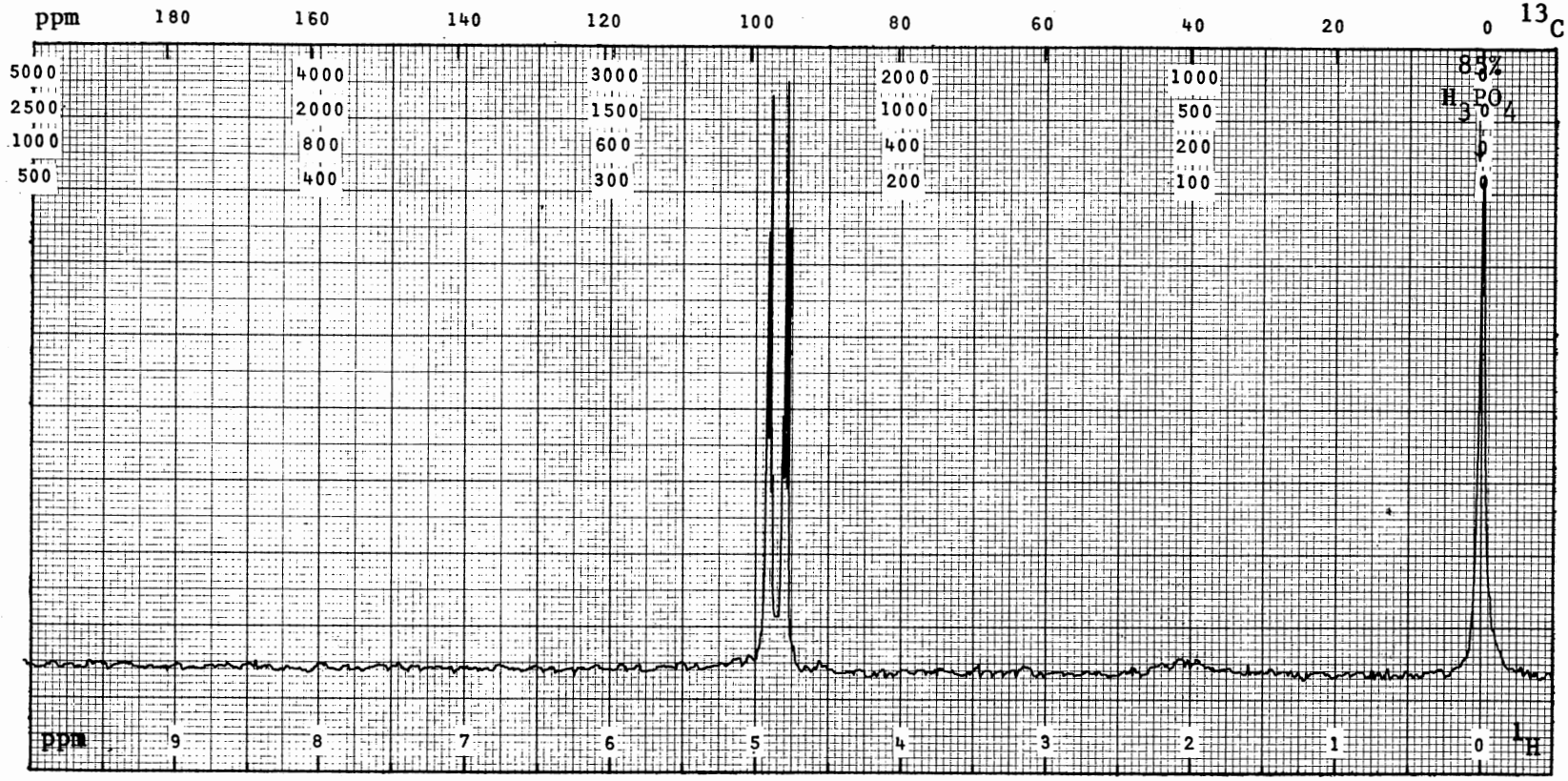
^{31}P NMR Spectrum of Cyclic Products from 112

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 40.

Size . .8 K; P2/RF . . . . 10 μs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^2H; D5/ST . . 5 s.

DC . . . ^1H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

PLATE LXXXVIII



^{31}P NMR Spectrum of Cyclic Products from 115

PFT X CW _; Solvent . . $DCCl_3$ + TFA; SO . . 49201 Hz; PW . . 1000 Hz; T. . . 27°C; Acq/SA . . 40.

Size . .8 K; P2/RF . . . . 10 μs/dB; SF . . 40.5 MHz; FB . . 3000 Hz; Lock . . ^2H; D5/ST . . 5 s.

DC . . . ^1H; Gated Off . . ; Offset . 45051 Hz; RF . . 9 W/dB; NBW . 100 Hz.

BIBLIOGRAPHY

(1) Abraham, R. J., Siverns, T. M., Org. Mag. Reson., 5, 253 (1973).

(2) Albright, T. A., Freeman, W. J., Schweizer, E. E., J. Am. Chem. Soc., 97, 2946 (1976).

(3) Albright, T. A., Freeman, W. J., Schweizer, E. E., J. Org. Chem., 40, 3437 (1975).

(4) Arcoria, A., Librando, V., Longo, M., Torre, M., Chim. Ind. (Milan), 60, 980 (1978); Chem. Abstr., 90, 188492x (1979).

(5) Beck, P., in Organophosphorus Compounds, Kosolapoff, G. M., Maier, L., Ed., Wiley-Interscience, New York, 1972, Vol. 2, pp. 189-508.

(6) Bentley, W. H., Haworth, E., Perkin, W. H., J. Chem. Soc., 69 161 (1896).

(7) Berenson, H., Dornbush, A. C., Wehner, D. C., (to American Cyanamid), U.S. Pat. 3506,577 (1970); Chem. Abstr., 73, 5251z (1970).

(8) Berkman, Z. A., Bartina, L. E., Kabachnik, M. I., Kossykh, V. G., Medved, T. Ya., Nesterova, N. P., Rozen, A. M., Yudina, K. S., Radiokhimiya, 17, 210 (1975); Chem. Abstr., 83, 66216v (1975).

(9) Berlin, K. D., Hellwege, D. M., in Topics in Phosphorus Chemistry, Grayson, M., Griffith, E. J., Ed., Interscience Publishers, New York, 1969, Vol. 6, pp. 1-86.

(10) Bestmann, H. J., Both, W., Chem. Ber., 107, 2923 (1974).

(11) Blaschke, G., Angew. Chem. Int. Ed. Engl., 19, 13 (1980).

(12) Bosnich, B., Wild, S. B., J. Am. Chem. Soc., 92, 459 (1970).

(13) Boyle, P. H., Quart. Rev., 25, 329 (1971).

(14) Braye, E. H., Caplier, I., Saussez, R., Tetrahedron, 27, 5523 (1971).

(15) Brazier, J. F., Houalla, D., Loenig, M., Wolf, R., in Topics in Phosphorus Chemistry, Griffith, E. J., Grayson, M., Ed., Interscience Publishers, New York, 1971, Vol. 8, pp. 132-133.

(16) Brenner, D., Oswald, A. A., (to Exxon), U.S. Pat. 4102,976 (1978); Chem. Abstr., 90, 24535n (1979).

(17) Brophy, J. J., Gallagher, M. J., Aust. J. Chem., 22, 1385 (1969).

(18) Brophy, J. J., Gallagher, M. J., Aust. J. Chem., 22, 1933 (1969).

(19) Brown, M., (to duPont), Ger. Offen. 2354, 757 (1974); Chem. Abstr., 81, 78750m (1974).

(20) Burger, A., J. Med. Chem., 21, 1 (1978).

(21) Butler, C. L., Cretche, L. H., J. Am. Chem. Soc., 55, 2605 (1933).

(22) Cahn, R. S., Ingold, C., Prelog, V., Angew. Chem. Int. Ed. Engl., 5, 385 (1966).

(23) Carman, C. J., Tarpley, A. R., Jr., Goldstein, J. H., J. Am. Chem. Soc., 93, 2864 (1971).

(24) Casini, G., Ferappi, M., Pietroni, B. R., Taddei, F., Schenetti, L., Tetrahedron, 28, 1497 (1972).

(25) Casy, A. F., in PMR Spectroscopy in Medicinal and Biological Chemistry, Academic Press, New York, 1971, p. 185.

(26) Chatt, J., Mann, F. G., J. Chem. Soc., 610 (1939).

(27) Chen, C. H., Berlin, K. D., J. Org. Chem., 36, 2791 (1971).

(28) Chen, C. H., Brighty, K. E., Michaels, F. M., J. Org. Chem., 46, 361 (1981).

(29) Chen, C. H., Ph.D. Dissertation, Oklahoma State University, Stillwater, Oklahoma, 1971.

(30) Christol, H., Cristau, H. J., Ann. Chim., 6, 179 (1971).

(31) Christol, H., Cristau, H. J., Ann. Chim., 6, 191 (1971).

(32) Christol, H., Cristau, H. J., Soleiman, M., Synthesis, 736 (1975).

(33) Cinquini, M., Colonna, S., Int. J. Sulfur Chem., 8, 603 (1976).

(34) Collet, A., Brienne, M., Jacques, J., Chem. Rev., 80, 215 (1980).

(35) Conley, R. T., in Infrared Spectroscopy, Allyn and Bacon, Inc., Boston, 1966, p. 192.

(36) Corfield, J. R., Shutt, J. R., Trippett, S., Chem. Commun., 789 (1969).

(37) Coyne, D. M., McEwen, W. E., Vanderwerf, C. A., J. Am. Chem. Soc., 78, 3601 (1956).

(38) D'Alelio, G. F., U.S. Pat. 373,406 (1973); Chem. Abstr., 79, 54070x (1973).

(39) Davis, M., Mann, F. G., J. Chem. Soc., 3770 (1964).

(40) Day, R. O., Husebye, S., Deiters, J. A., Holmes, R. R., J. Am. Chem. Soc., 102, 4387 (1980).

(41) Deanin, R. D., Bardoliwalla, D. F., Maher, P., Soc. Plast. Eng., Tech. Pap., 21, 105 (1975); Chem. Abstr., 83, 180135t (1975).

(42) Demmler, K., Lawonn, H., Hesse, A., (to BASF A.-G.) Ger. Offen. 2454,773 (1976); Chem. Abstr., 85, 64116e (1976).

(43) Dilbeck, G. A., Morris, D. L., Berlin, K. D., J. Org. Chem., 40, 1150 (1975).

(44) Dilbeck, G. A., Ph.D. Dissertation, Oklahoma State University, Stillwater, Oklahoma, 1974.

(45) Doddrell, D., Riggs, N. V., Aust. J. Chem., 25, 2715 (1972).

(46) El-Deek, M., Macdonell, G. D., Venkataramu, S. D., Berlin, K. D., J. Org. Chem., 41, 1403 (1976).

(47) Eliel, E. L., Pietrusiewicz, K. M., in Topics in Carbon-13 Spectroscopy, Levy, G. C., Ed., John-Wiley & Sons, New York, 1979, Vol. 3, pp. 171-182.

(48) Factor, A., Jaquiss, D. B. G., Mark, V., (to General Electric Co.), Ger. Offen. 2746,906 (1978); Chem. Abstr., 89, 164463s (1978).

(49) Ferrillo, R. G., Granzov, A., Thermochim. Acta., 38, 27 (1980); Chem. Abstr., 93, 8963g (1980).

(50) Fink, R., van der Helm, D., Berlin, K. D., Phosphorus and Sulfur., 8, 325 (1980).

(51) Flöther, F. V., Kraub, G., Zischunke, A., Kuzay, P., Sauer, W., Strüber, F. J., J. Prakt, Chem., 318, 1031 (1976).

(52) Fusco, R., (to Anic, S. P. A.), Austrian. 339,924 (1977); Chem. Abstr., 88, 89839t (1978).

(53) Fusco, R., (to Anic. S. P. A.), Ger. Offen. 2603,869 (1976); Chem. Abstr., 86, 5627v (1977).

(54) Gallagher, M. J., Jenkins, I. D., in Topics in Stereochemistry, Eliel, E. L., Allinger, N. L., Ed., Interscience Publishers, New York, 1968, Vol. 3, pp. 1-96.

(55) Gastrock, W. H., Pankavich, J. A., Carter, S. D., (to American Cyanamide Co.), U.S. 3957,978 (1976); Chem. Abstr., 85, 105198s (1976).

(56) Gaudemer, A., in Stereochemistry Fundamentals and Methods, Kagan, H. B., Ed., George-Thieme Publishers, Stuttgart, 1977, Vol. 1.

(57) Giardina, D., Ballini, R., Cingolani, G. M., Pietroni, B. R., Carotti, A., Casini, G., Tetrahedron, 35, 249 (1979).

(58) Goelte, E., Ger. Offen. 2,414,924 (1975); Chem. Abstr., 84, 110152t (1976).

(59) Gorden, M., Ph.D. Dissertation, University of Pittsburgh, Pittsburgh, Pennsylvania, 1965.

(60) Grayson, J. I., Norrish, H. K., Warren, S., J. Chem. Soc. Perkin I, 2556 (1976).

(61) Grayson, M., Griffith, E. J., Ed., Topics in Phosphorus Chemistry, Interscience Publishers, New York, 1967, Vol. 5

(62) Grim, S., McFarlane, W., Davidoff, E., Marts, J., J. Phys. Chem., 70, 581 (1966).

(63) Hall, C. R., Inch, T. D., Phosphorus and Sulfur, 7, 171 (1979).

(64) Hart, F. A., Mann, F. G., J. Chem. Soc., 4107 (1955).

(65) Hasan, M., Org. Magn. Reson., 14, 309 (1980).

(66) Haskins, T., Hudson, C. S., J. Am. Chem. Soc., 61, 1266 (1939).

(67) Holliman, F. G., Mann, F. G., J. Chem. Soc., 1634 (1947).

(68) Horner, L., Bercz, J. P., Bercz, C. V., Tetrahedron Lett., 5783 (1966).

(69) Horner, L., Doerges, H. J., Werkst. Korros., 23, 6 (1972); Chem. Abstr., 76, 116651m (1972).

(70) Horner, L., Ertel, H., Hinrichs, H., Werkst. Korros., 22, 924 (1971); Chem. Abstr., 76, 48785f (1972).

(71) Horner, L., Fuche, H., Winkler, H., Rapp, A., Tetrahedron Lett., 965 (1963).

(72) Horner, L., Henrichs, H., Werkst. Korros., 22, 864 (1971); Chem. Abstr., 76, 17044j (1972).

(73) Horner, L., Pure. Appl. Chem., 9, 225 (1964).

(74) Hughes, A. N., Amornraksa, K., Phisithkul, S., Reutrakul, V., J. Heterocyclic Chem., 13, 937 (1976).

(75) Hussain, M. S., Schmidbaur, H., J. Naturforsch., 31b, 721 (1976).

(76) Jung, D., Bothner-By, A. A., J. Am. Chem. Soc., 86, 4025 (1964).

(77) Kamai, G., Usacheva, G. M., Russ. Chem. Rev., 35, 601 (1966).

(78) Khaleeluddin, K., Scott, J. M. W., Chem. Ind. (London), 1034 (1976).

(79) Kienzle, F., Meyer, H. J., (to Hoffmann-La Roche), Ger. Offen. 2,526,796 (1976); Chem. Abstr., 85, 123411b (1976).

(80) Kinishi, R., Nakajima, Y., Oda, J., Inouye, Y., Agric. Biol. Chem., 42, 869 (1978).

(81) Kirby, A. J., Warren, S. G., in The Organic Chemistry of Phosphorus, Elsevier Publishing Co., New York, 1967, pp. 254-260.

(82) Klyne, W., Buckingham, J., in Atlas of Stereochemistry Absolute Configurations of Organic Molecules, Oxford University Press, New York, 1974, pp. 233-236.

(83) Krongauz, E. S., Rusanov, A. L., Renard, T. L., Russ. Chem. Rev., 39, 747 (1970).

(84) Kumli, K. F., McEwen, W. E., Vanderwerf, C. A., J. Am. Chem. Soc., 81, 248 (1959).

(85) Levy, G. C., Pehk, T., Lippmaa, E., Org. Magn. Reson., 14, 214 (1980).

(86) Lindeman, L. P., Adams, J. Q., Anal. Chem., 43, 1245 (1971).

(87) Maerky, M., (to Ciba-Geigy), Eur. Pat. Appl. 1991 (1979); Chem. Abstr., 92, 7841h (1980).

(88) Maier, L., J. Inorg. Nucl. Chem., 24, 275 (1962).

(89) Mann, F. G., in Progress in Stereochemistry, Klyne, W., de la Mare, P. B. D., Ed., Academic Press, New York, 1958, Vol. 2, pp. 196-227.

(90) Marcelin, G., Traynor, S. G., (to SCM Corp.), U.S. Pat. 4209,554 (1980); Chem. Abstr., 93, 142384x (1980).

(91) Märkl, G., Angew. Chem. Int. Ed. Engl., 4, 1023 (1965).

(92) Märkl, G., Heier, K. H., Agew. Chem. Int. Ed. Engl., 11, 1016 (1972).

(93) Marsi, K. L., Tuinstra, H., J. Org. Chem., 40, 1843 (1975).

(94) Masunaga, K., Shinohara, H., Hondo, T., (to Toyota Automobile Industry), U.S. Pat. 3720,589 (1973); Chem. Abstr., 79, 6945q (1973).

(95) Mathey, F., Thavard, D., C. R. Hebd. Seances Acad. Sci., Ser. C, 281, 243 (1975).

(96) Mavel, G., in Annual Reports on NMR Spectroscopy, Mooney, E. F., Ed., Academic Press, New York, 1973, Vol. 5B.

(97) McAllister, P. R., Dotson, M. J., Grim, S. O., Hillman, G. R., J. Med. Chem., 23, 862 (1980).

(98) McEwen, W. E., Berlin, K. D., Ed., Organophosphorus Stereochemistry, Part I and II, Appendix, D, H & R, Inc., Stroudsberg, Pennsylvania, 1975.

(99) McEwen, W. E., in Topics in Phosphorus Chemistry, Grayson, M., Griffith, E. J., Ed., Interscience Publishers, New York, 1965, Vol. 2, pp. 1-42.

(100) Michalski, P. J., Bull. Soc. Chim. Fr., 4, 1109 (1967).

(101) Mikolojczyk, M., Leitloff, M., Russ. Chem. Rev., 44, 670 (1975).

(102) Mislow, K., Raban, M., in Topics in Stereochemistry, Allinger, N. L., Eliel, E. L., Ed., Wiley-Interscience, New York, 1967, Vol. 1, pp. 1-38.

(103) Murray, R. W., Savides, C., (to American Cyanamid Co.), U.S. Pat. 3649,591 (1972); Chem. Abstr., 77, 6526n (1972).

(104) Needham, D. G., Griffin, R. D., (to Phillips Petroleum Co.), U.S. Pat. 3940,347 (1976); Chem. Abstr., 84, 181143b (1976).

(105) Newman, M. S., Chen, C. H., J. Org. Chem., 37, 1312 (1972).

(106) Nieuwenhuyse, H., Louw, R., J. Chem. Soc. Perkin I, 839 (1973).

(107) Ogata, M., Sato, M., Watanabe, Y., Suzuki, H., (to Hitachi Ltd.), Ger. Offen. 2025,469 (1970); Chem. Abstr., 74, 43048s (1971).

(108) Popp, F. D., McEwen, W. E., Chem. Rev., 58, 321 (1958).

(109) Poulin, J. C., Dang, T. P., Kagan, H. B., J. Organomet. Chem., 84, 87 (1975).

(110) Purdum, W. R., Dilbeck, G. A., Berlin, K. D., J. Org. Chem., 40, 3763 (1975).

(111) Quin, L. D., Breen, J. J., Org. Magn. Reson., 5, 17 (1973).

(112) Quin, L. D., in The Heterocyclic Chemistry of Phorphorus, John-Wiley and Sons, New York, 1981.

(113) Rabinovitz, M., Willner, I., Gamliel, A., Gazit, A., Tetrahedron, 35, 667 (1979).

(114) Radhakrishna, A. S., Berlin, K. D., van der Helm, D., Polish J. Chem., 54, 495 (1980).

(115) Redmore, D., (to Petrolite Corp.), U.S. Pat. 4117,236 (1978); Chem. Abstr., 90, 72343v (1979).

(116) Savides, C., Granzow, A., Cannelongo, J. F., J. Appl. Polymer Sci., 23, 2639 (1979).

(117) Smith, A. I., Bryan, R. J., Jr., (to Monsanto Co.), U.S. Pat. 3696,078 (1972); Chem. Abstr., 77, 166017a (1972).

(118) Snider, T. E., Berlin, K. D., J. Org. Chem., 38, 1657 (1973).

(119) Snider, T. E., Chen, C. H., Berlin, K. D., Phosphorus, 1, 81 (1971).

(120) Snider, T. E., Ph.D. Dissertation, Oklahoma State University, Stillwater, Oklahoma, 1972.

(121) Swan, J. M., (to Monash University), U.S. Pat. 3931,196 (1976); Chem. Abstr., 85, 21609a (1976).

(122) Taddei, F., Boll. Sci. Fac. Chim. Ind. Bologna, 26, 107 (1968).

(123) Technical Data, A Survey of the Literature on Applications of Polyphosphoric Acid, FMC Corporation, Inorganic Chemical Division, New York, 1964.

(124) Thomas, L. C., in Interpretation of the Infra-red Spectra of Organophosphorus Compounds, Heydon, London, 1979, Ch. 15.

(125) Troquet, M., Laveissiere, B., Pagetti, J., Met.:Corros.-Ind., 635-636, 235 (1978); Chem. Abstr., 90, 78309k (1979).

(126) Tumanov, A. A., Shevchuk, M. I., Postnov, I. E., Glukhova, M. N., Osipova, N. I., Tolocheko, A. F., Subbotina, G. M., Khim-Farm. Zh., 12, 49 (1978); Chem. Abstr., 90, 97999b (1976).

(127) Uhlig, F., Angew. Chem., 66, 435 (1954).

(128) Uhlig, F., Snyder, H. R., in Advances in Organic Chemistry: Methods and Results, Raphael, R. A., Taylor, E. C., Wynberg, H., Ed., Interscience Publishers, New York, 1960, Vol. 1, pp. 35-81.

(129) Valentine, D., Jr., Blount, J. F., Toth, K., J. Org. Chem., 45, 3691 (1980).

(130) Venkataramu, S. D., Berlin, K. D., Ealick, S. E., van der Helm, D., Phosphorus and Sulfur, 4, 187 (1978).

(131) Venkataramu, S. D., Macdonell, G. D., Purdum, W. R., Dilbeck, G. A., Berlin, K. D., J. Org. Chem., 42, 2195 (1977).

(132) Venkataramu, S. D., Macdonell, G. D., Purdum, W. R., El-Deek, M., Berlin, K. D., Chem. Rev., 77, 121 (1977).

(133) Vysotskii, V. I., Kalinov, S. M., Tilichenko, M. N., Zh. Obshch. Khim., 49, 2779 (1979); Chem. Abstr., 93, 8246a (1980).

(134) Vysotskii, V. I., Kalinov, S. M., Tilichenko, M. N., Zh. Obshch. Khim., 50, 1707 (1980); Chem. Abstr., 94, 4065p (1981).

(135) Vysotskii, V. I., Skobun, A. S., Tilichenko, M. N., Zh. Obshch. Khim., 49, 1956 (1979); Chem. Abstr., 92, 129014m (1980).

(136) Weast, R. C., Ed., CRC Handbook of Chemistry and Physics, 55th Edition, CRC Press, Cleveland, Ohio, 1974.

(137) Whitesides, G. M., Holtz, D., Roberts, J. D., J. Am. Chem. Soc., 86, 2628 (1964).

(138) Wiinikainan, R. A., Plast. Appliances, Natl. Tech. Conf., 100 (1975); Chem. Abstr., 84, 151389u (1976).

(139) Wilen, S. H., in Topics in Stereochemistry, Vol. 6, Eliel, E. L., Allinger, N. L., Ed., John Wiley and Sons, New York, 1971.

(140) Wilen, S. H., Tables of Resolving Agents and Optical Resolutions, Eliel, E. L., Ed., University of Notre Dam Press, Notre Dam, Indiana, 1972, pp. 249-255.

(141) Wilen, S. H., Tetrahedron, 33, 2725 (1977).

(142) Wilson, B. D., (to Eastman Kodak), U.S. Pat. 3511,849 (1970); Chem. Abstr., 73, 66448r (1970).

(143) Witschard, G., Griffin, C. E., Spectrochim. Acta, 19, 1905 (1963).

(144) Wittig, G., Eggers, H., Duffner, P., Liebigs Ann., 619, 10 (1958).

(145) Wolf, H., Jurb, R., Claussen, K., Chem. Ber., 107, 2887 (1974).

(146) Wu, K. K., van der Helm, D., Cryst. Struct. Comm., 6, 143 (1977); Chem. Abstr., 86, 114034v (1977).

(147) Zetsche, F., Hubacher, M., Helv. Chim. Acta, 9, 291 (1926).

VITA[2]

Narayanasamy Gurusamy

Candidate for the Degree of

Doctor of Philosophy

Thesis: SYNTHESIS AND RESOLUTION OF SELECTED α,ω-ALKANEDIYLBIS(1,2,3,4-TETRAHYDROPHOSPHINOLINIUM) SALTS. THE USE OF ^{31}P NMR ANALYSIS TO MONITOR THE RESOLUTION

Major Field: Chemistry

Biographical:

Personal Data: The author was born in Salaiyoor, India, on January 20, 1946, to G. Narayanasamy and N. Venkittammal; married to Vasantha on May 22, 1972; has two sons, Jayakumar and SriHari.

Education: The author was graduated from S. C. M. High School, Vadambacheri, India, in 1964; received the Bachelor of Science degree in Chemistry from PSG Arts College, University of Madras, India, in 1968; received the Master of Science degree in Chemistry from PSG Arts College, University of Madras, India, in 1970; completed requirements for the Doctor of Philosophy degree in Chemistry at Oklahoma State University, Stillwater, Oklahoma, in July, 1981.

Professional Experience: Demonstrator in Chemistry at PSG Arts College, Coimbatore, India, from June 1970-May 1971; Assistant Professor of Chemistry at PSG Arts College, Coimbatore, India, from June 1971-June 1972; Associate Lecturer in Chemistry at PSG College of Technology, Coimbatore, India, from July 1972-July 1978; Graduate Teaching Assistant in the Department of Chemistry at Oklahoma State University, Stillwater, Oklahoma, from September 1978-December 1979; received an Arts and Science Research Assistantship and an Alumni and Friends Scholarship and Research Assistantship for the summer of 1979 and was a research assistant from January 1980-July 1981 supported by the National Cancer Institute.

Membership in Professional Societies: The author is a member of Sigma Xi.