

Supporting Information

Visible light as a sole requirement for alkylation of α -C(sp³)-H of *N*-aryltetrahydroisoquinolines with alkylboronic acids

Feihu Cong,^a Wenjing Zhang,^a Gan Zhang,^a Jie Liu,^{*a} Yicheng Zhang,^a

Chao Zhou,^{*a} and Lei Wang^{a,b}

a. Key Laboratory of Green and Precise Synthetic Chemistry and Applications, Ministry of Education; Department of chemistry, Huaibei Normal University, Huaibei, Anhui 235000, P. R. China

b. College of Material Chemistry and Chemical Engineering, Key Laboratory of Organosilicon Chemistry and Material Technology, Ministry of Education, Hangzhou Normal University,

Hangzhou 311121, Zhejiang, P. R. China

E-mail: jieliu_1024@163.com, zhouch110@163.com

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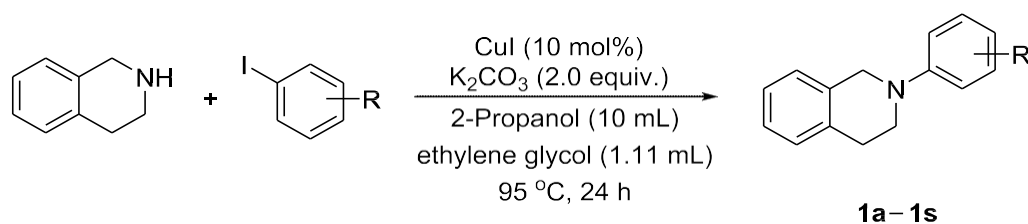
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1. General Information

All materials were obtained from commercial suppliers or prepared according to standard procedure unless otherwise noted. Solvents were purified and dried according to standard methods prior to use. For product purification by flash column chromatography, silica gel (200~300 mesh) and light petroleum ether (bp. 60~90) are used. All ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a 600 MHz Bruker FT-NMR spectrometer (600 MHz or 150 MHz or 565 MHz, respectively). All chemical shifts of ^1H NMR are given as δ value (ppm) with reference to tetramethylsilane (TMS) as an internal standard. The peak patterns are indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet) and td (triplet of doublet) The coupling constants, J , are reported in Hertz (Hz). High resolution mass spectroscopy data of the products were collected on a Thermo Scientific Q Exactive and Agilent Technologies 6540 UHD Accurate-Mass Q-TOF LC/MS (ESI).

2. Experimental Section

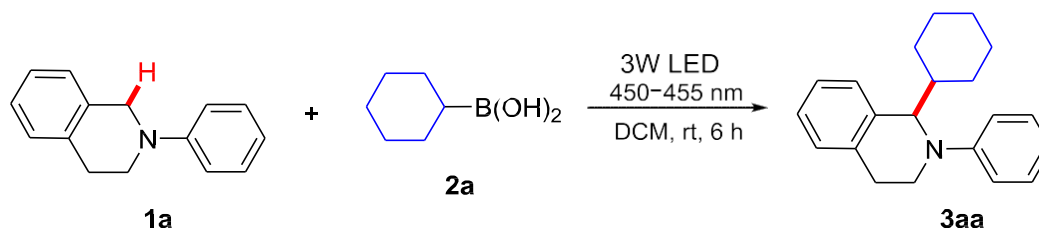
2.1 Typical procedure for the preparation of **1a–1s**



The substrates **1a–1s** were synthesized according to literature procedure.^[1] A typical procedure is described as following for the synthesis of **1a**: Copper(I) iodide (200 mg, 1.0 mmol) and potassium carbonate (2.76 g, 20.0 mmol) were added to a Schlenk tube. The tube was evacuated and back filled with nitrogen. 2-Propanol (10.0 mL), ethylene glycol (1.11 mL, 20.0 mmol), 1,2,3,4-tetrahydroisoquinoline (1.60 g,

12 mmol) and iodobenzene (1.11 mL, 10.0 mmol) were added successively via a micro-syringe at room temperature. The reaction mixture was heated at 95~100 °C and kept for 24 h and then allowed to cool to room temperature. Diethyl ether (20 mL) and water (20 mL) were then added. The aqueous layer was extracted by diethyl ether (2×20 mL). The combined organic phases were washed with brine, dried over anhydrous sodium sulfate and concentrated in vacuo. The residue was purified by flash column chromatography with mixed petroleum ether and ethyl acetate (petroleum ether/ethyl acetate = 98/2) to give the compound **1a** as a yellow solid (1.78 g, 85 % yield).

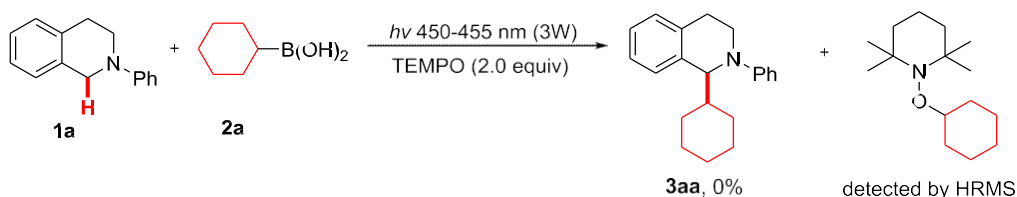
2.2 Representative procedure for the photoreaction of **1a** and **2a** to **3aa**



A 10 mL oven-dried reaction vessel equipped with a magnetic stirrer bar was charged with 2-phenyl-1,2,3,4-tetrahydroisoquinoline (**1a**, 0.20 mmol), cyclohexylboronic acid (**2a**, 0.40 mmol), and DCM (2.5 mL). The reaction mixture was exposed to blue LED (450–455 nm, 3 W) irradiation at room temperature with stirring for 6 h. The mixture was evaporated to dryness in vacuo and the residue was separated on a silica gel column with mixed petroleum ether and ethyl acetate (petroleum ether/ethyl acetate = 20: 1) as eluent to afford the desired products **3aa** as a yellow liquid (45.4 mg, 78% yield).

3. Preliminary Mechanistic Study

3.1 Free radical experiments



N-Phenyltetrahydroisoquinoline (**1a**, 0.2 mmol) with cyclohexylboronic acid (**2a**, 0.2 mmol), TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy, 0.40 mmol, 2.0 equiv.) were added to a Schlenk tube successively, which containing a magnetic stirring bar, then DCM (2.0 mL) was added via syringe. The reaction mixture was stirred for 6 hours under 3 W blue LED (450–455 nm) irradiation at room temperature. No corresponding product **3aa** was detected, the compound formed by **2a** and TEMPO was detected through HRMS (Figure S1), indicating that a radical pathway was involved in the reaction.

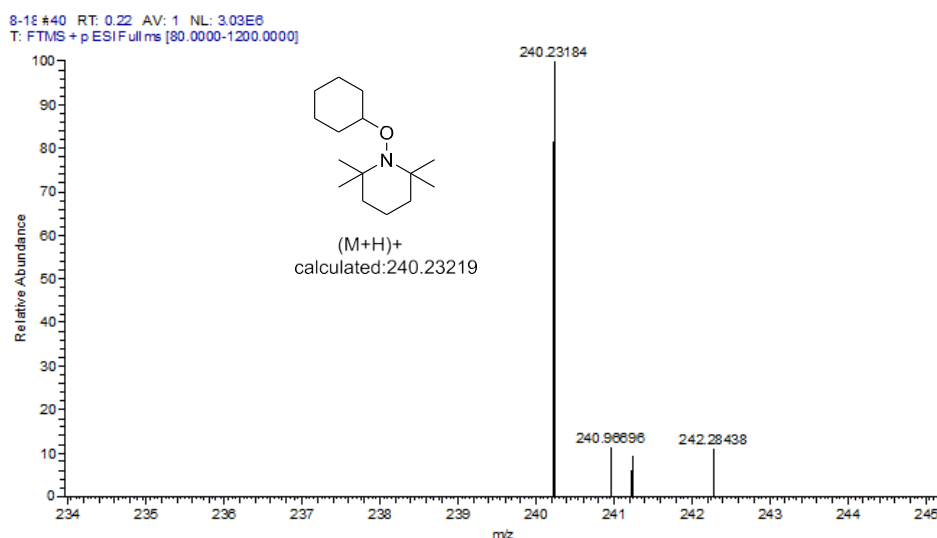


Figure S1. HRMS analysis of the compound formed by **2a** and TEMPO

3.2 UV/Vis absorption spectra

The UV/Vis absorption spectra of 2-phenyl-1,2,3,4-tetrahydroisoquinoline (**1a**, 0.03 mol/L), cyclohexylboronic acid (**2a**, 0.03 mol/L), and a mixture of **1a/2a** (1:1, 0.03 mol/L) in DCM were recorded in 1.0 cm path quartz cuvettes by using a SHIMADZU UV-2700i spectrometer, respectively. The obtained charge-transfer bands in UV/vis absorption spectra were shown in Figure S2.

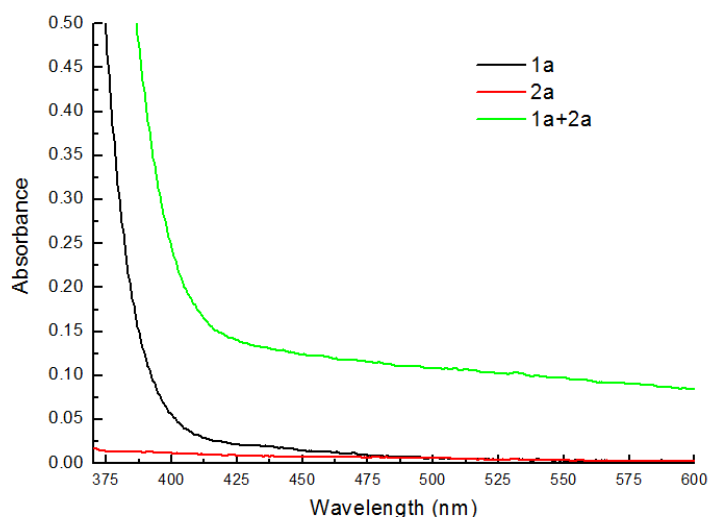


Figure S2. UV/Vis absorption spectra of **1a**, **2a** and a mixture of **1a/2a**

3.3 Determination of singlet oxygen species

For further exploration of the active species of singlet oxygen involved in the reaction, a general recommended reagent, 2,2,6,6-tetramethylpiperidine (TEMP) was used to trap $^1\text{O}_2$. When air-saturated DCM solution of *N*-phenyltetrahydroisoquinoline (**1a**) and cyclohexylboronic acid (**2a**), with TEMP under the irradiation of LED (450–455 nm, 3.0 W) resulted in the formation of a characteristic signal $^1\text{O}_2$ adduct with TEMP (Figure S3). The characteristic signal of $^1\text{O}_2$ was recorded by an EPR instrument (Figure S3), implying that $^1\text{O}_2$ was formed during the reaction.

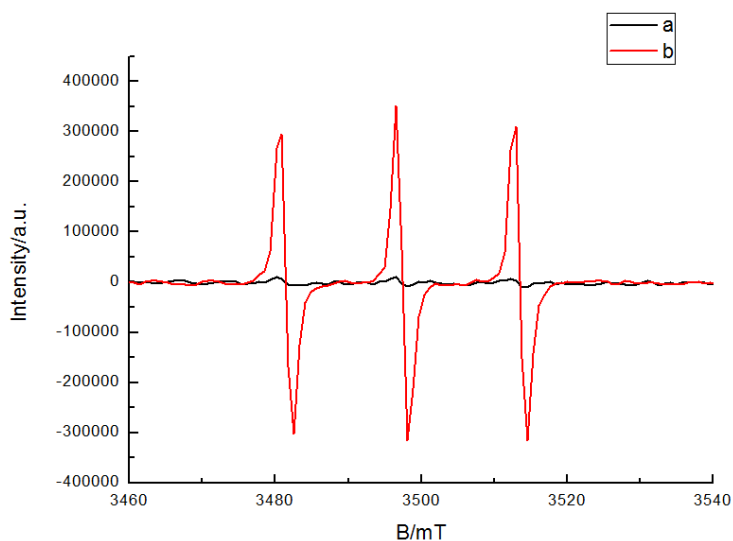
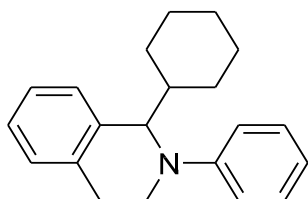


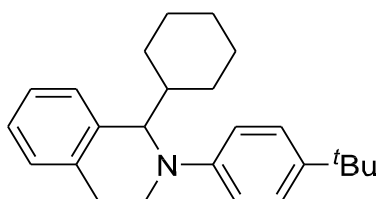
Figure S3. Electron spin resonance (ESR) spectra of characteristic signal of $^1\text{O}_2$ formed during the reaction

- (a) A solution of TEMP (0.2 mol/L) with *N*-phenyltetrahydroisoquinoline (**1a**) and cyclohexylboronic acid (**2a**) in air-saturated DCM without light irradiation
- (b) A solution of TEMP (0.2 mol/L) with *N*-phenyltetrahydroisoquinoline (**1a**) and cyclohexylboronic acid (**2a**) in air-saturated DME under LED (450–455 nm) irradiation for 10 s

4. Characterization Data for the Products

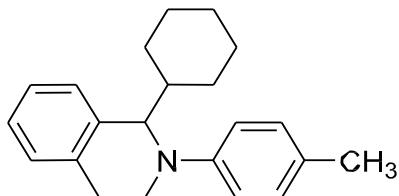


1-Cyclohexyl-2-phenyl-1,2,3,4-tetrahydroisoquinoline (3aa). Light yellow liquid, 45.4 mg, 78% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.22–7.19 (m, 2H), 7.15–7.10 (m, 3H), 7.06 (d, $J = 7.8$ Hz, 1H), 6.85 (d, $J = 7.8$ Hz, 2H), 6.66 (t, $J = 7.2$ Hz, 1H), 4.41 (d, $J = 8.4$ Hz, 1H), 3.73–3.69 (m, 1H), 3.47–3.43 (m, 1H), 3.03–2.94 (m, 2H), 1.97 (d, $J = 13.8$ Hz, 1H), 1.75–1.69 (m, 4H), 1.63–1.60 (m, 1H), 1.20–1.04 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 150.0, 137.9, 135.3, 129.2, 128.4, 128.2, 126.6, 125.2, 116.3, 113.0, 63.8, 44.1, 43.0, 31.0, 30.7, 27.4, 26.7, 26.5, 26.5. HRMS (ESI, m/z) [$\text{M} + \text{H}$] $^+$ Calcd. for $[\text{C}_{21}\text{H}_{26}\text{N}]^+$: 292.2060, found: 292.2055.

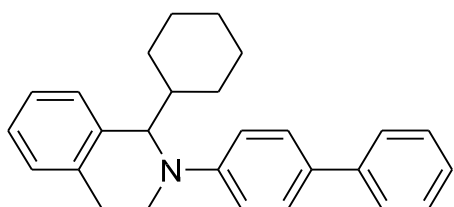


2-(4-(*tert*-Butyl)phenyl)-1-cyclohexyl-1,2,3,4-tetrahydroisoquinoline (3ba). Light yellow liquid, 48.6 mg, 70% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.25–7.22 (m, 2H), 7.14–7.07 (m, 3H), 7.05–7.02 (m, 1H), 6.81–6.78 (m, 2H), 4.37 (d, $J = 5.4$ Hz, 1H), 3.73–3.68 (m, 1H), 3.46–3.40 (m, 1H), 2.98–2.94 (m, 2H), 2.00 (d, $J = 11.4$ Hz, 1H), 1.77–1.68 (m, 4H), 1.61 (d, $J = 7.8$ Hz, 1H), 1.27 (s, 9H), 1.20–1.03 (m, 5H). ^{13}C

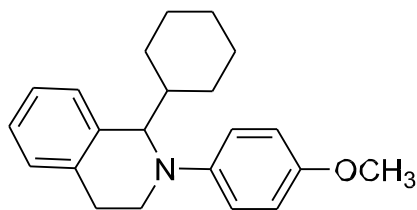
NMR (150 MHz, CDCl₃) δ : 147.8, 138.9, 137.9, 135.5, 128.4, 128.2, 126.5, 125.9, 125.1, 112.7, 64.1, 44.2, 43.1, 33.7, 31.6, 31.0, 30.6, 27.4, 26.8, 26.5, 26.5. HRMS (ESI, m/z) [M + H]⁺ Calcd. for [C₂₅H₃₄N]⁺: 348.2686, found: 348.2689.



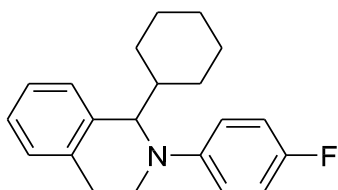
1-Cyclohexyl-2-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinoline (3ca). Light yellow liquid, 50.7 mg, 83% yield. ¹H NMR (600 MHz, CDCl₃) δ : 7.14–7.08 (m, 3H), 7.06–7.04 (m, 1H), 7.01 (d, J = 8.4 Hz, 2H), 6.76 (d, J = 9.0 Hz, 2H), 4.34 (d, J = 7.8 Hz, 1H), 3.71–3.67 (m, 1H), 3.46–3.42 (m, 1H), 2.95 (t, J = 6.6 Hz, 2H), 2.22 (s, 3H), 1.99–1.96 (m, 1H), 1.75–1.68 (m, 4H), 1.62–1.60 (m, 1H), 1.18–1.01 (m, 5H). ¹³C NMR (150 MHz, CDCl₃) δ : 148.1, 137.9, 135.4, 129.7, 128.5, 128.3, 126.5, 125.6, 125.1, 113.4, 64.0, 44.2, 43.1, 31.0, 30.8, 27.3, 26.7, 26.5, 20.3. HRMS (ESI, m/z) [M + H]⁺ Calcd. for [C₂₂H₂₈N]⁺: 306.2216, found: 306.2211.



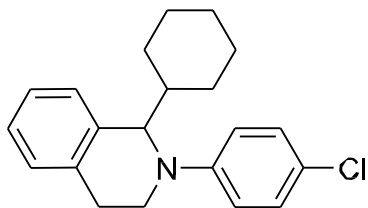
2-([1,1'-Biphenyl]-4-yl)-1-cyclohexyl-1,2,3,4-tetrahydroisoquinoline (3da). Light yellow liquid, 52.9 mg, 72% yield. ¹H NMR (600 MHz, CDCl₃) δ : 7.53 (dd, J = 8.4, 1.2 Hz, 2H), 7.48 (d, J = 9.0 Hz, 2H), 7.37 (t, J = 7.8 Hz, 2H), 7.24–7.23 (m, 1H), 7.18–7.12 (m, 3H), 7.08 (d, J = 8.4 Hz, 1H), 6.92 (d, J = 9.0 Hz, 2H), 4.47 (d, J = 8.4 Hz, 1H), 3.78–3.75 (m, 1H), 3.53–3.48 (m, 1H), 3.08–2.99 (m, 2H), 1.99–1.98 (m, 1H), 1.79–1.71 (m, 4H), 1.64–1.62 (m, 1H), 1.20–1.07 (m, 5H). ¹³C NMR (150 MHz, CDCl₃) δ : 149.3, 141.2, 137.8, 135.2, 128.9, 128.6, 128.4, 128.2, 127.7, 126.7, 126.2, 125.9, 125.3, 113.0, 63.8, 44.2, 43.1, 31.0, 30.7, 27.5, 26.7, 26.4, 26.4. HRMS (ESI, m/z) [M + H]⁺ Calcd. for [C₂₇H₃₀N]⁺: 368.2373, found: 368.2378.



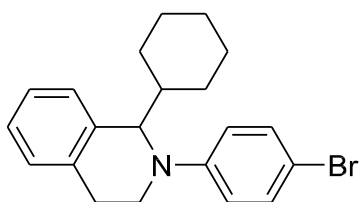
1-Cyclohexyl-2-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (3ea). Light yellow liquid, 53.3 mg, 83% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.18–7.12 (m, 3H), 7.10–7.08 (m, 1H), 6.84–6.80 (m, 4H), 4.26 (d, $J = 7.8$ Hz, 1H), 3.75 (s, 3H), 3.73–3.69 (m, 1H), 3.46 (dt, $J = 12.6, 6.6$ Hz, 1H), 2.99–2.91 (m, 2H), 2.04–2.01 (m, 1H), 1.78–1.72 (m, 4H), 1.66–1.63 (m, 1H), 1.21–1.06 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 151.6, 145.1, 137.8, 135.3, 128.5, 128.4, 126.4, 125.0, 115.4, 114.7, 64.6, 55.8, 44.0, 43.5, 31.0, 30.8, 26.9, 26.7, 26.5, 26.5. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{22}\text{H}_{28}\text{NO}]^+$: 322.2165, found: 322.2162.



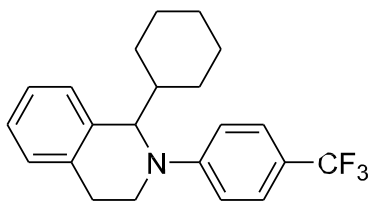
1-Cyclohexyl-2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (3fa). Light yellow liquid, 39.0 mg, 63% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.16–7.09 (m, 3H), 7.06–7.05 (m, 1H), 6.93–6.85 (m, 2H), 6.77–6.74 (m, 2H), 4.27 (d, $J = 7.8$ Hz, 1H), 3.69–3.64 (m, 1H), 3.43–3.38 (m, 1H), 2.94 (t, $J = 7.2$ Hz, 2H), 1.99–1.95 (m, 1H), 1.77–1.69 (m, 4H), 1.64–1.60 (m, 1H), 1.21–1.01 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 155.3 (d, $J = 233.9$ Hz), 146.9, 137.7, 135.2, 128.4 (d, $J = 6.0$ Hz), 126.7, 125.3, 115.4 (d, $J = 21.6$ Hz), 114.6 (d, $J = 7.1$ Hz), 64.5, 44.1, 43.5, 31.0, 30.8, 27.0, 26.7, 26.5, 26.5. ^{19}F NMR (564 MHz, CDCl_3) δ : –128.99. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{21}\text{H}_{25}\text{FN}]^+$: 310.1966, found: 310.1961.



2-(4-Chlorophenyl)-1-cyclohexyl-1,2,3,4-tetrahydroisoquinoline (3ga). Light yellow liquid, 42.9 mg, 66% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.16–7.10 (m, 5H), 7.04 (d, $J = 7.2$ Hz, 1H), 6.73 (d, $J = 8.4$ Hz, 2H), 4.33 (d, $J = 8.4$ Hz, 1H), 3.68–3.64 (m, 1H), 3.39–3.35 (m, 1H), 3.03–2.91 (m, 2H), 1.91 (d, $J = 12.6$ Hz, 1H), 1.74–1.67 (m, 4H), 1.62–1.56 (m, 1H), 1.17–1.02 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 148.6, 137.6, 135.1, 128.9, 128.4, 128.3, 126.8, 125.4, 121.0, 114.1, 64.0, 44.2, 43.3, 31.0, 30.7, 27.3, 26.7, 26.5, 26.4. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{21}\text{H}_{25}\text{ClN}]^+$: 326.1670, found: 326.1666.

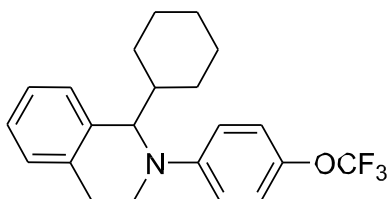


2-(4-Bromophenyl)-1-cyclohexyl-1,2,3,4-tetrahydroisoquinoline (3ha). Light yellow liquid, 48.0 mg, 65% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.27–7.24 (m, 2H), 7.17–7.14 (m, 1H), 7.13–7.10 (m, 2H), 7.06–7.04 (m, 1H), 6.71–6.68 (m, 2H), 4.34 (d, $J = 8.4$ Hz, 1H), 3.66 (dt, $J = 12.0, 6.0$ Hz, 1H), 3.40–3.35 (m, 1H), 3.05–3.00 (m, 1H), 2.97–2.92 (m, 1H), 1.92–1.89 (m, 1H), 1.75–1.67 (m, 4H), 1.63–1.60 (m, 1H), 1.19–0.97 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 149.0, 137.6, 135.0, 131.8, 128.3, 128.2, 126.8, 125.4, 114.5, 108.0, 63.9, 44.1, 43.2, 31.0, 30.7, 27.3, 26.7, 26.4, 26.4. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{21}\text{H}_{25}\text{BrN}]^+$: 370.1165, found: 370.1167.



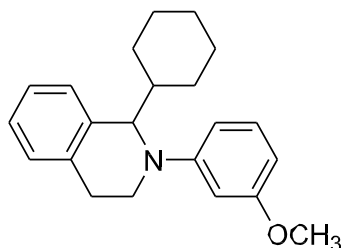
1-Cyclohexyl-2-(4-(trifluoromethyl)phenyl)-1,2,3,4-tetrahydroisoquinoline (3ia).

Light yellow liquid, 41.7 mg, 58% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.48 (d, $J = 9.0$ Hz, 2H), 7.25–7.18 (m, 3H), 7.12–7.11 (m, 1H), 6.89 (d, $J = 9.0$ Hz, 2H), 4.53 (d, $J = 8.4$ Hz, 1H), 3.77 (dt, $J = 11.4, 6.0$ Hz, 1H), 3.51–3.46 (m, 1H), 3.19–3.13 (m, 1H), 3.05–3.01 (m, 1H), 1.95–1.92 (m, 1H), 1.81–1.73 (m, 4H), 1.68–1.66 (m, 1H), 1.22–1.09 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 151.9, 137.4, 134.9, 128.2, 128.2, 127.0, 126.4 (q, $J = 3.8$ Hz), 125.6, 125.2 (q, $J = 268.5$ Hz), 117.4 (q, $J = 32.7$ Hz), 111.6, 63.6, 44.2, 43.3, 31.0, 30.7, 27.5, 26.6, 26.4, 26.3. ^{19}F NMR (564 MHz, CDCl_3) δ : –61.24. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{22}\text{H}_{25}\text{F}_3\text{N}]^+$: 360.1934, found: 360.1939.

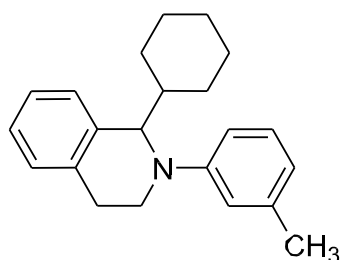


1-Cyclohexyl-2-(4-(trifluoromethoxy)phenyl)-1,2,3,4-tetrahydroisoquinoline (3ja).

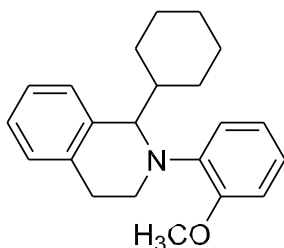
Light yellow liquid, 53.3 mg, 71% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.16–7.11 (m, 3H), 7.06–7.04 (m, 3H), 6.79–6.77 (m, 2H), 4.35 (d, $J = 8.4$ Hz, 1H), 3.71–3.67 (m, 1H), 3.42–3.38 (m, 1H), 3.04–3.00 (m, 1H), 2.98–2.94 (m, 1H), 1.95–1.92 (m, 1H), 1.76–1.68 (m, 4H), 1.63–1.61 (m, 1H), 1.16–1.01 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 148.8, 139.7, 137.5, 135.0, 128.3, 128.3, 126.8, 125.4, 122.1, 120.8 (q, $J = 253.5$ Hz), 113.3, 64.1, 44.1, 43.4, 31.0, 30.7, 27.3, 26.7, 26.4, 26.4. ^{19}F NMR (564 MHz, CDCl_3) δ : –58.36. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{22}\text{H}_{25}\text{F}_3\text{NO}]^+$: 376.1883, found: 376.1884.



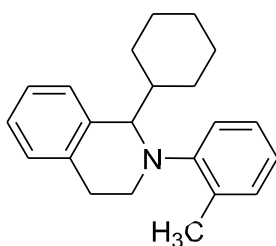
1-Cyclohexyl-2-(3-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (3ka). Light yellow liquid, 45.0 mg, 70% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.16–7.10 (m, 4H), 7.06–7.05 (m, 1H), 6.48 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.39 (t, $J = 2.4$ Hz, 1H), 6.25 (dd, $J = 7.8, 2.4$ Hz, 1H), 4.40 (d, $J = 8.4$ Hz, 1H), 3.77 (s, 3H), 3.72–3.68 (m, 1H), 3.46–3.42 (m, 1H), 3.04–2.95 (m, 2H), 1.97–1.94 (m, 1H), 1.75–1.68 (m, 4H), 1.63–1.60 (m, 1H), 1.17–1.02 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 160.7, 151.4, 137.9, 135.3, 129.7, 128.3, 128.2, 126.6, 125.2, 106.2, 100.7, 99.7, 63.9, 55.2, 44.1, 43.1, 30.9, 30.7, 27.5, 26.7, 26.5, 26.4. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{22}\text{H}_{28}\text{NO}]^+$: 322.2165, found: 322.2163.



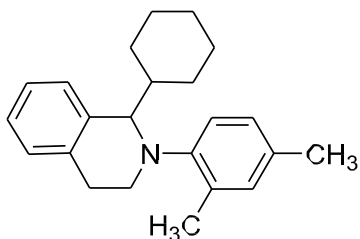
1-Cyclohexyl-2-(*m*-tolyl)-1,2,3,4-tetrahydroisoquinoline (3la). Light yellow liquid, 43.3 mg, 71% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.06–7.00 (m, 4H), 6.98–6.97 (m, 1H), 6.58 (d, $J = 6.6$ Hz, 2H), 6.42 (d, $J = 7.2$ Hz, 1H), 4.32 (d, $J = 8.4$ Hz, 1H), 3.62 (dt, $J = 12.0, 6.0$ Hz, 1H), 3.40–3.36 (m, 1H), 2.91–2.87 (m, 2H), 2.22 (s, 3H), 1.90–1.88 (m, 1H), 1.67–1.61 (m, 4H), 1.55–1.53 (m, 1H), 1.10–0.99 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 150.2, 138.8, 138.0, 135.4, 129.0, 128.4, 128.3, 126.6, 125.2, 117.4, 113.8, 110.3, 63.8, 44.2, 43.0, 31.0, 30.8, 27.4, 26.8, 26.5, 26.5, 22.2. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{22}\text{H}_{28}\text{N}]^+$: 306.2216, found: 306.2211.



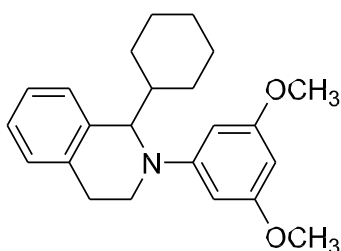
1-Cyclohexyl-2-(2-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (3ma). Light yellow liquid, 40.5 mg, 63% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.14–7.10 (m, 3H), 7.07–7.05 (m, 1H), 6.87–6.85 (m, 1H), 6.83 (dd, $J = 7.8, 1.2$ Hz, 1H), 6.76 (dd, $J = 7.8, 1.8$ Hz, 1H), 6.74–6.71 (m, 1H), 4.08 (d, $J = 7.8$ Hz, 1H), 3.84 (s, 3H), 3.64–3.61 (m, 2H), 2.85–2.79 (m, 1H), 2.71–2.66 (m, 1H), 2.12–2.08 (m, 1H), 1.74–1.62 (m, 5H), 1.19–1.03 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 152.8, 141.9, 138.4, 135.3, 129.0, 128.5, 126.0, 124.8, 121.7, 121.3, 121.0, 112.3, 65.0, 55.8, 43.3, 42.9, 31.3, 31.1, 26.7, 26.6, 26.5. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{22}\text{H}_{28}\text{NO}]^+$: 322.2165, found: 322.2169.



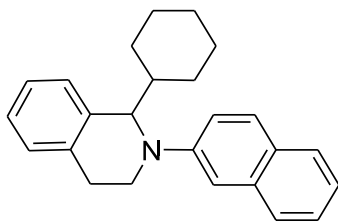
1-Cyclohexyl-2-(*o*-tolyl)-1,2,3,4-tetrahydroisoquinoline (3na). Light yellow liquid, 35.4 mg, 58% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.18–7.14 (m, 4H), 7.10–7.08 (m, 1H), 6.98–6.95 (m, 1H), 6.92–6.89 (m, 1H), 6.81–6.79 (m, 1H), 4.02 (d, $J = 6.6$ Hz, 1H), 3.51–3.47 (m, 1H), 3.16–3.12 (m, 1H), 2.75–2.69 (m, 1H), 2.65–2.60 (m, 1H), 2.39 (s, 3H), 1.98–1.94 (m, 1H), 1.73–1.61 (m, 5H), 1.17–1.07 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 152.1, 138.5, 136.2, 133.4, 131.0, 128.8, 128.1, 126.3, 125.9, 125.2, 123.0, 122.8, 66.0, 45.5, 44.9, 31.1, 30.4, 26.9, 26.7, 26.7, 26.3, 18.6. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$: Calcd. for $[\text{C}_{22}\text{H}_{28}\text{N}]^+$: 306.2216, found: 306.2212.



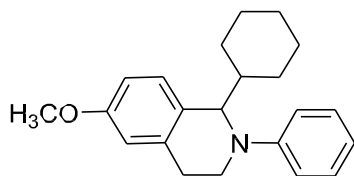
1-Cyclohexyl-2-(2,4-dimethylphenyl)-1,2,3,4-tetrahydroisoquinoline (30a). Light yellow liquid, 44.1 mg, 69% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.16–7.14 (m, 3H), 7.08 (d, $J = 5.4, 1.2$ Hz, 1H), 6.98 (d, $J = 2.4$ Hz, 1H), 6.76 (dd, $J = 8.4, 2.4$ Hz, 1H), 6.71 (d, $J = 8.4$ Hz, 1H), 4.00 (d, $J = 6.6$ Hz, 1H), 3.43–3.42 (m, 1H), 3.09–3.05 (m, 1H), 2.74–2.68 (m, 1H), 2.64–2.59 (m, 1H), 2.35 (s, 3H), 2.22 (s, 3H), 1.95–1.90 (m, 1H), 1.72–1.60 (m, 5H), 1.17–1.06 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 149.7, 138.6, 136.4, 133.5, 132.2, 131.8, 128.8, 128.2, 127.0, 125.9, 125.2, 123.1, 66.2, 46.0, 45.2, 31.1, 30.3, 27.0, 26.8, 26.7, 26.5, 20.8, 18.4. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{23}\text{H}_{30}\text{N}]^+$: 320.2373, found: 320.2372.



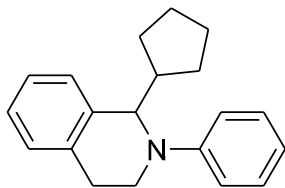
1-Cyclohexyl-2-(3,5-dimethoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (3pa). Light yellow liquid, 51.3 mg, 73% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.16–7.09 (m, 3H), 7.06–7.04 (m, 1H), 6.04 (d, $J = 2.4$ Hz, 2H), 5.88 (t, $J = 2.4$ Hz, 1H), 4.37 (d, $J = 7.8$ Hz, 1H), 3.77 (s, 6H), 3.71–3.67 (m, 1H), 3.46–3.41 (m, 1H), 3.04–2.94 (m, 2H), 1.96–1.93 (m, 1H), 1.75–1.68 (m, 4H), 1.63–1.60 (m, 1H), 1.16–1.07 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 161.6, 151.8, 137.8, 135.2, 128.3, 128.2, 126.7, 125.3, 92.5, 88.1, 64.0, 55.2, 44.1, 43.2, 31.0, 30.8, 27.5, 26.7, 26.4, 26.4. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{23}\text{H}_{30}\text{NO}_2]^+$: 352.2271, found: 352.2271.



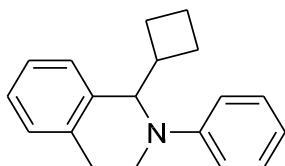
1-Cyclohexyl-2-(naphthalen-2-yl)-1,2,3,4-tetrahydroisoquinoline (3qa). Light yellow liquid, 38.8 mg, 57% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.66 (d, $J = 9.0$ Hz, 1H), 7.63 (d, $J = 7.8$ Hz, 1H), 7.59 (d, $J = 7.8$ Hz, 1H), 7.33–7.30 (m, 1H), 7.26 (dd, $J = 6.6, 2.4$ Hz, 1H), 7.17–7.10 (m, 5H), 6.99 (d, $J = 2.4$ Hz, 1H), 4.55 (d, $J = 8.4$ Hz, 1H), 3.81–3.76 (m, 1H), 3.63–3.59 (m, 1H), 3.01 (t, $J = 6.6$ Hz, 2H), 1.99–1.96 (m, 1H), 1.78–1.70 (m, 4H), 1.63–1.60 (m, 1H), 1.16–1.07 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 147.9, 137.9, 135.2, 135.2, 128.7, 128.5, 128.4, 127.4, 126.8, 126.7, 126.3, 126.2, 125.3, 122.0, 117.0, 106.9, 63.9, 44.1, 43.1, 31.1, 31.0, 27.3, 26.7, 26.5, 26.5. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{25}\text{H}_{28}\text{N}]^+$: 342.2216, found: 342.2217.



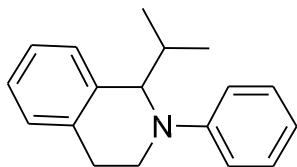
1-cyclohexyl-6-methoxy-2-phenyl-1,2,3,4-tetrahydroisoquinoline (3ra). Light yellow liquid, 54.6 mg, 85% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.22–7.18 (m, 2H), 6.99–6.96 (m, 1H), 6.84 (d, $J = 8.4$ Hz, 2H), 6.68–6.65 (m, 3H), 4.36–4.34 (m, 1H), 3.76 (s, 3H), 3.71–3.67 (m, 1H), 3.46–3.41 (m, 1H), 3.00–2.91 (m, 2H), 1.96 (d, $J = 12.6$ Hz, 1H), 1.75–1.69 (m, 4H), 1.63–1.61 (m, 1H), 1.17–1.02 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ : 158.2, 150.0, 136.5, 130.0, 129.3, 129.1, 116.3, 113.4, 113.1, 110.9, 63.3, 55.2, 44.2, 42.7, 30.9, 30.6, 27.7, 26.7, 26.5, 26.4. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{22}\text{H}_{28}\text{NO}]^+$: 322.2165, found: 322.2168.



1-Cyclopentyl-2-phenyl-1,2,3,4-tetrahydroisoquinoline (3ab).^[2] Light yellow liquid, 41.6 mg, 75% yield. ¹H NMR (600 MHz, CDCl₃) δ : 7.13–7.10 (m, 2H), 7.07–7.00 (m, 4H), 6.81–6.79 (m, 2H), 6.61–6.58 (m, 1H), 4.45–4.43 (m, 1H), 3.66–3.61 (m, 1H), 3.56–3.52 (m, 1H), 2.96–2.90 (m, 1H), 2.81–2.76 (m, 1H), 2.27–2.19 (m, 1H), 1.78–1.73 (m, 1H), 1.64–1.53 (m, 3H), 1.45–1.30 (m, 4H). ¹³C NMR (150 MHz, CDCl₃) δ : 150.1, 138.9, 134.9, 129.2, 128.7, 127.7, 126.5, 125.4, 116.9, 113.9, 62.8, 47.2, 42.0, 31.1, 30.7, 26.8, 25.2, 24.5.

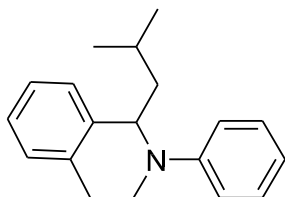


(1-Cyclobutyl-2-phenyl-1,2,3,4-tetrahydroisoquinoline (3ac).^[2] Light yellow liquid, 38.4 mg, 73% yield. ¹H NMR (600 MHz, CDCl₃) δ : 7.22–7.19 (m, 2H), 7.14–7.08 (m, 4H), 6.92–6.90 (m, 2H), 6.72–6.69 (m, 1H), 4.59 (d, $J = 7.8$ Hz, 1H), 3.59–3.57 (m, 2H), 3.01–2.96 (m, 1H), 2.86–2.79 (m, 1H), 2.76–2.71 (m, 1H), 1.95–1.84 (m, 4H), 1.78–1.65 (m, 2H). ¹³C NMR (150 MHz, CDCl₃) δ : 150.3, 137.6, 134.8, 129.1, 128.7, 127.2, 126.5, 125.5, 117.3, 114.4, 63.3, 41.9, 41.7, 27.4, 27.0, 26.7, 18.0.

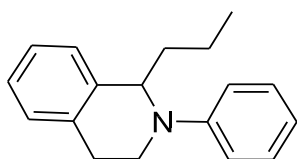


1-(*iso*-Propyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (3ad).^[3] Light yellow liquid, 34.7 mg, 69% yield. ¹H NMR (600 MHz, CDCl₃) δ : 7.22–7.19 (m, 2H), 7.14–7.07 (m, 4H), 6.85 (d, $J = 8.4$ Hz, 2H), 6.67 (t, $J = 7.2$ Hz, 1H), 4.37 (d, $J = 8.4$ Hz,

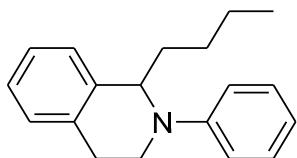
1H), 3.71 (dt, $J = 12.6, 6.0$ Hz, 1H), 3.46–3.42 (m, 1H), 2.98–2.95 (m, 2H), 2.15–2.07 (m, 1H), 1.05 (d, $J = 7.2$ Hz, 3H), 0.93 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ : 150.1, 137.9, 135.4, 129.2, 128.4, 128.3, 126.7, 125.4, 116.6, 113.3, 64.7, 43.1, 34.5, 27.5, 20.7, 20.2.



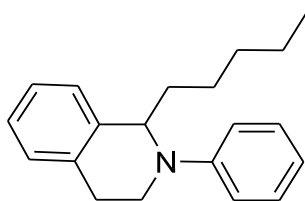
1-(*iso*-Butyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (3ae). Light yellow liquid, 37.1 mg, 70% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.23–7.20 (m, 2H), 7.15–7.07 (m, 4H), 6.89–6.88 (m, 2H), 6.71 (t, $J = 7.2$ Hz, 1H), 4.75 (t, $J = 7.2$ Hz, 1H), 3.64–3.58 (m, 2H), 3.01–2.97 (m, 1H), 2.79–2.75 (m, 1H), 1.91–1.87 (m, 1H), 1.75–1.71 (m, 1H), 1.54–1.49 (m, 1H), 1.04 (d, $J = 6.6$ Hz, 3H), 0.95 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ : 149.8, 139.4, 134.9, 129.3, 128.7, 127.2, 126.3, 125.7, 117.2, 114.2, 56.8, 45.9, 41.6, 26.5, 25.1, 22.9, 22.8. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{19}\text{H}_{24}\text{N}]^+$: 266.1903, found: 266.1901.



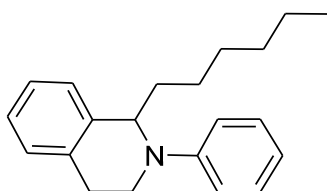
2-Phenyl-1(*n*-propyl)-1,2,3,4-tetrahydroisoquinoline (3af).^[4] Light yellow liquid, 36.7 mg, 73% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.24–7.21 (m, 2H), 7.14–7.08 (m, 4H), 6.86 (d, $J = 8.4$ Hz, 2H), 6.70 (t, $J = 6.6$ Hz, 1H), 4.66–4.63 (m, 1H), 3.62–3.55 (m, 2H), 3.02–2.98 (m, 1H), 2.86–2.82 (m, 1H), 1.95–1.91 (m, 1H), 1.70–1.66 (m, 1H), 1.50–1.40 (m, 2H), 0.93 (td, $J = 7.2, 1.8$ Hz, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ : 149.8, 139.2, 135.1, 129.3, 128.6, 127.4, 126.4, 125.8, 117.0, 113.7, 59.0, 41.9, 39.1, 27.2, 20.2, 14.2.



1-(*n*-Butyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (3ag).^[3] Light yellow liquid, 38.2 mg, 72% yield. ¹H NMR (600 MHz, CDCl₃) δ : 7.23–7.19 (m, 2H), 7.12–7.06 (m, 4H), 6.84 (d, $J = 7.8$ Hz, 2H), 6.69 (t, $J = 7.2$ Hz, 1H), 4.62 (t, $J = 7.2$ Hz, 1H), 3.59–3.51 (m, 2H), 2.99–2.94 (m, 1H), 2.79 (dt, $J = 16.2, 5.2$ Hz, 1H), 1.96–1.91 (m, 1H), 1.71–1.66 (m, 1H), 1.45–1.30 (m, 4H), 0.87 (t, 7.2 Hz, 3H). ¹³C NMR (150 MHz, CDCl₃) δ : 149.9, 139.4, 135.1, 129.4, 128.7, 127.5, 126.5, 125.9, 117.1, 113.9, 59.4, 42.0, 36.8, 29.3, 27.3, 23.0, 14.3.

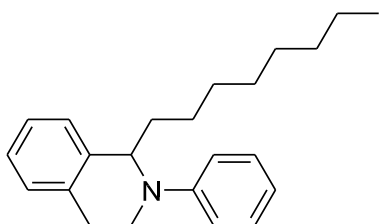


1-(*n*-Pentyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (3ah).^[2] Light yellow liquid, 37.4 mg, 67% yield. ¹H NMR (600 MHz, CDCl₃) δ : 7.18–7.14 (m, 2H), 7.10–7.02 (m, 4H), 6.79 (d, $J = 8.4$ Hz, 2H), 6.63 (t, $J = 7.2$ Hz, 1H), 4.56 (t, $J = 7.2$ Hz, 1H), 3.56–3.50 (m, 2H), 2.97–2.92 (m, 1H), 2.77 (dt, $J = 16.2, 5.4$ Hz, 1H), 1.90–1.85 (m, 1H), 1.64–1.60 (m, 1H), 1.42–1.38 (m, 1H), 1.35–1.31 (m, 1H), 1.24–1.21 (m, 4H), 0.82–0.78 (m, 3H). ¹³C NMR (150 MHz, CDCl₃) δ : 149.7, 139.2, 135.0, 129.2, 128.5, 127.3, 126.4, 125.7, 116.9, 113.7, 59.2, 41.8, 36.8, 31.9, 27.1, 26.6, 22.7, 14.1.



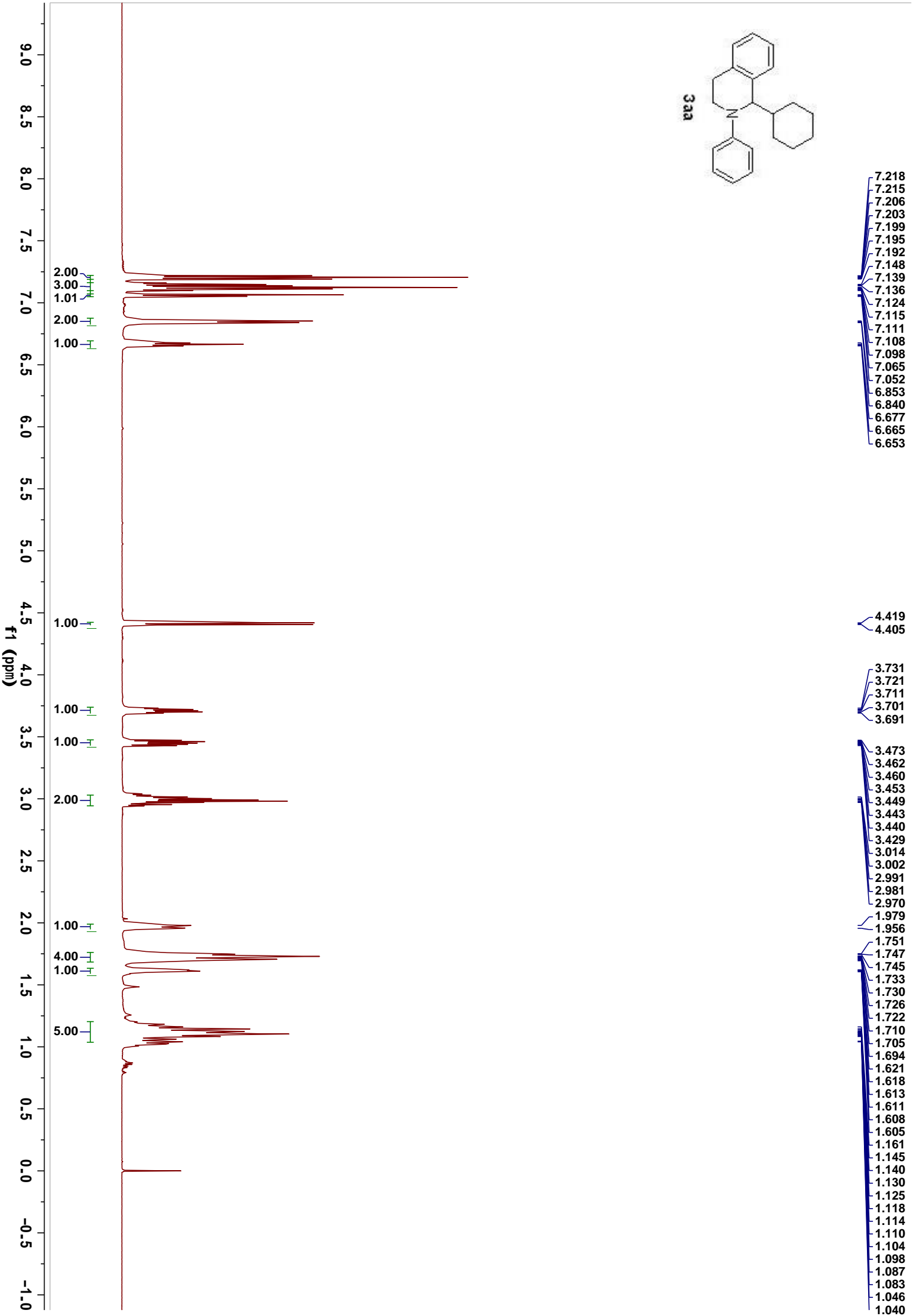
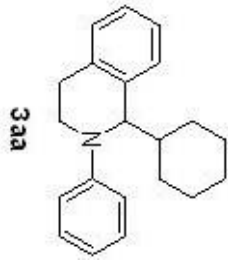
1-(*n*-Hexyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (3ai). Light yellow liquid, 40.5 mg, 69% yield. ¹H NMR (600 MHz, CDCl₃) δ : 7.24–7.21 (m, 2H), 7.16–7.09 (m,

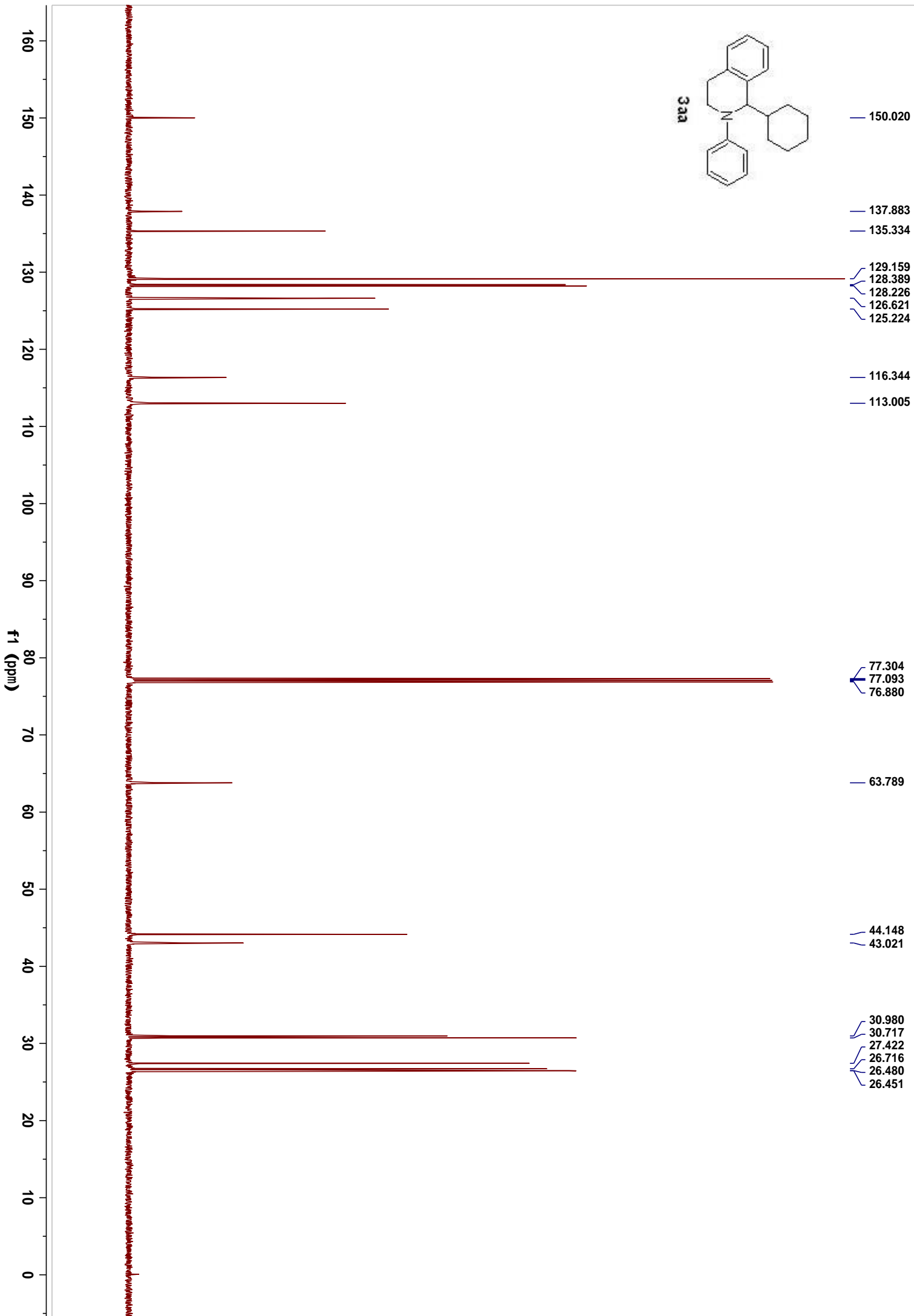
4H), 6.86 (d, $J = 7.8$ Hz, 2H), 6.70 (t, $J = 7.2$ Hz, 1H), 4.63 (t, $J = 7.2$ Hz, 1H), 3.64–3.55 (m, 2H), 3.03–2.98 (m, 1H), 2.86–2.82 (m, 1H), 1.98–1.91 (m, 1H), 1.72–1.66 (m, 1H), 1.49–1.45 (m, 1H), 1.40–1.36 (m, 1H), 1.32–1.25 (m, 6H), 0.86 (t, $J = 6.6$ Hz, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ : 149.7, 139.3, 135.0, 129.3, 128.5, 127.4, 126.4, 125.7, 116.9, 113.7, 59.3, 41.8, 36.9, 31.9, 29.4, 27.1, 26.9, 22.7, 14.1. HRMS (ESI, m/z) $[\text{M} + \text{H}]^+$ Calcd. for $[\text{C}_{21}\text{H}_{28}\text{N}]^+$: 294.2216, found: 294.2211.

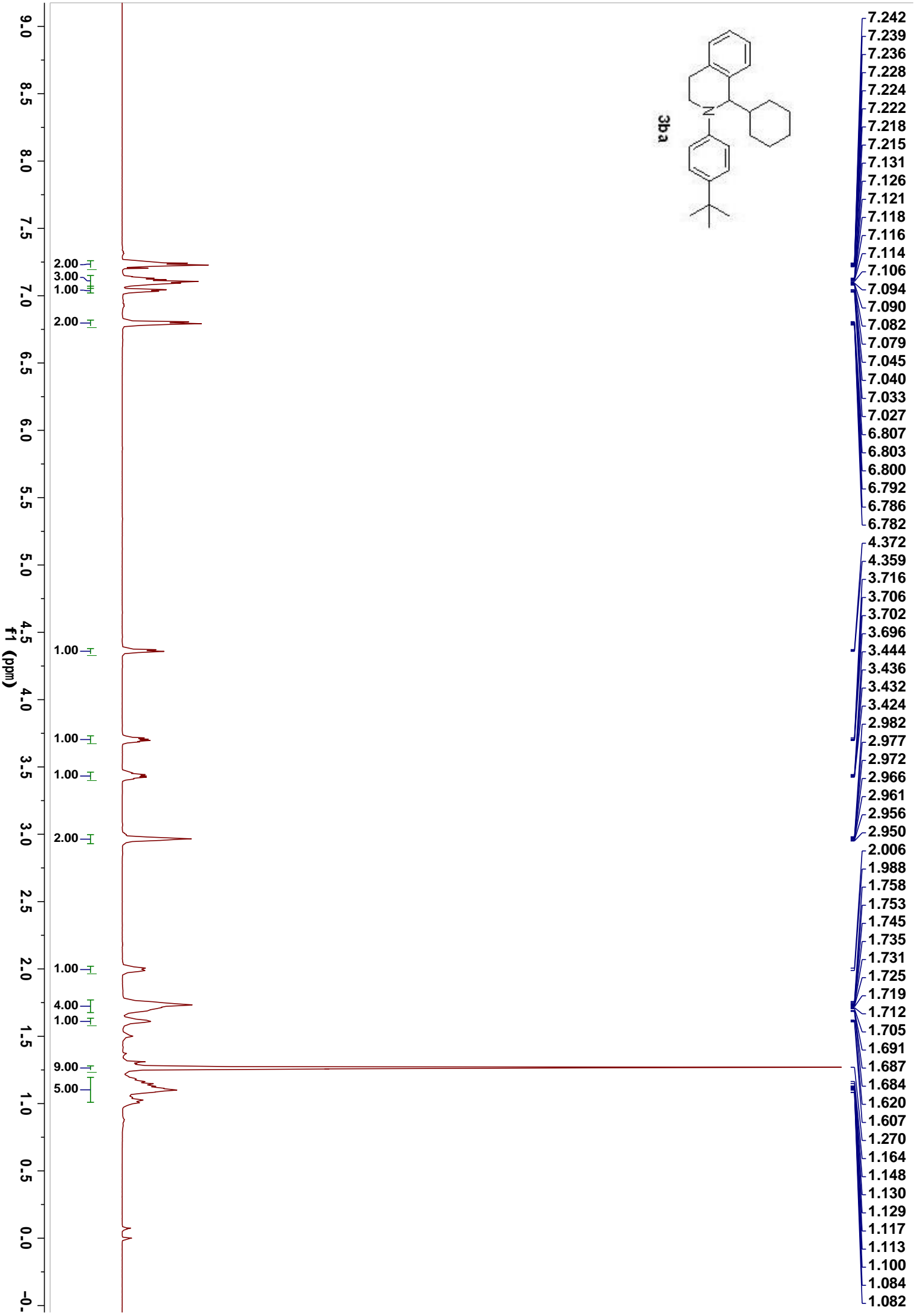
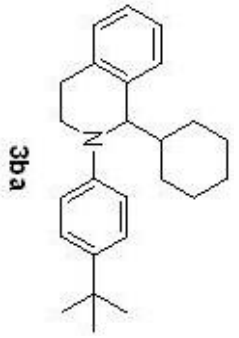


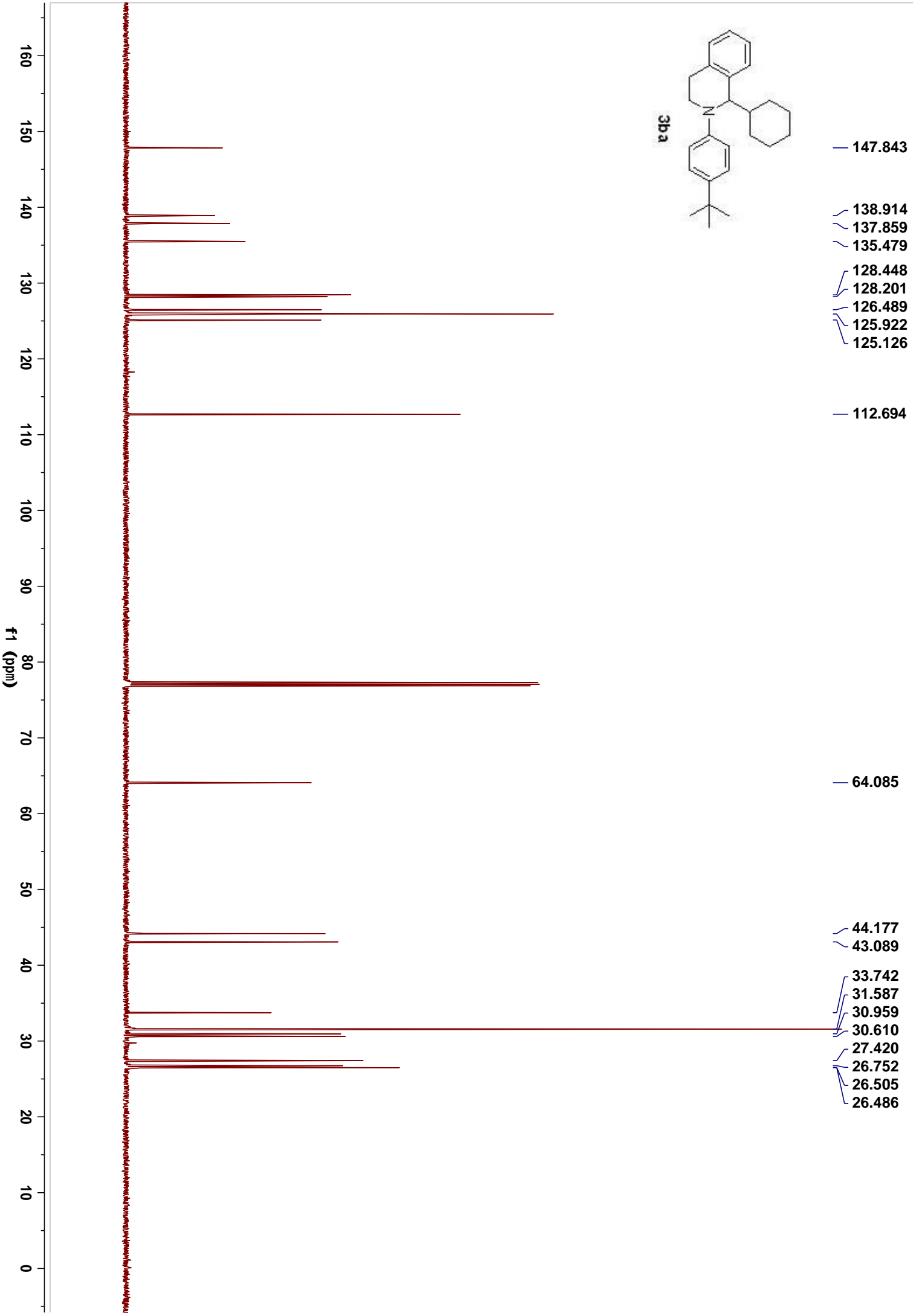
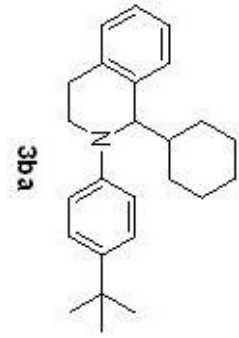
1-(*n*-Octyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (3aj).^[5] Light yellow liquid, 41.8 mg, 65% yield. ^1H NMR (600 MHz, CDCl_3) δ : 7.25–7.21 (m, 2H), 7.16–7.09 (m, 4H), 6.86 (d, $J = 8.4$ Hz, 2H), 6.70 (t, $J = 7.2$ Hz, 1H), 4.63 (t, $J = 7.2$ Hz, 1H), 3.64–3.56 (m, 2H), 3.04–2.99 (m, 1H), 2.84 (dt, $J = 15.6, 5.4$ Hz, 1H), 1.98–1.92 (m, 1H), 1.72–1.66 (m, 1H), 1.49–1.43 (m, 1H), 1.41–1.36 (m, 1H), 1.31–1.23 (m, 10H), 0.87 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ : 149.7, 139.3, 135.0, 129.2, 128.5, 127.3, 126.4, 125.7, 116.9, 113.7, 59.2, 41.8, 36.8, 31.9, 29.7, 29.6, 29.3, 27.1, 26.9, 22.7, 14.1.

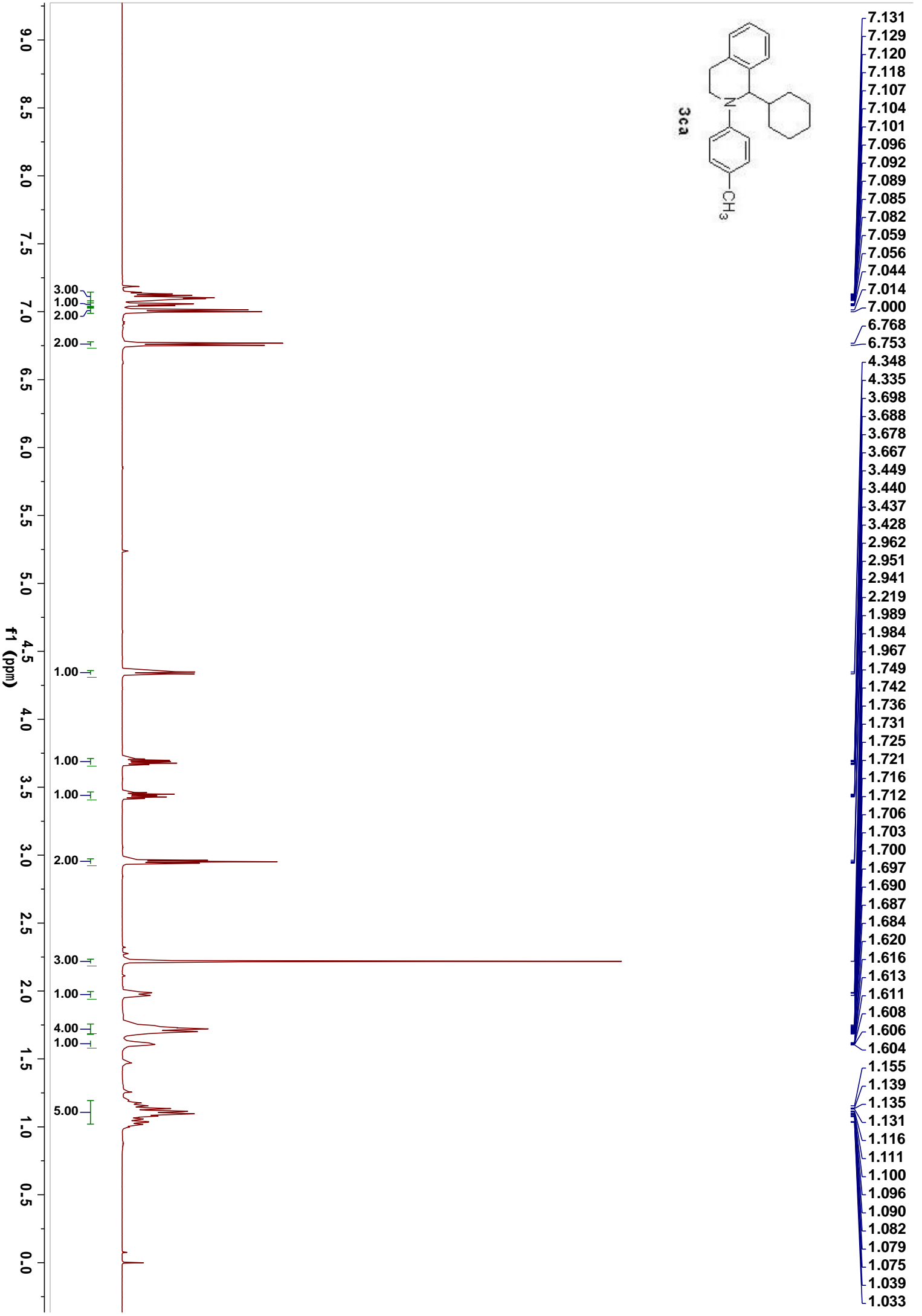
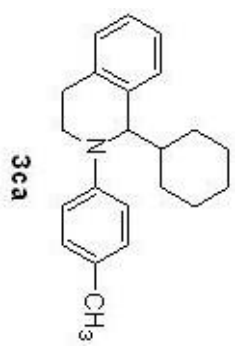
5. Copies of ^1H and ^{13}C NMR NMR Spectra of the Products

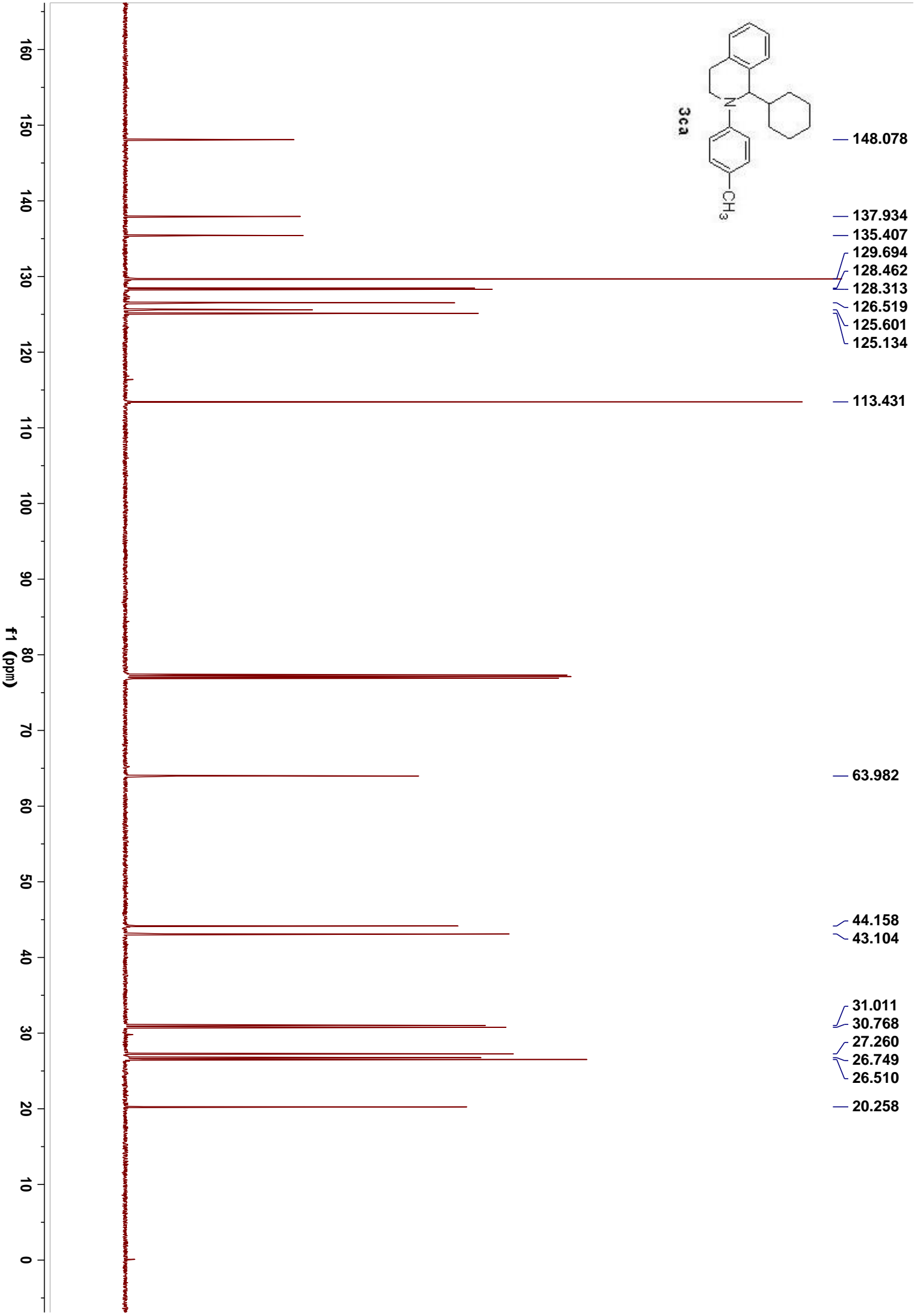
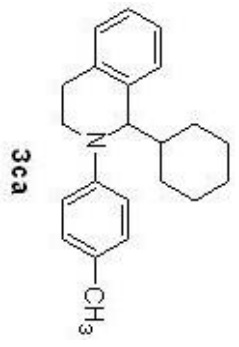


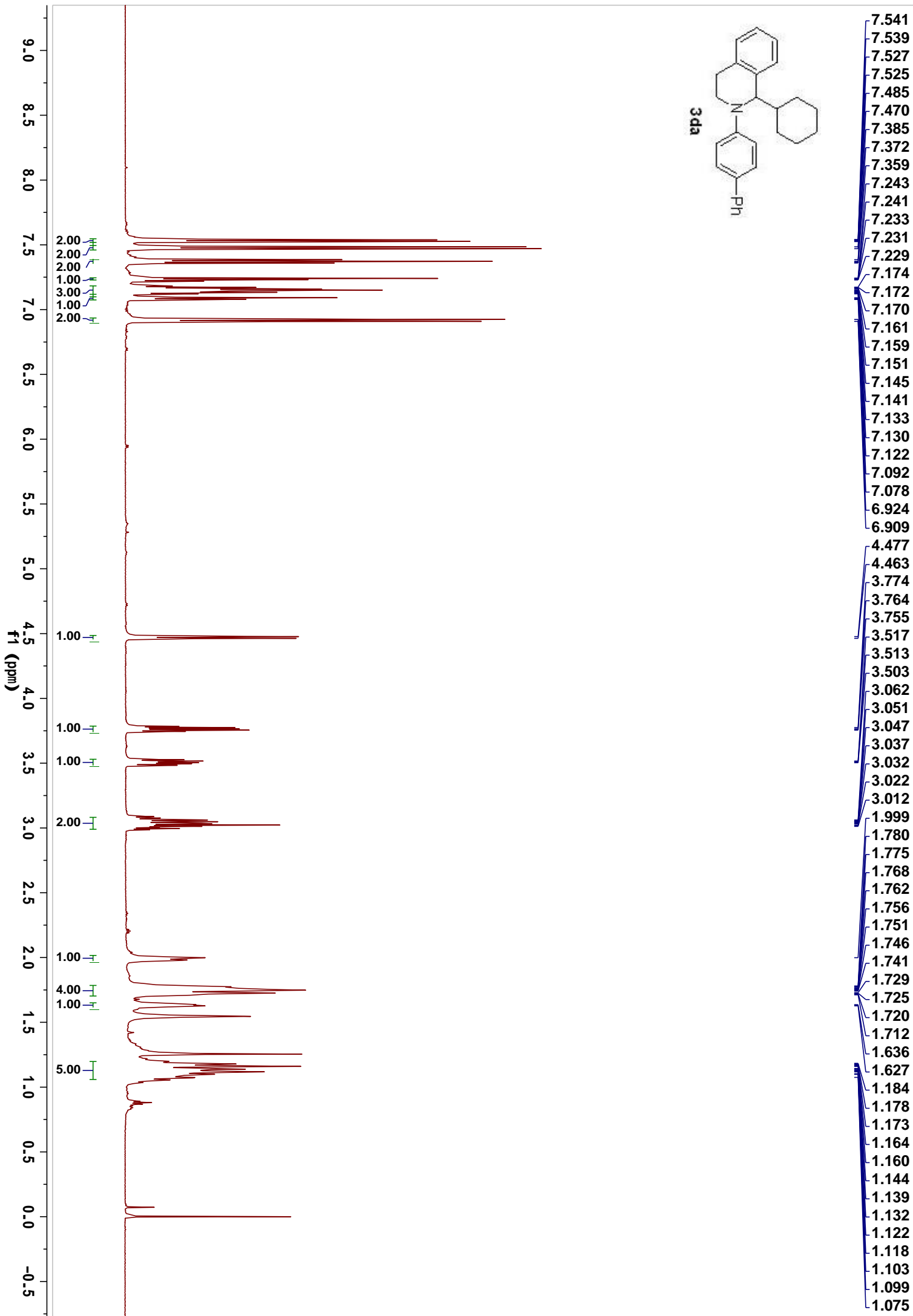
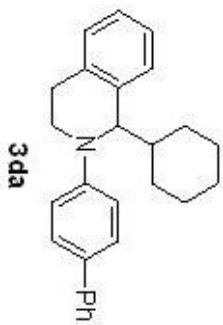


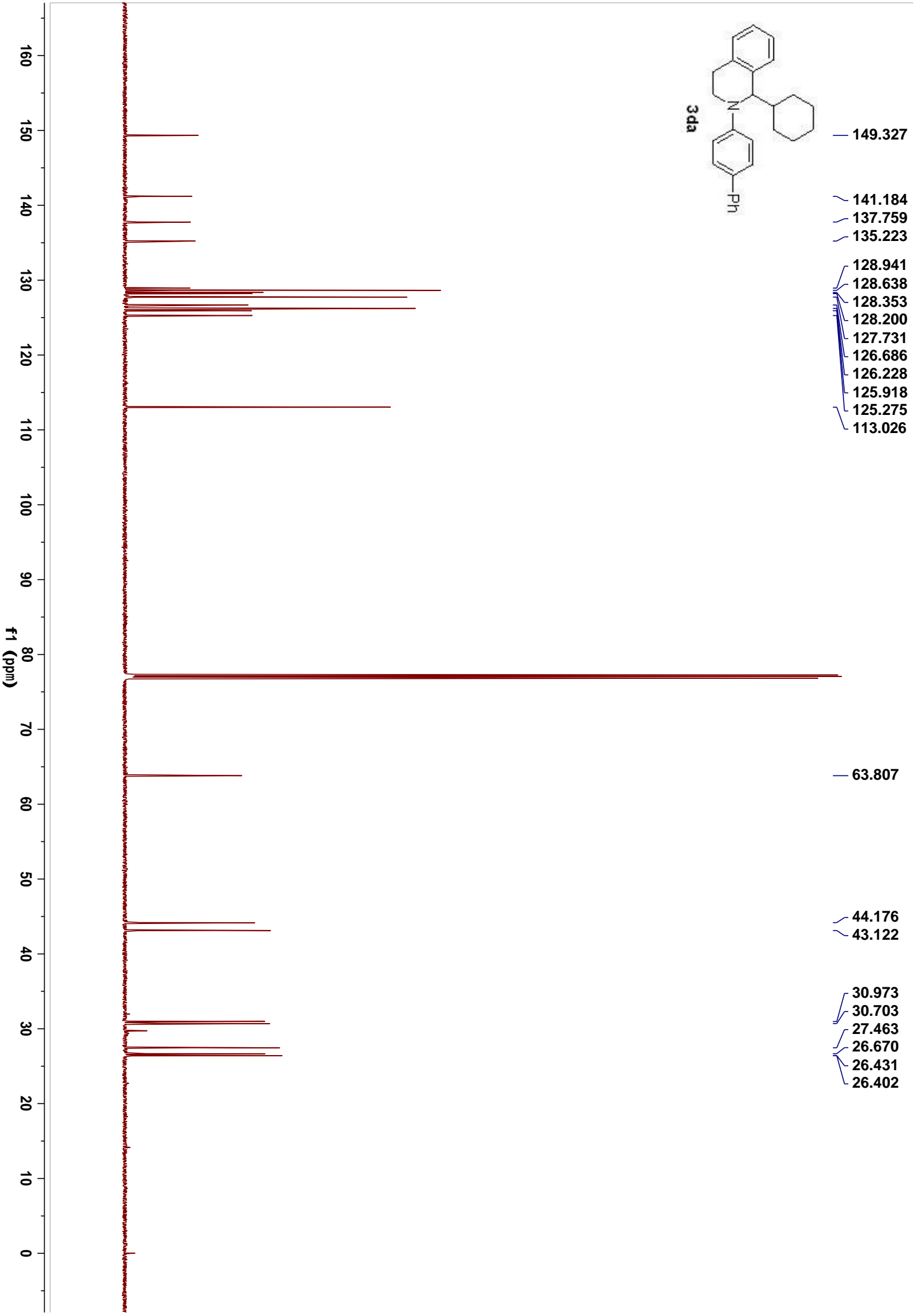
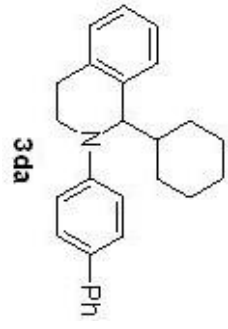


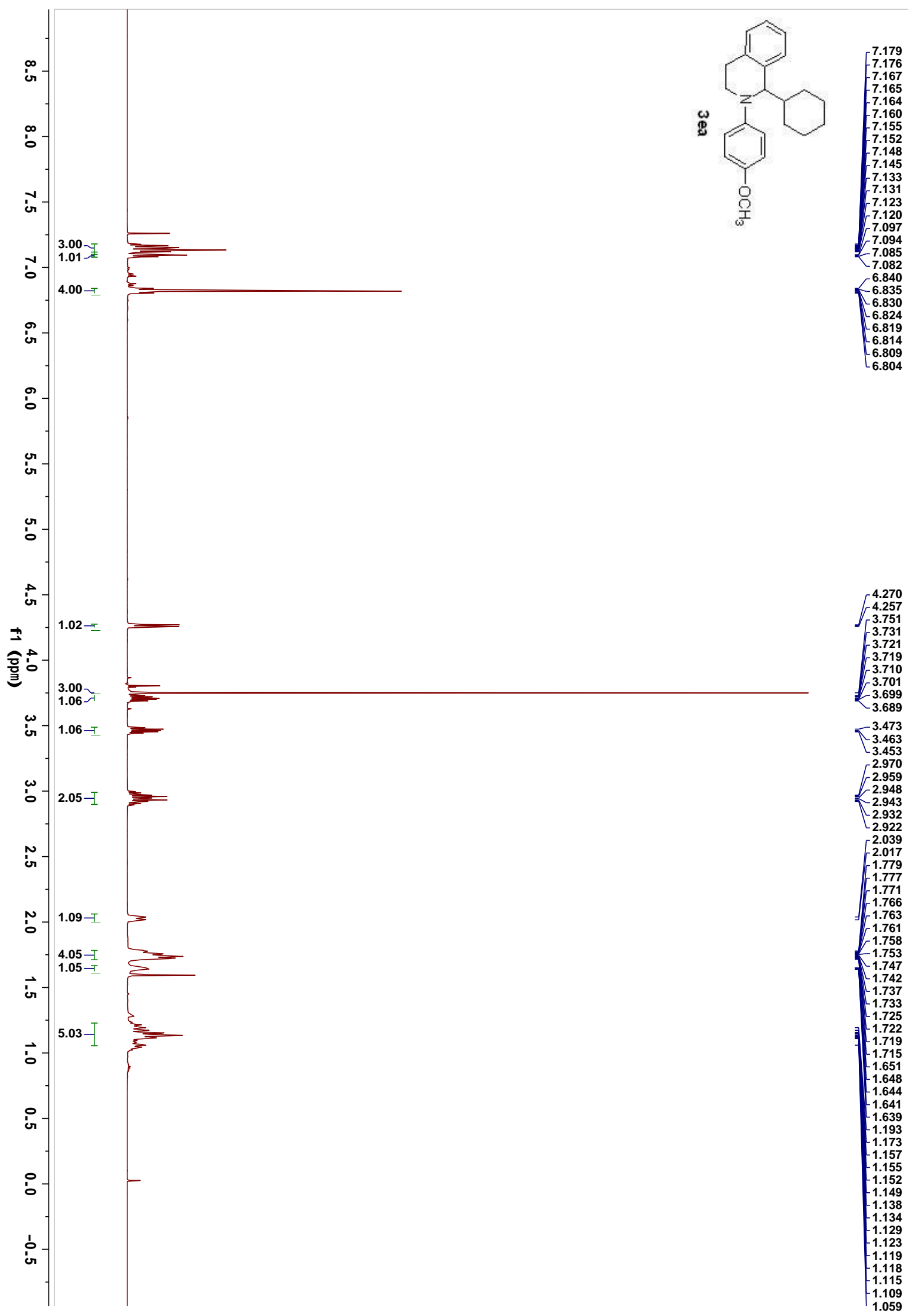
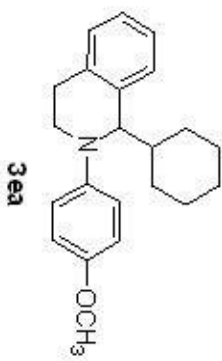


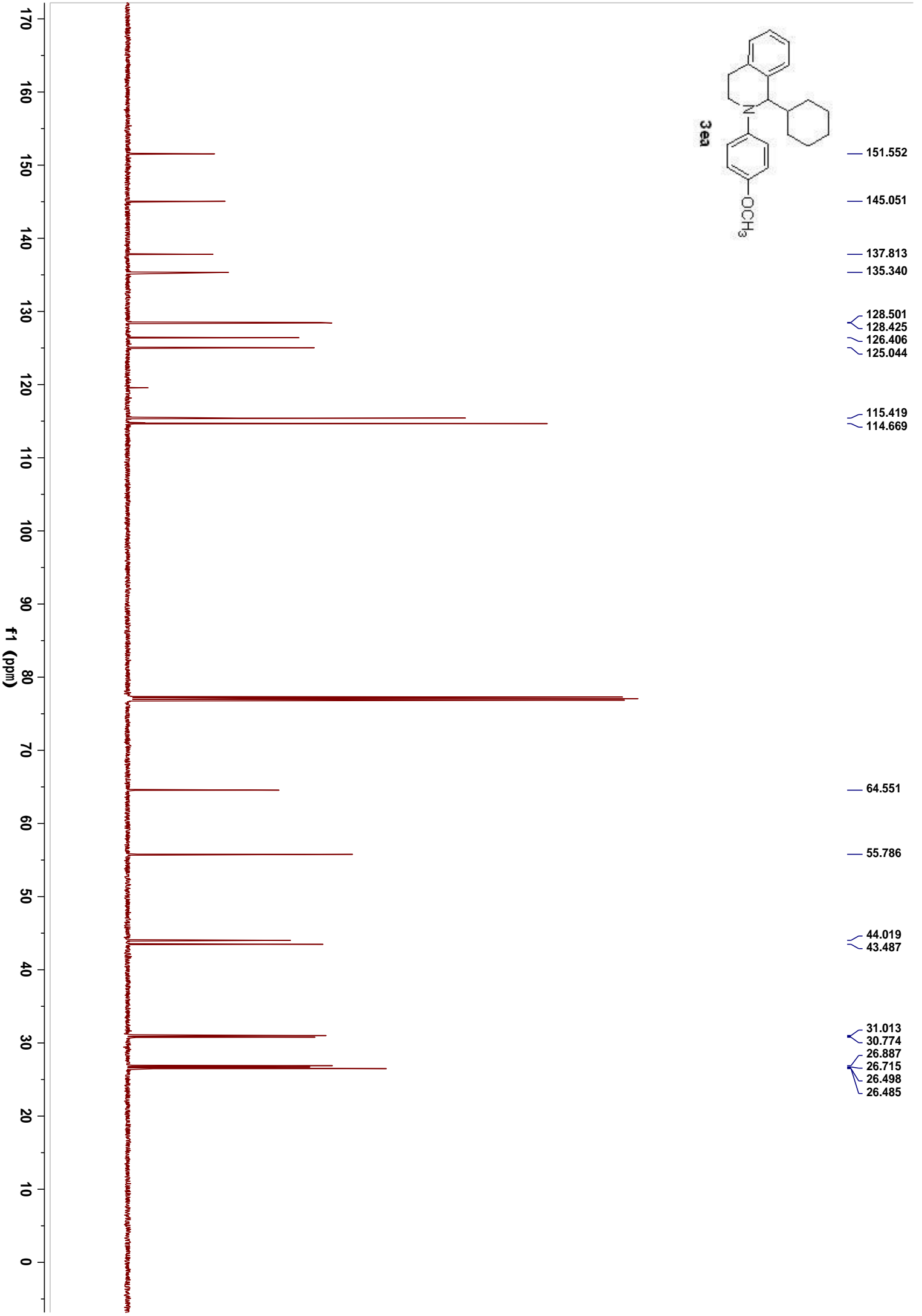
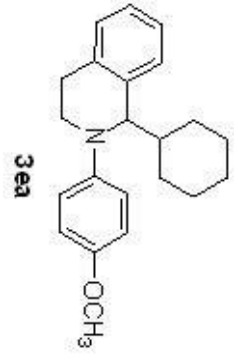


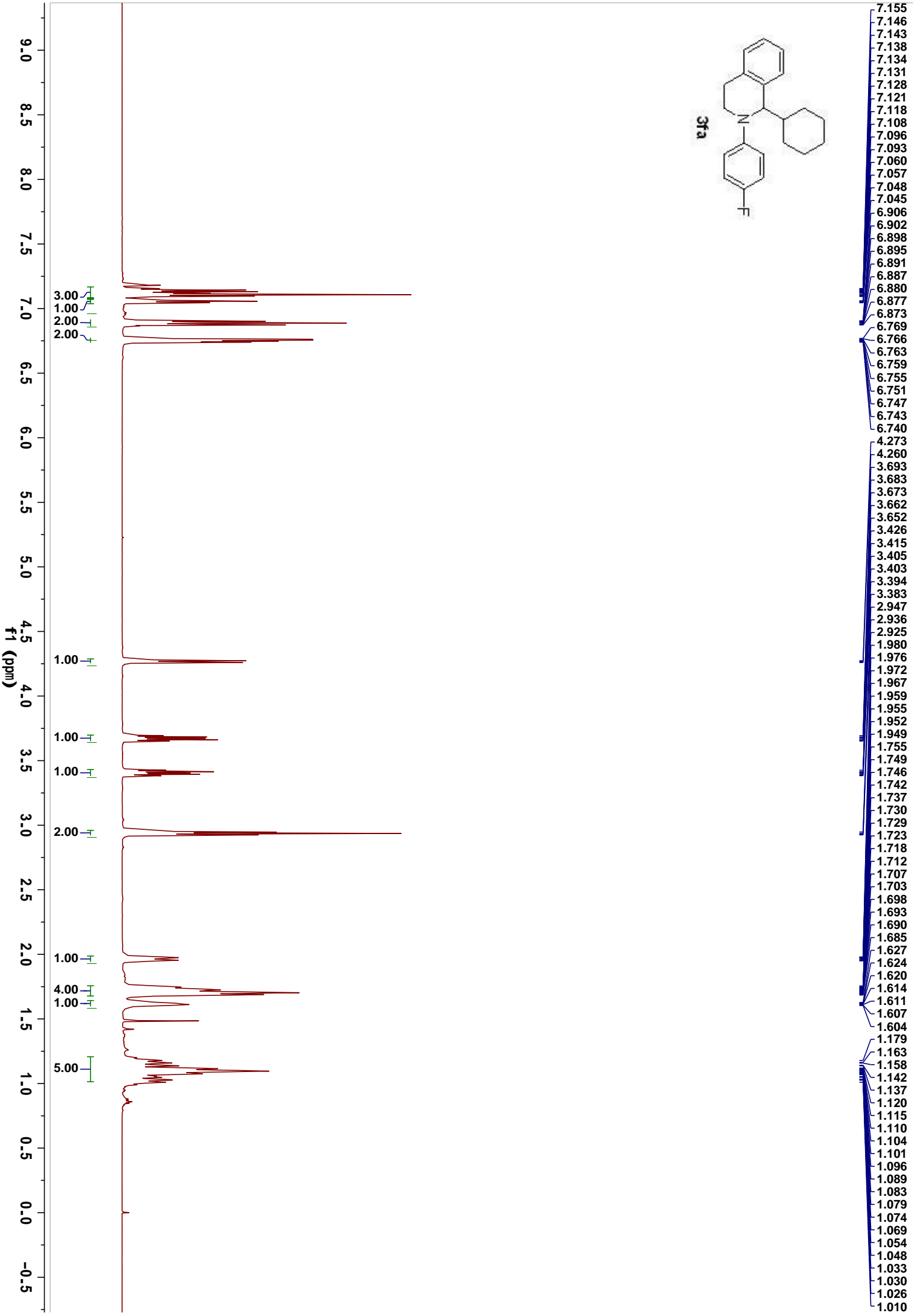
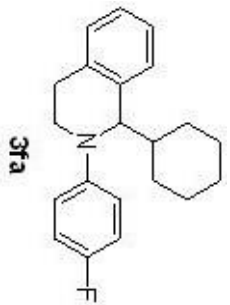


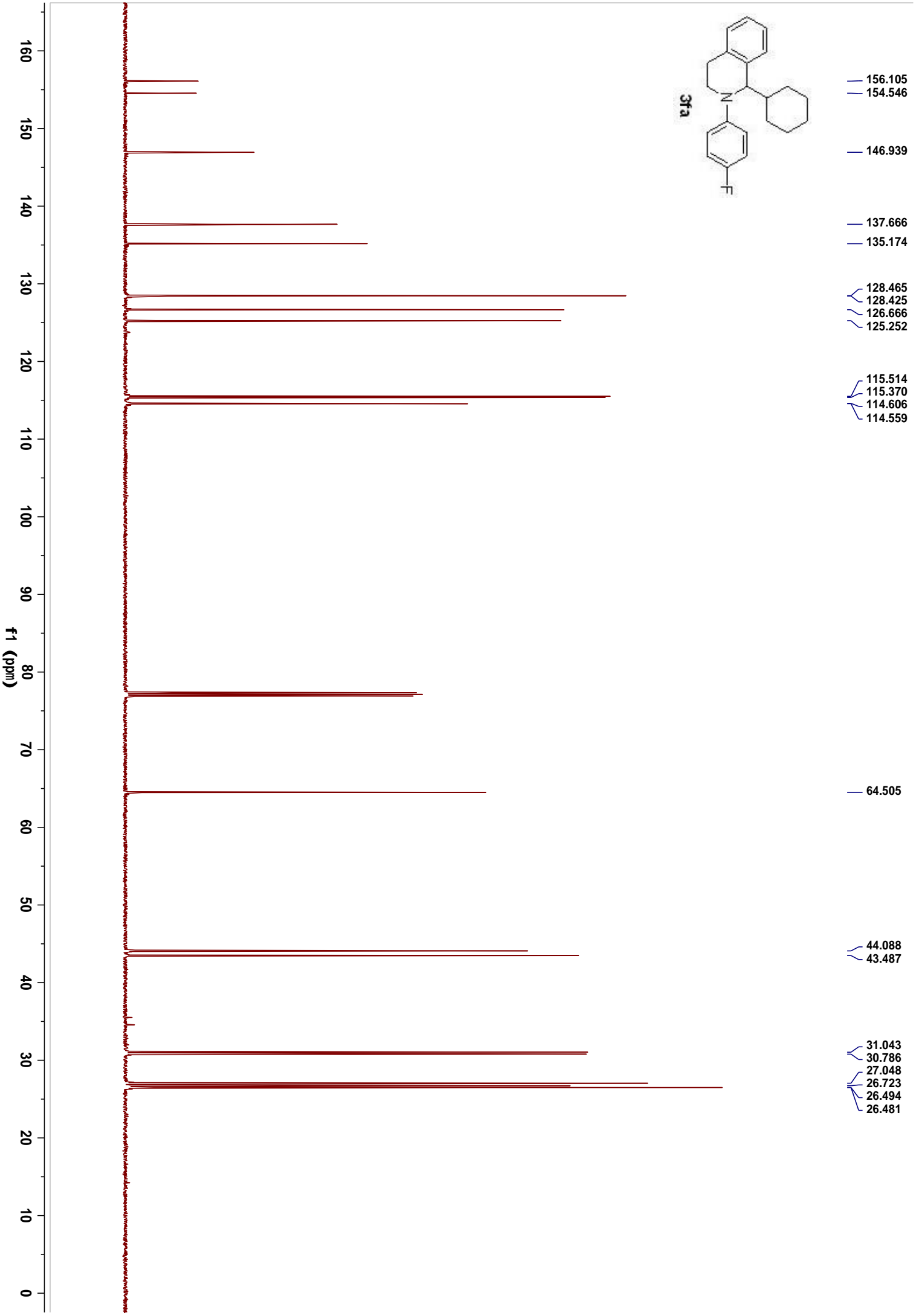
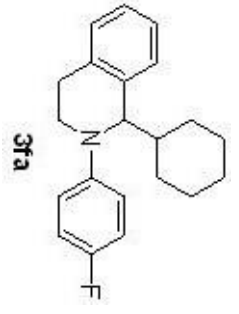


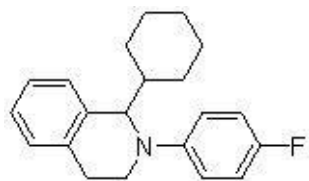








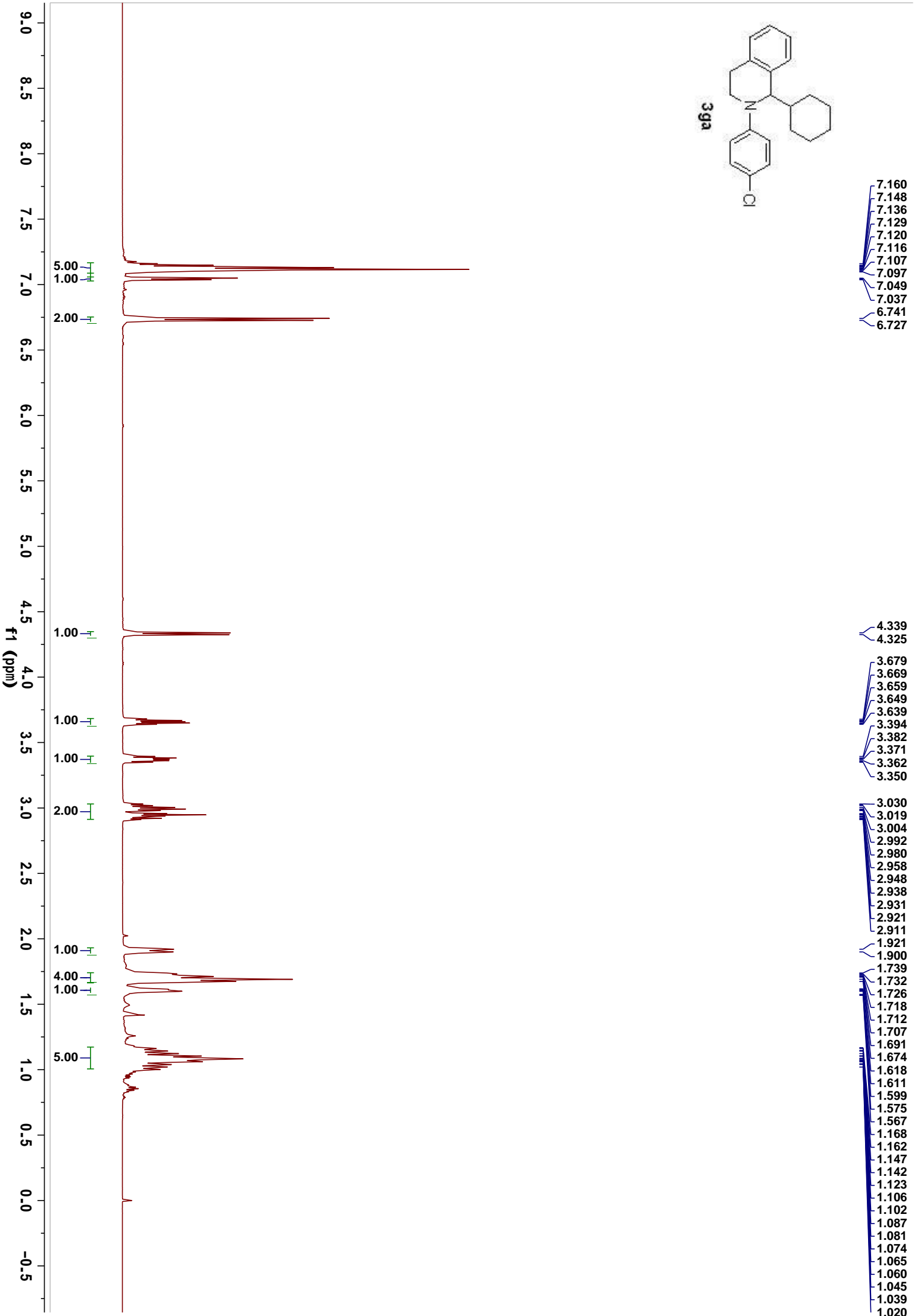
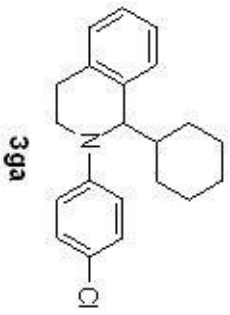


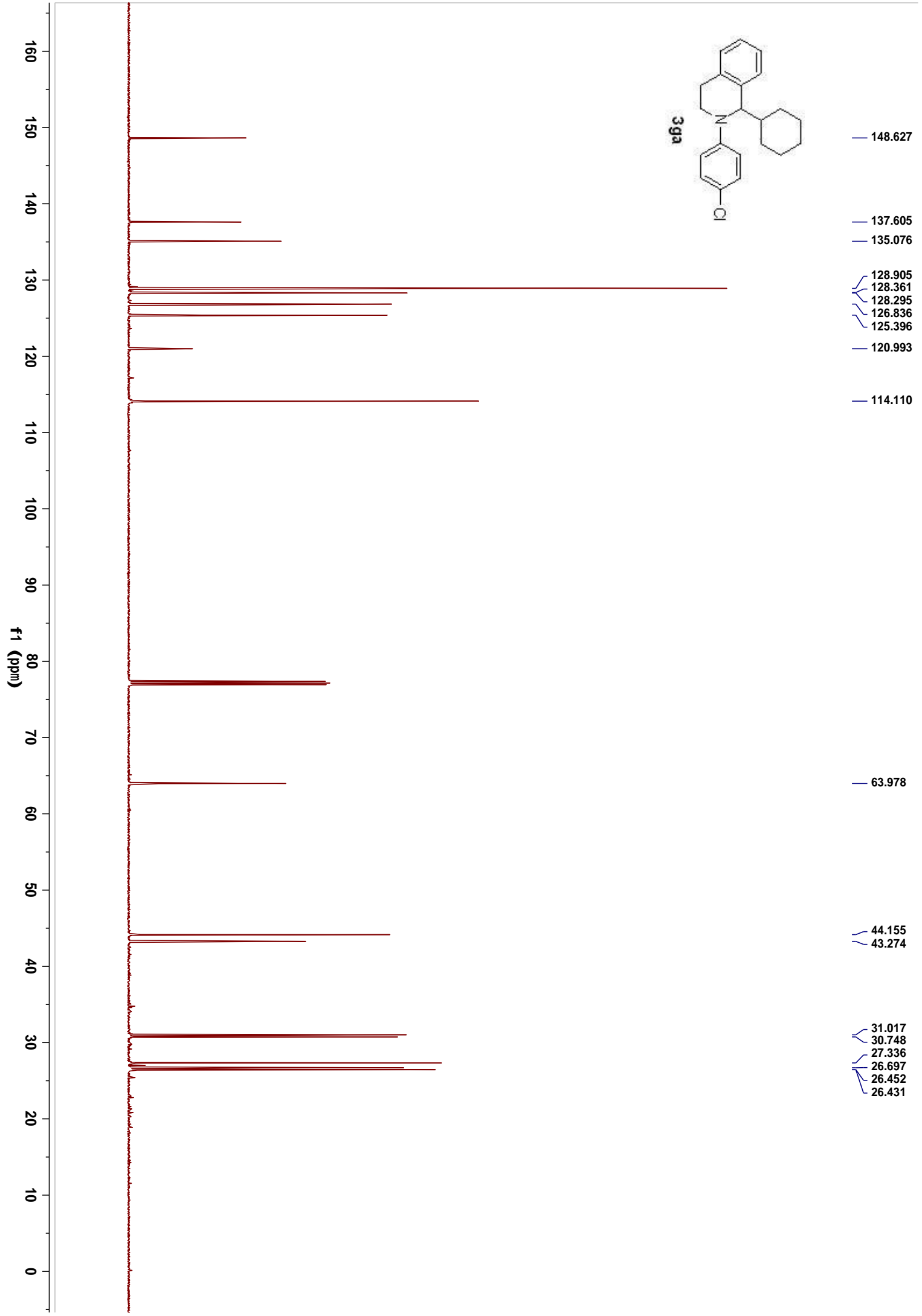
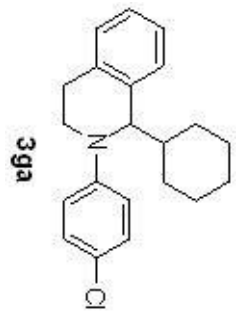


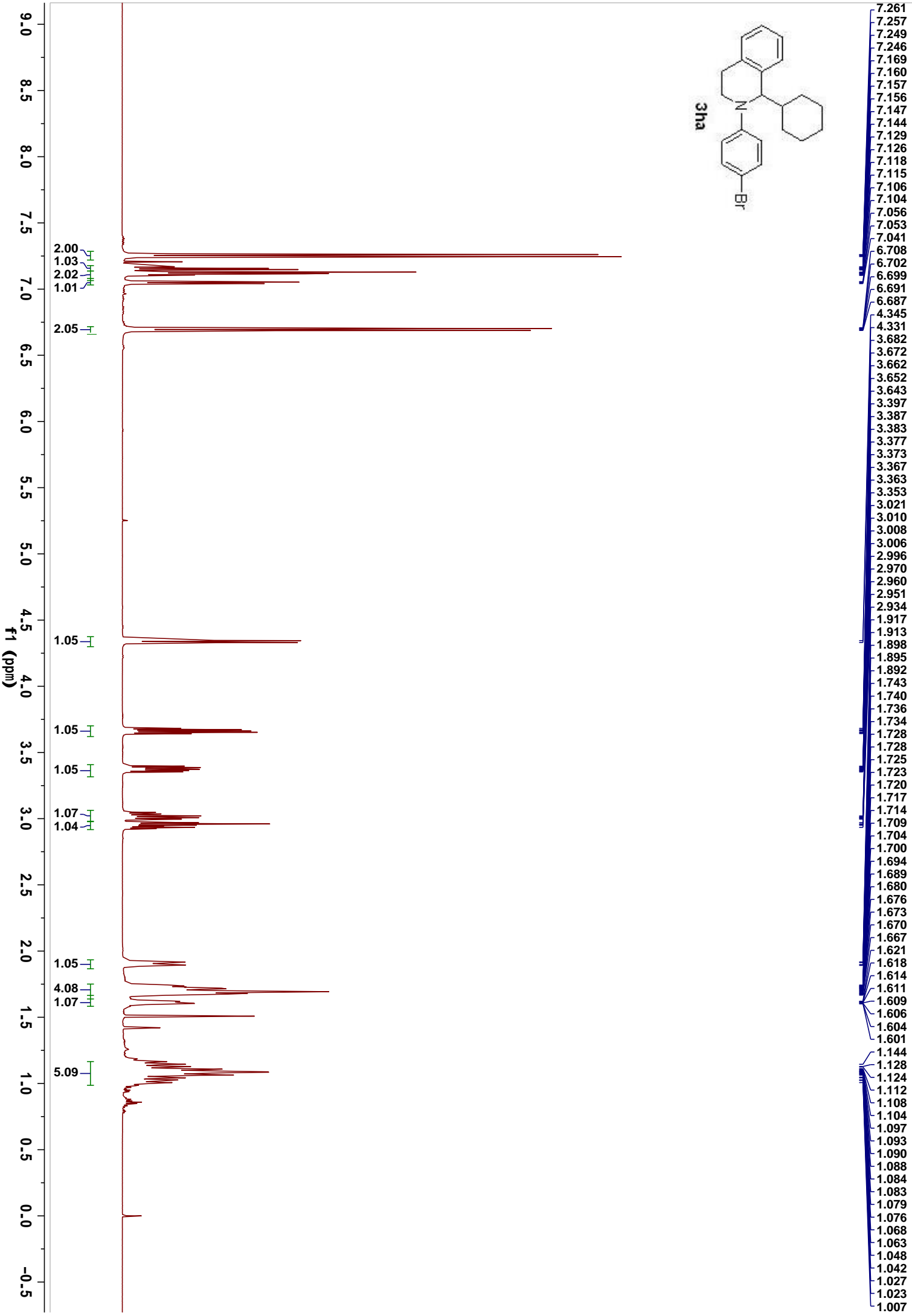
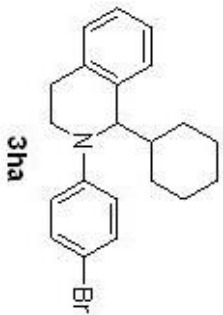
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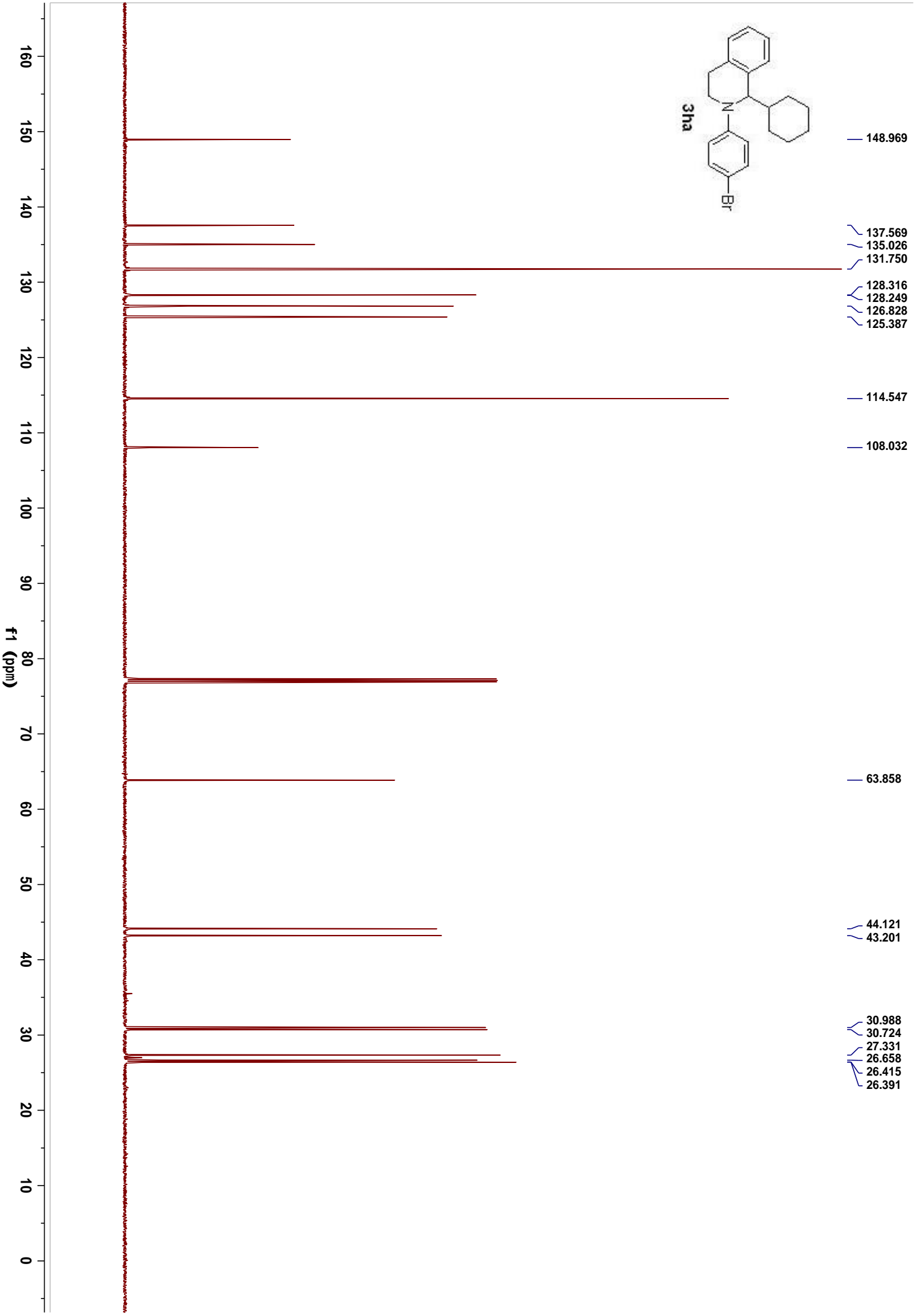
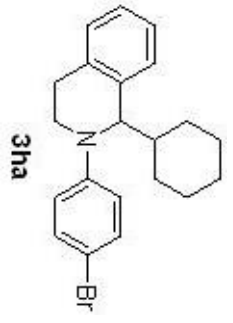
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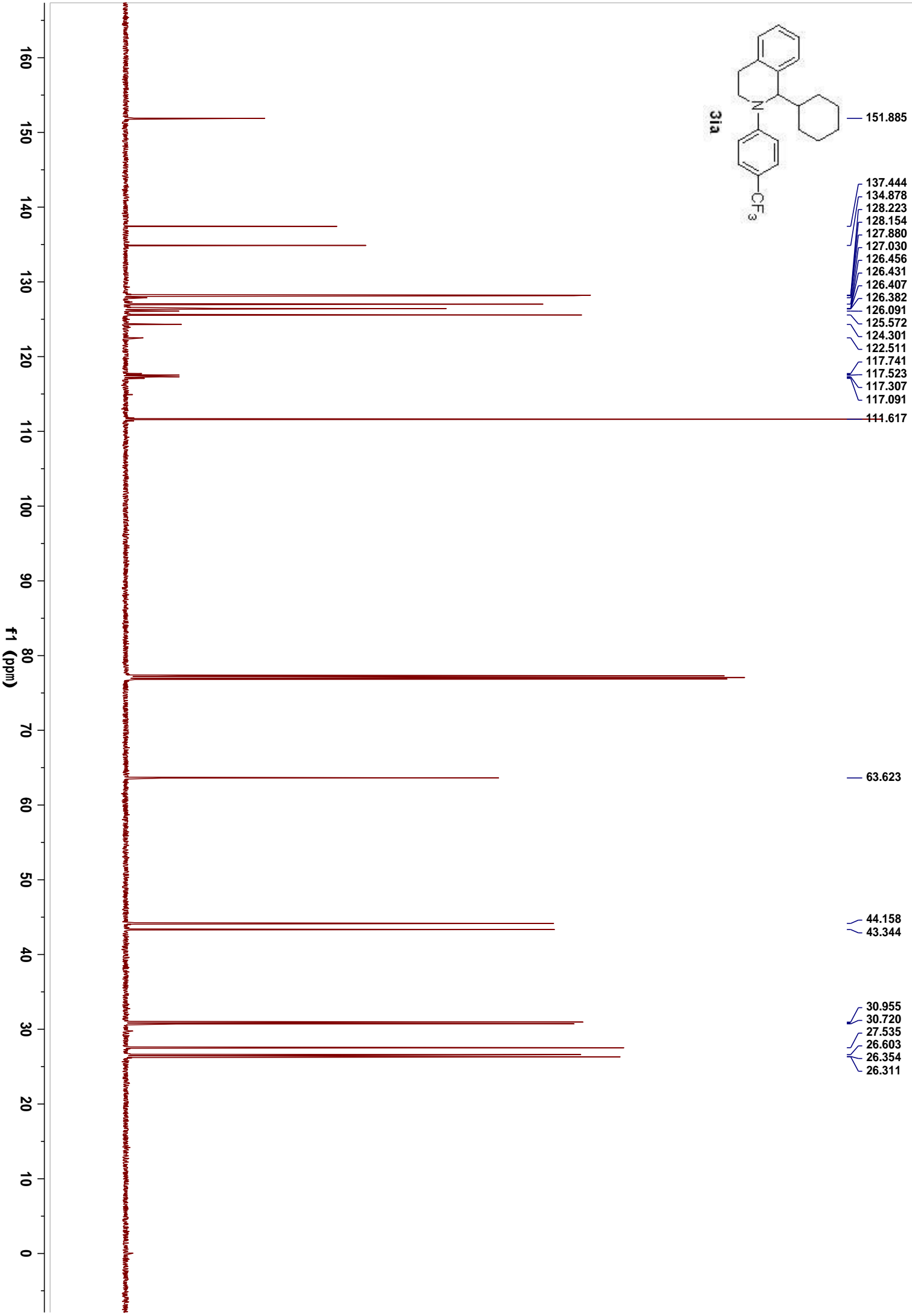
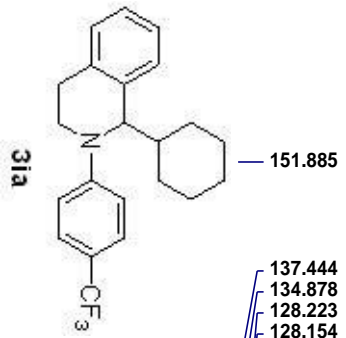
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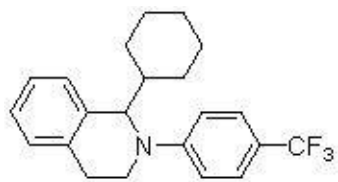










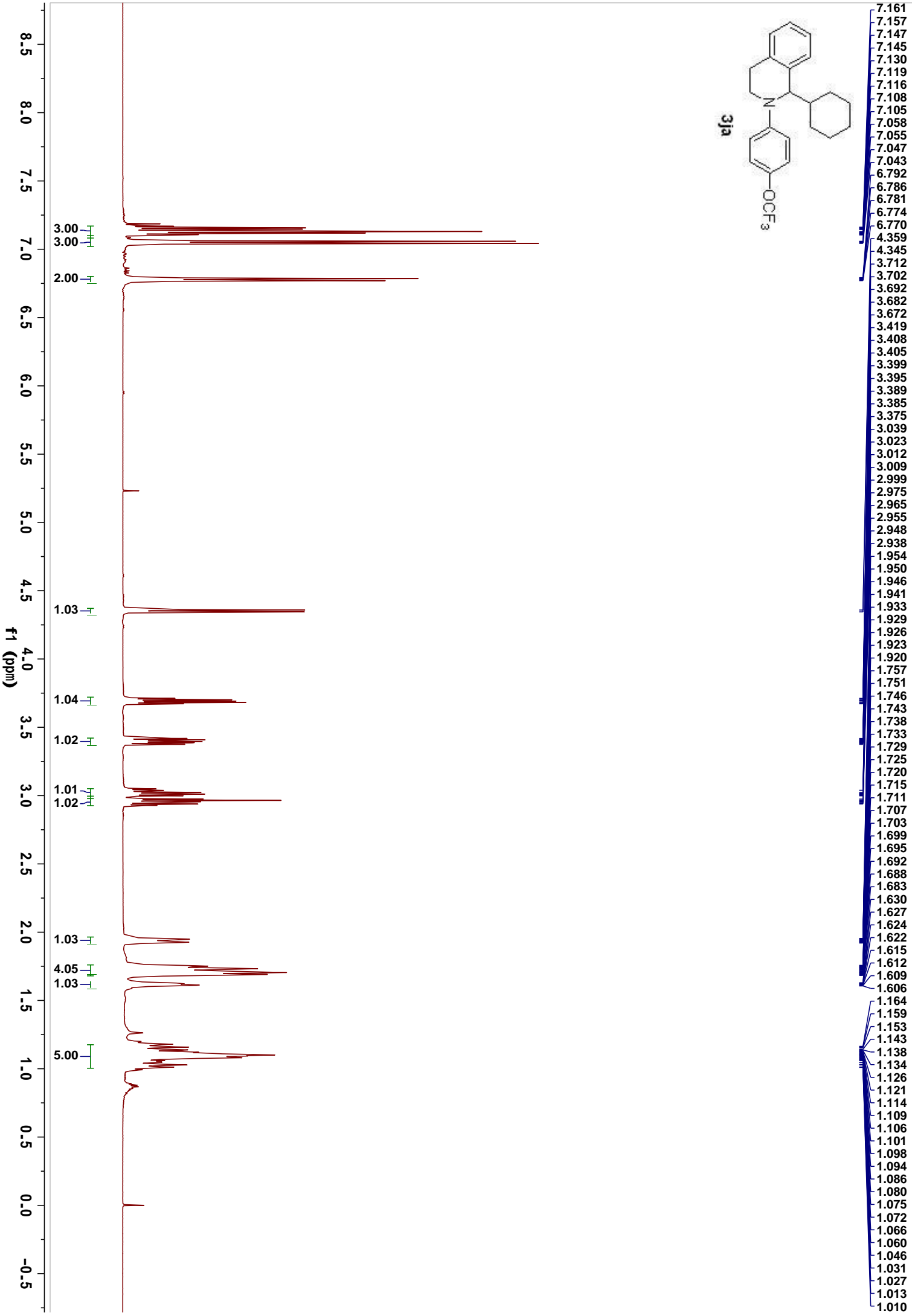
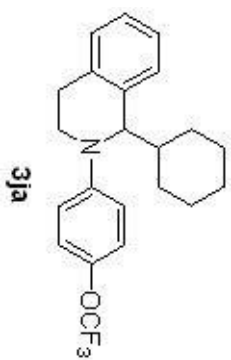


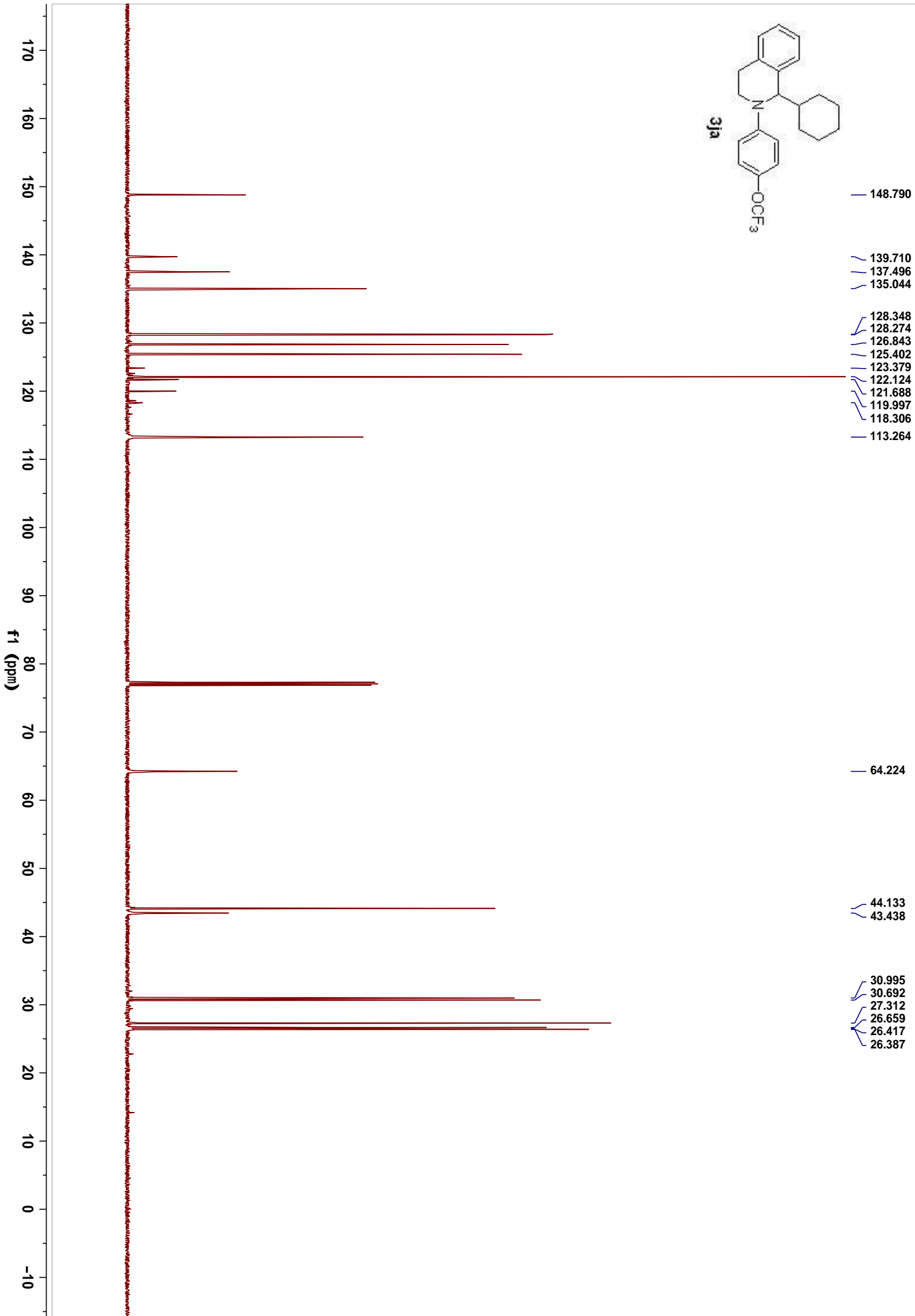
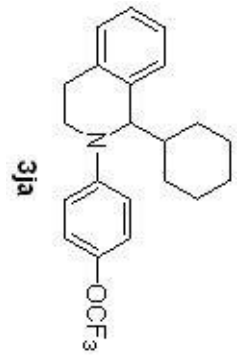
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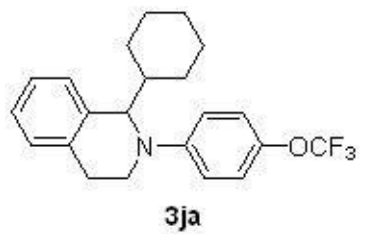
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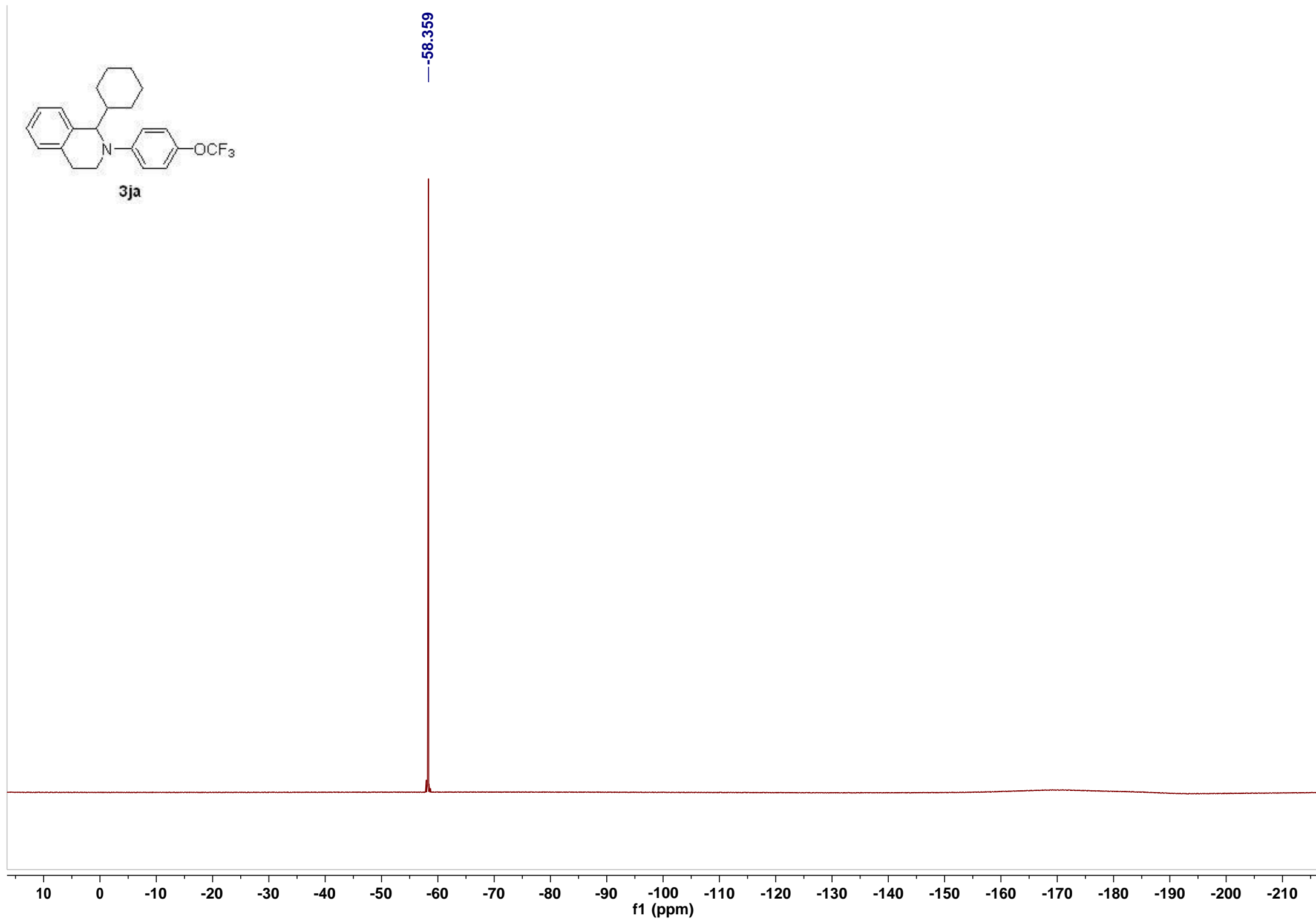
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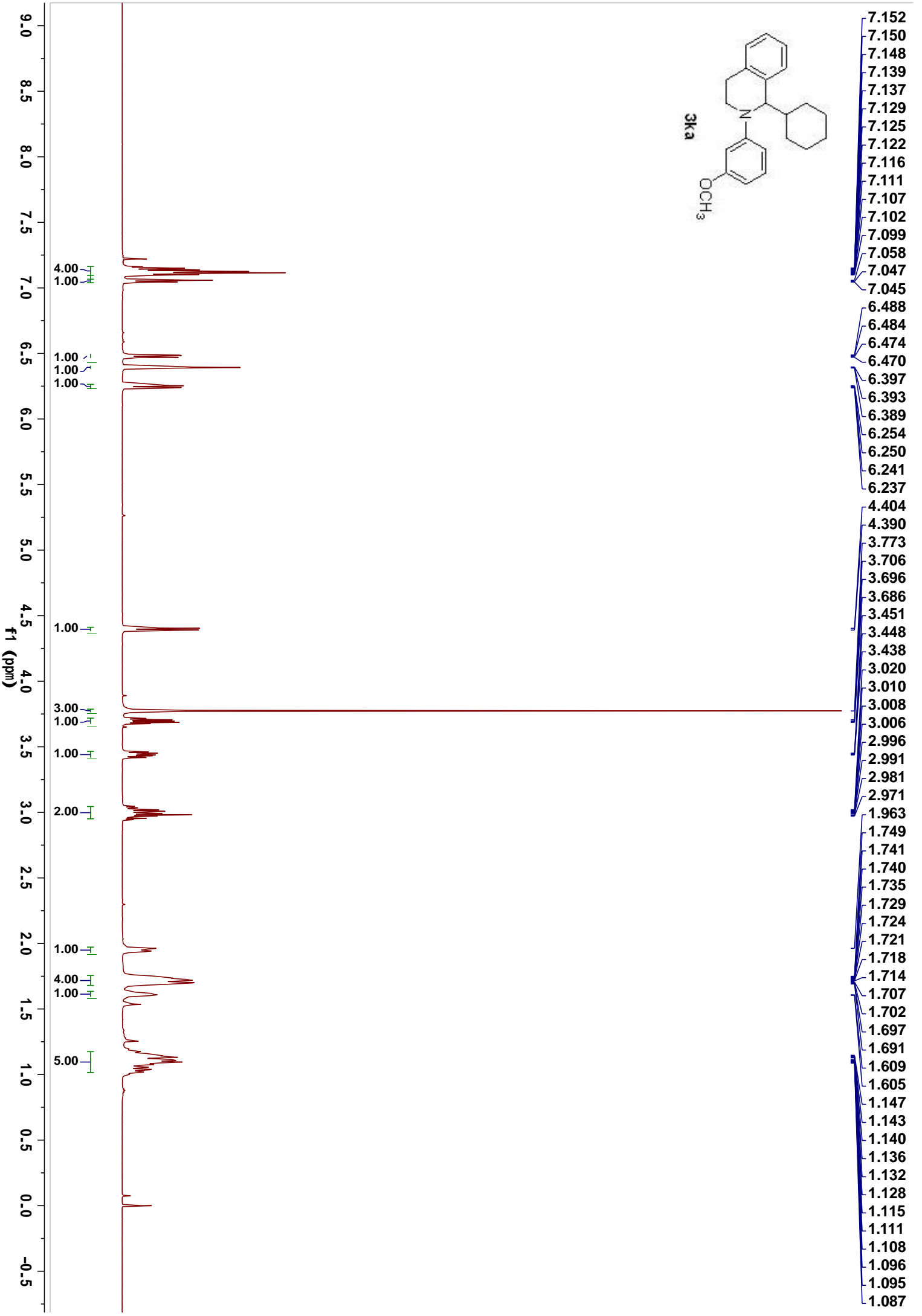
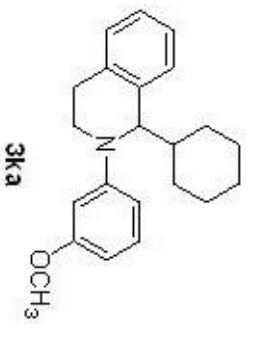


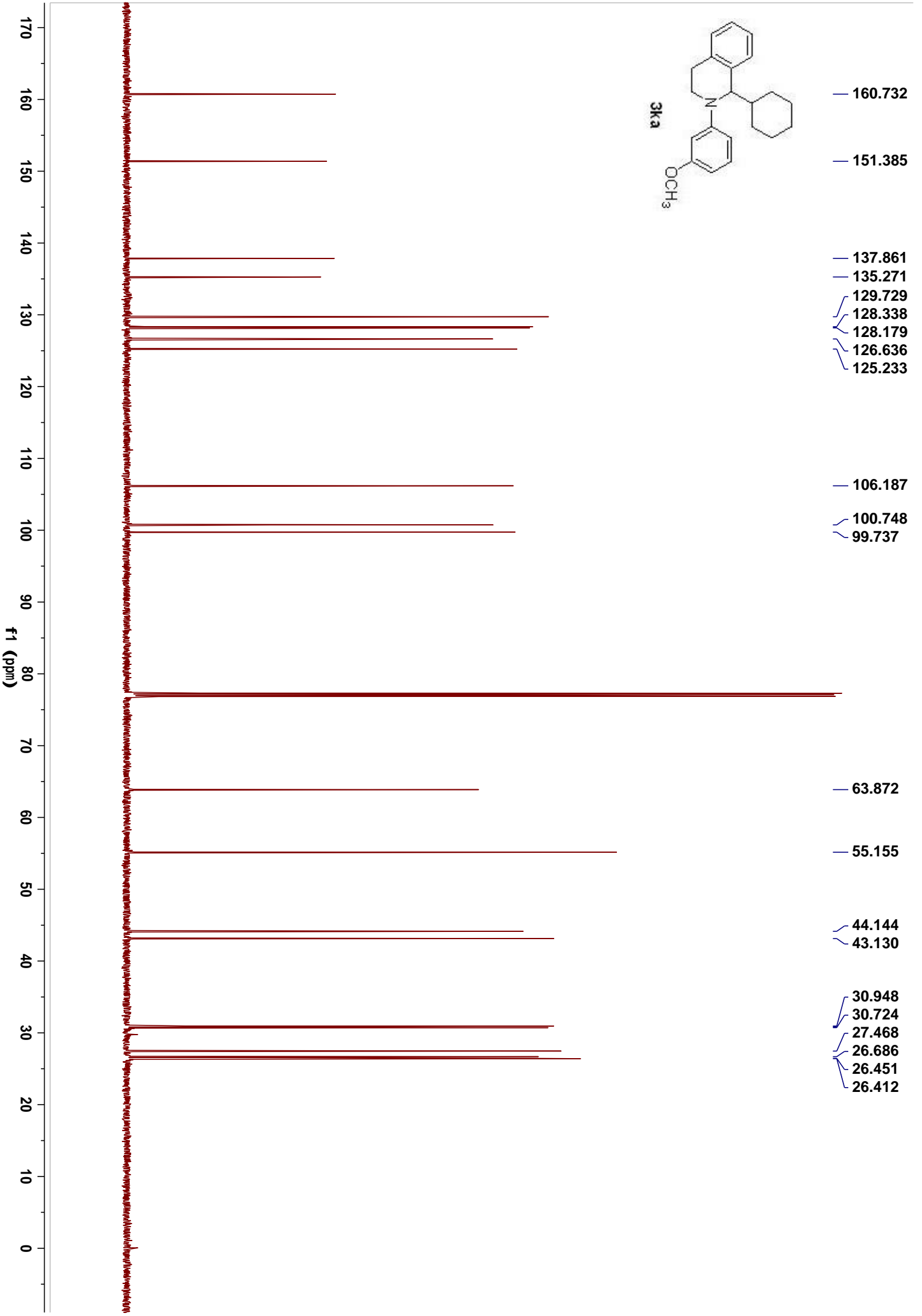
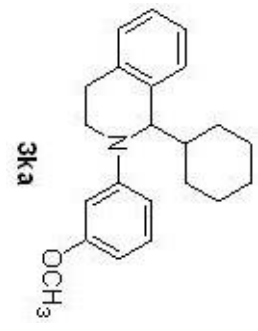


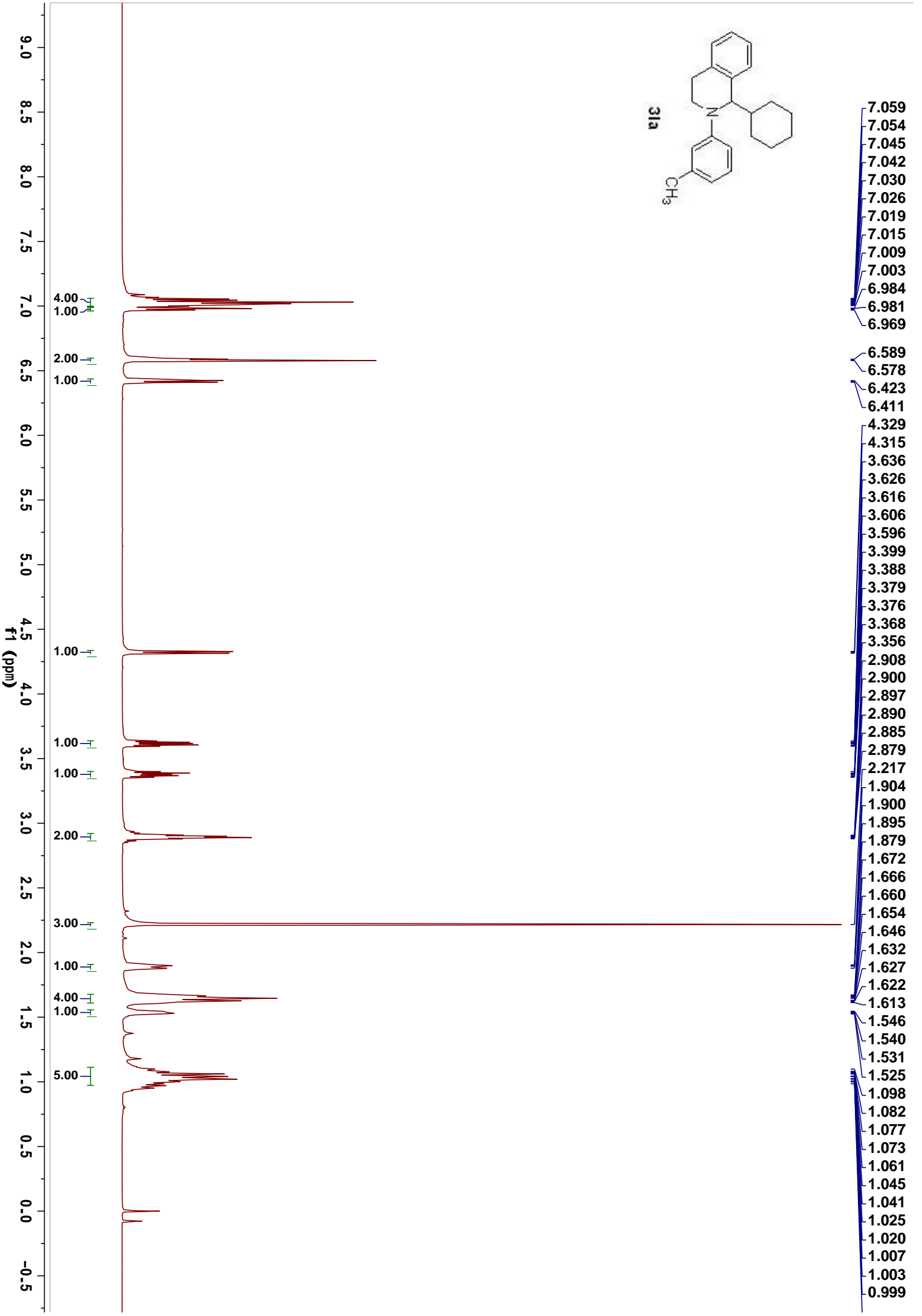
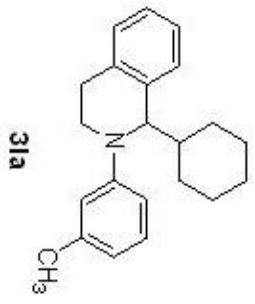


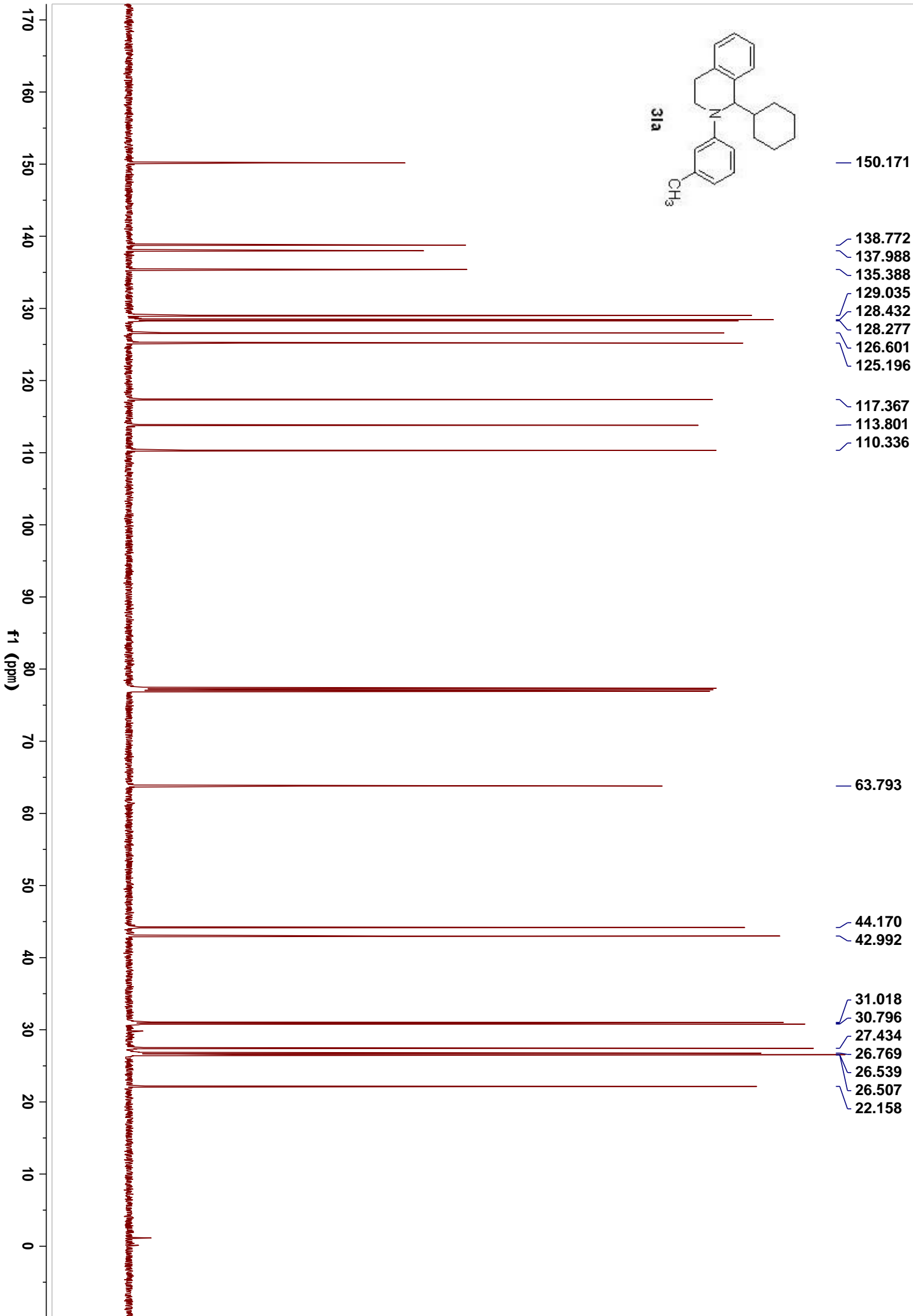
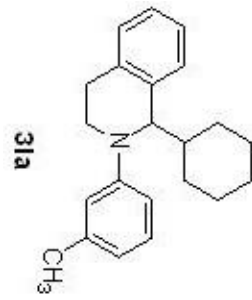
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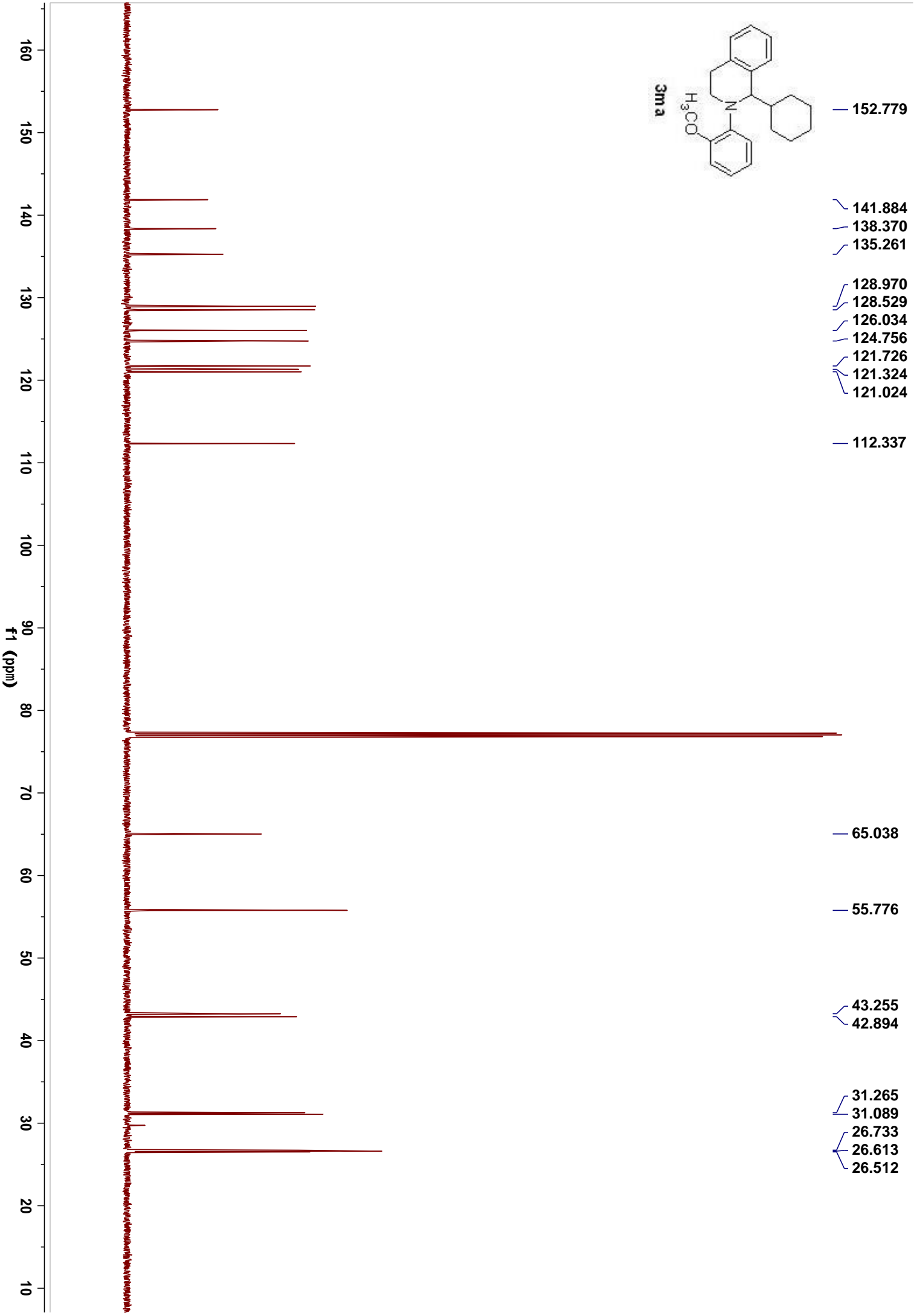
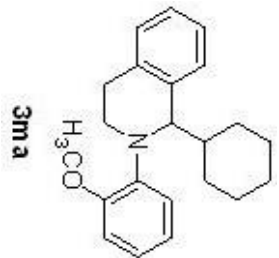


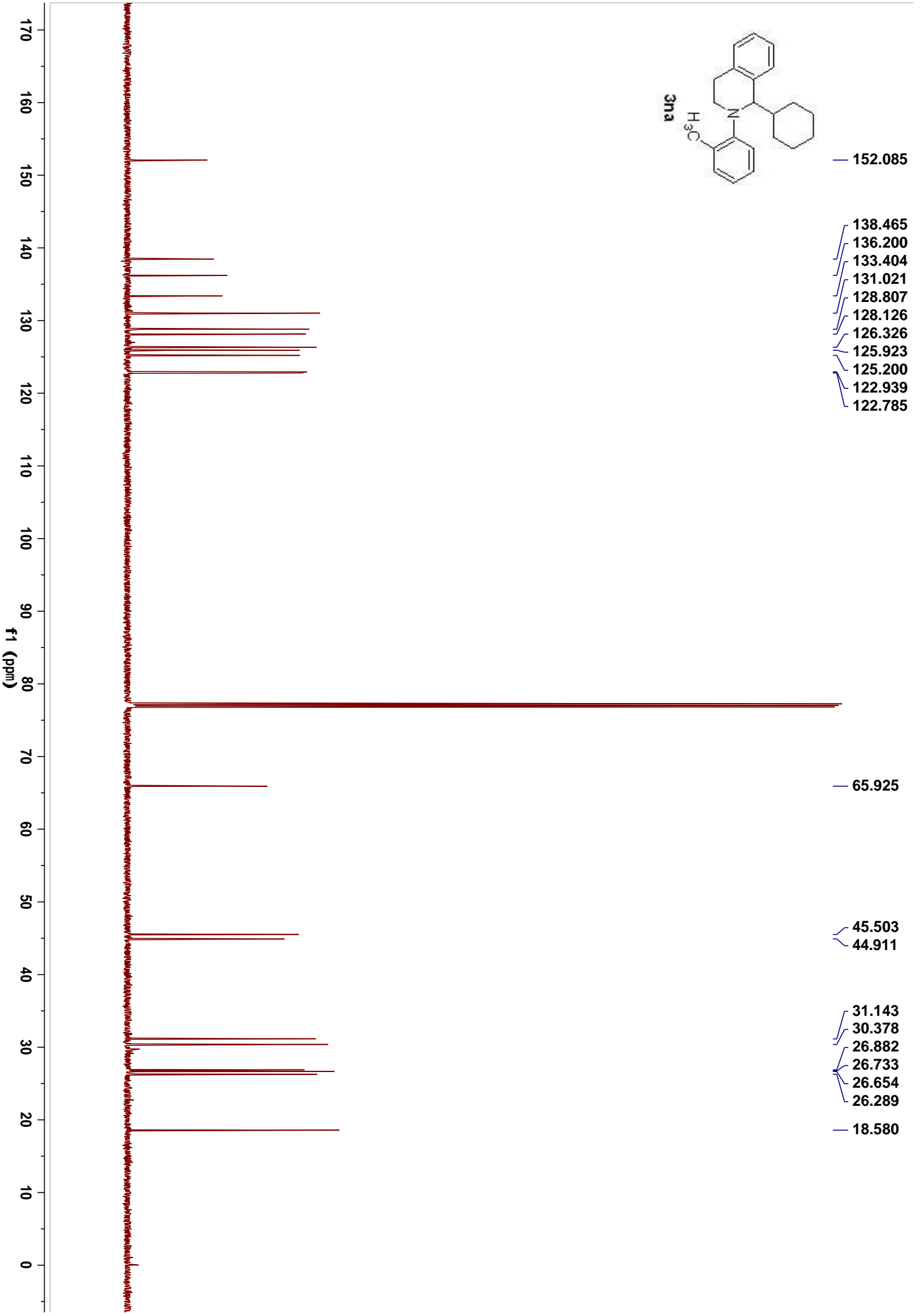
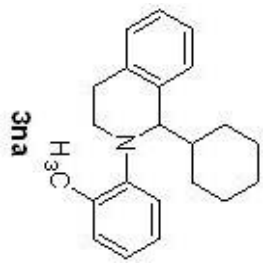


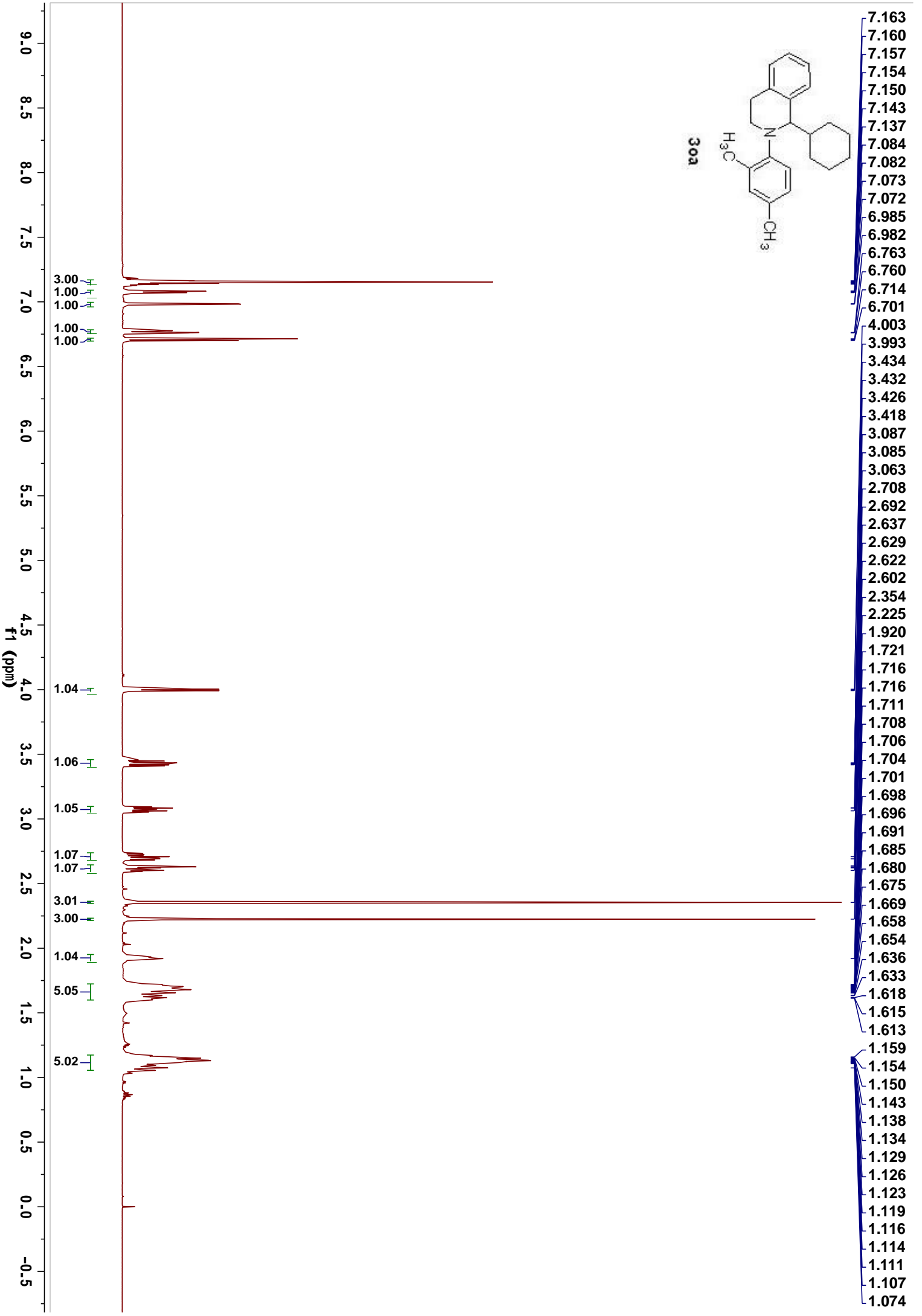
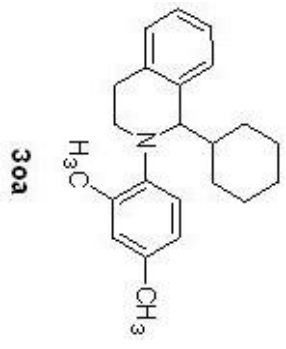


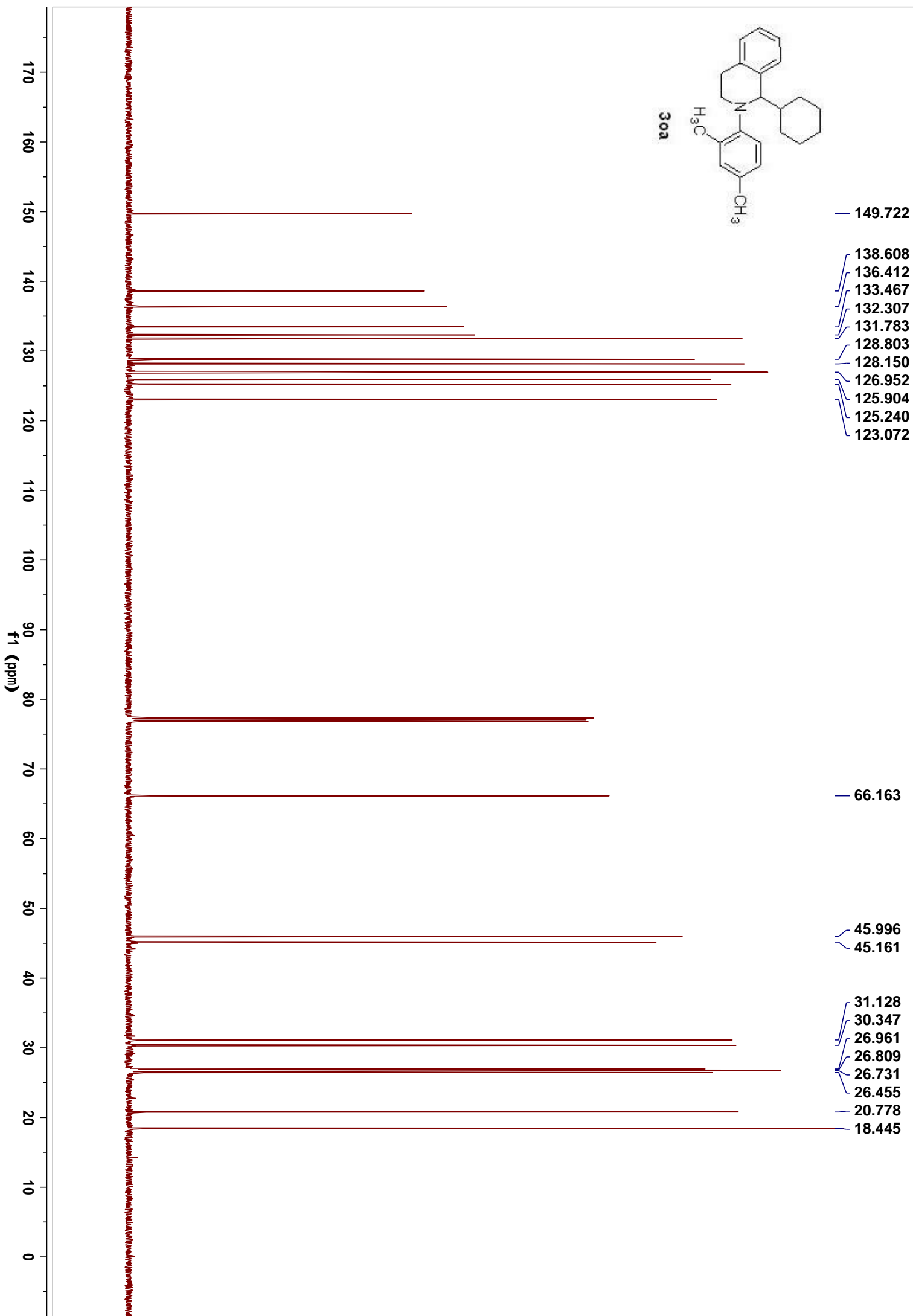
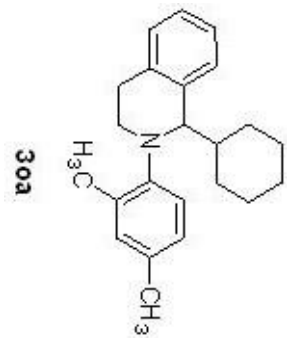


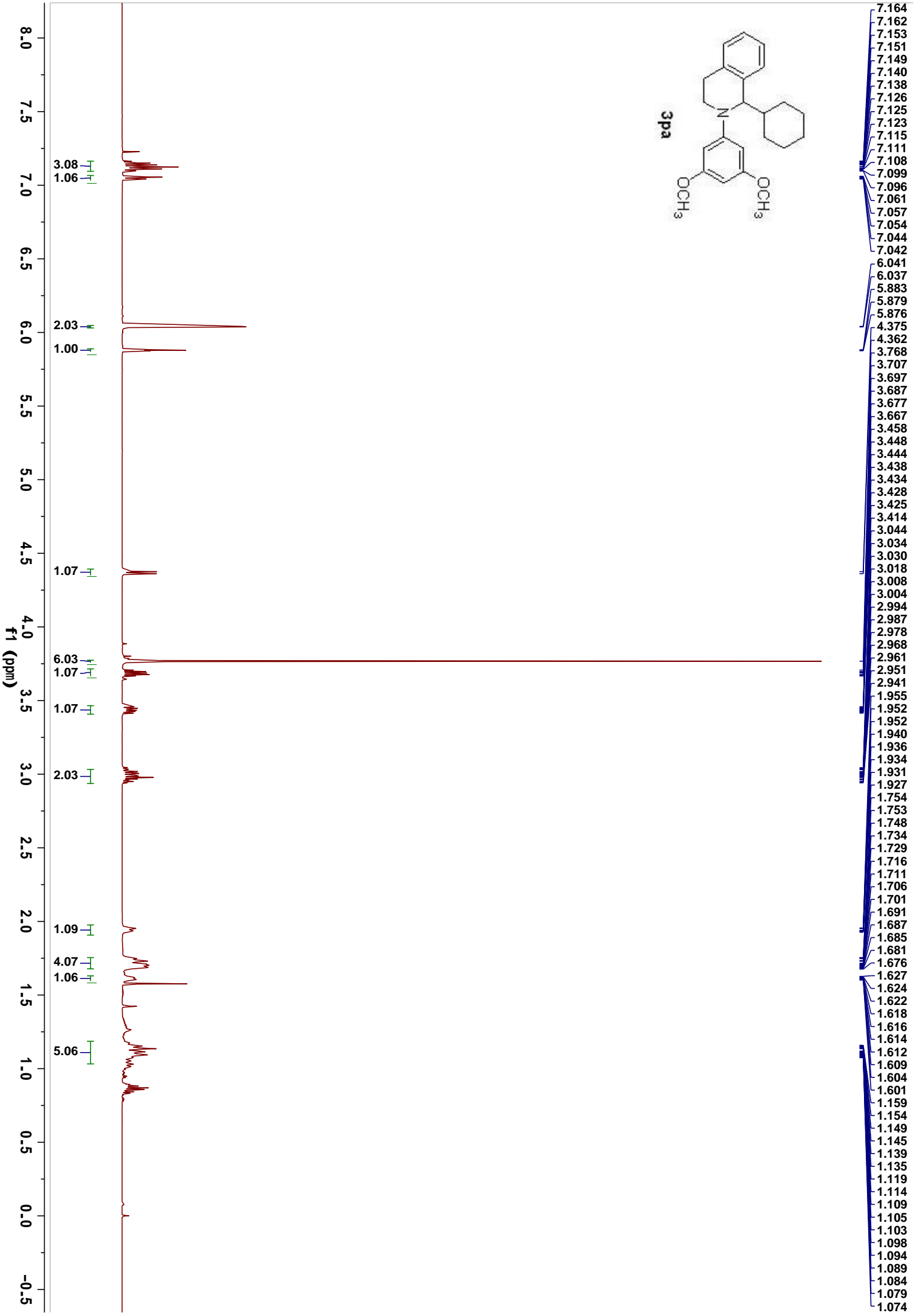
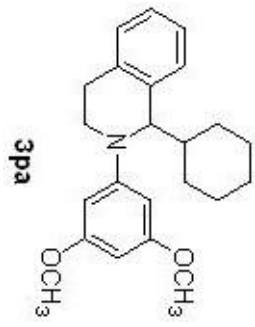


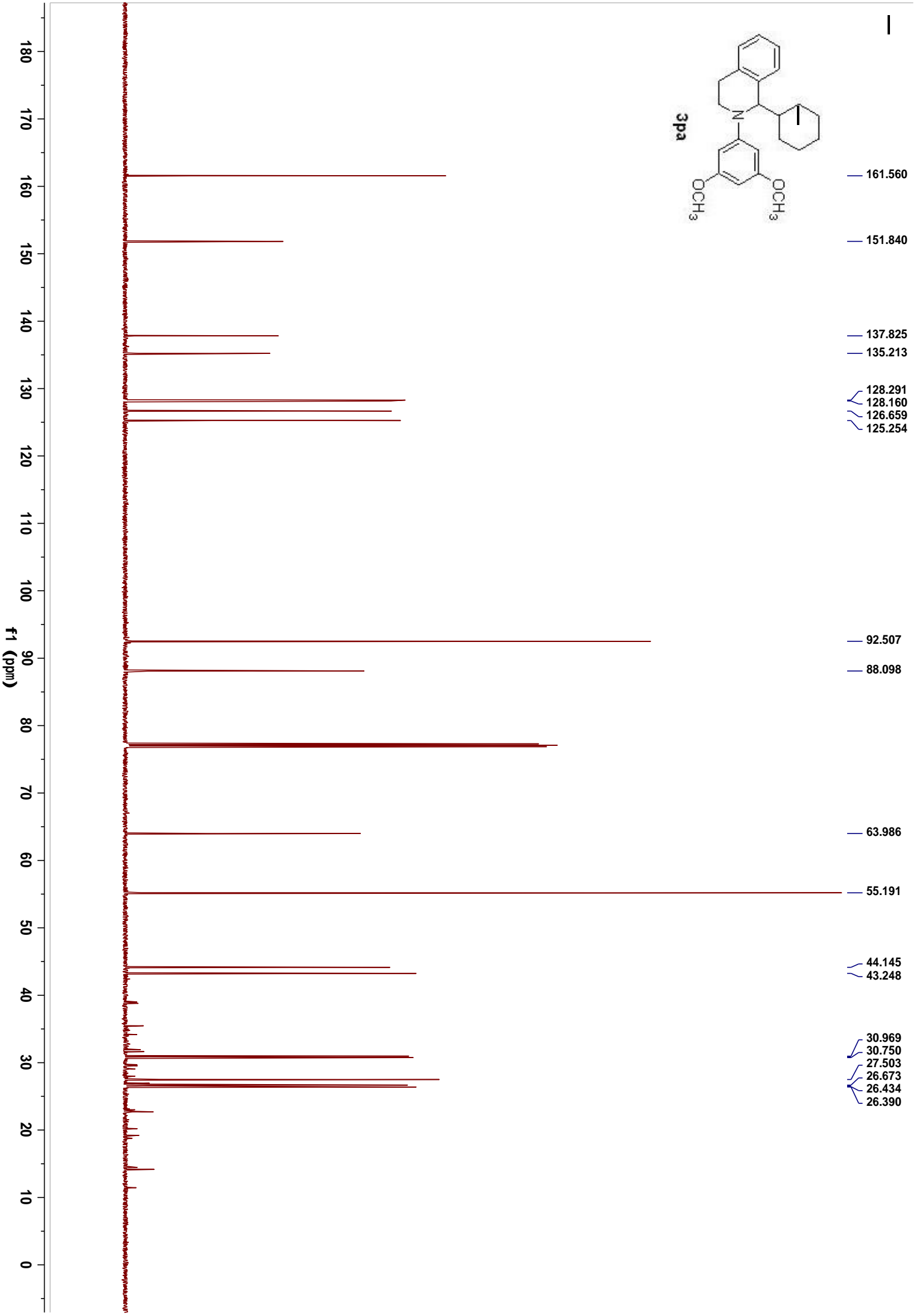
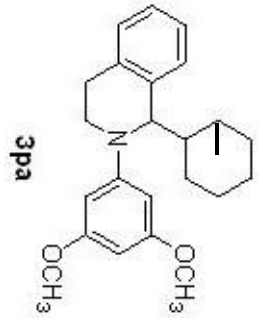


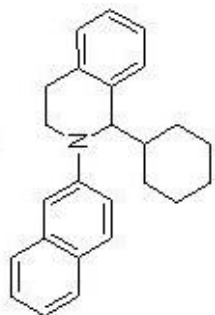




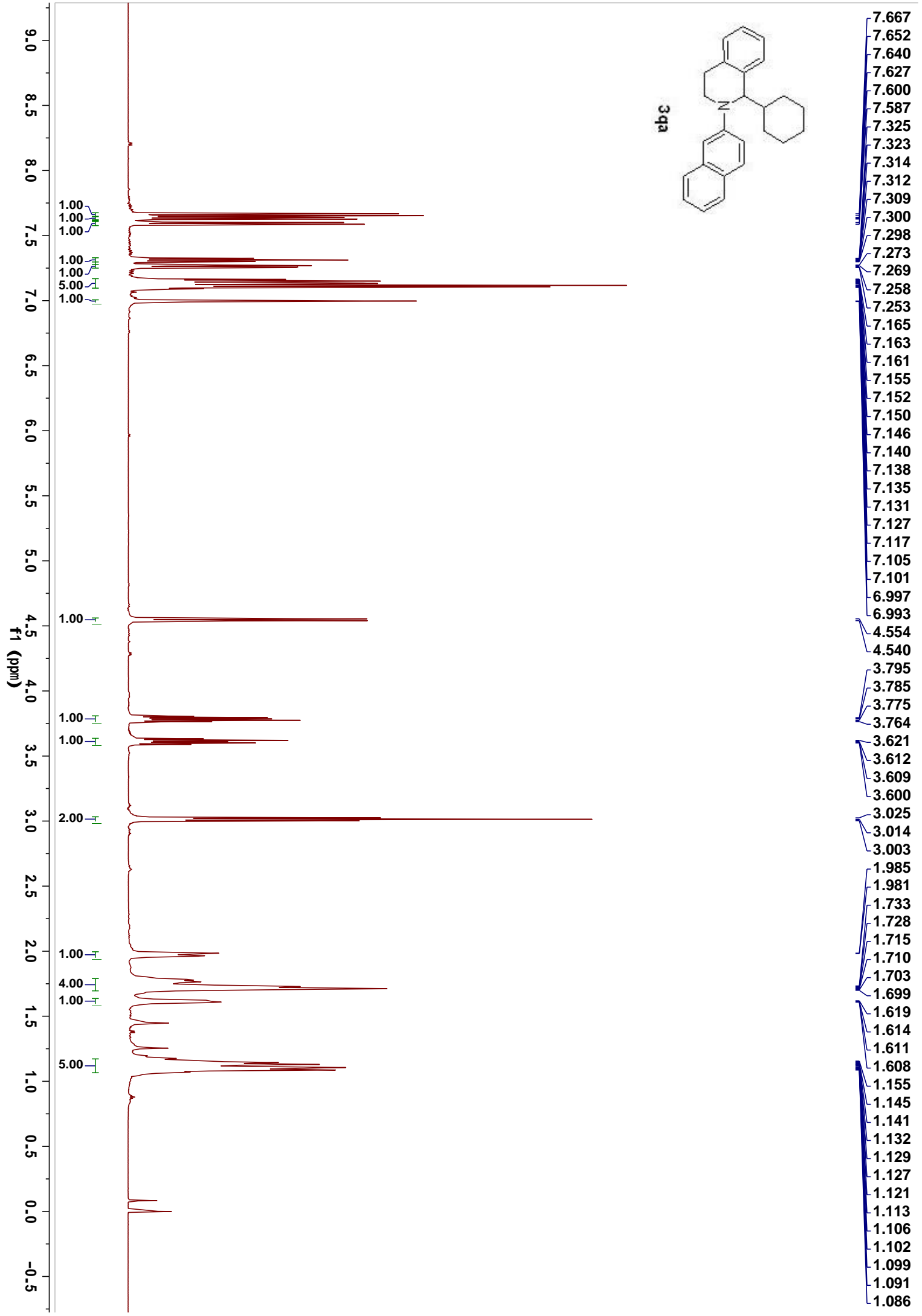


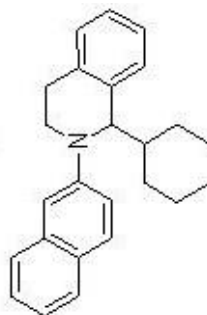




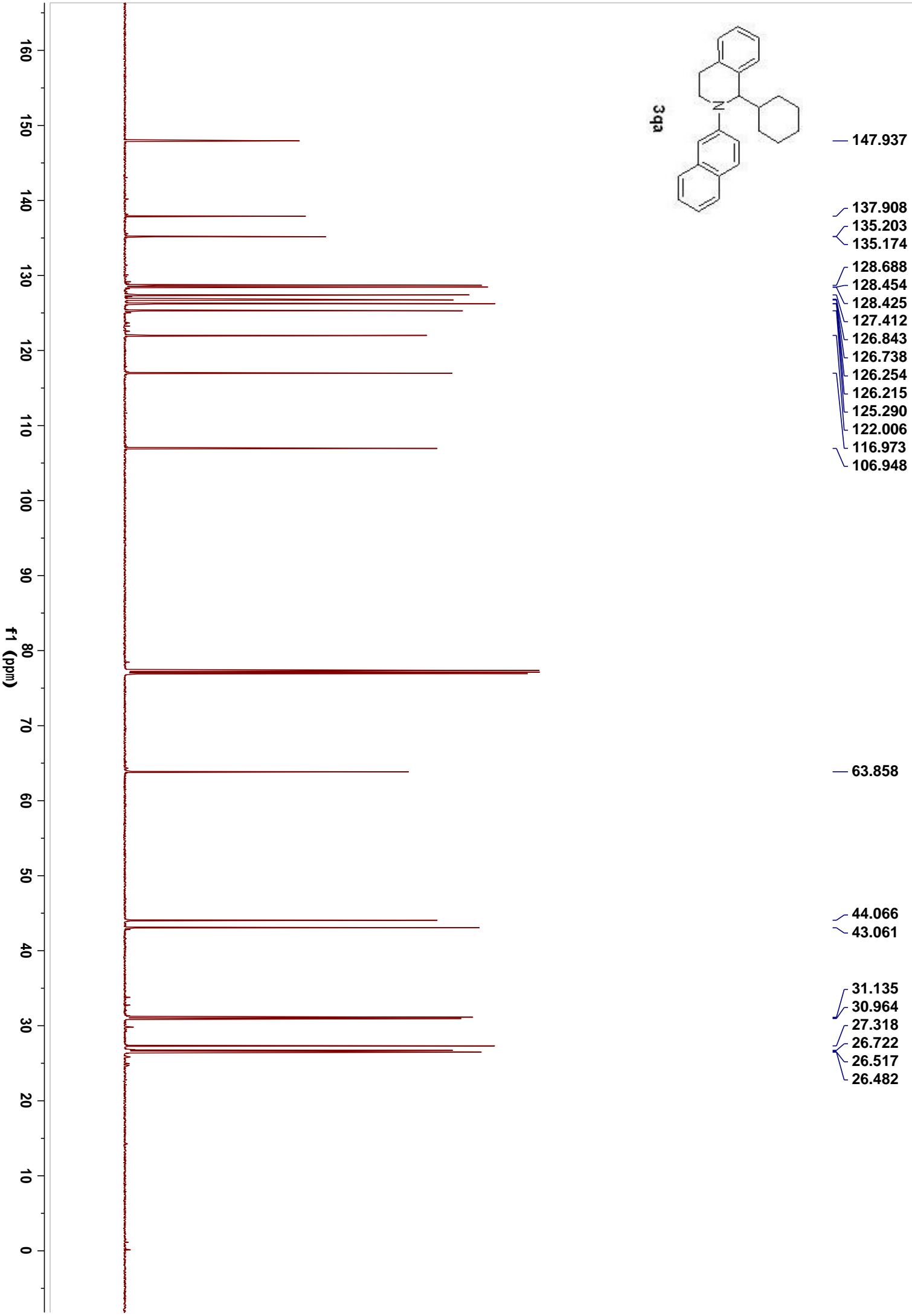


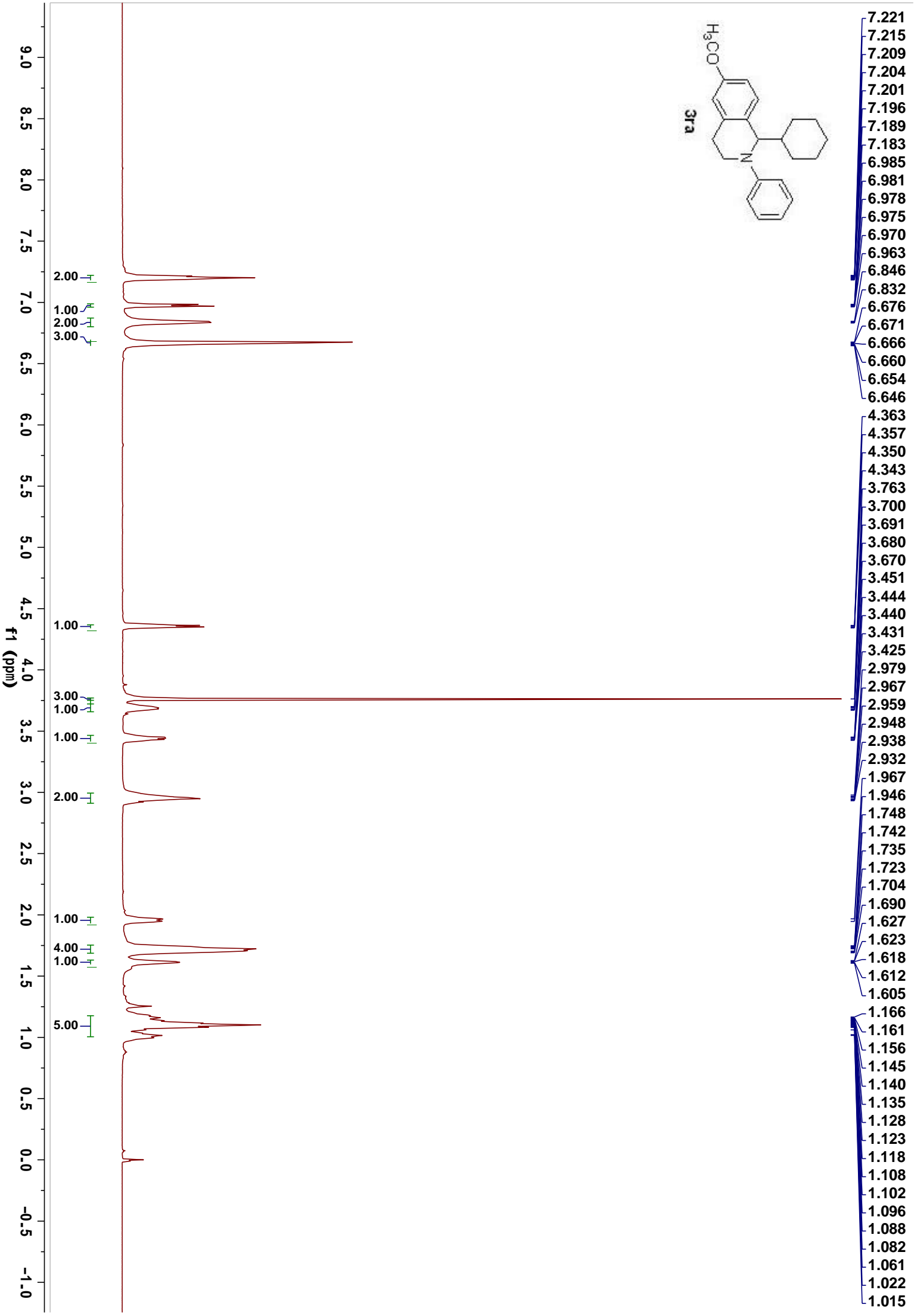
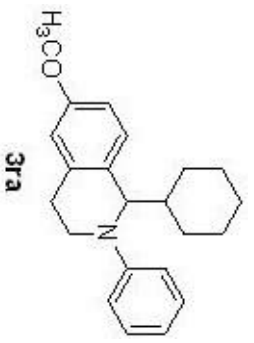
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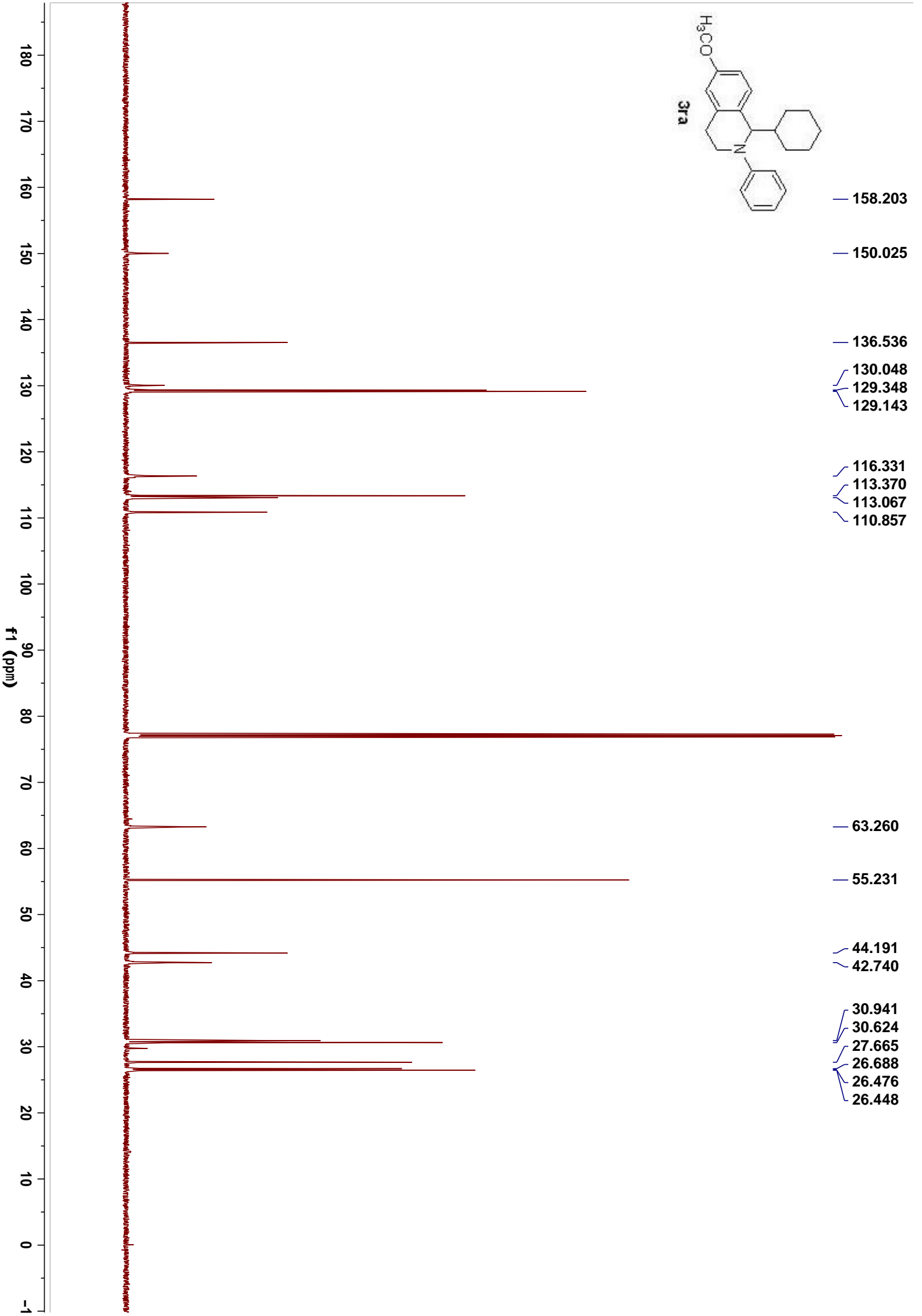
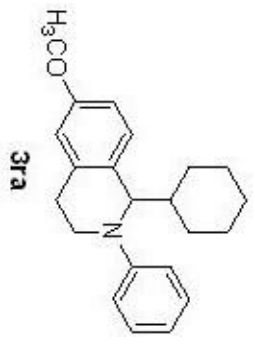


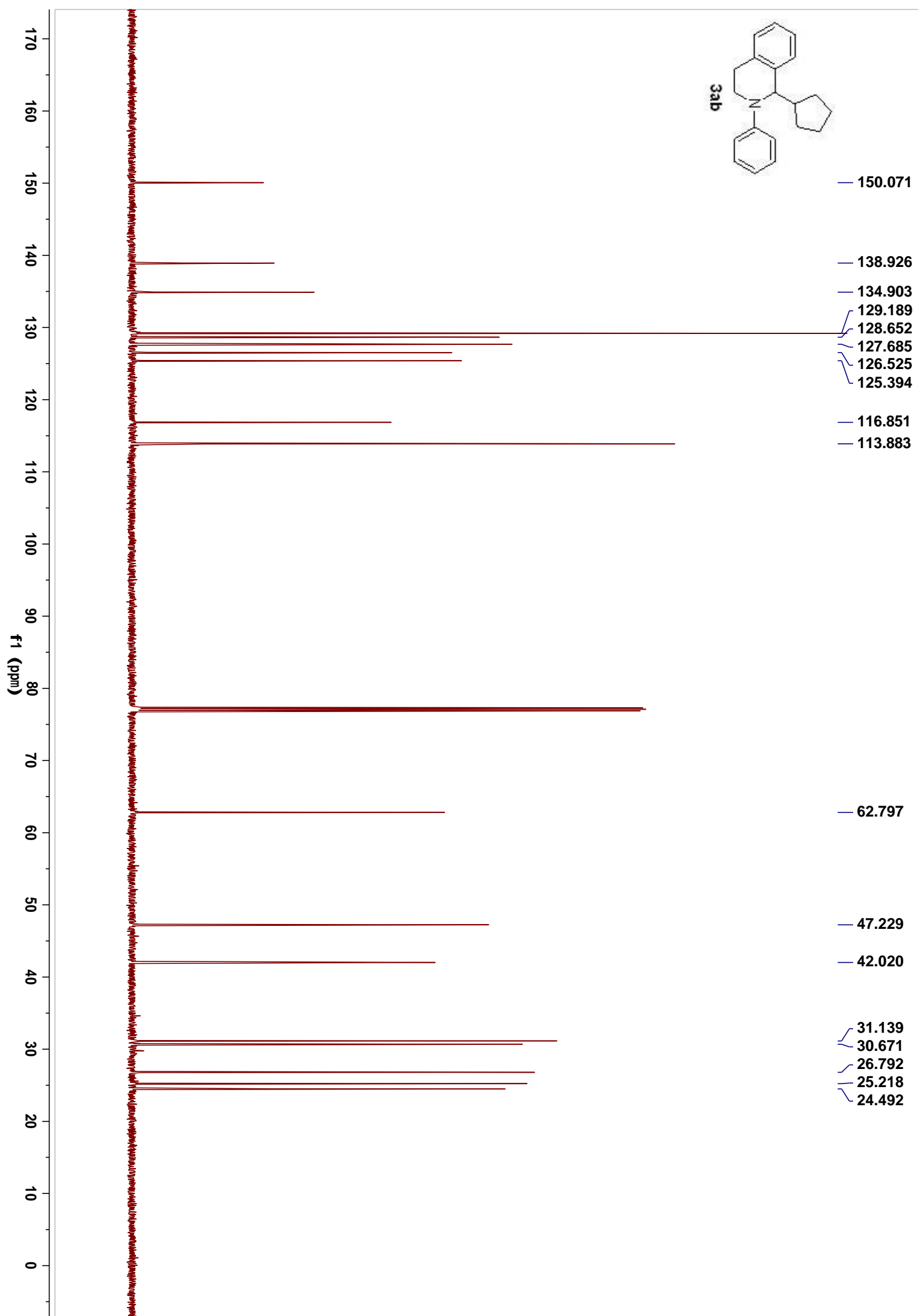
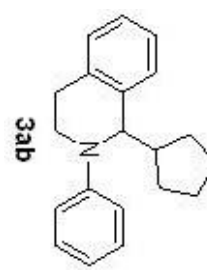


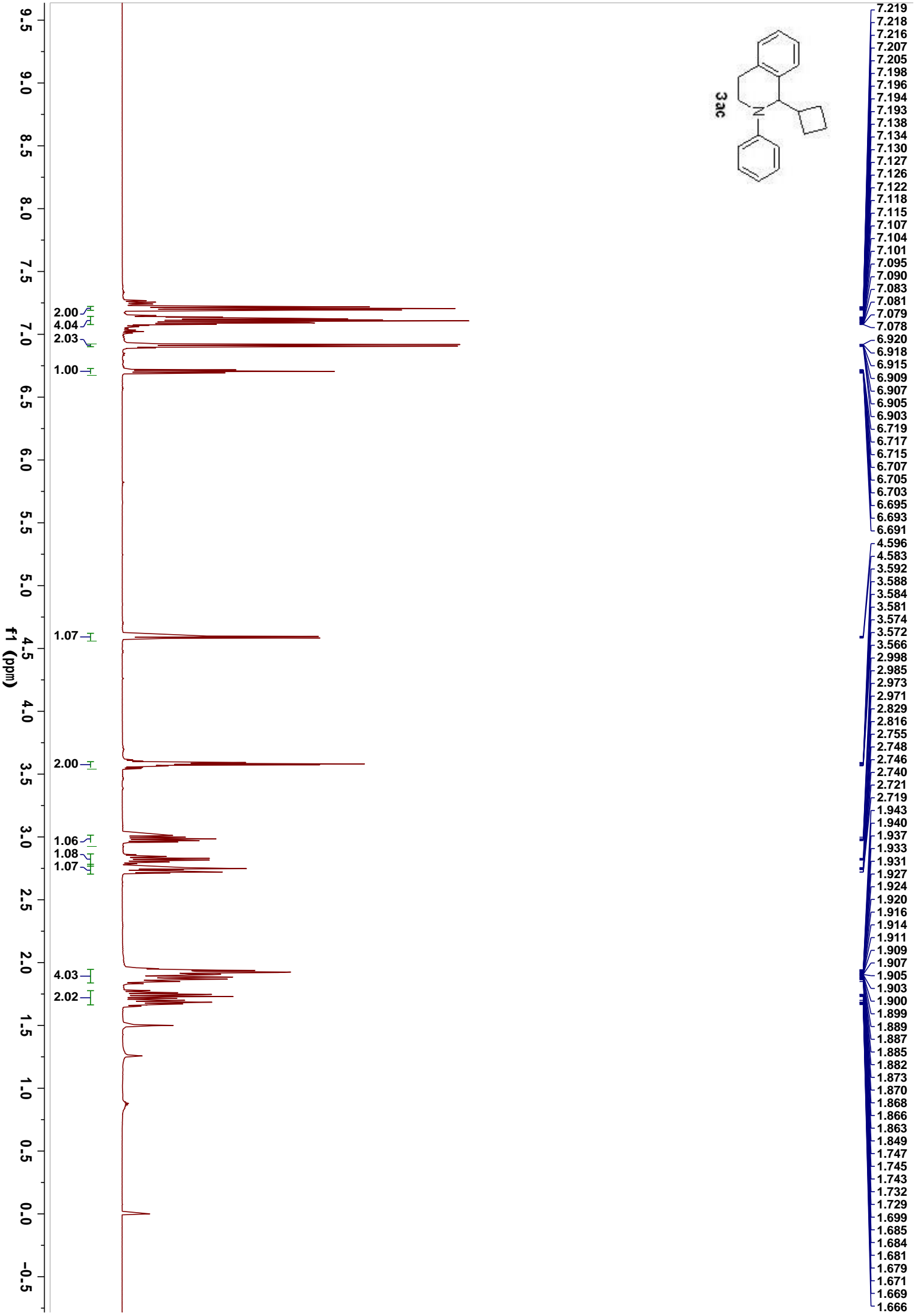
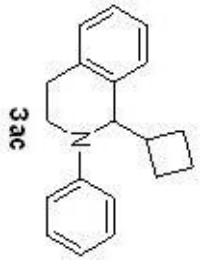
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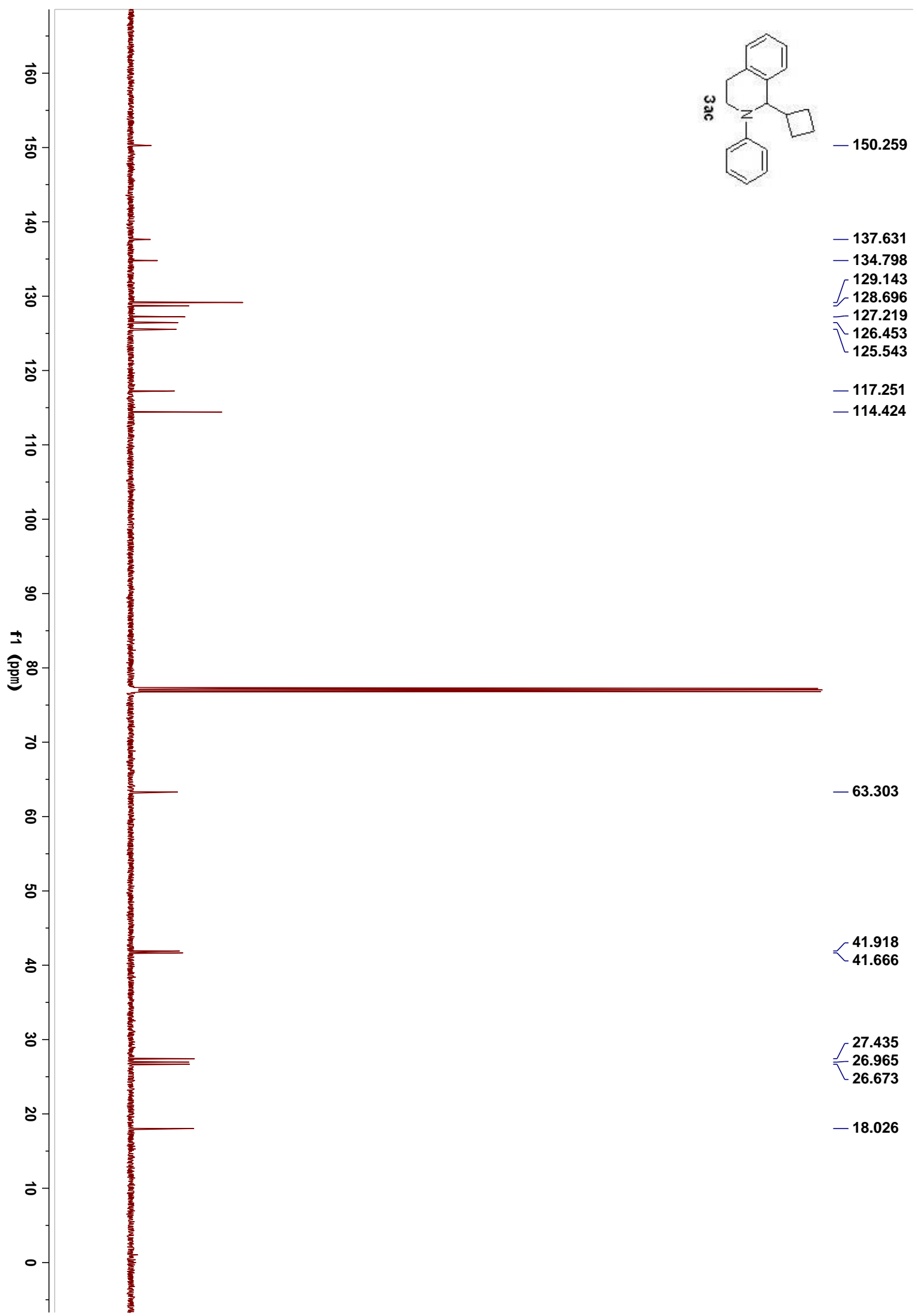
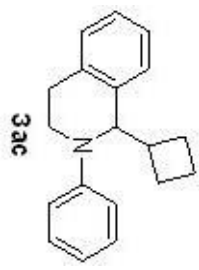


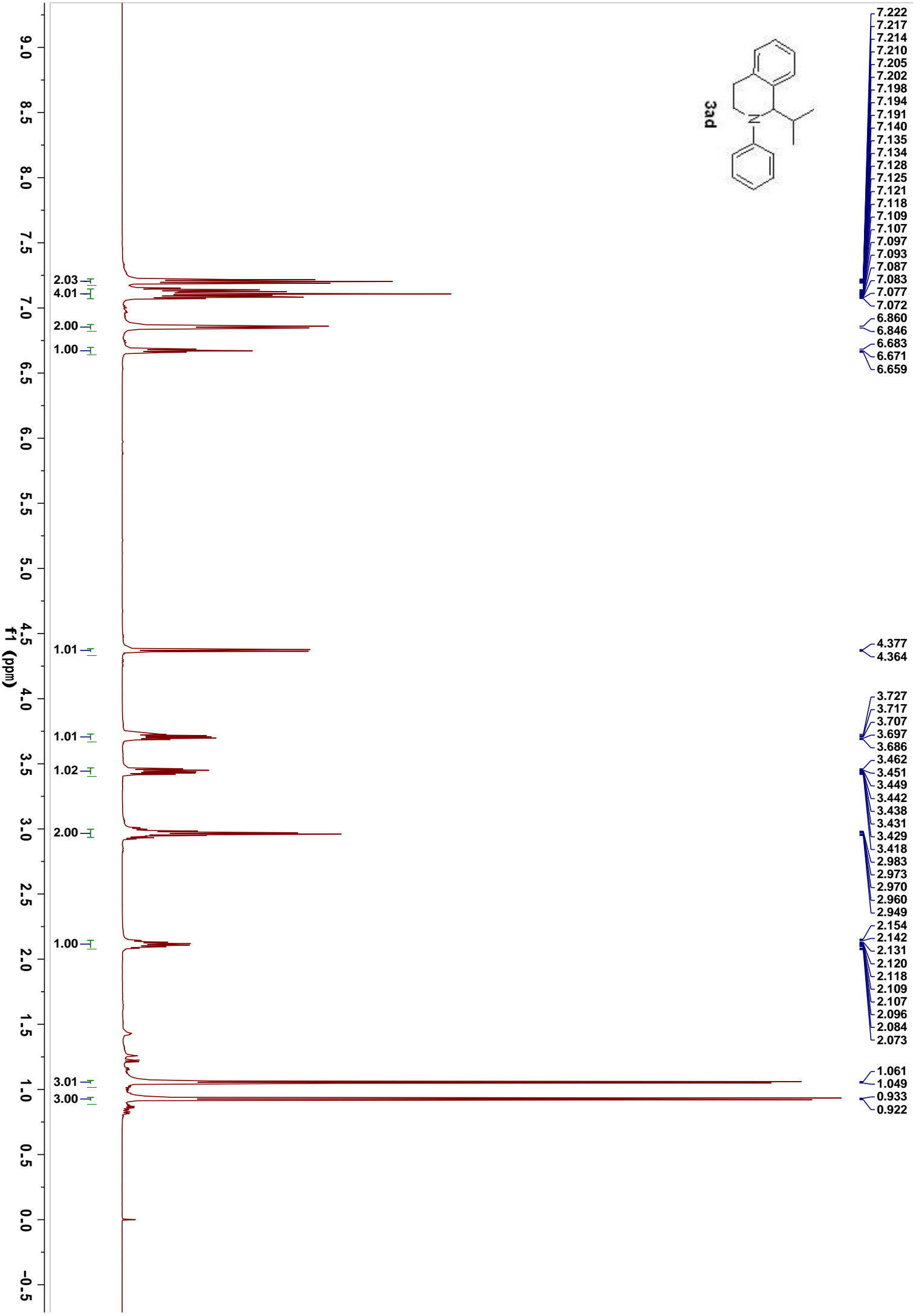
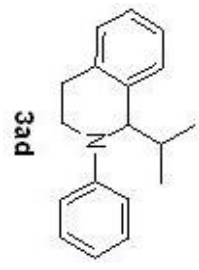


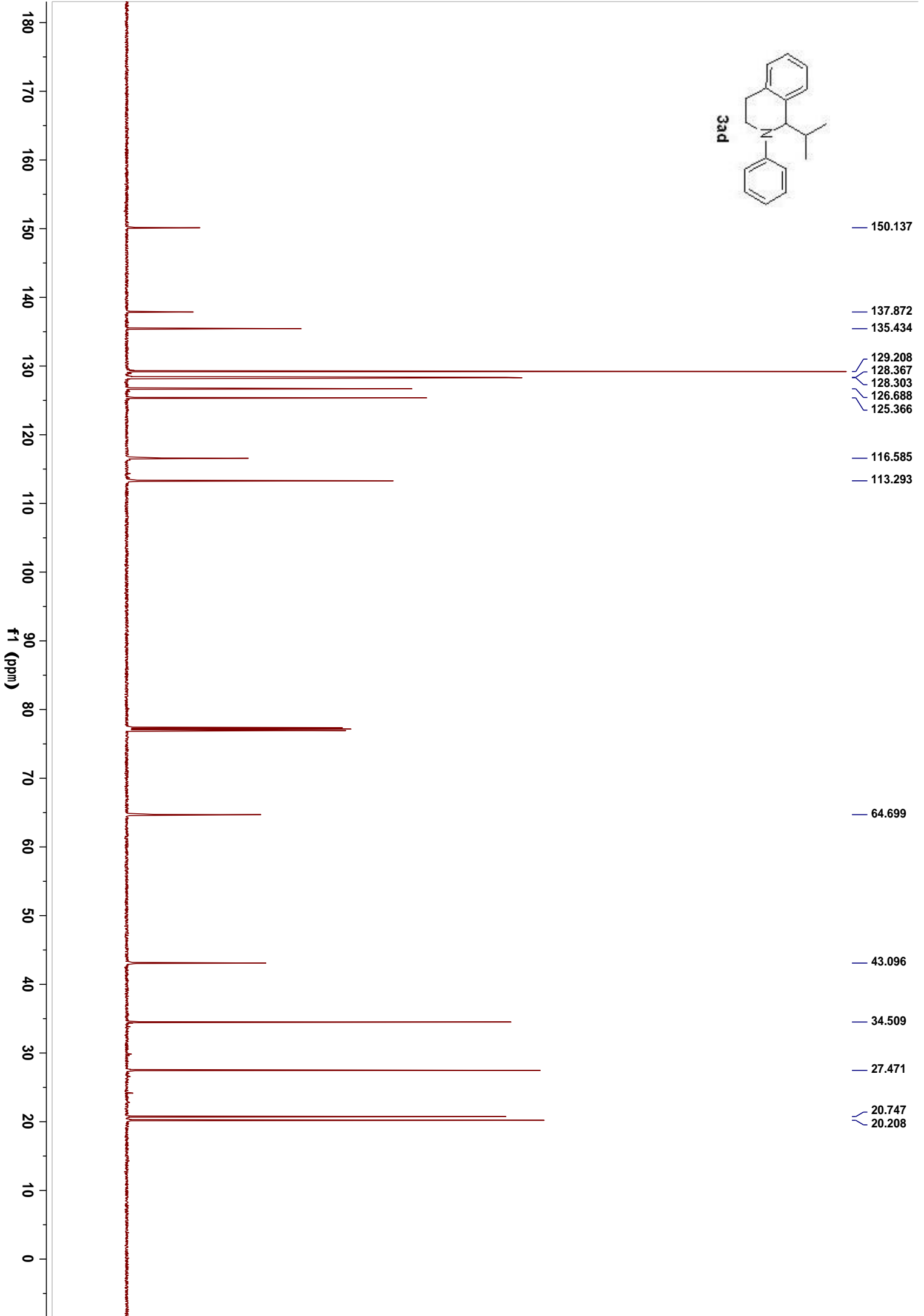
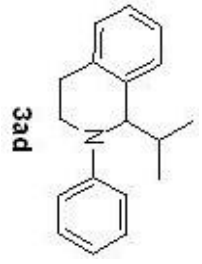


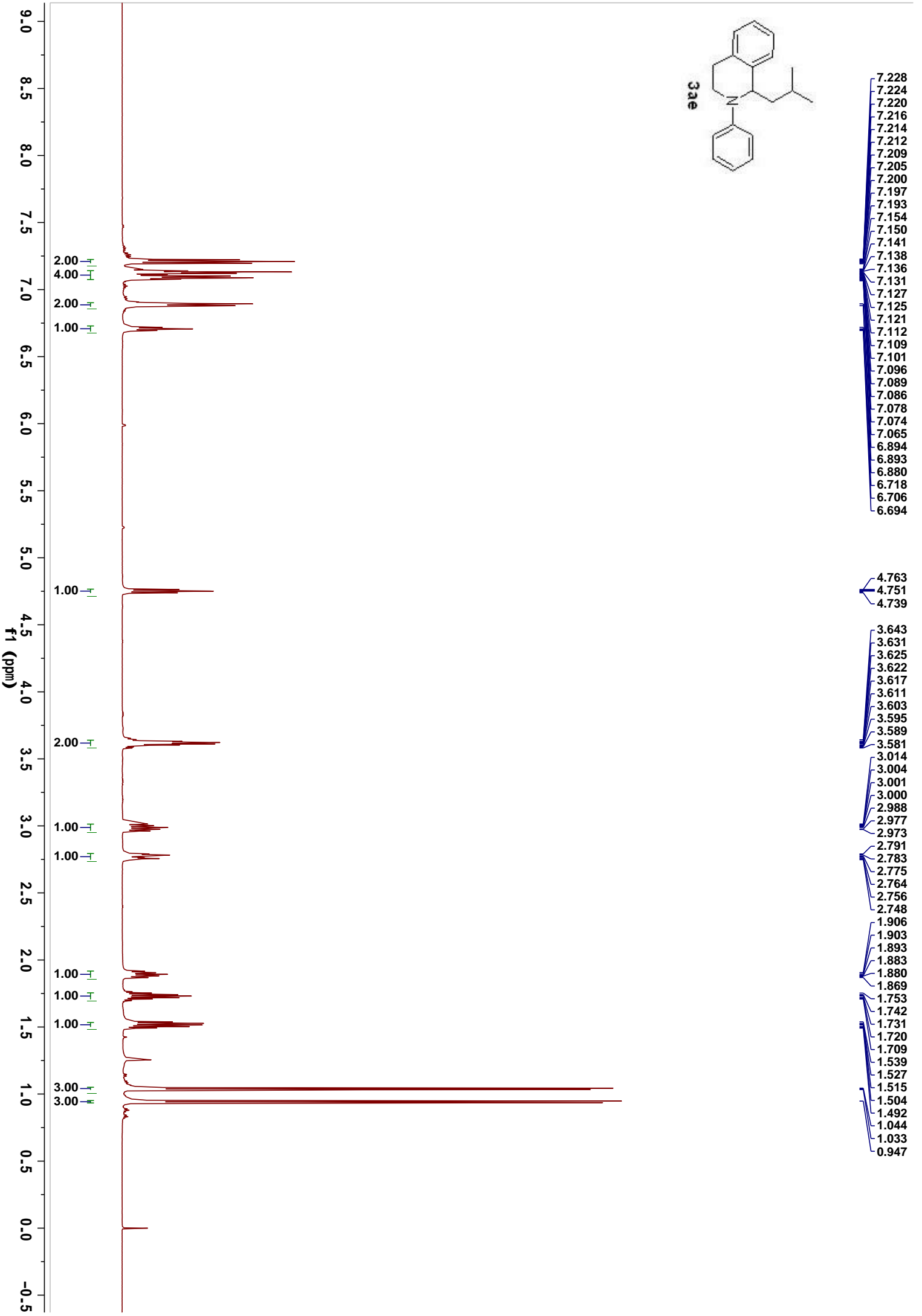
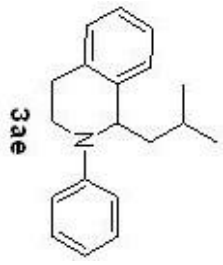


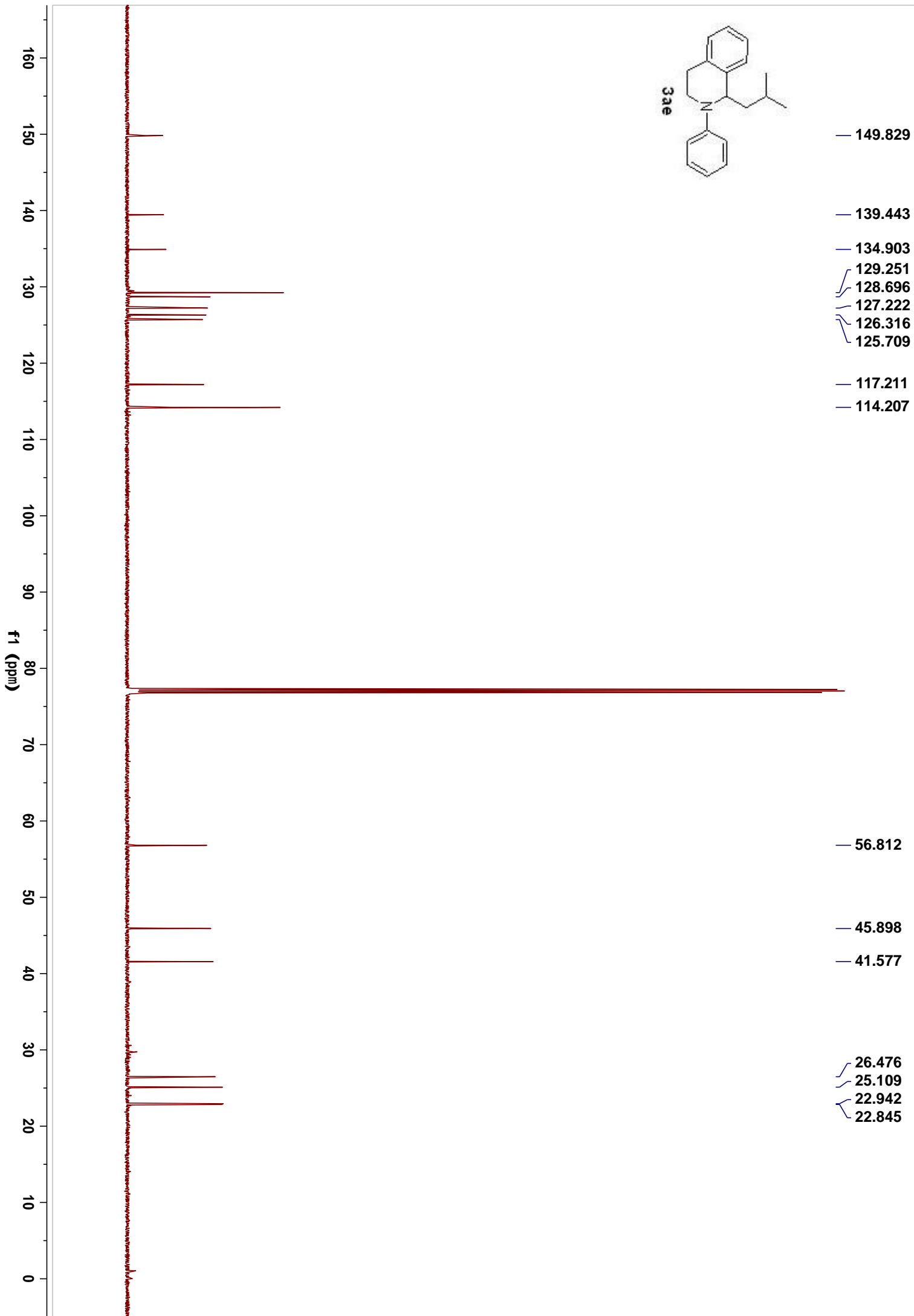
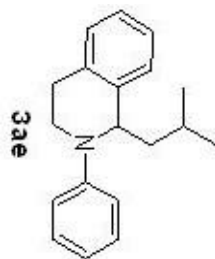


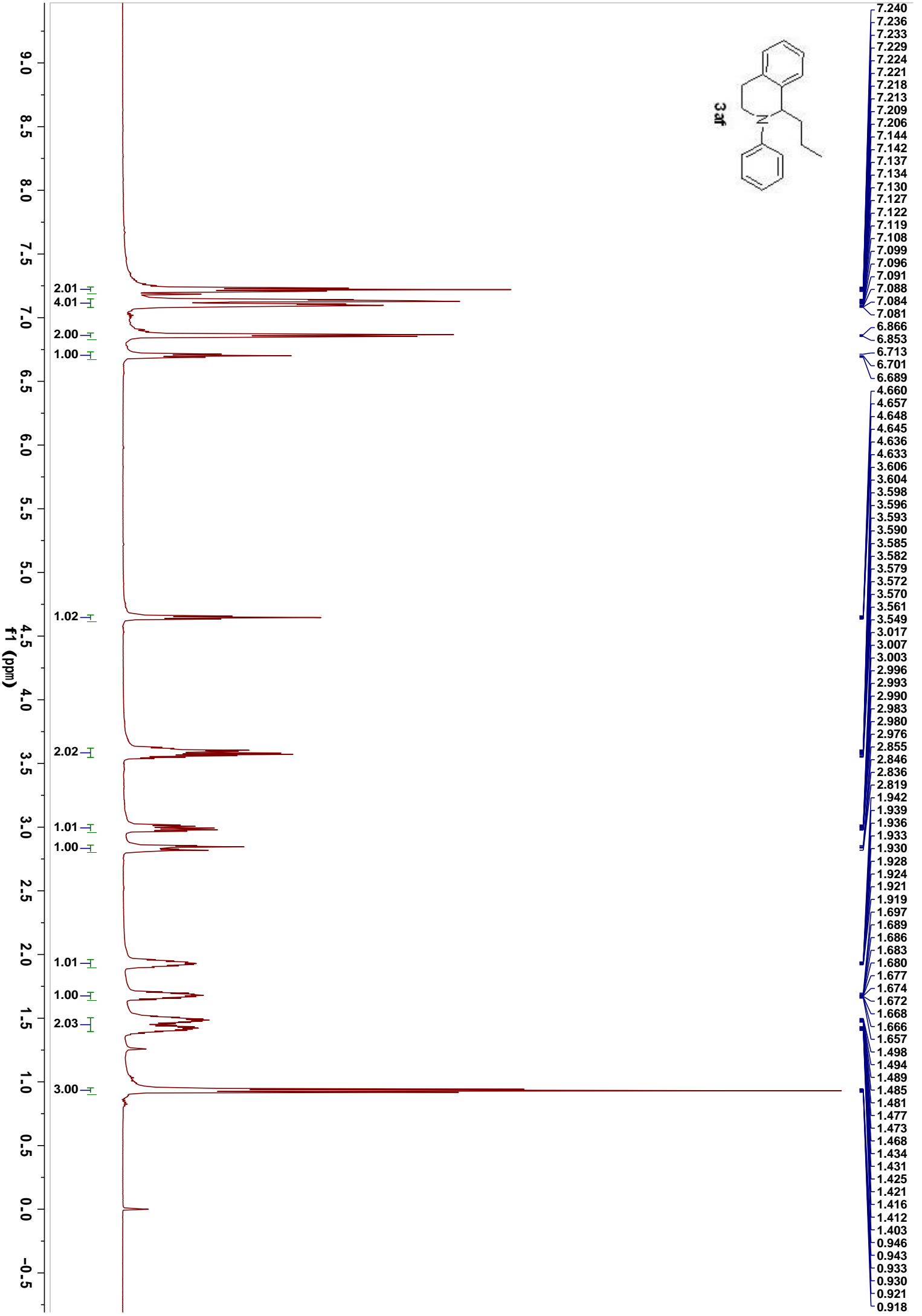
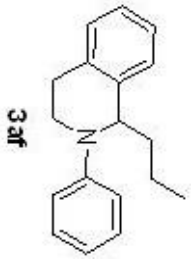


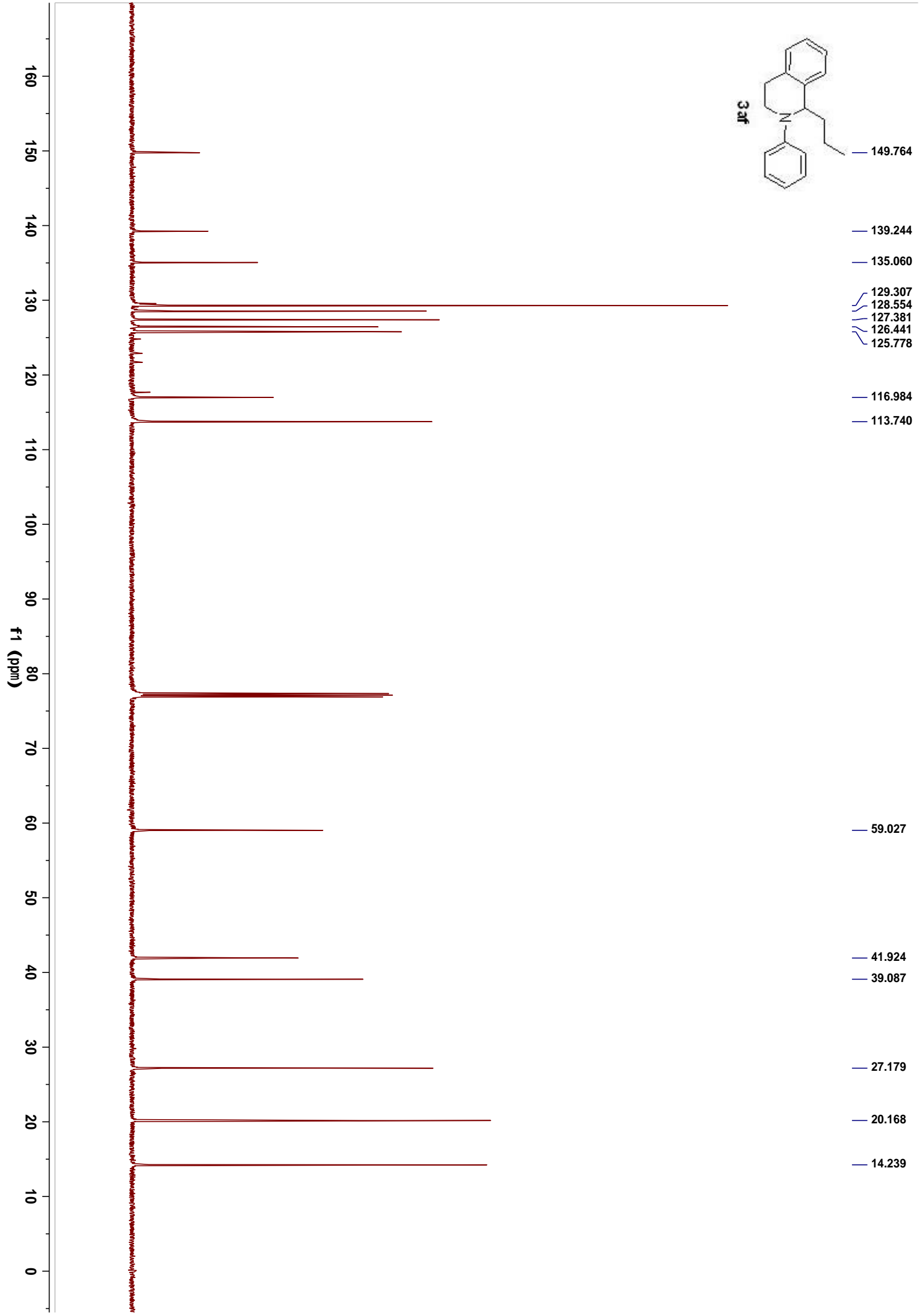
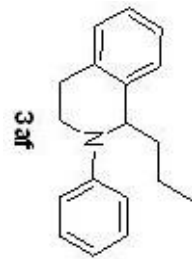


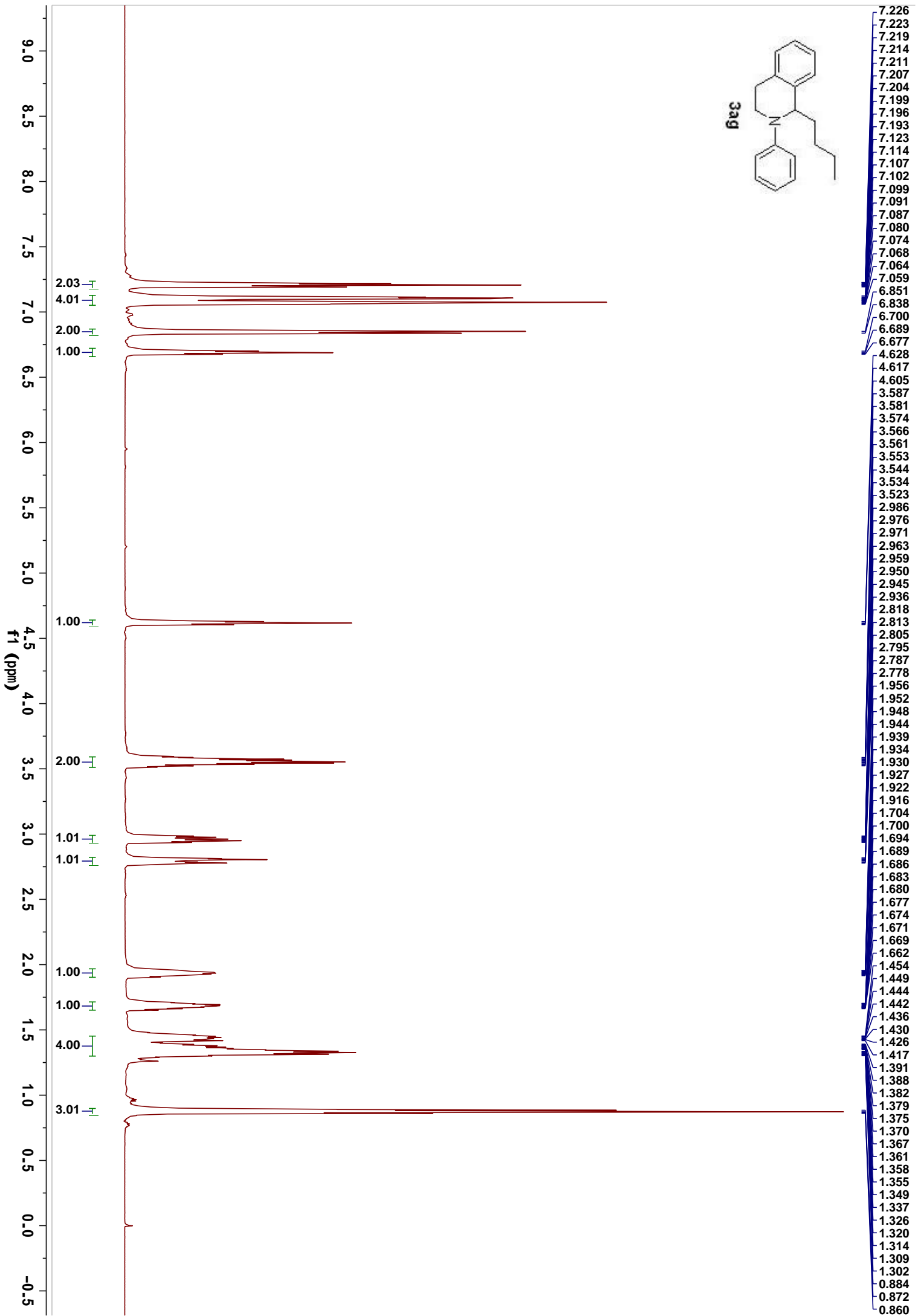


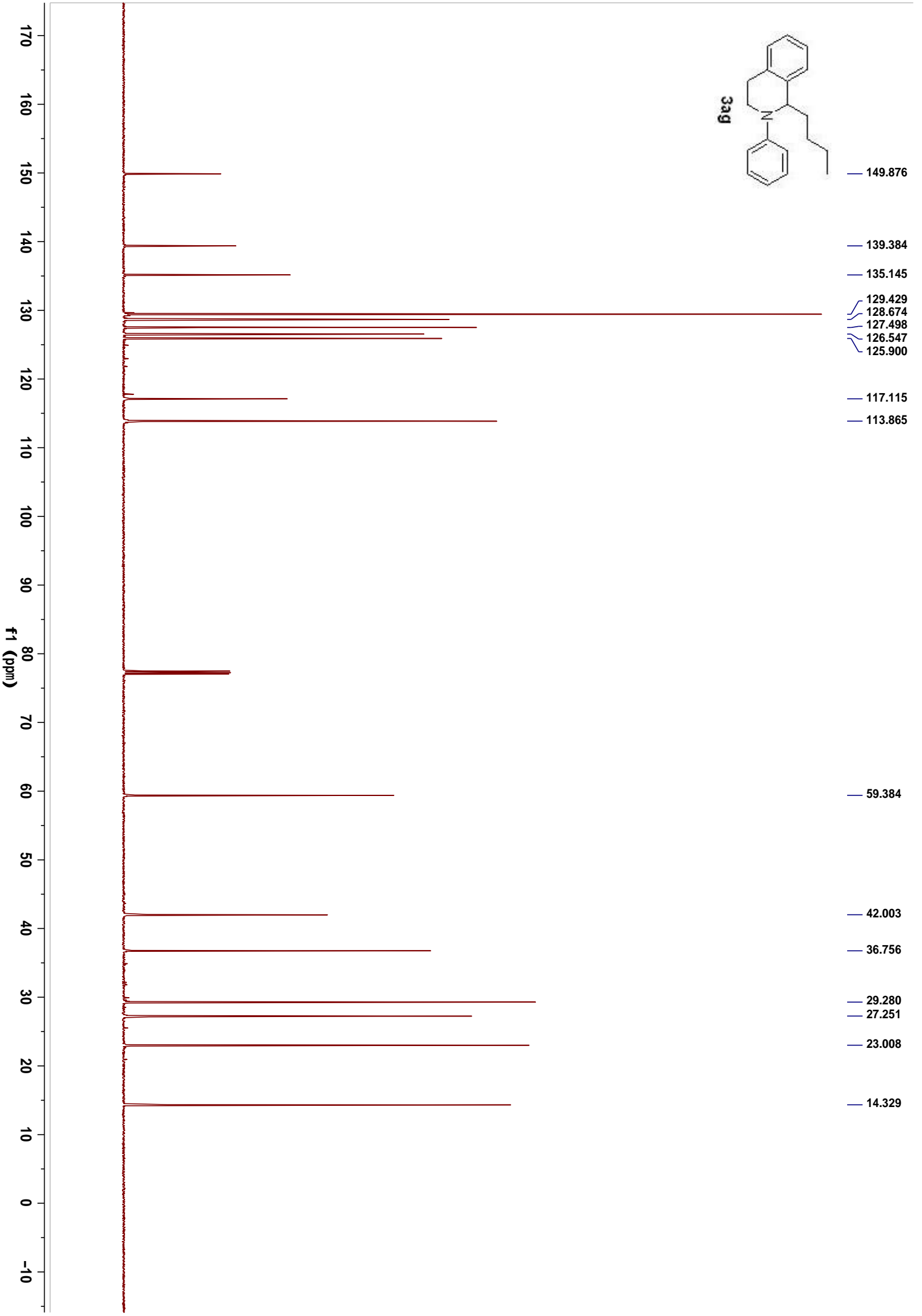
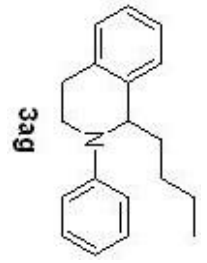


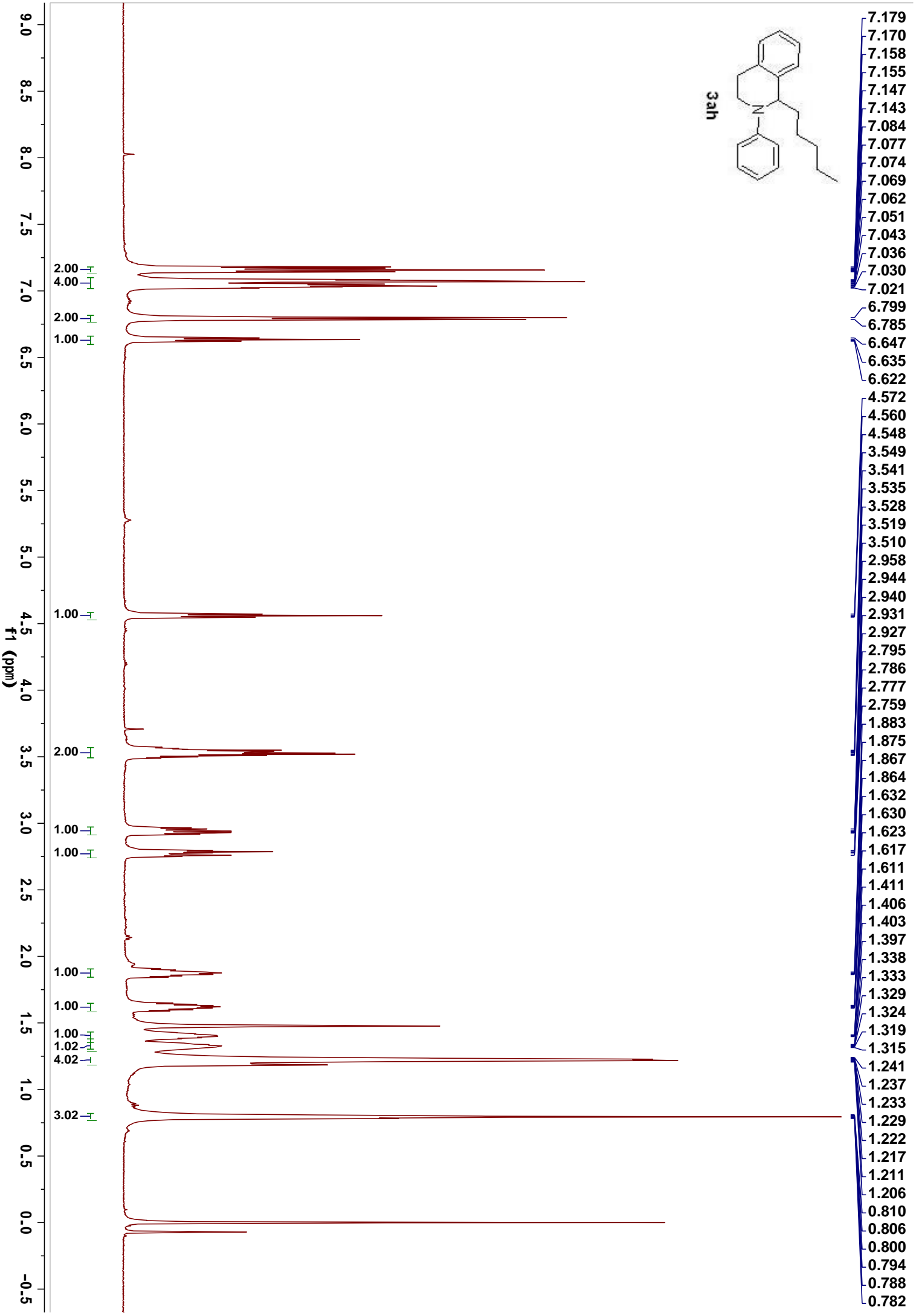
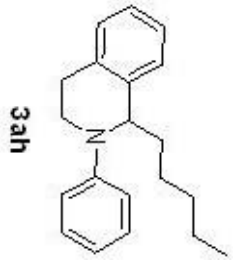


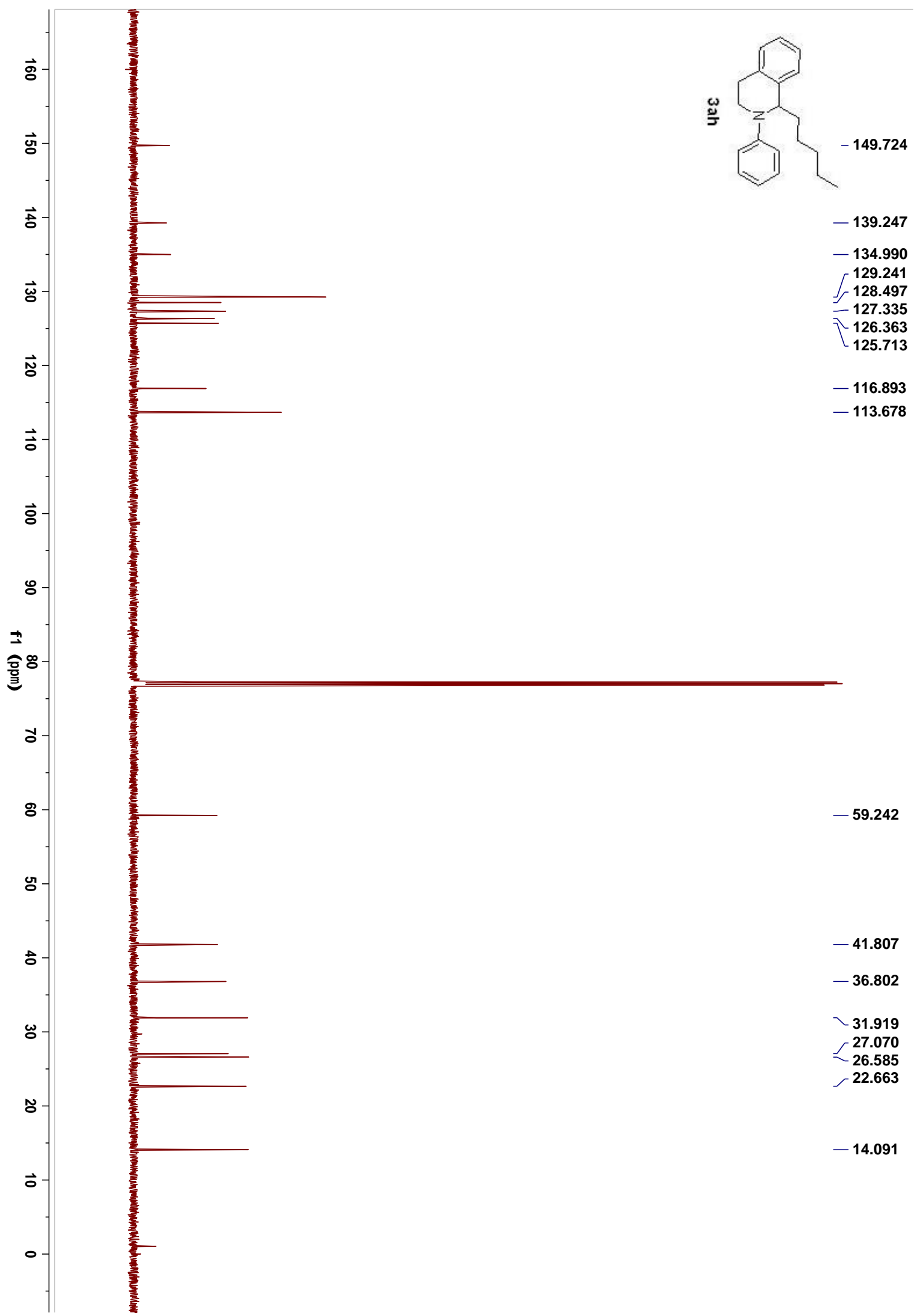
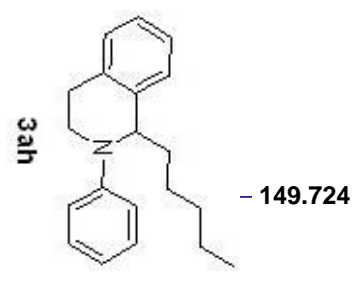


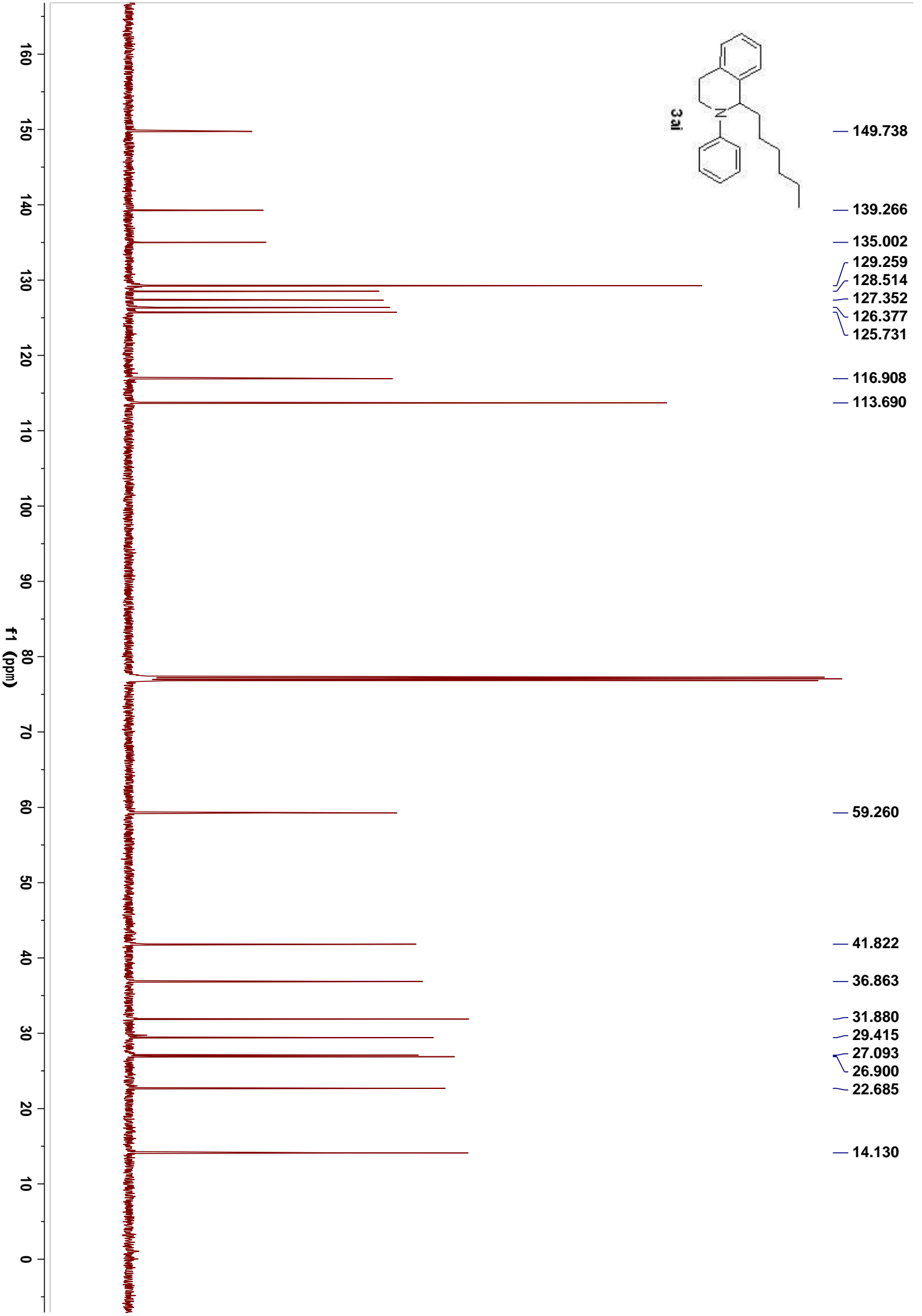
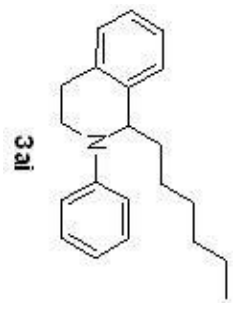


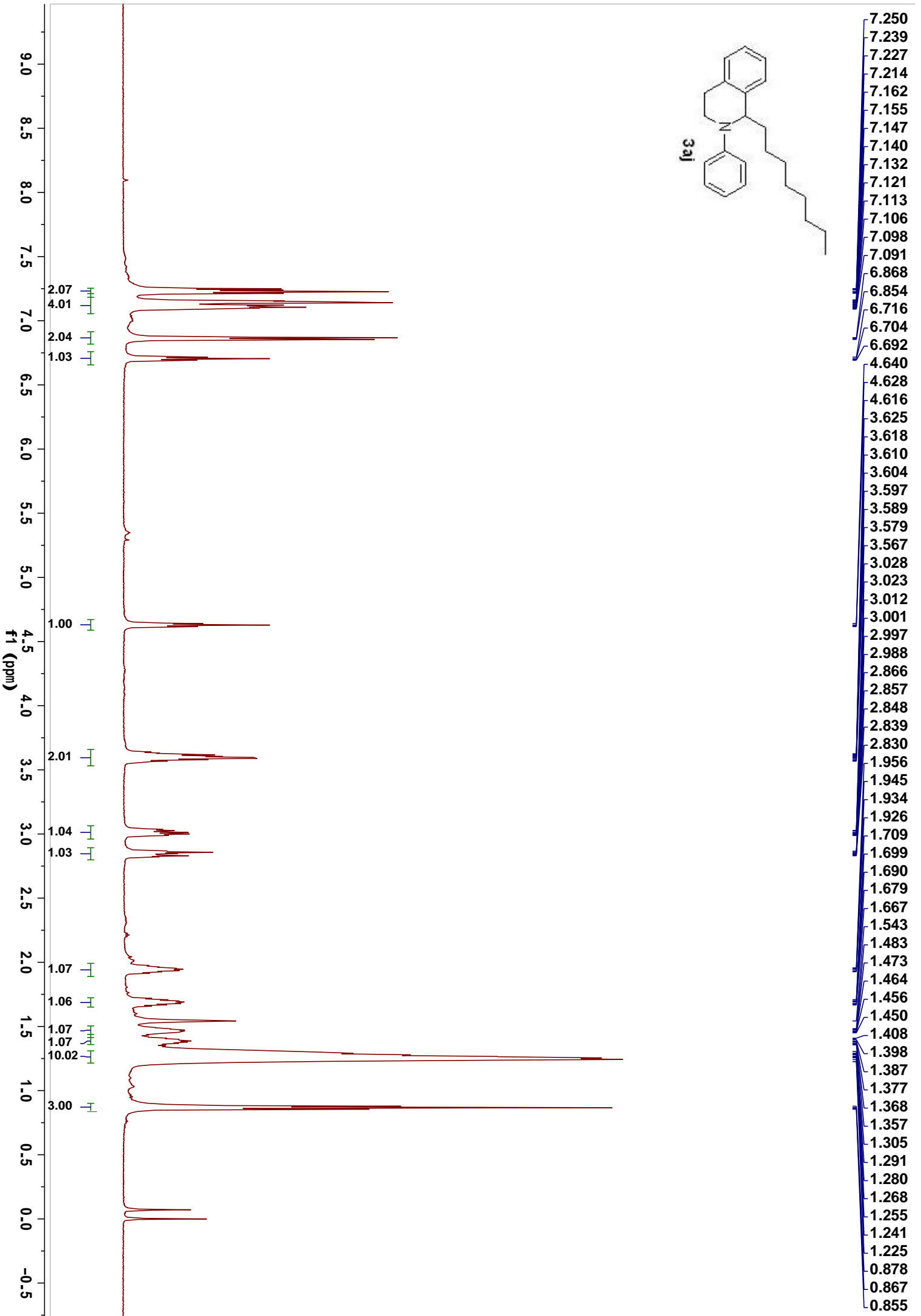
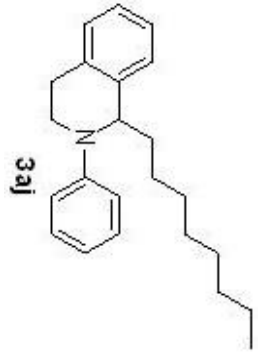


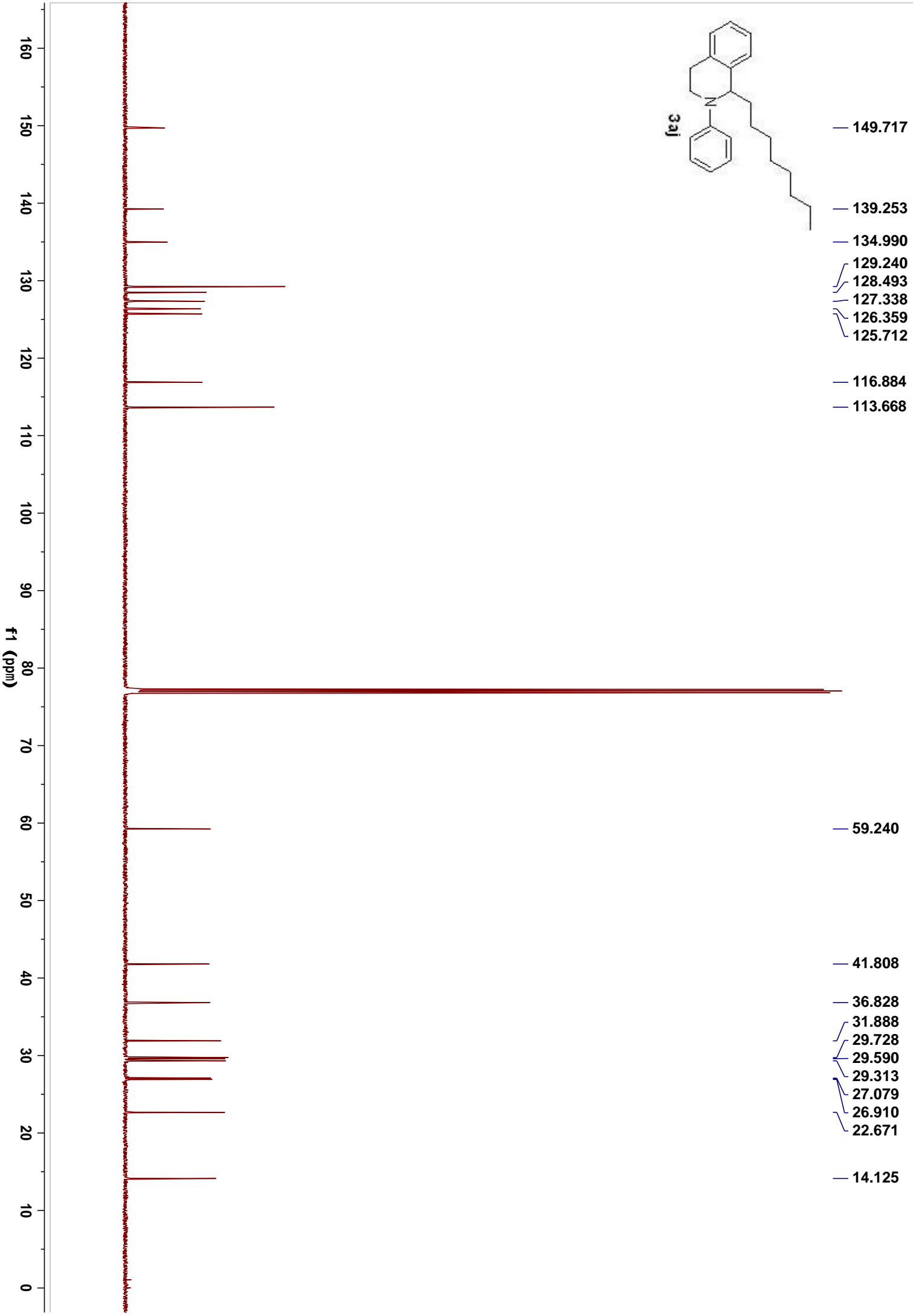
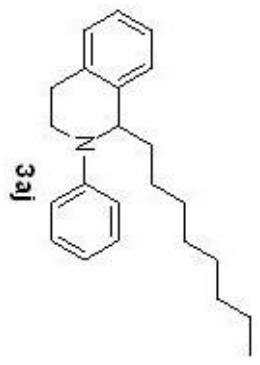












6. References

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