CHAPTER III

EXPERIMENTS

Instruments

1. Melting Point Apparatus ; Buchi Capillary Melting Point Apparatus
2. Infrared Spectrophotometer ; Perkin Elmer Model 2000.
3. Nuclear Magnetic resonance Spectrometer ; Bruker Spectrospin 300 and Jeol FT-NMR (JNM-A500)
4. Elemental Analysis; Perkin Elmer model 2000.

Chemicals

1. Absolute ethanol (Merck)
2. Acetic acid anhydride (BDH)
3. Ammonium acetate
4. Benzaldehyde (Merck)
5. Hydrochloric acid concentrated (Merck)
6. (37%) Formaldehyde solution (Lab-scan)
7. Glacial acetic acid (Lab-scan)
8. *p*-Nitrobenzoyl chloride
9. Nitromethane (TCI)
10. Nitroethane (Fluka)
11. (10%) Palladium on activated charcoal (TCI)
12. Phosphorus oxychloride (Sigma)

13. Phosphorus pentoxide (Sigma)
14. Potassium carbonate (Merck)
15. Silica (Merck)
16. Sodium hydroxide pellet (BHD)
17. Sodium borohydride (Fluka)
18. Tetrahydrofuran (Lab-scan)
19. Toluene (Merck)
20. Triethylamine (Fluka)
21. Xylene (Fluka)

General Procedures for Synthesis of *N*-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro isoquinoline derivatives

1. β-Nitrostyrene

Dissolved 6.1 g (0.1 mole) of nitromethane, 10.6 g (0.1 mol) of purified benzaldehyde with 20 ml of methanol in a 125 ml rounnd-bottom flask equipped with magnetic stirrer. The solution was cooled in ice bath and stirred for 10 min. Added dropwise a solution of 4.2 g sodium hydroxide in 10 ml of water, then a bulky white precipitate was formed. After standing for about 15 minutes, added 70 ml of ice-water containing crushed ice. Added dropwise the resulting cold solution into the 250 ml Erlenmeyer flask containing 50 ml of 4 M hydrochloric acid solution with continuous stirring, then pale yellow crystalline precipitate was separated. Filtered the residue by suction. Transfered the solid to a beaker immersed in hot water until two liquid layers formed. Then, cooled again until the lower layer of β-nitrostyrene solidified. β-

Nitrostyrene was recrystallized from ethanol as yellow neddle crystals. The yield of β-Nitrostyrene, m.p. 54-56°C, was 10.6 g (71 % yield)

β-Nitrostyrene

IR:	3110, 3044	cm^{-1}	(νC-H of aromatic and olefin)
(KBr)	1632	cm^{-1}	(νC=C of olefin)
(Figure 32)	1577, 1496, 1449	cm^{-1}	(νC=C of aromatic)
	1514	cm^{-1}	(νas NO_2)
	1342	cm^{-1}	(νs NO_2)
^{1}H-NMR:	7.41-7.52	ppm	(5H, m, aromatic proton)
(in $CDCl_3$)	7.57	ppm	(1H, d, ^3J = 13.8 Hz, β-H)
(Figure 33)	7.99	ppm	(1H, d, ^3J = 13.8 Hz, α-H)

2. β-Methyl-β-nitrostyrene

The mixture of 1 g (9.42 mmole) of benzaldehyde, 0.71 g (9.42 mmole) of nitroethane, 25 ml of glacial acetic acid and 25 ml of tetrahydrofuran were placed in 125 ml round-bottomed flask equipped with a magnetic stirrer, condenser and calcium chloride guard tube. 0.73 g (9.42 mmole) of Ammonium acetate was added to the stirred mixture at room temperature, and then the reaction was heated to reflux. Every an hour, another three parts of 0.71 g (9.42 mmole) of nitroethane and 0.73 g (9.42 mmole) of ammonium acetate were added to the reaction. After the reaction completed, 50 ml of water was added to the reaction mixture and extracted with 3 x50 ml dichloromethane. Glacial acetic acid in the extract was neutralized with 5% sodium bicarbonate solution. The extract was

washed with water and brine, respectively. It was dried over sodium sulfate anhydrous and filtrated. The filtrate was concentrated to give the brown oil. The crude oil was purified by using silica gel column chromatography and using hexane-dichloromethane (4:1) as eluent. The eluted product was recrystallized from ethanol to give 97 %yield of green-yellow needle crystals.

β-Methyl-β-nitrostyrene

IR:	3087, 3057	cm^{-1}	(νC-H of aromatic and olefin)
(KBr)	2975	cm^{-1}	(νC-H of CH_3 group)
(Figure 34)	1653	cm^{-1}	(νC=C of olefin)
	1574, 1449,1430	cm^{-1}	(νC=C of aromatic)
	1581	cm^{-1}	(νas O-N=O of aliphatic nitro group)
	1325	cm^{-1}	(νs O-N=O of aliphatic nitro group)
^{1}H-NMR:	2.44	ppm	(3H, s, β-CH_3)
(in $CDCl_3$)	7.38-7.47	ppm	(5H, m, aromatic proton)
(Figure 35)	8.07	ppm	(1H, s, α-H)

3. 1-Nitro-2-phenylethane and 2-Nitro-1-phenylpropane

1 g (6.71 mmole) of β-Nitrostyrene (or 1 g (6.13 mmole) of β-Methyl-β-nitrostyrene), 6 g of silica gel, 11 ml of iso-propanol and 35 ml of chloroform were placed in a 125 ml round-bottomed flask equipped with a magnetic stirrer. 4 equivalents of sodium borohydride was gradually added in portions into the slurry solution under cooling. Then the stirring was continued for 1 hour, at 0 °C under nitrogen atmosphere.

The reaction mixture was added with glacial acetic acid until the gas bubbles finished and then filtered. The filtrate was concentrated, and the resulting residue was dissolved in 100 ml ethylacetate. The solution was neutralized with 5 % w/v sodium bicarbonate solution and washed with water and brine. It was dried over sodium sulfate anhydrous, and filtered. The filtrate was concentrated to give yellow oil. The crude oil was purified by silica gel column chromatography using hexane-ethyl acetate (99:1) as eluent provided the colorless oil of product. The yield of 1-nitro-2-phenylethane and 2-nitro-1-phenylpropane were 0.882 g (87.0 %) and 0.872 g (86.2%), respectively.

1-Nitro-2-phenylethane

IR:	3089, 3065, 3031	cm^{-1}	(ν C-H of aromatic)
(Neat)	2950, 2920	cm^{-1}	(νas C-H and νs C-H of methylene
(Figure 36)			group)
	1550	cm^{-1}	(νas O-N=O of aliphatic nitro group)
	1380	cm^{-1}	(νs O-N=O of aliphatic nitro group)
	1600, 1455, 1431	cm^{-1}	(ν C=C of aromatic)

^{1}H-NMR:	3.27	ppm	(2H, t, ^{3}J = 7.5 Hz, 2-H)
(in CDCl3)	4.56	ppm	(2H, t, ^{3}J = 7.5 Hz, 1-H)
(Figure 37)	7.17-7.33	ppm	(5H, m, aromatic proton)

2-Nitro-1-phenylpropane

IR:	3089, 3065, 3031	cm^{-1}	(ν C-H of aromatic ring)
(Neat)	2992	cm^{-1}	(νas C-H of methyl group)

(Figure 38)	2940	cm^{-1}	(νs C-H of methyl group)
	1550	cm^{-1}	(νas O-N=O of nitro group)
	1388	cm^{-1}	(νs O-N=O of nitro group)
	1496	cm^{-1}	(ν C=C of aromatic ring)
	1454	cm^{-1}	(ν C=C of aromatic ring)
	1361	cm-1	(δs C-H of methyl group)
^{1}H-NMR:	1.49	ppm	(3H, d, ^3J = 6.6 Hz, 3-H)
(in $CDCl_3$)	2.96	ppm	(1H, dd, ^3J = 6.6 Hz, ^2J = 14.0, 1-Ha)
(Figure 39-40)	3.27	ppm	(1H, dd, ^3J = 7.5 Hz, ^2J = 14.0, 1-Hb)
	4.73	ppm	(1H, sextet, 2-H)
	7.11-7.31	ppm	(5H, aromatic)

4. 1-Amino-2-phenylethane (2-Phenylethylamine) and 2-Amino-1-phenylpropane (Amphetamine)

A solution of 1 g (6.62 mmole) of 1-nitro-2-phenylethane (or 1 g (6.06 mmole) of 2-nitro-1-phenylpropane), 3 ml glacial acetic acid in 20 ml of absolute ethanol was added to a Parr hydrogenation bottle along with 200 mg of 10% w/w palladium inactivated charcoal and subjected to shaking at low-pressure hydrogenation for 12 hours. The bottle was then removed, and the contents were filtered. The filtrate was concentrated, and the resulting residue was acidified by dissolving in 50 ml of 5 % w/v hydrochloric acid solution. The acidic solution was washed with dichloromethane, then the aqueous extract was cooled and basified by adding sodium hydroxide pellet and extracted with dichloromethane (50 ml x 3). The organic phase was washed with water and brine, dried over sodium sulfate anhydrous, and filtered. The filtrate was concentrated to give yellow

oil. The yields of 1-amino-2-phenylethane and 2-amino-1-phenylpropane were 0.550 g (68.6 %) and 0.636 g (77.8%), respectively.

1-Amino-2-phenylethane (2-Phenylethylamine)

IR:	3400-3300	cm^{-1}	(νas N-H of primary aliphatic amino group)
(Neat)	3330-3250	cm^{-1}	(νs N-H of primary aliphatic amino group)
(Figure 41)	3100-3000	cm^{-1}	(ν C-H of aromatic ring)
	2926	cm^{-1}	(νas C-H of methylene chain)
	2853	cm^{-1}	(νs C-H of methylene chain)
	1600	cm^{-1}	(δs N-H of primary aliphatic amino group)
	1500	cm^{-1}	(ν C=C of aromatic ring)
^{1}H-NMR:	2.74	ppm	(2H, t, ^3J = 6.6 Hz, 2-H)
(in $CDCl_3$)	2.96	ppm	(2H, t, ^3J = 6.6 Hz, 1-H)
(Figure 42-43)	7.18-7.32	ppm	(5H, aromatic)

2-Amino-1-phenylpropane (Amphetamine)

IR:	3400-3361	cm^{-1}	(νas N-H of primary amino group)
(Neat)	3330- 3250	m^{-1}	(νs N-H of primary amino group)
(Figure 44)	3100 -3000	cm^{-1}	(ν C-H of aromatic)
	2961 and 2872	cm^{-1}	(νas C-H and νs C-H of methyl group)
	2926 and 2853	cm^{-1}	(νas C-H and νs C-H of methylene group)

	1600	cm^{-1}	(δ N-H of primary amino group)
	1496 and1454 cm^{-1}	cm^{-1}	(ν C=C of aromatic)

^{1}H-NMR:	1.16	ppm	(3H, d, ^3J = 6.3 Hz, 3-H)
(in $CDCl_3$)	2.56	ppm	(1H, dd, ^3J = 7.8 Hz, ^2J = 13.2 Hz, 1-H)
(Figure 45-46)	2.75	ppm	(1H, dd, ^3J = 5.4 Hz, ^2J = 13.2 Hz, 1-H)
	3.20	ppm	(1H, septet, 2-H)
	7.21-7.36	ppm	(5H, m, (2'-6')-H, aromatic)

5. *N*-Acetyl-2-phenylethylamine and *N*-Acetylamphetamine

0.544 g (4.496 mmole) of 2-phenylethylamine, 0.909 g (8.992 mmole) of triethylamine and 10 ml of tetrahydrofuran were placed in 50 ml, two-necked round-bottomed flask provided with a reflux condenser, calcium chloride guard-tube and a dropping funnel. A solution of 0.688 g (6.74 mmole) of acetic acid anhydride in 10 ml of tetrahydrofuran was introduced through the dropping funnel. The acetic acid anhydride solution was added dropwise to the well-stirred mixture at room temperature. The reaction mixture was heated to reflux at 75 -80 °C for 1 hour. The reaction was stopped by adding 50 ml water into the reaction mixture, and extracted with dichloromethane (50 ml x 3). The extract was cleaned with 1 N hydrochloric acid solution and 1 N sodium hydroxide solution, respectively. The organic phase was washed with water and brine, dried over sodium sulfate anhydrous, and filtered. The filtrate was concentrated to give yellow oil. The crude oil was purified by silica gel column chromatography using hexane-ethylacetate (2:1) as eluent to give colorless viscous oil (semisolid). The yield of *N*-Acetyl-2-phenylethylamine was 0.646 g (88.2 %). As same as 2-phenylethylamine, 0.476 g (3.52

mmole) of amphetamine was used as substrate, the yield of product, *N*-acetyl amphetamine, colorless viscous oil (semisolid), was 0.574 g (92 %).

_N_-Acetyl-2-phenylethylamine

IR:	3330-2060	cm^{-1}	(ν N-H of secondary amide aroup)
(Neat)	3100-3000	cm^{-1}	(ν C-H of aromatic ring)
(Figure47)	2926	cm^{-1}	(νas C-H of methylene chain)
	2853	cm^{-1}	(νs C-H of methylene chain)
	1640	cm^{-1}	(ν C=O of amide)
^{1}H-NMR:	1.92	ppm	(3H, s, (CH_3CO)-H)
(in $CDCl_3$)	2.80	ppm	(2H, t, ^3J = 6.9Hz, 2-H)
(Figure 48-49)	3.50	ppm	(2H, q, ^3J = 6.9Hz, 1-H)
	5.39	ppm	(1H, br, s, amide-H)
	7.16-7.32	ppm	(5H, aromatic)

_N_-Acetylamphetamine

IR:	3330-2060	cm^{-1}	(ν N-H of secondary amide aroup)
(Neat)	3100-3000	cm^{-1}	(ν C-H of aromatic ring)
(Figure50)	2926	cm^{-1}	(νas C-H of methylene chain)
	2853	cm^{-1}	(νas C-H of methylene chain)
	1640	cm^{-1}	(ν C=O of amide)
^{1}H-NMR:	1.44	ppm	(3H, d, ^3J = 6.6 Hz, 3-H)

(in CDCl3)	1.93	ppm	(3H, s, (CH_3CO)-H)
(Figure 51-52)	2.77	ppm	(1H, dd, ^3J = 7.2 Hz, ^2J = 13.5 Hz, 1-H)
	2.89	ppm	(1H, dd, ^3J = 5.7 Hz, ^2J = 13.5 Hz, 1-H)
	4.32	ppm	(1H, septet, 2-H)
	5.38	ppm	(1H, br, s, amide-H)
	7.22-7.38	ppm	(5H, aromatic)

6. 3,4-Dihydro-1-methylisoquinoline

0.5 g (3.07 mmole) of *N*-Acetyl-2-phenylethylamine in 25 ml of dry xylene was placed in round-bottom flask provided with a reflux condenser, calcium chloride guard-tube. 1 g of phosphorus pentoxide and 1 g of phosphorus oxychloride were added to the mixture. The reaction mixture was refluxed for one hour. At the end of the refluxing time the flask was cooled in ice-bath while its contents were treated with ice-water 50 ml to hydrolyze excess dehydrating agents. The layers were separated, the aqeous layer was washed with benzene (50 ml x 3), and then made to strongly alkaline with sodium hydroxide pellet to the cool solution. The basic solution was extracted with dichloromethane (50 ml x 3), the extract was dried over sodium sulfate and filtered. The filtrate was concentrate to give brown oil, 0.376 g (70 %).

3,4-dimethyl-1-methylisoquinoline

IR :	3100-3000	cm^{-1}	(ν C-H of aromatic ring)
(Neat)	2960-2840	cm^{-1}	(νas and νs of CH_3 and CH_2 group)
(Figure 53)	1633	cm^{-1}	(ν C=N of imine group)
	1573, 1489, 1434	cm^{-1}	(ν C=C of aromatic ring)

	1450	cm^{-1}	(δas C-H of methyl group)
	1374	cm^{-1}	(δs C-H of methyl group)
^{1}H-NMR:	2.38	ppm	(3H, br s, 1-CH_3)
(in $CDCl_3$)	2.70	ppm	(2H, t, ^3J = 7.5 Hz, 4-H)
(Figure 54-55)	3.65	ppm	(2H, br t, ^3J = 7.5 Hz, 3-H)
	7.17	ppm	(1H, d, ^3J = 7.2 Hz, 5-H)
	7.28	ppm	(1H, t, ^3J = 7.2 Hz, 7-H)
	7.34	ppm	(1H, t, ^3J = 7.2 Hz, 6-H)
	7.47	ppm	(1H, d, ^3J = 7.5 Hz, 8-H)

7. 3,4-Dihydro-1,3-dimethylisoquinoline

A solution of 1.120 g (6.33 mmol) of *N*-acetylamphetamine and 3 ml of phosphorus oxychloride in 43 ml of dry toluene was refluxed for 3 hours. After cooling the reaction mixture was extracted with water (25 ml x 3). The aqueous phase was washed with dichloromethane (50 ml x 3), then it was cooled in ice bath and basified with sodium hydroxide pellet. The basified solution was extrated with dichloromethane (50 ml x 3), dried over anhydrous sodium sulfate and concentrated to give brown oil, 0.261 g, (26%).

3,4-Dihydro-1,3-dimethylisoquinoline

IR :	3100-3000	cm^{-1}	(ν C-H of aromatic ring)
(Neat)	2970-2840	cm^{-1}	(νas and νs of CH_3 and CH_2 group)
(Figure 56)	1651	cm^{-1}	(ν C=N of imine group)
	1564	cm^{-1}	(ν C=C of aromatic ring)

	1454	cm^{-1}	(δas C-H of methyl group)
	1376	cm^{-1}	(δs C-H of methyl group)
^{1}H-NMR:	1.36	ppm	(3H, d, ^3J = 6.9 Hz, 3-CH_3)
(in $CDCl_3$)	2.38	ppm	(3H, s, 1-CH_3)
(Figure 57-58)	2.46	ppm	(1H, t, $^3J = {}^2J$ = 14.1 Hz, 4-H)
	2.72	ppm	(1H, dd, ^3J = 5.1 Hz, ^2J = 15.6 Hz, 4-H)
	3.05	ppm	(1H, m, 3-H)
	7.14	ppm	(1H, d, ^3J = 6.9 Hz, 5-H, aromatic)
	7.26	ppm	(1H, t, ^3J = 7.2 Hz, 7-H, aromatic)
	7.33	ppm	(1H, t, ^3J = 7.2 Hz, 6-H, aromatic)
	7.46	ppm	(1H, d, ^3J = 7.2 Hz, 8-H, aromatic)

8. 1,2,3,4-Tetrahydro-1-methyl-isoquinoline and 1,2,3,4-Tetrahydro-1,3-dimethyl isoquinoline

A solution of 0.2 g (1.38 mmole) of 3,4-dihydro-1-methylisoquinoline in 5 ml of methanol was stirred in ice-bath. 0.150 g (4.14 mmole) of sodium borohydride was added in portions into the vigorously stirring solution at 0 °C within 1 hour. The reaction mixture was continuously stirred for another 1 hour. Then, 5 ml of glacial acetic acid was added to the reaction. The reaction mixture was concentrated. The resulting residue was dissolved in 30 ml of 5% w/v hydrochloric acid solution. The acidic solution was washed with dichloromethane (30 ml x 3). Then, the aqueous solution was cooled and basified with sodium hydroxide pellet and extracted with dichloromethane (30 ml x 3). The organic phase was washed with water and brine. It was dried over sodium sulfate anhydrous, and filtered. The filtrate was concentrated to give 1-methyl-1,2,3,4-tetrahydroisoquinoline as

yellow oil, 0.127 g (62.6 %). As same as 3,4-dihydro-1-methylisoquinoline, 0.152 g (0.96 mmole) of 3,4-dihydroisoquinoline-1,3-dimethyl was used as substrate to give product, 1,3-dimethyl-1,2,3,4-tetrahydroisoquinoline as yellow oil, 0.086 g (55.8 %).

1,2,3,4-Tetrahydro-1-methylisoquinoline

IR:	3350-3310	cm^{-1}	(ν N-H of secondary amine)
(Neat)	3100-3000	cm^{-1}	(νC-H of aromatic ring)
(Figure 59)	2960-2840	cm^{-1}	(νas and νs of CH_3 and CH_2 group)
	1600, 1492 and1429	cm^{-1}	(δC-H of aromatic ring)
	1447 and1372	cm^{-1}	(δas and δs of CH_3 and CH_2 group)

^{1}H-NMR:	1.45	ppm	(3H, d, ^3J = 6.6 Hz, 1-CH_3)
(in $CDCl_3$)	2.72	ppm	(1H, td, ^3J = 4.5 Hz, ^2J = 16.2 Hz, 4-Ha)
(Figure 60-61)	2.87	ppm	(1H, td, ^3J = 6 Hz, ^2J = 16.2 Hz, 4-Hb)
	3.01	ppm	(1H, td, ^3J = 4.5 Hz, 8.4 Hz, ^2J = 12.3 Hz, 3-Ha)
	3.25	ppm	(1H, dt, ^3J = 5.0 Hz, ^2J = 12.3 Hz, 3-Hb)
	4.10	ppm	(1H, q, ^3J = 6.6 Hz, 1-H)
	7.03-7.15	ppm	(4H, (5-8)-H)

1,2,3,4-Tetrahydro-1,3-dimethylisoquinoline

IR:	3350-3310	cm^{-1}	(ν N-H of secondary amine)
(Neat)	3100-3000	cm^{-1}	(ν C-H of aromatic ring)
(Figure 62)	2962 and 2872	cm^{-1}	(νas and νs of CH_3 group)

	2923 and 2827	cm^{-1}	(νas and νs of CH_2 group)
	1580, 1492 and 1430	cm^{-1}	(νC=C of aromatic ring)
	1453 and 1375	cm^{-1}	(δas and δs of CH_3 group)

^{1}H-NMR:	1.23	ppm	(3H, d, ^3J = 6.3 Hz, 3-CH_3)
(in CDCl3)	1.46	ppm	(3H, d, ^3J = 6.3 Hz, 1-CH_3)
(Figure 63-64)	2.56	ppm	(1H, dd, ^3J = 11.1 Hz, ^2J = 16.2 Hz, 4-H)
	2.73	ppm	(1H, dd, ^3J = 2.7 Hz, ^2J = 16.2 Hz, 4-H)
	3.05	ppm	(1H, m, 3-H)
	4.14	ppm	(1H, q, ^3J = 6.3 Hz, 1-H)
	7.03-7.15	ppm	(4H, (5-8)-H)

(Assignment for major diastereomer)

9. Attempt to Prepare 1,2,3,4-tetrahydro-3-methylisoquinoline

1-Phenyl-2-aminopropane (0.530g, 3.92 mmol) was treated with 37% formaldehyde (0.53 ml) to yield a colorless precipitate. Concentrated HCl (3.18 ml) was added, and the suspension was refluxed for 6 h. The brown solution was concentrated on a rotary evaporator, and the residue obtained was taken up in water (15 ml). The aqueous solution was washed with dichloromethane (15 ml x 3) to remove brown colored impurities. The yellow aqueous extract was cooled, basified with sodium hydroxide pellets, extract with dichloromethane (15 ml x 3), dried over anhydrous sodium sulfate, and evaporate to provide a red viscous oil (0.595g). Purification of this oil by silica gel column chromatography using dichloromethane-methanol-triethylamine (97:3:1) as the eluent provided the desired compound as a colorless oil (0.242 g, 42%). This followed as

the method of Grunewald, et al. The corresponding compound was not the desire product, but it was *N*-methylamphetamine. This result has been discussed in Chapter IV.

***N*-methylamphetamine**

IR:	3350-3310	cm^{-1}	(νN-H of secondary amine)
(Neat)	3100-3000	cm^{-1}	(νC-H of aromatic ring)
(Figure 66)	2965-2840	cm^{-1}	(νas and νs of CH_3 and CH_2 group)
	1604, 1494 and 1475	cm^{-1}	(νC=C of aromatic ring)
	1453 and 1373	cm^{-1}	(δas and δs of CH_3 group)

1H-NMR:	1.11	ppm	(3H, d, ^3J = 6.0 Hz, 3-H)
(in $CDCl_3$)	2.00	ppm	(1H, board, s, amino-H)
(Figure 67-68)	2.44	ppm	(3H, s, *N*-CH_3)
	2.65	ppm	(1H, dd, ^3J = 6.0, ^2J = 13.0, 1-H)
	2.76	ppm	(1H, dd, ^3J = 6.0, ^2J = 13.0, 1-H)
	2.84	ppm	(1H, m, 2-H)
	7.21-7.36	ppm	(5H, aromatic)

10. *N*-(*p*-Nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline and its derivatives

Placed 1 equivalent of 1,2,3,4-tetrahydroisoquinoline or derivatives, 2.0 equivalents of K_2CO_3, tetrahydrofuran in a two-necked, round-bottomed flask provided with magnetic stirrer, condenser, calcium chloride guard-tube and dropping funnel. A solution of 1.5 equivalents of *p*-nitrobenzoylchloride (PNBC) in tetrahydrofuran was introduced into the dropping funnel. The solution of acid chloride was added dropwise

into the vigorously-stirred solution within 30 minutes at room temperature. The reaction mixture was stirred and heated to reflux at 75-80 °C for 1 hour. The reaction was stopped by addition of water, then extracted with dichloromethane (thrice). After the extract was washed with 1 N hydrochloric acid solution and 1 N sodium hydroxide solution, respectively. It was washed with water and brine. The extract was filtered and concentrated. The resulting crude was purified by silica gel column chromatography using hexane-ethylacetate (4:1) as eluent and recrystallized from ethanol to provide the desire product, *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline, as a white solid. The conditions of the experiment are listed in Table 4.

Starting compound	PNBC	K_2CO_3	THF	Product
1,2,3,4-tetrahydroisoquinoline 0.500 g (3.75 mmole)	1.043 g, (5.62 mmole)	1.036 g, (7.50 mmole)	40 ml	*N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline 0.980 g (88.2%)
1,2,3,4-tetrahydro-1-methylisoquinoline 0.124 g (0.844 mmole)	0.234 g, (1.27 mmole)	0.233 g, (1.69 mmole)	15 ml	*N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline 0.209 g (83.7%)
1,2,3,4-tetrahydro-1,3-dimethylisoquinoline 0.080 g (0.500 mmole)	0.184 g, (0.750 mmole)	0.138 g, (1.00 mmole)	15 ml	*N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1,3-dimethylisoquinoline 0.060 g (52.0%)

Table 4. Details of reagents used in the synthesis of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline derivatives

N-(*p*-Nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline

Anal. Calcd. for $C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92; O, 17.00

Found : C, 68.06; H, 5.05; N, 10.09; O, 16.80

IR:	3100-3000	cm^{-1}	(ν C-H of aromatic ring)
(KBr)	2950-2840	cm^{-1}	(νas and νs of CH_2 group)
(Figure 68)	1627	cm^{-1}	(ν C=O of tertiary amide group)
	1517 and 1353	cm^{-1}	(νas and νs O-N=O of nitro group)
	1597, 1499 and 1446	cm^{-1}	(ν C=C of aromatic ring)

^{1}H-NMR: at room temperature. (Figure 69)

at low temperature (25°C, 15°C, 10°C, 0°C, -10°C). (Figure 70)

^{1}H-NMR: Assignment for major (A) and minor (B) conformations.

($CDCl_3$, (A : B = 3 : 2 ratio)

at -10°C)

(Figure 71-72)

2.87	ppm	(2H, t, ^{3}J = 6 Hz, 4-H (A))
2.99	ppm	(2H, t, ^{3}J = 6 Hz, 4-H (B))
3.58	ppm	(2H, t, ^{3}J = 6 Hz, 3-H (A))
4.00	ppm	(2H, t, ^{3}J = 6 Hz, 3-H (B))
4.51	ppm	(2H, s, 1-H (B))
4.90	ppm	(2H, s, 1-H (A))
6.89	ppm	(1H, d, ^{2}J = 7.6, 8-H(B))
7.13-7.26	ppm	(7H, m, 5-8 (A), 5-7 (B))
7.60-7.62	ppm	(2/3H, d/d, J = 7.32/7.63, (2', 6')-H (B)/(A))
8.29-8.30	ppm	(2/3H, d/d, J = 7.93/8.24, (3', 5')-H (B)/(A))

^{13}C-NMR: Assignment for major (A) and minor (B) conformations.

(Figure 73-74)

28.09	ppm	(4-C, (B))
29.46	ppm	(4-C, (A))
40.46	ppm	(3-C, (B))
44.79	ppm	(1-C, (A))
45.20	ppm	(3-C, (A))
49.62	ppm	(1-C, (B))
123.93	ppm	(3′ and 5′-C, (A)/(B))
125.79	ppm	(8-C, (B))
126.52	ppm	(7-C, (B))
126.75	ppm	(8-C, (A))
126.83	ppm	(7-C, (A))
127.26	ppm	(6-C, (B))
127.88	ppm	(2′ and 6′-C, (A)/(B))
128.16	ppm	(6-C, (B))
128.66	ppm	(5-C, (A))
129.13	ppm	(5-C, (B))
132.05	ppm	(8a-C, (B))
132.36	ppm	(8a-C, (A))
133.34	ppm	(4a-C, (A))
134.45	ppm	(4a-C, (B))
142.23	ppm	(1′-C, (A))
142.10	ppm	(1′-C, (B))
148.43	ppm	(4′-C, (A)/(B))
168.11	ppm	(carbonyl-C, (B))
168.55	ppm	(carbonyl-C, (A))

Other NMR experiments :

DEPT 135/DEPT90/^{13}C-NMR at room temperature (comparative spectrum) (Figure 75)

HH COSY (Figure 76)

HMQC (Figure 77)

HMBC (Figure 78-81)

_N_-(_p_-Nitrobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline

Anal. Calcd. for $C_{17}H_{16}N_2O_3$: C, 68.91; H, 5.44; N, 9.45; O, 16.20

Found : C, 69.35; H, 5.42; N, 9.90; O, 16.32

IR:	3100-3000	cm^{-1}	(ν C-H of aromatic ring)
(KBr)	2987-2840	cm^{-1}	(νas and νs of CH_3 and CH_2 group)
(Figure 82)	1625	cm^{-1}	(ν C=O of tertiary amide group)
	1519 and 1352	cm^{-1}	(νas and νs O-N=O of nitro group)
	1597, 1495 and 1438	cm^{-1}	(ν C=C of aromatic ring)
	1450	cm^{-1}	(δas C-H of CH_3 group)

^{1}H-NMR : Assignment for major (A) and minor (B) conformations.

(in $CDCl_3$) (A : B = 2 : 1 ratio)

(Figure 83-84)	1.49	ppm	(3H, d, ^{3}J = 6.3 Hz,1-CH_3, (B))
	1.59	ppm	(3H, d, ^{3}J = 7.2 Hz, 1-CH3, (A))
	2.76	ppm	(1H, t, ^{2}J = 16.5 Hz, 4-Ha, (A))
	2.94	ppm	(1H, d, ^{2}J = 18.0 Hz, 4-Ha, (B))

2.91	ppm	(1H, dd, ^{3}J = 5.7 Hz, ^{2}J = 16.5 Hz, 4-Hb, (A))
3.10	ppm	(1H, td, ^{3}J = 5.1 and 13.8 Hz, ^{2}J = 13.8 Hz, 4-Hb, (B))
3.27	ppm	(1H, td, ^{3}J = 2.7 and 12.3 Hz, ^{2}J = 12.3 Hz, 3-Ha, (B))
3.47	ppm	(2H, td, ^{3}J =3.6 and 12.6 Hz, ^{2}J = 12.6 Hz, 3-Ha, (A))
3.61	ppm	(2H, dd, ^{3}J =5.1 Hz, ^{2}J = 12.6 Hz, 3-Hb, (A))
4.67	ppm	(1H, q, ^{3}J = 6.3 Hz, 1-H, (B))
4.78	ppm	(1H, dd, ^{3}J = 4.5 Hz, ^{2}J = 12.3 Hz, 3-Hb, (B))
5.75	ppm	(2H, q, ^{3}J = 6.3 Hz, 1-H, (A))
6.87	ppm	(1H, d, ^{3}J = 6.6 Hz, 8-H, (B))
7.10-7.26	ppm	((4/3)H, m, (5-8)-H, (A)/(5-7)-H, (B))
7.57	ppm	((2/2)H, d/d, 2' and 6'-H (A)/(B))
8.29	ppm	((2/2)H, d/d, 3' and 5'-H (A)/(B))

^{13}C-NMR: Assignment for major (A) and minor (B) conformations.

(Figure 85-86)

21.72	ppm	(1-CH_3, (A))
23.42	ppm	(1-CH_3, (B))
28.34	ppm	(4-C, (B))
29.60	ppm	(4-C, (A))
35.55	ppm	(3-C, (B))
41.09	ppm	(3-C, (A))
49.03	ppm	(1-C, (A))
53.83	ppm	(1-C, (B))

123.88	ppm	(3′ and 5′-C,(A)/(B))
126.34	ppm	(aromatic-C)
126.60	ppm	(aromatic-C)
126.69	ppm	(aromatic-C)
127.10	ppm	(aromatic-C)
127.48	ppm	(2′ and 6′-C,(A)/(B))
128.71	ppm	(aromatic-C)
129.26	ppm	(aromatic-C)
132.29	ppm	(4a-C, (A))
133.49	ppm	(4a-C, (B))
136.81	ppm	(8a-C, (B))
137.56	ppm	(8a-C, (A))
142.48	ppm	(1′-C, (A)/(B))
148.16	ppm	(4′-C, (A)/(B))
167.62	ppm	(carbonyl-C, (A))
168.92	ppm	(carbonyl-C, (A))

Other NMR experiments :

DEPT 135 (Figure 87)

HH COSY (Figure 88)

HMQC (Figure 89)

HMBC (Figure 90-92)

N-(p-Nitrobenzoyl)-1,2,3,4-tetrahydro-1,3-dimethylisoquinoline

Anal. Calcd. for $C_{16}H_{14}N_2O_3$: C, 69.66; H, 5.85; N, 9.03; O, 15.47

Found : C, 69.71; H, 5.83; N, 9.02; O, 15.44

IR:	3100-3000	cm^{-1}	(ν C-H of aromatic ring)
(KBr)	2987-2840	cm^{-1}	(νas and νs of CH_3 and CH_2 group)
(Figure 93)	1625	cm^{-1}	(ν C=O of tertiary amide group)
	1519 and 1352	cm^{-1}	(νas and νs O-N=O of nitro group)
	1597, 1495 and 1438	cm^{-1}	(ν C=C of aromatic ring)
	1450	cm^{-1}	(δas C-H of CH_3 group)

^{1}H-NMR: (Assignment for major (A) conformation)

(in CDCl3) (A : B = 2 : 1 ratio)

(Figure 94-95)	1.23	ppm	(3H, board, 3-CH_3)
	1.68	ppm	(3H, board, 1-CH_3)
	2.86	ppm	(1H, board, 4-H)
	3.06	ppm	(1H, board, 4-H)
	4.11	ppm	(1H, board, 3-H)
	5.68	ppm	(1H, board, 1-H)
	7.10-7.26	ppm	(aromatic proton, 5′-8′)
	7.52	ppm	(2H, 2′ and 6′-H)
	8.26	ppm	(2H, 3′ and 5′-H)

^{13}C-NMR: (Assignment for major (A) conformation)

(Figure 96-97)	20.79	ppm	(3-CH_3)
	22.86	ppm	(1-CH3)
	35.48	ppm	(4-C)
	45.00	ppm	(1-C, (B))
	48.05	ppm	(1-C, (A))
	48.83	ppm	(3-C, (A))
	55.00	ppm	(3-C, (B))
	124.06	ppm	(3′ and 5′-C)
	126.41	ppm	(aromatic-C)
	126.91	ppm	(aromatic-C)
	127.08	ppm	(2′ and 6′-C)
	127.45	ppm	(aromatic-C)
	129.33	ppm	(aromatic-C)
	130.37	ppm	(8a-C)
	136.36	ppm	(4a-C)
	143.63	ppm	(1′-C)
	148.12	ppm	(4′-C)
	168.00	ppm	(carbonyl-C)

Other NMR experiments:

DEPT 135 (Figure 98)

HH COSY (Figure 99)

HMQC (Figure 100)

HMBC (Figure 101)

10. *N*-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydroisoquinoline derivatives and its derivative

A solution of 1 g of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in 20 ml of dichloromethane was added to a Parr hydrogenation bottle along with 0.3 g of 10% palladium on activated charcoal and subjected to shaking at low-pressure hydrogenation (60 psi) for 1 hour. The bottle was then removed, and the contents were filtered. The filtrate was evaporated, and the resulting residue (0.925 g, 103.5%) was dissloved in tetrahydrofuran, concentrated hydrochloric acid (excess) was added to it until the solution is couldy. The solution of the hydrochloride salt was evaporated to be white solid crude product (Acetone was also added to this solution to form azeotropic mixture with water). The hydrochloride salt was crystallized as a white solid from methanol-diethylether.

As same as above method, 1.0 g of *N*-(*p*-Nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline, 10 ml of CH_2Cl_2, 0.03 g of 10% Pd/C and hydrogenation at 60 psi; 1 hr, to give amino product 0.090 g, 100%.

***N*-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydroisoquinoline hydrochloride**

IR:	3100-3000	cm^{-1}	(νas and νs C-H of aromatic)
(KBr)	2800 and 2600	cm^{-1}	(νas and νs N-H of primary amine salt)
(Figure 102)			
	1613	cm^{-1}	(ν C=O of secondary amide)
	1570 and 1540	cm^{-1}	(δas and δs N-H of primary amine salt)

^{1}H-NMR:	2.84	ppm	(2H, board, s, 4-H)
(in CDCl3)	3.64	ppm	(2H, board, s, 3-H)
(Figure 103)	4.88	ppm	(2H, s, 1-H)
	7.16	ppm	(4H, board, s , (5-8)-H, aromatic)
	7.28	ppm	(2H, board, d, (2′, 6′)-H, aromatic)
	7.48	ppm	(2H, board, d, (3′, 5′)-H, aromatic)

^{13}C-NMR:	28.51	ppm	(4-C)
(Figure 104)	121.22	ppm	(2′ and 6′-C)
	126.36	ppm	(aromatic-C)
	126.53	ppm	(aromatic-C)
	128.71	ppm	(3′ and 5′-C)
	128.81	ppm	(aromatic-C)
	132.88	ppm	(1′-C)
	133.24	ppm	(8a-C)
	134.52	ppm	(4a-C)
	137.20	ppm	(4′-C)
	169.07	ppm	(carbonyl-C)

Other NMR experiments:

DEPT 135 (Figure 105)

HH COSY (Figure 106)

HMQC (Figure 107)

_N_-(_p_-Aminobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline hydrochloride

^{1}H-NMR :	1.46	ppm	(2H, d, ^{3}J = 6.9 Hz, 1-CH_3)
(in $CDCl_3$)	2.72	ppm	(1H, d, ^{3}J = 15.6 Hz, 4H)
(Figure 108-109)	2.93	ppm	(1H, ddd, 4-H)
	3.34	ppm	(2H, board, 3-H)
	3.75	ppm	(board, $NH3^{+}$)
	7.09	ppm	(2H, 3′and 5′-H)
	7.10-7.20	ppm	(4H, (5-8)-H)
	7.37	ppm	(2H, 2′ and 6′-H)
^{13}C-NMR:	22.00	ppm	(1-CH_3)
(Figure 110)	28.50	ppm	(4-C)
	49.00	ppm	(3-C)
	52.00	ppm	(1-C)
	119.18	ppm	(2′ and 6′-C)
	126.31	ppm	(aromatic-C)
	126.53	ppm	(aromatic-C)
	127.14	ppm	(aromatic-C)
	128.40	ppm	(3′ and 5′-C)
	129.03	ppm	(aromatic-C)
	130.70	ppm	(1′-C)
	133.67	ppm	(8a-C)
	138.21	ppm	(4a-C)
	140.50	ppm	(4′-C)
	169.00	ppm	(carbonyl-C)

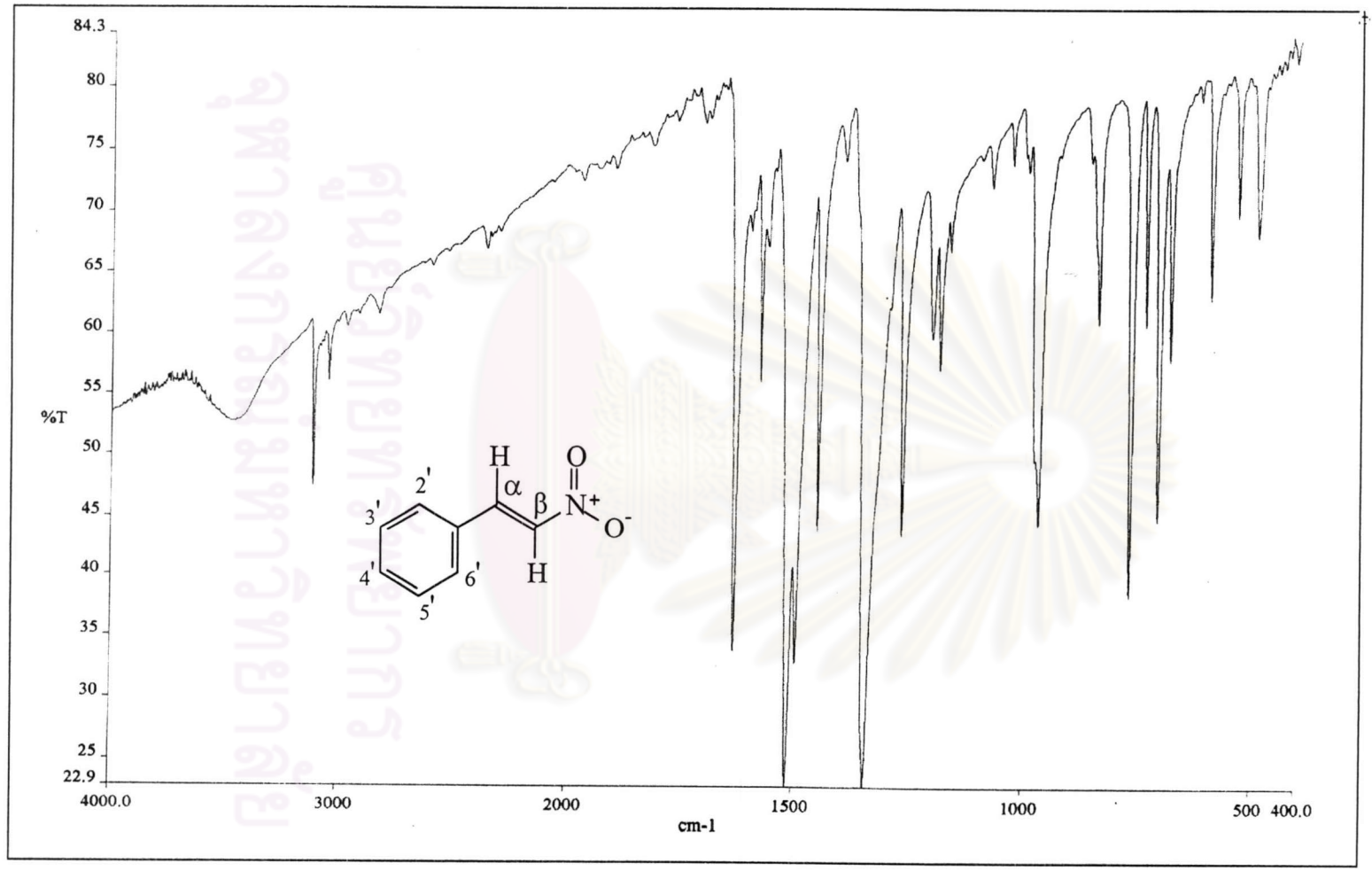


Figure 32. The IR spectrum (KBr) of β-nitrostyrene

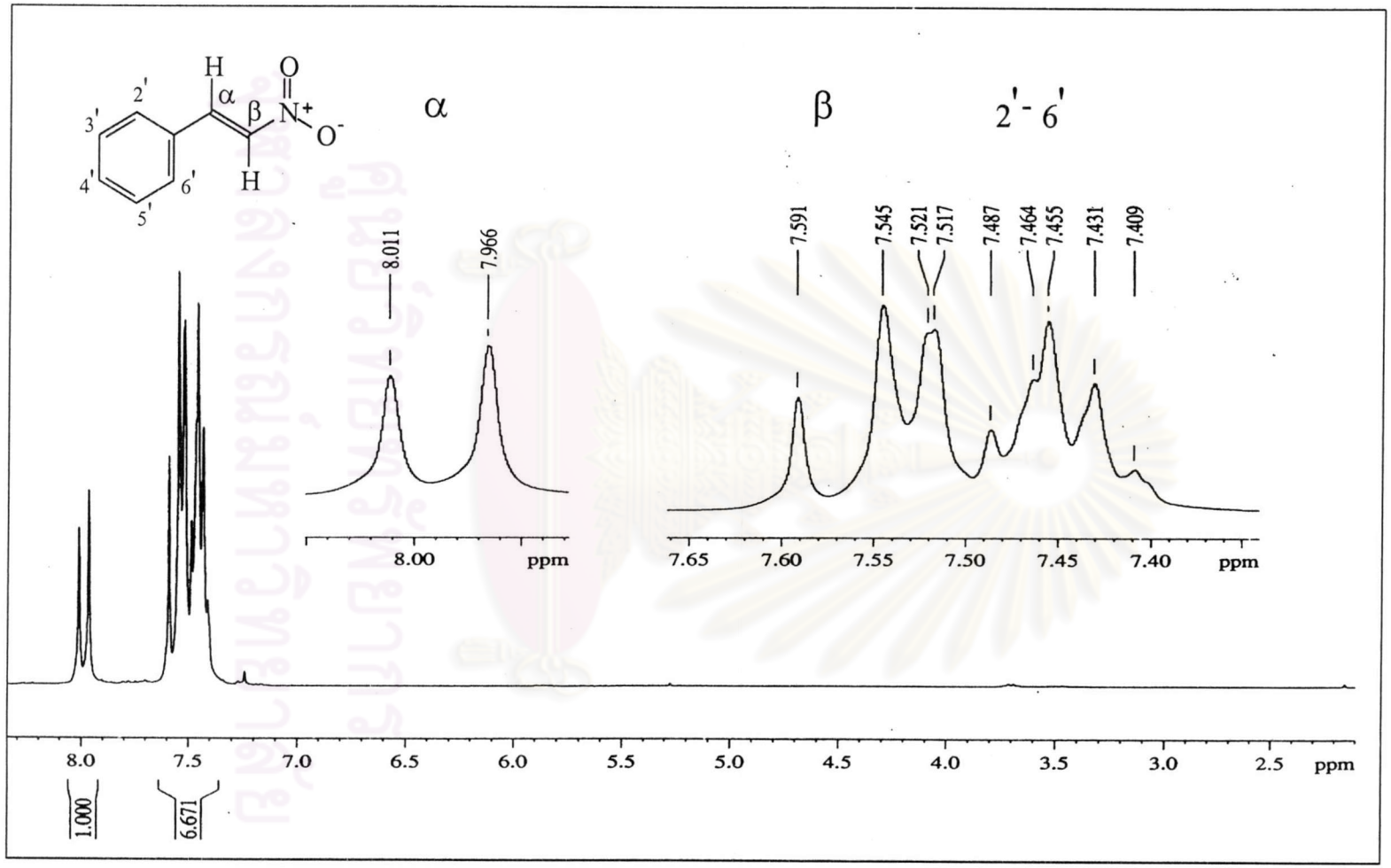


Figure 33.The 300 MHz spectrum of ^{1}H-NMR spectrum of β-nitrostyrene in $CDCl_3$

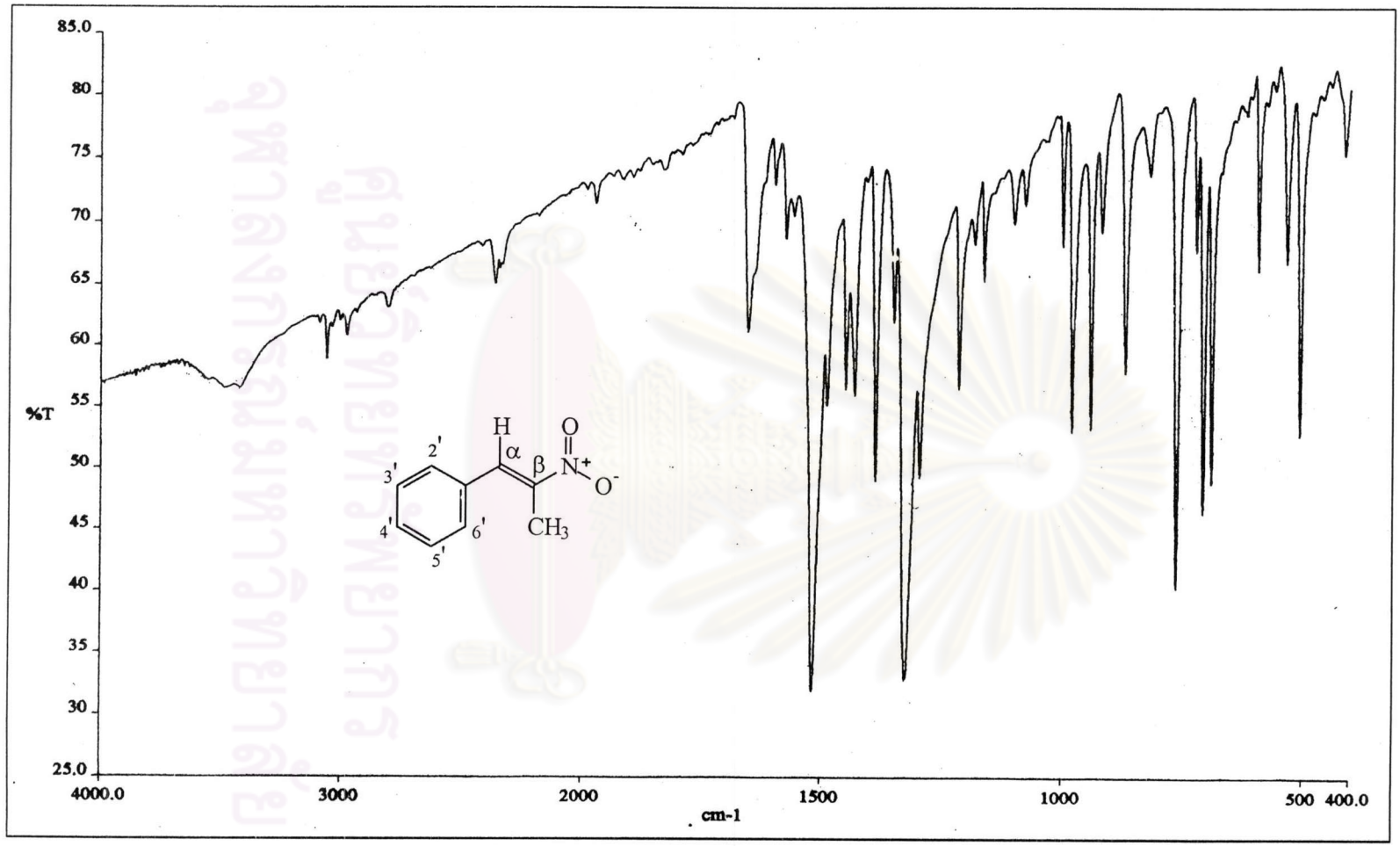


Figure 34. The IR spectrum (KBr) of β-methyl-β-nitrostyrene

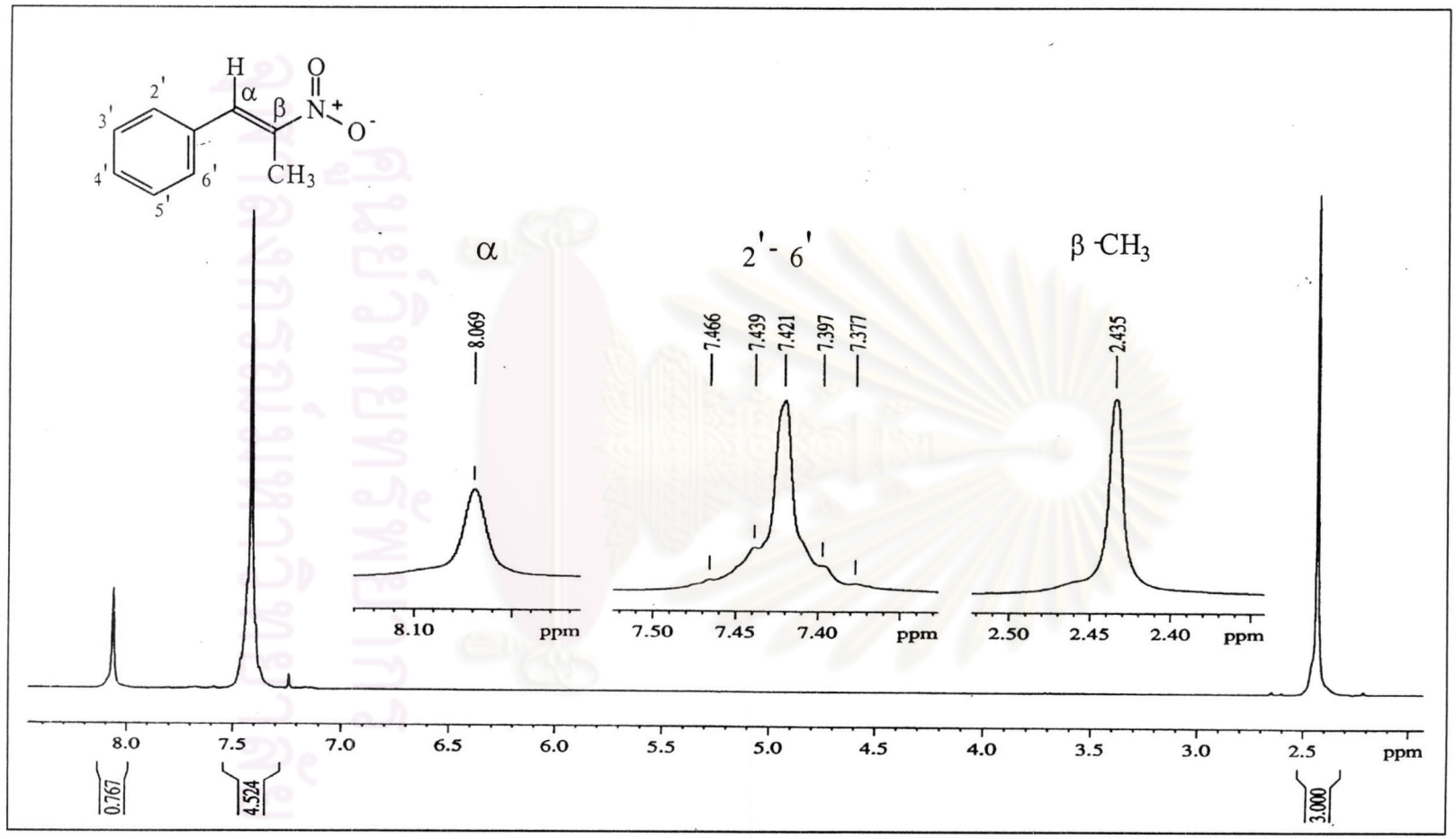


Figure 35. The 300 MHz ^{1}H-NMR spectrum of β-methyl-β-nitrostyrene in $CDCl_3$

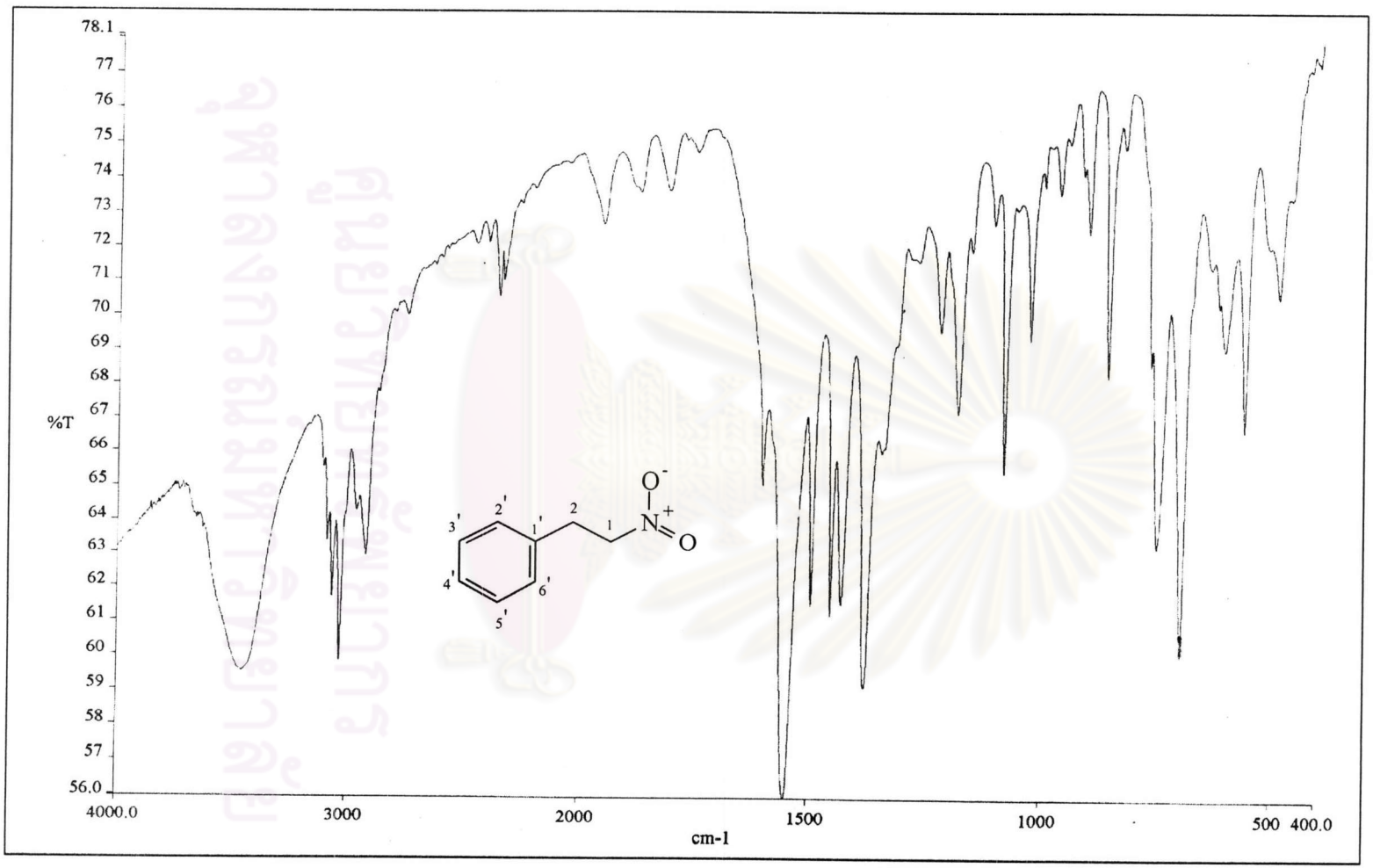


Figure 36. The IR spectrum (Neat) of 1-nitro-2-phenylethane

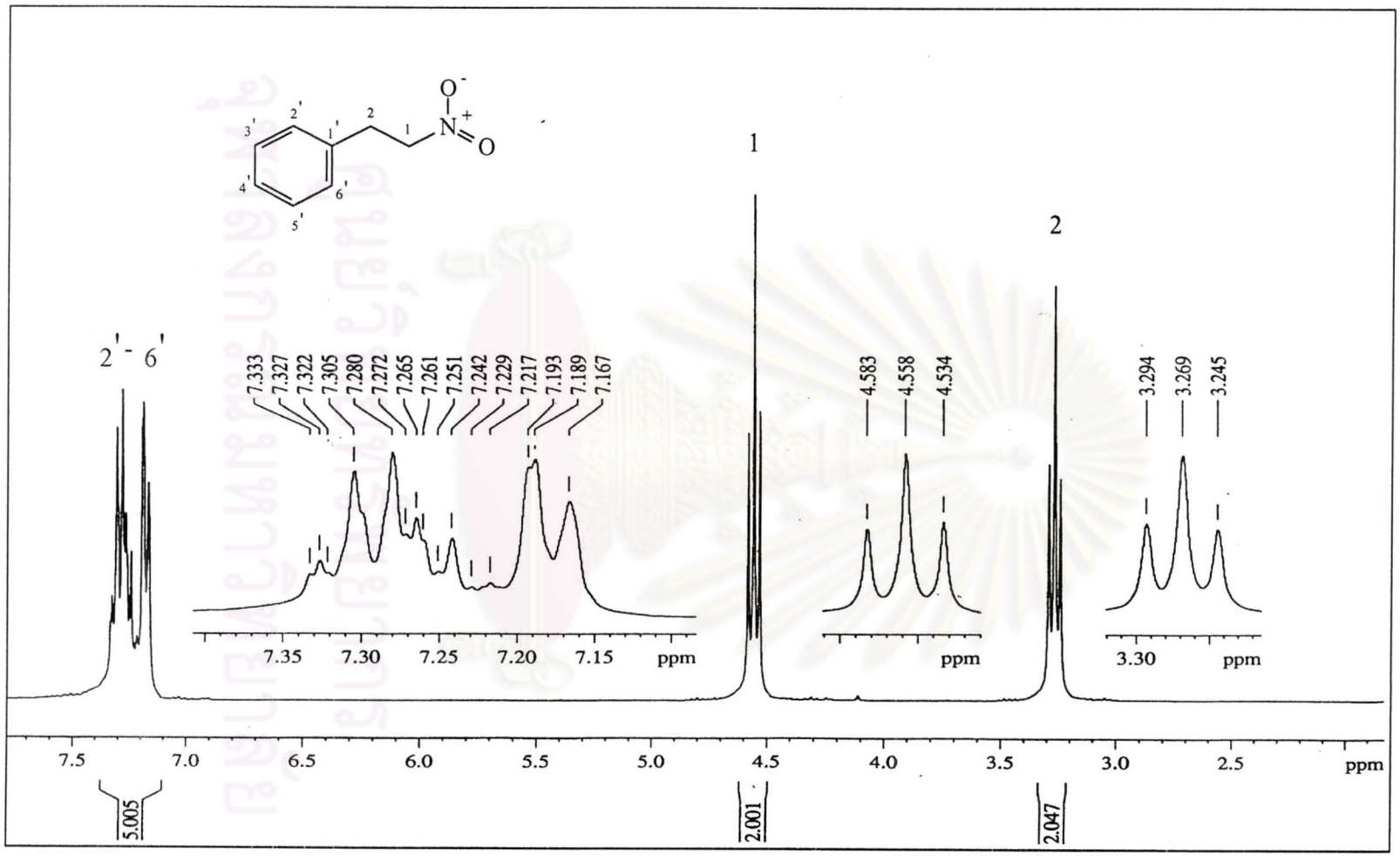


Figure 37. The 300 MHz ^{1}H-NMR spectrum of 1-nitro-2-phenylethane in $CDCl_3$

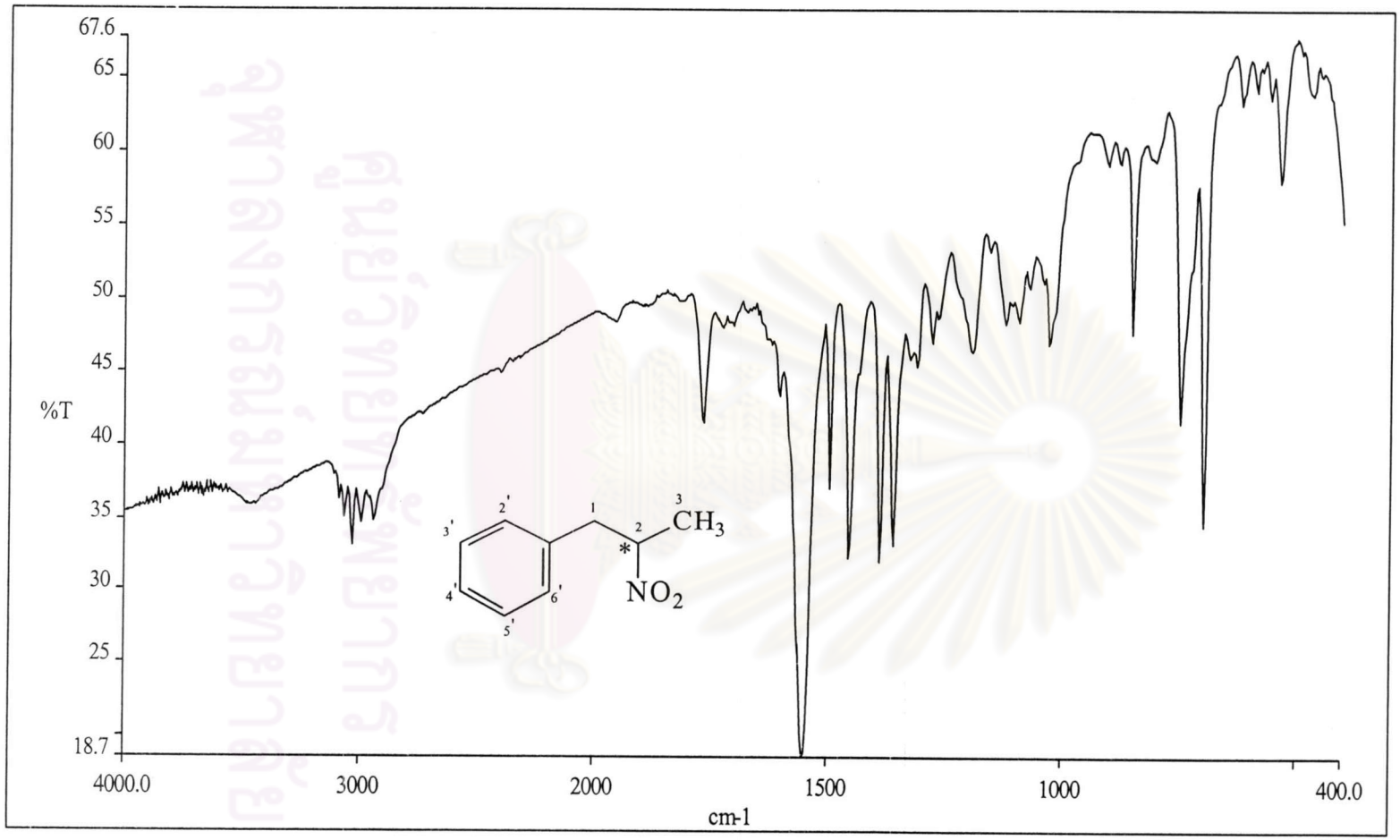


Figure 38. The IR spectrum (Neat) of 2-nitro-1-phenylpropane

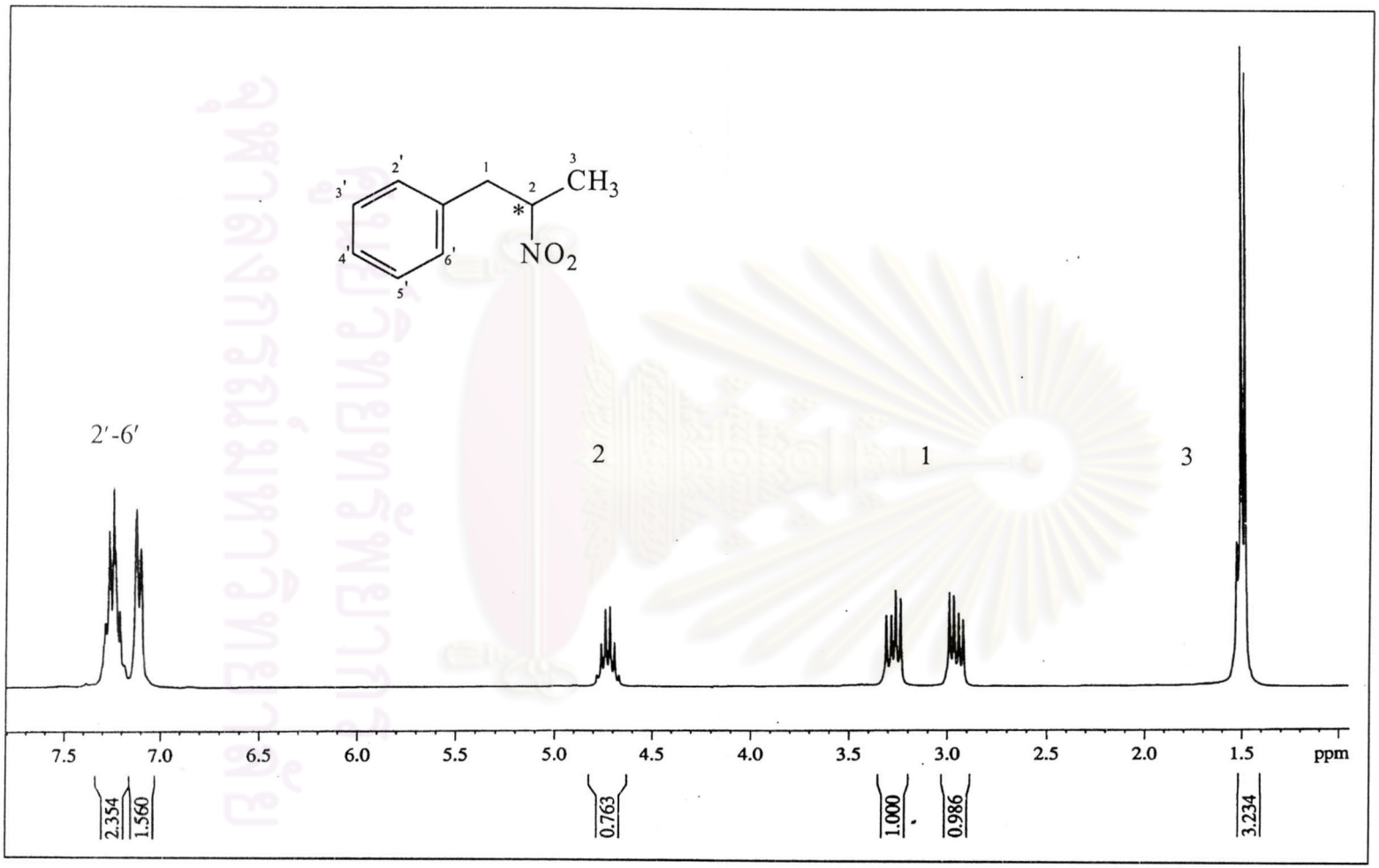


Figure 39. The 300 MHz ^{1}H-NMR spectrum of 2-nitro-1-phenylpropane in $CDCl_3$

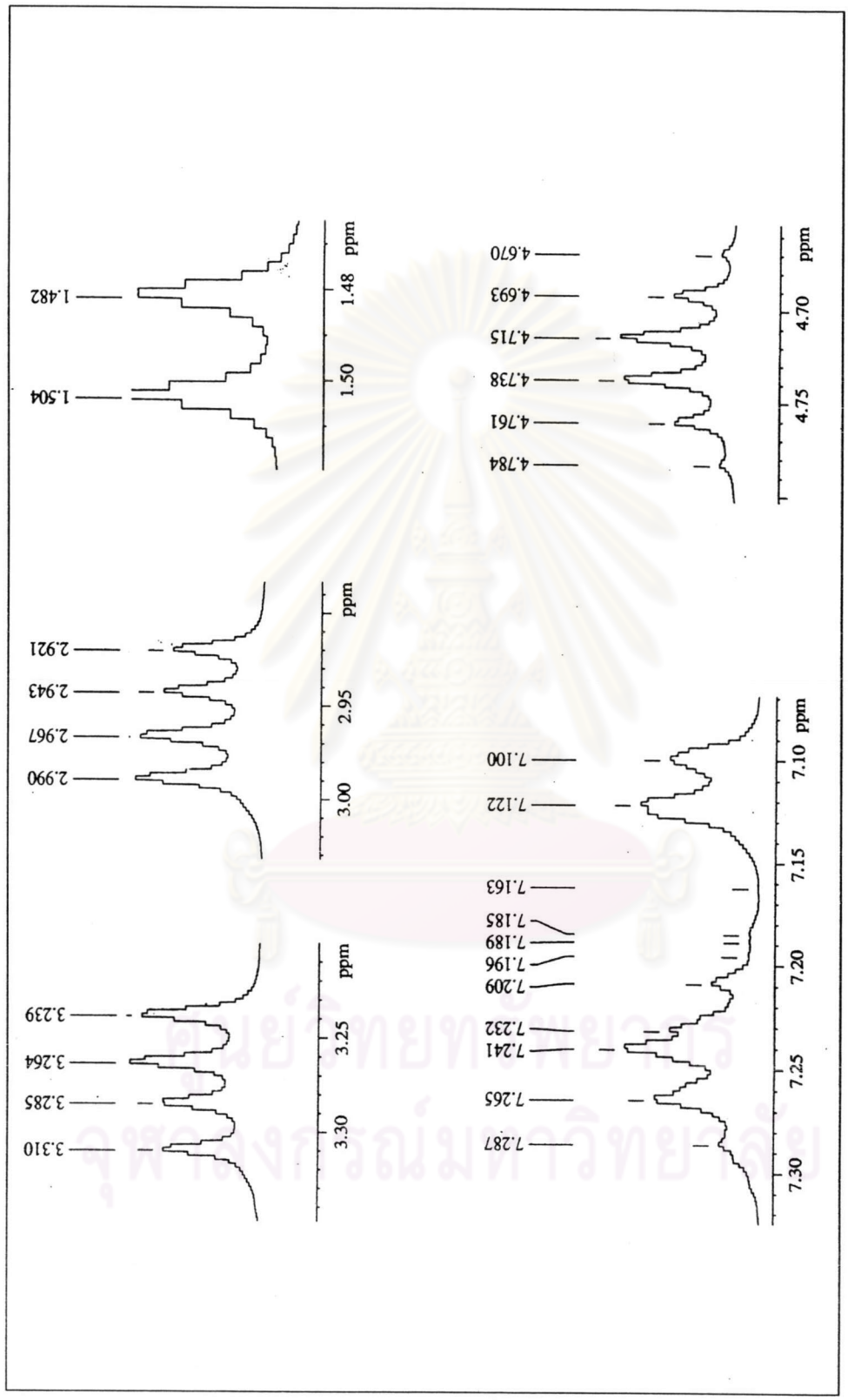


Figure 40. The 300 MHz ^{1}H-NMR spectrum of 2-nitro-1-phenylpropane in $CDCl_3$. (Enlarged-scale)

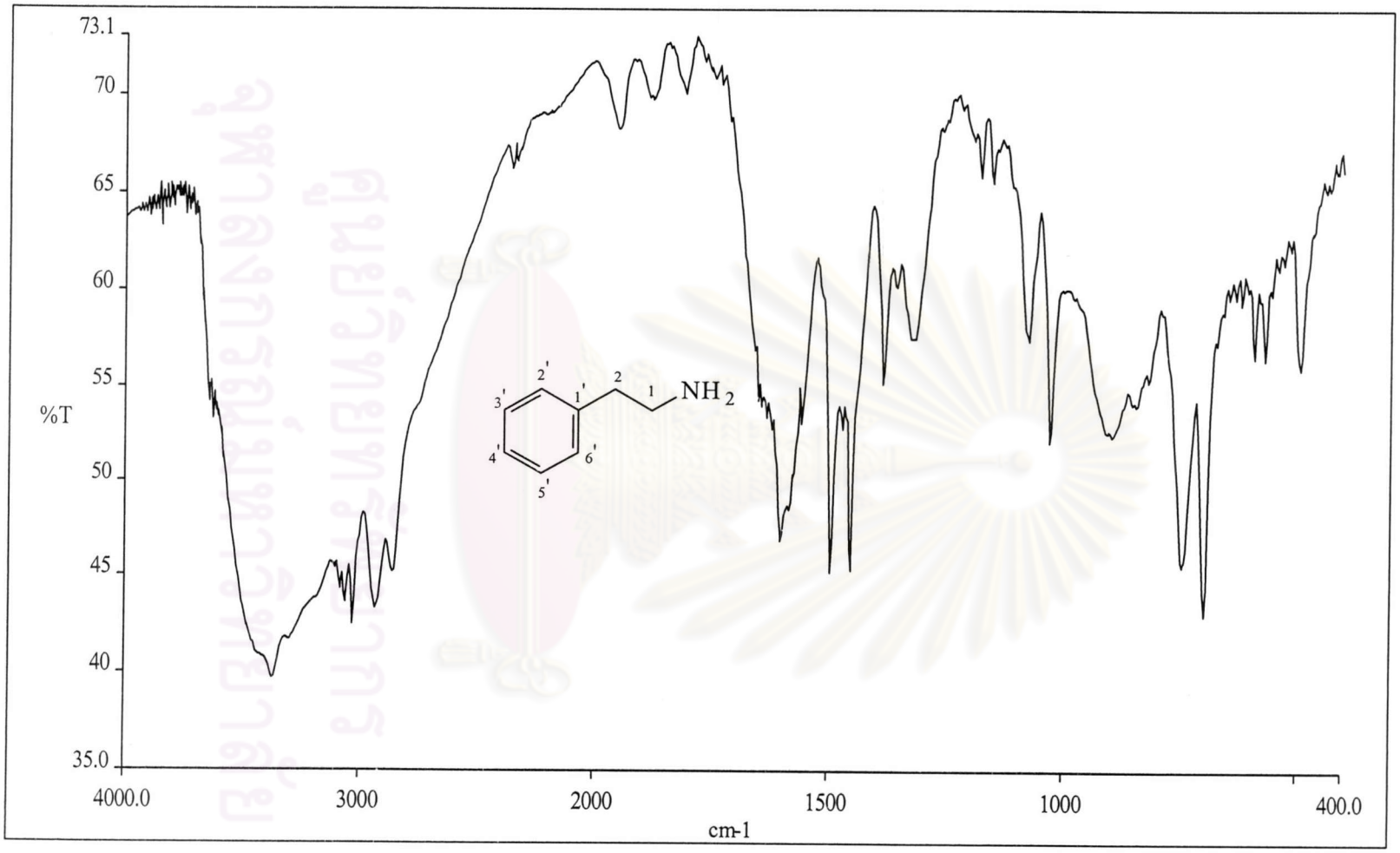


Figure 41. The IR spectrum (Neat) of 1-amino-2-phenylethane (2-phenylethylamine)

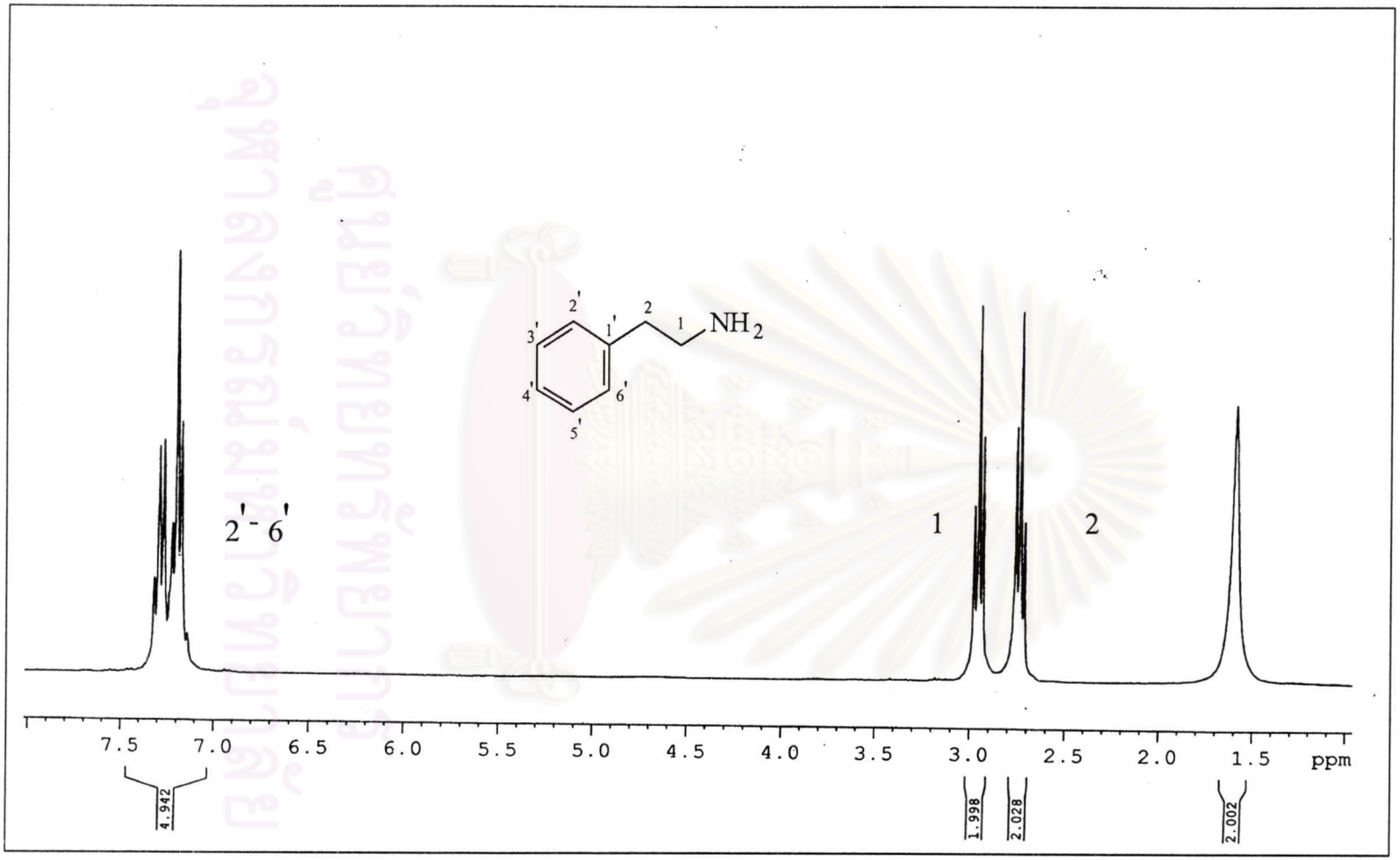


Figure 42. The 300 MHz ^{1}H-NMR spectrum of 1-amino-2-phenylethane (2-phenylethylamine) in $CDCl_3$

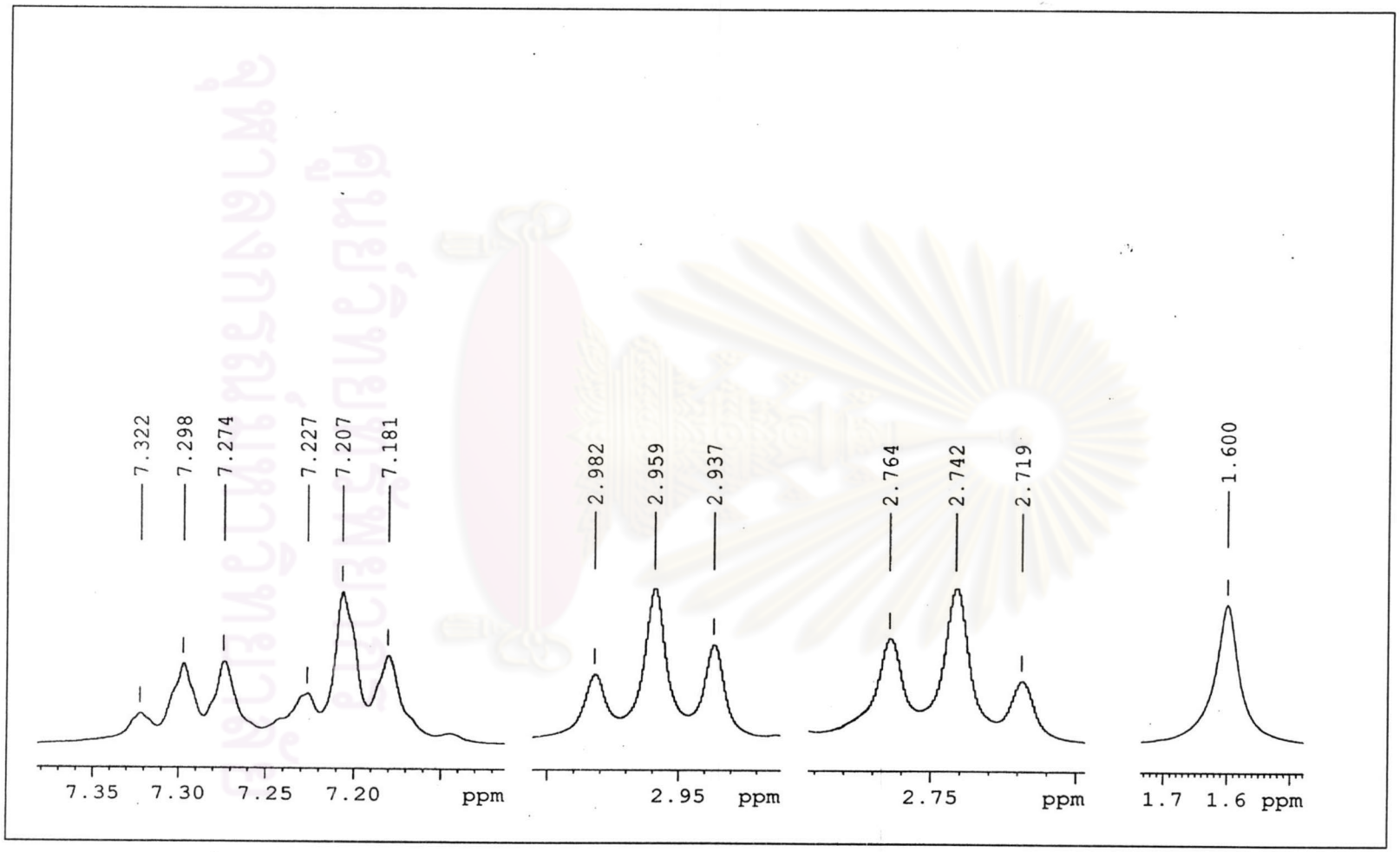


Figure 43. The 300MHz ^{1}H-NMR spectrum of 1-amino-2-phenylethane (2-phenylethylamine) in $CDCl_3$. (Enlarged-scale)

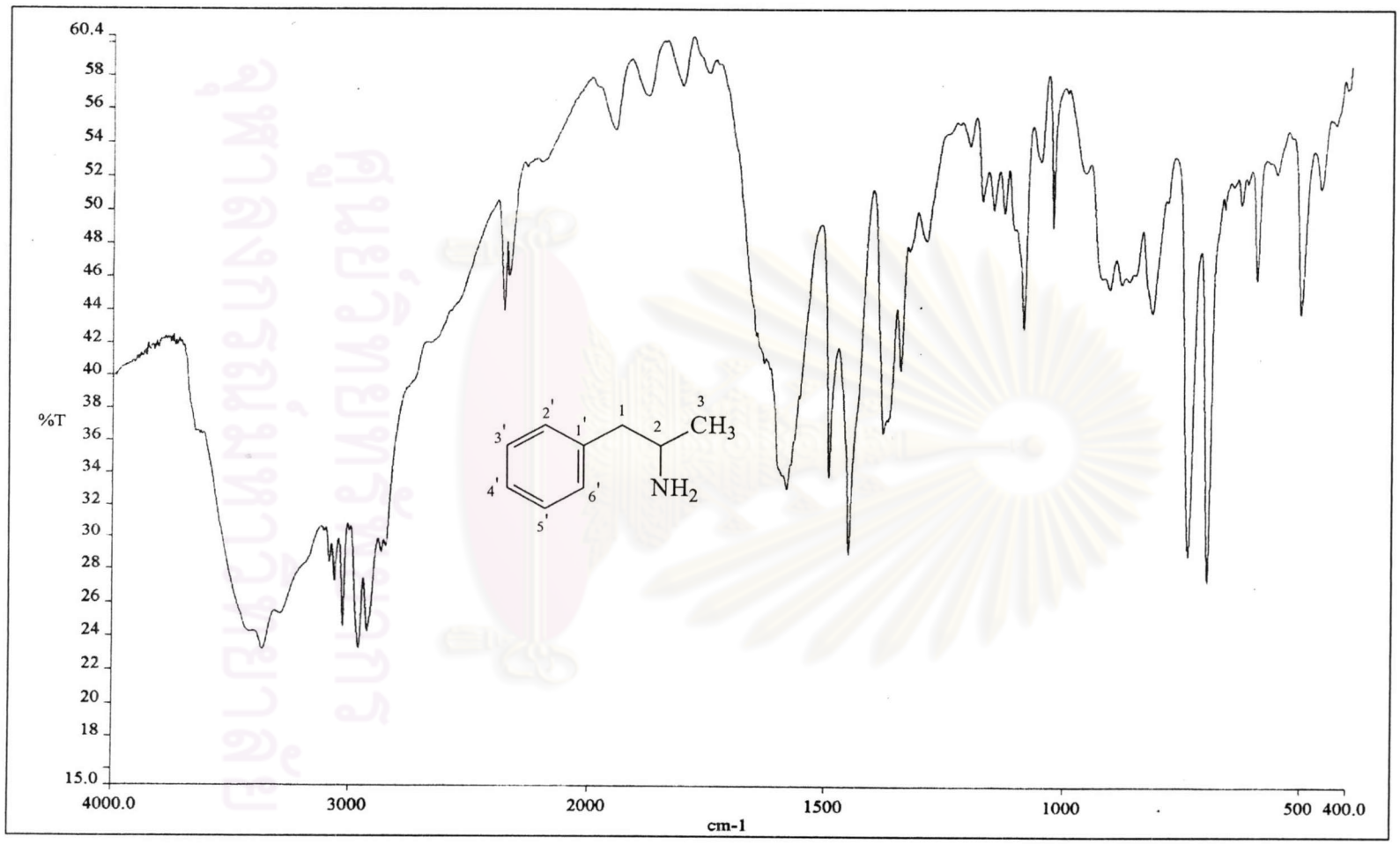


Figure 44. The IR spectrum (Neat) of 2-amino-1-phenylpropane (amphetamine)

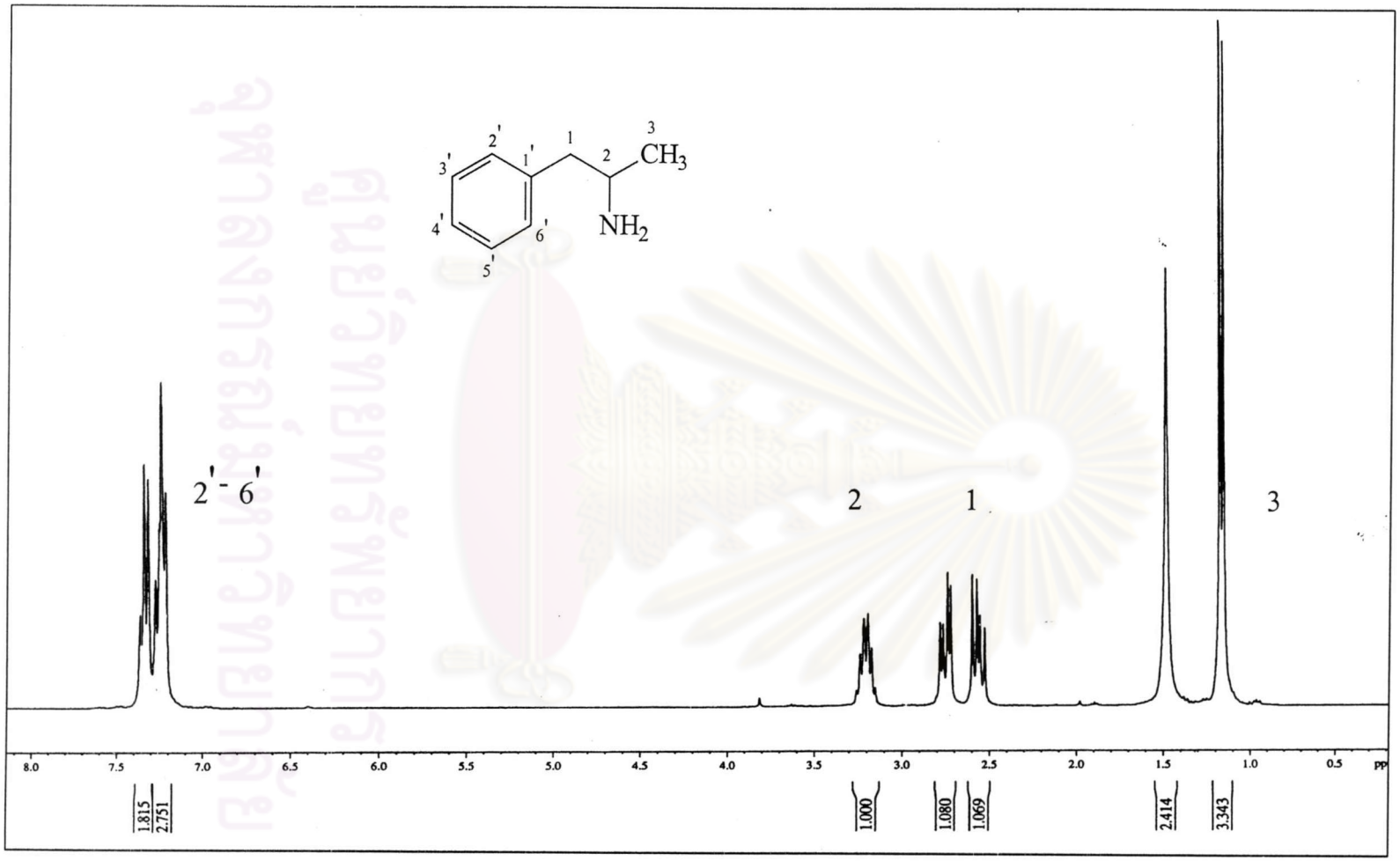


Figure 45. The 300 MHz ^{1}H-NMR spectrum of 2-amino-1-phenylpropane (amphetamine) in $CDCl_3$

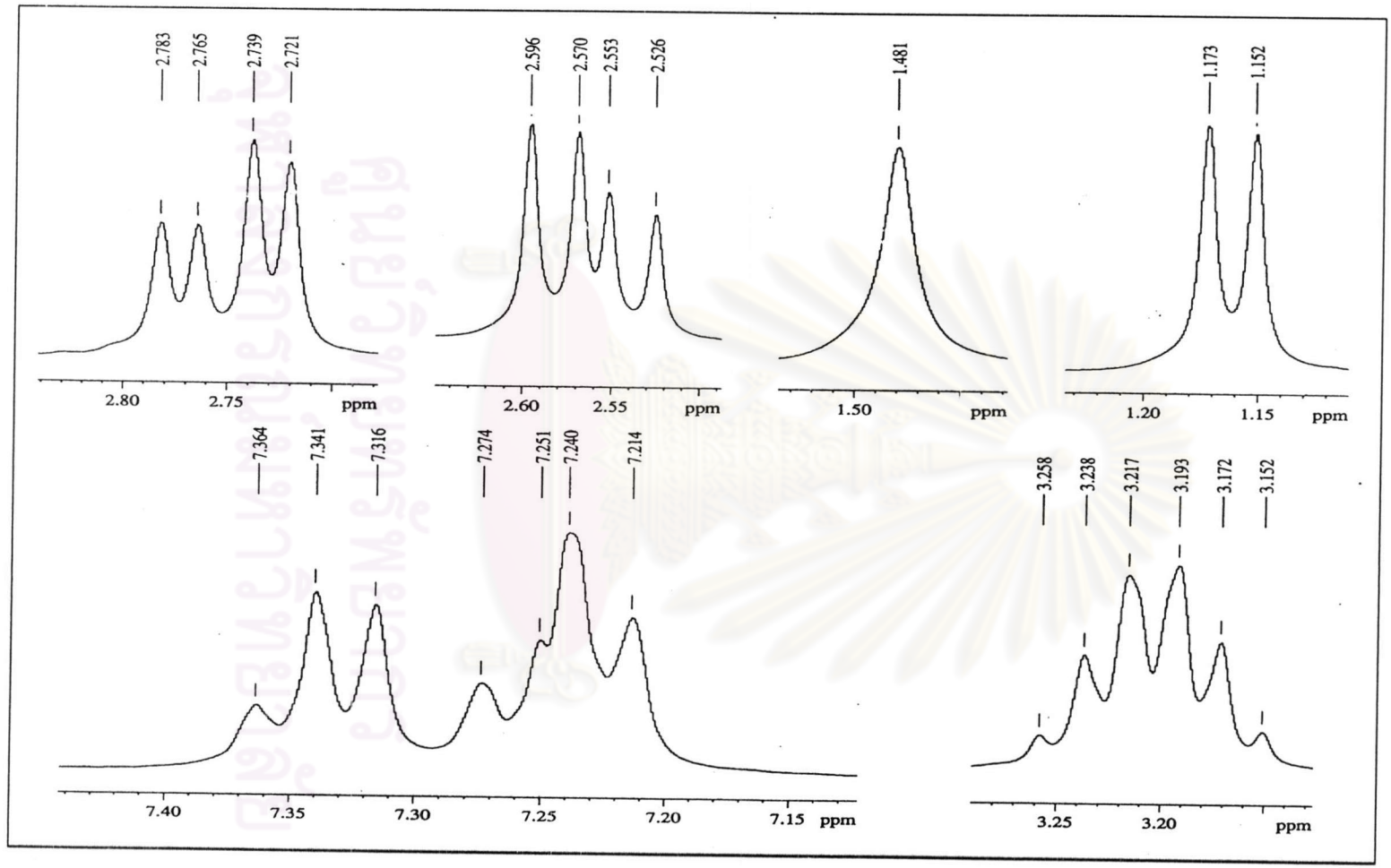


Figure 46. The 300 MHz ^{1}H-NMR spectrum of 2-amino-1-phenylpropane (amphetamine) in $CDCl_3$. (Enlarged-scale)

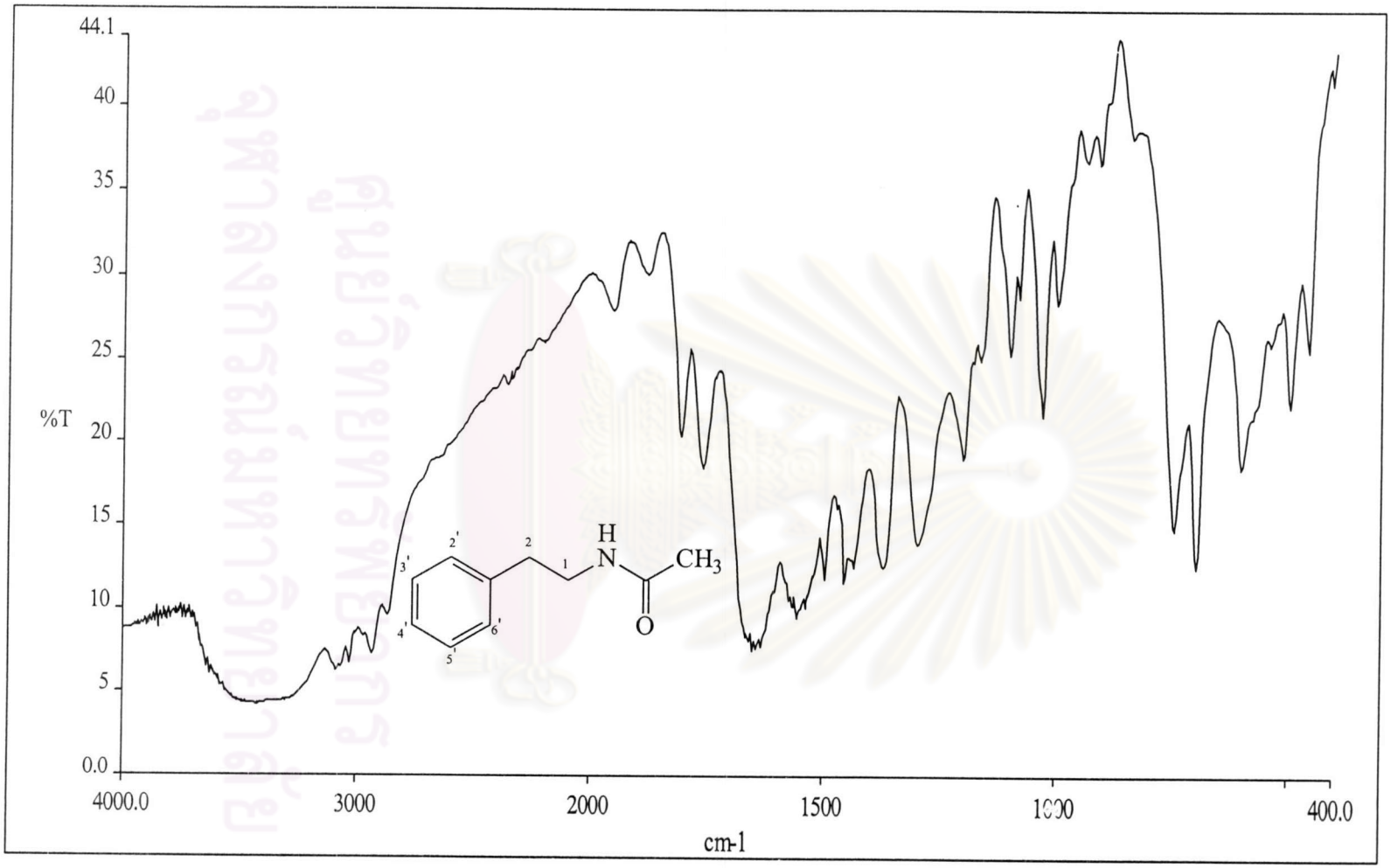


Figure 47. The IR spectrum (Neat) of *N*-acetyl-2-phenylethylamine

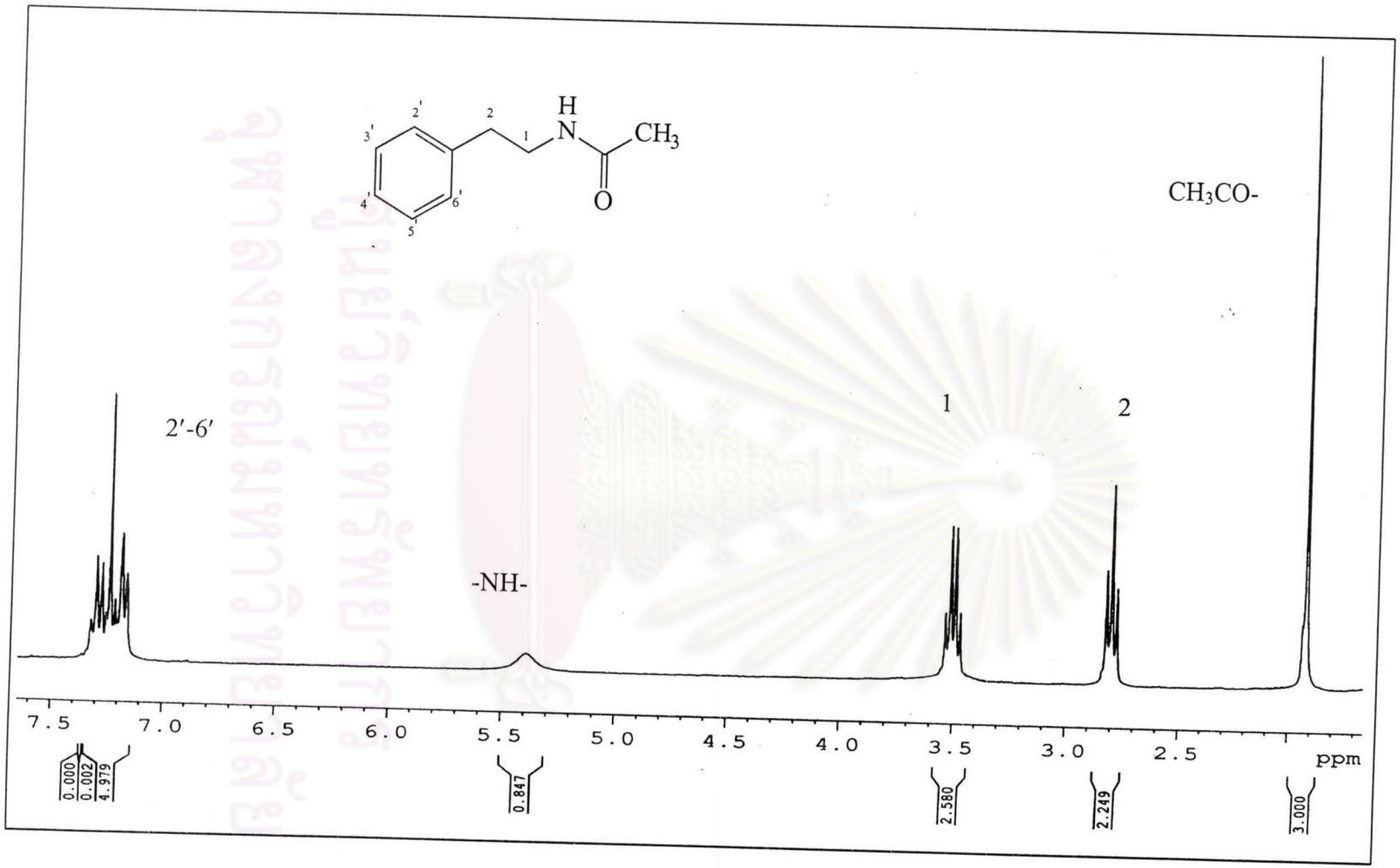


Figure 48. The 300 MHz ^{1}H-NMR spectrum of *N*-acetyl-2-phenylethylamine in $CDCl_3$

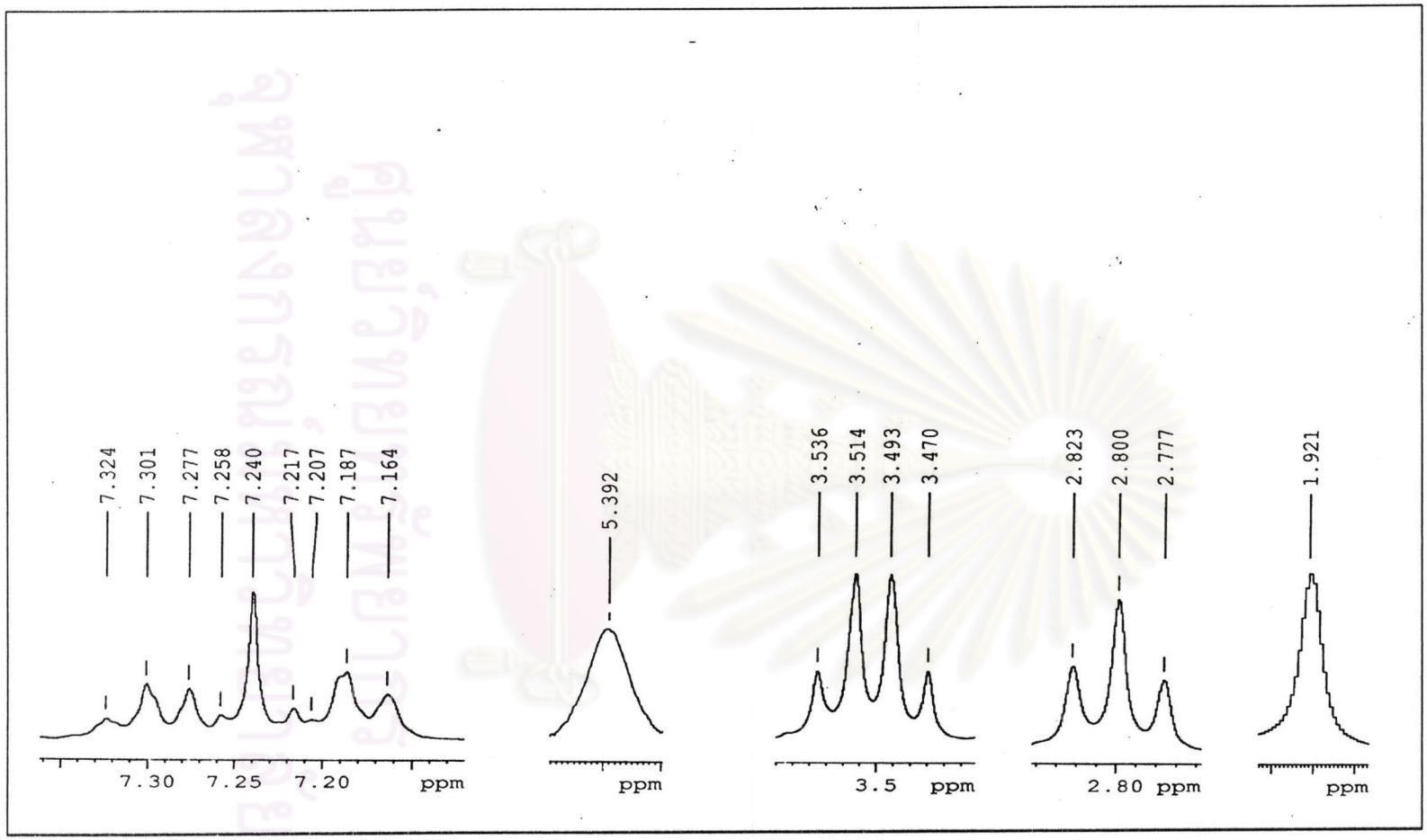


Figure 49. The 300 ^{1}H-NMR spectrum of *N*-acetyl-2-phenylethylamine in $CDCl_3$ (Enlarged-scale).

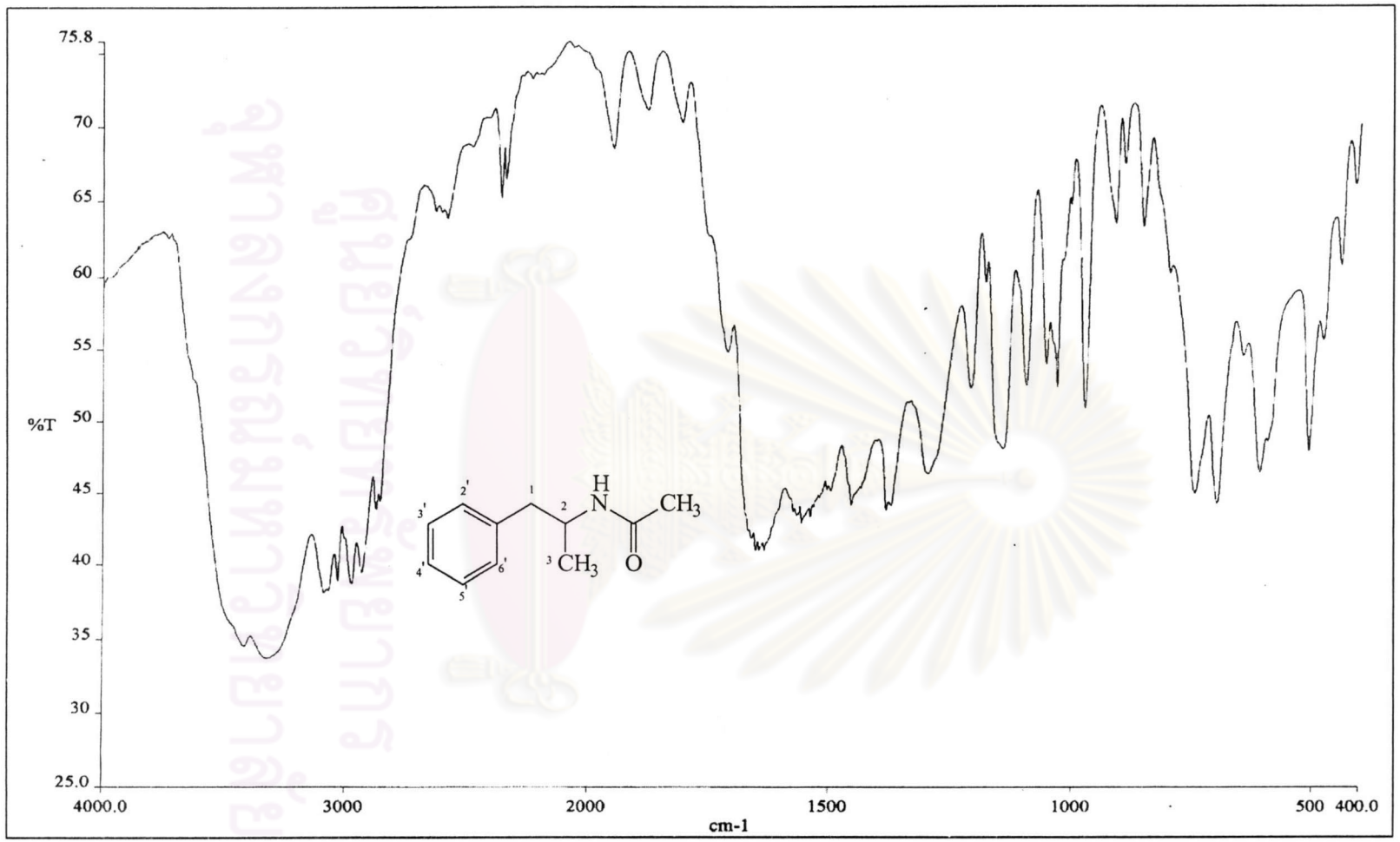


Figure 50. The IR spectrum (Neat) of *N*-acetylamphetamine

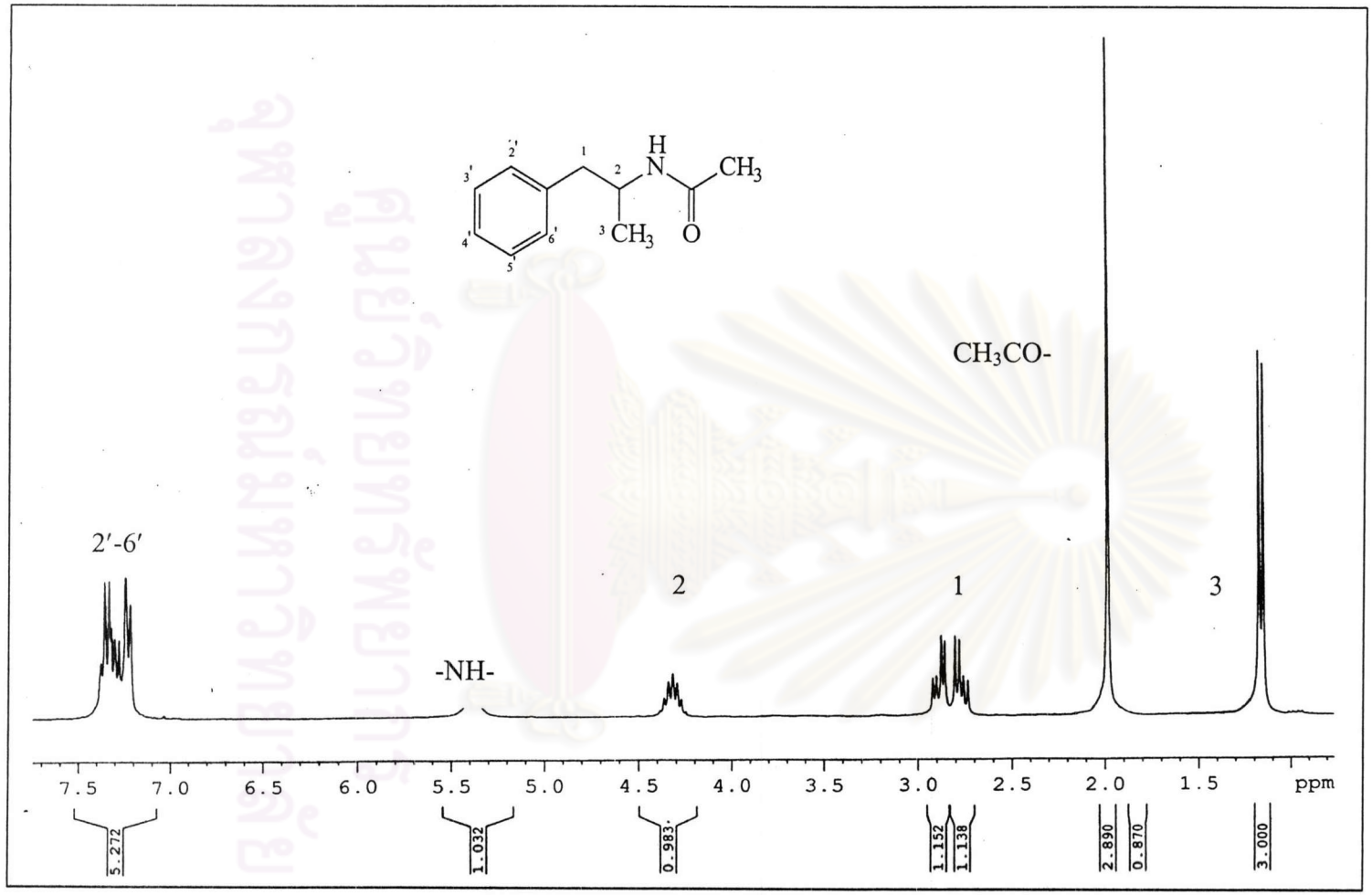


Figure 51. The 300 MHz ^{1}H-NMR spectrum of *N*-acetylamphetamine in $CDCl_3$

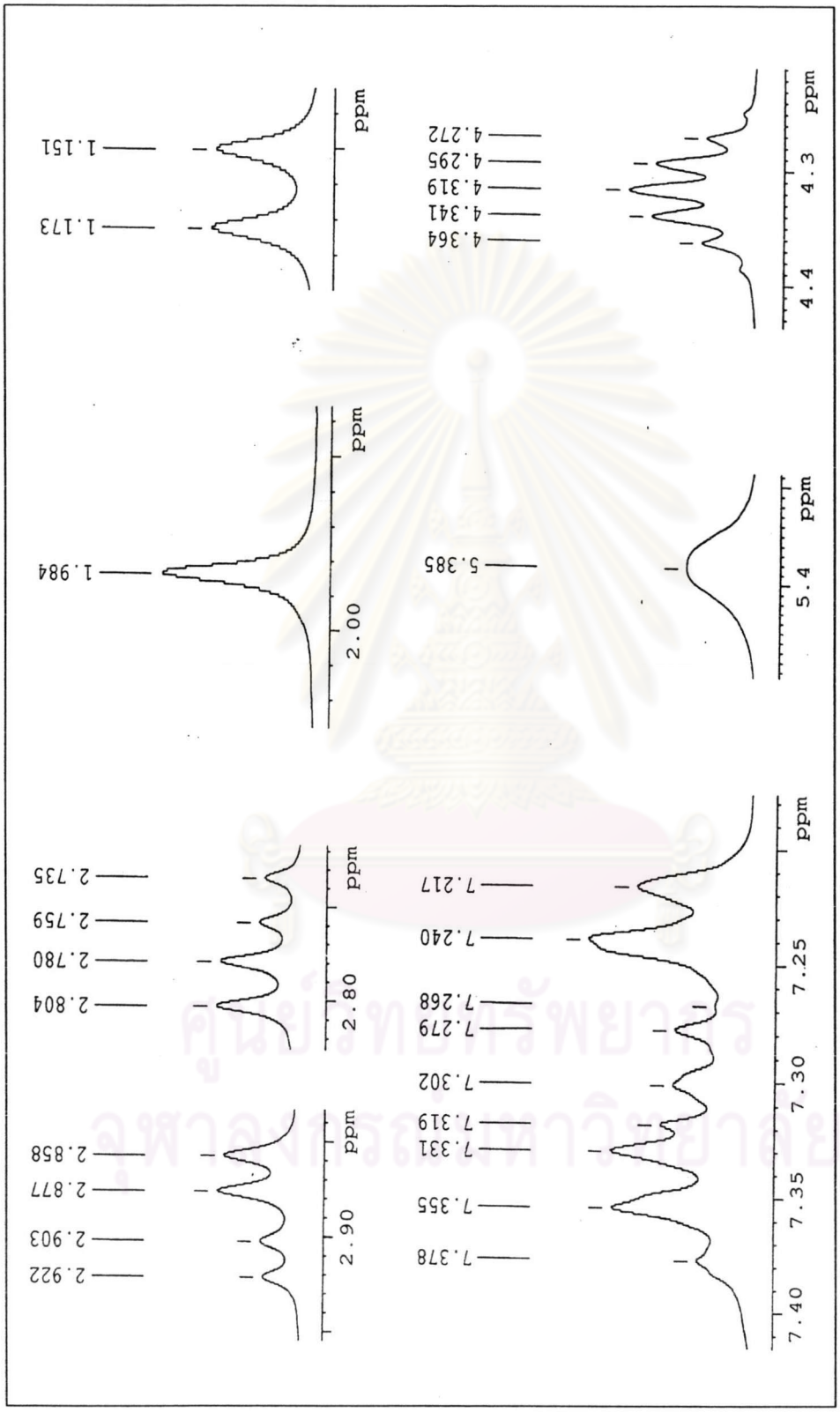


Figure 52. The 300 MHz ^{1}H-NMR spectrum of *N*-acetylamphetamine in $CDCl_3$. (Enlarged-scale)

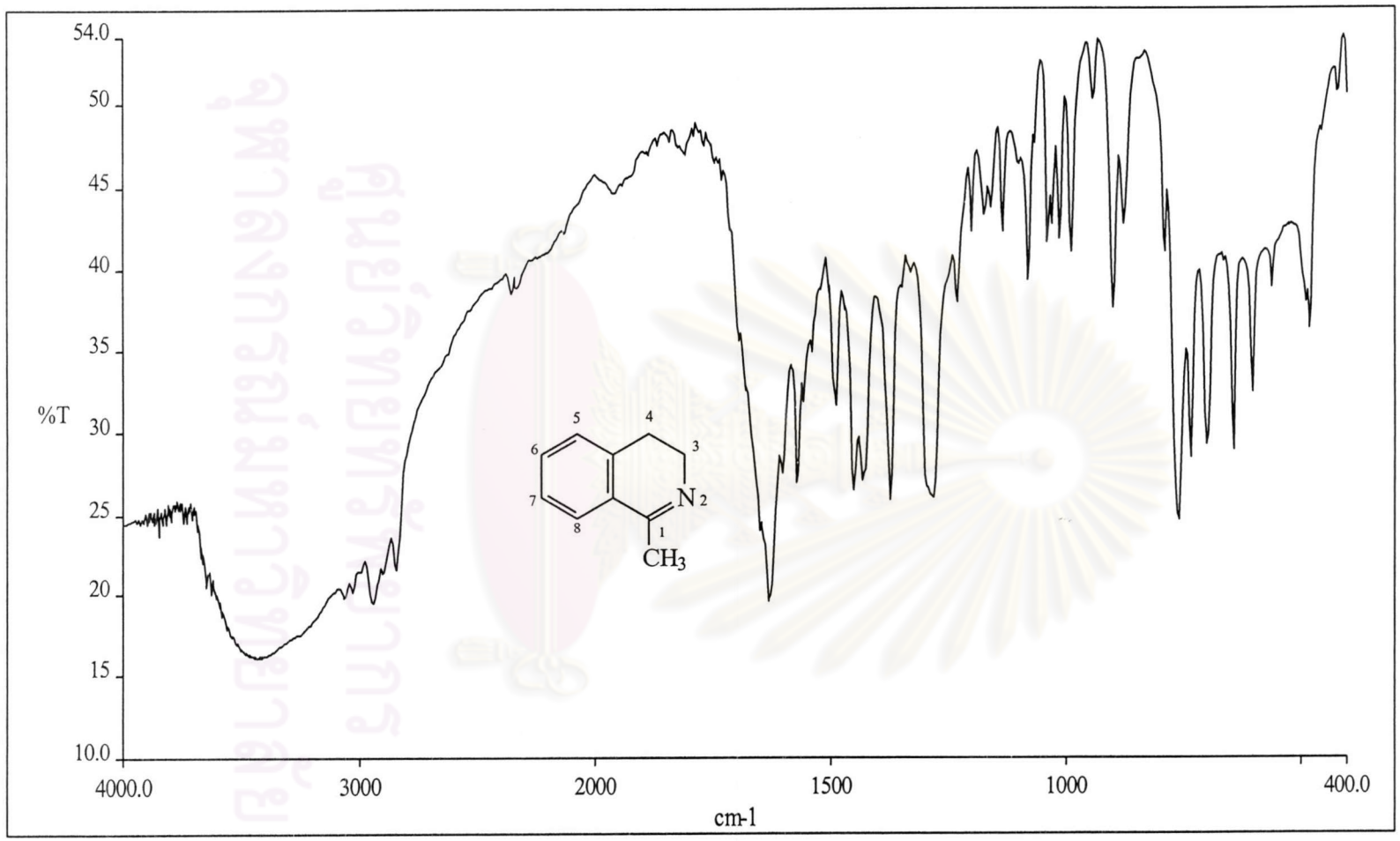


Figure 53. The IR spectrum (Neat) of 3,4-dihydro-1-methylisoquinoline

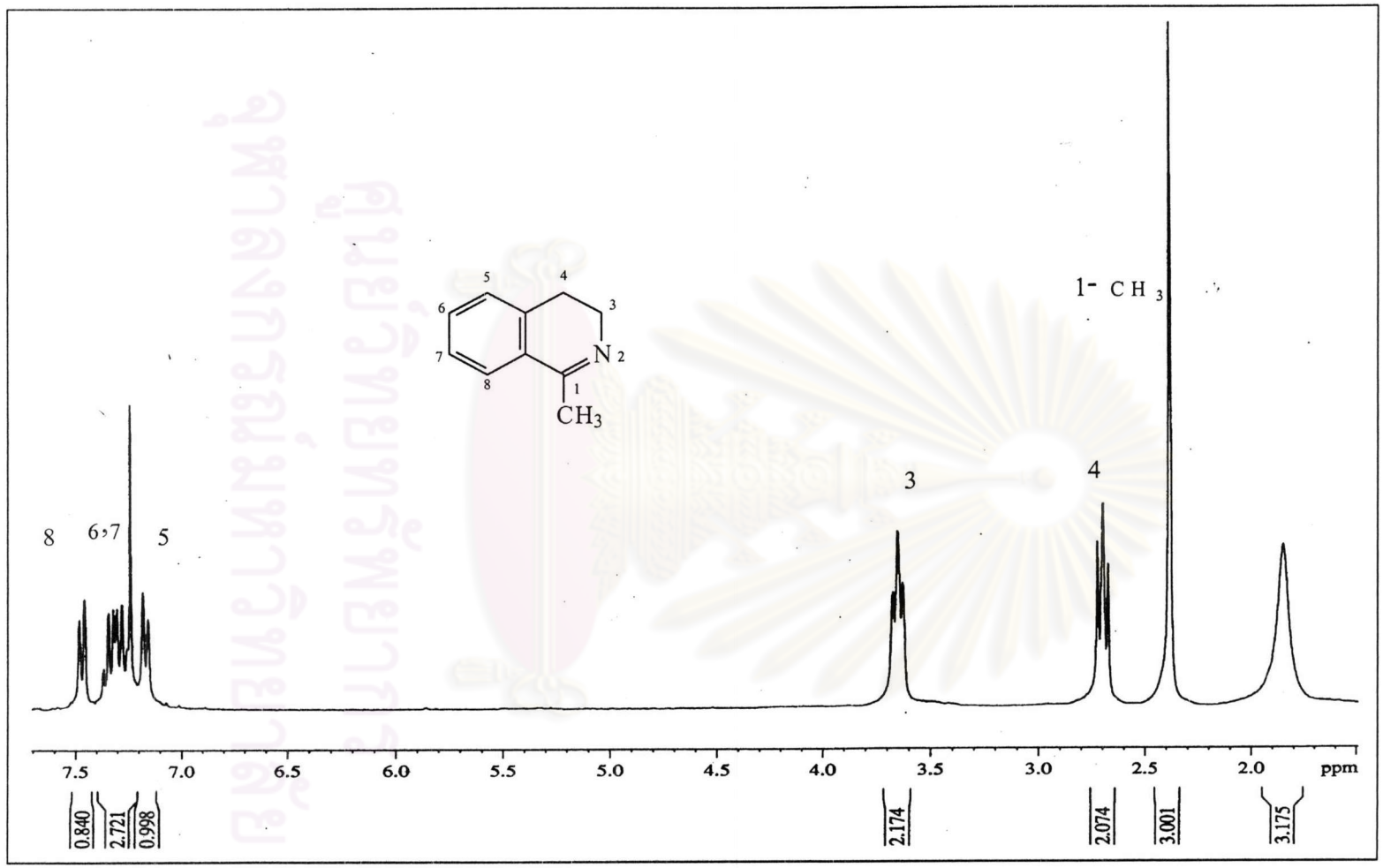


Figure 54. The 300 MHz ^{1}H-NMR spectrum of 3,4-dihydro-1-methylisoquinoline in $CDCl_3$

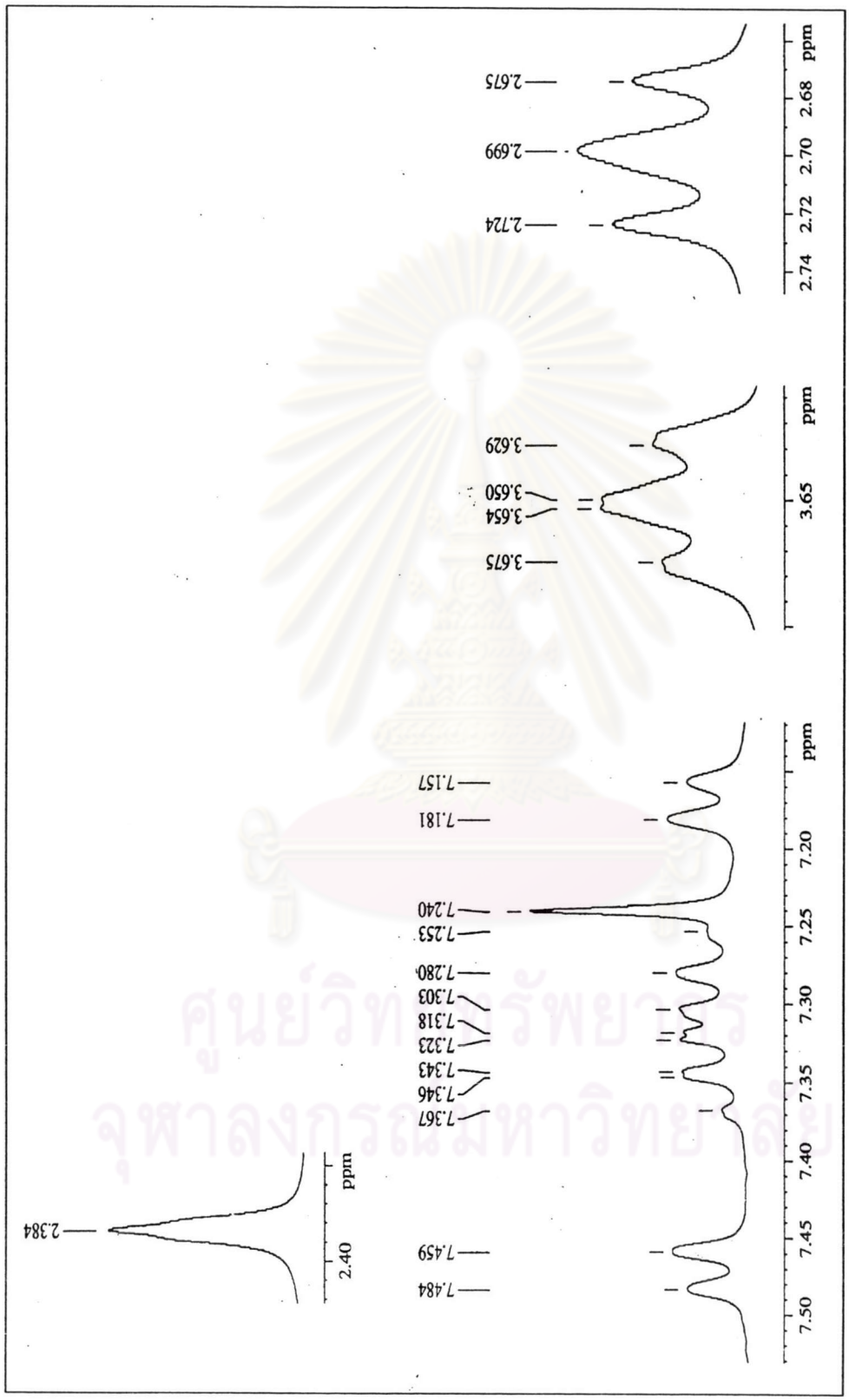


Figure 55. The 300 MHz ^{1}H-NMR spectrum of 3,4-dihydro-1-methylisoquinoline in $CDCl_3$ (Enlarged-scale)

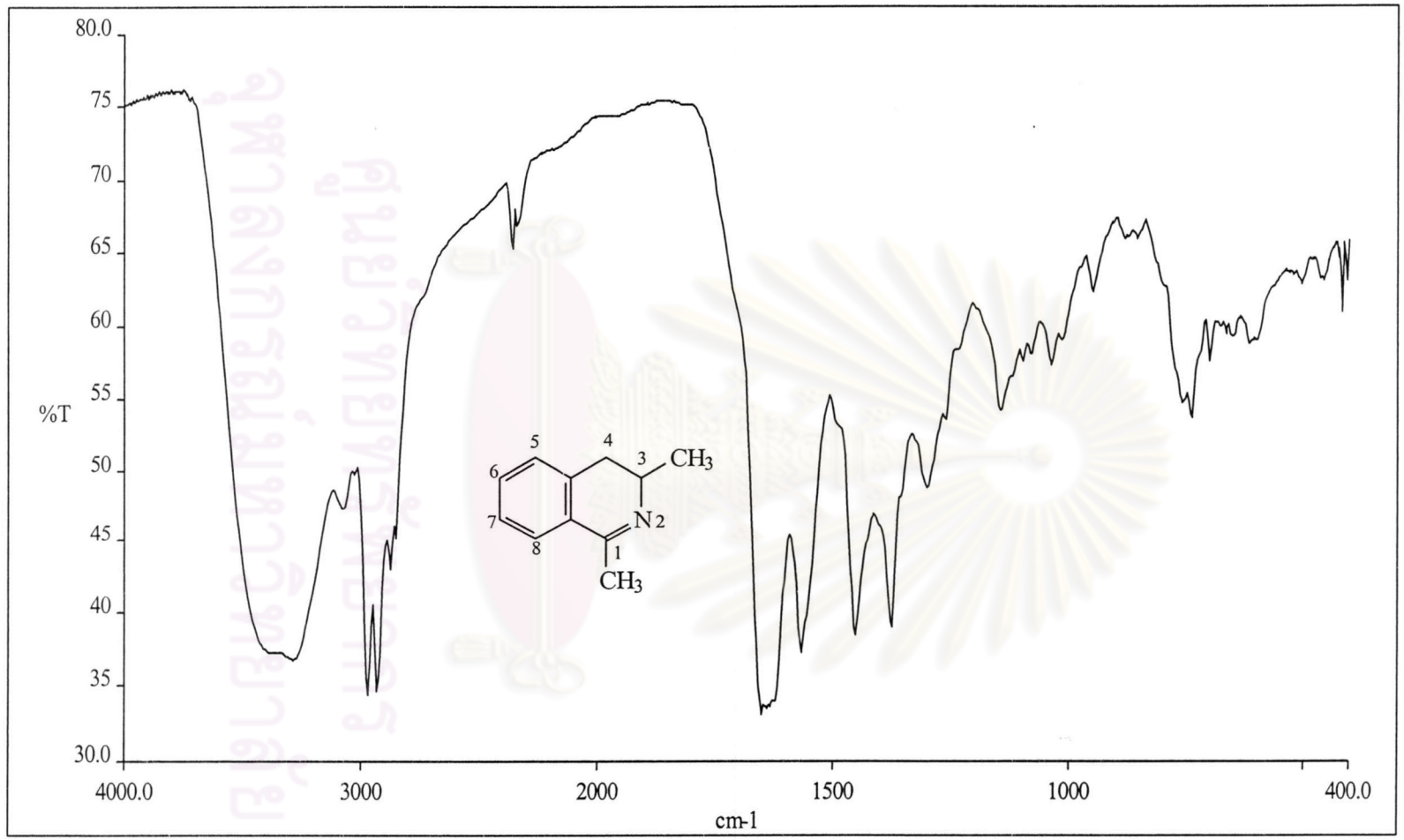


Figure 56. The IR spectrum (Neat) of 3,4-dimethyl-1,3-dimethylisoquinoline

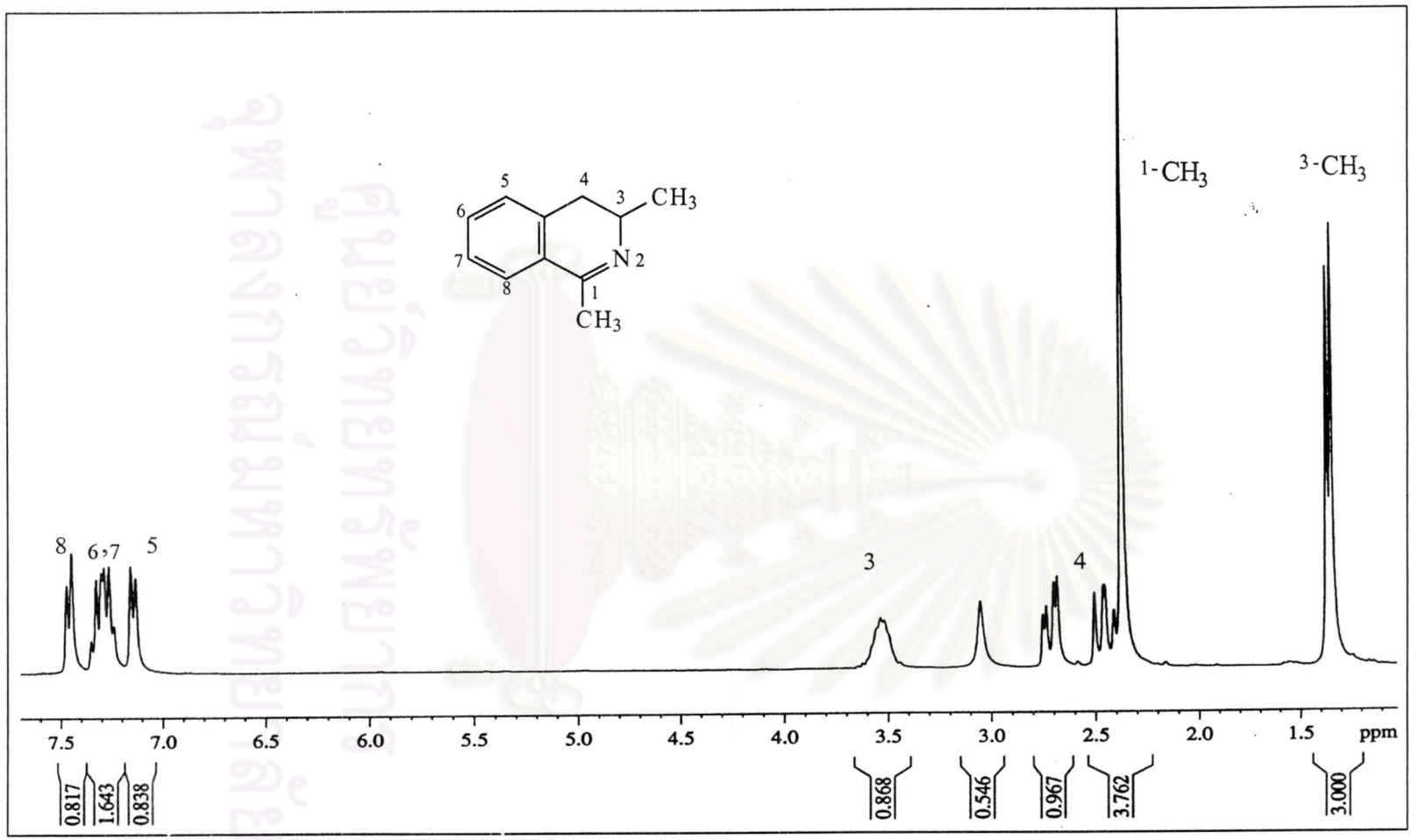


Figure 57. The 300 ^{1}H-NMR spectrum of 3,4-dihydro-1,3-dimethylisoquinoline in $CDCl_3$

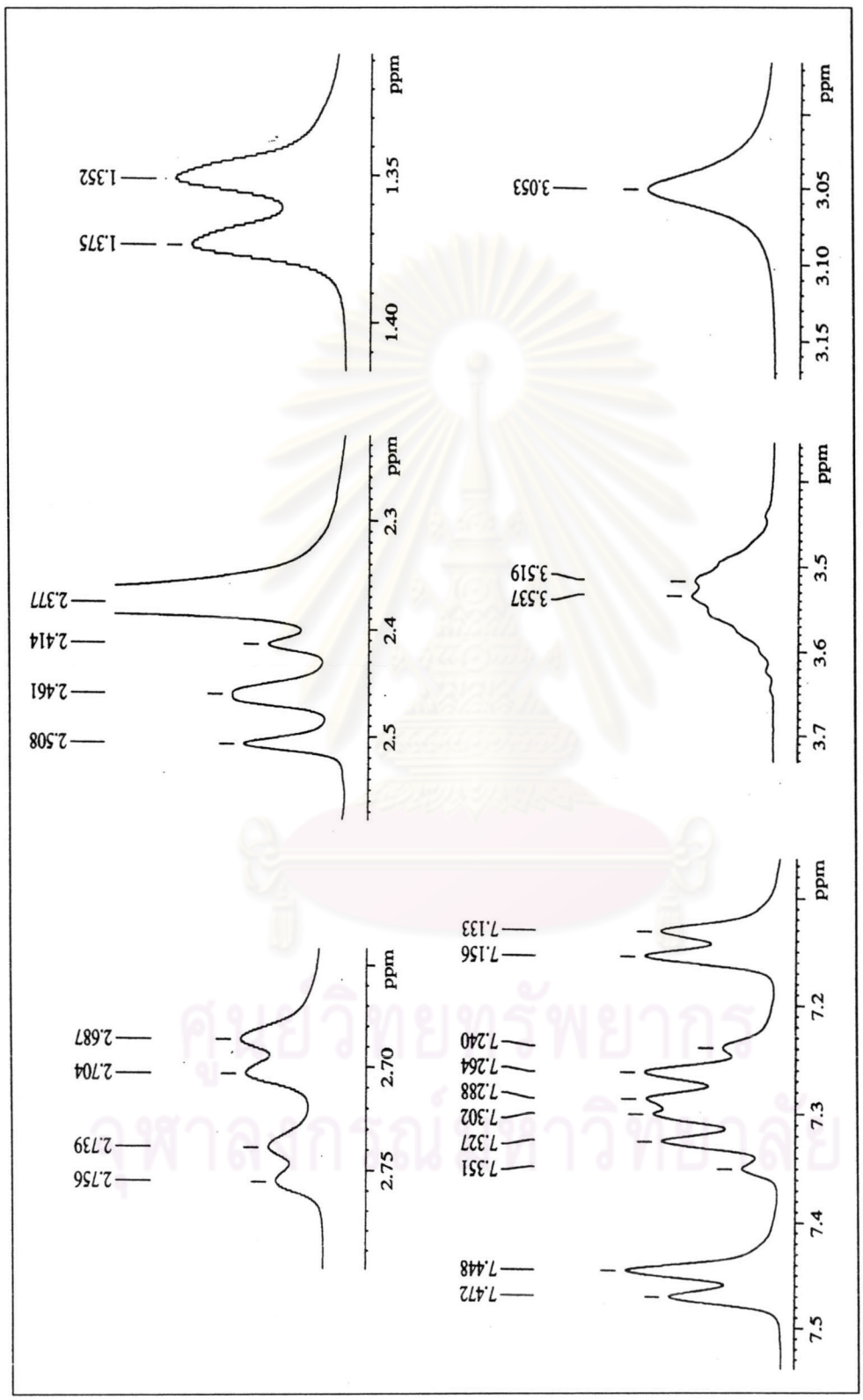


Figure 58. The 300 ^{1}H-NMR spectrum of 3,4-dihydro-1,3-dimethylisoquinoline in $CDCl_3$ (Enlarged-scale)

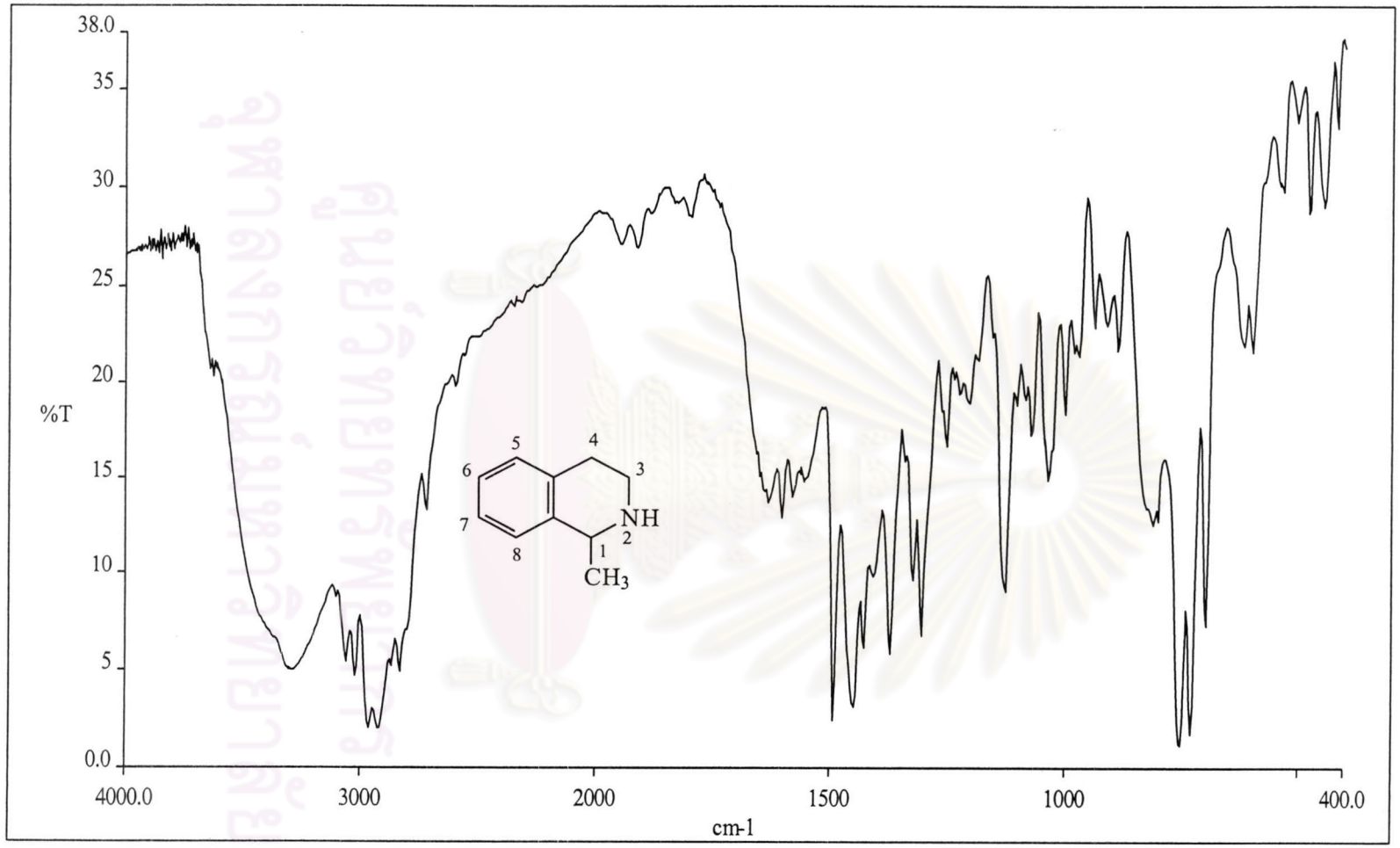


Figure 59. The IR spectrum (Neat) of 1,2,3,4-tetrahydro-1-methylisoquinoline

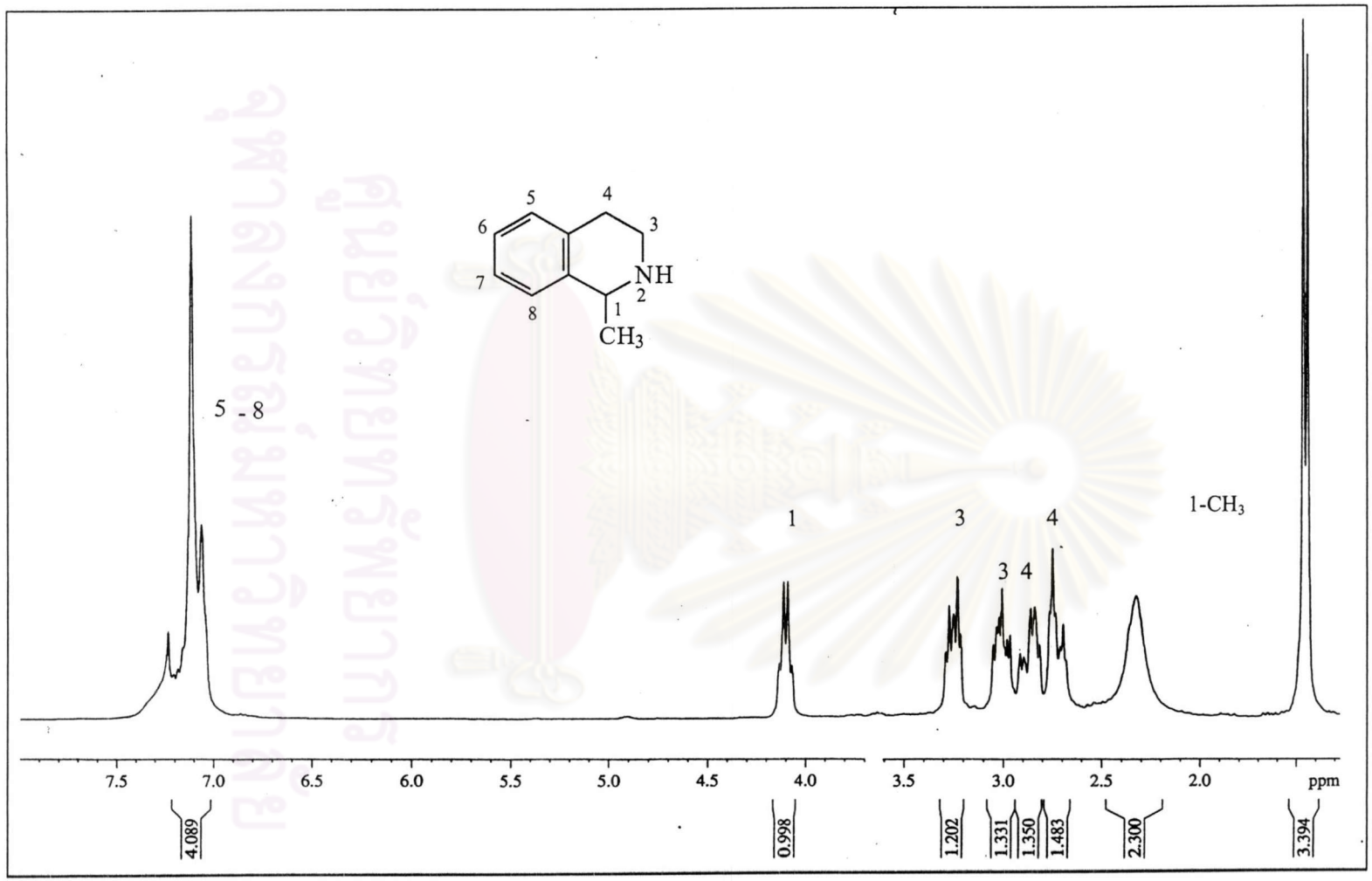


Figure 60. The 300 MHz ^{1}H-NMR spectrum of 1,2,3,4-tetrahydro-1-methylisoquinoline in $CDCl_3$

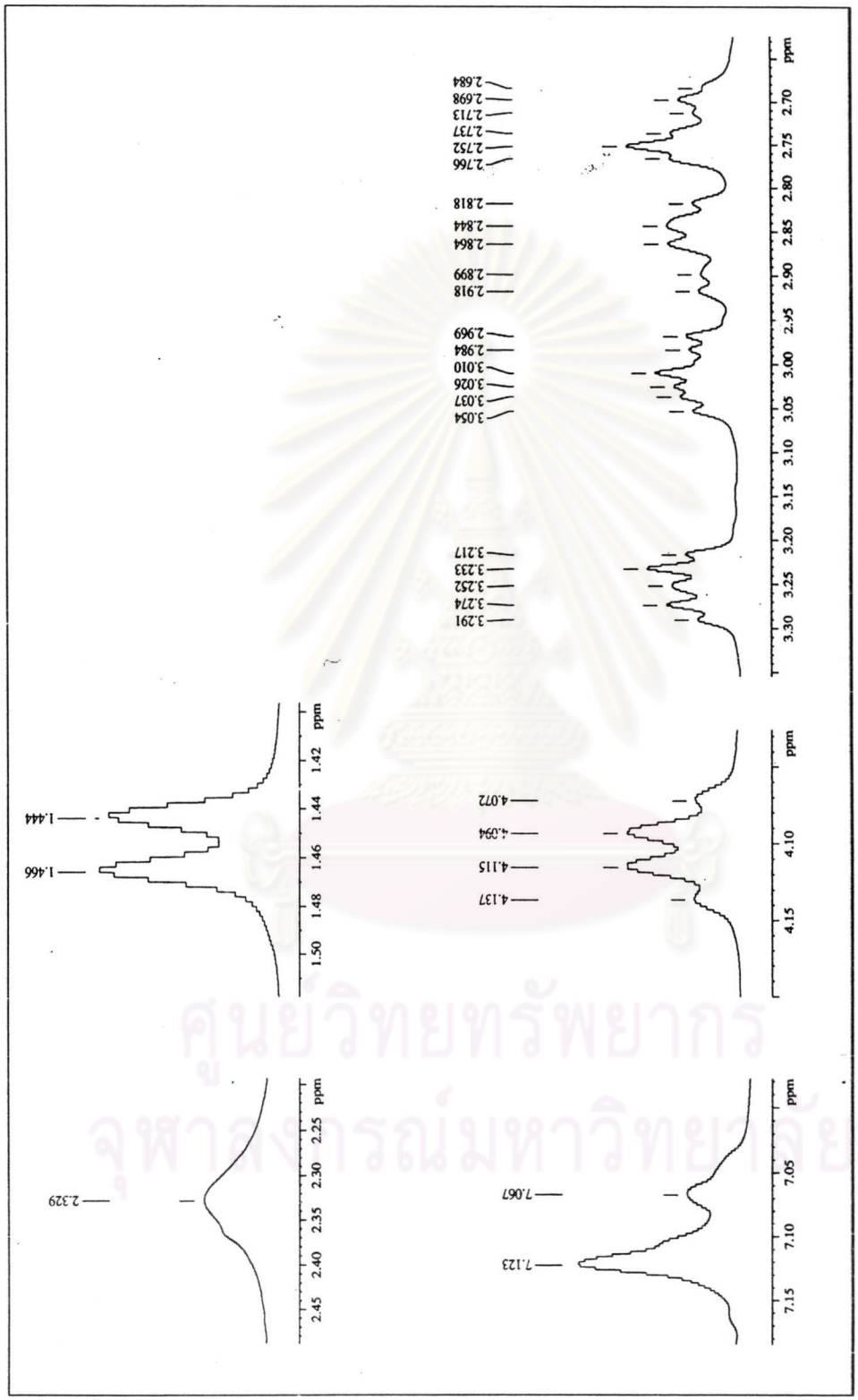


Figure 61. The 300 MHz ^{1}H-NMR spectrum of 1-methyl-1,2,3,4-tetrahydroisoquinoline in $CDCl_3$ (Enlarged-scale)

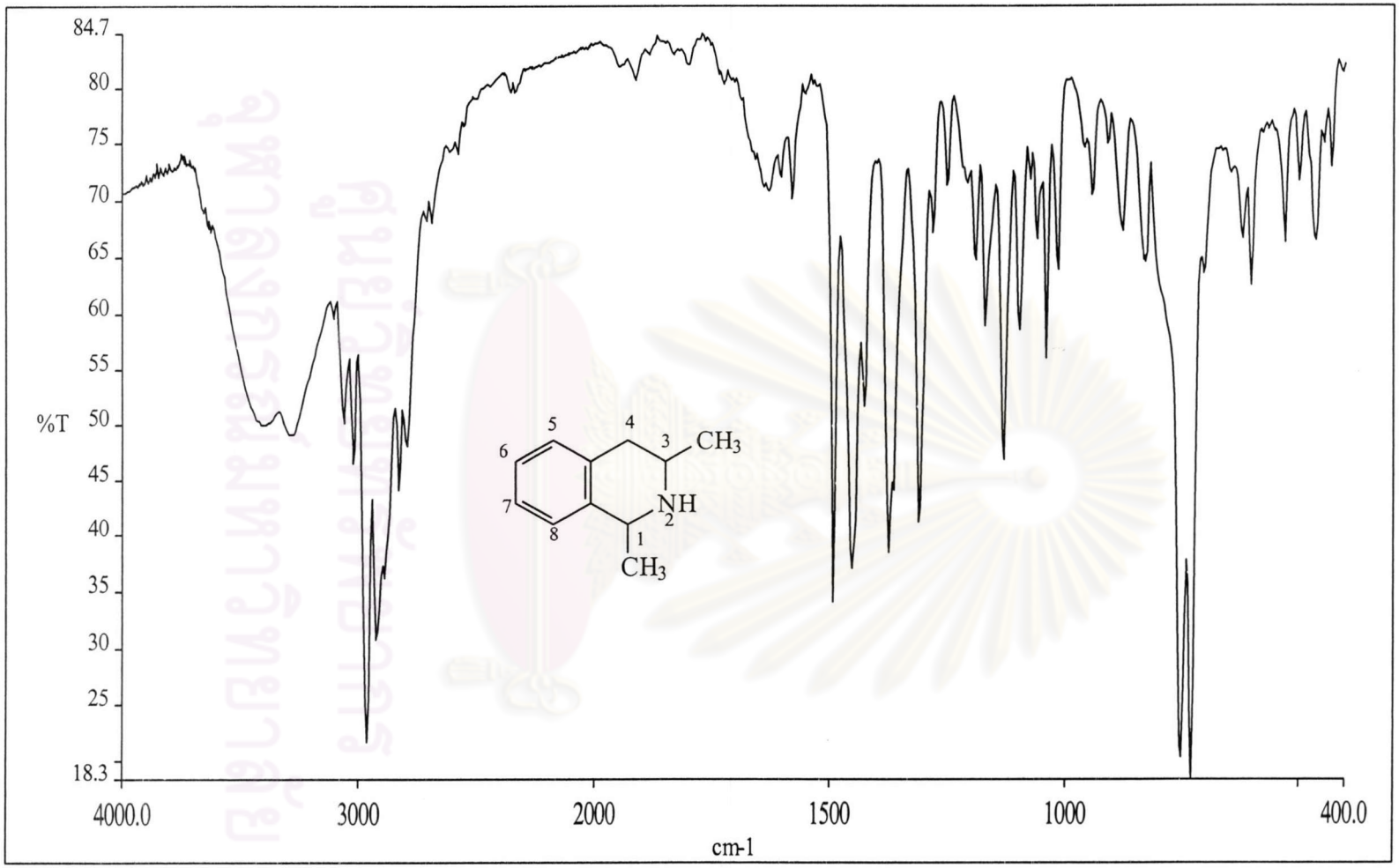


Figure 62. The IR spectrum (Neat) of 1,2,3,4-tetrahydro-1,3-dimethylisoquinoline

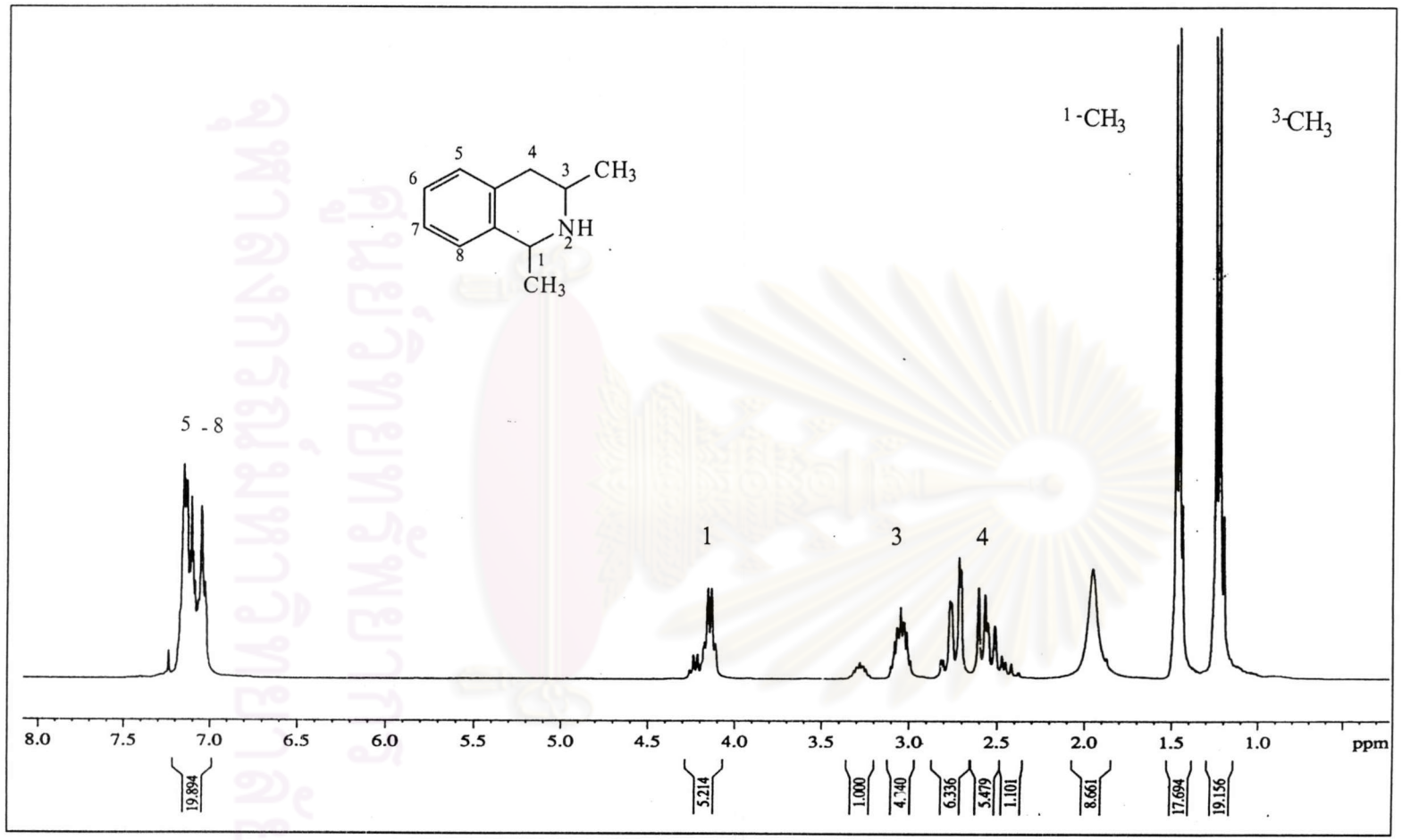


Figure 63. The 300 MHz ^{1}H-NMR spectrum of 1,2,3,4-tetrahydro-1,3-dimethyl-isoquinoline in $CDCl_3$

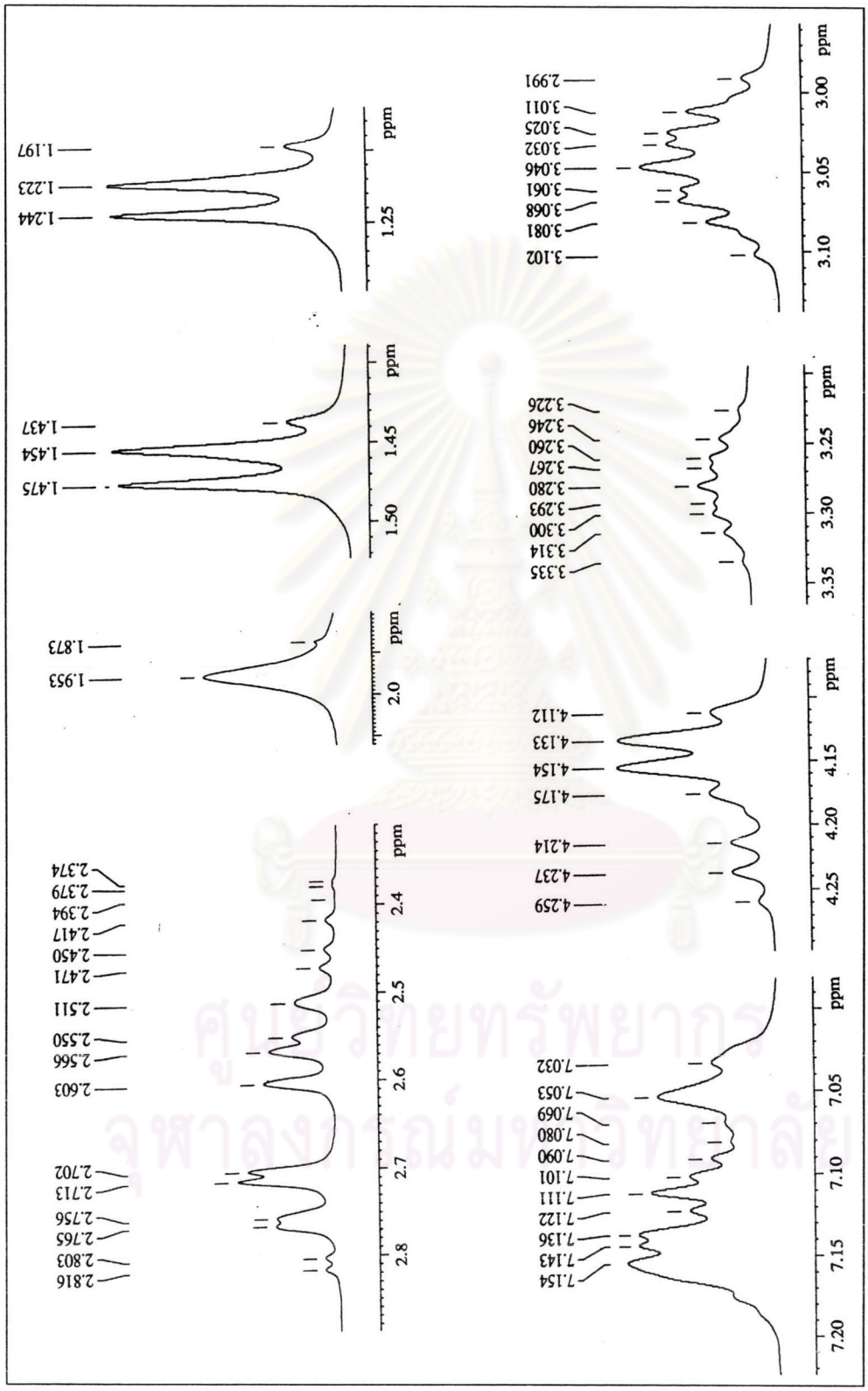


Figure 64. The 300 MHz ^{1}H-NMR spectrum of 1,2,3,4-tetrahydro-1,3-dimethyl-isoquinoline in $CDCl_3$ (Enlarged-scale)

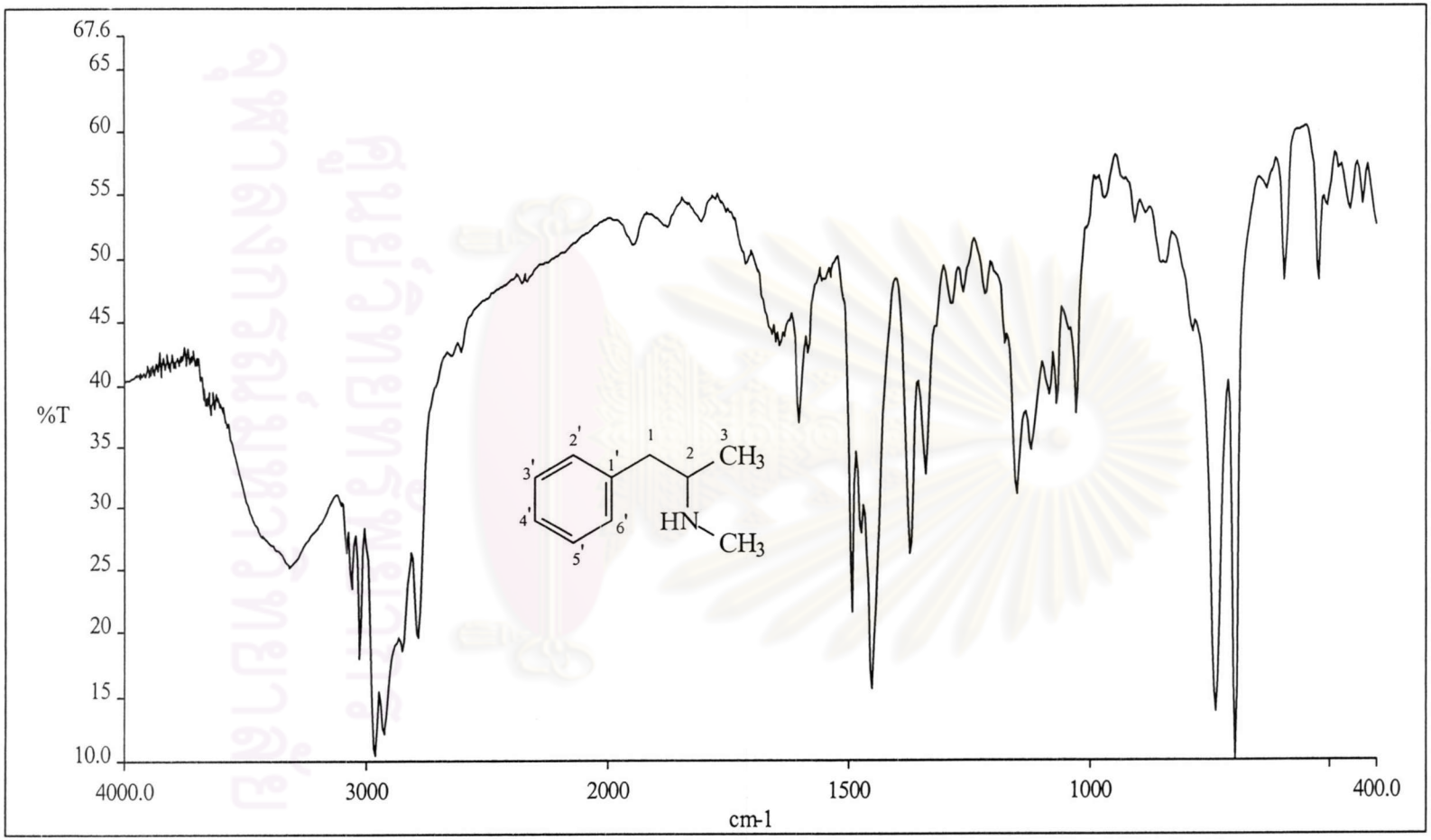


Figure 65. The IR spectrum (Neat) of *N*-methylamphetamine in $CDCl_3$

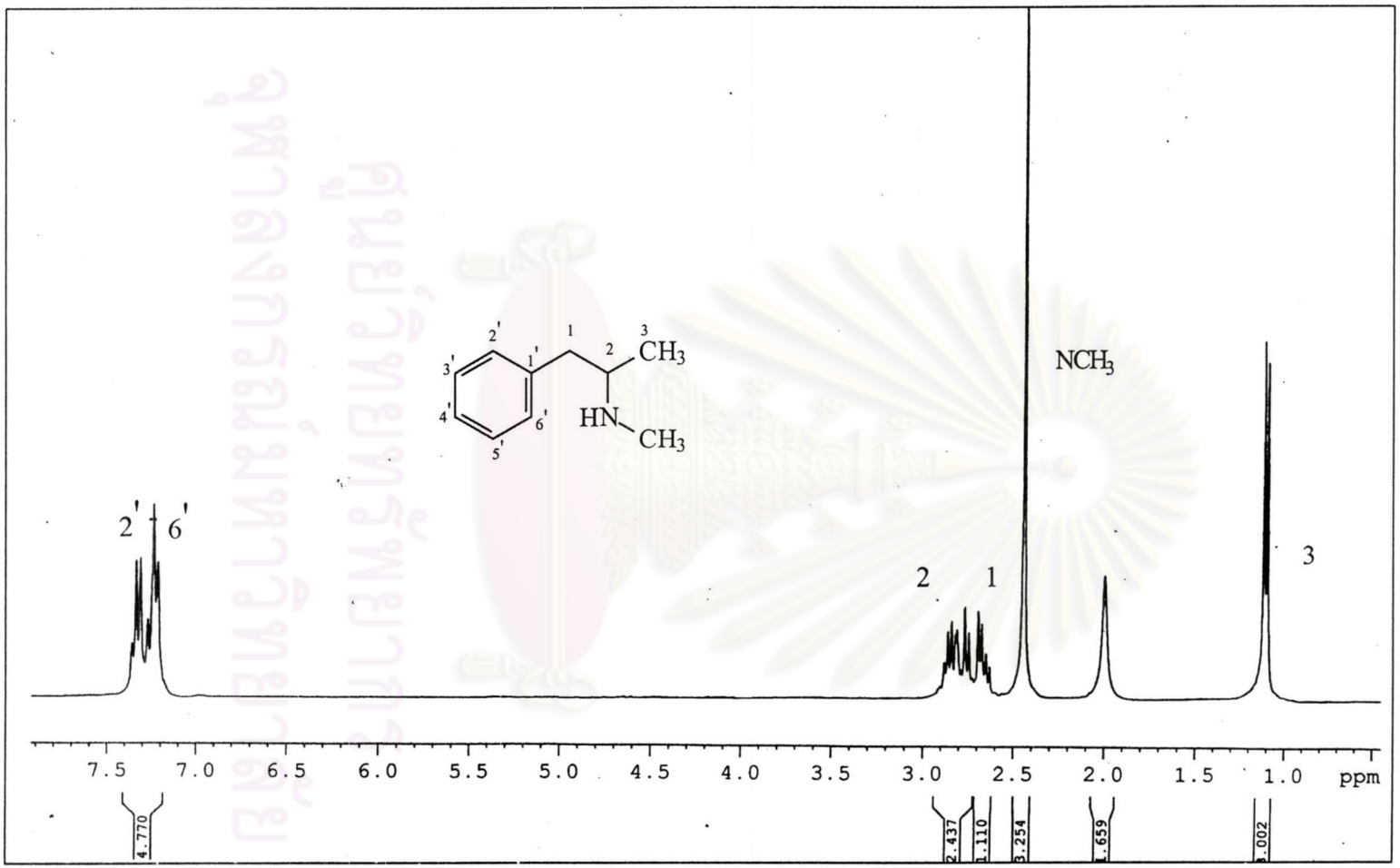


Figure 66. The 300 MHz ^{1}H-NMR spectrum of *N*-methylamphetamine in $CDCl_3$

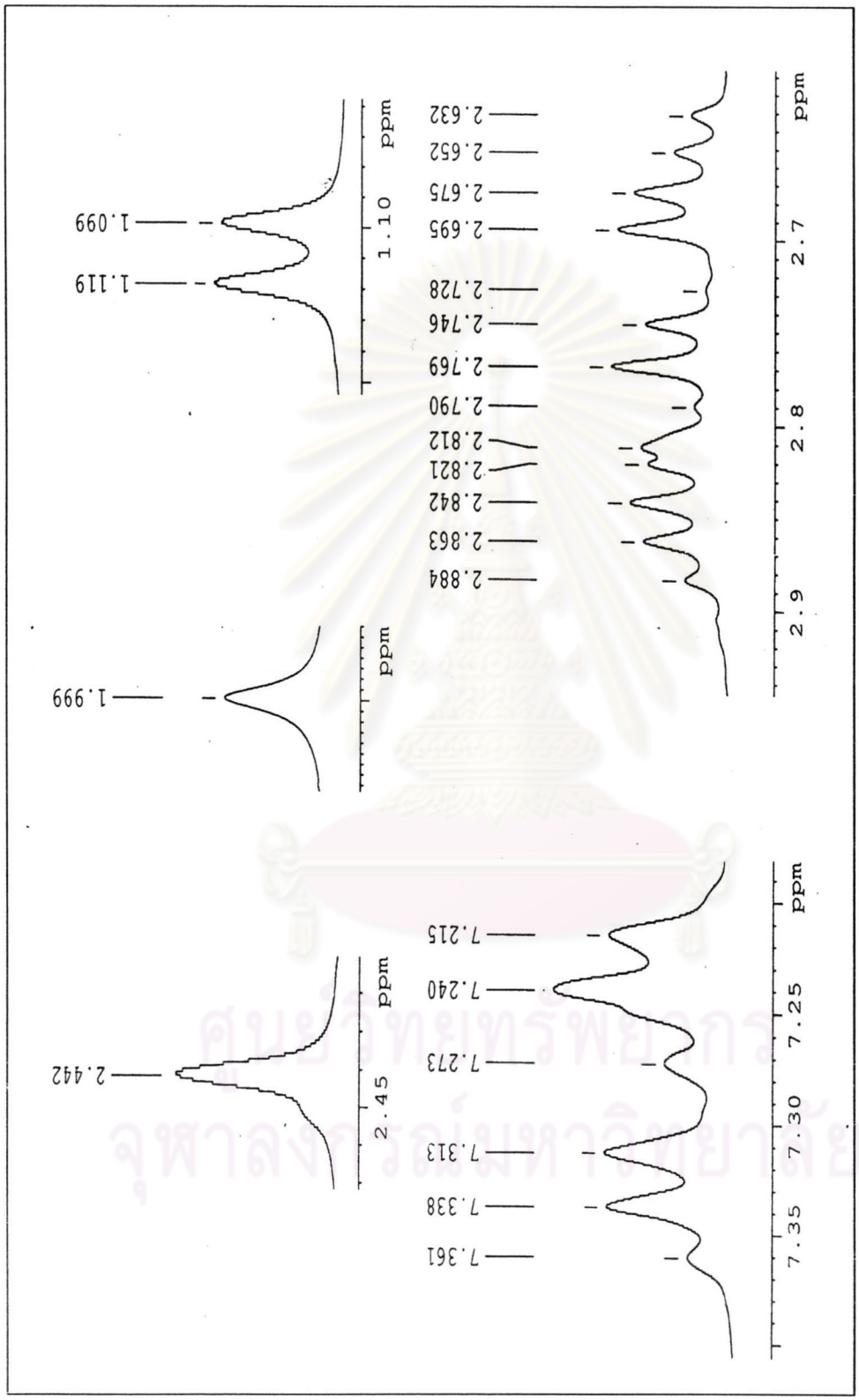


Figure 67. The 300 MHz ^{1}H-NMR spectrum of *N*-methylamphetamine in $CDCl_3$ (Enlarged-scale)

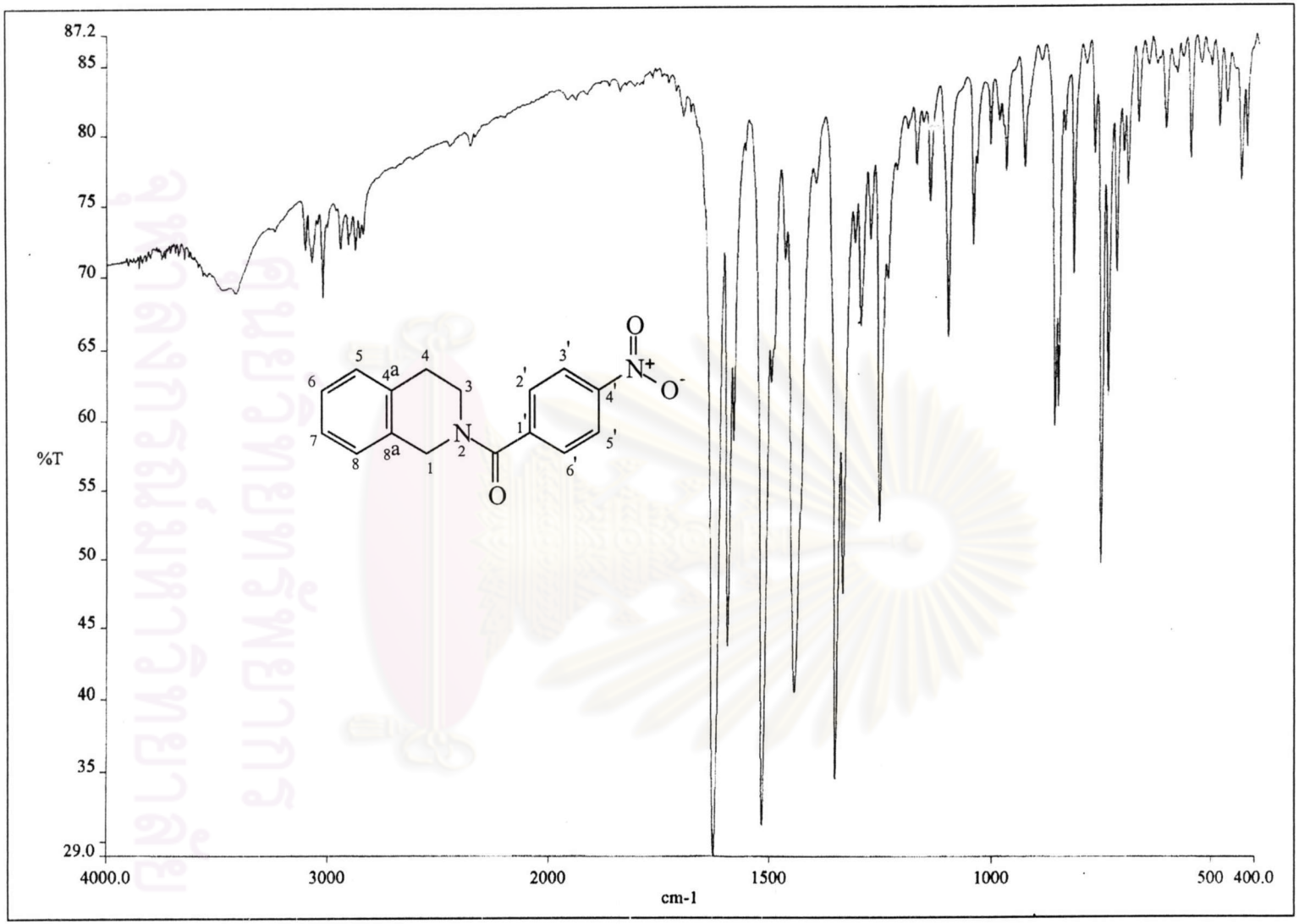


Figure 68. The IR spectrum (KBr) of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline

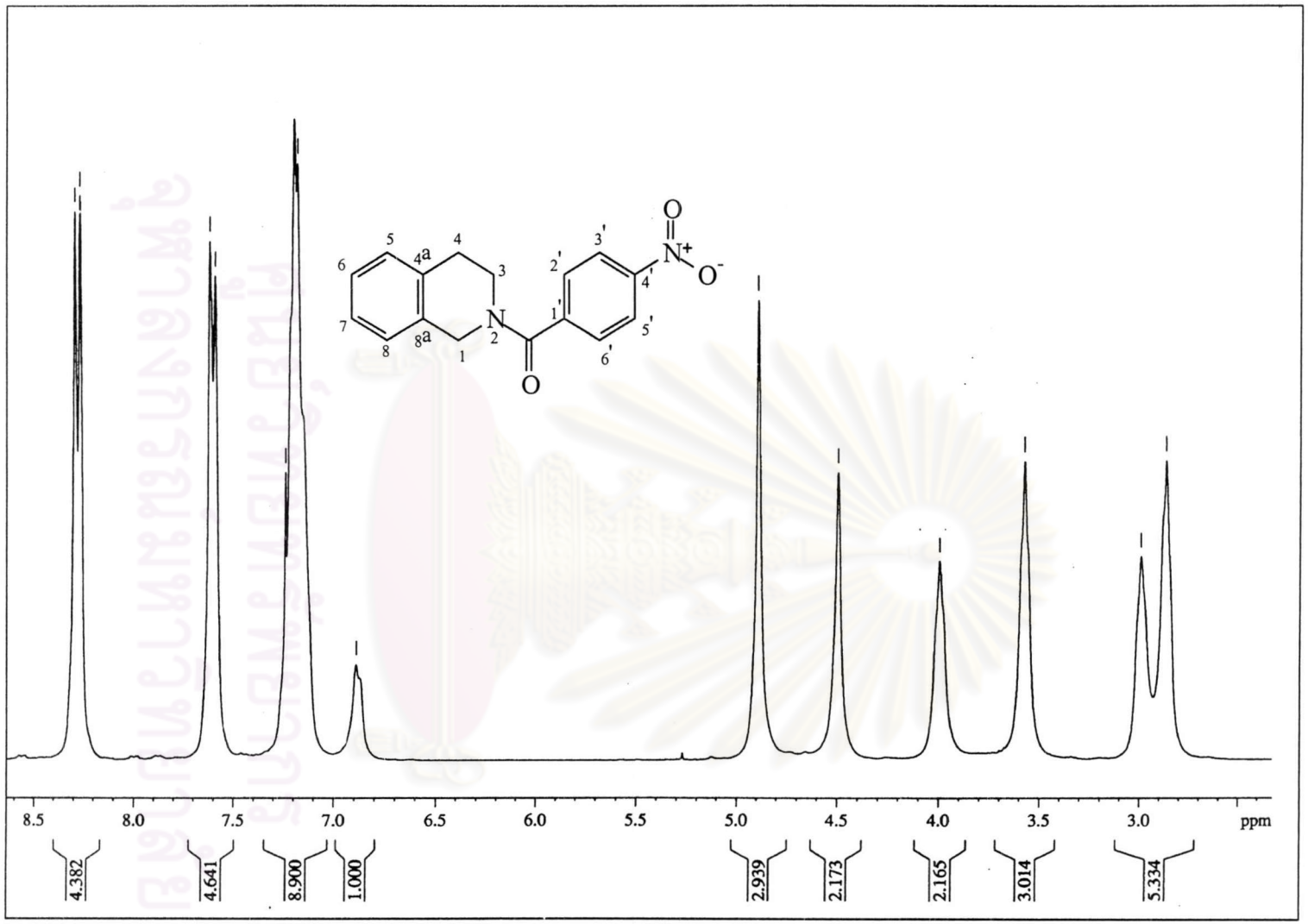


Figure 69. The 300 MHz ^{1}H-NMR spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in $CDCl_3$

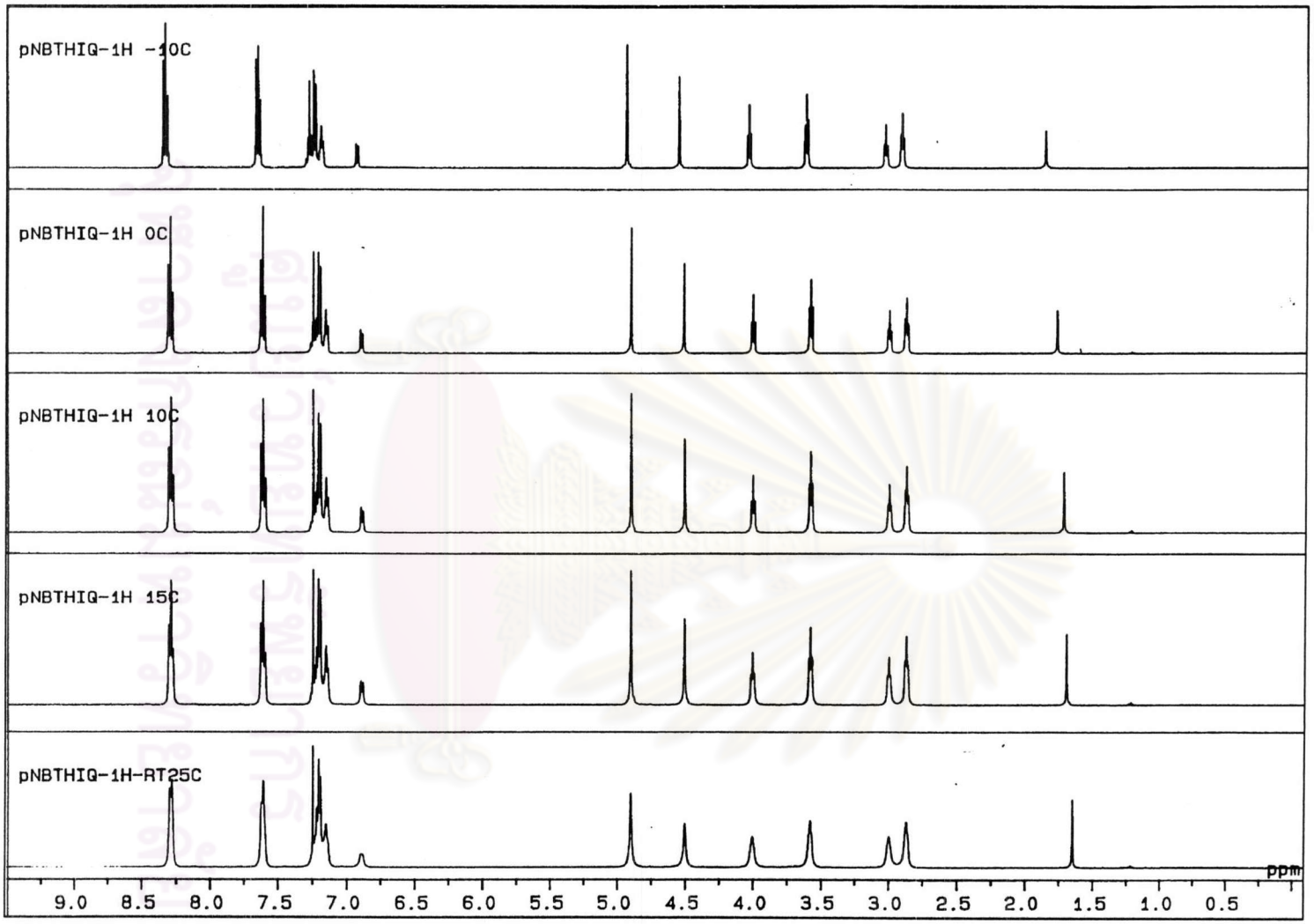


Figure 70. The 500 MHz ^{1}H-NMR spectra of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in $CDCl_3$, at room temperature (RT), 15 °C, 10 °C, 0 °C and -10 °C

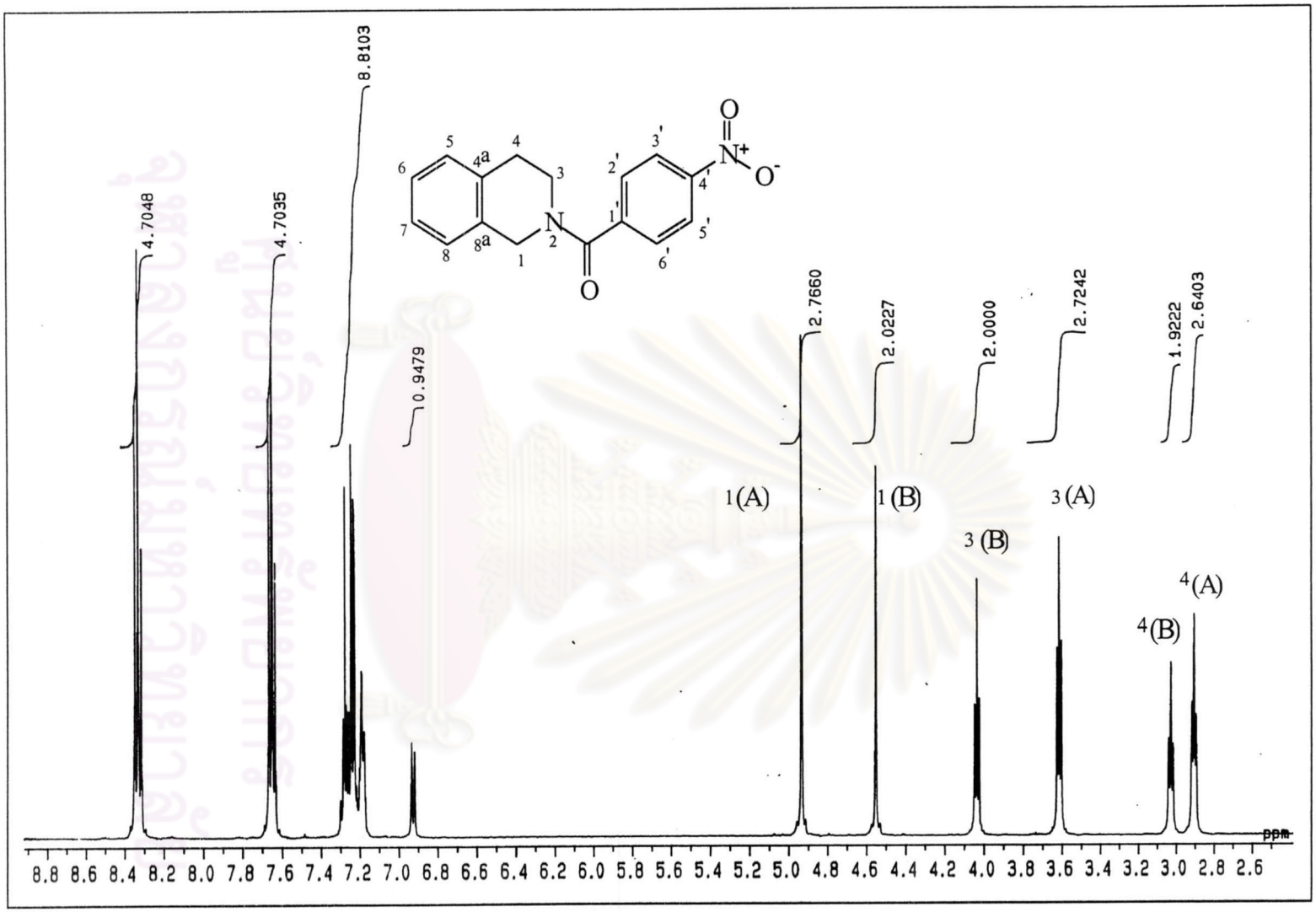


Figure 71. The 500 MHz ^{1}H-NMR of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in $CDCl_3$ at -10 °C.

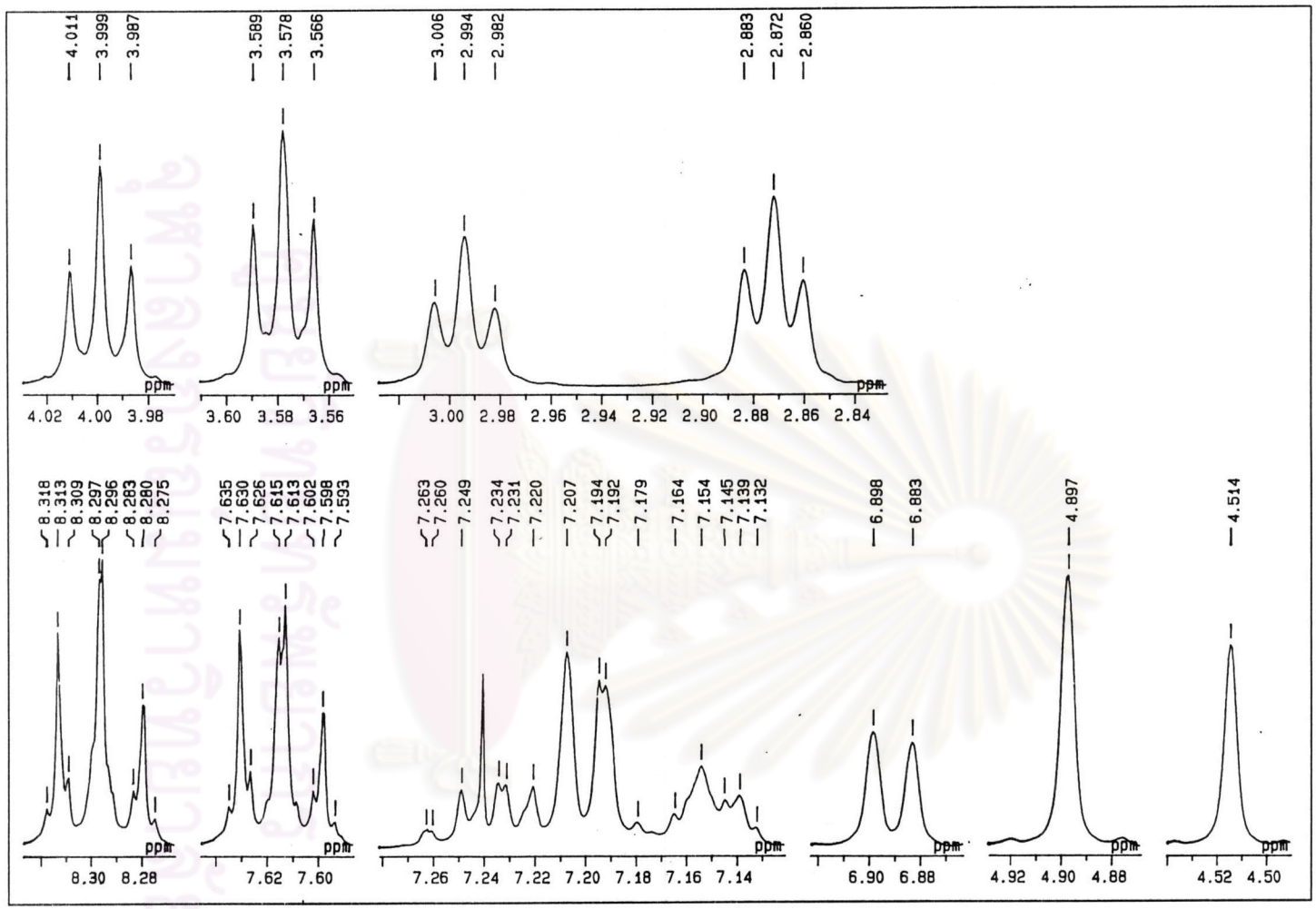


Figure 72. The 500 MHz ^{1}H-NMR spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in CDCl3 at -10°C.

(Enlarged- scale)

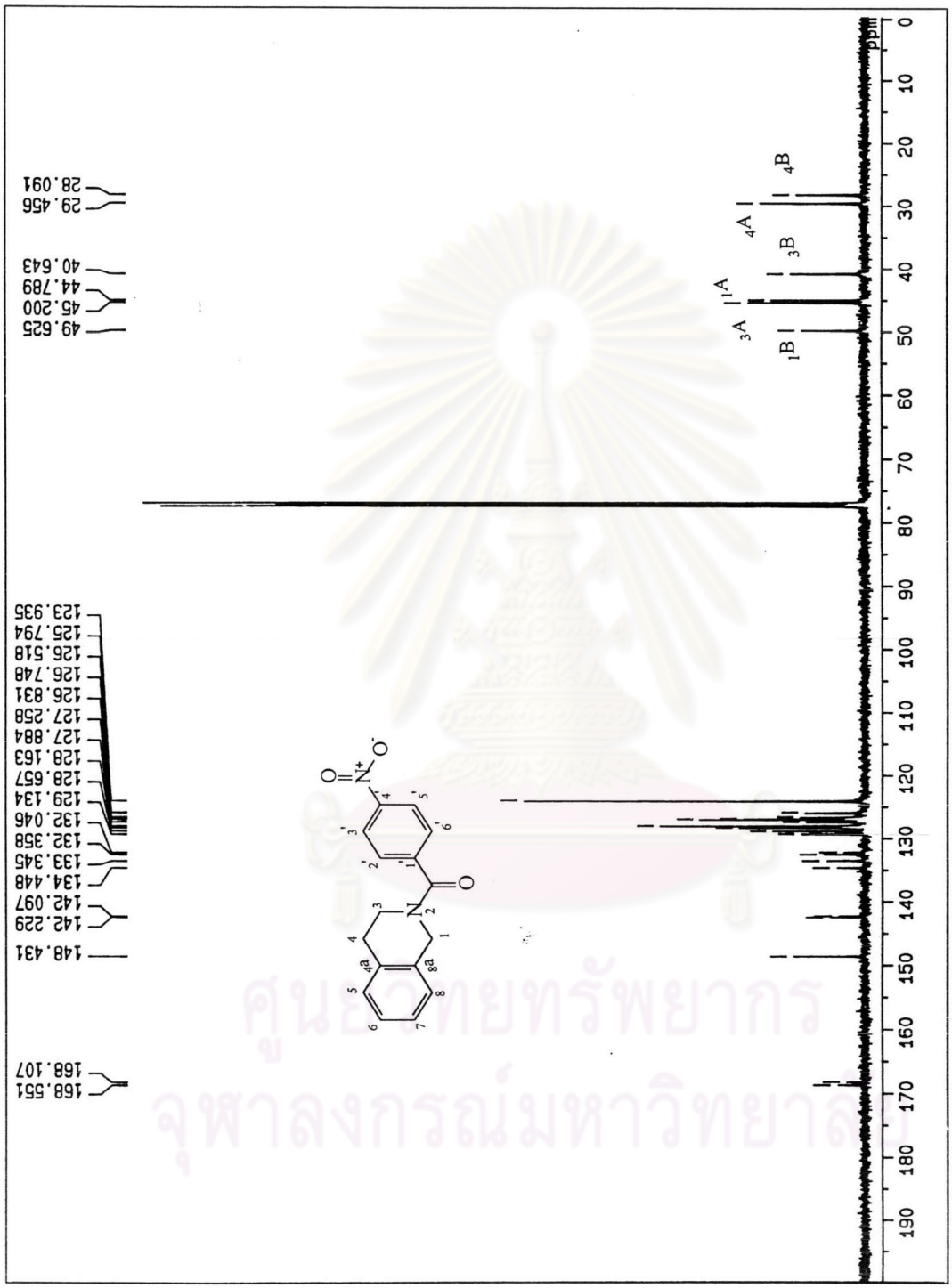


Figure 73. The 125 MHz ^{13}C-NMR of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in $CDCl_3$.

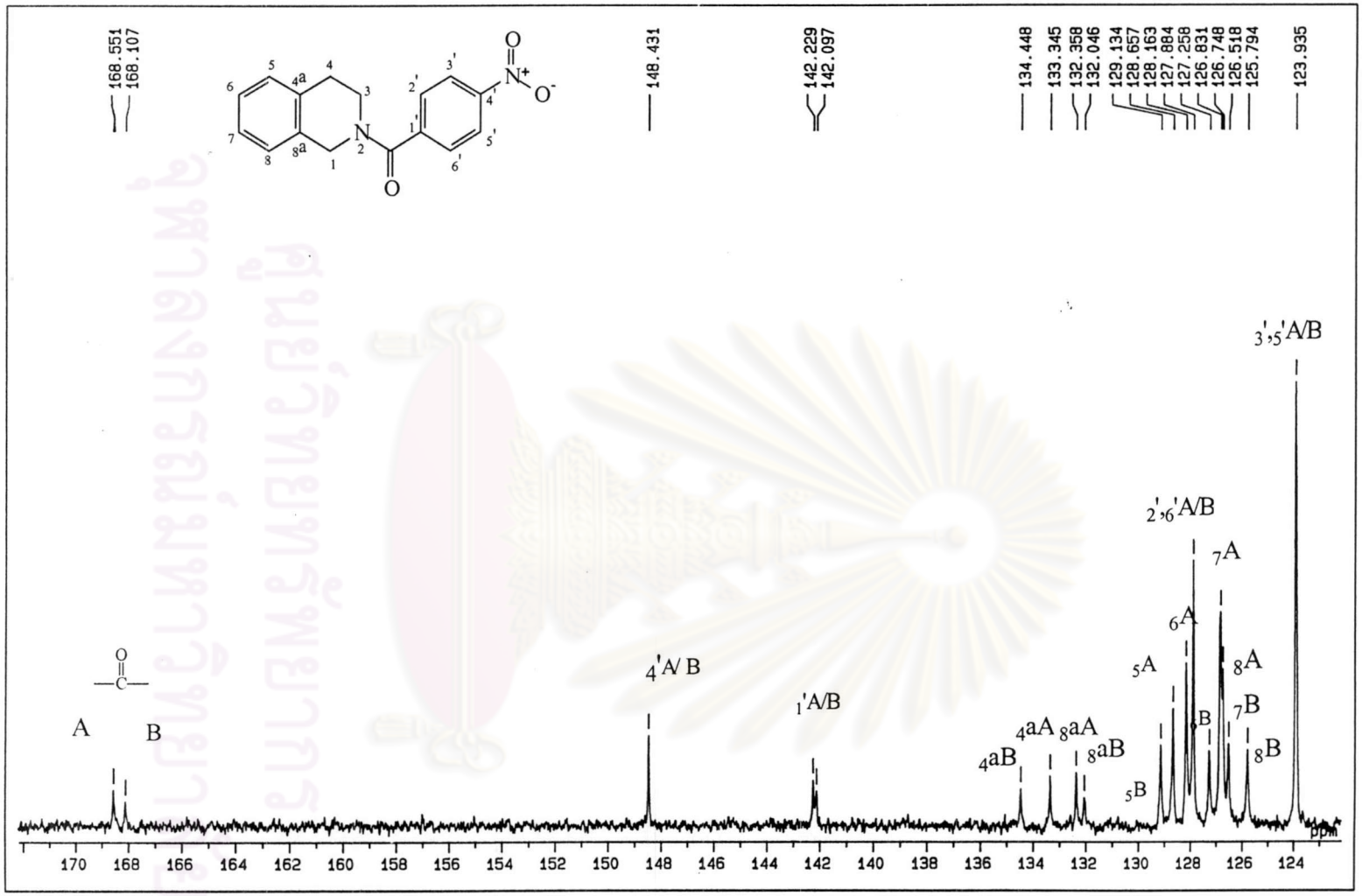


Figure 74. The 125 MHz ^{13}C-NMR of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in $CDCl_3$ (Enlarged-scale in123-170 ppm region)

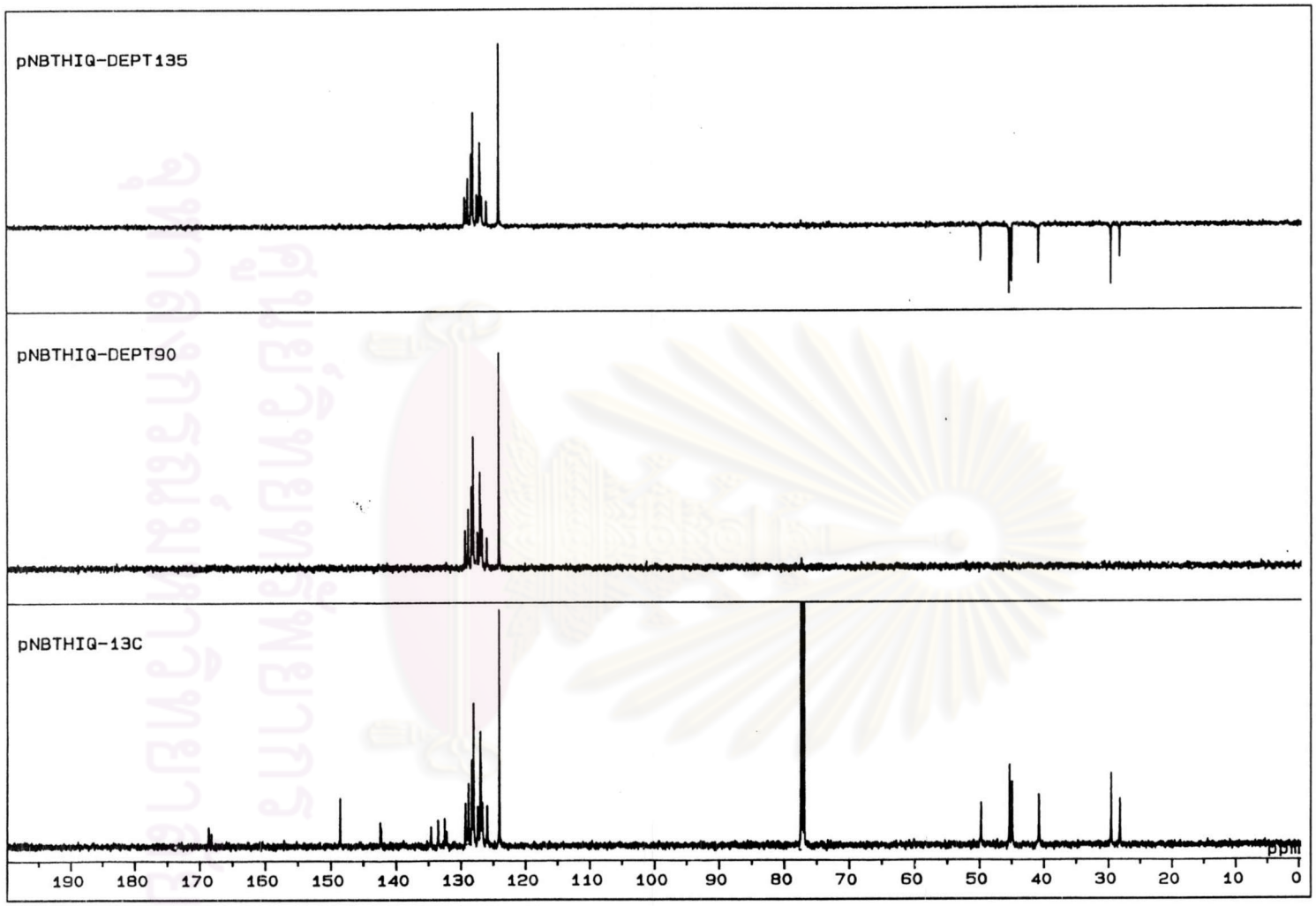


Figure 75. The 125 MHz ^{13}C-NMR, DEPT90 and DEPT135 spectra of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in $CDCl_3$

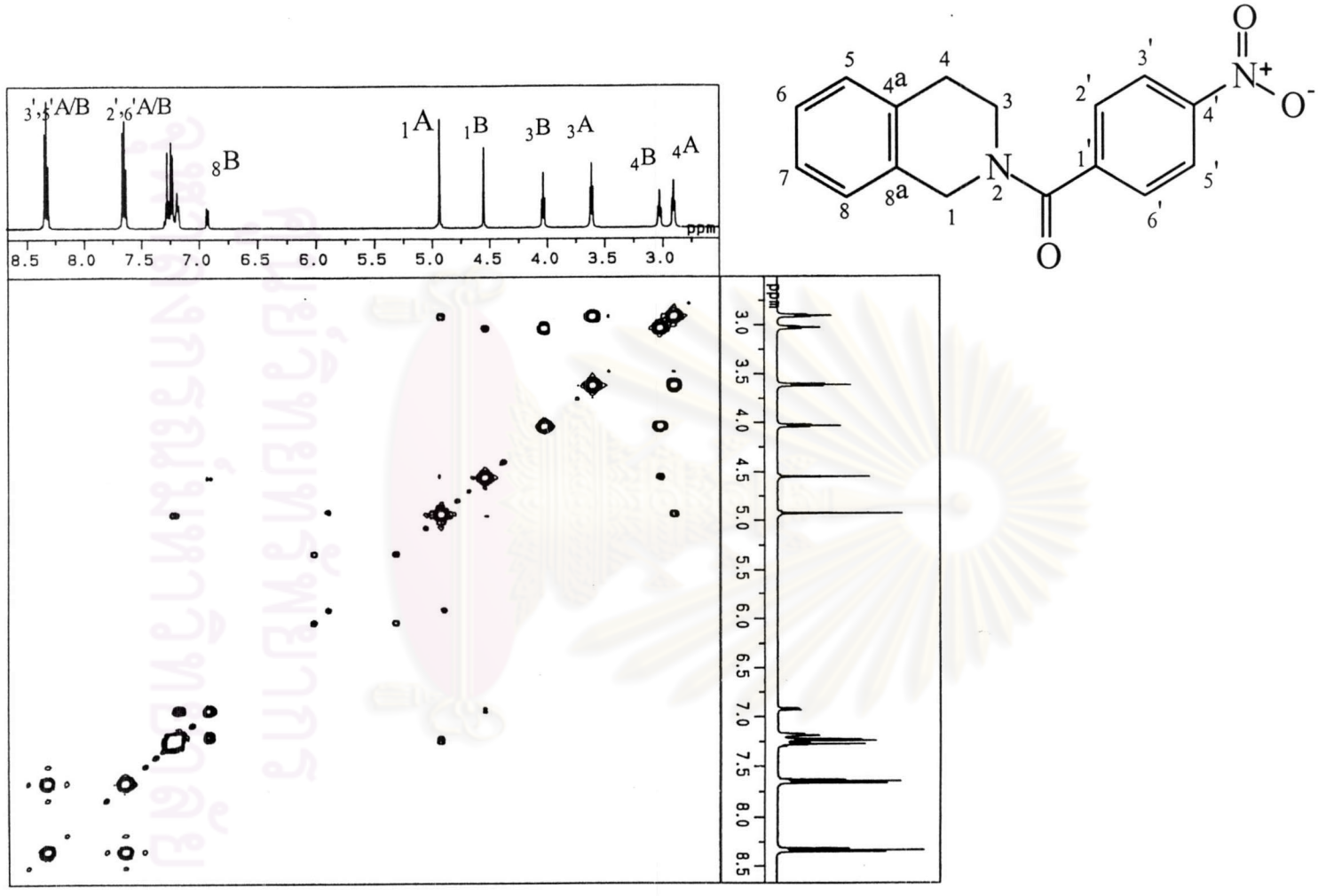


Figure 76. The 500 MHz HH COSY spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in $CDCl_3$ at -10°C

Figure 77. The 500 MHz HMQC spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in $CDCl_3$

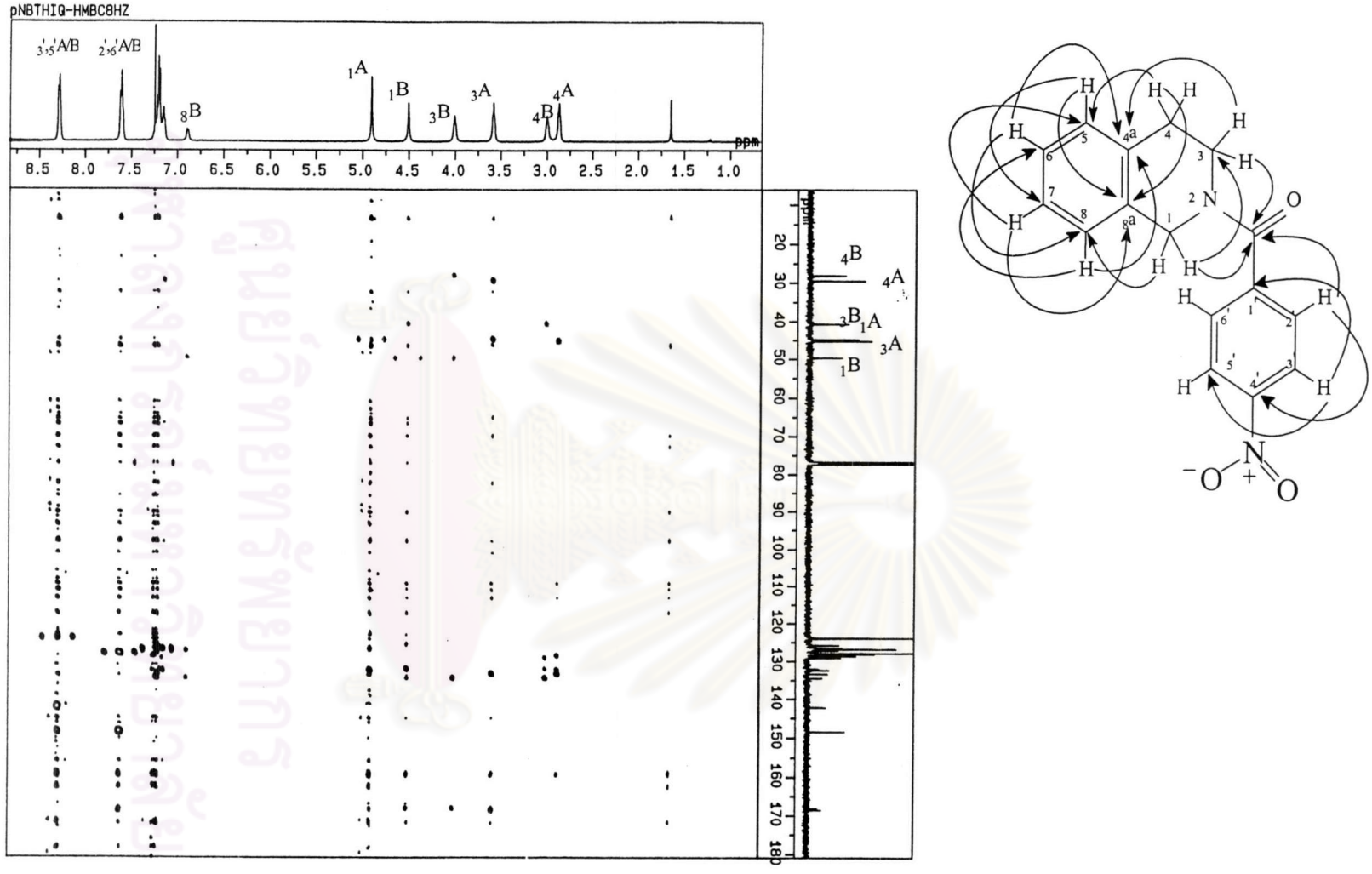


Figure 78. The 500 MHz HMBC spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in $CDCl_3$

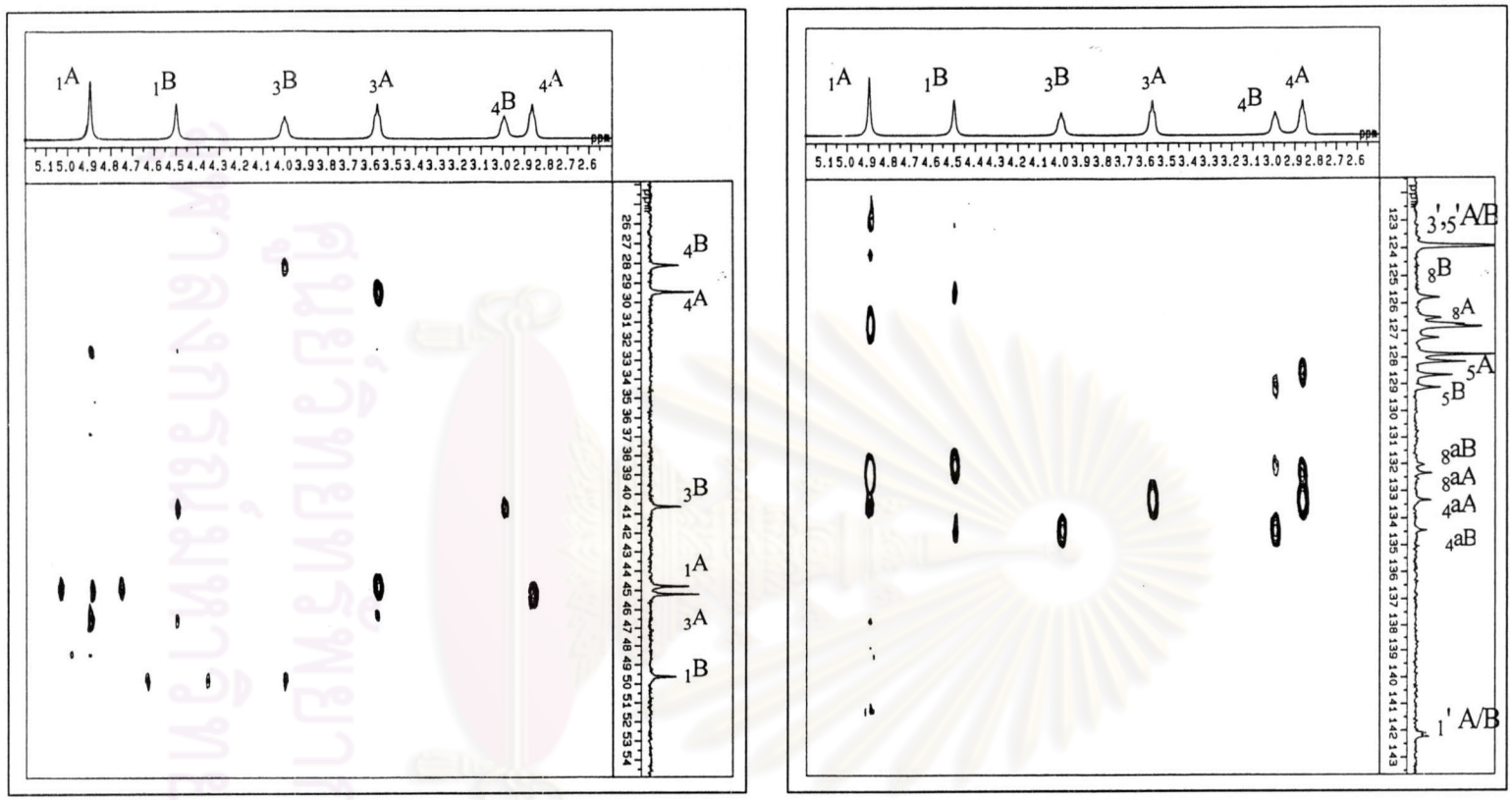


Figure 79. The 500 MHz HMBC spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in $CDCl_3$ (Enlarged-scale1)

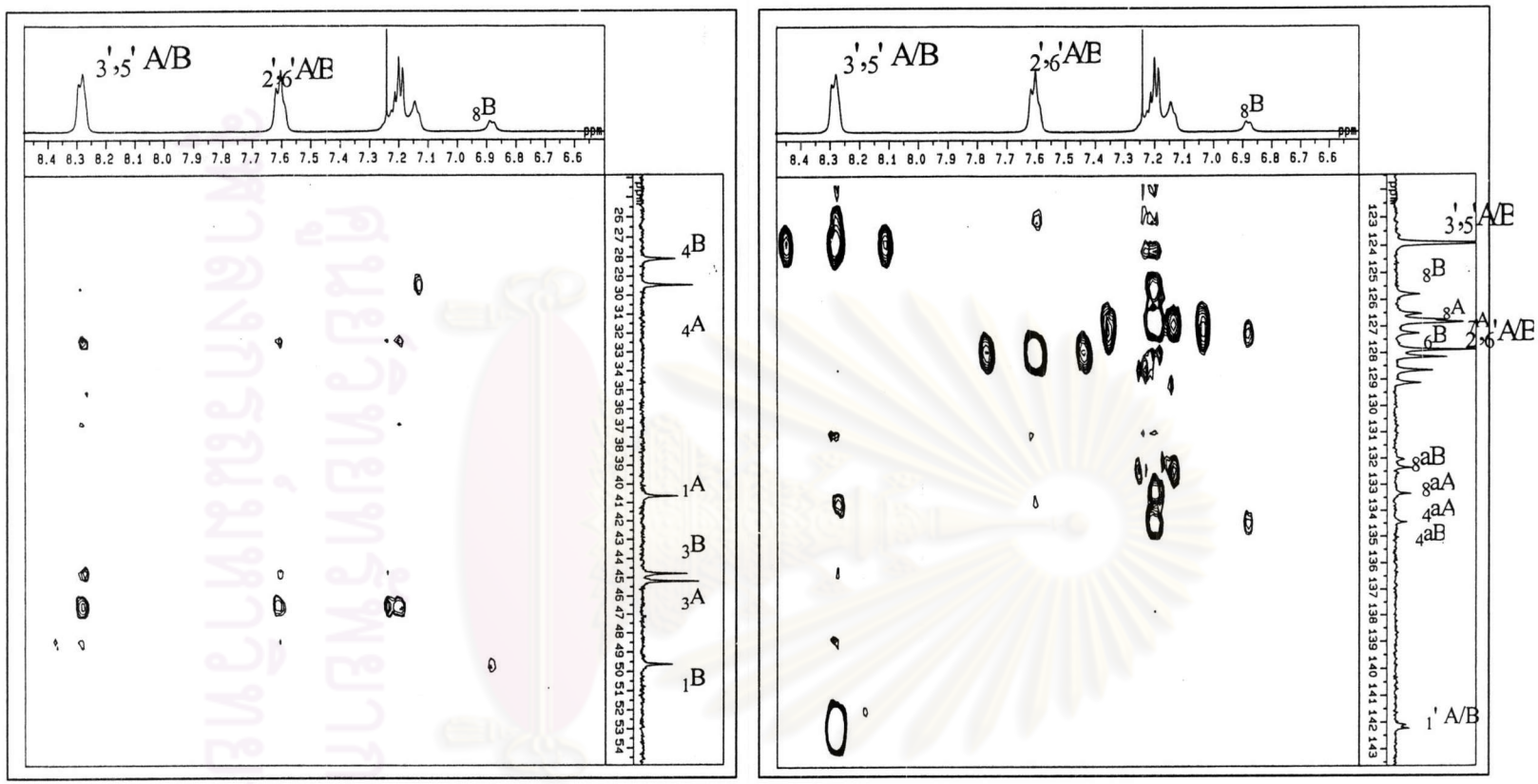


Figure 80. The 500 MHz HMBC spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in $CDCl_3$ (Enlarged-scale2)

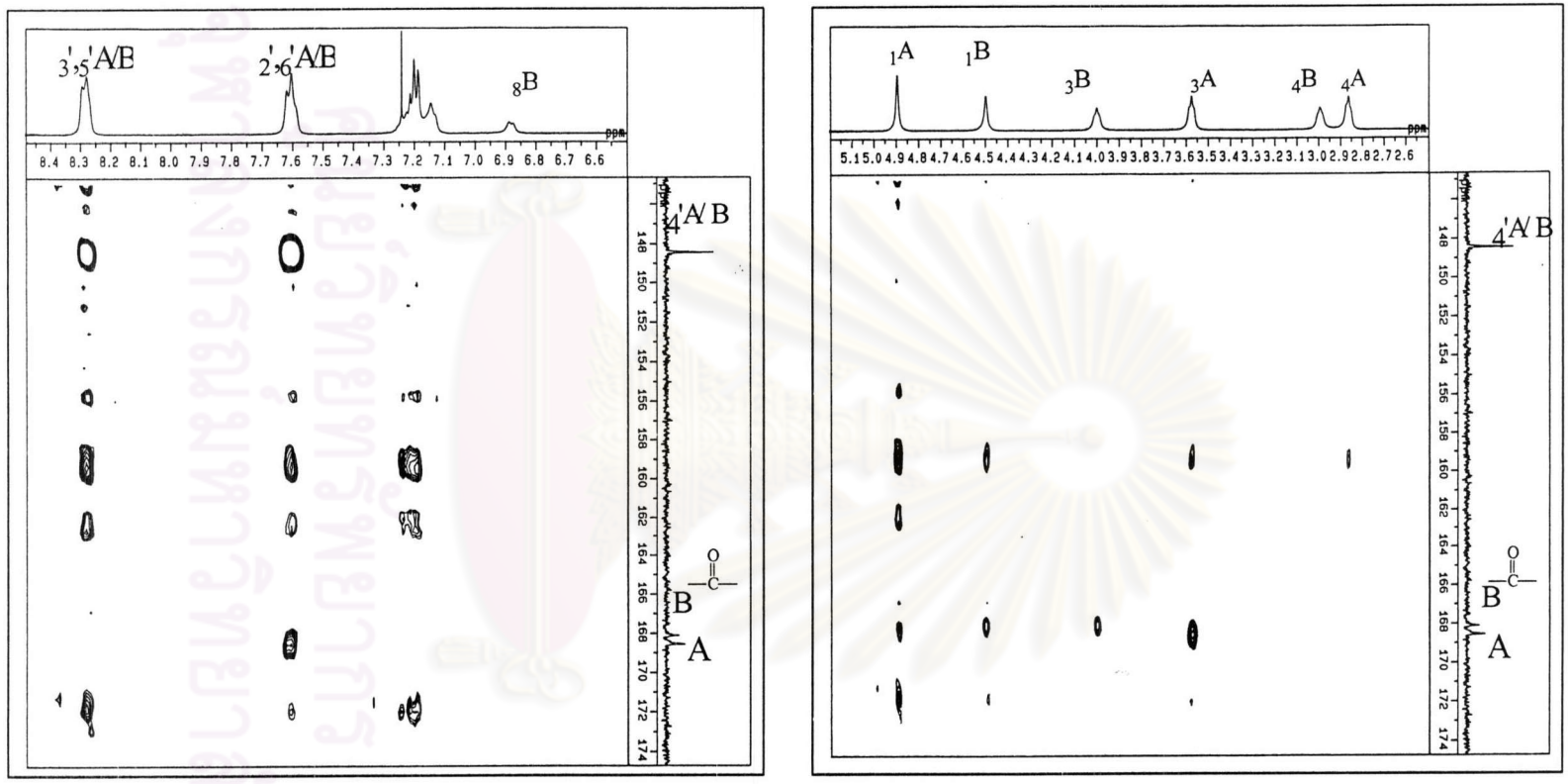


Figure 81. The 500 MHz HMBC spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydroisoquinoline in $CDCl_3$ (Enlarged-scale3)

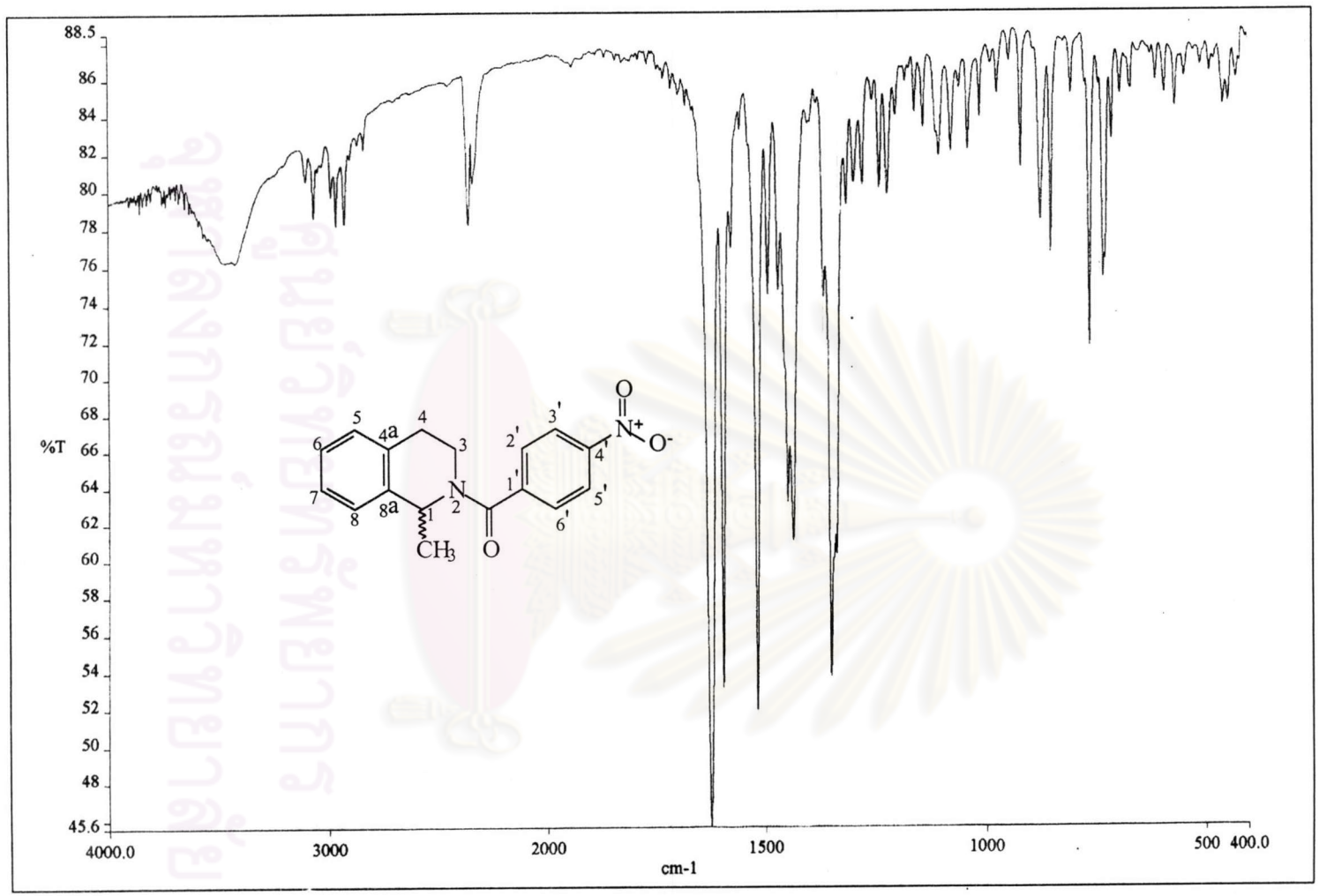


Figure 82. The IR spectrum (KBr) of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline

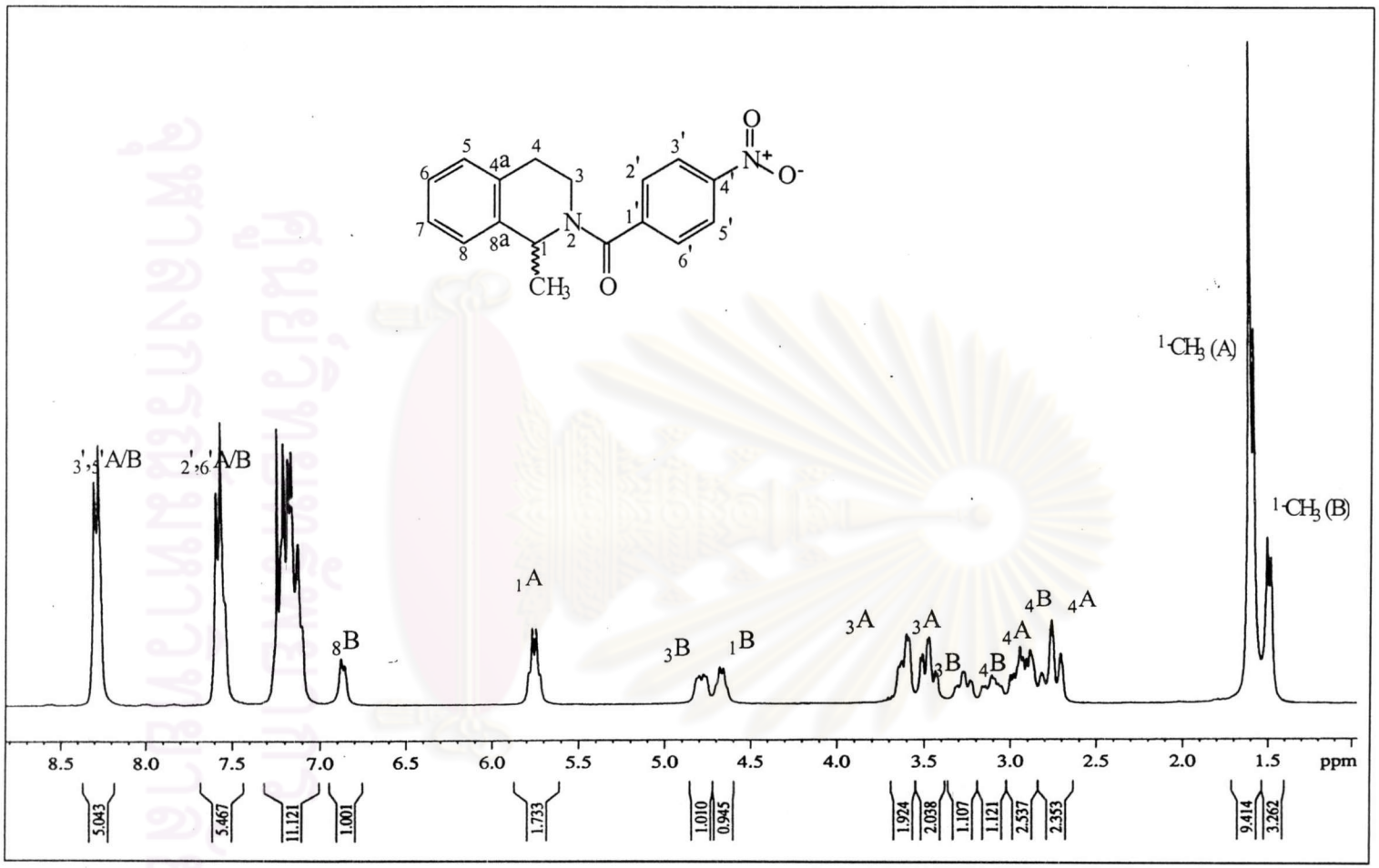


Figure 83. The 300 MHz ^{1}H-NMR spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline in $CDCl_3$

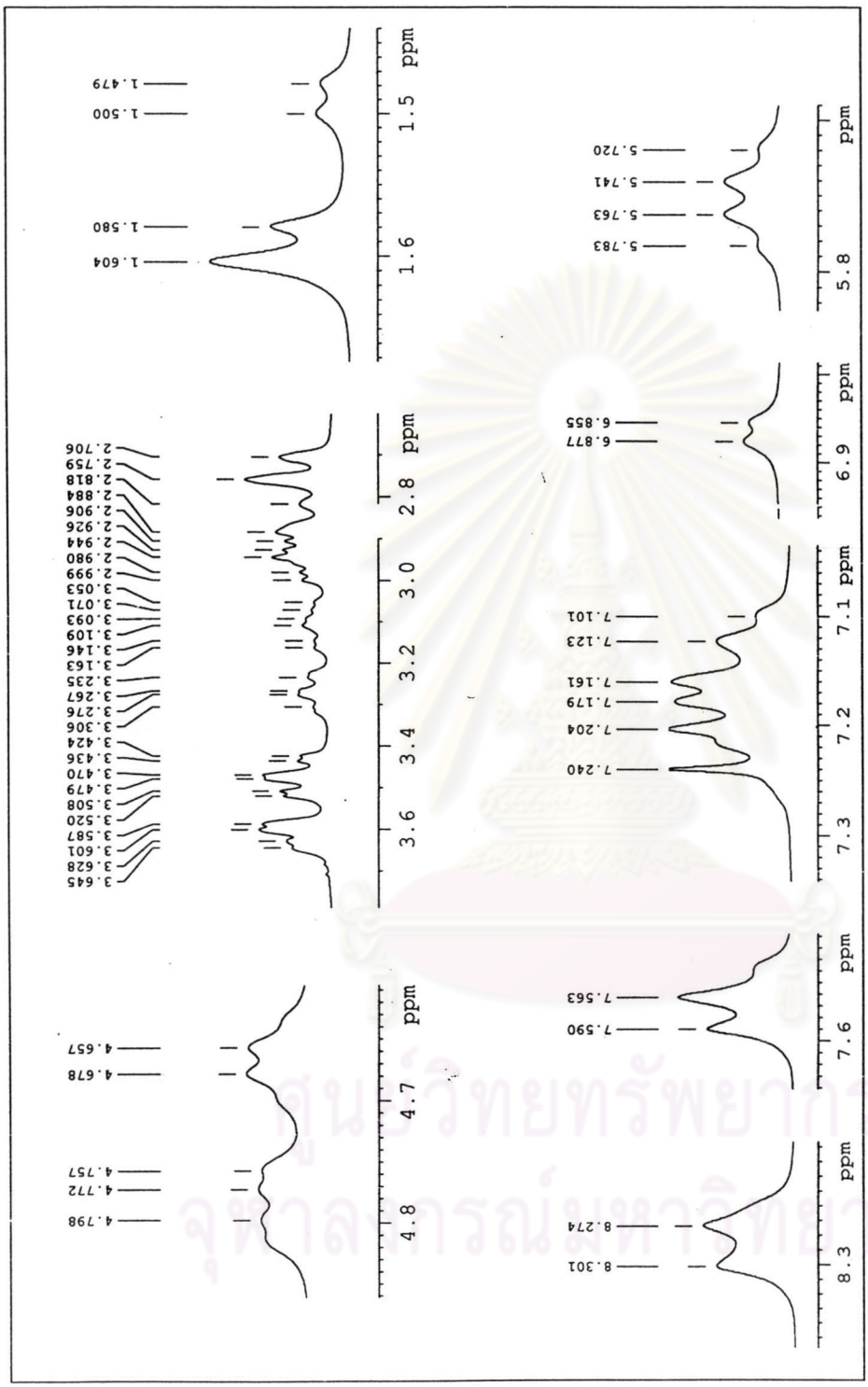


Figure 84. The 300 MHz ^{1}H-NMR spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline in $CDCl_3$

(Enlarged-scale)

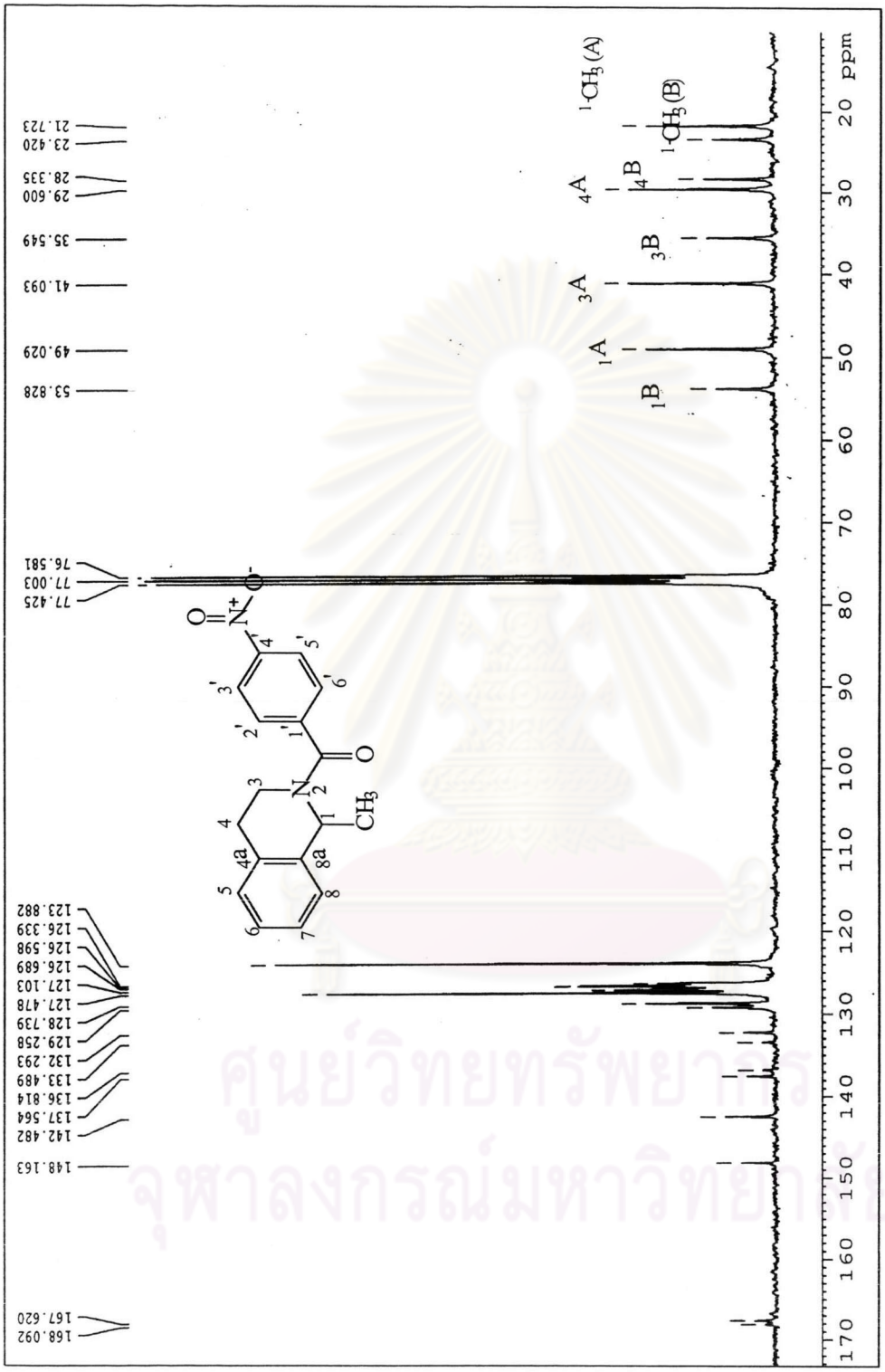


Figure 85. The 75 MHz ^{13}C-NMR spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline in $CDCl_3$

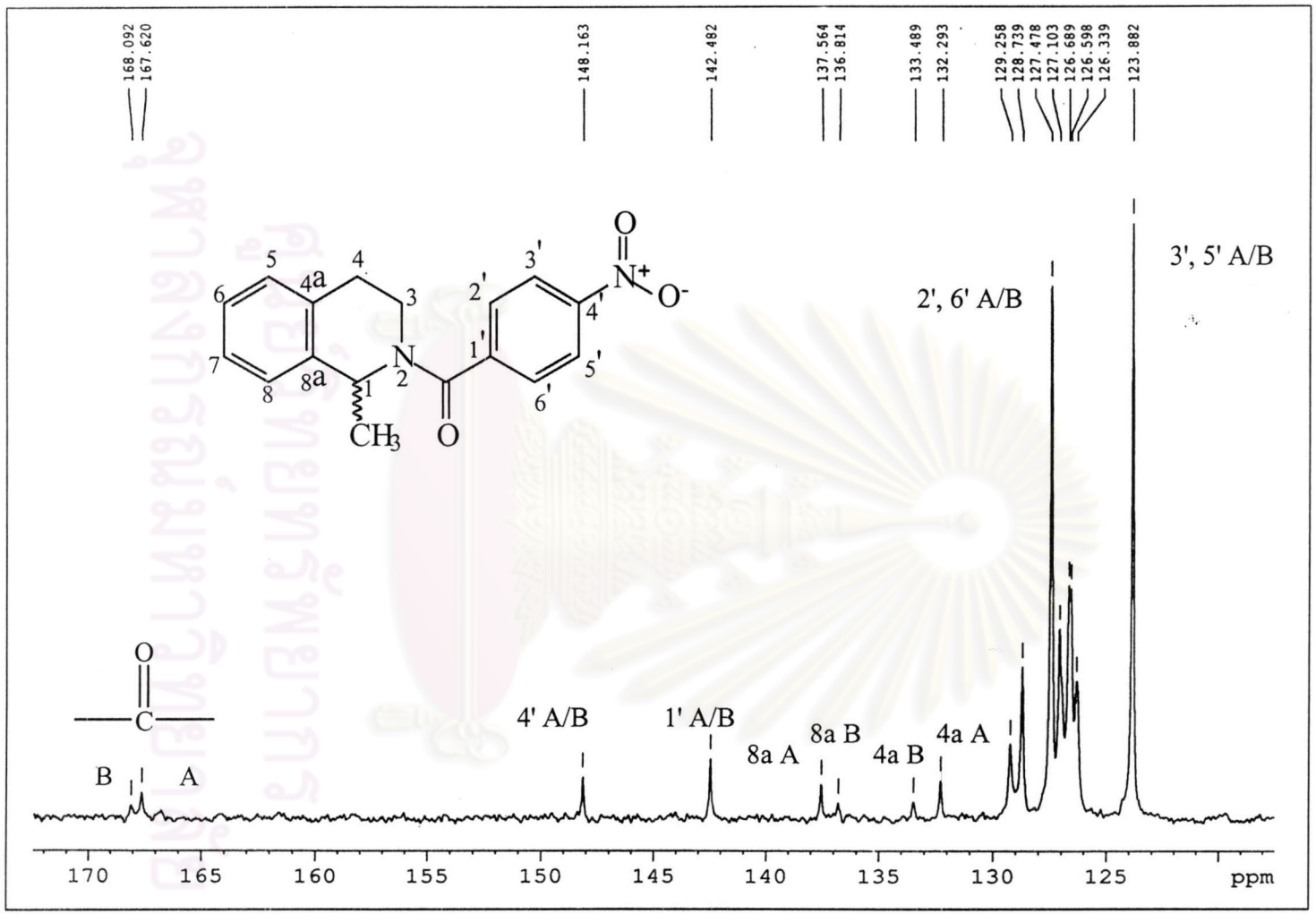


Figure 86. The 75 MHz ^{13}C-NMR spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline in $CDCl_3$ (Enlarged-scale in 120-170 ppm region)

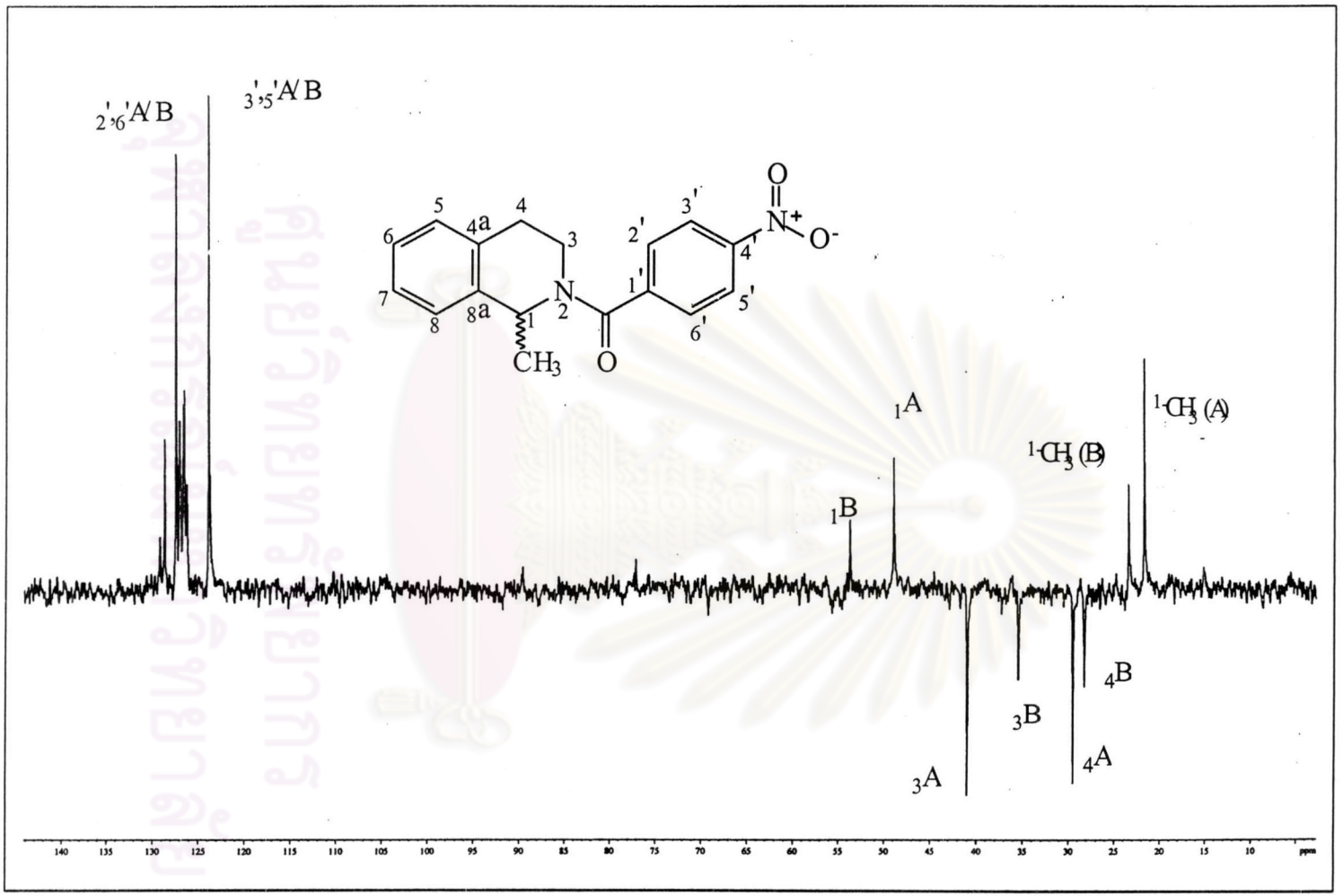
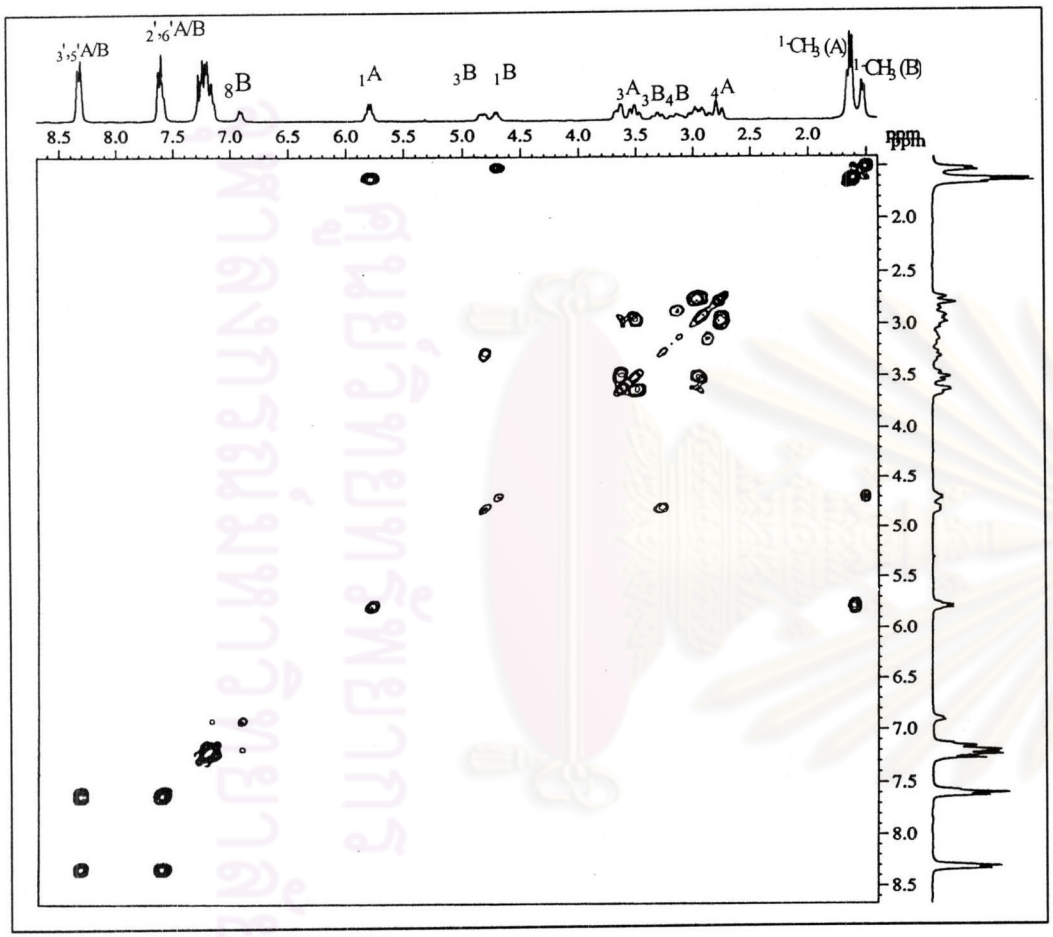


Figure 87. The 75 MHz DEPT 135 spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline in $CDCl_3$



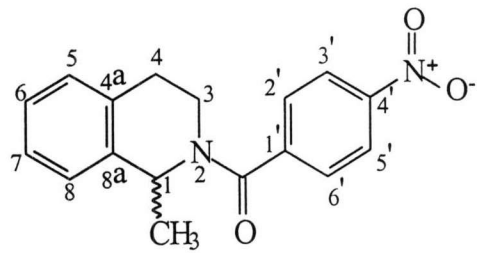


Figure 88. The 300 MHz HH COSY spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline in $CDCl_3$

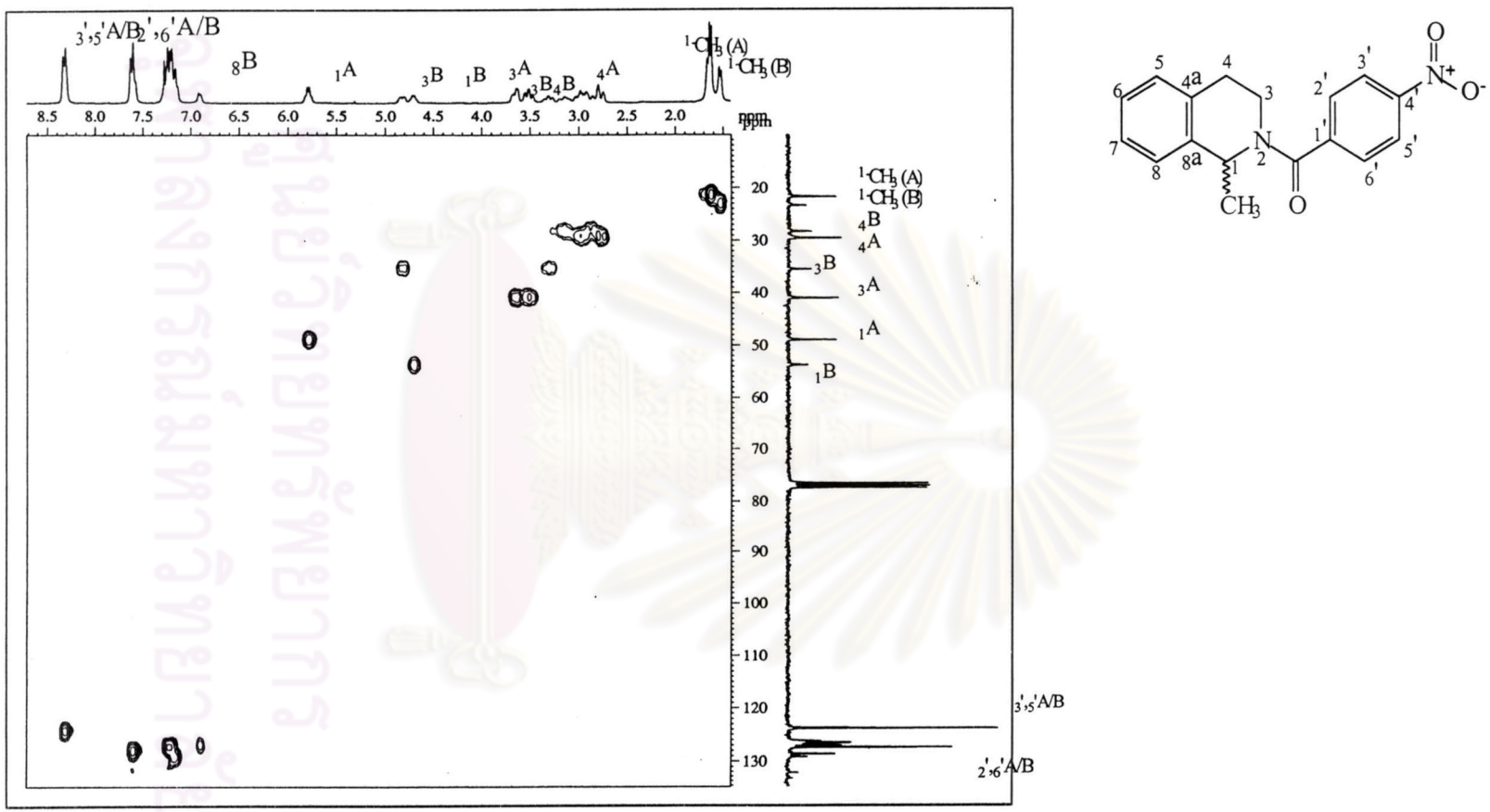


Figure 89. The 300 MHz HMQC spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline in $CDCl_3$

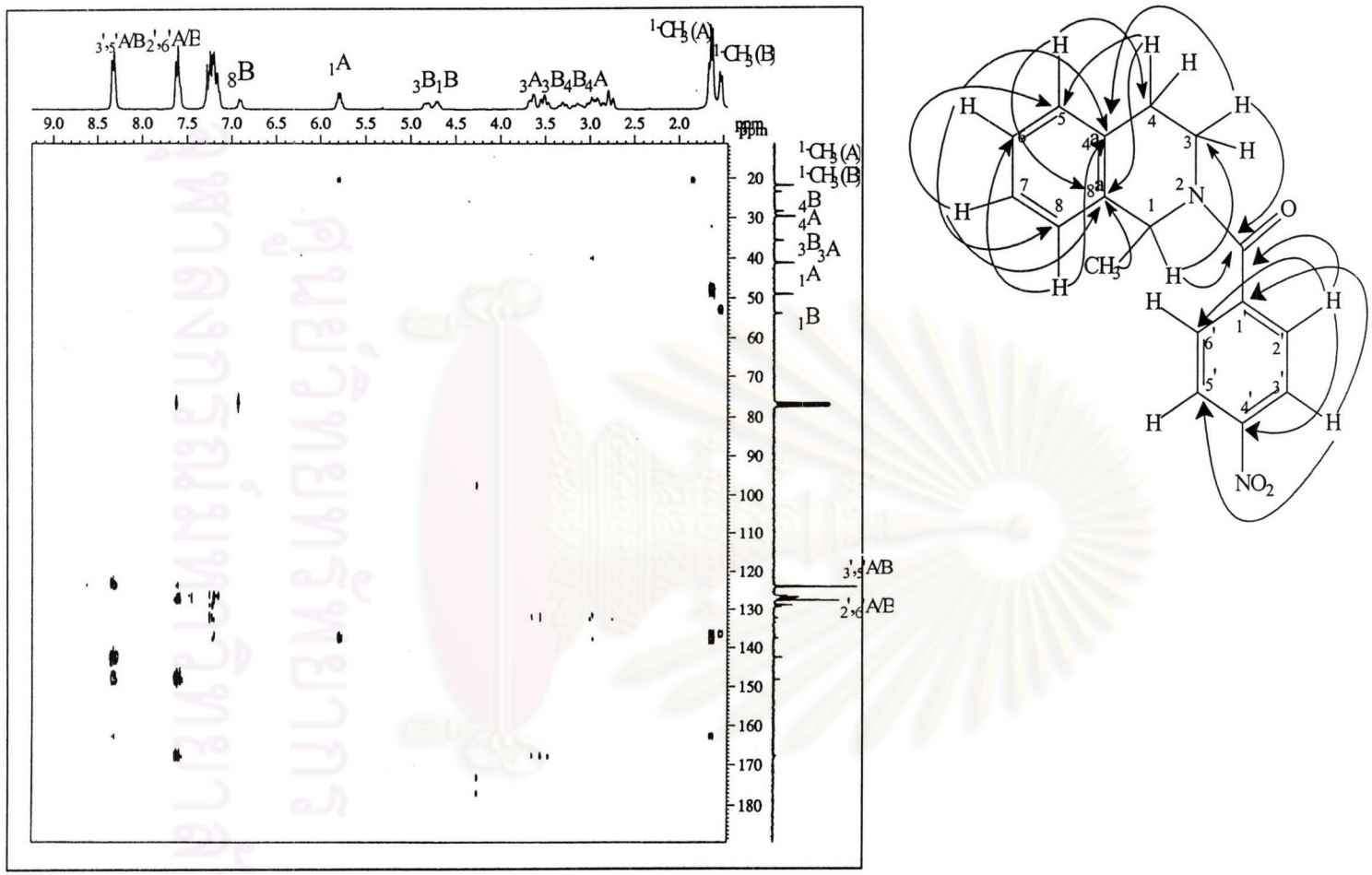


Figure 90. The 300 MHz HMBC spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline in $CDCl_3$

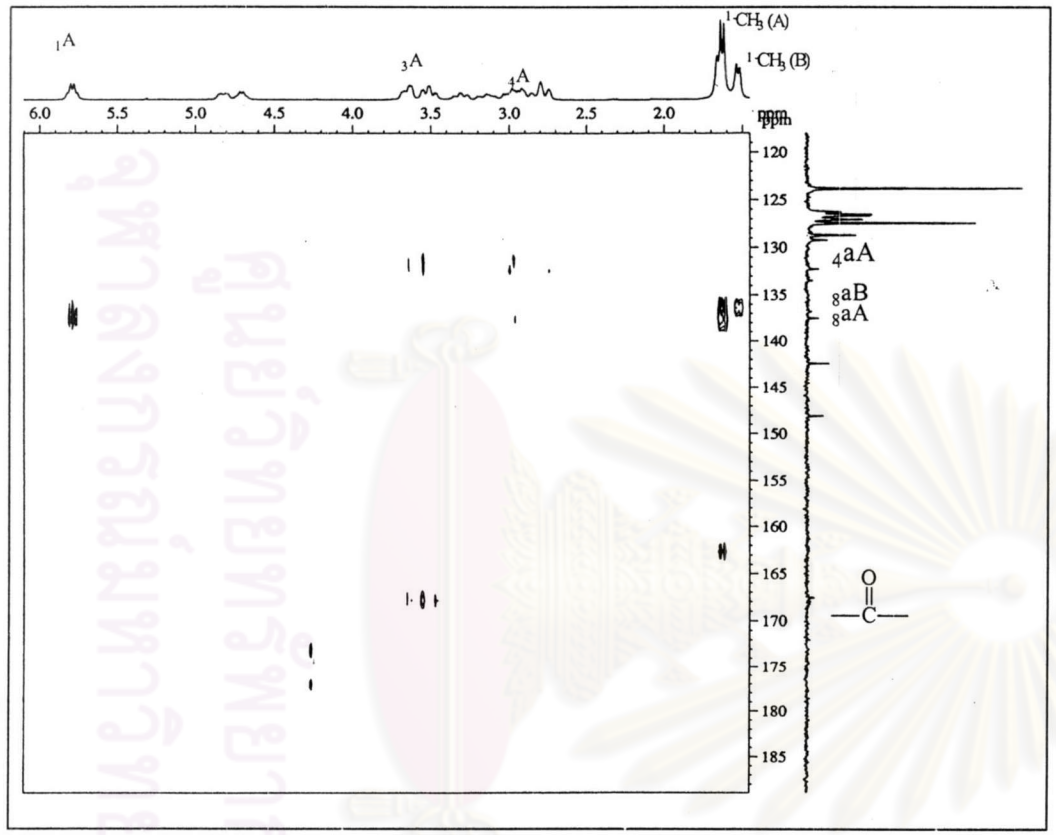


Figure 91. The 300 MHz HMBC spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline in $CDCl_3$ (Enlarged-scale1)

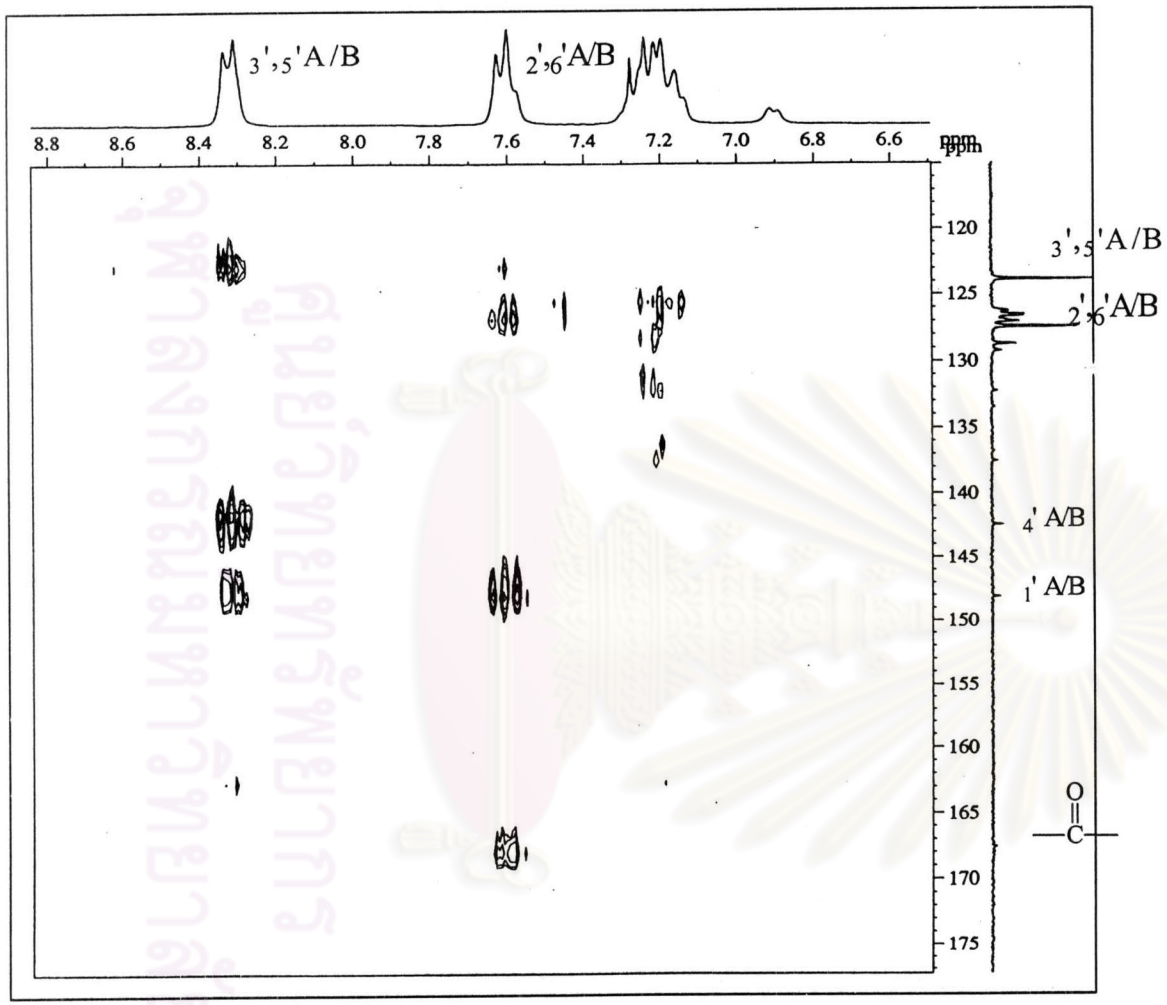


Figure 92. The 300 MHz HMBC spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline in $CDCl_3$ (Enlarged-scale2)

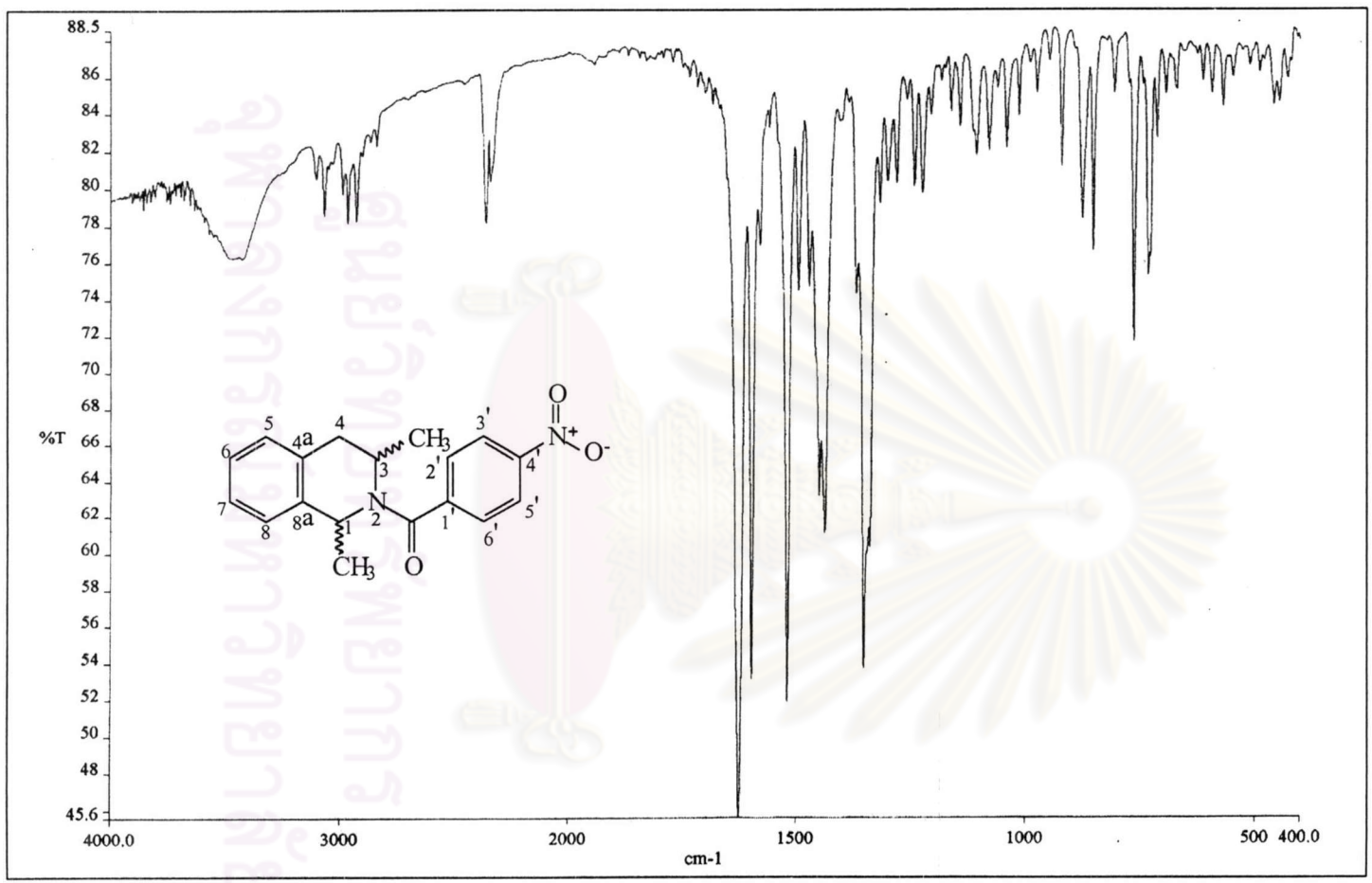


Figure 93. The IR spectrum (KBr) of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1,3-dimethylisoquinoline

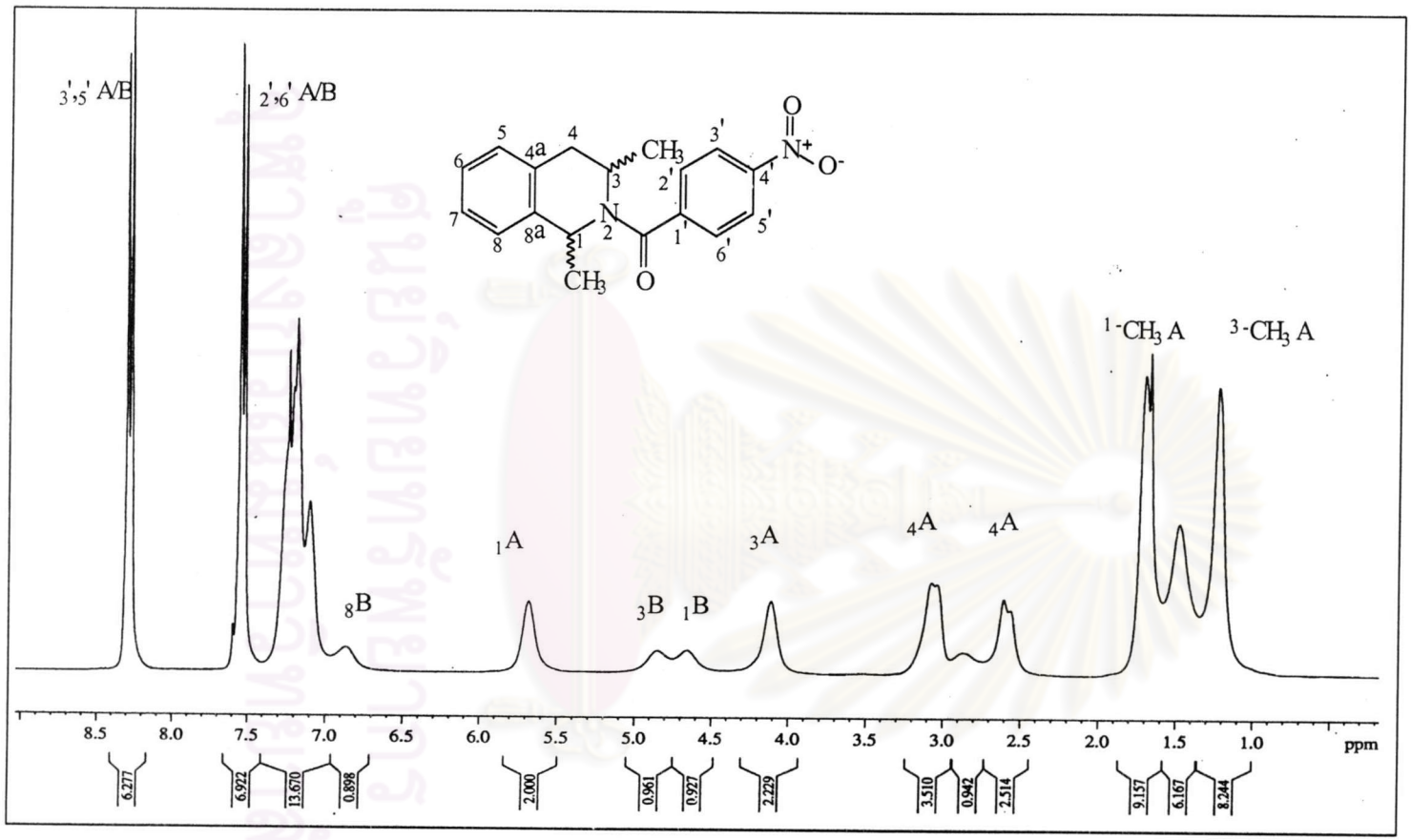


Figure 94. The 300 MHz ^{1}H-NMR spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1,3-dimethylisoquinoline in $CDCl_3$

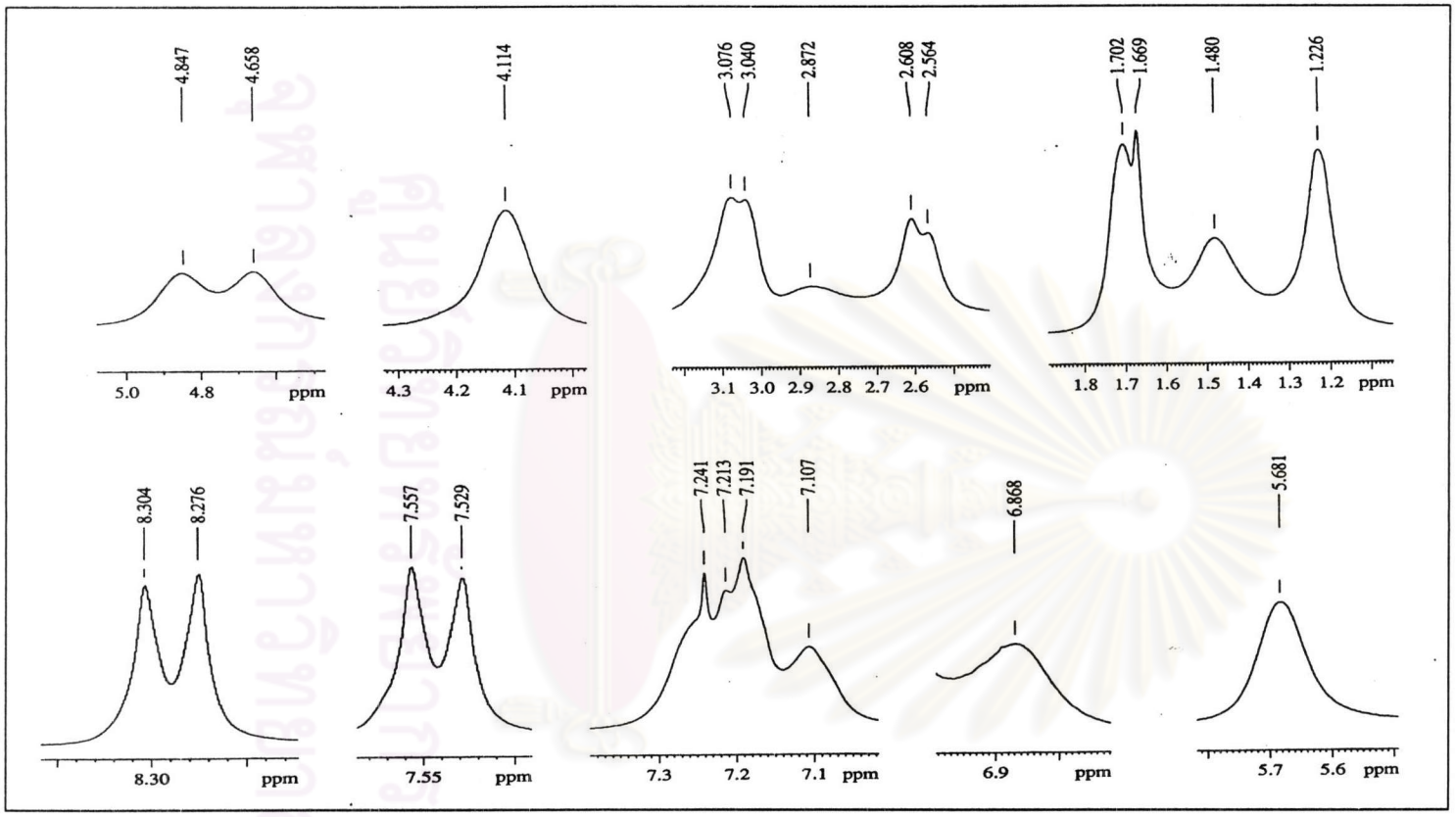


Figure 95. The 300 MHz ^{1}H-NMR spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1,3-dimethylisoquinoline in $CDCl_3$

(Enlarged-scale)

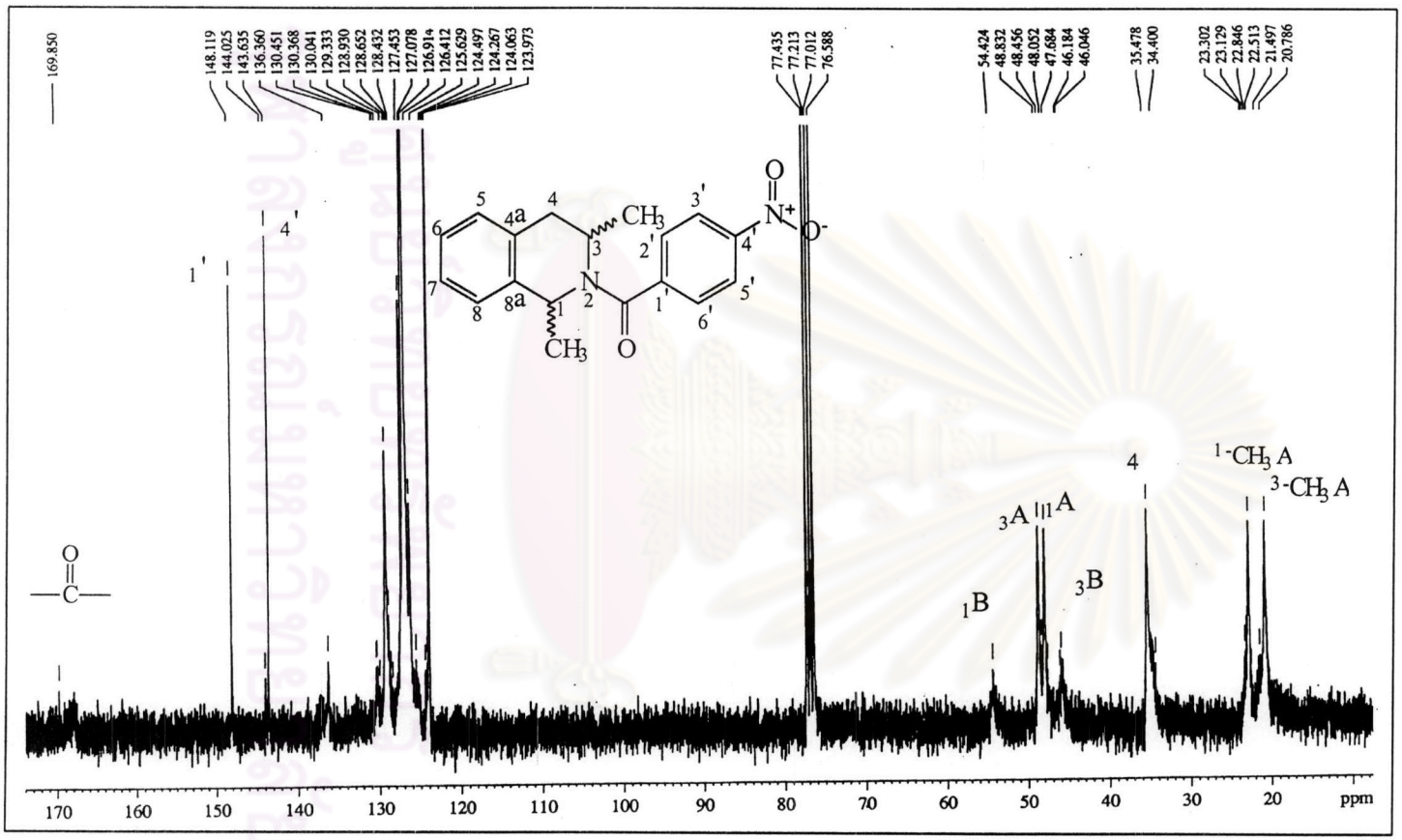


Figure 96. The 75 MHz ^{13}C-NMR spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1,3-dimethylisoquinoline in $CDCl_3$

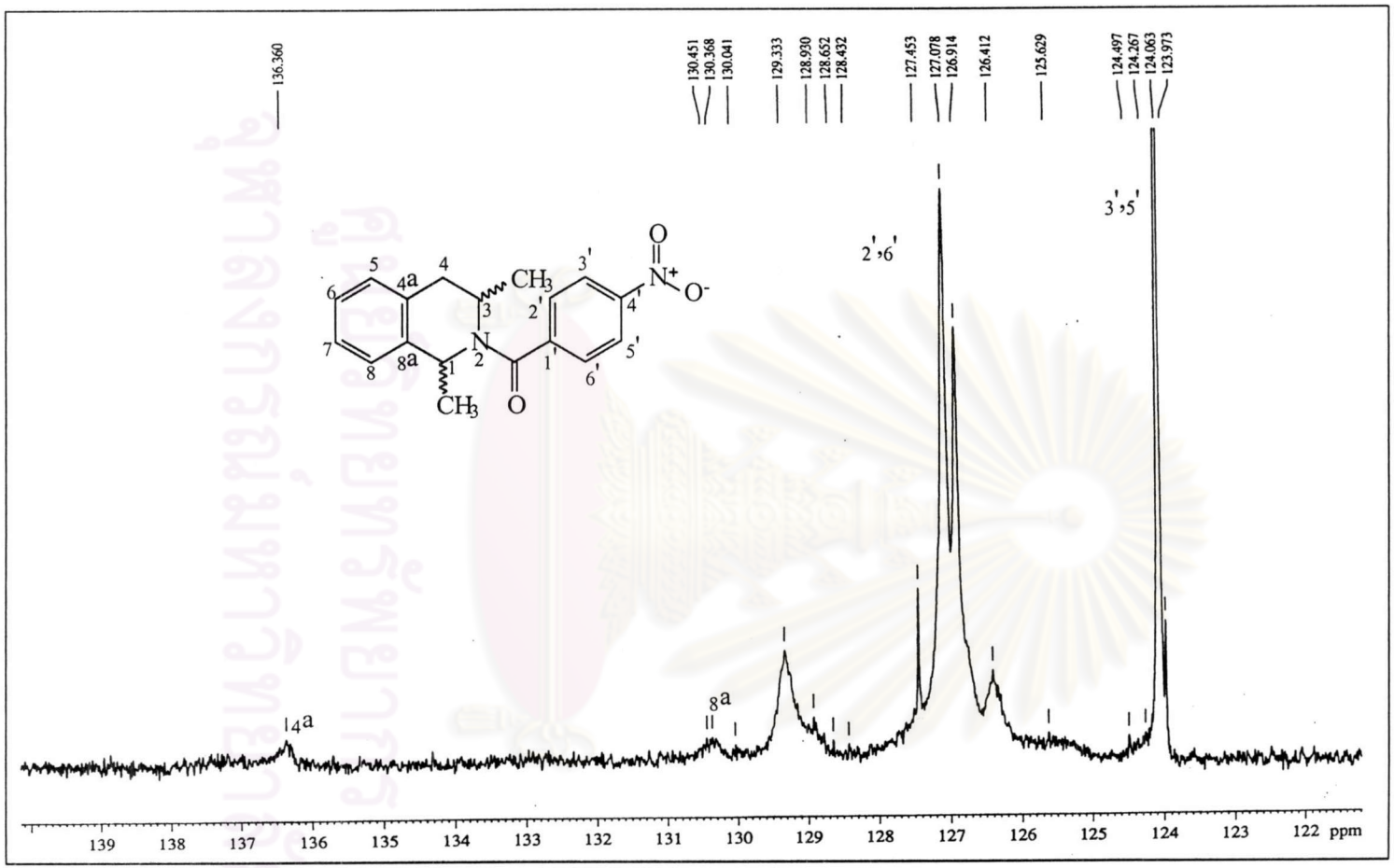


Figure 97. The 75 MHz ^{13}C-NMR spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1,3-dimethylisoquinoline in $CDCl_3$

(Enlarged-scale)

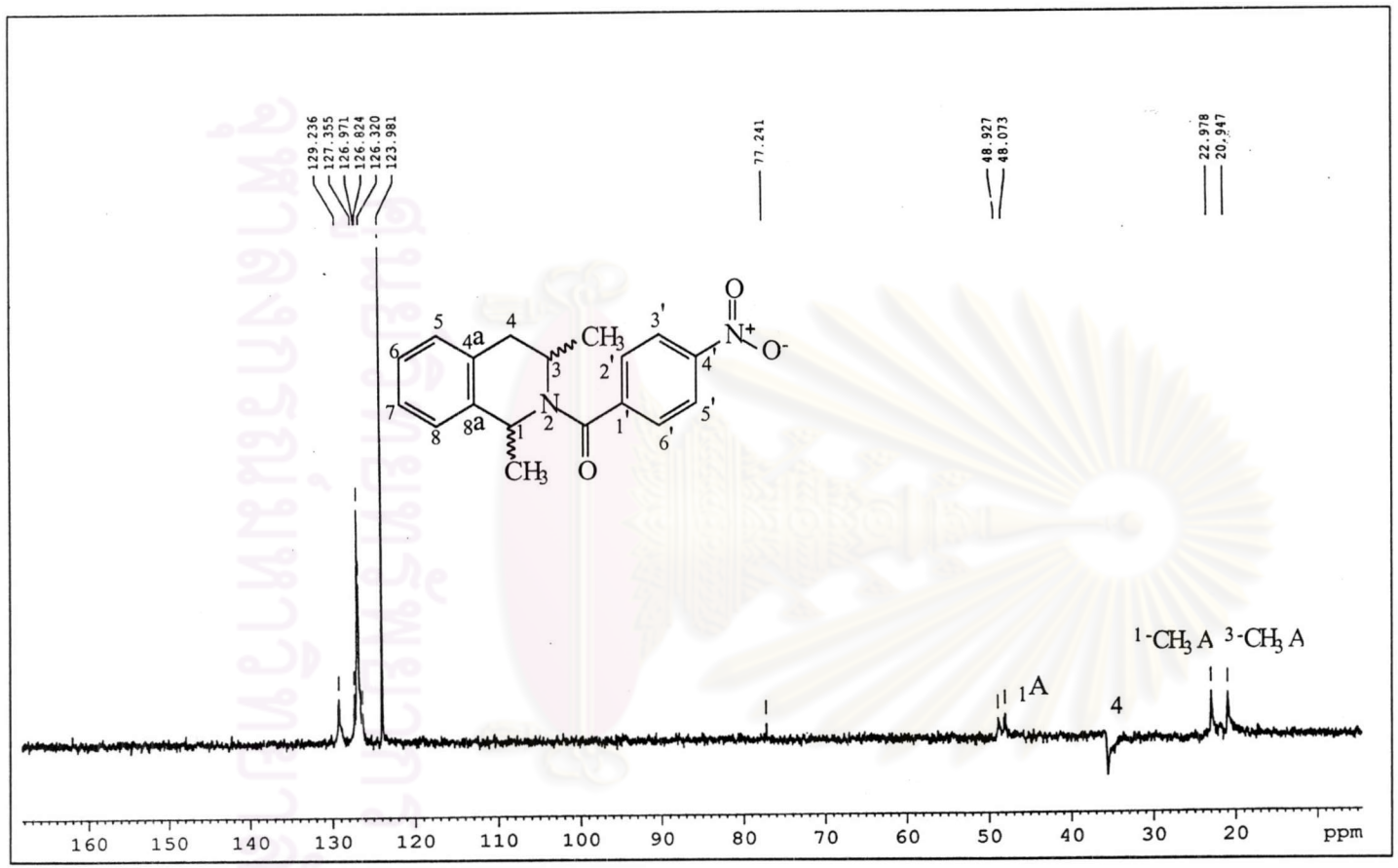


Figure 98. The 75 MHz DEPT 135 spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1,3-dimethylisoquinoline in $CDCl_3$

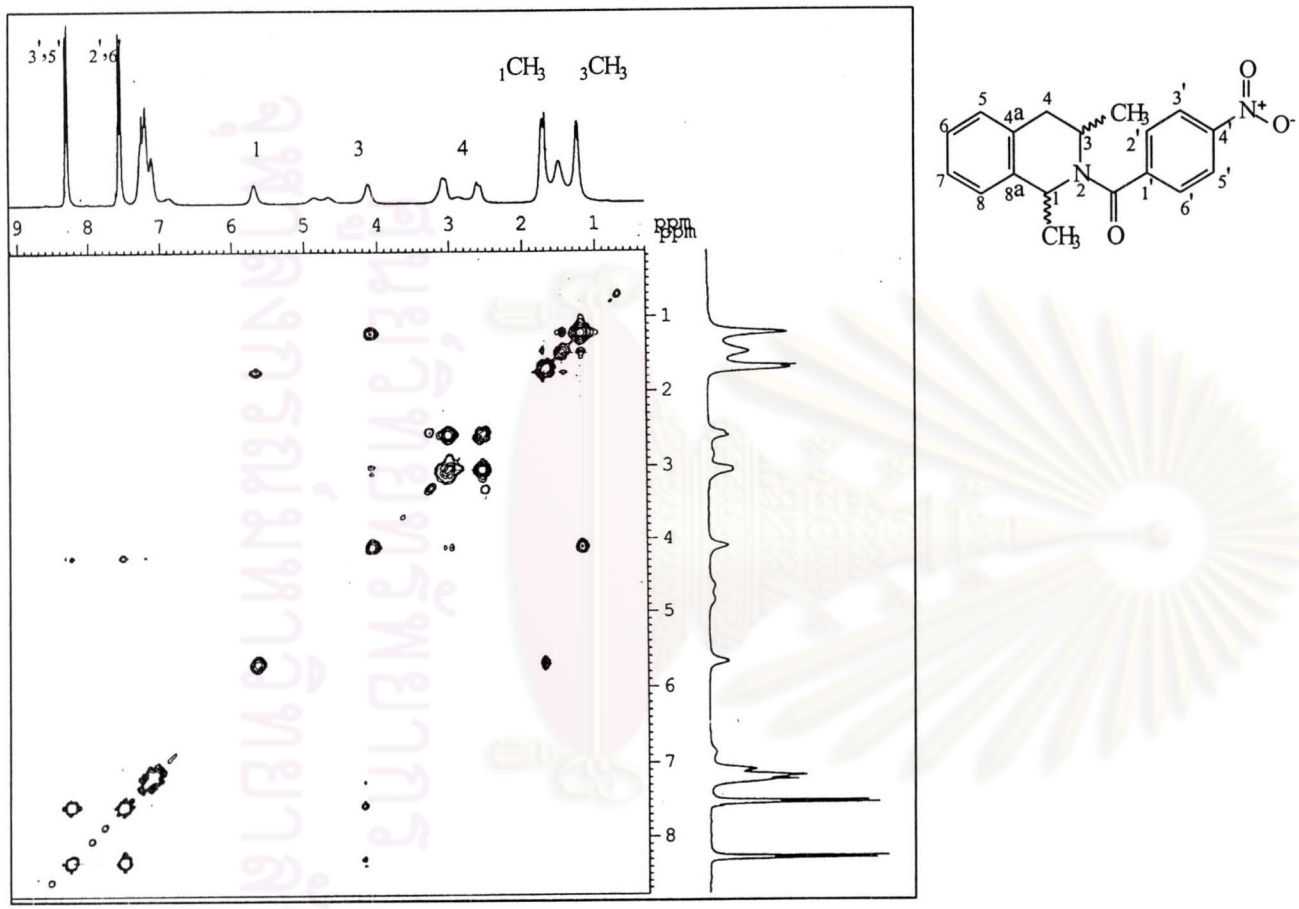


Figure 99. The 300 MHz HH COSY spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1,3-dimethylisoquinoline in $CDCl_3$

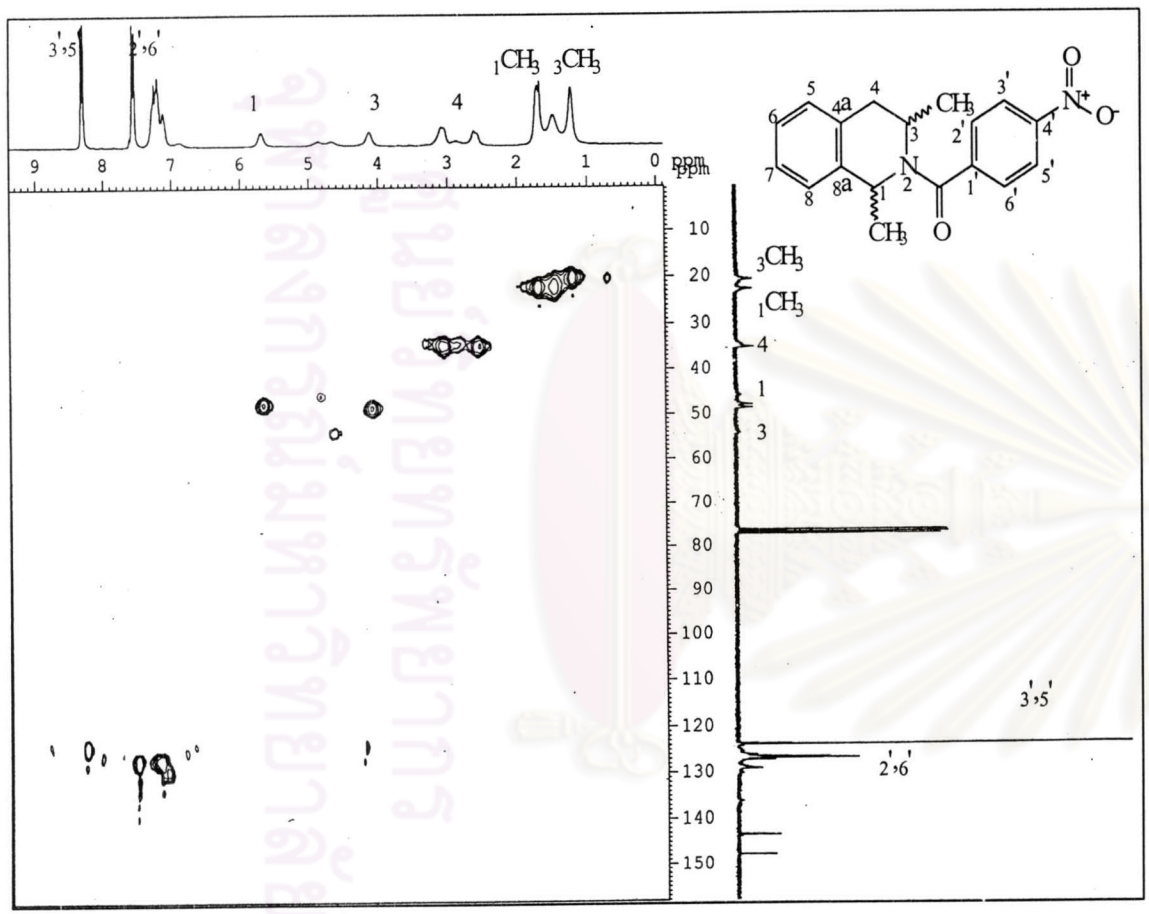


Figure 100. The 300 MHz HMQC spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1,3-dimethylisoquinoline in $CDCl_3$

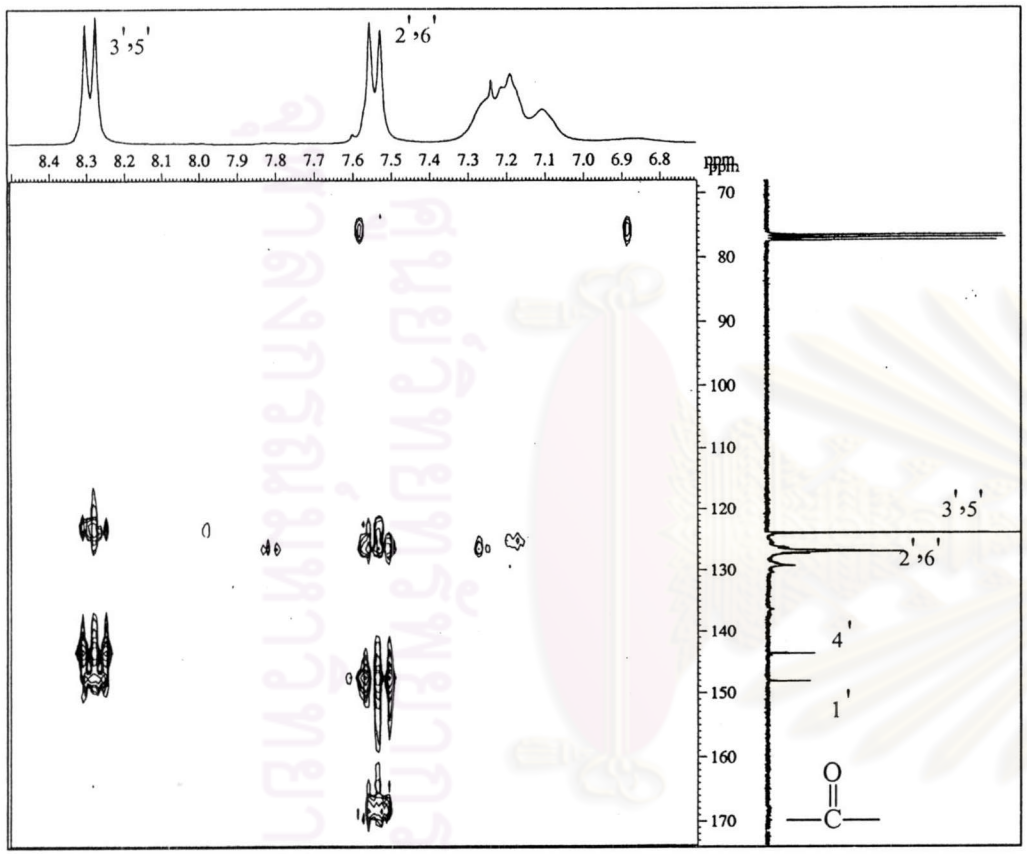


Figure 101. The 300 MHz HMBC spectrum of *N*-(*p*-nitrobenzoyl)-1,2,3,4-tetrahydro-1,3-dimethylisoquinoline in $CDCl_3$

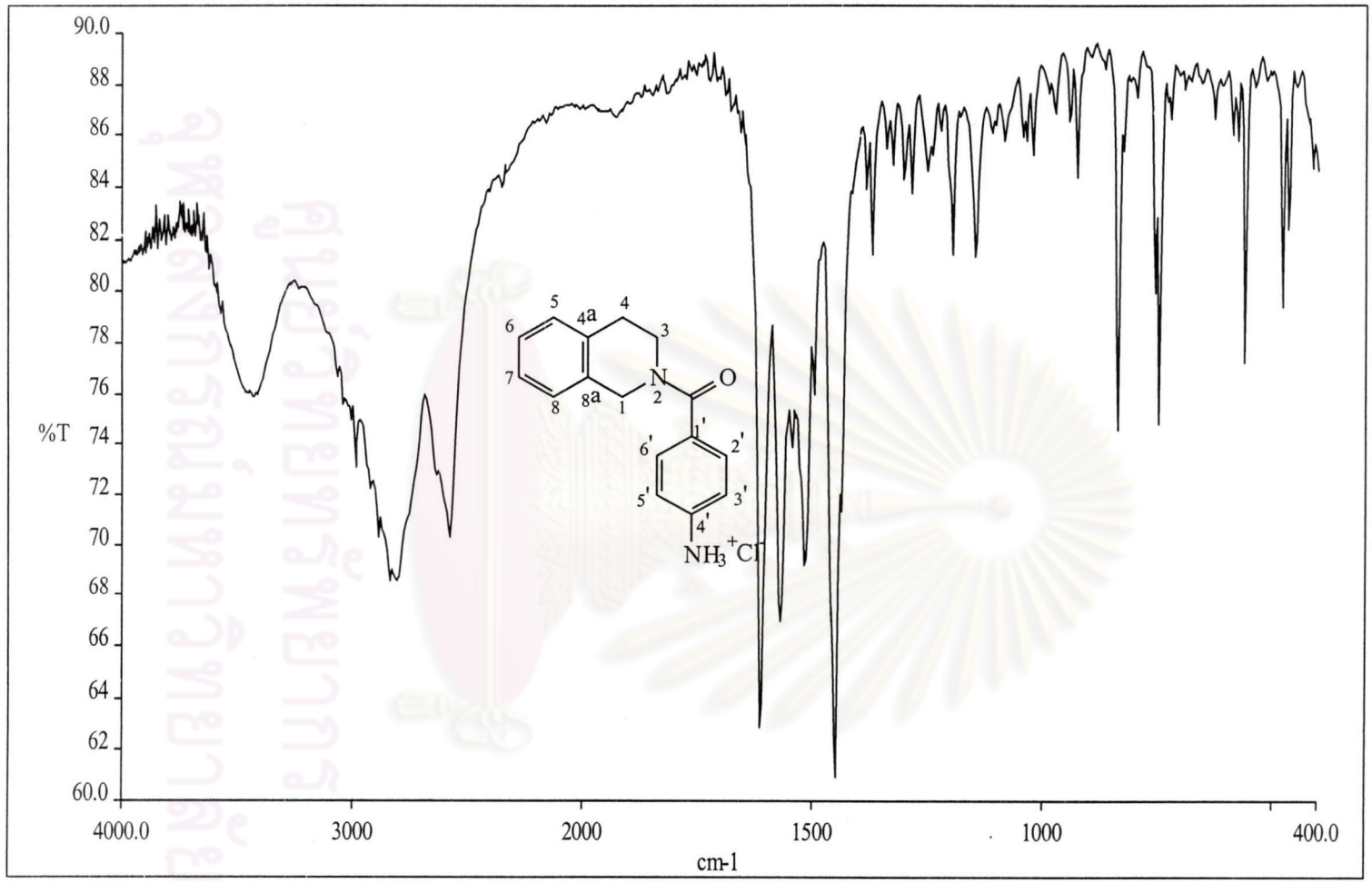


Figure 102. The IR spectrum (KBr) of *N*-(*p*-aminobenzoyl)-1,2,3,4-tetrahydroisoquinoline hydrochloride

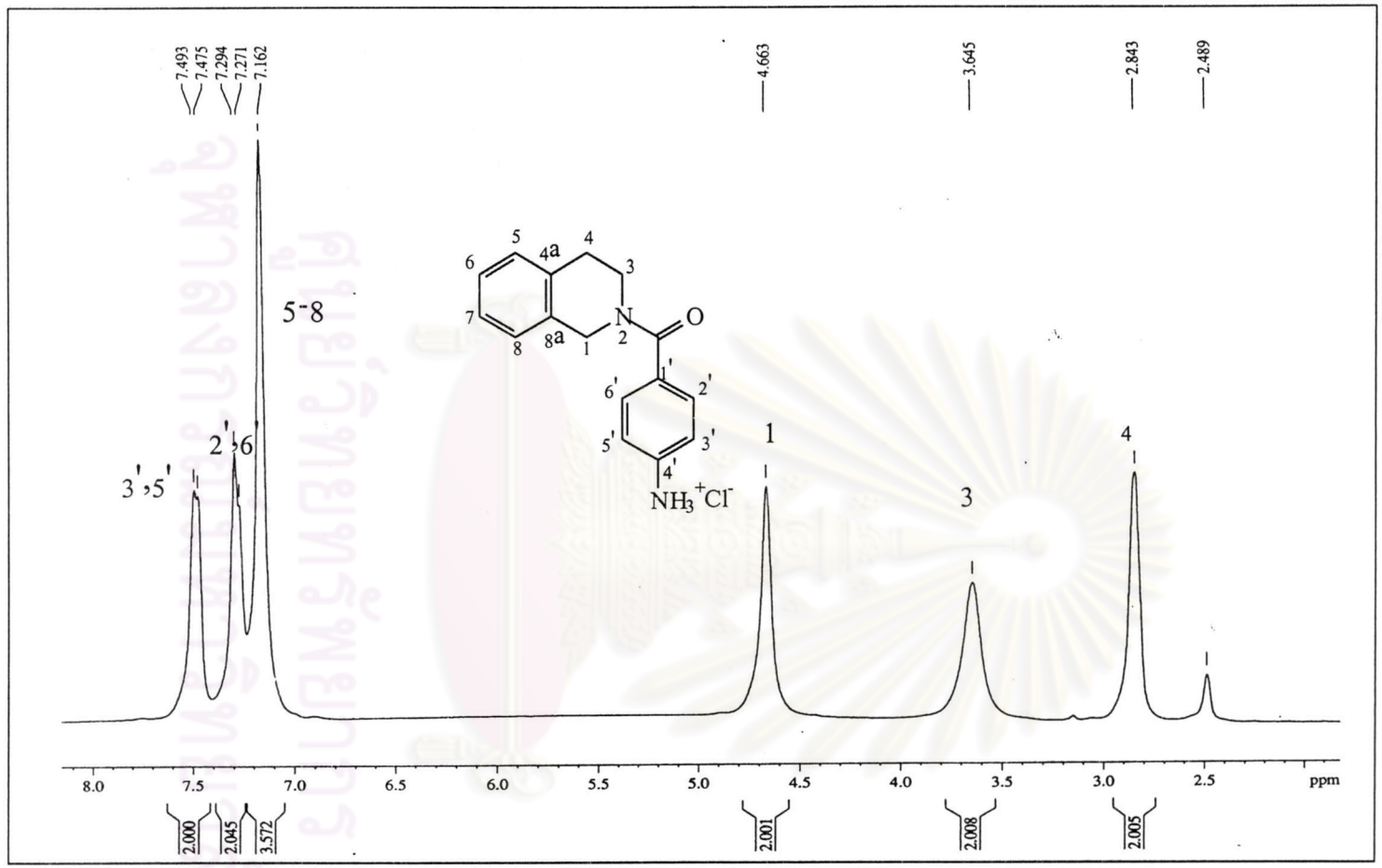


Figure 103. The 300 MHz ^{1}H-NMR spectrum of *N*-(*p*-aminobenzoyl)-1,2,3,4-tetrahydroisoquinoline hydrochloride in DMSO-d6

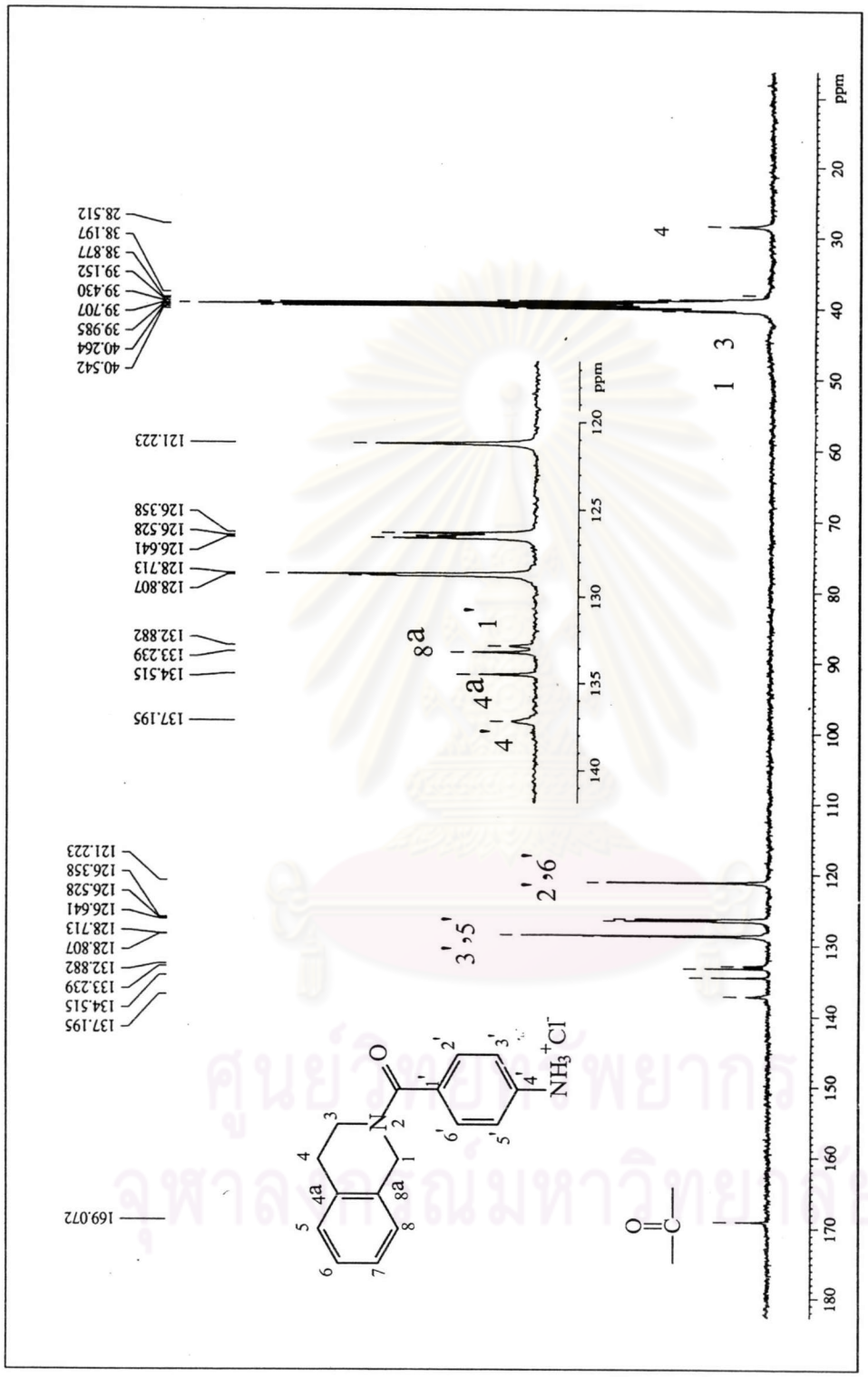


Figure 104. The 75 MHz ^{13}C-NMR spectrum of *N*-(*p*-aminobenzoyl)-1,2,3,4-tetrahydroisoquinoline hydrochloride in DMSO-d6

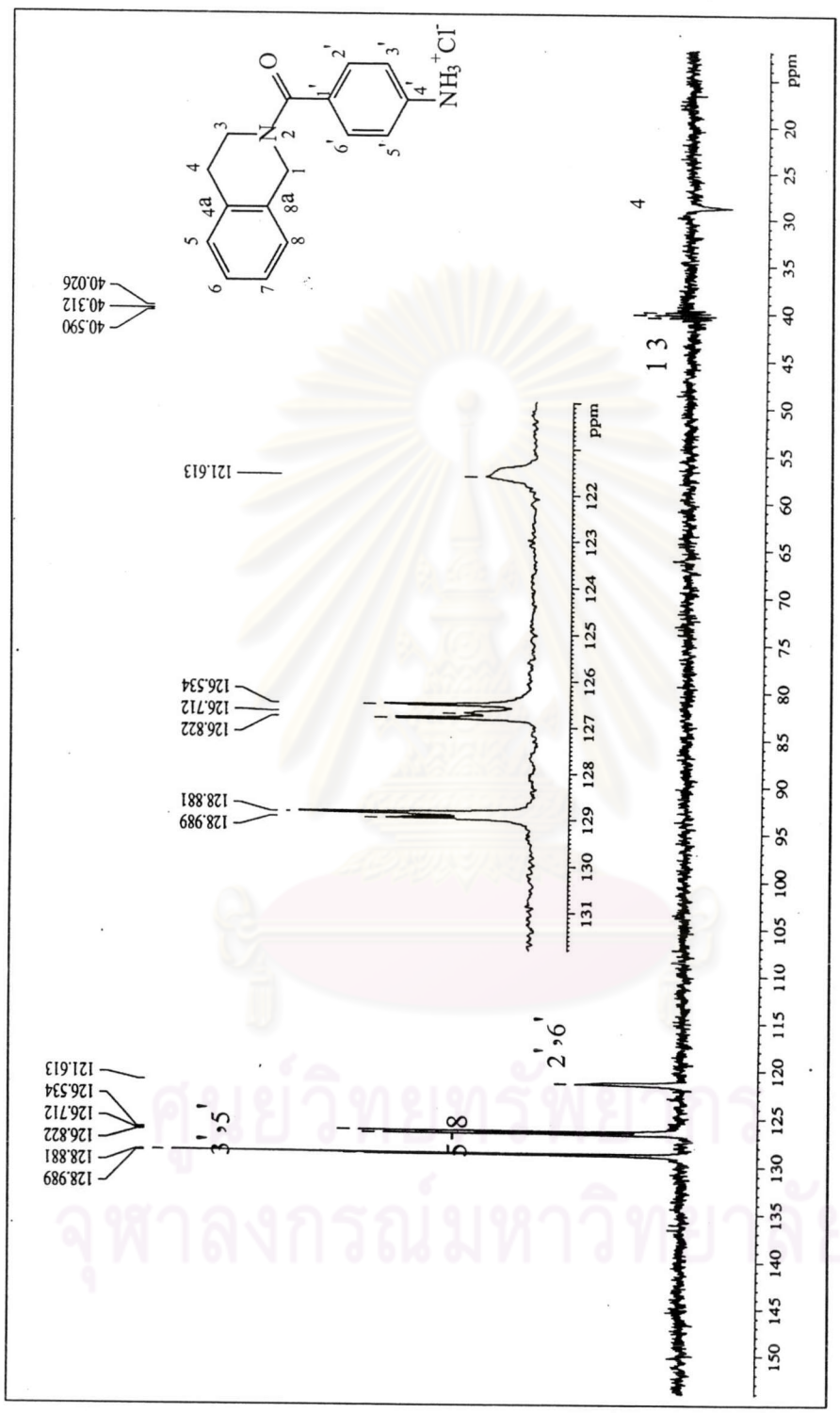
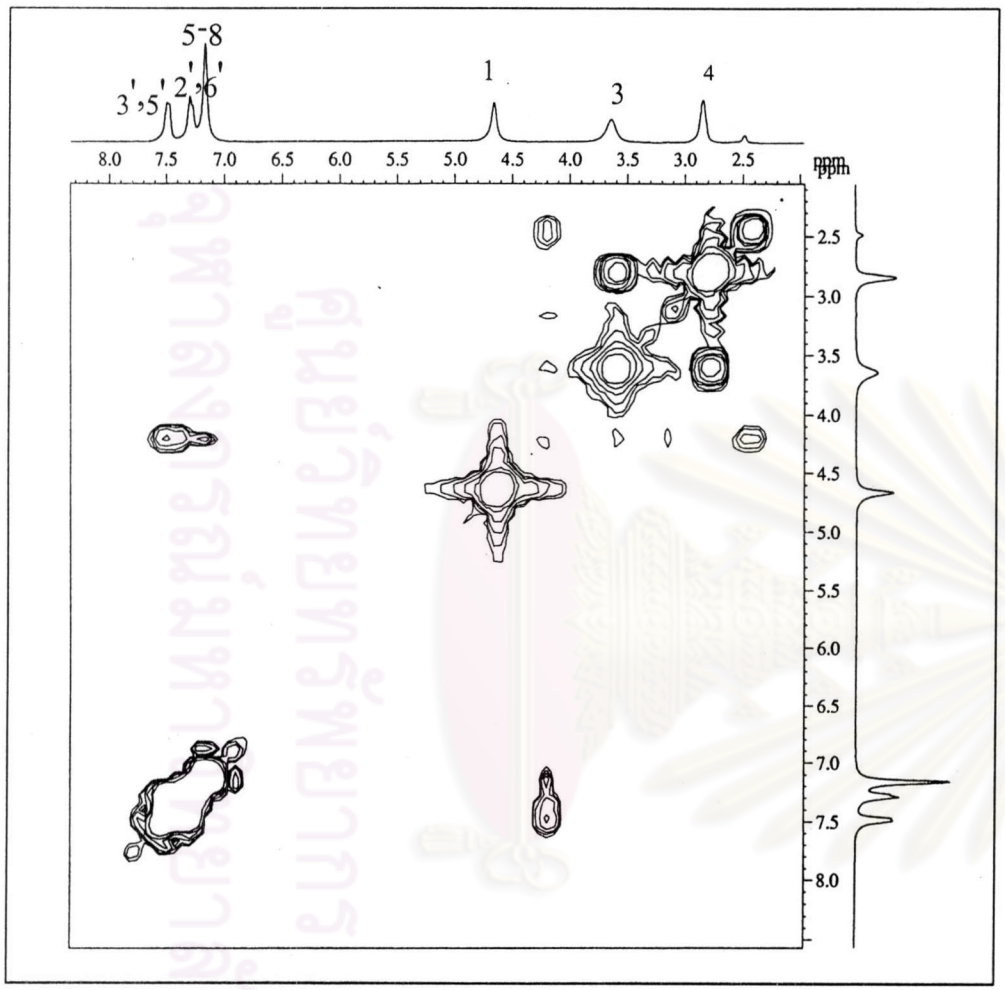


Figure 105. The 75 MHz ^{13}C-NMR spectrum of *N*-(*p*-aminobenzoyl)-1,2,3,4-tetrahydroisoquinoline hydrochloride in DMSO-d6



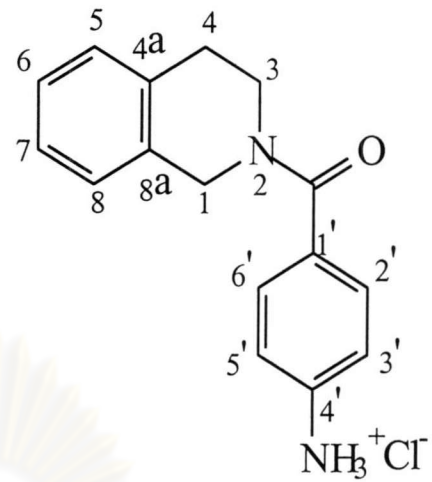


Figure 106. The 300 MHz HH COSY R spectrum of *N*-(*p*-aminobenzoyl)-1,2,3,4-tetrahydroisoquinoline hydrochloride in DMSO-d6

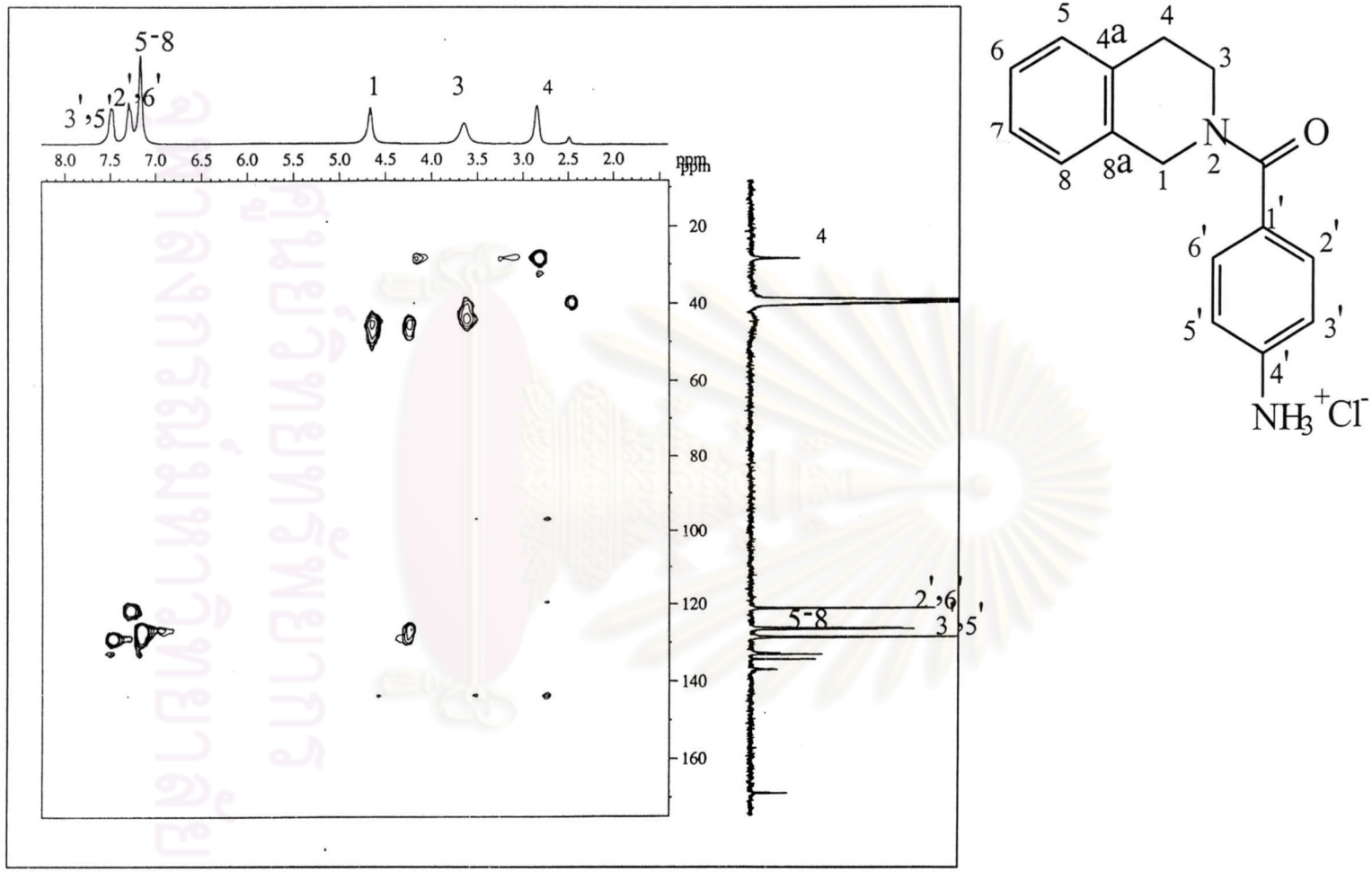


Figure 107. The 300 MHz HMQC spectrum of *N*-(*p*-aminobenzoyl)-1,2,3,4-tetrahydroisoquinoline hydrochloride in DMSO-d6

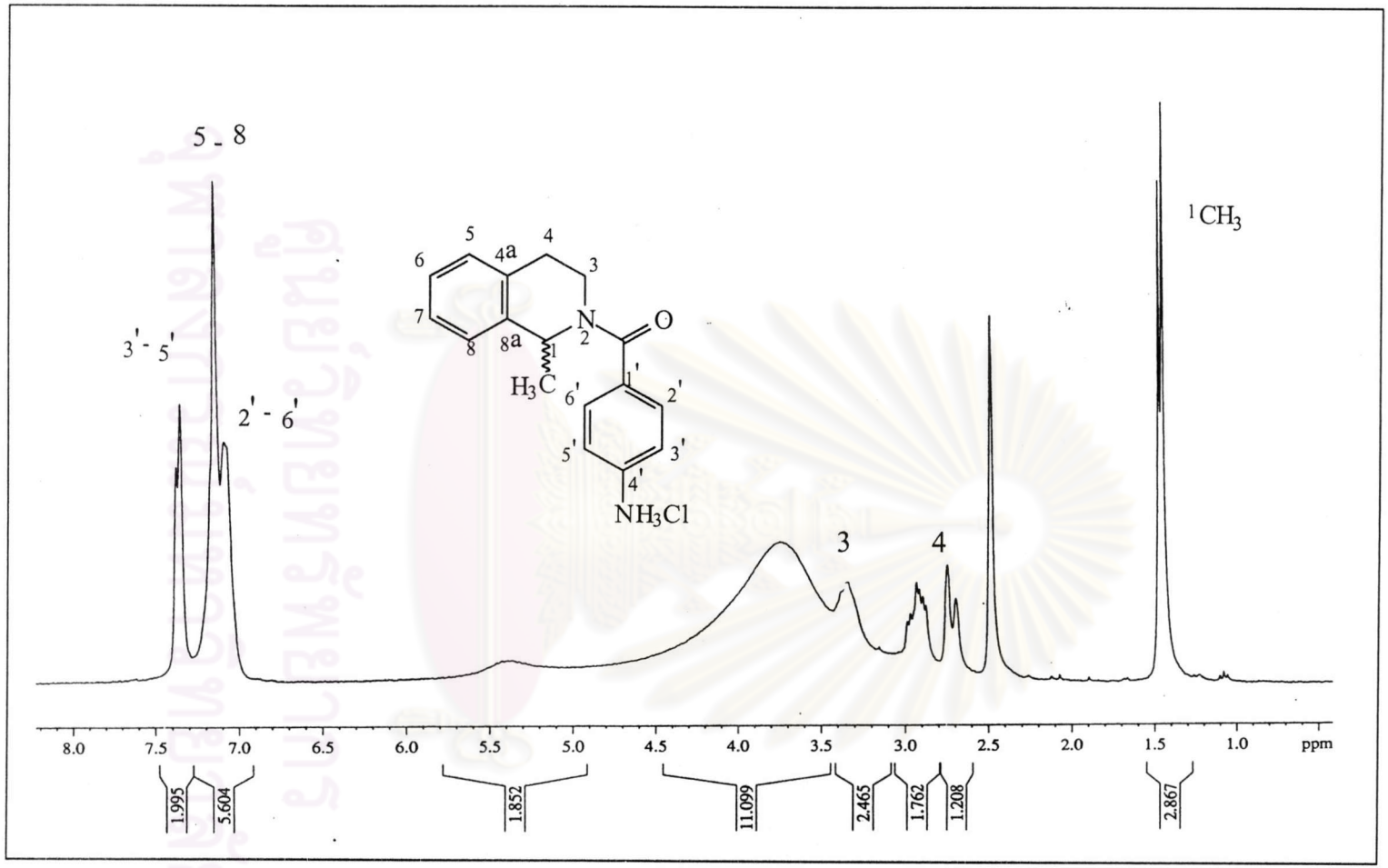


Figure 108. The 300 MHz ^{1}H-NMR spectrum of *N*-(*p*-aminobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline hydrochloride in DMSO-d6

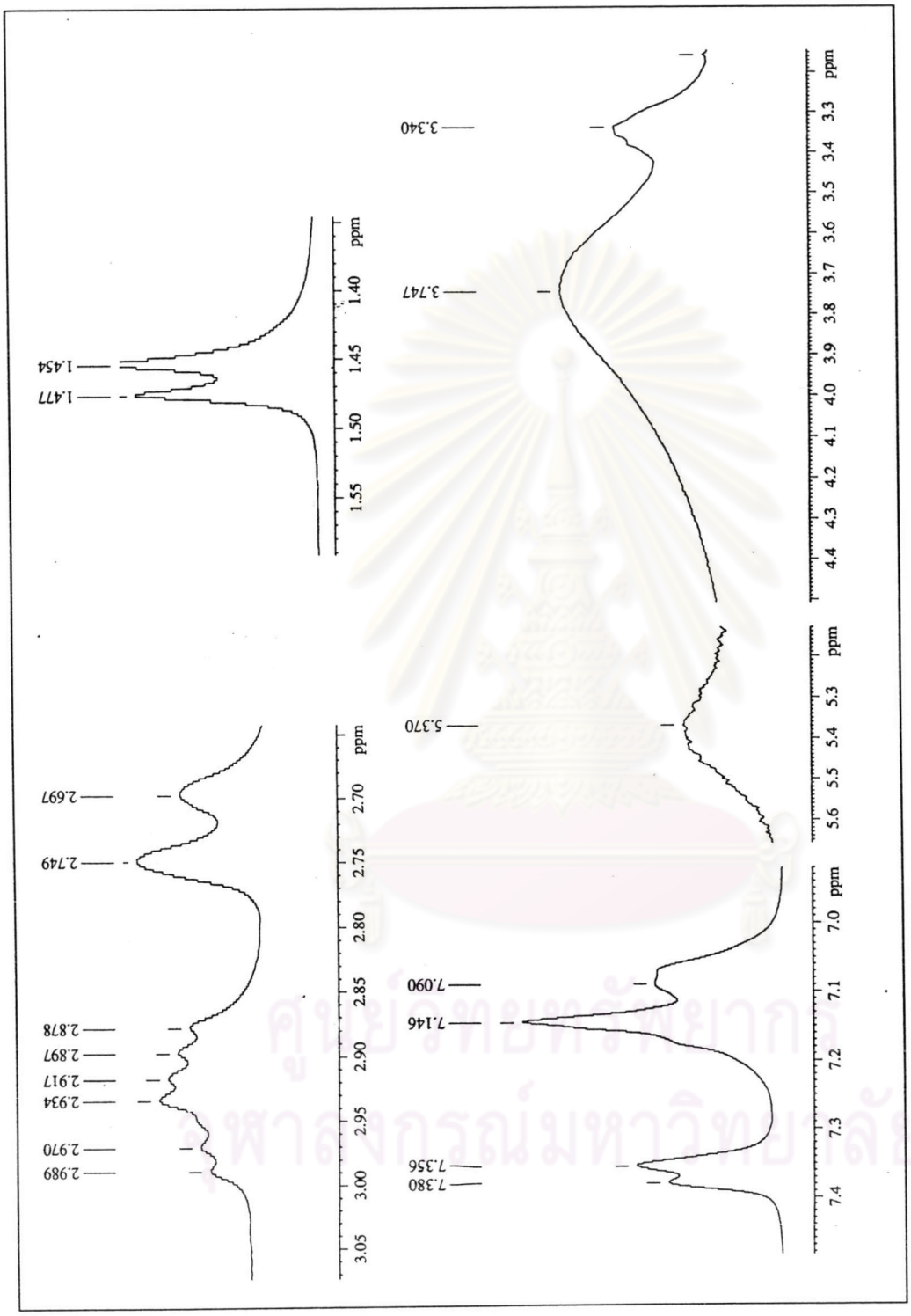


Figure 109. The 300 MHz ^{1}H-NMR spectrum of *N*-(*p*-aminobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline hydrochloride in DMSO-d6 (Enlarged-scale)

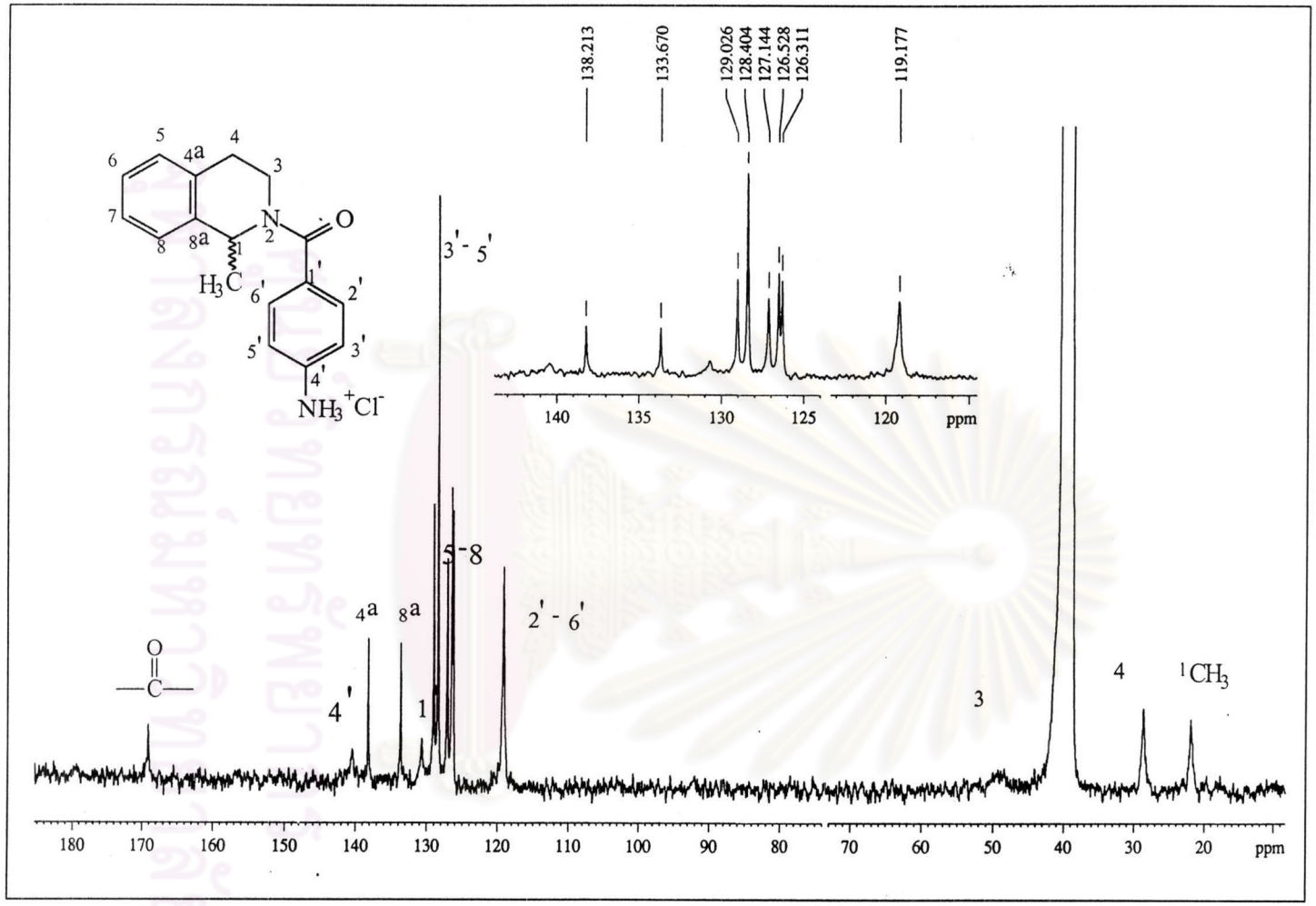


Figure 110. The 75 MHz ^{13}C-NMR spectrum of *N*-(*p*-aminobenzoyl)-1,2,3,4-tetrahydro-1-methylisoquinoline hydrochloride in DMSO-d6