Skeletal Diversity Construction via a Branching Synthetic Strategy

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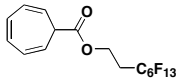
Publication data **[DO NOT ALTER/DELETE THIS TEXT]**
DOI: 10.1039/b000000x [DO NOT ALTER/DELETE THIS TEXT]

Supplementary Experimental Section

Synthesis of fluorous–tagged diazoacetate (1):

A mixture of glycine (1.90 g, 25.3 mmol), *p*-toluene sulfonic acid monohydrate (7.21 g, 37.9 mmol) and 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctan-1-ol (18.4 g, 50.6 mmol) in dry toluene was stirred rapidly and heated to reflux using a Dean-Stark apparatus. After 4 h the resultant colourless solution was cooled in ice for 30 min, leading to the formation of white crystals in the solution. The crystals were filtered and washed with a 1:1 mixture of THF: hexane. The solid was collected and dried *in vacuo* to yield the ester salt **4** as a white crystalline solid (14.37 g, 24.2 mmol, 96%). υ_{max} (neat)/cm^{-1} 1748s (ester); mp 143-145 $^{\circ}$C; δ_H (400 MHz; CD_3OD) 7.69 (2H, d, *J* 8.0), 7.22 (2H, d, *J* 8.0), 4.54 (2H, t, *J* 6.5), 3.86 (2H, s), 3.30-3.29 (2H, m), 2.36 (3H, s); δ_C (125 MHz; CD_3OD) 168.4, 143.5, 141.7, 129.8, 127.0, 59.1, 41.0, 31.2-30.9 (m, $C_6F_{13}\underline{C}H_2CH_2$); *m/z* (ES) 422 ([M-OTs]$^+$). Found C, 34.50; H, 2.62; N, 2.34%. $C_{17}H_{16}F_{13}ONS$ requires C, 34.41; H, 2.72; N, 2.36. The salt **4** (8.23 g, 13.9 mmol) was added to a solution of K_2CO_3 (1 equiv) in water. The free-base was extracted into $CHCl_3$. The organic fractions were combined and dried (Na_2SO_4). *Iso*-amyl nitrite (2.20 ml, 16.6 mmol) and acetic acid (0.16 ml, 2.8 mmol) were added and the solution heated to reflux with vigorous stirring. After 2 h the reaction was cooled in ice. The pale-yellow solution was washed with K_2CO_3 (10% w/v solution), dried (Na_2SO_4) and the solvent removed *in vacuo*. The crude product was purified by column chromatography (SiO_2; 7:3 pet. ether (30:40): Et_2O) to yield fluorous–tagged diazoacetate (**1**) as a yellow oil (5.35 g, 12.4 mmol, 89%). R_f 0.63 (SiO_2; 7:3 pet. ether (30:40): Et_2O); υ_{max} (neat)/cm^{-1} 2116s (C-N_2), 1698s (ester); δ_H (400 MHz; $CDCl_3$); 4.80 (1H, s), 4.50 (2H, t, *J* 6.4), 2.58-2.45 (2H, m); δ_C (125 MHz; $CDCl_3$) 165.9, 56.6, 46.3, 30.9-30.6 (m); HRMS found *m/z* (EI) 432.0140, $C_{10}H_5F_{13}N_2O_2$ (M^+) requires 432.0138. **Caution**: the fluorous–tagged diazoacetate (**1**) should be presumed to be toxic and potentially explosive; however, we have not experienced any problems and regard **1** to be comparable to commonly used ethyl diazoacetate.



Fluorous tagged diazoacetate (200 mg, 0.415 mmol, 1 equiv.) was added drop-wise to a green solution of $Rh_2(O_2CCF_3)$ (3.0 mg, 1.0 mol%) in benzene (0.8 ml, 9.35 mmol, 20 equiv.) over 30 min. The resultant brown solution was stirred at ambient temperature overnight and the solvent removed *in vacuo*. The crude product was purified by chromatography to yield the desired product as a pale yellow oil (156 mg, 0.32 mmol, 70%). $\mathbf{R}_f$ 0.34 (SiO_2; 10:1 hexane: ethyl acetate); $\boldsymbol{\upsilon}_{max}$ (neat)/cm^{-1} 1745 st (C(=O)OR), 1608 w (C=C), 1164 st (C-O); $\boldsymbol{\delta}_H$ (400 MHz; $CDCl_3$) 6.66-6.64 (2H, dd, *J* 2.5, 3.40 Hz, C(=O)CHCHCHC$\underline{H}$), 6.29-6.24 (2H, m, C(=O)CHCHC$\underline{H}$CH), 5.41-5.37 (2H, dd, *J* 9.0, 5.5 Hz, C(=O)CHC$\underline{H}$CHCH), 4.51-4.48 (2H, t, *J* 6.5 Hz, $C_6F_{13}CH_2C\underline{H}_2$), 2.58-.2.46 (3H, m, C(=O)C$\underline{H}$CHCHCH and $C_6F_{13}C\underline{H}_2CH_2$); $\boldsymbol{\delta}_C$ (125 MHz; $CDCl_3$) 172.6 (C), 130.9, 125.8, 115.9 (*aryl* $\underline{C}$H), 56.9 (CH_2), 43.6 (C), 30.5 (CH_2); **HRMS** (ESI+) *m/z* found 500.0895 ([M+NH_4]$^+$ calcd. 500.0890).

General method for synthesis of ecgonine analogues:

To a mixture of flurours-tagged cycloheptatriene (1 equiv.) and NaOH (11 equiv.) in H_2O contained in a borosilicate glass pressure tube with a screw-top was added a solution of primary amine (10 equiv.) in H_2O. The screw-top was closed and the mixture was heated with stirring at 180 °C for approximately 65 hr. After cooling, the solution was filtered concentrated and *in vacuo*. The dry residue was dissolved in 3N H_2SO_4 and extracted with diethyl ether (x 3) to remove any unreacted starting material. The aqueous phase was neutralised with 3N NaOH and the H_2O was removed *in vacuo*, leaving inorganic salts and product. This residue was suspended in absolute MeOH and conc. H_2SO_4 was added. The mixture was heated under reflux for approximately 48 hr. After this time the alcohol was removed *in vacuo* and the residue was dissolved in a minimum amount of H_2O. The aqueous solution was saturated with potassium carbonate, filtered and extracted with ether (x 4). The combined organic fractions were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude product was purified by column chromatography to yield the desired product.

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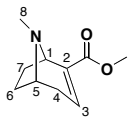
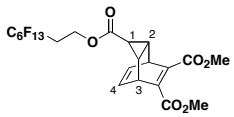


Isolated as a yellow oil (150 mg, 0.83 mmol, 35%); $\mathbf{R}_f$ 0.25 (SiO_2; 9.8:0.2 pet ether (30:40): ethyl acetate, triethylamine pre-treated TLC plates); υ_{max} (neat)/cm^{-1} 2950 (NCH_3), 1710 (C(=O)OR), 1640 (C=C); δ_H (400 MHz; *d*-DMSO) 6.72-6.70 (1H, m, H^3), 3.62 (3H, s, OCH_3), 3.54 (1H, d, *J* 5.5 Hz, H^1), 3.11-3.08 (1H, m, H^5), 2.51-2.45 (1H, m, H^4), 2.16 (3H, s, NCH_3), 2.04-1.91 (2H, m, H^6 and H^7), 1.77 (1H, dd, *J* 19.8 Hz, 4.3 Hz, H^4), 1.68-1.61 (1H, m, H^6 or H^7), 1.42-1.37 (1H, m, H^6 or H^7); δ_C (125 MHz; *d*-DMSO) 166.2 (C=O), 136.5 (C^3), 133.6 (C^2), 58.3, 56.4 (C^1 and C^5), 51.8 (OCH_3), 36.1 (NCH_3), 34.5, 31.3, 30.1 (C^4, C^6 and C^7); **HRMS** (ESI+) *m/z* found 182.1181 ($[M+H]^+$ calcd. 182.1181). This data is in accordance with that previously reported.[10]

General method for the synthesis of Diels-Alder analogues:

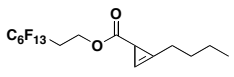
To a solution of cycloheptatriene (250 mg, 1.52 mmol, 1 equiv.) in toluene was added the appropriate dienophile (7.61 mmol, 5 equiv.) and the solution was heated to reflux for 3 hrs. Excess solvent was removed *in vacuo* and the crude product was purified by chromatography.



Isolated as a colourless oil (76 mg, 0.121 mmol, 59%); $\mathbf{R}_f$ 0.13 (SiO_2; 4:1 hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 1718 st (ester), 1638 m (C=C), 1602 w (C=C), 1230 st (C-O), 1144 st (C-O); δ_H (500 MHz: $CDCl_3$) 6.16 (2H, dd, *J* 4.5, 3.5 Hz, 2 C(4)H), 4.31 (2H, t, *J* 6.5 Hz, $CH_2CH_2C_6F_{13}$), 4.25 (2H, m, 2 C(3)H), 3.79 (6H, s, 2 CO_2CH_3), 2.43 (2H, tt, *J* 18.5, 6.5 Hz, $CH_2CH_2C_6F_{13}$), 2.68 (2H, dd, *J* 2.5, 2.0 Hz, 2 C(2)H), 1.76 (1H, t, *J* 2.5 Hz, C(1)H); δ_C (125 MHz: $CDCl_3$) 179.39 (C), 166.14 (C), 147.10 (C), 130.86 (CH), 56.45 (CH_2), 52.27 (CH_3), 40.61 (CH), 30.55 (CH_2), 30.13 (CH), 27.04 (CH); **HRMS** found MH^+ 625.0901, $C_{22}H_{18}F_{13}O_6^+$ required 625.0896.

General method for cyclopropenation:

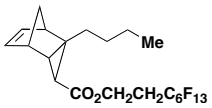
A solution of fluorous-tagged diazoacetate (1 equiv.) in anhydrous DCM was added dropwise to a mixture of $Rh_2(OAc)_4$ (1 mol%) and alkyne (3 equiv). The solution was stirred at ambient temperature for 12 hr. The solvent was removed *in vacuo* and the crude product was purified by column chromatography to give the desired cyclopropene product.



Isolated as a pale yellow oil (128 mg, 2.63 mmol, 57%); $\mathbf{R}_f$ 0.59 (SiO_2; 5:1 hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 1730 st (C(=O)OR), 1167 st (C-O); δ_H (400 MHz; $CDCl_3$) 6.30 (1H, app. q, *J* 1.5 Hz C(=O)CHCH), 4.40-4.30 (2H, m, $C_6F_{13}CH_2CH_2$), 2.51-2.39 (4H, m, $C_6F_{13}CH_2CH_2$ and C(=C)CH_2), 2.13 (1H, d, *J* 1.5 Hz C(=O)CHCH), 1.54 (2H, tt, *J* 7.5, 5.5 Hz $CH_2CH_2CH_2CH_3$), 1.37 (2H, qt, *J* 7.3, 5.3 Hz $CH_2CH_2CH_2CH_3$), 0.90 (3H, t, *J* 7.5 Hz, CH_2CH_3); δ_C (125 MHz; $CDCl_3$) 176.1 (C), 115.3 (C), 93.6 (CH), 56.1 ($C_6F_{13}CH_2CH_2$), 30.9-30.5 (m, $CH_2CH_2C_6F_{13}$), 28.7 (CH_2), 24.6 (CH_2), 22.2 (CH_2), 19.5 (CH), 13.5 (CH_3); **HRMS** (ESI+) *m/z* found 487.0942, ($[M+H]^+$ calcd. 487.0937).

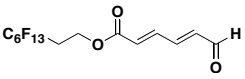
General method for Diels-Alder reaction of cyclopropenes:

Cyclopentadiene (20 equiv) was added drop-wise to an ice-cold solution of cyclopropene product (1 equiv) in anhydrous DCM. The solution was stirred at 0 °C for 30 min and at ambient temperature for 42 hr. The reaction was quenched with sat. aq. $NaHCO_3$ and the aqueous layer extracted with ethyl acetate (x 3). The combined organic layers were washed with sat. brine solution, dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude product was purified by column chromatography to yield the desired product Diels-Alder adduct.



Isolated as an amorphous white solid (286.6 mg, 0.52 mmol, 92%); $\mathbf{R}_f$ 0.31 (SiO_2; 9.8:0.2 hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 1726 st (C(=O)OR), 1171 st (C-O); **mp** 34-35 °C; δ_H (500 MHz; $CDCl_3$) 5.98-5.92 (1H, m, C=CH), 5.88 (1H, dd, *J* 3.3, 5.2 Hz, C=CH), 4.38-4.29 (2H, m, $C_6F_{13}CH_2CH_2$), 2.93-2.90 (1H, m), 2.81 (1H, s), 2.51-2.41 (2H, m, $C_6F_{13}CH_2CH_2$), 1.95 (1H, dd, *J* 3.1, 4.1 Hz), 1.92-1.86 (2H, m), 1.72-1.67 (1H, m) 1.63 (1H, d, *J* 7.1 Hz), 1.52 (1H, d, *J* 2.8 Hz), 1.49-1.40 (1H, m), 1.33-1.23 (2H, app. sextet, *J* 7.4 Hz), 1.18-1.10 (1H, m), 0.89 (3H, t, *J* 7.3 Hz); δ_C (125 MHz; $CDCl_3$) 170.8 (C), 132.6 (CH), 132.5 (CH), 61.8 (CH_2), 56.0 ($C_6F_{13}CH_2CH_2$), 48.8 (CH), 43.4 (CH), 34.6 (CH), 31.0 (CH_2), 30.7 ($C_6F_{13}CH_2CH_2$), 28.6 (CH_2), 27.0 (CH), 22.8 (CH_2), 13.9 (CH_3); **HRMS** (ESI+) *m/z* found 553.1412 ($[M+H]^+$ calcd. 553.1407); **Elemental analysis** calculated for $C_{21}H_{21}F_{13}O_2$ (%) C 45.66, H 3.83; Found C 45.77, H 3.75.

Polyene synthesis:

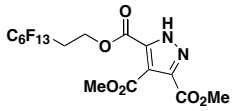


A solution of fluorous-tagged diazoacetate (137 mg, 0.32 mmol, 1 equiv.) in furan (3 ml) was added over 30 min to a green suspension of $Rh_2(OAc)_4$ (1.0 mg, 0.5 mol%) in furan (3 ml). The solution was stirred at ambient temperature for 12 hr, filtered and concentrated *in vacuo*. Iodine (2 mg) was added to a solution of the crude product mixture in anhydrous DCM (3 ml) and the reaction stirred at ambient temperature for 12 hr. The solution was concentrated *in vacuo* and extracted into diethyl ether (x 3). The combined organic fractions were washed with 10% sodium thiosulfate solution and with sat. brine solution, dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude product was purified by chromatography to yield the polyene product as an amorphous red/brown solid (89.7 mg, 0.19 mmol, 60%). $\mathbf{R}_f$ 0.31 (SiO_2; 4:1 hexane: ethyl

acetate); υ_{max} (neat)/cm^{-1} 1716 st (C(=O)OR), 1682 st (C(=O)H), 1641 w and 1602 m (C=C); δ_H (400 MHz; $CDCl_3$) 9.71-9.70 (1H, d, *J* 7.5 Hz, CHO), 7.49-7.43 (1H, dd, *J* 15.5 Hz, 11.0 Hz, CHCHCHCHCHO), 7.21-7.16 (1H, dd, *J* 15.5 Hz, 11.0 Hz, CHCHCHCHCHO), 6.48-6.44 (1H, dd, *J* 15.5 Hz, 7.7 Hz, CHCHCHCHCHO), 6.34-6.31 (1H, d, *J* 15.5 Hz, CHCHCHCHCHO), 4.54-4.51 (2H, t, *J* 6.5 Hz, $C_6F_{13}CH_2CH_2$), 2.61-2.51 (2H, m, $C_6F_{13}CH_2CH_2$); δ_C (125 MHz; $CDCl_3$) 192.6 (C), 165.9 (C), 146.5 (CH), 141.3 (CH), 137.5 (CH), 128.6 (CH), 56.9 ($C_6F_{13}CH_2CH_2$), 30.8-30.4 (m, $C_6F_{13}CH_2CH_2$).

General Method for the Formation of 1H-*N*-pyrazoles:

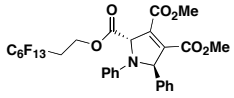
A solution of fluorous tagged diazoacetate (100 mg, 0.231 mmol, 6.5 equiv) in anhydrous dichloromethane (1 ml) was added dropwise to a solution of the appropriate dienophile (0.0355 mmol, 1 equiv.) in anhydrous dichloromethane (4 ml). The solution was stirred at ambient temperature for 24 hrs and the excess solvent was removed *in vacuo*. The crude product was purified by chromatography.



Isolated as a pale yellow oil (16.7 mg, 0.0291 mmol, 84 %); $\mathbf{R}_f$ 0.25 (SiO_2; 1:1 hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 3240 br (N-H), 1740 m (ester), 1570 w (C=C), 1240 st (C-O), 1200 st (C-F), 1150 st (C-F), 1030 m (C-O); δ_H (500 MHz; $CDCl_3$) 12.41 (1H, br s, NH), 4.65 (2H, t, *J* 6.5 Hz, $CH_2CH_3C_6F_{13}$), 3.95 (3H, s, CO_2CH_3), 3.95 (3H, s, CO_2CH_3), 2.61 (3H, tt, *J* 18.0, 6.9 Hz, $CH_2CH_3C_6F_{13}$); δ_C (125 MHz; $CDCl_3$) 163.11 (C), 119.64 (C), 57.74 (CH_2), 53.00 (CH_3), 52.90 (CH_3), 30.35 (CH_2); **HRMS** found MH^+ 575.0487, $C_{16}H_{12}F_{13}N_2O_6^+$ required 575.0488.

General method for three-component assembly of pyrrolidines

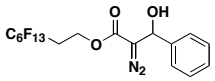
To a solution of imine (3 equiv.), dipolarophile (1 equiv.) and $Rh_2(OAc)_4$ (10 mol%) in anhydrous DCM was added drop-wise a solution of fluorous-tagged diazoacetate (1 equiv.) in anhydrous DCM. The solution was heated to 40 ºC for 2 hr. The resultant solution was cooled, filtered through silica gel and the solvent removed *in vacuo*. The crude product was purified by column chromatography to yield the desired product.



Isolated as a pale yellow oil (43 mg, 0.059 mmol, 51 %); $\mathbf{R}_f$ 0.25 (SiO_2; 4:1 hexane: ethyl acetate); υ_{max} (neat)/cm-1 1741 st (C(=O)OR), 1669 (C(=O)OR), 1235 st (C-O); δ_H (400 MHz; $CDCl_3$) 7.32-7.24 (5H, m, CHPh), 7.11-7.07 (2H, dd, *J* 8.5, 7.5 Hz, *meta*-NPh), 6.72-6.68 (1H, app. t, *J* 7.0 Hz, *para*-NPh), 6.56-6.54 (2H, d, *J* 8.0 Hz, *ortho*-NPh), 6.04-5.99 (1H, d, *J* 6.5 Hz, CHPh), 5.80-5.79 (1H, d, *J* 7.0 Hz, $CHCO_2CH_2CH_2C_6F_{13}$), 4.42-4.30 (2H, m, $C_6F_{13}CH_2CH_2$), 3.81 (3H, s, $CH(Ph)CCO_2CH_3$ or $CH(CO_2Et)CCO_2CH_3$), 3.63 (3H, s, $CH(Ph)CCO_2CH_3$ or $CH(CO_2Et)CCO_2CH_3$), 2.10-2.35 (3H, m, $C_6F_{13}CH_2CH_2$); δ_C (125 MHz; $CDCl_3$) 169.4 (C), 162.8 (C), 162.0 (C), 144.8 (C), 143.2 (C), 138.2 (C) 137.6 (C), 129.8 (CH), 129.1 (CH), 128.9 (CH), 128.5 (CH), 127.2 (CH), 118.6 (CH), 113.9 (CH), 71.1 (CH) , 69.5 (CH) 57.6 ($C_6F_{13}CH_2CH_2$), 52.6 (CH_3) , 52.3 (CH_3), 30.5-30.0 (m, $C_6F_{13}CH_2CH_2$); **HRMS** (ESI+) *m/z* found 728.1318 ($[M+H]^+$ calcd. 728.1318).

General method for β−dicarbonyl formation:

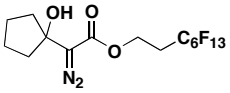
To a solution of the carbonyl compound (1.1 equiv. for aldehyde, 2 equiv for ketone) and fluorous-tagged diazoacetate (1 equiv.) in dry THF under nitrogen at -78 °C was added LDA (1.1 equiv. for aldehyde, 2 equiv. ketone) drop-wise over the course of several min. The reaction was stirred and allowed to warm up to ambient temperature. Upon complete consumption of starting material as observed by TLC (1-3 hr) the reaction was quenched with 50 % aq. NH_4Cl. The product was extracted into diethyl ether (x 3) and the combined organic fractions were washed with sat. aq. $NaHCO_3$, sat. brine solution, dried (Na_2SO_4) and the solvent removed *in vacuo*. The crude product was purified by column chromatography to yield the intermediate adduct. A solution of this adduct (1 equiv.) in anhydrous DCM was then added drop-wise to a suspension of $Rh_2(OAc)_4$ (1 mol%) in anhydrous DCM. The suspension was stirred at ambient temperature. Upon complete consumption of the starting material as observed by TLC (1-24 hr) the solvent was removed *in vacuo* and the crude product was purified by column chromatography to yield the desired β−dicarbonyl.



Isolated as a yellow oil (489 mg, 0.91 mmol, 78%); $\mathbf{R}_f$ 0.30 (SiO_2; 5:1 hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 2099 st (C-N_2), 1663 st (C(=O)OR); δ_H (400 MHz; $CDCl_3$) 7.43-7.29 (5H, m, CH aromatic), 5.90 (1H, d, *J* 3.5 Hz, CHOH), 4.52 (2H, t, *J* 6.0 Hz, $CH_2CH_2C_6F_{13}$), 2.82 (1H, br s, CHOH), 2.56-2.44 (2H, m, $CH_2CH_2C_6F_{13}$); δ_C (126 MHz; $CDCl_3$) 165.6 (C), 138.6 (C), 128.8 (CH), 128.5 (CH), 125.6 (CH), 68.6 (CH), 56.8 ($CH_2CH_2C_6F_{13}$), 30.9-30.6 (m, $CH_2CH_2C_6F_{13}$); **HRMS** (ESI-) *m/z* found 537.0498 ($[M-H]^-$ calcd. 537.0489).

Isolated as a white solid (57.9 mg, 0.113 mmol, 61 %). NMR and LCMS analysis showed that the product existed as a mixture of keto and enol forms in solution and that the relative ratio of keto:enol forms was approximately 2.5:1. $\mathbf{R}_f$ 0.32 (SiO_2; 1:1 hexane: toluene); υ_{max} (neat)/cm^{-1} 1761 st (C(=O)OR), 1643 and 1624 st (C(=O)) 1189 (C-O); **mp** 38-41 °C; **^{1}H NMR data for keto form**; δ_H (400 MHz; $CDCl_3$) 7.94-7.91 (2H, m, CH aromatic), 7.78-7.77 (1H, m, CH aromatic), 7.50-7.45 (2H, m, CH aromatic), 4.48-4.45 (2H, t, *J* 6.8 Hz, $C_6F_{13}CH_2CH_2$), 4.02 (2H, s,

C(=O)C<u>H</u>$_2$), 2.60-2.42 (keto and enol, 4H, m, $C_6F_{13}C\underline{H}_2CH_2$); **^{1}H NMR data for enol form; δ_H** (400 MHz; $CDCl_3$) 12.33 (1H, CH=C(O<u>H</u>), 7.79-7.78 (1H, m, C<u>H</u> aromatic), 7.62-7.58 (2H, m, C<u>H</u> aromatic), 7.44-7.39 (2H, m, C<u>H</u> aromatic), 5.68 (1H, s, C(OH)=C<u>H</u>), 4.52-4.49 (2H, t, *J* 6.5 Hz, $C_6F_{13}CH_2C\underline{H}_2$), 2.60-2.42 (keto and enol, 4H, m, $C_6F_{13}C\underline{H}_2CH_2$); **^{13}C NMR data: δ_C** (125 MHz; $CDCl_3$) 191.9 (keto C(=O)Ph), 172.5 (enol <u>C</u>(=O)Ph), 172.4 (enol <u>C</u>(-OH)$OCH_2CH_2C_6F_{13}$), 167.1 (keto <u>C</u>(=O)$OCH_2CH_2C_6F_{13}$), 135.8, 133.1 (keto and enol <u>C</u> aromatic), 133.9, 131.5, 128.8, 128.6, 128.4, 126.2 (keto and enol <u>C</u>H aromatic), 86.7 (enol C(=O)<u>C</u>H), 57.2, 56.1 (keto and enol, $C_6F_{13}CH_2CH_2$), 45.6 (keto C(=O)<u>C</u>H_2), 30.9, 30.7, 30.6, 30.5, 30.4, 30.3 (keto and enol $C_6F_{13}\underline{C}H_2CH_2$); **HRMS** (ESI+) *m/z* found 511.0574 ($[M+H]^+$ calcd. 511.0573; **Elemental analysis** calculated for $C_{17}H_{11}F_{13}O_3$ (%) C 40.02, H 2.17; Found C 40.42, H 2.22.

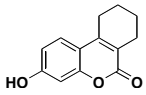


Isolated as a yellow oil (416 mg, 0.81 mmol, 81%); **R_f** 0.31 (SiO_2; 7.6:2.4 pet ether (30:40):diethyl ether); **υ_{max}** (neat)/cm^{-1} 2087 (C-N_2), 1660 (C(=O)OR); **δ_H** (500 MHz; $CDCl_3$) 4.52 (2 H, t, *J* 6.5 Hz, $C\underline{H}_2CH_2C_6F_{13}$), 3.01 (1 H, br s, OH), 2.57-2.47 (2 H, m, $CH_2C\underline{H}_2C_6F_{13}$), 2.08 (2 H, m, CH_2), 1.98-1.89 (2 H, m, CH_2), 1.86-1.79 (2 H, m, CH_2), 1.79-1.70 (2 H, m, CH_2); **δ_C** (126 MHz; $CDCl_3$) 166.4 (C), 78.6 (C), 56.5 ($\underline{C}H_2CH_2C_6F_{13}$), 39.4 ($CH_2$), 31.0-30.7 (m, $CH_2\underline{C}H_2C_6F_{13}$), 23.0 ($CH_2$); **HRMS** (ESI+) *m/z* found 517.0775 ($[M+H]^+$ calcd. 517.0791).

Isolated as a colourless oil (185 mg, 0.38 mmol, 84%). ^{1}H NMR analysis showed that the product existed as a mixture of keto and enol forms in solution and that the relative ratio of keto:enol was approximately 1:4. **R_f** 0.25 (SiO_2; 9.8:0.2 pet ether (30:40): ethyl acetate); **υ_{max}** (neat)/cm^{-1} 1754 (C(=O)OR), 1720 (C=O), 1660 (α, β-C=O), 1615 (C=C); **^{1}H NMR data for keto form; δ_H** (400 MHz; $CDCl_3$) 12.00 (1H, C=C(O<u>H</u>)), 4.51-4.39 (2H, m, $C_6F_{13}CH_2C\underline{H}_2$), 2.57-2.42 (2H, m, $C_6F_{13}C\underline{H}_2CH_2$), 2.29-2.24 (2H, m, CH_2), 2.23-2.17 (2H, m, CH_2), 1.71-1.64 (2H, m, CH_2), 1.63-1.56 (2H, m, CH_2); **^{13}C NMR data: δ_C** (126 MHz; $CDCl_3$) 205.7 (keto, <u>C</u>(=O)CHC(=O)O), 173.2 (enol <u>C</u>(=O)CHC(=O)O), 172.0 (enol <u>C</u>(OH)$OCH_2CH_2C_6F_{13}$), 169.6 (keto <u>C</u>(=O)$OCH_2CH_2C_6F_{13}$), 97.3 (enol <u>C</u>=C(OH)), 56.8 (keto CH), 56.0, 55.9 (keto and enol, $C_6F_{13}CH_2\underline{C}H_2$), 41.6 ($CH_2$), 30.7-30.3 (keto and enol $C_6F_{13}\underline{C}H_2CH_2$), 29.8 ($CH_2$), 29.1 ($CH_2$), 27.0 ($CH_2$), 23.4 ($CH_2$), 22.2 ($CH_2$), 22.1 ($CH_2$), 21.8 ($CH_2$); **HRMS** (ESI+) *m/z* found 489.0733 ($[M+H]^+$ calcd. 489.0730).

General method for Coumarin formation:

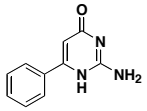
Conc. H_2SO_4 (5 equiv.) was added dropwise to a mixture of β–dicarbonyl (1 equiv.) and phenol derivative (1 equiv). EtOAc was added (if required) to form a solution which was stirred at ambient temperature for 12 hr. The crude product was purified by column chromatography to remove the fluorous-tagged alcohol by-product and to yield the desired coumarin.



Isolated as a white solid (23.9 mg, 0.11 mmol, 74%); **υ_{max}** (neat)/cm^{-1} 3210 br (OH), 1678 st (C(=O)OR), 1614 st (C=C), 1574 st; **mp** (recrystallised from MeOD) 188-193 °C **δ_H** (400 MHz; MeOD) 7.52 (1 H, d, *J* = 8.7 Hz, OHCCHC<u>H</u>), 6.78 (1 H, dd, *J* = 8.7, 2.4 Hz, OHCC<u>H</u>CH), 6.67 (1 H, d, *J* = 2.4 Hz, OHCC<u>H</u>C(O)), 2.79 (2 H, m, C(=C)CH_2), 2.47 (2 H, m, C(=C)CH_2), 1.89-1.76 (4 H, m, C(=C)$CH_2C\underline{H}_2$ and C(=C)$CH_2CH_2C\underline{H}_2$); **δ_C** (125 MHz; MeOD) 164.4 (C=O), 161.6 (C), 154.8 (C), 150.2 (C), 125.9 (CH), 120.1 (C), 114.1 (C), 114.0 (CH), 103.2 (CH), 26.2 (CH_2), 24.8 (CH_2), 22.8 (CH_2), 22.5 (CH_2); **HRMS** (ESI+) *m/z* found 217.0864 ($[M+H]^+$ calcd. 217.0865).

General method for the synthesis of Pyrimidinones:

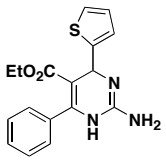
A solution of β-ketoester (1 equiv.) and guanidine carbonate (1 equiv.) in ethanol was heated to reflux for 5 hrs. The resultant precipitate was collected by filtration, washed with cold ethanol, water and acetone and dried under vacuum to give the desired product as a white solid.



Isolated as a white solid (60.6 mg, 0.324 mmol, 62 %); **υ_{max}** (neat)/cm^{-1} 3336 m (N-H), 3060 m (N-H), 1643 m (amide), 1559 st (C-NH_2), 1515 m (C=C); **δ_H** (500 MHz; DMSO) 10.85 (1H, br s, N<u>H</u>), 7.93 (2H, t, *J* 3.5 Hz, aryl H), 7.43 (3H, m, aryl H), 6.61 (2H, br s, N<u>H</u>$_2$), 6.10 (1H, s, C<u>H</u>); **δ_C** (125 MHz; $CDCl_3$) 163.29 (C), 162.52 (C), 155.65 (C), 137.242 (C), 129.78 (CH), 128.24 (CH), 126.50 (CH), 97.44 (CH); **HRMS** found MH^+ 188.0819, $C_{10}H_{10}N_3O^+$ required 188.0819; **m.p**. 281-286 °C.

General Method for the three-component Biginelli Reaction:

To a suspension of guanidine hydrochloride (1.2 equiv.) and sodium bicarbonate (4 equiv.) in anhydrous DMF was added the appropriate β-ketoester (1.1 equiv) and aldehyde (1 equiv.). The mixture was heated to 70 °C for 16 hrs. After cooling to room temperature the solution was poured onto crushed ice to facilitate precipitation and the yellow solid was collected by filtration.

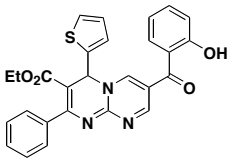


Isolated as a yellow solid (1.31 g, 4.00 mmol, 85 %); **υ_{max}** (neat)/cm^{-1} 3398 w (N-H), 3357 w (N-H), 1671 m (ester), 1579 m (C-NH_2), 1529 w (C=C), 1230 st (C=O); **δ_H** (500 MHz; DMSO) 7.64 (1H, br s, N<u>H</u>), 7.35

(1H, dd, *J* 4.0, 1.0 Hz, aryl H), 7.25 (5H, m, aryl H), 7.00 (2H, m, aryl H), 6.39 (2H, br s, N$\underline{H}_2$), 5.58 (1H, s, C$\underline{H}$), 3.74 (2H, q, *J* 7.0 Hz, C$\underline{H}_2$CH$_3$), 0.80 (3H, t, *J* 7.0 Hz, CH$_2$C$\underline{H}_3$); **δ$_C$** (125 MHz; $CDCl_3$) 165.64 (C), 155.22 (C), 150.60 (C), 127.99 (CH), 126.95 (CH), 126.62 (CH), 126.33 (CH), 124.29 (CH), 122.91 (CH), 97.75 (C), 58.00 (CH_2), 48.44 (CH), 13.60 (CH_3); **HRMS** found MH^+ 328.1103, $C_{17}H_{18}N_3O_2S^+$ required 328.1120; **m.p**. 247-252 °C.

General method for the reaction with Chromones:

A suspension of dihydropyrimidine (1 equiv.) and the appropriate chromone (1 equiv.) in ethanol was heated to reflux for 5 hrs. After cooling to room temperature the yellow solid was collected by filtration, washed with EtOH and dried under vacuum to give the desired product.



Isolated as a yellow solid (745 mg, 1.54 mmol, 50 %); **υ$_{max}$** (neat)/cm^{-1} 2753 br (O-H), 1694 m (ester), 1664 st (ketone), 1622 m (C=C), 1531 m (C=N); **δ$_H$** (500 MHz; DMSO) 11.84 (1H, br s, O$\underline{H}$), 7.90 (1H, dd, *J* 6.5, 1.0 Hz, aryl H), 7.51 (2H, m, aryl H), 7.44 (2H, t, *J* 7.5 Hz, aryl H), 7.38 (2H, m, aryl H), 7.30 (1H, d, *J* 5.0 Hz, aryl H), 7.14 (1H, d, *J* 3.0 Hz, aryl H), 7.10 (1H, t, *J* 7.5 Hz, aryl H), 7.06 (1H, d, *J* 8.0 Hz, aryl H), 6.96 (1H, dd, *J* 5.0, 3.5 Hz, aryl H), 6.23 (1H, s, N=C$\underline{H}$), 6.17 (1H, s, N-C$\underline{H}$), 5.45 (1H, s, C$\underline{H}$), 3.90 (2H, qd, *J* 7.0, 3.0 Hz, C$\underline{H}_2$CH$_3$), 0.80 (3H, t, *J* 7.0 Hz, CH$_2$C$\underline{H}_3$); **δ$_C$** (125 MHz; $CDCl_3$) 179.45 (C), 164.58 (C), 155.94 (C), 148.60 (C), 142.09 (CH), 140.08 (CH), 135.71 (CH), 135.09 (C), 130.20 (CH), 128.49 (CH), 128.22 (CH), 127.40 (CH), 126.96 (CH), 126.73 (CH), 126.56 (CH), 124.05 (C), 122.55 (CH), 118.10 (CH), 108.81 (C), 103.44 (C), 82.89 (CH), 60.30 (CH_2), 52.89 (CH), 13.50 (CH_3); **HRMS** found MH^+ 484.1326, $C_{27}H_{22}N_3O_4S^+$ required 484.1331; **m.p.** 232-245 °C.

General method for cleavage to the amide:

Me_2AlCl (1M in hexane, 5 equiv.) was added dropwise to a solution of cyclohexylamine (5 equiv.) in anhydrous toluene. After stirring at ambient temperature for 10 minutes the appropriate Diels-Alder adduct (1 equiv.) was added drop wise as a solution in toluene and the solution heated to 50 °C for 5 hrs. After cooling to room temperature the reaction was quenched by the drop wise addition of sat. aq. NH_4Cl solution. The organic layer was separated and the aqueous layer was washed with EtOAc (×3). The combined organic layers were washed with brine, dried ($MgSO_4$) and the solvent removed *in vacuo*. The crude product was purified by chromatography.

General method for transesterification:

^{n}BuLi (1.6 M in hexane, 8 equiv.) was added dropwise to a solution of alcohol (8.2 equiv.) in THF at 0 °C. After stirring for 10 minutes the substrate (1 equiv.) was added as a single portion in THF and the solution stirred for a further 3 hrs. After warming to room temperature the reaction was washed with sat. aq. $NaHCO_3$ and extracted into diethyl ether (× 3). The combined organic extracts were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by chromatography.

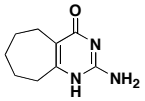
General method for reduction to the alcohol:

To a solution of fluorous tagged ester (1 equiv.) in THF at -78 °C was added DIBAL-H (1M in hexane, 5 equiv.). The solution was stirred for 2 hrs at -78 °C, warmed to room temperature and quenched by addition of Rochelle's Salts. The product was extracted into EtOAc (× 3) and the combined organic layers were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by chromatography.

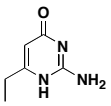
General method for hydrolysis to the acid:

To a solution of LiOH (5 equiv.) in H_2O was added a solution of fluorous tagged ester (1 equiv.) in THF and the mixture was heated to reflux for 3 hrs. After cooling to room temperature the mixture was washed with EtOAc. The aqueous layer was acidified (3M HCl) and re-extracted with EtOAc (× 3). The organic fractions from the second washing were combined, washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give a white solid.

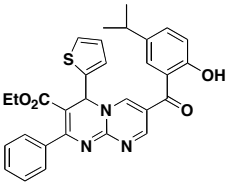
Library Demonstration Compounds:



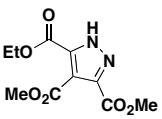
υ$_{max}$ (neat)/cm^{-1} 3323 m (N-H), 3120 m (N-H), 1654 st (amide), 1639 st (C-NH_2), 1607 m (C=C); **δ$_H$** (500 MHz; DMSO) 10.74 (1H, br s, N$\underline{H}$), 6.63 (2H, br s, N$\underline{H}_2$), 2.46 (4H, s, 2 C$\underline{H}_2$), 1.70 (2H, quint, *J* 5.5 Hz, C$\underline{H}_2$), 1.50 (2H, quint, *J* 5.0 Hz, C$\underline{H}_2$), 1.37 (2H, quint, *J* 5.0 Hz, C$\underline{H}_2$); **δ$_C$** (125 MHz; DMSO) 152.92 (C), 112.46 (C), 31.78 (CH_2), 27.09 (CH_2), 25.22 (CH_2), 22.82 (CH_2); **HRMS** found MH^+ 180.1137, $C_9H_{14}N_3O^+$ required 180.1138; **m.p**. 258-266 °C.



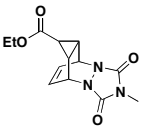
υ$_{max}$ (neat)/cm^{-1} 3320 m (N-H), 3180 m (N-H), 1646 st (amide), 1576 m (C-NH_2), 1525 m (C=C); **δ$_H$** (500 MHz; MeOD) 5.59 (1H, s, C$\underline{H}$), 4.90 (2H, s, N$\underline{H}_2$), 2.37 (2H, q, *J* 7.5 Hz, C$\underline{H}_2$CH$_3$), 1.18 (3H, q, *J* 7.5 Hz, CH$_2$C$\underline{H}_3$); **δ$_C$** (125 MHz; $CDCl_3$) 174.07 (C), 170.68 (C), 161.67 (C), 100.17 (CH), 30.67 (CH_2), 13.08 (CH_3); **HRMS** found MNa^+ 162.0645, $C_6H_9N_3ONa^+$ required 162.0643; **m.p.** 250-254 °C.



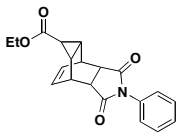
υ_{max} (neat)/cm^{-1} 2720 br (O-H), 1675 m (ester), 1621 m (ketone), 1599 m (C=C), 1541 m (C=N), 1243 st (C-O); δ_H (500 MHz; DMSO) 10.88 (1H, br s, OH), 7.63 (1H, m, aryl H), 7.53 (2H, m, aryl H), 7.36 (5H, m, aryl H), 7.24 (1H, d, *J* 3.0 Hz, aryl H), 7.12 (1H, d, *J* 8.5 Hz, aryl H), 7.01 (1H, t, *J* 4.0 Hz, aryl H), 6.44 (1H, s, N=CH), 6.04 (1H, s, N-CH), 3.83 (2H, q, *J* 7.0 Hz, CH_2CH_3), 2.93 (1H, septuplet, *J* 7.0 Hz, CH_3CHCH_3), 1.20 (6H, d, *J* 7.0 Hz, CH_3CHCH_3), 0.78 (3H, t, *J* 7.0 Hz, CH_2CH_3); δ_C (125 MHz; $CDCl_3$) 179.01 (C), 164.64 (C), 154.29 (C), 142.61 (C), 134.84 (C), 134.51 (CH), 128.95 (CH), 128.54 (CH), 127.71 (CH), 127.19 (CH), 127.19 (CH), 126.84 (CH), 126.41 (C), 125.62 (C), 125.43 (C), 123.76 (CH), 123.38 (CH), 118.41 (CH), 108.23 (C), 103.06 (C), 82.77 (CH), 59.72 (CH_2), 59.32 (CH), 52.49 (CH), 32.75 (CH), 23.962 (CH_3), 23.874 (CH_3), 13.50 (CH_3); **HRMS** found MH^+ 526.1799, $C_{30}H_{28}N_3O_4S^+$ required 526.1801; **m.p.** 247-252 °C.



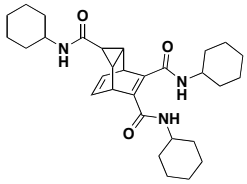
$\mathbf{R}_f$ 0.17 (SiO_2; 1:1 hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 3240 br (N-H), 1750 m (ester), 1710 st (ester), 1570 m (C=C), 1260 st (C-O), 1030 st (C-O); δ_H (500 MHz; $CDCl_3$) 11.95 (1H, br s, NH), 4.39 (2H, q, *J* 7.0 Hz, CH_2CH_3), 3.95 (3H, s, CO_2CH_3), 3.93 (3H, s, CO_2CH_3), 1.36 (3H, t, *J* 7.0 Hz, CH_2CH_3); δ_C (125 MHz; $CDCl_3$) 163.34 (C), 119.39 (C), 62.20 (CH_2), 52.98 (CH_3), 52.80 (CH_3), 13.98 (CH_3); **HRMS** found MH^+ 279.0601, $C_{10}H_1N_2O_6Na^+$ required 279.0593; **m.p.** 91-94 °C.



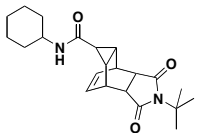
$\mathbf{R}_f$ 0.08 (SiO_2; 2:1 hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 1775 m (imide), 1705 st (imide), 1179 st (C-O); δ_H (500 MHz; $CDCl_3$) 6.07 (2H, t, *J* 4.0 Hz, CH=CH), 5.14 (2H, m, NCH), 4.13 (2H, q, *J* 7.0 Hz, CH_2CH_3), 3.00 (3H, s, CH_3), 2.12 (2H, dd, *J* 5.0, 3.0 Hz, CH-CH), 1.40 (1H, t, *J* 3.0 Hz, COCH), 1.25 (3H, t, *J* 7.0 Hz, CH_2CH_3); δ_C (125 MHz; $CDCl_3$) 170.48 (C), 158.38 (C), 125.86 (CH), 61.23 (CH_2), 52.10 (CH), 25.40 (CH_3), 23.61 (CH), 15.49 (CH), 14.15 (CH_3); **HRMS** found MH^+ 278.1151, $C_{13}H_{16}N_3O_4^+$ required 278.1141; **m.p.** 123-129 °C.



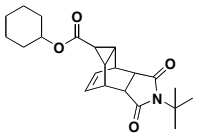
$\mathbf{R}_f$ 0.15 (SiO_2; 2:1 hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 1770 w (imide), 1744 w (ester), 1698 st (imide), 1184 st (C-O); δ_H (500 MHz; $CDCl_3$) 7.43 (2H, m, aryl 2H), 7.36 (1H, m, aryl 1H), 7.15 (2H, m, aryl 2H), 5.96 (2H, dd, *J* 4.5, 3.5 Hz, CH=CH), 4.11 (2H, q, *J* 7.0 Hz, CH_2CH_3), 3.63 (2H, m, NCOCHCH), 3.19 (2H, t, *J* 1.5 Hz, NCOCHCH), 1.83 (2H, q, *J* 2.5 Hz, 2COCHCH), 1.44 (1H, t, *J* 3.0 Hz, COCH), 1.26 (3H, t, *J* 7.0 Hz, CH_2CH_3); δ_C (125 MHz; $CDCl_3$) 176.89 (C), 172.41 (C), 131.65 (C), 129.31 (CH), 129.15 (CH), 128.73 (CH), 128.56 (CH), 60.84 (CH_2), 44.69 (CH), 33.25 (CH), 20.45 (CH), 20.07 (CH), 14.23 (CH_3); **HRMS** found MH^+ 338.1391, $C_{20}H_{20}NO_4^+$ required 338.1392; **m.p.** 173-178 °C.



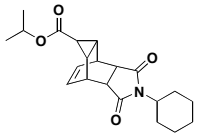
$\mathbf{R}_f$ 0.14 (SiO_2; hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 3277 w (N-H), 1636 st (amide), 1526 m (amide); δ_H (500 MHz; $CDCl_3$) 7.03 (2H, d, *J* 8.0 Hz, 2NH), 6.07 (2H, d, *J* 8.0 Hz, CH=CH), 5.67 (1H, d, *J* 8.0 Hz, NH), 4.21 (2H, apparent m, CCH), 3.75 (2H, m, 2NHCH), 3.64 (1H, m, NHCH), 1.95 (2H, d, *J* 2.0 Hz, CH-CH), 1.84 (6H, m, cyclohexyl 6H), 1.67 (6H, m, cyclohexyl 6H), 1.57 (3H, m, cyclohexyl 3H), 1.39 (1H, t, *J* 2.5 Hz COCH), 1.31 (6H, m, cyclohexyl 6H), 1.14 (9H, m, cyclohexyl 9H); δ_C (125 MHz; $CDCl_3$) 169.08 (C), 166.10 (C), 146.99 (C), 131.25 (CH), 48.56 (CH), 48.10 (CH), 41.56 (CH), 33.11 (CH_2), 32.76 (CH_2), 32.69 (CH_2), 32.59 (CH), 26.13 (CH), 25.41 (CH_2), 24.80 (CH_2), 24.71 (CH_2); **HRMS** found MH^+ 516.3216, $C_{30}H_{43}N_3O_3Na^+$ required 494.3383; **m.p.** 151-161 °C.



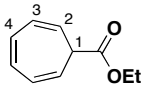
$\mathbf{R}_f$ 0.31 (SiO_2; hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 3340 w (N-H), 1761 w (imide), 1683 st (imide), 1652 st (amide), 1530 m (amide); δ_H (500 MHz; $CDCl_3$) 5.80 (2H, m, CH=CH), 5.45 (1H, d, *J* 7.5 Hz, NH), 3.87 (1H, m, NCH), 3.42 (2H, s, CHCHCH), 2.85 (2H, d, *J* 1.5 Hz, NCOCH), 1.86 (2H, d, *J* 12.0 Hz, cyclohexyl 2H), 1.76 (1H, m, cyclohexyl 1H), 1.67 (4H, m, cyclohexyl 2H + CH-CH), 1.58 (2H, s, ^{t}butyl 2H), 1.46 (7H, m, ^{t}butyl 7H), 1.32 (2H, m, cyclohexyl 2H), 1.08 (3H, m, cyclohexyl 3H), 0.99 (1H, t, *J* 2.5 Hz, NHCOCH); δ_C (125 MHz; $CDCl_3$) 179.10 (C), 169.93 (C), 128.45 (CH), 58.19 (C), 48.27 (CH), 44.52 (CH), 33.21 (CH), 33.09 (CH_2), 28.28 (CH_3), 25.46 (CH_2), 24.80 (CH_2), 21.95 (CH), 19.18 (CH); **HRMS** MH^+ 371.2322, $C_{22}H_{31}N_2O_3^+$ required 371.2335; **m.p.** 238-245 °C.



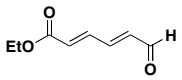
$\mathbf{R}_f$ 0.20 (SiO_2; 4:1 30-40 petroleum ether: ethyl acetate); υ_{max} (neat)/cm^{-1} 1767 w (imide), 1692 st (imide), 1161 st (C-O); δ_H (500 MHz; $CDCl_3$) 5.81 (2H, dd, *J* 4.5, 3.5 Hz, C<u>H</u>=C<u>H</u>), 4.68 (1H, m, $CO_2C\underline{H}$), 3.46 (2H, m, CHC<u>H</u>CH), 2.85 (2H, t, *J* 1.5 Hz, NCOC<u>H</u>), 1.80 (2H, m, cyclohexyl 2<u>H</u>), 1.69 (4H, m, cyclohexyl 2<u>H</u> + C<u>H</u>-C<u>H</u>), 1.52 (1H, m, cyclohexyl 1<u>H</u>), 1.47 (9H, s, ^{t}butyl 9<u>H</u>), 1.33 (5H, m, cyclohexyl 4<u>H</u> + COC<u>H</u>), 1.23 (1H, m, cyclohexyl 1<u>H</u>); δ_C (125 MHz; $CDCl_3$) 178.93 (C), 171.89 (C), 128.27 (CH), 72.94 (CH), 58.26 (C), 44.43 (CH), 33.20 (CH), 31.62 (CH_2), 28.29 (CH_3), 25.31 (CH_2), 23.76 (CH_2), 20.38 (CH), 20.12 (CH); **HRMS** found MH^+ 372.2286, $C_{22}H_{30}NO_4^+$ required 372.2176; **m.p.** 179-182 °C.



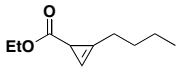
$\mathbf{R}_f$ 0.43 (SiO_2; 2:1 30-40 petroleum ether: ethyl acetate); υ_{max} (neat)/cm^{-1} 1766 w (imide), 1704 st (ester), 1691 st (imide), 1190 m (C-O); δ_H (500 MHz; $CDCl_3$) 5.78 (2H, dd, *J* 4.5, 3.5 Hz, C<u>H</u>=C<u>H</u>), 4.94 (1H, septuplet, *J* 6.0 Hz, $CO_2C\underline{H}$), 3.82 (1H, tt, *J* 12.5, 4.0 Hz, NC<u>H</u>), 3.48 (2H, apparent m, CHC<u>H</u>CH), 2.92 (2H, apparent m, NCOC<u>H</u>), 2.02 (2H, qd, *J* 12.5, 3.5 Hz, cyclohexyl 2<u>H</u>), 1.76 (4H, m, cyclohexyl 2<u>H</u> + C<u>H</u>-C<u>H</u>), 1.60 (1H, d, *J* 11.5 Hz, cyclohexyl <u>H</u>), 1.44 (2H, m, cyclohexyl 2<u>H</u>), 1.32 (1H, t, *J* 3.0 Hz, COC<u>H</u>), 1.25 (2H, m, cyclohexyl 2<u>H</u>), 1.20 (6H, d, *J* 6.5 Hz, $2C\underline{H}_3$), 1.15 (1H, m, cyclohexyl <u>H</u>); δ_C (125 MHz; $CDCl_3$) 177.90 (C), 171.88 (C), 128.15 (CH), 67.99 (CH), 51.48 (CH), 44.22 (CH), 33.05 (CH), 28.65 (CH_2), 25.75 (CH_2), 25.01 (CH_2), 21.79 (CH), 20.36 (CH), 20.24 (CH_3); **HRMS** found MH^+ 358.2049, $C_{21}H_{28}NO_4^+$ required 358.2018; **m.p.** 177-181 °C.



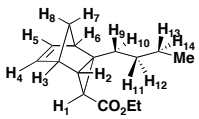
$\mathbf{R}_f$ 0.34 (SiO_2; 10:1 Hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 1734 st (ester), 1605 w (C=C), 1161 st (C-O); δ_H (400 MHz; $CDCl_3$) 6.64 (2H, m, 2 C(4)<u>H</u>), 6.25 (2H, m, 2 C(3)<u>H</u>), 5.43 (2H, dd, *J* 9.0 Hz, 5.5 Hz, 2 C(2)<u>H</u>), 4.25 (2H, qd, *J* 7.0, 1.0 Hz, $C\underline{H}_2CH_3$), 2.53 (1H, td, *J* 5.5, 1.0 Hz, C(1)<u>H</u>), 1.30 (3H, t, *J* 7.0, 1.0 Hz, $CH_2C\underline{H}_3$); δ_C (125 MHz; $CDCl_3$) 172.84 (C), 130.75 (CH), 125.41 (CH), 117.11 (CH), 60.84 (CH_2), 43.93 (CH), 14.09 (CH_3); **HRMS** found MH^+ 187.0445, $C_{10}H_{12}O_2Na^+$ required 187.0737. Data consistent with the literature [A. J. Anciaux, A. J.Hubert, A. F. Noels, N. Petiniot, P. Teyssie, *J. Org. Chem.* **1980**, *45*, 695-702].



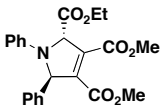
$\mathbf{R}_f$ 0.21 (SiO_2; 4:1 Hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 1712 st (ester), 1682 st (aldehyde), 1636 w and 1601 m (C=C); δ_H (400 MHz; $CDCl_3$) 9.60-9.59 (1H, d, *J* 7.5 Hz, C<u>H</u>O), 7.38-7.31 (1H, dd, *J* 15.5 Hz, 11.5 Hz, CHCH<u>H</u>CHCHO), 7.15-7.08 (1H, dd, *J* 15.5 Hz, 11.5 Hz, CHC<u>H</u>CHCHCHO), 6.37-6.31 (1H, dd, *J* 15.5 Hz, 8.0 Hz, CHCHCHC<u>H</u>CHO), 6.26-6.22 (1H, dd, *J* 15.5 Hz, C<u>H</u>CHCHCHCHO), 4.20-4.15 (2H, q, *J* 7.0 Hz, $C\underline{H}_2CH_3$), 1.26-1.22 (3H, t, *J* 7.0 Hz, $CH_2C\underline{H}_3$); δ_C (125 MHz; $CDCl_3$) 192.77 (CHO), 165.24 (C), 147.09 (CH), 140.14 (CH), 136.77 (CH), 129.76 (CH), 60.86 (CH_2), 13.99 (CH_3). Data consistent with the literature [E. Wenkhert, M. Guo, R. Lavilla, B. Porter, K. Ramachandran, J. H. Sheu, *J. Org. Chem.* **1990**, *55*, 6203-6214].



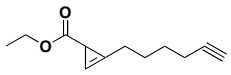
$\mathbf{R}_f$ 0.39 (SiO_2; 5:1 Hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 1719 st (ester), 1178 st (C-O); δ_H (400 MHz; $CDCl_3$), 6.27 (1H, s, $CH_3CH_2O_2CHC\underline{H}$), 4.11-4.03 (2H, m, $C\underline{H}_2CH_3$), 2.46-2.43 (2H, t, *J* 7.0 Hz, $C\underline{H}_2CH_2CH_2CH_3$), 2.07 (1H, s, $CH_3CH_2O_2C\underline{H}CH$), 1.56-1.48 (2H, quintet, *J* 7.0 Hz, $CH_2C\underline{H}_2CH_2CH_3$), 1.39-1.29 (2H, quintet, *J* 7.0 Hz, $CH_2CH_2C\underline{H}_2CH_3$), 1.21-1.18 (3H, t, *J* 7.0 Hz, $CH_2C\underline{H}_3$), 0.88-0.85 (3H, t, *J* 7.0 Hz, $CH_2CH_2CH_2C\underline{H}_3$); δ_C (125 MHz; $CDCl_3$) 176.41 (C), 115.47 (C), 93.83 (CH), 59.93 (CH_2), 28.60 (CH_2), 24.50 (CH_2), 22.05 (CH_2), 19.55 (CH), 14.21 (CH_3), 13.53 (CH_3). Data consistent with the literature [P. Muelleru, C. Graenicher, *Helv. Chim. Acta.* **1993**, *76*, 521-534].



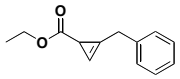
$\mathbf{R}_f$ 0.32 (SiO_2; 24:1 Hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 1722 st (ester), 1174 st (C-O); δ_H (400 MHz; C_6D_6) 5.76-5.74 (1H, at, *J* 3.5 Hz, 5.0 Hz CH^4CH^5), 5.68-6.64 (1H, at, *J* 3.5 Hz, 5.0 Hz CH^4CH^5), 4.15-4.02 (2H, m, $C\underline{H}_2CH_3$), 2.76 (1H, s, H^3 or H^6), 2.68 (1H, s, H^3 or H^6), 2.29-2.23 (1H, m, H^9), 2.11-2.10 (1H, t, *J* 3.5 Hz, H^2), 1.81-1.79 (1H, d, *J* 7.0 Hz, H^7), 1.78-1.72 (1H, m, H^{11} or H^{12}), 1.77-1.76 (1H, d, *J* 3.0 Hz, H^1), 1.62-1.60 (1H, d, *J* 7.0 Hz, H^8), 1.57-1.50 (1H, m, H^{11} or H^{12}), 1.46-1.37 (3H, m, H^{10}, H^{13} and H^{14}), 1.10-1.07 (3H, t, *J* 7.0, $CH_2C\underline{H}_3$), 1.02-1.00 (3H, t, *J* 7.0 Hz, CH_3); δ_C (125 MHz; C_6D_6) 170.69 (C), 132.71 (CH), 132.58 (CH), 61.97 (CH_2), 59.94 (CH_2), 49.02 (CH), 43.72 (CH), 35.45 (CH), 33.92 (C), 31.52 (CH_2), 29.01 (CH_2), 26.12 (CH), 23.22 (CH_2), 14.56 (2 × CH_3); **HRMS** found MH^+ 235.1700, $C_{15}H_{23}O_2^+$ required 235.1698.



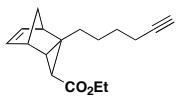
R$_f$ 0.15 (SiO_2; 1:1 Hexane: ethyl acetate); υ_{max} (neat)/cm^{-1} 1749 st (ester), 1727 st (ester), 1232 st (C-O); δ_H (400 MHz; $CDCl_3$) 7.33-7.21 (5H, m, aryl C<u>H</u>), 7.10-6.53 (5H, m, *N*-aryl C<u>H</u>), 6.02-6.00 (1H, d, *J* 7.0 Hz, C<u>H</u>Ph), 5.76-5.75 (1H, d, *J* 7.0 Hz, C<u>H</u>CO_2Et), 4.22-4.06 (2H, m, C<u>H</u>$_2$$CH_3$), 3.82 (3H, s, CH(Ph)$CCO_2C$<u>H</u>$_3$), 3.62 (3H, s, CH($CO_2$Et)$CCO_2C$<u>H</u>$_3$), 1.12-1.08 (3H, t, *J* 7.0 Hz, CH_2C<u>H</u>$_3$); δ_C (125 MHz; CDCl3) 169.57 (C), 162.88 (C), 162.24 (C), 143.91 (C), 143.42 (C), 137.93 (C), 130.86 (C), 128.99 (CH), 128.86 (CH), 128.38 (CH), 127.27 (CH), 118.26 (CH), 113.87 (CH), 70.99 (CH), 69.71 (CH), 61.73 (CH_2), 52.57 (CH_3), 52.30 (CH_3), 14.02 (CH_3); **HRMS** found MH^+ 410.1587, $C_{23}H_{24}NO_6^+$ required 410.1604; **m.p.** 102-107 °C.



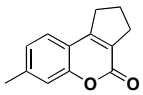
R$_f$ 0.23 (SiO_2; 9.4:0.6 pet ether (30:40): ethyl acetate); υ_{max} (neat)/cm^{-1} 1717 st (C(=O)OR), 1180 st (C-O); δ_H (400 MHz; $CDCl_3$) 6.37 (1H, app. q, *J* 1.4 Hz C(=O)CHC<u>H</u>), 4.19-4.09 (2H, m, C(=O)C<u>H</u>$_2$$CH_3$), 2.55 (2H, td, *J* 7.1, 1.4 Hz, C(=CH)C<u>H</u>$_2$$CH_2$ or C(=CH)$CH_2CH_2CH_2C$<u>H</u>$_2$), 2.23 (2H, td, *J* 7.0, 2.6 Hz, C(=CH)C<u>H</u>$_2$$CH_2$ or C(=CH)$CH_2CH_2CH_2C$<u>H</u>$_2$), 2.15 (1H, d, *J* 1.4 Hz C(=O)C<u>H</u>CH), 1.96 (1H, t, *J* 2.7 Hz, C≡C<u>H</u>), 1.77-1.70 (2H, m, C(=CH)CH_2C<u>H</u>$_2$ or C(=CH)CH_2CH_2C<u>H</u>$_2CH_2$), 1.65-1.59 (2H, m, C(=CH)CH_2C<u>H</u>$_2$ or C(=CH)CH_2CH_2C<u>H</u>$_2CH_2$), 1.26 (3H, t, *J* 7.3 Hz, CH_2C<u>H</u>$_3$); δ_C (125 MHz; $CDCl_3$) 176.5 (C), 115.1 (C), 94.5 (CH), 84.0 (C), 68.5 (CH), 60.2 (CH_2), 27.7 (CH_2), 25.7 (CH_2), 24.5, (CH_2) 19.7 (CH), 18.1 (CH_2), 13.5 (CH_3); **HRMS** (ESI+) *m/z* found 193.1223, ([M+H]$^+$ calcd. 193.1223).



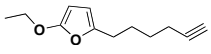
R$_f$ 0.32 (SiO_2; 9.6:0.4 pet ether (30:40): ethyl acetate); υ_{max} (neat)/cm^{-1} 1717 st (C(=O)OR), 1180 st (C-O); δ_H (400 MHz; $CDCl_3$) 7.33-7.24 (5H, m, C<u>H</u> aromatic) 6.47-6.46 (1H, app. q, *J* 1.5 Hz C(=O)CHC<u>H</u>), 4.12-4.03 (2H, m, C(=O)OC<u>H</u>$_2$$CH_3$), 3.90-3.77 (2H, app. q, *J* 17.6 Hz, C(=C)C<u>H</u>$_2$), 2.22 (1H, d, *J* 1.5 Hz C(=O)C<u>H</u>CH), 1.20 (3H, t, *J* 7.3 Hz, CH_2C<u>H</u>$_3$); δ_C (125 MHz; $CDCl_3$) 176.0 (C), 136.2 (C), 128.6 (2 CH), 126.8 (CH), 114.7 (C), 95.7 (CH), 60.2 (CH_2), 31.4 (CH_2), 20.4 (CH), 14.3 (CH_3); **HRMS** (ESI+) *m/z* found 203.1075, ([M+H]$^+$ calcd. 203.1072).



R$_f$ 0.14 (SiO_2; 9.8:0.2 pet ether (30:40): ethyl acetate); υ_{max} (neat)/cm^{-1} 1720 st (C(=O)OR), 1156 st (C-O); δ_H (500 MHz; C_6D_6) 5.62-5.58 (1 H, m, C=CH), 5.56-5.51 (1 H, m, C=CH), 4.06-3.91 (2 H, m, C(=O)C<u>H</u>$_2$$CH_3$), 2.63-2.58 (1 H, m), 2.53 (1 H, s), 2.12-2.03 (1 H, m), 2.02-1.96 (1 H, m), 1.77 (3 H, t, *J* = 2.7 Hz, C≡CH), 1.67-1.63 (1 H, m), 1.55 (2 H, ddd, *J* = 10.6, 9.1, 4.8 Hz), 1.50-1.46 (1 H, m), 1.43-1.33 (4 H, m), 0.98 (3 H, t, *J* = 7.13 Hz, CH_3); δ_C (125 MHz; C_6D_6) 170.5 (C), 132.5 (CH), 132.4 (CH), 84.2 (C), 68.6 (CH), 61.8 (CH_2), 59.8 (CH_2), 48.8(CH), 43.5 (CH), 35.2 (CH), 33.6 (C), 28.7 (CH_2) , 28.5 (CH_2), 28.0 (CH_2), 26.8 (CH), 18.5 (CH_2), 14.2 (CH_3); **HRMS** (ESI+) *m/z* found 259.1686 ([M+H]$^+$ calcd. 259.1698).



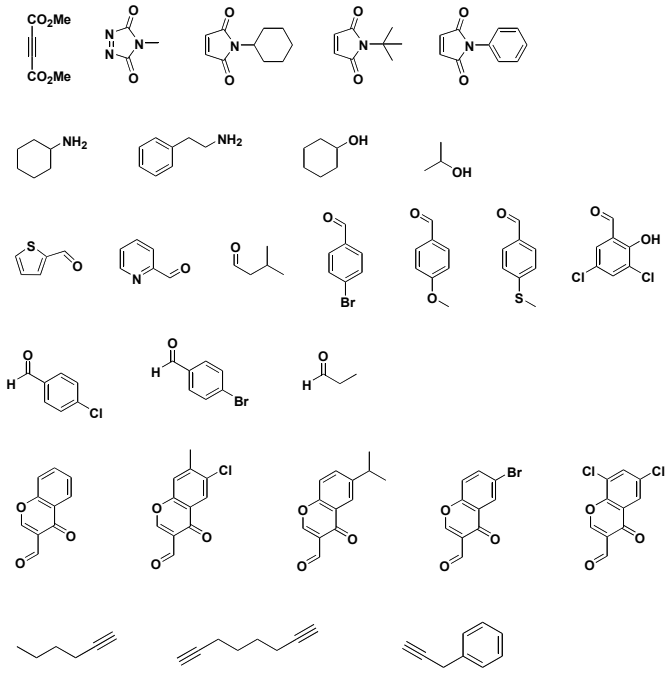
υ_{max} (neat)/cm^{-1} 1716 st (C(=O)OR), 1614 (C=C), 1558 (aromatic C=C); **mp** 87-92 °C δ_H (400 MHz; MeOD) 7.41 (1 H, d, *J* 8.5 Hz, CH aromatic), 7.16-7.14 (2H, m, CH aromatic), 3.10-3.05 (2H, m, C=CCH_2), 2.83-2.79 (2H, m, C=CCH_2), 2.43 (3H, s, CH_3) 2.22 (2H, app quintet, *J* 7.9 Hz, C=CCH_2C<u>H</u>$_2$); δ_C (126 MHz; MeOD) 162.3 (C=O), 158.7 (C), 155.4 (C), 143.7 (C), 127.4 (C), 126.7 (CH), 126.0 (CH), 117.59 (CH), 117.56 (C), 32.8 (CH_2), 31.3 (CH_2), 23.5 (CH_2), 21.7 (CH_3); **HRMS** (ESI+) *m/z* found 201.0911 ([M+H]$^+$ calcd. 201.0910).



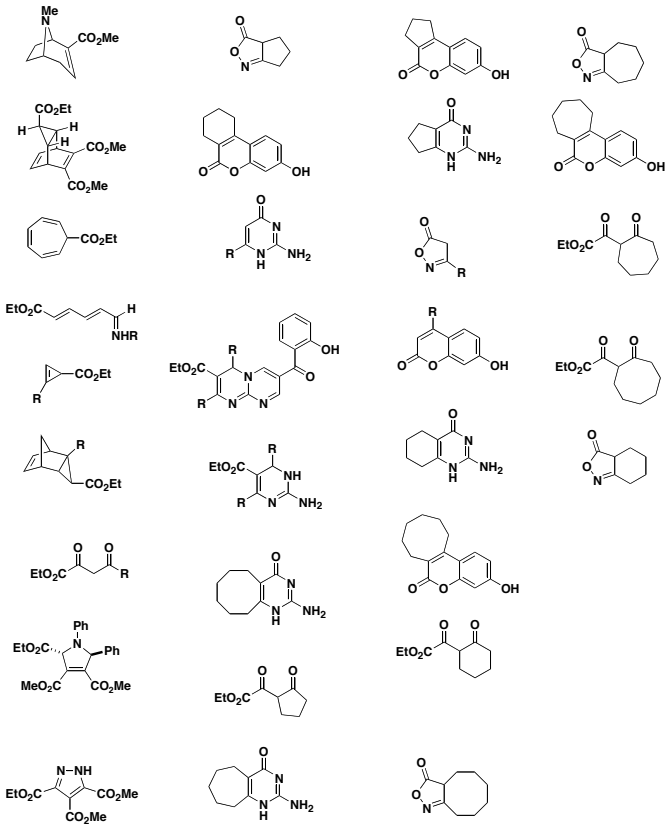
A solution of alkyne-tethered cyclopropene (50 mg, 0.26 mmol) in dry toluene (15 ml) under an ethylene atmosphere was heated to reflux. A solution of Grubbs II catalyst (11mg, 1 mol%) in dry toluene (4 ml) was added dropwise over the course of 5 hr. The resulting green solution was heated at reflux for 12 hr. The solution was cooled, filtered through SiO_2 and the solvent removed *in vacuo*. The crude product was purified by column chromatography (SiO_2, 9.8:0.2 pet ether (30:40): diethyl ether) to yield the substituted furan as a wet white solid (15 mg, 0.08 mmol, 30%).

R$_f$ 0.44 (SiO_2; 9.8:0.2 pet ether (30:40): ethyl acetate); υ_{max} (in $CDCl_3$)/cm^{-1} 1618, 1587, 1259; δ_H (400 MHz; $CDCl_3$) 5.81-5.80 (1H, m, CH_2CC<u>H</u>CH), 4.99 (1H, d, *J* 3.0 Hz, CH_2CCHC<u>H</u>), 4.03 (2H, q, *J* 7.0 Hz, CH_3C<u>H</u>$_2$), 2.51 (2H, td, *J* 7.3, 1.0 Hz, C<u>H</u>$_2$$CH_2CH_2CH_2C$≡CH), 2.19 (2H, td, *J* 7.0, 2.5 Hz, $CH_2CH_2CH_2C$<u>H</u>$_2$C≡CH), 1.93 (1H, t, *J* 2.8 Hz, C=C<u>H</u>), 1.74-1.67 (2H, m, CH_2C<u>H</u>$_2CH_2CH_2$C≡CH or CH_2CH_2C<u>H</u>$_2CH_2$C≡CH), 1.60-1.54 (2H, m, CH_2C<u>H</u>$_2CH_2CH_2$C≡CH or CH_2CH_2C<u>H</u>$_2CH_2$C≡CH), 1.38 (3H, t, *J* 7.0 Hz, CH_3); δ_C (125 MHz; $CDCl_3$) 159.4 (C), 145.6 (C), 105.5 (CH), 84.3 (C), 80.4 (CH), 68.3 (CH), 66.7 (CH_2), 27.8 (CH_2), 27.4 (CH_2), 27.0 (CH_2), 18.2 (CH_2), 14.6 (CH_3); **HRMS** (ESI+) *m/z* found 193.1224 ([M+H]$^+$ calcd. 193.1229).

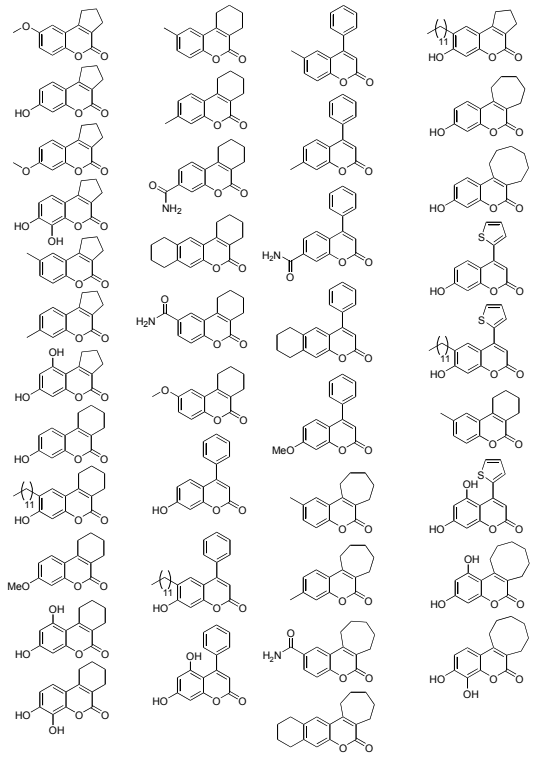
Library Building Blocks:

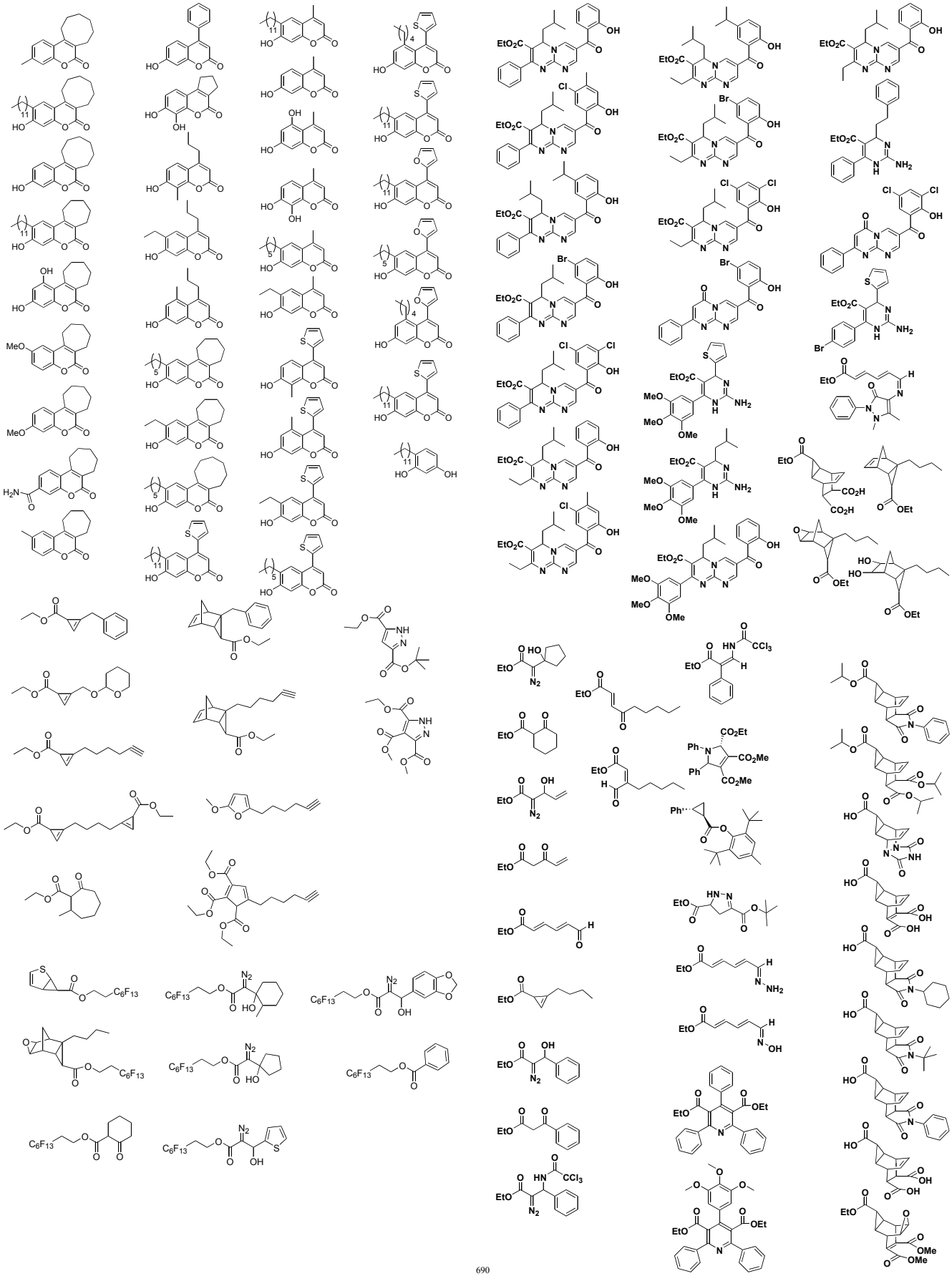


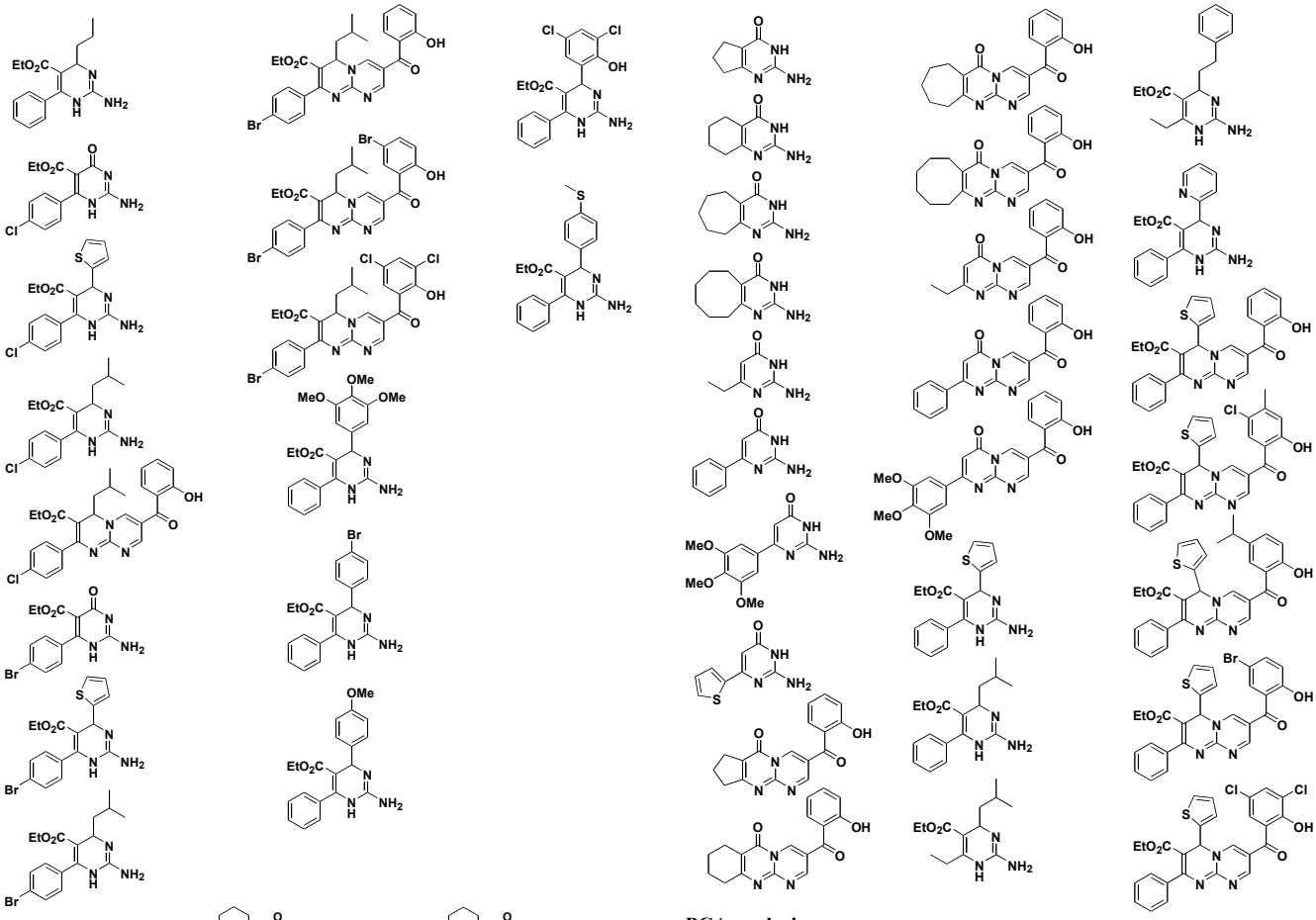
Molecular Frameworks Produced in the Library Synthesis:

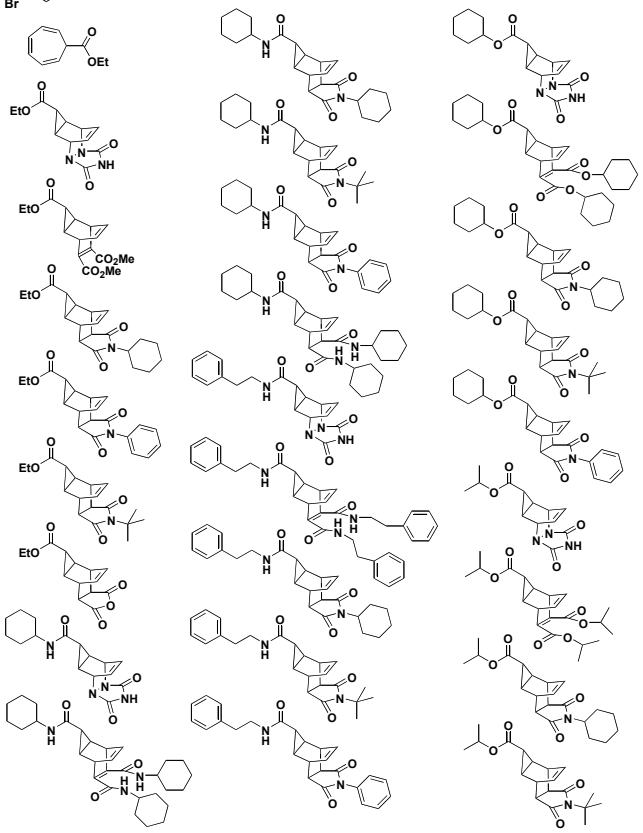


Compounds Produced in the Library Synthesis:







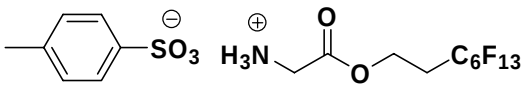


PCA analysis:

In order to assess the diversity of the small molecule collection, we calculated 184 physicochemical and topological molecular descriptors properties (e.g. size, polarity, charges, degree of branching) using MOE 2005.06 [MOE (Molecular Operating Environment); Chemical Computing Group Inc.: Montreal, Quebec, Canada]. Structures were washed (ionized to formal charge, acids and bases protonated according to neutral pH) and PEOE partial charges [J. Gasteiger and M. Marsili, Tetrahedron Lett. 1978, 34, 3181-3184.] were assigned for the calculation of descriptors involving partial surface charges. Subsequently, principal component analysis (PCA) of the resulting property space was performed for visualization and numerical diversity estimation using Statistica 6 [StatSoft, Inc. 2001. STATISTICA (data analysis software system), version 6. www.statsoft.com. Distributor: StatSoft Inc., Tulsa, OK.]. Numerical diversity values were calculated as the product of the standard deviations of the first three principal components, which gives an estimate of the average size of chemical space occupied per compound in this representation. To gauge the degree of overall diversity obtained in our diversity–oriented synthesis we compared the diversity of our library to the chemical space spanned by 'benchmark collections': (1) the MDL Drug Data Report (MDDR) database [MDL Drug Data Report, Elsevier MDL, http://www.mdli.com] and (2) a focused library of histamine H3 receptor antagonists (where a common biphenyl scaffold was functionalized at two positions) [R. Faghih, W. Dwight, J. Bao Pan, G. B. Fox, K. M. Krueger, T.

A. Esbenshade, J. M. McVey, K. Marsh, Y. L. Bennani and A. A. Hancock, Bioorg. Med. Chem. Lett. 2003, 13, 1325-1328.].

Library diversity can be described as the standard deviation of properties in this PCA space, normalized to a per-compound-basis. Normalization to give a value of 100% for the most diverse library (MDDR) gives values of 40% for the DOS library and 3% for the focused library. Therefore, employing the quantitative measure developed here we can compare directly the diversity of compound collections, and assess the relative success of any diversity–oriented synthesis. It should be noted that the PCA plot shows a projection of whole-molecule physicochemical and topological molecular descriptors into 2-D space, and perhaps does not reward appropriately the synthesis of diverse and complex molecular frameworks.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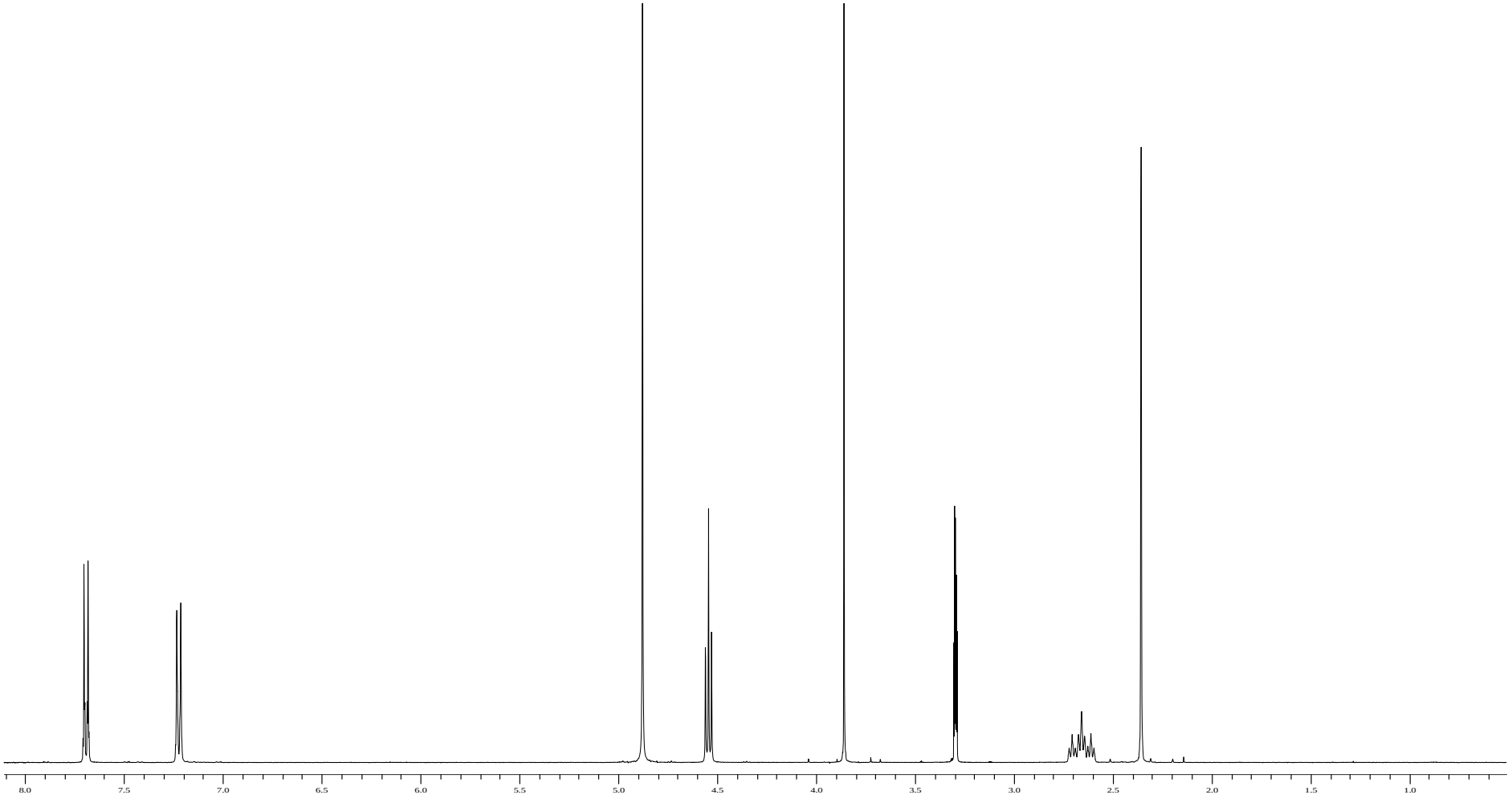
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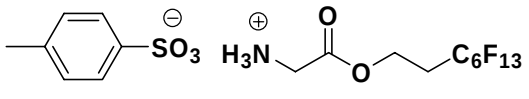
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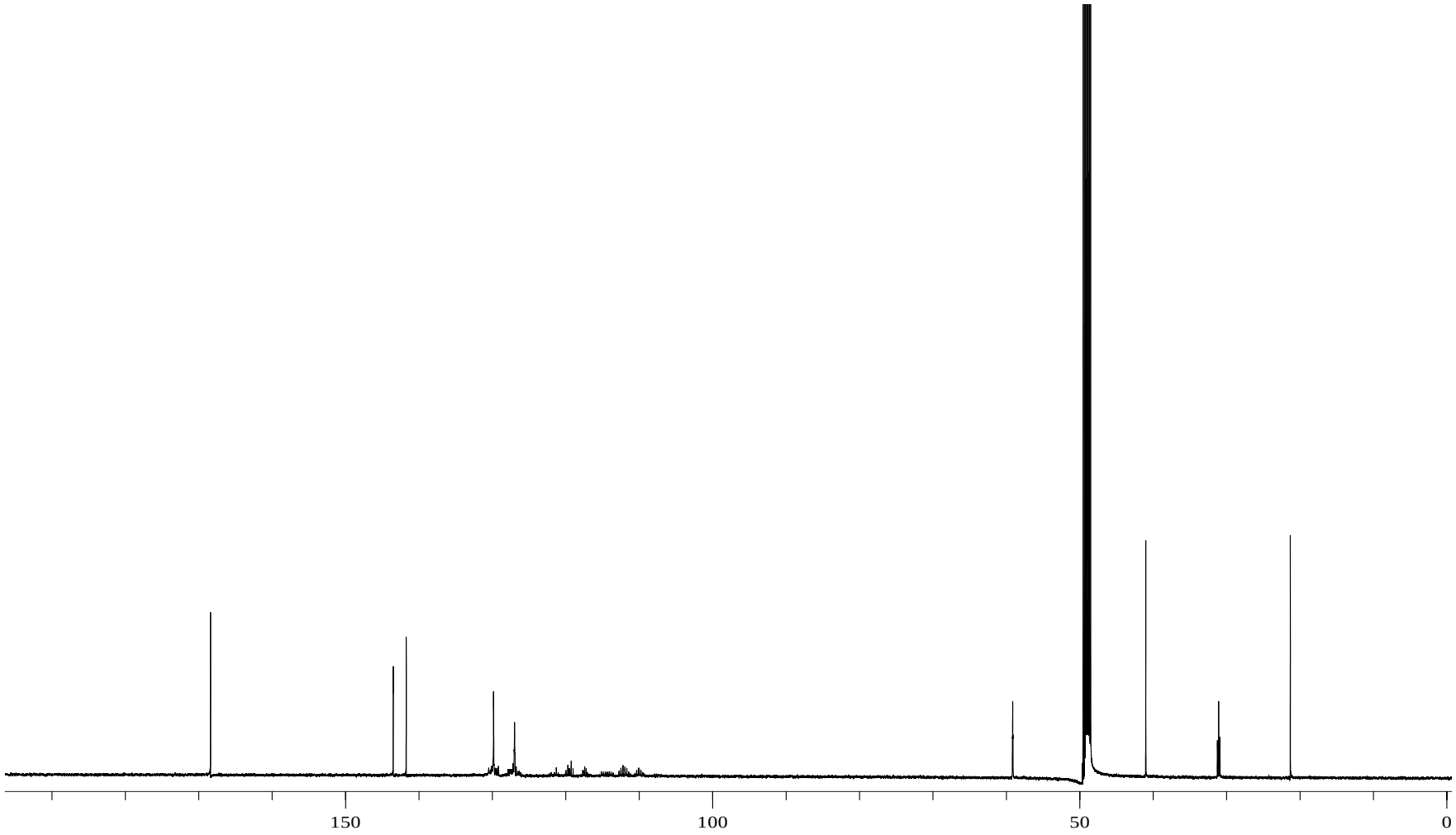
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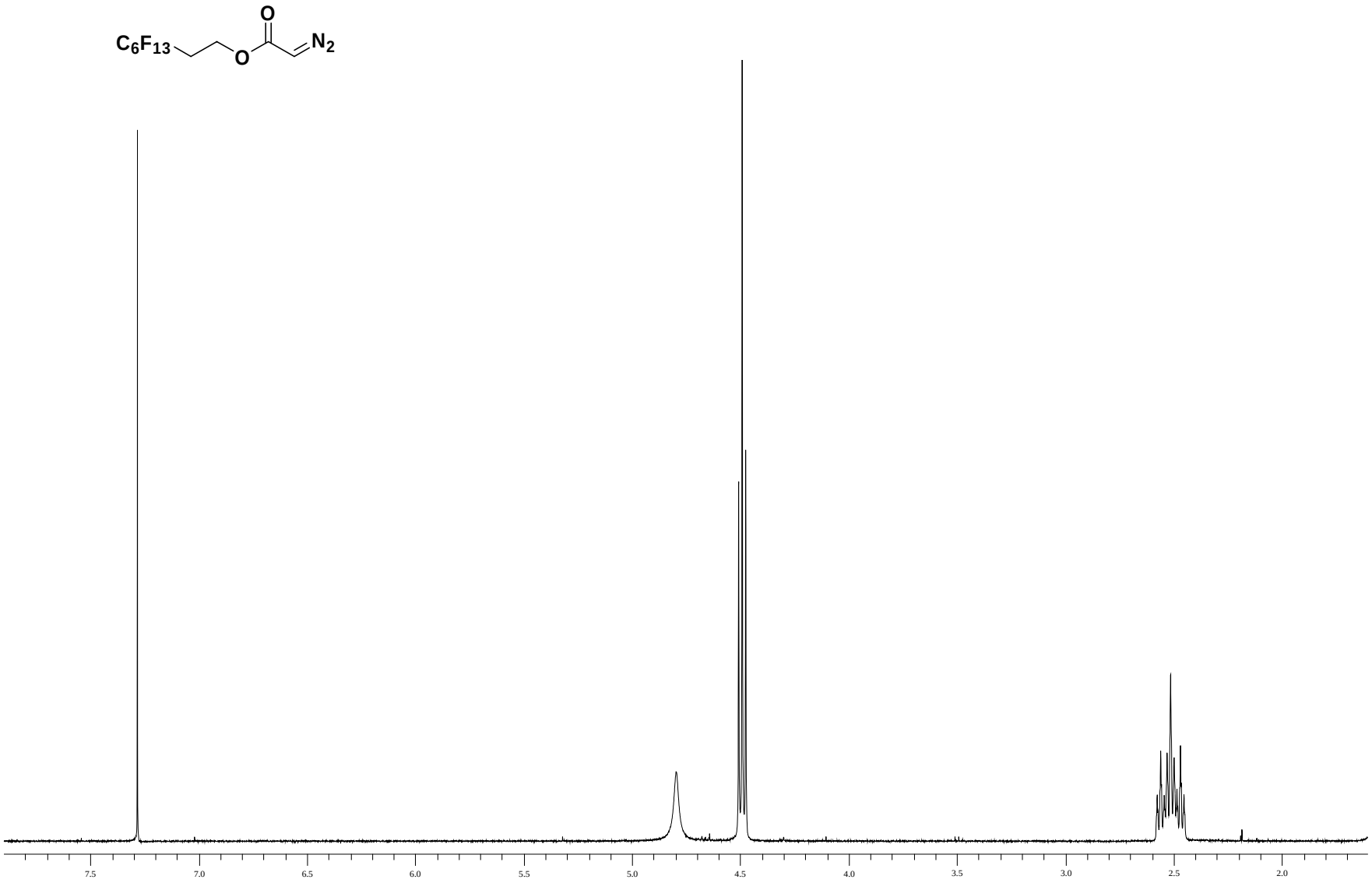
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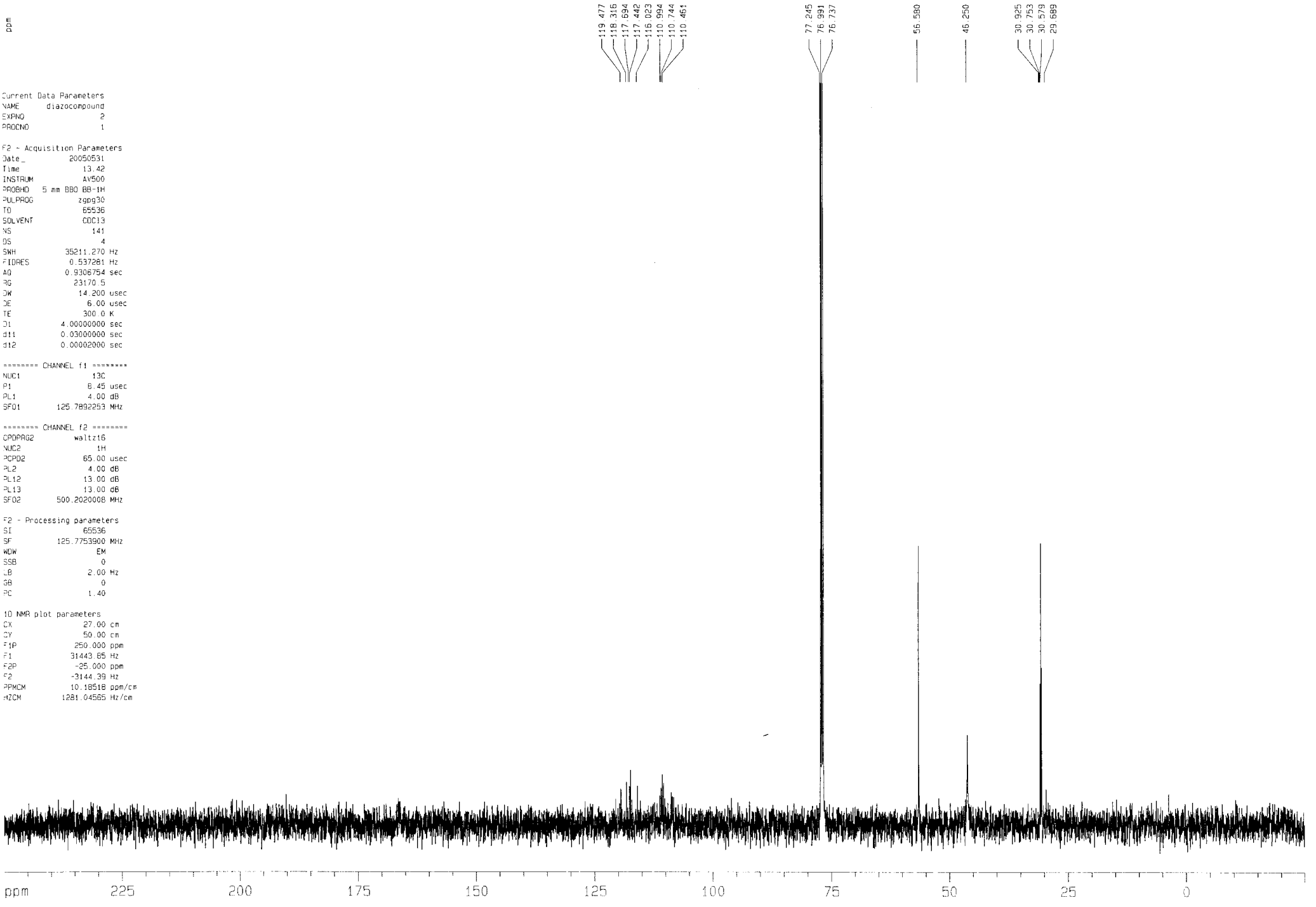

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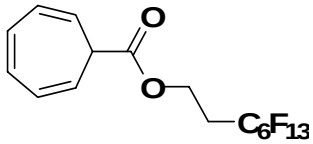
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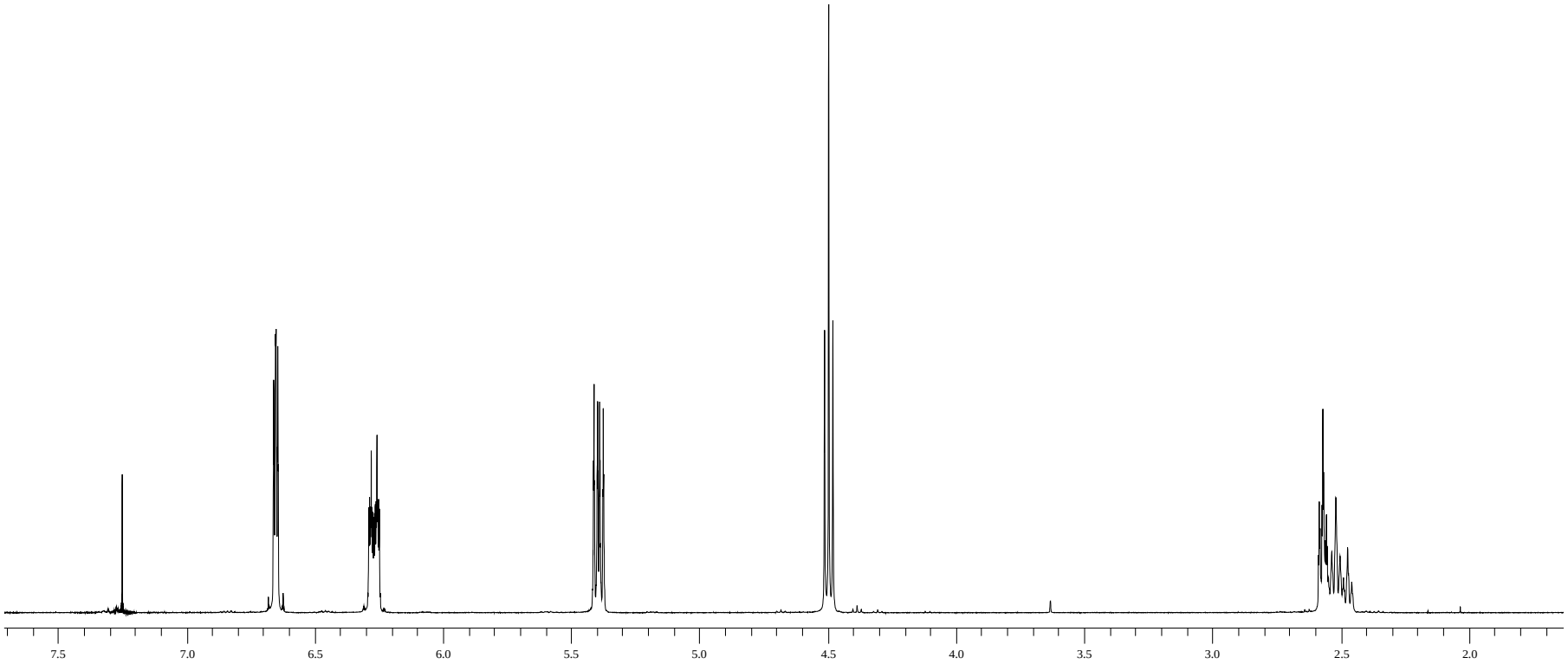
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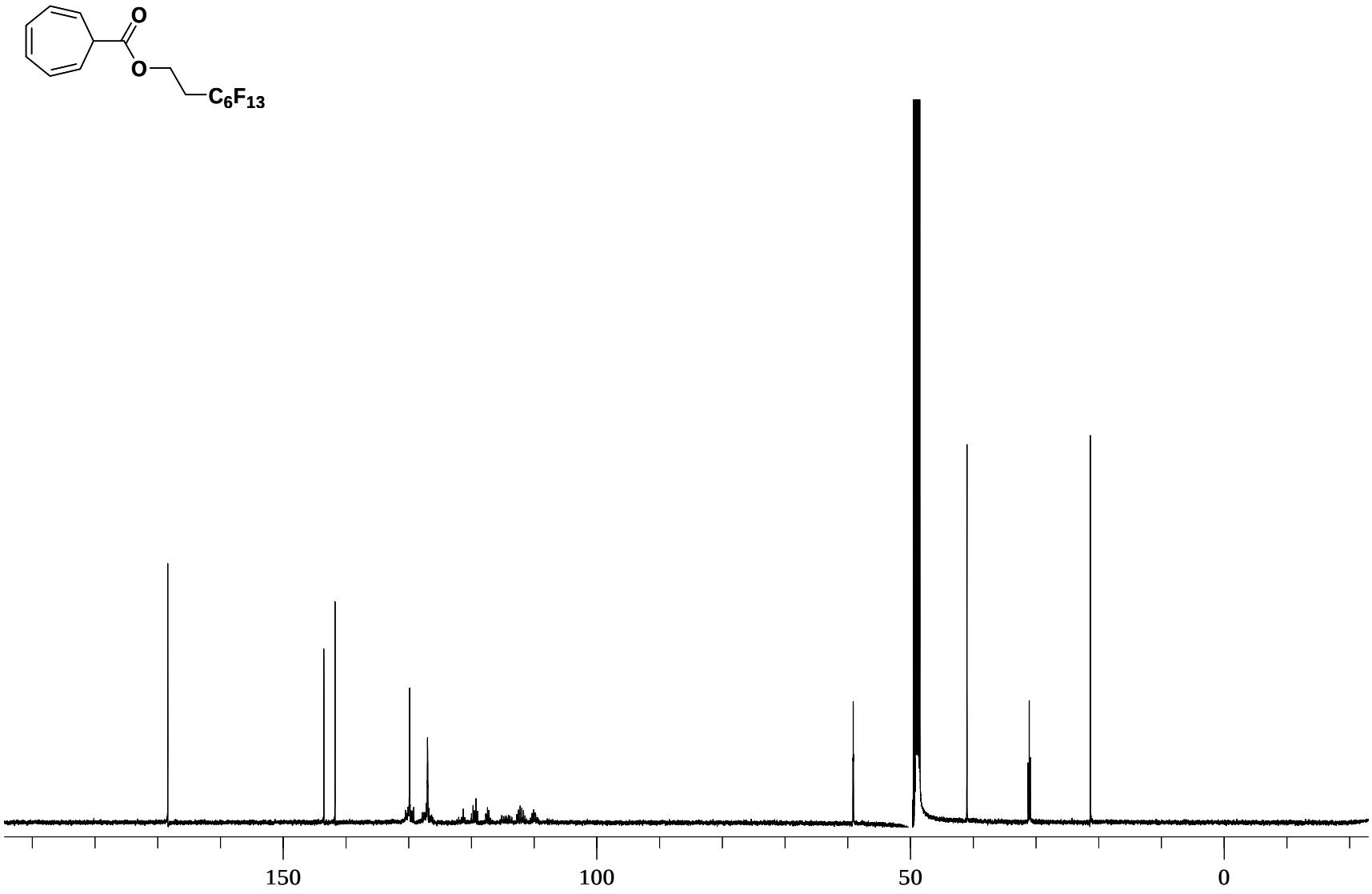
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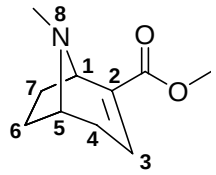
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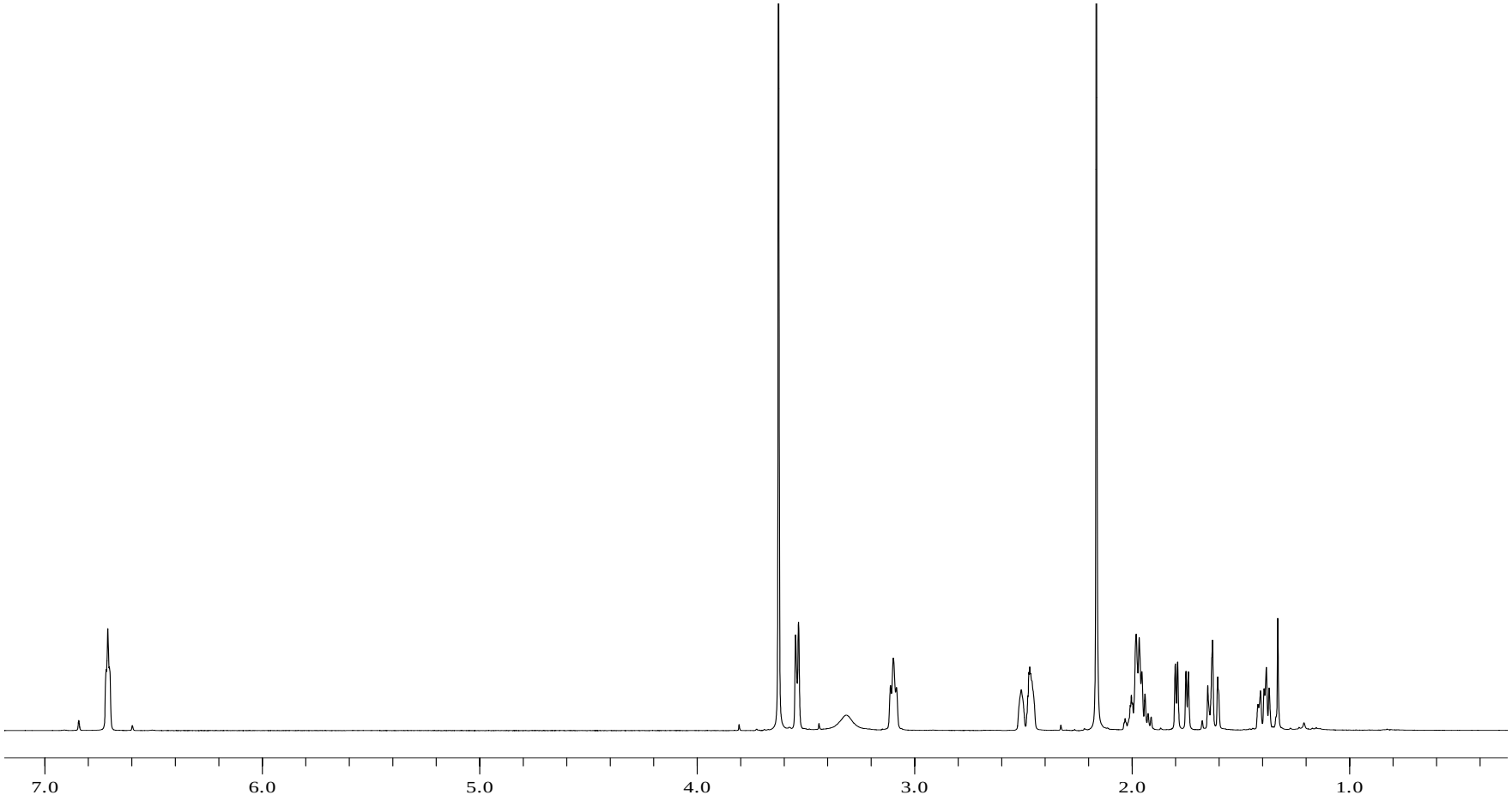
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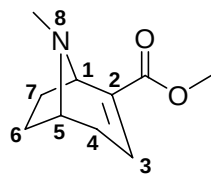
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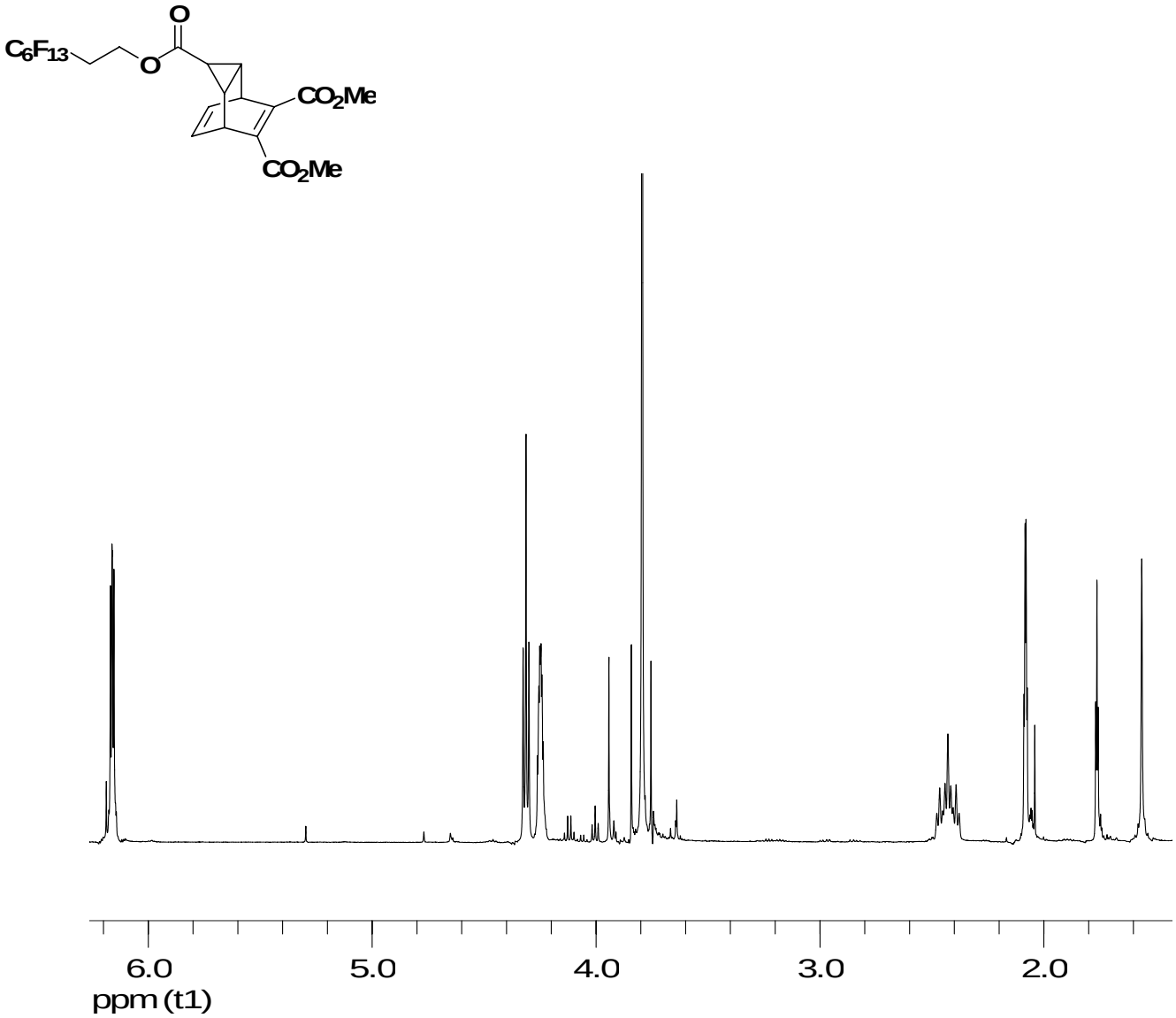
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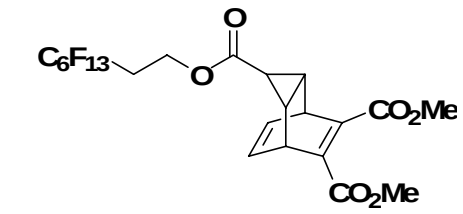
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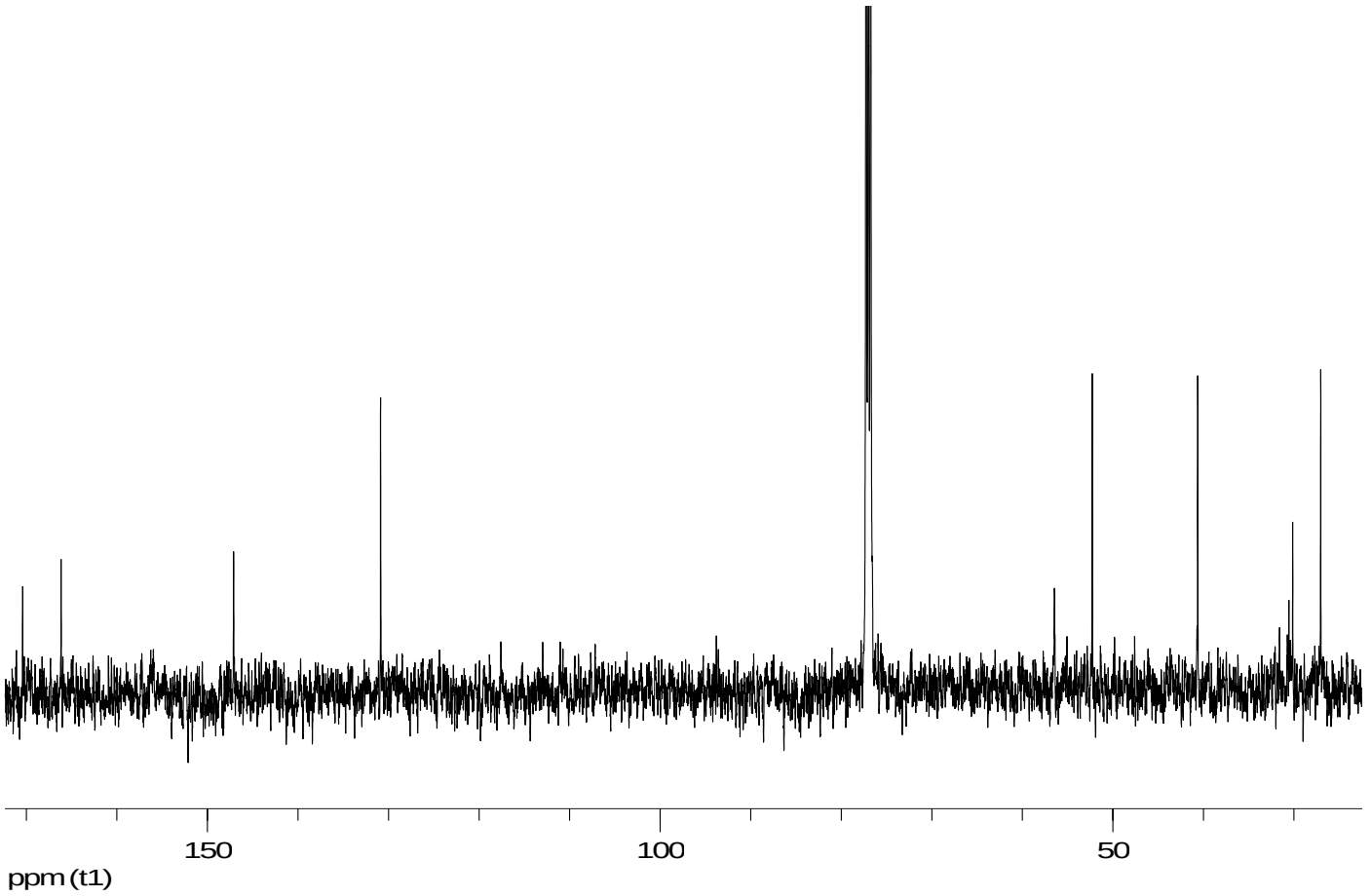
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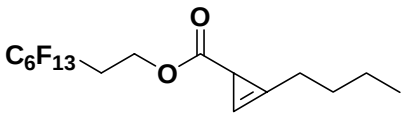
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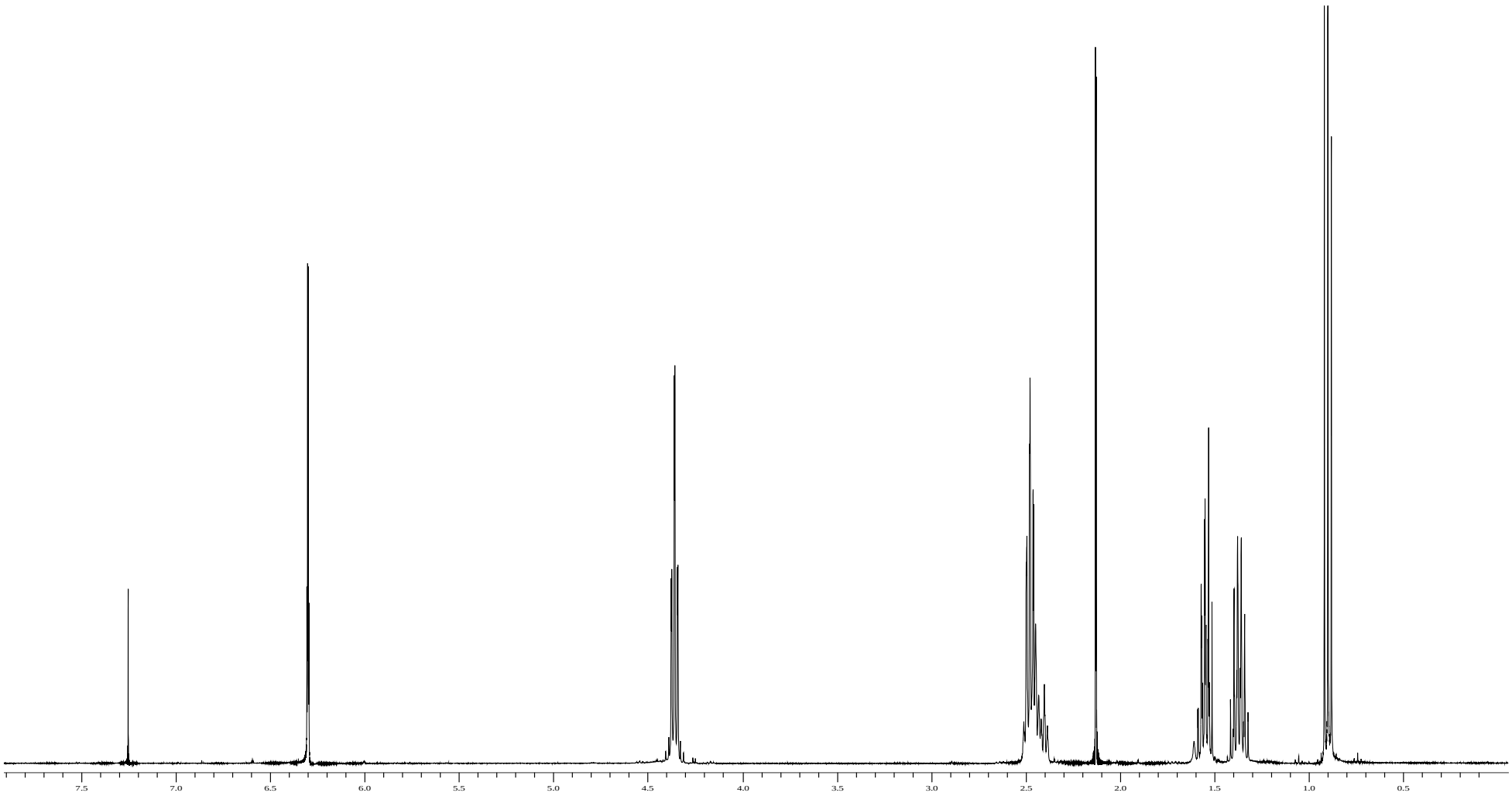
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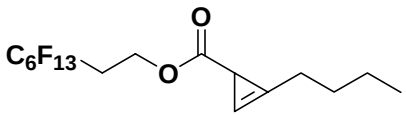
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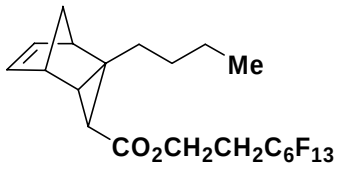
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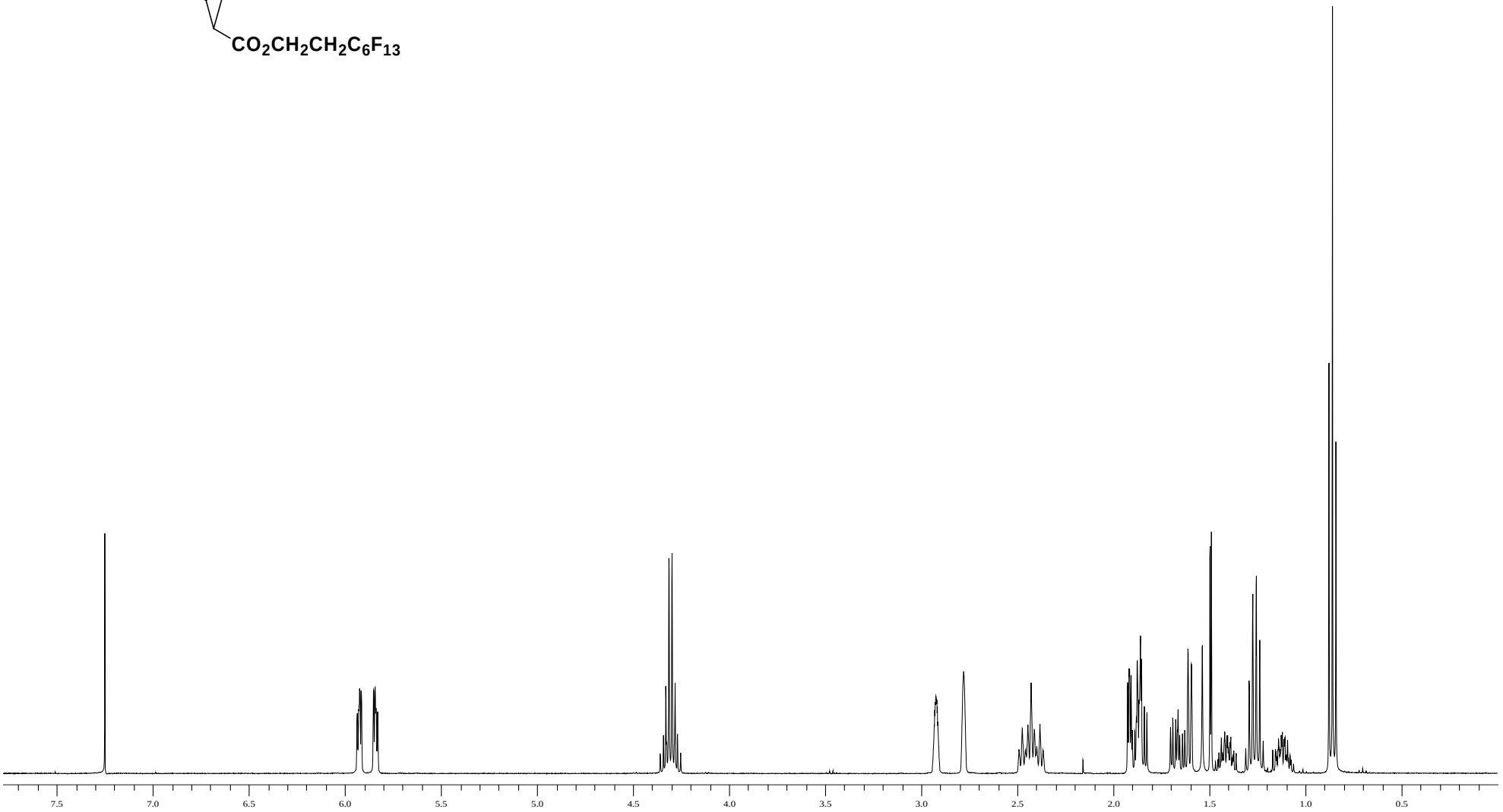
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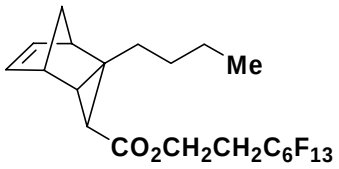
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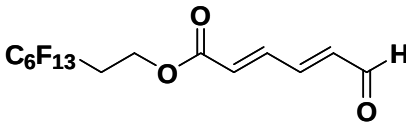
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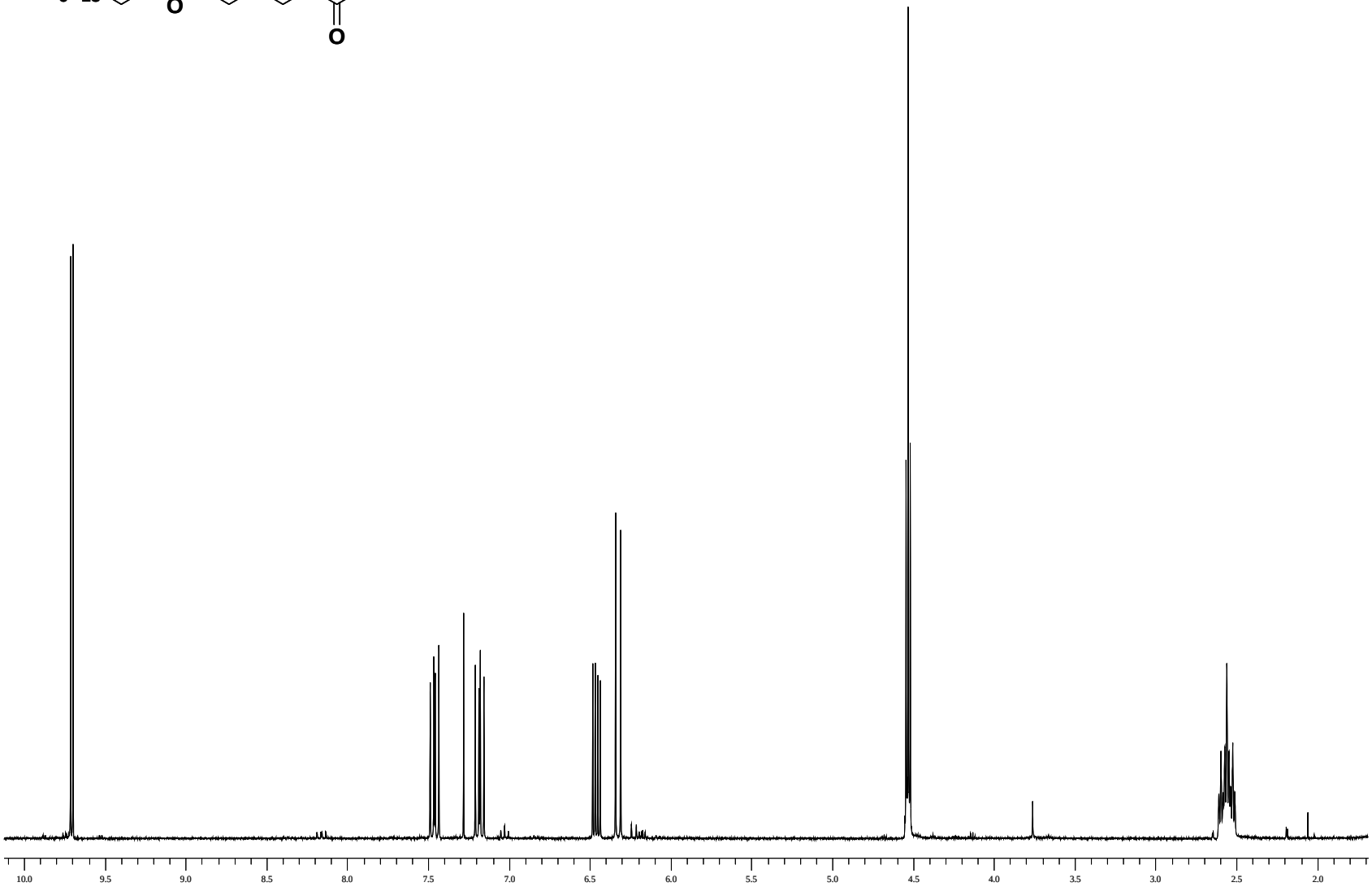
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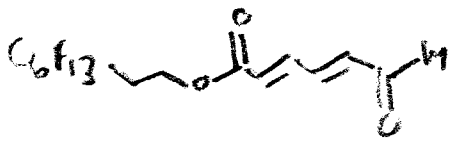
DW 14.200 usec
DE 6.00 usec
TE 300.0 K
D1 4.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec

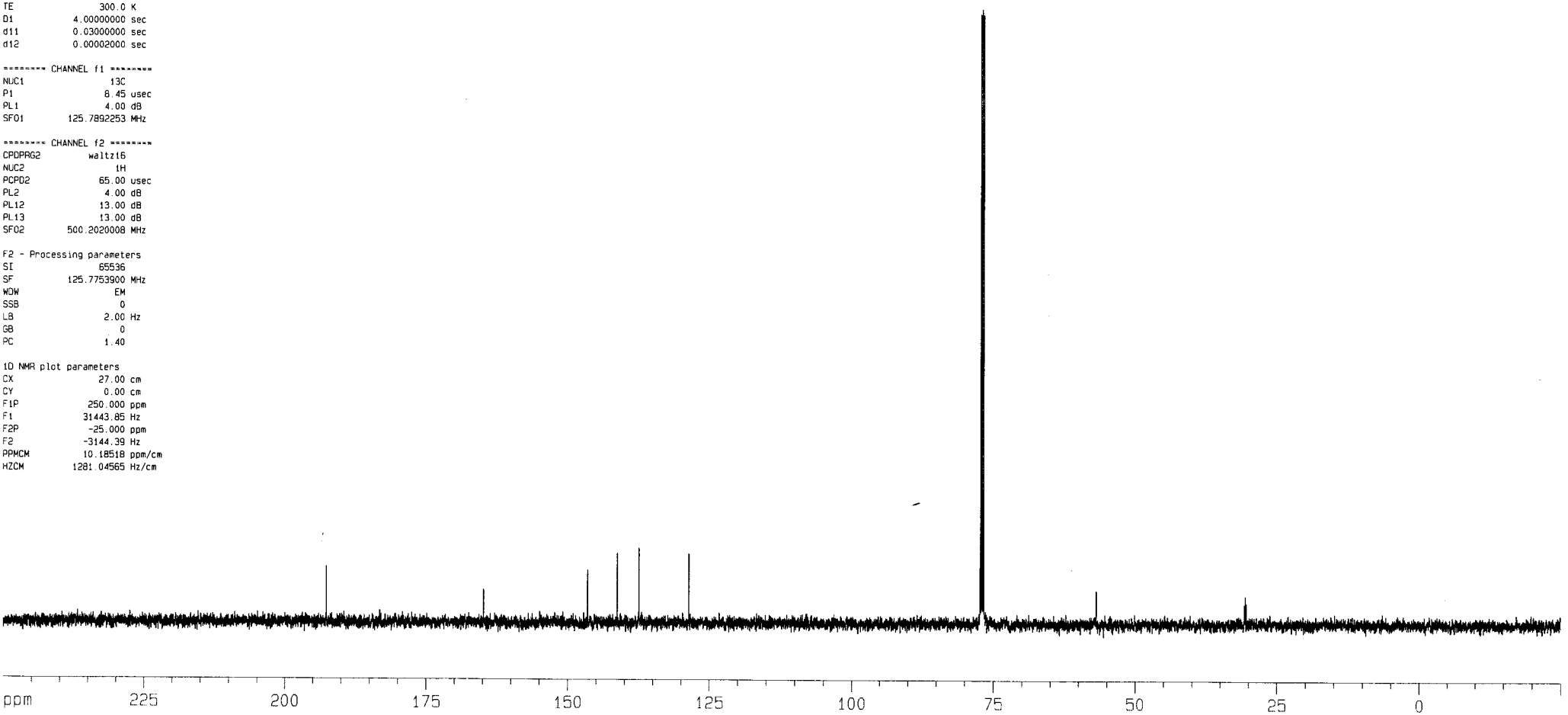
======== CHANNEL f1 ========
NUC1 13C
P1 8.45 usec
PL1 4.00 dB
SFO1 125.7892253 MHz

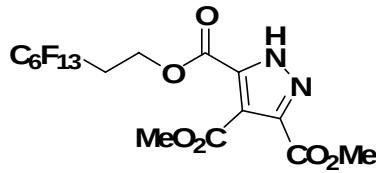
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 4.00 dB
PL12 13.00 dB
PL13 13.00 dB
SFO2 500.2020008 MHz

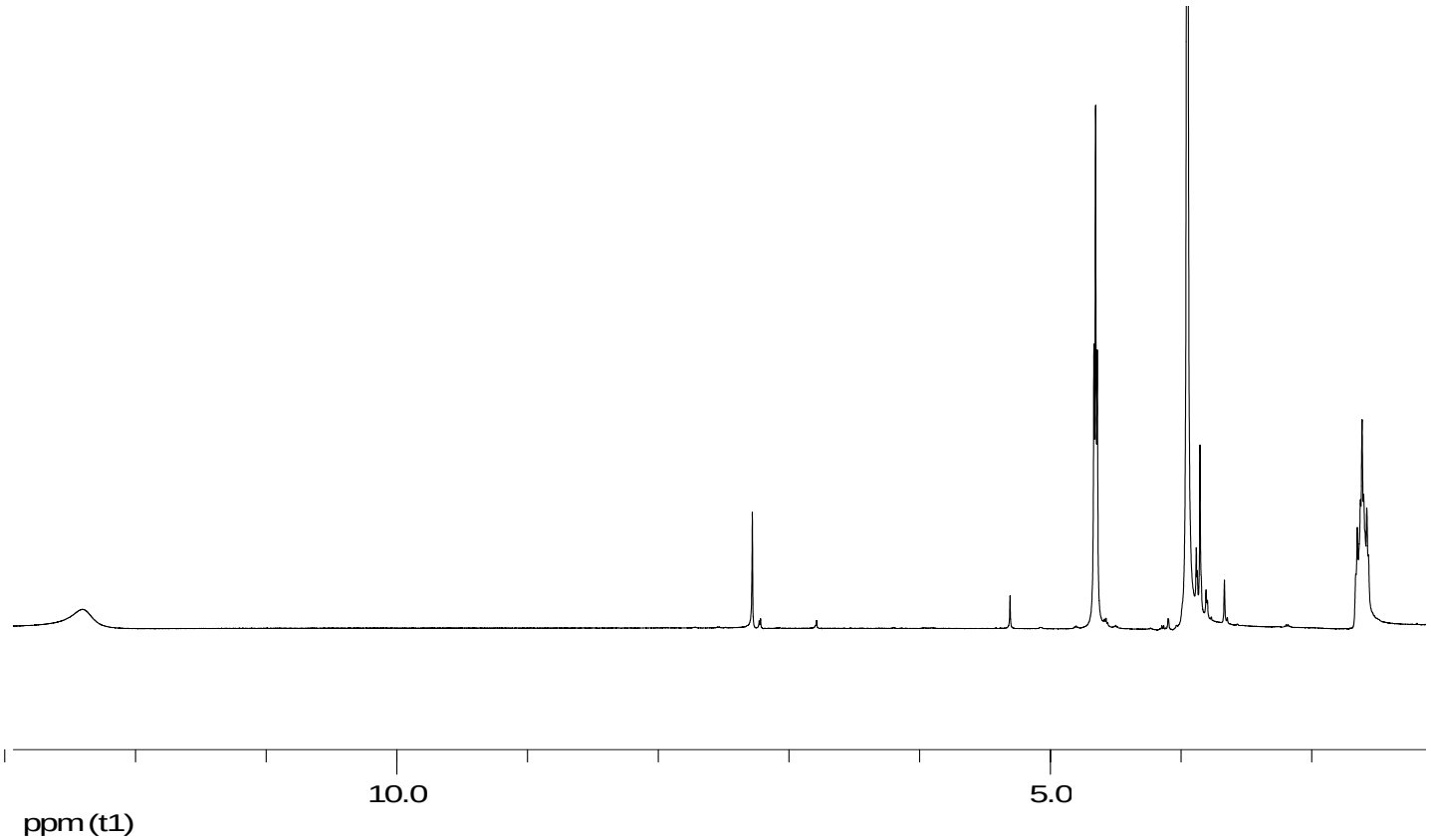
F2 - Processing parameters
SI 65536
SF 125.7753900 MHz
WDW EM
SSB 0
LB 2.00 Hz
GB 0
PC 1.40

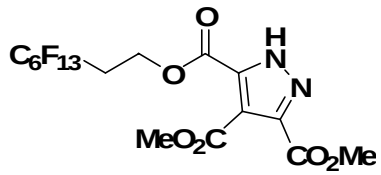
1D NMR plot parameters
CX 27.00 cm
CY 0.00 cm
F1P 250.000 ppm
F1 31443.85 Hz
F2P -25.000 ppm
F2 -3144.39 Hz
PPMCM 10.18518 ppm/cm
HZCM 1281.04565 Hz/cm

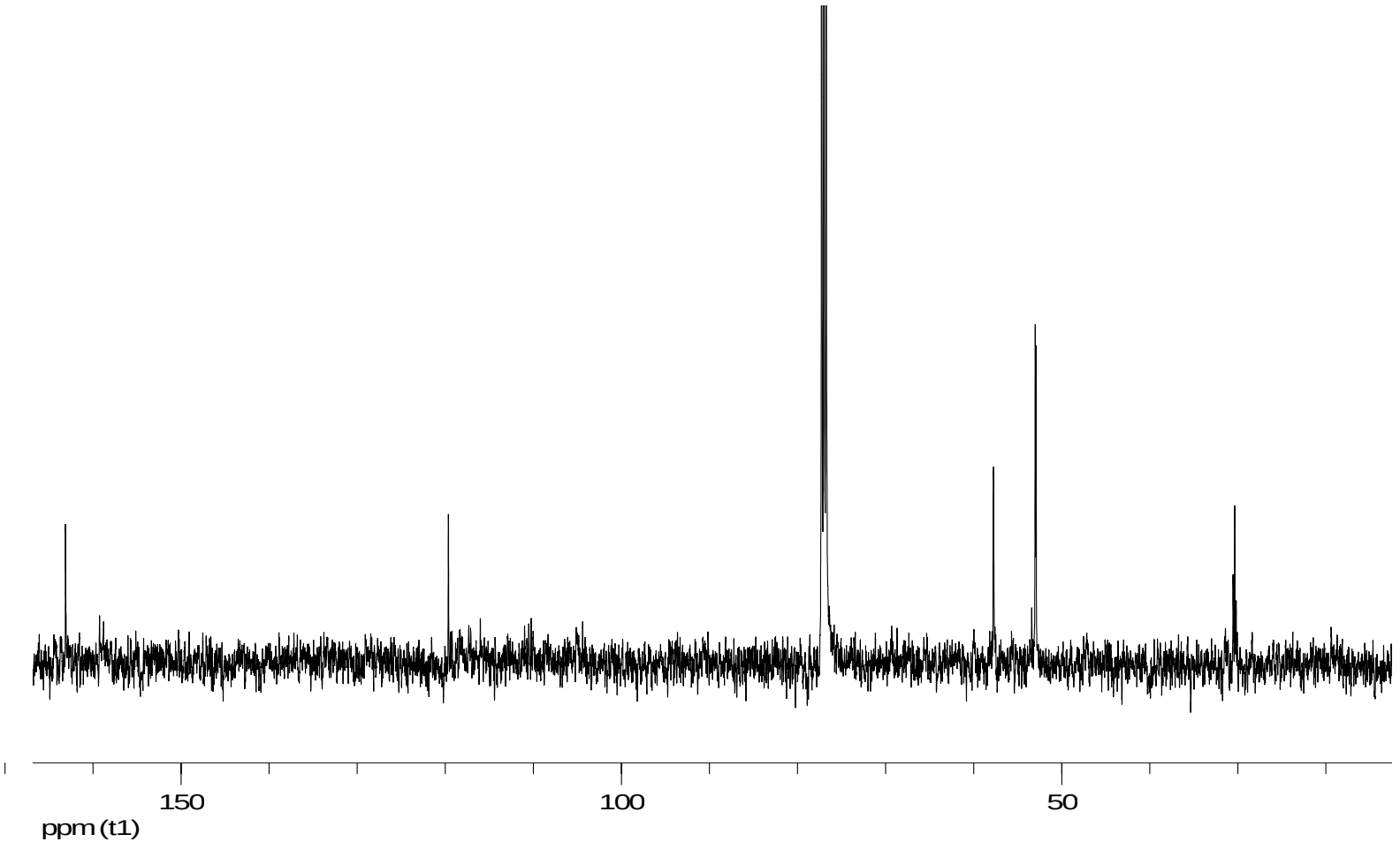


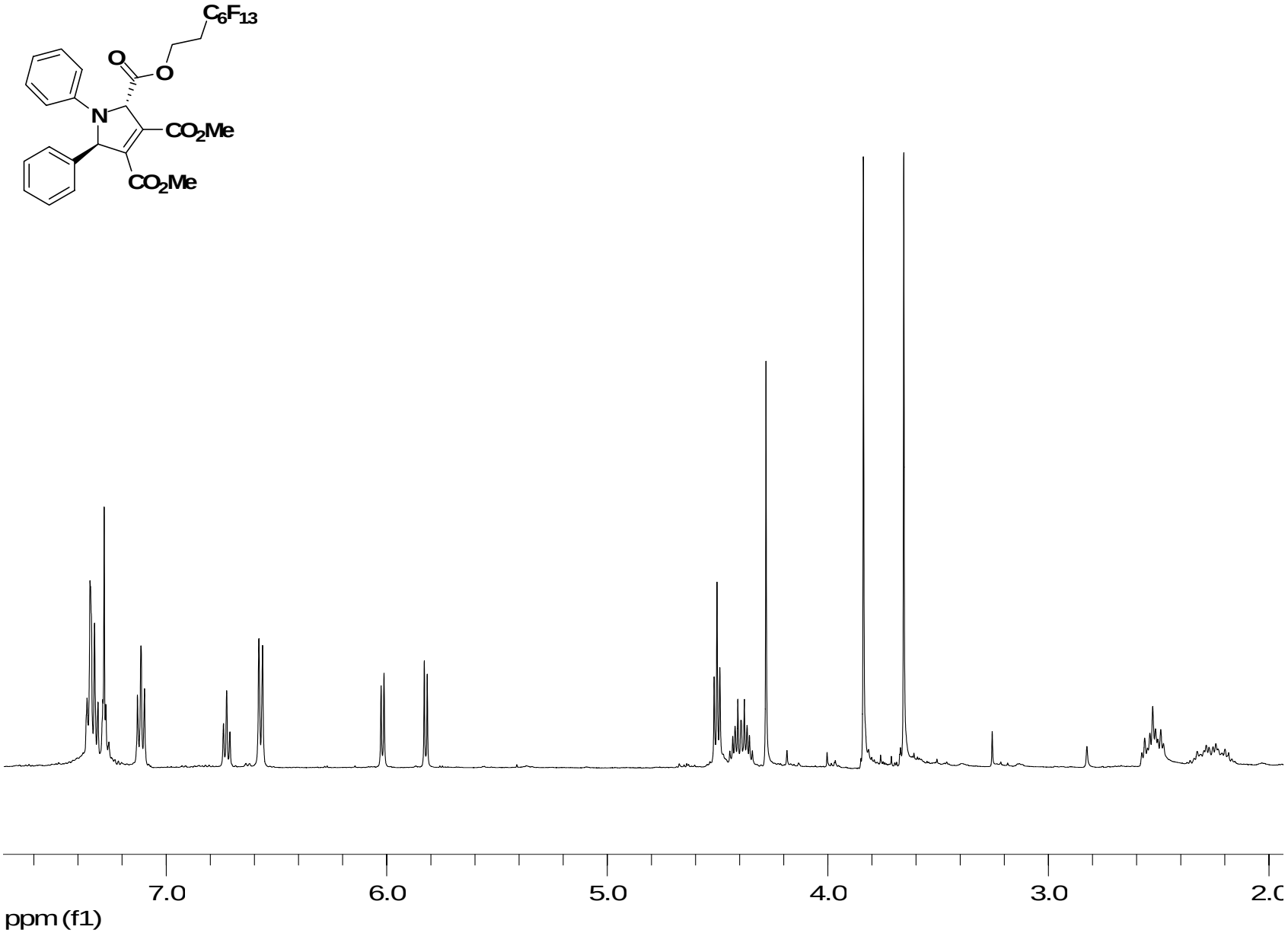


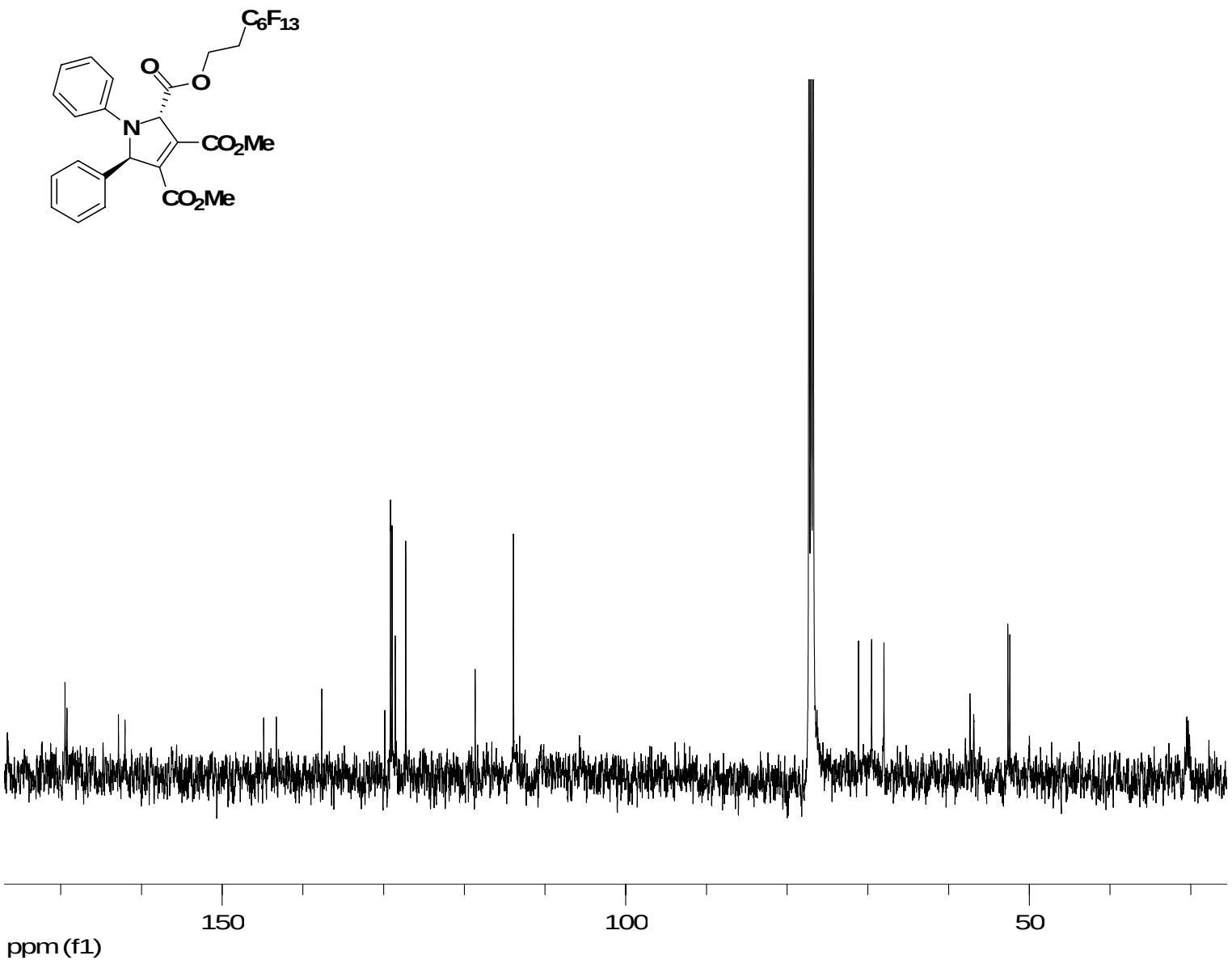

O
H
N
N
C6F13
O
MeO2C
CO2Me

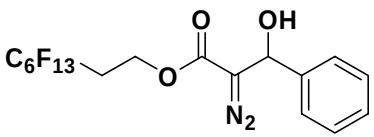

10.0
5.0
ppm (t1)

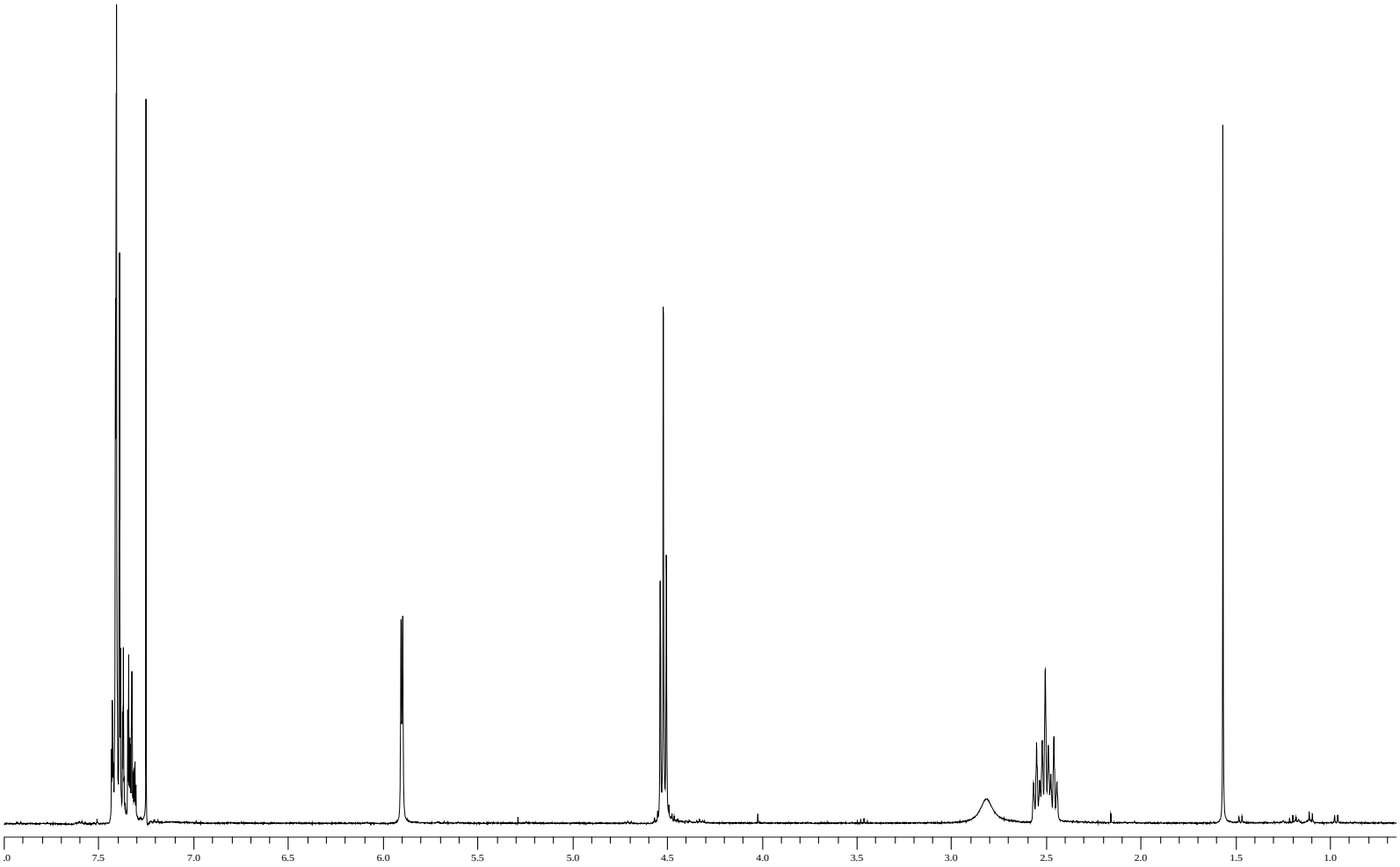

O
H
N
N
O
C6F13
MeO2C
CO2Me

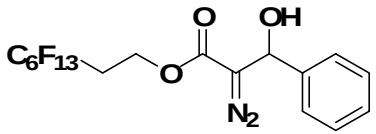

150
100
50
ppm (t1)

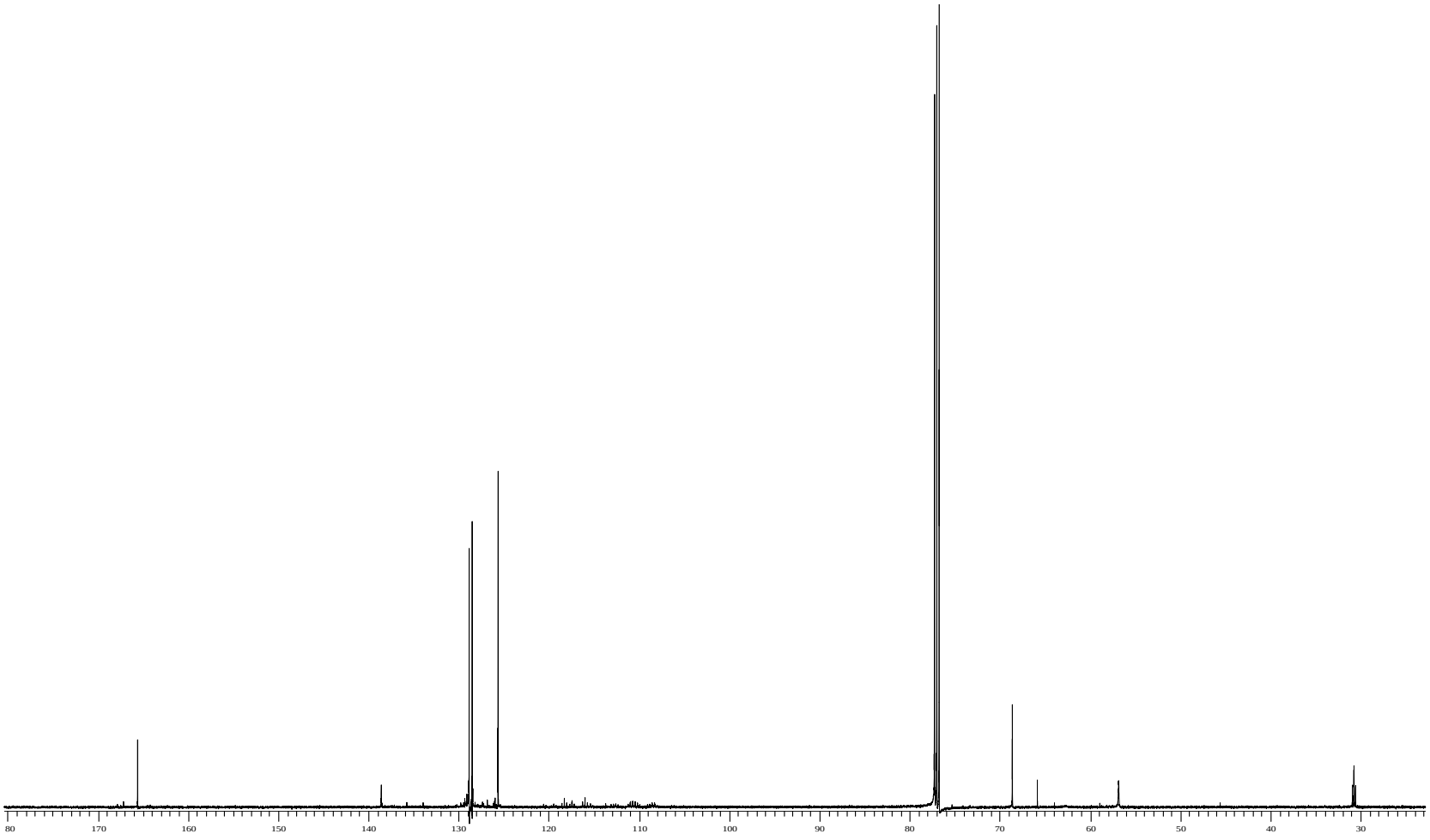

C6F13
O
O
N
CO2Me
CO2Me
7.0
6.0
5.0
4.0
3.0
2.0
ppm (f1)

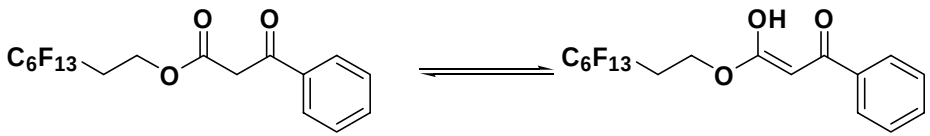

C6F13
O
O
N
CO2Me
CO2Me
150
100
50
ppm (f1)


O
OH
C6F13
O
N2

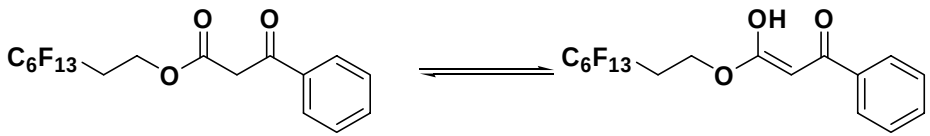

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0

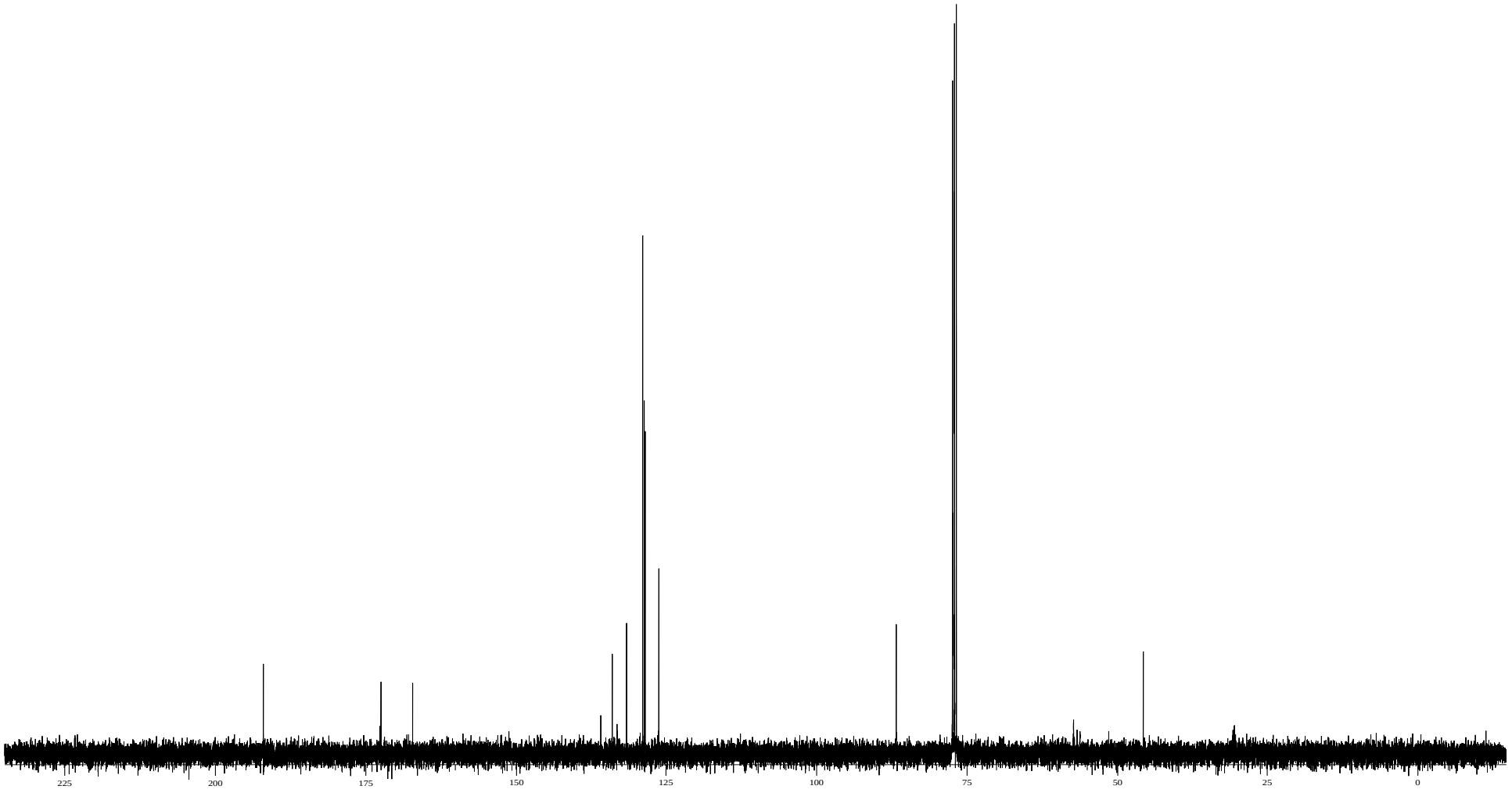

O
OH
C6F13
O
N2

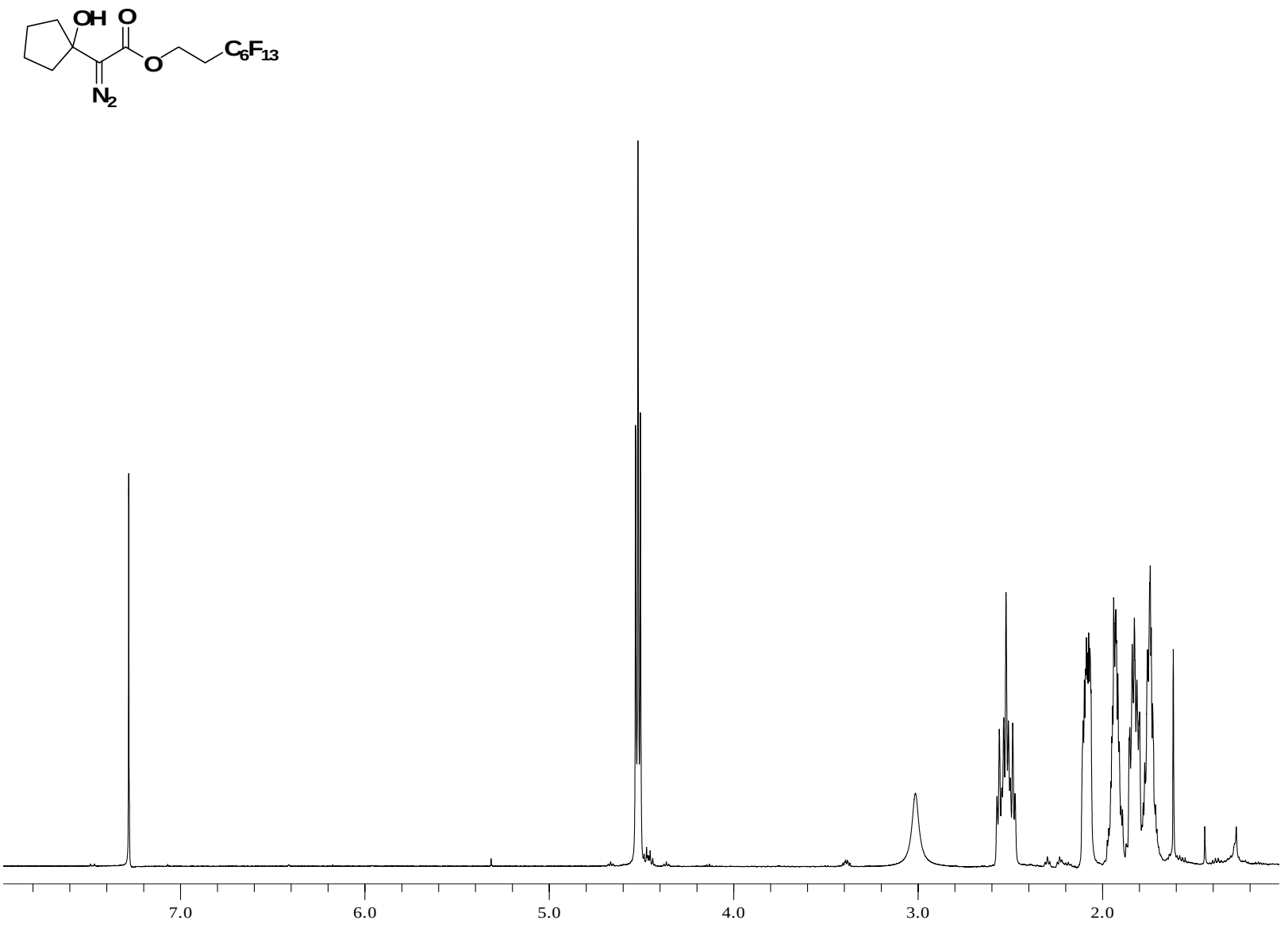

80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30

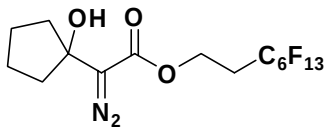

C6F13
O
O
O
C6F13
O
OH
O

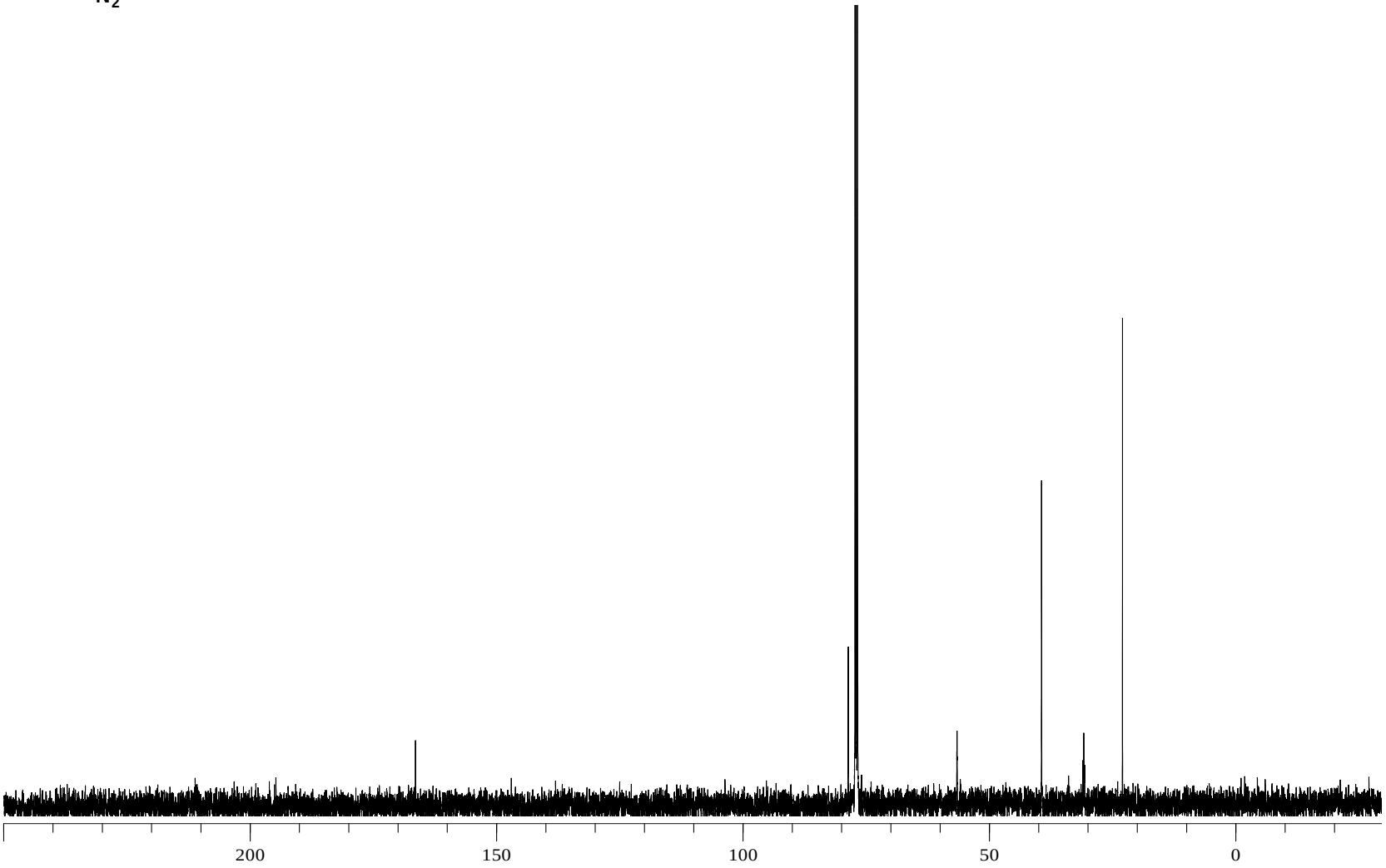
13
12
11
10
9
8
7
6
5
4
3
2

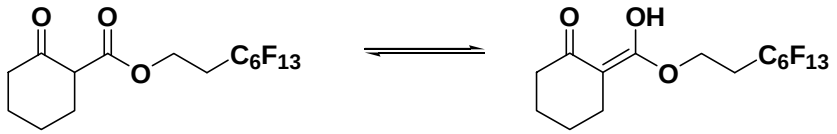

C6F13
O
O
O
C6F13
O
OH
O

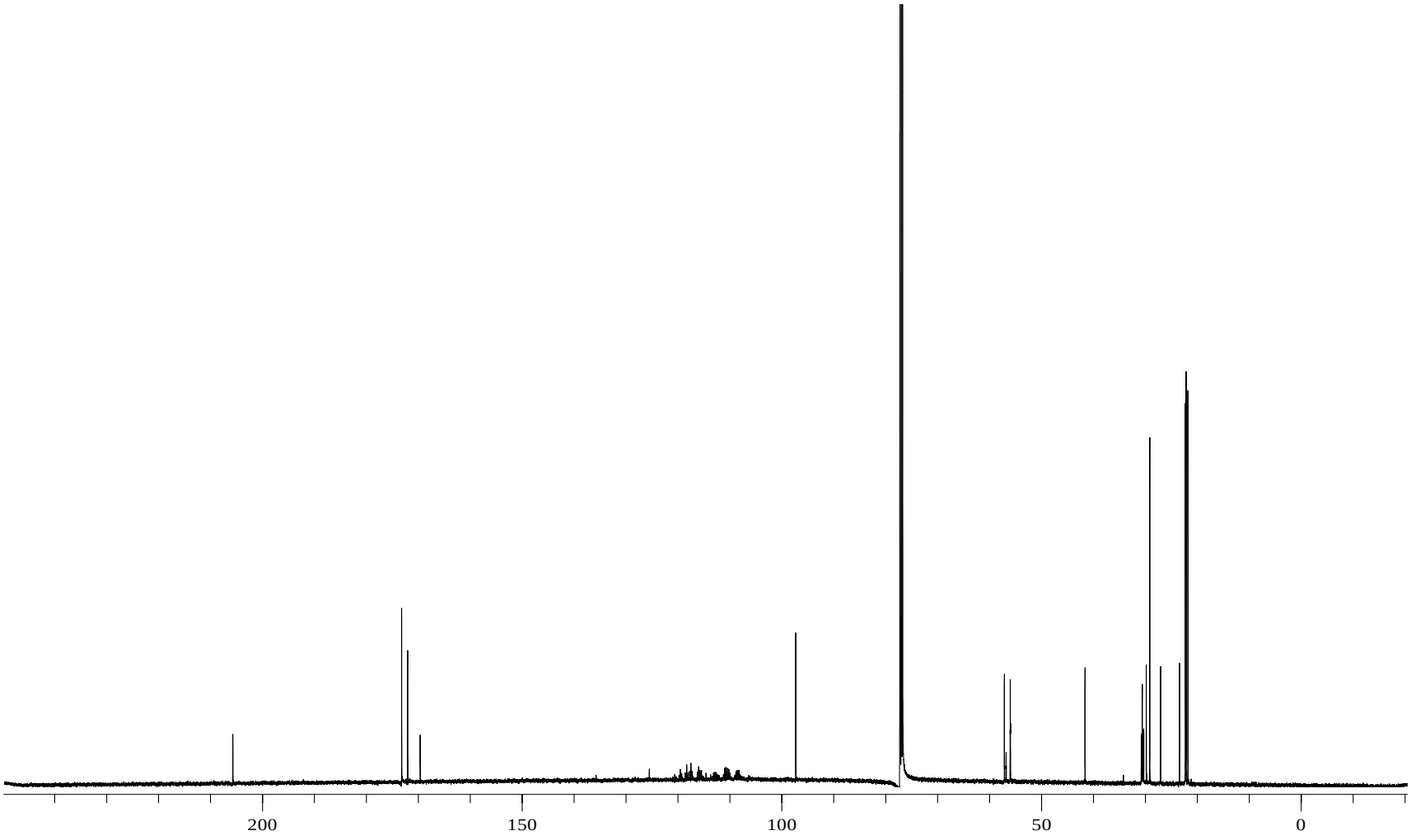

225
200
175
150
125
100
75
50
25
0

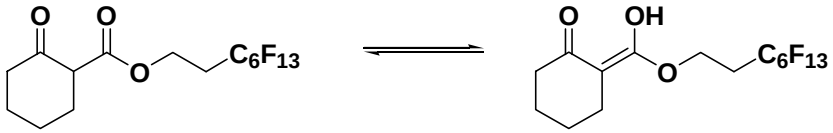

OH
O
O
C6F13
N2
7.0
6.0
5.0
4.0
3.0
2.0

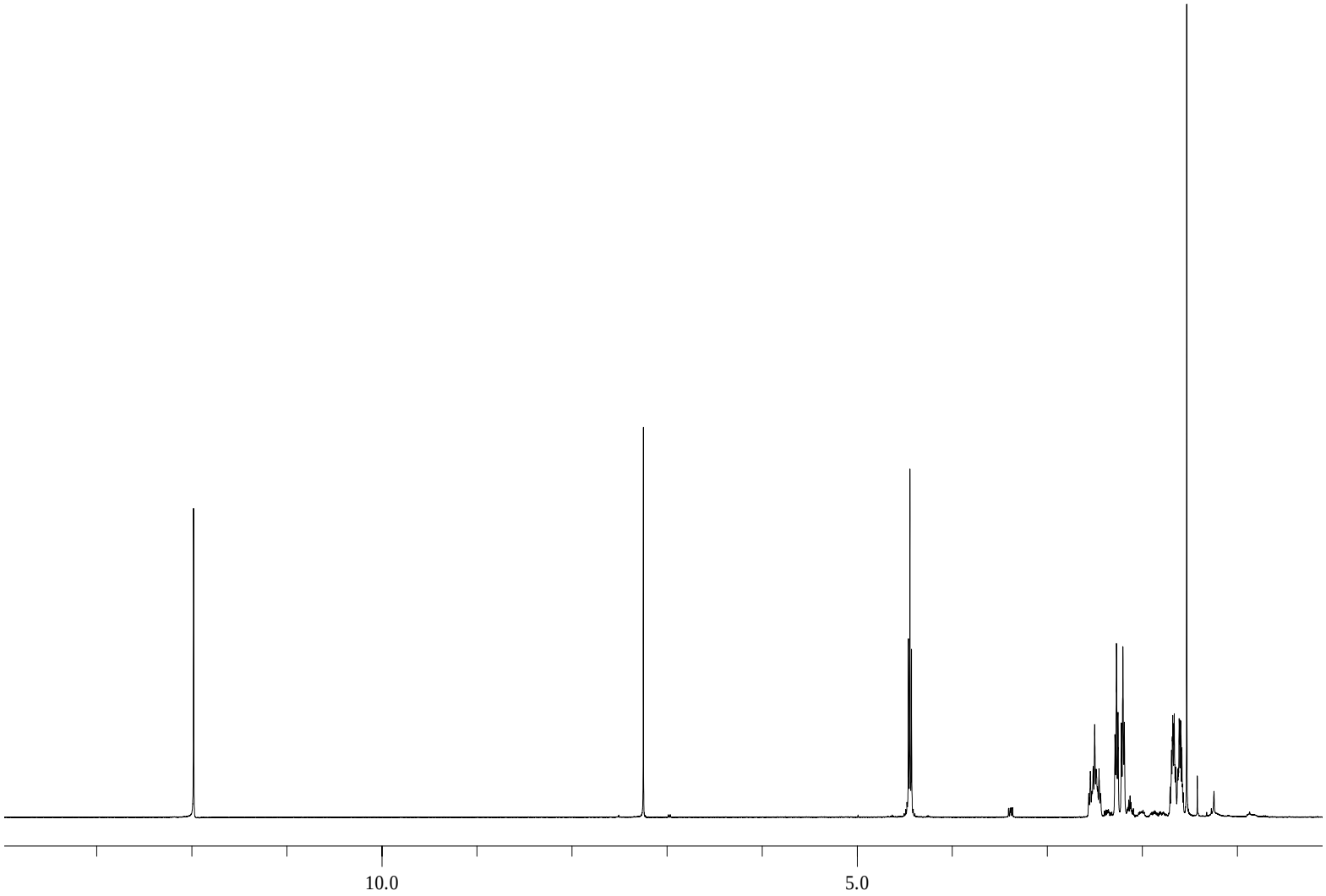

OH
O
O
C_6F_{13}
N_2

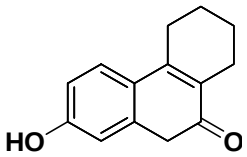

200
150
100
50
0

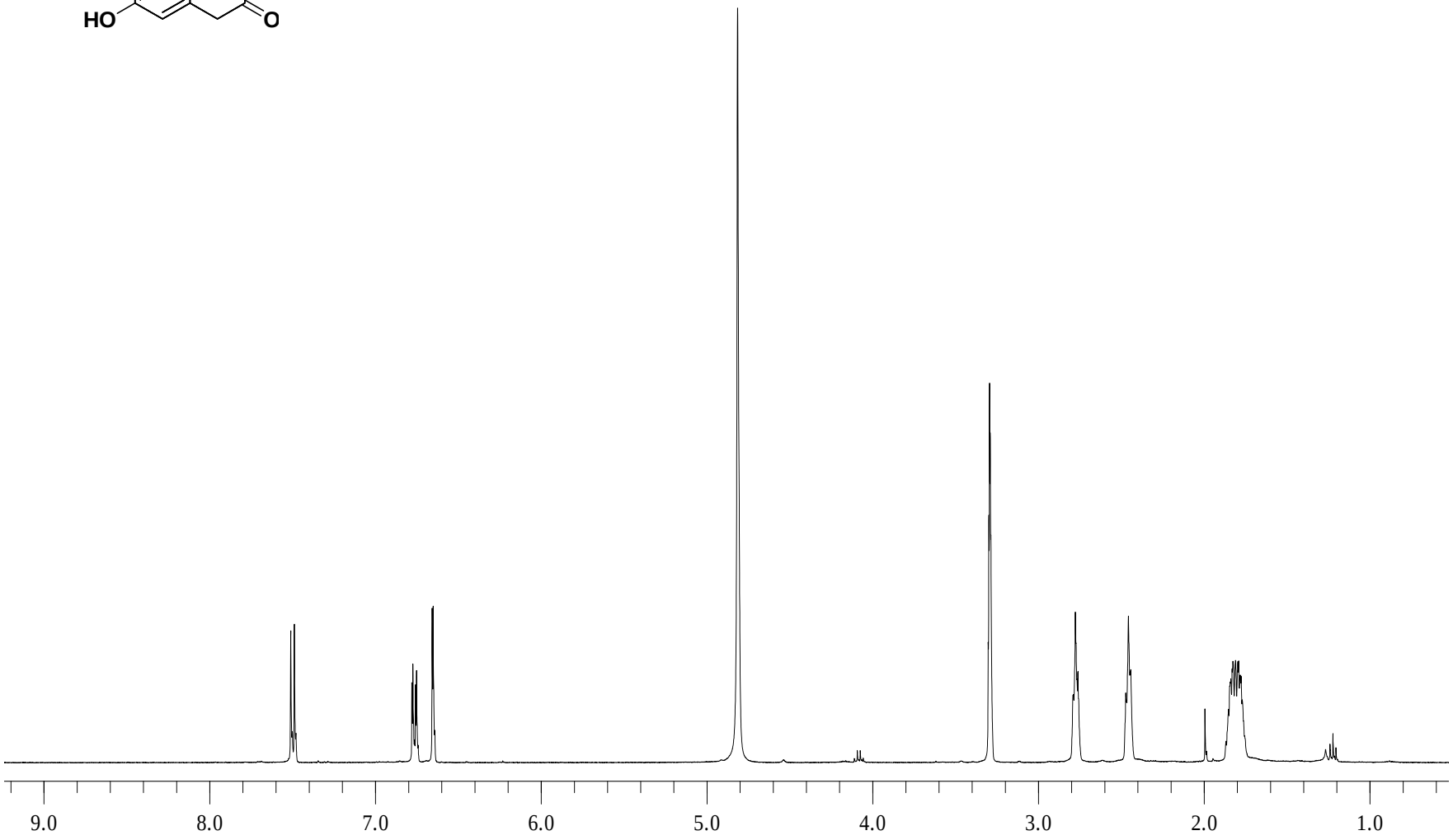

O
O
O
C6F13
O
OH
O
C6F13

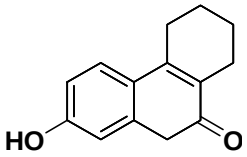

200
150
100
50
0

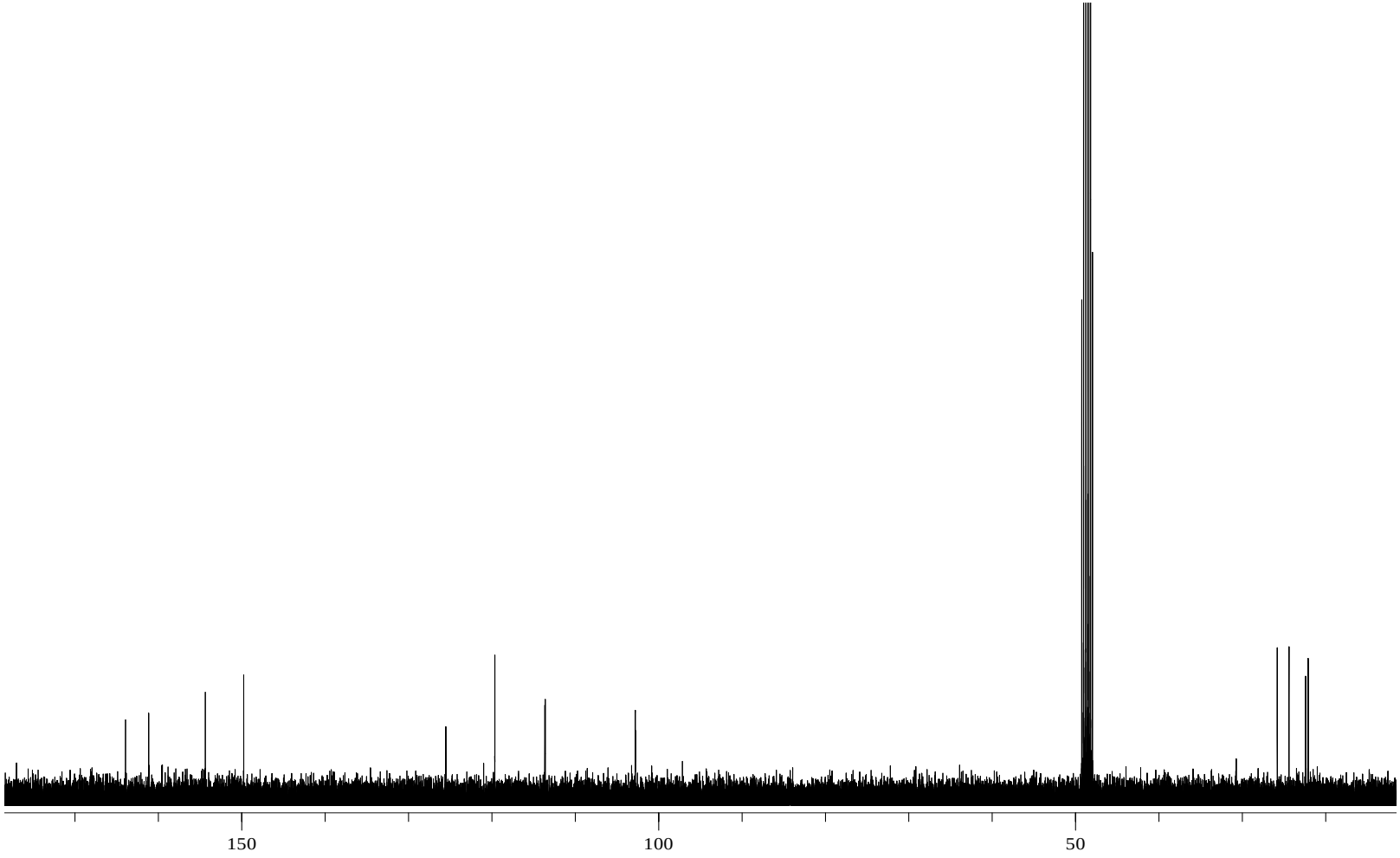

O
O
O
C6F13
O
OH
O
C6F13

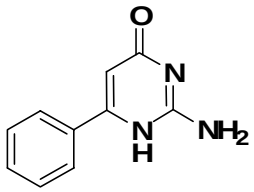

10.0
5.0

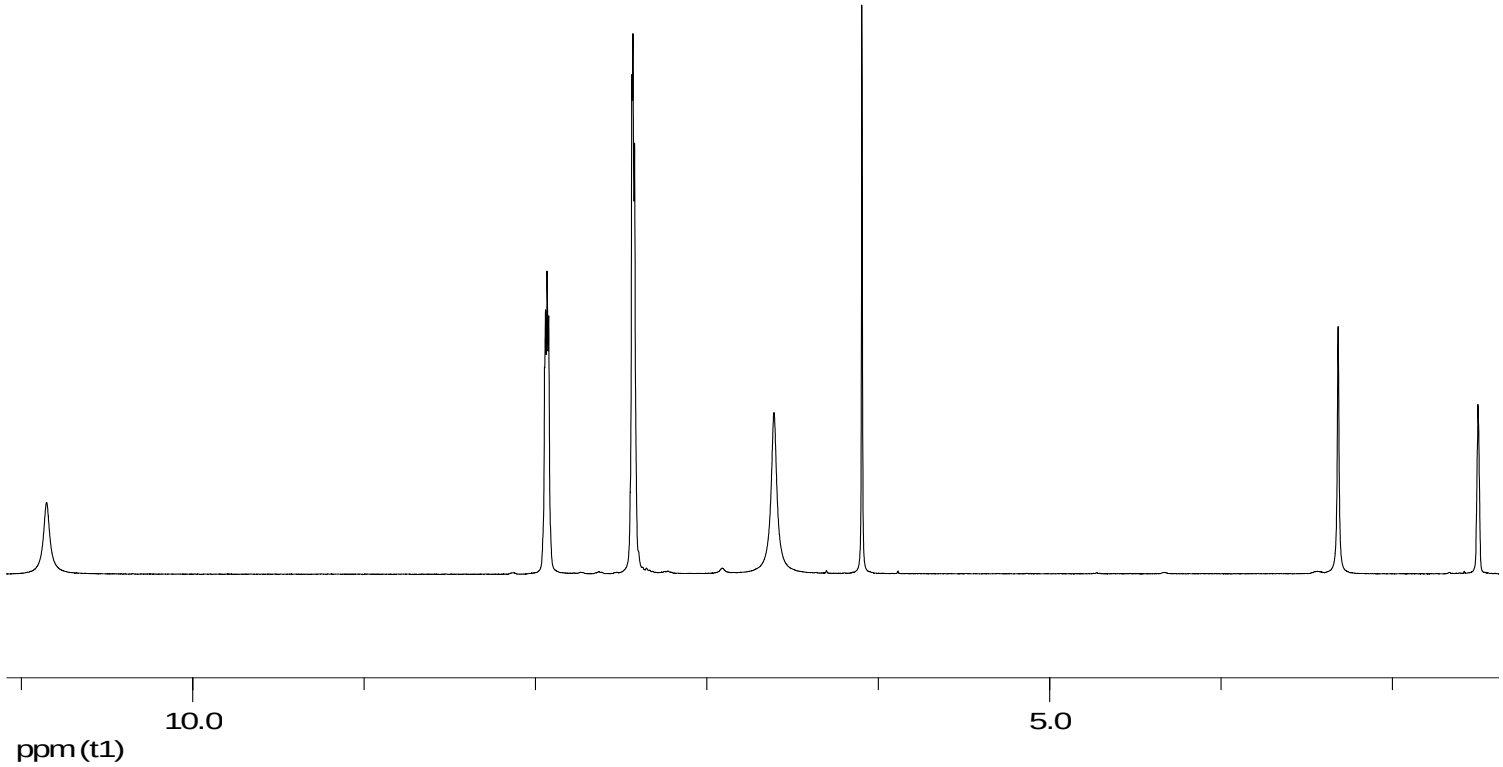

HO
O


9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0


HO
O


150
100
50


O
N
N
H
NH2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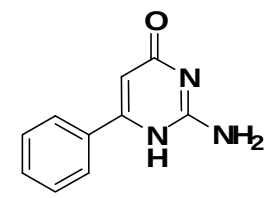
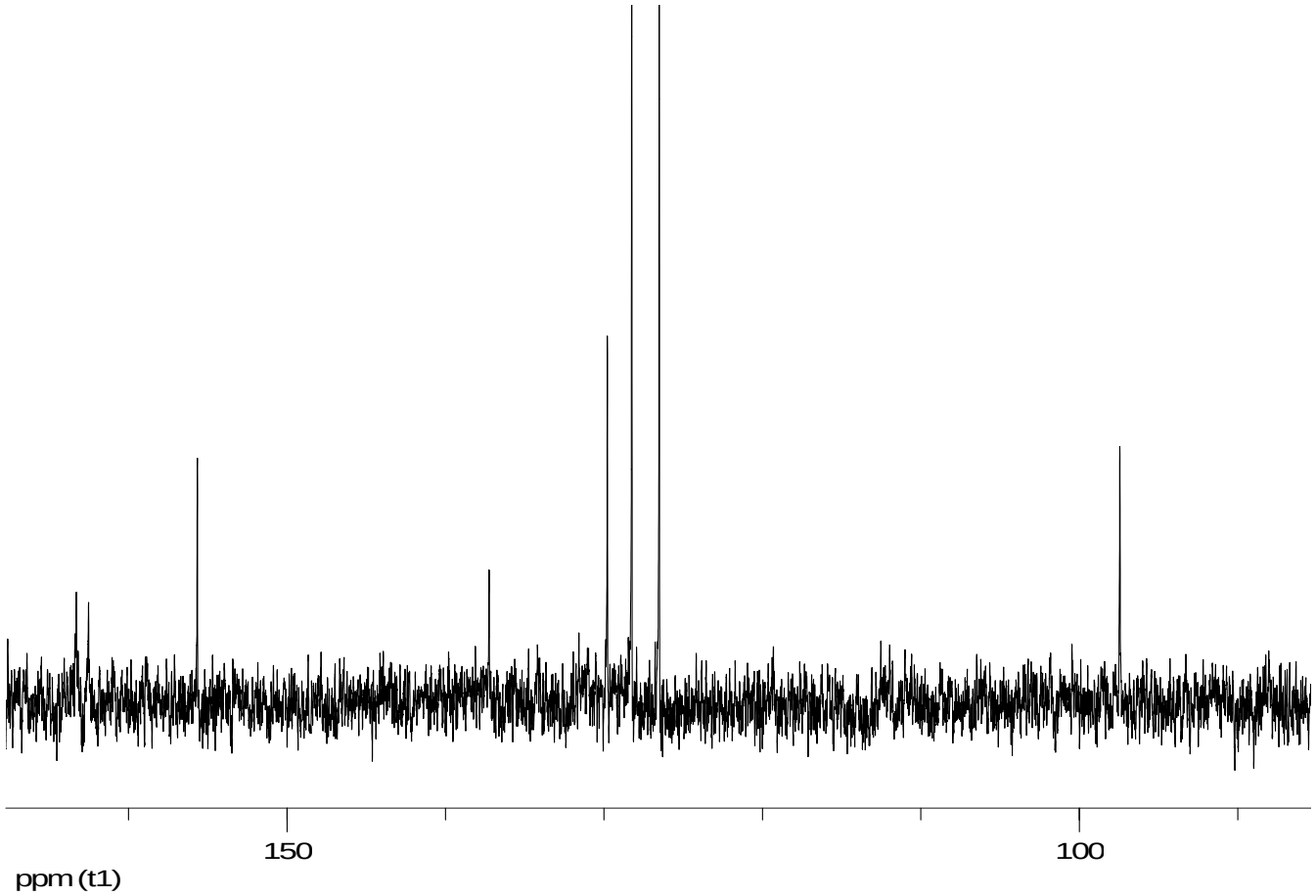
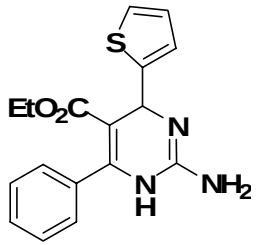
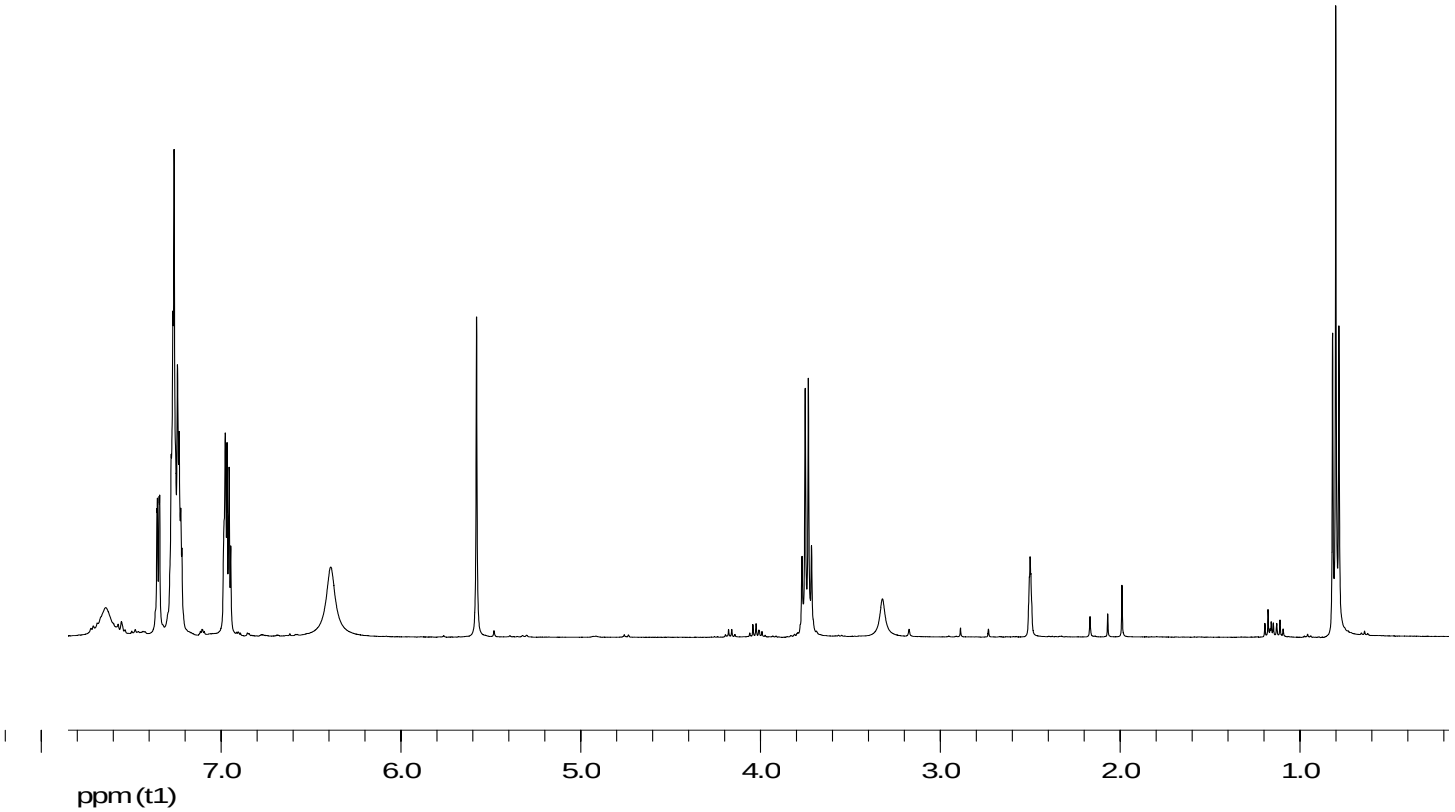
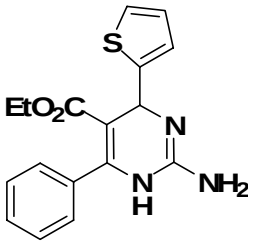
5.0
ppm (t1)


O
N
N
H
NH2


150
100
ppm (t1)


S
EtO2C
N
N
H
NH2


7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)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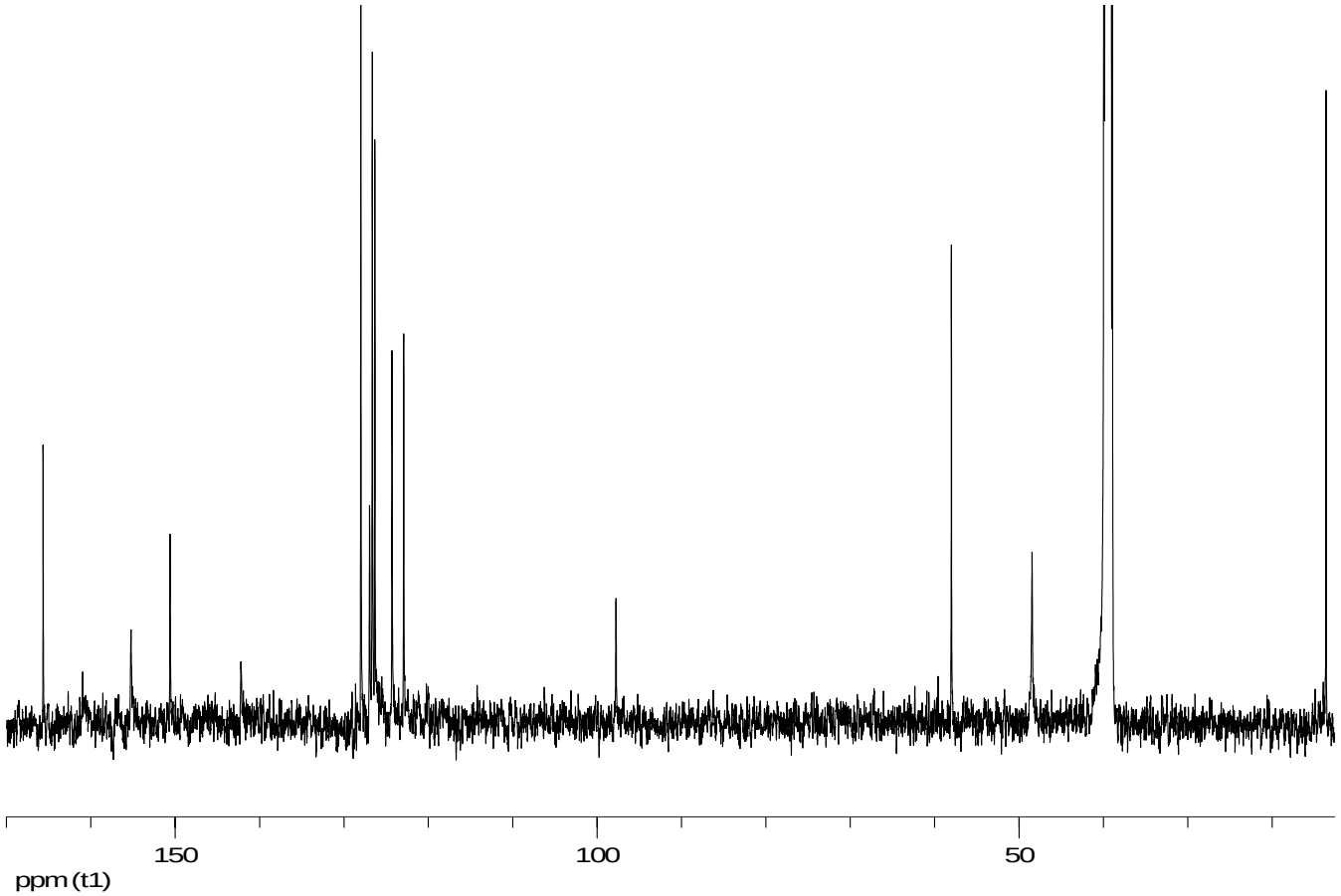
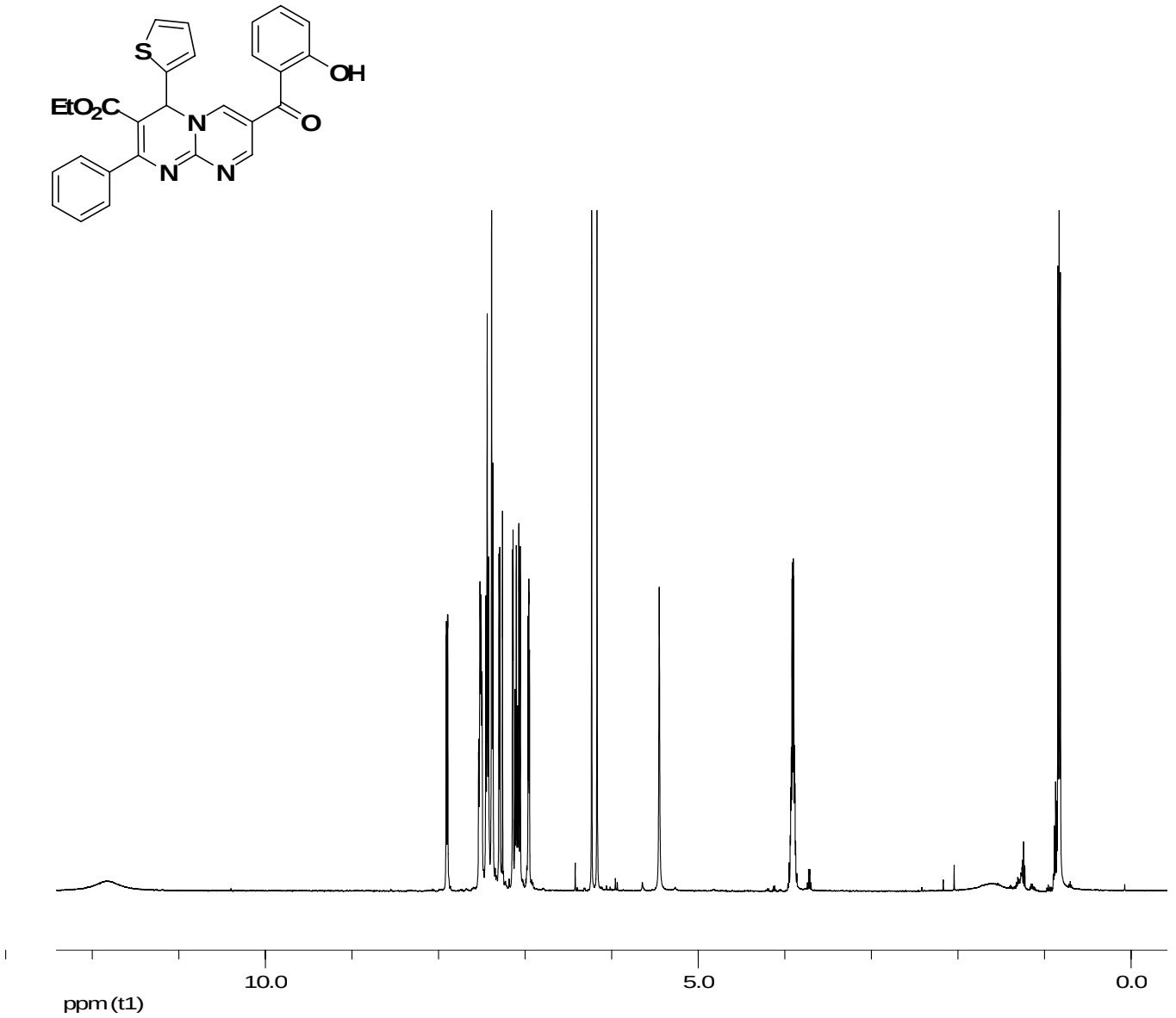
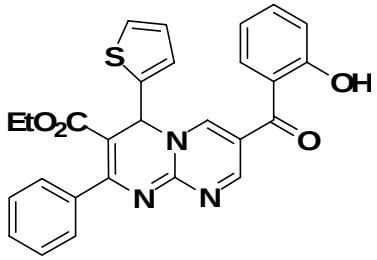
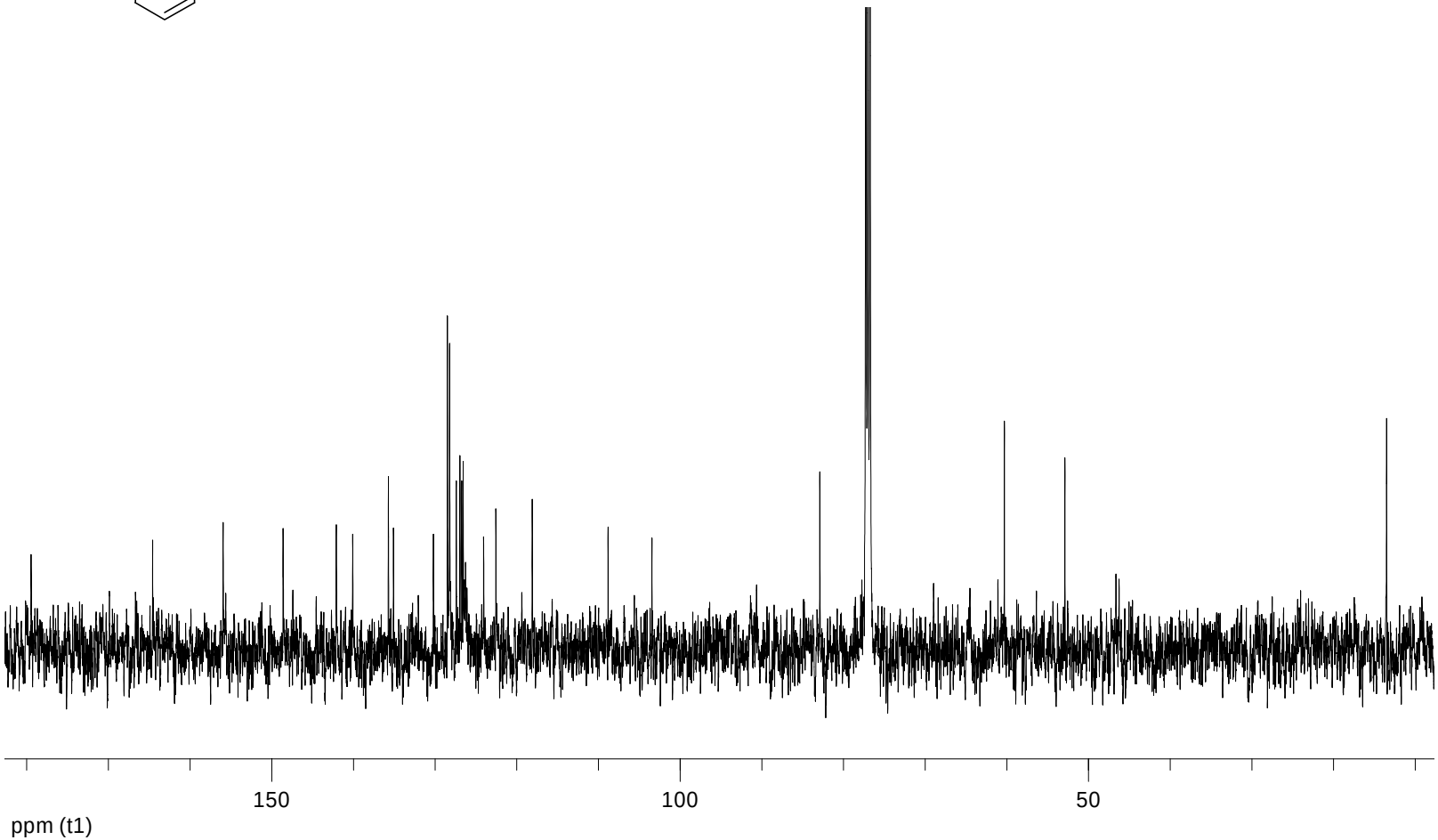
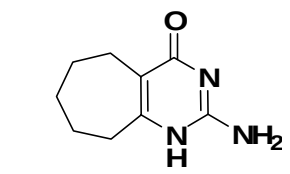
N
N
H
NH2

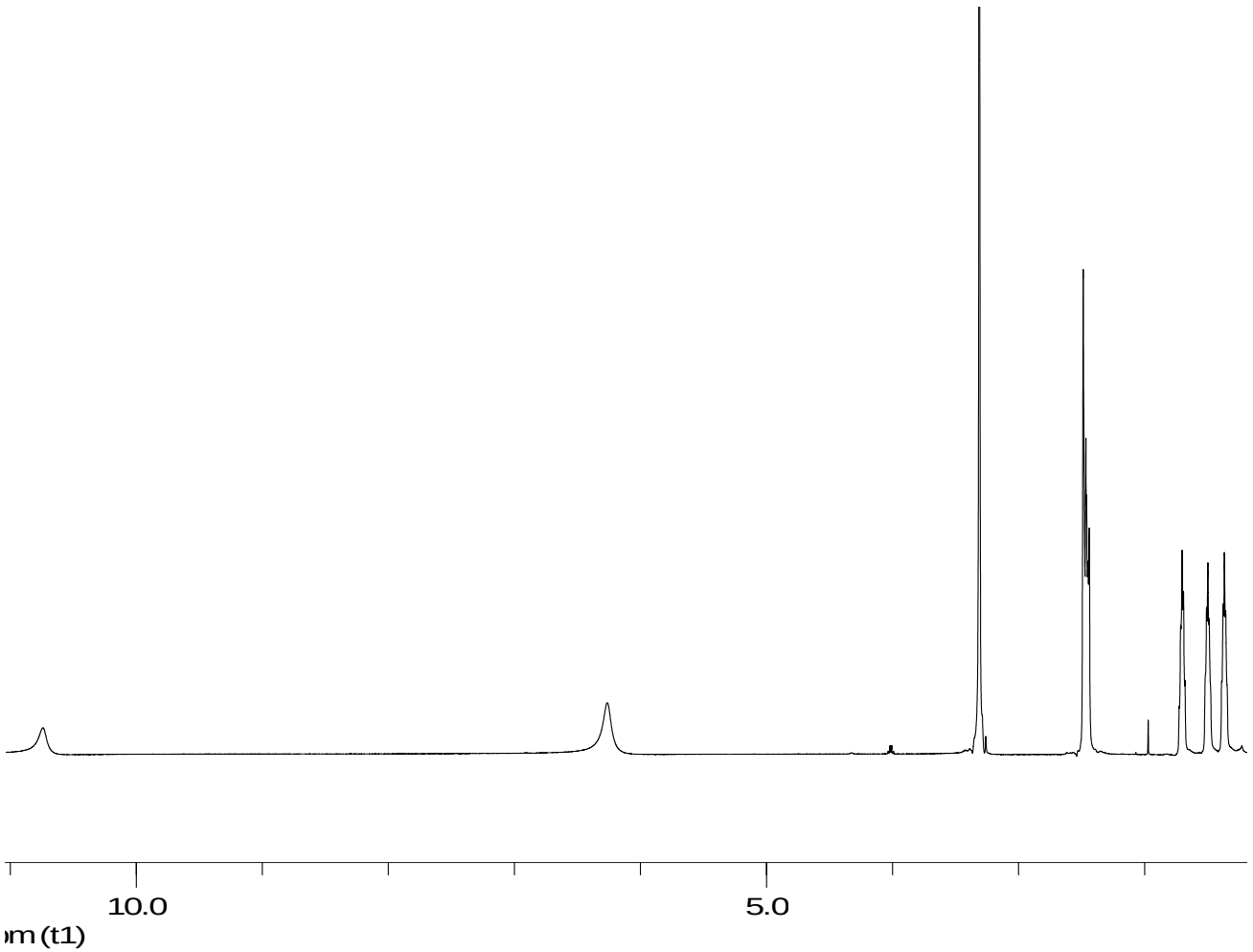

150
100
50
ppm (t1)

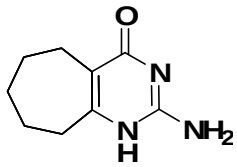

S
OH
EtO2C
N
O
N
N
10.0
5.0
0.0
ppm (t1)

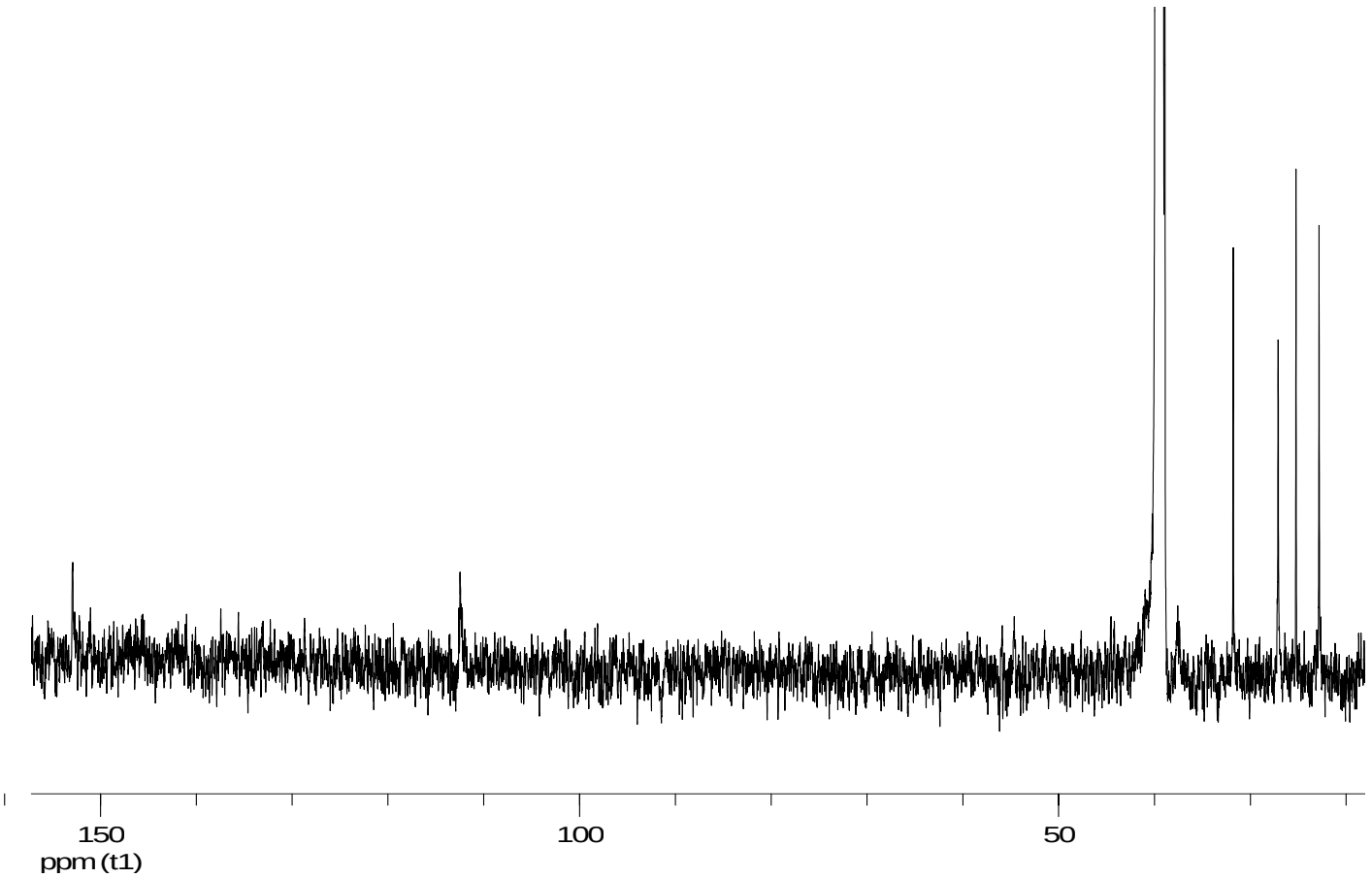

S
OH
EtO2C
N
O
N
N

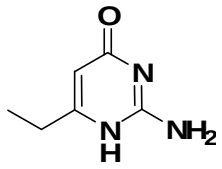

150
100
50
ppm (t1)


O
N
N
H
NH2


10.0
5.0
m (t1)


O
N
N
H
NH2


150
100
50
ppm (t1)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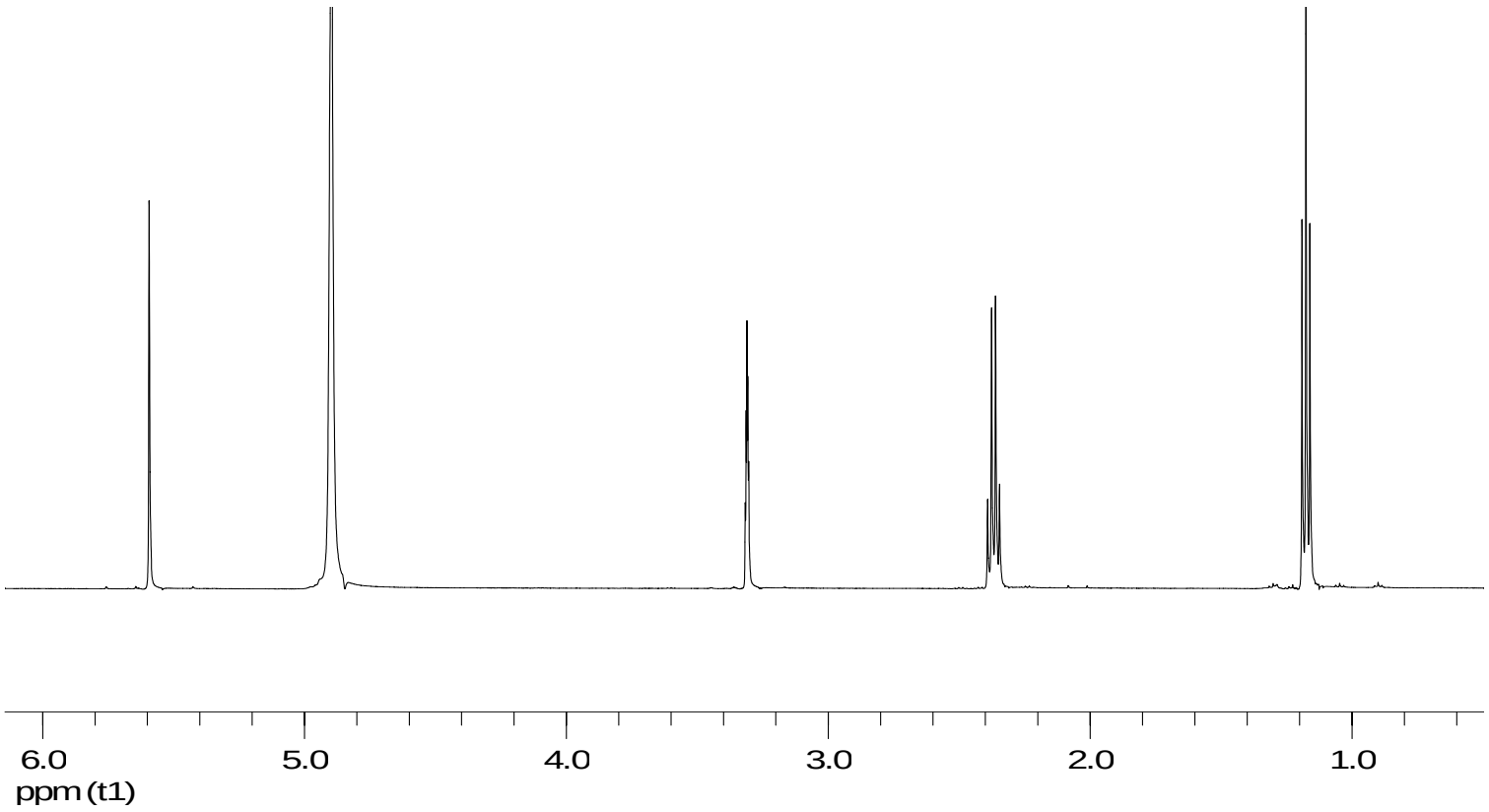
N
N
H
NH2


6.0
5.0
4.0
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2.0
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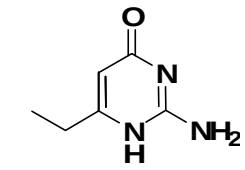
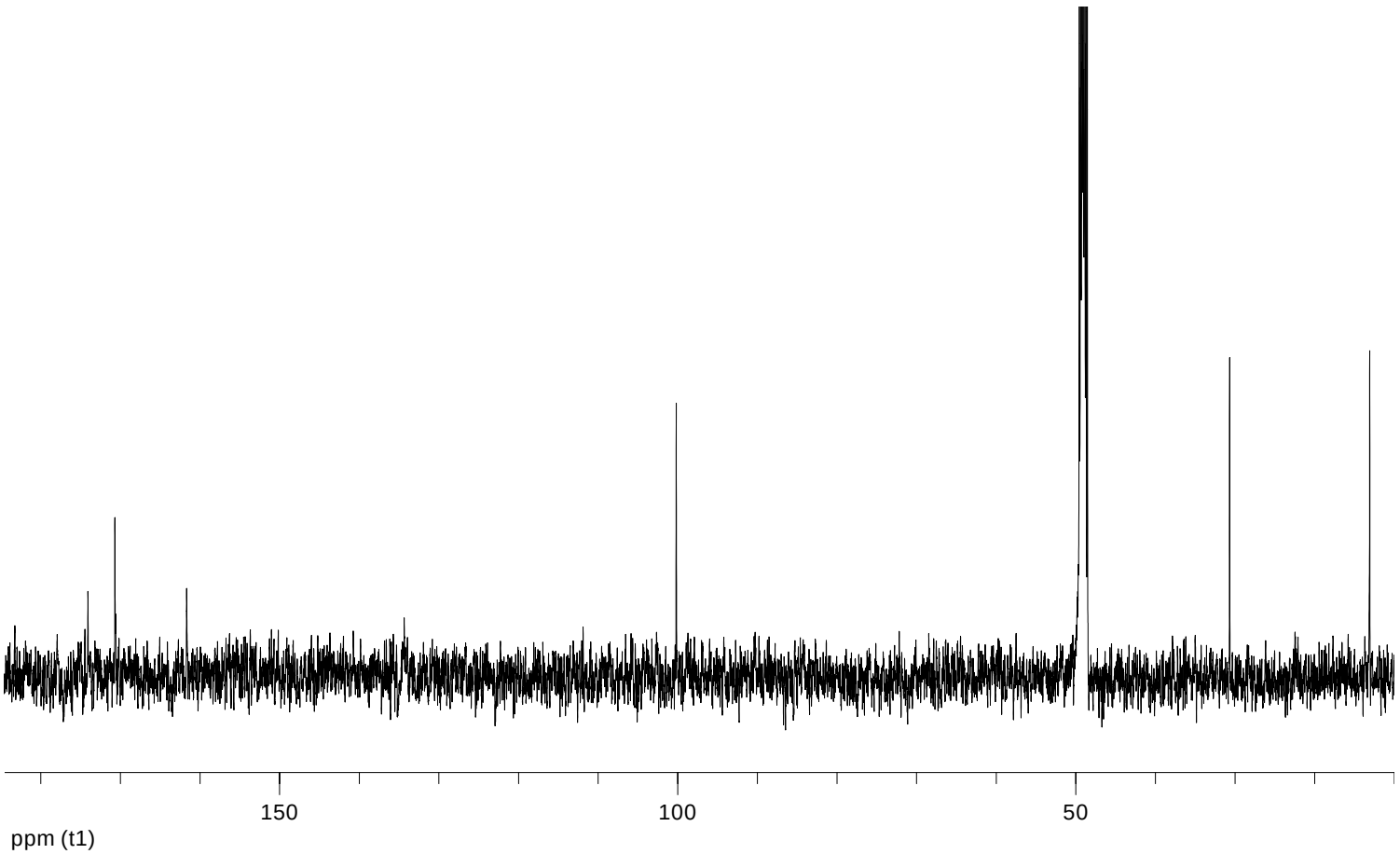
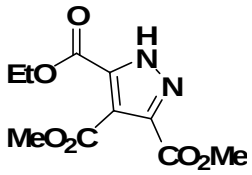
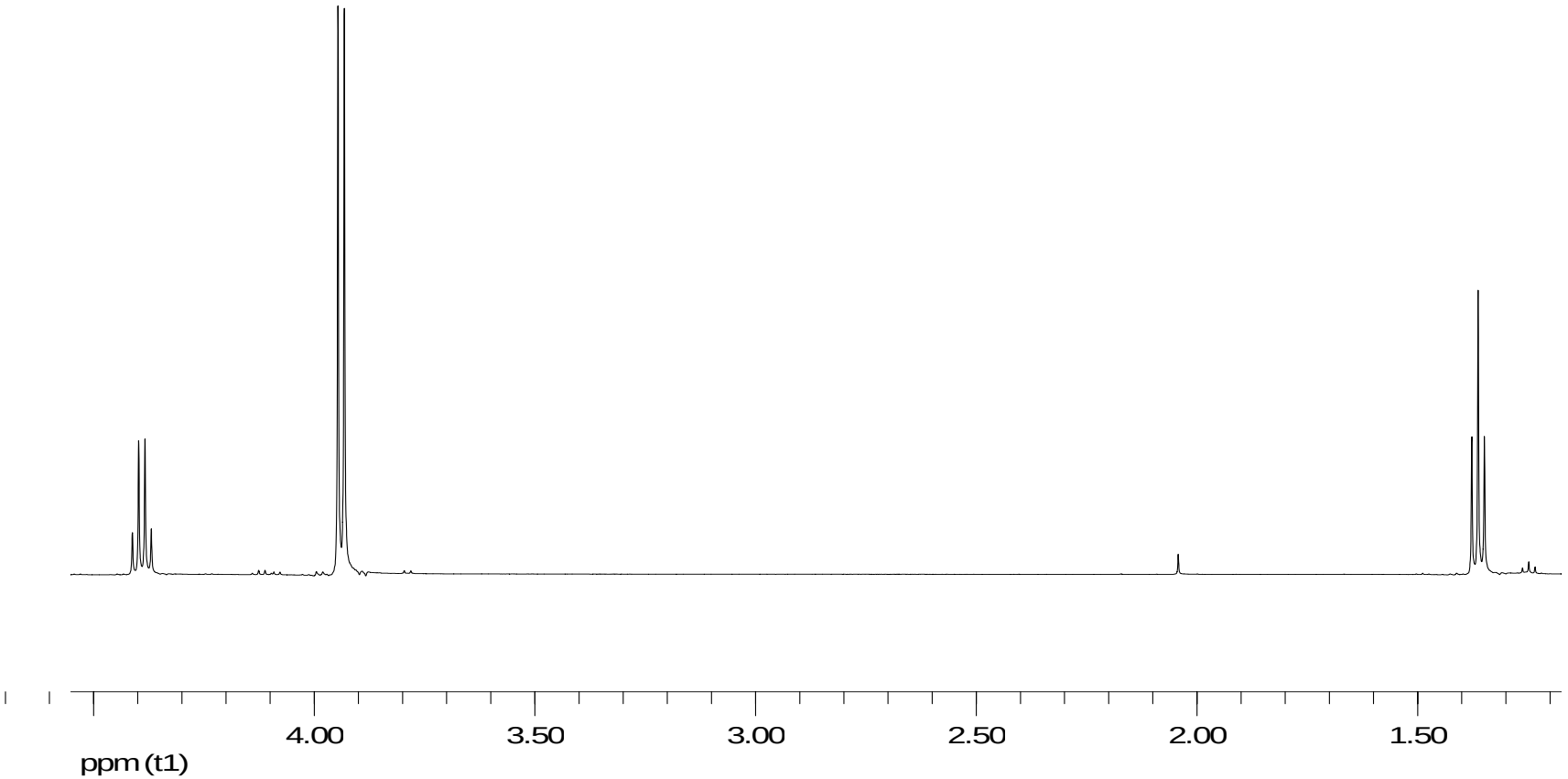
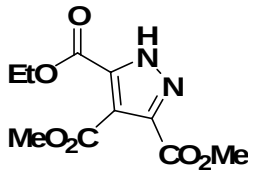
ppm (t1)

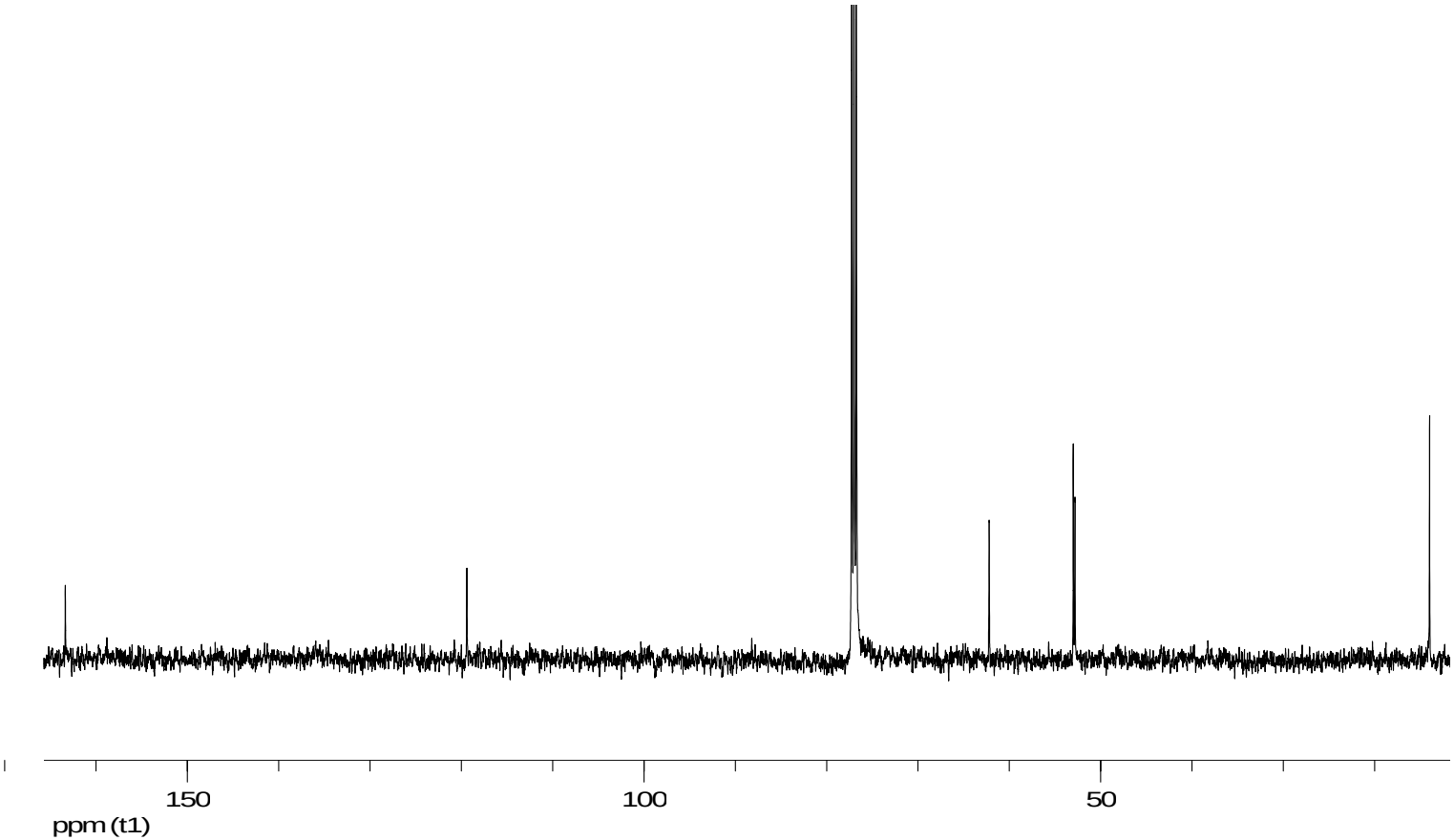

O
N
N
H
NH2

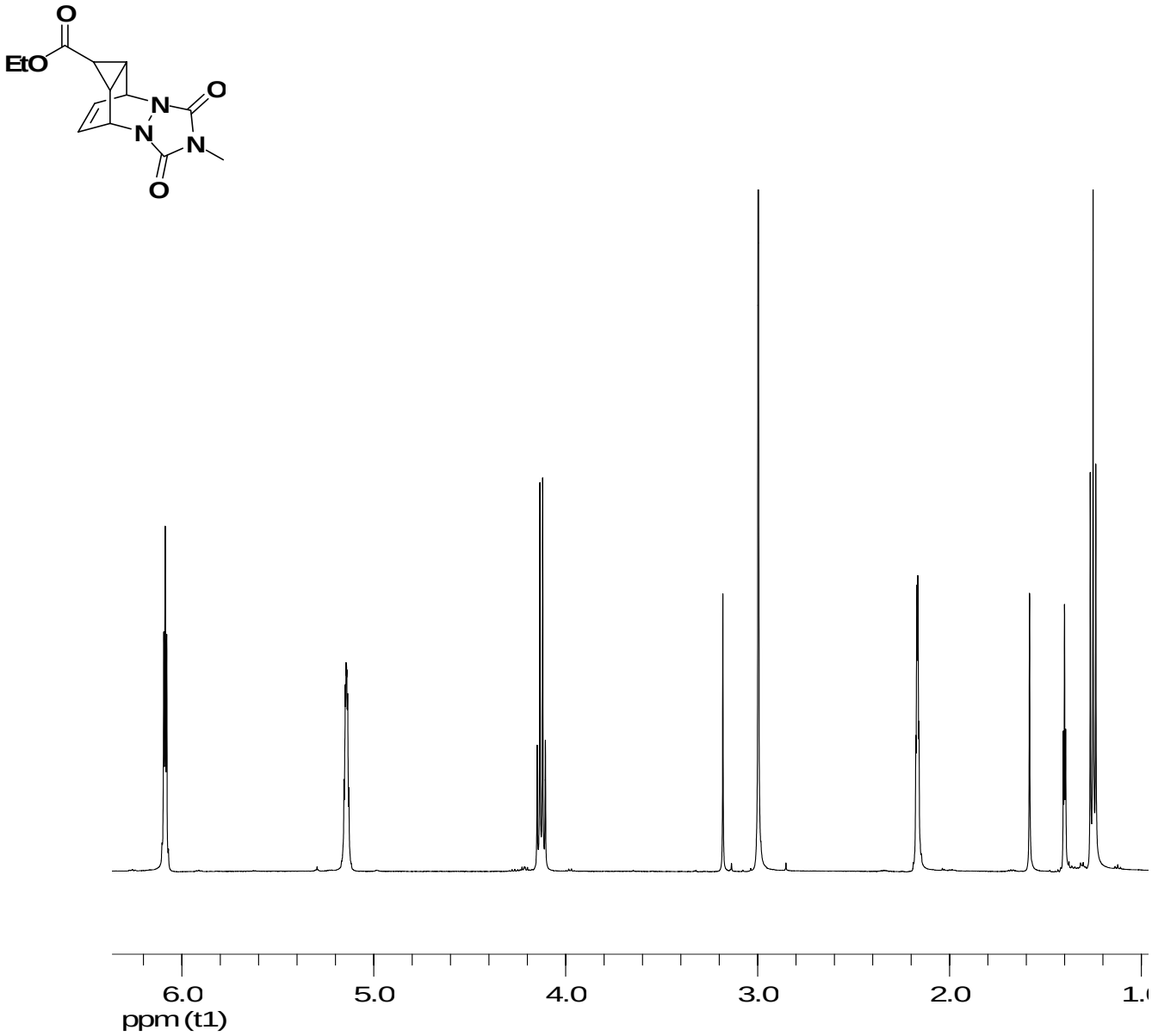

150
100
50
ppm (t1)

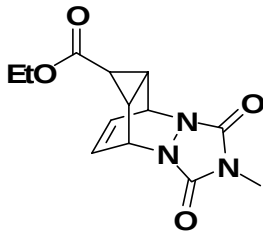

O
H
N
EtO
N
MeO2C
CO2Me


4.00
3.50
3.00
2.50
2.00
1.50
ppm (t1)


O
H
N
N
EtO
MeO2C
CO2Me


150
100
50
ppm (t1)


O
EtO
N
O
N
N
O
6.0
5.0
4.0
3.0
2.0
ppm (t1)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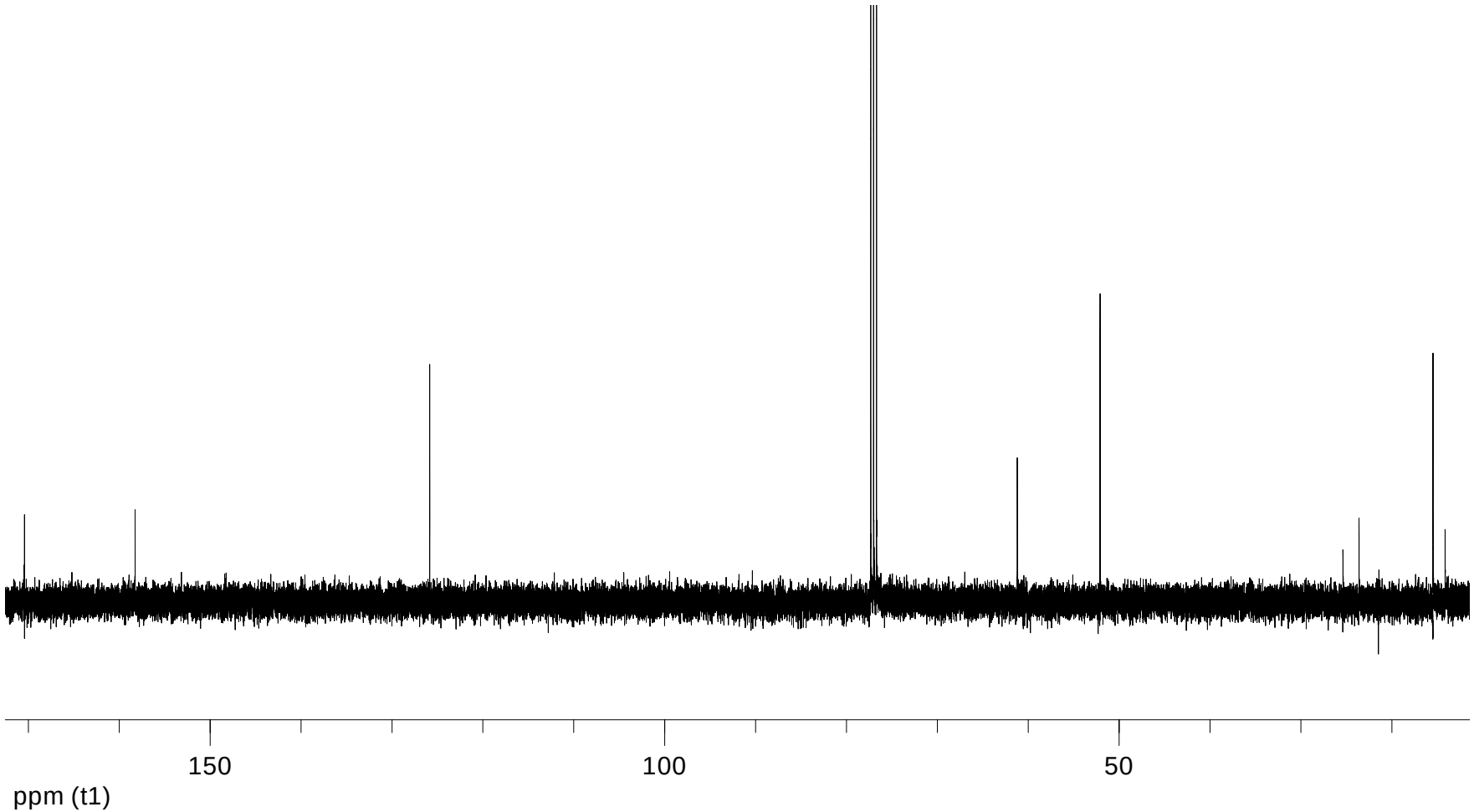
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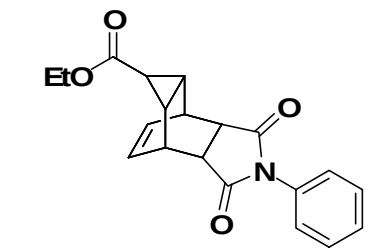
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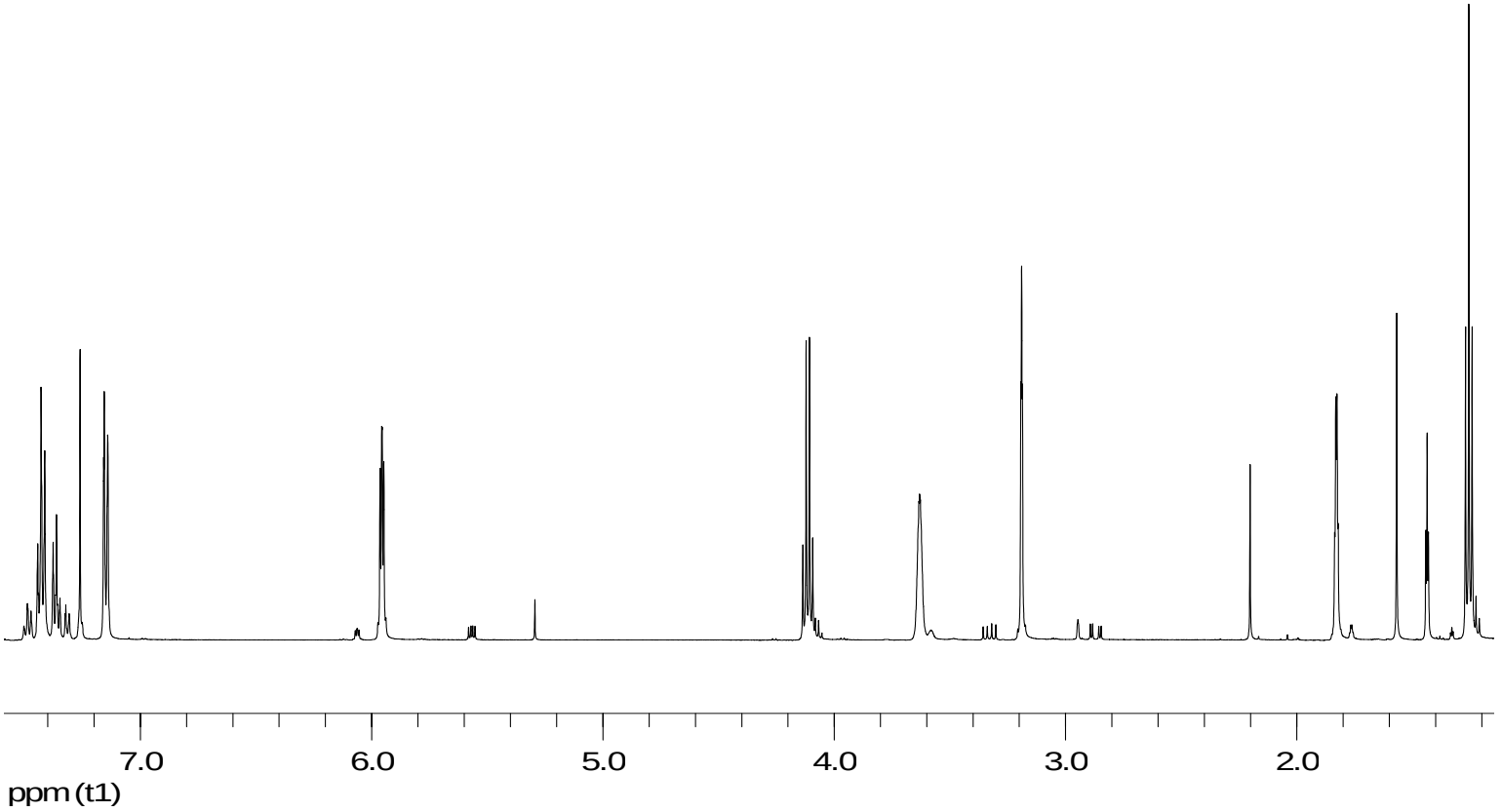
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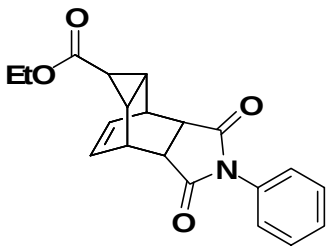
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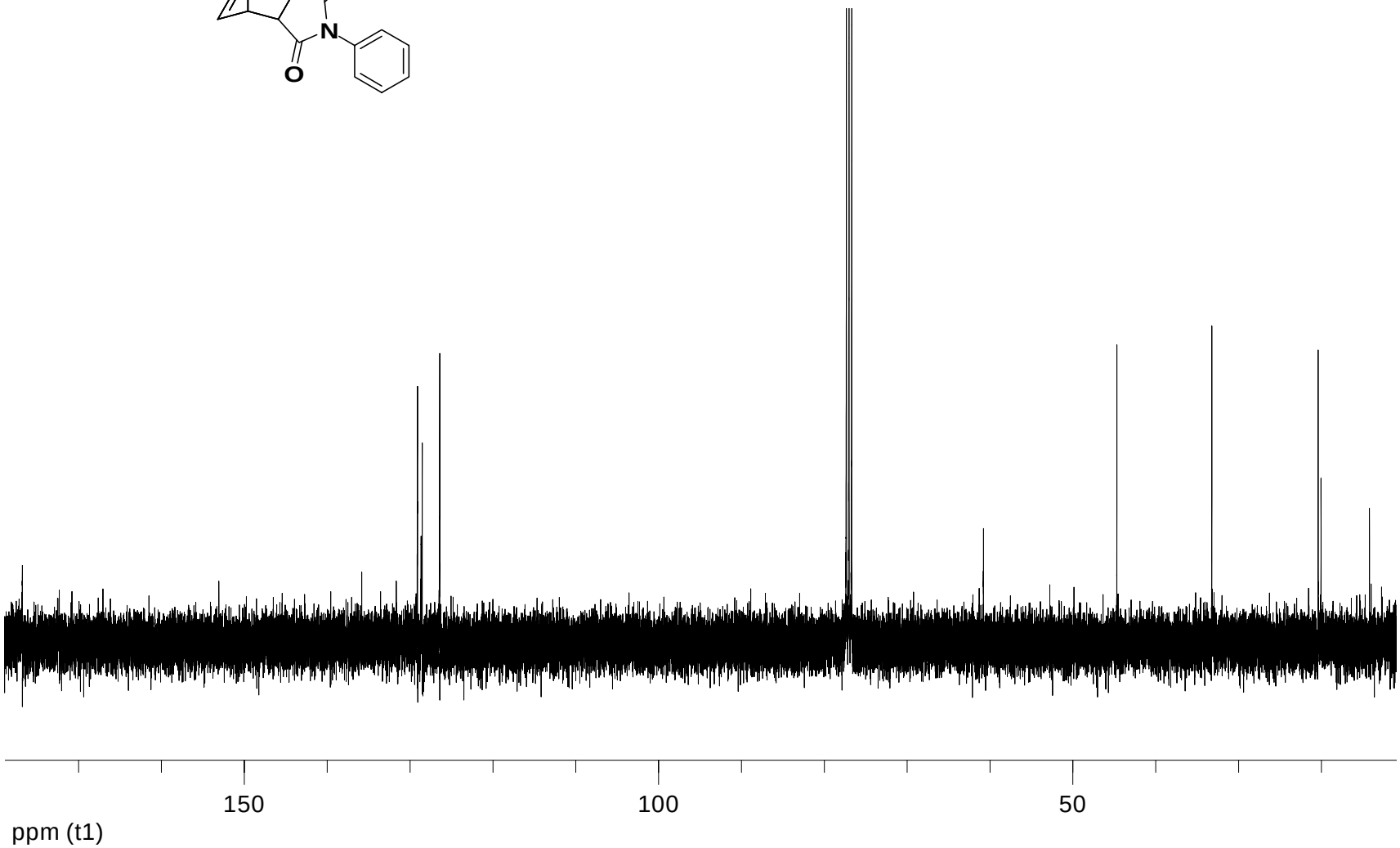
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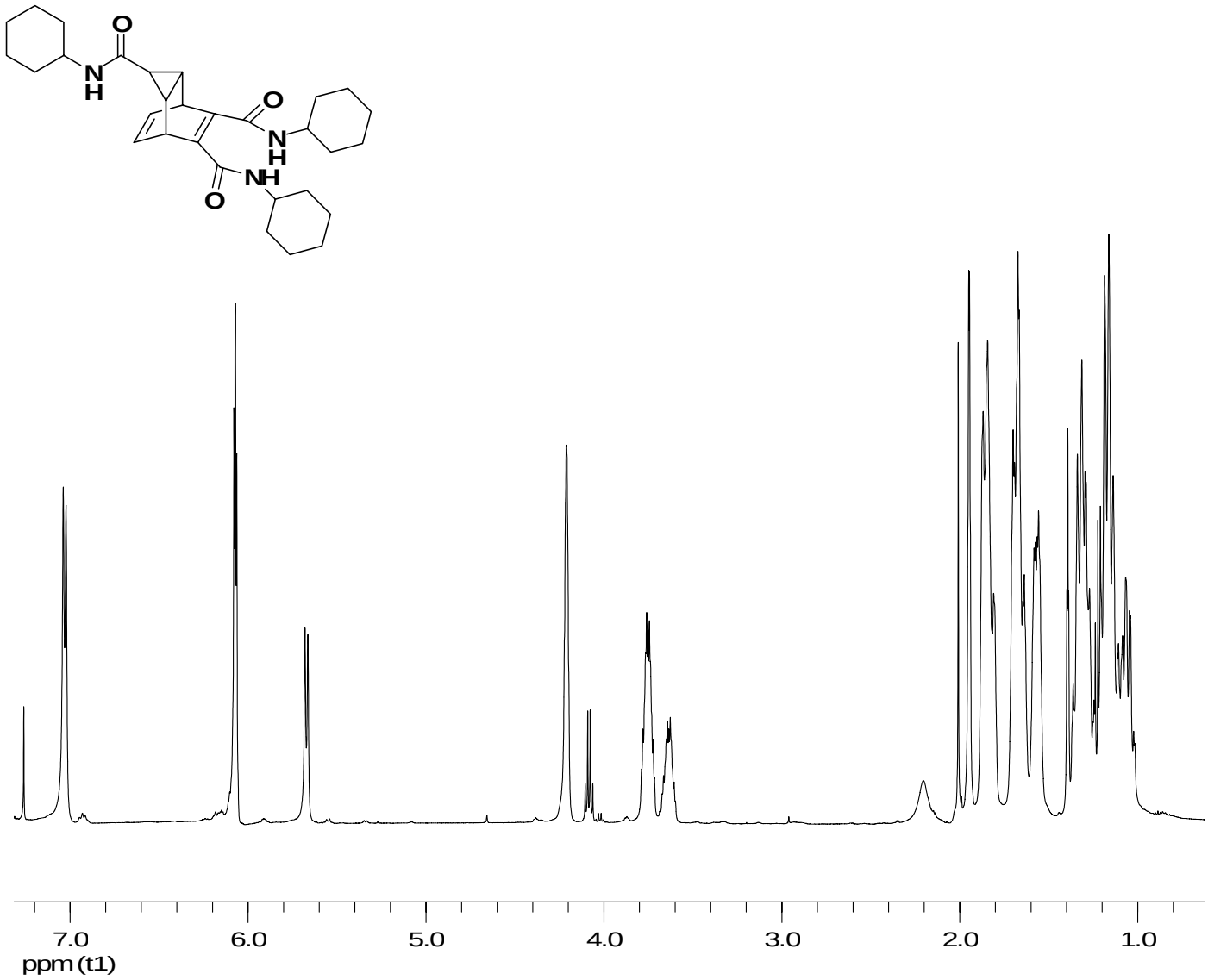
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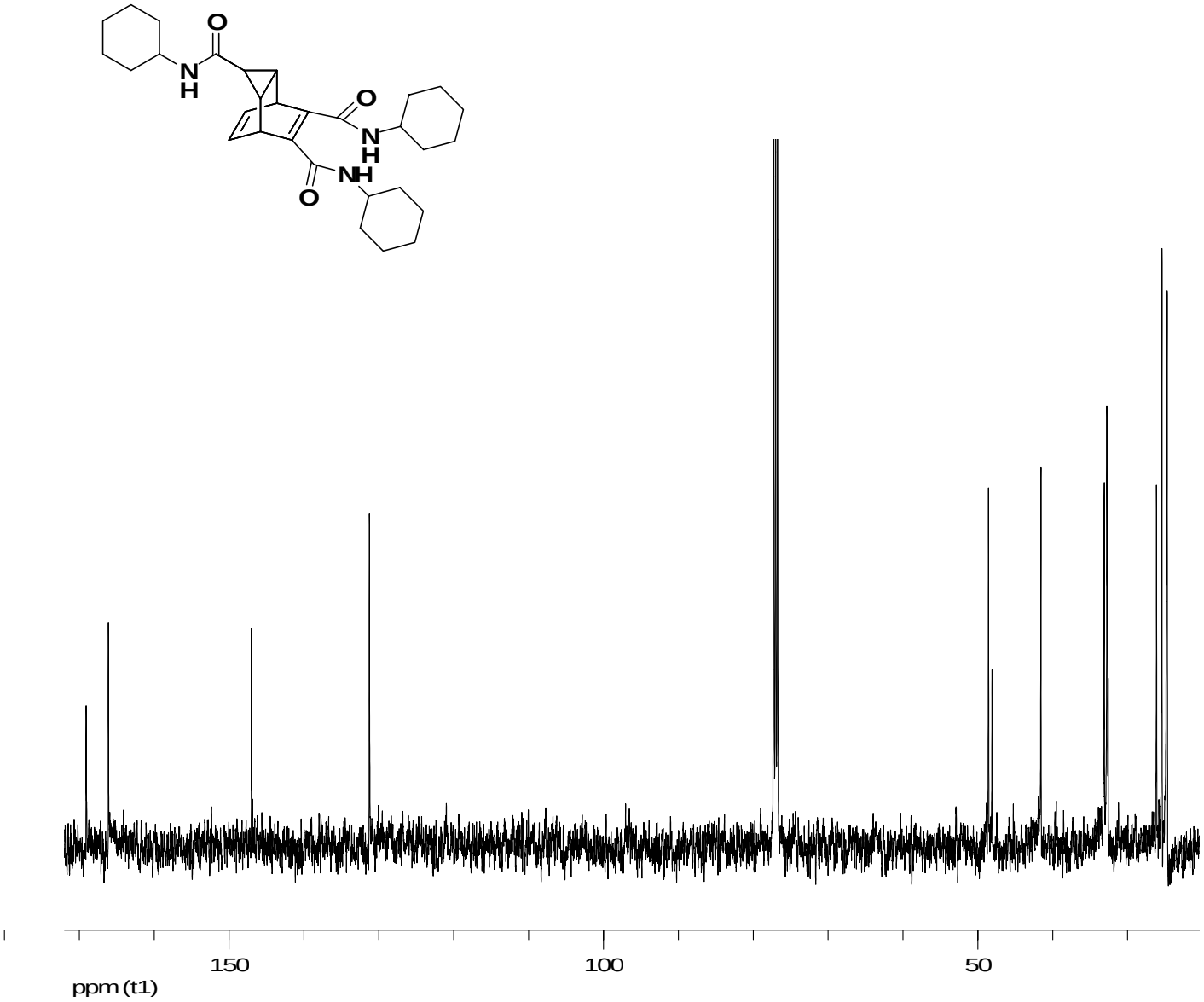
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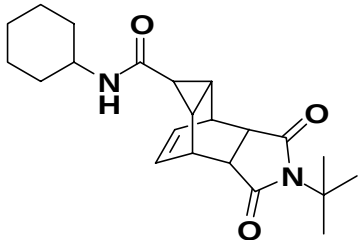
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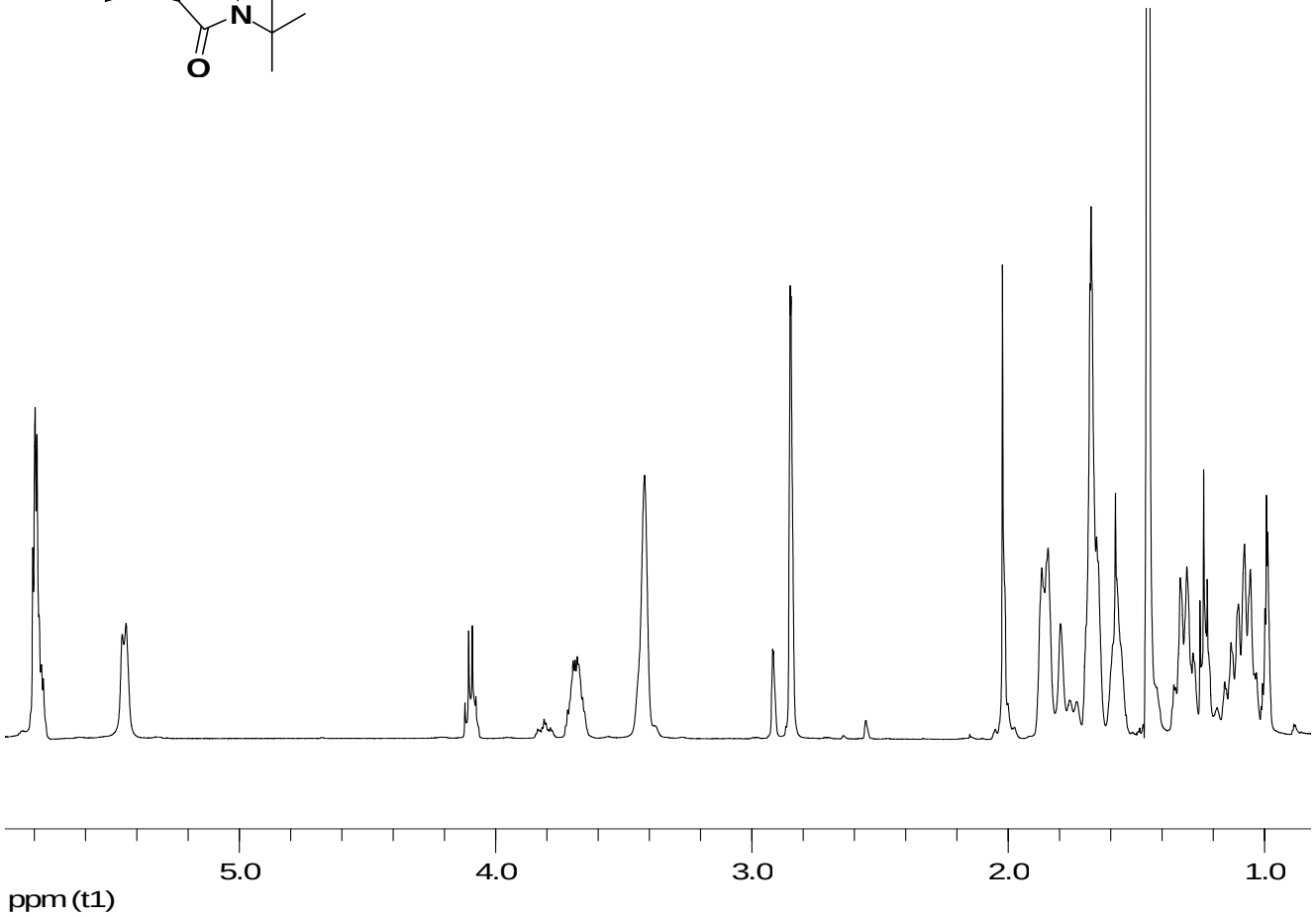
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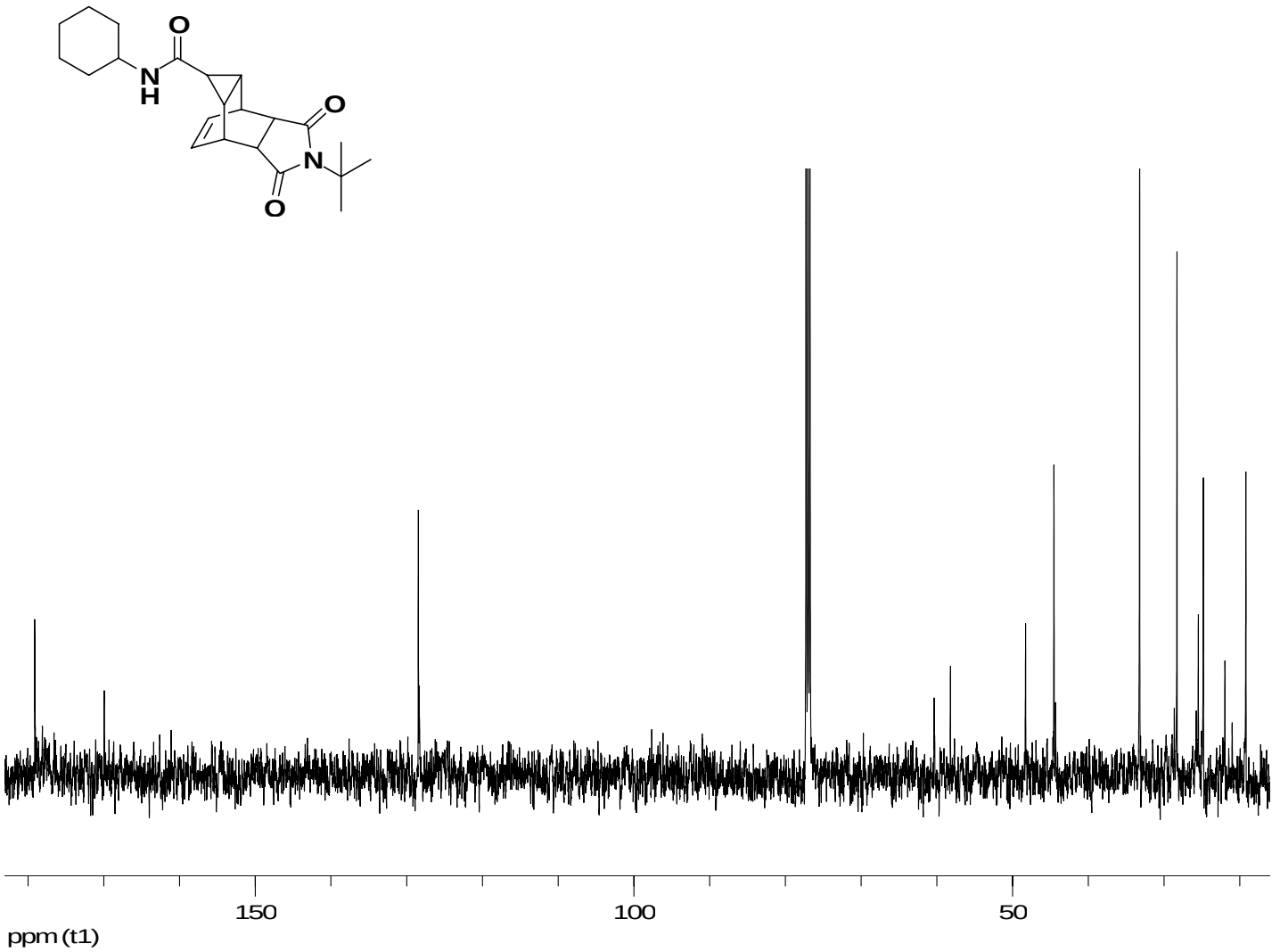
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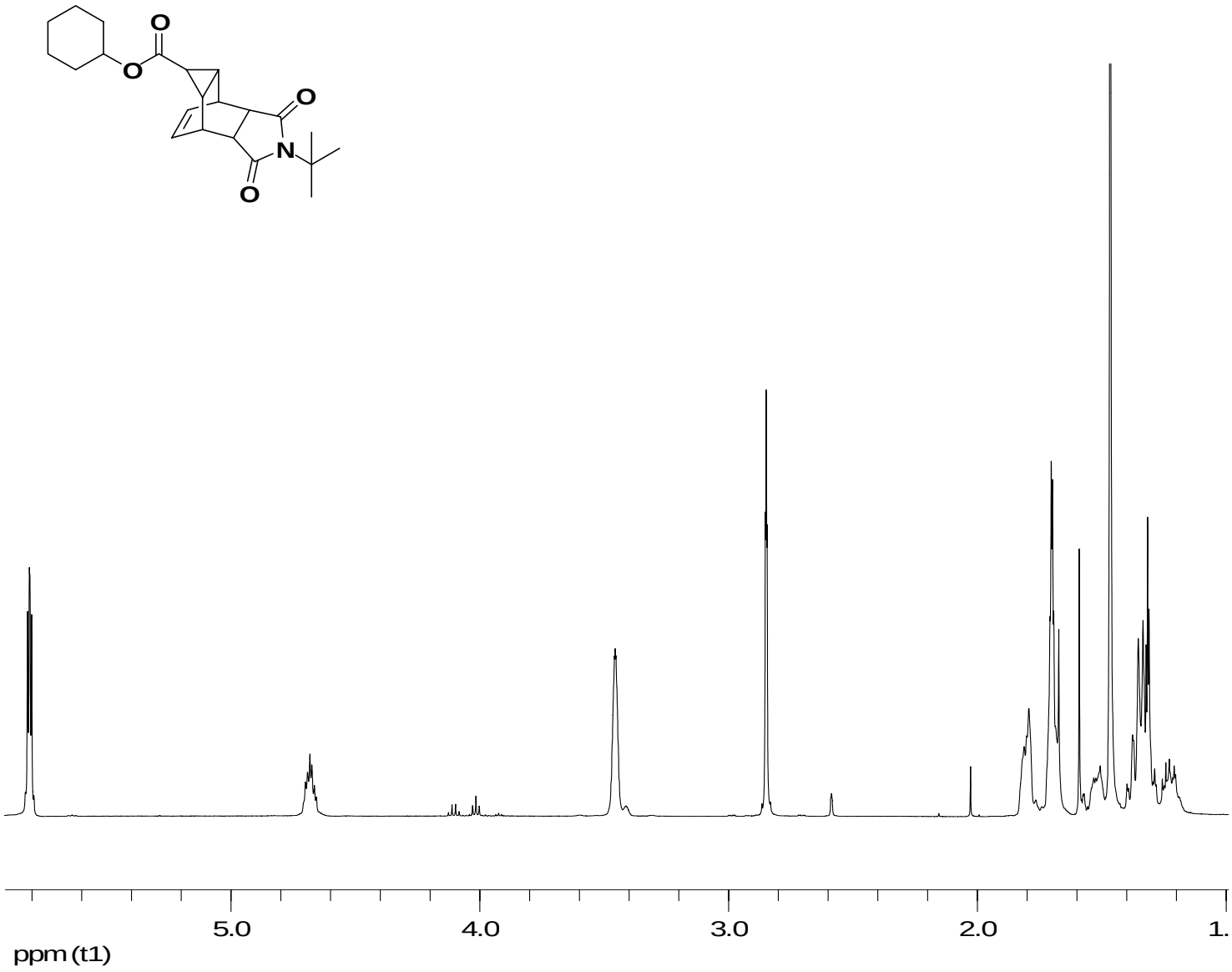
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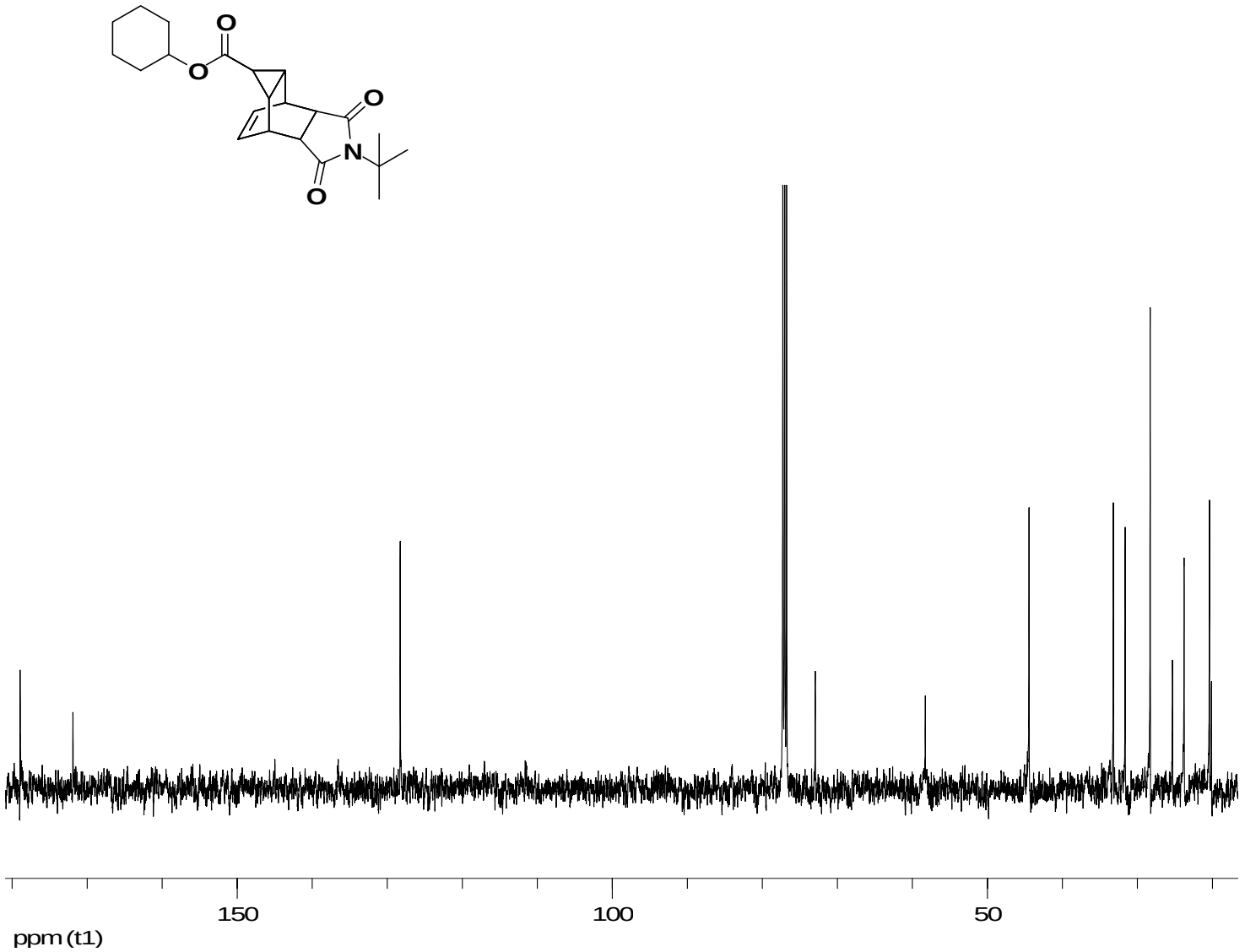
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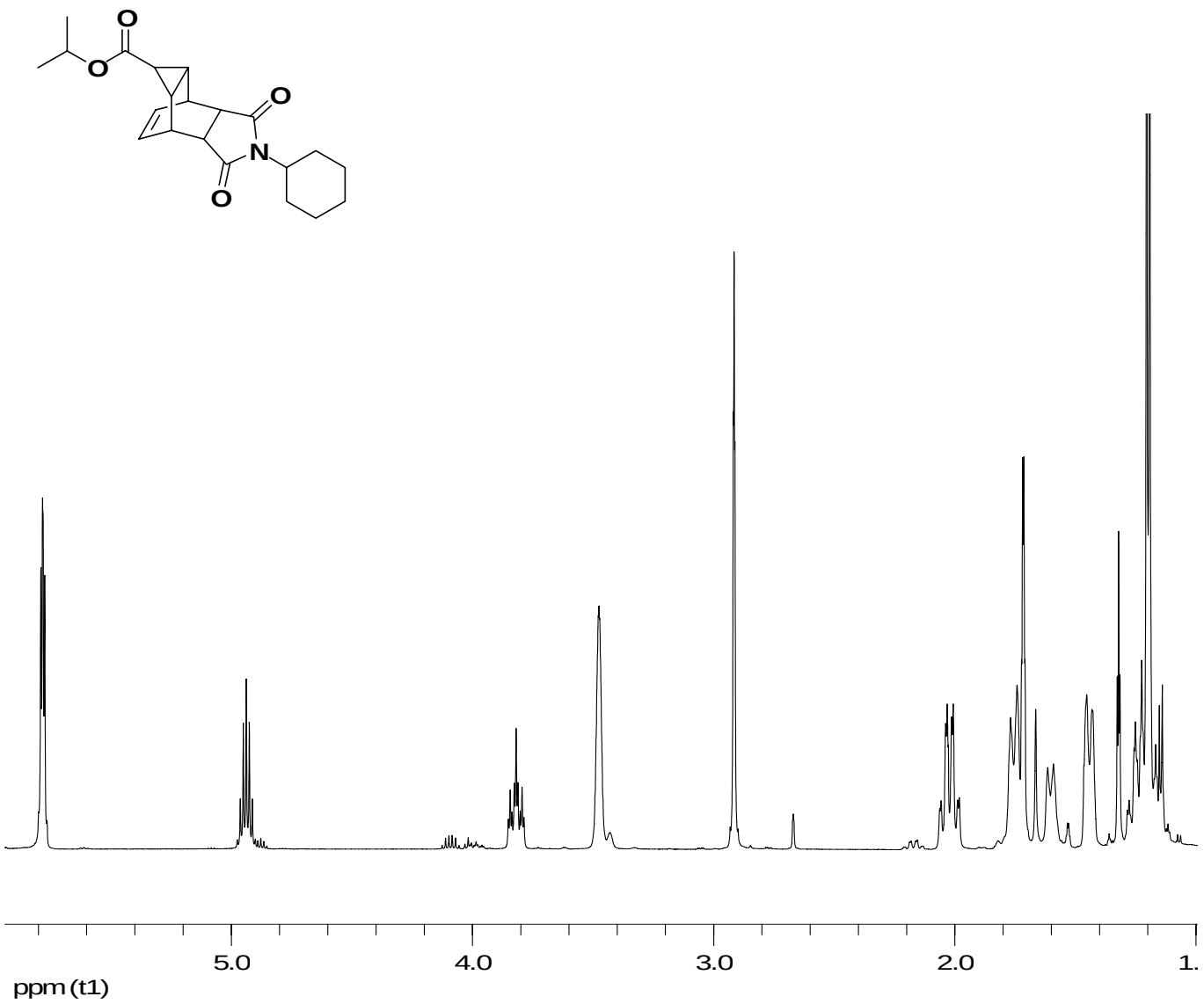
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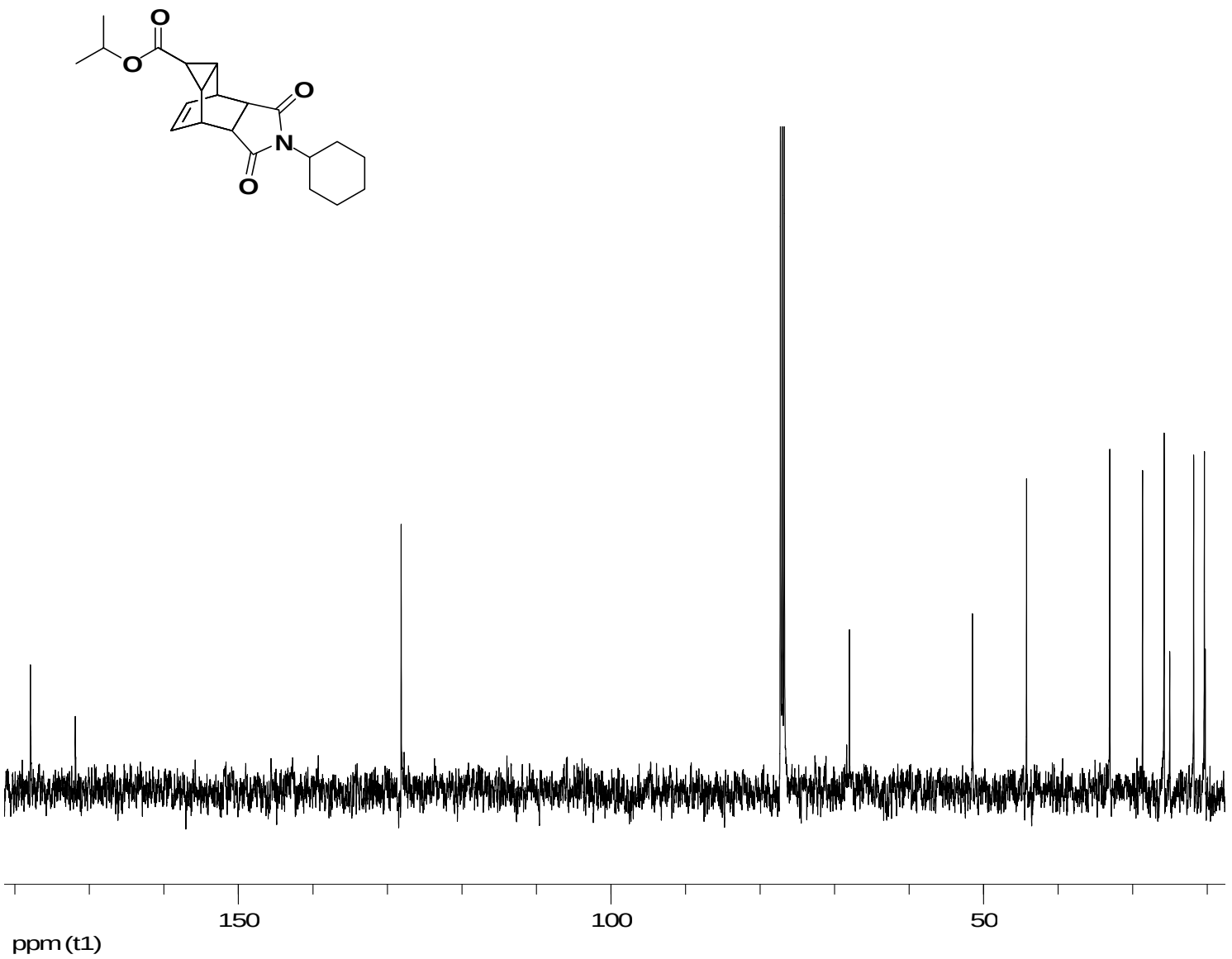
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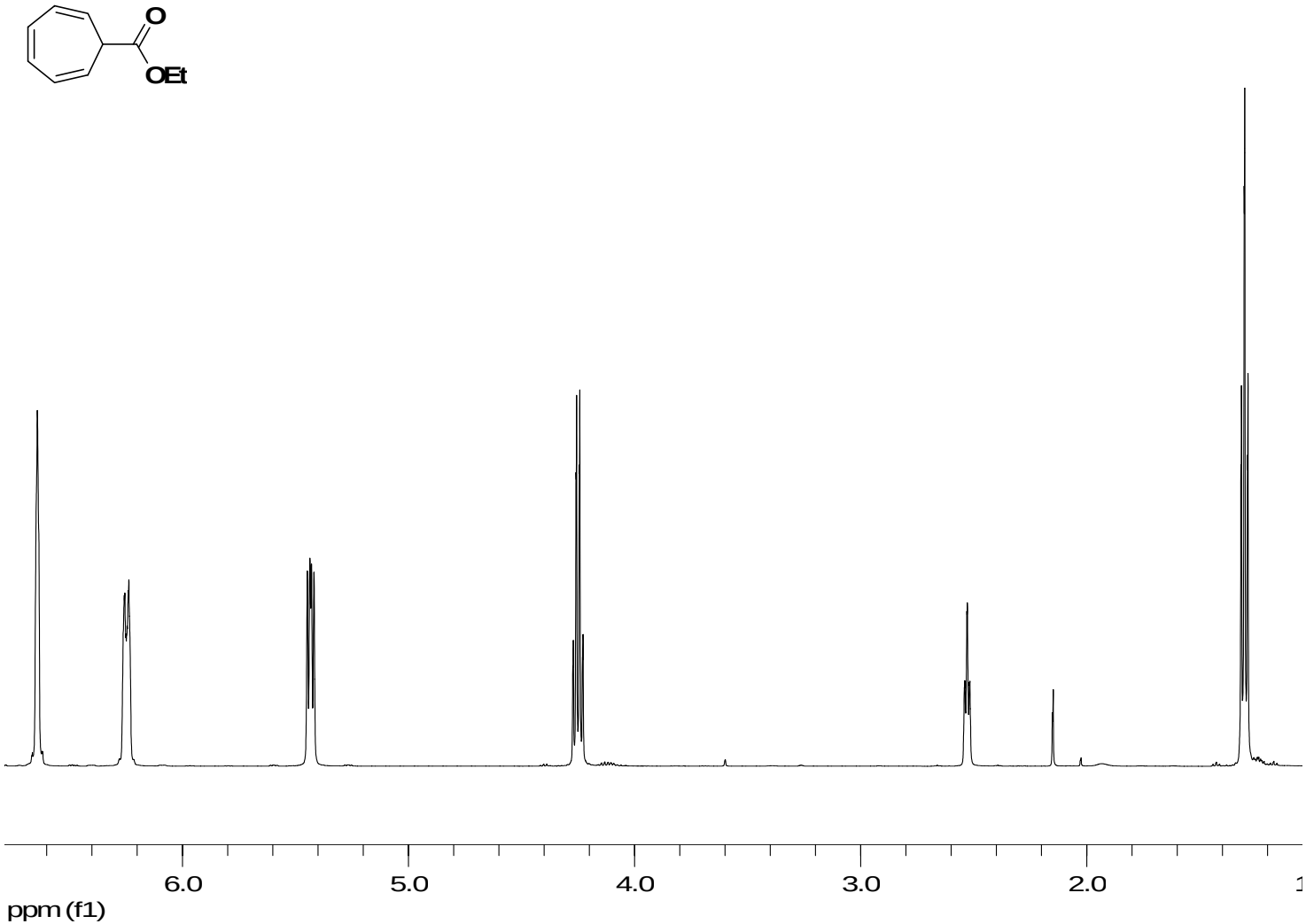
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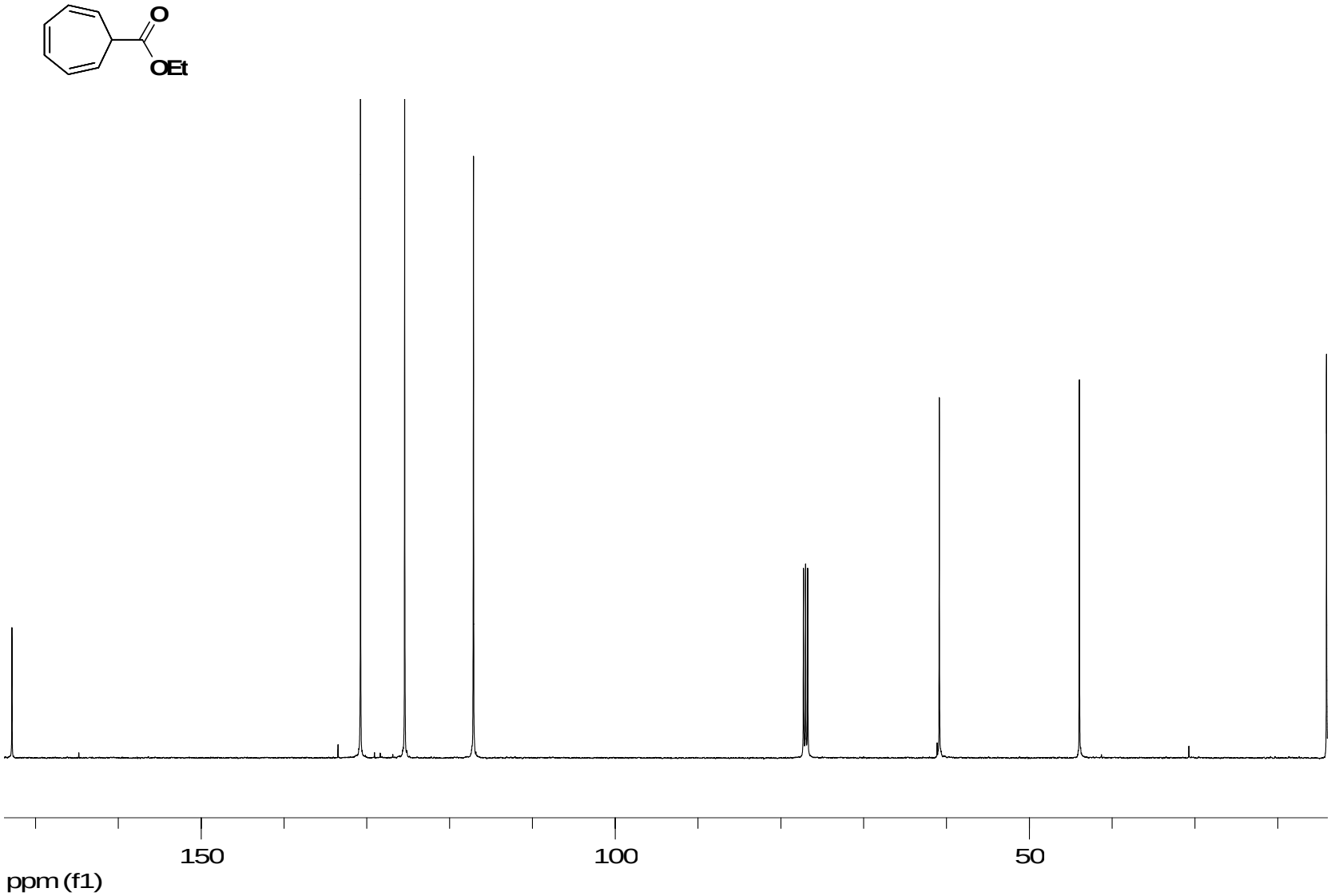
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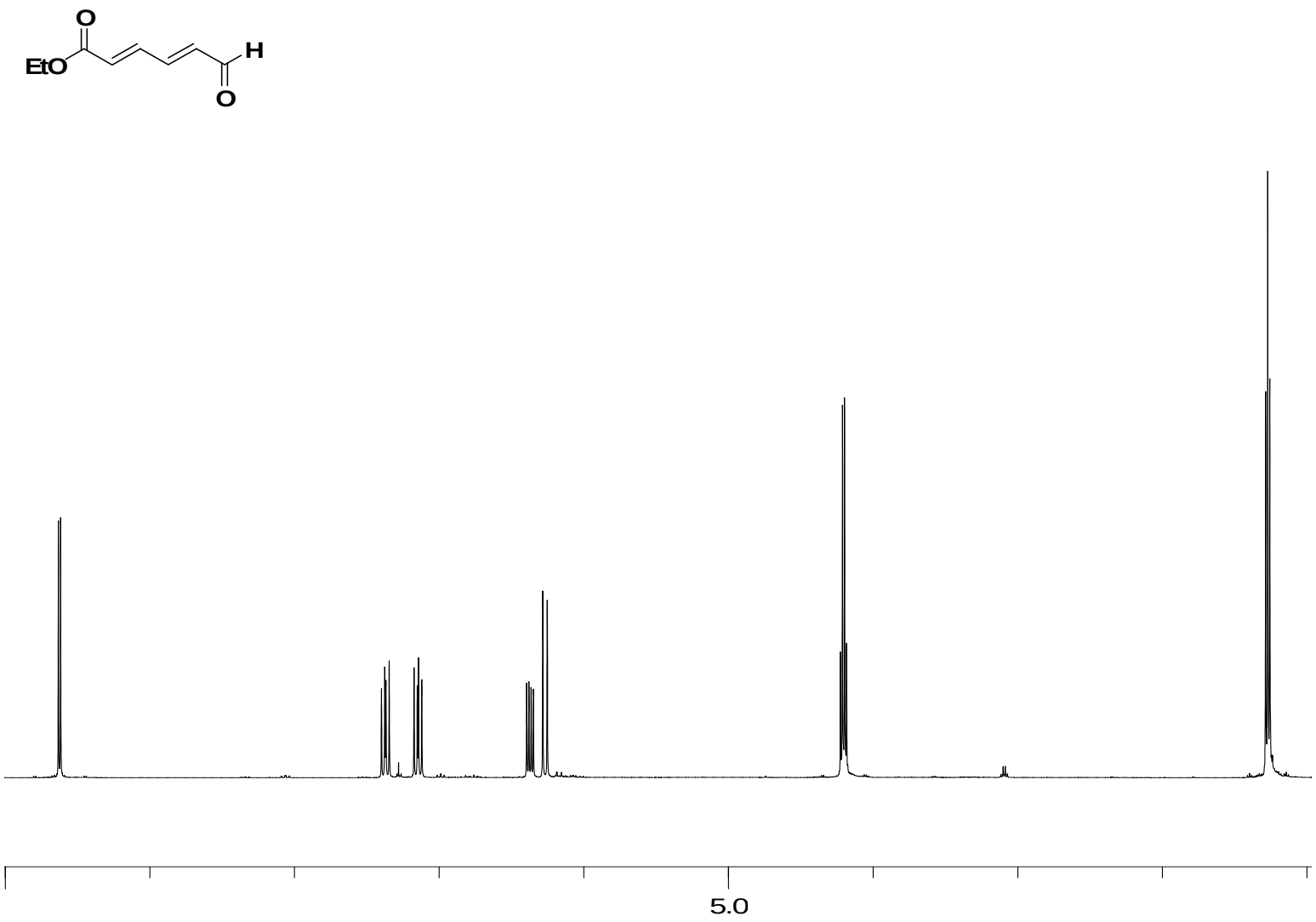
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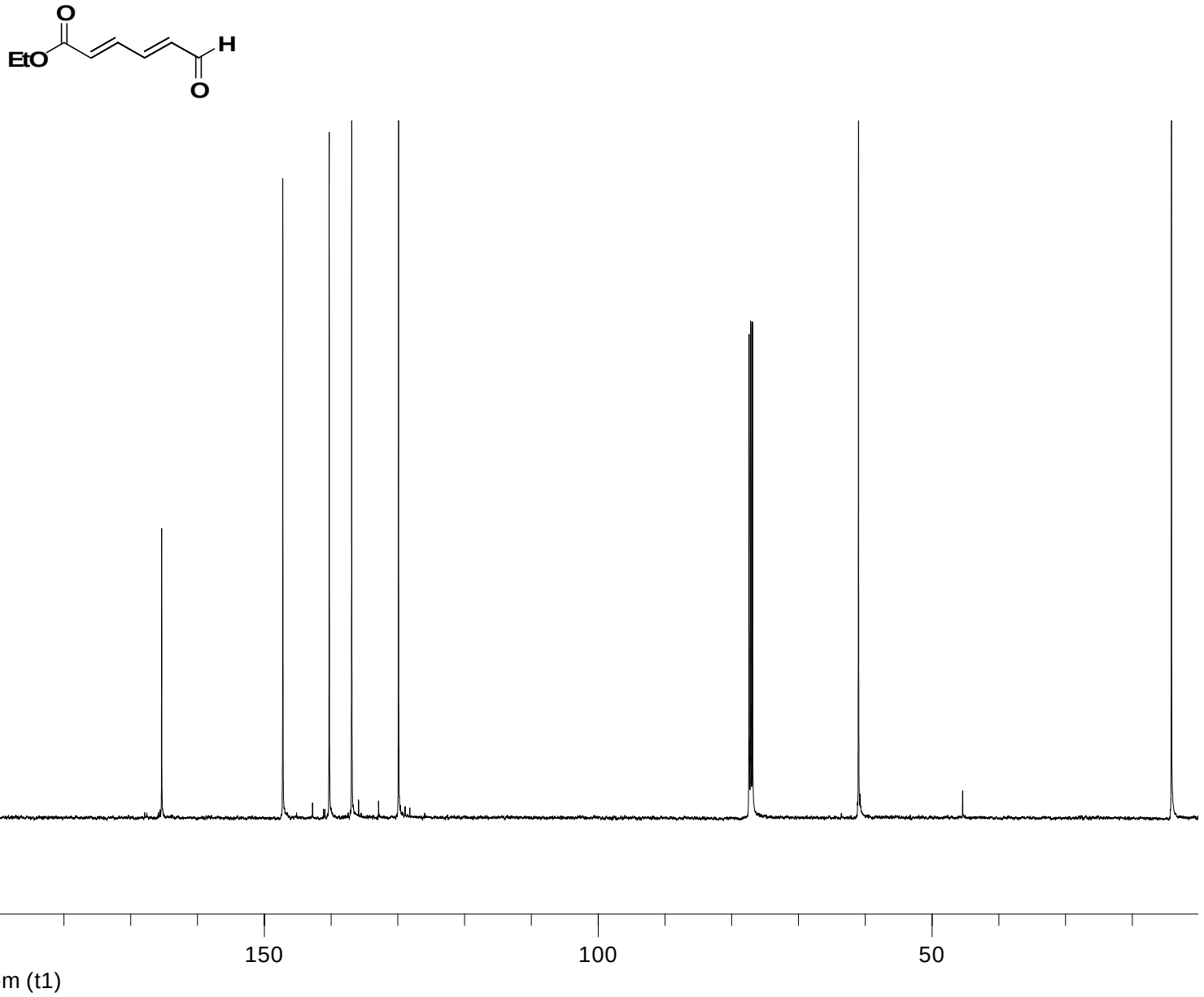
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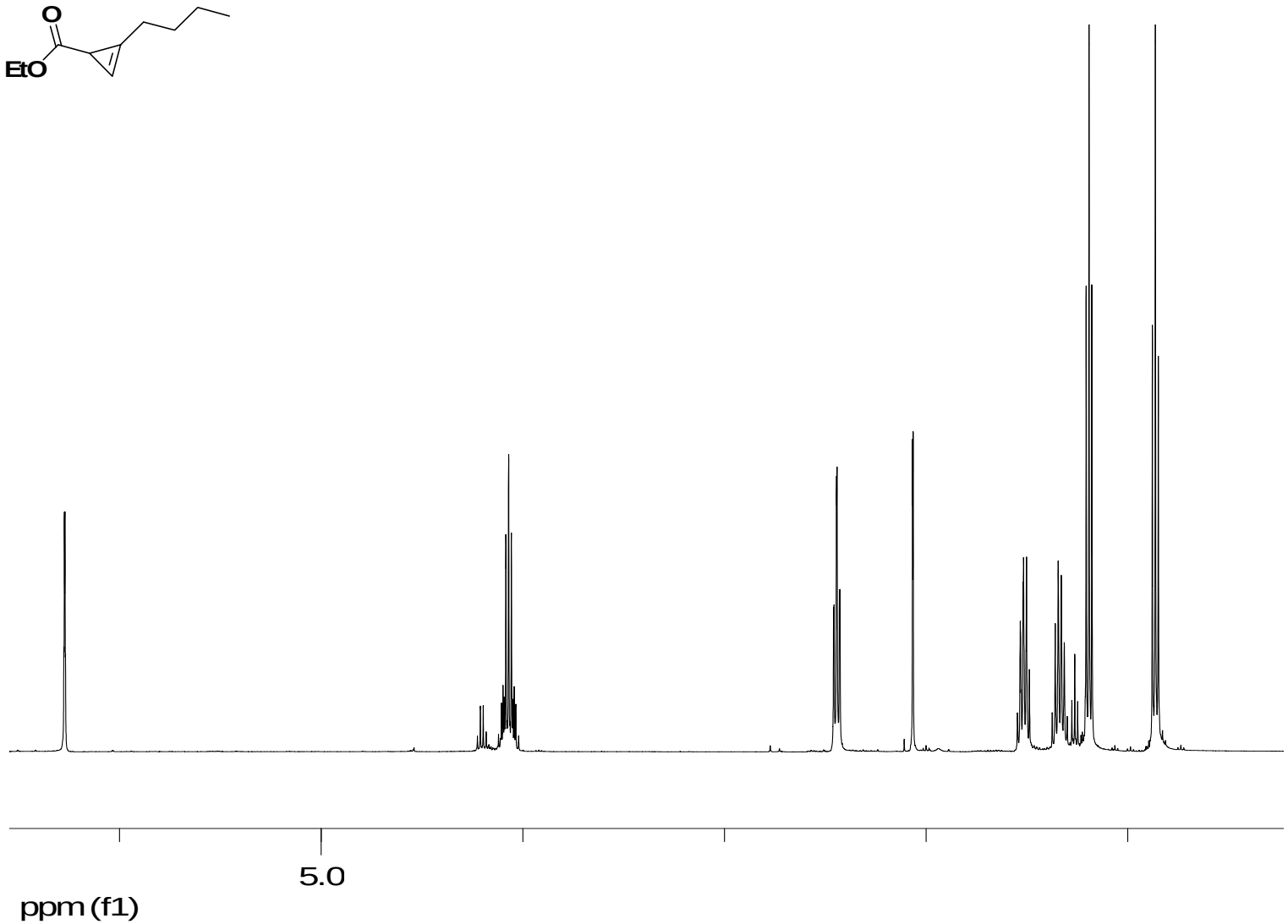
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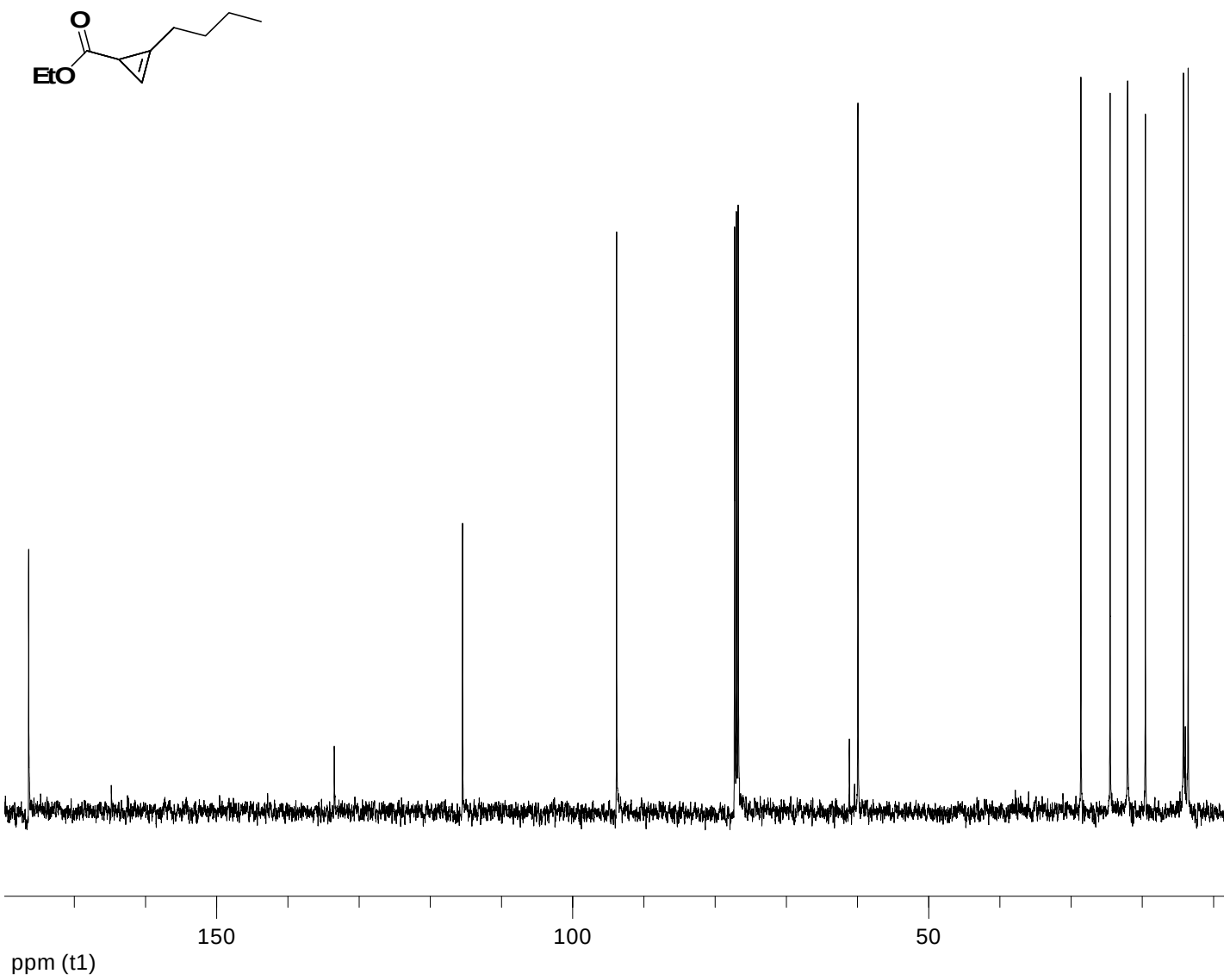
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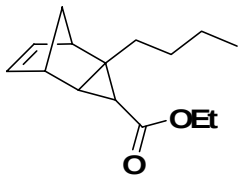
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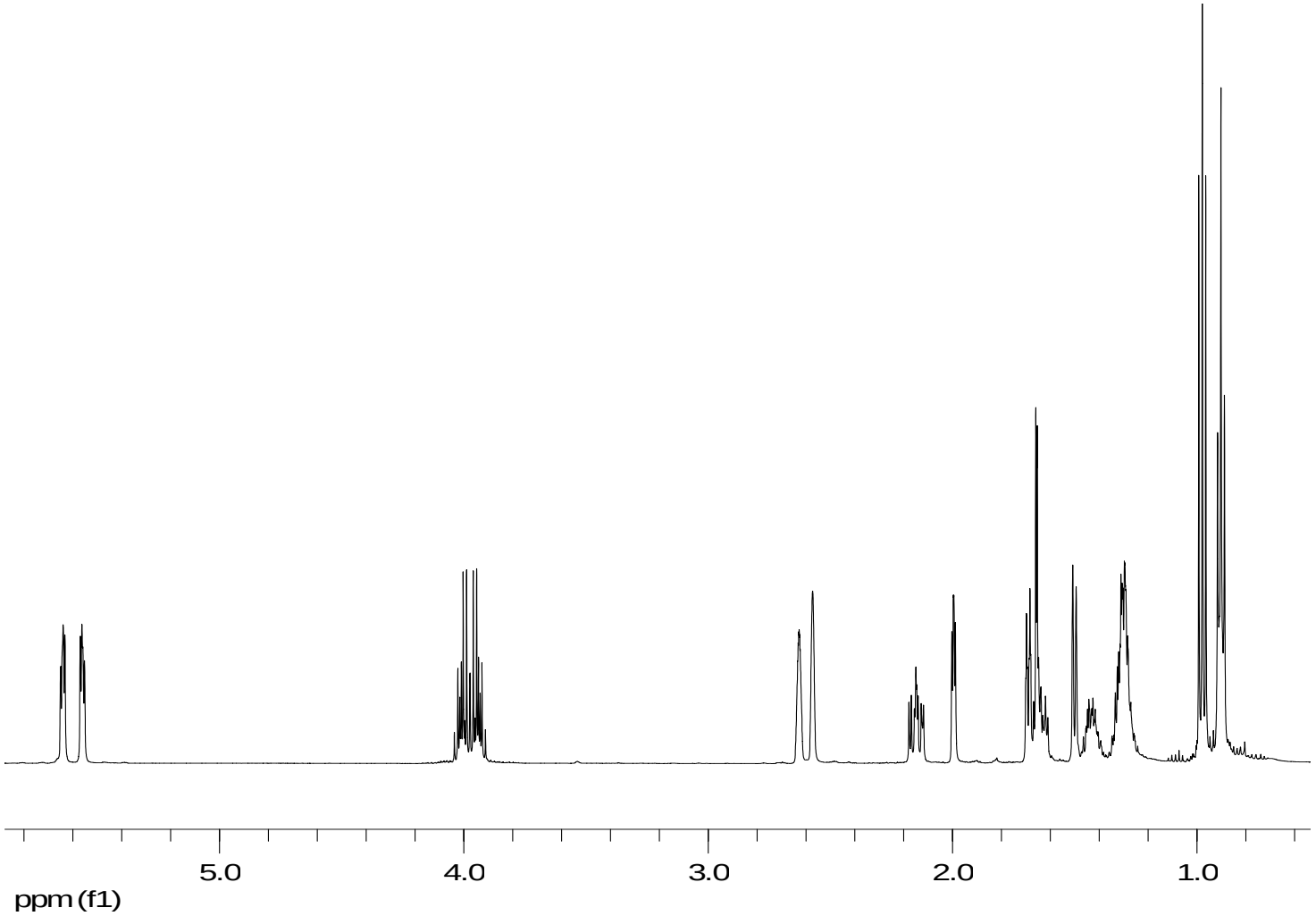
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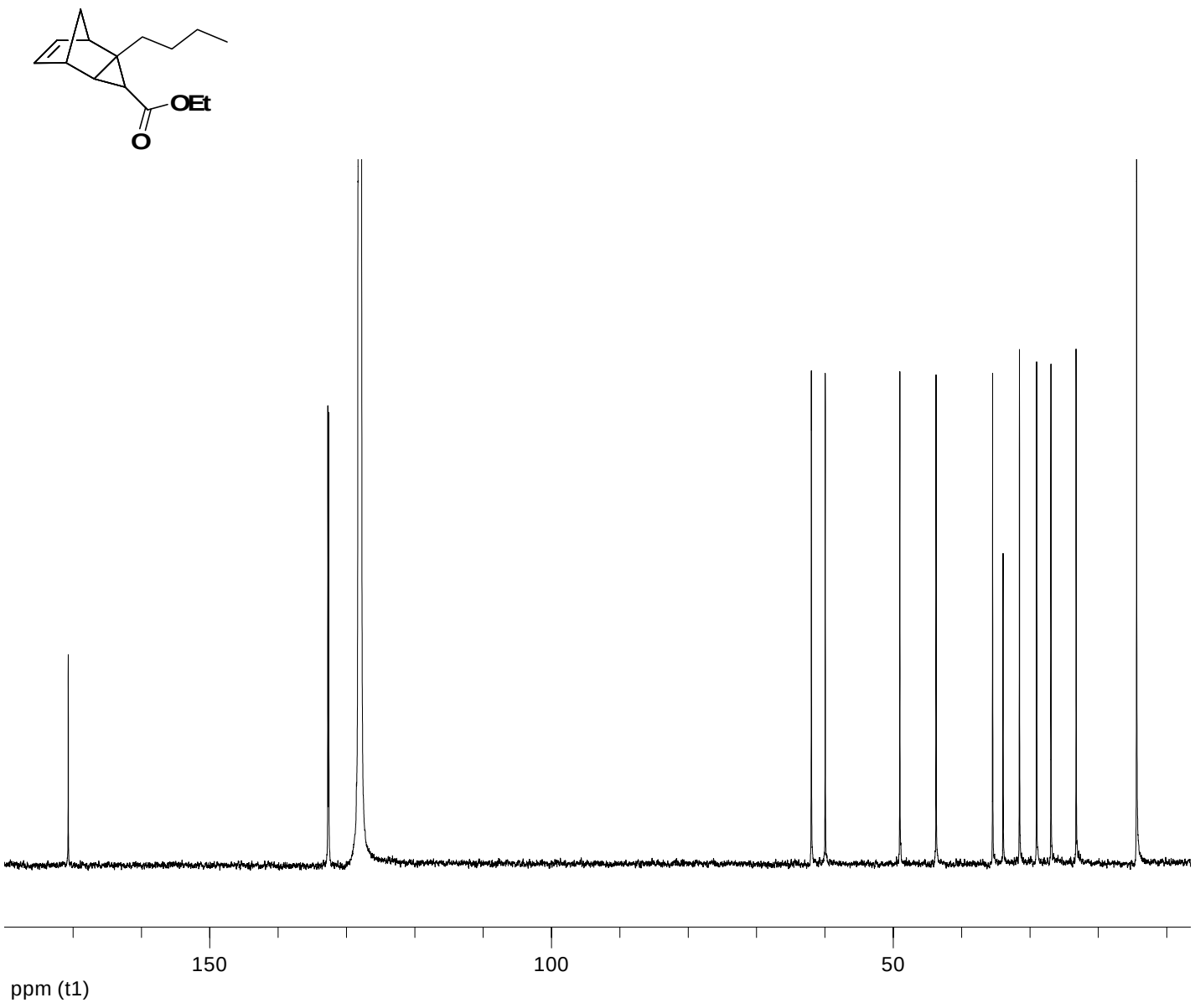
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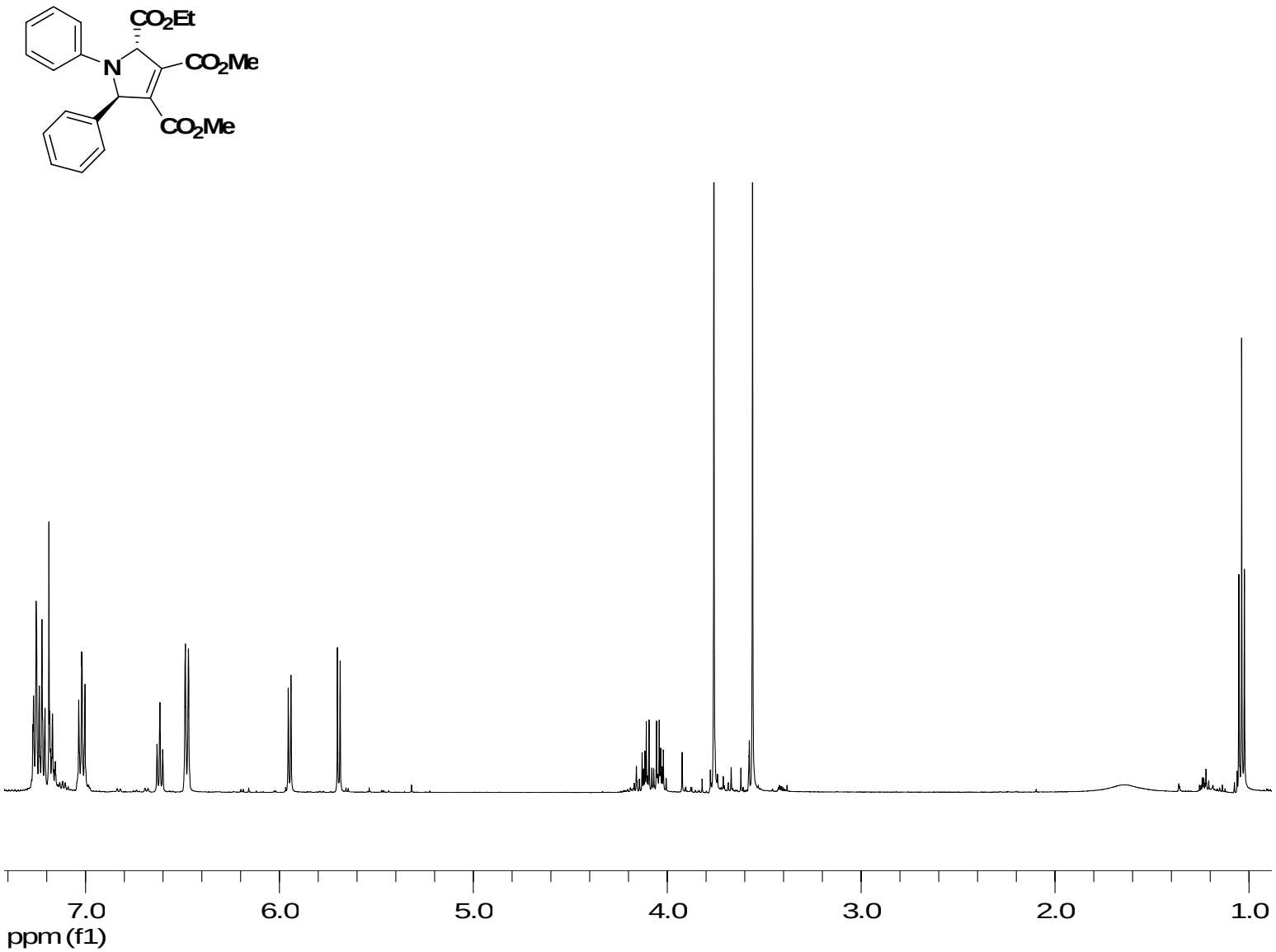
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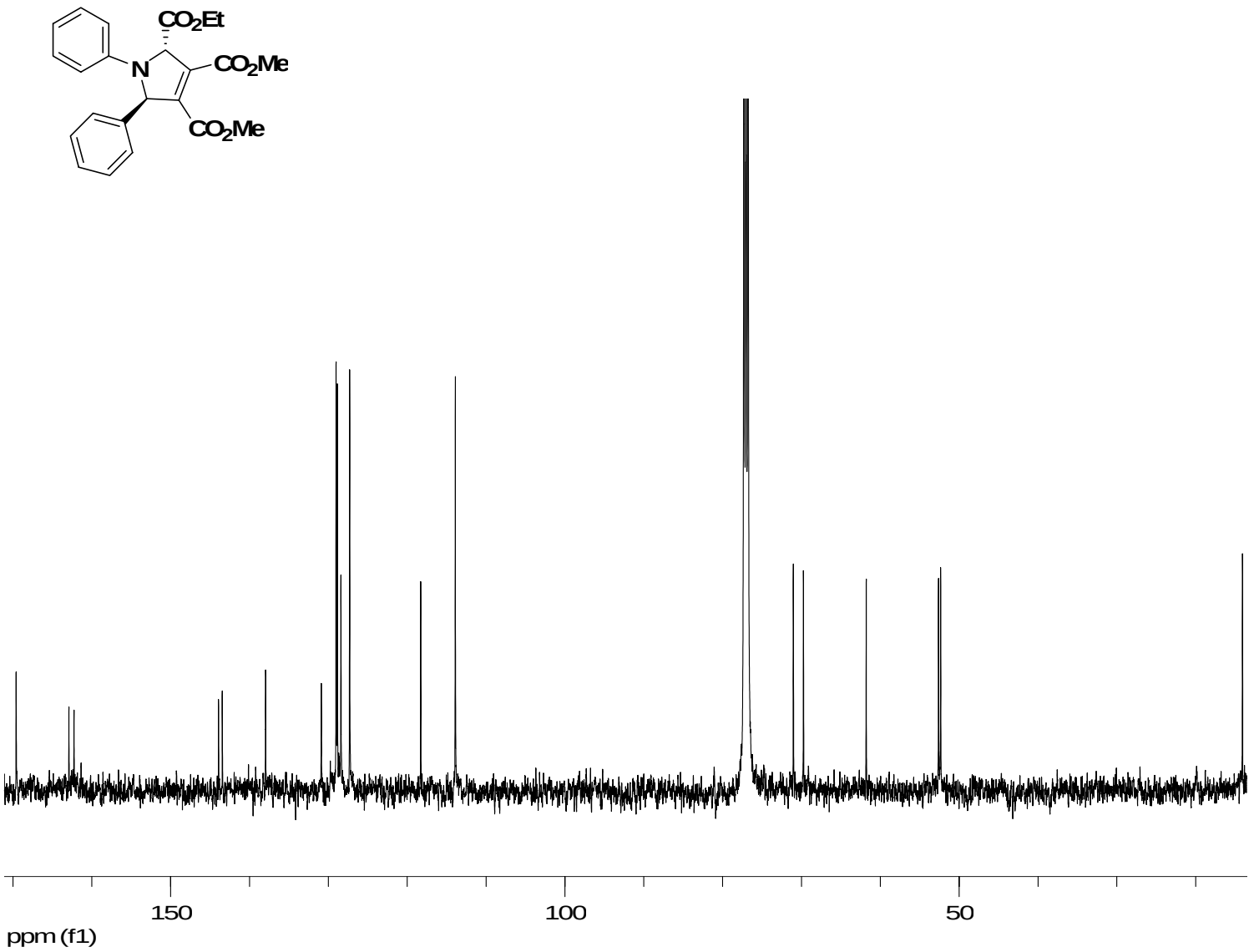
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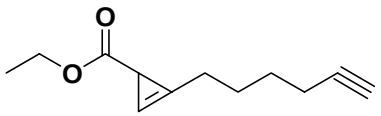
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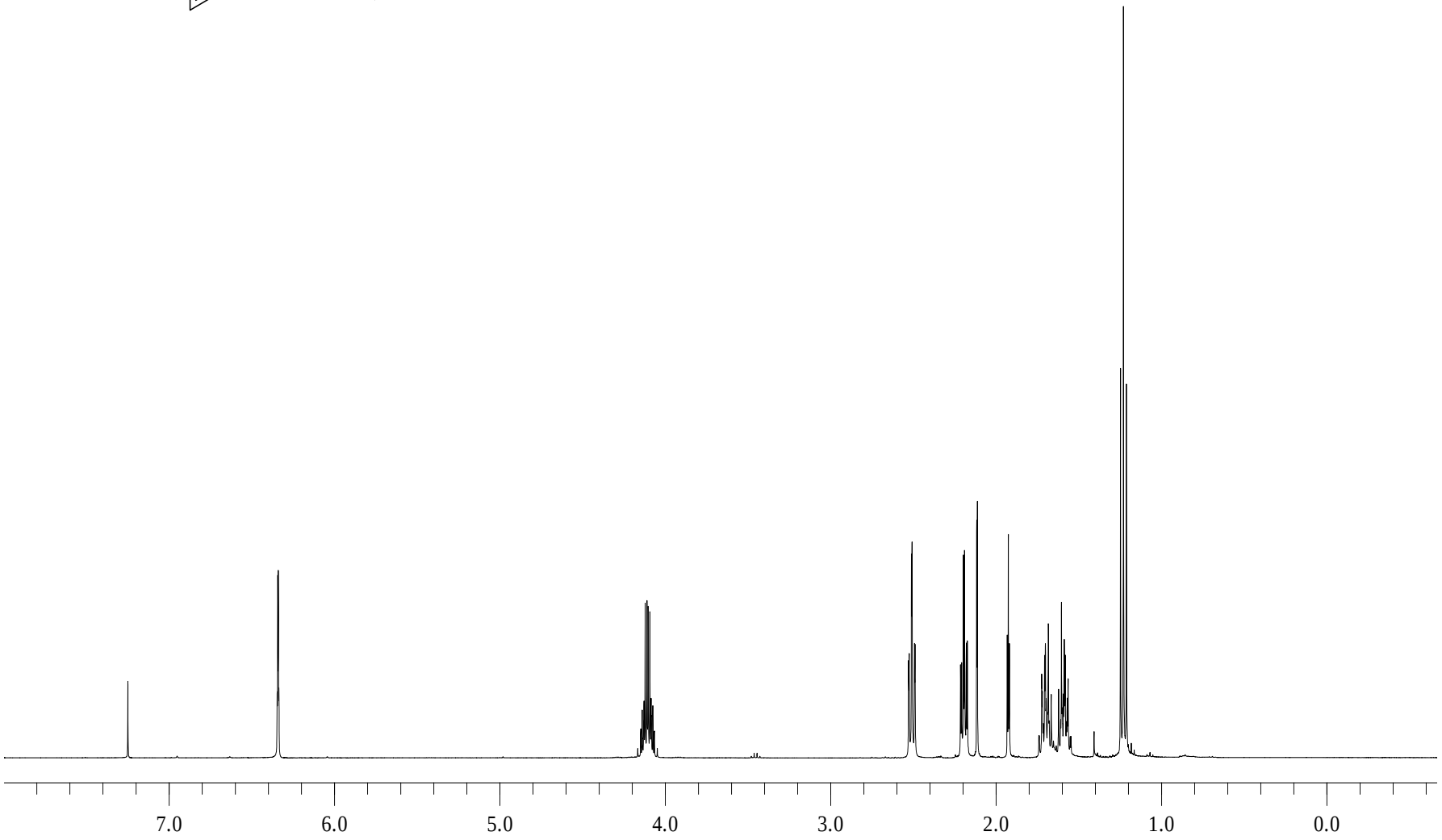
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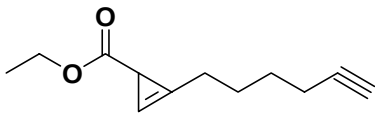
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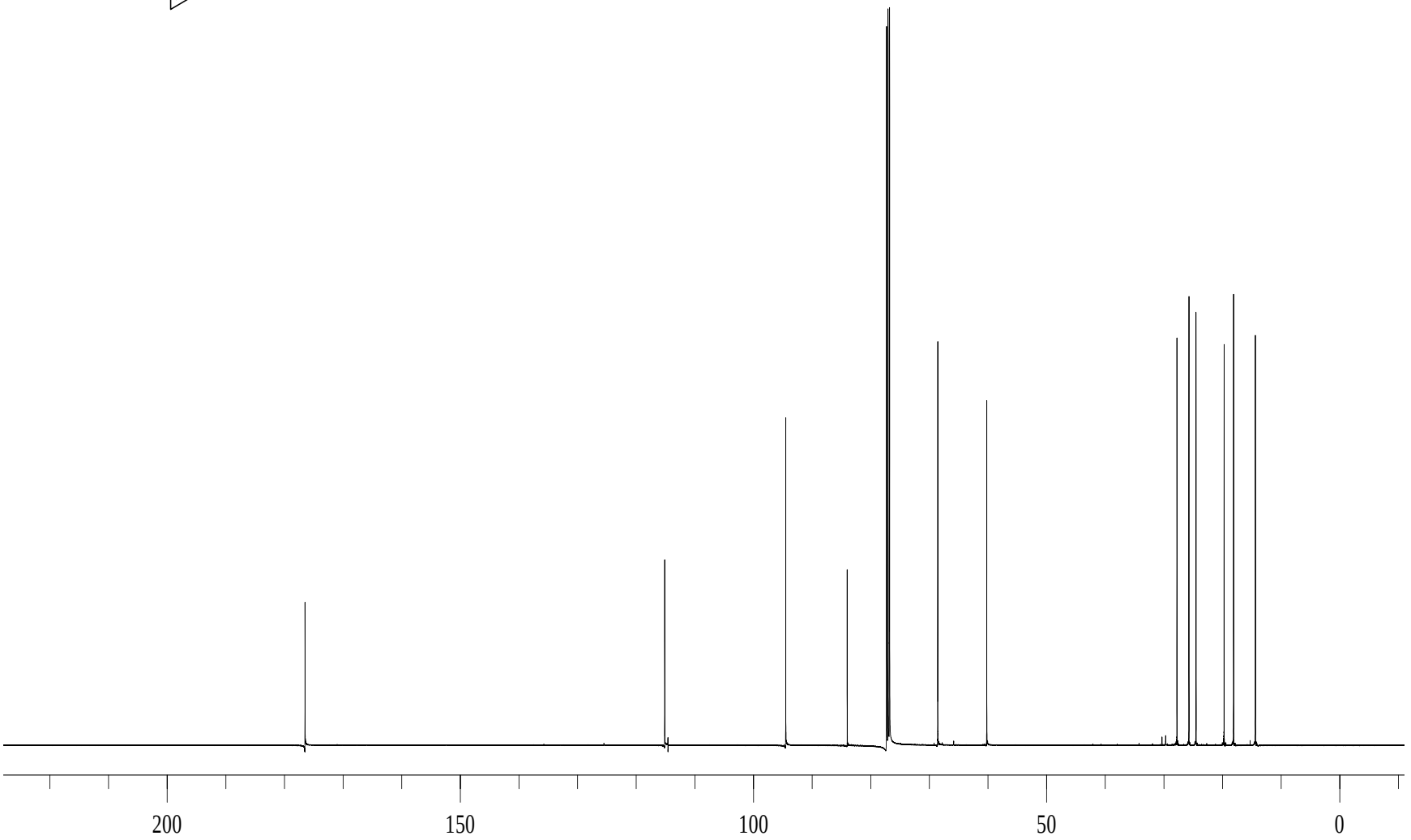
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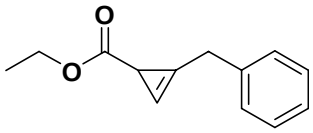
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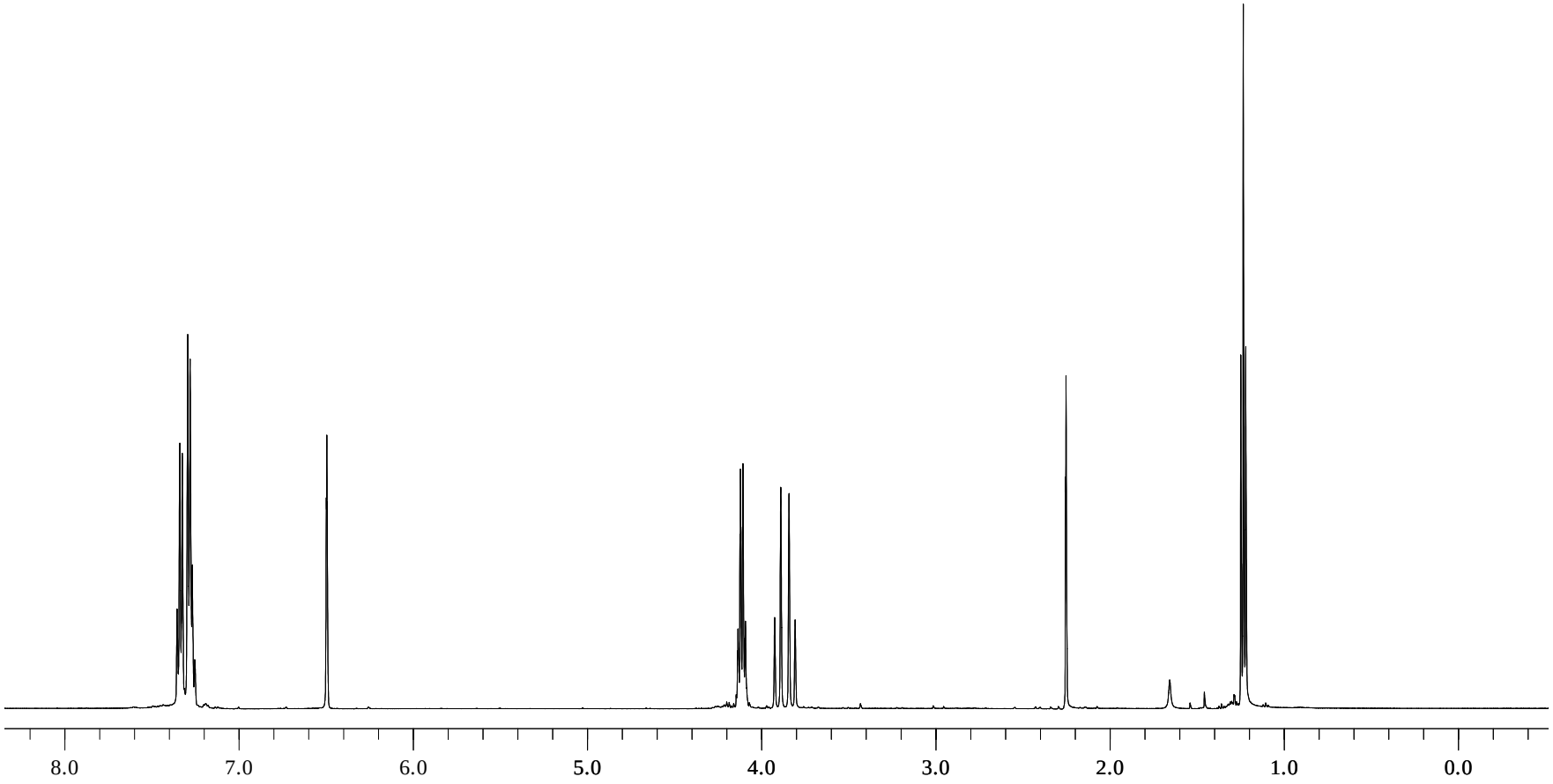
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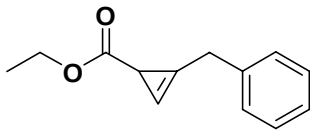
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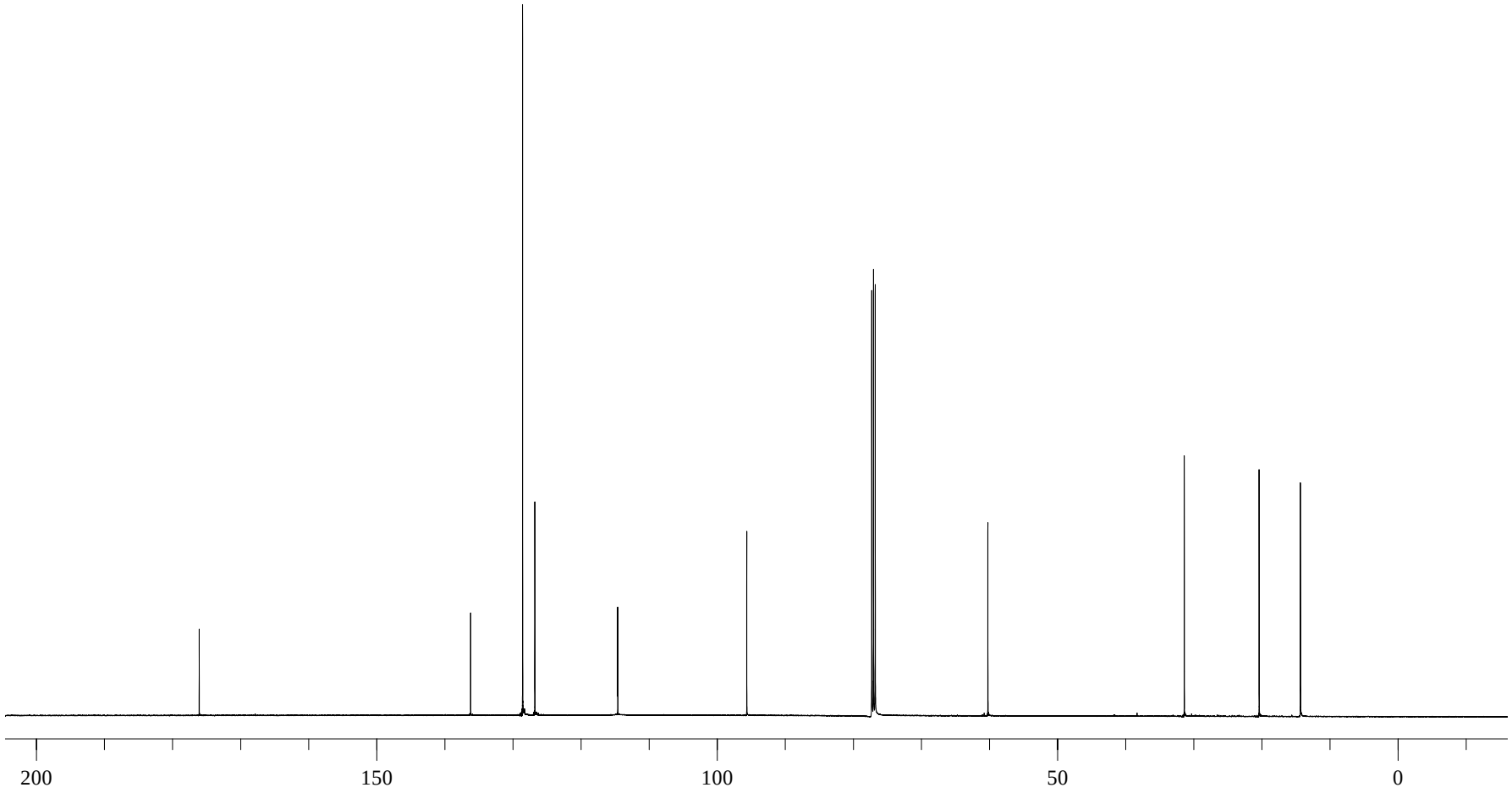
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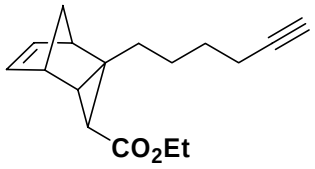
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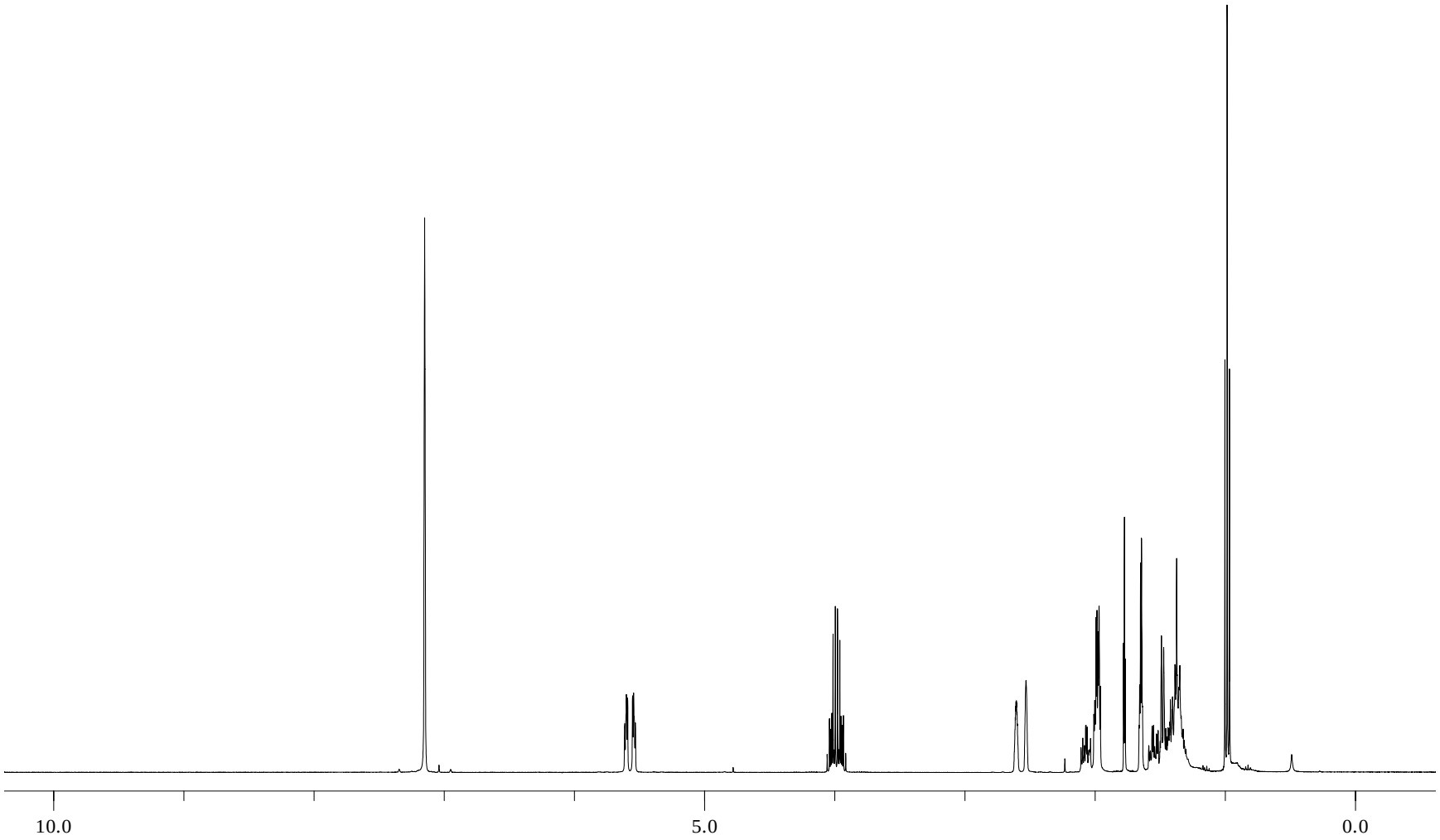
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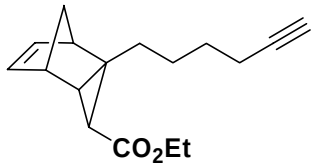
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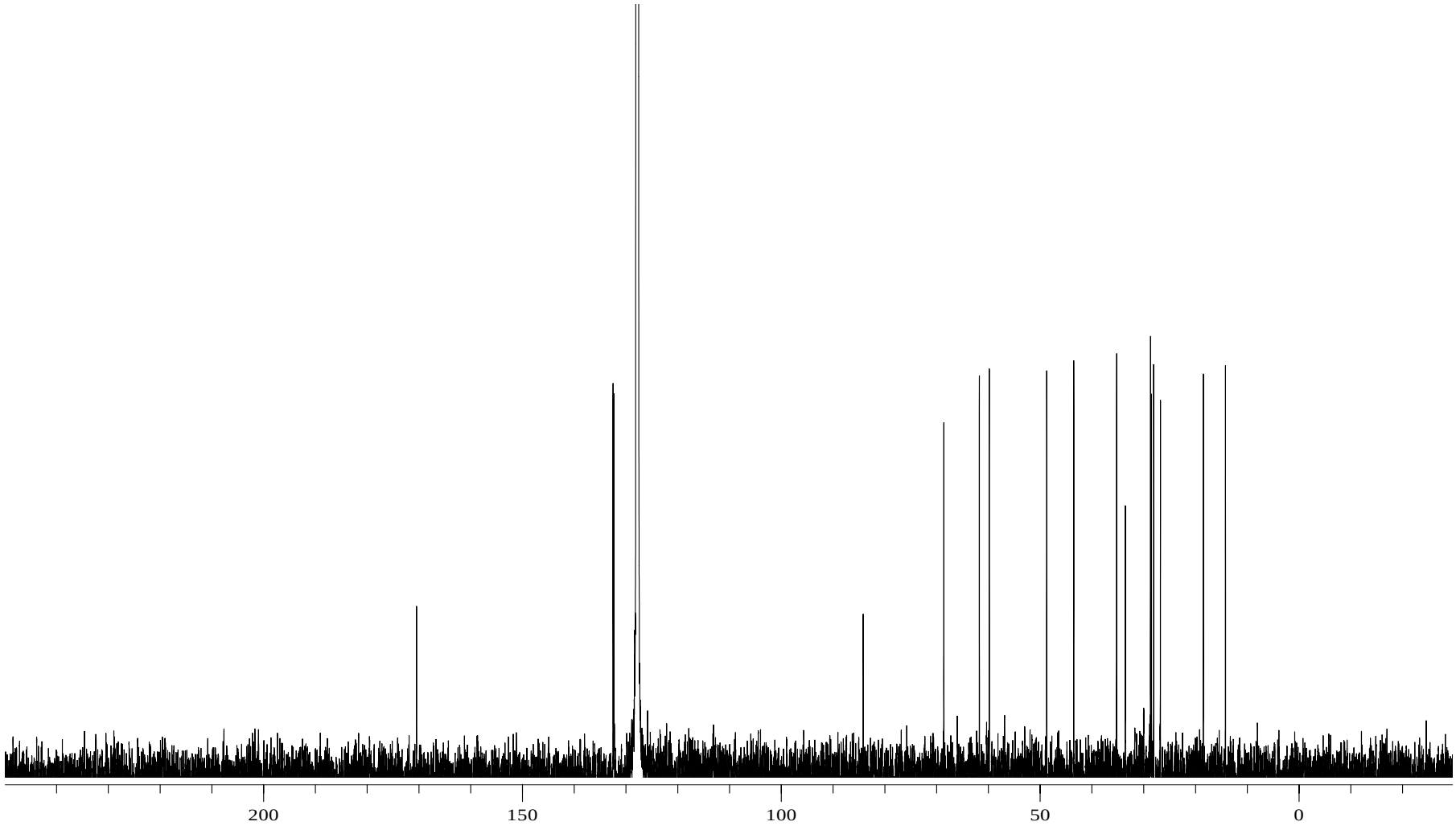
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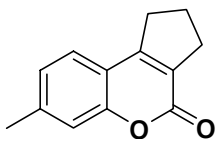
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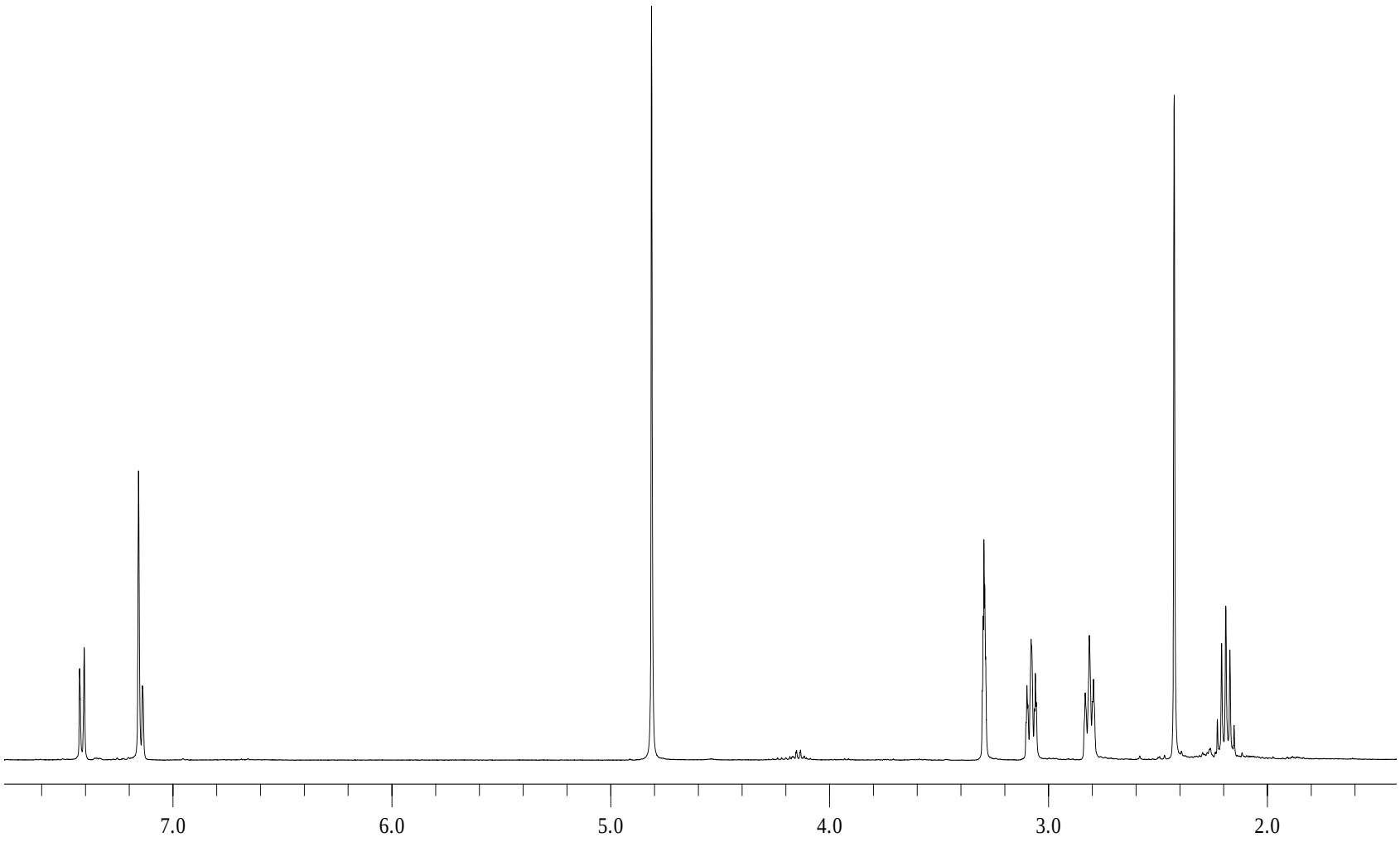
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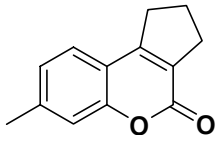
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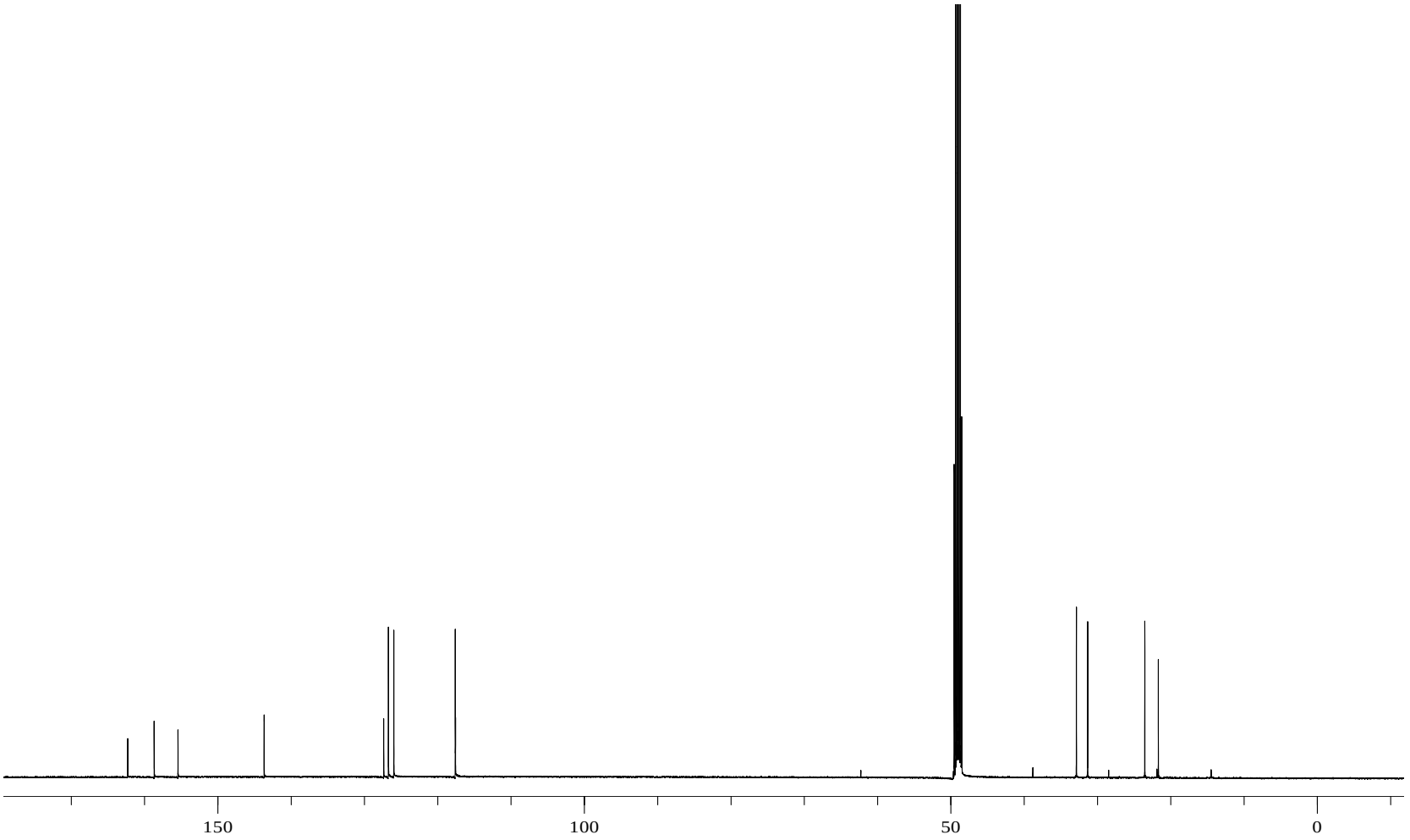
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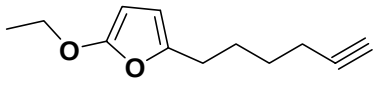
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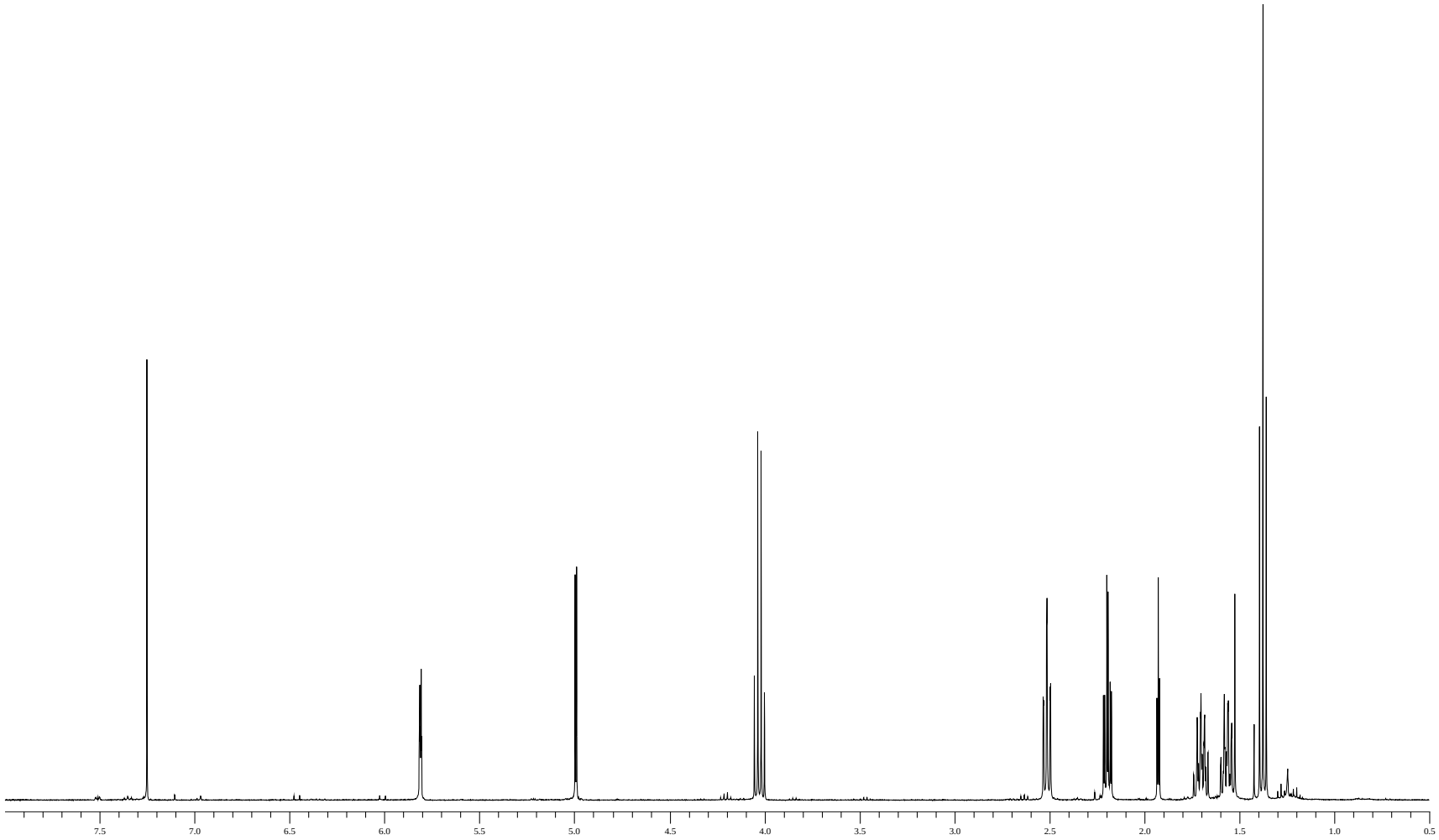
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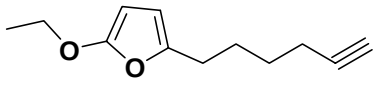
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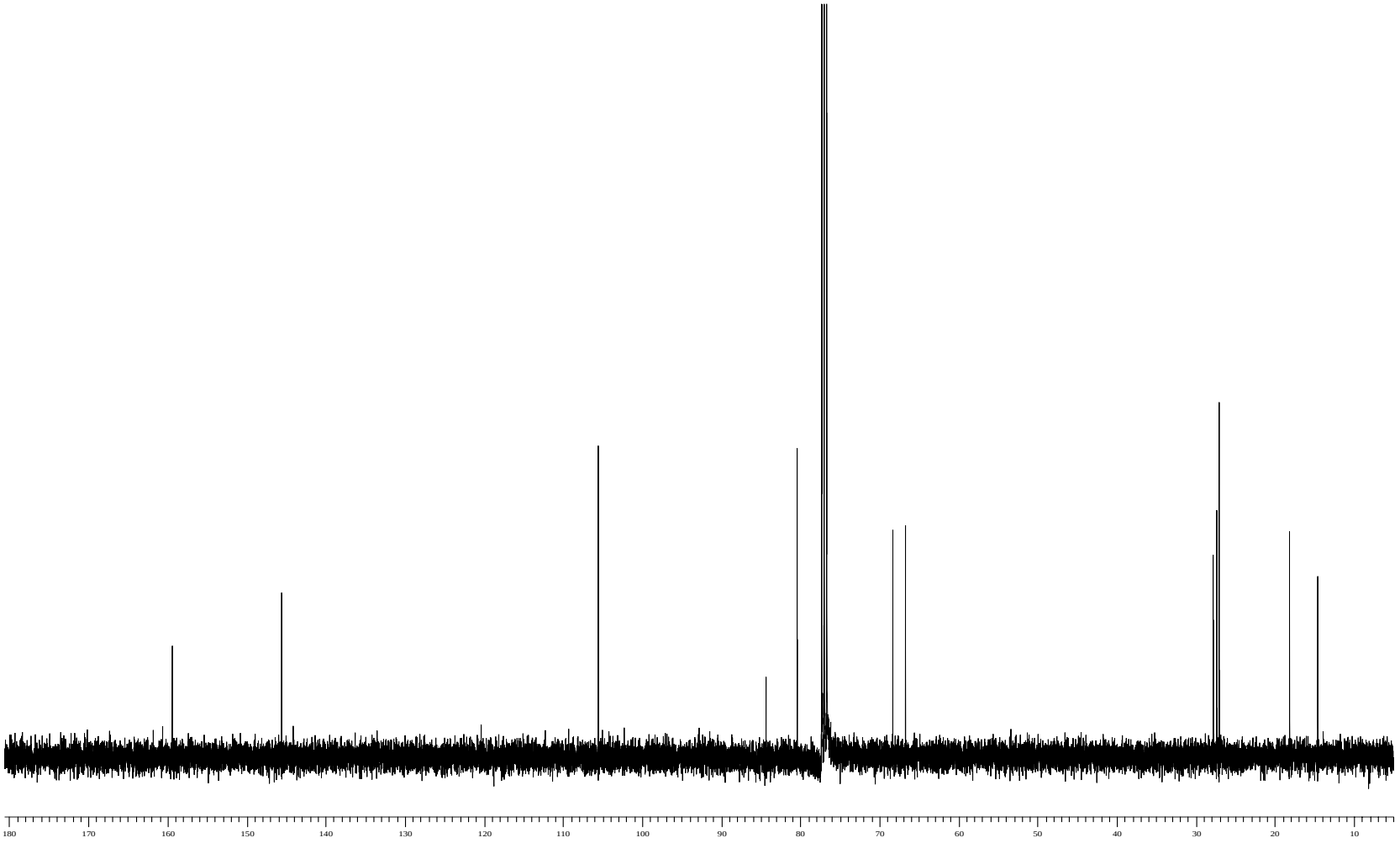
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