

# Intermolecular Cross-Double-Michael Addition between Nitro and Carbonyl Activated Olefins as A New Approach in C-C Bond Formation

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## **I. General Methods and materials:**

Unless otherwise noted, all commercial reagents and solvents were obtained from the commercial provider and used without further purification. Air and/or moisture-sensitive reactions were carried out under an atmosphere of nitrogen using oven/flame-dried glassware and standard syringe/septa techniques.  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra were recorded on Joel 270 and Varian 600 MHz spectrometers. Chemical shifts were reported relative to internal tetramethylsilane ( $\delta$  0.00 ppm) or  $\text{CDCl}_3$  ( $\delta$  7.26 ppm) or DMSO ( $\delta$  2.49 ppm) for  $^1\text{H}$  and  $\text{CDCl}_3$  ( $\delta$  77.0 ppm) or DMSO ( $\delta$  39.5 ppm) for  $^{13}\text{C}$ . Infrared (IR) spectra were obtained on a Prospect MIDAC FT-IR spectrometer. Flash column chromatography was performed on 230-430 mesh silica gel. Analytical thin layer chromatography was performed with precoated glass baked plates (250 $\mu$ ) and visualized by fluorescence and by charring after treatment with potassium permanganate stain.  $R_f$  values were obtained by elution in the stated solvent ratios.

**General Procedure for Intermolecular tandem double Michael addition reaction:** The nitroalkene (1.0 eq.) was added to a solution of  $\alpha,\beta$ -unsaturated ketone/ester (2.0 eq.), L-Proline (20 mol%) and  $\text{NaN}_3$  (1.0 eq.) in DMSO. The resulting reaction mixture was stirred at room temperature for 5 hrs followed by the dilution with dichloromethane. The organic layer was washed with water and brine. The combined organic layer was dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure with flash silica gel chromatography to give the pure product.

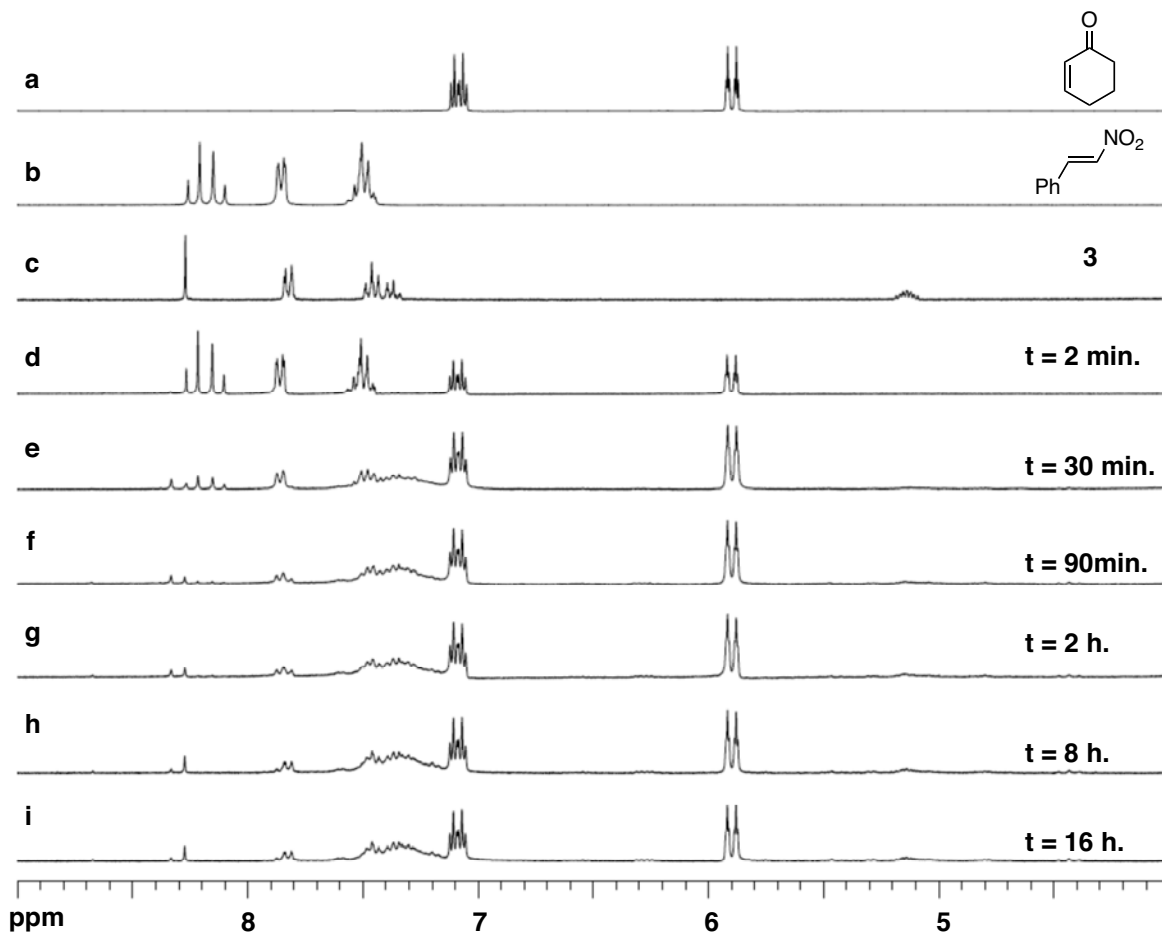
**Synthesis of compound 6a:** The zinc powder (440 mg, 6.76 mmols) was added into the solution of **5f** (720 mg, 3.38 mmols) in acetic acid (2.5 mL) over 10 minutes at 0  $^\circ\text{C}$ . The resulting reaction mixture was stirred at room temperature for 1.5 hr. followed by the filtration through Celite with washing by ether (20 mL). The filtrate was then diluted with water and cooled to 0  $^\circ\text{C}$ . The 10 M sodium hydroxide solution was added until the aqueous layer pH was 12. After separation, the aqueous phase was extracted with ether (2 x 50 mL). The combined organic layer was washed with water (50 mL), dried over sodium sulfate and removed by vacuum. Purification by column chromatography gave the desired amine **6a**.

**Synthesis of allylic alcohol 6b:** Compound **5j** (175 mg, 1.0 eq.) was dissolved in 1,2-dichlorobenzene to which was added DABCO (56 mg, 1.0 eq.). The resulting reaction mixture was then refluxed at 180 °C for 3hrs. The crude product was purified by flash chromatography (Hex/EA 8:2) to give 131 mg of **6b** as a pale red oil an exclusively as a single diastereomer.

**General procedure for Nef reaction for synthesis of compound 6c:** To a solution of compound **5q** (227 mg, 1.0 mmols) in methanol was added sodium methoxide (25 mg) in methanol at 0 °C and the mixture was stirred for 0.5 hrs. To the nitronate solution was added a mixture of conc. sulfuric acid (0.2 mL) and methanol (10 mL). During the addition, the mixture was kept at 0 °C and after additional stirring at 0 °C for an hour, it was poured into dichloromethane (20 mL). The organic layer was washed with cold water and the water layer was extracted with dichloromethane. The combined organic layer was dried over sodium sulfate and the solvent was removed under vacuum pressure. Dichloromethane and 2N hydrochloric acid was added and the mixture was stirred at room temperature for 2hrs. The water layer was then washed with dichloromethane and the organic layer was dried over sodium sulfate and removed under vacuum and the crude product was then purified by column chromatography to give **6c** in 72% yield.

**Preparation of single crystal for X-ray diffraction:** Single crystal suitable for X-ray diffraction analysis was obtained by slow evaporation of the solution of **5d** and **6a** in acetone.

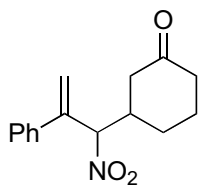
## II. NMR spectra of the reaction between 1a and 2a forming 3.



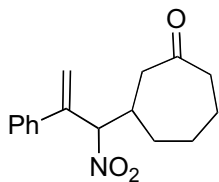
**Figure S-1.** The NMR spectra of the reaction between **1a** and **2a**: a) **2a**; b) **1a**; c) **3**, a mixture of two double bond isomers with a ration of 2:1; d) reaction between **1a** and **2a** when time is 2 min.; e) 30 min.; f) 90 min.; g) 2 h.; h) 8 h.; i) 2 h.

Based on the spectra, the nitroalkene was consumed rapidly. At 30 minutes, more than 90% **1a** was consumed while no **3** forming. The amount of **3** kept increasing even almost all **1a** was consumed. These spectra clearly revealed two important mechanistic facts: 1) nitroalkene is more reactive Michael receptor than enone; and 2) the oligomerization of **1a** is equilibrium and can come back to simple nitroalkene before polymerization. This result set up our key hypothesis that installation of a  $\beta$ -alkyl group will help the reaction to reach the desired cross double Michael addition.

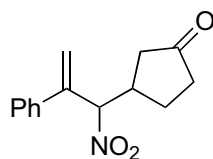
### III. Compound Characterization:



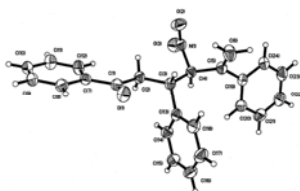
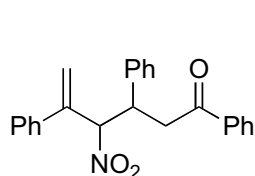
**(S)-3-((R)-1-nitro-2-phenylallyl) cyclohexanone** (d:r = 1:1) (**5a**): **5a** was purified by flash chromatography (Hexane-EtOAc, v/v 5/1) as yellow oil with overall isolated yield: 87%. The two diastereomer were isolated. Isomer 1:  $^1\text{H-NMR}$  (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.37-1.82 (m, 2H), 1.82-1.98 (m, 2H), 2.00-2.26 (m, 2H), 2.32-2.52 (m, 2H), 2.60-2.82 (m, 1H), 5.24 (d,  $J = 10.4$  Hz, 1H), 5.65 (s, 1H), 5.71 (s, 1H), 7.30-7.40 (m, 5H);  $^{13}\text{C-NMR}$  (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  24.1, 28.5, 41.0, 42.3, 43.2, 94.1, 119.3, 126.6, 128.7, 129.0, 139.5, 141.7, 208.5; IR ( $\text{cm}^{-1}$ ) : 2940, 2346, 1708, 1547, 1446; HRMS Calculated for  $[\text{C}_{15}\text{H}_{17}\text{NO}_3\text{Na}]^+$ : 282.1106, Found: 282.1101. Isomer 2:  $^1\text{H-NMR}$  (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.52-2.53 (m, 8H), 2.81-3.02 (m, 1H), 5.27 (d,  $J = 7.4$  Hz, 1H), 5.62 (s, 1H), 5.67 (s, 1H), 7.20-7.45 (m, 5H);  $^{13}\text{C-NMR}$  (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  24.3, 27.1, 40.9, 42.0, 44.4, 94.1, 118.9, 126.6, 128.7, 129.0, 139.5, 139.5, 208.2.



**3-(1-nitro-2-phenylallyl)cycloheptanone** (d:r = 1.2:1) (**5b**) : **5b** was purified by flash chromatography (Hexane-EtOAc, v/v 5/1) as yellow oil with overall isolated yield: 72%. The two diastereomers cannot be separated. Two sets of signals were obtained for the  $^1\text{H}$  and  $^{13}\text{C}$  NMR.  $^1\text{H-NMR}$  (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.35-1.64 (m, 6H), 1.85-1.92 (m, 4H), 2.1-2.2 (m, 4H), 2.48-2.58 (m, 8H), 5.21 (d,  $J=9.7\text{Hz}$ , 1H), 5.26 (d,  $J=8.9\text{Hz}$ , 1H), 5.64 (s, 1H), 5.67 (s, 1H), 5.70 (s, 1H), 5.75 (s, 1H), 7.33-7.40 (m, 5H);  $^{13}\text{C-NMR}$  (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  24.3, 24.4, 28.2, 28.3, 32.0, 33.4, 39.2, 39.7, 43.5, 45.0, 46.0, 94.1, 94.3, 119.0, 119.4, 126.6, 126.7, 128.7 (overlapped), 128.9 (overlapped), 139.3, 139.4, 142.3, 142.5, 211.4, 211.5; IR ( $\text{cm}^{-1}$ ): 2944, 2355, 1698 1542, 1438; HRMS Calculated for  $[\text{C}_{16}\text{H}_{19}\text{NO}_3\text{Na}]^+$ : 296.12626, Found: 296.12576.



**3-(1-nitro-2-phenylallyl) cyclopentanone** (d:r = 1.1:1) (**5c**): **5c** was purified by flash chromatography (Hexane-EtOAc, v/v 3/1) as yellow oil, isolated yield 55%. The two diastereomers cannot be separated. Two sets of signals were obtained for the  $^1\text{H}$  and  $^{13}\text{C}$  NMR.  $^1\text{H}$ -NMR (270 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.20-1.82 (m, 4H), 2.03-2.62 (m, 10H), 3.05-3.22 (m, 2H), 5.27 (d,  $J=10.3\text{Hz}$ , 2H), 5.62 (s, 1H), 5.67 (s, 1H), 5.69 (s, 1H), 5.74 (s, 1H), 7.34-7.65 (m, 10H);  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ ):  $\delta$  25.8, 27.3, 37.9, 38.1, 40.1, 40.2, 41.3, 42.8, 94.1, 94.2, 119.5, 119.7, 126.7, 126.8, 128.7 (overlapped), 128.9 (overlapped), 138.9, 139.0, 142.5, 142.8, 215.4, 215.5; IR ( $\text{cm}^{-1}$ ): 2195, 1690, 1546, 1497, 1436; HRMS calculated for  $[\text{C}_{14}\text{H}_{15}\text{NO}_3\text{Na}]^+$ : 268.0949, found 286.09486



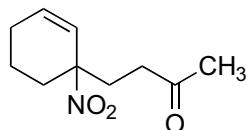
Crystal structure of *anti* isomer

**(3S, 4R)-4-nitro-1,3,5-triphenylhex-5-en-one** (d:r = 1.6:1) (**5d**): **5d** was purified by flash chromatography (Hexane-EtOAc, v/v 3/1) as White solid, isolated yield: 70%, m.p. 165 °C. The two diastereomers cannot be separated by column chromatography. The purification was achieved by recrystallization of anti-isomer. IR ( $\text{cm}^{-1}$ ): 2175, 1674, 1534, 1497, 1446; HRMS Calculated for  $[\text{C}_{24}\text{H}_{21}\text{NO}_3\text{Na}]^+$ : 394.1419, Found: 394.1415.

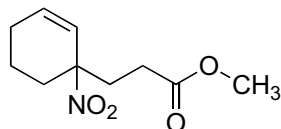
For anti isomer,  $^1\text{H}$ -NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  3.22 (dd,  $J = 16.8, 3.5\text{ Hz}$ , 1H), 3.21 (dd,  $J = 17.1, 9.6\text{ Hz}$ , 1H), 4.44 (ddd,  $J = 16.8, 9.9, 3.5\text{ Hz}$ , 1H), 5.75 (s, 1H), 5.89 (d,  $J = 11.6\text{ Hz}$ , 1H), 6.01 (s, 1H), 7.12-7.57 (m, 13H), 7.66-7.69 (m, 2H);  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  41.1, 45.2, 93.9, 120.1, 126.7, 127.9, 128.0, 128.2, 128.7, 128.9 (overlapped), 129.1, 133.4, 136.2, 138.9, 139.9, 142.2, 196.5.

For syn isomer.  $^1\text{H}$ -NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  3.33 (dd,  $J = 16.8, 2.9\text{ Hz}$ , 1H), 3.69 (dd,  $J = 17.1, 7.2\text{ Hz}$ , 1H), 4.34 (ddd,  $J = 16.8, 10.3, 3.2\text{ Hz}$ , 1H), 5.48 (s, 1H), 5.78 (s, 1H), 5.86 (d,  $J = 10.6\text{ Hz}$ , 1H), 6.01 (s, 1H), 7.12-7.57 (m, 13H), 7.66-7.69 (m, 2H);  $^{13}\text{C}$ -NMR (67.5 MHz,

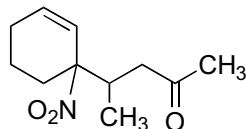
CDCl<sub>3</sub>)  $\delta$  41.6, 44.8, 93.6, 119.5, 126.5, 127.5, 128.1, 128.2, 128.3, 128.5, 128.6, 128.7, 128.8, 133.3, 136.9, 137.5, 139.9, 142.5, 196.6.



**4-((S)-1-nitrocyclohex-2-en-1-yl)butan-2-one (5e):** **5e** was purified by flash chromatography (Hexane-EtOAc, v/v 3/1) as yellow oil, isolated yield: 93%. <sup>1</sup>H-NMR (270 MHz, CDCl<sub>3</sub>)  $\delta$  1.40-1.56 (m, 1H), 1.59-1.73 (m, 2H), 1.86-2.16 (m, 7H), 2.36-2.52 (m, 3H), 5.81 (ddd,  $J$  = 10.1, 3.6, 2.1 Hz, 1H), 6.02 (ddd,  $J$  = 10.1, 4.1, 3.5 Hz, 1H); <sup>13</sup>C-NMR (67.5 MHz, CDCl<sub>3</sub>)  $\delta$  18.8, 24.8, 30.0, 31.9, 34.0, 37.6, 88.4, 125.1, 134.2, 206.4; IR (cm<sup>-1</sup>) : 2294, 2331, 1708, 1534, 1444; HRMS Calculated for [C<sub>10</sub>H<sub>15</sub>NO<sub>3</sub>Na]<sup>+</sup>: 220.0950, Found: 220.0945.

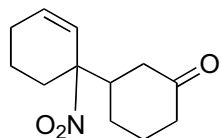


**Methyl 3-((S)-1-nitrocyclohex-2-en-1-yl) propionate (5f):** **5f** was purified by flash chromatography (Hexane-EtOAc, v/v 3/1) as yellow oil, isolated yield: 85%. <sup>1</sup>H-NMR (270 MHz, CDCl<sub>3</sub>)  $\delta$  1.40-1.75 (m, 3H), 1.85-2.33 (m, 6H), 2.38-2.54 (m, 1H), 3.60 (s, 3H), 5.81 (ddd,  $J$  = 9.9, 3.7, 2.2 Hz, 1H), 6.02 (ddd,  $J$  = 10.2, 4.2, 3.2 Hz, 1H); <sup>13</sup>C-NMR (67.5 MHz, CDCl<sub>3</sub>)  $\delta$  18.8, 24.7, 28.5, 31.6, 35.3, 51.9, 88.3, 124.9, 134.4, 172.5; IR (cm<sup>-1</sup>) : 2956, 2331, 1742, 1538, 1448; HRMS Calculated for [C<sub>10</sub>H<sub>15</sub>NO<sub>4</sub>Na]<sup>+</sup>: 236.0899, Found: 236.0896.

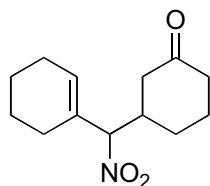


**4-Methyl-5-((S)-1-nitrocyclohex-2-en-1-yl) pentan-2-one (d/r=1.6/1) (5g):** **5g** was purified by flash chromatography (Hexane-EtOAc, v/v 3/1) as yellow oil, isolated yield: 81%. The two diastereomers cannot be separated. Two sets of signals were obtained for the <sup>1</sup>H and <sup>13</sup>C NMR. <sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>)  $\delta$  0.77 (d,  $J$  = 6.6 Hz, 3H), 0.81 (d,  $J$  = 6.6 Hz, 3H), 1.28-2.53 (m, 16H), 2.04 (s, 3H), 2.05 (s, 3H), 2.65-2.74 (m, 2H), 5.71-5.79 (m, 2H), 5.99-6.08 (m, 2H); Isomer 1: <sup>13</sup>C NMR (67.5 MHz, CDCl<sub>3</sub>)  $\delta$  14.6, 18.6, 24.9, 27.3, 30.5, 37.2, 45.6, 92.2, 125.4,

135.6, 206.1; Isomer 2:  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  15.1, 18.7, 24.8, 27.6, 30.5, 37.1, 45.1, 92.2, 124.9, 135.0, 206.2; HRMS Calculated for  $[\text{C}_{11}\text{H}_{17}\text{NO}_3\text{Na}]^+$ : 234.1106, Found: 214.1101.

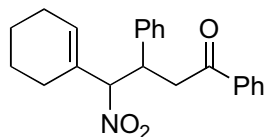


**(S)-3-((S)-1-nitrocyclohex-2-enyl) cyclohexanone** (d:r = 1.3:1) (**5h**) : Both isomers of **5h** were purified by flash chromatography (Hexane-EtOAc, v/v 3/1) as yellow oils, with overall isolated yield: 76%. The two diastereomers cannot be separated. Two sets of signals were obtained for the  $^1\text{H}$  and  $^{13}\text{C}$  NMR.  $^1\text{H}$ -NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.31-2.62 (m, 30H), 5.81-5.92 (m, 2H), 6.08-6.19 (m, 2H); Isomer 1:  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  18.8, 24.5, 25.0, 25.9, 28.5, 41.0, 42.5, 46.5, 91.8, 123.7, 135.8, 209.2; Isomer 2:  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  18.7, 24.5, 24.8, 25.6, 27.4, 41.0, 42.7, 46.7, 91.6, 124.7, 135.4, 209.2; HRMS Calculated for  $[\text{C}_{12}\text{H}_{17}\text{NO}_3\text{Na}]^+$ : 246.1106, Found: 246.1101.



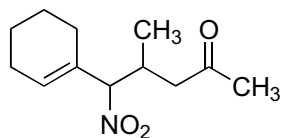
**(S)-3-((R)-cyclohexenyl)nitromethyl cyclohexanone** (d:r = 1.2:1) (**5i**): **5i** was purified by flash chromatography (Hexane-EtOAc, v/v 3/1) as yellow oil, isolated yield: 90%. The two diastereomers cannot be separated. Two sets of signals were obtained for the  $^1\text{H}$  and  $^{13}\text{C}$  NMR.  $^1\text{H}$ -NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.11-1.79 (m, 14H), 1.79-2.07 (m, 12H), 2.10-2.35 (m, 6H), 2.49-2.68 (m, 2H), 4.58 (d,  $J$  = 10.6 Hz, 1H), 4.60 (d,  $J$  = 11.8 Hz, 1H), 5.87-5.90 (br, 2H); Isomer 1:  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  21.7, 22.3, 23.7, 24.3, 25.5, 26.9, 38.4, 41.0, 44.4, 98.9, 130.7, 133.3, 208.5; Isomer 2:  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  21.6, 22.2, 23.6, 24.2, 25.5, 28.2, 38.3, 41.0, 43.1, 98.8, 130.2, 133.7, 209.1; IR ( $\text{cm}^{-1}$ ): 2294, 2331, 1713, 1534, 1439; HRMS Calculated for  $[\text{C}_{13}\text{H}_{19}\text{NO}_3\text{Na}]^+$ : 260.1263, Found: 260.1258.





**4-cyclohexenyl-4-nitro-1,3-diphenylbutan-1-one (5j)**; **5j** was purified by flash chromatography (Hexane-EtOAc, v/v 3/1) with overall isolated yield: 70% (d:r = 4:1). The two diastereomers were separated by column chromatography. Isomer 1 (major) is white solid, m.p. is 186 °C; isomer 2 (minor) colorless oil.

Isomer 1:  $^1\text{H-NMR}$  (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.24-1.43(m, 4H), 1.71-2.04(m, 4H), 3.19(dd,  $J=16.6\text{Hz}$ , 1H), 3.49(dd,  $J=16.8\text{Hz}$ , 1H), 4.2-4.32(m, 1H), 5.21(d,  $J=11.1\text{Hz}$ , 1H), 5.77(s, 1H), 7.12-7.24(m, 1H), 7.36-7.41(m, 2H), 7.47-7.53(m, 1H), 7.79-7.82(m, 2H);  $^{13}\text{C-NMR}$  (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  21.53, 22.2, 24.5, 42.1, 97.8, 127.4, 128.0, 132.9, 133.3, 196.7; IR ( $\text{cm}^{-1}$ ): 2274, 2355, 1709, 1534, 1469; HRMS Calculated for  $[\text{C}_{22}\text{H}_{23}\text{NO}_3\text{Na}]^+$ : 372.1575, Found: 372.15732; Isomer 2:  $^1\text{H-NMR}$  (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.50-1.63(m, 4H), 1.99-2.18(m, 4H), 3.13(dd,  $J=4.2\text{Hz}$ , 1H), 3.23(dd,  $J=8.9\text{Hz}$ , 1H), 4.34-4.38(m, 1H), 5.30(d,  $J=11.8\text{Hz}$ , 1H), 6.13(s, 1H), 7.21-7.42(m, 7H);  $^{13}\text{C-NMR}$  (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  21.7, 22.3, 23.7, 25.6, 41.2, 98.8, 127.6, 128.0, 133.3, 134.4, 196.7

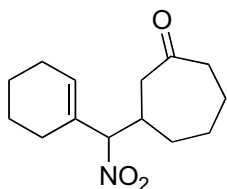


**(4R, 5R)-5-methyl-5-nitropentan-2-one (5k)**: Both isomers of **5k** was purified by flash chromatography (Hexane-EtOAc, v/v 3/1) as yellow oils with overall isolated yield: 81% (d/r = 1.6/1). The two diastereomers were separated by column chromatography.

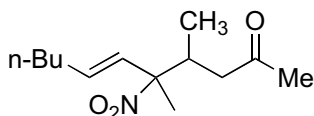
Isomer-1 (major):  $^1\text{H-NMR}$  (270 MHz,  $\text{CDCl}_3$ )  $\delta$  0.89 (d,  $J = 6.9\text{ Hz}$ , 3H), 1.52-1.69 (m, 5H), 2.01-2.19 (m, 6H), 2.33 (dd,  $J = 17.1, 8.9\text{ Hz}$ , 1H), 2.45 (dd,  $J = 17.1, 3.2\text{ Hz}$ , 1H), 2.80-2.90 (m, 1H), 4.69 (d,  $J = 10.9\text{ Hz}$ , 1H), 5.90-6.00 (br, 1H);  $^{13}\text{C-NMR}$  (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  15.90, 21.8, 22.3, 23.7, 25.5, 29.8, 30.5, 46.6, 98.6, 130.1, 132.7, 206.3; HRMS Calculated for  $[\text{C}_{12}\text{H}_{19}\text{NO}_3\text{Na}]^+$ : 248.1263, Found: 248.1258.

Isomer-2 (minor):  $^1\text{H-NMR}$  (270 MHz,  $\text{CDCl}_3$ )  $\delta$  0.98 (d,  $J = 6.2\text{ Hz}$ , 3H), 1.45-1.74 (m, 4H), 1.89-2.20 (m, 7H), 2.26 (dd,  $J = 17.6, 8.9\text{ Hz}$ , 1H), 2.41 (dd,  $J = 17.3, 3.5\text{ Hz}$ , 1H), 2.83-3.06 (m,

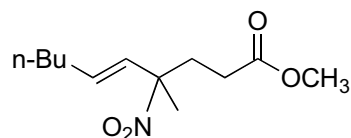
1H), 4.72 (d,  $J = 11.1$  Hz, 1H), 5.90-6.10 (br, 1H);  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  16.9, 21.7, 22.3, 23.8, 25.5, 29.8, 30.7, 45.6, 99.2, 131.3, 133.2, 206.1.



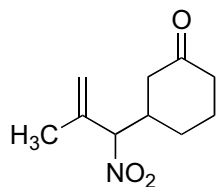
**(S)-3-((R)-cyclohexenylnitromethyl)-cyclopentanone** (d:r = 1:1) (**5l**) : **5l** was purified by flash chromatography (Hexane-EtOAc, v/v 3/1) as yellow oil, isolated yield: 76%. The two diastereomers cannot be separated. Two sets of signals were obtained for the  $^1\text{H}$  and  $^{13}\text{C}$  NMR.  $^1\text{H}$ -NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.08-2.64 (m, 38H), 4.60 (s, 1H), 4.65 (s, 1H), 5.92-6.08 (br, 2H); Isomer 1 (major):  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  21.7, 22.2, 23.5, 24.4, 25.5, 28.2, 33.5, 36.0, 43.6, 44.9, 99.2, 130.8, 134.1, 211.8; Isomer 2 (minor):  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  21.7, 22.3, 23.8, 24.6, 25.5, 28.5, 31.4, 35.7, 43.6, 46.4, 98.8, 131.0, 133.7, 211.3; HRMS Calculated for  $[\text{C}_{14}\text{H}_{21}\text{NO}_3\text{Na}]^+$ : 274.1419, Found: 274.1414



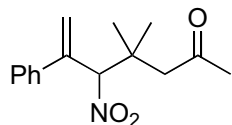
**(E)-methyl 3,4-dimethyl-4-nitrodec-5-enoate (5m)**: **5m** was purified by flash chromatography (Hexane-EtOAc, v/v 5/1) as yellow oil, isolated yield: 82%. The two diastereomers cannot be separated. Two sets of signals were obtained for the  $^1\text{H}$  and  $^{13}\text{C}$  NMR.  $^1\text{H}$ -NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  0.84-0.91(m, 12H), 1.23-1.40(m, 8H), 1.55(s, 3H), 1.58(s, 3H), 2.07-2.47(m, 14H), 2.84-3.01(m, 2H), 5.76-7.83(m, 4H). Isomer 1:  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  13.8, 14.8, 17.5, 22.2, 30.4, 31.0, 32.1, 37.1, 45.7, 94.4, 128.7, 135.9, 206.0. Isomer 2:  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  13.8, 15.3, 16.9, 22.1, 30.2, 30.9, 32.0, 37.0, 45.7, 94.5, 128.8, 135.2, 206.1. IR ( $\text{cm}^{-1}$ ): 2930, 2346, 1718, 1537, 1456; HRMS Calculated for  $[\text{C}_{13}\text{H}_{23}\text{NO}_3\text{Na}]^+$ : 264.15756, Found: 264.15695



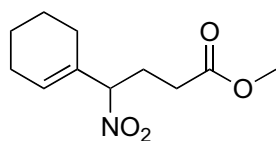
**(*R,E*)-methyl 4-methyl-4-nitrodec-5-enoate (5n):** **5n** was purified by flash chromatography (Hexane-ETOAc, v/v 5/1) as yellow oil, isolated yield: 70%.  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  0.83 (t,  $J = 6.9$  Hz, 3H), 1.97-2.06 (m, 2H), 1.59 (s, 3H), 1.98-2.06 (m, 2H), 2.17-2.39 (m, 4H), 3.61 (s, 3H), 5.65-5.80 (m, 2H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  13.9, 22.2, 29.1, 30.9, 32.0, 34.5, 51.9, 90.2, 128.7, 134.8, 172.6; IR ( $\text{cm}^{-1}$ ) : 2956, 2346, 1738, 1538, 1437; HRMS Calculated for  $[\text{C}_{12}\text{H}_{21}\text{NO}_4\text{Na}]^+$ : 266.1368, Found: 266.1365.



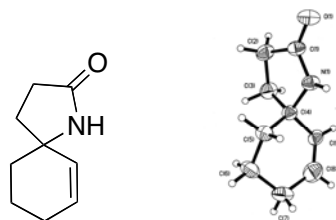
**(*S*)-3-((*R*)-2-methyl-1-nitroallyl) cyclohexanone (d/r=1.1/1) (5o):** **5o** was purified by flash chromatography (Hexane-EtOAc, v/v 5/1) as yellow oil, isolated yield: 67%. The two diastereomers cannot be separated. Two sets of signals were obtained for the  $^1\text{H}$  and  $^{13}\text{C}$  NMR.  $^1\text{H}$ -NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.21-2.47 (m, 22H), 2.55-2.71 (m, 2H), 4.74 (d,  $J = 10.4$  Hz, 1H), 4.75 (d,  $J = 10.8$  Hz, 1H), 5.19-5.21 (m, 4H); Isomer 1 (major):  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  17.9, 24.3, 26.8, 38.7, 40.9, 44.2, 97.9, 120.9, 137.2, 208.2; Isomer 2:  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  17.7, 24.2, 28.2, 38.6, 41.0, 43.0, 97.8, 121.4, 136.7, 208.7; HRMS Calculated for  $[\text{C}_{10}\text{H}_{15}\text{NO}_3\text{Na}]^+$ : 220.0949, Found: 220.0946.



**(*R*)-4,4-dimethyl-5-nitro-6-phenylhept-6-en-2-one (5p):** **5p** was purified by flash chromatography (Hexane-EtOAc, v/v 5/1) as yellow oil, isolated yield: 45%.  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.06 (s, 3H), 1.19 (s, 3H), 1.78 (s, 3H), 2.39(q,  $J=18.03\text{Hz}$ , 2H), 5.55(s, 1H), 5.70(s, 1H), 7.31-7.37(m, 5H);  $^{13}\text{C}$ -NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  23.9, 24.2, 31.1, 37.9, 51.1, 93.8, 126.9, 128.3, 128.9, 141.2, 206.7; HRMS Calculated for  $[\text{C}_{15}\text{H}_{19}\text{NO}_3\text{Na}]^+$ : 284.12626, Found: 284.12587.

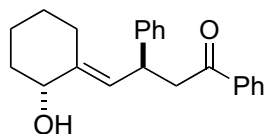


**(R)-Methyl-4-cyclohexenyl-4-nitrobutanoate (5q):** 5q was purified by flash chromatography (Hexane-EtOAc, v/v 5/1) as yellow oil, isolated yield: 85%.  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.38-1.65 (m, 4H), 1.80-2.18 (m, 5H), 2.26 (t,  $J = 6.9$  Hz, 2H), 2.32-2.45 (m, 1H), 3.61 (s, 3H), 4.84 (t,  $J = 7.4$  Hz, 1H), 5.86-5.89 (br, 1H).  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  21.7, 22.2, 23.4, 25.3, 25.7, 30.1, 51.9, 92.4, 131.5, 131.6, 172.4; IR ( $\text{cm}^{-1}$ ) : 2916, 2346, 1706, 1478, 1433; HRMS Calculated for  $[\text{C}_{11}\text{H}_{17}\text{NO}_4\text{Na}]^+$ : 250.1055, Found: 250.1051.



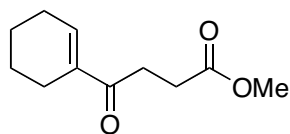
Crystal structure of *anti* isomer

**6a:** (444 mg, 72% yield). IR ( $\text{cm}^{-1}$ ) : 3175, 2901, 1975, 1703, 1547, 1425  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.53-1.69 (m, 2H), 1.85-2.17 (m, 6H), 2.38 (dd,  $J = 8.4, 6.9$  Hz, 2H), 5.56 (d,  $J = 10.2$  Hz, 1H), 5.93-5.99 (m, 1H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  19.6, 24.2, 26.3, 30.0, 30.8, 63.3, 129.8, 132.0, 169.5; HRMS Calculated for  $[\text{C}_9\text{H}_{13}\text{NONa}]^+$ : 174.0895, Found: 174.0890.



**6b:**  $^1\text{H}$  NMR (270 MHz,  $\text{CDCl}_3$ )  $\delta$  1.27-1.48 (m, 4H), 1.60-2.00 (m, 3H), 2.47-2.60 (m, 1H), 3.30 (dd,  $J = 15.8, 7.9$  Hz, 1H), 3.39 (dd,  $J = 15.8, 6.2$  Hz, 1H), 3.98 (dd,  $J = 6.4, 4.1$  Hz, 1H), 4.36 (ddd,  $J = 14.4, 6.2, 3.5$  Hz, 1H), 5.56 (d,  $J = 9.9$  Hz, 1H), 7.13-7.21 (m, 1H), 7.24-7.29 (m, 3H), 7.36-7.45 (m, 2H), 7.51-7.60 (m, 1H), 7.89-7.93 (m, 2H);  $^{13}\text{C}$  NMR (67.5 MHz,  $\text{CDCl}_3$ )  $\delta$  23.3, 26.9, 27.1, 36.3, 39.0, 45.9, 73.4, 123.0, 126.4, 127.3, 128.3, 128.6, 128.7, 133.1, 137.2, 142.0, 144.8, 198.9; HRMS Calculated for  $[\text{C}_{22}\text{H}_{24}\text{NO}_2\text{Na}]^+$ : 343.1674, Found: 343.1669. (the absolute stereochemistry of the product is not determined. However, the single diastereomer of **5j** gave single diastereomer of **6b**, while the mixture of 1.5:1 syn/anti isomers gave 1.5:1 mixture

of two stereoisomers. Therefore, the conversion is concerted and the structure of the product can be rationalized by the starting material **5j**, whose relative stereo-chemistry was determined by the comparison with the **5d** X-ray structure).

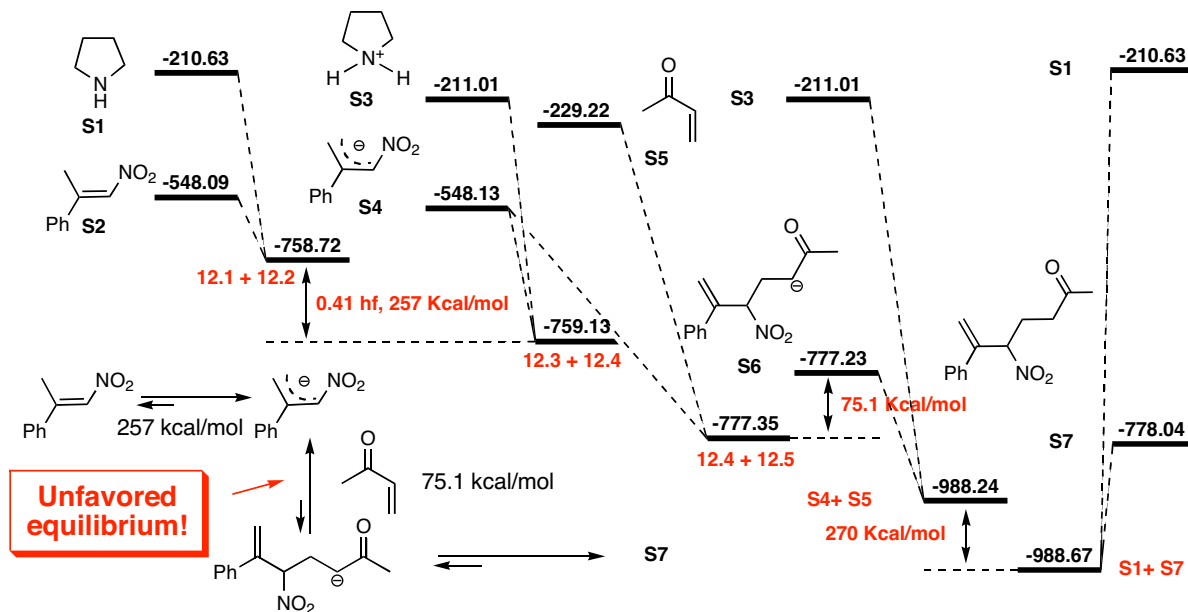


**6c**: IR (cm<sup>-1</sup>) : 3394, 2934, 1735, 1666, 1436 <sup>1</sup>H NMR (270 MHz, CDCl<sub>3</sub>) δ 1.56-1.67 (m, 4H), 2.21-2.25 (m, 4H), 2.61 (t, *J* = 6.6 Hz, 2H), 2.97 (t, *J* = 6.6 Hz, 2H), 3.67 (s, 3H), 6.94-6.97 (br, 1H); <sup>13</sup>C NMR (67.5 MHz, CDCl<sub>3</sub>) δ 21.5, 21.9, 23.0, 26.0, 28.1, 31.7, 51.7, 138.8, 140.2, 173.7, 198.9; HRMS Calculated for [C<sub>11</sub>H<sub>16</sub>NO<sub>3</sub>H]<sup>+</sup>: 197.1178, Found: 197.1173.

#### IV. The Computation Studies.

The computational studies were performed using the GAMESS-US package at the MP2/6-31G\* level of theory. The results are summarized in **Scheme S1**.

**Scheme S1.** Computation studies revealed the unfavored equilibrium for simple cabanion addition



Based on the calculation, a clear unfavored equilibrium for the carbanion **S4** addition to the enone **S5** was revealed, which supported the nucleophilic addition mechanism and agreed with the experimental data.

## V. ORTEP Drawing of the Crystal Structures

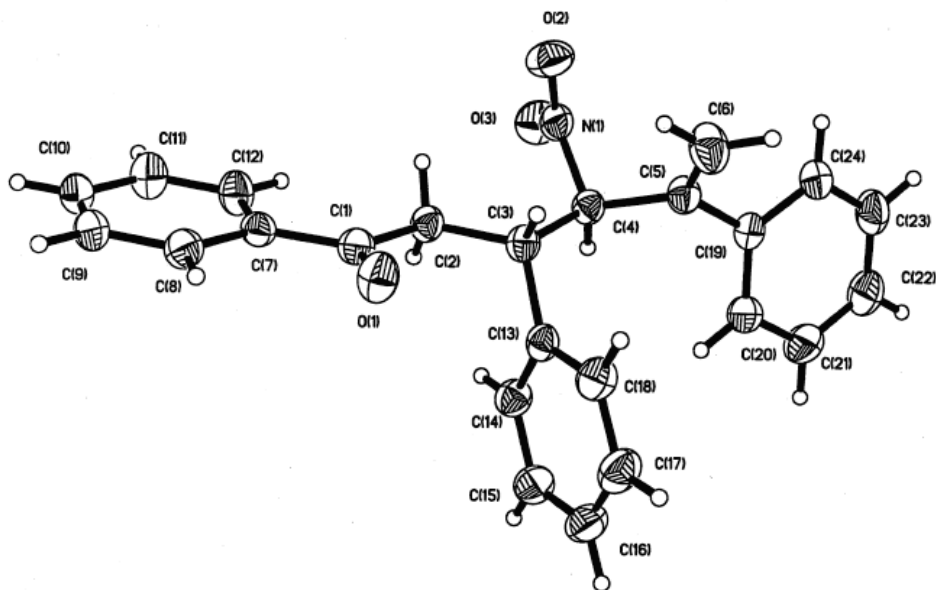


Figure S2. ORTEP drawing of the crystal structure of compound **5d**.

**Compound 5d:**  $C_{24}H_{21}NO_3$ ; 371.42; 0.22 x 0.40 x 0.42mm; Triclinic; P1;  $a = 5.7208\text{\AA}$ ,  $b = 9.9178\text{\AA}$ ,  $c = 19.0024\text{\AA}$ ,  $\alpha = 79.479^\circ$ ,  $\beta = 82.596^\circ$ ,  $\gamma = 84.090^\circ$ ; Vol. =  $971.64\text{ \AA}^3$   $Z = 2$ ;  $\rho = 1.270\text{g/cm}^3$ ;  $\mu = 0.84\text{cm}^{-1}$ ; Radiation source: MoK $\alpha$ ,  $\lambda = 0.71073\text{\AA}$ ;  $T = 293\text{K}$ ;  $2\theta$  max = 28; Reflections collected: 7011, Independent reflections 4340; Data collection consisted of the measurement of a total of 1650 frames in five different runs covering a hemisphere of data.; A colorless crystal of  $C_{24}H_{21}NO_3$  was washed with the perfluoropolyether PFO-XR75 (Lancaster) and wedged in a glass capillary. **CCDC # is 656161.**

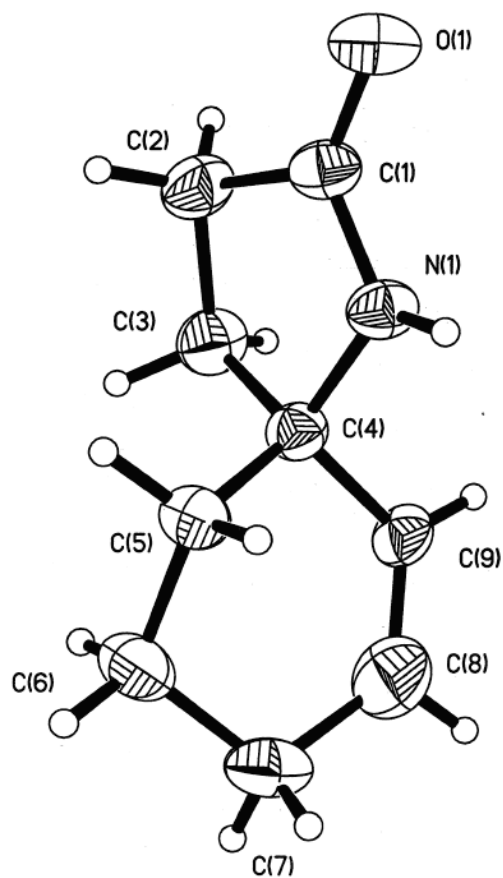
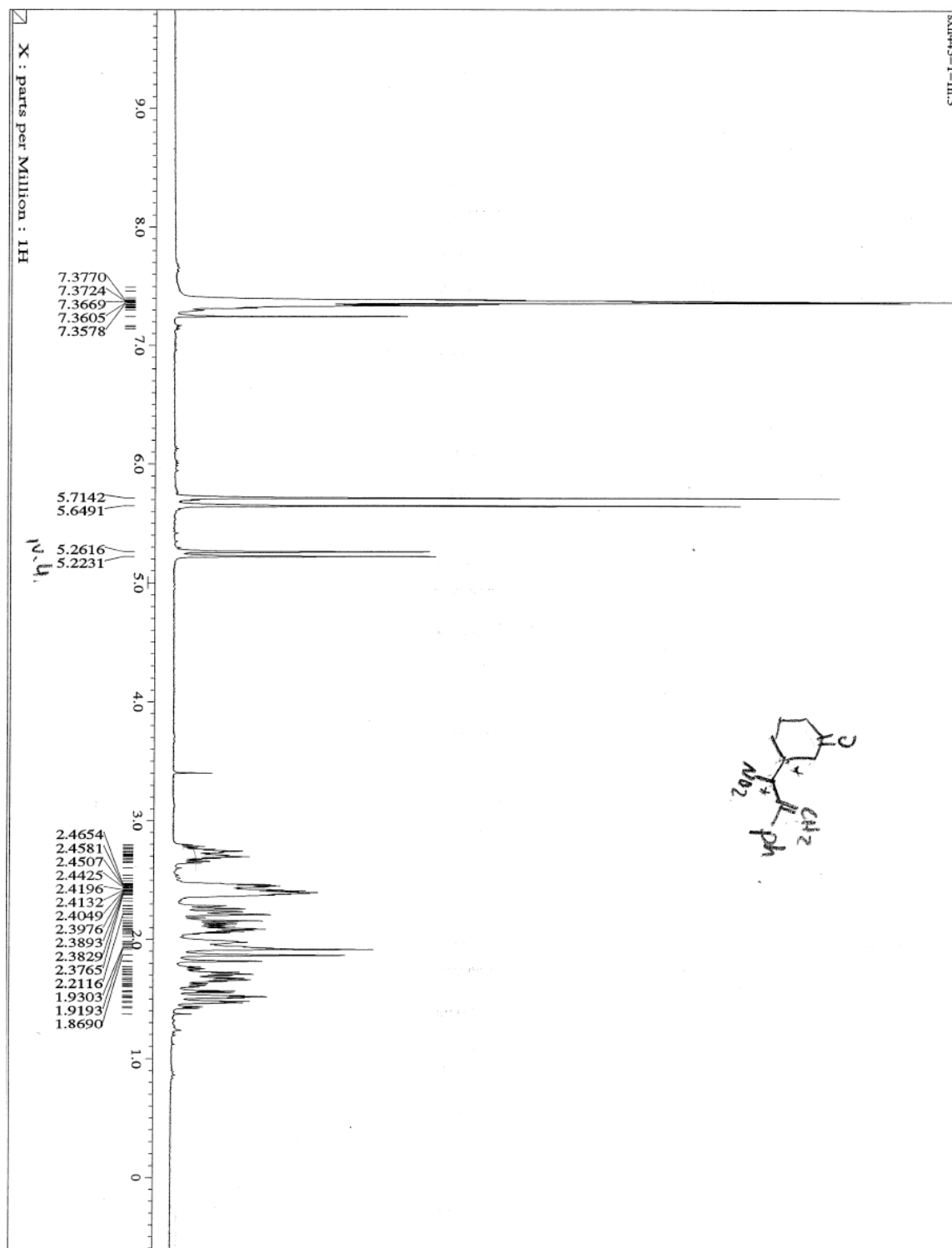


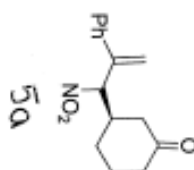
Figure S3. ORTEP drawing of the crystal structure of compound **6a**

**Compound 6a:**  $\text{C}_9\text{H}_{13}\text{NO}$ ; 151.20; 0.28 x 0.40 x 0.42mm; Monoclinic;  $P2_1/c$ ;  $a = 11.2786\text{\AA}$ ,  $b = 7.629\text{\AA}$ ,  $c = 9.9808\text{\AA}$ ,  $\alpha = 90^\circ$ ,  $\beta = 98.141^\circ$ ,  $\gamma = 90^\circ$ ; Vol. =  $850.15\text{\AA}^3$   $Z = 4$ ;  $\rho = 1.181\text{g/cm}^3$ ;  $\mu = 0.77\text{cm}^{-1}$ ; Radiation source:  $\text{MoK}\alpha$ ,  $\lambda = 0.71073\text{\AA}$ ;  $T = 293\text{K}$ ;  $2\theta$  max = 28; Reflections collected: 5520, Independent reflections 1912; Data collection consisted of the measurement of a total of 1650 frames in five different runs covering a hemisphere of data.; A colorless crystal of  $\text{C}_9\text{H}_{13}\text{NO}$  was washed with the perfluoropolyether PFO-XR75 (Lancaster) and wedged in a glass capillary. **CCDC # is 656162.**

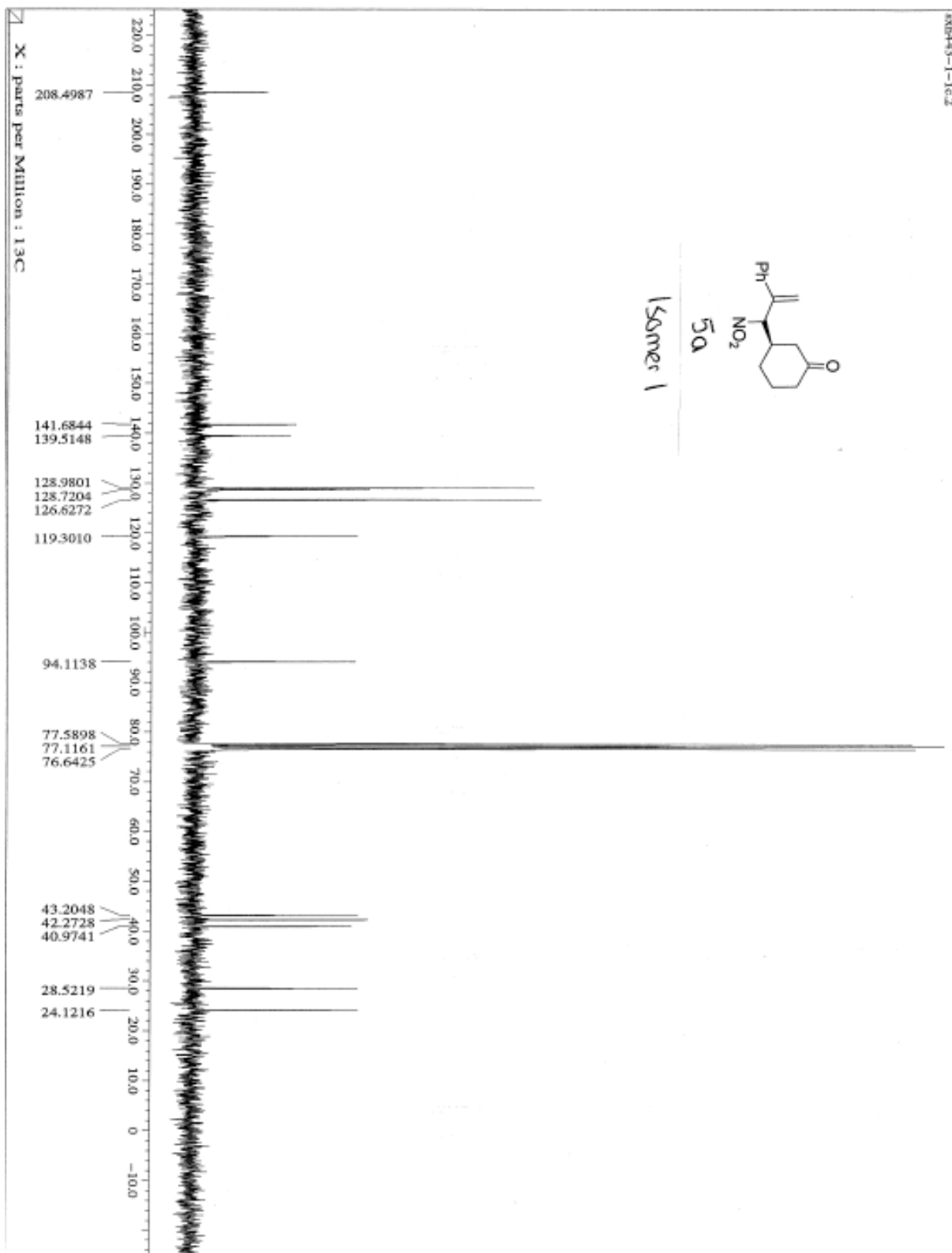


# VII. $^1\text{H}$ -NMR and $^{13}\text{C}$ -NMR Spectra

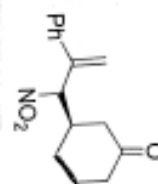




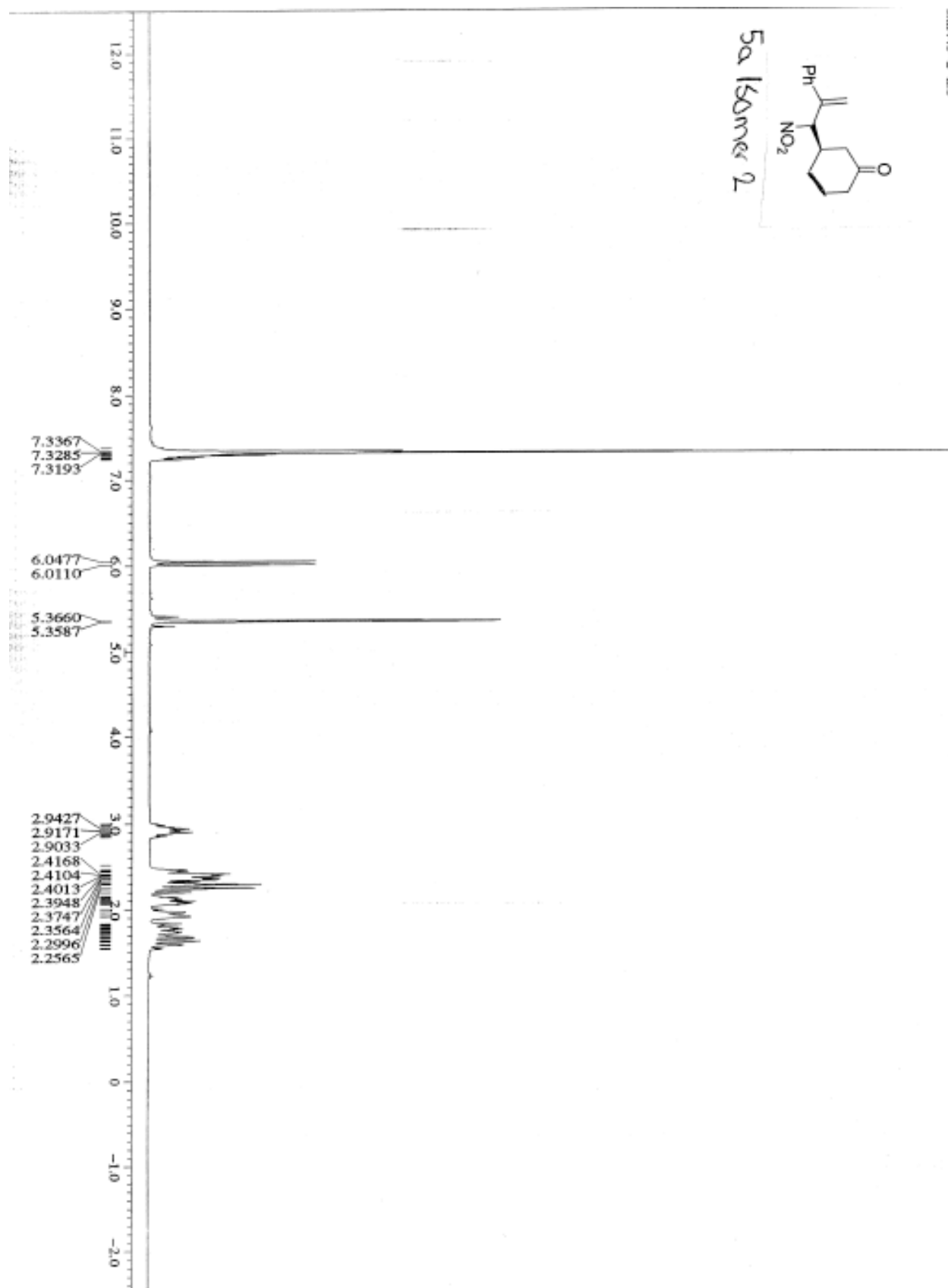
Isomer 1

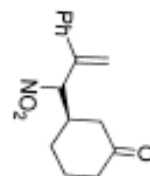


Isomer 1

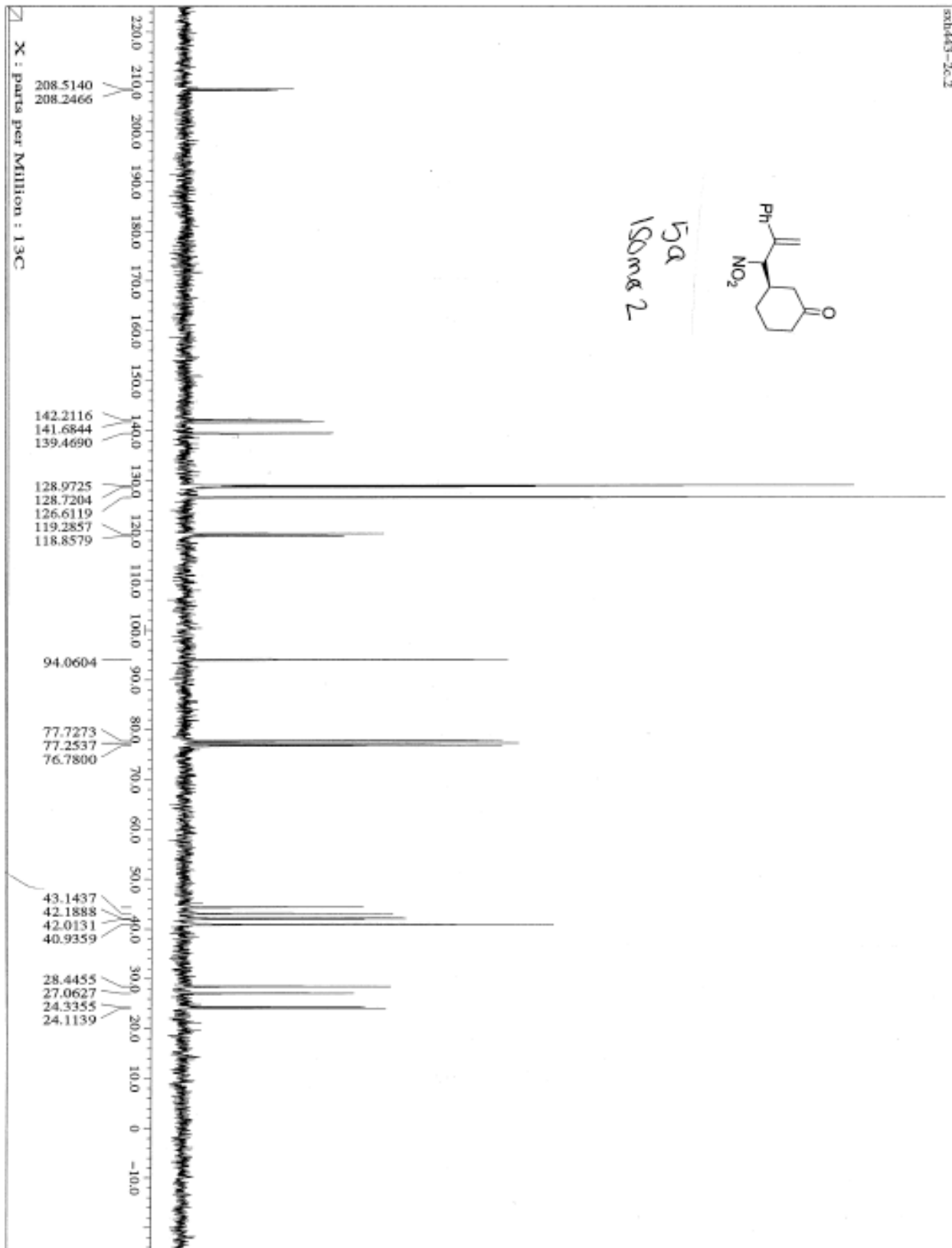


5a isomer 2

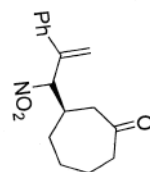




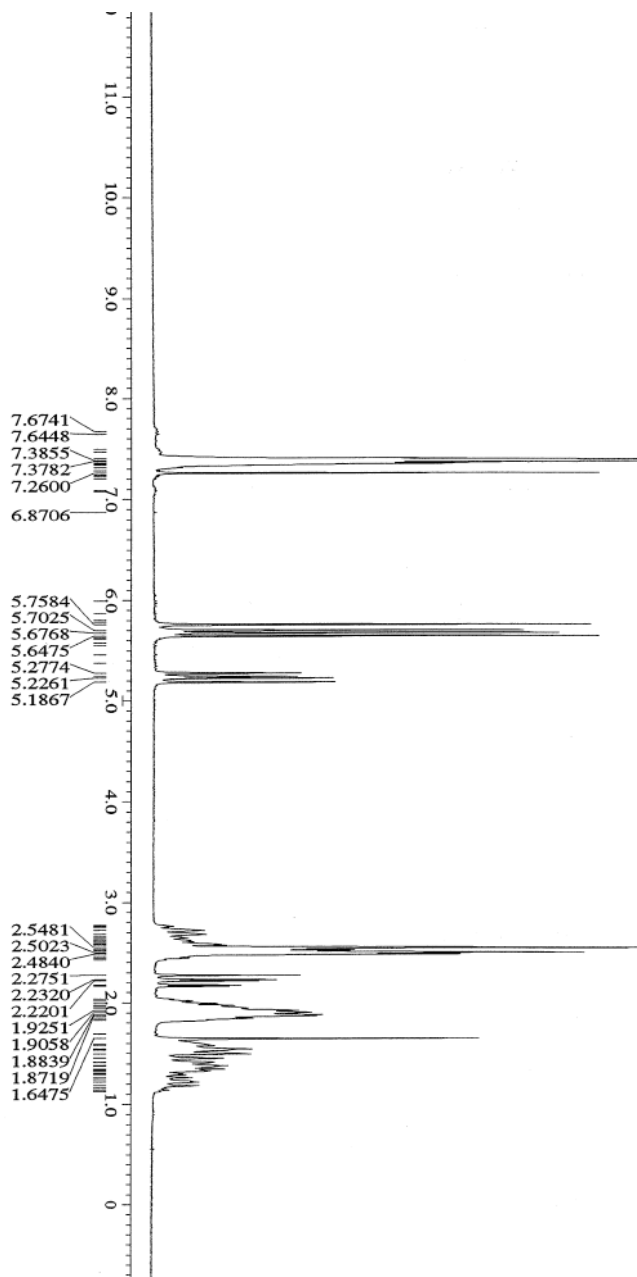
5a  
Isomer 2

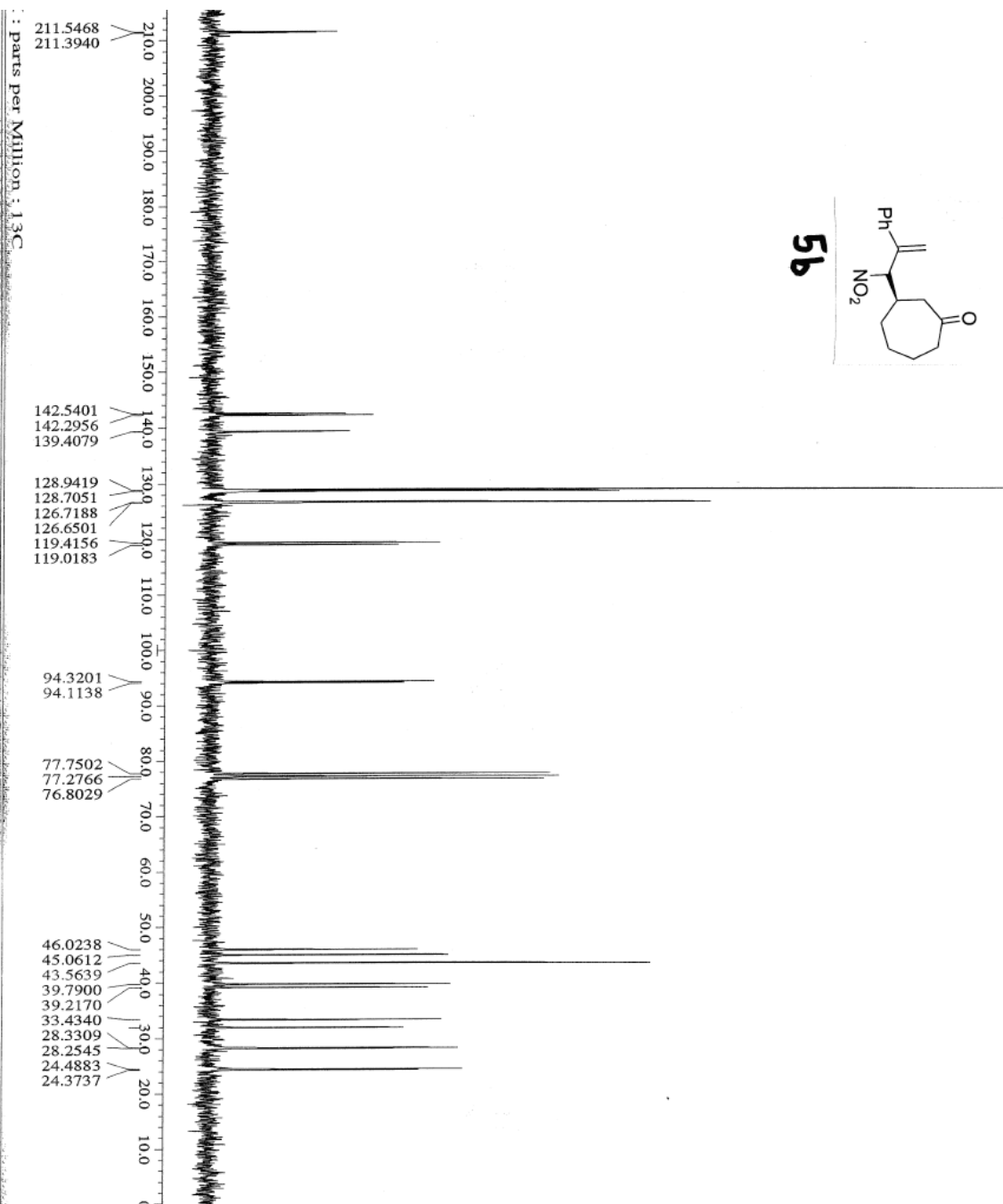
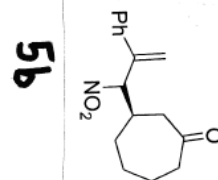


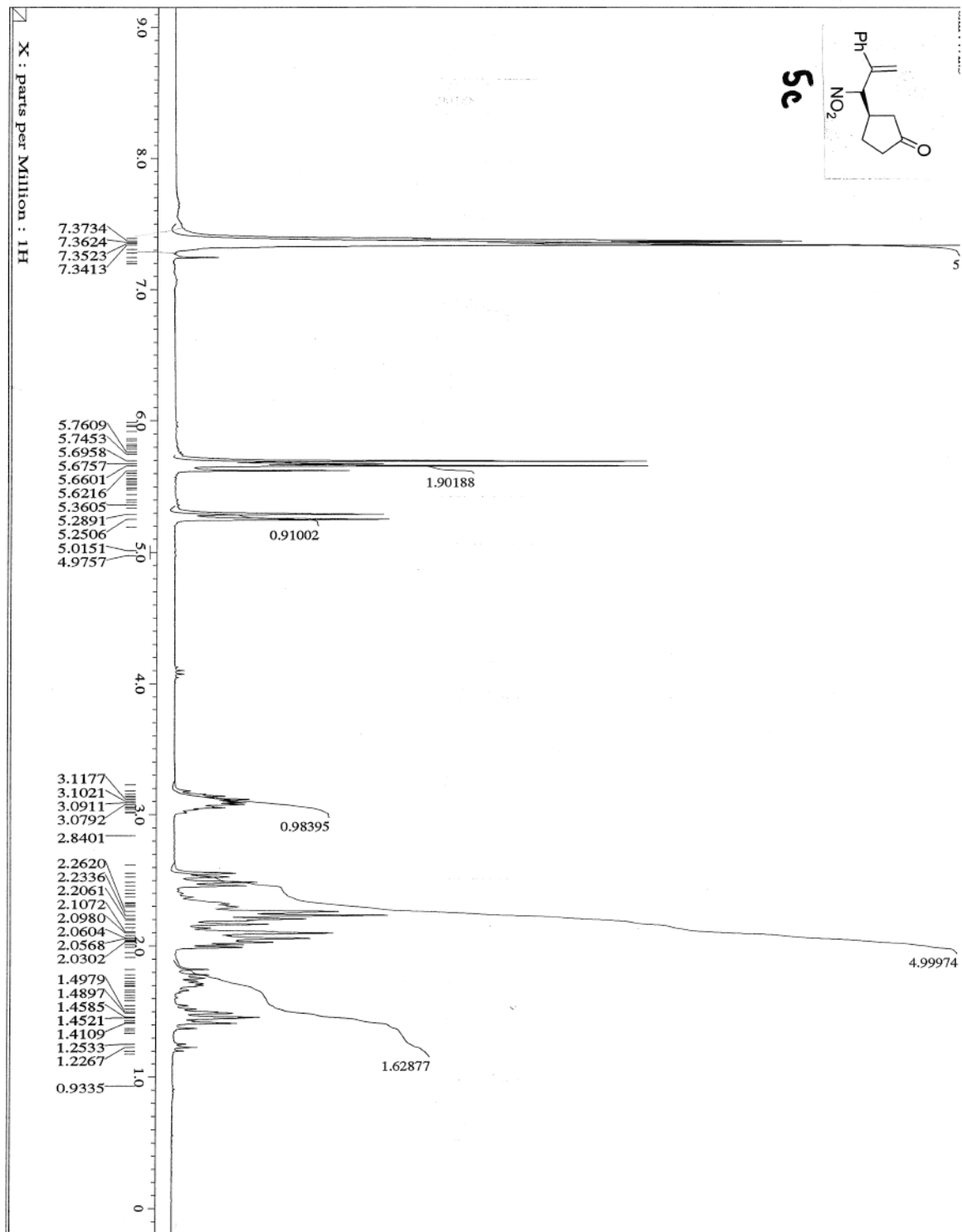
5b

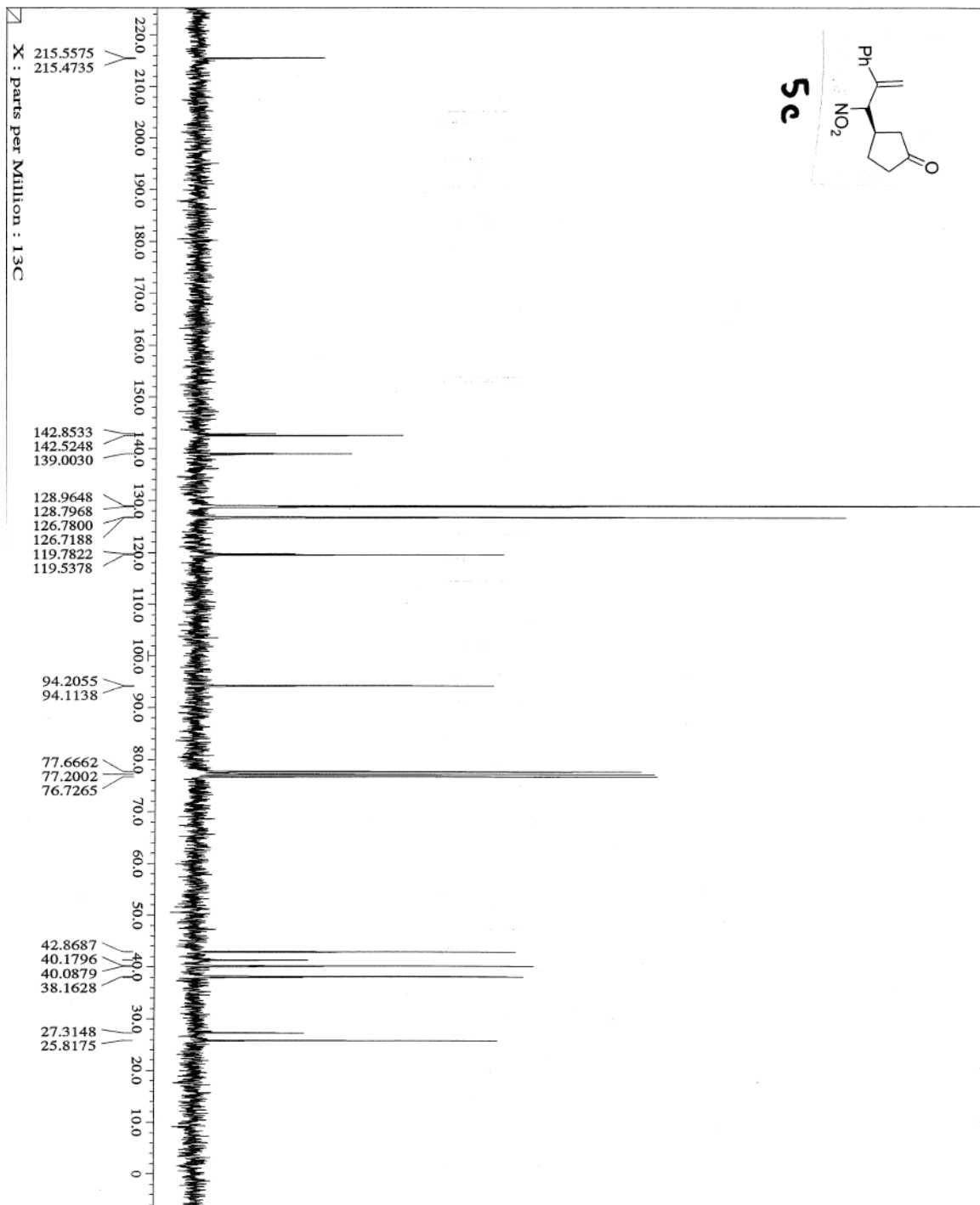


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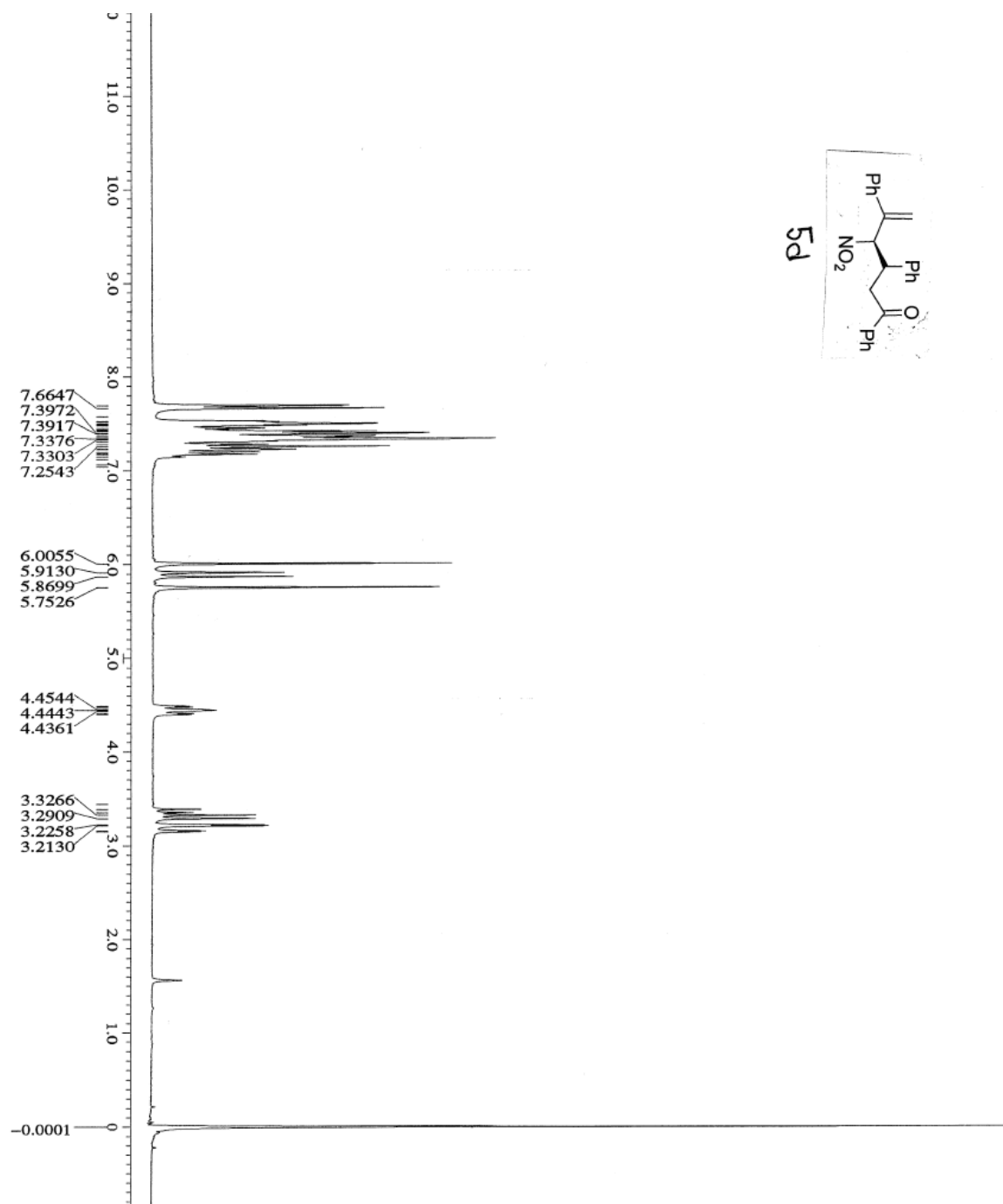
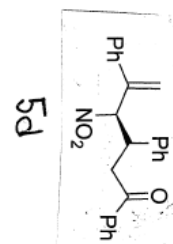


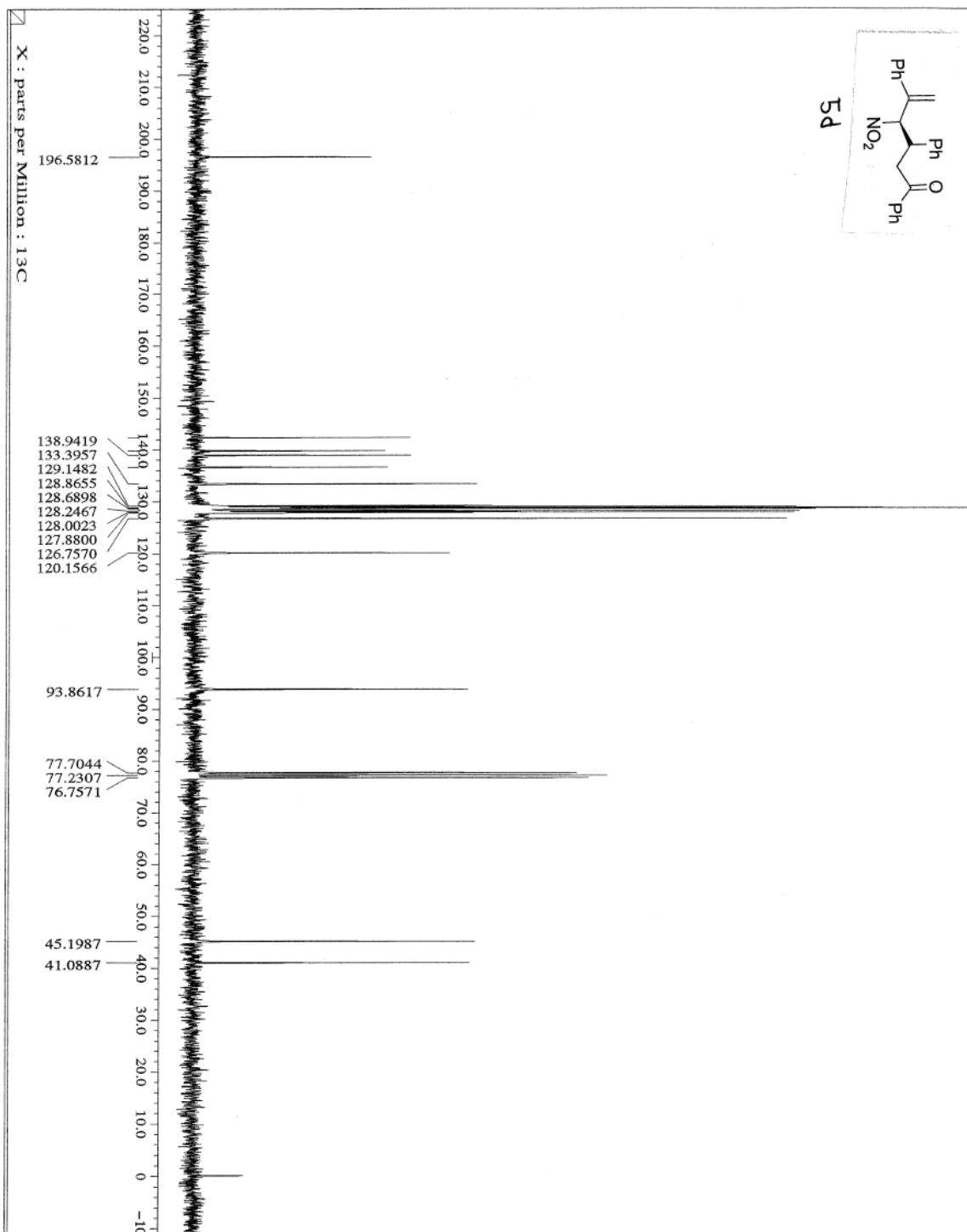


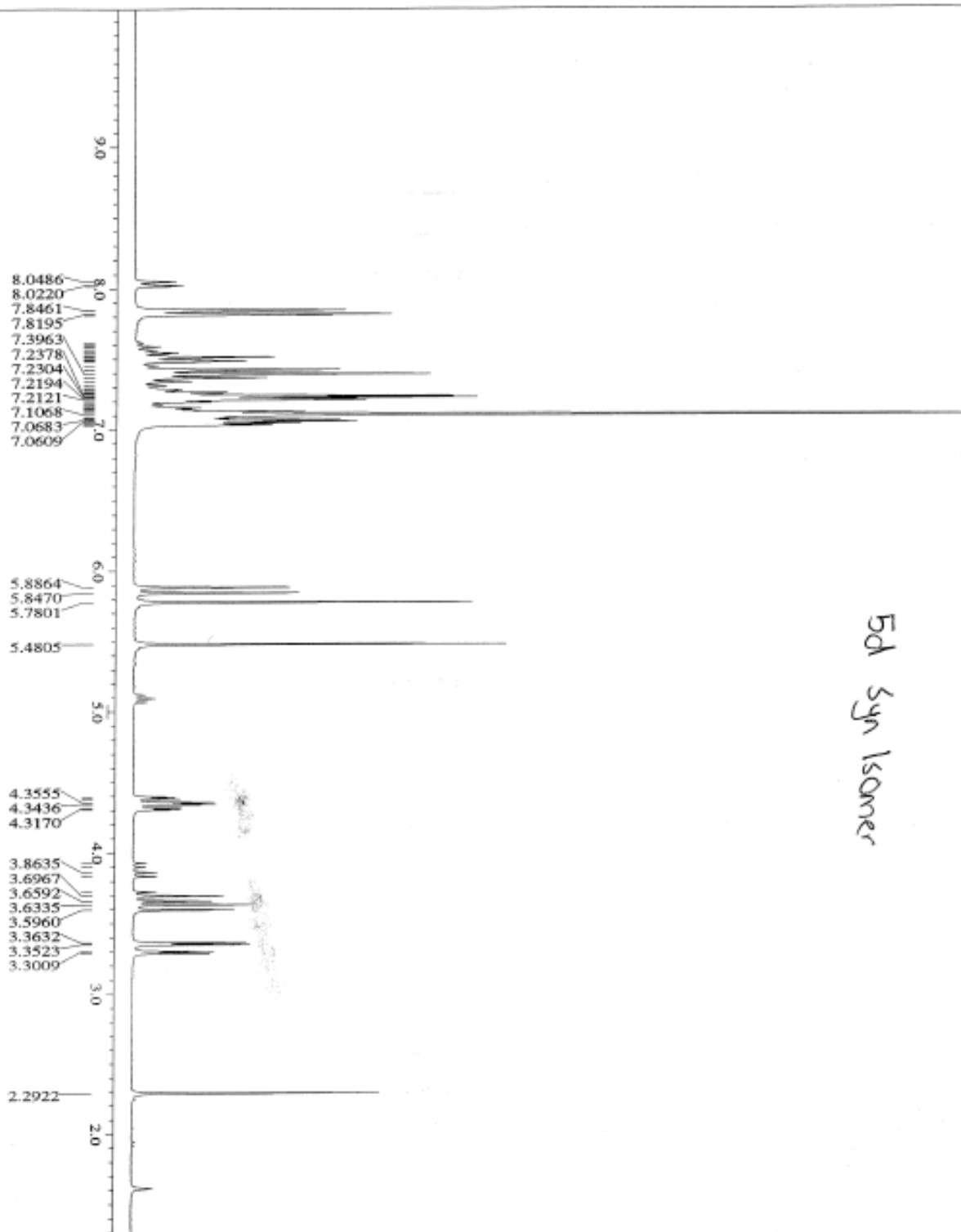




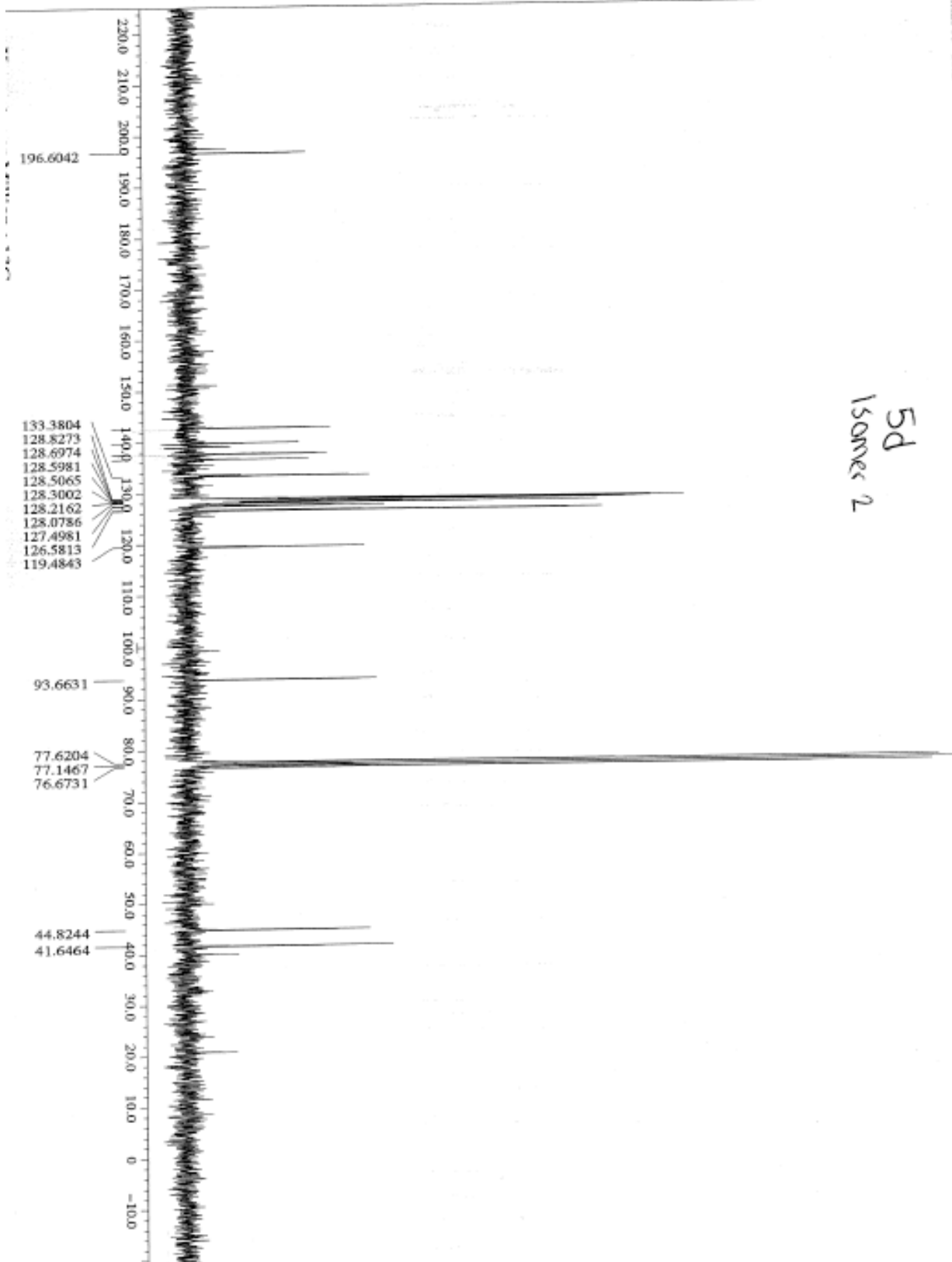




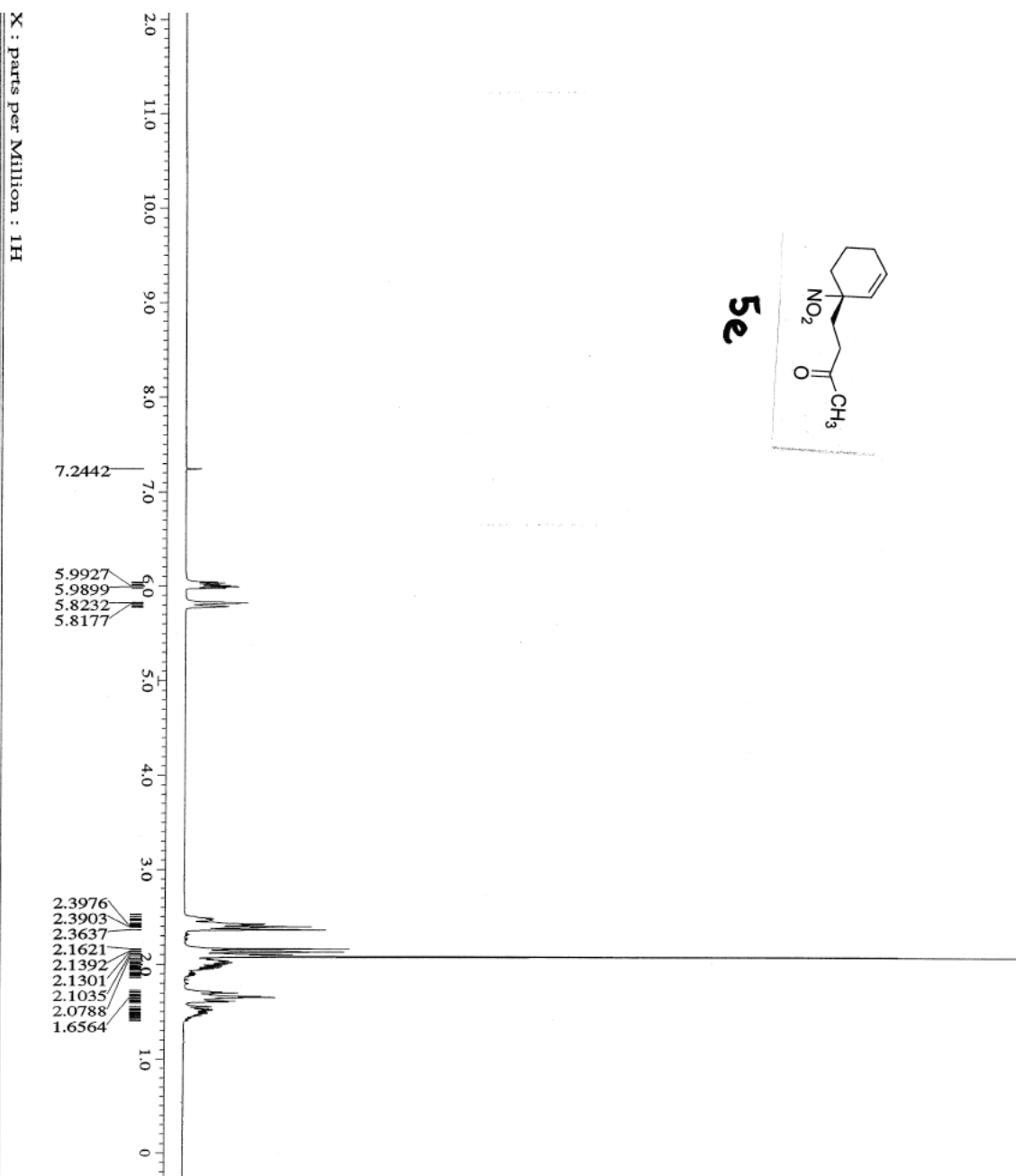
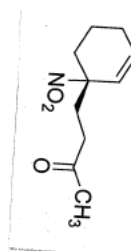


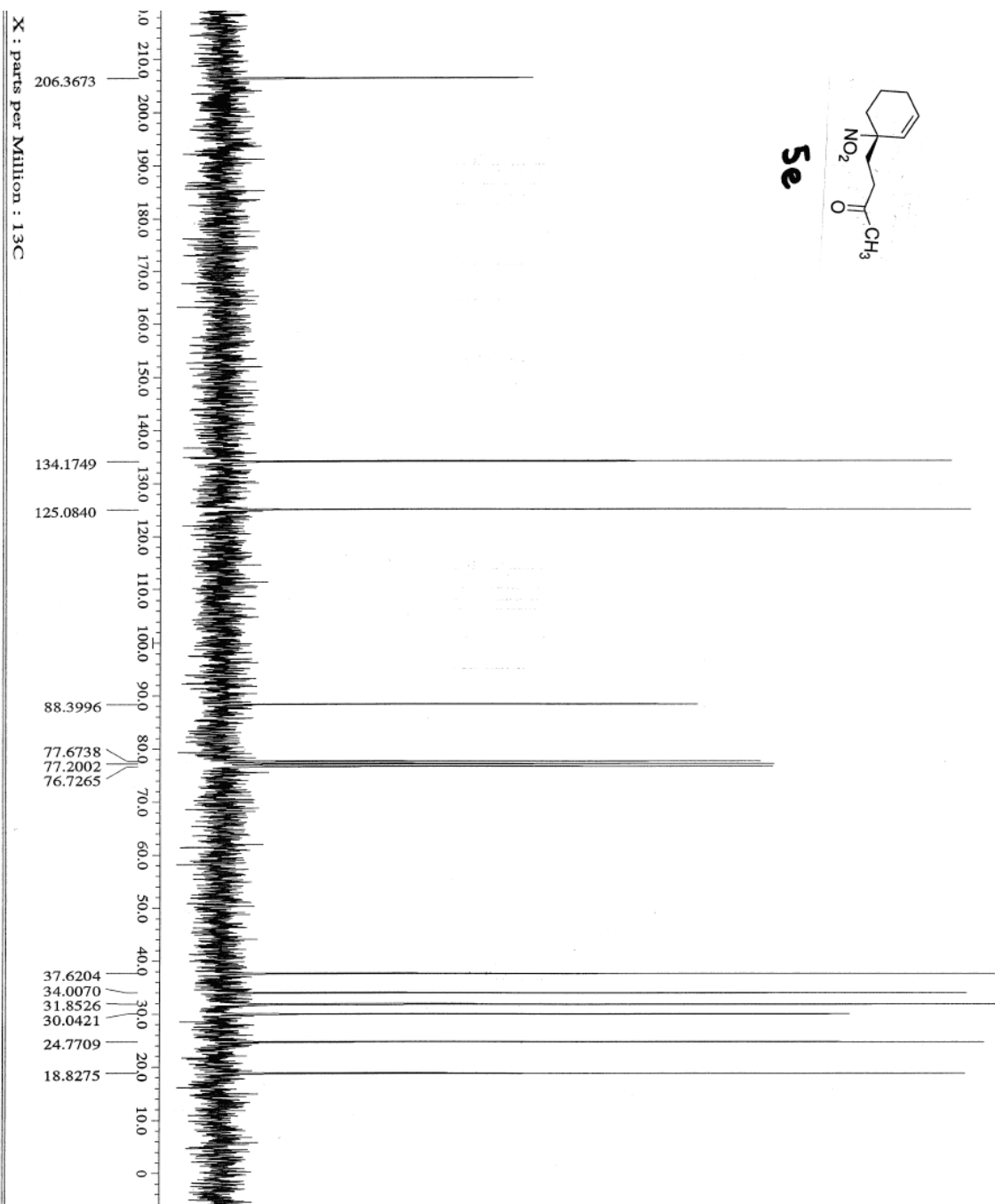
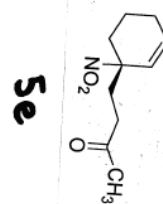


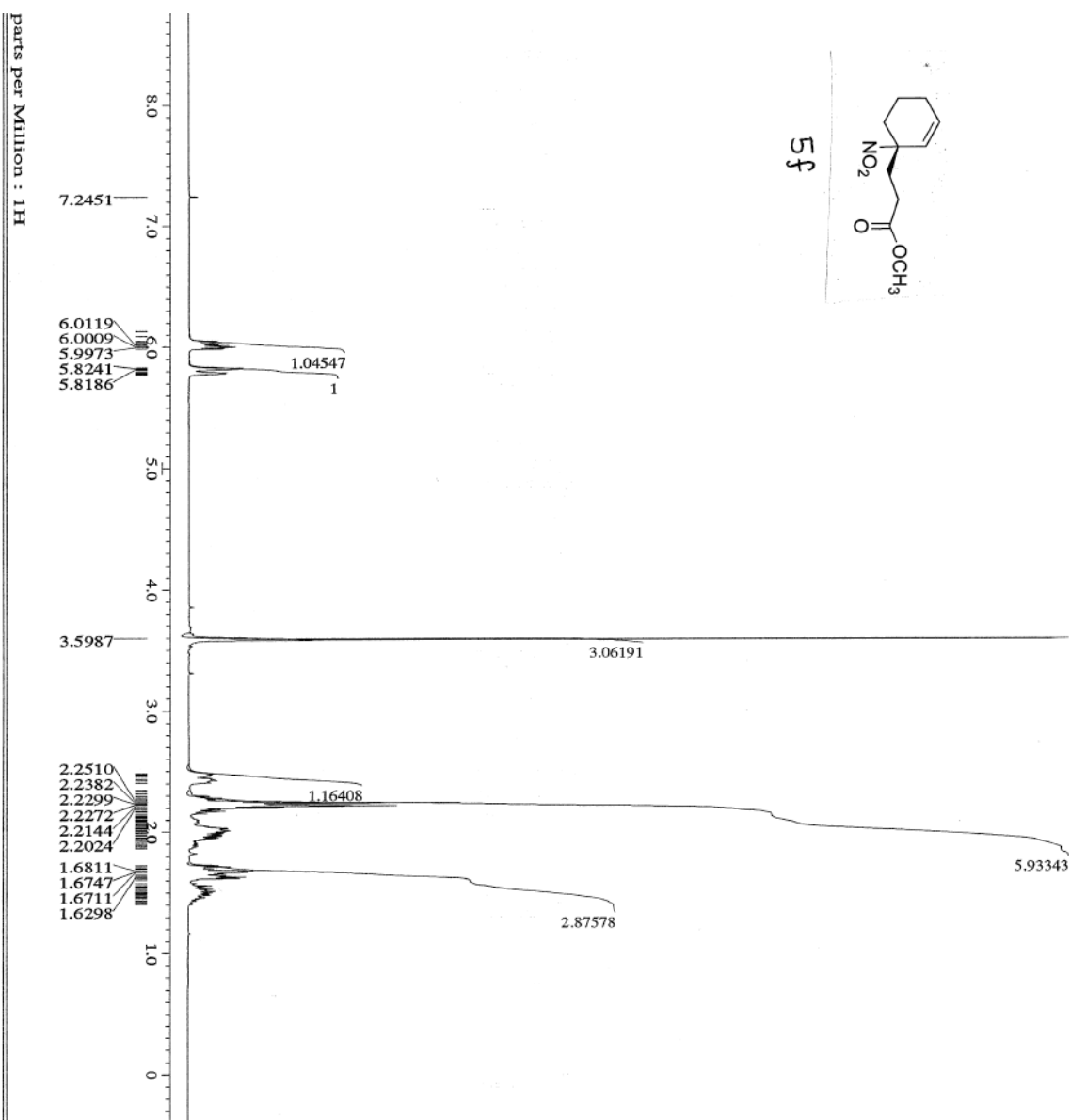
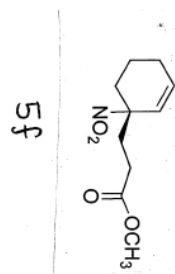
5d  
Isomer 2

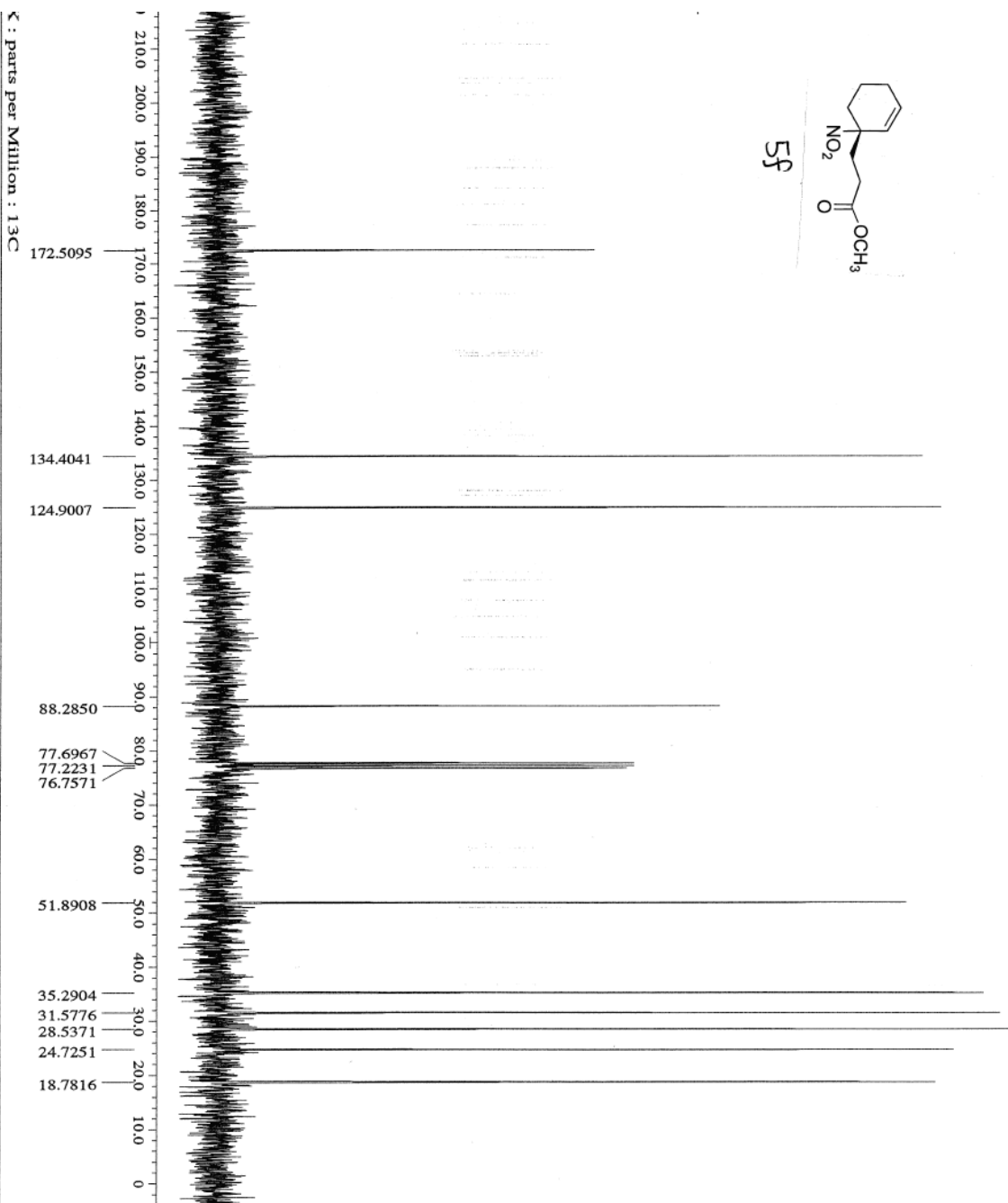


5e



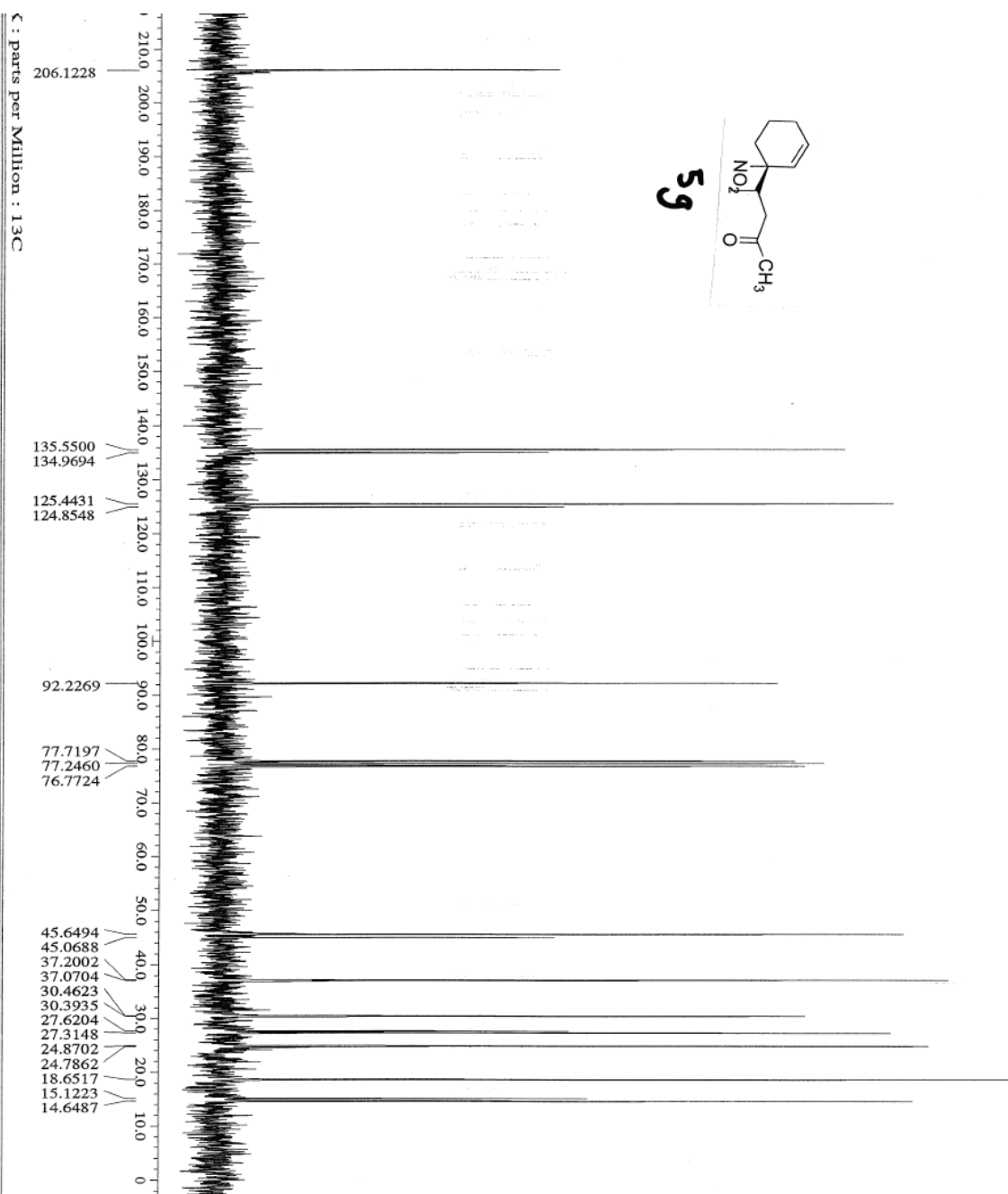
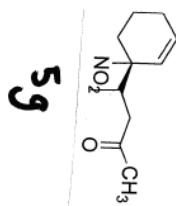


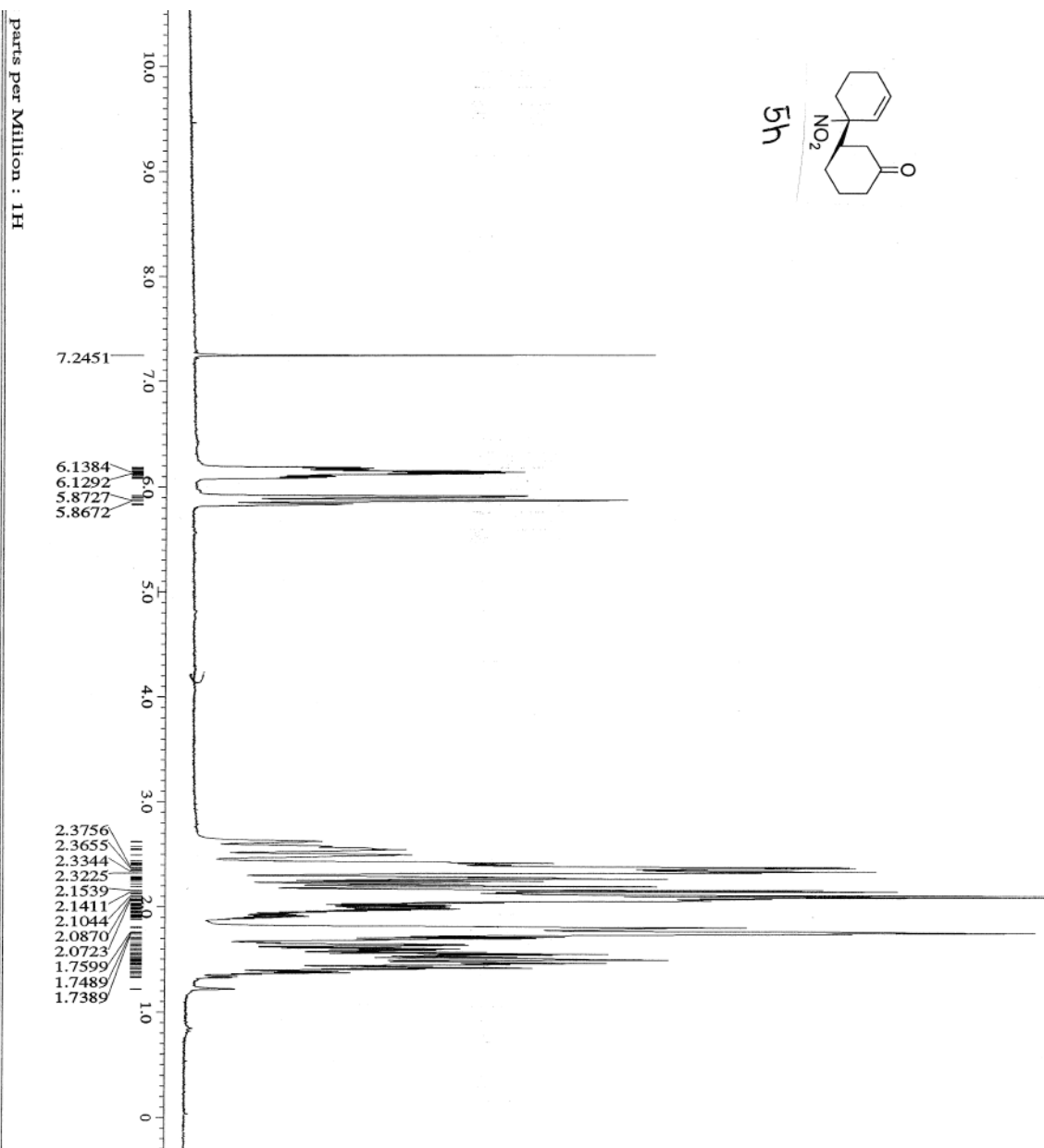
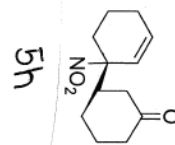


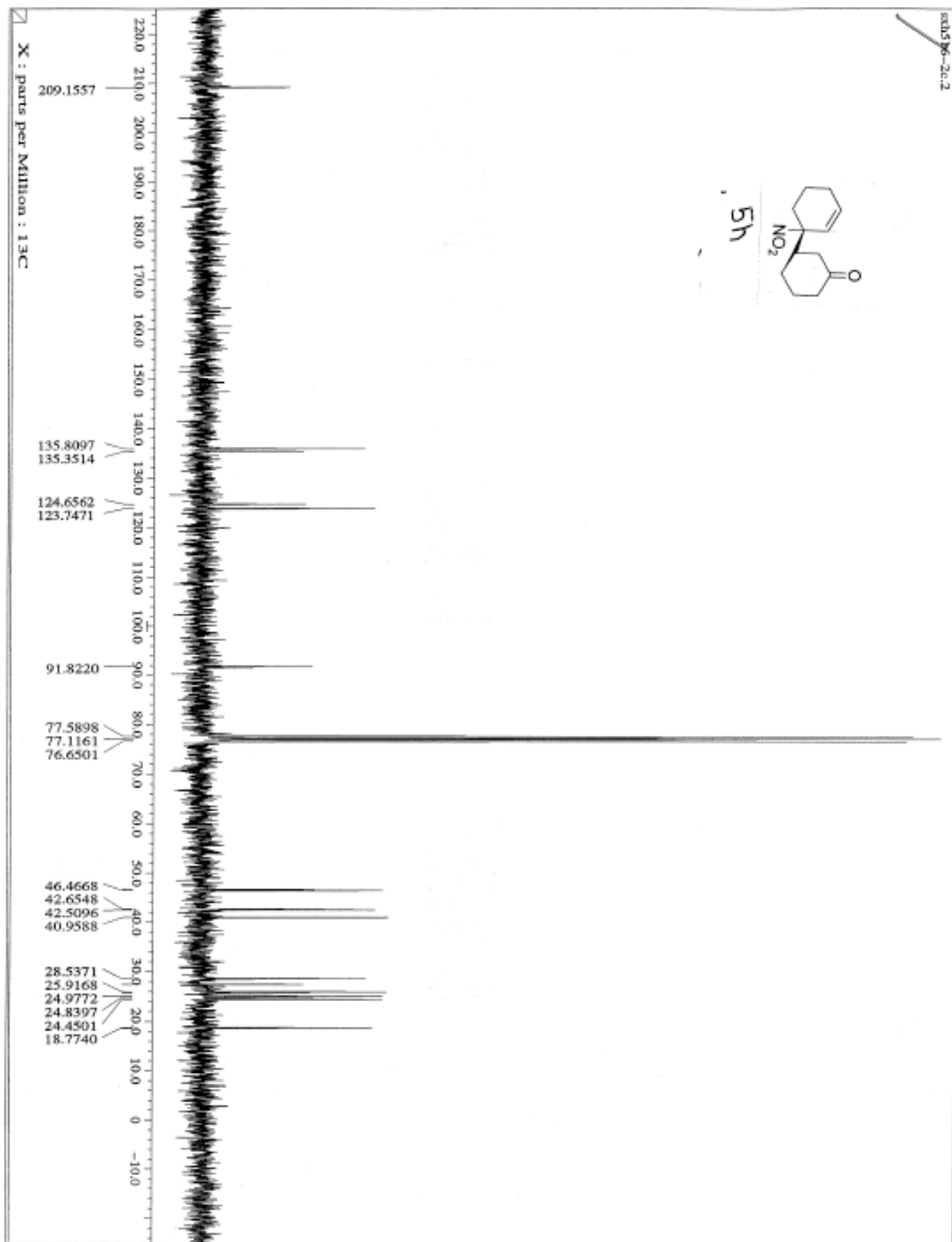




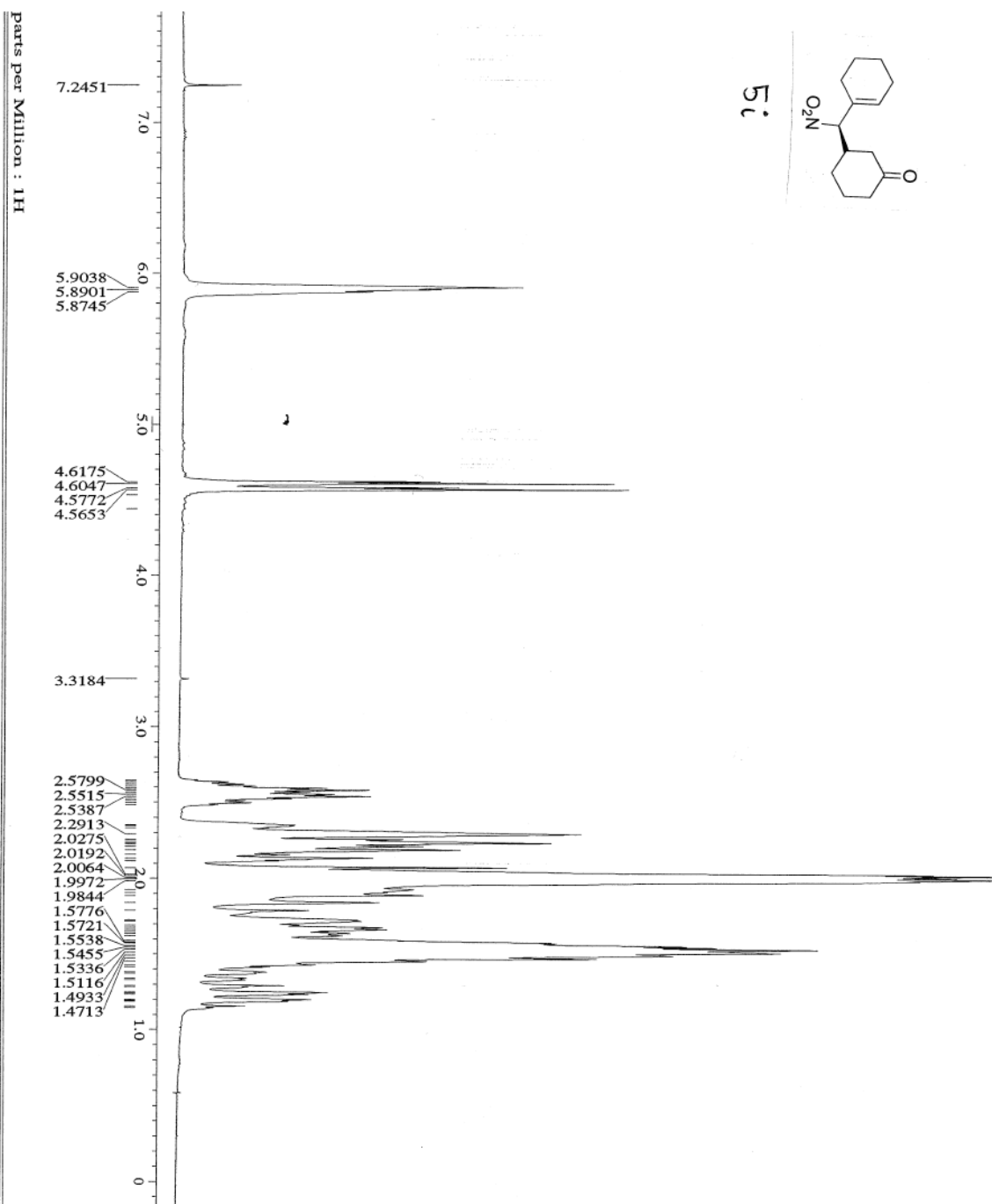
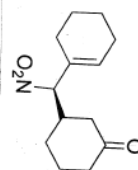


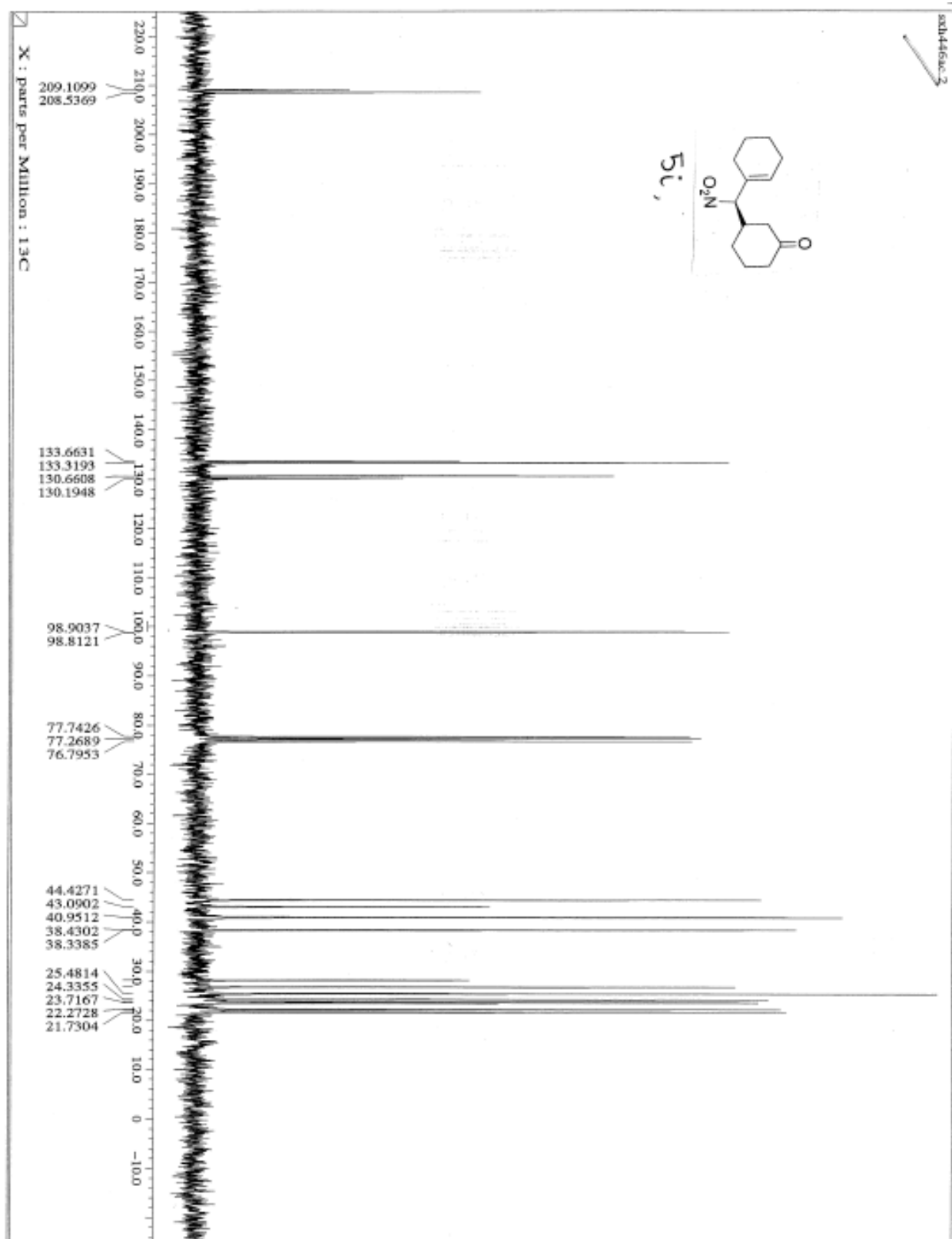


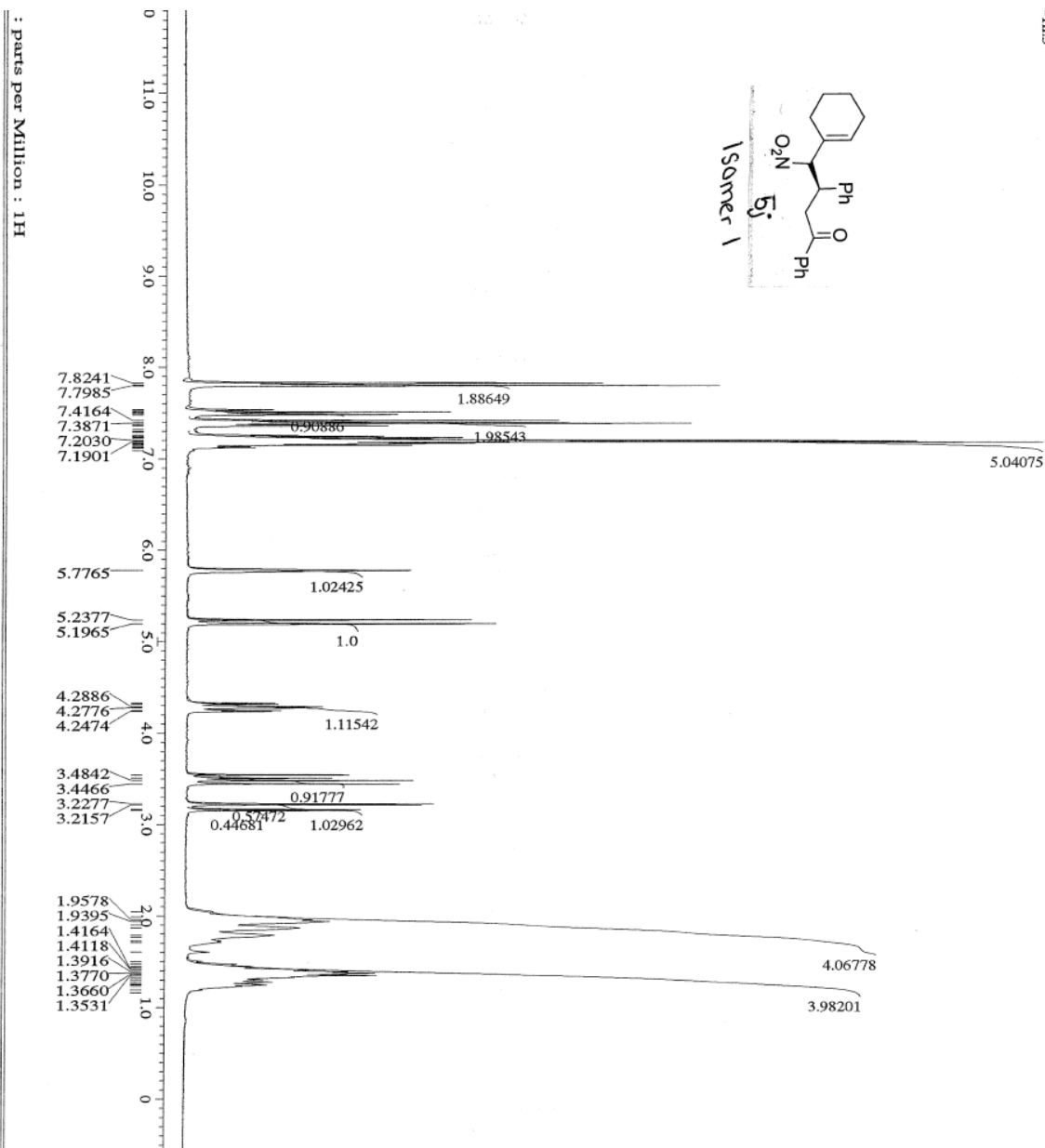
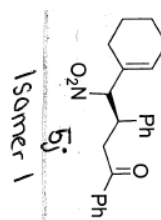


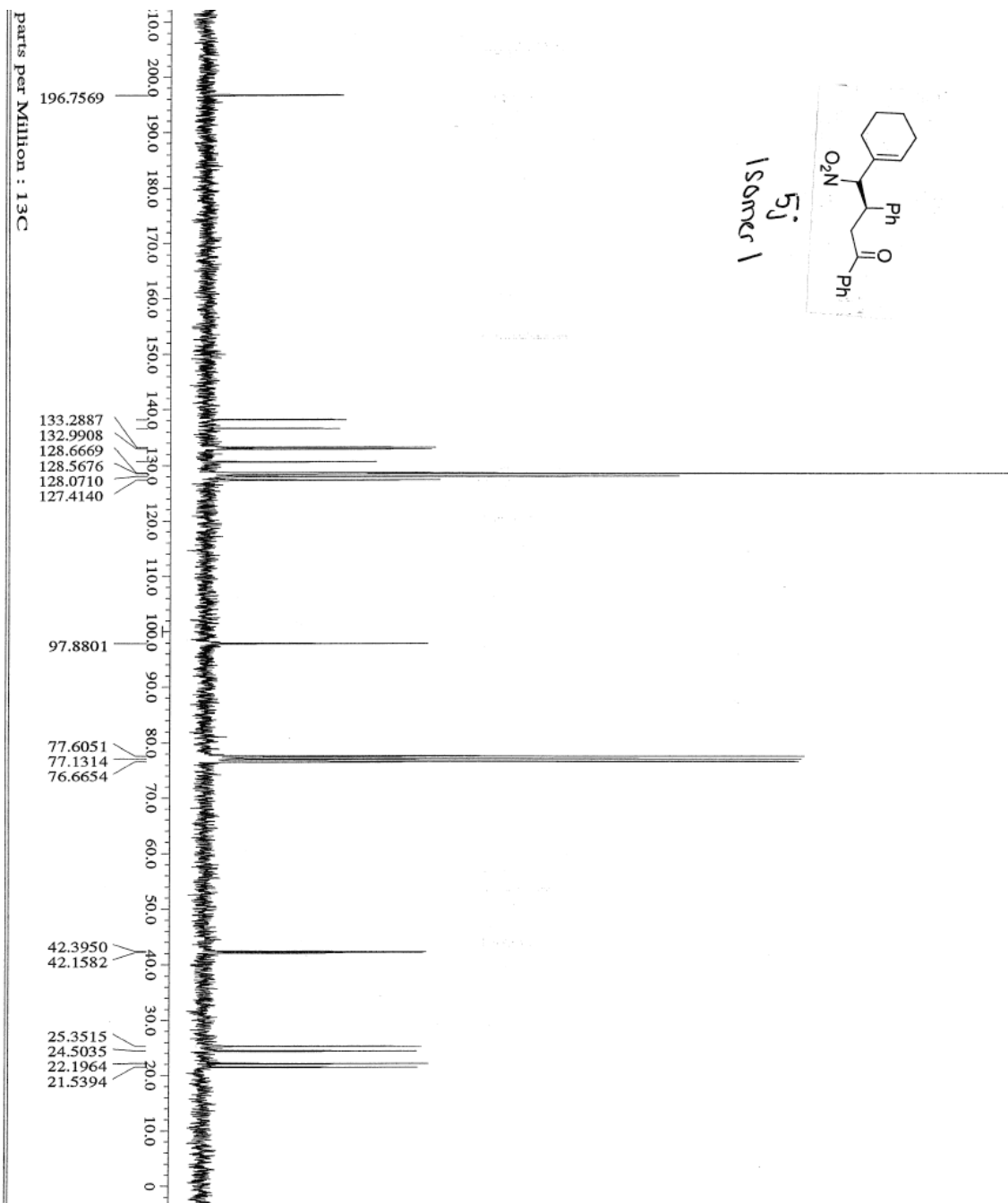


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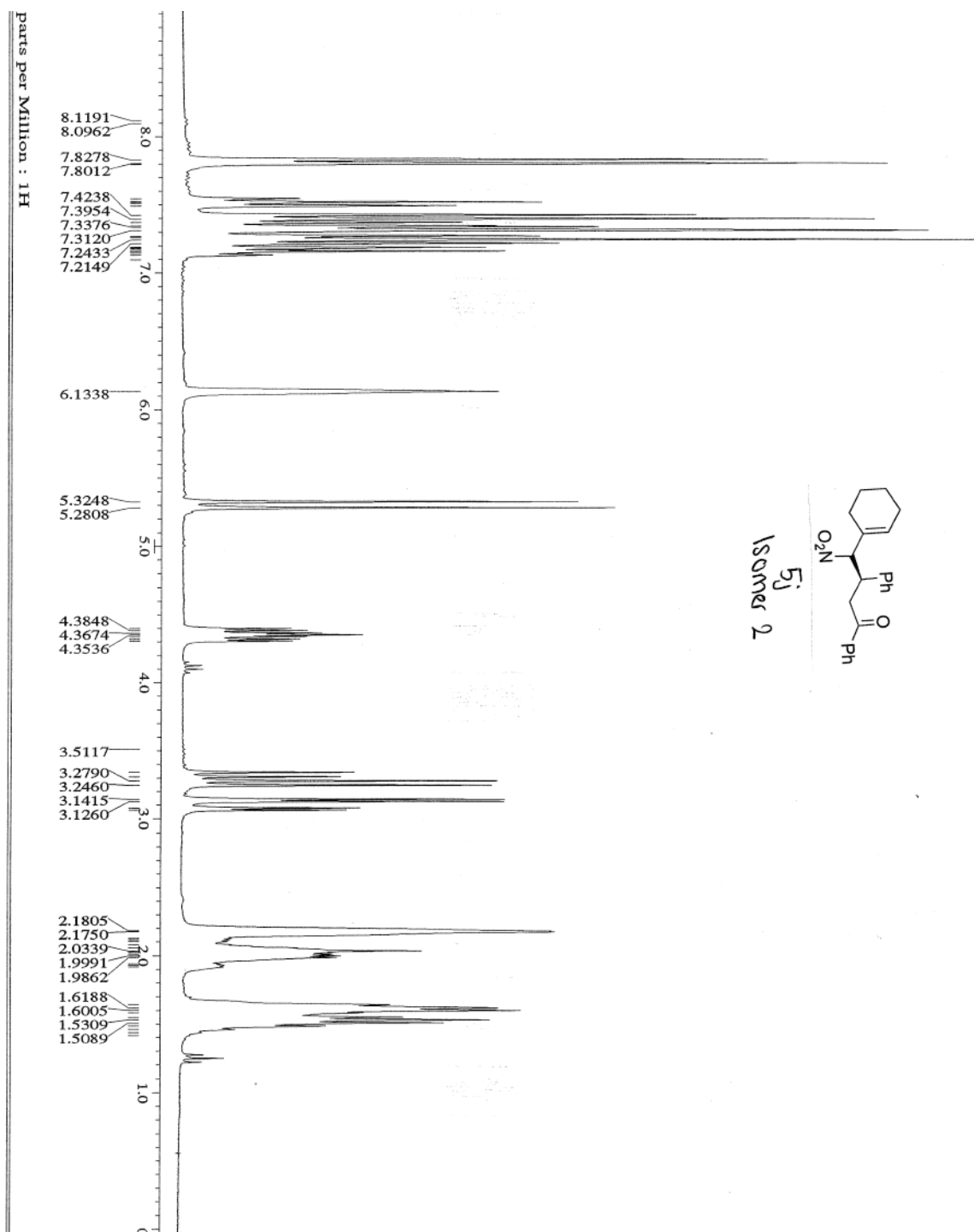


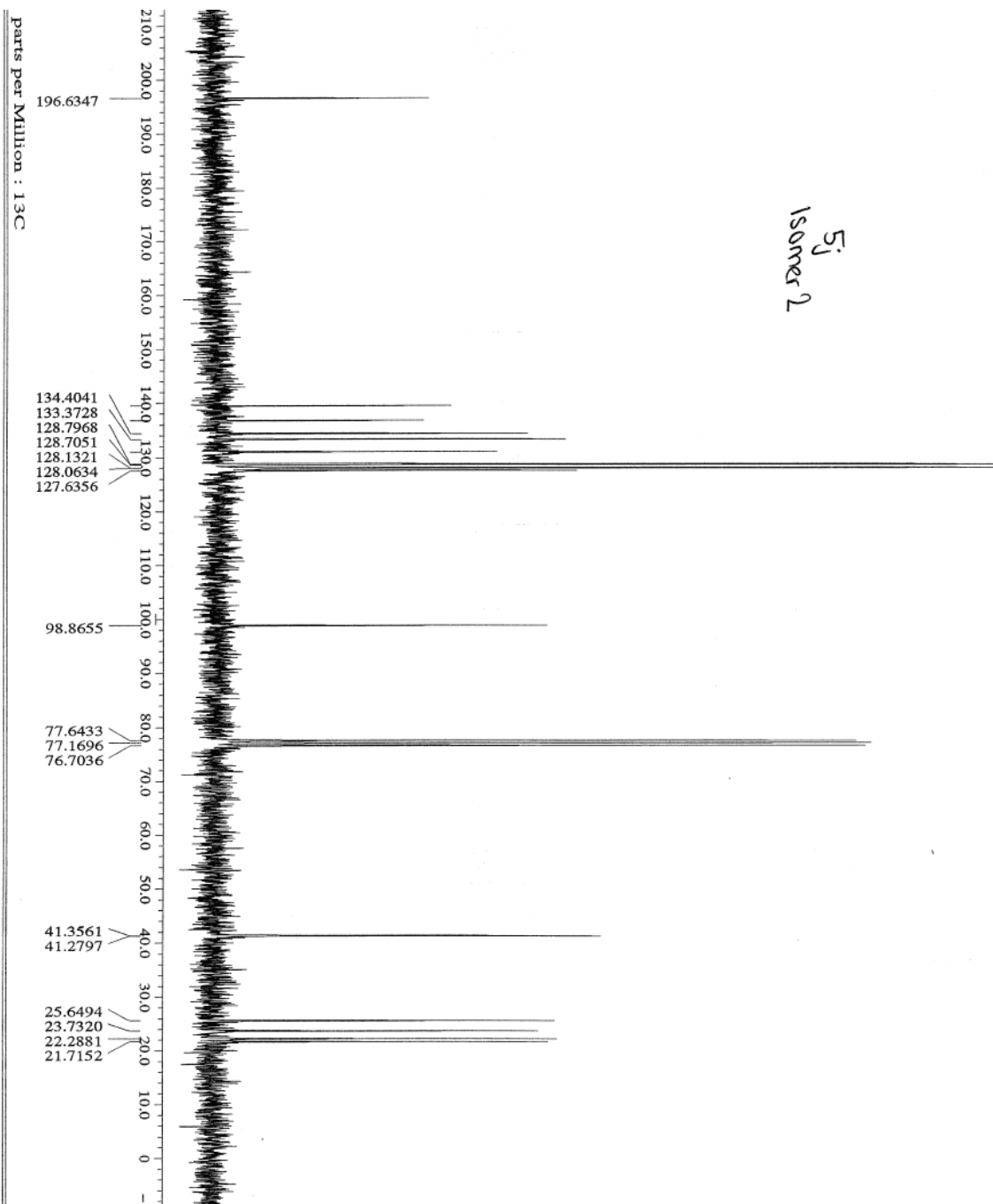


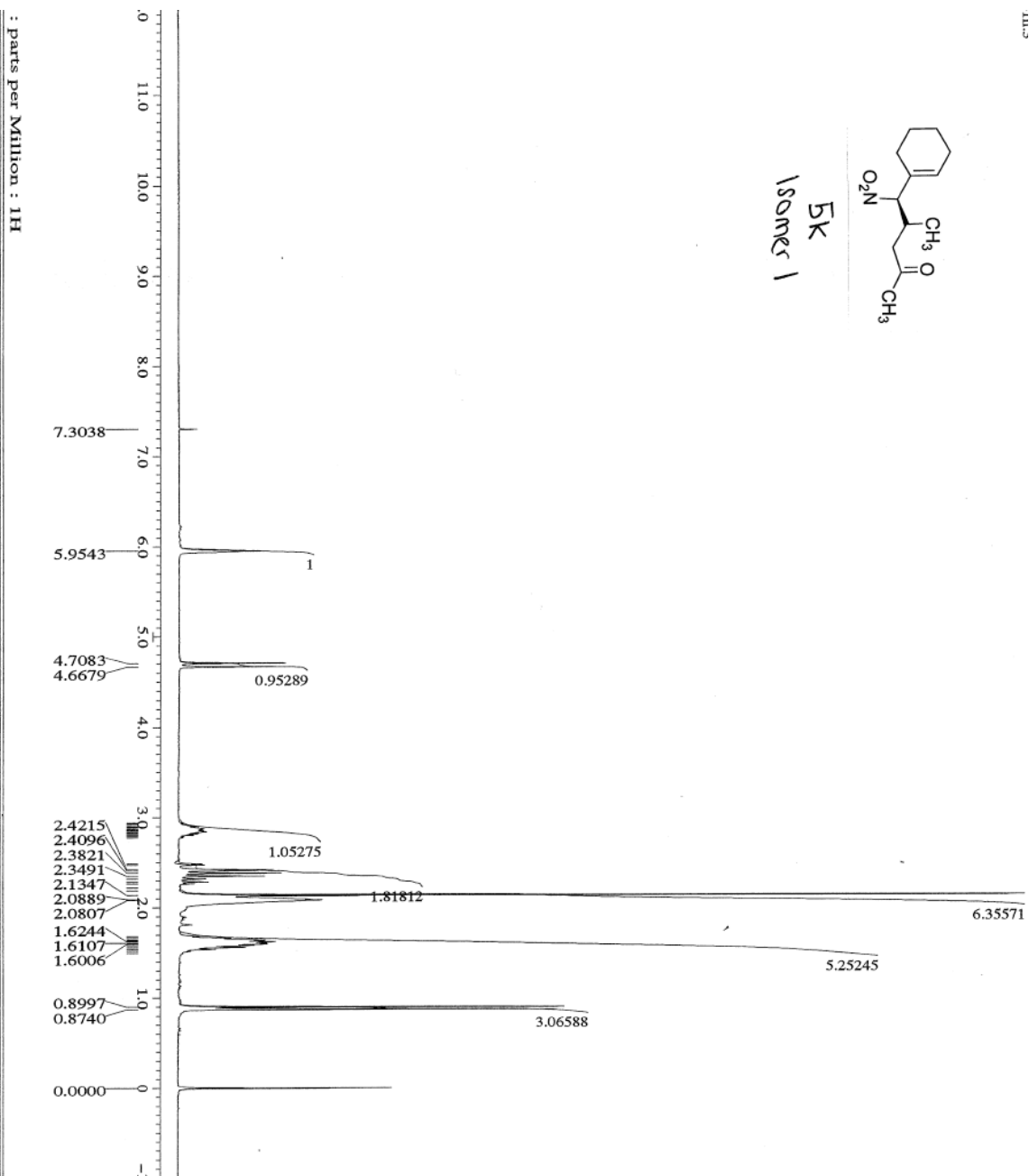
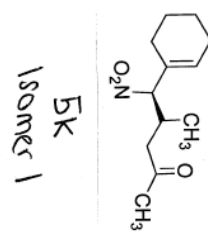


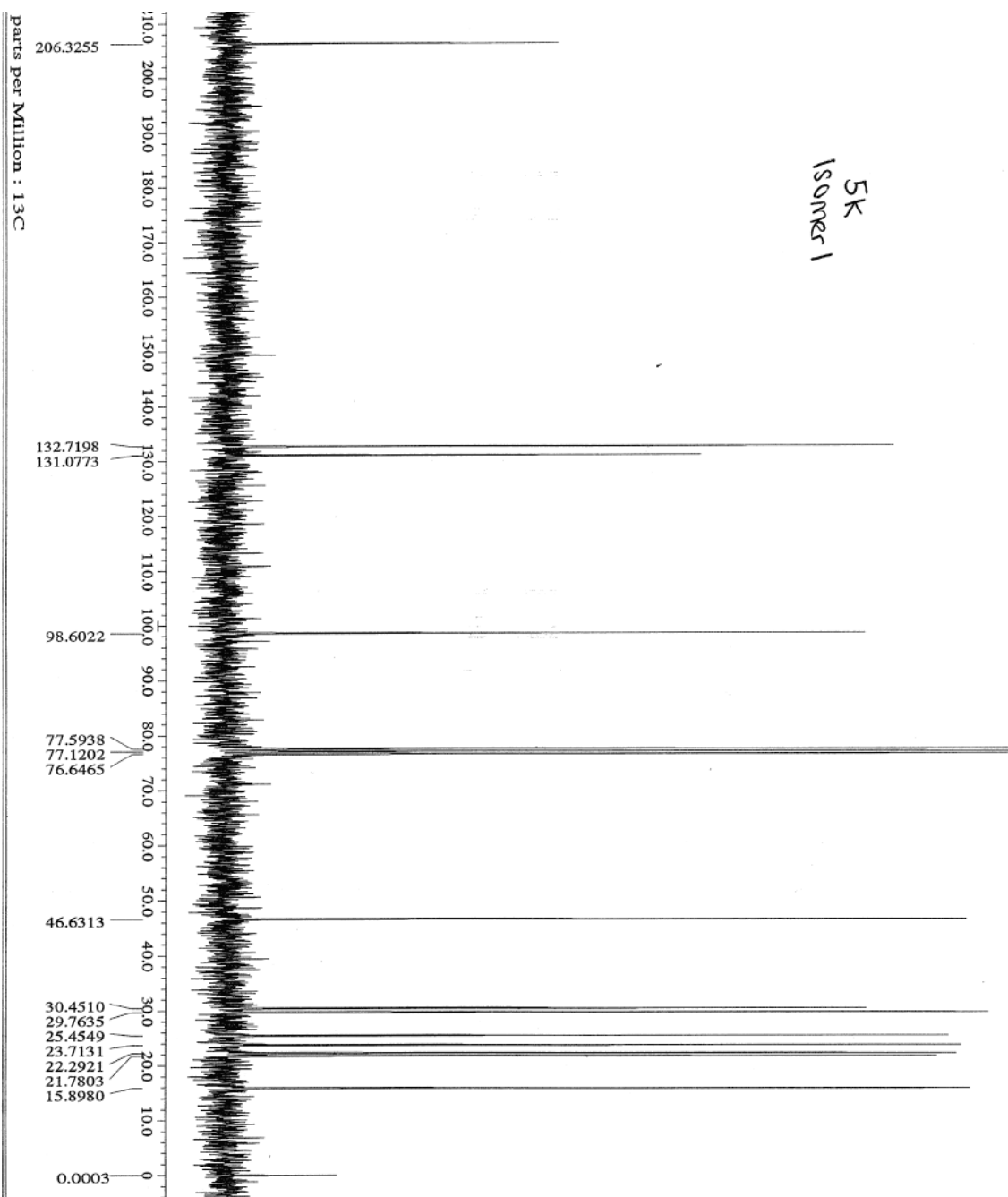


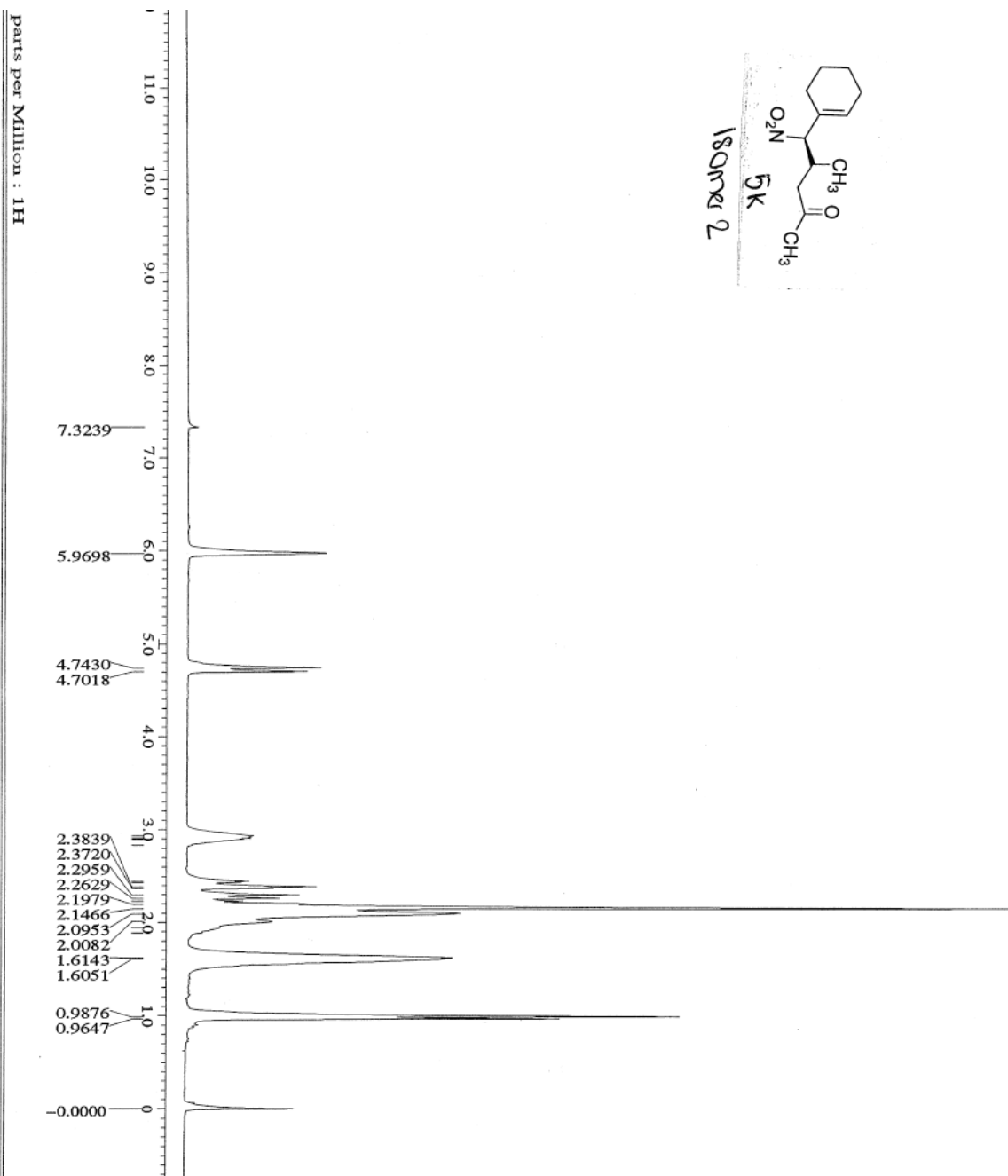
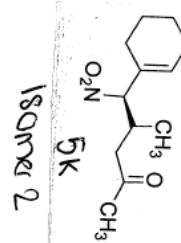


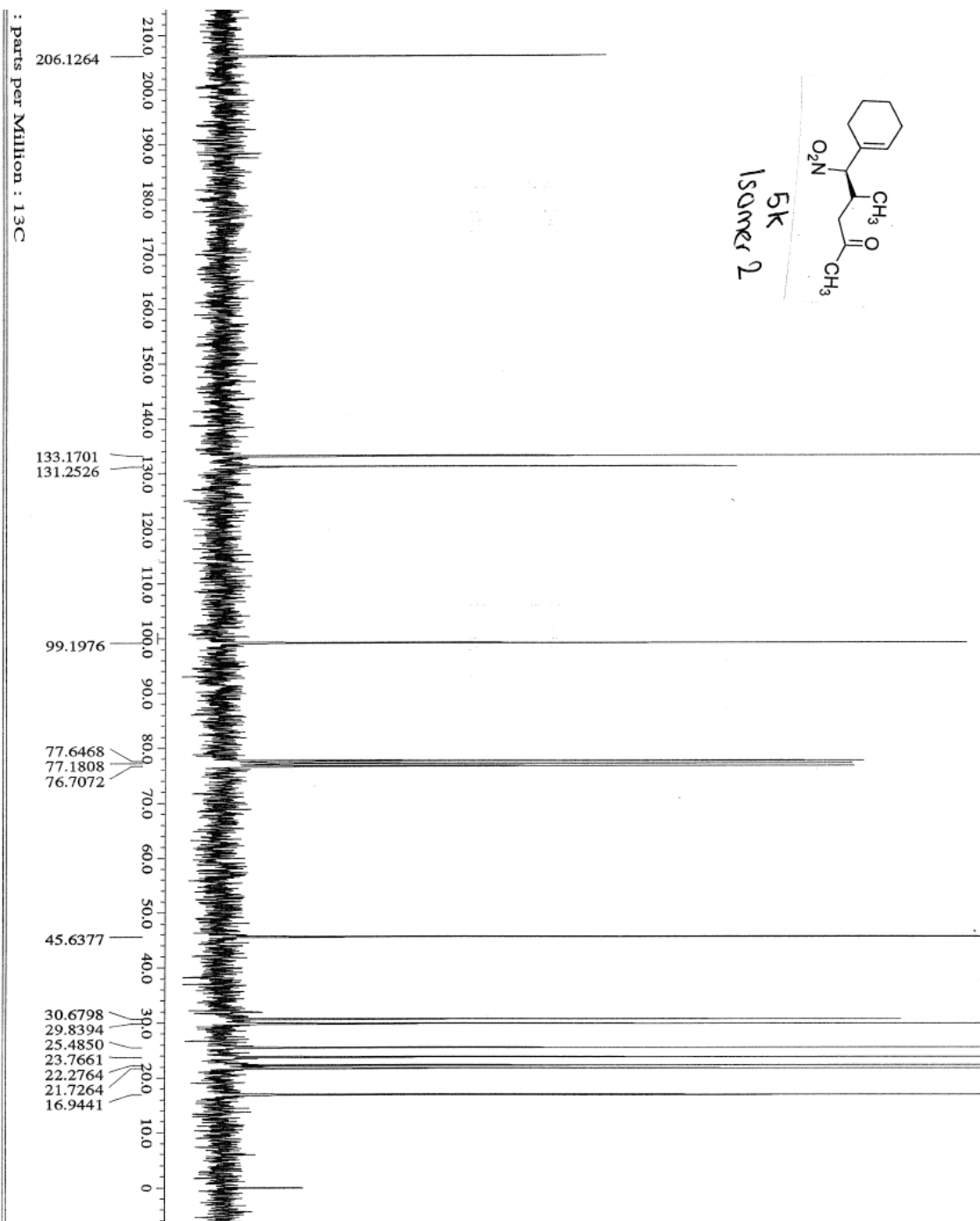


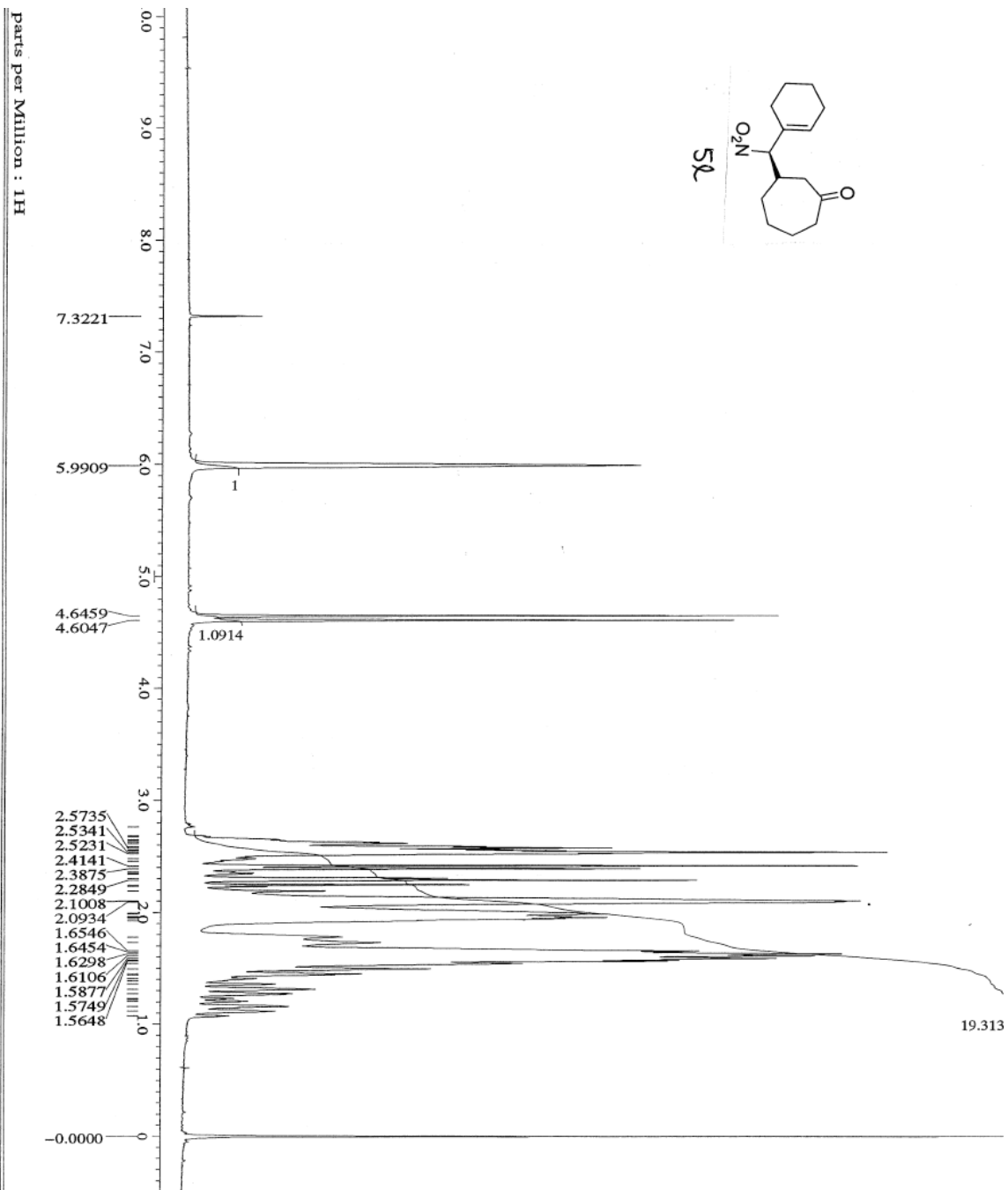


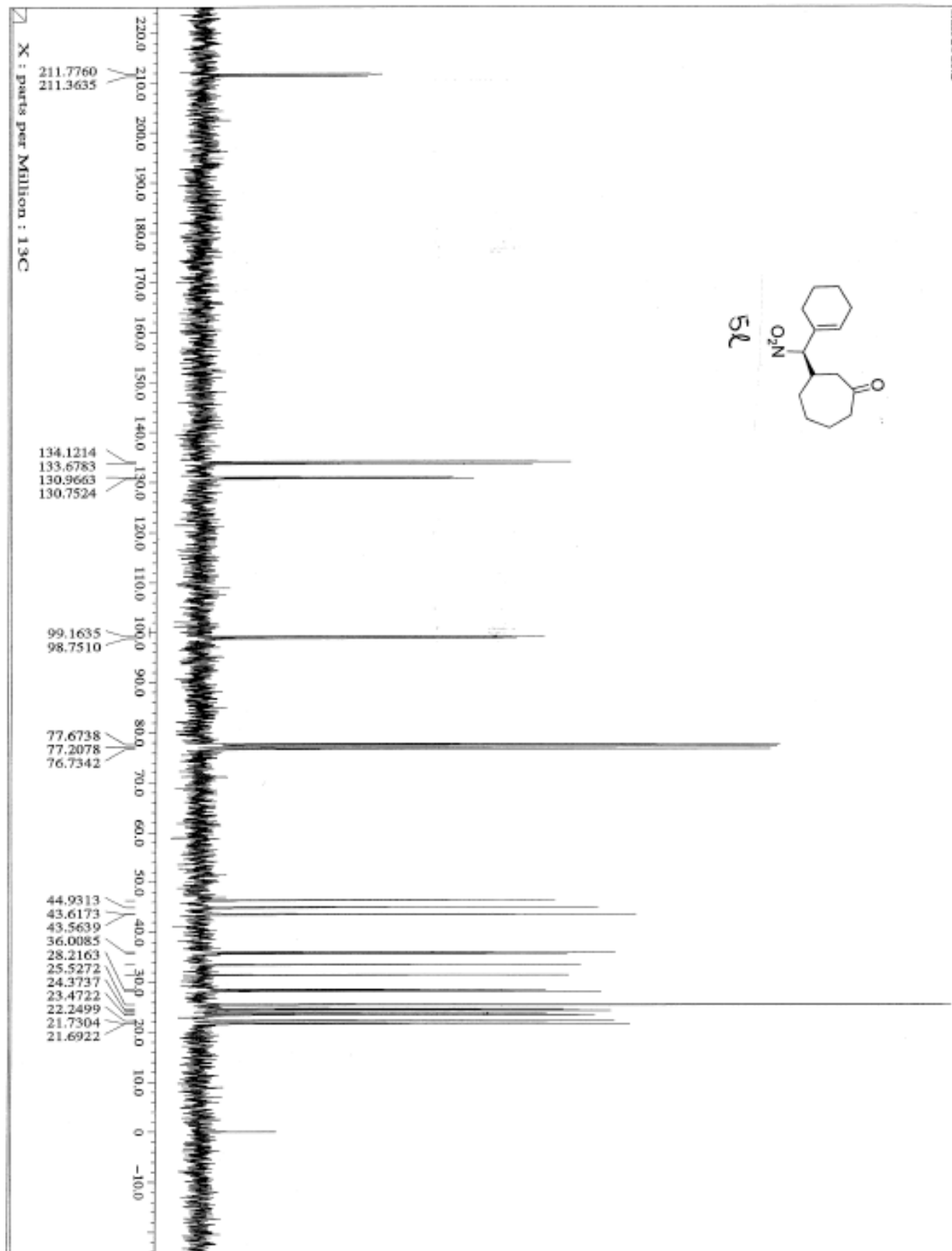
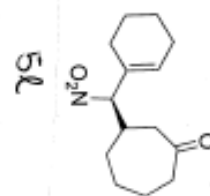




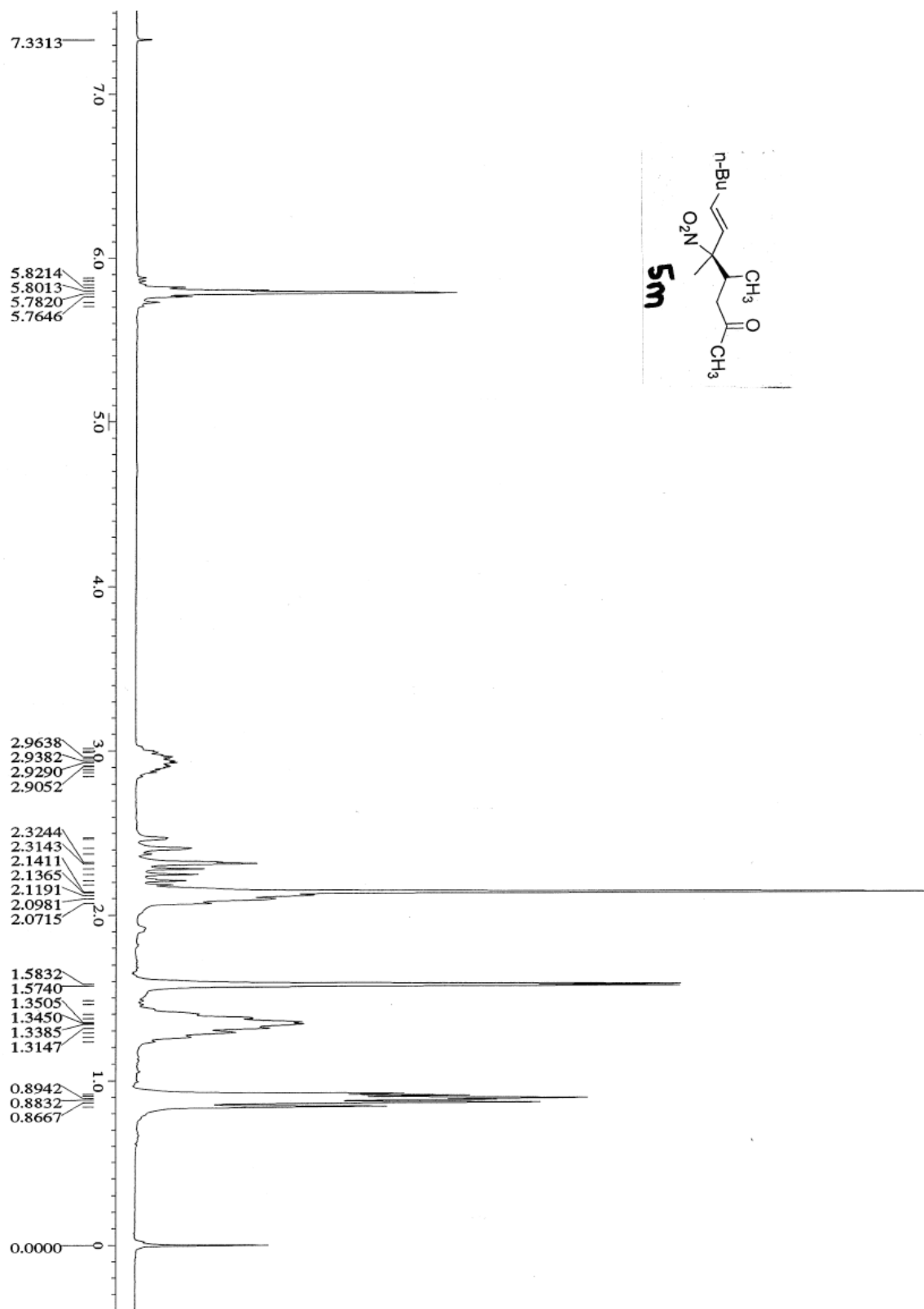


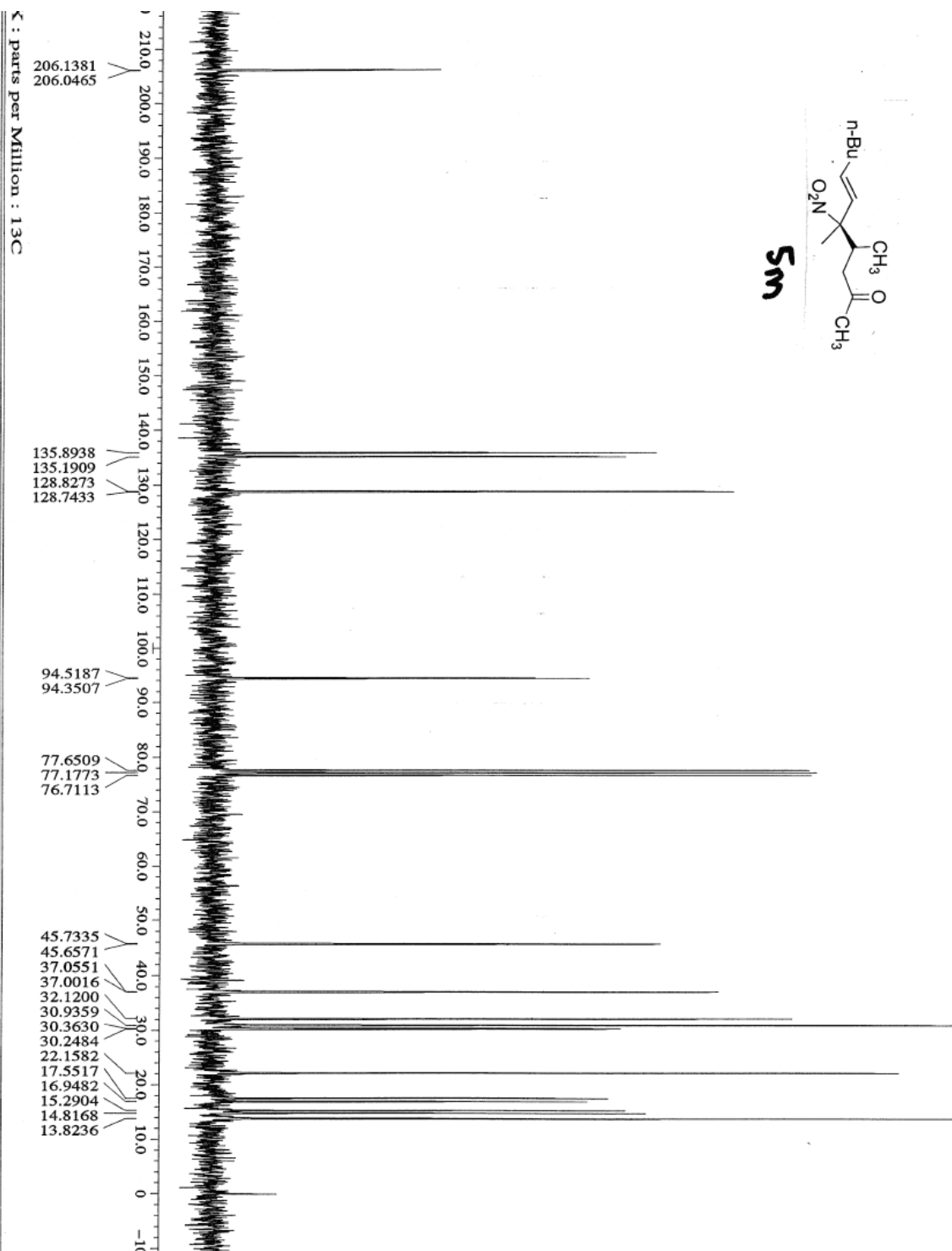


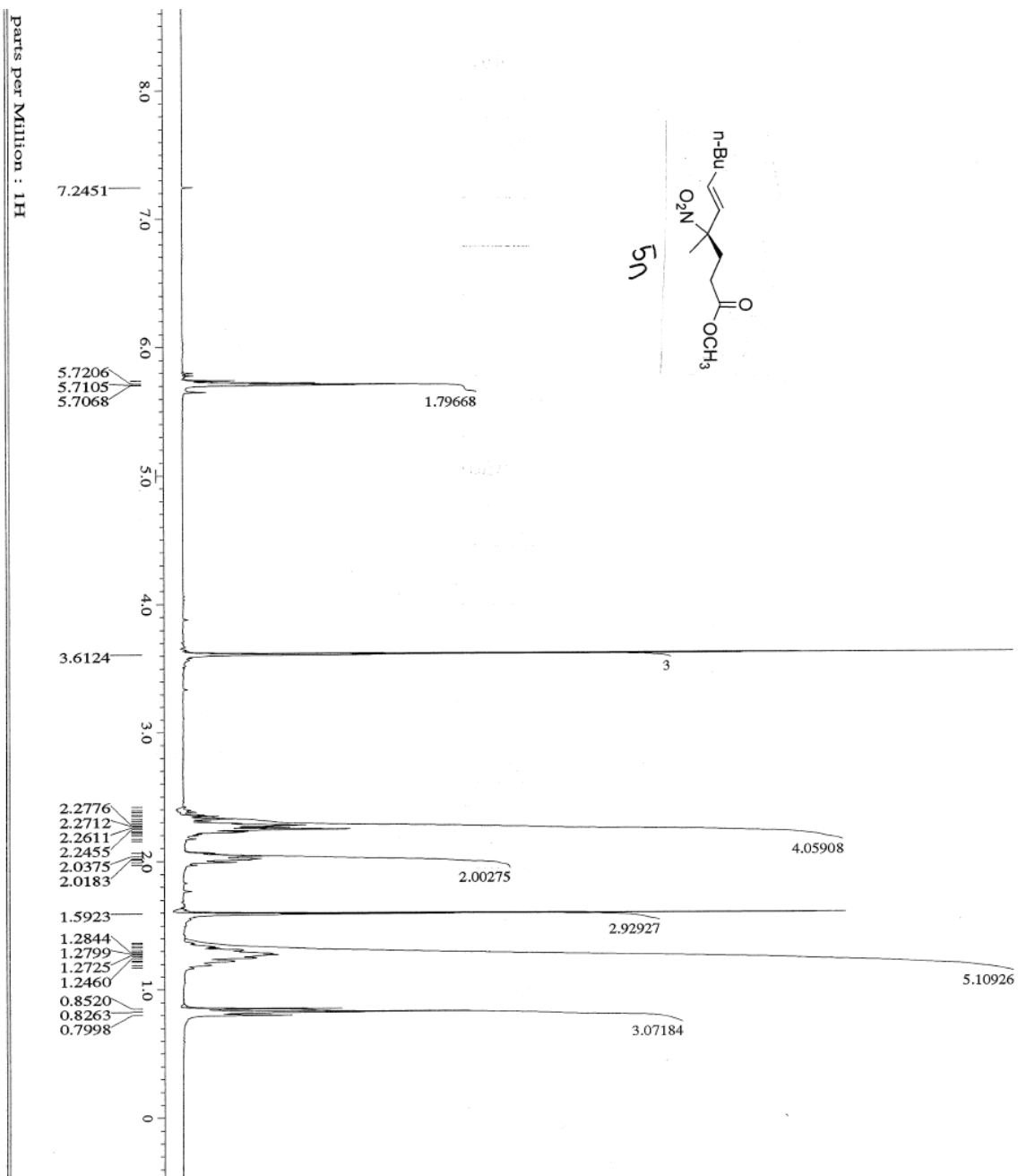




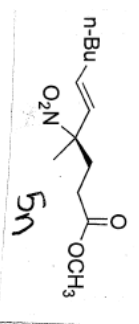
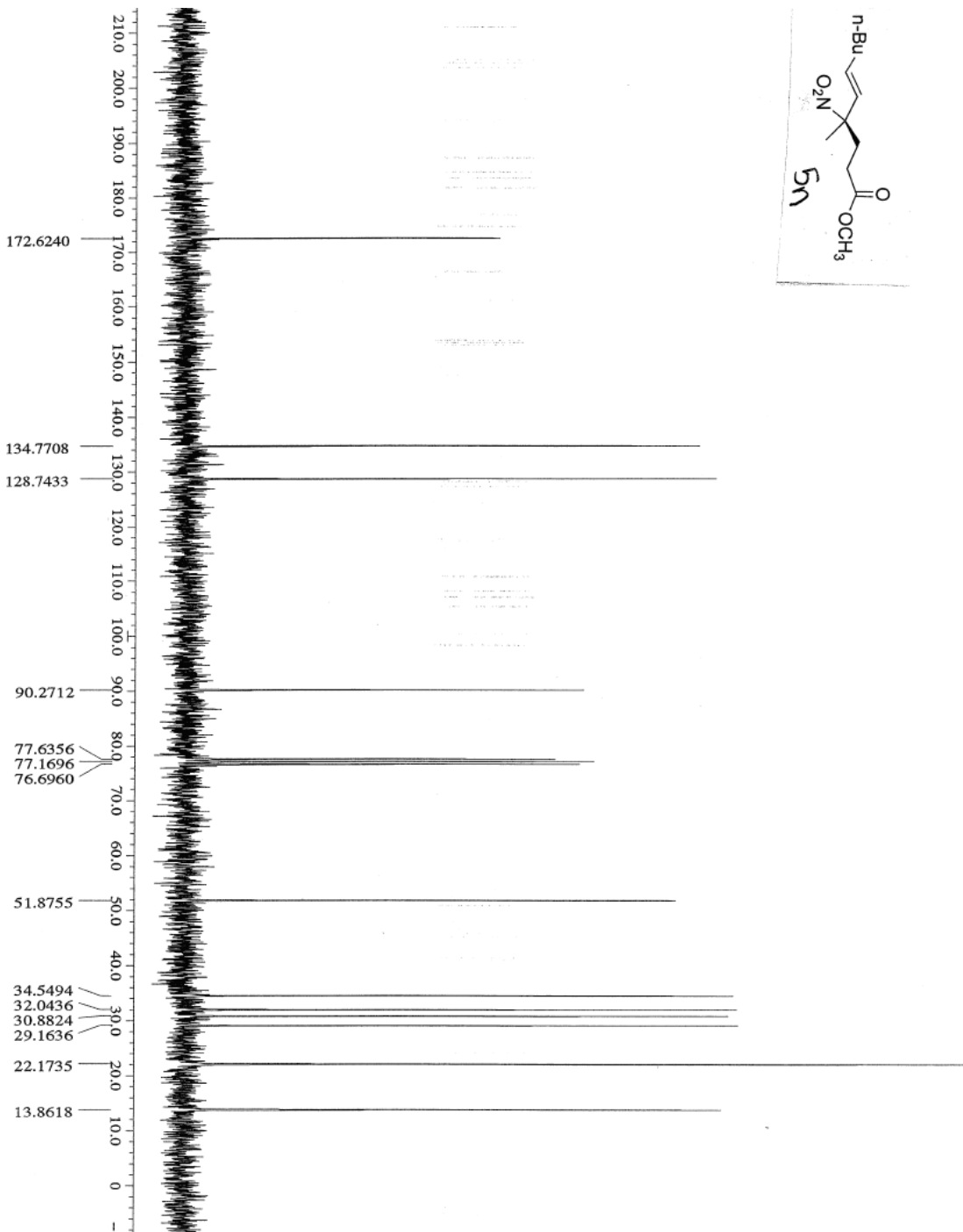


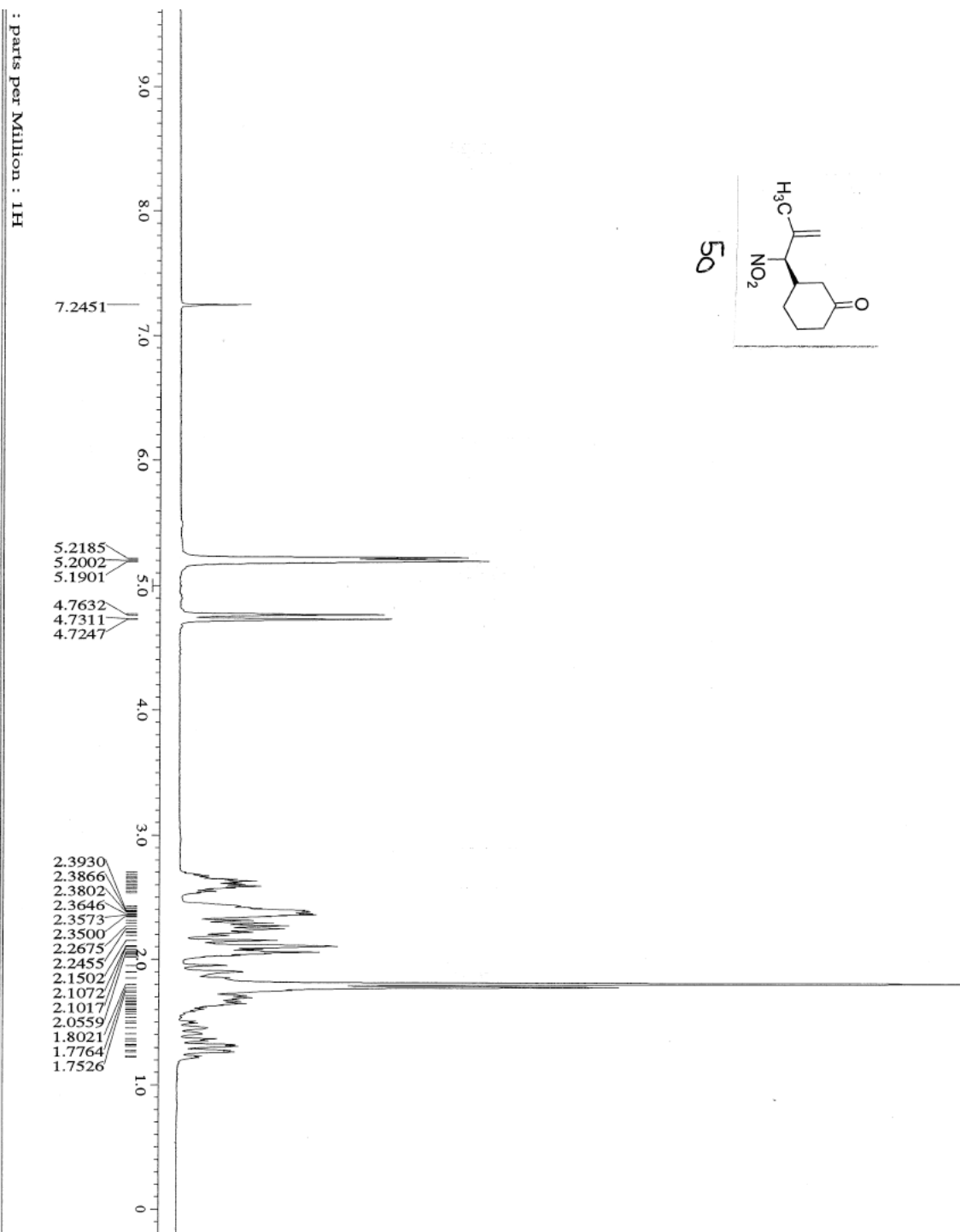
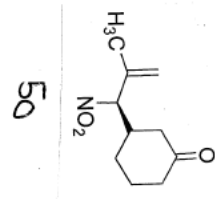


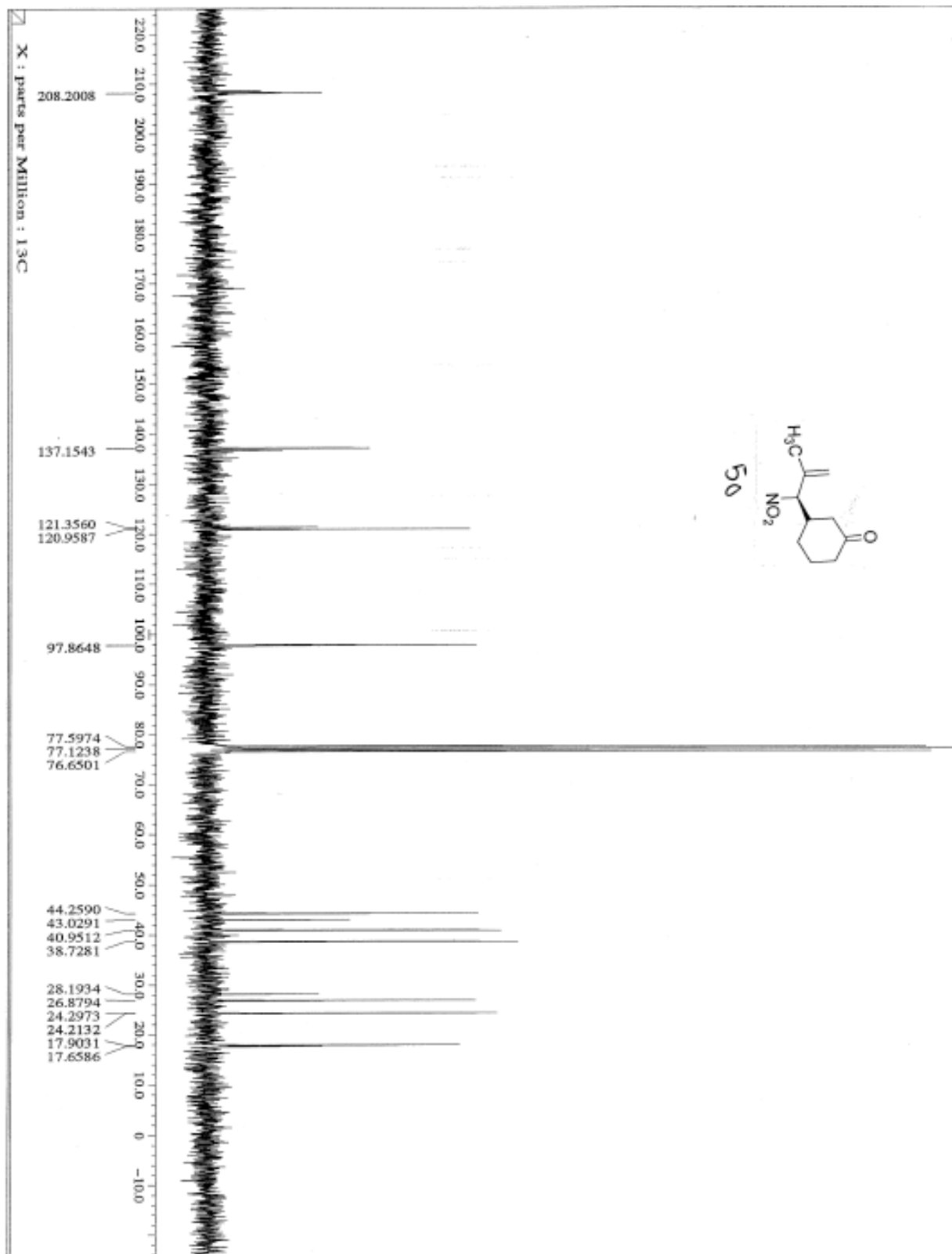


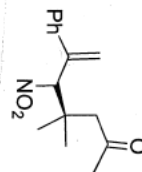


: parts per Million : 13C

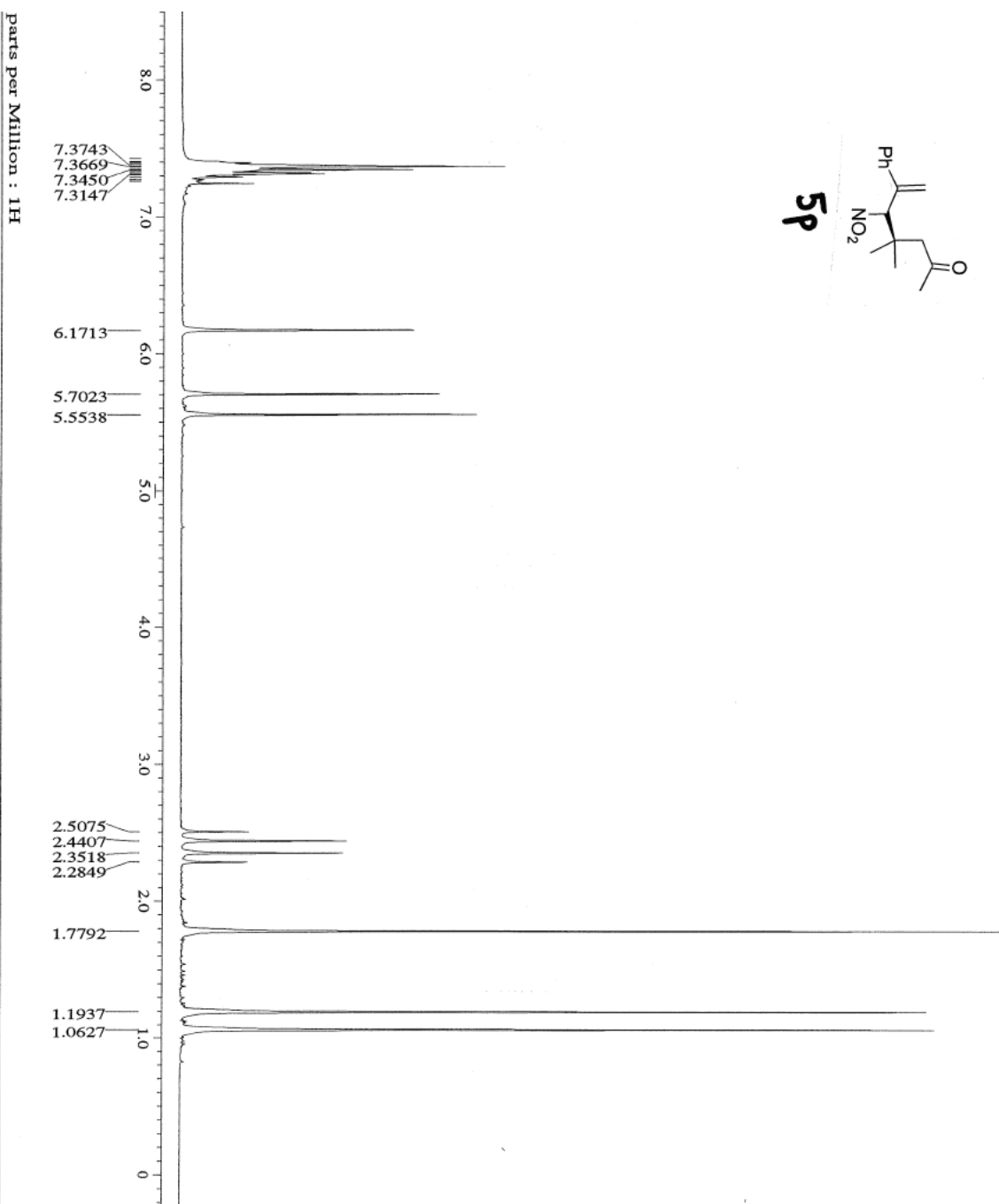


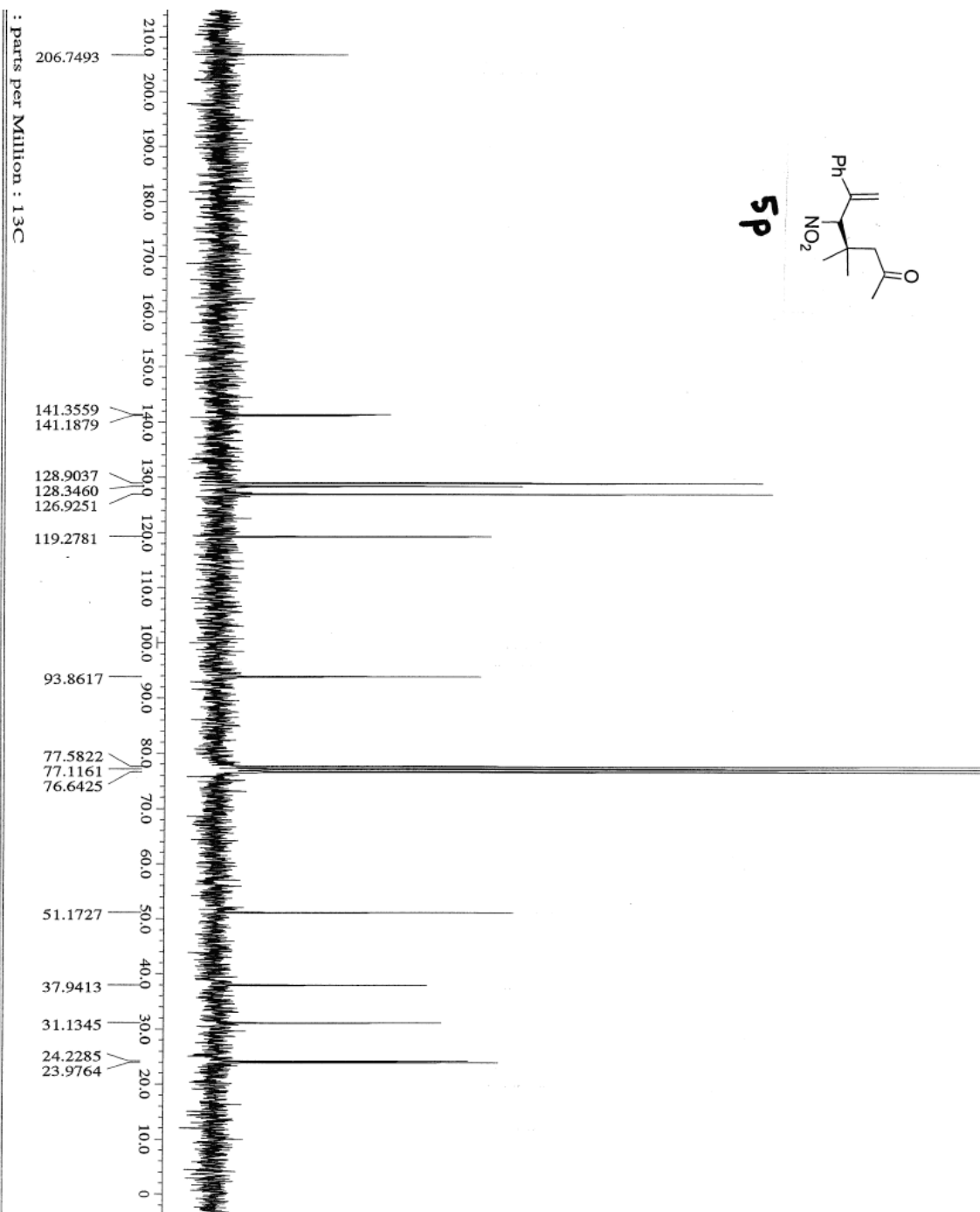




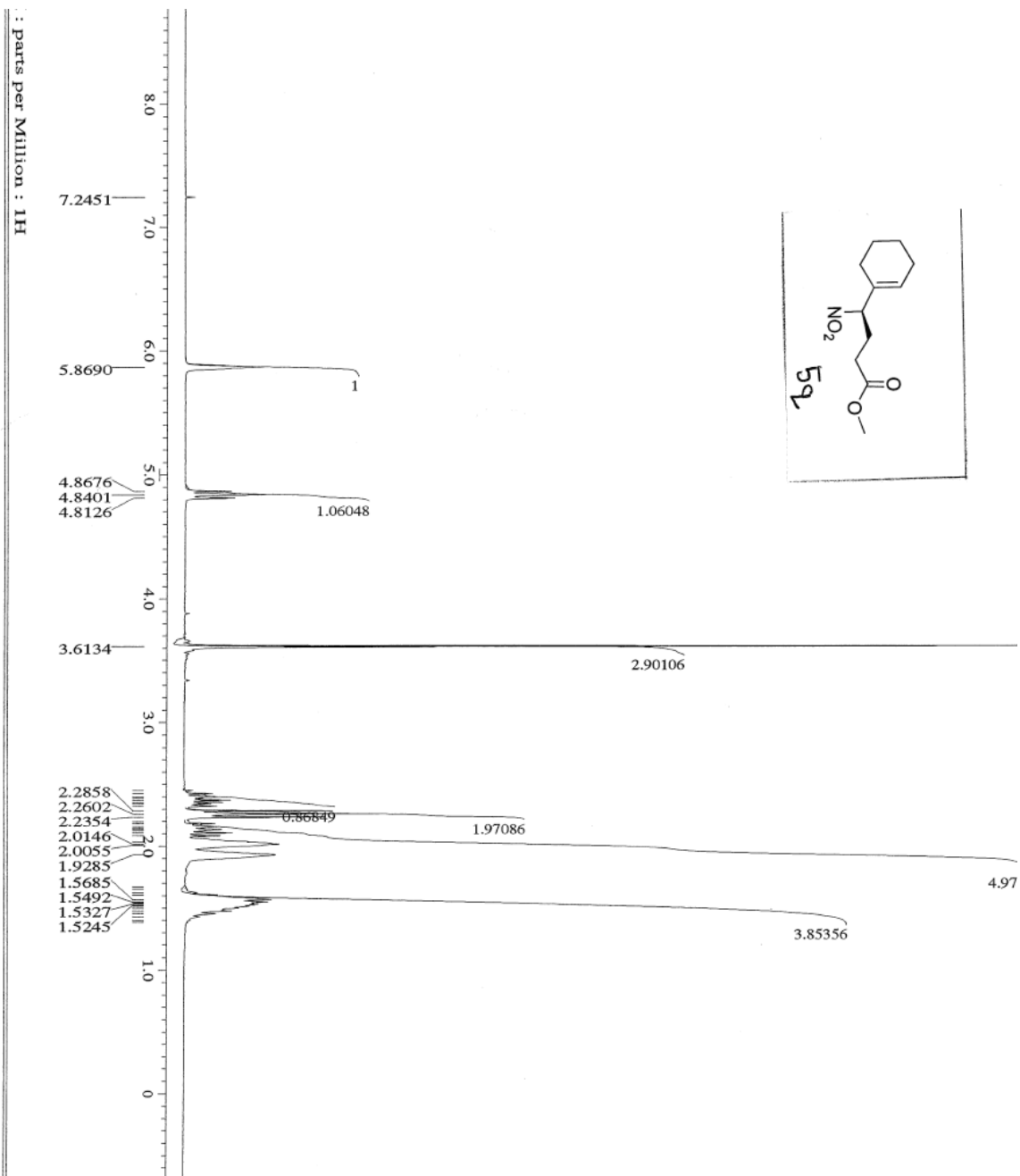


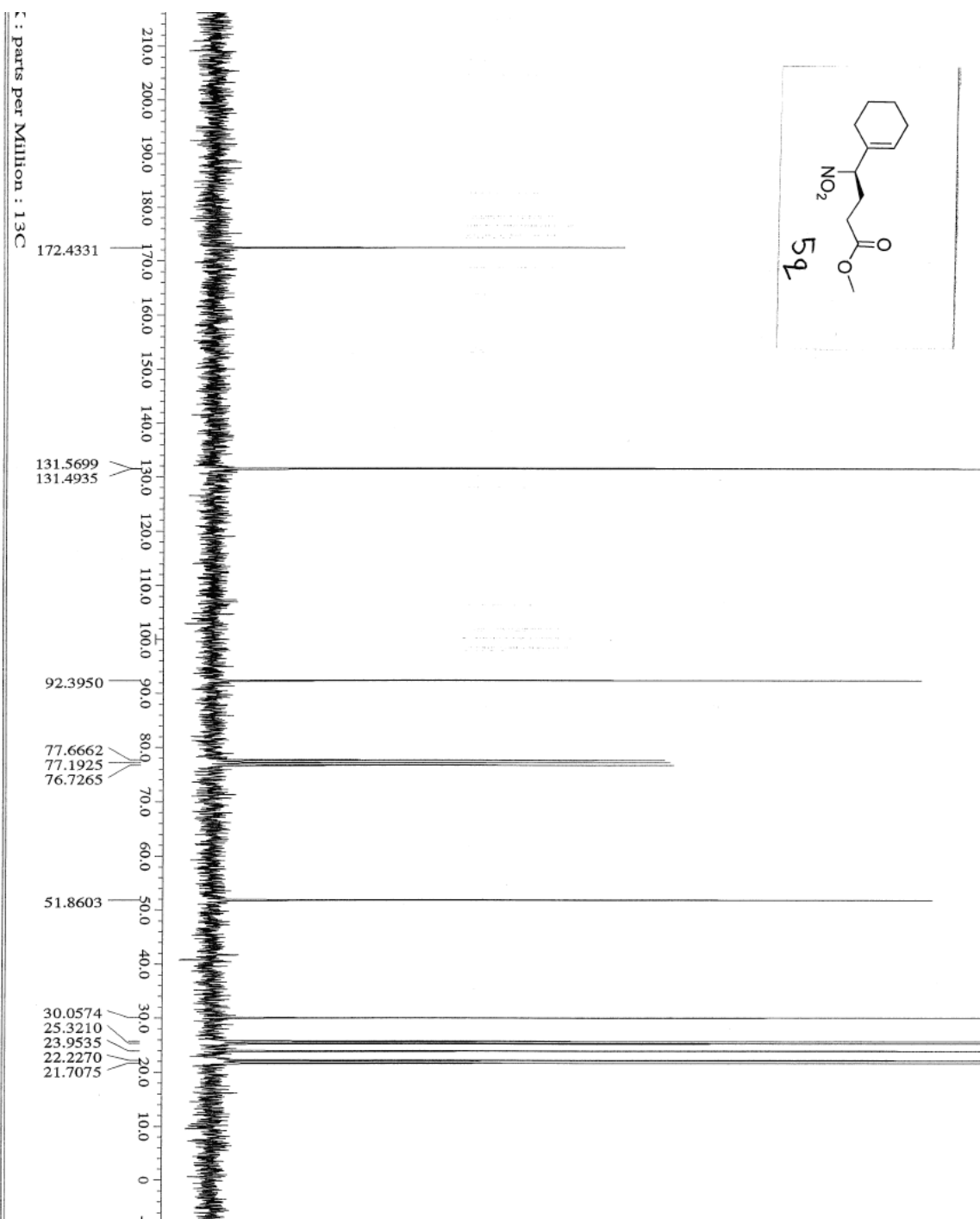
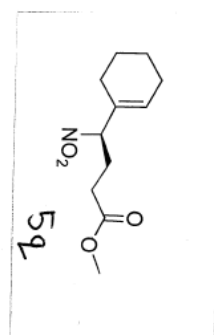
5p



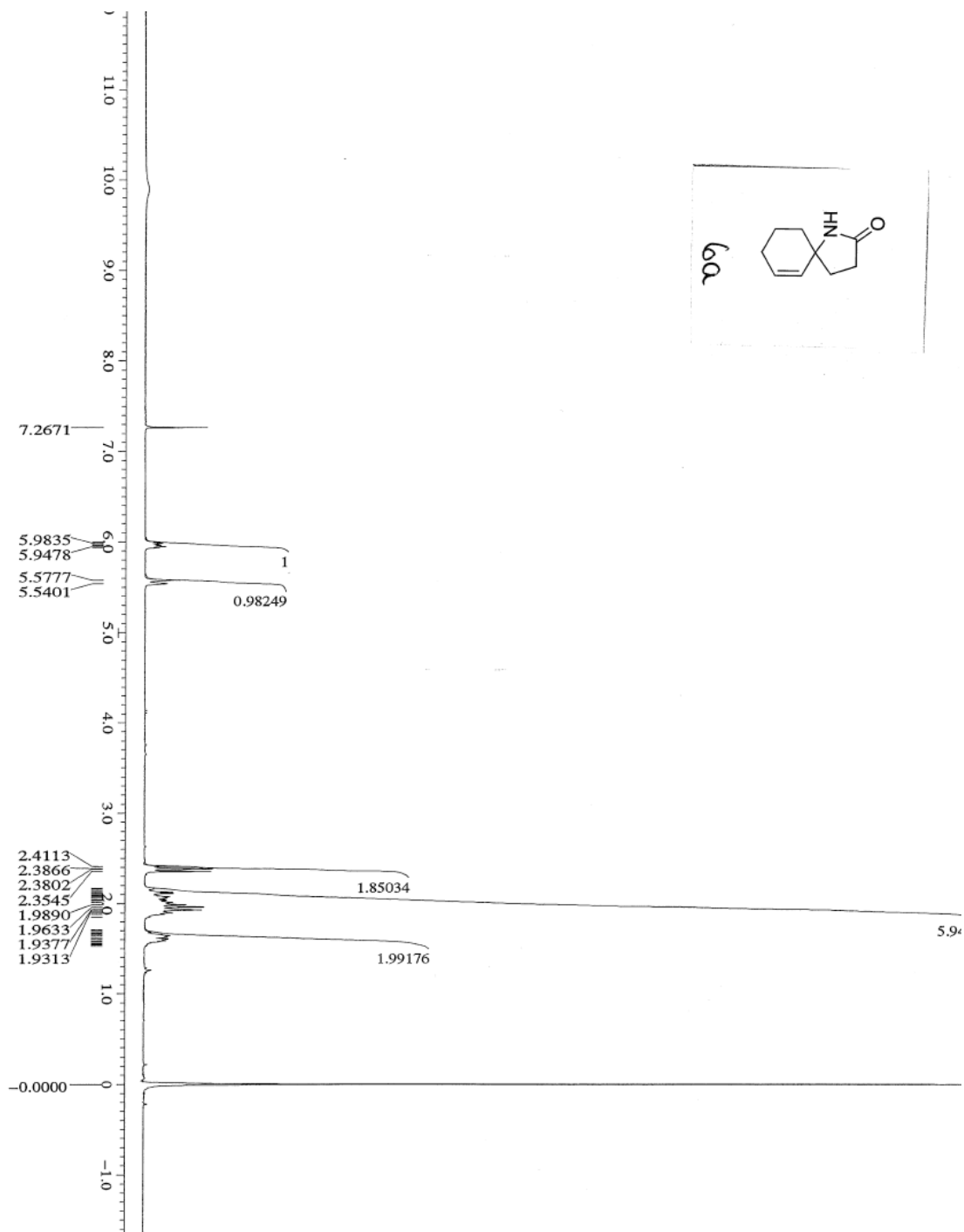


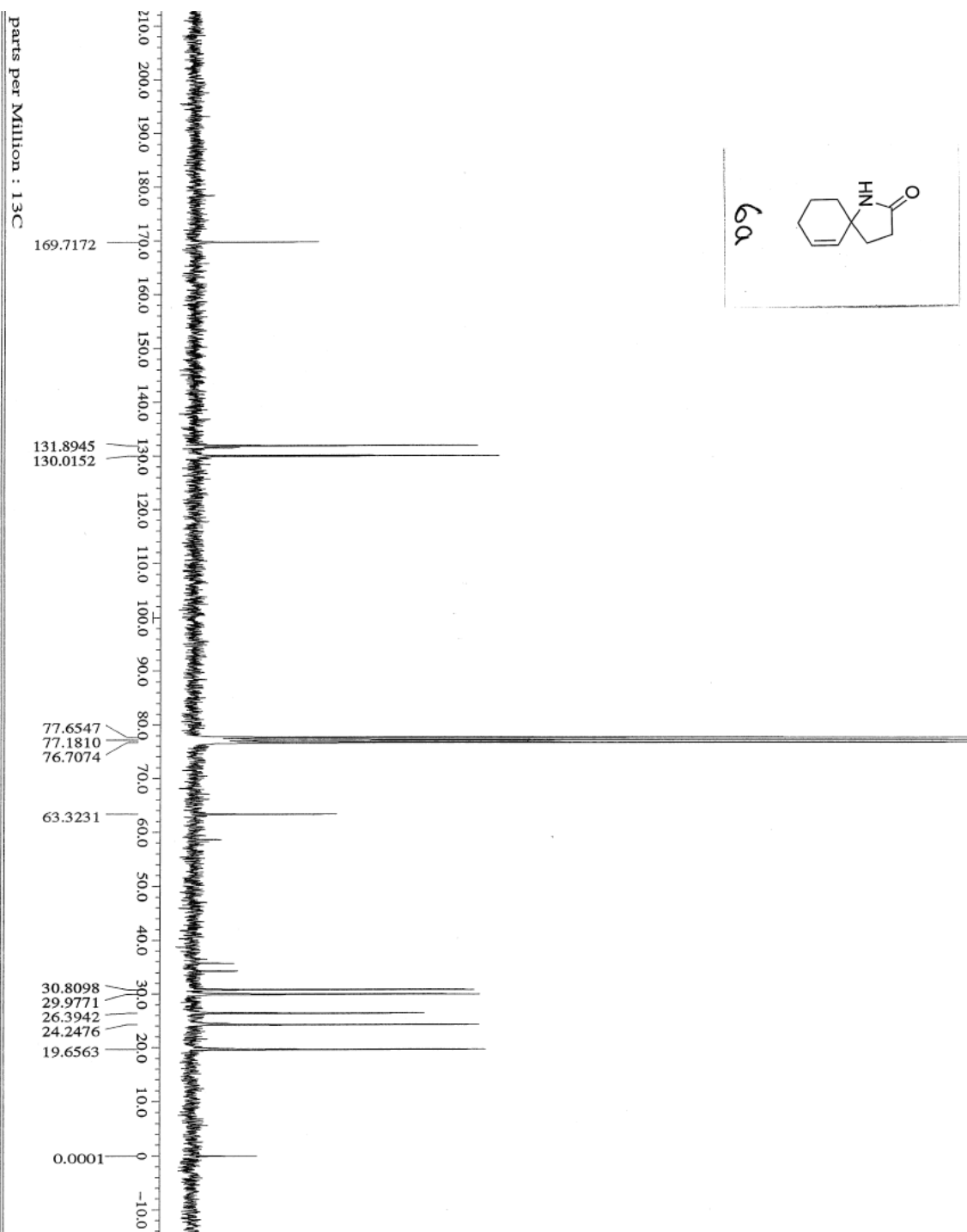
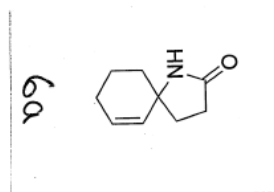


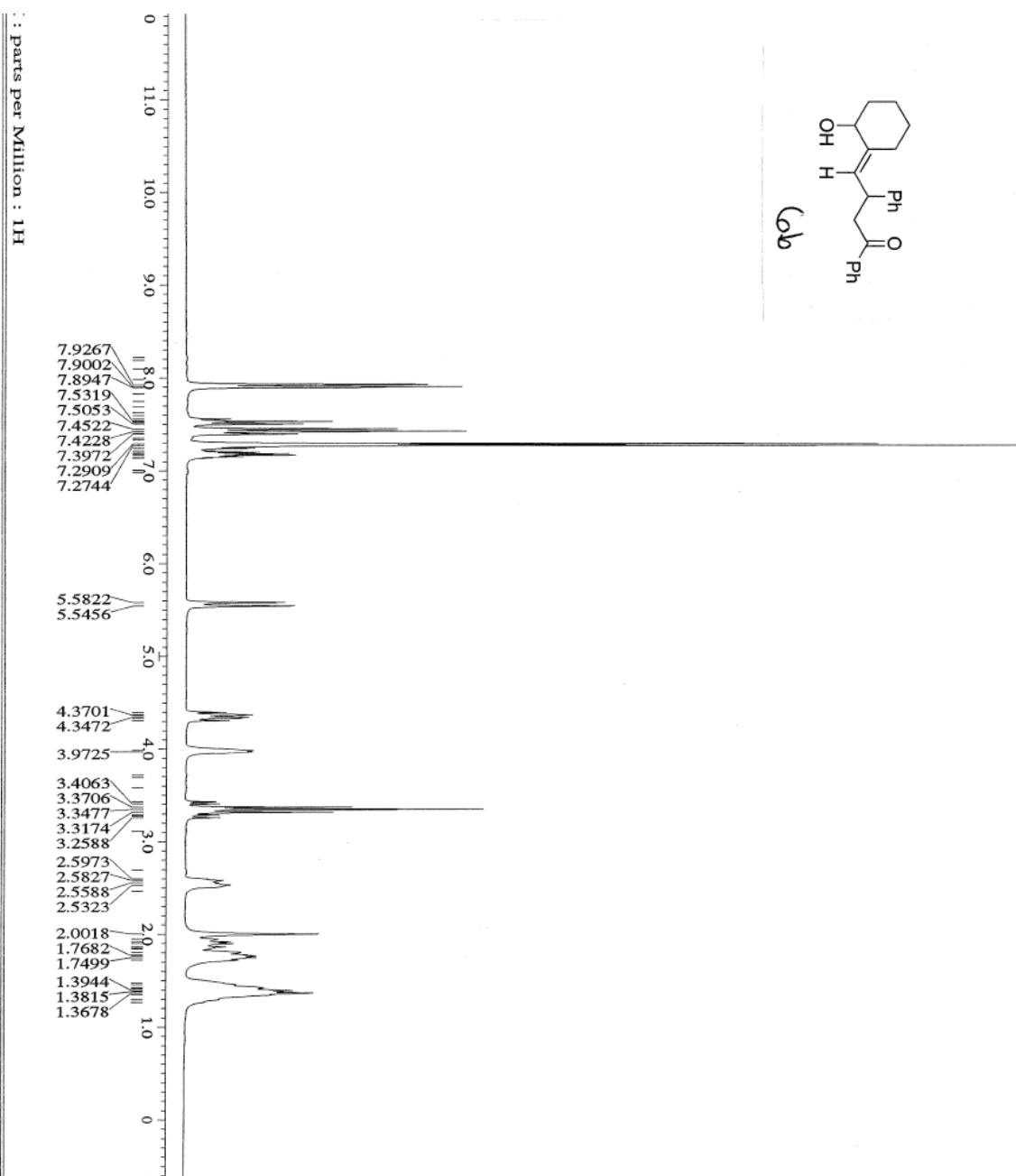




: parts per Million : 1H







: parts per Million : <sup>13</sup>C

