CHAPTER III

EXPERIMENTAL

Instruments.

1. Infrared Spectrophotometers : Perkin-Elmer FT-IR 1760 X (The Scientific and Technological Research Equipment Center, Chulalongkorn University); Perkin-Elmer 283 (Faculty of Pharmaceutical Sciences, Chulalongkorn University).

2. Nuclear Magnetic Resonance Spectrophotometers : Brucker FT-NMR (80 MHz) (Department of Science Service, Ministry of Science, Technology and Energy); Brucker ACF200 (200 MHz) (Department of Chemistry, Faculty of Sciences, Chulalongkorn University); Jeol JNM-A500 (500 MHz) (The Scientific and Technological Research Equipment Center, Chulalongkorn University).

3. Mass Spectrometer : Jeol FX 3000 double focusing (The Scientific and Technological Research Equipment Center, Chulalongkorn University).

4. Melting Point Apparatus : Buchi capillary melting point apparatus (Department of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Chulalongkorn University).

Chemicals.

Benzoyl chloride (May & Baker LTD.).

Tetrahydrofuran (Merck).

Zinc chloride (Merck).

4-Toluidine (Sigma).

Sodium hydroxide (B.P. grade).

Formic acid 85% (Carlo Erba).

Aluminium chloride (Fluka Chemie AG).

Potassium carbonate (Merck).

p-Nitrotoluene (Laboratory grade).

Sodium dichromate dihydrate (Laboratory grade)

p-Nitrobenzoic acid (Fluka Chemie AG).

Phosphorus pentachloride (May & Baker LTD.).

Sulphuric acid 95-97% (Merck).

Palladium on activated charcoal (10% Pd) (Merck).

All solvents used were either B.P. or laboratory grade.

Chemical Preparations.

1. *p*-Nitrobenzoic acid.

46 g (0.33 mol) of *p*-nitrotoluene, 136 g of sodium dichromate dihydrate and 300 ml of water were placed in a 1-litre, two-necked round-bottomed flask equipped with a magentic stirrer. By means of a dropping funnel, 340 g (185 ml) of concentrated sulphuric acid was added during about 30 minutes to the well-stirred mixture. The heat of dilution of the acid caused

the *p*-nitrotoluene to melt and oxidation took place. When all the sulphuric acid had been introduced and the temperature of the mixture commenced to fall, a reflux condenser was attached to the flask, and the mixture was heated to gentle boiling for half an hour. Then the reaction mixture was cooled and poured into 400-500 ml. of water. The crude *p*-nitrobenzoic acid was filter at the pump and was washed with about 200 ml of water. The solid was transferred to a 1-litre beaker, about 200 ml of 5 per cent sulphuric acid (11 g or 6 ml of concentrated sulphuric acid added to 200 ml of water) was added and the mixture was digested on a water bath, with agitation, in order to remove the chromium salts as completely as possible. Then the mixture was allowed to cool and filtered again. The acid was transferred to a beaker, any lumps of material were broken up and treated with 5 per cent sodium hydroxide solution until the liquid remained alkaline. The *p*-nitrobenzoic acid passed into solution, any unchanged *p*-nitrotoluene remained undissolved and chromium salts are converted into chromic hydroxide and/or sodium chromite. About 5 g of decolourising carbon was added and the mixture was warmed to about 50°c with stirring for 5 minutes and filtered with suction. The alkaline solution of sodium *p*-nitrobenzoate was run into about 450 ml of well-stirred 15 per cent sulphuric acid (74 g or 40 ml of concentrated sulphuric acid in 400 ml of water). The acid should not be added to the alkaline solution, for in this way the acid is liable to be contaminated by the sodium salt. Finally, the purified acid was filtered at the pump, washed thoroughly with cold water and dried in the oven. The yield of *p*-nitrobenzoic acid, m.p.236°c, was 48 g (86%) : this is sufficiently pure for most purposes. Reference m.p. in literature is 237°c (Furniss et al., 1991).

IR	: 3117-2840	cm^{-1}	(ν O-H combined with ν aromatic C-H)
(KBr	1692	cm^{-1}	(ν C=O carboxylic acid)
pellet)	1606	cm^{-1}	(ν aromatic C-C ring)
	1542	cm^{-1}	(ν_{as} N-O)
	1429	cm^{-1}	(δ O-H)
	1351	cm^{-1}	(ν_{sym} N-O)
	1293-1279	cm^{-1}	(ν C-O)
	929	cm^{-1}	(δ out-of-plane O-H)
	800	cm^{-1}	(δ out-of-plane aromatic C-H)

(Figure 23.)

2. *p*-Nitrobenzoyl chloride.

100 g (0.6 mol) of pure *p*-nitrobenzoic acid and 126 g (0.6mol) of pure phosphorus pentachloride were mixed in a 500-ml round-bottomed flask. The flask was fitted with a calcium chloride guard-tube and the latter was connected to a gas absorption device. The flask was heated on a water bath, with occasional shaking, until the reaction commenced and then for a further 30 minutes or until the vigorous evolution of hydrogen chloride had almost ceased : a pale yellow homogeneous liquid was formed. A still-head connected with a water-cooled condenser was attached, and the phosphorus oxychloride (b.p. 107°c) was removed at ordinary pressure either by heating in an oil bath gradually to 200-220°c or by heating in an air bath until the boiling point was about 150°c. The mixture was allowed to cool and the excess phosphorus pentachloride was washed with diethyl ether. The yield of *p*-nitrobenzoyl chloride (a yellow crystalline solid, m.p. 70°c) was 105 g (95%) and was pure enough for most purposes. Reference m.p. is 71°c (Furniss et al.,1991). A

perfectly pure product, m.p. 73°c, was obtained by recrystallising from carbon tetrachloride.

IR : 1775 cm^{-1} (ν C=O acid chloride)
(Nujol 1613,1545 cm^{-1} (ν aromatic C-C ring)
mull) 842 cm^{-1} (δ out-of-plane aromatic C-H)
(The bands at 3000-2860,1470,1383 cm^{-1} are Nujol's.)
(Figure 24.)

3. 4-Chlorobutyl benzoate.

94.50 g (0.69 mol) of anhydrous zinc chloride and 50.00 g (0.69 mol) of tetrahydrofuran were placed in a 500-ml, two-necked round-bottomed flask provided with a reflux condenser and a dropping funnel. The flask was cooled in a water bath and 97.47 g (0.69 mol) of benzoyl chloride was introduced into the dropping funnel; a calcium chloride guard-tube was inserted into the mouth of the funnel. The acid chloride was added dropwise (45 minutes) to the well-stirred mixture with frequent shaking. If the reaction shows signs of becoming vigorous the rate of addition must be decreased. When all of the acid chloride had been introduced and the temperature of the mixture began to fall, the mixture was heated to gentle boiling for three hours. Then, the reaction mixture was poured into water. The crude product was extracted with 100-ml chloroform for three times. The chloroform extract was washed with a little 5% w/v sodium hydroxide solution, then with three 100-ml portions of water and dried with anhydrous sodium sulphate. The crude 4-Chlorobutyl benzoate was distilled through a fractionating column under diminished pressure. The 4-Chlorobutyl benzoate was collected as a colourless liquid at

136°c/2 bar; the yield was 146.88 g. (99.60%)

IR :	3080-3030	cm^{-1}	(ν aromatic C-H)
(Neat)	3000-2840	cm^{-1}	(ν aliphatic C-H)
	1720	cm^{-1}	(ν C=O ester)
	1602,1584	cm^{-1}	(ν aromatic C-C ring)
	1450	cm^{-1}	(δ CH_2)
	1275	cm^{-1}	(ν C(=O)-O)
	1115	cm^{-1}	(ν O-C(alkyl))
	1070,1026	cm^{-1}	(δ in-plane aromatic C-H)
	710	cm^{-1}	(δ out-of-plane aromatic C-H)

(Figure 25.)

^{1}H-NMR :	1.93	ppm (4H, complex)
($CDCl_3$)	3.59	ppm (2H, t)
	4.35	ppm (2H, t)
	7.40-7.51	ppm (3H, complex)
	8.04	ppm (2H, dd)

(Figure 26.)

4. 4-[N-(*o*-Toluidino)]butyl benzoate hydrochloride salt.

140.00 g (0.66 mol) of 4-Chlorobutyl benzoate and 176.50 g (1.65 mol) of *o*-Toluidine were mixed, divided, and filled in twelve test tubes with screw caps. The caps were screwed tightly. Then, the test tubes and contents were heated in an oil bath to 125°c-130°c for 6 hours. The tubes were allowed to cool and the liquid mixture solidified. *n*-Hexane was added to dissolved the

crude product. The insoluble *o*-Toluidine hydrochloride was filtered off. A 10% w/v hydrochloric acid solution was added to the hexane filtrate. The hydrochloride salt of the product was formed and precipitated. Then, it was filtered off. Upon recrystallisation from absolute ethanol, 157.24 g (74.70%) of 4-[N-(*o*-Toluidino)]butyl benzoate hydrochloride salt, m.p. 176-178°c (decomposed), was obtained.

IR	: 3080-3030	cm^{-1}	(ν aromatic C-H)
(KBr	3000-2840	cm^{-1}	(ν aliphatic C-H)
pellet)	3000-2455	cm^{-1}	(ν $^{+}NH_2$)
	1716	cm^{-1}	(ν C=O ester)
	1577	cm^{-1}	(ν aromatic C-C ring)
	1501,1479,1447	cm^{-1}	(δ C-H mixed with ν aromatic C-C ring)
	1278	cm^{-1}	(ν C(=O)-O)
	1115	cm^{-1}	(ν O-C(alkyl))
	755,711	cm^{-1}	(δ out-of-plane aromatic C-H)
	(Figure 27.)		

^{1}H-NMR :	1.79	ppm (2H, tt, J=7.6, 7.6 Hz)
($CDCl_3$)	2.09	ppm (2H, tt, J=7.6, 7.6 Hz)
	2.58	ppm (3H, s)
	3.35	ppm (2H, t, J=7.9 Hz)
	4.19	ppm (2H, t, J=7.6 Hz)
	7.19-7.22	ppm (2H, complex)
	7.27	ppm (1H, m)
	7.41	ppm (2H, m)
	7.54	ppm (1H, tt, J=7.6, 1.2 Hz)

7.73 ppm (1H, d, J=7.6 Hz)

7.97 ppm (2H, dd, J=8.2, 1.2 Hz)

11.37 ppm (1H, broad, s)

(Figure 28-31.)

5. 4-[N-(*o*-Toluidino)]butanol.

56.34 g (1.41 mol) of sodium hydroxide was dissolved in 300 ml of water in a 1-litre round-bottomed flask. 150.00 g (0.47 mol) of 4-[N-(*o*-Toluidino)]butyl benzoate hydrochloride salt was added into the flask with shaking. Then, 200 ml of absolute ethanol was added to produce a homogeneous solution. A reflux condenser was attached to the flask and the mixture was refluxed for 3 hours; hydrolysis was then completed. Ethanol was distilled off as much as possible by a rotary evaporator. After that, the mixture was extracted with three 100-ml portions of chloroform. The combined chloroform extract was washed with water to remove the contaminated sodium hydroxide. Subsequently, the chloroform extract was dried with anhydrous sodium sulphate and chloroform was evaporated by the rotary evaporator. The crude aminoalcohol was then purified by distillation through a fractionating column under reduced pressure. The 4-[N-(*o*-Toluidino)]butanol was collected at 150°c/1.5 bar. The yield was 71.01 g (84.50%).

IR	: 3420	cm^{-1}	(ν O-H, intermolecular hydrogen bonding)
(Neat)	3080-3030	cm^{-1}	(ν aromatic C-H)
	3000-2840	cm^{-1}	(ν aliphatic C-H)
	1618,1600	cm^{-1}	(ν aromatic C-C ring)
	1521,1482,1458	cm^{-1}	(δ C-H mixed with ν aromatic C-C ring)

1058 cm^{-1} (ν C-O)

750 cm^{-1} (δ out-of-plane aromatic C-H)

(Figure 32.)

^{1}H-NMR : 1.66 ppm (2H, tt, J=6.7, 6.7 Hz)

($CDCl_3$) 1.72 ppm (2H, tt, J=6.7, 6.7 Hz)

2.12 ppm (3H, s)

3.16 ppm (2H, t, J=6.7 Hz)

3.65 ppm (2H, t, J=6.1 Hz)

6.61 ppm (1H, d, J=7.9 Hz)

6.65 ppm (1H, ddd, J=7.3, 7.3, 0.9 Hz)

7.04 ppm (1H, d, J=7.1 Hz)

7.11 ppm (1H, ddd, J=7.9, 7.9, 0.9 Hz)

(Figure 33-36.)

6. N-(4-Hydroxybutyl)-N-(*o*-tolyl)formamide.

50.00 g (0.28 mol) of 4-[N-(*o*-Toluidino)]butanol was placed in a 500-ml two-necked round-bottomed flask fitted with a reflux condenser and a dropping funnel. 12.62 ml (0.28 mol) of 85% w/w formic acid solution was filled in the dropping funnel. The acid solution was introduced dropwise to the well-stirred liquid. After all of the acid solution had been added, the mixture was heated on a boiling water bath for 3 hours. The mixture was then allowed to cool and 100 ml of chloroform was added. Later, the chloroform mixture was washed with water to remove the unreacted formic acid and with 5% w/v hydrochloric acid solution to remove the unreacted 4-[N-(*o*-Toluidino)]butanol. Chloroform was evaporated by a rotary evaporator. The residual oily product

was purified with a silica gel column, eluted with chloroform. The yield of N-(4-Hydroxybutyl)-N-(*o*-tolyl) formamide was 38.68 g (66.90%).

IR	: 3419	cm^{-1}	(ν O-H)
(Neat)	3080-3030	cm^{-1}	(ν aromatic C-H)
	3000-2840	cm^{-1}	(ν aliphatic C-H)
	1668	cm^{-1}	(ν C=O amide)
	1602,1586	cm^{-1}	(ν aromatic C-C ring)
	1494,1459	cm^{-1}	(δ C-H mixed with ν aromatic C-C ring)
	1067	cm^{-1}	(ν C-O)
	769,731	cm^{-1}	(δ out-of-plane aromatic C-H)
	(Figure 37.)		

^{1}H-NMR	: 1.26-1.36	ppm (4H, complex)
($CDCl_3$+	1.95 (minor), 2.01 (major)	ppm (3H, s)
CD_3OD)	3.30	ppm (2H, t, J=5.9 Hz)
(1:1)	3.41	ppm (2H, t, J=6.6 Hz)
	4.14	ppm (1H, broad, s)
	6.81-7.07	ppm (3H, complex)
	7.79 (major), 8.03 (minor)	ppm (1H, s)
	(Figure 38.)	

7. N-(4-Chlorobutyl)-N-(*o*-tolyl)formamide.

20.69 g (12.69 ml, 0.17 mol) of redistilled thionyl chloride was placed in the 100-ml round-bottomed flask and 30.00 g (0.15 mol) of N-(4-Hydroxybutyl)-N-(*o*-tolyl)formamide was placed in the dropping funnel. The

alcohol was added with stirring during 2 hours; there was a slight evolution of heat, sulphur dioxide was evolved and the liquid darkened considerably. When all the alcohol had been added, the mixture was heated in the hot water bath (temperature 40-50°c) for 3 hours. The apparatus for distillation was rearranged and the excess of thionyl chloride was distilled slowly, passing over below 80°c. The residual substance was poured into iced water. The oily product was separated and added with 100-ml chloroform. Subsequently, the mixture was washed with two 50-ml portions of 5% w/v sodium hydroxide solution and three 100-ml portions of water, successively. The chloroform layer was dried with anhydrous sodium sulphate. The solvent was 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 N-(4-Chlorobutyl)-N-(*o*-tolyl)formamide was 26.90 g (82.30%).

IR	: 3080-3030	cm^{-1}	(ν aromatic C-H)
(Neat)	3000-2840	cm^{-1}	(ν aliphatic C-H)
	1678	cm^{-1}	(ν C=O amide)
	1602,1582	cm^{-1}	(ν aromatic C-C ring)
	1494,1459	cm^{-1}	(δ C-H mixed with ν aromatic C-C ring)
	758,729	cm^{-1}	(δ out-of-plane aromatic C-H)
	(Figure 39.)		

^{1}H-NMR	: 1.58-1.80	ppm (4H, complex)
($CDCl_3$)	2.18 (minor), 2.22 (major)	ppm (3H, s)
	3.49	ppm (2H, t, J=6.3 Hz)
	3.65	ppm (2H, t, J=7.2 Hz)
	7.04-7.28	ppm (4H, complex)

8.05 (major), 8.27 (minor) ppm (1H, s)

(Figure 40.)

8. N-Formyl-1,2,3,4-tetrahydro-4,8-dimethylquinoline.

23.65 g (0.177 mol) of anhydrous aluminium chloride and 100 ml of carbon disulphide were placed in the 500-ml round-bottomed flask. The mixture was stirred and the solution of 20.00 g (0.089 mol) of N-(4-Chlorobutyl)-N-(*o*-tolyl)formamide in 100 ml. carbon disulphide was added slowly from the dropping funnel during 1-2 hours. When all the solution had been run in, the stirring was continued for 3 hours longer. Then, the contents of the flask were poured very cautiously on to 300 g of crushed ice. Chloroform was added to dissolve the solid mass. The organic layer was separated and washed with 100-ml water three times. The solvent extract was dried with anhydrous sodium sulphate. The solvent was evaporated by a rotary evaporator. Purification was achieved by column chromatographic method using silica gel as a stationary phase and chloroform as a mobile phase. The yield of product was 10.41 g (62.10%).

IR	: 3080-3030	cm^{-1}	(ν aromatic C-H)
(Neat)	3000-2840	cm^{-1}	(ν aliphatic C-H)
	1677	cm^{-1}	(ν C=O amide)
	1592	cm^{-1}	(ν aromatic C-C ring)
	1475-1450	cm^{-1}	(δ C-H mixed with ν aromatic C-C ring)
	783,755	cm^{-1}	(δ out-of-plane aromatic C-H)

(Figure 41.)

^{1}H-NMR : 1.28 ppm (3H, d, J=6.9 Hz)

($CDCl_3$) 1.58 ppm (1H, m)

2.07 ppm (1H, m)

2.19 (minor), 2.31 (major) ppm (3H, s)

2.75 ppm (1H, m)

3.59 ppm (1H, ddd, J=-12.7, 7.1, 5.3 Hz)

3.98 ppm (1H, ddd, J=-13.0, 7.7, 7.7 Hz)

7.05-7.13 ppm (3H, complex)

8.24 (minor), 8.30 (major) ppm (1H, s)

(Figure 42.)

9. 1,2,3,4-Tetrahydro-4,8-dimethylquinoline.

8.00 g (0.042 mol) of N-Formyl-1,2,3,4-tetrahydro-4,8-dimethylquinoline and 30 ml of 10% w/v sodium hydroxide solution was placed in the 100-ml round-bottomed flask. Then 20 ml of absolute ethanol was added to produce a homogeneous solution. A reflux condenser was fitted to the flask and the mixture was refluxed for 3 hours; hydrolysis is then completed. Ethanol was disfilled off as much as possible by a rotary evaporator until the residue becomed pasty. The mixture was then extracted with three 100-ml portions of chloroform. The combined chloroform extract was washed with water to remove the residual sodium hydroxide and dried with anhydrous sodium sulphate. Later, the solvent was evaporated *in vacuo*. The oily product was purified by the column chromatography using silica gel as a stationary phase and chloroform as a mobile phase. The yield of the product was 5.80 g (85.10%).

IR : 3450 cm^{-1} (ν N-H)

(Neat) 3080-3030 cm^{-1} (ν aromatic C-H)

3000-2840 cm^{-1} (ν aliphatic C-H)

1610 cm^{-1} (ν aromatic C-C ring)

1505,1491,1478 cm^{-1} (δ C-H mixed with ν aromatic C-C ring)

770,742 cm^{-1} (δ out-of-plane aromatic C-H)

(Figure 43.)

^{1}H-NMR : 1.36 ppm (3H, d, J=7.4 Hz)

($CDCl_3$) 1.75 ppm (1H, m)

2.05 ppm (1H, m)

2.14 ppm (3H, s)

3.00 ppm (1H, m)

3.36-3.70 ppm (3H, complex)

6.65 ppm (1H, dd, J=7.5, 7.5 Hz)

6.95 ppm (1H, d, J=7.3 Hz)

7.03 ppm (1H, d, J=7.5 Hz)

(Figure 44.)

10. N-(*p*-Nitrobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline.

A solution of 4.00 g (0.025 mol) of 1,2,3,4-Tetrahydro-4,8-dimethylquinoline in 25 ml of tetrahydrofuran and 3.43 g of potassium carbonate were added to a 100-ml two-necked round-bottomed flask equipped with a magnetic stirrer, a reflux condenser, an addition funnel, and a hot plate. A solution of 5.53 g (0.030 mol) of *p*-nitrobenzoyl chloride in 25 ml of tetrahydrofuran was added dropwise, and the resulting mixture was refluxed for

12 hours. The solution was then cooled to room temperature, poured into 100 ml of water, and extracted with chloroform (3 x 100 ml). The extracts were combined, washed with 5% w/v of sodium hydroxide solution (1 x 100 ml) and water (3 x 100 ml), successively, and dried over anhydrous sodium sulphate. Later, the solvent was evaporated. The resulting residue was purified by recrystallization from absolute ethanol. The yield of N-(*p*-Nitrobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethyquinoline, m.p.140-142°c, was 6.29 g (81.70%).

IR	: 3080-3030	cm^{-1}	(ν aromatic C-H)
(KBr	3000-2840	cm^{-1}	(ν aliphatic C-H)
pellet)	1648	cm^{-1}	(ν C=O amide)
	1600	cm^{-1}	(ν aromatic C-C ring)
	1517	cm^{-1}	(ν_{as} N-O)
	1477-1409	cm^{-1}	(δ C-H mixed with ν aromatic C-C ring)
	1343	cm^{-1}	(ν_{sym} N-O)
	861-709	cm^{-1}	(δ out-of-plane aromatic C-H)
	(Figure 45.)		

^{1}H-NMR : Assignment for only major conformer.

($CDCl_3$)	1.43	ppm (1H, m)
	1.47	ppm (3H, d, J=6.7 Hz)
	1.75	ppm (3H, s)
	2.39	ppm (1H, dddd, J=-12.8, 9.5, 4.6, 3.4 Hz)
	2.85	ppm (1H, m)
	3.25	ppm (1H, ddd, J=-12.8, 9.5, 3.4 Hz)
	4.74	ppm (1H, ddd, J=-12.8, 9.5, 8.2 Hz)
	6.85	ppm (1H, d, J=7.3 Hz)

7.15 ppm (1H, dd, J=7.3, 7.3 Hz)

7.19 ppm (1H, d, J=7.3 Hz)

7.35 ppm (2H, d, J=8.9 Hz)

7.98 ppm (2H, d, J=8.9 Hz)

(Figure 46-49.)

11. N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline.

A solution of 5.00 g (0.016 mol) of N-(*p*-Nitrobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in absolute ethanol (50 ml) was added to a Parr hydrogenation bottle along with 150 mg of 10% palladium on activated charcoal and subjected to low-pressure hydrogenation (45 psi) for 3 hours. The bottle was then removed, and the contents were filtered. The filtrate was evaporated, and the resulting residue was purified by recrystallisation from benzene. The yield of the product, m.p. 170-172°c, was 3.32 g (73.60%).

IR :	3442	cm^{-1}	(ν_{as} N-H)
(KBr	3349	cm^{-1}	(ν_{sym} N-H)
pellet)	3227	cm^{-1}	(overtone of δ -NH_2)
	3080-3030	cm-1	(ν aromatic C-H)
	3000-2840	cm^{-1}	(ν aliphatic C-H)
	1650-1604	cm^{-1}	(ν C=O amide combined with δ -NH_2)
	1564	cm^{-1}	(ν aromatic C-C ring)
	1516,1477	cm^{-1}	(δ C-H mixed with ν aromatic C-C ring)
	838,783,756	cm^{-1}	(δ out-of-plane aromatic C-H)

(Figure 50.)

EIMS : 281.0 (1.94%), 280.0 (9.48%), 161.0 (2.79%), 121.0 (4.83%),
(m/e) 120.0 (57.49%), 92.0 (7.84%), 65.0 (5.16%)
(Figure 51.)

^{1}H-NMR : -at room temperature. See figure 52.
($CDCl_3$) -at high temperature (40°c, 50°c). See figure 53.
-at low temperature (15°c, 0°c, -15°c, -30°c). See figure 54-56.

^{1}H-NMR : Assignment for only major conformer.

($CDCl_3$, at -30°c)		
	1.38	ppm (1H, m)
	1.45	ppm (3H, d, J=6.7 Hz)
	1.76	ppm (3H, s)
	2.34	ppm (1H, dddd, J=-12.8, 9.8, 4.6, 2.8 Hz)
	2.82	ppm (1H, m)
	3.24	ppm (1H, ddd, J=-12.5, 9.5, 2.4 Hz)
	3.94	ppm (2H, s)
	4.61	ppm (1H, ddd, J=-12.9, 9.8, 8.6 Hz)
	6.38	ppm (2H, d, J=8.9 Hz)
	6.88	ppm (1H, d, J=6.7 Hz)
	7.03	ppm (2H, d, J=8.3 Hz)
	7.13	ppm (1H, dd, J=7.3, 7.3 Hz)
	7.16	ppm (1H, d, J=6.3 Hz)

(Figure 57-60.)

^{13}C-NMR : -at room temperature. See figure 61.
($CDCl_3$) -at low temperature (-30°c). See figure 62-64.

Other NMR experiments : DEPT135 See figure 65.

HH COSY See figure 66-68.

CH COSY See figure 69-71.

HMBC See figure 72-74.

HH NOESY See figure 75-77.

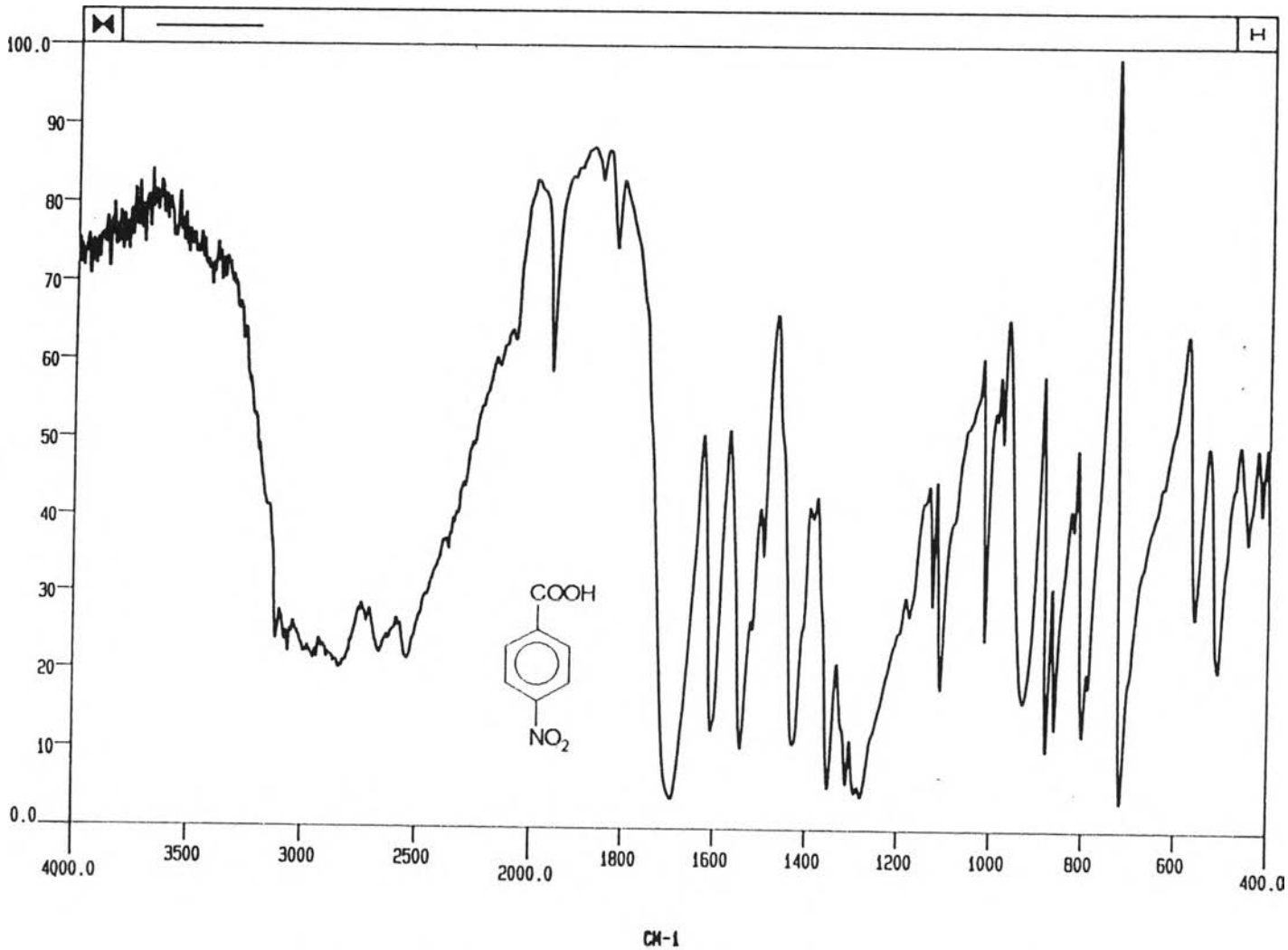

Figure 23. The IR spectrum (KBr pellet) of *p*-Nitrobenzoic acid.

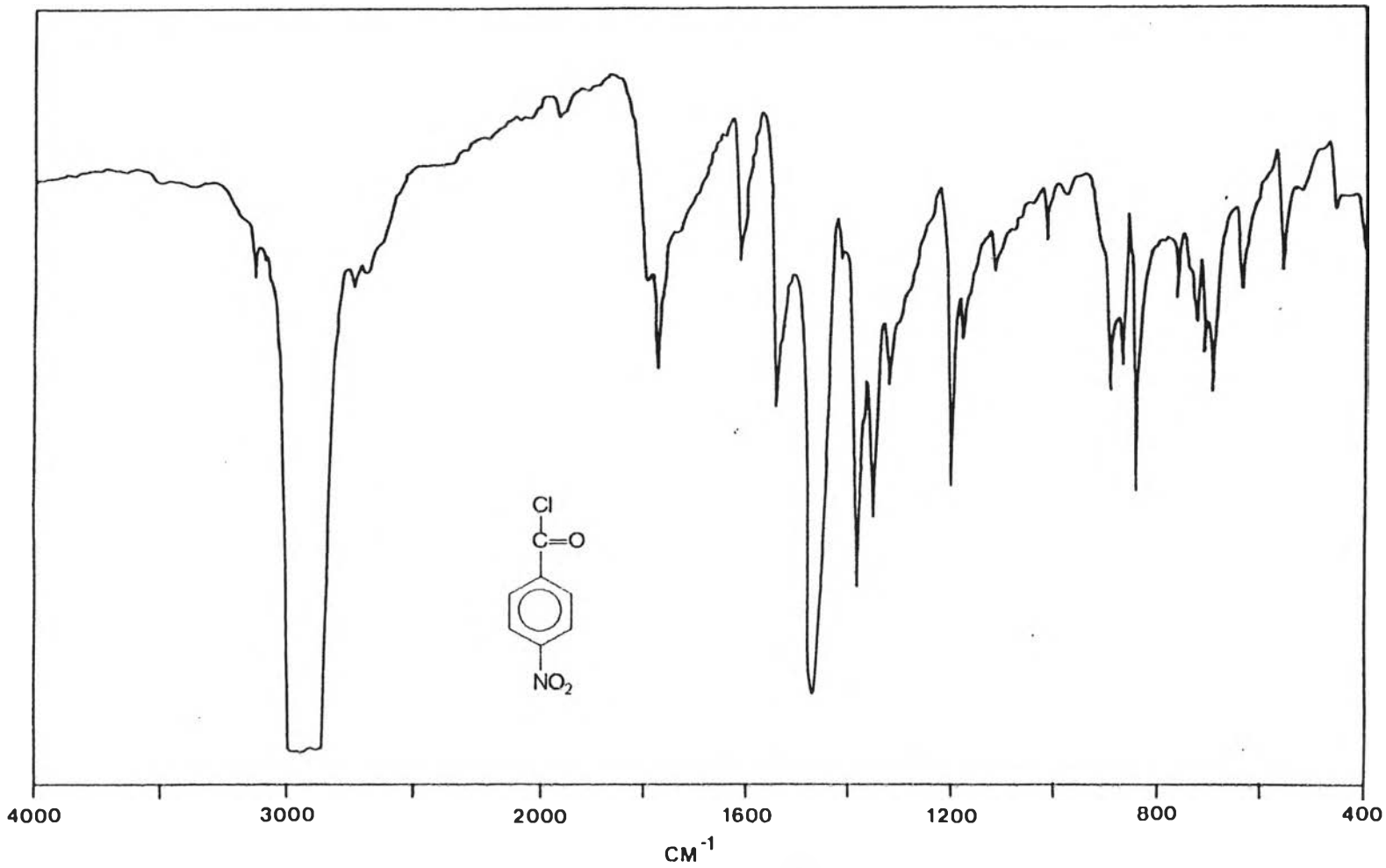

Figure 24. The IR spectrum (Nujol mull) of *p*-Nitrobenzoyl chloride.

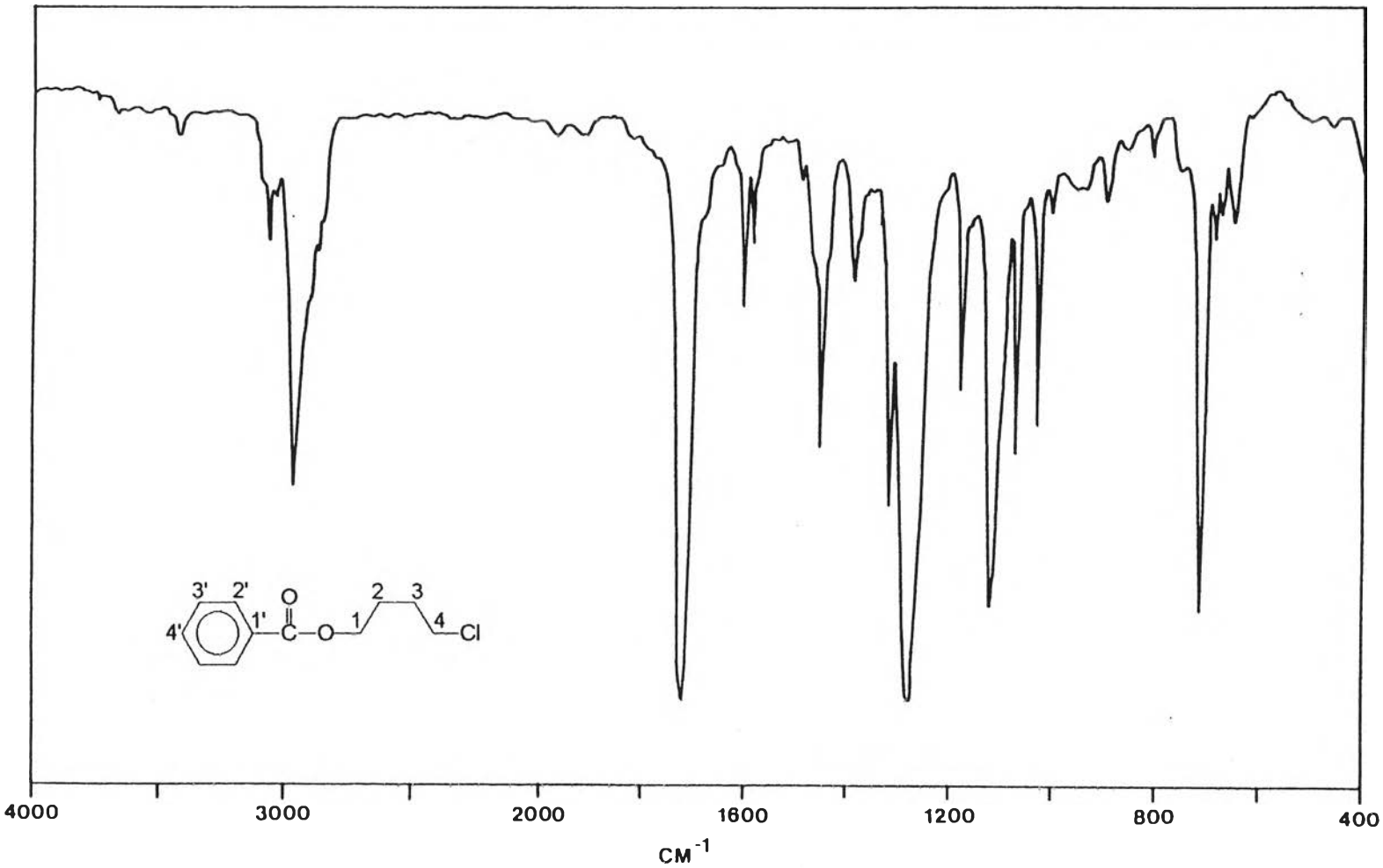

Figure 25. The IR spectrum (Neat) of 4-Chlorobutyl benzoate.

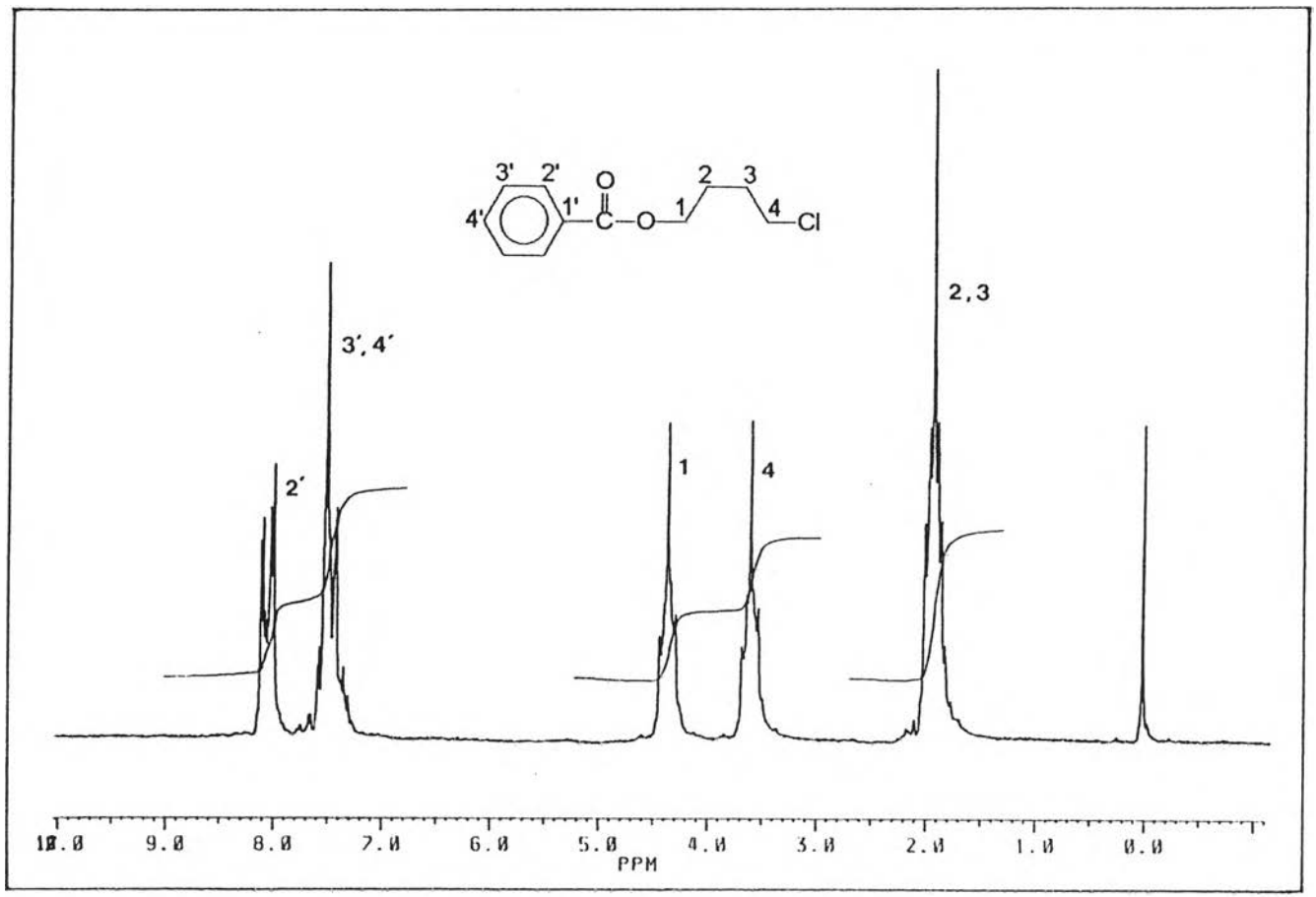

Figure 26. The 80 MHz ^{1}H-NMR spectrum of 4-Chlorobutyl benzoate in $CDCl_3$.

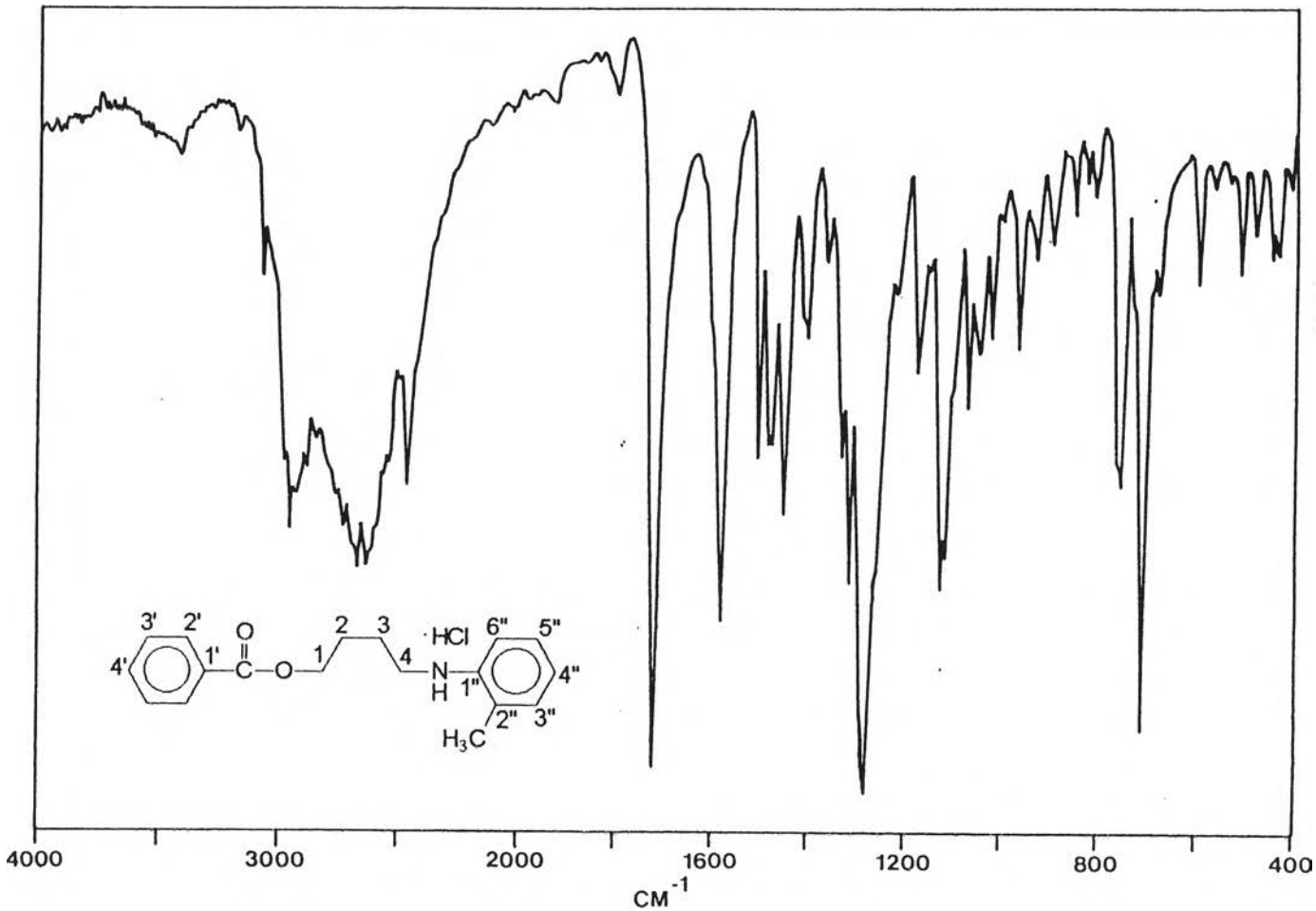

Figure 27. The IR spectrum (KBr pellet) of 4-[N-(*o*-Toluidino)]butyl benzoate hydrochloride salt.

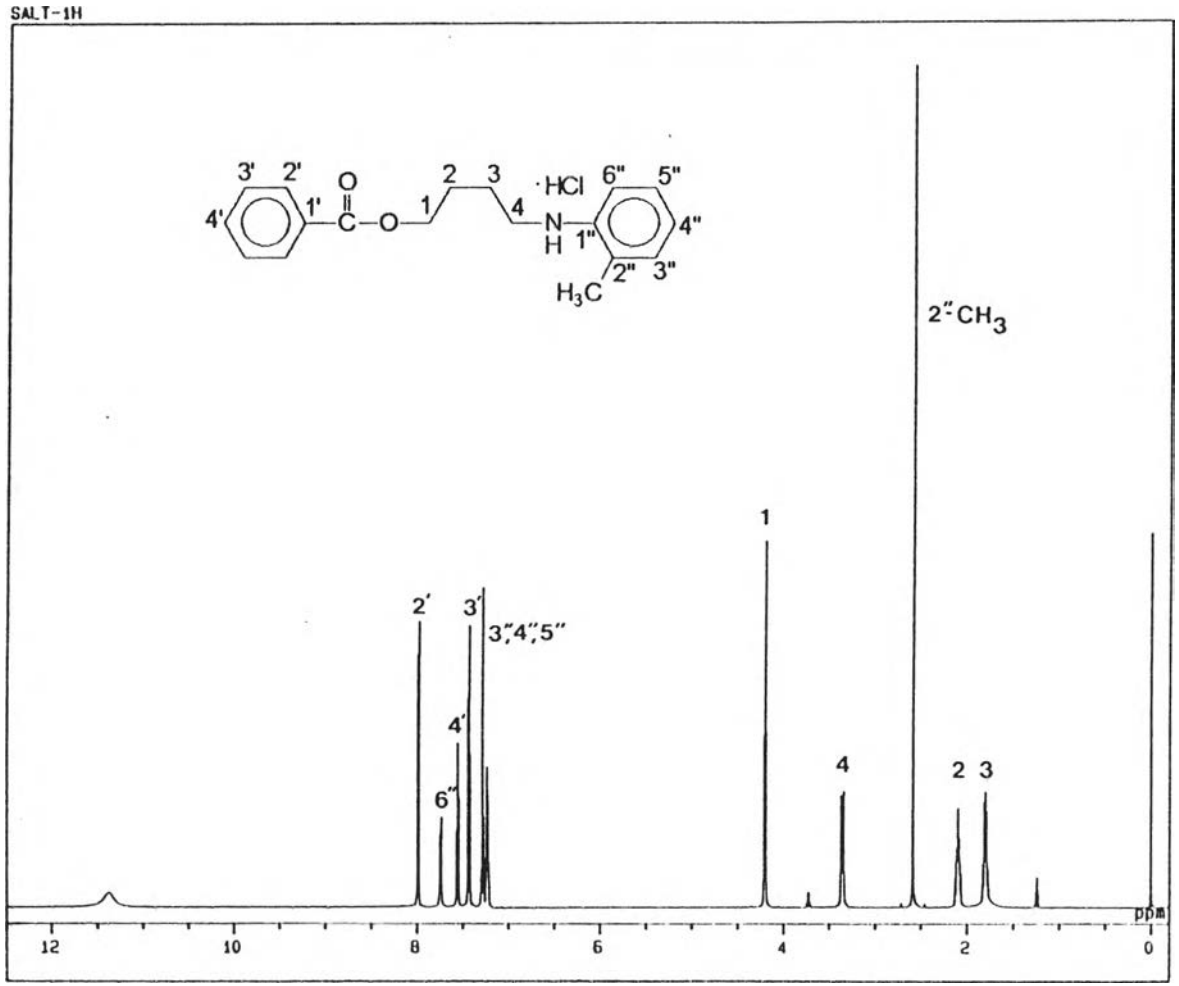

Figure 28. The 500 MHz ^{1}H-NMR spectrum of 4-[N-(*o*-Toluidino)]butyl benzoate hydrochloride salt in $CDCl_3$.

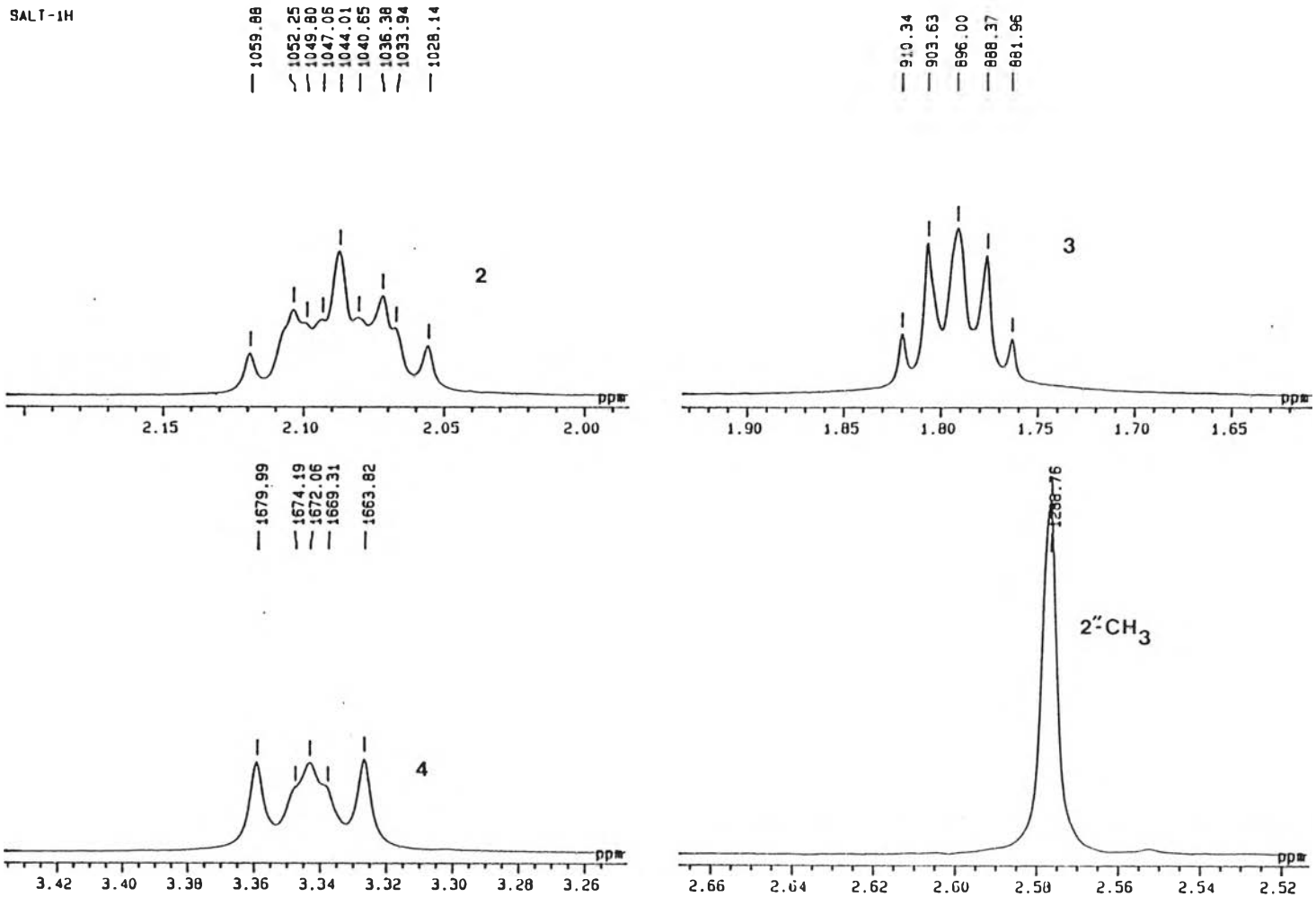

Figure 29. The 500 MHz ^{1}H-NMR spectrum of 4-[N-(*o*-Toluidino)]butyl benzoate hydrochloride salt in $CDCl_3$.

(Enlarged scale : 1.6-3.4 ppm)

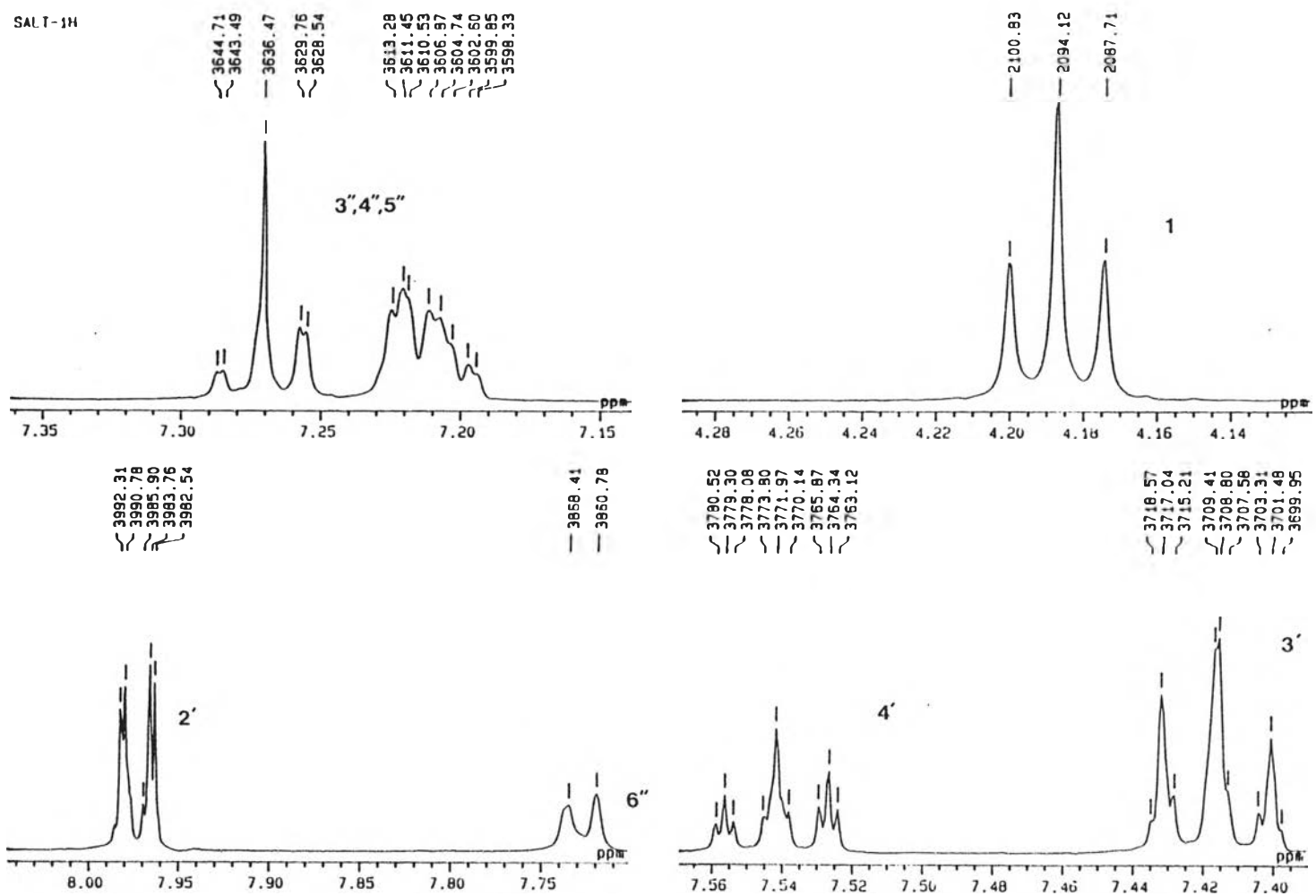

Figure 30. The 500 MHz ^{1}H-NMR spectrum of 4-[N-(*o*-Toluidino)]butyl benzoate hydrochloride salt in $CDCl_3$.

(Enlarged scale : 4.1-8.0 ppm)

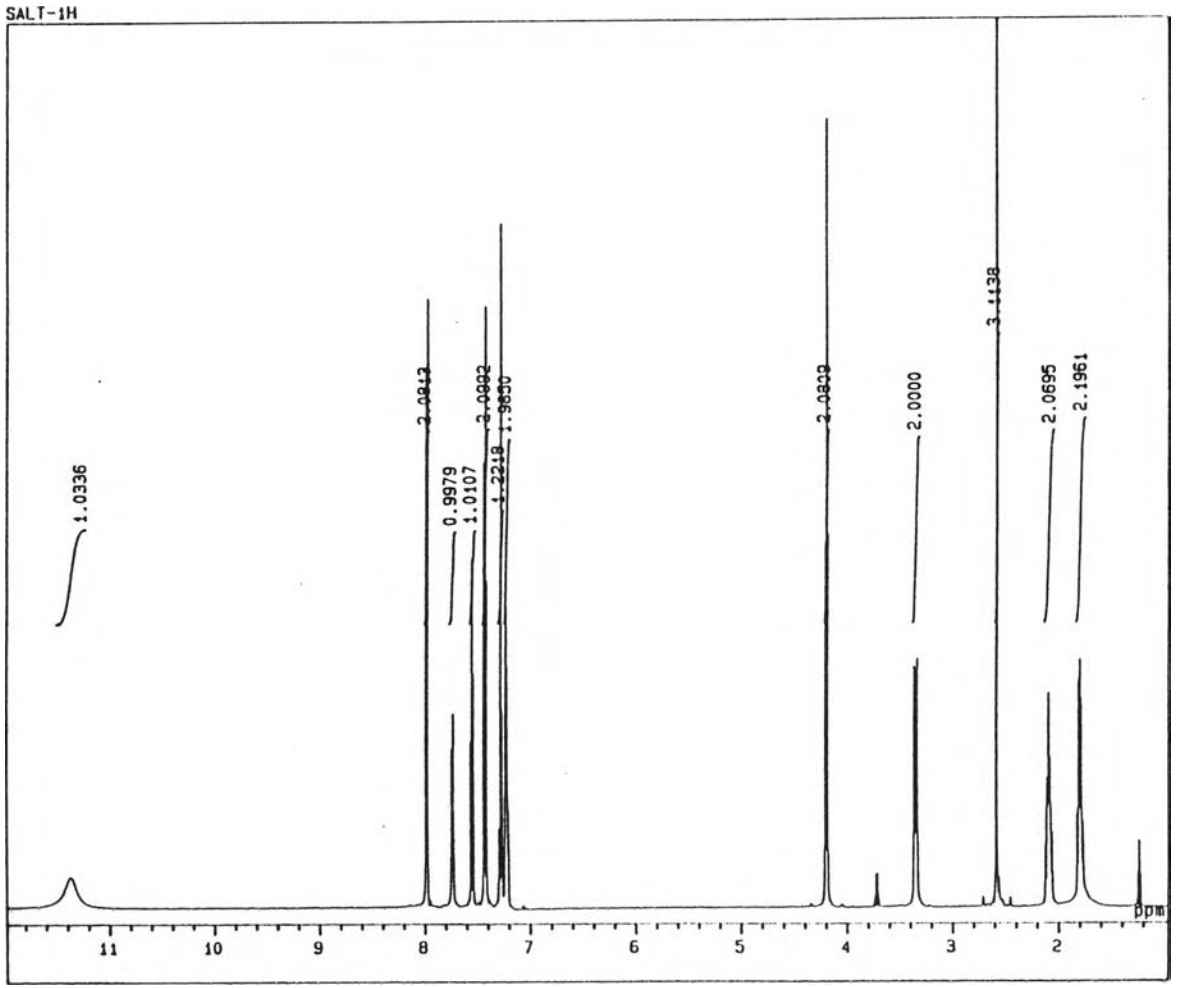

Figure 31. The 500 MHz ^{1}H-NMR spectrum of 4-[N-(*o*-Toluidino)]butyl benzoate hydrochloride salt in $CDCl_3$. (Exhibit the integration.)

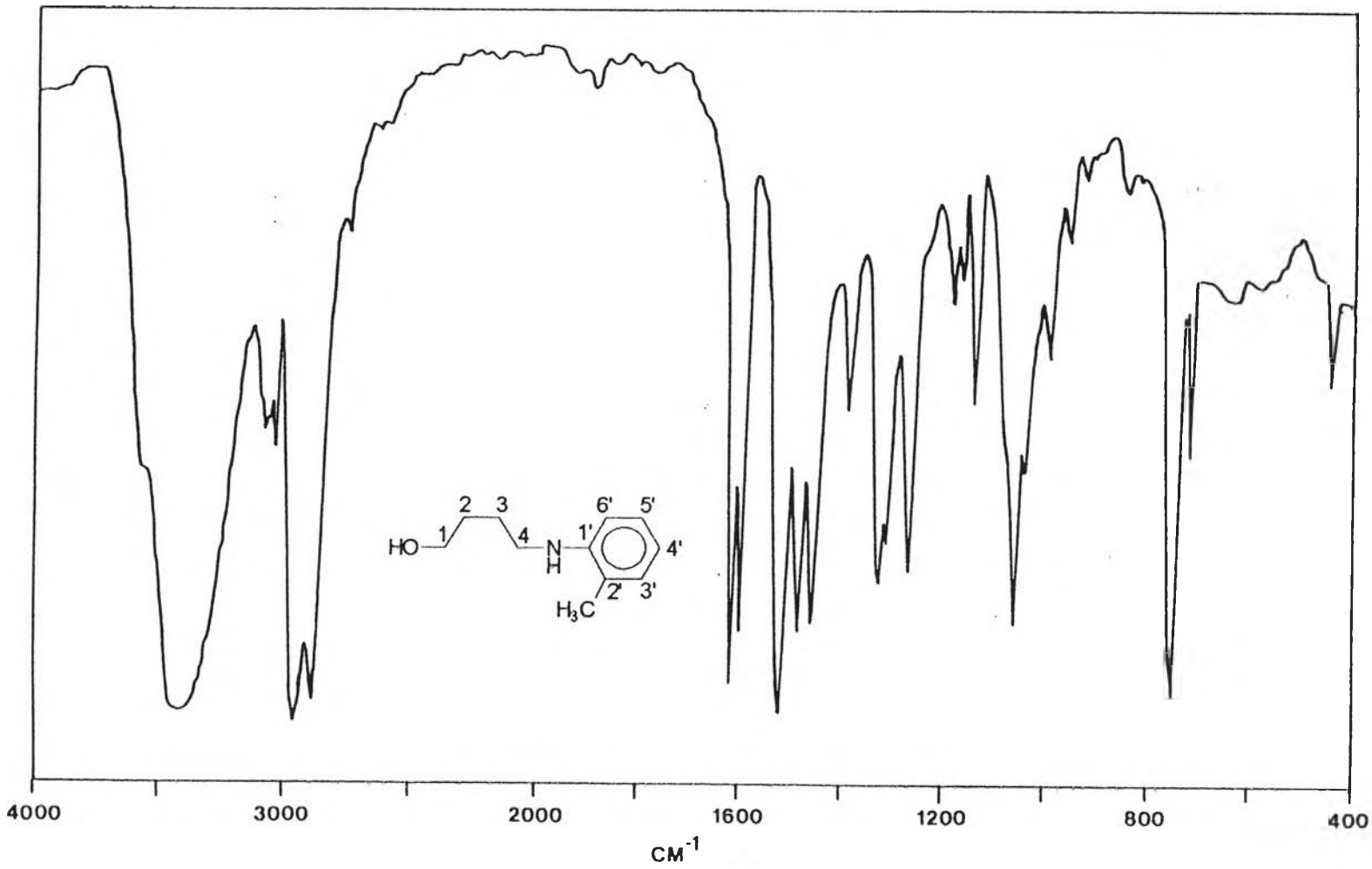

Figure 32. The IR spectrum (Neat) of 4-[N-(*o*-Toluidino)]butanol.

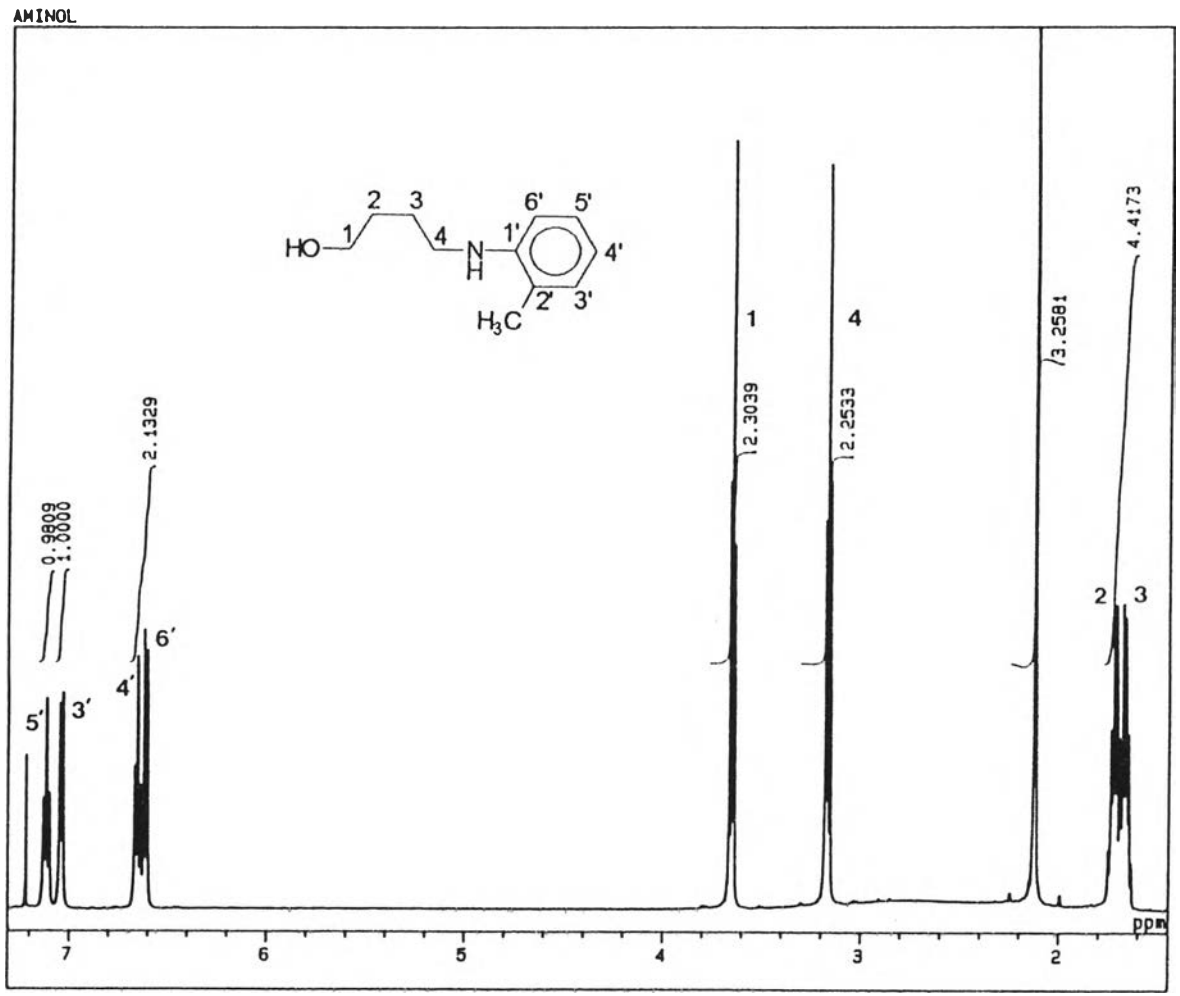

Figure 33. The 500 MHz ^{1}H-NMR spectrum of 4-[N-(*o*-Toluidino)]butanol in $CDCl_3$.

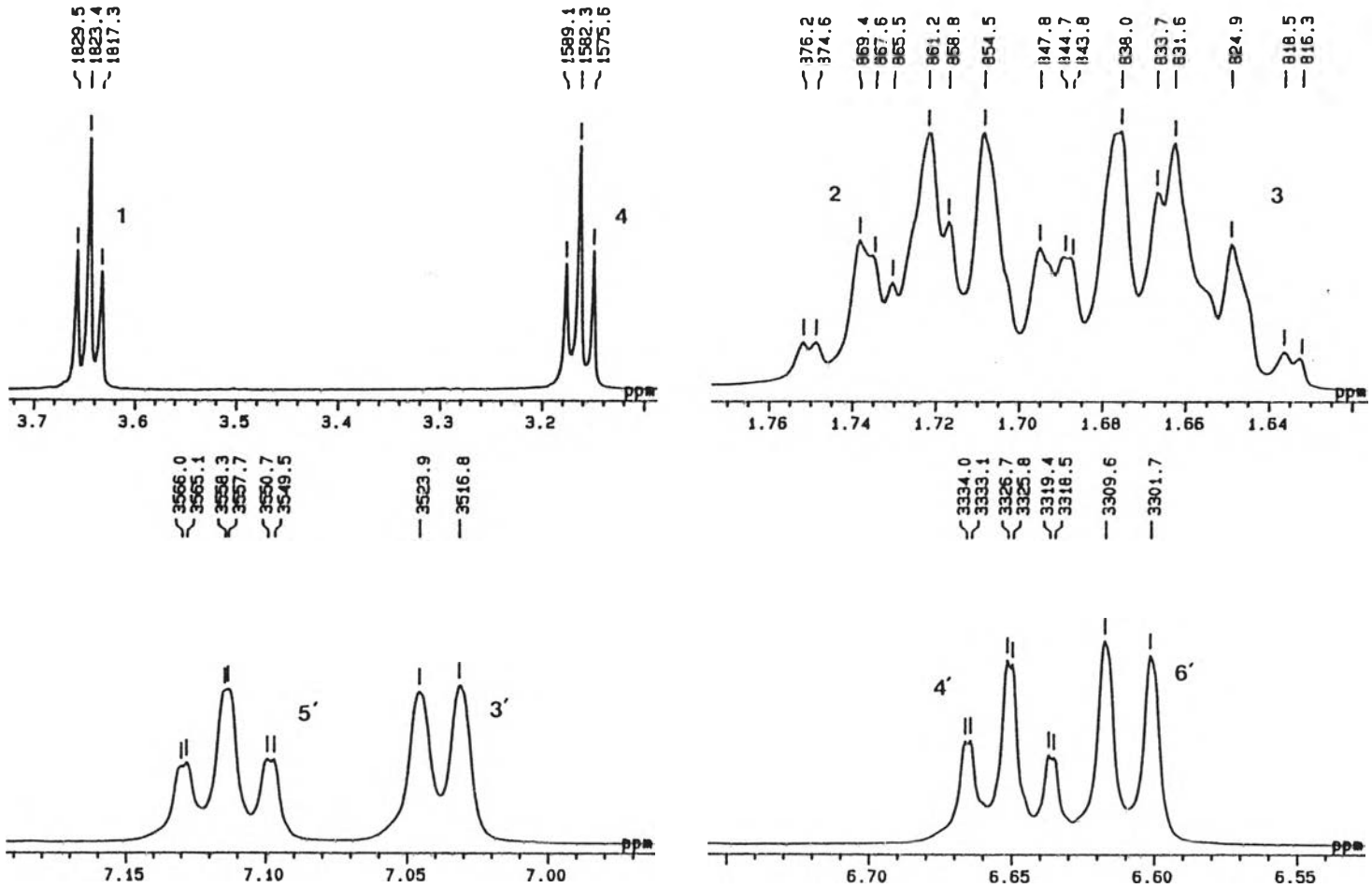

Figure 34. The 500 MHz ^{1}H-NMR spectrum of 4-[N-(*o*-Toluidino)]butanol in $CDCl_3$. (Enlarged scale : 1.6-7.2 ppm)

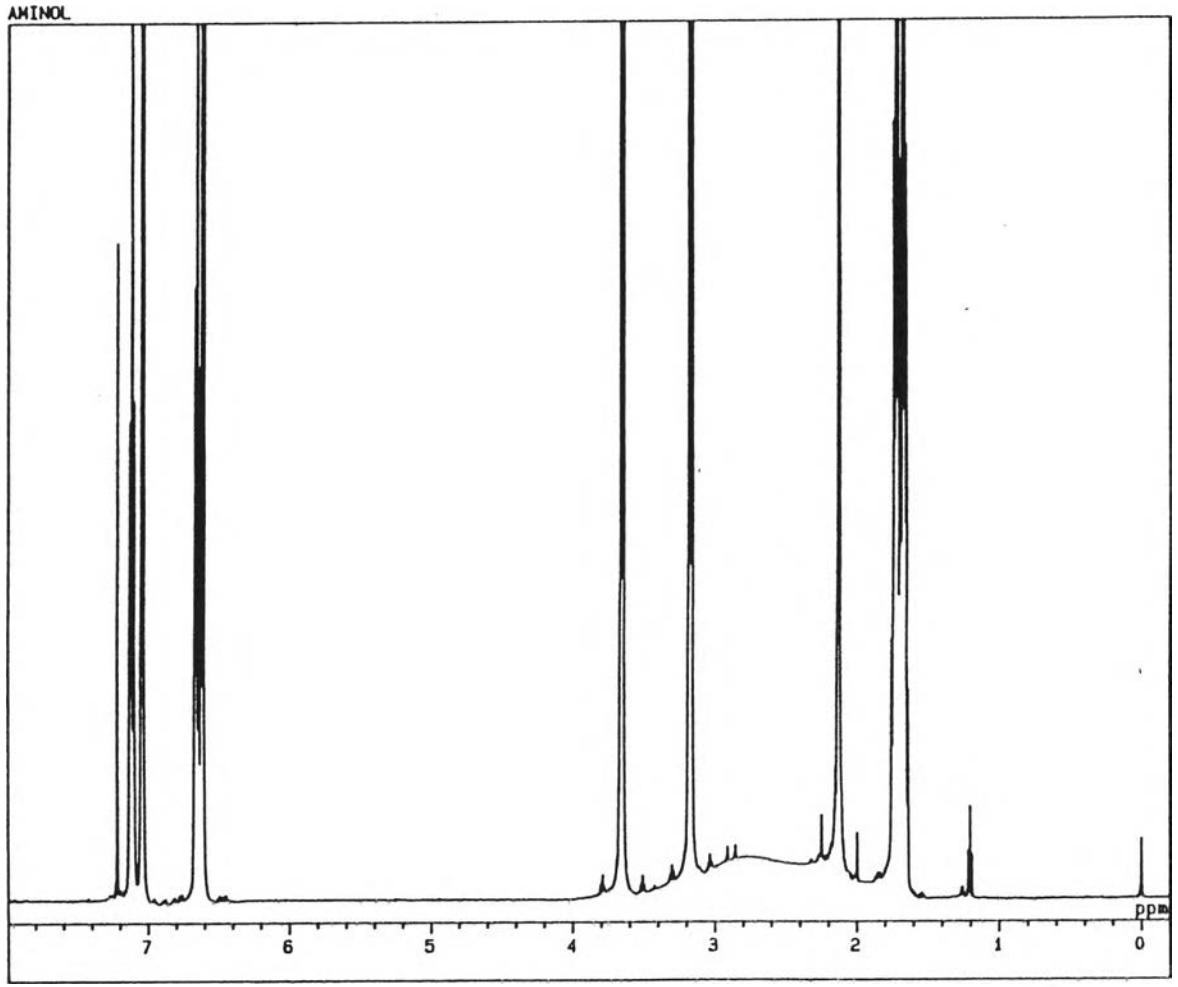

Figure 35. The 500 MHz ^{1}H-NMR spectrum of 4-[N-(*o*-Toluidino)]butanol in $CDCl_3$. (Exhibit the broad signal.)

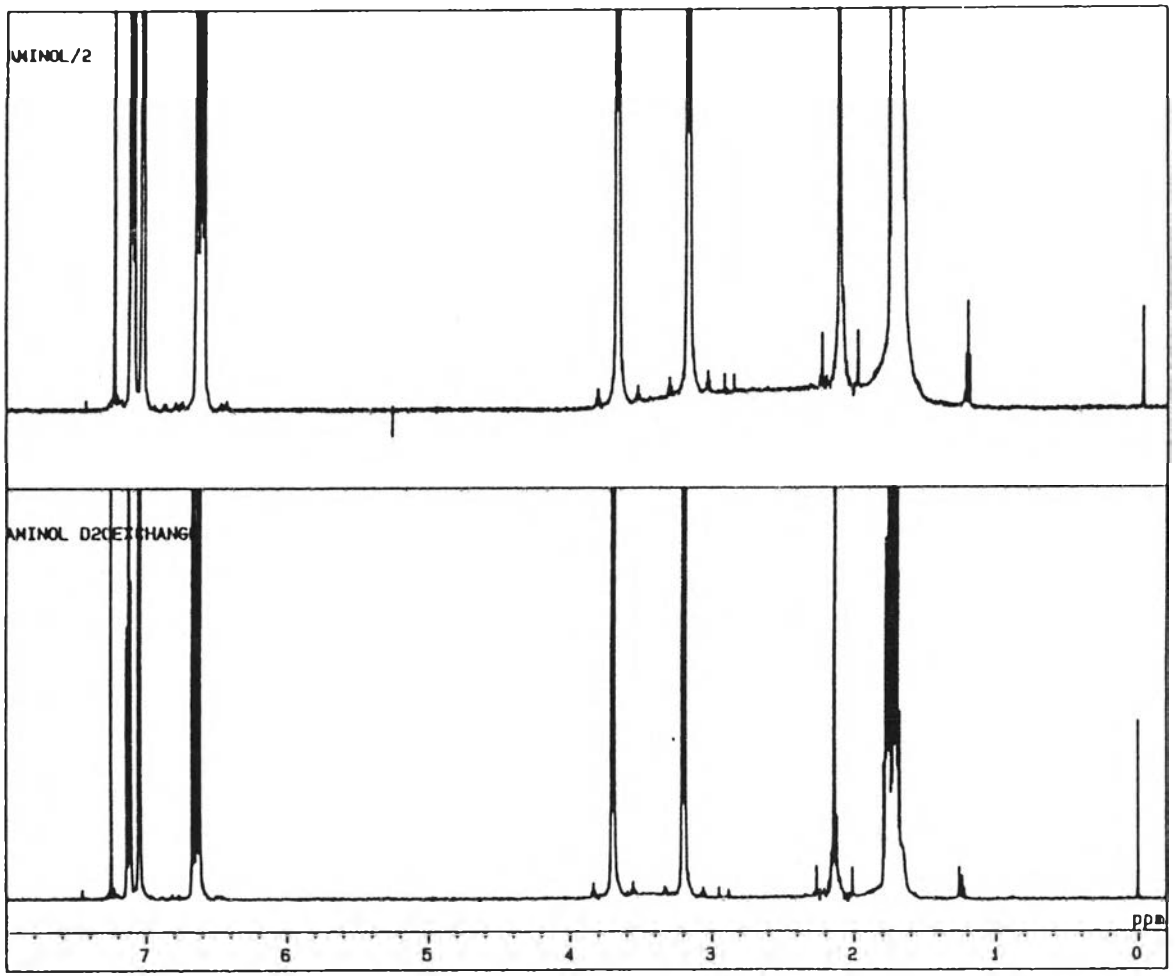

Figure 36. The 500 MHz ^{1}H-NMR spectrum of 4-[N-(*o*-Toluidino)]butanol in $CDCl_3$. (Before and after D_2O exchange)

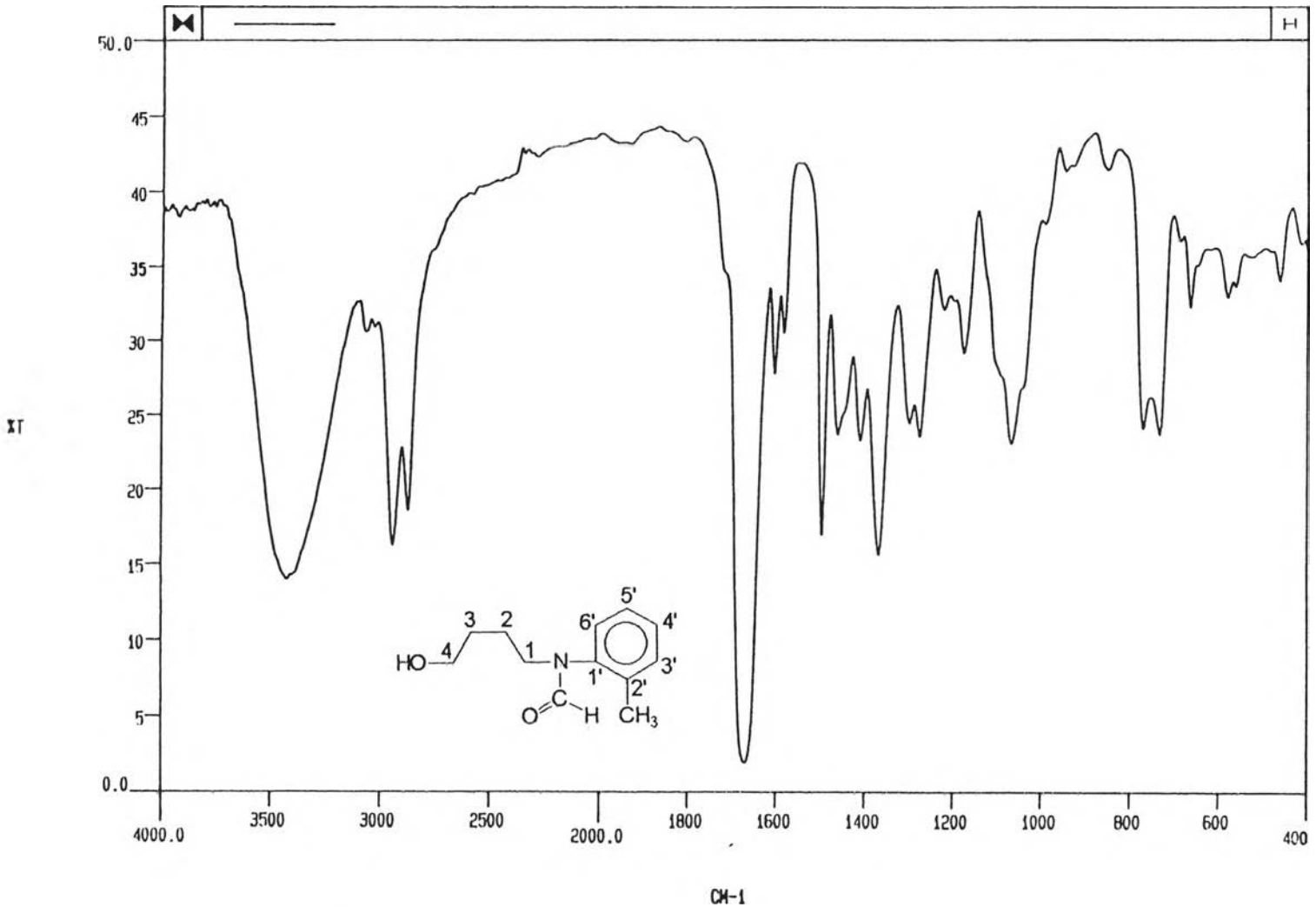

Figure 37. The IR spectrum (Neat) of N-(4-Hydroxybutyl)-N-(*o*-tolyl)formamide.

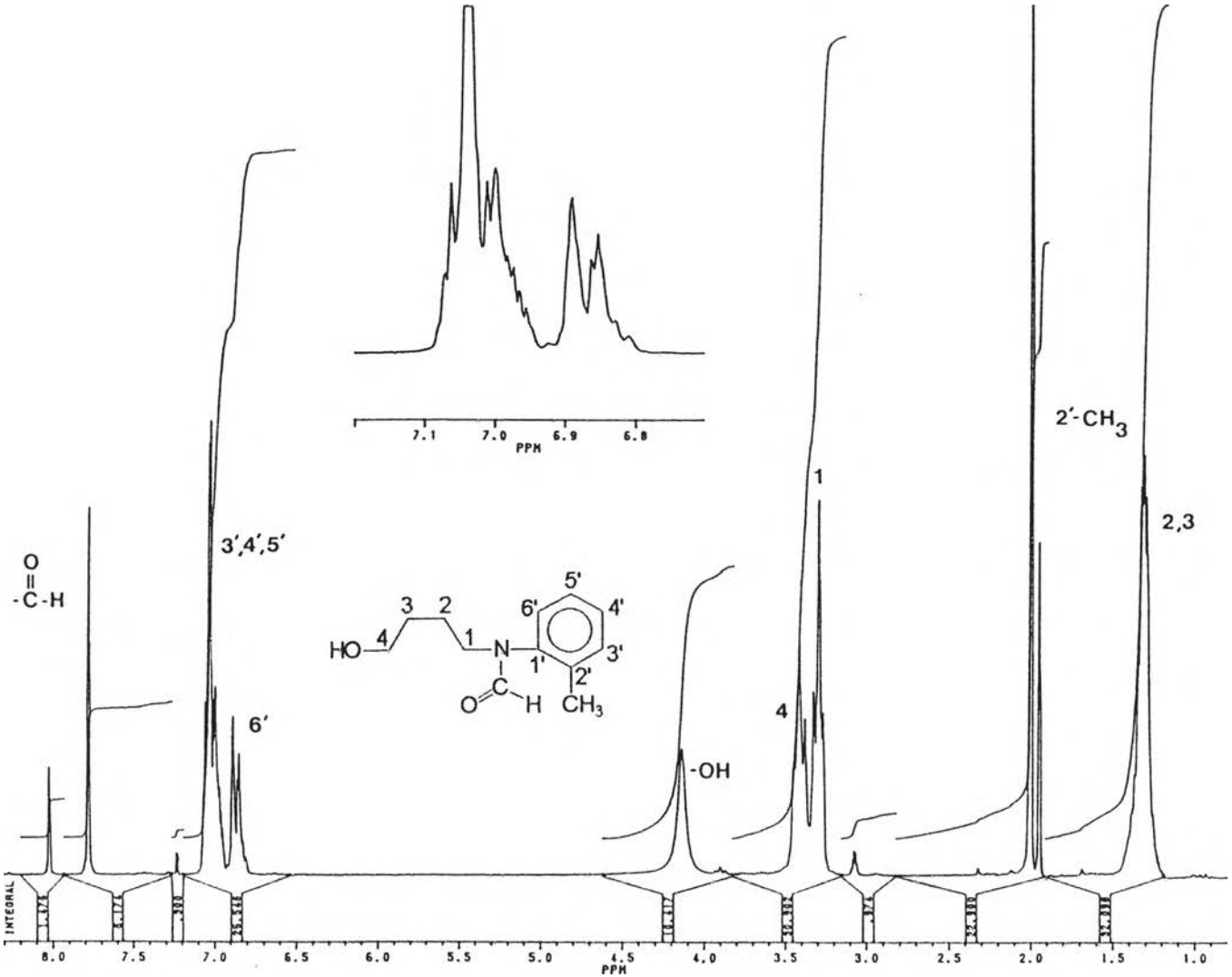

Figure 38. The 200 MHz ^{1}H-NMR spectrum of N-(4-Hydroxybutyl)-N-(*o*-tolyl)formamide in $CDCl_3$ + CD_3OD (1:1).

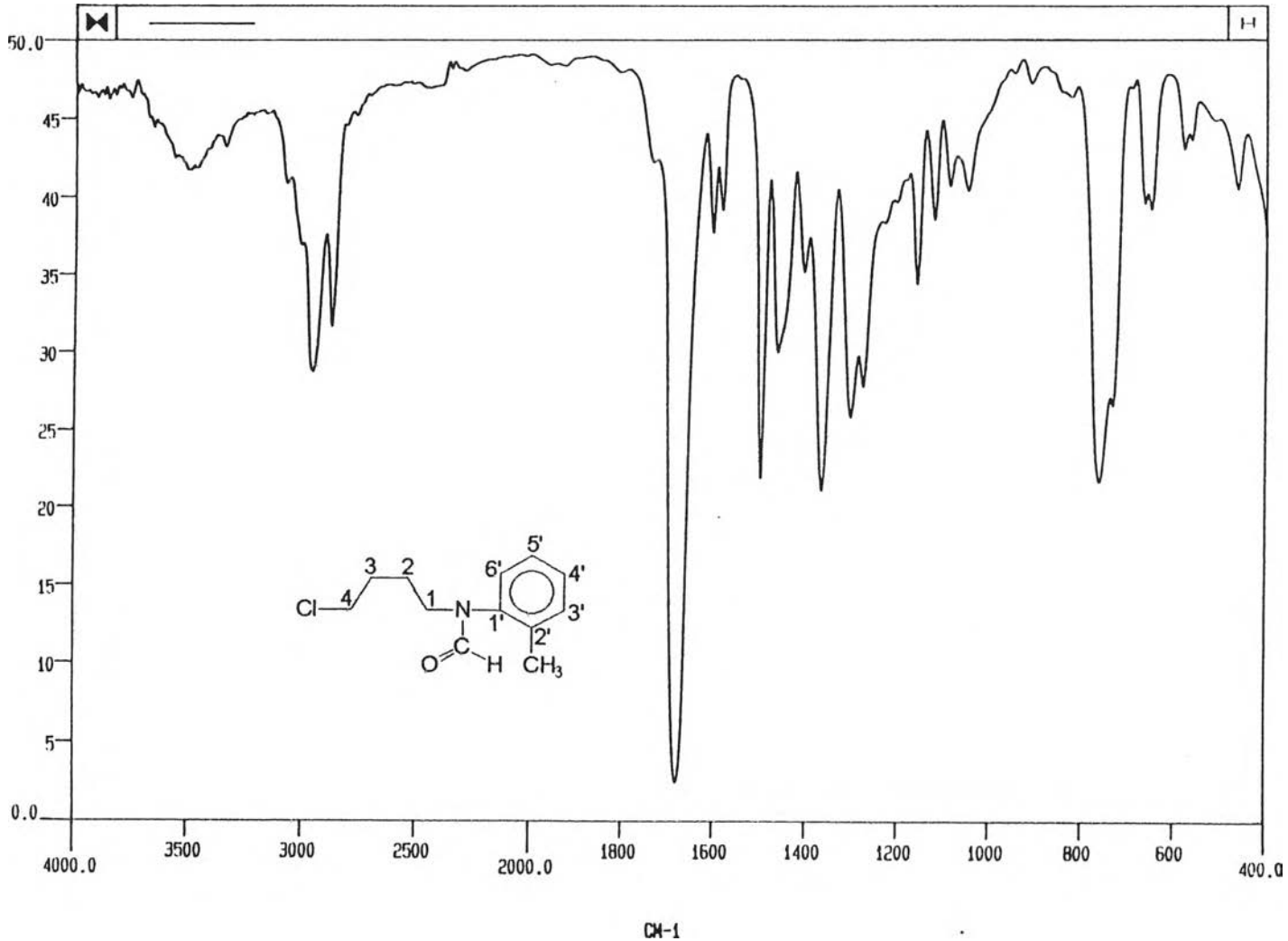

Figure 39. The IR spectrum (Neat) of N-(4-Chlorobutyl)-N-(*o*-tolyl)formamide.

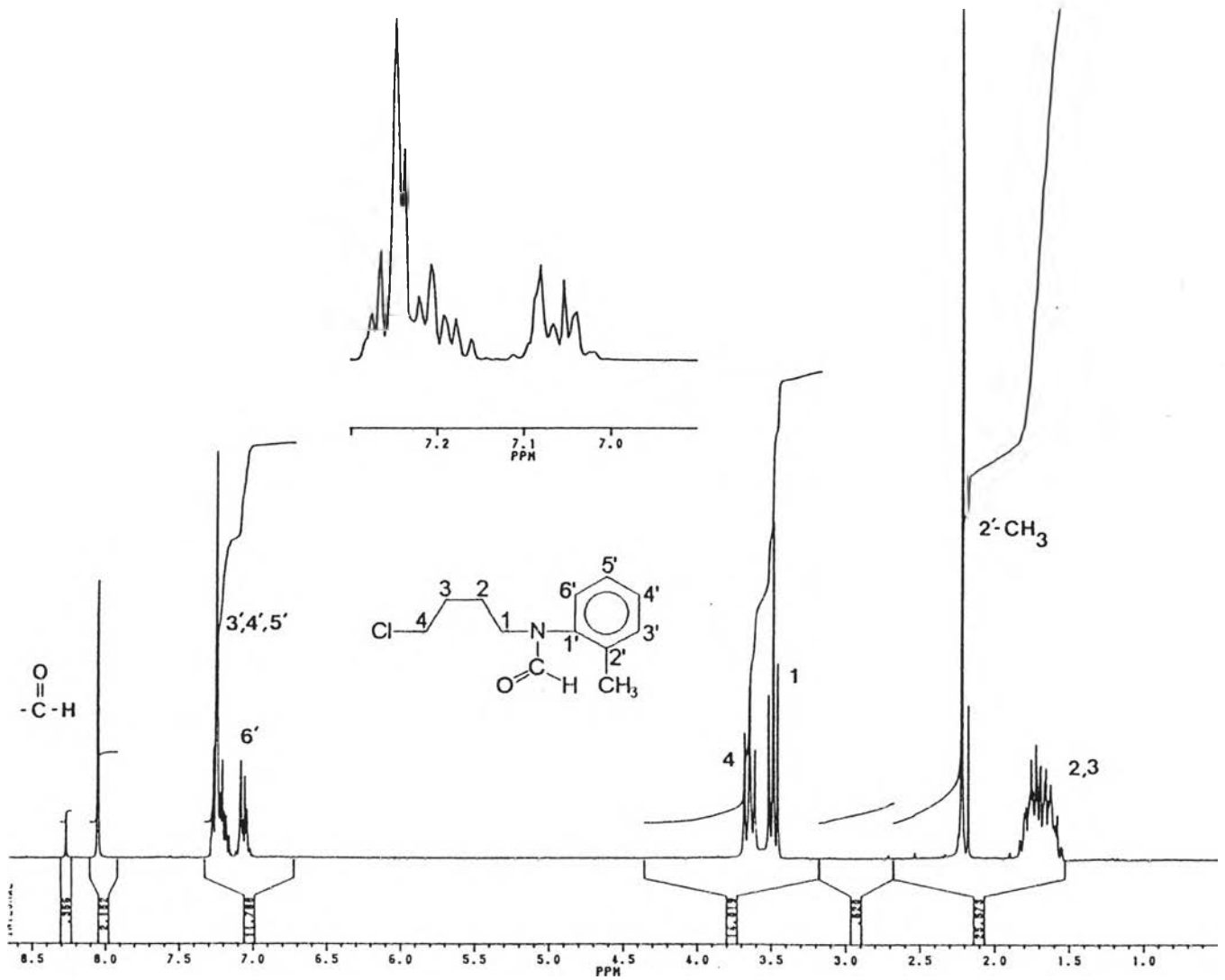

Figure 40. The 200 MHz ^{1}H-NMR spectrum of N-(4-Chlorobutyl)-N-(*o*-tolyl)formamide in $CDCl_3$.

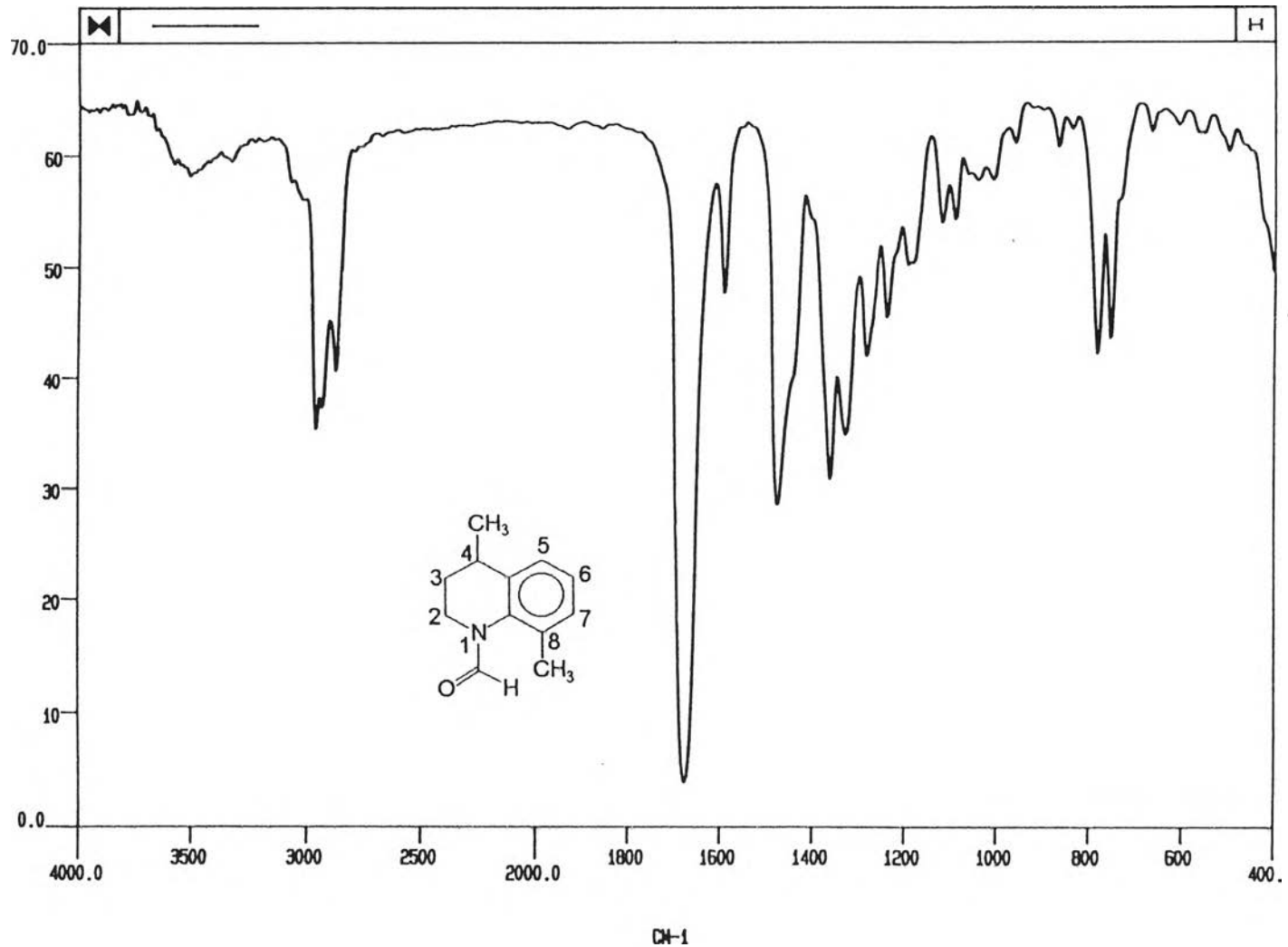

Figure 41. The IR spectrum (Neat) of N-Formyl-1,2,3,4-tetrahydro-4,8-dimethylquinoline.

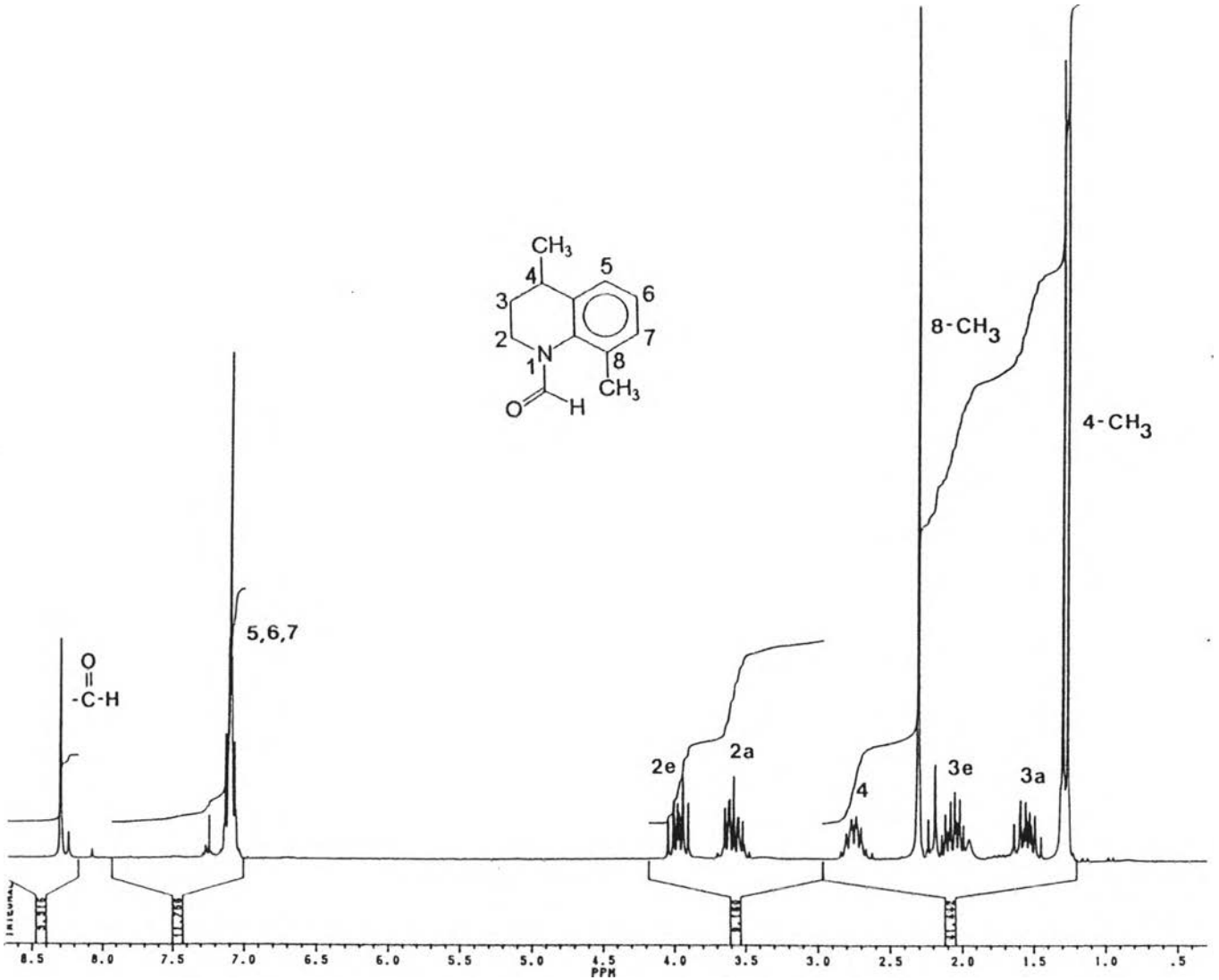

Figure 42. The 200 MHz ^{1}H-NMR spectrum of N-Formyl-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$.

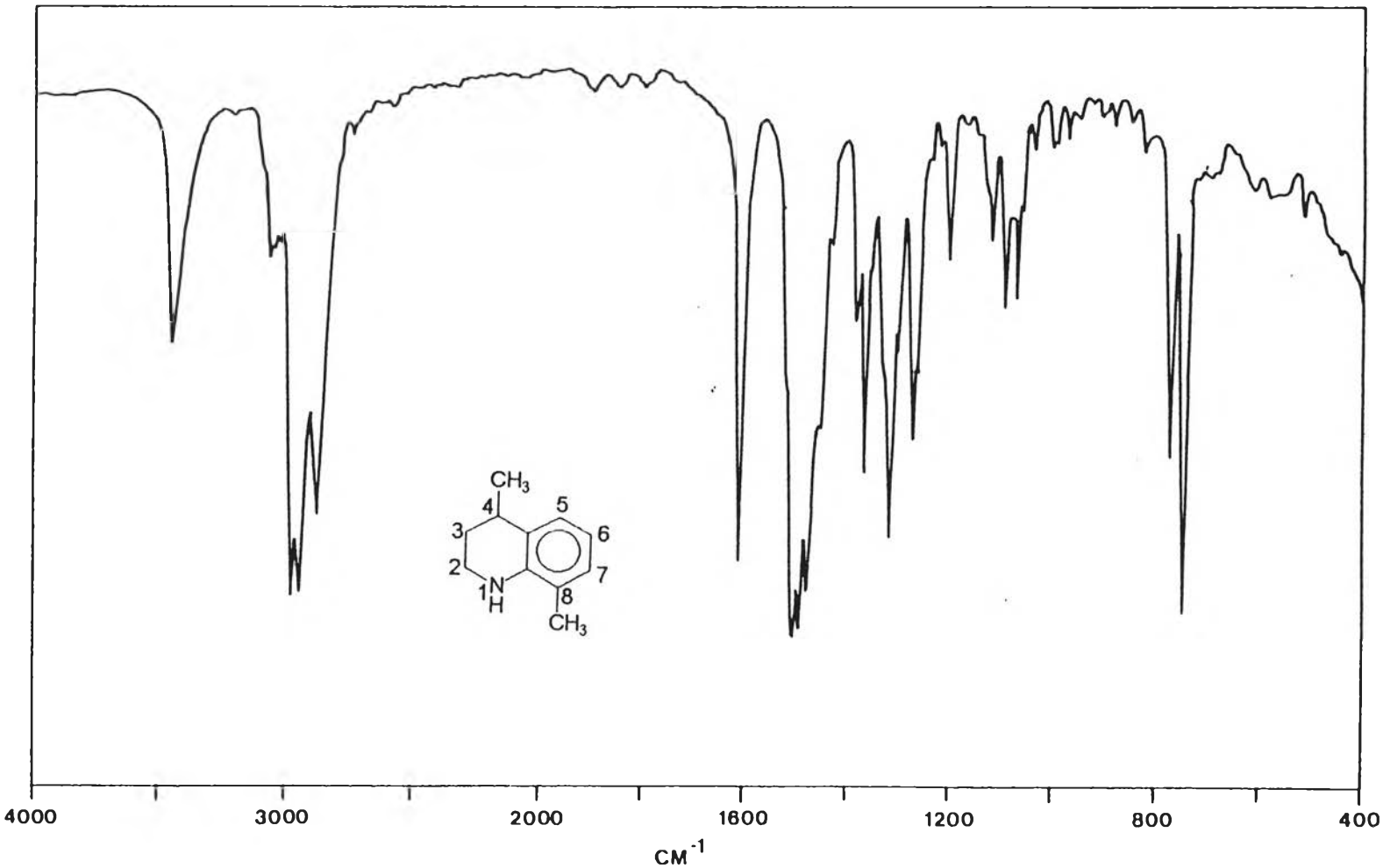

Figure 43. The IR spectrum (Neat) of 1,2,3,4-Tetrahydro-4,8-dimethylquinoline.

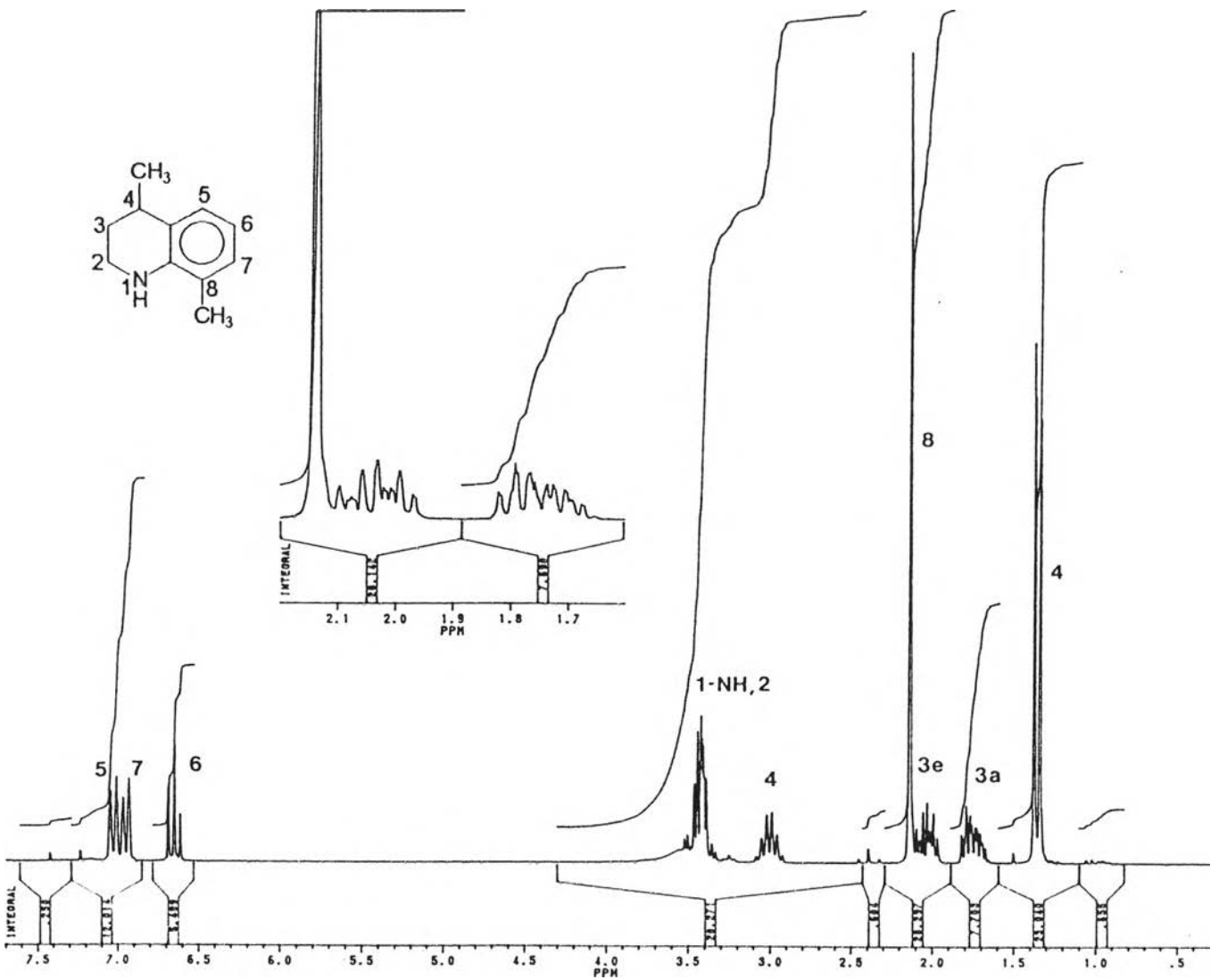

Figure 44. The 200 MHz ^{1}H-NMR spectrum of 1,2,3,4-Tetrahydro-4,8-dimethylquinoline in $CDCl_3$.

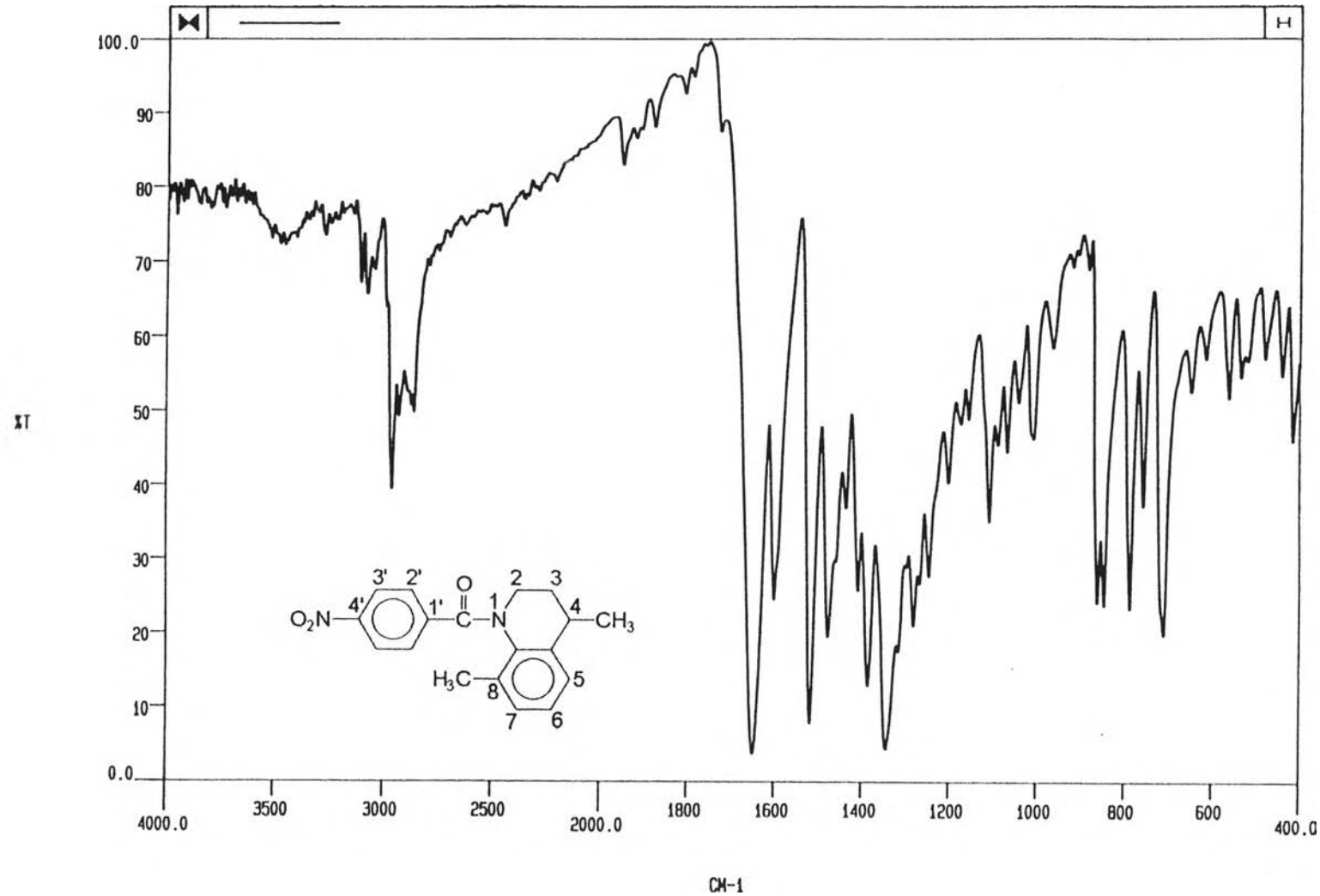

Figure 45. The IR spectrum (KBr pellet) of N-(*p*-Nitrobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline.

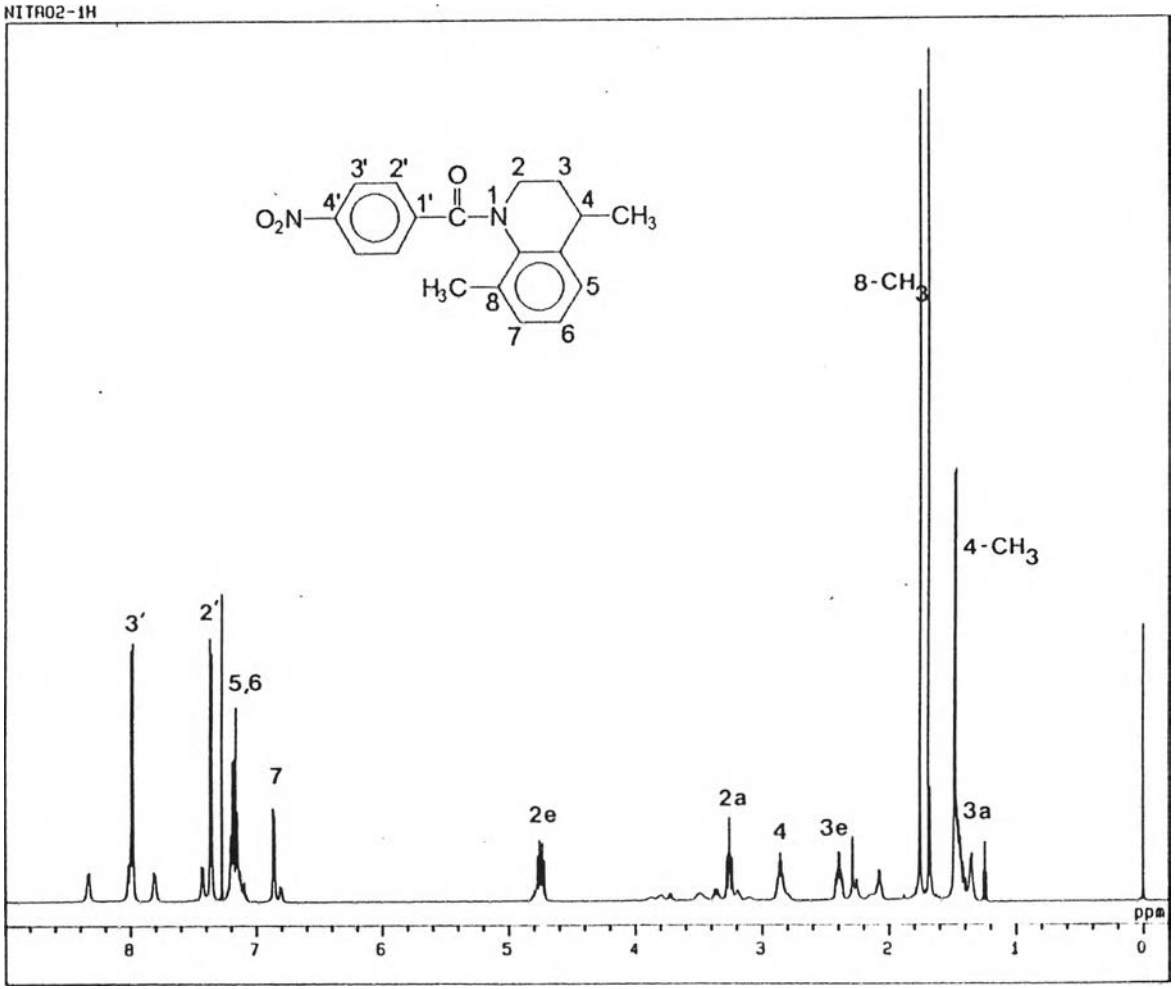

Figure 46. The 500 MHz ^{1}H-NMR spectrum of N-(*p*-Nitrobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$.

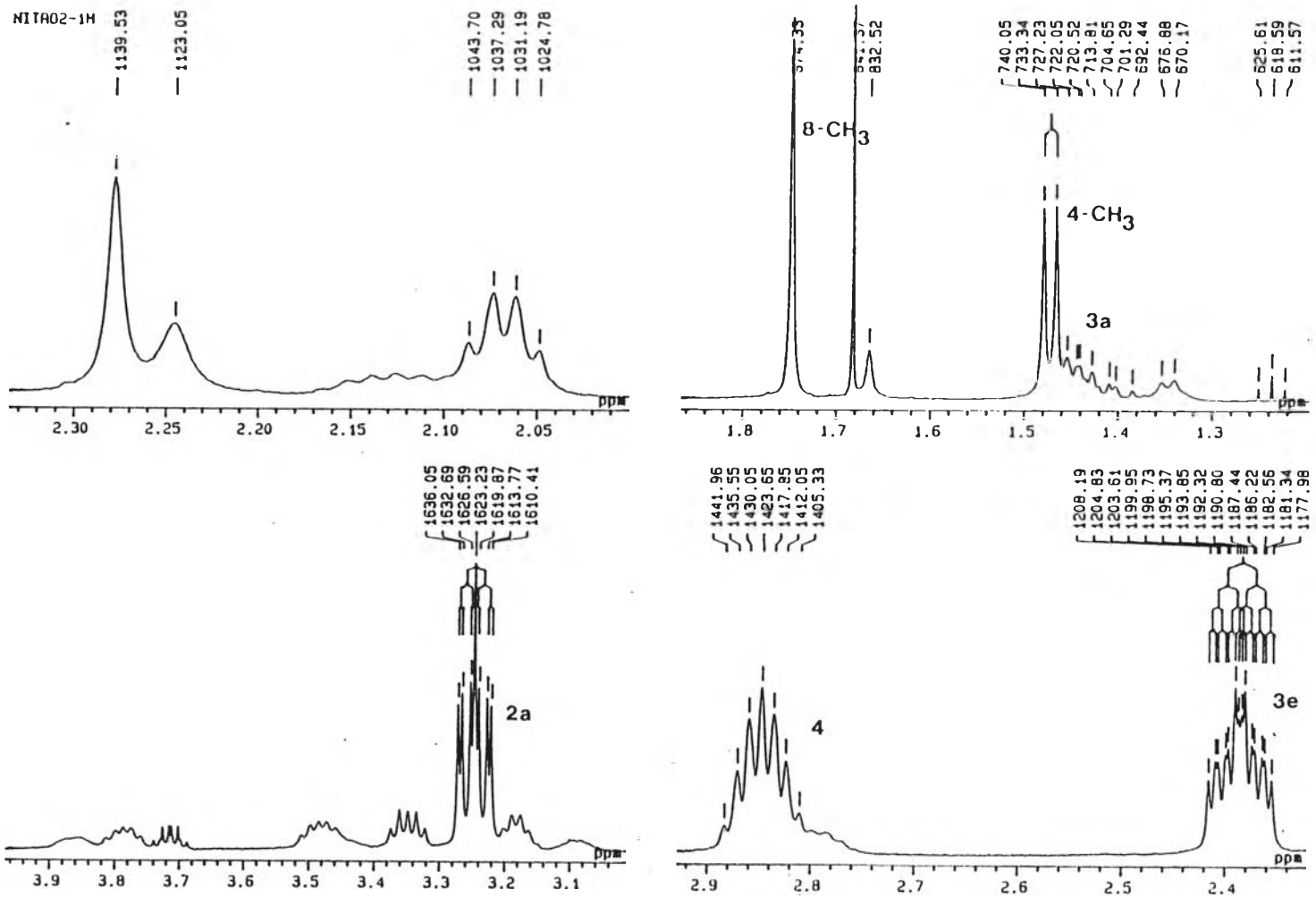

Figure 47. The 500 MHz ^{1}H-NMR spectrum of N-(*p*-Nitrobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$.

(Enlarged scale : 1.2-4.0 ppm)

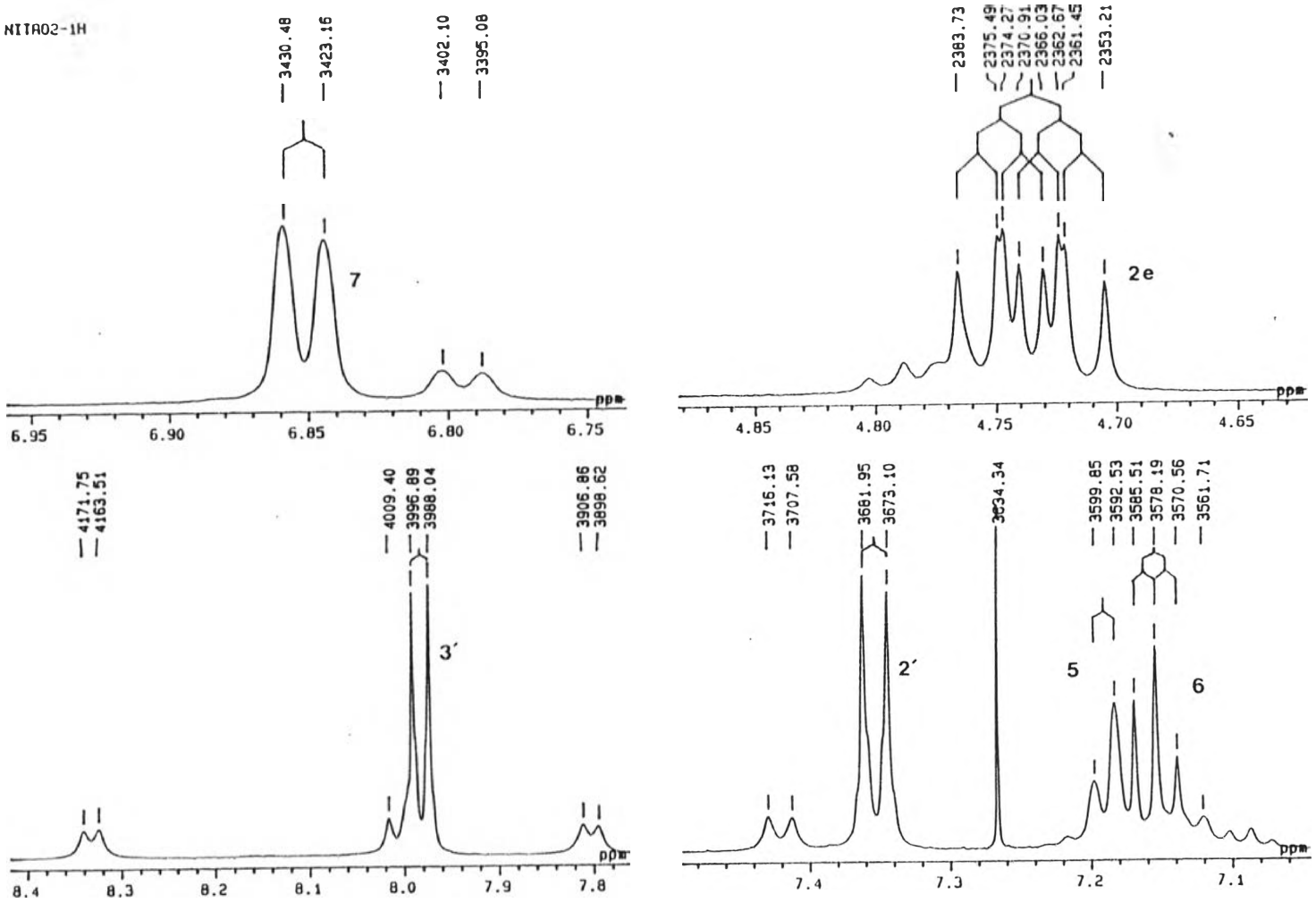

Figure 48. The 500 MHz ^{1}H-NMR spectrum of N-(*p*-Nitrobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$.

(Enlarged scale : 4.6-8.4 ppm)

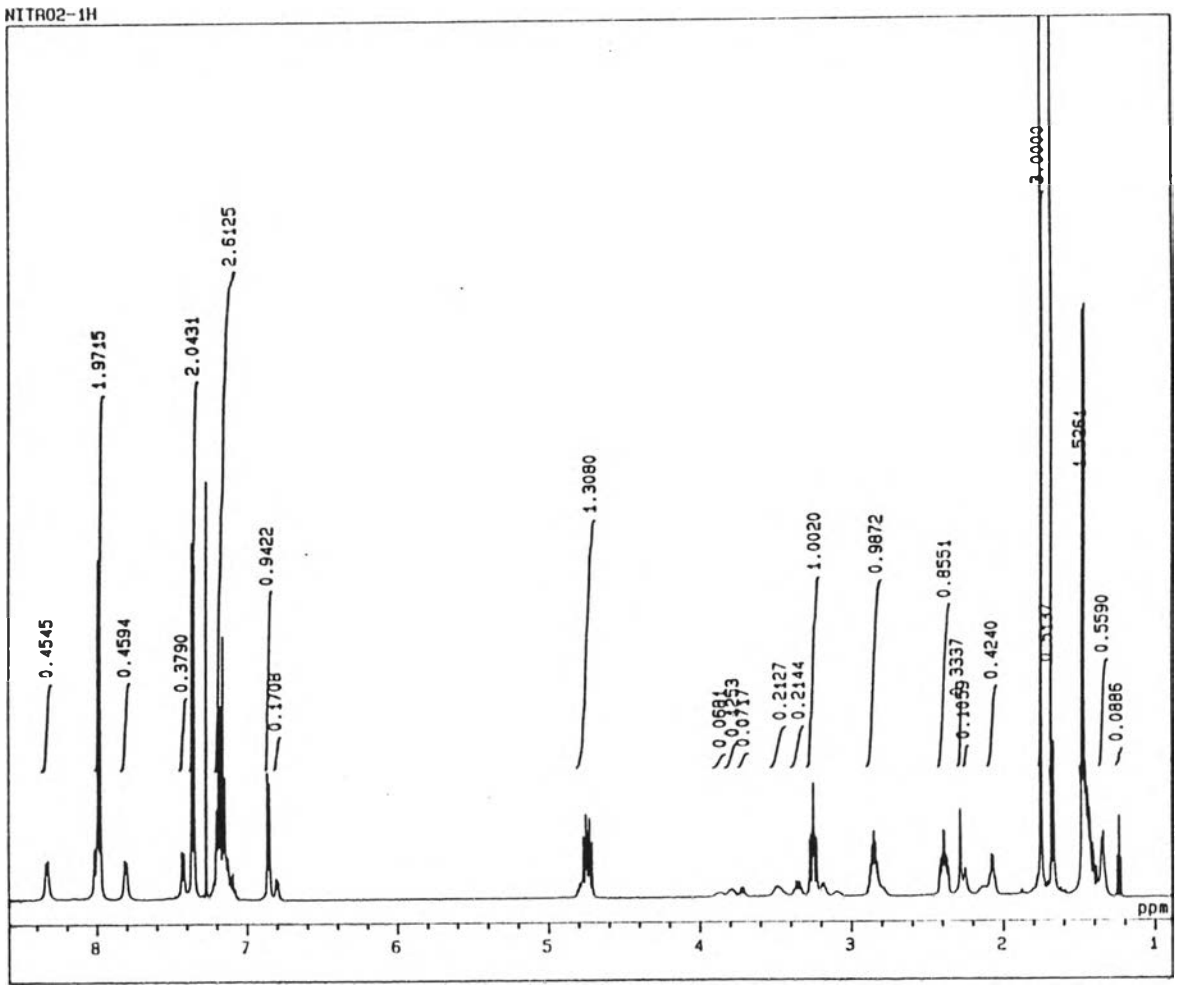

Figure 49. The 500 MHz ^{1}H-NMR spectrum of N-(*p*-Nitrobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$.

(Exhibit the integration.)

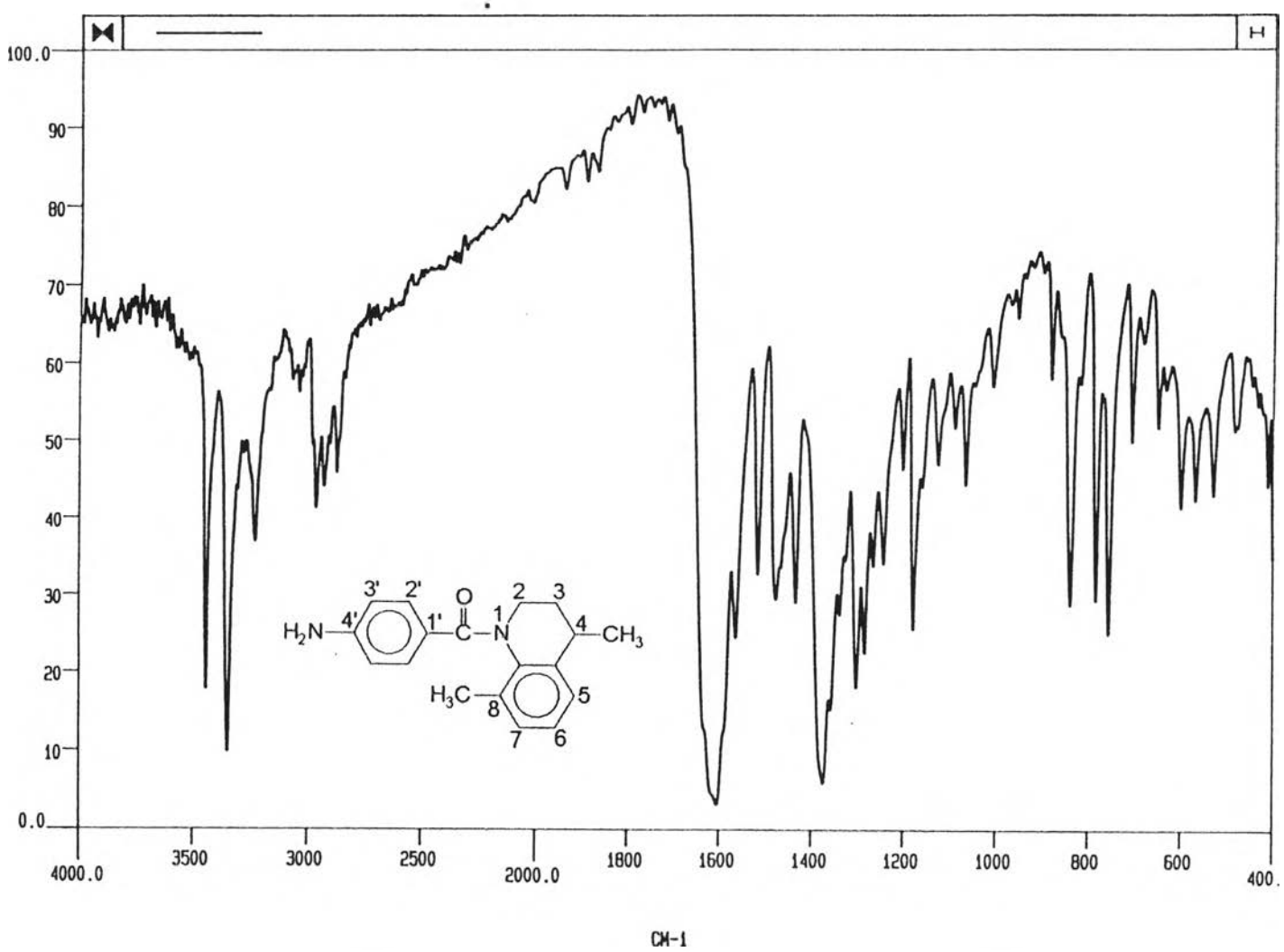

Figure 50. The IR spectrum (KBr pellet) of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline.

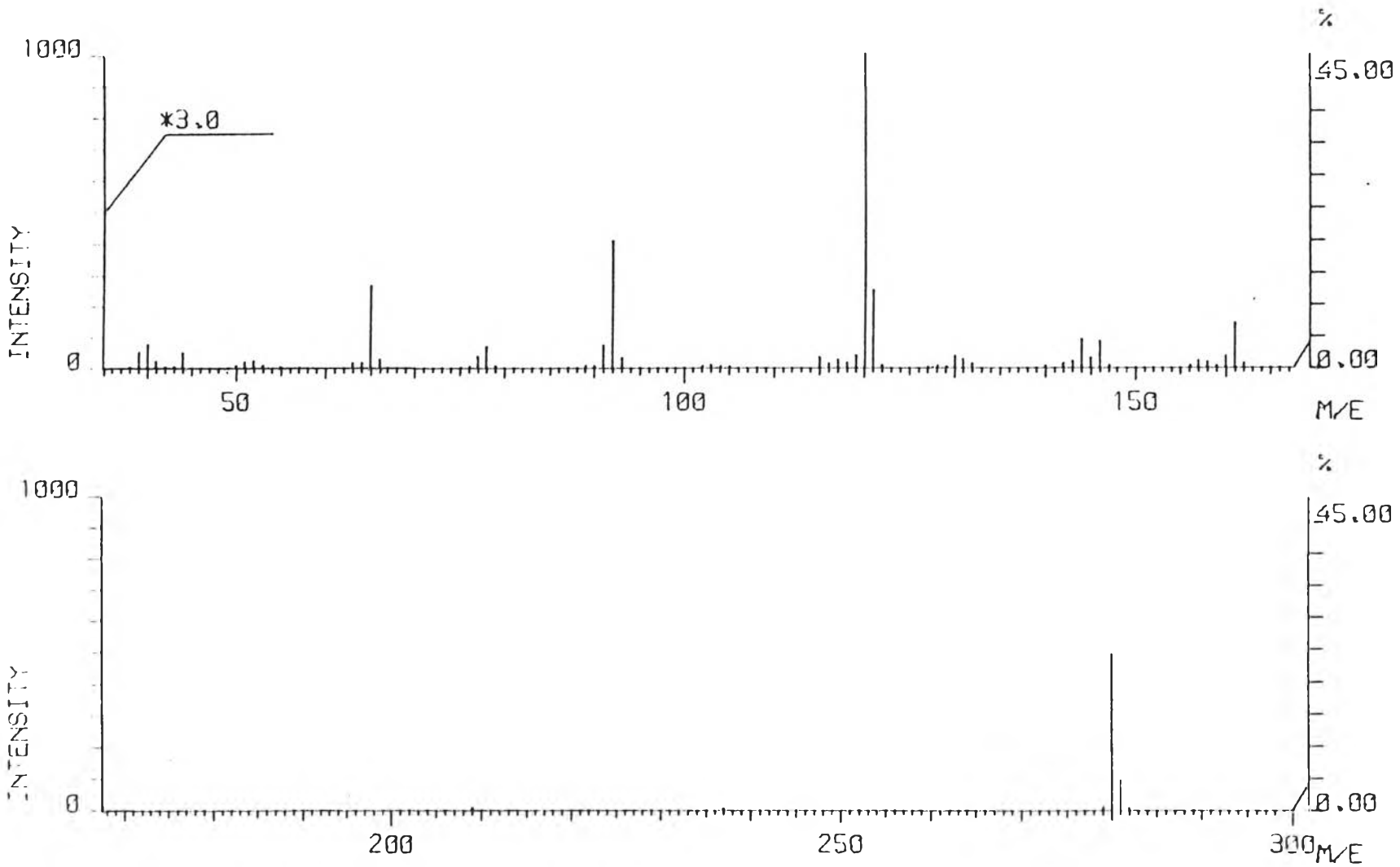

Figure 51. The EIMS spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline.

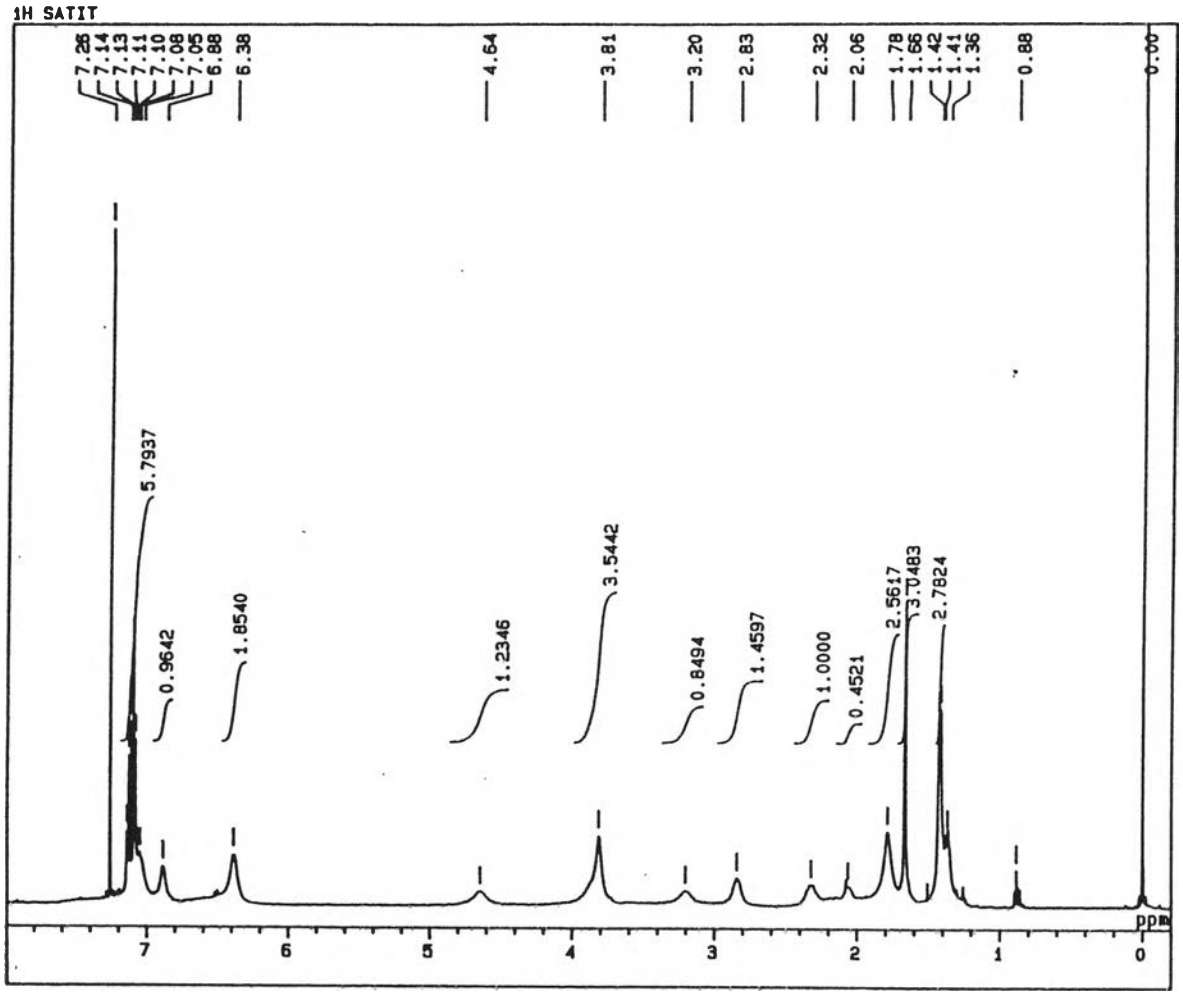

Figure 52. The 500 MHz ^{1}H-NMR spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at room temperature.

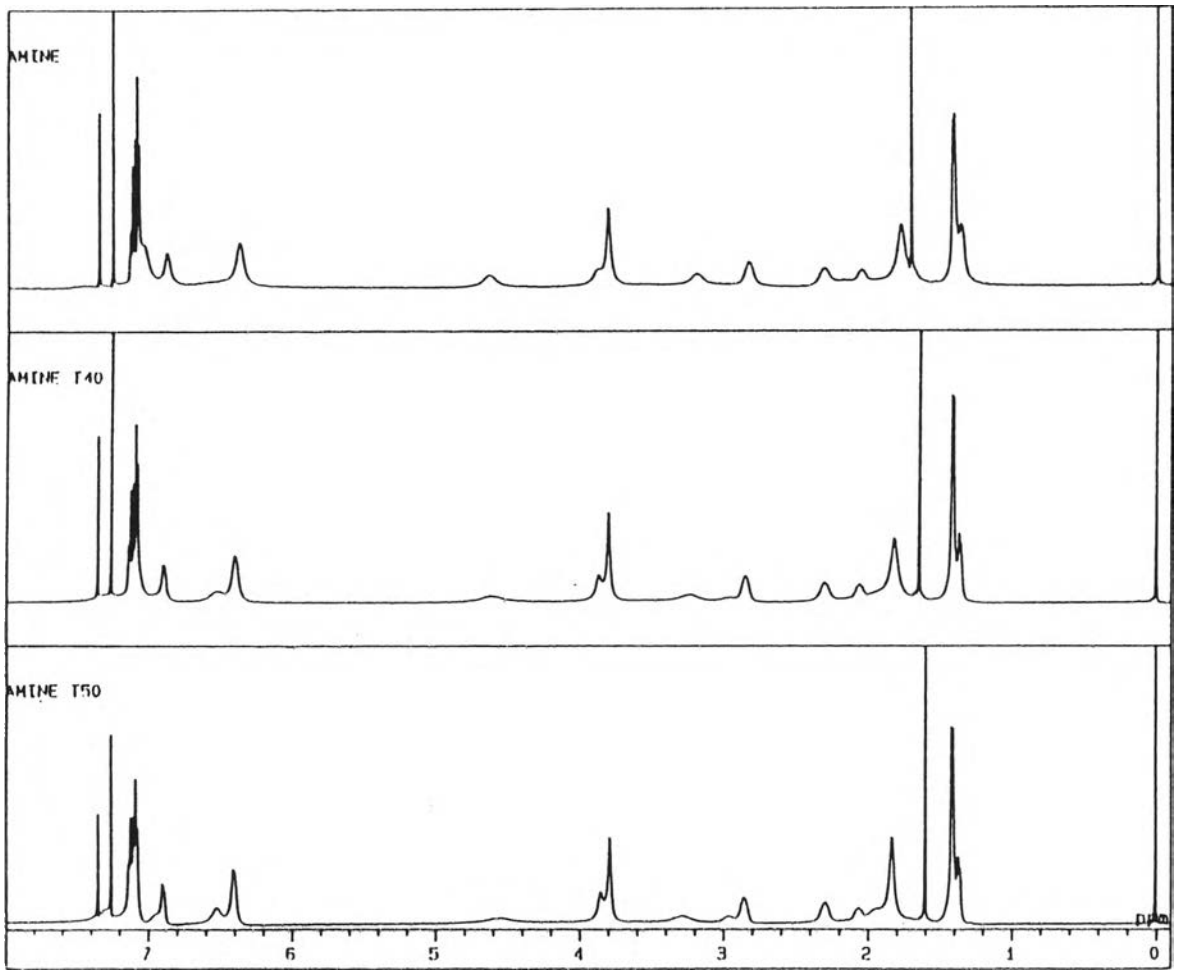

Figure 53. The 500 MHz ^{1}H-NMR spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at high temperature (at room temperature, 40°c, and 50°c, respectively).

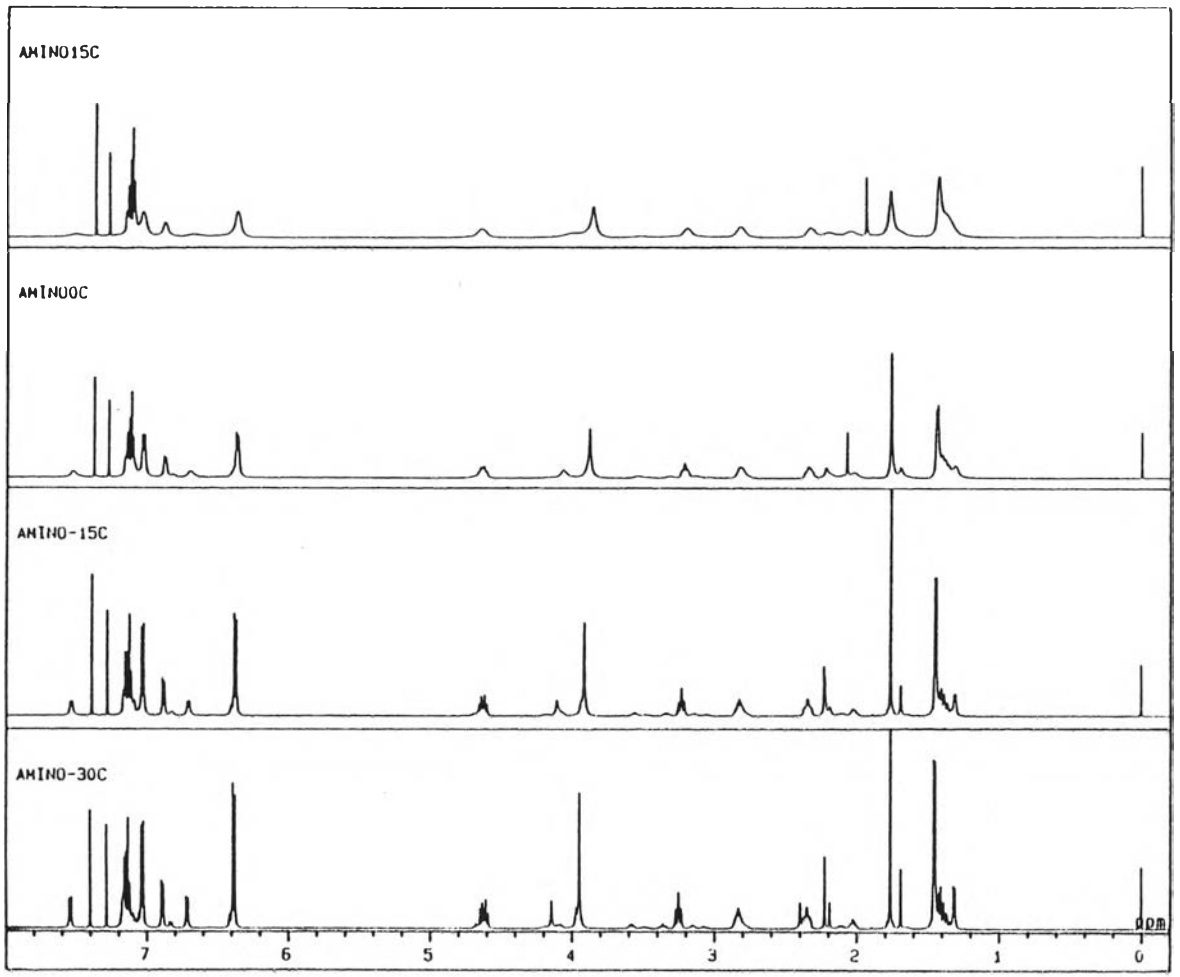

Figure 54. The 500 MHz ^{1}H-NMR spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at low temperature (at 15°c, 0°c, -15°c, and -30°c, respectively).

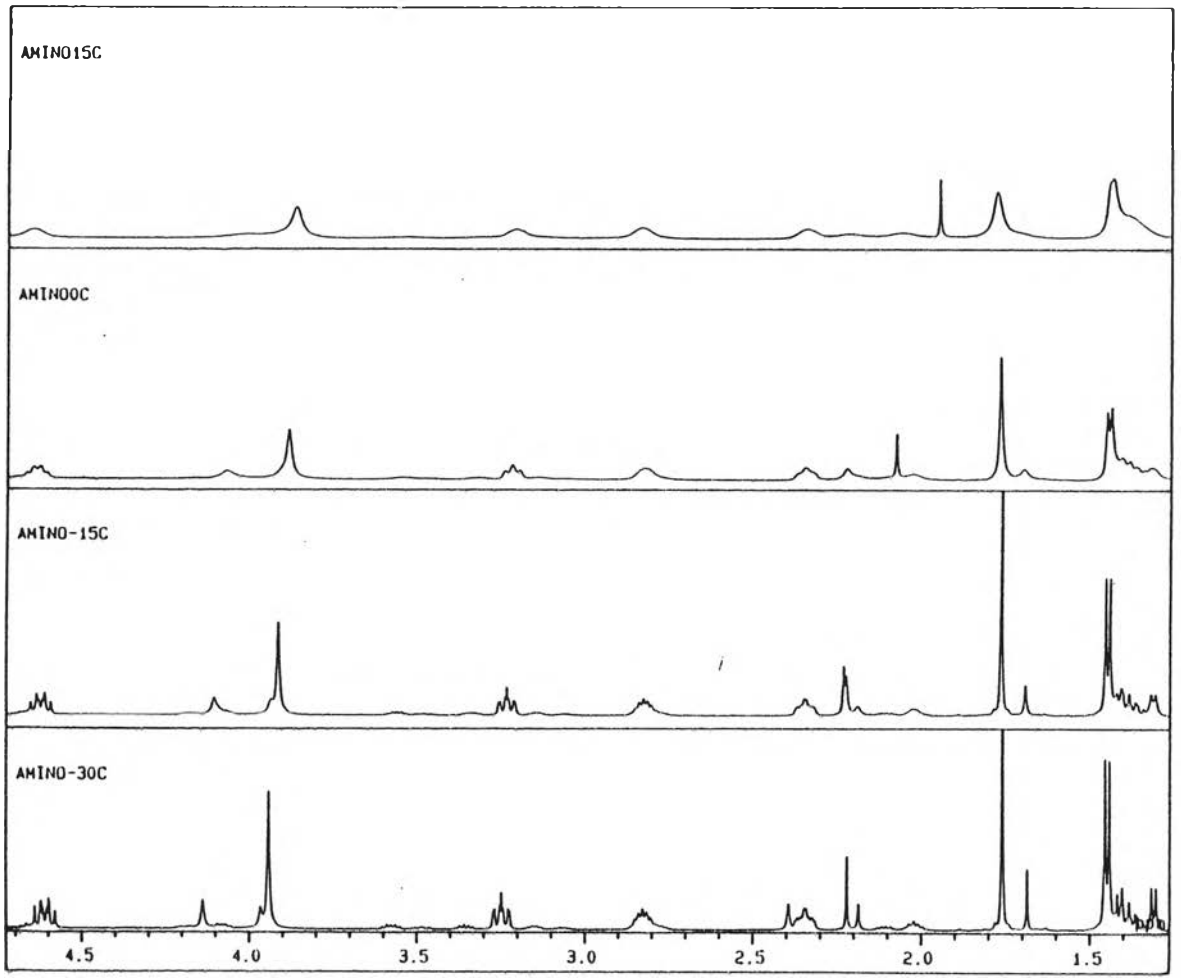

Figure 55. The 500 MHz ^{1}H-NMR spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at low temperature (at 15°c, 0°c, -15°c, and -30°c, respectively). (Enlarged scale : 1.3-4.7 ppm)

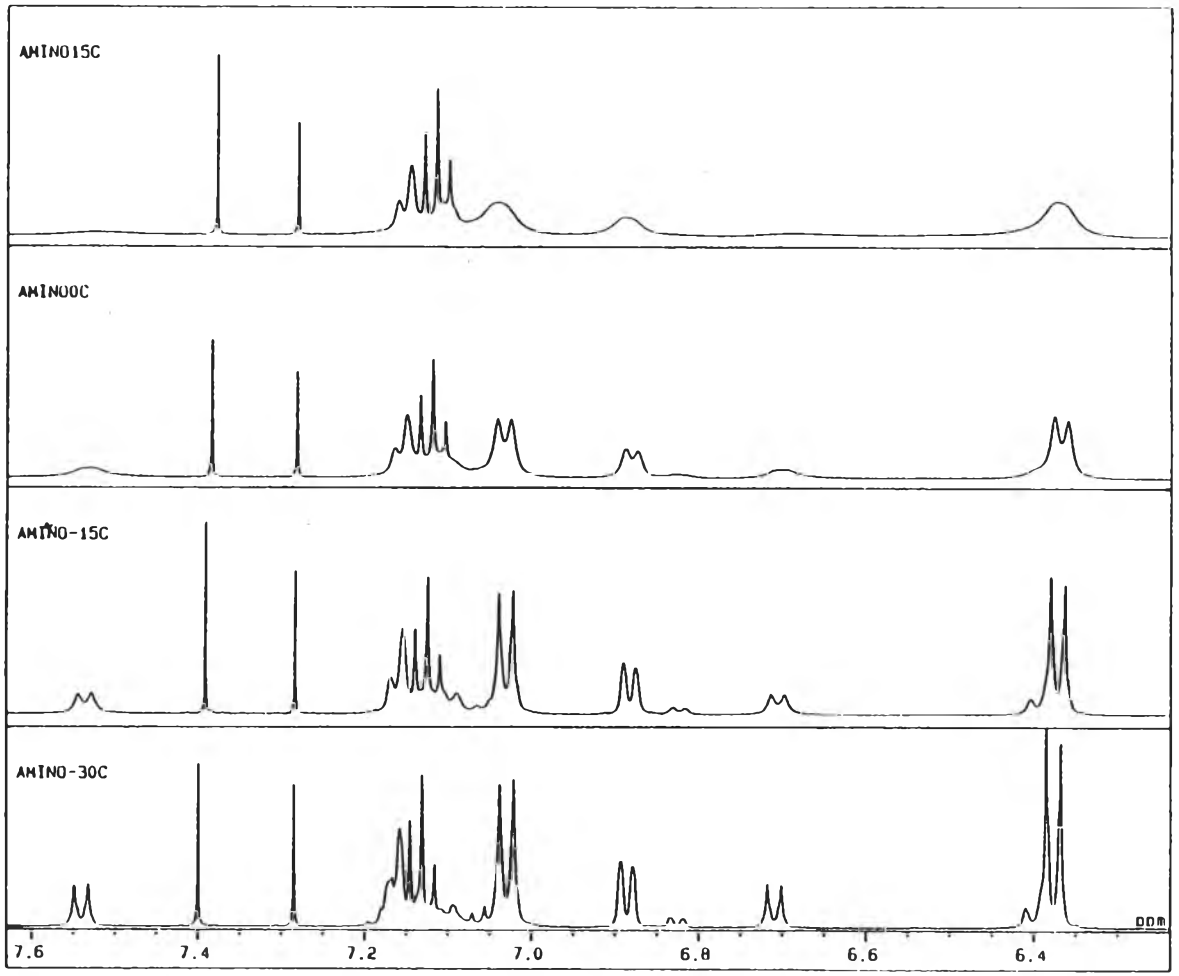

Figure 56. The 500 MHz ^{1}H-NMR spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at low temperature (at 15°c, 0°c, -15°c, and -30°c, respectively). (Enlarged scale : 6.3-7.6 ppm)

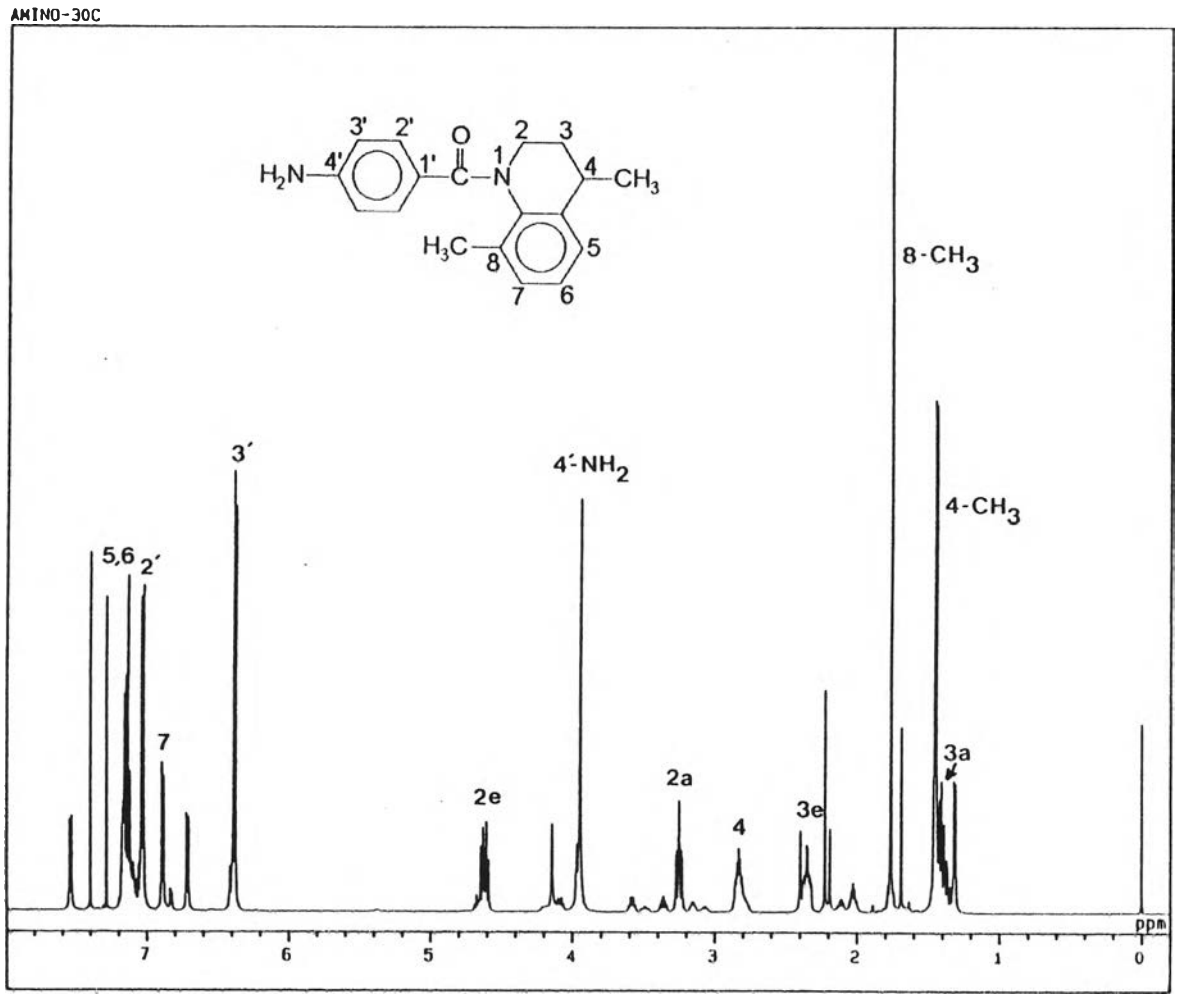

Figure 57. The 500 MHz ^{1}H-NMR spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c.

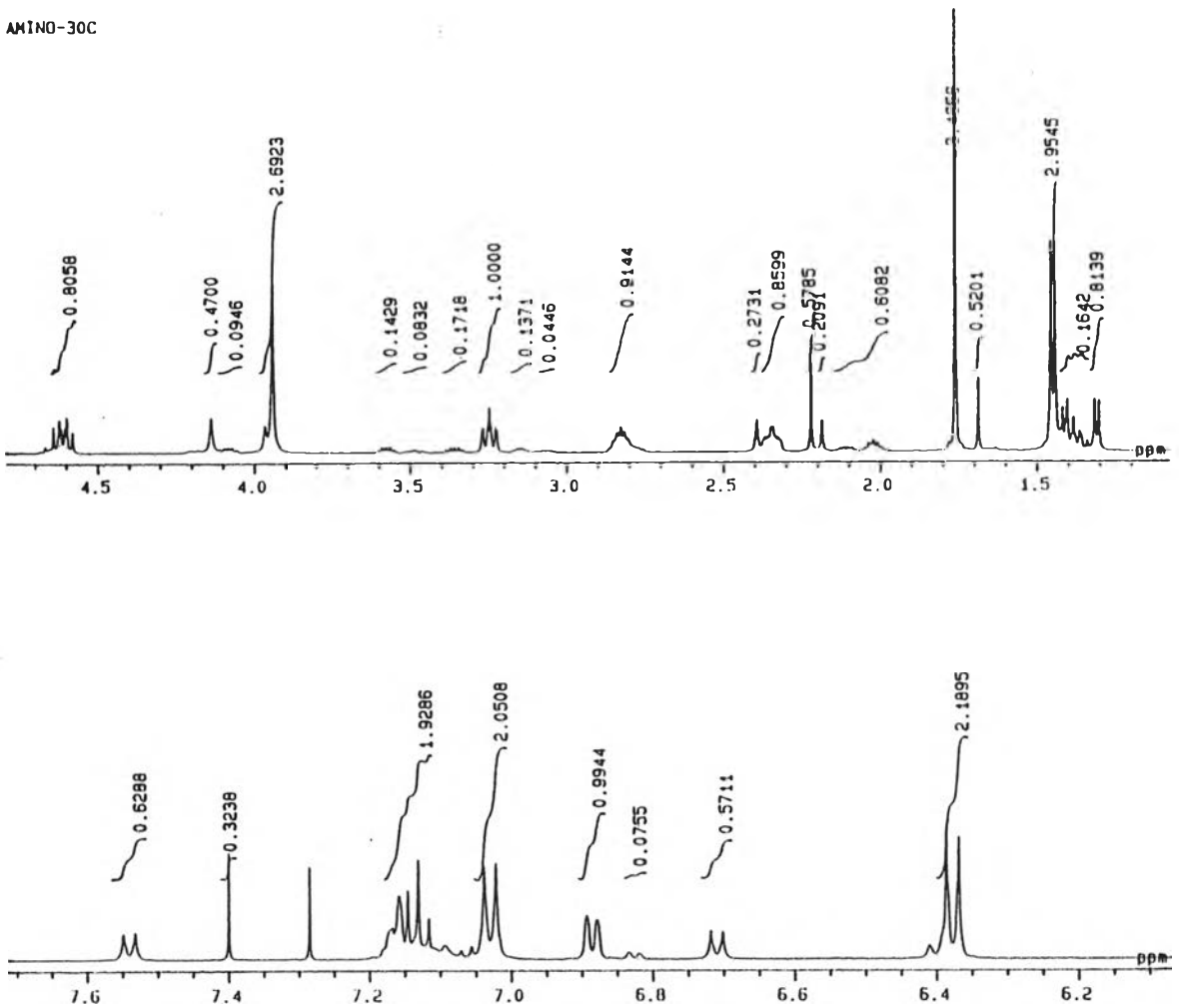

Figure 58. The 500 MHz ^{1}H-NMR spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c. (Exhibit the integration.)

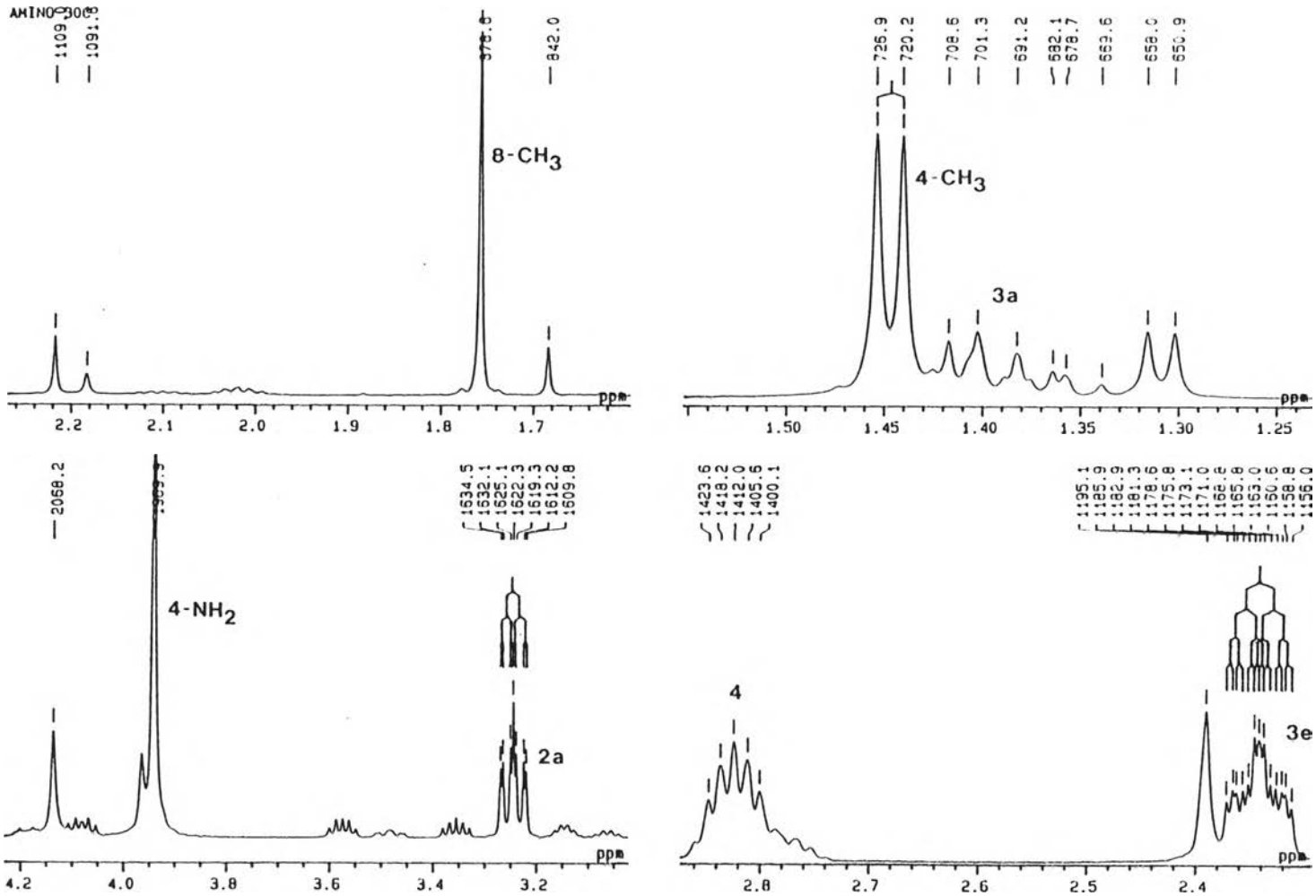

Figure 59. The 500 MHz ^{1}H-NMR spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c. (Enlarged scale : 1.2-4.2 ppm)

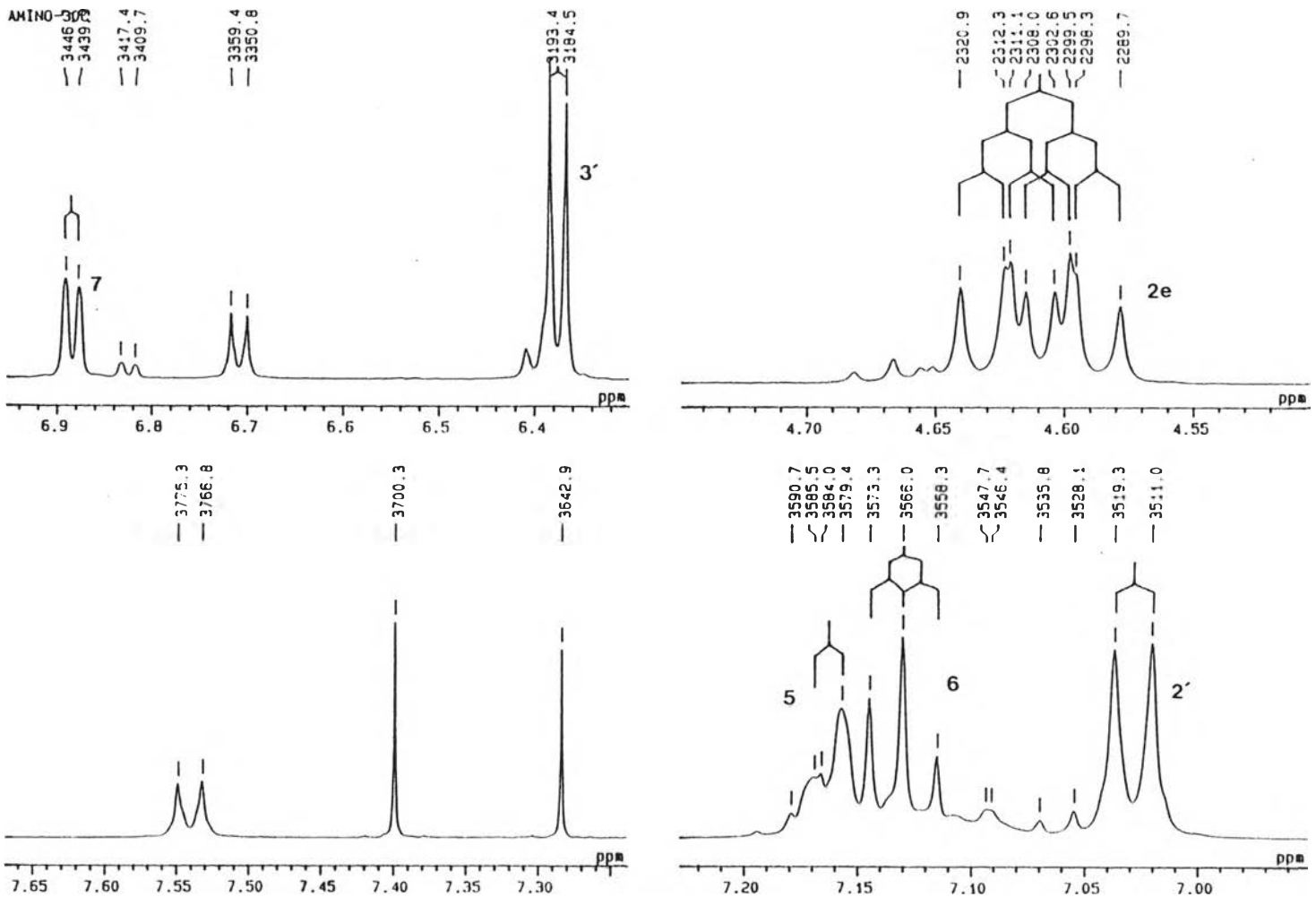

Figure 60. The 500 MHz ^{1}H-NMR spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c. (Enlarged scale : 4.5-7.7 ppm)

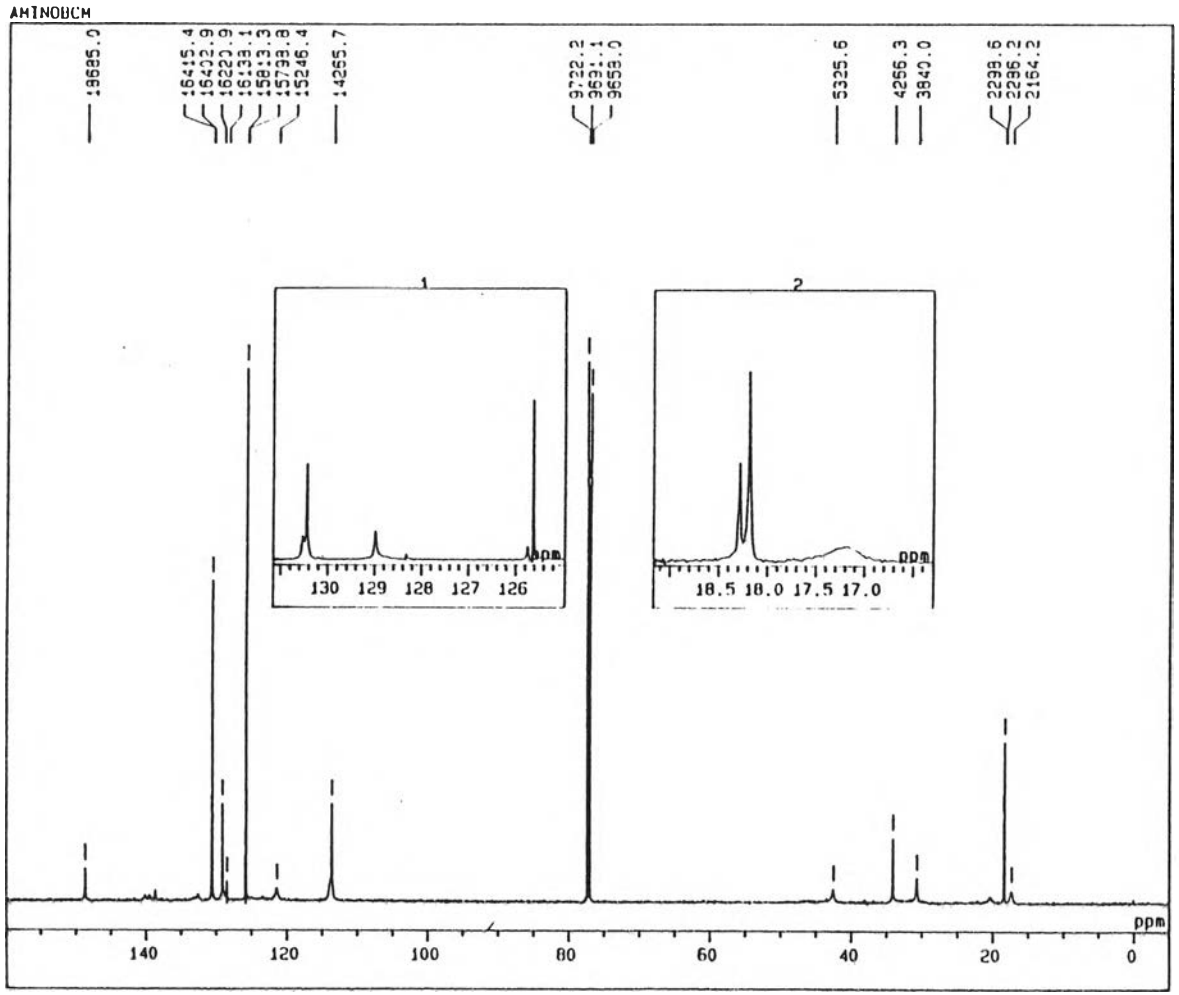

Figure 61. The 125 MHz ^{13}C-NMR decoupled spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at room temperature.

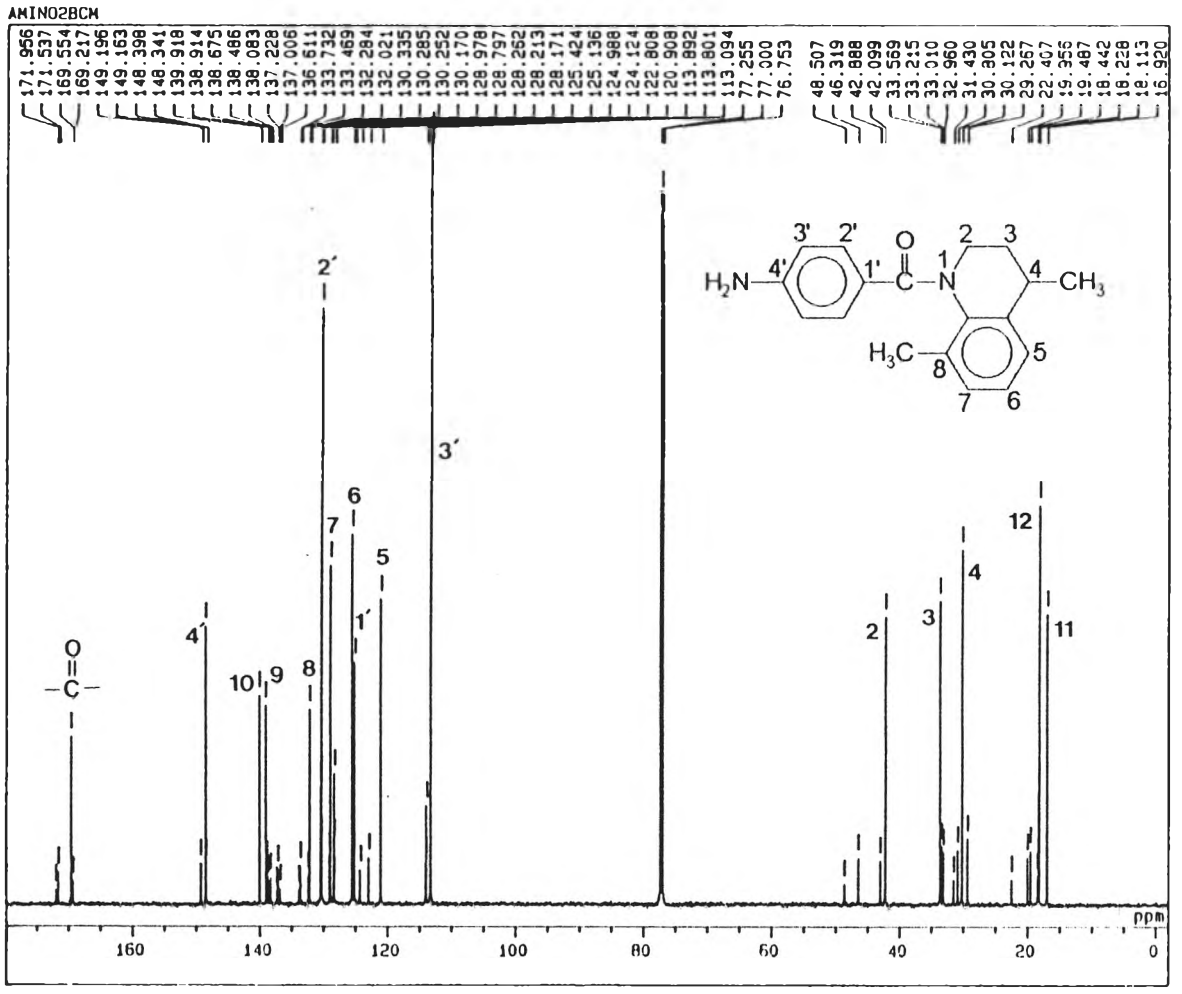

Figure 62. The 125 MHz ^{13}C-NMR decoupled spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c.

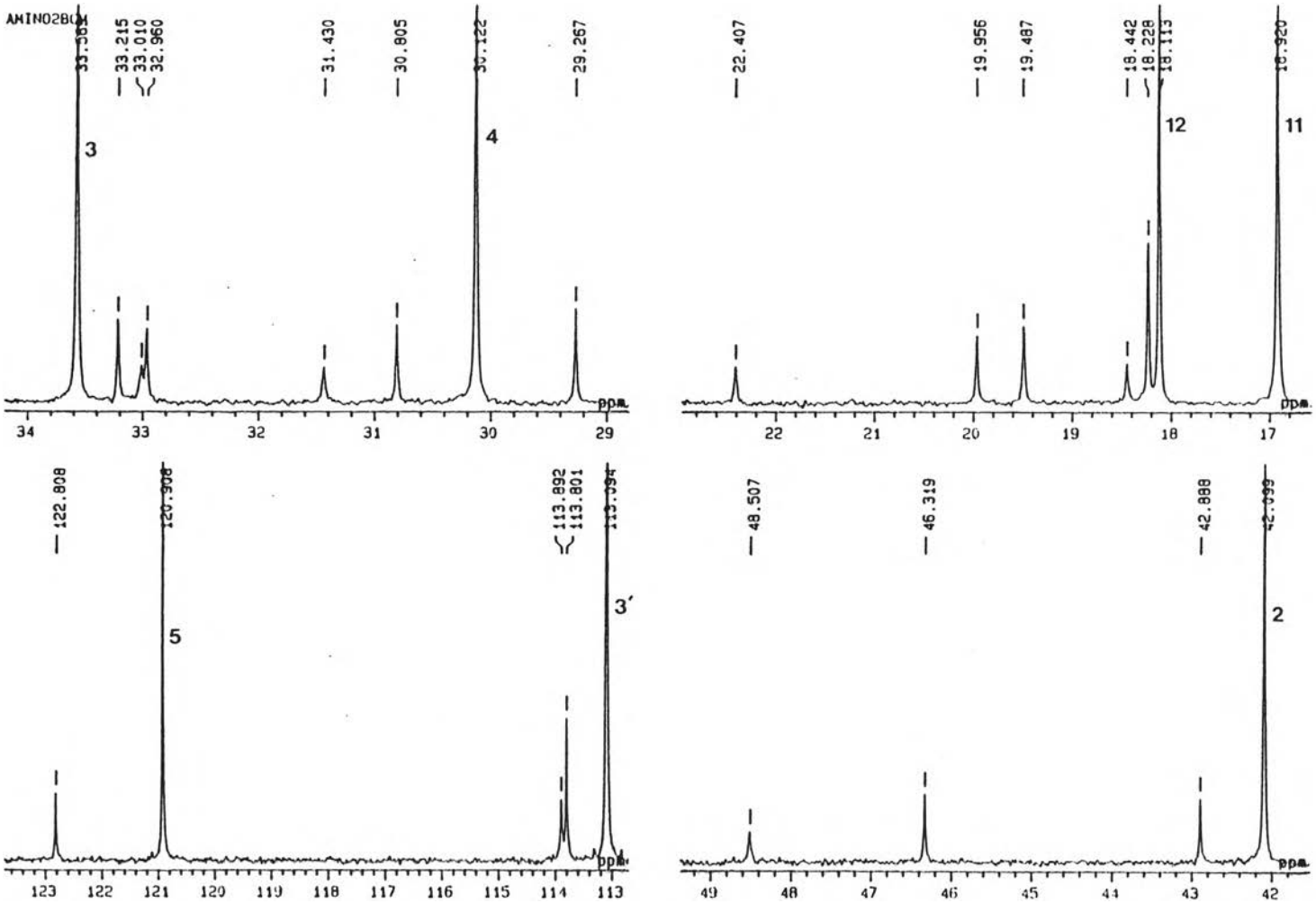

Figure 63. The 125 MHz ^{13}C-NMR decoupled spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c. (Enlarged scale : 16-123 ppm)

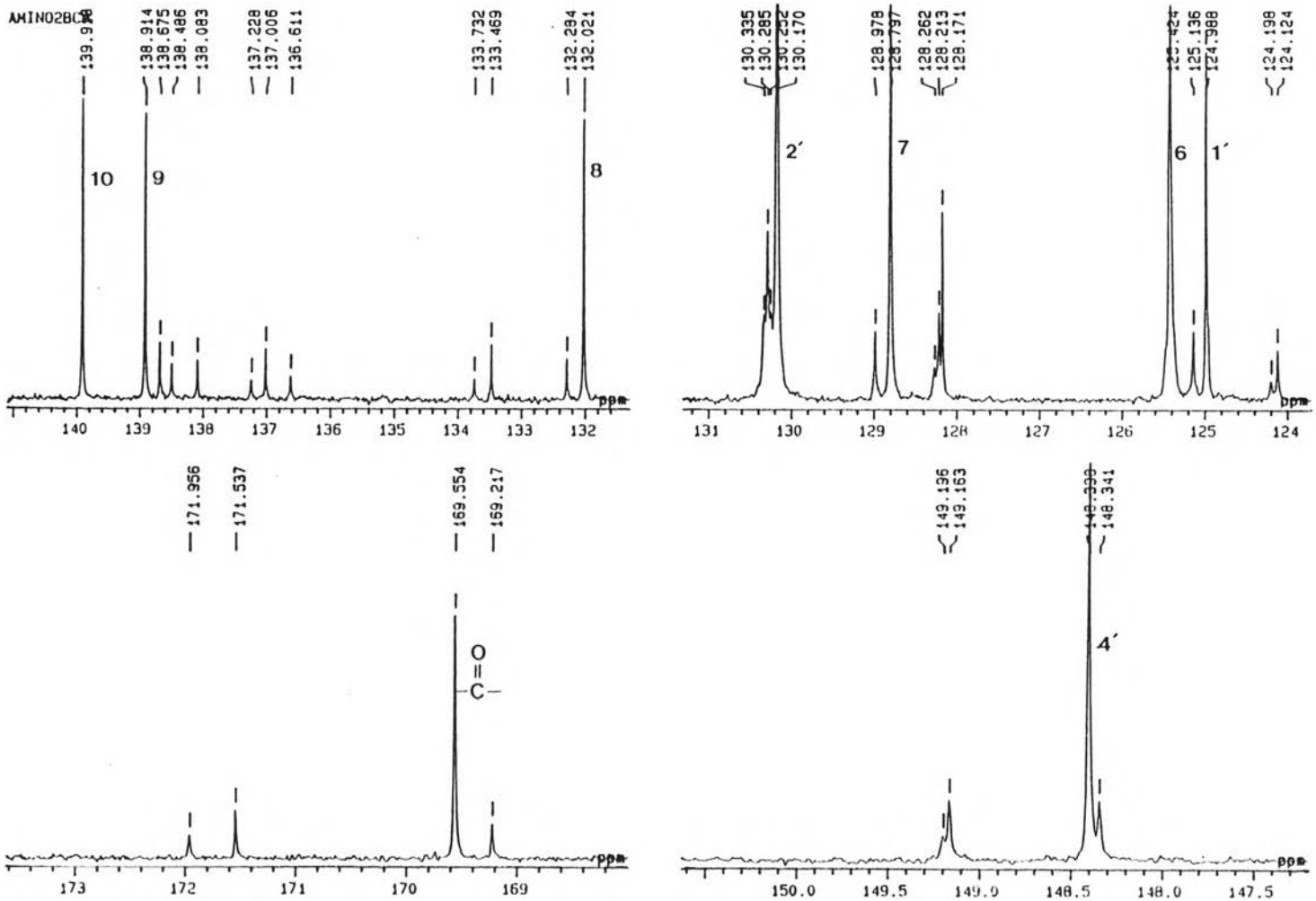

Figure 64. The 125 MHz ^{13}C-NMR decoupled spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c. (Enlarged scale : 124-173 ppm)

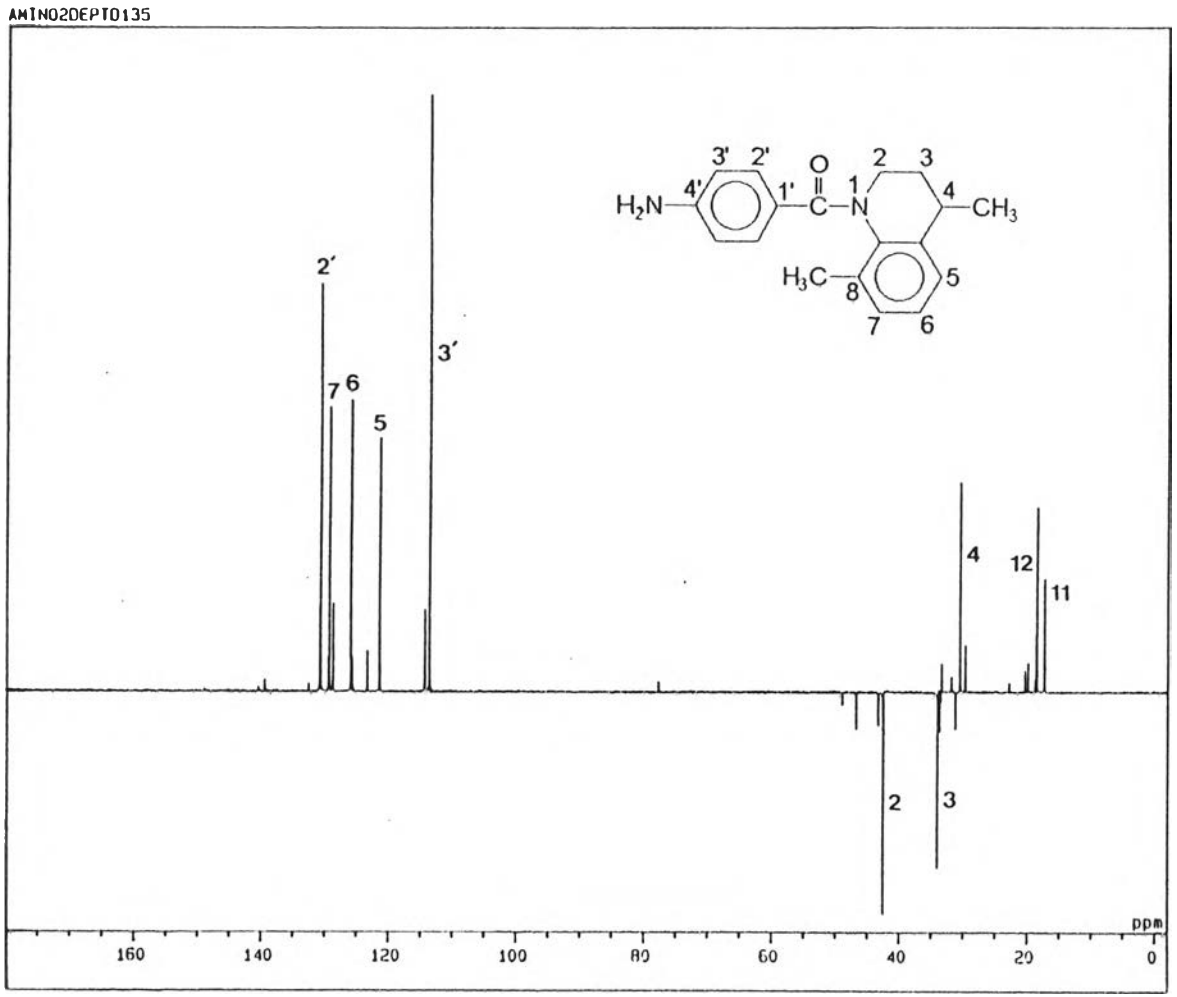

Figure 65. The 125 MHz DEPT135 spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c.

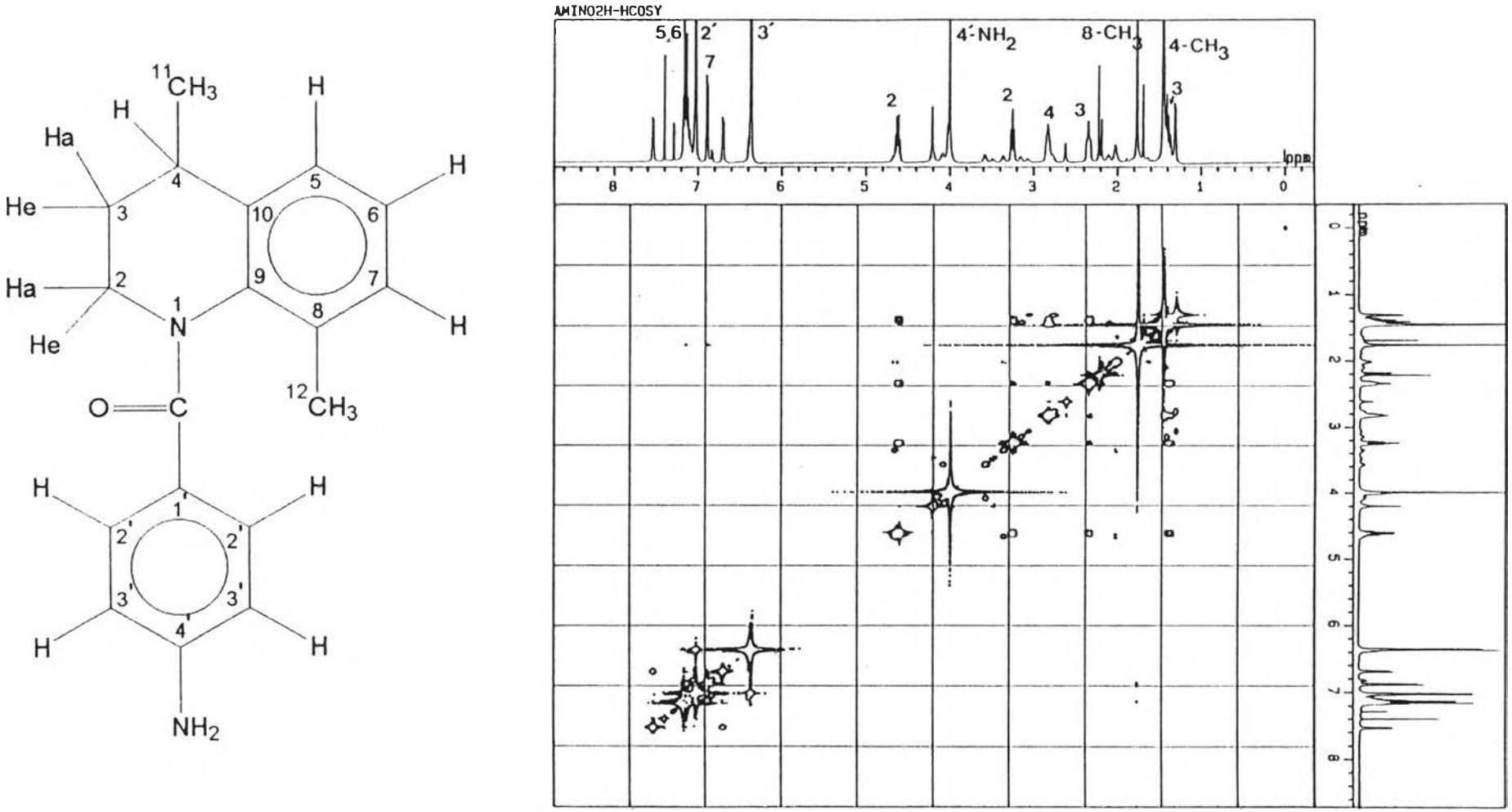

Figure 66. The 500 MHz HH COSY spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c.

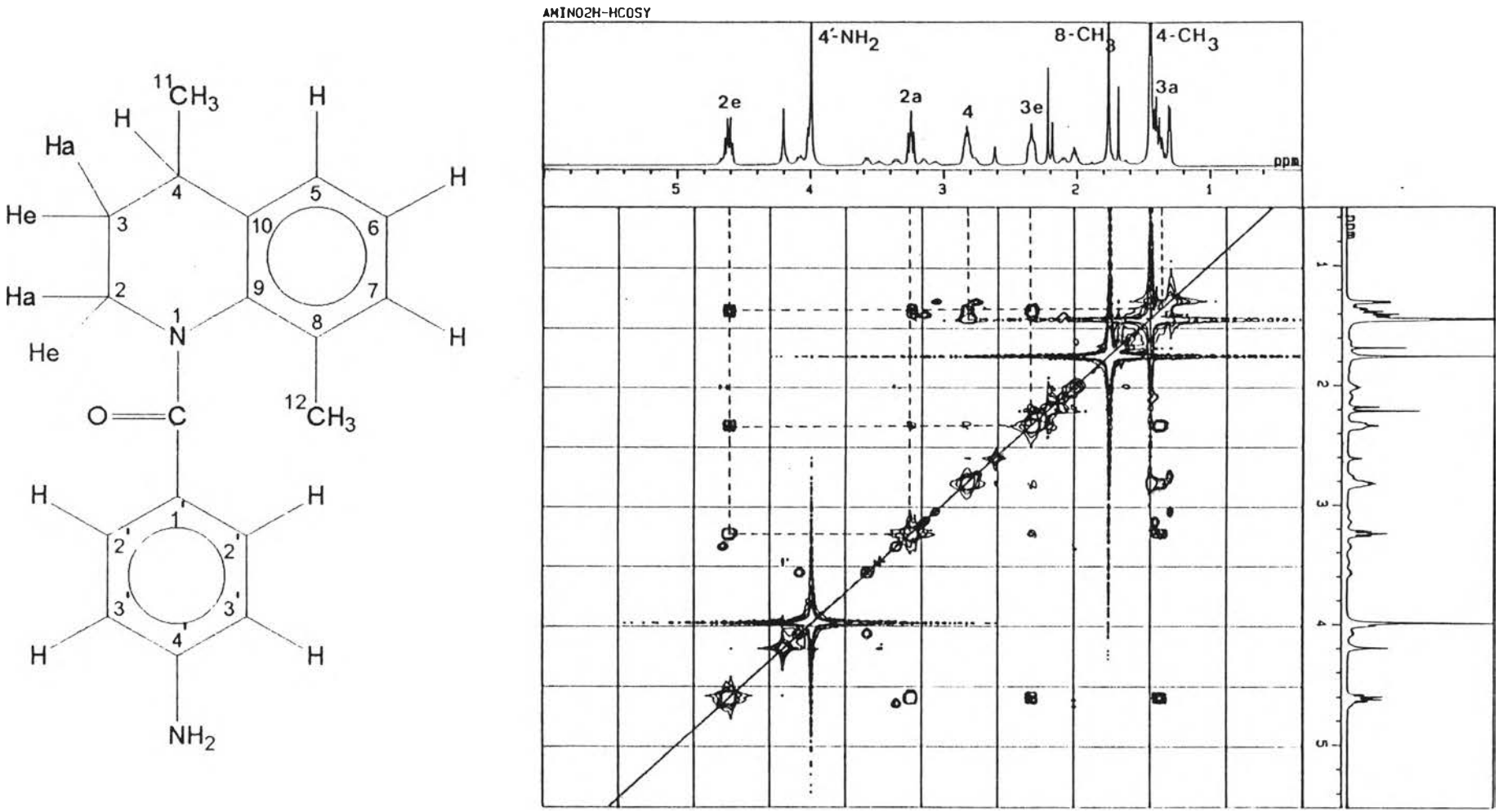

Figure 67. The 500 MHz HH COSY spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c. (Expansion between 0.5-6.0 ppm)

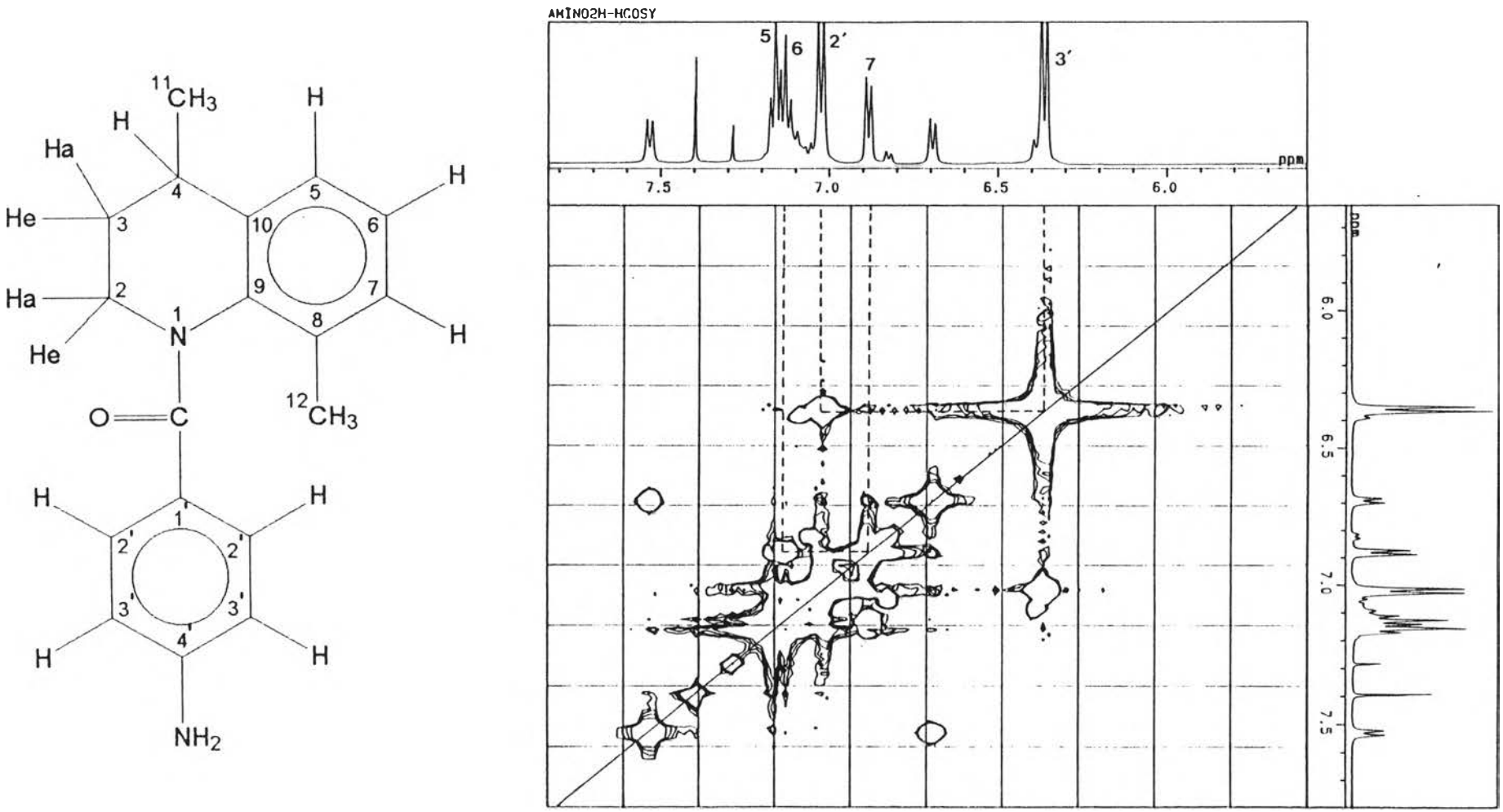

Figure 68. The 500 MHz HH COSY spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c. (Expansion between 6.4-7.8 ppm)

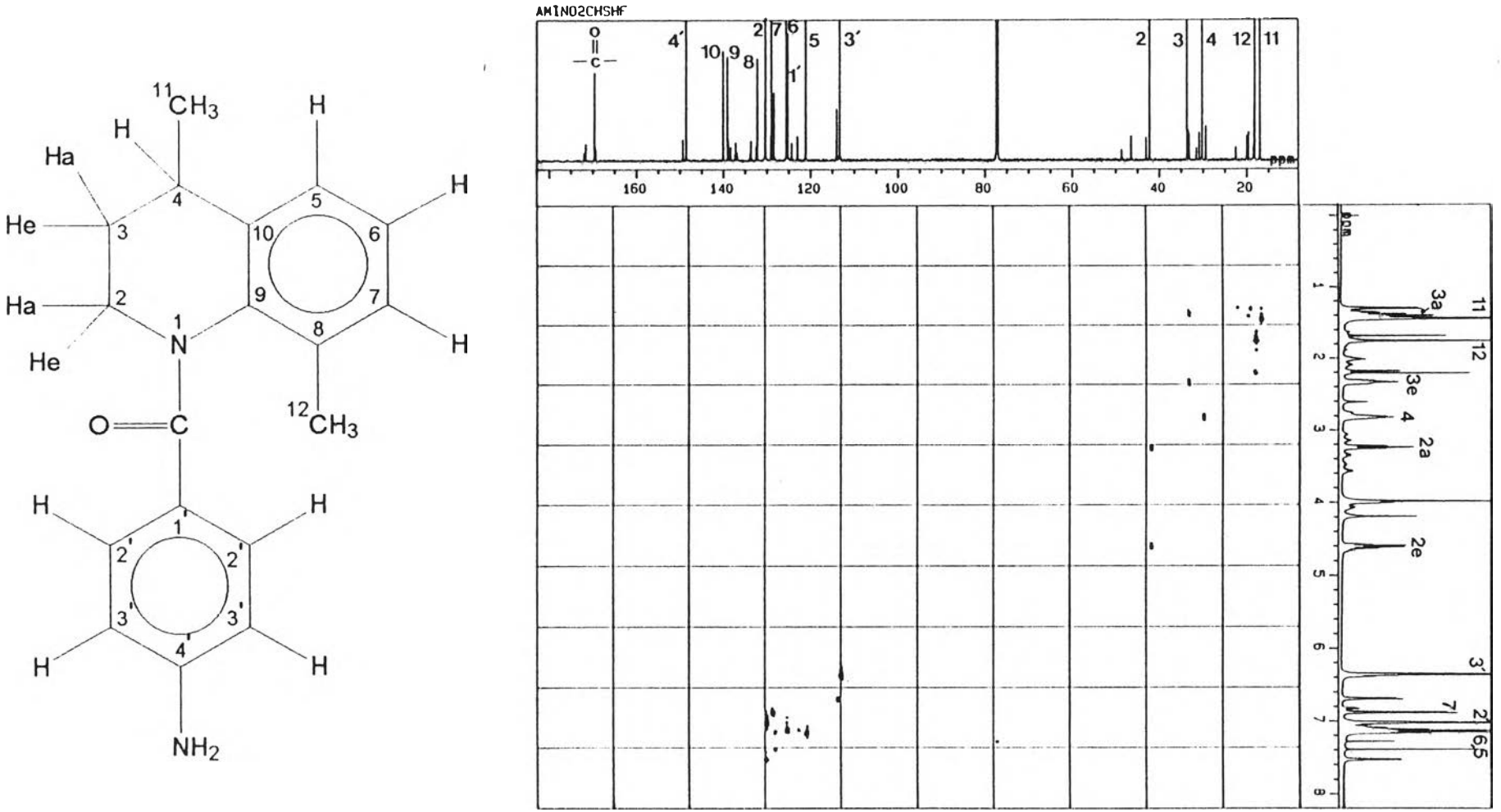

Figure 69. The 125 MHz CH COSY spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c.

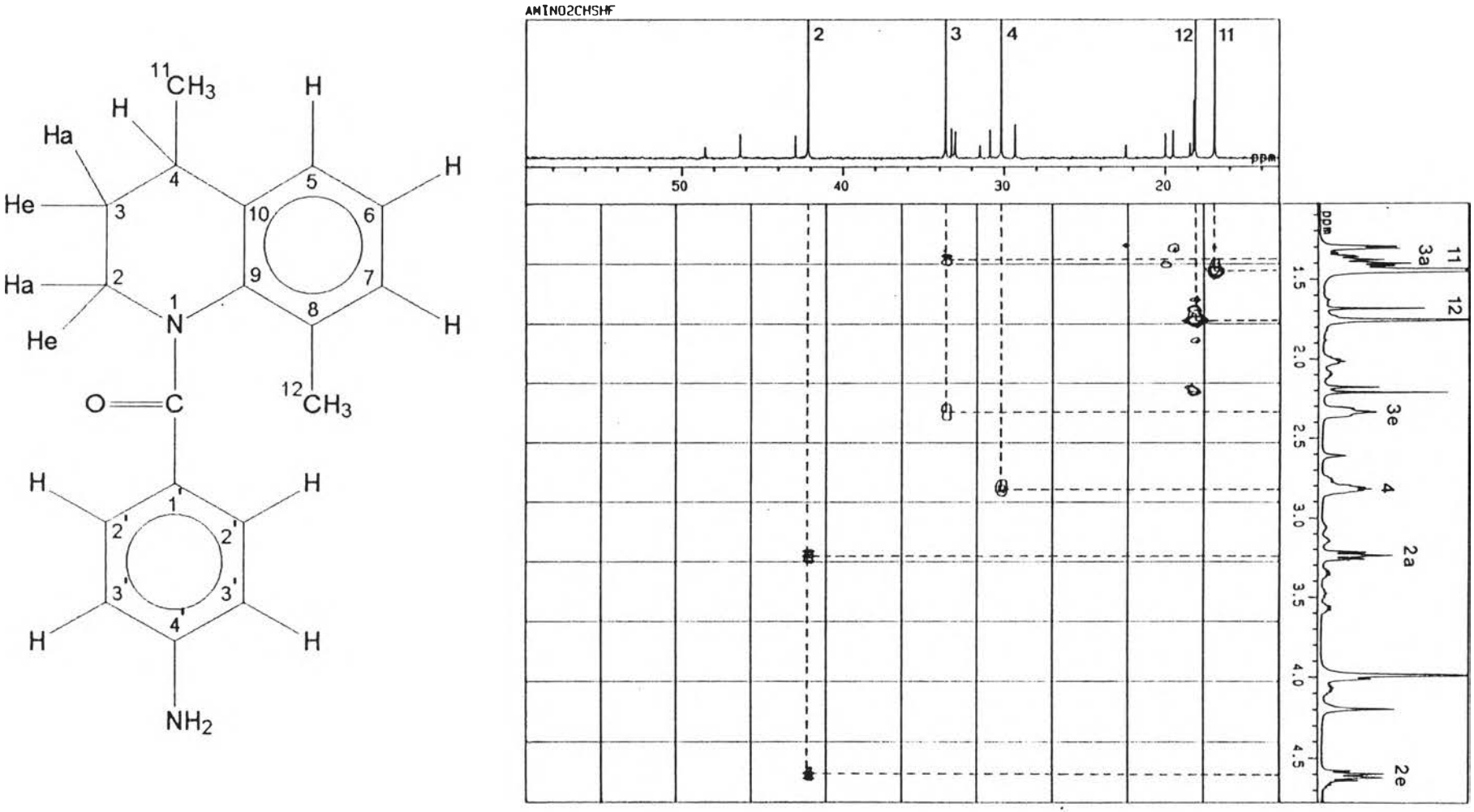

Figure 70. The 125 MHz CH COSY spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c. (Expansion : X scale between 22-60 ppm and Y scale between 1.0-4.8 ppm)

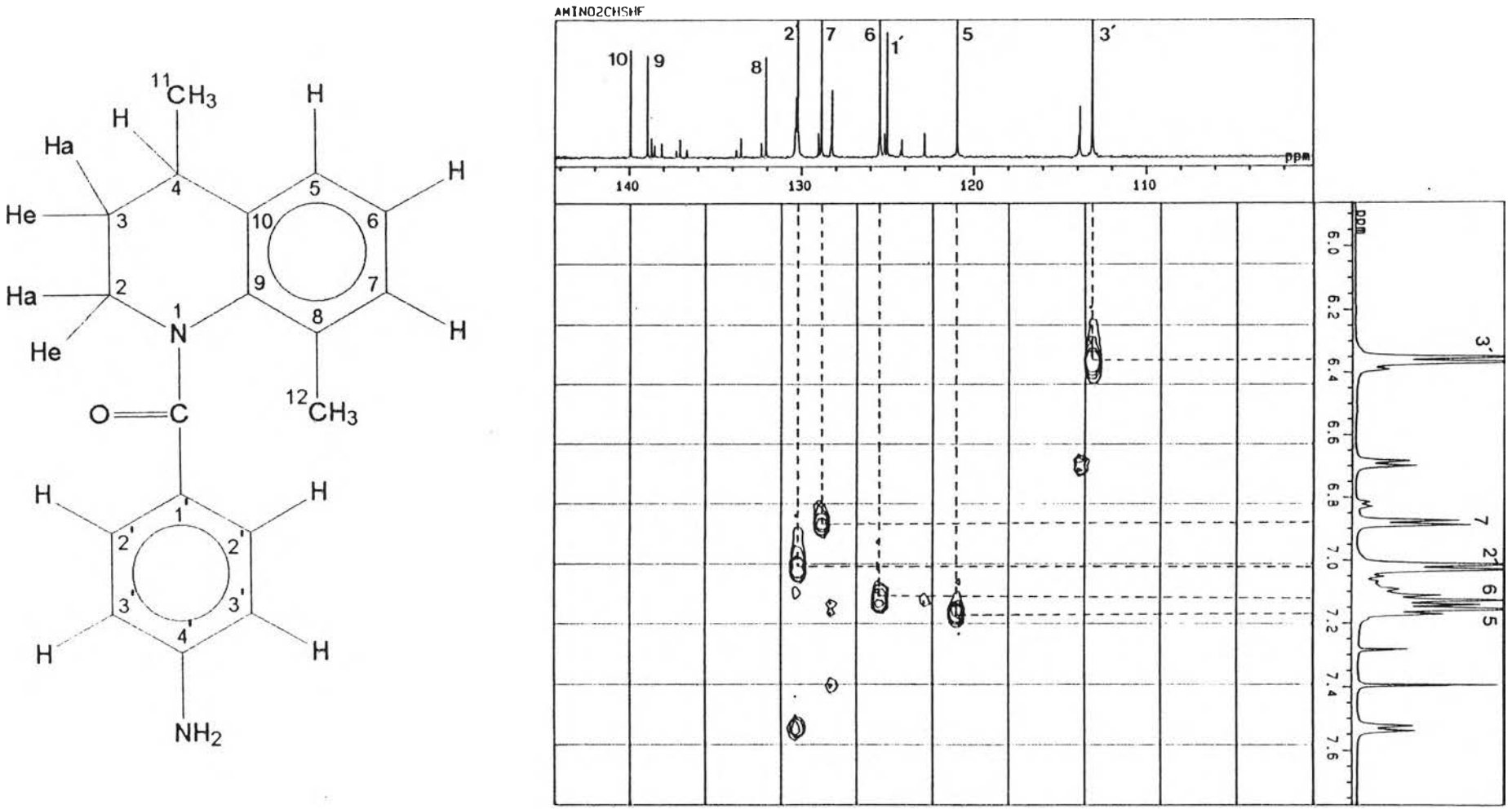

Figure 71. The 125 MHz CH COSY spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c. (Expansion : X scale between 100-144 ppm and Y scale between 5.9-7.8 ppm)

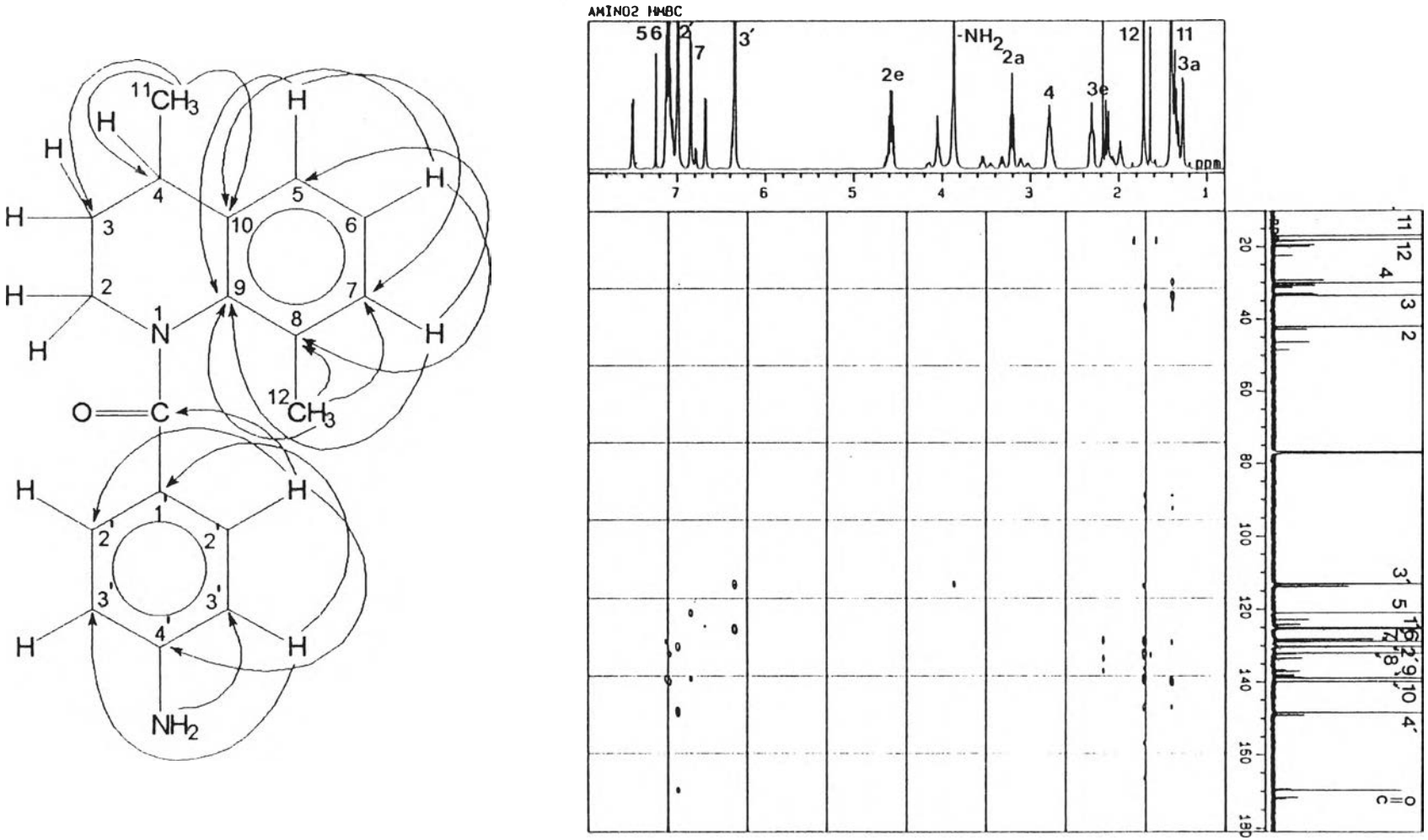

Figure 72. The 125 MHz HMBC spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c.

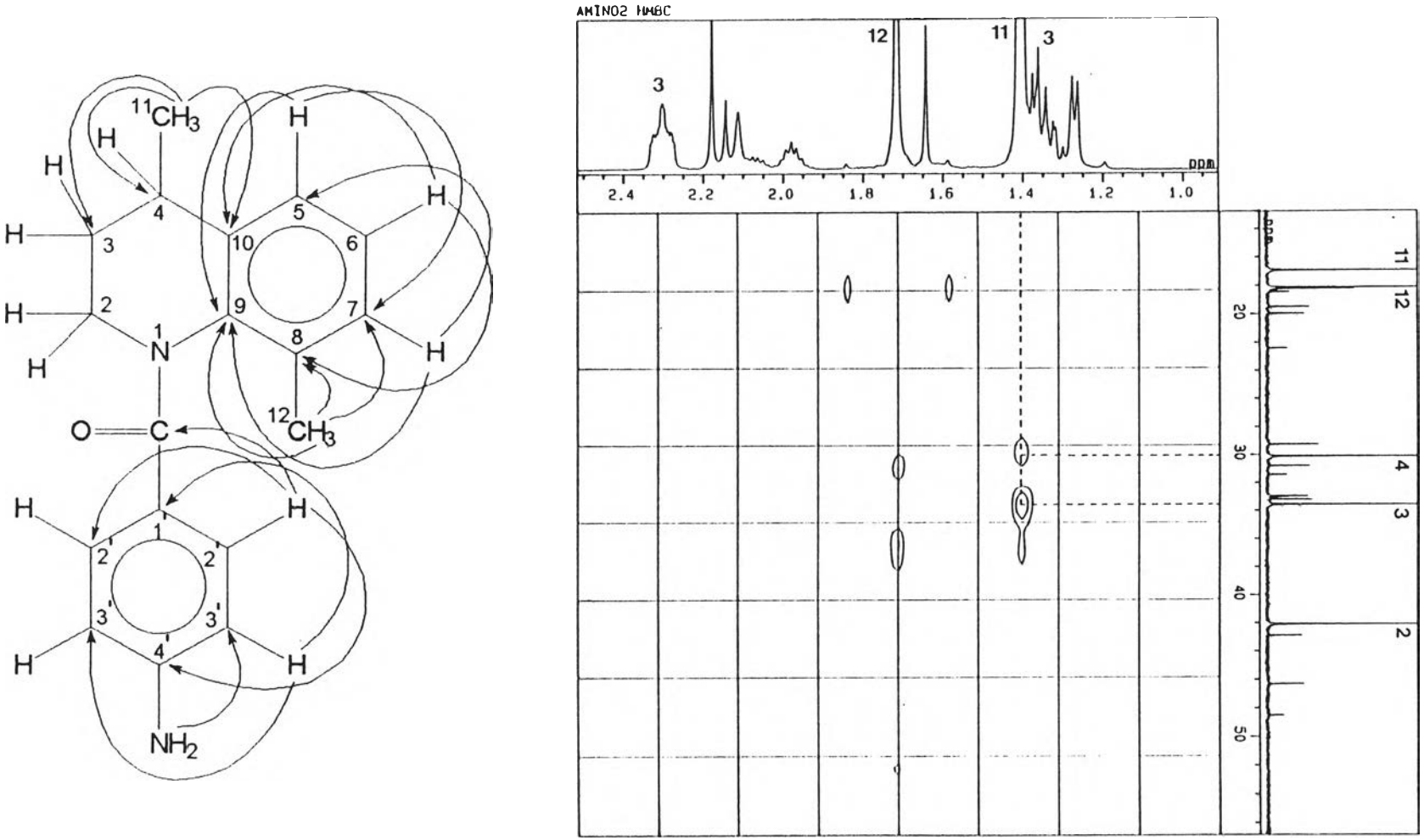

Figure 73. The 125 MHz HMBC spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c. (Expansion : X scale between 0.9-2.5 ppm and Y scale between 10-60 ppm)

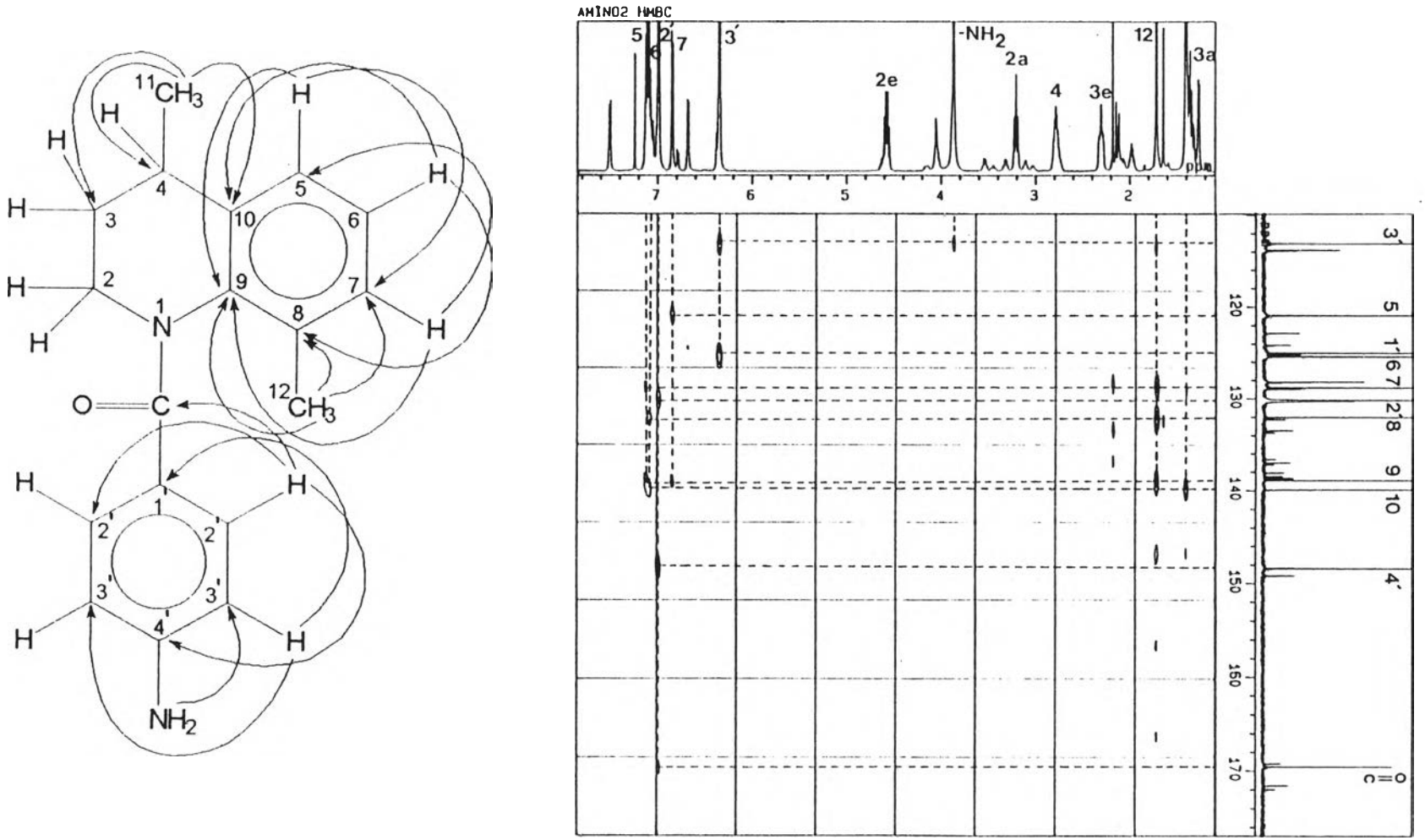

Figure 74. The 125 MHz HMBC spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c. (Expansion : X scale between 1.1-7.9 ppm and Y scale between 110-176 ppm)

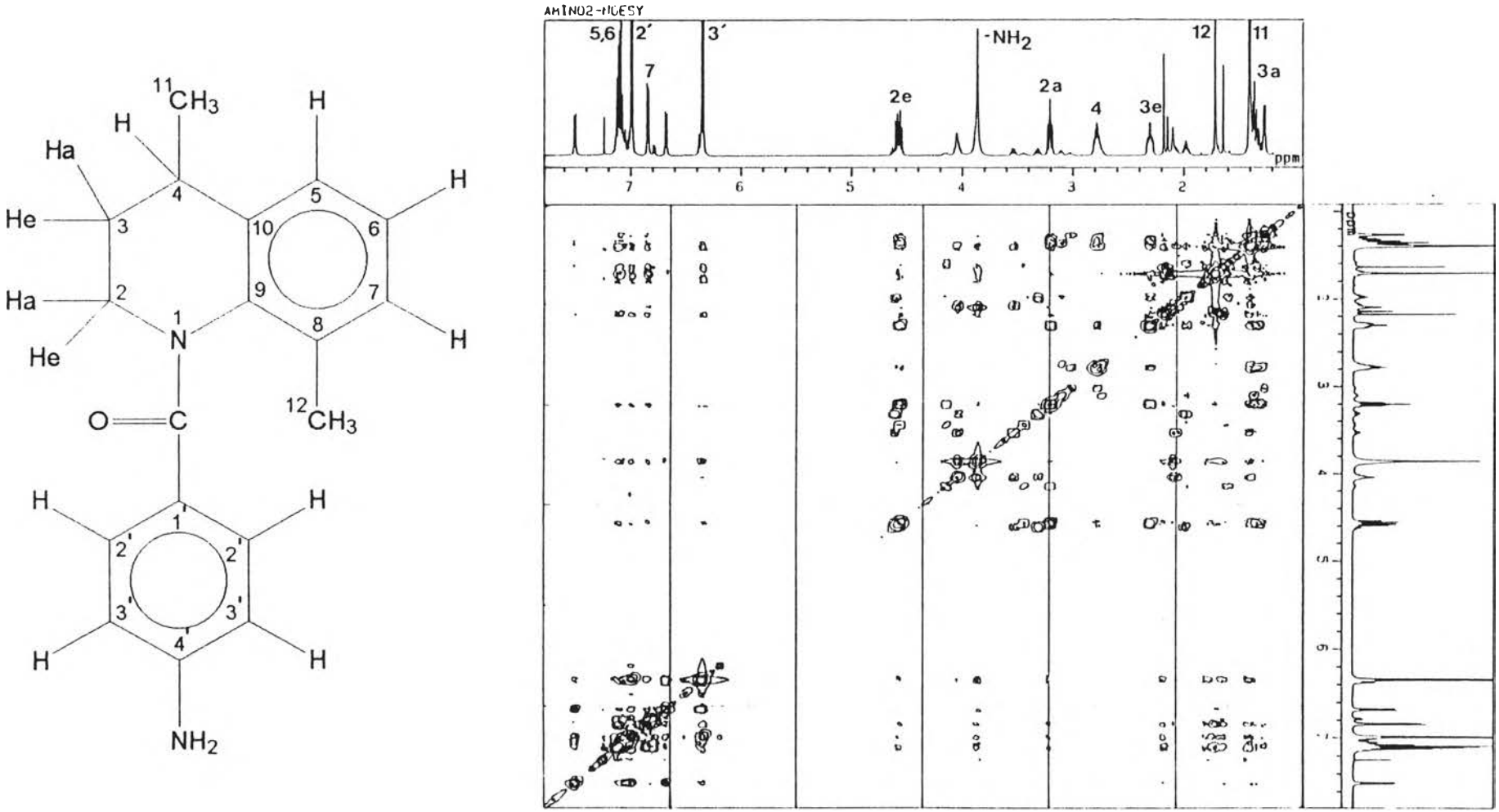

Figure 75. The 500 MHz HH NOESY spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c.

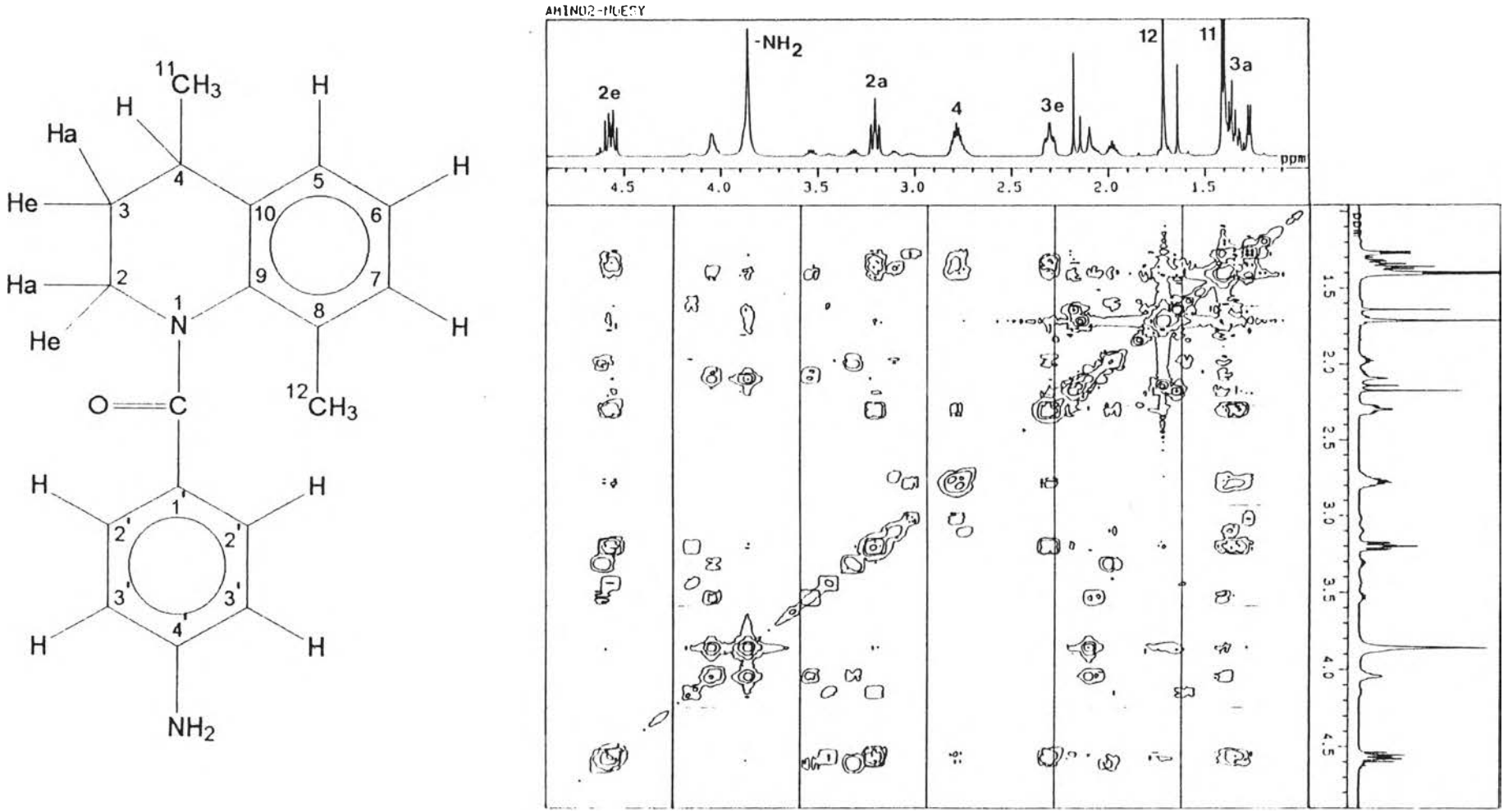

Figure 76. The 500 MHz HH NOESY spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c. (Expansion between 1.0-4.9 ppm)

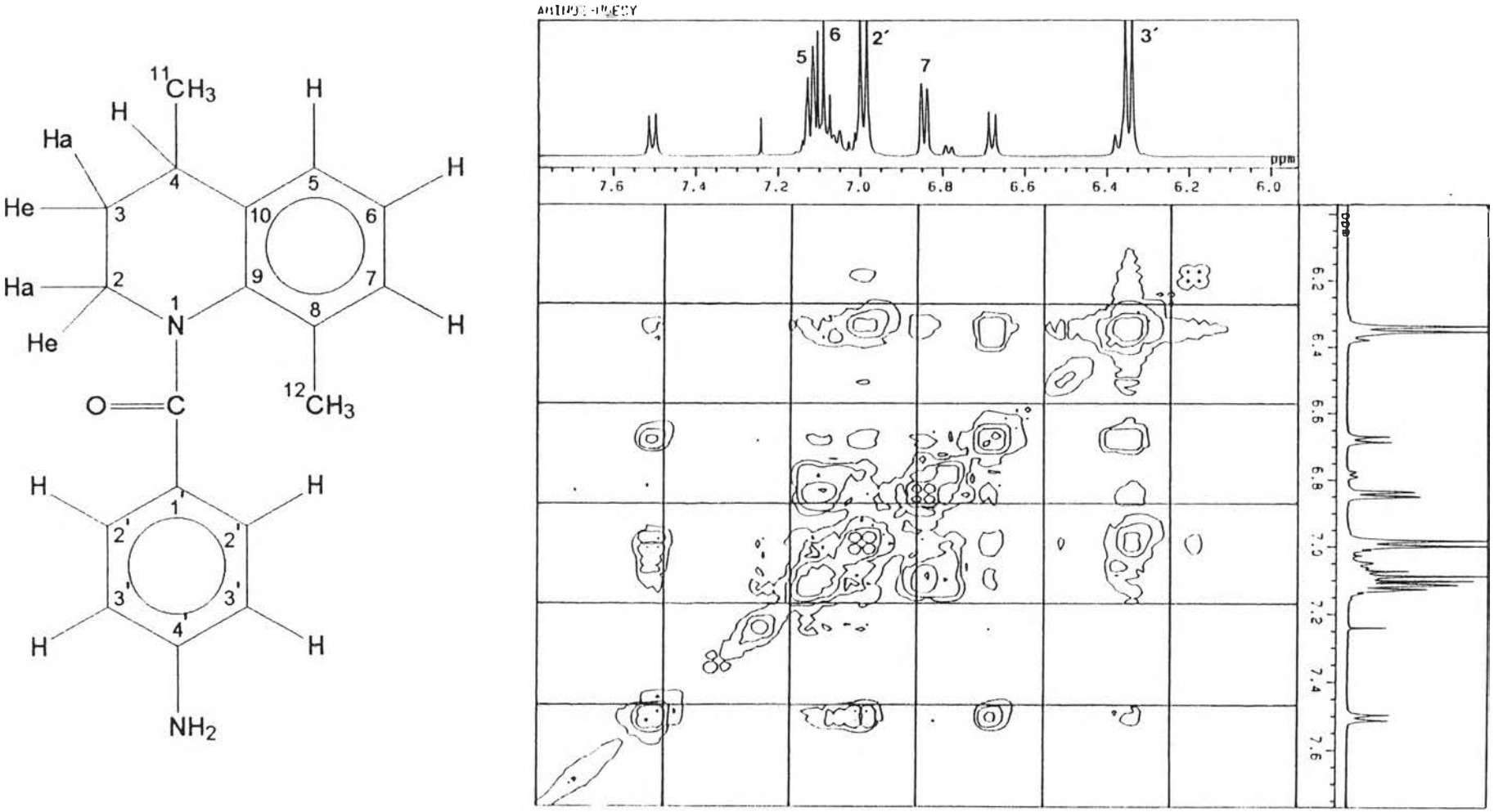

Figure 77. The 500 MHz HH NOESY spectrum of N-(*p*-Aminobenzoyl)-1,2,3,4-tetrahydro-4,8-dimethylquinoline in $CDCl_3$ at -30°c. (Expansion between 6.0-7.8 ppm)