ADDITION OF AMMONIA TO DIALKYL meso-AND dl-DIBROMOSUCCINATES AND TO DIALKYL BROMOFUMARATES AND DIALKYL BROMOMALEATES--FORMATION OF AZIRIDINES AND ENAMINES

By

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INTRODUCTION

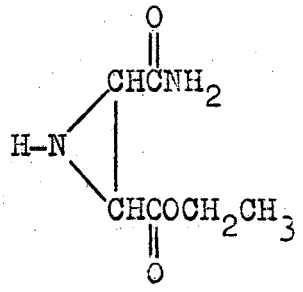
The reaction of ammonia with α-bromo-α,β-unsaturated carboxylic acid esters has been observed to proceed with formation of alkyl aziridine-2-carboxylates. However, no dialkyl aziridine-2,3-dicarboxylates, not otherwise substituted, have been reported until now. Several N-substituted derivatives have been prepared by the action of organic azides on dialkyl fumarates. The reaction of primary amines with α-bromo-α,β-unsaturated monocarboxylic esters is recorded to give cis/trans isomers of the alkyl 2-alkyl-aziridine-3-carboxylates. Ammonia and bromomaleic or bromofumaric acid esters react to form only one of the stereoisomers of each dialkyl aziridine-2,3-dicarboxylate.

CHAPTER I

HISTORICAL

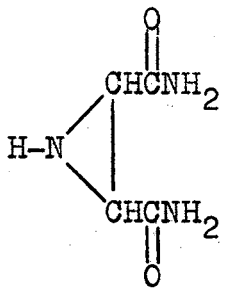
Aziridines from the Action of Ammonia on α,β-Dibromo and α-Bromo-α,β-Unsaturated Ketones and Esters

In 1881, Lehrfeld[33] reported that when diethyl dibromosuccinate was treated with alcoholic ammonia at 60-80°, a cyclic compound of structure I was formed in low yield.



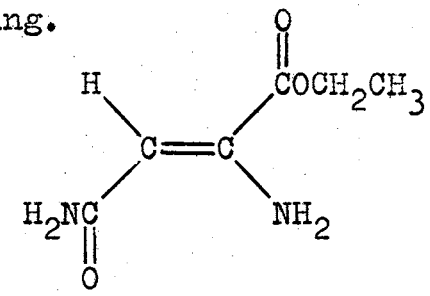
I

Hell and Poliakoff[26] repeated this work using the same conditions and obtained I together with resinous products. When the reaction was carried out at higher temperatures, large amounts of resinous products were formed. Only once when the reaction was run at 120-130° with alcoholic ammonia was a crystalline product obtained of structure II. Since

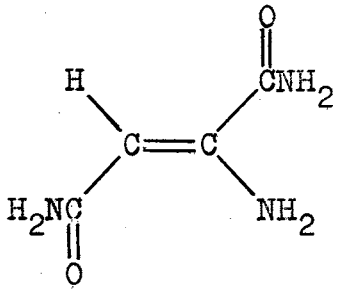


II

then, it has been suggested that I and II may better be assigned structures III and IV,[20] but experimental data is lacking.

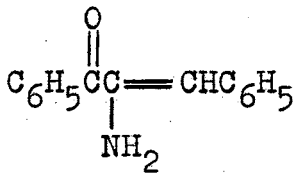


III



IV

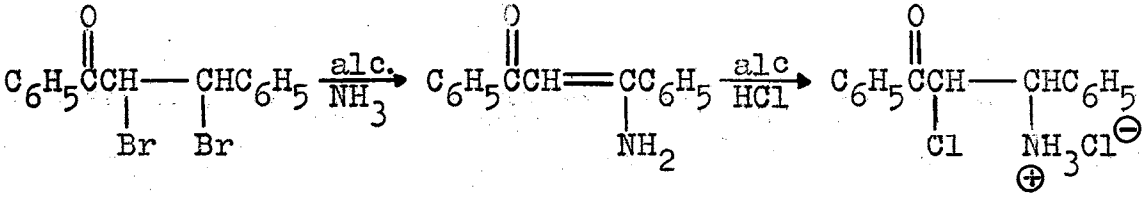
Early reports in the literature concerning the reaction of ammonia with α,β-dibromobenzylacetophenone and α-bromobenzalacetophenone state that almost colorless products were obtained, one structure of which was assigned to V.[39]



V

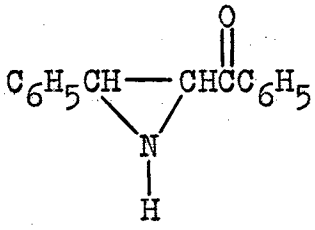
Cromwell's investigations have since shown that all substances of the structure V obtained from the reaction of secondary amines with α-bromobenzalacetophenone are highly colored and it seems doubtful that structure V is the true one for these light-colored substances.[15]

In 1943, Algar and coworkers[1] published some work involving the reaction of ammonia with α,β-dibromobenzylacetophenone. They did not attempt to isolate the intermediate products from the reaction but treated the crude mixture with alcoholic hydrogen chloride and obtained products to which they assigned the structure VI.



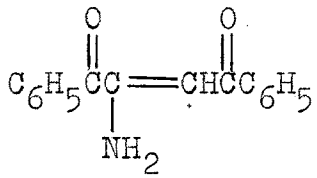
VI

Almost simultaneous investigations by Cromwell and coworkers[12] indicated the true structure for the compound obtained from the reaction of ammonia with the dibromo ketones to be aziridine of structure VII.



VII

Lutz[34] found that the reaction of ammonia with dibenzoylethylene dibromide did not proceed with the formation of the aziridine-type structure but instead gave the isomeric aminodibenzoylethylene VIII. This compound was shown to possess the enamine structure by its synthesis from dibenzoylmethoxyethylene and dibenzoylacetylene. Most ethylenimine ketones are now prepared from the reaction of the ap-

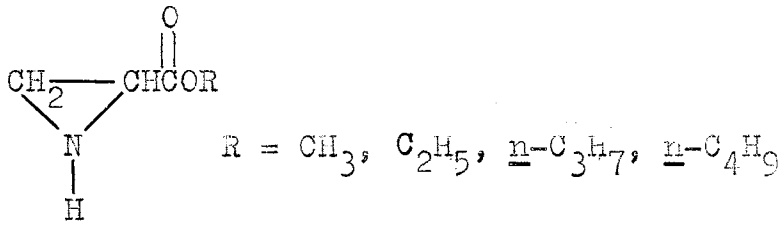


VIII

propriate primary amine and an α-bromo-α,β-unsaturated ketone or an α,β-dibromo ketone.

Very little work has been published in the area of ammonia reactions with α,β-dibromo and α-bromo-α-β-unsaturated carboxylic acid esters. Presumably this area has been avoided because of the ease of formation of amides by ammonia attacking the ester moiety.

In 1960,[28] the formation of aziridines IX was reported from the reactions of ammonia on α,β-dibromopropionic and α-bromoacrylic esters. The formation of ethyl-2-methyl-



IX

aziridine-3-carboxylate was also recorded. The stereochemistry and yields of products were not given.

In the research for a simple synthesis of N-unsubstituted alkyl aziridine-2-carboxylates, Kyburz and coworkers[32] prepared several esters of IX by the reaction of liquid ammonia with the corresponding α,β-dibromo carboxylic acid esters using N-phenyl-2-naphthylamine as a stabilizer. After extraction with ether and distillation of the extracts

$$CH_2BrCHBrCO_2R \xrightarrow[NH_3]{liq.} \quad IX$$

$$R = CH_3,\ C_2H_5,\ \underline{n}\text{-}C_3H_7,\ \text{iso-}C_3H_7,\ \underline{n}\text{-}C_4H_9$$

at reduced pressure yields ranging from 7.6 percent for the methyl to 76 percent for the isopropyl ester were obtained.

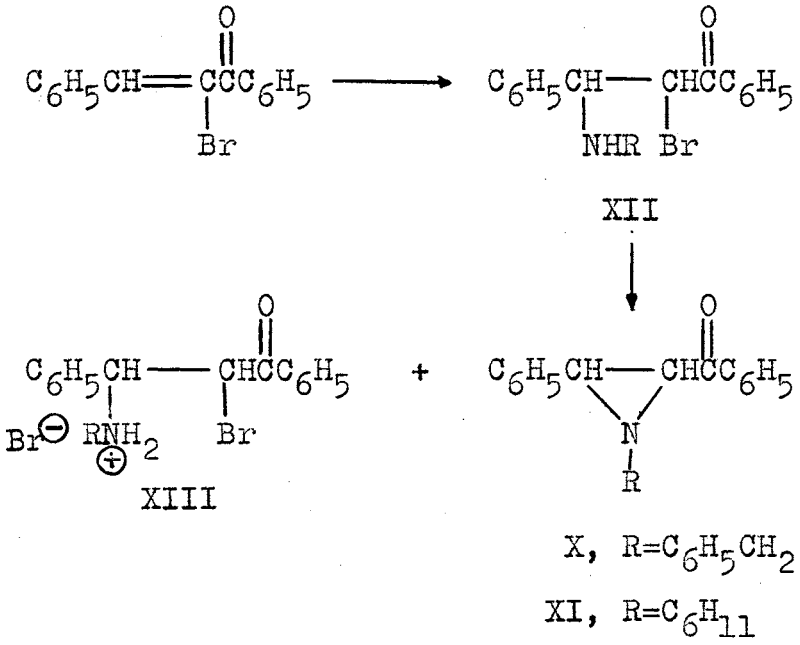
Henery-Logan and Limburg[27] obtained the corresponding benzyl ester of IX in the same manner but the product was isolated by treatment of the extract with an ethereal solution of oxalic acid. This afforded the colorless monooxalate salt of benzyl aziridine-2-carboxylate. The aziridine was released from its oxalate salt by treatment of an aqueous solution of the salt with sodium bicarbonate.

Aziridines from the Action of Primary Amines on α,β-Dibromo and α-Bromo-α,β-unsaturated Ketones and Esters

Since the first aziridines with a ketone carbonyl group attached to the ring were described in 1943,[12] the reaction of primary amines with α,β-dibromo ketones and α-bromo-α,β-unsaturated ketones have been used to prepare many N-alkyl derivatives. A discussion of the reactions of amines with bromo ketones was included in a review in 1946.[9]

Cromwell and coworkers[12] have investigated the reaction of benzylamine and cyclohexylamine with α,β-dibromobenzylacetophenone and α-bromobenzalacetophenone and found them

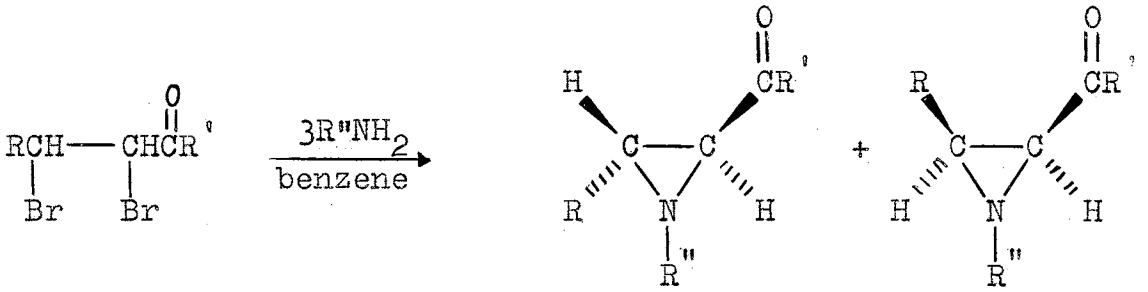
to give colorless substances which are consistent only with aziridine-type structures X and XI. When the α-bromobenzalacetophenone was treated with one mole of benzylamine under special conditions, it was possible to isolate the intermediate, β-benzylamino-α-bromo-β-propiophenone XII. The bromo amino ketone XII was unstable and reacted readily in



solution with itself to form X and the hydrobromide XIII. This salt (XIII) was also obtained by treating X with dry hydrogen bromide gas in benzene.[44] The dibromide XIII reacted with alcoholic potassium hydroxide to give X.

It was evident from these early studies that ammonia and primary amines react with α-bromo-α,β-unsaturated ketones to give first an α-bromo-β-amino ketone[15] which then forms the aziridine ring by splitting out hydrogen bromide. In most of the early reactions of primary amines with α,β-dibromc ketones, the aziridines were obtained in yields of

only about 25%. Cromwell and Hoeksema[16] suggested that these low yields might be due to the formation of pairs of geometrical isomers of which only the less soluble was isolated. The reaction of benzylamine with α,β-dibromobenzyl-p-methylacetophenone was found to give the isomeric products XIV (29%) and XV (37%).[16] The cis form was found to be the



$R = C_6H_5$
$R' = p\text{-}CH_3C_6H_4$
$R'' = C_6H_5CH_2$

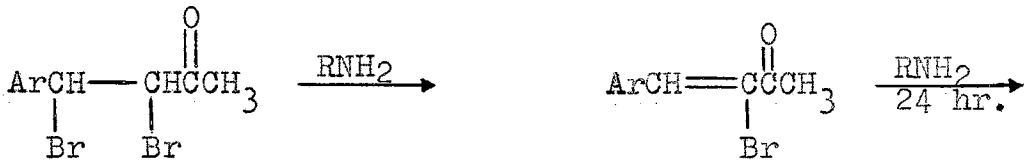
XIV, trans XV, cis

less stable of the two since it rearranged to the trans isomer when exposed to sunlight in a saturated petroleum ether solution.

The reaction of cyclohexylamine with 2,3-dibromo-3-(o-nitrophenyl)propiophenone is reported to give an 89% yield of a nearly 50-50 mixture of cis- and trans-aziridines.[18] The isomers were separated by column chromatography on alumina. The cis isomer was found to be more strongly absorbed on the alumina which appears to be a general property of these aziridines.[19]

The cis isomer reacted with phenylhydrazine to form 1,3-diphenyl-5-(o-nitrophenyl)pyrazole. The trans isomer did not react in this manner.

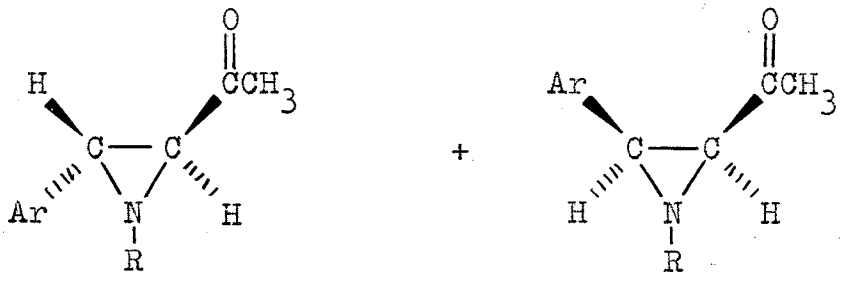
The first report of the synthesis and characterization of arylacetylaziridines was made in 1958.[13] Earlier attempts to prepare 1-benzyl-2-phenyl-3-acetylaziridine from benzalacetone dibromide resulted in a very unstable, oily product which was difficult to purify. p-Phenylbenzalacetone dibromide (XVI) was selected as a starting point to insure that the product would be a solid. Surprisingly, one mole of cyclohexylamine only dehydrobrominated XVI to give XVII and no addition product was found. Only after standing at room temperature for 24 hours with three moles of cyclohexylamine in benzene did the reaction give a good yield of aziridines XVIIIa and XVIIIb.



XVI XVII

Ar = p-$C_6H_5C_6H_5$

R = C_6H_{11}

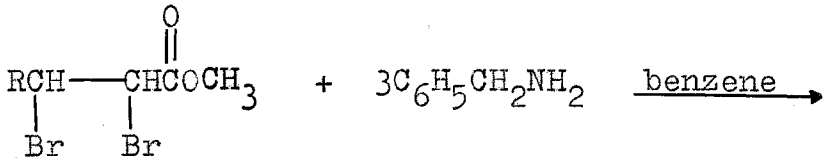


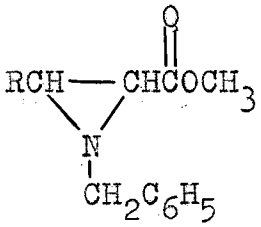
XVIIIa, trans XVIIIb, cis

The cis-trans mixture was separated into approximately two parts of XVIIIa and one part of XVIIIb. The exact ratio

was not determined since the overall yield of XVIII was only 68 percent.

α,β-Dibromo-and α-bromo-α,β-unsaturated esters also react with primary amines in a manner similar to that of α,β-dibromo ketones. In 1953 Stolberg and coworkers[41] reported the formation of some aziridines from the reaction of benzylamine with methyl α,β-dibromopropionate and methyl α,β-dibromobutyrate. The dibromo esters were treated with 3 moles of benzylamine in benzene. Colorless oils whose analyses corresponded to structures XIX and XX (50 percent) were isolated by high vacuum distillation. The yields could be increased to about 75 percent when one mole of benzylamine and two moles of triethylamine was allowed to react with one mole of the ester.

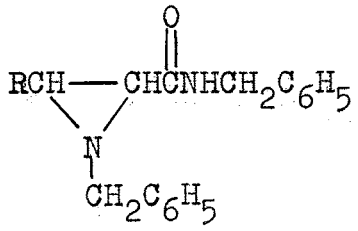




XIX, R = H

XX, R = CH_3

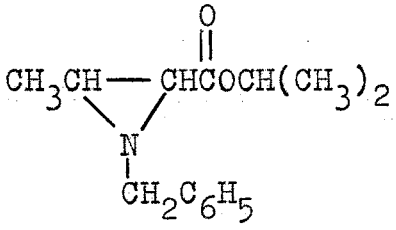
A compound whose empirical formula corresponded to the structure XXI was isolated in about 0.5 - 1% yield. The formation of the ring structures XIX and XX were confirmed by the molar refractions found. The stereochemistry of XX was not determined but the trans structure was favored on



XXI

the basis of its infrared (IR) absorption.

Independent investigations by Prostenik and coworkers[38] showed that the reaction of benzylamine with isopropyl α,β-dibromobutyrate, isopropyl α-bromocrotonate and isopropyl α-bromoisocrotonate gave the same aziridine of structure XXII in 65 - 85% yields.



XXII

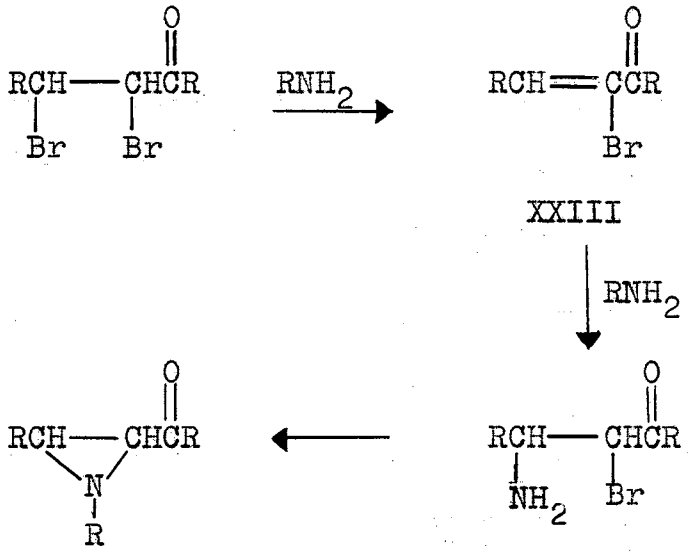
The product from each of the three esters showed two bands in the IR carbonyl region, one at 1718 $cm.^{-1}$ and the other at 1736 $cm.^{-1}$. An interpretation was that XXII consisted of a mixture of cis and trans isomers. Chromatography of this mixture over acid-washed alumina produced the cis and trans isomers of XXII. Proof of structure was accomplished by debenzylation, by hydrogenolysis over palladium on charcoal, ring opening by aqueous perchloric acid and hydrolysis by hydrogen chloride resulting in the formation of the 2-amino-3-hydroxybutyric acids. The isomer be-

lieved to be the cis form gave a good yield of dl-threonine; the trans isomer gave dl-allothreonine. This evidence lends support to the work of Paris and Fanta [37] and Dickey and co-workers[21] who established that ring opening of the aziridine ring proceeds with a single Walden inversion.

Numerous other aziridines derived from the reaction of primary amines with α,β-dibromo and α-bromo-α,β-unsaturated esters have been reported.[7,36]

Mechanism and Stereochemistry in the Reaction of Ammonia and Primary Amines with α,β-Dibromo and α-Bromo-α,β-unsaturated Ketones and Esters

There is general agreement that the first step in the reaction of a primary amine with an α,β-dibromo carbonyl compound proceeds with dehydrohalogenation to give the α-bromo-α,β-unsaturated compound (XXIII).[10,15] Amines are well-recognized nucleophilic[8] reagents indicating attack of the amino group will take place at the β-carbon to give the α-bromo-β-amino intermediate XXIV by 1,4-addition.[15] An internal S_N2 type ring closure would then be expected to produce the mixed cis- and trans-aziridines XXV. Studies have revealed that each ring closure of the halo-amine involves a single Walden inversion.[17]



XXIII

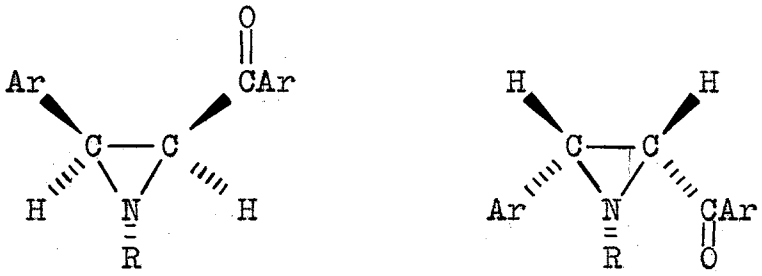
cis and trans

XXV

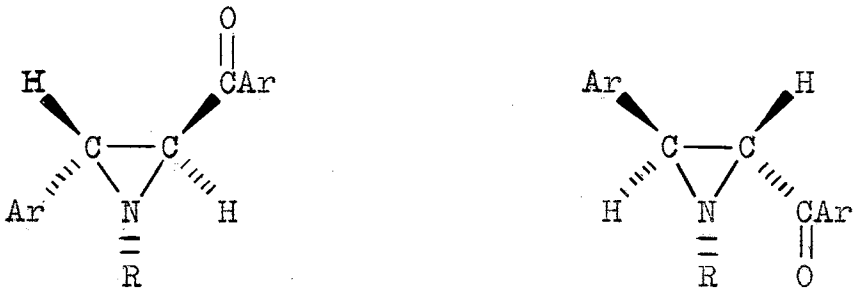
erythro and threo

XXIV

If it is assumed that these trisubstituted aziridines possess an asymmetric nitrogen atom,[10] then it is theoretically possible for there to exist two cis isomers and two trans isomers as shown. However, no isomers due to asymmetry at nitrogen have been reported owing to the fast inversion rate at nitrogen. Three-ring carbonyl hyperconjugation, resulting from orbital overlap of bent bonds of the ring with π orbitals of attached groups, is expected to increase this rate considerably.[10]



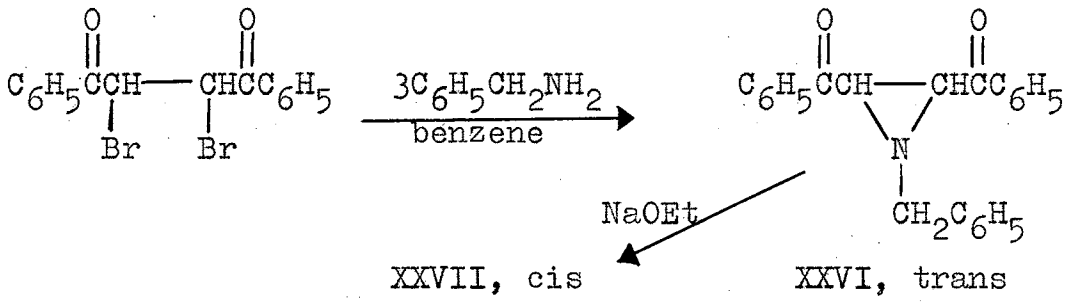
cis isomers



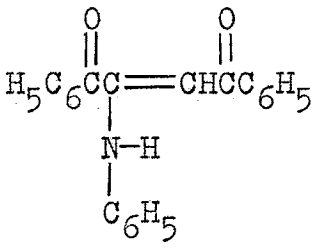
trans isomers

Cromwell[14] has suggested that the cis/trans product ratio is determined by the product ratio of the intermediate erythro and threo forms of XXIV. It has been shown that the cis/trans product ratio of products derived from α-bromo-α, β-unsaturated ketones is the same as the ratio derived from the corresponding dibromide, supporting dehydrohalogenation in the first step.[14] Experimental results obtained suggest that there is a most favored conformation of the enol resulting from 1,4-addition of the amine and that a rationale based on relative sizes of groups in the intermediate α-bromo-β-amino ketone and favored conformations in the transition state can be used to explain cis/trans product ratios.[11]

The reaction of benzylamine with either meso- or d,l-2,3-dibromo-1,4-diphenyl-1,4-butanedione formed the identical 1-benzyl-2,3-dibenzoylaziridine (XXVI).[43] Lutz had previously observed the same result using methylamine.[34] Aziridine XXVI was shown to be the trans isomer. When XXVI was treated briefly with hot sodium ethoxide, it isomerized to the corresponding cis isomer (XXVII). The cis/trans re-



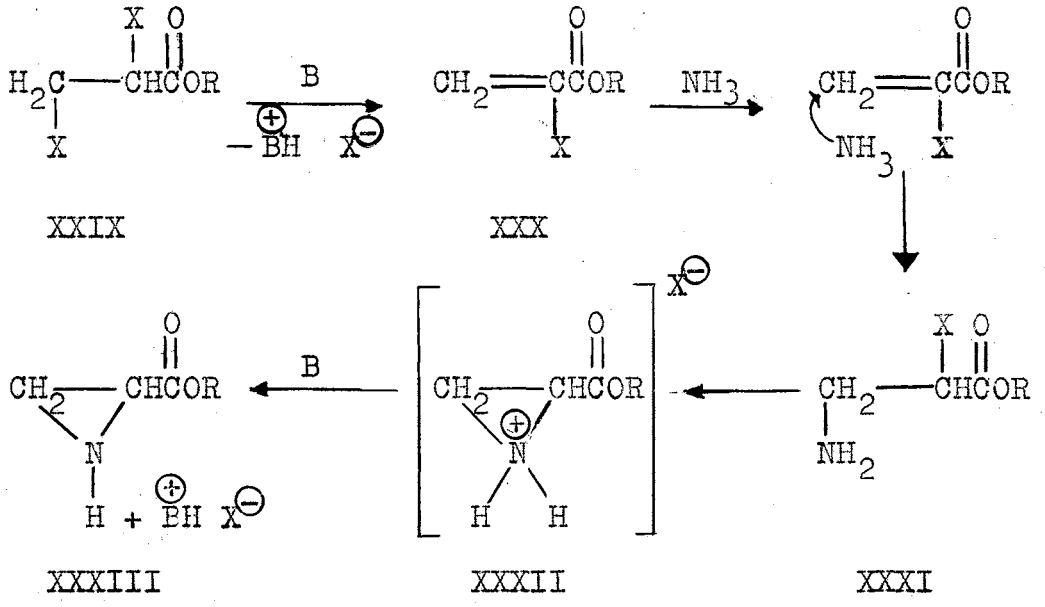
lationship of these aziridines was proven by their elementary analysis, IR spectra, ultraviolet (UV) spectra and nuclear magnetic resonance (NMR) spectra. Both XXVI and XXVII were converted to the identical enamine XXVIII by



XXVIII

treatment with glacial acetic acid.

Kyburz and coworkers [32] have postulated the course of the reaction of ammonia with α,β-dihalo carboxylic acid ester XXIX as proceeding with dehydrohalogenation to give XXX and attack of ammonia at the β-carbon to give β-amino-α-haloester XXXI. Formation of the enol is enhanced by polar solvents through stabilization of the charge developing on oxygen. Intramolecular attack of the amine on the α-halogen results in the formation of aziridine XXXIII via the ammonium intermediate XXXII.



XXIX XXX XXXI XXXII XXXIII

No examples of the reaction of ammonia with α,β-dibromocarboxylic acid esters in which mixtures of cis- or trans-aziridines were observed have been reported.

CHAPTER II

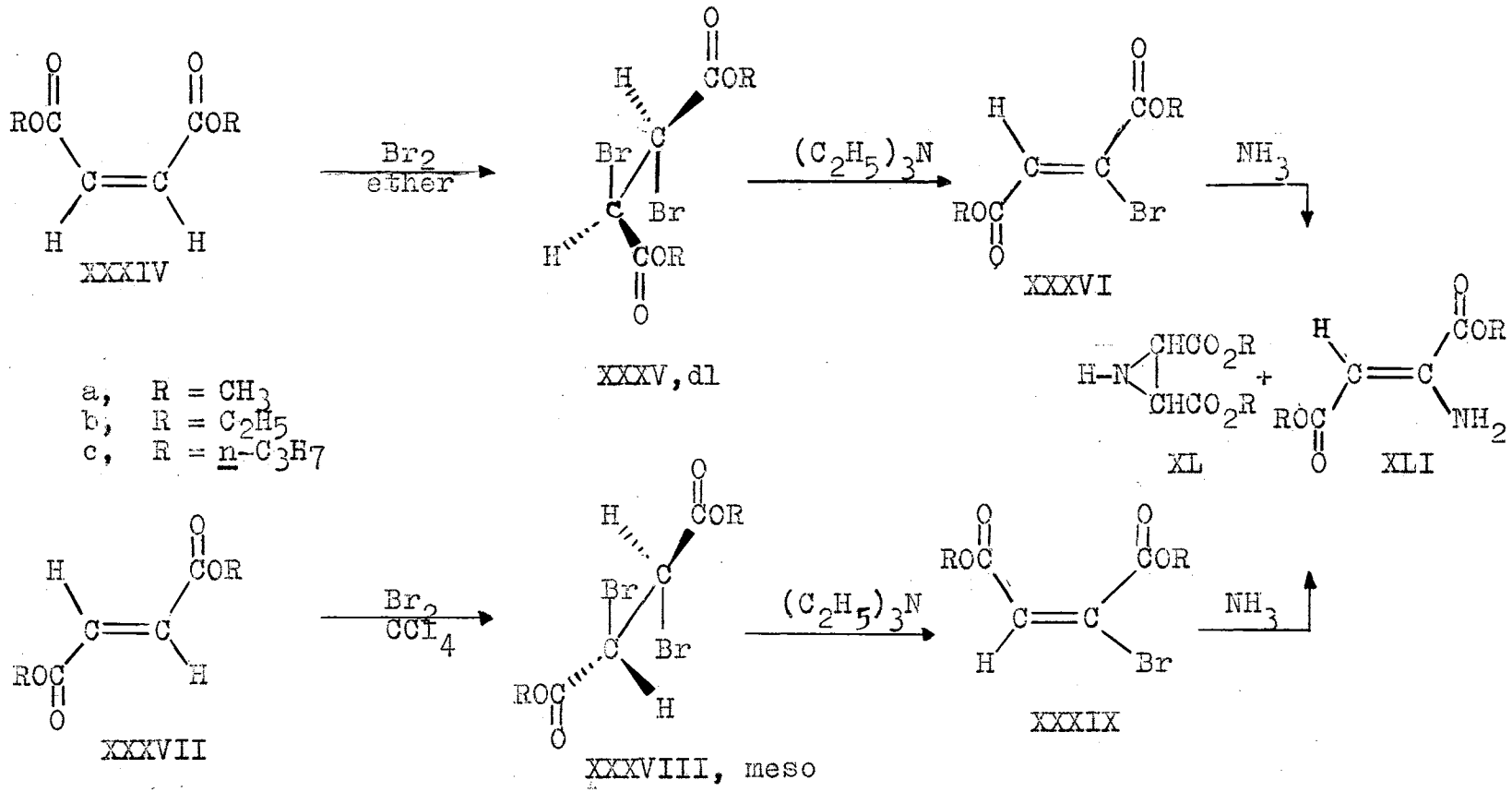
DISCUSSION OF RESULTS AND CONCLUSIONS

The object of this research was to study the reaction of ammonia with some esters of α,β-dibromosuccinic acid and identify and determine the stereochemistry of the products. Several aziridines have been obtained and the chemistry of these heterocycles has been examined.

The reaction of ammonia with diethyl meso-dibromosuccinate (XXXVIIIb) had previously been reported to proceed with the formation of aziridine I and II in low yield.[26,33] Some workers believe these compounds to possess the enamine structures III and IV.[20] Under the reaction conditions used in this research, amide formation was apparently minor and none were isolated.

The present sequence of reactions (Scheme 1) began with dialkyl maleates XXXIV and dialkyl fumarates XXXVII. Bromination of XXXIV and XXXVII gave dialkyl dibromosuccinates XXXV and XXXVIII, respectively, in good yield. Dehydrohalogenation of dibromides XXXV and XXXVIII afforded dialkyl bromofumarates XXXVI and dialkyl bromomaleates XXXIX, respectively, in nearly quantitative yield.

It was found that the action of ammonia on meso- and dl-dibromides XXXV and XXXVIII, or on cis and trans-vinylic


ROC
COR
H
XXXIV
Br2
ether
Br
Br
H
COR
XXXV, dl
(C2H5)3N
XXXVI
NH3
a, R = CH3
b, R = C2H5
c, R = n-C3H7
H-N
CHCO2R
CHCO2R
XL
NH2
XLI
Br2
CCl4
XXXVII
XXXVIII, meso
XXXIX

Scheme 1

bromides XXXVI and XXXIX, gave one aziridine XL and one enamine XLI as the only two products identifiable by GLC.

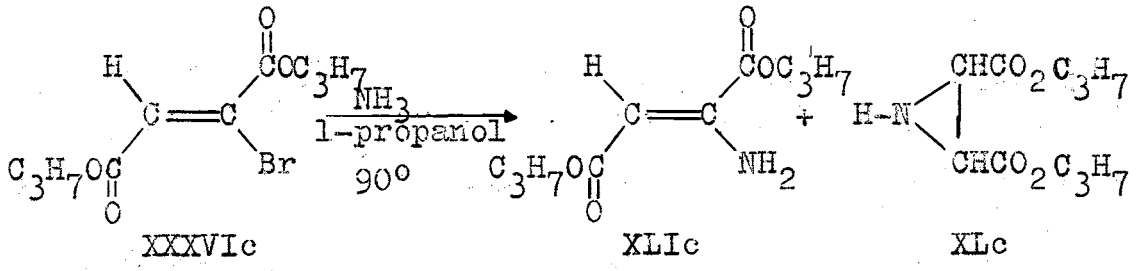
The solvent in which each reaction was performed was the alcohol corresponding to the ester used.

When dibromides XXXVb and XXXVIIIb were treated with ammonia in a 1:3 mole ratio at 65° for four hours, the reaction was found to be incomplete and to leave considerable amounts of vinylic bromides XXXVIb and XXXIXb, respectively, unreacted. Maximum yield of aziridine XLb was obtained when XXXVb or XXXVIIIb was treated with one mole of triethylamine in absolute ethanol. Subsequent treatment of the resulting vinylic bromides with an excess of ammonia in refluxing ethanol (78°) gave XLb in yields averaging 40-45 percent. The reaction could be followed by GLC by observing the disappearance of the vinylic bromides. This technique allowed the reaction time to be kept at a minimum and prevented formation of major amounts of amide. Most of the reactions were complete in about two hours. It appeared that the temperature of the reaction mixture was also a factor since lower yields (~30%) of XLb were obtained when the reaction was run at 60-65°. In one experiment when the reaction was conducted at room temperature, only a minute amount of aziridine XLb was observed by GLC.

Reaction of ammonia with dimethyl bromomaleate (XXXIXa) and dimethyl bromofumarate (XXXVIa) gave very similar results, yielding only aziridine XLa and enamine XLIa; however, lower yields were realized (~28%). The amount of

ether-soluble material obtained from these reactions was only 68-72 percent of the theoretical yield assuming that the products consist of only aziridine XLa and enamine XLIa. It was observed that the amount of aziridine XLa present in the reaction mixtures slowly decreased and a brown solid appeared in the bottom of the bottle. This process was not very fast since there was still some aziridine XLa remaining after three months. This decomposition was observed only in the case of aziridine XLa.

The reaction of ammonia with di-n-propyl bromofumarate (XXXVIc) was observed to be fast. GLC was used to follow the



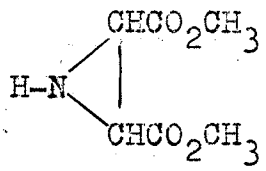
XXXVIc XLIc XLc

reaction; the disappearance of vinylic bromide XXXVIc was complete in less than two hours to yield 90 percent of a mixture of aziridine XLc and enamine XLIc. NMR analysis showed this mixture to consist of about 56 percent of aziridine XLc. This is somewhat higher than the yields obtained of aziridine XLa and XLb. This possibly results from the higher temperatures (90°) which could be obtained using 1-propanol as the solvent.

Isolation of aziridine XL was in some cases very difficult. None of the aziridine-enamine mixtures could be sep-

arated by distillation. Only mixtures were obtained in which the amount of aziridine XL was always smaller than before distillation, indicating some decomposition of XL.

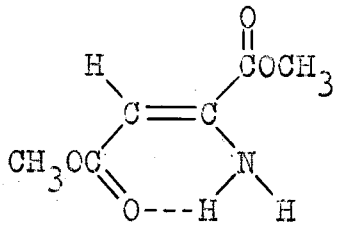
Separation of the mixture consisting of XLa and XLIa was accomplished by chromatography over neutral alumina and by preparative gas chromatography. Aziridine XLa was identified by elemental analysis and IR and NMR spectral data. The IR spectrum of XLa (Plate XII) showed a band at



XLa

3250 cm.$^{-1}$, indicative of a secondary amine. The NMR spectrum of XLa (Plate XXX) showed a singlet at δ3.75 for the two equivalent methyl groups, a broad singlet at δ 1.91 for the amine proton and a singlet at δ 2.81 attributed to the two ring protons.

The compound identified as enamine XLIa exhibited bands in the IR (Plate IX) at 3470 and 3350 cm.$^{-1}$, which supports the structure of a primary amine.[45] Bands at 1730 and 1675 cm.$^{-1}$ were attributed to free carbonyl group and hydrogen-bonded carbonyl group, respectively.[24] The double bond absorbed at 1620 cm.$^{-1}$. The NMR spectrum (Plate XXVII) of XLIa showed peaks attributed to two nonequivalent methyl groups at δ 3.63 and δ 3.83. Signals at δ 5.35 and δ 6.55 were observed for the vinyl proton and amine protons, re-

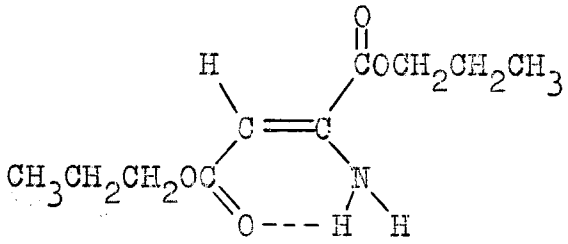


XLIa

spectively. Based on this data XLIa was given the trans structure.

Attempts to separate the mixture of aziridine XLc and enamine XLIc over neutral and acid-washed alumina were unsuccessful. It was found that enamine XLIc could be obtained quite pure by fractional distillation, which caused isomerization of aziridine XLc to XLIc.

Enamine XLIc was identified by its elemental analysis and IR and NMR spectral data. Its IR spectrum (Plate XI) showed bands almost identical to those of XLIa, suggesting

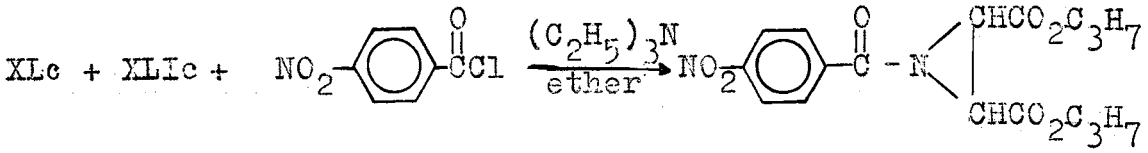


XLIc

the trans structure. The NMR spectrum (Plate XXIX) of enamine XLIc showed peaks attributed to nonequivalent propyl groups and singlets at δ 5.37 and δ 6.50 attributed to the vinyl proton and amine protons, respectively.

Aziridine XLc was not obtained as the unsubstituted

compound but was isolated by treating the mixture of XLc and XLIc with p-nitrobenzoyl chloride and separating XLc as its p-nitrobenzoyl derivative (XLII). This proved to be



XLII

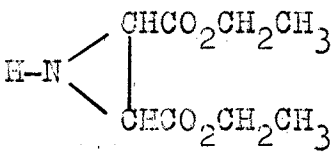
a successful method of separation since no reaction of enamine XLIc with p-nitrobenzoyl chloride could be observed.

The structure of XLII was confirmed by elemental analysis and IR and NMR spectral data. Bands in the IR spectrum (Plate XVIII) occurred at 1729 $cm.^{-1}$ for an ester carbonyl group and at 1696 $cm.^{-1}$ for an amide carbonyl group. The NMR spectrum (Plate XXXVII) showed peaks characteristic of the n-propyl groups and a singlet at δ 3.70 attributed to the two ring protons.

Separation of the mixture of aziridine XLb and enamine XLIb proved to be a much easier process. During the earlier stages of this research analytical samples of XLb and XLIb were obtained by preparative gas chromatography and by chromatography over neutral and acid-washed alumina. When yields of XLb were increased to 40-45 percent, it was found that aziridine XLb could be obtained pure by cooling the mixture of XLb and XLIb dissolved in n-hexane in a Dry Ice-acetone bath. Care had to be taken not to freeze the entire

mixture since enamine XLIb also crystallized at low temperatures. Recovery of XLb by this method gave yields up to 21 percent. Purification of XLb was achieved quite nicely by recrystallization from n-hexane.

The IR spectrum of XLb (Plate XIII) showed a band at 3280 $cm.^{-1}$ for secondary amines. Two carbonyl bands were observed, one at 1744 $cm.^{-1}$ and the other at 1720 $cm.^{-1}$. The peak at lower frequency could possibly be due to intermolecular hydrogen bonding since a dilute chloroform solution gave only a single band at 1730 $cm.^{-1}$. An NMR spectrum of XLb (Plate XXXI) exhibited peaks showing equivalency of the ethyl groups. A singlet at δ 1.85 assigned to the amine proton and a sharp singlet at δ 2.84 arising from two equivalent ring protons were observed. Addition of deuterium



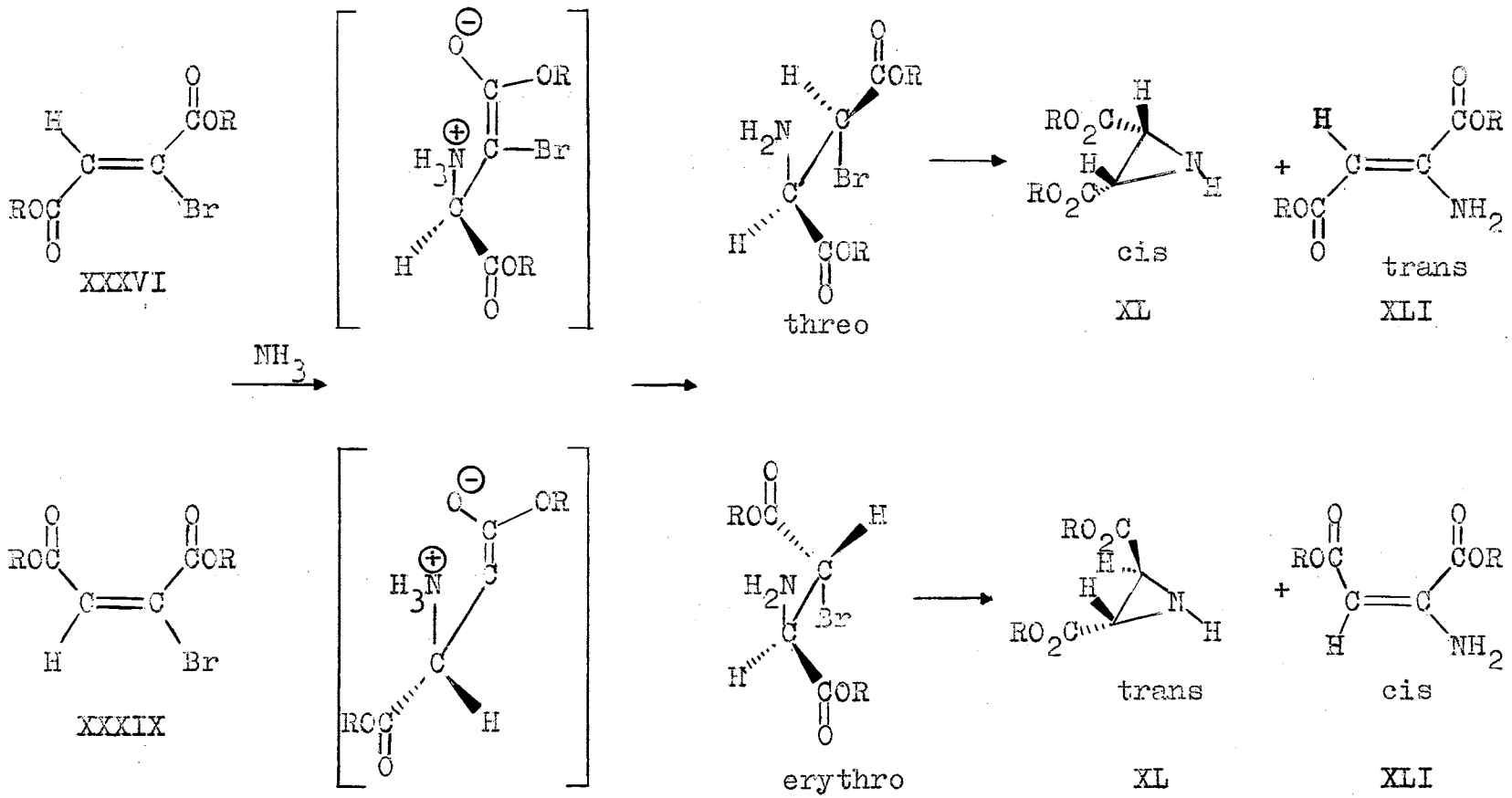
XLb

oxide caused the peak at δ 1.85 to disappear. When XLb was heated with sodium carbonate in acetonitrile, it gave an NMR spectrum (Plate XXXVI) which indicated coupling between the amine protons and the ring protons. In addition to the normal splitting pattern for the ethyl groups a doublet centered at δ 2.86 (J=9.0 c.p.s.) and a broad triplet centered at δ 1.83 (J=9.0 c.p.s.) were observed. This coupling may be caused by the removal of all traces of acid by the

sodium carbonate giving a completely dry compound. This phenomenon also occurs in the case of anhydrous ethanol.[40] The IR spectrum of XLb after treatment with sodium carbonate was identical to that of XLb before treatment. When the dry XLb was allowed to stand for a few days, its NMR spectrum was identical to that of the original XLb.

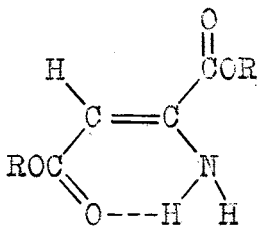
Although the formation of only one stereoisomer of aziridine XL and enamine XLI was observed in all of the reactions of ammonia with the dibromides or the vinylic bromides, to date it has not been possible by the physical methods available to determine whether aziridine XL is the cis or the trans isomer. It has been established that the reactions of amines with α,β-dibromo ketones and esters, in general, first proceeds with elimination of hydrogen bromide[10,15] to give the corresponding vinylic bromides. There is no reason to believe that this is not the case with dibromides XXXV and XXXVIII.

The reaction of ammonia with vinylic bromides XXXVI and XXXIX can be visualized as proceeding in the manner indicated in Scheme 2. The enolic form of the ester, which results when ammonia attacks the β-carbon, can be stabilized by the polar solvents used in all reactions.[32] Each of the bromides XXXVI and XXXIX is expected to give a racemic form of this enol which then collapses into a mixture of erthyro- and threo-α-bromo-β-aminosuccinic esters. The composition of this mixture can not be determined since the components are very unstable and collapse immediately into aziridine


XXXVI
XXXIX
NH3
threo
erythro
cis
XL
trans
XLI
trans
XL
cis
XLI

Scheme 2

XL and enamine XLI. It can easily be seen that the threo form can react by two routes; intramolecular displacement of bromine can occur to give cis-aziridine XL or the more favorable trans elimination of hydrogen bromide may result to yield trans-enamine XLI. On the other hand the erythro form can react with intramolecular displacement of bromine to give trans-aziridine XL, or trans elimination of hydrogen bromide can occur with formation of cis-enamine XLI. Infrared analysis indicates that strong intramolecular hydrogen bonding occurs in XLI between an ester carbonyl group and the amine protons indicating the trans structure. It is

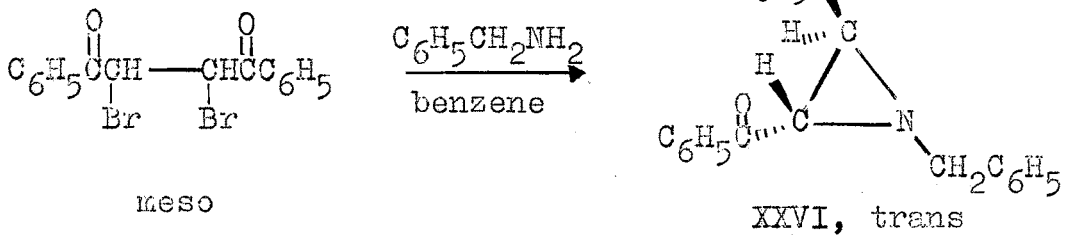


XLI

assumed that the cis form of XL is more sterically hindered than the trans form of XLI, we might draw the conclusion that the threo form of the α-bromo-β-amino intermediate would give mostly the more sterically favorable trans-enamine XLI. In addition the erythro form of the intermediate would give mostly the trans-aziridine XL and very little of the cis-enamine XLI. However, these conclusions alone are not sufficient evidence to constitute proof of structure of aziridine XL.

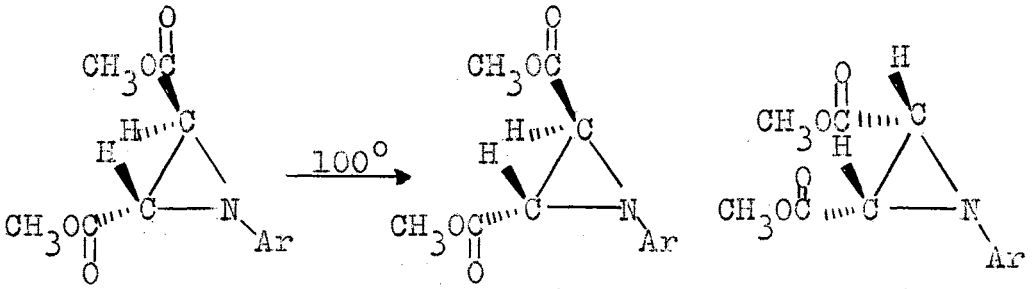
Turner and coworkers[43] have shown that when meso-1,2-

dibenzoyl-1,2-dibromoethane is treated with three moles of benzylamine in benzene only trans-1-benzyl-2,3-benzoylaziridine (XXVI) is formed. Treatment of XXVI with hot sodium



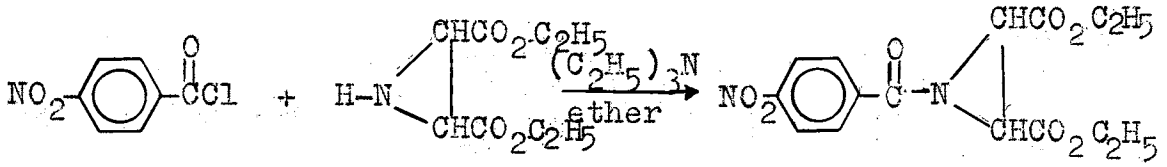
ethoxide afforded cis-1-benzyl-2,3-dibenzoylaziridine (XXVII) in about 80 percent yield indicating that the cis isomer may be the more stable of the two forms. Similar treatment of aziridine XLb with sodium ethoxide afforded only the dry aziridine whose IR and NMR spectra were identical to those of the compound obtained by treatment of XLb with sodium carbonate.

Huisgen and coworkers[29] have reported that when dimethyl 1-(p-methoxyphenyl)aziridine-2,3-dicarboxylate is heated to about 100°, an equilibrium is established between



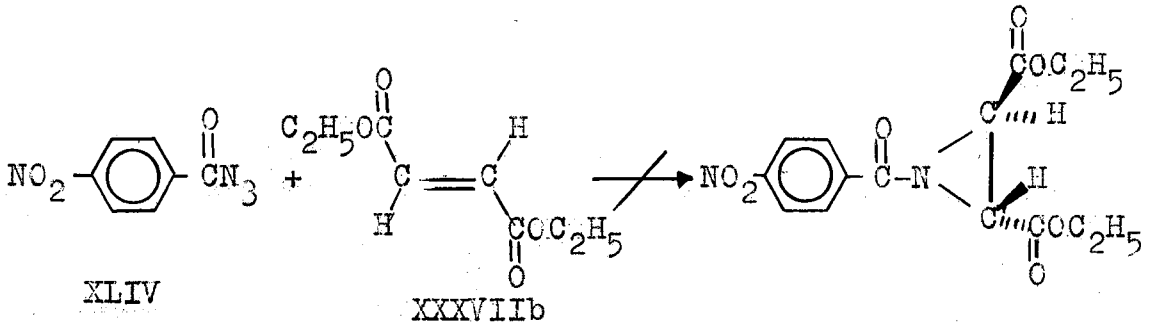
the cis and trans isomers. The trans isomer is highly favored and makes up about 80 percent of the total. When aziri-

dine XLb was heated at 125° for two hours, no equilibration between cis and trans forms could be observed by NMR, but instead XLb was converted almost completely to enamine XLb. Szeimies and Huisgen[42] have also shown that aryl azides add across the double bonds of dialkyl fumarates to form trans-dialkyl aziridine-2,3-dicarboxylates. It was thought that this might be a way of establishing the stereochemistry of XLb. Since the p-nitrobenzoyl derivative (XLIII) of XLb was readily prepared by treating the aziridine with p-nitrobenzoyl chloride, this route was chosen. Comparison of the NMR



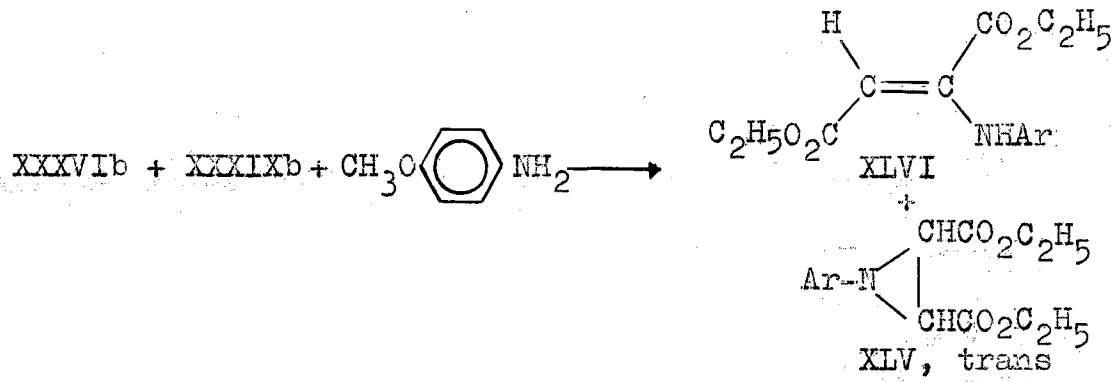
XLb XLIII

and IR spectra of amide XLIII with those of the product obtained from the reaction of p-nitrobenzoyl azide (XLIV) with diethyl fumarate (XXXVIIb) might give some indication of the stereochemistry of XLb. This assumes that addition of the nitrene from XLIV across the double bond of XXXVIIb is stereospecific. Treatment of XXXVIIb with p-nitrobenzoyl azide (XLIV) in benzene for one month did not proceed as expected, but gave only N,N'-bis(p-nitrophenyl)urea. Photolysis of a mixture of XLIV and XXXVII for ten hours with ultraviolet (UV) light gave the same result.



XLIV XXXVIIb

Huisgen[42] has prepared dimethyl 1-(p-methoxyphenyl)aziridine-2,3-dicarboxylate by the reaction of p-methoxyphenyl azide with dimethyl fumarate. We prepared diethyl 1-(p-methoxyphenyl)aziridine-2,3-dicarboxylate by treating vinylic bromides XXXVI and XXXIX with p-anisidine in ethanol. A mixture of products was obtained. Analysis of this



XLVI

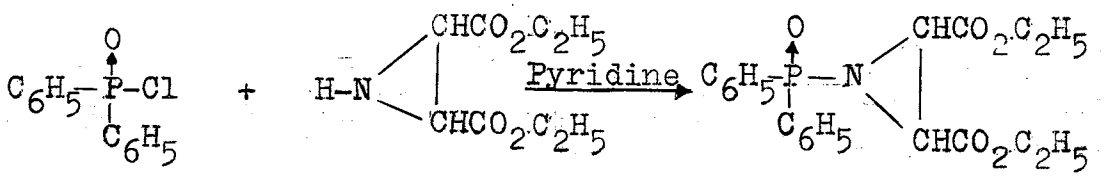
XLV, trans

by NMR (CCl_4) showed peaks characteristic of the ethyl groups, a singlet at δ 5.28 attributed to the vinyl proton on enamine XLVI, a singlet at δ 3.29 which could be assigned to the ring protons on trans-aziridine XLV and a very minor singlet at δ 2.85 attributed to the ring protons on the cis isomer of XLV.

Huisgen[29] reported chemical shifts in CCl_4 for the ring protons on trans-dimethyl 1-(p-methoxyphenyl)aziridine-2,3-

dicarboxylate at δ 3.31 and the ring protons of the cis isomer at δ 2.86. Since the chemical shifts of the ring protons should not be affected much by the type of ester group, this indicates that the reaction of bromides XXXVIb and XXXIXb with p-anisidine forms only the trans isomer of XLV. This lends further support to the belief that trans XLb is formed from the reaction of ammonia with bromides XXXVI and XXXIX.

Attempted phosphorylation of XLb with a number of phosphorus chlorides using triethylamine as the base were unsuccessful. A complex appeared to be forming between the phosphorus chloride and triethylamine preventing addition to XLb. However, when XLb was treated with dry diphenylphosphinic chloride in pyridine, an addition product (XLVII) was obtained but purification could not be effected.



XLVII

Attempted crystallization from a number of solvent combinations produced only very viscous oils. A doublet in the NMR spectrum of XLVII (Plate XXXV) centered at δ 3.61 ($J_{P-N-C-H}$ = 12.5 c.p.s.) showed addition had occurred. This coupling is very similar to that observed in 1-(diphenylphosphinyl)aziridine, $J_{P-N-C-H}$ = 14.5 c.p.s..[2] The IR

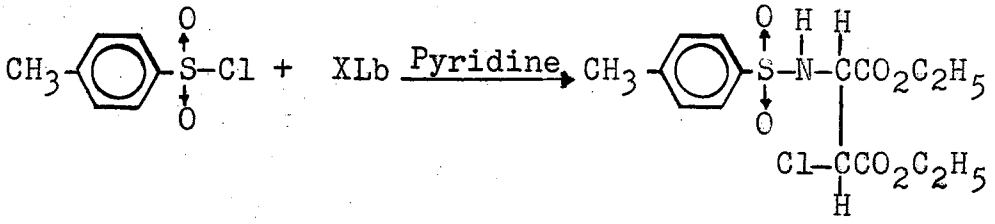
spectrum of XLVII (Plate XVII) showed the presence of a weak band at 3460 $cm.^{-1}$ possibly due to some ring opening product.

A nice crystalline derivative could also be obtained when XLb was treated with 2,4-dichlorophenoxyacetyl chloride in ether with triethylamine as the base. The structure of

XLVIII

XLVIII was confirmed by elemental analysis and NMR and IR spectral data (Plates XVI and XXXIV).

Surprisingly, when XLb was treated with p-toluenesulfonyl chloride in pyridine, a product was obtained which appeared to have a structure XLIX. A solution of XLIX

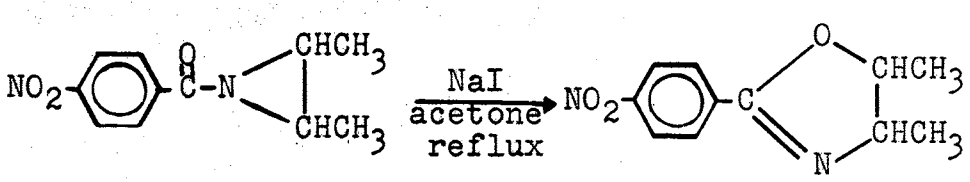


XLIX

precipitated silver chloride when treated with an ethanolic silver nitrate solution, so the presence of chlorine was indicated. The NMR spectrum of XLIX showed a broad signal at δ 5.74 which disappeared when deuterium oxide was added and was attributed to the amide proton. The IR spectrum of

XLIX showed a strong band at 3240 cm.$^{-1}$ also indicative of a primary amide.

Heine and coworkers[25] have reported the isomerization of cis- and trans-1-p-nitrobenzoyl-2,3-dimethylaziridine to



cis and trans cis and trans

cis- and trans-2-p-nitrophenyl-4,5-dimethyl-2-oxazoline, respectively, by treating the aziridine with sodium iodide in refluxing acetone.

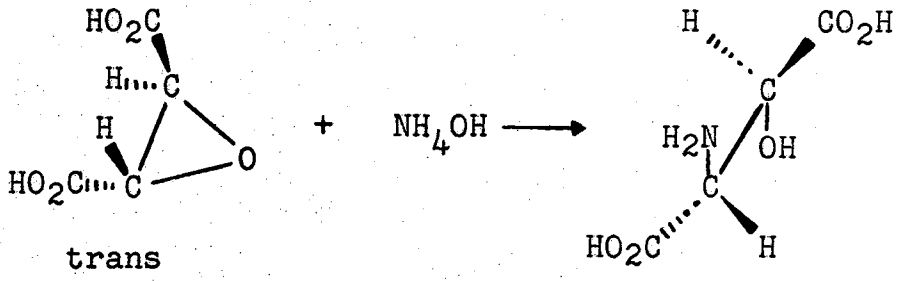
Similar treatment of aziridine XLIII afforded a compound (L) whose NMR spectrum (Plate XXXIII) agreed quite closely with the expected structure, showing an AB quartet composed of two doublets centered at δ 5.01 (J=6.8 c.p.s.) and δ 5.41 (J=6.8 c.p.s.) as expected. The IR spectrum of L (Plate XV) showed bands at 1652 cm.$^{-1}$ (C=N) and nonequivalent ester carbonyls at 1750 cm.$^{-1}$ and 1735 cm.$^{-1}$.

XLIII L

On the information obtained from this research, the stereochemistry of aziridine XL cannot be absolutely de-

termined. However, there is strong evidence which points to the trans structure.

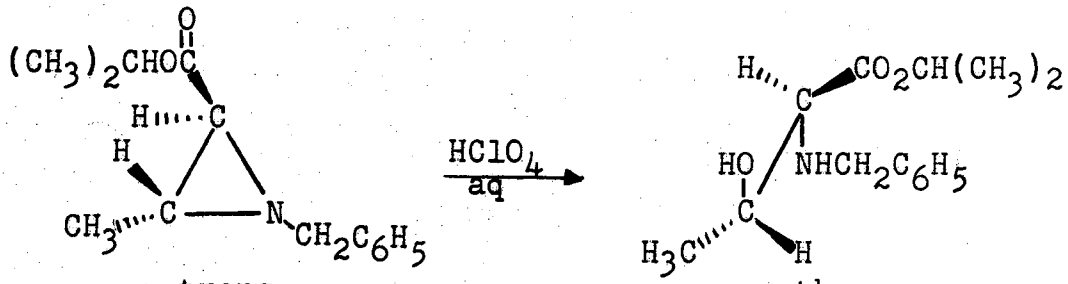
A method of absolute proof of structure of XL is hereby proposed. It is well known that epoxide rings open by a simple S_N2 mechanism.[5] Miller[35] has shown that when (-) trans-epoxysuccinic acid was treated with ammonium hydroxide, erythro-β-hydroxy-L-aspartic acid (LI) was formed.



trans

LI, erythro

Prostenik[38] has also shown that aziridine rings are opened by perchloric acid in a stereospecific manner involving a single inversion.



trans

erythro

If aziridine XLb is of the trans configuration, opening of the ring with aqueous perchloric acid and subsequent hydrolysis should yield the erythro-β-hydroxyaspartic acid. If XLb is the cis isomer then the threo-β-hydroxyaspartic acid should result. These are both known compounds.[23]

TABLE I

INFRARED ABSORPTION BANDS ($cm.^{-1}$) OF PRODUCTS

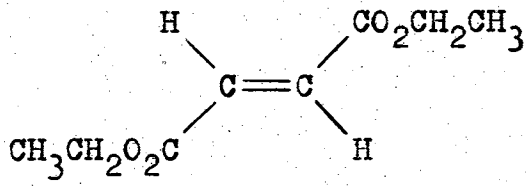
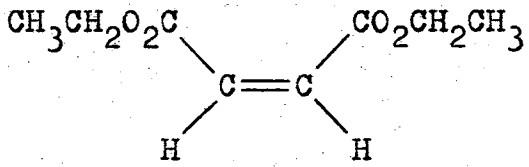
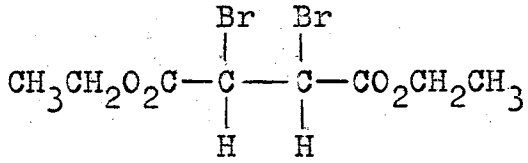
Compound	Plate	Amine	C=O	C=C	Additional Bands
 XXXVIIb	I	---	1724	1652	1158, 1038, 980, 860, 775
 XXXIVb	II	---	1724	1640	1168, 1030, 865, 808
 XXXVIIIb	III	---	1731	---	1471, 1267, 1228, 1028, 955, 860, 670

TABLE I (CONTINUED)

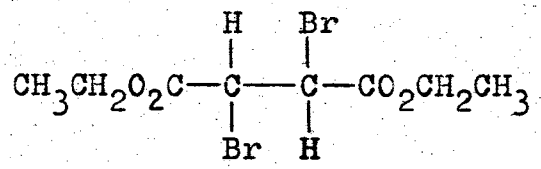
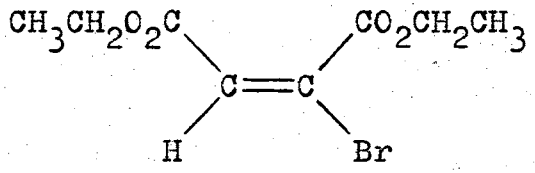
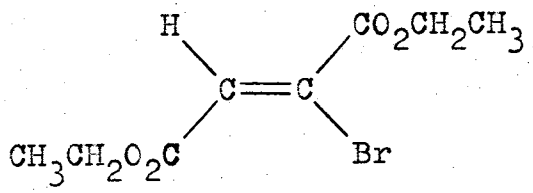
Compound	Plate	Amine	C=O	C=C	Additional Bands
 XXXVb	IV	---	1740	---	1377, 1310, 1250, 1025, 861
 XXXIXb	V	---	1730	1630	1450, 1370, 1330, 1037, 865, 684
 XXXVIIb	VI	---	1728	1630	1371, 1251, 1188, 1037, 863

TABLE I (CONTINUED)

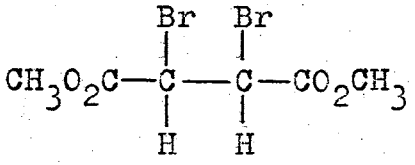
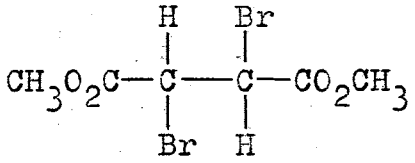
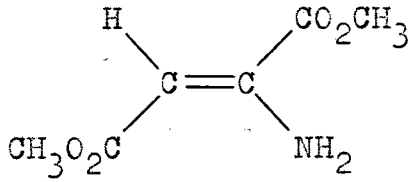
Compound	Plate	Amine	C=O	C=C	Additional Bands
 XXXVIIIa	VII	---	1735	---	1440, 1400, 1163, 1140, 991, 877, 675
 XXXVa	VIII	---	1728	---	1443, 1302, 1172, 995, 970, 919, 900, 795, 687
 XLIa	IX	3470, 3350	1730, 1675	1620	1440, 1300, 1152, 1027, 783

TABLE I (CONTINUED)

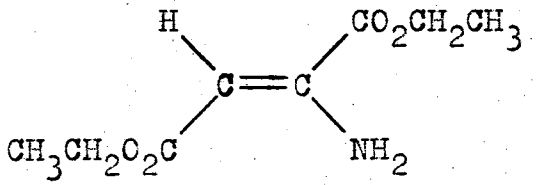
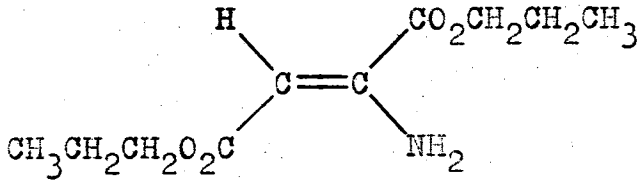
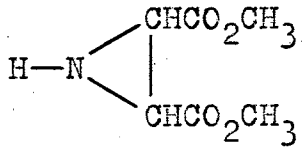
Compound	Plate	Amine	C=O	C=C	Additional Bands
 XLIb	X	3470, 3350	1730, 1676	1620	1557, 1371, 1295, 1155, 1100, 1040, 862, 781
 XLIc	XI	3470, 3350	1730, 1676	1620	1558, 1465, 1392 1160, 1061, 948, 782
 XLa	XII	3250	1730	---	1442, 1350, 1030, 863, 749

TABLE I (CONTINUED)

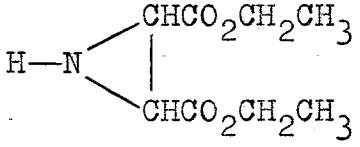
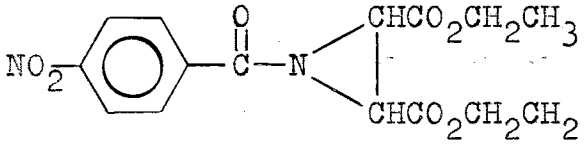
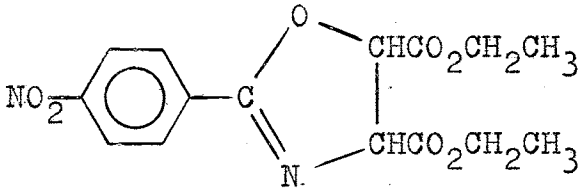
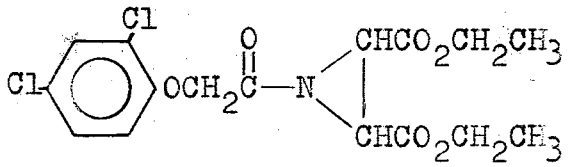
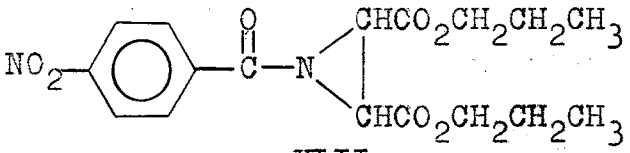
Compound	Plate	Amine	C=O	C=C	Additional Bands
 XLb	XIII	3280	1744, 1720	---	1451, 1371, 1340, 1261, 1190, 843, 764
 XLIII	XIV	---	1729, 1695[a]	1613[b]	1540, 1040, 878, 855, 724, 710
 L	XV	---	1750, 1735	1652, 1605[b]	1530, 909, 866, 703

TABLE I (CONTINUED)

Compound	Plate	Amine	C=O	C=C	Additional Bands
 XLVIII	XVI	---	1730, 1707[a]	---	1482, 1331, 1220, 1155, 1110, 1080, 1036, 865, 822, 757
 XLII	XVIII	---	1729, 1696[a]	1610[b]	1516, 1090, 1055, 1011, 967, 878, 853, 804, 723

Compounds XXXVIIIa, XXXVa, XLb, LIII, XLVIII and XLII, (KBr Pellets).

Compounds XXXVIIb, XXXIVb, XXXVIIIb, XXXVb, XXXIXb, XLIa, XLIb, XLIc, XLa, L and XLVII, (NaCl Cells).

[a] amide bands

[b] C=C Skeletal in-plane vibrations

TABLE II

NMR CHEMICAL SHIFTS AND COUPLING CONSTANTS OF PRODUCTS.

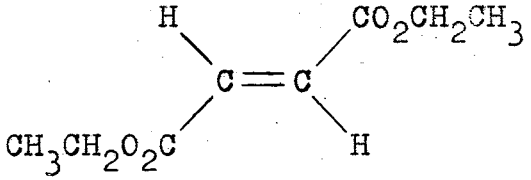
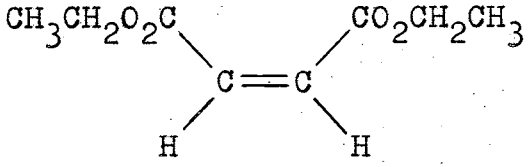
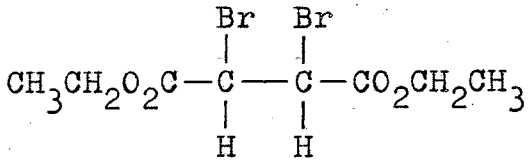
Compound	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Assignment
 XXXVIIb	XIX	$CDCl_3$	1.31t 4.29q 6.89s	7.0 7.0 —	CH_3 CH_2 H
 XXXIVb	XX	$CDCl_3$	1.29t 4.25q 6.29s	7.0 7.0 —	CH_3 CH_2 H
 XXXVIIIb	XXI	$CDCl_3$	1.32t 4.32q 4.68s	7.0 7.0 —	CH_3 CH_2 H

TABLE II (CONTINUED)

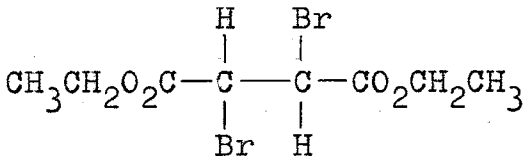
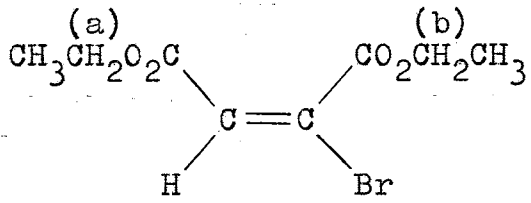
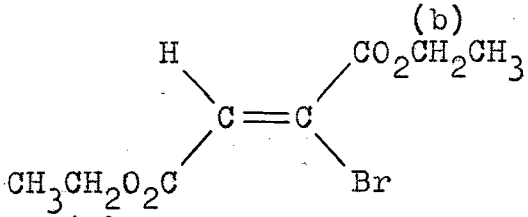
Compound	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Assignment
 XXXVb	XXII	$CDCl_3$	1.29t 4.27q 4.66s	7.0 7.0 --	CH_3 CH_2 H
 XXXIXb	XXIII	$CDCl_3$	1.27t 1.32t 4.20q 4.32q 6.49s	7.0 7.0 7.0 7.0 --	CH_3(a) CH_3(b) CH_2(a) CH_2(b) H
 XXXVIb	XXIV	$CDCl_3$	1.32t 1.35t 4.29q 4.35q 7.48s	7.0 7.0 7.0 7.0 --	CH_3(a) CH_3(b) CH_2(a) CH_2(b) H

TABLE II (CONTINUED)

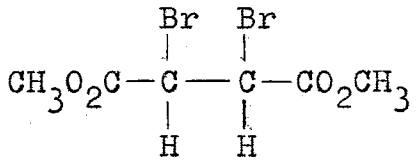
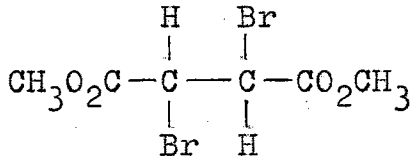
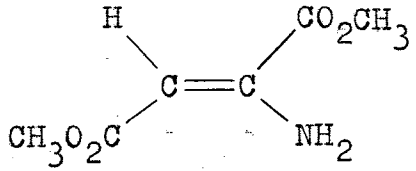
Compound	Plate	Solvent	δ(values) (p.p.m.) a	J(c.p.s.)	Assignment
 XXXVIIIa	XXV	CCl_4	3.80s 4.55s	-- --	CH_3 H
 XXXVa	XXVI	CCl_4	3.75s 4.52s	-- --	CH_3 H
 XLIa	XXVII	CCl_4	3.63s 3.83s 5.35s 6.55s (broad)	-- -- -- --	CH_3 CH_3 H NH_2

TABLE II (CONTINUED)

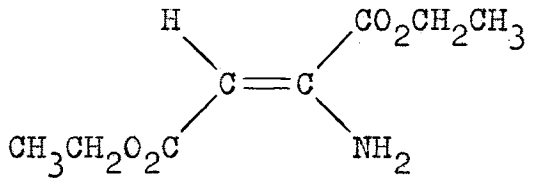
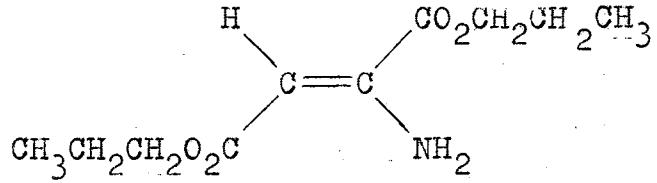
Compound	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Assignment
 XLIb	XXVIII	$CDCl_3$	1.27t 1.31t 4.15q 4.29q 5.45s 6.59s (broad)	7.0 7.0 7.0 7.0 -- --	CH_3 CH_3 CH_2 CH_2 H NH_2
 XLIc	XXIX	CCl_4	0.96t 1.00t 1.62m 4.01t 4.18t 5.37s 6.50s (broad)	7.0 7.0 -- 6.7 6.7 -- --	CH_3 CH_3 CH_2 OCH_2 OCH_2 OCH_2 NH_2

TABLE II (CONTINUED)

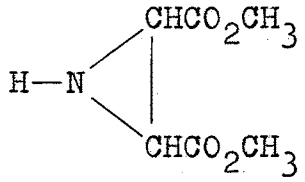
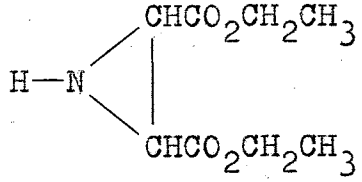
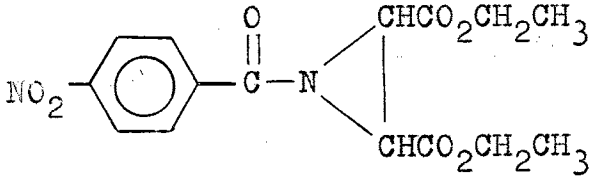
Compound	Plate	Solvent	δ(values) (p.p.m.)a	J(c.p.s.)	Assignment
 XLa	XXX	CCl_4	1.91s (broad) 2.81s 3.75s	-- -- --	NH H CH_3
 XLb	XXXI	$CDCl_3$	1.30t 1.85s 2.84s 4.20q	7.0 -- -- 7.0	CH_3 NH^3 H CH_2
 XLIII	XXXII	$CDCl_3$	1.22t 3.67s 4.13q 8.16m	7.0 -- 7.0 --	CH_3 H 3 CH_2 C_6H_4

TABLE II (CONTINUED)

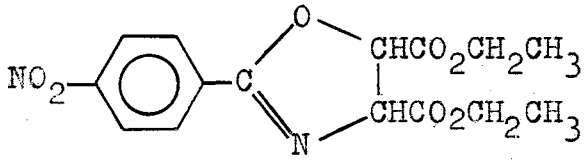
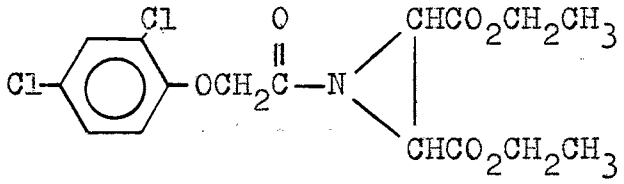
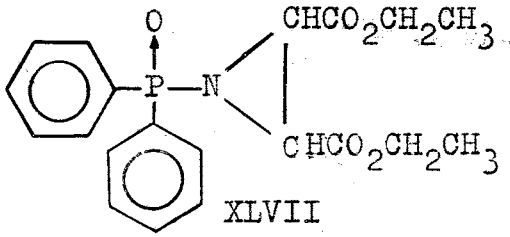
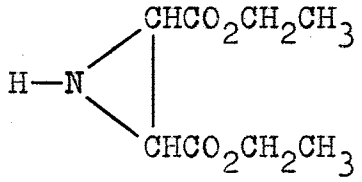
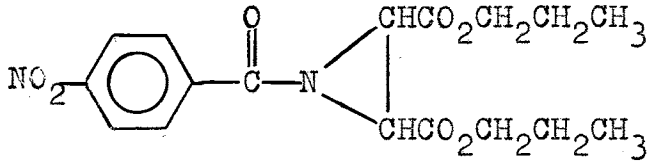
Compound	Plate	Sol-vent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Assign-ment
 L	XXXIII	$CDCl_3$	1.31t 1.35t 4.29q 5.01d 5.41d 8.17s	7.0 7.0 7.0 6.8 6.8 --	CH_3 CH_3 CH_2 H H C_6H_4
 XLVII	XXXIV	$CDCl_3$	1.25t 3.53s 4.18q 4.62s 7.00m	7.0 -- 7.0 -- --	CH_3 H CH_2 OCH_2 C_6H_3
 XLVII	XXXV	$CDCl_3$	1.14t 3.61d 4.04q 7.38m 7.82m	7.0 12.5(P-N-C-H) 7.0 -- --	CH_3 H CH_2 C_6H_5 C_6H_5

TABLE II (CONTINUED)

Compound	Plate	Solvent	δ(values) (p.p.m.)[a]	J(c.p.s.)	Assignment
 XLb, Dry	XXXVI	$CDCl_3$	1.31t 1.83t (broad) 2.86d 4.26q	7.0 9.0 9.0 7.0	CH_3 NH H CH_2
 XLII	XXXVII	$CDCl_3$	0.91t 1.62h 3.70s 4.09t 8.21m	7.0 7.0 -- 7.0 --	CH_3 CH_2 H OCH_2 C_6H_4

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

CHAPTER III

EXPERIMENTAL[a-e]

Preparation of Diethyl Fumarate (XXXVIIb). This procedure and that used in the preparation of diethyl maleate (XXXIV) employs the method of Arthur[3] for removing water formed in the esterification. A 500-ml., three-necked flask was equipped with a drying tube ($CaCl_2$), a Soxhlet extractor, a condenser, a thermometer and a magnetic stirrer. The extractor was filled with 125 g. of type 5A mole sieve. Fumaric acid (100 g., 0.86 mole) was placed in the flask and 200 ml. of absolute ethanol and 4 ml. of concentrated sulfuric acid were added. The reaction mixture was boiled

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

[b]The infrared spectra were determined on a Beckman IR-5A as films on sodium chloride cells or as potassium bromide pellets unless otherwise specified.

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

[d]Gas chromatographic analyses were performed using an Aerograph Model A-700 Autoprep unit and a Varian-Aerograph Model 1520 with a thermal conductivity detector. The column used was a 10' x ¼" 15% DEGS on 60/80-mesh acid-washed Chromosorb W.

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

for 2.5 hours after which time the mole sieve was renewed and boiling was continued for an additional 2.5 hours. When cooled, the mixture was shaken with a 10% sodium carbonate solution until it was neutral to indicator paper. The ester was separated and the aqueous layer was shaken with benzene. The ester and benzene extracts were combined, and the benzene was removed through a fractionating column. Distillation of the ester was achieved in a side arm flask at atmospheric pressure. The fraction boiling at 212-215° was collected (lit.[31] b. p. 98°/10mm.); yield, 125 g. (86%).

The IR (Plate I) and NMR (Plate XIX) spectral data (Tables I and II) were identical with those of an authentic sample.

Preparation of Diethyl Maleate (XXXIVb). The previously described apparatus was charged with 100 g. (0.86 mole) of maleic acid dissolved in 250 ml. of absolute ethanol and 4 ml. of sulfuric acid. Type 5A mole sieve (100 g.) was placed in the extractor, and the reaction mixture was boiled for 6 hours. The mole sieve was replaced every 2 hours. The workup was the same as for the previous reaction. The ester was distilled and the fraction boiling at 218-222° was collected (lit.[31] b. p. 99°/10 mm.); yield, 139 g. (92%).

The IR (Plate II) and NMR (Plate XX) spectral data (Tables I and II) were identical with those of an authentic sample.

Preparation of Diethyl meso-Dibromosuccinate (XXXVIIIb). The procedure follows that of Ing and Perkin[30] with modifi-

cations. A 200-ml., three-necked flask was equipped with a mechanical stirrer, an addition funnel and a Friedrichs condenser. Diethyl fumarate (30 g., 0.17 mole) dissolved in 50 ml. of carbon tetrachloride was placed in the flask and heated to reflux. Bromine (27.8 g., 0.20 mole) was added dropwise from the addition funnel over a period of 1 hour and heating was continued for 2 hours. The volume was reduced by evaporation of the carbon tetrachloride leaving an oil which crystallized upon cooling to 10°. In subsequent runs an aqueous solution of sodium thiosulfate was added until the bromine color disappeared. Crystallization of the oil from absolute ethanol yielded 45 g. (81%) of white crystals; m. p. 57-58° (lit.[30] m. p. 58°).

Anal. Calcd. for $C_8H_{12}Br_2O_4$: C, 28.94; H, 3.64; Br, 48.13.
Found: C, 29.29; H, 3.69; Br, 47.92.

The IR (Plate III) and NMR (Plate XXI) spectral date (Tables I and II) further substantiate the structure of this known compound.

Preparation of Diethyl dl-Dibromosuccinate (XXXVb). This procedure employs the method of Ing and Perkin[30] with modifications. A 500-ml., three-necked flask was equipped as in the previous reaction and charged with a solution of 50 g. (0.29 mole) of diethyl maleate in 250 ml. of dry ether which was cooled by a cold water bath. The flask was protected from direct sunlight by a cloth, and bromine (46.5 g., 0.29 mole) was added dropwise over a 5-hour period, while stirring. The reaction mixture was stirred for an additional

4 hours. Excess bromine was removed by shaking with an aqueous solution of sodium thiosulfate, and the ether was distilled from the organic layer. Distillation of the crude ester gave a fraction boiling at 115-117°/1 mm. (lit.[30] b. p. 137-138°/11 mm.); yield 76 g. (80%).

The IR (Plate IV) and NMR (Plate XXII) spectral data (Tables I and II) are consistent with the structure of this known compound.

Preparation of Diethyl Bromomaleate (XXXIXb). A 500-ml., three-necked flask was equipped with a condenser, an addition funnel and a magnetic stirrer. A solution of XXXVIIIb (25 g., 0.075 mole) in 200 ml. of absolute ethanol was placed in the flask. Triethylamine (8.1 g., 0.080 mole) in 50 ml. of absolute ethanol was added dropwise over a period of 1 hour. The mixture was stirred at room temperature for 24 hours. Removal of alcohol was accomplished on a flask evaporator, and the residue was taken up with ether and filtered. The ether was removed leaving 18.1 g. (97%) of a yellow oil.

An ether solution of this oil was analyzed by GLC on the usual column[d] at a column temperature of 200°. The helium flow-rate was 49 ml./min. This analysis showed the presence of two compounds in a 3.5:1 ratio. The larger peak (retention time, 8.1 min.) was collected by preparative gas chromatography using the same column as above and identified as XXXIXb which was analyzed, n_D^{25} 1.4738.

Anal. Calcd. for $C_8H_{11}BrO_4$: C, 38.22; H, 4.41; Br, 31.82.
Found: C, 38.33; H, 4.37; Br, 31.82.

The IR (Plate V) and NMR (Plate XXIII) spectral data (Tables I and II) are consistent with the structure of this compound.

Preparation of Diethyl Bromofumarate (XXXVIb). The procedure and reagents used were the same as in the previous reaction except that dl-dibromide XXXVb was used instead of meso-dibromide XXXVIIIb. The yield was 17.8 g. (95%).

An ether solution of the oil was analyzed by GLC as in the previous reaction and showed the presence of two products in a ratio of 32.4:1. The larger peak (XXXVIb; retention time, 11.3 min.) was collected as before and analyzed; n_D^{25} 1.4775 (lit.[4] $n_{He}^{19.1}$ 1.4819).

Anal. Calcd. for $C_8H_{11}BrO_4$: C, 38.22; H, 4.41; Br, 31.82.
Found: C, 38.36; H, 4.35; Br, 32.03.

Mixed injections on GLC column showed that the minor product was vinylic bromide XXXIXb.

The IR (Plate VI) and NMR (Plate XXIV) spectral data (Tables I and II) for XXXVIb consistent with the assigned structure.

Preparation of Dimethyl meso-Dibromosuccinate(XXXVIIIa). The procedure used employs the method of Ing and Perkin[30] with modifications. Dimethyl fumarate (XXXVIIa) (50 g., 0.35 mole) was dissolved in 150 ml. of carbon tetrachloride and placed in a 500-ml., three-necked flask equipped in the usual manner (see page 35). Bromine (56 g., 0.35 mole) was

added dropwise over a period of 0.5 hour, and the reaction mixture was boiled for 5 hours and stirred overnight at room temperature. Workup in the usual manner (see page 49) gave a nearly colorless oil which was crystallized from n-hexane, m. p. 64-65° (lit.[30] m. p. 65°); yield, 97 g. (91%).

The IR (Plate VII) and NMR (Plate XXV) spectral data (Tables I and II) substantiate the structure of this known compound.

Preparation of Dimethyl dl-Dibromosuccinate (XXXVa). The procedure used follows closely that of Ing and Perkin[30] and is the same as that used in the preparation of XXXVb (page 49) except for materials used and reaction time. A 500-ml., three-necked flask equipped as usual was charged with a solution of 50 g. (0.35 mole) of dimethyl maleate (XXXIVa) in 250 ml. of ether. The flask was cooled by an ice bath and protected from direct sunlight by a cloth. Bromine (56 g., 0.35 mole) was added from the addition funnel over a period of 0.25 hour. The reaction mixture was stirred for about 7 hours until the pale yellow color indicated the end of the reaction. Workup in the manner previously described (see page 49) resulted in a yellow oil which was crystallized from n-hexane to yield 40 g. (38%) of white crystals of XXXVa, m. p. 40-42° (lit.[30] 43°).

The IR (Plate VIII) and NMR (Plate XXVI) spectral data (Tables I and II) further substantiate the structure of this known compound.

Preparation of Di-n-Propyl Bromofumarate (XXXVIc). A

1-liter, three-necked flask was equipped in a manner previously described (see page 49) and charged with a solution of 98.3 g. (0.49 mole) of di-n-propyl maleate (XXXIVc) in 250 ml. of dry ether. The flask was cooled in an ice bath and protected from direct sunlight by a cloth. Bromine (80 g., 0.50 mole) was added from the addition funnel over a period of 1 hour and the mixture was stirred for 24 hours. The same workup as in previous experiments was followed (see page 49). Triethylamine (50.5 g., 0.50 mole) was added to the ether solution and stirred for 12 hours and filtered. The ether was removed and the resulting yellow oil was distilled, b. p. 110°/1.8 mm., yield 110 g. (81%).

The NMR spectrum showed a triplet centered at δ 1.10 ($-CH_2CH_2C\underline{H}_3$), a multiplet centered at δ 1.67 ($-CH_2C\underline{H}_2CH_3$), two nonequivalent triplets centered at δ 4.13 and δ 4.19 and a singlet at δ 7.39 ($-C\underline{H}CBr$). Minor impurities displayed singlets at δ 6.74 and δ 6.43.

Reaction of Ammonia with Dimethyl meso-Dibromosuccinate (XXXVIIIa). A 500-ml., three-necked flask was equipped with an addition funnel, a condenser filled with dry ice, a thermometer, a drying tube ($CaCl_2$) and a magnetic stirrer. A solution of XXXVIIIa (25 g., 0.82 mole) in 200 ml. of methanol was placed in the flask and 8.3 g. (0.082 mole) of triethylamine was added and the reaction mixture was heated at 65° for 1 hour. A solution of 3.2 g. (0.20 mole) of ammonia in 100 ml. of methanol was added dropwise from the addition funnel over a period of 6 hours while the re-

action mixture was being heated at 60-65°. Heating was continued for 2 additional hours. The methanol was evaporated, the residue was extracted with ether and the resulting solution filtered. The ether was removed leaving 9.3 g. of a brown oil. An ether solution of this oil was analyzed by GLC on the usual column[d] with the following temperature settings: Column, 200°; injector, 260°; detector, 288°. The helium flow-rate was 49 cc./min. Two peaks were observed at retention times of 10.6 and 12.8 min. in a ratio of 2.6:1.

A portion of the oil (2.0 g.) placed on a column of neutral alumina and successively eluted with n-hexane, benzene and ether gave analytical amounts of two components. The first compound eluted was a colorless oil which partially crystallized after several hours. Its melting point could not be determined since it was not fully crystalline at room temperature. Analysis by GLC on the column used above showed that this compound had a retention time of 10.6 min., and subsequently identified by IR (Plate IX) and NMR (Plate XXVII) spectral[1] date (Tables I and II) as dimethyl aminofumarate (XLIa).

Anal. Calcd. for $C_6H_9NO_4$: C, 45.28; H, 5.70; N, 8.80.
Found: C, 45.29; H, 5.79; N, 8.86.

The second component eluted from the alumina column was a colorless oil which had a retention time of 12.8 min. by GLC analysis using the column and conditions previously described. This compound was identified by IR (Plate XII) and NMR (Plate XXX) spectral data (Tables I and II) as

dimethyl aziridine-2,3-dicarboxylate (XLa).

Anal. Calcd. for $C_6H_9NO_4$: C, 45.28; H, 5.70; N, 8.80.
Found: C, 44.62; H, 5.76; N, 8.99.

After a few days a brown solid which was insoluble in ether formed in the bottom of the bottle containing the reaction mixture. NMR analysis also showed that the peaks attributed to aziridine XLa were decreasing in size.

Reaction of Ammonia with Dimethyl dl-Dibromosuccinate (XXXVa). The same reaction conditions and workup were used as in the previous reaction. Materials were the same except that dl-dibromide XXXVa was used instead of meso-dibromide XXXVIIIa. Workup of the reaction yielded 11.6 g. of a brown oil which was analyzed by GLC using the same column and conditions as with the previous reaction. Mixed injections of this oil and the oil obtained from the previous run showed the presence of enamine XLIa and aziridine XLa. Analysis of this mixture by NMR was performed by integrating the peaks at δ 5.35 and δ 2.81 attributed to the vinyl proton on enamine XLIa and the ring protons on aziridine XLa, respectively. This analysis showed an enamine-aziridine ratio of 6.1:1. After a few days the same brown substance appeared in the bottom of the reaction mixture as in the previous reaction.

Reaction of Ammonia with Diethyl meso-Dibromosuccinate (XXXVIIIb)-Run 1. A 500-ml., three-necked flask was equipped as usual (see page 53) and charged with a solution of XXXVIIIb (25 g., 0.075 mole) in 100 ml. of absolute ethanol

and heated to 65°. Ammonia (3.74 g., 0.23 mole) in 150 ml. of ethanol was added dropwise from the addition funnel over a period of 3 hours and heating at 65° was continued for 1 additional hour. Evaporation of the ethanol was done on a flask evaporator to give a residue which was extracted with dry ether. The resulting solution was filtered to remove the ammonium bromide, and the ether was evaporated from the extract leaving a brown oil. Distillation of the oil gave a fraction boiling at 111-116°/1.4 mm.; yield, 11.5 g. of a yellow liquid.

GLC analysis using the same column and temperature settings as before showed three peaks at retention times of 8.1, 11.5 and 13.1 minutes. The peak at 8.1 min. was identified by mixed injections as the vinylic bromide XXXIXb. The peaks at 11.5 min. and 13.1 min. were collected by preparative gas chromatography using the same GLC column[d] and analyzed.

The peak which had a retention time of 11.5 min. was identified by IR (Plate X) and NMR (Plate XXVIII) spectral data (Tables I and II) as diethyl aminofumarate (XLIb) n_D^{24} 1.4899 (lit. n_D^{20} 1.4928).[22]

Anal. Calcd. for $C_8H_{13}NO_4$: C, 51.33; H, 7.00; N, 7.48.
Found: C, 49.81; H, 6.92; N, 7.02.

Obviously some of vinylic bromide XXXVIb was present since XXXVIb and XLIb have almost identical retention times and small amounts would be hard to detect.

The peak which had a retention time of 13.1 min. was

subsequently identified by IR (Plate XIII) and NMR (Plate XXXI) spectral data (see Tables I and II) as diethyl aziridine-2,3-dicarboxylate (XLb), m. p. 52-53°.

Anal. Calcd. for $C_8H_{13}NO_4$: C, 51.33; H, 7.00; N, 7.48.
Found: C, 51.46; H, 6.80; N, 7.52.

It was later found that pure XLb could be obtained by cooling a hexane solution of the mixture to Dry Ice-acetone temperature and filtering.

Reaction of Ammonia with Diethyl dl-Dibromosuccinate (XXXVb)-Run 1. The procedure and materials employed were the same as in the previous reaction (page 55) except that dibromide XXXVb was used instead of XXXVIIIb. Workup in the usual manner showed the presence of the same products (XXXIXb, XXXVIb, XLb and XLIb) as in the previous reaction. Exact ratios could not be determined because of overlapping peaks attributed to vinylic bromide XXXVIb and enamine XLIb. Subsequent reactions were followed by GLC and NMR and carried essentially to completion by observing the disappearance of vinylic bromides (XXXIXb and XXXVIb).

Reaction of Ammonia with XXXVIIIb-Run 2. A 500-ml., three-necked flask was equipped as in Run 1 and charged with a solution of XXXVIIIb (25 g., 0.075 mole) in 150 ml. of absolute ethanol. The mixture was heated to 65° and a saturated solution of ethanolic ammonia (150 ml.) was added from the addition funnel over a period of 1.5 hours; heating at 65° was continued for 1 more hour. The usual workup (page 55) gave 12.7 g. of a brown oil which was analyzed by

GLC and showed the presence of only two products identified by mixed injections and NMR analysis as aziridine XLb and enamine XLIb. Integration of the area under the peaks showed the aziridine-enamine ratio to be 1:2.

Reaction of Ammonia with XXXVb -Run 2. The procedure employed was the same as for Run 1 using 25 g. (0.075 mole) of XXXVb. Workup in the usual manner yielded 11.8 g. of a brown oil. GLC and NMR analysis showed the same two products (enamine XLIb and aziridine XLb) as from the reaction of ammonia with XXXVIIIb. The aziridine-enamine ratio was 1:1.9.

Reaction of Ammonia with a Mixture of Vinylic Bromides XXXIXb and XXXVIb. A 1-liter, three-necked flask was equipped in the usual way (page 55) with the exception of a dry ice condenser which was replaced by a Friedrichs condenser. A solution of 85 g. (0.34 mole) of XXXIXb and XXXVIb (previously analyzed as containing 60% XXXIXb and 40% XXXVIb) in 500 ml. of absolute ethanol was placed in the flask and heated to reflux. Dry ammonia gas was bubbled into the solution through a gas inlet so as to maintain the temperature at 75-80°. After 2.5 hours the solution was cooled and the ethanol was removed on a flash evaporator. The residue was taken up with 200 ml. of dry ether and the resulting solution was filtered. Removal of the ether left 58 g. of an orange oil. Analysis of this oil by NMR showed the presence of aziridine XLb and enamine XLIb in a 1:1 ratio. This analysis showed no peaks attributable to vinylic bromides

XXXIXb or XXXVIb or any other products.

The orange oil was dissolved in about 200 ml. of n-hexane and cooled in a Dry Ice-acetone bath. After several minutes of stirring, crystals began to form and after about 15 min. the mixture was filtered. Recrystallization of the solid from n-hexane yielded 13 g. (21%) of pure XLb, m. p. 52-53°. Molecular weight, 181; theoretical, 187.

The NMR and IR spectra of XLb obtained here were identical to those obtained of the solid material from all previous reactions of ammonia with XXXVIIIb, XXXVb, XXXIXb and XXXVIb.

Reaction of Ammonia with Di-n-propyl Bromofumarate (XXXVIc). A 1-liter, three-necked flask was equipped as usual (page 55) and charged with a solution of XXXVIc (100 g., 0.36 mole) in 300 ml. of 1-propanol. The mixture was heated to 90° and ammonia (18.3 g., 1.1 mole) dissolved in 200 ml. of 1-propanol was added dropwise over a period of 1 hour. The reaction was heated at 90° and followed by taking aliquots every 15 min., evaporating the 1-propanol, extracting with ether and analyzing the solution by GLC on the usual column.[d] It was possible to follow the reaction by noting the disappearance of vinylic bromide (XXXVIc). After heating for 1 hour (after the ammonia was added), GLC analysis showed that the reaction was essentially complete on the basis of the absence of peaks attributed to vinylic bromide XXXVIb.

The reaction mixture when worked up in the manner de-

scribed above left 69 g. of an orange oil.

GLC analysis of the oil was possible with the same column employed above using the following temperature settings: column, 200°; injector, 260°; detector, 288°. Helium flow-rate was 49 cc./min. Two peaks were observed at retention times of 16.7 and 18.5 min. The ratio could not be determined accurately because of slight overlap of the two peaks, but the peak at 16.7 min. was the larger of the two.

NMR analysis of the mixture showed a singlet at δ 5.48 attributed to di-n-propyl aminofumarate XLIc and a singlet at δ 2.86 attributed to the ring protons on aziridine XLc. Integration of these two peaks gave a product ratio of 56:44, XLc to XLIc.

Attempts to freeze out one of the products at Dry Ice-acetone temperatures failed. Chromatography on acid-washed and neutral alumina was unsuccessful, yielding only mixtures of the two products.

Distillation of a few ml. of the mixture gave about 40% yield of a yellow liquid, b. p. 92-94°/0.1 mm. The remainder of the material appeared to polymerize and turn black in the pot. GLC analysis of this oil showed it to be a pure product (XLIc) corresponding to the peak at 16.7 min. retention time.

Anal. Calcd. for $C_{10}H_{17}NO_4$: C, 55.80; H, 7.96; N, 6.51.
Found: C, 55.98; H, 7.99; N, 6.48.

The IR (Plate XI) and NMR (Plate XXIX) are consistent with the proposed structure (see Tables I and II).

Reaction of p-Anisidine with Vinylic Bromides XXXIXb and XXXVIb. A 200-ml., three-necked flask was equipped as usual (page 58). A solution of vinylic bromides XXXIXb and XXXVIb (10.3 g., 0.04 mole), which had been analyzed as a 60:40 mixture, and 4.1 g. (0.04 mole) of triethylamine in 50 ml. of absolute ethanol were placed in the flask. p-Anisidine (5.0 g., 0.04 mole) in 25 ml. of ethanol was added over a period of 5 minutes and the mixture heated at reflux for 3 hours. The ethanol was evaporated and the mixture was filtered. Evaporation of the ether left a yellow oil (11.9 g.) which was analyzed by NMR.

The NMR spectrum of the crude reaction product in CCl_4 showed a singlet at δ 3.29 attributed to the ring protons on the diethyl 1-(p-methoxyphenyl)aziridine-2,3-dicarboxylate (XLV) and a singlet at δ 5.28 attributed to the vinyl proton on the corresponding enamine XLVI. A very small peak was observed at δ 2.85 which was attributed to the ring protons on the cis isomer of XLV.

The ratio of enamine XLVI to aziridine XLV was 1.7:1. cis-Aziridine XLV made up less than 5% of the total product.

Preparation of Diethyl 1-(p-Nitrobenzoyl)aziridine-2,3-dicarboxylate (XLIII). This procedure is similar to the one employed by Heine.[25] A 200-ml., three-necked flask was equipped with a condenser, a drying tube ($CaCl_2$), a nitrogen inlet, an additional funnel and a magnetic stirrer. Aziridine XLb (1.0 g., 0.0054mole) dissolved in 25 ml. of dry ether and 0.54 g. (0.0054mole) of triethylamine was placed

in the flask. p-Nitrobenzoyl chloride in 25 ml. of dry ether was added dropwise over a period of 45 minutes and the reaction was stirred for 10 hours under nitrogen. The triethylamine hydrochloride was removed by filtering and the filtrate concentrated on a flask evaporator leaving a yellow oil. The oil was dissolved in a minimum amount of benzene, and n-hexane was added until the solution became cloudy. After a few hours a yellow crystalline solid precipitated. Recrystallization from benzene-hexane gave 1.4 g. (75%) of pure XLIII, m. p. 86-87°.

Anal. Calcd. for $C_{15}H_{16}N_2O_7$: C, 53.57; H, 4.80; N, 8.33.
Found: C, 54.21; H, 5.05; N, 8.17.

The NMR (Plate XXXII) and IR (Plate XIV) spectral data (see Tables I and II) are consistent with the assigned structure of this compound.

Several other derivatives were prepared including the 1-benzoyl, 1-acetyl and 1-chloroacetyl derivatives, but the products were not crystalline and were consequently difficult to purify.

Preparation of Diethyl 1-(2,4-dichlorophenoxyacetyl)-aziridine-2,3-dicarboxylate (XLVIII). A 200-ml., three-necked flask was equipped with a condenser, a drying tube ($CaCl_2$) and an addition funnel, and charged with 2.0 g. (0.011 mole) of XLb. A solution of 2,4-dichlorophenoxyacetyl chloride (2.6 g., 0.011 mole) in 30 ml. of dry ether was added dropwise from the addition funnel over a period of 0.5 hour. The reaction mixture was stirred at room tempera-

ture for 18 hours and filtered. Removal of the ether from the filtrate left a white crystalline solid (XLVIII) which was recrystallized from benzene-hexane (m. p. 110-111°), yield 3.4 g. (82%).

Anal. Calcd. for $C_{16}H_{17}Cl_2NO_6$: C, 49.22; H, 4.38; N, 3.59.
Found: C, 48.97; H, 4.20; N, 3.78.

The IR (Plate XVI) and NMR (Plate XXXIV) spectral data (Tables I and II) are consistent with the structure of this compound.

Isomerization of XLIII with Sodium Iodide. This procedure follows the method of Heine.[25] A 50-ml., one-necked flask was equipped with a condenser, a drying tube ($CaCl_2$) and a magnetic stirrer. A mixture of 200 mg. (0.00107 mole) of XLIII and 89 mg. of sodium iodide in 20 ml. of dry acetone was placed in the flask, and the mixture was heated at reflux for 3 hours. After stirring at room temperature overnight, the acetone was evaporated and the residue extracted with ether, and the resulting solution was filtered. The ether was evaporated from the filtrate and a yellow oil remained (approx. 200 mg.). NMR analysis did not show a peak at δ 3.67 for the ring protons on XLIII, but instead showed a AB quartet (J=6.8 c.p.s.) centered at δ 5.23 (ring protons on oxazoline L).

The IR (Plate XV) and NMR (Plate XXXIII) substantiate the structure of this compound.

Preparation of Di-n-propyl 1-(p-Nitrobenzoyl)aziridine-2,3-dicarboxylate (XLII). A three-necked flask was equipped

in the usual manner (see page 61) and charged with a solution of 5.0 g. of the reaction mixture from the reaction of ammonia with XXXVIb (containing 2.3 g., 0.011 mole) of XLc in 10 ml. of dry ether. p-Nitrobenzoyl chloride (2.3 g., 0.012 mole) was added from the addition funnel and the reaction mixture was stirred for 6 hours under nitrogen. Filtration of the mixture and evaporation of the ether gave a yellow oil. The oil was dissolved in a minimum amount of benzene, and n-hexane was added until the solution became cloudy. The solution was placed in the refrigerator, and after 3 days the yellow solid which had precipitated was filtered out. Recrystallization from benzene-hexane yielded 1.5 g. (53%) of XLII, m. p. 63-63.5°.

Anal. Calcd. for $C_{17}H_{20}N_2O_7$: C, 56.04; H, 5.53; N, 7.69.
Found: C, 56.18; H, 5.58; N, 7.80.

The IR (Plate XVIII) and NMR (Plate XXXVII) spectral data (see Table I and II) further substantiated the structure of this compound.

Attempted Epimerization of Aziridine XLb with Sodium Carbonate in Acetonitrile. A 50-ml., one-necked flask was equipped with a condenser, a drying tube ($CaCl_2$) and a magnetic stirrer. A solution of XLb (1.0 g., 0.0054 mole) in 4 ml. of acetonitrile was placed in the flask, and 0.57 g. of Na_2CO_3 was added. The reaction mixture was heated at reflux for 3 hours. The acetonitrile was evaporated and the residue taken up in ether and filtered. The resulting yellow oil was crystallized from n-hexane and gave 0.8 g.

of crystals, m. p. 52-53°.

The NMR spectrum (Plate XXXVI) showed that the singlet at δ 2.85 in XLb had been split into a doublet (J=9.0c.p.s.) and the singlet at δ 1.80 was split into a broad triplet (J= 9.0 c.p.s.). Addition of D_2O caused the peak at δ 1.80 to disappear and the doublet at δ 2.85 coalesced into a singlet. The IR spectrum of this compound was identical to that of XLb.

Attempted Epimerization of Aziridine XLb with Sodium Ethoxide. A 50-ml., one-necked flask was equipped as in the previous reaction and charged with 1.0 g. (0.0054 mole) of XLb in 10 ml. of 0.5 molar sodium ethoxide. The mixture was heated at reflux for 5 min. and cooled to room temperature. Ten ml. of water was added but no precipitate was observed. The mixture was extracted with two 50-ml. portions of ether. The ether was evaporated from the extract to give a yellow oil which on crystallization from hexane yielded 0.5 g. of white crystals, m. p. 52-53°.

The NMR spectrum of this compound was identical to that of the compound (XLb) obtained from the previous reaction.

Isomerization of Aziridine XLb into Enamine XLIb. A 10-ml., two-necked flask was equipped with a thermometer, a condenser and a drying tube ($CaCl_2$). Aziridine XLb (0.2 g.) was placed in the flask and heated at 125-135° for 1.5 hours. The compound turned dark on heating. Analysis of the residue by NMR showed that there had been an 85% conversion to enamine XLIb.

Attempted Preparation of Diethyl 1-(Diphenylphosphinyl)-

aziridine-2,3-dicarboxylate (XLVII). A 50-ml., one-necked flask was equipped with a magnetic stirrer and charged with 1.0 g. (0.0054 mole) of XLb and 4 ml. of pyridine. Diphenylphosphinic chloride (1.0 g., 0.0064 mole) was added and the flask sealed with a cork. The reaction mixture was stirred at room temperature for 6 hours and the pyridine was removed under vacuum. The residue was taken up in ether and filtered to remove the pyridine hydrochloride. Evaporation of the ether gave 1.9 g. (92%) of a honey-like substance which was dried in a vacumn oven at 60° for 3 hours to remove traces of pyridine. The material could not be crystallized by use of methylene chloride-n-hexane or benzene-hexane.

The NMR spectrum (Plate XXXV) indicated that addition did take place since the ring protons are split into a doublet($J_{P-N-C-H}$ = 12.5 c.p.s.).

The IR spectrum (Plate XVII) indicates some ring opening did occur due to the presence of a band at 3460 $cm.^{-1}$ (NH).

Attempted Preparation of Diethyl 1-(p-Toluenesulfonyl)-aziridine-2,3-dicarboxylate(XLVIX). A 50-ml., three-necked flask was equipped with an addition funnel, a condenser, a drying tube ($CaCl_2$), a nitrogen inlet and a magnetic stirrer. A solution of XLb (1.0 g., 0.0054 mole) in 3 ml. of pyridine was placed in the flask. p-Toluenesulfonyl chloride (1.02 g., 0.0054 mole) in 2 ml. of pyridine was added from the addition funnel, and the reaction mixture was stirred under

nitrogen for 4 hours. The pyridine was removed under vacumn, the residue extracted with ether, and the solution filtered. The ether was removed and the resulting oil was crystallized from benzene-hexane, m. p. 104-105°; yield 1.1 g.

When treated with a silver nitrate solution, an ethanolic solution of this solid gave a precipitate.

The NMR showed a broad peak at δ 5.74 (NH) which disappeared when D_2O was added to the sample. The presence of a band at 3240 $cm.^{-1}$ in the IR spectrum also indicated that ring opening had occurred.

Attempted Phosphorylation of Aziridine XLb using Triethylamine as the Acid Scavenger. Attempted phosphorylation of XLb with phosphorus oxychloride, phenylphosphinous dichloride, diphenylphosphinic chloride, diphenyl phosphorochloridate and phenylphosphonic dichloride using benzene or ether as the solvent and triethylamine as the base, failed to give any addition to the aziridine. There appeared to be some type of complex forming between the phosphorus halide and triethylamine, possibly the phosphonium salt.

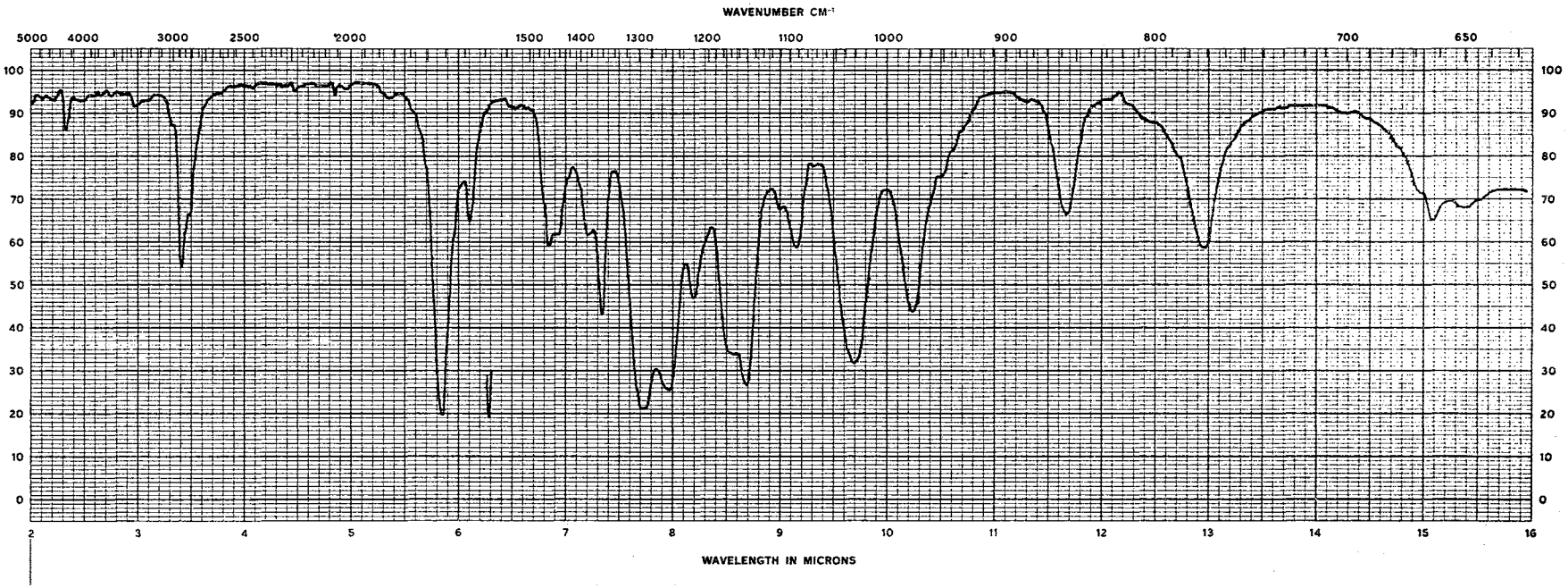
Preparation of p-Nitrobenzoyl Azide (XLIV). The procedure follows closely that of Cabat[6] used in the preparation of benzoyl azide. A 200-ml. three-necked flask was equipped with an addition funnel, a drying tube ($CaCl_2$), a thermometer and a magnetic stirrer. A solution of sodium azide (7 g., 0.108 mole) in 20 ml. of water and 10 ml. of acetone was placed in the flask and cooled to 10°. A solution of p-nitrobenzoyl chloride in 10 ml. of acetone was

added from the addition funnel over a period of 0.5 hour. The reaction was allowed to stir overnight while coming to room temperature. The mixture was extracted with 125 ml. of ether. After the ether solution was washed three times with 15-ml. portions of 10% NaOH and twice with 50-ml. portions of water, it was dried overnight ($MgSO_4$). Removal of the ether under aspirator pressure at room temperature gave product, yield 9.4 g. (90%). m. p. 64-65° (lit.[46] m. p. 65°).

Reaction of p-Nitrobenzoyl Azide (XLIV) with XXXVIIb. A 200-ml. three-necked flask was equipped as in the previous reaction. A solution of diethyl fumarate (XXXVIIb) (8.4 g., 0.049 mole) in 50 ml. of benzene was placed in the flask, and 9.4 g. (0.049 mole) of azide XLIV dissolved in 50 ml. of benzene was added dropwise over a period of 2 hours. The reaction was stirred at room temperature for 2 weeks. The progress of the reaction was checked frequently by NMR, but no addition to the diethyl fumarate could be observed. A yellow precipitate formed as the reaction progressed. It was identified as N,N'-bis(p-nitrophenyl)urea by comparison of its IR spectrum with that of a known sample.

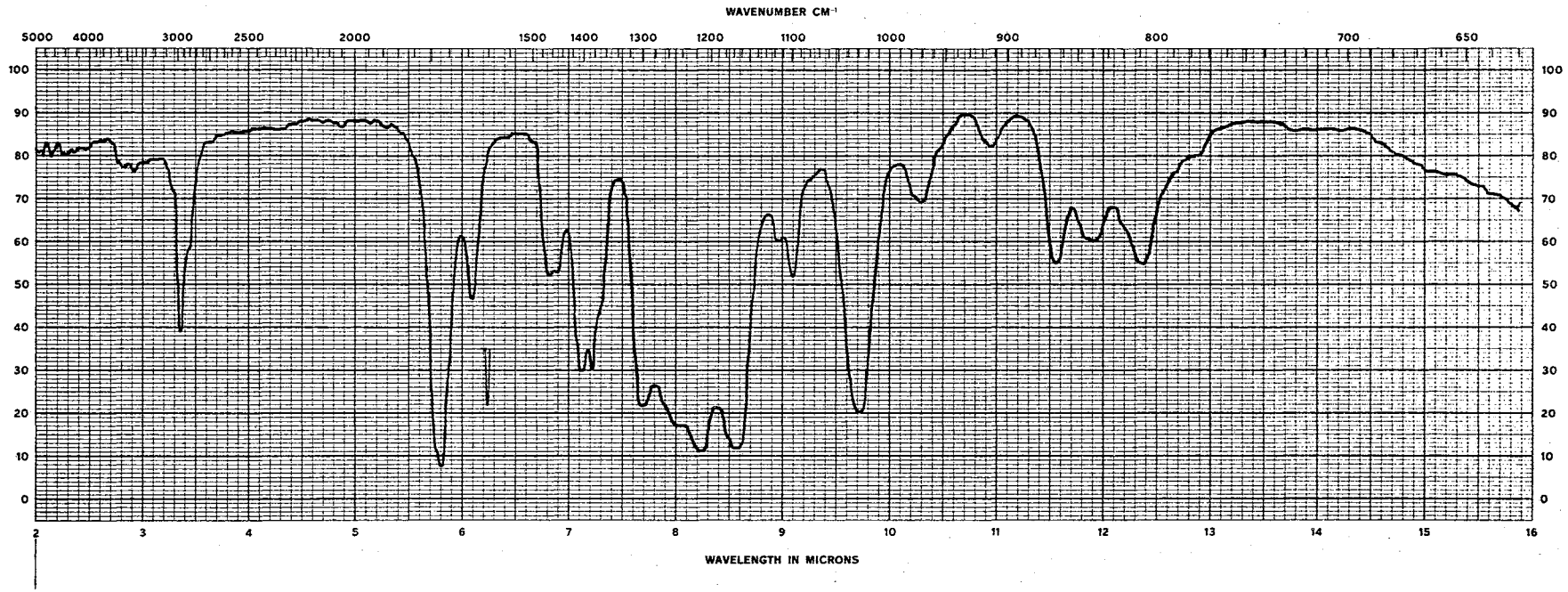
Photolysis of a mixture of azide XLIV and diethyl fumarate in hexane for 10 hours with UV light gave only N,N'-bis(p-nitrophenyl)urea as the product.

Plate I



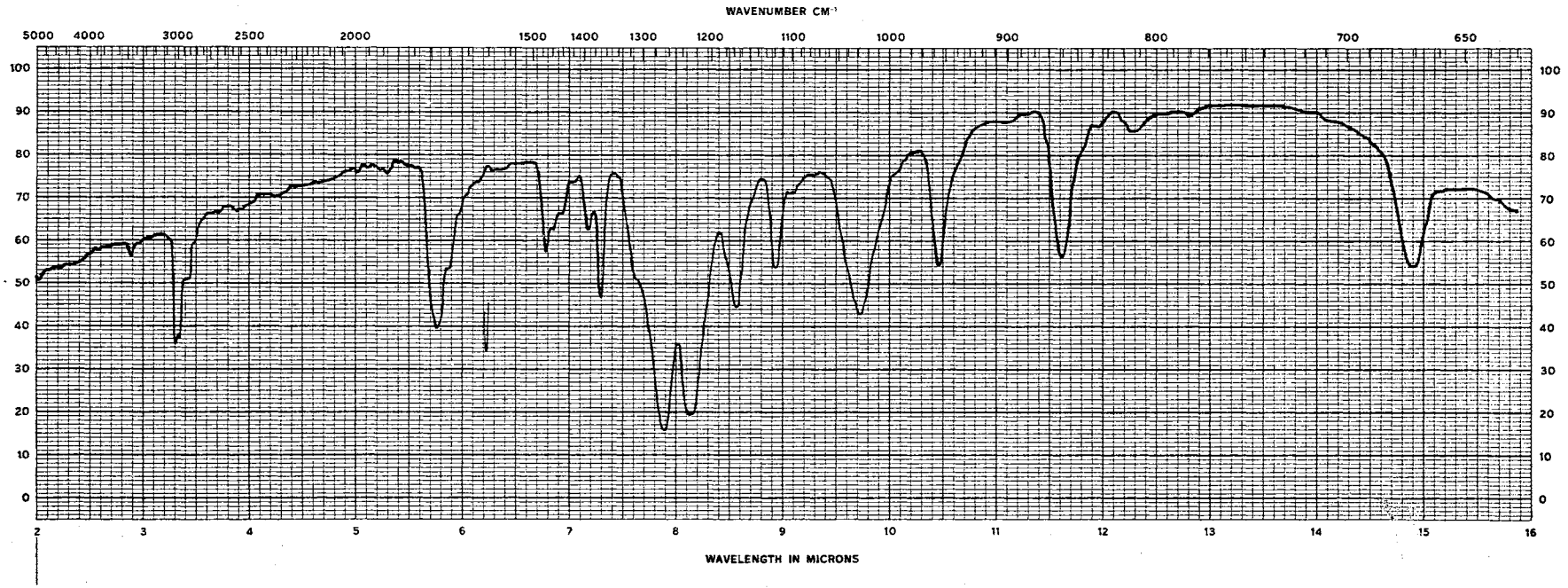
Diethyl Fumarate (XXXVIIb), Film on NaCl Plates

Plate II



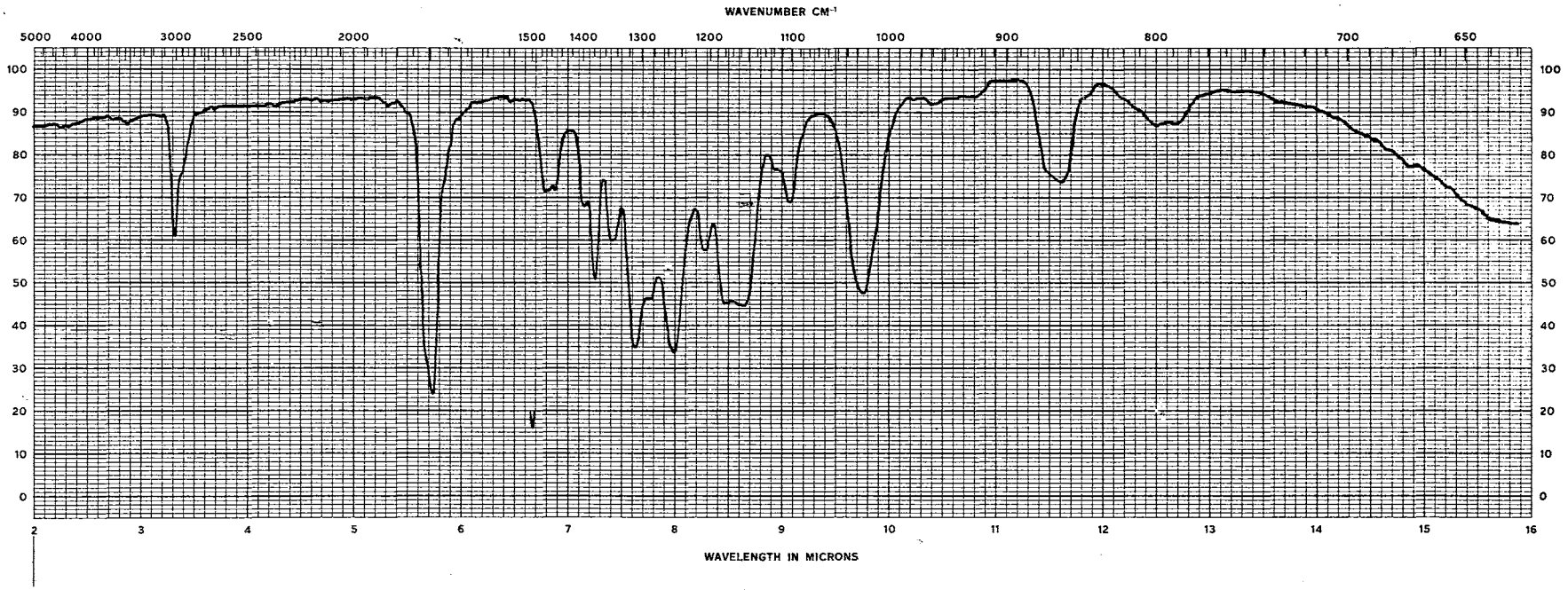
Diethyl Maleate (XXXIVb), Film on NaCl Plates

Plate III



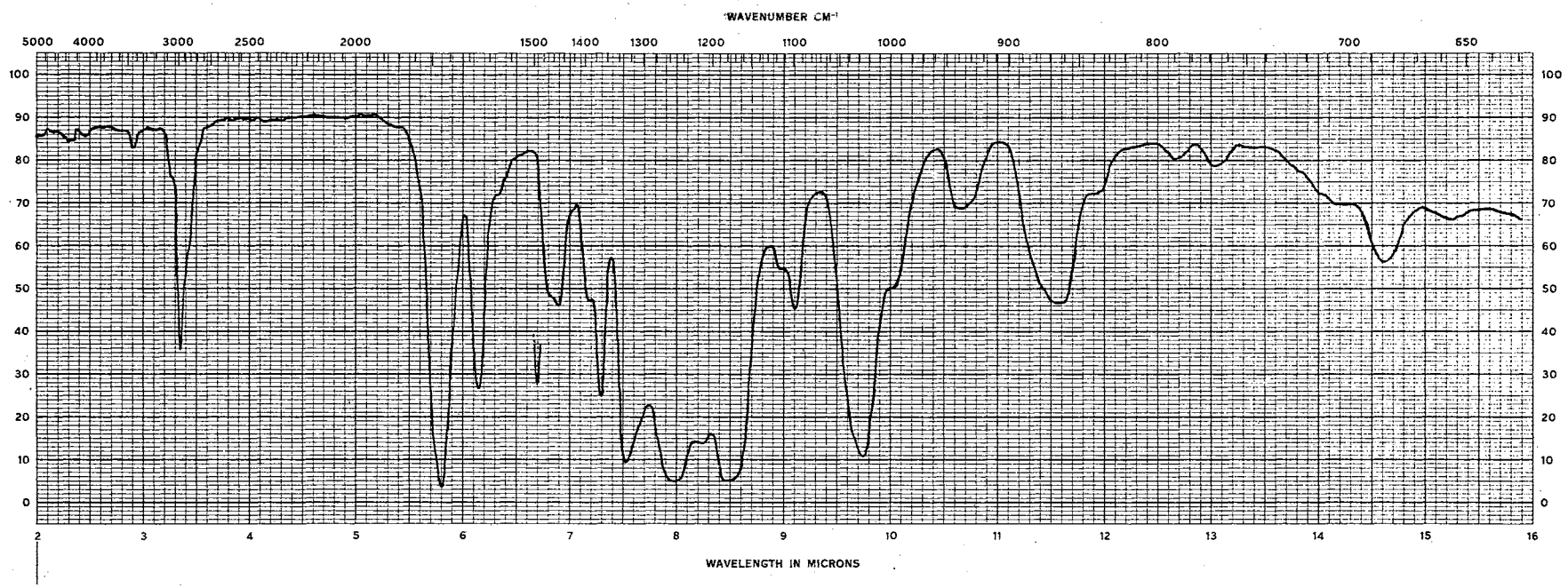
Diethyl meso-Dibromosuccinate (XXXVIIIb), Film on NaCl Plates

Plate IV



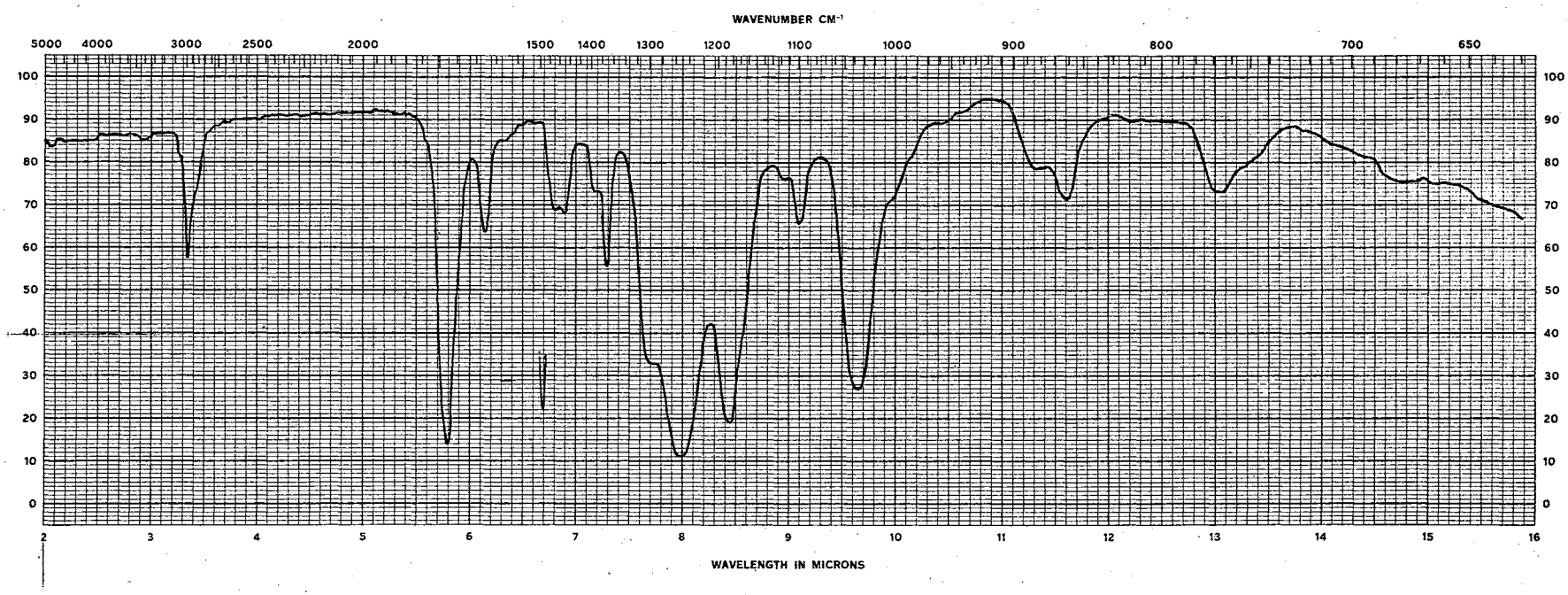
Diethyl dl-Dibromosuccinate (XXXVb), Film on NaCl Plates

Plate V



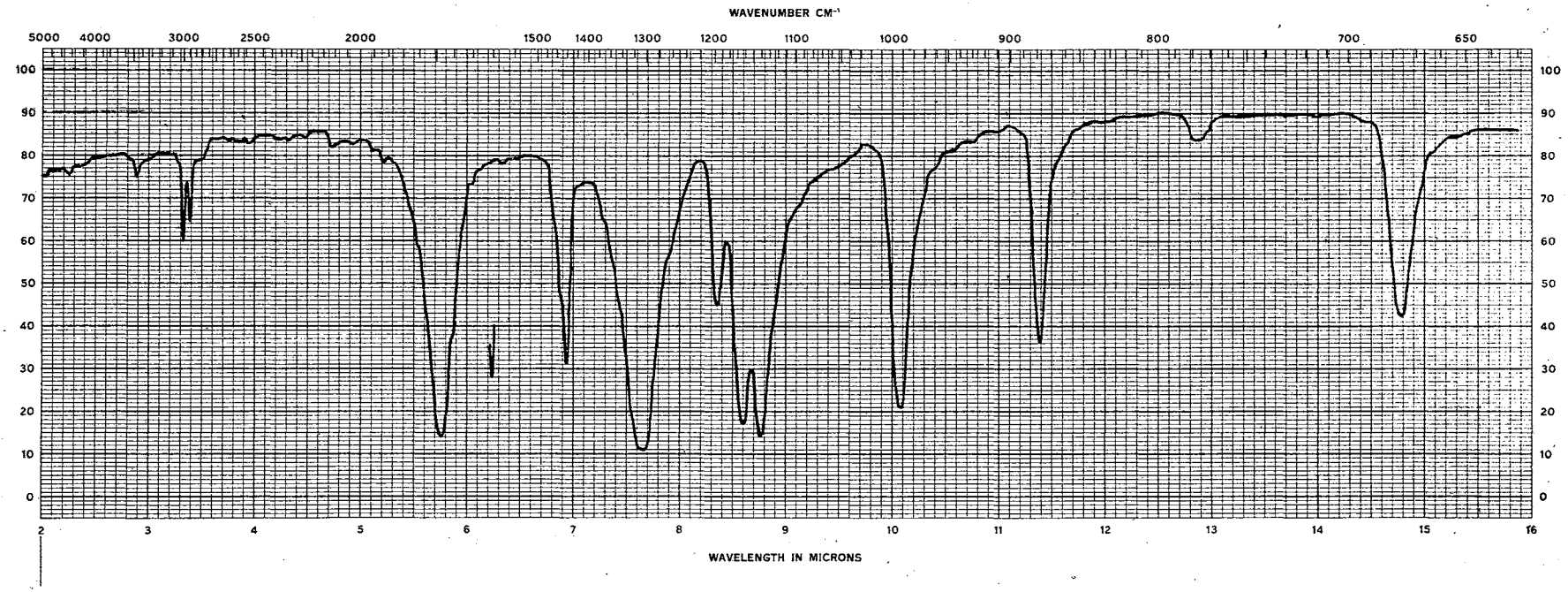
Diethyl Bromomaleate (XXXIXb), Film on NaCl Plates

Plate VI



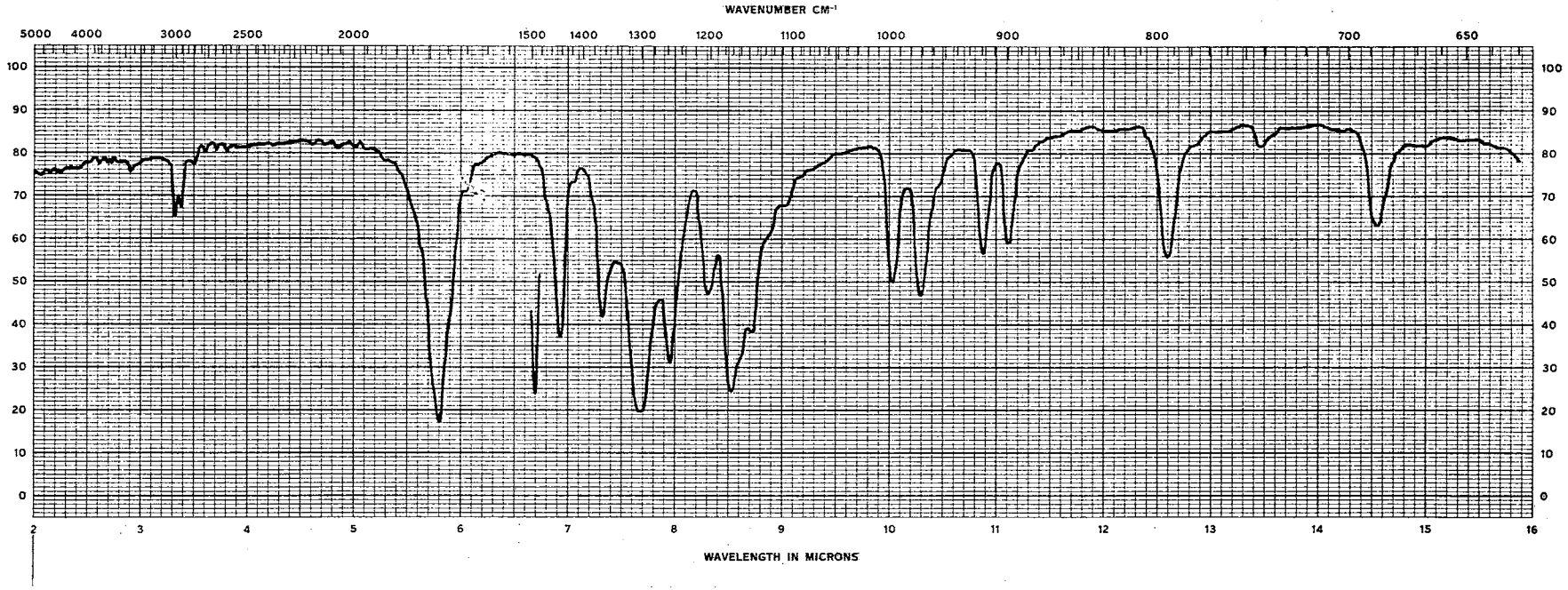
Diethyl Bromofumarate (XXXVIb), Film on NaCl Plates

Plate VII



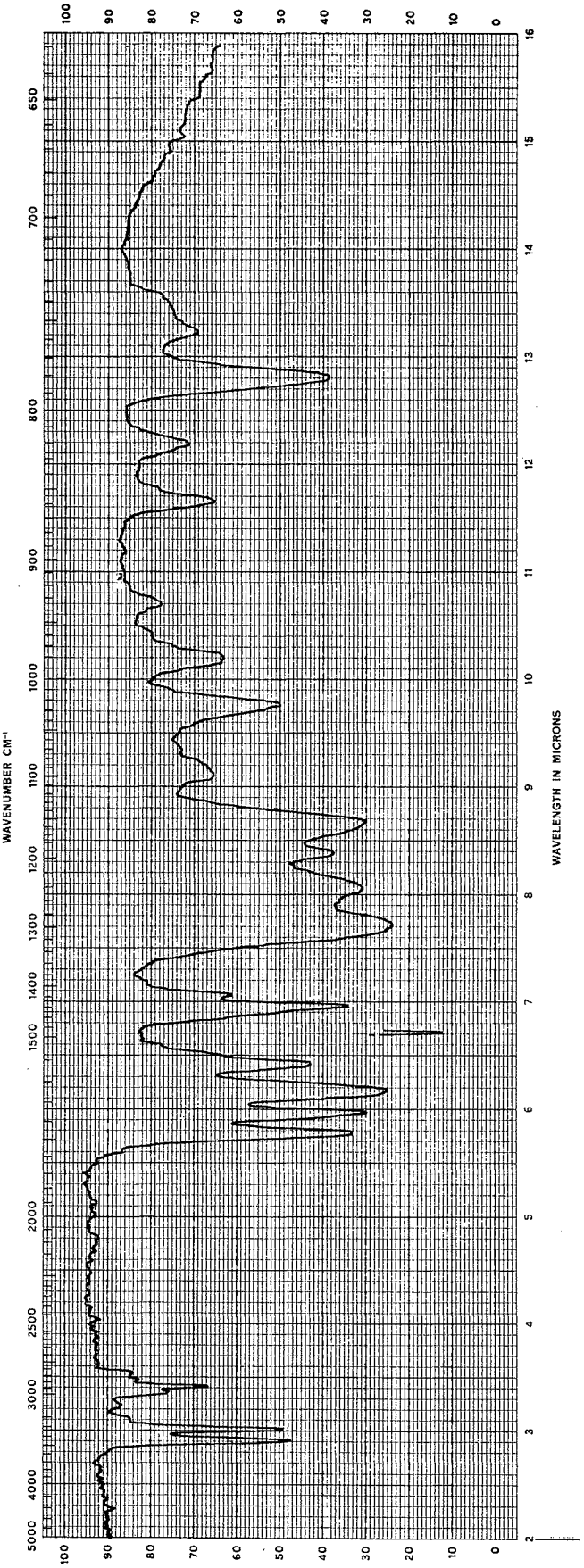
Dimethyl meso-Dibromosuccinate (XXXVIIIa), KBr Pellet

Plate VIII



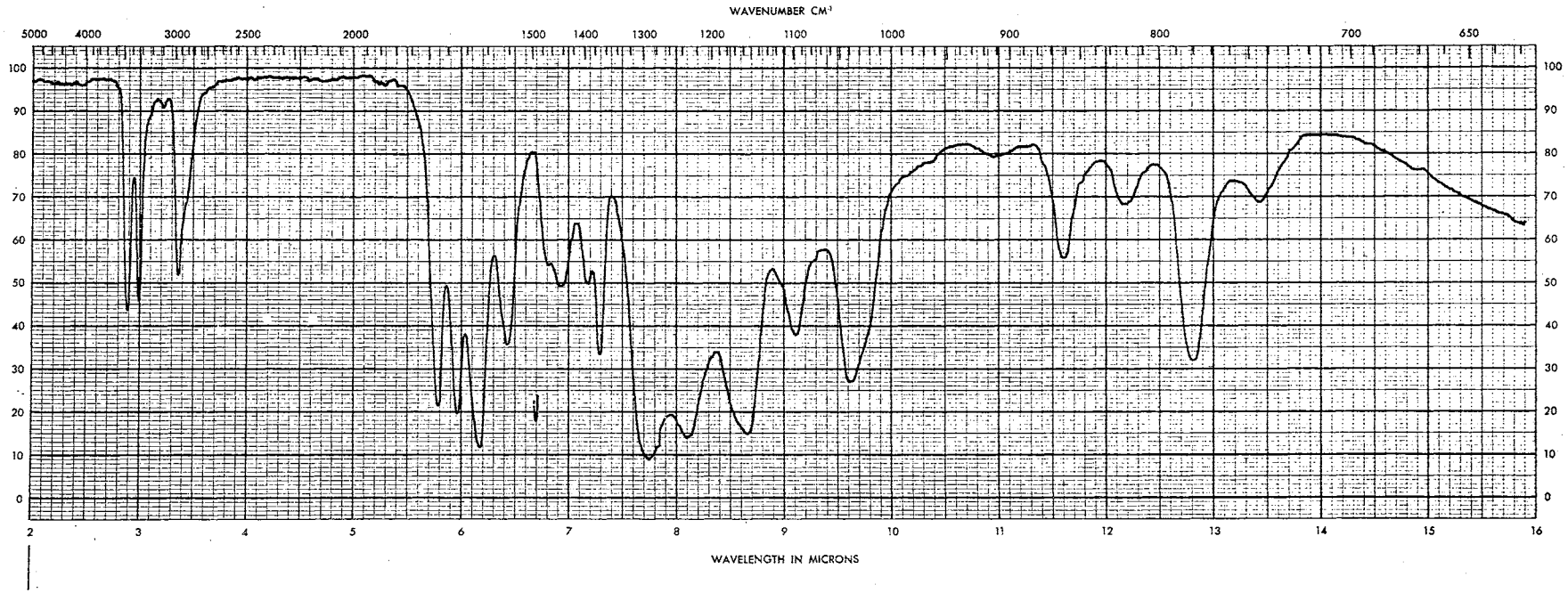
Dimethyl dl-Dibromosuccinate (XXXVa), KBr Pellet

Plate IX



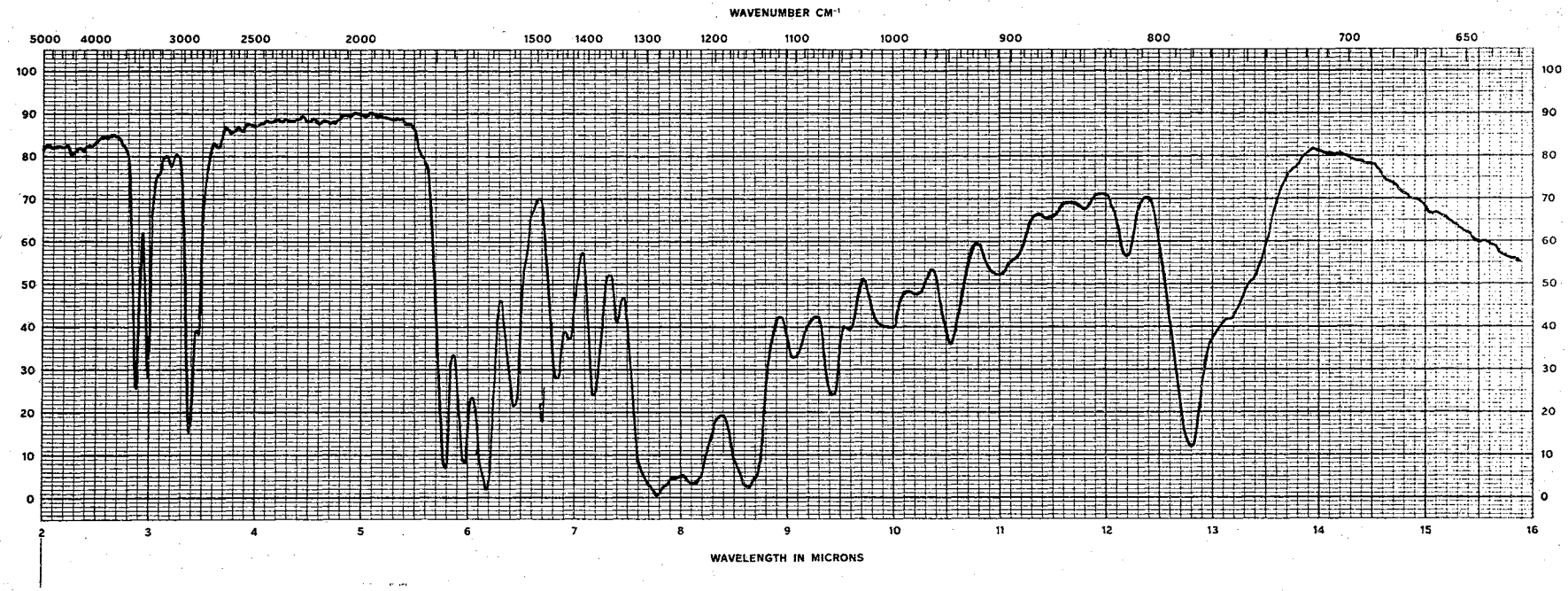
Dimethyl Aminofumarate (XLIa), Film on NaCl Plates

Plate X



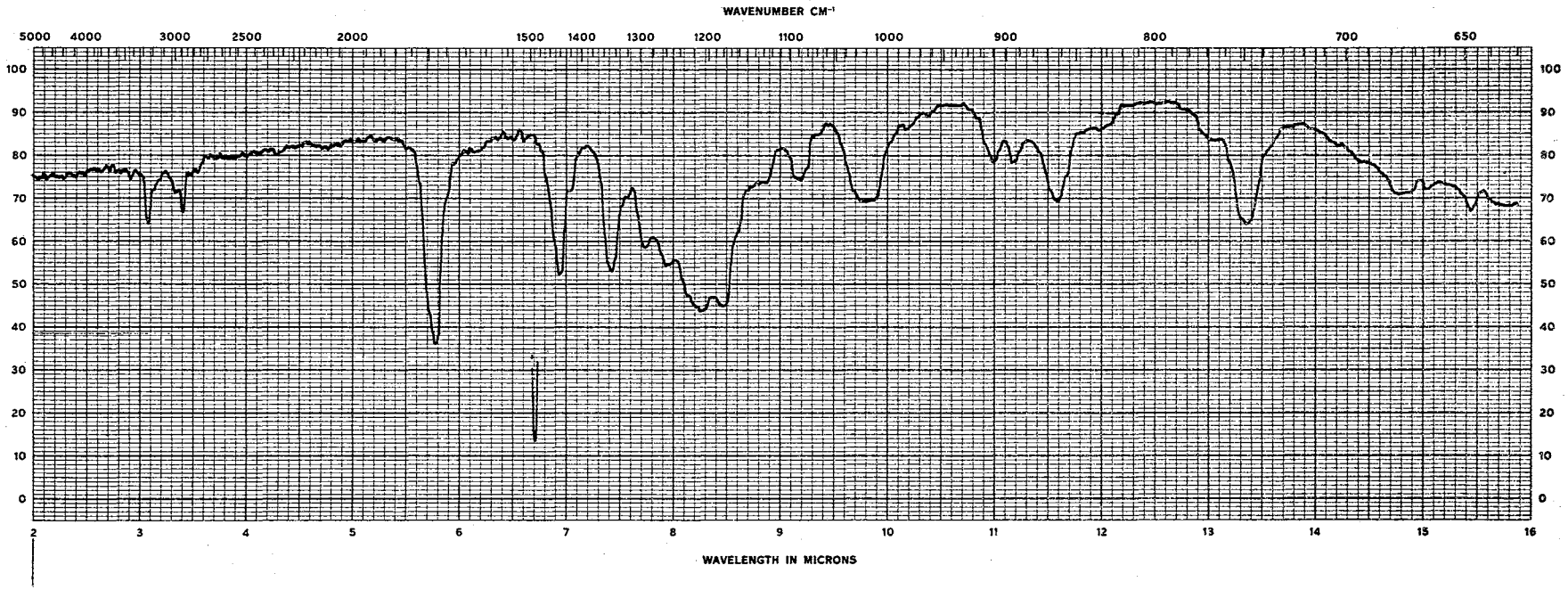
Diethyl Aminofumarate (XLIb), Film on NaCl Plates

Plate XI



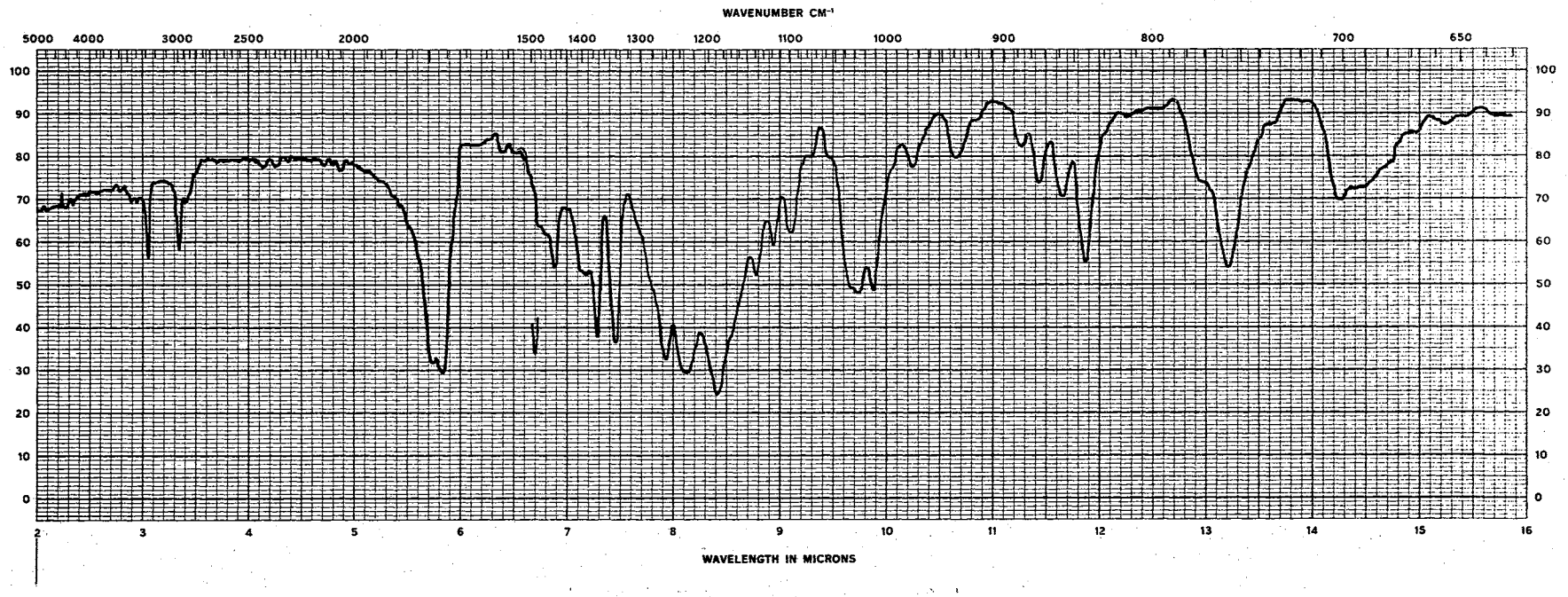
Di-n-propyl Aminofumarate (XLIc), Film on NaCl Plates

Plate XII



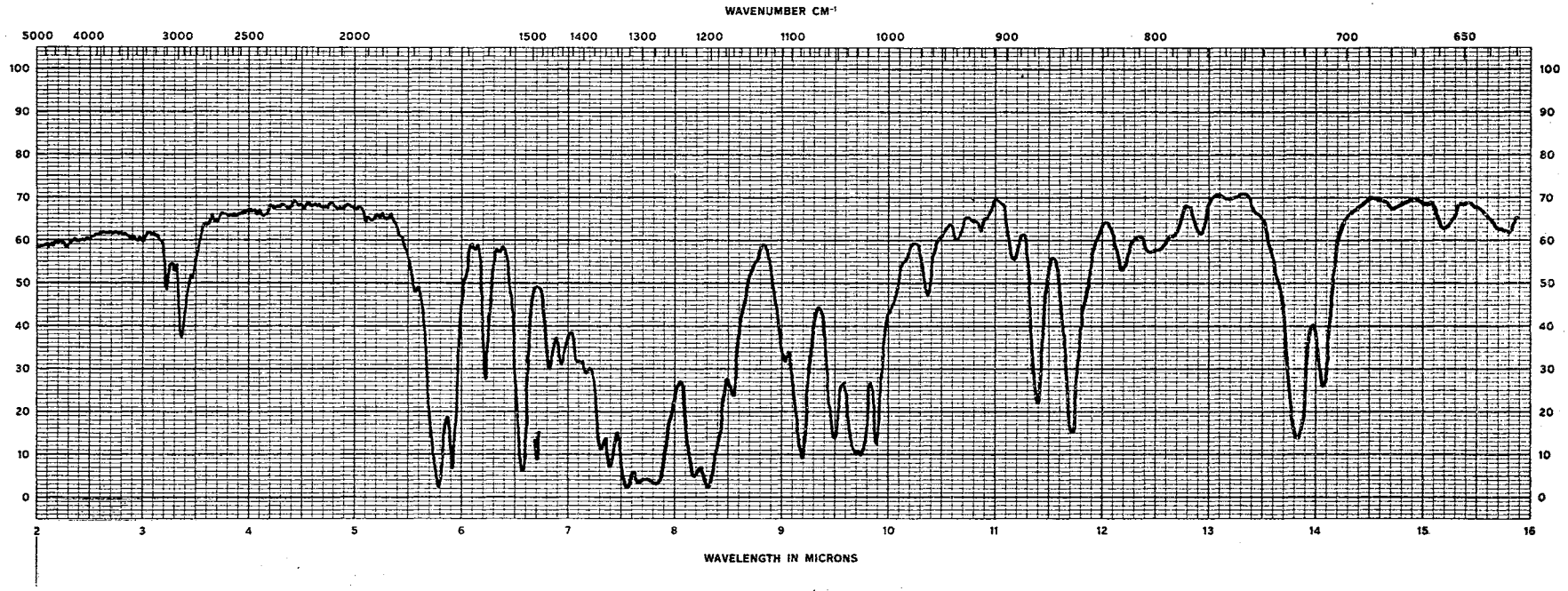
Dimethyl Aziridine-2,3-dicarboxylate (XLa), Film on NaCl Plates

Plate XIII



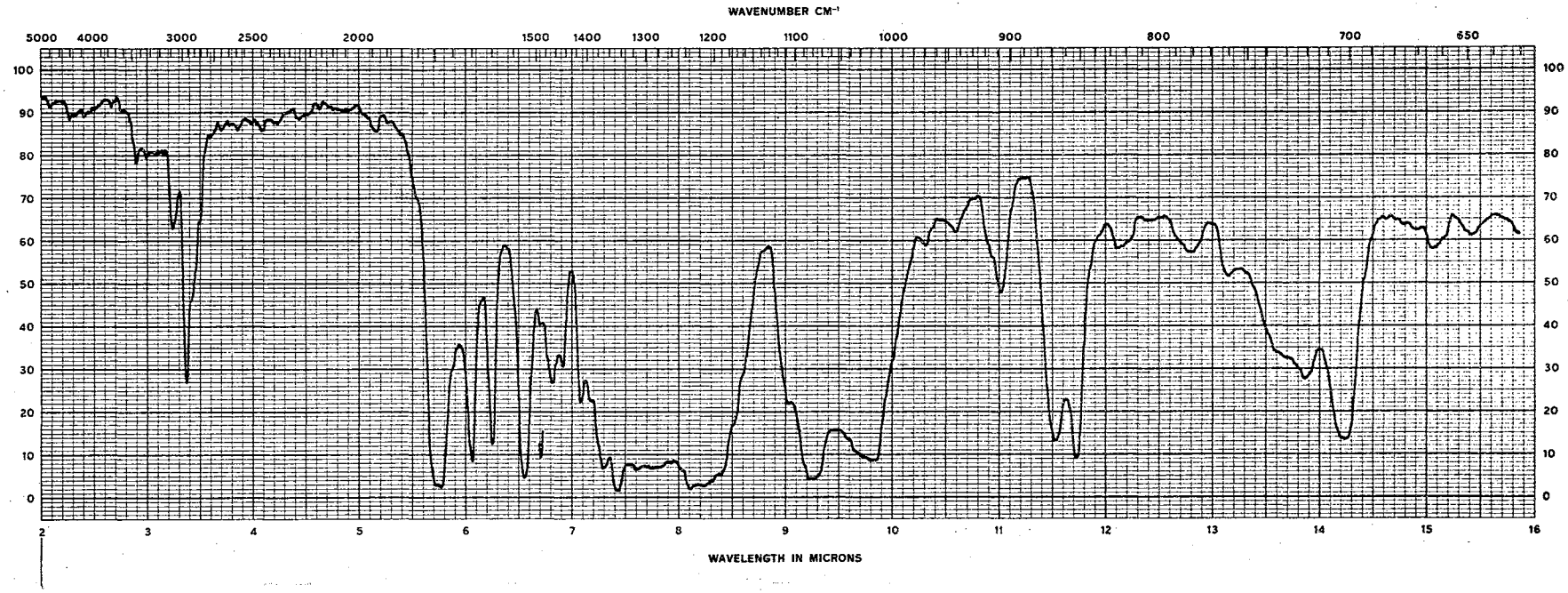
Diethyl Aziridine-2,3-dicarboxylate (XLb), KBr Pellet

Plate XIV



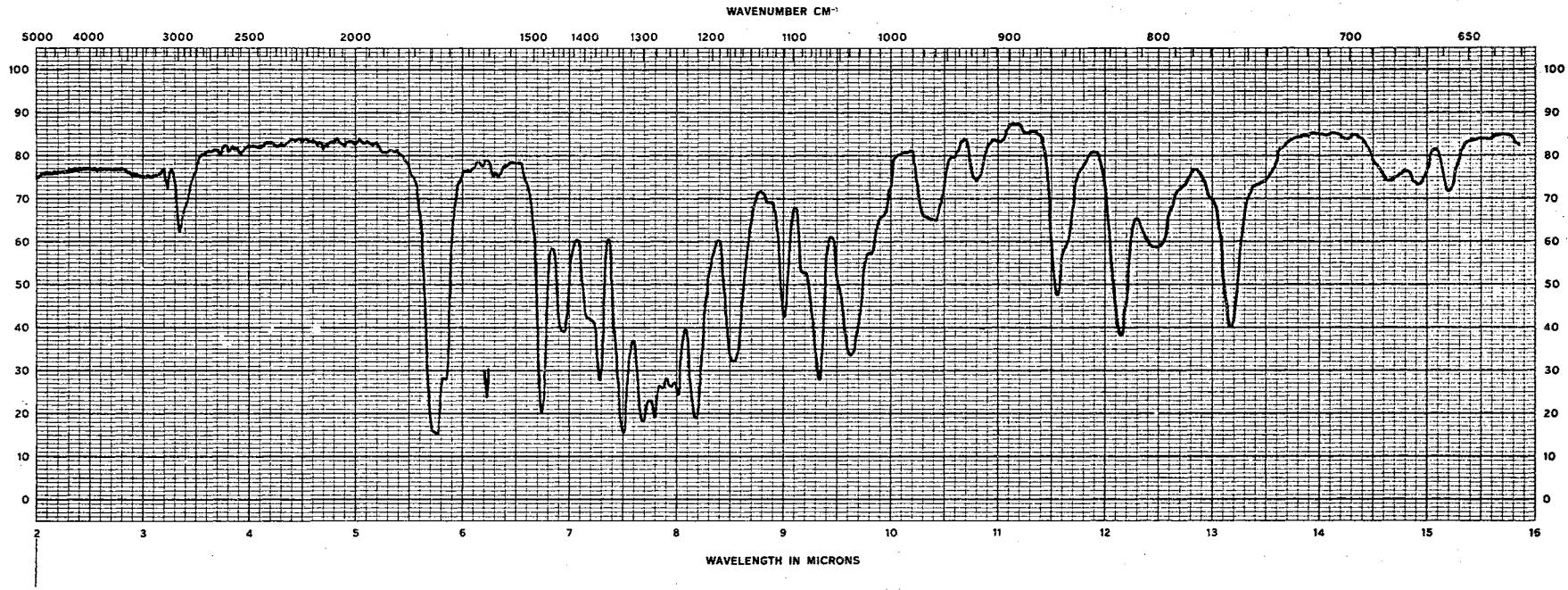
Diethyl 1-(p-Nitrobenzoyl)aziridine-2,3-dicarboxylate (XLIII), KBr Pellet

Plate XV



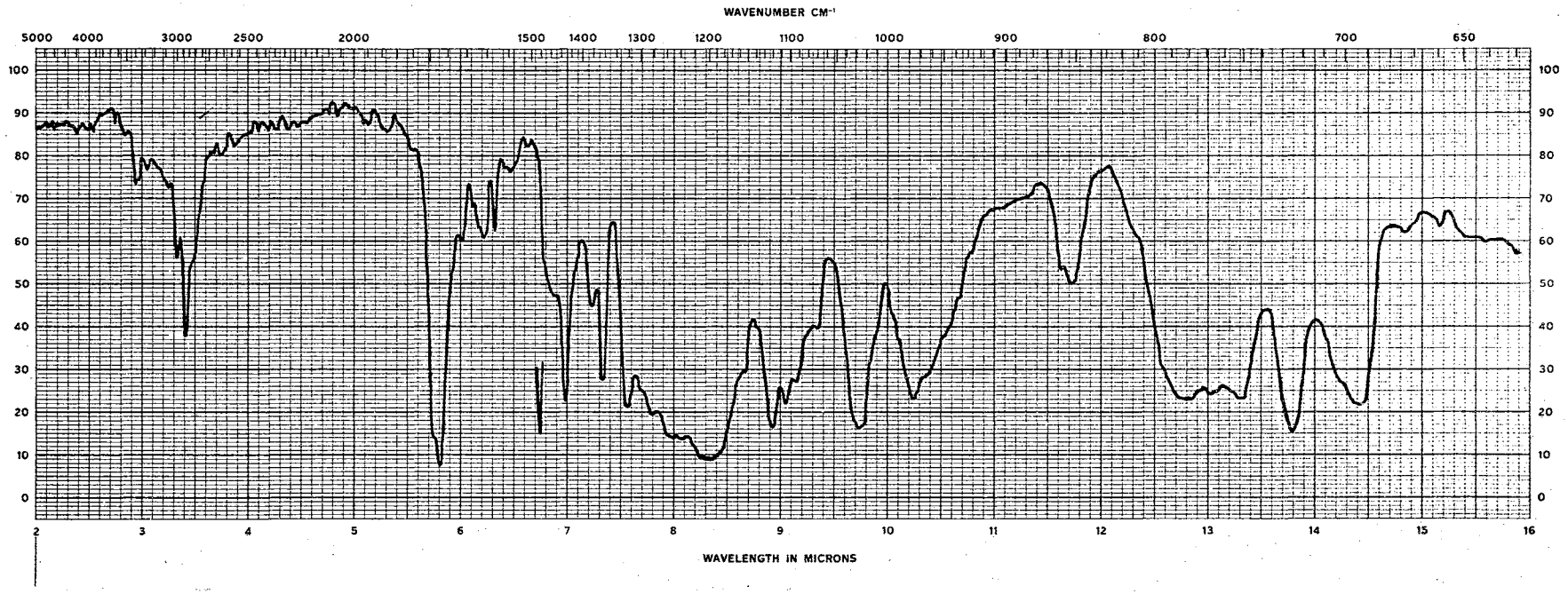
Diethyl 2-p-Nitrophenyl-2-oxazoline-2,3-dicarboxylate (L), Film on NaCl Plates

Plate XVI



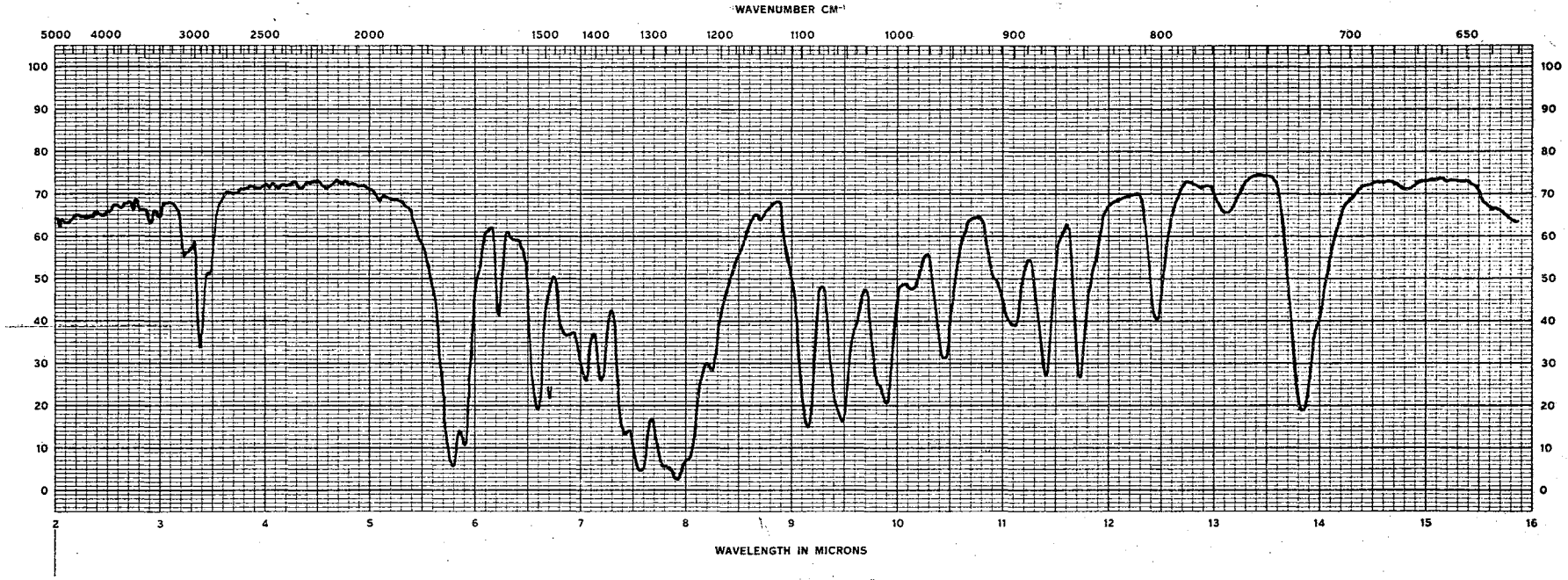
Diethyl 1-(2,4-Dichlorophenoxyacetyl)aziridine-2,3-dicarboxylate (XLVIII), KBr Pellet

Plate XVII



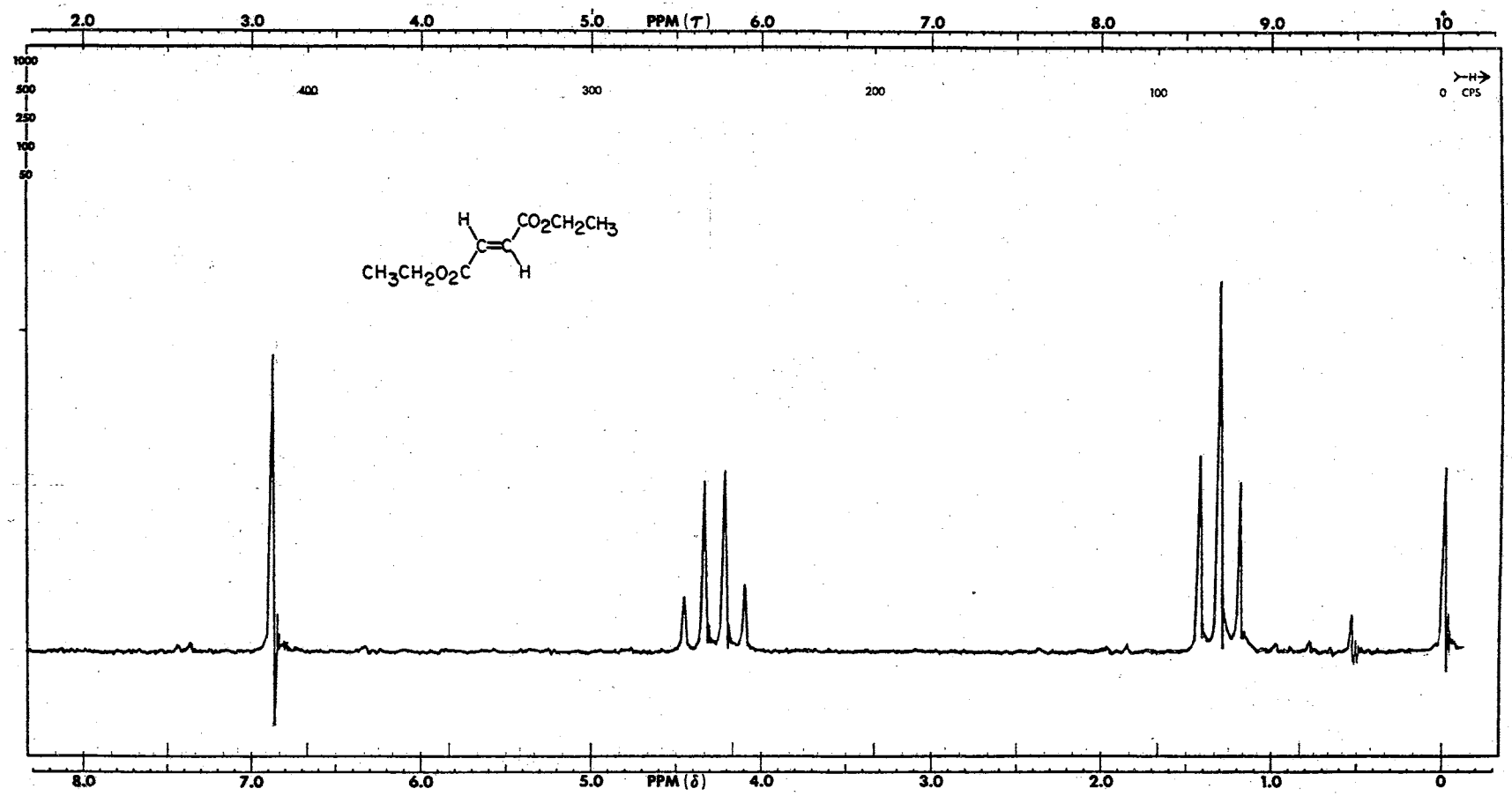
Diethyl 1-(Diphenylphosphinyl)aziridine-2,3-dicarboxylate (XLVII), Film on NaCl Plates

Plate XVIII



Di-n-propyl 1-(Nitrobenzoyl)aziridine-2,3-dicarboxylate (XLII), KBr Pellet

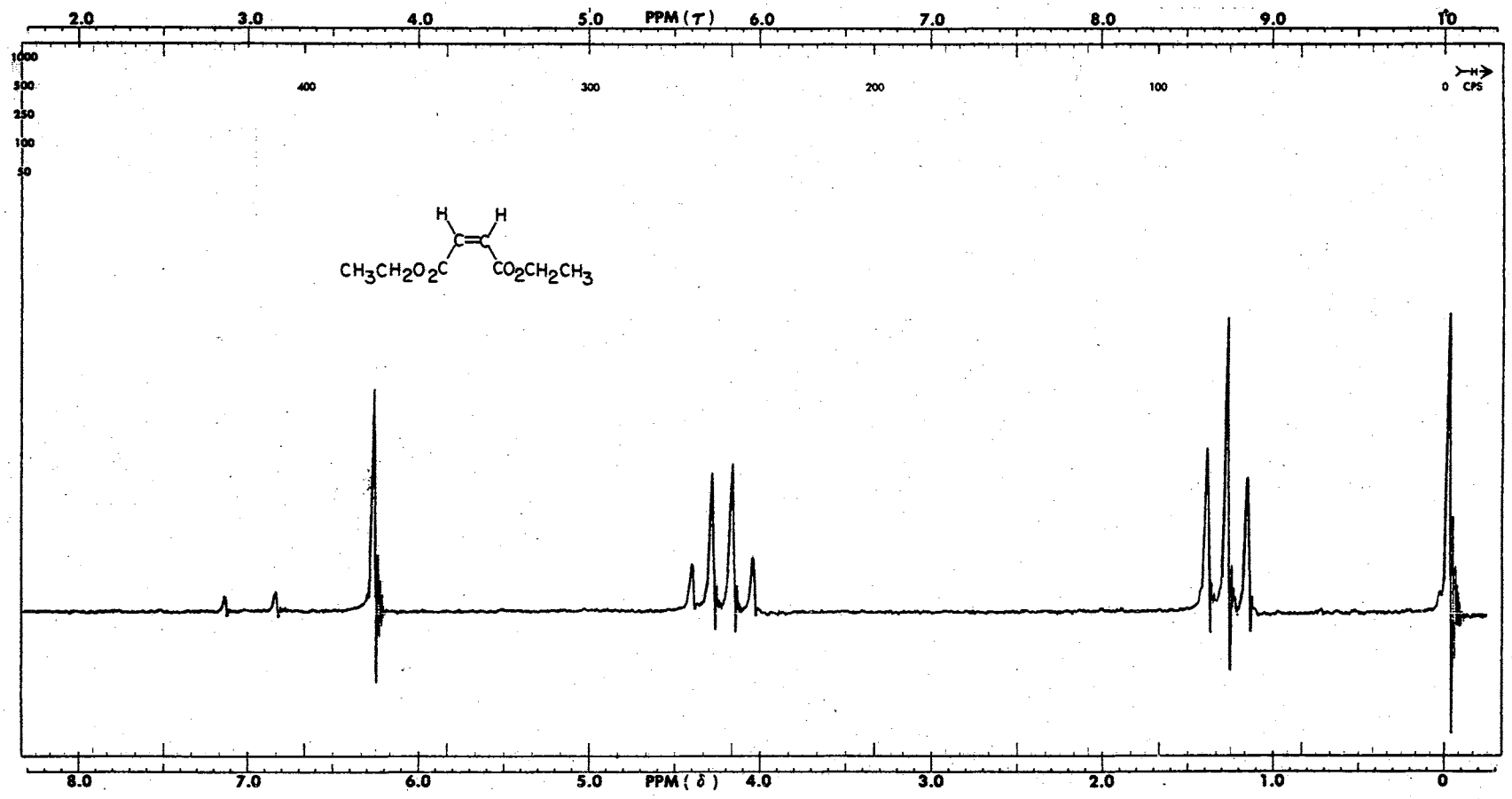
Plate XIX



Diethyl Fumarate (XXXVIIb)

Solvent.....$CDCl_3$	R.F. Field..0.05 mG	S.W.....500 cps	S.A.....2.5
F.B.....4.0 cps	S.T.....250 sec	S.O.....000 cps	I.A.....off

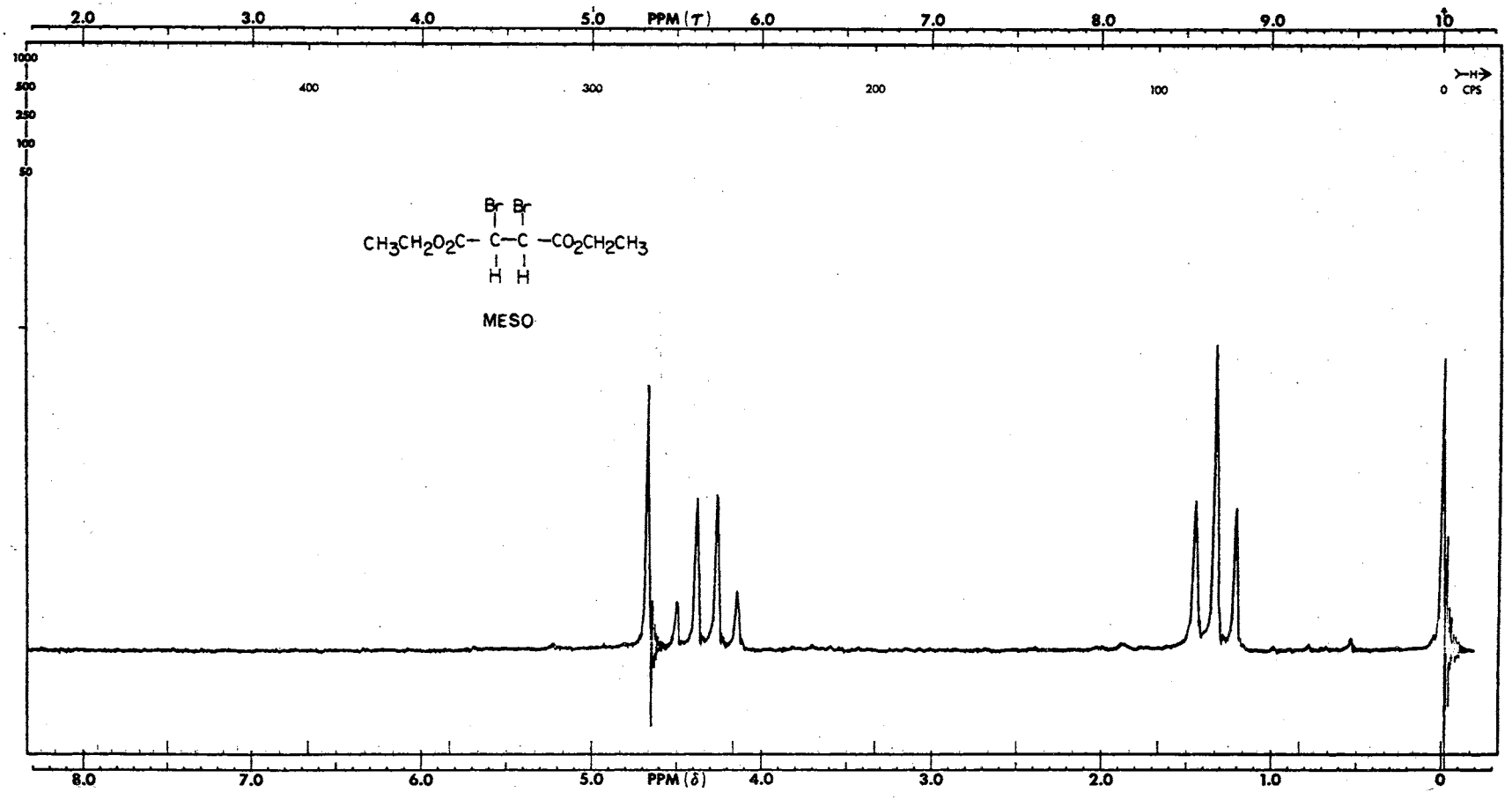
Plate XX



Diethyl Maleate (XXXIVb)

Solvent.....$CDCl_3$	R.F. Field..0.05 mG	S.W.....500 cps	S.A.....1.0
F.B.. . . . . 4 cps	S.T.....250 sec	S.O.....000 cps	I.A.....off

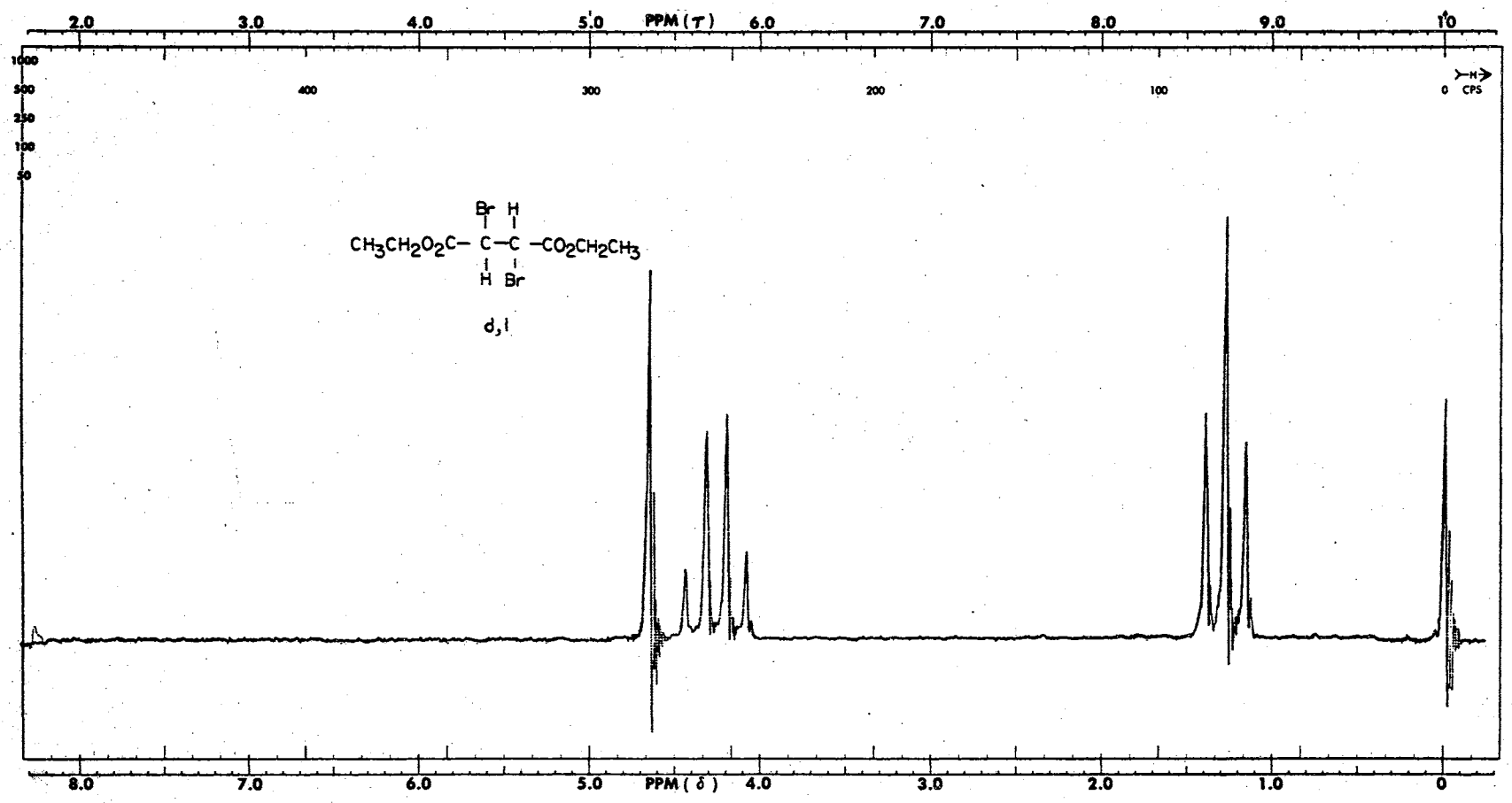
Plate XXI



Diethyl meso-Dibromosuccinate (XXXVIIIb)

Solvent.....$CDCl_3$	R.F. Field..0.05 mG	S.W.....500 cps	S.A.....1.6
F.B.....4.0 cps	S.T.....250 sec	S.O.....000 cps	I.A.....off

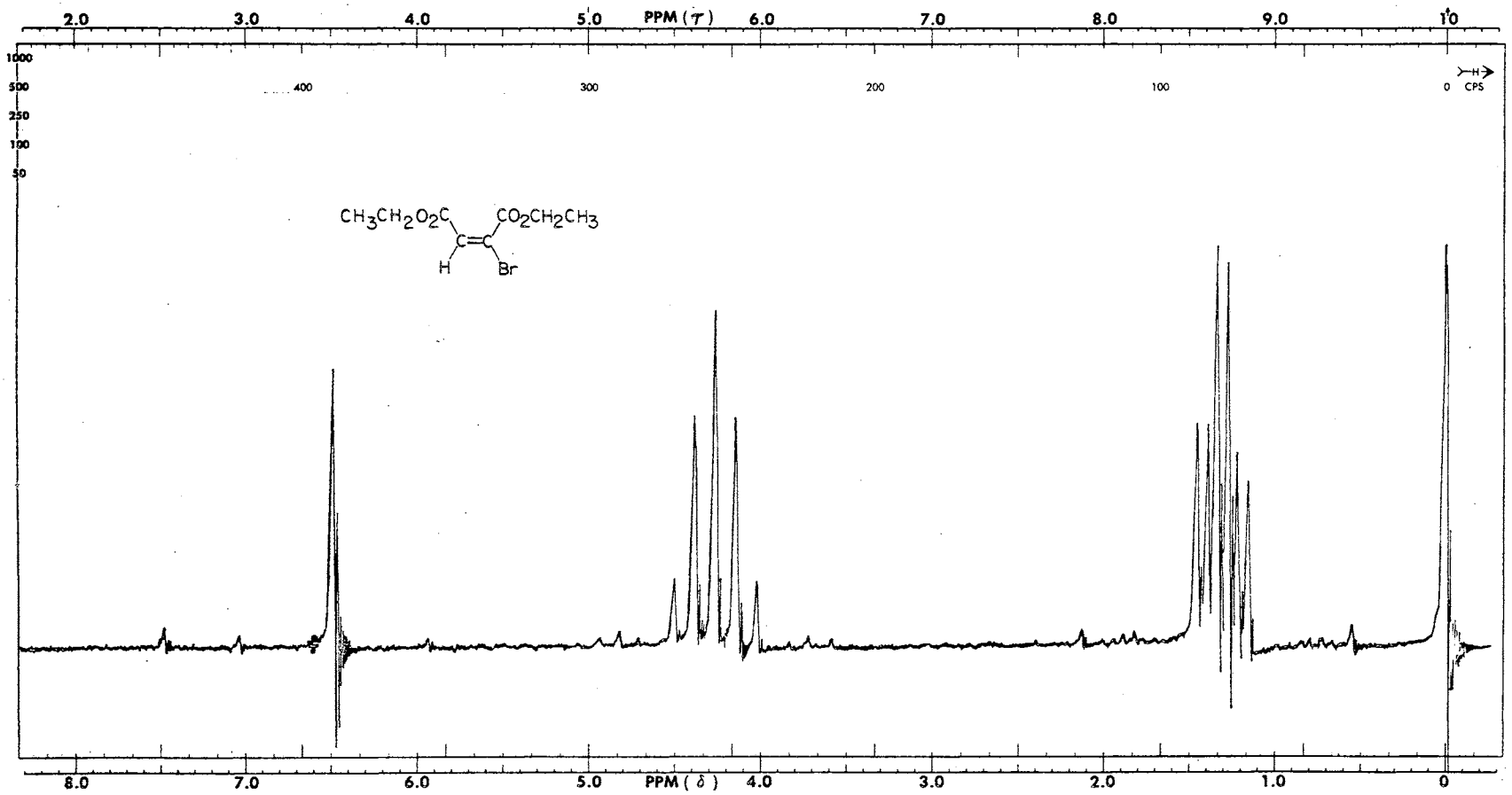
Plate XXII



Diethyl dl-Dibromosuccinate (XXXVb)

Solvent.....$CDCl_3$	R.F. Field..0.05 mG	S.W.....500 cps	S.A.....1.6
F.B.....4.0 cps	S.T.....250 sec	S.O.....000 cps	I.A.....off

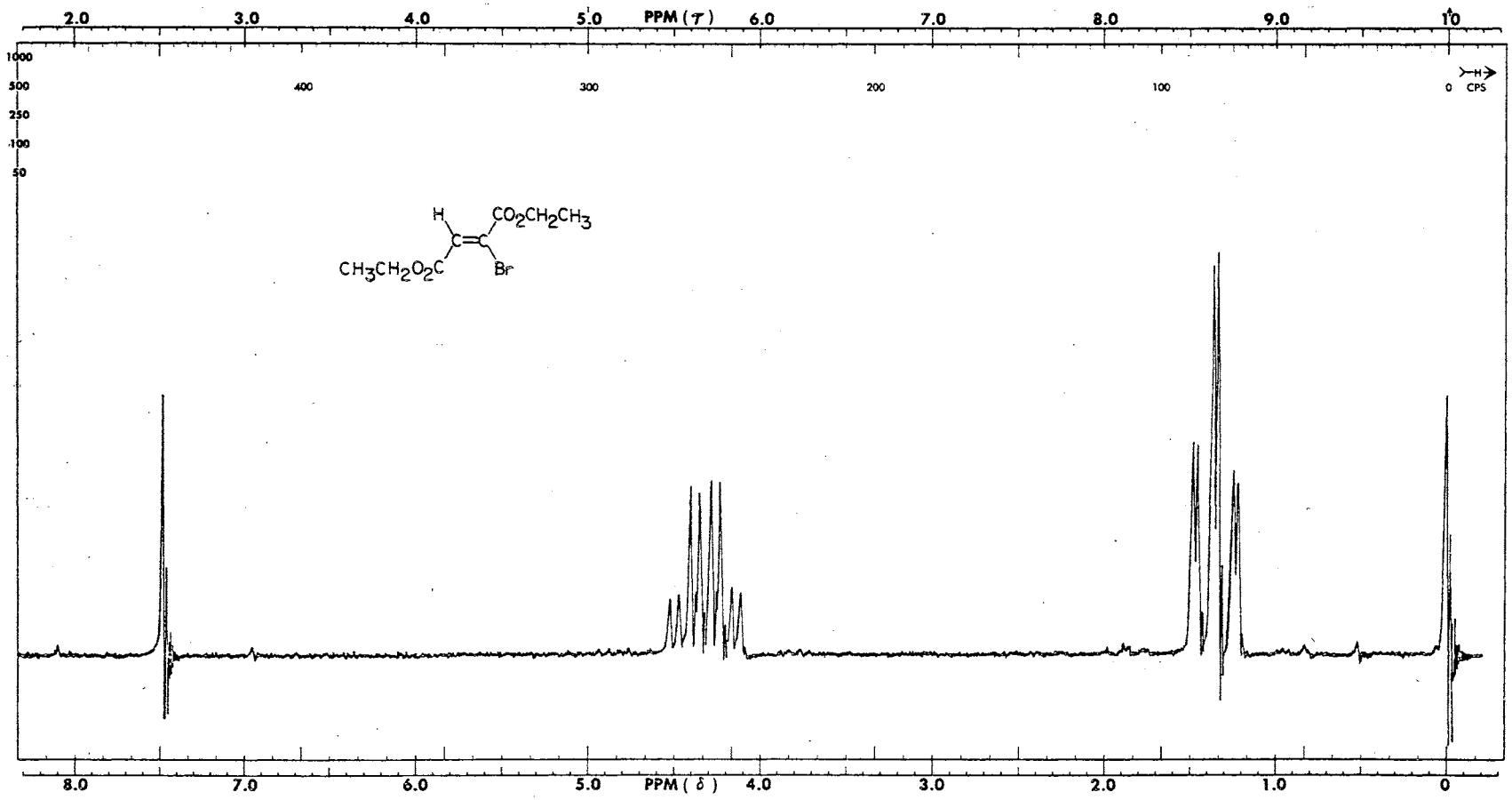
Plate XXIII



Diethyl Bromomaleate (XXXIXb)

Solvent.....$CDCl_3$ R.F. Field..0.05 mG S.W.....500 cps S.A.....2.0
F.B.....4.0 cps S.T.....250 sec S.O.....000 cps I.A.....off

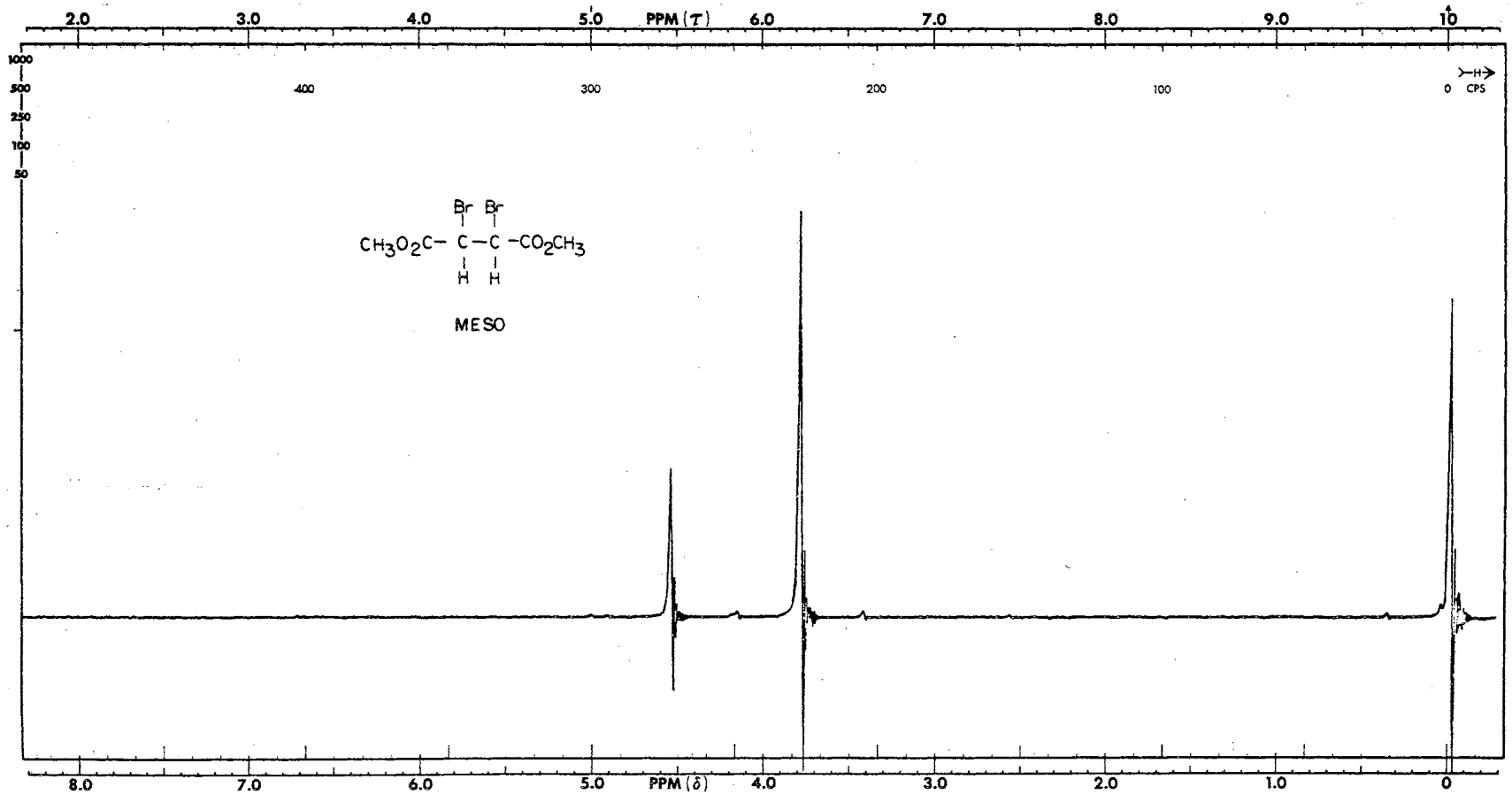
Plate XXIV



Diethyl Bromofumarate (XXXVIb)

Solvent.....$CDCl_3$	R.F. Field..0.05 mG	S.W.....500 cps	S.A.....2.0
F.B.....4.0 cps	S.T.....250 sec	S.O.....000 cps	I.A.....off

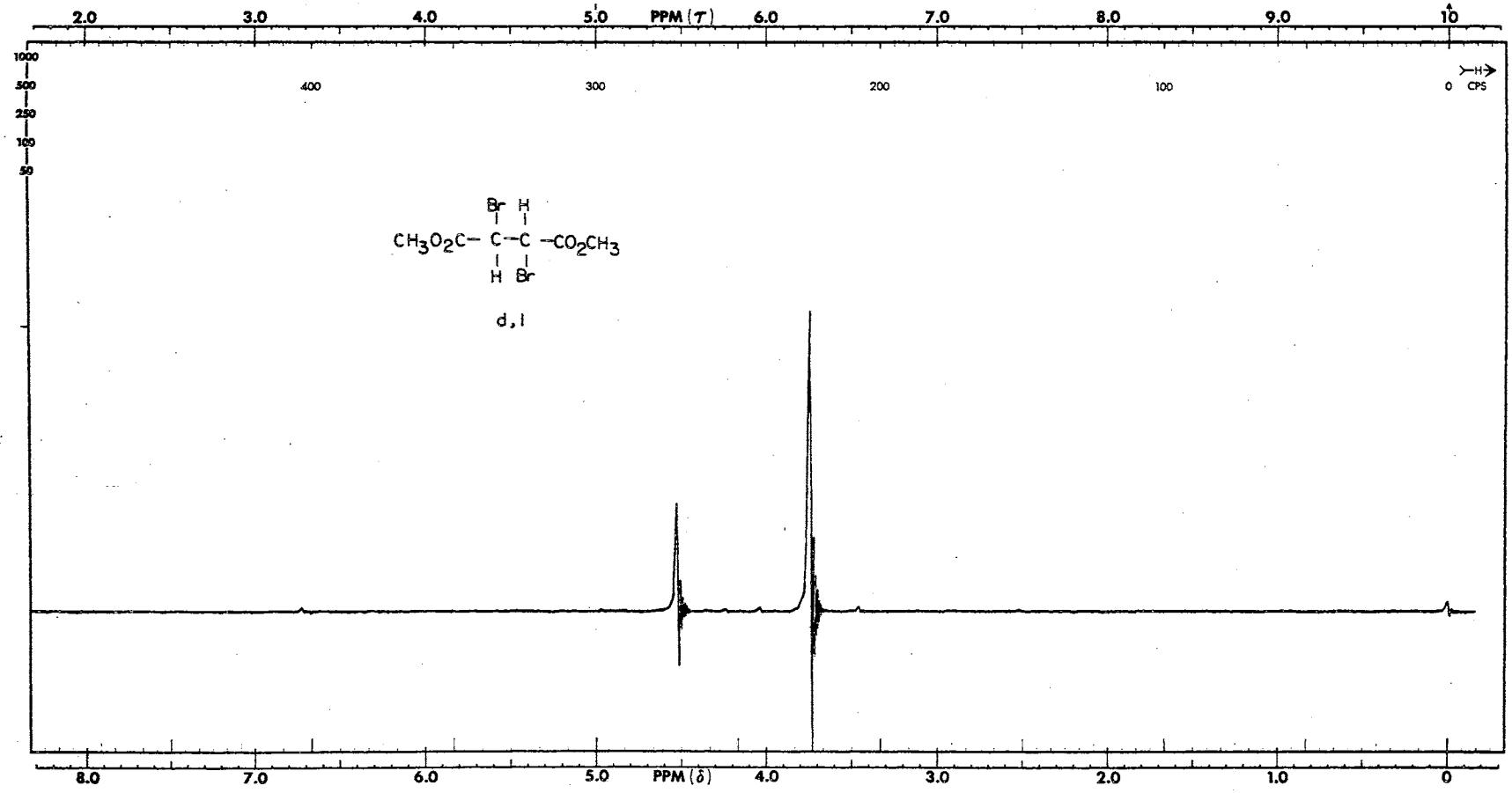
Plate XXV



Dimethyl meso-Dibromosuccinate (XXXVIIIa)

Solvent.....CCl_4	R.F. Field..0.05 mG	S.W.....500 cps	S.A.....1.0
F.B.....4.0 cps	S.T.....250 sec	S.O.....000 cps	I.A.....off

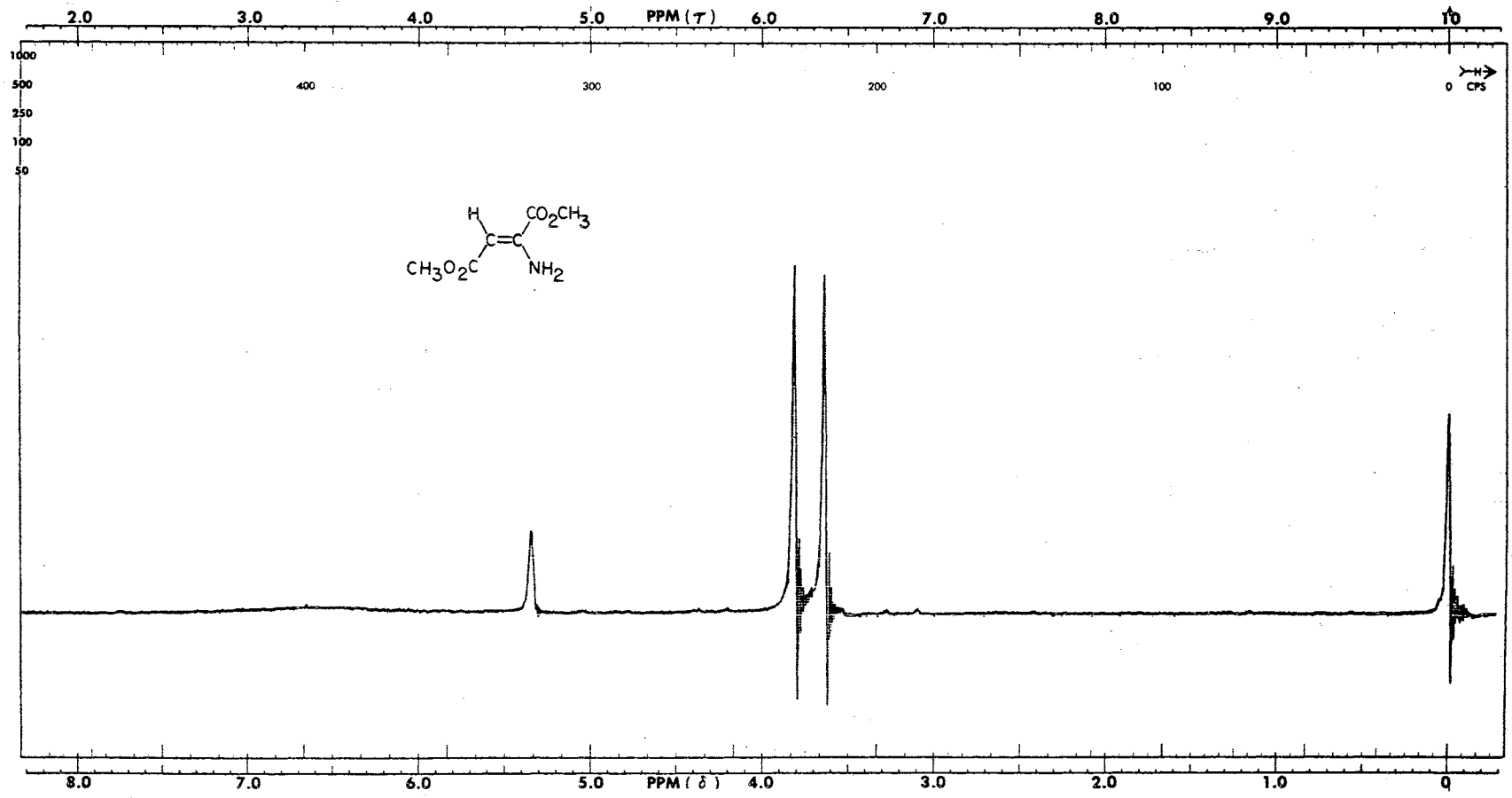
Plate XXVI



Dimethyl dl-Dibromosuccinate (XXXVa)

Solvent.....CCl_4	R.F. Field..0.05 mG	S.W.....500 cps	S.A.....0.4
F.B.....4.0 cps	S.T.....250 sec	S.O.....000 cps	I.A.....off

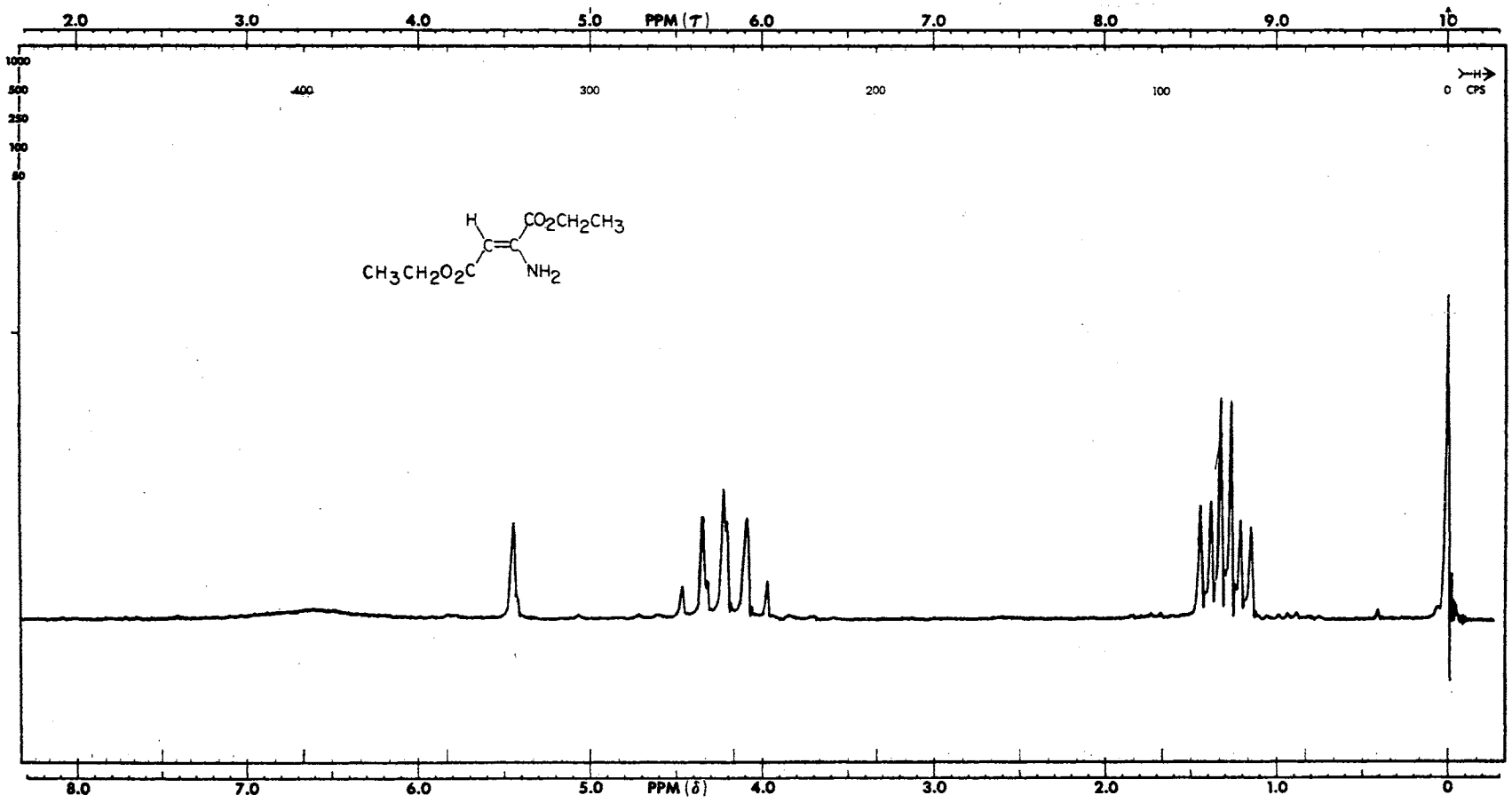
Plate XXVII



Dimethyl Aminofumarate (XLIa)

Solvent.....CCl_4 R.F. Field..0.05 mG S.W.....500 cps S.A.....1.6
F.B.....4.0 cps S.T.....250 sec S.O.....000 cps I.A.....off

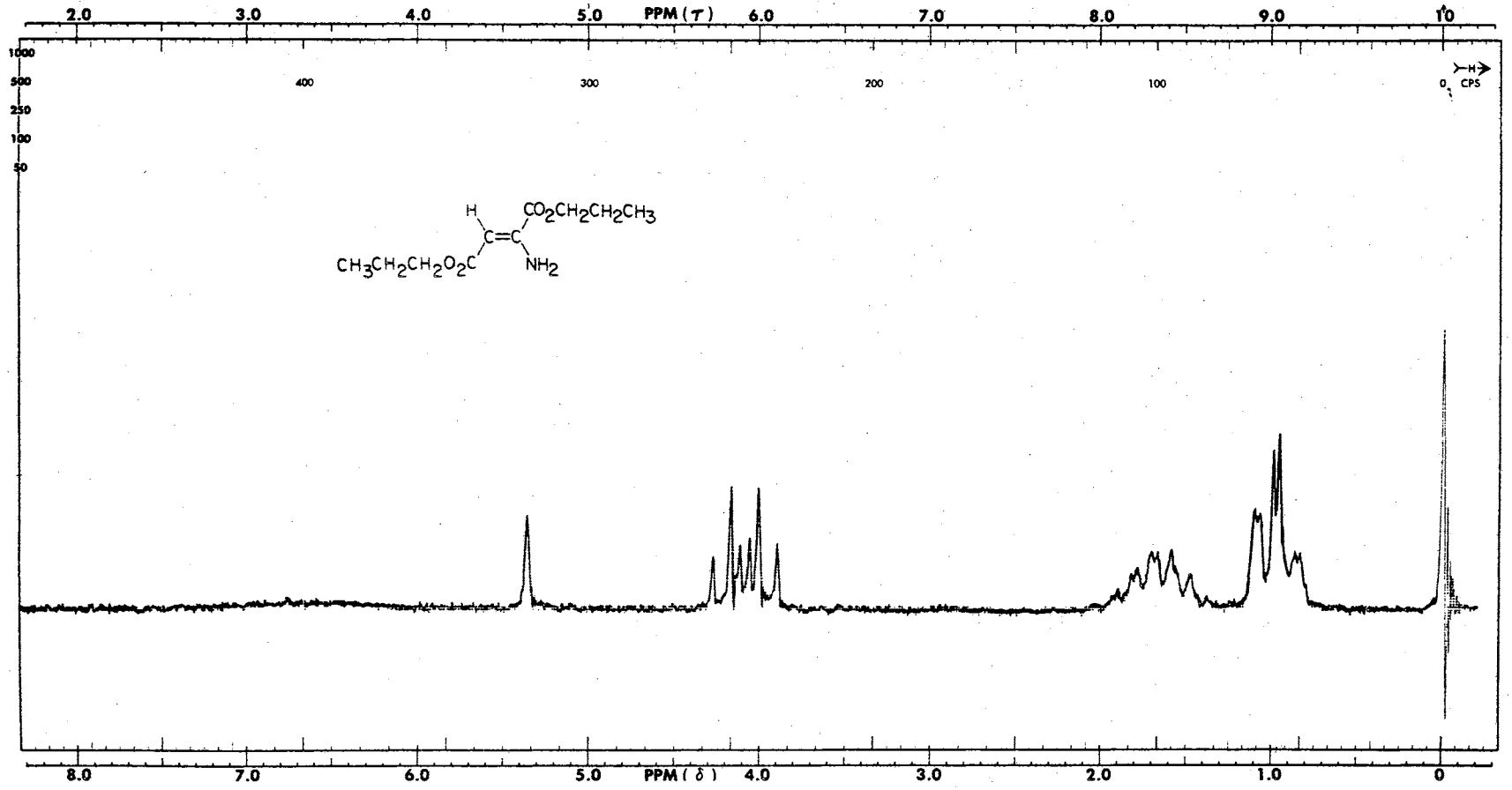
Plate XXVIII



Diethyl Aminofumarate (XLIb)

Solvent.....$CDCl_3$ R.F. Field..0.05 mG S.W.....500 cps S.A.....1.2
F.B.....4.0 cps S.T.....250 sec S.O.....000 cps I.A.....off

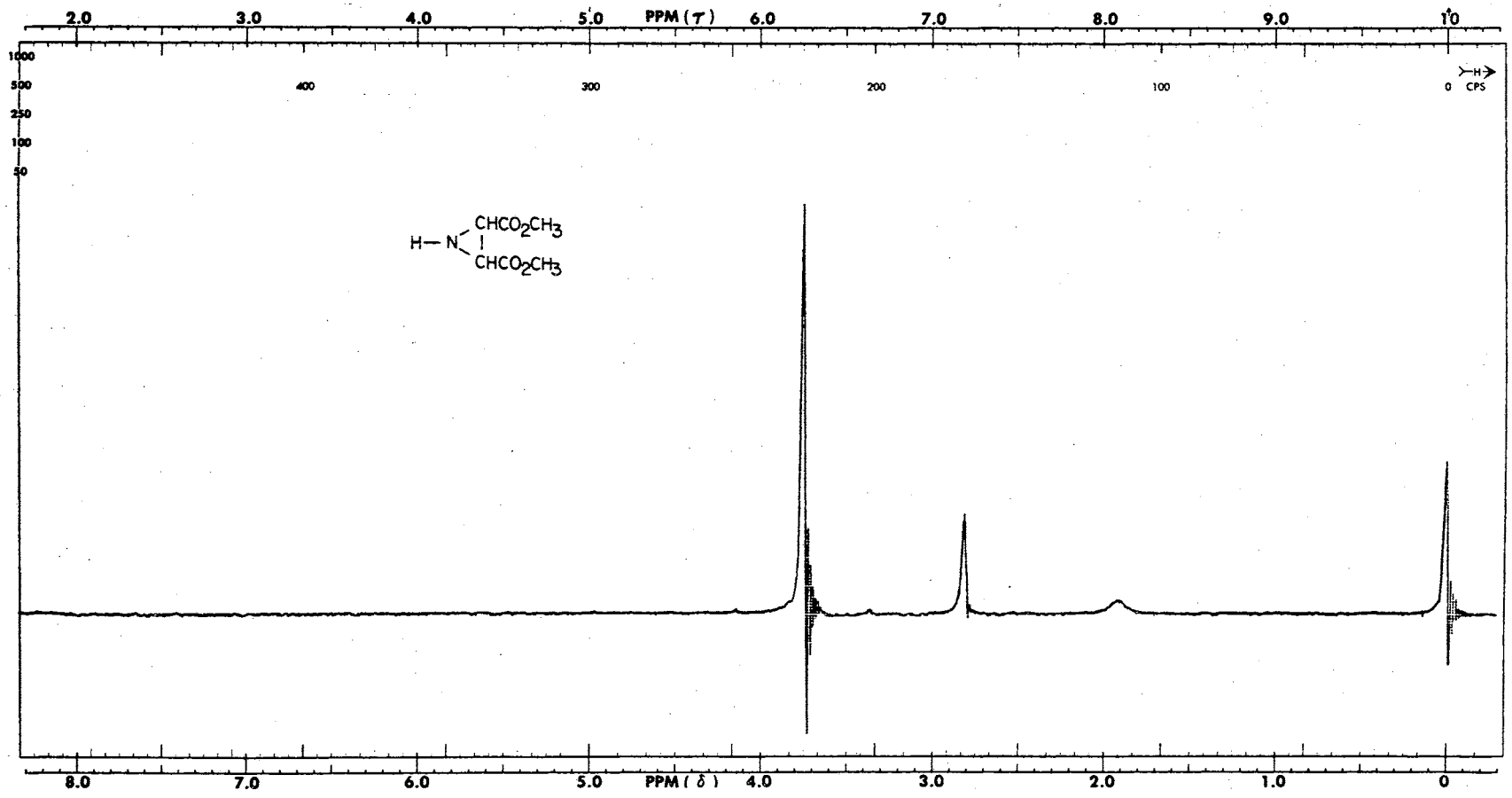
Plate XXIX



Di-n-propyl Aminofumarate (XLIc)

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

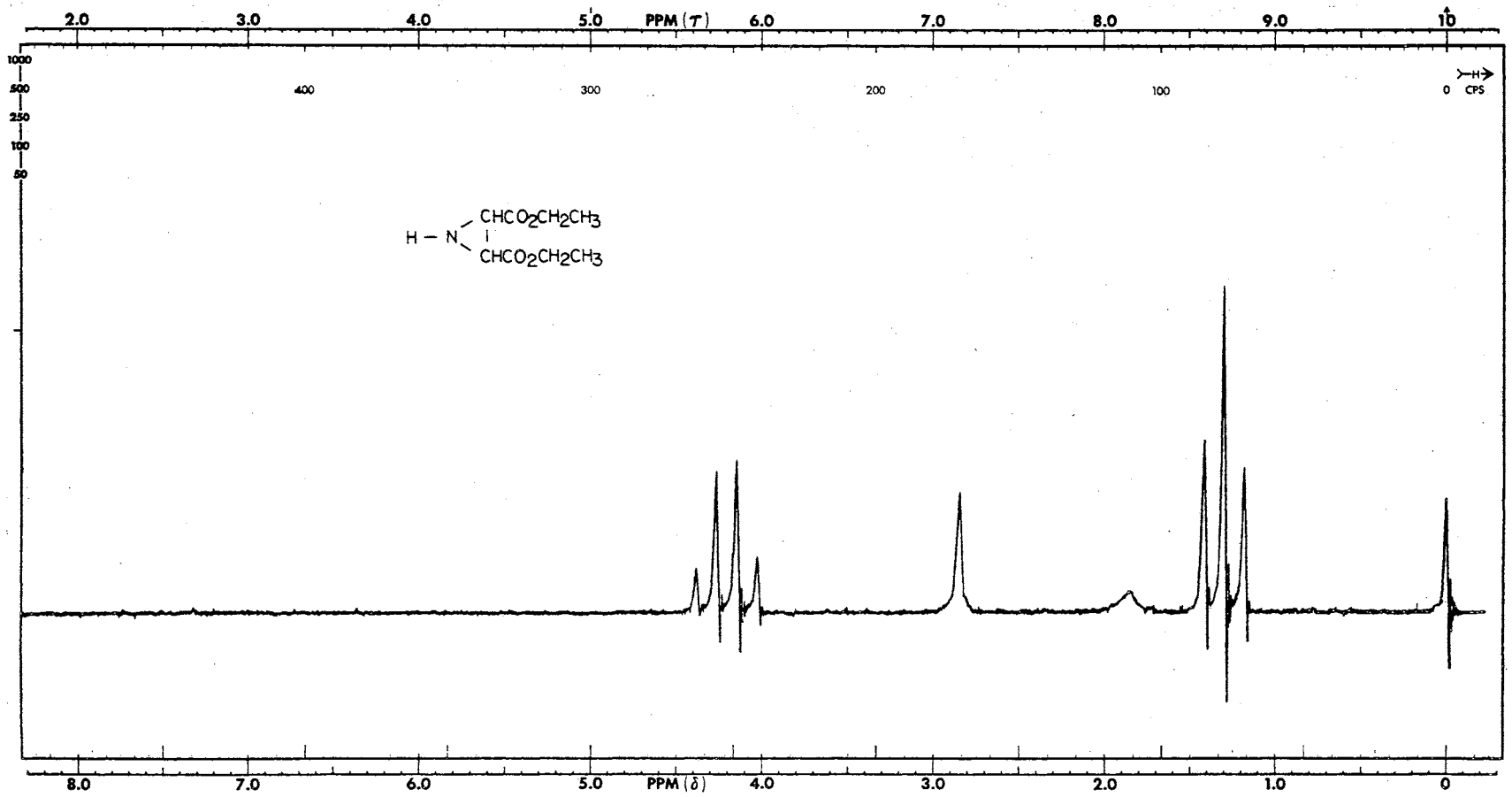
Plate XXX



Dimethyl Aziridine-2,3-dicarboxylate (XLa)

Solvent.....CCl_4	R.F. Field..0.05 mG	S.W.....500 cps	S.A.....1.6
F.B.....4.0 cps	S.T.....250 sec	S.O.....000 cps	I.A.....off

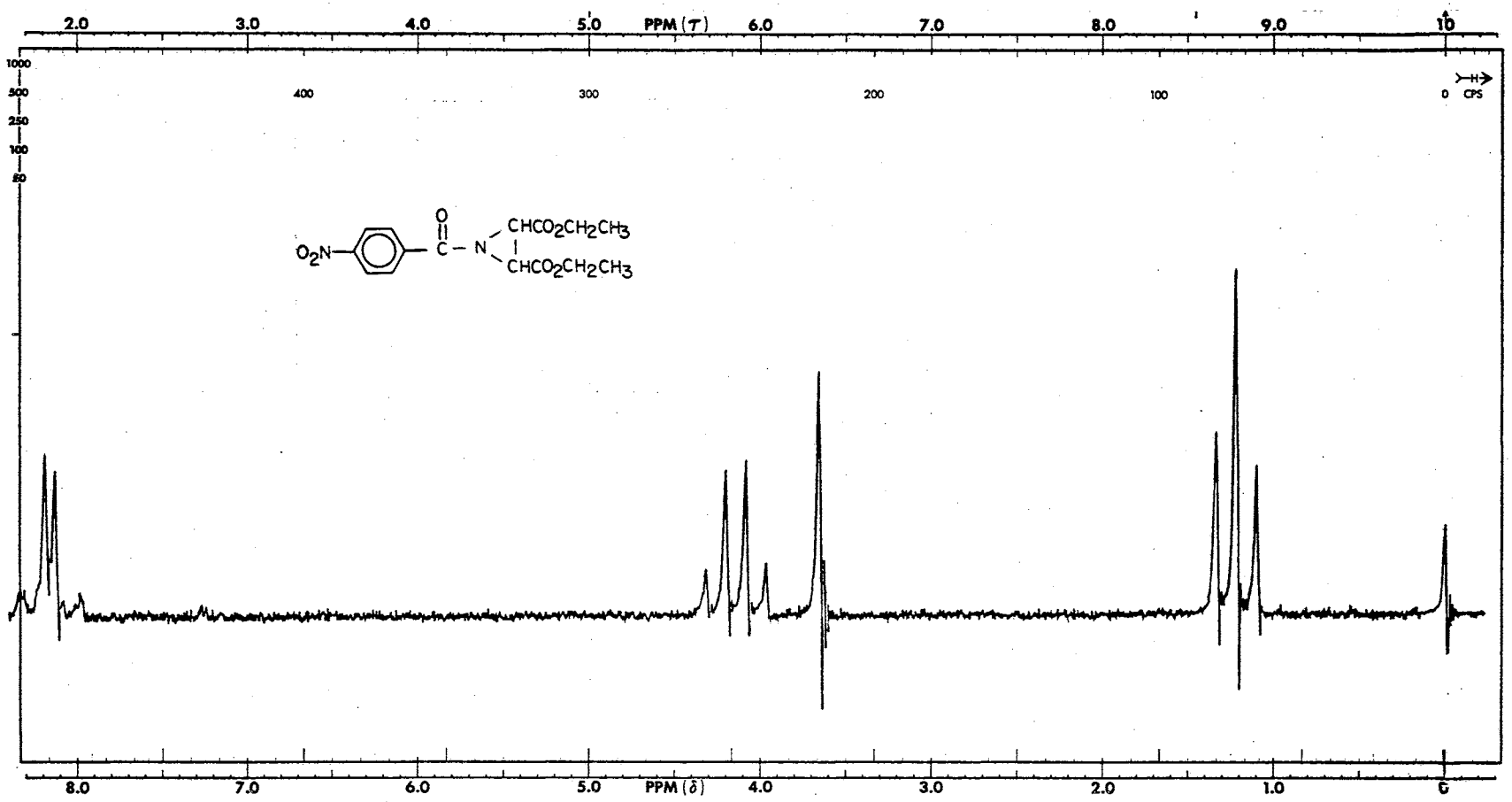
Plate XXXI



Diethyl Aziridine-2,3-dicarboxylate (XLb)

Solvent.....$CDCl_3$	R.F. Field..0.034 mG	S.W.....500 cps	S.A.....3.2
F.B.....4.0 cps	S.T.....250 sec	S.O.....000 cps	I.A.....off

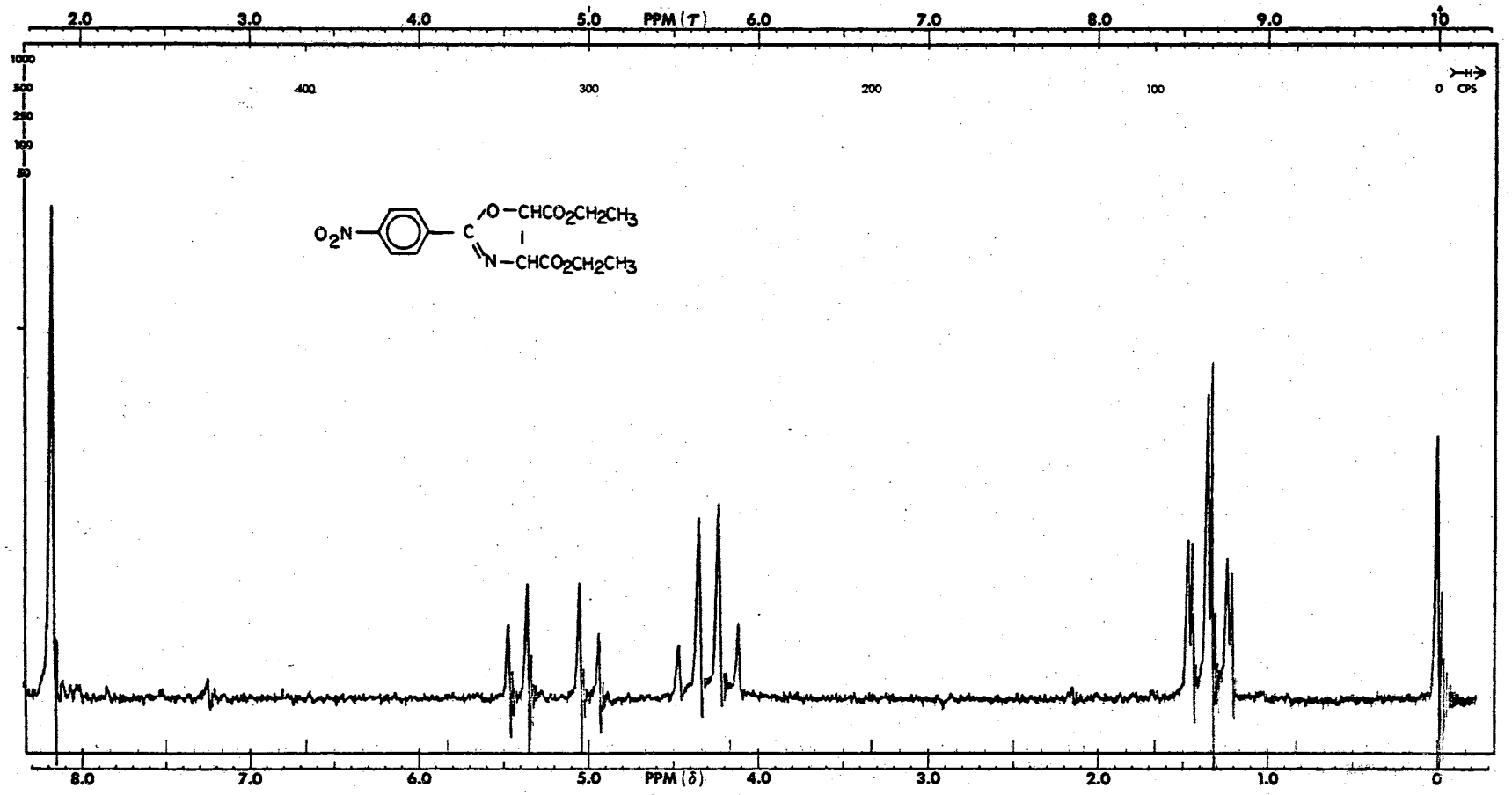
Plate XXXII



Diethyl 1-(p-Nitrobenzoyl)aziridine-2,3-dicarboxylate (XLIII)

Solvent.....$CDCl_3$	R.F. Field..0.033 mG	S.W.....500 cps	S.A.....6.3
F.B.....4.0 cps	S.T.....250 sec	S.O.....000 cps	I.A.....off

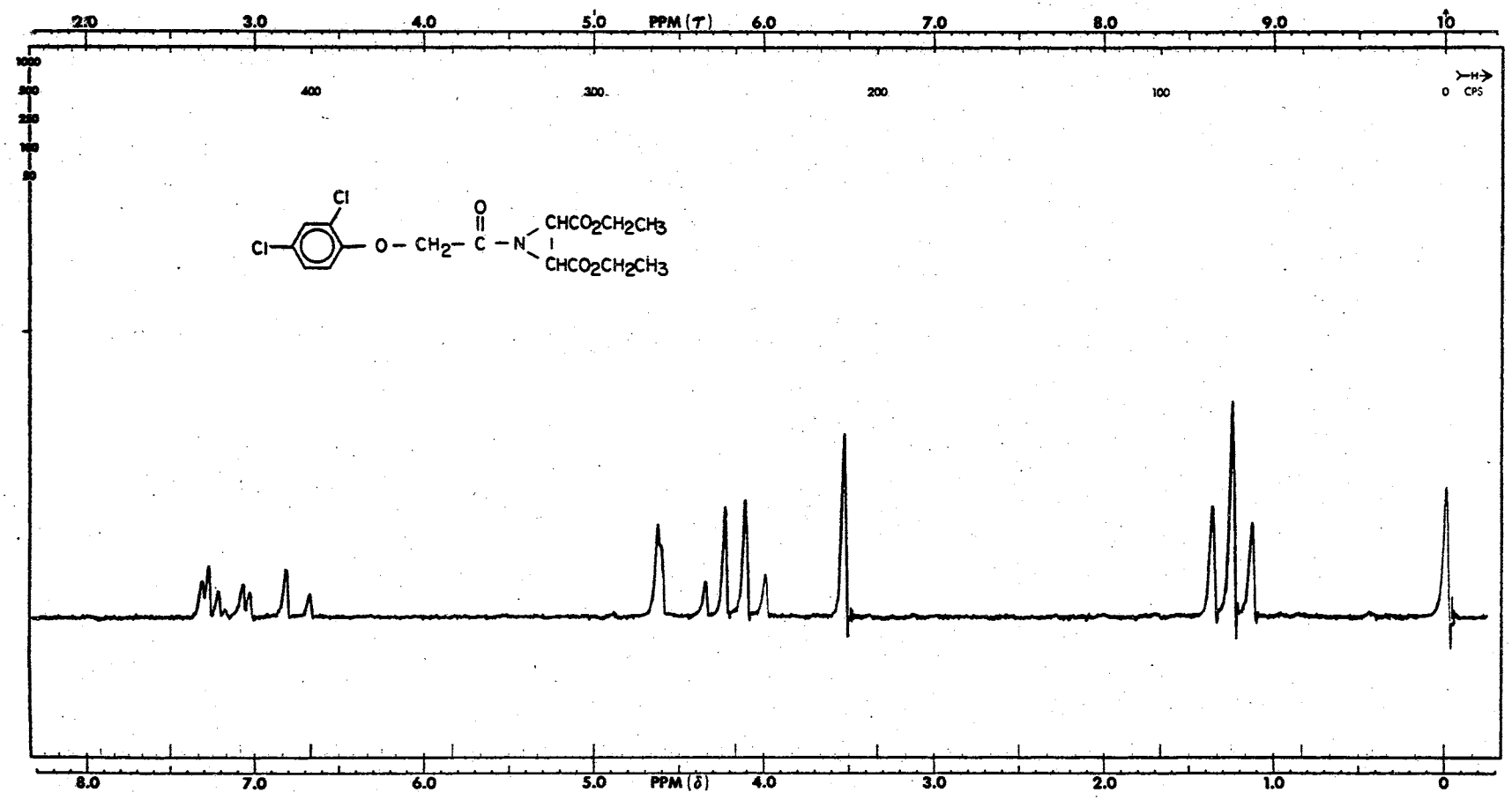
Plate XXXIII



Diethyl 2-p-Nitrophenyl-2-oxazoline-4,5-dicarboxylate (L)

Solvent.....$CDCl_3$	R.F. Field..0.02 mG	S.W.....500 cps	S.A.....6.3
F.B.....4.0 cps	S.T.....250 sec	S.O.....000 cps	I.A.....off

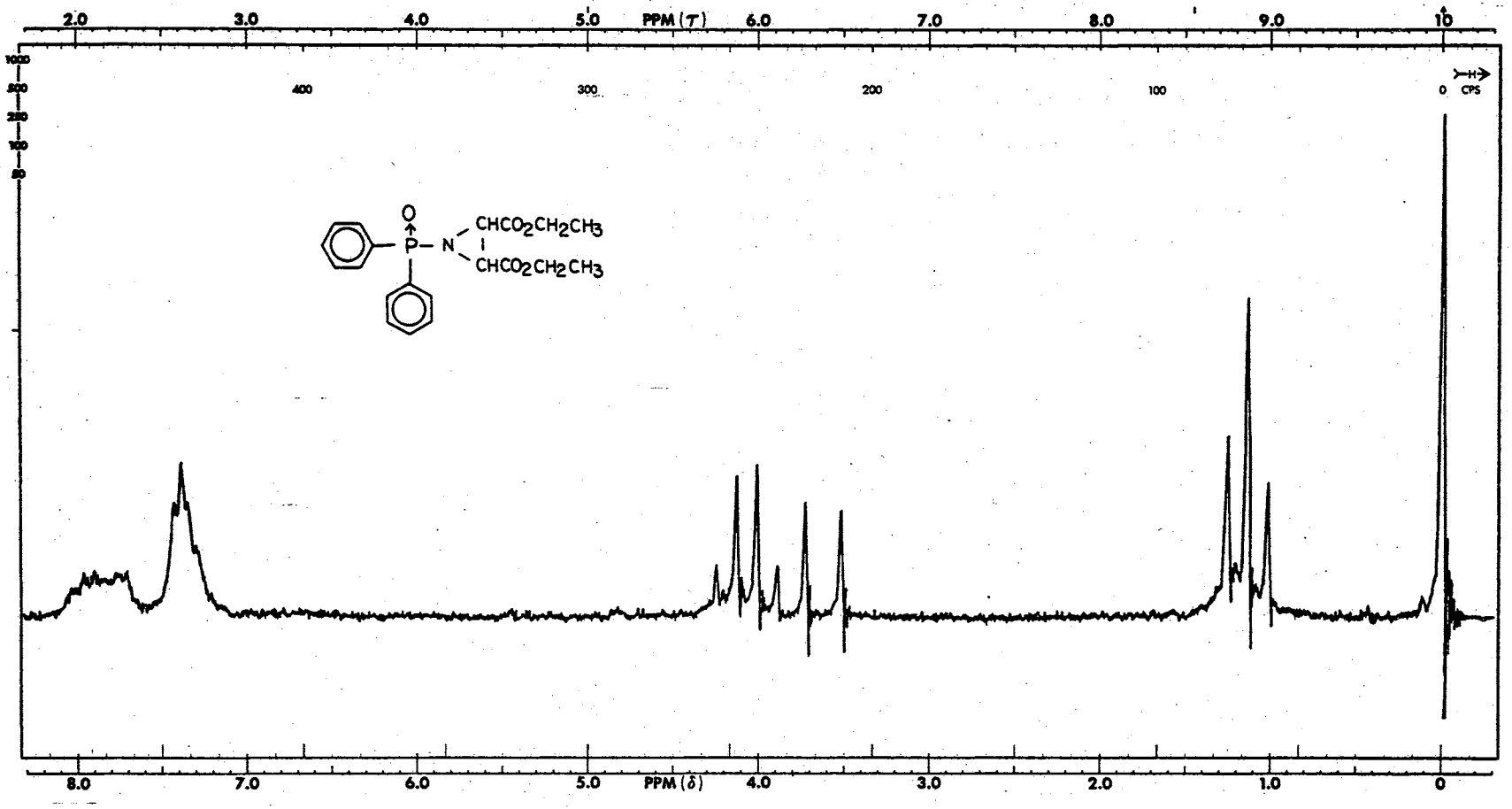
Plate XXXIV



Diethyl 1-(2,4-Dichlorophenoxyacetyl)aziridine-2,3-dicarboxylate (XLVIII)

Solvent.....$CDCl_3$	R.F. Field..0.05 mG	S.W.....500 cps	S.A.....3.2
F.B.....4.0 cps	S.T.....250 sec	S.O.....000 cps	I.A.....off

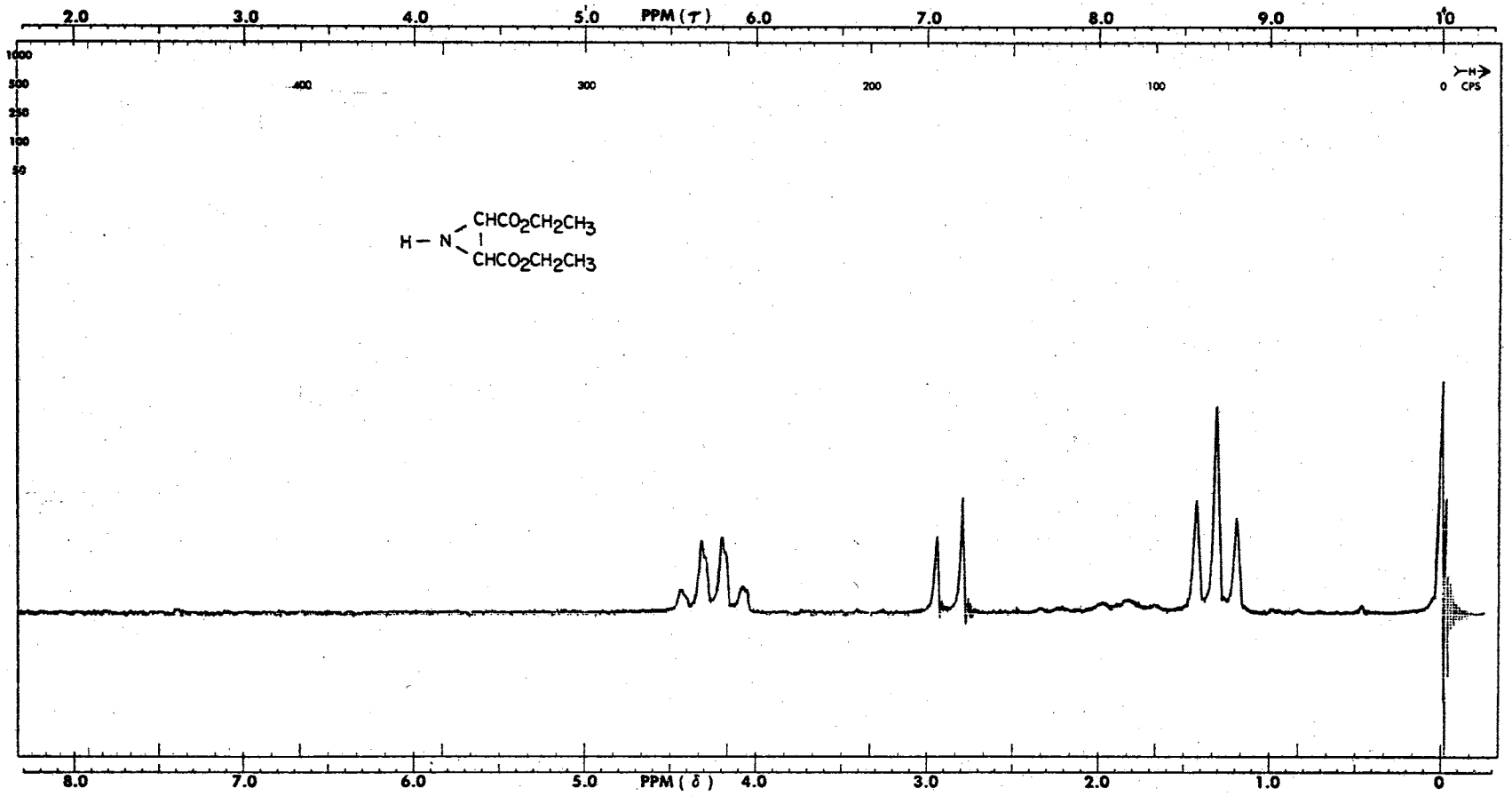
Plate XXXV



Diethyl 1-(Diphenylphosphinyl)aziridine-2,3-dicarboxylate (XLVII), Crude

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

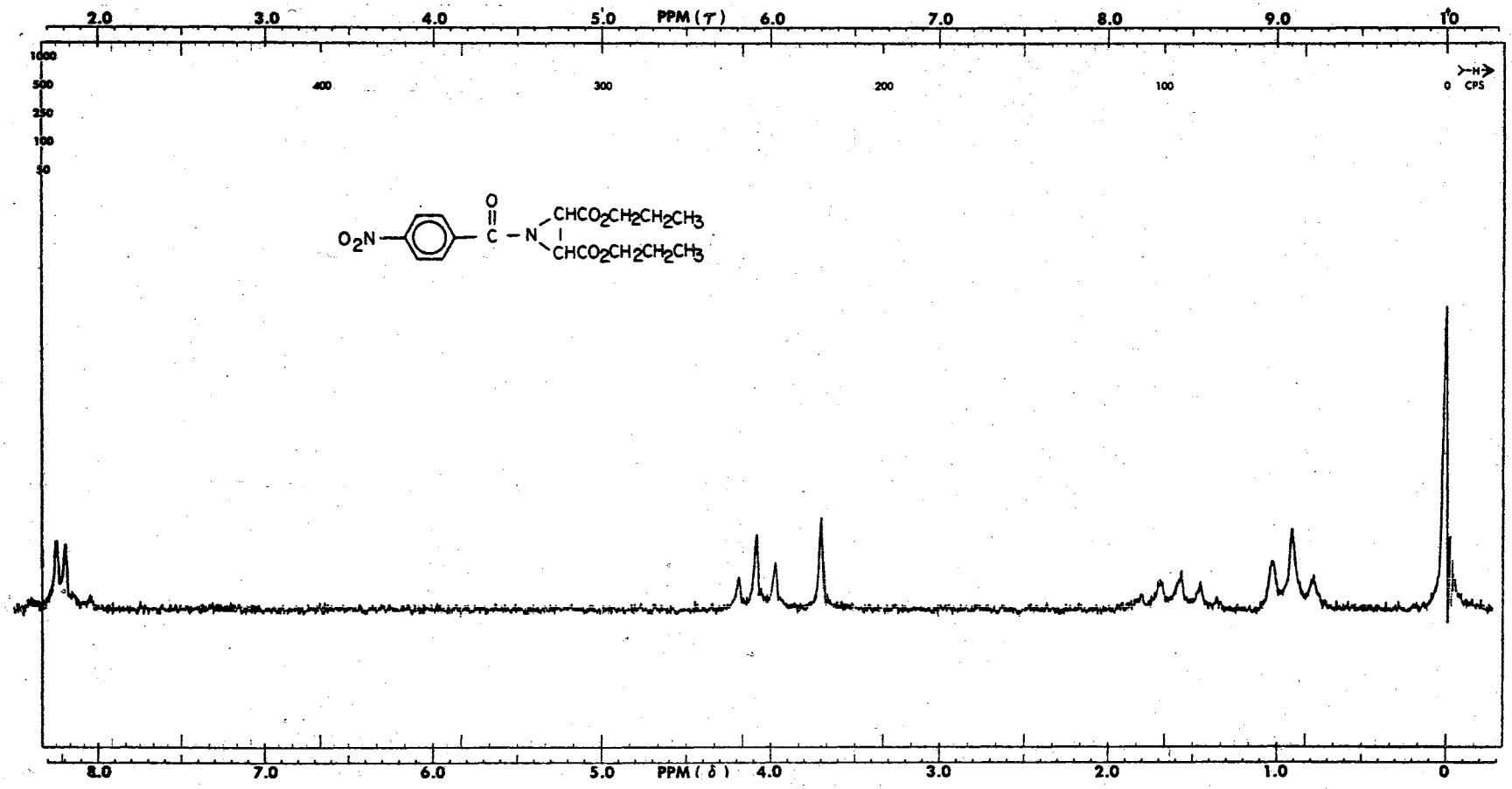
Plate XXXVI



Diethyl Aziridine-2,3-dicarboxylate (XLb), Dry

Solvent.....$CDCl_3$	R.F. Field..0.05 mG	S.W.....500 cps	S.A.....3.2
F.B.....4.0 cps	S.T.....250 sec	S.O.....000 cps	I.A.....off

Plate XXXVII



Di-n-propyl 1-(p-Nitrobenzoyl)aziridine-2,3-dicarboxylate (XLII)

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

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VITA

Lenton Gay Williams

Candidate for the Degree of

Master of Science

Thesis: ADDITION OF AMMONIA TO DIALKYL meso-AND dl-DIBROMOSUCCINATES AND TO DIALKYL BROMOFUMARATES AND DIALKYL BROMOMALEATES--FORMATION OF AZIRIDINES AND ENAMINES

Major Field: Organic Chemistry

Biographical:

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Professional Experience: The author has been on active duty in the United States Army since May, 1961, and in the Chemical Corps since May, 1963. He has had various jobs associated with chemical agents, munitions and equipment and has attended several military and chemical warfare schools.

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