Diversity-Oriented Synthesis of Quinolines via Friedländer annulation reaction under mild catalytic conditions

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EXPERIMENTAL

General Information

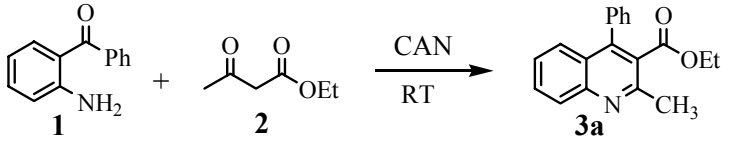
All moisture-sensitive reactions were carried out under N_2 atmosphere in flame-dried glassware sealed by rubber septa. Unless otherwise specified, materials were obtained from commercial sources and used without purification. All solvents were dried according to standard procedures and purified by distillation prior to use. Addition of chemicals was performed by using disposable plastic syringes. Column chromatography was performed using Acme's silica gel (60-120 mesh). Solvents for chromatography (*n*-hexane, cyclohexane, EtOAc) were distilled prior to use. For analytical TLC, Merck precoated silica gel 60 F-254 plates using UV light (254 nm) as visualizing agent. Melting points were obtained using a precision digital melting point Veego VMP-DS apparatus and are uncorrected. Optical rotations were measured on a Jasco P-1030 polarimeter. IR spectra were recorded on a thermo Nicolet Nexus 670 FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on either a Bruker Avance 300 (300.132 MHz for ^{1}H, 75.473 for ^{13}C), or Varian FT-200MHz (Gemini) spectrometer in $CDCl_3$. Chemicals shifts are reported in parts per million (δ) relative to tetramethylsilane (δ 0.0) as an internal standard. Elemental analyses were performed on a Elementar's Vario EL microanalyzer. Low-resolution mass spectra (ESI-MS) and HRMS were recorded on Quattro LC, Micromass, and Q STAR XL, Applied Biosystems respectively.

Reaction optimization study:

In an attempt to find the optimum reaction conditions, a systematic study was carried out on a representative case by varying the concentration of the catalyst, solvent and the reaction temperature (Table 1). In screening a set of solvents, we observed a direct correlation between polarity and yield (MeOH >EtOH > CH_3CN > THF > CH_2Cl_2 > toluene). Thus, the high yields were obtained in polar solvents particularly MeOH, whereas cyclohexane proved to be the least effective. Both the amount of catalyst and

choice of solvent were found to influence the course of reaction. However, increase in the concentration of CAN from 25% to 50% resulted in 10% decrease in the yield of the reaction. In the absence of catalyst, the reaction did not yield any product even after prolonged reaction time (10-15 h).

TABLE 1[a]: Optimization of the catalyst equivalents, solvent and reaction time for the reaction of *o*-aminoarylketone (**1**) with ethyl acetoacetate (**2**)



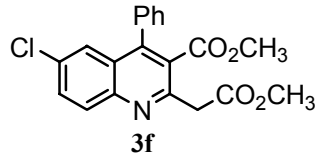
Entry	Catalyst (mol %)	Solvent	Time (min)	Yield (%)[c]	TON[b]
1	None	CH_3CN	-	-	-
2	CAN (5)	CH_3CN	90	70	1400
3	CAN (5)	MeOH	45	80	1600
4	CAN (10)	CH_3CN	120	75	750
5	CAN (10)	MeOH	45	96	960
6	CAN (10)	EtOH	45	92	920
7	CAN (10)	THF	90	60	600
8	CAN (10)	CH_2Cl_2	120	45	450
9	CAN (10)	H_2O	180	10	100
10	CAN (25)	CH_3CN-H_2O(4:1)	180	65	260
11	CAN (25)	Toluene	180	15	60
12	CAN (50)	CH_3CN	90	65	130
13	CAN (50)	MeOH	30	86	172

[a]Reactions conditions: *o*-aminoarylketone (1 mmol), ethyl acetoaetate (1 mmol), RT.
[b]TON =turn-over number (defined as 100 x mmol of product/ mmol of catalyst).
[c]Isolated yield after column chromatography.

Experimental procedures and characterization data:

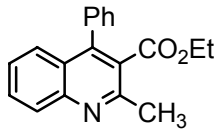
Typical procedure for the synthesis of methyl 6-chloro-2-(2-methoxy-2-oxoethyl)-4-phenyl-3-quinolinecarboxylate (3f). A mixture of 2-amino-5-chlorobenzophenone (2.31 g, 10.0 mmol), dimethyl 1,3-acetonedicarboxylate (1.74 g, 10.0 mmol), and CAN (0.548 g, 1 mmol, 10 mol%) in methanol (10 mL) was stirred at room temperature for 45 min. After completion of the reaction (monitored by TLC), the reaction mixture was diluted with EtOAc (30 mL), and washed with water (15 mL), dried (Na_2SO_4) and concentrated

in vacuo. The resulting residue was purified by silica gel column chromatography using EtOAc: petroleum ether (1:10) to afford the pure product **3f** (3.48 g, 94%).



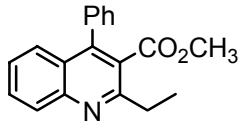
3f

m.p. 110-120 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 3.47 (s, 3H, CH_3), 3.71 (s, 3H, CH_3), 4.18 (s, 2H, $ArCH_2$), 7.31-7.35 (m, 2H, ArH), 7.47-7.55 (m, 4H, ArH), 7.64-7.69 (dd, 1H, J_1 = 9.06, J_2 =2.26 Hz, ArH), 8.02-8.06 (d, 1H, J = 9.06 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 43.1, 52.2, 125.4, 126.5, 127.2, 128.4, 128.5, 128.8, 129.0, 129.1, 131.0, 131.5, 133.2, 135.3, 146.2, 147.1, 151.6, 168.2, 170.3. HRMS (ESI) calcd for $C_{20}H_{16}NO_4Cl$ 370.0846 $[M+H]^+$, found 370.0837.



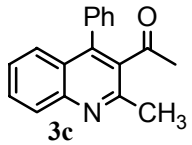
3a

ethyl 2-methyl-4-phenyl-3-quinolinecarboxylate (3a). m.p. 99-102 ^{o}C (Lit. m.p.[20] 99-100 ^{o}C). ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 0.89-0.96 (t, 3H, J = 7.55 Hz, CH_3), 2.76 (s, 3H, $ArCH_3$), 3.98-4.06 (q, 2H, J = 7.55 Hz, CH_2), 7.32-7.56 (m, 7H, ArH), 7.65-7.71 (m, 1H, ArH), 8.02-8.06 (d, 1H, J = 8.31 Hz, ArH). MS (EI): m/z (%) = 291 (M^+, 95), 246 (100), 218 (50), 176 (20), 85 (20), 71 (40), 57 (80), 43 (70).



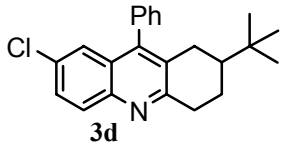
3b

methyl 2-ethyl-4-phenyl-3-quinolinecarboxylate (3b). m.p. 105-106 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.38-1.47 (t, 3H, J = 7.43 Hz, CH_3), 2.95-3.08 (q, 2H, J = 7.43 Hz, $ArCH_2$), 3.53 (s, 3H, CO_2CH_3), 7.31-7.58 (m, 7H, ArH), 7.64-7.73 (m, 1H, ArH), 8.05-8.11 (d, 1H, J = 8.18 Hz, ArH). MS (EI): m/z (%) = 291 (M^+, 100), 276 (95), 260 (10), 232 (40), 204 (45), 177 (10), 71 (10), 57 (30), 43 (25).



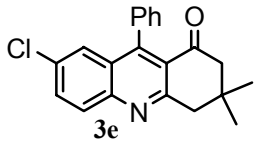
3c

1-(2-methyl-4-phenyl-3-quinolyl)ethanone (3c). m.p. 111-112 ^{o}C (Lit. m.p.[21] 113-114 ^{o}C). ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.96 (s, 3H, $COCH_3$), 2.67 (s, 3H, $ArCH_3$), 7.32-7.73 (m, 8H, ArH), 8.01-8.07 (d, 1H, J = 8.17 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.7, 31.7, 124.9, 126.0, 126.3, 128.5, 128.7, 129.9, 134.7, 135.1, 143.7, 147.4, 153.3, 205.4. MS (EI): m/z (%) = 261 (M^+, 50), 246 (100), 218 (55), 176 (25), 57 (10), 43 (25).



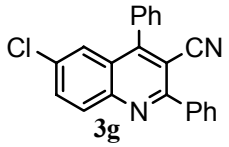
3d

2-(*tert*.butyl)-7-chloro-9-phenyl-1,2,3,4-tetrahydroacridine (3d). m.p. 148-150 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 0.87 (s, 9H, 3 x CH_3), 1.41-1.62 (m, 2H, CH_2), 2.10-2.18 (m, 1H, CH), 2.22-2.34 (m, 1H, ArCH), 2.59-2.68 (m, 1H, ArCH), 3.00-3.15 (m, 1H, ArCH), 3.22-3.33 (m, 1H, ArCH), 7.18-7.23 (m, 3H, ArH), 7.46-7.58 (m, 4H, ArH), 7.89-7.92 (d, 1H, J = 8.87 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.1, 27.1, 29.4, 32.5, 34.8, 44.6, 124.5, 127.4, 128.1, 128.7, 128.8, 128.9, 129.2, 129.8, 130.0, 131.1, 136.3, 144.6, 145.9, 159.7. HRMS (ESI) calcd for $C_{23}H_{24}NCl$ 350.1675 $[M + H]^+$, found 350.1680.



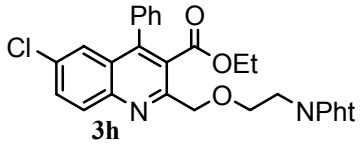
3e

7-chloro-3,3-dimethyl-9-phenyl-1,2,3,4-tetrahydro-1-acridinone (3e). m.p. 219-220 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.17 (s, 6H, 2 x CH_3), 2.52 (s, 2H, $COCH_2$), 3.23 (s, 2H, $ArCH_2$), 7.11-7.15 (m, 2H, ArH), 7.36-7.37 (m, 1H, ArH), 7.48-7.53 (m, 3H, ArH), 7.64-7.69 (dd, 1H, J_1 = 9.06, J_2 =2.26 Hz, ArH), 7.95-7.99 (d, 1H, J = 9.06 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.3, 32.2, 48.2, 54.1, 123.2, 126.7,127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 130.1, 132.4, 136.7, 147.3, 150.0, 161.4, 197.6. MS (ESI) m/z 336 ($[M+H]^+$, 100). HRMS (ESI) calcd for $C_{21}H_{18}NOCl$ 336.1155 $[M + H]^+$, found 336.1146.



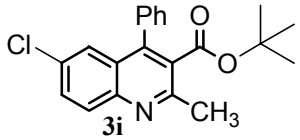
3g

6-chloro-3-cyano-2,4-diphenylquinoline (3g). m.p. 192-194 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 7.46-7.72 (m, 9H, ArH), 7.75-7.81 (dd, 1H, J_1 = 9.63, J_2 =3.02 Hz, ArH), 7.96-8.02 (m, 2H, ArH), 8.15 (d, 1H, J = 8.87 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 116.8, 128.6, 129.0, 129.1, 129.2, 129.3, 129.6, 130.0, 130.1, 130.8, 131.7, 133.4, 133.9, 133.8, 137.7, 147.0, 155.5, 158.7. EIMS: m/z (%) 343 ($M^{+2,}$ 25), 341 (72), 157 (12), 117 (15), 101 (45), 79 (100). Anal. Calcd for $C_{22}H_{13}N_2Cl$: C, 77.53, H, 3.84, N, 8.22. Found: C, 77.38, H, 3.76, N, 8.17. IR (KBr): 2219 cm^{-1}



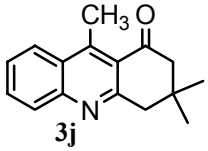
3h

ethyl 6-chloro-2-(2-phthalimidoethoxy)methyl-4-phenylquinoline-3-carboxylate (3h). m.p. 165-166 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 0.92 (t, 3H, J = 7.55 Hz, CH_3), 3.68-3.74 (t, 2H, J = 6.04 Hz, OCH_2), 3.81-3.87 (t, 2H, J = 6.04 Hz, NCH_2), 4.00-4.08 (q, 2H, J = 7.55 Hz, CO_2CH_2), 4.91 (s, 2H, $ArCH_2$), 7.29-7.34 (m, 2H, ArH), 7.45-7.51 (m, 4H, ArH), 7.61-7.73 (m, 3H, ArH), 7.77-7.83 (m, 2H, ArH), 7.80-8.02 (d, 1H, J = 9.06 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.5, 37.4, 61.4, 67.6, 73.5, 123.2, 123.3, 125.3, 127.0, 127.1, 128.3, 128.5, 128.7, 129.3, 131.0, 131.2, 132.1, 133.2, 133.8, 134.9, 145.5, 146.4, 155.0, 167.5, 168.1. HRMS (ESI) calcd for $C_{29}H_{23}N_2O_5Cl$ 515.1373 $[M+H]^+$, found 515.1359.



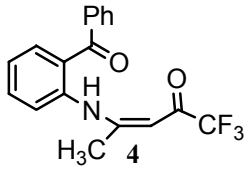
3i

***tert*-butyl 6-chloro-2-methyl-4-phenyl-3-quinolinecarboxylate (3i).** m.p. 141-143 ^{o}C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.21 (s, 9H, 3 x CH_3), 2.73 (s, 3H, $ArCH_3$), 7.22(tt, 2H, J = 8.6, 2.1 Hz, ArH), 7.32-7.37 (m, 2H, ArH), 7.42-7.44 (d, 1H, J = 2.26 Hz, ArH), 7.47-7.54 (m, 3H, ArH), 7.58-7.63 (dd, 1H, J_1 = 9.06, J_2 =2.26 Hz, ArH), 7.96-8.00 (d, 1H, J = 9.06 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.5, 27.5, 82.6, 125.1, 126.1, 128.3, 128.6, 129.5, 130.4, 130.8, 132.1, 135.0, 144.5, 145.8, 154.8, 167.0. MS (ESI) m/z (%) 354 (M+H, 100). HRMS (ESI) calcd for $C_{21}H_{21}NO_2Cl$ 354.1260 $[M + H]^+$, found 354.1246.



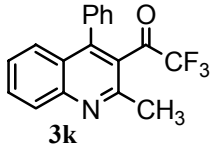
3j

3,3,-dimethyl-9-methyl-1,2,3,4-tetrahydro-1-acridinone (3j). m.p. 104-106°C. ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.12 (s, 6H, 2 x CH_3), 2.66 (s, 2H, $ArCH_3$), 3.06 (s, 2H, $COCH_2$), 3.18 (s, 2H, $ArCH_2$), 7.55 (ddd, 1H, *J* = 8.2, 6.8, 1.2 Hz, ArH), 7.75 (ddd, 1H, *J* = 8.2, 6.8, 1.2 Hz, ArH), 8.02 (d, 1H, *J* = 8.2 Hz, ArH), 8.21 (d, 1H, *J* = 8.2 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.6, 28.2, 31.2, 47.9, 54.7, 124.1, 125.5, 126.3, 127.5, 129.1, 130.7, 148.1, 150.0, 160.6, 200.2. HRMS (ESI) calcd for $C_{16}H_{17}NO$ 239.1310 $[M+H]^+$, found 239.1304.



4

(Z)-4-(2-Benzoylphenylamino)-1,1,1-trifluoropent-3-en-2-one (4). ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.05 (s, 3H, CH_3), 5.42 (s, 1H, =CH), 7.26-7.69 (m. 9H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.3, 91.5, 114.5 (q, *J* = 218 Hz), 127.1, 127.3, 128.5, 129.4, 130.3, 130.7, 131.7, 133.5, 134. 4, 137.6, 176.6 (q, *J* = 34 Hz), 195.3. MS (ESI) m/z (%) 334 (M+H, 100).

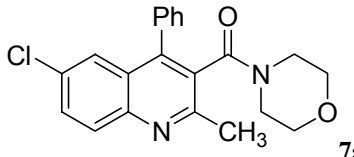


3k

2,2,2-Trifluoro-1-(2-methyl-4-phenylquinolin-3-yl)ethanone (3k). m.p. 82-84 °C (Lit.[16c] m.p. 80-81 °C). ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.61 (s, 3H, $ArCH_3$), 7.36-7.41 (m, 2H, ArH), 7.57-7.68 (m, 5H, ArH), 7.92 (m, 1H, ArH), 8.12 (d, *J* = 8.4 Hz, 1H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.8, 115.6 (q, *J* = 308 Hz), 126.1, 127.1, 127.6, 128.5, 129.1, 129.4, 130.3, 131.3, 131.6, 147.5, 148.3, 153.3, 189.2 (q, *J* = 38 Hz). MS (ESI) m/z (%) 316 (M+H, 100).

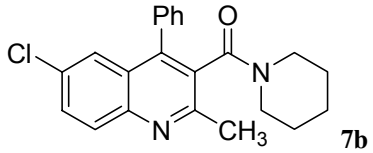
Typical procedure for the preparation of (6-chloro-2-methyl-4-phenyl-3-quinolyl)(morpholino)methanone (7a). A mixture of 2-amino-5-chlorobenzophenone (1.155 g, 5.0 mmol), 1-morpholino-1,3-butanedione, **6a** (0.855 g, 5.0 mmol), and CAN

(0.274 g, 0.5 mmol, 10 mol %) in methanol (5 mL) was stirred at room temperature for 60 minutes. After completion of the reaction (monitored by TLC), the mixture was diluted with ethyl acetate (30 mL), and washed with water (15 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography using EtOAc: petroleum ether (1:10) to afford the pure product **7a** (1.65 g, 90 %).



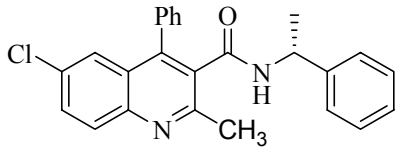
7a

m.p. 187-189 ^{o}C; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 2.68 (s, 3H, $ArCH_3$), 2.75-2.91 (m, 2H, CH_2), 2.97-3.22 (m, 2H, CH_2), 3.27-3.40 (m, 2H, CH_2), 3.45-3.63 (m, 2H, CH_2), 7.23-7.33 (m, 1H, ArH), 7.46-7.68 (m, 6H, ArH), 7.95-8.03 (d, 1H, *J*= 9.14 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.4, 41.36, 46.4, 66.3, 124.9, 125.7, 128.1, 129.0, 129.1, 129.3, 130.1, 130.5, 130.9, 132.4, 134.2, 143.2, 146.1, 155.1, 167.0. MS (ESI): m/z (%) = 367 (M+H, 100).



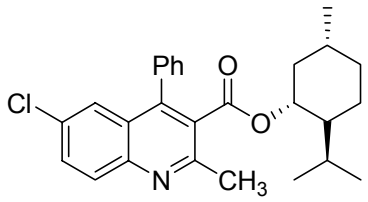
7b

(6-chloro-2-methyl-4-phenyl-3-quinolyl)(piperidino)methanone (7b). m.p.170-171 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.15-1.58 (m, 6H, 3 x CH_2), 2.71 (s, 3H, $ArCH_3$), 2.76-2.86 (m, 1H, CH), 3.00-3.09 (m, 1H, CH), 3.33-3.42 (m, 1H, CH), 3.48-3.59 (m, 1H, CH), 7.29-7.35 (m, 1H, ArH), 7.46-7.67 (m, 6H, ArH), 7.98-8.03 (d, 1H, *J*= 8.30 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.4, 24.0, 25.1, 25.9, 124.9, 125.9, 127.7, 128.8, 129.0, 129.4, 130.0, 130.4, 130.5, 132.2, 134.3, 142.9, 145.9, 155.3, 166.6. MS (ESI): m/z (%) = 365 (M+H, 100).



7c

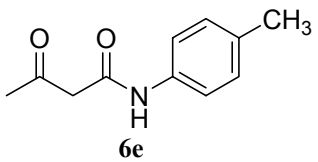
***N*3-[(1*R*)-1-phenylethyl]-6-chloro-2-methyl-4-phenyl-3-quinolinecarboxamide (7c).** m.p. 225-227 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.13-1.91 (d, 3H, *J*= 6.80 Hz, CH_3), 2.77 (s, 3H, $ArCH_3$), 4.99-5.10 (q, 1H, J_1= 6.80 Hz, J_2= 7.55 Hz, CH), 5,48-5.58 (broad doublet, 1H, *J*= 7.55 Hz, CONH), 6.91-7.00 (m, 2H, ArH), 7.19-7.29 (m, 4H, ArH), 7.34-7.43 (m, 2H, ArH), 7.47-7.56 (m, 3H, ArH), 7.61-7.66 (dd, 1H, J_1= 9.06 Hz, J_2= 2.26 Hz, ArH), 7.97-8.02 (d, 1H, *J*= 9.06 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.4, 23.5, 48.6, 125.1, 126.0, 127.3, 128.7, 128.8, 129.3, 129.4, 130.5, 130.7, 130.8, 132.2, 134.7, 141.8, 144.0, 145.9, 155.8, 166.7. MS (ESI): m/z (%) = 401 (M+H, 100).



7d

(1*R*,2*R*,5*R*)-2-isopropyl-5-methylcyclohexyl-6-chloro-2-methyl-4-phenyl-3-quinolinecarboxylate (7d). $[\alpha]_D$ –68.93^{o} (c 1.03, $CHCl_3$, 20 ^{o}C). m.p.146-147 ^{o}C; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 0.55-0.63 (d, 1H, *J*= 7.03 Hz, CH), 0.69-0.89 (dd, 6H, J_1= 15.62 Hz, J_2= 7.03 Hz, 2 x CH_3), 0.90-1.28 (m, 3H, CH_3), 1.29-1.69 (m, 7H, 3 x CH_2 + CH), 2.73 (s, 3H, $ArCH_3$), 4.57-4.72 (dt, 1H, J_1= 10.94 Hz, J_2= 4.68 Hz, OCH), 7.27-7.67 (m, 7H, ArH), 7.94-8.03 (d, 1H, *J*= 8.59 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.8, 20.9, 22.0, 22.9, 23.8, 25.6, 31.4, 39.9, 46.7, 75.9, 125.2, 126.2, 128.6, 128.9, 129.6, 129.9, 130.0, 132.4, 134.8, 144.7, 146.1, 154.8, 167.9. MS (ESI): m/z (%) = 436 (M+H, 100).

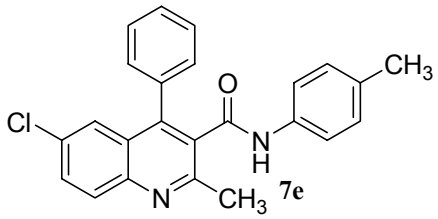
***N*1-(4-methylphenyl)-3-oxobutanamide (6e).** A mixture of *tert*-butyl acetoacetate (1.58 g, 10.0 mmol), and *p*-toluidine (1,07 g, 10.0 mmol), in 10 mL dry xylene was heated in a 50 mL beaker for a period of 5 minutes till colorless vapors of *tert*-butanol came out. TLC (EtOAc: petroleum ether, 1:2), showed the completion of the reaction. The reaction mixture was cooled and washed with hexane. Upon flash chromatography of this crude solid resulted in a pure cream-colored solid **6e** (1.81 g, 95 % yield).



6e

m.p. 92-93 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.30 (s, 3H, $COCH_3$), 2.31 (s, 3H, $ArCH_3$), 3.51 (s, 2H, $COCH_2CO$), 7.04-7.10 (d, 1H, *J*= 8.31 Hz, ArH), 7.36-7.41 (d, 1H, *J*= 8.31 Hz, ArH), 9.09 (broad singlet, 1H, CONH). MS (ESI): m/z (%) = 192 (M+H, 100), 214 ($M+Na^+$, 20).

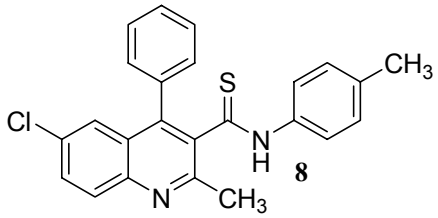
***N*3-(4-methylphenyl)-6-chloro-2-methyl-4-phenyl-3-quinolinecarboxamide (7e).** A mixture of 2-amino-5-chlorobenzophenone (1.155 g, 5.0 mmol), *N*1-(4-methylphenyl)-3-oxobutanamide, **6e** (0.955 g, 5.0 mmol), and CAN (0.274 g, 0.5 mmol, 10 mol %) in methanol (5 mL) was stirred at room temperature for 60 min. After completion of the reaction (monitored by TLC), the reaction mixture was diluted with ethyl acetate (30 mL), and washed with water (15 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography using EtOAc: petroleum ether (1:1) to afford the pure product **7e** (1.74 g, 90 %).



7e

m.p. 227-229 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.29 (s, 3H, $ArCH_3$), 2.83 (s, 3H, $ArCH_3$), 6.80 (s, 1H, CONH), 6.93-7.01 (m, 4H, ArH), 7.40-7.55 (m, 6H, ArH), 7.62-7.67 (dd, 1H, J_1= 9.06 Hz, J_2= 2.66 Hz, ArH), 7.97-8.01 (d, 1H, *J*= 9.06 Hz, ArH). MS (ESI): m/z (%) = 387.20 (M+H, 100).

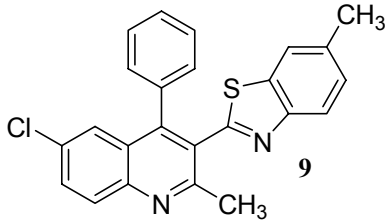
***N*3-(4-methylphenyl)-6-chloro-2-methyl-4-phenyl-3-quinolinecarbothioamide (8).** Lawesson's reagent (0.404 g, 1.0 mmol) was added to the stirred solution of quinoline amide **7f** (0.774 g, 2.0 mmol) in dry toluene 5 mL at 60 ^{o}C. The reaction mixture was refluxed for 1-2 hours and after the completion of the reaction (monitored by TLC) toluene was removed by vacuo distillation. Sodium hypochlorite was added to the residue to quench the reaction. Ice-cubes was added to get dark yellow colored crude solid which was filtered through Buchner funnel. Recrystallization using Acetone: water afforded pure pale yellow colored prisms of compound **8** (0.645 g) in 80 % yield.



8

m.p. 179-180 ^{o}C; ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 2.35 (s, 3H, $ArCH_3$), 2.75 (s, 3H, $ArCH_3$), 6.34 (s, 1H, CSNH), 7.05-7.17 (d, 1H, *J*= 8.53 Hz, ArH), 7.29-7.63 (m, 9H, ArH), 7.98-8.05 (d, 1H, *J*= 9.30 Hz, ArH). MS (ESI): m/z (%) = 403 (M+H, 100).

2-(6-chloro-2-methyl-4-phenyl-3-quinolyl)-6-methyl-1,3-benzothiazole (9). Dess-Martin periodinane (0.424 g, 1.1 mmol) was added to a stirred solution of quinoline thioformanilide, **8** (0.403 g, 1.0 mmol) in CH_2Cl_2 (5 mL) at room temperature. The progress of the reaction was monitored with TLC. After completion, it was quenched with H_2O (2 x 5 mL) and extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and concentrated in vacuo to afford the crude product which was purified by column chromatography on silica gel using EtOAc: petroleum ether (1:3) as eluent to give compound **9** as a light yellow solid (0.341 g) in 85 % yield.

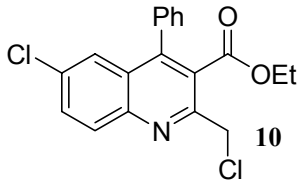


9

m.p.185-187 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.47 (s, 3H, $ArCH_3$), 2.65 (s, 3H, $ArCH_3$), 7.23-7.33 (m, 6H, ArH), 7.50-7.52 (m, 2H, ArH), 7.64-7.69 (m, 1H, ArH), 7.88-7.92 (d, 1H, *J*= 8.50 Hz, ArH), 8.03-8.07 (d, 1H, *J*= 9.06 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 24.7, 121.1, 122.9, 126.4, 127.5, 127.7, 128.2, 128.4, 130.0, 130.6, 131.2, 132.2, 134.8, 135.5, 136.6, 146.3, 147.8, 151.0, 157.7, 163.6. MS (ESI): m/z (%) = 401 (M+H, 100).

ethyl 6-chloro-2-(chloromethyl)-4-phenyl-3-quinolinecarboxylate (10). A mixture of 2-amino-5-chlorobenzophenone (2.31 g, 10.0 mmol), ethyl 4-chloroacetoacetate (2.07 g, 10 mmol), and CAN (0.548 g, 1 mmol, 10 mol %) in methanol (15 mL) was stirred at room temperature for 60 minutes. After completion of the reaction (monitored by TLC),

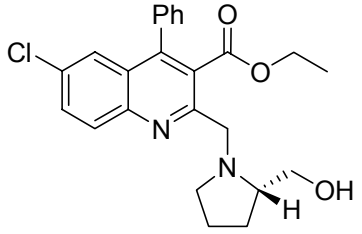
the mixture was diluted with ethyl acetate (40 mL), and washed with water (25 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography using petroleum ether to afford the pure product **10** (3.41 g, 95 %).



10

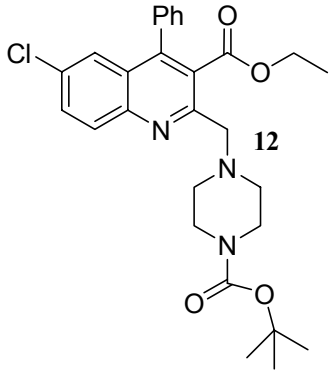
m.p. 105-106 ^{o}C; Lit. 106-108 ^{o}C.[24] ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 0.87-0.93 (t, 3H, *J*= 7.55 Hz, CH_3), 3.97-4.05 (q, 2H, *J*= 7.55 Hz, CO_2CH_2), 4.97 (s, 2H, $ArCH_2$), 7.32-7.36 (m, 2H, ArH), 7.48-7.55 (m, 4H, ArH), 7.66-7.70 (dd, 1H, J_1= 9.06 Hz, J_2= 2.66 Hz, ArH), 8.04-8.08 (d, 1H, *J*= 9.06 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.1, 45.5, 61.4, 124.7, 126.3, 126.6, 128.5, 128.9, 129.0, 131.4, 131.8, 132.9, 134.1, 145.1, 146.9, 153.0, 166.2. MS (FAB): m/z (%) = 360 (M^+, 45), 362 (M+2, 28), 363 (M+3, 4), 364 (M+4, 4).

Ethyl 6-chloro-2-[(2*S*)-2-(hydroxymethyl)tetrahydro-1*H*-1-pyrrolyl]methyl-4-phenyl-3-quinolinecarboxylate (11). (0.718 g, 2) mmol of compound **10** was dissolved in CH_3CN followed by the addition of Et_3N (1 mL) and catalytic DMAP. Stirring was continued for a period of 30 minutes at room temperature followed by the addition of *S*-prolinol (0.202 g, 2 mmol). Reaction was continued till complete disappearance of the starting material was observed with TLC. CH_3CN was removed *in vacuo,* quenched with cold water and extracted with ethyl acetate (2 x 5 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and concentrated in vacuo to afford the crude product. Column chromatography of the crude product gave a dark red color solid compound **11** (0.637 g, 75 % yield).

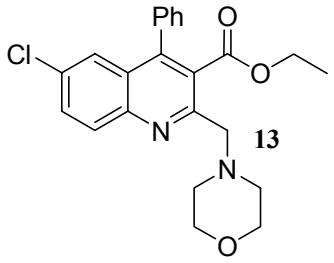


11

$[\alpha]_D$ –21.20^o (c 1.02, $CHCl_3$, 20 ^oC). m.p. 172-174 ^oC; ^1H NMR (200 MHz, $CDCl_3$, TMS) δ 0.76-0.86 (t, 3H, *J*= 7.35 Hz, CH_3), 1.49-1.90 (m, 4H, 2 x CH_2), 2.33 (m, 1H, CH), 2.62-2.74 (m, 1H, CH), 2.85-2.97 (m, 1H, asymmetric CH), 3.24-3.36 (m, 1H, OCH), 3.48-3.58 (m, 1H, OCH), 3.80-4.03 (m, 3H, CO_2CH_2 + ArCH), 4.35-4.45 (m, 1H, ArCH), 7.26-7.41 (m, 2H, ArH), 7.45-7.57 (m, 4H, ArH), 7.61-7.69 (dd, 1H, J_1= 8.81 Hz, J_2= 2.20 Hz, ArH), 7.99-8.05 (d, 1H, *J*= 8.81 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.3, 23.8, 26.7, 55.1, 57.8, 62.0, 61.5, 68.3, 125.4, 126.8, 129.0, 129.0, 129.2, 131.0, 131.9, 133.8, 134.7, 145.4, 147.4, 167.7. MS (ESI): m/z (%) = 425 (M+H, 100).



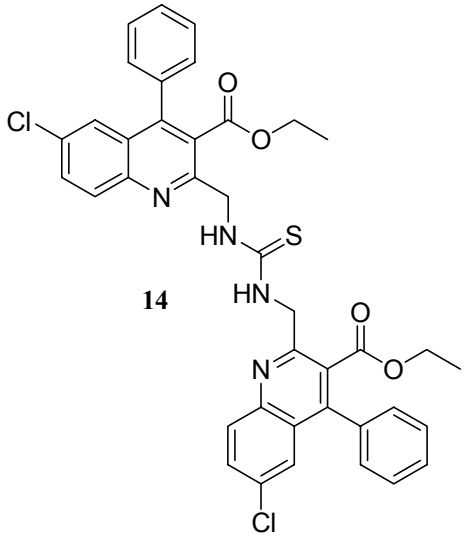
Ethyl 2-[4-(*tert*-butoxycarbonyl)piperazino]methyl-6-chloro-4-phenyl-3-quinolinecarboxylate (12). m.p. 169-171 ^oC; ^1H NMR (300 MHz, $CDCl_3$, TMS) δ 0.79-0.84 (t, 3H, *J*= 7.55 Hz, CH_3), 1.43 (s, 9H, 3 x CH_3), 2.40-2.48 (m, 4H, 2 x CH_2), 3.26-3.33 (m, 4H, 2 x CH_2), 3.88-3.96 (m, 4H, CO_2CH_2 + $ArCH_2$), 7.31-7.36 (m, 2H, ArH), 7.47-7.54 (m, 4H, ArH), 7.62-7.67 (dd, 1H, J_1= 9.06 Hz, J_2= 2.26 Hz, ArH), 7.99-8.03 (d, 1H, *J*= 9.06 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.4, 28.3, 43.7, 52.4, 60.8, 63.6, 79.6, 125.2, 127.0, 127.5, 128.3, 128.6, 129.2, 130.8, 131.0, 132.8, 135.0, 145.4, 146.2, 154.6, 156.5, 167.8. MS (ESI): m/z (%) = 510 (M+H, 100).



Ethyl 6-chloro-2-(morpholinomethyl)-4-phenyl-3-quinolinecarboxylate (13). m.p. 162-164 ^oC; ^1H NMR (300 MHz, $CDCl_3$, TMS) δ 0.82-0.91 (t, 3H, *J*= 7.34 Hz, CH_3), 2.45-2.53 (t, 4H, *J*= 5.14 Hz, 2 x CH_2), 3.56-3.64 (t, 4H, *J*= 5.14 Hz, 2 x CH_2), 3.92-4.05

(m, 4H, CO_2CH_2 + $ArCH_2$), 7.31-7.39 (m, 2H, ArH), 7.46-7.58 (m, 4H, ArH), 7.63-7.70 (dd, 1H, J_1= 8.81 Hz, J_2= 2.20 Hz, ArH), 8.01-8.08 (d, 1H, J= 9.55 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.5, 53.1, 60.9, 64.0, 66.9, 125.3, 127.0, 127.6, 128.3, 128.6, 129.3, 130.8, 131.0, 132.8, 135.1, 145.4, 146.1, 156.5, 167.8. MS (ESI): m/z (%) = 411 (M+H, 100).

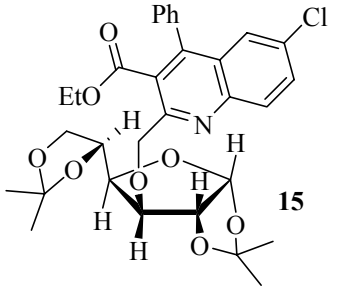
Ethyl 6-chloro-2-([([6-chloro-3-(ethoxycarbonyl)-4-phenyl-2-quinolyl]methylamino) carbothioyl]aminomethyl)-4-phenyl-3-quinolinecarboxylate (14). To a solution of thiourea (0.152 g, 2 mmol), in dry CH_3CN was added NaH, 60 % w/w (0.177 g, 4.4 mmol), in portions at 0 ^oC. After stirring for 30 minutes compound **10** (1.436 g, 4.0 mmol) was added and the reaction mixture was refluxed for 5-6 hours till TLC showed complete disappearance of the starting materials. CH_3CN was removed *in vacuo* and the reaction was quenched with cold water (5 mL). Ethyl acetate (2 x 5 mL) was used for extraction, which was washed simultaneously with brine and dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography on silica gel (EtOAc: petroleum ether 1:3) gave a pale yellow solid compound **14** (1.084 g, 75 % yield).



14

^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 0.79-0.86 (t, 6H, J= 6.80 Hz, 2 x CH_3), 1.85 (s, 2 x NH), 3.90-3.98 (q, 4H, J= 7.55 Hz, 2 x CH_2), 4.28 (s, 4H, 2 x $ArCH_2$), 7.12-7.19 (m, 2H, ArH), 7.42-7.51 (m, 4H, ArH), 7.60-7.66 (dd, 1H, J_1= 9.06 Hz, J_2= 2.26 Hz, ArH), 7.81-7.86 (d, 1H, J= 9.06 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.4, 37.6, 61.3, 125.2, 126.4, 126.9, 128.3, 128.6, 129.1, 131.0, 131.1, 132.8, 135.3, 145.5, 146.6, 155.7, 167.5. MS (ESI): m/z (%) = 724 (M+H, 100).

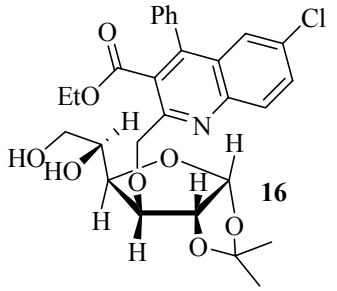
Ethyl 2-[((3a*S*,5*S*,6*S*,6a*S*)-5-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2,2-dimethylperhydrofuro[2,3-*d*][1,3]dioxol-6-yloxy)methyl]-6-chloro-4-phenyl-3-quinolinecarboxylate (15). To a solution of *D*-glucose diacetonide (1.30 g, 5 mmol), in dry THF was added NaH, 60 % w/w (0.200 g, 5.5 mmol), in portions at 0°C. After stirring for 30 minutes compound **10** (1.795 g, 5 mmol) was added and stirring was continued for further 2-4 hours at room temperature till TLC showed complete disappearance of the starting materials. CH_3CN was removed *in vacuo* and the reaction was quenched with cold water (5 mL) and extracted with ethyl acetate (2 x 5 mL). The combined extracts were washed with brine and dried (Na_2SO_4) and concentrated under reduced pressure to afford a solid residue, which was purified by silica gel column chromatography (EtOAc: petroleum ether 2:5) gave a gummy compound **15** (2.482 g, 85 % yield).



$[\alpha]_D$ –28.481° (c 1.58, $CHCl_3$, 20 °C). ^{1}H NMR (200 MHz, $CDCl_3$, TMS) δ 0.77-0.86 (t, 3H, *J*= 7.41 Hz, CH_3), 1.24-1.49 (m, 12H, 4 x CH_3), 3.86-4.08 (m, 6H, CO_2CH_2 + OCH_2 + 2 x CH), 4.18-4.30 (m, 1H, CH), 4.59-4.63 (d, 1H, *J*= 3.70 Hz, CH), 4.98-5.05 (d, 2H, *J*= 5.92 Hz, $ArCH_2$), 5.76-5.81 (d, 1H, *J*= 3.70 Hz, CH), 7.25-7.39 (m, 2H, ArH), 7.45-7.55 (m, 4H, ArH), 7.63-7.71 (dd, 1H, J_1= 8.89 Hz, J_2= 2.22 Hz, ArH), 8.02-8.09 (d, 1H, *J*= 8.89 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.3, 25.4, 26.2, 26.8, 61.3, 67.0, 72.4, 73.2, 81.0, 82.0, 83.0, 105.2, 108.9, 111.7, 125.3, 126.9, 127.0, 128.3, 128.8, 129.0, 129.3, 131.1, 131.4, 133.4, 135.0, 145.6, 146.6, 154.3, 167.6. MS (ESI): m/z (%) = 584 (M+H, 100).

Ethyl 2-[((3a*S*,5*R*,6*S*,6a*S*)-5-[(1*S*)-1,2-dihydroxyethyl]-2,2-dimethylperhydrofuro[2,3-*d*][1,3]dioxol-6-yloxy)methyl]-6-chloro-4-phenyl-3-quinolinecarboxylate (16). To a stirred solution of compound **15** (1.168 g, 2 mmol) in MeOH (15 mL), was added aqueous 0.8 % H_2SO_4 solution and stirred for overnight. TLC

(ethyl acetate: hexane, 1:1), showed the completion of the reaction. Methanol was removed *in vacuo* and the residue was treated with saturated solution of $NaHCO_3$ and extracted with ethyl acetate (2 x 5 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered and the solvent was removed *in vacuo*. Purification by column chromatography using EtOAc: petroleum ether (1:2) afforded a colorless solid compound **16** (0.707 g, 65 % yield).

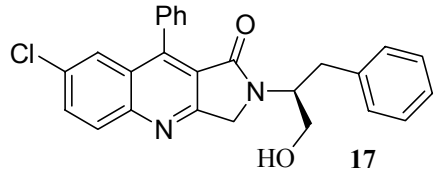


16

$[\alpha]_D$ –40.19^o (c 1.02, $CHCl_3$, 20 ^{o}C). m.p. 104-106 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 0.80-0.90 (t, 3H, *J*= 7.55 Hz, CH_3), 1.22-1.33 (m, 6H, 2 x CH_3), 2.03 (s, 1H, OH), 2.07 (s, 1H, OH), 3.70-3.77 (m, 1H, CH), 3.89-4.15 (m, 5H, CO_2CH_2, + OCH_2 + CH), 4.22-4.30 (m, 1H, CH), 4.62-4.66 (d, 1H, *J*= 3.77 Hz, CH), 4.86-4.94 (d, 1H, *J*= 16.61 Hz, ArCH), 5.12-5.20 (d, 1H, *J*= 16.61 Hz, ArCH), 5.93-5.97 (d, 1H, *J*= 3.77 Hz, CH), 7.27-7.34 (m, 2H, ArH), 7.49-7.56 (m, 4H, ArH), 7.69-7.74 (dd, 1H, J_1= 9.06 Hz, J_2= 2.26 Hz, ArH), 8.18-8.23 (d, 1H, *J*= 9.06 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.4, 26.3, 26.8, 61.9, 64.7, 68.12, 69.1, 80.4, 81.9, 82.9, 105.8, 111.8, 125.4, 126.8, 128.5, 129.0, 130.0, 133.6, 132.1, 134.6, 145.2, 147.6, 153.9, 166.8. MS (ESI): m/z (%) = 545 (M+H, 100).

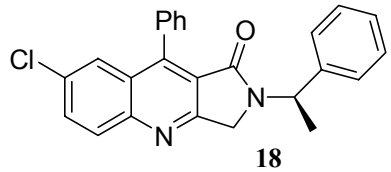
2-[(1*S*)-1-Benzyl-2-hydroxyethyl]-7-chloro-9-phenyl-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]quinolin-1-one (17). To a mixture of compound 10 (0.718 g, 2 mmol), and Et_3N (1 mL) in CH_3CN (5 mL) was added *S*-phenylalaninol (0.302 g, 2 mmol). The stirring was continued for a period of 2-3 hours at room temperature. TLC showed the appearance of a new spot corresponding to the intermediate ester **17a**. The reaction mixture was further stirred at 40-45 ^{o}C for a period of 12 hours, till the TLC showed the complete disappearance of the intermediate **17a**. CH_3CN was removed *in vacuo,* quenched with cold water (5 mL) and extracted with ethyl acetate (2 x 5 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered and the solvent was removed *in*

vacuo. Column chromatography of the crude product gave a light red color compound **17** (0.686 g, 80 %).



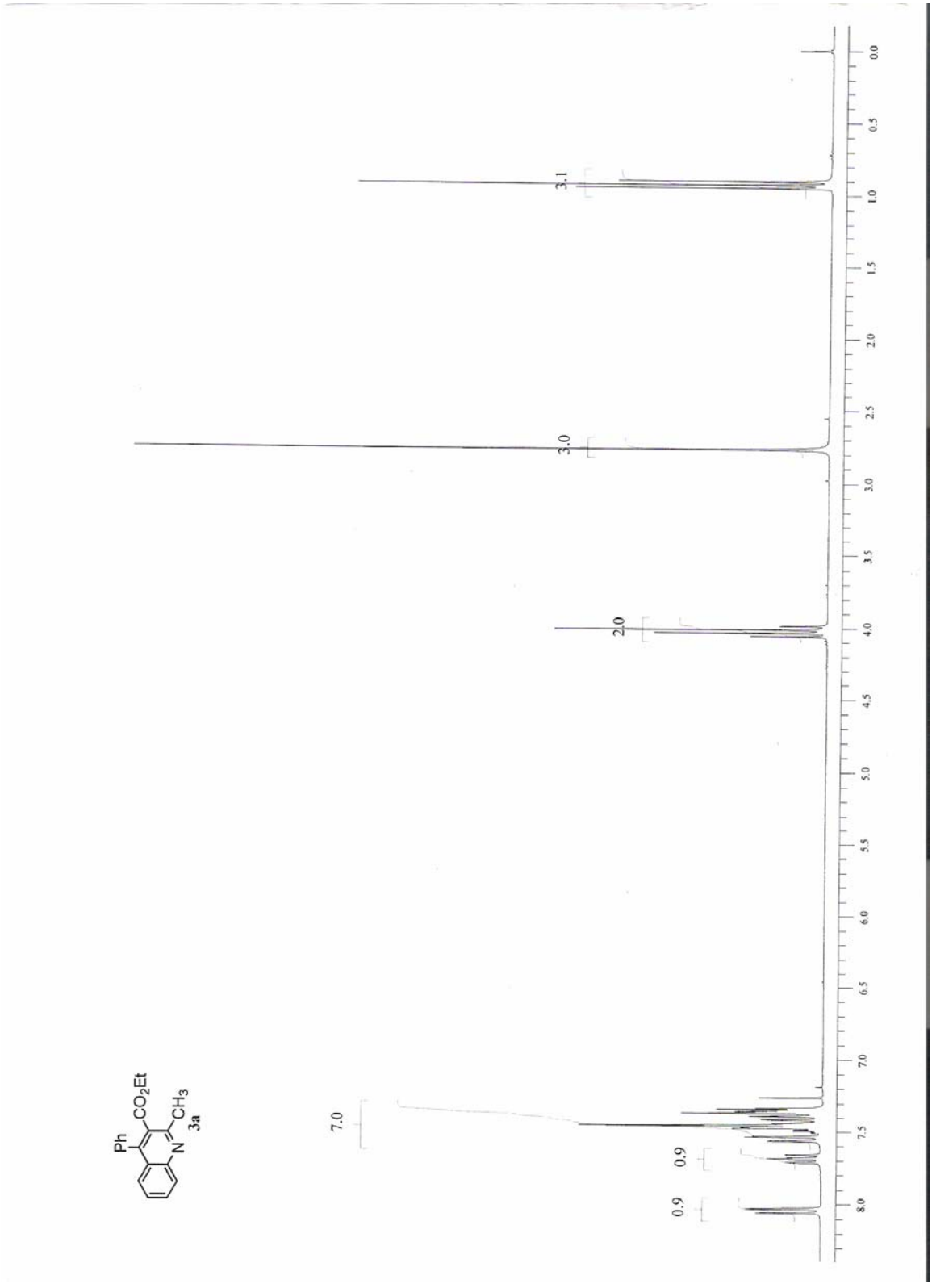
17

$[\alpha]_D$ –91.000^o (c 1.00, $CHCl_3$, 20 ^{o}C). m.p. 80-82 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 2.71 (broad singlet, 1H, OH), 3.00-3.07 (d, 2H, *J*= 7.55 Hz, $ArCH_2$), 3.72-3.85 (m, 2H, CH_2), 4.42-4.53 (m, 3H, CH_2-pyrrolone + asymmetric CH), 7.08-7.39 (m, 7H, ArH), 7.50-7.56 (m, 3H, ArH), 7.65-7.72 (m, 2H, ArH), 7.98-8.04 (d, 1H, *J*= 9.06 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): 35.1, 49.3, 56.0, 62.7, 120.7, 126.0, 126.5, 127.8, 128.0, 128.5, 128.7, 129.0, 129.7, 130.4, 131.8, 132.7, 137.4, 146.7, 147.7, 160.9, 166.3. MS (ESI): m/z (%) = 430 (M+H, 30), 380 (35), 366 (100).



18

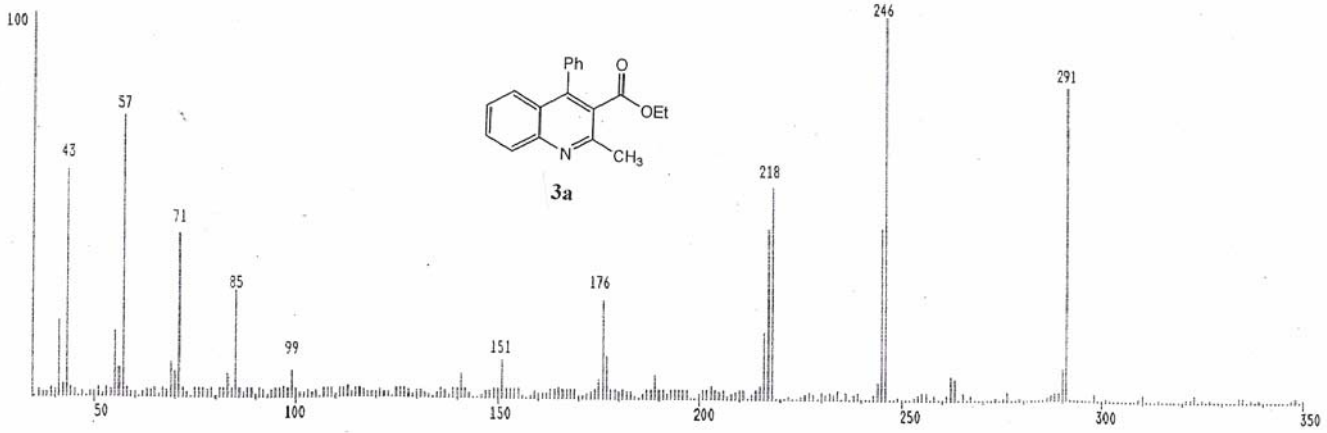
7-Chloro-9-phenyl-2-[(1*R*)-1-phenylethyl]-2,3-dihydro-1*H*-pyrrolo[3,4-*b*]quinolin-1-one (18). $[\alpha]_D$ 266.05^o (c 1.09, $CHCl_3$, 20 ^{o}C). m.p. 125-127 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ 1.68-1.73 (d, 3H, *J*= 7.55 Hz, CH_3), 4.10-4.17 (d, 1H, *J*= 16.61 Hz, CH-pyrrolone), 4.43-4.50 (d, 1H, *J*= 16.61 Hz, CH-pyrrolone), 5.75-5.83 (q, 1H, *J*= 7.55 Hz, asymmetric CH), 7.21-7.39 (m, 5H, ArH), 7.41-7.47 (m, 2H, ArH), 7.54-7.62 (m, 3H, ArH), 7.66-7.70 (dd, 1H, J_1= 9.06 Hz, J_2= 2.26 Hz, ArH), 7.74-7.76 (d, 1H, *J*= 2.26 Hz, ArH), 8.00-8.04 (d, 1H, *J*= 9.06 Hz, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 17.0, 46.4, 49.1, 120.9, 126.1, 127.2, 127.8, 128.1, 128.7, 129.0, 129.8, 129.9, 130.6, 131.8, 132.0, 132.7, 139.9, 146.9, 148.0, 160.9, 165.0. MS (ESI): m/z (%) = 399 (M+H, 15).


Ph
CO2Et
CH3
3a
7.0
0.9
0.9
2.0
3.0
3.1

AEA.LRP DSB AEA

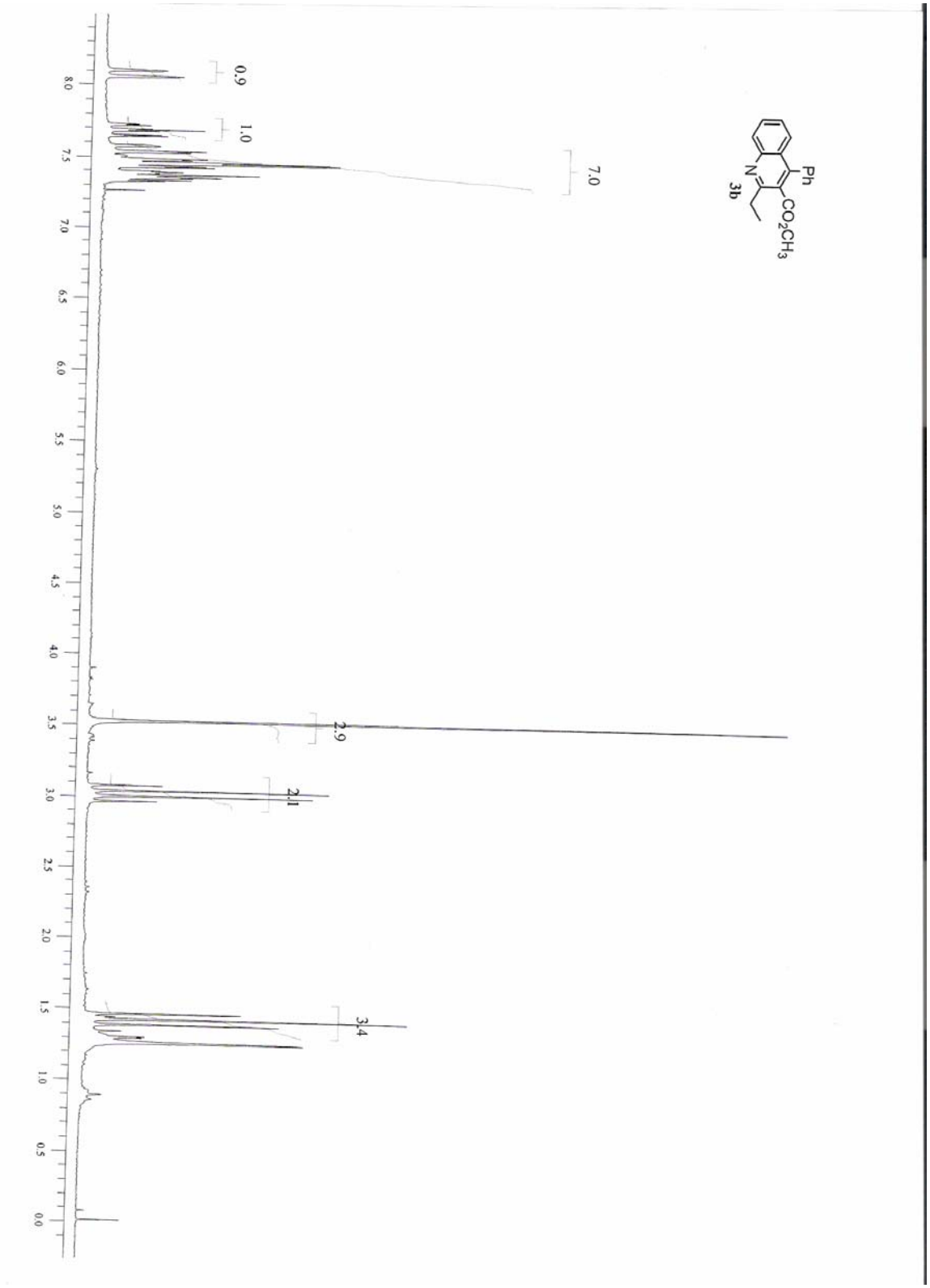
Date run : 04-26-2005(16:39:49) Instr. : VG 7070H Operator : NCMS

Scan 3 RT= 0:13 No.ions= 277 Base= 84.4%F TIC=327299



3a

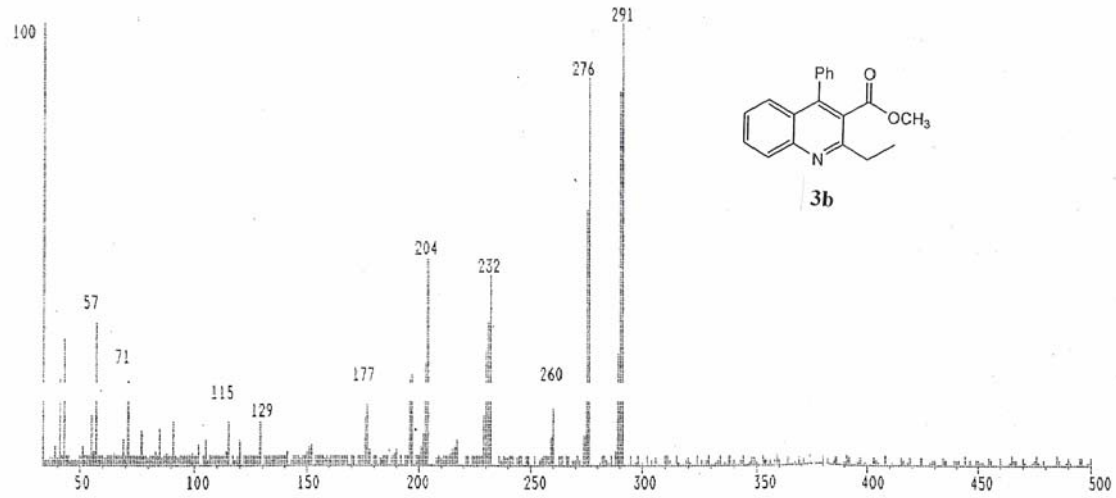
MASS SPECTRUM OF COMPOUND 3a


Ph
CO2CH3
N
3b
0.9
1.0
7.0
2.9
2.1
3.4

IICT NCMS
06-21-2005

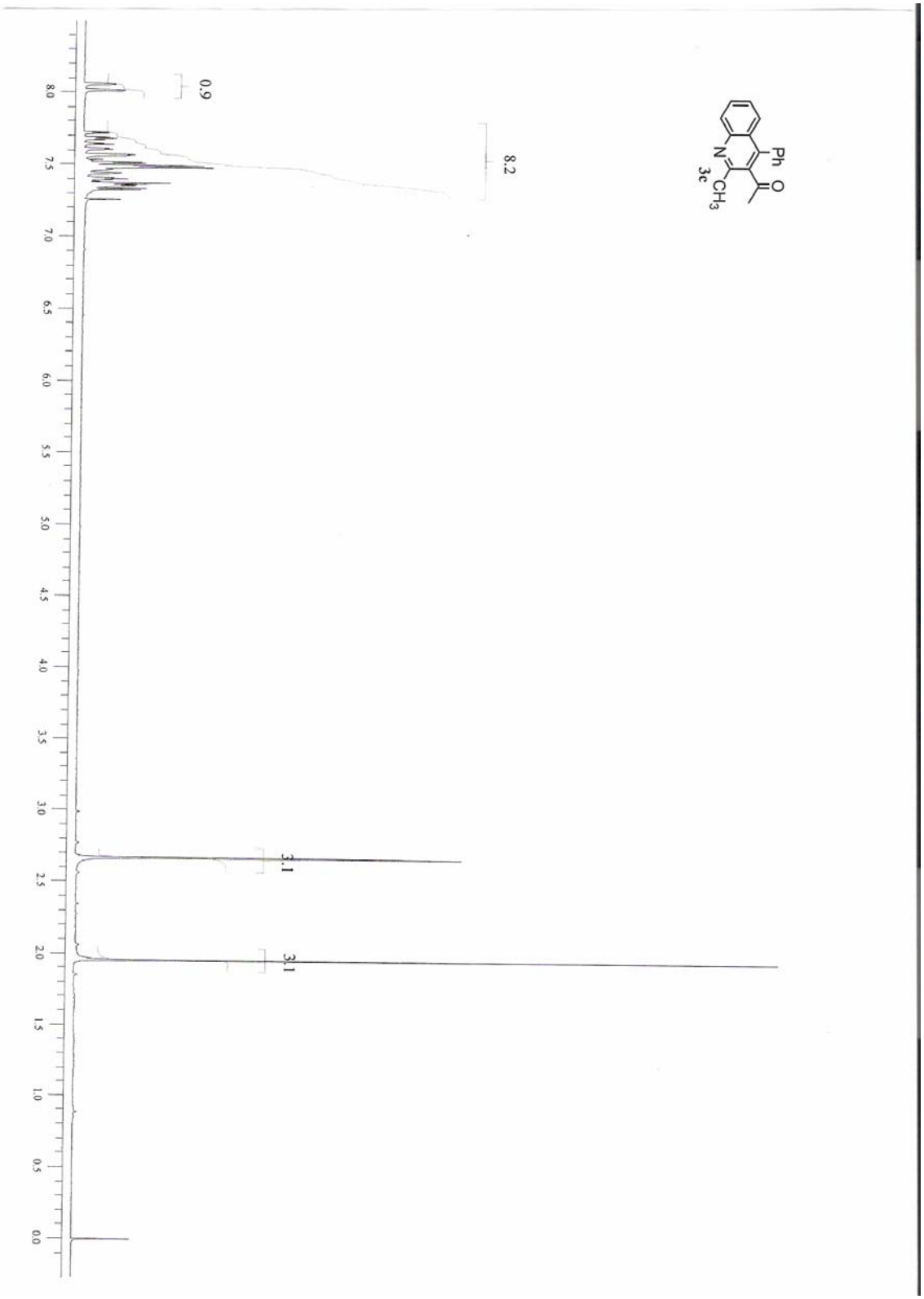
OXA.LRP DSB OXA
Date run : 06-20-2005(09:33:33) Instr. : VG 7070H Operator : NCMS

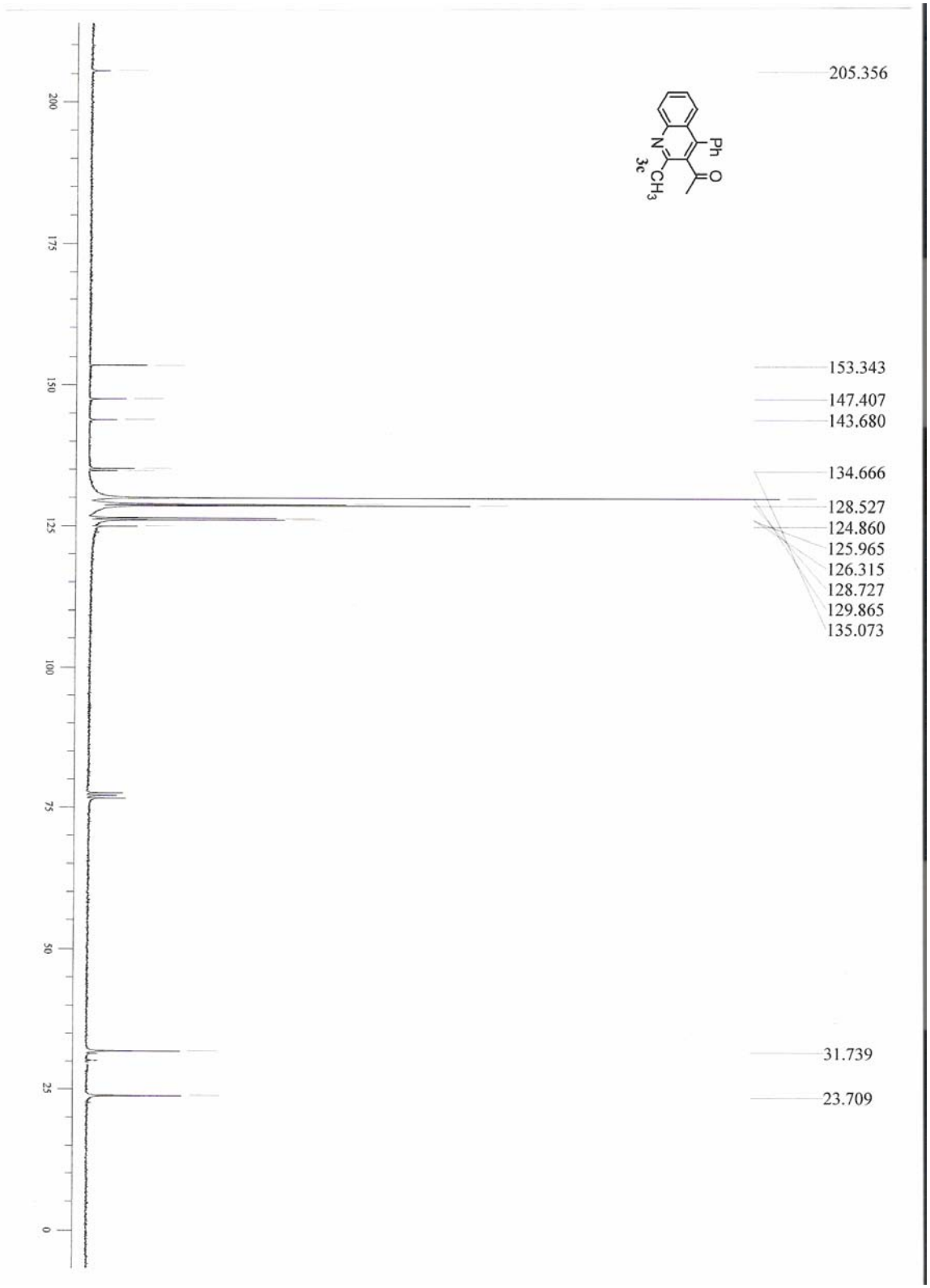
Scan 4 RT= 0:16 No.ions= 483 Base= 41.5%F TIC=310858



3b

MASS SPECTRUM OF COMPOUND 3b

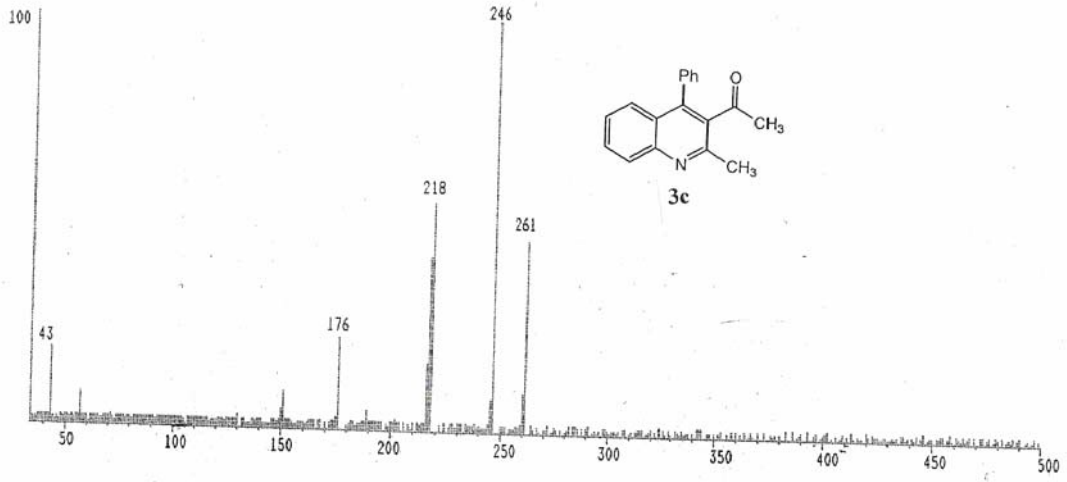

Ph
O
N
CH3
3c
0.9
8.2
3.1
3.1
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


205.356
153.343
147.407
143.680
134.666
128.527
124.860
125.965
126.315
128.727
129.865
135.073
31.739
23.709
Ph
O
N
CH3
3c
200
175
150
125
100
75
50
25
0

IICT NCMS
05-31-2005

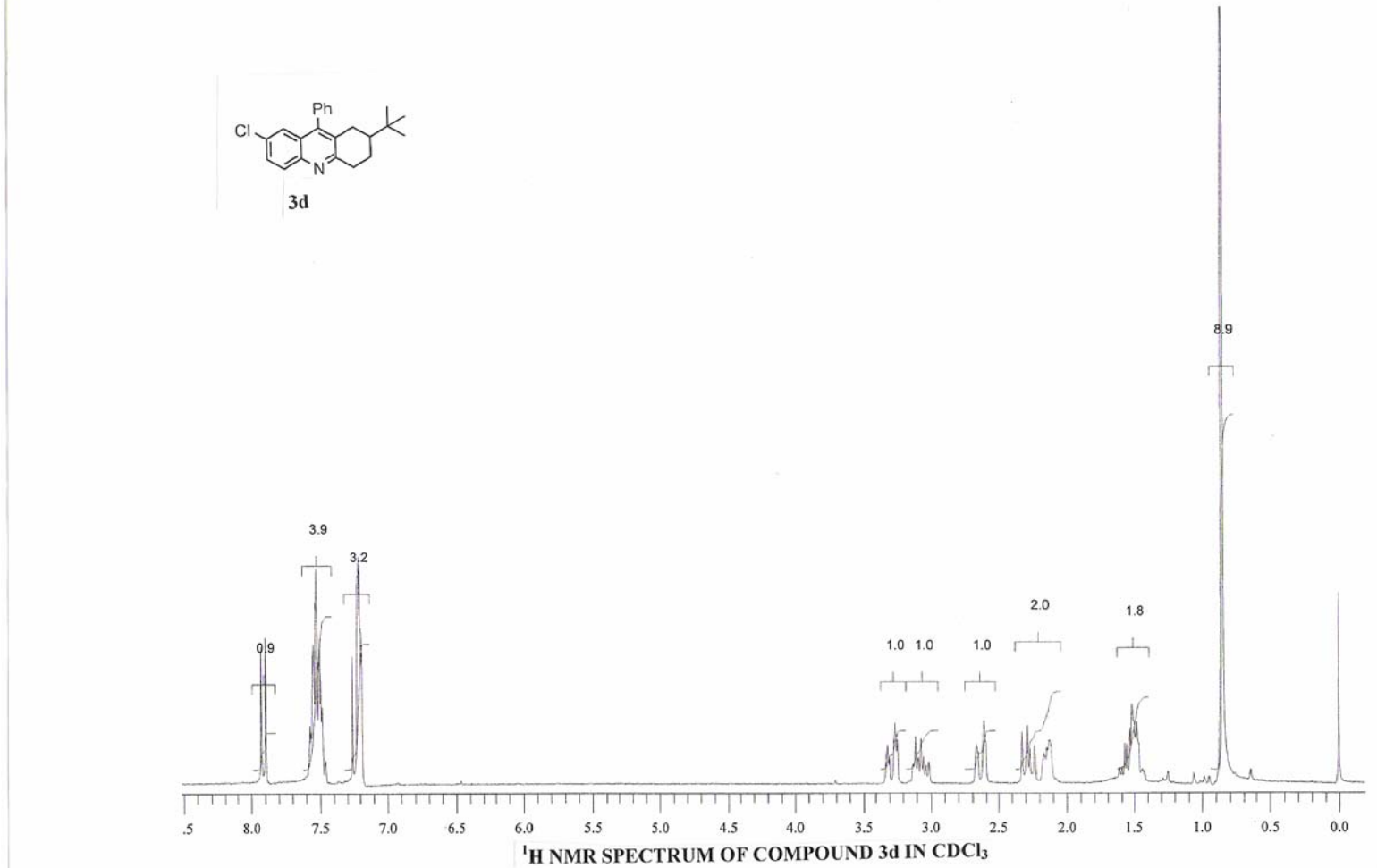
ACE.LRP DSB ACE
Date run : 05-31-2005(16:06:17) Instr. : VG 7070H Operator : NCMS

Scan 12 RT= 0:48 No.ions= 501 Base= 84.8%F TIC=372520

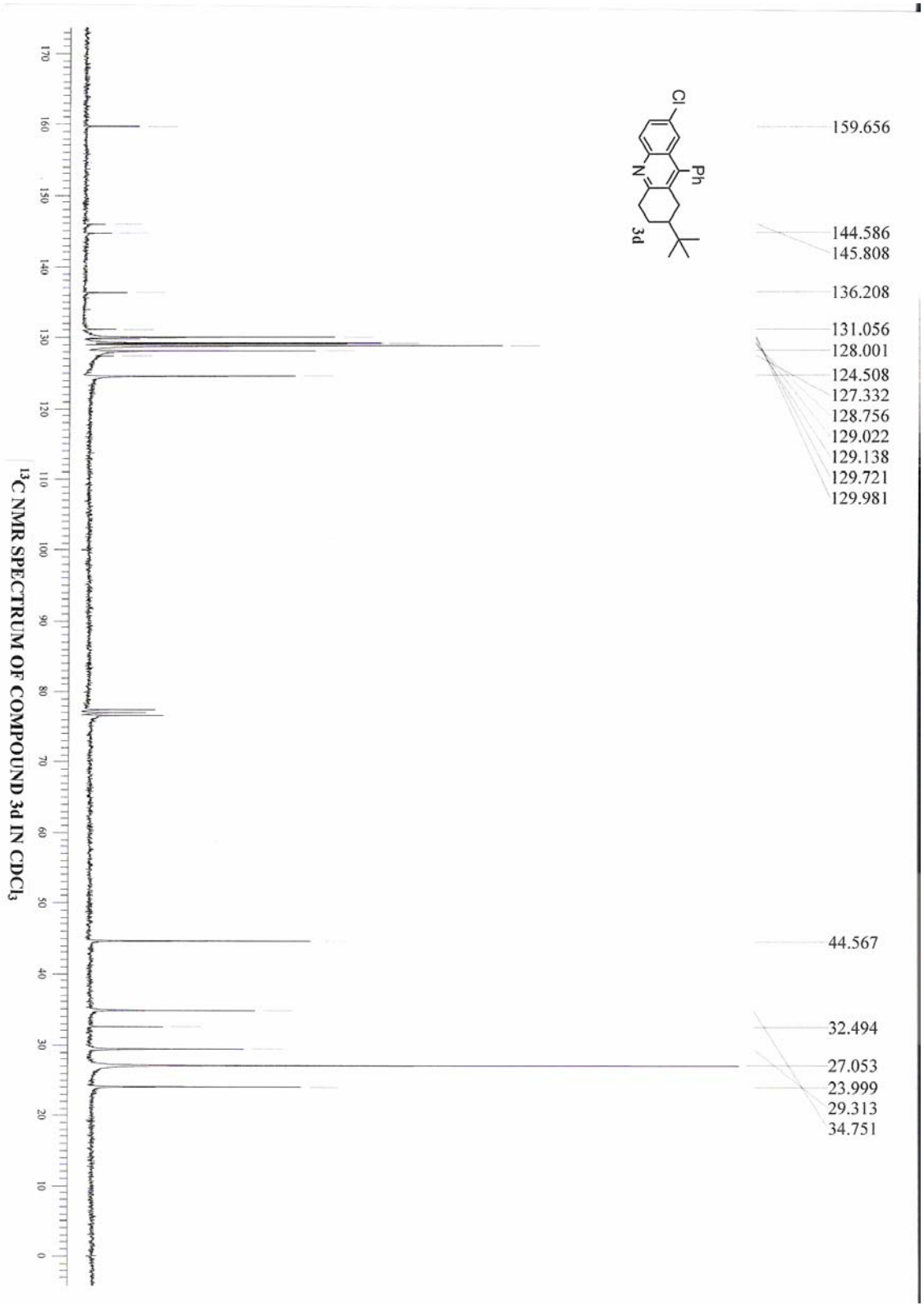


3c

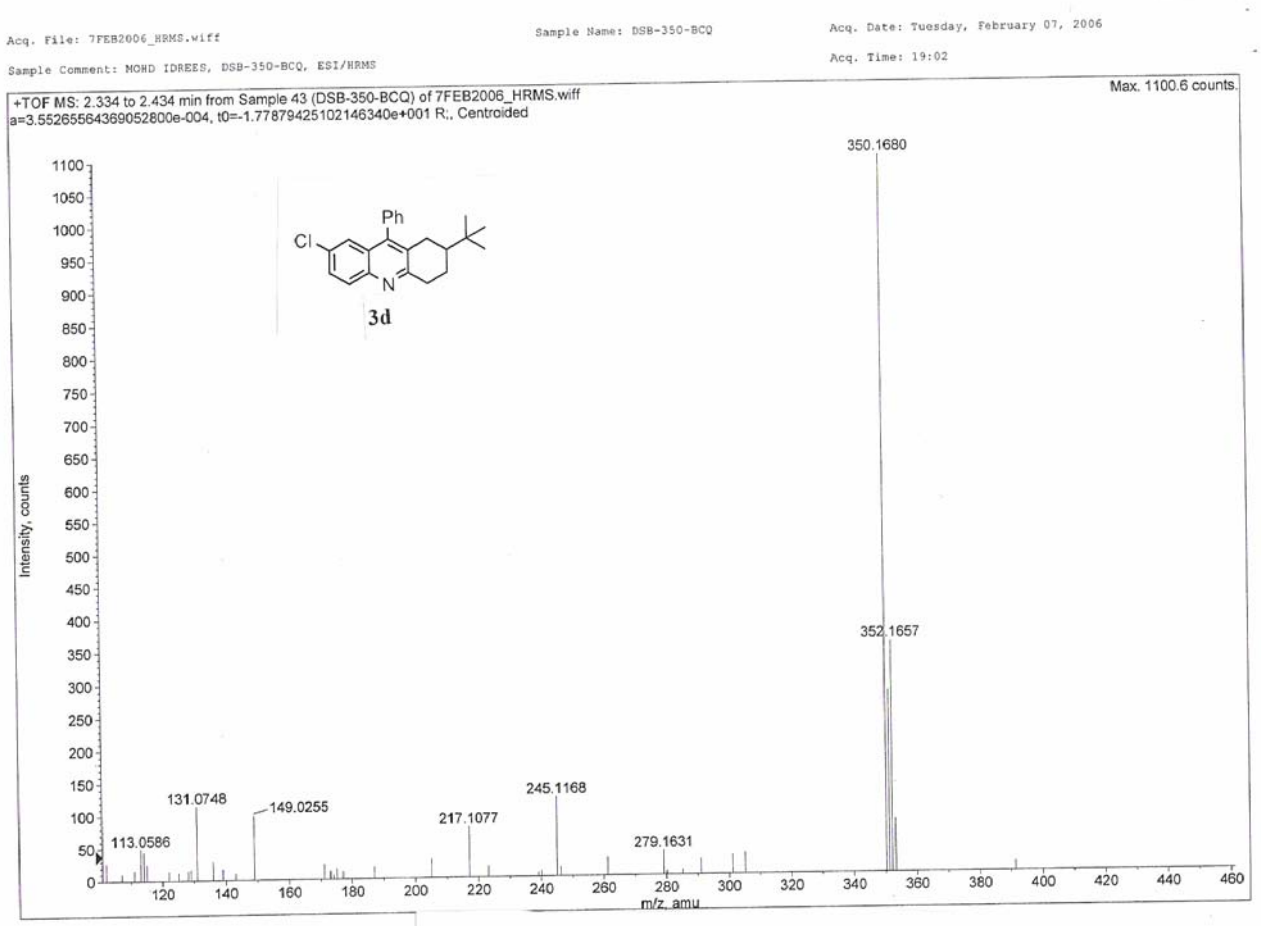
MASS SPECTRUM OF COMPOUND 3c



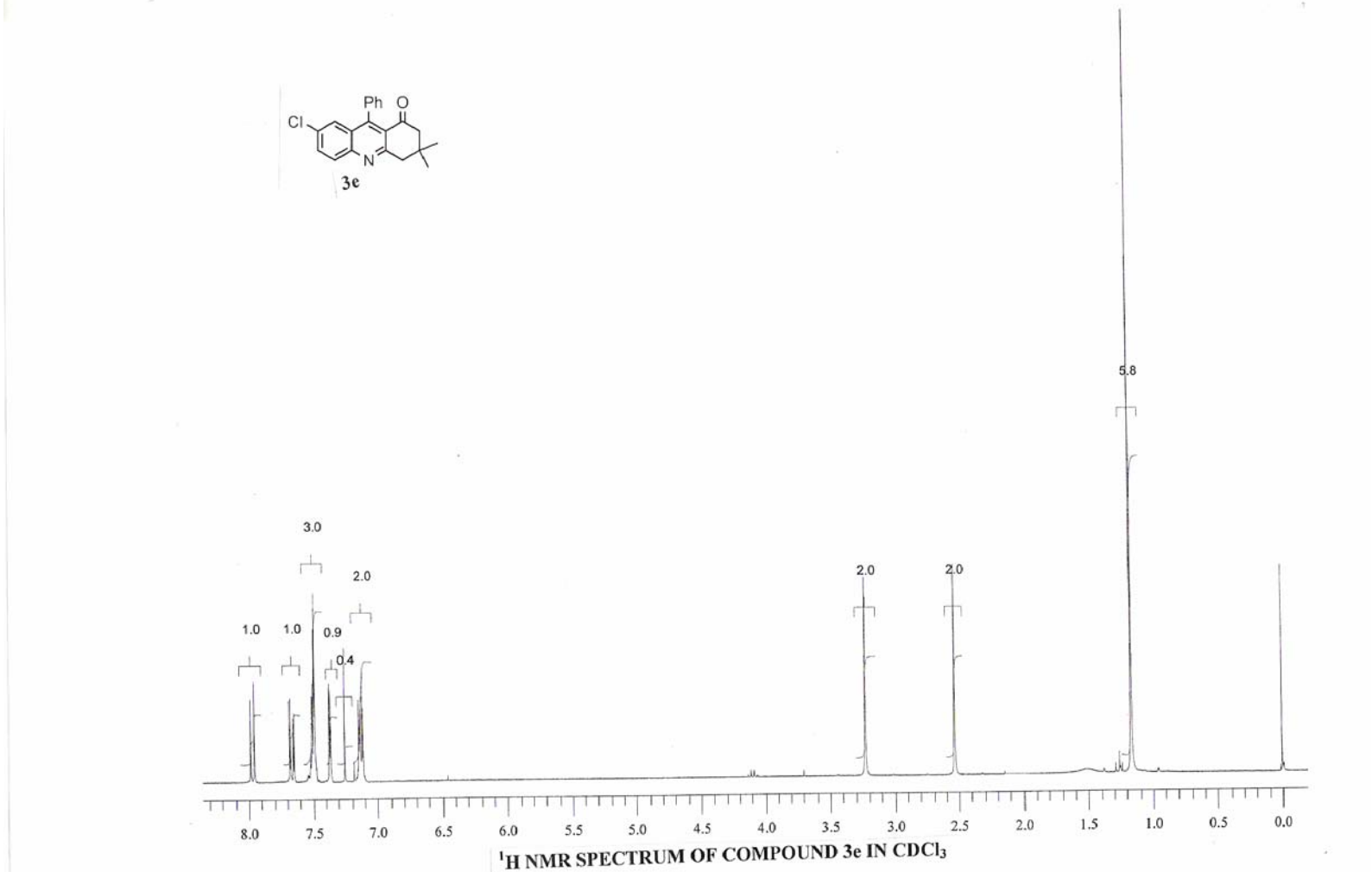
^{1}H NMR SPECTRUM OF COMPOUND 3d IN $CDCl_3$



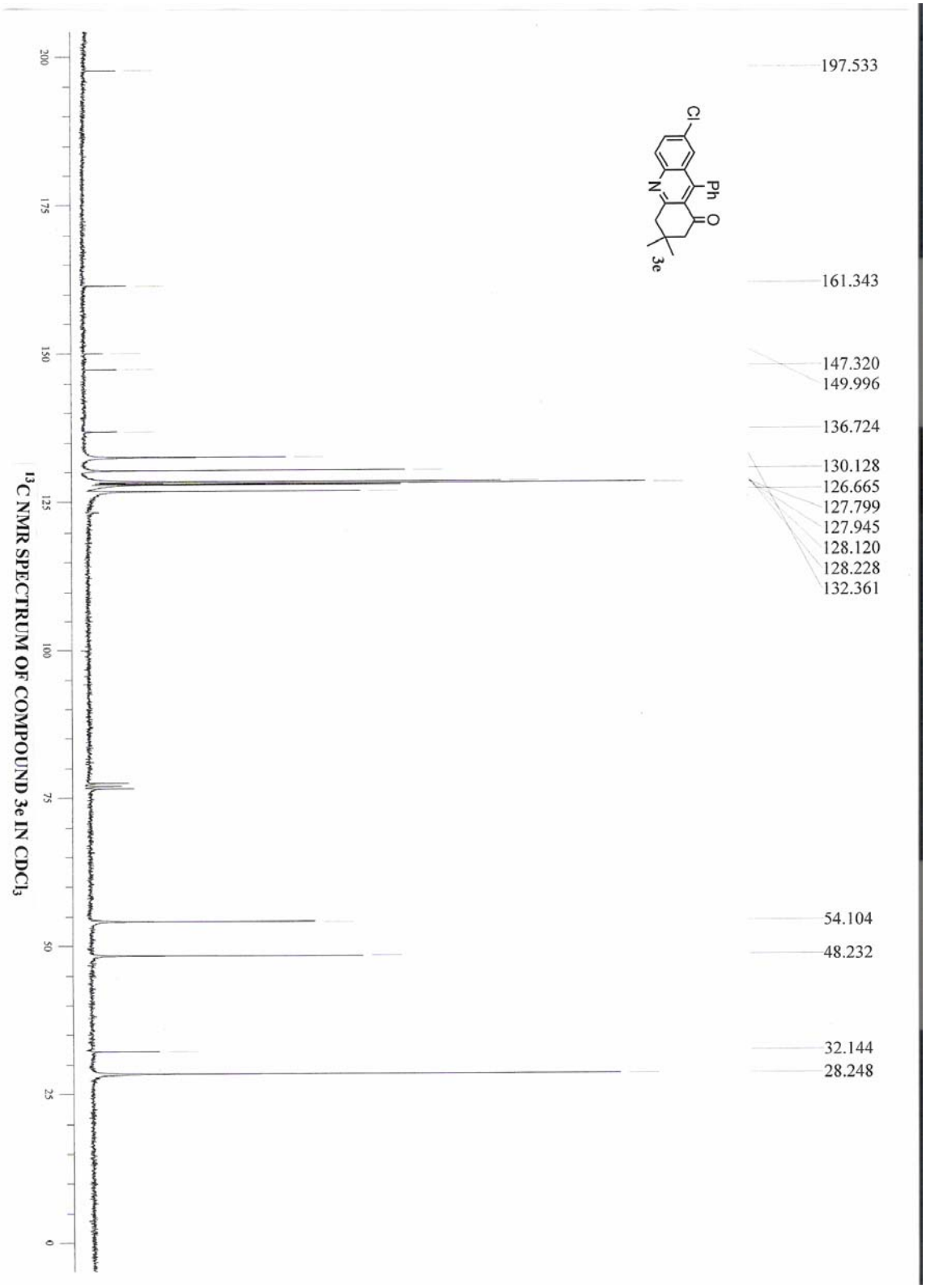
^{13}C NMR SPECTRUM OF COMPOUND 3d IN $CDCl_3$



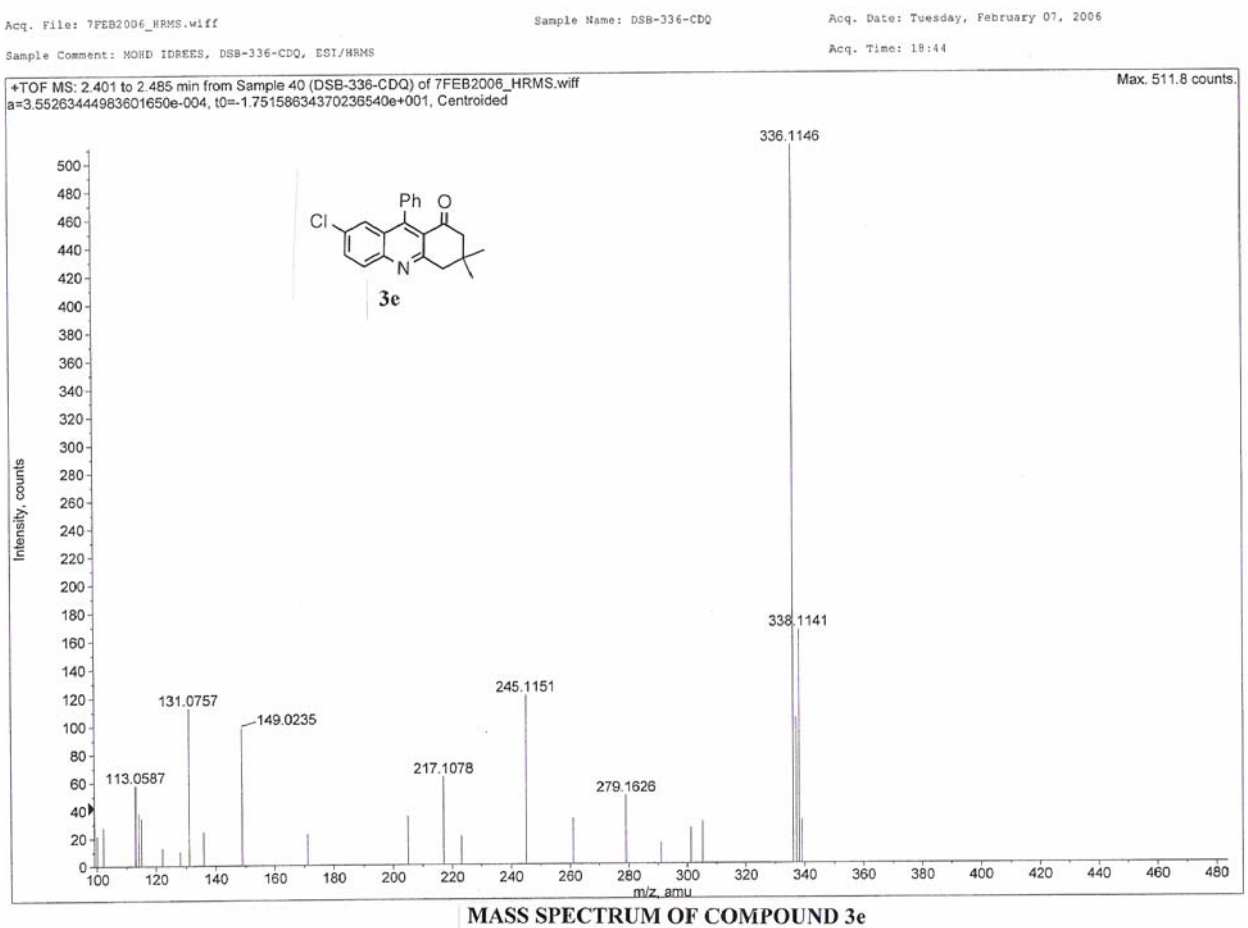
MASS SPECTRUM OF COMPOUND 3d



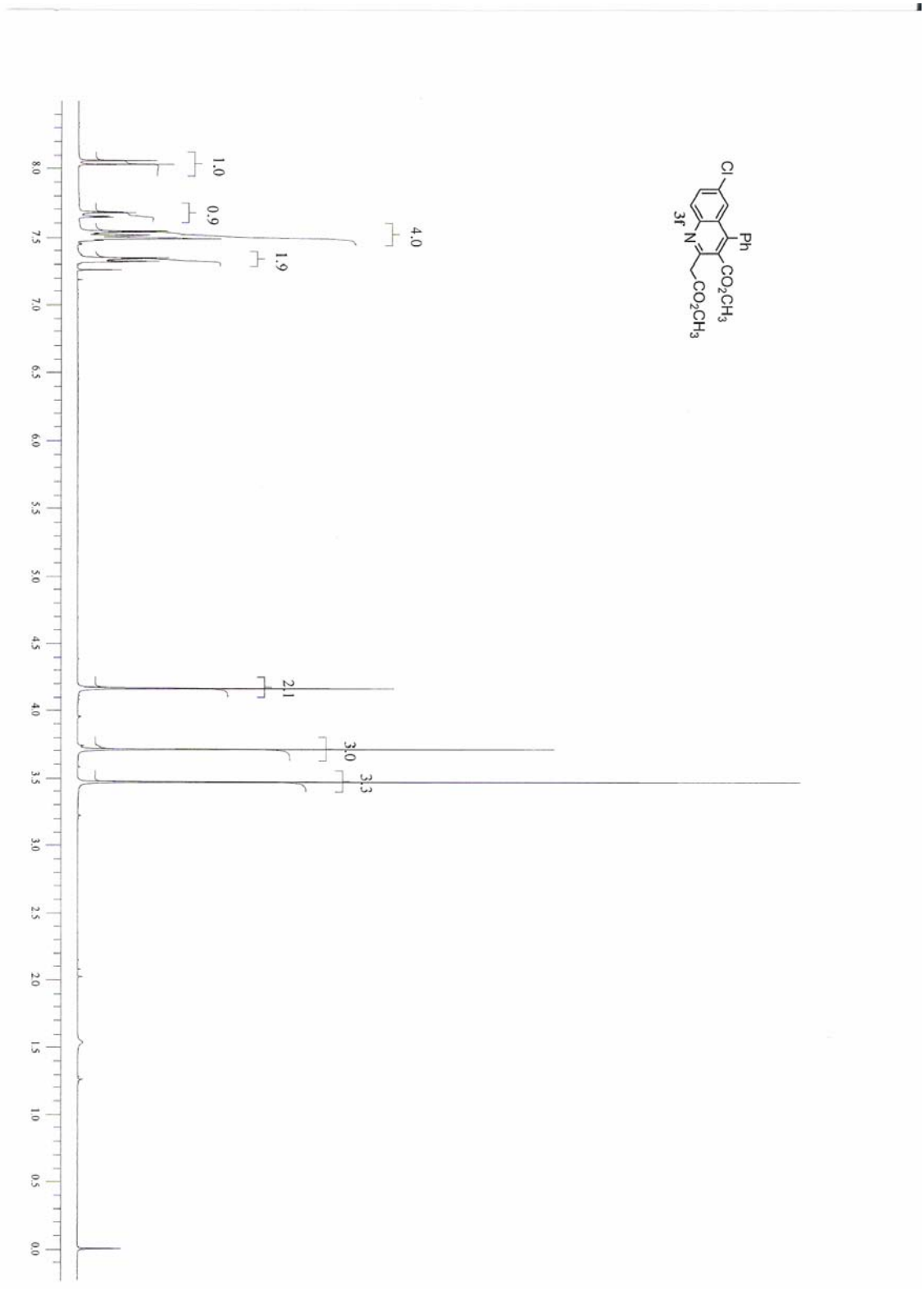
^{1}H NMR SPECTRUM OF COMPOUND 3e IN $CDCl_3$

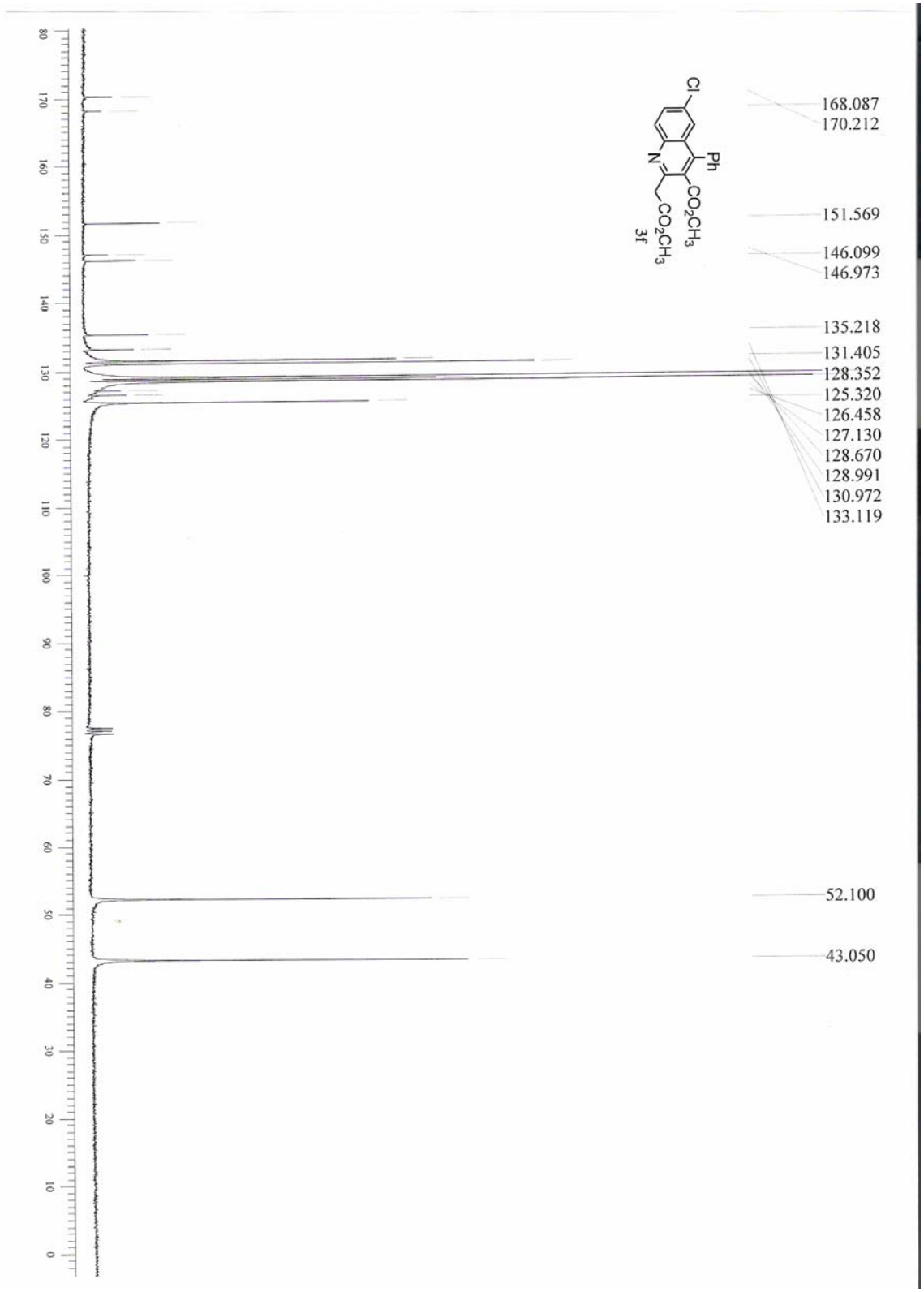


^{13}C NMR SPECTRUM OF COMPOUND 3e IN $CDCl_3$



MASS SPECTRUM OF COMPOUND 3e


Cl
Ph
3f
N
CO2CH3
CO2CH3
1.0
0.9
4.0
1.9
2.1
3.0
3.3


Cl
Ph
N
CO2CH3
CO2CH3
3f
168.087
170.212
151.569
146.099
146.973
135.218
131.405
128.352
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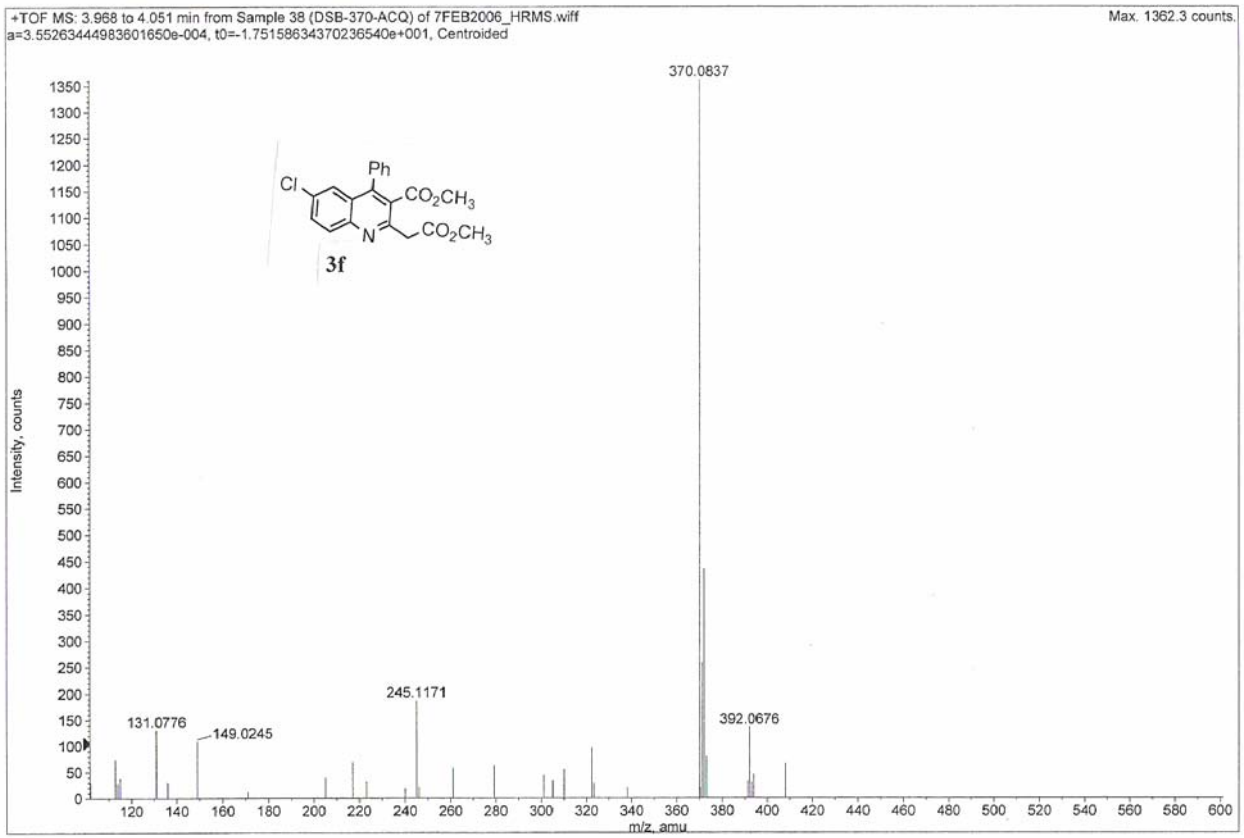
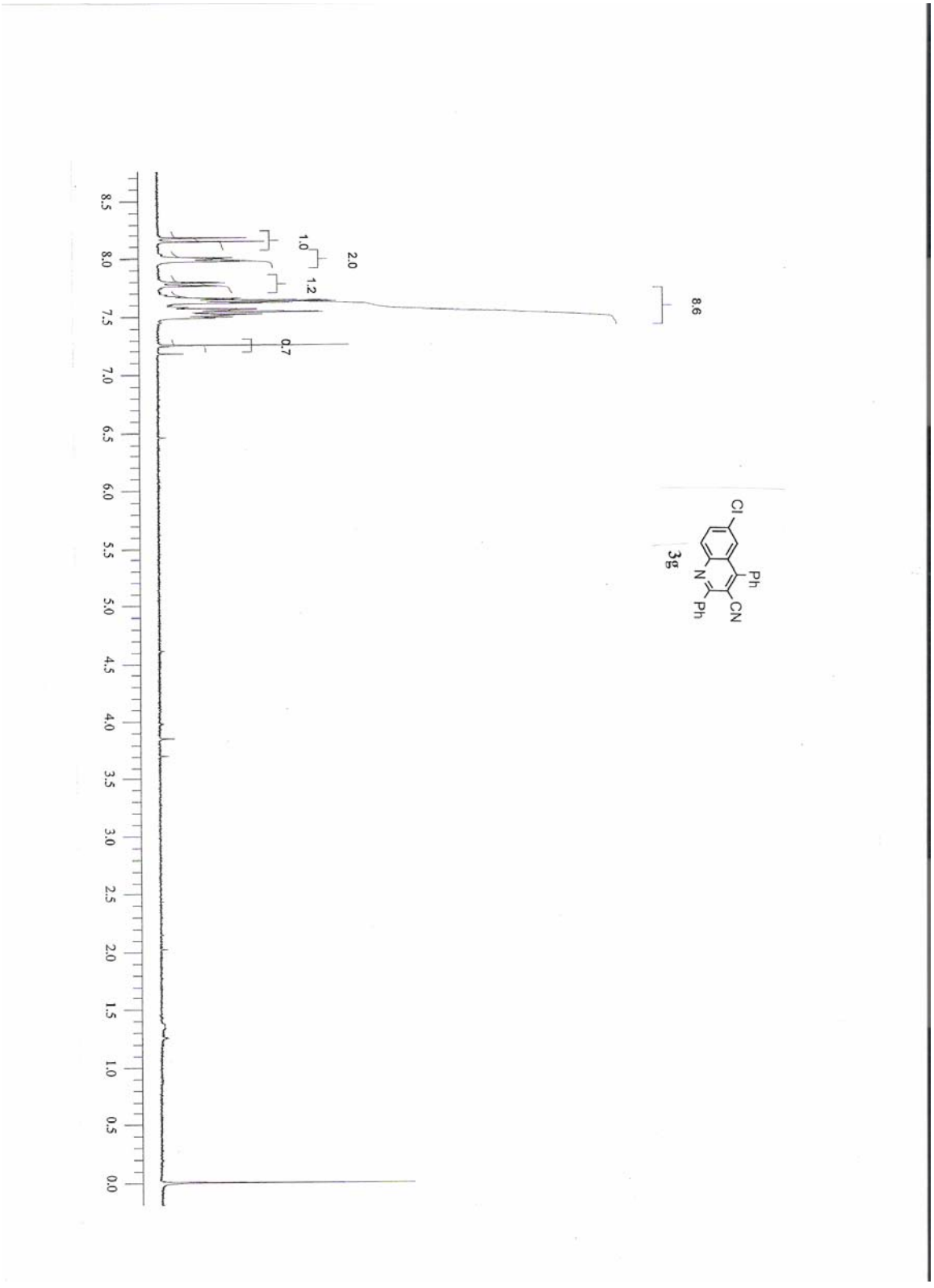
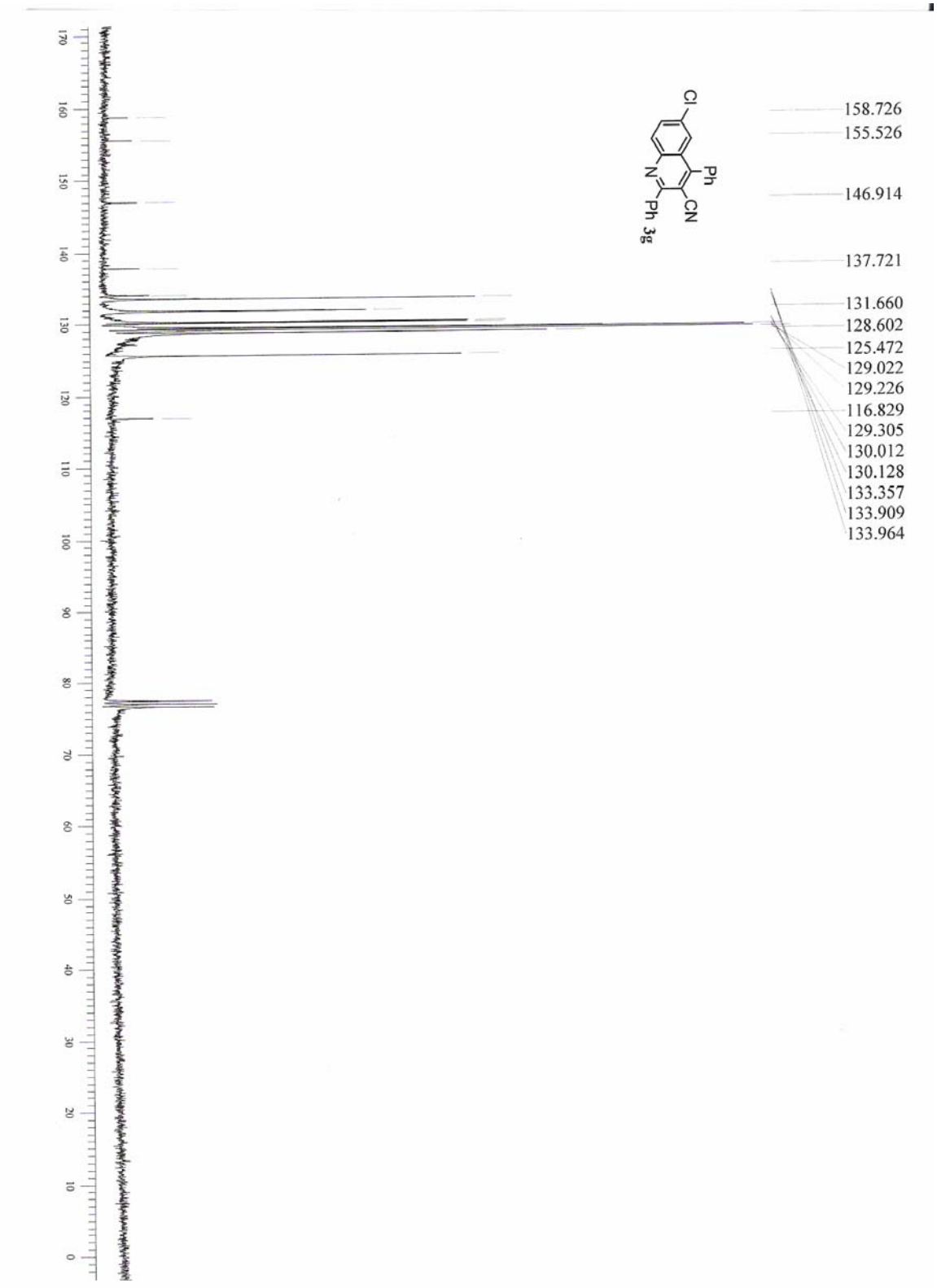
127.130
128.670
128.991
130.972
133.119
52.100
43.050

Acq. File: 7FEB2006_HRMS.wiff Sample Name: DSB-370-ACQ Acq. Date: Tuesday, February 07, 2006

Sample Comment: MOHD IDREES, DSB-370-ACQ, ESI/HRMS Acq. Time: 18:30




Cl
Ph
CN
N
Ph
3g
8.6
2.0
1.0
1.2
0.7
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


Cl
Ph
N
CN
Ph 3g
158.726
155.526
146.914
137.721
131.660
128.602
125.472
129.022
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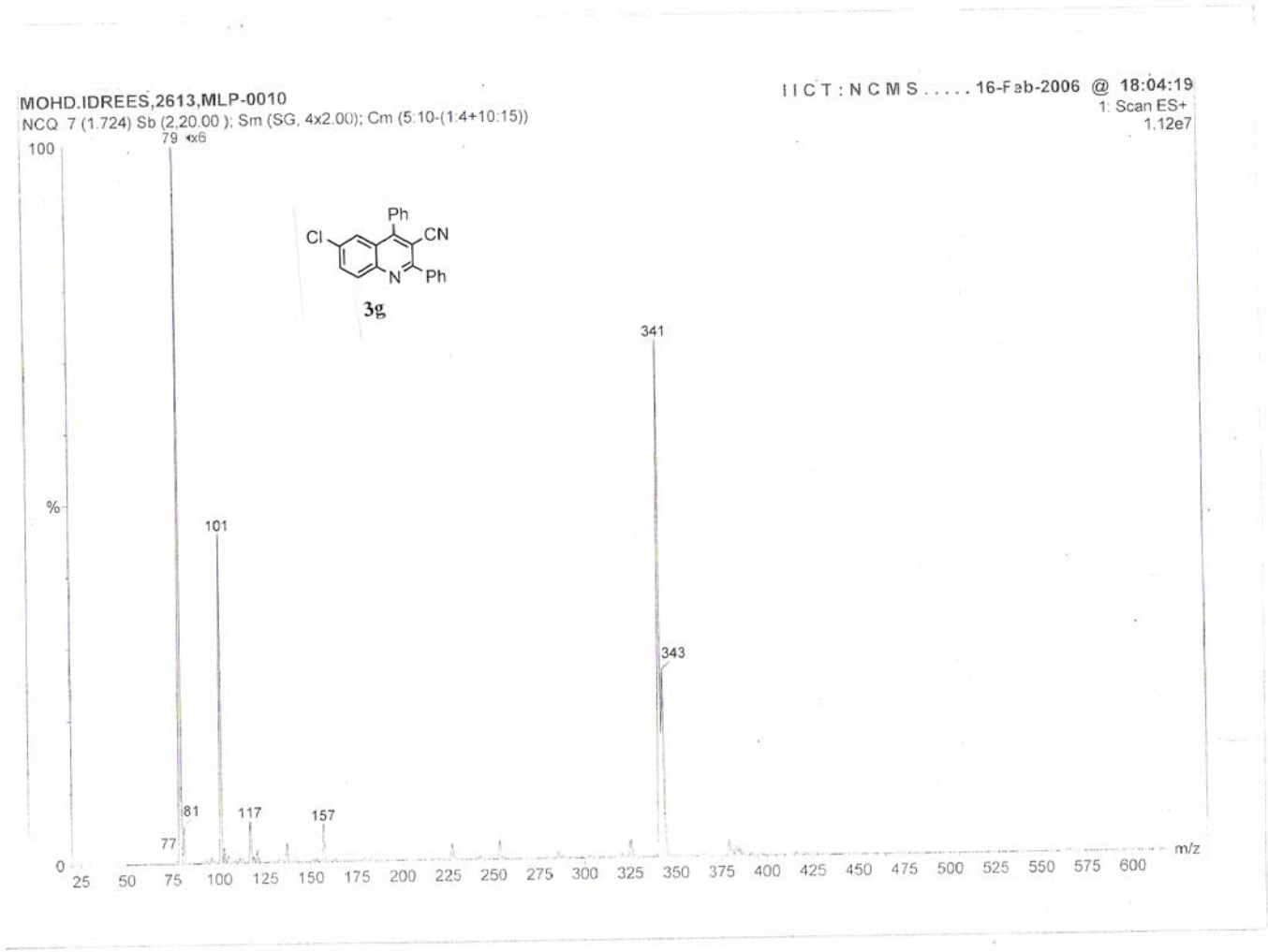
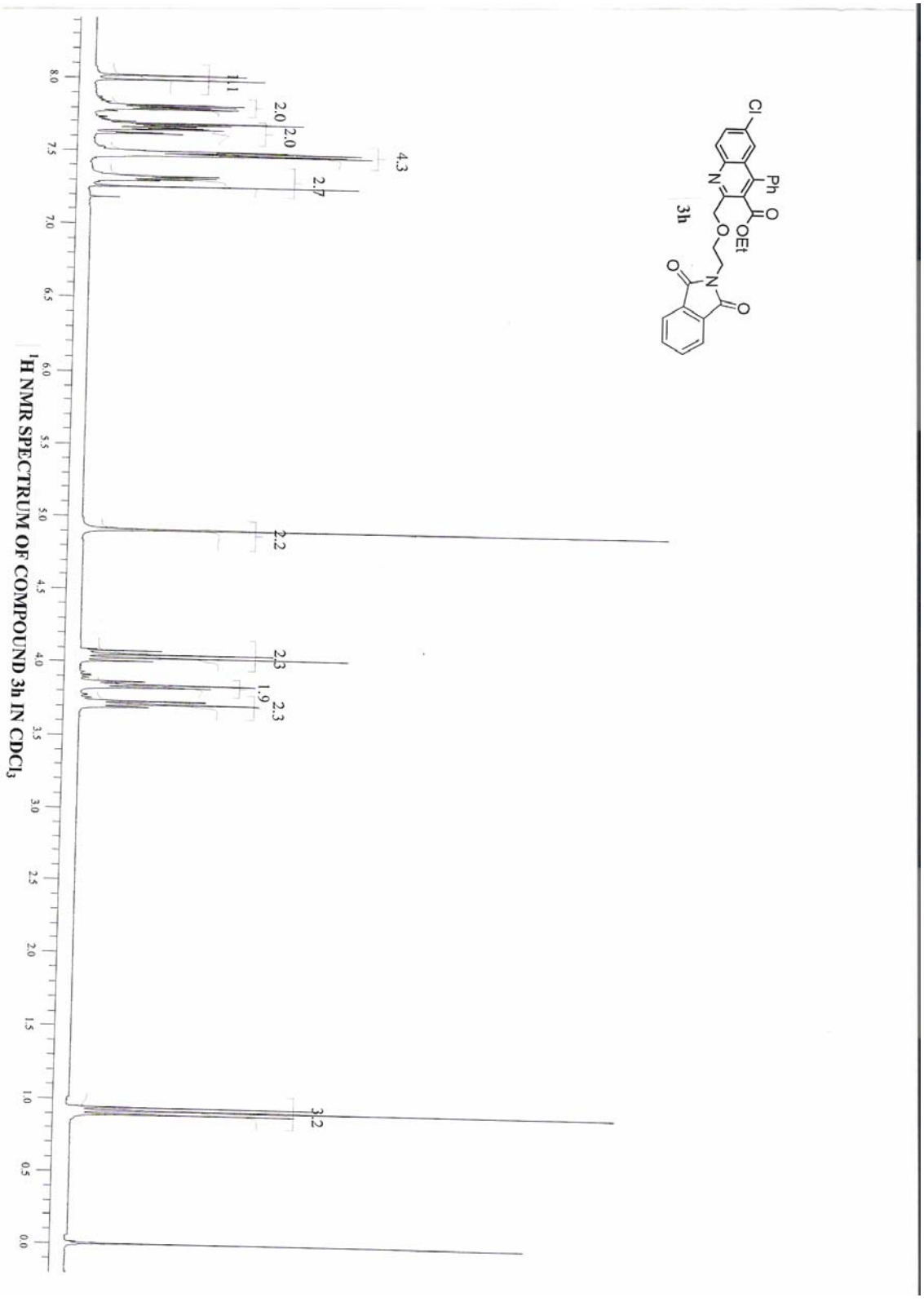
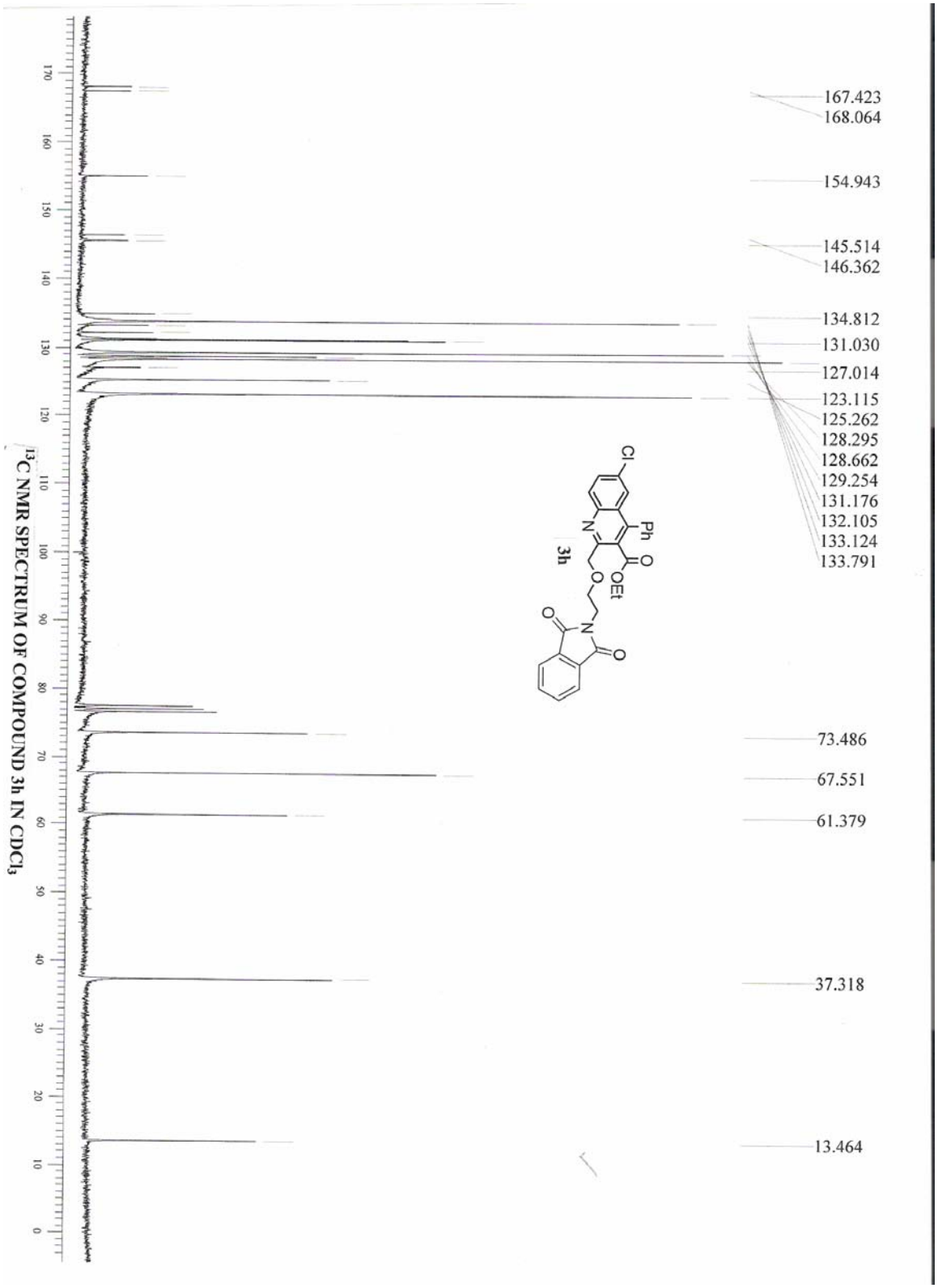
129.305
130.012
130.128
133.357
133.909
133.964


MOHD.IDREES,2613,MLP-0010
NCQ 7 (1.724) Sb (2,20.00); Sm (SG, 4x2.00); Cm (5:10-(1:4+10:15))
I I C T : N C M S . . . . . 16-Feb-2006 @ 18:04:19
1: Scan ES+
1.12e7
79 4x6
100
%
0
Ph
Cl
CN
N
Ph
3g
341
343
101
81
117
157
77
m/z
25 50 75 100 125 150 175 200 225 250 275 300 325 350 375 400 425 450 475 500 525 550 575 600

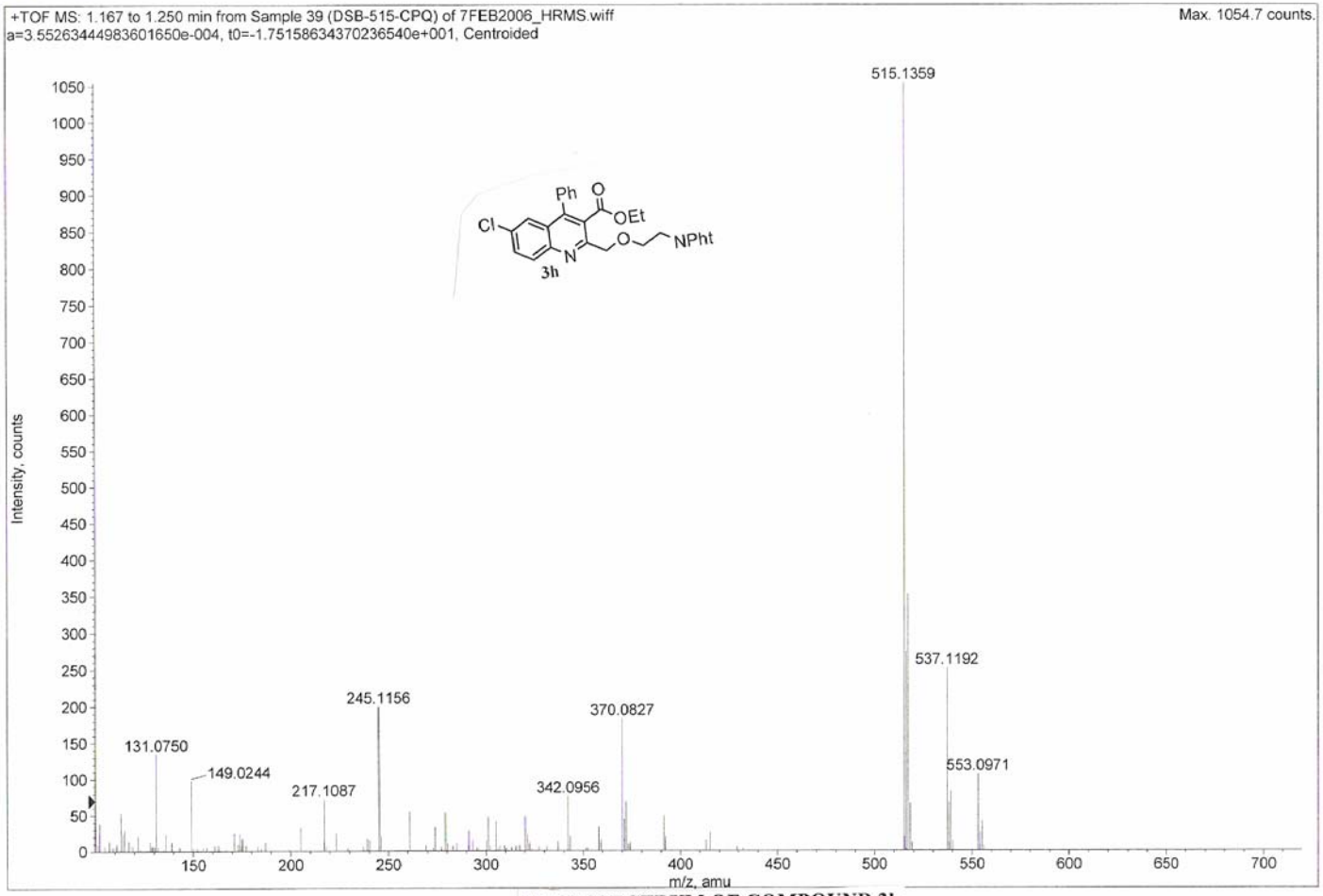


^{1}H NMR SPECTRUM OF COMPOUND 3h IN $CDCl_3$

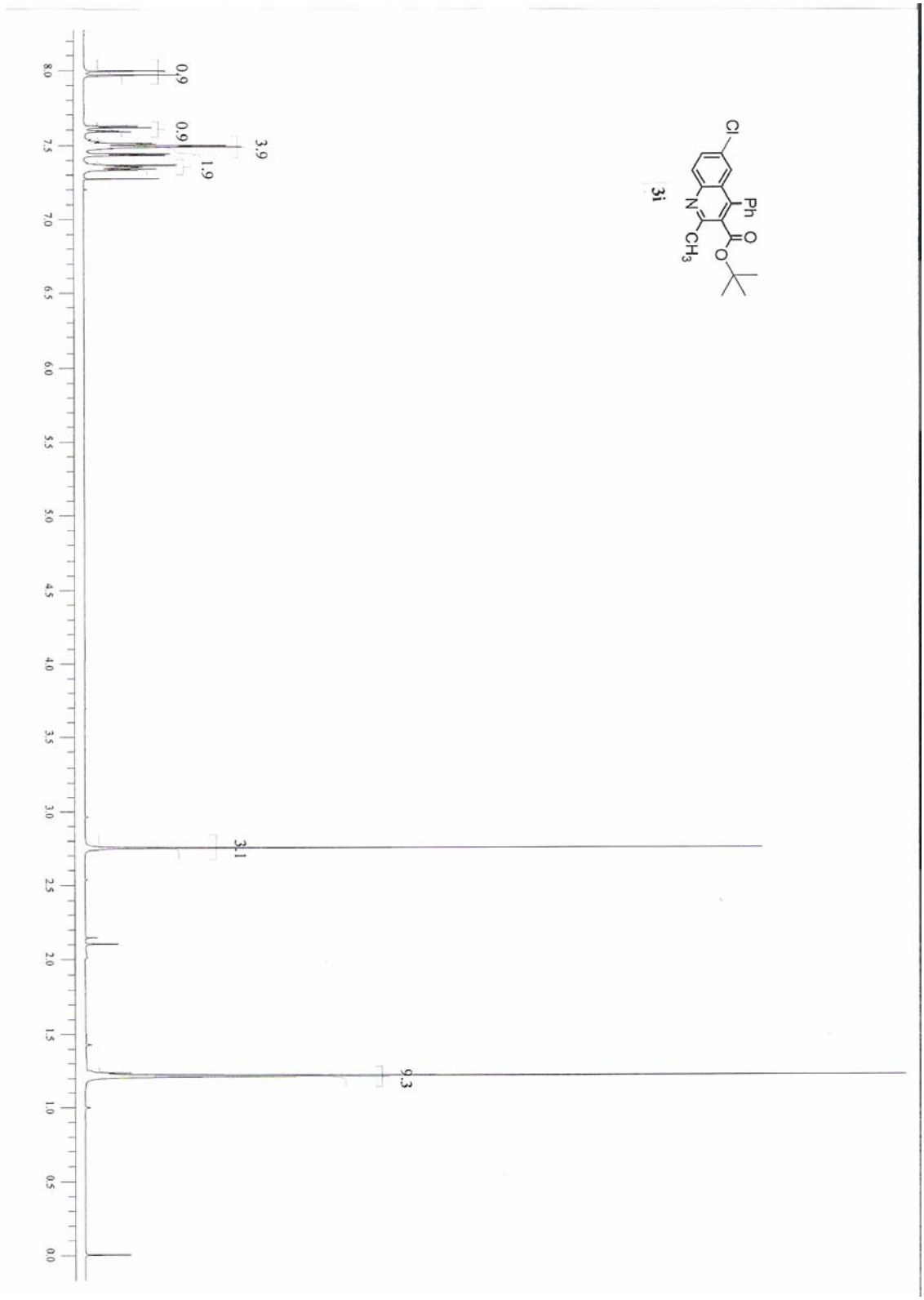

^{13}C NMR SPECTRUM OF COMPOUND 3h IN $CDCl_3$
167.423
168.064
154.943
145.514
146.362
134.812
131.030
127.014
123.115
125.262
128.295
128.662
129.254
131.176
132.105
133.124
133.791
73.486
67.551
61.379
37.318
13.464
3h
Cl
Ph
OEt
O
N

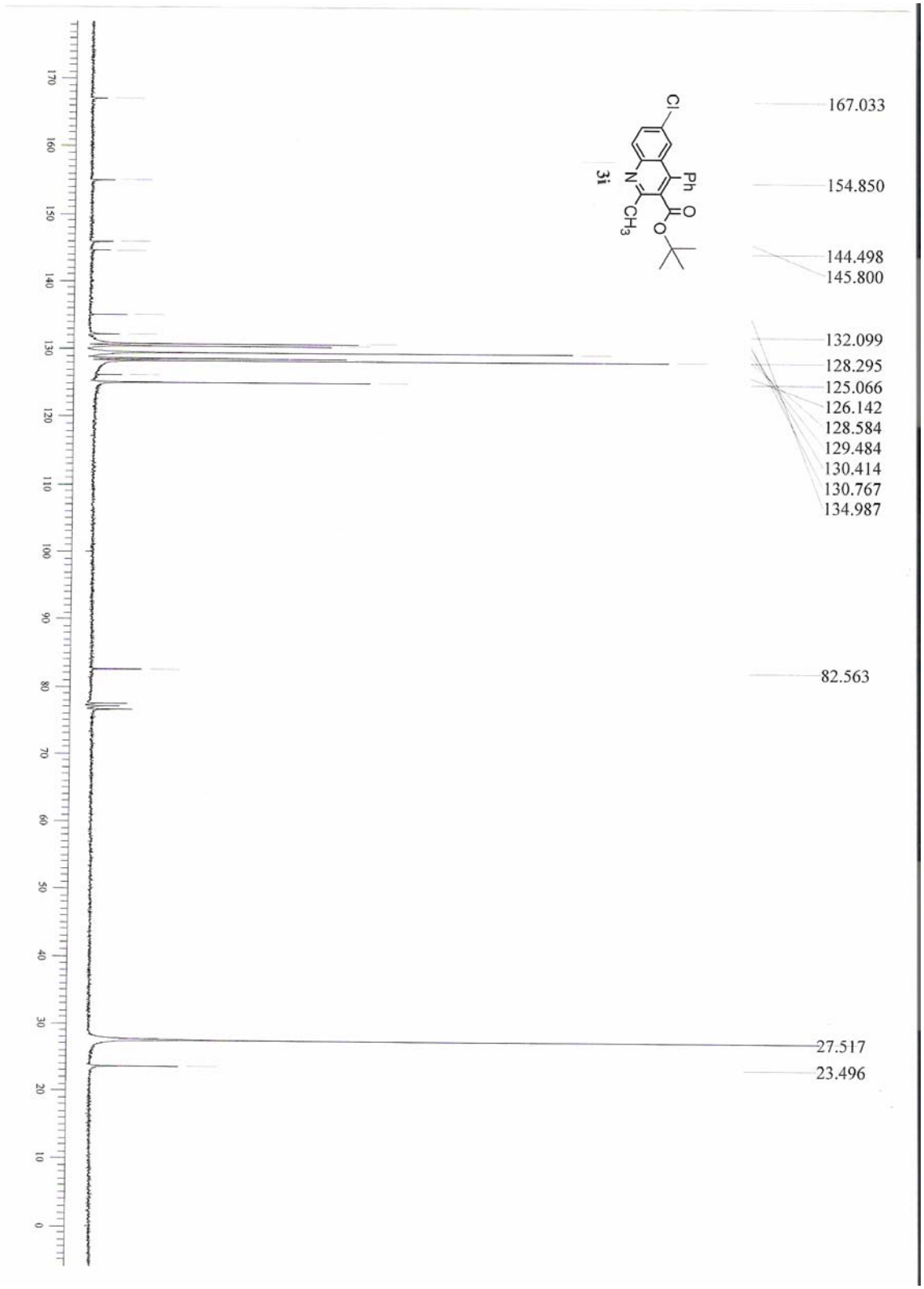
Acq. File: 7FEB2006_HRMS.wiff Sample Name: DSB-515-CPQ Acq. Date: Tuesday, February 07, 2006

Sample Comment: MOHD IDREES, DSB-515-CPQ, ESI/HRMS Acq. Time: 18:40



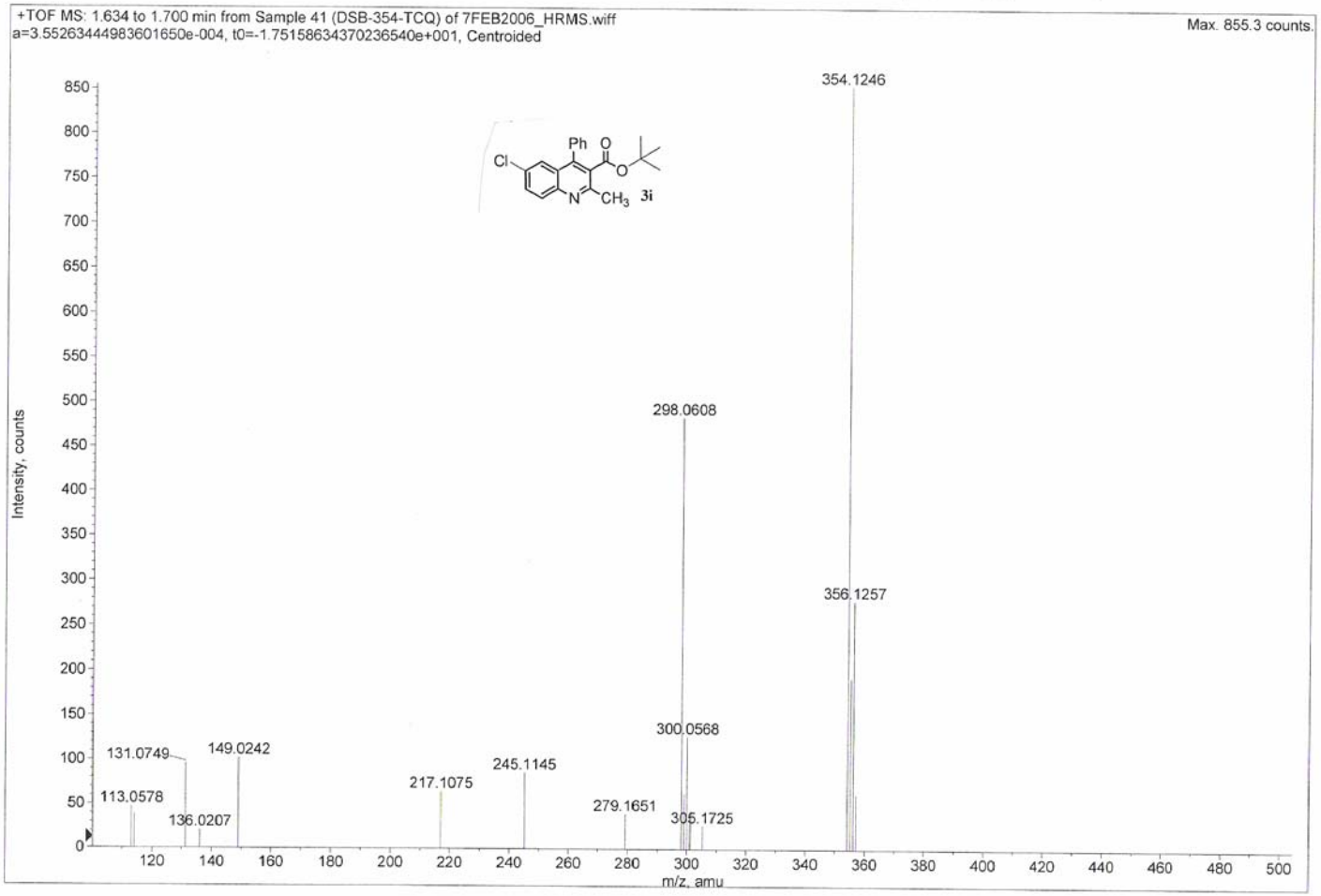
MASS SPECTRUM OF COMPOUND 3h

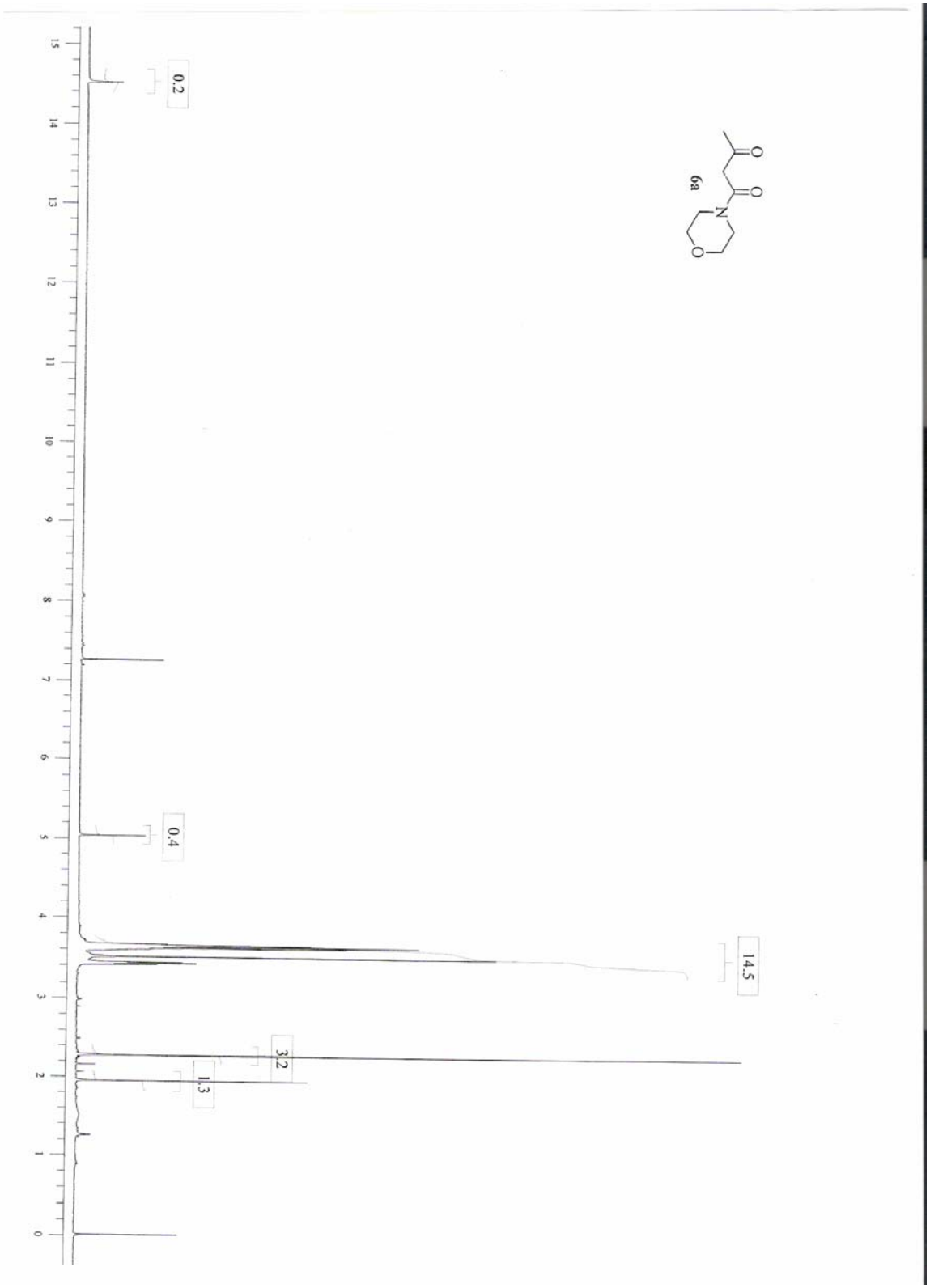

Cl
Ph
O
N
CH3
O
3i
0.9
0.9
3.9
1.9
3.1
9.3
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

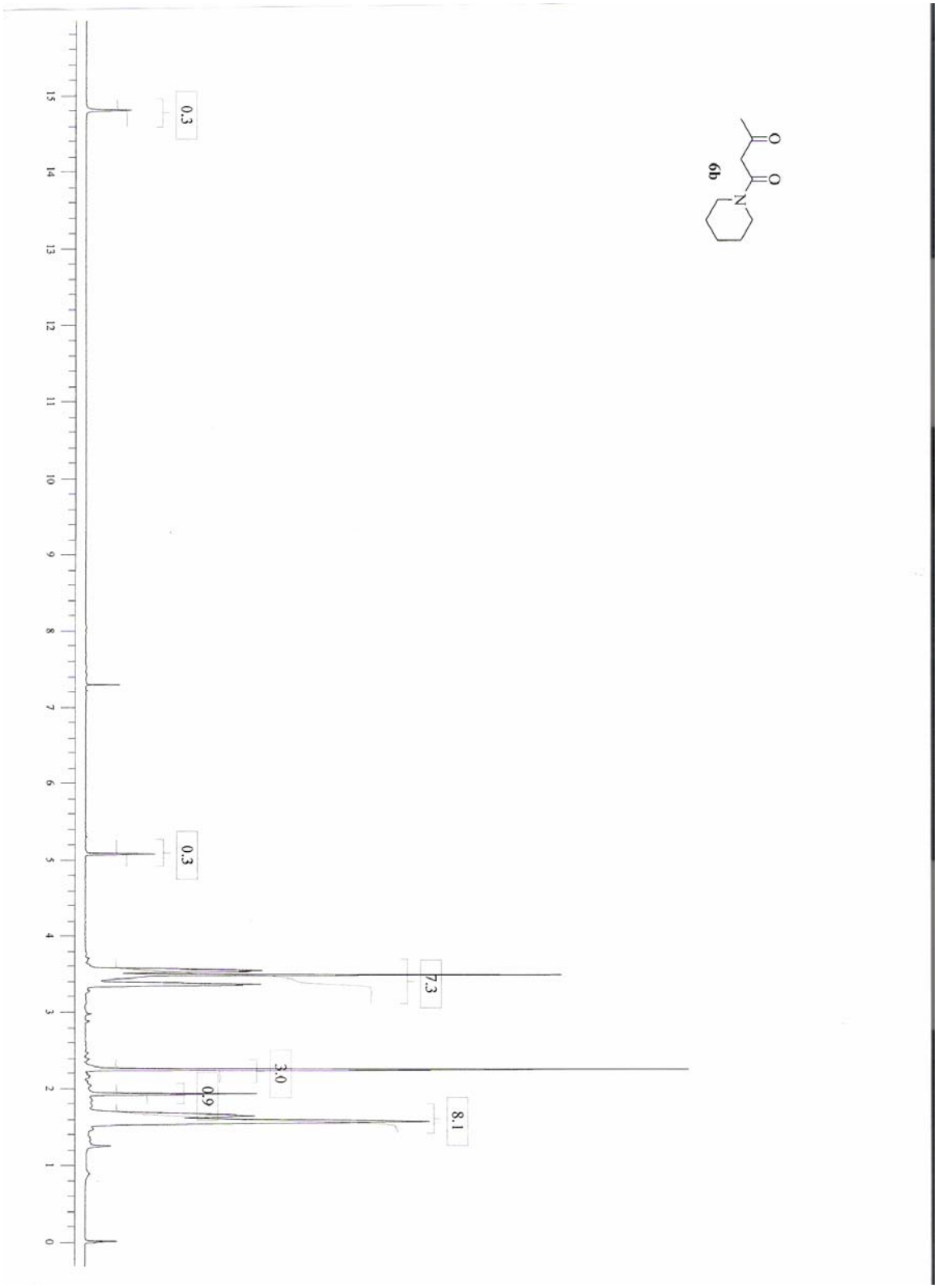

Cl
Ph
O
O
N
CH3
3i
167.033
154.850
144.498
145.800
132.099
128.295
125.066
126.142
128.584
129.484
130.414
130.767
134.987
82.563
27.517
23.496

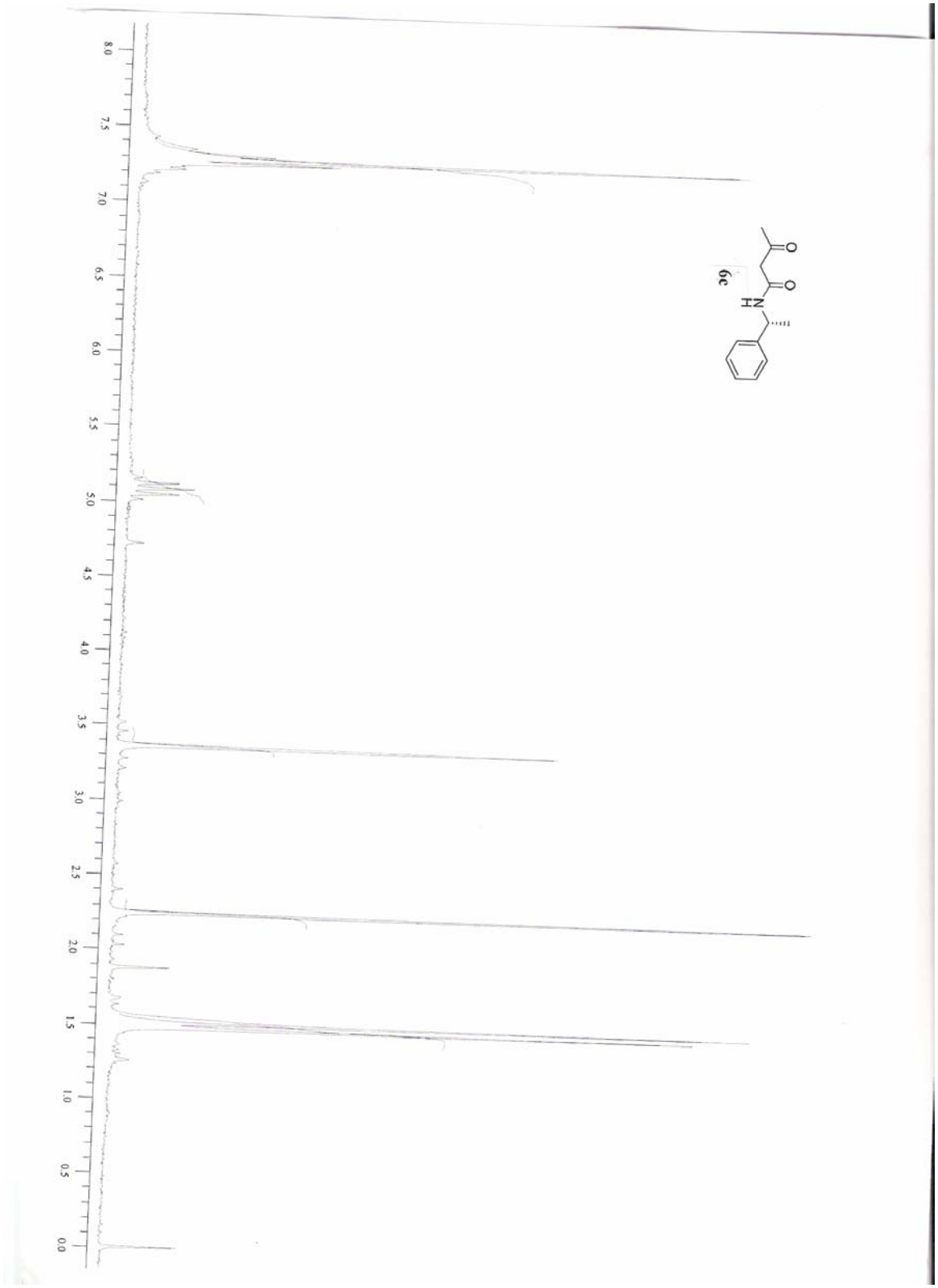
Acq. File: 7FEB2006_HRMS.wiff Sample Name: DSB-354-TCQ Acq. Date: Tuesday, February 07, 2006

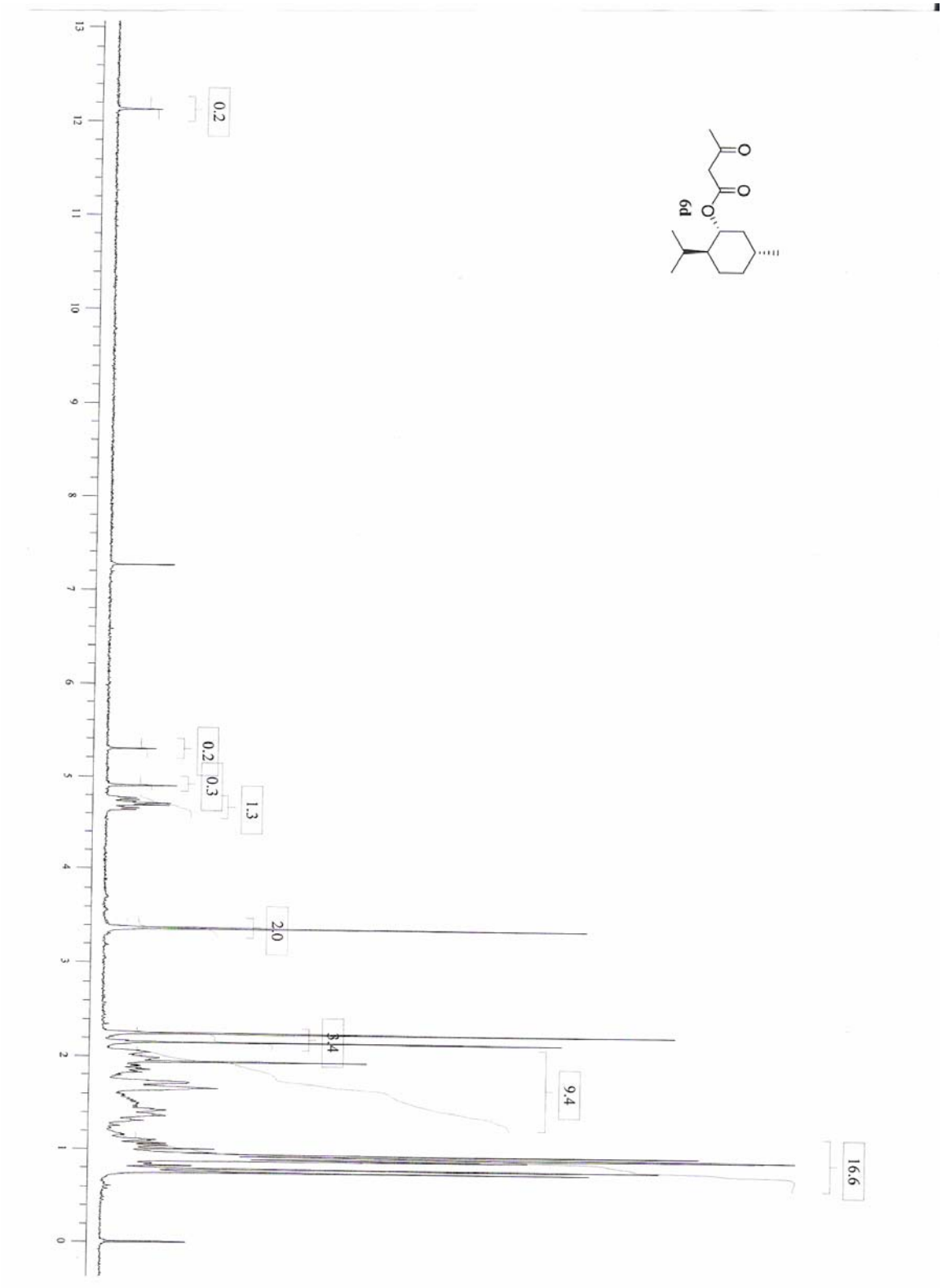
Sample Comment: MOHD IDREES, DSB-354-TCQ, ESI/HRMS Acq. Time: 18:51

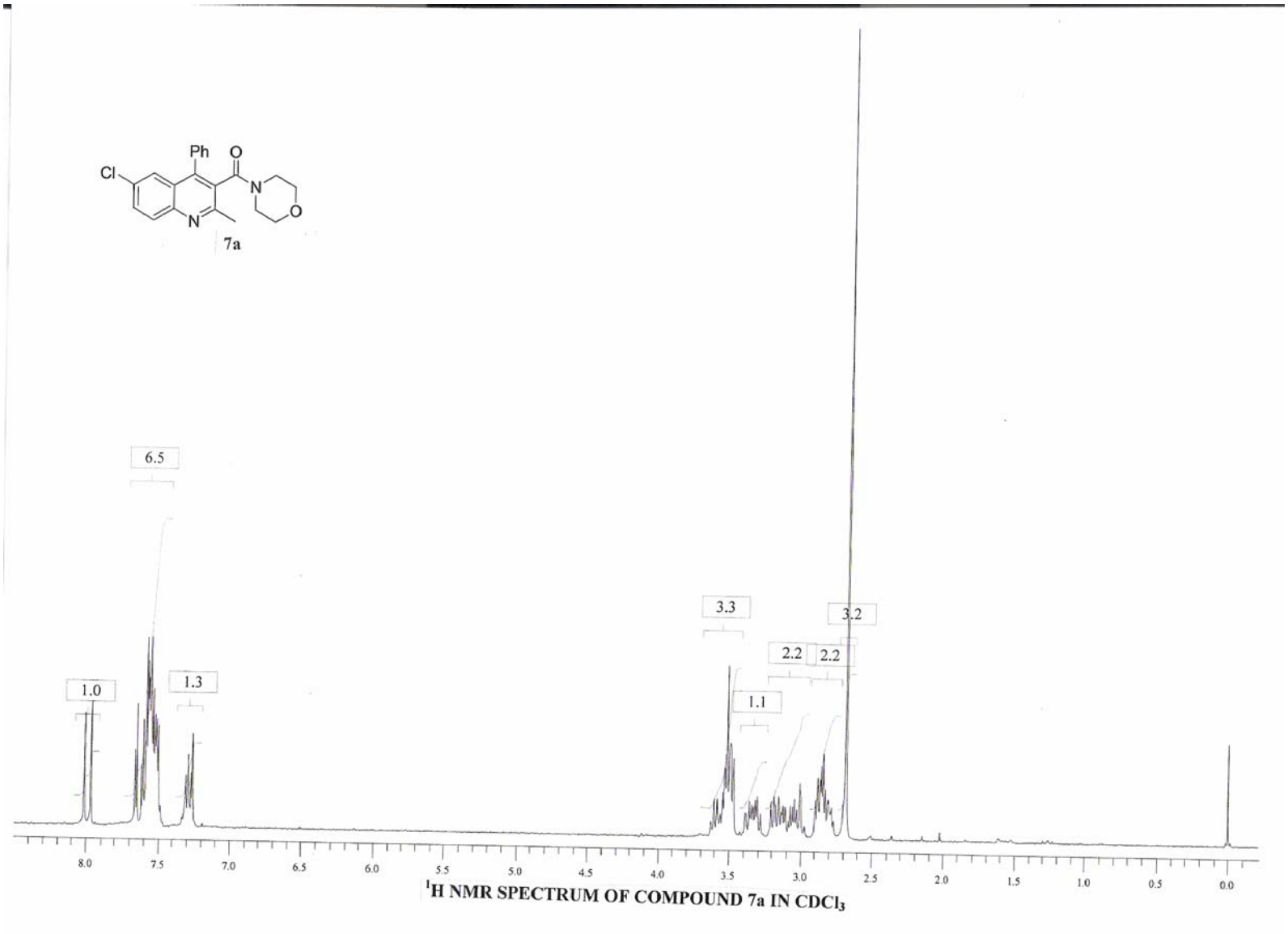



6a
0.2
0.4
14.5
3.2
1.3

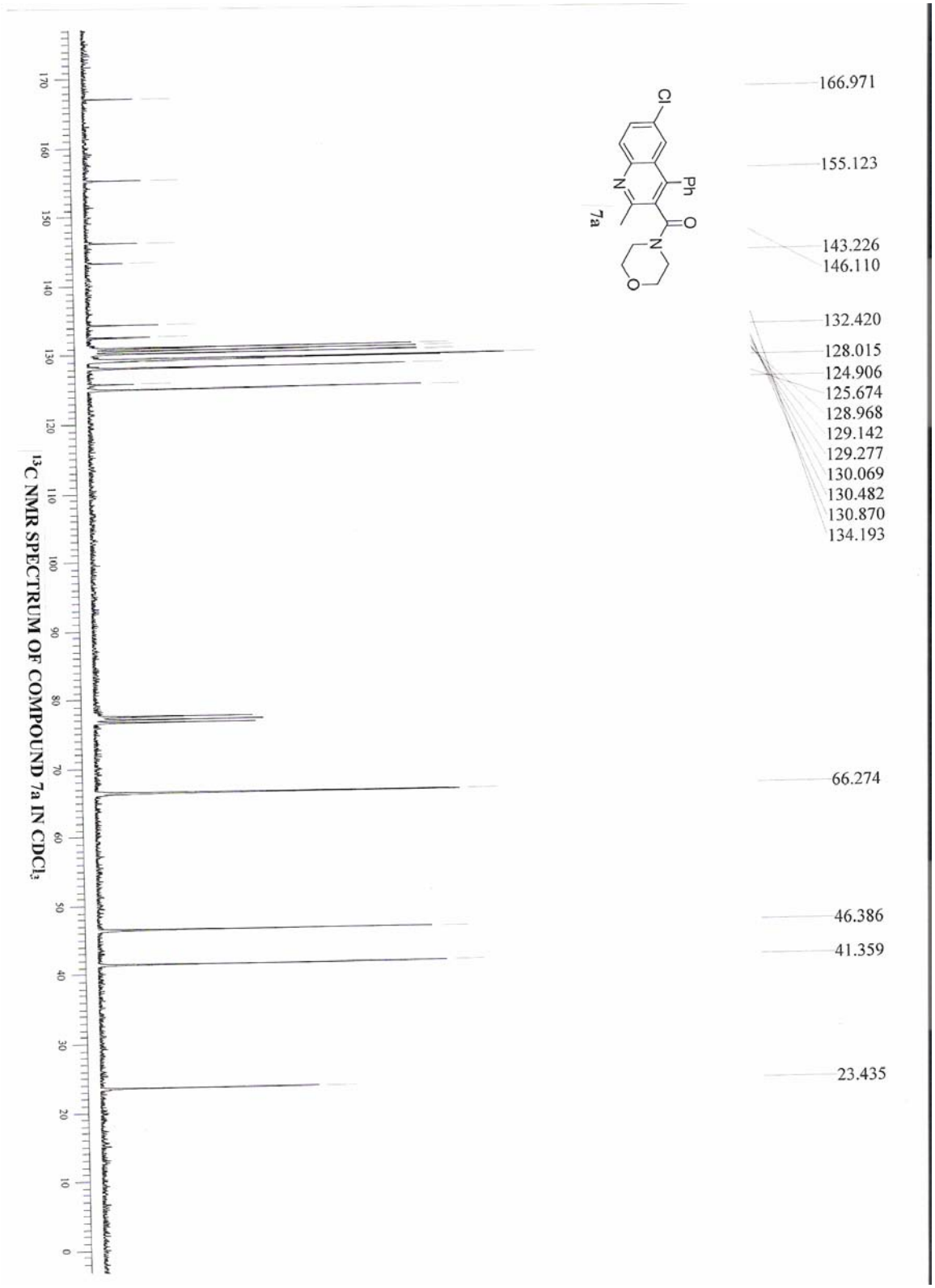

6b
0.3
0.3
7.3
3.0
0.9
8.1

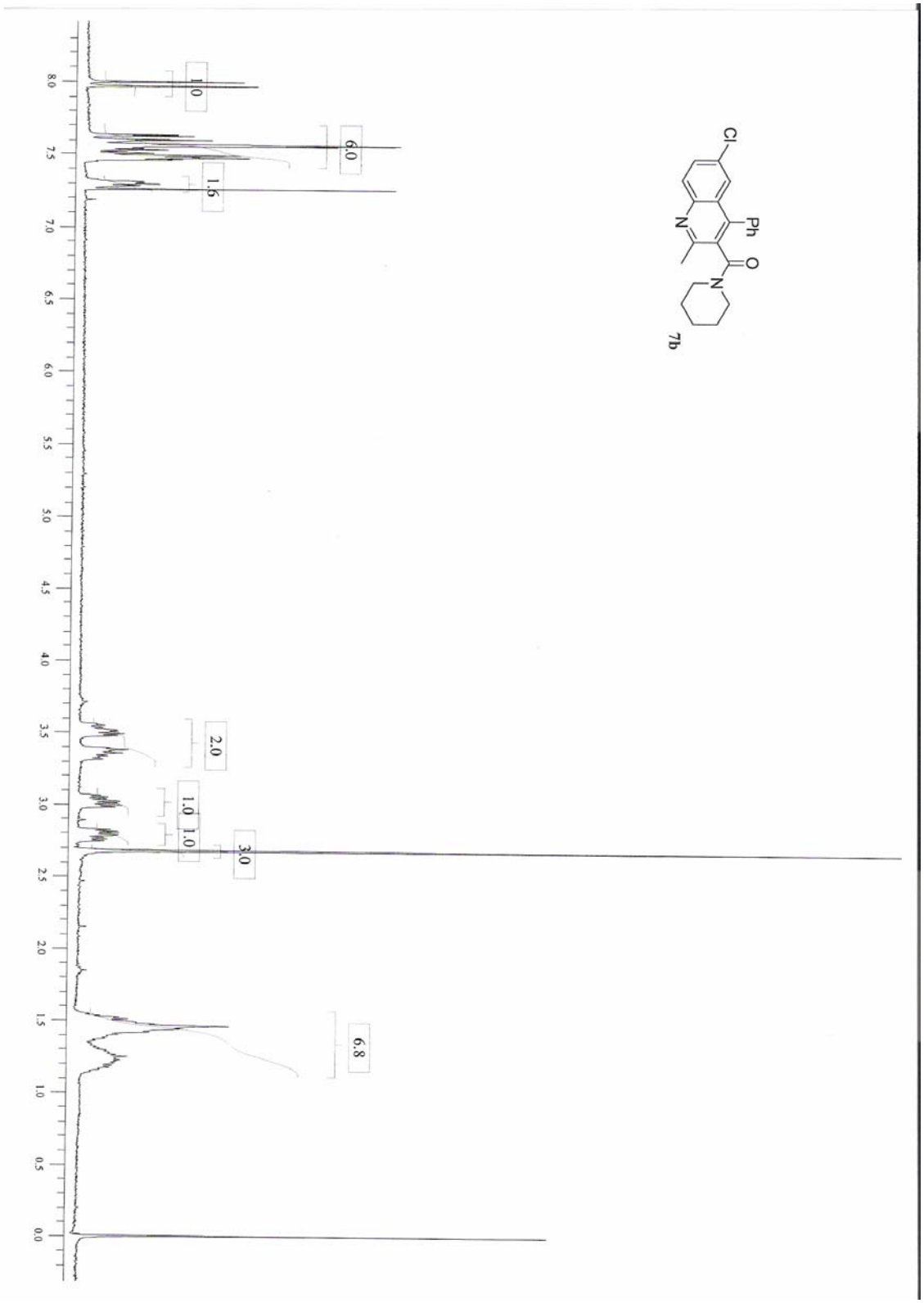

3g
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

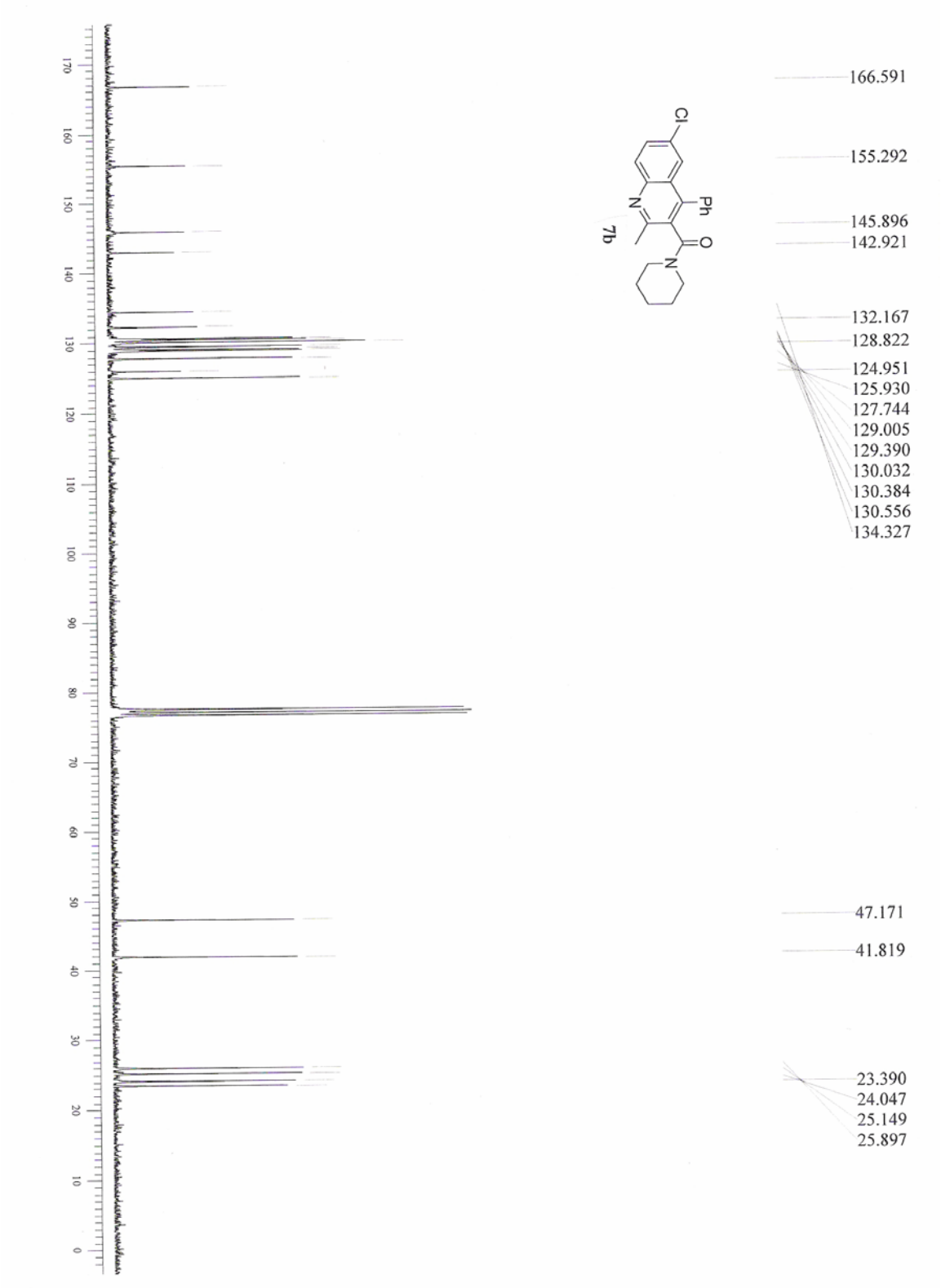

6d
0.2
0.2
0.3
1.3
2.0
8.4
9.4
16.6

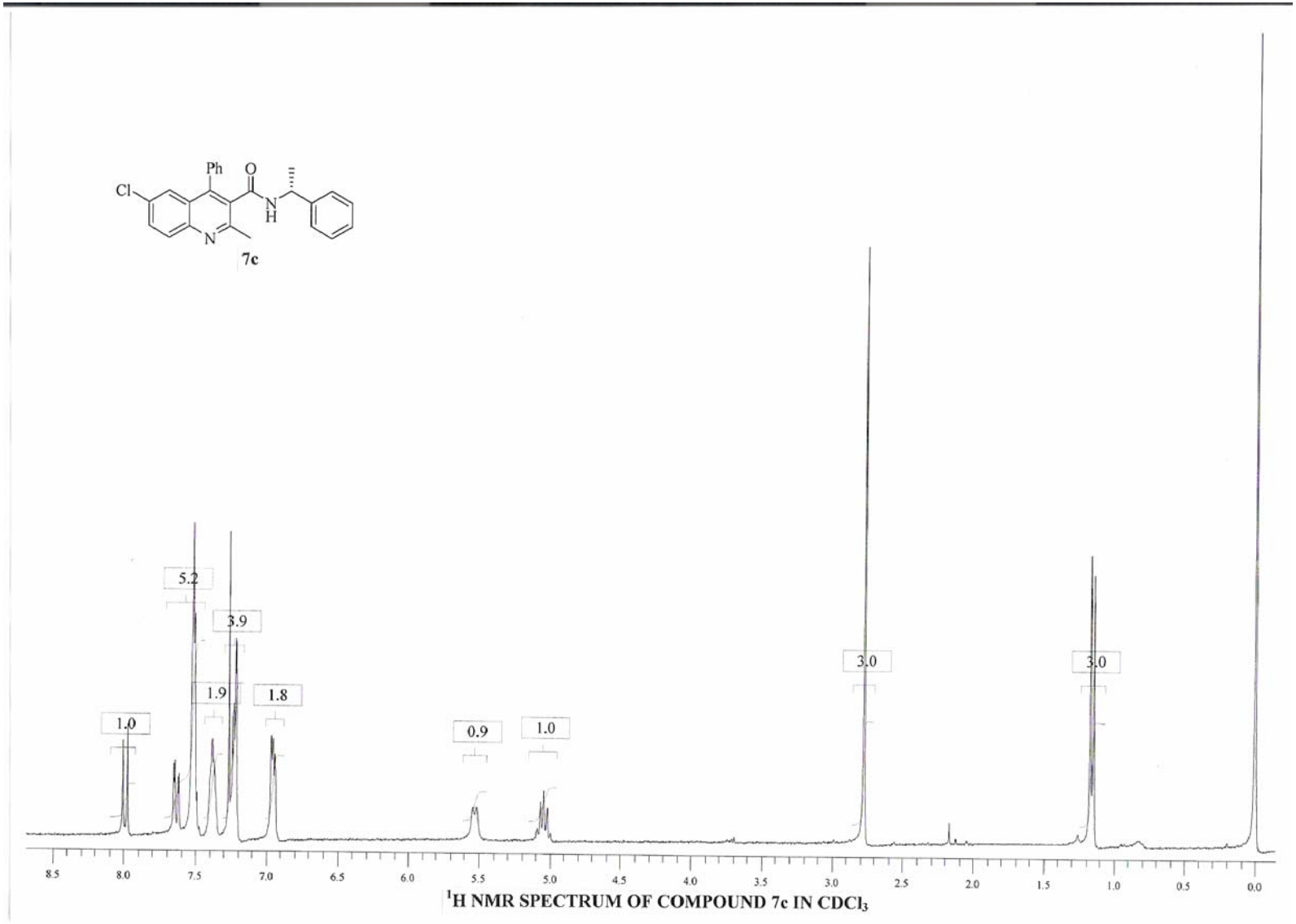


^{1}H NMR SPECTRUM OF COMPOUND 7a IN $CDCl_3$

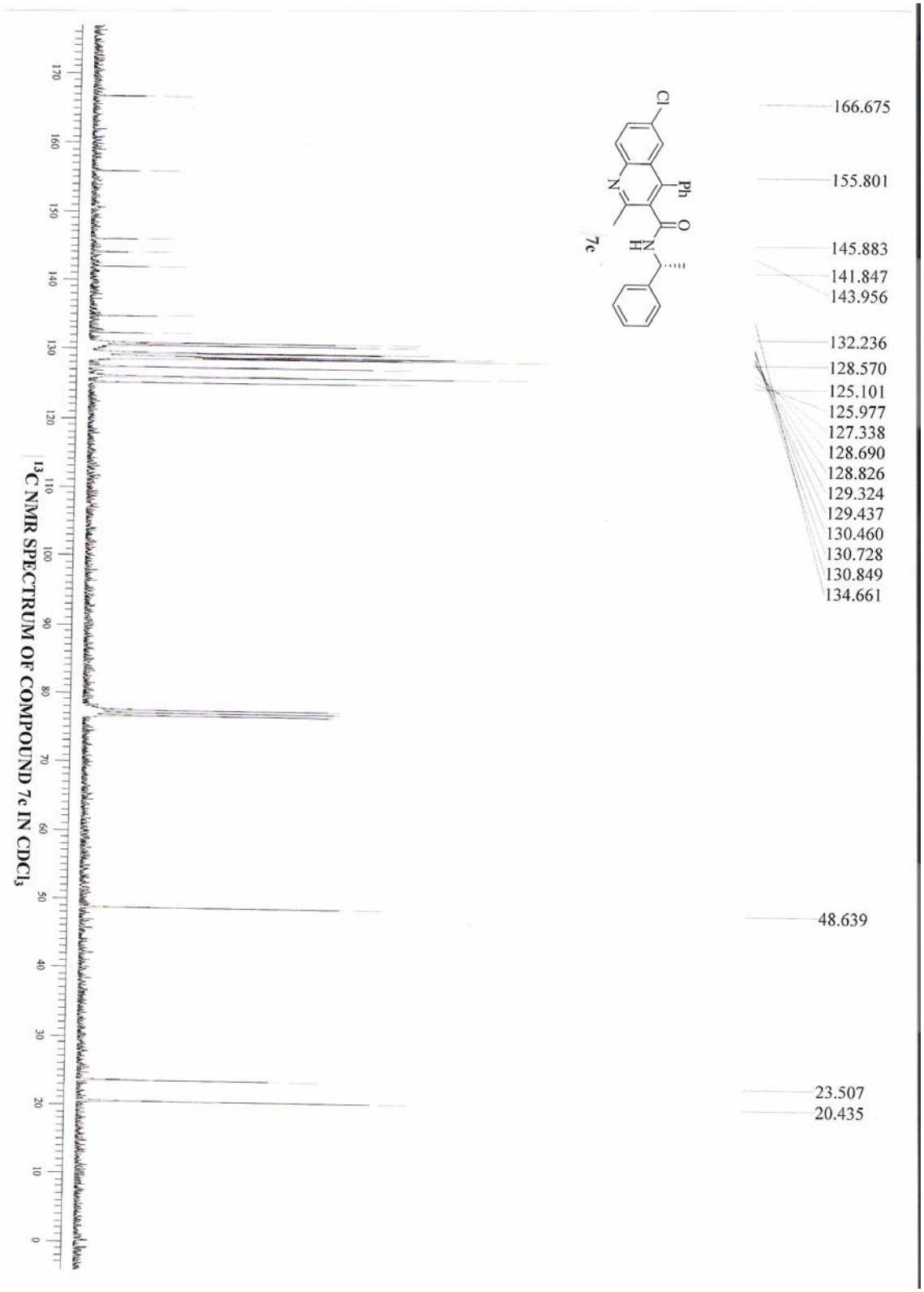

166.971
155.123
143.226
146.110
132.420
128.015
124.906
125.674
128.968
129.142
129.277
130.069
130.482
130.870
134.193
66.274
46.386
41.359
23.435
Cl
Ph
O
N
O
7a
^{13}C NMR SPECTRUM OF COMPOUND 7a IN $CDCl_3$

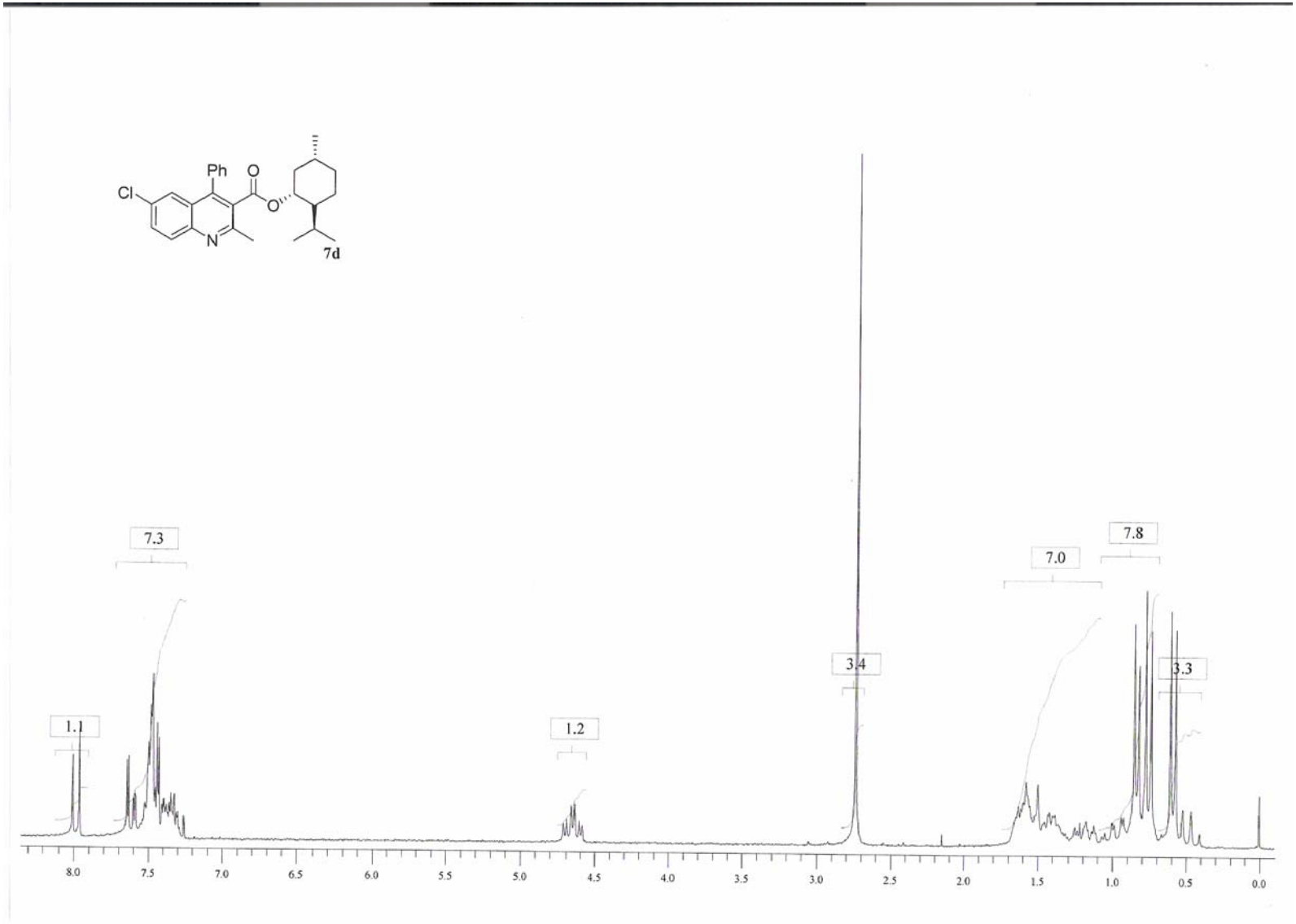

Cl
Ph
O
N
N
7b
1.0
6.0
1.6
2.0
1.0
1.0
3.0
6.8

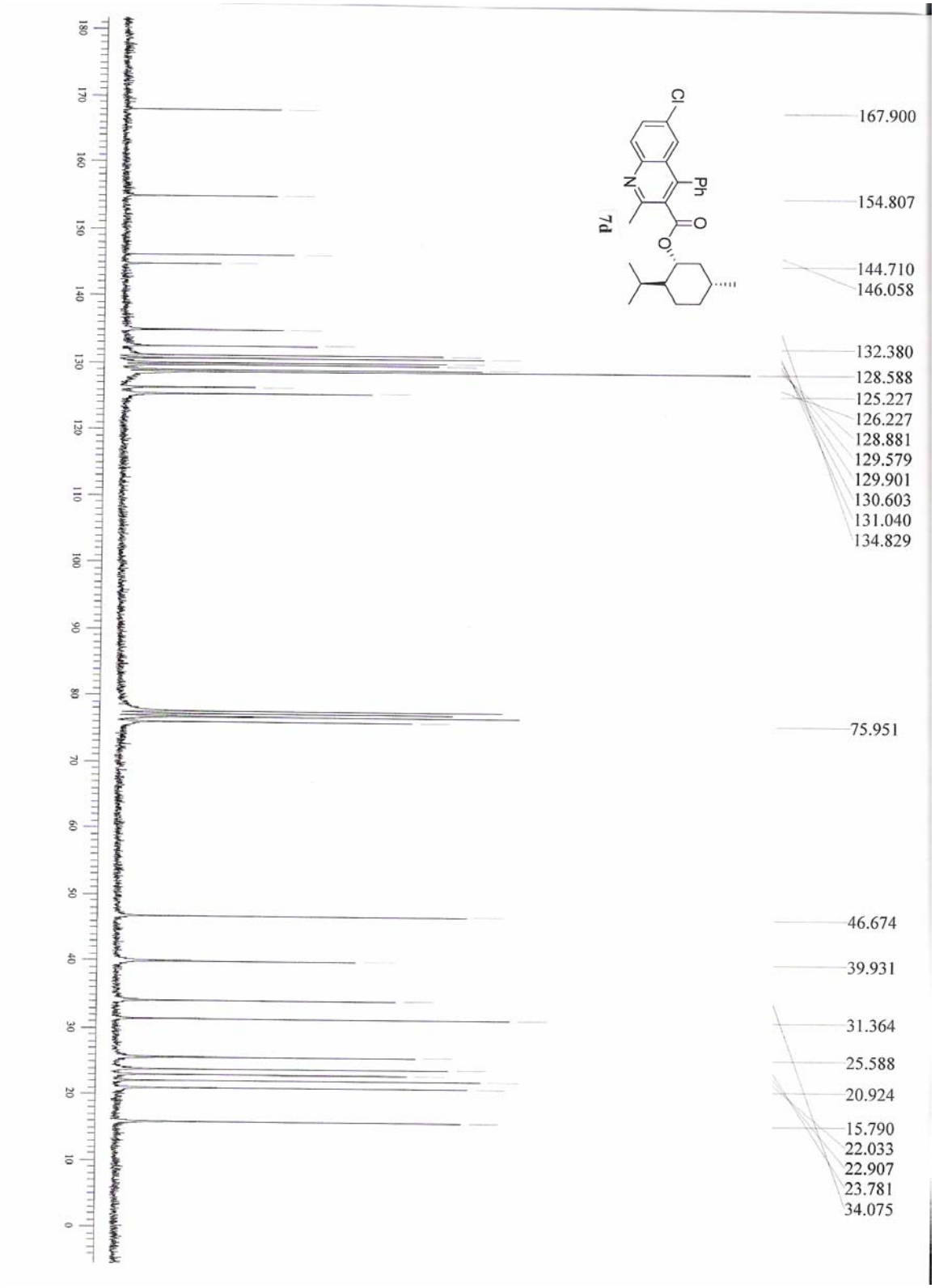

166.591
155.292
145.896
142.921
132.167
128.822
124.951
125.930
127.744
129.005
129.390
130.032
130.384
130.556
134.327
47.171
41.819
23.390
24.047
25.149
25.897
Cl
Ph
O
N
N
7b

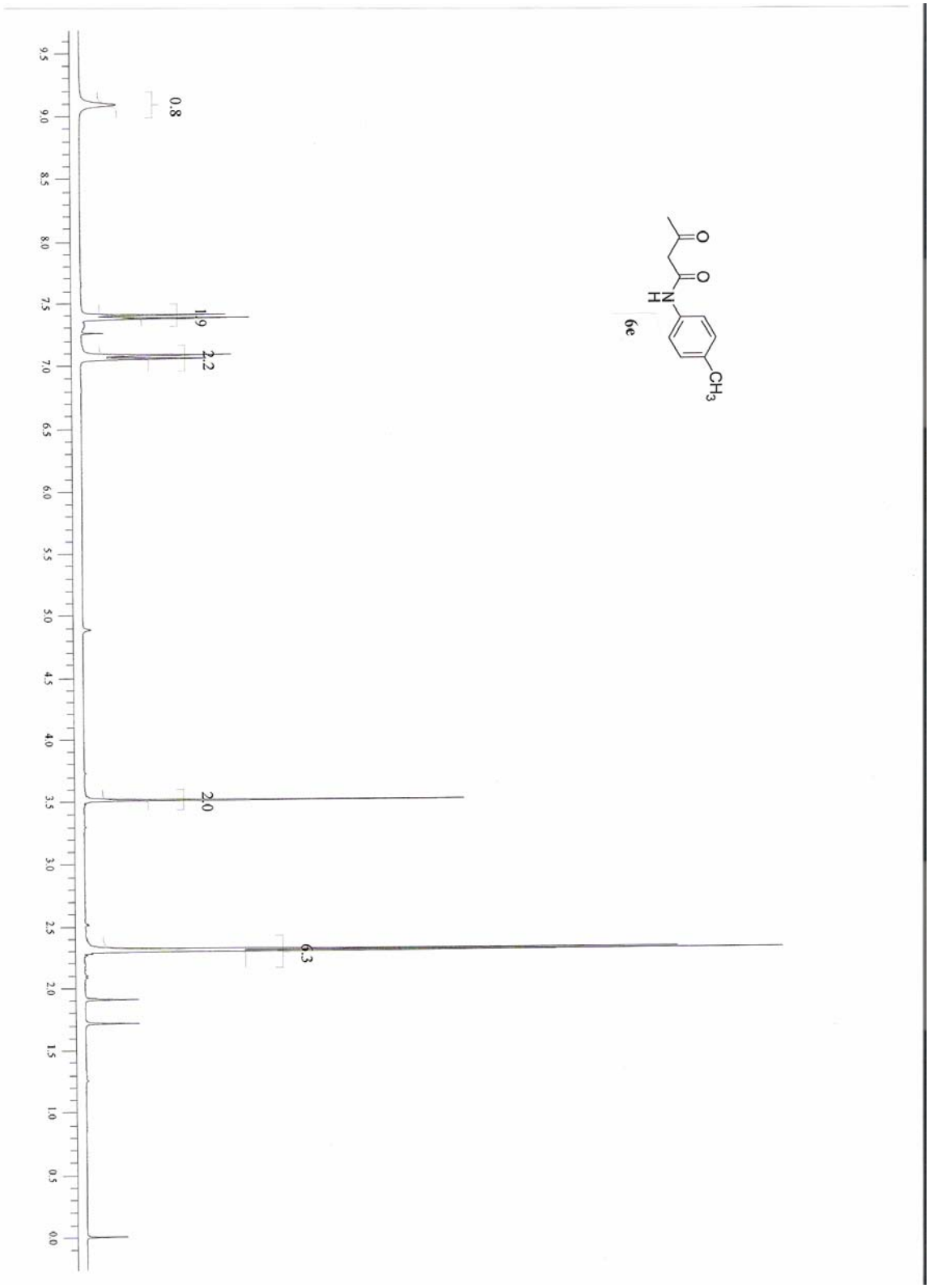


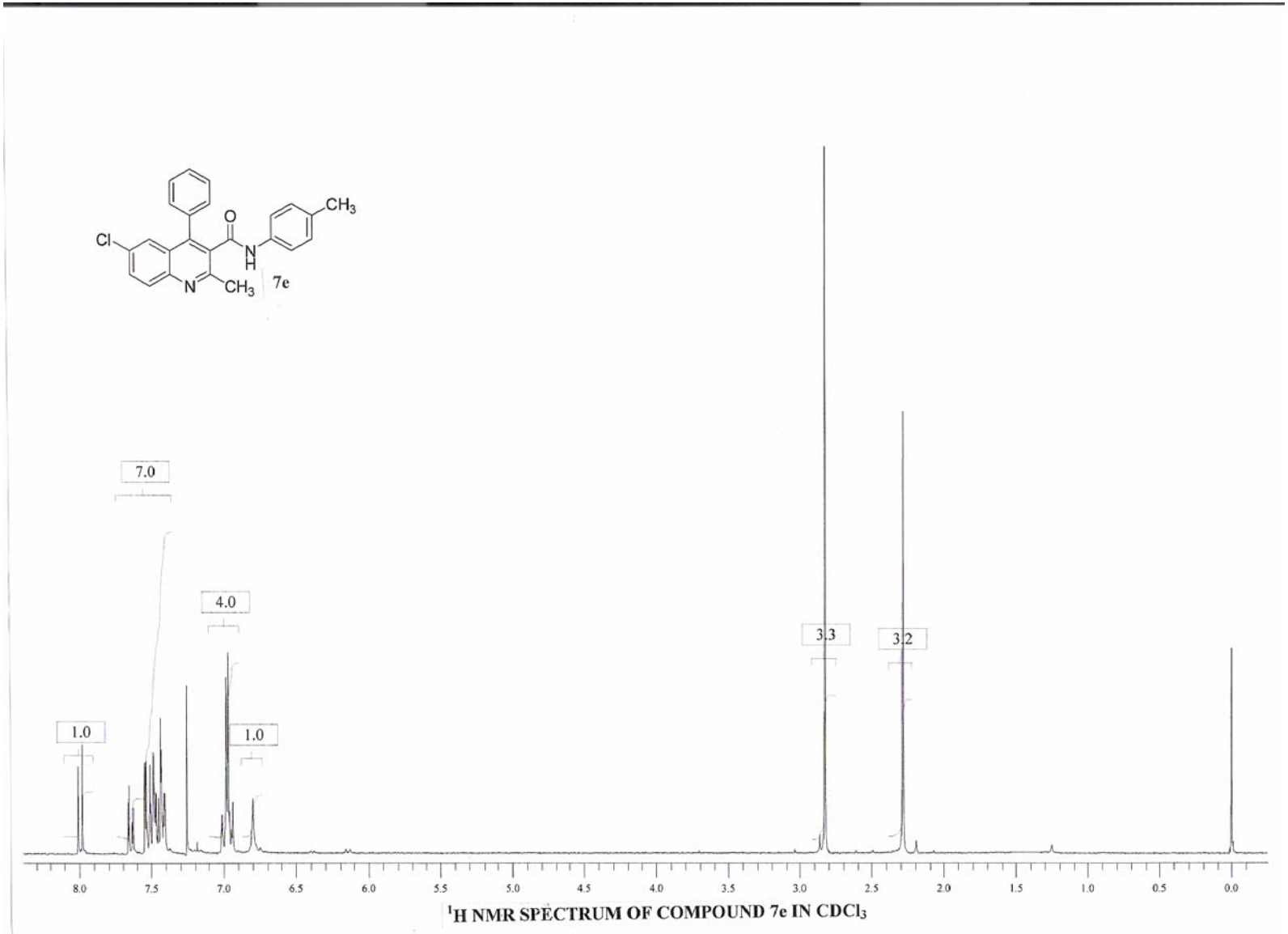
^{1}H NMR SPECTRUM OF COMPOUND 7c IN $CDCl_3$


^{13}C NMR SPECTRUM OF COMPOUND 7c IN CDCl$_3$
7c
166.675
155.801
145.883
141.847
143.956
132.236
128.570
125.101
125.977
127.338
128.690
128.826
129.324
129.437
130.460
130.728
130.849
134.661
48.639
23.507
20.435


Ph
O
Cl
O
N
7d
7.3
7.8
7.0
3.4
3.3
1.1
1.2
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


Cl
Ph
N
O
O
7d
167.900
154.807
144.710
146.058
132.380
128.588
125.227
126.227
128.881
129.579
129.901
130.603
131.040
134.829
75.951
46.674
39.931
31.364
25.588
20.924
15.790
22.033
22.907
23.781
34.075

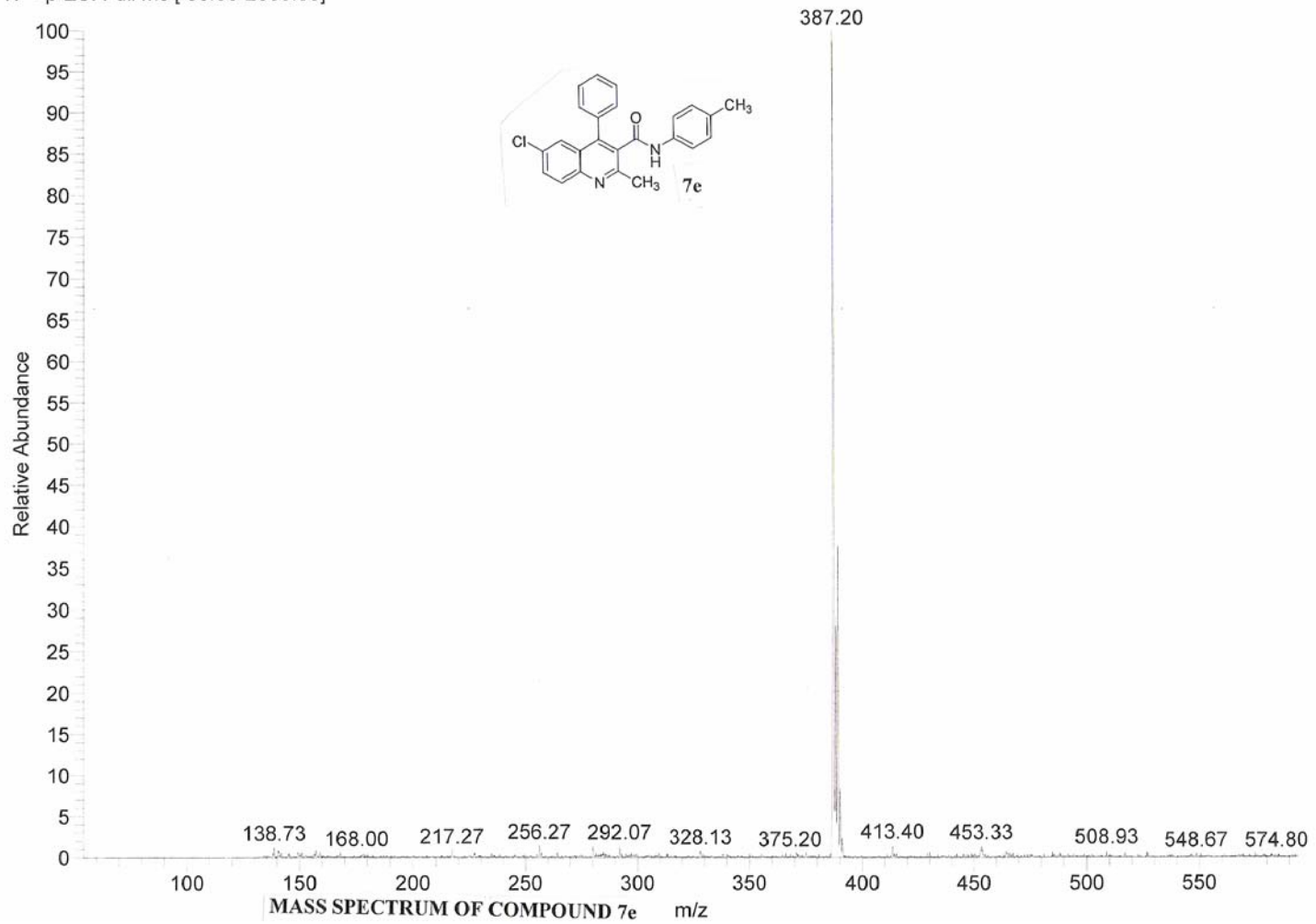

6e
0.8
1.9
2.2
2.0
6.3



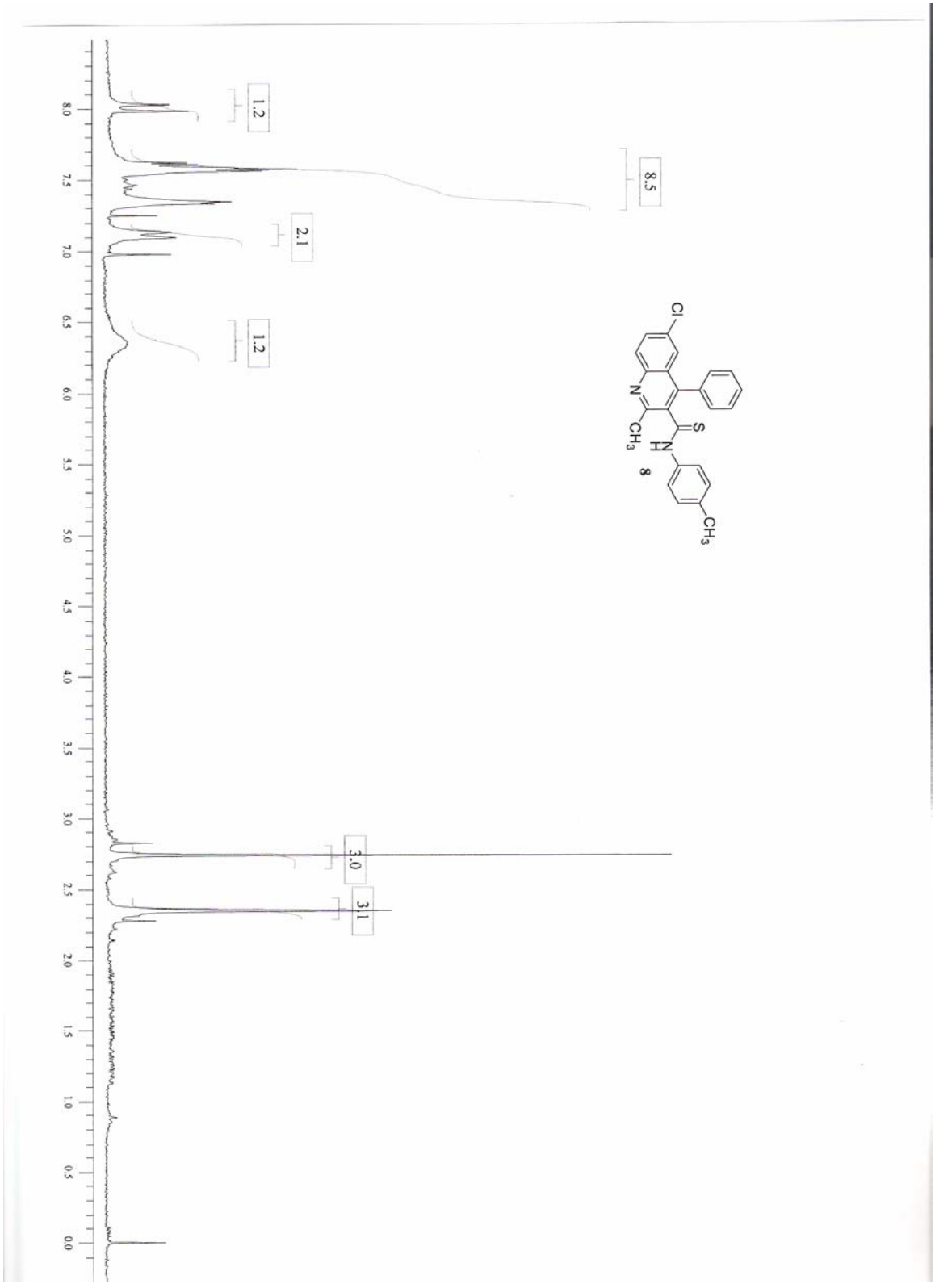
^{1}H NMR SPECTRUM OF COMPOUND 7e IN $CDCl_3$

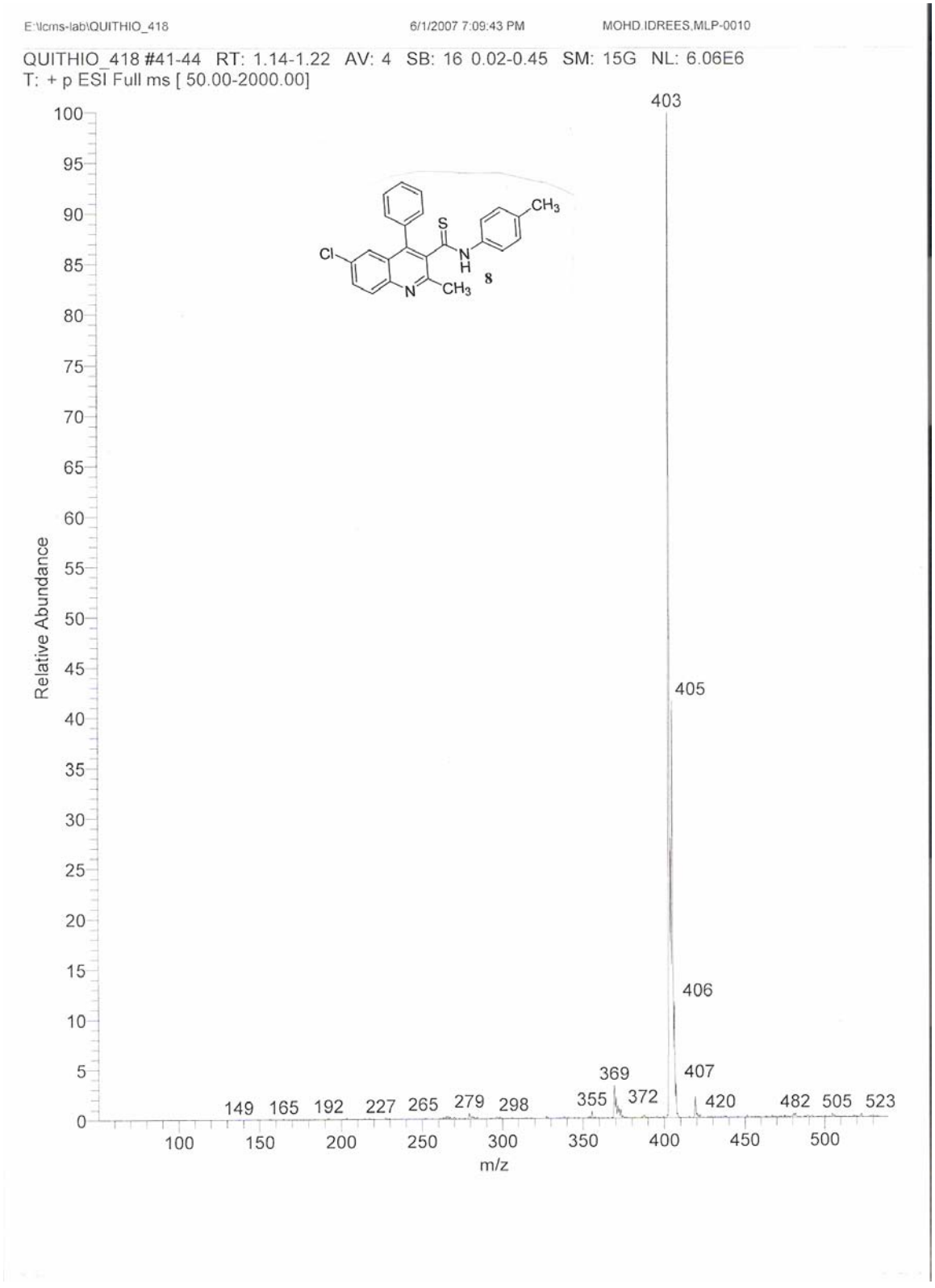
DSB402QUINAM_070509155045 5/9/2007 3:50:45 PM MOHD. IDREES, MLP-0010

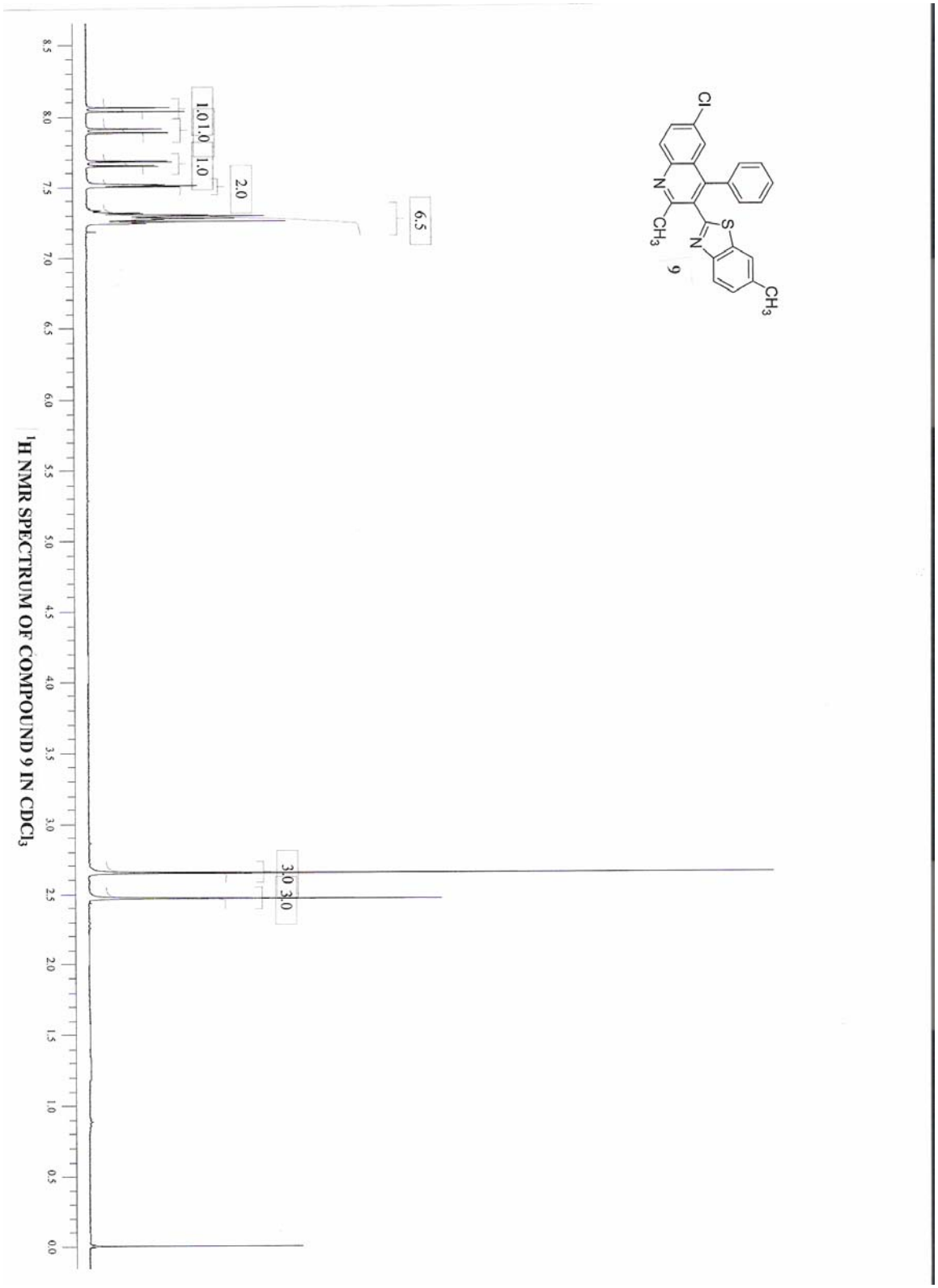
DSB402QUINAM_070509155045 #31-40 RT: 0.93-1.19 AV: 10 NL: 4.56E6
T: + p ESI Full ms [50.00-2000.00]



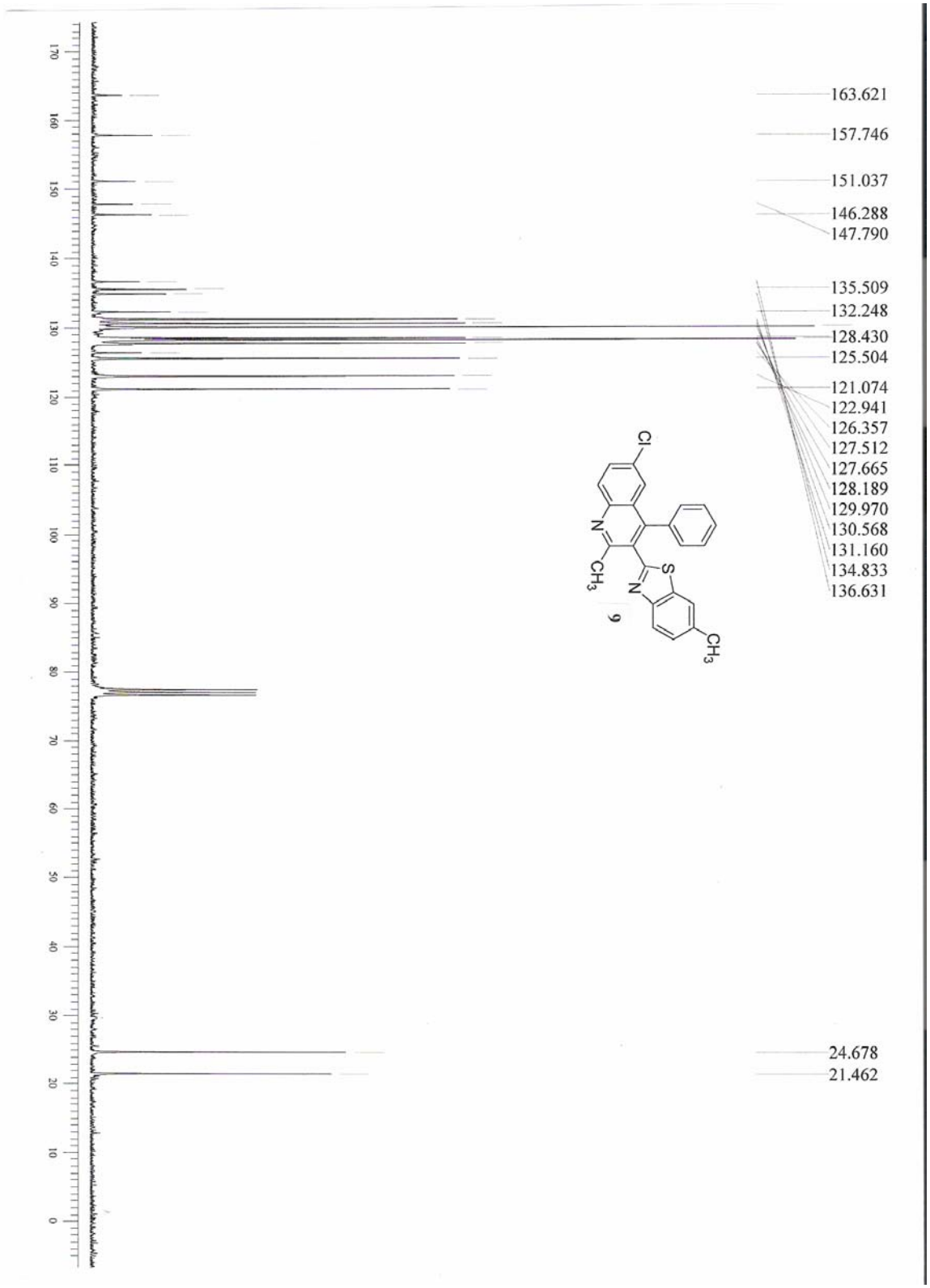
MASS SPECTRUM OF COMPOUND 7e

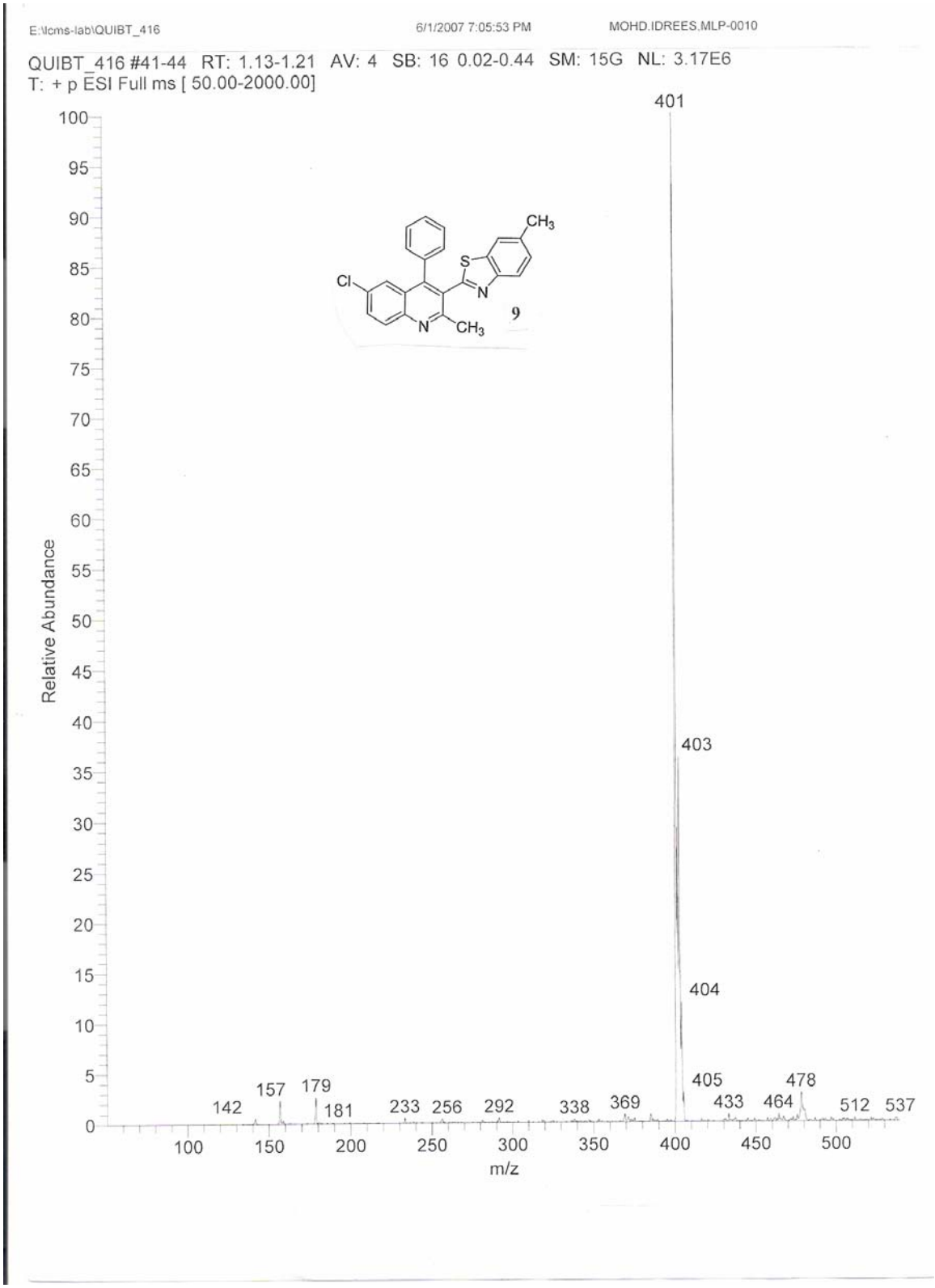

8.5
1.2
2.1
1.2
3.0
3.1
Cl
N
CH3
S
N
H
8
CH3
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

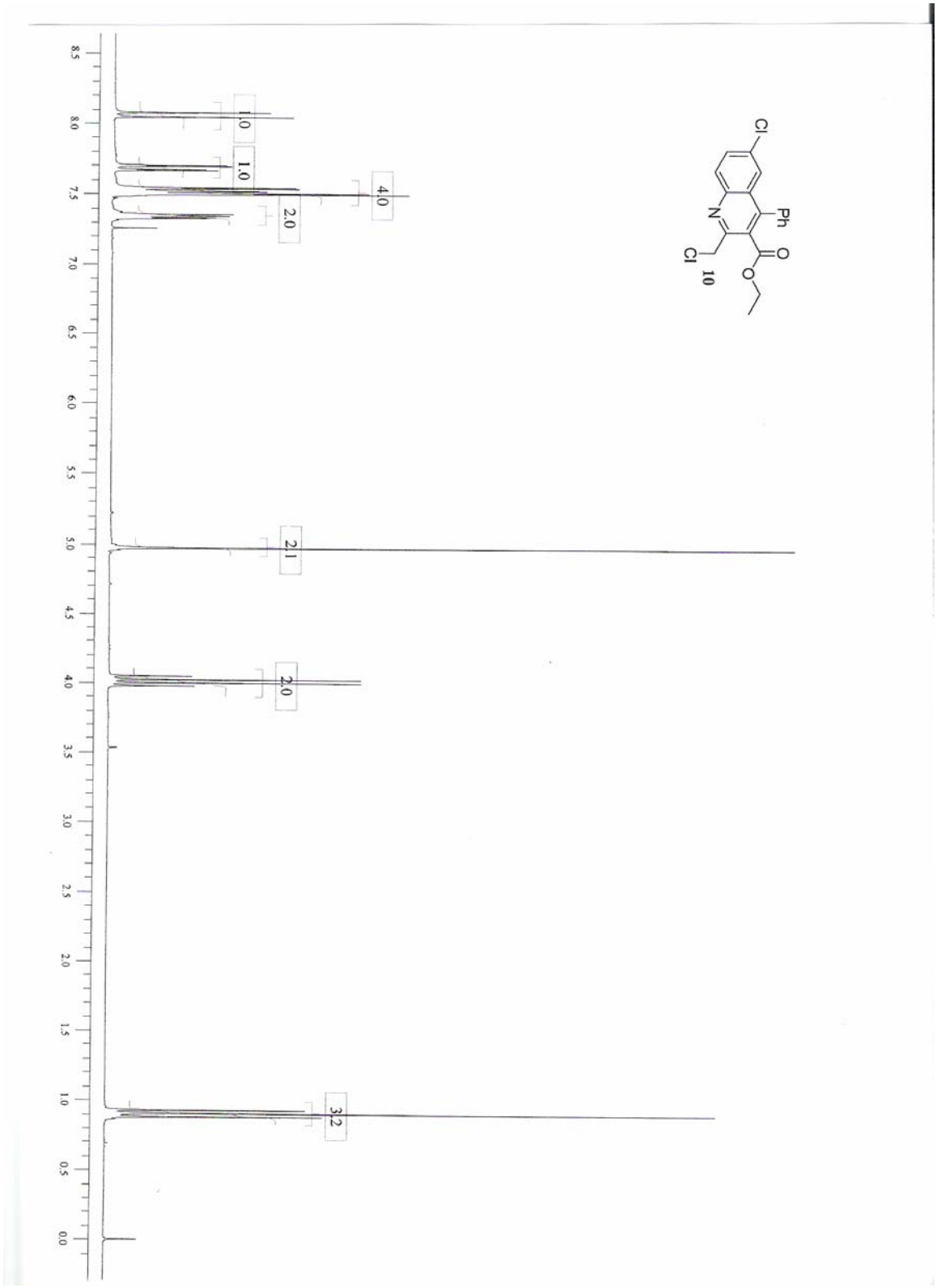

E:\lcms-lab\QUITHIO_418
6/1/2007 7:09:43 PM
MOHD.IDREES,MLP-0010
QUITHIO_418 #41-44 RT: 1.14-1.22 AV: 4 SB: 16 0.02-0.45 SM: 15G NL: 6.06E6
T: + p ESI Full ms [50.00-2000.00]
Cl
S
N
H
CH3
N
CH3
8
Relative Abundance
m/z
403
405
406
407
369
355
372
149
165
192
227
265
279
298
420
482
505
523

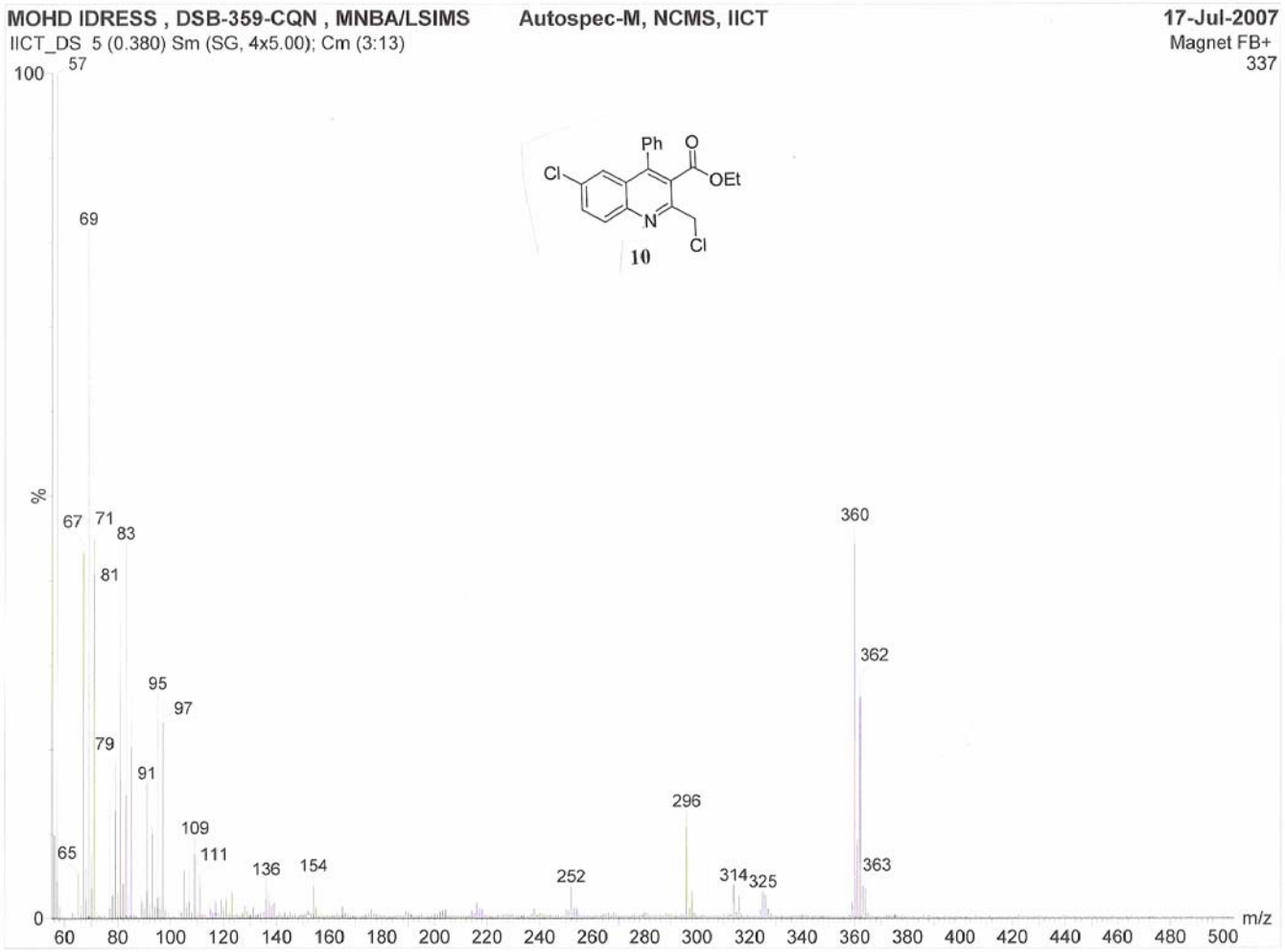


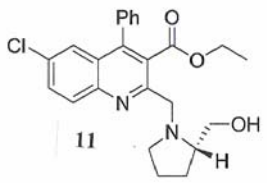
^{1}H NMR SPECTRUM OF COMPOUND 9 IN $CDCl_3$


163.621
157.746
151.037
146.288
147.790
135.509
132.248
128.430
125.504
121.074
122.941
126.357
127.512
127.665
128.189
129.970
130.568
131.160
134.833
136.631
24.678
21.462
Cl
N
CH3
S
N
CH3
9

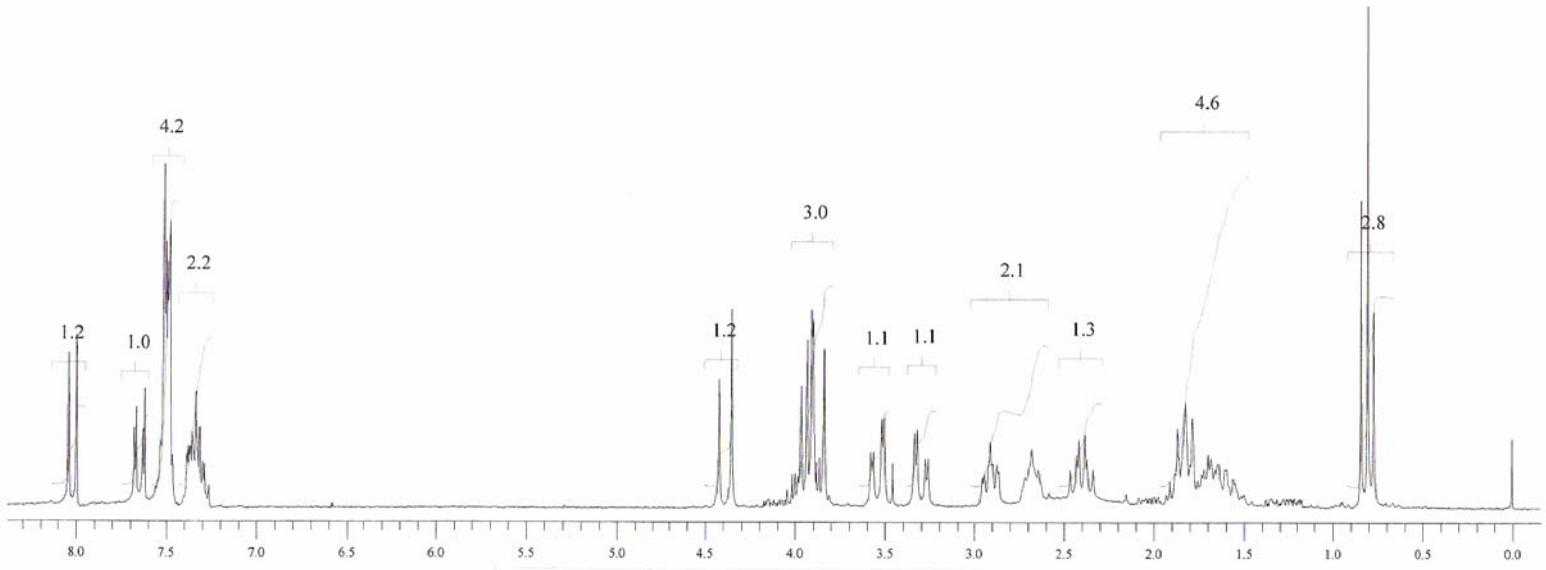

E:\lcms-lab\QUIBT_416
6/1/2007 7:05:53 PM
MOHD.IDREES,MLP-0010
QUIBT_416 #41-44 RT: 1.13-1.21 AV: 4 SB: 16 0.02-0.44 SM: 15G NL: 3.17E6
T: + p ESI Full ms [50.00-2000.00]
Cl
S
N
CH3
N
CH3
9
Relative Abundance
m/z
401
403
404
405
478
157
179
142
181
233
256
292
338
369
433
464
512
537


Cl
Ph
O
N
Cl
10
O
1.0
1.0
4.0
2.0
2.1
2.0
3.2

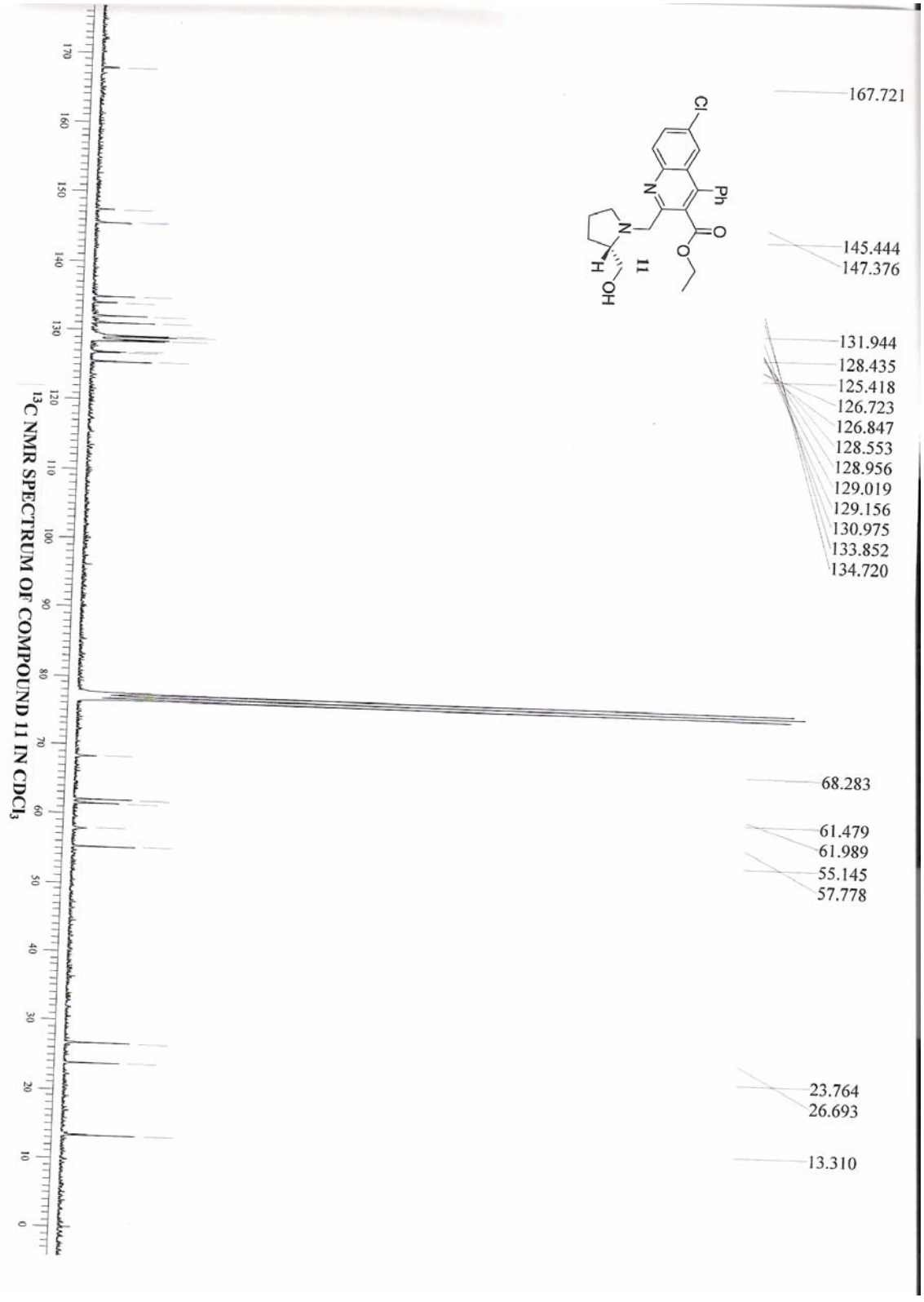

MOHD IDRESS , DSB-359-CQN , MNBA/LSIMS
IICT_DS 5 (0.380) Sm (SG, 4x5.00); Cm (3:13)
Autospec-M, NCMS, IICT
17-Jul-2007
Magnet FB+
337
Ph
O
Cl
OEt
N
Cl
10
100
%
0
57
69
67
71
83
81
95
97
79
91
109
111
65
136
154
252
296
314
325
360
362
363
m/z
60 80 100 120 140 160 180 200 220 240 260 280 300 320 340 360 380 400 420 440 460 480 500

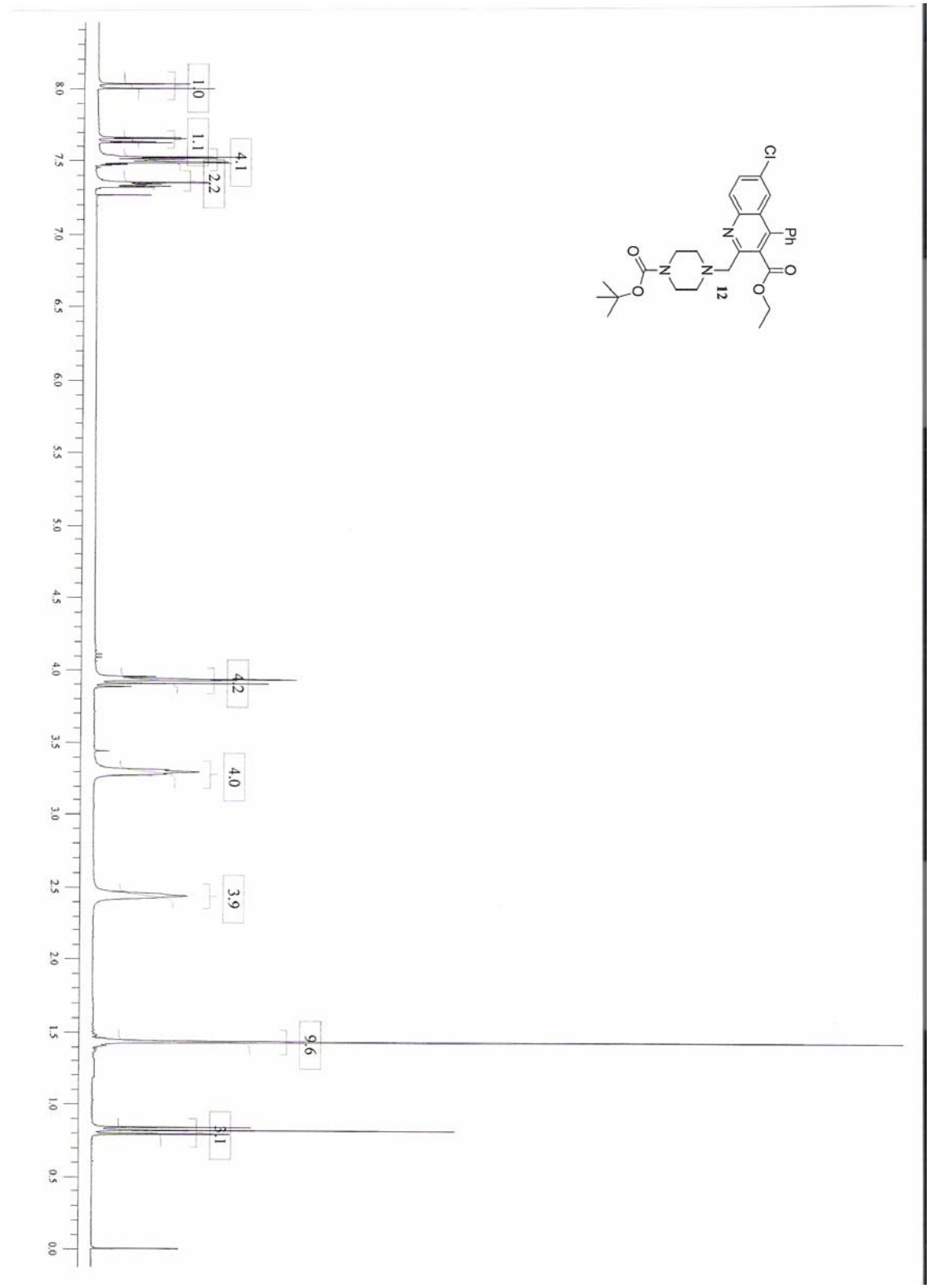


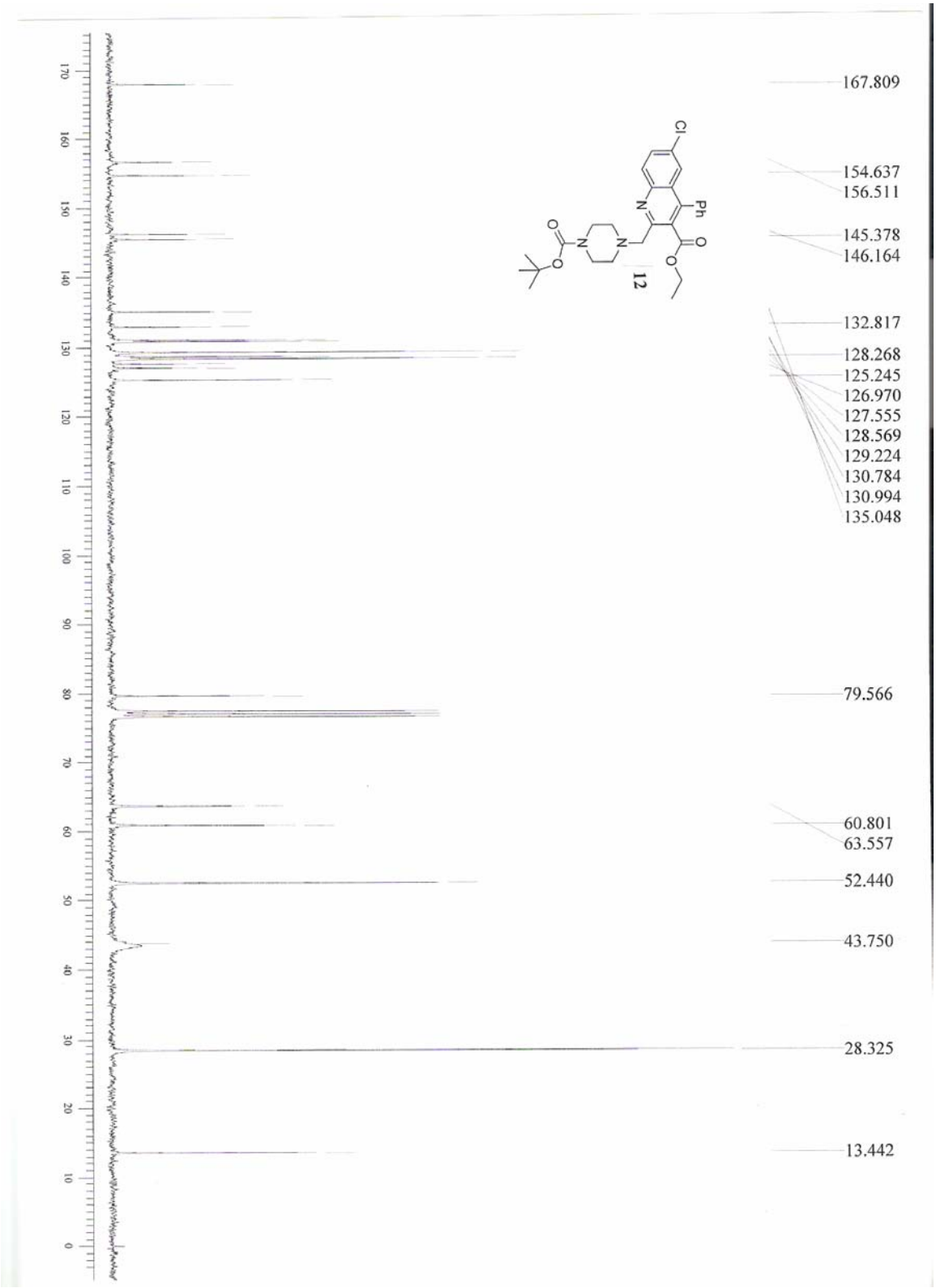
11

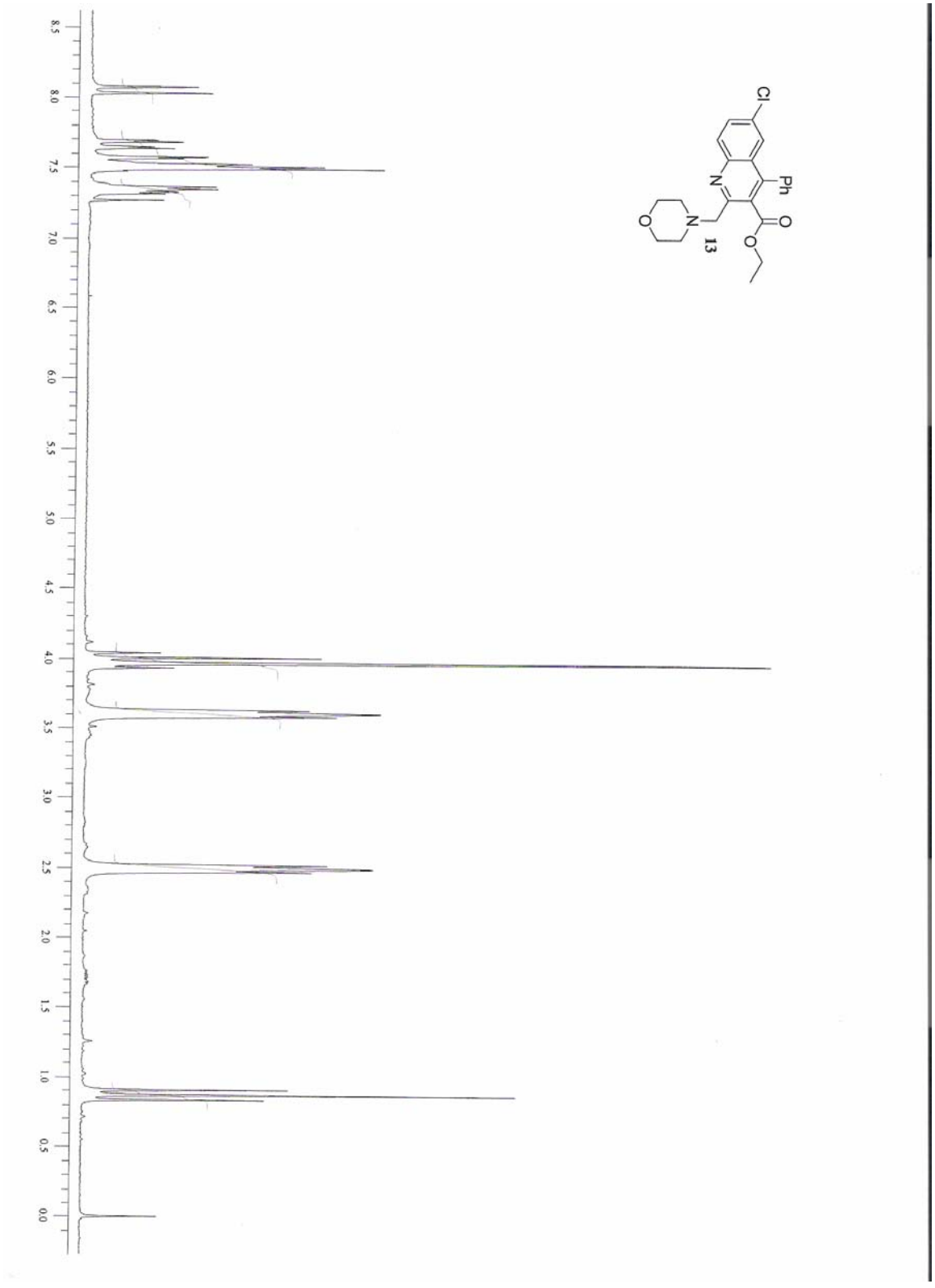


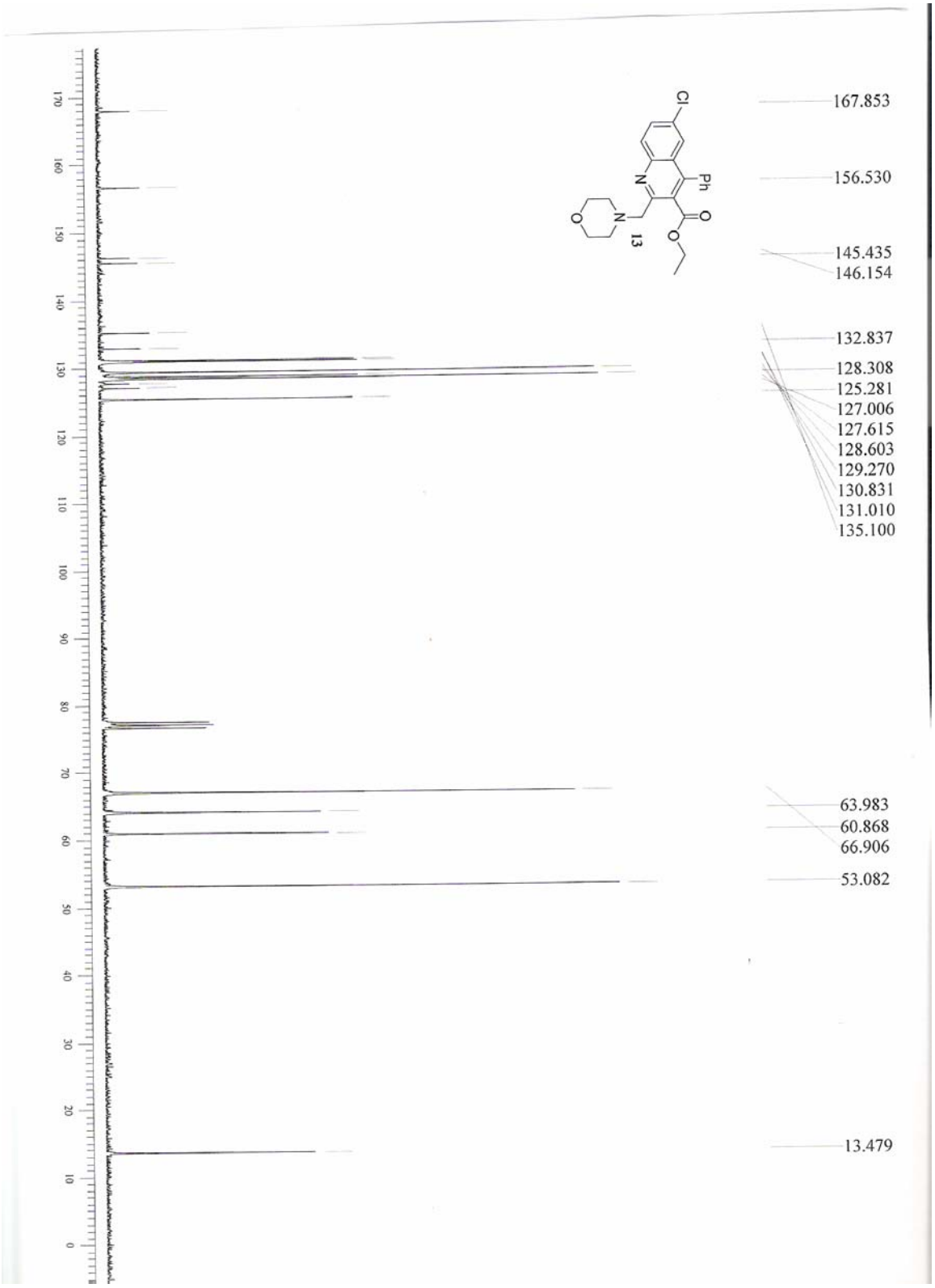
^{1}H NMR SPECTRUM OF COMPOUND 11 IN $CDCl_3$

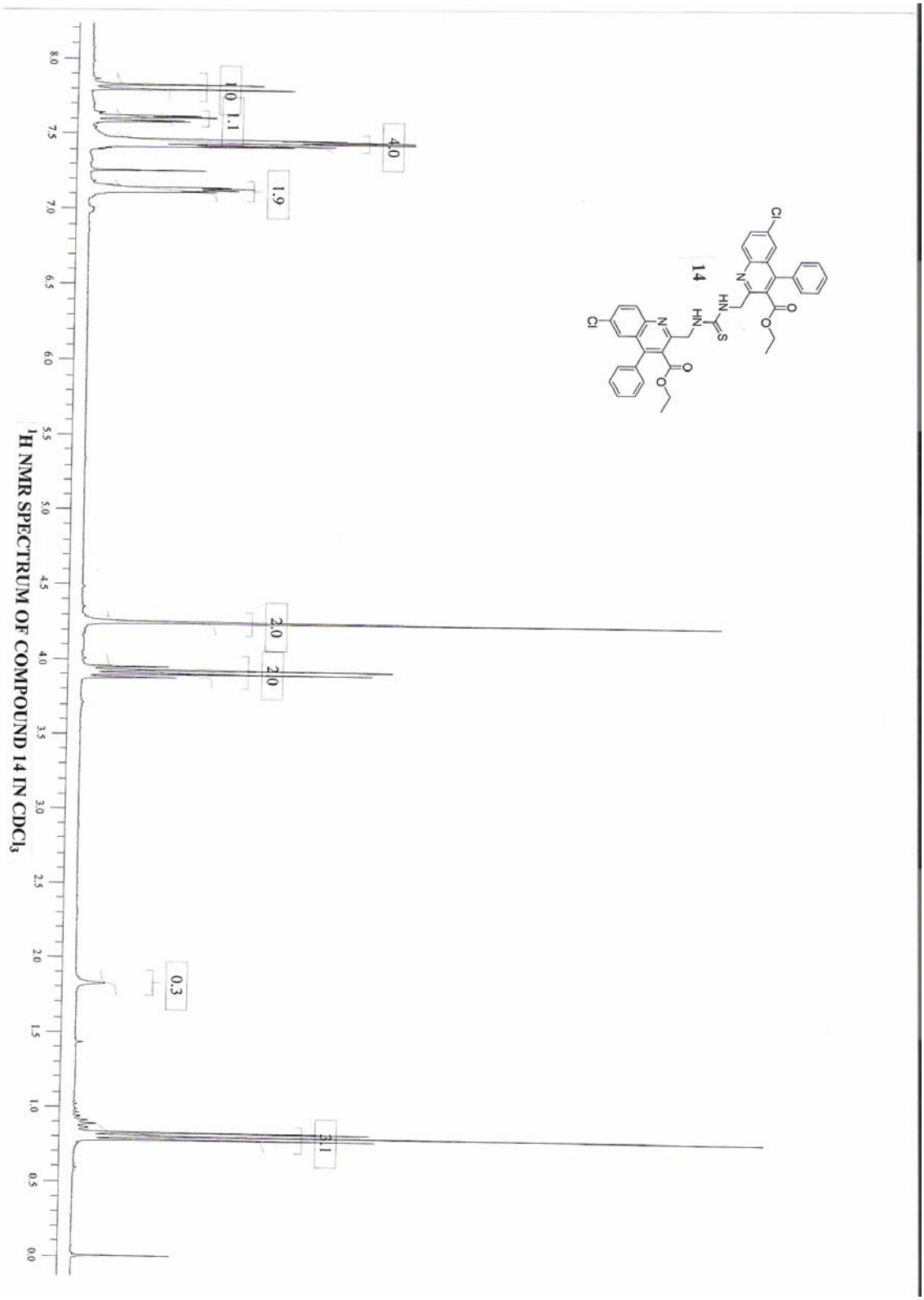

^{13}C NMR SPECTRUM OF COMPOUND 11 IN $CDCl_3$
Cl
Ph
N
N
O
O
H
OH
11
167.721
145.444
147.376
131.944
128.435
125.418
126.723
126.847
128.553
128.956
129.019
129.156
130.975
133.852
134.720
68.283
61.479
61.989
55.145
57.778
23.764
26.693
13.310


Cl
Ph
N
O
O
N
N
O
O
12
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1.0
1.1
2.2
4.1
4.2
4.0
3.9
9.6
3.1

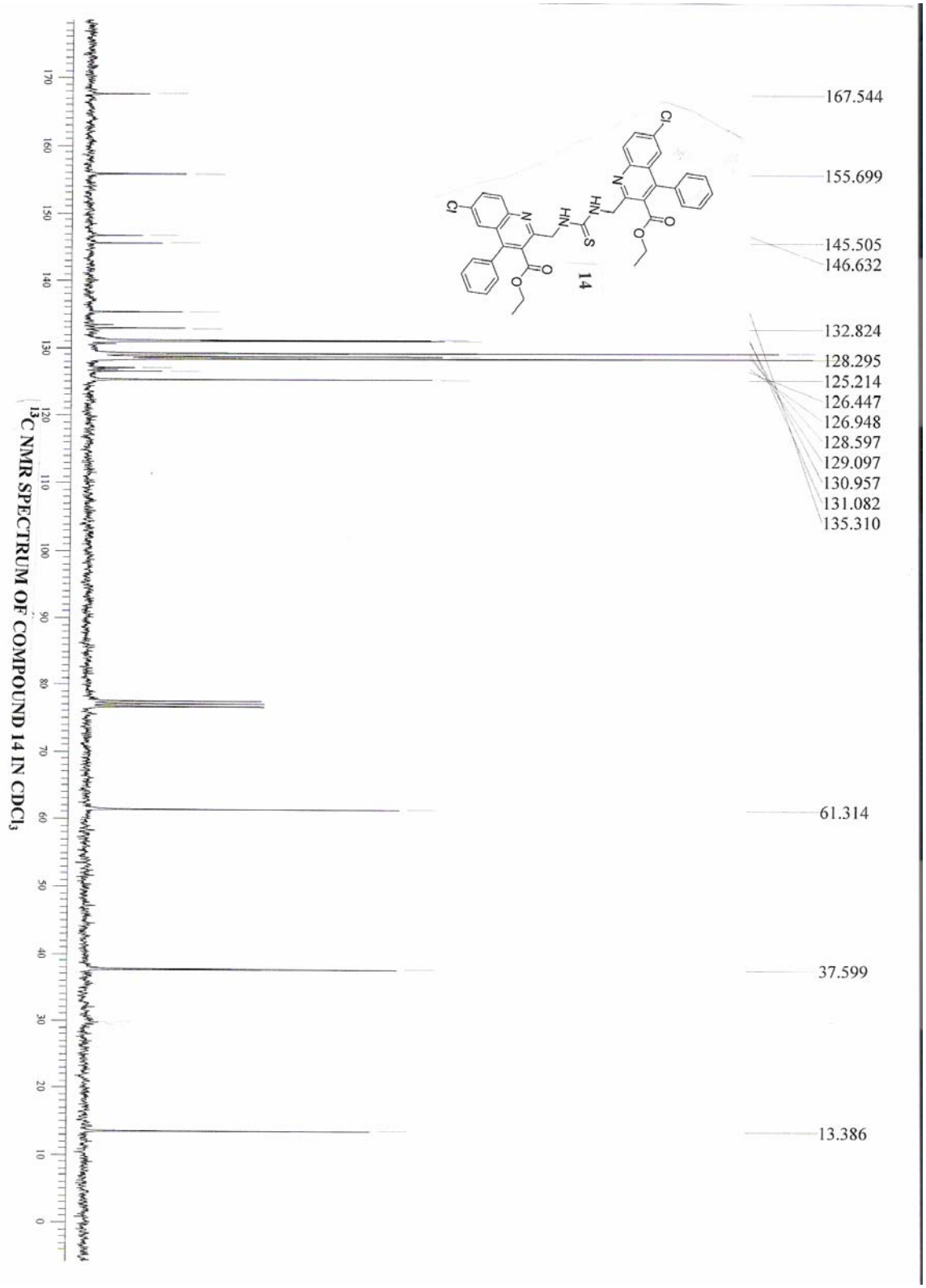

167.809
154.637
156.511
145.378
146.164
132.817
128.268
125.245
126.970
127.555
128.569
129.224
130.784
130.994
135.048
79.566
60.801
63.557
52.440
43.750
28.325
13.442
Cl
Ph
N
O
O
O
12

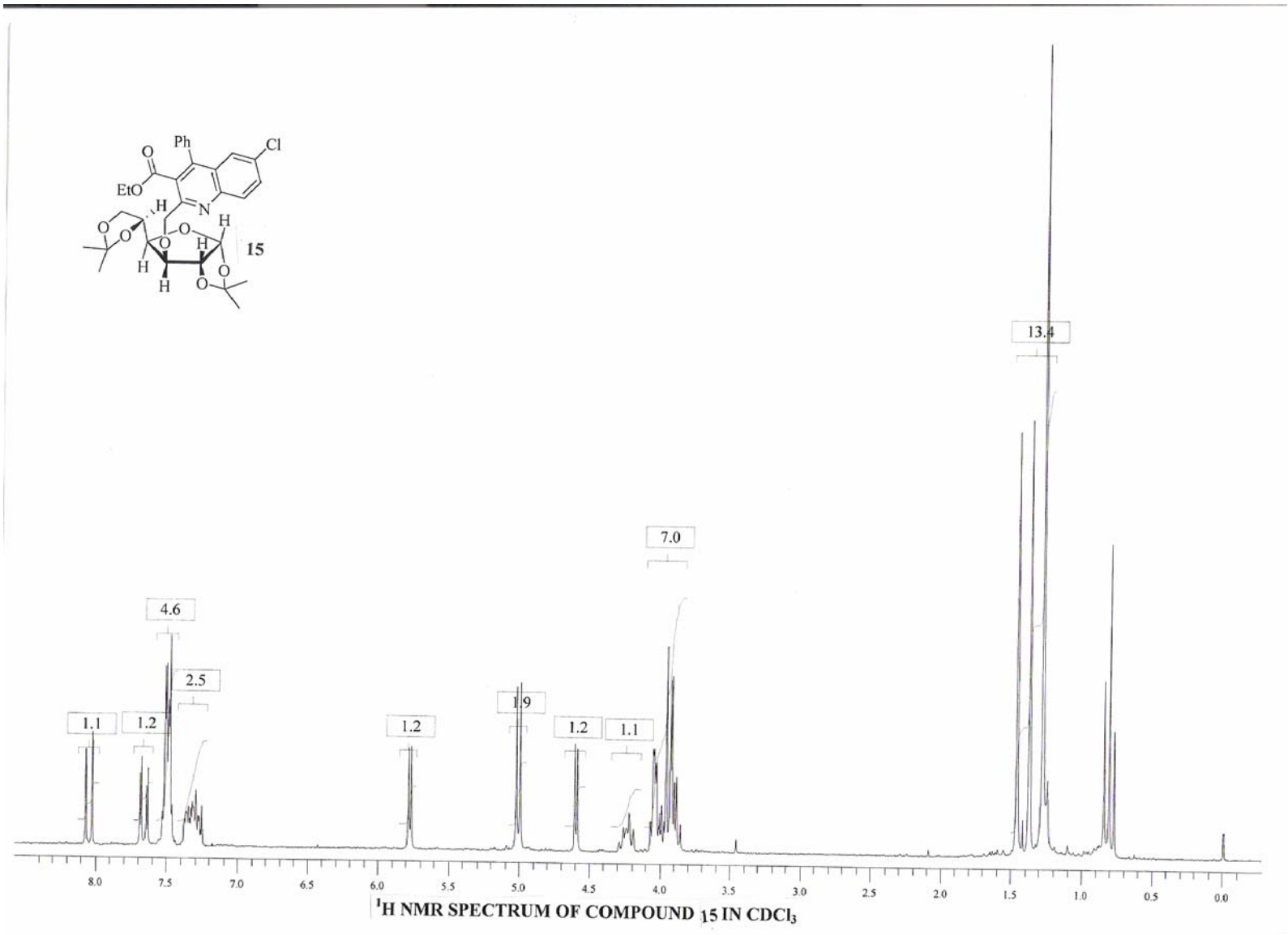

Cl
Ph
O
O
N
N
O
13
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


Cl
Ph
N
O
N
O
13
167.853
156.530
145.435
146.154
132.837
128.308
125.281
127.006
127.615
128.603
129.270
130.831
131.010
135.100
63.983
60.868
66.906
53.082
13.479

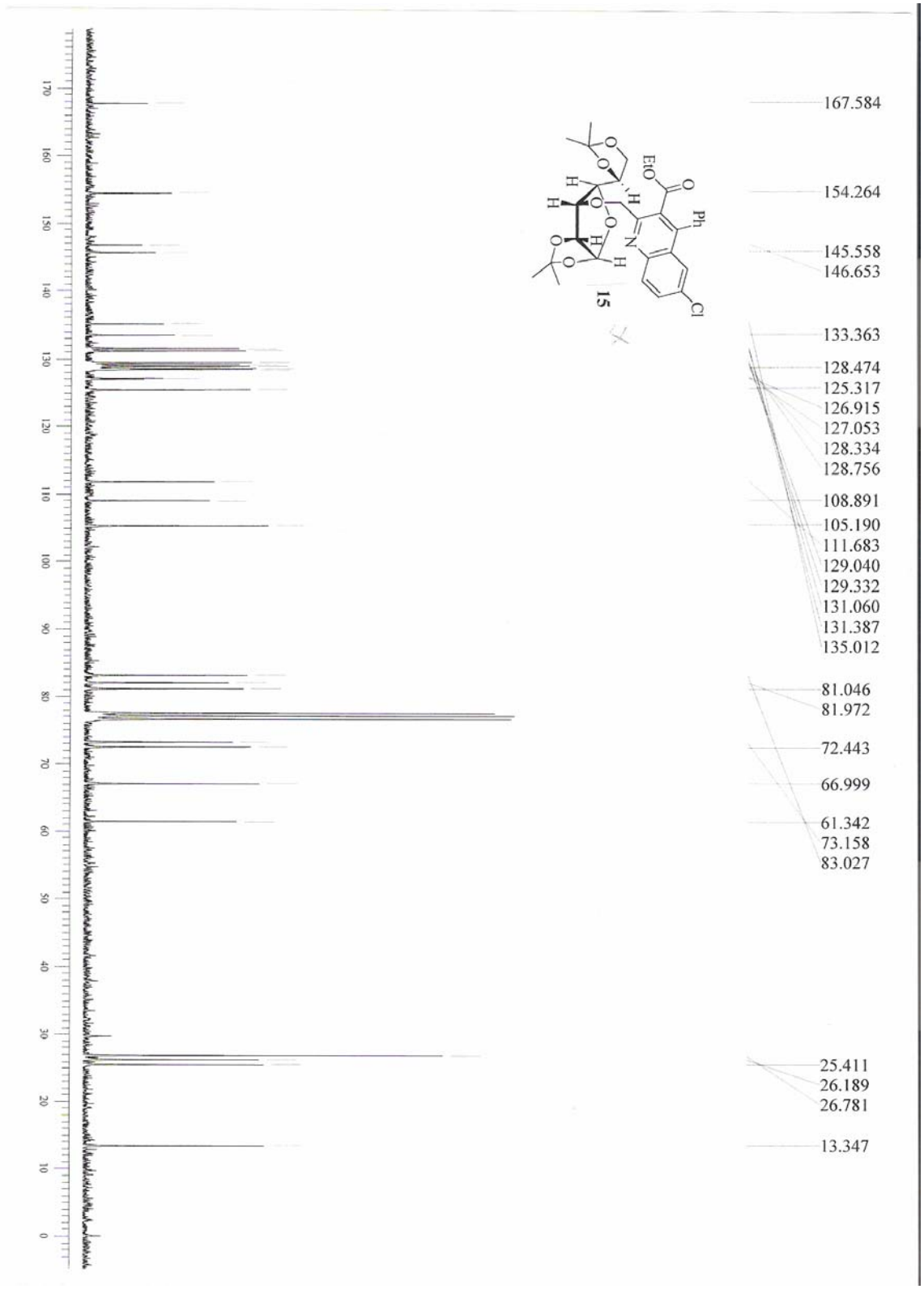


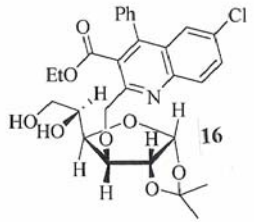
^{1}H NMR SPECTRUM OF COMPOUND 14 IN $CDCl_3$

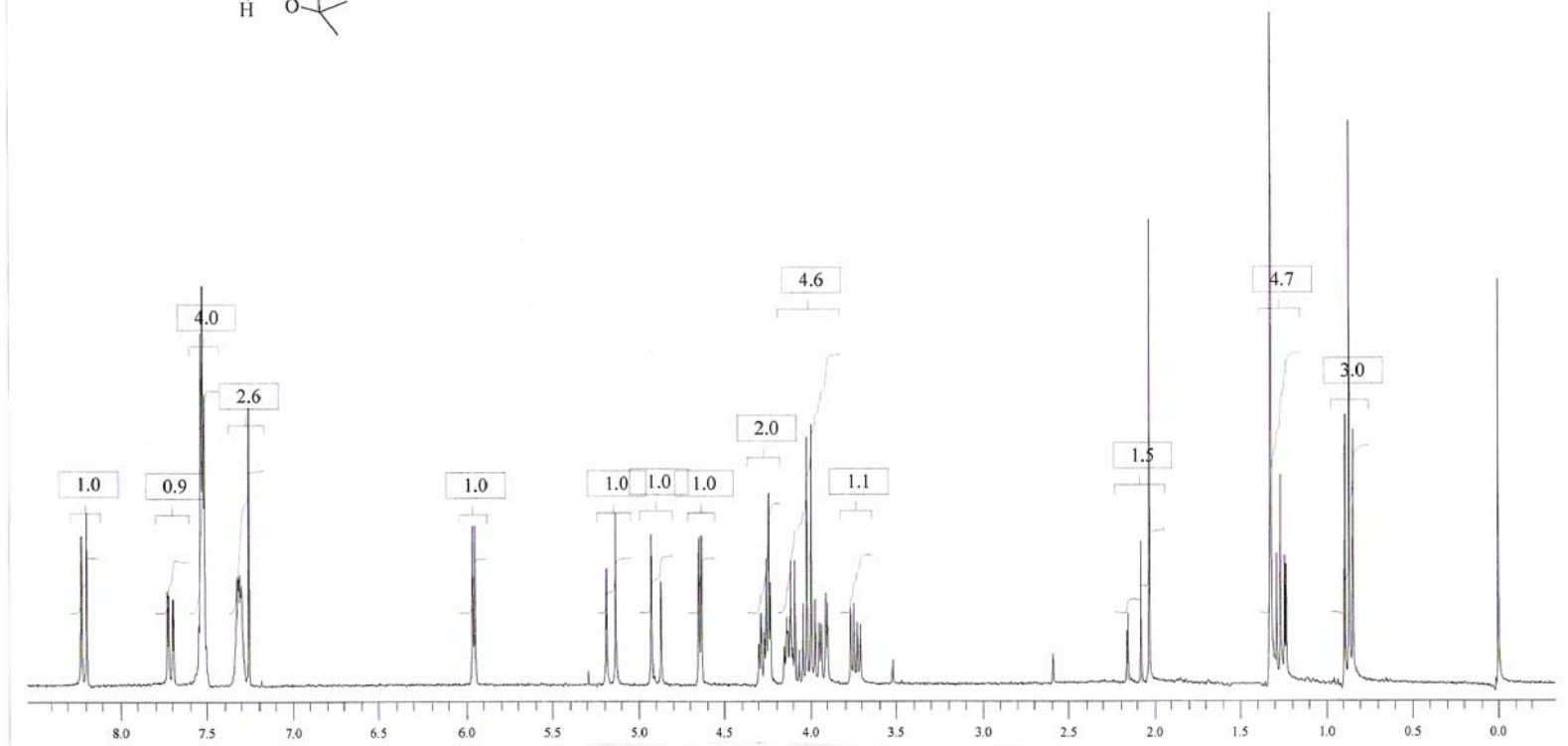

167.544
155.699
145.505
146.632
132.824
128.295
125.214
126.447
126.948
128.597
129.097
130.957
131.082
135.310
61.314
37.599
13.386
14
^{13}C NMR SPECTRUM OF COMPOUND 14 IN $CDCl_3$



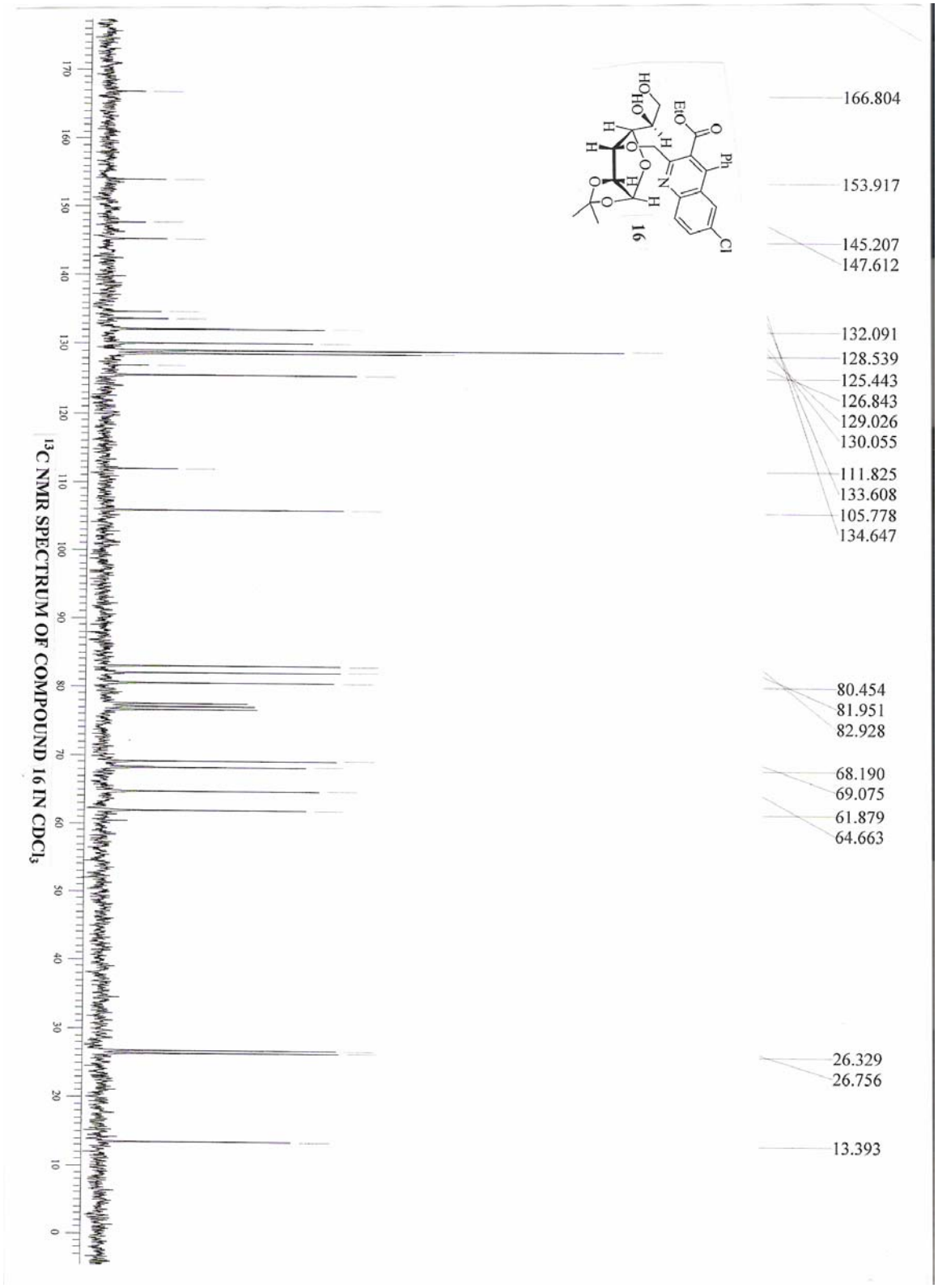
^{1}H NMR SPECTRUM OF COMPOUND 15 IN $CDCl_3$

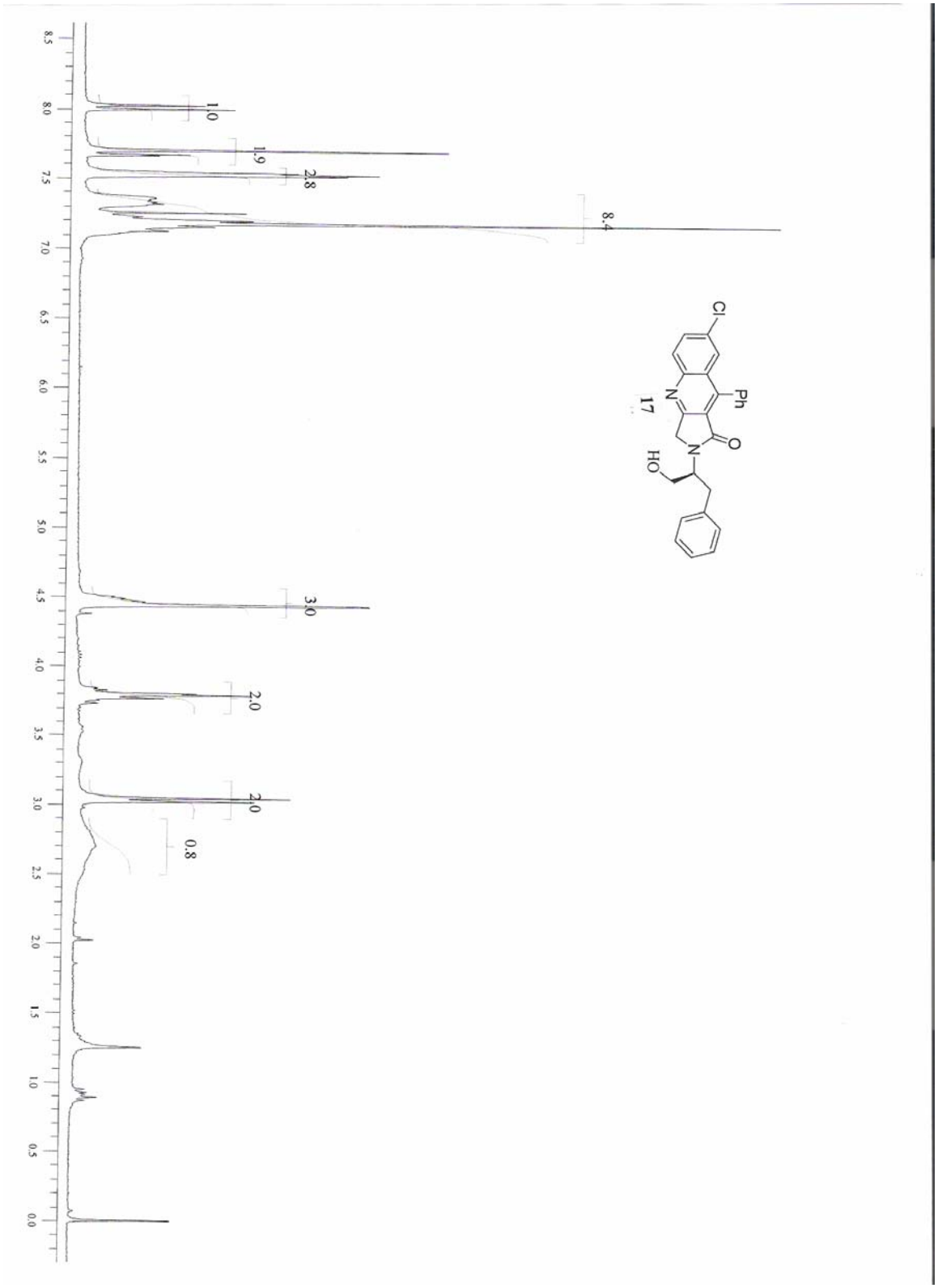

167.584
154.264
145.558
146.653
133.363
128.474
125.317
126.915
127.053
128.334
128.756
108.891
105.190
111.683
129.040
129.332
131.060
131.387
135.012
81.046
81.972
72.443
66.999
61.342
73.158
83.027
25.411
26.189
26.781
13.347
15

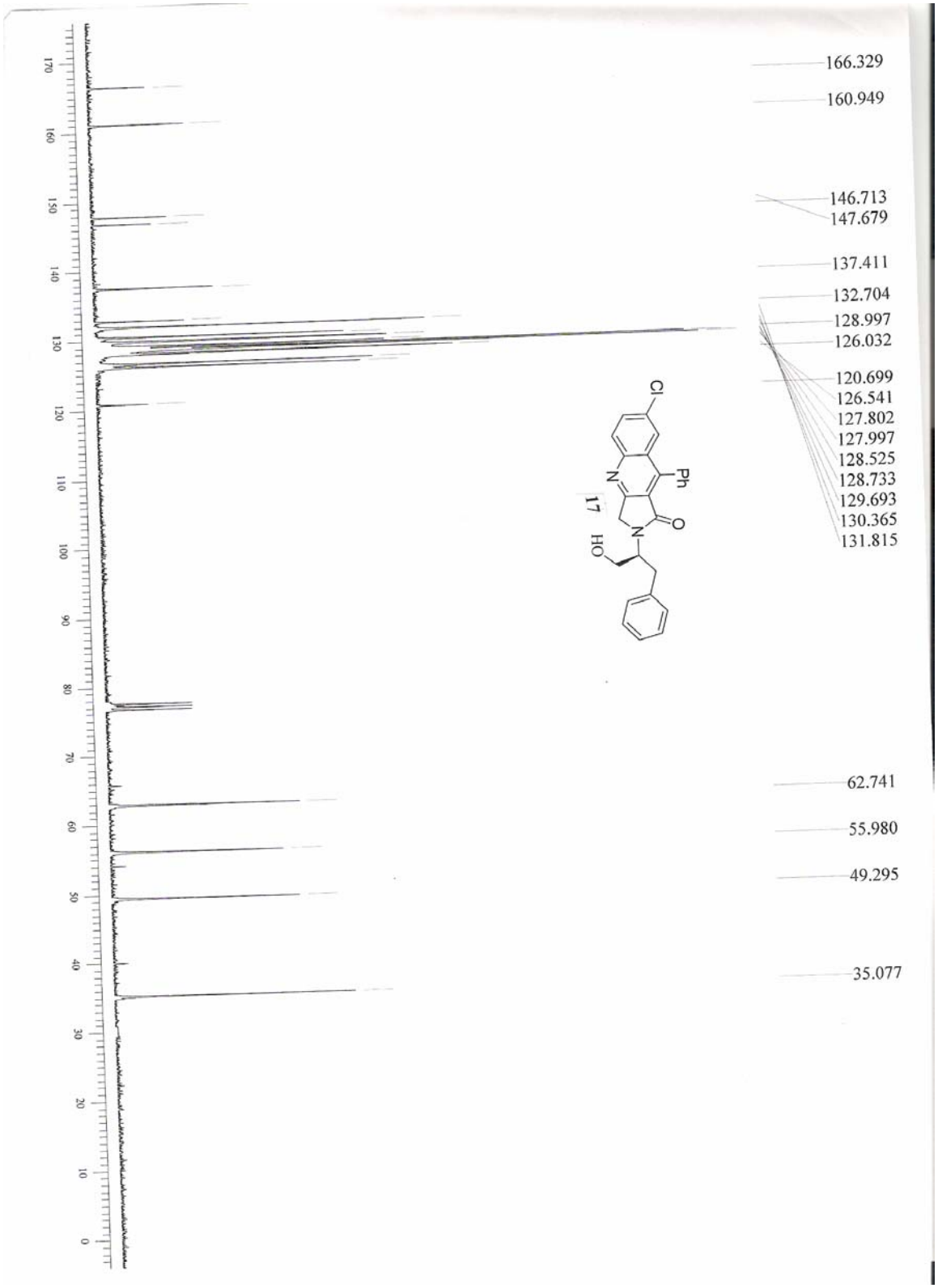


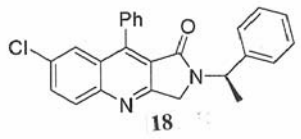


^{1}H NMR SPECTRUM OF COMPOUND 16 IN $CDCl_3$

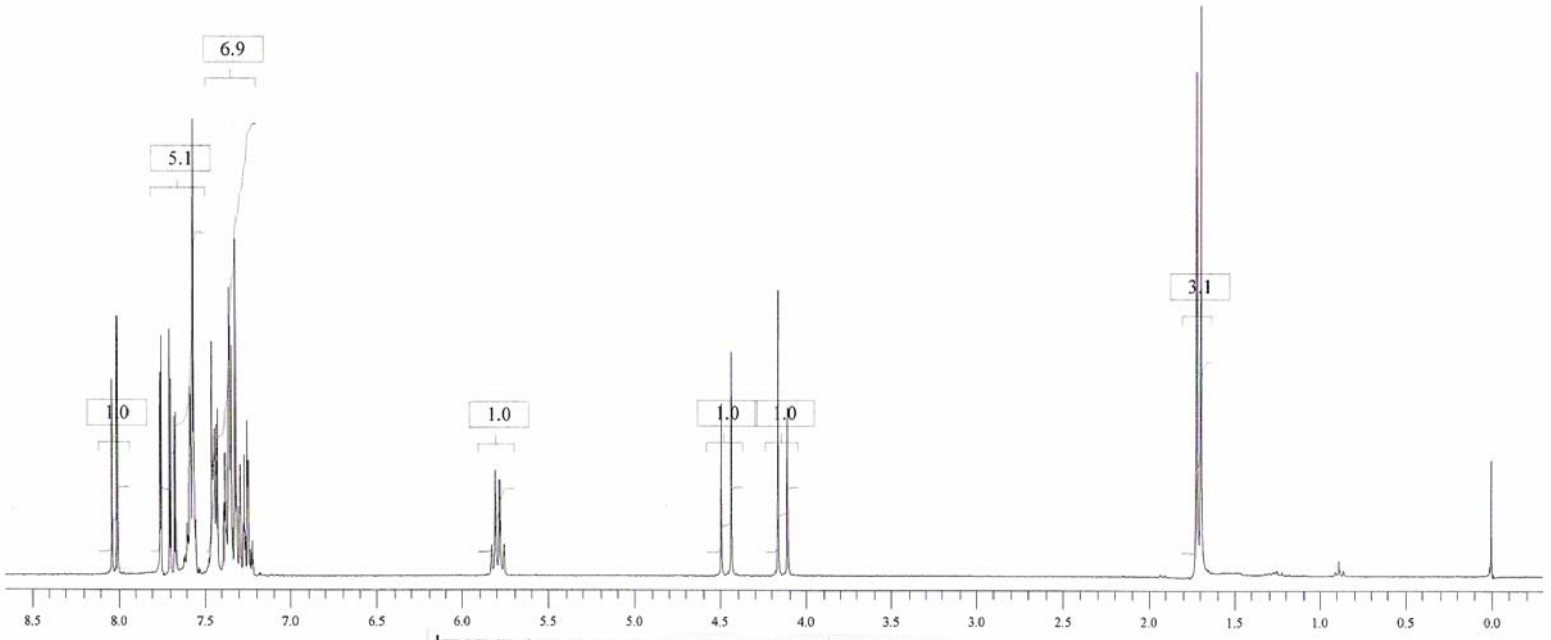

166.804
153.917
145.207
147.612
132.091
128.539
125.443
126.843
129.026
130.055
111.825
133.608
105.778
134.647
80.454
81.951
82.928
68.190
69.075
61.879
64.663
26.329
26.756
13.393
16
^{13}C NMR SPECTRUM OF COMPOUND 16 IN $CDCl_3$


Cl
Ph
O
N
N
HO
17
1.0
1.9
2.8
8.4
3.0
2.0
2.0
0.8

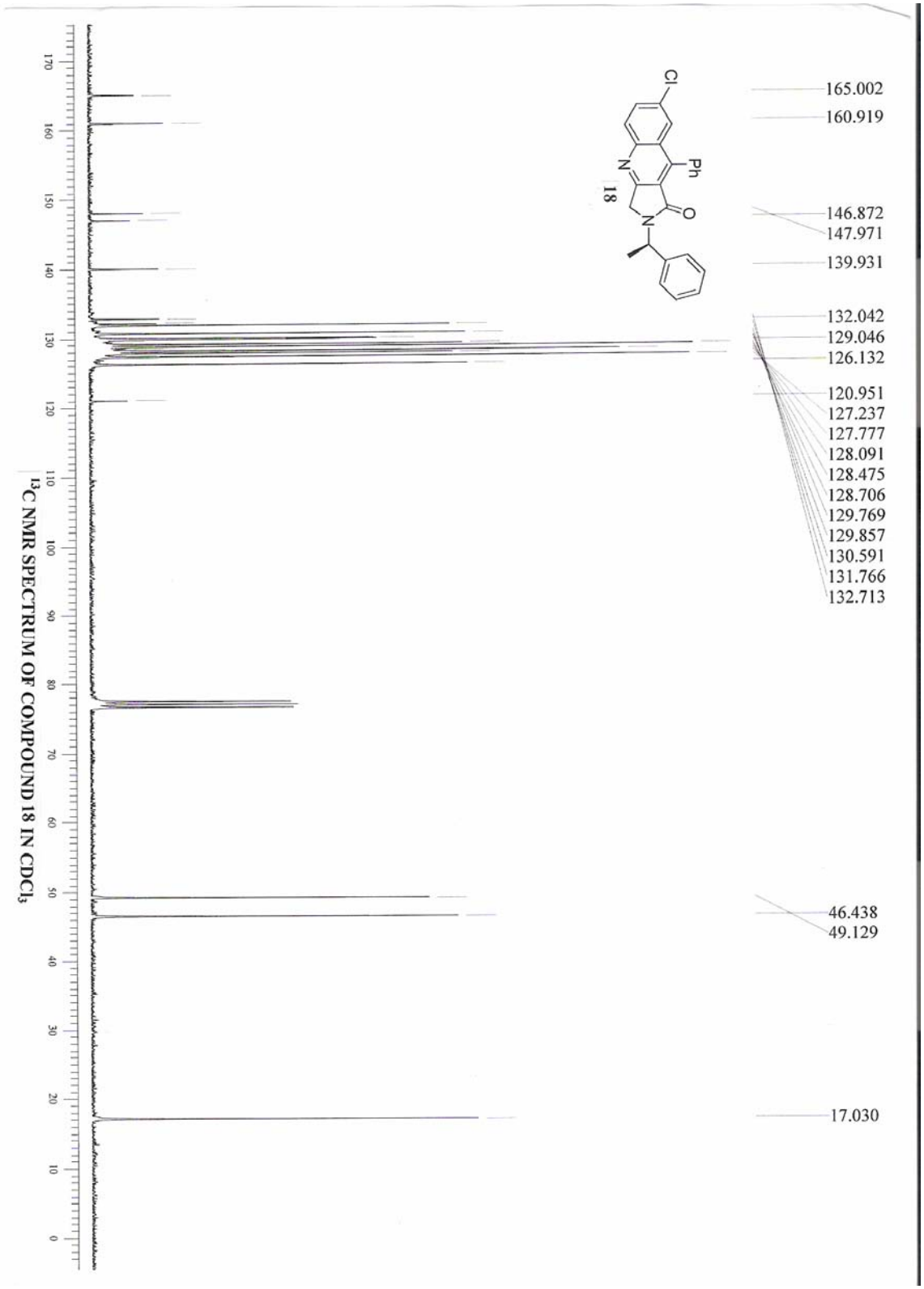

166.329
160.949
146.713
147.679
137.411
132.704
128.997
126.032
120.699
126.541
127.802
127.997
128.525
128.733
129.693
130.365
131.815
62.741
55.980
49.295
35.077
Cl
Ph
O
N
N
HO
17



18



^{1}H NMR SPECTRUM OF COMPOUND 18 IN $CDCl_3$



^{13}C NMR SPECTRUM OF COMPOUND 18 IN $CDCl_3$