

CHAPTER III

EXPERIMENTS

Instruments.

1. Infrared Spectrophotometer.
 - : Perkin-Elmer model FT-IR 1760 X.
 - : Perkin Elmer model FT-IR 1600 Series.
 - : Perkin Elmer model FT-IR 16 PC.
 - : Perkin Elmer model 283.
2. Nuclear Magnetic Resonance Spectrophotometer.
 - : Jeol JNM-A500.
3. Mass Spectrophotometer.
 - : Kratos model Profile.
4. Melting Point Apparatus.
 - : Buchi capillary melting point apparatus.
5. CHNS/O Analyser
 - : Perkin Elmer PE 2400 Series II.

Chemicals.

Acetone (Merck)
DL-Alanine (Aldrich)
1-Bromopropane (Fluka Chemika)
2-Butene-1,4-diol (Aldrich)
Chloroacetic acid (Fluka Chemika)
Ethanol, absolute (Merck)
Formamide (Fluka Chemika)
Formic acid, 85 % (Carlo Erba)
Hydrochloric acid, concentrated (BDH Laboratory-supplier)
Magnesium, turning (Merck-Schuchardt)

Oxalic acid, dihydrate (Mallinckrodt Chemical-Works)
 Phosphorus pentoxide (Merck)
 Potassium hydroxide (Laboratory grade)
 Pyridine (Merck)
 Pyridoxine (B.P. grade)
 Sodium bicarbonate (Laboratory grade)
 Sodium carbonate, anhydrous (Carlo Erba)
 Sodium sulfate, anhydrous (Merck)
 Sulfuric acid, concentrated (Merck)
 Thionyl chloride (Laboratory grade)
p-Toluenesulfonic acid, monohydrate (Sigma)
 Valproic acid (Sigma)
 All Solvents used were either B.P. or laboratory-grade.

Ethyl Chloroacetate.

A mixture of 50 g (0.53 mol) of chloroacetic acid and 250 ml of absolute ethanol was refluxed in the presence of 1 ml of concentrated sulfuric acid for 10 hours. An azeotropic mixture of water formed and ethanol was distilled at 78 °c. The residue was distilled and ethyl chloroacetate was collected at 144.5 °c. The yield was about 30.0 g (46.3%).

IR. : 2984-2800 cm^{-1} (ν C-H, aliphatic)
 (neat) 1754 cm^{-1} (ν C=O, α -halogenated ester)
 1466-1369 cm^{-1} (δ C-H)
 1313,1096 cm^{-1} (ν C(=O)-O-C)
 1026 cm^{-1} (ν C(=O)-O-C)
 781 cm^{-1} (ν C-Cl)
 (Figure 26)

Ethyl Ethoxyacetate.

A solution of sodium ethoxide was prepared by dissolving 18.76 g (0.82 mol) of sodium in 300 ml of absolute ethanol. The stirrer was started, and to the solution of sodium ethoxide, 100 g (103.1 ml, 0.82 mol) of ethyl chloroacetate was run in from of the dropping funnel during 2 hours and reaction mixture was refluxed for 30 minutes with stirring. The stirrer was stopped and sodium chloride formed was let to precipitate. The supernatant liquor was decanted and the solvent was

evaporated. If there was some precipitate left in the residue, it was filtered until a clear solution was obtained. The residue was distilled and ethyl ethoxyacetate was collected at 156-157 °c. The yield was about 65.4 g (61%).

IR. : 2979-2903 cm^{-1} (ν C-H, aliphatic)
 (neat) 1755 cm^{-1} (ν C=O, ester)
 1274,1203 cm^{-1} (ν C(=O)-O-C)
 1136 cm^{-1} (ν_{as} C-O-C)
 1034 cm^{-1} (ν C(=O)-O-C)
 (Figure 27)

2-Propylpentanal.

A solution of propylmagnesium bromide was prepared from 130 g (96 ml, 1.06 mol) of 1-bromopropane, magnesium turning 27 g (1.10 mol) and 500 ml of dry ether in a 1-litre flask. The flask containing the resulting Grignard reagent was cooled in an ice bath. A solution of 67.8 g (69.7 ml, 0.53 mol) of ethyl ethoxyacetate in 100 ml of dry ether was placed in the separatory funnel. The solution of the Grignard reagent was stirred and the ethyl ethoxyacetate was run into it at such a rate that the ether refluxed gently. The ice bath was removed and the stirring was continued for 6 hours.

About 100 ml of water was placed in the separatory funnel and run into the vigorously stirred reaction at such a rate that rapid refluxing occurred. This was followed by a cold solution of 300 ml of 10% sulfuric acid. Two practically clear layers were present in the flask. The ethereal layer was decanted as much as possible into a 500-ml round-bottomed flask. The remainder, including the aqueous layer was transferred into a separatory funnel. The residue solid was then washed with two 50 ml portions of ether and these washings were combined with the liquid in the separatory funnel which was then washed well with water, dried over anhydrous sodium sulfate and the solvent was evaporated. The residue was crude 1,1-dipropyl-2-ethoxyethanol (Figure 28). It was not further purified. The yield was 72 g (80%). Then crude 1,1-dipropyl-2-ethoxyethanol was transformed to 2-propylpentanal as described below.

IR. : 3600-3300 cm^{-1} (ν O-H)
 (neat) 3000-2800 cm^{-1} (ν C-H, aliphatic)

1462-1380 cm^{-1} (δ C-H)
 1200-1000 cm^{-1} (ν C-O, ether)
 1200-878 cm^{-1} (ν C-O, alcohol)
 (Figure 28)

The mixture of 72 g (0.41 mol) of crude 1,1-dipropyl-2-ethoxyethanol and 75 g (0.82 mol) of anhydrous oxalic acid was refluxed at 110-115 °c for 4 hours. The reaction mixture was cooled and filtered. The filtrate was washed with sodium bicarbonate solution. The residue was washed well with water, dried over anhydrous sodium sulfate and the solvent was then evaporated. The aldehyde was isolated by steam distillation. The distillate was extracted with ether. The combined ether extract was washed well with water, dried over anhydrous sodium sulfate and then solvent was the evaporated. The yield was about 43 g (80%).

IR. : 2960-2872 cm^{-1} (ν C-H, aliphatic)
 (neat) 2810, 2702 cm^{-1} (ν C-H, aldehydic hydrogen)
 1728 cm^{-1} (ν C=O, aldehyde)
 1462-1310 cm^{-1} (δ C-H)
 (Figure 29)

5-Hydroxymethyl-8-methyl-2-(1-propylbutyl)-4*H*-dioxino[4,5-*c*]pyridine or α^4 ,3-O-(2-Propylpentanylidene)pyridoxine (LXIX).

2.0 g (9.7 mmol) of pyridoxine hydrochloride was suspended in 10 ml of dry 2-propylpentanal and cooled in ice. A fine stream of dry hydrogen chloride gas was passed into the suspension with protection from moisture. After about an hour, the particles of the vitamin disappeared and finally a clear solution was obtained. The mixture was stirred at room temperature for 2 hours to complete the reaction. Then 200 ml of dry ether was added to the mixture. Precipitation had by then begun and the precipitates were quickly filtered off and immediately washed with dry ether. Recrystallization of the crystalline precipitates from ethanol/ether give 3.0 g (97.9%) of 5-hydroxymethyl-8-methyl-2-(1-propylbutyl)-4*H*-dioxino[4,5-*c*]pyridine hydrochloride or α^4 , 3-O-(2-propylpentanylidene)pyridoxine hydrochloride, m.p.172-174 °c (dec.). It gave a negative ferric chloride test.

Anal. Calcd. for $C_{16}H_{25}O_3N \cdot HCl$: C, 60.85; H, 8.30; N, 4.43.
 Found : C, 60.62; H, 8.32; N, 4.14.

IR : 3289 cm^{-1} (v O-H)
 (KBr) 3100-3000 cm^{-1} (v C-H, aromatic)
 2958-2870 cm^{-1} (v C-H, aliphatic)
 2815 cm^{-1} (v C-H, acetal)
 2750-2008 cm^{-1} (v N^+ -H)
 1966-1746 cm^{-1} (overtone or combination)
 1637-1422 cm^{-1} (v $C=C-C=N$, pyridine ring)
 1283 cm^{-1} (v_{as} C-O-C, aryl alkyl ether)
 1219 cm^{-1} (δ O-H)
 1037, 1002 cm^{-1} (v C-O, primary alcohol)
 (Figure 30)

1H -NMR : 0.91-0.95 ppm ($-CH_3$, 6H, complex)
 ($CDCl_3$) 1.34-1.59 ppm ($-CH_2-$, 8H, complex)
 1.85-1.93 ppm ($-CH-$, 1H, complex)
 2.72 ppm ($-CH_3$, 3H, s)
 4.74 ppm ($-HCH-O-$, 1H, d, $J = 14.95$ Hz)
 4.68 ppm ($-HCH-O-$, 1H, d, $J = 14.95$ Hz)
 5.05 ppm ($-CH_2-O-$, 2H, s)
 5.09 ppm ($-O-CH-O-$, 1H, d, $J = 3.96$ Hz)
 8.36 ppm (aromatic H, 1H, s)
 (Figure 31-32)

^{13}C -NMR : 13.78 ppm ($-CH_3$)
 ($CDCl_3$) 14.32 ppm ($-CH_3$)
 20.23, 20.26, 30.69, 30.84 ppm ($-CH_2-$)
 41.33 ppm ($-CH-$)
 57.97 ppm ($-CH_2-O-$)
 64.19 ppm ($-CH_2-O-$)
 103.39 ppm ($-O-CH-O-$)
 129.81, 135.70, 136.46, 141.14, 150.08 ppm (aromatic C)
 (Figure 33)

The free base has been obtained from an aqueous solution of the hydrochloride by making the solution alkaline with sodium bicarbonate and extracting with chloroform. The chloroform solution was washed with water, dried, and evaporated to give an oily liquid free base.

EIMS : 279 (35.2%), 180 (55.5%), 151 (56.1%), 123 (17.2%),
 (m/e) 122 (15.9%), 106 (100.0%), 94 (71.4%), 57 (33.7%),
 55 (24.1%), 43 (25.5%), 41 (30.3%)
 (Figure 34)

5-Hydroxymethyl-2,2,8-trimethyl-4*H*-dioxino[4,5-*c*]pyridine or $\alpha^4,3$ -*O*-Isopropylidenepyridoxine.

2.0 g (9.7 mmol) of pyridoxine hydrochloride was suspended in 40 ml of dry, freshly distilled acetone and cooled in ice. A fine stream of dry hydrogen chloride gas was passed into the suspension with protection from moisture. After about an hour, the particles of the vitamin disappeared and finally a clear solution was obtained. The mixture was stirred at room temperature for 2 hours to complete the reaction. Then 200 ml of dry ether was added to the mixture. Precipitation had by then begun and the precipitates were quickly filtered off and immediately washed with dry ether. Recrystallization of the crystalline precipitates from ethanol/ether give 2.0 g (83.9%) of 5-hydroxymethyl-2,2,8-trimethyl-4*H*-dioxino[4,5-*c*]pyridine hydrochloride or $\alpha^4,3$ -*O*-isopropylidenepyridoxine hydrochloride, m.p.210-212 °c (dec.). It gave a negative ferric chloride test.

IR : 3325 cm⁻¹ (v O-H)
 (KBr) 3089 cm⁻¹ (v C-H, aromatic)
 2985-2861 cm⁻¹ (v C-H, aliphatic)
 2494 cm⁻¹ (v N⁺-H)
 1916-1731 cm⁻¹ (overtone or combination)
 1622-1444 cm⁻¹ (v C=C-C=N, pyridine ring)
 1298 cm⁻¹ (v_{as} C-O-C, aryl alkyl ether)
 1212 cm⁻¹ (δ O-H)
 1065,1051 cm⁻¹ (v C-O, primary alcohol)
 (Figure 35)

¹H-NMR : 1.58 ppm (-CH₃, 6H, s)
 (D₂O) 2.54 ppm (-CH₃, 3H, s)
 4.65 ppm (-CH₂-O-, 2H, s)
 5.07 ppm (-CH₂-O-, 2H, s)
 8.09 ppm (aromatic H, 1H, s)
 (Figure 36)

$^{13}\text{C-NMR}$: 16.19 ppm (-CH₃)
 (D₂O) 26.89 ppm (-CH₃)
 60.16 ppm (-CH₂-O-)
 61.22 ppm (-CH₂-O-)
 105.29 ppm (-O-C-O-)
 131.54, 137.14, 137.84, 145.82, 150.87 ppm (aromatic C)
 (Figure 37)

5-(2-Propylpentanoyl)oxymethyl-2,2,8-trimethyl-4H-dioxino[4,5-c]pyridine or $\alpha^4,3$ -O-Isopropylidenepyridoxine-5-valproate.

To a 1.3 g (9.0 mmol) of 2-propylpentanoic acid, a 1.3 g (10.9 mmol) of thionyl chloride was added dropwise with stirring at room temperature. After completion of the addition, the mixture was stirred for 24 hours. The excess thionyl chloride was removed *in vacuo*. The residue acid chloride was dissolved with 10 ml of dry alcohol-free chloroform and was added dropwise with stirring at room temperature to the solution of 2 g (8.1 mmol) of $\alpha^4,3$ -O-isopropylidenepyridoxine hydrochloride in a mixture of 50 ml of dry, alcohol-free chloroform and 10 ml of dry pyridine. After completion of the addition, the mixture was then stirred for 24 hours at room temperature to complete the reaction.

The 5-(2-propylpentanoyl)oxymethyl-2,2,8-trimethyl-4H-dioxino[4,5-c]pyridine or $\alpha^4,3$ -O-isopropylidenepyridoxine-5-valproate was extracted with chloroform. The extract was washed well with 0.5 N hydrochloric acid, 5% sodium carbonate solution and with water successively. After dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure. The oily liquid obtained was dissolved in hexane, a fine stream of dry hydrogen chloride gas was pass into the solution. Precipitation had by then begun and the precipitates were quickly filtered off and washed with hexane. Recrystallization of the crystalline precipitates from ethyl acetate give 1.8 g (59.5%) of 5-(2-propylpentanoyl)oxymethyl-2,2,8-trimethyl-4H-dioxino[4,5-c]pyridine hydrochloride or $\alpha^4,3$ -O-isopropylidenepyridoxine-5-valproate hydrochloride, m.p.154-156 °c (dec.). It gave a negative ferric chloride test.

Anal. Calcd. for C₁₉H₂₉O₄N·HCl : C, 61.36; H, 8.13; N, 3.37.
 Found : C, 61.56; H, 7.90; N, 3.75.

IR : 3021 cm^{-1} (v C-H, aromatic)
 (KBr) 2958-2712 cm^{-1} (v C-H, aliphatic)
 2597-2040 cm^{-1} (v $\text{N}^+\text{-H}$)
 1736 cm^{-1} (v C=O, ester)
 1620-1430 cm^{-1} (v C=C-C=N, pyridine ring)
 1296 cm^{-1} (v_{as} C-O-C, aryl alkyl ether)
 1170, 1141 cm^{-1} (v C-O, ester)
 (Figure 38)

$^1\text{H-NMR}$: 0.88-0.91 ppm (- CH_3 , 6H, complex)
 (CDCl_3) 1.21-1.61 ppm (- CH_2 -, 8H, complex)
 1.63 ppm (- CH_3 , 6H, s)
 2.42-2.47 ppm (-CH-, 1H, complex)
 2.80 ppm (- CH_3 , 3H, s)
 5.02 ppm (- $\text{CH}_2\text{-O}$ -, 2H, s)
 5.07 ppm (- $\text{CH}_2\text{-O}$ -, 2H, s)
 8.20 ppm (aromatic H, 1H, s)
 (Figure 39-40)

$^{13}\text{C-NMR}$: 13.86 ppm (- CH_3)
 (CDCl_3) 13.91 ppm (- CH_3)
 20.59 ppm (- CH_3)
 24.54, 34.34 ppm (- CH_2 -)
 44.94 ppm (-CH-)
 58.41, 58.90 ppm (- $\text{CH}_2\text{-O}$ -)
 102.48 ppm (-O-C-O-)
 129.40, 130.35, 134.20, 143.86, 148.66 ppm (aromatic C)
 175.56 ppm (carbonyl C)
 (Figure 41)

3-Hydroxy-4-hydroxymethyl-2-methyl-5-(2-propylpentanoyl)oxy methylpyridine or Pyridoxine-5-valproate (LXXI).

0.5 g (1.3 mmol) of $\alpha^4,3\text{-O-isopropylidenepyridoxine-5-valproate hydrochloride}$ was suspended in 20 ml of 9 % aqueous formic acid and refluxed for 30 minutes on a steam-bath. The solution was made alkaline with sodium bicarbonate, evaporated *in vacuo*, and some ether was added. Recrystallization of the crystalline precipitate from hot ethyl acetate gave 0.3 g (67.2%) of 3-hydroxy-4-hydroxymethyl-2-methyl-5-

(2-propylpentanoyl)oxymethylpyridine or pyridoxine-5-valproate, m.p. 122-123 °c. It gave a positive ferric chloride test.

Anal. Calcd. for $C_{16}H_{25}O_4N$: C, 65.06; H, 8.53; N, 4.74.
Found: C, 65.33; H, 8.22; N, 4.42.

IR : 3180-3140 cm^{-1} (v O-H, hydrogen bonded)
(KBr) 2959-2871 cm^{-1} (v C-H, aliphatic)
2608-2028 cm^{-1} (v N^+H)
1729 cm^{-1} (v C=O, ester)
1622-1429 cm^{-1} (v C=C=N, pyridine ring)
1289 cm^{-1} (v C-O, phenol)
1165, 1142 cm^{-1} (v C-O, ester)
1036 cm^{-1} (v C-O, primary alcohol)
(Figure 42)

1H -NMR : 0.87-0.90 ppm (- CH_3 , 6H, complex)
($CDCl_3$) 1.20-1.61 ppm (- CH_2 -, 8H, complex)
2.40-2.46 ppm (-CH-, 1H, complex)
2.73 ppm (- CH_3 , 3H, s)
5.14 ppm (- CH_2O -, 2H, s)
5.19 ppm (- CH_2O -, 2H, s)
8.36 ppm (aromatic H, 1H, s)
(Figure 43-45)

^{13}C -NMR : 13.88 ppm (- CH_3)
($CDCl_3$) 14.31 ppm (- CH_3)
20.56, 34.31 ppm (- CH_2 -)
44.95 ppm (-CH-)
59.63, 60.12 ppm (- CH_2O -)
129.40, 131.06, 140.21, 143.00, 154.83 ppm (aromatic C)
175.63 ppm (carbonyl C)
(Figure 46)

EIMS : 295 (1.6%), 151 (18.9%), 127 (5.1%), 106 (31.6%),
(m/e) 102 (23.1%), 99 (10.4%), 94 (20.1%), 73 (58.8%), 57 (73.8%),
55 (79.3%), 43 (64.8%), 41 (100.0%)
(Figure 47)

4-Hydroxymethyl-5-hydroxymethyl-2-methyl-3-(2-propylpentanoyl)oxypyridine or Pyridoxine-3-valproate (LXXII).

To a 0.9 g (6.2 mmol) of 2-propylpentanoic acid, a 0.9 g (7.6 mmol) of thionyl chloride was added dropwise with stirring at room temperature. After completion of the addition, the mixture was stirred for 24 hours. The excess thionyl chloride was removed *in vacuo*. The residue acid chloride was dissolved with 25 ml of dry tetrahydrofuran and was added dropwise with stirring at room temperature to the solution of 1.0 g (4.9 mmol) of pyridoxine hydrochloride and 1.0 g of anhydrous sodium carbonate in 7 ml of water. After completion of the addition, the mixture was then stirred for 3 hours at room temperature to complete the reaction.

The 4-hydroxymethyl-5-hydroxymethyl-2-methyl-3-(2-propylpentanoyl)oxypyridine or pyridoxine-3-valproate was extracted with chloroform. The extract was washed well with 0.5 N hydrochloric acid, 5 % sodium carbonate solution and with water successively. After dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure. The oily liquid obtained was dissolved in hexane, a fine stream of dry hydrogen chloride gas was passed into the solution. Precipitation had by then begun and the precipitates were quickly filtered off and washed with hexane. Recrystallization of the crystalline precipitates from ethanol/ether give 0.9 g (55.8%) of 4-hydroxymethyl-5-hydroxymethyl-2-methyl-3-(2-propylpentanoyl)oxypyridine hydrochloride or pyridoxine-3-valproate hydrochloride, m.p.138-139 °c (dec.). It gave a negative ferric chloride test.

Anal. Calcd. for $C_{16}H_{25}O_4N \cdot HCl$: C, 57.91; H, 7.90; N, 4.22.
Found : C, 57.62; H, 7.60; N, 4.26.

IR : 3372-3113 cm^{-1} (v O-H)
(KBr) 2957-2872 cm^{-1} (v C-H, aliphatic)
2772-2024 cm^{-1} (v N^+H)
1748 cm^{-1} (v C=O, ester)
1636-1433 cm^{-1} (v C=C-C=N, pyridine ring)
1219 cm^{-1} (v C-O, phenol ester)
1050,1035 cm^{-1} (v C-O, primary alcohol)
(Figure 48)

¹H-NMR : 0.88-0.91 ppm (-CH₃, 6H, complex)
 (D₂O) 1.22-1.63 ppm (-CH₂-, 8H, complex)
 2.53-2.59 ppm (-CH-, 1H, complex)
 2.79 ppm (-CH₃, 3H, s)
 5.01 ppm (-CH₂-O-, 2H, s)
 5.48 ppm (-CH₂-O-, 2H, s)
 8.36 ppm (aromatic H, 1H, s)
 (Figure 49-51)

¹³C-NMR : 16.61 ppm (-CH₃)
 (D₂O) 17.37 ppm (-CH₃)
 22.42, 35.49 ppm (-CH₂-)
 47.28 ppm (-CH-)
 59.42, 60.71 ppm (-CH₂-O-)
 132.58, 139.97, 141.22, 145.45, 155.09 ppm (aromatic C)
 181.08 ppm (carbonyl C)
 (Figure 52)

The free base has been obtained from an aqueous solution of the hydrochloride by making the solution alkaline with sodium bicarbonate and extracting with chloroform. The chloroform solution was washed with water, dried, and evaporated to give an oil from which crystals of the free base separated, m.p. 94-95 °c.

EIMS : 295 (3.3%), 151 (12.9%), 127 (5.6%), 106 (20.6%),
 (m/e) 102 (43.1%), 99 (8.7%), 94 (25.9%), 73 (100.0%), 57 (60.0%),
 55 (62.4%), 43 (61.7%), 41 (70.6%)
 (Figure 53)

4-Hydroxymethyl-2-methyl-3-[(2-propylpentanoyl)oxy]-5-[(2-propylpentanoyl)oxymethyl]pyridine or Pyridoxine-3,5-divalproate (LXXIV).

To a 0.5 g (3.5 mmol) of 2-propylpentanoic acid, a 0.5 g (4.2 mmol) of thionyl chloride was added dropwise with stirring at room temperature. After completion of the addition, the mixture was stirred for 24 hours. The excess thionyl chloride was removed *in vacuo*. The residue acid chloride was dissolved with 10 ml of dry alcohol-free chloroform and was added dropwise with stirring at room temperature to the solution of 1.0 g (3.0 mmol) of pyridoxine-5-valproate hydrochloride

in a mixture of 50 ml of dry, alcohol-free chloroform and 10 ml of dry pyridine.

The 4-hydroxymethyl-2-methyl-3- [(2-propylpentanoyl)oxy] -5- [(2-propylpentanoyl)oxymethyl]pyridine or pyridoxine-3,5-divalproate was extracted with chloroform. The extract was washed well with 0.5 N hydrochloric acid, 5% sodium carbonate solution and with water successively. After dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure. The oily liquid obtained did not appear to form the solid precipitates of the hydrochloride salt when dissolved in hexane and pass into the solution with a fine stream of dry hydrogen chloride gas. The purification was performed by column chromatographic technique, mobile phase used was chloroform and stationary phase was silica gel. The yield of 4-hydroxymethyl-2-methyl-3-[(2-propyl pentanoyl)oxy]-5-[(2-propylpentanoyl)oxymethyl]pyridine or pyridoxine-3,5-divalproate was 0.5 g (39.4%). It gave a negative ferric chloride test.

Anal. Calcd. for $C_{24}H_{39}O_5N$: C, 68.38; H, 9.32; N, 3.32.
Found : C, 68.38; H, 9.24; N, 3.36.

IR : 3380-3100 cm^{-1} (v O-H)
(neat) 2959-2874 cm^{-1} (v C-H, aliphatic)
1737 cm^{-1} (v C=O, aliphatic ester)
1604-1419 cm^{-1} (v C=C=N, pyridine ring)
1241, 1208 cm^{-1} (v C-O, phenol ester)
1168, 1141 cm^{-1} (v C-O, ester)
1057, 1027 cm^{-1} (v C-O, primary alcohol)
(Figure 54)

1H -NMR : 0.82-0.89 ppm (-CH₃, 12H, complex)
(CDCl₃) 1.13-1.64 ppm (-CH₂-, 16H, complex)
2.38-2.46 ppm (-CH-, 2H, complex)
2.53 ppm (-CH₃, 3H, s)
5.19 ppm (-CH₂-O-, 2H, s)
5.25 ppm (-CH₂-O-, 2H, s)
8.12 ppm (aromatic H, 1H, s)
(Figure 55-57)

^{13}C -NMR : 13.76, 13.89 ppm (-CH₃)
 (CDCl₃) 19.45 ppm (-CH₃)
 20.33, 20.57, 34.38, 34.47 ppm (-CH₂-)
 44.96, 45.18 ppm (-CH-)
 57.64, 60.94 ppm (-CH₂-O-)
 127.44, 129.07, 141.14, 149.79, 150.42 ppm (aromatic C)
 176.12, 179.16 ppm (carbonyl C)
 (Figure 58)

EIMS : 422 (1.9%), 379 (2.5%), 262 (11.3%), 151 (5.0%),
 (m/e) 127 (11.9%), 106 (3.5%), 102 (93.2%), 99 (10.1%),
 73 (100.0%), 57 (31.7%), 55 (23.0%), 43 (13.6%), 41 (17.2%)
 (Figure 59)

2-Methyl-3-[(2-propylpentanoyl)oxy]-4-[(2-propylpentanoyl)oxy methyl]-5-hydroxymethylpyridine or Pyridoxine-3,4-divalproate (LXXIII).

To a 3.6 g (25 mmol) of 2-propylpentanoic acid, a 3.6 g (30 mmol) of thionyl chloride was added dropwise with stirring at room temperature. After completion of the addition, the mixture was stirred for 24 hours. The excess thionyl chloride was removed *in vacuo*. The residue acid chloride was dissolved with 10 ml of dry alcohol-free chloroform and was added dropwise with stirring at room temperature to the suspension of 2.0 g (9.7 mmol) of pyridoxine hydrochloride in a mixture of 50 ml of dry, alcohol-free chloroform and 10 ml of dry pyridine.

While the reaction proceeded the particles of the pyridoxine hydrochloride disappeared and finally a clear solution was obtained, the mixture was then set aside for 24 hours at room temperature to complete the reaction.

The 2-methyl-3-[(2-propylpentanoyl)oxy]-4-[(2-propylpentanoyl)oxymethyl]-5-hydroxymethylpyridine or pyridoxine-3,4-divalproate was extracted with chloroform. The extract was washed well with 0.5 N hydrochloric acid, 5% sodium carbonate solution and with water successively. After dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure. The oily liquid obtained was dissolved in hexane, a fine stream of dry hydrogen chloride gas was

passed into the solution. Precipitation had by then begun and the precipitates were quickly filtered off and washed with hexane. Recrystallization of the crystalline precipitates from ethanol/ether give 2.2 g (49.4%) of 2-methyl-3-[(2-propylpentanoyl)oxy]-4-[(2-propylpentanoyl)oxymethyl]-5-hydroxymethylpyridine hydrochloride or pyridoxine-3,4-divalproate hydrochloride, m.p. 118-120 °c (dec.). It gave a negative ferric chloride test.

Anal. Calcd. for $C_{24}H_{39}O_5N \cdot HCl$: C, 62.93; H, 8.80; N, 3.06.
 Found : C, 63.06; H, 8.72; N, 2.95.

IR : 3297 cm^{-1} (v O-H)
 (KBr) 2960-2873 cm^{-1} (v C-H, aliphatic)
 1772, 1743 cm^{-1} (v C=O, ester)
 1623-1465 cm^{-1} (v C=C=N, pyridine ring)
 1241-1060 cm^{-1} (v C-O, ester, primary alcohol)
 (Figure 60)

1H -NMR : 0.86-1.00 ppm (-CH₃, 12H, complex)
 (CDCl₃) 1.18-1.84 ppm (-CH₂, 16H, complex)
 2.34-2.40, 2.74-2.80 ppm (-CH-, 2H, complex)
 2.72 ppm (-CH₃, 3H, s)
 5.05 ppm (-CH₂-O-, 2H, s)
 5.09 ppm (-CH₂-O-, 2H, s)
 8.99 ppm (aromatic H, 1H, s)
 (Figure 61-62)

^{13}C -NMR : 13.84 ppm (-CH₃)
 (CDCl₃) 15.33 ppm (-CH₃)
 20.47, 33.44, 34.23 ppm (-CH₂-)
 44.74, 44.84 ppm (-CH-)
 56.09, 58.49 ppm (-CH₂-O-)
 137.39, 141.49, 143.83, 146.29, 146.49 ppm (aromatic C)
 172.65, 175.41 ppm (carbonyl C)
 (Figure 63)

The free base has been obtained from an aqueous solution of the hydrochloride by making the solution alkaline with sodium bicarbonate and extracting with chloroform. The chloroform solution was washed with water, dried, and evaporated to give an oily liquid free base.

EIMS : 421 (1.2%), 151 (9.4%), 127 (23.9%), 99 (33.4%), 94 (11.0%),
 (m/e) 73 (16.3%), 57 (100.0%), 55 (29.7%), 43 (37.3%), 41 (35.7%)
 (Figure 64)

2-Methyl-3-[(2-propylpentanoyl)oxy]-4,5-di[(2-propylpentanoyl)oxy methyl]pyridine or Pyridoxine Trivalproate (LXXV).

To a 5.6 g (39 mmol) of 2-propylpentanoic acid, a 5.6 g (47 mmol) of thionyl chloride was added dropwise with stirring at room temperature. After completion of the addition, the mixture was stirred for 24 hours. The excess thionyl chloride was removed *in vacuo*. The residue acid chloride was dissolved with 10 ml of dry alcohol-free chloroform and was added dropwise with stirring at room temperature to the suspension of 2.0 g (9.7 mmol) of pyridoxine hydrochloride in a mixture of 50 ml of dry, alcohol-free chloroform and 10 ml of dry pyridine.

While the reaction proceeded the particles of the pyridoxine hydrochloride disappeared and finally a clear solution was obtained, the mixture was then set aside for 24 hours at room temperature to complete the reaction.

The 2-methyl-3-[(2-propylpentanoyl)oxy]-4,5-di[(2-propylpentanoyl)oxymethyl]pyridine or pyridoxine trivalproate was extracted with chloroform. The extract was washed well with 0.5 N hydrochloric acid, 5% sodium carbonate solution and with water successively. After dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure. The oily liquid obtained did not appear to form the solid precipitates of the hydrochloride salt when dissolved in hexane and pass into the solution with a fine stream of dry hydrogen chloride gas. The purification was performed by column chromatographic technique, mobile phase used was chloroform and stationary phase was silica gel. The yield of 2-methyl-3-[(2-propylpentanoyl)oxy]-4,5-di[(2-propylpentanoyl)oxymethyl]pyridine or pyridoxine trivalproate was 3.9 g. (68.6%).

Anal. Calcd. for $C_{32}H_{53}O_6NHCl$: C, 70.17; H, 9.75; N, 2.56.
 Found : C, 70.35; H, 9.50; N, 2.43.

IR : 2960-2874 cm^{-1} (ν C-H, aliphatic)
 (neat) 1761, 1739 cm^{-1} (ν C=O, ester)
 1643-1409 cm^{-1} (ν C=C=N, pyridine ring)
 1241-1140 cm^{-1} (ν C-O, ester)
 (Figure 65)

$^1\text{H-NMR}$: 0.79-0.94 ppm ($-\text{CH}_3$, 18H, complex)
 (CDCl_3) 1.14-1.81 ppm ($-\text{CH}_2-$, 24H, complex)
 2.28-2.35, 2.63-2.69 ppm ($-\text{CH}-$, 3H, complex)
 2.36-2.37 ppm ($-\text{CH}_3$, 3H, s)
 5.01-5.02 ppm ($-\text{CH}_2\text{-O}-$, 2H, s)
 5.22 ppm ($-\text{CH}_2\text{-O}-$, 2H, s)
 8.38-8.39 ppm (aromatic H, 1H, s)
 (Figure 66-68)

$^{13}\text{C-NMR}$: 13.78-13.84 ppm ($-\text{CH}_3$)
 (CDCl_3) 19.82 ppm ($-\text{CH}_3$)
 20.41, 20.47, 33.64, 34.29, 34.42 ppm ($-\text{CH}_2-$)
 44.82, 44.95, 45.07 ppm ($-\text{CH}-$)
 56.67, 60.78 ppm ($-\text{CH}_2\text{-O}-$)
 129.81, 135.34, 144.55, 147.16, 152.44 ppm (aromatic C)
 173.45, 175.62, 175.79 ppm (carbonyl C)
 (Figure 69)

EIMS : 548 (26.2%), 506 (5.4%), 422 (16.2%), 379 (43.9%),
 (m/e) 151 (18.2%), 127 (100.0%), 123 (7.3%), 122 (6.5%),
 106 (14.1%), 102 (54.1%), 99 (67.5%), 73 (47.4%),
 57 (85.5%), 55 (32.0%), 43 (19.3%), 41 (20.1%)
 (Figure 70)

Ethyl Alaninate Hydrochloride.

10 g (84.1 mmol) of thionyl chloride was slowly added to the cooled suspension of 7.5 g (84.1 mmol) of alanine in 125 ml of absolute ethanol. While the reaction proceeded the particles of alanine disappeared and finally a clear solution was obtained. The mixture was refluxed for 2 hours, and then the excess ethanol was evaporated. Addition of anhydrous ether made the residual oily liquid obtained crystallized on prolonged standing to give a hygroscopic ethyl alaninate

hydrochloride in almost quantitative yield, and no further purification was required.

IR : 3449-2600 cm^{-1} (νNH_3^+)
 (nujol) 1744 cm^{-1} ($\nu \text{C=O}$)
 1609-1513 cm^{-1} (δNH_3^+)
 1246-1211 cm^{-1} ($\nu \text{C-O}$, ester)
 (Figure 71)

Ethyl-*N*-formylalaninate.

10 g (22.2 mmol) of formamide was added to 35 g (22.8 mmol) of ethyl alaninate hydrochloride, the mixture was slowly heated to 105 °c, and held at 105 °c for 4 hours. The solution was cooled, ammonium chloride formed was removed, and the residue was then distilled to give ethyl-*N*-formylalaninate, b.p._{0.8} 100 °c. The yield was about 25 g (77.8%).

IR : 3284 cm^{-1} ($\nu \text{N-H}$)
 (neat) 2986-2878 cm^{-1} ($\nu \text{C-H}$, aliphatic)
 1736 cm^{-1} ($\nu \text{C=O}$)
 1667 cm^{-1} ($\nu \text{C=O}$)
 1532 cm^{-1} ($\delta \text{N-H}$)
 1380 cm^{-1} ($\nu \text{C-N}$)
 1206-1138 cm^{-1} ($\nu \text{C-O}$)
 (Figure 72)

4-Methyl-5-ethoxyoxazole.

To a mixture of 72.0 g (0.5 mol) of phosphorus pentoxide and 150 ml of dry, alcohol-free chloroform was added, over 20 min at 25-30 °c with cooling, a solution of 36.2 g (0.25 mol) of ethyl-*N*-formylalaninate in 100 ml of dry, alcohol-free chloroform. Vigorous stirring was maintained throughout. While the reaction proceeded, the mass was too thick to stirred, but with gentle external heating reflux was maintained for 4 hours.

After cooling, the chloroform was decanted and the residue is the hard mass. To the residual hard mass, a solution of 80 g of potassium hydroxide in 400 ml of water was added with ice cooling and vigorous

stirring. After cautious warming to room temperature, the mixture was refluxed for 1 hour, cooled and extracted with 4x50 ml of dichloromethane. The combined extracts were washed well with water, dried over anhydrous sodium sulfate and the solvent was then evaporated and the residue was distilled *in vacuo*. 4-Methyl-5-ethoxyoxazole was collected at 78-80 °c, 50 mmHg. The yield was about 17.8 g (56.1%).

IR : 3134cm⁻¹ (v C-H, unsaturated)
 (neat) 2982-2930 cm⁻¹ (v C-H, aliphatic)
 1670-1406 cm⁻¹ (v C=N-C=C, oxazole ring)
 1221-1020 cm⁻¹ (v C-O-C)
 (Figure 73)

¹H-NMR : 1.36 ppm (-CH₃, 3H, t, J = 7.02 Hz)
 (CDCl₃) 2.05 ppm (-CH₃, 3H, s)
 4.16 ppm (-CH₂, 2H, q, J = 7.02 Hz)
 7.38 ppm (aromatic H, 1H, s)
 (Figure 74)

2-(1-Propylbutyl)-1,3-dioxep-5-ene.

A mixture of 12.8 g (0.1 mol) of 2-propylpentanal, 8.8 g (0.1 mol) of *cis*-2-butene-1,4-diol, 0.5 g of *p*-toluenesulfonic acid monohydrate and 150 ml of benzene was refluxed under a Dean-Stark trap until the removal of water was complete (about 3 hours). The mixture was then cooled and washed with sodium bicarbonate solution. The residue was washed well with water, dried over anhydrous sodium sulfate and the solvent was then evaporated *in vacuo*. The purification was performed by column chromatographic technique, mobile phase used was chloroform and stationary phase was silica gel. The yield of 2-(1-propylbutyl)-1,3-dioxep-5-ene was 12.0 g (60.5%).

IR : 3031cm⁻¹ (v C-H, unsaturated)
 (neat) 2958-2871 cm⁻¹ (v C-H, aliphatic)
 1650 cm⁻¹ (v C=C)
 1121-996 cm⁻¹ (v_{as} C-O-C)
 (Figure 75)

$^1\text{H-NMR}$: 0.88-0.91 ppm ($-\text{CH}_3$, 6H, complex)
 (CDCl_3) 1.25-1.47 ppm ($-\text{CH}_2-$, 8H, complex)
 1.65-1.67 ppm ($-\text{CH}-$, 1H, complex)
 4.13-4.18 ppm ($-\text{HCH-O}-$, 2H, complex)
 4.38-4.43 ppm ($-\text{HCH-O}-$, 2H, complex)
 4.54 ppm ($-\text{O-CH-O}-$, 1H, d)
 5.71-5.72 ppm ($-\text{CH}=\text{}$, 2H, t)
 (Figure 76-77)

$^{13}\text{C-NMR}$: 14.37 ppm ($-\text{CH}_3$)
 (CDCl_3) 19.80, 31.38 ppm ($-\text{CH}_2-$)
 41.10 ppm ($-\text{CH}-$)
 65.98 ppm ($-\text{CH}_2\text{-O}-$)
 106.97 ppm ($-\text{O-CH-O}-$)
 129.45 ppm ($-\text{CH}=\text{}$)
 (Figure 78)

An Attempt to Synthesize 9-Hydroxy-8-methyl-3-(1-propylbutyl)-4*H*,9*H*-dioxepino[5,6-*c*]pyridine or α^4, α^5 -O-(2-Propylpentanylidene)pyridoxine (LXX).

An effort to prepare 9-hydroxy-8-methyl-3-(1-propylbutyl)-4*H*,9*H*-dioxepino[5,6-*c*]pyridine or α^4, α^5 -O-(2-propylpentanylidene)pyridoxine was made by the following procedures.

Firstly, the 2-(1-propylbutyl)-1,3-dioxep-5-ene and 4-methyl-5-ethoxyoxazole was mixed and stirred at room temperature for upto 240 hours under nitrogen gas. This procedure was done in three kind of solvents, dry ether, benzene, and 2-(1-propylbutyl)-1,3-dioxep-5-ene.

Secondly, the 2-(1-propylbutyl)-1,3-dioxep-5-ene and 4-methyl-5-ethoxyoxazole was allowed to react at 80-180 °c (the solvent used were xylene or 2-(1-propylbutyl)-1,3-dioxep-5-ene) for upto 120 hours in a sealed tube under nitrogen gas.

In addition to the two former procedures, the use of the catalyst was decided, finally. Trichloroacetic or hydrogen chloride was used as the catalyst for the Diels-Alder reaction of 2-(1-propylbutyl)-1,3-dioxep-5-ene and 4-methyl-5-ethoxyoxazole. The mixture was either stirred at room temperature for 120 hours (either in ether or 2-(1-propylbutyl)-1,3-

dioxep-5-ene), and refluxed at 180 °c (either in xylene or 2-(1-propylbutyl)-1,3-dioxep-5-ene) in sealed tube under nitrogen gas for 48 hours.

These procedures gave the same result. The reaction mixture darkened and resinified, slowly at room temperature and rapidly when heated. The TLC chromatogram of the reaction mixture showed that the reaction of these two reactants was not occurred under all of the procedures used. These resinous mixtures contained 2-(1-propylbutyl)-1,3-dioxep-5-ene, 4-methyl-5-ethoxyoxazole and the compounds that were believed to be the degraded products of 4-methyl-5-ethoxyoxazole. An attempt to isolate these degraded products failed.

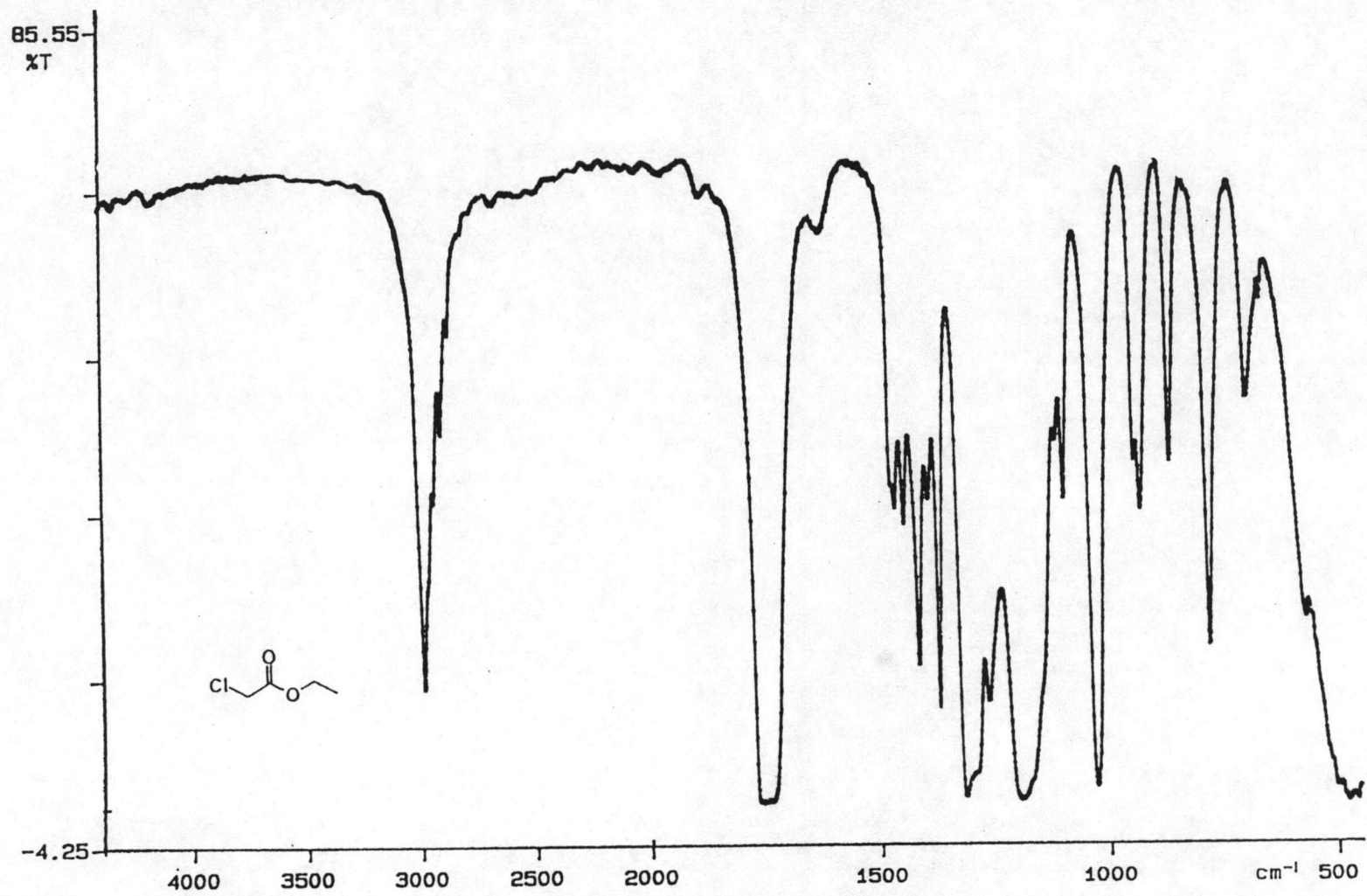


Figure 26. The IR spectrum (neat) of ethyl chloroacetate.

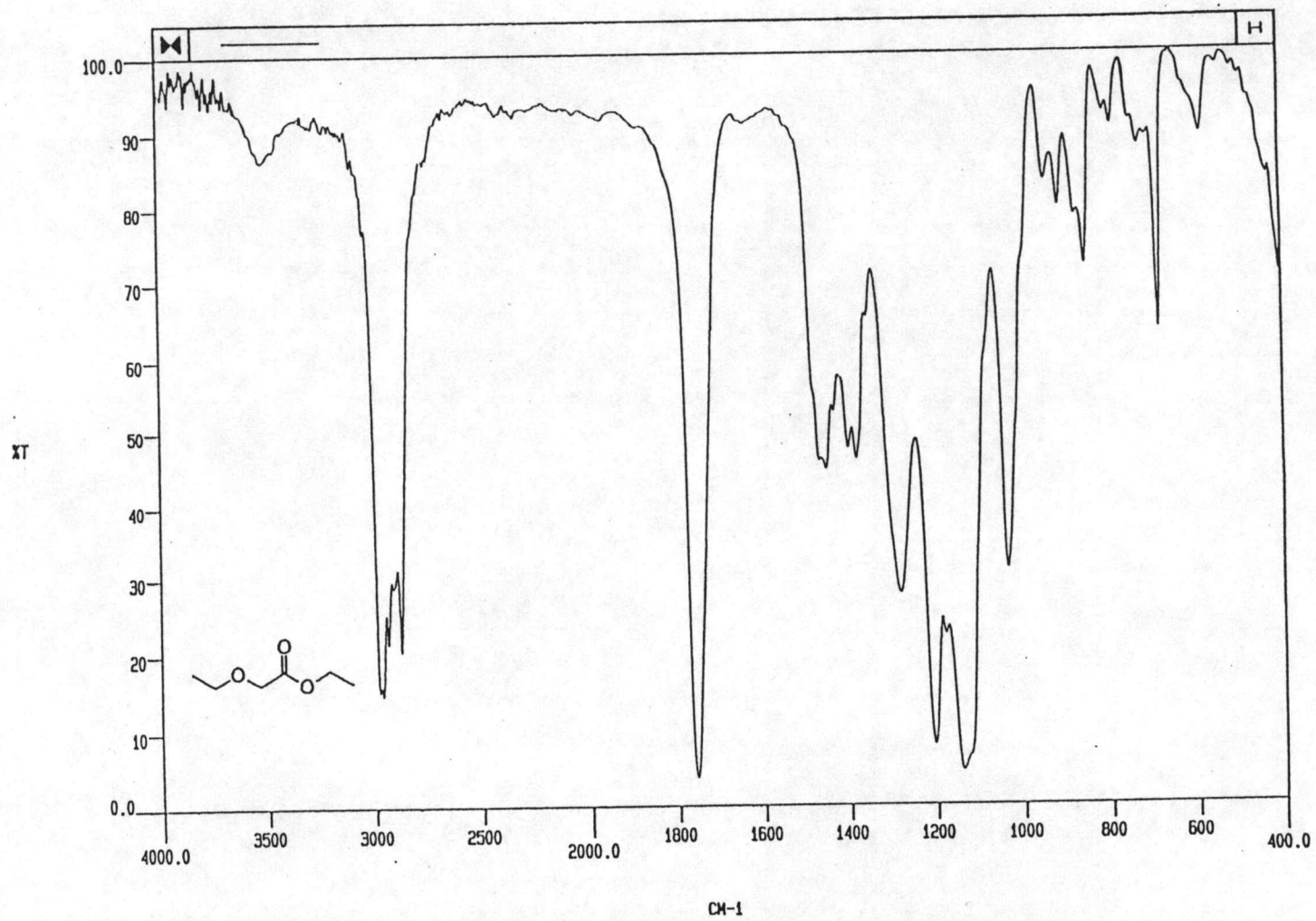


Figure 27. The IR spectrum (neat) of ethyl ethoxyacetate.

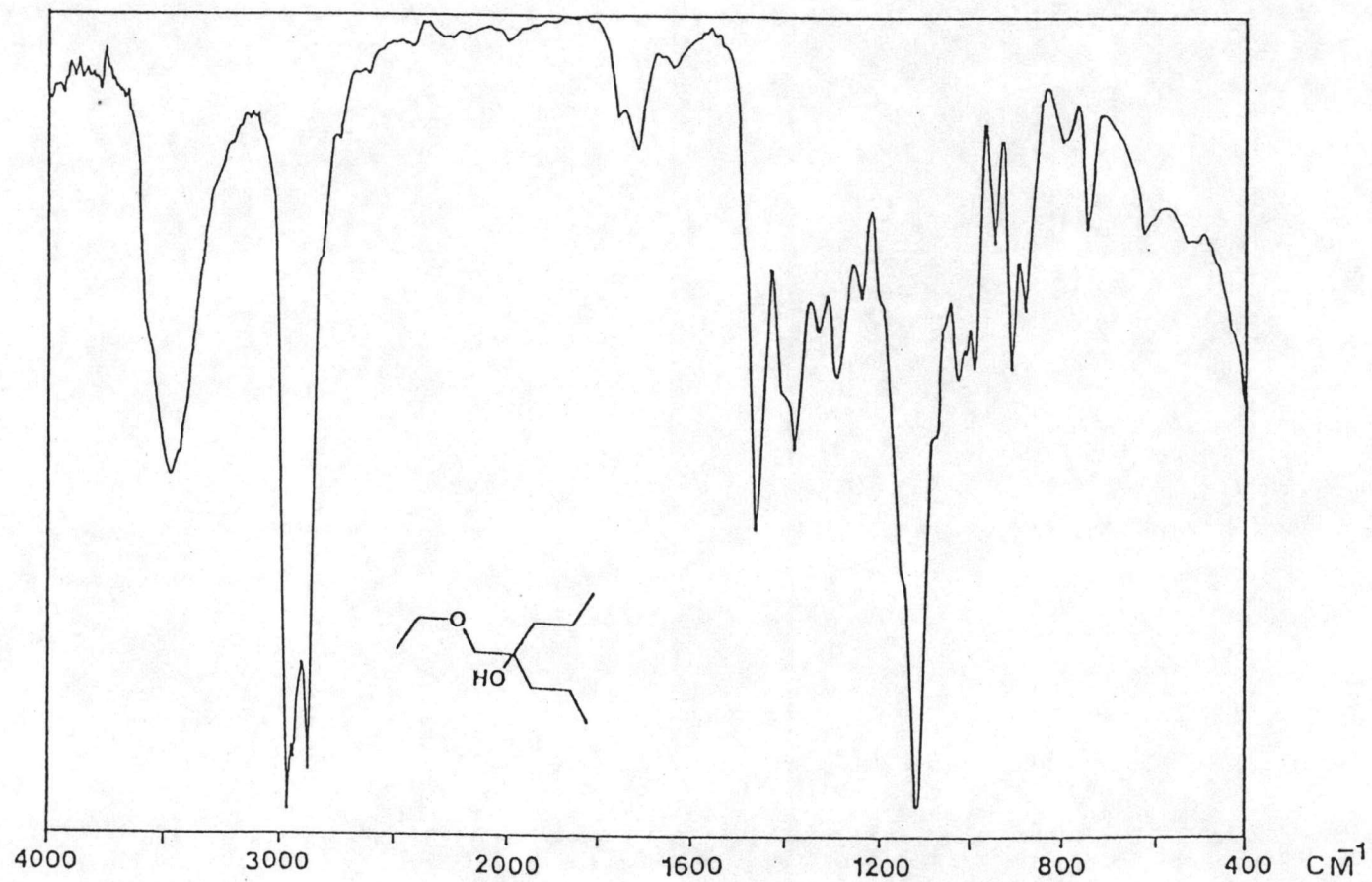


Figure 28. The IR spectrum (neat) of crude 1,1-dipropyl-2-ethoxyethanol.

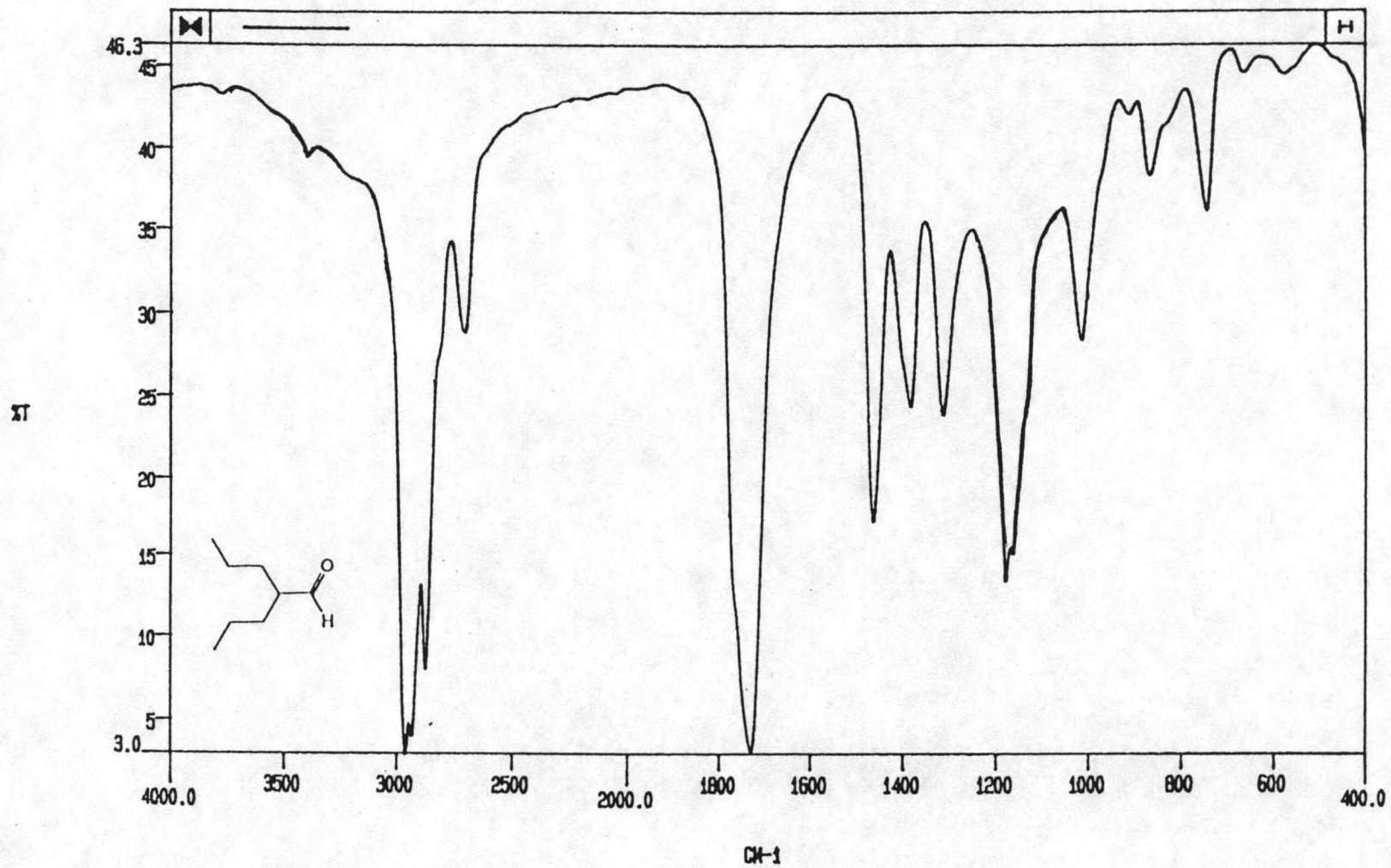


Figure 29. The IR spectrum (neat) of 2-propylpentanal.

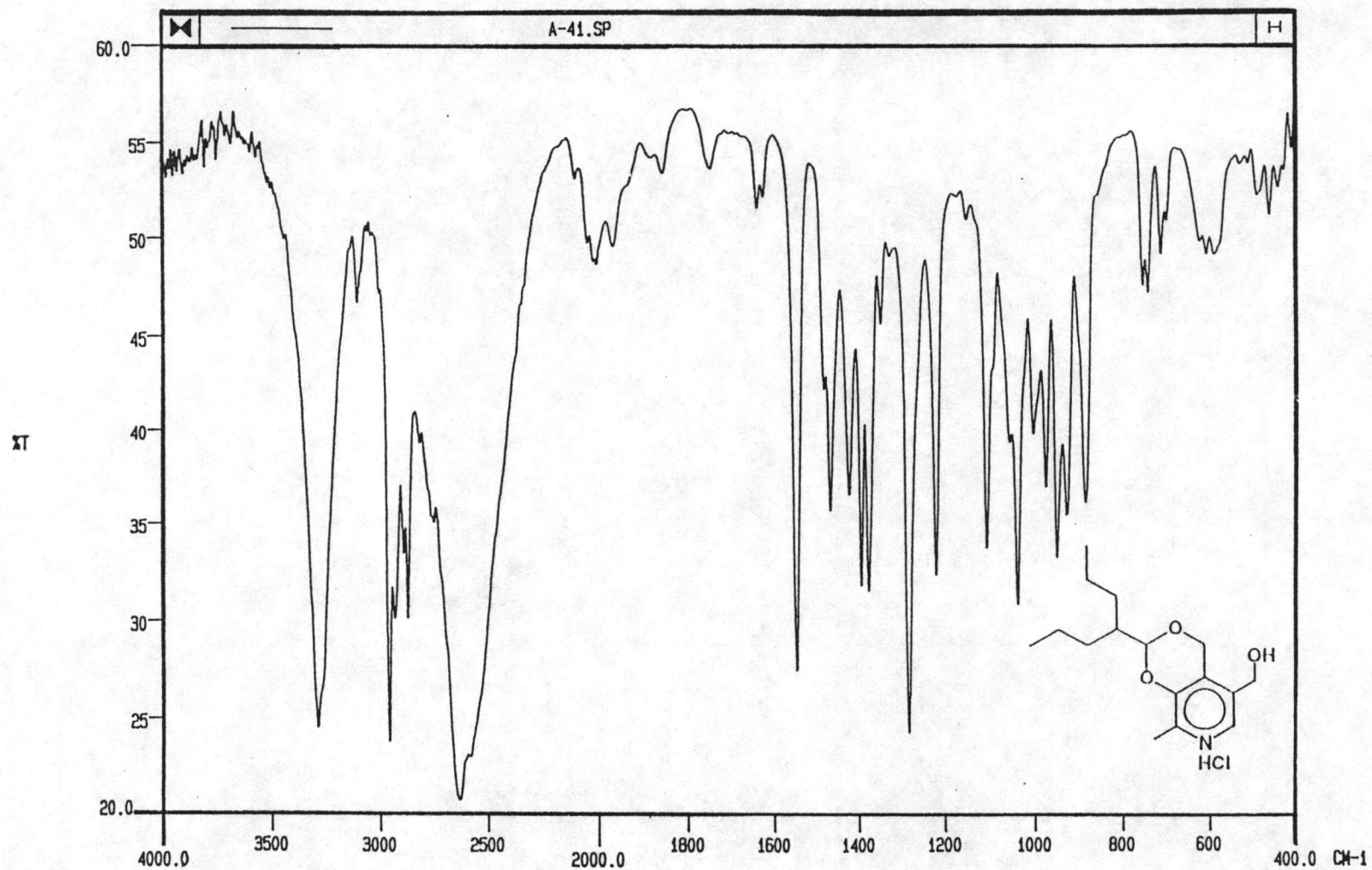


Figure 30. The IR spectrum (KBr) of $\alpha^4,3$ -O-(2-propylpentanylidene)pyridoxine (LXIX) hydrochloride

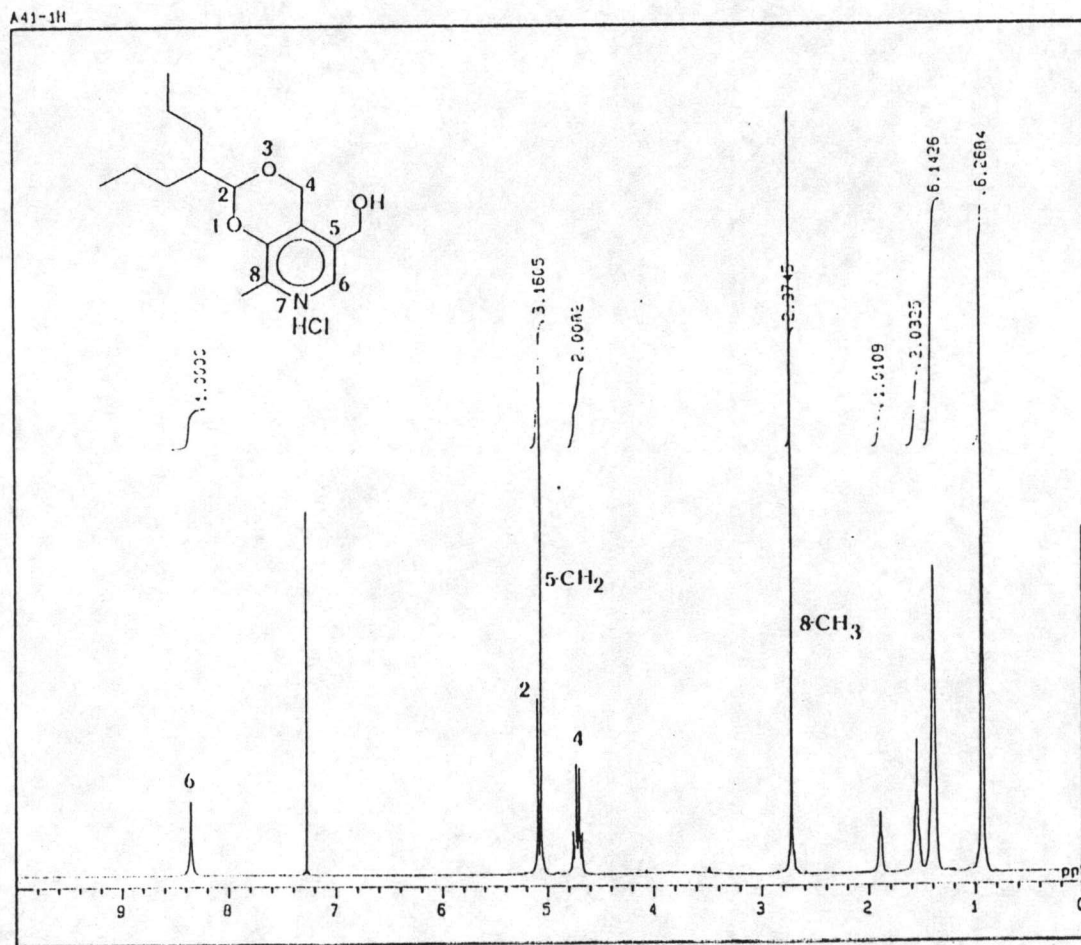


Figure 31. The $^1\text{H-NMR}$ spectrum of $\alpha^4,3\text{-O-(2-propylpentanylidene)pyridoxine}$ (LXIX) hydrochloride (in CDCl_3).

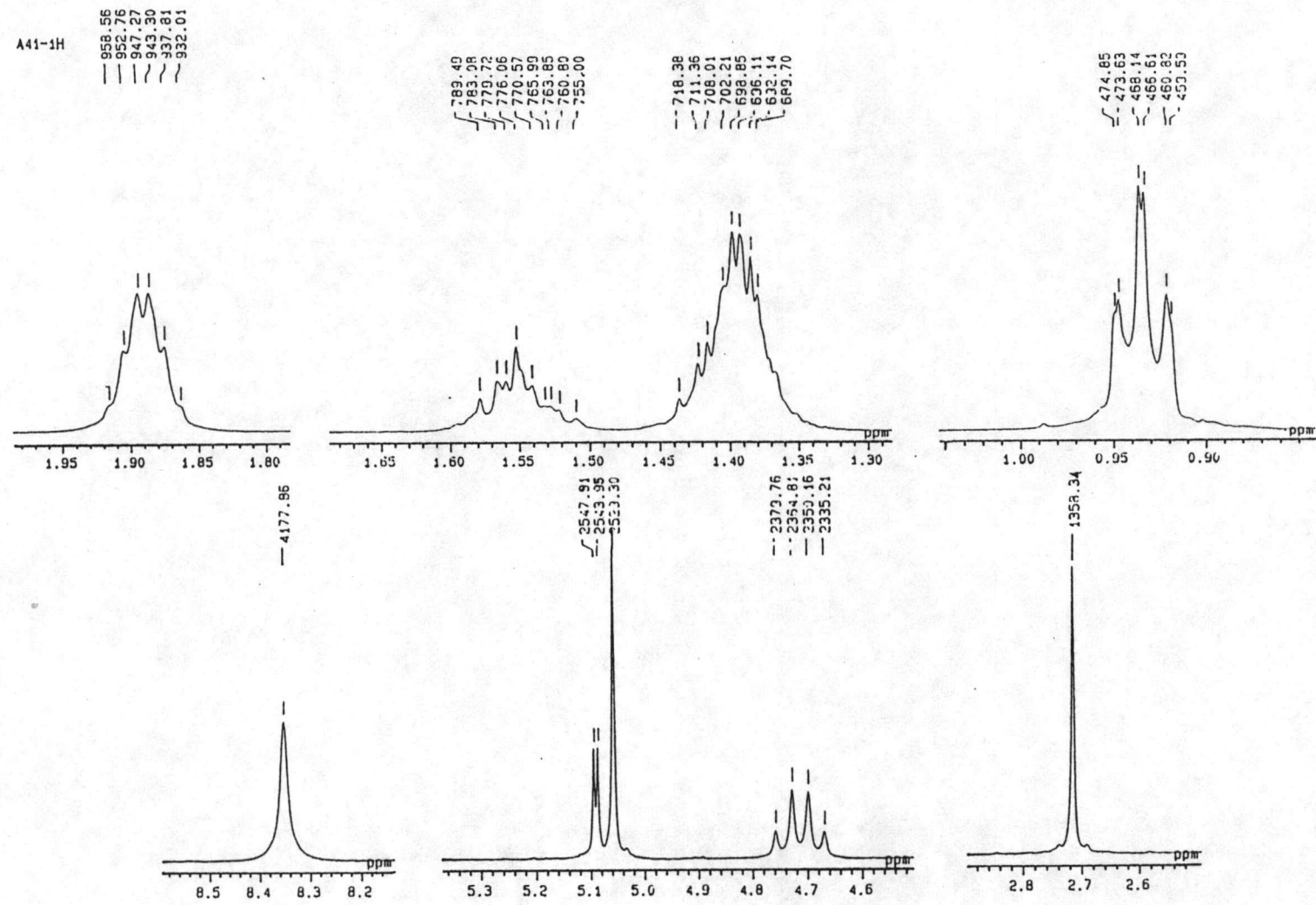


Figure 32. The ¹H-NMR spectrum of $\alpha^4,3$ -O-(2-propylpentanylidene)pyridoxine (LXIX) hydrochloride (Enlarged scale)

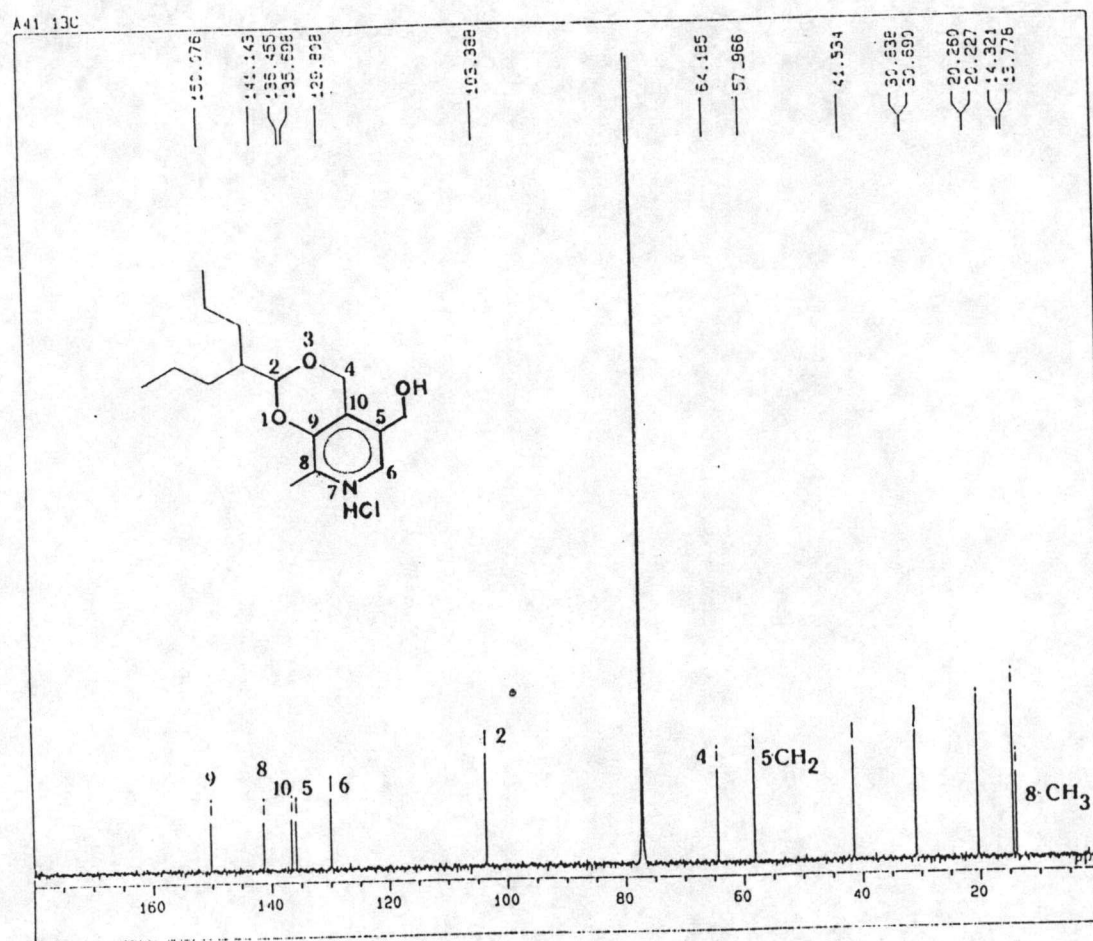


Figure 33. The ^{13}C -NMR spectrum of $\alpha^4,3$ -O-(2-propylpentanylidene)pyridoxine (LXIX) hydrochloride (in CDCl_3).

SM6410002 Scan 174 RT=6:07 100%=69080 mv 20 Dec 95 9:23
LRP +EI A41

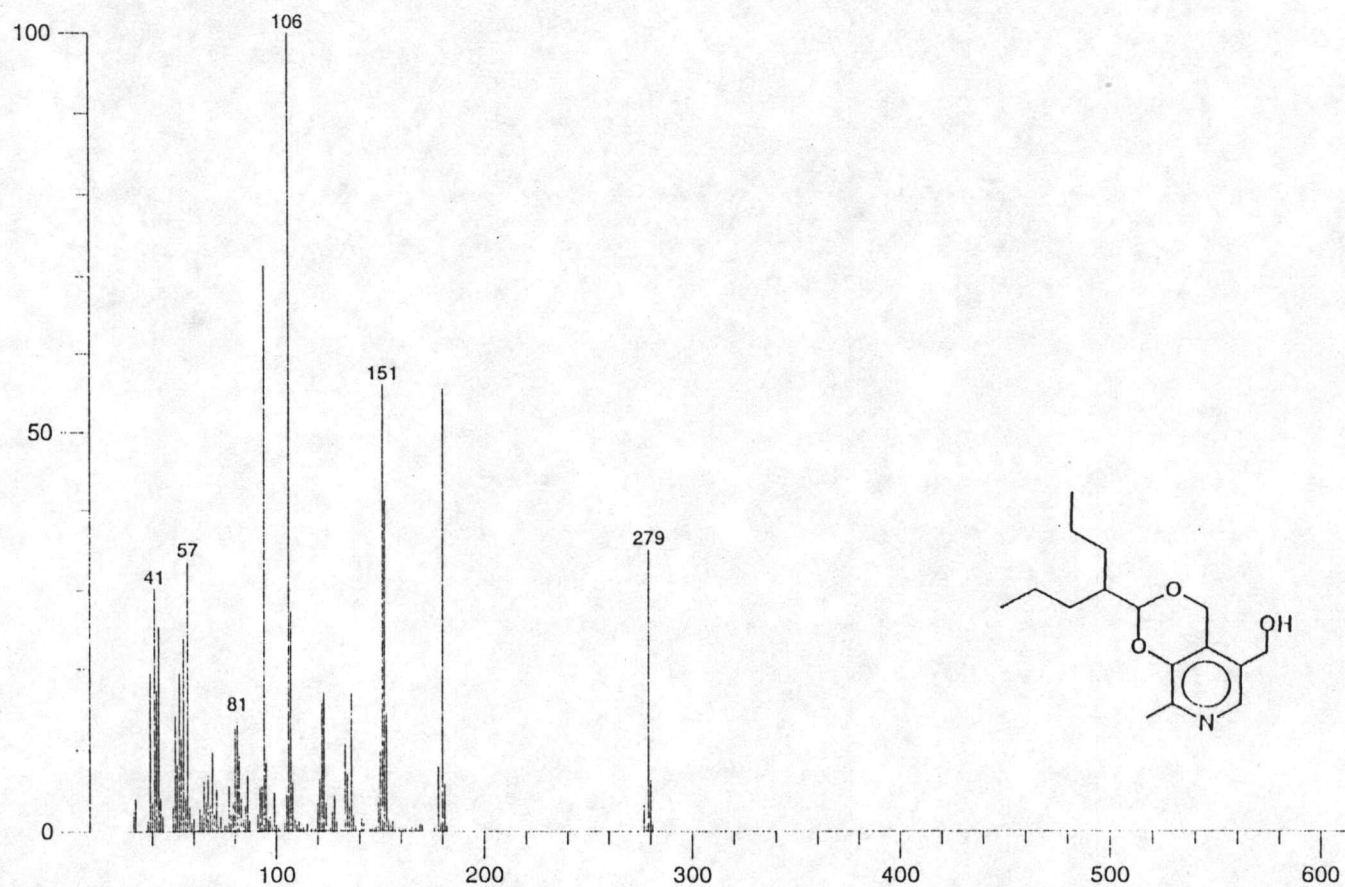


Figure 34. The mass spectrum of $\alpha^4,3$ -O-(2-propylpentanylidene)pyridoxine (LXIX)

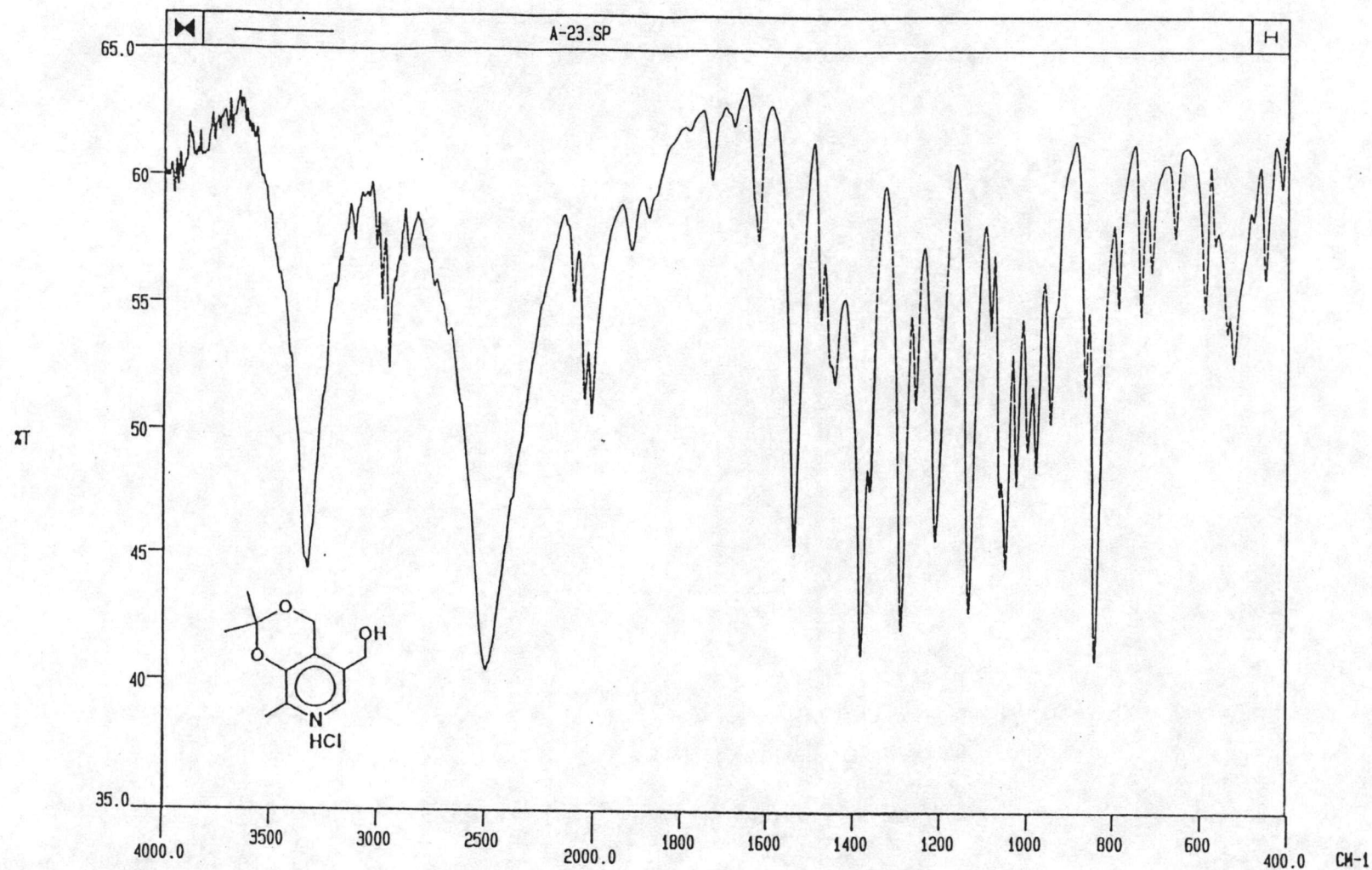


Figure 35. The IR spectrum (KBr) of $\alpha^4,3$ -O-isopropylidene pyridoxine hydrochloride.

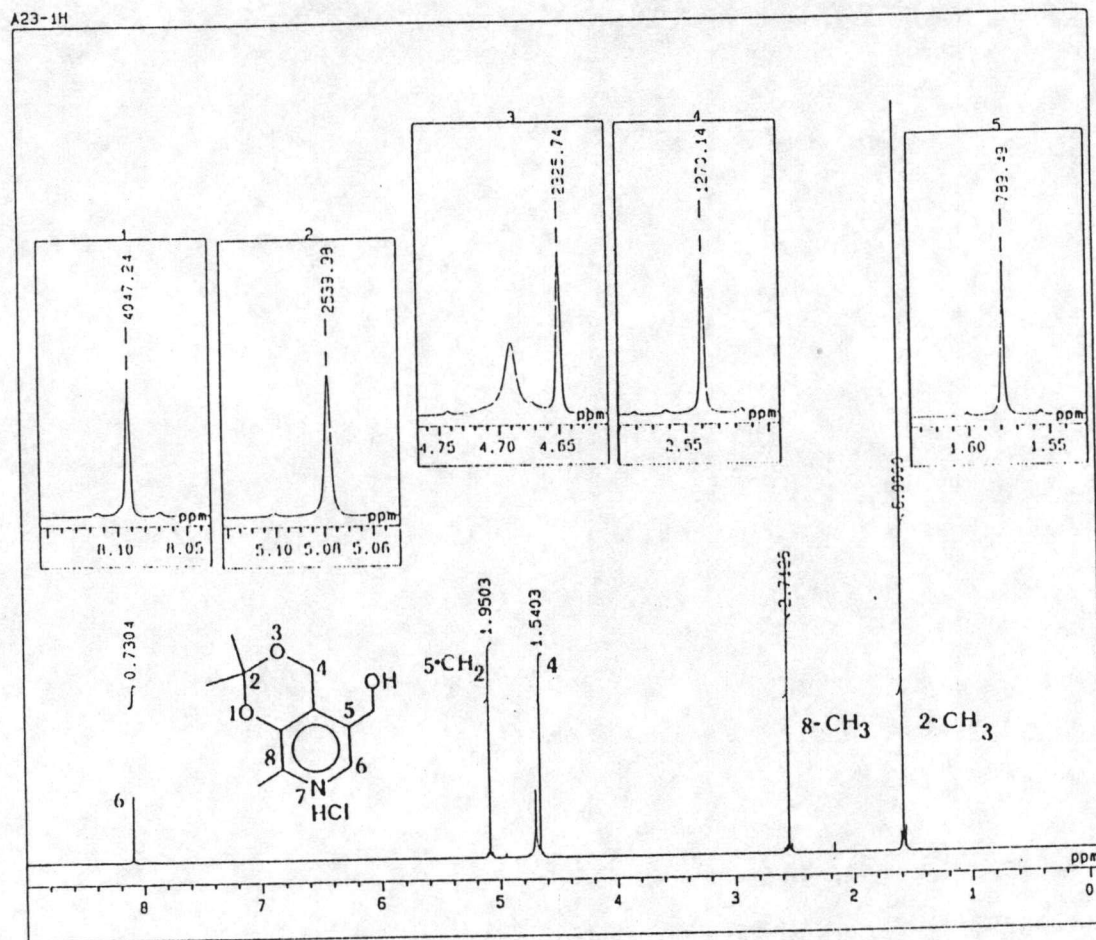


Figure 36. The $^1\text{H-NMR}$ spectrum of $\alpha^4,3$ -O-isopropylidene pyridoxine hydrochloride (in D_2O).

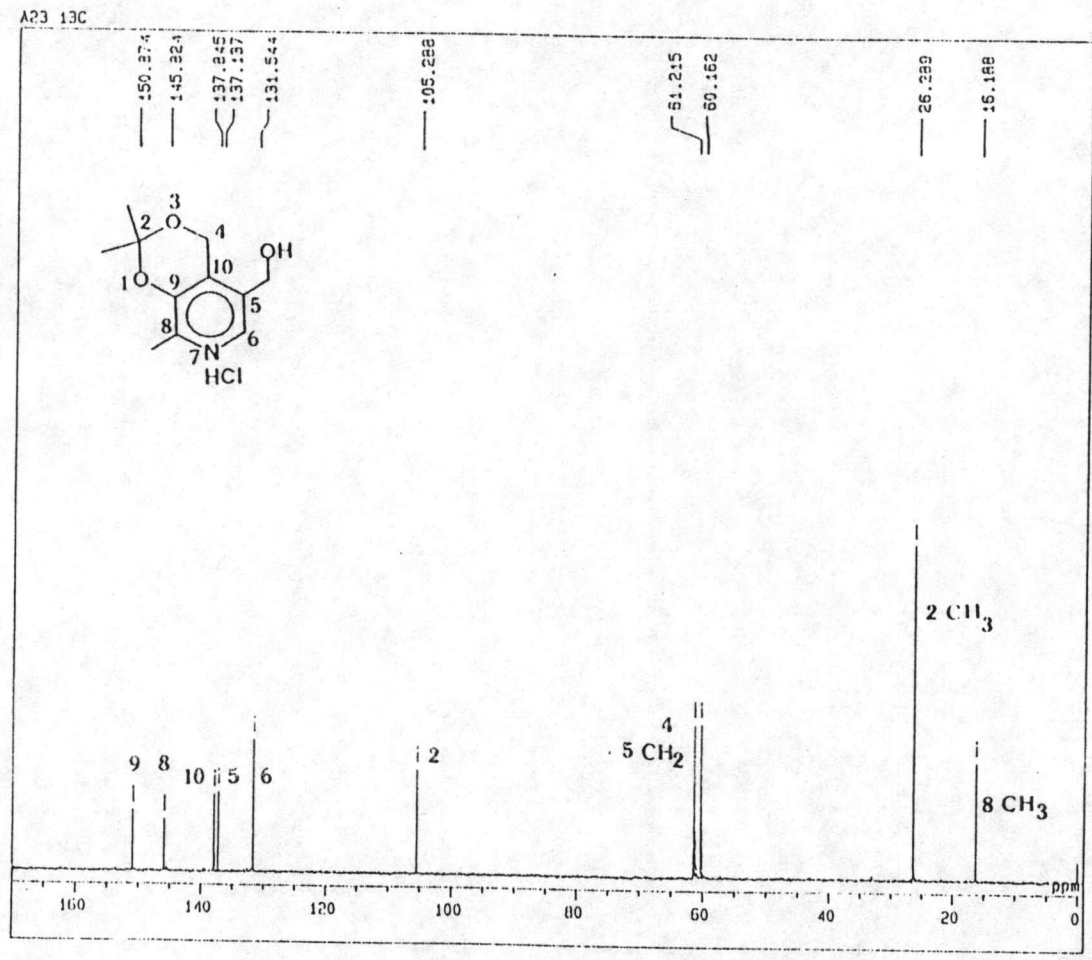


Figure 37. The ^{13}C -NMR spectrum of $\alpha^4,3$ -O-isopropylidene pyridoxine hydrochloride (in D_2O).

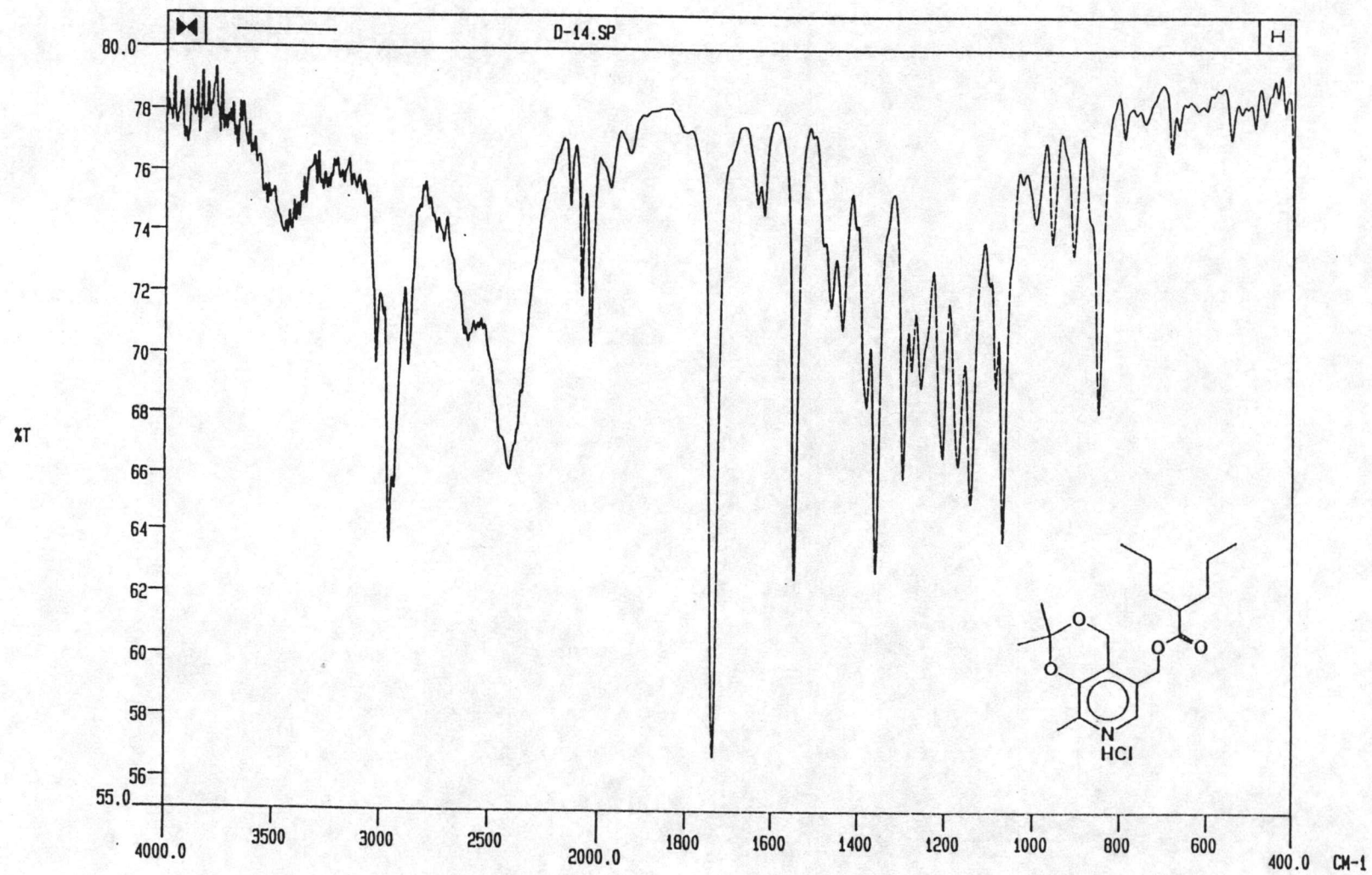


Figure 38. The IR spectrum (KBr) of $\alpha^4,3$ -O-isopropylidene pyridoxine-5-valproate hydrochloride.

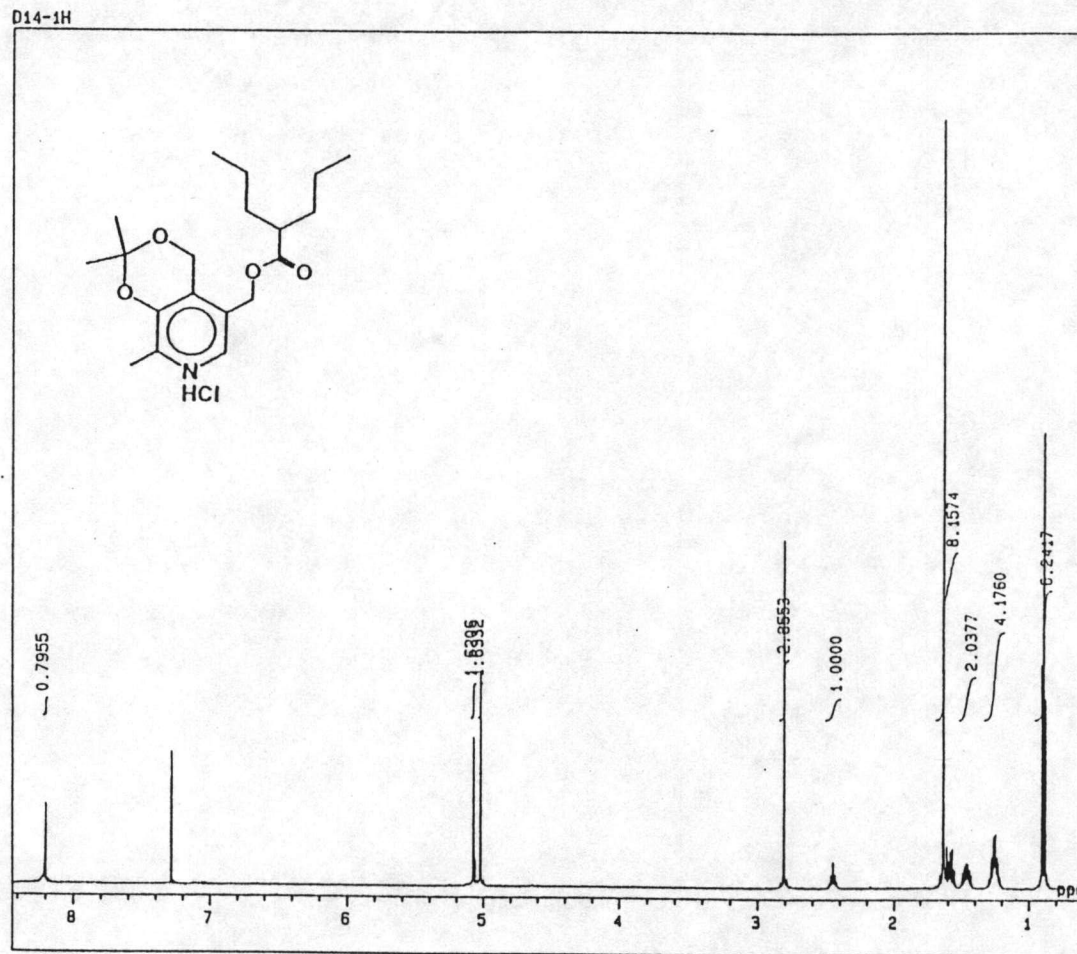


Figure 39. The $^1\text{H-NMR}$ spectrum of $\alpha^4,3$ -O-isopropylidene pyridoxine-5-valproate hydrochloride (in CDCl_3).

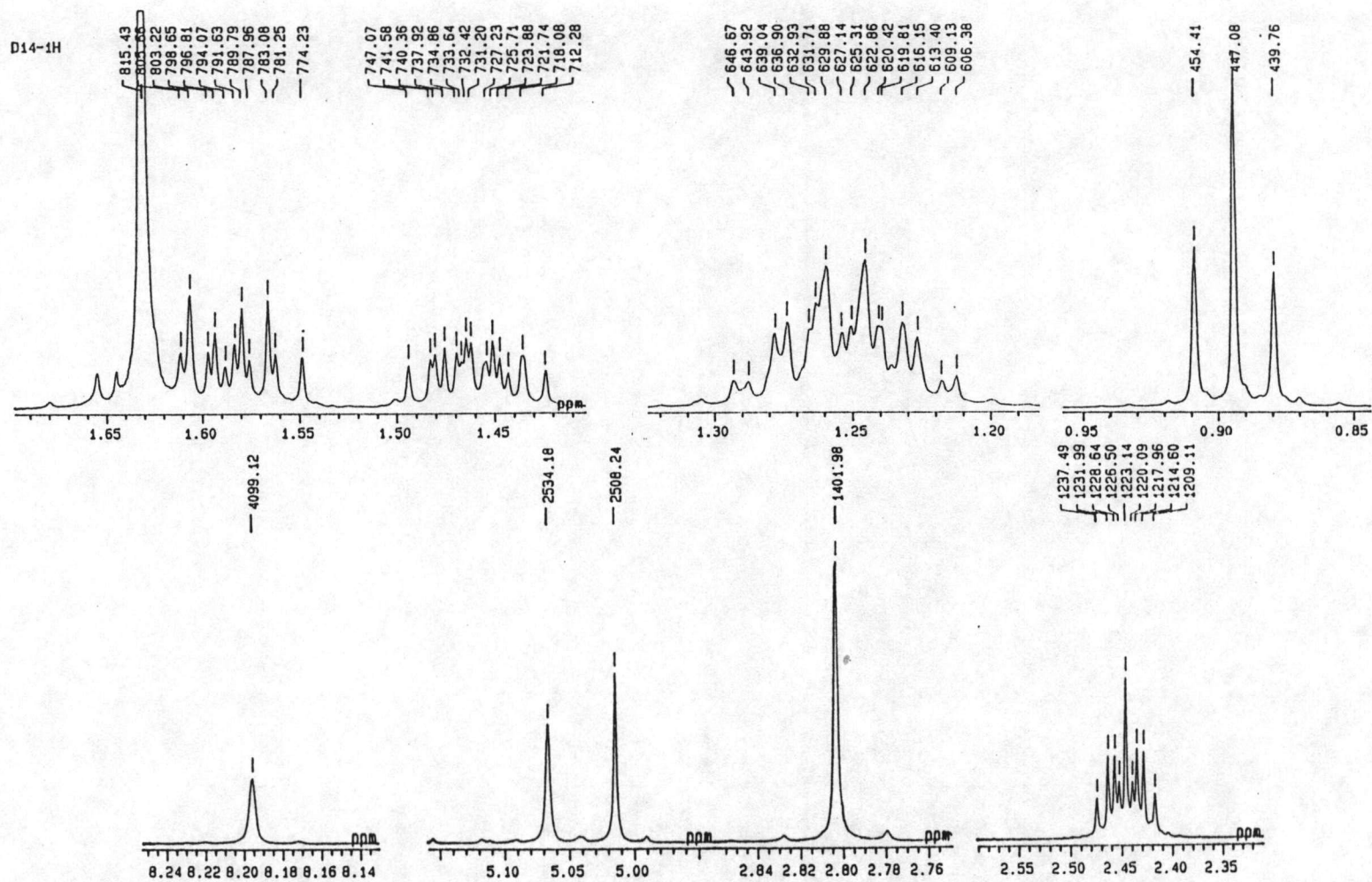


Figure 40. The $^1\text{H-NMR}$ spectrum of $\alpha^4,3\text{-O-isopropylidenpyridoxine-5-valproate hydrochloride}$ (in CDCl_3). (Enlarged scale)

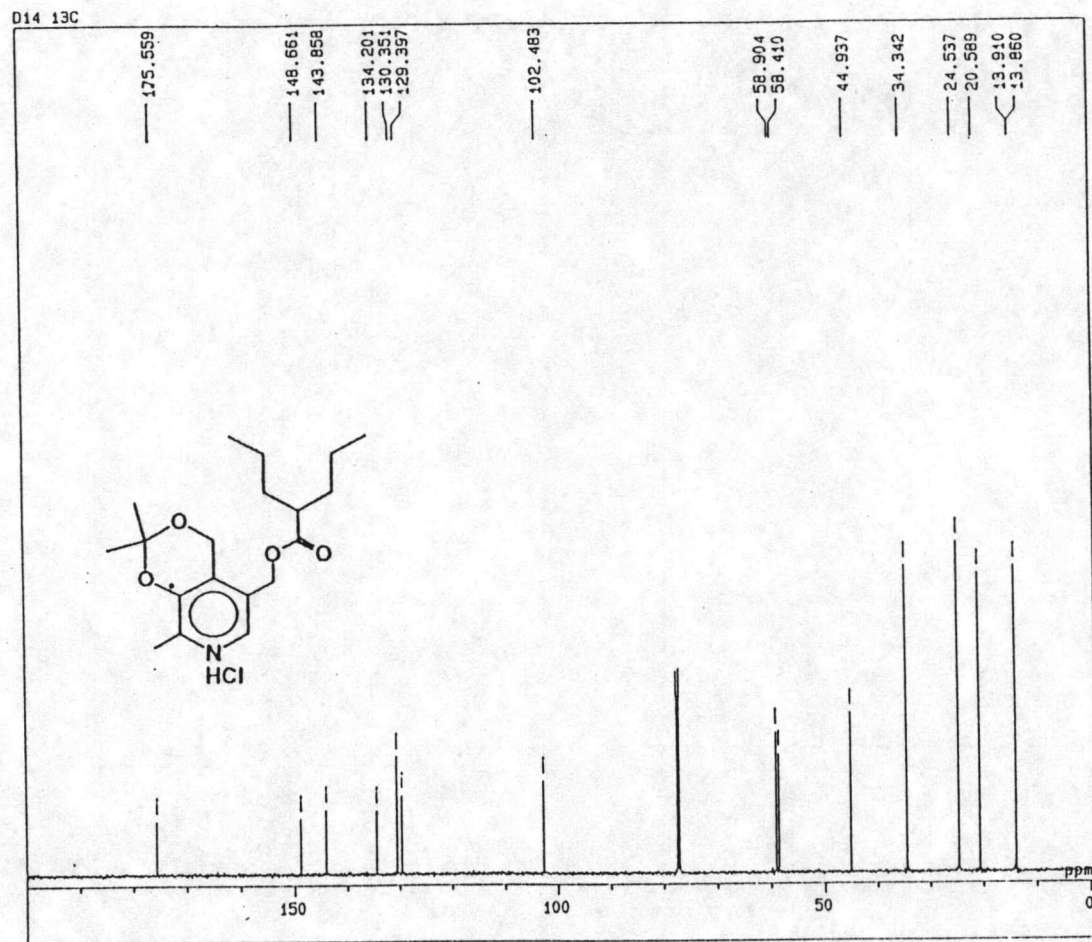


Figure 41. The ^{13}C -NMR spectrum of $\alpha^4,3$ -O-isopropylidene pyridoxine-5-valproate hydrochloride (in CDCl_3).

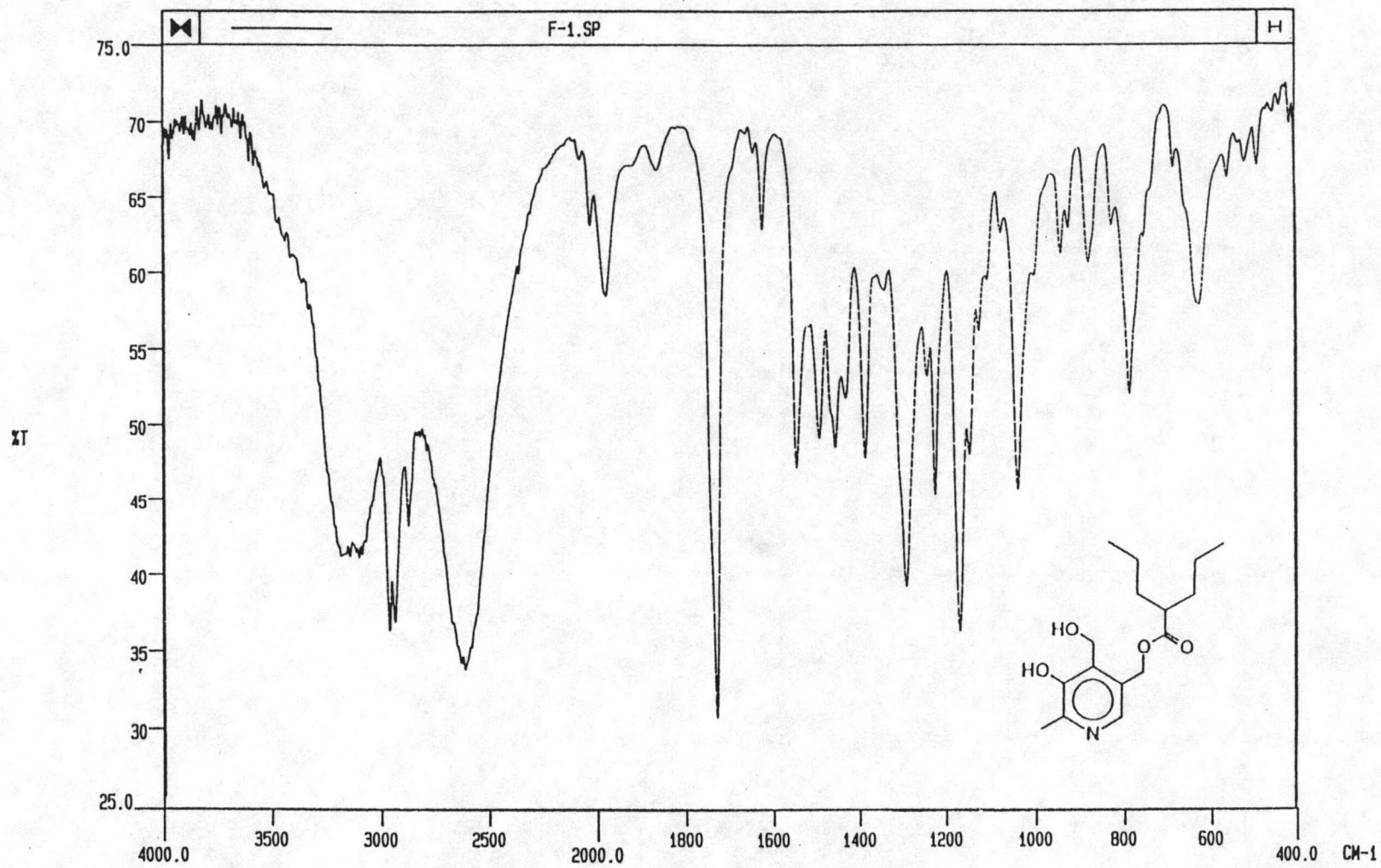


Figure 42. The IR spectrum (KBr) of pyridoxine-5-valproate (LXXI)

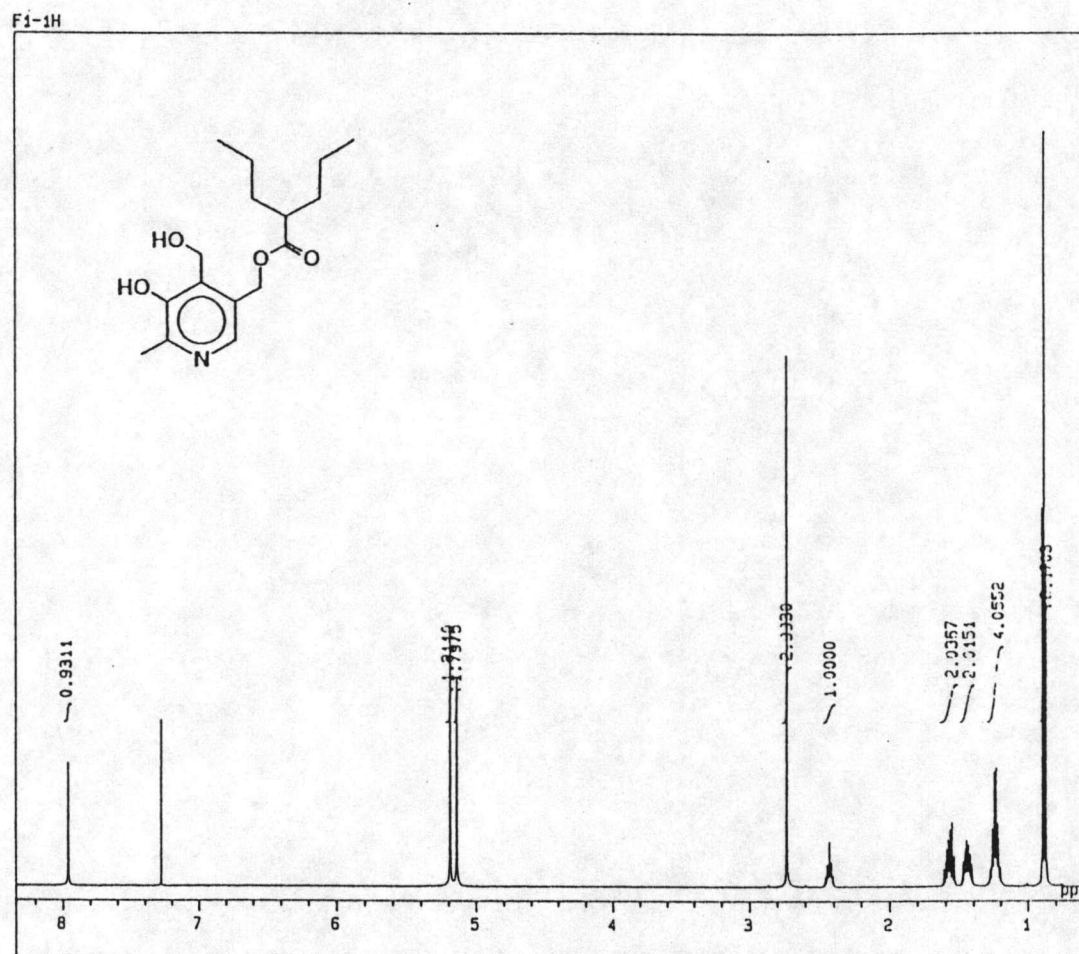


Figure 43. The ^1H -NMR spectrum of pyridoxine-5-valproate (LXXI, in CDCl_3)

F1-1H

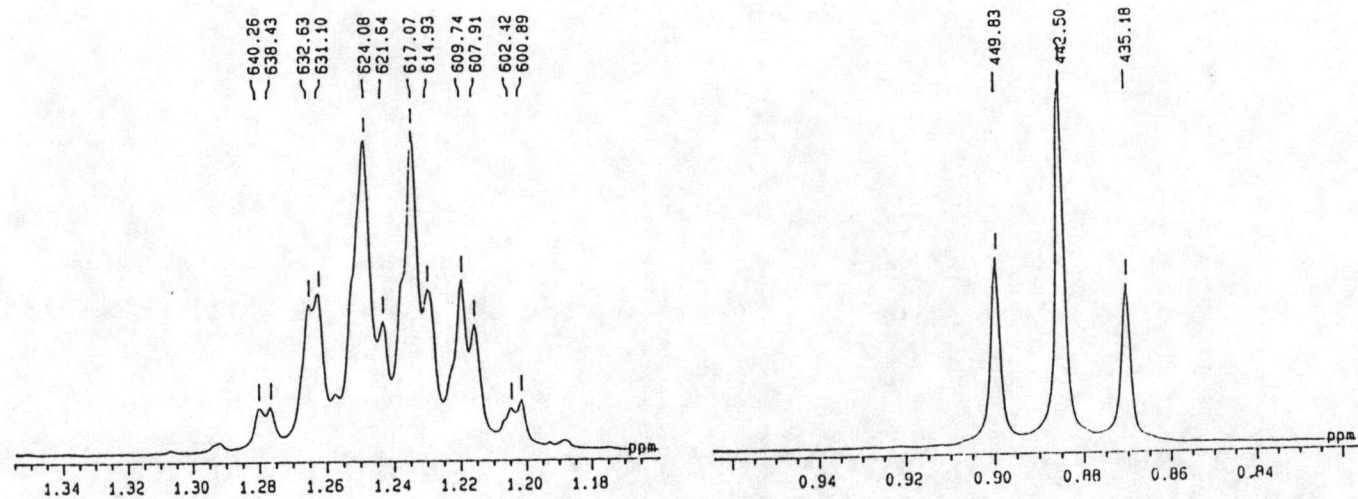


Figure 44. The ^1H -NMR spectrum of pyridoxine-5-valproate (LXXI, in CDCl_3)
(Enlarged scale : 0.8-1.3 ppm)

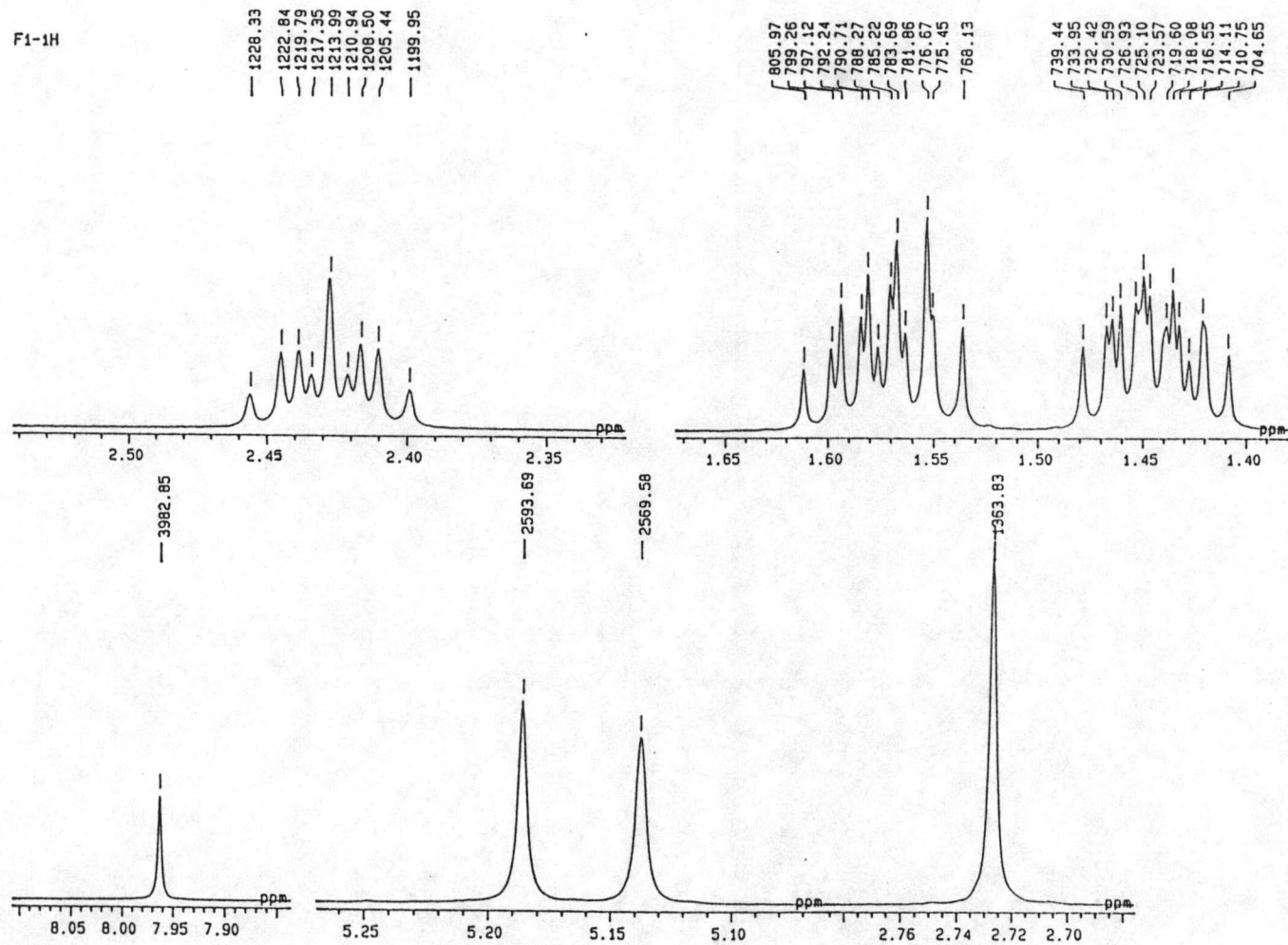


Figure 45. The ^1H -NMR spectrum of pyridoxine-5-valproate (LXXI, in CDCl_3)
(Enlarged scale : 1.4-8.0 ppm)

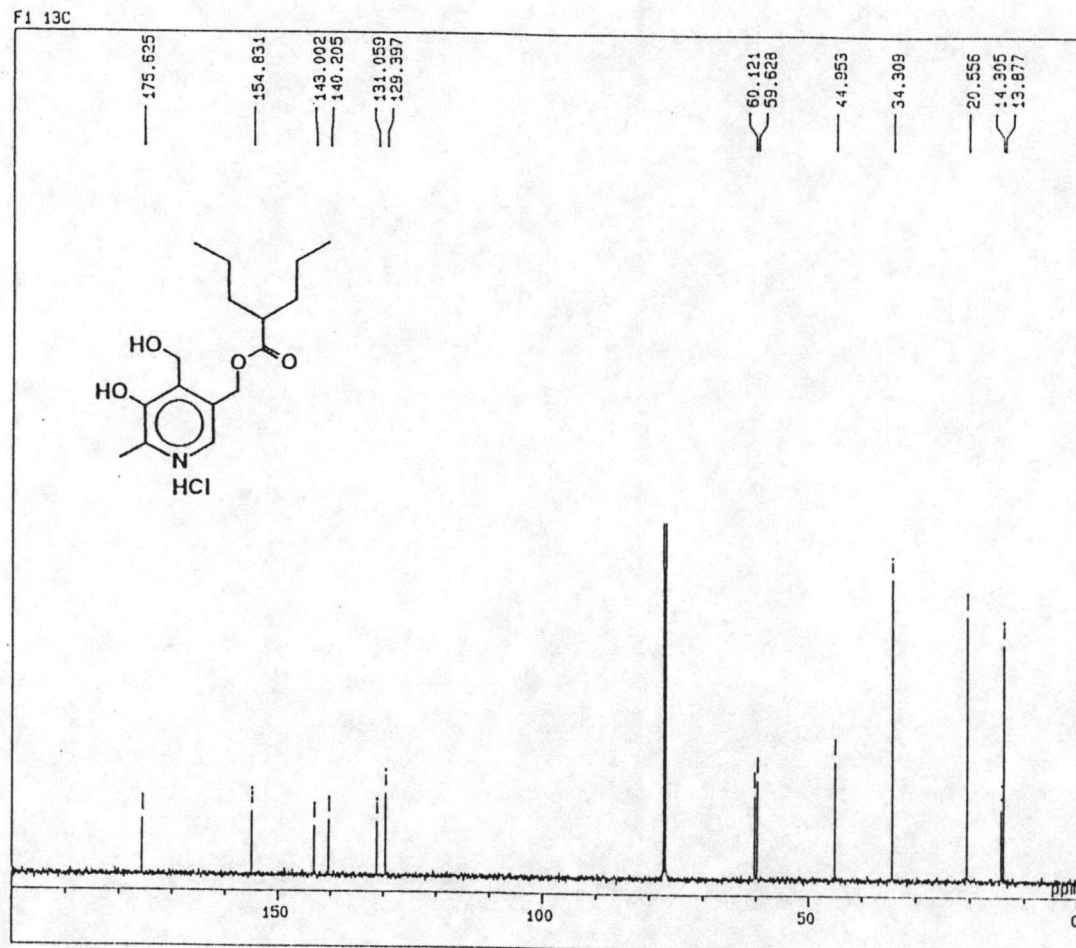


Figure 46. The ^{13}C -NMR spectrum of pyridoxine-5-valproate (LXXI, in CDCl_3)

SN8030001 Scan 171 RT=6:02 100%=121009 mv 15 Jan 96 13:32
LRP +EI F1

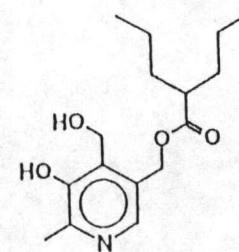
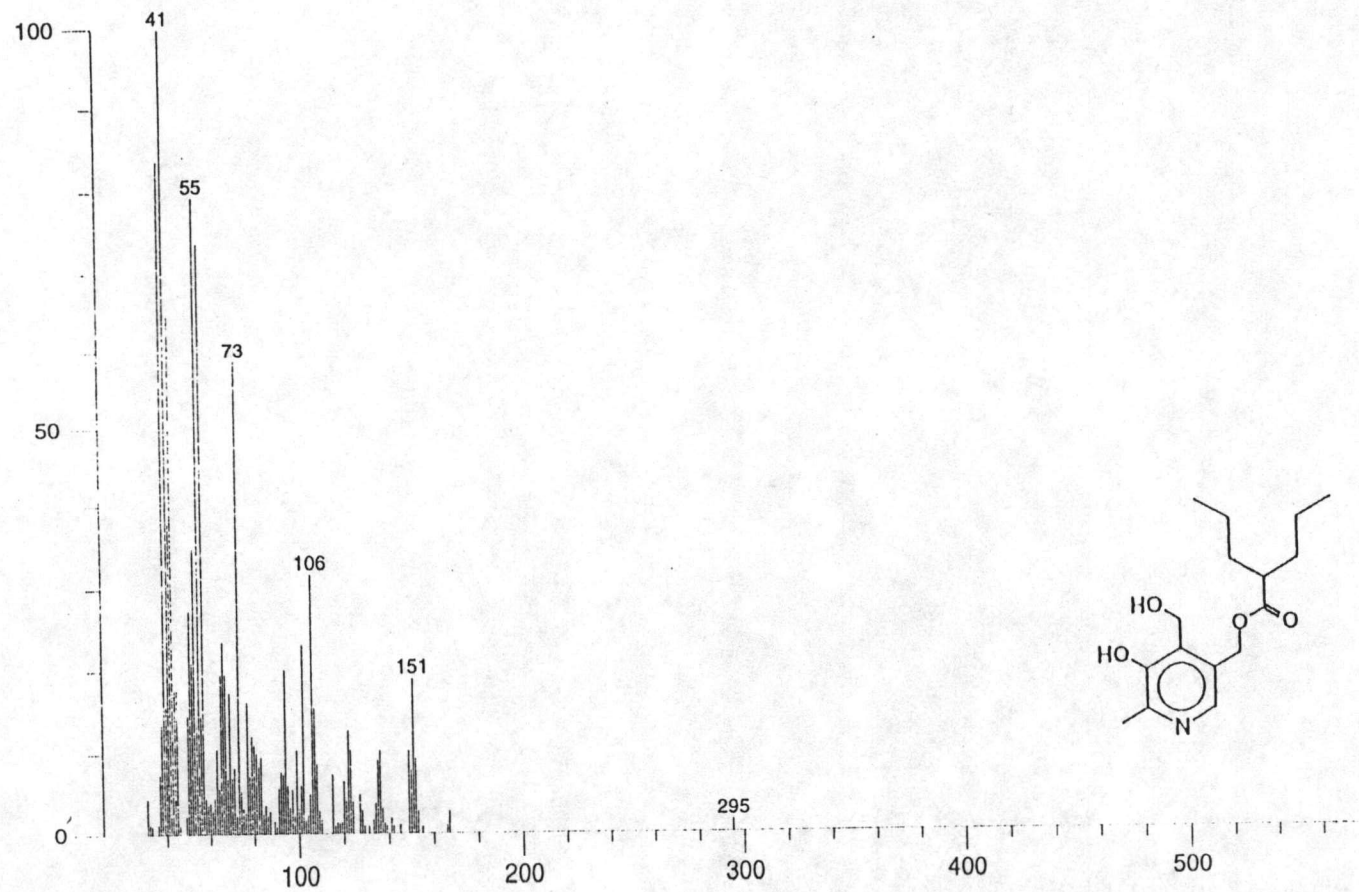


Figure 47. The mass spectrum of pyridoxine-5-valproate (LXXI)

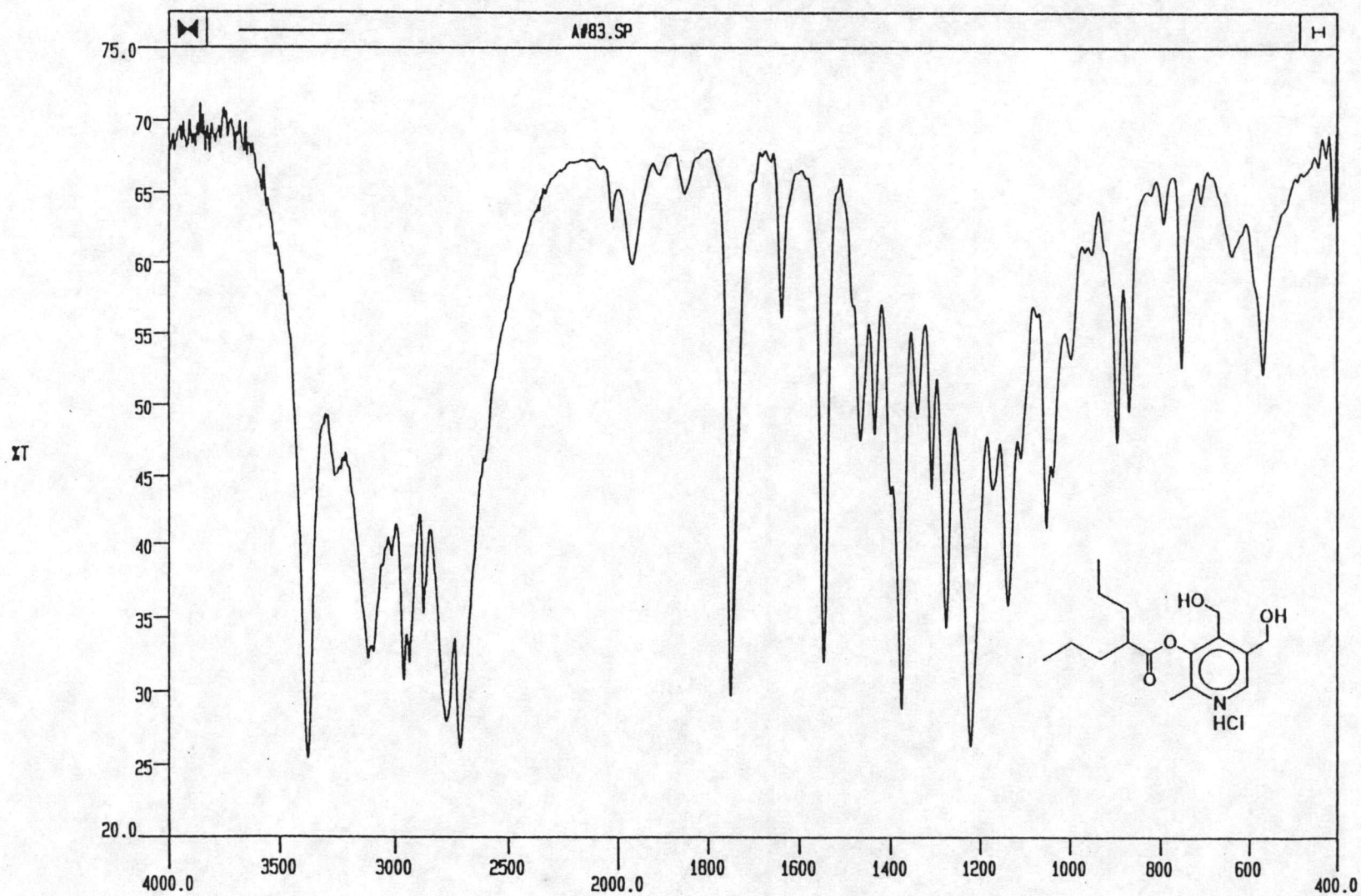


Figure 48. The IR spectrum (KBr) of pyridoxine-3-valproate hydrochloride (LXXII) hydrochloride

CT-1

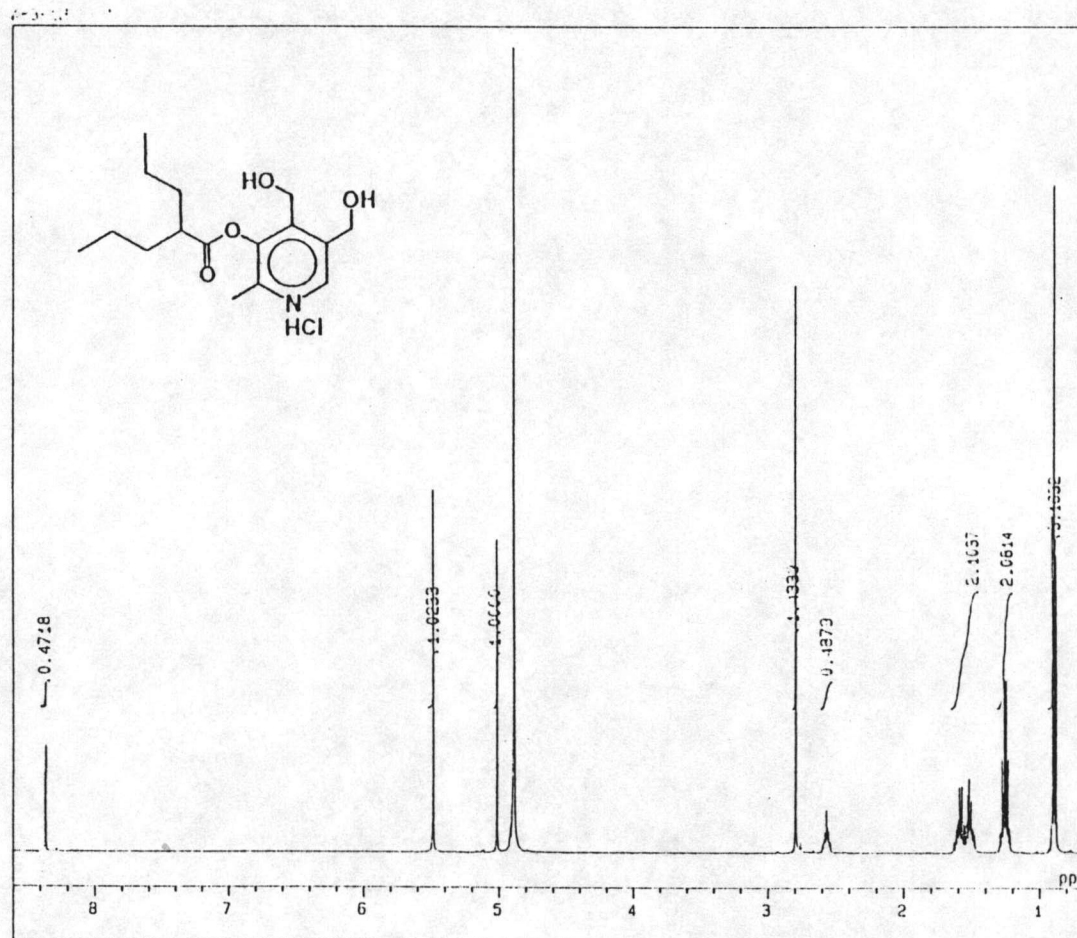


Figure 49. The ¹H-NMR spectrum of pyridoxine-3-valproate (LXXII) hydrochloride (in D₂O)

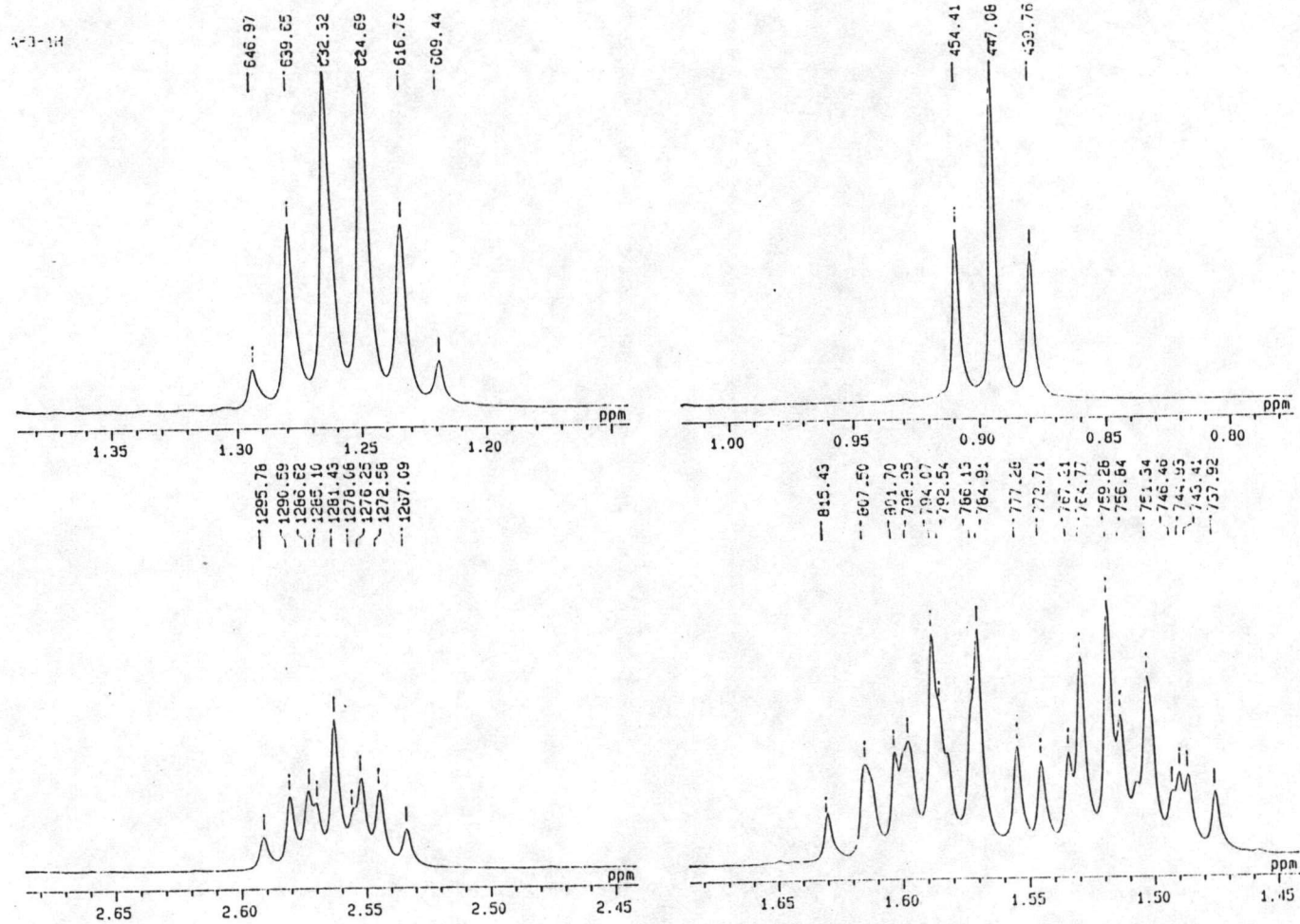


Figure 50. The $^1\text{H-NMR}$ spectrum of pyridoxine-3-valproate (LXXII) hydrochloride (in D_2O)
 (Enlarged scale : 0.8-2.6 ppm)

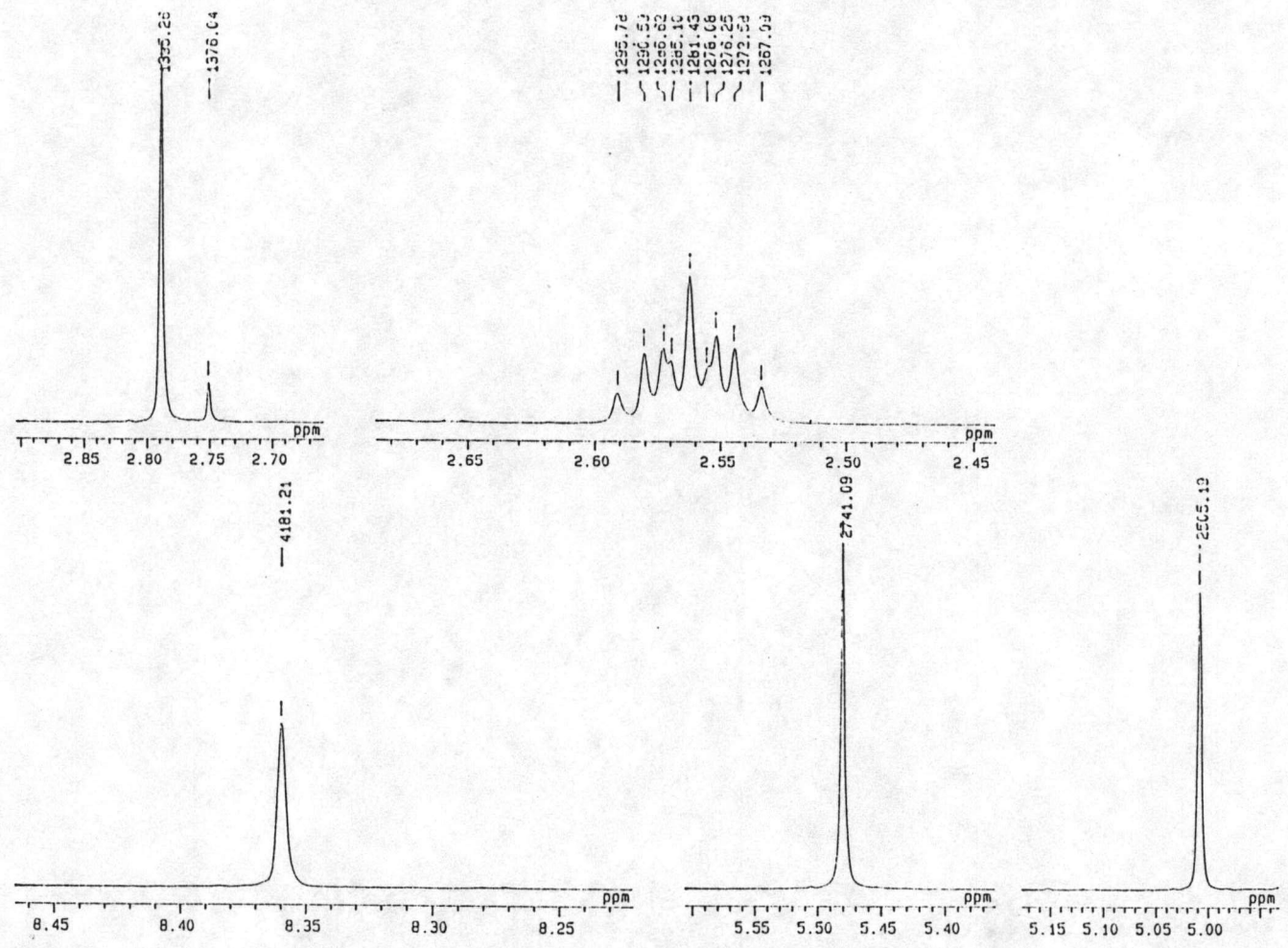


Figure 51. The $^1\text{H-NMR}$ spectrum of pyridoxine-3-valproate (LXXII) hydrochloride (in D_2O)
(Enlarged scale : 2.5-8.4 ppm)

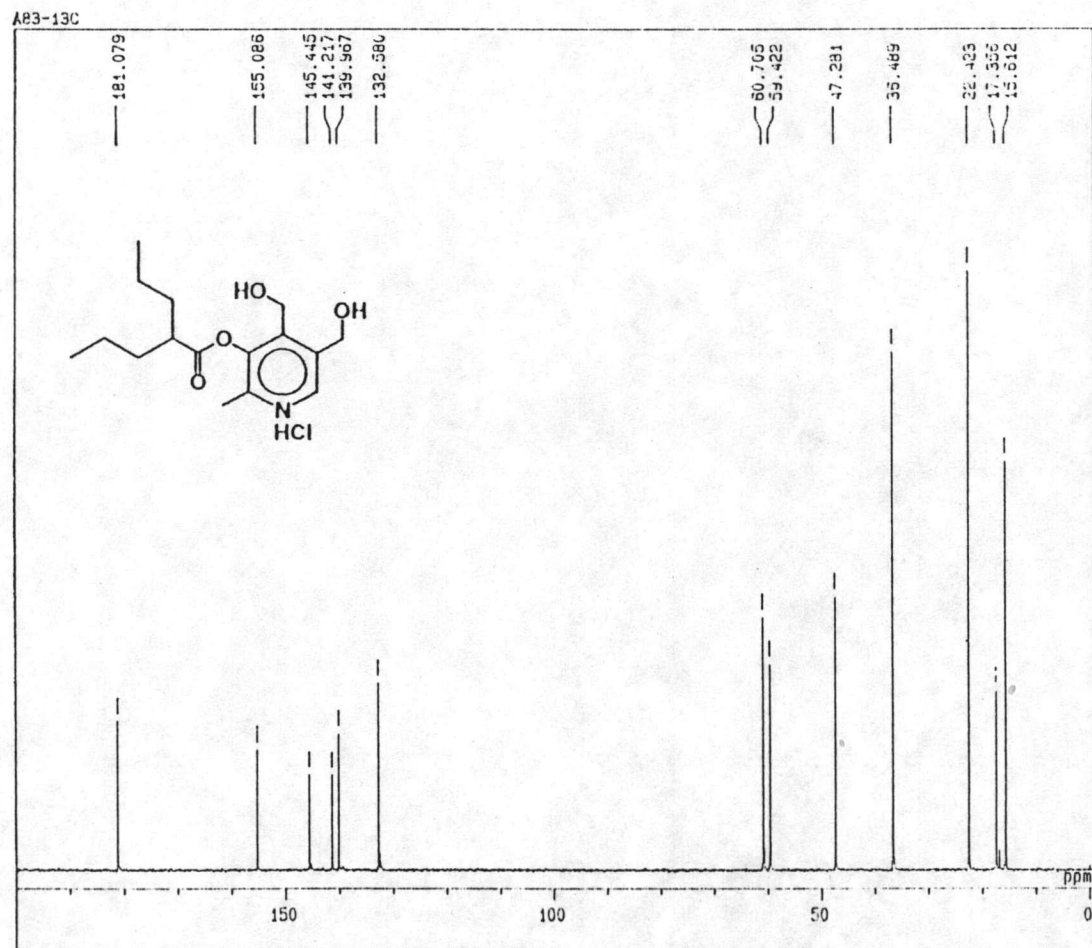


Figure 52. The ¹³C-NMR spectrum of pyridoxine-3-valproate (LXXII) hydrochloride (in D₂O)

SN9240002 Scan 119 RT=4:11 100%=36755 mv 17 Jan 96 12:56
LRP +EI A83

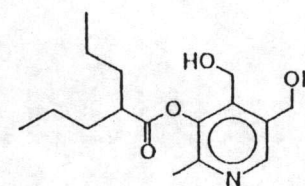
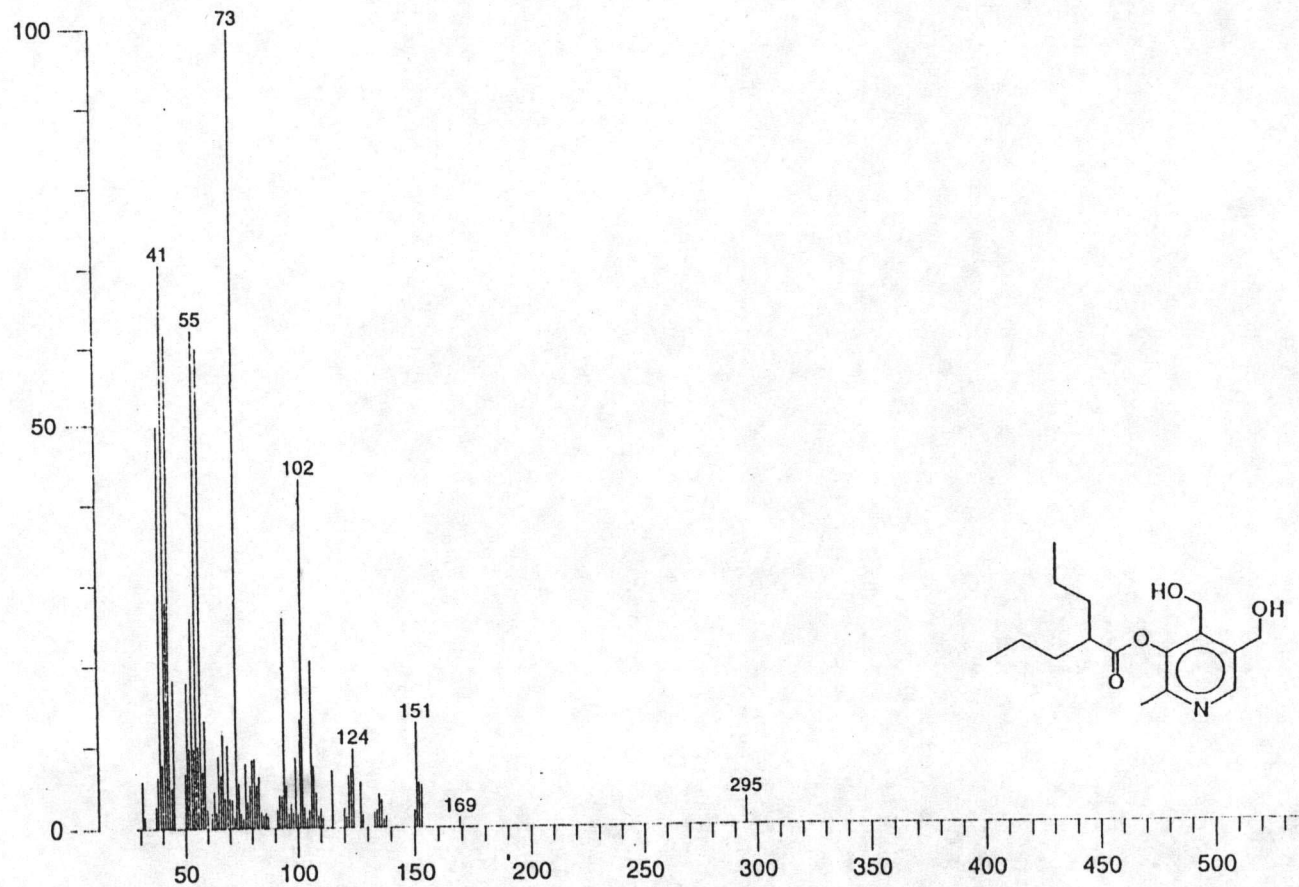


Figure 53. The mass spectrum of pyridoxine-3-valproate (LXXII)

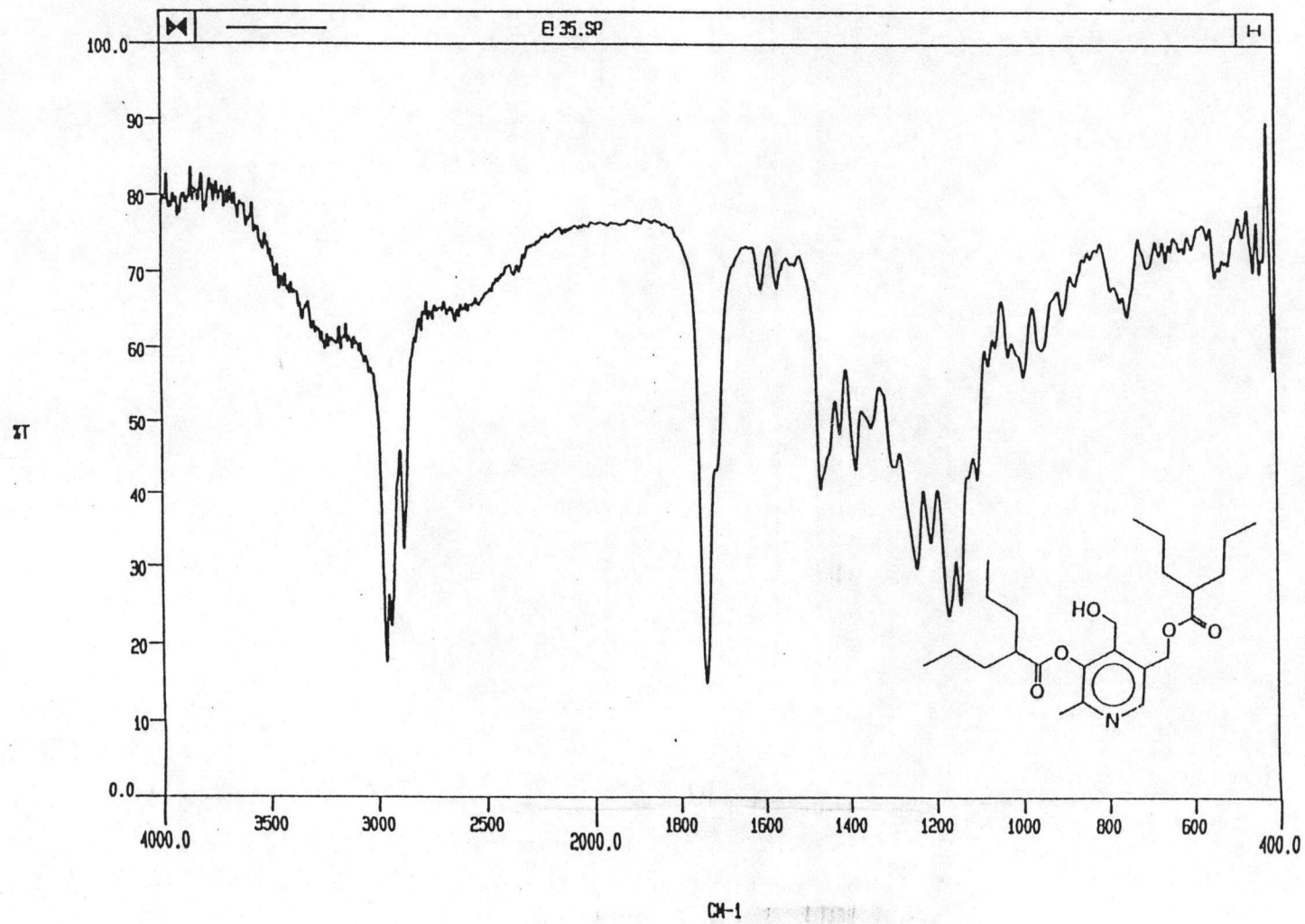


Figure 54. The IR spectrum (neat) of pyridoxine-3,5-divalproate (LXXIV)

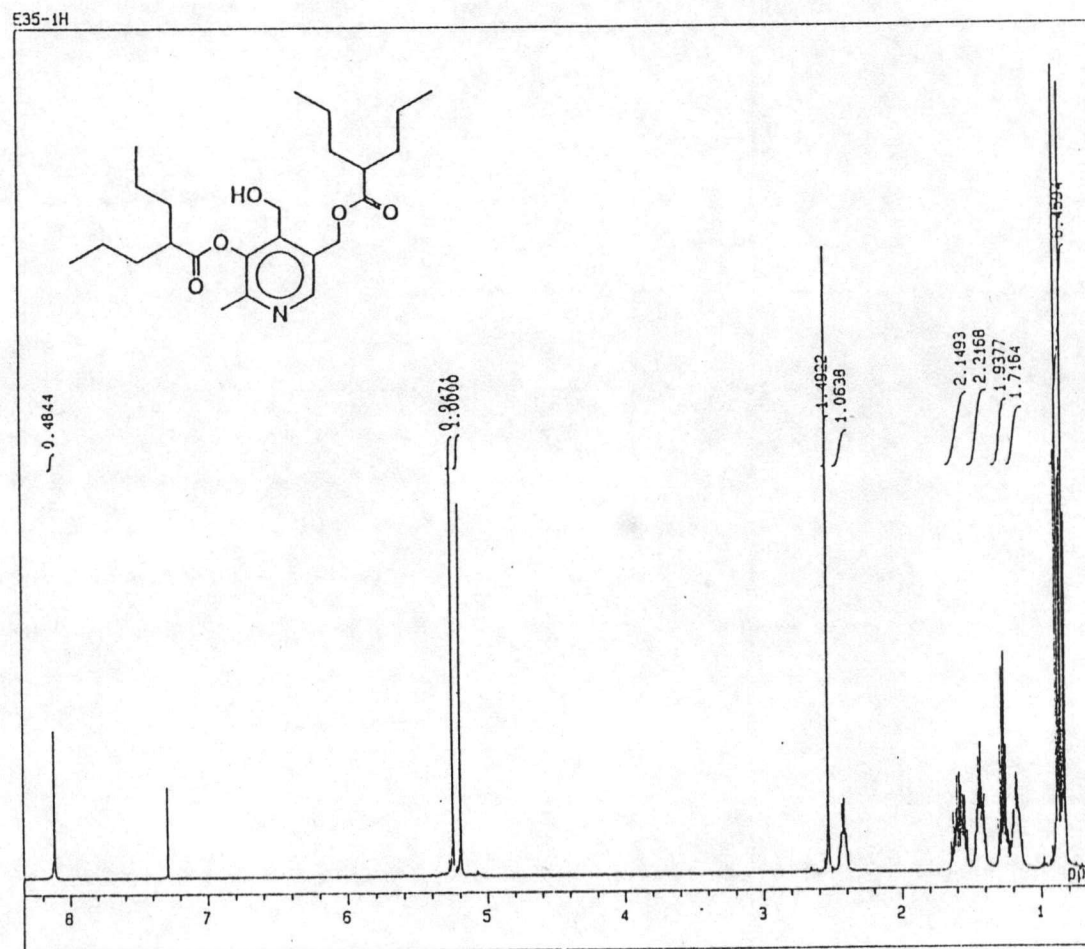


Figure 55. The ¹H-NMR spectrum of pyridoxine-3,5-divalproate (LXXIV, in CDCl₃)

E35-1H

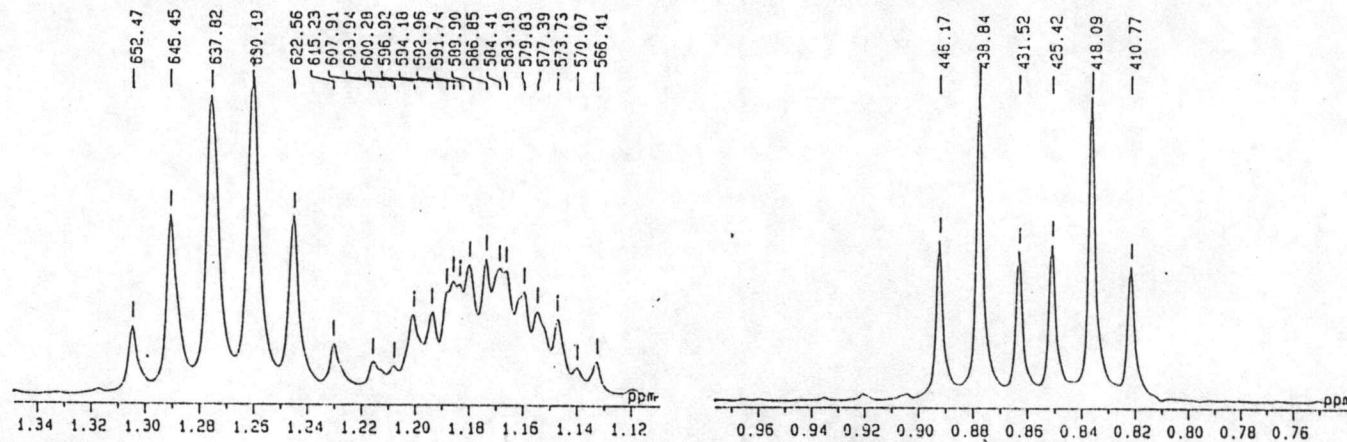


Figure 56. The $^1\text{H-NMR}$ spectrum of pyridoxine-3,5-divalproate (LXXIV, in CDCl_3)
(Enlarged scale : 0.8-1.4 ppm)

E35-1H

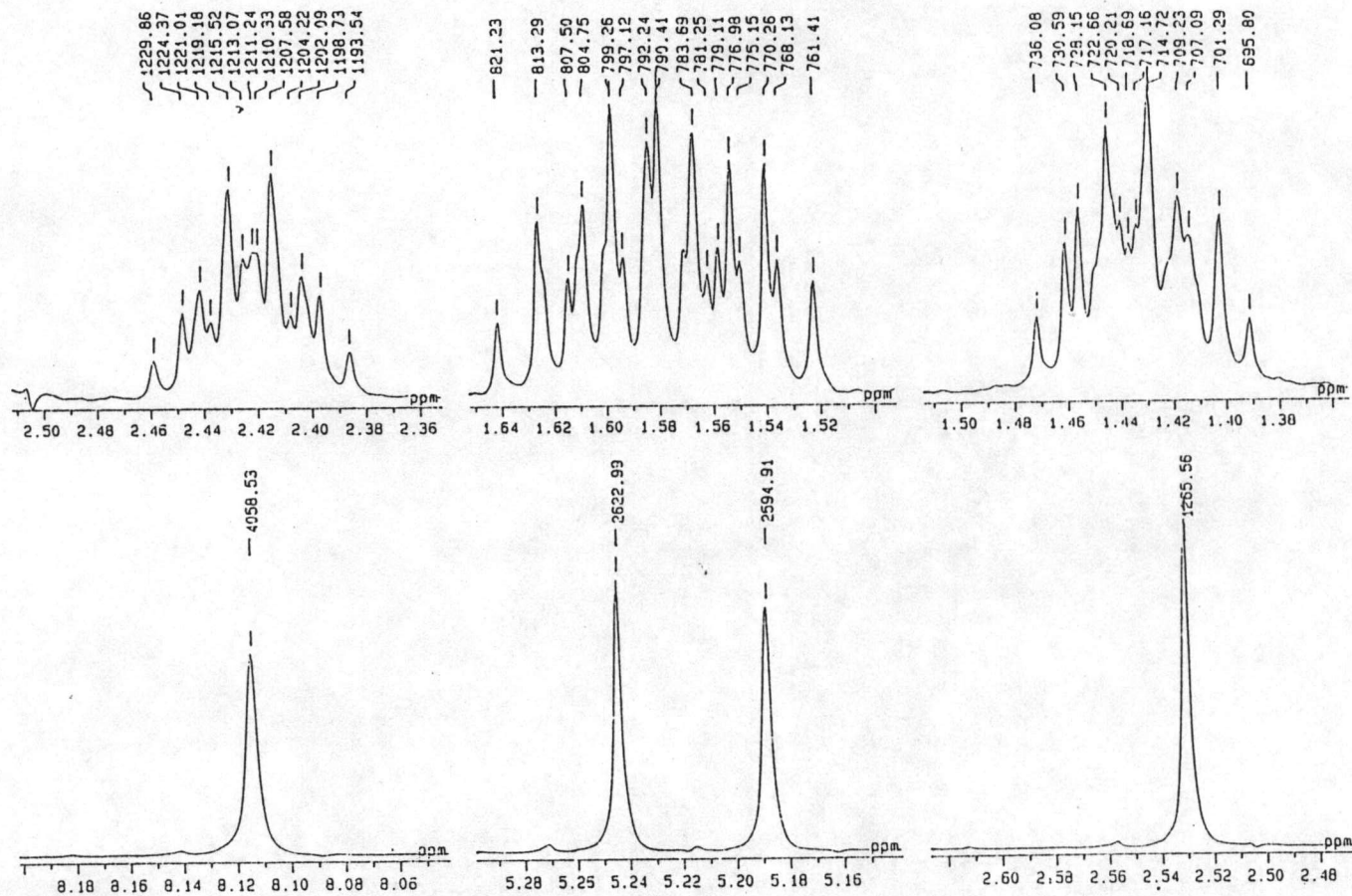


Figure 57. The ^1H -NMR spectrum of pyridoxine-3,5-divalproate (LXXIV, in CDCl_3)
(Enlarged scale : 1.4-8.2 ppm)

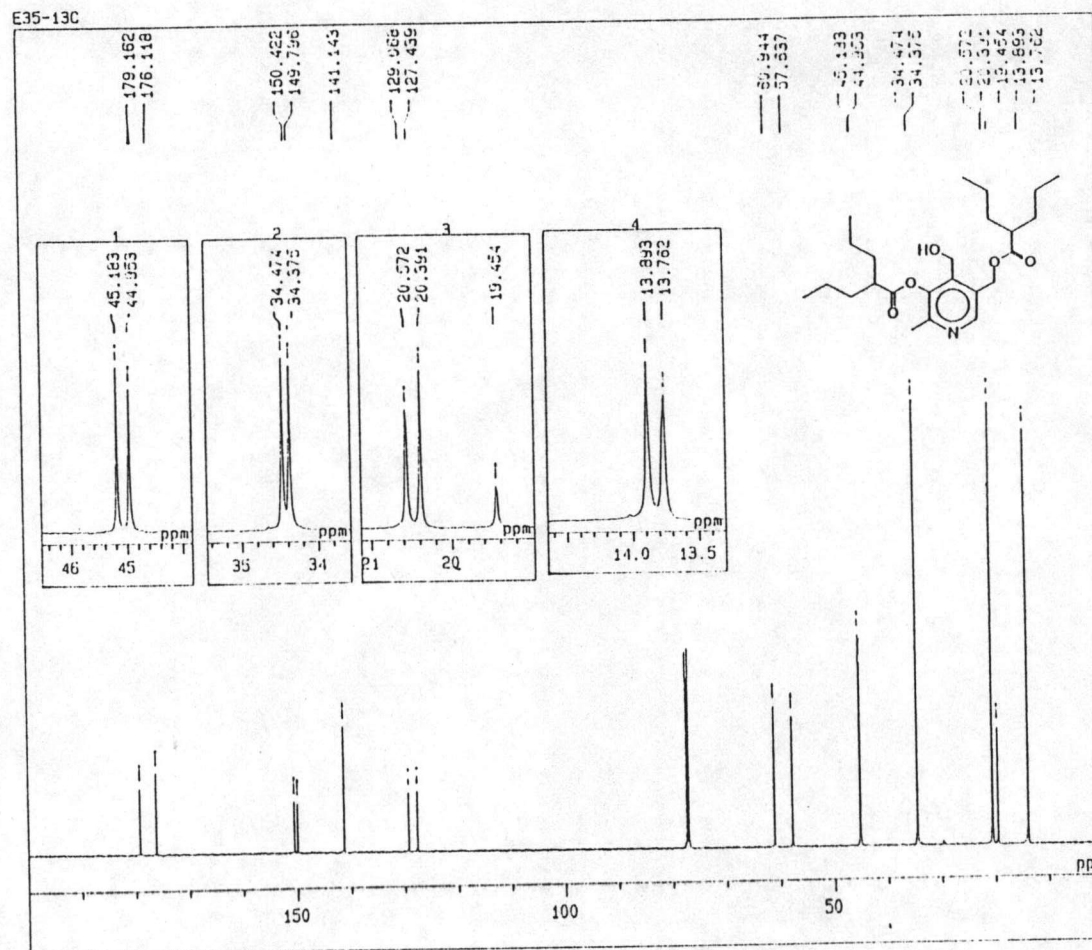


Figure 58. The ^{13}C -NMR spectrum of pyridoxine-3,5-divalproate (LXXIV, in CDCl_3)

SM6430001 Scan 237 RT=8:20 100%=127637 mv 20 Dec 95 14:14
LRP +EI E35

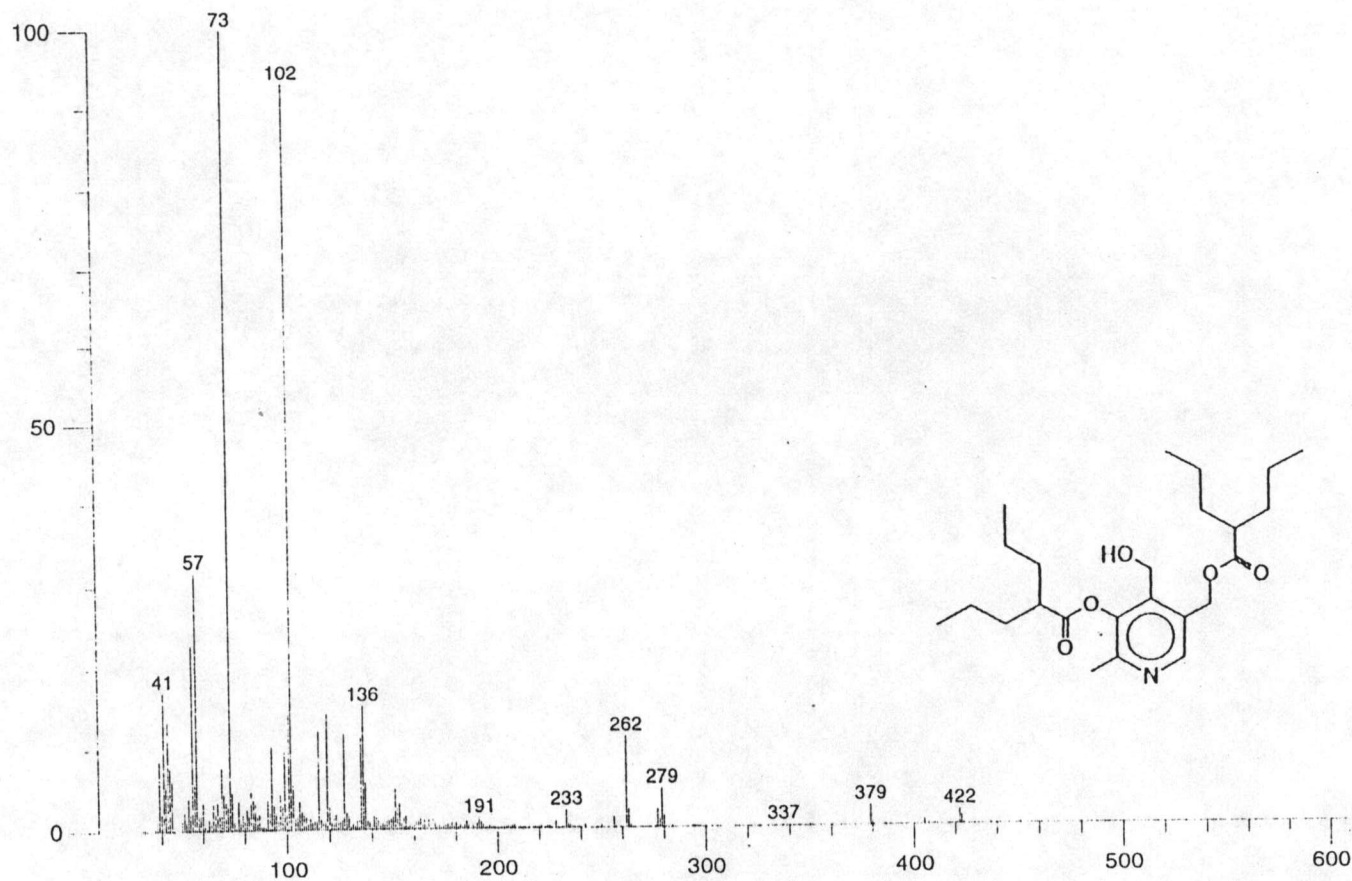


Figure 59. The mass spectrum of pyridoxine-3,5-divalproate (LXXIV)

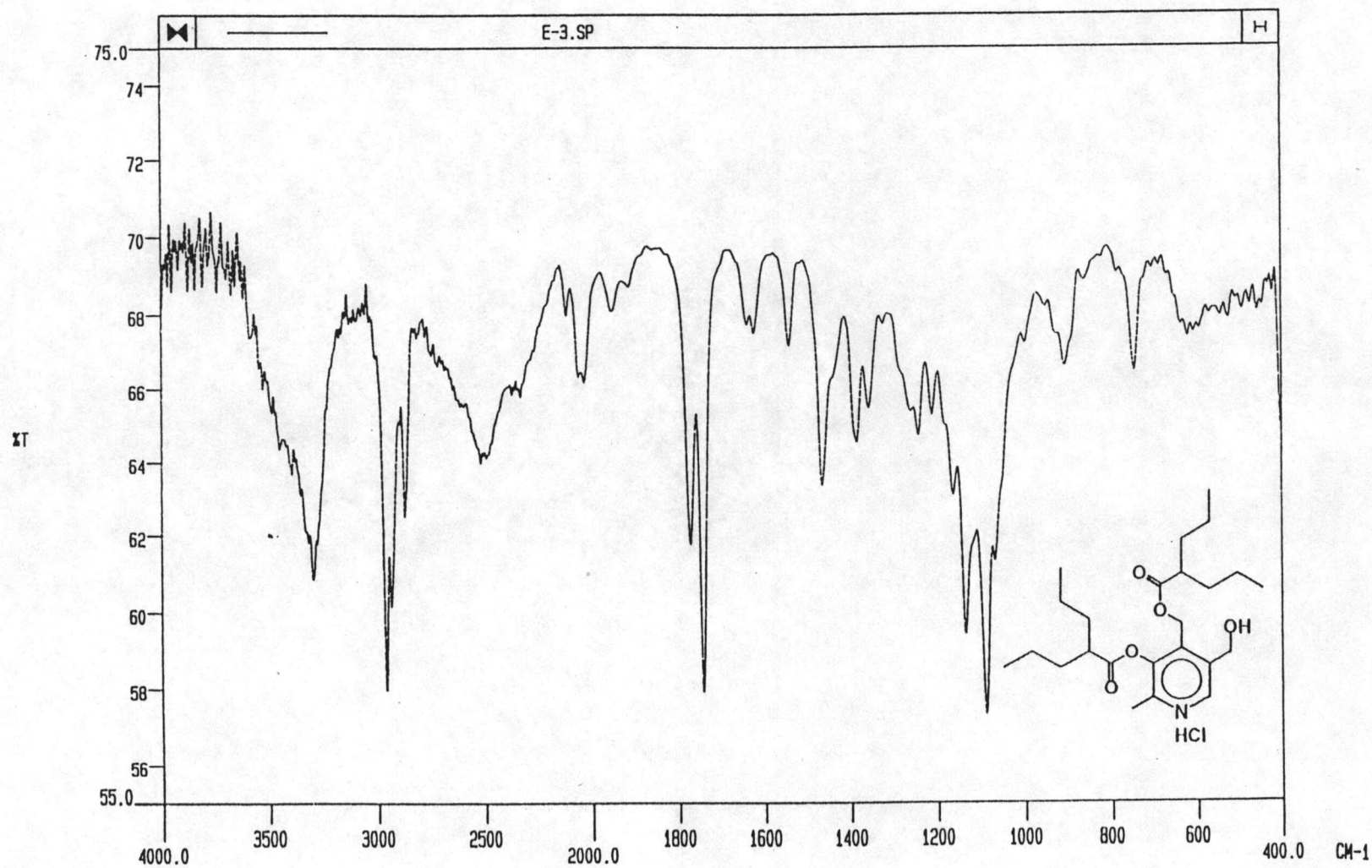


Figure 60. The IR spectrum (KBr) of pyridoxine-3,4-divalproate (LXXIII) hydrochloride

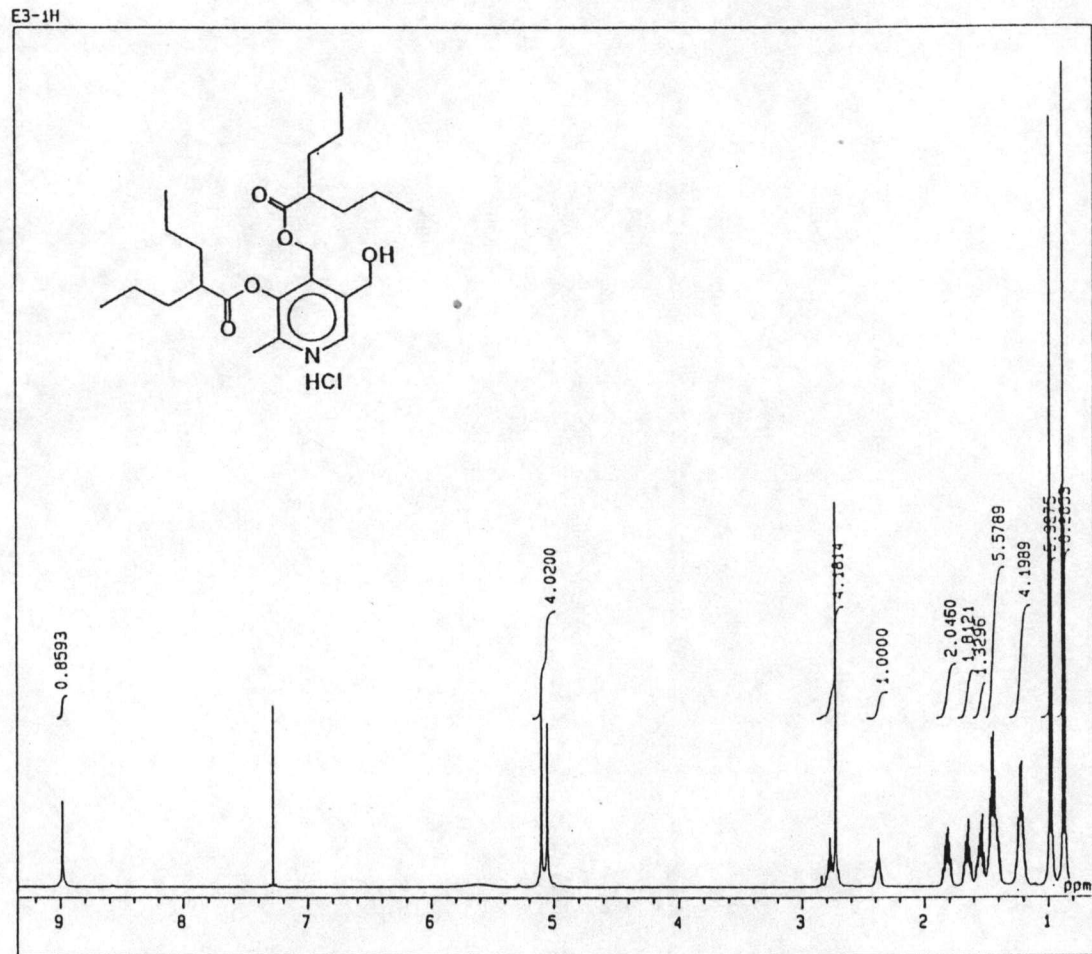


Figure 61. The ¹H-NMR spectrum of pyridoxine-3,4-divalproate (LXXIII) hydrochloride (in CDCl₃)

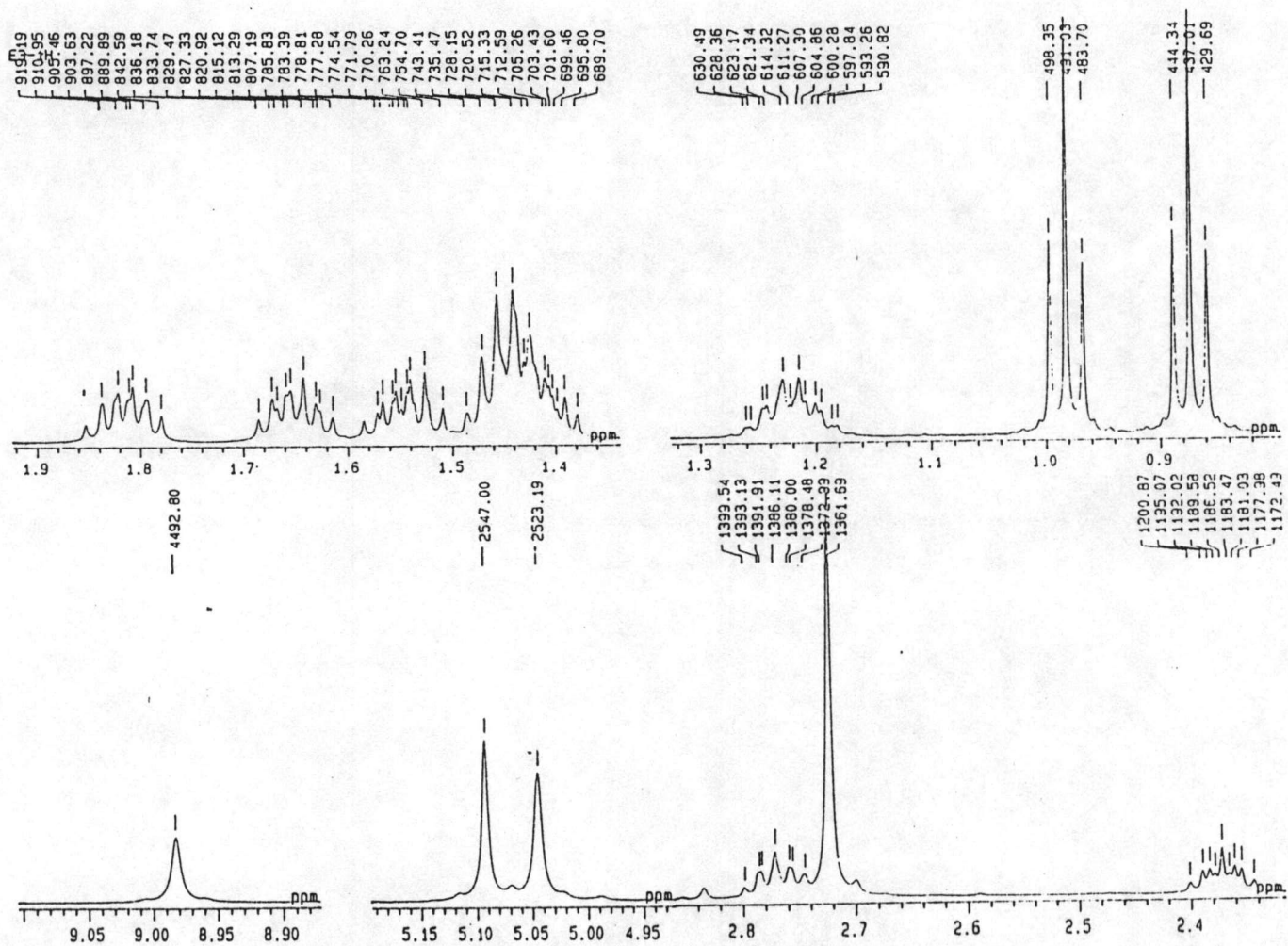


Figure 62. The ^1H -NMR spectrum of pyridoxine-3,4-divalproate (LXXIII) hydrochloride (in CDCl_3) (Enlarged scale : 0.8-9.0 ppm)

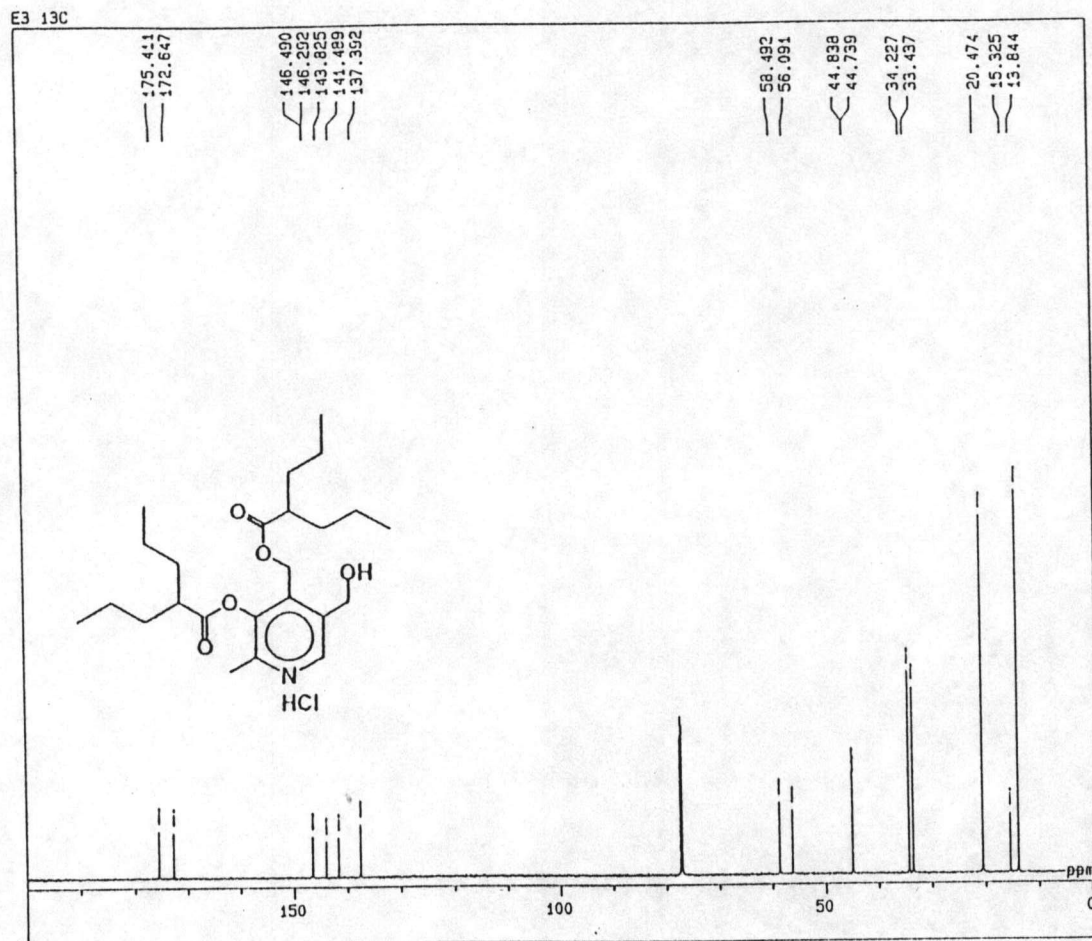


Figure 63. The ^{13}C -NMR spectrum of pyridoxine-3,4-divalproate (LXXIII) hydrochloride (in CDCl_3)

SN8040003 Scan 87 RT=3:03 100%=110357 mv 17 Jan 96 8:49
LRP +EI E34

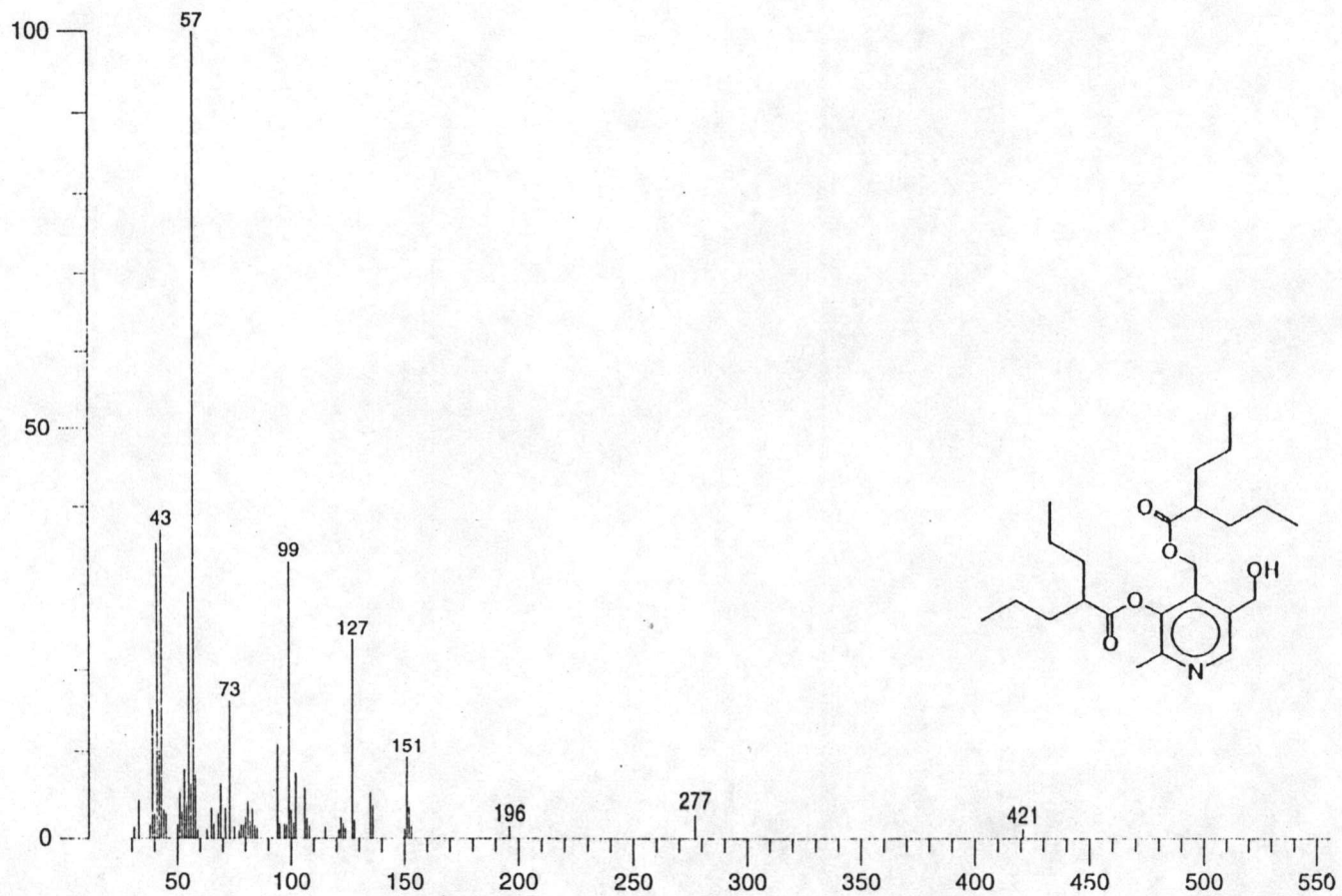


Figure 64. The mass spectrum of pyridoxine-3,4-divalproate (LXXIII)

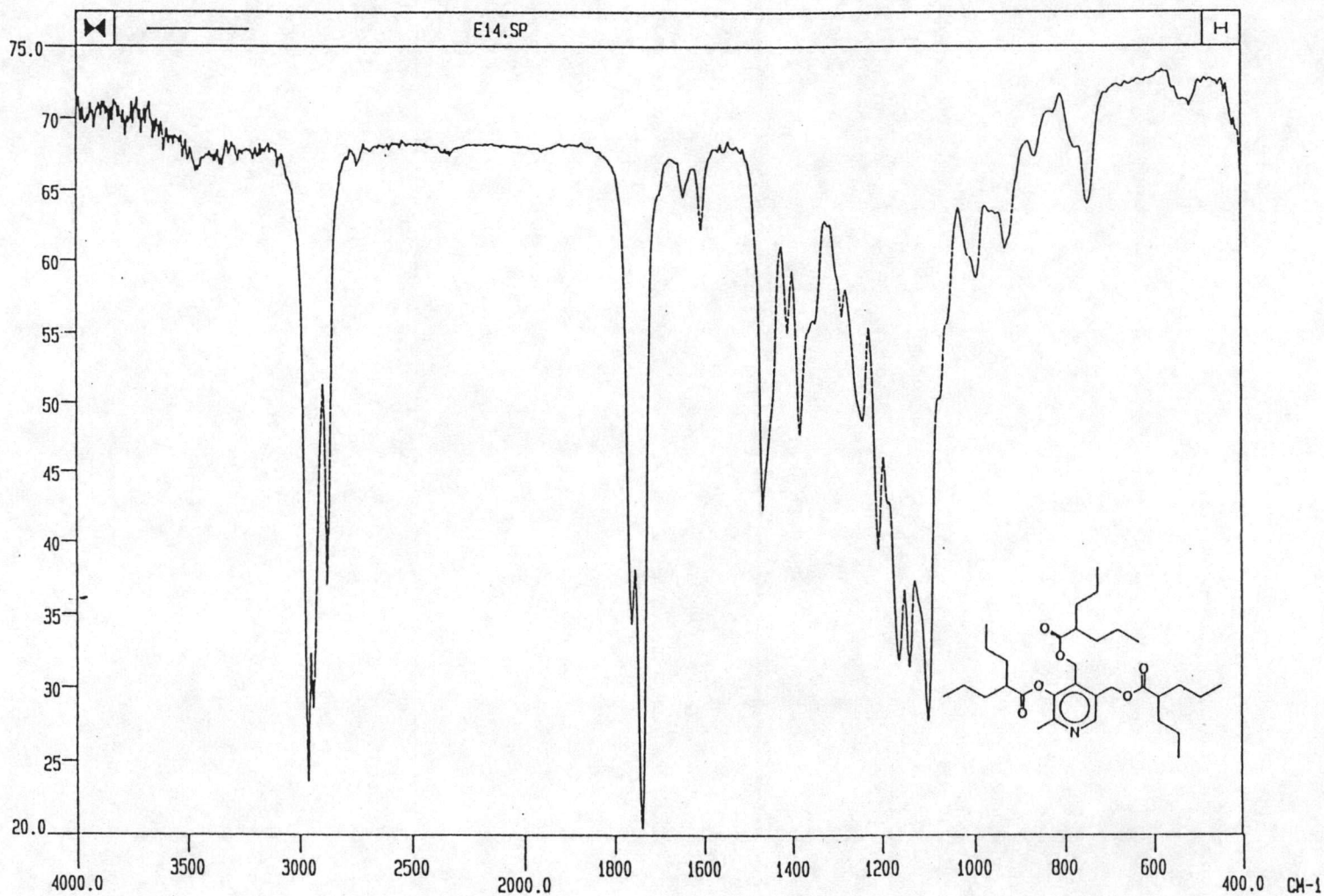


Figure 65. The IR spectrum (neat) of pyridoxine trivalproate (LXXV)

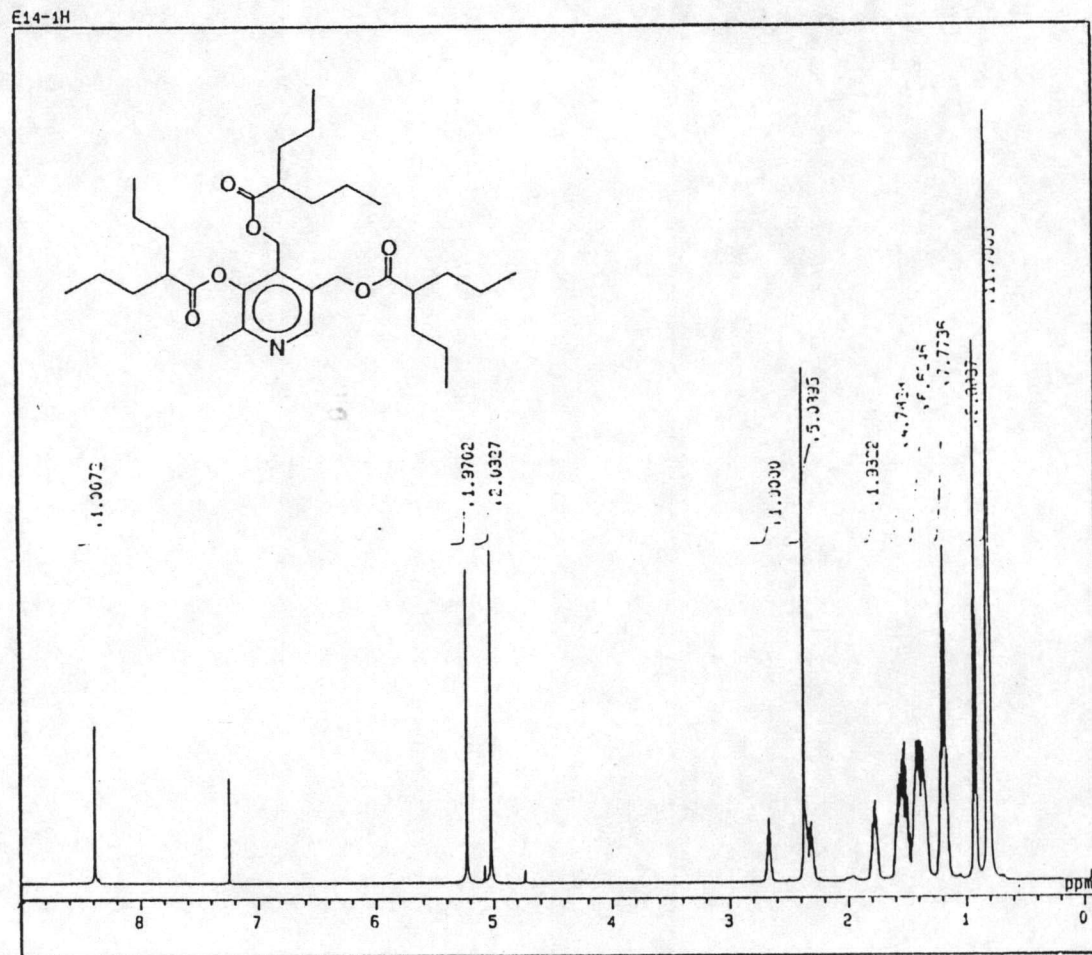


Figure 66. The ¹H-NMR spectrum of pyridoxine trivalproate (LXXV, in CDCl₃)

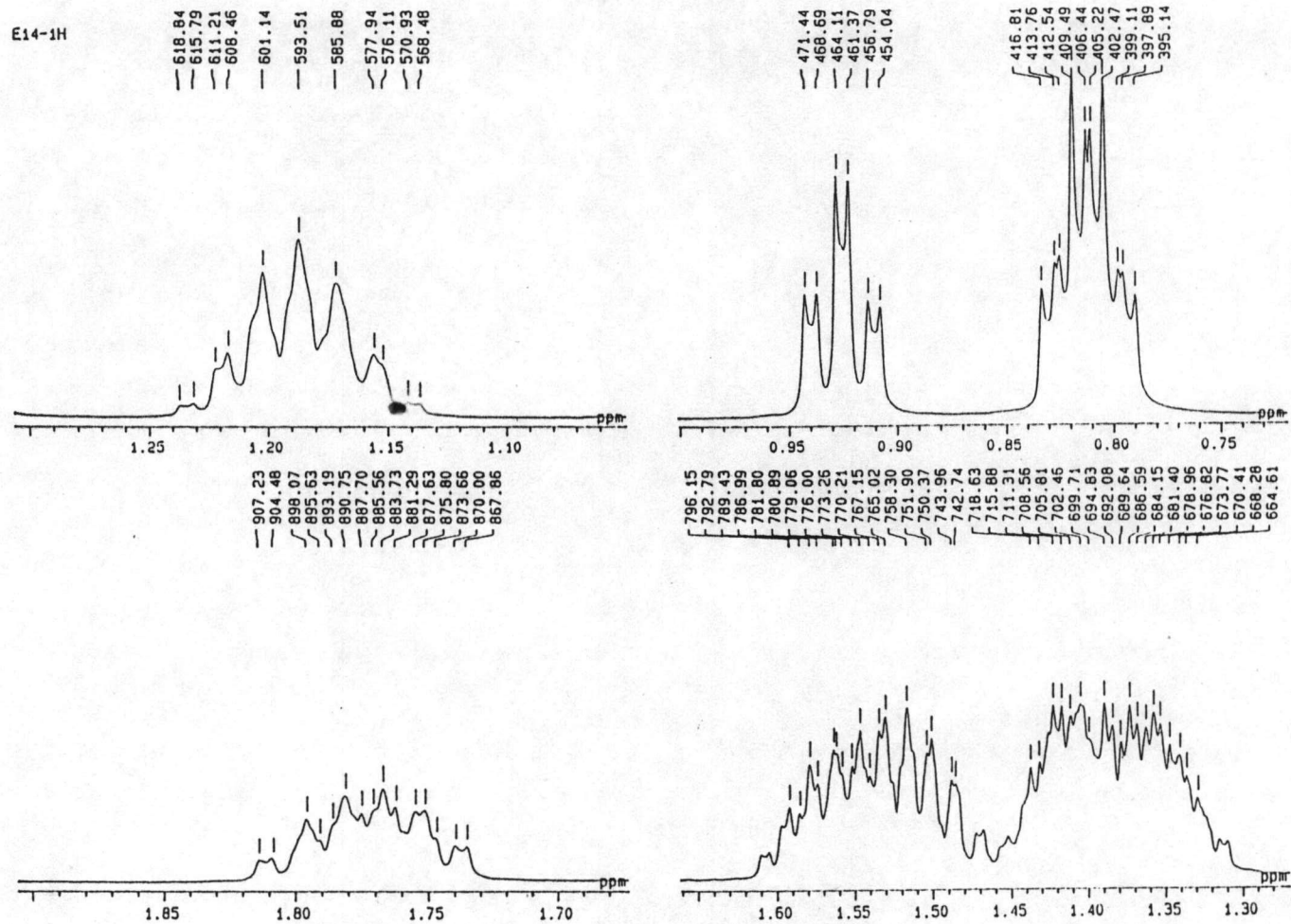


Figure 67. The $^1\text{H-NMR}$ spectrum of pyridoxine trivalproate (LXXV, in CDCl_3) (Enlarged scale ; 0.7-1.9 ppm).

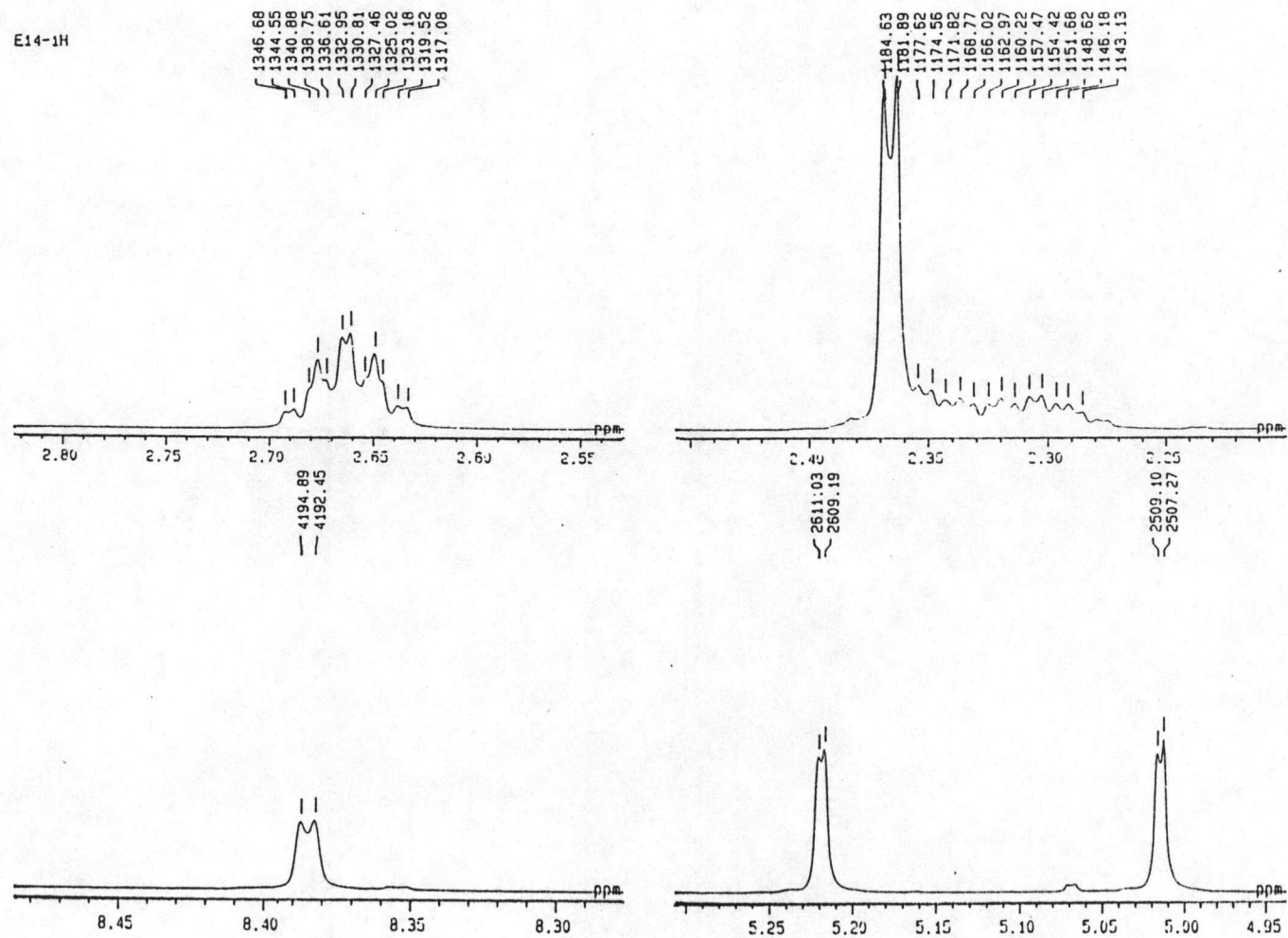


Figure 68. The ^1H -NMR spectrum of pyridoxine trivalproate (LXXV, in CDCl_3)
(Enlarged scale : 2.2-8.4 ppm)

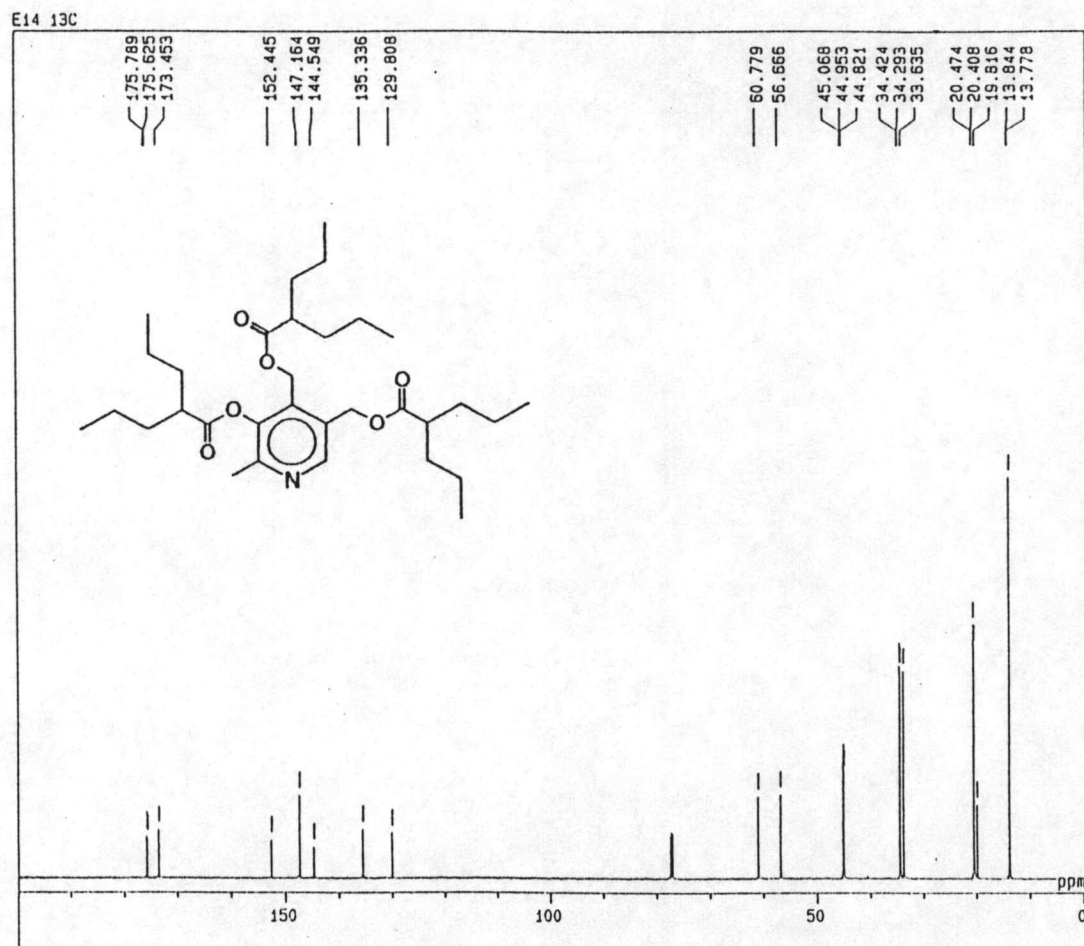


Figure 69. The ^{13}C -NMR spectrum of pyridoxine trivalproate (LXXV, in CDCl_3)

SM6420001 Scan 466 RT=16:28 100%=98482 mv 20 Dec 95 10:27
LRP +EI E14

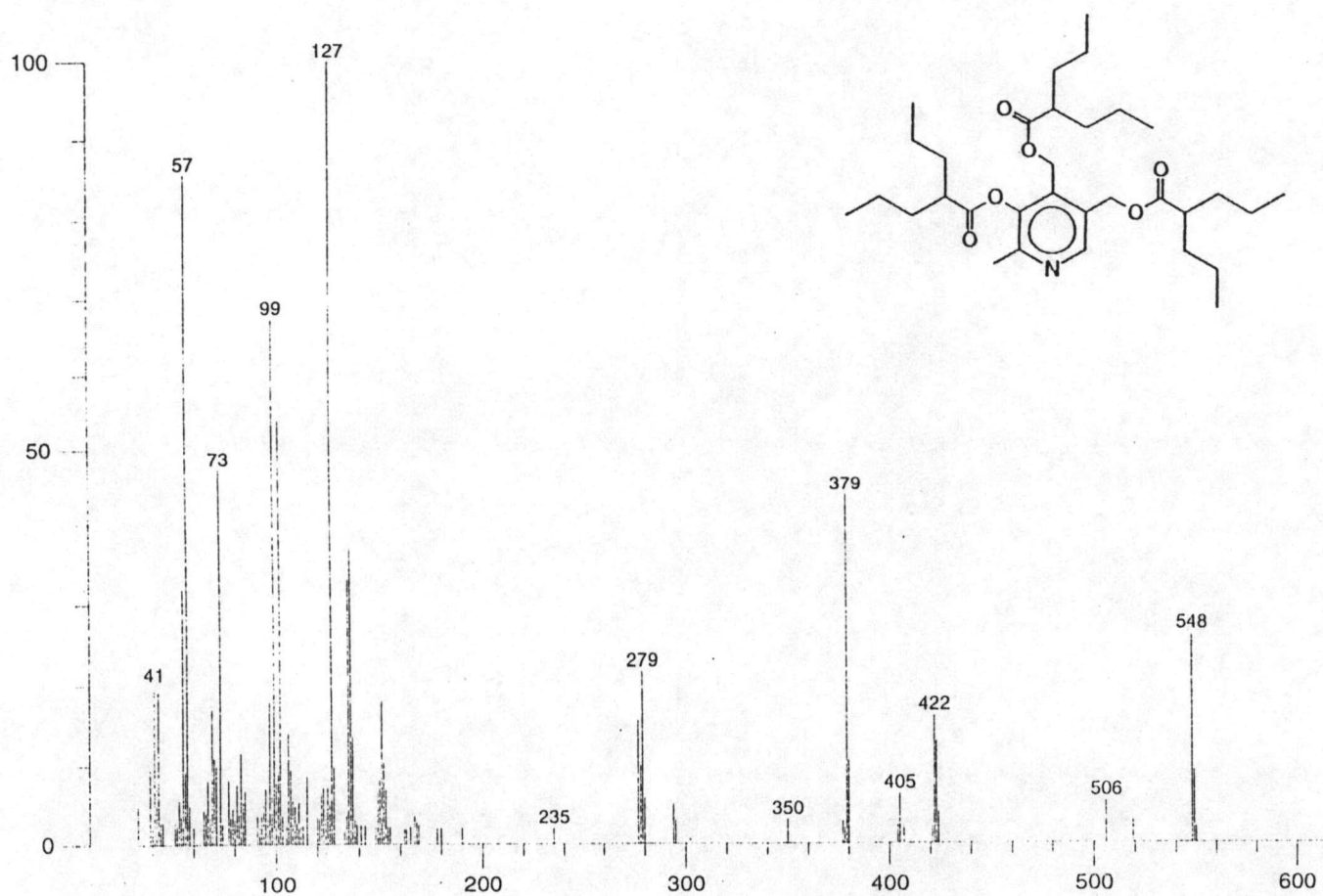


Figure 70. The mass spectrum of pyridoxine trivalproate (LXXV)

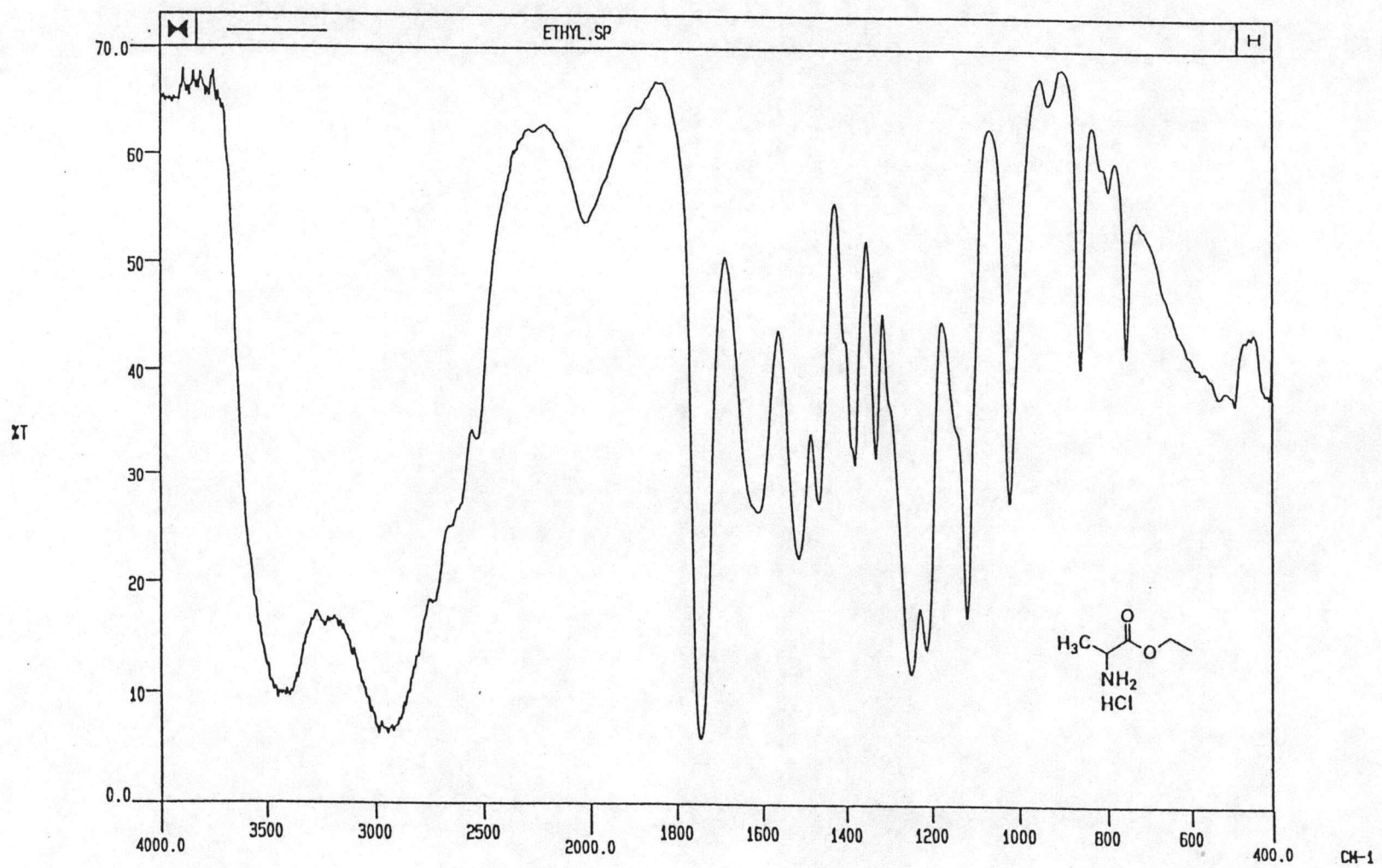


Figure 71. The IR spectrum (nujol) of ethyl alaninate hydrochloride.

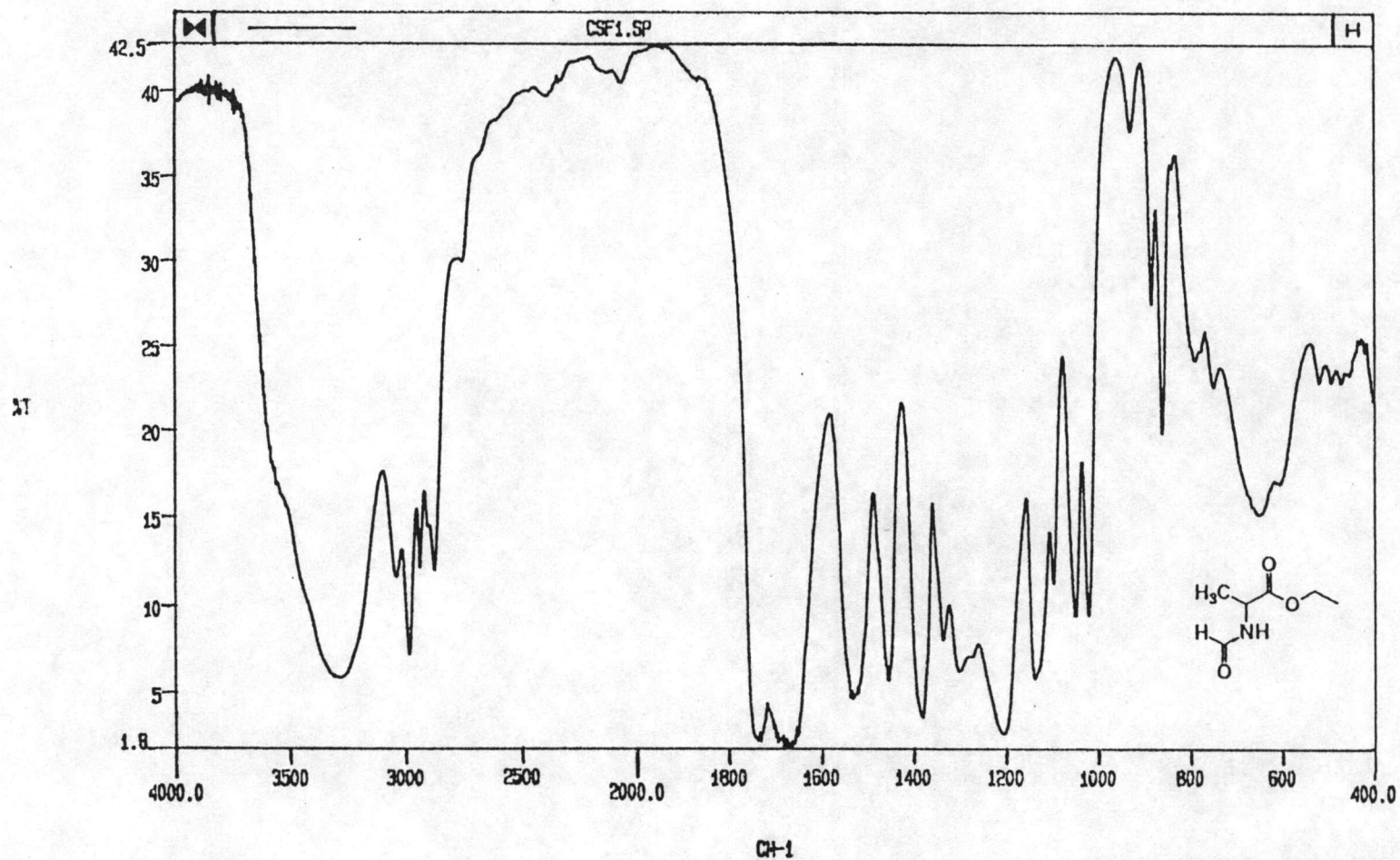


Figure 72. The IR spectrum (neat) of ethyl-N-formylalaninate.

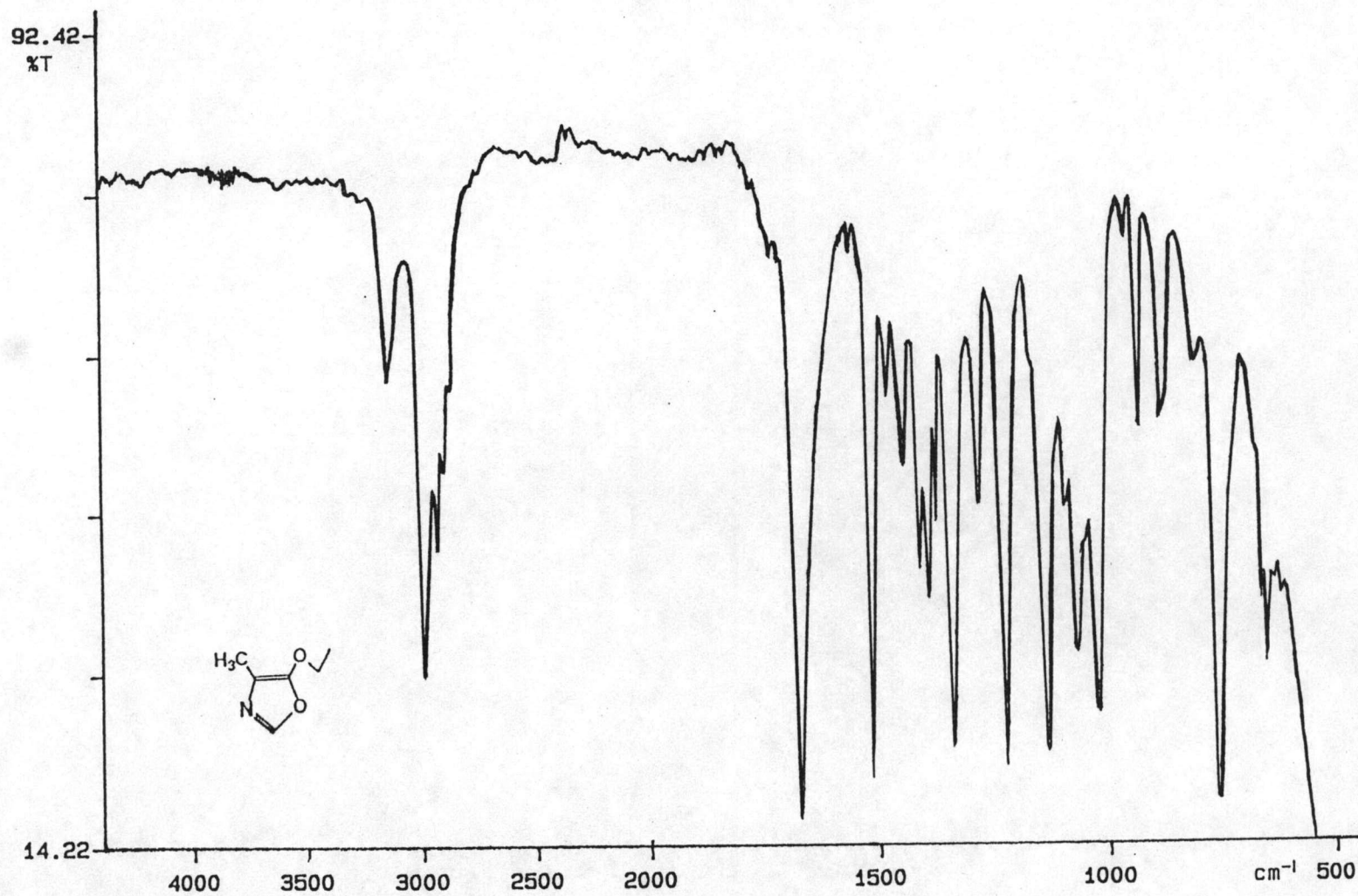


Figure 73. The IR spectrum (neat) of 4-methyl-5-ethoxyoxazole.

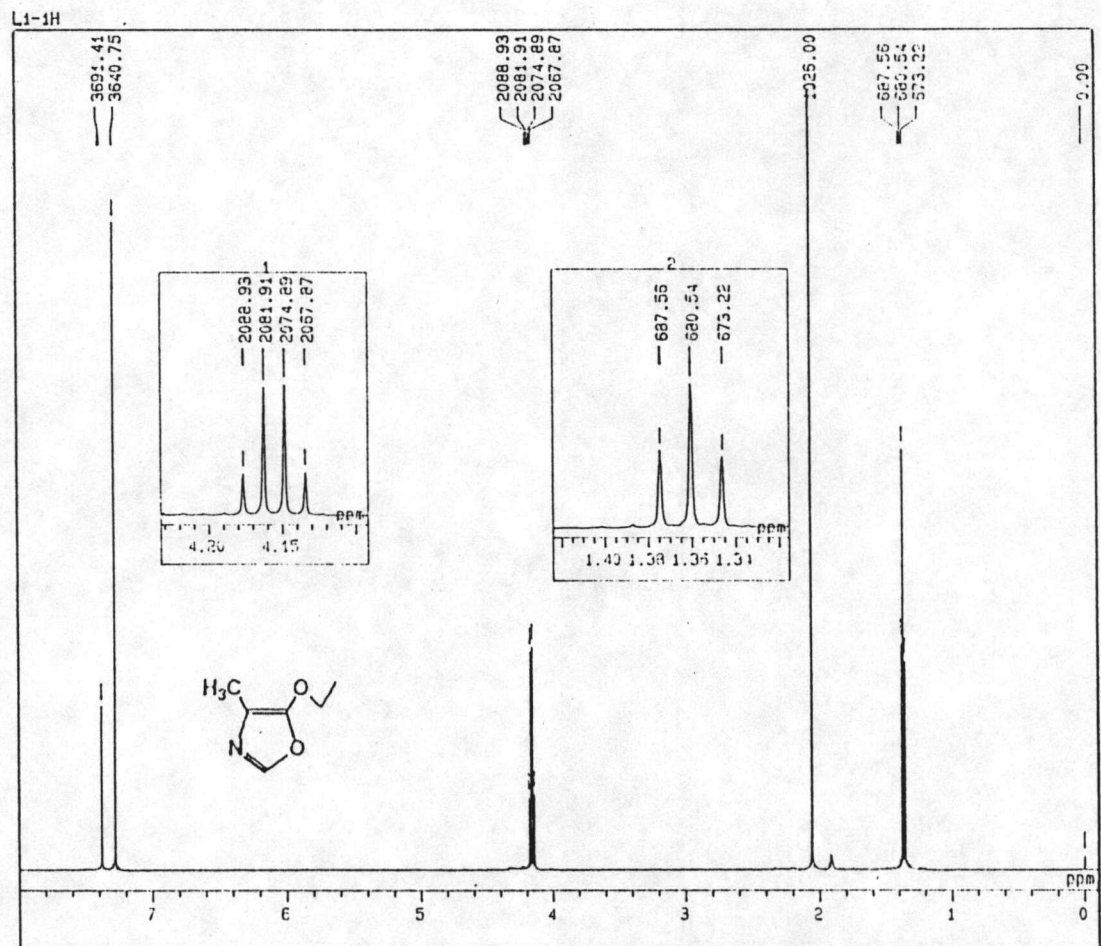


Figure 74. The ^1H -NMR spectrum of 4-methyl-5-ethoxyoxazole (in CDCl_3).

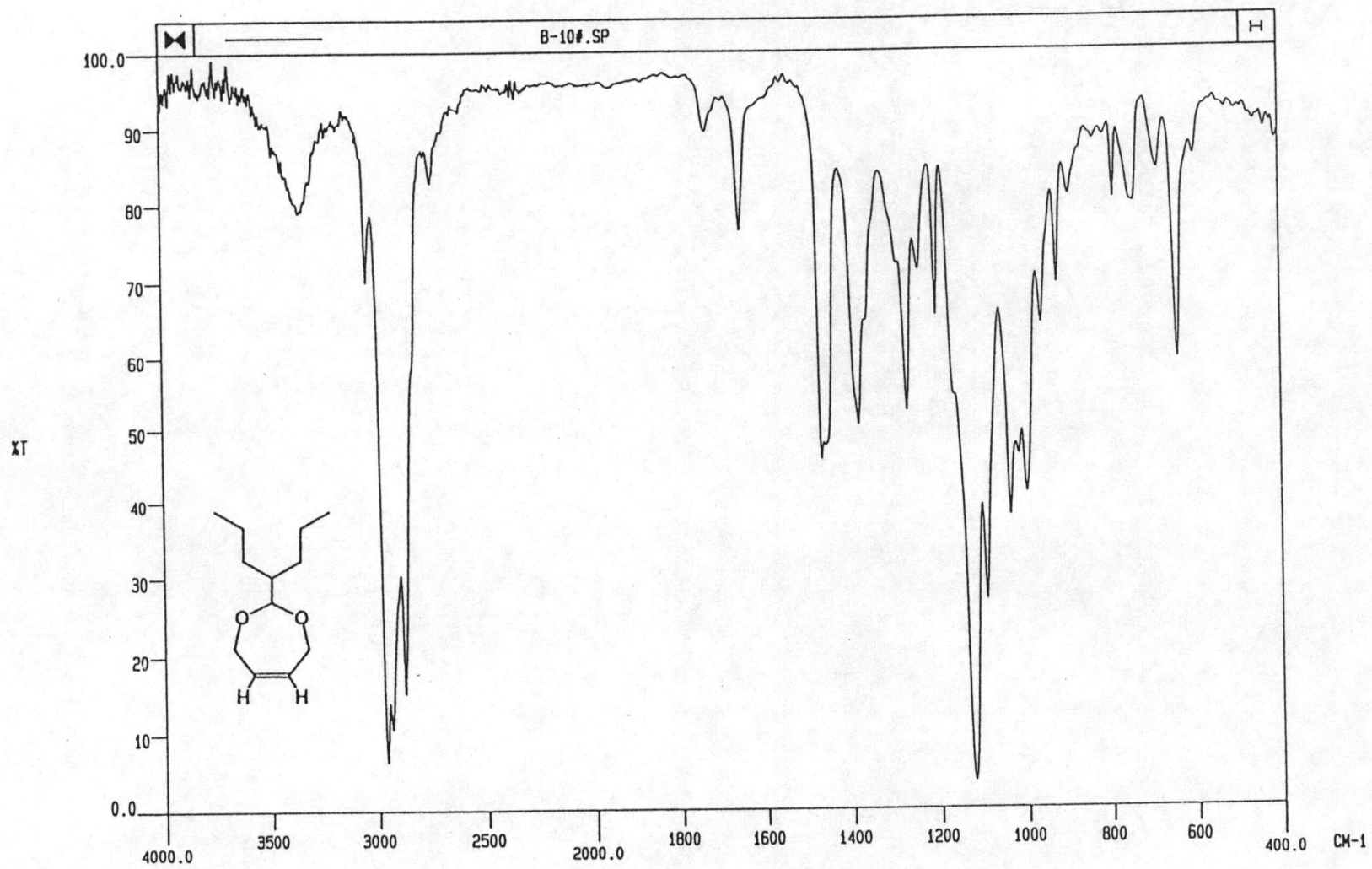


Figure 75. The IR spectrum (neat) of 2-(1-propylbutyl)-1,3-dioxep-5-ene.

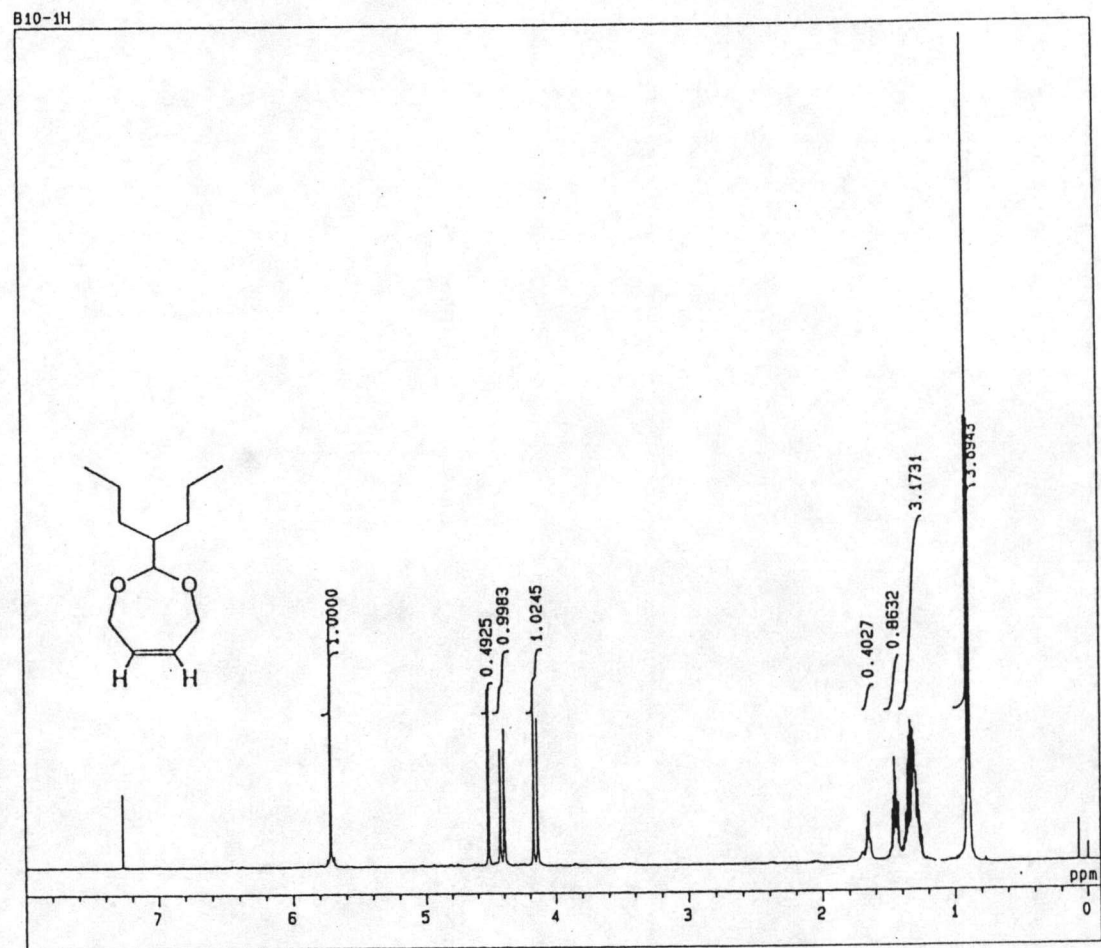


Figure 76. The ^1H -NMR spectrum of 2-(1-propylbutyl)-1,3-dioxep-5-ene (in CDCl_3).

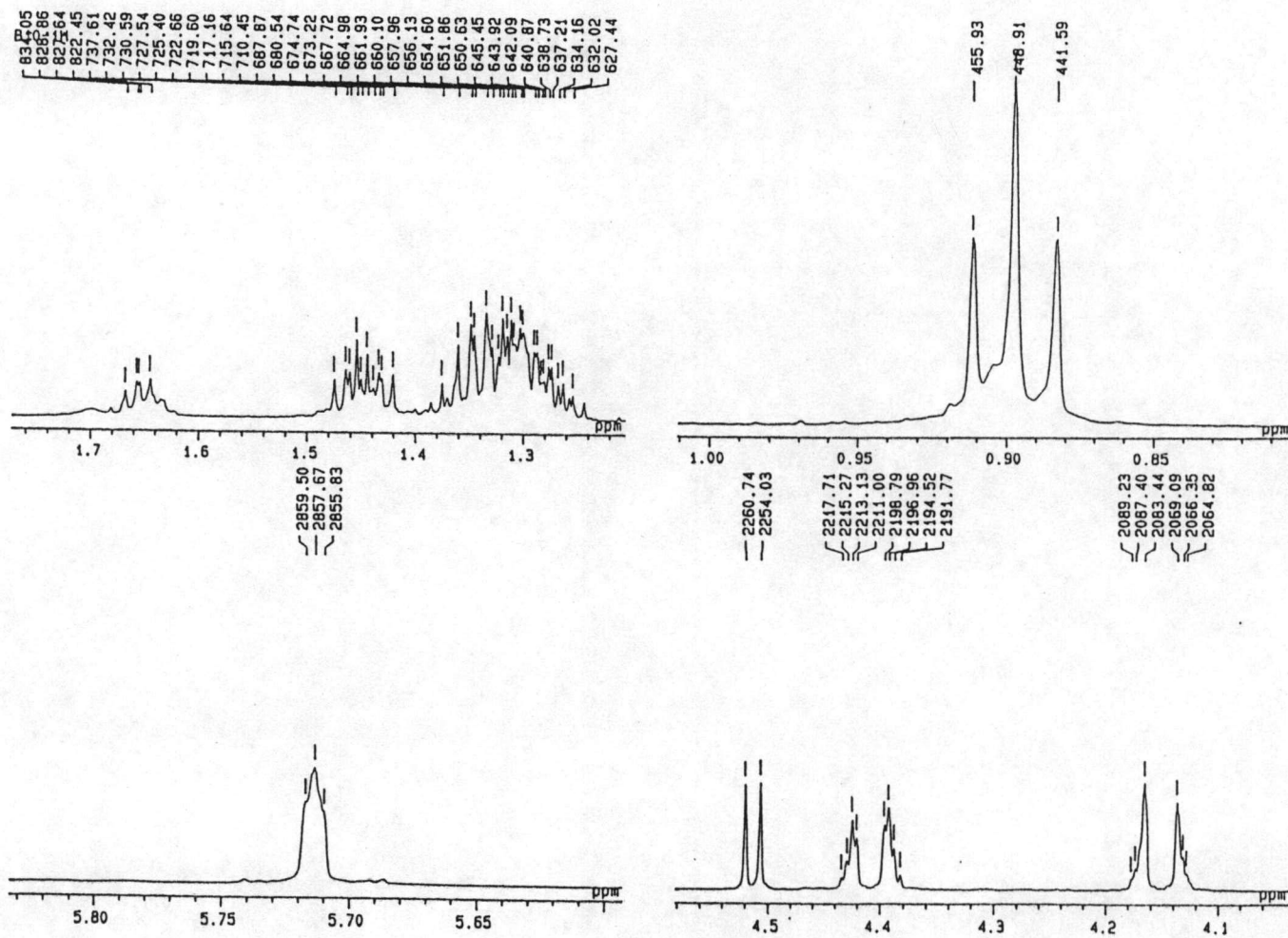


Figure 77. The ¹H-NMR spectrum of 2-(1-propylbutyl)-1,3-dioxep-5-ene (in CDCl₃). (Enlarged scale)

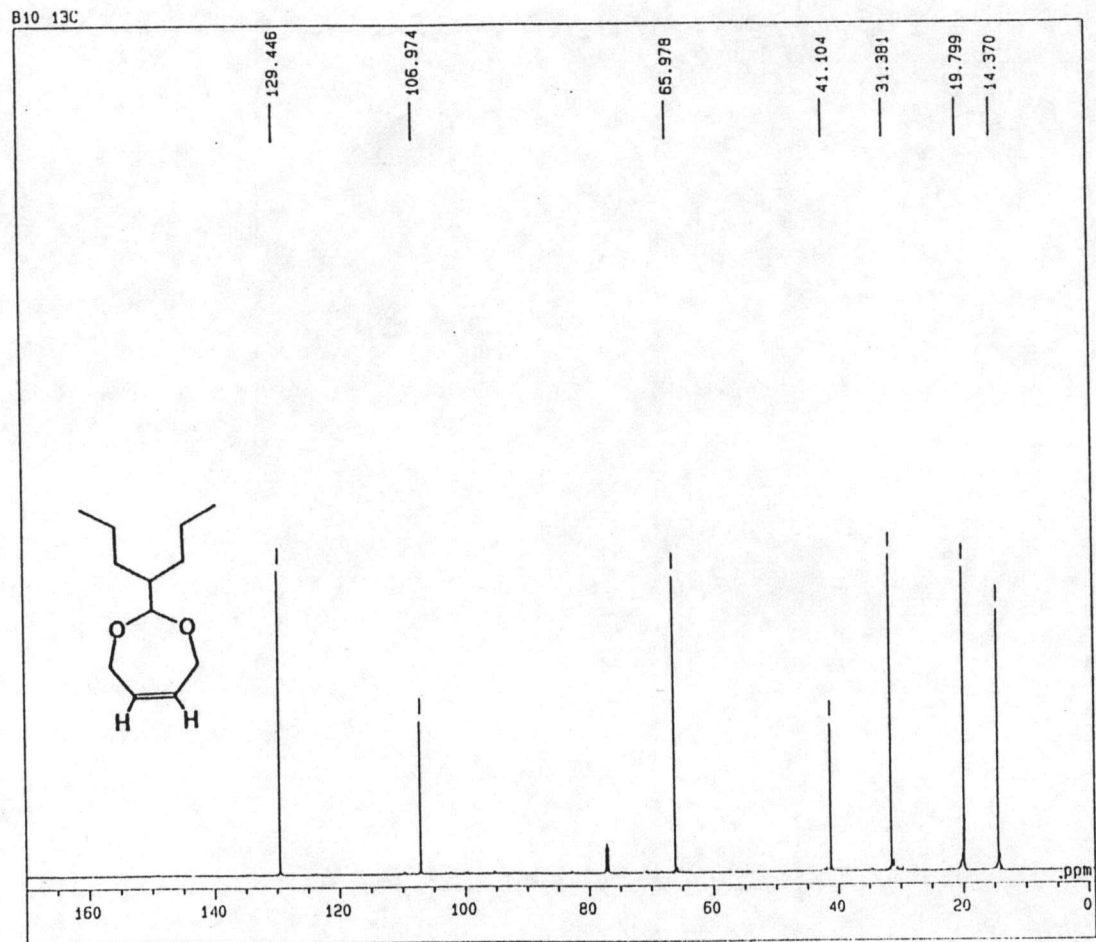


Figure 78. The ^{13}C -NMR spectrum of 2-(1-propylbutyl)-1,3-dioxep-5-ene (in CDCl_3).