

## CHAPTER III

### EXPERIMENTS

#### Instruments

1. Melting Point Apparatus; Buchi Capillary Melting Point B-545 Apparatus.
2. Infrared Spectrophotometer; Perkin Elmer 2000.
3. Nuclear magnetic Resonance Spectrophotometer; Bruker AMX 300 FT (300 MHz).
4. Nuclear magnetic Resonance Spectrophotometer; Bruker AMX 500 FT (500 MHz).
5. Elemental Analysis; CHNS/O Analyzer (Perkin Elmer PE2400 Series II)

#### Chemicals

1. Benzaldehyde (Merck, Darmstadt, Germany)
2. 4-Biphenyl boronic acid (Aldrich, )
3. n-Butanol (Labscan, Bangkok, Thailand)
4. Dibutyl L-(+)-tartate (TCI, Tokyo, Japan)
5. 3,5-Dimethoxybenzaldehyde (TCI, Tokyo, Japan)
6. 3,4 Dimethoxyphenyl boronic acid (Aldrich, USA)
7. Ethanol (Merck, Darmstadt, Germany)
8. Gacial acetic acid (Labscan, Bangkok, Thailand)
9. Iodine (Merck, Darmstadt, Germany)
10. Isopropyl alcohol (Labscan, Bangkok, Thailand)
11. 4-methylphenyl boronic acid (TCI, Tokyo, Japan)
12. 4-methoxyphenyl boronic acid (TCI, Tokyo, Japan)
13. Methanol (Labscan, Bangkok, Thailand)
14. Nitroethane (Fluka, St. Gallen, Switzerland)

15. 10 % Palladium on activated charcoal (Fluka, St. Gallen, Switzerland)
16. Paraformaldehyde (Merck, Darmstadt, Germany)
17. Periodic acid (Fluka, St. Gallen, Switzerland)
18. Phenyl boronic acid (TCI, Tokyo, Japan)
19. Silver Nitrate (Fluka, St. Gallen, Switzerland)
20. Sodium borohydride (Fluka, St. Gallen, Switzerland)
21. Trifluoroacetic acid (Fluka, St. Gallen, Switzerland)
22. Tetrahydrofuran (Labscan, Bangkok, Thailand)
23. Tetrakis(triphenylphosphine) palladium (TCI, Tokyo, Japan)



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## General procedures for the synthesis of 3-Methyl-1,2,3,4-tetrahydro-isoquinoline derivatives

I. Procedures for the synthesis of *N*-benzyl-2-(3',5'-dimethoxyphenyl)-1-methylethylamine, the starting material

### 1. 2-(3',5'-Dimethoxyphenyl)-1-methyl-1-nitroethene (CU-19-01)

Ammonium acetate (9.29 g, 120.5 mmol) was added to a gently stirred solution of 3,5-dimethoxybenzaldehyde (20.0 g, 120.5 mmol) in tetrahydrofuran (20 ml). Nitroethane (30 ml) was slowly added to the stirred reaction. The mixture was refluxed for 2 hours, and then tetrahydrofuran was removed under vacuo. The residue was poured into water (100 ml) and extracted with ethyl acetate (3 x 100 ml). The combined organic extracts were dried over anhydrous  $\text{Na}_2\text{SO}_4$ . The residue was concentrated in vacuo and purified via recrystallization from methanol to afford yellow crystalline solid to yeild 26.37 g. (98%); m.p. 84.0-85.5 °C

IR	3053	$\text{cm}^{-1}$ ( $\text{V}_s$ C-H, aromatic)
(KBr)	2977	$\text{cm}^{-1}$ ( $\text{V}_s$ C-H, aliphatic)
	1649	$\text{cm}^{-1}$ ( $\text{V}_s$ C=C, aliphatic)
	1600	$\text{cm}^{-1}$ ( $\text{V}_s$ C=C, aromatic)
	1519	$\text{cm}^{-1}$ ( $\text{V}_{as}$ N-O)
	1321	$\text{cm}^{-1}$ ( $\text{V}_s$ N-O)
	1210	$\text{cm}^{-1}$ ( $\text{V}_{as}$ C=C-O-C)
	1157	$\text{cm}^{-1}$ ( $\text{V}_{as}$ C-O-C)
	1060	$\text{cm}^{-1}$ ( $\text{V}_s$ C=C-O-C)

(Figure 16)

$^1\text{H-NMR}$	2.45	ppm (s, 3H, 1- $\text{CH}_3$ )
( $\text{CDCl}_3$ )	3.82	ppm (s, 2 x 3H, 3' and 5'- $\text{OCH}_3$ )
	6.52	ppm (d, $J_m = 2.1$ Hz, 1H, H-4')
	6.55	ppm (d, $J_m = 2.1$ Hz, 2H, H-2' and H-6')
	8.01	ppm (s, 1H, H-2)

(Figure 17)

$^{13}\text{C-NMR}$	14.54	ppm (1- $\text{CH}_3$ )
( $\text{CDCl}_3$ )	55.89	ppm (3' and 5'- $\text{OCH}_3$ )
	102.13	ppm (CH-4')
	108.31	ppm (CH-2' and 6')
	133.95	ppm (CH-1)
	134.58	ppm (C-1')
	148.55	ppm (C-2)
	161.36	ppm (C-3' and C-5')

(Figure 18)

## 2. 2-(3',5'-Dimethoxyphenyl)-1-methyl-1-nitroethane (CU-19-02)

A well stirred solution of 2-(3',5'-dimethoxyphenyl)-1-methyl-1-nitroethane (0.723 g, 3.24 mmol), silica gel (6.0 g) in the mixtures of  $\text{CH}_2\text{Cl}_2$  (35 ml) and IPA (isopropyl alcohol) (35 ml) was cooled in an ice-bath, and consequently, sodium borohydride (0.491 g, 13.0 mmol, 4 eq.) was added portion over 1 hour. The reaction was stirred at room temperature for 3 hours. Glacial acetic acid was slowly added to the stirred reaction until the solution was acidic pH. The silica gel was separated out by filtration and washed with dichloromethane (100 ml). The combined filtrates were washed with 5% sodium bicarbonate (3 x 100 ml) to neutralize the excess glacial acetic acid; the organic phase was washed with water (3 x 100 ml) and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . The solution was concentrated under reduced pressure to give the

yellowish oil of product. The residue was purified by column chromatography (SiO<sub>2</sub>, hexanes:EtOAc = 4:1) to yield 0.722 g (99 %) as colorless thick oil.

IR	3010-3125	cm <sup>-1</sup> (V C-H, aromatic)
(Neat)	2995	cm <sup>-1</sup> (V C-H, aliphatic)
	1600	cm <sup>-1</sup> (V <sub>s</sub> C=C, aromatic)
	1550	cm <sup>-1</sup> (V <sub>as</sub> N-O)
	1353-1322	cm <sup>-1</sup> (V <sub>s</sub> N-O)
	1205	cm <sup>-1</sup> (V <sub>as</sub> C=C-O-C)
	1153	cm <sup>-1</sup> (V <sub>as</sub> C-O-C)
	1065	cm <sup>-1</sup> (V <sub>s</sub> C=C-O-C)

(Figure 19)

<sup>1</sup> H-NMR	1.55	ppm (d, <i>J</i> = 6.5 Hz, 3H, 1-CH <sub>3</sub> )
(CDCl <sub>3</sub> )	2.91	ppm (dd, <i>J</i> <sub>gem</sub> = 13.7 Hz, <i>J</i> <sub>vic</sub> = 6.7 Hz, 1H, H-2)
	3.29	ppm (dd, <i>J</i> <sub>gem</sub> = 13.7 Hz, <i>J</i> <sub>vic</sub> = 7.3 Hz, 1H, H-2)
	3.77	ppm (s, 2 x 3H, 3' and 5'-O-CH <sub>3</sub> )
	4.77	ppm (m, 1H, H-1)
	6.31	ppm (s, 2H, H-2' and H-6')
	6.39	ppm (s, 1H, H-4')

(Figure 20)

<sup>13</sup> C-NMR	19.25	ppm (1-CH <sub>3</sub> )
(CDCl <sub>3</sub> )	41.75	ppm (CH <sub>2</sub> -2)
	55.69	ppm (3' and 5'-OCH <sub>3</sub> )
	84.62	ppm (CH-1)
	99.56	ppm (CH-4')
	107.48	ppm (CH-2' and 6')

138.14 ppm (C-1')  
 161.46 ppm (C-3' and C-5')

(Figure 21)

DEPT 135 (Figure 22)

### 3. 2-(3',5'-Dimethoxyphenyl)-1- methylethylamine (CU-19-03)

A solution of 2-(3,5-dimethoxyphenyl)-1-methyl-1-nitroethane(4.220 g, 18.76 mmol) in ethanol (10 ml) and glacial acetic acid (5 ml) was hydrogenated over 10 % Pd/C (0.94 g, 5% mmol of the starting material) under pressure of hydrogen gas for 72 hours. The catalyst was removed by filtration and washed with ethanol (100-200 ml). The combined filtrates were evaporated to give the yellow oily residues. The resulting residues were dissolved in 100 ml of ethyl acetate and extracted with 0.5 N hydrochloric acid (3 x 100 ml). The aqueous portion was basified and adjusted to pH = 9-10 with ammonia solution, and then extracted with dichloromethane (3 x 100 ml). The combined organic layers were concentrated under vacuum and dissolved in 100 ml of ethyl acetate and then washed with water (3 x 100 ml). The organic residues were dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure to afford pale yellowish oil of product. This product was purified by column chromatography (SiO<sub>2</sub>, Hexanes:EtOAc = 4:1 with 3 % Et<sub>3</sub>N) to yield 3.07 g. (84 %) as a colorless thick oil.

IR	3300-3500	cm <sup>-1</sup> (V <sub>s</sub> N-H, broad)
(Neat)	3125	cm <sup>-1</sup> (V C-H, aromatic)
	2995	cm <sup>-1</sup> (V C-H, aliphatic)
	1596	cm <sup>-1</sup> (V <sub>s</sub> C=C, aromatic)
	1205	cm <sup>-1</sup> (V <sub>as</sub> C=C-O-C, aromatic)
	1152	cm <sup>-1</sup> (V <sub>as</sub> C-O-C)
	1058	cm <sup>-1</sup> (V <sub>s</sub> C=C-O-C)

(Figure 24)

<sup>1</sup> H-NMR	1.12	ppm (d, $J = 6.3$ Hz, 3H, 1-CH <sub>3</sub> )
(CDCl <sub>3</sub> )	1.52	ppm (s, 1H, NH)
	2.44	ppm (dd, $J_{gem} = 13.1$ Hz, $J_{vic} = 8.3$ Hz, 1H, H-2)
	2.66	ppm (dd, $J_{gem} = 13.1$ Hz, $J_{vic} = 5.1$ Hz, 1H, H-2)
	3.16	ppm (m, 1H, H-1)
	3.77	ppm (s, 2 x 3H, 3' and 5'-OCH <sub>3</sub> )
	6.34	ppm (m, 3H, H-2', H-4' and H-6')

(Figure 25)

<sup>13</sup> C-NMR	23.98	ppm (1-CH <sub>3</sub> )
(CDCl <sub>3</sub> )	47.33	ppm (CH <sub>2</sub> -2)
	48.71	ppm (CH-1)
	55.65	ppm (3' and 5'-OCH <sub>3</sub> )
	98.54	ppm (CH-4')
	107.65	ppm (CH-2' and 6')
	142.48	ppm (C-1')
	161.18	ppm (C-3' and C-5')

(Figure 26)

DEPT 135 (Figure 27)

4. *N*-Benzyl-2-(3',5'-dimethoxyphenyl)-1-methylethylamine (CU-19-04)

Benzaldehyde (6.22 g, 73.35 mmol) was added to a solution of 2-(3',5'-dimethoxyphenyl)-1-methylethylamine (2.86 g, 14.67 mmol) in benzene (100 ml). The mixture was refluxed under a Dean-Stark separator for 6 hours. The solvent was removed under reduced pressure to generate the intermediate imines yellowish oil. This residue was dissolved in ethanol (100 ml) and 3-5 equivalents of NaBH<sub>4</sub> were slowly added. The reaction mixture was stirred on ice bath. The stirring mixture was slowly allowed to warm at the room temperature overnight. The excess NaBH<sub>4</sub> was

decomposed with glacial acetic acid, evaporated under vacuum to give the residue. The residue was diluted with ethyl acetate (100 ml) and extracted with water (3 x 100 ml). The collected aqueous fractions were basified and adjusted to pH 9-10 with concentrated ammonium solution. The basic aqueous fraction was extracted with dichloromethane (3 x 100 ml). The collected o washed with water (3 x 100), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated under reduced pressure to give the pale yellowish oil. The residue was purified by column chromatography ( $\text{SiO}_2$ , hexanes:EtOAc = 9.5:0.5 with 3 %  $\text{Et}_3\text{N}$ ) to yield 3.14 g (75 %) of colorless thick oil.

IR	3296	$\text{cm}^{-1}$ ( $\text{V}_s$ N-H, broad)
(Neat)	3075	$\text{cm}^{-1}$ ( $\text{V}$ C-H, aromatic)
	2990	$\text{cm}^{-1}$ ( $\text{V}_s$ C-H, aliphatic)
	1596	$\text{cm}^{-1}$ ( $\text{V}_s$ C=C, aromatic)
	1445-1432	$\text{cm}^{-1}$ ( $\text{V}_s$ O- $\text{CH}_3$ )
	1205	$\text{cm}^{-1}$ ( $\text{V}_{as}$ C=C-O-C)
	1152	$\text{cm}^{-1}$ ( $\text{V}_{as}$ C-O-C)
	1054	$\text{cm}^{-1}$ ( $\text{V}_s$ C=C-O-C)

(Figure 29)

$^1\text{H-NMR}$	1.11	ppm (d, $J = 6.2$ Hz, 3H, 1- $\text{CH}_3$ )
( $\text{CDCl}_3$ )	1.80	ppm (s, 1H, NH)
	2.60	ppm (dd, $J_{gem} = 13.2$ Hz, $J_{vic} = 6.2$ Hz, 1H, H-2)
	2.70	ppm (dd, $J_{gem} = 13.2$ Hz, $J_{vic} = 7.4$ Hz, 1H, H-2)
	2.93	ppm (m, 1H, H-1)
	3.70	ppm (d, $J = 13.2$ Hz, 1H, N- $\text{CH}_2\text{Ph}$ )
	3.75	ppm (s, 6H, 3' and 5'- $\text{OCH}_3$ )
	3.88	ppm (d, $J = 13.2$ Hz, 1H, N- $\text{CH}_2\text{Ph}$ )
	6.32	ppm (s, 3H, H-2', H-4' and H-6')



7.18-7.34 ppm (5H, aromatic ring)  
(Figure 30)

<sup>13</sup> C-NMR	20.66	ppm (1-CH <sub>3</sub> )
(CDCl <sub>3</sub> )	44.35	ppm (CH <sub>2</sub> -2)
	51.61	ppm (N-CH <sub>2</sub> )
	53.61	ppm (CH-1)
	55.64	ppm (3' and 5'-OCH <sub>3</sub> )
	98.76	ppm (CH-4')
	107.77	ppm (CH-2' and 6')
	127.29	ppm (CH-4'')
	128.40	ppm (CH-2'' and 6'')
	128.53	ppm (CH-3'' and 5'')
	142.19	ppm (C-1'')
	142.22	ppm (C-1')
	161.18	ppm (C-3'' and C-5'')

(Figure 31)

DEPT 135 (Figure 32)

#### Note 1

When sodium borohydride was less used than 3 equivalents, the Schiff base intermediate was incompletely reduced and was consequently cyclized to obtain the 1-phenyl THIQ when the excess glacial acetic acid was added to eliminate the unreacted sodium borohydride in the workup process. The structure of the cyclized product (m.p. 106.5-107.0 °C) was proven by <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy. Therefore, 3-5 equivalents of sodium borohydride was essential to afford the highest yield of the required product and the lowest isoquinoline by-product.

Anal. Cal. For C<sub>19</sub>H<sub>23</sub>NO<sub>2</sub> C 76.26 %; H 7.47 %; N 4.94 %

Found C 76.38 %; H 7.41 %; N 4.94 %

IR	3100-3400	$\text{cm}^{-1}$ ( $\text{V}_s$ N-H, broad)
(Neat)	3159	$\text{cm}^{-1}$ ( $\text{V}$ C-H, aromatic)
	2912	$\text{cm}^{-1}$ ( $\text{V}_s$ C-H, aliphatic)
	1597	$\text{cm}^{-1}$ ( $\text{V}_s$ C=C, aromatic)
	1457-1420	$\text{cm}^{-1}$ ( $\text{V}_s$ O-CH <sub>3</sub> )
	1201	$\text{cm}^{-1}$ ( $\text{V}_{as}$ C=C-O-C)
	1146	$\text{cm}^{-1}$ ( $\text{V}_{as}$ C-O-C)
	1051	$\text{cm}^{-1}$ ( $\text{V}_s$ C=C-O-C)

(Figure 176)

<sup>1</sup> H-NMR	1.10	ppm (d, $J = 6.2$ Hz, 3H, 1-CH <sub>3</sub> )
(CDCl <sub>3</sub> /TMS)	2.00	ppm (s, 1H, NH)
	2.58	ppm (dd, $J_{gem} = 16.5$ Hz, $J_{ax} = 11.0$ Hz, 1H, H-4)
	2.79	ppm (dd, $J_{gem} = 16.5$ Hz, $J_{eq} = 4.0$ Hz, 1H, H-4)
	3.00	ppm (m, 1H, H-1)
	3.55	ppm (s, 3H, 6- or 8-OCH <sub>3</sub> )
	3.82	ppm (s, 3H, 8- or 6-OCH <sub>3</sub> )
	5.30	ppm (s, 1H)
	6.25	ppm (s, 1H, H-7)
	6.30	ppm (s, 1H, H-5)
	7.09-7.28	ppm (5H, aromatic-H)

(Figure 177 and 178)

<sup>13</sup> C-NMR	22.68	ppm (3-CH <sub>3</sub> )
(CDCl <sub>3</sub> /TMS)	37.83	ppm (CH <sub>2</sub> -4)
	42.39	ppm (CH-3)
	55.67	ppm (6- or 8-OCH <sub>3</sub> )

	55.77	ppm (8- or 6-OCH <sub>3</sub> )
	55.84	ppm (CH-1)
	96.88	ppm (CH-7)
	104.53	ppm (CH-5)
	117.75	ppm (C-4a)
	127.00	ppm (CH-4')
	137.86	ppm (CH-2',3' and 5',6')
	137.85	ppm (C-1')
	145.07	ppm (C-4a)
	157.90	ppm (C-6 or C-8)
	159.81	ppm (C-8 or C-6)
	(Figure 179)	
DEPT 135	(Figure 180)	
HMQC	(Figure 182 and 183)	
NOESY	(Figure 184 and 185)	

II. The Procedure for cyclization of *N*-benzyl-2-(3',5'-dimethoxyphenyl)-1-methylethylamine to the tetrahydroisoquinoline with paraformaldehyde

#### 1.2-Benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05)

A solution of *N*-benzyl-2-(3,5-dimethoxyphenyl)-1-methylethylamine (1.00 g, 3.5 mmol) and potassium carbonate (1.94 g, 14.0 mmol) in ethanol (25 ml) was stirred for 10 min at room temperature. Paraformaldehyde (0.16 g, 5.3 mmol, 1.5 eq.) was then added in one portion; the mixture was stirred overnight at room temperature and then filtered. The filtrate was evaporated under reduced pressure to give the *O,N*-acetal intermediate which was used without purification. The acetal residue was dissolved in CH<sub>2</sub>Cl<sub>2</sub> which was added 0.5 M TFA in CH<sub>2</sub>Cl<sub>2</sub> (7 ml, 3.5 mmol). The

mixture was stirred at 0 °C for 1 hour, then diluted with cool water and adjusted to pH 9-12 with ammonia solution. The aqueous mixture was extracted with dichloromethane (3 x 100 ml). The combined extracts were washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and consequently, concentrated under reduced pressure to give the pale yellowish oil. The residue was purified by column chromatography (SiO<sub>2</sub>, hexanes:EtOAc = 9.5:0.5 with 3 % Et<sub>3</sub>N) to yield 0.95 g (91 %) as a colorless crystalline solid.

Anal. Cal. For C<sub>19</sub>H<sub>23</sub>NO<sub>2</sub> C 76.77 %; H 7.81 %; N 4.72 %

Found C 76.56 %; H 7.62 %; N 4.75 %

IR 2961 cm<sup>-1</sup> (V C-H ,aliphatic )

(KBr pellet) 1602 cm<sup>-1</sup> (V<sub>s</sub> C=C, aromatic)

1205 cm<sup>-1</sup> (V<sub>as</sub> C=C-O-C)

1147 cm<sup>-1</sup> (V<sub>as</sub> C-O-C)

1051 cm<sup>-1</sup> (V<sub>s</sub> C=C-O-C)

(Figure 34)

<sup>1</sup>H-NMR 1.09 ppm (d, *J* = 6.4 Hz, 3H, 3-CH<sub>3</sub>)

(CDCl<sub>3</sub>) 2.55 ppm (dd, *J*<sub>gem</sub> = 16.4 Hz, *J*<sub>vic</sub> = 4.7 Hz, 1H, H-4)

3.00 ppm (dd, *J*<sub>gem</sub> = 16.4 Hz, *J*<sub>vic</sub> = 4.8 Hz, 1H, H-4)

3.10 ppm (m, 1H, H-3)

3.57 ppm (d, 2H, H-1)

3.65 ppm (d, *J* = 13.4 Hz, 1H, N-CH<sub>2</sub>Ph)

3.74 ppm (s, 3H, 6- or 8-OCH<sub>3</sub>)

3.79 ppm (s, 3H, 8- or 6-OCH<sub>3</sub>)

3.85 ppm (d, *J* = 13.4 Hz, 1H, N-CH<sub>2</sub>Ph)

6.25 ppm (s, 1H, H-5 or H-7)

6.27 ppm (s, 1H, H-7 or H-5)

7.20-7.41 ppm (5H, aromatic)

(Figure 36 and 37)

$^{13}\text{C-NMR}$	14.21	ppm (3- $\text{CH}_3$ )
( $\text{CDCl}_3$ )	36.47	ppm ( $\text{CH}_2$ -4)
	46.76	ppm ( $\text{CH}_2$ -1)
	51.31	ppm (CH-3)
	55.62	ppm (6- or 8- $\text{OCH}_3$ )
	55.70	ppm (8- or 6- $\text{OCH}_3$ )
	58.18	ppm (N- $\text{CH}_2\text{Ph}$ )
	96.27	ppm (C-7)
	104.77	ppm (C-5)
	116.15	ppm (C-8a)
	127.19	ppm (C-4')
	128.67	ppm (C-2' and C-6')
	129.30	ppm (C-3' and C-5')
	136.04	ppm (C-1')
	140.00	ppm (C-4a)
	157.49	ppm (C-6 or C-8)
	159.20	ppm (C-8 or C-6)

(Figure 37)

DEPT 135 (Figure 38)

H-H COSY (Figure 40 and 41)

HMQC (Figure 42 and 43)

III. The procedures for cyclization of *N*-benzyl-2-(3',5'-dimethoxyphenyl)-1-methylethylamine to the tetrahydroisoquinoline with butyl glyoxal

1. Butyl glyoxalate

To a solution of dibutyl-L-(+)-tatrante (19.06 g, 72.74 mmol) in dry ether (150 ml) cooled in an ice water-bath, was added (16.58 g, 72.74 mmol) of periodic acid ( $\text{HIO}_4$ ) in a small portion over 1 hour under nitrogen atmosphere with stirring. The milky reaction was vigorously stirred at room temperature until the ether layer became almost clear solution and then the ether phase was decanted to separate out the white solid, dried over anhydrous  $\text{Na}_2\text{SO}_4$ . Finally, the filtrate was distilled in a short-path distillation to give the butyl glyoxal as colorless oil (Kelly, 1972) yield 27.5 g (72 %)

2. Butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10)

A mixture solution of *N*-benzyl-2-(3,5-dimethoxyphenyl)-1-methylethylamine (1.99 g, 7.0 mmol), butyl glyoxal (9.10 g, 70.0 mmol),  $\text{K}_2\text{CO}_3$  (4.83 g, 35 mmol) in *n*-butanol (10 ml) was gently stirred overnight at room temperature, and then the solution was filtered and washed with *n*-butanol. The filtrate was evaporated under reduced pressure to give the *O,N*-acetal intermediate. The residue was dissolved with dichloromethane (10 ml), then slowly added 0.5 M TFA in  $\text{CH}_2\text{Cl}_2$  (14 ml, 7.0 mmol) into the solution mixture. This mixture was stirred in ice water-bath for 1 hour. The reaction was poured into basified cool water (100 ml) and extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 100 ml). The combined extracts were concentrated under vacuum to give the residue of product. This residue was purified by column chromatography ( $\text{SiO}_2$ , hexanes:EtOAc = 9.5:0.5 with 3 %  $\text{Et}_3\text{N}$ ) and recrystallized with MeOH to give yield 2.52 g (91 %), m.p. 81.0-82.0 °C as a colorless crystalline solid.

Anal. Cal. For  $\text{C}_{24}\text{H}_{31}\text{NO}_4$ : C, 72.61; H, 7.87; N, 3.53

Found : C, 72.52; H, 7.80; N, 3.52

IR	3330	$\text{cm}^{-1}$ (overtone C=O)
(KBr pellet)	1735	$\text{cm}^{-1}$ (V C=O, ester)
	1596	$\text{cm}^{-1}$ (V C=C, aromatic)
	1261	$\text{cm}^{-1}$ (V <sub>as</sub> C=C-O-C)
	1193	$\text{cm}^{-1}$ (V <sub>as</sub> C-O-C)
	1172-1148	$\text{cm}^{-1}$ (V <sub>s</sub> C-O-C)

(Figure 44)

<sup>1</sup> H-NMR	0.91	ppm (t, $J = 7.3$ Hz, 3H, H-4')
(CDCl <sub>3</sub> )	1.17	ppm (d, $J = 6.6$ Hz, 3H, 3-CH <sub>3</sub> )
	1.35	ppm (m, 2H, H-3')
	1.57	ppm (m, 2H, H-2')
	2.62	ppm (dd, $J_{gem} = 16.6$ Hz, $J_{ax} = 9.3$ Hz, 1H, H-4)
	2.74	ppm (dd, $J_{gem} = 16.6$ Hz, $J_{eq} = 4.4$ Hz, 1H, H-4)
	3.46	ppm (m, 1H, H-3)
	3.59	ppm (d, $J = 14.5$ Hz, 1H, N-CH <sub>2</sub> Ph)
	3.65	ppm (s, 3H, 6- or 8-OCH <sub>3</sub> )
	3.78	ppm (s, 3H, 8- or 6-OCH <sub>3</sub> )
	3.90	ppm (d, $J = 14.5$ Hz, 1H, N-CH <sub>2</sub> Ph)
	4.08	ppm (m, 2H, H-1')
	4.41	ppm (s, 1H, H-1)
	6.26	ppm (s, 2H, H-5 and H-7)
	7.20-7.42	ppm (5H, aromatic-H)

(Figure 45 and 46)

<sup>13</sup> C-NMR	14.06	ppm (CH <sub>3</sub> -4')
(CDCl <sub>3</sub> )	18.29	ppm (3-CH <sub>3</sub> )
	19.45	ppm (CH <sub>2</sub> -3')

31.13	ppm (CH <sub>2</sub> -2')
33.75	ppm (CH <sub>2</sub> -4)
49.04	ppm (CH-1)
51.63	ppm (CH-3)
55.56	ppm (6- or 8-OCH <sub>3</sub> )
55.67	ppm (8- or 6-OCH <sub>3</sub> )
60.37	ppm (N-CH <sub>2</sub> Ph)
64.59	ppm (C-1')
96.59	ppm (CH-7)
104.76	ppm (CH-5)
114.12	ppm (C-8a)
127.04-128.79	ppm (aromatic-CH)
137.86	ppm (C-1'')
140.54	ppm (C-4a)
158.62	ppm (C-6 or C-8)
159.93	ppm (C-8 or C-6)
173.32	ppm (C-carbonyl ester)

(Figure 47)

DEPT 135 (Figure 48)

H-H COSY (Figure 50 and 51)

HMQC (Figure 52 and 53)

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IV. The Procedure for halogenation of 1,2,3,4-tetrahydroisoquinoline derivatives

1. 5-Iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01)

A solution of the corresponding THIQ (55 mg, 0.1851 mmol) in EtOH (10 ml) and  $\text{CH}_2\text{Cl}_2$  (2 ml) was slowly added to a stirred solution mixture of iodine (70 mg, 0.278 mmol) and silver nitrate (94.33 mg, 0.553 mmol, 3 eq.) in EtOH (10 ml). The reaction mixture was stirred at room temperature for 8 hours. The solids were removed by filtration. The residue was dissolved in  $\text{CH}_2\text{Cl}_2$  (50 ml) and this organic solution was washed with a saturated  $\text{NaHCO}_3$  (2 x 50 ml) and  $\text{H}_2\text{O}$  (2 x 50 ml), dried over anhydrous  $\text{Na}_2\text{SO}_4$  and concentrated under vacuum. The residue was purified by column chromatography ( $\text{SiO}_2$ / hexanes:EtOAc = 4:1) and crystallization to yield 62.62 mg (80.0 %); m.p. 127.5-128.0 °C as a colorless solid.

Anal. Cal. For  $\text{C}_{19}\text{H}_{22}\text{NO}_2\text{I}$ : C, 53.91; H, 5.24; N, 3.31

Found : C, 53.81; H, 5.12; N, 3.35

IR	3006	$\text{cm}^{-1}$ (V C-H, aromatic)
(KBr pellet)	2961	$\text{cm}^{-1}$ (V C-H, aliphatic)
	1589	$\text{cm}^{-1}$ (V <sub>s</sub> C=C, aromatic)
	1213	$\text{cm}^{-1}$ (V <sub>as</sub> C=C-O-C)
	1147	$\text{cm}^{-1}$ (V <sub>as</sub> C-O-C)
	1077	$\text{cm}^{-1}$ (V <sub>s</sub> C=C-O-C)

(Figure 53)

$^1\text{H-NMR}$	1.15	ppm (d, $J = 6.5$ Hz, 3H, 3- $\text{CH}_3$ )
( $\text{CDCl}_3$ )	2.55	ppm (dd, $J_{gem} = 16.9$ Hz, $J_{vic} = 5.6$ Hz, 1H, H-4)
	2.85	ppm (dd, $J_{gem} = 16.9$ Hz, $J_{vic} = 4.9$ Hz, 1H, H-4)
	3.10	ppm (m, 1H, H-3)

3.51	ppm (d, $J = 16.1$ Hz, 1H, H-1)
3.59	ppm (d, $J = 13.4$ Hz, 1H, N-CH <sub>2</sub> Ph)
3.60	ppm (d, $J = 16.5$ Hz, 1H, H-1)
3.78	ppm (s, 3H, 6- or 8-OCH <sub>3</sub> )
3.82	ppm (d, $J = 13.4$ Hz, 1H, N-CH <sub>2</sub> Ph)
3.89	ppm (s, 3H, 8- or 6-OCH <sub>3</sub> )
6.32	ppm (s, 1H, H-7)
7.23-7.40	ppm (5-H, aromatic)

(Figure 55 and 56)

<sup>13</sup>C-NMR  
(CDCl<sub>3</sub>)

15.29	ppm (3-CH <sub>3</sub> )
42.54	ppm (CH <sub>2</sub> -4)
47.16	ppm (CH <sub>2</sub> -1)
52.57	ppm (CH-3)
55.76	ppm (6- or 8-OCH <sub>3</sub> )
57.03	ppm (8- or 6-OCH <sub>3</sub> )
57.45	ppm (N-CH <sub>2</sub> Ph)
82.96	ppm (C-5)
93.76	ppm (C-7)
118.43	ppm (C-8a)
127.27	ppm (C-4')
128.67	ppm (C-3' and C-5')
129.24	ppm (C-2' and C-6')
138.82	ppm (C-1')
139.79	ppm (C-4a)
157.46	ppm (C-8 or C-6)
157.74	ppm (C-6 or C-8)

(Figure 57)

DEPT 135	(Figure 58)
H-H COSY	(Figure 60 and 61)
HMQC	(Figure 62 and 63)
HMBC	(Figure 64)

2. Butyl-5-iodo-2- benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydro-isoquinoline-1-carboxylate(CU-20-02)

A solution mixture of the corresponding THIQ (50 mg, 0.126 mmol) and silver nitrate (64 mg ,0.378 mmol, 3 eq.) in EtOH (10 ml) and CH<sub>2</sub>Cl<sub>2</sub> (2 ml) was slowly added with an iodine (48 mg , 0.189 mmol, 1.5 eq.) in EtOH (10 ml). The reaction mixture was stirred at room temperature for 8 hours. The solids were removed by filtration. The residue was concentrated under reduced pressure. The residue was purified by column chromatography (SiO<sub>2</sub>/ hexanes:EtOAc = 4:1 with 3% Et<sub>3</sub>N) and crystallization provided the corresponding iodinated THIQ (52.71 mg, 80.0 %); m.p. 102.5-103.5 °C as a colorless solid.

Anal. Cal. For C<sub>24</sub>H<sub>30</sub>NO<sub>4</sub>I: C, 55.07; H, 5.78; N, 2.68

Found : C, 55.05; H, 5.78; N, 2.67

IR	3031	cm <sup>-1</sup> (V C-H, aromatic)
(KBr pellet)	2962	cm <sup>-1</sup> (V C-H, aliphatic)
	1724	cm <sup>-1</sup> (V C=O, ester)
	1589	cm <sup>-1</sup> (V <sub>s</sub> C=C, aromatic)
	1265	cm <sup>-1</sup> (V <sub>as</sub> C=C-O-C)
	1195	cm <sup>-1</sup> (V <sub>as</sub> C-O-C)
	1064	cm <sup>-1</sup> (V <sub>s</sub> C-O-C)

(Figure 65)

<sup>1</sup> H-NMR	0.95	ppm (t, $J = 7.3$ Hz, 3H, H-4')
(CDCl <sub>3</sub> )	1.28	ppm (d, $J = 6.6$ Hz, 3H, 3-CH <sub>3</sub> )
	1.35	ppm (m, 2H, H-3')
	1.65	ppm (m, 2H, H-2')
	2.49	ppm (dd, $J_{gem} = 17.2$ Hz, $J_{ax} = 10.5$ Hz, 1H, H-4)
	2.70	ppm (dd, $J_{gem} = 17.2$ Hz, $J_{eq} = 4.1$ Hz, 1H, H-4)
	3.42	ppm (m, 1H, H-3)
	3.41	ppm (d, $J = 14.5$ , 1H, N-CH <sub>2</sub> Ph)
	3.70	ppm (s, 3H, 6- or 8-OCH <sub>3</sub> )
	3.85	ppm (s, 3H, 8- or 6-OCH <sub>3</sub> )
	3.90	ppm (d, $J = 14.5$ , 1H, N-CH <sub>2</sub> Ph)
	4.10	ppm (m, 2H, H-1')
	4.40	ppm (s, 1H, H-1)
	6.35	ppm (s, 1H, H-7)
	7.22-7.45	ppm (5H, aromatic-H)

(Figure 66 and 67)

<sup>13</sup> C-NMR	14.07	ppm (CH <sub>3</sub> -4')
(CDCl <sub>3</sub> )	19.06	ppm (3-CH <sub>3</sub> )
	19.45	ppm (CH <sub>2</sub> -3')
	31.12	ppm (CH <sub>2</sub> -2')
	39.24	ppm (CH <sub>2</sub> -4)
	49.99	ppm (CH-3)
	50.76	ppm (N-CH <sub>2</sub> Ph)
	55.80	ppm (6-OCH <sub>3</sub> or 8-OCH <sub>3</sub> )
	56.93	ppm (8-OCH <sub>3</sub> or 6-OCH <sub>3</sub> )
	60.71	ppm (C-1)
	64.75	ppm (CH <sub>2</sub> -1')

83.17	ppm (C-5)
93.94	ppm (C-7)
116.39	ppm (C-8a)
127.11	ppm (C-4'')
128.57	ppm (C-3'' and C-5'')
128.75	ppm (C-2'' and C-6'')
140.27	ppm (C-1'')
140.49	ppm (C-4a)
158.21	ppm (C-8 or C-6)
159.07	ppm (C-6 or C-8)
172.87	ppm (C-carbonyl ester)

(Figure 68)

DEPT 135

(Figure 69)

H-H COSY

(Figure 71 and 72)

HMQC

(Figure 73 and 74)

HMBC

(Figure 75)

V. The corresponding 5-Aryl-3-methyl-1,2,3,4-tetrahydroisoquinoline derivatives synthesis via Suzuki Coupling reaction.

1. 5-Phenyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-01)

The corresponding 5-iodo-THIQ (50 mg, 0.118 mmol) and phenyl boronic acid (29 mg, 0.237 mmol) were dissolved in toluene (10 ml). Saturated aqueous  $\text{NaHCO}_3$  (7.5 ml) and  $\text{Pd}(\text{PPh}_3)_4$  (33 mg, 0.028 mmol, 0.24 eq.) were added, and the mixture was stirred under nitrogen atmosphere and heated at 110 °C for 12 hours. The reaction mixture was cooled to room temperature and extracted with EtOAc (2 x 10 ml). The combined organics were washed with brine (2 x 10 ml) and dried over anhydrous

$\text{Na}_2\text{SO}_4$ . Purification via column chromatography ( $\text{SiO}_2$ , Hexane:EtOAc = 4:1) and crystallization to yield 37 mg (85 %) the corresponding 5-Aryl-THIQ derivative as a colorless solid; m.p. 152.0-153.0 °C.

Anal. Cal. For  $\text{C}_{25}\text{H}_{27}\text{NO}_2$  : C, 80.40; H, 7.29; N, 3.75

Found : C, 80.22; H, 7.28; N, 3.85

IR	3028	$\text{cm}^{-1}$ (V C-H, aromatic)
(KBr pellet)	2948	$\text{cm}^{-1}$ (V C-H, aliphatic)
	1601	$\text{cm}^{-1}$ (V <sub>s</sub> C=C, aromatic)
	1203	$\text{cm}^{-1}$ (V <sub>as</sub> C=C-O-C)
	1172	$\text{cm}^{-1}$ (V <sub>as</sub> C-O-C)
	1088	$\text{cm}^{-1}$ (V <sub>s</sub> C=C-O-C)

(Figure 76)

$^1\text{H-NMR}$	1.03	ppm (d, $J = 6.3$ Hz, 3H, 3- $\text{CH}_3$ )
( $\text{CDCl}_3$ )	2.23	ppm (dd, $J_{\text{gem}} = 16.9$ Hz, $J_{\text{vic}} = 5.4$ Hz, 1H, H-4)
	2.65	ppm (dd, $J_{\text{gem}} = 16.9$ Hz, $J_{\text{vic}} = 4.6$ Hz, 1H, H-4)
	2.98	ppm (m, 1H, H-3)
	3.60	ppm (d, $J = 13.6$ Hz, 1H, N- $\text{CH}_2\text{Ph}$ )
	3.65	ppm (s, 2H, H-1)
	3.70	ppm (s, 3H, 6-, or 8- $\text{OCH}_3$ )
	3.84	ppm (s, 3H, 8-, or 6- $\text{OCH}_3$ )
	3.86	ppm (d, $J = 13.6$ Hz, 1H, N- $\text{CH}_2\text{Ph}$ )
	6.42	ppm (s, 1H, H-7)
	7.10-7.40	ppm (10H, aromatic-H)

(Figure 77 and 78)

$^{13}\text{C-NMR}$	14.66	ppm (3- $\text{CH}_3$ )
( $\text{CDCl}_3$ )	35.40	ppm ( $\text{CH}_2$ -4)

47.34	ppm (CH <sub>2</sub> -1)
51.76	ppm (CH-3)
55.65	ppm (6- or 8-OCH <sub>3</sub> )
56.51	ppm (8- or 6-OCH <sub>3</sub> )
58.09	ppm (N-CH <sub>2</sub> Ph)
93.45	ppm (CH-7)
115.92	ppm (C-8a)
123.27	ppm (C-5)
126.94-130.92	ppm (CH-aromatic)
134.71	ppm (C-1')
137.67	ppm (C-1'')
139.91	ppm (C-4a)
156.26	ppm (C-6 or C-8)
156.45	ppm (C-8 or C-6)

(Figure 79)

DEPT

(Figure 80)

2. 5-(4''-Biphenyl)-2- benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydro-isoquinoline (CU-21-02)

The corresponding 5-iodo-THIQ (50 mg, 0.118 mmol) and 4-Biphenyl boronic acid (47 mg, 0.236 mmol) were dissolved in toluene (10 ml). Saturated aqueous NaHCO<sub>3</sub> (7.5 ml) and Pd (PPh<sub>3</sub>)<sub>4</sub> (33 mg, 0.028 mmol, 0.24 eq.) were added, and the mixture was stirred under nitrogen atmosphere and heated at 110 °C for 5 hours. The reaction mixture was cooled to room temperature and extracted with EtOAc (2 x 10 ml). The combined organics were washed with brine (2 x 10 ml) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Purification via column chromatography (SiO<sub>2</sub>, Hexane:EtOAc = 4:1) and crystallization to yield 53 mg (100 %) the corresponding 5-Aryl-THIQ derivative as a colorless solid; m.p. 151.0-152.0 °C.

Anal. Cal. For  $C_{31}H_{31}NO_2$  : C, 82.82; H, 6.95; N, 3.12

Found : C, 82.85; H, 6.95; N, 3.09

IR	3027	$cm^{-1}$ (V C-H, aromatic)
(KBr pellet)	2935	$cm^{-1}$ (V C-H, aliphatic)
	1600	$cm^{-1}$ (V <sub>s</sub> C=C, aromatic)
	1210	$cm^{-1}$ (V <sub>as</sub> C=C-O-C)
	1166	$cm^{-1}$ (V <sub>as</sub> C-O-C)
	1070	$cm^{-1}$ (V <sub>s</sub> C=C-O-C)

(Figure 82)

$^1H$ -NMR	1.03	ppm (d, $J = 6.2$ Hz, 3H, 3-CH <sub>3</sub> )
(CDCl <sub>3</sub> )	2.31	ppm (dd, $J_{gem} = 16.8$ Hz, $J_{vic} = 5.3$ Hz, 1H, H-4)
	2.71	ppm (dd, $J_{gem} = 16.8$ Hz, $J_{vic} = 4.5$ Hz, 1H, H-4)
	3.00	ppm (s, 1H, H-3)
	3.65	ppm (s, 2H, H-1)
	3.63	ppm (d, $J = 13.7$ Hz, 1H, N-CH <sub>2</sub> Ph)
	3.74	ppm (s, 3H, 6- or 8-OCH <sub>3</sub> )
	3.86	ppm (s, 3H, 8- or 6-OCH <sub>3</sub> )
	3.88	ppm (d, $J = 13.7$ Hz, 1H, N-CH <sub>2</sub> Ph)
	6.45	ppm (s, 1H, H-7)
	7.23-7.74	ppm (14H, aromatic-H)

(Figure 83 and 84)

$^{13}C$ -NMR	14.69	ppm (3-CH <sub>3</sub> )
(CDCl <sub>3</sub> )	35.54	ppm (CH <sub>2</sub> -4)
	47.39	ppm (CH <sub>2</sub> -1)
	51.79	ppm (CH-3)



	55.67	ppm (6- or 8-OCH <sub>3</sub> )
	56.53	ppm (8- or 6-OCH <sub>3</sub> )
	58.14	ppm (N-CH <sub>2</sub> Ph)
	93.38	ppm (CH-7)
	115.99	ppm (C-8a)
	122.74	ppm (C-5)
	127.19-131.25	ppm (CH-aromatic)
	134.81	ppm (C-1')
	137.67	ppm (C-1'')
	139.61	ppm (C-4'')
	139.82	ppm (C-4a)
	141.52	ppm (C-1''')
	156.52	ppm (C-6 or C-8)
	156.55	ppm (C-8 or C-6)
	(Figure 85)	
DEPT	(Figure 86)	
HH COSY	(Figure 88 and 89)	
HMQC	(Figure 90 and 91)	

### 3. 5-(4''-Methylphenyl)-2- benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03)

The corresponding 5-iodo-THIQ (50 mg, 0.118 mmol) and 4-methylphenyl boronic acid (32 mg, 0.236 mmol) were dissolved in toluene (10 ml). Saturated aqueous NaHCO<sub>3</sub> (7.5 ml) and Pd(PPh<sub>3</sub>)<sub>4</sub> (33 mg, 0.028 mmol) were added, and the mixture was stirred under nitrogen atmosphere and heated at 110 °C for 17 hours. The reaction mixture was cooled to room temperature and extracted with EtOAc (2 x 10 ml). The combined organics were washed with brine (2 x 10 ml) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Purification via column chromatography (SiO<sub>2</sub>, Hexane:EtOAc =

4:1) and crystallization to yield 43 mg (95 %) the corresponding 5-Aryl-THIQ derivative as a colorless solid; m.p. 108.0-109.5 °C.

Anal. Cal. For  $C_{26}H_{29}NO_2$ : C, 80.59; H, 7.54; N, 3.61

Found : C, 80.47; H, 7.51; N, 3.32

IR	3010	$cm^{-1}$ (V C-H, aromatic)
(KBr pellet)	2930	$cm^{-1}$ (V C-H, aliphatic)
	1595	$cm^{-1}$ (V <sub>s</sub> C=C, aromatic)
	1208	$cm^{-1}$ (V <sub>as</sub> C=C-O-C)
	1148	$cm^{-1}$ (V <sub>as</sub> C-O-C)
	1069	$cm^{-1}$ (V <sub>s</sub> C=C-O-C)
	(Figure 92)	
<sup>1</sup> H-NMR	1.04	ppm (d, $J = 6.4$ Hz, 3H, 3-CH <sub>3</sub> )
(CDCl <sub>3</sub> )	2.25	ppm (dd, $J_{gem} = 16.8$ Hz, $J_{vic} = 5.4$ Hz, 1H, H-4)
	2.40	ppm (s, 3H, 4''-CH <sub>3</sub> )
	2.65	ppm (dd, $J_{gem} = 16.8$ Hz, $J_{vic} = 4.7$ Hz, 1H, H-4)
	2.96	ppm (m, 1H, H-3)
	3.61	ppm (d, $J = 13.5$ Hz, 1H, N-CH <sub>2</sub> Ph)
	3.62	ppm (s, 2H, H-1)
	3.71	ppm (s, 3H, 6- or 8-OCH <sub>3</sub> )
	3.84	ppm (s, 3H, 8- or 6-OCH <sub>3</sub> )
	3.86	ppm (d, $J = 13.5$ Hz, 1H, N-CH <sub>2</sub> Ph)
	6.42	ppm (s, 1H, H-7)
	7.09	ppm (d, $J_o = 8.0$ Hz, 2H, 3'', 5'' -aromatic-H)
	7.21	ppm (d, $J_o = 8.0$ Hz, 2H, 2'', 6'' -aromatic-H)
	7.25-7.34	ppm (m, 3H, 3', 4', 5' - aromatic-H)

7.40 ppm (d,  $J = 7.1$  Hz, 2H, 2', 6' -aromatic-H)

(Figure 93 and 94)

$^{13}\text{C-NMR}$	14.72	ppm (3- $\text{CH}_3$ )
( $\text{CDCl}_3$ )	21.71	ppm ( $\text{CH}_3$ -Ph)
	35.40	ppm ( $\text{CH}_2$ -4)
	47.35	ppm ( $\text{CH}_2$ -1)
	51.80	ppm (CH-3)
	55.65	ppm (6- or 8- $\text{OCH}_3$ )
	56.59	ppm (8- or 6- $\text{OCH}_3$ )
	58.07	ppm (N- $\text{CH}_2$ Ph)
	93.38	ppm (CH-7)
	115.85	ppm (C-8a)
	123.13	ppm (C-5)
	127.11-130.75	ppm (CH-aromatic)
	134.53	ppm (C-1'')
	134.82	ppm (C- $\text{CH}_3$ )
	136.44	ppm (C-1')
	139.86	ppm (C-4a)
	156.34	ppm (C-6 and C-8)

(Figure 95)

DEPT 135

(Figure 96)

HH COSY

(Figure 98 and 99)

HMQC

(Figure 100 and 101)

4. 5-(4''-Methoxy phenyl)-2- benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-04)

The corresponding 5-iodo-THIQ (50 mg, 0.118 mmol) and 4-methoxy phenyl boronic acid (36 mg, 0.237 mmol) were dissolved in toluene (10 ml). Saturated aqueous  $\text{NaHCO}_3$  (7.5 ml) and  $\text{Pd}(\text{PPh}_3)_4$  (33 mg, 0.028 mmol) were added, and the mixture was stirred under nitrogen atmosphere and heated at  $110^\circ\text{C}$  for 48 hours. The reaction mixture was cooled to room temperature and extracted with EtOAc (2 x 10 ml). The combined organics were washed with brine (2 x 10 ml) and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . Purification via column chromatography ( $\text{SiO}_2$ , Hexane:EtOAc = 4:1) and crystallization to yield 37 mg (78 %) the corresponding 5-Aryl-THIQ derivative as a colorless solid;  $123.5\text{-}124.5^\circ\text{C}$ .

Anal. Cal. For  $\text{C}_{26}\text{H}_{29}\text{NO}_3$ : C, 77.39; H, 7.24; N, 3.47

Found : C, 77.29; H, 7.29; N, 3.42

IR	3054	$\text{cm}^{-1}$ (V C-H, aromatic)
(KBr pellet)	2944	$\text{cm}^{-1}$ (V C-H, aliphatic)
	1600	$\text{cm}^{-1}$ ( $\text{V}_s$ C=C, aromatic)
	1203	$\text{cm}^{-1}$ ( $\text{V}_{as}$ C=C-O-C)
	1172	$\text{cm}^{-1}$ ( $\text{V}_{as}$ C-O-C)
	1066	$\text{cm}^{-1}$ ( $\text{V}_s$ C=C-O-C)

(Figure 102)

$^1\text{H-NMR}$	1.04	ppm (d, $J = 6.4$ Hz, 3H, 3- $\text{CH}_3$ )
( $\text{CDCl}_3$ )	2.28	ppm (dd, $J_{gem} = 16.9$ Hz, $J_{vic} = 5.5$ Hz, 1H, H-4)
	2.64	ppm (dd, $J_{gem} = 16.9$ Hz, $J_{vic} = 4.6$ Hz, 1H, H-4)
	2.96	ppm (m, 1H, H-3)
	3.59	ppm (d, $J = 13.3$ Hz, 1H, N- $\text{CH}_2\text{Ph}$ )
	3.62	ppm (d, 2H, H-1)

3.71	ppm (s, 3H, 6- or 8-OCH <sub>3</sub> )
3.81	ppm (s, 3H, 4''-OCH <sub>3</sub> )
3.85	ppm (s, 3H, 8- or 6-OCH <sub>3</sub> )
3.86	ppm (d, $J = 13.3$ Hz, 1H, N-CH <sub>2</sub> Ph)
6.41	ppm (s, 1H, H-7)
6.95	ppm (d, $J_o = 8.6$ Hz, 2H, 3'', 5'' -aromatic-H)
7.13	ppm (d, $J_o = 8.6$ Hz, 2H, 2'', 6'' -aromatic-H)
7.22-7.35	ppm (m, 3H, 3', 4', 5' - aromatic-H )
7.40	ppm (d, $J = 7.1$ Hz, 2H, 2', 6' -aromatic-H )

(Figure 103 and 104)

<sup>13</sup>C-NMR  
(CDCl<sub>3</sub>)

14.76	ppm (3-CH <sub>3</sub> )
35.49	ppm (CH <sub>2</sub> -4)
47.40	ppm (CH <sub>2</sub> -1)
51.83	ppm (CH-3)
55.56	ppm (6- or 8-OCH <sub>3</sub> )
55.65	ppm (4''-OCH <sub>3</sub> )
56.52	ppm (8- or 6-OCH <sub>3</sub> )
58.07	ppm (CH <sub>2</sub> -1)
93.41	ppm (CH-7)
113.97	ppm (3'', 5''-CH)
115.85	ppm (C-8a)
122.78	ppm (C-5)
127.21-129.30	ppm (CH-aromatic)
129.72	ppm (C-1'')
131.94	ppm (2'', 6''-CH)
135.04	ppm (C-1')
139.87	ppm (C-4a)

156.28	ppm (C-6)
156.34	ppm (C-8)
158.58	ppm (C-4'')

(Figure 105)

DEPT 135	(Figure 106)
H-H COSY	(Figure 108 and 109)
HMQC	(Figure 110 and 111)

5. 5-(3'',4''-Dimethoxy phenyl)-2- benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05)

The corresponding 5-iodo-THIQ (50 mg, 0.118 mmol) and 3,4-dimethoxy phenyl boronic acid (43 mg, 0.237 mmol) were dissolved in toluene (10 ml). Saturated aqueous NaHCO<sub>3</sub> (7.5 ml) and Pd(PPh<sub>3</sub>)<sub>4</sub> (33 mg, 0.028 mmol) were added, and the mixture was stirred under nitrogen atmosphere and heated at 110 °C for 48 hours. The reaction mixture was cooled to room temperature and extracted with EtOAc (2 x 10 ml). The combined organics were washed with brine (2 x 10 ml) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Purification via column chromatography (SiO<sub>2</sub>, Hexane:EtOAc = 4:1) and crystallization to yield 36.83 mg (72 %) the corresponding 5-Aryl-THIQ derivative as a colorless solid; m.p. 122.0-123.0 °C.

Anal. Cal. For C<sub>27</sub>H<sub>31</sub>NO<sub>4</sub> : C, 74.80; H, 7.21; N, 3.23

Found : C, 74.51; H, 7.27; N, 3.32

IR	3010	cm <sup>-1</sup> (V C-H,aromatic)
(KBr pellet)	2938	cm <sup>-1</sup> (V C-H,aliphatic )
	1599	cm <sup>-1</sup> (V <sub>s</sub> C=C,aromatic)
	1210	cm <sup>-1</sup> (V <sub>as</sub> C=C-O-C)
	1177	cm <sup>-1</sup> (V <sub>as</sub> C-O-C)

1068  $\text{cm}^{-1}$  ( $\nu_s \text{C}=\text{C}-\text{O}-\text{C}$ )

(Figure 112)

$^1\text{H-NMR}$	1.03	ppm (d, $J = 6.4$ Hz, 3H, 3- $\text{CH}_3$ )
( $\text{CDCl}_3$ )	2.26	ppm (dd, $J_{gem} = 16.8$ Hz, $J_{vic} = 5.5$ Hz, 1H, H-4)
	2.67	ppm (dd, $J_{gem} = 16.8$ Hz, $J_{vic} = 5.2$ Hz, 1H, H-4)
	2.95	ppm (m, 1H, H-3)
	3.61	ppm (m, 1H, N- $\text{CH}_2\text{Ph}$ )
	3.62	ppm (m, 2H)
	3.71	ppm (s, 3H, 8- or 6- $\text{OCH}_3$ )
	3.81	ppm (s, 3H, 4'' - or 3''- $\text{OCH}_3$ )
	3.85	ppm (s, 3H, 6- or 8- $\text{OCH}_3$ )
	3.91	ppm (s, 3H, 3'' - or 4''- $\text{OCH}_3$ )
	3.86	ppm (m, 1H, N- $\text{CH}_2\text{Ph}$ )
	6.41	ppm (s, 1H, H-7)
	6.73	ppm (d, $J_m = 1.8$ Hz, 1H, 2'' - aromatic-H)
	6.75	ppm (dd, $J_m = 1.8$ Hz, $J_o = 7.9$ Hz, 1H, 6'' - aromatic-H)
	6.92	ppm (d, $J_o = 7.9$ Hz, 1H, 5'' - aromatic-H)
	7.24	ppm (m, 1H, 4' -aromatic-H)
	7.31	ppm (m, 2H, 3' and 5' -aromatic-H)
	7.39	ppm (dd, $J_m = 1.2$ Hz, $J_o = 7.6$ Hz, 2H, 2' and 6' -aromatic-H)

(Figure 113, 114 and 115)

$^{13}\text{C-NMR}$	14.09, 14.42	ppm (3- $\text{CH}_3$ )
( $\text{CDCl}_3$ )	35.18, 35.31	ppm ( $\text{CH}_2$ -4)
	46.94, 47.11	ppm ( $\text{CH}_2$ -1)

51.39	ppm (CH-3)
55.19	ppm (6- or 8-OCH <sub>3</sub> or 3''- or 4''-OCH <sub>3</sub> )
55.68	ppm (6- or 8-OCH <sub>3</sub> or 3''- or 4''-OCH <sub>3</sub> )
55.76	ppm (6- or 8-OCH <sub>3</sub> or 3''- or 4''-OCH <sub>3</sub> )
56.03	ppm (6- or 8-OCH <sub>3</sub> or 3''- or 4''-OCH <sub>3</sub> )
57.79	ppm (N-CH <sub>2</sub> Ph)
92.74	ppm (CH-7)
110.73, 110.79	ppm (5''-CH)
113.65	ppm (2''-CH)
115.53	ppm (C-8a)
122.29, 122.36	ppm (C-5)
122.44, 122.49	ppm (6''-CH)
126.72	ppm (4'-CH)
128.16	ppm (3' and 5'-CH)
128.80	ppm (2' and 6'-CH)
129.59	ppm (C-1'')
134.68	ppm (C-1')
139.48	ppm (C-4a)
147.48	ppm (C-3'' or C-4'')
148.40	ppm (C-4'' or C-3'')
155.85	ppm (C-6 and C-8)

(Figure 118 and 119)

DEPT

(Figure 120-122)

HH COSY

(Figure 121-122)

HMQC

(Figure 125-127)

NOESY

(Figure 128-129)



6. Butyl-(5-phenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-06)

The corresponding 5-iodo-THIQ (50 mg, 0.096 mmol), phenyl boronic acid (23 mg, 0.191 mmol) and Pd(PPh<sub>3</sub>)<sub>4</sub> (27 mg, 0.023 mmol) were dissolved in a mixture of toluene (10 ml) and saturated NaHCO<sub>3</sub> (7.5 ml). The reaction mixture was sealed under nitrogen atmosphere and heated at 110 °C for 15 h. The reaction mixture was cooled down to room temperature and extracted with EtOAc (2 x 20 ml). The combined organics were washed with brine (2 x 20 ml) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Purification via column chromatography (SiO<sub>2</sub>, Hexane:EtOAc = 4:1) and crystallization to yield 43 mg (96 %) the corresponding 5-Aryl-THIQ derivative as a colorless solid; m.p. 117.0-118.0 °C.

Anal. Cal. For C<sub>25</sub>H<sub>27</sub>NO<sub>4</sub>: C, 76.08; H, 7.45; N, 2.96

Found : C, 75.95; H, 7.85; N, 2.97

IR	3026	cm <sup>-1</sup> (V C-H, aromatic)
(KBr pellet)	2962	cm <sup>-1</sup> (V C-H, aliphatic)
	1725	cm <sup>-1</sup> (V C=O, ester)
	1592	cm <sup>-1</sup> (V <sub>s</sub> C=C, aromatic)
	1322	cm <sup>-1</sup> (V <sub>as</sub> C=C-O-C)
	1190	cm <sup>-1</sup> (V <sub>as</sub> C-O-C)
	1072	cm <sup>-1</sup> (V <sub>s</sub> C-O-C)

(Figure 130)

<sup>1</sup> H-NMR	0.96	ppm (t, J = 7.3 Hz, 3H, H-4')
(CDCl <sub>3</sub> )	1.07	ppm (d, J = 6.6 Hz, 3H, 3-CH <sub>3</sub> )
	1.42	ppm (m, 2H, H-3')
	1.65	ppm (m, 2H, H-2')
	2.33	ppm (m, 2H, H-4)

3.37	ppm (m, 1H, H-3)
3.60	ppm (d, $J = 14.6$ , 1H, N-CH <sub>2</sub> Ph)
3.73	ppm (s, 3H, 6- or 8-OCH <sub>3</sub> )
3.78	ppm (s, 3H, 8- or 6-OCH <sub>3</sub> )
3.89	ppm (d, $J = 14.6$ , 1H, N-CH <sub>2</sub> Ph)
4.12	ppm (m, 2H, H-1')
4.53	ppm (s, 1H, H-1)
6.43	ppm (s, 1H, H-7)
7.25-7.41	ppm (5H, aromatic-H)

(Figure 131 and 132)

<sup>13</sup>C-NMR  
(CDCl<sub>3</sub>)

14.12	ppm (CH <sub>3</sub> -4')
18.66	ppm (3-CH <sub>3</sub> )
19.51	ppm (CH <sub>2</sub> -3')
31.18	ppm (CH <sub>2</sub> -2')
32.02	ppm (CH <sub>2</sub> -4)
49.24	ppm (CH-3)
51.52	ppm (N-CH <sub>2</sub> Ph)
55.68	ppm (6- or 8-OCH <sub>3</sub> )
56.30	ppm (8- or 6-OCH <sub>3</sub> )
60.62	ppm (CH-1)
64.64	ppm (CH <sub>2</sub> -1')
93.46	ppm (CH-7)
113.69	ppm (C-5)
122.95	ppm (C-8a)
127.06-131.16	ppm (CH-aromatic)
136.48	ppm (C-1''')
137.48	ppm (C-1'')

140.56	ppm (C-4a)
157.06	ppm (C-6 or C-8)
157.72	ppm (C-8 or C-6)
173.53	ppm (C-carbonyl)

(Figure 133)

DEPT 135 (Figure 134)

7. Butyl-5-(4'''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07)

The corresponding 5-iodo-THIQ (100 mg, 0.191 mmol) and 4-biphenyl boronic acid (76 mg, 0.382 mmol) were dissolved in toluene (10 ml). Saturated aqueous  $\text{NaHCO}_3$  (7.5 ml) and  $\text{Pd}(\text{PPh}_3)_4$  (53 mg, 0.046 mmol) were added, and the mixture was stirred under nitrogen atmosphere and heated at 110 °C for 5 hours. The reaction mixture was cooled down to room temperature and extracted with EtOAc (2 x 10 ml). The combined organics were washed with brine (2 x 10 ml) and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . Purification via column chromatography ( $\text{SiO}_2$ , Hexane:EtOAc = 4:1) and crystallization to yield 104.99 mg (100 %) the corresponding 5-Aryl-THIQ derivative as a colorless solid; m.p. 92.0-93.0 °C.

Anal. Cal. For  $\text{C}_{36}\text{H}_{39}\text{NO}_4$ : C, 78.66; H, 7.15; N, 2.55

Found : C, 78.67; H, 7.05; N, 2.61

IR	3027	$\text{cm}^{-1}$ (V C-H, aromatic)
(KBr pellet)	2960	$\text{cm}^{-1}$ (V C-H, aliphatic)
	1731	$\text{cm}^{-1}$ (V C=O, ester)
	1595	$\text{cm}^{-1}$ ( $\text{V}_s$ C=C, aromatic)
	1323	$\text{cm}^{-1}$ ( $\text{V}_{as}$ C=C-O-C)
	1177	$\text{cm}^{-1}$ ( $\text{V}_{as}$ C-O-C)
	1073	$\text{cm}^{-1}$ ( $\text{V}_s$ C-O-C)

(Figure 136)

<sup>1</sup> H-NMR	0.95	ppm (t, $J = 7.3$ Hz, 3H, H-4')
(CDCl <sub>3</sub> )	1.13	ppm (d, $J = 6.5$ Hz, 3H, 3-CH <sub>3</sub> )
	1.47	ppm (m, 2H, H-3')
	1.63	ppm (m, 2H, H-2')
	2.39	ppm (m, 2H, H-4)
	3.39	ppm (m, 1H, H-3)
	3.64	ppm (d, $J = 14.4$ , 1H, N-CH <sub>2</sub> Ph)
	3.76	ppm (s, 3H, 6- or 8-OCH <sub>3</sub> )
	3.79	ppm (s, 3H, 8- or 6-OCH <sub>3</sub> )
	3.93	ppm (d, $J = 14.4$ , 1H, N-CH <sub>2</sub> Ph)
	4.13	ppm (m, 2H, H-1')
	4.56	ppm (s, 1H, H-1)
	6.46	ppm (s, 1H, H-7)
	7.20-7.80	ppm (14H, aromatic-H)

(Figure 137 and 138)

<sup>13</sup> C-NMR	14.12	ppm (CH <sub>3</sub> -4')
(CDCl <sub>3</sub> /TMS)	18.66	ppm (3-CH <sub>3</sub> )
	19.52	ppm (CH <sub>2</sub> -3')
	31.20	ppm (CH <sub>2</sub> -2')
	32.16	ppm (CH <sub>2</sub> -4)
	49.29	ppm (CH-3)
	51.60	ppm (N-CH <sub>2</sub> Ph)
	55.71	ppm (6- or 8-OCH <sub>3</sub> )
	56.34	ppm (8- or 6-OCH <sub>3</sub> )
	60.65	ppm (CH-1)

	64.65	ppm (CH <sub>2</sub> -1')
	93.50	ppm (CH-7)
	113.82	ppm (C-5)
	122.51	ppm (C-8a)
	127.07-131.60	ppm (CH-aromatic)
	136.50	ppm (C-4''')
	136.59	ppm (C-1''')
	139.74	ppm (C-1'')
	140.56	ppm (C-4a)
	141.51	ppm (C-1''''')
	157.15	ppm (C-6 or C-8)
	157.80	ppm (C-8 or C-6)
	173.53	ppm (C-carbonyl)
	(Figure 139)	
DEPT 135	(Figure 140)	
HH COSY	(Figure 142 and 143)	
HMQC	(Figure 144 and 145)	

8. Butyl-5-(4'''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08)

The corresponding 5-iodo-THIQ (50 mg, 0.096 mmol) and 4-methylphenyl boronic acid (26 mg, 0.192 mmol) were dissolved in toluene (10 ml). Saturated aqueous NaHCO<sub>3</sub> (7.5 ml) and Pd(PPh<sub>3</sub>)<sub>4</sub> (27 mg, 0.023 mmol) were added, and the mixture was stirred under nitrogen atmosphere and heated at 110 °C for 20 hours. The reaction mixture was cooled down to room temperature and extracted with EtOAc (2 x 10 ml). The combined organics were washed with brine (2 x 10 ml) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Purification via column chromatography (SiO<sub>2</sub>, Hexane:

EtOAc = 4:1) and crystallization to yield 45 mg (96 %) the corresponding 5-Aryl-THIQ derivative as a colorless solid; m.p. 102.0-103.0 °C.

Anal. Cal. For  $C_{31}H_{37}NO_4$ : C, 76.36; H, 7.65; N, 2.87

Found : C, 76.09; H, 7.72; N, 2.72

IR	3029	$cm^{-1}$ (V C-H, aromatic)
(KBr pellet)	2932	$cm^{-1}$ (V C-H, aliphatic)
	1737	$cm^{-1}$ (V C=O, ester)
	1593	$cm^{-1}$ (V <sub>s</sub> C=C, aromatic)
	1321	$cm^{-1}$ (V <sub>as</sub> C=C-O-C)
	1198	$cm^{-1}$ (V <sub>as</sub> C-O-C)
	1074	$cm^{-1}$ (V <sub>s</sub> C-O-C)
	(Figure 146)	
<sup>1</sup> H-NMR	0.95	ppm (t, $J = 7.3$ Hz, 3H, H-4')
(CDCl <sub>3</sub> )	1.07	ppm (d, $J = 6.6$ Hz, 3H, 3-CH <sub>3</sub> )
	1.41	ppm (m, 2H, H-3')
	1.63	ppm (m, 2H, H-2')
	2.34	ppm (m, 2H, H-4)
	2.41	ppm (s, 3H, 4'''-CH <sub>3</sub> )
	3.40	ppm (m, 1H, H-3)
	3.60	ppm (d, $J = 14.5$ Hz, 1H, N-CH <sub>2</sub> Ph)
	3.72	ppm (s, 3H, 6- or 8-OCH <sub>3</sub> )
	3.77	ppm (s, 3H, 8- or 6-OCH <sub>3</sub> )
	3.90	ppm (d, $J = 14.5$ Hz, 1H, N-CH <sub>2</sub> Ph)
	4.13	ppm (m, 2H, H-1')
	4.50	ppm (s, 1H, H-1)
	6.42	ppm (s, 1H, H-7)

7.13	ppm (m, 2H, 2 <sup>'''</sup> and 6 <sup>'''</sup> -aromatic-H)
7.22	ppm (d, $J = 8.0$ Hz, 2H, 3 <sup>'''</sup> and 5 <sup>'''</sup> -aromatic-H)
7.24-7.35	ppm (3H, aromatic-H)
7.47	ppm (d, $J = 7.2$ Hz, 2H, 2 <sup>''</sup> and 6 <sup>''</sup> -aromatic-H)

(Figure 147 and 148)

<sup>13</sup> C-NMR (CDCl <sub>3</sub> )	14.10	ppm (CH <sub>3</sub> -4')
	18.67	ppm (3-CH <sub>3</sub> )
	19.50	ppm (CH <sub>2</sub> -3')
	21.72	ppm (CH <sub>3</sub> -Ph)
	31.17	ppm (CH <sub>2</sub> -2')
	32.02	ppm (CH <sub>2</sub> -4)
	49.28	ppm (CH-3)
	51.52	ppm (N-CH <sub>2</sub> -Ph )
	55.67	ppm (6- or 8-OCH <sub>3</sub> )
	56.28	ppm (8- or 6-OCH <sub>3</sub> )
	60.63	ppm (CH-1 )
	64.61	ppm (CH <sub>2</sub> -1')
	93.45	ppm (CH-7 )
	113.67	ppm (C-5)
	122.86	ppm (C-8a)
	127.03-130.96	ppm (CH-aromatic)
	134.33	ppm (C-1 <sup>'''</sup> )
	136.54	ppm (C-4 <sup>'''</sup> )
	136.58	ppm (C-1 <sup>''</sup> )
	140.58	ppm (C-4a)
	157.16	ppm (C-6 or C-8)
	157.60	ppm (C-8 or C-6)

	173.52	ppm (C-carbonyl)
	(Figure 149)	
DEPT 135	(Figure 150)	
HH COSY	(Figure 152 and 153)	
HMQC	(Figure 154 and 155)	

9. Butyl-5-(4<sup>'''</sup>-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09)

The corresponding 5-iodo-THIQ (50 mg, 0.096 mmol) and 4-methoxyphenyl boronic acid (29 mg, 0.191 mmol) were dissolved in toluene (10 ml). Saturated aqueous NaHCO<sub>3</sub> (7.5 ml) and Pd(PPh<sub>3</sub>)<sub>4</sub> (26.52 mg, 0.023 mmol) were added, and the mixture was stirred under nitrogen atmosphere and heated at 110 °C for 24 hours. The reaction mixture was cooled down to room temperature and extracted with EtOAc (2 x 10 ml). The combined organics were washed with brine (2 x 10 ml) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Purification via column chromatography (SiO<sub>2</sub>, Hexane:EtOAc = 4:1) and crystallization to yield 42 mg (86 %) the corresponding 5-Aryl-THIQ derivative as a colorless solid; m.p. 161.0-162.0 °C.

Anal. Cal. For C<sub>31</sub>H<sub>37</sub>NO<sub>5</sub>: C, 73.93; H, 7.41; N, 2.78

Found : C, 73.94; H, 7.45; N, 2.74

IR	3027	cm <sup>-1</sup> (V C-H, aromatic)
(KBr pellet)	2954	cm <sup>-1</sup> (V C-H, aliphatic)
	1728	cm <sup>-1</sup> (V C=O, ester)
	1595	cm <sup>-1</sup> (V <sub>s</sub> C=C, aromatic)
	1243	cm <sup>-1</sup> (V <sub>as</sub> C=C-O-C)
	1182	cm <sup>-1</sup> (V <sub>as</sub> C-O-C)
	1074	cm <sup>-1</sup> (V <sub>s</sub> C-O-C)

(Figure 156)



<sup>1</sup> H-NMR (CDCl <sub>3</sub> )	0.95	ppm (t, $J = 7.3$ Hz, 3H, H-4')
	1.07	ppm (d, $J = 6.6$ Hz, 3H, 3-CH <sub>3</sub> )
	1.42	ppm (m, 2H, H-3')
	1.63	ppm (m, 2H, H-2')
	2.32	ppm (m, 2H, H-4)
	3.37	ppm (m, 1H, H-3)
	3.60	ppm (d, $J = 14.5$ , 1H, N-CH <sub>2</sub> Ph)
	3.72	ppm (s, 3H, 6- or 8-OCH <sub>3</sub> )
	3.76	ppm (s, 3H, 8- or 6-OCH <sub>3</sub> )
	3.86	ppm (s, 4 <sup>'''</sup> -OCH <sub>3</sub> )
	3.90	ppm (d, $J = 14.5$ , 1H, N-CH <sub>2</sub> Ph)
	4.13	ppm (m, 2H, H-1')
	4.51	ppm (s, 1H, H-1)
	6.41	ppm (s, 1H, H-7)
	6.96	ppm (d, $J = 8.5$ Hz, 2H, 3 <sup>'''</sup> and 5 <sup>'''</sup> -aromatic-H)
	7.17	ppm (m, 2 <sup>'''</sup> and 6 <sup>'''</sup> aromatic-H)
	7.21-7.34	ppm (5H, aromatic-H)
7.45	ppm (d, $J = 7.1$ Hz, 2H, 2 <sup>''</sup> and 6 <sup>''</sup> -aromatic-H)	

(Figure 157 and 158)

<sup>13</sup> C-NMR (CDCl <sub>3</sub> )	14.09	ppm (CH <sub>3</sub> -4')
	18.67	ppm (3-CH <sub>3</sub> )
	19.49	ppm (CH <sub>2</sub> -3')
	31.16	ppm (CH <sub>2</sub> -2')
	32.09	ppm (CH <sub>2</sub> -4)
	49.26	ppm (CH-3)
	51.52	ppm (N-CH <sub>2</sub> Ph)

55.56	ppm (6- or 8-OCH <sub>3</sub> )
55.67	ppm (CH <sub>3</sub> O-Ph)
56.29	ppm (8- or 6-OCH <sub>3</sub> )
60.62	ppm (CH-1)
64.61	ppm (CH <sub>2</sub> -1')
93.45	ppm (CH-7)
113.69	ppm (C-5)
114.00	ppm (CH-3''' and 5''')
122.51	ppm (C-8a)
127.02-128.82	ppm (CH-aromatic)
129.51	ppm (C-1''')
131.80, 132.13	ppm (CH-2''' and 6''')
136.80	ppm (C-1'')
140.57	ppm (C-4a)
157.26	ppm (C-6 or C-8)
157.57	ppm (C-8 or C-6)
158.68	ppm (C-4''')
173.54	ppm (C-carbonyl)

(Figure 159)

DEPT 135

(Figure 160)

H-H COSY

(Figure 162 and 163)

HMQC

(Figure 164 and 165)

10. Butyl-5-(3''',4'''-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10)

The corresponding 5-iodo-THIQ (50 mg, 0.096 mmol) and 3,4-dimethoxy phenyl boronic acid (35 mg, 0.191 mmol) were dissolved in toluene(10 ml). Saturated aqueous NaHCO<sub>3</sub> (7.5 ml) and Pd(PPh<sub>3</sub>)<sub>4</sub> (27 mg, 0.023 mmol) were added,

and the mixture was stirred under nitrogen atmosphere and heated at 110 °C for 48 hours. The reaction mixture was cooled to room temperature and extracted with EtOAc (2 x 10 ml). The combined organics were washed with brine (2 x 10 ml) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Purification via column chromatography (SiO<sub>2</sub>, Hexane:EtOAc = 4:1) and crystallization to yield 37 mg (72 %) the corresponding 5-Aryl-THIQ derivative as a colorless solid ; m.p. 139.0-140.0 °C.

Anal. Cal. For C<sub>32</sub>H<sub>39</sub>NO<sub>6</sub>: C, 72.02; H, 7.37; N, 2.62

Found : C, 71.94; H, 7.47; N, 2.52

IR	3015	cm <sup>-1</sup> (V C-H, aromatic)
(KBr pellet)	2834, 2960	cm <sup>-1</sup> (V C-H, aliphatic)
	1726	cm <sup>-1</sup> (V C=O, ester)
	1594	cm <sup>-1</sup> (V <sub>s</sub> C=C, aromatic)
	1247	cm <sup>-1</sup> (V <sub>as</sub> C=C-O-C)
	1177	cm <sup>-1</sup> (V <sub>as</sub> C-O-C)
	1073	cm <sup>-1</sup> (V <sub>s</sub> C-O-C)

(Figure 166)

<sup>1</sup> H-NMR	0.90	ppm (t, <i>J</i> = 7.3 Hz, 3H, H-4')
(CDCl <sub>3</sub> )	1.07	ppm (d, <i>J</i> = 6.5 Hz, 3H, 3-CH <sub>3</sub> )
	1.41	ppm (m, 2H, H-3')
	1.63	ppm (m, 2H, H-2')
	2.35	ppm (m, 2H, H-4)
	3.35	ppm (m, 1H, H-3)
	3.62	ppm (m, 1H, N-CH <sub>2</sub> Ph)
	3.73	ppm (s, 3H, 6- or 8-OCH <sub>3</sub> )
	3.77	ppm (s, 3H, 8- or 6-OCH <sub>3</sub> )
	3.89	ppm (s, 3H, 3''' - or 4''' - OCH <sub>3</sub> )

3.93	ppm (s, 3H, 4 <sup>'''</sup> - or 3 <sup>'''</sup> - OCH <sub>3</sub> )
3.92	ppm (d, 1H, N-CH <sub>2</sub> Ph)
4.11	ppm (m, 2H, H-1')
4.52	ppm (s, 1H, H-1)
6.42	ppm (s, 1H, H-7)
6.75	ppm (s, 1H, 2 <sup>'''</sup> -aromatic-H)
6.79	ppm (d, $J_o = 7.9$ Hz, 1H, 6 <sup>'''</sup> -aromatic-H)
6.93	ppm (d, $J_o = 7.9$ Hz, 1H, 5 <sup>'''</sup> -aromatic-H)
7.22-7.35	ppm (m, 3H, aromatic-H)
7.45	ppm (d, $J = 7.2$ Hz, 2H, 2 <sup>''</sup> and 6 <sup>''</sup> -aromatic-H)

(Figure 167 and 168)

<sup>13</sup>C-NMR

(CDCl<sub>3</sub>/TMS)

14.09	ppm (CH <sub>3</sub> -4')
18.63	ppm (3-CH <sub>3</sub> )
19.49	ppm (CH <sub>2</sub> -3')
31.17	ppm (CH <sub>2</sub> -2')
32.01, 31.90	ppm (CH <sub>2</sub> -4)
49.26	ppm (CH-3)
51.57, 51.71	ppm (N-CH <sub>2</sub> Ph)
55.07	ppm (6- or 8-OCH <sub>3</sub> )
56.18	ppm (3 <sup>'''</sup> -or 4 <sup>'''</sup> -OCH <sub>3</sub> )
56.33	ppm (6- or 8- OCH <sub>3</sub> and 3 <sup>'''</sup> - or 4 <sup>'''</sup> -OCH <sub>3</sub> )
60.57	ppm (CH-1)
64.63	ppm (CH-1')
93.45	ppm (CH-7)
111.33	ppm (CH-6 <sup>'''</sup> )
113.68, 113.83	ppm (C-5)
114.35	ppm (CH-5 <sup>'''</sup> )

122.86 ppm (C-8a)  
 122.68, 123.25 ppm (CH-2<sup>'''</sup>)  
 127.05-128.84 ppm (CH-aromatic)  
 129.92 ppm (C-1<sup>'''</sup>)  
 136.83 ppm (C-1<sup>''</sup>)  
 140.51 ppm (C-4a)  
 148.11 ppm (C-3<sup>'''</sup> or C-4<sup>'''</sup>)  
 148.99 ppm (C-4<sup>'''</sup> or C-3<sup>'''</sup>)  
 157.25 ppm (C-6 or C-8)  
 157.62 ppm (C-8 or C-6)  
 173.60 ppm (C-carbonyl)

(Figure 169)

DEPT 135

(Figure 170)

HH COSY

(Figure 172 and 173)

HMQC

(Figure 174 and 175)

ศูนย์วิทยทรัพยากร  
 จุฬาลงกรณ์มหาวิทยาลัย

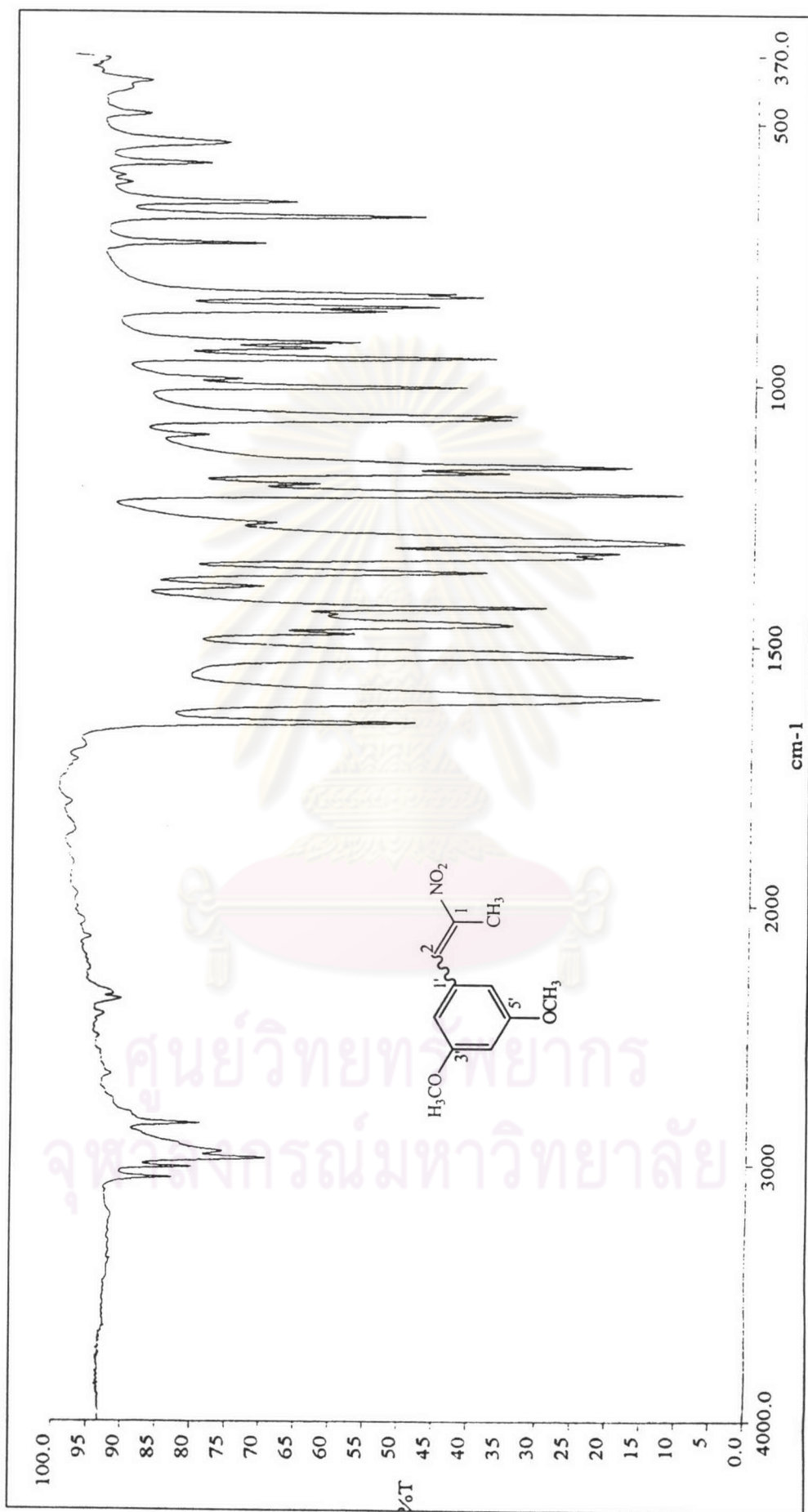


Figure 16 The IR spectrum (KBr) of 2-(3,5'-dimethoxyphenyl)-1-methyl-1-nitroethene (CU-19-01)

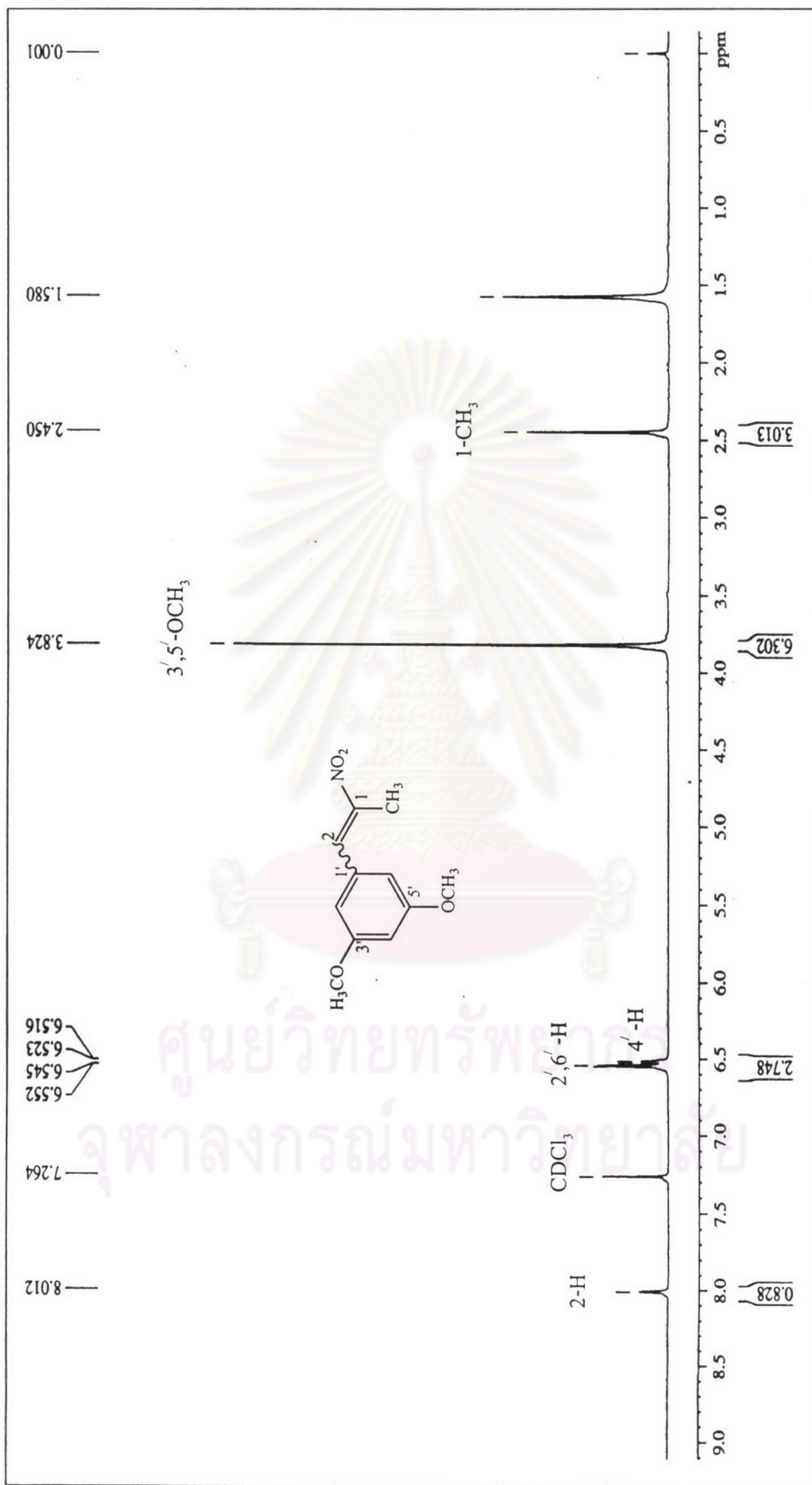


Figure 17 The 300 MHz <sup>1</sup>H-NMR spectrum of 2-(3,5'-dimethoxyphenyl)-1-methyl-1-nitroethene (CU-19-01)

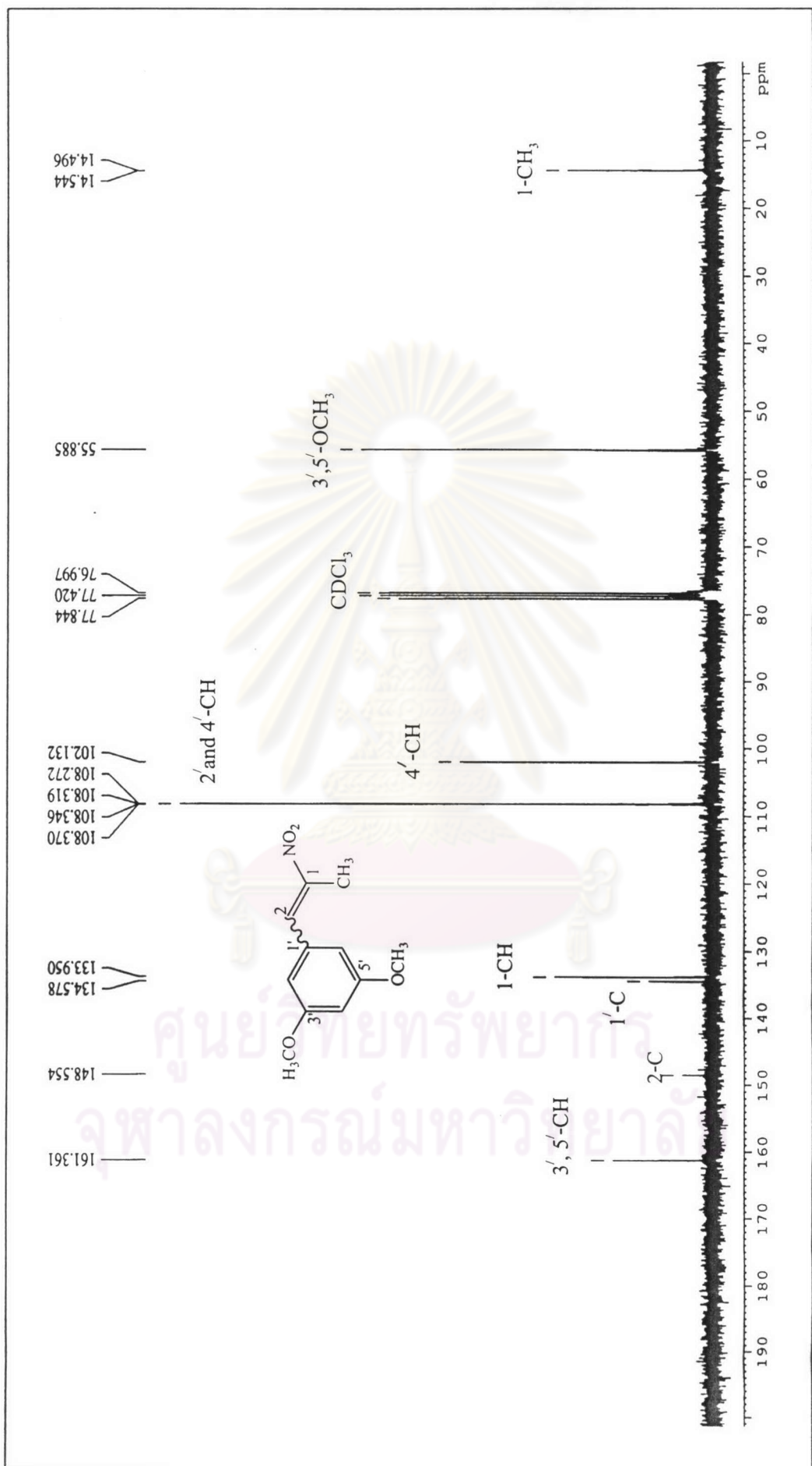


Figure 18 The 75 MHz  $^{13}\text{C}$ -NMR spectrum of 2-(3',5'-dimethoxyphenyl)-1-methyl-1-nitroethene (CU-19-01)



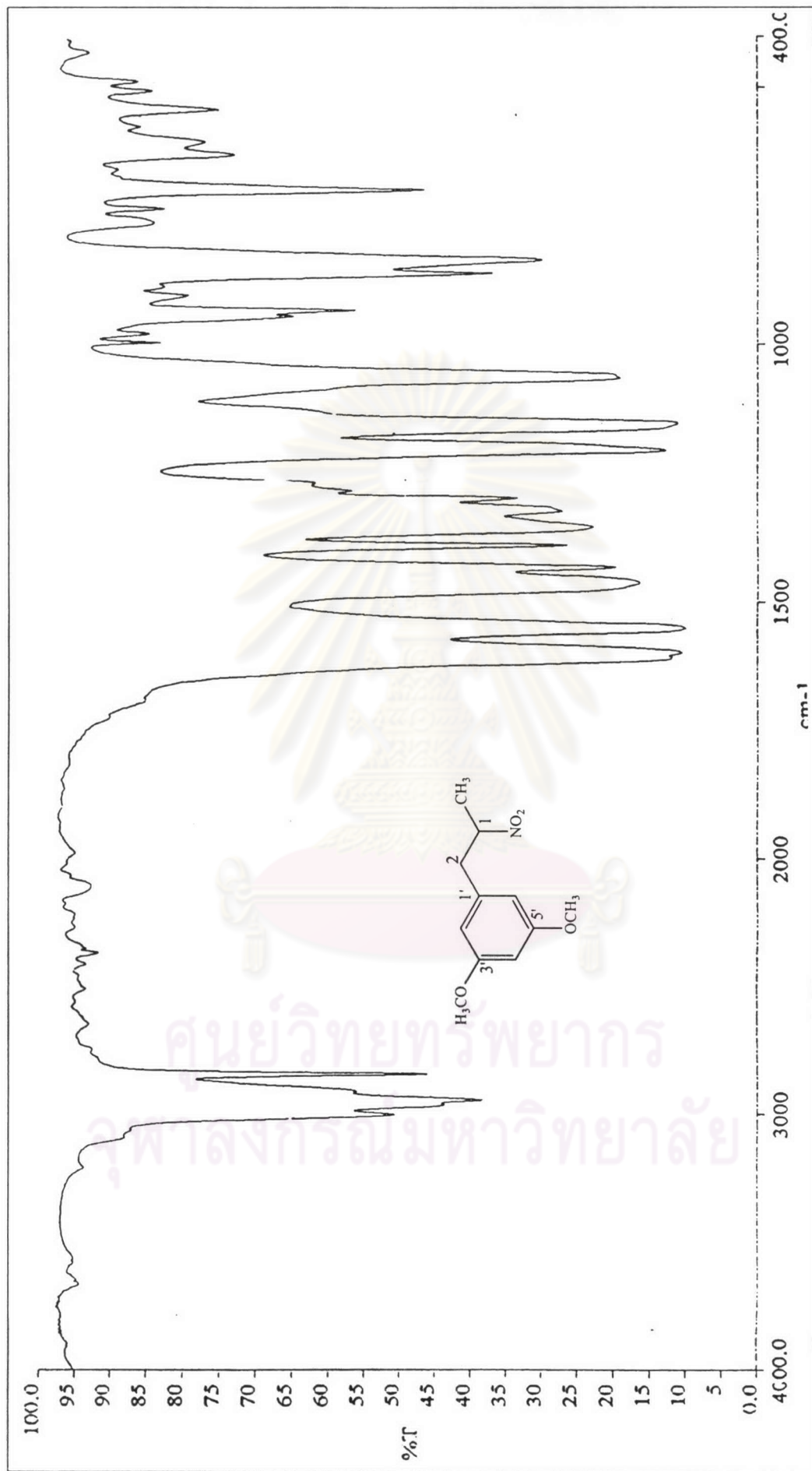


Figure 19 The IR spectrum (KBr) of 2-(3,5'-dimethoxyphenyl)-1-methyl-1-nitroethane (CU-19-02)

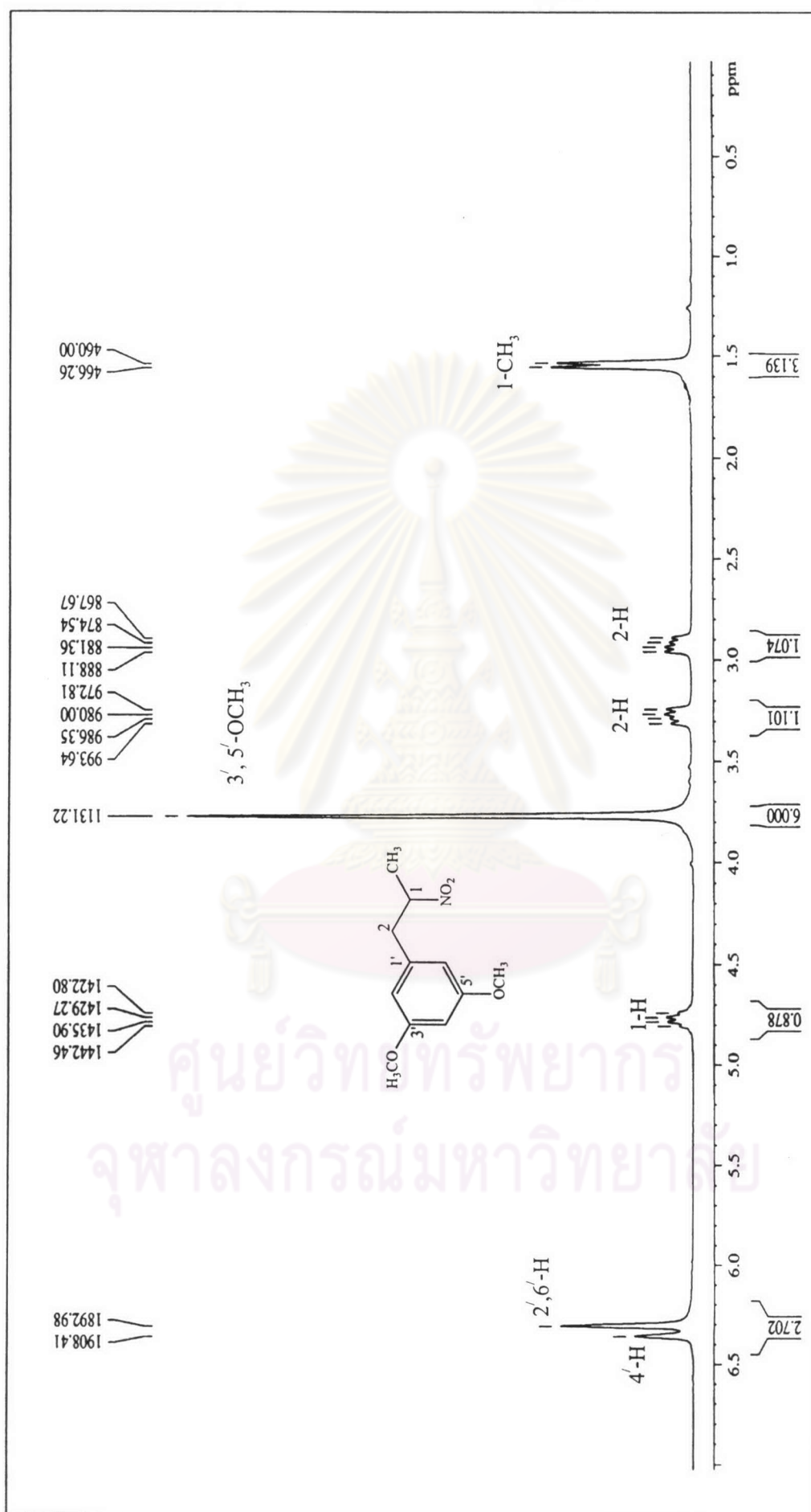


Figure 20 The 300 MHz <sup>1</sup>H-NMR spectrum of 2-(3,5'-dimethoxyphenyl)-1-methyl-1-nitroethane (CU-19-02)

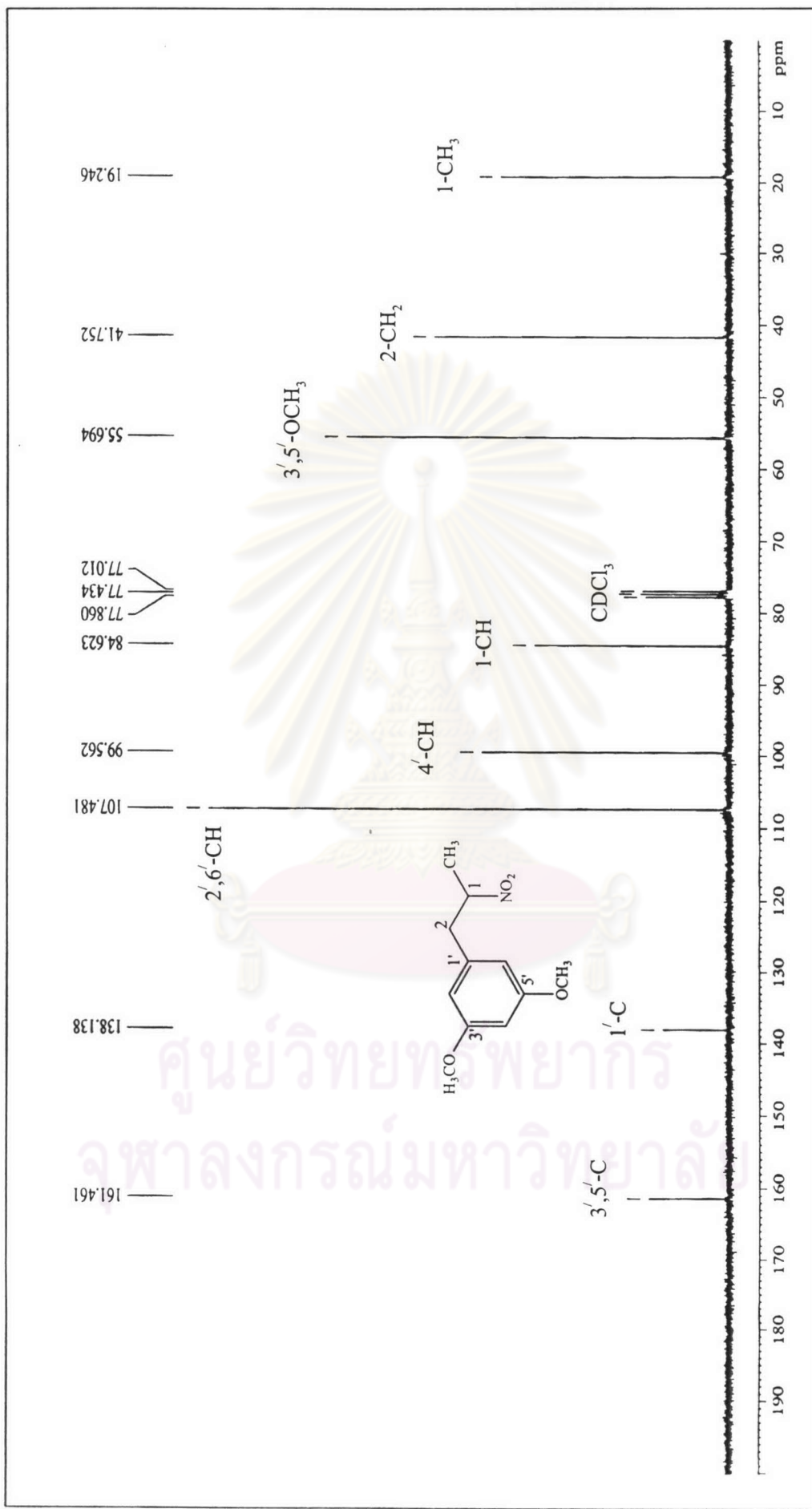


Figure 21 The 75 MHz  $^{13}\text{C}$ -NMR spectrum of 2-(3',5'-dimethoxyphenyl)-1-methyl-1-nitroethane (CU-19-02)

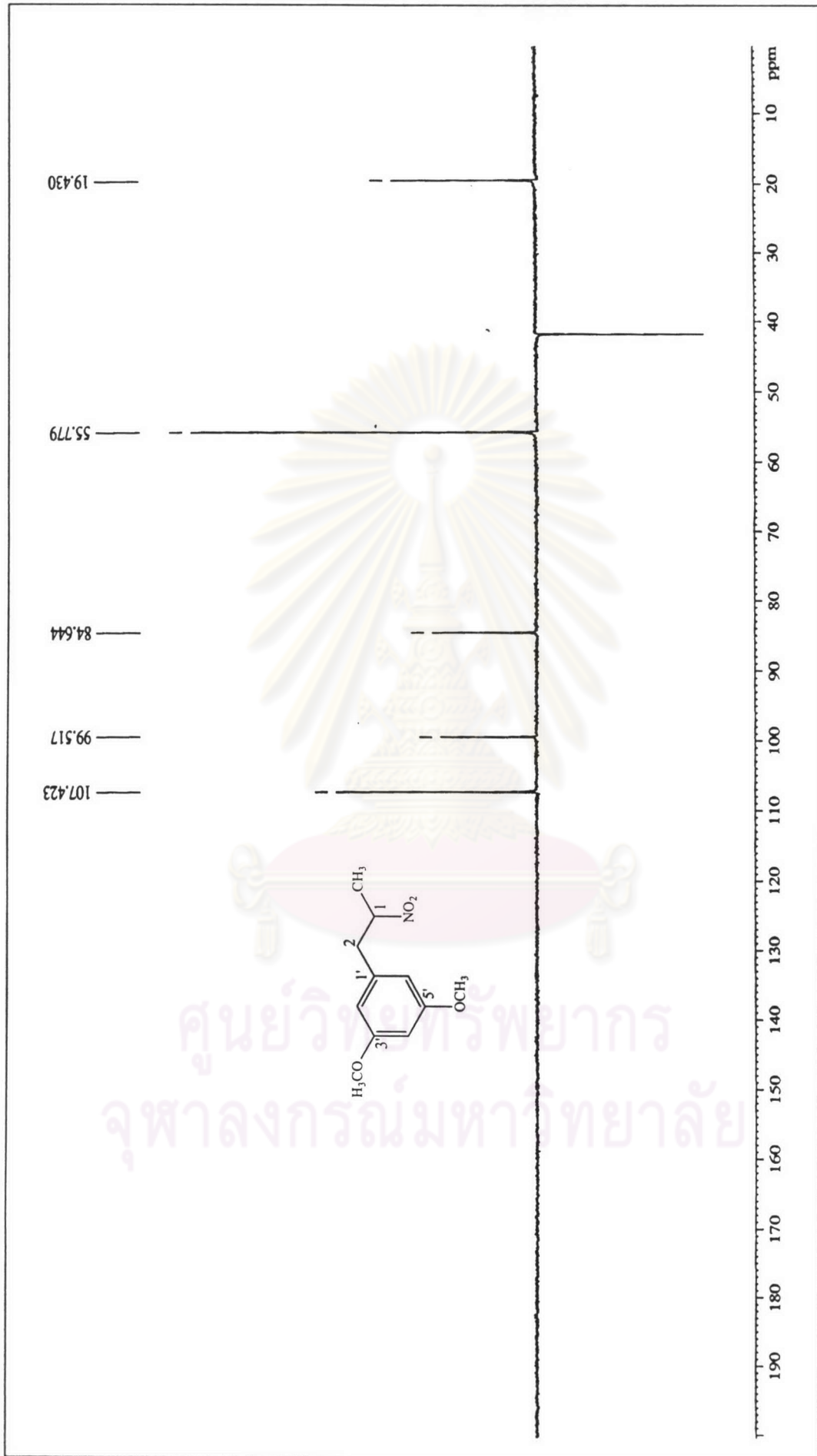


Figure 22 The 75 MHz DEPT 135 spectrum of 2-(3',5'-dimethoxyphenyl)-1-methyl-1-nitroethane (CU-19-02)

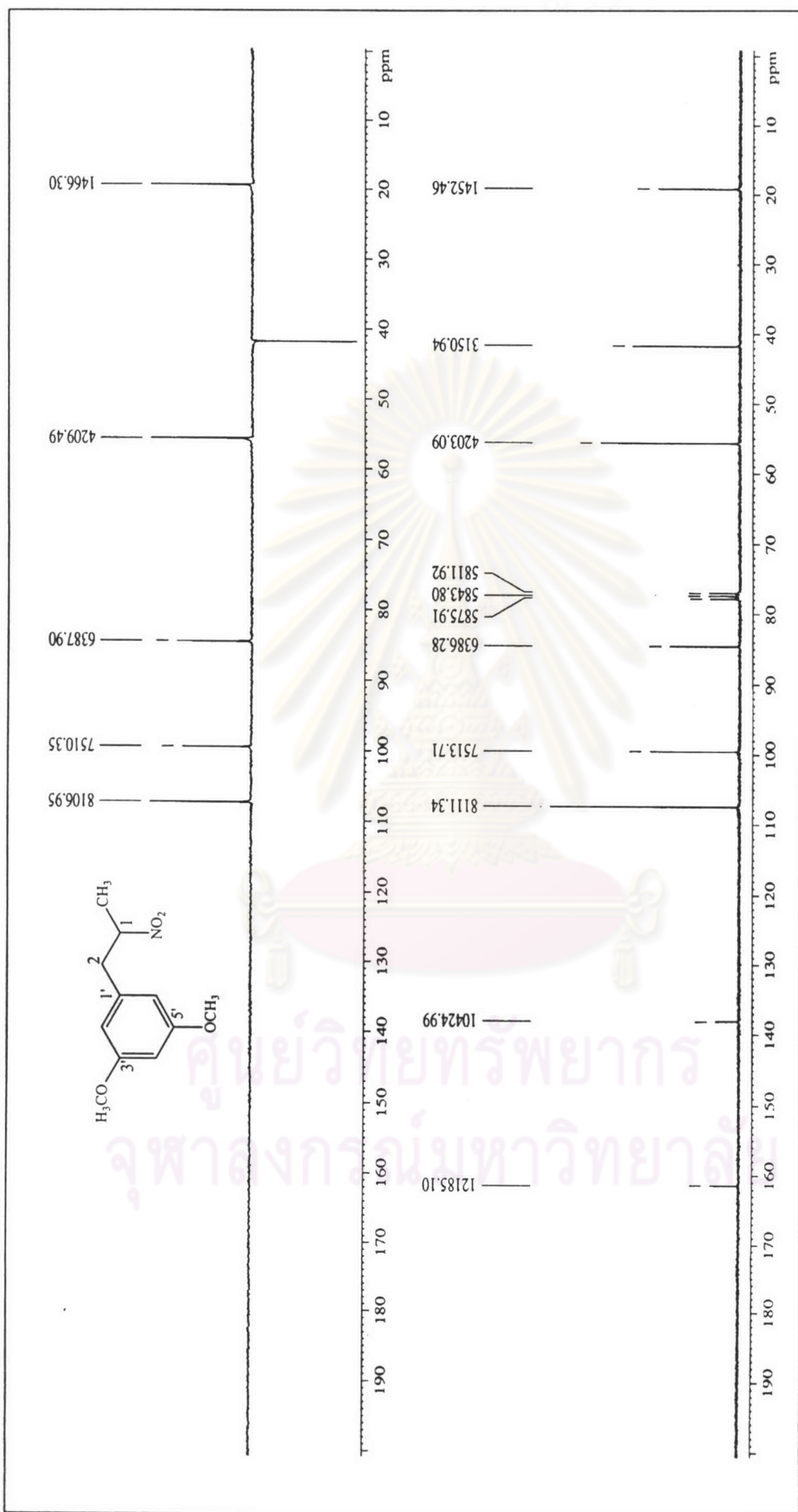


Figure 23 The 75 MHz DEPT 135 and  $^{13}\text{C}$ -NMR spectrum comparison of 2-(3',5'-dimethoxyphenyl)-1-methyl-1-nitroethane (CU-19-02)

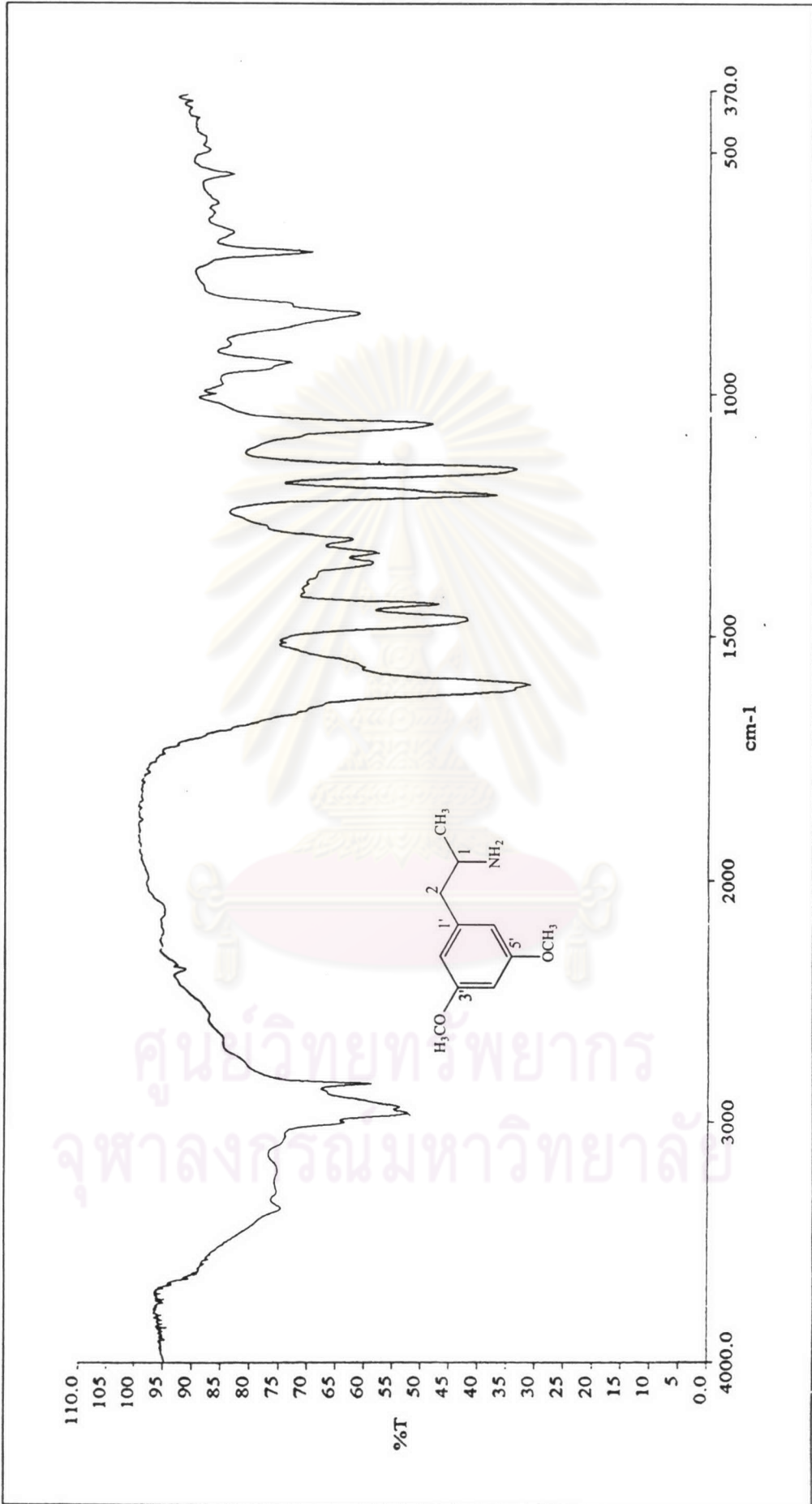


Figure 24 The IR spectrum (KBr) of 2-(3,5'-dimethoxyphenyl)-1-methylethylamine (CU-19-03)

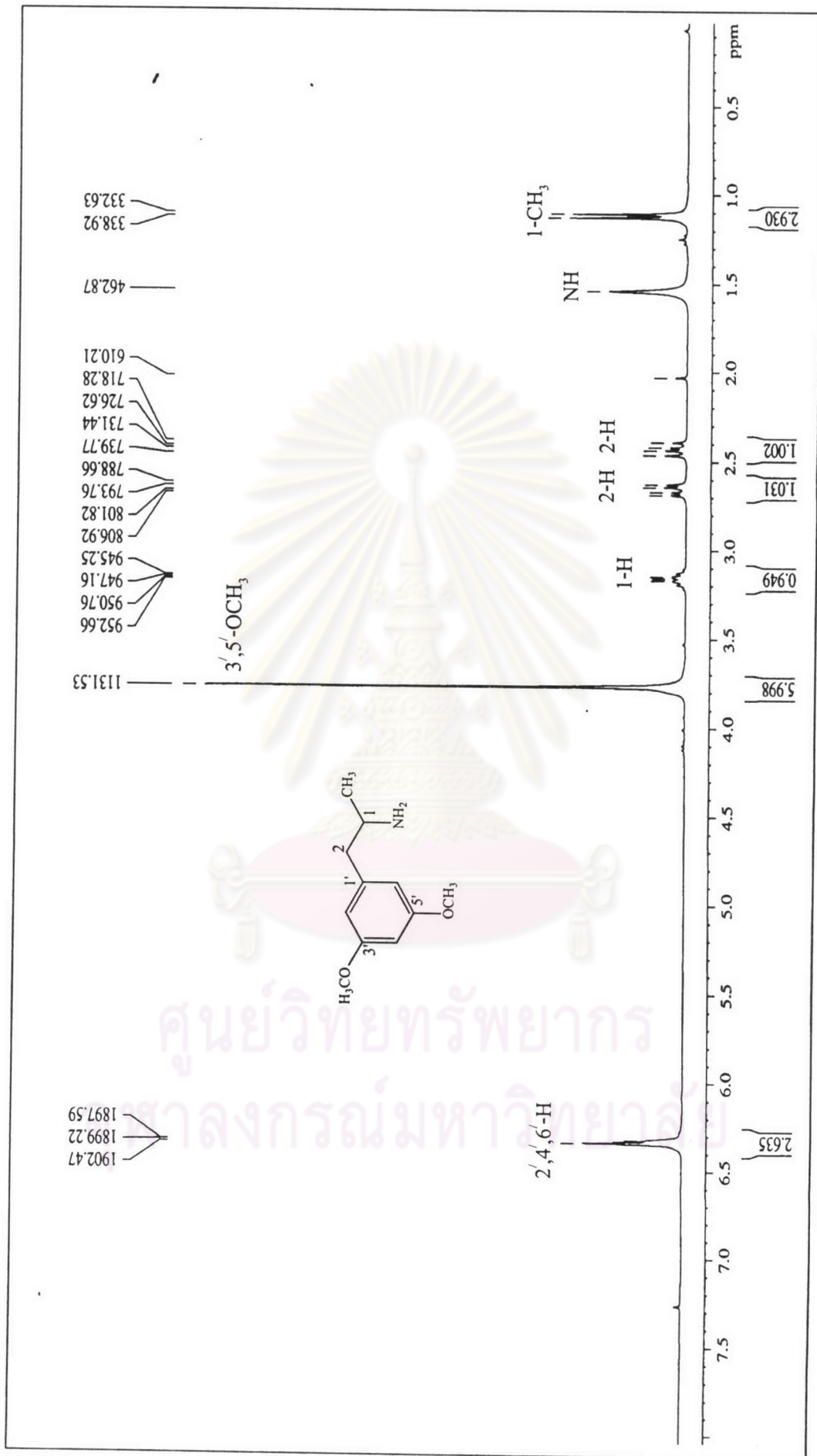


Figure 25 The 300 MHz <sup>1</sup>H-NMR spectrum of 2-(3,5'-dimethoxyphenyl)-1-1-methylethylamine (CU-19-03)

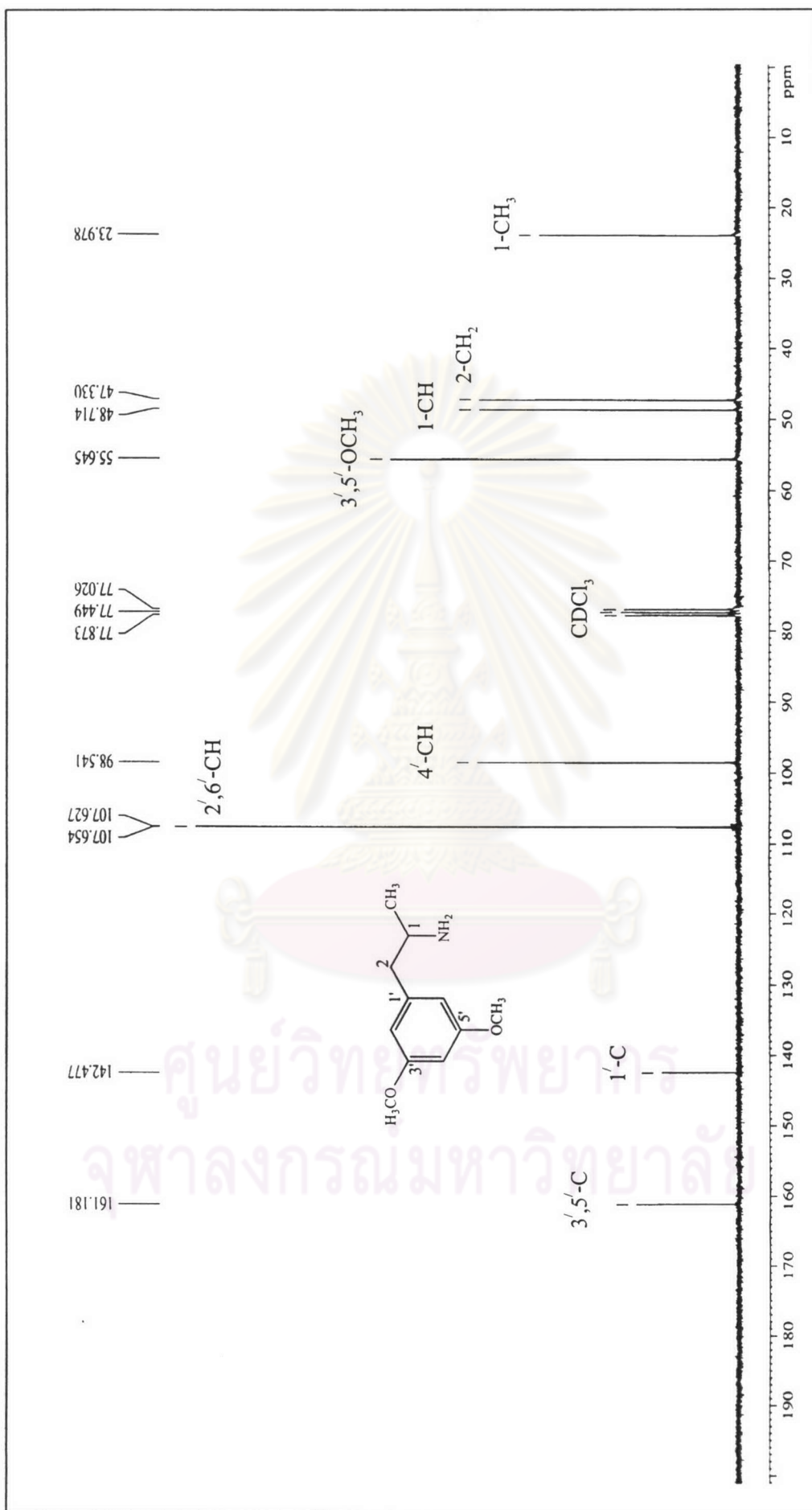


Figure 26 The 75 MHz  $^{13}\text{C}$ -NMR spectrum of 2-(3',5'-dimethoxyphenyl)-1-methylethylamine (CU-19-03)



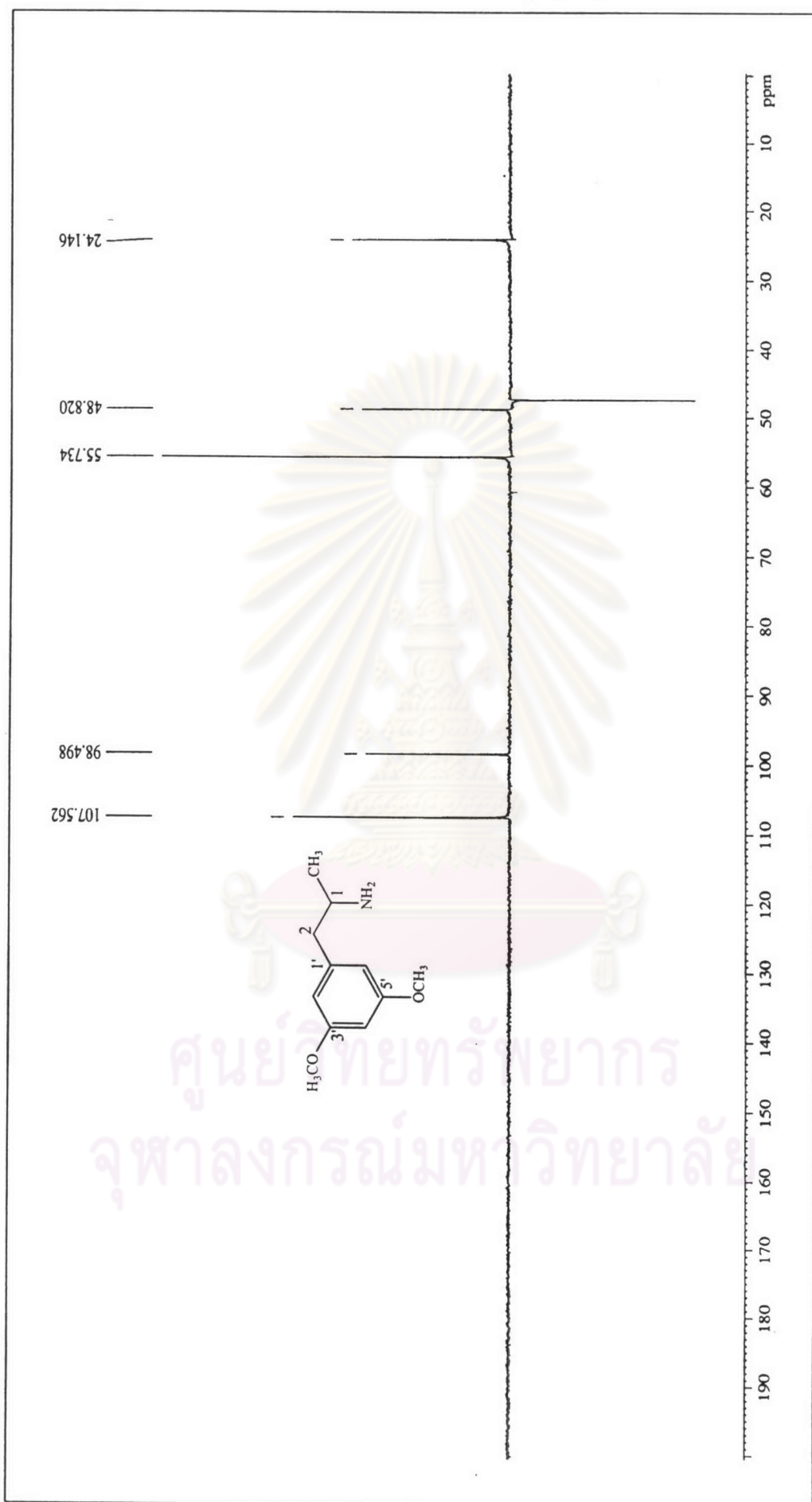


Figure 27 The 75 MHz DEPT 135 spectrum of 2-(3',5'-dimethoxyphenyl)-1-methylethylamine (CU-19-03)

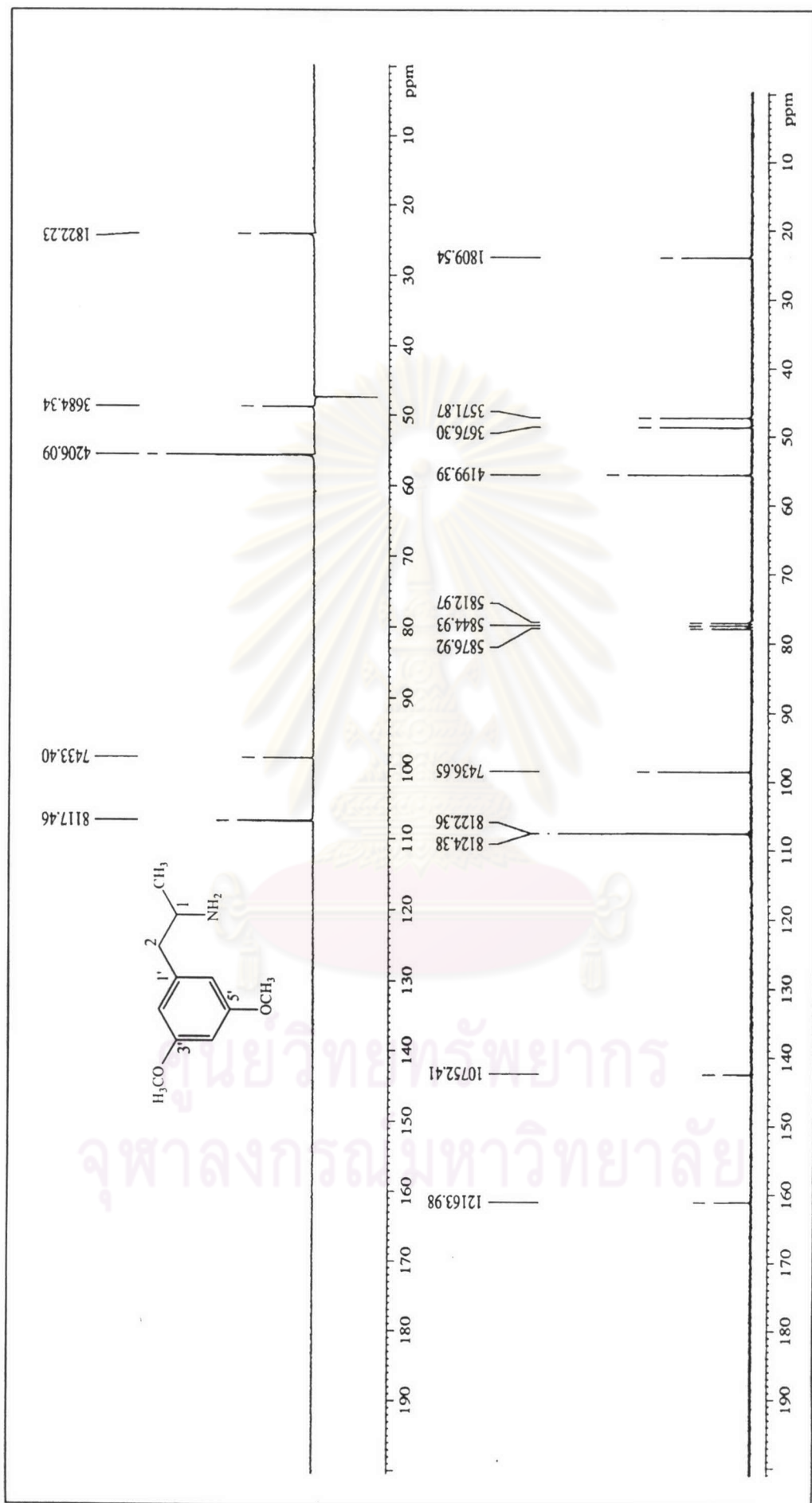


Figure 28 The 75 MHz DEPT  $^{13}\text{C}$ -NMR spectrum comparison of 2-(3,5'-dimethoxyphenyl)-1- methylethylamine (CU-19-03)

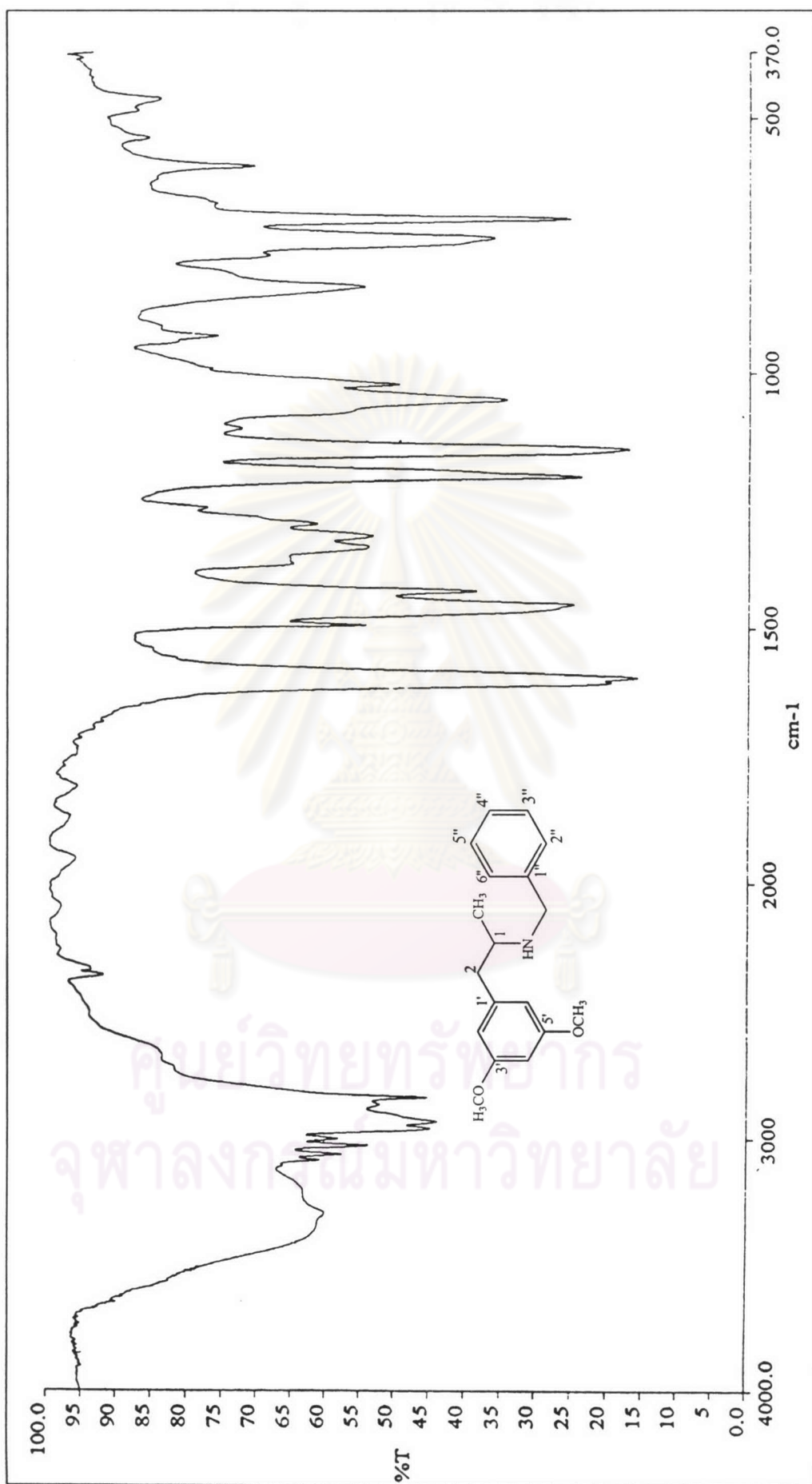


Figure 29 The IR spectrum (KBr) of *N*-benzyl-2-(3,5'-dimethoxyphenyl)-1-methylethylamine (CU-19-04)

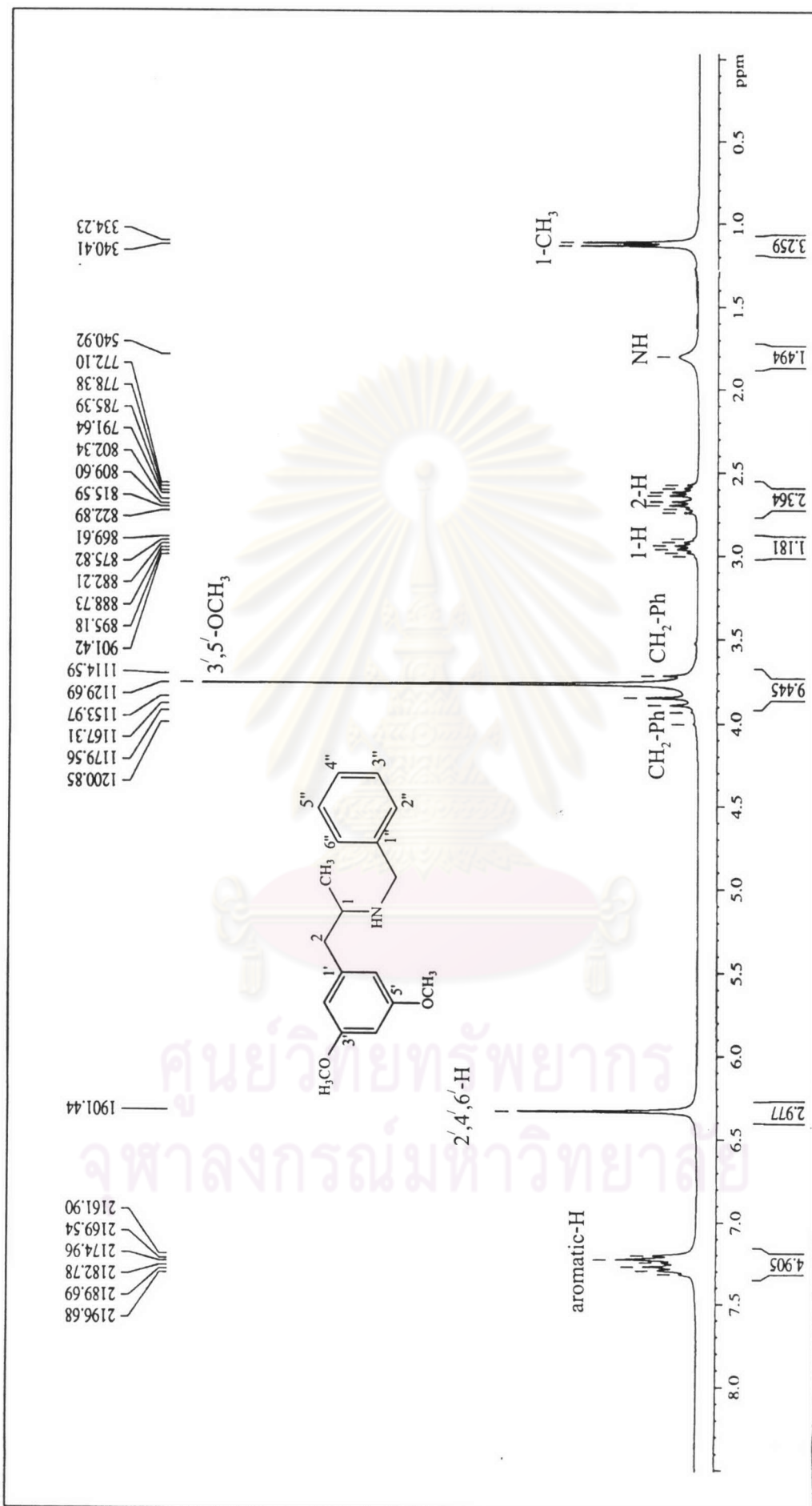


Figure 30 The 300 MHz <sup>1</sup>H-NMR spectrum of *N*-benzyl-2-(3,5-dimethoxyphenyl)-1-methylethylamine (CU-19-04)

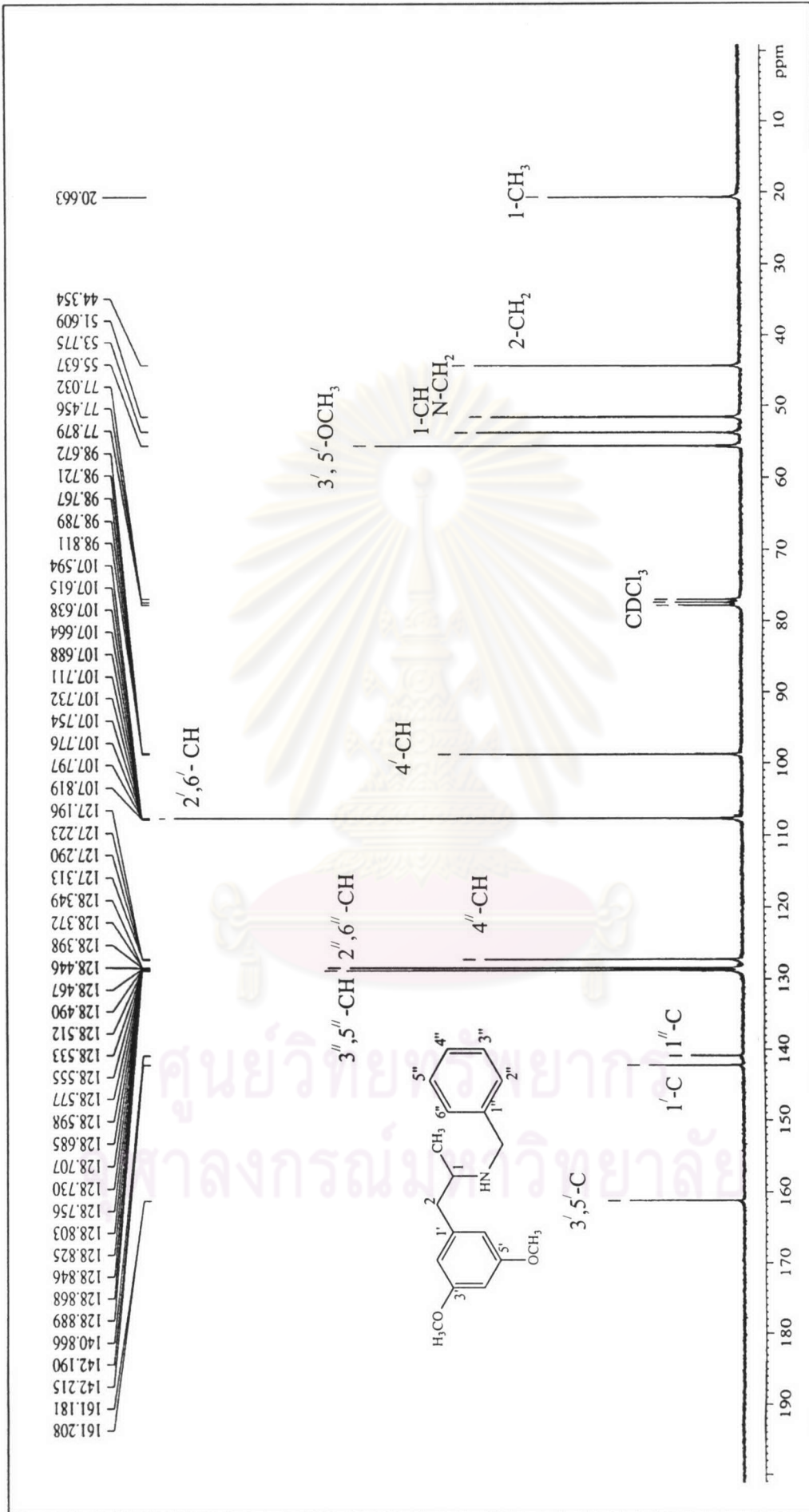


Figure 31 The 75 MHz  $^{13}\text{C}$ -NMR spectrum of *N*-benzyl-2-(3,5-dimethoxyphenyl)-1-methylethylamine (CU-19-04)

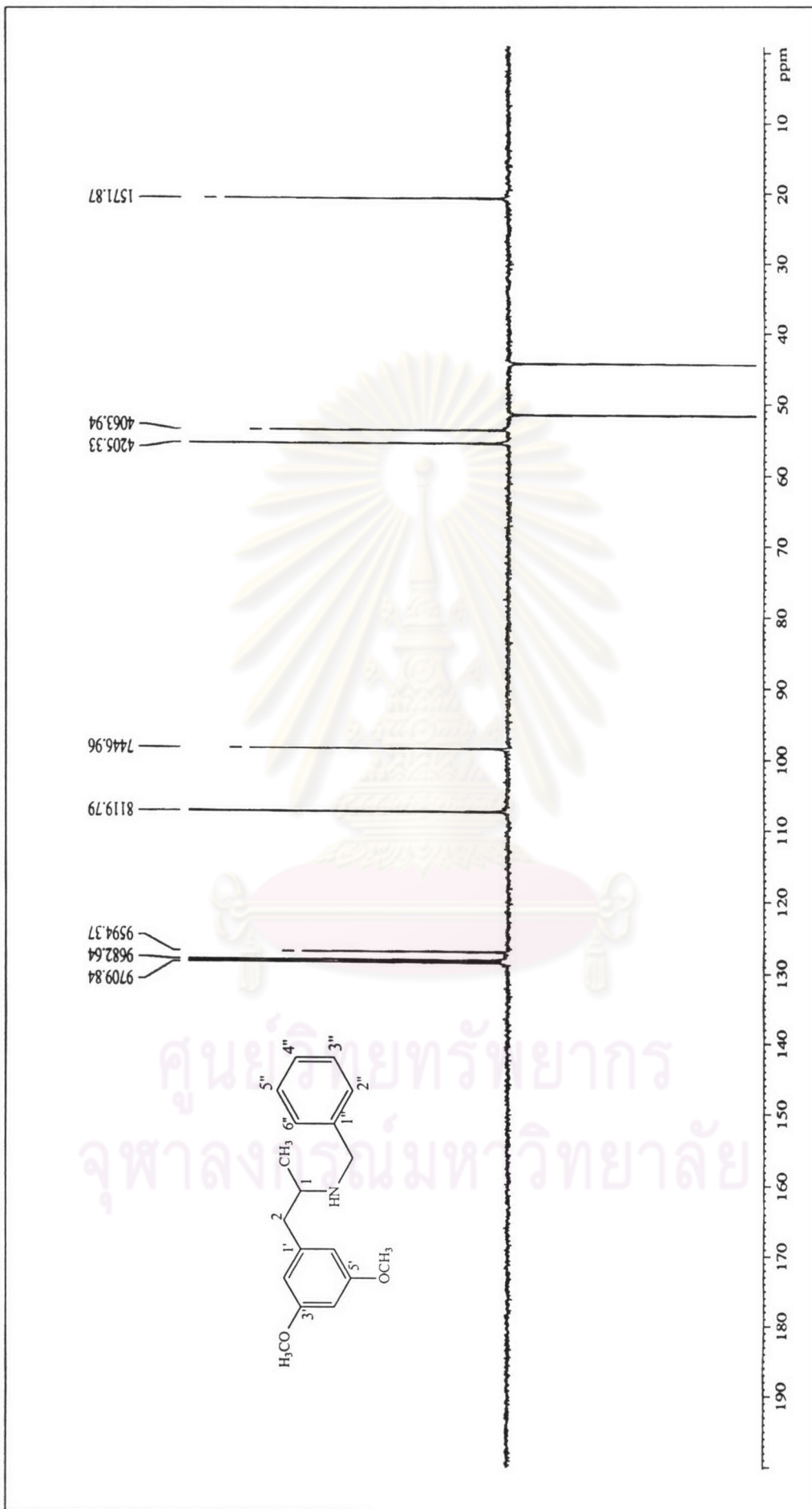


Figure 32 The 75 MHz DEPT 135 spectrum of *N*-benzyl-2-(3,5'-dimethoxyphenyl)-1-methylethylamine (CU-19-04)

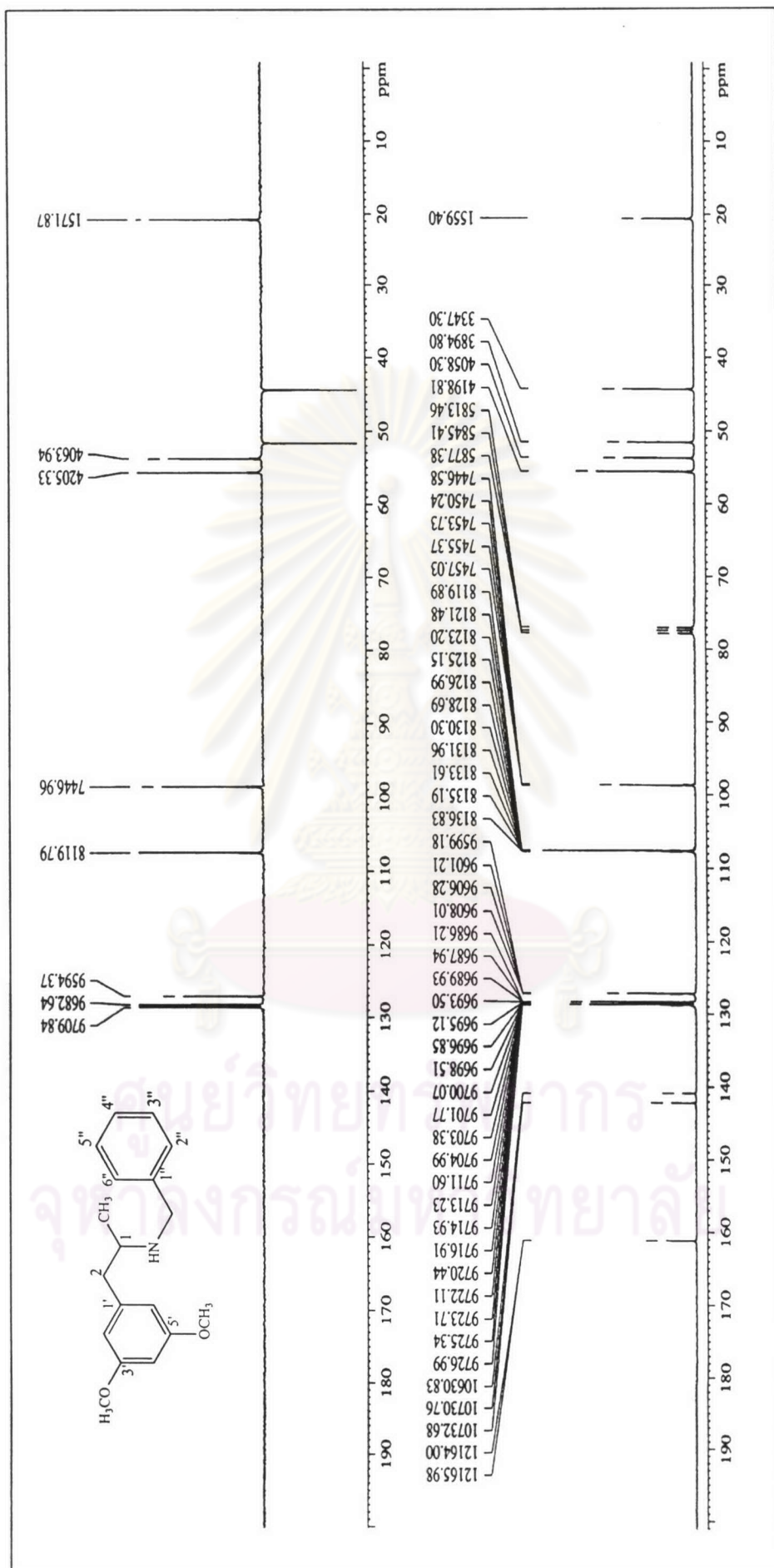


Figure 33 The 75 MHz DEPT 135 and  $^{13}\text{C}$ -NMR spectrum comparison of *N*-benzyl-2-(3,5-dimethoxyphenyl)-1-methylethylamine (CU-19-04)

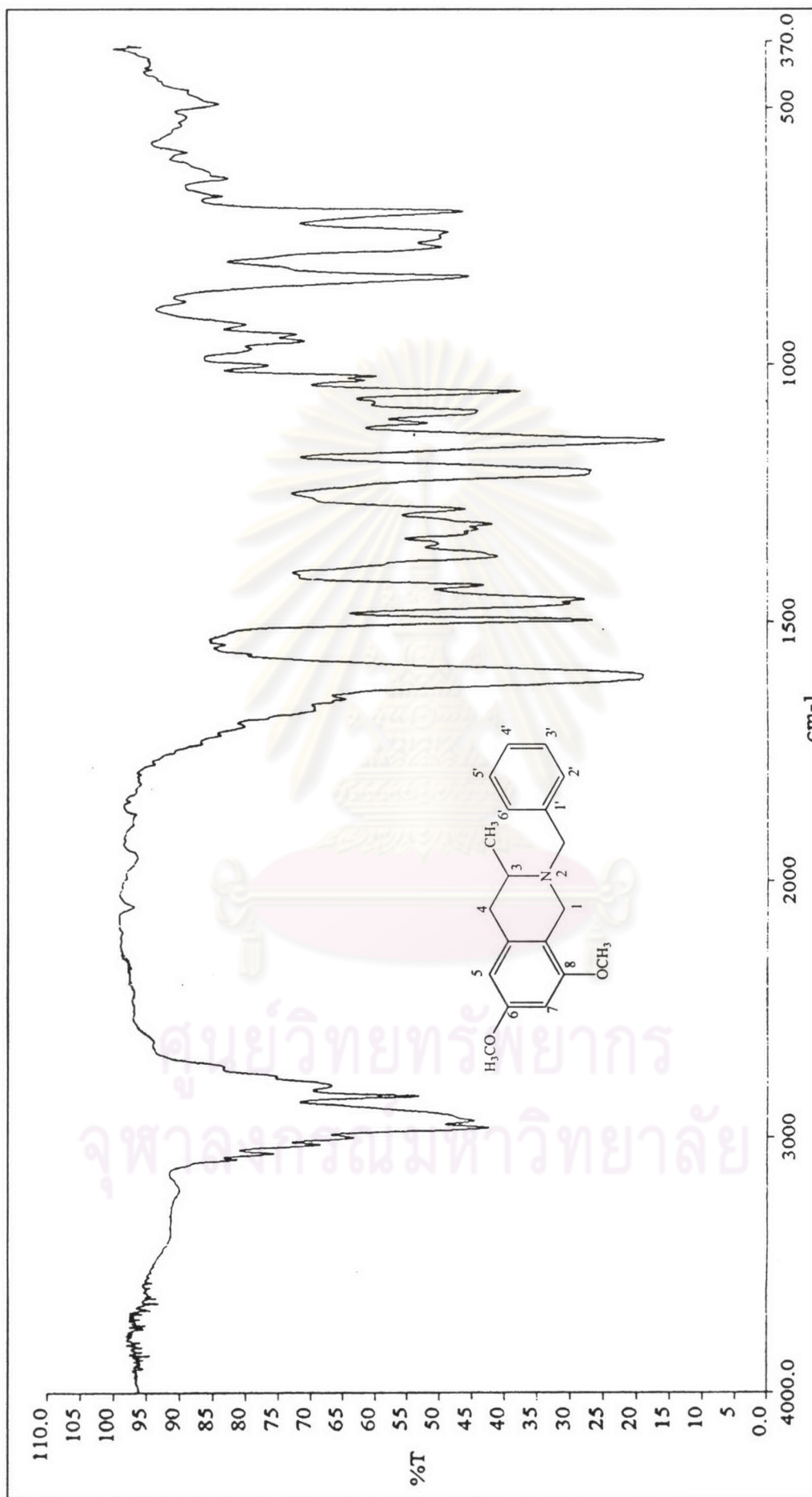


Figure 34 The IR spectrum (KBr) of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05)



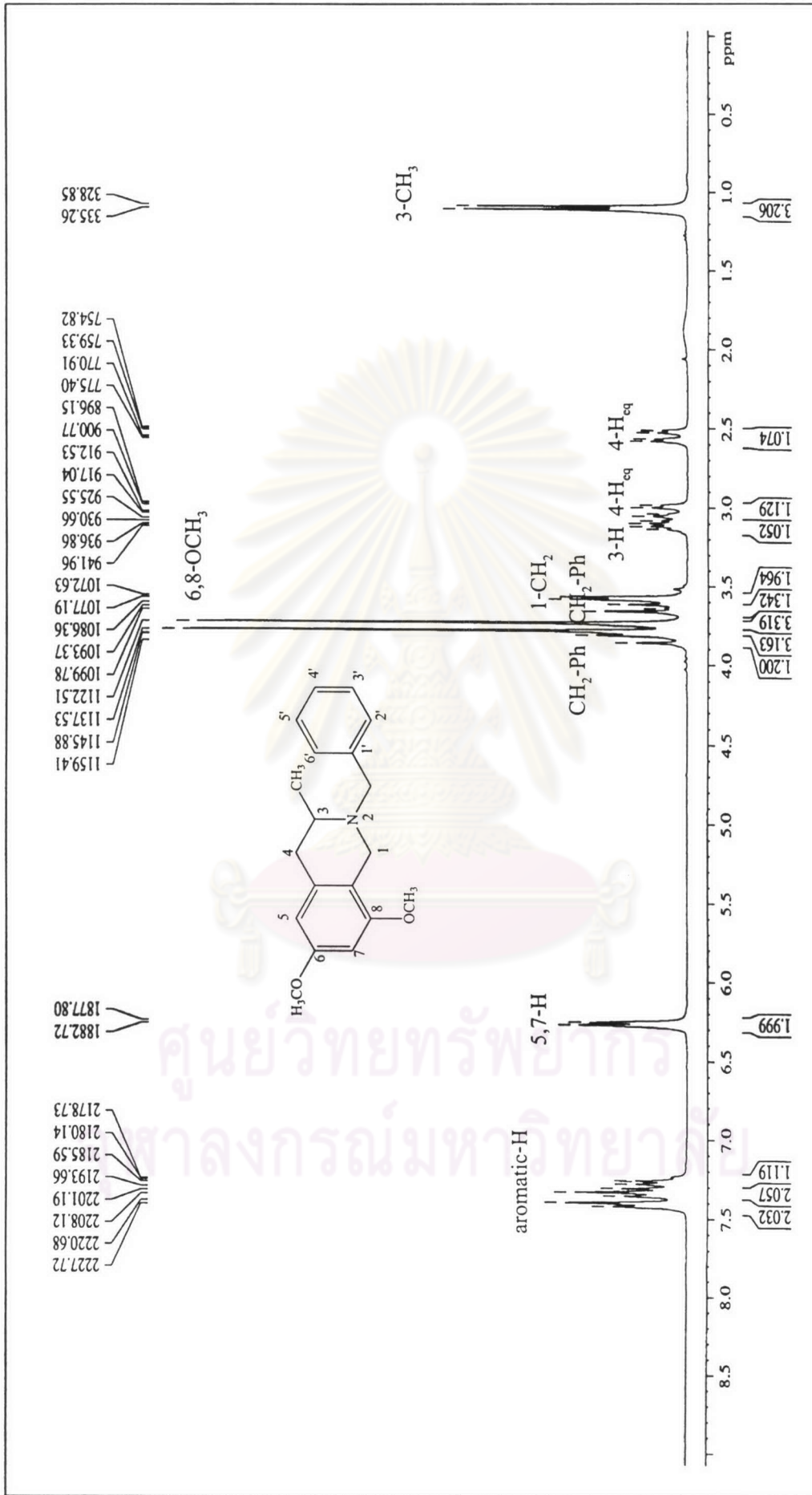


Figure 35 The 300 MHz <sup>1</sup>H-NMR spectrum of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05)

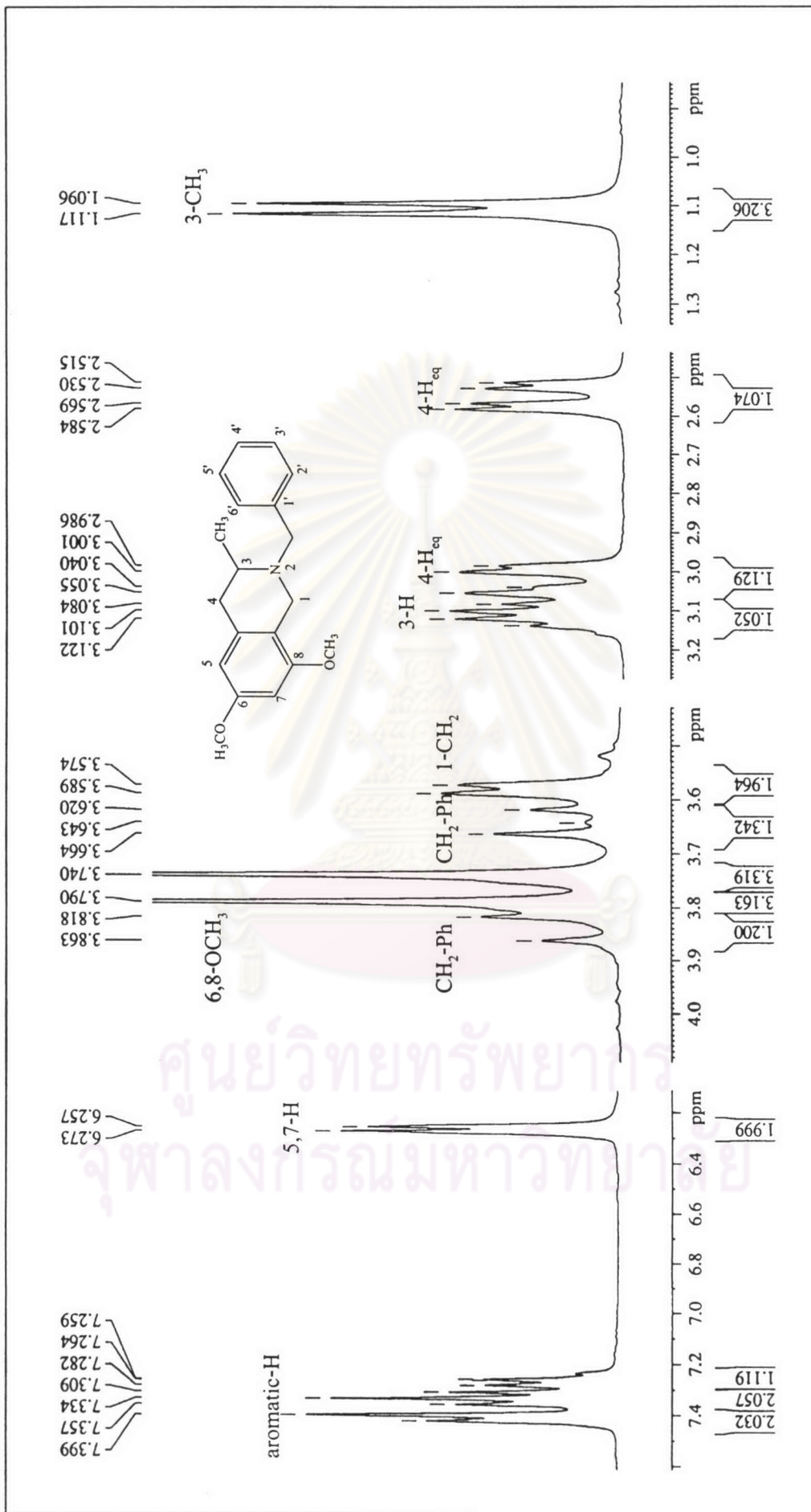


Figure 36 The 300 MHz <sup>1</sup>H-NMR spectrum of 2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-19-05) (Enlarged scale)

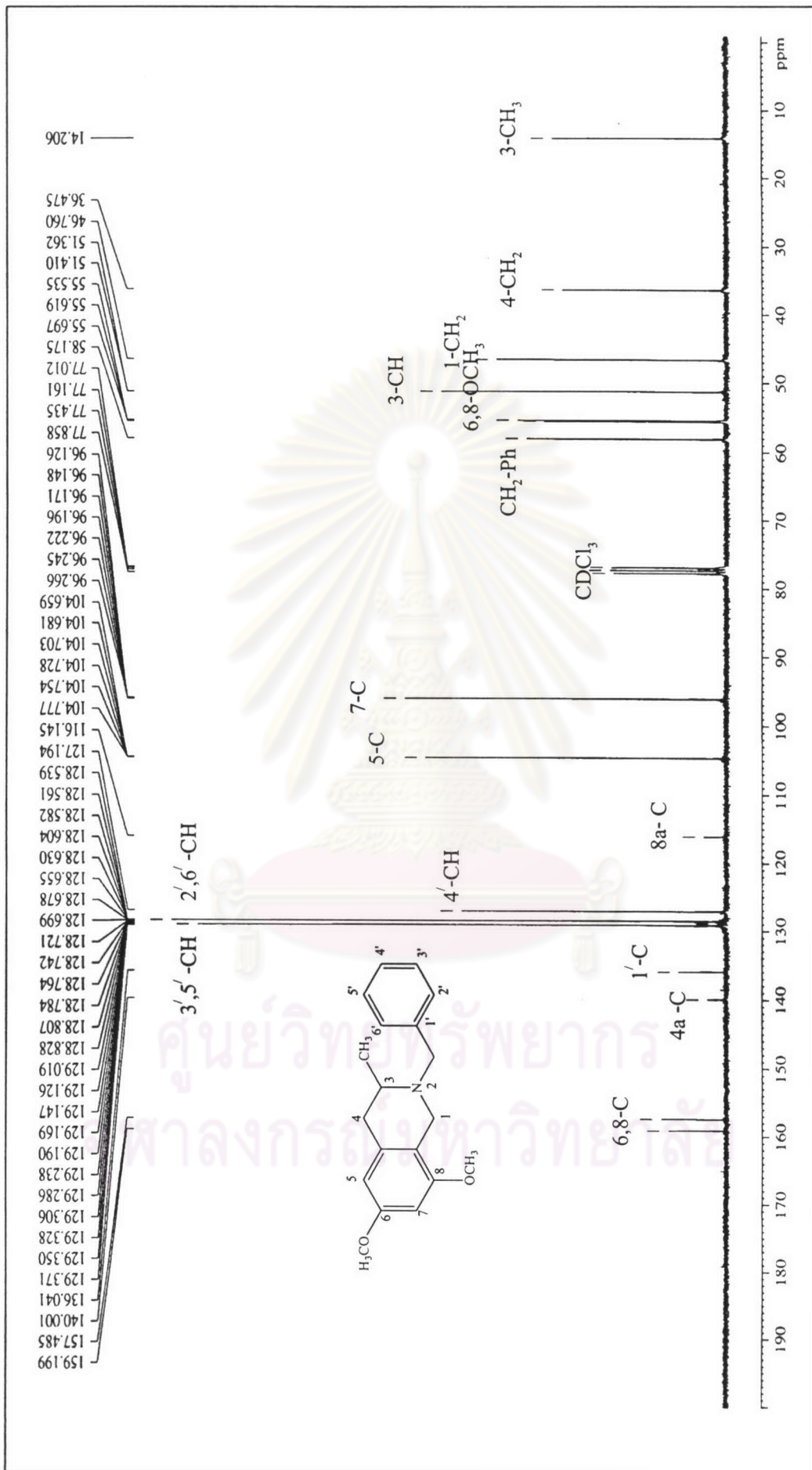


Figure 37 The 75 MHz  $^{13}\text{C}$ -NMR spectrum of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05)

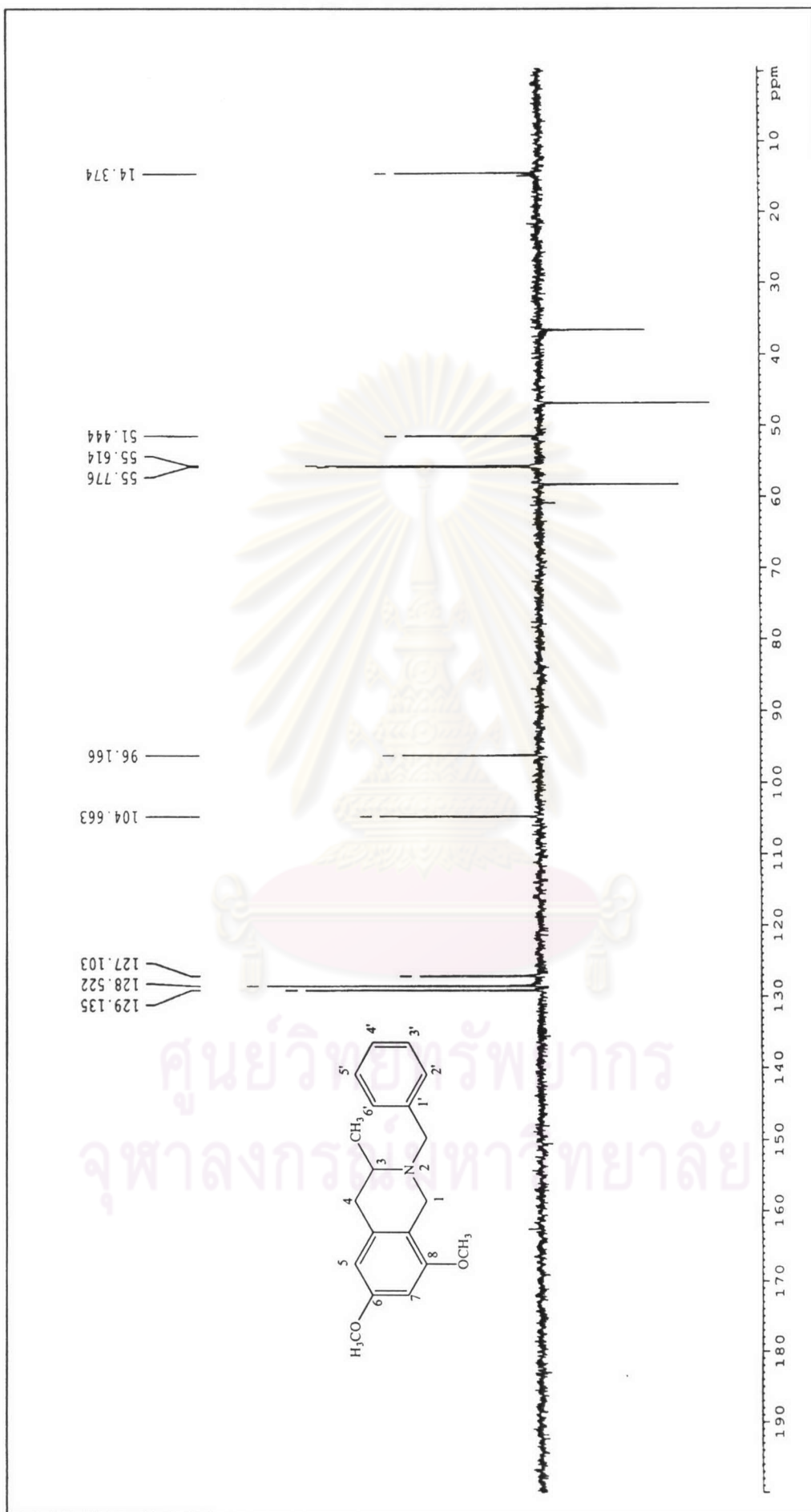


Figure 38 The 75 MHz DEPT 135 spectrum of 2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-19-05)

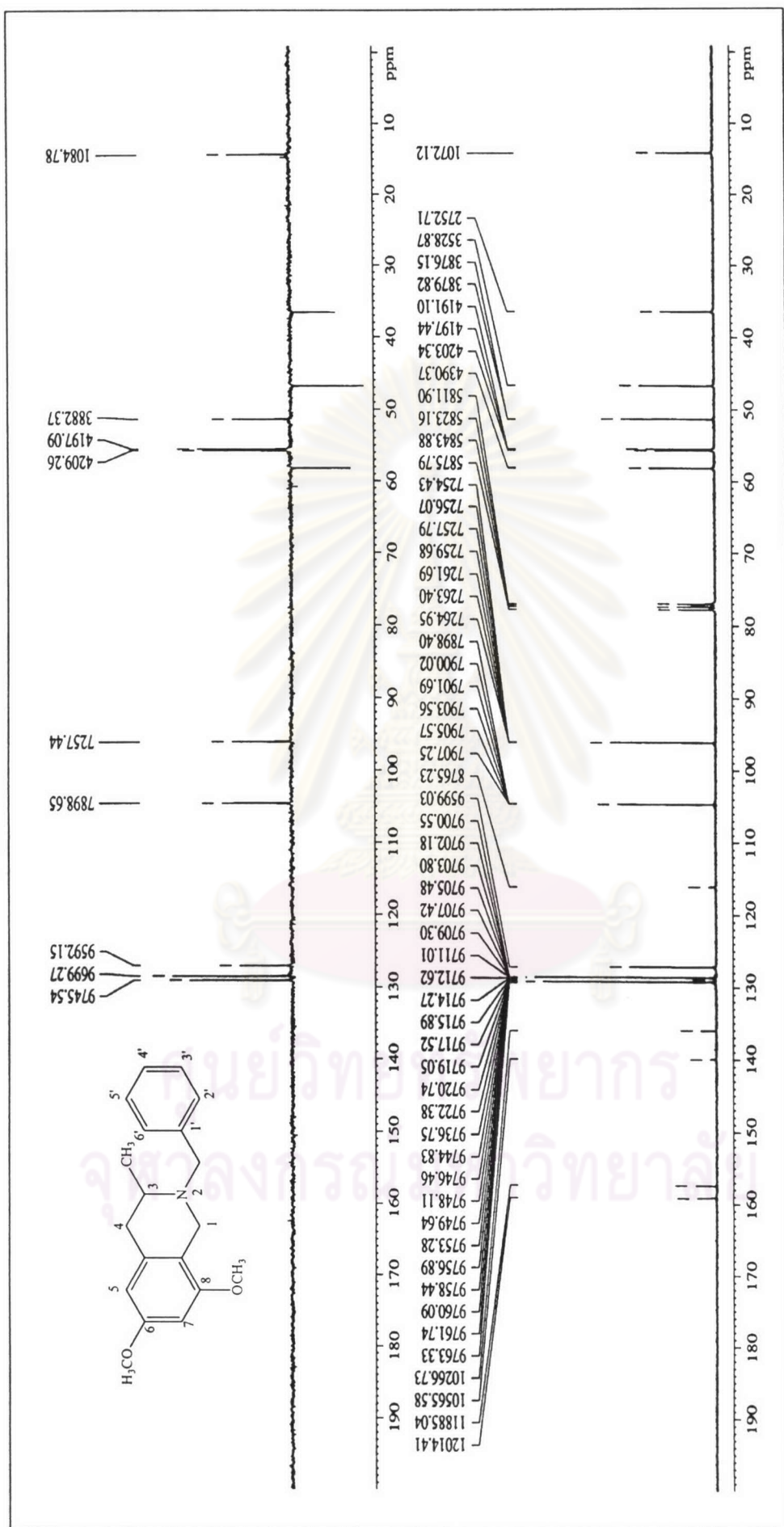


Figure 39 The 75 MHz DEPT 135 and  $^{13}\text{C}$ -NMR spectrum comparison of 2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline(CU-

19-05)

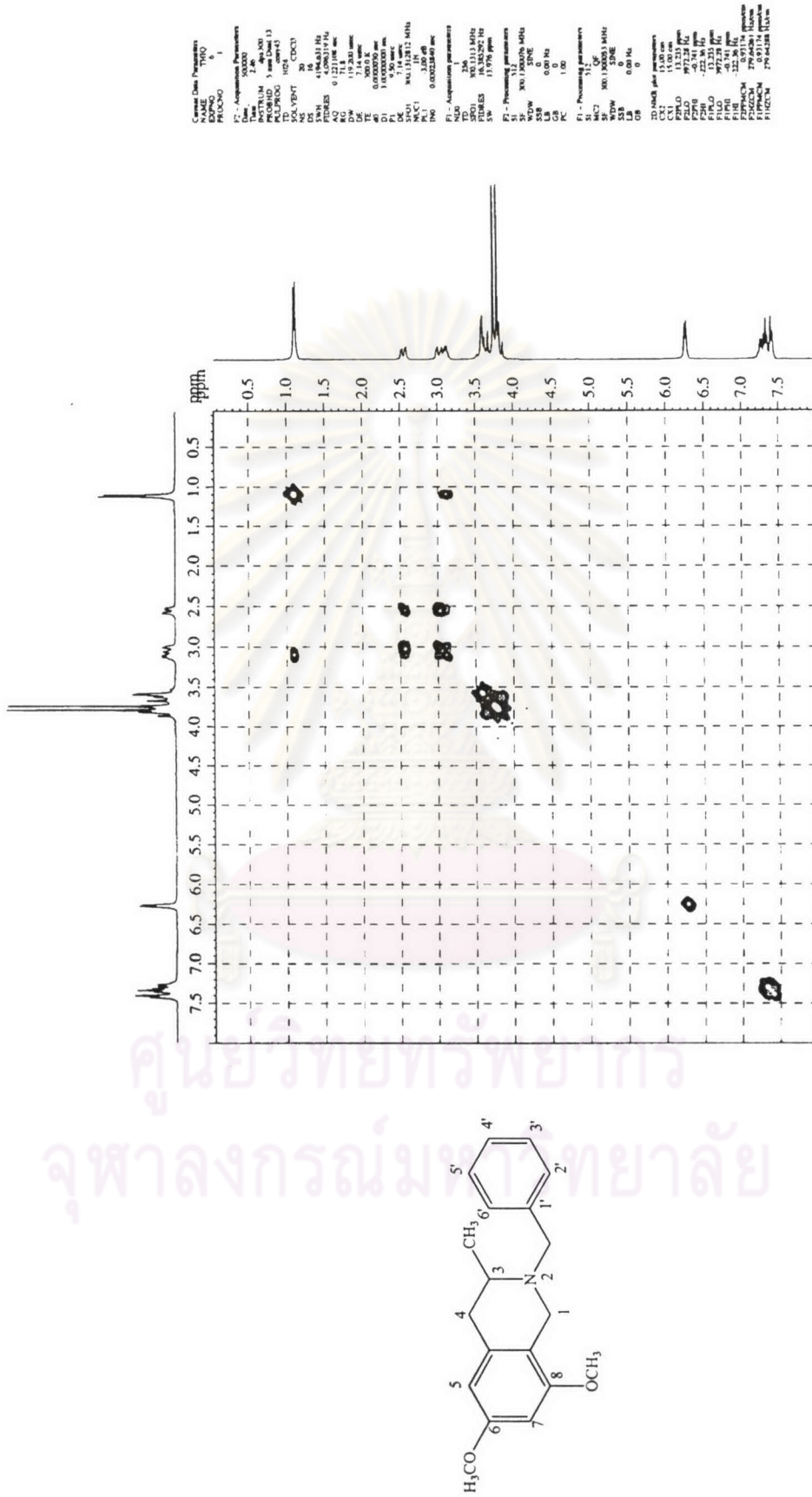
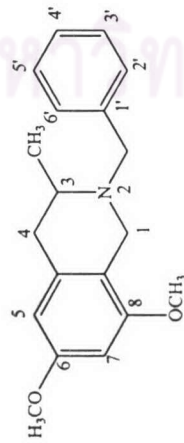


Figure 40 The 300 MHz <sup>1</sup>H-<sup>1</sup>H COSY spectrum of 2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-19-05)



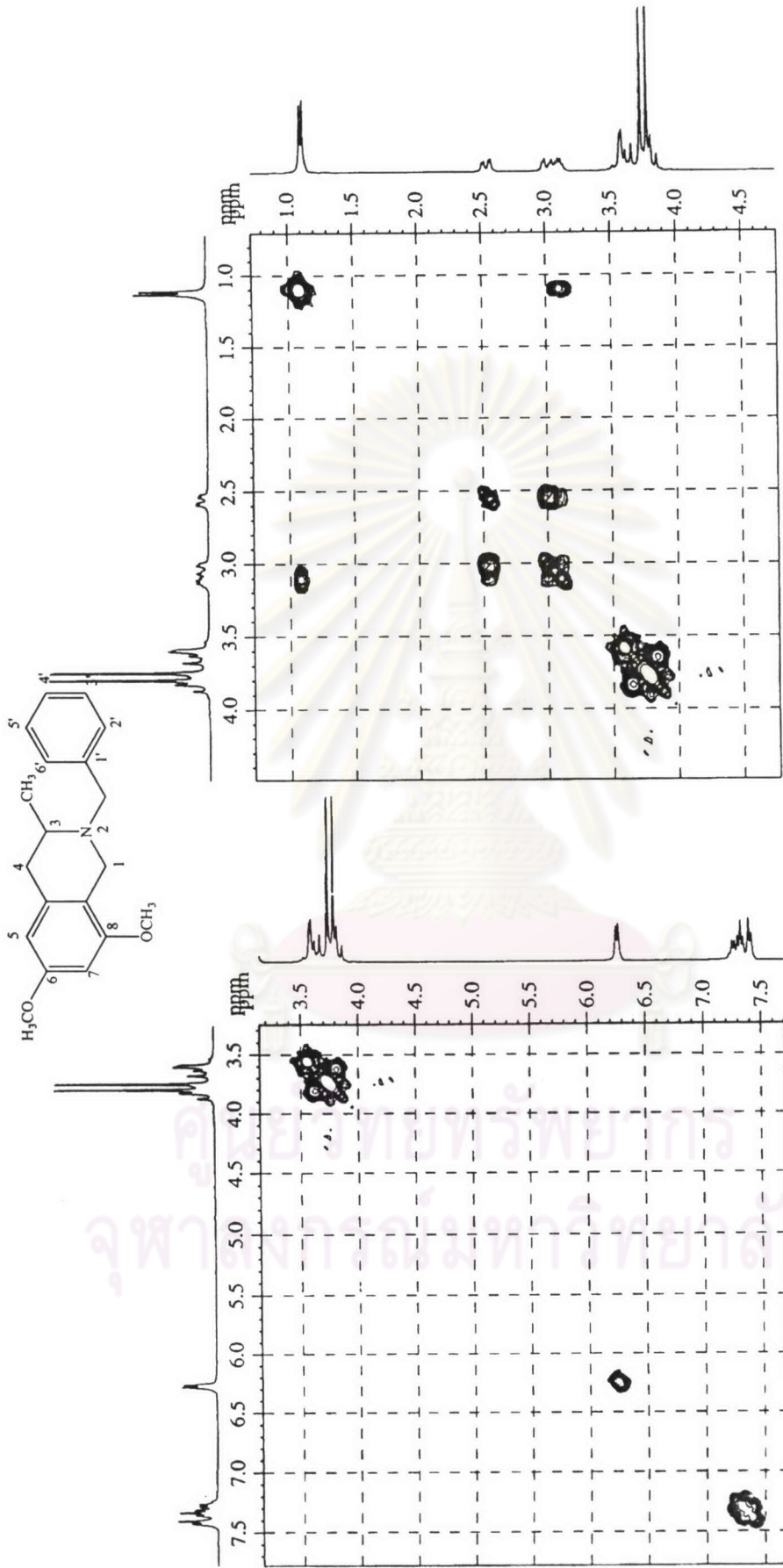


Figure 41 The 300 MHz HH COSY spectrum of 2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-19-05) (Enlarged scale)

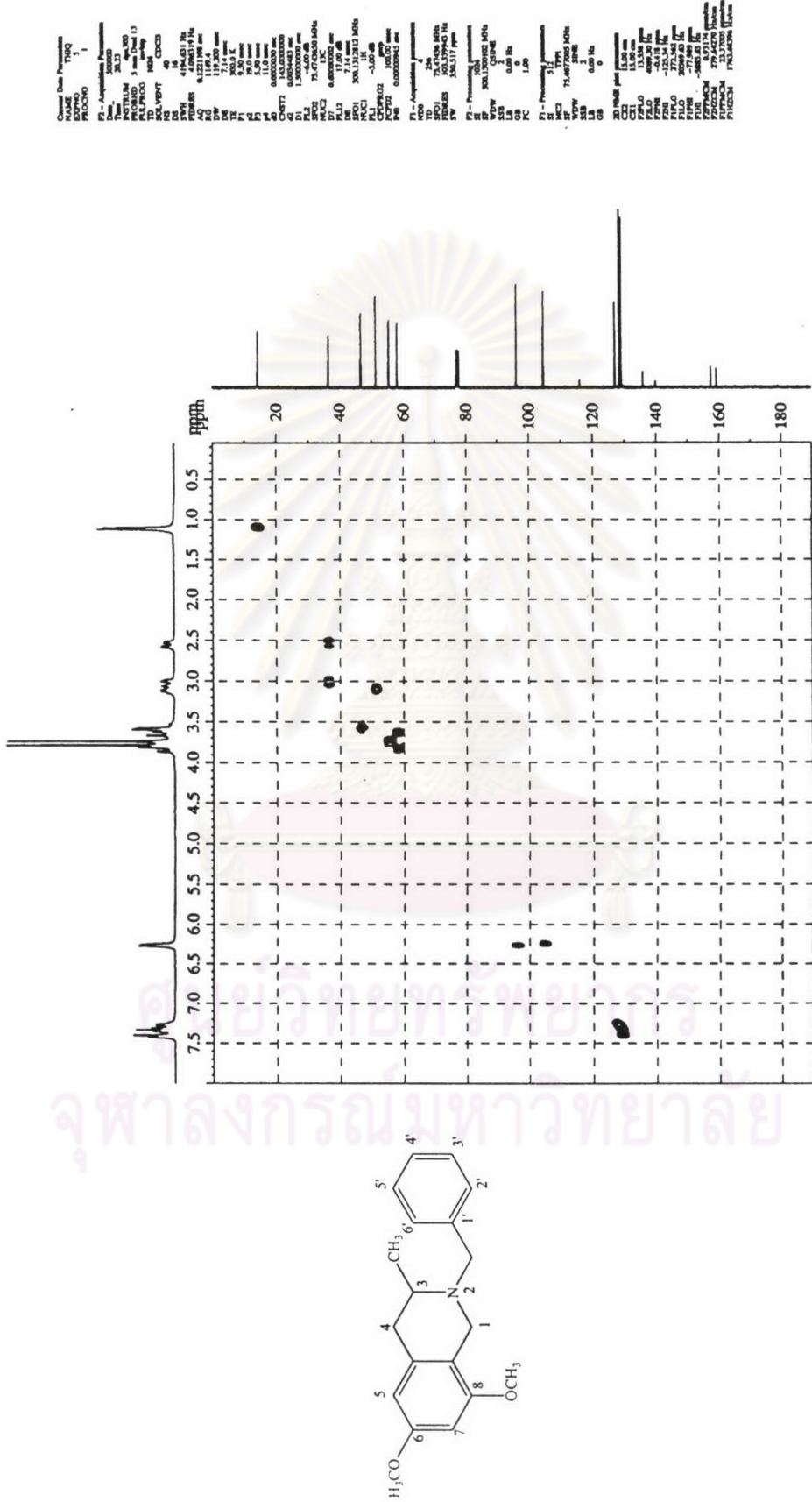


Figure 42 The 300 MHz HMQC spectrum of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-19-05)



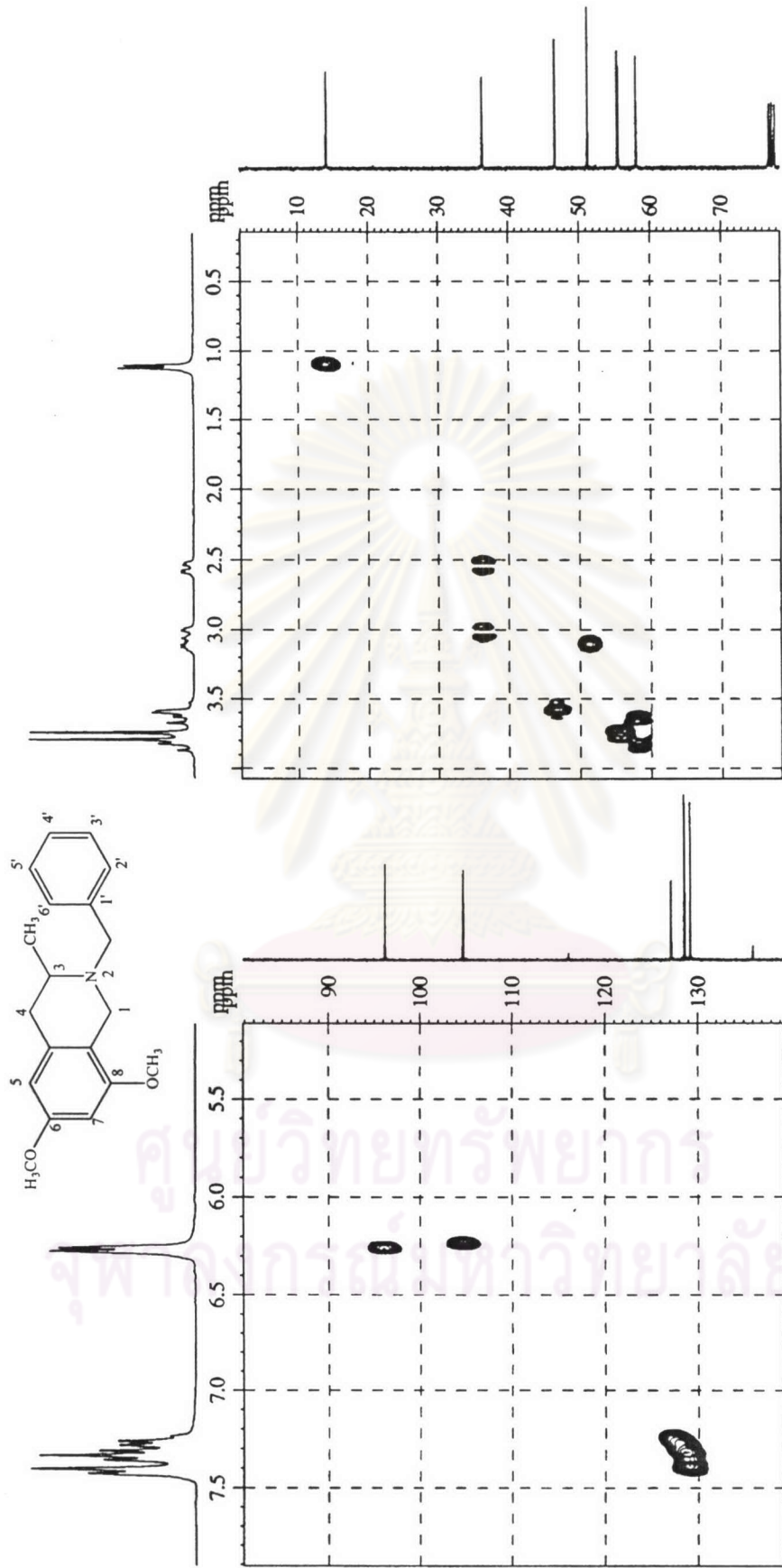


Figure 43 The 300 MHz HMQC spectrum of 2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline(CU-19-05) (Enlarged scale)

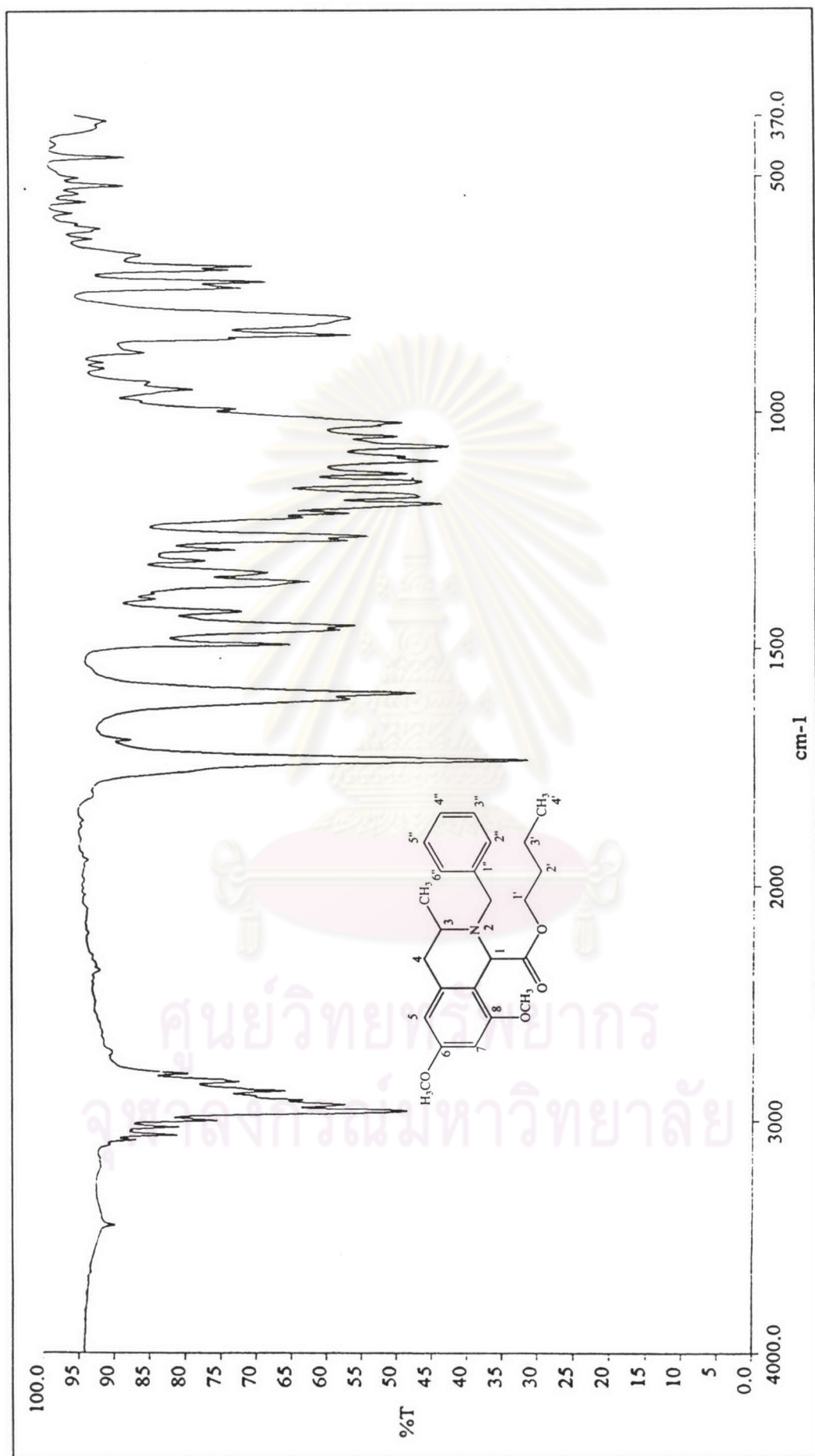


Figure 44 The IR spectrum (KBr) of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10)

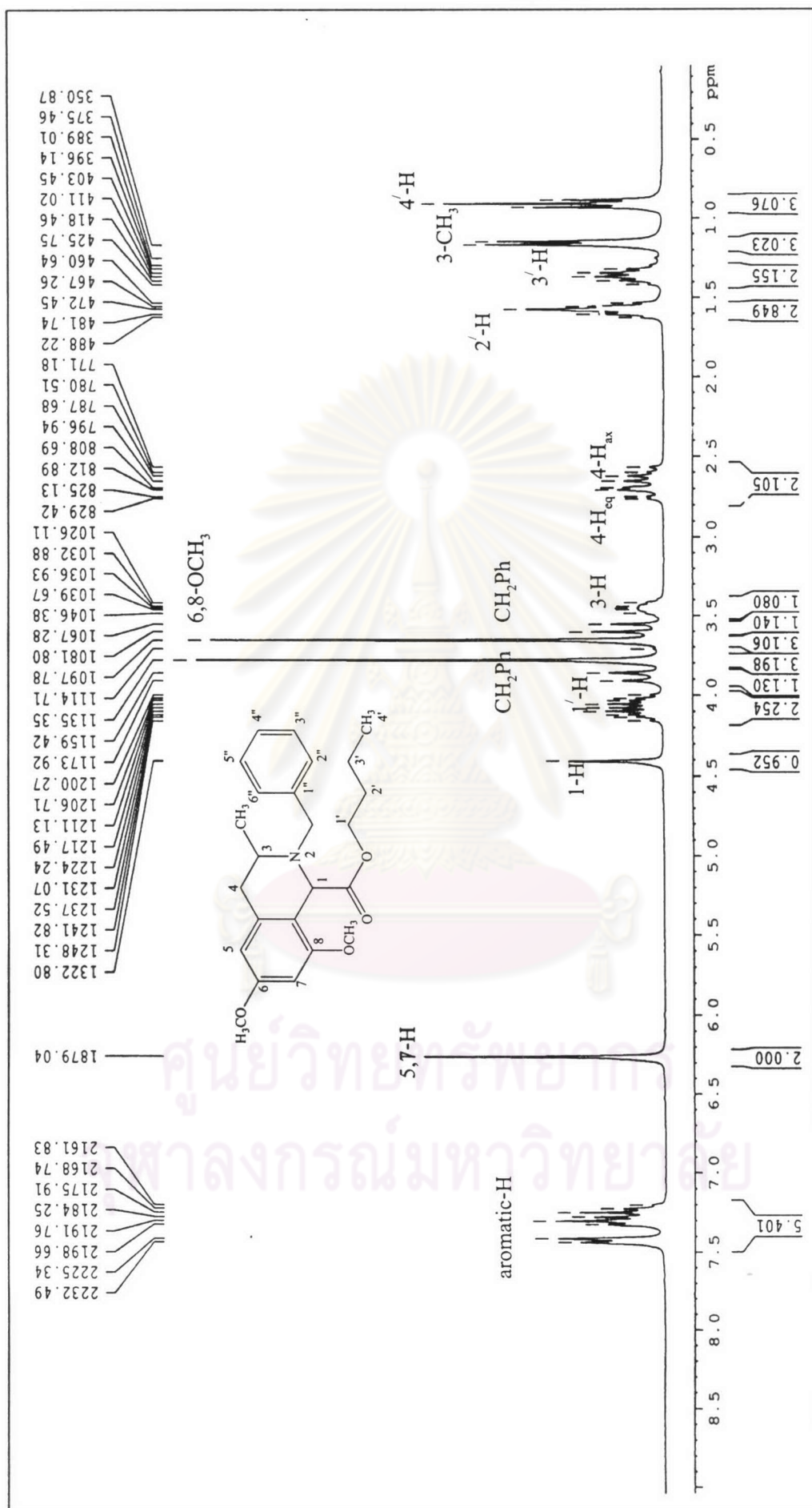


Figure 45 The 300 MHz <sup>1</sup>H-NMR spectrum of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10)

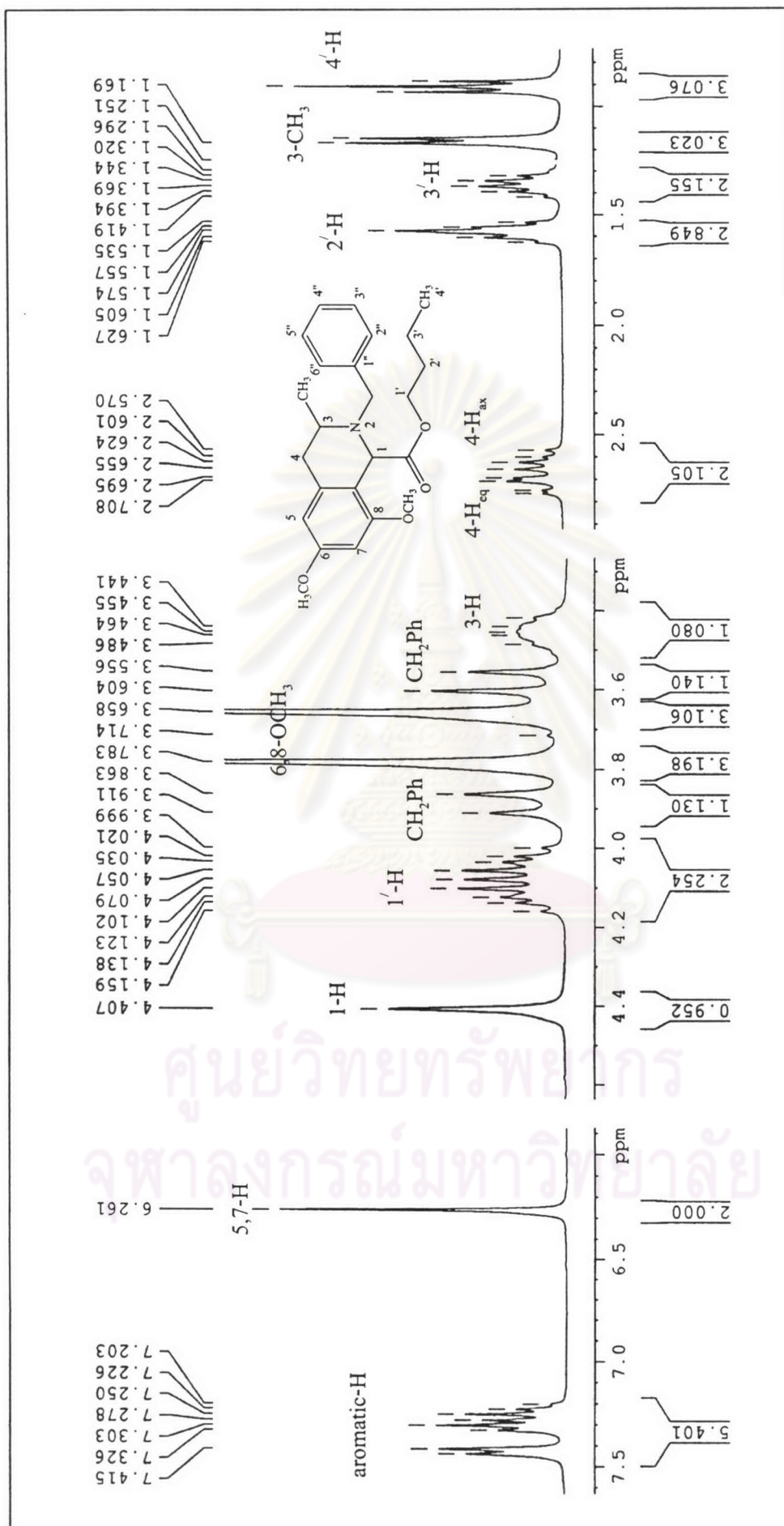


Figure 46 The 300 MHz <sup>1</sup>H-NMR spectrum of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10)

(Enlarged scale)

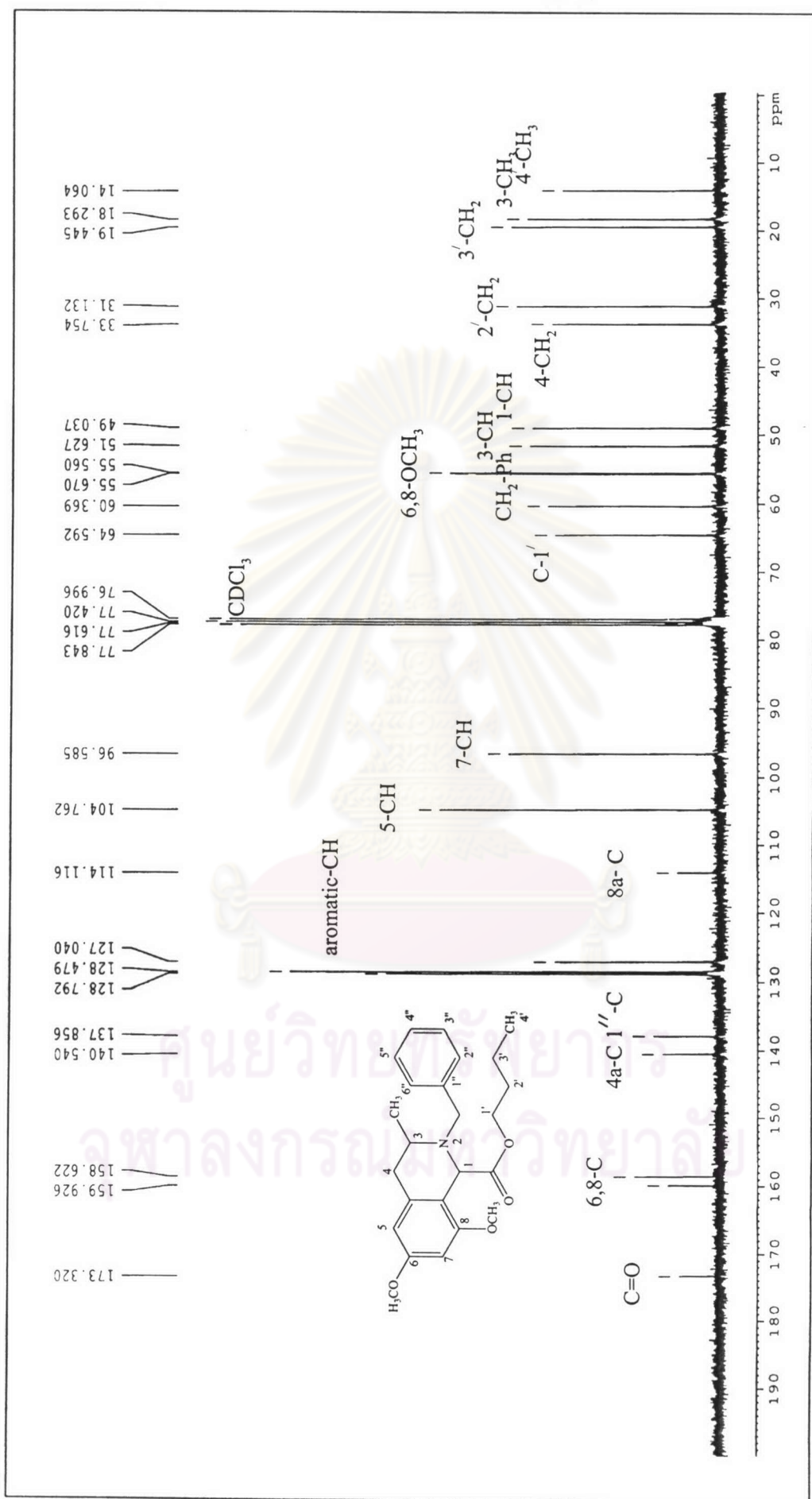


Figure 47 The 75 MHz  $^{13}\text{C}$ -NMR spectrum of butyl-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10)

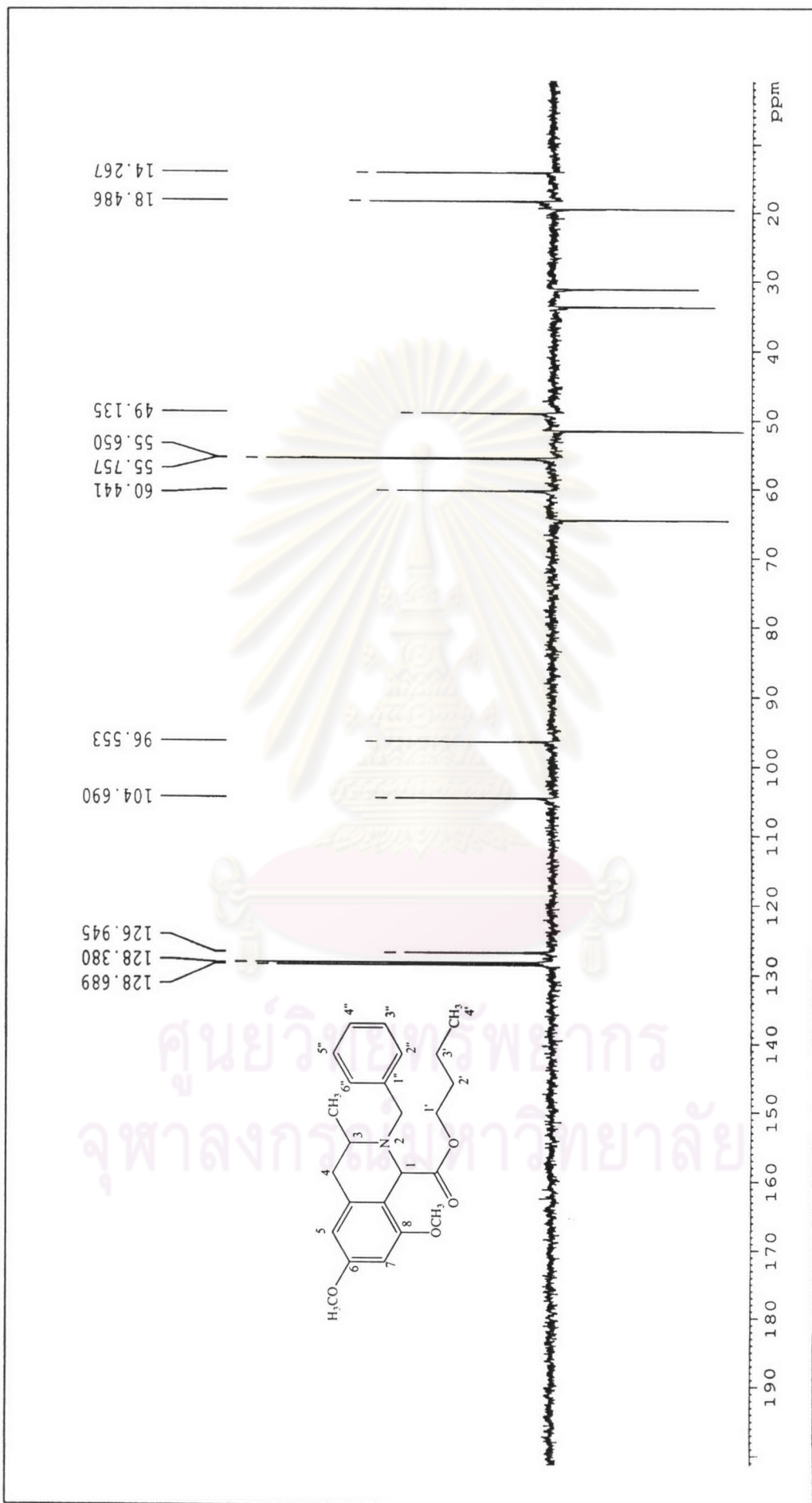


Figure 48 The 75 MHz DEPT 135 spectrum of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10)

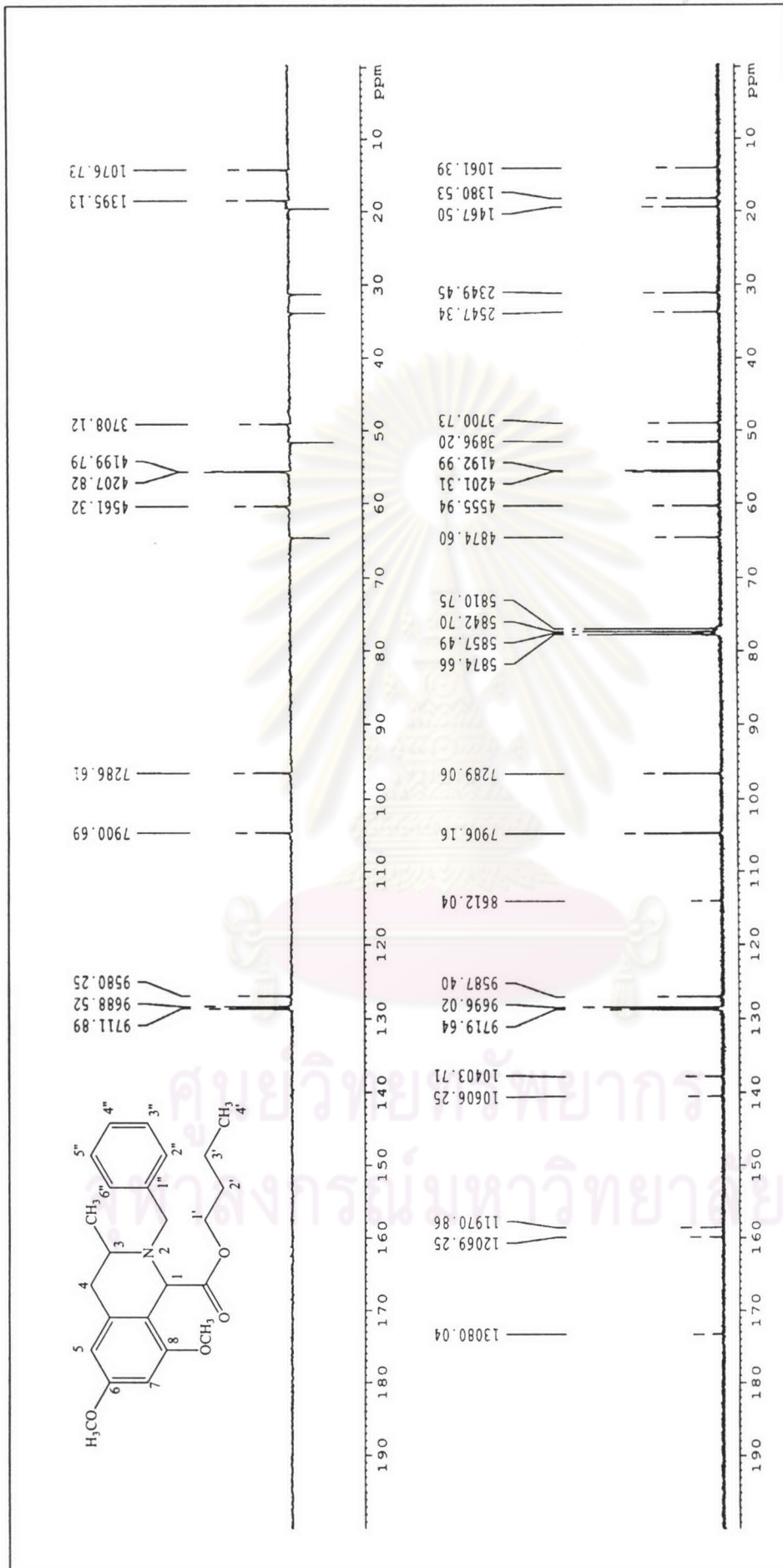


Figure 49 The 75 MHz DEPT 135 and  $^{13}\text{C}$ -NMR spectrum comparison of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10)

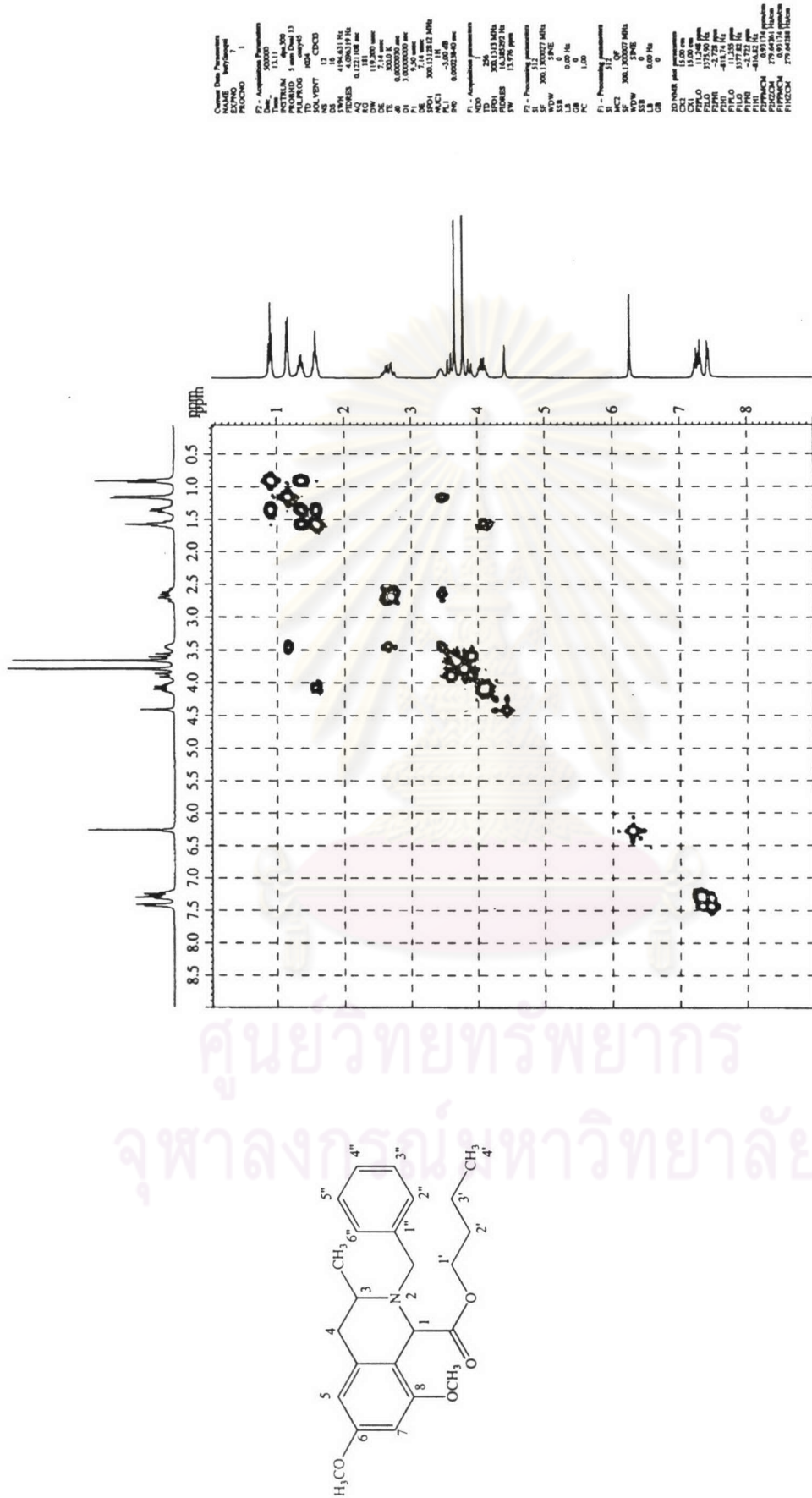


Figure 50 The 300 MHz 1H-1H COSY spectrum of butyl-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10)



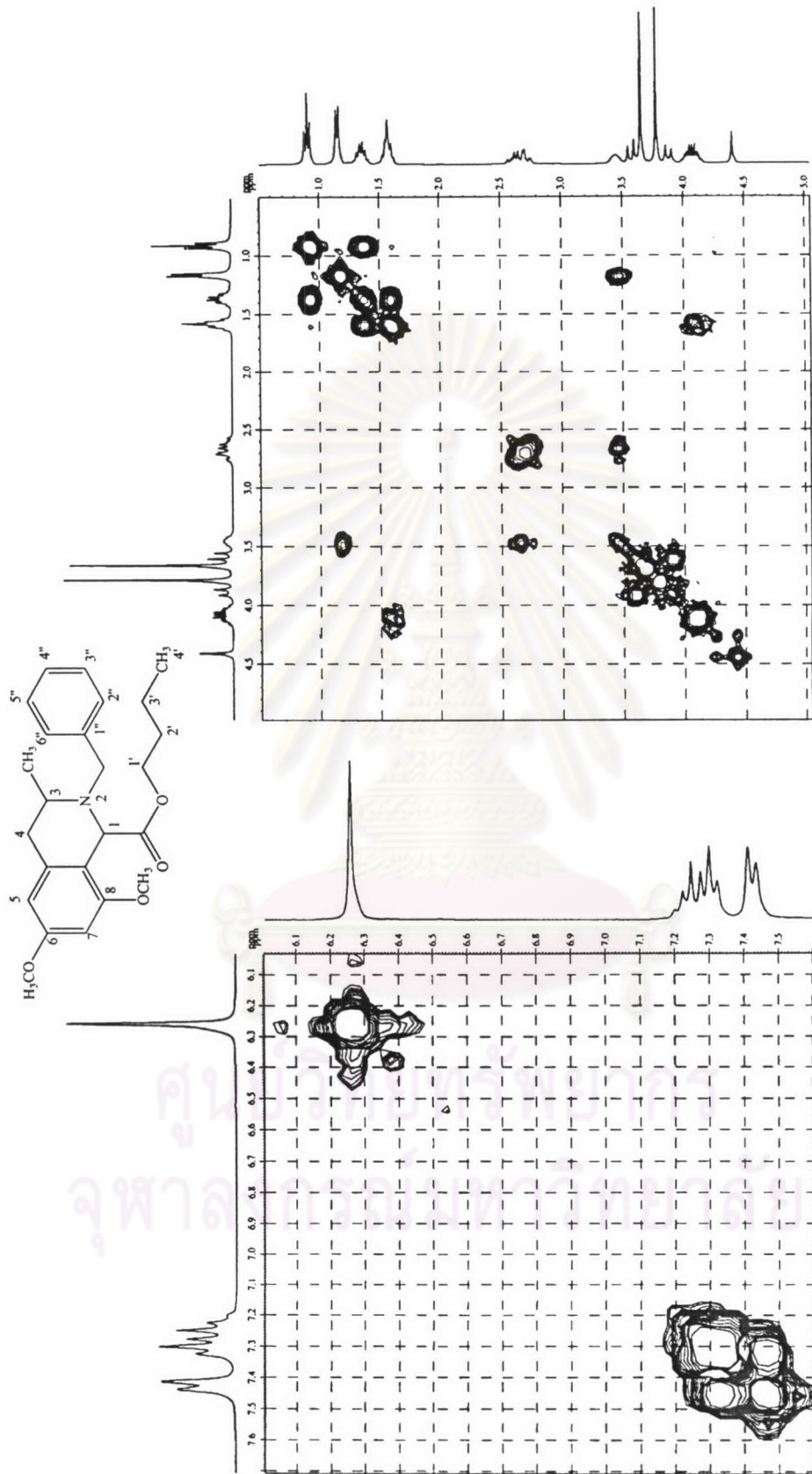


Figure 51 The 300 MHz <sup>1</sup>H-<sup>1</sup>H COSY spectrum of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10)

(Enlarged scale)

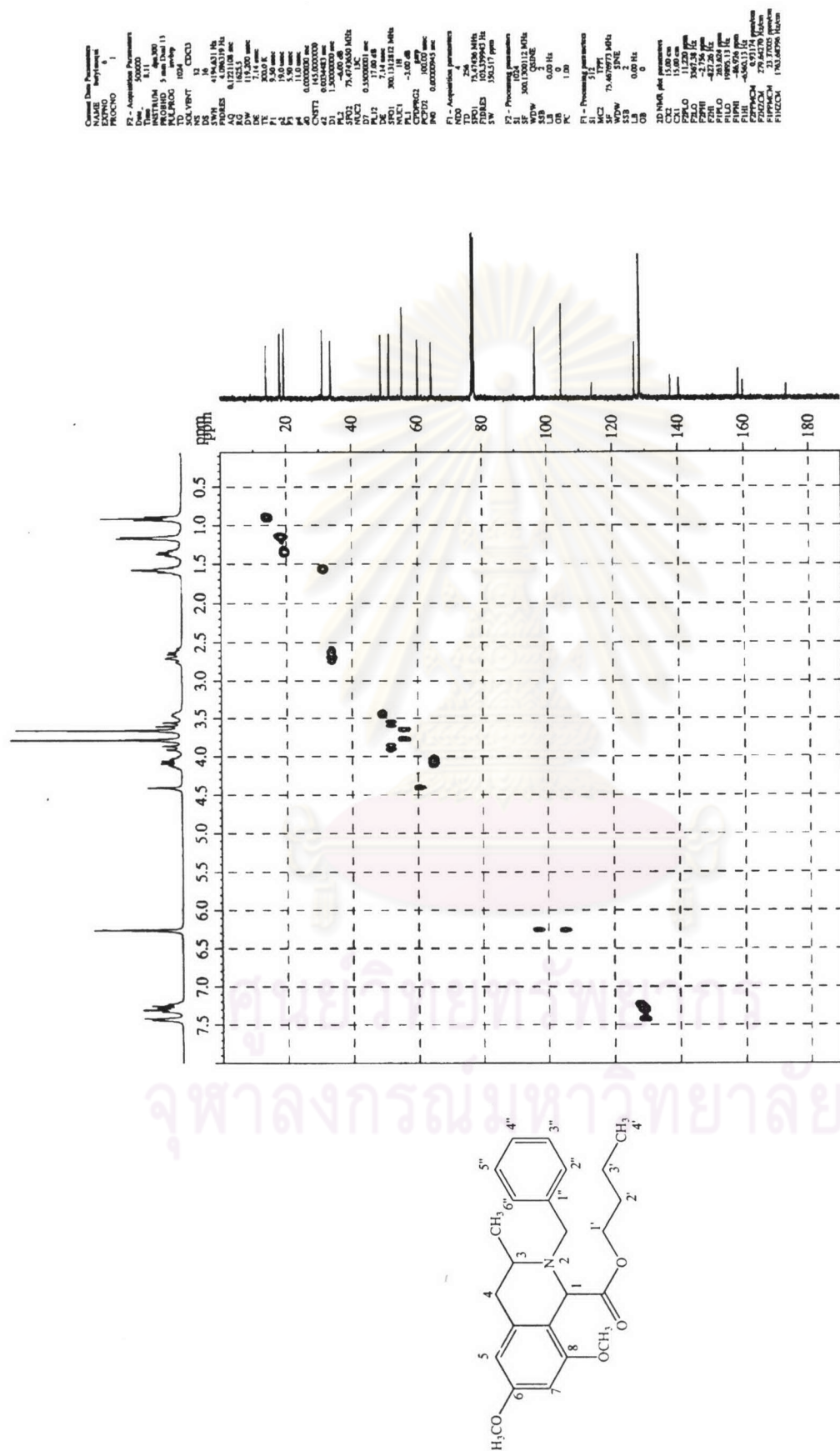


Figure S2 The 300 MHz HMQC spectrum of butyl-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10)

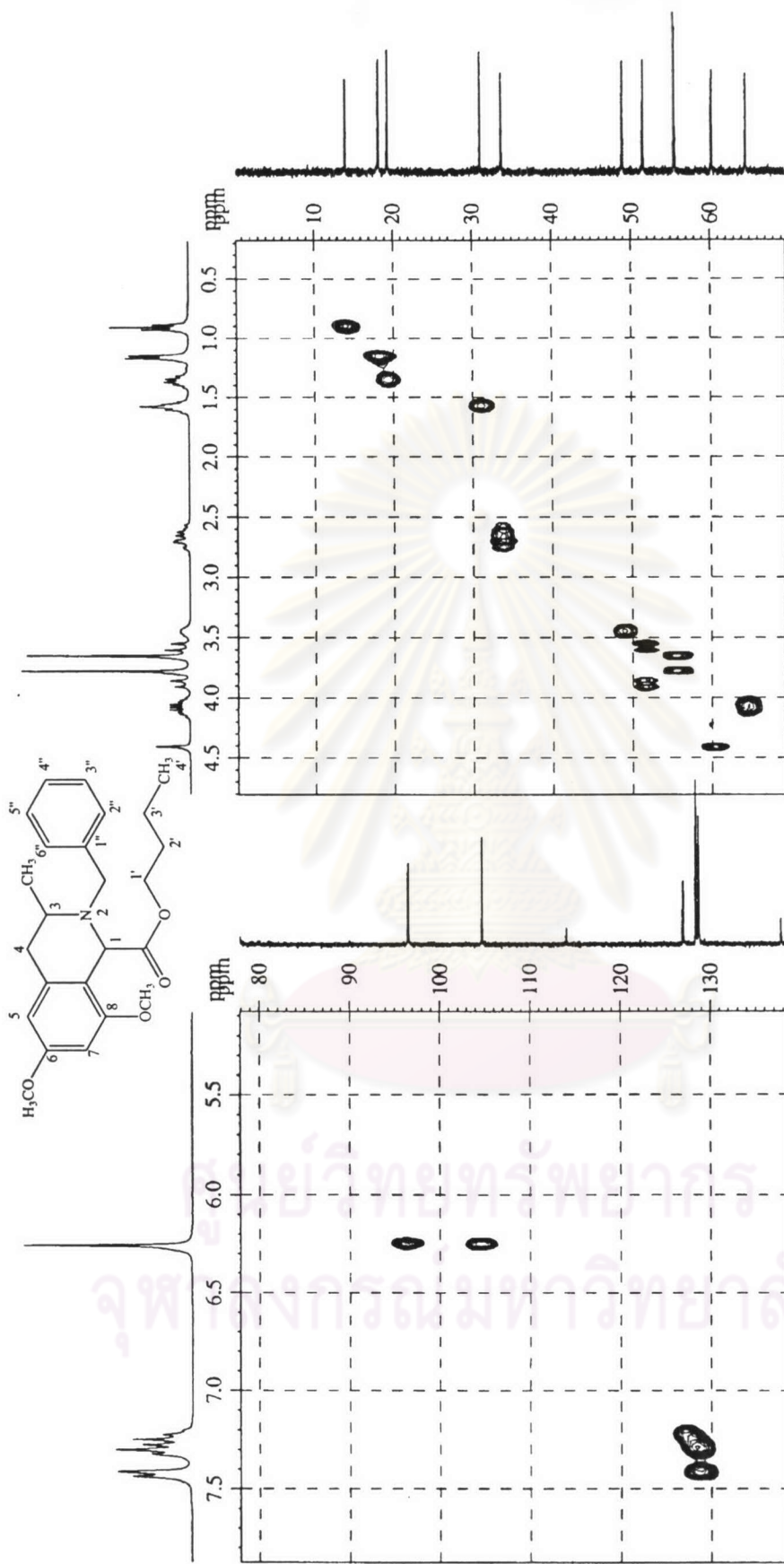


Figure 53 The 300 MHz HMQC spectrum of butyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-19-10) (Enlarged scale)

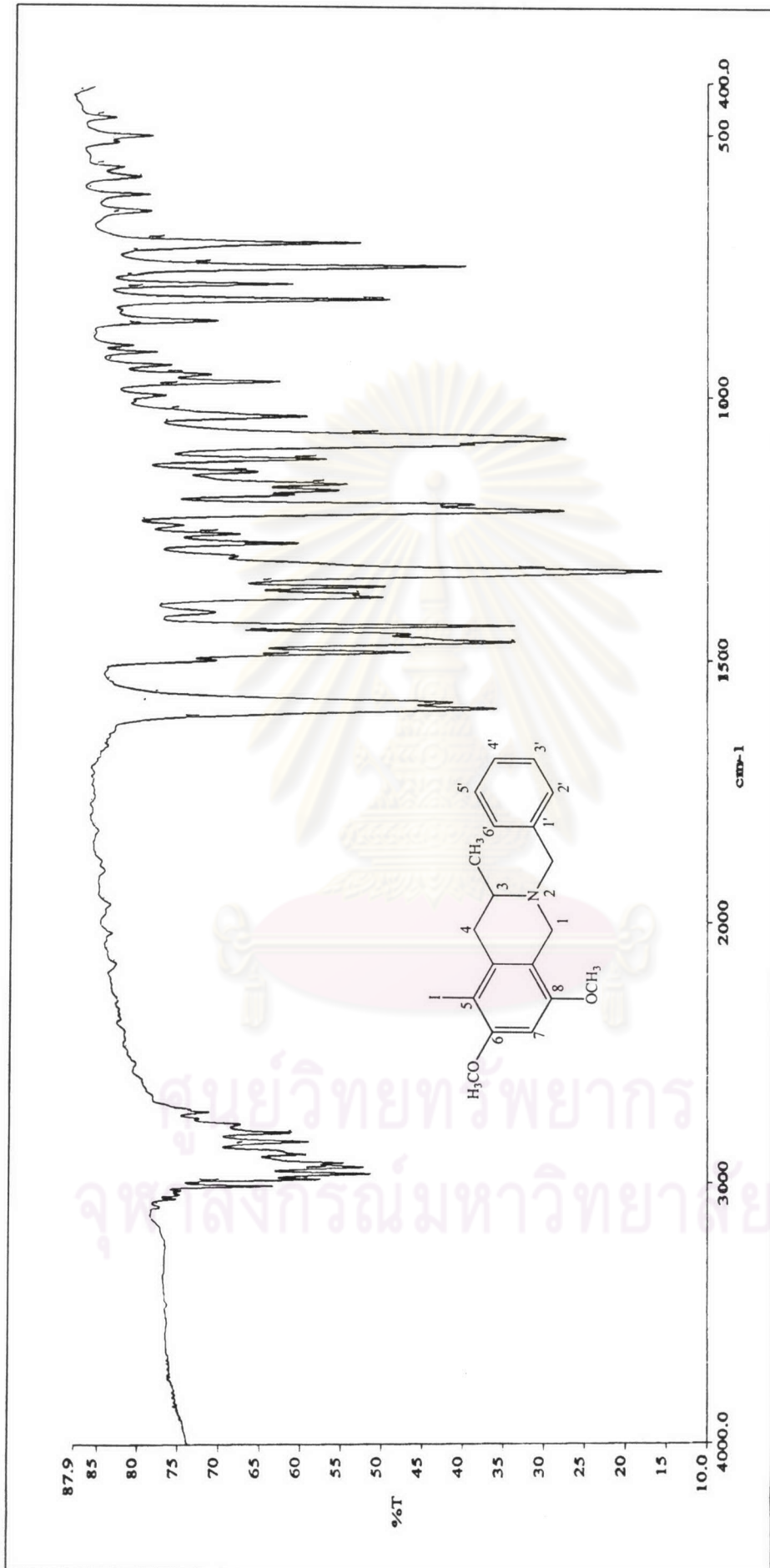


Figure 54 The IR spectrum (KBr) of 5-Iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01)

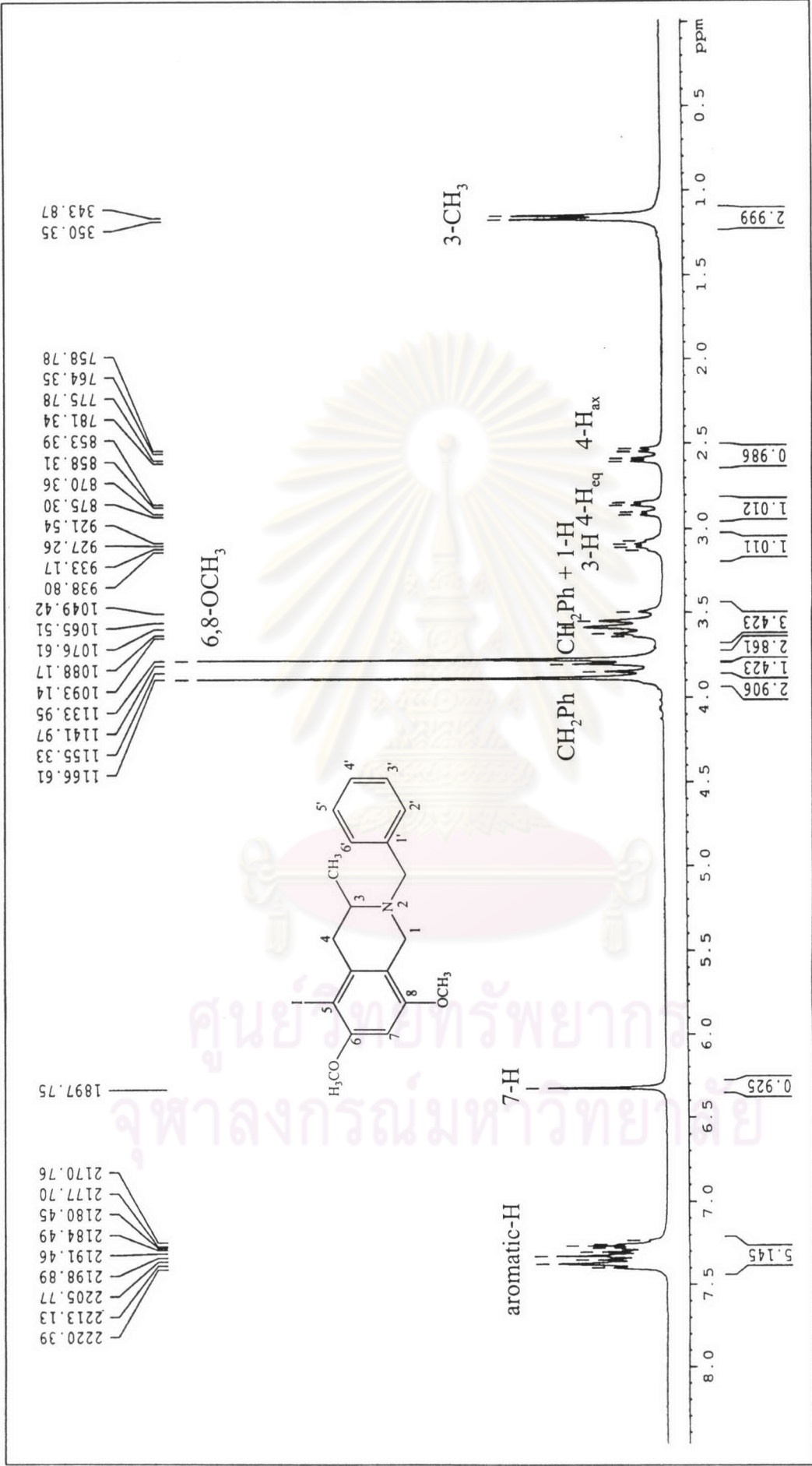


Figure S5 The 300 MHz <sup>1</sup>H-NMR spectrum of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01)

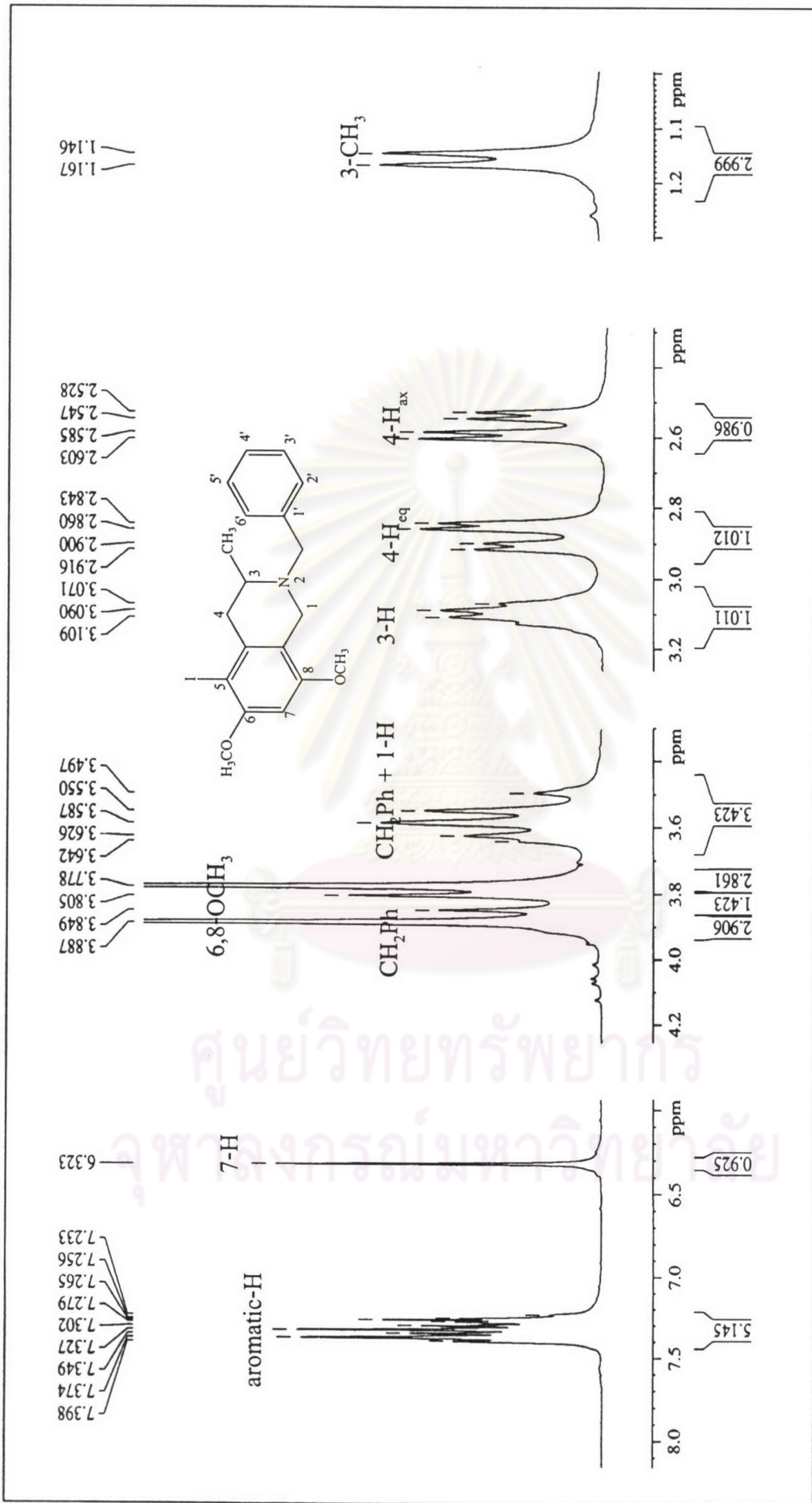


Figure 56 The 300 MHz <sup>1</sup>H-NMR spectrum of 5-iodo-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-20-01) (Enlarged scale)

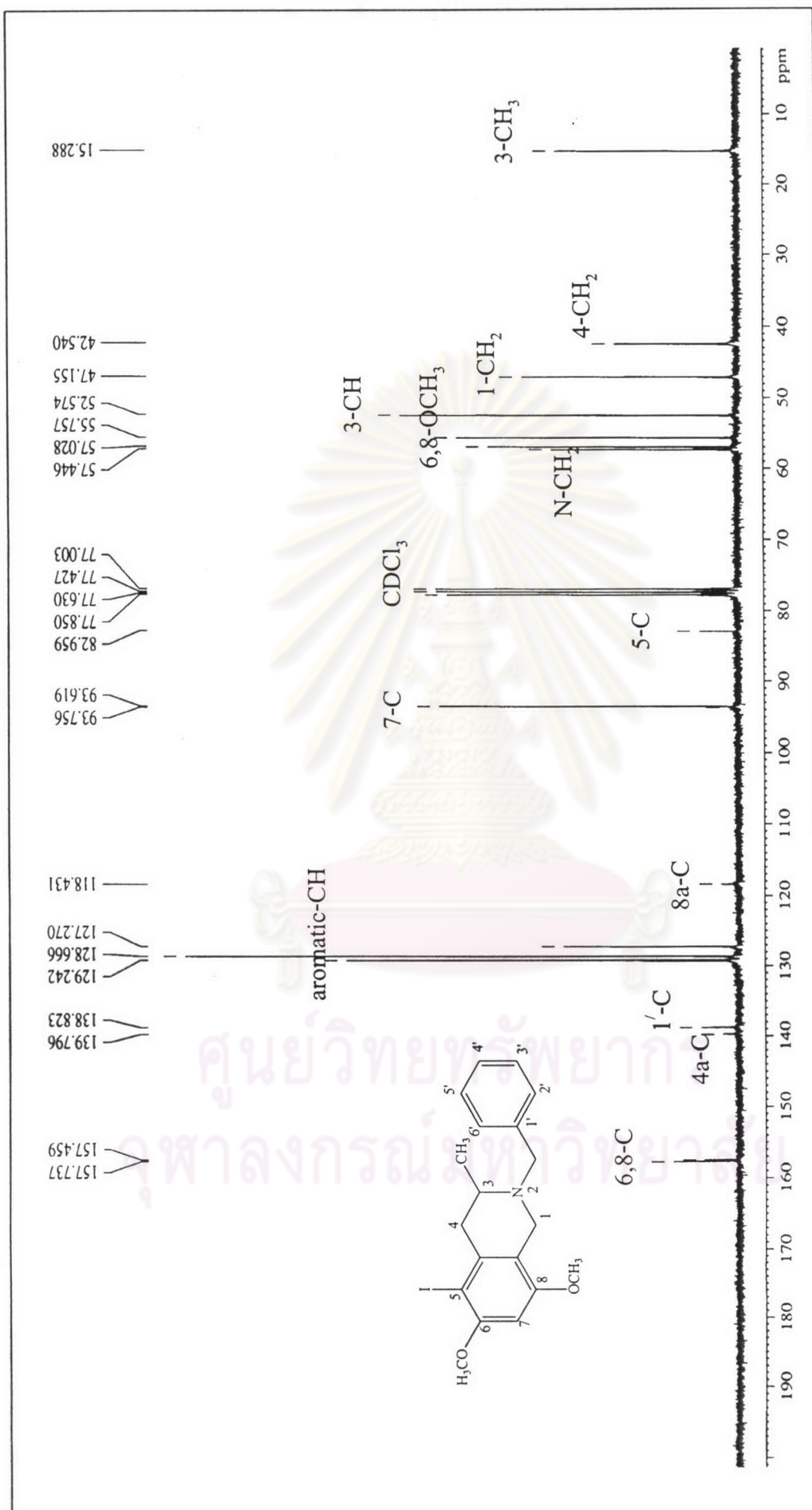


Figure 57 The 75 MHz <sup>13</sup>C-NMR spectrum of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01)

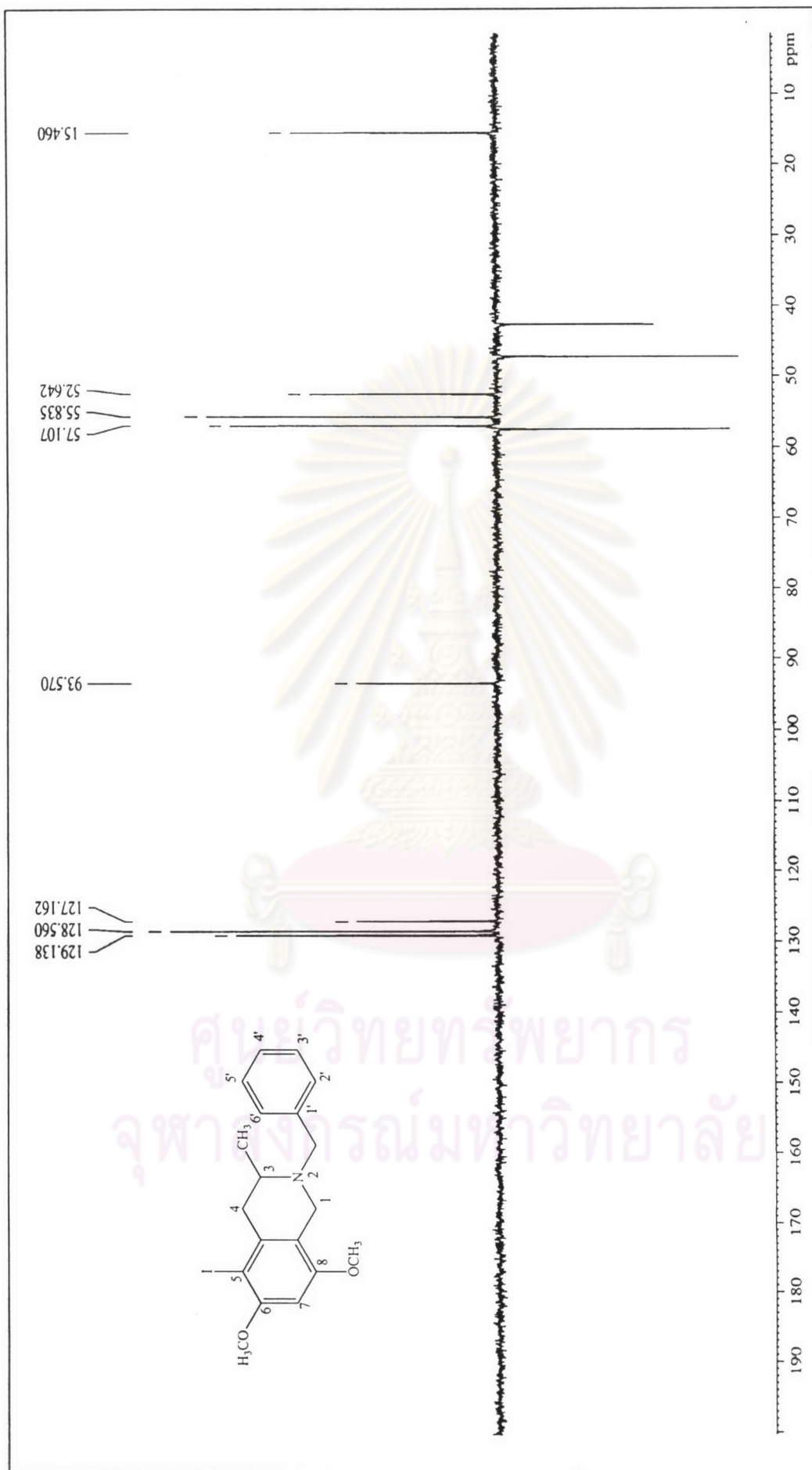


Figure 58 The 75 MHz DEPT 135 spectrum of 5-iodo-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-20-01)



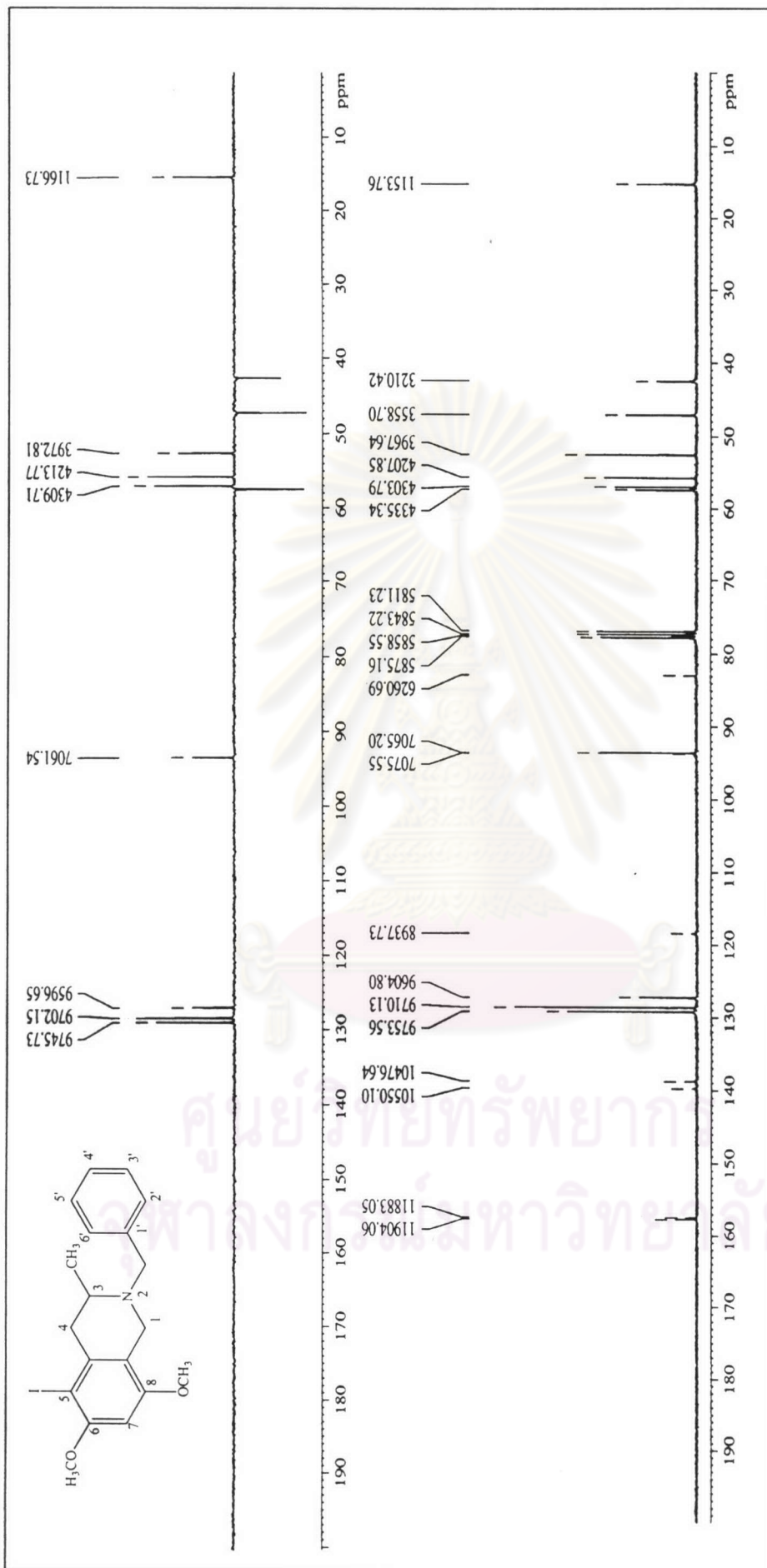


Figure 59 The 75 MHz DEPT 135 and <sup>13</sup>C-NMR spectrum comparison of 5-iodo-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline

(CU-20-01)



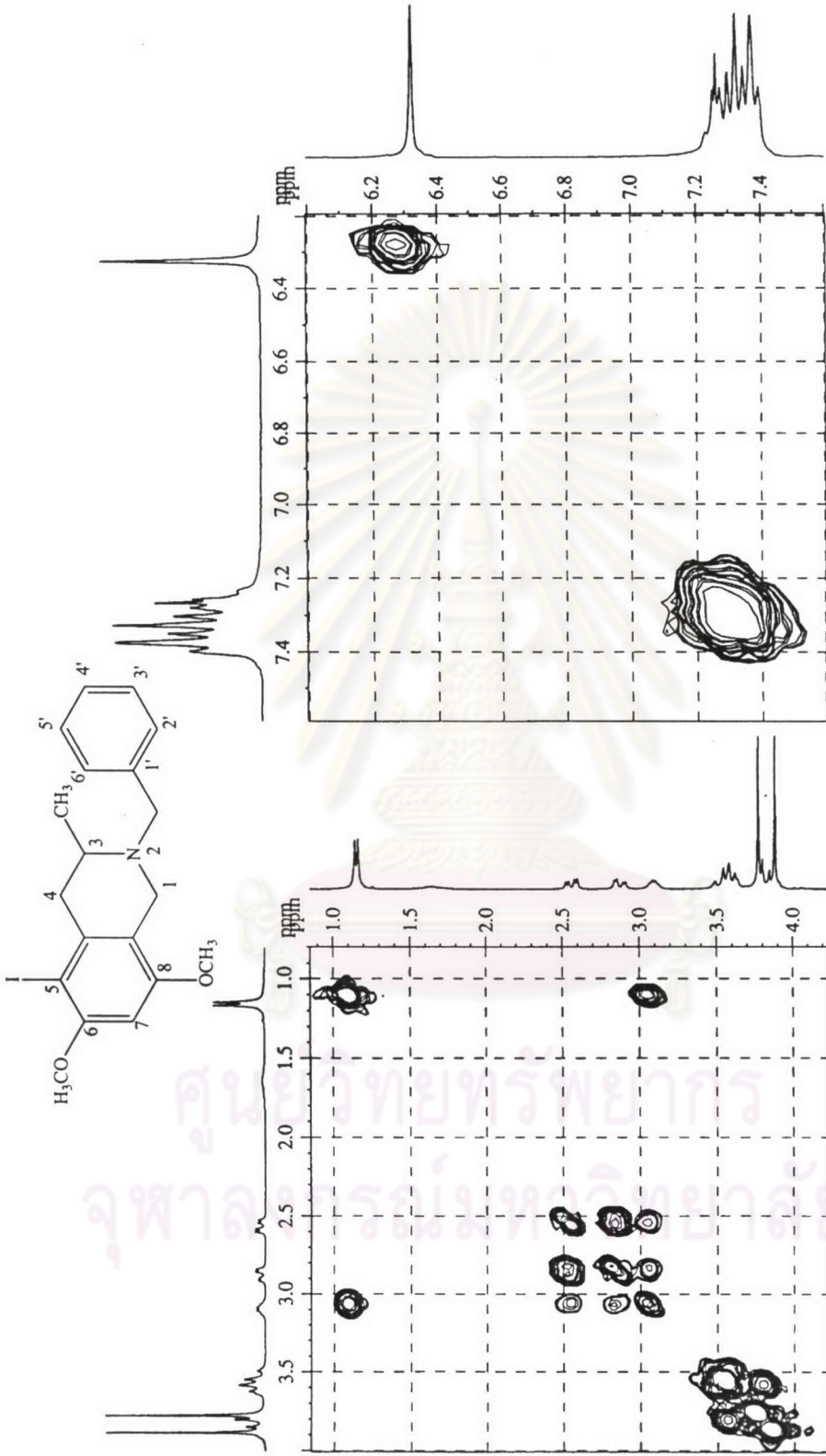


Figure 61 The 300 MHz HH COSY spectrum of 5-iodo-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-20-01) (Enlarged scale)

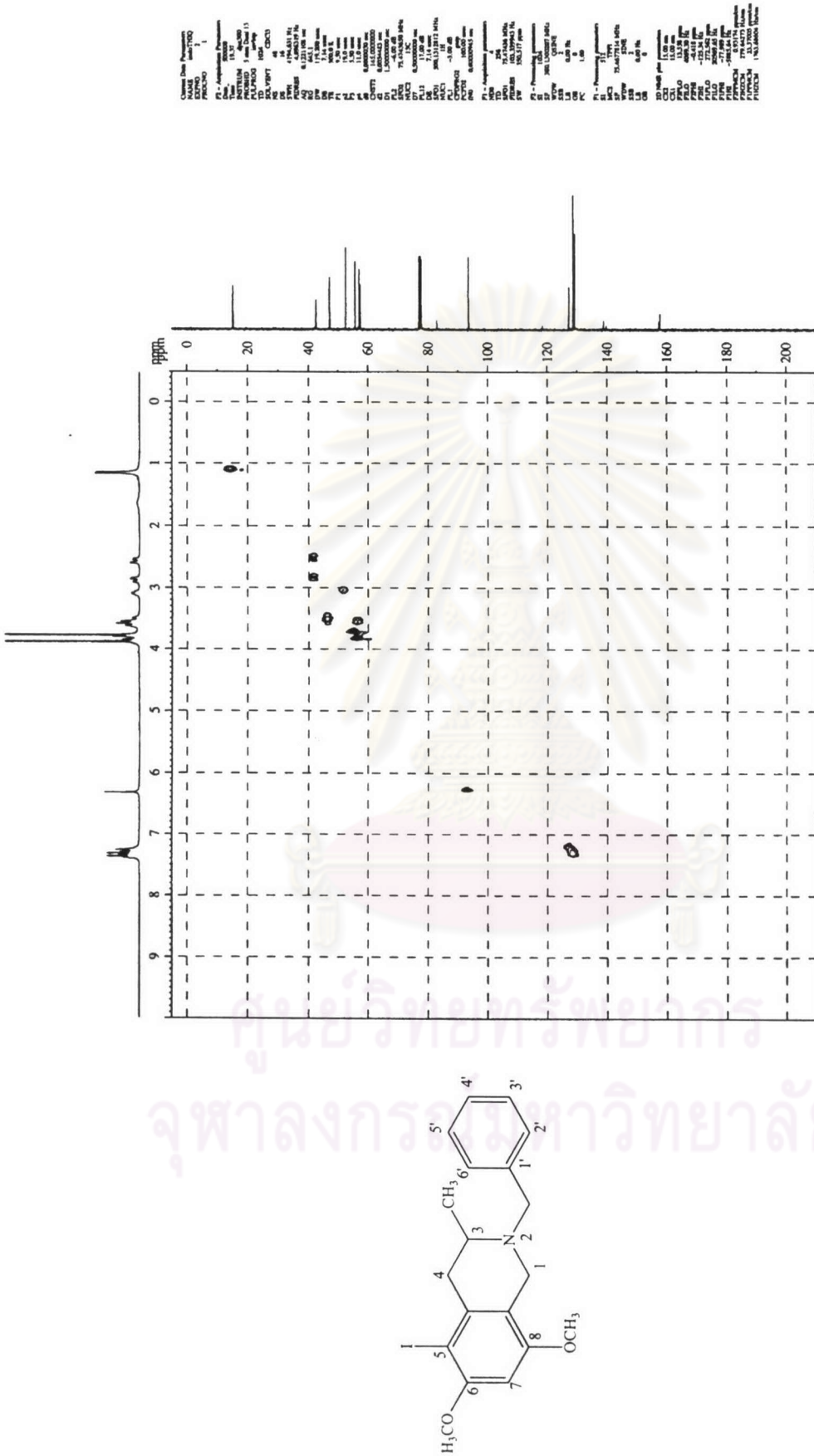


Figure 62 The 300 MHz HMQC spectrum of 5-iodo-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-20-01)

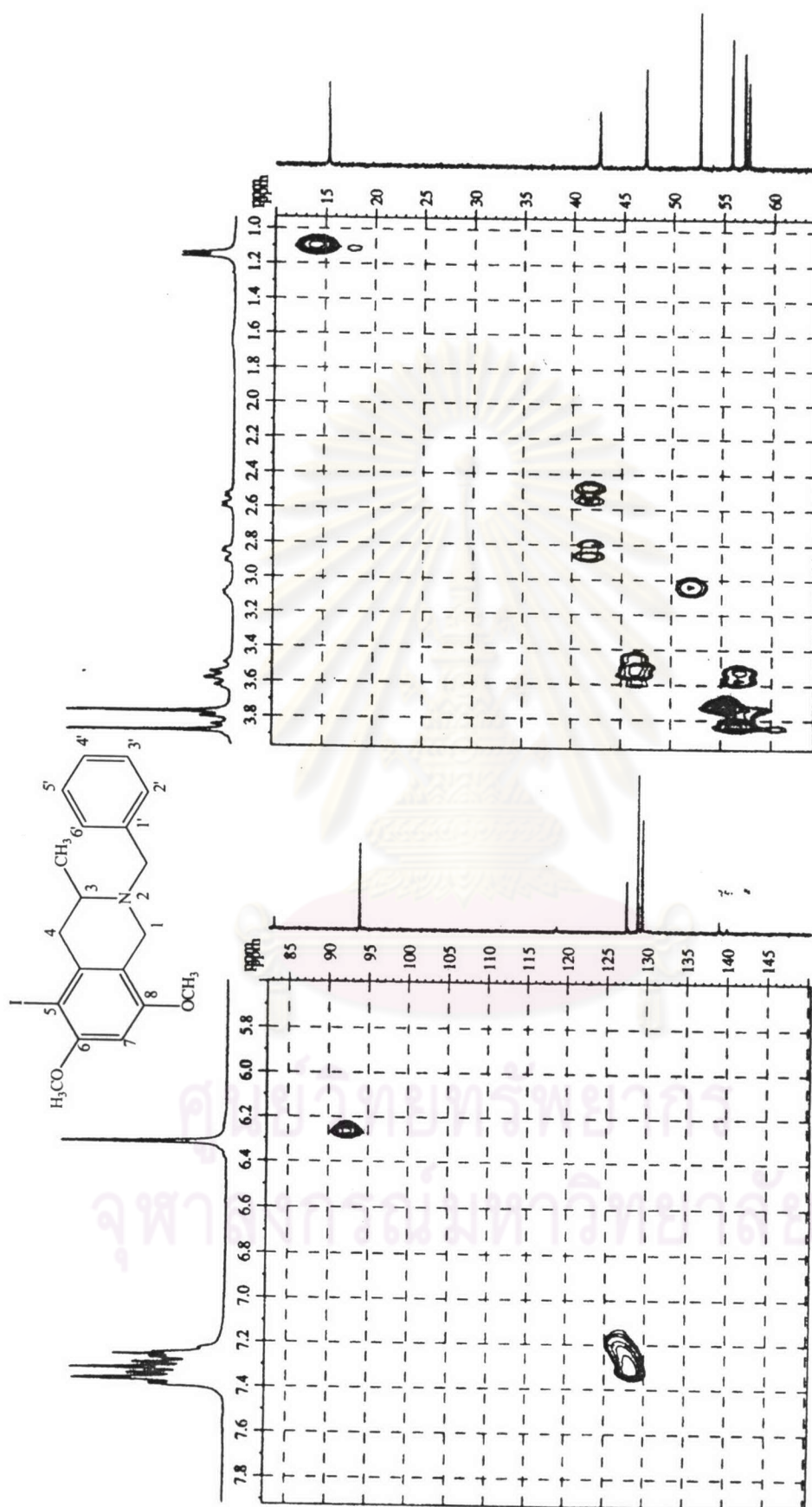


Figure 63 The 300 MHz HMQC spectrum of 5-iodo-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-20-01) (Enlarged scale)

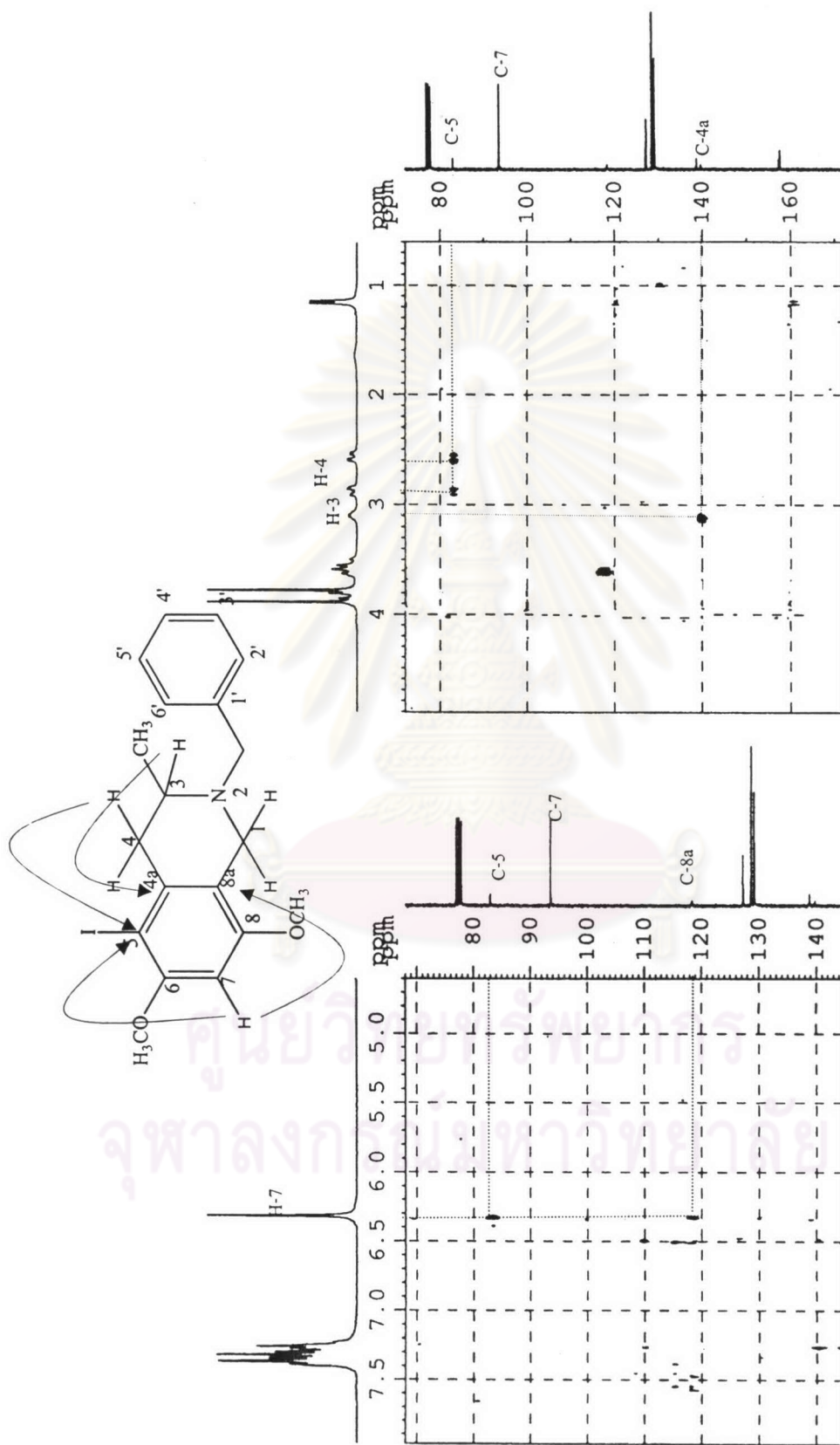


Figure 64 The 300 MHz HMBC spectrum of 5-iodo-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-20-01) (Enlarged scale)

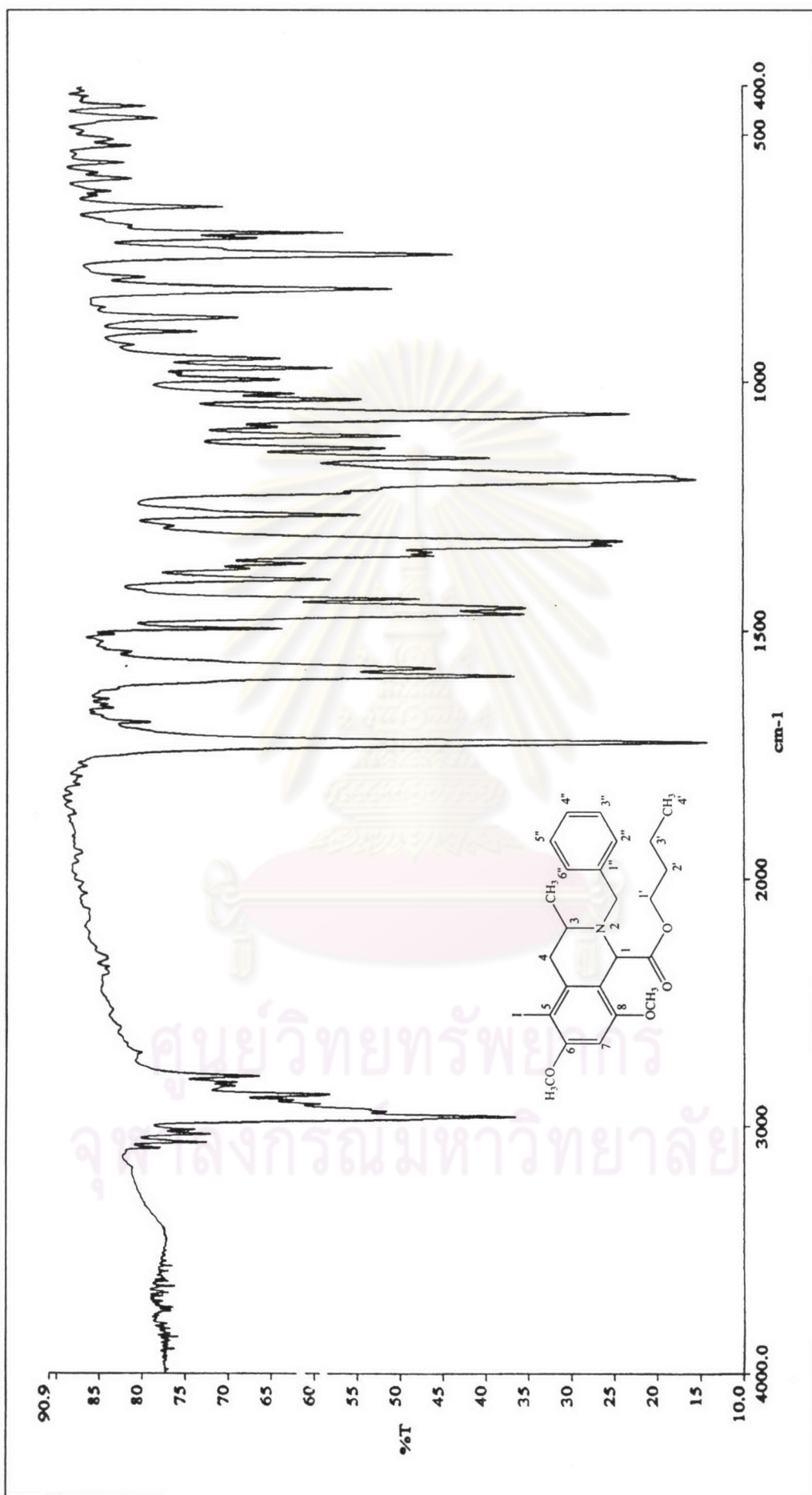


Figure 65 The IR spectrum (KBr) of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-20-02)

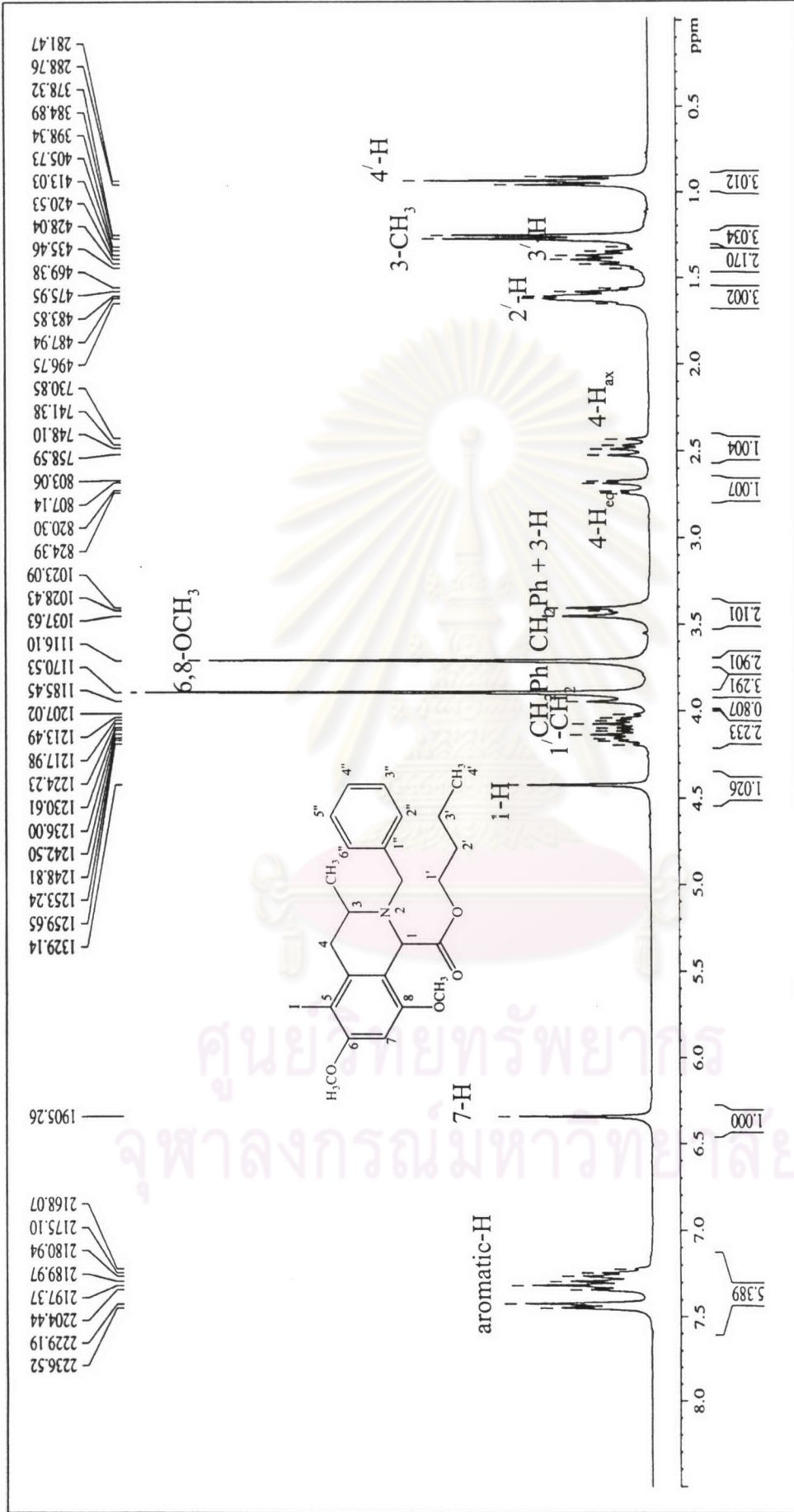


Figure 66 The 300 MHz <sup>1</sup>H-NMR spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate

(CU-20-02)



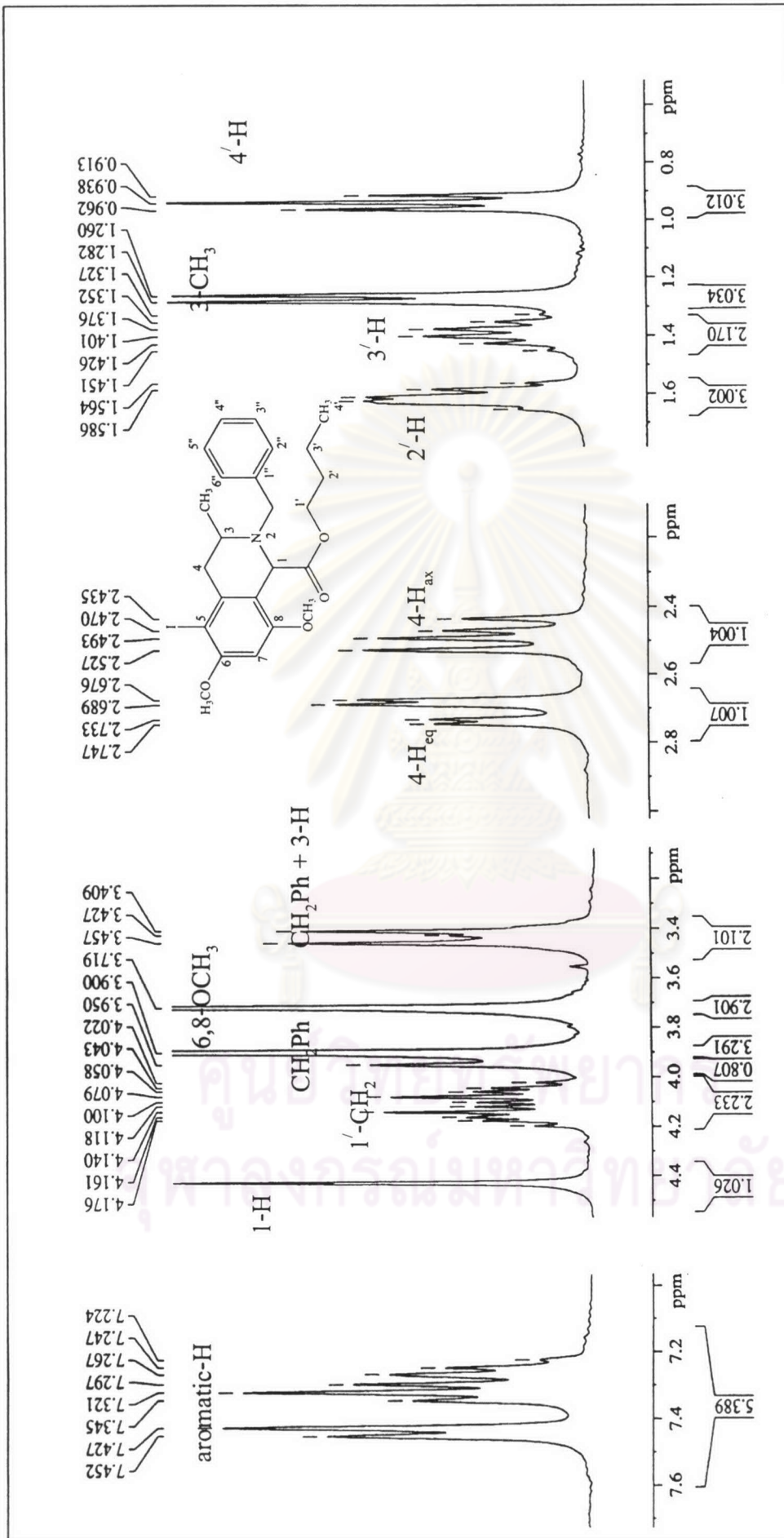


Figure 67 The 300 MHz <sup>1</sup>H-NMR spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-20-02) (Enlarged scale)

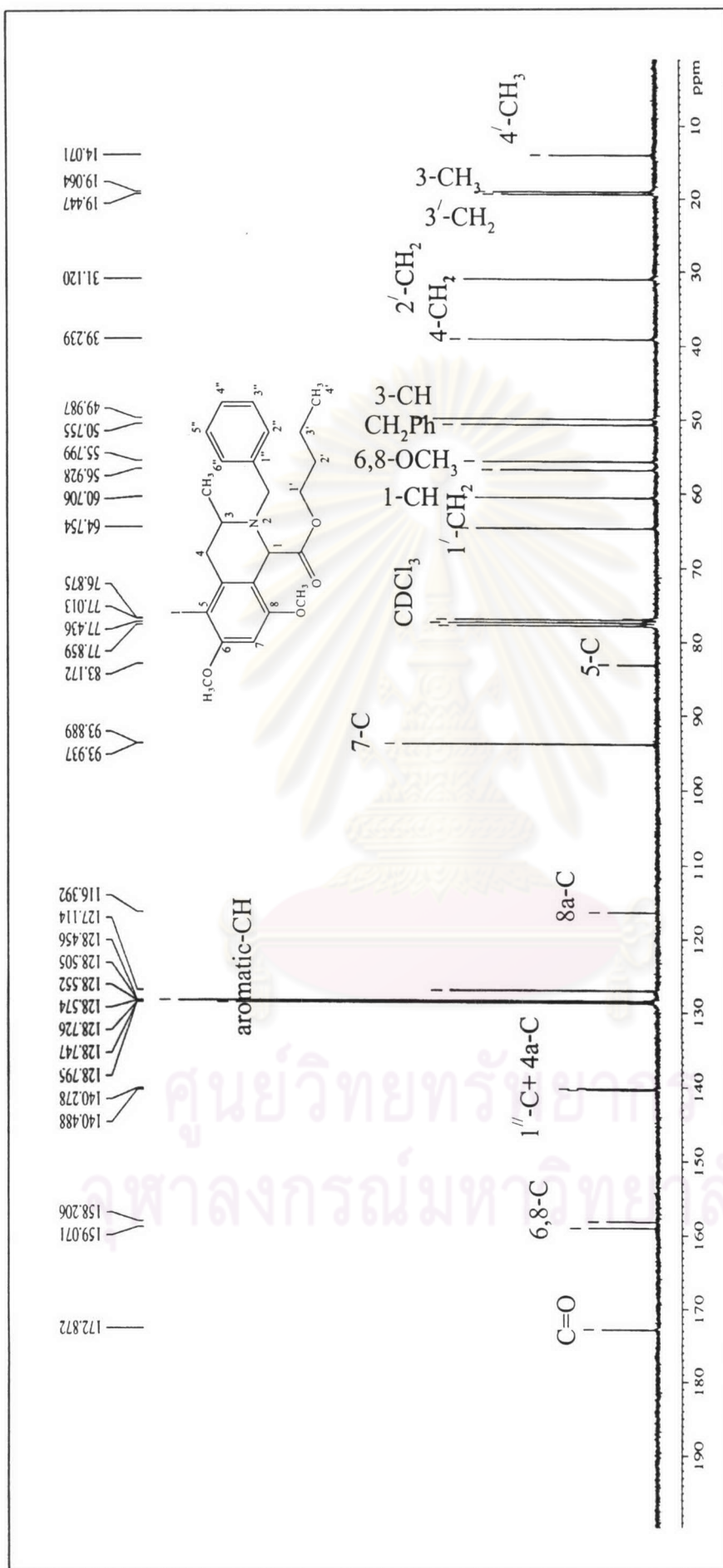


Figure 68 The 75 MHz <sup>13</sup>C-NMR spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate

(CU-20-02)

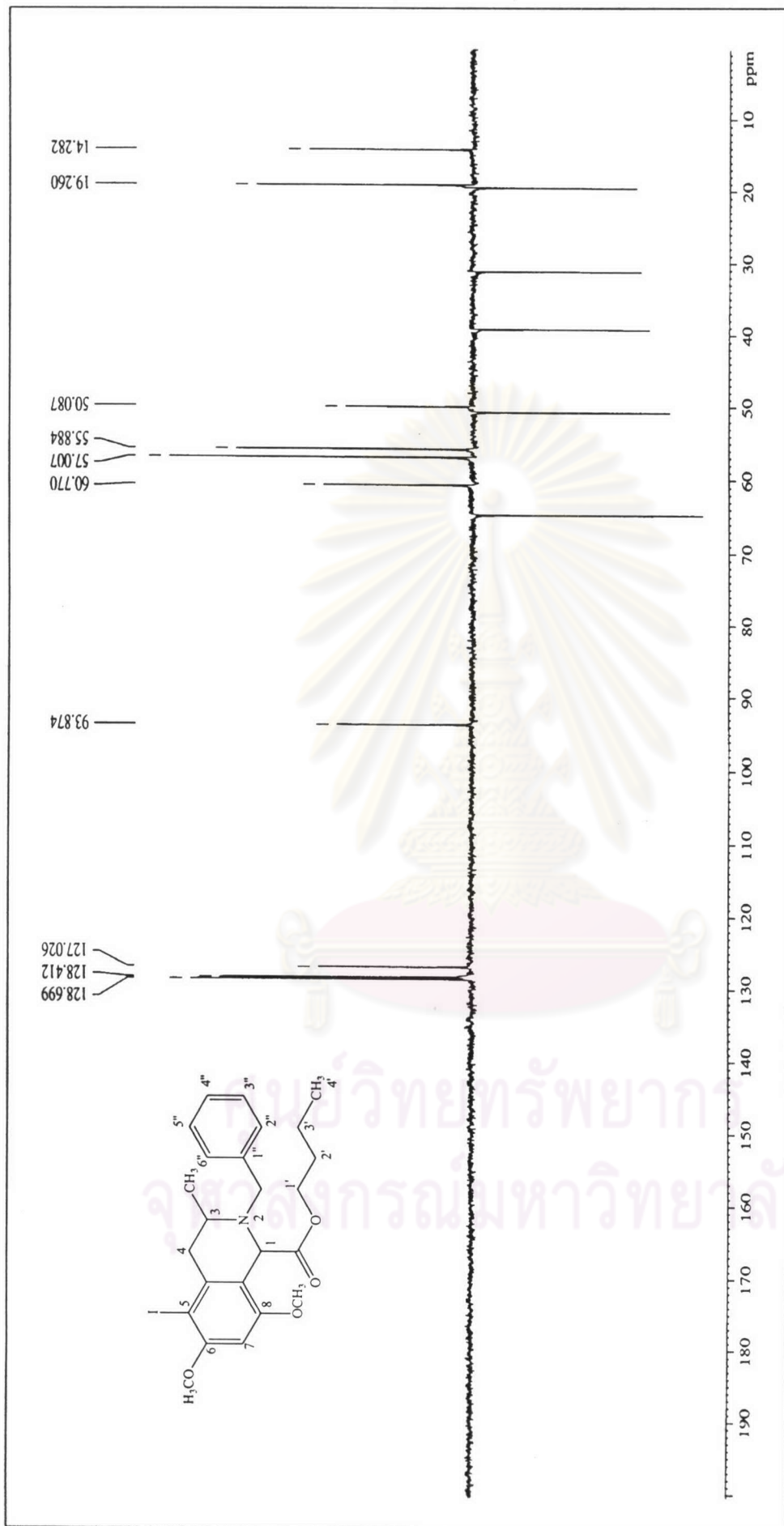


Figure 69 The 75 MHz DEPT 135 spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate

(CU-20-02)

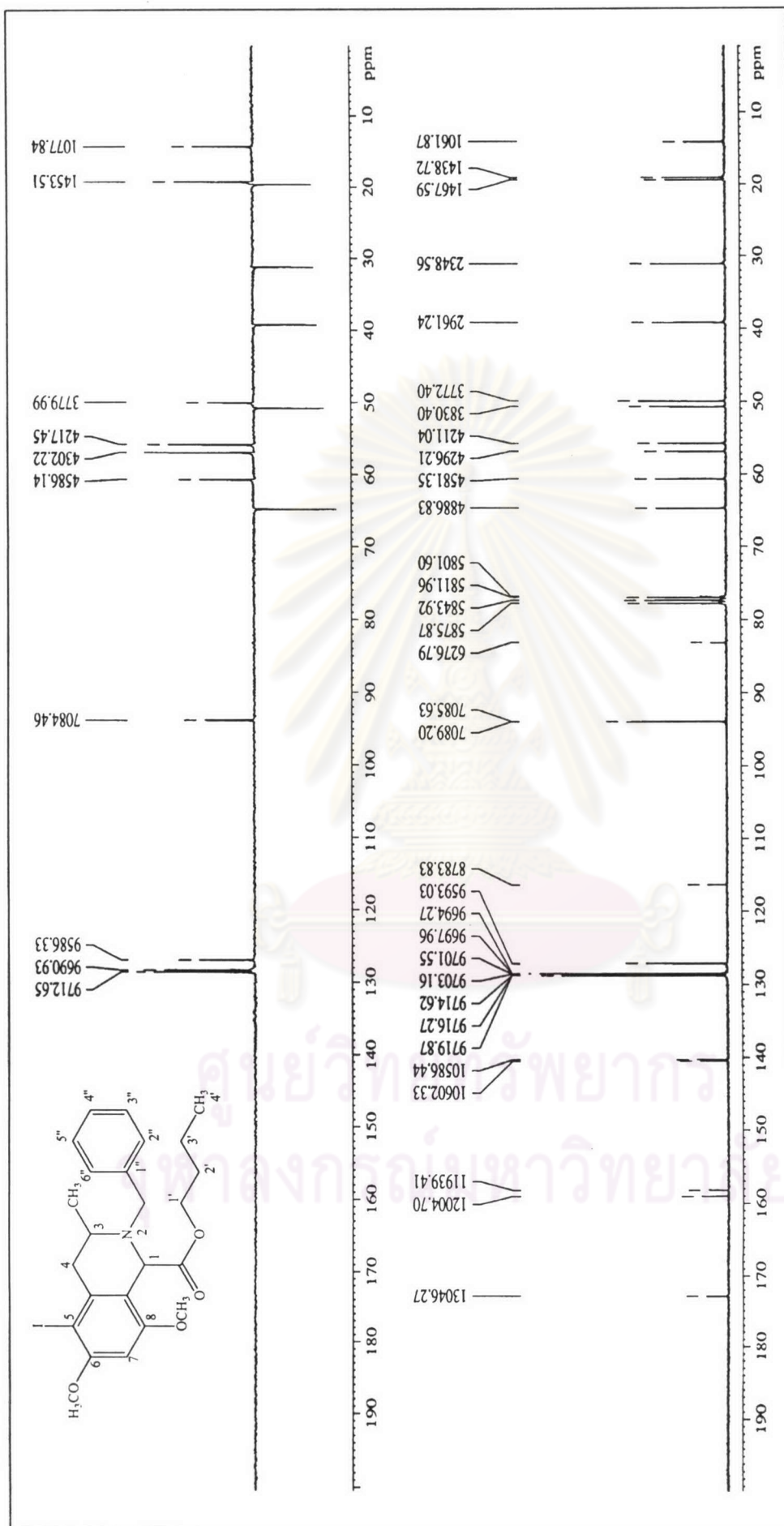


Figure 70 The 75 MHz DEPT 135 and <sup>13</sup>C-NMR spectrum comparison of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-20-02)

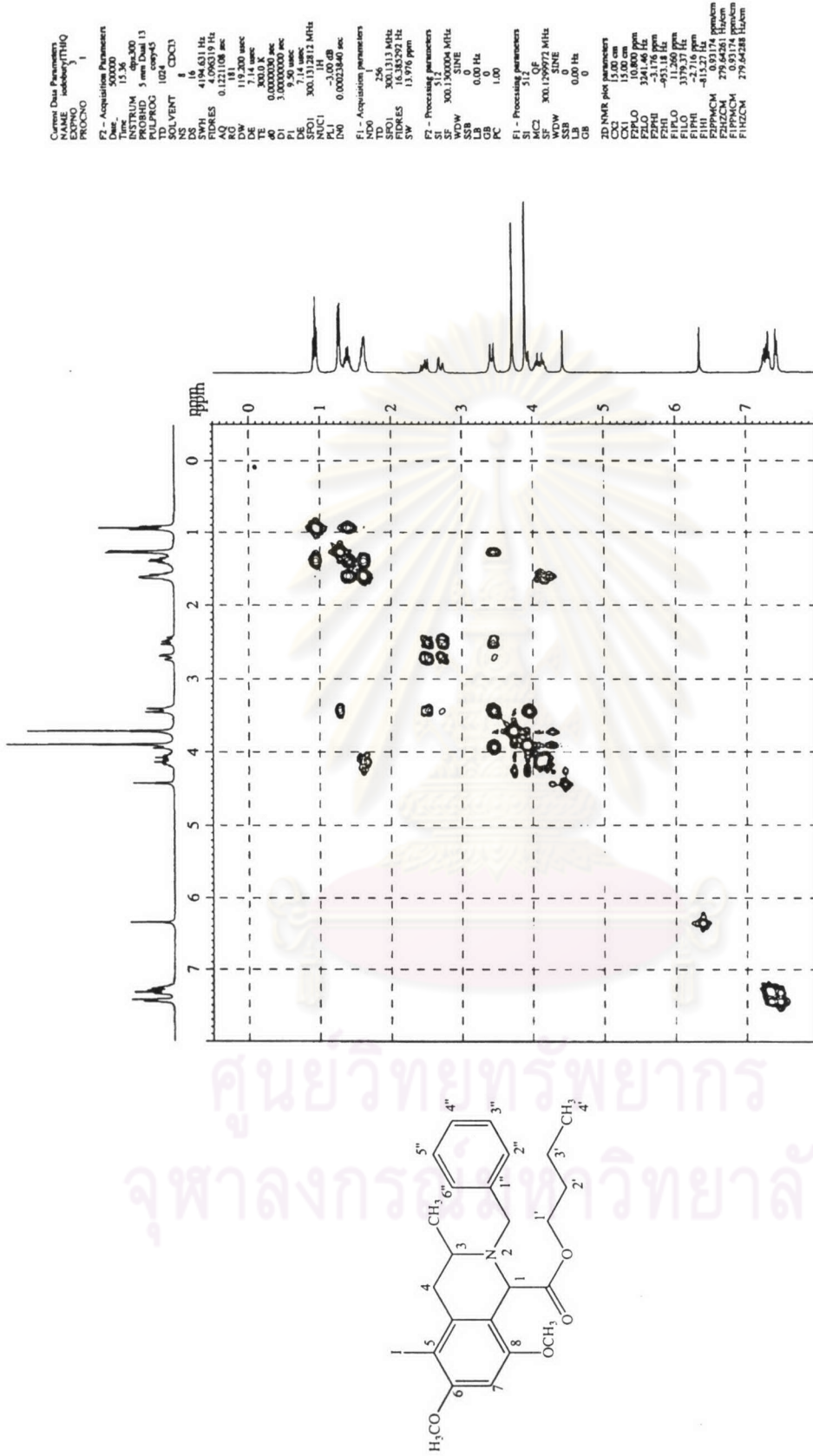


Figure 71 The 300 MHz <sup>1</sup>H-<sup>1</sup>H COSY spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline-1-carboxylate

(CU-20-02)

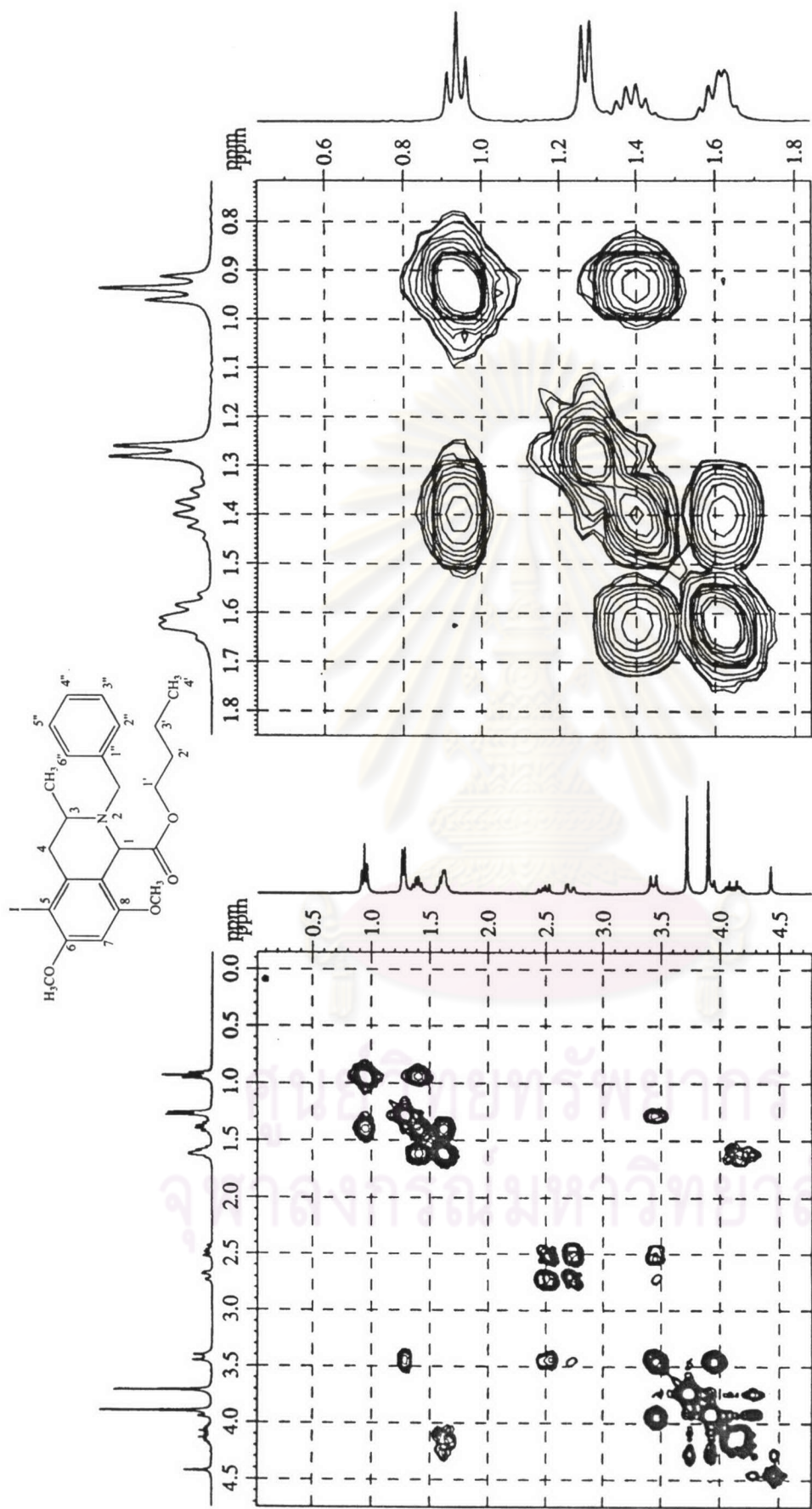


Figure 72 The 300 MHz <sup>1</sup>H-<sup>1</sup>H COSY spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-20-02) (Enlarged scale)

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DE           7.14 nsec
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P2           19.0 nsec
P3           11.0 nsec
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D1           1.50000000 sec
PL1         -6.00 dB
SFO2         75.4743000 MHz
D2           0.50000000 sec
PL2         17.00 dB
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ZD NMR job parameters
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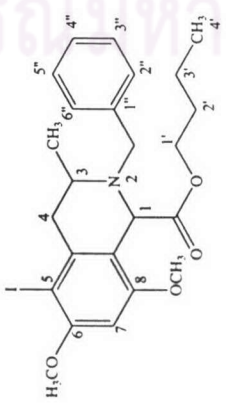
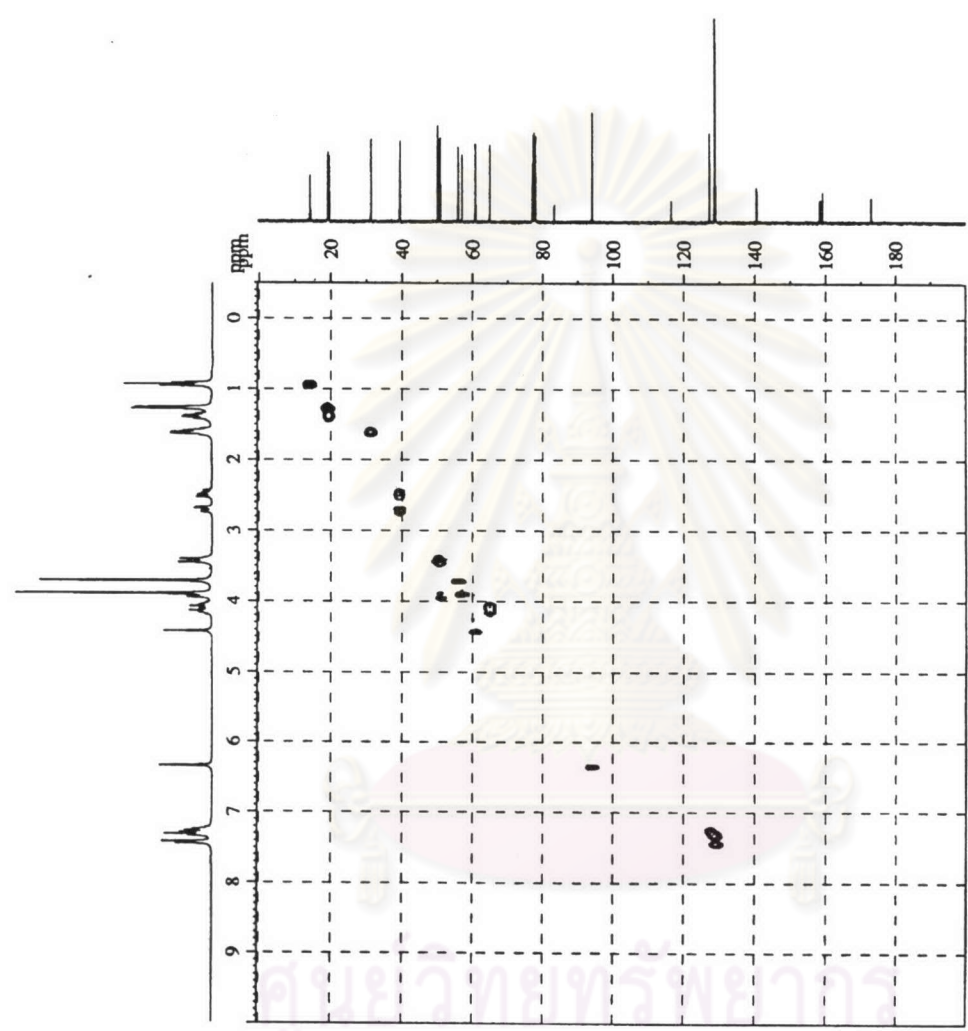


Figure 73 The 300 MHz <sup>1</sup>H NMR spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-

20-02)

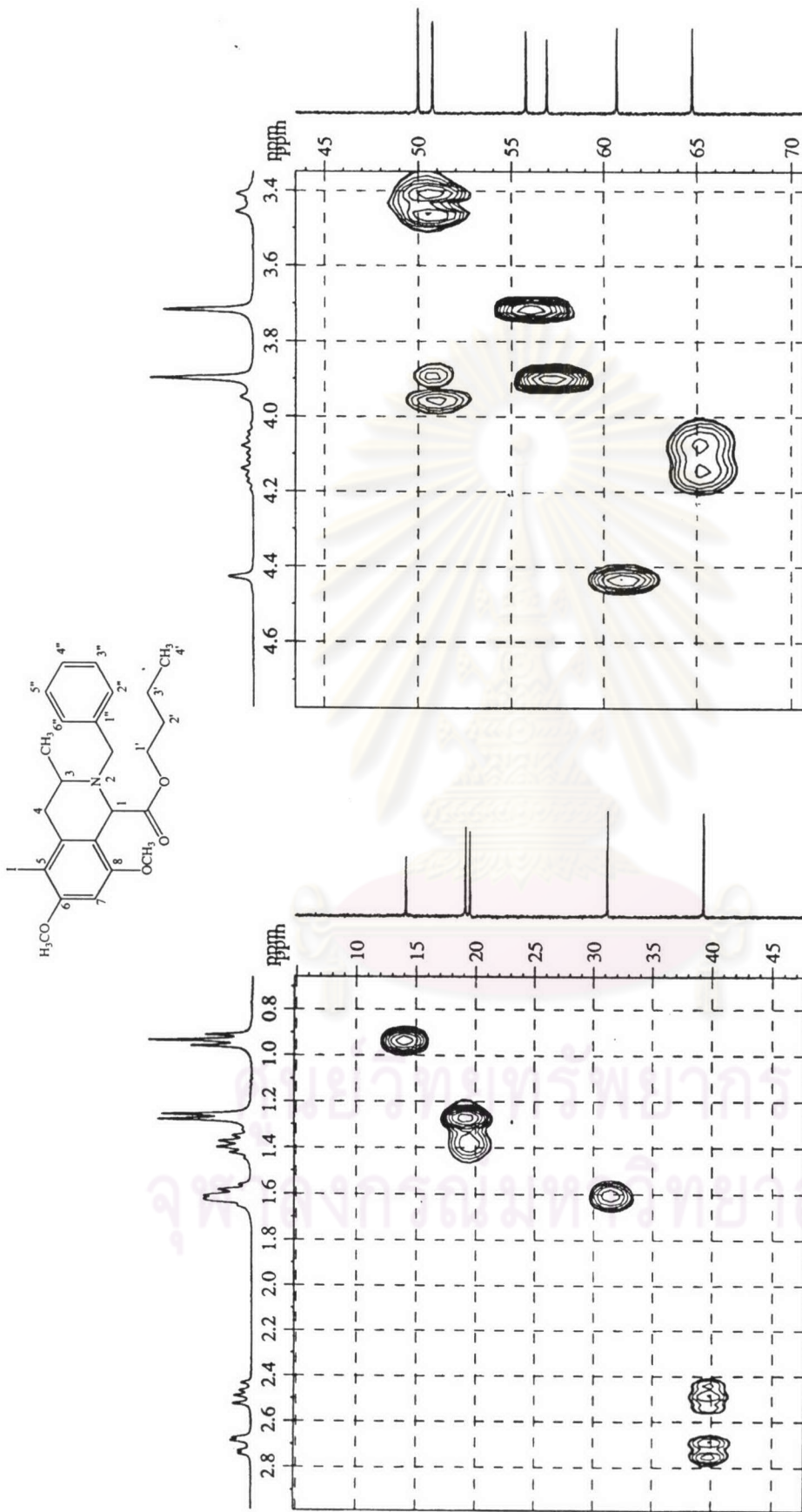


Figure 74 The 300 MHz HMQC spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-20-02) (Enlarged scale)



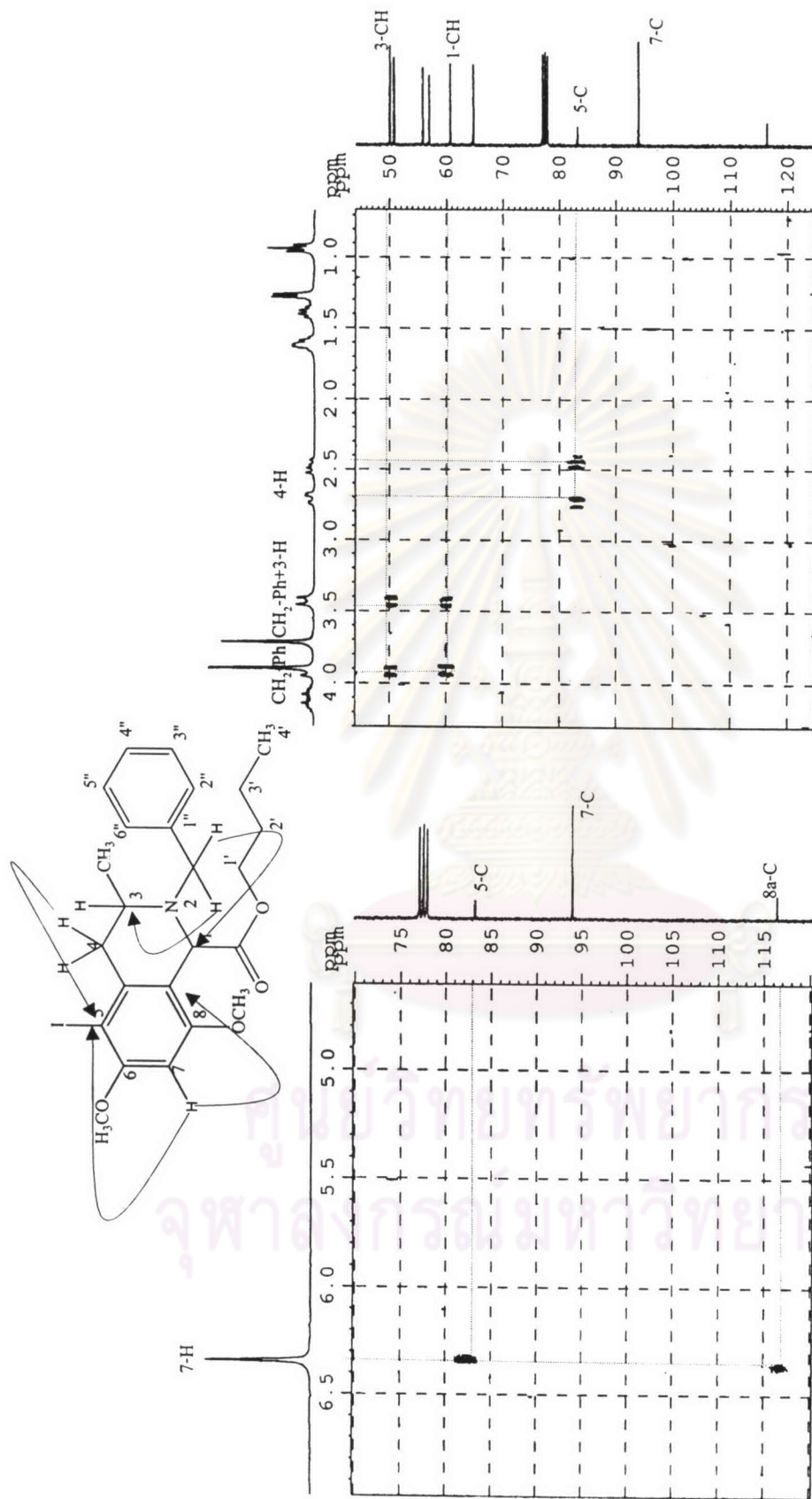


Figure 75 The 300 MHz HMBC spectrum of butyl-5-iodo-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-20-02) (Enlarged scale)

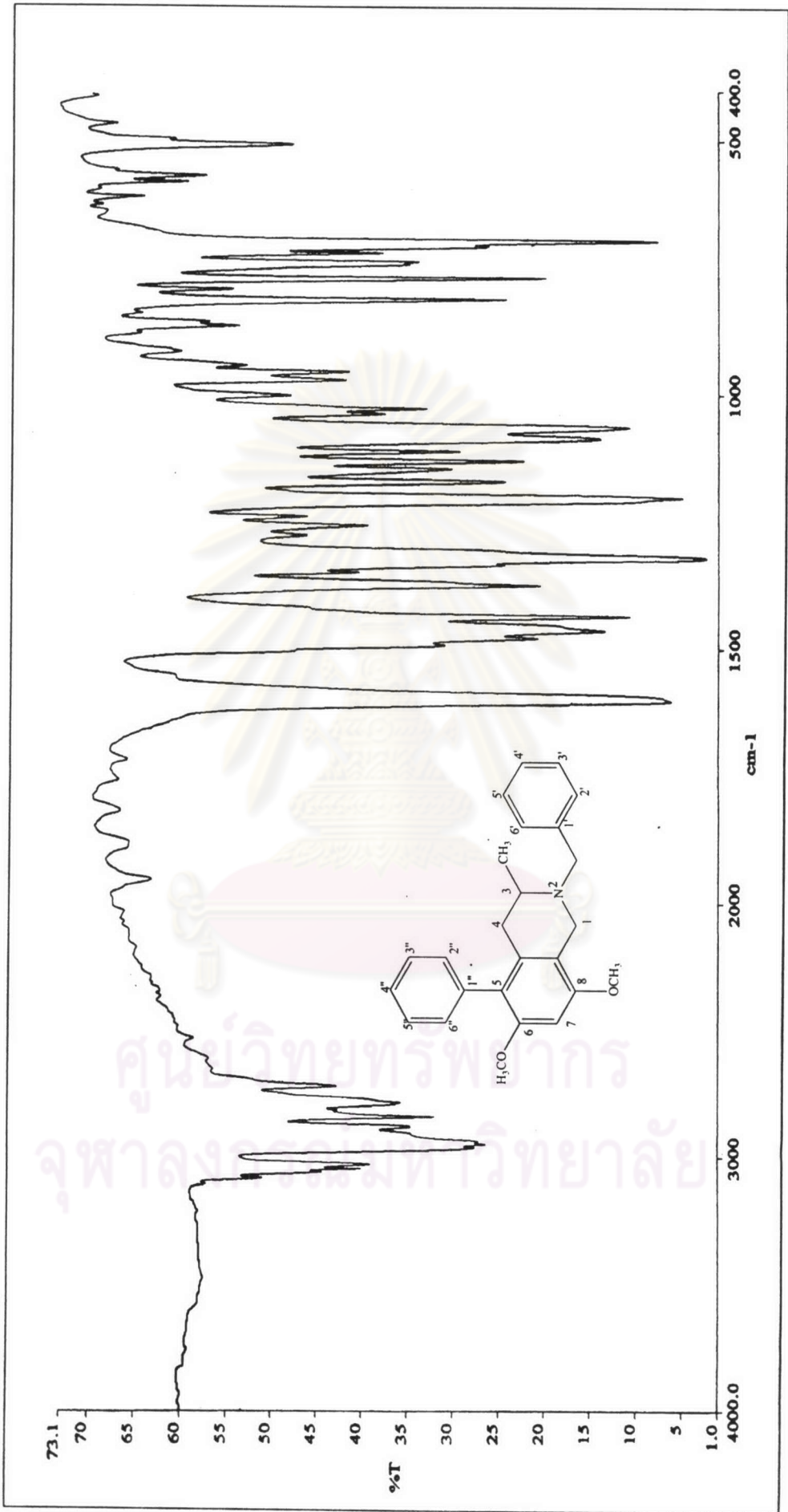


Figure 76 The IR spectrum (KBr) of 5-phenyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-01)

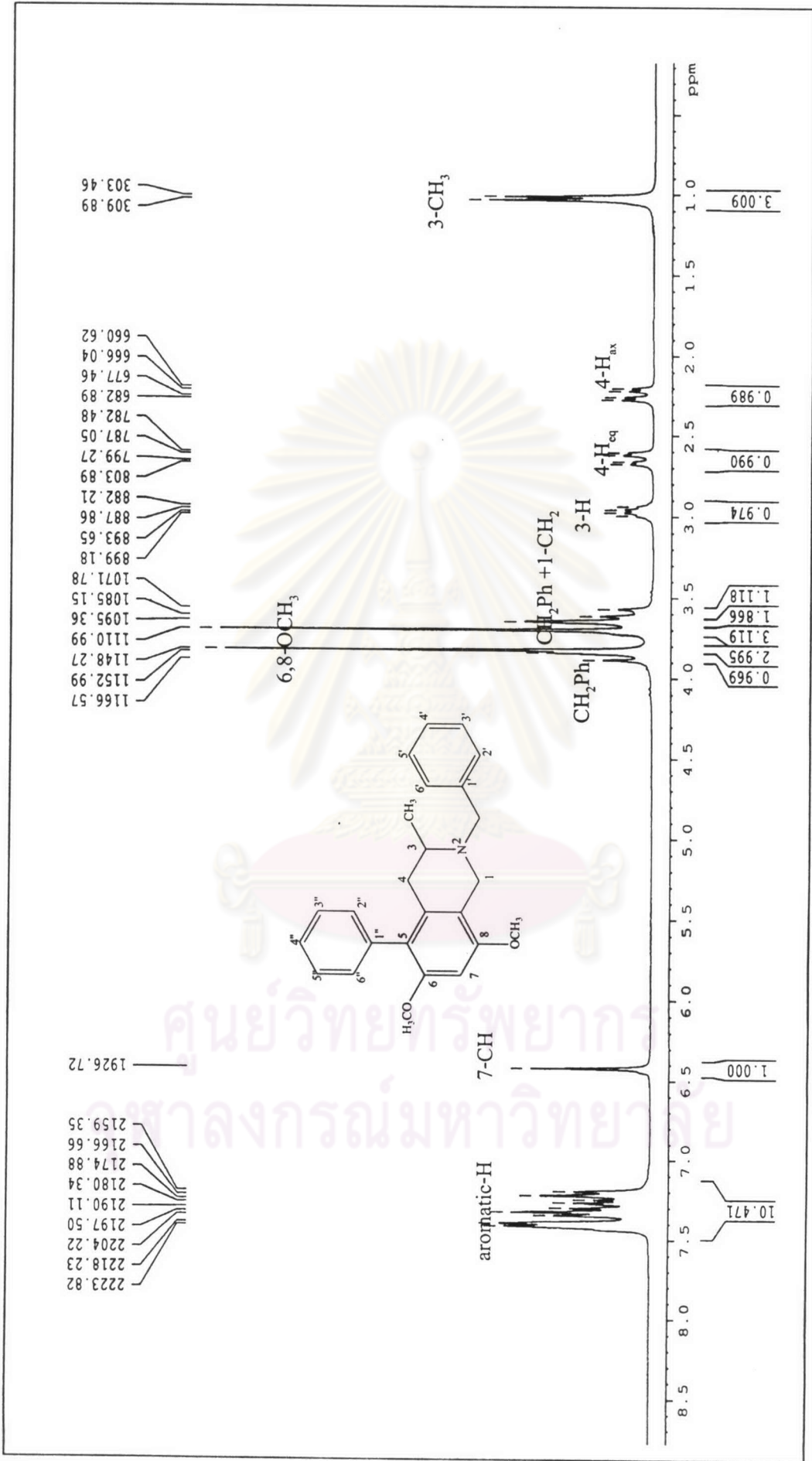


Figure 77 The 300 MHz <sup>1</sup>H-NMR spectrum of 5-phenyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-01)

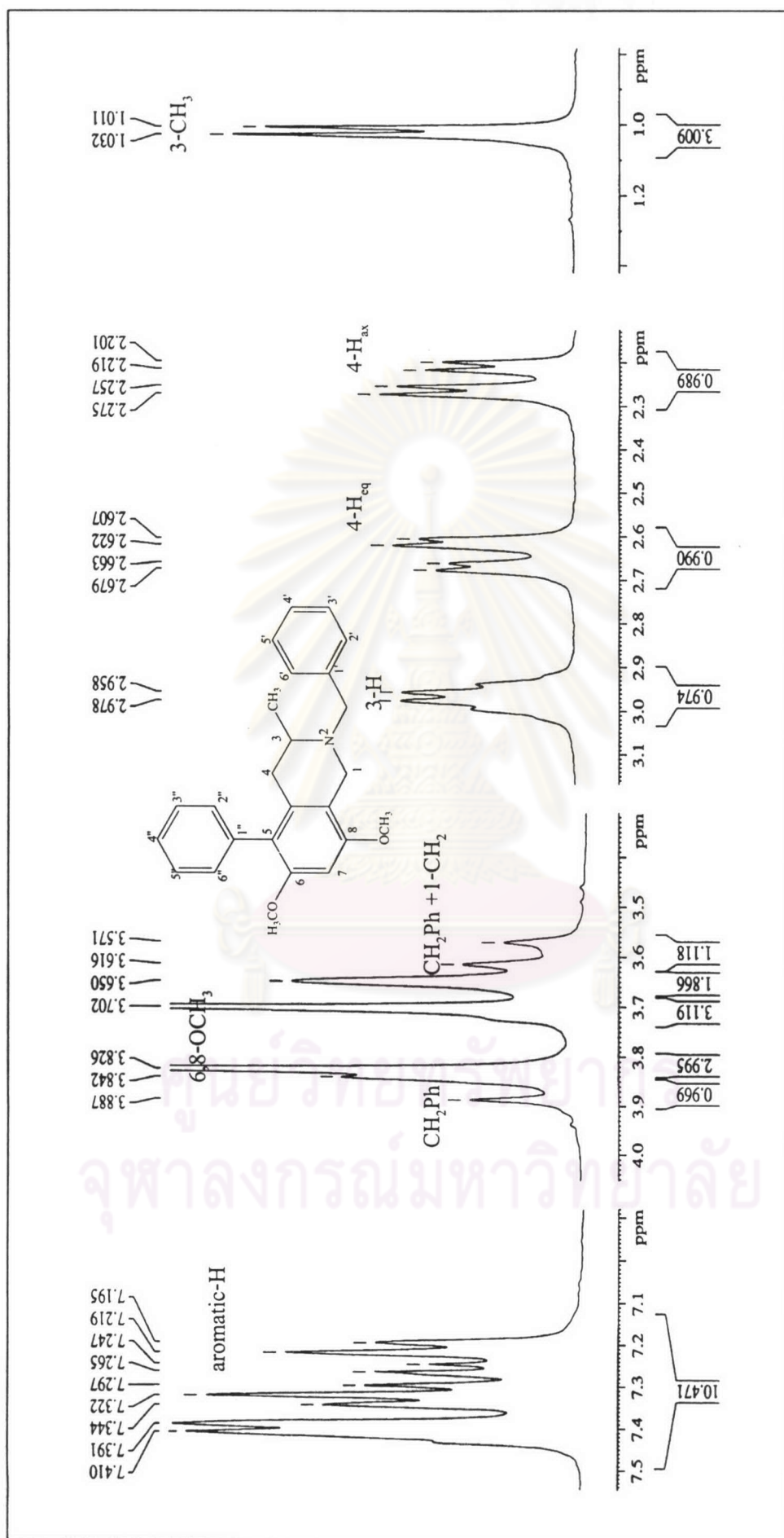


Figure 78 The 300 MHz <sup>1</sup>H-NMR spectrum of 5-phenyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-01)

(Enlarged scale)

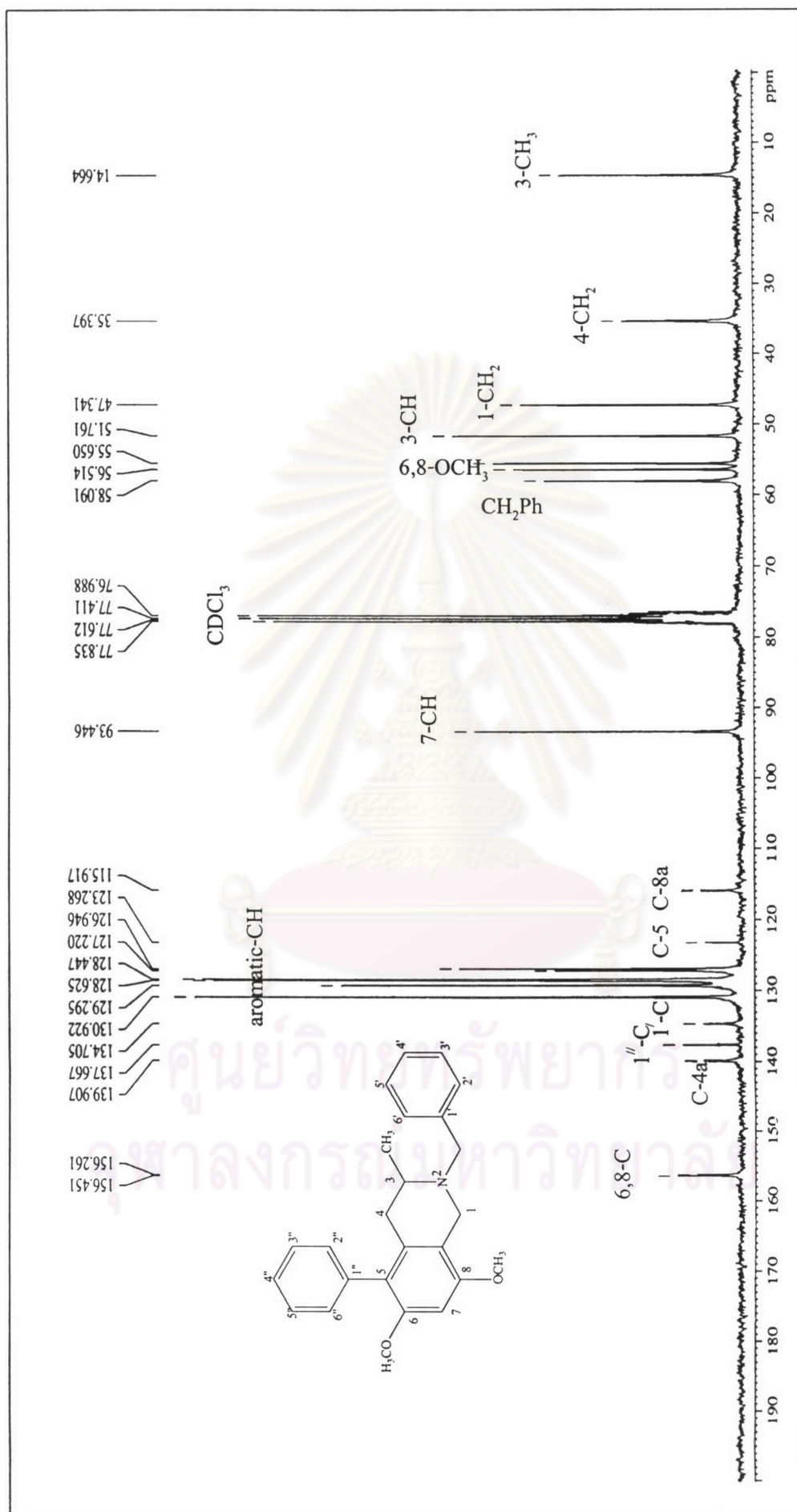


Figure 79 The 75 MHz  $^{13}\text{C}$ -NMR spectrum of 5-phenyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-01)

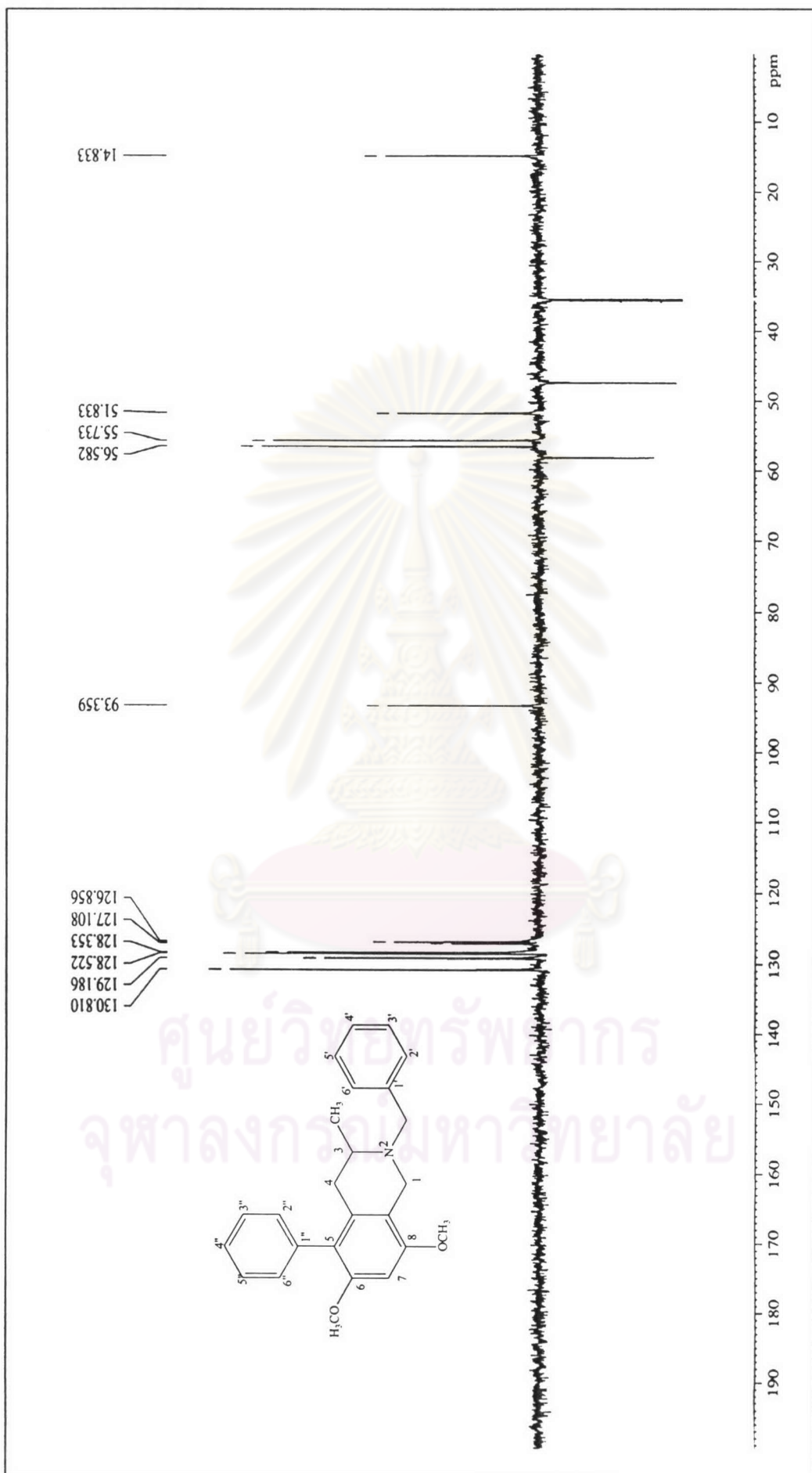


Figure 80 The 75 MHz DEPT 135 spectrum of 5-phenyl-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-21-01)

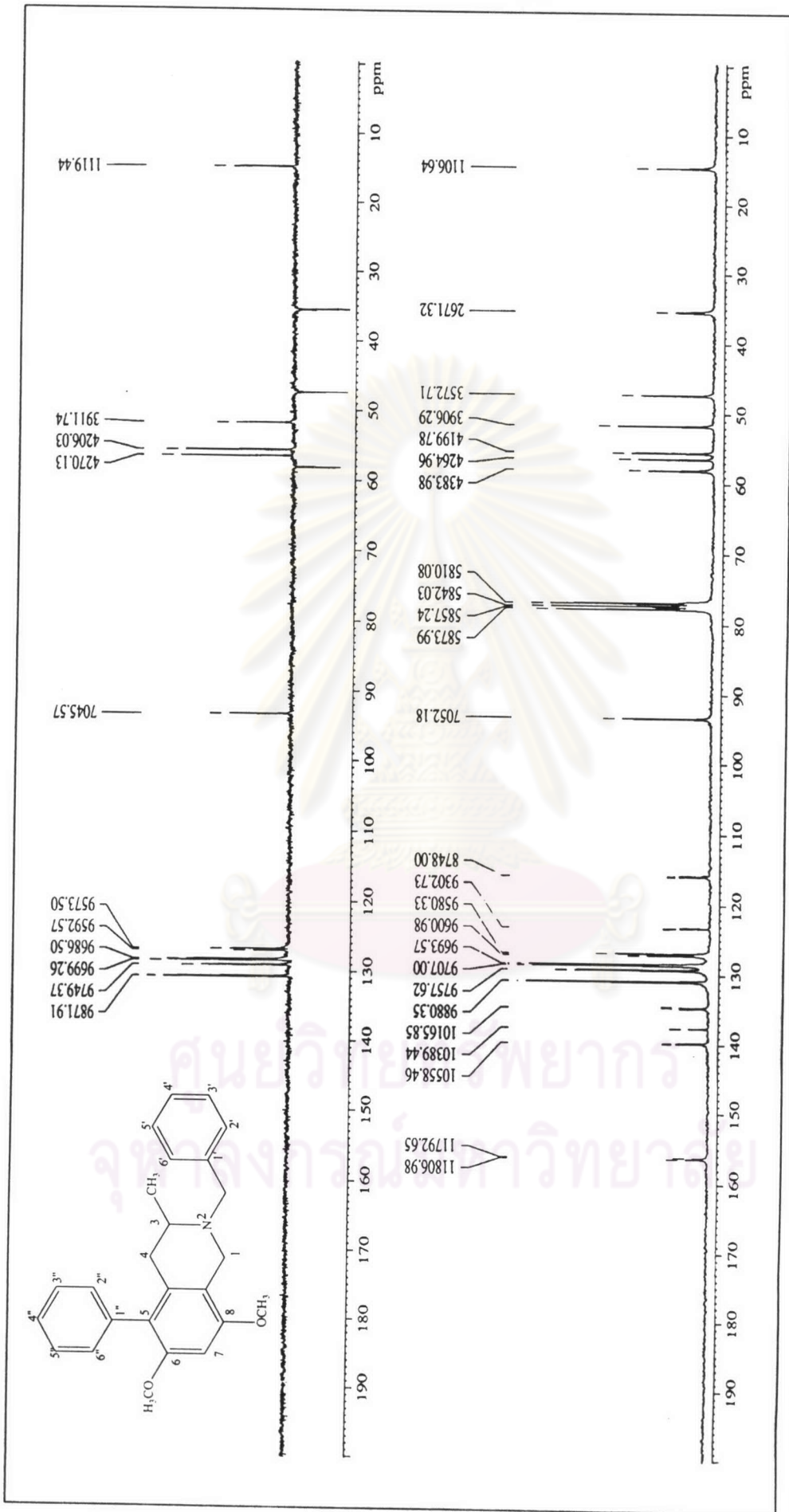


Figure 81 The 75 MHz DEPT 135 and <sup>13</sup>C-NMR spectrum comparison of 5-phenyl-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-01)

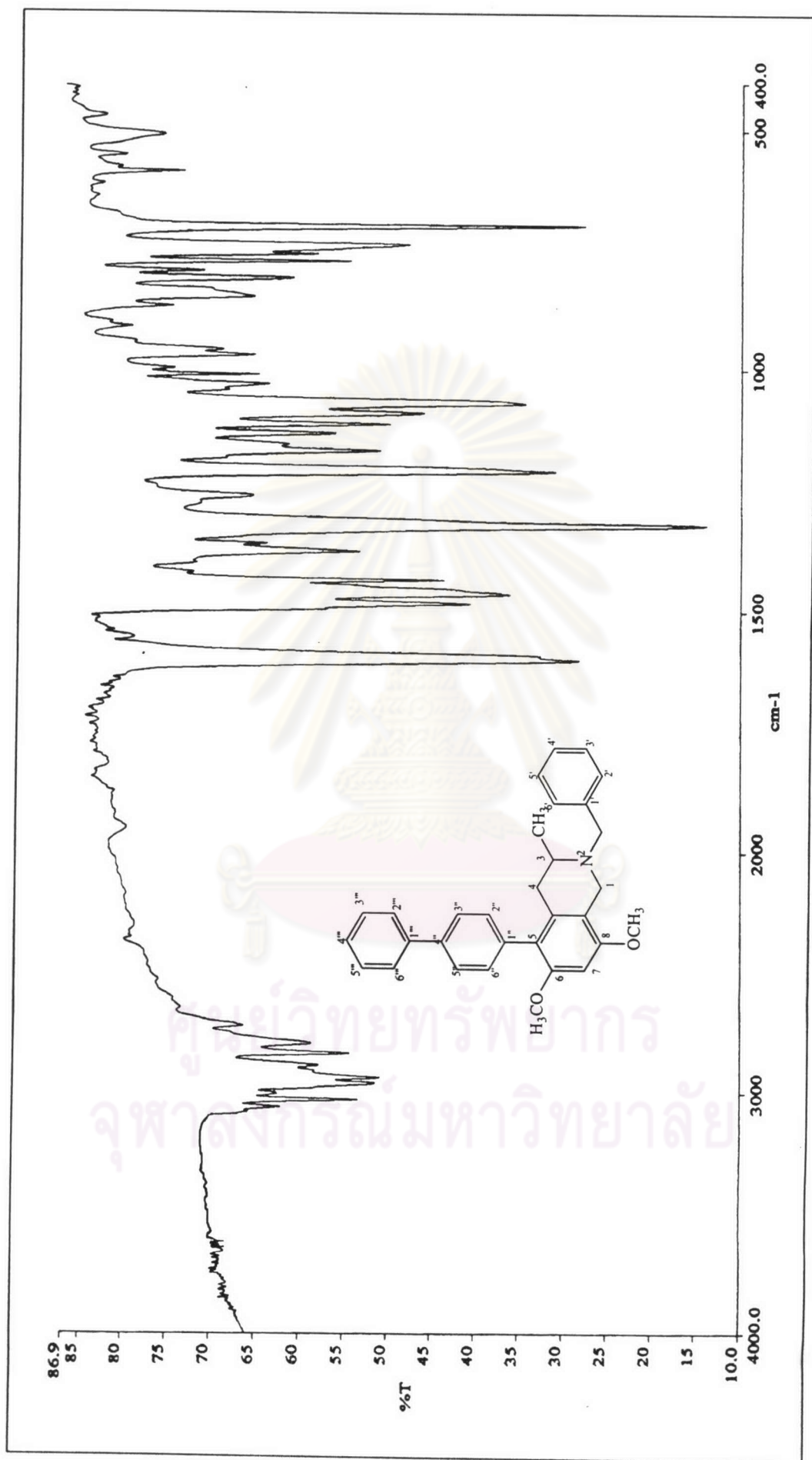


Figure 82 The IR spectrum (KBr) of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydro-isoquinoline (CU-21-02)



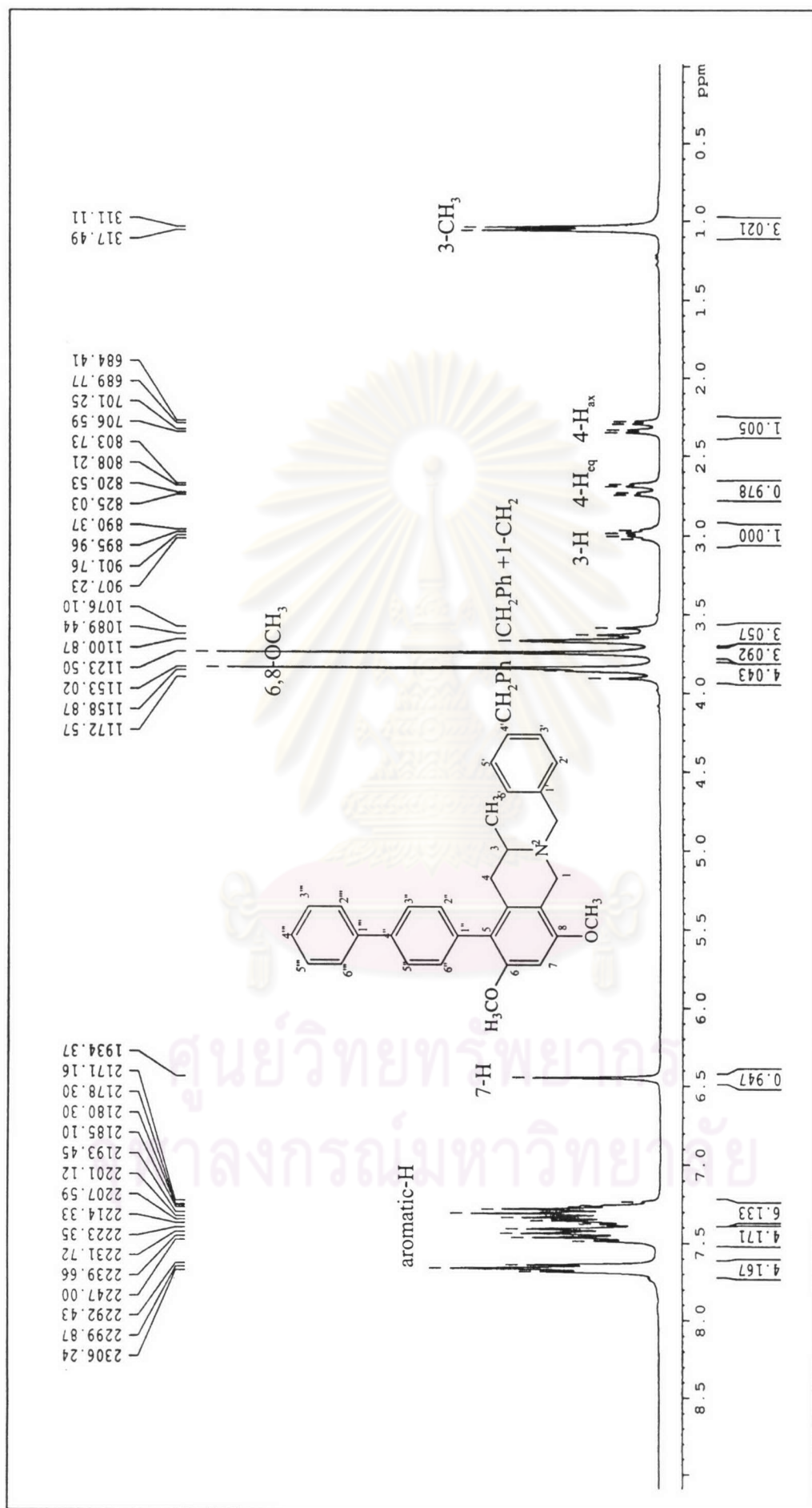


Figure 83 The 300 MHz <sup>1</sup>H-NMR spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-21-02)

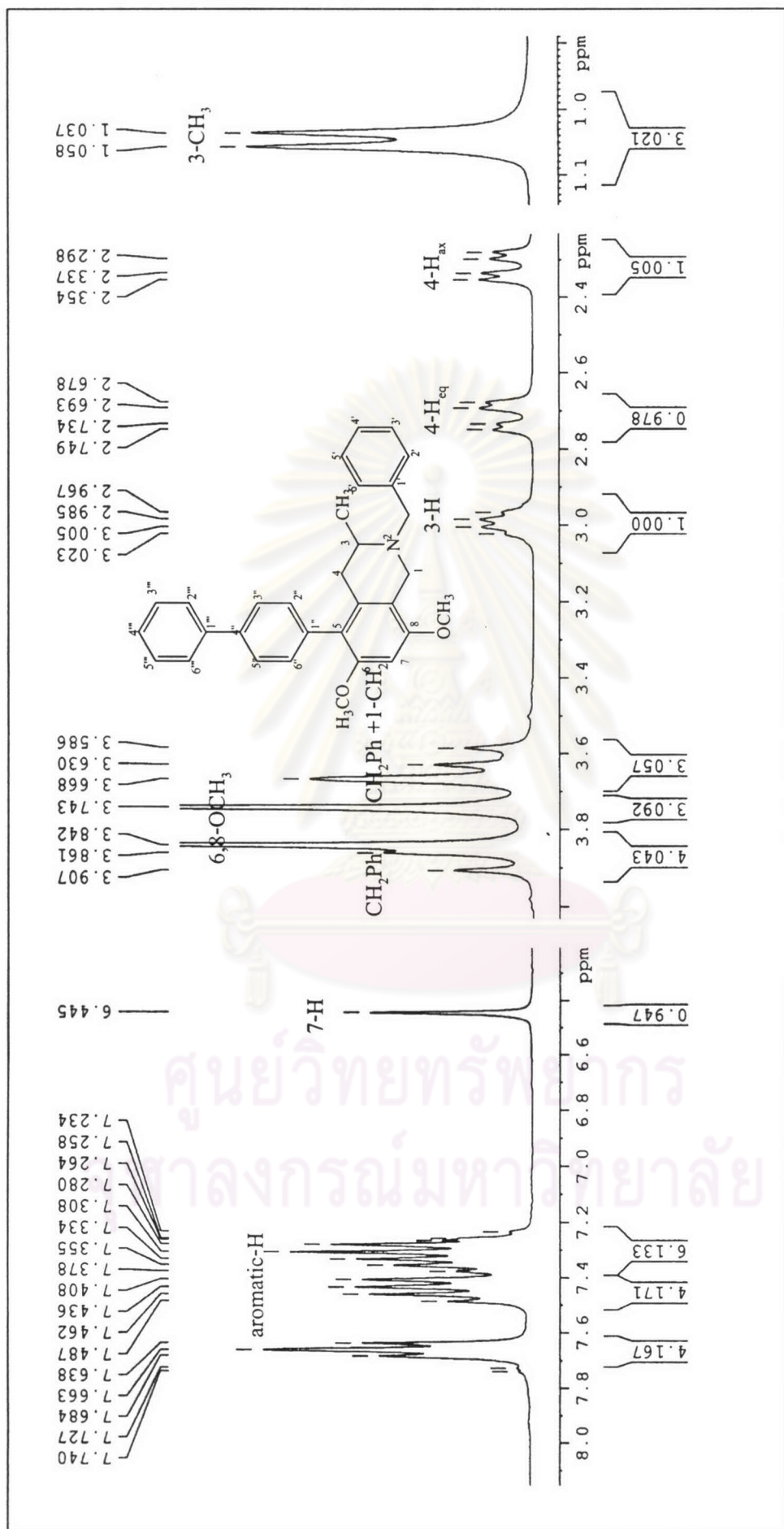


Figure 84 The 300 MHz <sup>1</sup>H-NMR spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-02)

(Enlarged scale)

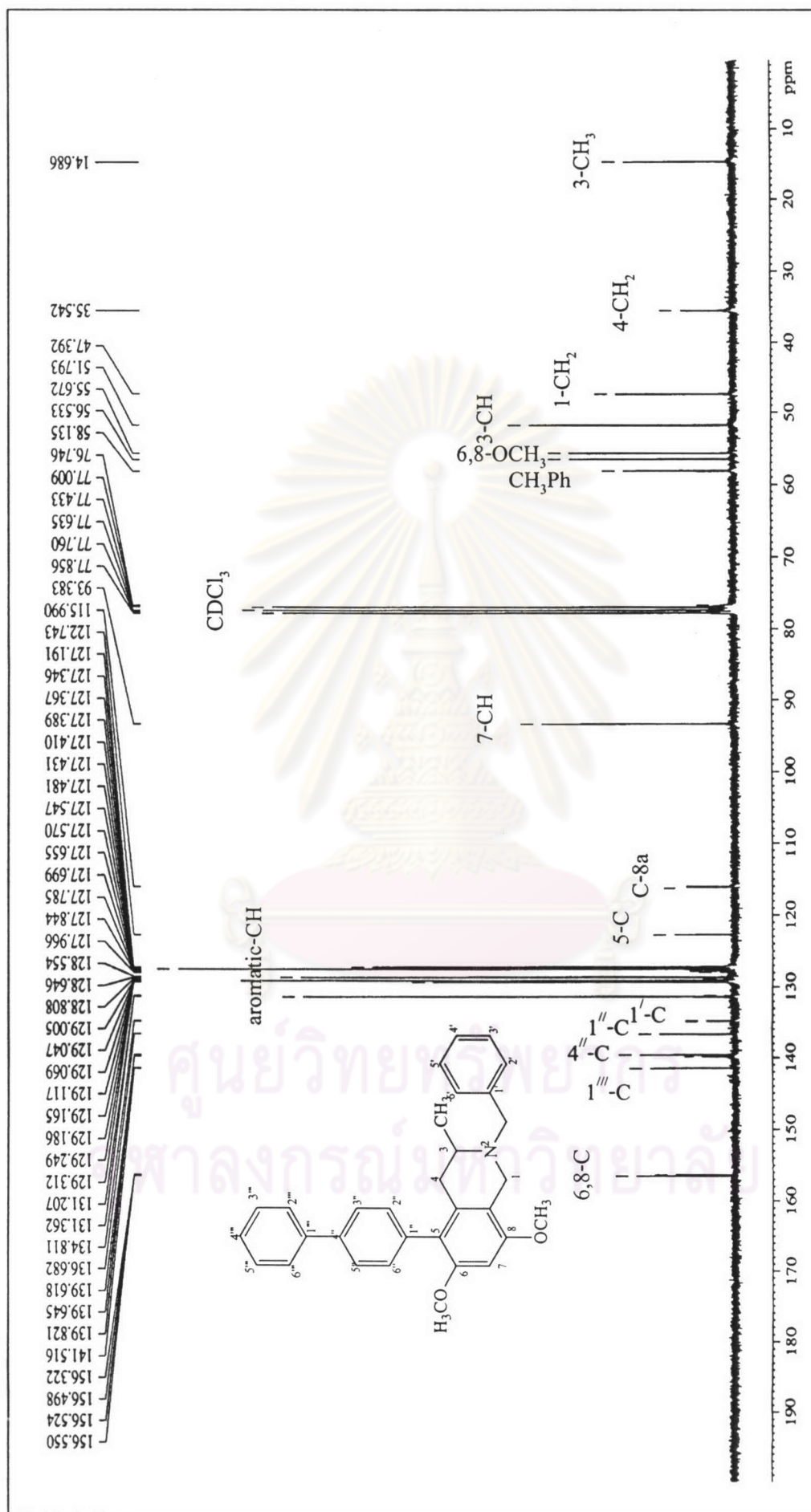


Figure 85 The 75 MHz  $^{13}\text{C}$ -NMR spectrum of 5-(4-biphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-21-02)

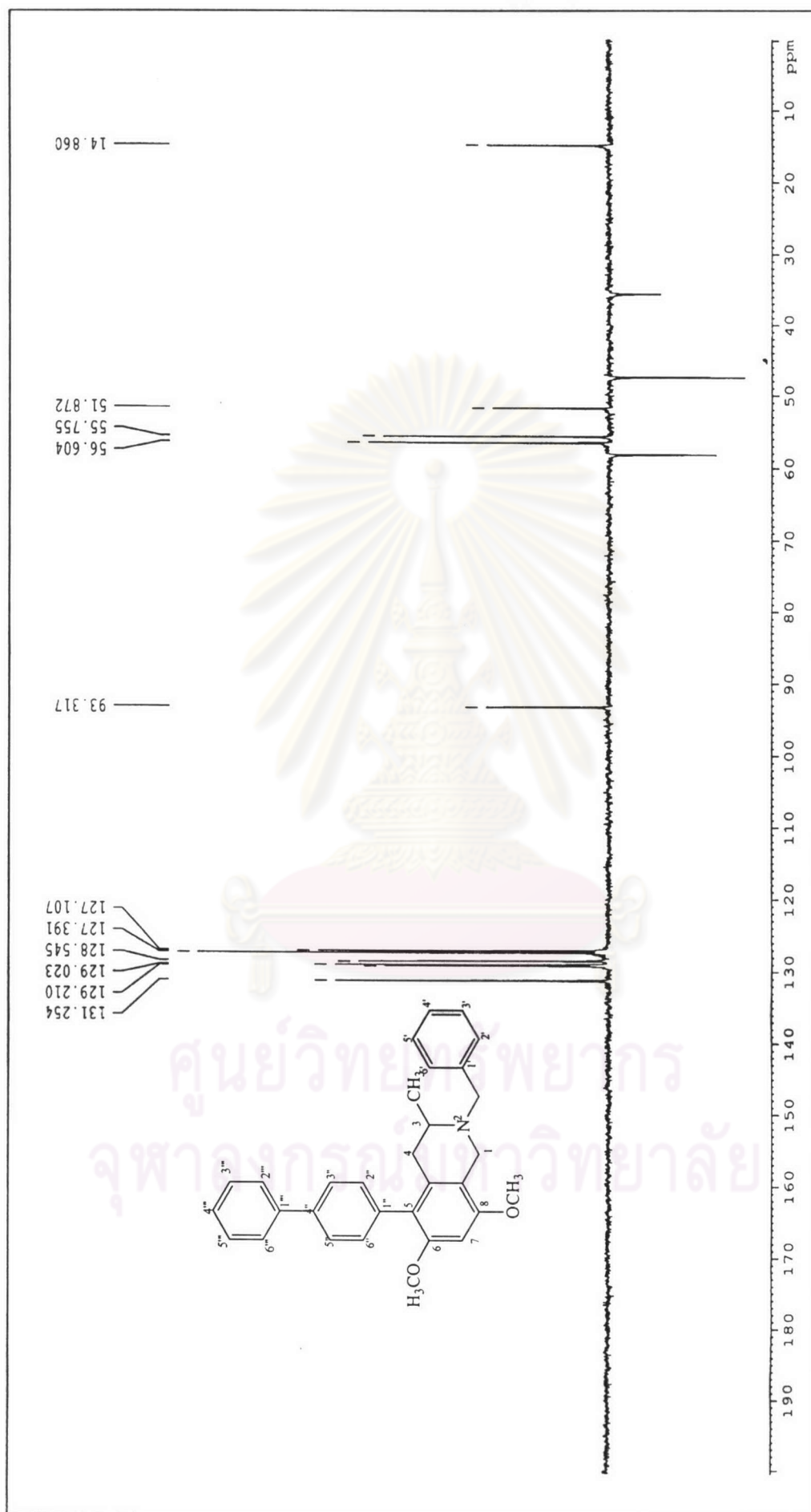


Figure 86 The 75 MHz DEPT 135 spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline(CU-21-02)

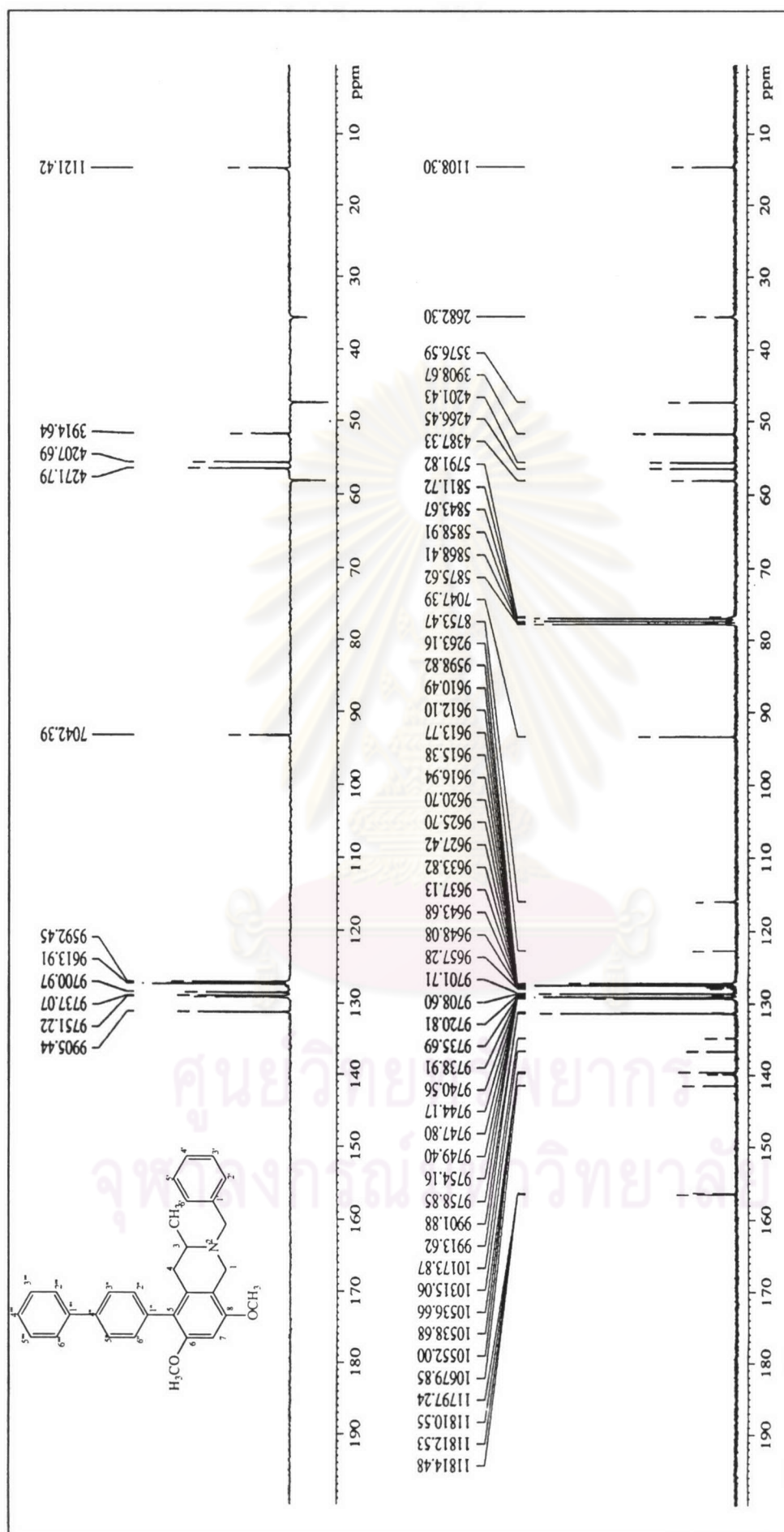


Figure 87 The 75 MHz DEPT 135 and <sup>13</sup>C-NMR spectrum comparison of 5-(4'-biphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-21-02)

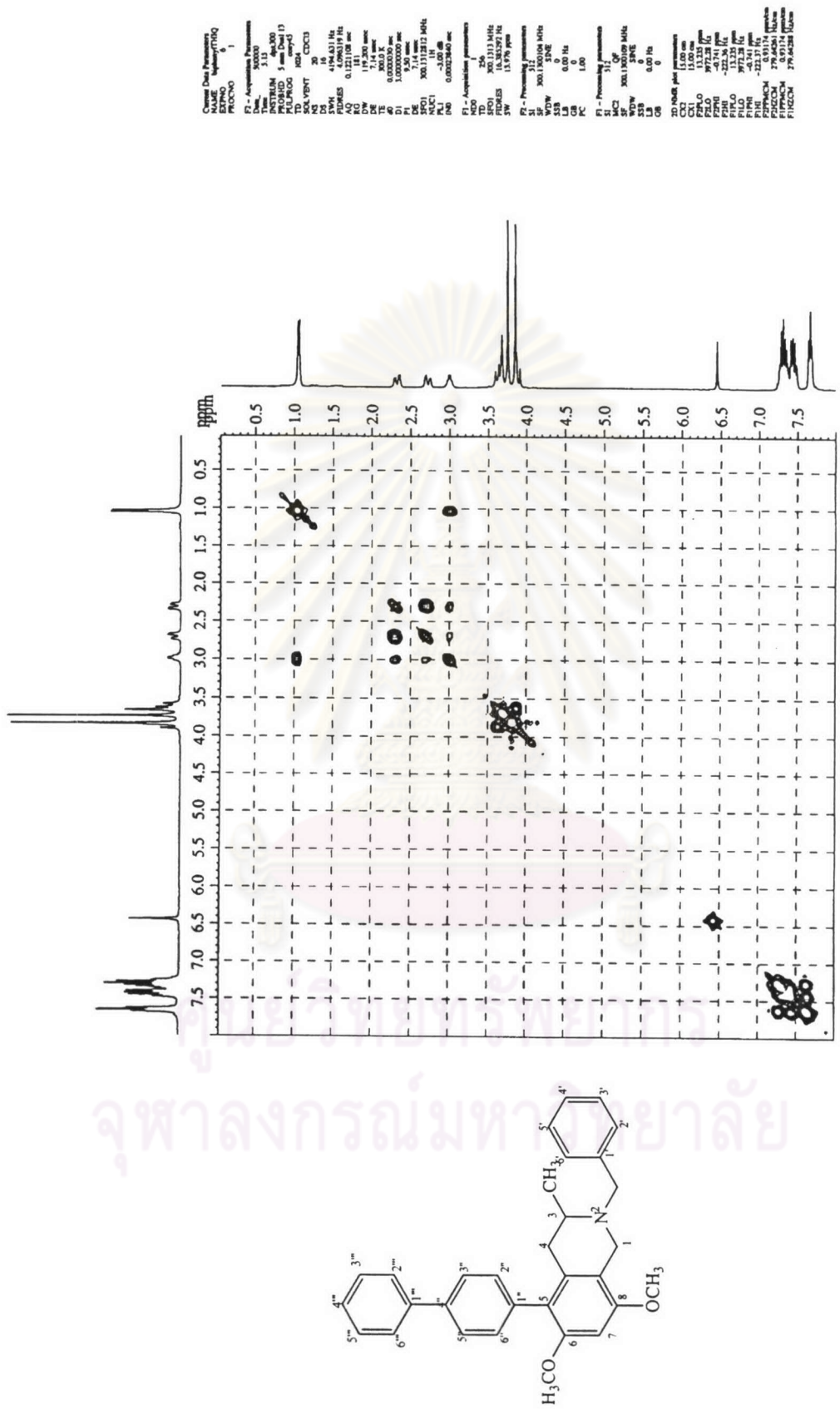


Figure 88 The 300 MHz HH COSY spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-21-02)

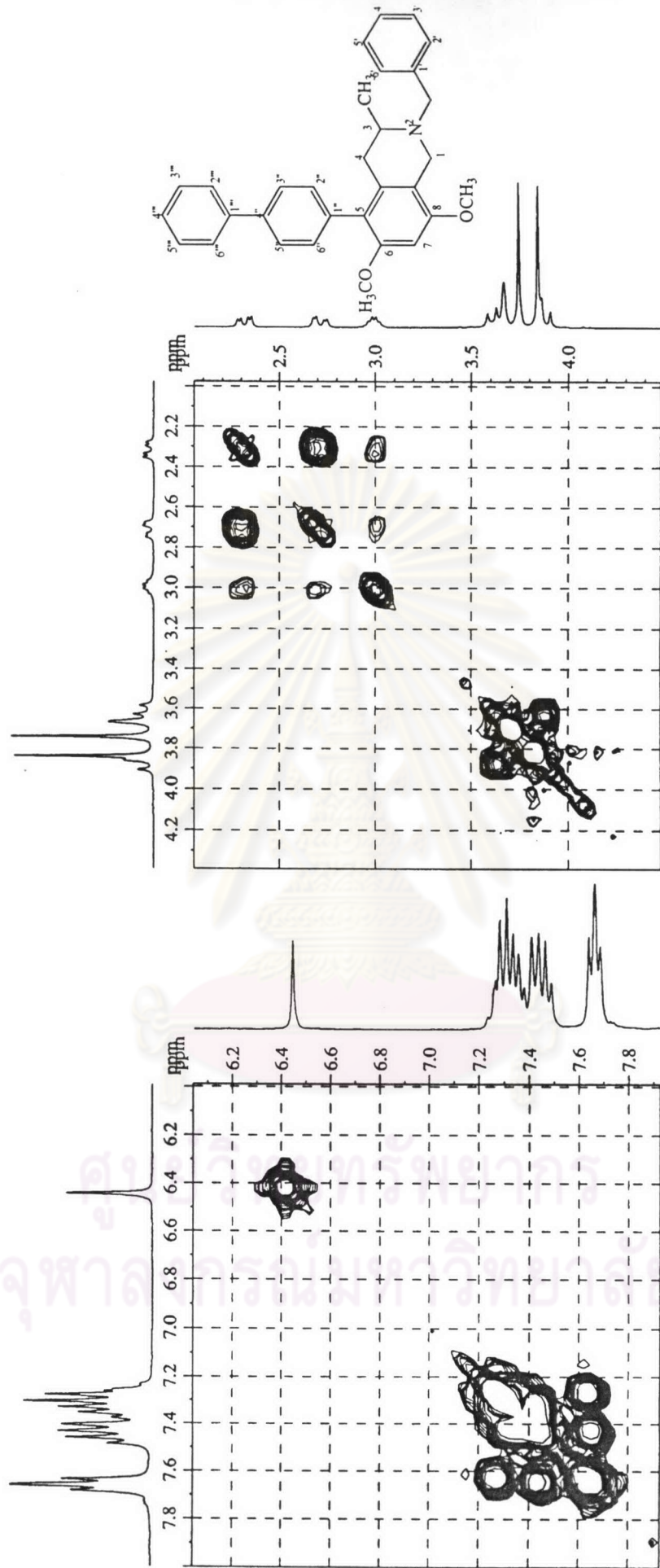


Figure 89 The 300 MHz <sup>1</sup>H-<sup>1</sup>H COSY spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-02)

(Enlarged scale)

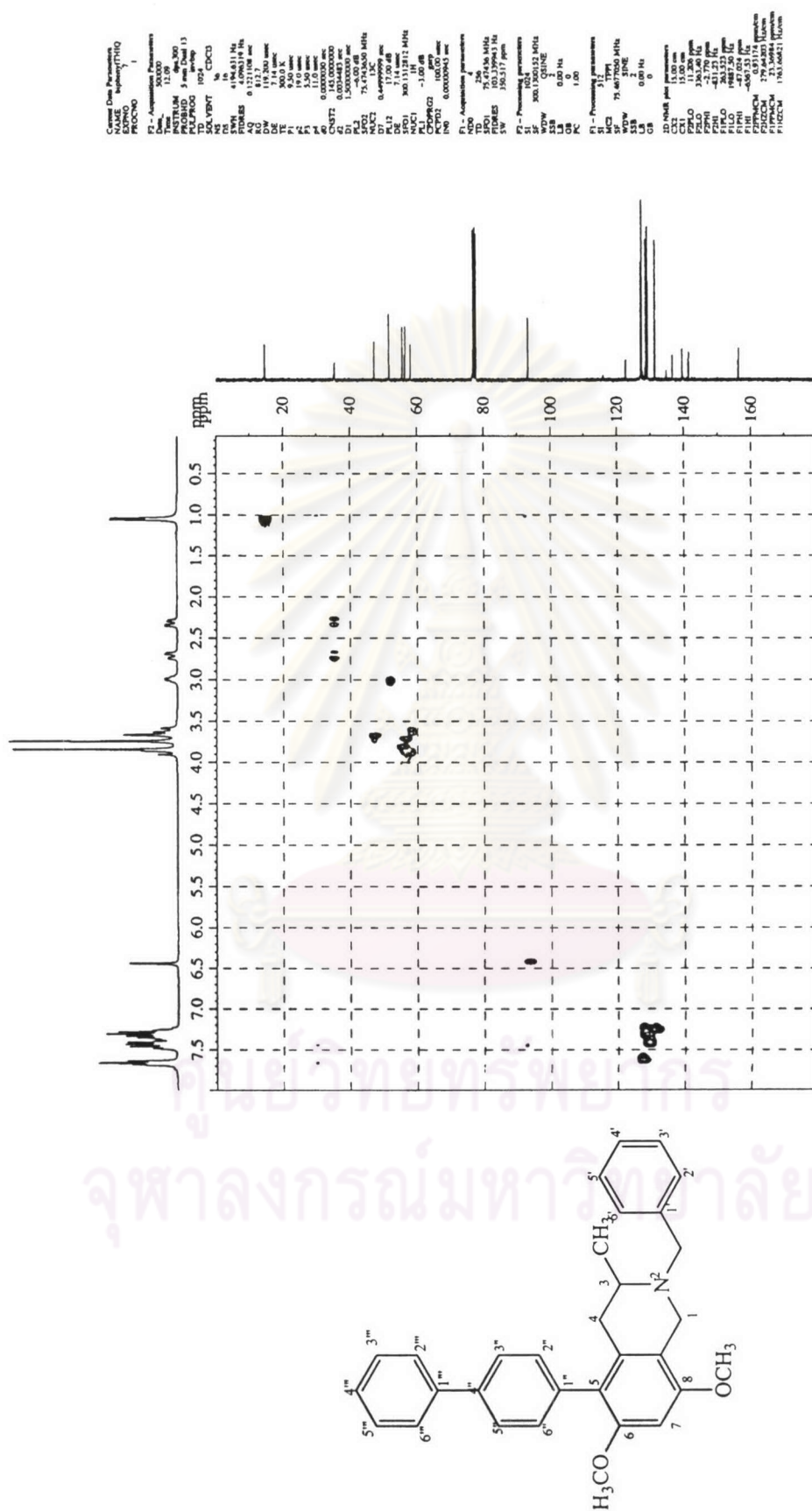


Figure 90 The 300 MHz HMQC spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline(CU-21-02)



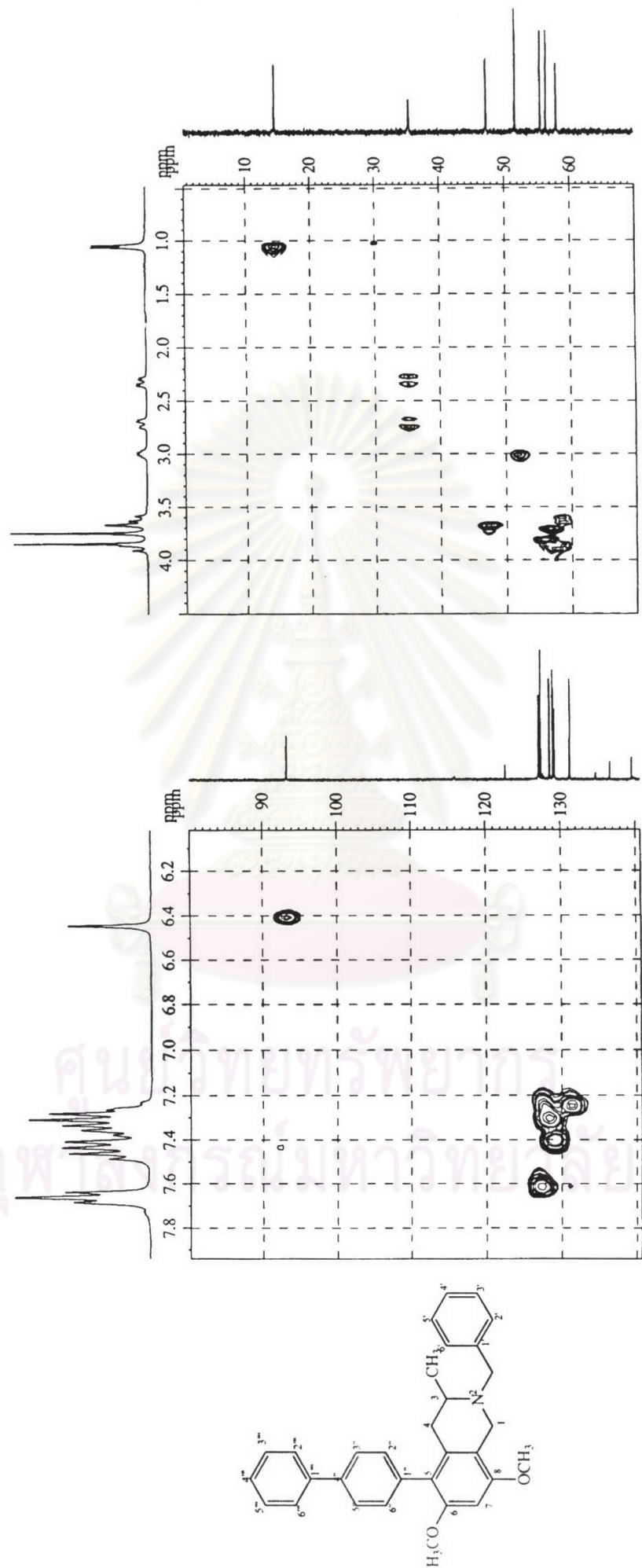


Figure 91 The 300 MHz HMQC spectrum of 5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline(CU-21-02)  
(Enlarged scale)

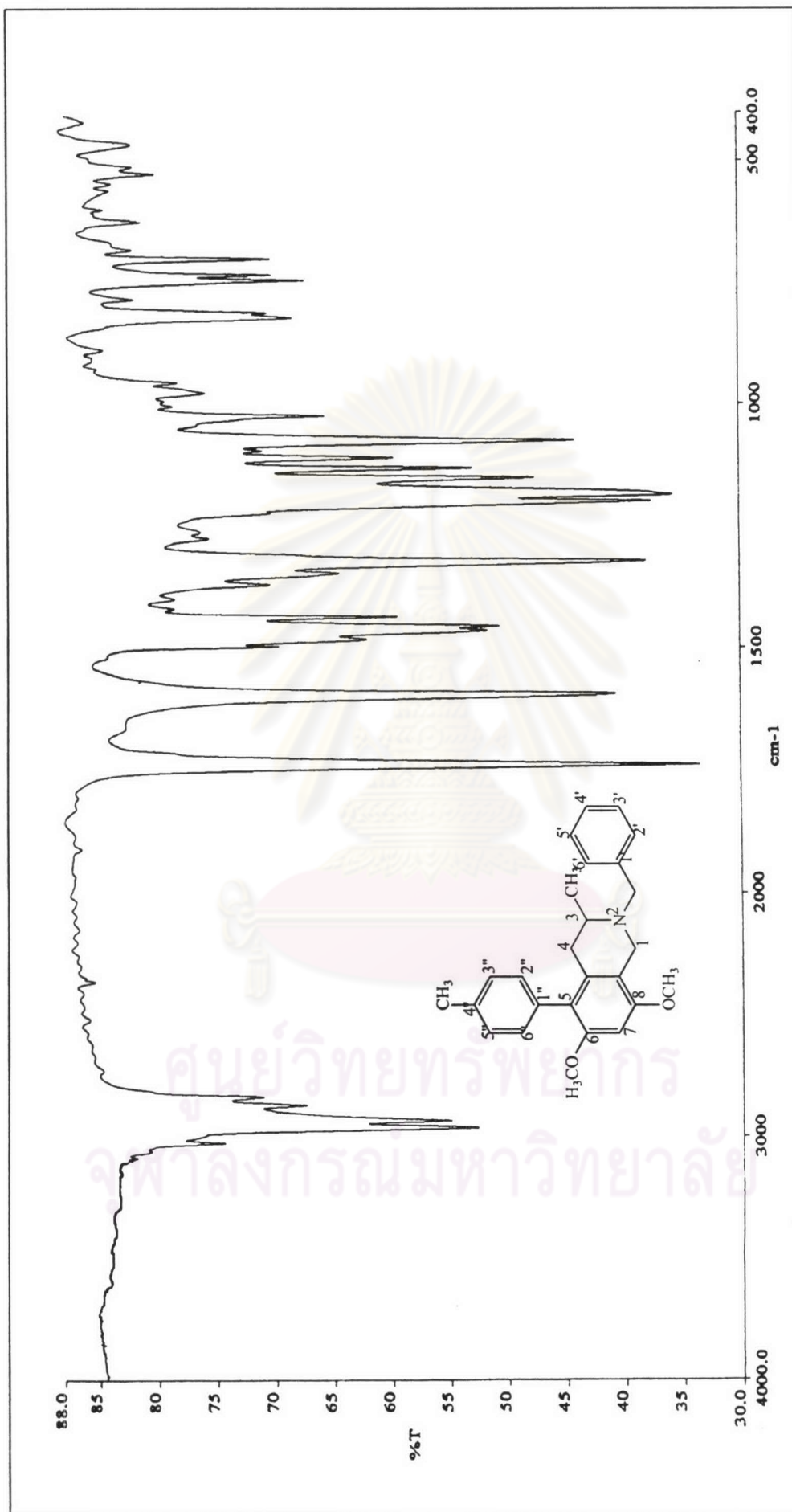


Figure 92 The IR spectrum (KBr) of 5-(4-methylphenyl)-2-benzyl-6,8-dimethoxy-3,3,4-tetrahydroisoquinoline (CU-21-03)

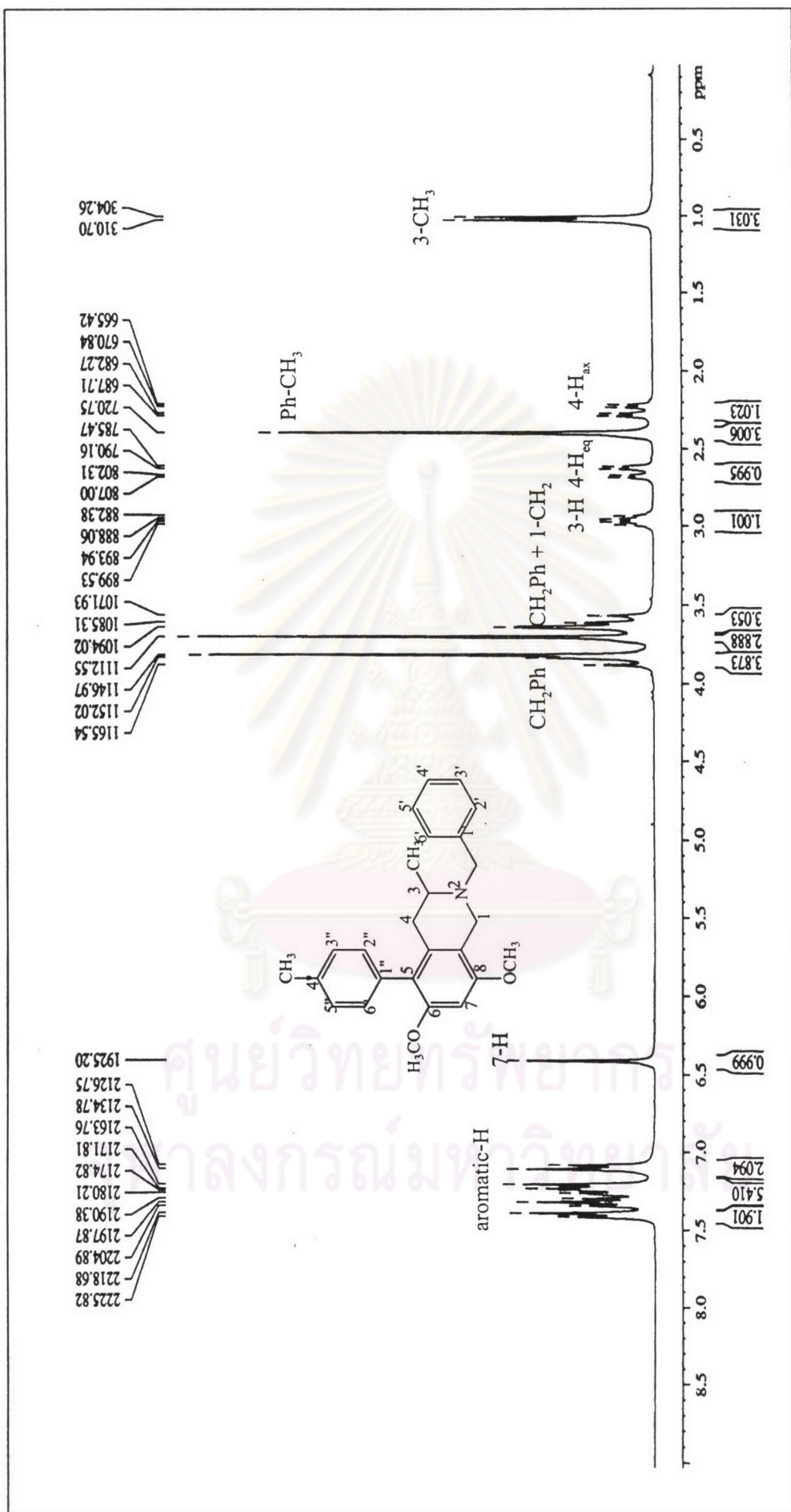


Figure 93 The 300 MHz <sup>1</sup>H-NMR spectrum of 5-(4'-methylphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-21-03)

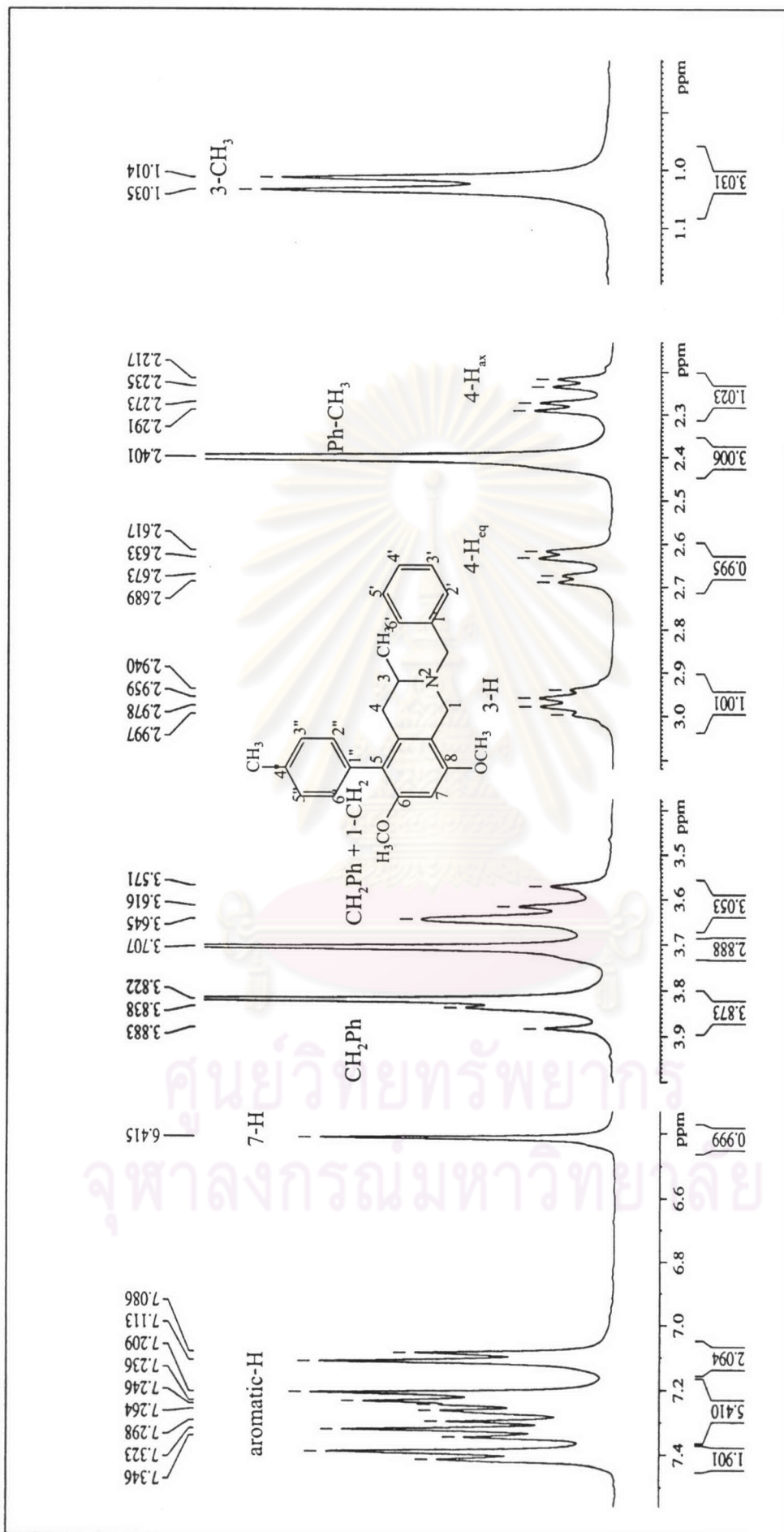


Figure 94 The 300 MHz <sup>1</sup>H-NMR spectrum of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-21-03)

(Enlarged scale)

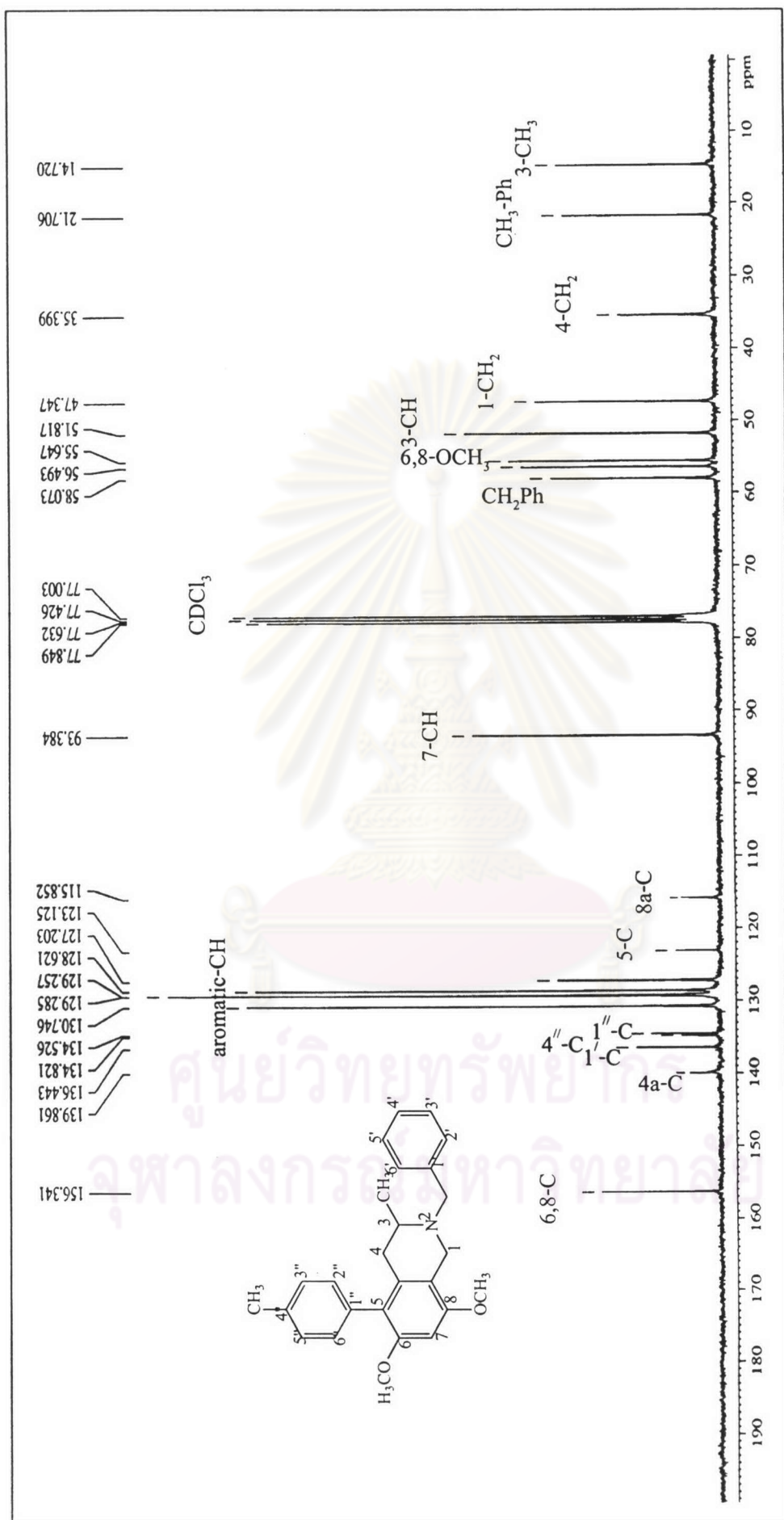


Figure 95 The 75MHz  $^{13}\text{C}$ -NMR spectrum of 5-(4''-methylphenyl)-2-(2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03)

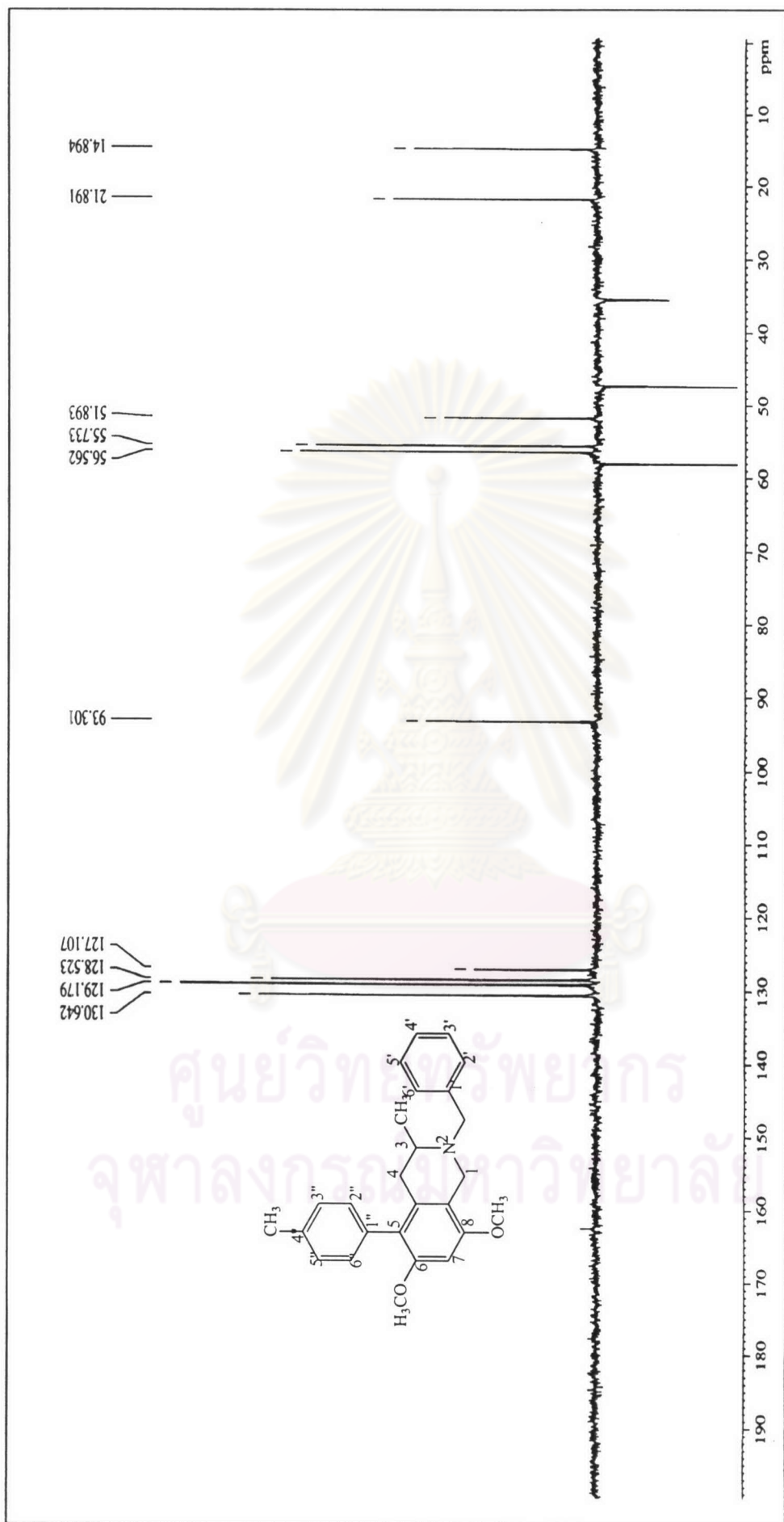


Figure 96 The 75 MHz DEPT 135 spectrum of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03)

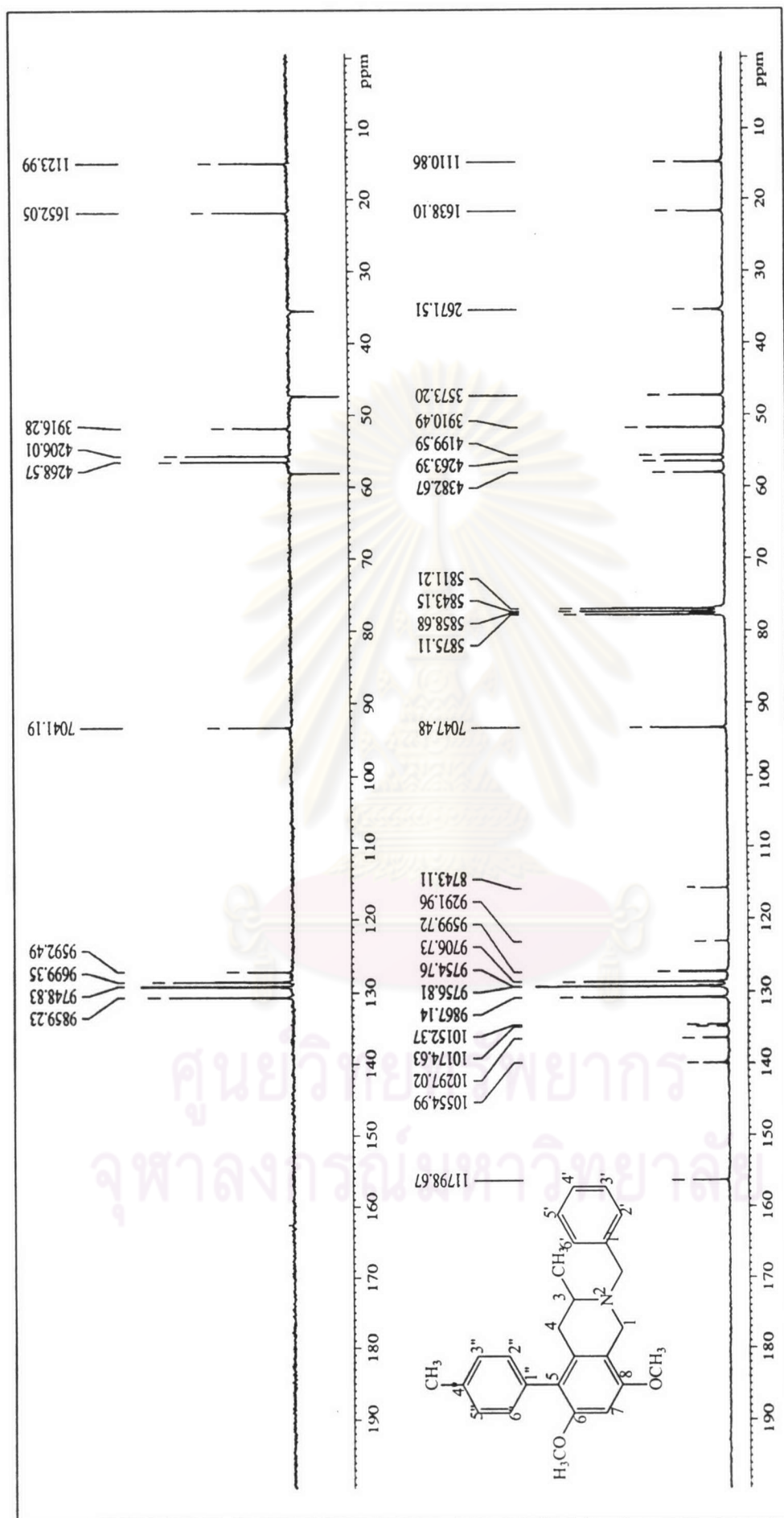


Figure 97 The 75 MHz DEPT 135 and <sup>13</sup>C-NMR spectrum comparison of 5-(4'-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-03)





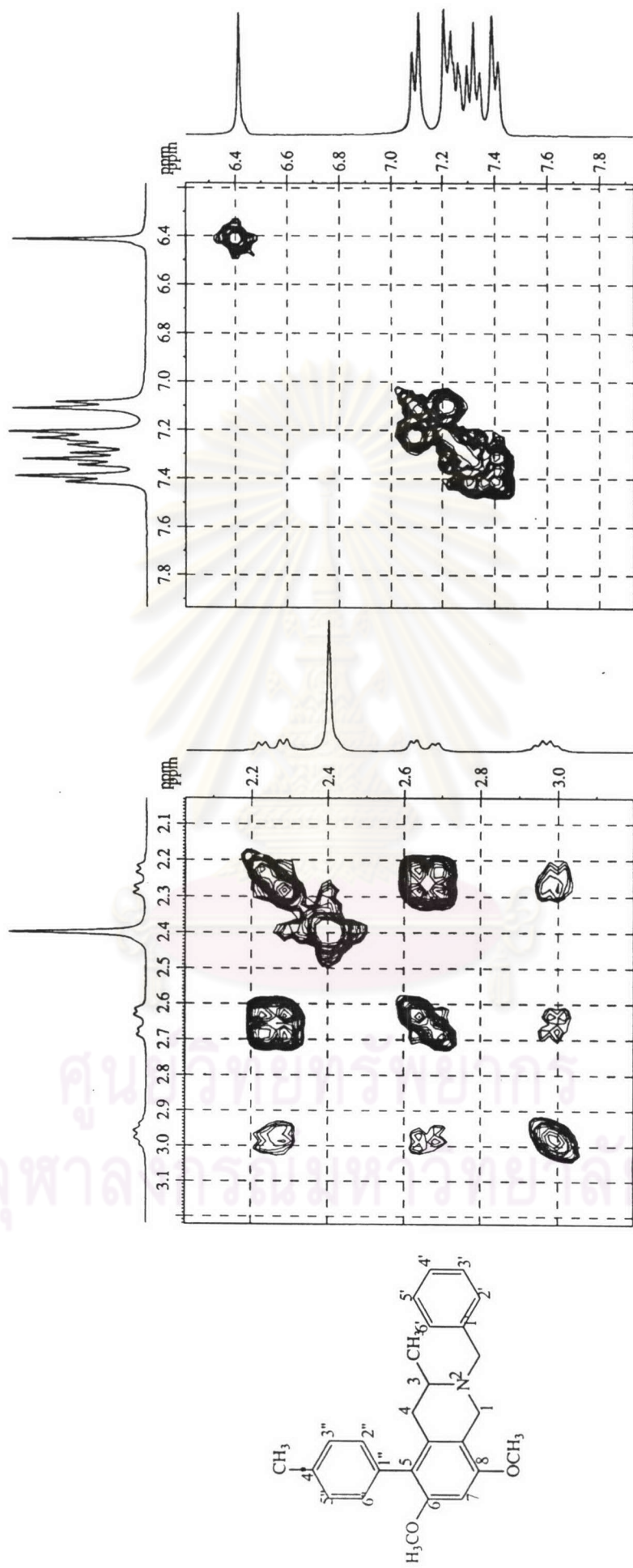


Figure 99 The 300 MHz HH COSY spectrum of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-21-03) (Enlarged scale)



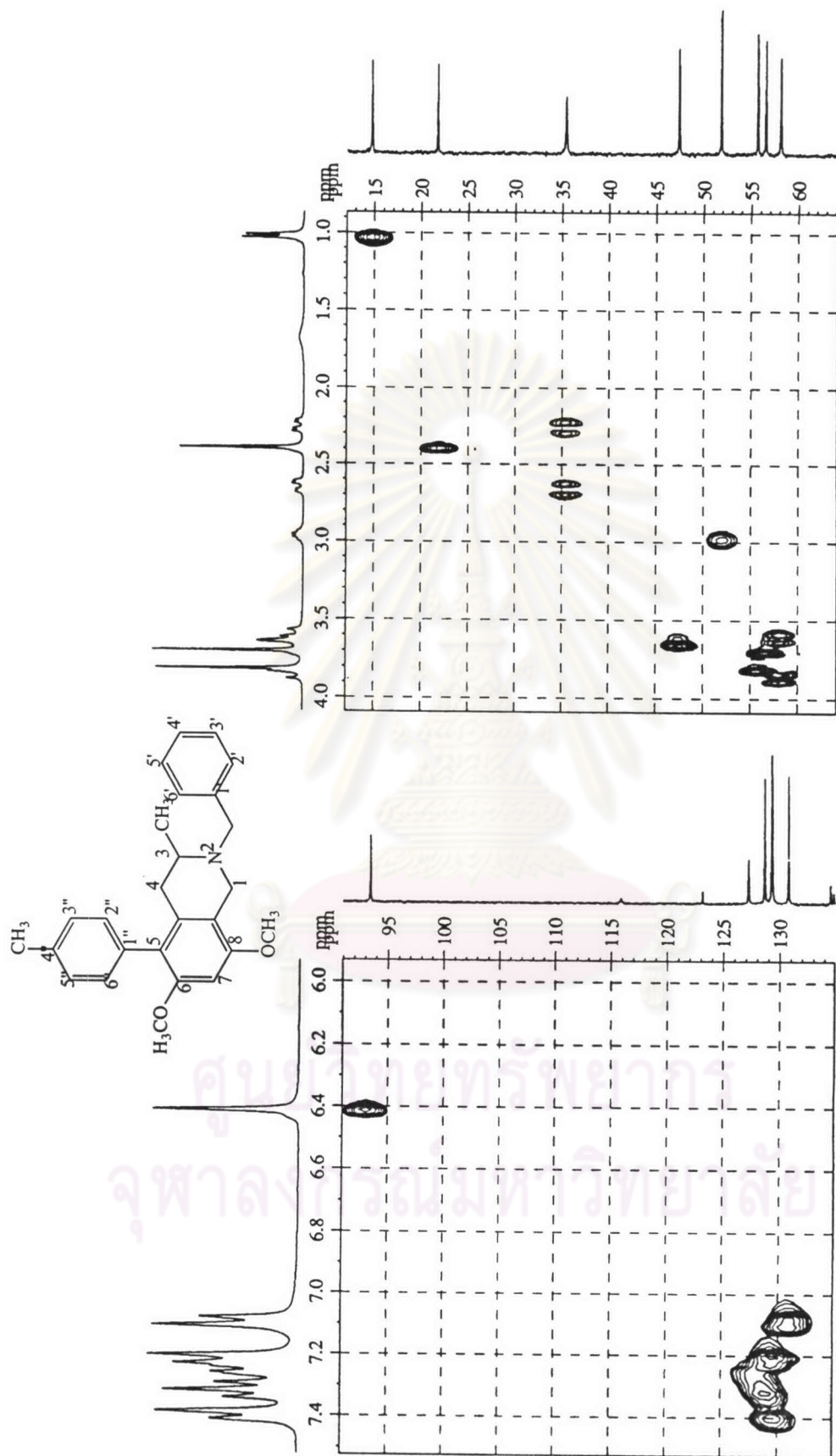


Figure 101 The 300 MHz HMQC spectrum of 5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CUJ-21-03)

(Enlarged scale)

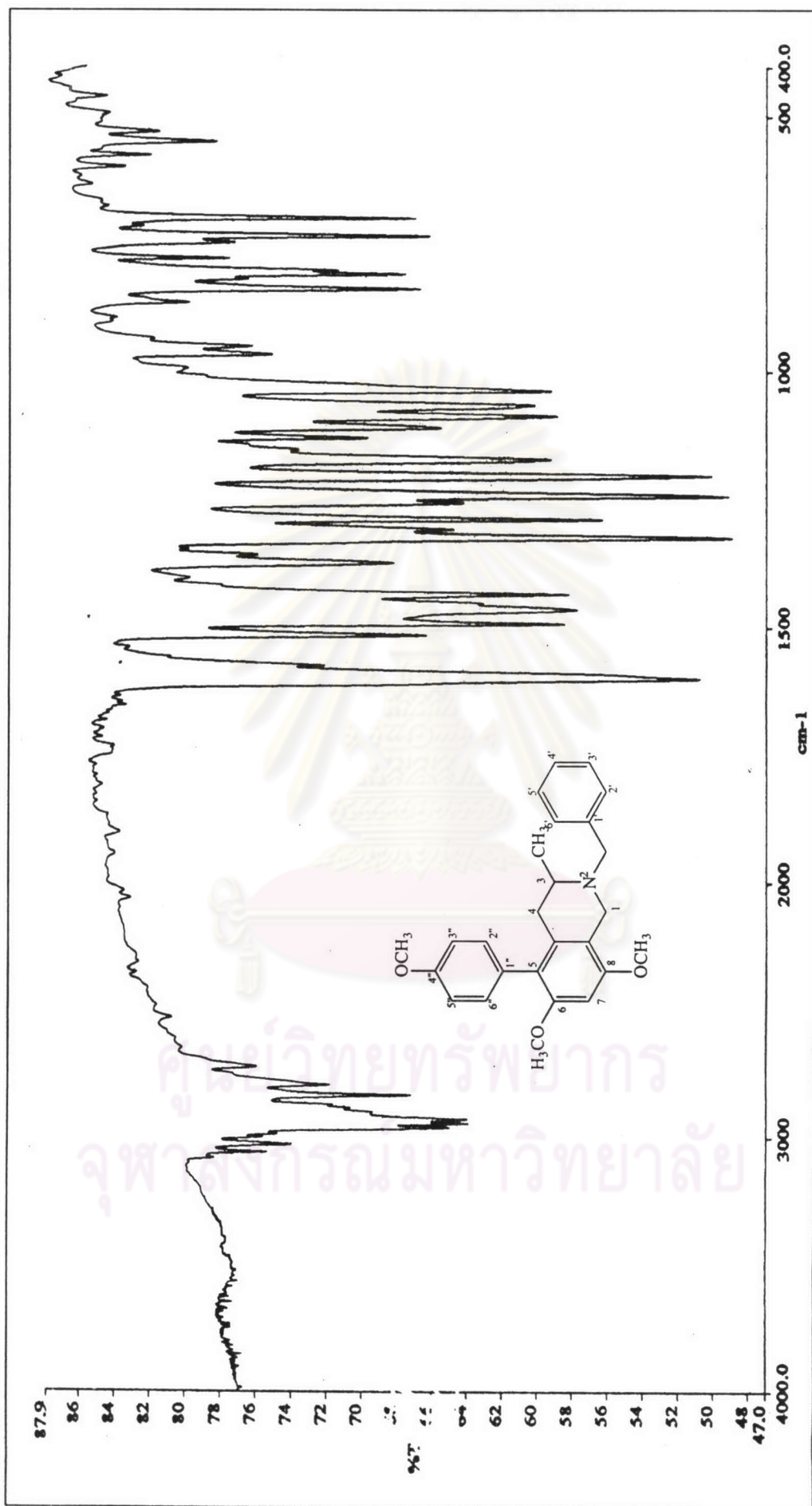


Figure 102 The IR spectrum (KBr) of 5-(4''-methoxy phenyl)-2- benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-211-04)

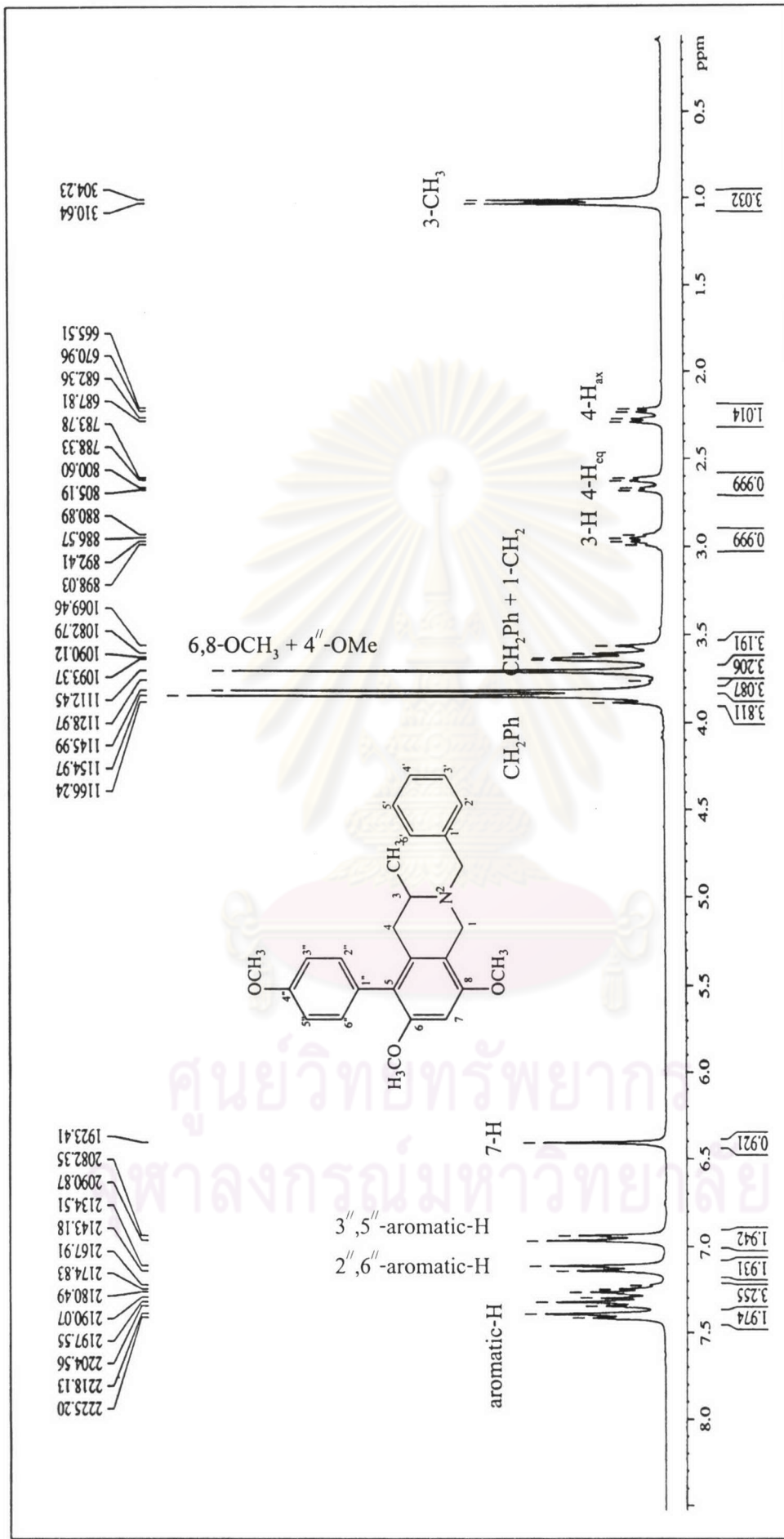


Figure 103 The 300 MHz <sup>1</sup>H-NMR spectrum of 5-(4'-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-

04)

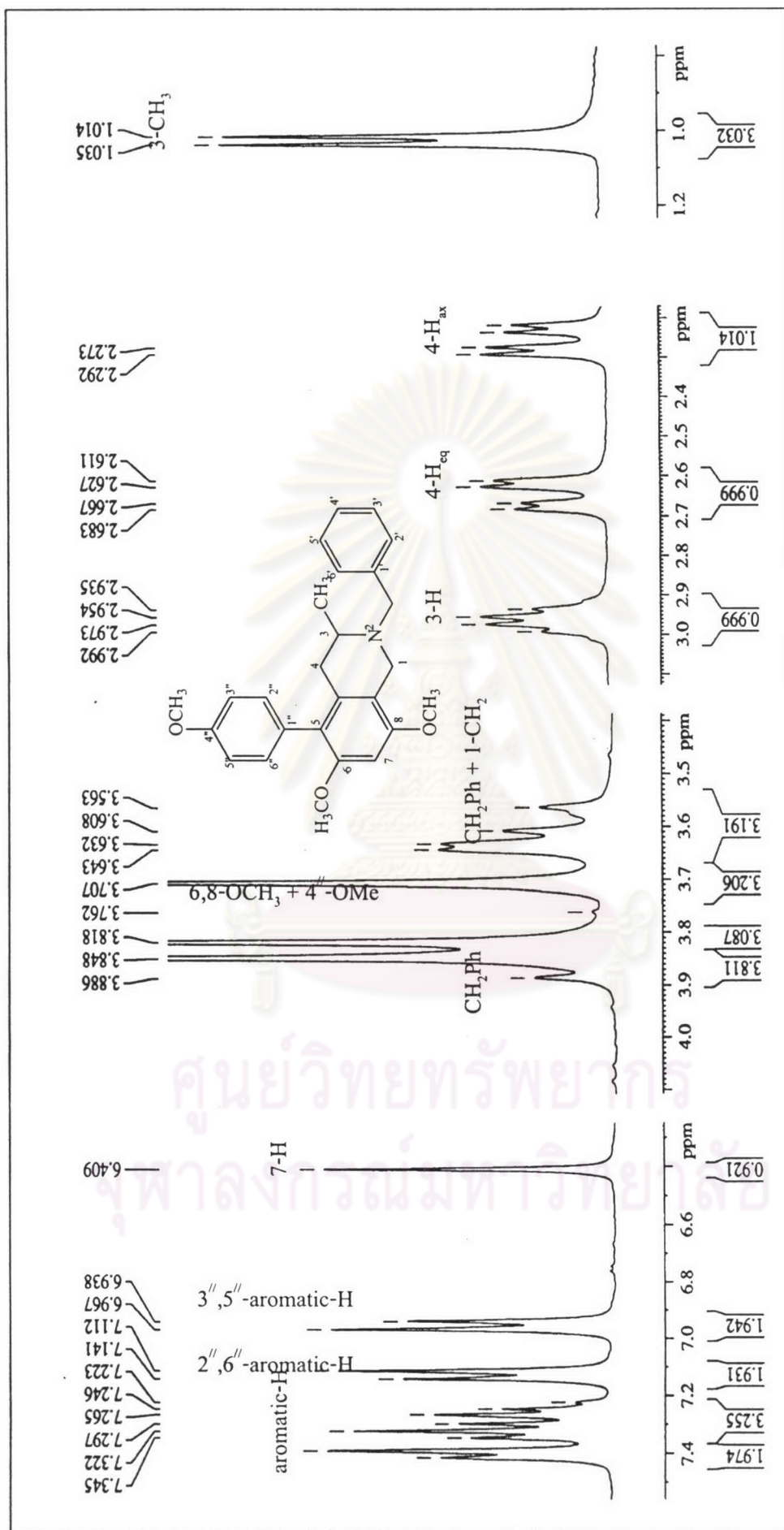


Figure 104 The 300 MHz <sup>1</sup>H-NMR spectrum of 5-(4'-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-

04) (Enlarge scale)

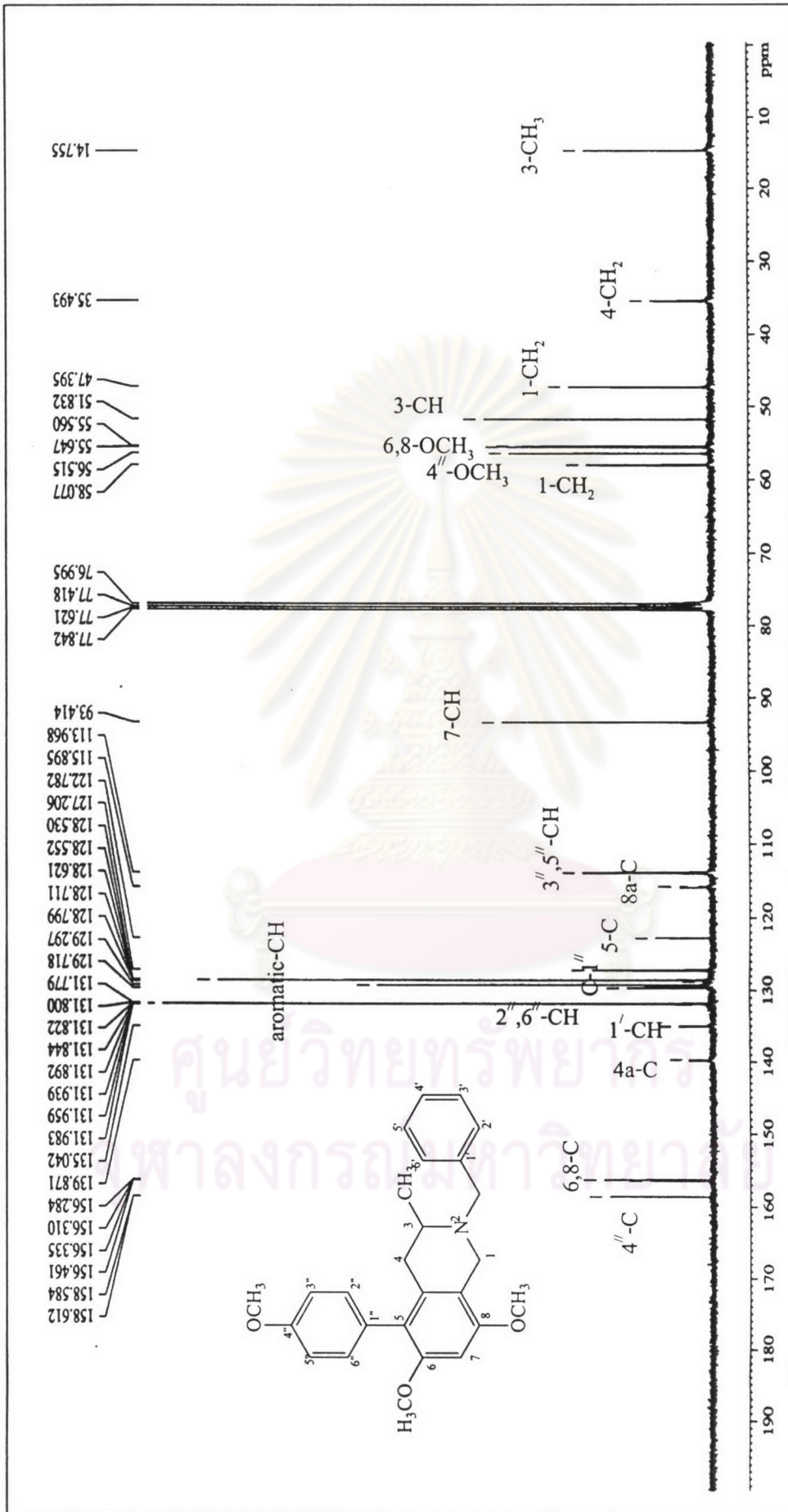


Figure 105 The 75 MHz  $^{13}\text{C-NMR}$  spectrum of 5-(4-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline

(CU-21-04)

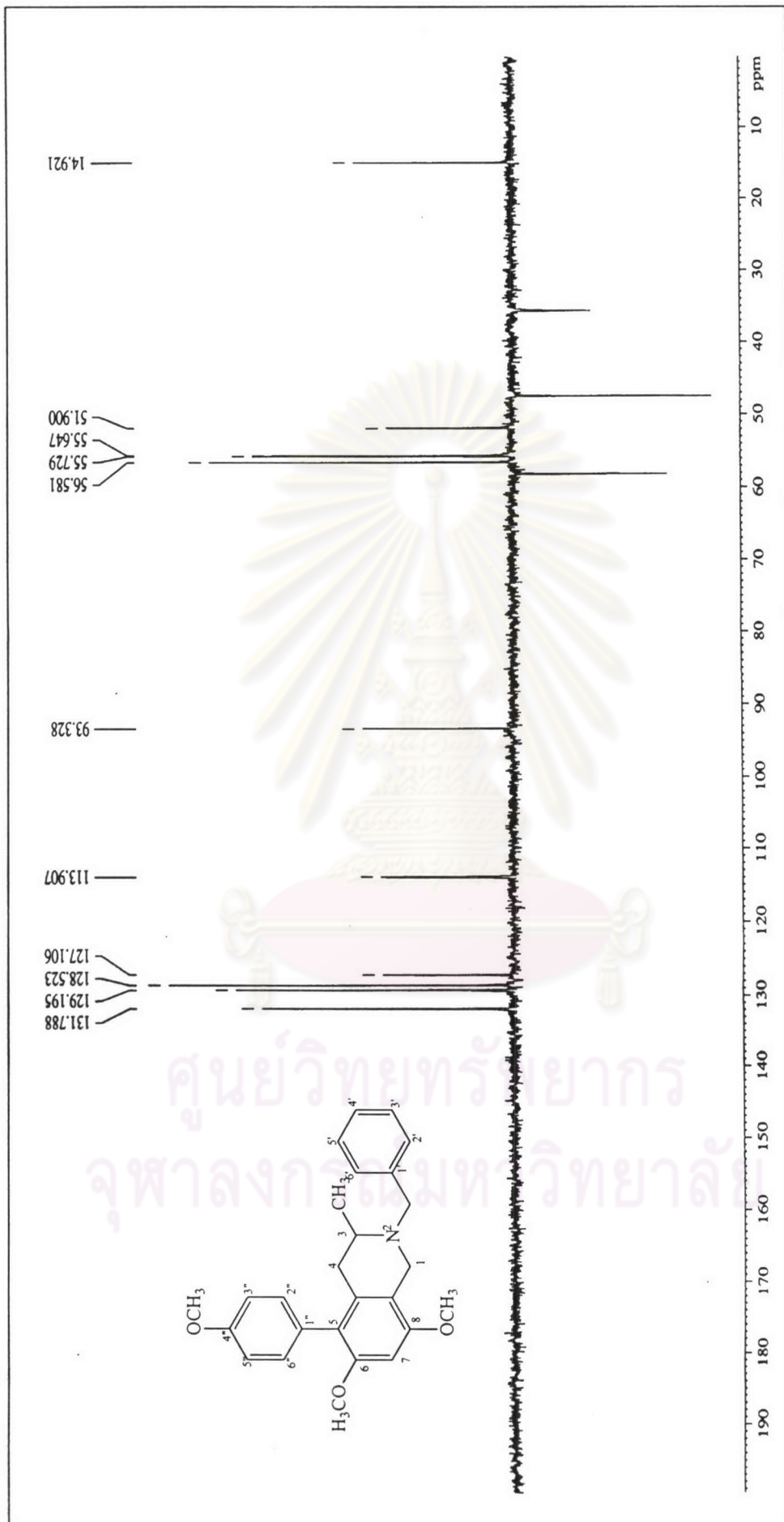


Figure 106 The 75 MHz DEPT 135 spectrum of 5-(4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline

(CU-21-04)



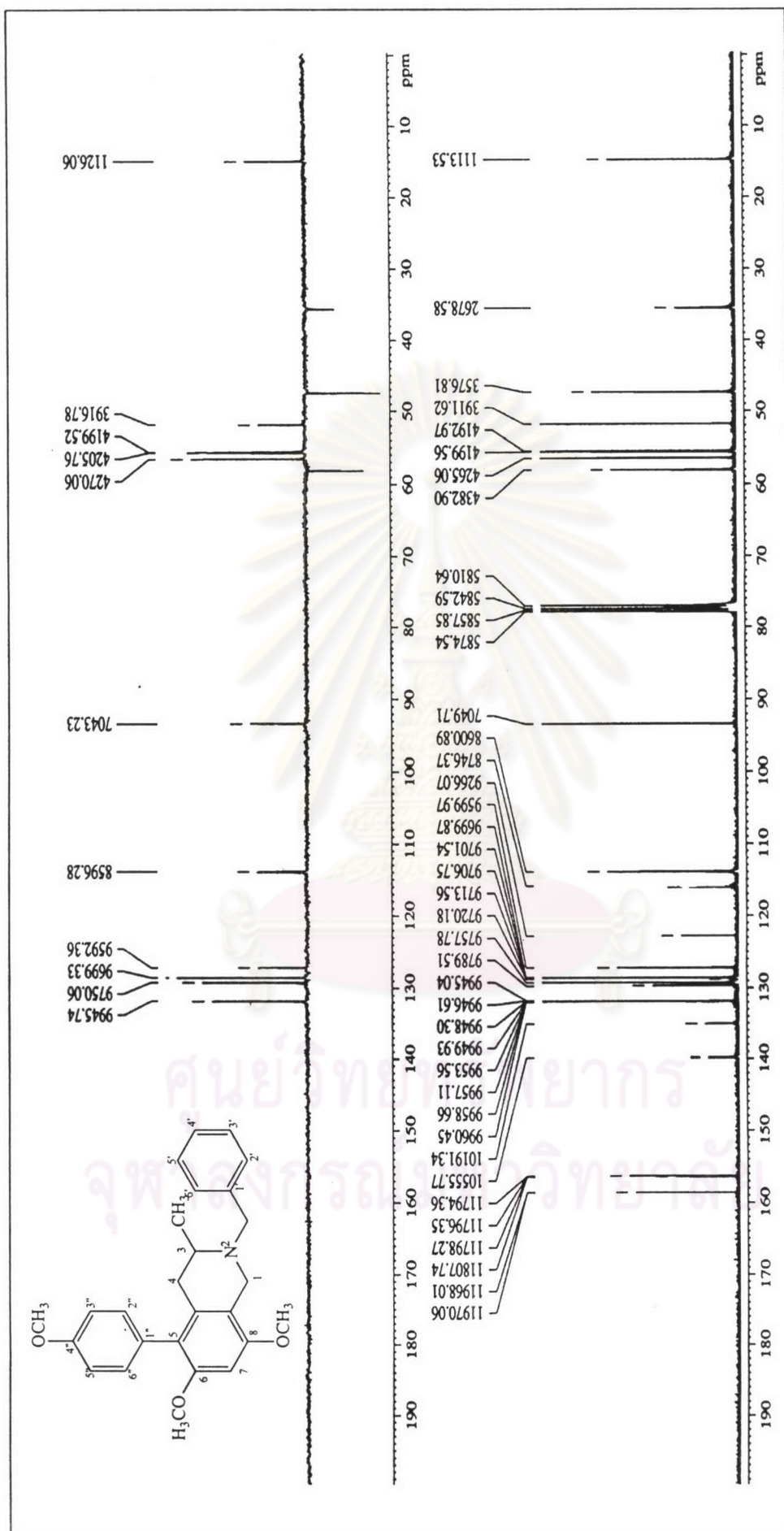


Figure 107 The 75 MHz DEPT 135 and  $^{13}\text{C}$ -NMR spectrum comparison of 5-(4'-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-04)

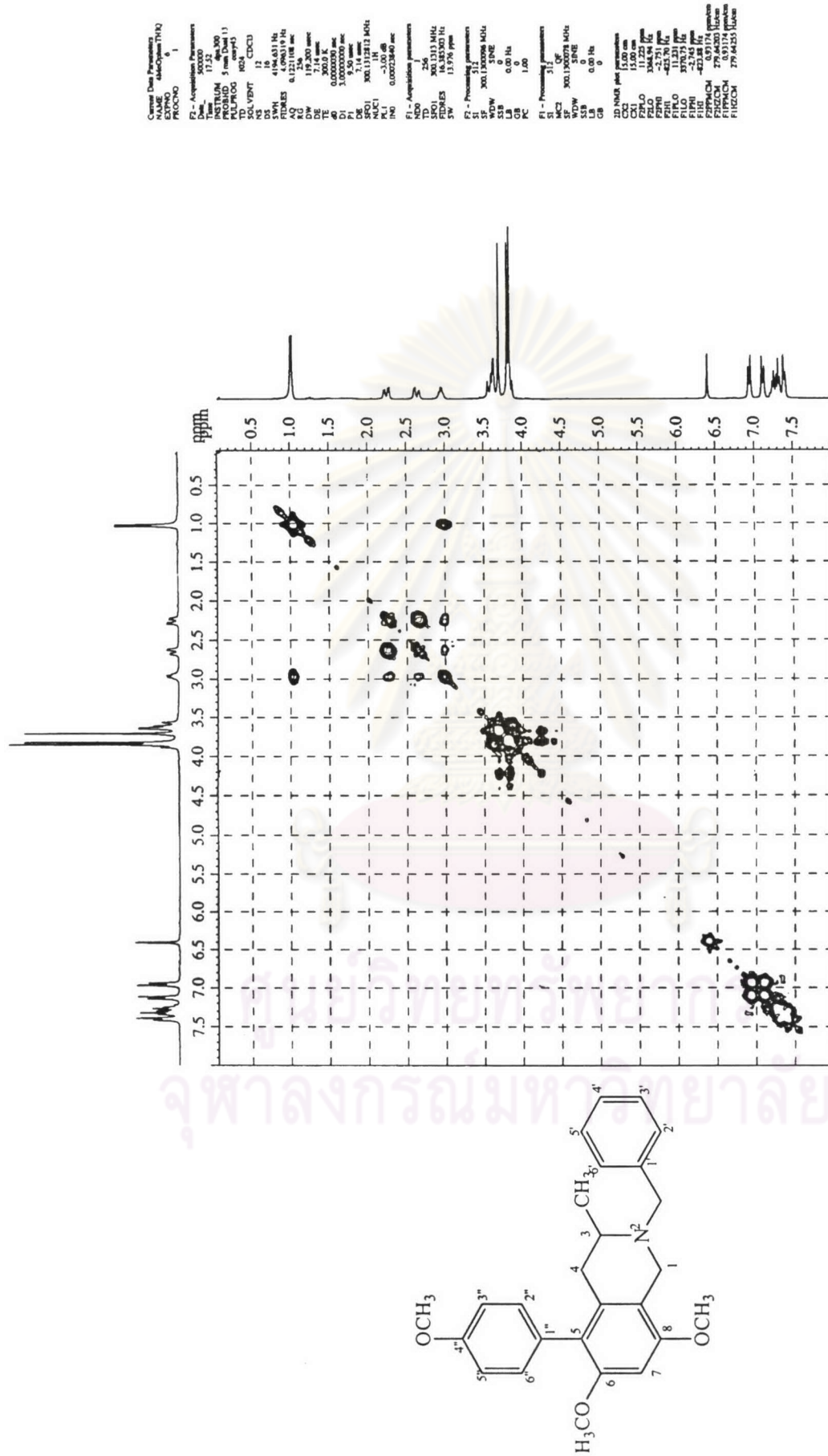


Figure 108 The 300 MHz <sup>1</sup>H-<sup>1</sup>H COSY spectrum of 5-(4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-

21-04)

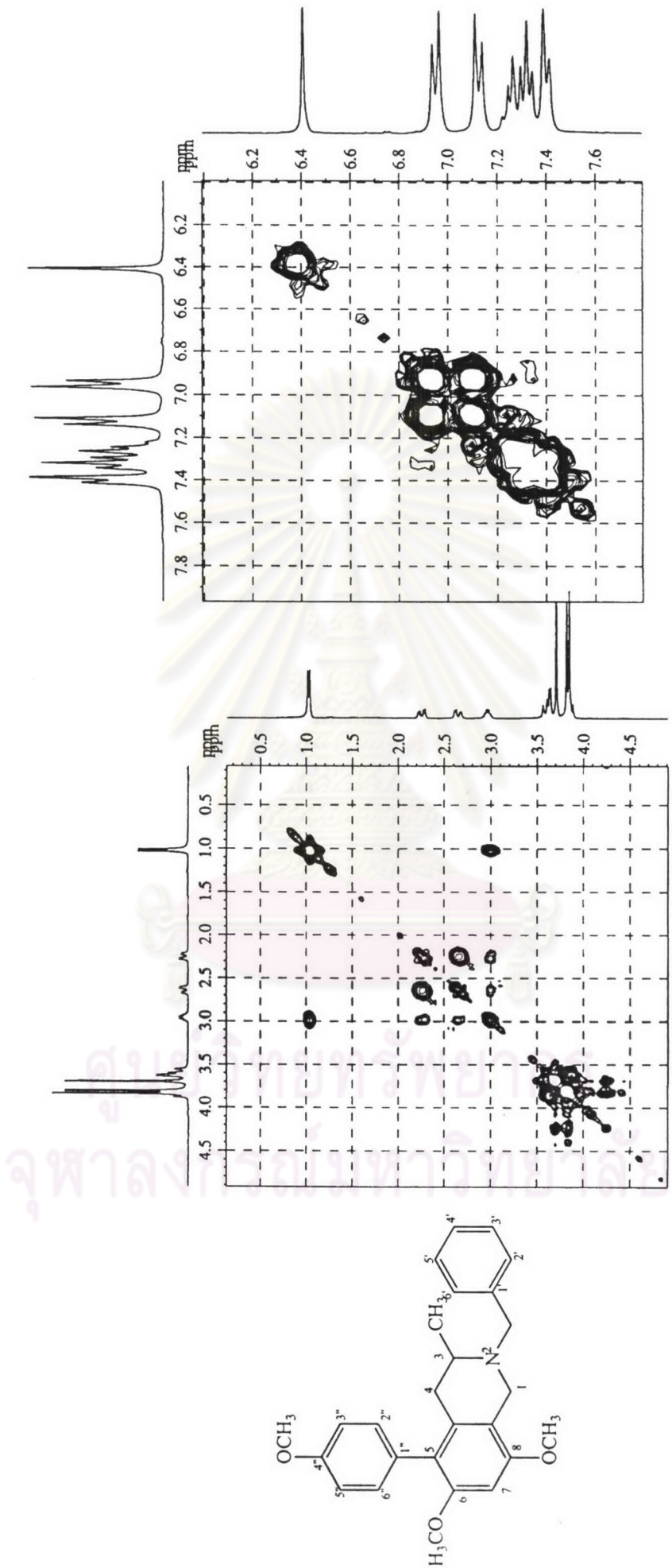


Figure 109 The 300 MHz <sup>1</sup>H-<sup>1</sup>H COSY spectrum of 5-(4'-methoxyphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-21-04) (Enlarged scale)



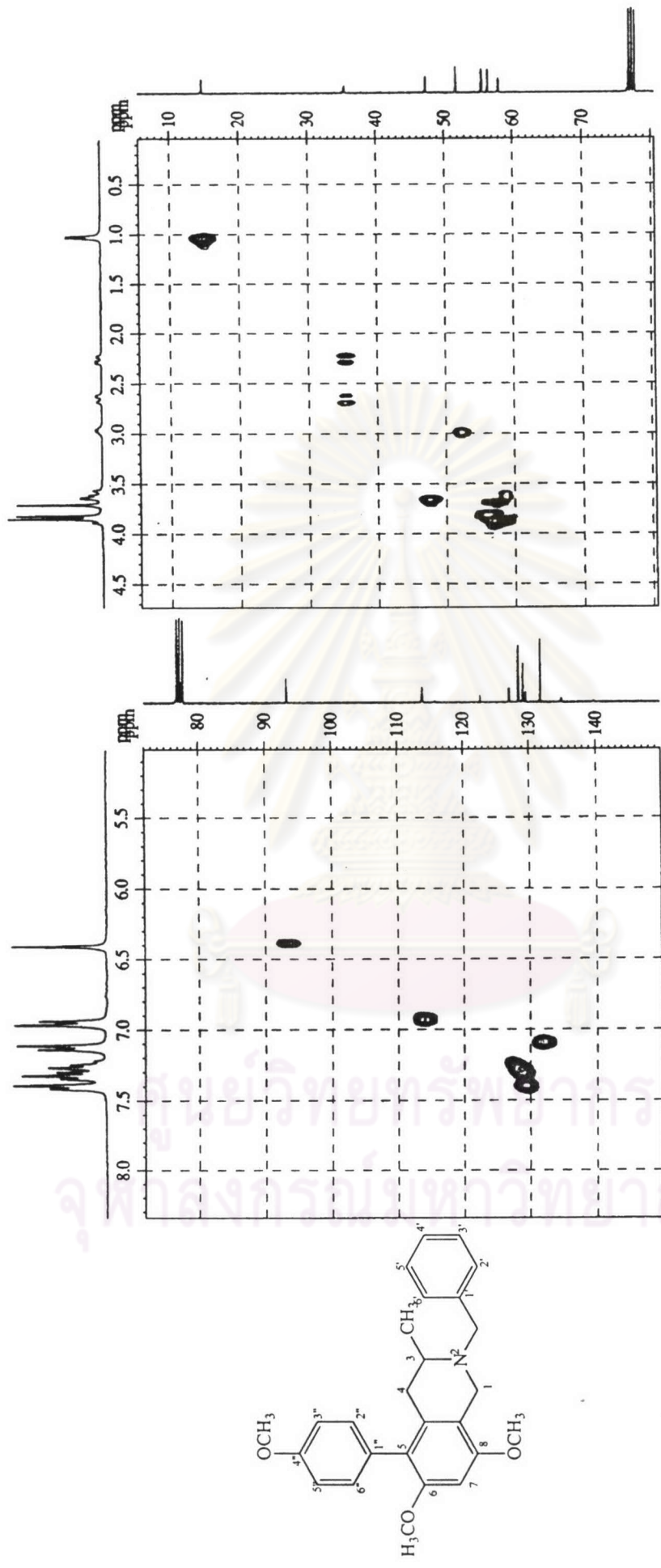


Figure 111 The 300 MHz HMQC spectrum of 5-(4'-methoxy phenyl)-2-(benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline(CU-21-04)) (Enlarged scale)

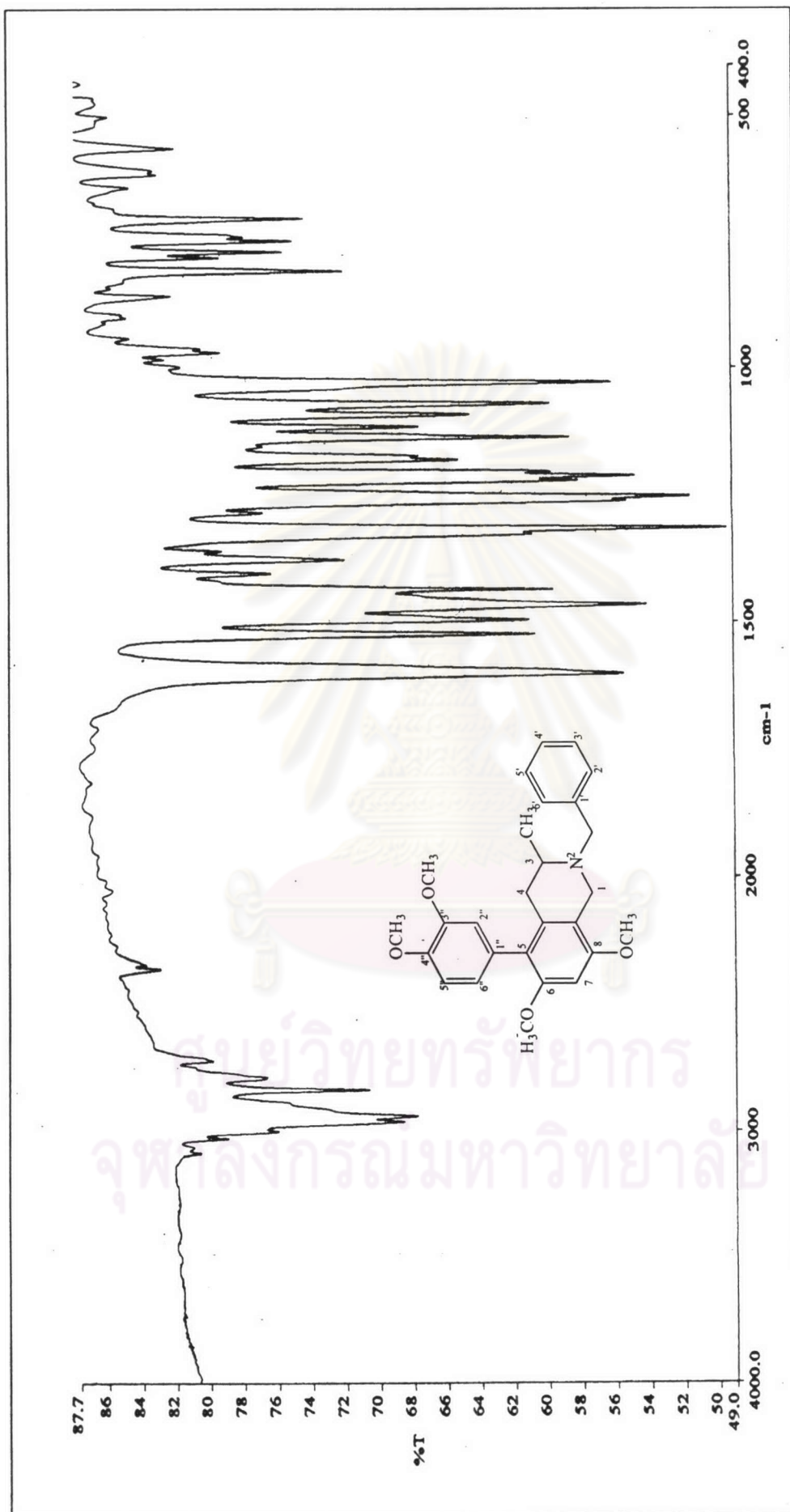


Figure 112 The IR spectrum (KBr) of 5-(3,4''-dimethoxy phenyl)-2- benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydro-isoquinoline (CU-21-05)

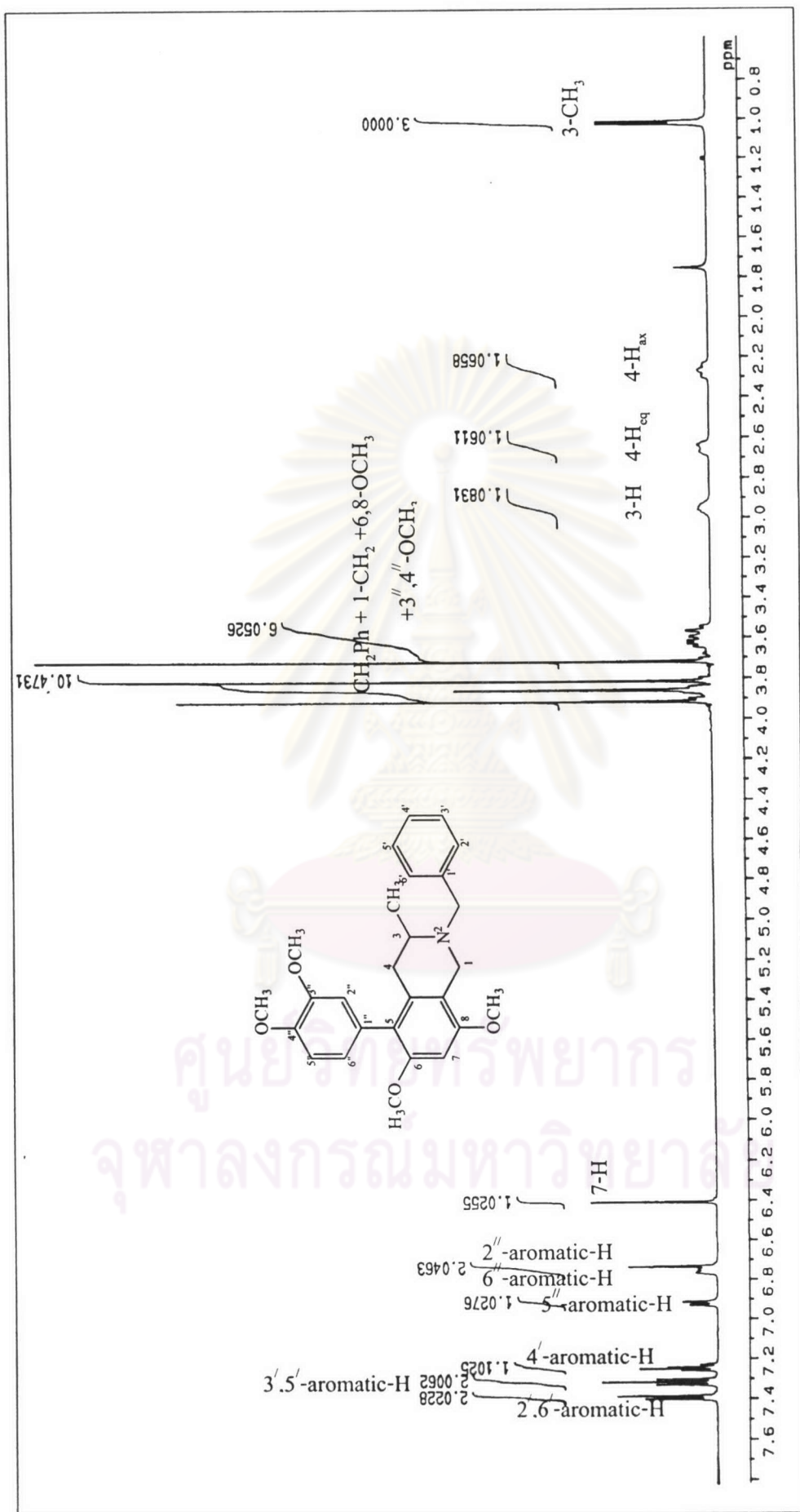


Figure 113 The 500 MHz <sup>1</sup>H-NMR spectrum of 5-(3'',4''-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline

(CU-21-05)

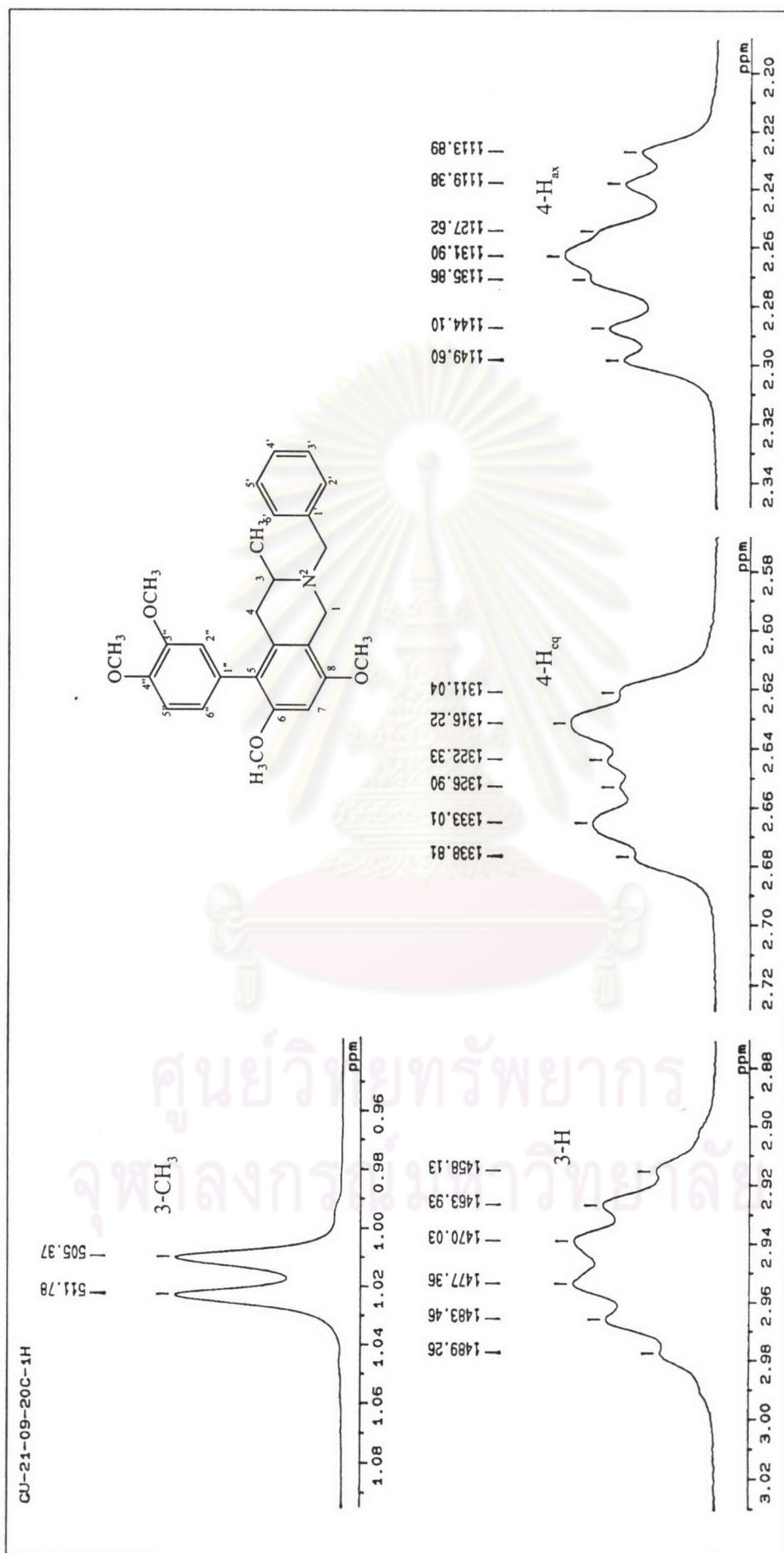


Figure 114 The 500 MHz <sup>1</sup>H-NMR spectrum of 5-(3',4'-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) (Enlarged scale)



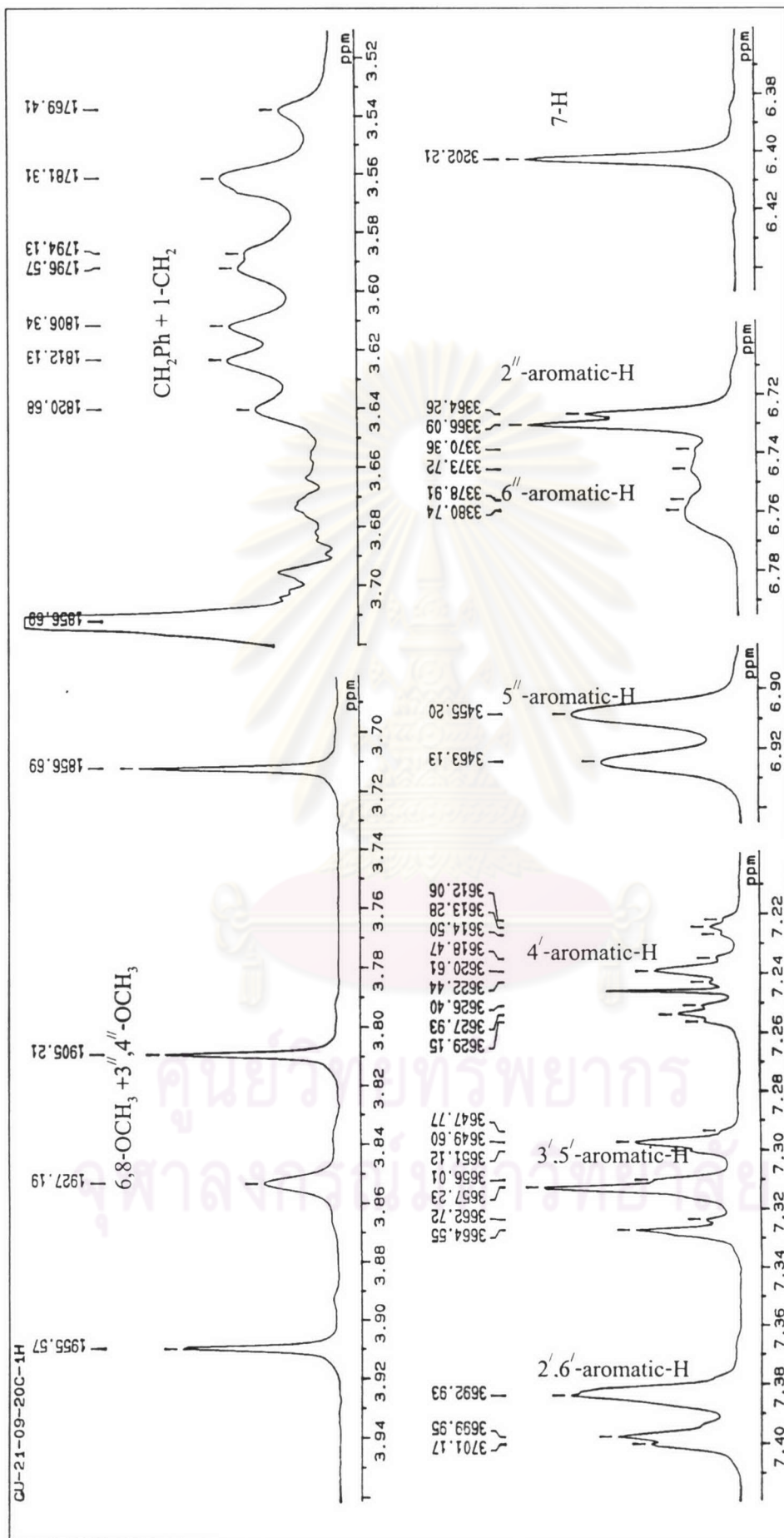


Figure 115 The 500 MHz <sup>1</sup>H-NMR spectrum of 5-(3,4-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline

(CU-21-05) ( Enlarged scale 2)

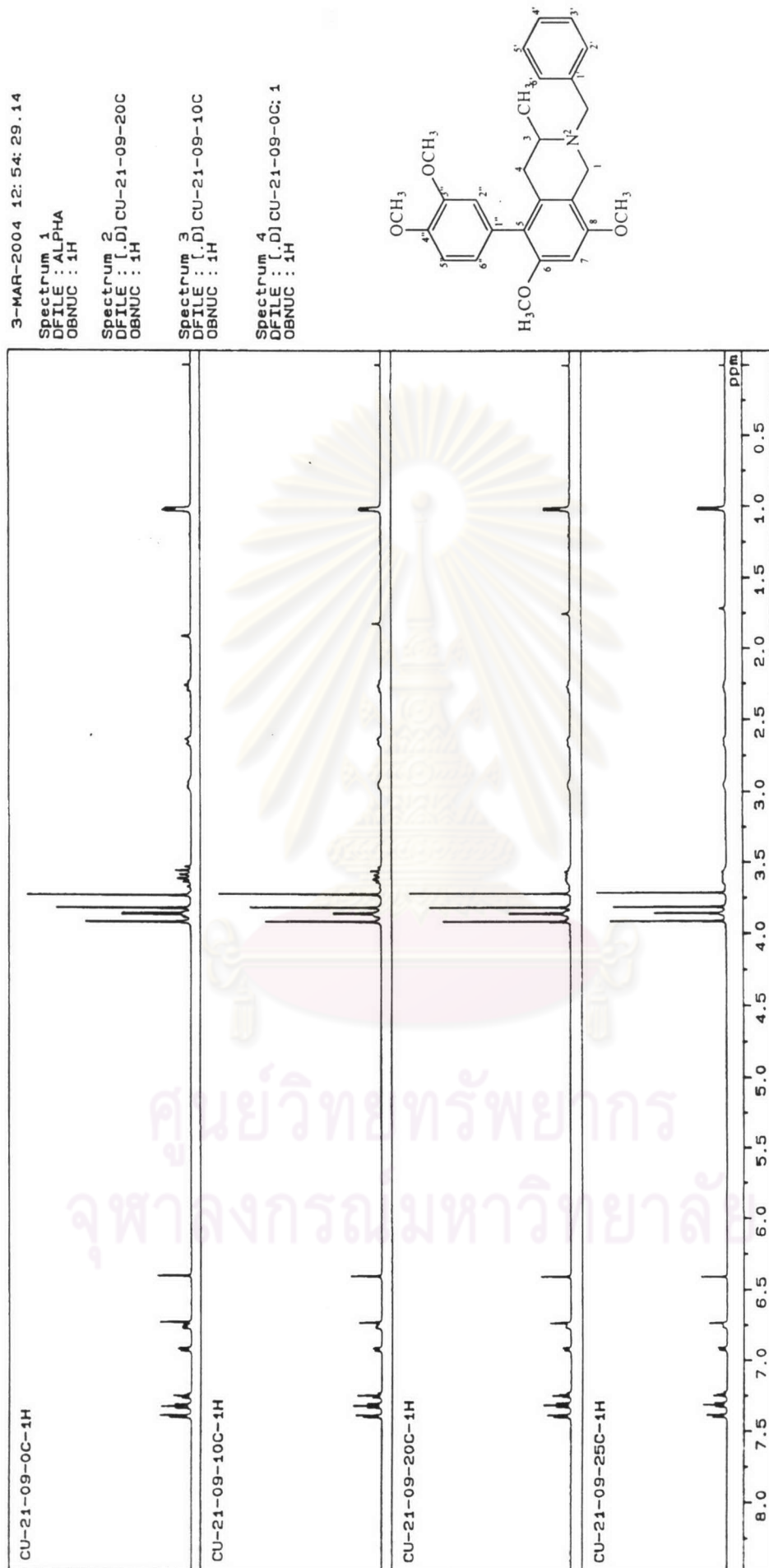


Figure 116 The 500 MHz  $^1\text{H-NMR}$  spectra of 5-(3',4'-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) at 25 °C, 20 °C, 10 °C, and 0 °C.



Figure 117 The 500 MHz <sup>1</sup>H-NMR spectra of 5-(3,4-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) at 25 °C, 20 °C, 10 °C, and 0 °C. (Enlarged scale)

CU-21-09-13C

3-MAR-2004 13: 23: 56.29

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 \* CHULALONGKORN UNIVERSITY \*  
 \* JNM-A500 \*  
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SF1LE : [D]CU-21-09-BCM  
 COMNT : CU-21-09-13C

EXMOD : SINGL  
 IRMOD : BCM  
 POINT : 16384  
 FREQU : 33898.31 Hz  
 SCANS : 1200  
 DUMMY : 4  
 ACQTM : 0.4833 sec  
 PD : 2.0000 sec  
 RGAIN : 23  
 PW1 : 4.75 usec  
 OBNUC : 13C  
 OBFRQ : 125.65 MHz  
 OBSSET : 127958.00 Hz

IRNUC : 1H  
 IRFRQ : 500.00 MHz  
 IRSET : 162410.00 Hz  
 IRATN : 120  
 IRBPW : 55.0 usec  
 IRBP1 : 30  
 IRBP2 : 6  
 IRBNS : 0

ADBIT : 16  
 CTEMP : 20.0 C  
 CSVPD : 12 Hz  
 SLVNT : CDCL3  
 RESOL : 2.07 Hz  
 B1FVL : 2.07 Hz  
 REFVL : 77.00 ppm  
 XE : 22134.04 Hz  
 XS : 1696.57 Hz

OPERATOR :

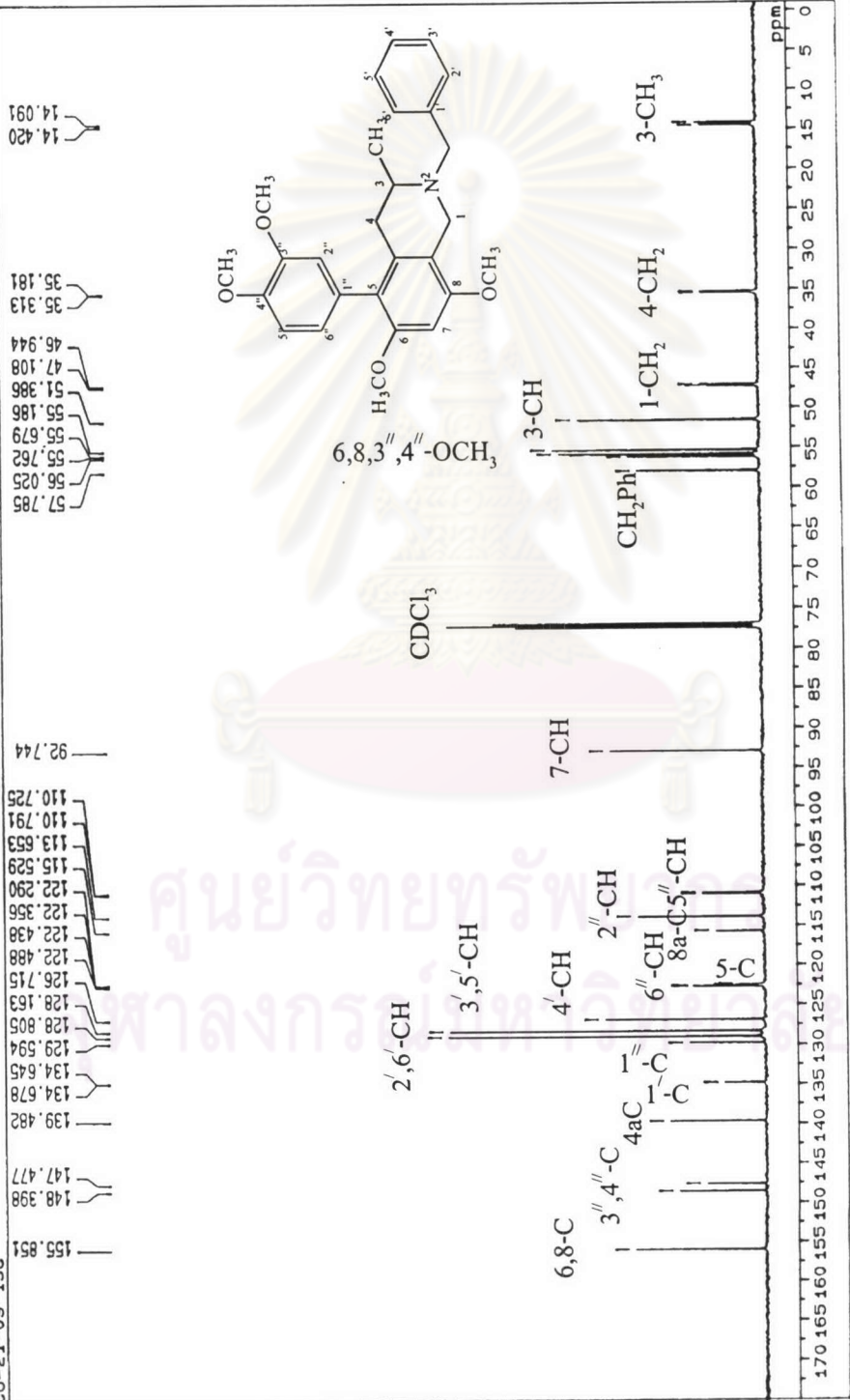


Figure 118 The 125 MHz <sup>13</sup>C-NMR spectrum of 5-(3,4'-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05)

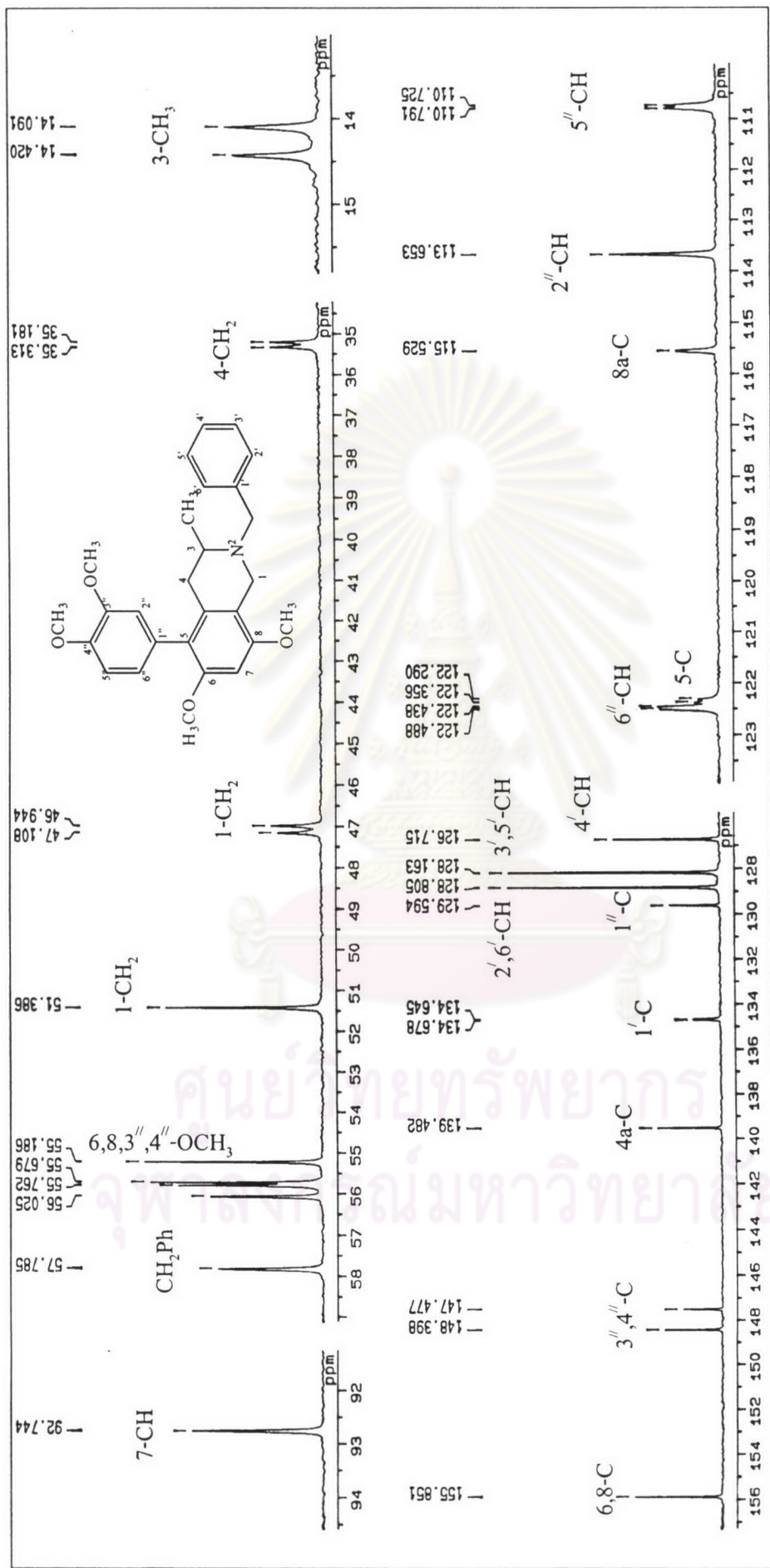


Figure 119 The 125 MHz <sup>13</sup>C-NMR spectrum of 5-(3,4'-dimethoxy phenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) (Enlarged scale)

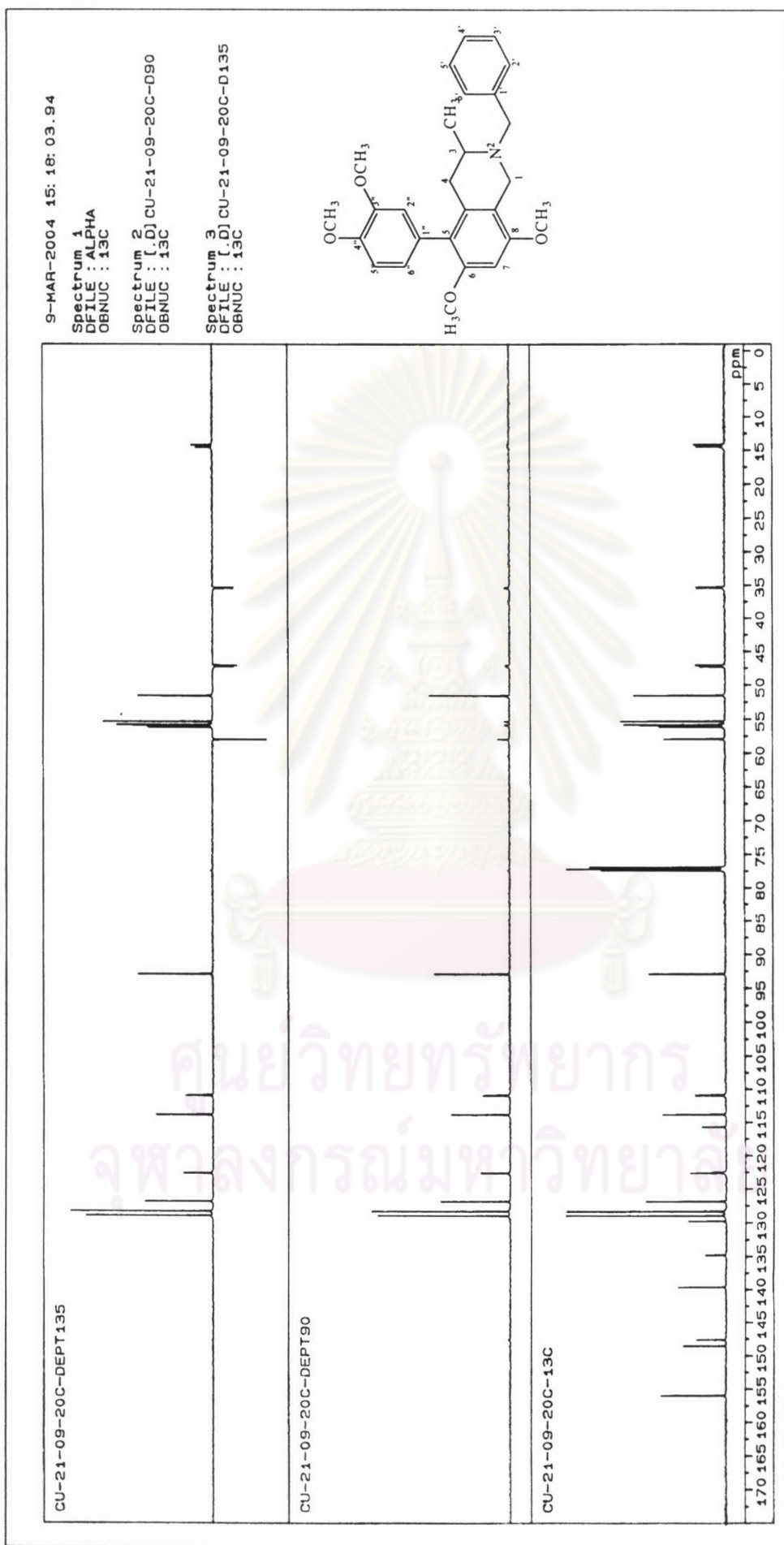


Figure 120 The 125 MHz DEPT -90 and 135 spectrum of 5-(3',4''-dimethoxy phenyl)-2- benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroiso-quinoline (CU-21-05)

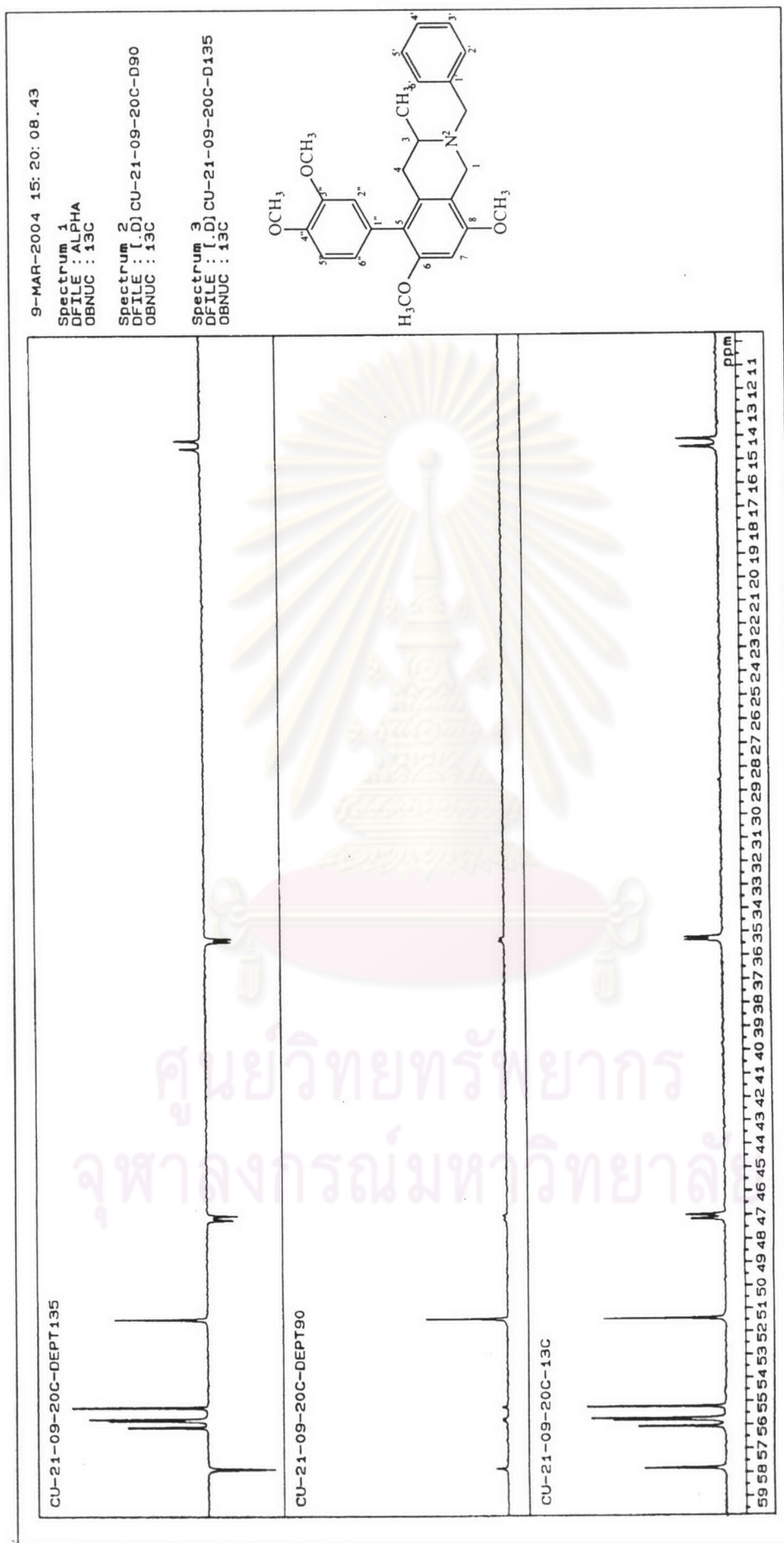


Figure 121 The 125 MHz DEPT -90 and 135 spectrum of 5-(3,4'-dimethoxy phenyl)-2- benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline (CU-21-05) (Enlarged scale 1)

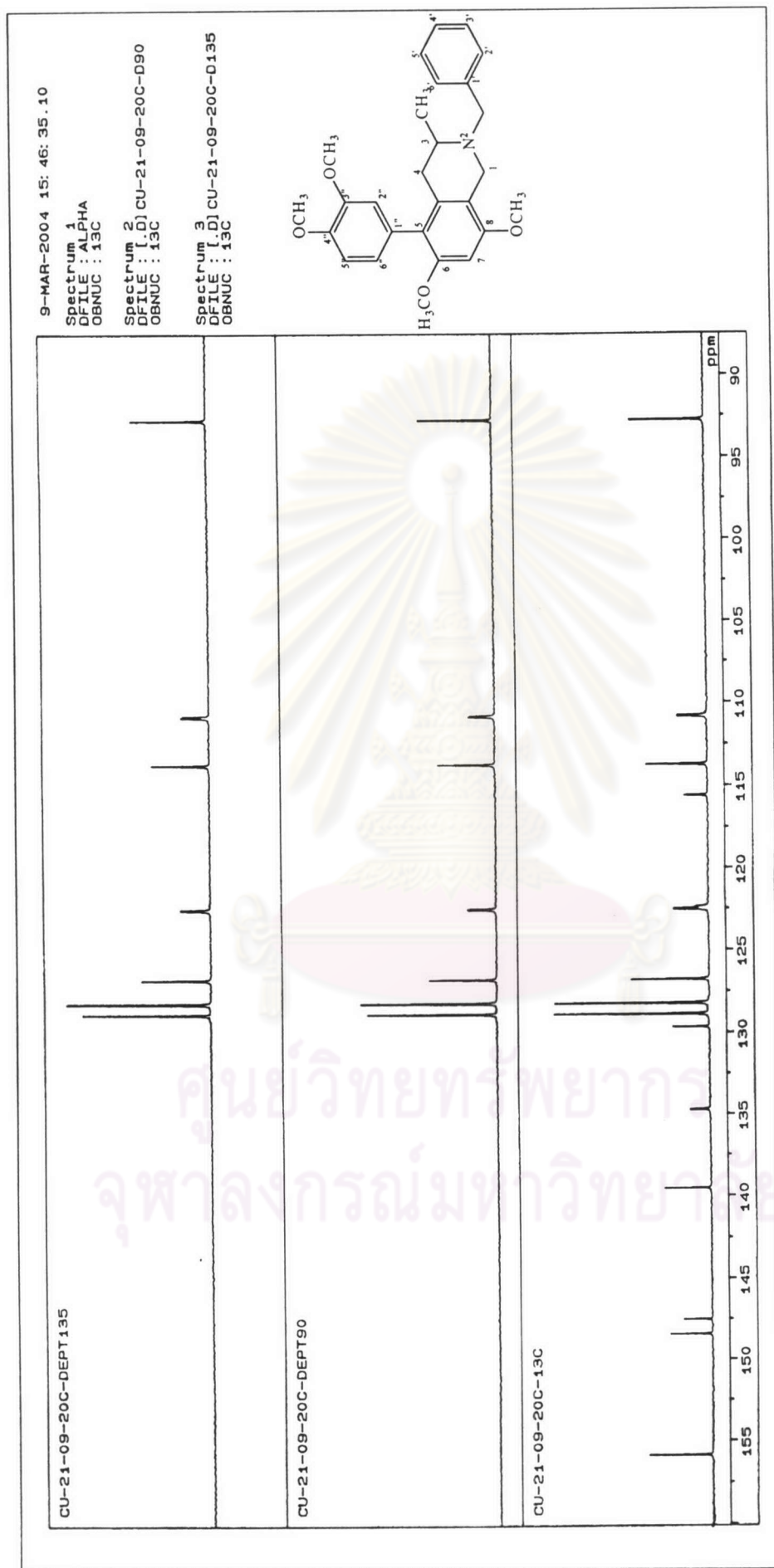


Figure 122 The 125 MHz DEPT -90 and 135 spectrum of 5-(3',4'-dimethoxy phenyl)-2- benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) (Enlarged scale 2)



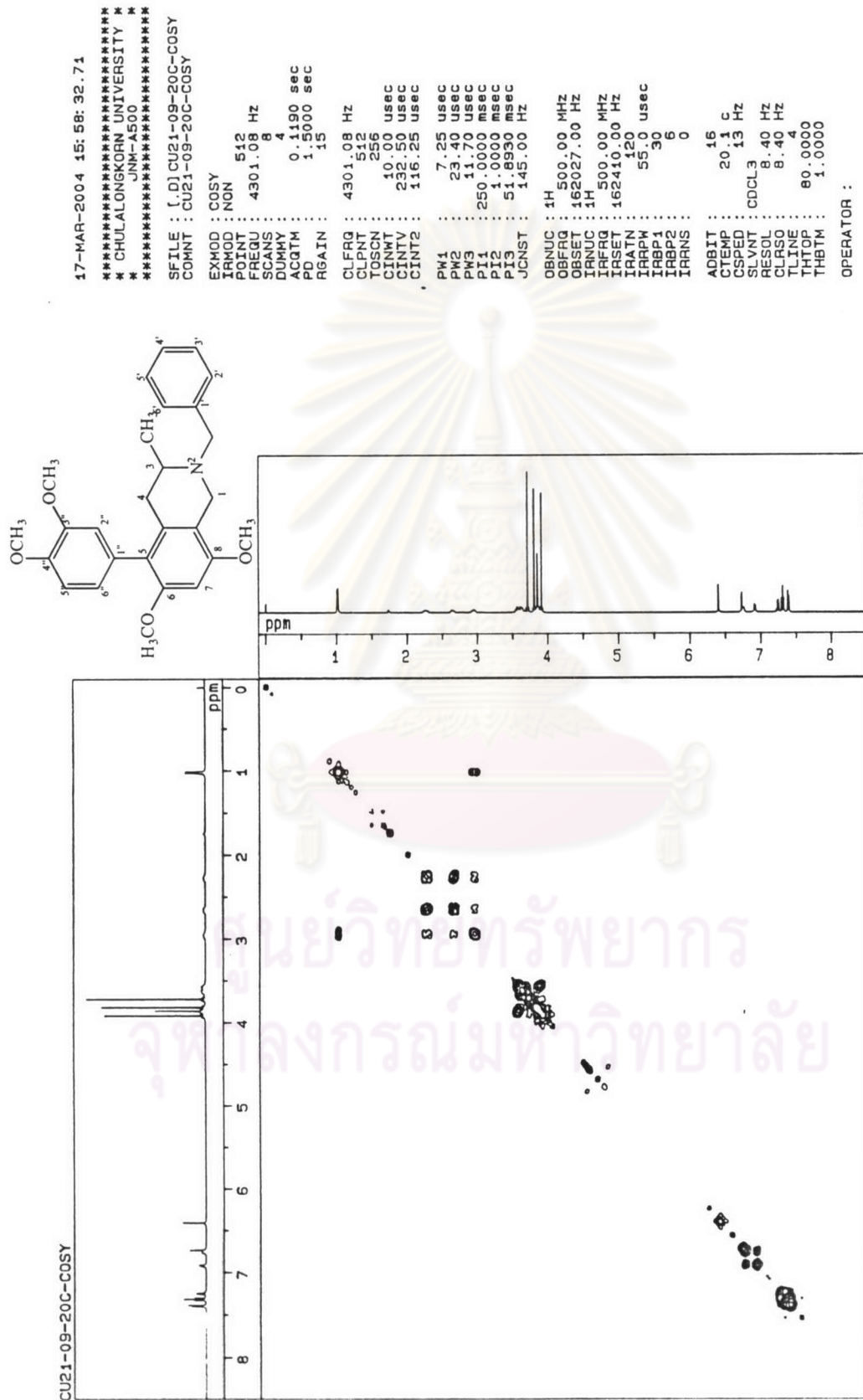


Figure 123 The 500 MHz HH COSY spectrum of 5-(3,4-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline

(CU-21-05)

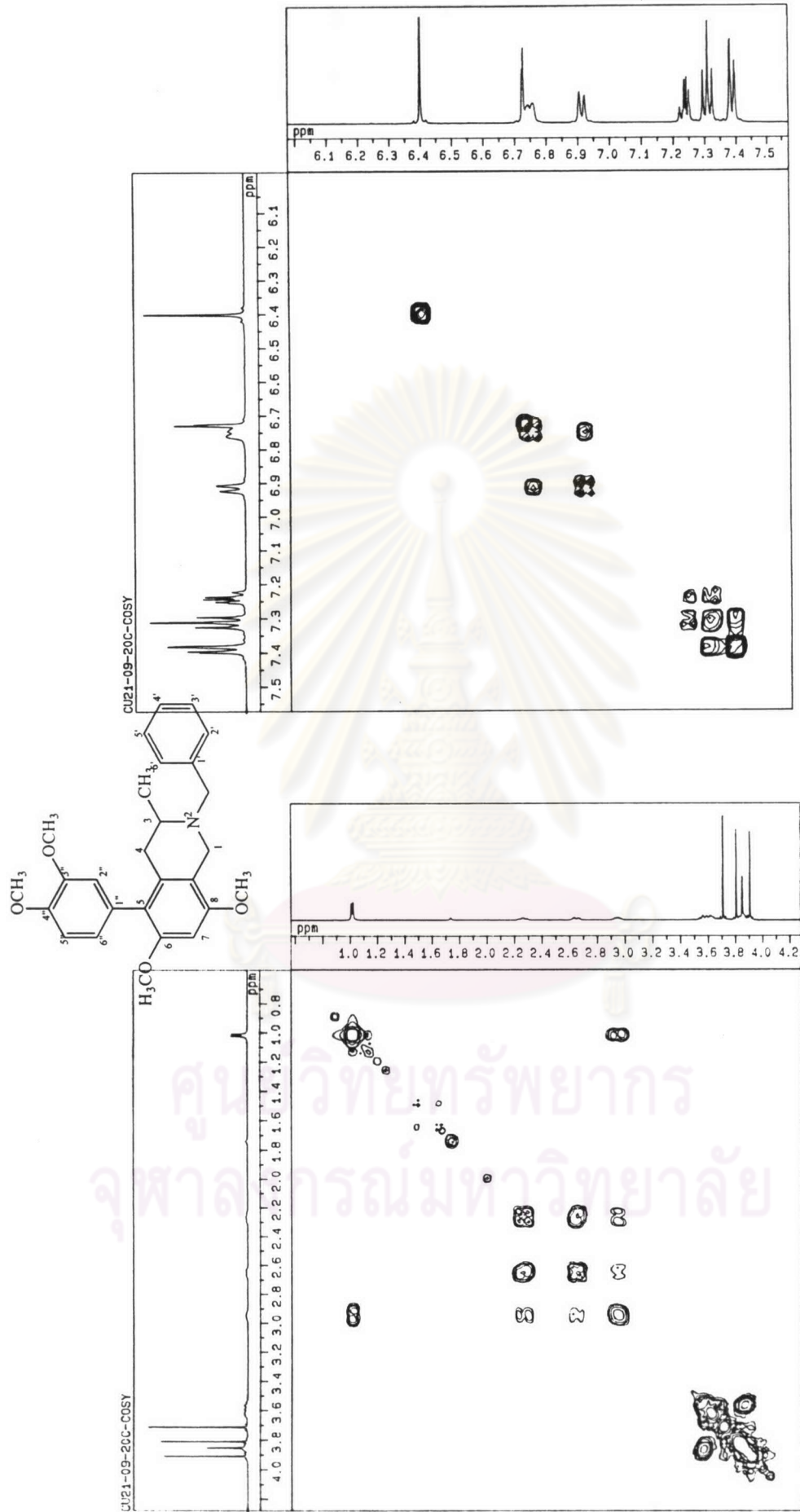


Figure 124 The 500 MHz HH COSY spectrum of 5-(3',4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline

(CU-21-05) (Enlarged scale)

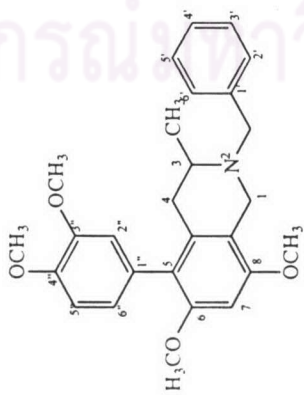
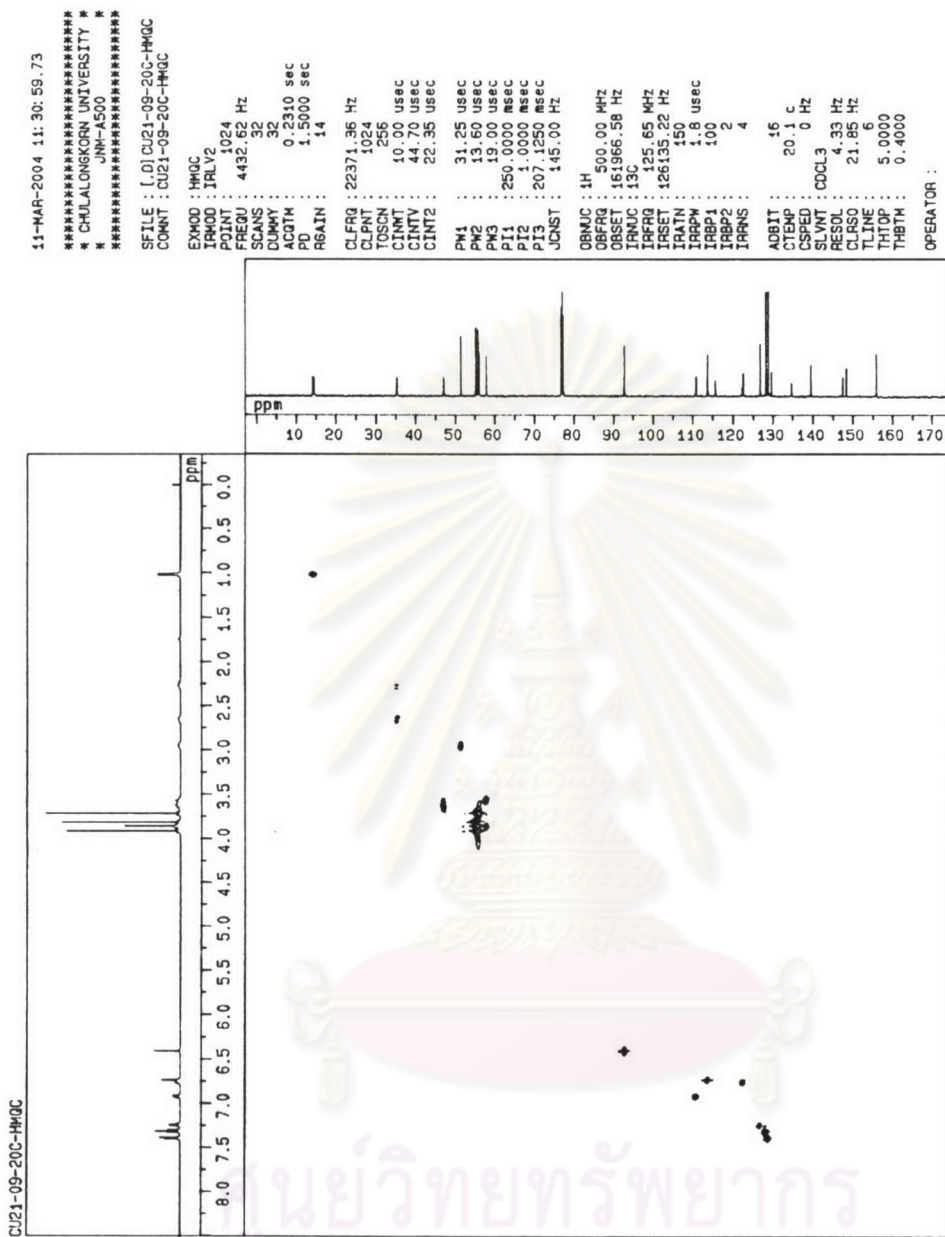


Figure 125 The 500 MHz HMQC spectrum of 5-(3,4-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline

(CU-21-05)

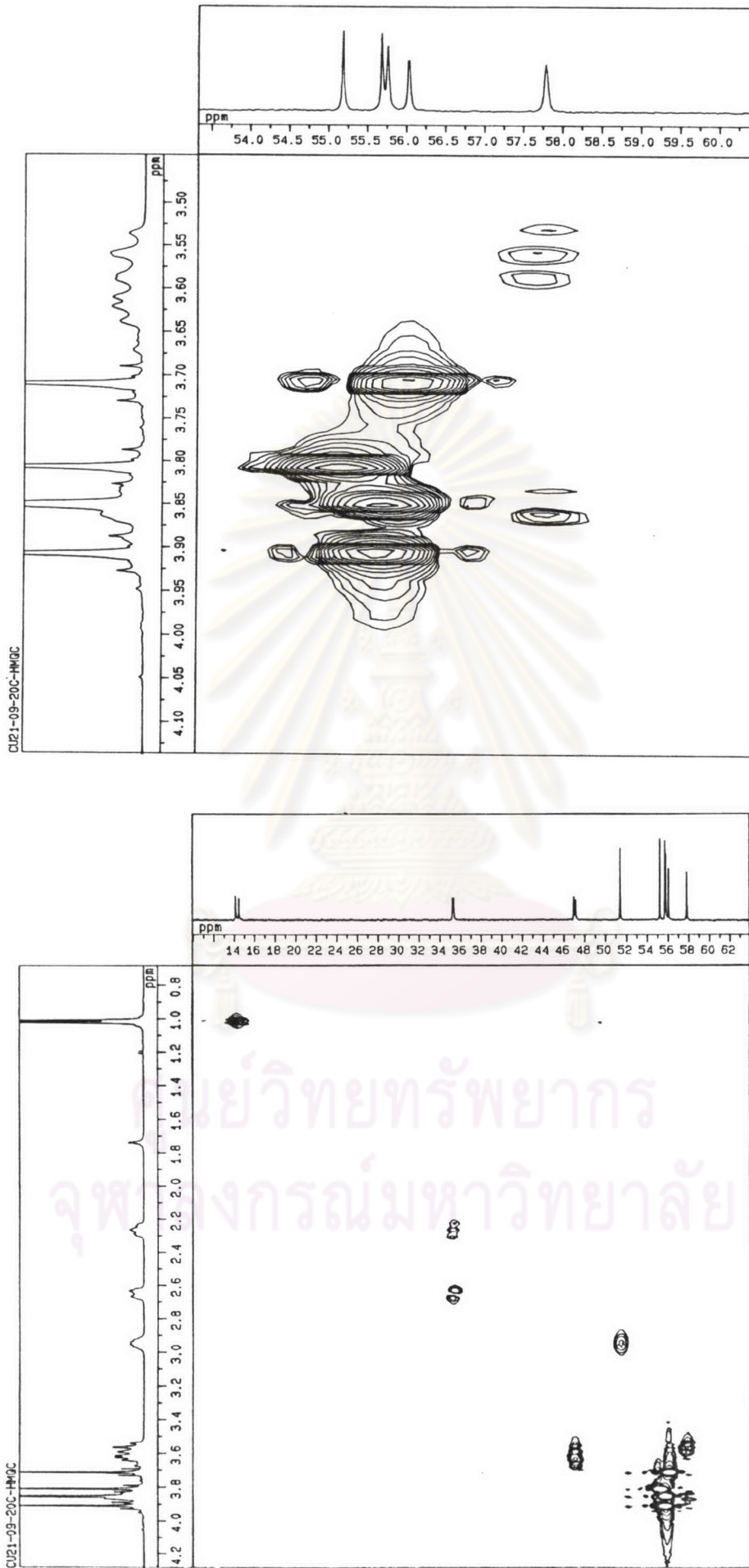


Figure 126 The 500 MHz HMQC spectrum of 5-(3',4'-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) (Enlarged scale 1)

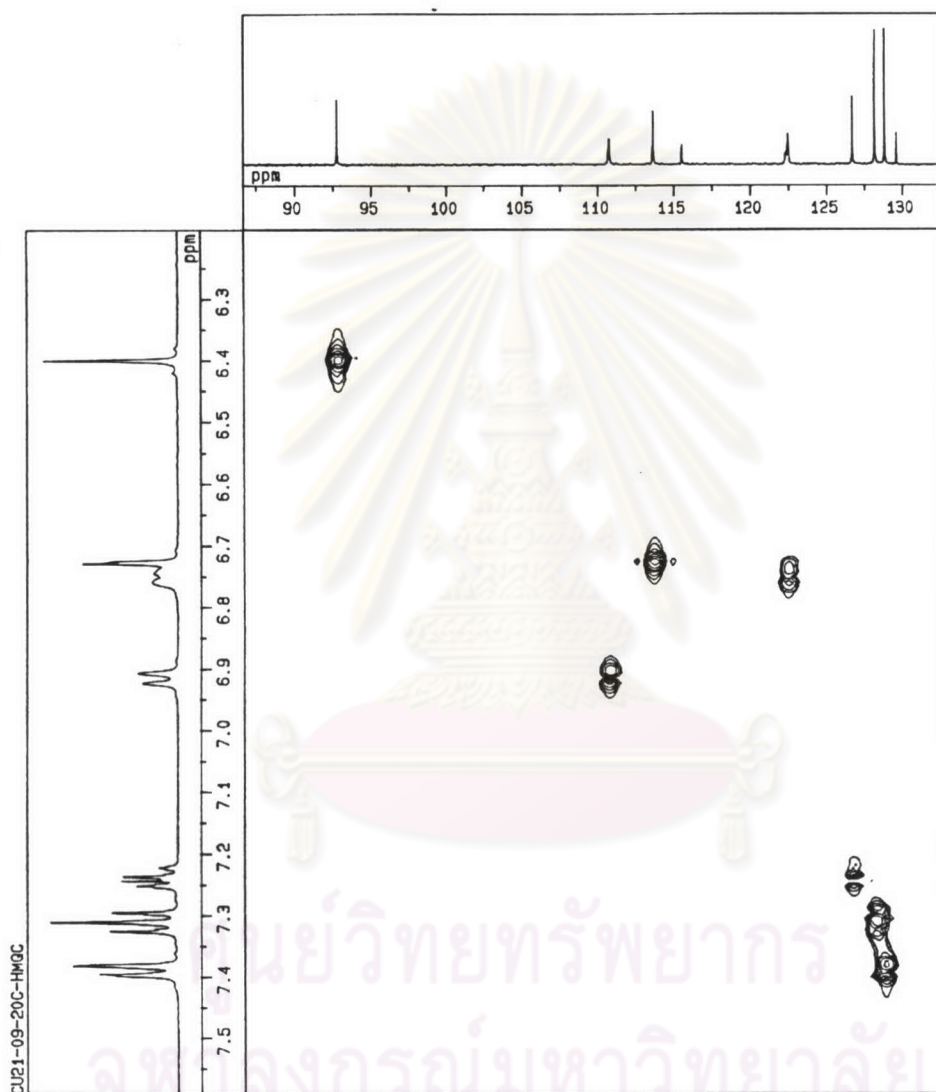


Figure 127 The 500 MHz HMQC spectrum of 5-(3',4'-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) (Enlarged scale 2)

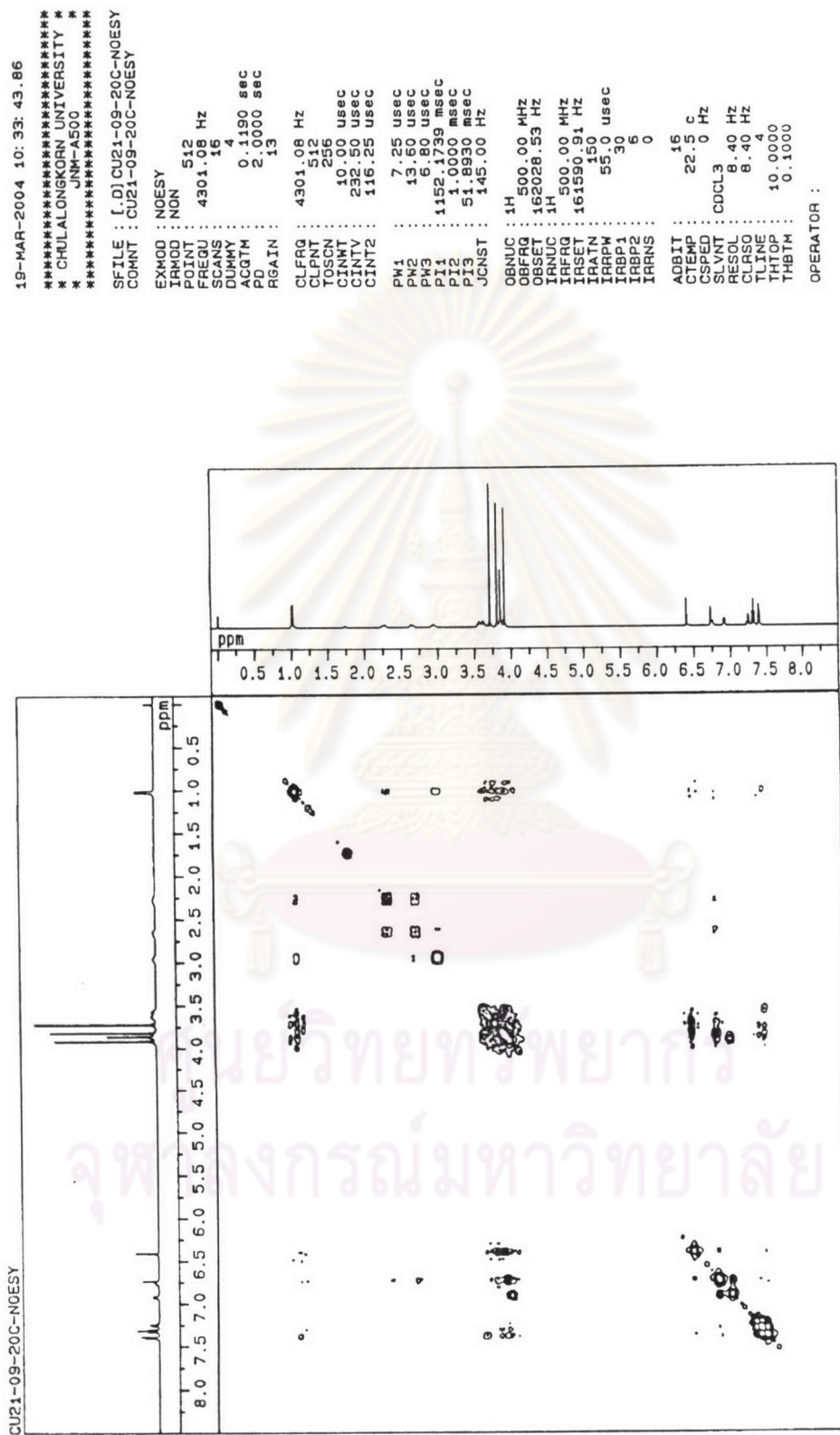


Figure 128 The 500 MHz NOESY spectrum of 5-(3',4'-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline

(CU-21-05)

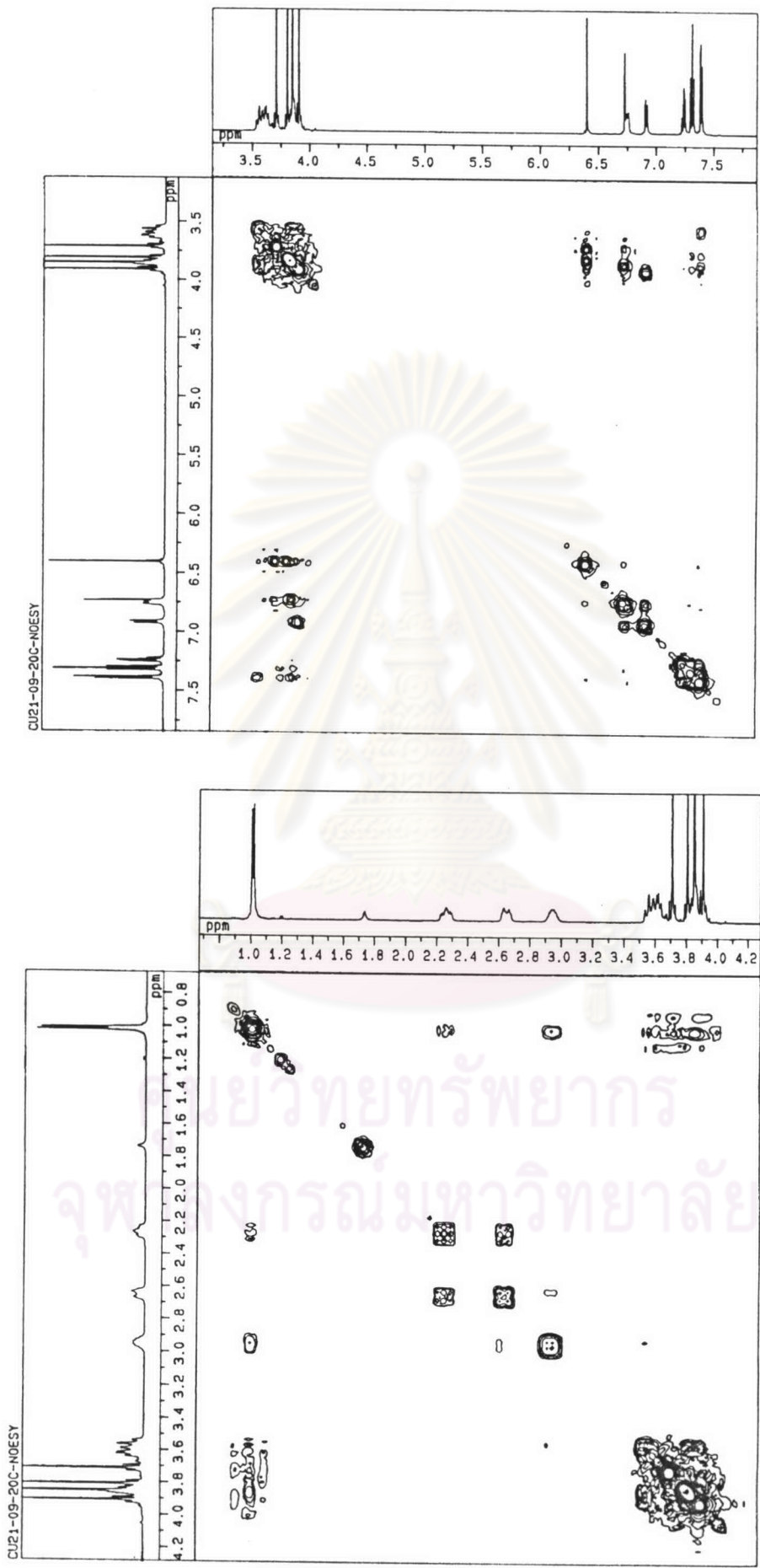


Figure 129 The 500 MHz NOESY spectrum of 5-(3,4'-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-21-05) (Enlarged scale)

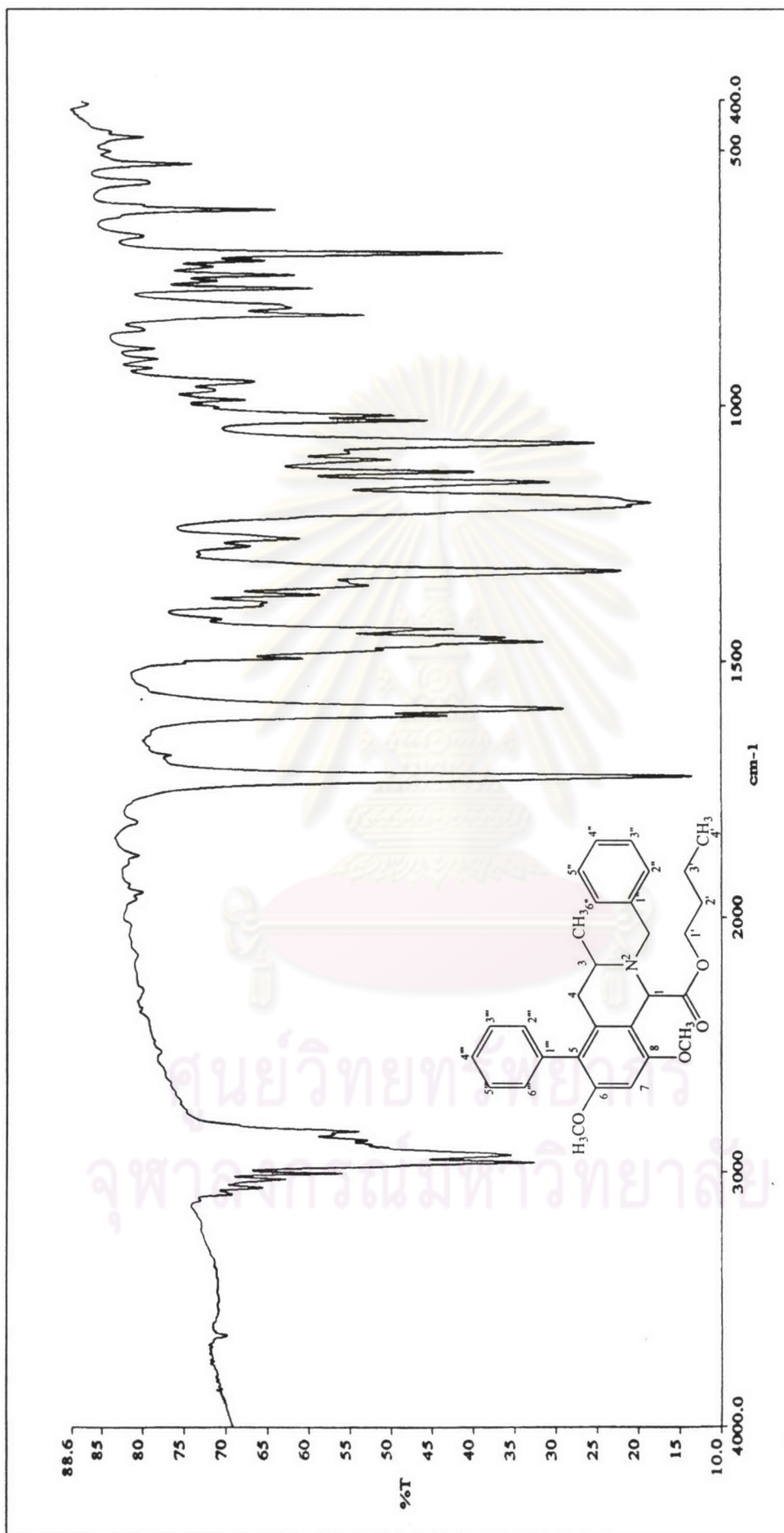


Figure 130 The IR spectrum (KBr) of butyl-(5-phenyl)-2-(benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate

(CU-21-06)



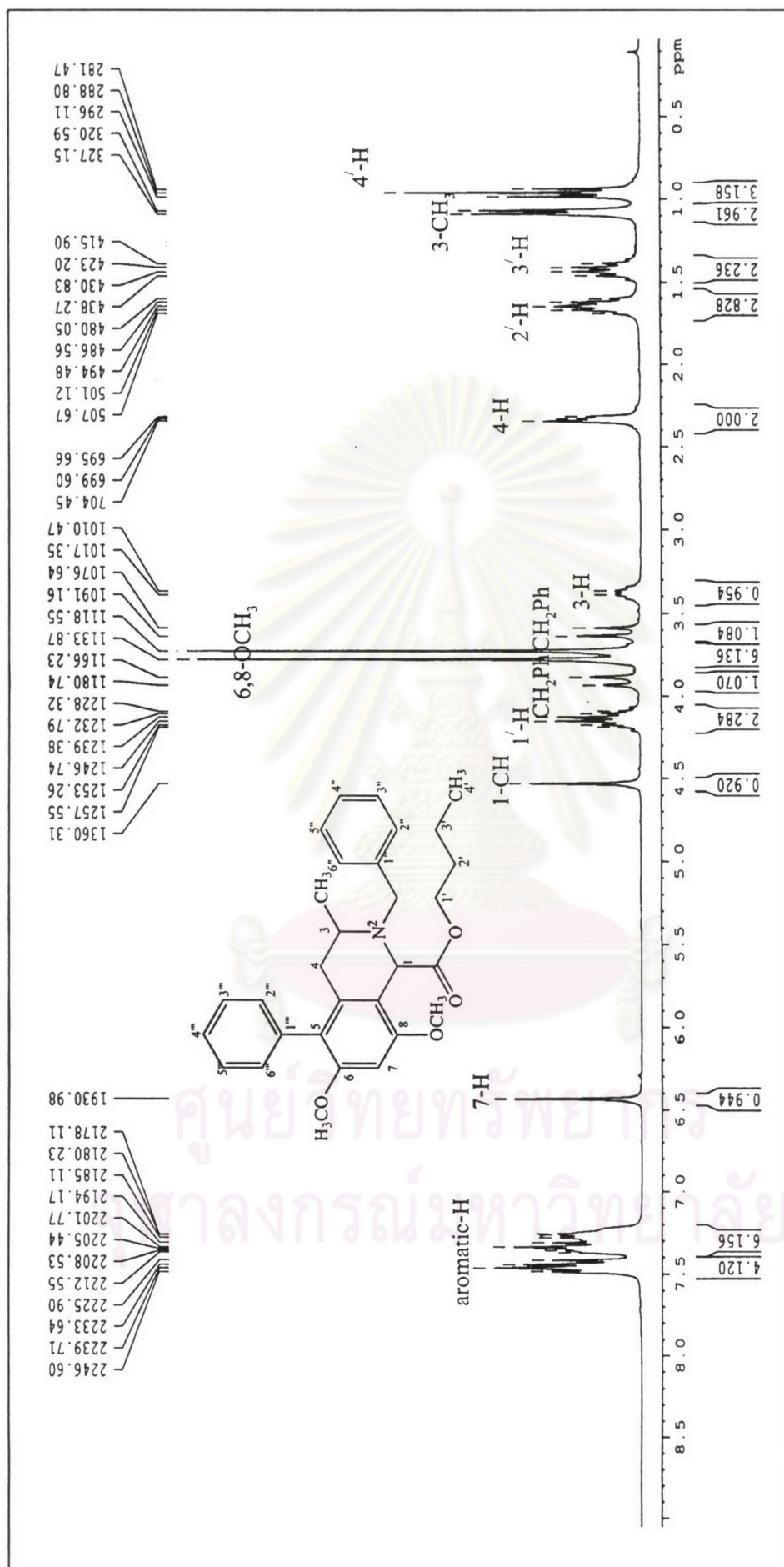


Figure 131 The 300 MHz <sup>1</sup>H-NMR spectrum of butyl-(5-phenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate

(CU-21-06)

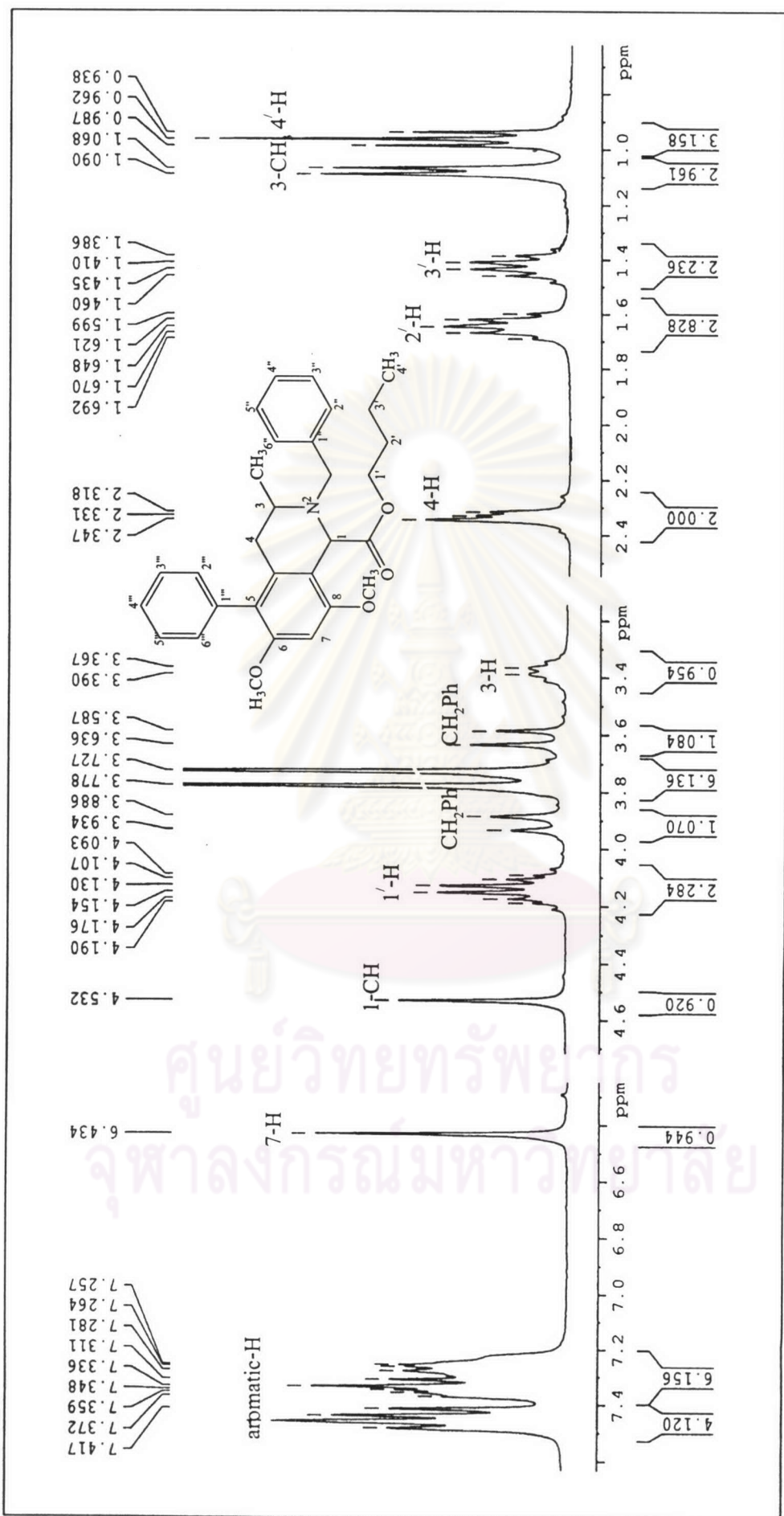


Figure 132 The 300 MHz <sup>1</sup>H-NMR spectrum of butyl-(5-phenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-06) (Enlarged scale)

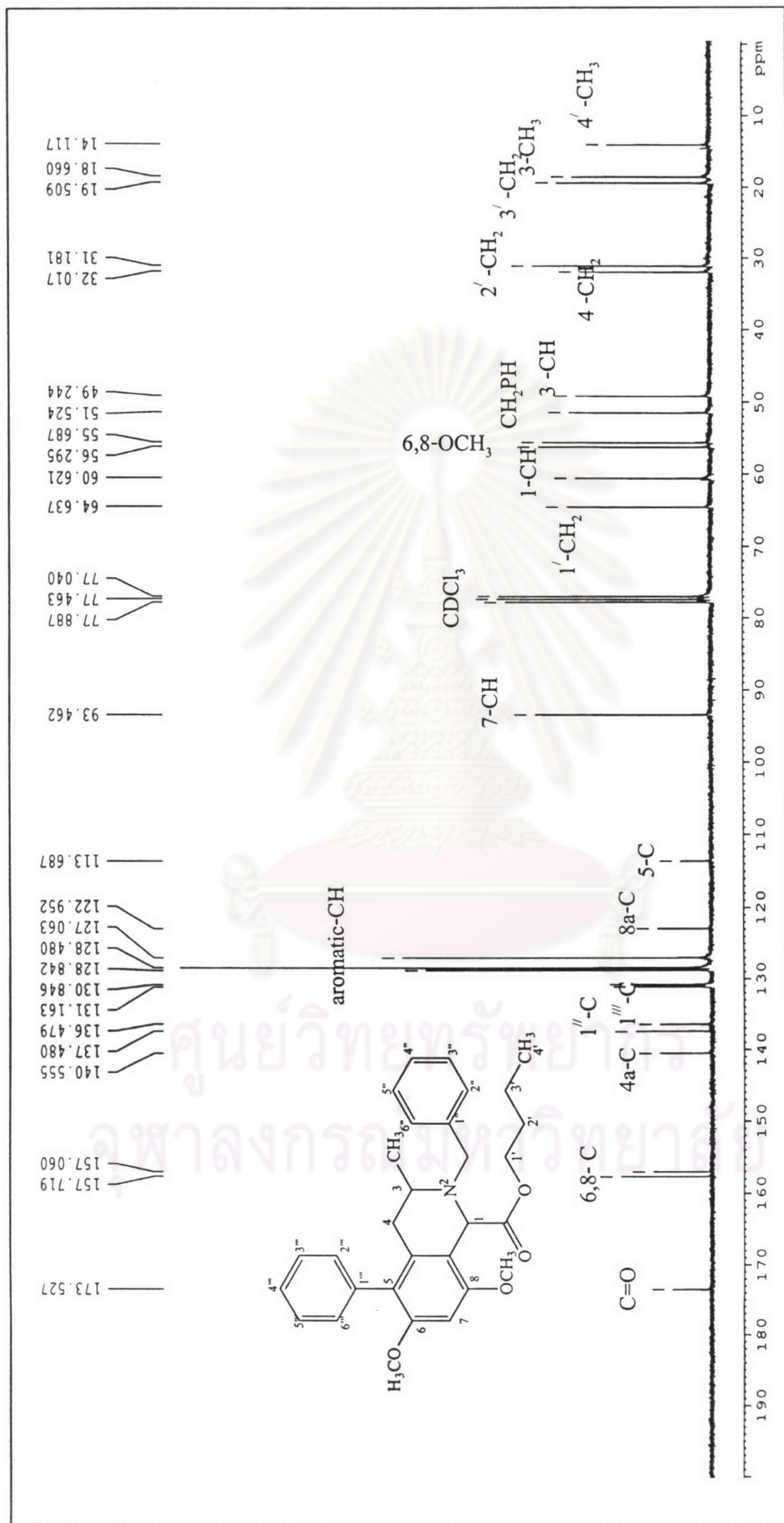


Figure 133 The 75 MHz <sup>13</sup>C-NMR spectrum of butyl-(5-phenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate

(CU-21-06)

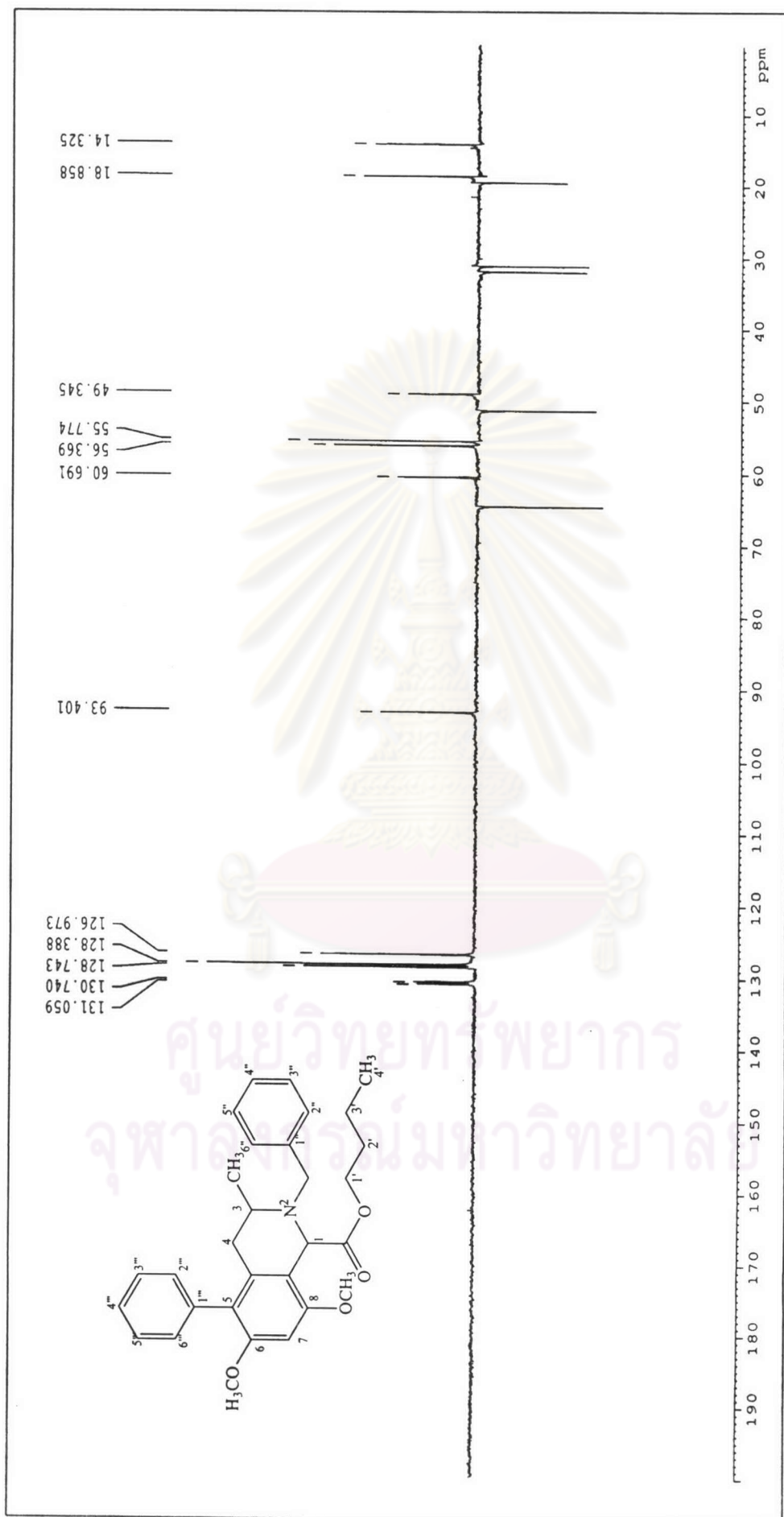


Figure 134 The 75 MHz DEPT 135 spectrum of butyl-(5-phenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-06)

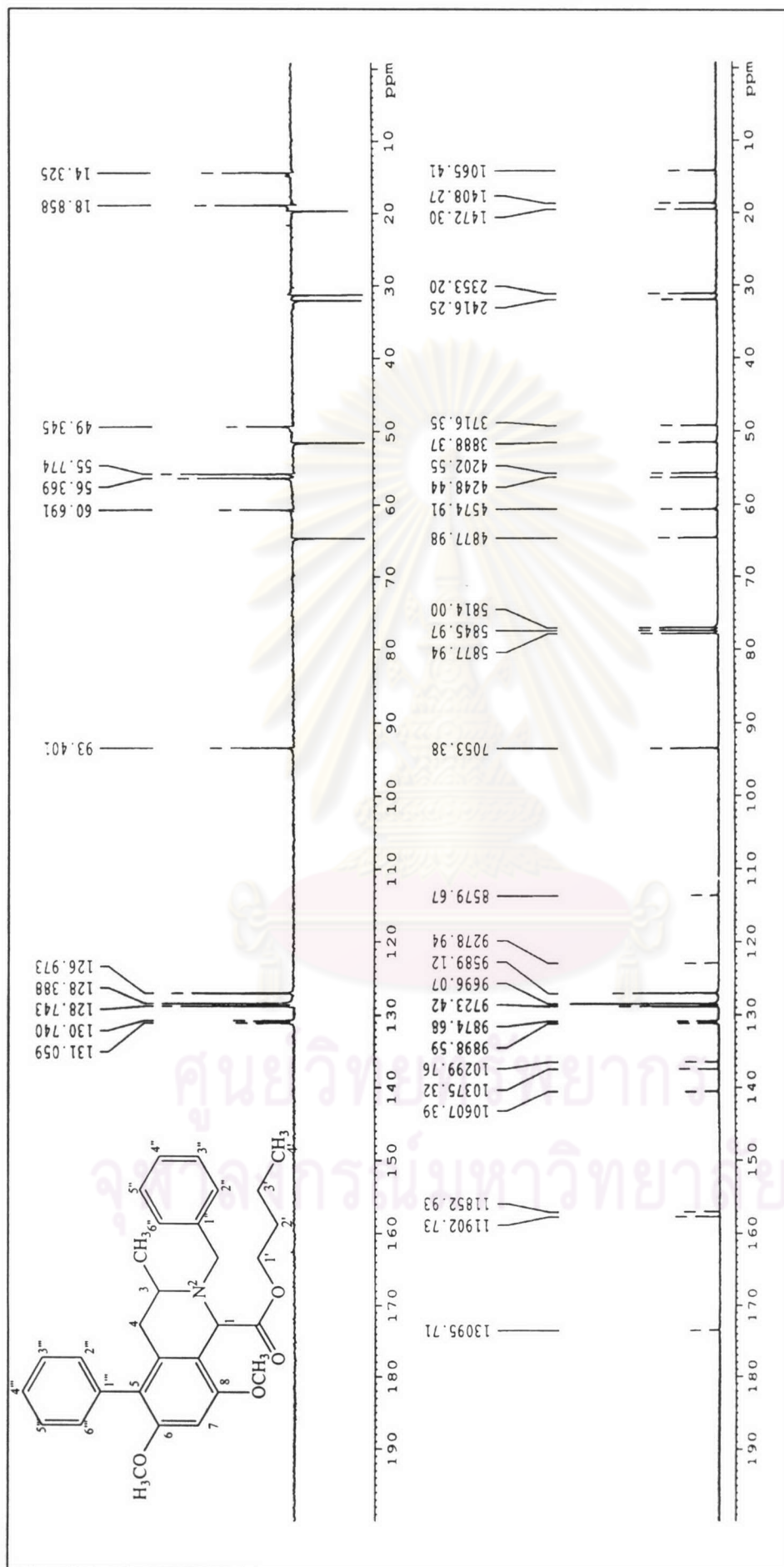


Figure 135 The 75 MHz DEPT 135 and <sup>13</sup>C NMR spectrum comparison of butyl-(5-phenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-06)

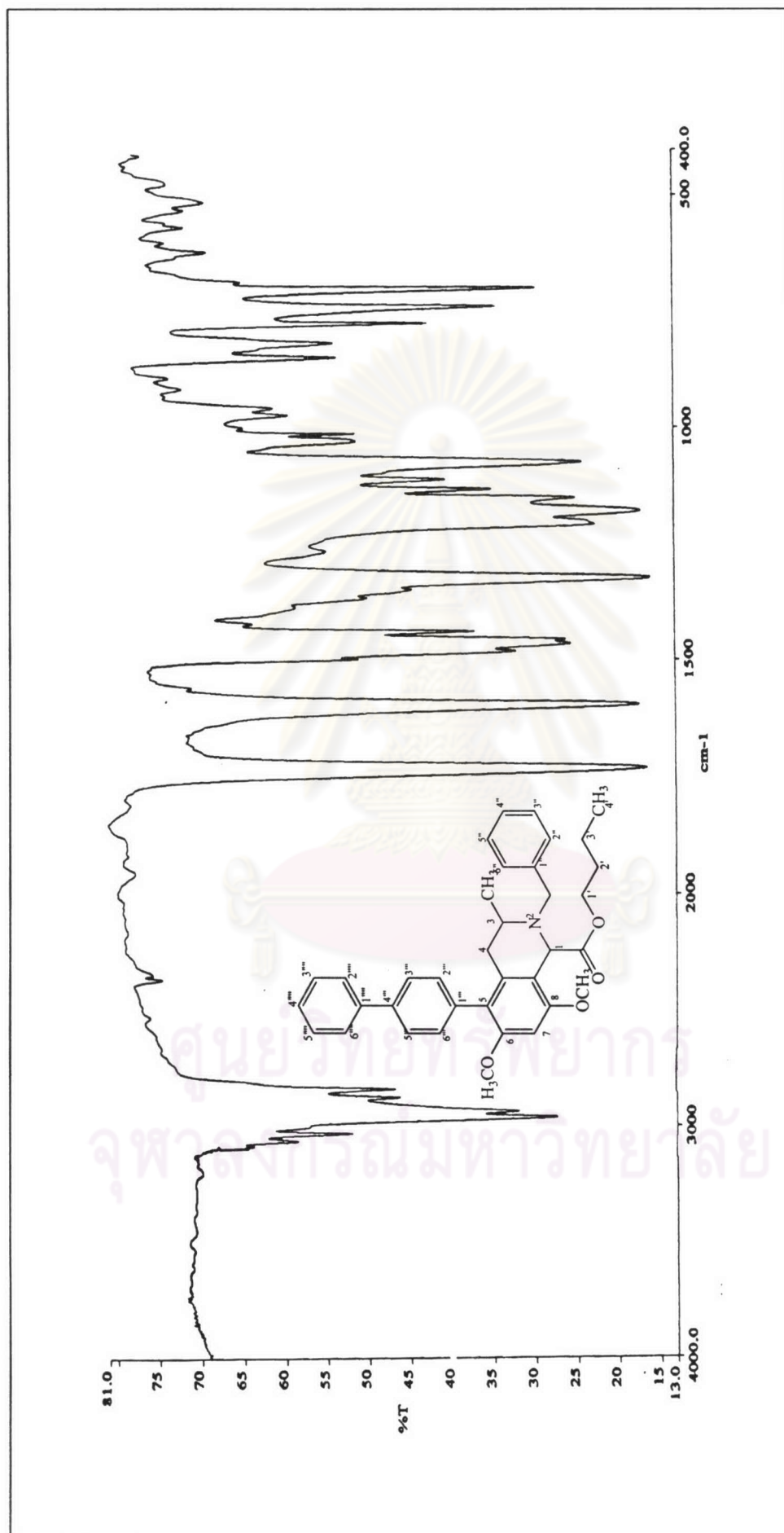


Figure 136 The IR spectrum (KBr) of butyl-5-(4'-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-

21-07)

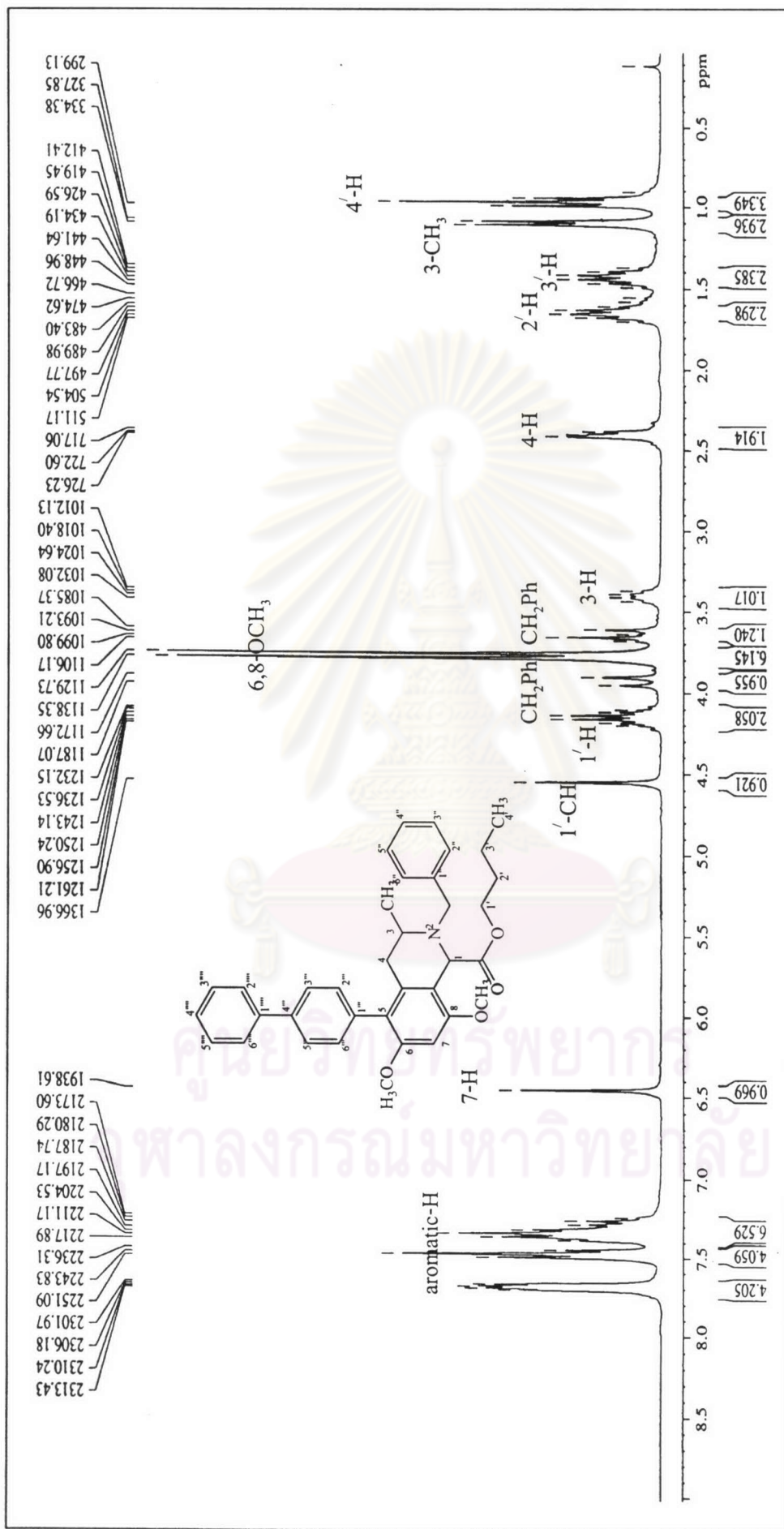


Figure 137 The 300 MHz <sup>1</sup>H-NMR spectrum of butyl-5-(4'-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07)

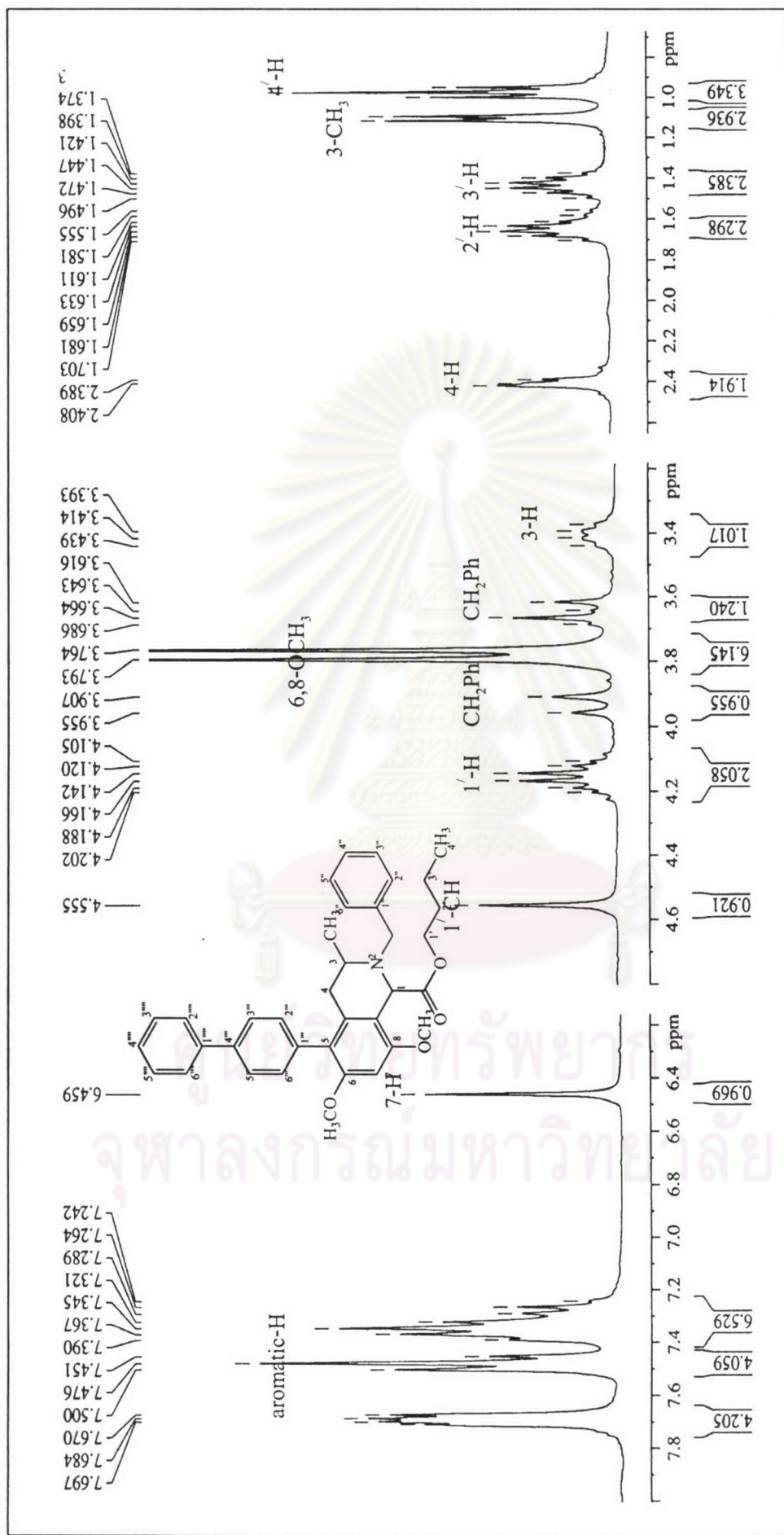


Figure 138 The 300 MHz <sup>1</sup>H-NMR spectrum of butyl-5-(4-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07) (Enlarged scale)



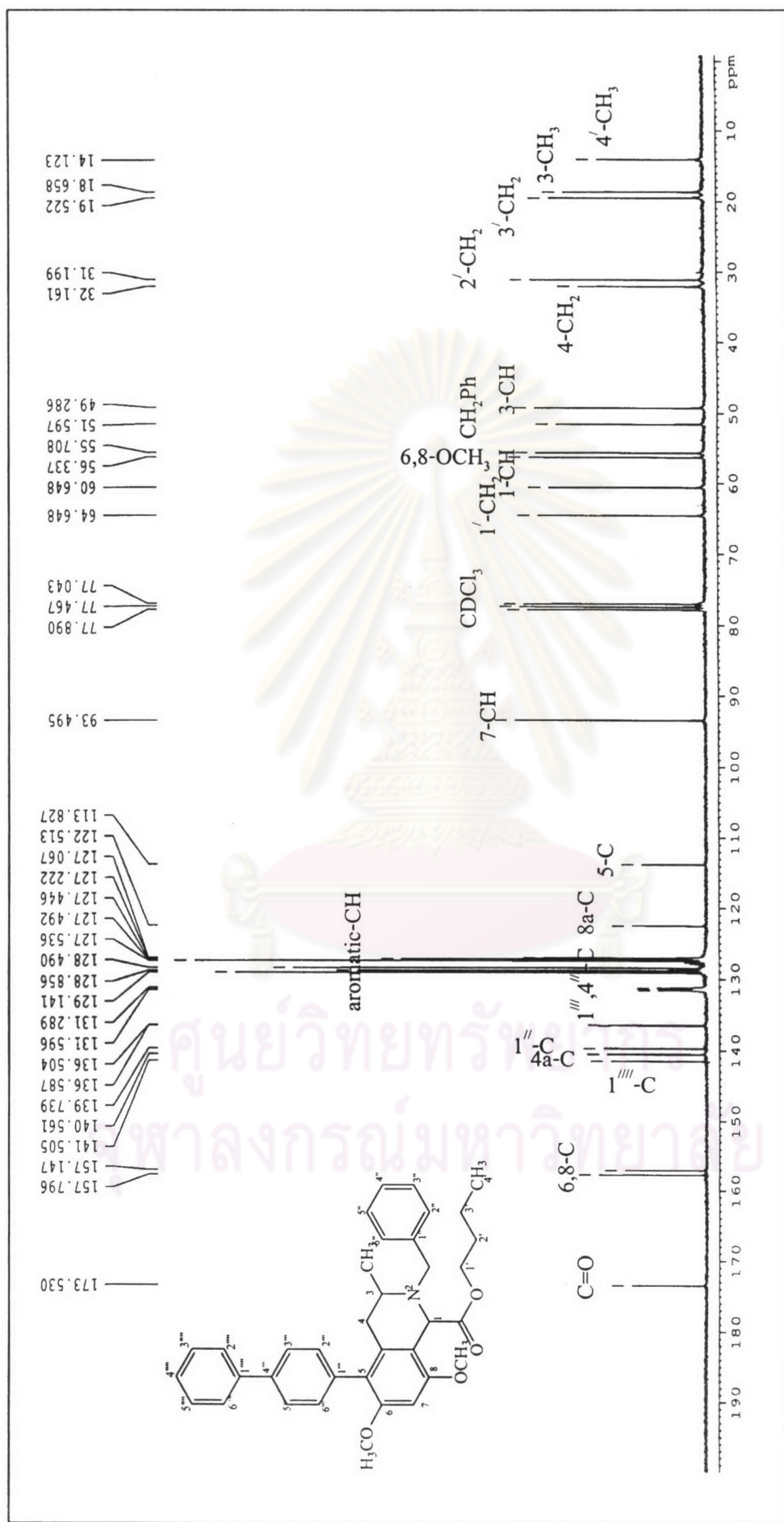


Figure 139 The 75 MHz  $^{13}\text{C}$ -NMR spectrum of butyl-5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07)

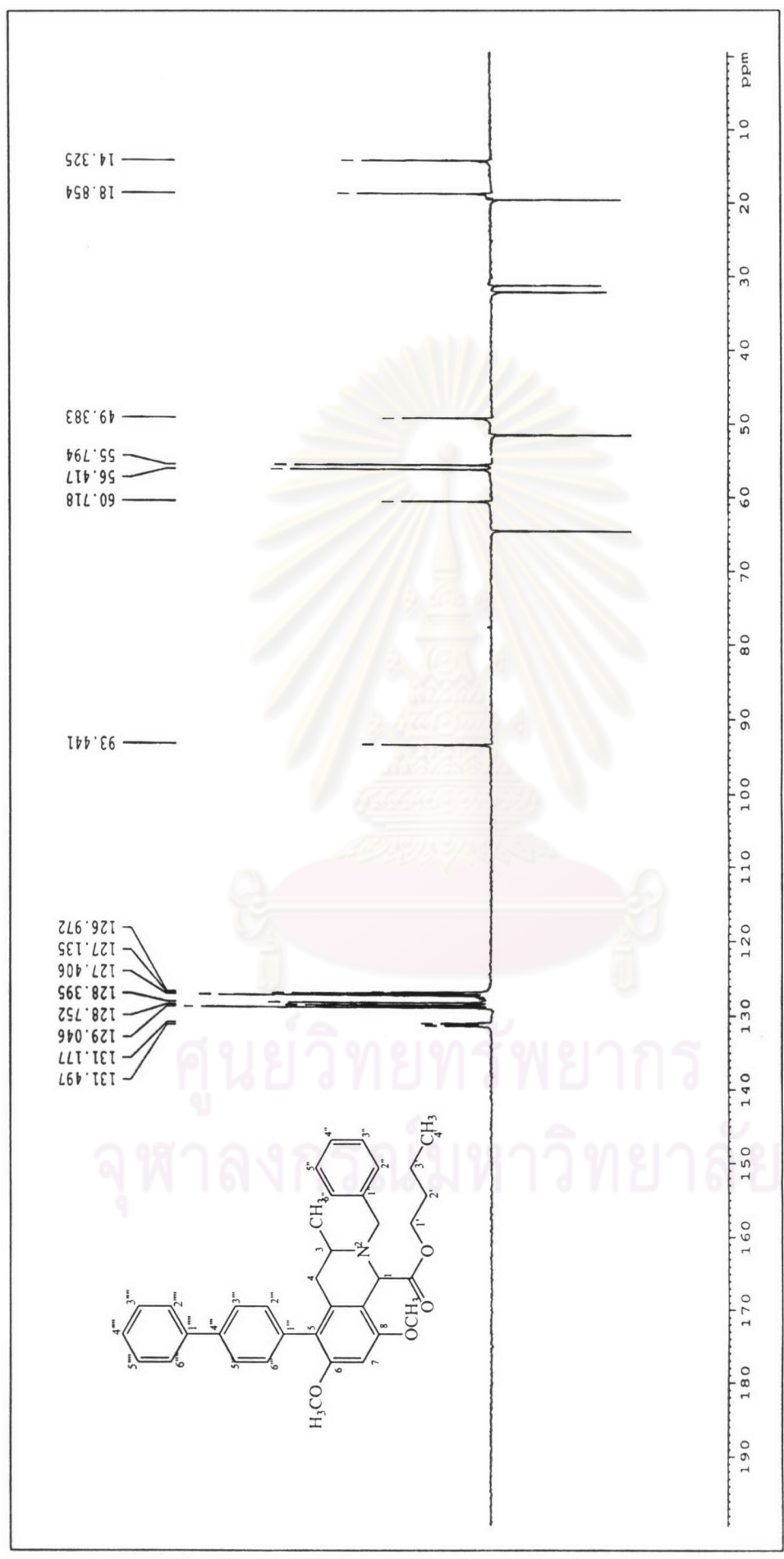


Figure 140 The 75 MHz DEPT 135 spectrum of butyl-5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07)

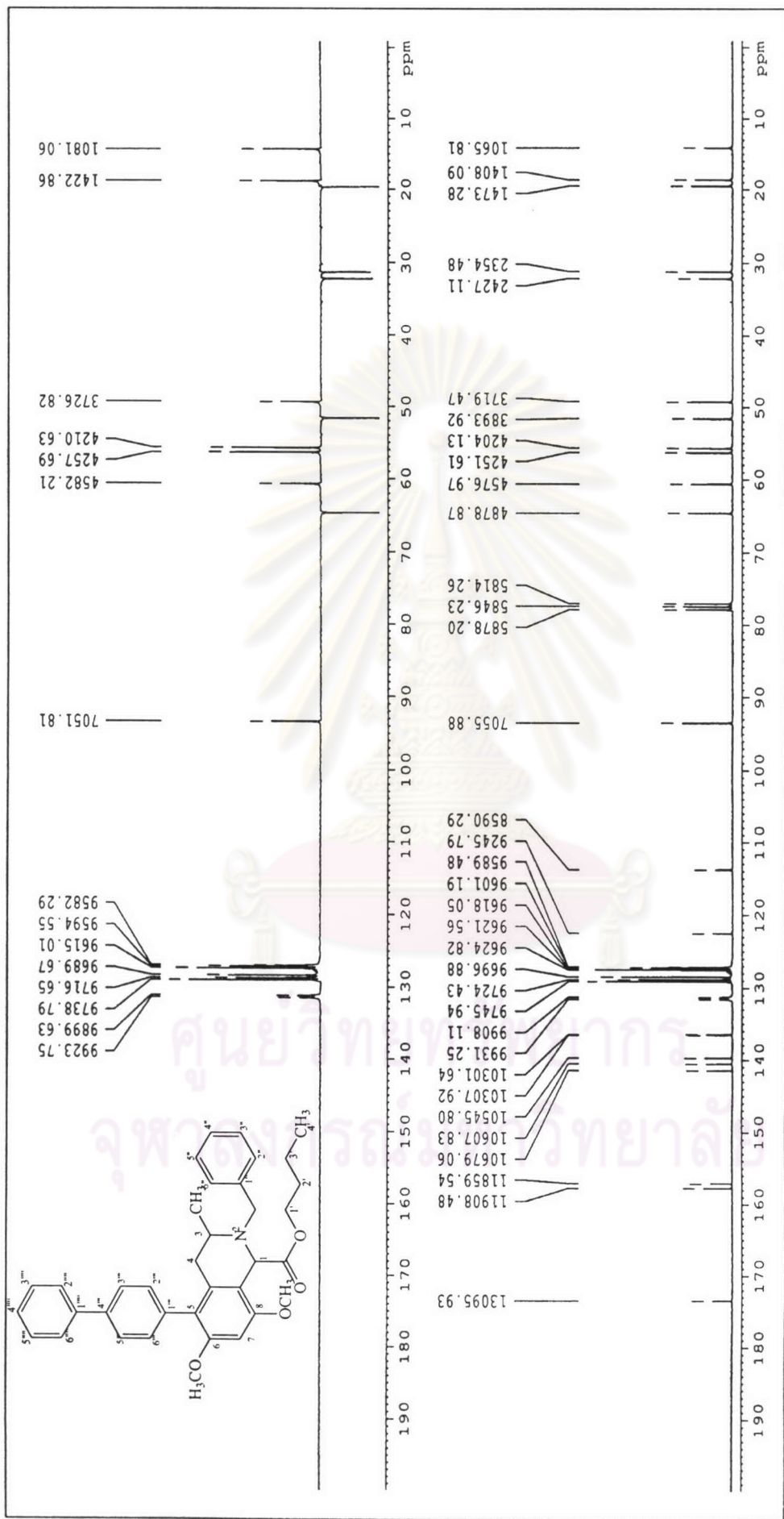


Figure 141 The 75 MHz DEPT 135 and <sup>13</sup>C-NMR spectrum comparison of butyl-5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07)

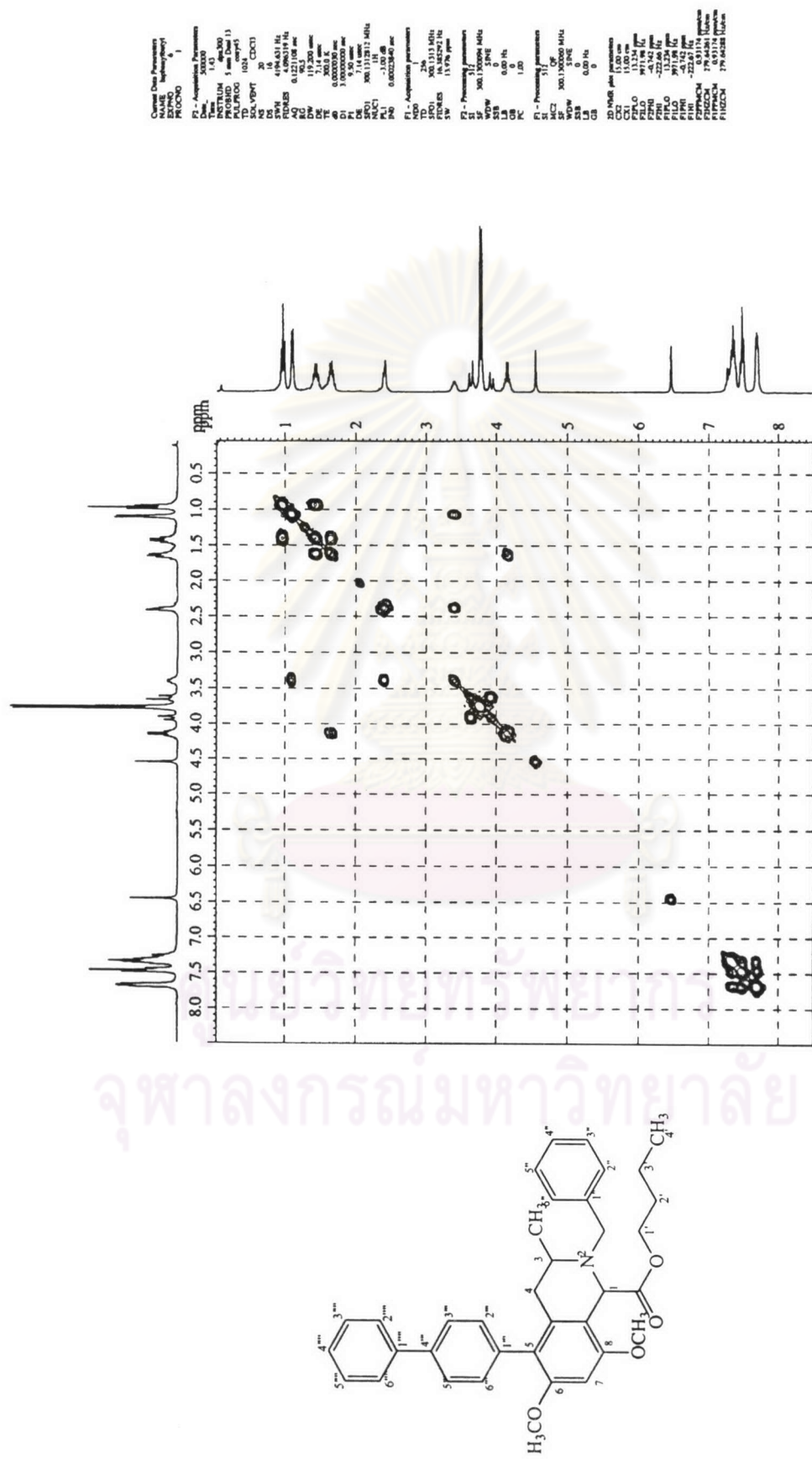


Figure 142 The 300 MHz <sup>1</sup>H-<sup>1</sup>H COSY spectrum of butyl-5-(4'-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate(CU-21-07)

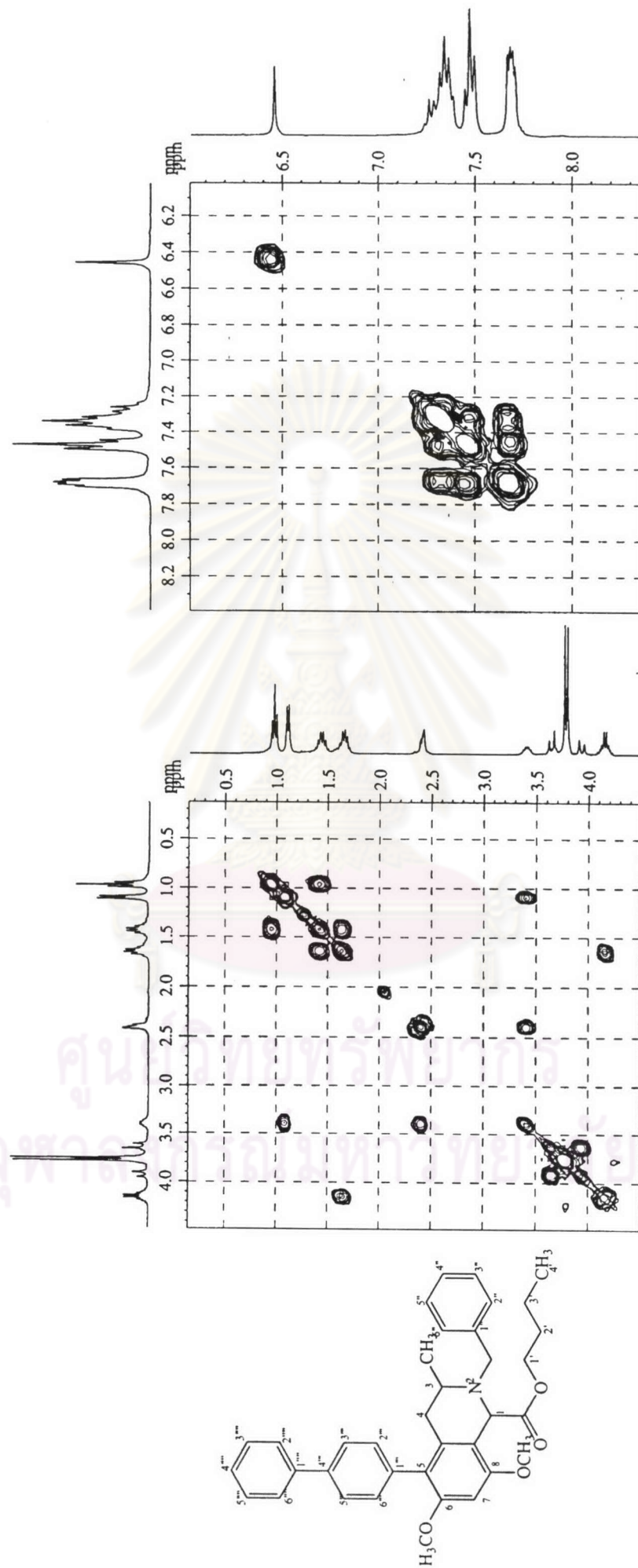


Figure 143 The 300 MHz  $^1\text{H}$ - $^1\text{H}$  COSY spectrum of butyl-5-(4'-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07) (Enlarged scale)



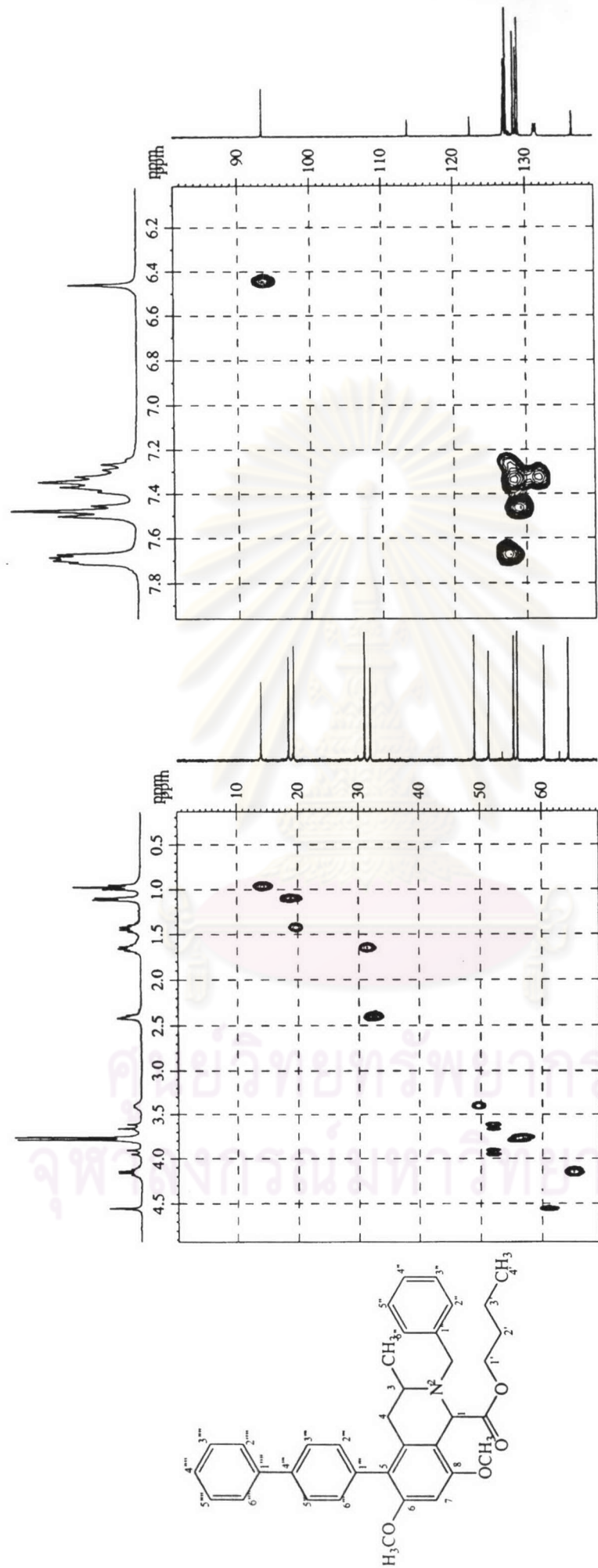


Figure 145 The 300 MHz HMQC spectrum of butyl-5-(4''-biphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-07) (Enlarged scale)

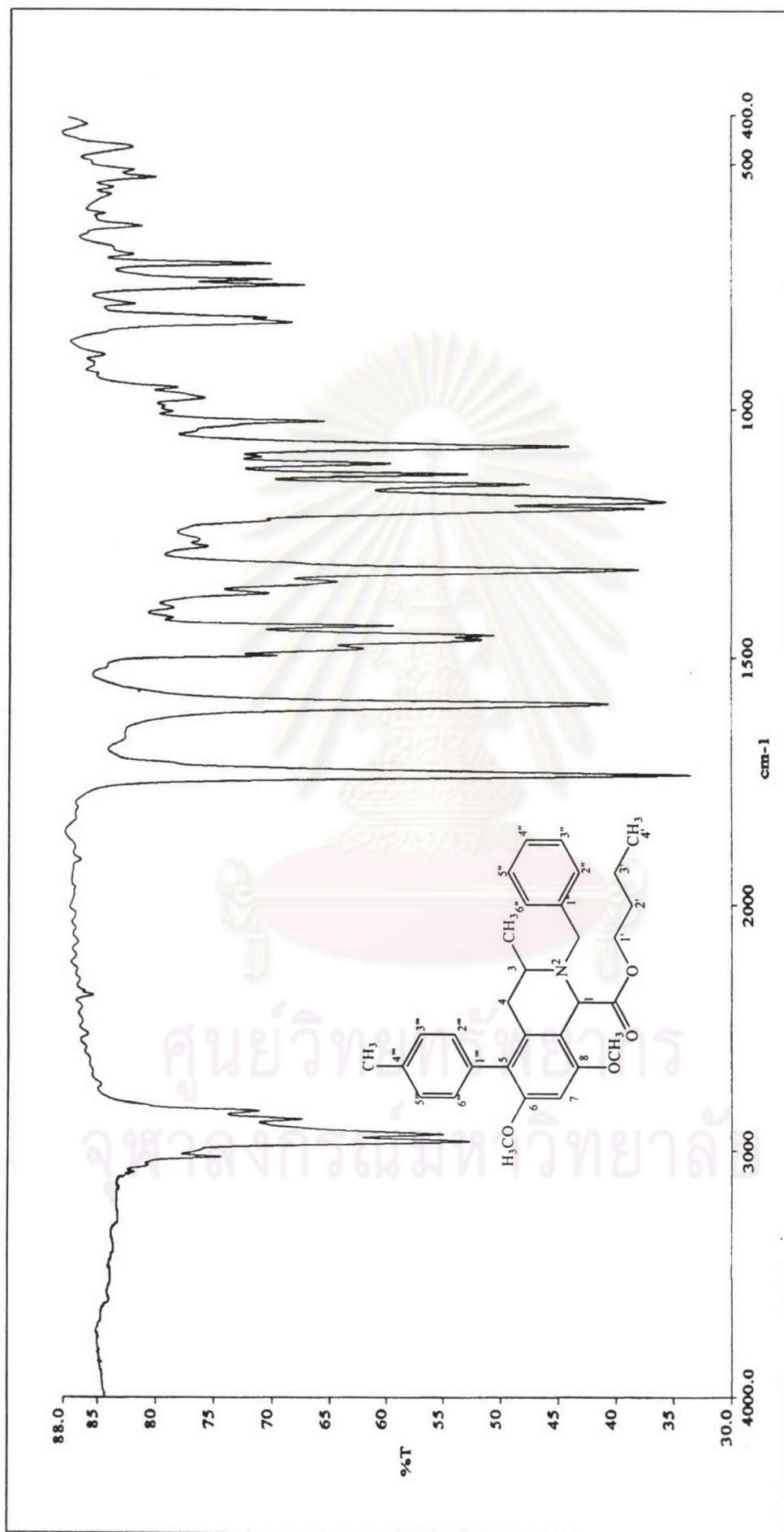


Figure 146 The IR spectrum (KBr) of butyl-5-(4-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate(CU-21-08)



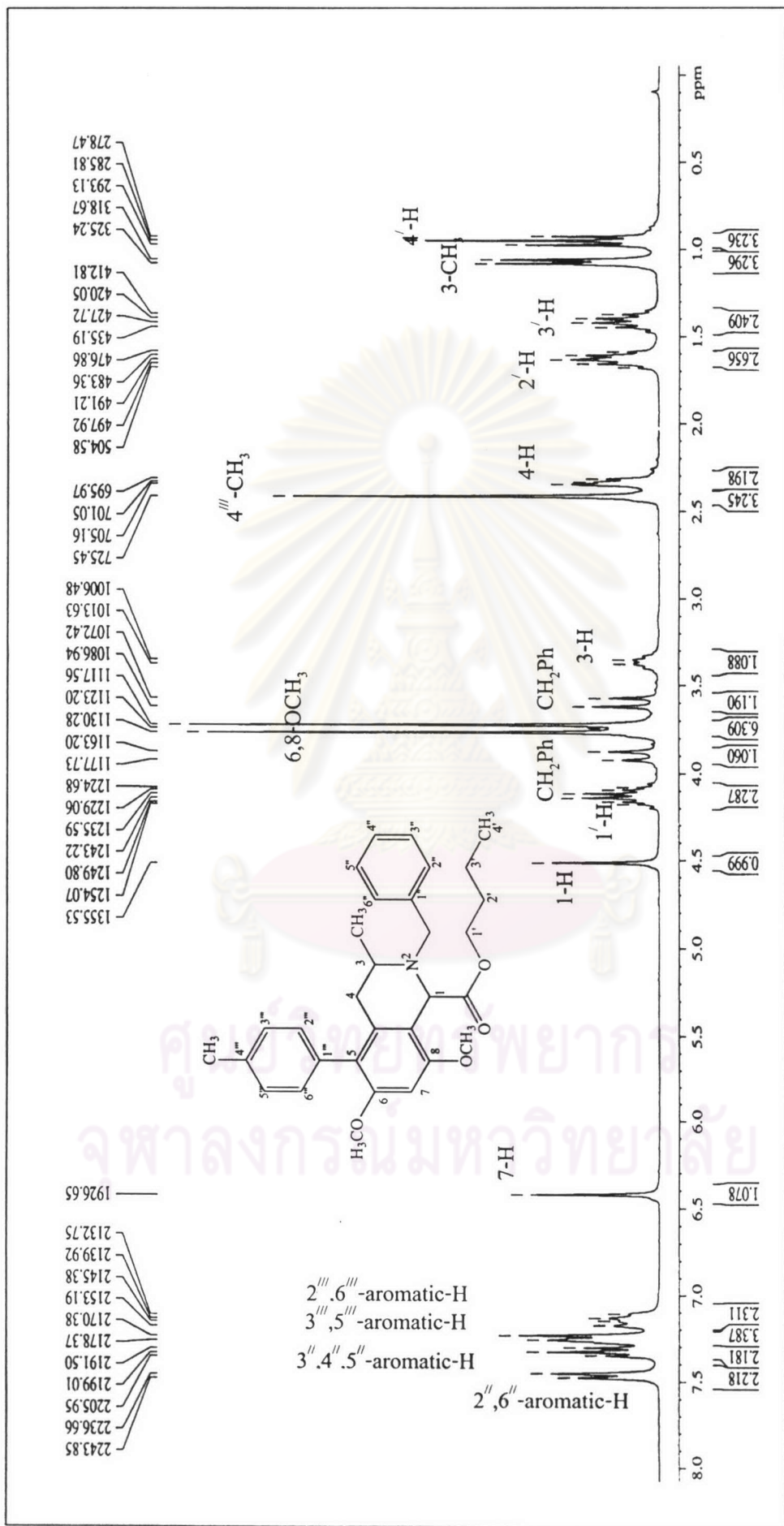


Figure 147 The 300 MHz <sup>1</sup>H-NMR spectrum of butyl-5-(4-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08)

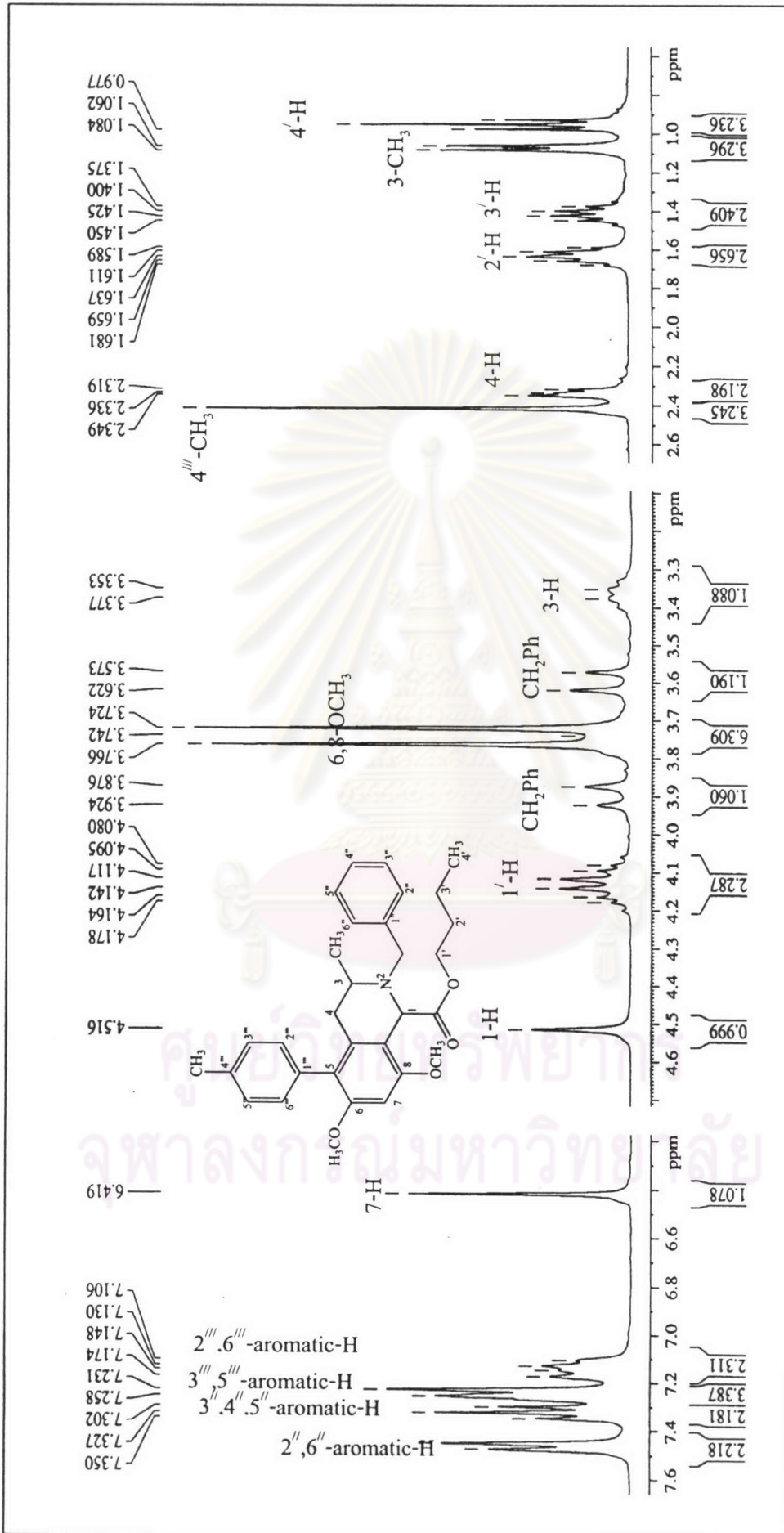


Figure 148 The 300 MHz <sup>1</sup>H-NMR spectrum of butyl-5-(4'''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08) (Enlarged scale)

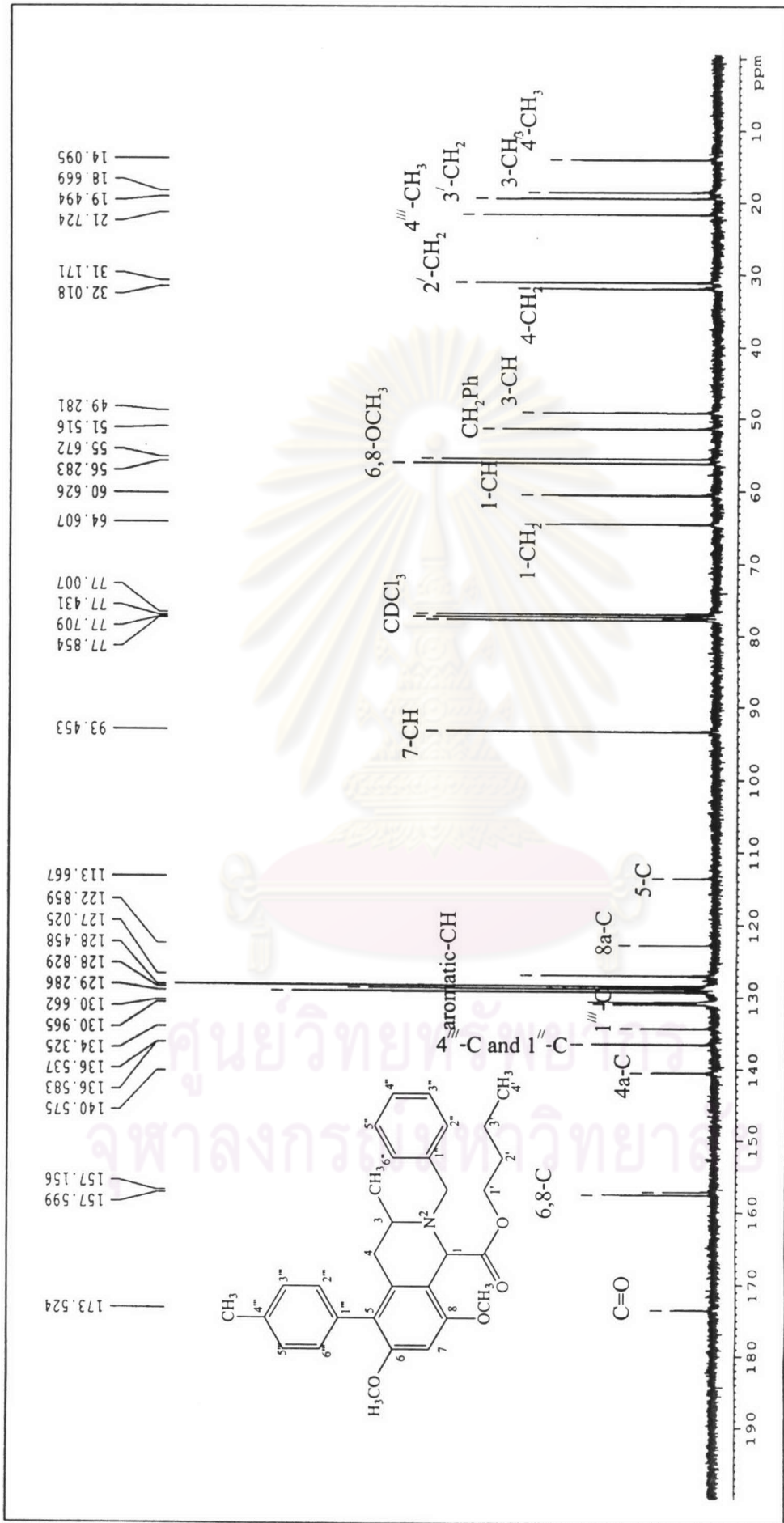


Figure 149 The 75 MHz  $^{13}\text{C}$ -NMR spectrum of butyl-5-(4'''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08)

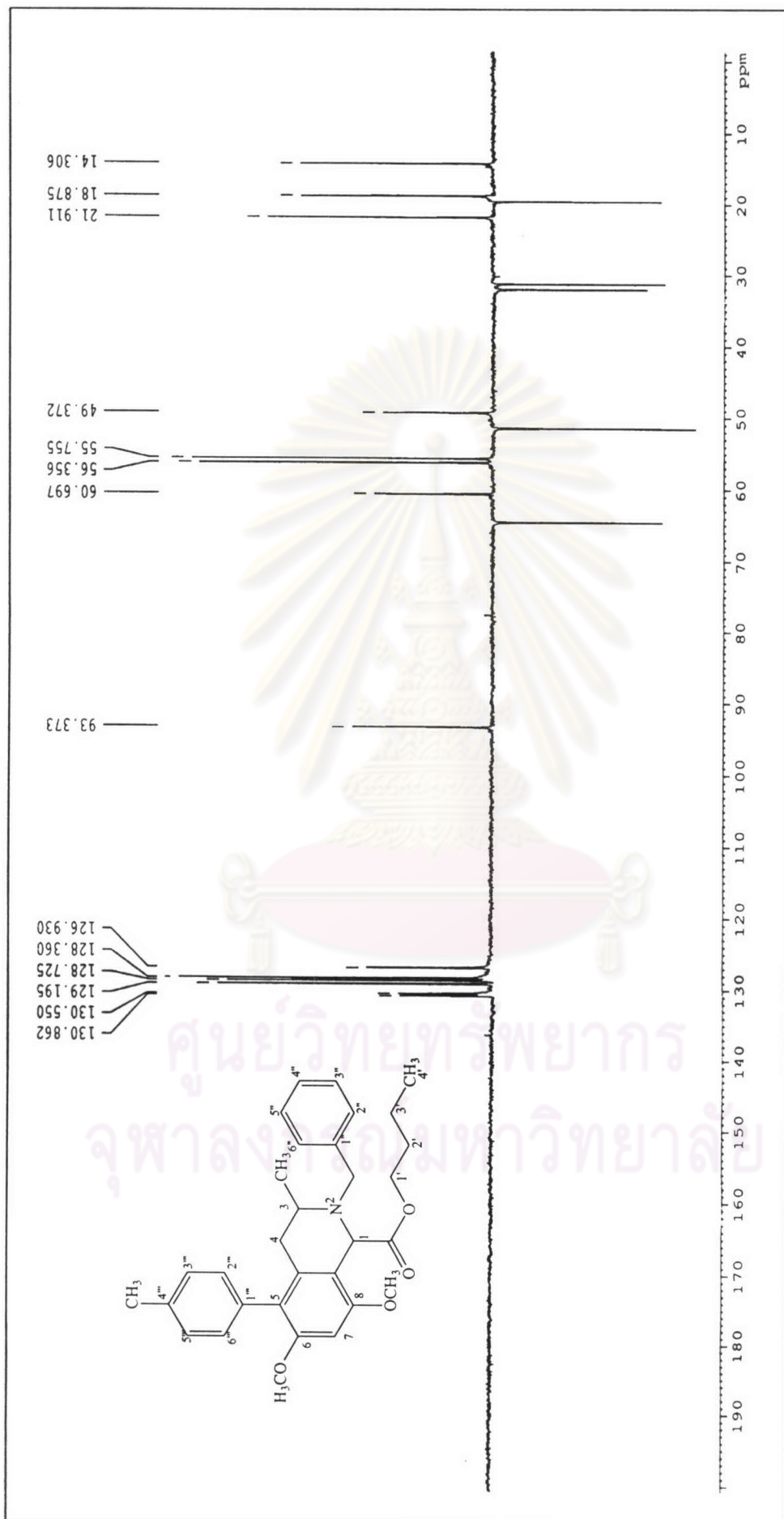


Figure 150 The 75 MHz DEPT 135 spectrum of butyl-5-(4'''-methylphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08)

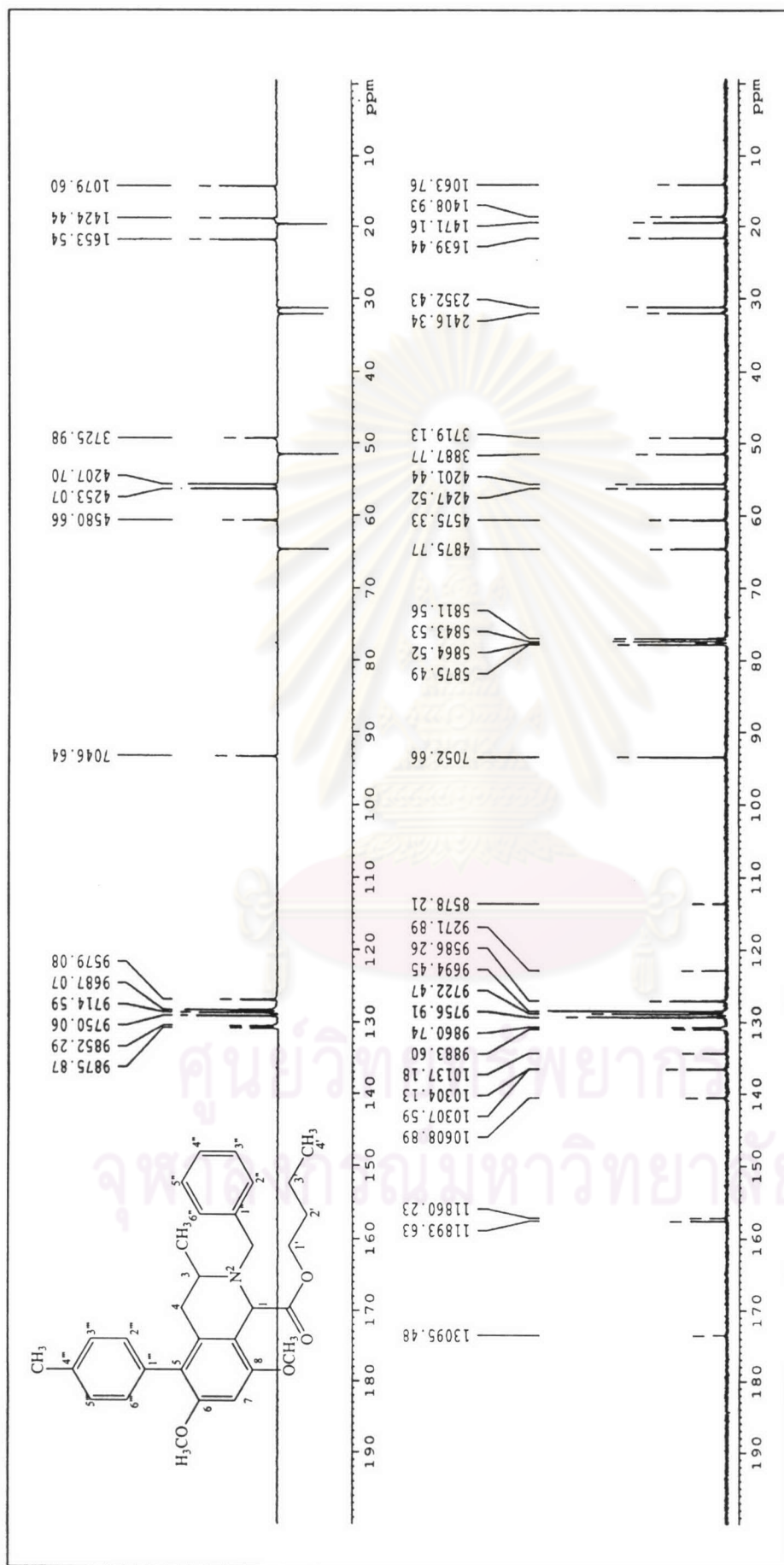


Figure 151 The 75 MHz DEPT 135 and <sup>13</sup>C-NMR spectrum comparison of butyl-5-(4-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08)

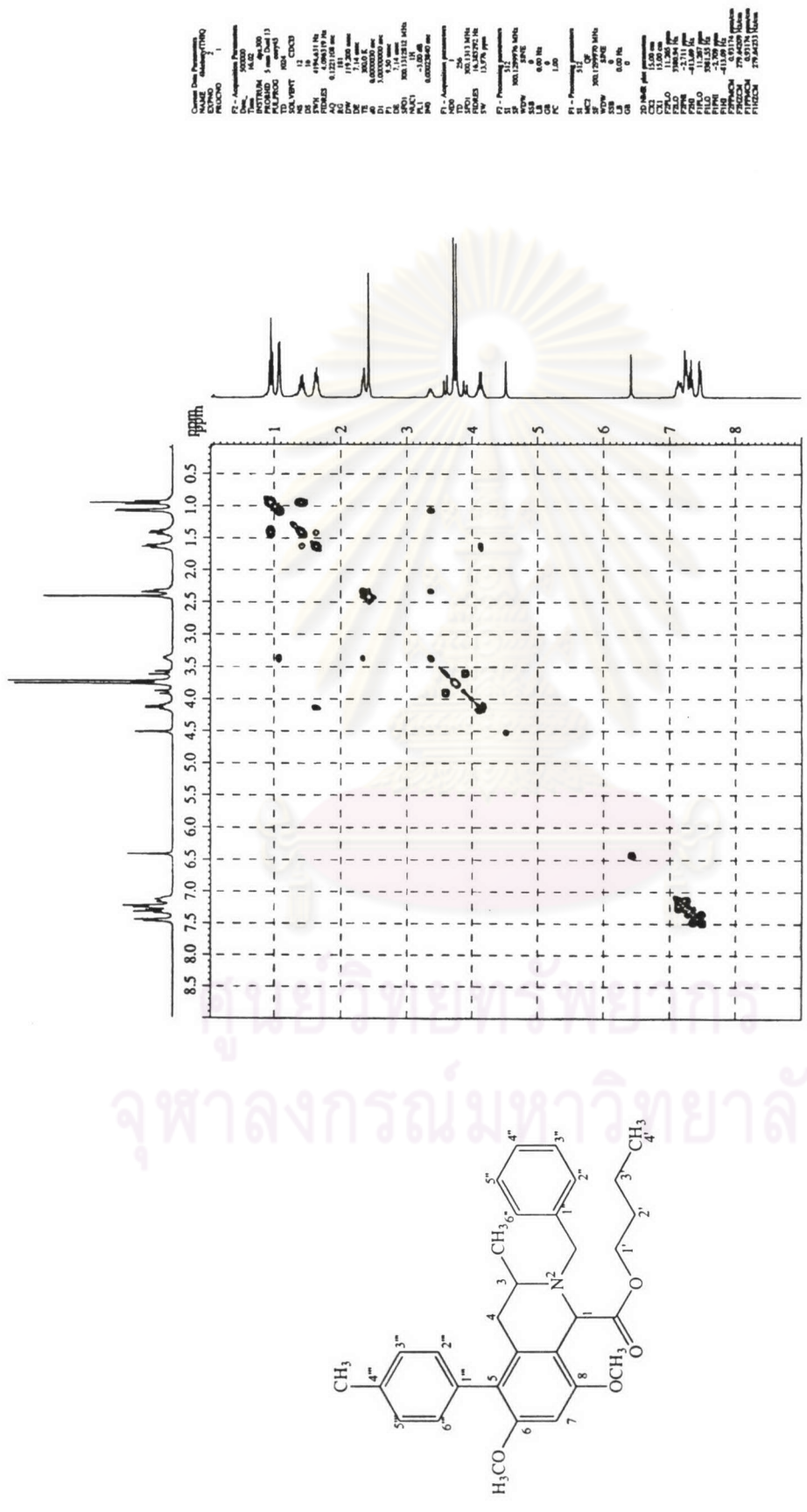


Figure 152 The 300 MHz <sup>1</sup>H-<sup>1</sup>H COSY spectrum of butyl-5-(4-methylphenyl)-2-benzyl-6,8-dimethoxy-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08)

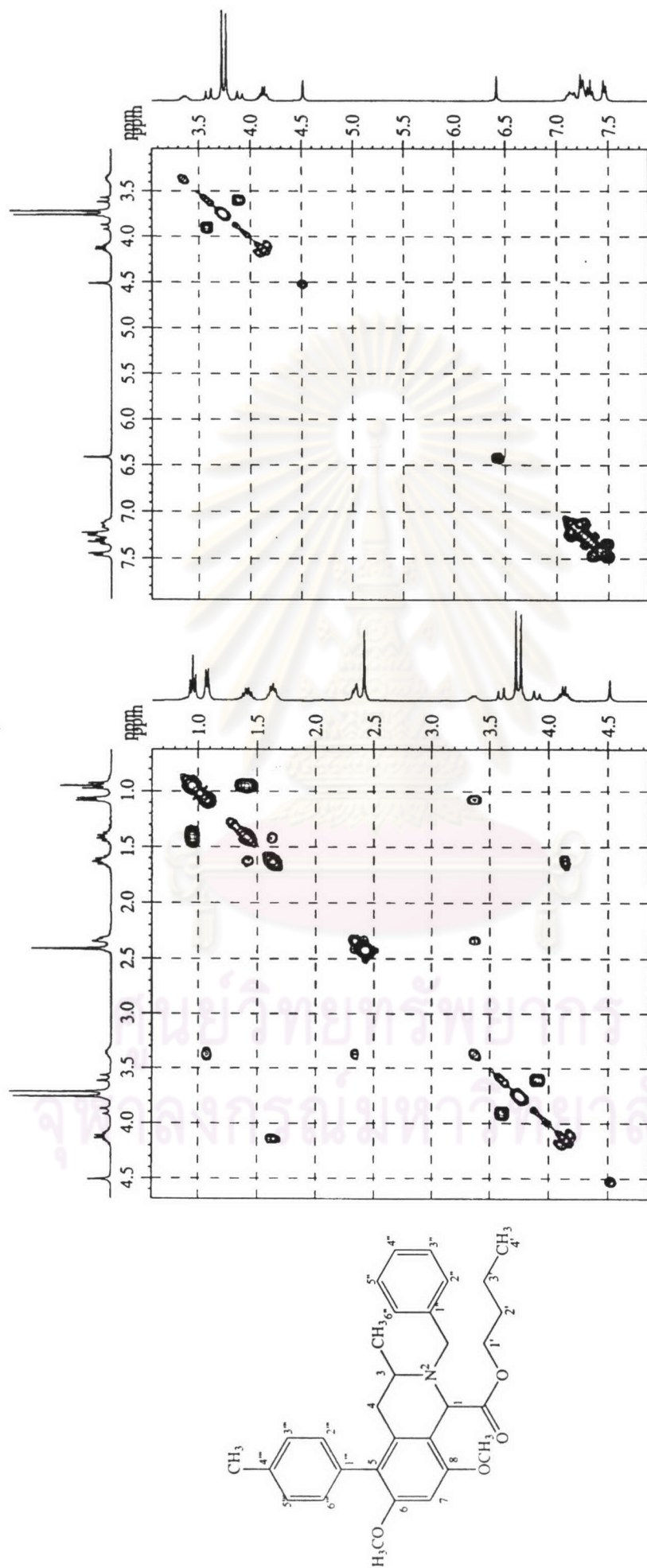


Figure 153 The 300 MHz HH COSY spectrum of butyl-5-(4''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08) (Enlarged scale)

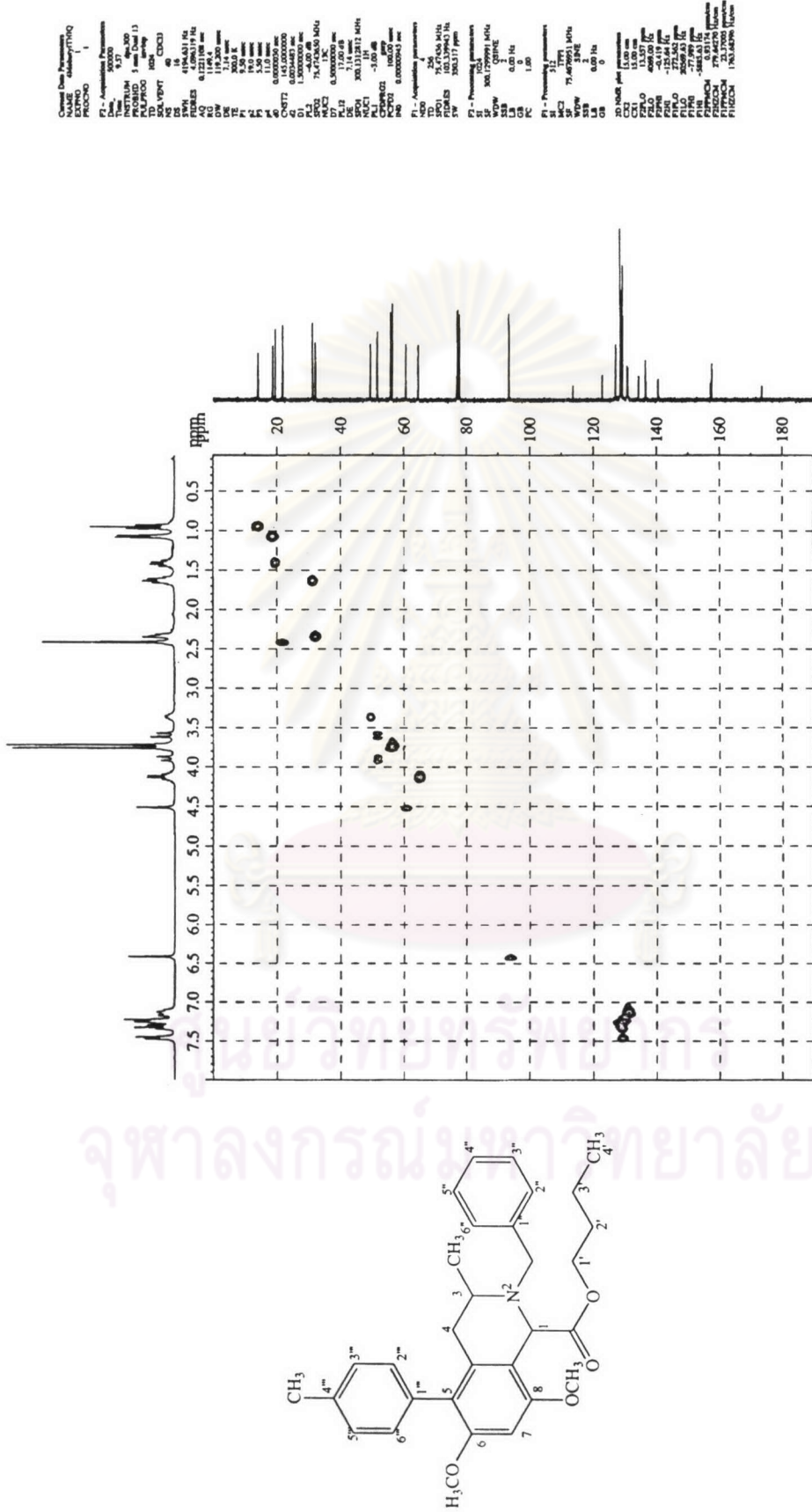


Figure 154 The 300 MHz HMQC spectrum of butyl-5-(4'''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08)



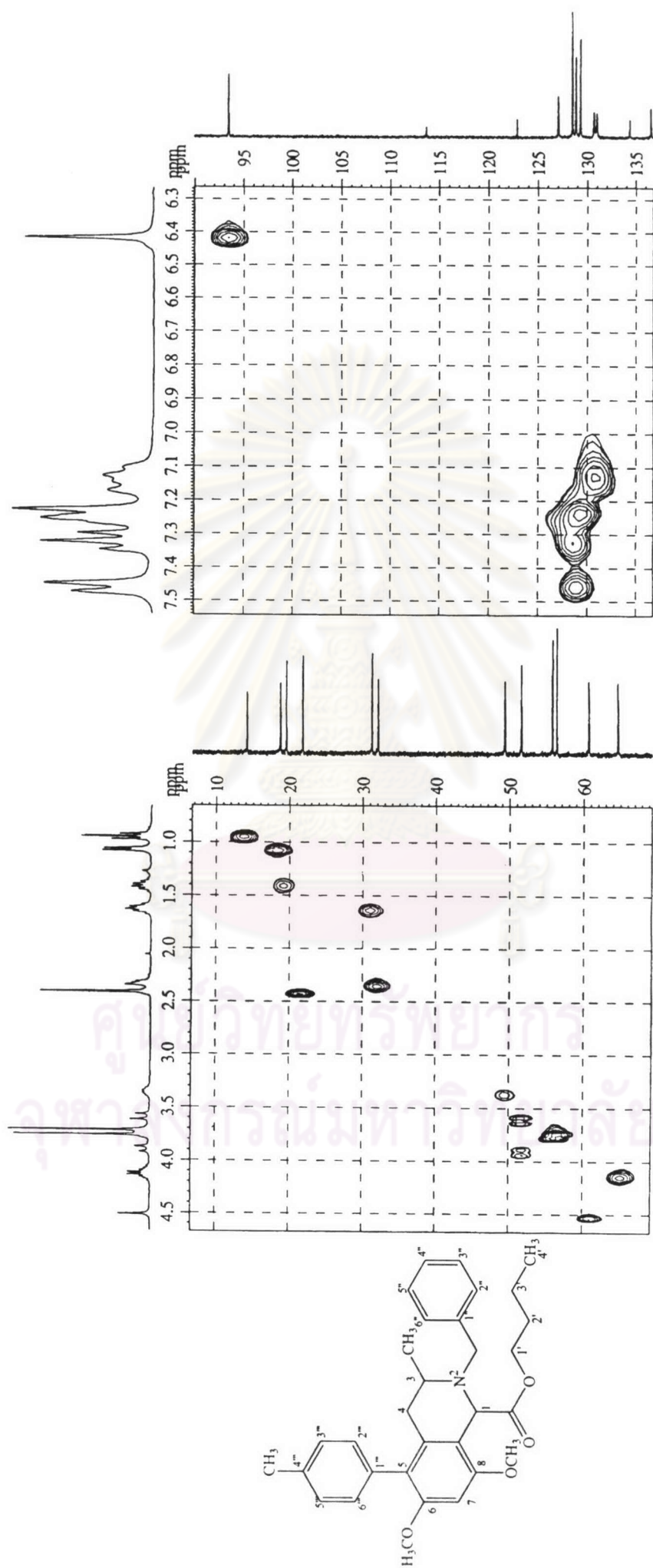


Figure 155 The 300 MHz HMQC spectrum of butyl-5-(4'''-methylphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-08) (Enlarged scale)

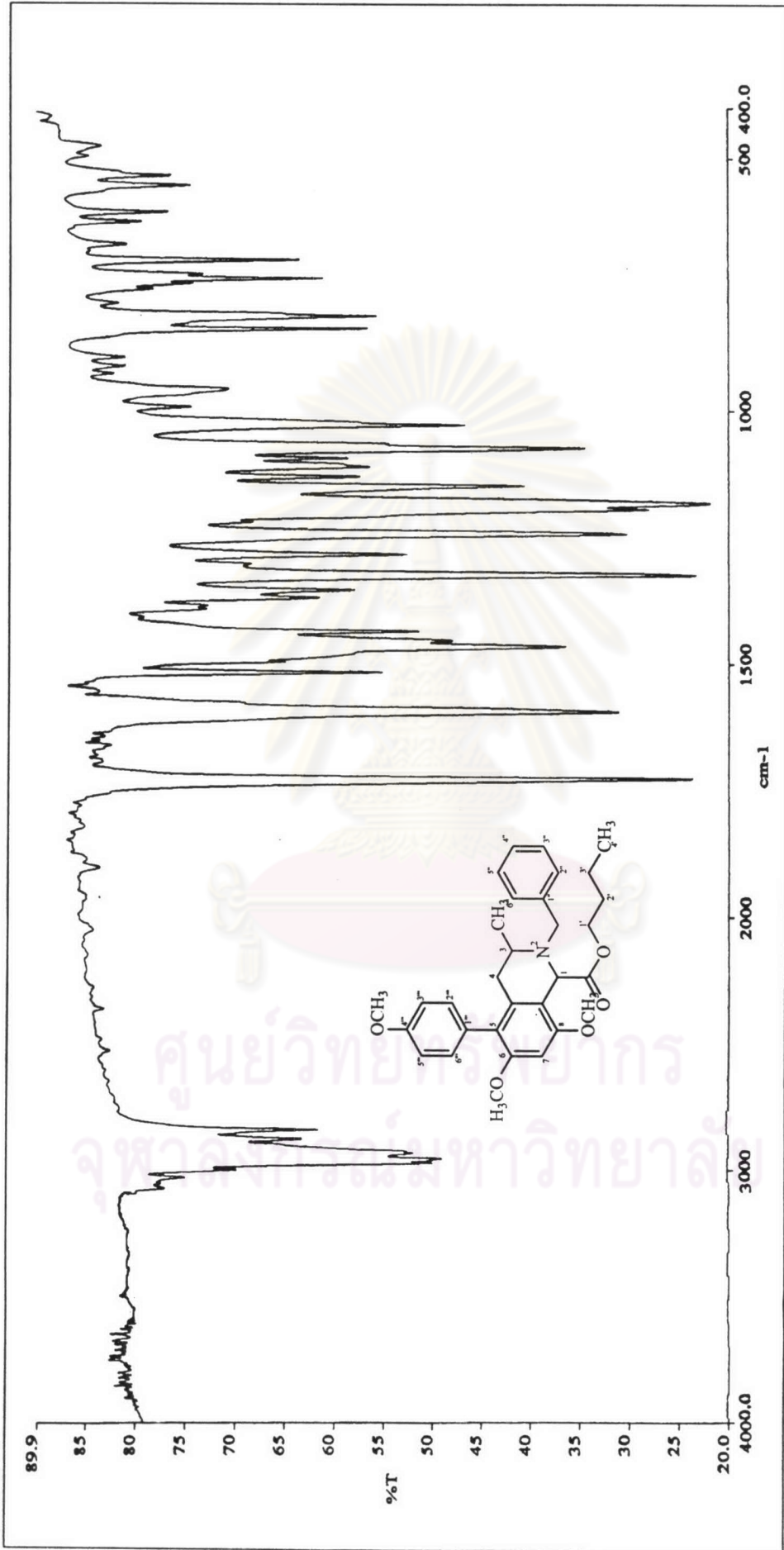


Figure 156 The IR spectrum (KBr) of butyl-5-(4-methoxyphenyl)-2-benzyl 6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09)

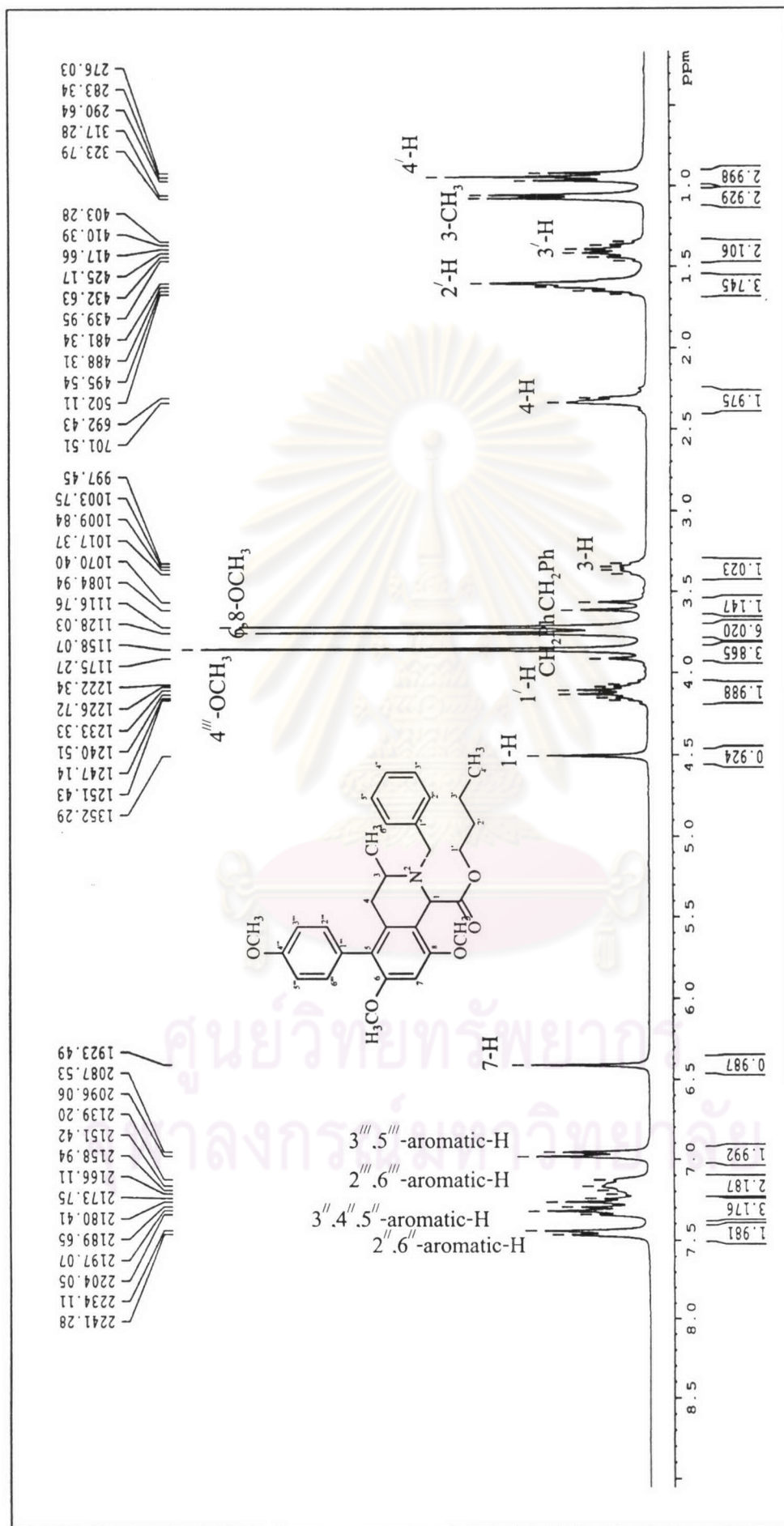


Figure 157 The 300 MHz  $^1\text{H-NMR}$  spectrum of butyl-5-(4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09)

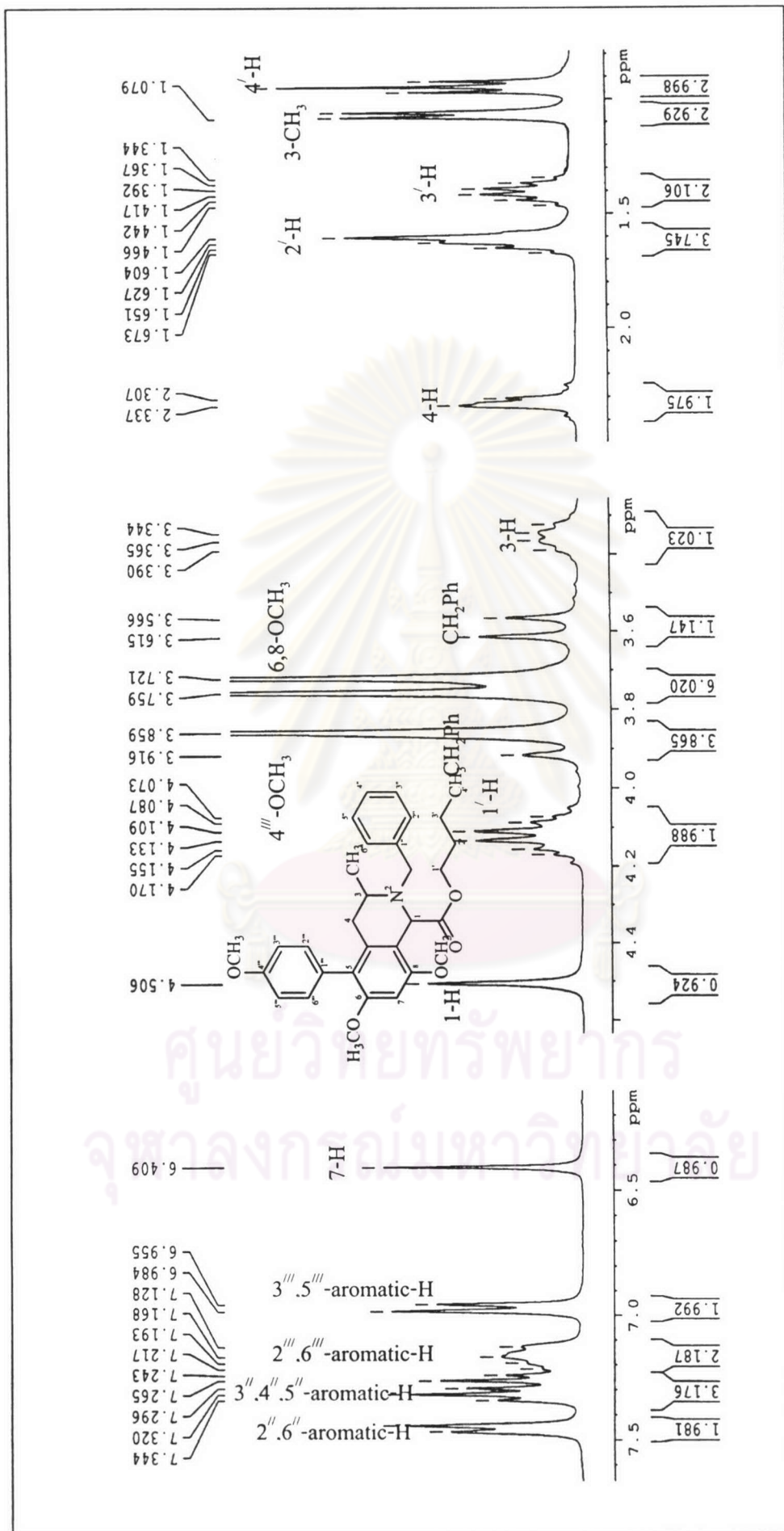


Figure 158 The 300 MHz <sup>1</sup>H-NMR spectrum of butyl-5-(4'''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09) (Enlarged scale)

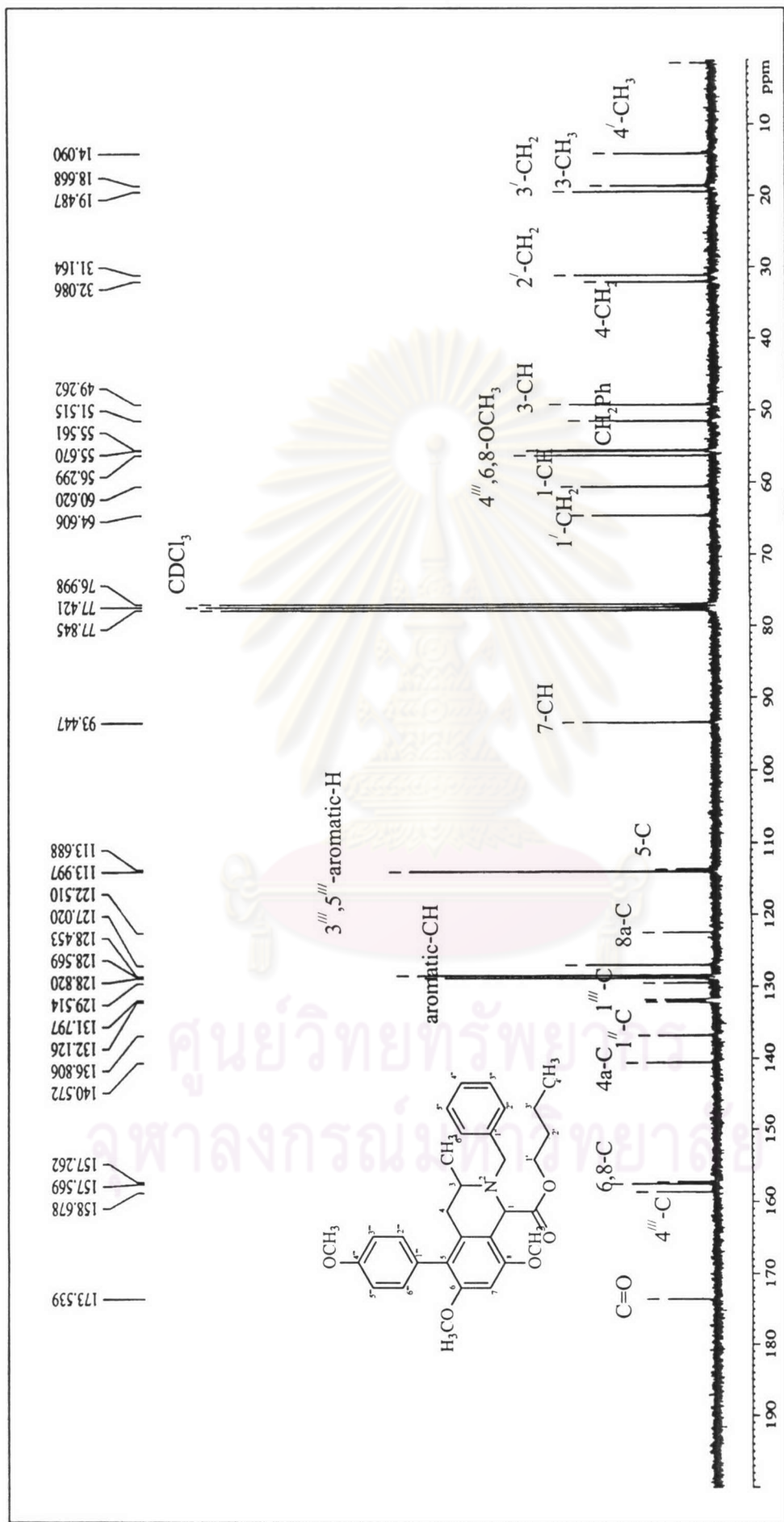


Figure 159 The 75 MHz <sup>13</sup>C-NMR spectrum of butyl-5-(4'''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09)

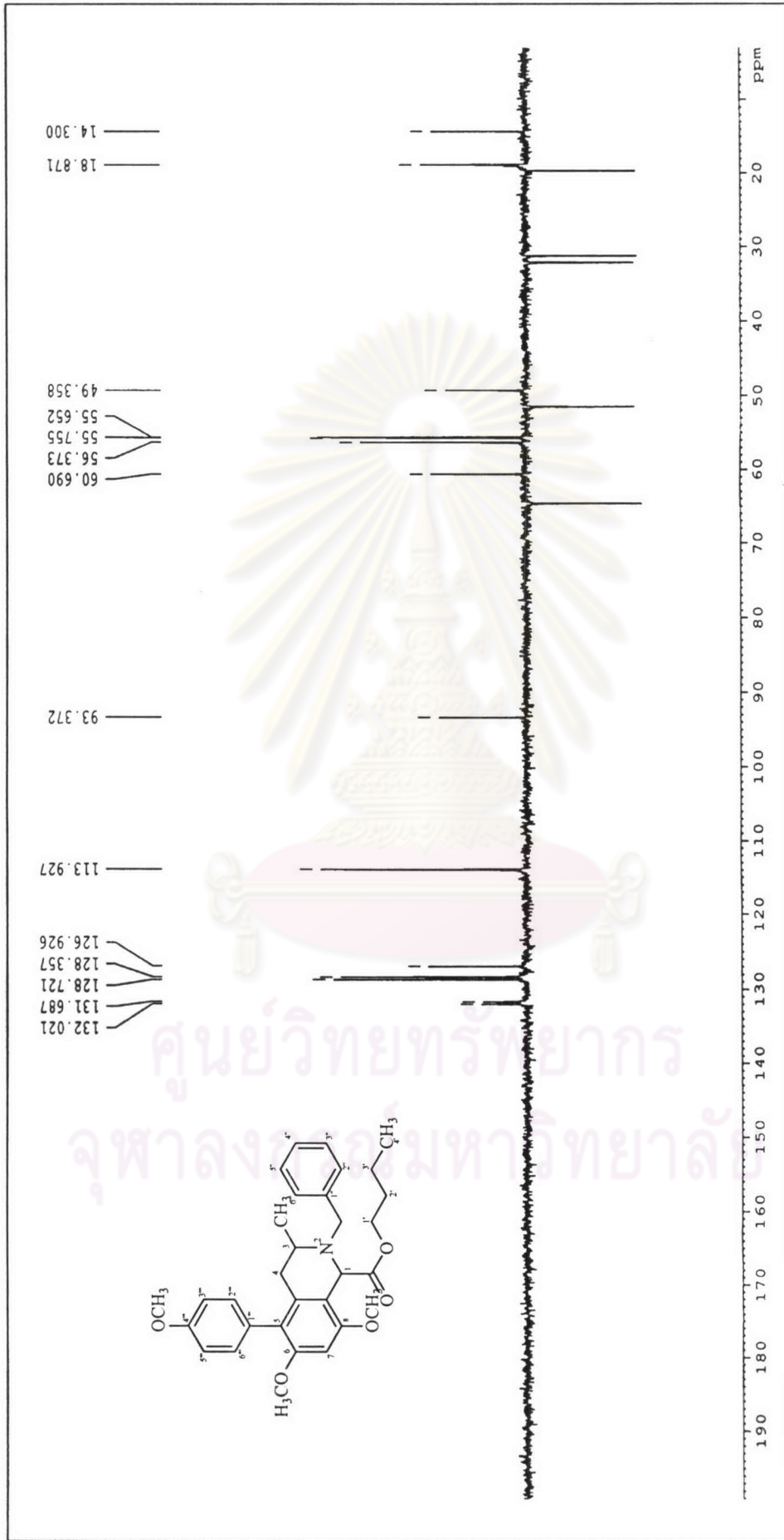


Figure 160 The 75 MHz  $^{13}\text{C}$ -NMR spectrum of butyl-5-(4'''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09)

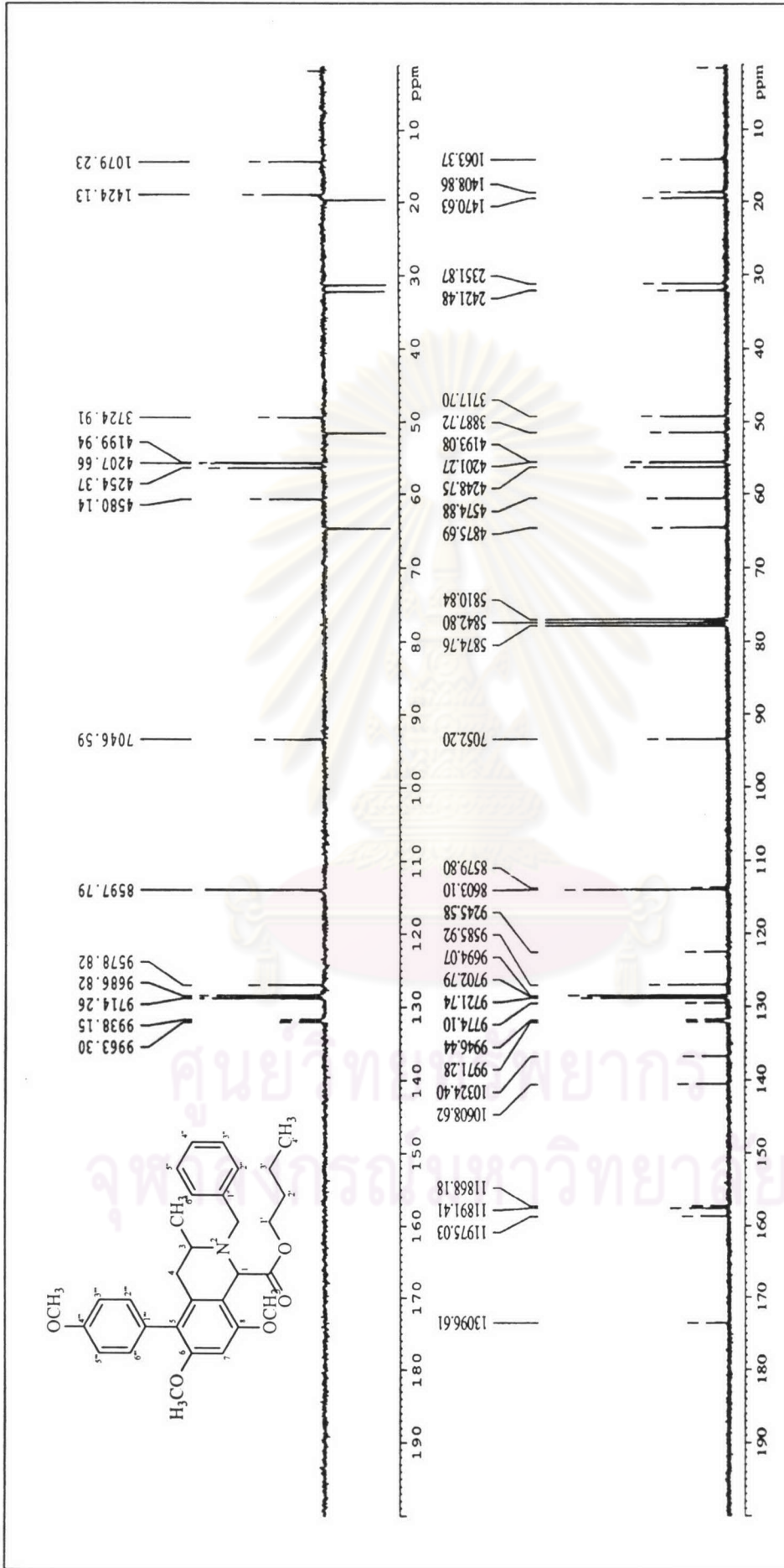


Figure 161 The 75 MHz DEPT 135 and  $^{13}\text{C}$ -NMR spectrum comparison of butyl-5-(4-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09)

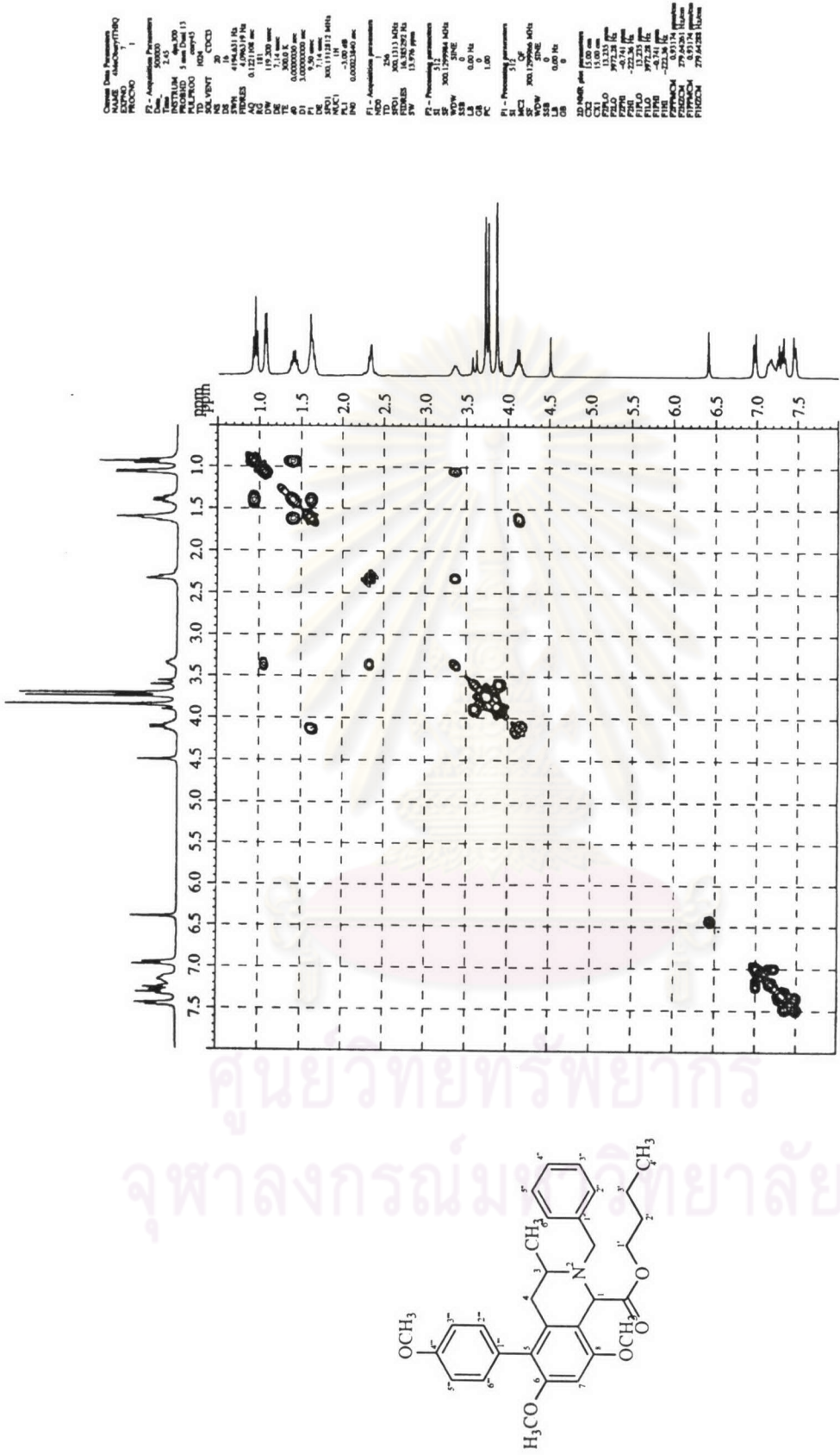


Figure 162 The 300 MHz HH COSY spectrum of butyl-5-(4'''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09)



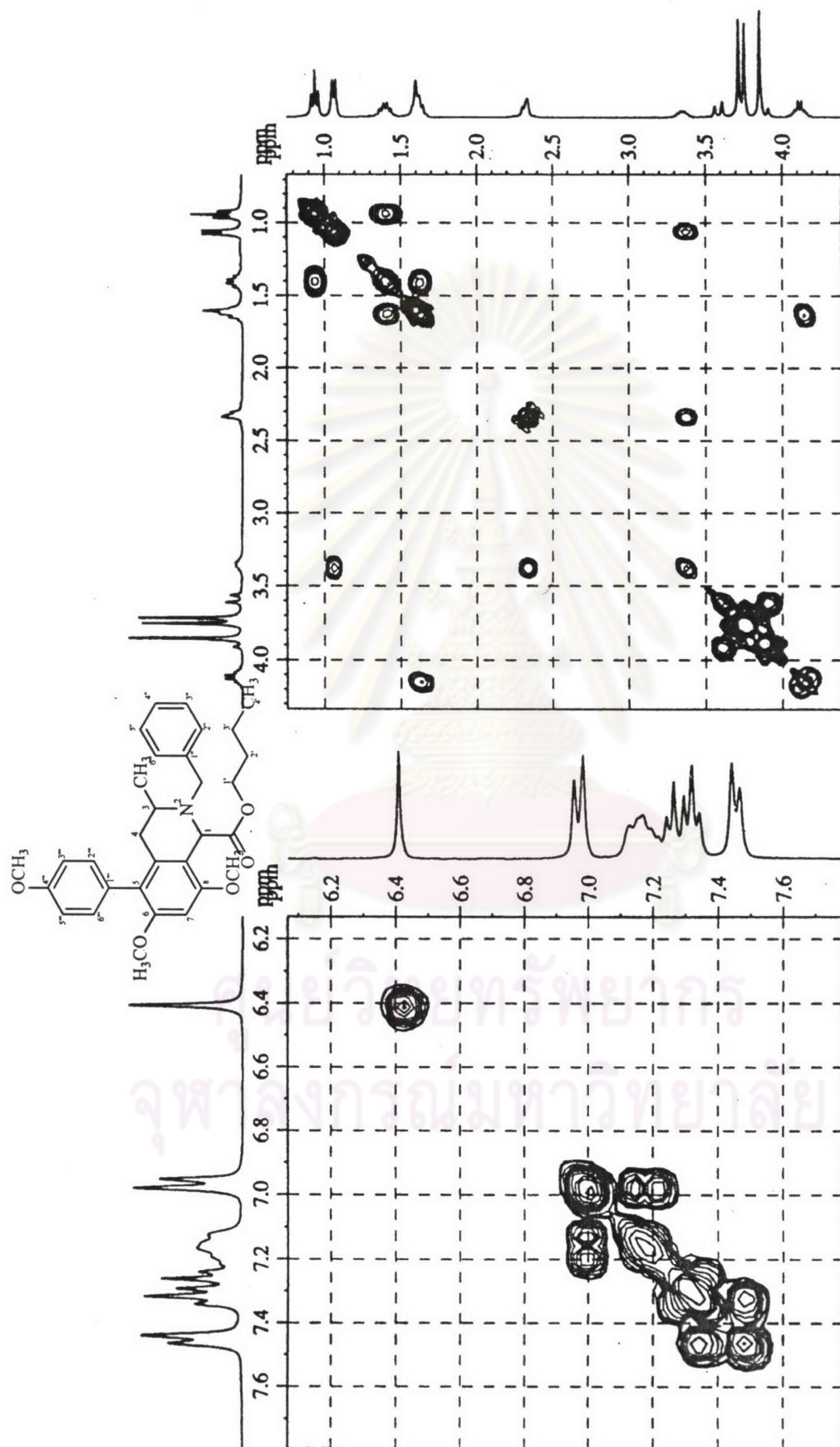
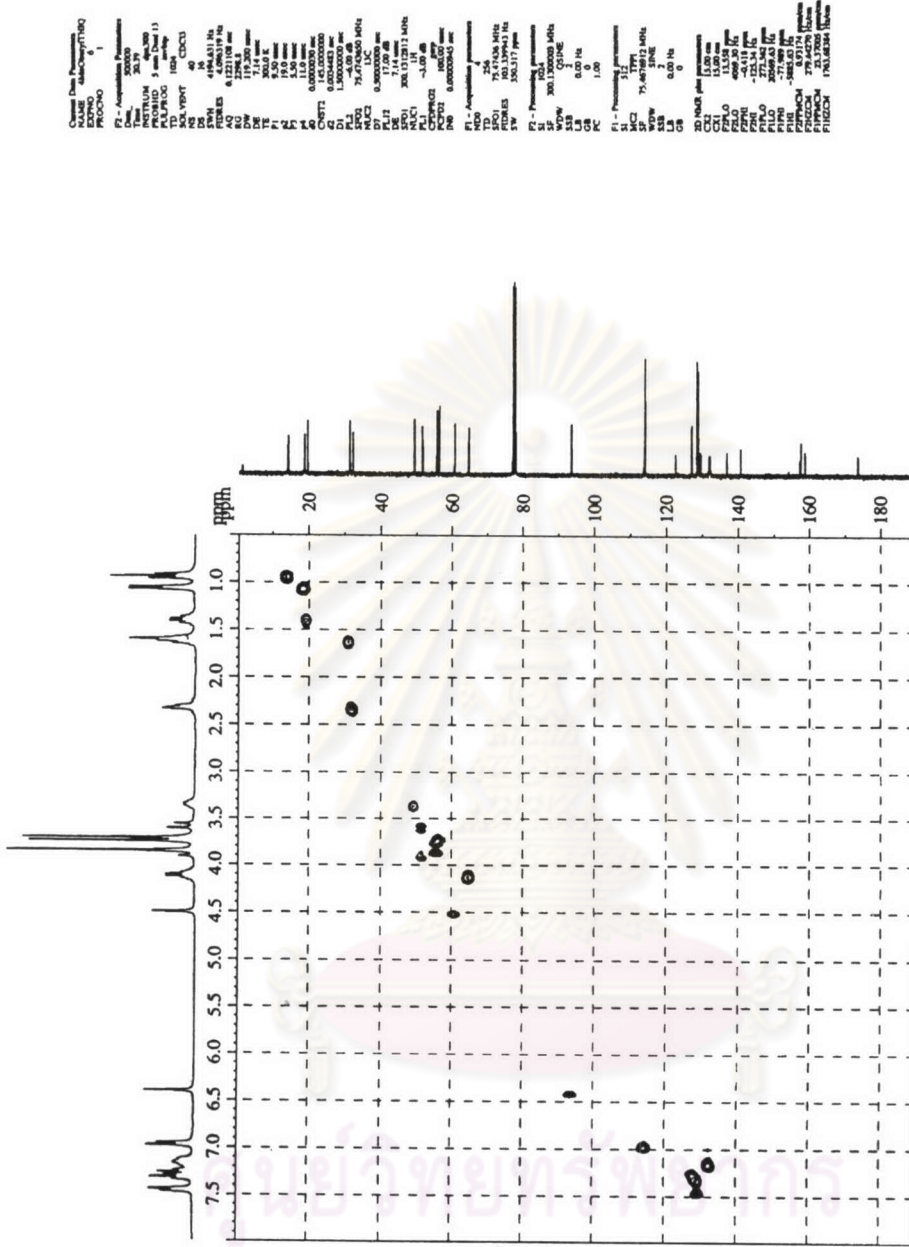


Figure 163 The 300 MHz <sup>1</sup>H-<sup>1</sup>H COSY spectrum of butyl-5-(4''-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09) (Enlarged scale)



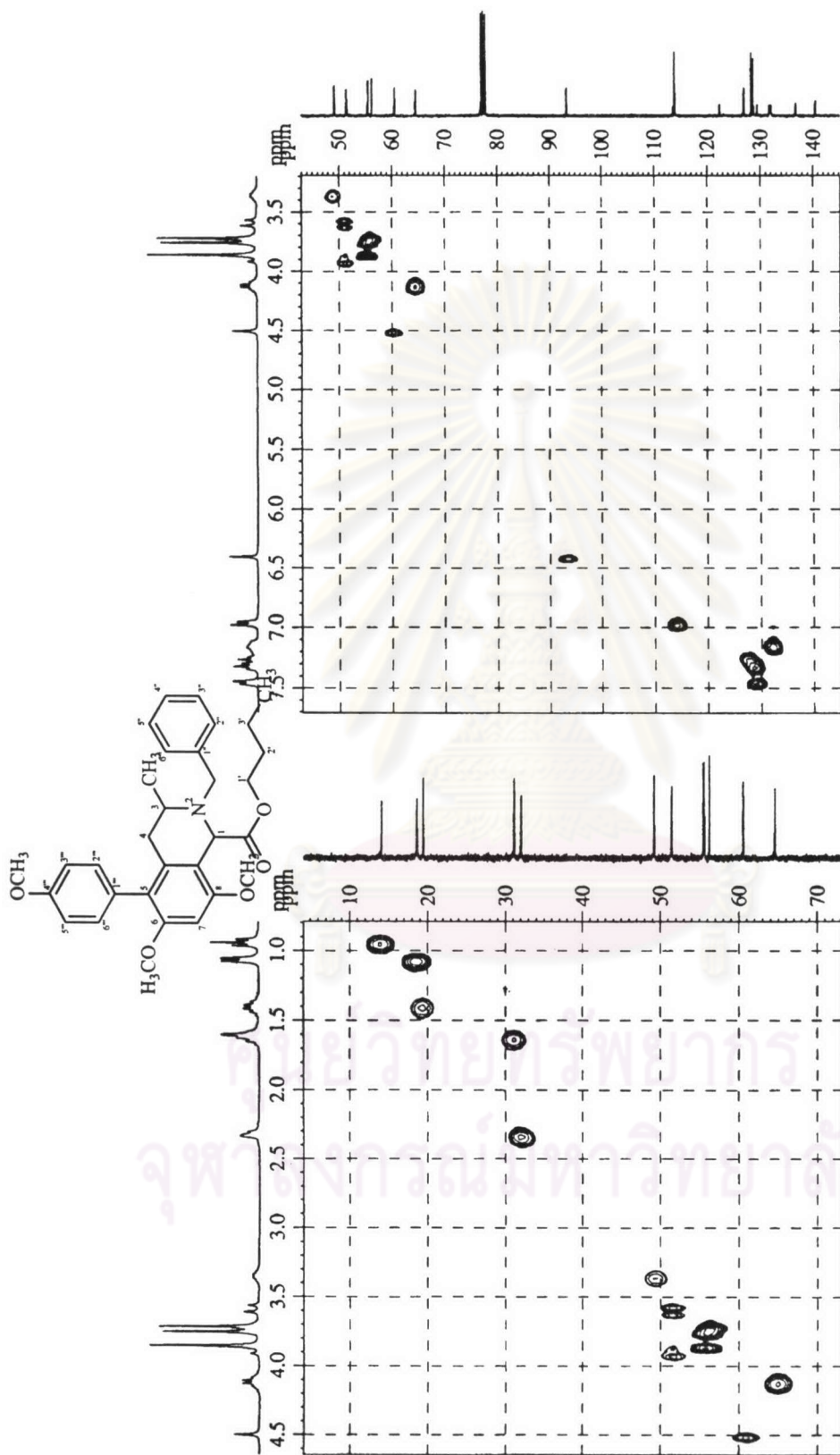


Figure 165 The 300 MHz HMQC spectrum of butyl-5-(4-methoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-09) (Enlarged scale)

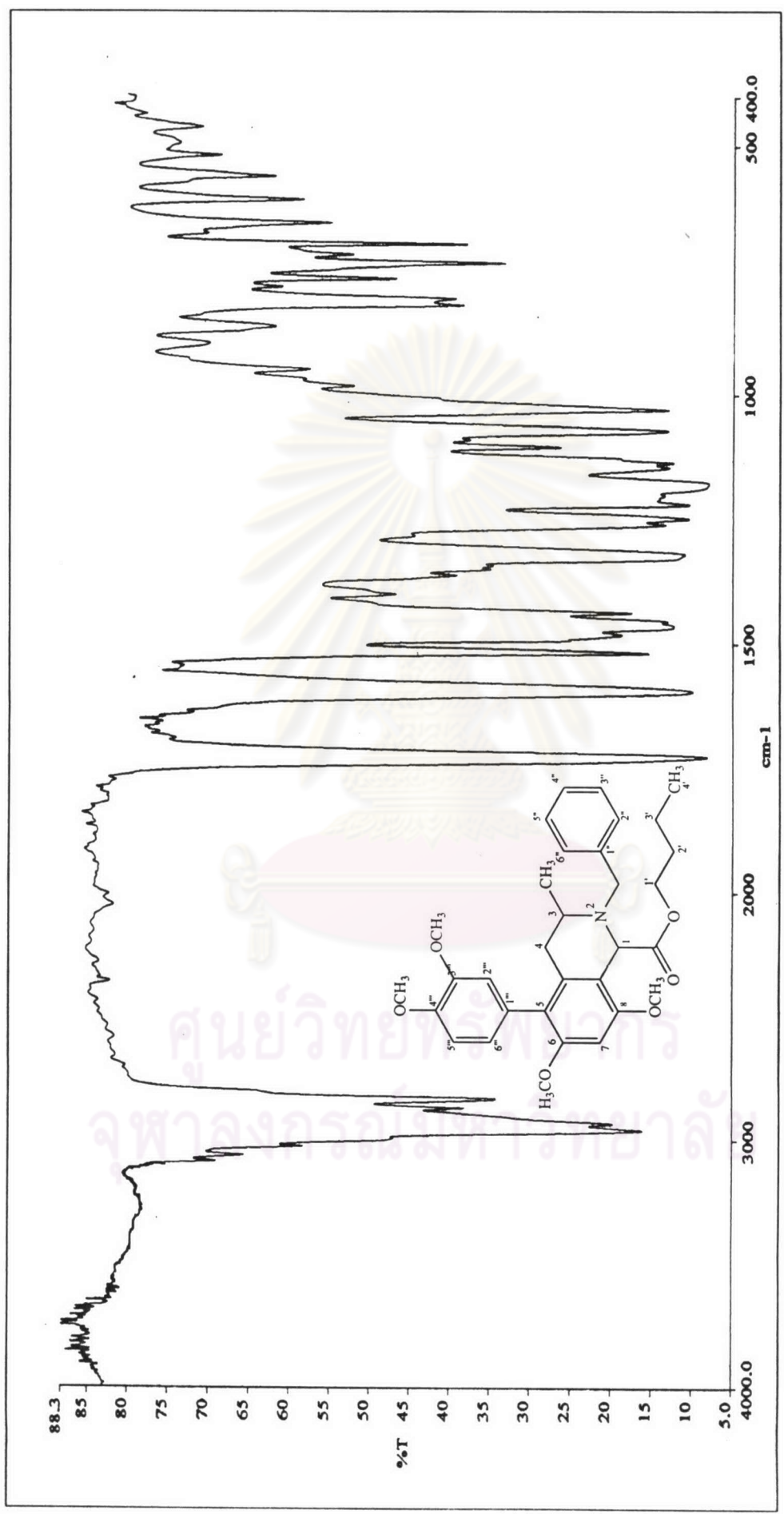


Figure 166 The IR spectrum (KBr) of butyl-5-(3<sup>'''</sup>,4<sup>'''</sup>-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10)

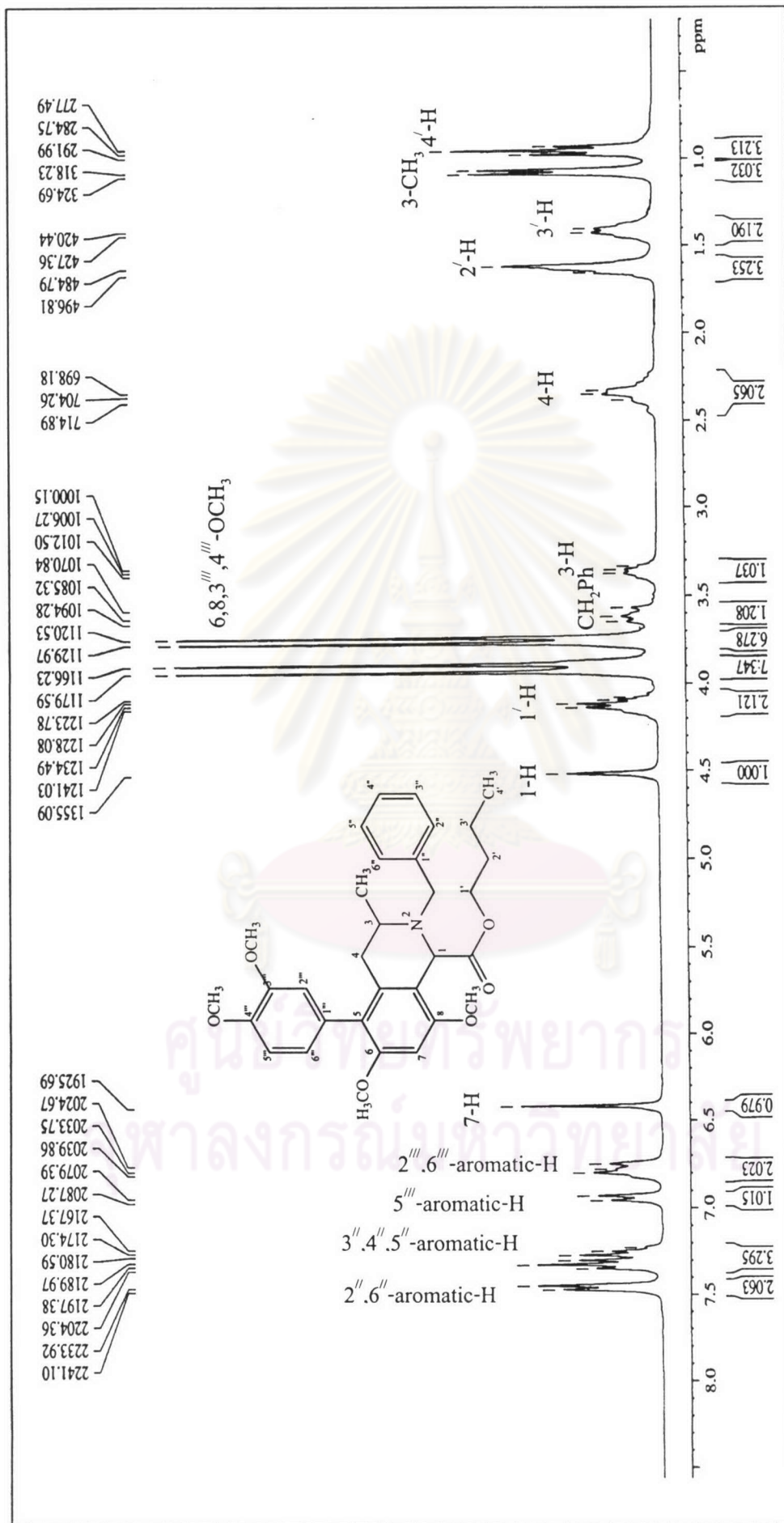


Figure 167 The 300 MHz <sup>1</sup>H-NMR spectrum of butyl-5-(3,4-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10)

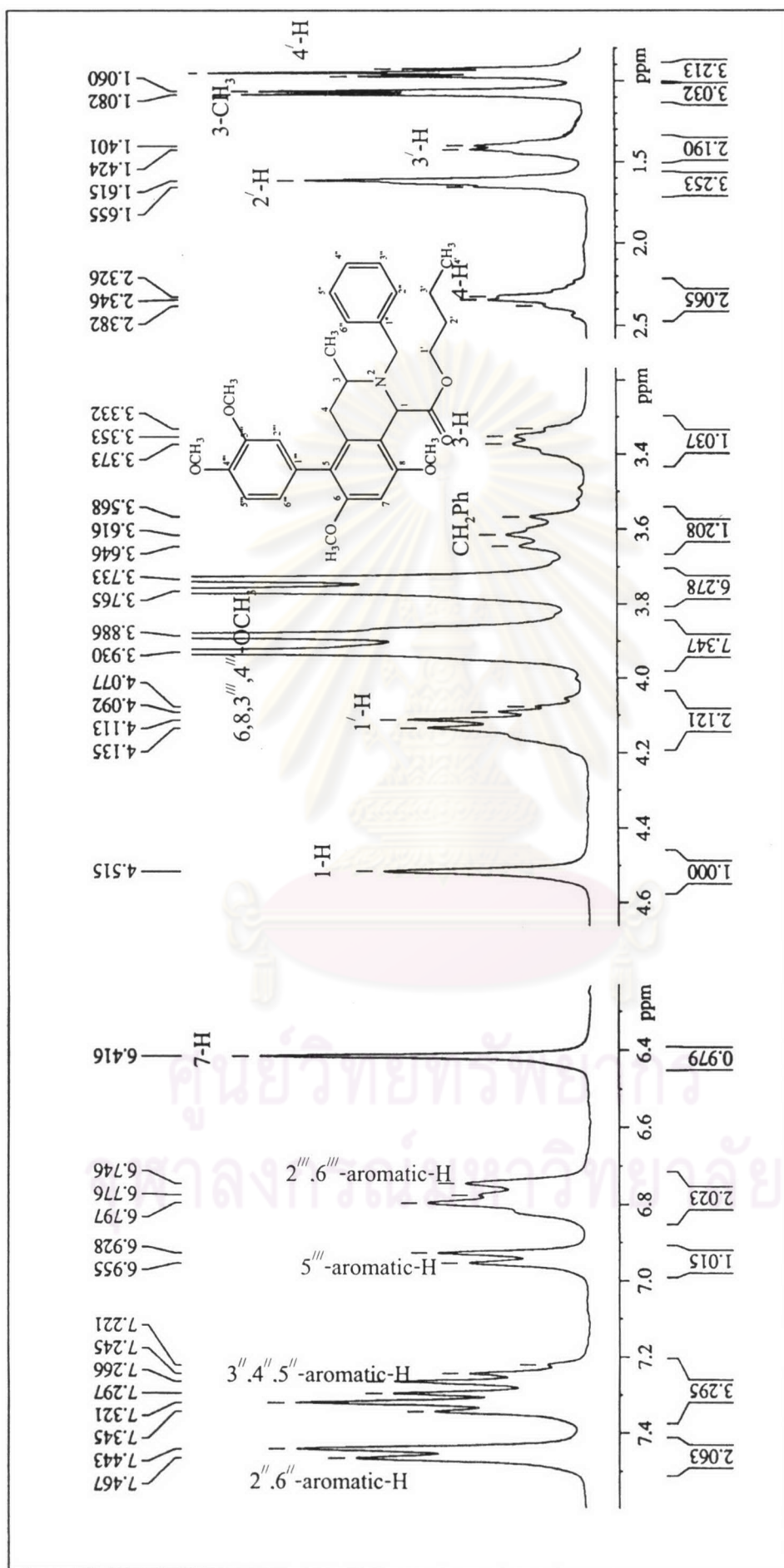


Figure 168 The 300 MHz  $^1\text{H-NMR}$  spectrum of butyl-5-(3,4-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10) (Enlarged scale)

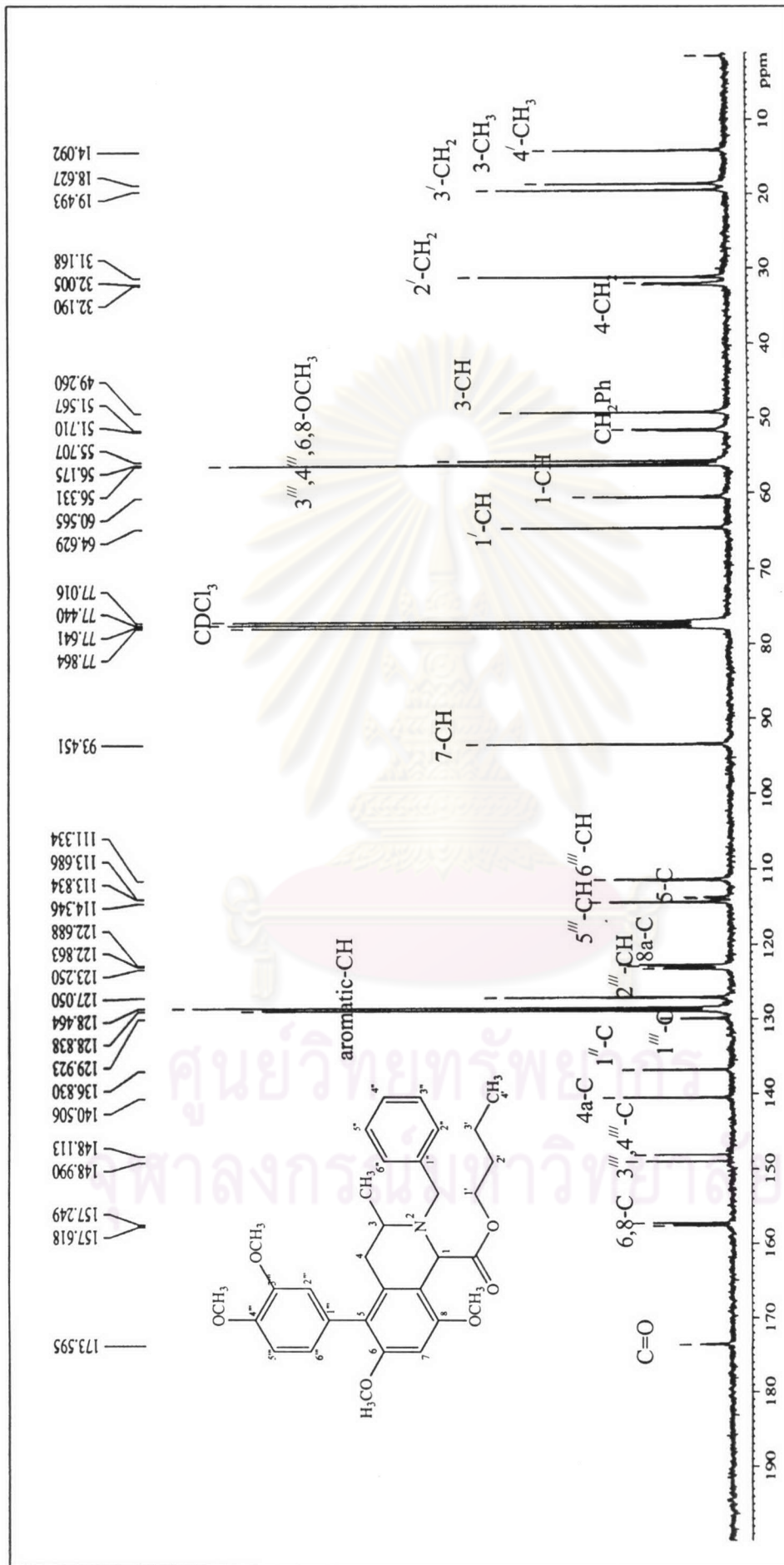


Figure 169 The 75 MHz <sup>13</sup>C-NMR spectrum of butyl-5-(3,4-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10)

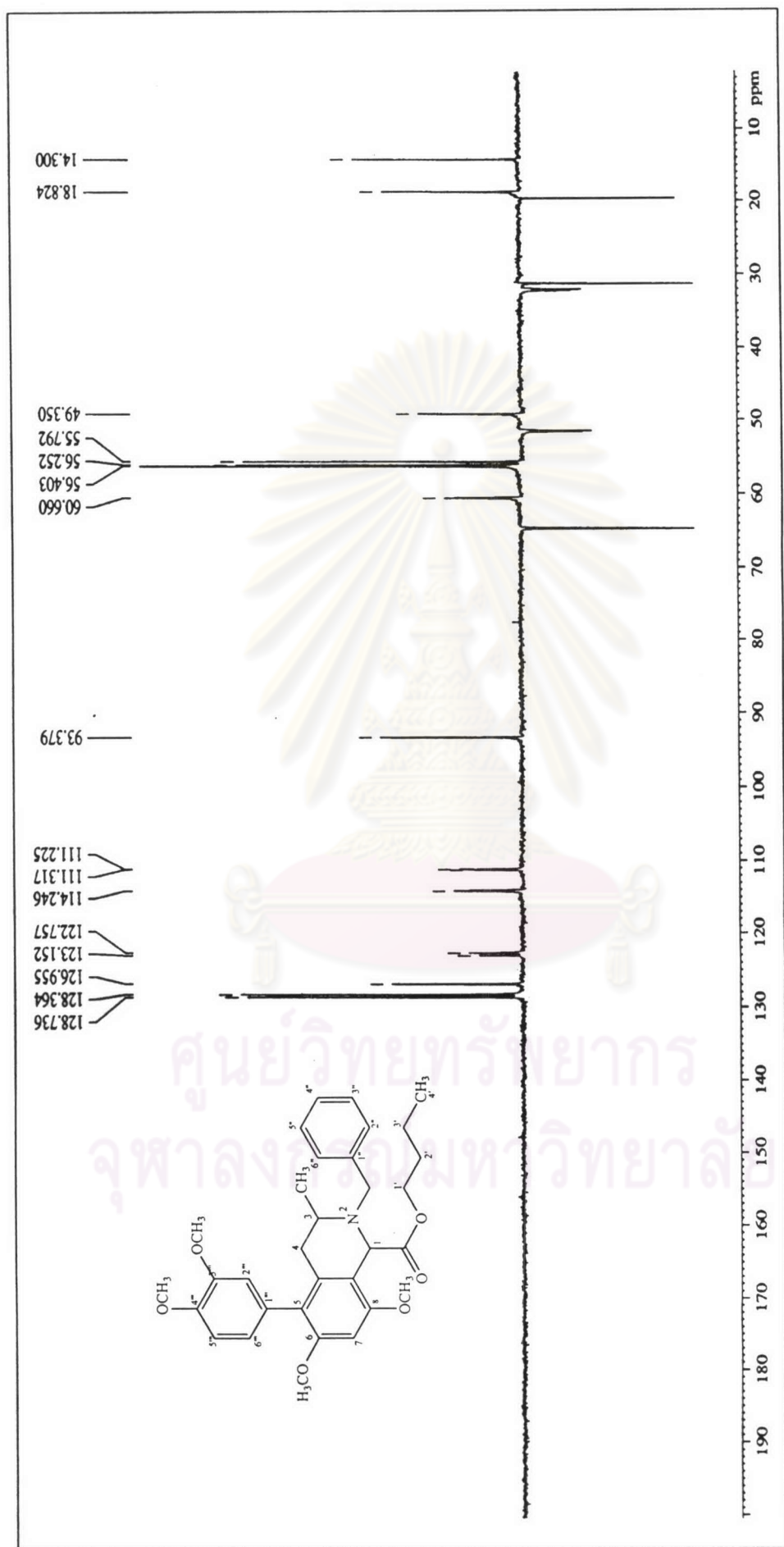


Figure 170 The 75 MHz  $^{13}\text{C}$ -NMR spectrum of butyl-5-(3<sup>'''</sup>, 4<sup>'''</sup>-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10)



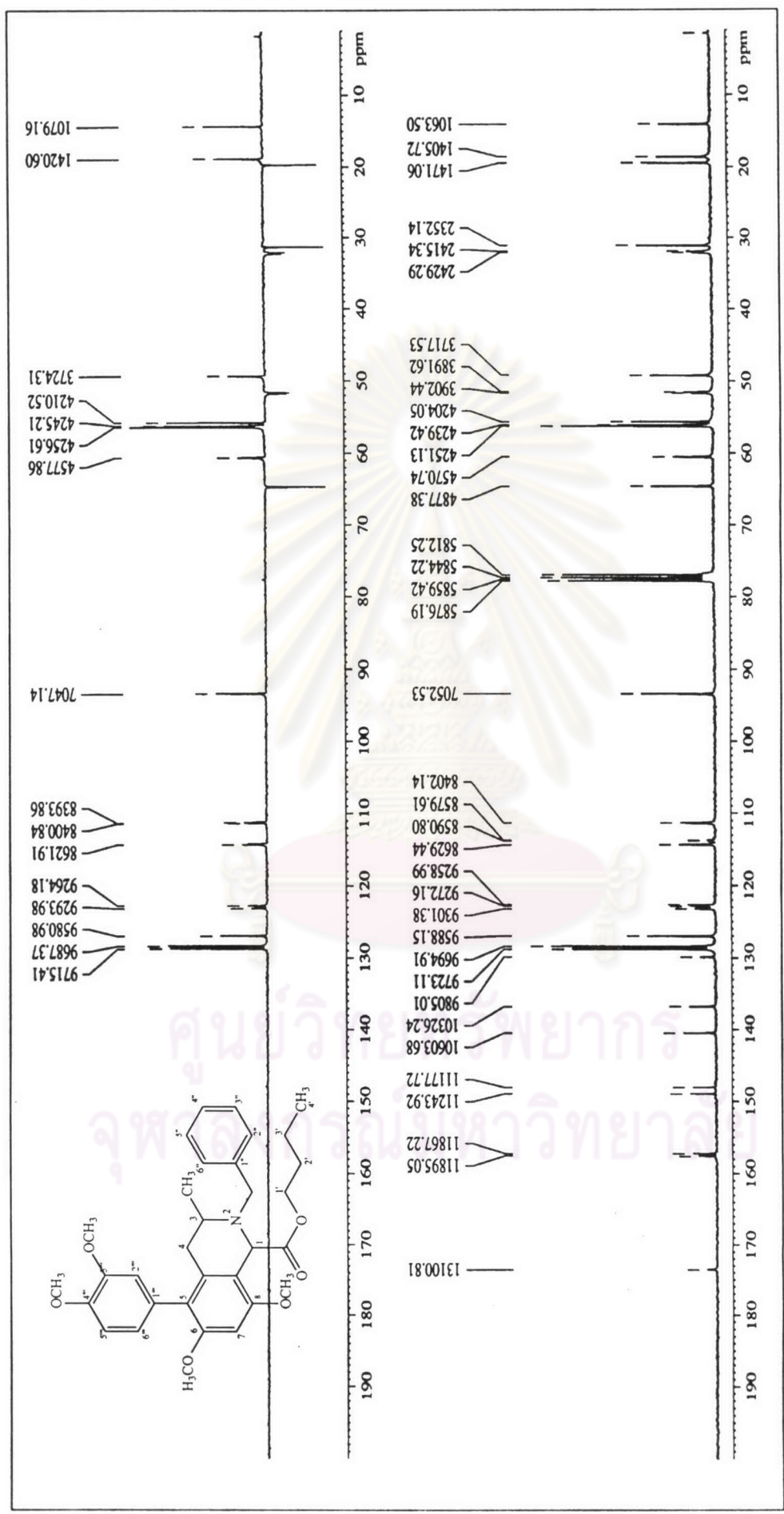


Figure 171 The 75 MHz DEPT 135 and <sup>13</sup>C-NMR spectrum comparison of butyl-5-(3<sup>'''</sup>, 4<sup>'''</sup>-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10)

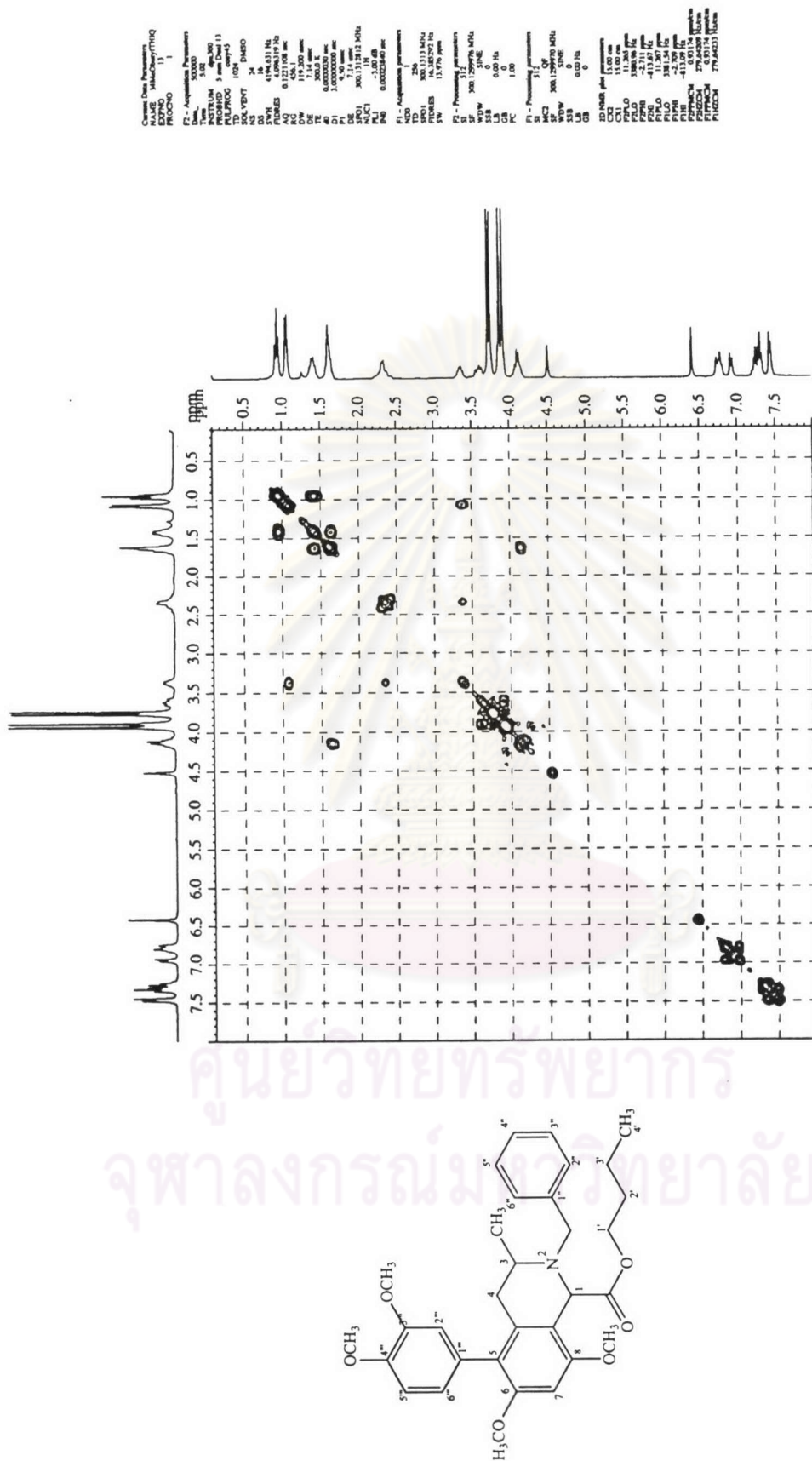


Figure 172 The 300 MHz HH COSY spectrum of butyl-5-(3<sup>'''</sup>,4<sup>'''</sup>-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10)

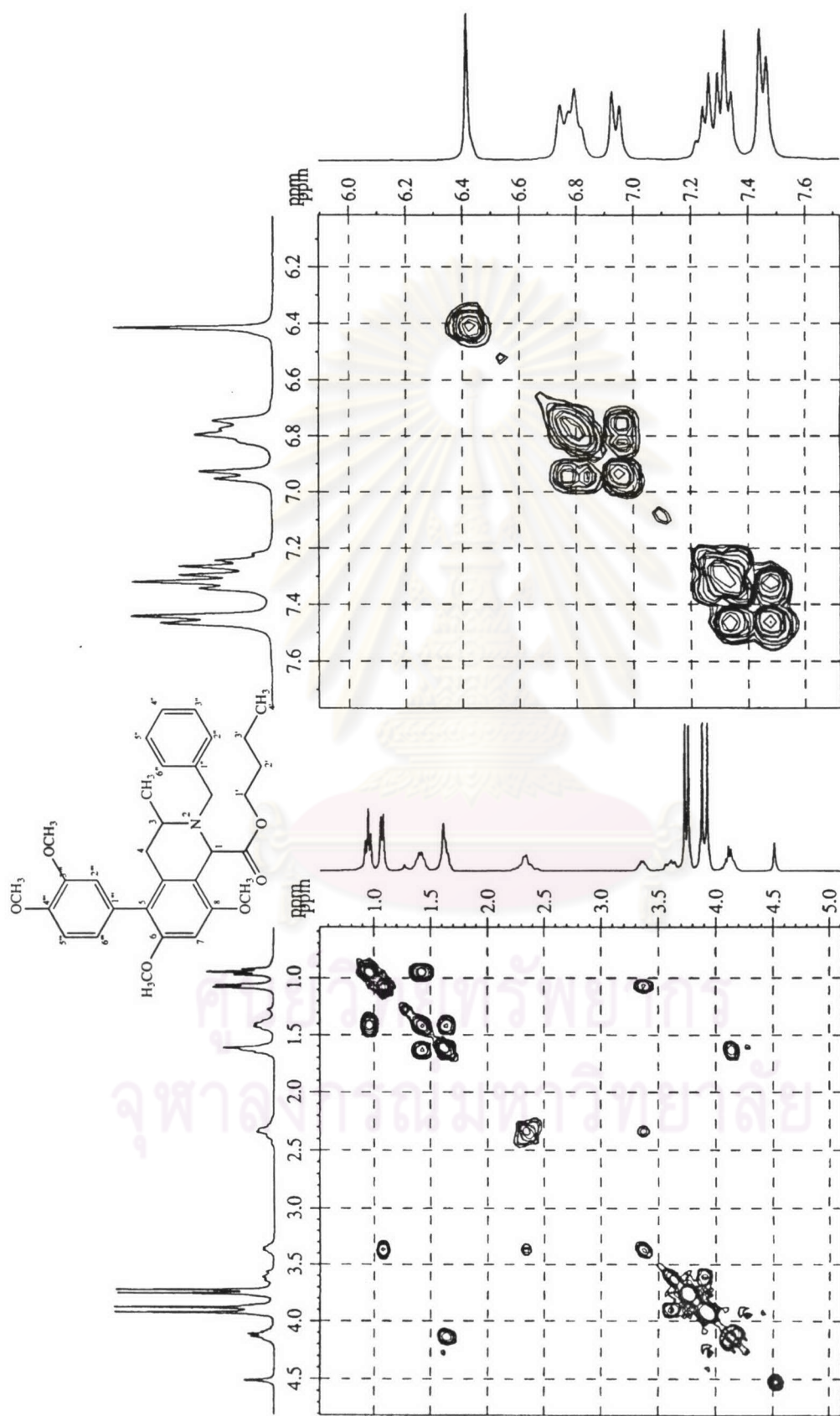


Figure 173 The 300 MHz HH COSY spectrum of butyl-5-(3,4-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10) (Enlarged scale)



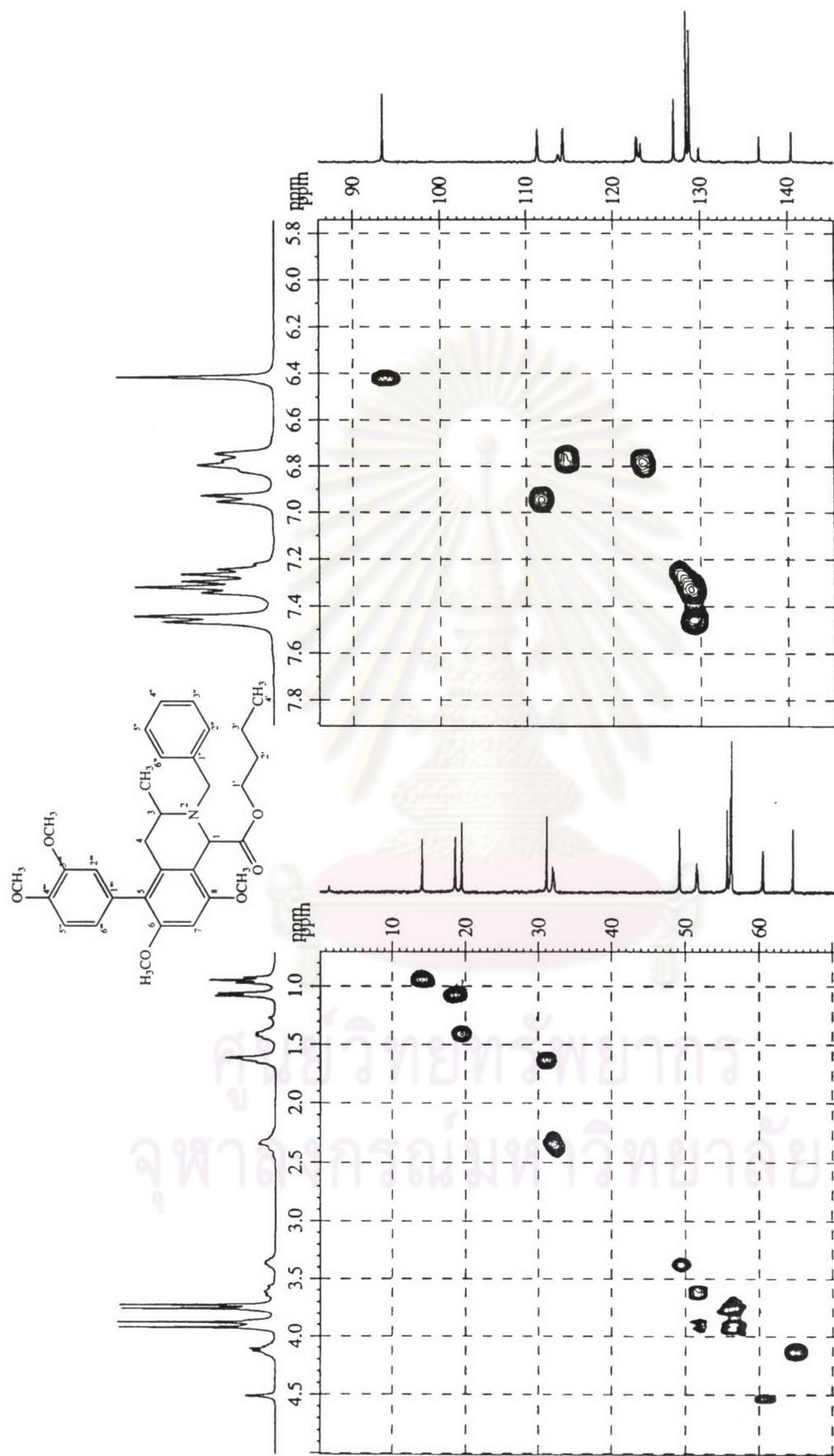


Figure 175 The 300 MHz HMQC spectrum of butyl-5-(3<sup>'''</sup>, 4<sup>'''</sup>-dimethoxyphenyl)-2-benzyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline-1-carboxylate (CU-21-10) (Enlarged scale)

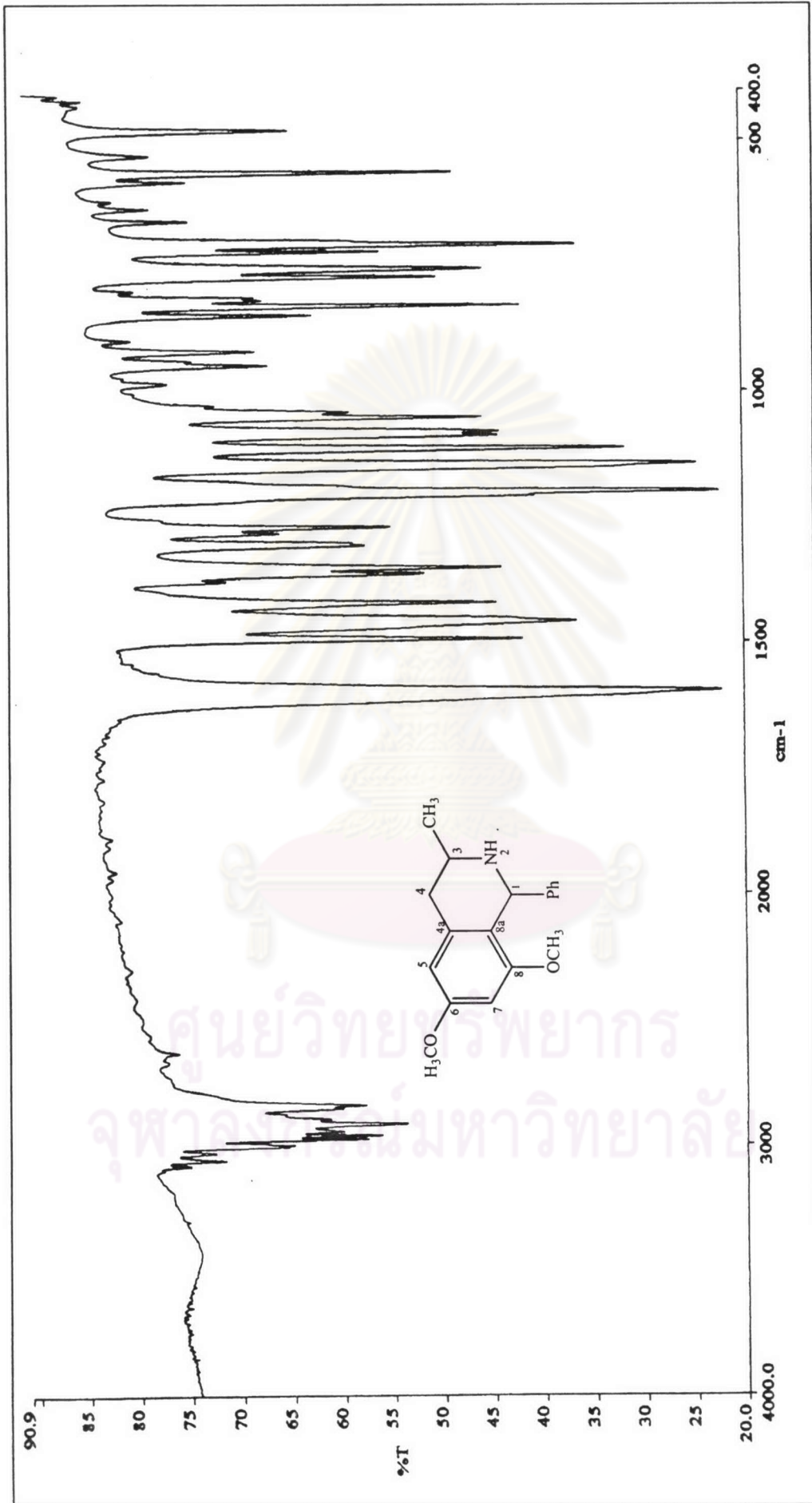


Figure 176 The IR spectrum (KBr) of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01)

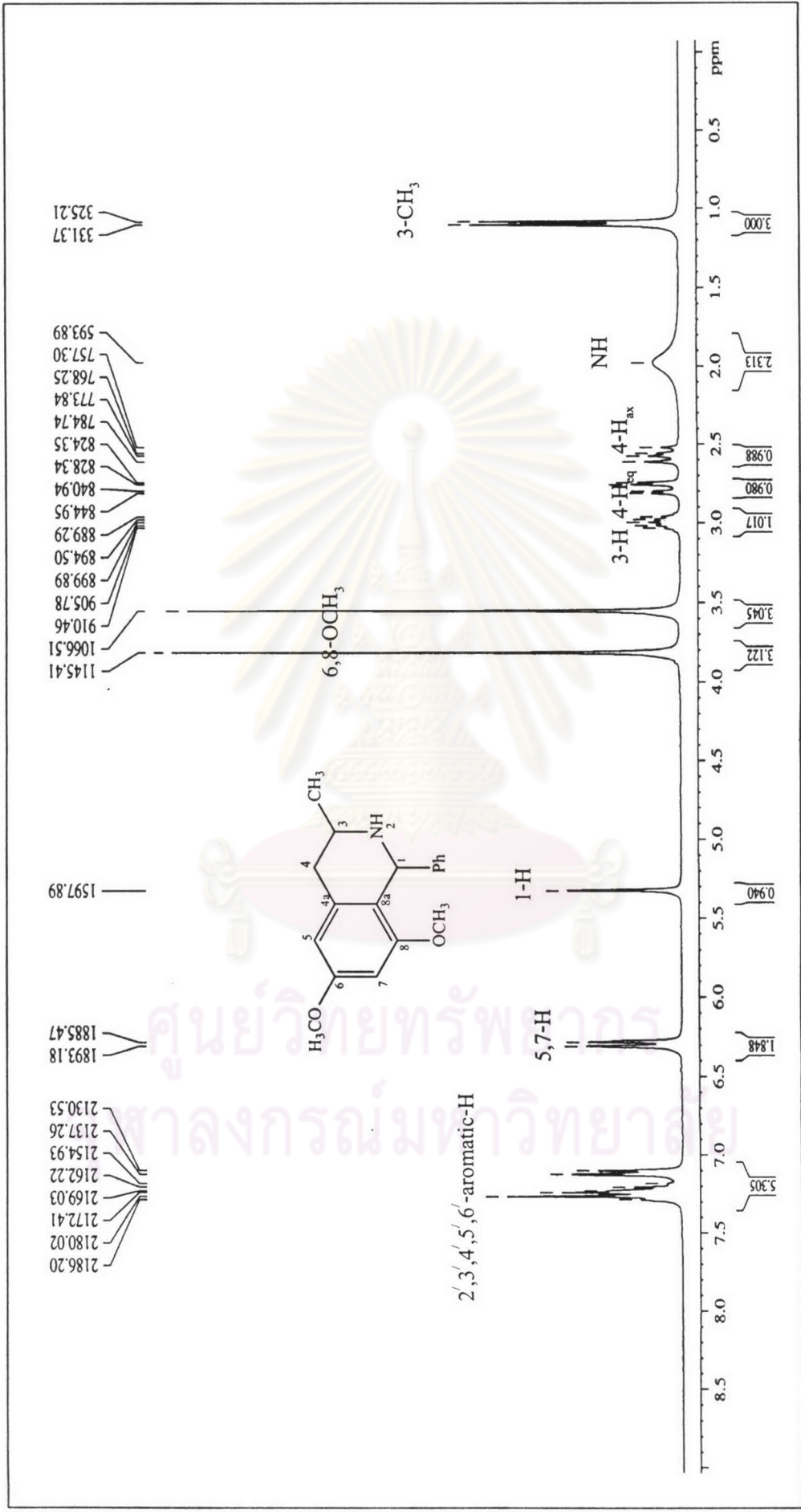


Figure 177 The 300 MHz <sup>1</sup>H-NMR spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01)

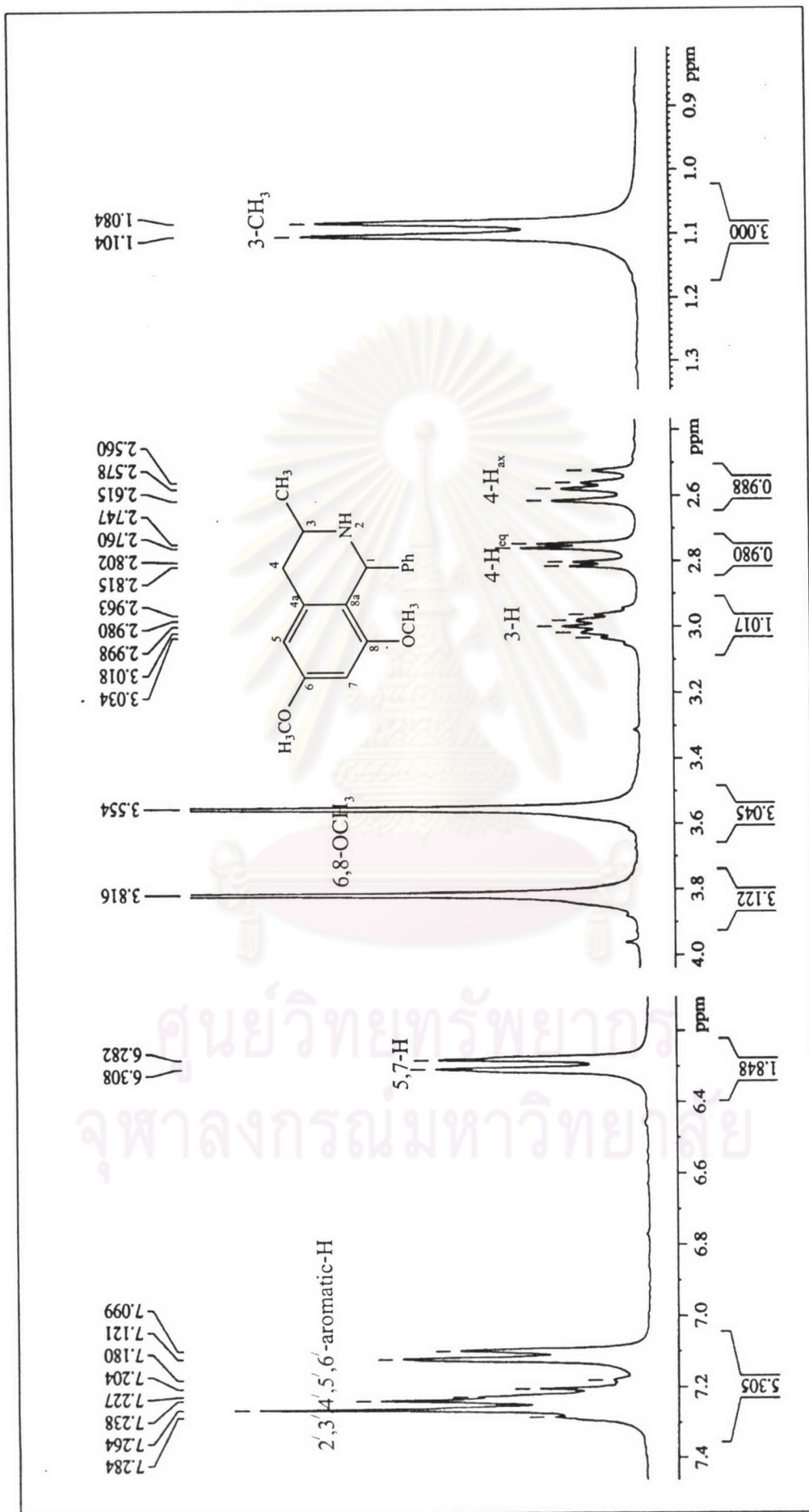


Figure 178 The 300 MHz <sup>1</sup>H-NMR spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01) (Enlarged scale)



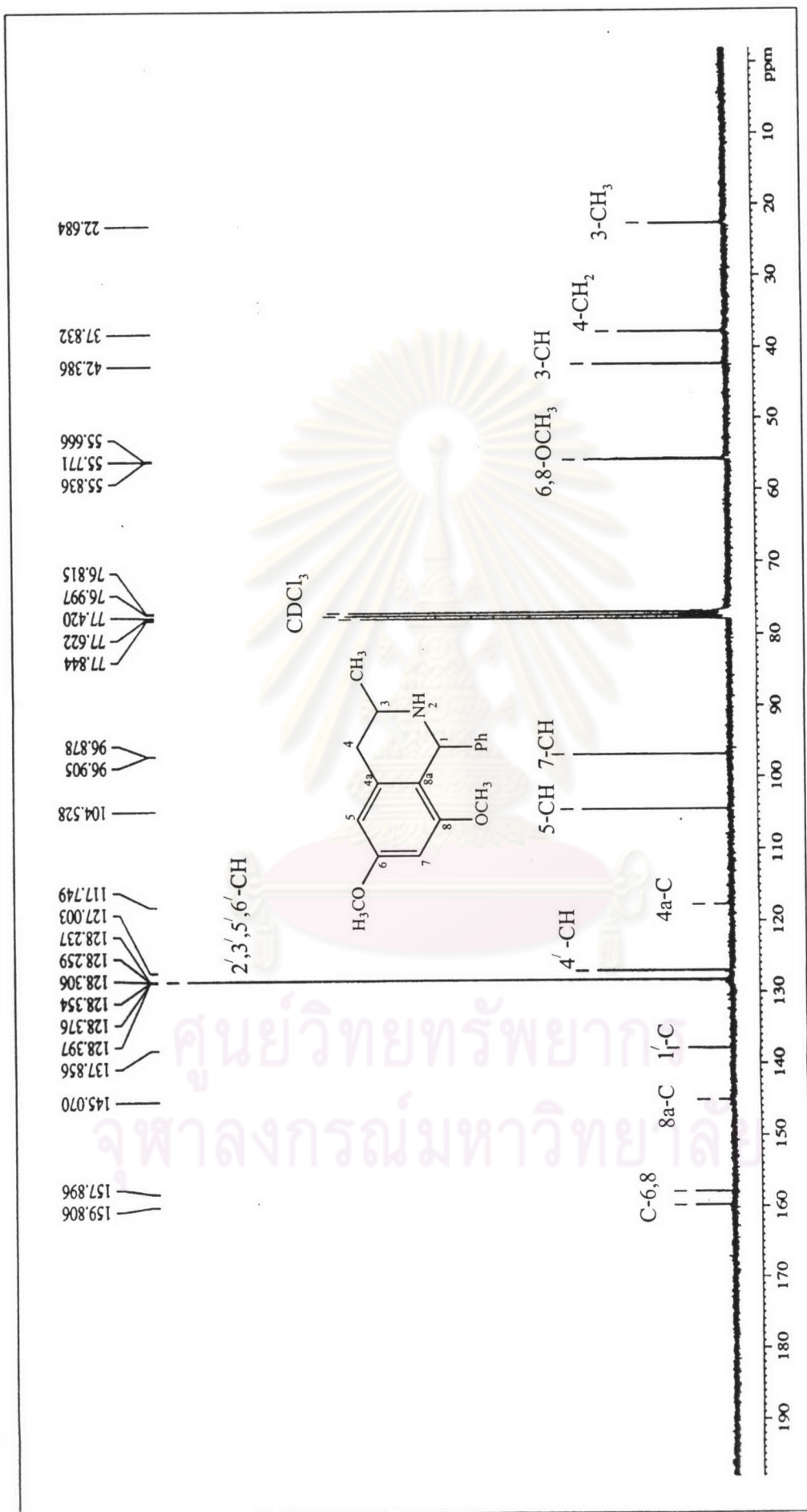


Figure 179 The 75 MHz <sup>13</sup>C-NMR spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01)

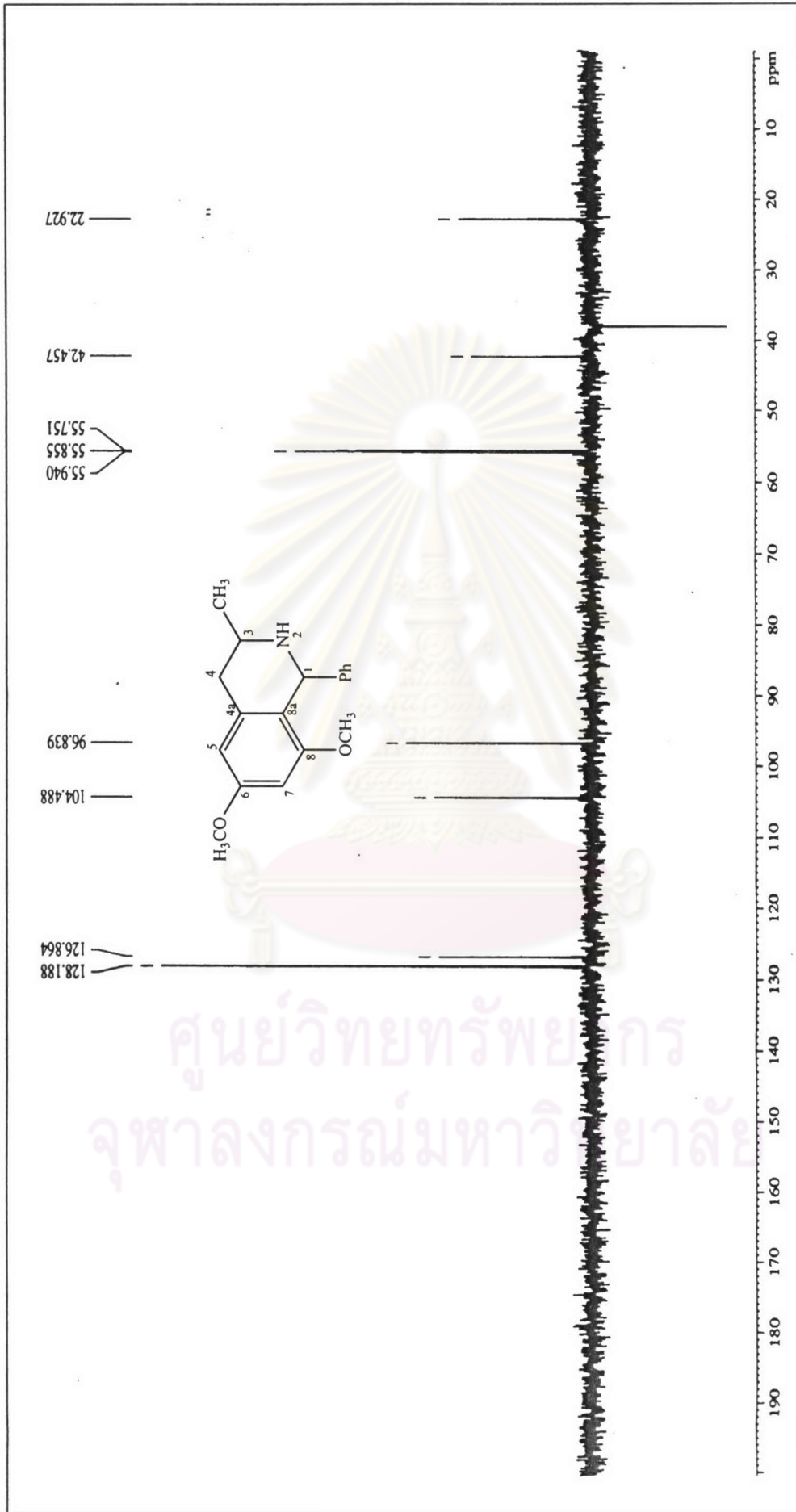


Figure 180 The 75 MHz DEPT 135 spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01)

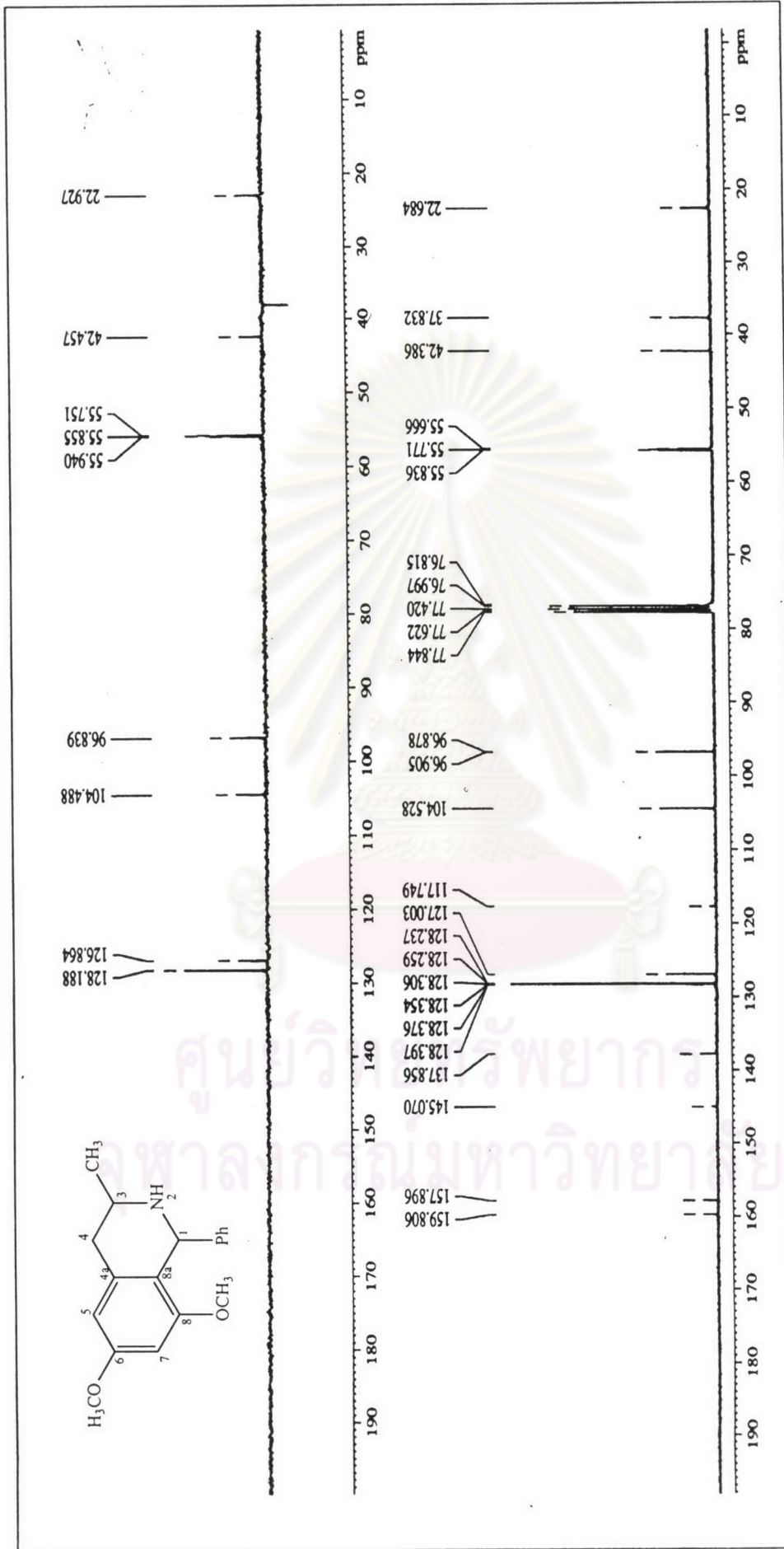


Figure 181 The 75 MHz DEPT 135 and <sup>13</sup>C-NMR spectrum comparison of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline

(CU-22-01)



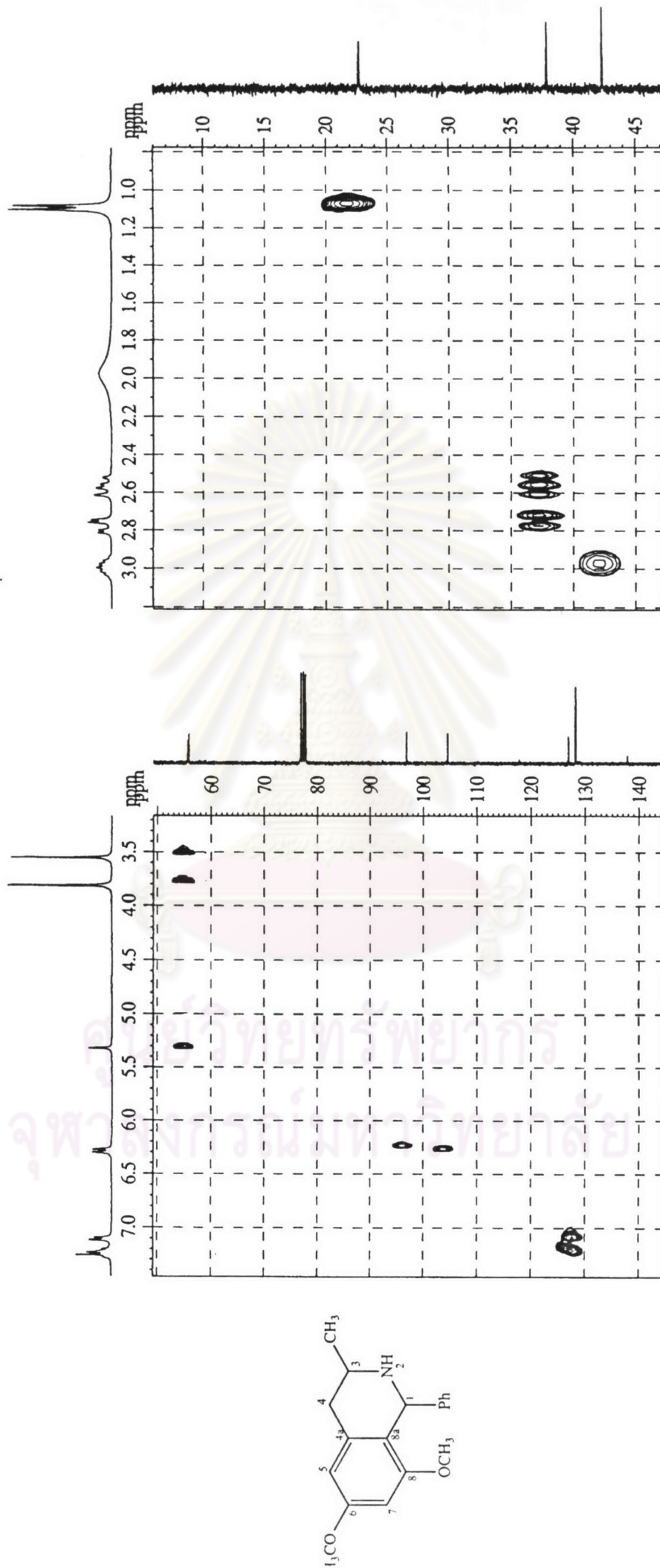
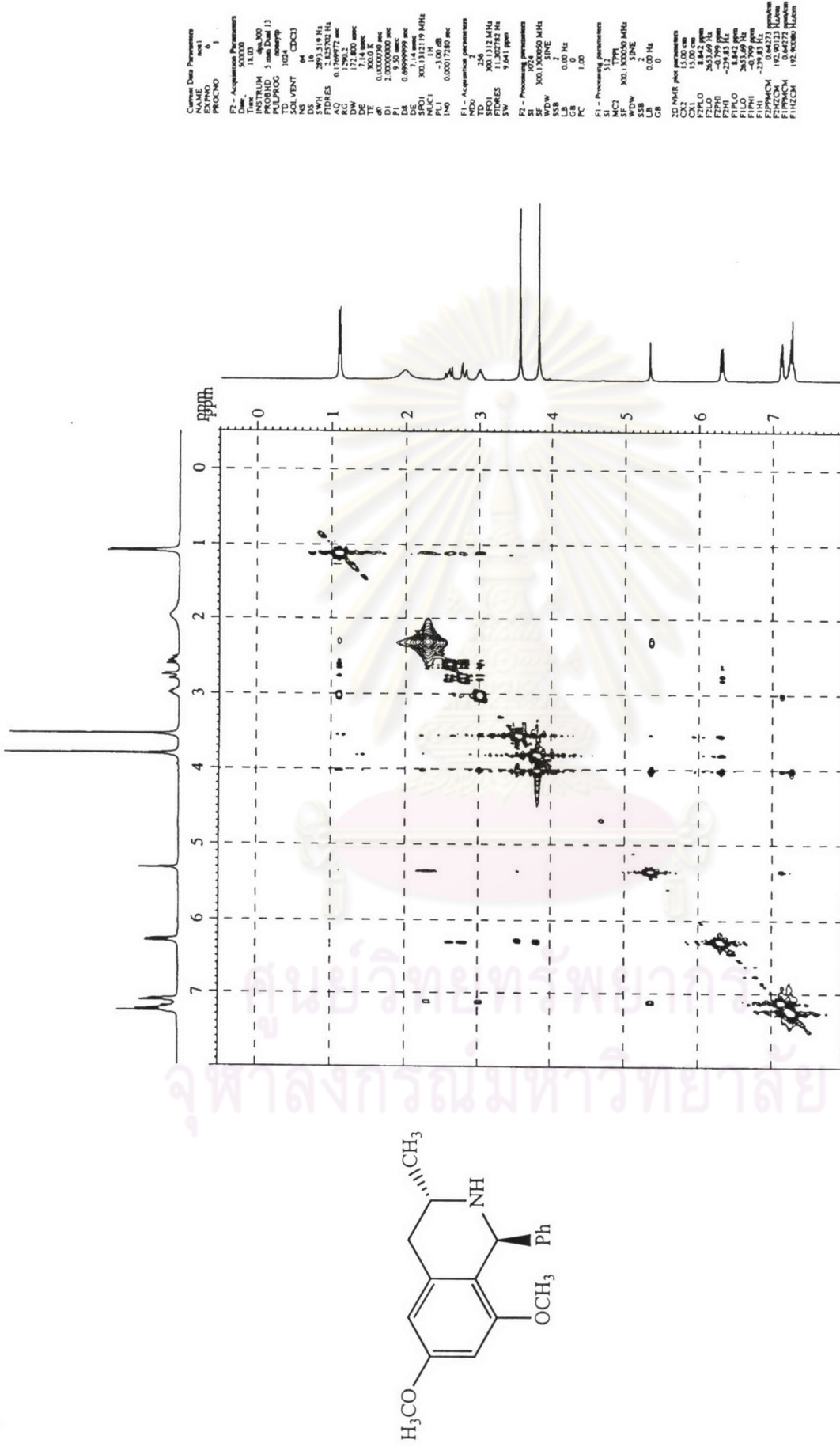


Figure 183 The 300 MHz HMQC spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline(CU-22-01) (Enlarged scale)



Current Data Parameters  
NAME: test1  
PROCNO: 1  
F1 - Acquisition Parameters  
Date\_: 200808  
Time: 18.03  
PROBHD: 5 mm DAI 13  
PULPROG: zgpg30  
SOLVENT: DMSO  
NS: 64  
SWH: 2893.518 Hz  
FIDRES: 1.63702 Hz  
AQ: 0.12962 sec  
RG: 1280  
DW: 17.800 nsec  
DE: 2.000 nsec  
TE: 300.2 K  
d1: 0.000000 sec  
d11: 0.000000 sec  
P1: 1.500000 sec  
P2: 0.69999999 sec  
SFO1: 300.131219 MHz  
NUC1: 1H  
IN1: 40  
RG1: 0.00017680 sec  
F2 - Acquisition parameters  
MDS: 256  
TD: 65536  
SFO2: 300.131219 MHz  
FIDRES: 11.82732 Hz  
SW: 9.641 ppm  
F3 - Processing parameters  
SI: 1024  
SF: 300.131219 MHz  
WDW: 2  
SSB: 0 Hz  
CB: 0  
PC: 1.00  
F4 - Processing parameters  
SI: 512  
SF: 150.065609 MHz  
WDW: 2  
SSB: 0 Hz  
CB: 0  
PC: 1.00  
2D NMR plot parameters  
CX2: 12.00 cm  
CY2: 12.00 cm  
PZLO: 1.842 Hz  
PZLH: 2653.69 Hz  
F2H1: -29.43 Hz  
F1FLO: 8.842 ppm  
F1F1H: -40.799 Hz  
F1H1: -239.43 Hz  
F2H2: 172.800 Hz  
F1F2H2: 0.64777 Hz  
F1F2H1: 172.80000 Hz

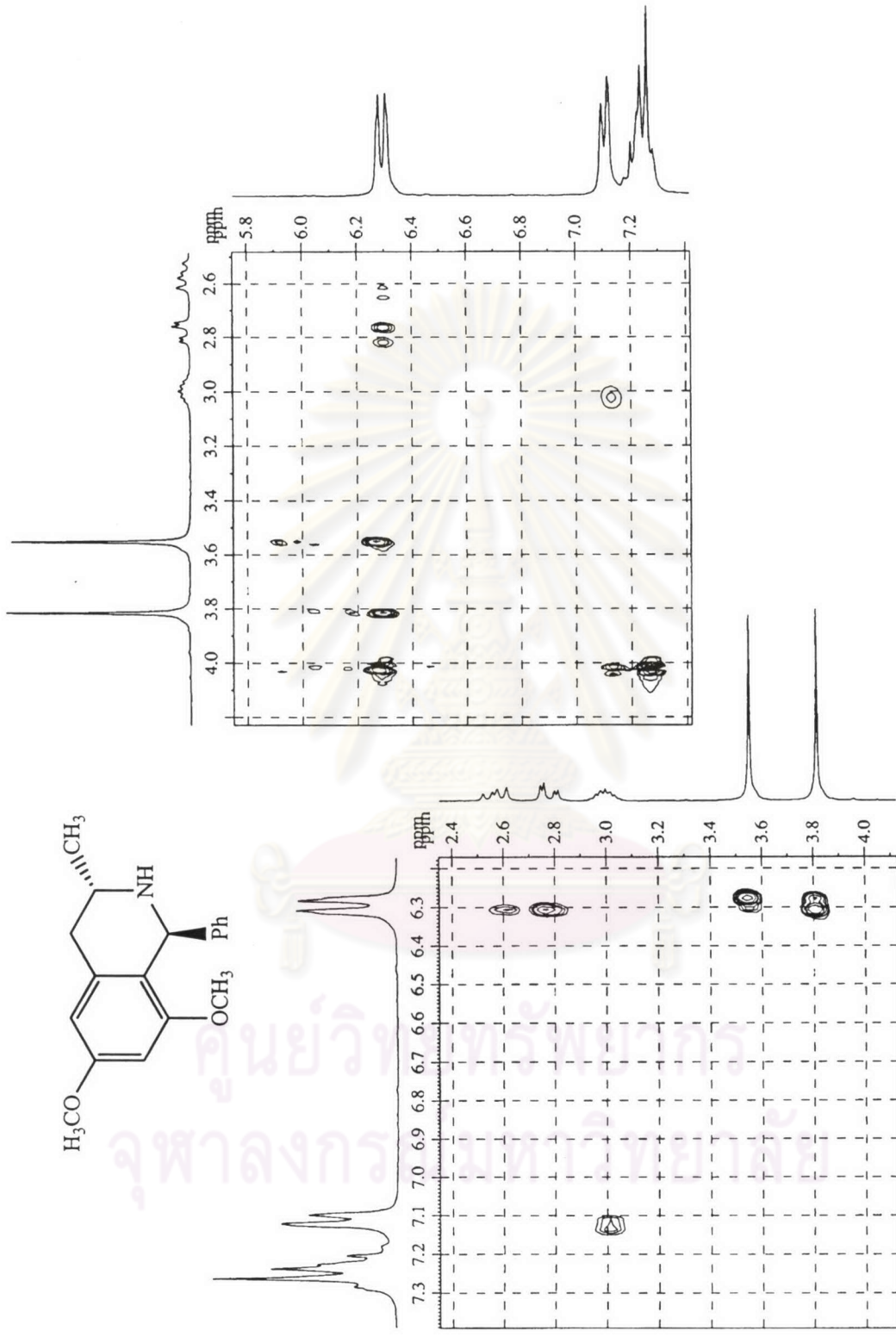


Figure 185 The 300 MHz NOESY spectrum of 1-phenyl-6,8-dimethoxy-3-methyl-1,2,3,4-tetrahydroisoquinoline (CU-22-01) (Enlarged scale)