Supporting Information

Amide linked Redox-Active Naphthoquinones for the Treatment of Mitochondrial Dysfunction

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General Experimental

Nuclear Magnetic Resonance Spectroscopy

Proton (^{1}H) and carbon (^{13}C) nuclear magnetic resonance spectra were recorded in deuterated chloroform ($CDCl_3$) or DMSO-D_6 on a Varian Mercury 2000 operating at 300 MHz or 75 MHz respectively or alternatively on a Bruker Avance III operating at 400 MHz and 100 Mhz respectively as specified in text. Chemical shifts were recorded as δ values in parts per million (ppm) and referenced to the solvent used. In the case of $CDCl_3$ solvent references were at 7.26 ppm and 77.16 ppm for ^{1}H and ^{13}C respectively, similarly for DMSO-D_6 solvent references were at 2.50 ppm and 39.52 ppm for ^{1}H and ^{13}C respectively).[31] The following abbreviations were used to describe ^{1}H spectra peak splitting patterns; s = singlet, bs = broad singlet, d = doublet, bd = broad doublet, dd = doublet of doublets, t = triplet, ddt = doublet of doublets of triplets, qd = quartet of doublets, q = quartet, quin = quintet, sex = sextet, m = multiplet.

Infrared Spectroscopy

Infrared spectrometry was performed on a Shimadzu FTIR 8400s spectrometer, using NaCl plates. Liquids and solids were recorded as thin films by evaporation from CH_2Cl_2.

Mass Spectroscopy

Mass spectroscopy was performed on Kratos Concept ISQ using electron ionisation with 70eV electrons with an accelerating voltage of 5.3 kV or a Water Xero Triple Quadrupole using 2.5 kV needle voltage with direct infusion electrospray ionisation measuring positive ions. Accurate Mass was also measured by ‘peak matching’ at 10,000 resolution against perfluorokerosene.

Analytical analyses were performed by The Central Science Laboratory at the University of Tasmania. The molecular ions and fragments are quoted with the relative intensities of the peaks referenced to the most intense taken as 100 %.

Column Chromatography

Merck flash grade silica (32-63 μm) was used for column and flash chromatography and were performed according to the general method of Still *et al.*[32]

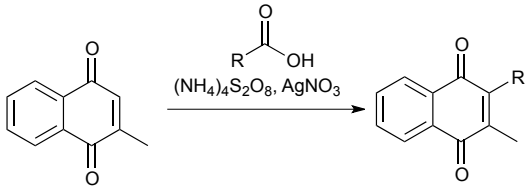
Thin Layer Chromatography (TLC)

Merck Silica gel 60 F254 aluminium backed sheets were used for analytical thin layer chromatography. TLC plates were visualised under a 254 nm UV lamp and/or by treatment with a phosphomolybdic acid (37.5 g), ceric acid (7.5 g), sulphuric acid (37.5 mL), water (720 mL) dip or a potassium permanganate dip (3g, $KMnO_4$, 20 g K_2CO_3, 5 mL 5 % aqueous NaOH, 300 mL), followed by heating.

Solvents and Reagents

All standards and reagents were purified by standard laboratory procedures.[33] Anhydrous magnesium sulphate was used as the drying agent for organic extracts unless otherwise stated and solvents removed under reduced pressure on a rotary evaporator.

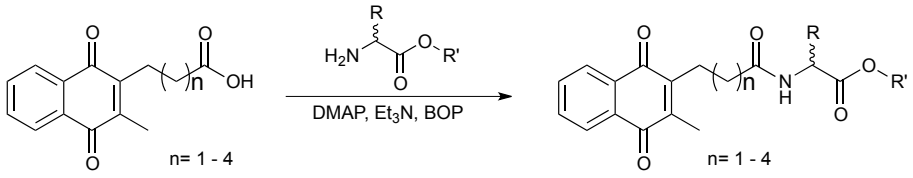
General Procedure A: Silver assisted radical decarboxylation general method:



Carboxylic acid (2 equiv.) was added to a solution of menadione (1 equiv.) in CH_3CN/H_2O (3:1) and the mixture was heated to 75 °C. To this solution, $AgNO_3$ (0.1 equiv.) was added followed by the slow addition of $(NH_4)_2S_2O_8$ (2.5 equiv.) in H_2O (5 mL) over 10 mins. The resulting mixture was stirred for a further 2 h. The mixture was cooled to room temperature, extracted with CH_2Cl_2 and the organic extract

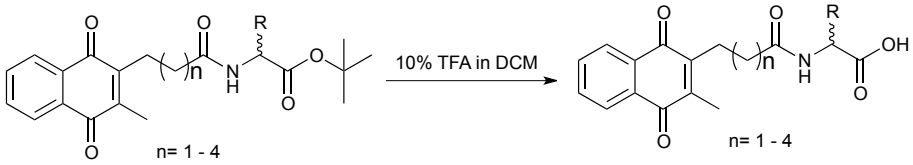
washed with sat. $NaHCO_3$ and H_2O (unless specified otherwise). The organic layer was dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to give the crude product, which was purified by flash chromatography (silica gel).

General Procedure B: Quinone peptide coupling general method:



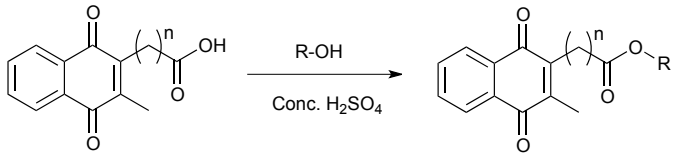
Quinone acid (1 equiv.) was added to anhydrous dichloromethane (5-10ml) under an atmosphere of N_2 and cooled to 0 °C. Amino acid (1 equiv.), dimethylaminopyridine (DMAP, 0.1 equiv.), triethylamine (Et_3N, 2.5 equiv.) and a coupling agent (1.4 equiv.) were added consecutively and the reaction mixture warmed slowly to room temperature before leaving overnight. The reaction was quenched with H_2O (20mL) and the organic layer washed with sat. $KHSO_4$ solution, sat. $NaHCO_3$ solution and H_2O. The organic layer was dried with $MgSO_4$, filtered and the solvent removed under reduced pressure to give a crude product, which was purified by flash chromatography (silica gel) to give the pure analogue.

General Procedure C: t-butyl ester deprotection method:



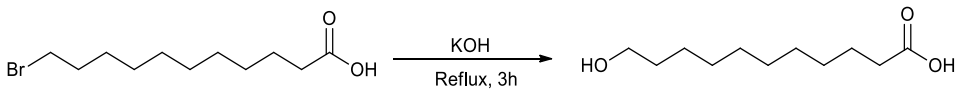
The t-butyl esters were added to 10% TFA in dichlormethane (5.0 mL) and the reaction mixture left stirring at room temperature over night before being removed under reduced pressure. The crude product was obtained and purified by flash chromatography (silica gel) to give the pure analogue.

General Proceedure D: Esterification Procedure



A solution of **12 – 17** in R-OH was stirred at room temperature overnight in the presence a catalytic amount of conc. H_2SO_4. Reaction was quenched with $NaHCO_3$ $_{(aq)}$ until solution was weakly alkaline and the compound extracted with CH_2Cl_2 (20 mL), dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to give the pure product.

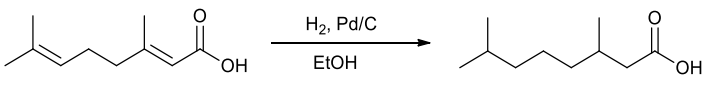
11-Hydroxyundecanoic acid



As described by Duveau *et al.* a solution of 11-bromoundecanoic acid (2.01 g, 7.56 mmol) in aqueous KOH (1.027 g, 18.3 mmol) was refluxed for 3h. Reaction was quenched with approximately 5M H_2SO_4 resulting in the formation of a thick white precipitate which was filtered and the precipitate collected to give the pure product as a white solid in a quantitative yield. Spectral data was consistent with that reported [1].

^{1}H NMR δ ($CDCl_3$, 300 MHz): 1.24 – 1.37 (m, 12H), 1.51 – 1.64 (m, 4H), 2.33 (t, J = 7.4 Hz, 2H), 3.63 (t, J = 6.6 Hz, 2H), 5.14 (s, 1H).

3,7-Dimethyloctanoic acid

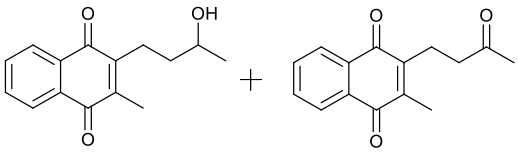


To a solution of geranic acid (500 mg, 2.97 mmol) in ethanol (30 mL) 10 % palladium on carbon was added to the reaction vessel under an atmosphere of nitrogen. Reaction vessel was placed on Parr Shaker Hydrogenator under an

atmosphere of hydrogen at 35 psi for 2h. Reaction mixture was filtered through a celite plug and the solvent removed under reduced pressure to give the product in a quantitative yield (583 mg, 3.38 mmol).

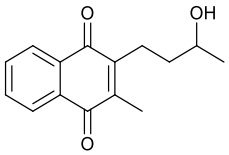
^{1}H NMR δ ($CDCl_3$, 300 MHz): 0.86 (d, *J* = 6.6 Hz, 6H), 0.96 (d, *J* = 6.6 Hz, 3H), 1.11 – 1.33 (m, 6H), 1.52 (nonet, *J* = 6.6 Hz, 1H), 1.94 – 1.97 (m, 1H), 2.13 (dd, *J* = 14.9, 8.1 Hz, 1H), 2.34 (dd, *J* = 14.9, 5.8 Hz, 1H)

2-(3-Hydroxybutyl)-3-methyl-1,4-naphthoquinone (6) and 2-(3-Oxobutyl)-3-methyl-1,4-naphthoquinone (7)



6 and **7** were prepared according to general procedure A from menadione (**4**) (548 mg, 3.18 mmol) and γ-valerolactone (0.56 mL, 5.85 mmol) and the products purified by flash chromatography (30 % ethyl acetate/hexanes followed by 50 % ethyl acetate/hexanes) to give **6** as a brown semi-solid in a 9 % yield (74 mg, 0.302 mmol) and **7** as yellow crystalline solid in 3 % yield (25 mg, 0.103 mmol) with a melting point of 84-87 °C.

2-(3-Hydroxybutyl)-3-methyl-1,4-naphthoquinone (6)



^{1}H NMR δ ($CDCl_3$, 300 MHz): 1.22 (d, *J* = 6.2, 3H), 1.59 – 1.68 (m, 2H), 2.21 (s, 3H), 2.65 – 2.86 (m, 2H), 3.69 – 3.77 (m, 1H), 7.67 – 7.70 (m, 2H), 8.05 – 8.08 (m, 2H)

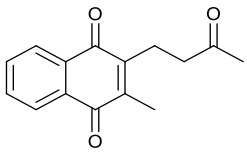
^{13}C NMR δ (CDCl3, 75 MHz): 12.8, 23.2, 23.5, 37.9, 67.1, 126.4, 126.6, 132.2, 132.3, 133.6, 133.7, 144.1, 147.0, 185.3, 185.5

HRMS: For $C_{15}H_{16}O_3$, predicted 244.10994, found 244.11002

MS *m/z* (EI+): 244 (M+, 15), 226 (34), 202 (100), 186 (50), 173 (32), 157 (45), 128 (60)

IR V_{max}: 3488, 2970, 1780, 1703, 1658, 1595, 1377, 1329, 1296, 714

2-(3-Oxobutyl)-3-methyl-1,4-naphthoquinone (7)



^{1}H NMR δ ($CDCl_3$, 400 MHz): 2.17 (s, 3H), 2.20 (s, 3H), 2.65 (t, *J* = 7.7 Hz, 2H), 2.87 (t, *J* = 7.7 Hz, 2H), 7.67 – 7.69 (m, 2H), 8.03 – 8.07 (m, 2H)

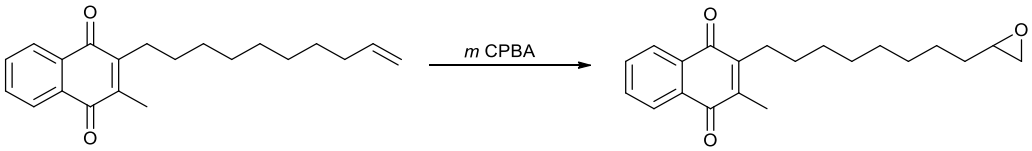
^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.86, 21.84, 29.96, 42.11, 126.42, 126.52, 132.28, 132.32, 133.63, 133.68, 144.26, 145.98, 184.85, 185.17, 207.14

HRMS: For $C_{15}H_{14}O_3$, predicted 242.09424, found 242.09421

MS *m/z* (EI+): 242 (M+, 16), 200 (100), 171 (16), 128 (24)

IR V_{max}: 2946, 2359, 1713, 1661, 1619, 1595, 1376, 1328, 1297, 1164, 712

2-Methyl-3-(9,10-epoxydecyl)-1,4-naphthoquinone (8)



29 was added slowly to a solution of *m*-CPBA (50 %, 85 mg, 0.493 mmol) in CH_2Cl_2 (5 mL) at 0 °C with continuous stirring for a 10 min period before the reaction mixture was warmed to room temperature and left stirring overnight. The reaction mixture was washed with sat. $NaHCO_3$ solution and H_2O. The organic layer was dried with $MgSO_4$, filtered and the solvent removed under reduced pressure to give the

crude product which was purified by flash chromatography (20 % ethyl acetate/hexanes) to give **8** as a yellow powdered solid in 73 % yield (38 mg, 0.117 mmol) with a melting point of 66-67°C.

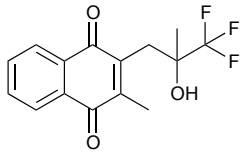
^{1}H NMR δ ($CDCl_3$, 300 MHz): 1.30 – 1.51 (m, 14H), 2.16 (s, 3H), 2.42 – 2.45 (m, 1H), 2.60 (t, *J* = 7.5 Hz, 2H), 2.70 – 2.73 (m, 1H), 2.86 – 2.89 (m, 1H), 7.64 – 7.68 (m, 2H), 8.03 – 8.06 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 75 MHz): 12.81, 26.11, 27.25, 28.89, 29.47. 29.56, 29.59, 30.10, 32.63, 47.28, 52.55, 126.33, 126.42, 132.33, 132.37, 133.44, 133.48, 143.26, 147.68, 184.87, 185.52

HRMS: For $C_{21}H_{26}O_3$, predicted 326.18819, found 326.18887, MS *m/z* (EI+): 326 (M+, 45), 310 (10), 211 (15), 187 (100), 158 (25)

IR V_{max} : 2927, 2849, 1659, 1616, 1594, 1464, 1377, 1328, 1295, 717

2-methyl-3-(3,3,3-trifluoro-2-hydroxy-2-methylpropyl)-1,4-naphthoquinone (10)



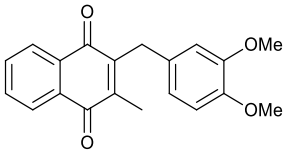
10 was prepared according to general procedure A from menadione (**4**) (748 mg, 4.342 mmol) and 3-(trifluoro)-3-hydroxybutyric acid (245 mg, 1.4253 mmol) and the product purified by flash chromatography (90 % CH_2Cl_2/hexanes) to give **10** as a crystalline yellow solid in 14 % yield (60 mg, 0.2008 mmol) with a melting point of 42-44 °C.

^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.32 (s, 3H), 2.25 (s, 3H), 2.94 (d, *J* = 14.0 Hz, 1H), 3.23 (d, *J* = 14.0 Hz, 1H), 4.12 (bs, 1H), 7.72 – 7.74 (m, 2H), 8.07 – 8.10 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 14.2, 20.8, 3.28, 74.1 (q, $J_{C\text{-}F}$ = 28.2 Hz), 126.2 (q, $J_{C\text{-}F}$ = 285.0 Hz), 126.7, 126.9, 131.7, 132.0, 133.9, 134.3, 140.8, 148.0, 184.6, 187.6

IR V_{max}: 3462, 1662, 1618, 1539, 1462, 1381, 1332, 1286, 1153, 1097, 779

2-(3,4-Dimethoxybenzyl)-3-methyl-1,4-naphthoquinone (11)



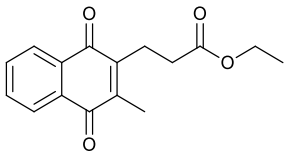
11 was prepared according to general procedure A from menadione (**4**) (503 mg, 2.918 mmol) and 3,4-dimethoxyphenylacetic acid (1.140 g, 5.932 mmol) and the product purified by flash chromatography (40 % ethyl acetate/hexanes) to give **11** as a crystalline yellow solid in 18 % yield (171 mg, 0.5309 mmol) with a melting point of 65-70 °C. Spectral data was consistent with that reported [2].

^{1}H NMR δ ($CDCl_3$, 300 MHz): 2.25 (s, 3H), 3.80 (s, 3H), 3.83 (s, 3H), 3.95 (s, 2H), 6.73 (s, 2H), 6.80 (s, 1H), 7.66 – 7.69 (m, 2H), 8.05 – 8.08 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 75 MHz): 13.45, 32.19, 56.09, 111.51, 112.44, 120.68, 126.47, 126.66, 130.69, 132.26, 132.33, 133.66, 133.68, 144.34, 145.62, 147.90, 149.24, 184.99, 185.64

IR V_{max}: 2945, 2835, 1658, 1616, 1595, 1514, 1464, 1375, 1331, 1293, 1261, 1237, 1141, 1028, 747, 701

Ethyl-3-(3-methyl-1,4-naphthoquinone-2-yl)propanoate (12)



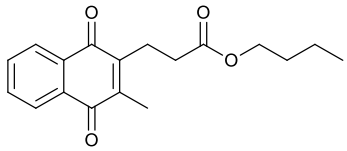
12 was prepared according to general procedure D from **20** (33 mg, 0.135 mmol) in ethanol to give the **12** as a viscous yellow oil in 85 % yield (31 mg, 0.115 mmol). Spectral data was consistent with that reported [3].

^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.22 (t, *J* = 7.2 Hz, 3H), 2.20 (s, 3H), 2.51 (t, *J* = 7.6 Hz, 2H), 2.95 (t, *J* = 7.9Hz, 2H), 4.11 (q, *J* = 7.2. 2H), 7.66 – 7.68 (m, 2H), 8.04 – 8.06 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.89, 14.36, 22.97, 33.01, 60.85, 126.47, 126.48, 132.26, 132.28, 133.63, 133.64, 144.45, 145.39, 172.56, 184.59, 185.22

IR V_{max}: 2983, 1733, 1661, 1595, 1294, 1259

Butyl-3-(3-methyl-1,4-naphthoquinone-2-yl)propanoate (13)



13 was prepared according to general procedure D from **20** (32 mg, 0.130 mmol) in butanol to give **5o** as a viscous yellow oil in 86 % yield (33 mg, 0.111 mmol).

^{1}H NMR δ ($CDCl_3$, 400 MHz): 0.88 (t, *J* = 7.4 Hz, 3H), 1.33 (sextet, *J* = 7.3 Hz, 2H), 1.53 – 1.60 (m, 2H), 2.21 (s, 3H), 2.52 (t, *J* = 7.9 Hz), 2.95 (t, *J* =7.9 Hz, 2H), 4.06 (t, *J* = 6.7 Hz, 2H), 7.67 – 7.69 (m, 2H), 8.04 – 8.07 (m, 2H)

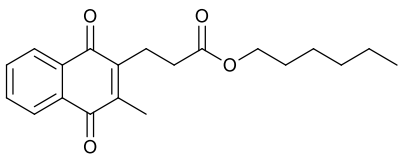
^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.90, 13.86, 19.30 23.02, 30.80, 33.03, 64.80, 126.48, 126.50, 132.28, 132.30, 133.64, 133.65, 144.47, 145.42, 172.66, 184.60, 185.22

HRMS: For $C_{18}H_{20}O_4$, predicted 300.13616, found 300.13678

MS *m/z* (EI+): 300 (M+, 5), 243 (15), 226 (84), 198 (100), 181 (14)

IR V_{max}: 2959, 2874, 1733, 1660, 1596, 1379, 1329, 1294, 789, 714

Hexyl-3-(3-methyl-1,4-naphthoquinone-2-yl)propanoate (14)



14 was prepared according to general procedure D from **20** (32 mg, 0.136 mmol) in hexanol to give **14** as a viscous brown oil in 93 % yield (41 mg, 0.123 mmol).

^{1}H NMR δ ($CDCl_3$, 400 MHz): 0.85 (t, *J* = 6.9 Hz, 3H), 1.25 – 1.31 (m, 6H), 1.55 – 1.59 (m, 2H), 2.21 (s, 3H), 2.52 (t, *J* = 7.8 Hz, 2H), 2.95 (t, *J* = 7.9 Hz, 2H), 4.04 (t, *J* = 6.8 Hz, 2H), 7.66 – 7.69 (m, 2H), 8.04 – 8.06 (m, 2H)

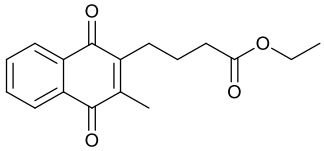
^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.89, 14.15, 22.66, 23.01, 25.74, 28.70, 31.57, 33.05, 126.47, 126.49, 132.26, 132.28, 133.64, 133.65, 144.47, 145.41, 172.71, 184.60, 185.23

HRMS: For $C_{20}H_{24}O_4$, predicted 328.16746, found 328.16812

MS *m/z* (EI+): 328 (M+, 5), 244 (22), 226 (82), 198 (100)

IR V_{max}: 2930, 2857, 1733, 1661, 1596, 1329, 1329, 1293, 1172, 790, 714

Ethyl-4-(3-methyl-1,4-naphthoquinone-2-yl)butanoate (15)



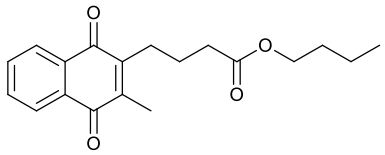
15 was prepared according to general procedure D from **21** (31 mg, 0.119 mmol) in ethanol to give **15** as a viscous yellow oil in 91 % yield (31 mg, 0.108 mmol). Spectral data was consistent with that reported [3].

^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.80 (quin, *J* = 7.8 Hz, 2H), 1.24 (t, *J* =7.1 Hz, 3H), 2.19 (s, 3H), 2.39 (t, *J* = 7.2, 2H), 2.67 (t, *J* = 7.9 Hz, 2H), 4.11 (q, *J* = 7.1 Hz, 2H), 7.66 – 7.68 (m, 2H), 8.04 – 8.06 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.84, 14.41, 23.91, 26.50, 34.20, 60.61, 126.41, 126.47, 132.29, 132.31, 133.56, 133.57, 144.04, 146.47, 173.29, 184.72, 185.38

IR V_{max}: 2976, 1733, 1659, 1377, 1327, 1294, 1260, 1158, 717

Butyl-4-(3-methyl-1,4-naphthoquinone-2-yl)butanoate (16)



16 was prepared according to general procedure D from **21** (28 mg, 0.110 mmol) in butanol to give **16** as a viscous yellow oil in >95 % yield (37 mg, 0.119 mmol).

^{1}H NMR δ ($CDCl_3$, 400 MHz): 0.91 (at, *J* = 7.4 Hz, 3H), 1.35 (sextet, *J* = 7.6 Hz, 2H), 1.58 (quin, *J* = 7.2 Hz, 2H), 1.80 (quin, *J* =7.6 Hz, 2H), 2.19 (s, 3H), 2.39 (t, *J* = 7.2 Hz, 2H) 2.67 (t, *J* = 7.9 Hz, 2H), 4.06 (t, *J* = 6.7 Hz, 2H), 7.66 – 7.68 (m, 2H), 8.04 – 8.06 (m, 2H)

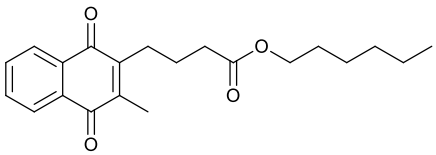
^{13}C NMR δ ($CDCl_3$, 100 MHz): 13.84, 13.87, 19.31, 23.92, 26.51, 30.84, 34.18, 64.56, 126.41, 126.47, 132.29, 132.31, 133.55, 133.56, 144.03, 146.47, 173.40, 184.71, 185.38

HRMS: For $C_{19}H_{22}O_4$, predicted 314.15181, found 314.15127

MS *m/z* (EI+): 314 (M+, 45), 257 (18), 240 (64), 225 (55), 212 (100), 198 (66), 181 (15)

IR V_{max}: 2959, 2874, 1733, 1660, 1596, 1379, 1328, 1294, 1166, 717

Hexyl-4-(3-methyl-1,4-naphthoquinone-2-yl)butanoate (17)



17 was prepared according to general procedure D from **21** (301 mg, 0.118 mmol) in hexanol to give **17** as a viscous brown oil in >95 % yield (44 mg, 0.128 mmol).

^{1}H NMR δ ($CDCl_3$, 400 MHz): 0.86 (t, *J* = 6.8 Hz, 3H), 1.23 – 1.34 (m, 6H), 1.59 (quin, *J* = 7.0 Hz, 2H), 1.80 (quin, *J* = 7.6 Hz, 2H), 2.19 (s, 3H), 2.39 (t, *J* = 7.2 Hz,

2H), 2.67 (t, *J* = 7.9 Hz, 2H), 4.04 (t, *J* = 6.8 Hz, 2H), 7.65 – 7.67 (m, 2H), 8.03 – 8.06 (m, 2H)

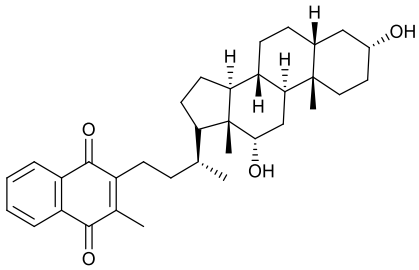
^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.83, 14.15, 22.68, 23.92, 25.75, 26.50, 28.76, 31.59, 34.18, 64.87, 126.40, 126.46, 132.28, 132.30, 133.54, 133.56, 144.03, 146.46, 173.41, 184.71, 185.37

HRMS: For $C_{21}H_{26}O_4$, predicted 342.18311, found 342.18321

MS *m/z* (EI+): 342 (M+, 35), 258 (22), 240 (60), 225 (50), 212 (100), 198 (50)

IR V_{max}: 2956, 2870, 1733, 1661, 1596, 1379, 1328, 1295, 1166, 717

Deoxycholic Quinone Derivative (18)



18 was prepared according to general procedure A from menadione (**4**) (507 mg, 2.94 mmol) and deoxycholic acid (2.320 g, 5.91 mmol) and the product purified by flash chromatography (80 % ethyl acetate/hexanes) to give **18** as a yellow semisolid in 19 % yield (288 mg , 0.555 mmol).

^{1}H NMR δ (CDCl3, 300 MHz): 0.68 (s, 3H), 0.95 – 1.89 (m, 32H), 2.16 (s, 3H), 2.46 – 2.53 (m, 1H), 2.65 – 2.71 (m, 1H), 3.57 – 3.62 (m, 1H), 4.00 (s, 1H), 7.66 – 7.68 (m, 2H), 8.04 – 8.06 (m, 2H)

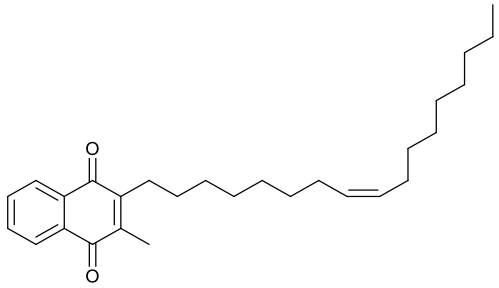
^{13}C NMR δ (CDCl3, 75 MHz): 12.6, 12.9, 17.8, 23.3, 23.8, 24.0, 26.3, 27.3, 27.7, 28.8, 30.6, 33.8, 34.3, 34.7, 35.4, 36.2, 36.3, 36.5, 42.2, 46.7, 47.2, 48.4, 72.0, 73.4, 126.3, 126.4, 132.3, 132.4, 133.4, 133.5, 143.0, 148.2, 184.0, 185.5

HRMS: For $C_{34}H_{46}O_4$, predicted 518.33961, found 518.33835

MS *m/z* (EI+): 518 (M+, 100), 500 (25), 313 (28), 271 (42), 227 (40), 187 (88)

IR V_{max}: 3395, 2936, 2865, 1695, 1659, 1652, 1615, 1596, 1447, 1377, 1327, 1293, 1042, 910, 732, 718, 693

(Z) 2-(8-Heptadecenyl)-3-methyl-1,4-naphthoquinone (19)



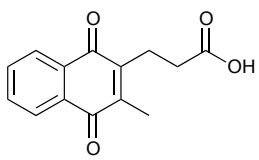
19 was prepared according to general procedure A from menadione (**4**) (298 mg, 1.73 mmol) and oleic acid (1.25 mL, 3.96 mmol) and the product purified by flash chromatography (40 % ethyl acetate/hexanes) to give **19** as a yellow opaque oil in 8 % yield (57 mg, 0.140 mmol). Spectral data was consistent with that reported [4].

^{1}H NMR δ ($CDCl_3$, 300 MHz): 0.86 (t, *J* = 6.6, 3H), 1.25 – 1.46 (m, 24H), 1.96 – 2.03 (m, 4H), 2.17 (s, 3H), 2.61 (t, *J* = 7.5, 2H), 5.31 – 5.35 (m, 2H), 7.65 – 7.68 (m, 2H), 8.04 – 8.07 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 75 MHz): 12.81, 14.30, 22.87, 27.30, 27.37, 27.41, 28.95, 29.38, 29.52, 29.63, 29.72, 29.81, 29.92, 30.07, 30.17, 32.10, 126.34. 126.45, 129.94, 130.19, 132.36, 132.40, 133.44, 133.47, 143.26, 147.75, 184.82, 185.51

IR V_{max}: 2926, 2854, 1703, 1661, 1464, 1377, 1327, 1286, 718

3-(3-methyl-1,4-naphthoquinone-2-yl)propanoic acid (**20**)



20 was prepared according to general procedure A from menadione (**4**) (1.995 g, 11.59 mmol) and succinic acid (2.757 g, 23.34 mmol) and the product purified by

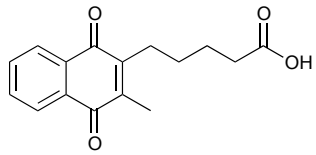
flash chromatography (100% dichloromethane followed by 100% ethyl acetate) to give **20** as a crystalline yellow solid in 20 % yield (0.561 g, 2.296 mmol) with a melting point of 68 – 72 °C.

^{1}H NMR δ ($CDCl_3$, 400 MHz): 2.23 (s, 3H), 2.60 (t, *J* = 7.9 Hz, 2H), 2.98 (t, *J* = 7.9 Hz, 2H), 7.69 – 7.71 (m, 2H), 8.06 – 8.09 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.9, 22.7, 32.6, 126.5, 126.5, 132.2, 132.3, 133.75, 133.76, 144.7, 144.9, 177.8, 184.6, 185.2

IR V_{max}: 2932, 1738, 1706, 1658 1595, 1379, 1330, 1296, 716

5-(3-Methyl-1,4-naphthoquinone-2-yl)pentanoic acid (22)



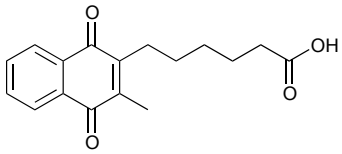
22 was prepared according to general procedure A from menadione (**4**) (2.164 g, 12.57 mmol) and adipic acid (3.724 g, 25.48 mmol) and the product purified by flash chromatography (100% dichloromethane followed by 100% ethyl acetate) to give **22** as a crystalline yellow solid in 78 % yield (2.653 g, 9.742 mmol) with a melting point of 66 – 70 °C.

^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.49 – 1.57 (m, 2H), 1.70 – 1.77 (m, 2H), 2.17 (s, 3H), 2.40 (t, *J* = 7.4 Hz, 2H), 2.64 (t, *J* = 7.9 Hz, 2H), 7.66 – 7.68 (m, 2H), 8.03 – 8.05 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.7, 24.9, 26.7, 28.1, 33.8, 126.3, 126.4, 132.20, 132.21, 133.4, 133.5, 143.5, 146.8, 179.6, 184.7, 185.3

IR V_{max}: 2939, 1705, 1658, 1618, 1595, 1379, 1327, 1294, 1261, 715

6-(3-Methyl-1,4-naphthoquinone-2-yl)hexanoic acid (23)



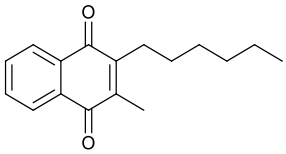
23 was prepared according to general procedure A from menadione (**4**) (2.010 g, 11.68 mmol) and pimelic acid (3.720 g, 23.23 mmol) and the product purified by flash chromatography (100% dichl;oromethane followed by 100% ethyl acetate) to give **23** as a crystalline yellow solid in 57 % yield (1.921 mg, 6.710 mmol) with a melting point of 49 – 51 °C.

^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.45 – 1.51 (m, 4H), 1.69 (quin, *J* = 7.3 Hz, 2H), 2.18 (s, 3H), 2.36 (t, *J* = 7.4 Hz, 2H), 2.63 (t, *J* = 7.5 Hz, 2H), 7.66 – 7.69 (m, 2H), 8.05 – 8.07 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.7, 24.5, 26.9, 28.4, 29.4, 33.9, 126.3, 126.4 132.2, 132.3, 133.46, 133.49, 143.4, 147.2, 179.6, 184.8, 185.4

IR V_{max}: 2937, 1707, 1658, 1595, 1327, 1294, 1259, 715

2-Methyl-3-hexyl-1,4-naphthoquinone (24)



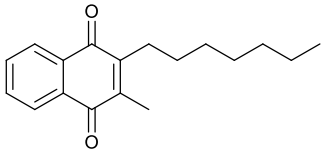
24 was prepared according to general procedure A from menadione (**4**) (208 mg, 1.21 mmol) and heptanoic acid (0.35 mL, 2.93 mmol) with the use of $K_2S_2O_8$ instead of $(NH_4)_2S_2O_8$ and the product purified by flash chromatography (50 % CH_2Cl_2/hexanes) to give **24** as an yellow crystalline solid in 22 % yield (68 mg, 0.266 mmol) with a melting point of 50-54 °C. Spectral data was consistent with that reported [5].

^{1}H NMR δ ($CDCl_3$, 300 MHz): 0.88 – 0.93 (t, *J* = 6.8 Hz, 3H), 1.28 – 1.45 (m, 8H), 2.15 (s, 3H), 2.59 (t, *J* = 8.2 Hz, 2H), 7.62 – 7.67 (m, 2H), 8.01 – 8.04 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 75 MHz): 12.63, 14.11, 22.61, 27.12, 28.73, 29.69, 31.64, 126.14, 126.24, 132.13. 132.18, 133.26, 133.30, 143.06, 147.53, 184.60, 185.29

IR V_{max}: 2950, 2922, 2855, 1661, 1652, 1619, 1594, 1460, 1379, 1327, 1296, 718, 690

2-Methyl-3-heptyl-1,4-naphthoquinone (25)



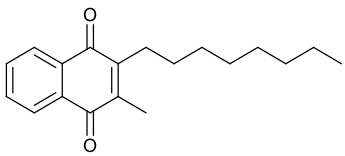
25 was prepared according to general procedure A from menadione (**4**) (504 mg, 2.93 mmol) and octanoic acid (0.97 mL, 6.12 mmol) and the product purified by flash chromatography (50 % CH_2Cl_2/hexanes) to give **25** as a crystalline yellow solid in 56 % yield (443 mg, 1.64 mmol) with a melting point of 59-61 °C. Spectral data was consistent with that reported [6].

^{1}H NMR δ ($CDCl_3$, 300 MHz): 0.83 – 0.87 (m, 3H), 1.26 – 1.44 (m, 10H), 2.15 (s, 3H), 2.59 (t, J = 7.5 Hz, 2H), 7.63 – 7.66 (m, 2H), 8.02 – 8.05 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 75 MHz): 12.78, 14.25, 22.80, 27.26, 28.92, 29.26, 30.12, 31.93, 126.29, 126.39, 132.29, 132.33, 133.41, 133.44, 143.21, 147.70, 184.83, 185.50

IR V_{max}: 2950, 2923, 2854, 1661, 1619, 1596, 1460, 1377, 1329, 1293, 716, 690

2-Methyl-3-octyl-1,4-naphthoquinone (26)



26 was prepared according to general procedure A from menadione (**4**) (200 mg, 1.16 mmol) and nonanoic acid (0.45 mL, 2.56 mmol) and the product purified by flash chromatography (50 % CH_2Cl_2/hexanes) to give **26** as a yellow crystalline solid in 57 % yield (188 mg, 0.661 mmol) with a melting point of 58-61 °C.

^{1}H NMR δ ($CDCl_3$, 300 MHz): 0.87 (t, *J* = 6.8 Hz, 3H), 1.27 – 1.44 (m, 12H), 2.18 (s, 3H), 2.63 (t, *J* = 7.5, 2H), 7.66 – 7.69 (m, 2H), 8.05 – 8.08 (m, 2H)

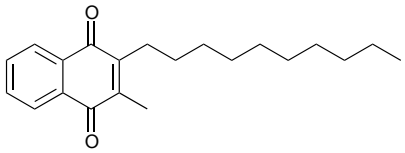
^{13}C NMR δ ($CDCl_3$, 75 MHz): 12.8, 14.3, 22.8, 27.3, 28.9, 29.4, 29.6, 30.2, 32.0, 126.4, 126.5, 132.3, 132.4, 133.4, 133.5, 143.2, 147.8, 184.9, 185.6

HRMS: For $C_{19}H_{24}O_2$, predicted 284.17763, found 284.17718

MS *m/z* (EI+): 284 (M+, 55), 227 (18), 186 (100), 158 (34)

IR V_{max}: 2949, 2921, 2850, 1661, 1619, 1594, 1460, 1376, 1329, 1291, 717, 690

2-Decyl-3-methyl-1,4-naphthoquinone (27)

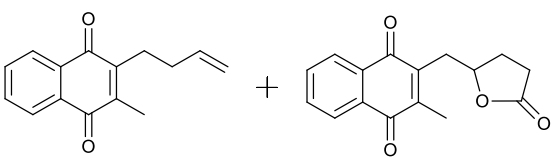


27 was prepared according to general procedure A from menadione (**4**) (320 mg, 1.86 mmol) and undecanoic acid (692 mg, 3.71 mmol) and the product purified by flash chromatography (50 % CH_2Cl_2/hexanes) to give **27** as a yellow crystalline solid in 11 % yield (62 mg, 0.198 mmol). Spectral data was consistent with that reported [7].

^{1}H NMR δ ($CDCl_3$, 300 MHz): 0.85 (t, *J* = 6.9 Hz, 3H), 1.24 – 1.51 (m, 16H), 2.16 (s, 3H), 2.60 (t, *J* = 8.1, 2H), 7.64 – 7.67 (m, 2H), 8.03 – 8.06 (m, 2H)

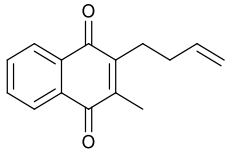
^{13}C NMR δ ($CDCl_3$, 75 MHz): 12.8, 14.3, 22.9, 27.3, 28.9, 29.5, 29.6, 29.7, 29.8, 30.2, 32.1, 126.3, 126.4, 132.2, 132.4, 133.4, 133.5, 143.2, 147.7, 184.9, 185.5

2-(3-Butenyl)-3-methyl-1,4-naphthoquinone (28) and 5-(3-methyl-1,4-naphthoquinone-2-yl)-γ-pentolactone (9)



28 and **9** were prepared according to general procedure A from menadione (**4**) (505 mg, 2.94 mmol) and 4-pentenoic acid (0.59 mL, 5.78 mmol) and the products separated and purified by flash chromatography (15 % ethyl acetate/hexanes followed by 50 % ethyl acetate/hexanes) to give the product **28** as a yellow semi-solid in a 5 % yield (31 mg, 0.136 mmol) and **9** in 6 % yield (50 mg, 0.184 mmol) as a brown semi-solid.

2-(3-Butenyl)-3 methyl-1,4-naphthoquinone (28)



^{1}H NMR δ ($CDCl_3$, 300 MHz) 2.19 (s, 3H), 2.23 – 2.28 (m, 2H), 2.71 – 2.76 (m, 2H), 4.96 – 5.07 (m, 2H), 5.86 (ddt, *J* = 17.2, 10.2, 6.7 Hz, 1H), 7.67 – 7.70 (m, 2H), 8.04 – 8.08 (m, 2H)

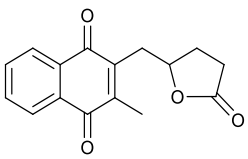
^{13}C NMR δ ($CDCl_3$, 75 MHz) 13.01, 26.83, 32.89, 115.77, 126.42, 126.49, 132.3, 133.54, 133.58, 137.49, 143.85, 146.66, 184.79, 185.47

HRMS: For $C_{15}H_{14}O_2$, predicted 226.09938, found 226.09927

MS *m/z* (EI+): 226 (M+, 42), 211 (100), 197 (28), 172 (22), 129 (18), 105 (20)

IR V_{max} 2976, 2927, 1661, 1618, 1596, 1377, 1329, 1295, 715

5-(3-Methyl-1,4-naphthoquinone-2-yl)-γ-pentolactone (9)



^{1}H NMR δ ($CDCl_3$, 300 MHz): 1.99 – 2.04 (m, 1H), 2.24 (s, 3H), 2.40 – 2.46 (m, 1H), 2.50 – 2.67 (m, 2H), 2.93 (dd, *J* = 13.4, 8.9 Hz, 1H), 3.12 (dd, *J* = 13.5, 4.4, 1H), 4.69 – 4.76 (m, 1H), 7.68 – 7.74 (m, 2H), 8.02 – 8.09 (m, 2H)

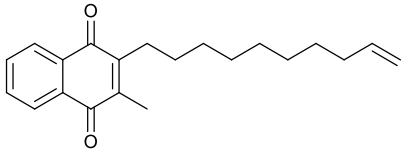
^{13}C NMR δ ($CDCl_3$, 75 MHz): 13.43, 28.24, 28.63, 33.11, 79.44, 126.35, 126.50, 131.82, 132.13, 133.59, 133.73, 141.40, 146.27, 176.56, 184.74, 184.76

HRMS: For $C_{16}H_{14}O_4$, predicted 270.08921, found 270.08926

MS *m/z* (Es+): 293 (M+ NH_4, 100), 288 (M+ Na, 75), 271 (M+ H, 86)

IR V_{max}:3380, 2976, 2939, 1774, 1688, 1660, 1621, 1596, 1459, 1379, 1331, 1296, 1180, 1022, 732, 721, 694

2-(9-Decenyl)-3-methyl-1,4-naphthoquinone (29)



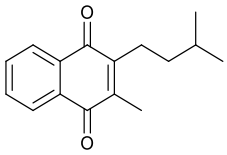
29 was prepared according to general procedure A from menadione (**4**) (208 mg, 1.20 mmol) and 10-undecenoic acid (0.47 mL, 2.80 mmol) and the product purified by flash chromatography (50 % CH_2Cl_2/hexanes) to give **29** as a crystalline yellow solid in 37 % yield (136 mg, 0.437 mmol) with a melting point of 47-49 °C (Ref. [8] = 68 °C).

^{1}H NMR δ ($CDCl_3$, 300 MHz) 1.29 – 1.49 (m, 12H), 1.99 – 2.03 (m, 2H), 2.18 (s, 3H), 2.59 – 2.64 (t, *J* = 7.5Hz, 2H), 4.89 – 5.01 (m, 2H), 5.73 – 5.86 (ddt, *J* = 17.2, 10.2, 6.7 Hz, 1H), 7.66 – 7.70 (m, 2H), 8.05 – 8.09 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 75 MHz) 12.83, 27.29, 28.94, 29.08, 29.28, 29.56, 30.16, 33.97, 114.34, 126.35, 126.45, 132.37, 132.41, 133.46, 133.49, 139.37, 143.27, 147.75, 184.90, 185.56 (one carbon overlapping)

IR V_{max} 3073, 2925, 2853, 1661, 1641, 1618, 1596, 1459, 1378, 1328, 1294, 909, 716, 691

2-Isopentyl-3-methyl-1,4-naphthoquinone (30)



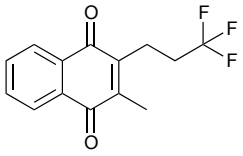
30 was prepared according to general procedure A from menadione (**4**) (505 mg, 2.93 mmol) and 4-methyl-*n*-valeric acid (0.75 mL, 7.01 mmol) and the product purified by flash chromatography (50 % CH_2Cl_2/hexanes) to give **30** as a yellow viscous oil in 36 % yield (253 mg, 1.04 mmol).

^{1}H NMR δ ($CDCl_3$, 300 MHz): 0.97 (d, *J* = 6 Hz, 6H), 1.28 – 1.36 (m, 2H), 1.61 – 1.71 (m, 1H), 2.18 (s, 3H), 2.59 – 2.64 (m, 2H), 7.66 – 7.69 (m, 2H), 8.05 – 8.08 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 75 MHz): 12.7, 22.5, 25.3, 28.8, 37.8, 126.3, 126.4, 132.3, 132.4, 133.4, 133.5, 143.1, 148.0, 184.8, 185.5

IR V_{max}: 2956, 2870, 1661, 1596, 1466, 1377, 1329, 1297, 713

2-Methyl-3-(3,3,3-trifluoropropyl)-1,4-naphthoquinone (31)



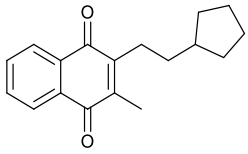
31 was prepared according to general procedure A from menadione (**4**) (910 mg, 5.2840 mmol) and trifluorobutyric acid (268 mg, 1.8834 mmol) and the product purified by flash chromatography (70 % CH_2Cl_2/hexanes) to give **31** as a bright yellow crystalline solid in 59 % yield (299 mg, 1.1147 mmol) with a melting point of 61-62 °C.

^{1}H NMR δ ($CDCl_3$, 400 MHz): 2.13 (s, 3H) 2.21 – 2.33 (m, 2H), 2.81 (t, *J* = 7.8Hz, 2H), 7.60 – 7.62 (m, 2H), 7.93 – 7.95 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.4, 20.1 (q, $J_{C\text{-}F}$ = 3.5 Hz), 32.2 (q, $J_{C\text{-}F}$ = 29.1 Hz), 126.2, 126.3, 126.6 (q, $J_{C\text{-}F}$ = 277.6 Hz), 131.8, 131.9, 133.56, 133.59, 143.6, 144.6, 184.0, 184.6

IR V_{max}: 1660, 1622, 1595, 1456, 1381, 1294, 1251, 1238, 1138, 991, 717

2-(2-Cylclopentylethyl)-3-methyl-1,4-naphthoquinone (32)



32 was prepared according to general procedure A from menadione (**4**) (501 mg, 2.91 mmol) and 3-cyclopentylpropionic acid (0.85 mL, 5.95 mmol) and the product purified by flash chromatography (50 % CH_2Cl_2/hexanes) to give **32** as a viscous yellow oil in 33 % yield (255 mg, 0.948 mmol).

^{1}H NMR δ ($CDCl_3$, 300 MHz): 1.12 – 1.16 (m, 2H), 1.37 – 1.60 (6H), 1.76 – 1.83 (m, 3H), 2.18 (s, 3H), 2.55 – 2.60 (m, 2H), 7.60 – 7.63 (m, 2H), 7.98 – 8.01 (m, 2H)

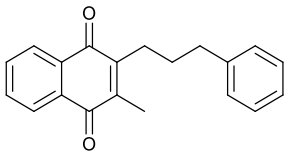
^{13}C NMR δ ($CDCl_3$, 75 MHz): 12.62, 25.40, 26.53, 27.72, 35.19, 40.59, 126.23, 126.30, 132.22, 132.28, 133.34, 133.38, 142.95, 147.74, 184.69, 185.38

HRMS: For $C_{18}H_{20}O_2$, predicted 268.14633, found 268.14710

MS *m/z* (EI+): 268 (M+, 12), 253 (5), 168 (100), 174 (10), 158 (40)

IR V_{max}: 2949, 2865, 1661, 1616, 1453, 1377, 1329, 1295, 715

2-Methyl-3-(3-phenpropyl)-1,4-naphthoquinone (33)



33 was prepared according to general procedure A from menadione (**4**) (503 mg, 2.92 mmol) and 4-phenylbutyric acid (976 mg, 5.94 mmol) and the product purified by

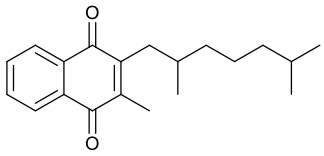
flash chromatography (55 % CH_2Cl_2/hexanes) to give **33** as a crystalline yellow solid in 37 % yield (316 mg, 1.09 mmol) with a melting point of 34-36 °C.

^{1}H NMR δ ($CDCl_3$, 300 MHz): 1.78 – 1.84 (m, 2H), 2.10 (s, 3H), 2.63 – 2.76 (m, 4H), 7.17 – 7.30 (m, 5H), 7.65 – 7.68 (m, 2H), 8.03 – 8.07 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 75 MHz): 12.77, 26.99, 30.33, 36.30, 126.17, 126.41, 126.48, 128.58, 132.37, 132.39, 133.53, 133.55, 141.84, 143.51, 147.33, 184.88, 185.49 (one carbon overlapping)

IR V_{max}: 2933, 2362, 1657, 1617, 1596, 1453, 1329, 1294, 714, 699

2-(2,6-Dimethylheptyl)-3-methyl-1,4-naphthoquinone (34)



34 was prepared according to general procedure A from menadione (**4**) (446 mg, 2.59 mmol) and 3,7-dimethyloctanoic acid (218 mg, 1.26 mmol) and the product purified by flash chromatography (50 % CH_2Cl_2/hexanes) to give **34** as a yellow oil in 56 % yield (222 mg, 0.743 mmol).

^{1}H NMR δ ($CDCl_3$, 300 MHz): 0.82 – 0.87 (m, 9H), 1.09 – 1.39 (m, 1H), 1.43 – 1.54 (m, 1H), 1.68 – 1.79 (m, 1H), 2.17 (s, 3H), 2.47 (dd, *J* = 12.5, 8.6 Hz, 1H), 2.64 (dd, *J* = 12.5, 6.0 Hz, 1H), 7.64 – 7.69 (m, 2H), 8.03 – 8.06 (m, 2H)

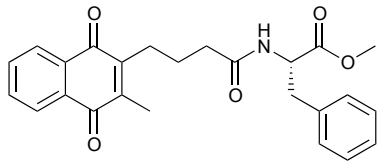
^{13}C NMR δ ($CDCl_3$, 75 MHz): 13.48, 19.91, 22.74, 22.89, 25.09, 28.14, 33.80, 34.52, 37.92, 39.35, 126.32, 126.51, 132.33, 132.35, 133.42, 133.48, 144.13, 147.11, 185.11, 185.46

HRMS: For $C_{20}H_{26}O_2$, predicted 298.19328, found 298.19338

MS *m/z* (EI+): 298 (M+, 38), 186 (100), 158 (20)

IR V_{max}: 2955, 2928, 2869, 1661, 1597, 1460, 1379, 1329, 1294, 716

(*S*)-Methyl-2(4-(3-methyl-1,4-naphthoquinone-2-yl)butamido)-3-phenylpropanoate (35)



35 was prepared according to general procedure B from **21** (108 mg, 0.4170 mmol) and (*S*)-phenylalanine methyl ester (90 mg, 0.4193 mmol). The product purified by a Reveleris ® X2 automated flash chromatography system (Eluent: gradient 100 % Hexanes - 100 % ethyl acetate, Column: Reveleris ® Silica 4 g, Flow rate: 18 mL/min) to give **35** as a yellow oil in 29 % yield (51 mg, 0.1223 mmol).

^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.80 (quin, *J* = 8.2 Hz, 2H), 2.20 (s, 3H), 2.29 (t, *J* = 7.2 Hz, 2H), 2.63 – 2.67 (m, 2H), 3.15 (qd, *J* = 14.0, 6.0 Hz, 2H), 3.74 (s, 3H), 6.11 (d, *J* = 7.8, 1H), 4.92 (q, *J* = 6.1 Hz, 1H), 7.12 – 7.14 (m, 2H), 7.24 – 7.31 (m, 3H), 7.70 – 7.72 (m, 2H), 8.07 – 8.10 (m, 2H)

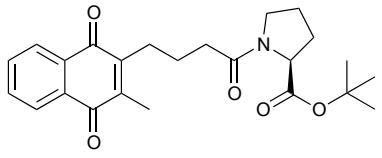
^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.9, 24.3, 26.4, 23.9, 38.1, 52.5, 53.2, 126.4, 126.5, 127.3 128.7 (two carbons), 129.4 (two carbons), 132.2, 132.3, 133.5, 133.6, 136.1, 144.2, 146.4, 172.0, 172.3, 184.9, 185.3

HRMS: For $C_{25}H_{25}N_1O_5$, predicted 419.17327, found 419.17403

MS *m/z* (EI+): 419 (M+, 45), 241 (100), 197 (50), 162 (100), 120 (45)

IR V_{max} : 3371, 3293, 2951, 1745, 1652, 1596, 1538, 1436, 1378, 1329, 1295, 1215, 717

(*S*)-*tert*-Butyl-1-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanoyl)pyrrolidine-2-carboxylate (37)



37 was prepared according to general procedure B from **21** (197 mg, 0.7623 mmol) and L-Proline t-butyl ester.HCl (139 mg, 0.6716 mmol) and the product purified by flash chromatography (60 % ethyl acetate/hexanes) to give **37** as yellow oil in 53 % yield (146 mg, 0.3543 mmol).

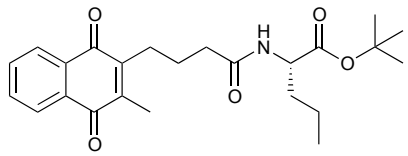
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.44 (s, 9H), 1.82 – 1.88 (m, 2H), 1.90 – 1.96 (m, 2H), 2.04 – 2.13 (m, 2H), 2.21 (s, 3H), 2.36 – 2.48 (m, 2H), 2.67 – 2.71 (m, 2H), 3.47 – 3.52 (m, 1H), 3.59 – 3.64 (m, 1H), 4.37 (dd, *J* = 8.5, 3.9 Hz, 1H), 7.66 – 7.68 (m, 2H), 8.03 – 8.07 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 23.7, 24.7, 26.5, 28.0, 29.3, 34.1, 47.1, 59.5, 81.2, 126.2 (two carbons), 132.23, 132.26, 133.3 (two carbons), 144.0, 146.7, 171.0, 171.6, 184.7, 185.3

$[\alpha]_D^{20}$: +48.70° (*c* 0.97, $CHCl_3$)

IR V_{max}: 2976, 2935, 1735, 1654, 1618, 1595, 1456, 1425, 1367, 1294, 1153, 719

(*S*)-*tert*-Butyl-2-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)pentanoate (38)



38 was prepared according to general procedure B from **21** (209 mg, 0.8096 mmol) and L-Norvaline t-butyl ester.HCl (159 mg, 0.7587 mmol) and the product purified by flash chromatography (50 % ethyl acetate/hexanes) to give **38** as yellow oil in 44 % yield (140 mg, 0.3376 mmol).

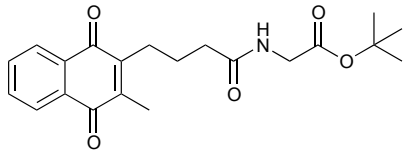
^{1}H NMR δ ($CDCl_3$ 400 MHz): 0.90 (t, *J* = 7.3 Hz, 3H), 1.29 – 1.33 (m, 2H), 1.43 (s, 9H), 1.58 – 1.65 (m, 2H), 1.77 -1.84 (m, 2H), 2.17 (s, 3H), 2.31 (t, *J* = 7.2 Hz, 2H), 2.64 – 2.68 (m, 2H), 4.45 – 4.50 (m, 1H), 6.27, d, *J* = 8.0 Hz, 1H), 7.64 – 7.67 (m, 2H), 8.01 – 8.03 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 13.9, 18.6, 24.4, 26.4, 28.1, 34.9, 36.2, 52.6, 82.0, 126.40, 126.45, 132.23, 132.29, 133.51, 133.55, 144.1, 146.4, 171.9, 172.2, 184.9, 185.3

$[\alpha]_D^{20}$: -3.43° (*c* 0.17, $CHCl_3$)

IR V_{max}: 3354, 3296, 2962, 1734, 1660, 15595, 1521, 1458, 1367, 1329, 1294, 1149, 717

***tert*-Butyl 2-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)acetate (39)**



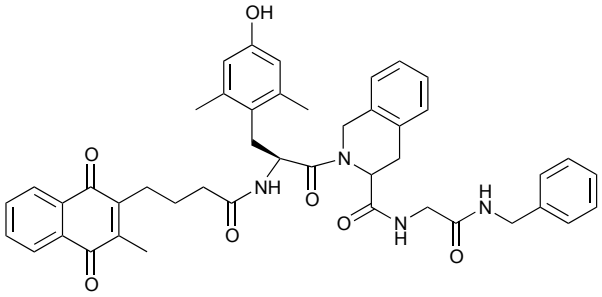
39 was prepared according to general procedure B from **21** (165 mg, 0.6381 mmol) and glycine t-butyl ester (148 mg, 0.8852 mmol) and the product purified by flash chromatography (50 % ethyl acetate/hexanes) to give **39** as yellow viscous oil in 36 % yield (85 mg, 0.2294 mmol).

^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.41 (s, 9H), 1.79 (quin, *J* = 7.2 Hz, 2H), 2.15 (s, 3H), 2.31 (t, *J* = 7.2 Hz, 2H), 2.62 – 2.66 (m, 2H), 3.89 (d, 5.1 Hz, 2H), 6.27 – 6.29 (m, 1H), 7.60 – 7.65 (m, 2H), 7.98 – 8.01 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.7, 24.3, 26.3, 28.0, 35.8, 42.0, 82.2, 126.25, 126.29, 132.13, 132.17, 133.3, 133.4, 144.0, 146.3, 169.2, 172.4, 184.7, 185.1

IR V_{max}: 3369, 2978, 1743, 1660, 1595, 1521, 1369, 1329, 1294, 1224, 1157, 717

***N*-(2-(Benzylamino)-2-oxoethyl)-2-((*S*)-3-(4-hydroxy-2,6-dimethylphenyl)-2-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)propanoyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide (40)**



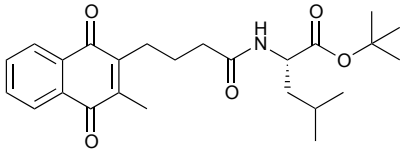
40 was prepared according to general procedure B from **21** (31 mg, 01181 mmol) and DMT-Tic-Gly-Bnz.HCl (49 mg, 0.0785 mmol) and the product purified by flash chromatography (95:5:1 methanol/ethyl acetate/H_2O) to give **40** as an opaque yellow semi-solid in 27 % yield (15 mg, 0.0196 mmol).

MS *m/z* (ES+): 777 (M+Na, 45), 755 (M+, 48), 591 (100)

$[\alpha]_D^{20}$: -26.67° (*c* 0.05, $CHCl_3$)

IR V_{max}: 3306, 1653, 1595, 1539, 1456, 1437, 1379, 1294, 1267, 1143, 1030, 734

(*S*)-*tert*-Butyl-4-methyl-2-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)pentanoate (41)



41 was prepared according to general procedure B from **21** (194 mg, 0.7496 mmol) and L-Leucine t-butyl ester.HCl (168 mg, 0.7509 mmol) and the product purified by flash chromatography (40 % ethyl acetate/hexanes) to give **41** as yellow oil in 39 % yield (124 mg, 0.2898 mmol).

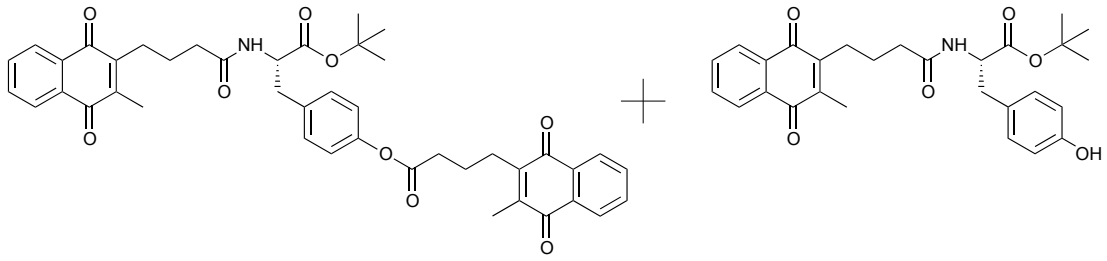
^{1}H NMR δ ($CDCl_3$, 400 MHz): 0.90 (d, *J* = 6.5 Hz, 6H), 1.42 (s, 9H), 1.46 – 1.65 (m, 3H), 1.79 (quin, *J* = 7.4 Hz, 2H), 2.16 (s, 3H), 2.29 (t, *J* = 7.4 Hz, 2H), 2.62 – 2.66 (m, 2H), 4.49 (td, *J* = 8.4, 5.3 Hz, 1H), 6.16 (d, *J* = 8.4 Hz, 1H), 7.62 – 7.66 (m, 2H), 7.98 – 8.03 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.7, 22.1, 22.8, 24.3, 25.0, 26.4, 28.0, 36.1, 41.9, 51.4, 81.8, 126.2, 126.3, 132.1, 132.2, 133.40, 133.43, 144.0, 146.4, 171.9, 172.5, 184.8, 185.2

$[\alpha]_D^{20}$: -2.62 ° (*c* 1.06, $CHCl_3$)

IR V_{max}: 3354, 2958, 2870, 1734, 1660, 1595, 1541, 1521, 1456, 1367, 1329, 1294, 1149, 717

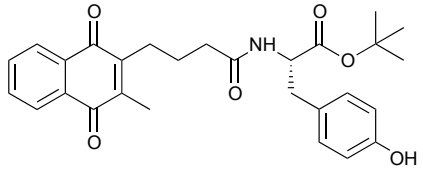
(*S*)-*tert*-Butyl-3-(4-hydroxyphenyl)-2-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)propanoate (42) and **(*S*)-4-(3-(*tert*-butoxy)-2-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)-3-oxopropyl)phenyl 4-(3-methyl-1,4-naphthoquinone-2-yl)butanoate (43)**



42 was prepared according to general procedure B from **21** (98 mg, 0.3810 mmol) and L-tyrosine t-butyl ester.HCl (168 mg, 0.7509 mmol). Purification by flash chromatography resulted in the identification of **42** and **43**. Compounds were combined and dissolved in 10 mL methanol, excess potassium carbonate added and the reaction left stirring at r.t for 1hour. The mixture was extracted with dichloromethane 3x 30 mL and the organic layer dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to give crude **42** which was purified by flash chromatography (silica gel) (50 % ethyl acetate/hexanes) to give **42** as yellow oil in 20 % yield (42 mg, 0.0871 mmol).

Note: **43** (14.9 mg, 0.0208 mmol) was kept for analysis (yellow viscous oil).

(*S*)-*tert*-Butyl-3-(4-hydroxyphenyl)-2-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)propanoate (42)



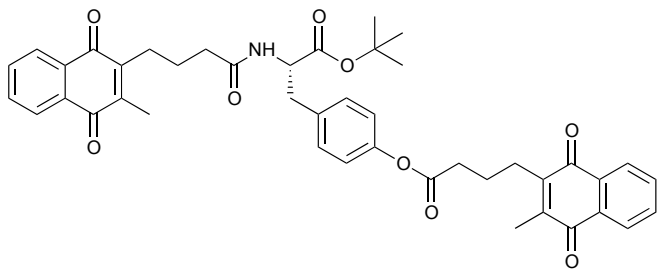
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.42 (s, 9H), 1.78 (quin, *J* = 7.5 Hz, 2H), 2.17 (s, 3H), 2.27 (t, *J* = 7.5 Hz, 2H), 2.61 – 2.65 (m, 2H), 2.98 (dd, *J* = 14.1, 6.1 Hz, 1H), 3.05 (dd, *J* = 14.1 Hz, 6.1 Hz, 1H), 4.72 – 4.76 (m, 1H), 6.09 (d, *J* = 8.0 Hz, 1H), 6.72 (d, *J* = 8.3 Hz, 2H), 7.01 (d, *J* = 8.3Hz, 2H), 7.67 – 7.72 (m, 2H), 8.05 – 8.08 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 24.3, 26.4, 28.1, 36.2, 37.4, 77.3, 82.5, 115.4 (two carbons), 126.42, 126.47, 130.7 (two carbons), 132.3, 133.5, 144.2, 146.5, 154.9, 171.1, 171.9, 184.9, 185.3

$[\alpha]_D^{20}$: +14.86.$^{\circ}$ (*c* 0.18, $CHCl_3$)

IR V_{max}: 3367, 2987, 2931, 1732, 1654, 1616, 1695, 1516, 1506, 1369, 1330, 1294, 1259, 1153, 734

(*S*)-4-(3-(*tert*-Butoxy)-2-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)-3-oxopropyl)phenyl 4-(3-methyl-1,4-naphthoquinone-2-yl)butanoate (43)



^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.40 (s, 9H), 1.78 (quin, *J* = 7.8 Hz, 2H), 1.90 (quin, *J* = 7.7 Hz, 2H), 2.18 (s, 3H), 2.22 (s, 3H), 2.28 (t, *J* = 7.3 Hz, 2H), 2.61 – 2.65 (m, 4H), 2.73 – 2.77 (m, 2H), 3.09 (d, *J* = 6.1 Hz, 2H), 4.73 – 4.78 (m, 1H), 6.10 (d, *J* =

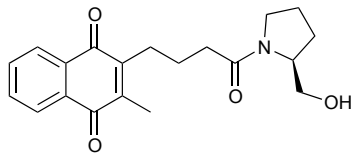
7.7 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 7.66 – 7.71 (m, 4H), 8.04 – 8.09 (m, 4H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.84, 12.87, 23.7, 24.3, 26.3, 26.4, 28.1, 34.1, 36.1, 37.6, 53.5, 82.6, 121.5, 126.3, 126.43, 126.45, 126.47, 130.5, 132.23, 132.25, 132.29, 132.3, 133.51, 133.52, 133.59, 134.0, 144.1, 146.2, 146.4, 149.7, 170.8, 171.6, 172.8, 184.7, 184.9, 185.31, 185.35

$[\alpha]_D^{20}$: +17.91° (*c* 0.34, $CHCl_3$)

IR V_{max}: 3366, 2978, 2933, 1734, 1654, 1595, 1506, 1456, 1369,1296, 1259, 1201, 1153, 734

(*S*)-2-(4-(2-(Hydroxymethyl)pyrrolidin-1-yl)-4-oxobutyl)-3-methyl-1,4-naphthoquinone (44)



44 was prepared according to general procedure B from **21** (117 mg, 0.4522 mmol) and L-Prolinol (159 mg, 0.7587 mmol) and the product purified by flash chromatography (100 % ethyl acetate) to give **44** as yellow oil in 36 % yield (50 mg, 1459 mmol).

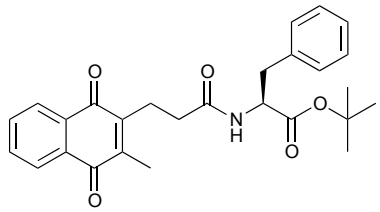
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.60 (quin, *J* = 6.2 Hz, 2H), 1.82 – 2.02 (m, 6H), 2.21 (s, 3H), 2.39 (t, *J* = 7.2 Hz, 2H), 2.67 – 2.72 (m, 2H), 3.50 – 3.55 (m, 1H), 3.66 (dd, *J* = 11.3, 2.8 Hz, 1H), 4.15 – 4.22 (m, 1H), 7.66 – 7.68 (m, 2H), 8.03 – 8.07 (m, 2H).

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 23.6, 24.5, 26.4, 28.3, 34.6, 48.1, 61.2, 67.3, 126.33, 126.37, 132.1, 132.2, 133.4, 133.5, 144.1, 146.6, 173.6, 184.9, 185.3

$[\alpha]_D^{20}$: -35.12° (*c* 0.41, $CHCl_3$)

IR V_{max}: 3367, 2953, 2877, 1695, 1654, 1616, 1595, 1454, 1329, 1296, 1047, 732, 719

(*S*)-*tert*-Butyl-2-(3-(3-methyl-1,4-naphthoquinone-2-yl)propanamido)-3-phenylpropanoate (46)



46 was prepared according to general procedure B from **21** (119 mg, 0.4876 mmol) and L-phenyl alanine t-butyl ester.HCl (115 mg, 0.4462 mmol) and the product purified by flash chromatography (30 % ethyl acetate/hexanes) to give **46** as yellow oil in 22 % yield (45 mg, 0.0997 mmol).

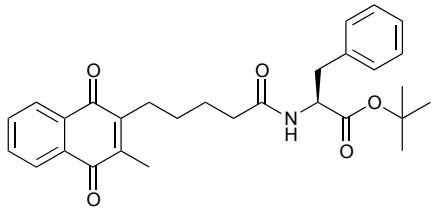
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.37 (s, 9H), 2.94 (s, 3H), 2.37 – 2.41 (m, 2H), 2.92 (t, *J* = 7.8 Hz, 2H), 3.05 (d, *J* = 6.1 Hz, 2H), 4.71 – 4.76 (m, 1H), 6.08 (d, *J* = 7.7 Hz, 1H), 7.09 – 7.21 (m, 5H), 7.66 – 7.68 (m, 2H), 8.02 – 8.05 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 23.4, 28.0, 34.9, 38.1, 53.5, 82.4, 126.33, 126.39, 127.0, 128.4 (two carbons), 129.5 (two carbons), 132.1, 132.2, 133.50, 133.54, 136.2, 144.5, 145.4, 170.7, 171.0, 184.7, 185.0

$[\alpha]_D^{20}$: +29.91° (*c* 0.54, $CHCl_3$)

IR V_{max}: 3365, 2978, 1732, 1660, 1595, 1521, 1456, 1367, 1294, 1153, 700

(*S*)-*tert*-Butyl-2-(5-(3-methyl-1,4-naphthoquinone-2-yl)pentanamido)-3-phenylpropanoate (47)



47 was prepared according to general procedure B from **22** (205 mg, 0.7525 mmol) and L-phenyl alanine t-butyl ester.HCl (188 mg, 0.7308 mmol) and the product

purified by flash chromatography (40 % ethyl acetate/hexanes) to give **47** as bright yellow oil in 69 % yield (240.4 mg, 0.5055 mmol).

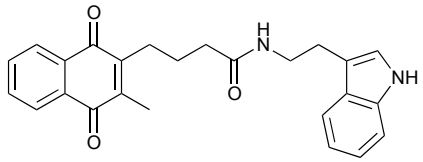
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.35 (s, 9H), 1.39 - 1.47 (m, 2H), 1.67 (quin, *J* = 7.5 Hz, 2H), 2.11 (s, 3H), 2.20 (t, *J* = 7.6 Hz, 2H), 2.58 (t, *J* = 7.9 Hz, 2H), 2.98 – 3.08 (m, 2H), 4.70 – 4.75 (m, 1H), 6.09 (d, *J* = 7.6 Hz, 1H), 7.09 – 7.12 (m, 5H), 7.60 – 7.64 (m, 2H), 7.98 – 8.02 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.6, 25.6, 26.5, 27.9, 28.0, 36.0, 38.0, 53.4, 82.2, 126.1, 126.2, 126.8, 128.3 (two carbons), 129.4 (two carbons), 132.11, 132.12, 133.3 (two carbons), 136.2, 143.4, 146.8, 170.8, 172.1, 184.6, 185.1

$[\alpha]_D^{20}$: +37.83° (*c* 0.92, $CHCl_3$)

IR V_{max}: 3306, 2978, 2933, 1732, 1658, 1595, 1531, 1367, 1329, 1257, 1294, 1155, 715

_N_-(2-(1_H_-Indol-3-yl)ethyl)-4-(3-methyl-1,4-naphthoquinone-2-yl)butanamide (48)



48 was prepared according to general procedure B from **21** (194 mg, 0.7507 mmol) and tryptamine (124 mg, 0.7708 mmol) and the product purified by flash chromatography (80 % ethyl acetate/hexanes) to give **48** as a brown viscous oil in 42 % yield (127 mg, 0.3178 mmol).

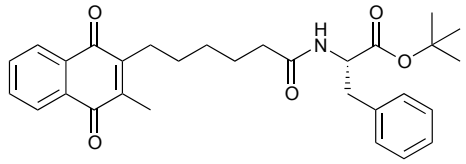
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.77 (quin, *J* = 7.4 Hz, 2H), 2.14 (s, 3H), 2.22 (t, *J* = 7.4 Hz, 2H), 2.57 – 2.61 (m, 2H), 2.97 (t, *J* = 6.8 Hz, 2H), 3.58 – 3.63 (m, 2H), 6.13 (t, *J* = 5.2 Hz, 1H), 7.01 (bs, 1H), 7.04 – 7.08 (m, 1H), 7.11 – 7.15 (m, 1H), 7.32 (d, *J*

= 8.0 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.64 – 7.67 (m, 2H), 7.99 – 8.04 (m, 2H), 8.69 (bs, 1H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.7, 24.3, 25.2, 26.3, 36.1, 39.9, 111.4, 112.7, 118.6, 119.3, 122.0, 122.2, 126.2 (two carbons), 127.3, 132.02, 132.09, 133.42, 133.47, 136.4, 143.9, 146.2, 172.6, 184.8, 185.1

IR V_{max}: 3392, 3294, 2935, 1705, 1653, 1595, 1527, 1458, 1332, 1296, 740, 715

(*S*)-*tert*-Butyl-2-(6-(3-methyl-1,4-naphthoquinone-2-yl)hexanamido)-3-phenylpropanoate (50)



50 was prepared according to general procedure B from **23** (240 mg, 0.8396 mmol) and L-phenyl alanine t-butyl ester.HCl (180 mg, 0.7001 mmol) and the product purified by flash chromatography (40 % ethyl acetate/hexanes) to give **50** as yellow oil in 48 % yield (167 mg, 0.3383 mmol).

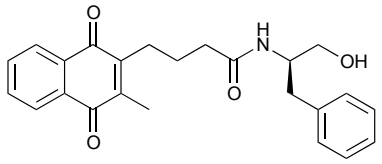
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.40 (s, 9H), 1.41 – 1.47 (m, 4H), 1.64 (quin, *J* = 7.5 Hz, 2H), 2.16 (s, 3H), 2.18 – 2.29 (m, 2H), 2.60 (t, *J* = 7.8 Hz, 2H), 3.02 – 3.10 (m, 2H), 4.73 – 4.78 (m, 1H), 6.05 (d, *J* = 7.7 Hz, 1H), 7.13 – 7.15 (m, 2H), 7.21 – 7.28 (m, 3H), 7.65 – 768 (m, 2H), 8.03 – 8.06 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.6, 25.2, 26.8, 27.9, 28.3, 29.4, 36.3, 38.1, 53.3, 82.3, 126.20, 126.28, 126.9, 128.3 (two carbons), 129.5 (two carbons), 132.17, 132.19, 133.32, 133.35, 134.18, 136.3, 143.2, 147.2, 170.9, 172.3, 184.6, 185.3

$[\alpha]_D^{20}$: +23.33° (*c* 0.66, $CHCl_3$)

IR V_{max}: 3290, 2978, 2933, 1734, 1695, 1653, 1595, 1521, 1456, 1369, 1294, 1155, 702

(*R*)-*N*-(1-Hydroxy-3-phenylpropan-2-yl)-4-(3-methyl-1,4-naphthoquione-2-yl)butanamide (52)



52 was prepared according to general procedure B from **21** (180 mg, 0.6954 mmol) and D-phenyl alaninol (117 mg, 0.7731 mmol) and the product purified by flash chromatography (100 % ethyl acetate) to give **52** as a brown oil in 55 % yield (186 mg, 0.4300 mmol).

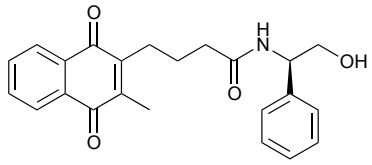
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.72 – 1.78 (m, 2H), 2.17 (s, 3H), 2.25 (t, *J* = 6.9 Hz, 2H), 2.56 – 2.50 (m, 2H), 2.86 – 2.91 (m, 2H), 3.60 (dd, *J* = 11.2, 5.2 Hz, 1H), 3.74 (dd, *J* = 11.2, 3.5 Hz, 1H), 4.21 – 4.25 (m, 1H), 6.09 (d, *J* = 7.7 Hz 1H), 7.19 – 7.29 (m, 5H), 7.68 – 7.71 (m, 2H), 8.03 – 8.08 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 24.3, 26.2, 36.2, 37.1, 53.0, 64.4, 126.45, 126.47, 126.7, 128.7, 129.3, 132.1, 132.2, 33.5, 133.7, 137.8, 144.3, 146.3, 173.0, 185.22, 185.27

$[\alpha]_D^{20}$: -13.88° (*c* 0.25, $CHCl_3$)

IR V_{max}: 3369, 3306, 3064, 2933, 1653, 1595, 1533, 1456, 1377, 1330, 1294, 1041, 734, 702

(*R*)-*N*-(2-Hydroxy-1-phenylethyl)-4-(3-methyl-1,4-naphthoquinone-2-yl)butanamide (53)



53 was prepared according to general procedure B from **21** (178 mg, 0.6877 mmol) and D-phenyl glycinol (109 mg, 0.7953 mmol) and the product purified by dissolving in dichloromethane and adding hexanes dropwise until a precipitate was formed to give **53** as yellow crystalline solid in 62 % yield (161 mg, 0.4266 mmol) with a melting point of 150 – 154 °C.

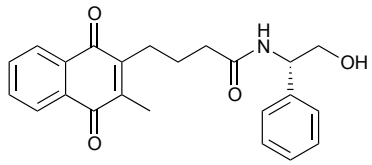
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.80 – 1.90 (m, 2H) 2.29 (s, 3H), 2.36 (t, *J* = 7.1 Hz, 2H), 2.65 – 2.73 (m, 2H), 3.92 (d, *J* = 5.0 Hz, 2H), 5.10 – 5.14 (m, 1H), 6.50 (d, *J* = 6.8 Hz, 1H), 7.27 – 7.38 (m, 5H), 7.67 – 7.72 (m, 2H), 8.03 – 8.10 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 24.4, 26.3, 36.2, 56.1, 66.8, 126.4, 126.9, 128.0, 129.0 (two carbons), 132.1, 132.3, 133.5, 133.7, 139.0, 144.4, 146.3, 172.9, 185.2, 185.3

$[\alpha]_D^{20}$: -31.81° (*c* 0.64, $CHCl_3$)

IR V_{max}: 3296, 2935, 1658, 1595, 1541, 1456, 1377, 1330, 1294, 719, 700

(*S*)-*N*-(2-Hydroxy-1-phenylethyl)-4-(3-methyl-1,4-naphthoquinone-2-yl)butanamide (54)



54 was prepared according to general procedure B from **21** (187 mg, 0.7252 mmol) and L-phenyl glycinol (106 mg, 0.7690 mmol) and the product purified by dissolving in dichloromethane and adding hexanes dropwise until a precipitate was formed to give **54** as yellow crystaline solid in 69 % yield (188 mg, 0.4992 mmol) with a melting point of 140 – 144 °C.

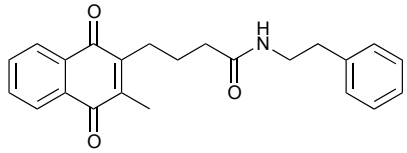
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.80 – 1.90 (m, 2H), 2.19 (s, 3H), 2.37 (t, *J* = 7.1 Hz, 2H), 2.65 – 2.72 (m, 2H), 3.92 (d, *J* = 5.0 Hz, 2H), 5.09 – 5.14 (m, 1H), 6.53 (d, *J* = 6.3 Hz, 1H), 7.27 – 7.38 (m, 5H), 7.68 – 7.70 (m, 2H), 8.04 – 8.08 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 128, 24.4, 26.3, 36.1, 56.2, 66.7, 12.4, 126.9, 128.0, 128.9 (two carbons), 132.1, 132.3, 133.5, 133.7, 139.0, 144.4, 146.3, 173.0, 185.2, 185.3

$[\alpha]_D^{20}$: +18.01° (*c* 0.66, $CHCl_3$)

IR V_{max}: 3294, 2937, 1656, 1595, 1535, 1454, 1377, 1330, 1294, 1070, 700

4-(3-Methyl-1,4-naphthoquinone-2-yl)-*N*-phenethylbutanamide (55)



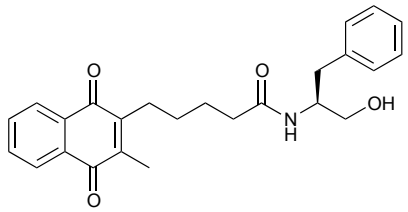
55 was prepared according to general procedure B from **21** (179 mg, 0.6942 mmol) and phenethylamine (98 mg, 0.8088 mmol) and the product purified by flash chromatography (70 % ethyl acetate/hexanes) to give **55** as yellow solid in 59 % yield (148 mg, 0.4086 mmol) with a melting point of 106 – 107 °C.

^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.80 (quin, *J* = 7.3 Hz, 2H), 2.20 (s, 3H), 2.25 (t, *J* = 7.3 Hz, 2H), 2.62 – 2.66 (m, 2H), 2.85 (t, *J* = 7.0 Hz, 2H), 3.53 – 3.58 (m, 2H), 5.92 (bs, 1H), 7.20 – 7.23 (m, 3H), 7.28 – 7.32 (m, 2H), 7.67 (m, 2H), 7.71 (m, 2H), 8.03 – 8.09 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 24.4, 26.4, 35.7, 36.1, 40.7, 126.3, 126.4, 126.6, 128.7 (two carbons), 128.8 (two carbons), 132.1, 132.2, 133.5, 133.6, 138.9, 144.2, 146.3, 172.4, 185.0, 185.2

IR V_{max}: 3298, 3064, 2933, 1653, 1595, 1541, 1456, 1377, 1329, 1294, 717

(*S*)-*N*-(1-Hydroxy-3-phenylpropan-2-yl)-5-(3-methyl-1,4-naphthoquinone-2-yl)pentanamide (56)



56 was prepared according to general procedure B from **22** (149 mg, 0.5483 mmol) and L-phenyl alaninol (88 mg, 0.5800 mmol) and the product purified by flash chromatography (2 % methanol/ethyl acetate) to give **56** as bright yellow/brown oil in 59 % yield (131 mg, 0.3236 mmol).

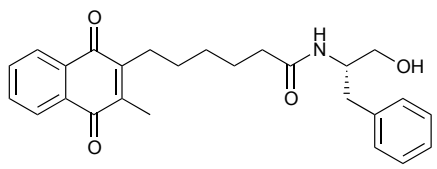
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.43 (quin, *J* = 7.7 Hz, 2H), 1.66 – 1.75 (m, 2H), 2.17 (s, 3H), 2.24 – 2.28 (m, 2H), 2.56 – 2.64 (m, 2H), 2.83 – 2.94 (m, 2H), 3.39 (bs, 1H), 3.58 (dd, *J* = 11.2, 5.1 Hz, 1H), 3.70 (dd, *J* = 11.2, 3.5 Hz, 2H), 4.19 – 4.23 (m, 1H), 6.26 (d, *J* = 7.7 Hz, 1H), 7.15 – 7.28 (m, 5H), 7.68 – 7.72 (m, 2H), 8.03 – 8.09 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 25.8, 26.5, 27.7, 36.0, 37.0, 53.0, 64.1, 126.32, 126.39, 126.6, 128.6 (two carbons), 129.2 (two carbons), 132.1, 132.2, 133.5, 133.6, 137.7, 143.7, 146.7, 173.7, 185.0, 185.2

$[\alpha]_D^{20}$: -16.60° (*c* 2.12, $CHCl_3$)

IR V_{max}: 3296, 2935, 1656, 1595, 1531, 1456, 1377, 1329, 1294, 702

(*S*)-*N*-(1-Hydroxy-3-phenylpropan-2-yl)-6-(3-methyl-1,4-naphthoquione-2-yl)hexanamide (57)



57 was prepared according to general procedure B from **23** (148 mg, 0.5176 mmol) and L-phenyl alaninol (92 mg, 0.6071 mmol) and the product purified by flash chromatography (2 % methanol/ethyl acetate) to give **57** as yellow semi solid in 34 % yield (74 mg, 0.1759 mmol).

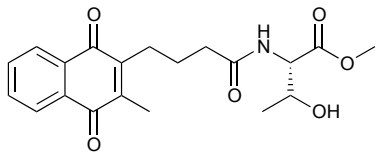
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.34 – 1.48 (m, 4H), 1.62 (quin, *J* = 7.4 Hz, 2H), 2.16 (s, 3H), 2.17 (t, *J* = 7.5 Hz, 2H), 2.56 – 2.60 (m, 2H), 2.78 (bs, 1H), 2.81 – 2.92 (m, 2H), 3.59 (dd, *J* = 11.1, 5.2 Hz, 1H), 3,69 (dd, *J* = 11.1, 3.5 Hz, 1H), 4.16 – 4.20 (m, 1H), 5.97 (d, *J* = 7.0 Hz, 1H), 7.19 – 7.23 (m, 3H), 7.27 - 7.31 (m, 2H), 7.67 – 7.70 (m, 2H), 8.03 – 8.07 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 25.4, 26.9, 28.3, 29.3, 36.4, 37.1, 53.1, 64.4, 126.3 (two carbons), 126.8, 128.7, 129.3, 132.26, 132.28, 133.51, 133.53, 137.7, 143.4, 147.2, 174.1, 184.9, 185.4

$[\alpha]_D^{20}$: +15.15° (*c* 2.31, $CHCl_3$)

IR V_{max}: 3336, 2935, 1695, 1658, 1595, 1541, 1456, 1377, 1329, 1296, 715, 702 M

(2*S*,3*R*)-methyl-3-hydroxy-2-(4-(3-methyl-naphthoquione-2-yl)butanamido)butanoate (58)



58 was prepared according to general procedure B from **21** (151 mg, 0.5827 mmol) and L-threonine methyl ester.HCl (104 mg, 0.6102 mmol) and the product purified by flash chromatography (90 % ethyl acetate/hexane) to give **58** as yellow crystalline solid in 39 % yield (84 mg, 0.2252 mmol) with a melting point of 50 – 52 °C.

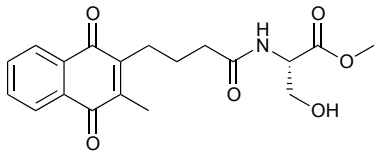
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.25 (d, *J* = 6.5 Hz, 3H), 1.81 – 1.89 (m, 2H), 2.20 (s, 3H), 2.39 (t, *J* = 7.1 Hz, 2H), 2.67 – 2.72 (m, 2H), 3.76 (s, 3H), 4.36 (dq, *J* = 6.4, 2.5 Hz, 1H), 4.63 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.50 (d, *J* = 8.8 Hz, 1H), 7.67 – 7.70 (m, 2H), 8.02 – 8.08 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 20.2, 24.3, 26.3, 36.0, 52.6, 57.4, 68.1, 126.3, 126.4, 132.0, 132.2, 133.5, 133.6, 144.2, 146.3, 171.7, 173.0, 185.0, 185.2

$[\alpha]_D^{20}$: -2.42° (*c* 1.60, $CHCl_3$)

IR V_{max}: 3358, 2974, 1743, 1658, 1595, 1529, 1437, 1379, 1329, 1294, 1209, 717

(*S*)-Methyl-3-hydroxy-2-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)propanoate (59)



59 was prepared according to general procedure B from **21** (149 mg, 0.5777 mmol) and L-serine methyl ester.HCl (98 mg, 0.6286 mmol) and the product purified by flash chromatography (100 % ethyl acetate) to give **59** as yellow crystalline needles in 53 % yield (110 mg, 0.3069 mmol) with a melting point of 94 – 98 °C.

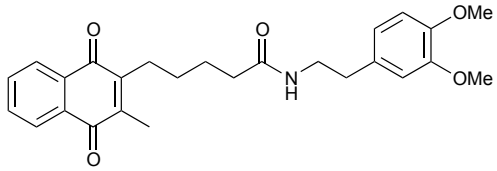
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.78 – 1.94 (m, 2H), 2.21 (s, 3H), 2.37 (td, *J* = 7.1, 2.7 Hz, 2H), 2.46 (bs, 1H), 2.62 – 2.77 (m, 2H), 3.79 (s, 3H), 4.02 (d, *J* = 3.5 Hz, 2H), 4.70 (dt, *J* = 7.1, 3.5 Hz, 1H), 6.64 (d, *J* = 7.0 Hz, 1H), 7.68 – 7.70 (m, 2H), 8.03 – 8.08 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 24.2, 26.1, 35.8, 53.9, 54.9, 63.4, 126.4, 126.5, 132.0, 132.2, 133.6, 133.7, 144.5, 146.3, 171.1, 172.7, 185.2, 185.3

$[\alpha]_D^{20}$: +6.17 ° (*c* 0.75, $CHCl_3$)

IR V_{max}: 3280, 2955, 1734, 1645, 1616, 1558, 1521, 1506, 1456, 1338, 1296

***N*-(3,4-Dimethoxyphenethyl)-5-(3-methyl-1,4-naphthoquinone-2-yl)pentanamide (60)**



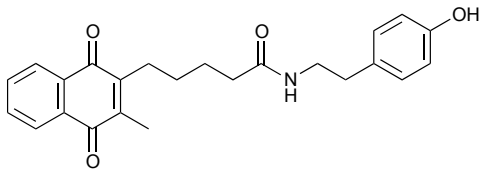
60 was prepared according to general procedure B from **22** (170 mg, 0.6243 mmol) and 3,4-dimethoxyphenylethylamine (105 mg, 0.5777 mmol) and the product purified by flash chromatography (90 % ethyl acetate/hexanes) to give **60** as bright yellow solid in 35 % yield (95 mg, 0.2170 mmol) with a melting point of 106 – 108 °C.

^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.46 (quin, *J* = 7.5 Hz, 2H), 1.70 (quin, *J* = 7.5 Hz, 2H), 2.14 (s, 3H), 2.18 (t, *J* = 7.5 Hz, 2H), 2.58 – 2.62 (m, 2H), 2.73 (t, *J* = 7.1 Hz, 2H), 3.44 – 3.49 (m, 2H), 3.80 (s, 3H), 3.82 (s, 3H), 5.75 (t, *J* = 5.4 Hz, 1H), 6.66 – 6.68 (m, 2H), 6.73 – 6.73 (m, 1H), 7.64 – 7.67 (m, 2H), 7.99 – 8.04 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.7, 25.8, 26.5, 28.0, 35.3, 36.3, 40.7, 55.90, 55.94, 111.3, 111.8, 120.6, 126.25, 126.29, 131.4, 132.14, 132.17, 133.43, 133.47, 143.5, 146.8, 147.7, 149.0, 172.8, 184.7, 185.2

IR V_{max}: 3381, 3292, 2935, 1658, 1595, 1516, 1462, 1329, 1294, 1261, 1236, 1157, 1141, 1028, 715,

_N_-(4-Hydroxyphenethyl)-5-(3-methyl-1,4-naphthoquinone-2-yl)pentanamide (61)



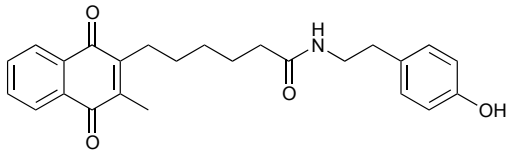
61 was prepared according to general procedure B from **22** (159 mg, 0.5831 mmol) and tyramine (77 mg, 0.5628 mmol) and the product purified by flash chromatography (85 % ethyl acetate/hexanes) to give **61** as orange solid in 20 % yield (45 mg, 0.1137 mmol) with a melting point of 136 – 138 °C.

^{1}H NMR δ (CD_3OD, 400 MHz): 1.42 – 1.50 (m, 2H), 1.66 (quin, *J* = 7.5 Hz, 2H), 2.15 (s, 3H), 2.19 (t, *J* = 7.3 Hz, 2H), 2.62 – 2.68 (m, 4H), 3.33 (t, *J* = 7.2 Hz, 2H), 6.67 (d, *J* = 8.5 Hz, 2H), 7.00 (d, *J* = 8.5 Hz, 2H), 7.72 – 7.74 (m, 2H), 8.01 – 8.04 (m, 2H)

^{13}C NMR δ (CD_3OD, 100 MHz): 12.7, 27.1, 27.4, 29.1, 35.6, 36.8, 42.2, 116.1 (two carbons), 127.0, 127.1, 130.7 (two carbons), 131.2, 133.4, 134.5 (two carbons), 144.6, 148.0, 156.8, 175.8, 185.8, 186.3

IR V_{max}: 3369, 3296, 2937, 1755, 1693, 1653, 1616, 1595, 1516, 1329, 1294, 1197, 734, 715

_N_-(4-Hydroxyphenethyl)-6-(3-methyl-1,4-naphthoquinone-2-yl)hexanamide (62)



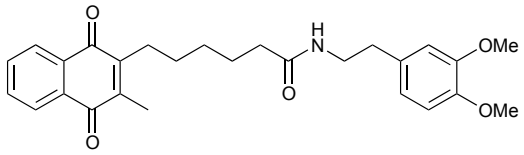
62 was prepared according to general procedure B from **23** (137 mg, 0.4778 mmol) and tyramine (74 mg, 0.5423 mmol) and the product purified by flash chromatography (90 % ethyl acetate/hexanes) to give **62** as orange crystalline solid in 39 % yield (75 mg, 0.1842 mmol) with a melting point of 90 – 92 °C.

^{1}H NMR δ (CD_3OD, 400 MHz): 1.33 – 1.42 (m, 2H), 1.45 – 1.54 (m, 2H), 1.62 (quin, *J* = 7.4 Hz, 2H), 2.13 – 2.16 (m, 2H), 2.17 (s, 3H), 2.62 – 2.69 (m, 2H), 3.34 (t, *J* = 7.3 Hz, 2H), 6.68 – 6.70 (m, 2H), 6.99 – 7.03 (m, 2H), 7.72 – 7.78 (m, 2H), 8.02 – 8.05 M, 2H)

^{13}C NMR δ (CD_3OD, 100 MHz): 12.6, 26.6, 27.6, 29.2, 30.3, 35.7, 36.9, 42.0, 116.3 (, 127.00, 127.08, 130.6 (two carbons), 131.3, 133.51, 133.55, 134.52, 134.54, 144.5, 148.4, 156.8, 175.9, 185.9, 186.4

IR V_{max}: 3369, 3296, 2935, 1695, 1654, 1595, 1541, 1516, 1329, 1296, 734, 713

***N*-(3,4-Dimethoxyphenethyl)-6-(3-methyl-1,4-naphthoquinone-2-yl)hexanamide (63)**



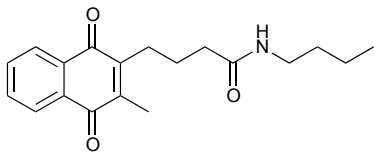
63 was prepared according to general procedure B from **23** (165 mg, 0.5773 mmol) and 3,4-dimethoxyphenyletheylamine (126 mg, 0.6932 mmol) and the product purified by flash chromatography (90 % ethyl acetate/hexanes) to give **63** as yellow solid in 60 % yield (155 mg, 0.3457 mmol) with a melting point of 98 – 100 °C.

^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.39 – 1.48 (m, 4H), 1.65 (quin, *J* = 7.4 Hz, 2H), 2.14 (t, *J* = 7.7 Hz, 2H), 2.16 (s, 3H), 2.57 – 2.61 (m, 2H), 2.74 (t, *J* = 7.0 Hz, 2H), 3.49 (q, *J* = 6.3 Hz, 2H), 3.83 (s, 3H), 3.84 (s, 3H), 5.61 (bs, 1H), 6.70 – 6.72 (m, 2H), 6.77 – 6.80 (m, 1H), 7.65 – 7.68 (m, 2H), 8.02 – 8.06 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.7, 25.4, 26.9, 28.3, 29.5, 35.3, 36.5, 40.7, 55.9, 56.0, 111.4, 112.0, 120.7, 126.31, 126.32, 131.4, 132.2, 133.44, 133.45, 143.3, 147.2, 147.8, 149.1, 173.0, 184.8, 185.3

IR V_{max}: 3369, 3304, 2935, 1656, 1595, 1516, 1456, 1329, 1294, 1261, 1236, 1028, 715

***N*-Butyl-4-(3-methyl-1,4-naphthoquione-2-yl)butanamide (64)**



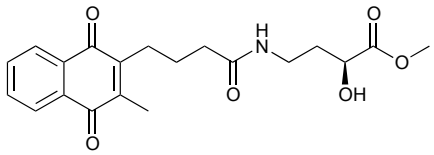
64 was prepared according to general procedure B from **21** (149 mg, 0.5533 mmol) and butylamine (67 mg, 0.9106 mmol) and the product purified by flash chromatography (70 % ethyl acetate/hexanes) to give **64** as yellow solid in 40 % yield (73 mg, 0.2336 mmol) with a melting point of 136 – 138 °C.

^{1}H NMR δ ($CDCl_3$, 400 MHz): 0.91 (t, *J* = 7.3 Hz, 3H), 1.35 (sextet, *J* = 7.3 Hz, 2H), 1.49 (quin, *J* = 7.3 Hz, 2H), 1.83 (quin, *J* = 7.3 Hz, 2H), 2.21 (s, 3H), 2.27 (t, *J* = 7.3 Hz, 2H), 2.65 – 2.69 (m, 2H), 3.24 – 3.29 (m, 2H), 5.78 (bs, 1H), 7.67 – 7.69 (m, 2H), 8.04 – 8.08 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 13.8, 20.2, 24.5, 26.5, 31.8, 36.2, 39.4, 126.40, 126.43, 132.2, 132.3, 133.5, 133.6, 144.2, 146.4, 172.2, 185.1, 185.2

IR V_{max}: 3302, 2931, 2862, 1660, 1639, 1595, 1554, 1458, 1323, 1296, 717

(*R*)-Methy-2-hydroxy-4-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)butanoate (65)



65 was prepared according to general procedure B from **21** (153 mg, 0.5905 mmol) and (*R*)-2-hydroxy-4-aminobutyric acid methyl ester.HCl (103 mg, 0.6073 mmol) and the product purified by a Reveleris ® X2 automated flash chromatography system (Eluent: gradient 50 – 80% ethyl acetate/hexanes, Column: Reveleris ® Silica 4 g, Flow rate: 18 mL/min) to give **65** as a bright yellow oil in 16 % yield (34 mg, 0.0921 mmol).

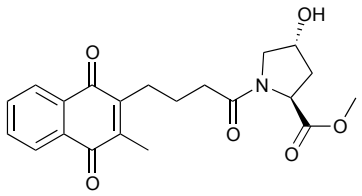
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.74 – 1.81 (m, 2H), 2.16 (s, 3H), 2.28 (t, *J* = 7.2 Hz, 2H), 2.60 – 2.64 (m, 2H), 3.32 – 3.39 (m, 2H), 3.47 – 3.53 (m, 2H), 3.73 (s, 3H), 4.25 (dd, *J* = 8.8, 3.7 Hz, 1H), 6.54 (t, *J* = 5.7 Hz, 1H), 7.64 – 7.67 (m, 2H), 7.99 – 8.03 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.7, 24.3, 26.4, 33.7, 36.0, 36.2, 52.6, 69.0, 126.3 (two carbons), 132.0, 132.1, 133.5, 133.6, 144.2, 146.2, 173.4, 174.0, 185.0, 185.1

$[\alpha]_D^{20}$: -2.47.$^{\circ}$ (*c* 0.97, $CHCl_3$)

IR V_{max}: 3367, 3306, 2953, 2929, 1739, 1658, 1595, 1539, 1456, 1437, 1329, 1294, 1215, 1122, 846, 717

(2*S*,4*R*)-Methyl-4-hydroxy-1-(4-(3-methyl-1,4-dioxo-1,4-dihydronaphthalen-2-yl)butanoyl)pyrrolidine-2-carboxylate (66)



66 was prepared according to general procedure B from **21** (143 mg, 0.5536 mmol) and *trans*-4-Hydroxy-L-proline methyl ester.HCl (103 mg, 0.5693 mmol) and the product purified by flash chromatography (90 % ethyl acetate/hexanes) to give **66** as yellow viscous oil in 59 % yield (126 mg, 0.3256 mmol).

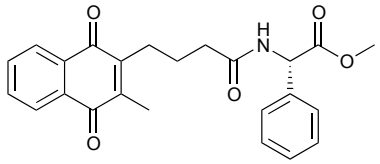
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.77 – 1.85 (m, 2H), 2.05 (ddd, *J* = 13.3, 8.1, 5.0 Hz, 1H), 2.18 (s, 3H), 2.25 – 2.31 (m, 1H), 2.41 (t, *J* = 7.2 Hz, 2H), 2.66 (t, *J* = 7.9 Hz, 2H), 3.47 (bs, 1H), 3.54 – 3.56 (m, 1H), 3.69 (s, 3H), 3.73 – 3.76 (m, 1H), 4.56 (t, *J* = 8.0 Hz, 2H), 7.63 – 7.67 (m, 2H), 7.99 – 8.04 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 23.5, 26.3, 34.0, 37.8, 52.4, 55.3, 57.7, 70.3, 126.3 (two carbons), 132.1, 132.2, 133.4, 133.5, 144.2, 146.5, 172.0, 172.8, 184.9, 185.3

$[\alpha]_D^{20}$: -58.57° (*c* 1.33, $CHCl_3$)

IR V_{max}: 3396, 2951, 1747, 1653, 1622, 1595, 1456, 1437, 1327, 1296, 1199, 1084, 717

(*S*)-Methyl-2-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)-2-phenylacetate (67)



67 was prepared according to general procedure B from **21** (209 mg, 0.8100 mmol) and S-(+)-phenyl glycine methyl ester.HCl (169 mg, 0.8396 mmol) and the product purified by flash chromatography (45 % ethyl acetate/hexanes) to give **67** as yellow solid in 72 % yield (236 mg, 0.5826 mmol) with a melting point of 100 – 102 °C.

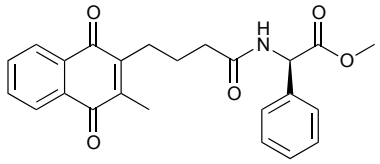
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.78 – 1.85 (m, 2H), 2.13 (s, 3H), 2.35 (td, *J* = 7.3, 3.2 Hz, 2H), 2.63 – 2.67 (m, 2H), 3.70 (s, 3H), 5.59 (d, *J* = 7.2 Hz, 1H), 6.87 (d, *J* = 6.6 Hz, 1H), 7.28 – 7.37 (m, 5H), 7.63 – 7.66 (m, 2H), 7.99 – 8.03 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.7, 24.2, 26.3, 35.8, 52.8, 56.5, 126.3, 126.4, 127.4, 128.6, 129.1, 132.1, 132.2, 133.4, 133.5, 136.5, 144.1, 146.3, 171.5, 171.7, 184.9, 185.2

$[\alpha]_D^{20}$: +99.11° (*c* 1.13, $CHCl_3$)

IR V_{max}: 3306, 3030, 2953, 1743, 1647, 1597, 1597, 1537, 1456, 1435, 1379, 1330, 1296, 1213, 1127, 754, 717, 698

(*R*)-Methyl-2-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)-2-phenylacetate (68)



68 was prepared according to general procedure B from **21** (202 mg, 0.7810 mmol) and R-(-)-phenyl glycine methyl ester.HCl (161 mg, 0.8396 mmol) and the product purified by flash chromatography (45 % ethyl acetate/hexanes) to give **68** as yellow solid in 69 % yield (219 mg, 0.5394 mmol) with a melting point of 90 – 92 °C.

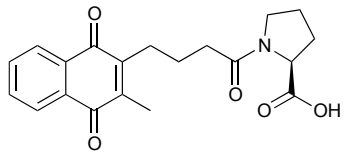
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.78 – 1.86 (m, 2H), 2.15 (s, 3H), 2.35 (td, *J* = 7.3, 3.0 Hz, 2H), 2.64 – 2.68 (m, 2H), 3.71 (s, 3H), 5.60 (d, *J* = 7.2 Hz, 1H), 6.79 (d, *J* = 7.2 Hz, 1H), 7.30 – 7.36 (m, 5H), 7.64 – 7.69 (m, 2H), 8.00 – 8.06 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.7, 24.3, 26.3, 35.9, 52.9, 56.5, 126.3, 126.4, 127.4 (two carbons), 128.7, 129.1 (two carbons), 132.20, 132.27, 133.50, 133.54, 136.6, 144.1, 146.4, 171.5, 171.7, 184.9, 185.3

$[\alpha]_D^{20}$: -93.58° (*c* 0.78, $CHCl_3$)

IR V_{max}: 3304, 3032, 2953, 1743, 1656, 1647, 1597, 1521, 1456, 1435, 1379, 1323, 1296, 1259, 1213, 1172, 754, 717, 696

(*S*)-1-(4-(3-Methyl-1,4-naphthoquinone-2-yl)butanoyl)pyrrolidine-2-carboxylic acid (70)



70 was prepared from the deprotection of **37** (114 mg, 0.2766 mmol), using general procedure C. The product was purified by flash chromatography (3 % methanol/ethyl acetate) to give **70** as brown viscous oil in 65 % yield (64 mg, 0.1798 mmol).

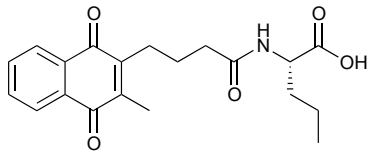
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.82 – 1.90 (m, 2H), 2.02 – 2.08 (m, 2H), 2.21 (s, 3H), 2.13 – 2.33 (m, 2H), 2.45 – 2.50 (m, 2H), 2.68 – 2.72 (m, 2H), 3.49 – 3.53 (m, 1H), 3.60-3.63 (m, 1H), 4.55 – 4.58 (m, 1H), 7.53 (bs, 1H), 7.68 – 7.07 (m, 2H), 8.04 – 8.08 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 23.3, 24.8, 26.4, 28.0, 34.1, 47.8, 59.7, 126.34, 126.38, 132.1, 132.2, 133.51, 133.56, 144.2, 146.3, 173.4, 173.9, 184.8, 185.3

$[\alpha]_D^{20}$: -65.80° (*c* 1.69, $CHCl_3$)

IR V_{max}: 2976, 2956, 1732, 1658, 1616, 1595, 1456, 1329, 1294, 1188, 717

(*S*)-2-(4-(3-Methyl-1,4-naphthoquinone-2-yl)butanamido)pentanoic acid (71)



71 was prepared from the deprotection of **38** (140 mg, 0.3376 mmol), using general procedure C. The product was purified by silica plug (gradient 5-10 % methanol/ethyl acetate) to give **71** as yellow/brown viscous oil in 36 % yield (44 mg, 0.1223 mmol).

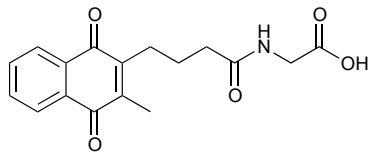
^{1}H NMR δ (CD_3OD, 400 MHz): 0.92 (t, *J* = 7.3 Hz, 3H), 1.35 – 1.45 (m, 2H), 1.61 – 1.70 (m, 2H), 1.78 (quin, *J* = 7.5 Hz, 2H), 2.14 (s, 3H), 2.34 (t, *J* = 7.4, 2H), 2.62 – 2.62 (m, 2H), 4.29 – 4.32 (m, 1H), 7.68 – 7.72 (m, 2H), 7.94 – 7.98 (m, 2H)

^{13}C NMR δ (CD_3OD, 100 MHz): 12.7, 14.0, 20.1, 25.7, 27.3, 35.0, 36.6, 127.00, 127.08, 133.3, 134.5, 144.9, 147.5, 175.3 (two carbons), 185.6, 186.2

$[\alpha]_D^{20}$: -24.44 ° (*c* 0.09, $CHCl_3$)

IR V_{max}: 3336, 3296, 2960,2874, 1660, 1595, 1558, 1456, 1296, 1205, 1139, 1026, 721

2-(4-(3-Methyl-1,4-naphthoquinone-2-yl)butanamido)acetic acid (72)



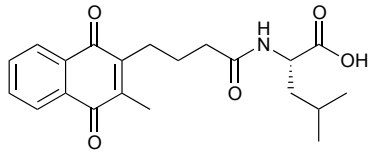
72 was prepared from the deprotection of **39** (75 mg, 0.1952 mmol), using general procedure C. The product purified by precipitation from dichloromethane and the solvent was decanted to give **72** as brown solid in 54 % yield (34 mg, 0.1062 mmol) with a melting point of 62 – 66 °C.

^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.82 (quin, *J* = 7.5 Hz, 2H), 2.16 (s, 3H), 2.41 (t, *J* = 7.2 Hz, 2H), 2.64 – 2.68 (m, 2H), 4.09 (d, *J* = 5.2 Hz, 2H), 6.96 – 6.99 (m, 1H), 7.65 – 7.68 (m, 2H), 7.99 – 8.04 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 24.3, 26.3,35.7, 41.6, 126.45, 126.48, 132.0, 132.2, 133.6, 133.7, 144.5, 146.0, 172.6, 174.7, 185.2, 185.3

IR V_{max}: 3296, 2939, 1734, 1654, 1595, 1533, 1330, 1296, 1024, 717

(*S*)-4-Methyl-2-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)pentanoic acid (73)



73 was prepared from the deprotection of **41** (109 mg, 0.2559 mmol), using general procedure C. The product purified by flash chromatography (5 % methanol/ethyl acetate) to give **73** as a dark yellow viscous oil in 61 % yield (58 mg, 0.1612 mmol).

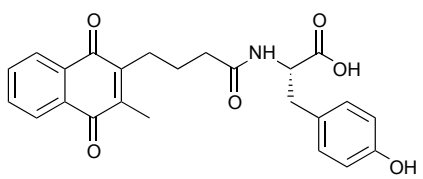
^{1}H NMR δ ($CDCl_3$, 400 MHz): 0.93 – 0.95 (m, 6H), 1.61 – 1.73 (m, 3H) 1.82 (quin, *J* = 7.4 Hz, 2H), 2.17 (s, 3H), 2.38 (t, *J* = 7.4 Hz, 2H), 2.64 – 2.68 (m, 2H), 4.59 – 4.64 (m, 1H), 6.73 (d, *J* = 8.0 Hz, 1H), 7.65 – 7.67 (m, 2H), 7.99 – 8.03 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.7, 21.8, 22.9, 24.3, 25.0, 26.3, 35.9, 41.0, 51.0, 126.3 (two carbons), 132.0, 132.1, 133.5, 133.6, 144.3, 146.2, 173.5, 176.2, 185.1, 185.2

$[\alpha]_D^{20}$: -5.35 ° (*c* 0.93, $CHCl_3$)

IR V_{max}: 3321, 1716, 1660, 1618, 1595, 1539, 1506, 1330, 1294, 1207, 717

(*S*)-3-(4-Hydroxyphenyl)-2-(4-(3-methyl-1,4-naphthoquinone-2-yl)butanamido)propanoic acid (74)



74 was prepared from the deprotection of **42** (30 mg, 0.06213 mmol), using general procedure C. The product purified by precipitation from dichloromethane and the solvent decanted to give **74** as a dark yellow viscous oil in 76 % yield (20 mg, 0.0479 mmol).

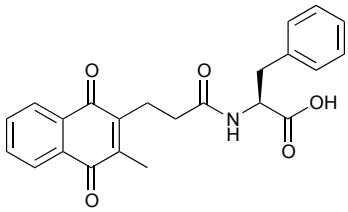
^{1}H NMR δ (CD_3OD, 400 MHz): 1.67 (quin, *J* = 7.7 Hz, 2H), 2.08 (s, 3H), 2.23 – 2.30 (m, 2H), 2.37 – 2.45 (m, 1H), 2.52 – 2.59 (m, 1H), 2.82 (dd, *J* = 14.0, 9.5 Hz, 1H), 3.12 (dd, *J* = 14.0, 4.9 Hz, 1H), 4.60 – 4.64 (m,1H), 6.65 (d, *J* = 8.3 Hz, 2H), 7.04 (d, *J* = 8.3 Hz, 2H), 7.71 – 7.73 (m, 2H), 7.99 – 8.02 (m, 2H)

^{13}C NMR δ (CD_3OD, 100 MHz): 12.6, 25.6, 27.1, 36.5, 37.6, 55.2, 116.1 (two carbons), 127.0, 127.1, 129.1, 131.2 (two carbons), 133.4, 134.56, 134.57, 145.0, 147.5, 157.2, 174.9, 175.3, 185.7, 186.3

$[\alpha]_D^{20}$: +2.21 ° (*c* 0.81, $CHCl_3$)

IR V_{max}: 3365, 2937, 1734, 1716, 1647, 1616, 1595, 1516, 1456, 1296, 1232

(*S*)-2-(3-(3-Methyl-1,4-naphthoquinone-2-yl)propanamido)-3-phenylpropanoic acid (76)



76 was prepared from the deprotection of **46** (18 mg, 0.0407 mmol), using general procedure C. The product purified by flash chromatography (5 % methanol/ethyl acetate) to give **76** as a yellow oil in 80 % yield (13 mg, 0.0327 mmol).

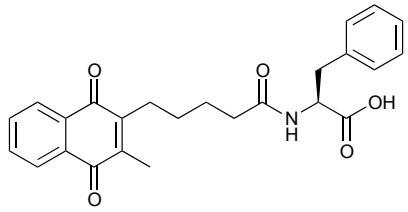
^{1}H NMR δ (CD_3OD, 400 MHz): 2.08 (s, 3H), 2.37 (td, *J* = 7.6, 3.5 Hz, 2H), 2.82 (t, *J* = 7.6 Hz, 2H), 2.89 (dd, *J* = 13.9, 9.3 Hz, 1H), 3.17 (dd, *J* = 13.9, 4.9 Hz, 1H), 4.64 (dd, *J* = 9.3, 5.0 Hz, 1H), 7.11 – 7.17 (m, 5H), 7.72 – 7.75 (m, 2H), 8.00 – 8.02 (m, 2H)

^{13}C NMR δ (CD_3OD, 100 MHz): 12.7, 24.3, 35.1, 38.4, 55.0, 127.0, 127.7, 129.3 (two carbons), 130.1 (two carbons), 133.4, 134.590, 134.598, 138.4, 145.5, 146.4, 174.4, 185.6, 186.1

$[\alpha]_D^{20}$: -3.95° (*c* 0.45, $CHCl_3$)

IR V_{max}: 3306, 2926, 1732, 1658, 1595, 1454, 1330, 1296, 1195, 734, 702

(*S*)-2-(5-(3-Methyl-1,4-naphthoquinone-2-yl)pentanamido)-3-phenylpropanoic acid (77)



77 was prepared from the deprotection of **47** (215 mg, 0.4517 mmol), using general procedure C. The product purified by flash chromatography (35 % ethyl acetate/hexane) to give **77** as a brown oil in 85 % yield (161 mg, 0.3843 mmol).

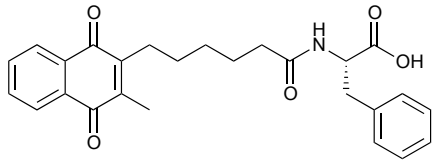
^{1}H NMR δ (CD_3OD, 400 MHz): 1.26 – 1.40 (m, 2H), 1.58 (quin, *J* = 7.6 Hz, 2H), 2.09 (s, 3H), 2.17 – 2.22 (m, 2H), 2.55 (t, *J* = 7.9 Hz, 2H), 2.90 (dd, *J* = 14.0, 9.6 Hz, 1H), 3.19 (dd, *J* = 14.1, 4.7 Hz, 1H), 4.67 (dd, *J* = 9.7, 4.9 Hz, 2H), 7.14 – 7.21 (m, 5H), 7.70 – 7.74 (m, 2H), 7.99 – 8.02 (m, 2H)

^{13}C NMR δ (CD_3OD, 100 MHz): 12.7, 26.9, 27.4, 28.9, 36.4, 38.3, 54.8, 127.0, 127.1, 127.6, 129.3 (two carbons), 130.1 (two carbons), 133.40, 133.42, 134.5 (two carbons), 138.5, 144.5, 148.0, 174.7, 175.7, 185.7, 186.3

$[\alpha]_D^{20}$: +25.16° (*c* 1.06, $CHCl_3$)

IR V_{max}: 3316, 2939, 1734, 1656, 1595, 1525, 1456, 1294, 1190, 736, 702

(*S*)-2-(6-(3-Methyl-1,4-naphthoquinone-2-yl)hexanamido)-3-phenylpropanoic acid (78)



78 was prepared from the deprotection of **50** (166 mg, 0.3382 mmol), using general procedure C. The product purified by precipitation from dichloromethane and the solvent was decanted to give **78** as brown solid in 84 % yield (124 mg, 0.2854 mmol) with a melting point of 72 – 76 °C.

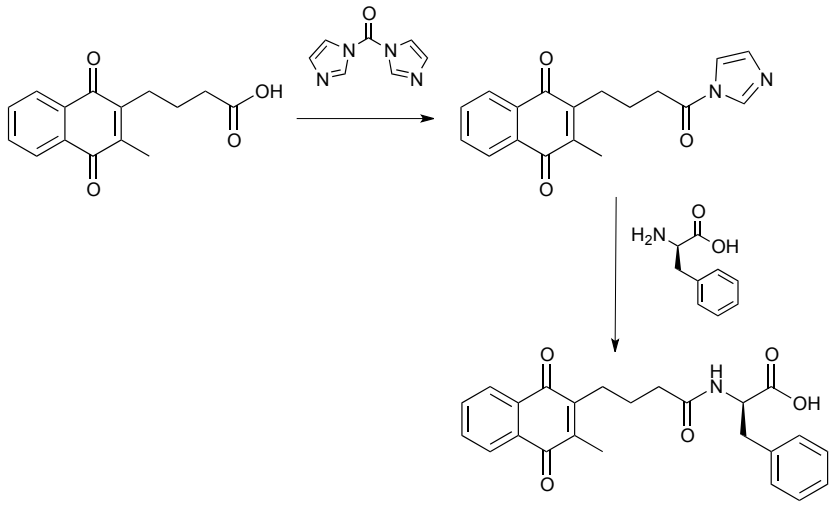
^{1}H NMR δ (CD_3OD, 400 MHz): 1.30 – 1.35 (m, 2H), 1.39 – 1.46 (m, 2H), 1.56 (quin, *J* = 7.5 Hz, 2H), 2.16 (s, 3H), 2.17 – 2.20 (m, 2H), 2.58 – 2.62 (m, 2H), 2.93 (dd, *J* = 14.0, 9.5 Hz, 1H), 3.22 (dd, *J* = 14.0, 4.9 Hz, 1H), 4.69 (dd, *J* = 9.5, 4.9 Hz, 1H), 7.20 – 7.28 (m, 5H), 7.74 – 7.76 (m, 2H), 8.03 – 8.05 (m, 2H)

^{13}C NMR δ (CD_3OD, 100 MHz): 12.7, 26.5, 27.6, 29.3, 30.2, 36.5, 38.4, 54.8, 127.02, 127.09, 127.7, 129.4, 130.2, 133.46, 133.49, 134.57, 134.58, 138.5, 144.4, 148.3, 174.7, 175.9, 185.8, 186.3

$[\alpha]_D^{20}$: +24.71 ° (*c* 0.78, $CHCl_3$)

IR V_{max}: 3288, 2937, 1732, 1660, 1595, 1531, 1456, 1377, 1330, 1294, 1172, 736, 702

(*R*)-2-(4-(3-Methyl-1,4-naphthoquinone-2-yl)butanamido)-3-phenylpropanoic acid (79)



21 (200 mg, 0.7736 mmol) was added to anhydrous dichloromethane (5-10ml) under an atmosphere of N_2. Carbonyl diimidazole (145 mg, 0.8930 mmol) was added and the resulting mixture stirred for 3.5 h at room temperature. The reaction was quenched with H_2O (20mL) and the organic layer washed with H_2O (2 x 20 mL). The organic layer was dried with $MgSO_4$, filtered and the solvent removed under reduced pressure to give the crude intermediate as a yellow oil (222 mg, 0.7190 mmol). To the crude intermediate in THF (5 mL) a solution of D-phenyl alanine (650 mg, 3.9373 mmol) and pyridine (0.28 mL, 3.6084 mmol) in H_2O (15 mL) was added and the reaction stirred under an atmosphere of nitrogen for 6 h. The reaction was quenched with 20 mL 2M HCl and extracted DCM (3 x 20 mL) and the organic layer was dried with $MgSO_4$, filtered and the solvent removed under reduced pressure to give a crude product, which was purified by flash chromatography (7 % methanol/ethyl acetate) to give **79** as yellow oil in 14 % yield (44 mg, 0.1080 mmol).

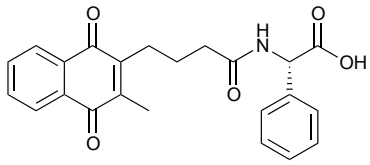
^{1}H NMR δ ($CDCl_3$, 400 MHz): 1.72 – 1.79 (m, 2H), 2.15 (s, 3H), 2.30 (t, J = 7.3 Hz, 2H), 2.57 – 2.61 (m, 2H), 3.13 (dd, J = 14.1, 7.0 Hz, 2H), 3.27 (dd, J = 14.2, 5.5 Hz, 2H), 4.88 – 4.93 (m, 1H), 6.51 (d, J = 7.5 Hz, 1H), 7.18 – 7.29 (m, 5H), 7.67 – 7.71 (m 2H), 8.03 – 8.07 (m, 2H)

^{13}C NMR δ ($CDCl_3$, 100 MHz): 12.8, 24.2, 26.2, 35.9, 37.4, 53.4, 126.4, 127.2, 128.7(two carbons), 129.4 (two carbons), 132.1, 132.2, 133.5, 133.6, 135.9, 144.3, 146.2, 173.3, 174.8, 185.0, 185.2

$[\alpha]_D^{20}$: -38.75° (*c* 0.16, $CHCl_3$)

IR V_{max}: 3370, 2928, 1732, 1658, 1595, 1527, 1456, 1330, 1294, 734, 717, 702

(*S*)-2-(4-(3-Methyl-1,4-naphthoquinone-2-yl)butanamido)-2-phenylacetic acid (80)



67 (76.1 mg, 0.1877 mmol) was added to 6M HCl (4 mL) with a catalytic amount of glacial acetic acid. Solution was refluxed for 2h and reaction quenched with the addition of H_2O (20 mL) and dichlormethane (20 mL), and the aqueous layer extracted with a further 2 x 20 mL dichloromethane. The organic layer dried with $MgSO_4$ and the solvent removed under reduced pressure to give a crude product, which was purified by precipitation from dichloromethane and the solvent decanted to give **80** as pale yellow solid in 46 % yield (34.0 mg, 0.0869 mmol) with a melting point of 168 – 170 °C.

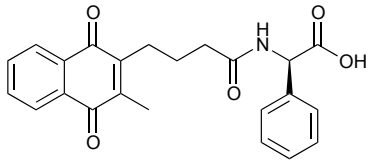
^1H NMR δ (CD_3OD, 400 MHz): 1.81 (quin, *J* = 7.6 Hz, 2H), 2.14 (s, 3H), 2.35 – 2.40 (m, 2H), 2.65 – 2.70 (m, 2H), 5.42 (s, 1H), 7.31 – 7.42 (m, 5H), 7.72 – 7.75 (m, 2H), 8.02 – 8.04 (m, 2H)

^{13}C NMR δ (CD_3OD, 100 MHz): 12.7, 25.6, 27.2, 36.2, 58.2, 127.0, 127.1, 128.8 (two carbons), 129.3, 129.7 (two carbons), 133.510, 133.51, 134.5, 134.6, 138.1, 145.9, 147.5, 175.1, 185.8, 186.3

$[\alpha]_D^{20}$: +90.34° (*c* 0.74, $CHCl_3$)

IR V_{max}: 3350, 3030, 2933, 1732, 1658, 1647, 1597, 1533, 1456, 1379, 1330, 1296, 1259, 1219, 754, 717, 698

(*R*)-2-(4-(3-Methyl-1,4-naphthoquinone-2-yl)butanamido)-2-phenylacetic acid (81)



68 (49 mg, 0.1208 mmol) was added to 6M HCl (4 mL) with a catalytic amount of glacial acetic acid. Solution was refluxed for 2h and reaction quenched with the addition of H_2O (20 mL) and dichlormethane (20 mL), and the aqueous layer extracted with a further 2 x 20 mL dichloromethane. The organic layer dried with $MgSO_4$ and the solvent removed under reduced pressure to give a crude product, which was purified by precipitation from dichloromethane and the solvent decanted to give **81** as pale yellow solid in 14 % yield (7 mg, 0.0169 mmol) with a melting point of 128 – 130 °C.

^{1}H NMR δ (CD_3OD, 400 MHz): 1.81 (quin, J = 7.5 Hz, 2H), 2.14 (s, 3H), 2.35 – 2.40 (m, 2H), 2.65 – 2.70 (m, 2H), 5.42 (s, 1H), 7.31 – 7.42 (m, 5H), 7.73 – 7.75 (m, 2H), 8.02 – 8.04 (m, 2H)

^{13}C NMR δ (CD_3OD, 100 MHz): 12.7, 25.6, 27.2, 36.2, 58.3, 127.0, 127.1, 128.8 (two carbons), 129.3, 129.7 (two carbons), 133.50, 133.52, 134.57, 134.59, 138.2, 145.0, 147.5, 175.1, 185.8, 186.3 (Note: one carbon signal missing or overlapped)

$[\alpha]_D^{20}$: -127.41° (c 0.14, $CHCl_3$)

IR V_{max}: 3348, 3066, 2928, 1732, 1658, 1647, 1597, 1496, 1456, 1379, 1330, 1296, 1259, 1217, 1178, 754, 717, 698

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7. H. R. Nasiri, M. G. Madej, R. Panisch, M. Lofantaine, J. W. Bats, C. R. D. Lancaster, H. Schwalbe, *J. Med. Chem.*, **2013**, *56*, 9530 - 9541
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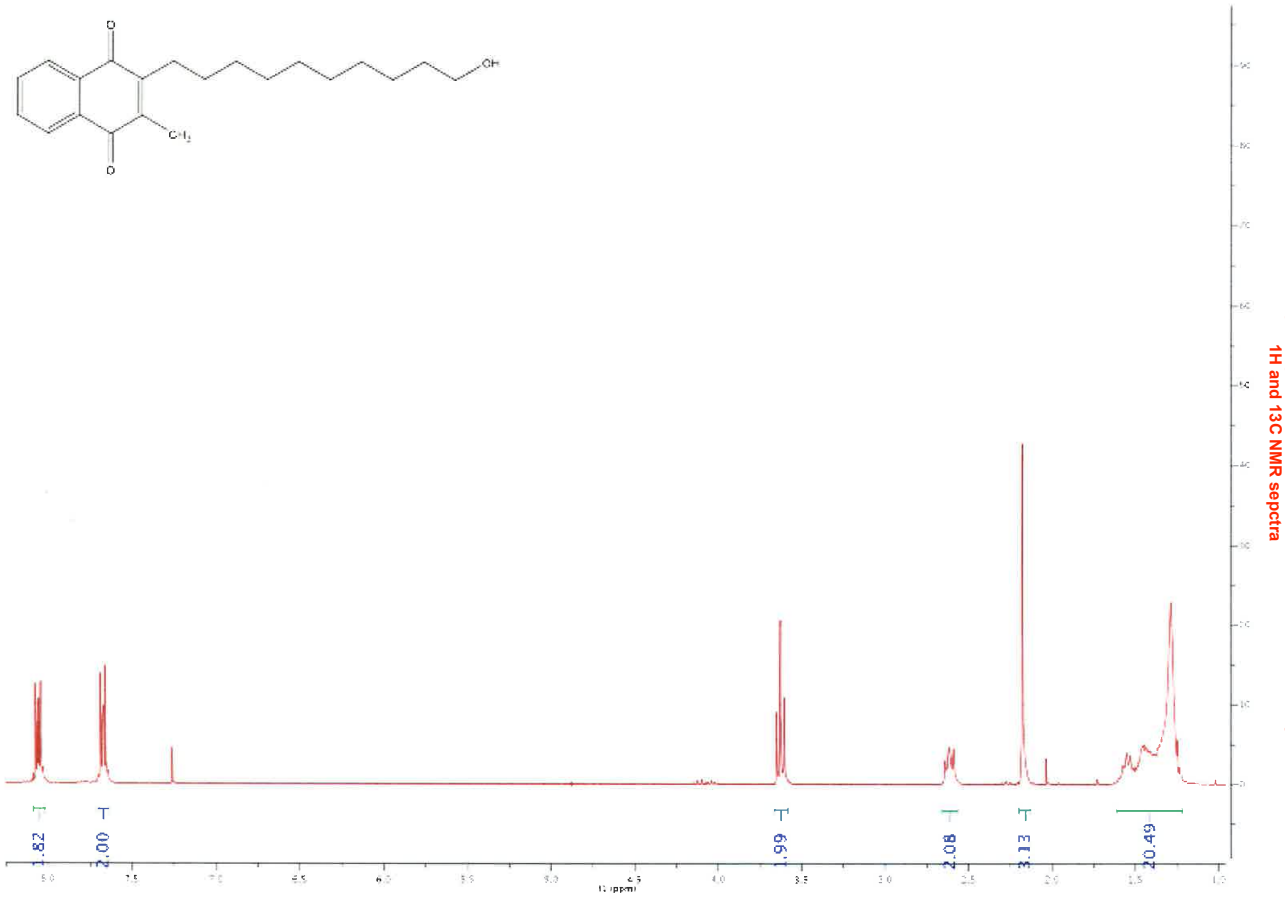

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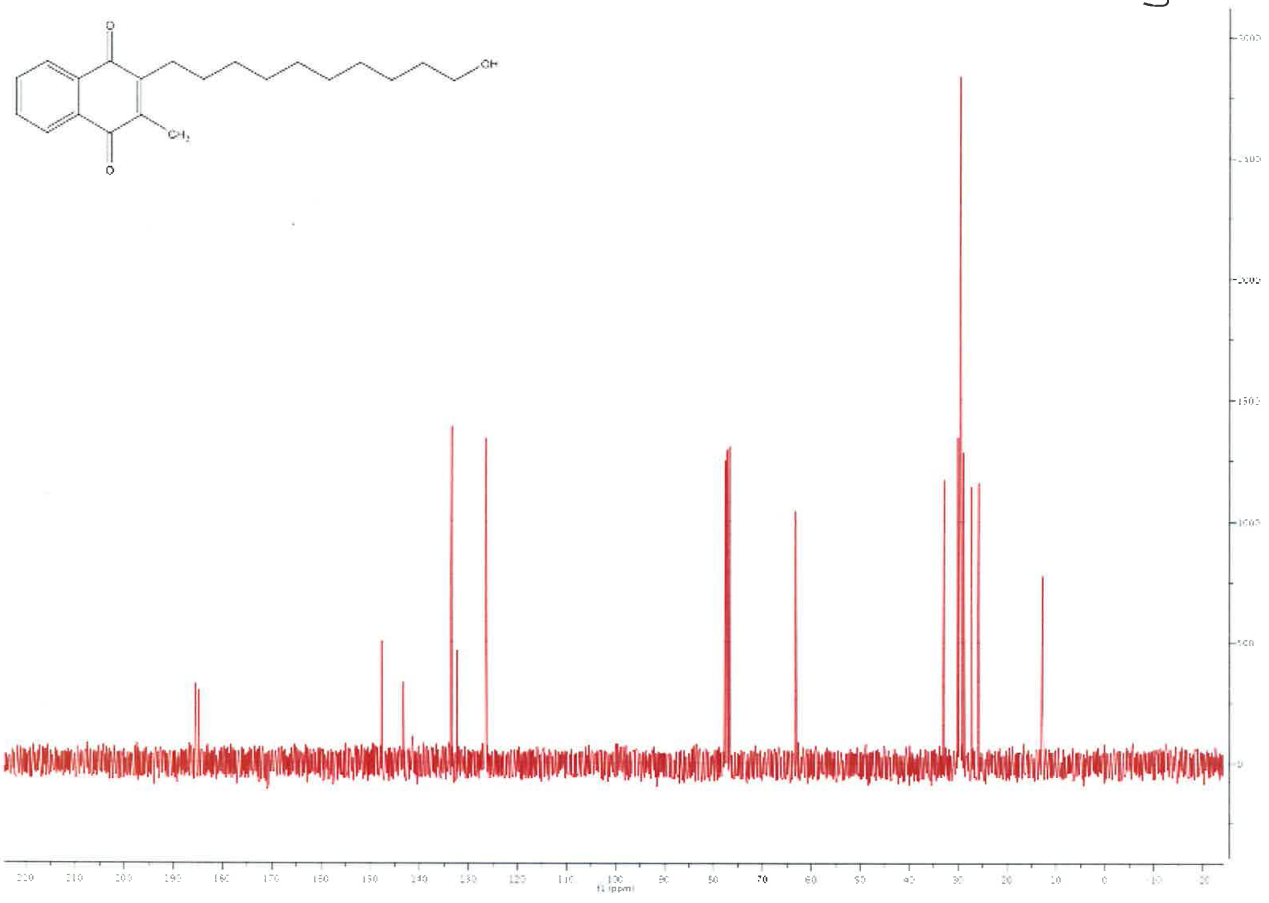

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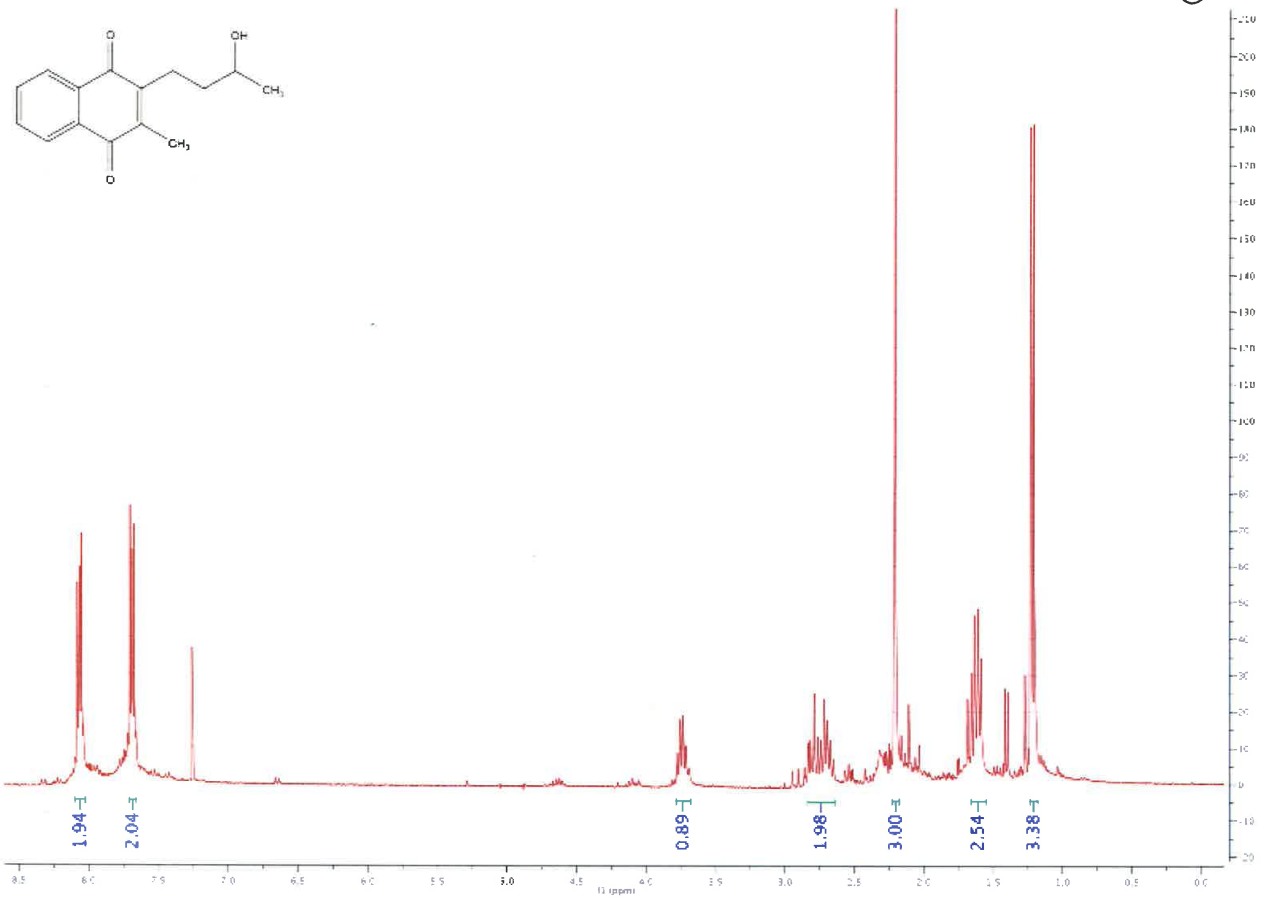

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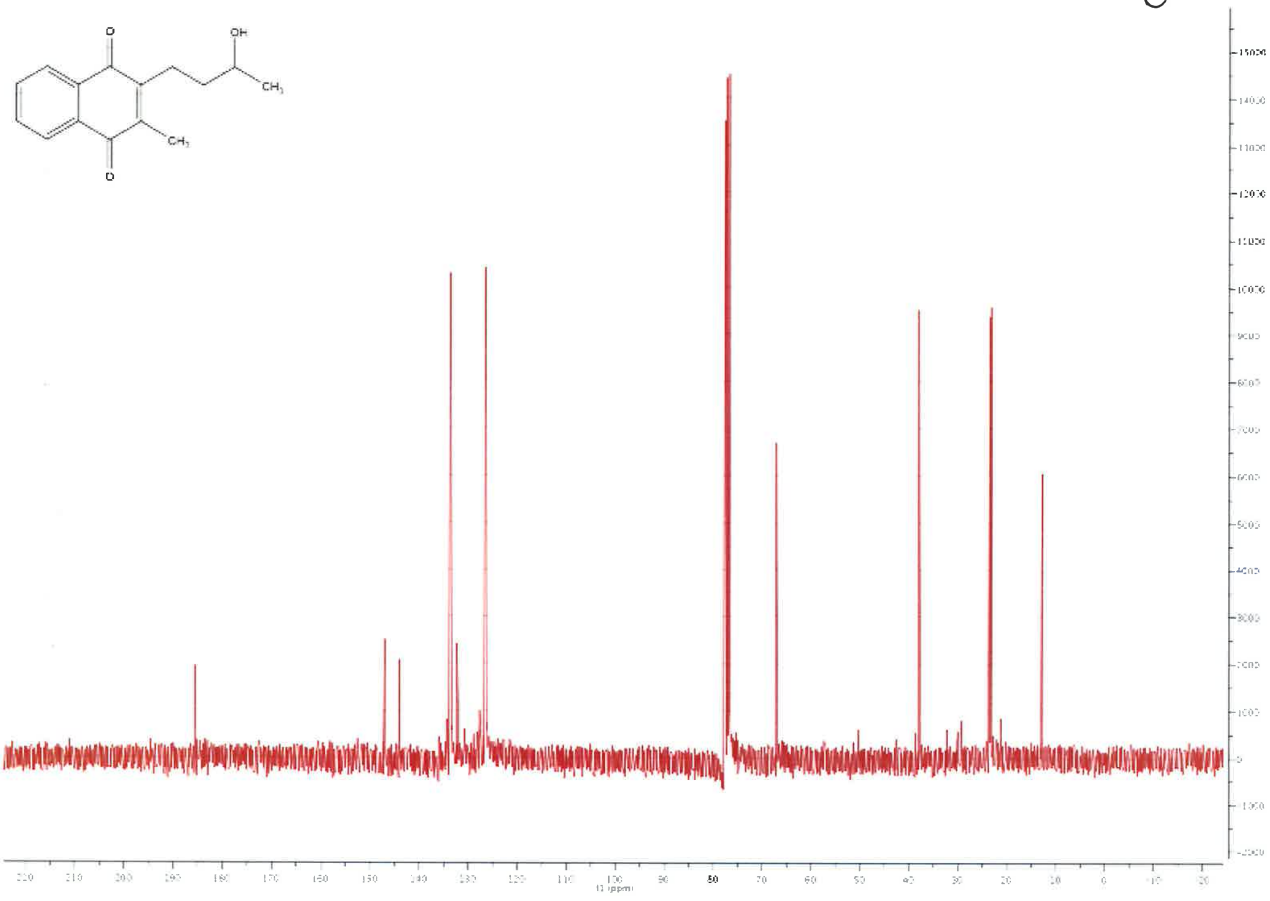

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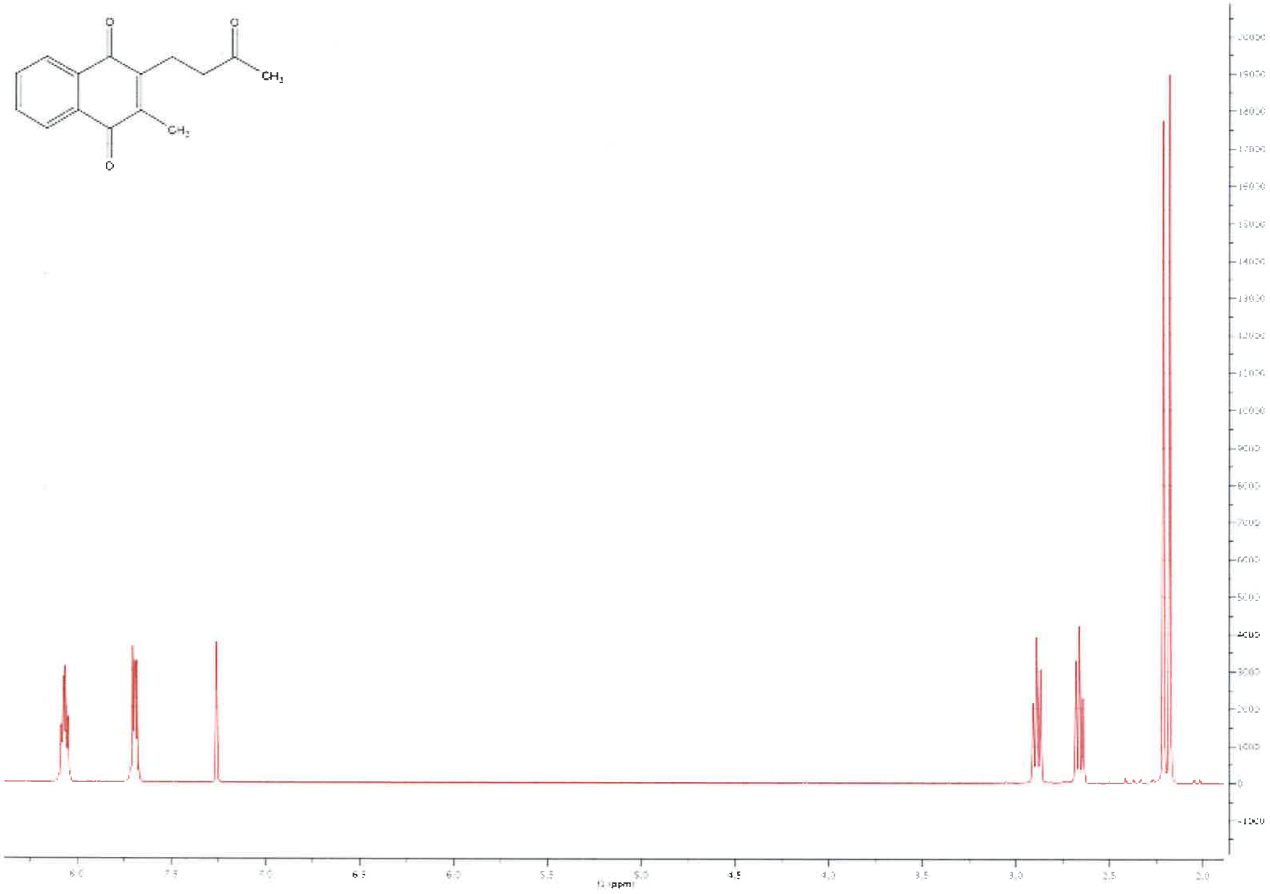

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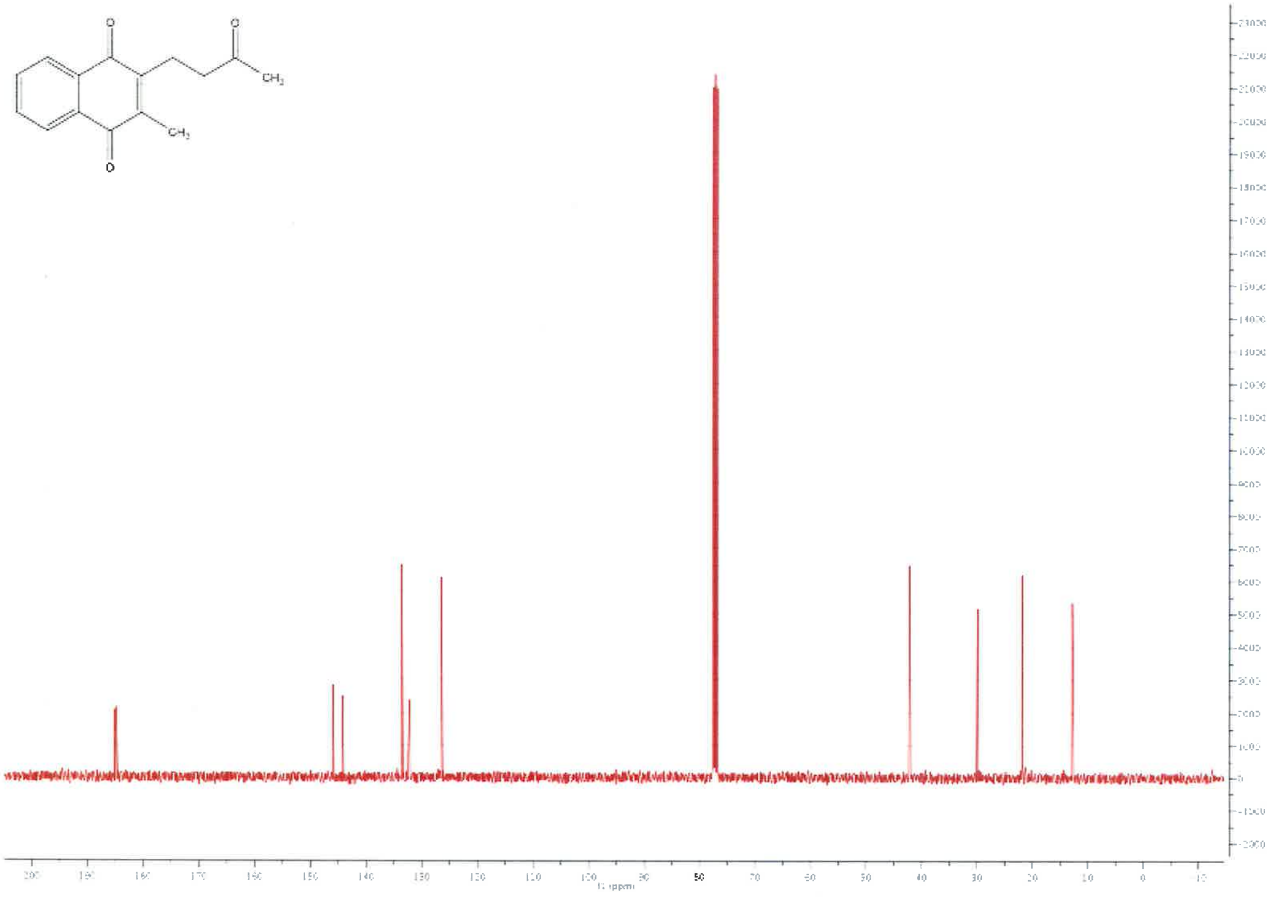

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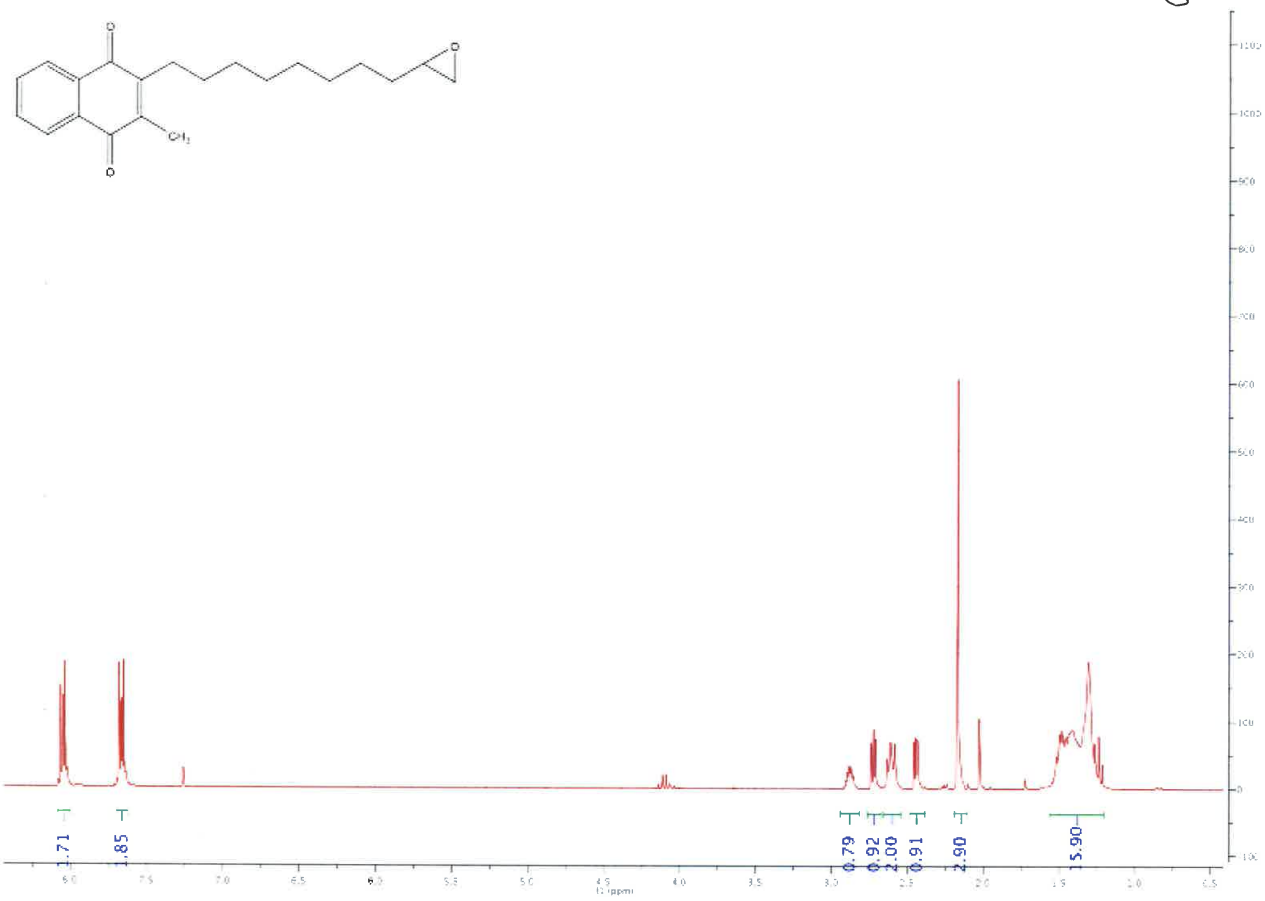

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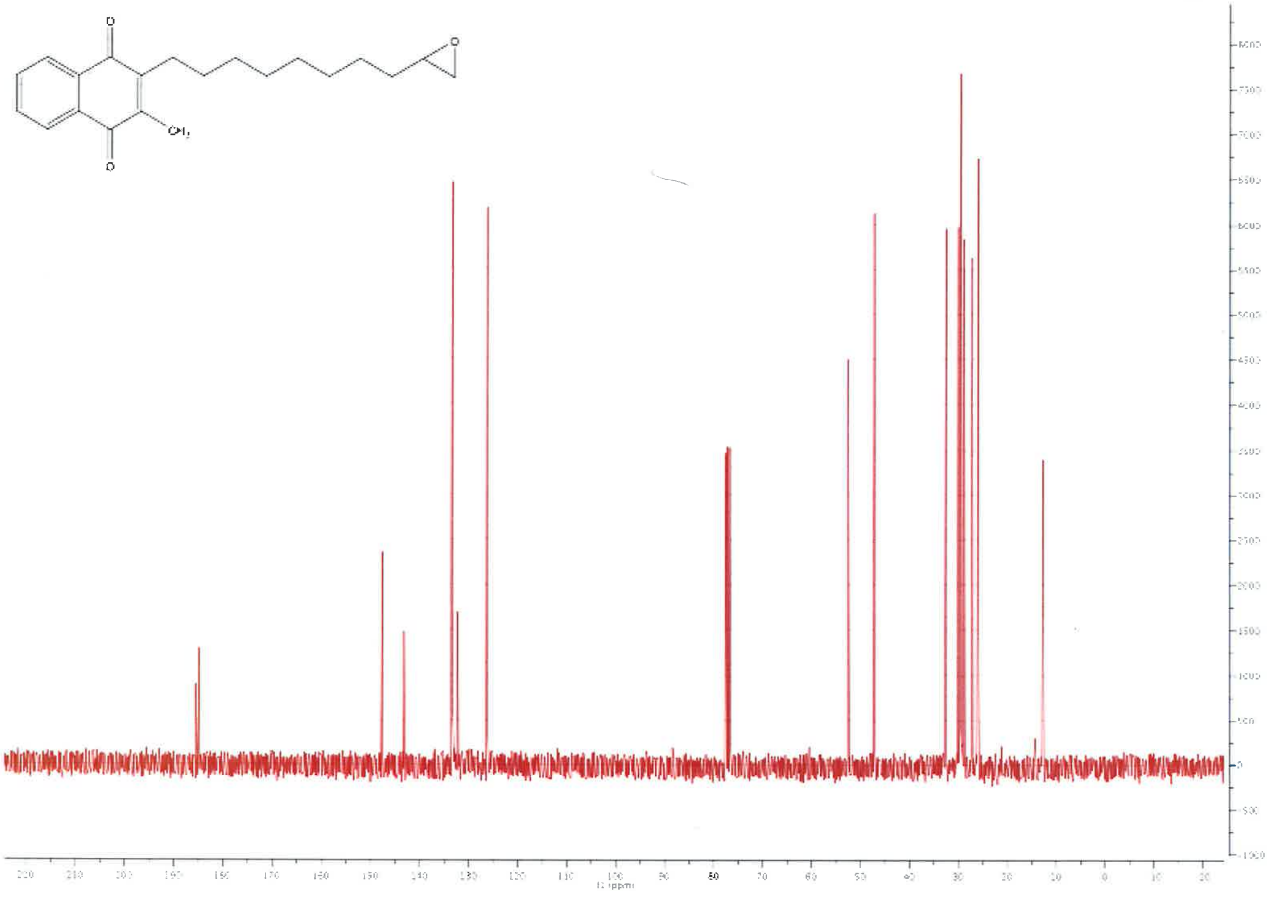

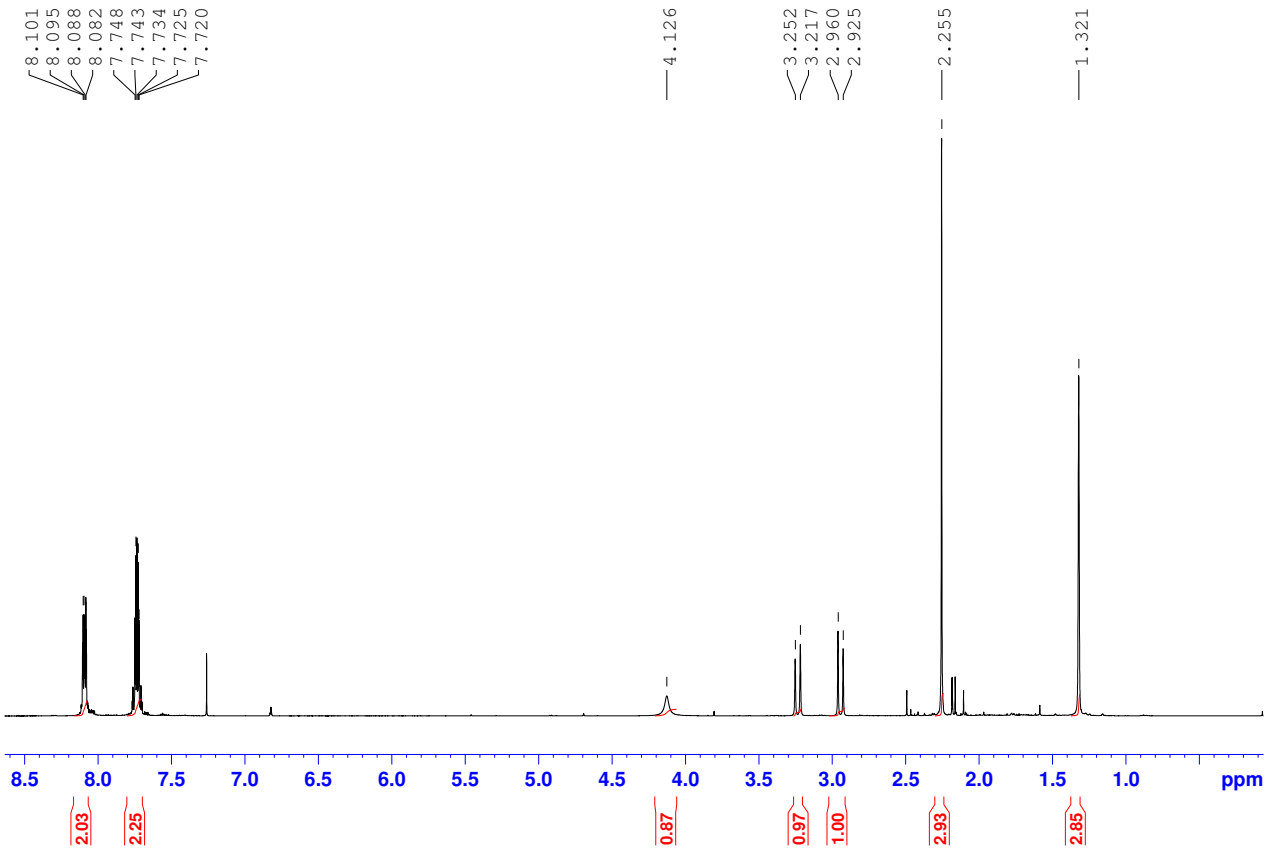
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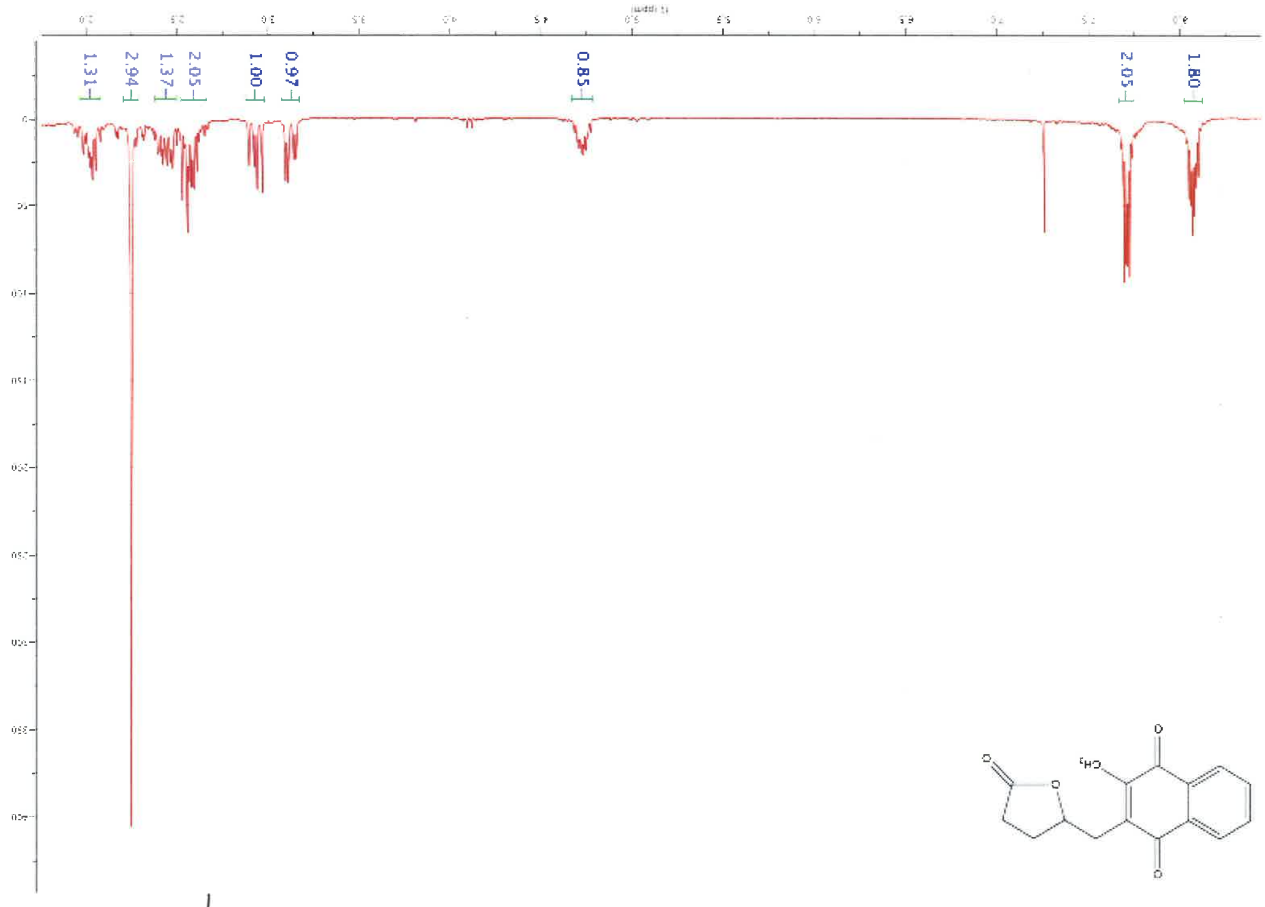
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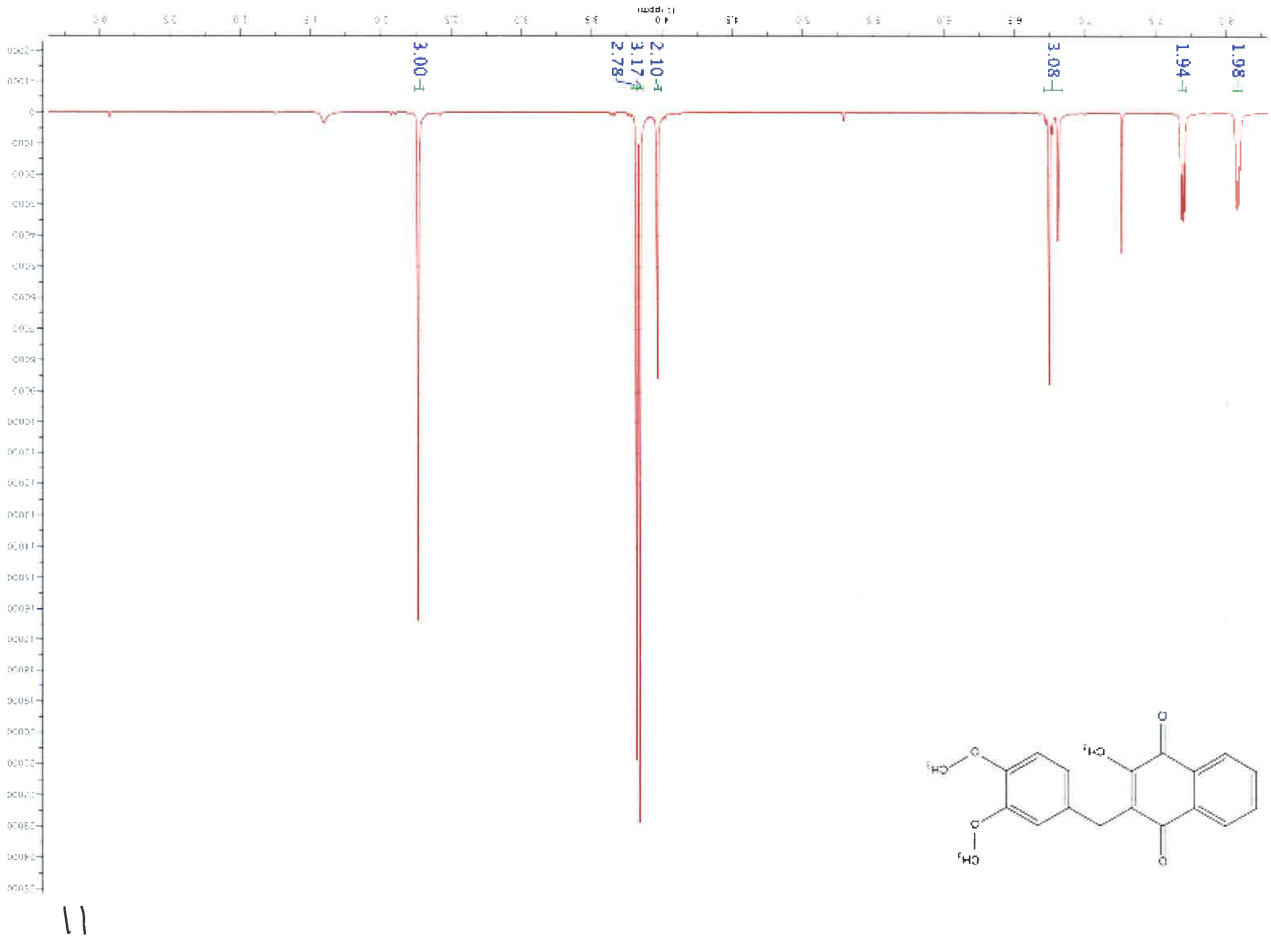

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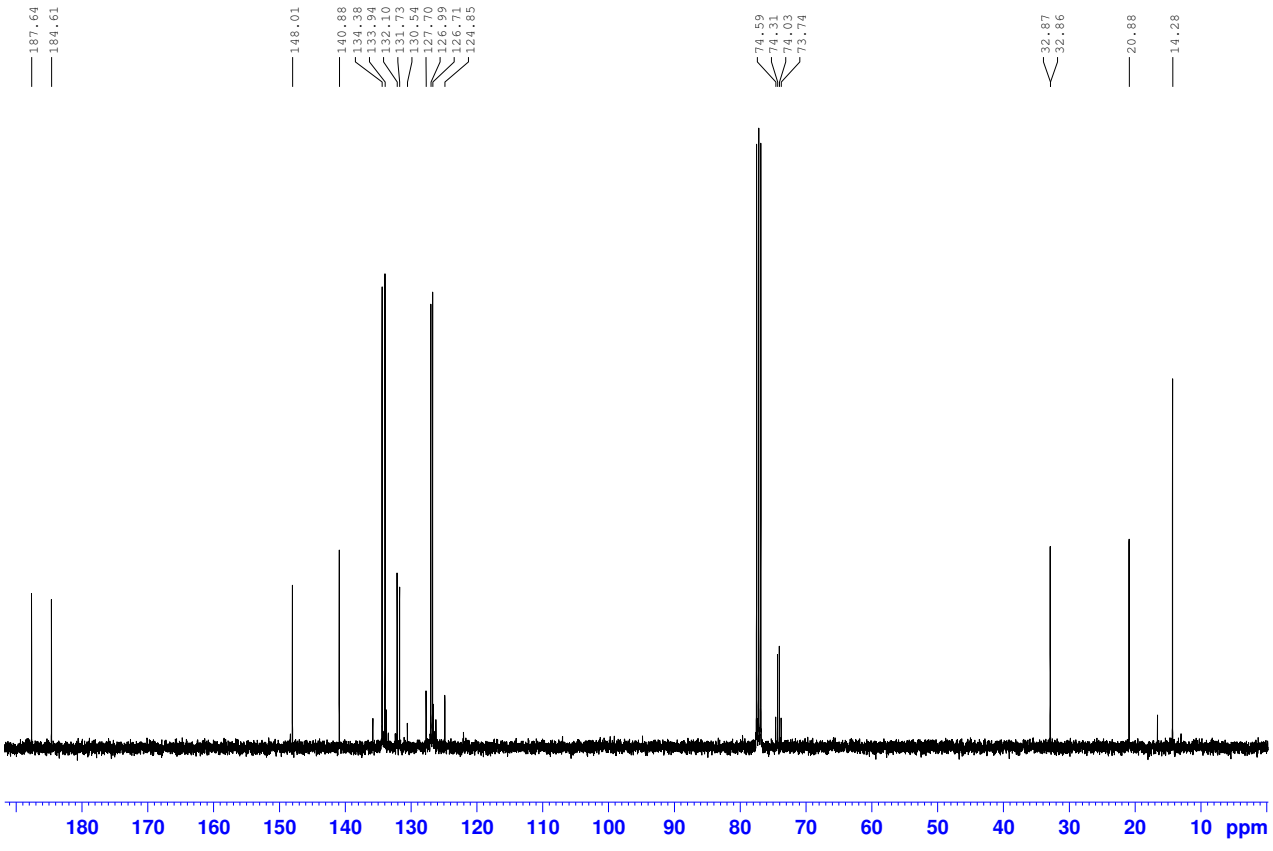
Avance III - 13C with 1H Power-gated Decoupling



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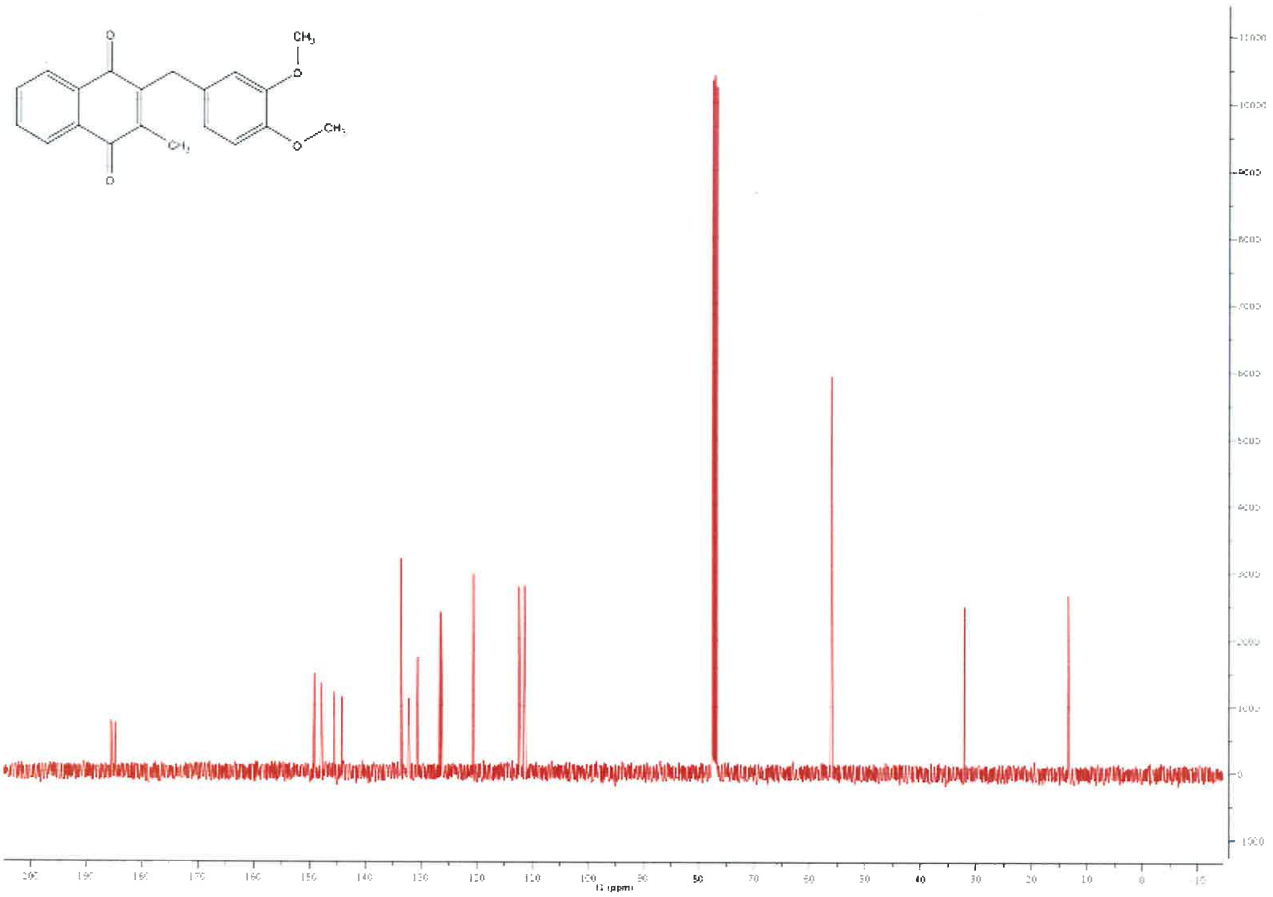

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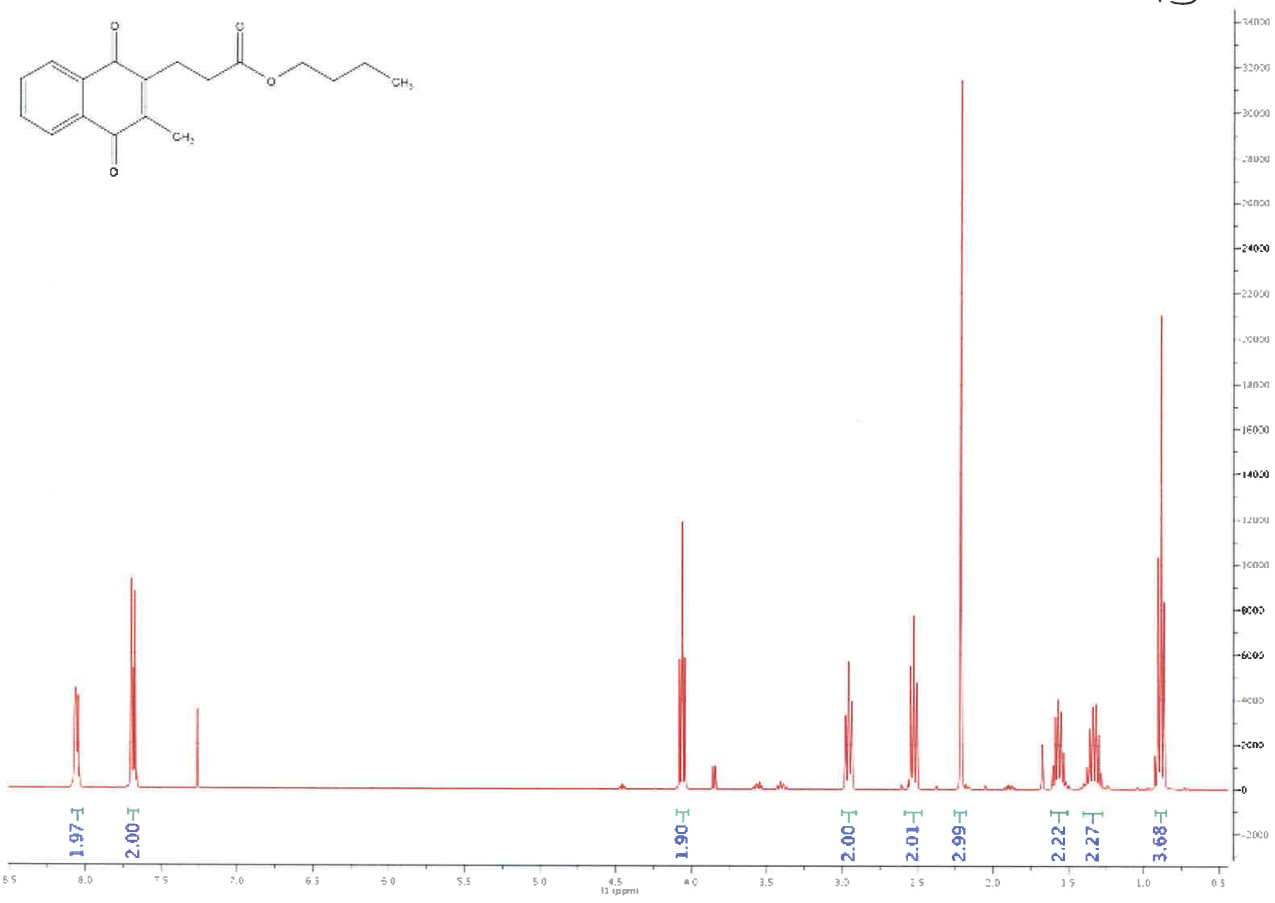

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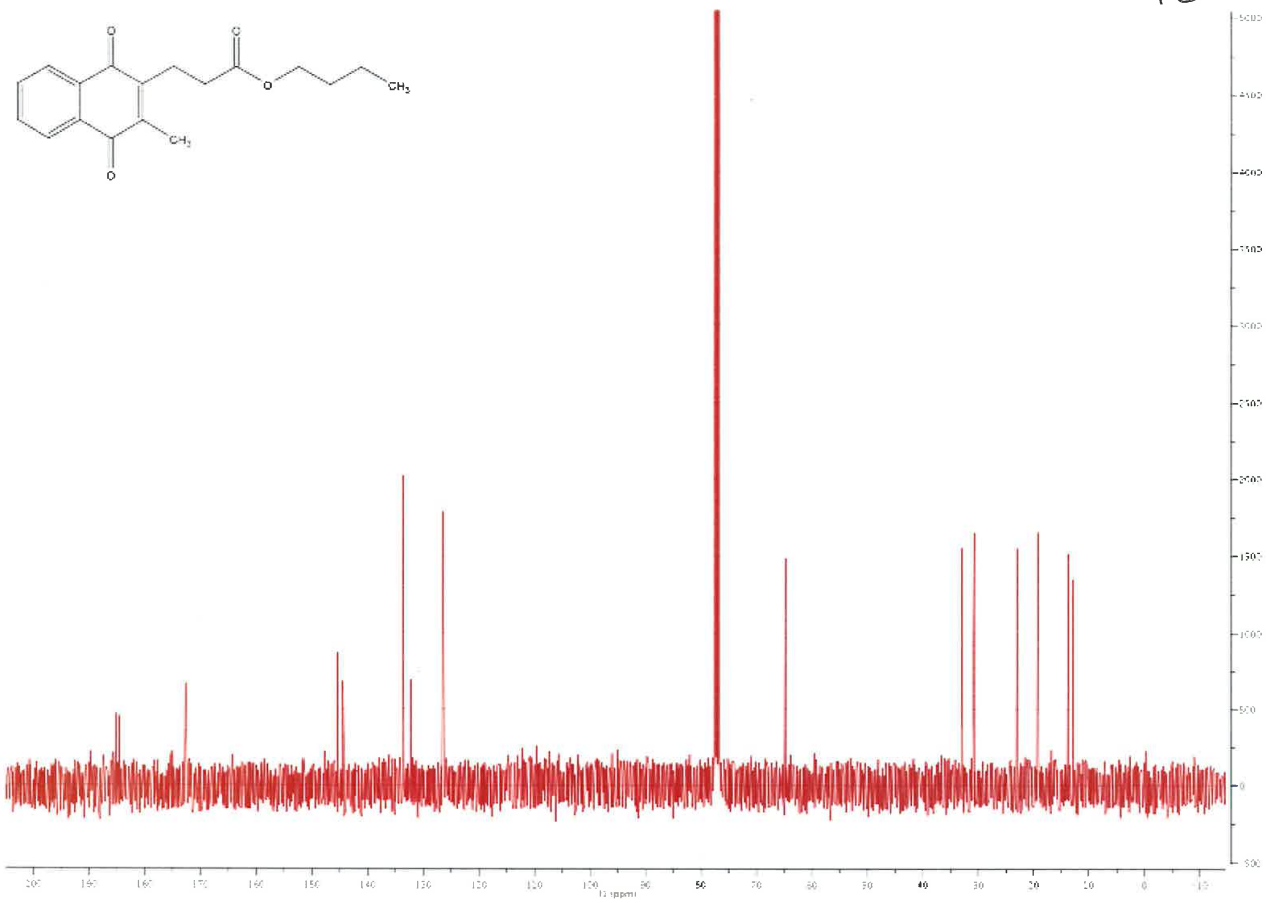

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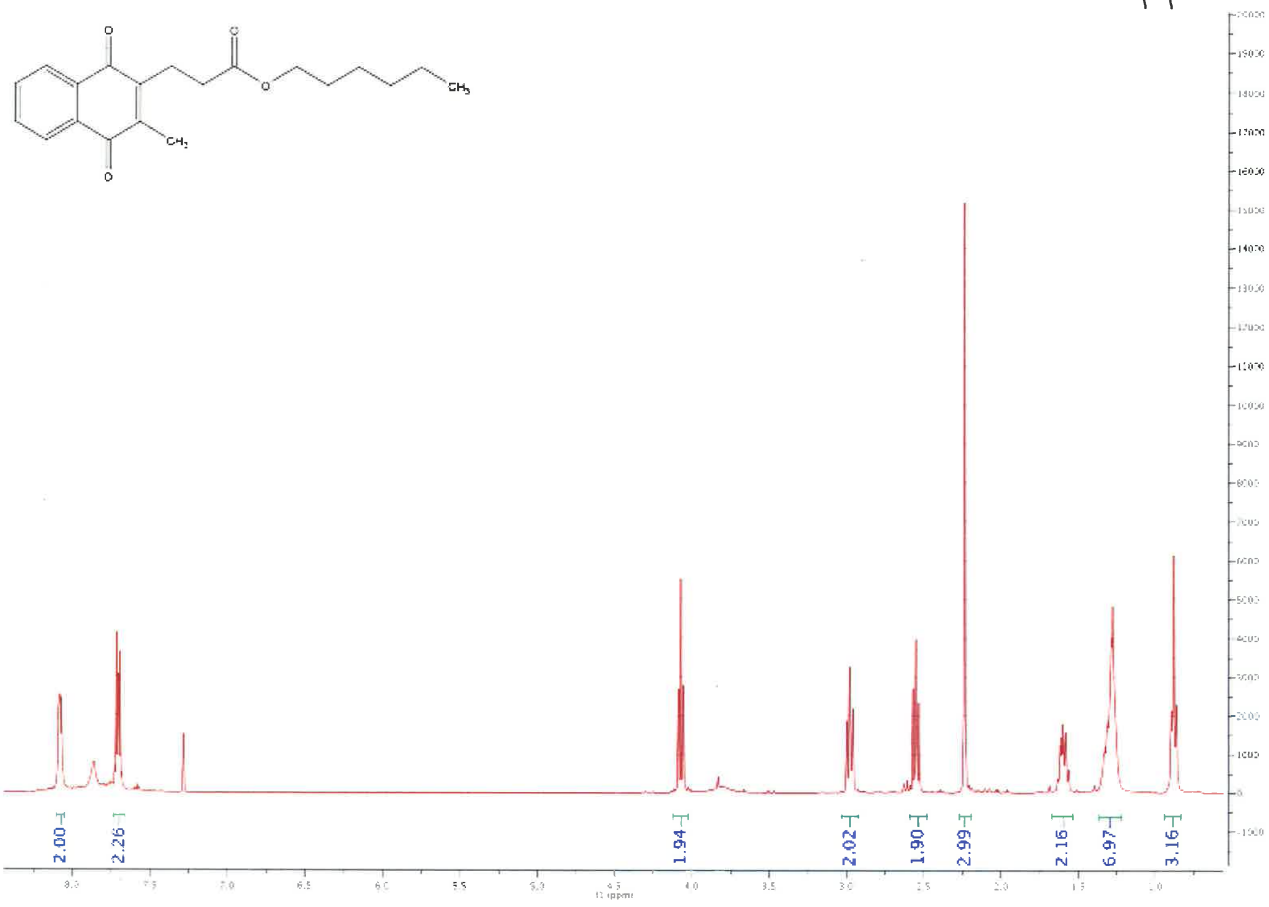

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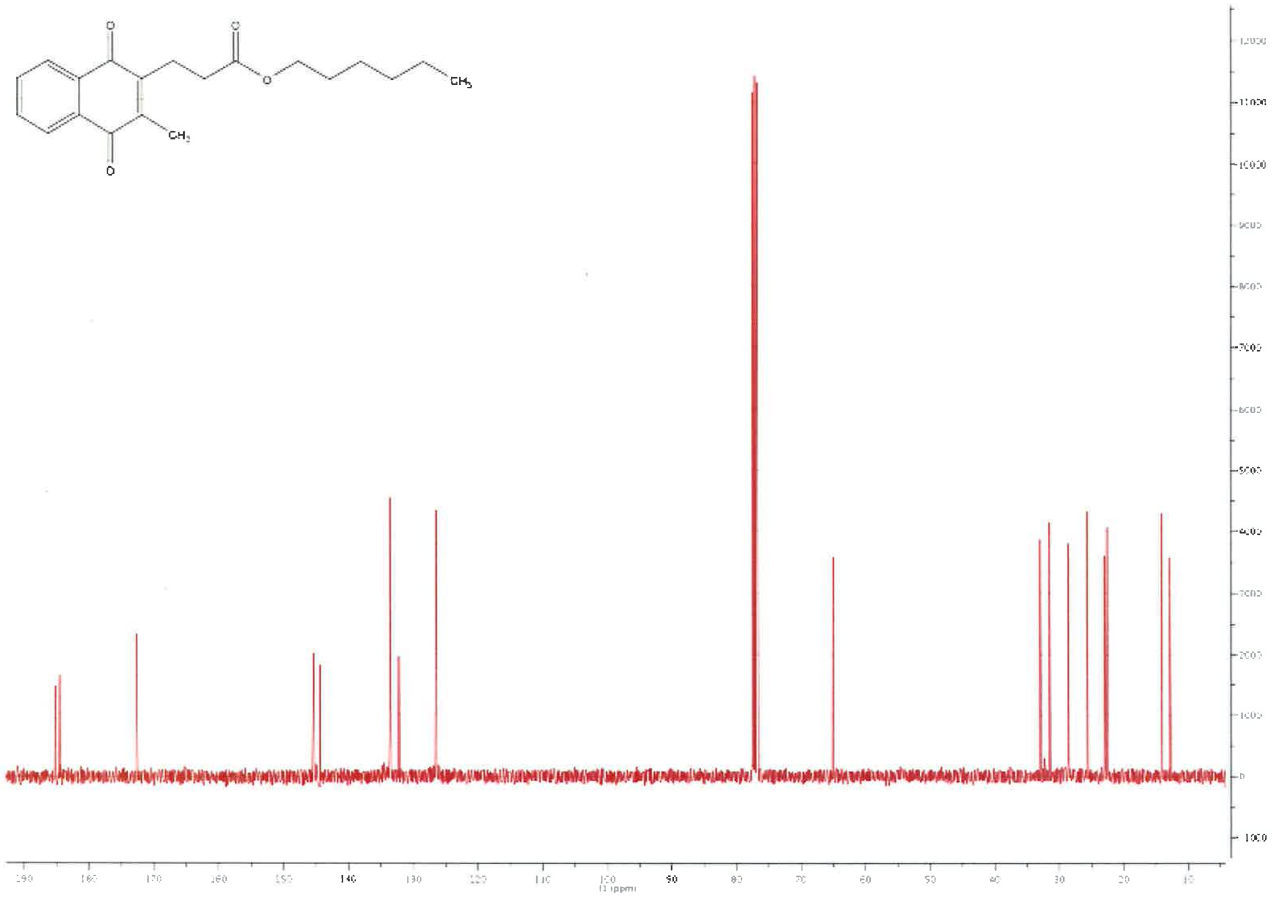

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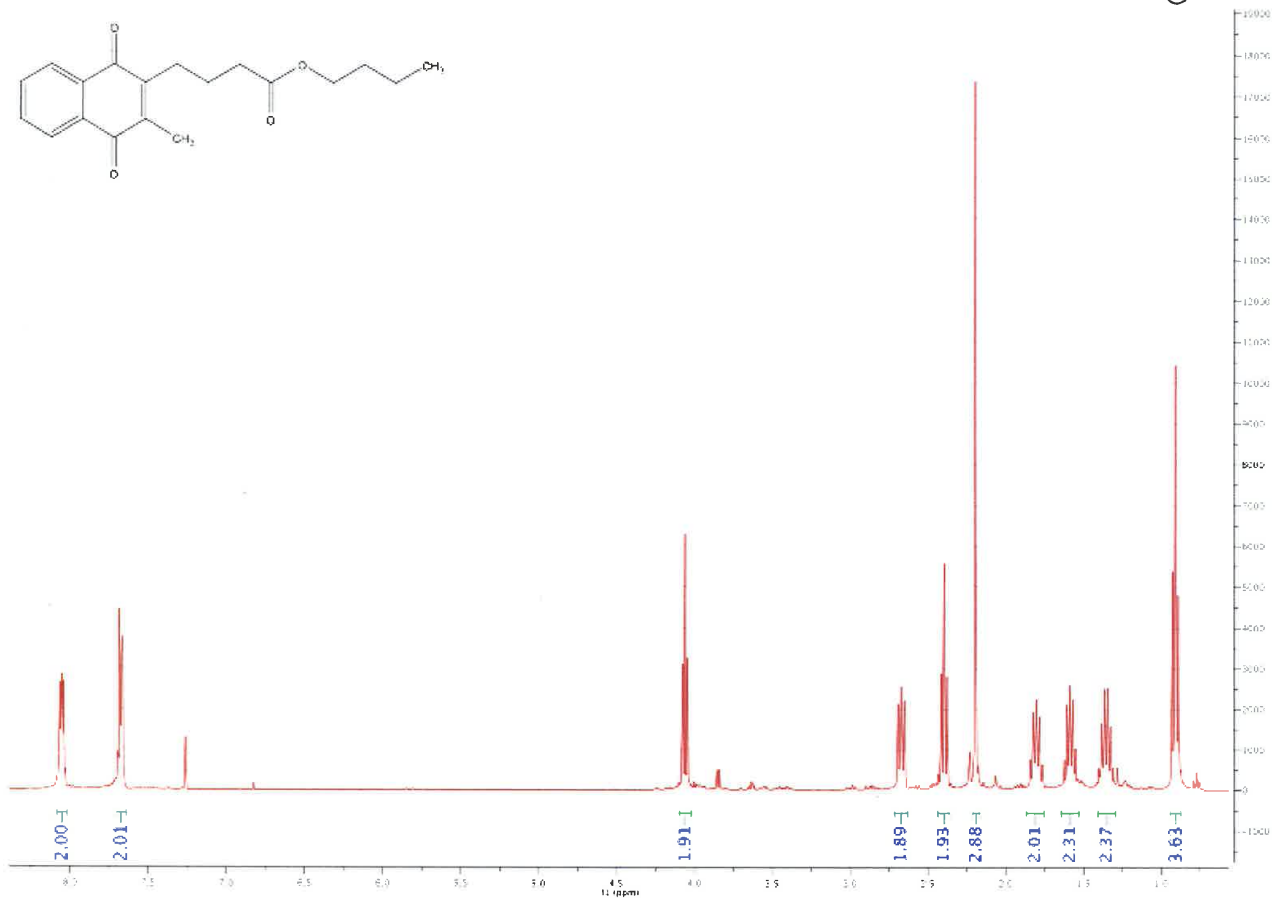

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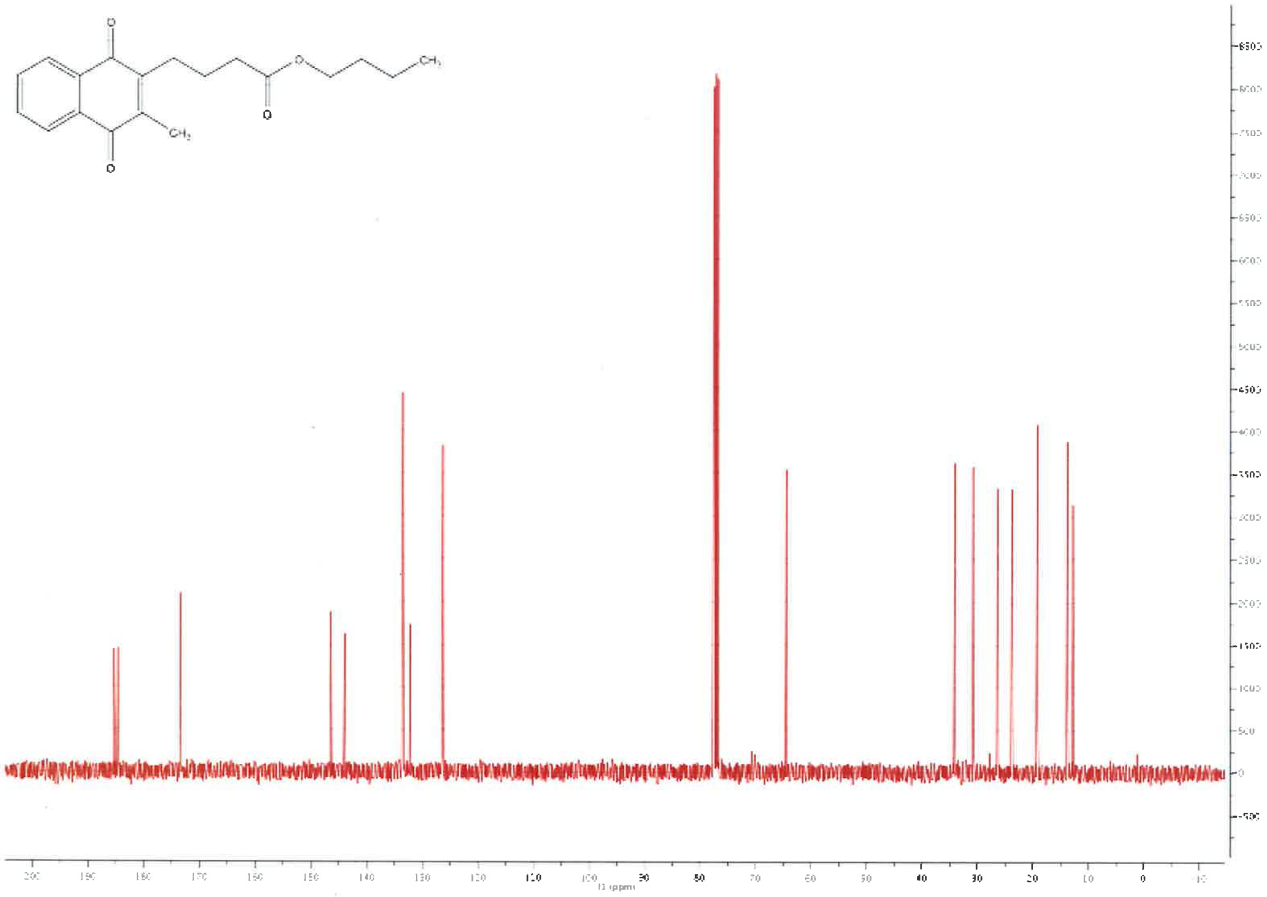

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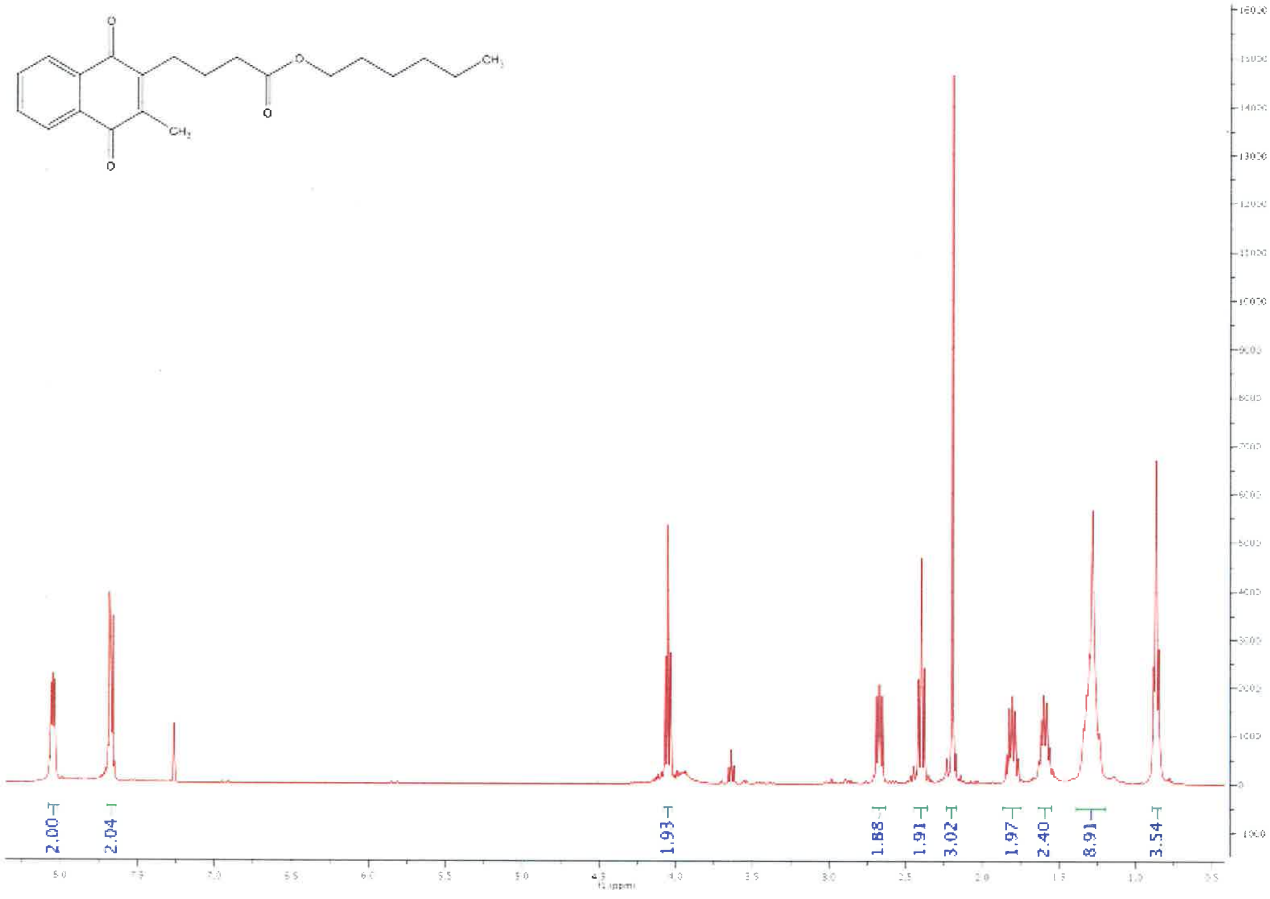

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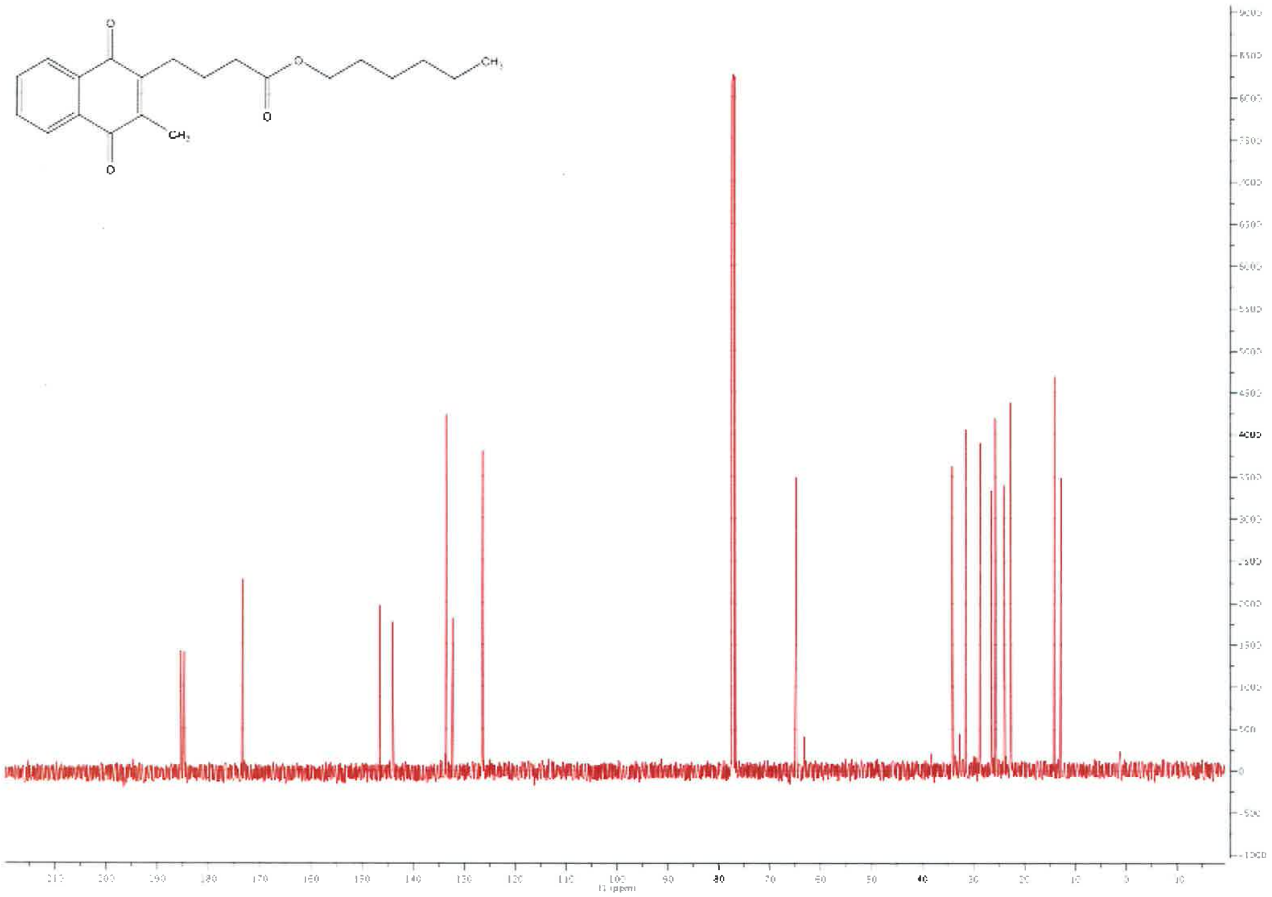

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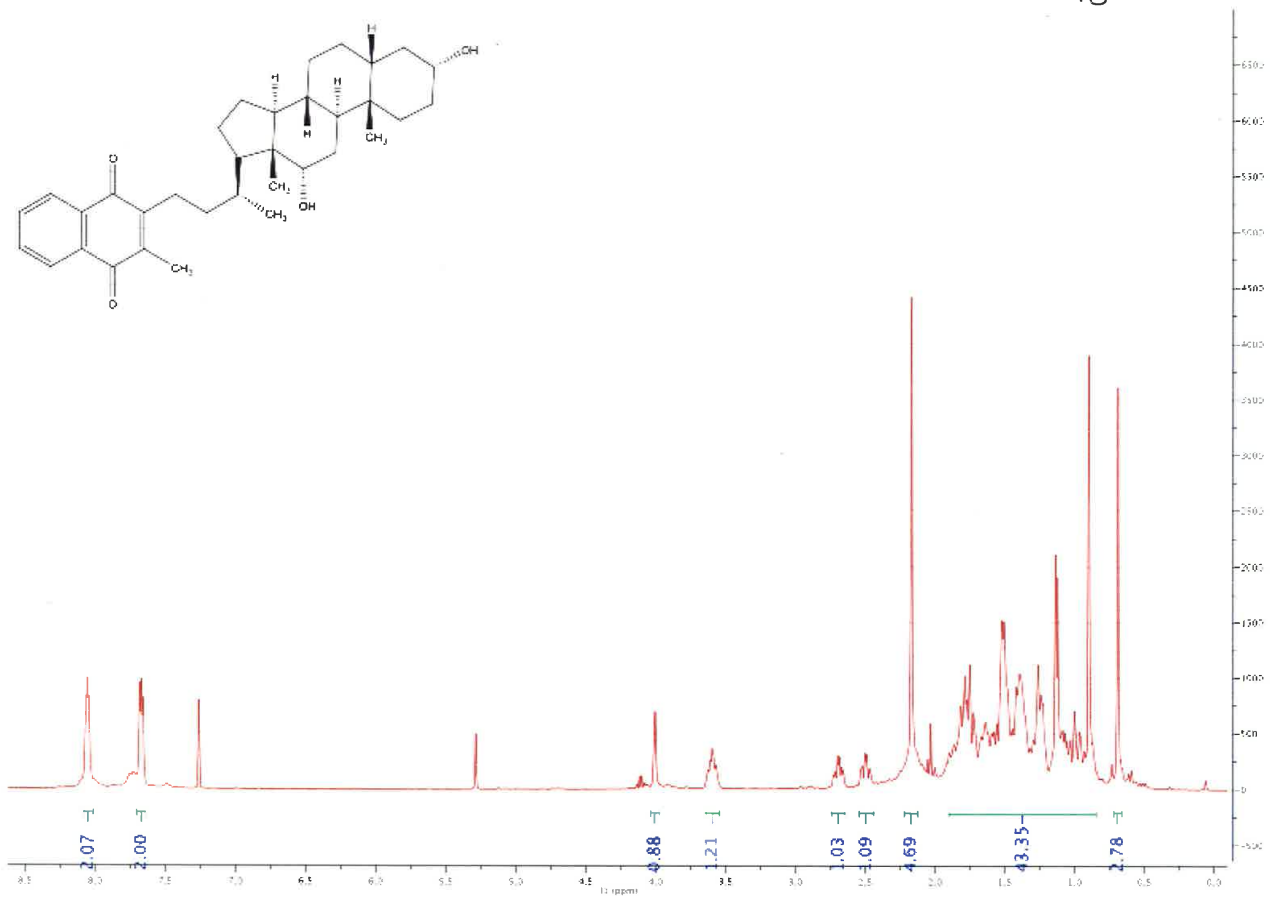
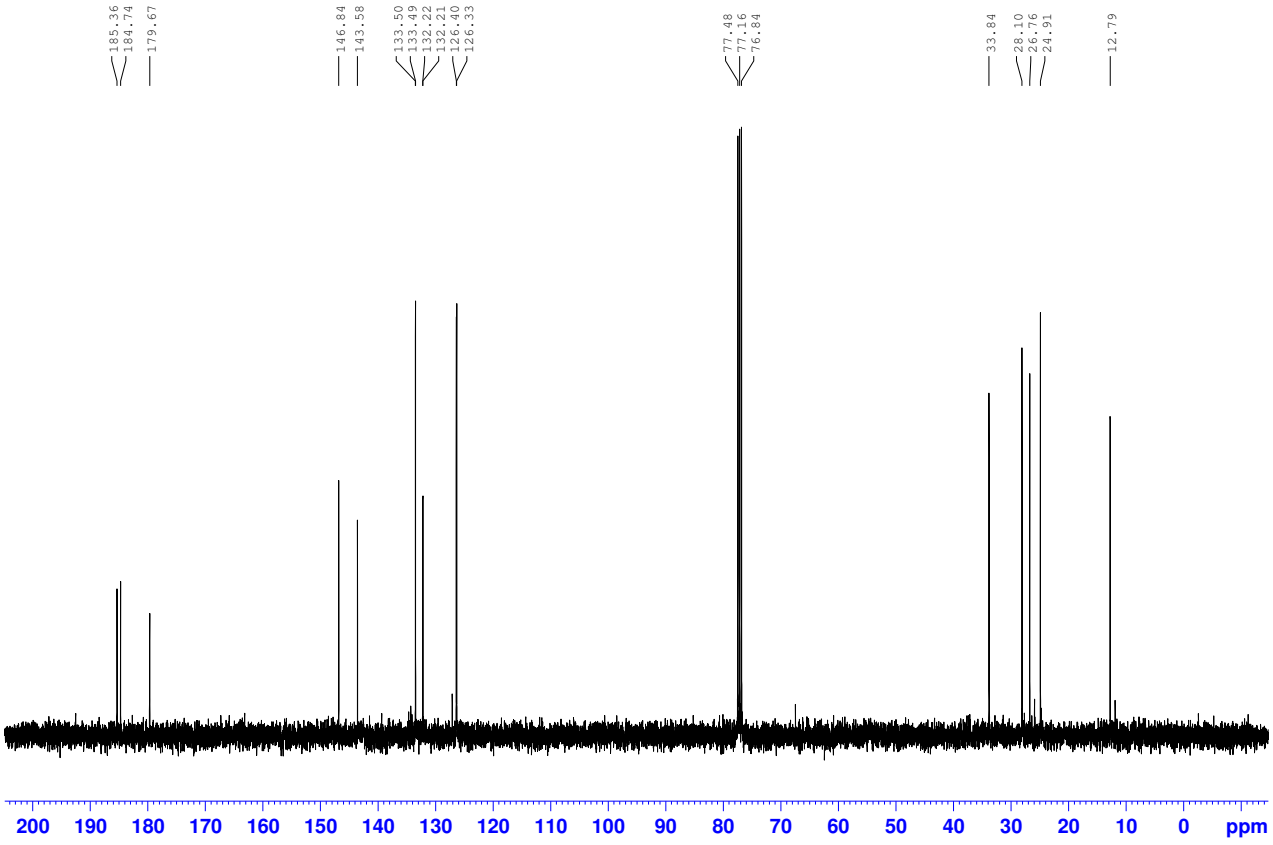
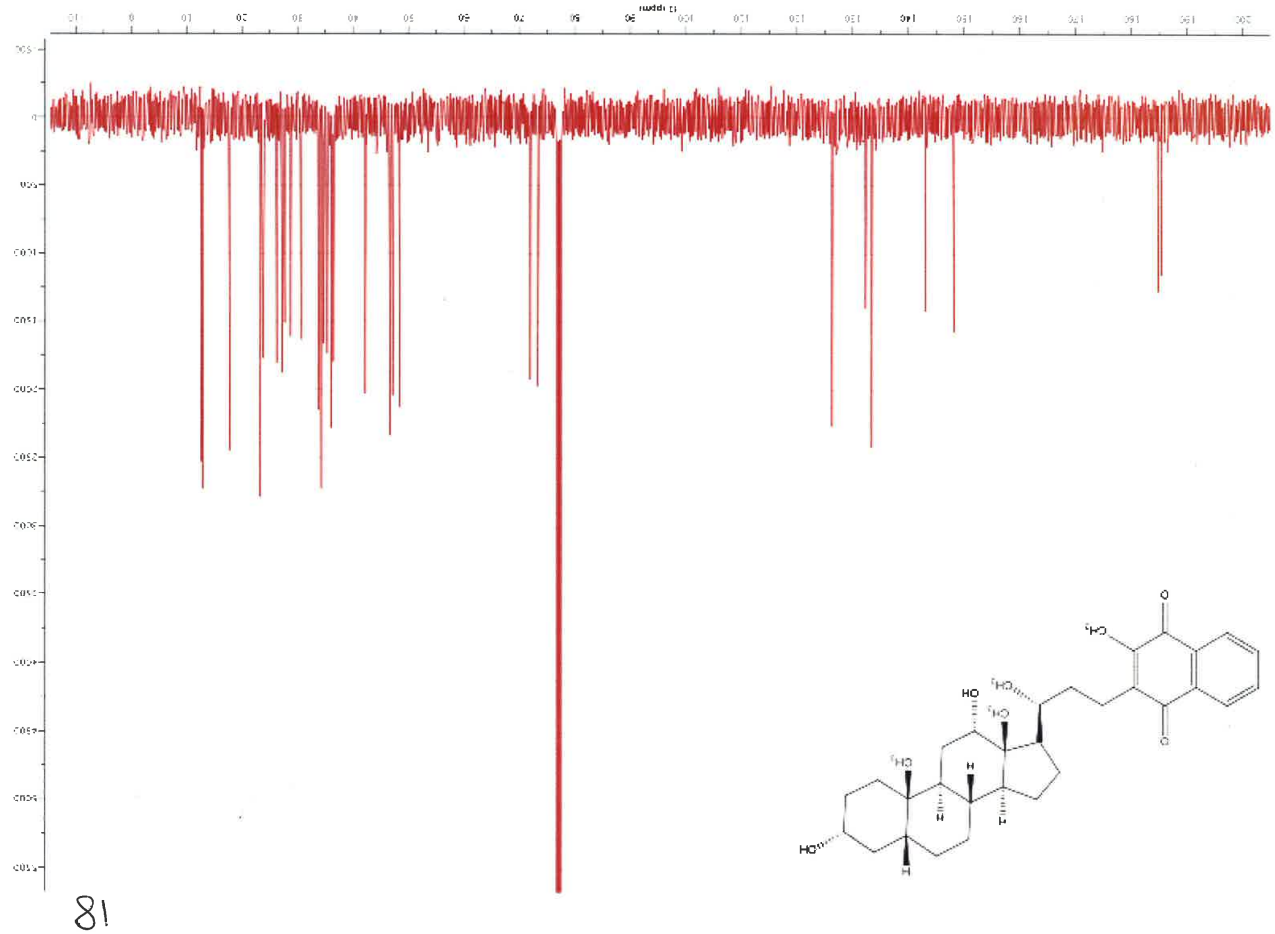


Avance III - 13C with 1H Power-gated Decoupling





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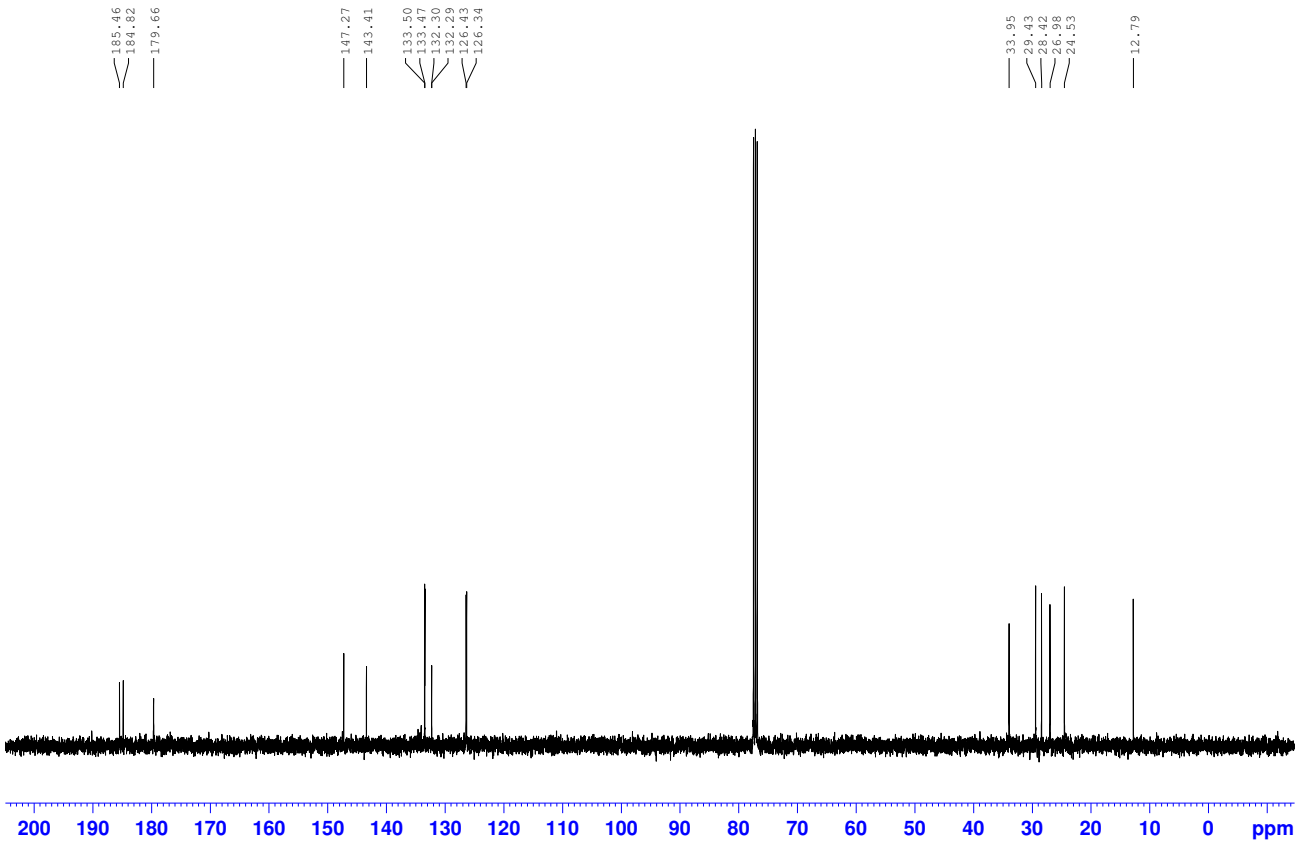
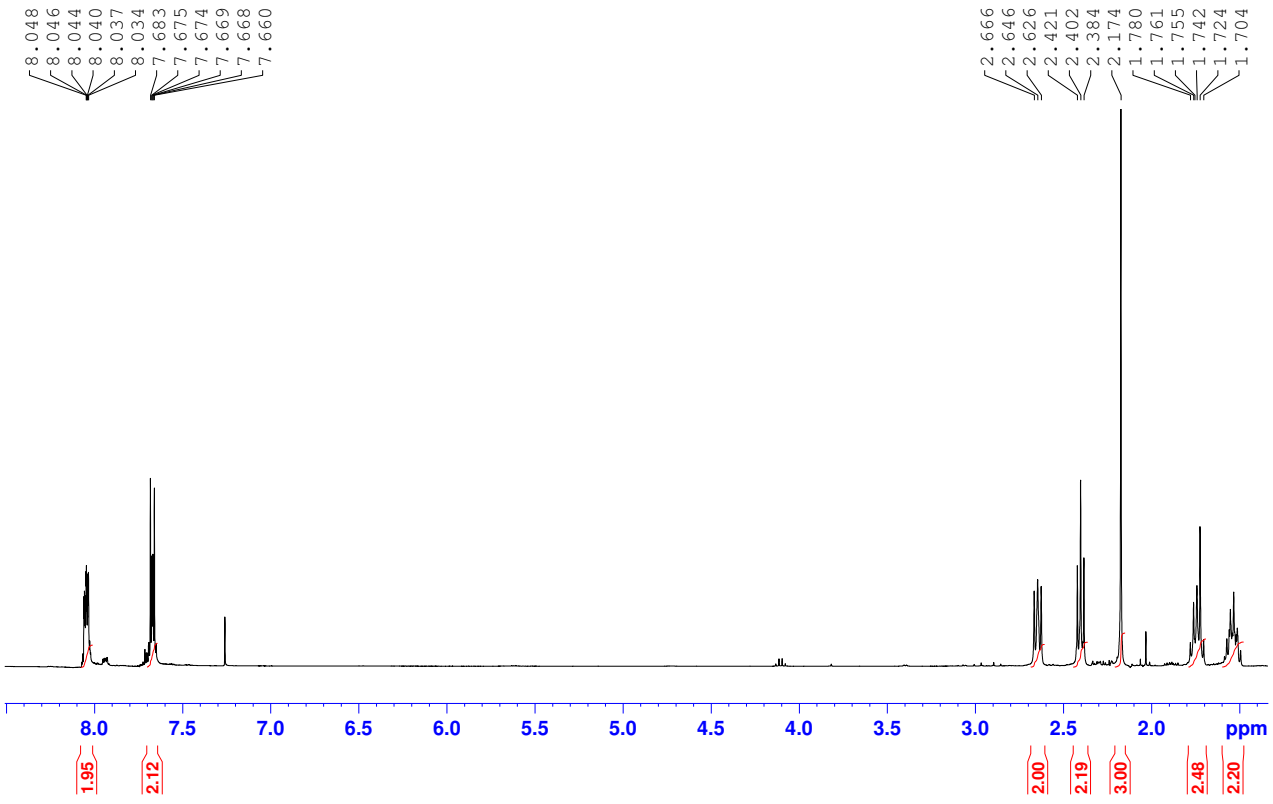
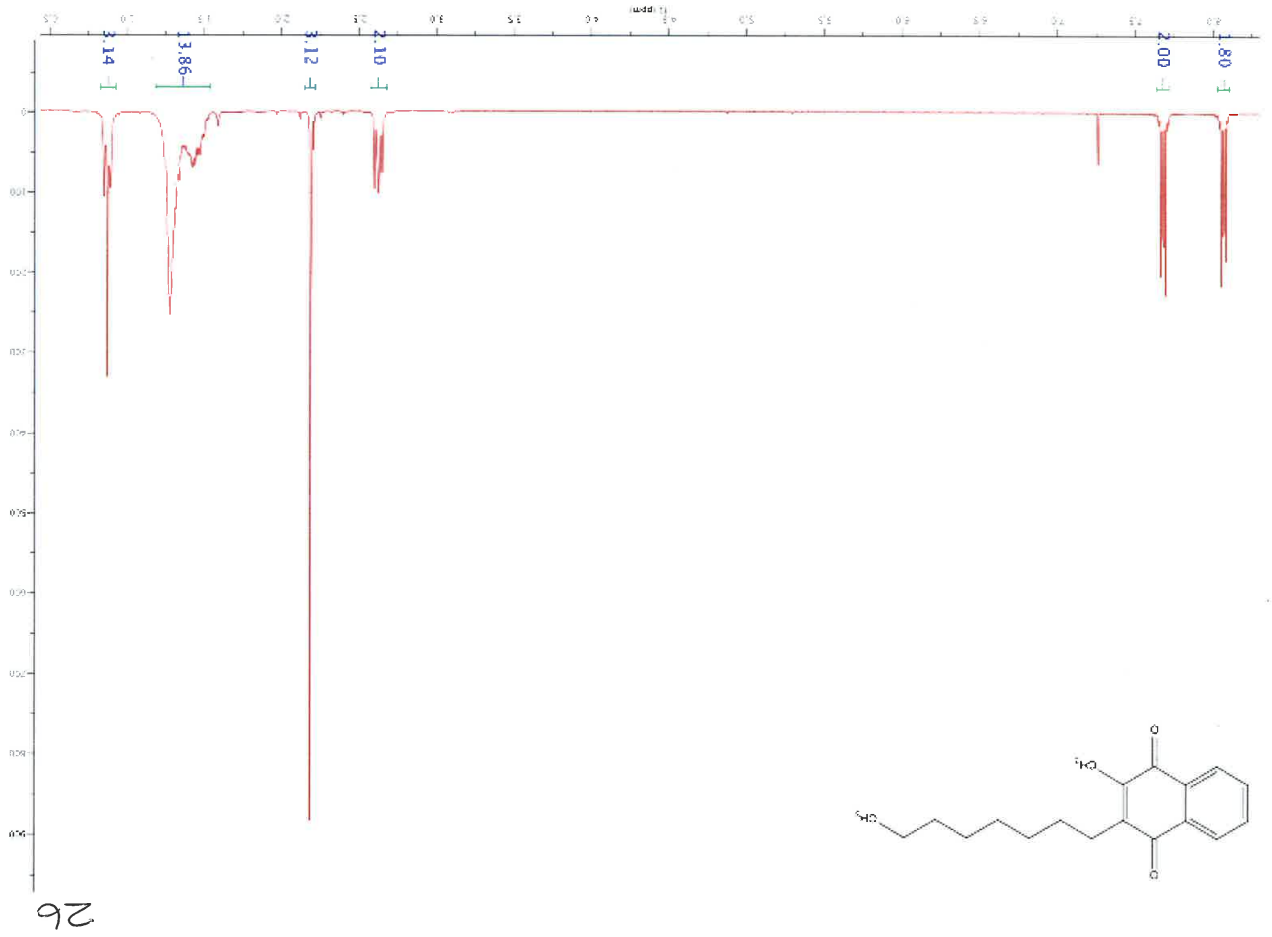
Avance III - 13C with 1H Power-gated Decoupling



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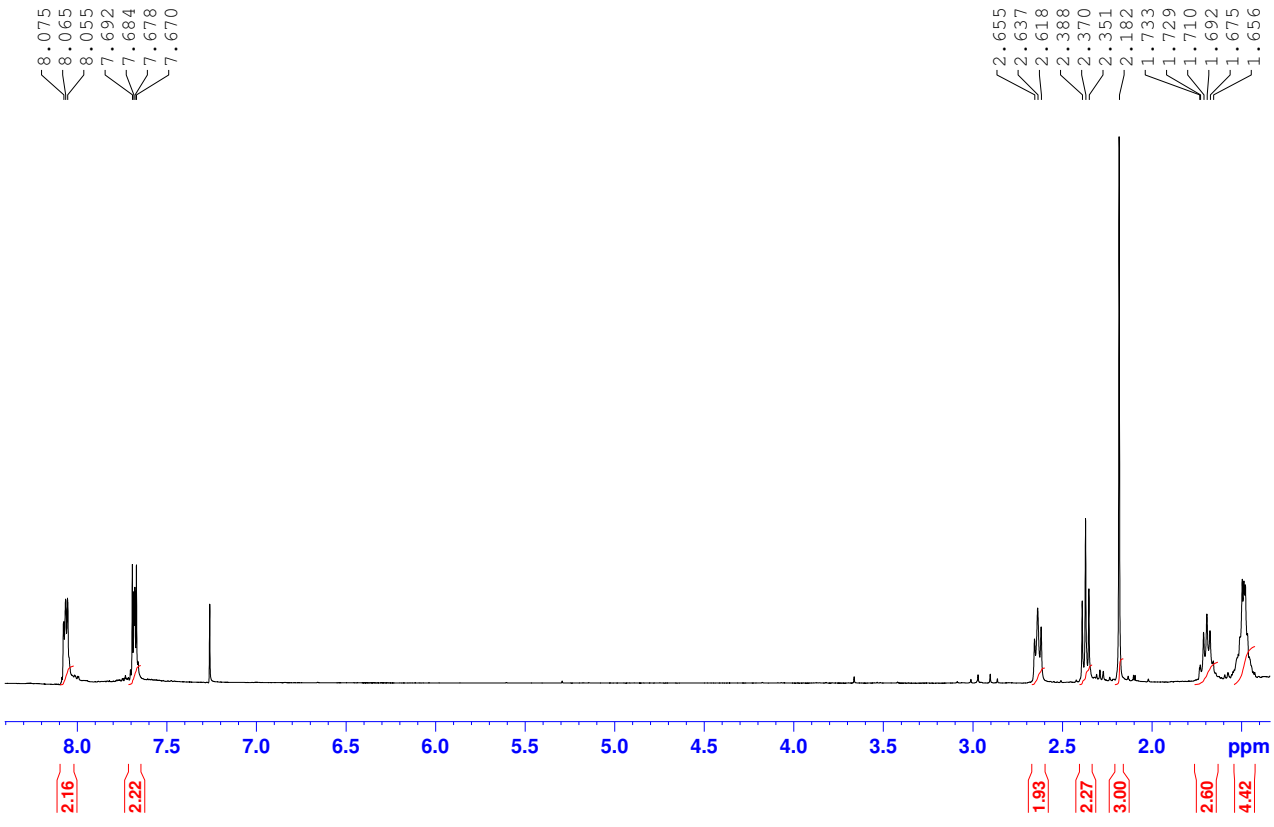
13.86
3.12
2.10
2.00
1.80
26

23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8.055
7.692
7.684
7.678
7.670
2.655
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2.618
2.388
2.370
2.351
2.182
1.733
1.729
1.710
1.692
1.675
1.656
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm
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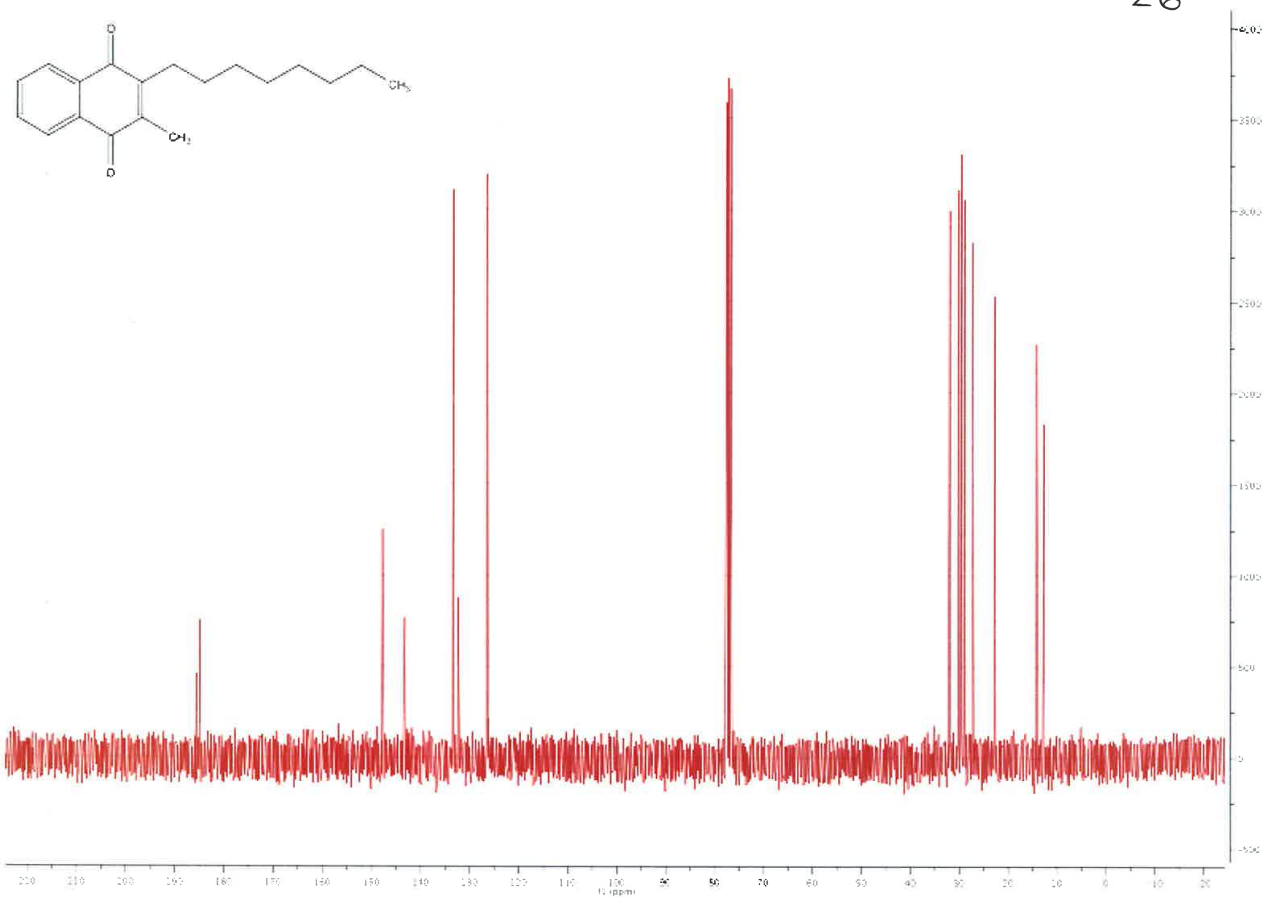
2.22
1.93
2.27
3.00
2.60
4.42

26



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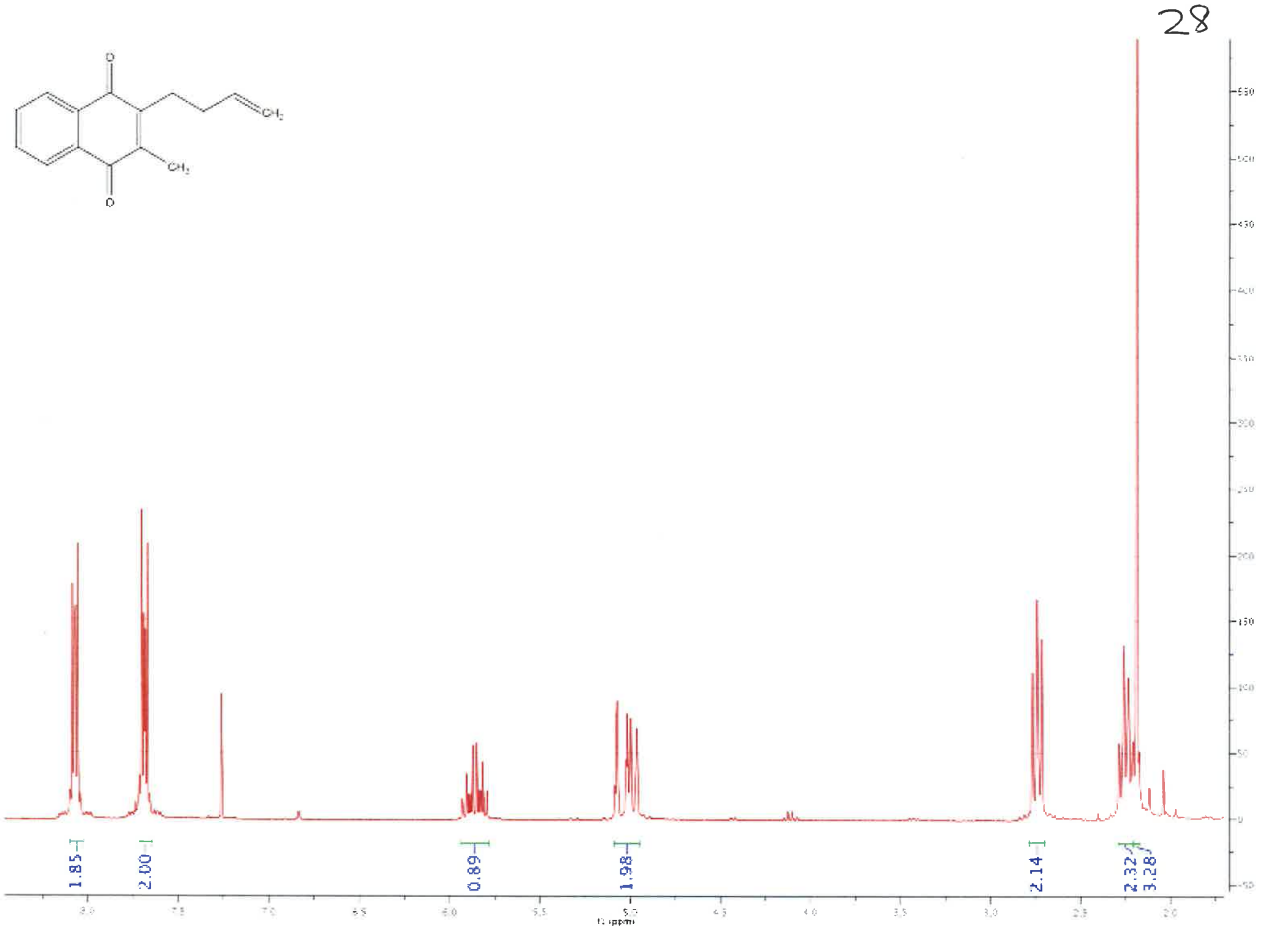

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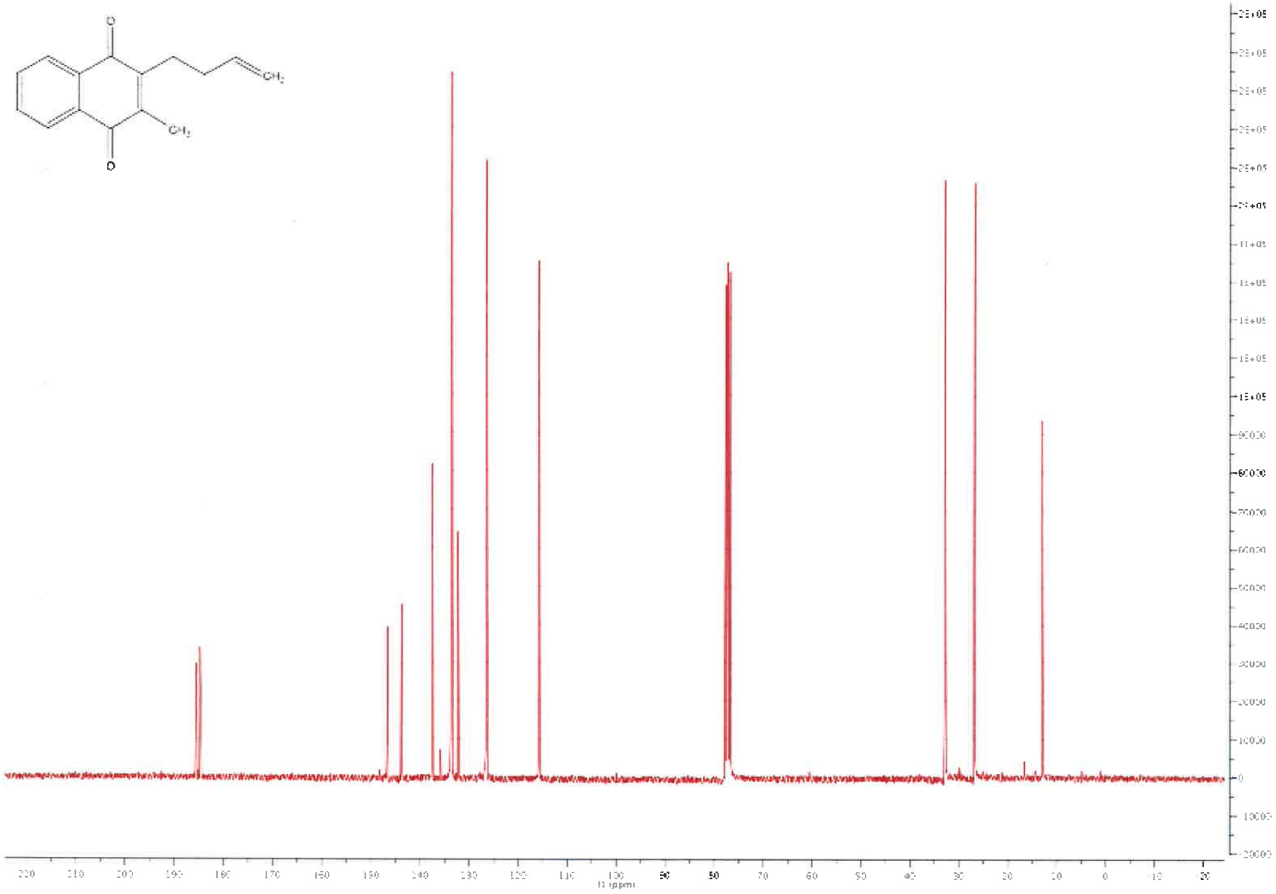

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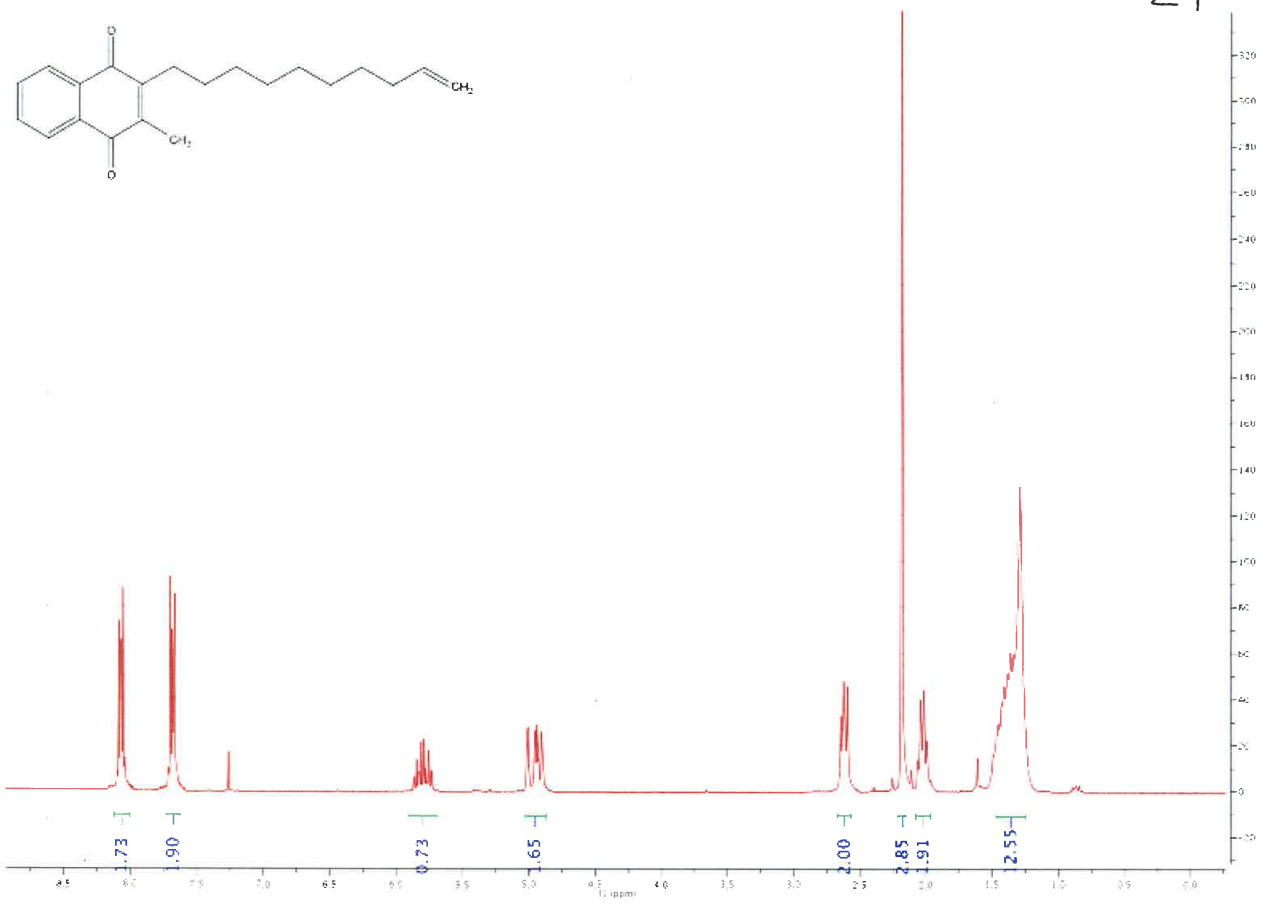

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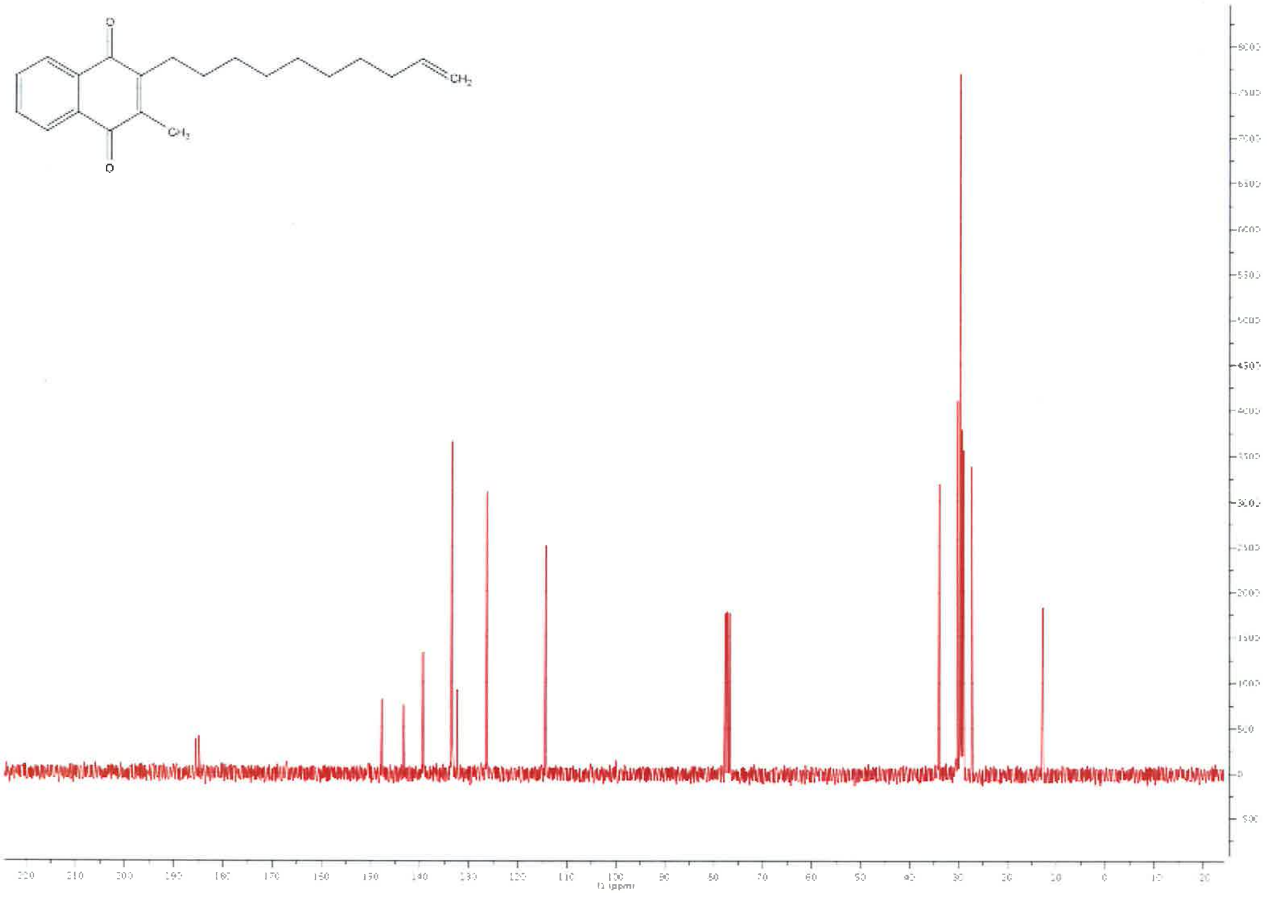

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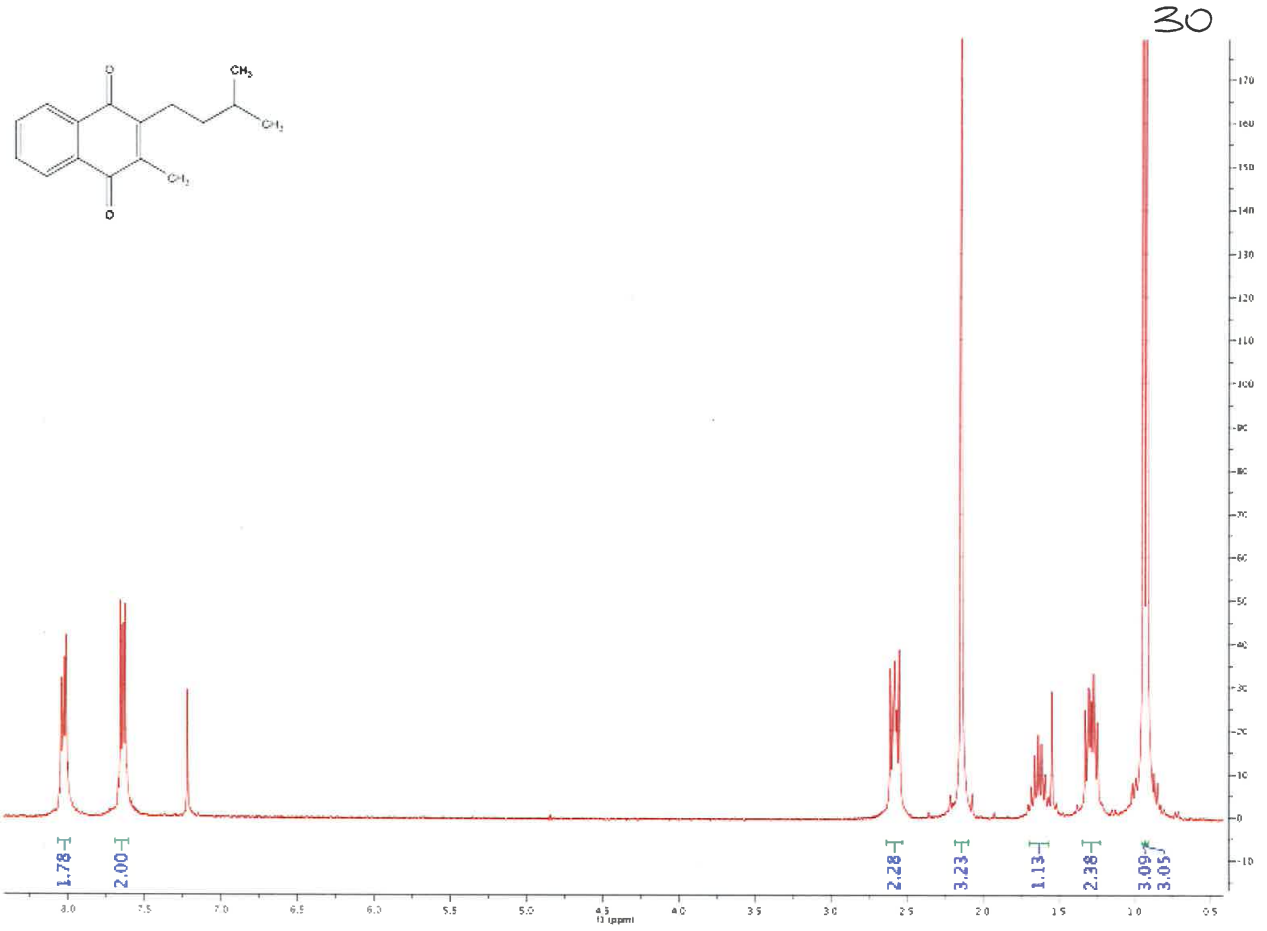

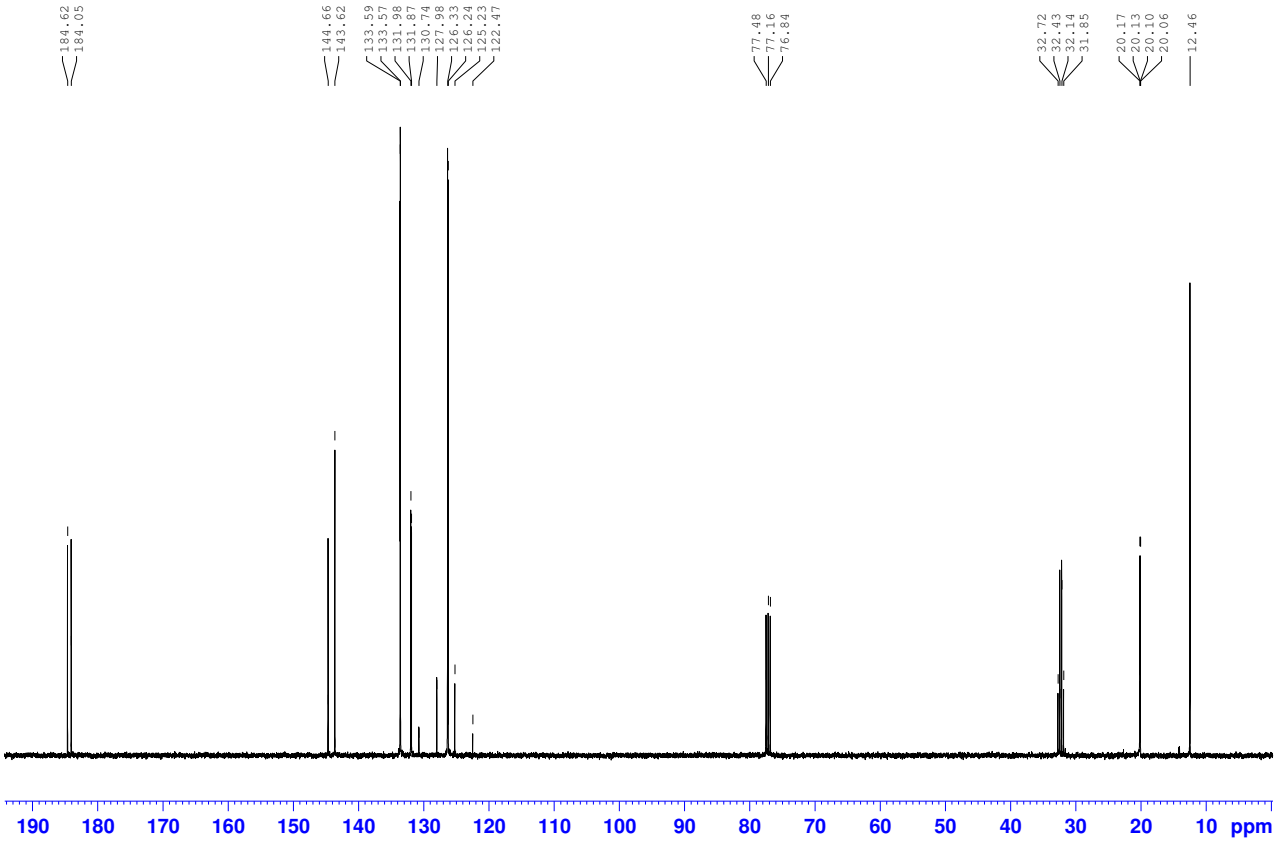
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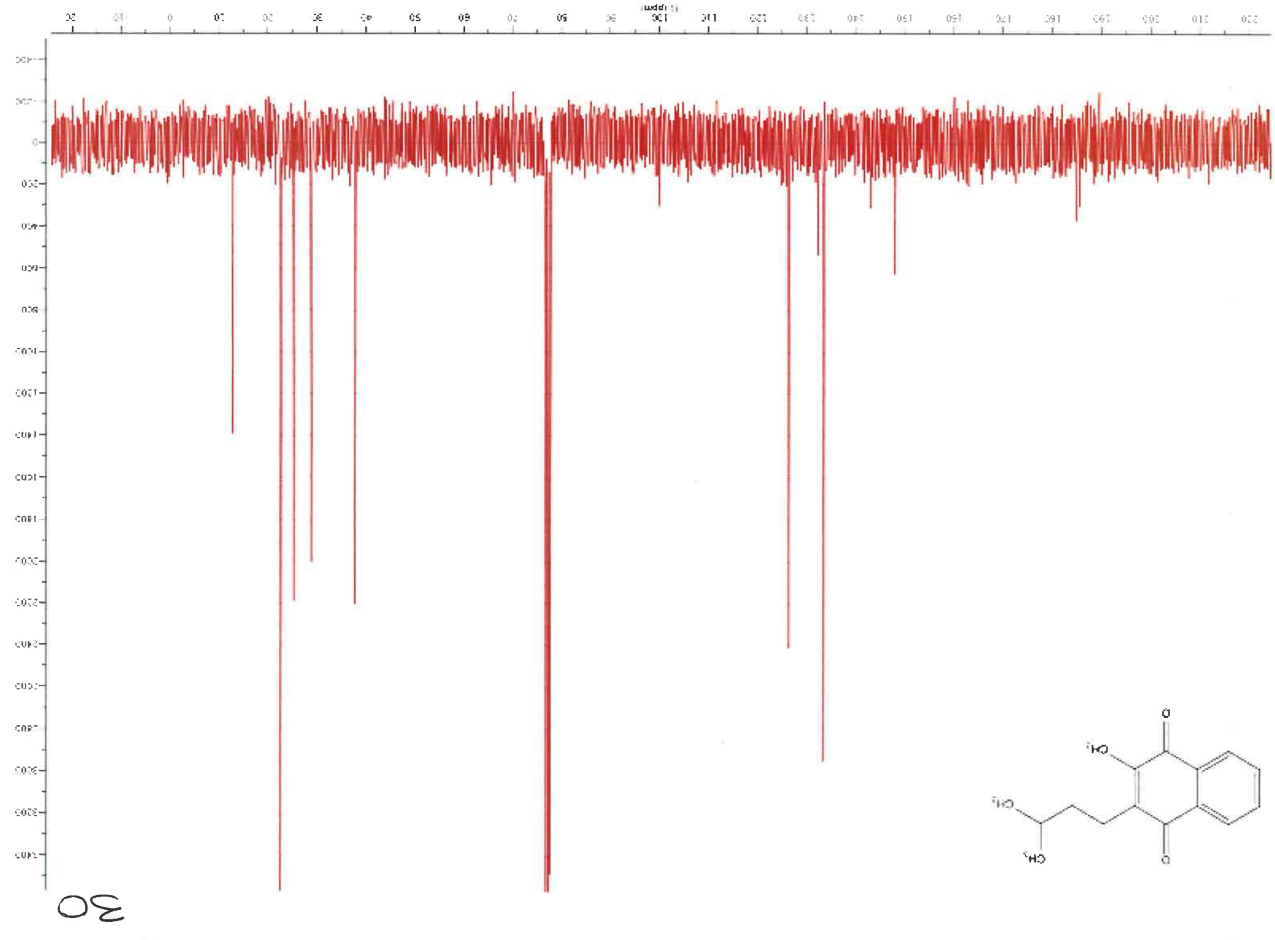
144.66
143.62
133.59
133.57
131.98
131.87
130.74
127.98
126.33
126.24
125.23
122.47
77.48
77.16
76.84
32.72
32.43
32.14
31.85
20.17
20.13
20.10
20.06
12.46
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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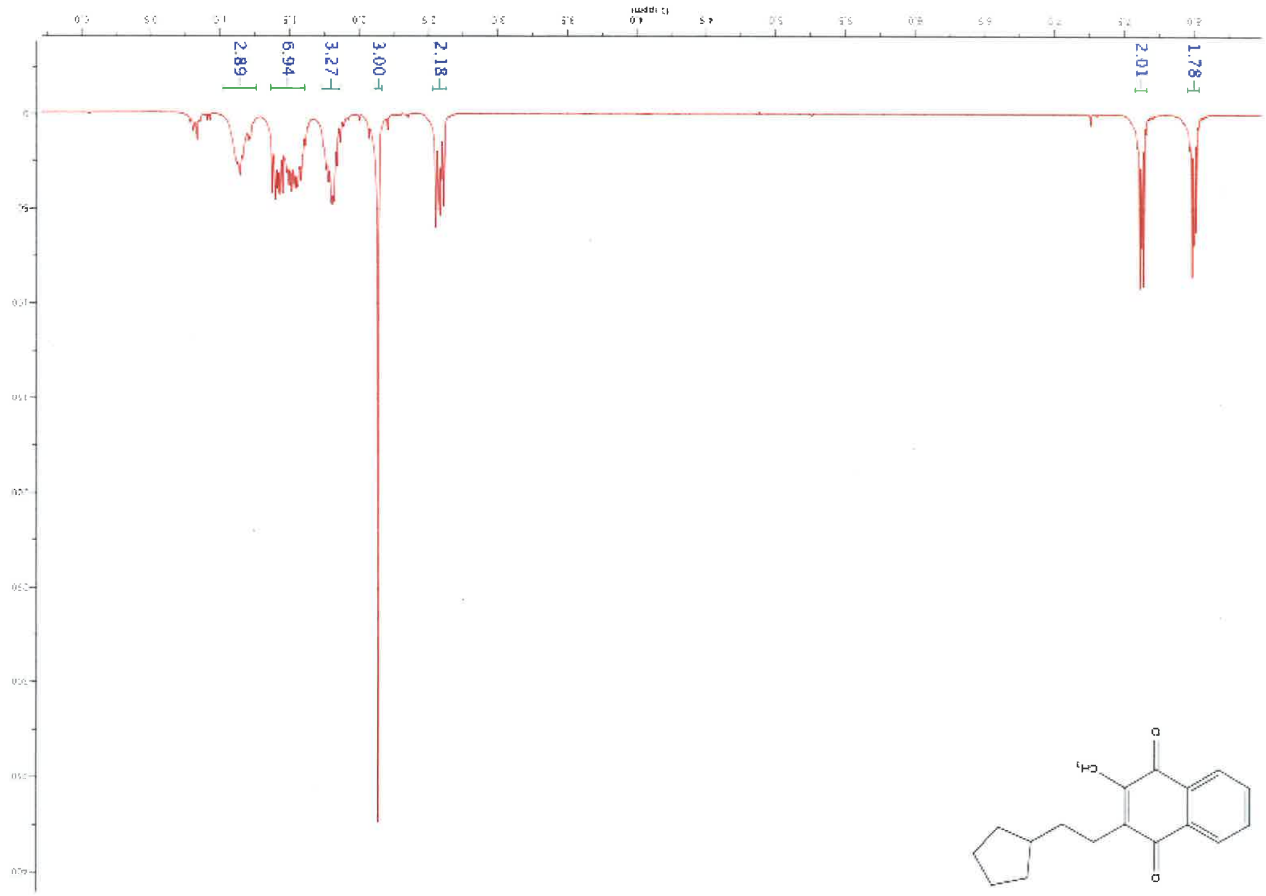
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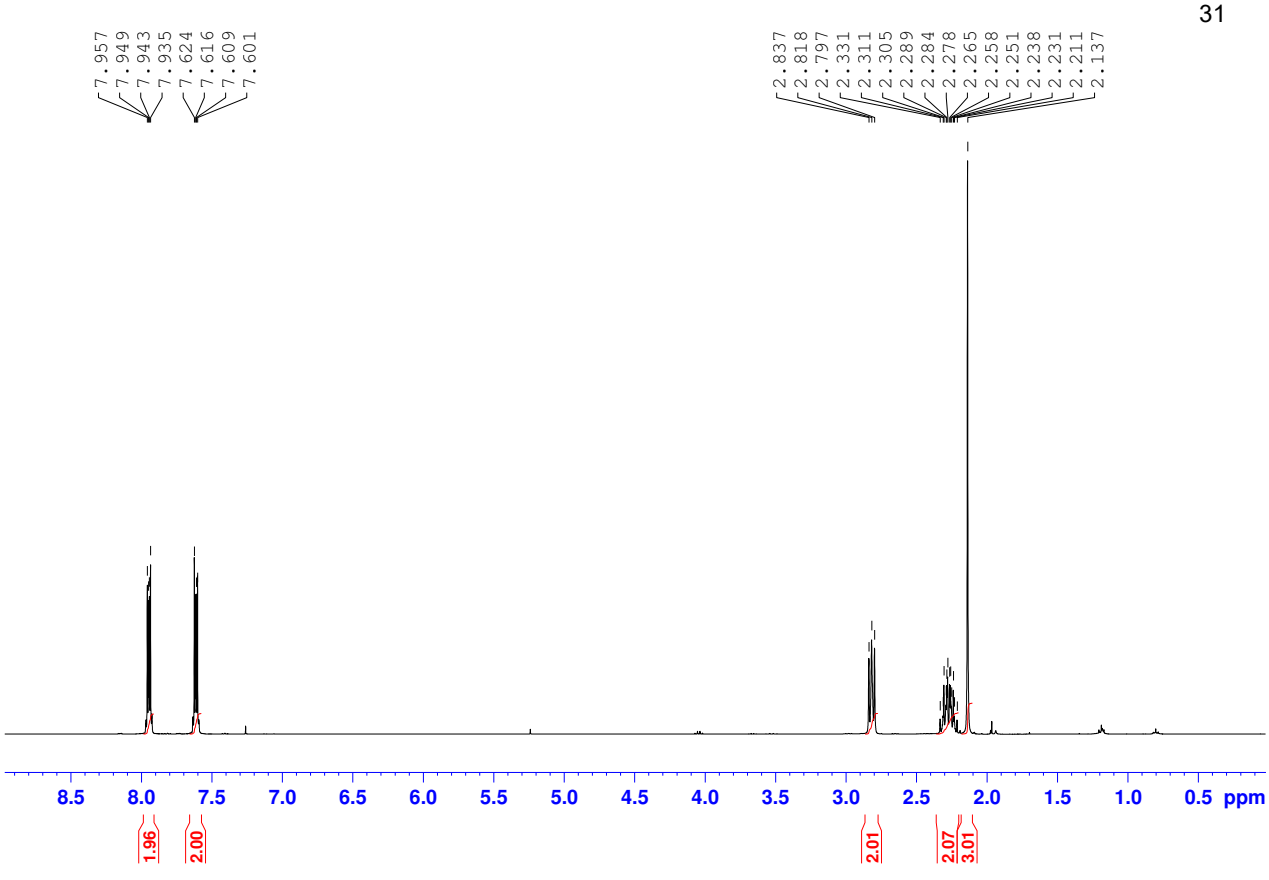
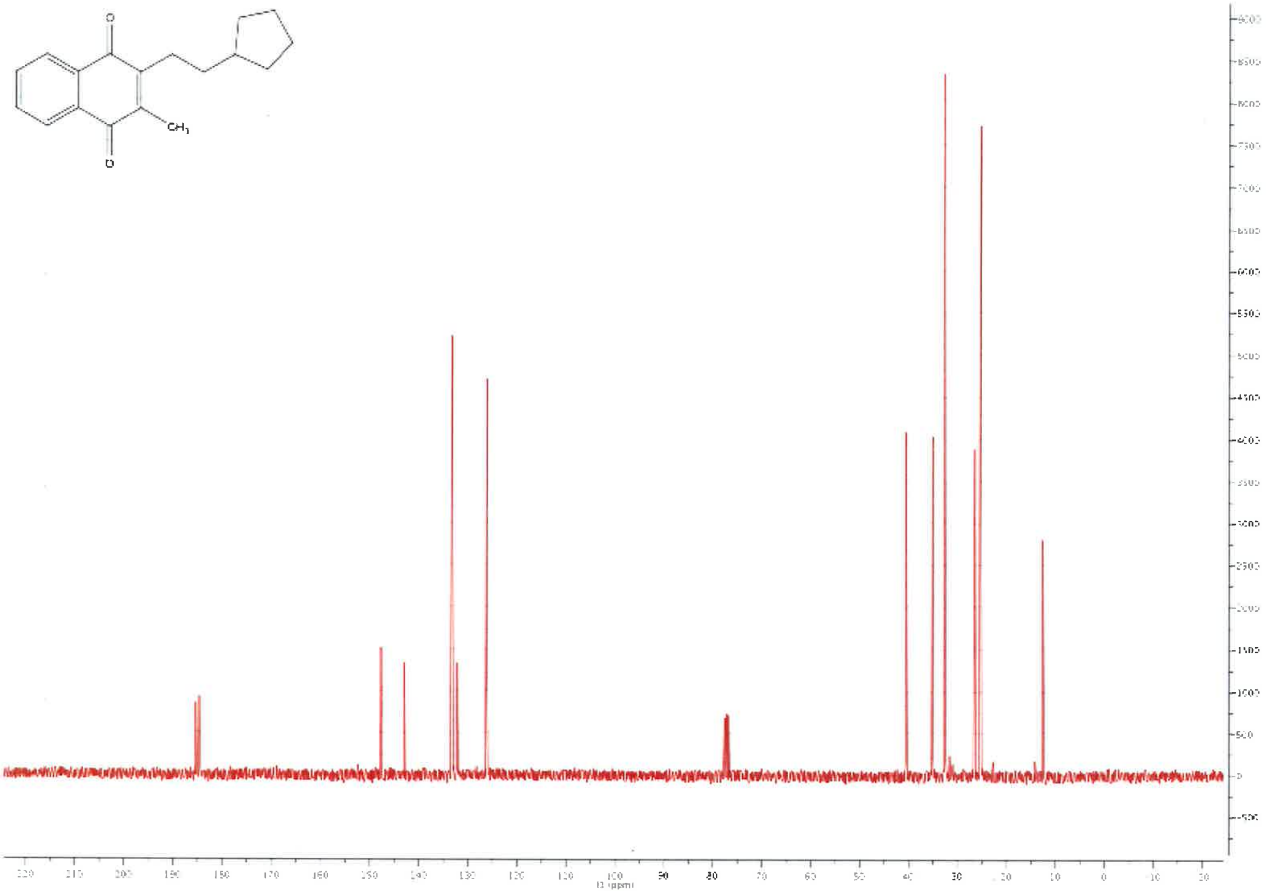
6.94
3.27
3.00
2.18
2.01
1.78
O
CH3
O

32

31


7.957
7.949
7.943
7.935
7.624
7.616
7.609
7.601
2.837
2.818
2.797
2.331
2.311
2.305
2.289
2.284
2.278
2.265
2.258
2.251
2.238
2.231
2.211
2.137
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.96
2.00
2.01
2.07
3.01

32



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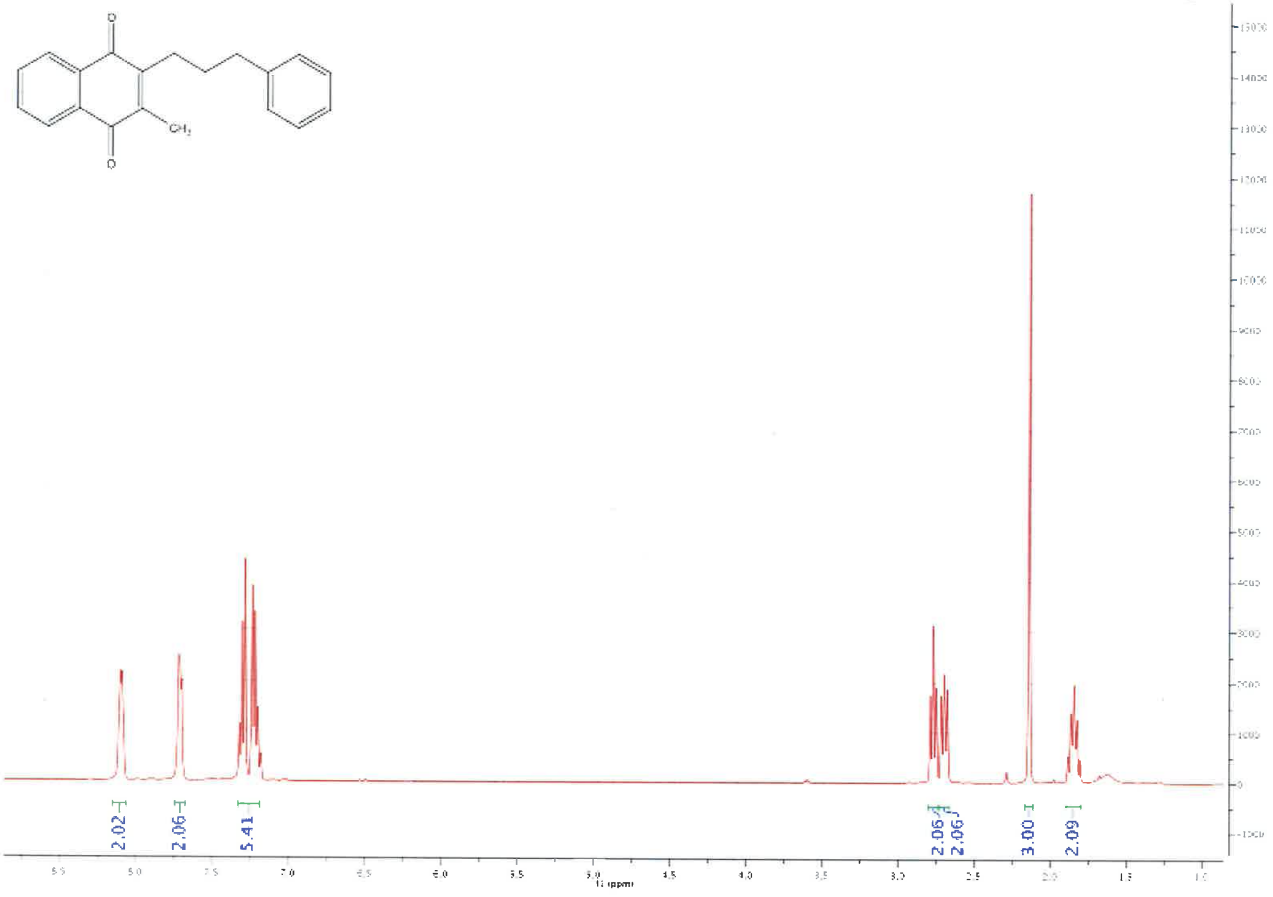

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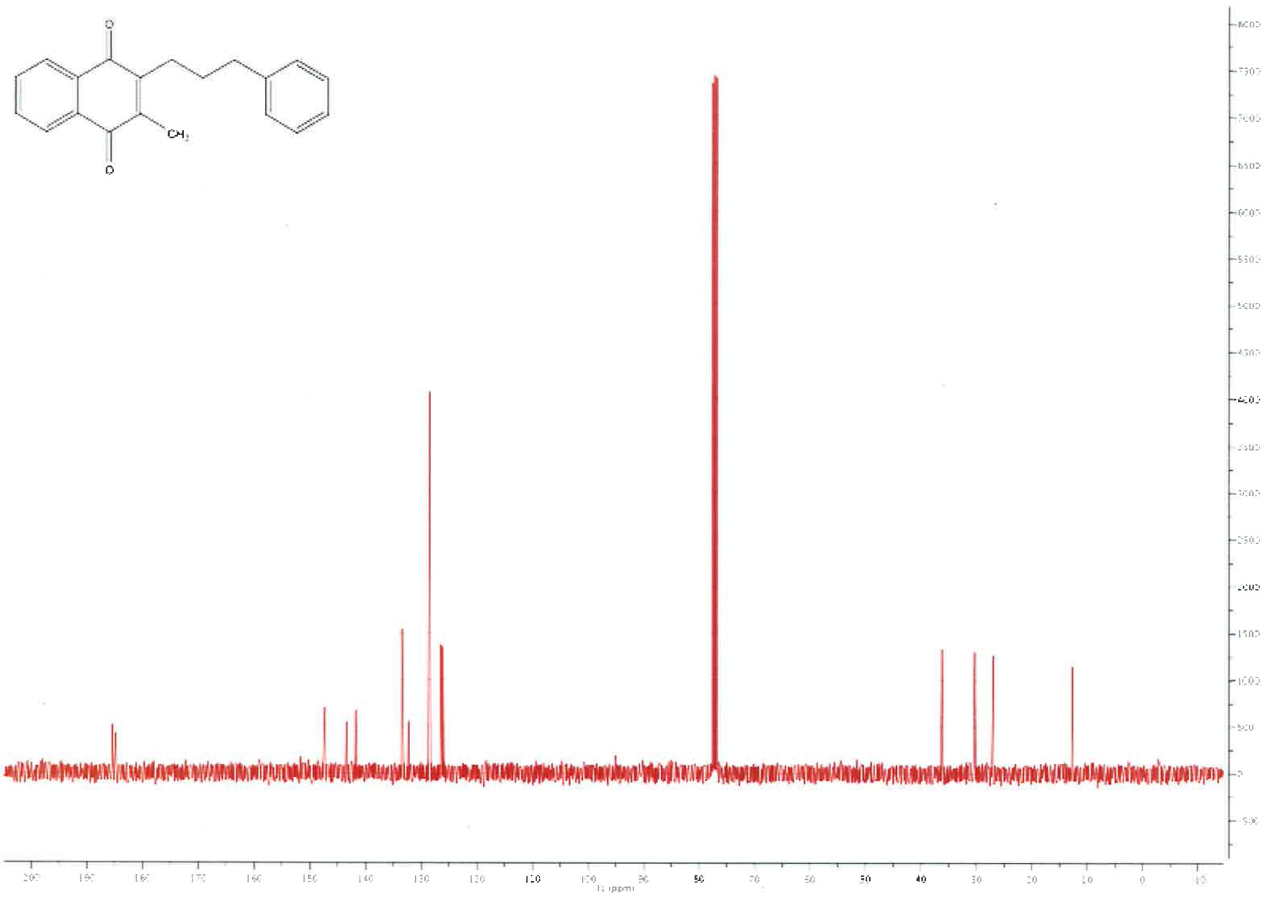

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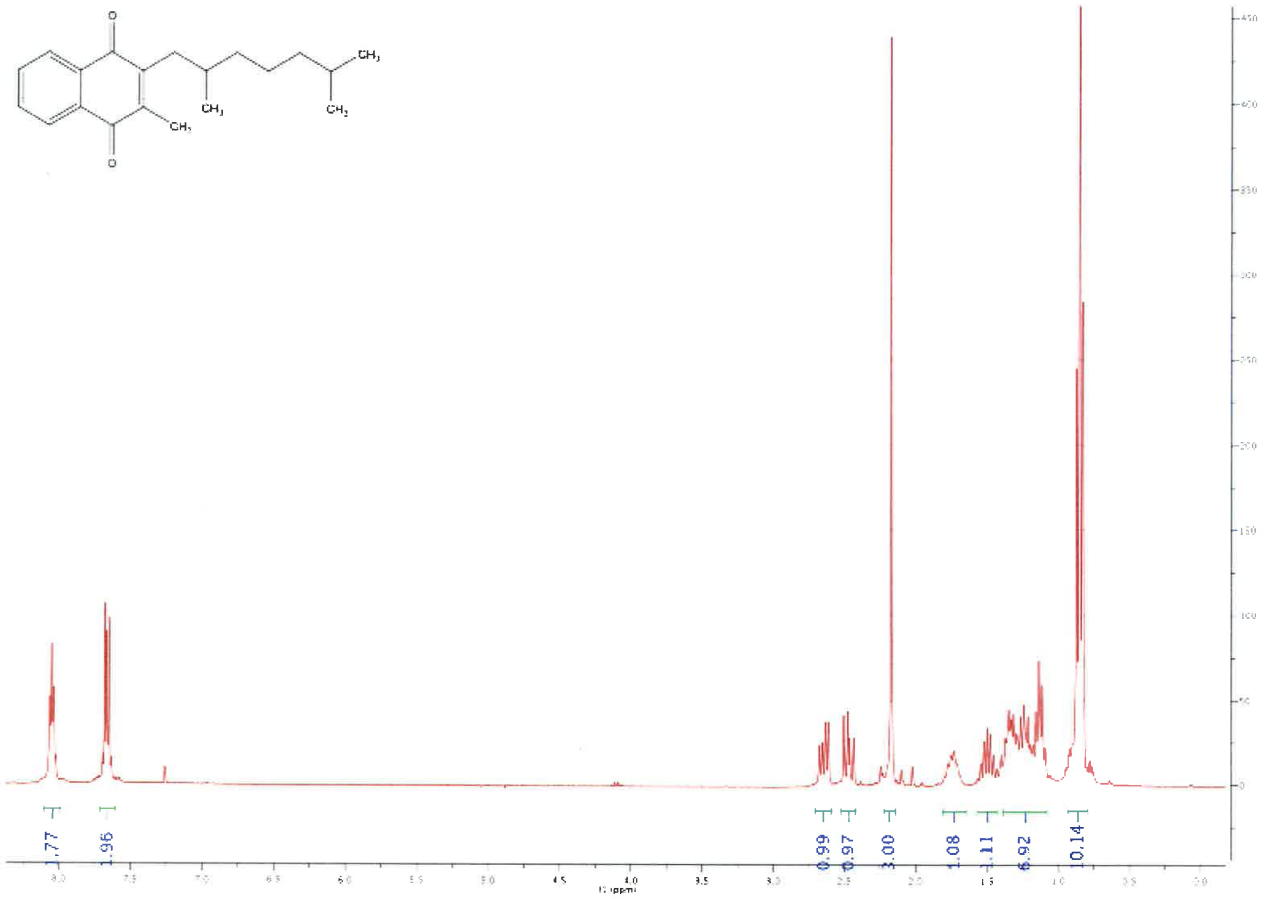

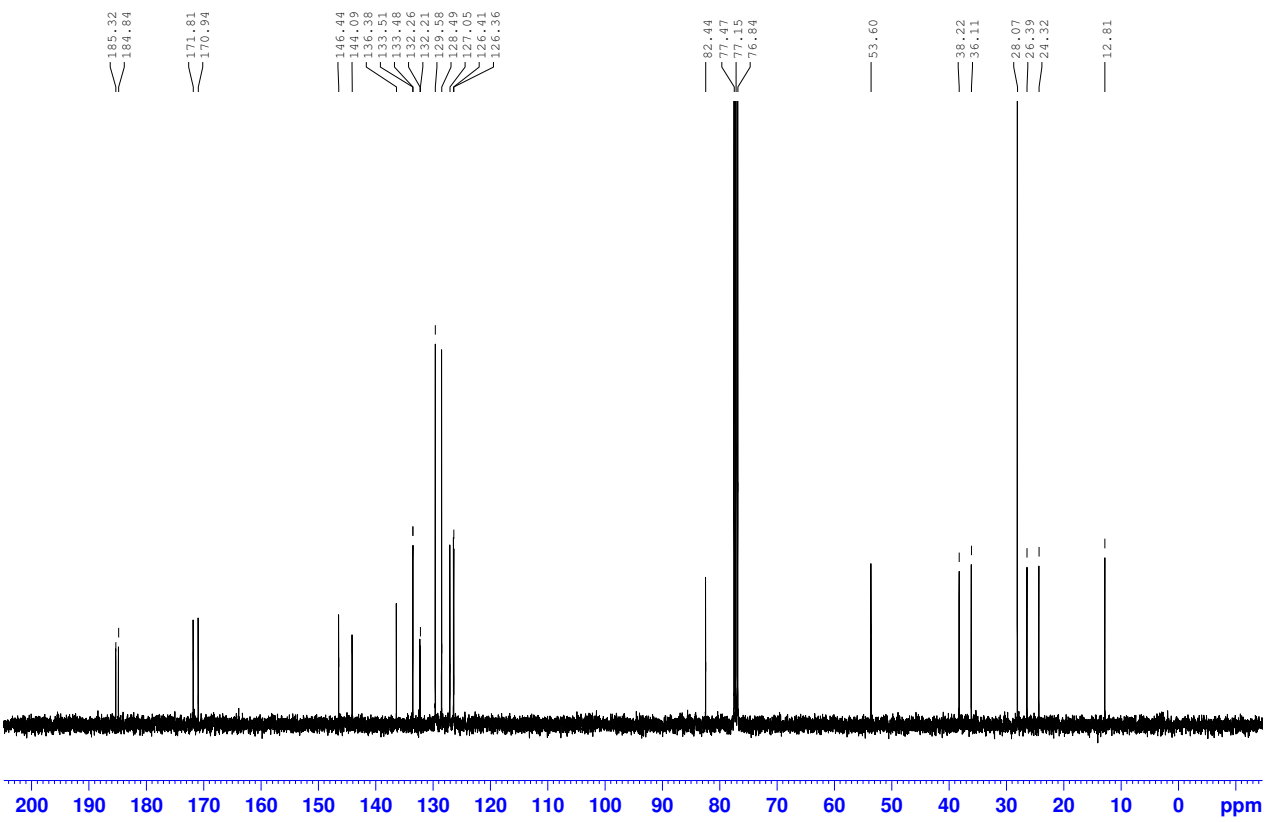
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170.94
146.44
144.09
136.38
135.51
133.48
132.26
132.21
129.58
128.49
127.05
126.41
126.36
82.44
77.47
77.15
76.84
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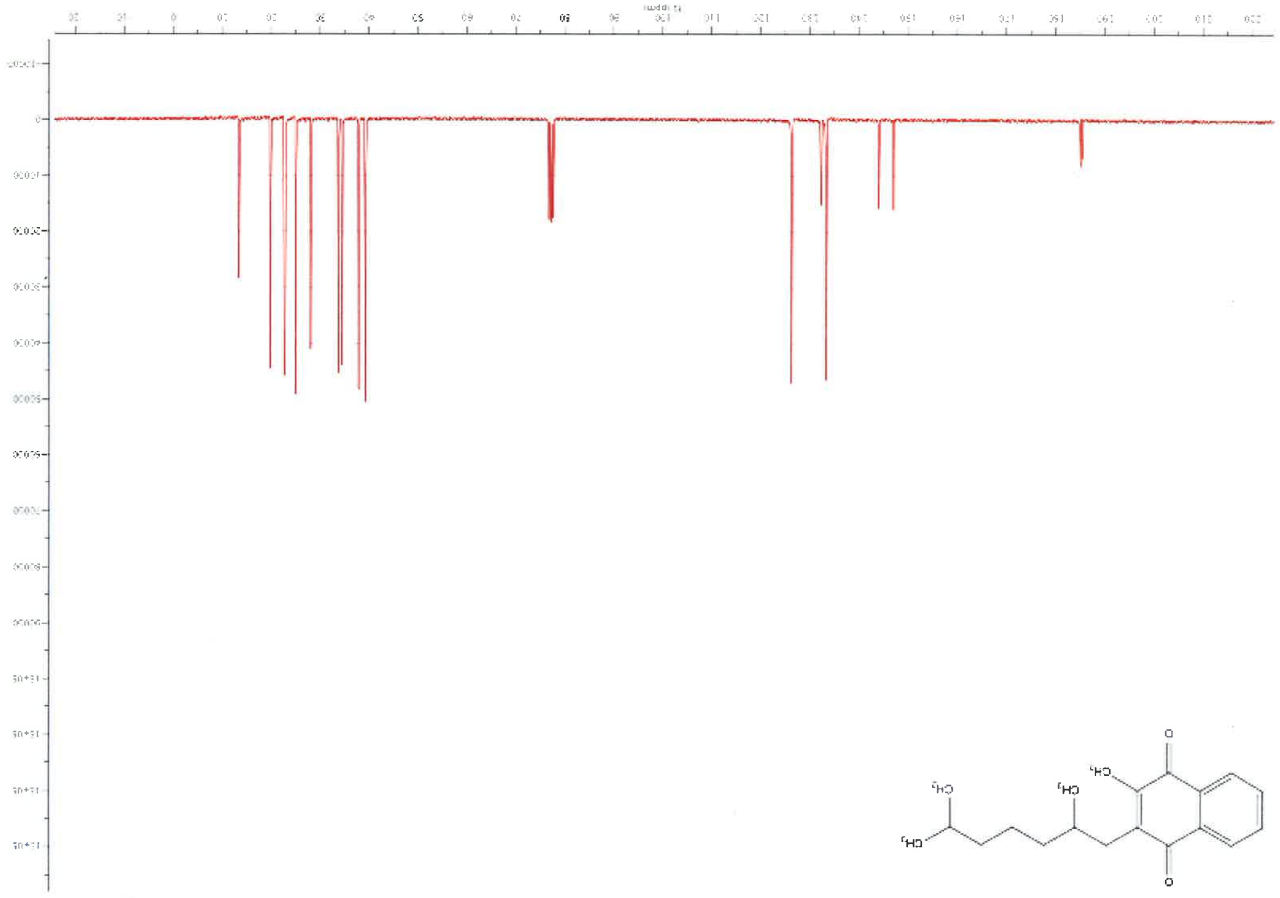
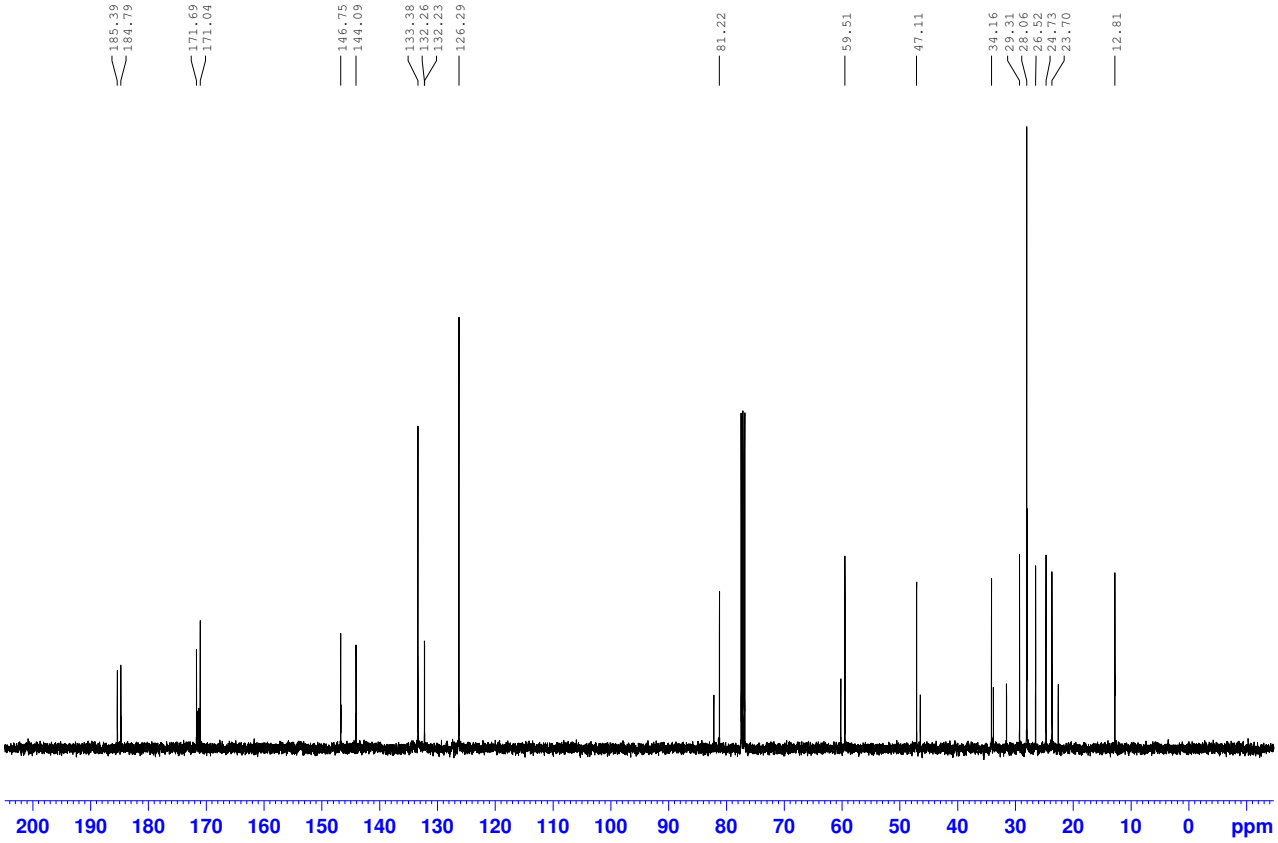
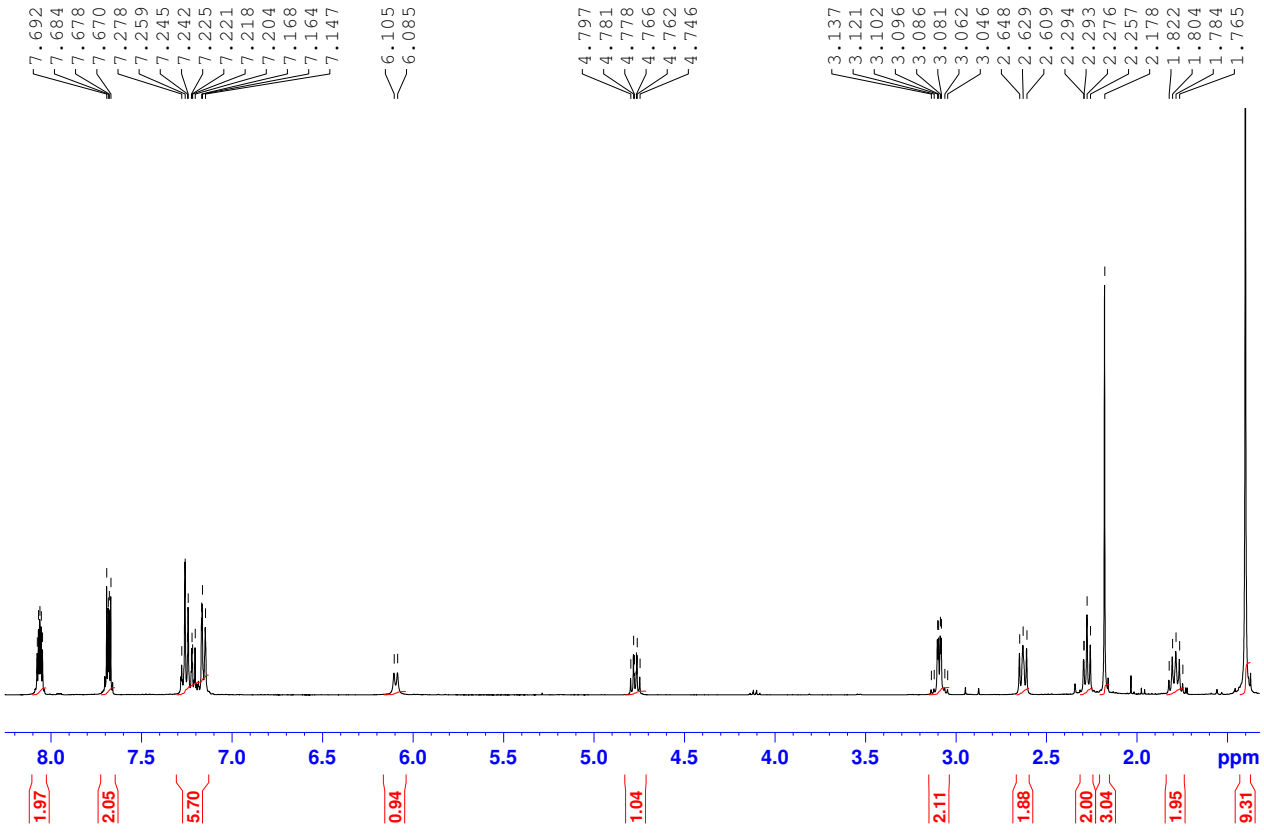
36.11
28.07
26.39
24.32
12.81
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



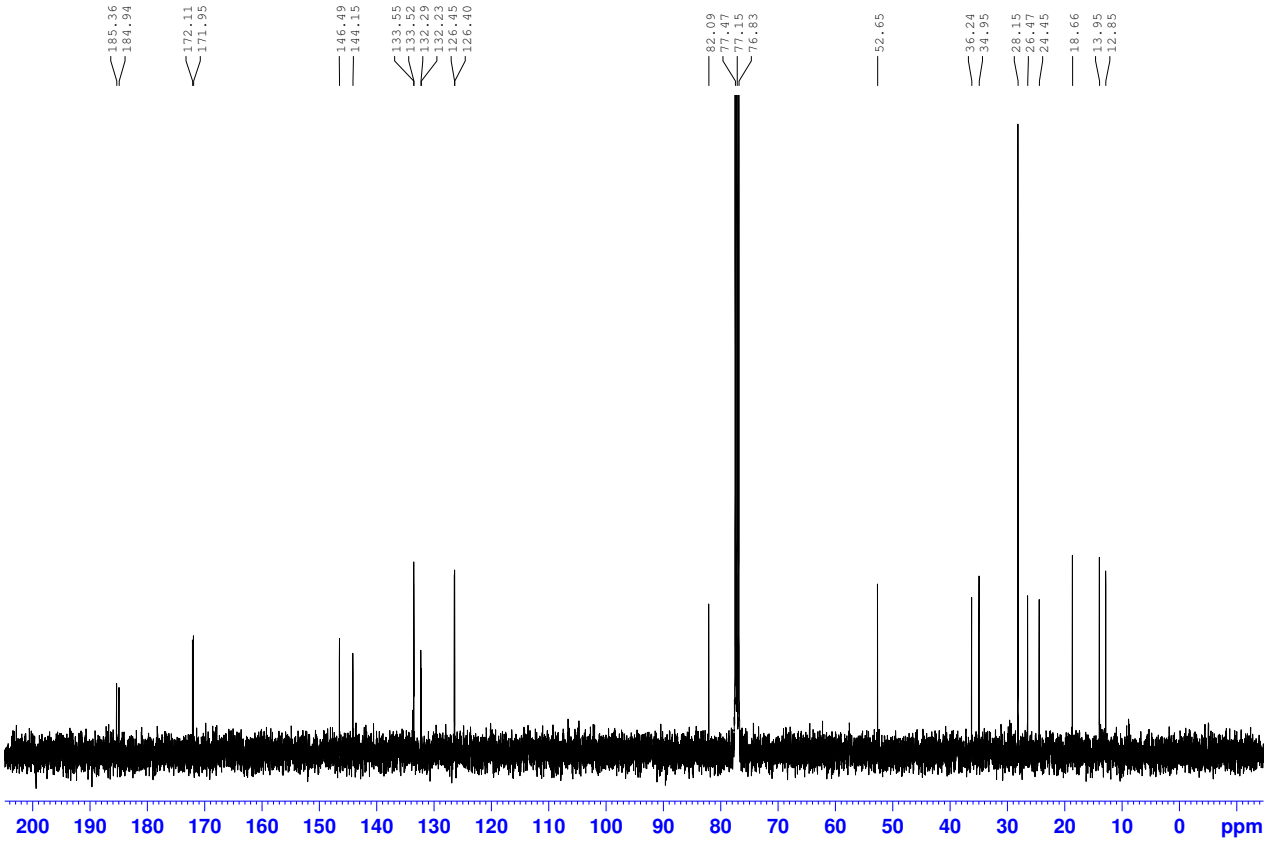
34

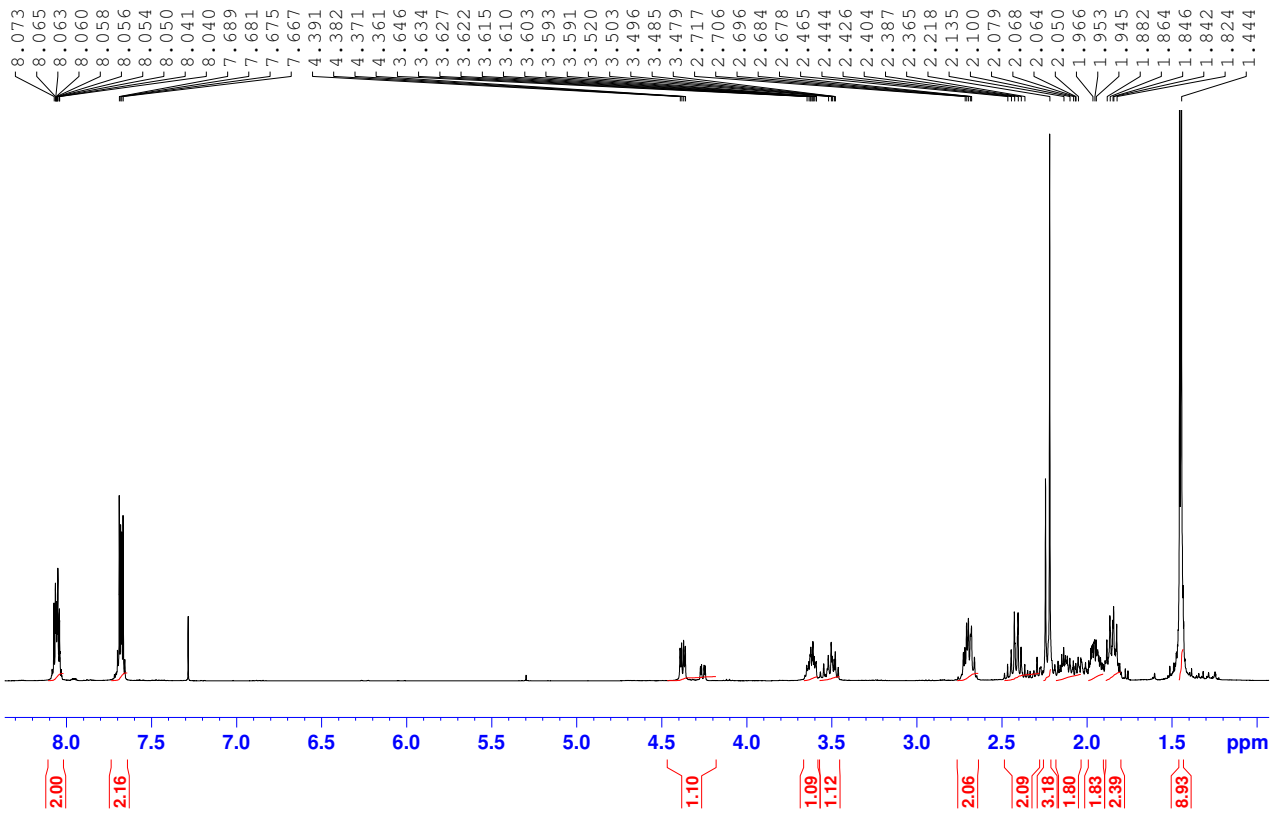
Avance III - 13C with 1H Power-gated Decoupling





Avance III - 13C with 1H Power-gated Decoupling





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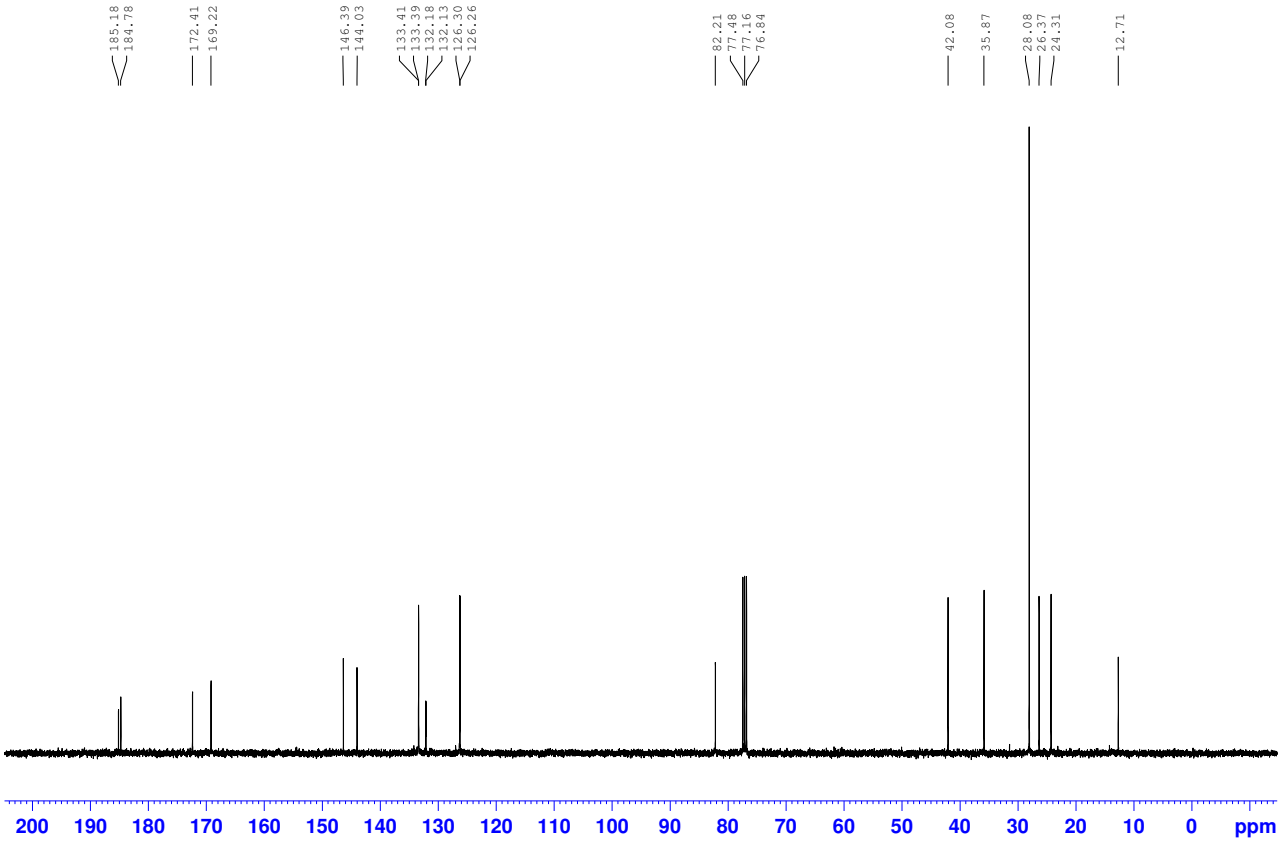
Avance III - 13C with 1H Power-gated Decoupling



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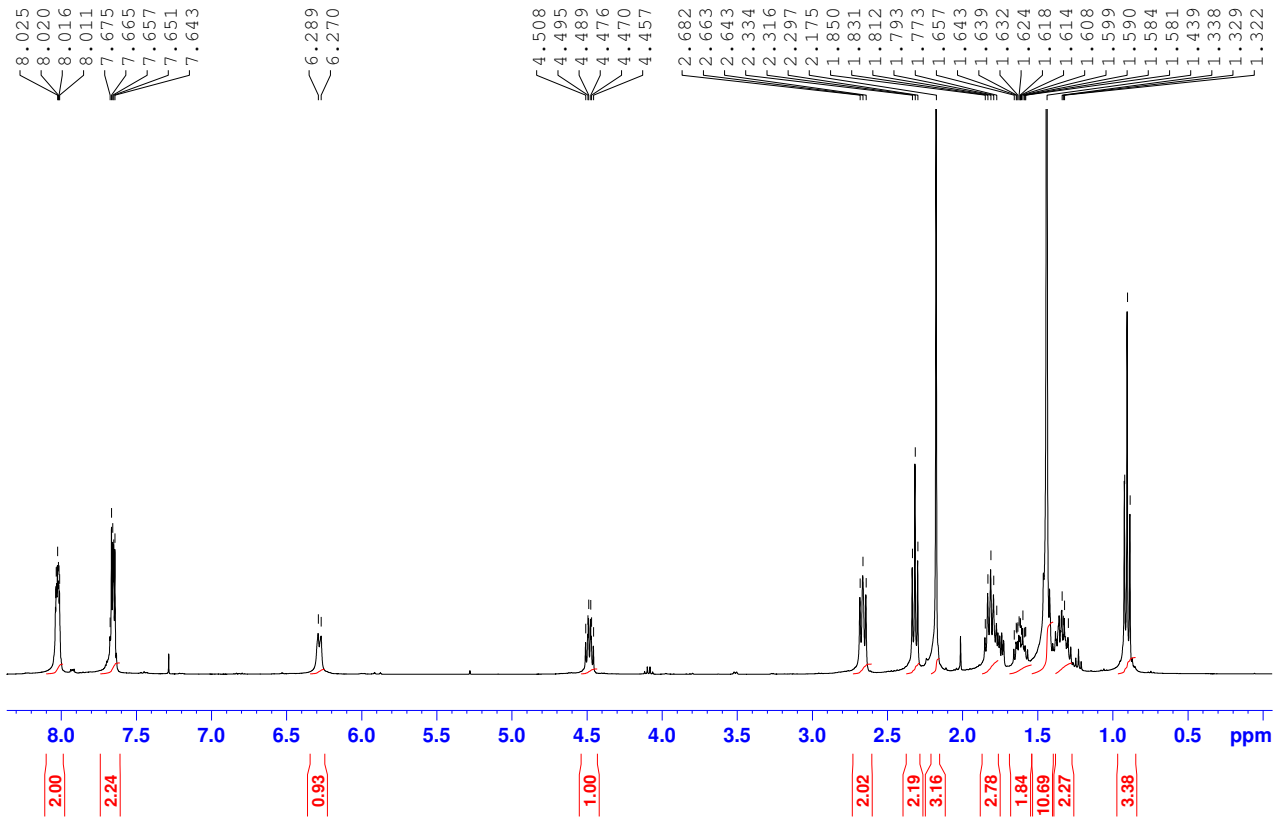
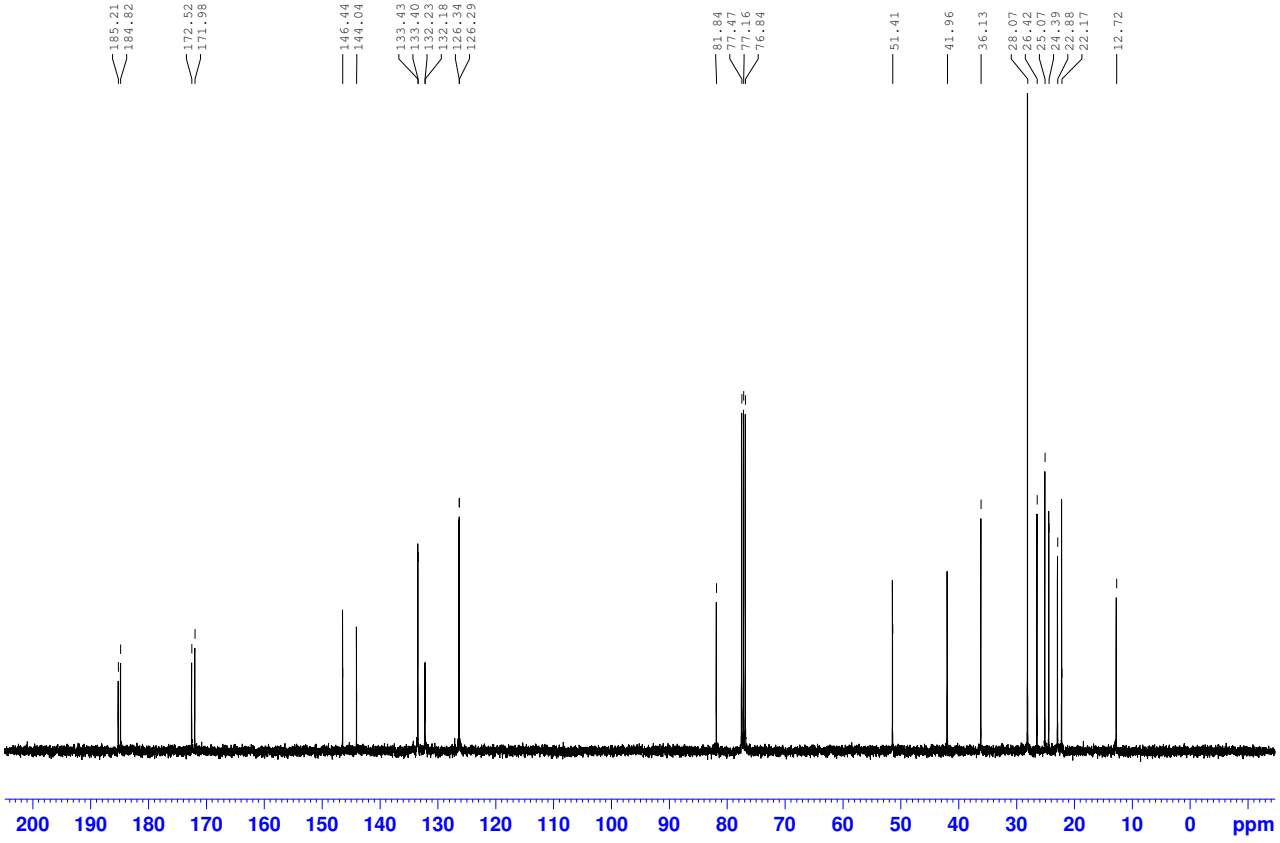
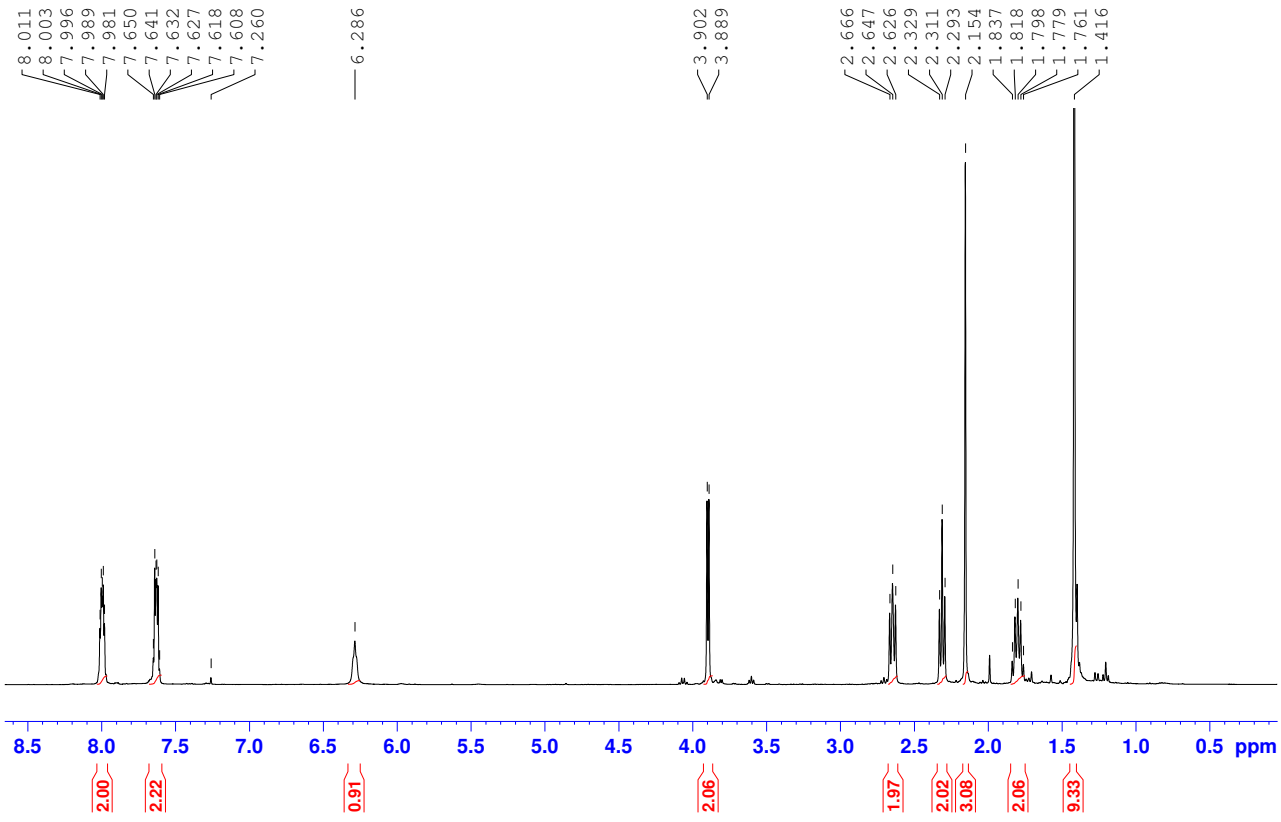
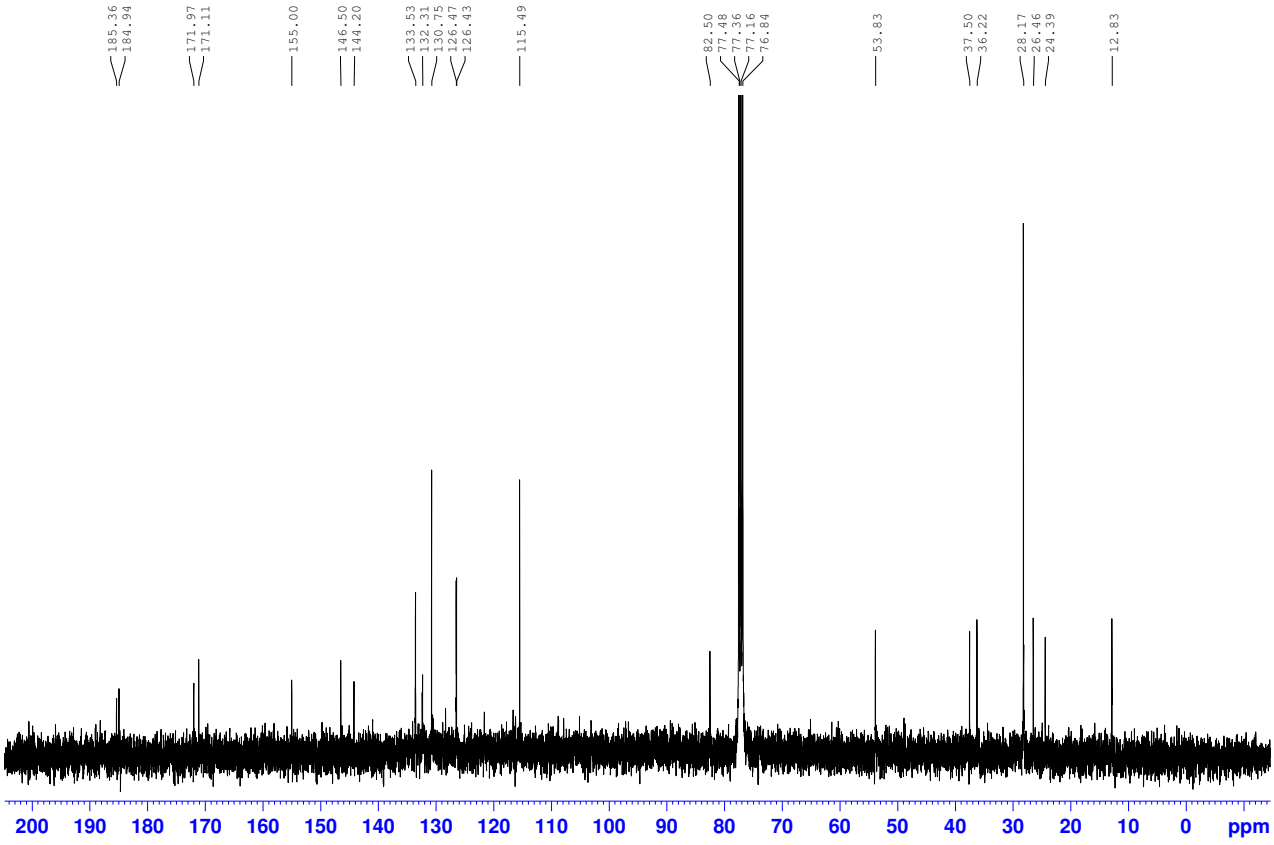


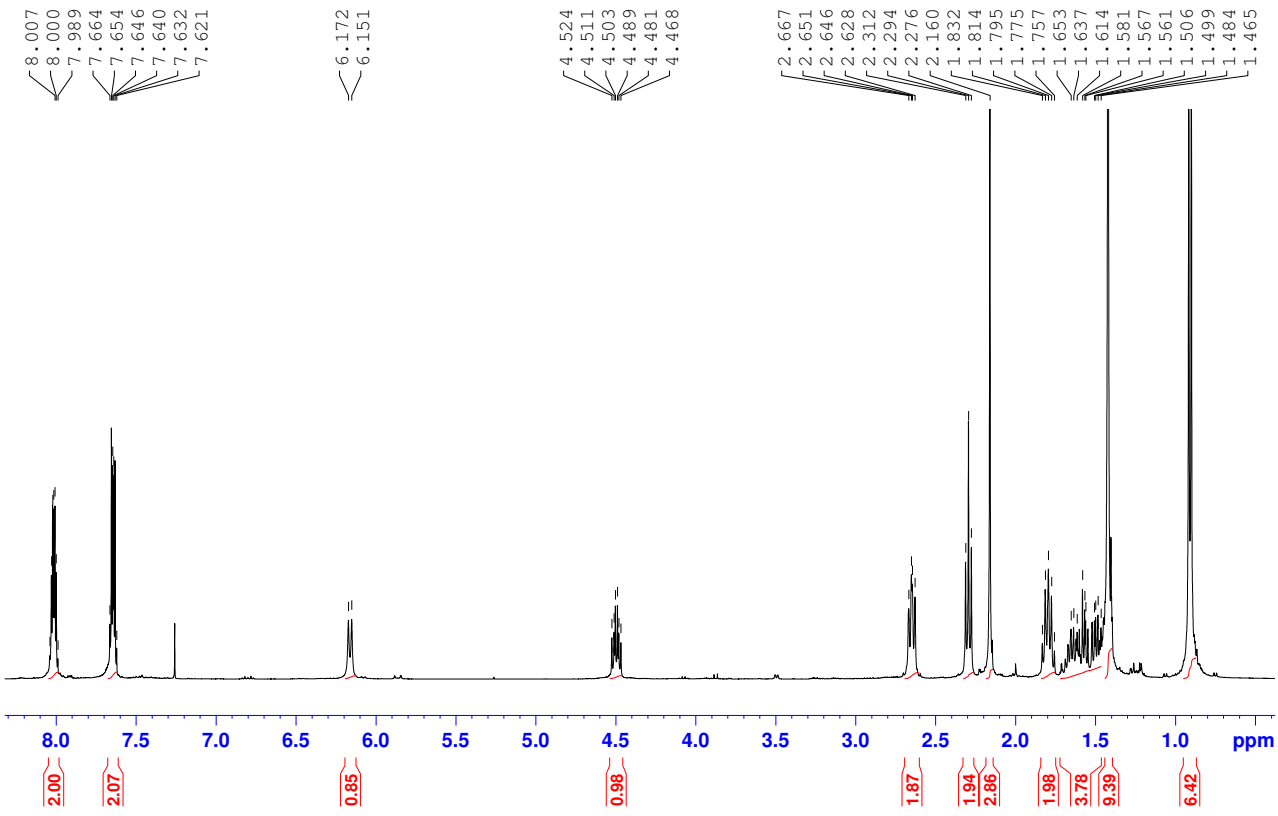
Avance III - 13C with 1H Power-gated Decoupling



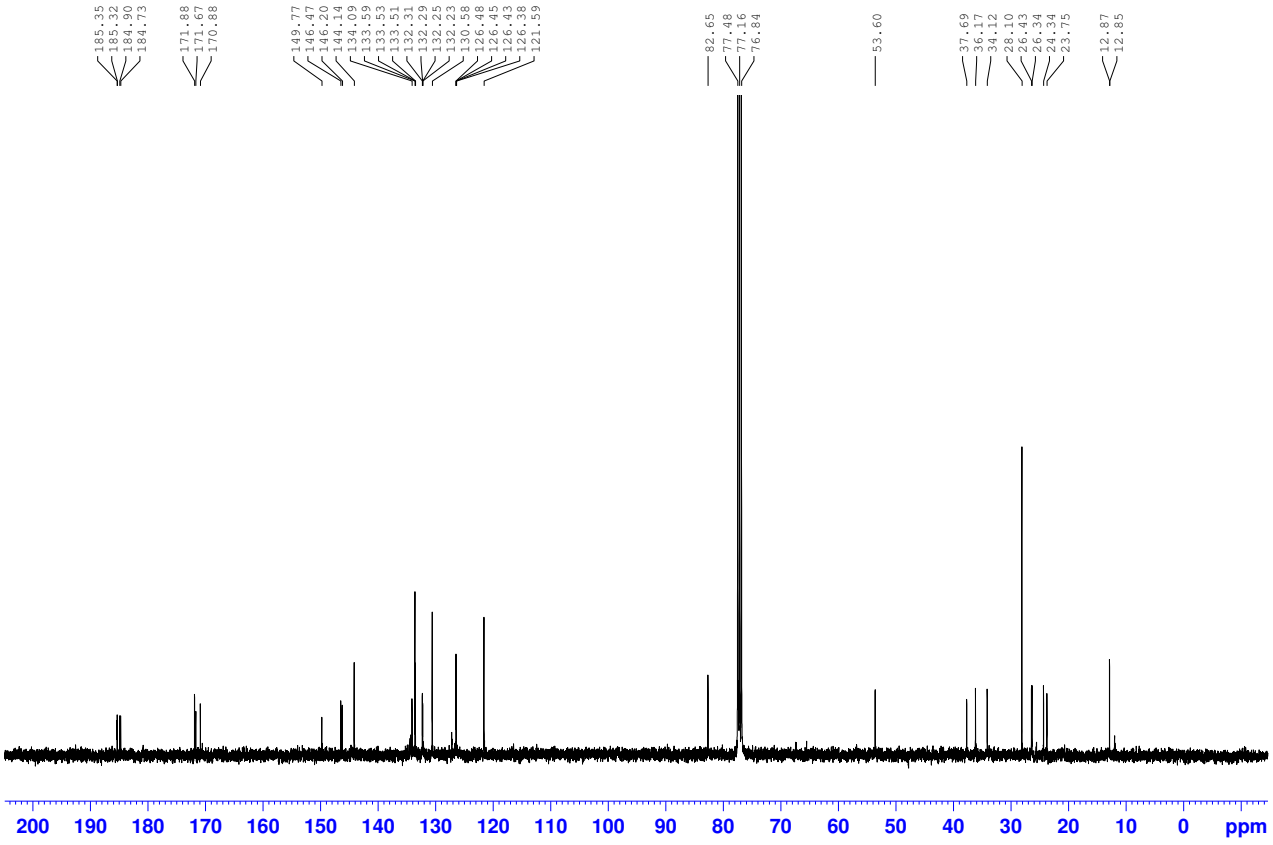


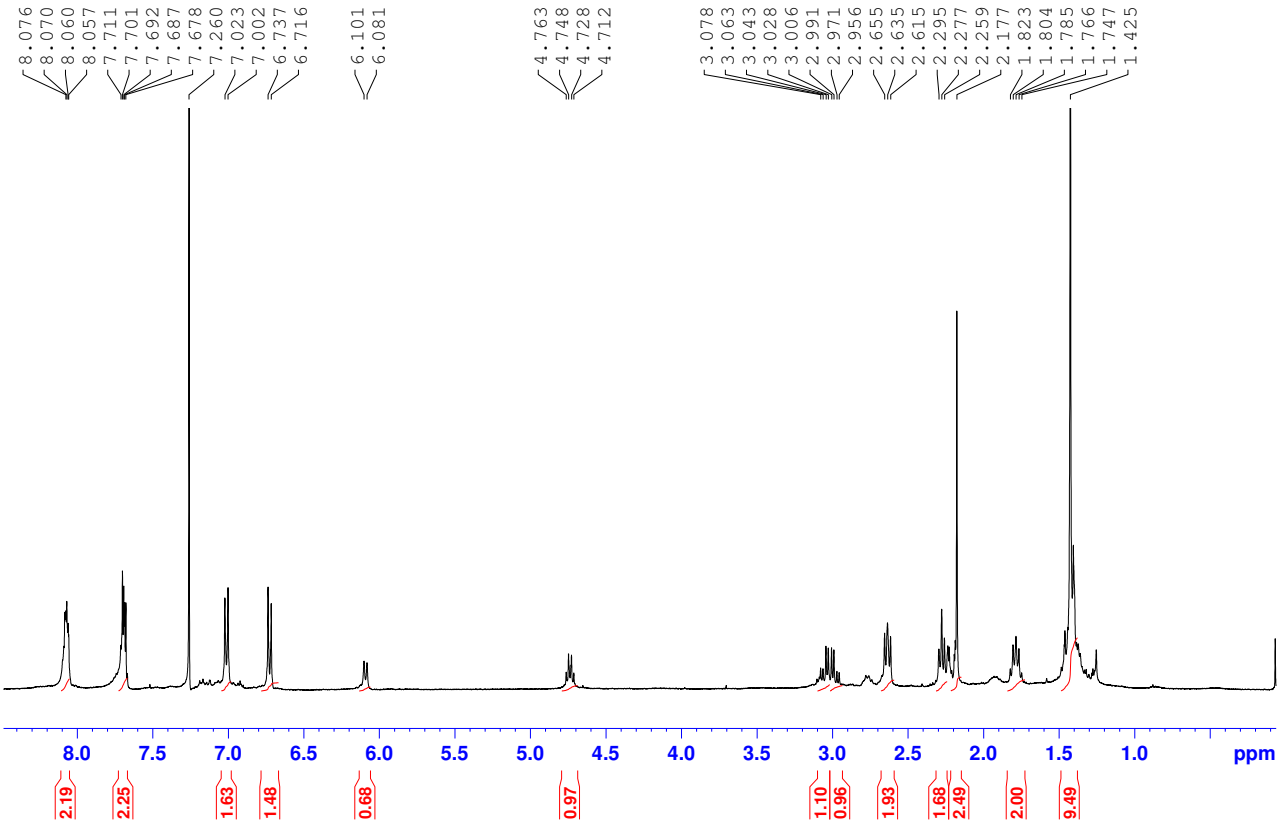
Avance III - 13C with 1H Power-gated Decoupling



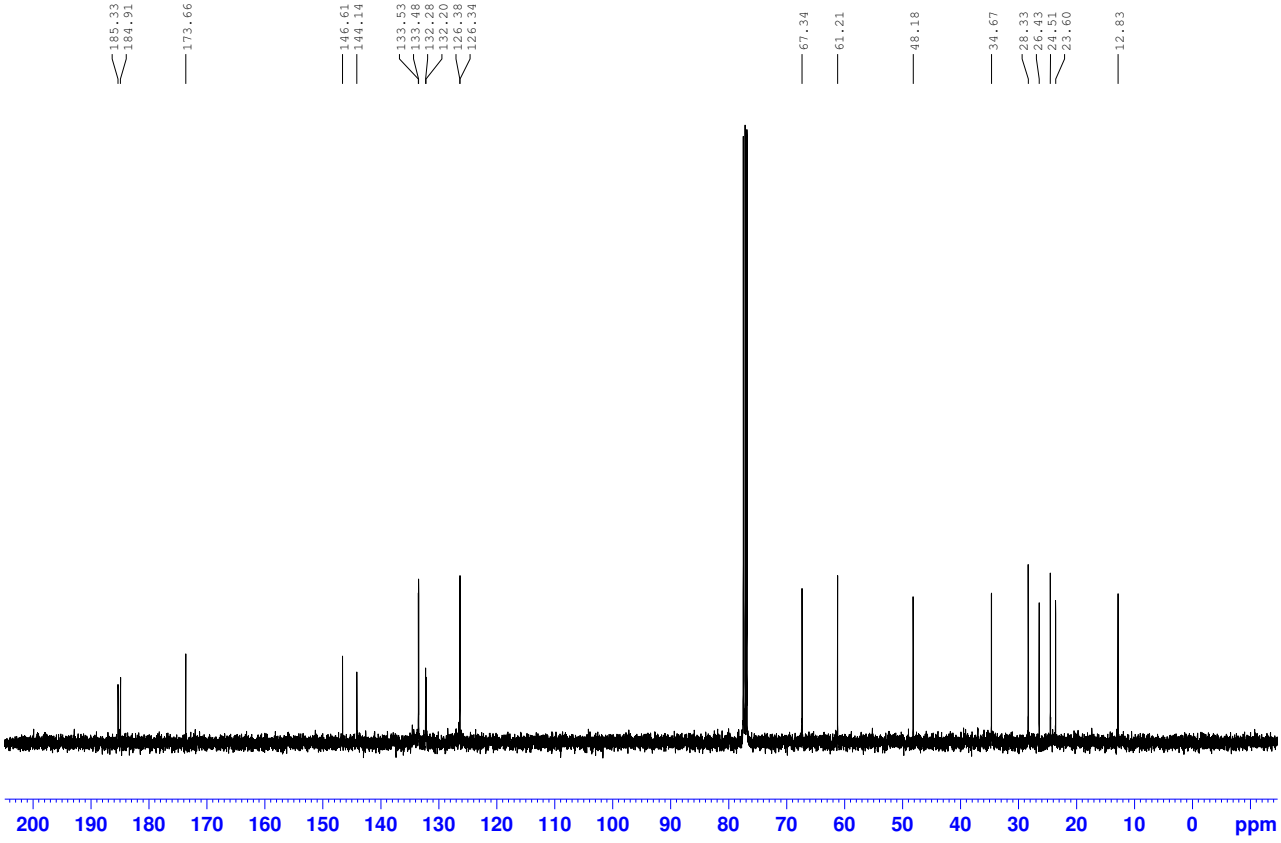


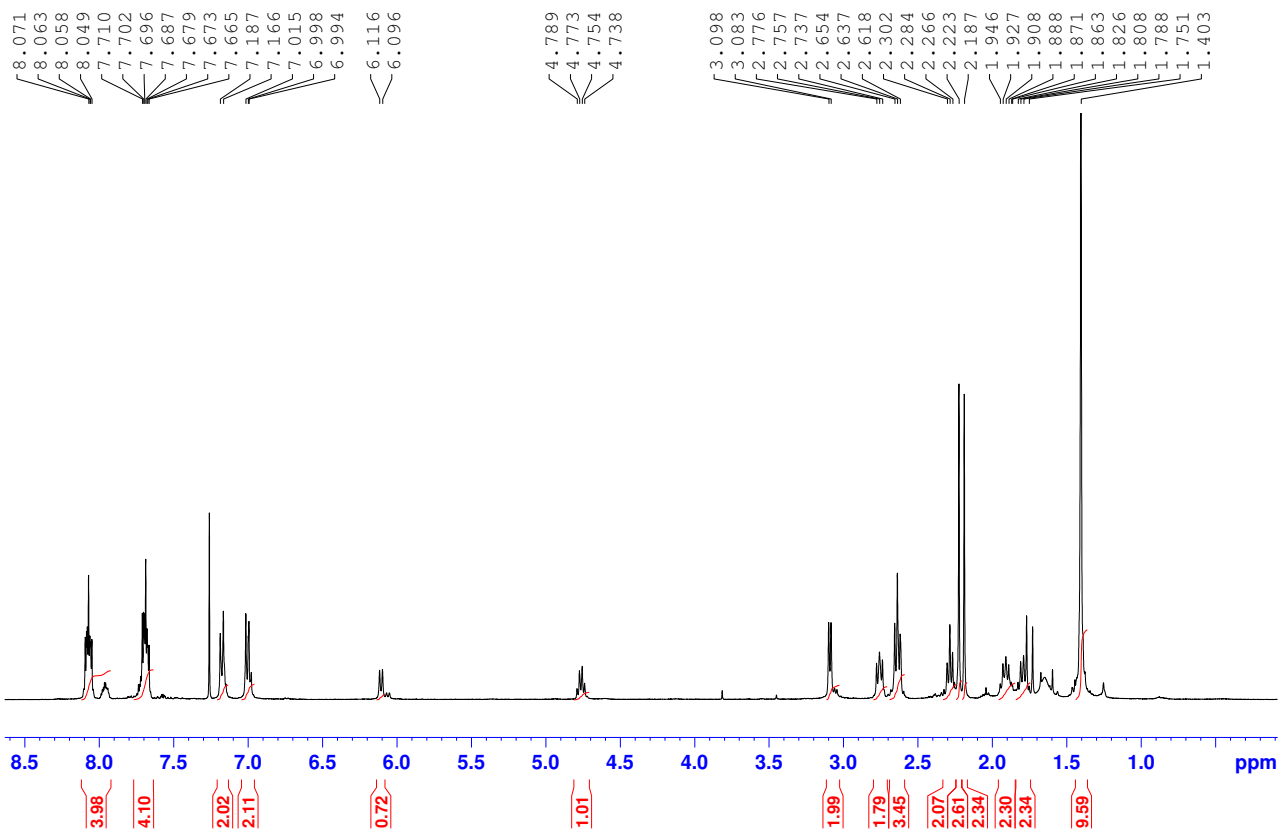
Avance III - 13C with 1H Power-gated Decoupling



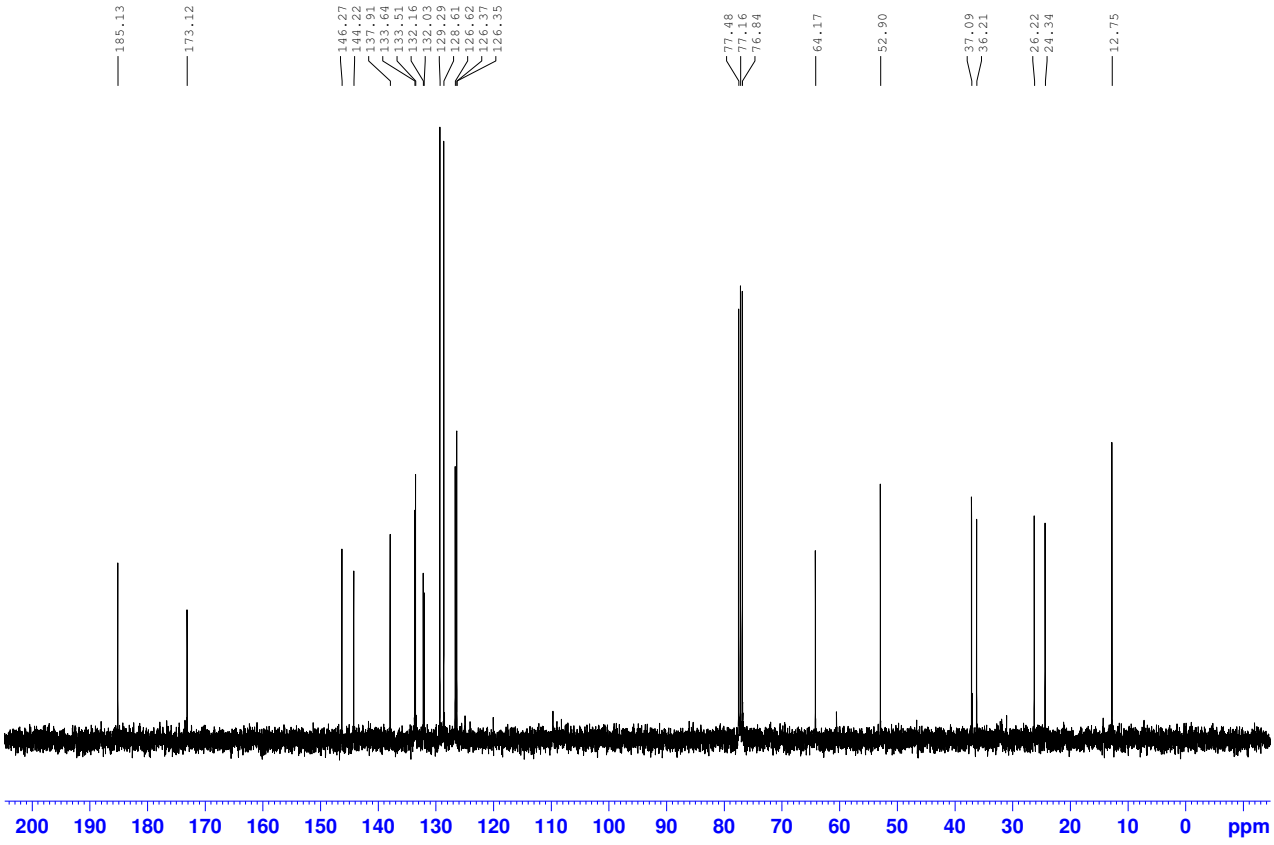


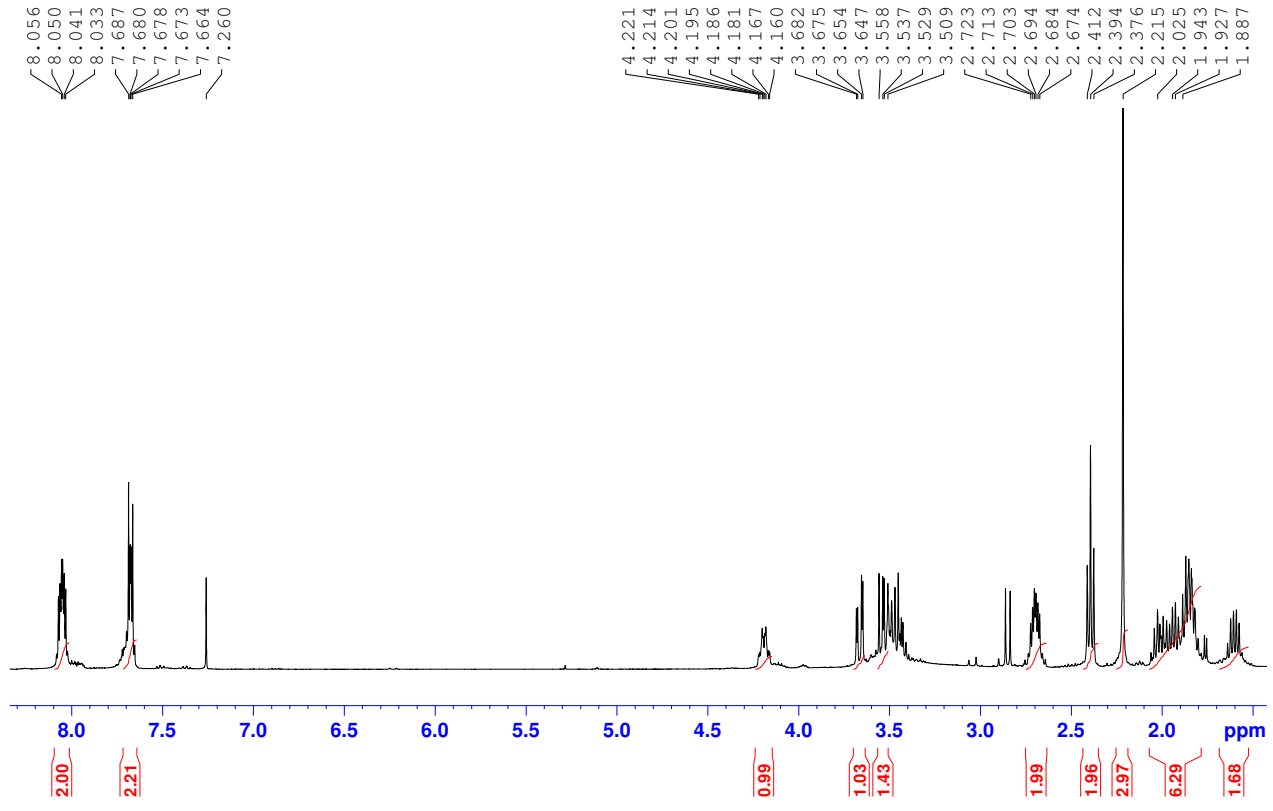
Avance III - 13C with 1H Power-gated Decoupling



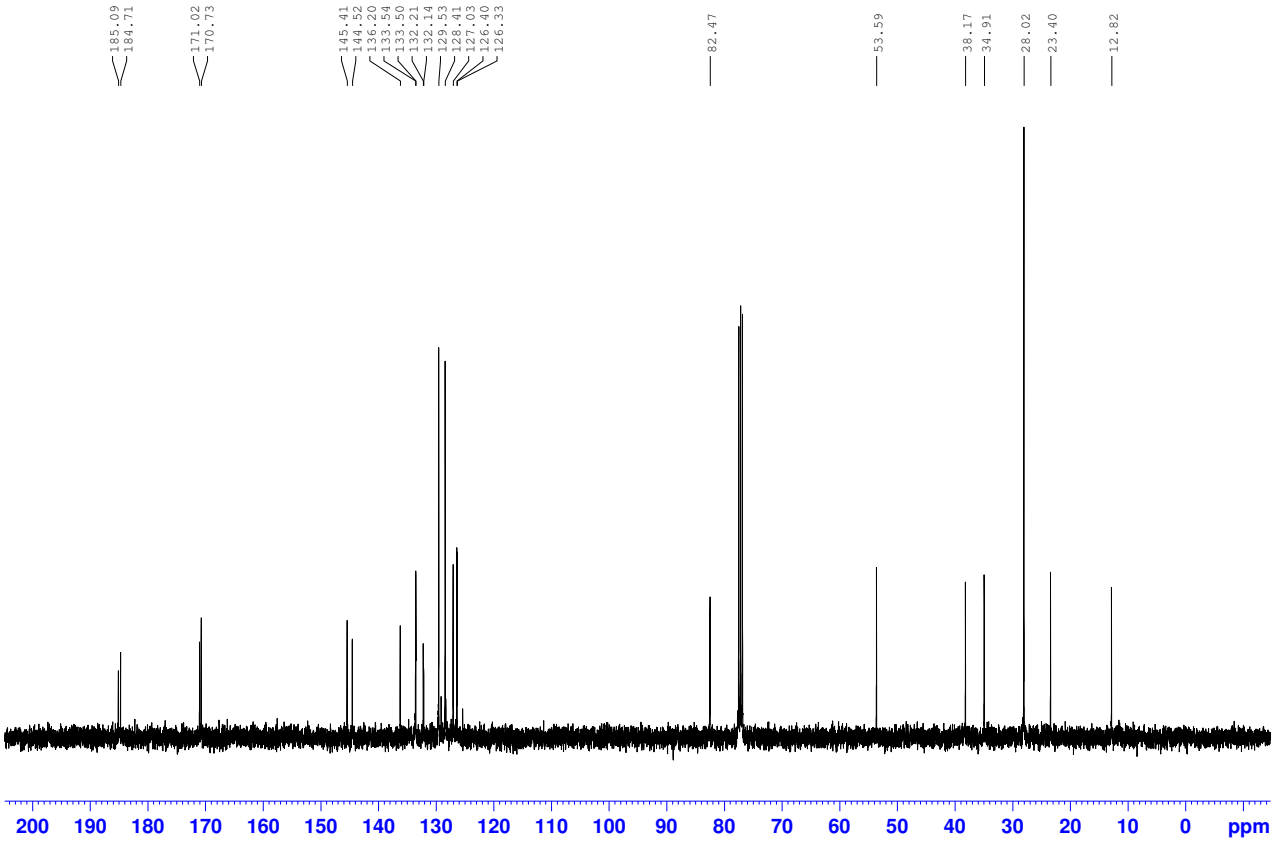


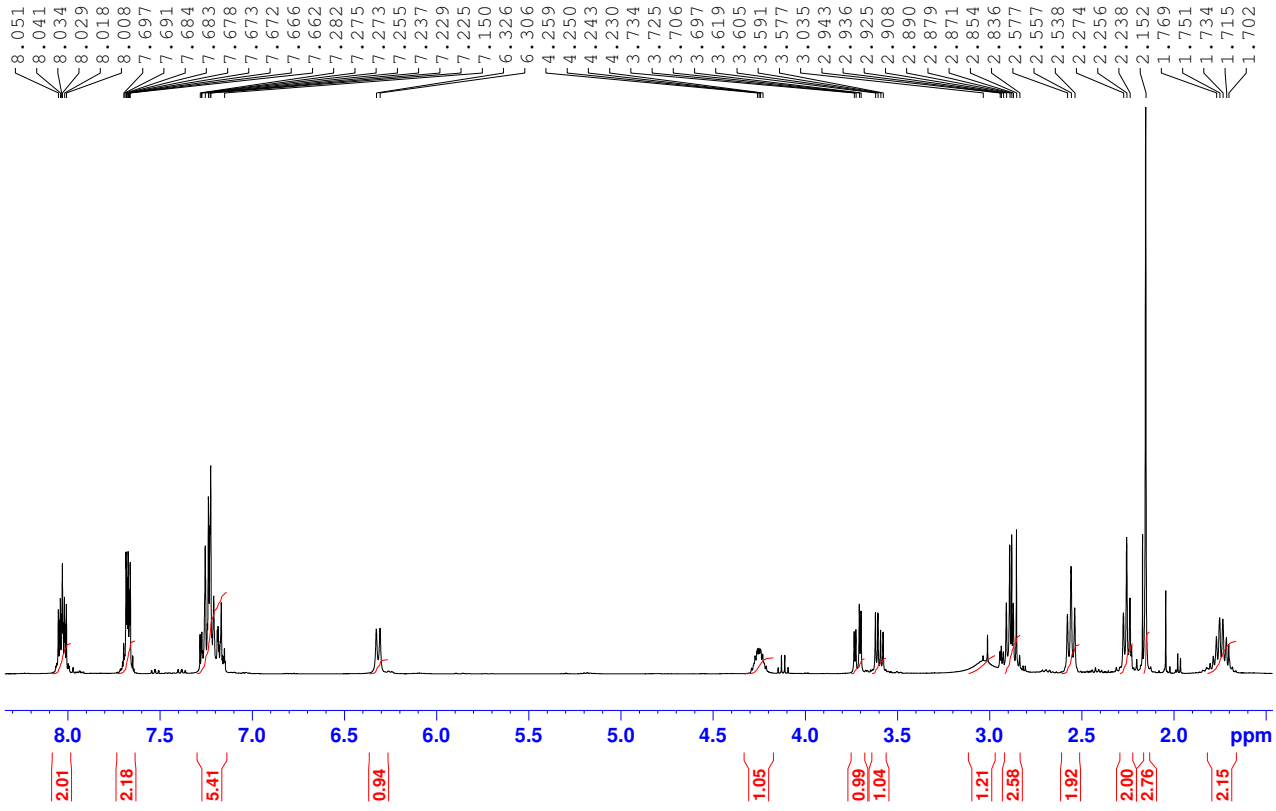
Avance III - 13C with 1H Power-gated Decoupling



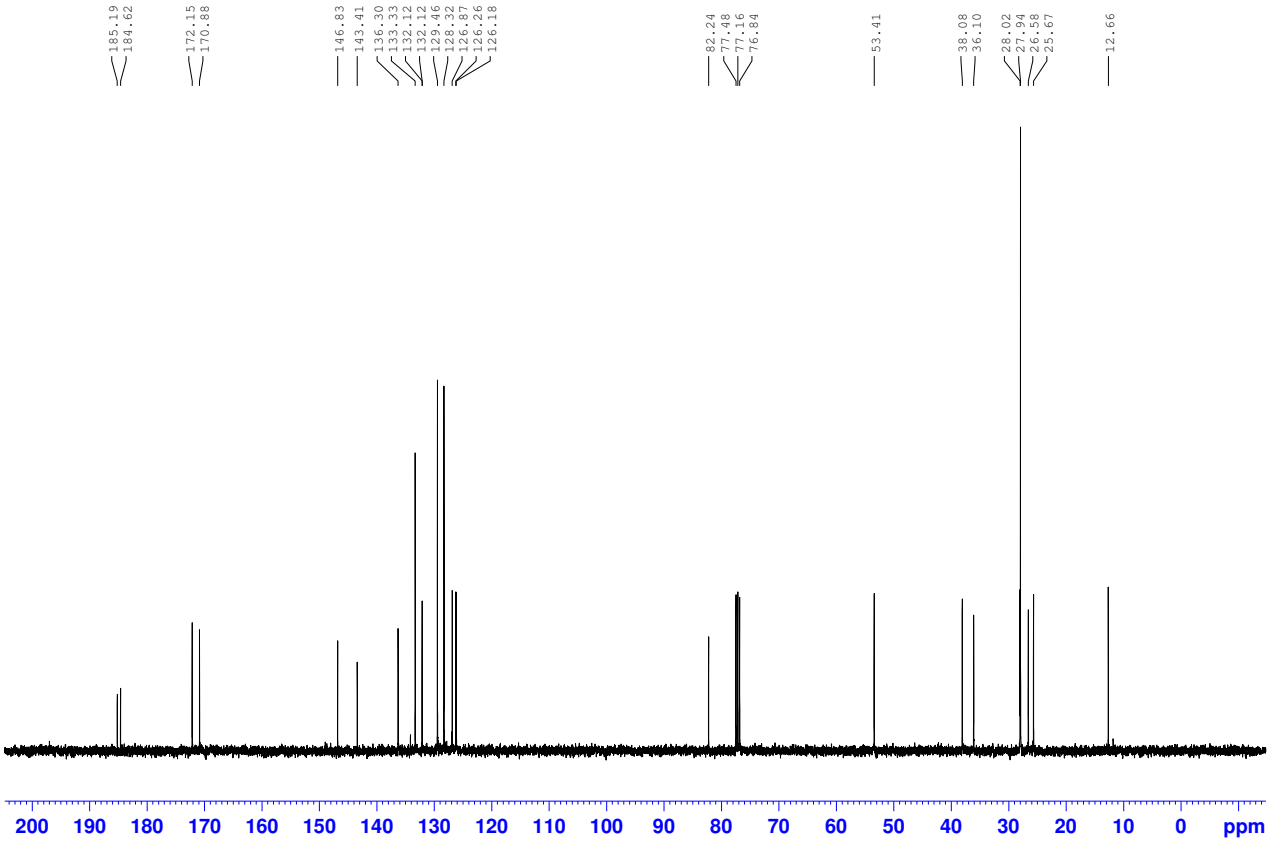


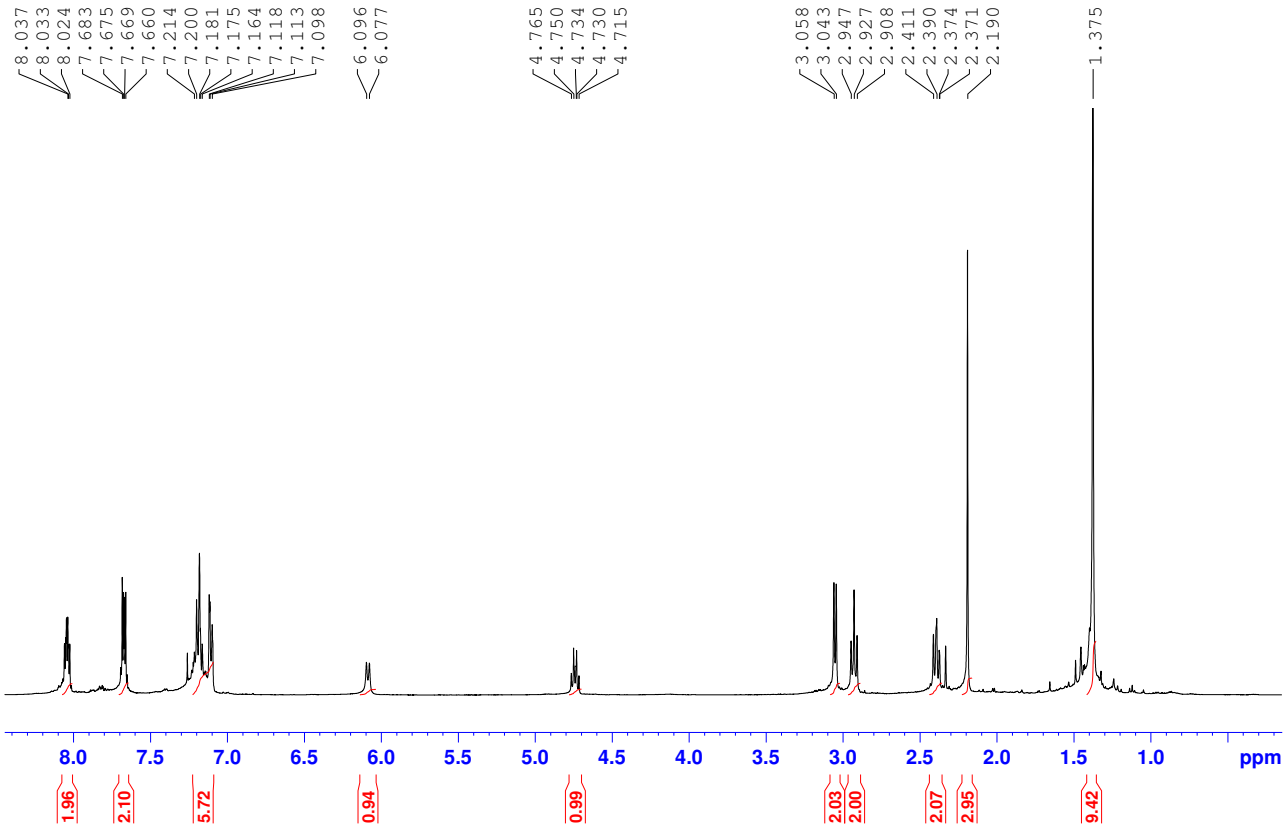
Avance III - 13C with 1H Power-gated Decoupling



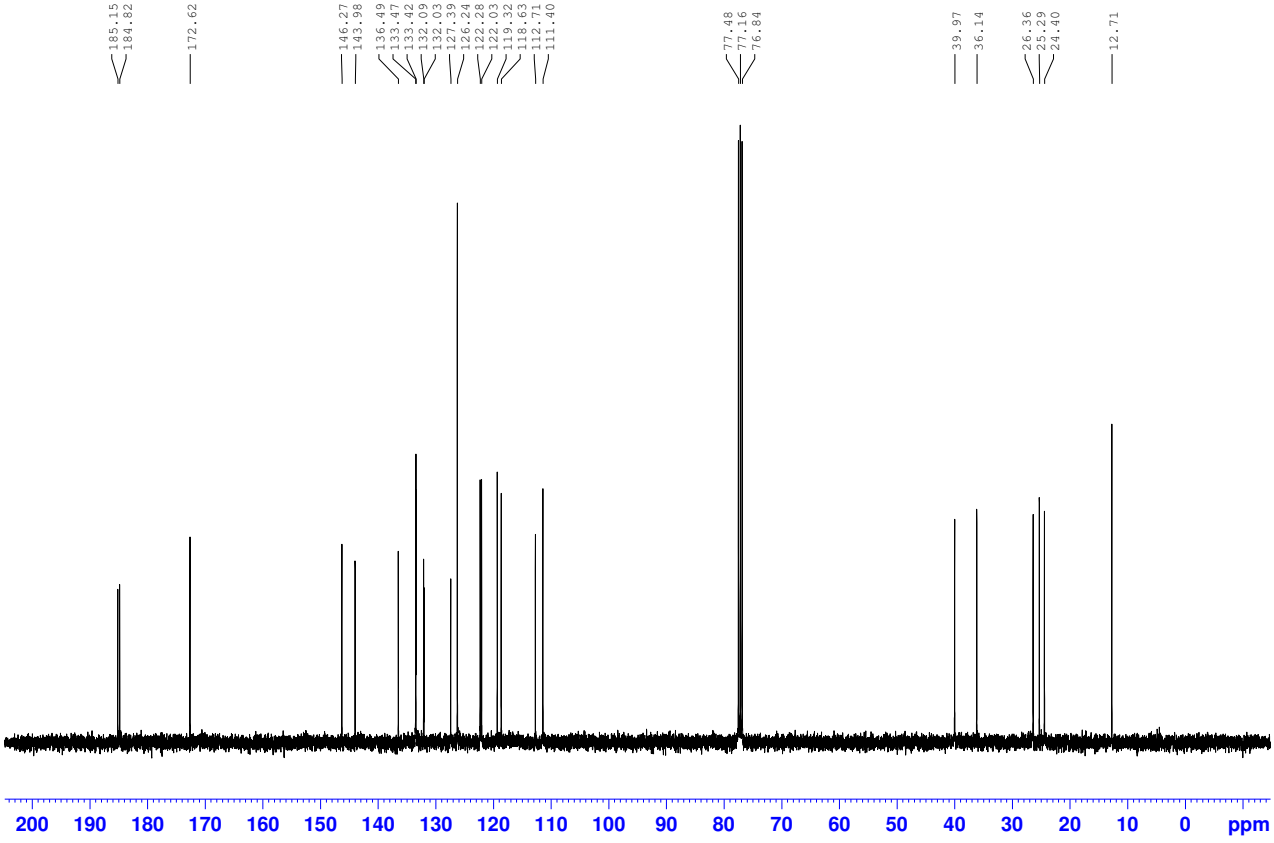


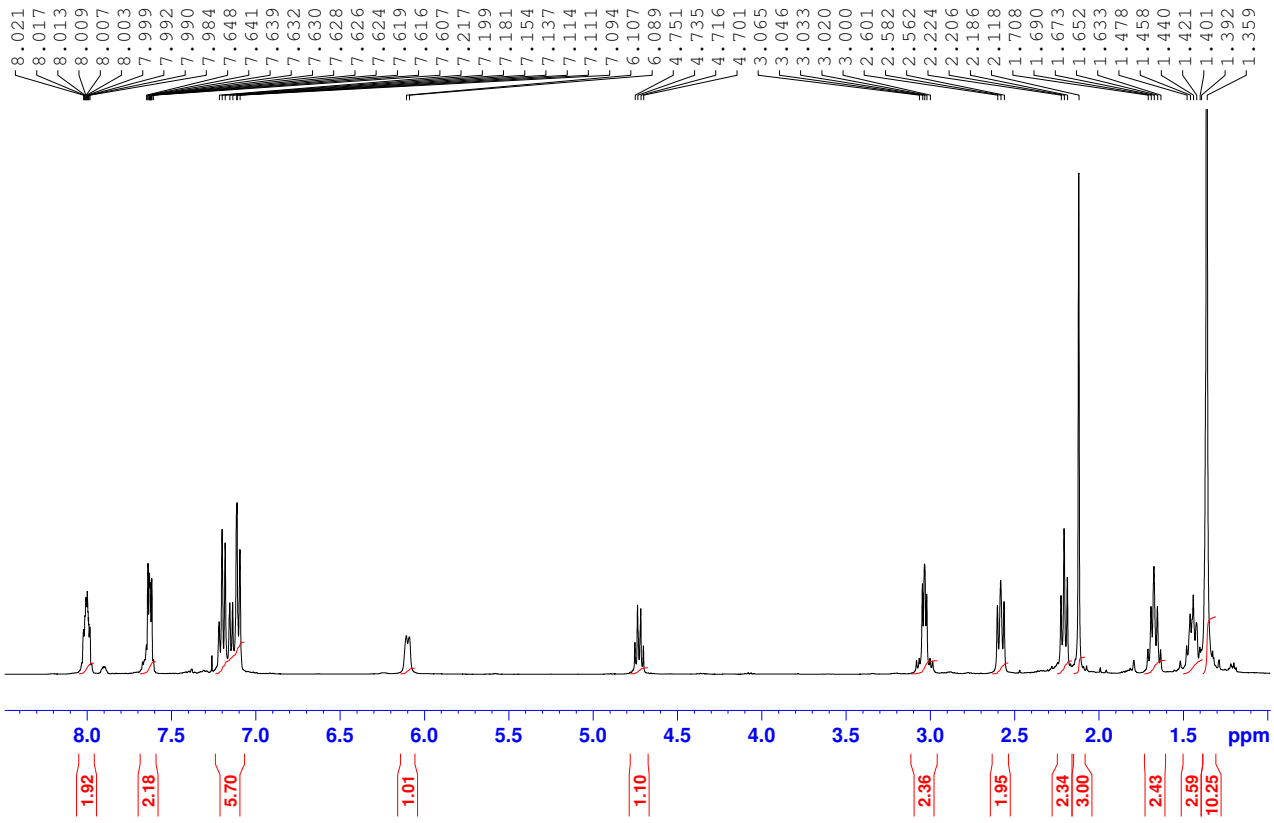
Avance III - 13C with 1H Power-gated Decoupling



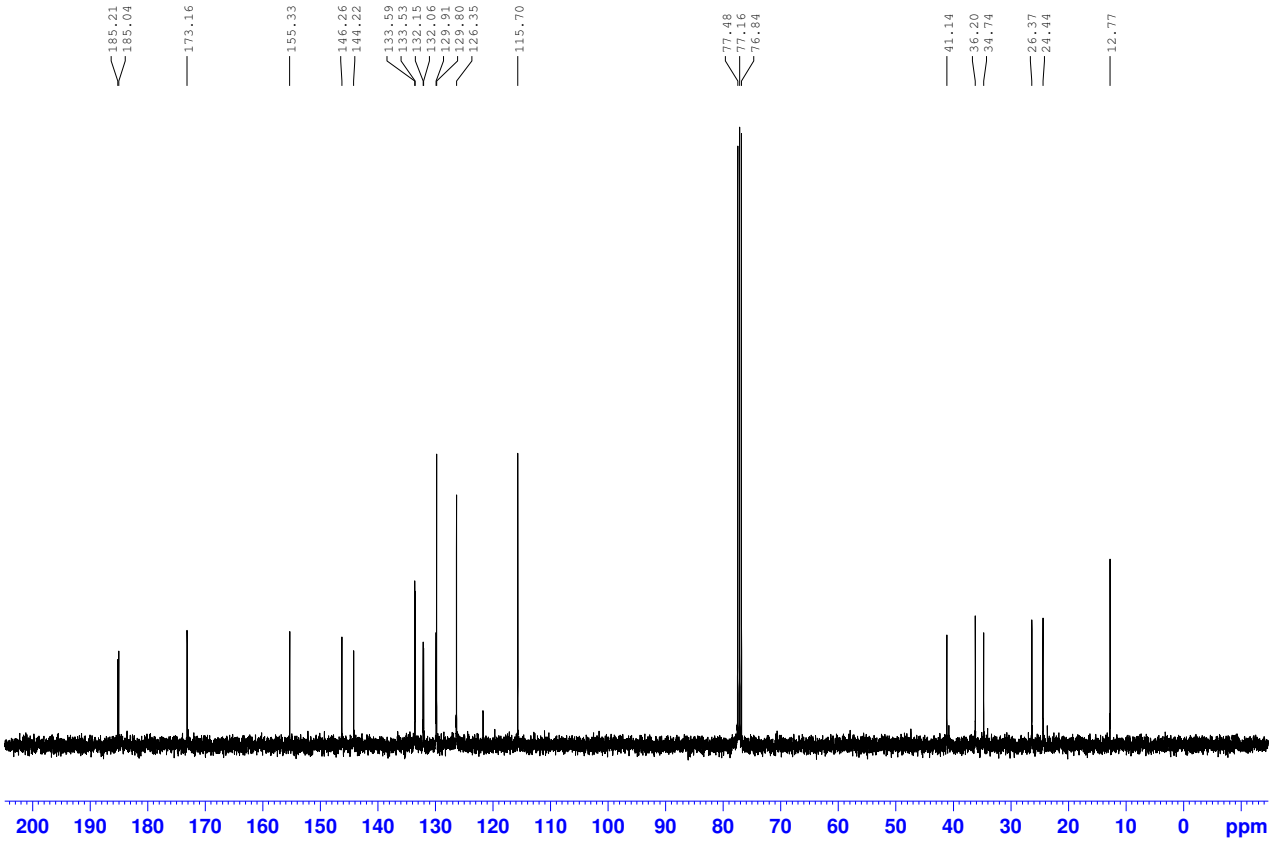


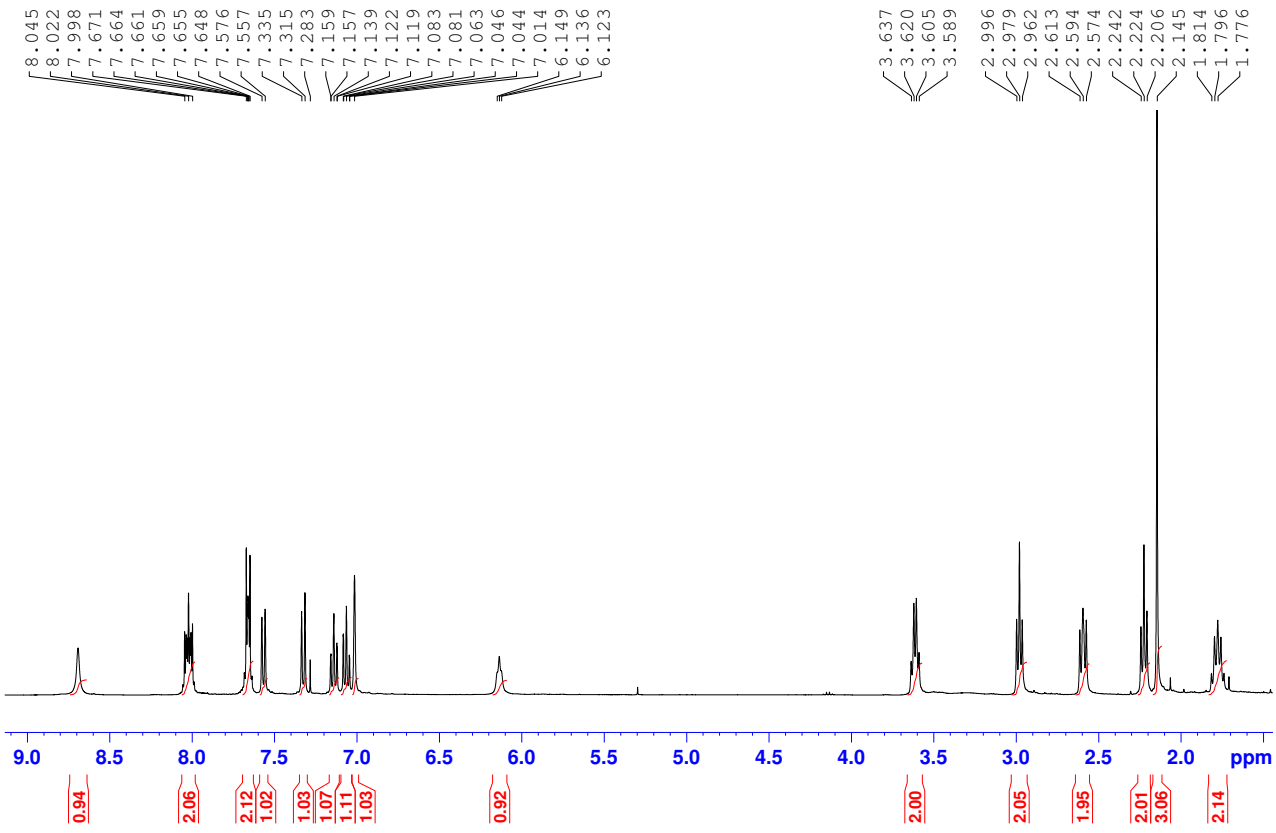
Avance III - 13C with 1H Power-gated Decoupling



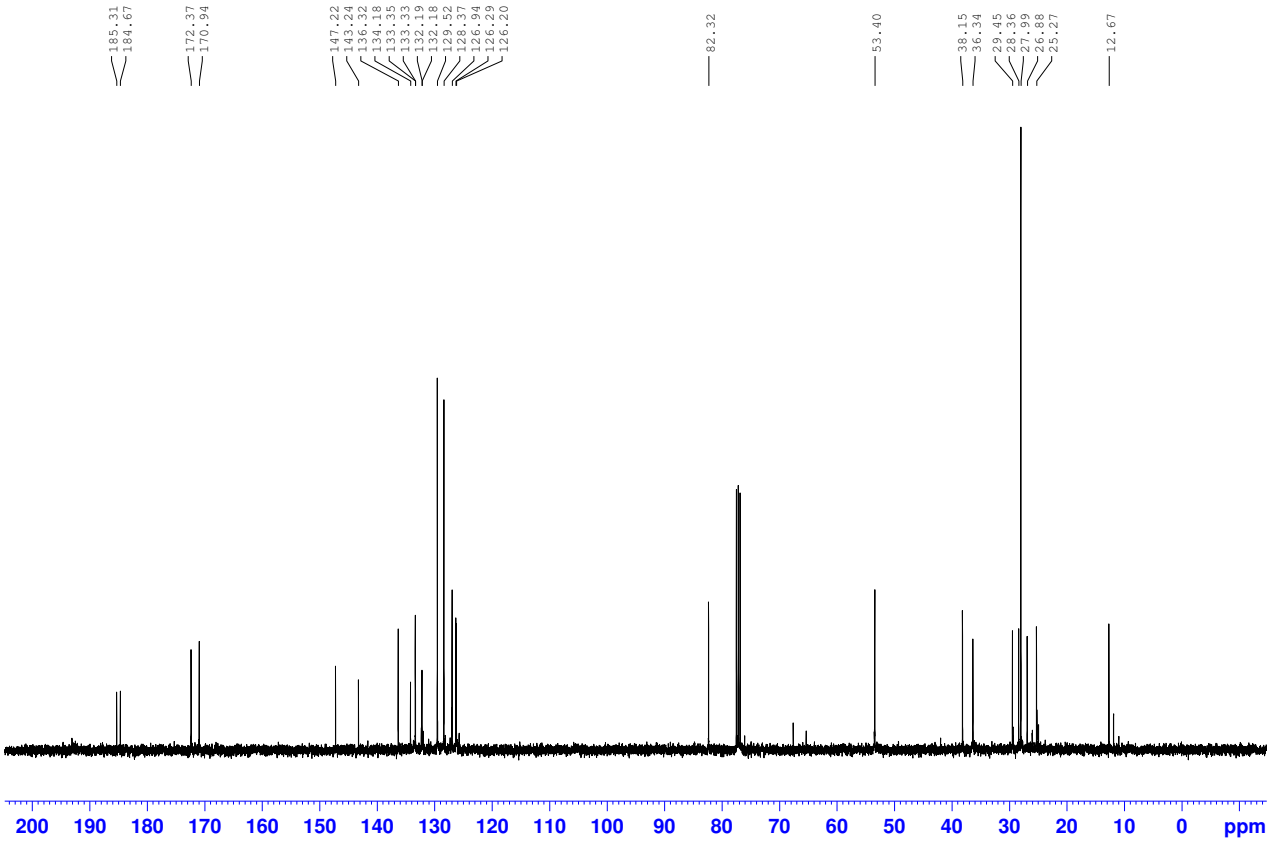


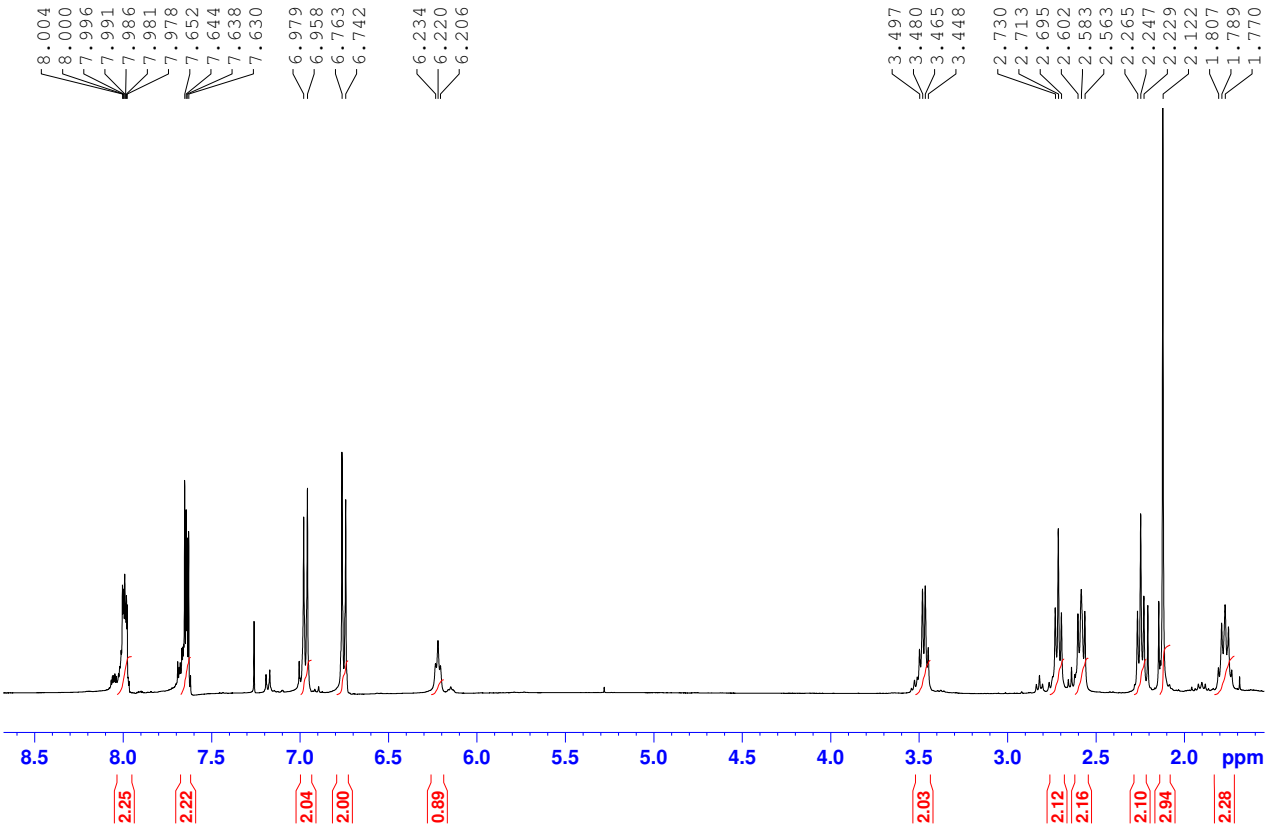
Avance III - 13C with 1H Power-gated Decoupling



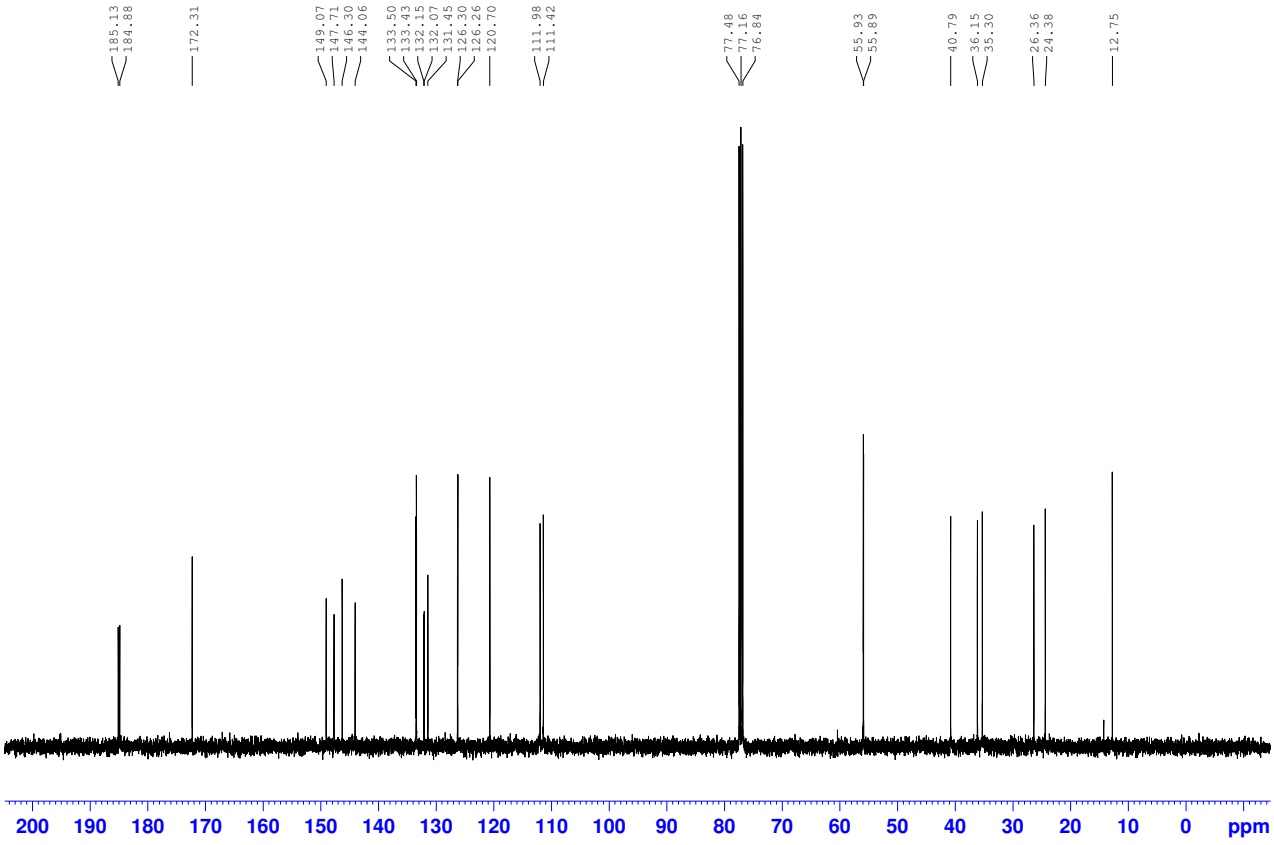


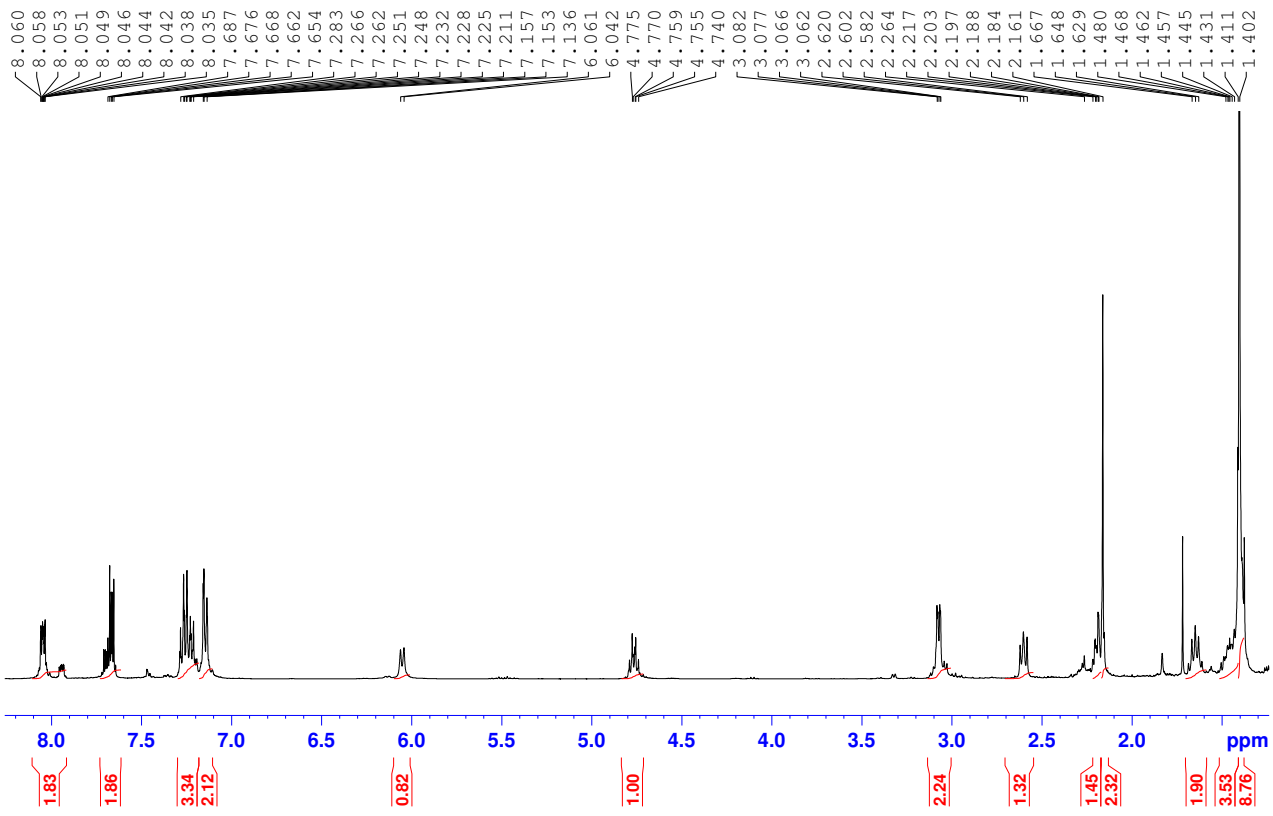
Avance III - 13C with 1H Power-gated Decoupling



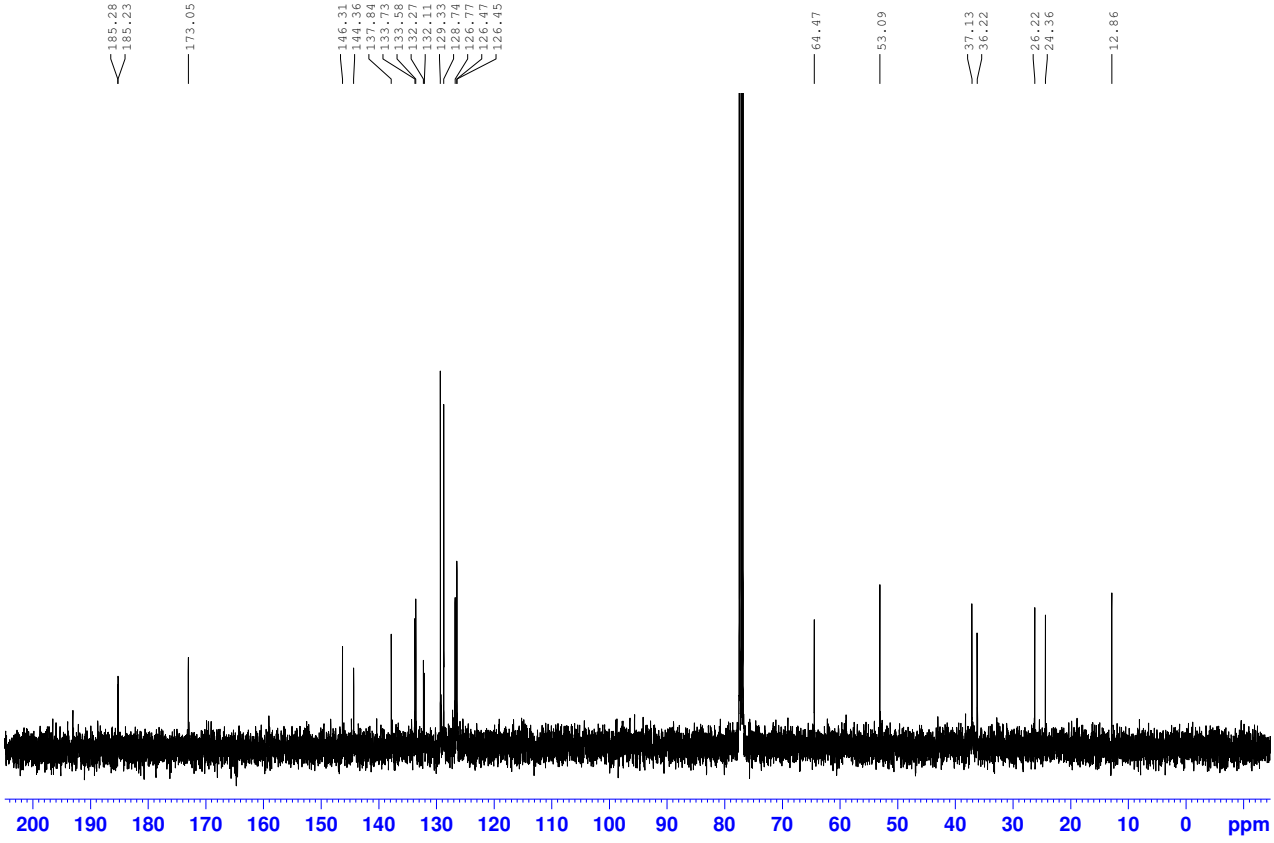


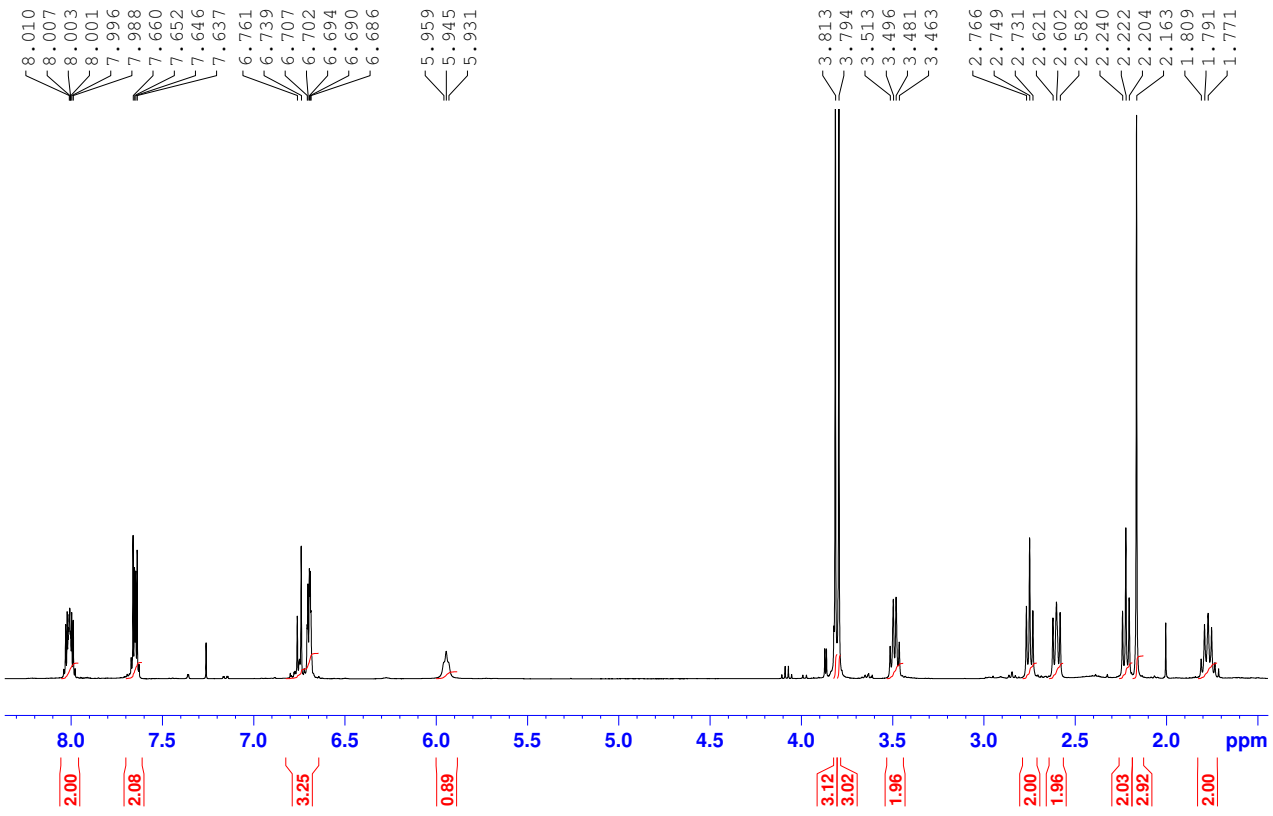
Avance III - 13C with 1H Power-gated Decoupling





Avance III - 13C with 1H Power-gated Decoupling





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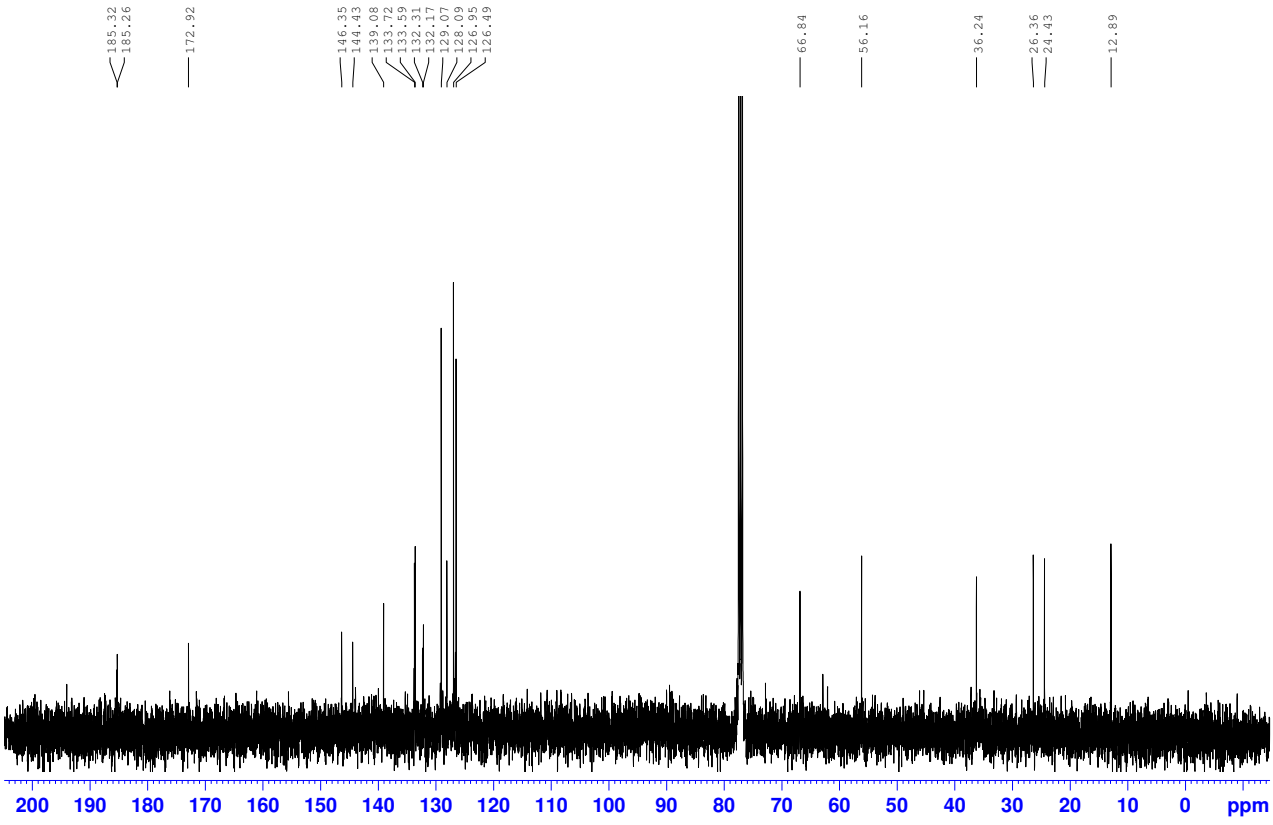
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133.59
132.31
132.17
129.07
128.09
126.95
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66.84
56.16
36.24
26.36
24.43
12.89
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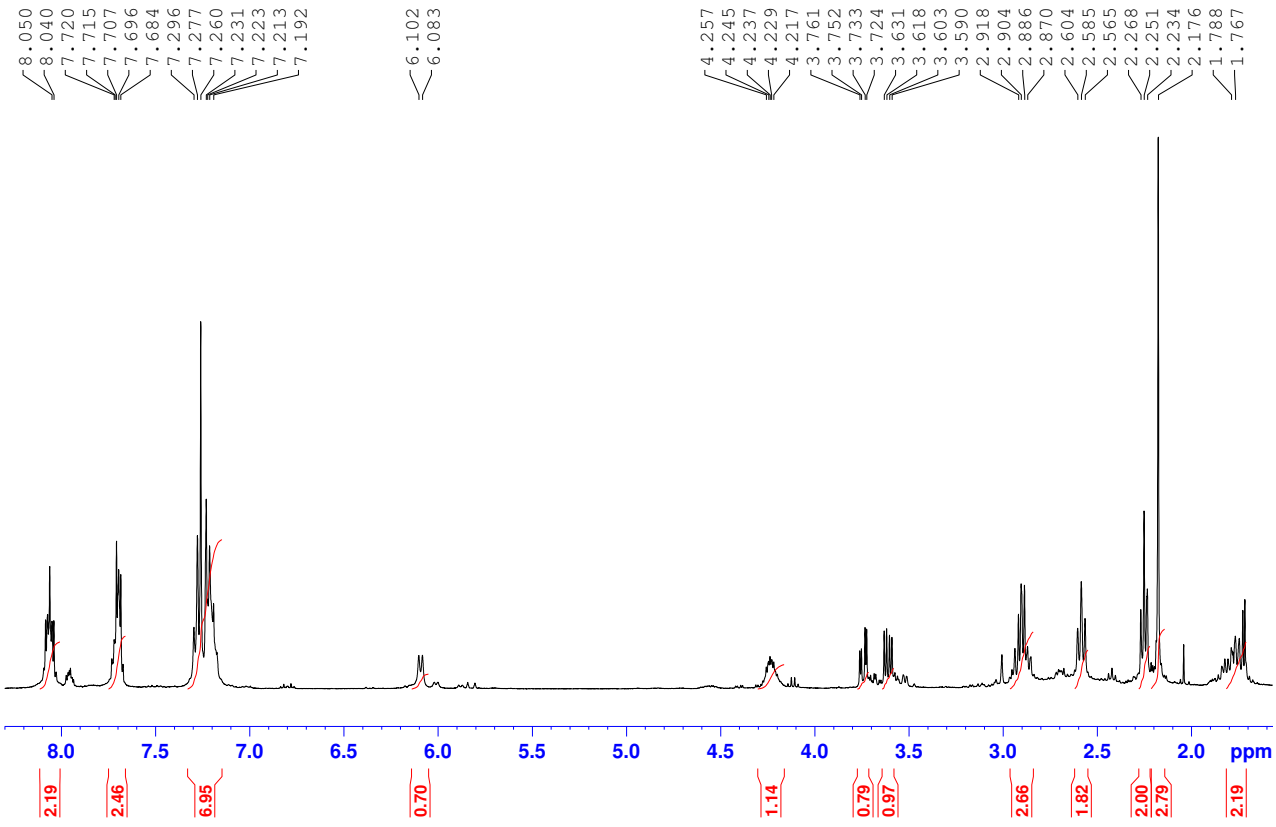
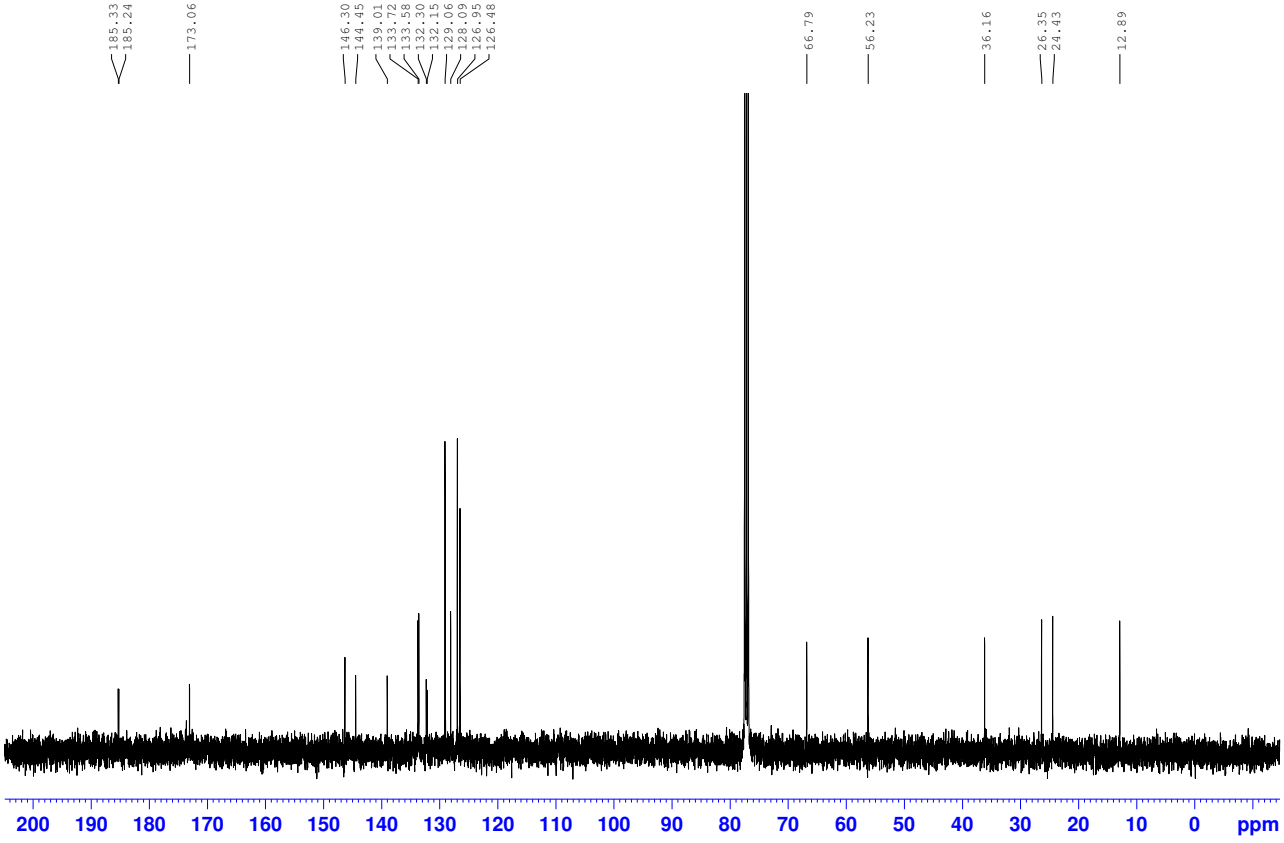
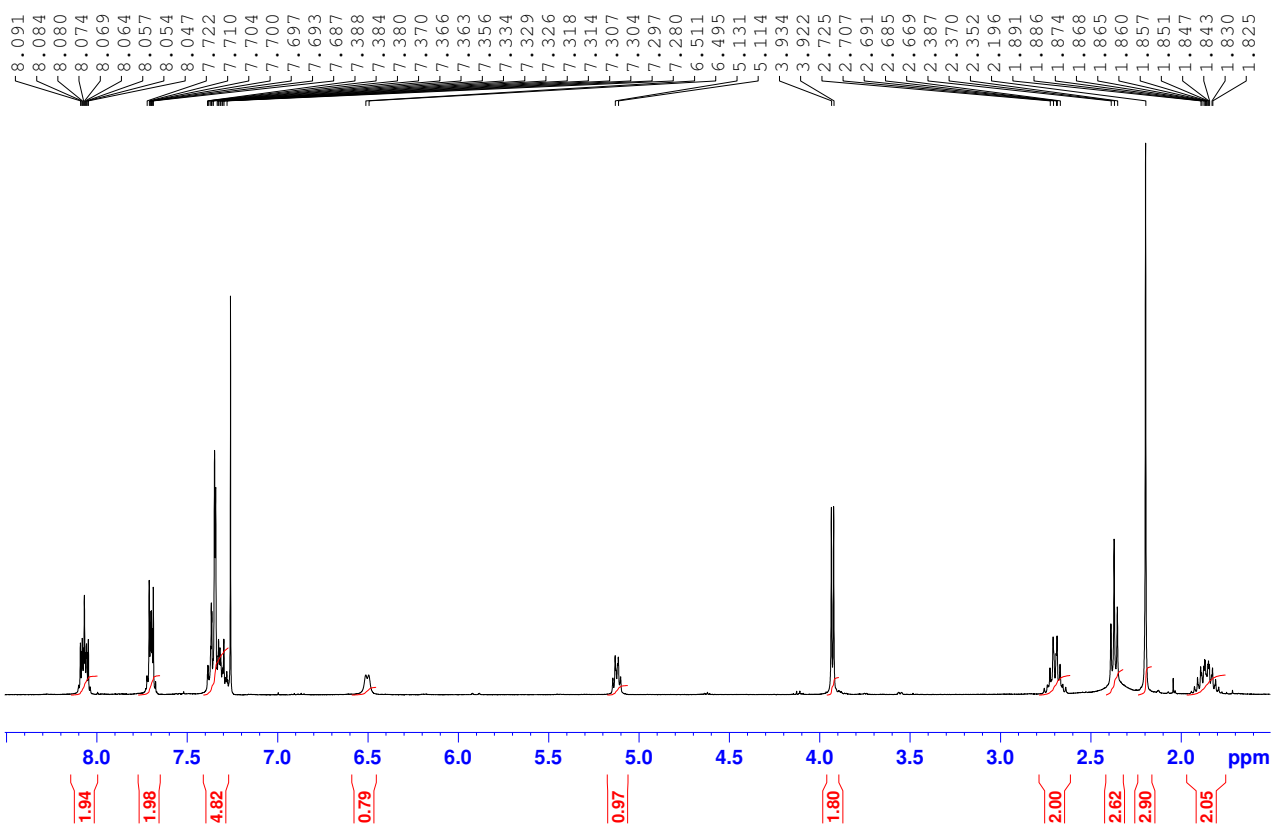
52

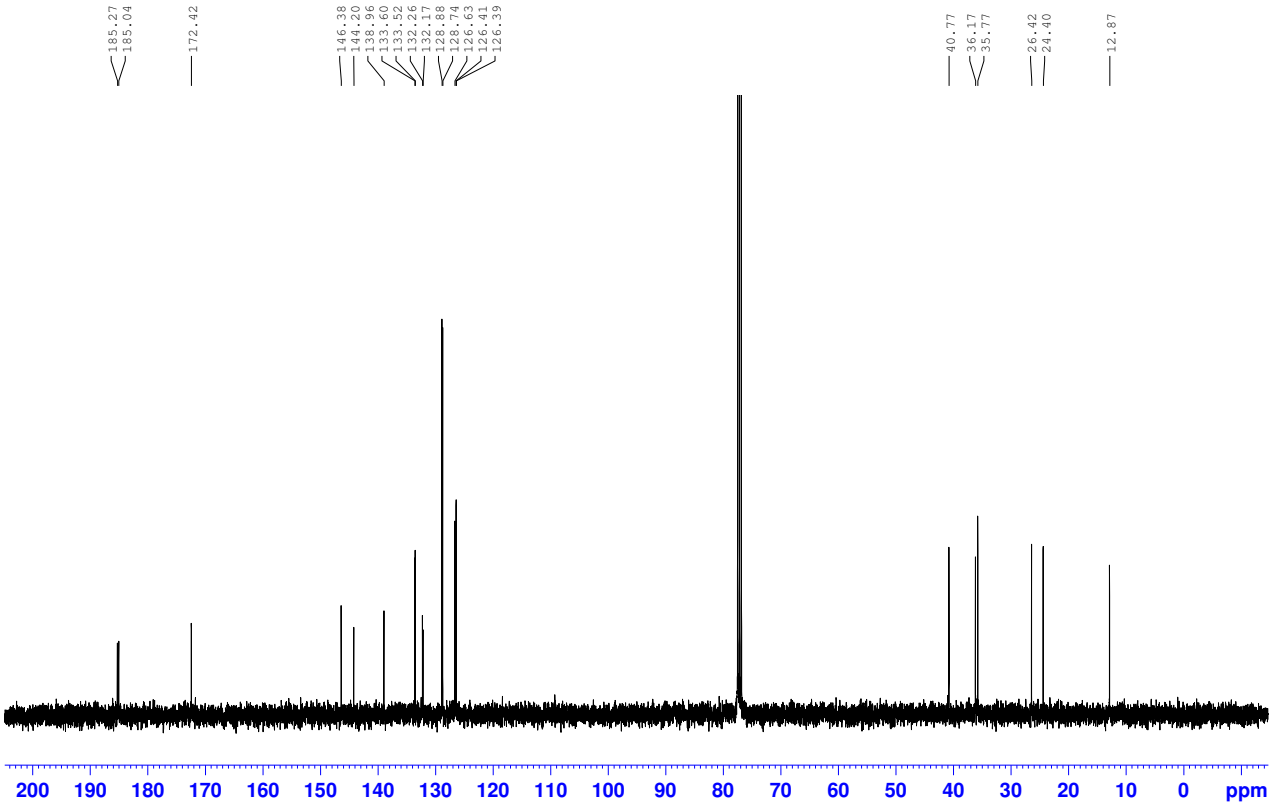

8.050
8.040
7.720
7.715
7.707
7.696
7.684
7.296
7.277
7.260
7.231
7.223
7.213
7.192
6.102
6.083
4.257
4.245
4.237
4.229
4.217
3.761
3.752
3.733
3.724
3.631
3.618
3.603
3.590
2.918
2.904
2.886
2.870
2.604
2.585
2.565
2.268
2.251
2.234
2.176
1.788
1.767
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 ppm
2.19
2.46
6.95
0.70
1.14
0.79
0.97
2.66
1.82
2.00
2.79
2.19

Avance III - 13C with 1H Power-gated Decoupling

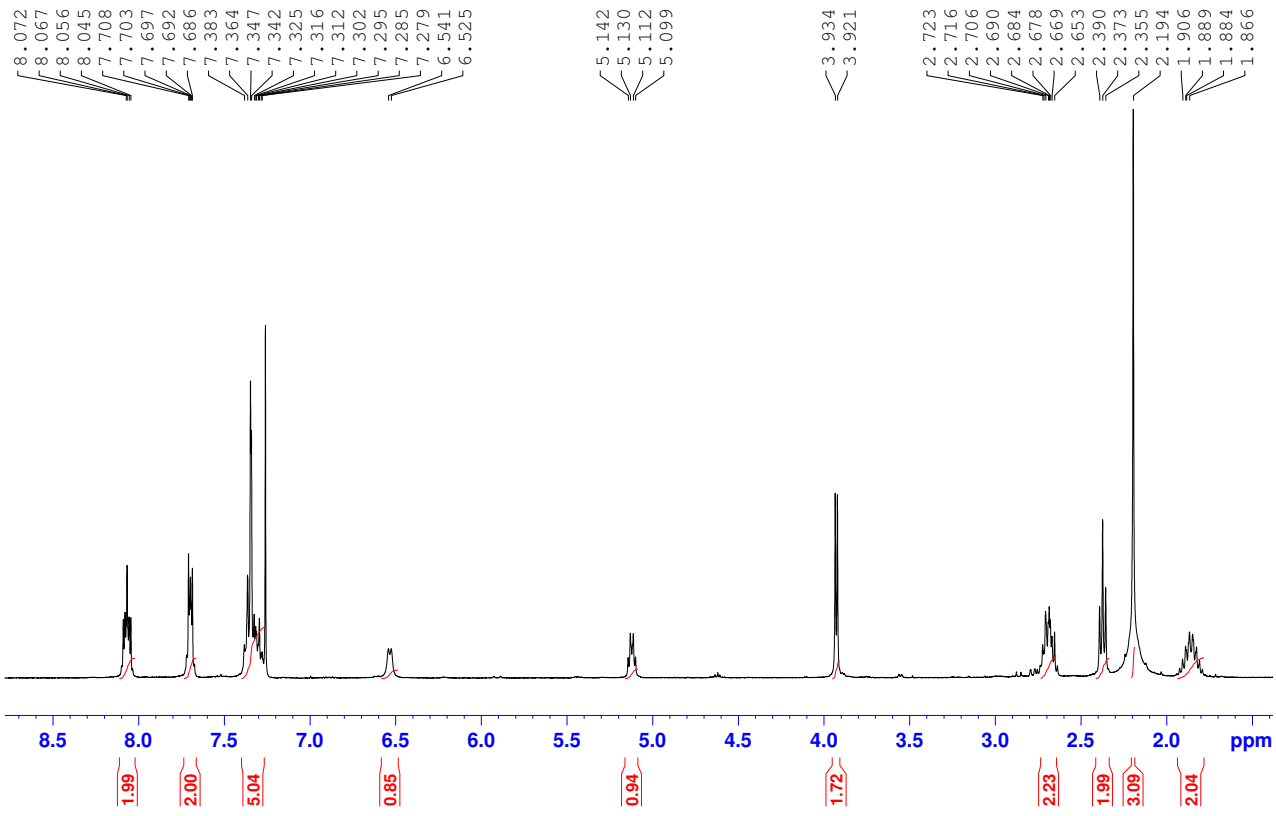


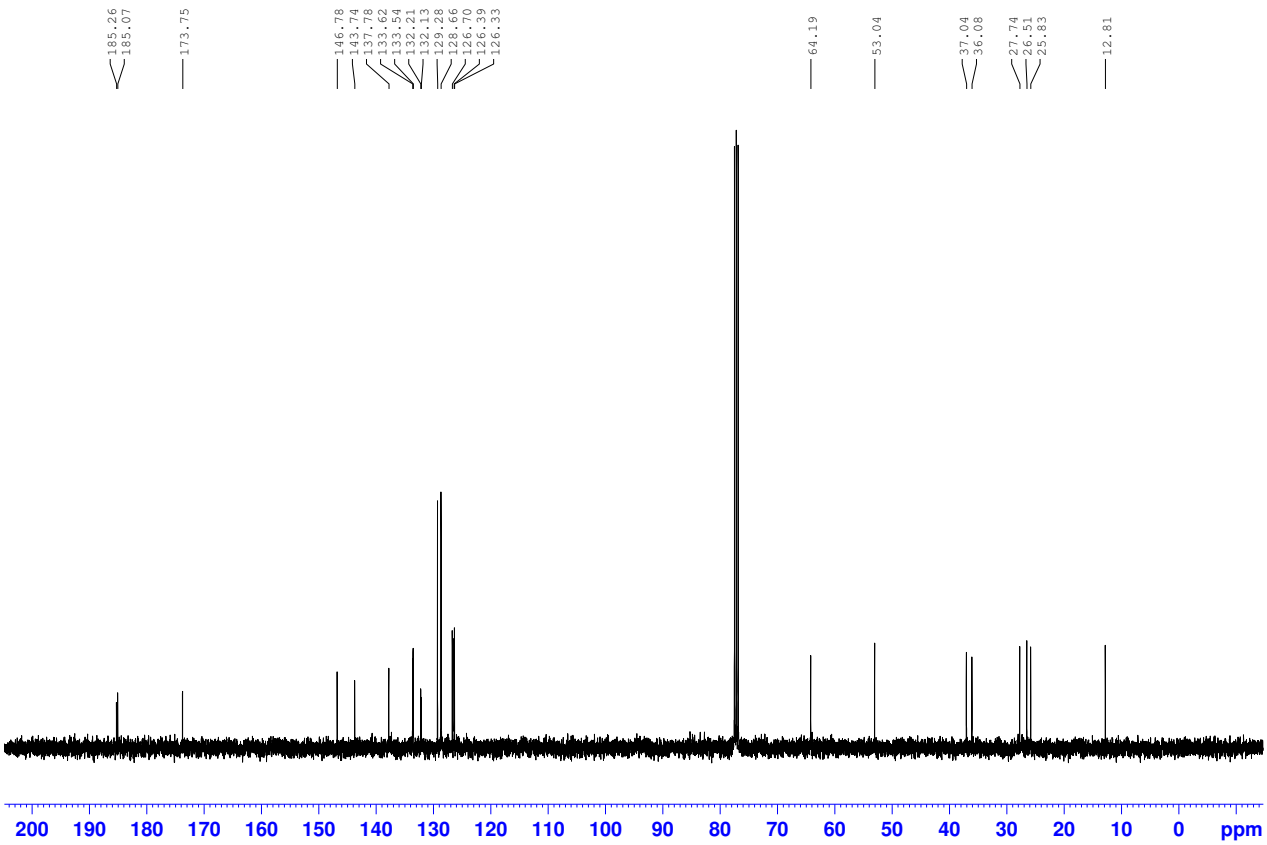


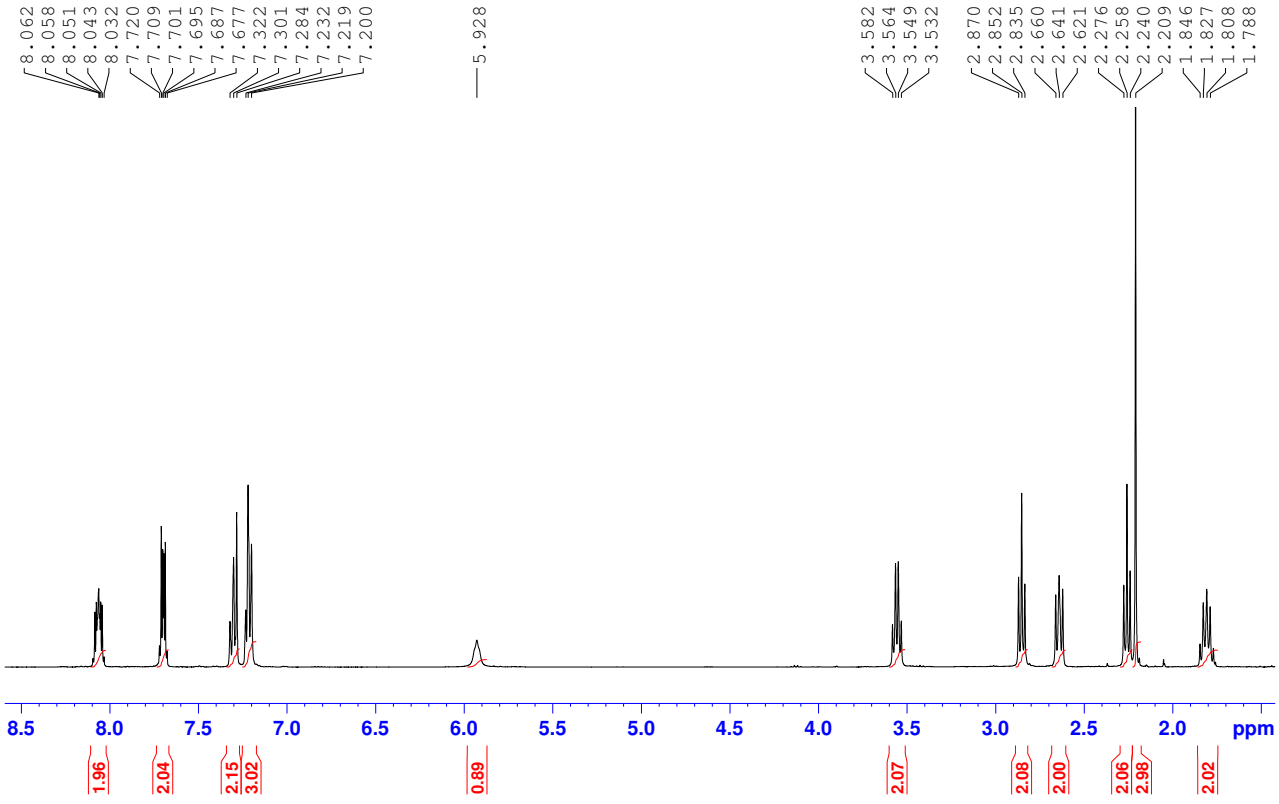
55

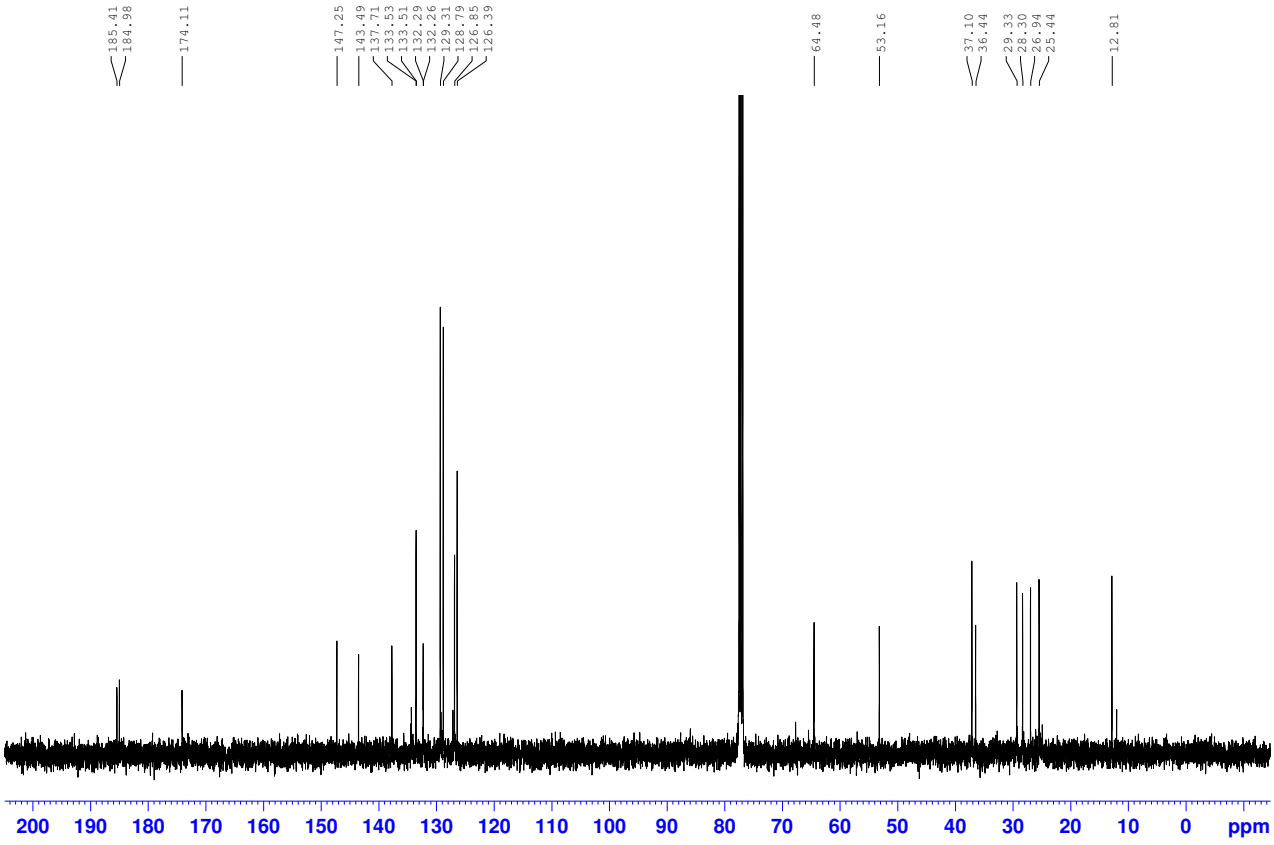

185.27
185.04
172.42
146.38
144.20
138.96
133.60
133.52
132.26
132.17
128.88
128.74
126.63
126.41
126.39
40.77
36.17
35.77
26.42
24.40
12.87
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

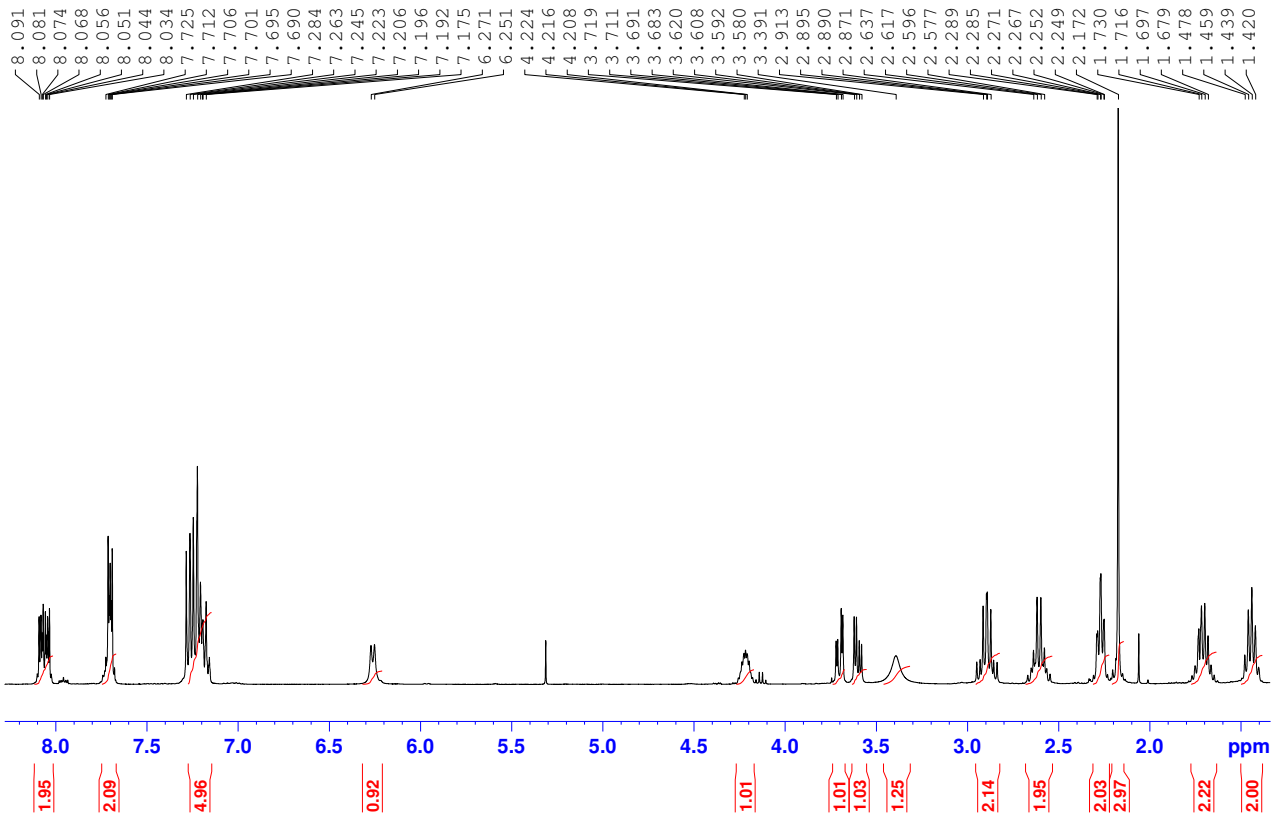
54


8.072
8.067
8.056
8.045
7.708
7.703
7.697
7.692
7.686
7.383
7.364
7.347
7.342
7.325
7.316
7.312
7.302
7.295
7.285
7.279
6.541
6.525
5.142
5.130
5.112
5.099
3.934
3.921
2.723
2.716
2.706
2.690
2.684
2.678
2.669
2.653
2.390
2.373
2.355
2.194
1.906
1.889
1.884
1.866
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 ppm
1.99
2.00
5.04
0.85
0.94
1.72
2.23
1.99
3.09
2.04

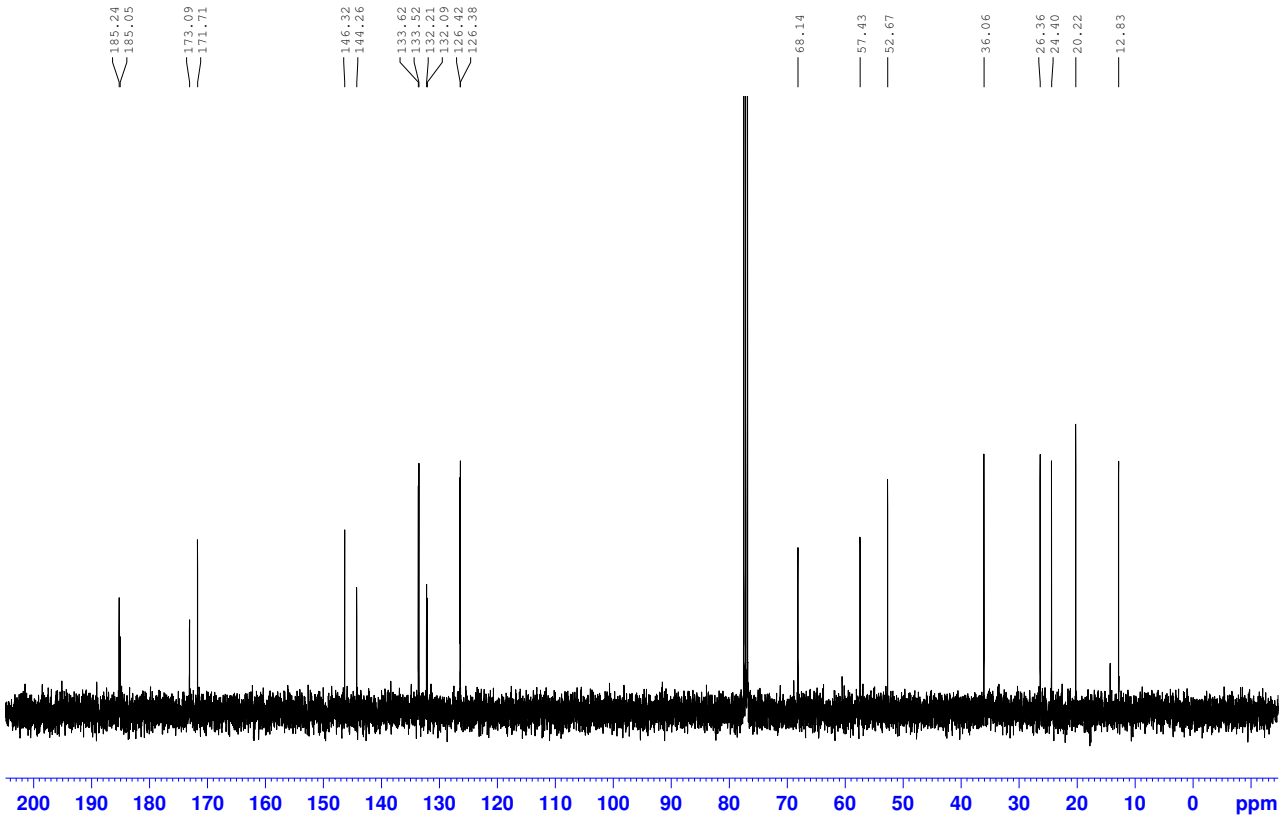

185.26
185.07
173.75
146.78
143.74
137.78
133.62
133.54
132.21
132.13
129.28
128.66
126.70
126.39
126.33
64.19
53.04
37.04
36.08
27.74
26.51
25.83
12.81
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.062
8.058
8.051
8.043
8.032
7.720
7.709
7.701
7.695
7.687
7.677
7.322
7.301
7.284
7.232
7.219
7.200
5.928
3.582
3.564
3.549
3.532
2.870
2.852
2.835
2.660
2.641
2.621
2.276
2.258
2.240
2.209
1.846
1.827
1.808
1.788
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 ppm
1.96
2.04
2.15
3.02
0.89
2.07
2.08
2.00
2.06
2.98
2.02

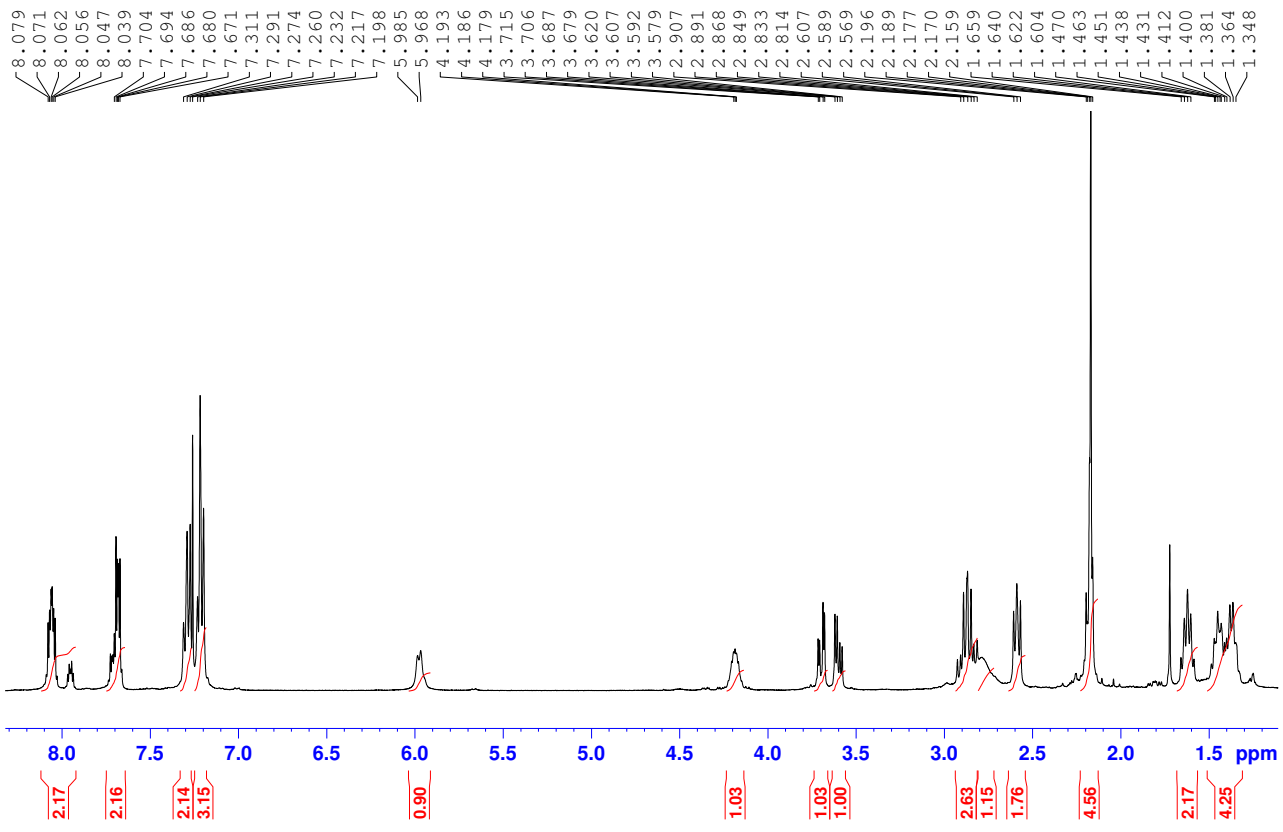

185.41
184.98
174.11
147.25
143.49
137.71
133.53
133.51
132.29
132.26
129.31
128.79
126.85
126.39
64.48
53.16
37.10
36.44
29.33
28.30
26.94
25.44
12.81
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


8.091
8.081
8.074
8.068
8.056
8.051
8.044
8.034
7.725
7.712
7.706
7.701
7.695
7.690
7.284
7.263
7.245
7.223
7.206
7.196
7.192
7.175
6.271
6.251
4.224
4.216
4.208
3.719
3.711
3.691
3.683
3.620
3.608
3.592
3.580
3.391
2.913
2.895
2.890
2.871
2.637
2.617
2.596
2.577
2.289
2.285
2.271
2.267
2.252
2.249
2.172
1.730
1.716
1.697
1.679
1.478
1.459
1.439
1.420
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 ppm
1.95
2.09
4.96
0.92
1.01
1.01
1.03
1.25
2.14
1.95
2.03
2.97
2.22
2.00

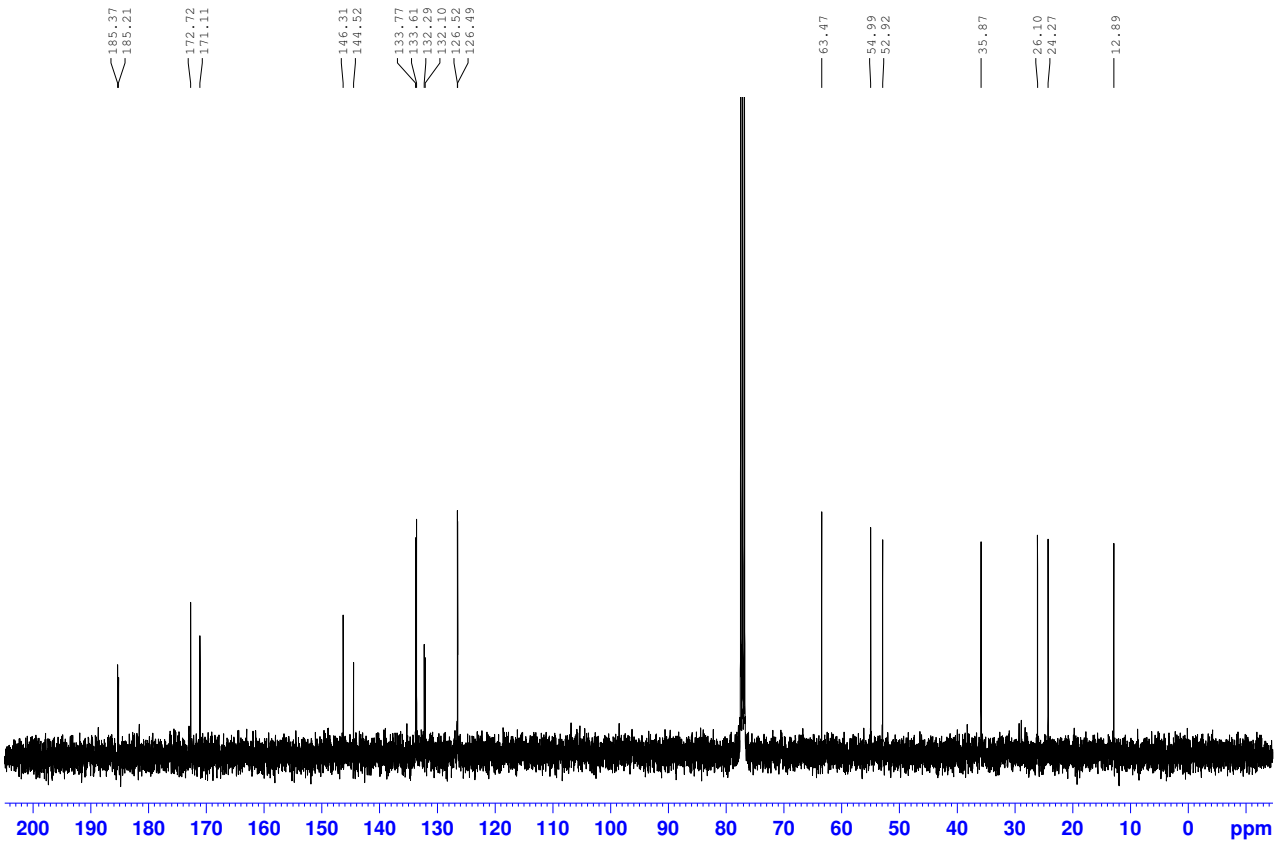
58


185.24
185.05
173.09
171.71
146.32
144.26
133.62
133.52
132.21
132.09
126.42
126.38
68.14
57.43
52.67
36.06
26.36
24.40
20.22
12.83
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

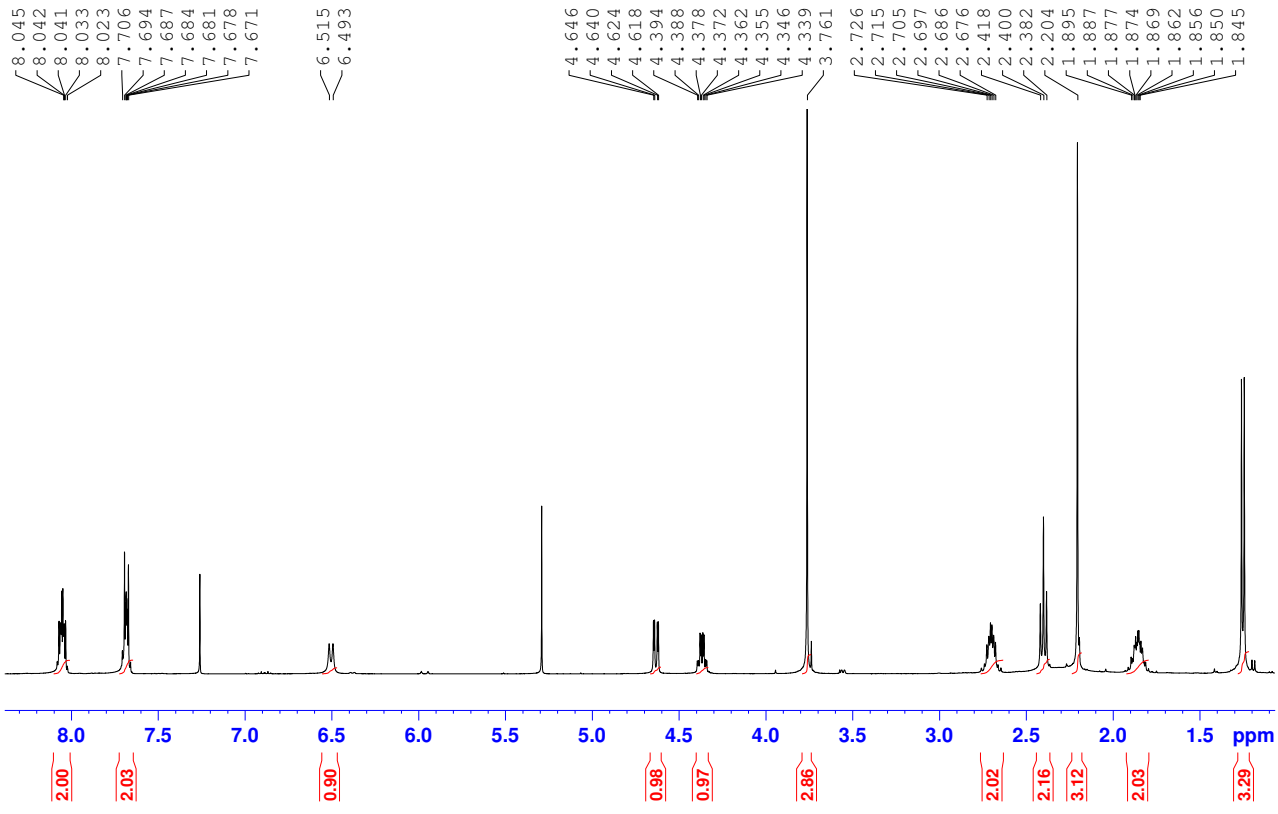
57


8.079
8.071
8.062
8.056
8.047
8.039
7.704
7.694
7.686
7.680
7.671
7.311
7.291
7.274
7.260
7.232
7.217
7.198
5.985
5.968
4.193
4.186
4.179
3.715
3.706
3.687
3.679
3.620
3.607
3.592
3.579
2.907
2.891
2.868
2.849
2.833
2.814
2.607
2.589
2.569
2.196
2.189
2.177
2.170
2.159
1.659
1.640
1.622
1.604
1.470
1.463
1.451
1.438
1.431
1.412
1.400
1.381
1.364
1.348
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm
2.17
2.16
2.14
3.15
0.90
1.03
1.03
1.00
2.63
1.15
1.76
4.56
2.17
4.25

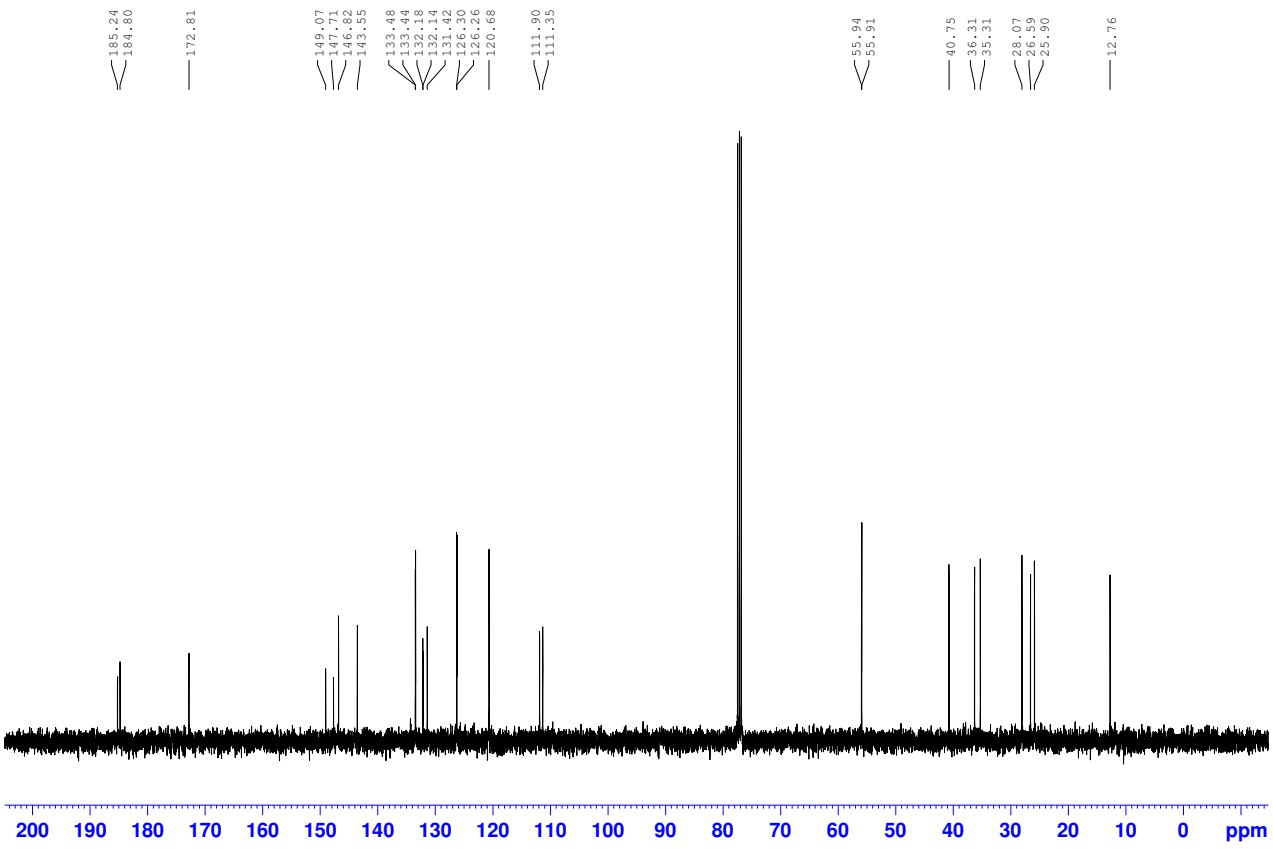
59

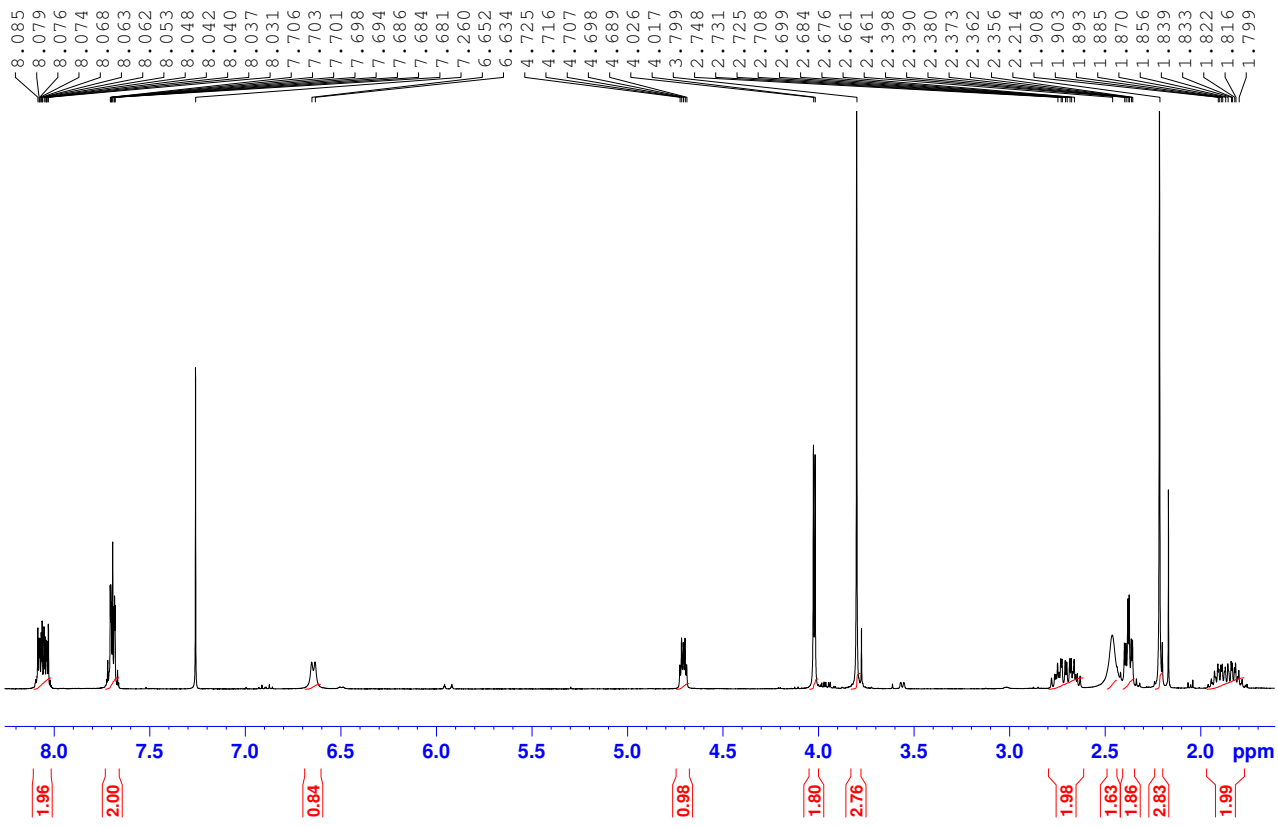

185.37
185.21
172.72
171.11
146.31
144.52
133.77
133.61
132.29
132.10
126.52
126.49
63.47
54.99
52.92
35.87
26.10
24.27
12.89
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

58

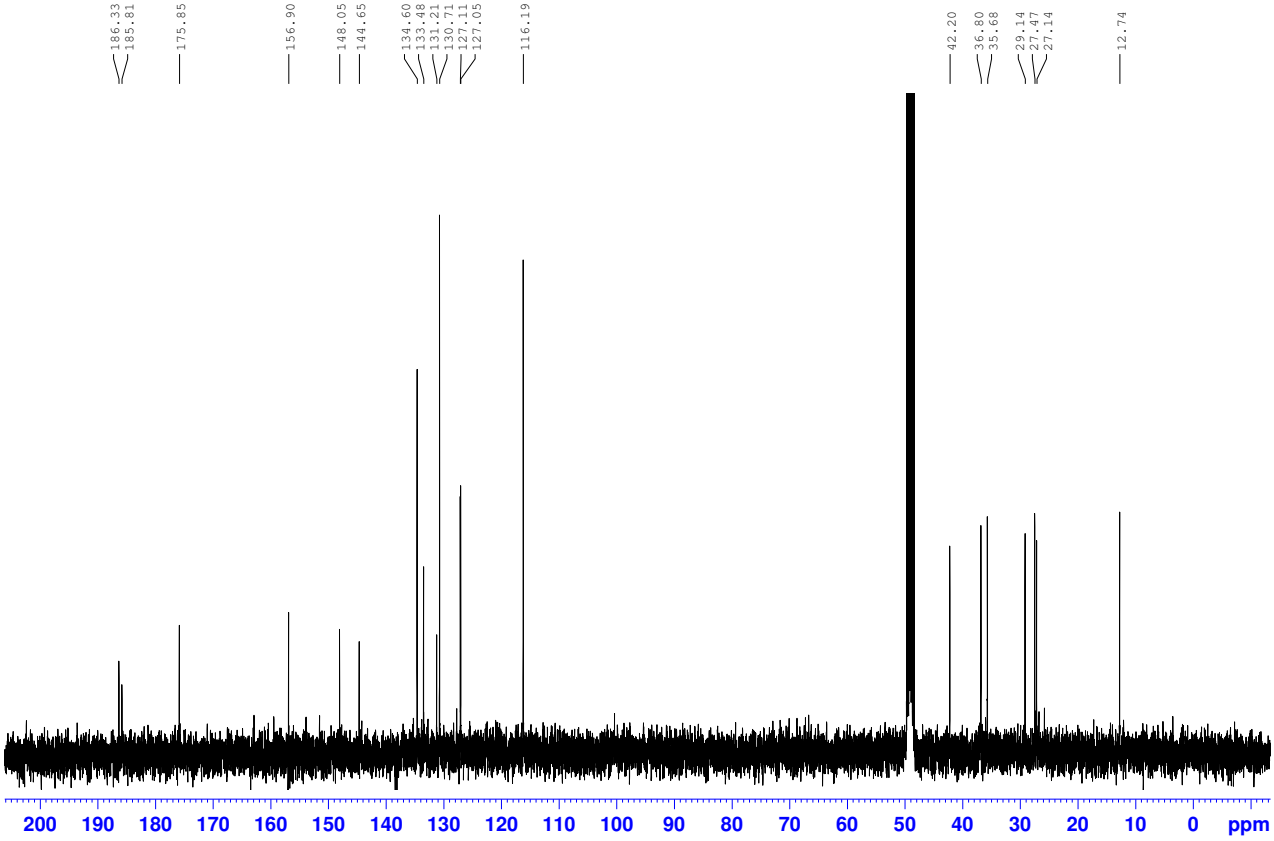

8.045
8.042
8.041
8.033
8.023
7.706
7.694
7.687
7.684
7.681
7.678
7.671
6.515
6.493
4.646
4.640
4.624
4.618
4.394
4.388
4.378
4.372
4.362
4.355
4.346
4.339
3.761
2.726
2.715
2.705
2.697
2.686
2.676
2.418
2.400
2.382
2.204
1.895
1.887
1.877
1.874
1.869
1.862
1.856
1.850
1.845
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm
2.00
2.03
0.90
0.98
0.97
2.86
2.02
2.16
3.12
2.03
3.29

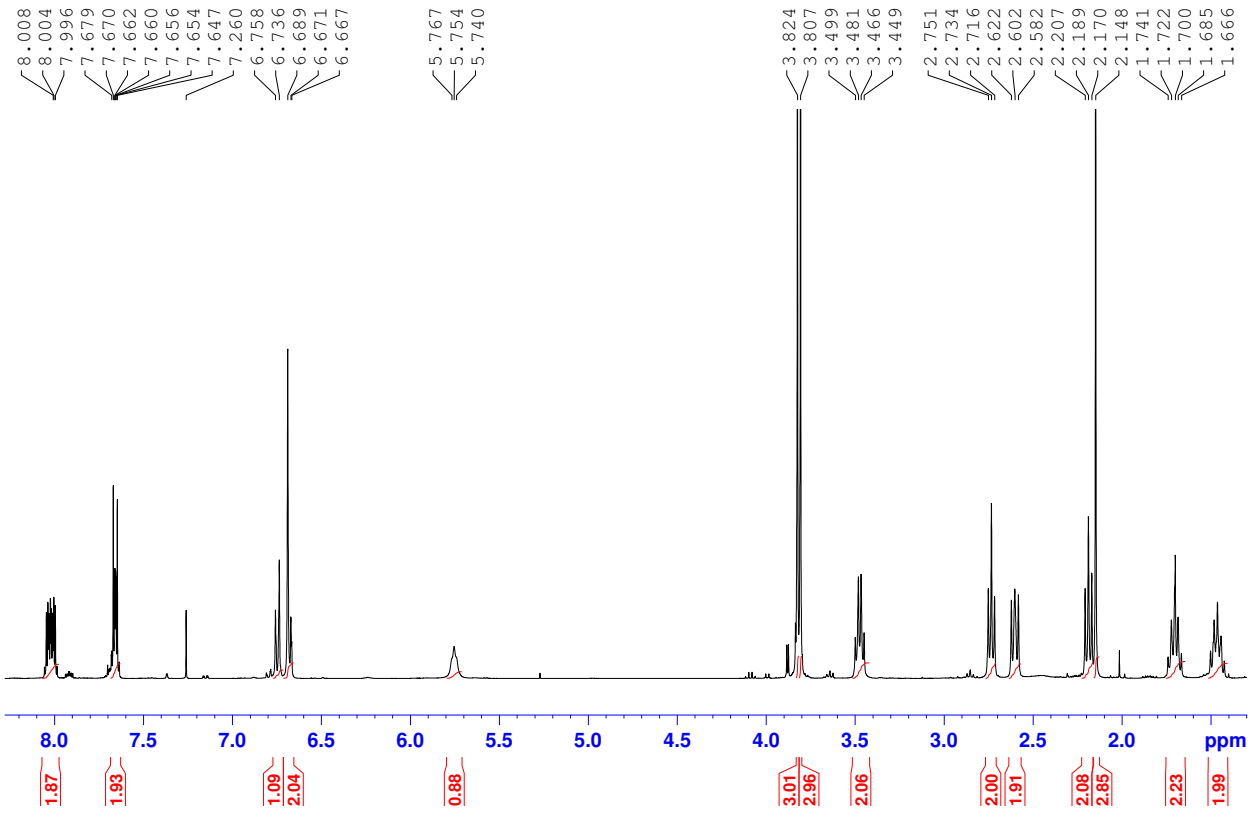
Avance III - 13C with 1H Power-gated Decoupling



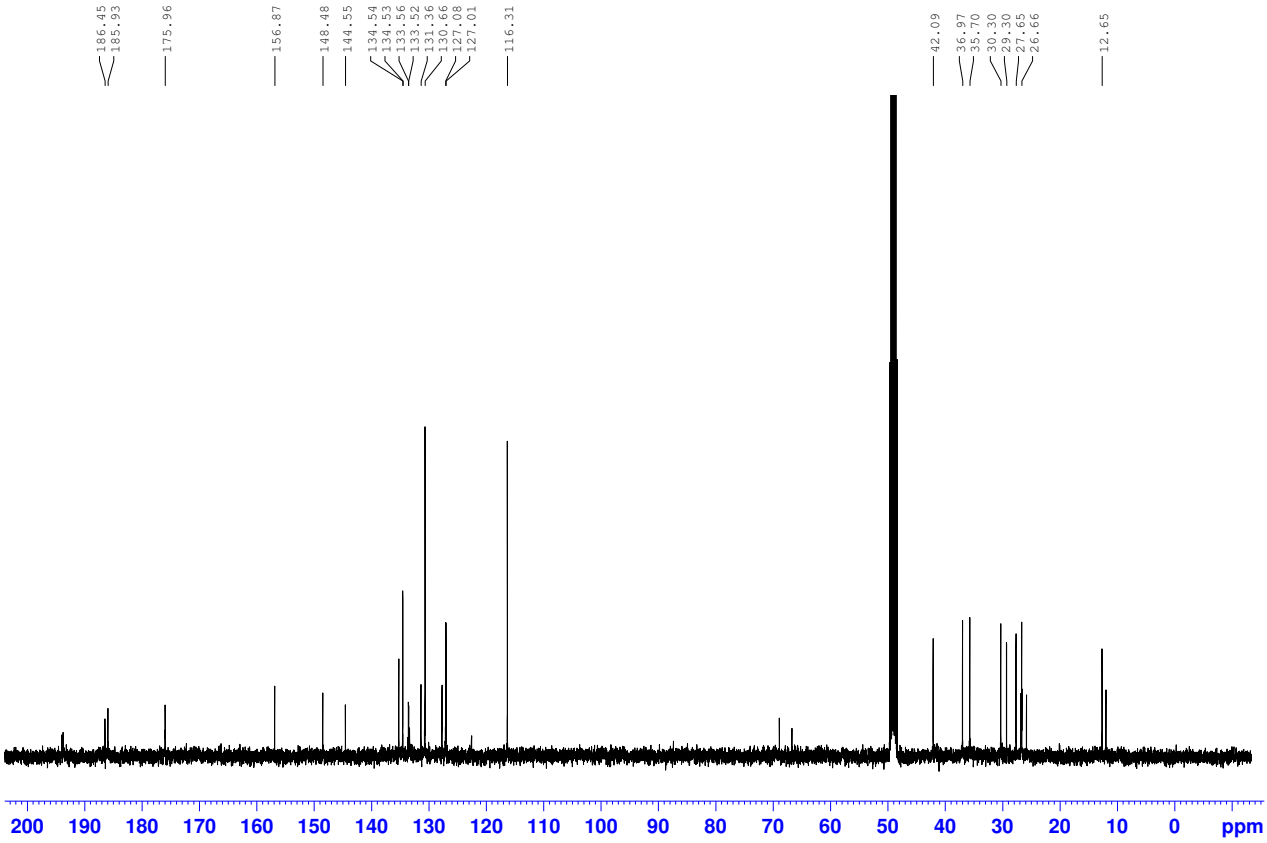


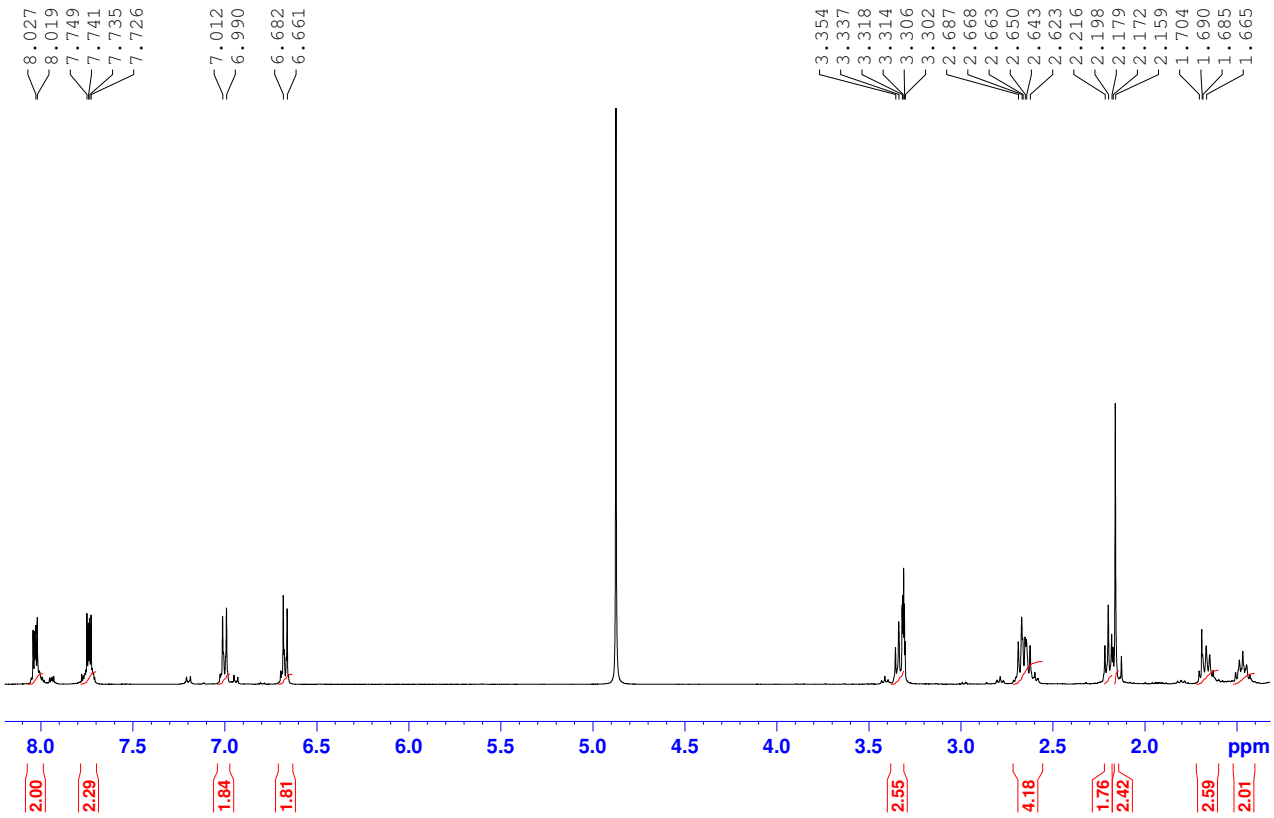
Avance III - 13C with 1H Power-gated Decoupling



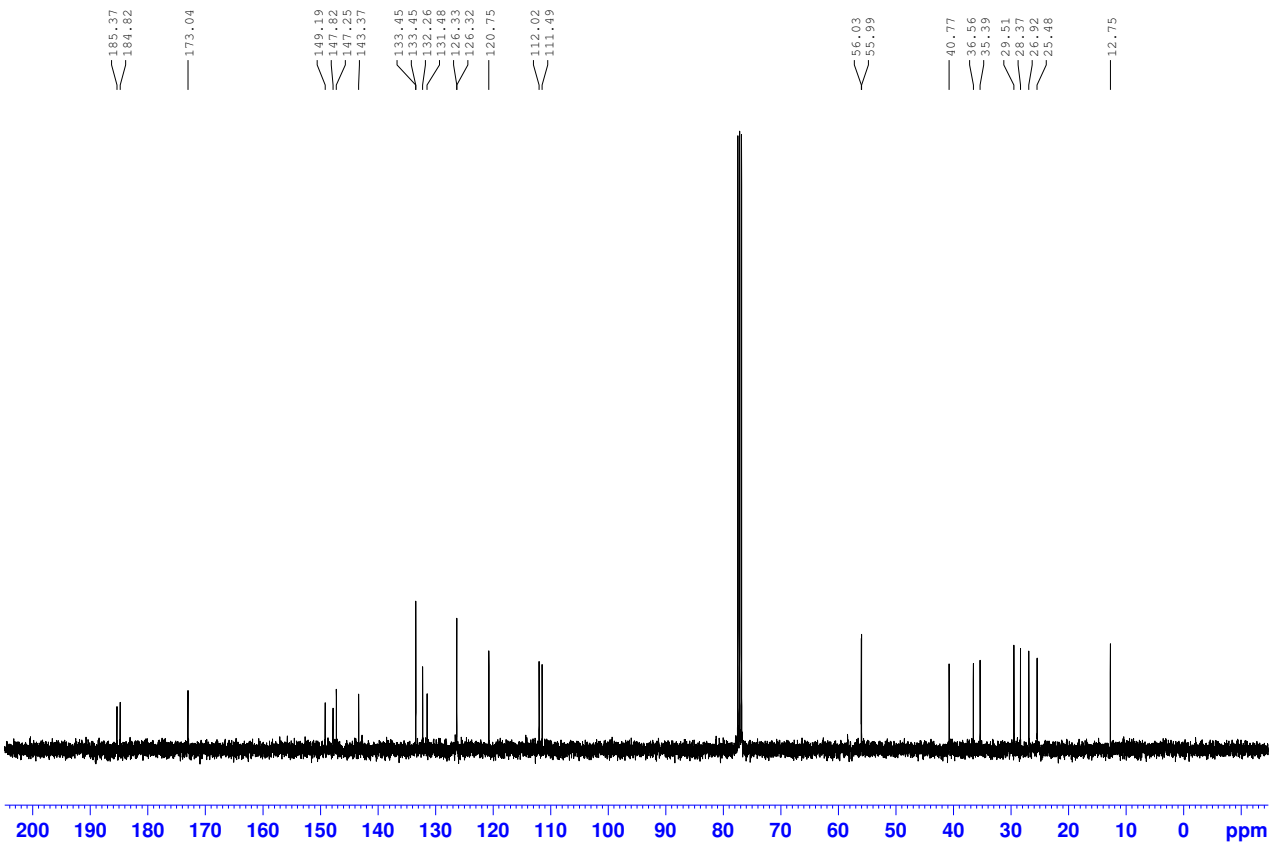


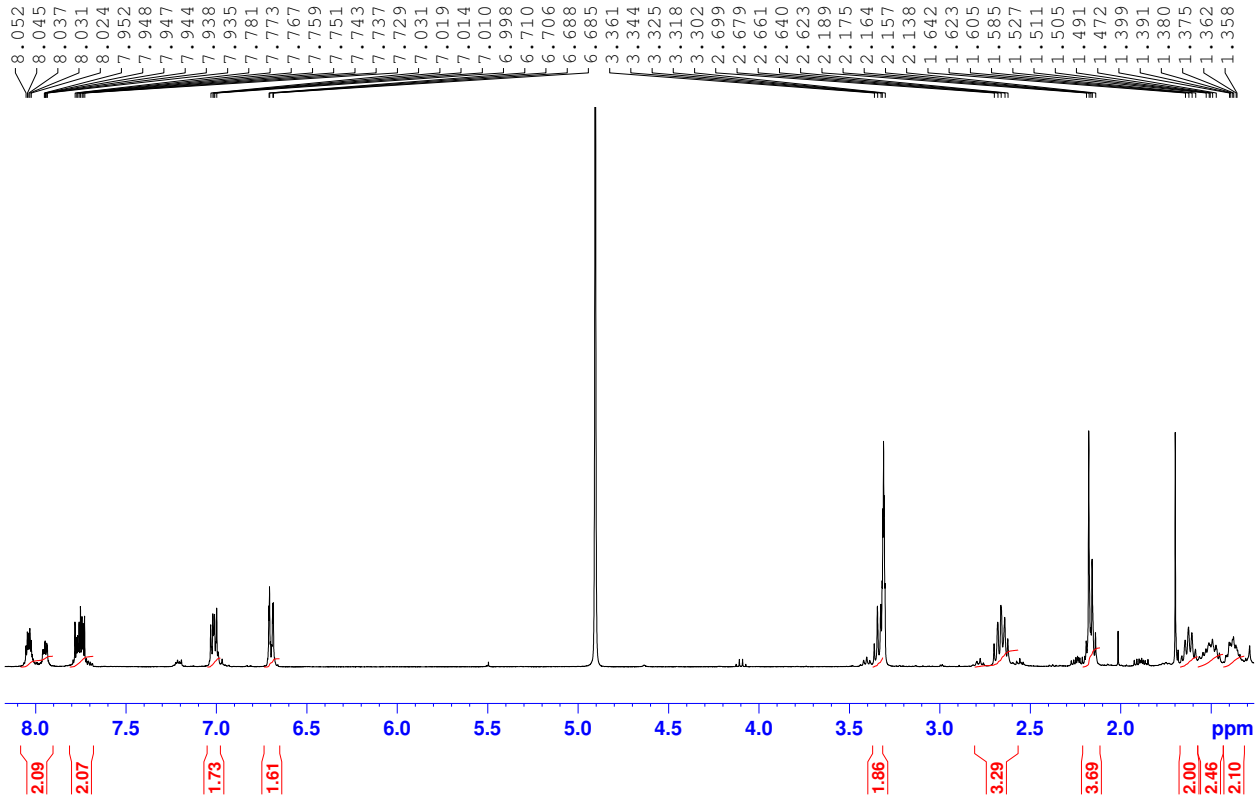
Avance III - 13C with 1H Power-gated Decoupling





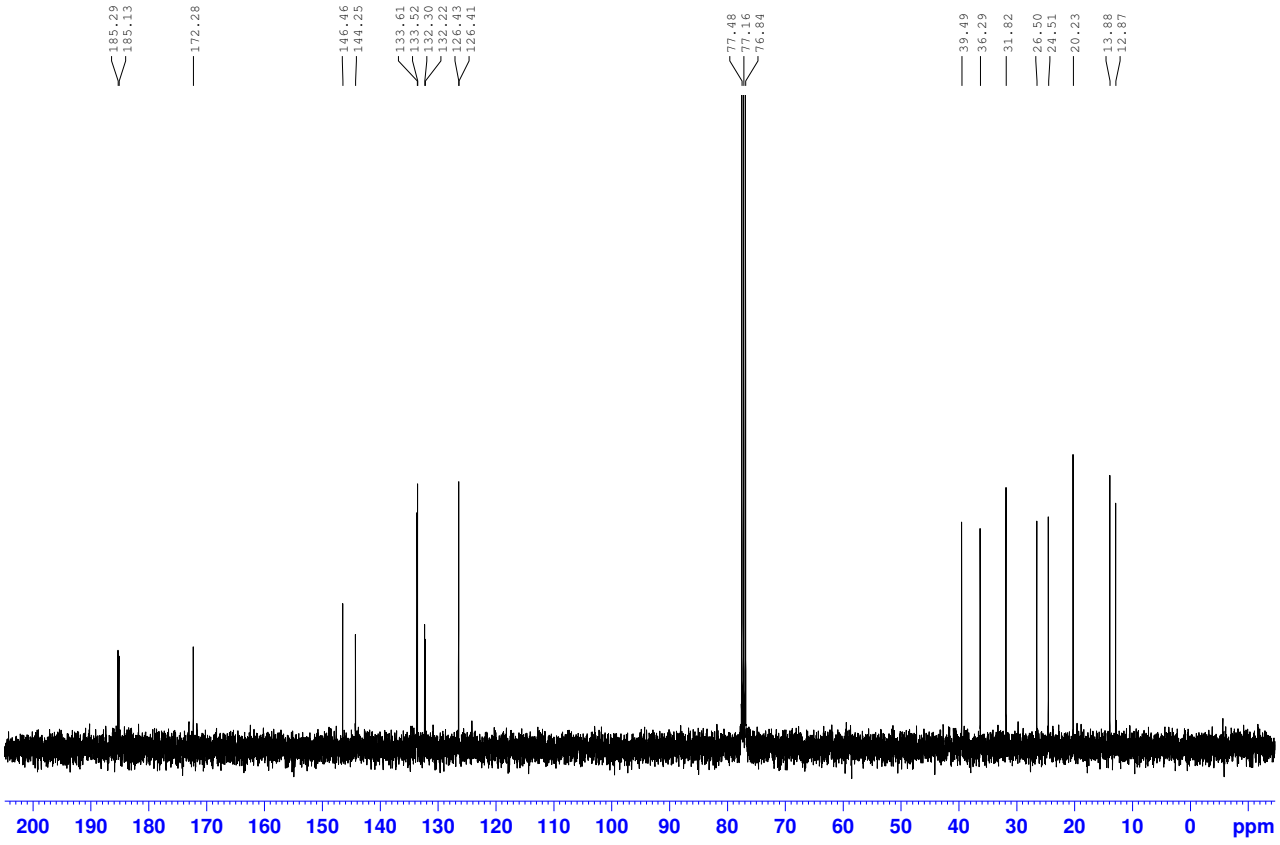
Avance III - 13C with 1H Power-gated Decoupling





64

Avance III - 13C with 1H Power-gated Decoupling



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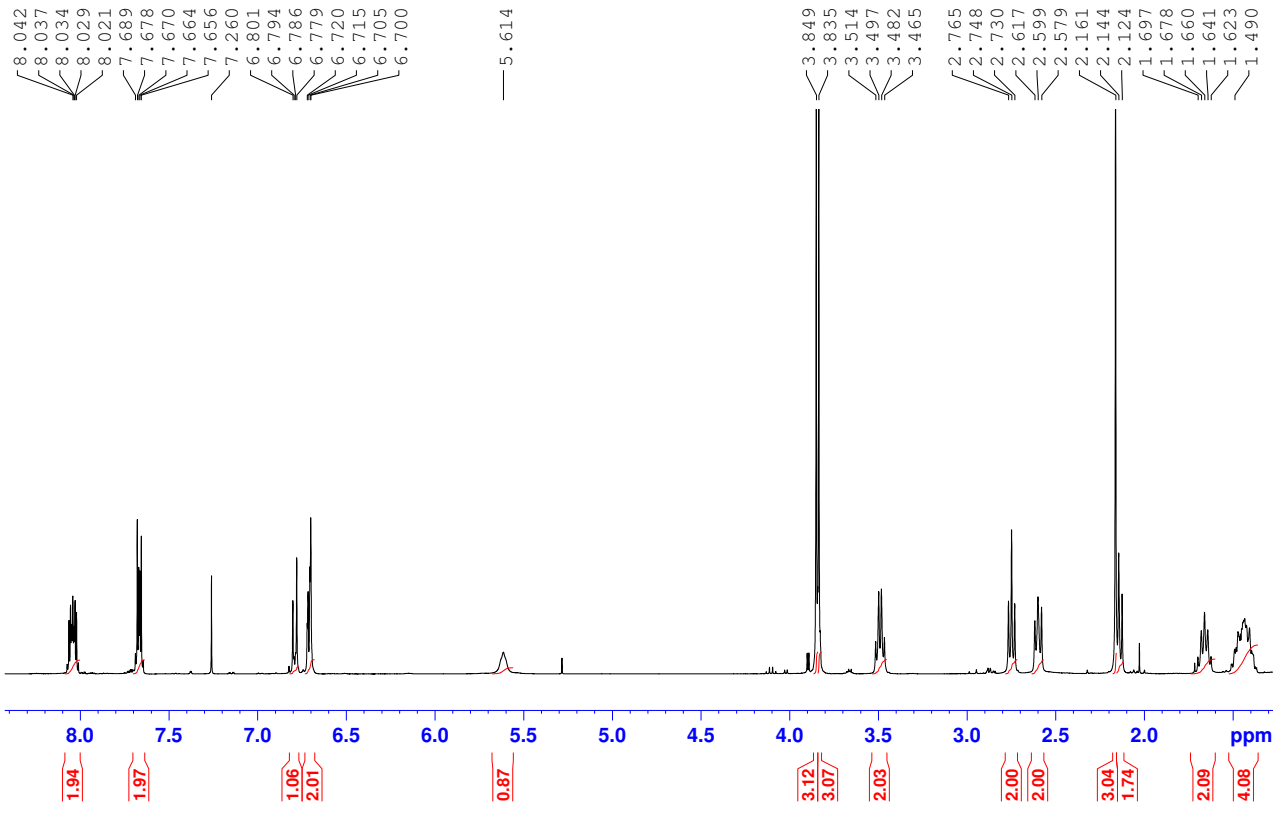
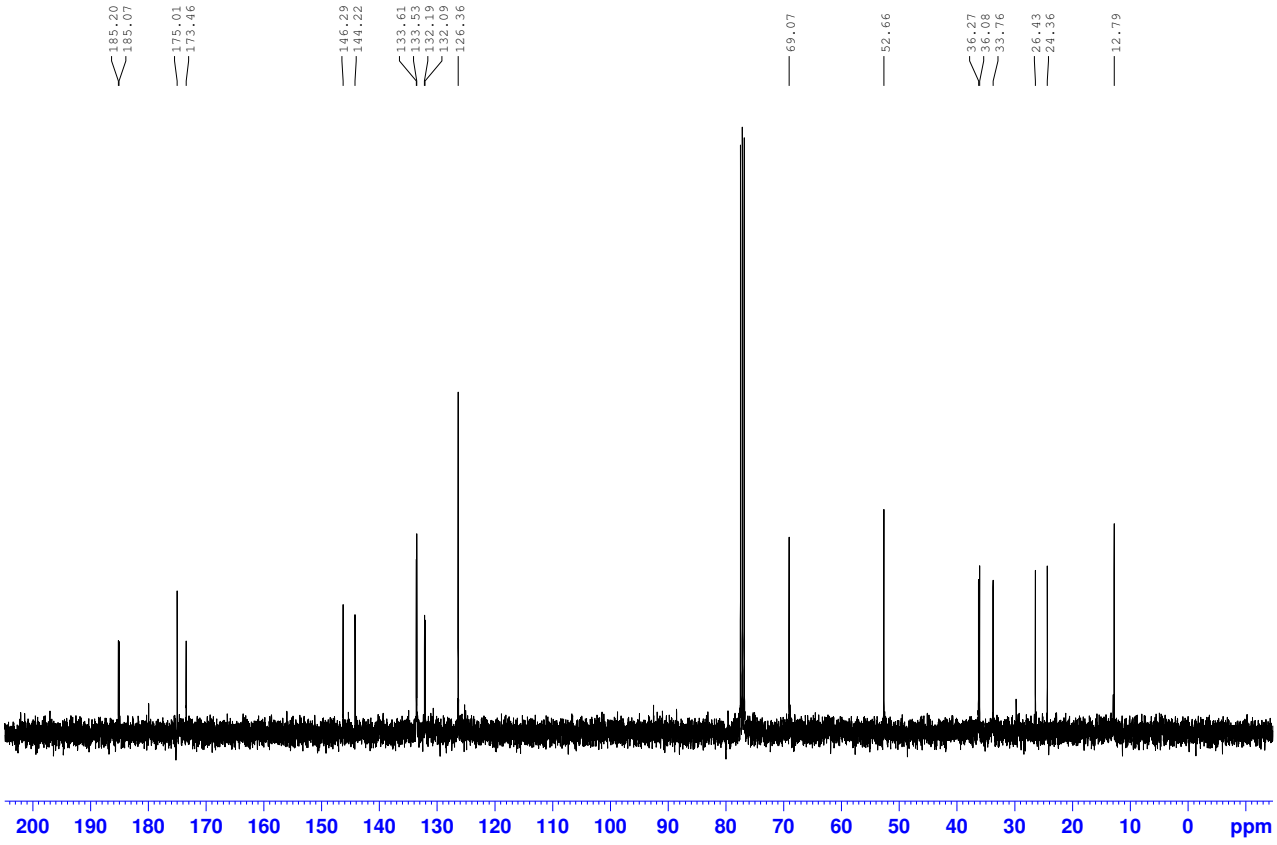


65

Avance III - 13C with 1H Power-gated Decoupling



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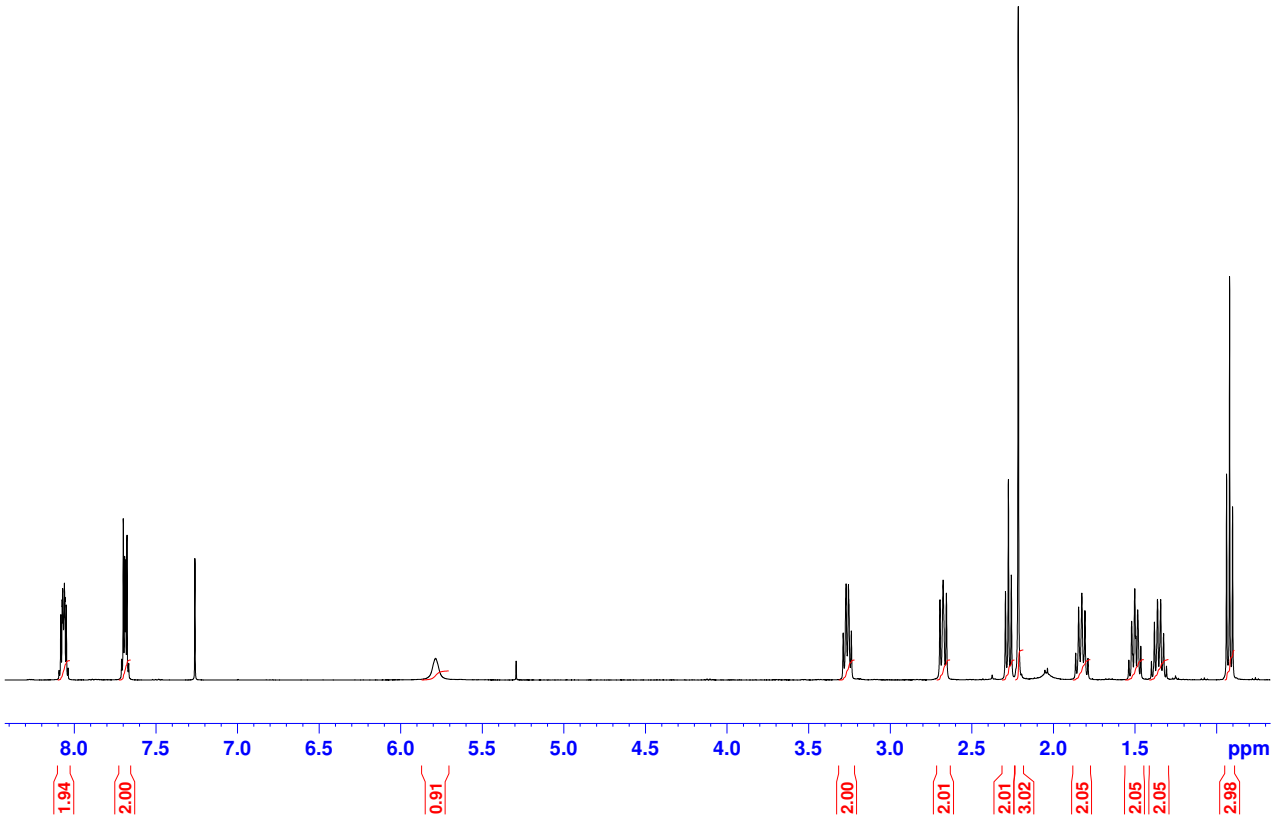
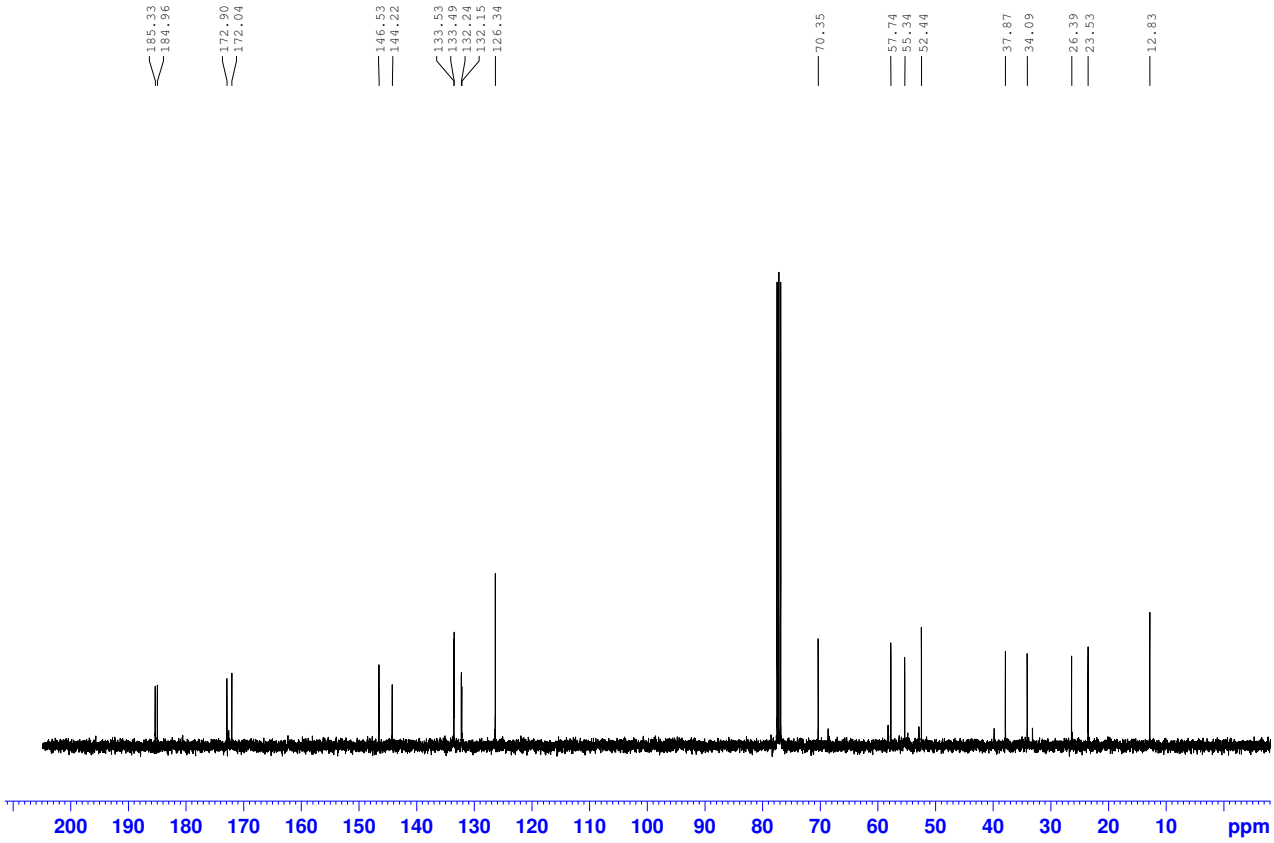
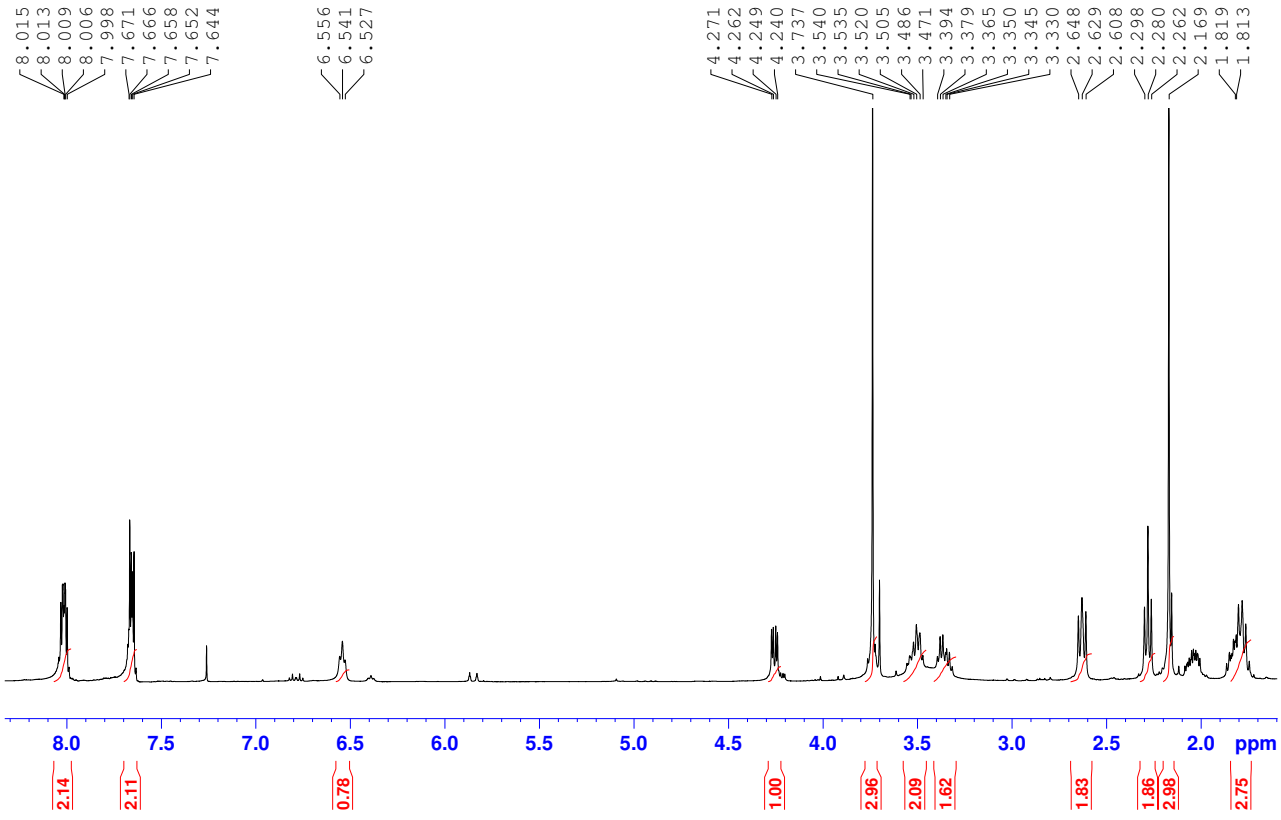
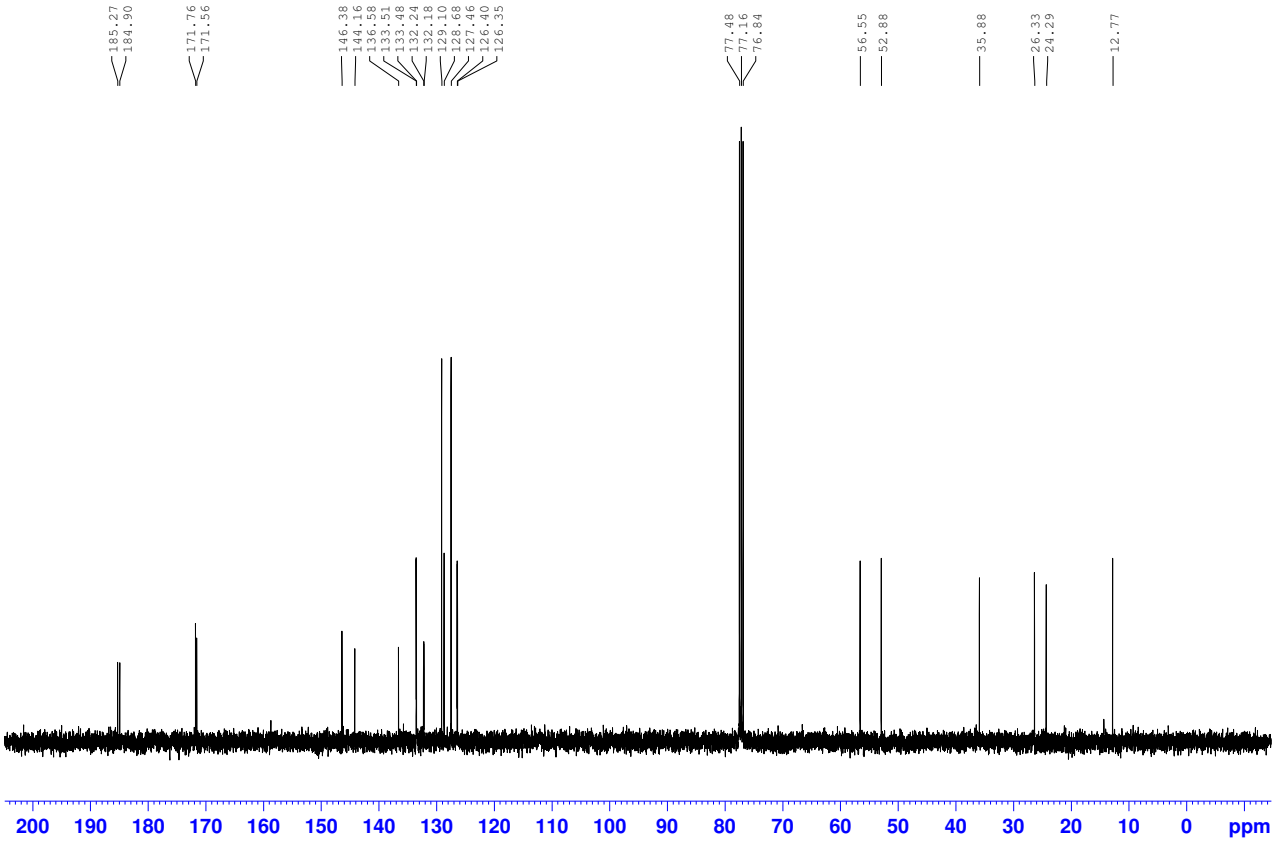


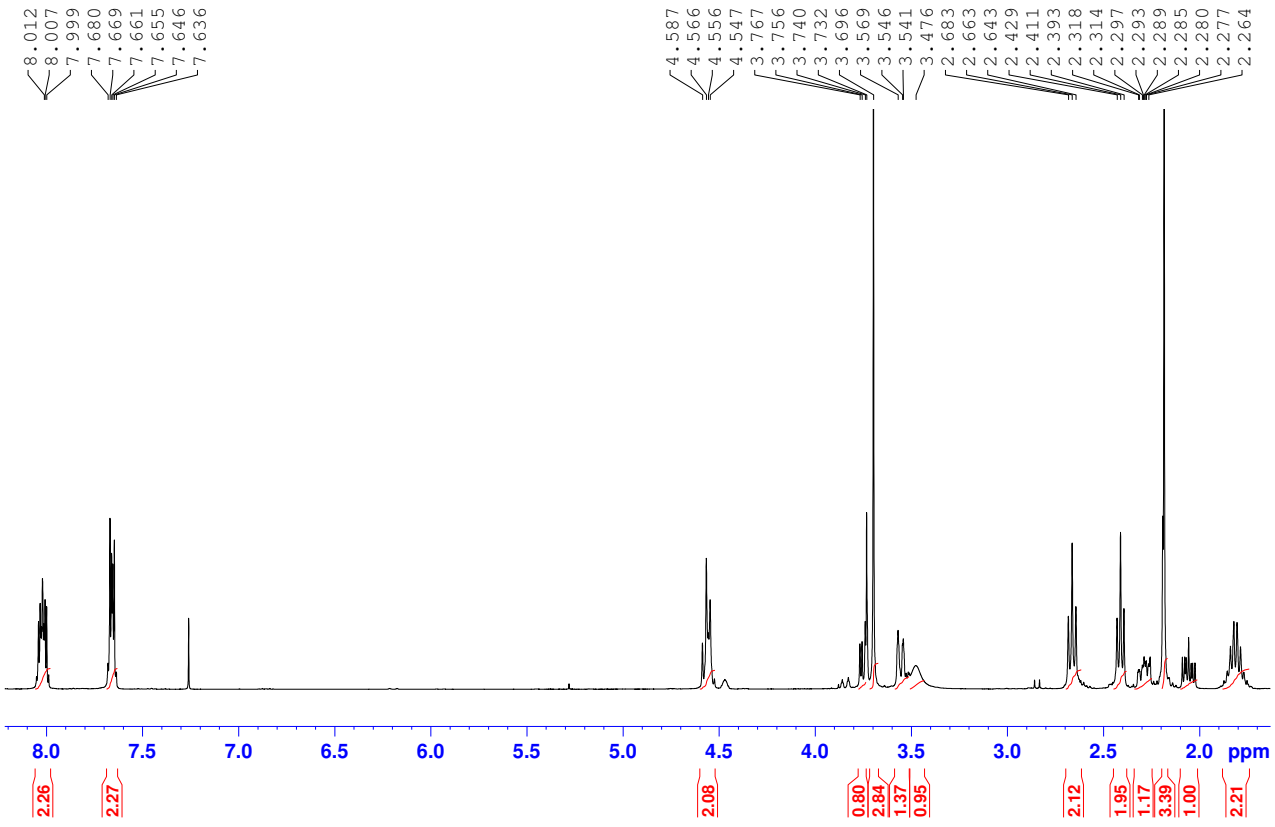
Avance III - 13C with 1H Power-gated Decoupling



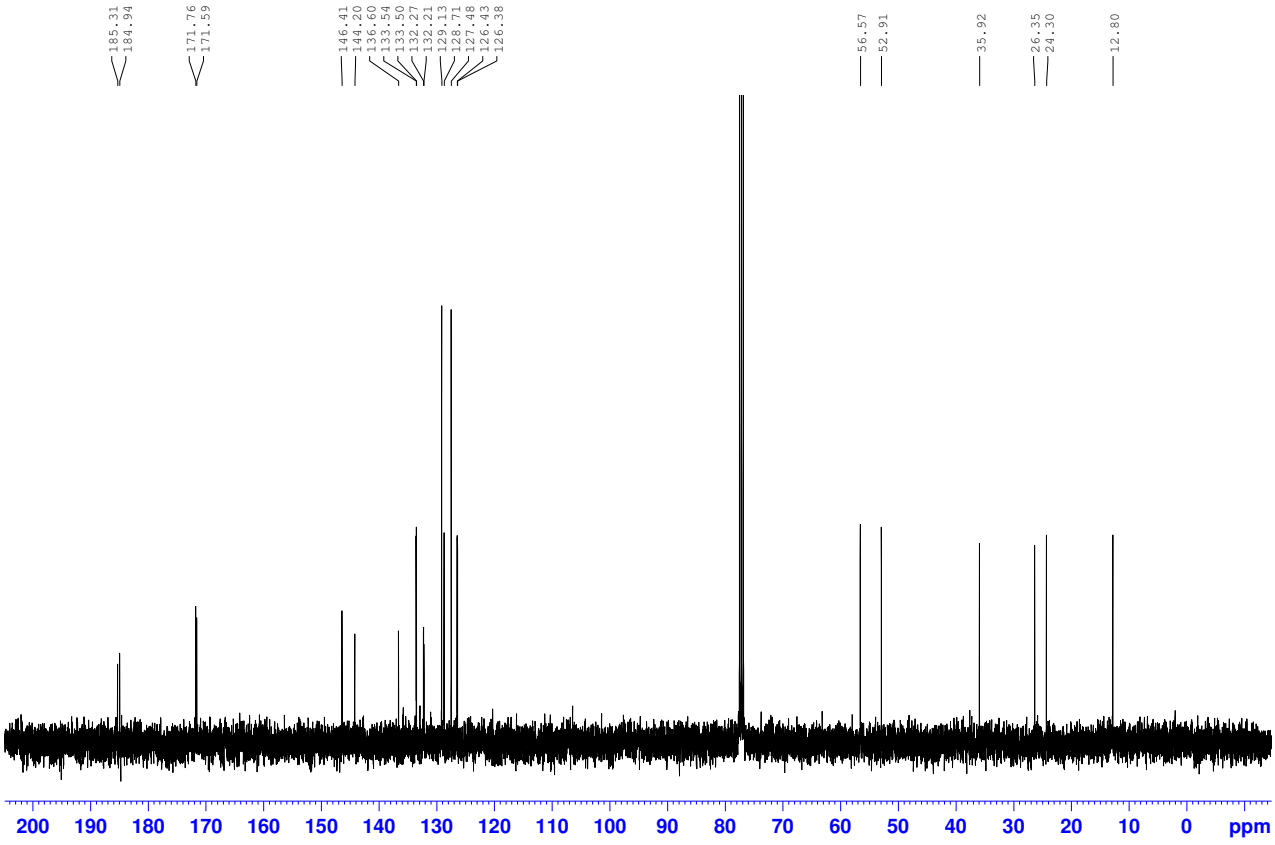


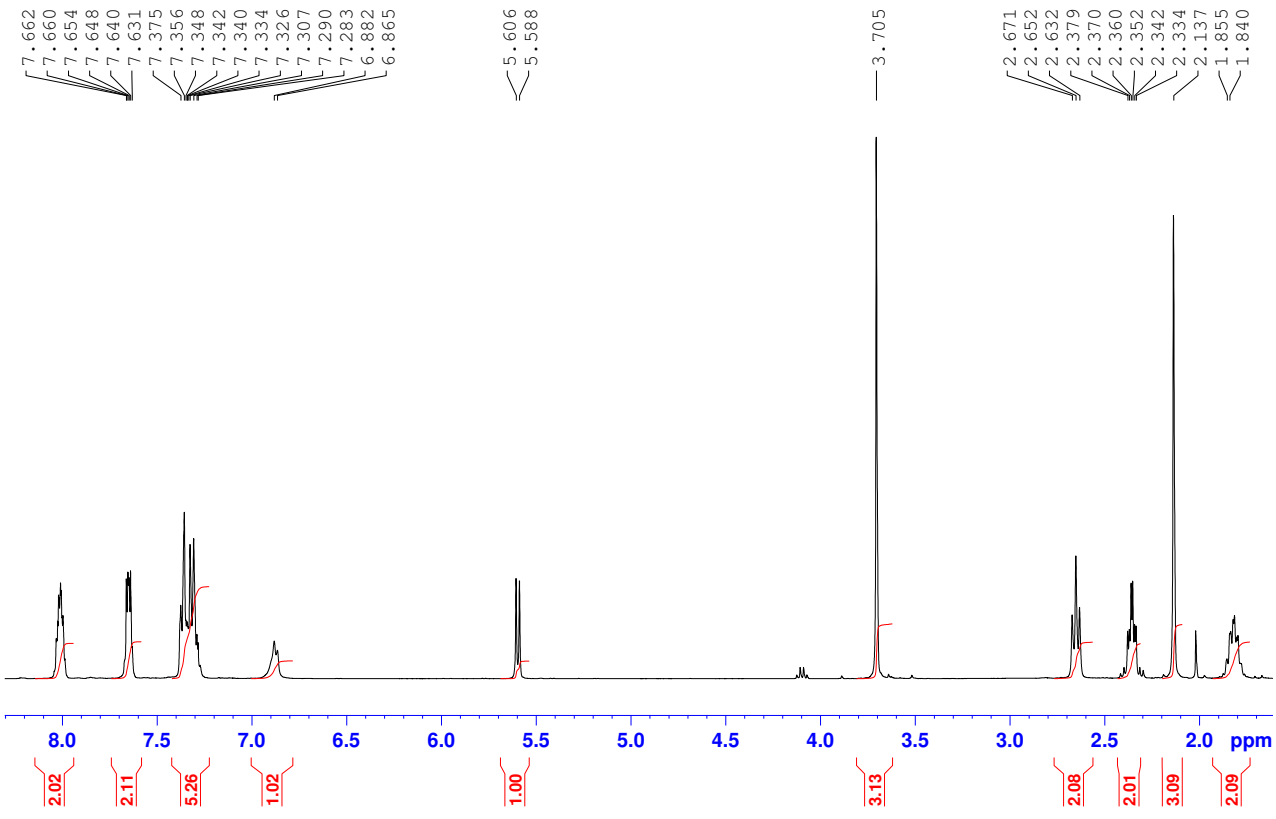
Avance III - 13C with 1H Power-gated Decoupling





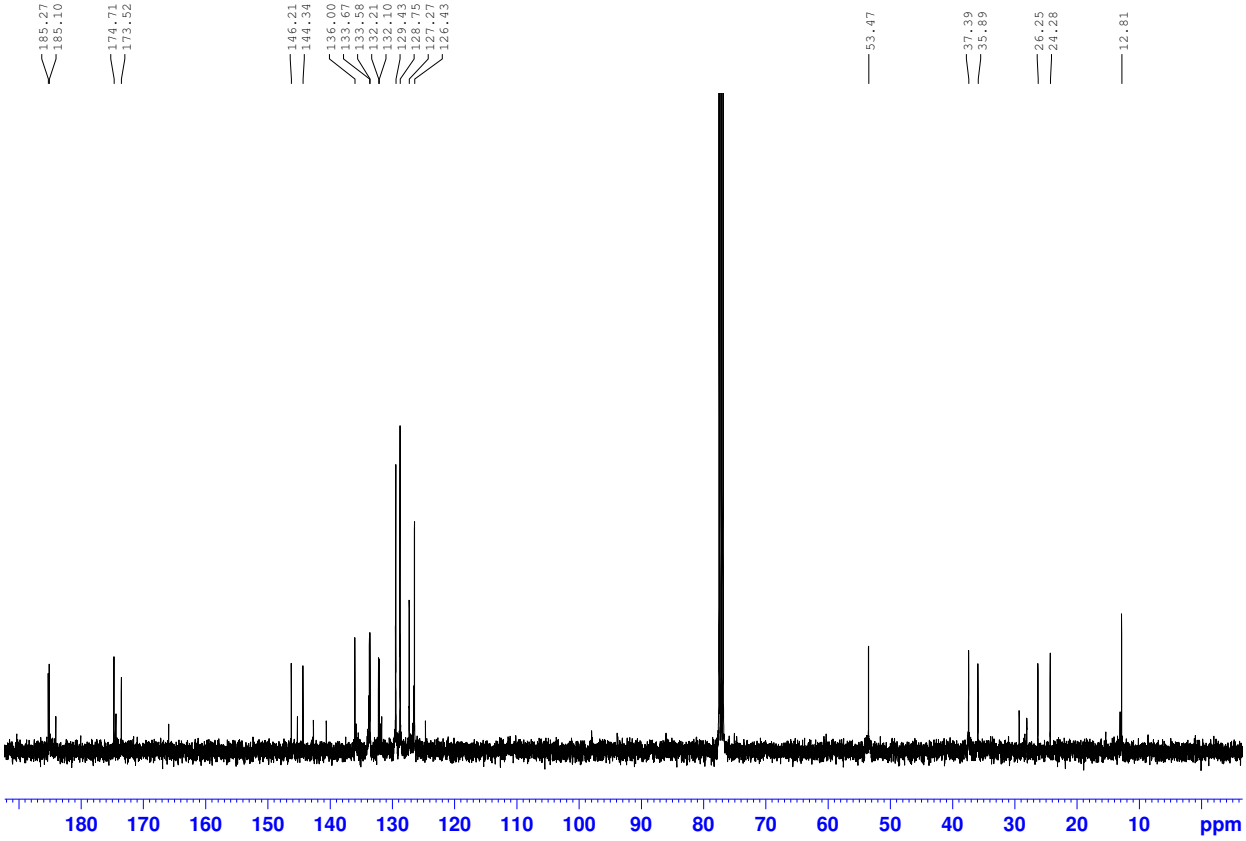
Avance III - 13C with 1H Power-gated Decoupling



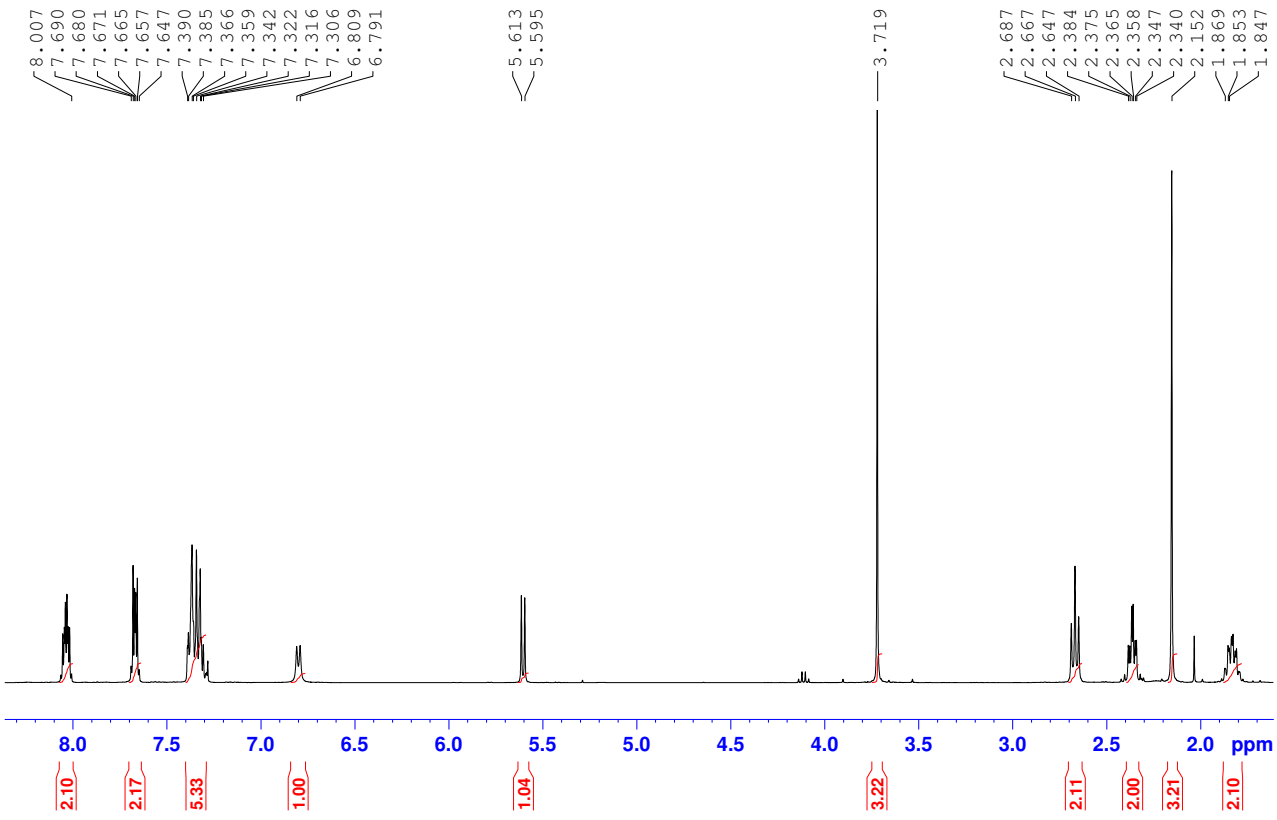


69

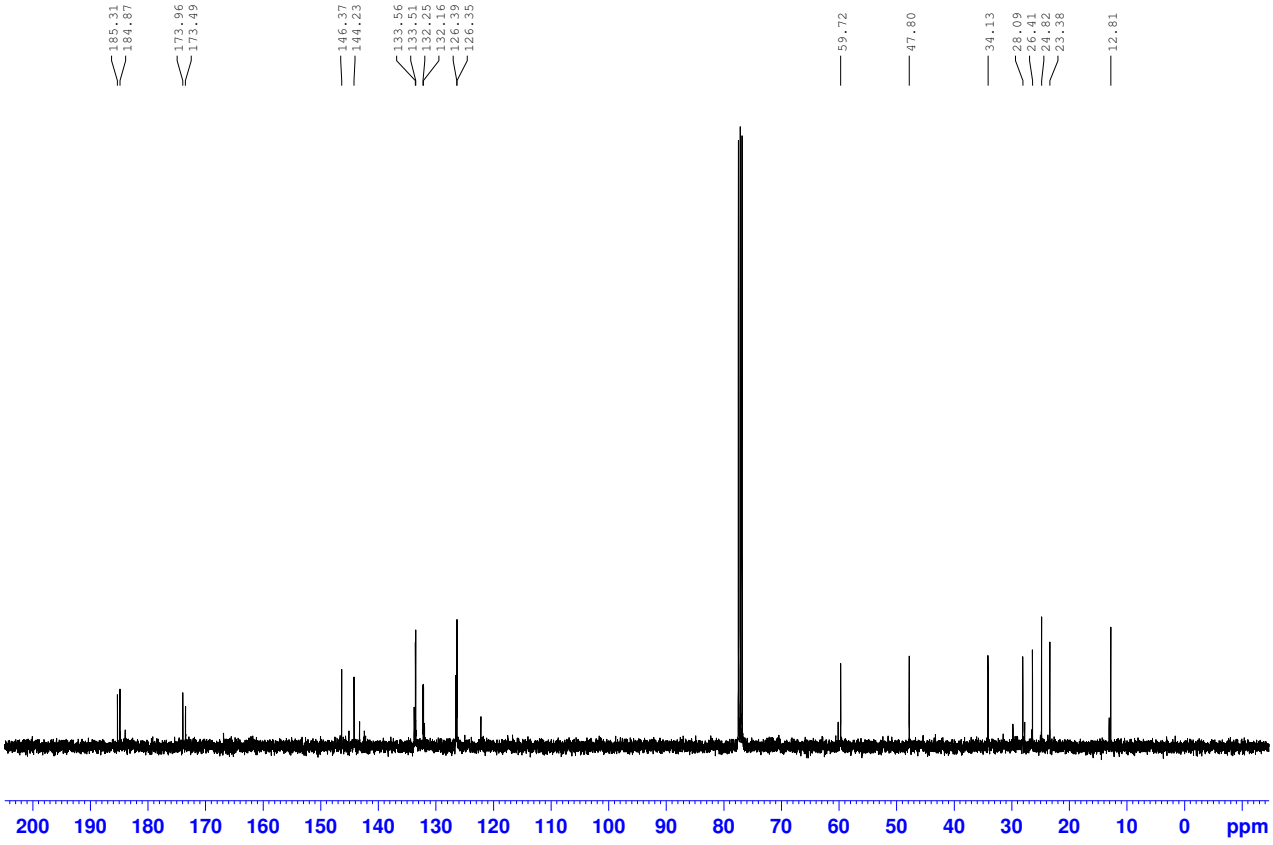
Avance III - 13C with 1H Power-gated Decoupling

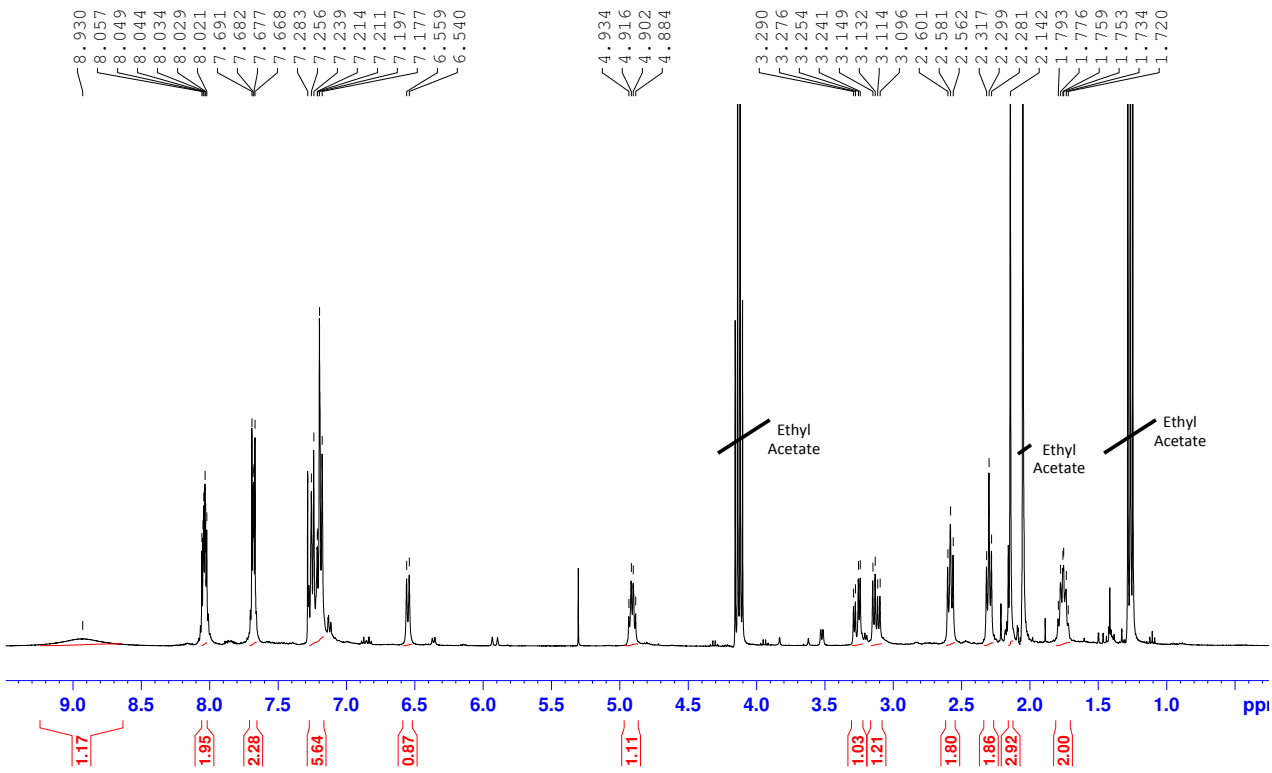


68

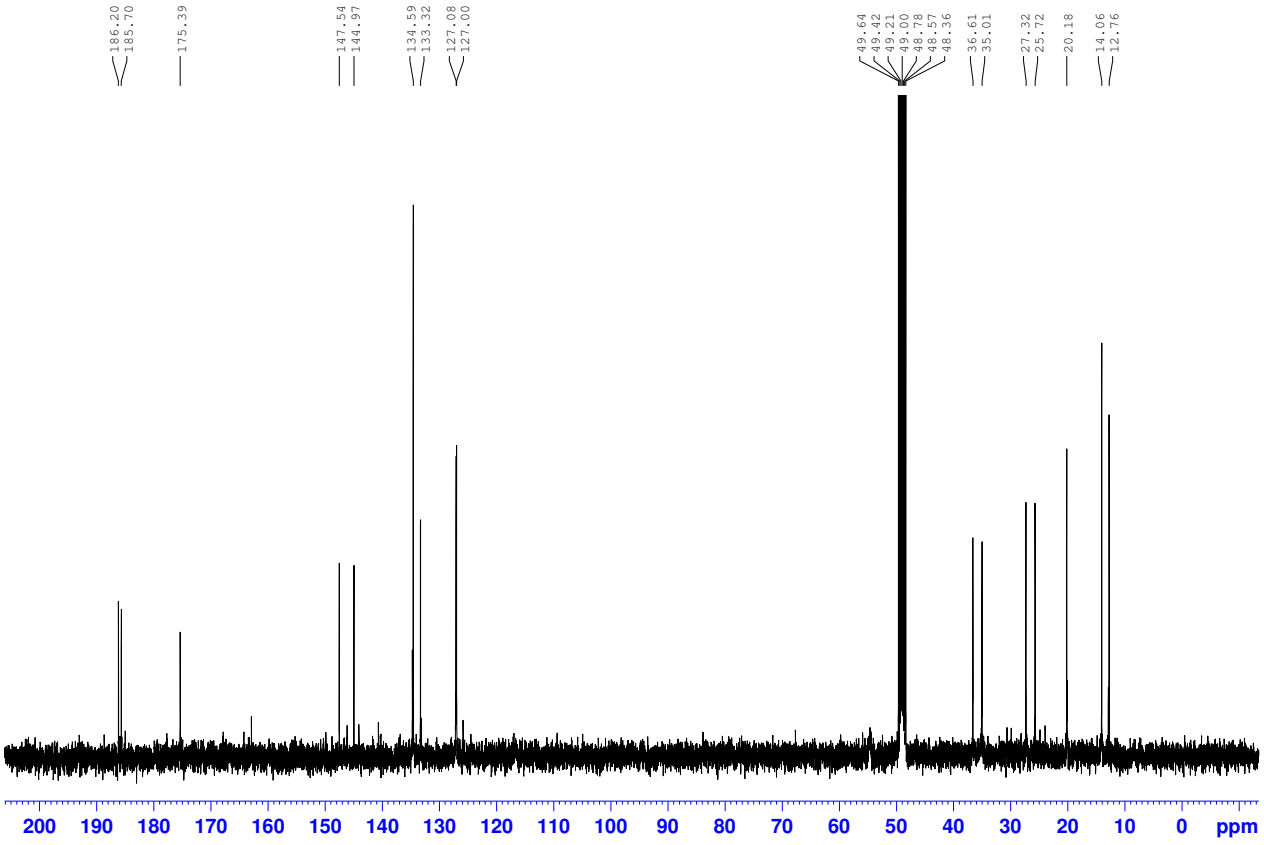


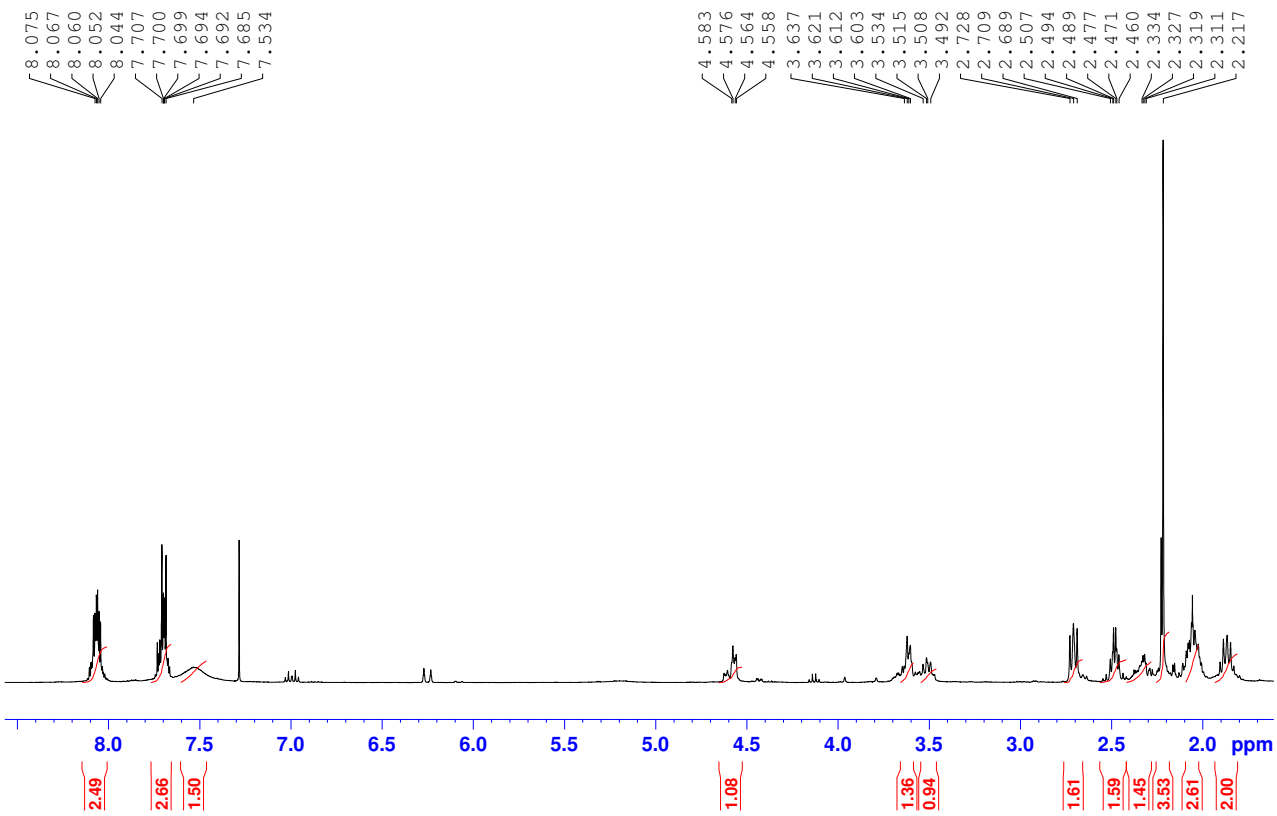
Avance III - 13C with 1H Power-gated Decoupling



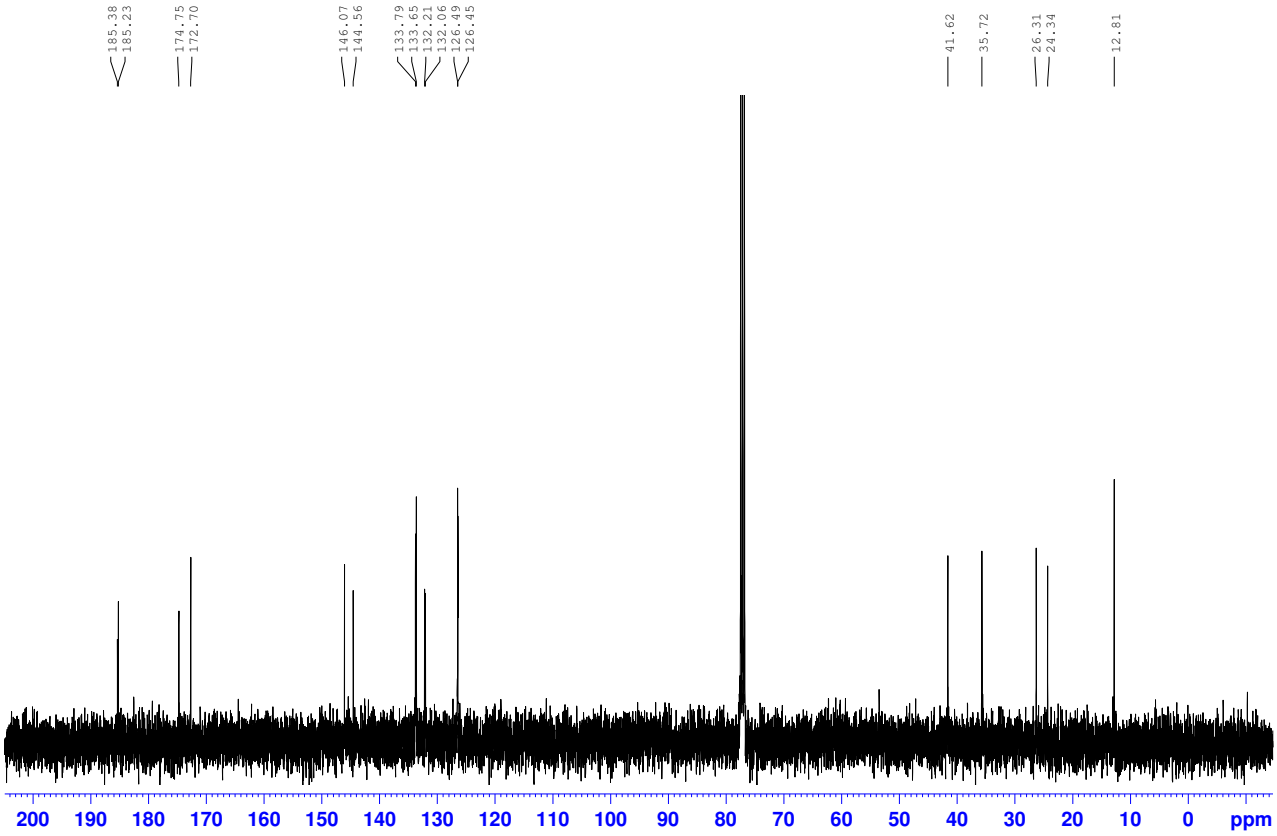


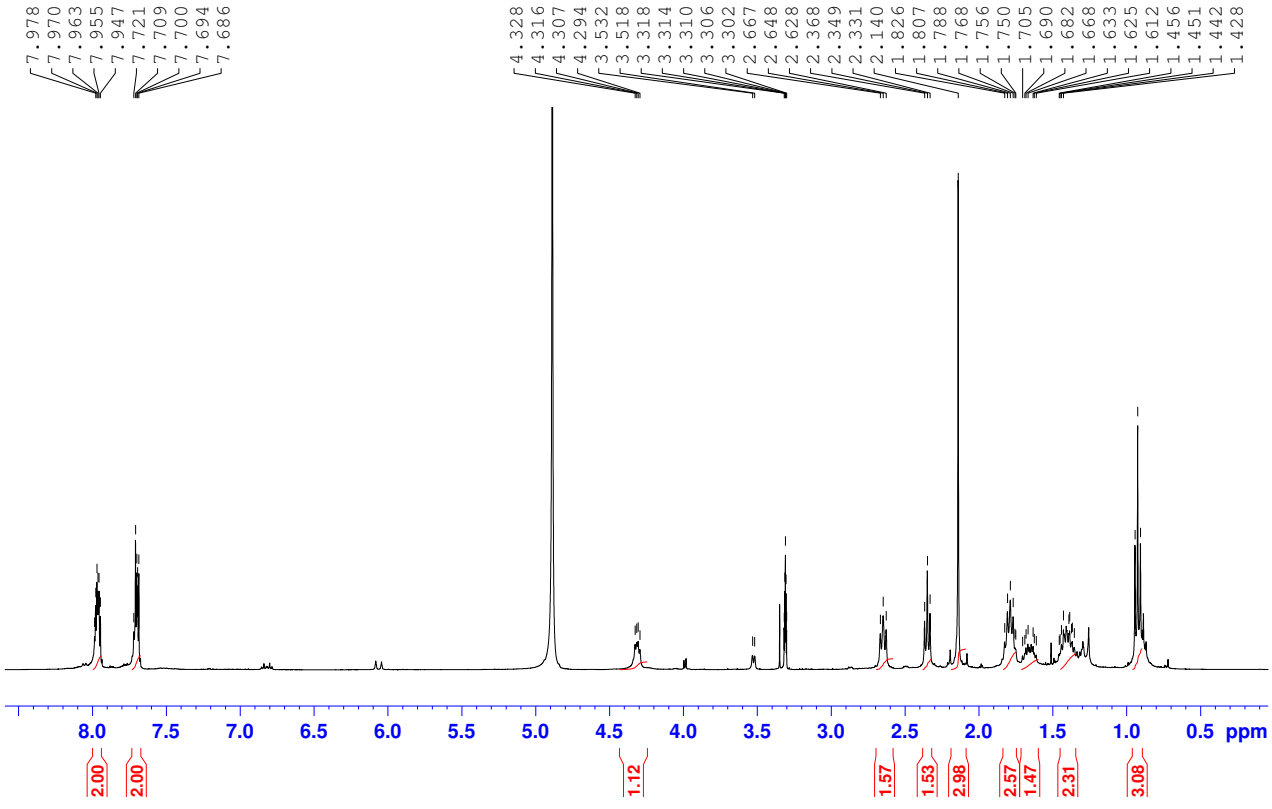
Avance III - 13C with 1H Power-gated Decoupling



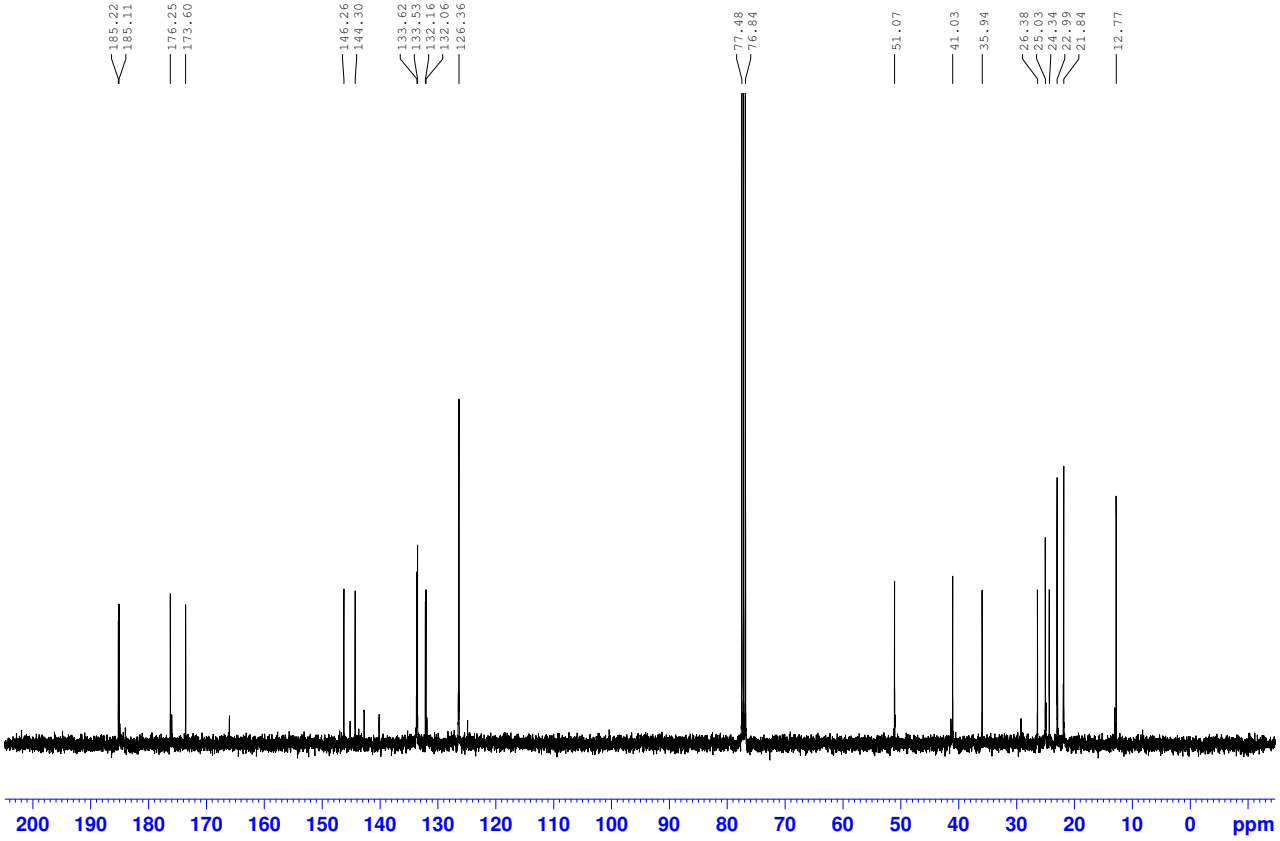


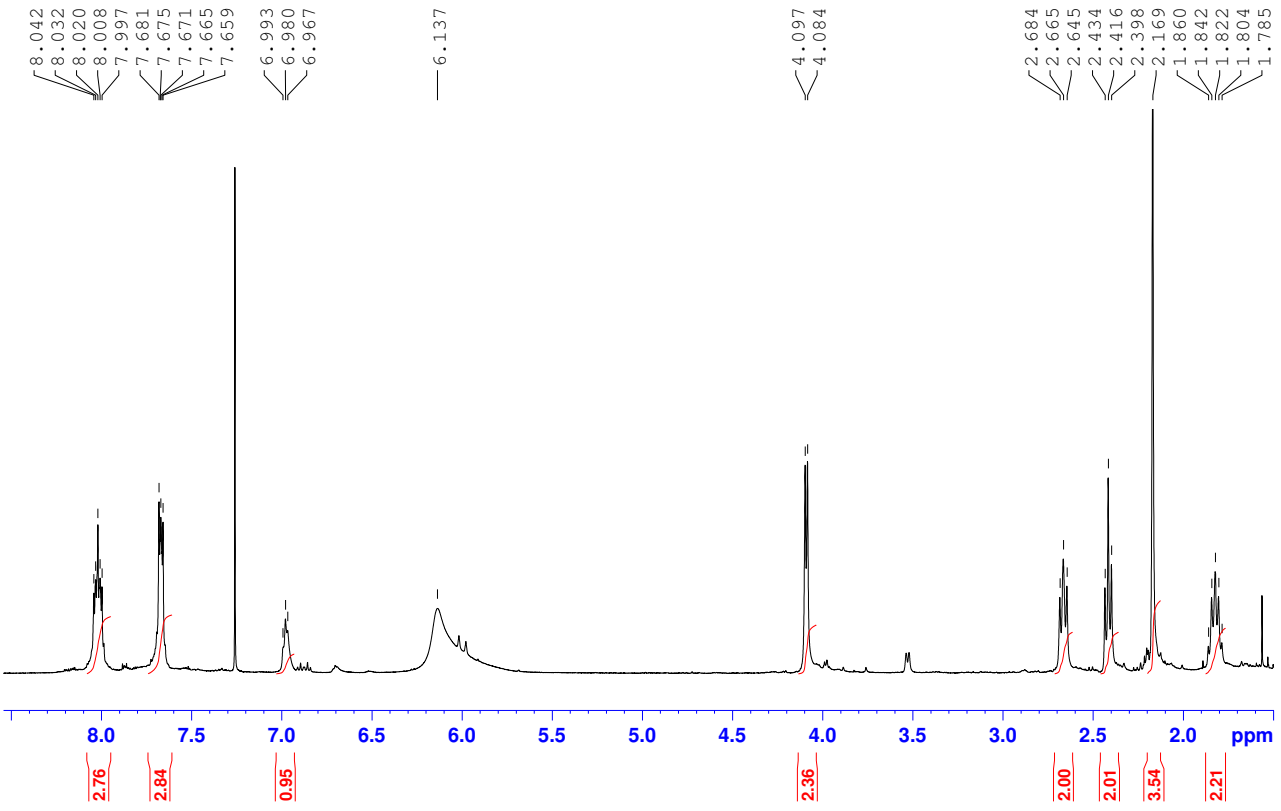
Avance III - 13C with 1H Power-gated Decoupling



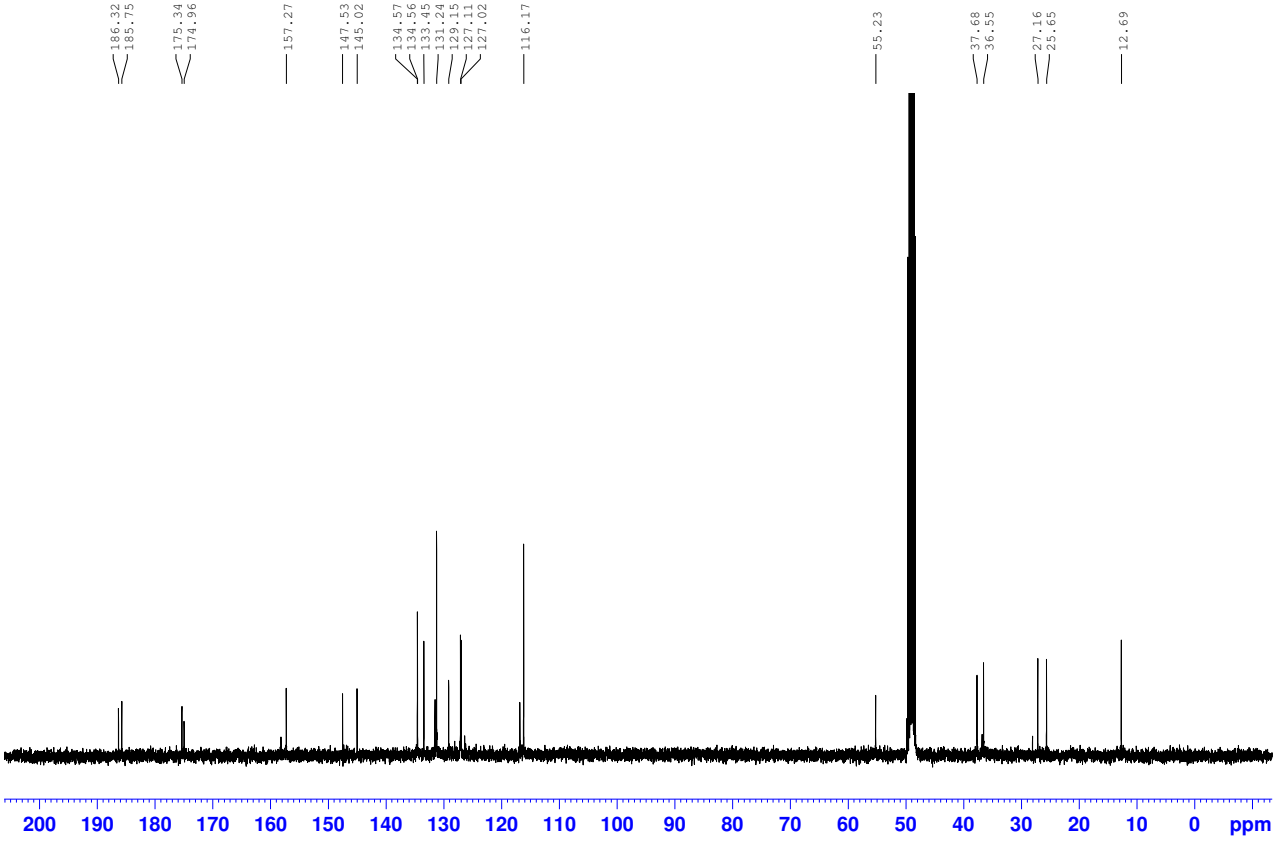


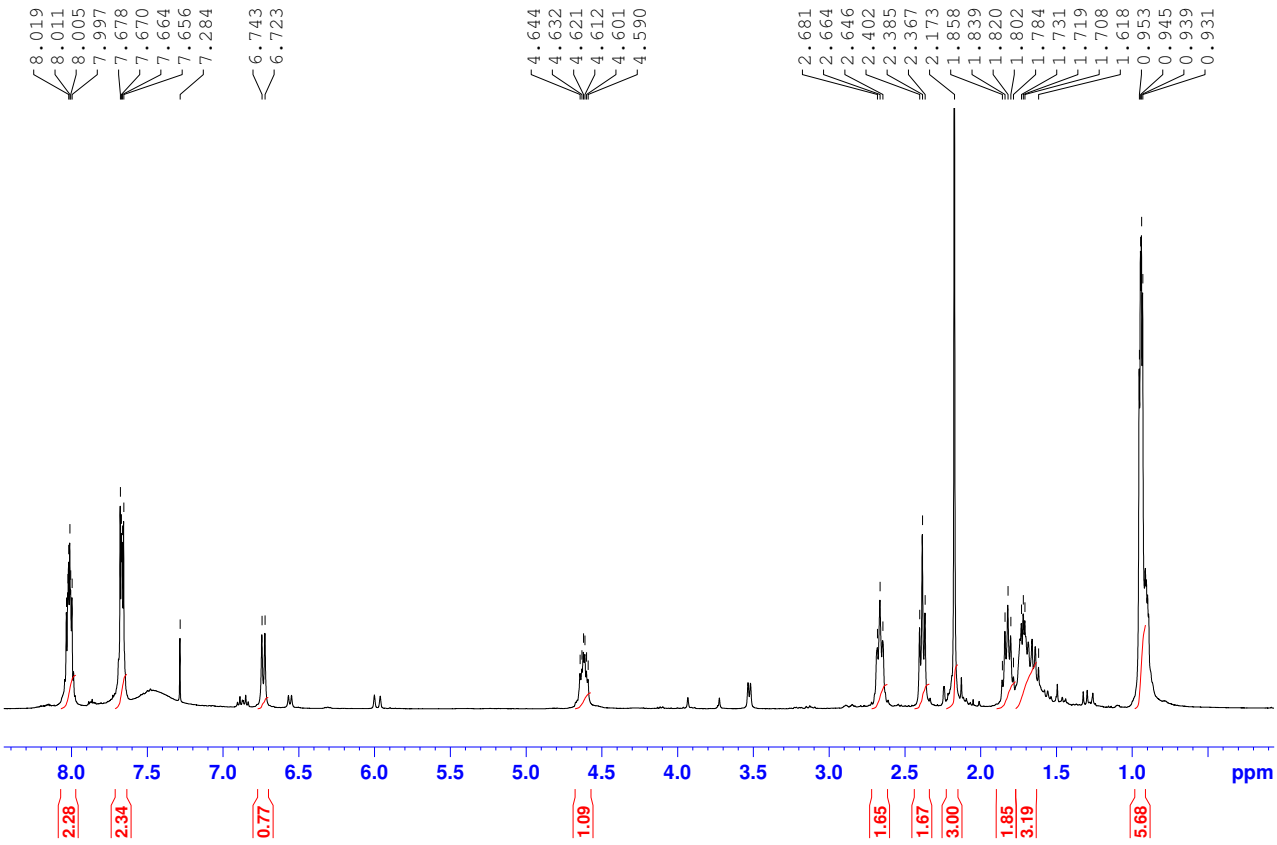
Avance III - 13C with 1H Power-gated Decoupling



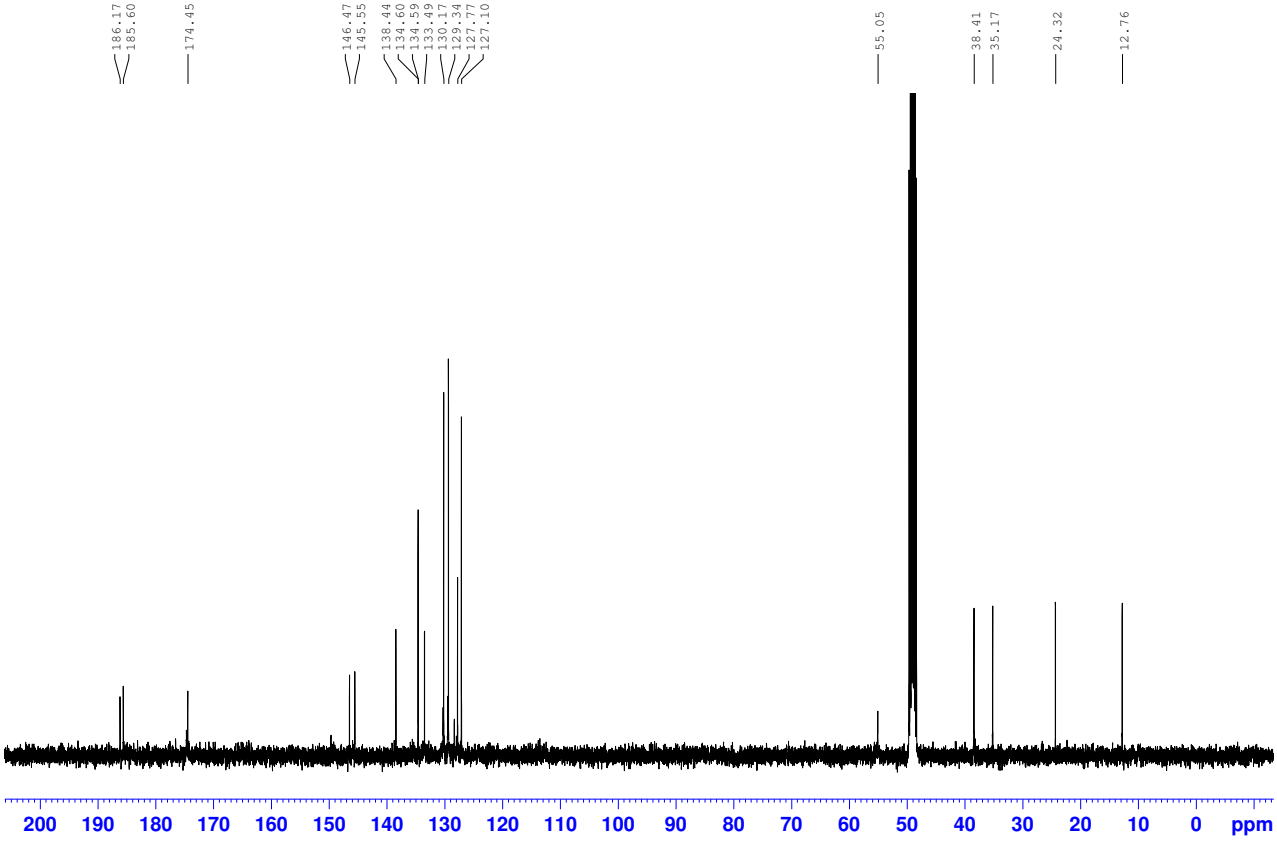


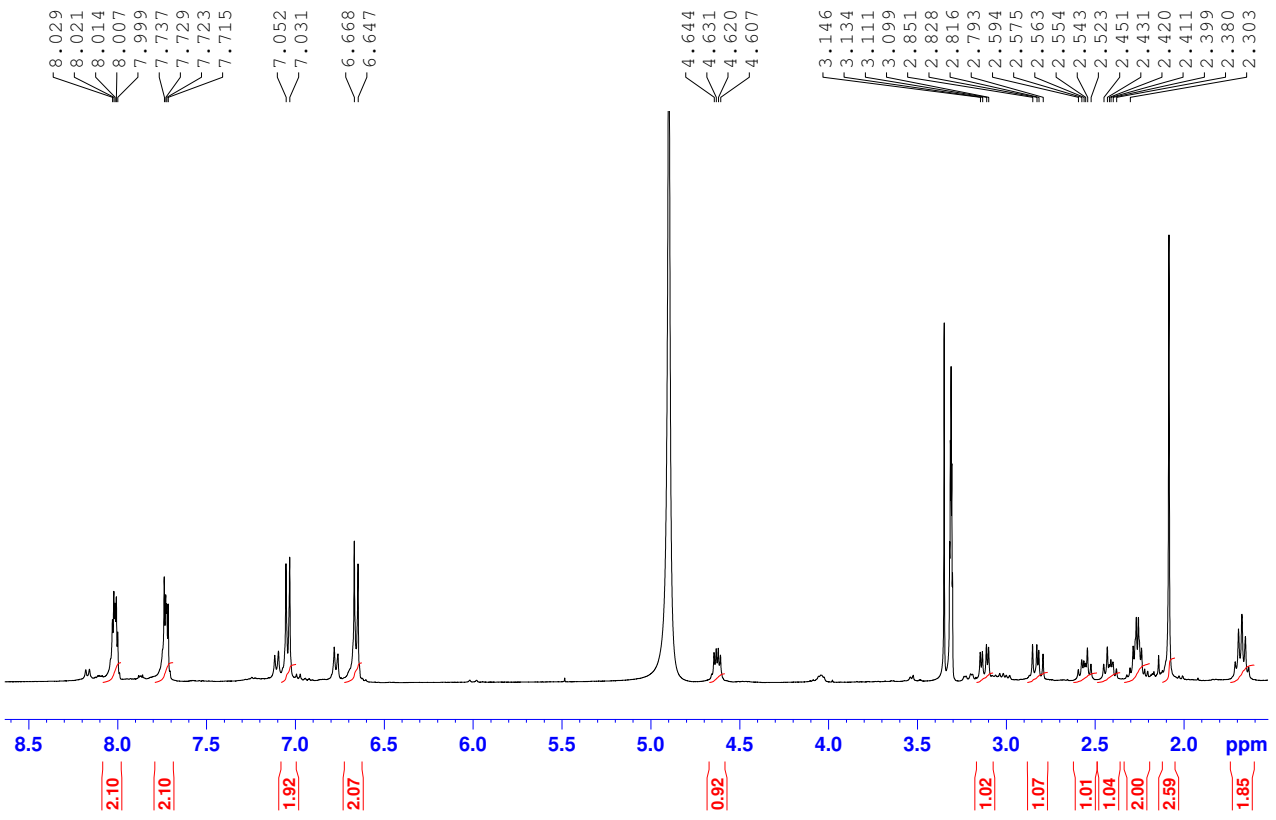
Avance III - 13C with 1H Power-gated Decoupling



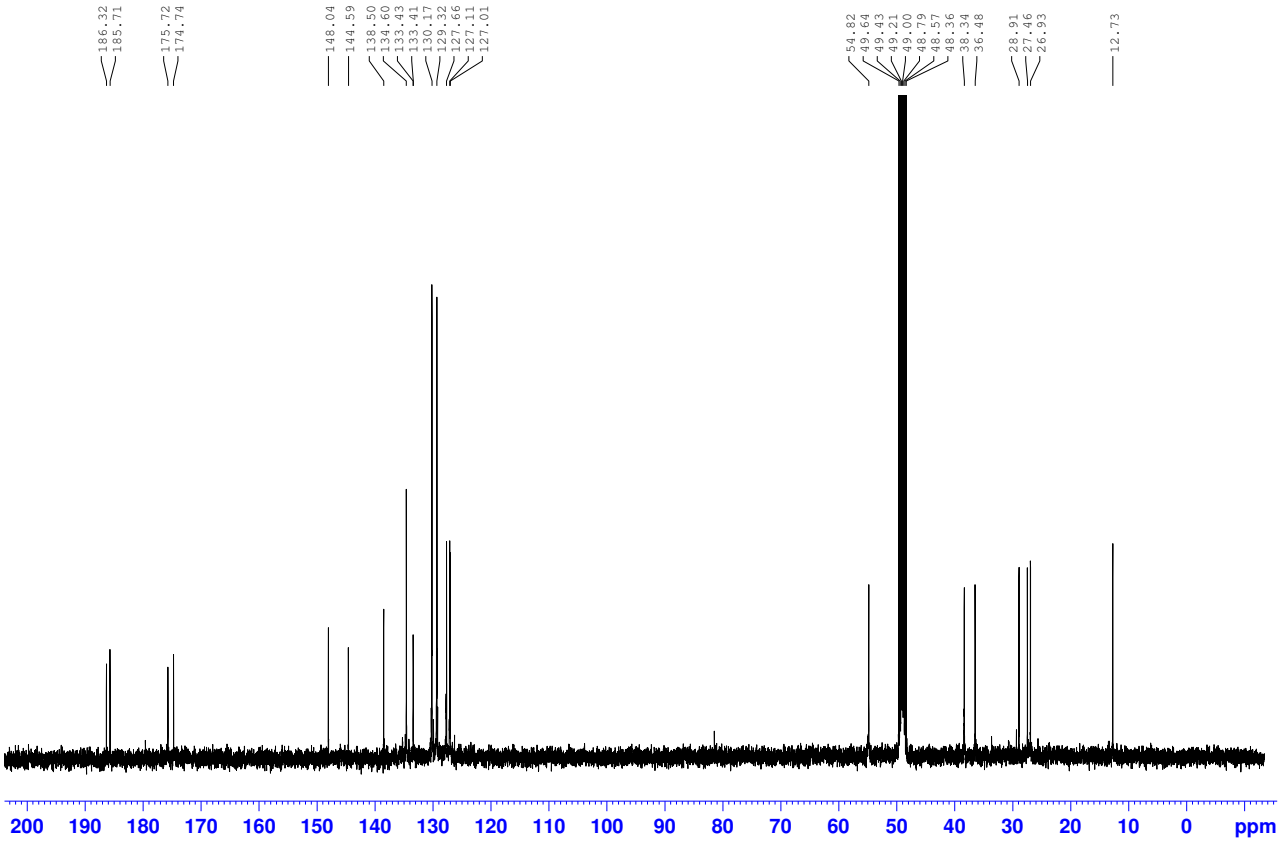


Avance III - 13C with 1H Power-gated Decoupling

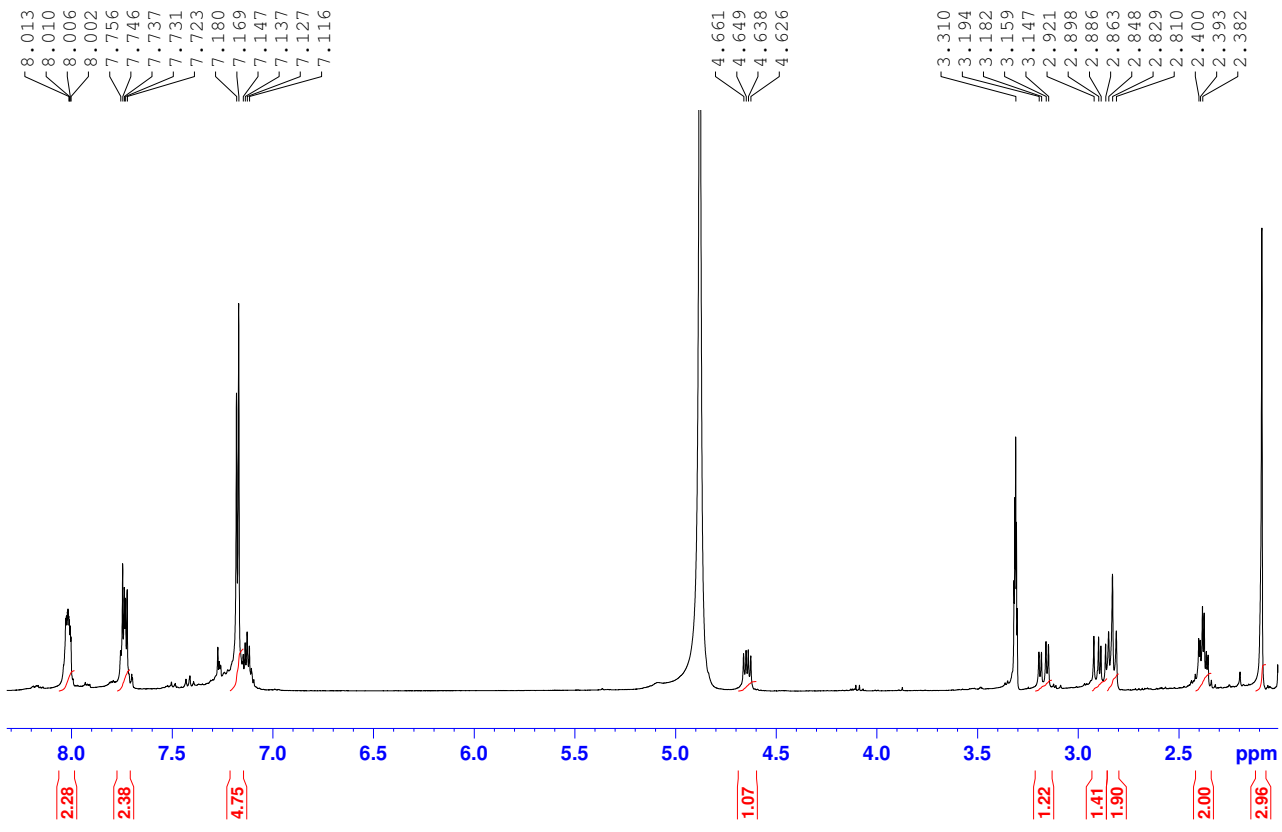


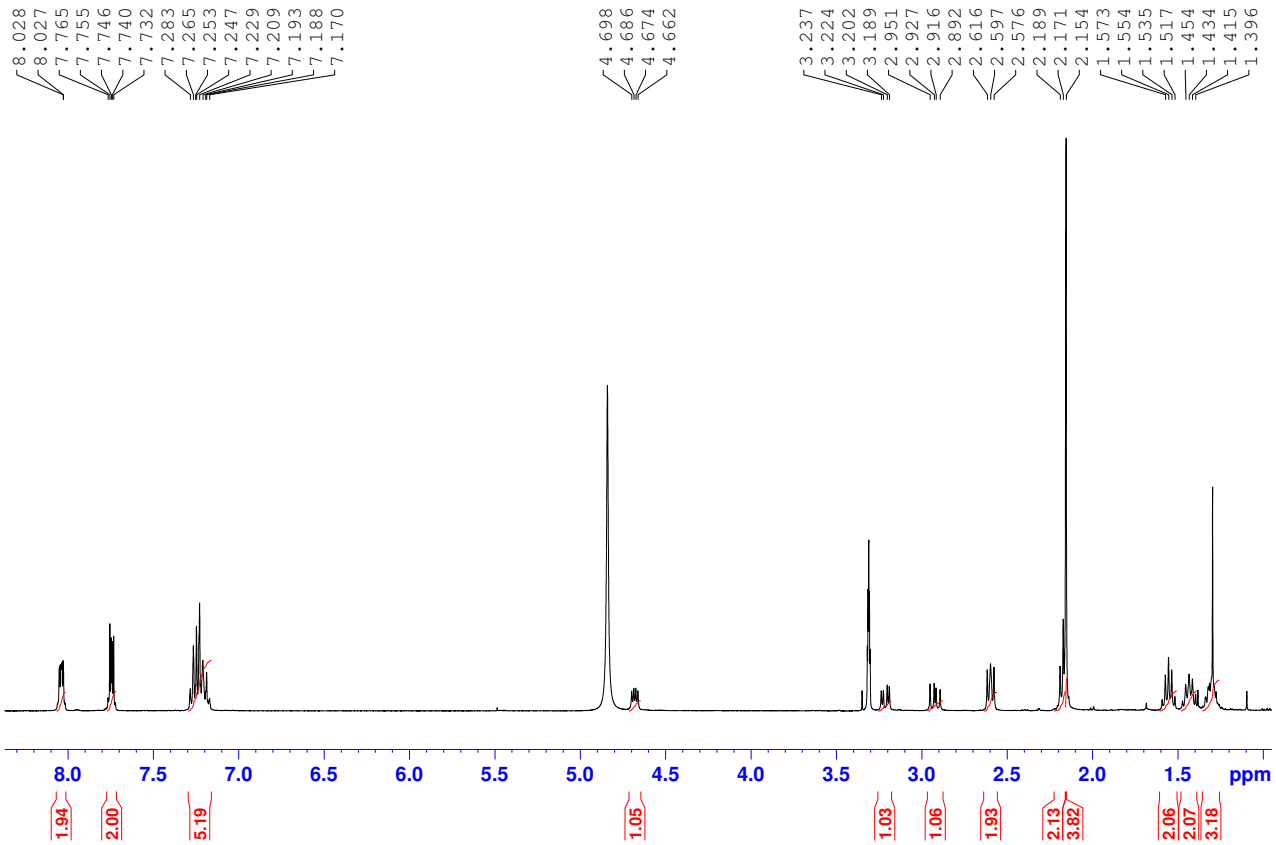


Avance III - 13C with 1H Power-gated Decoupling



KW-PhD-B1-Pg137-PURE

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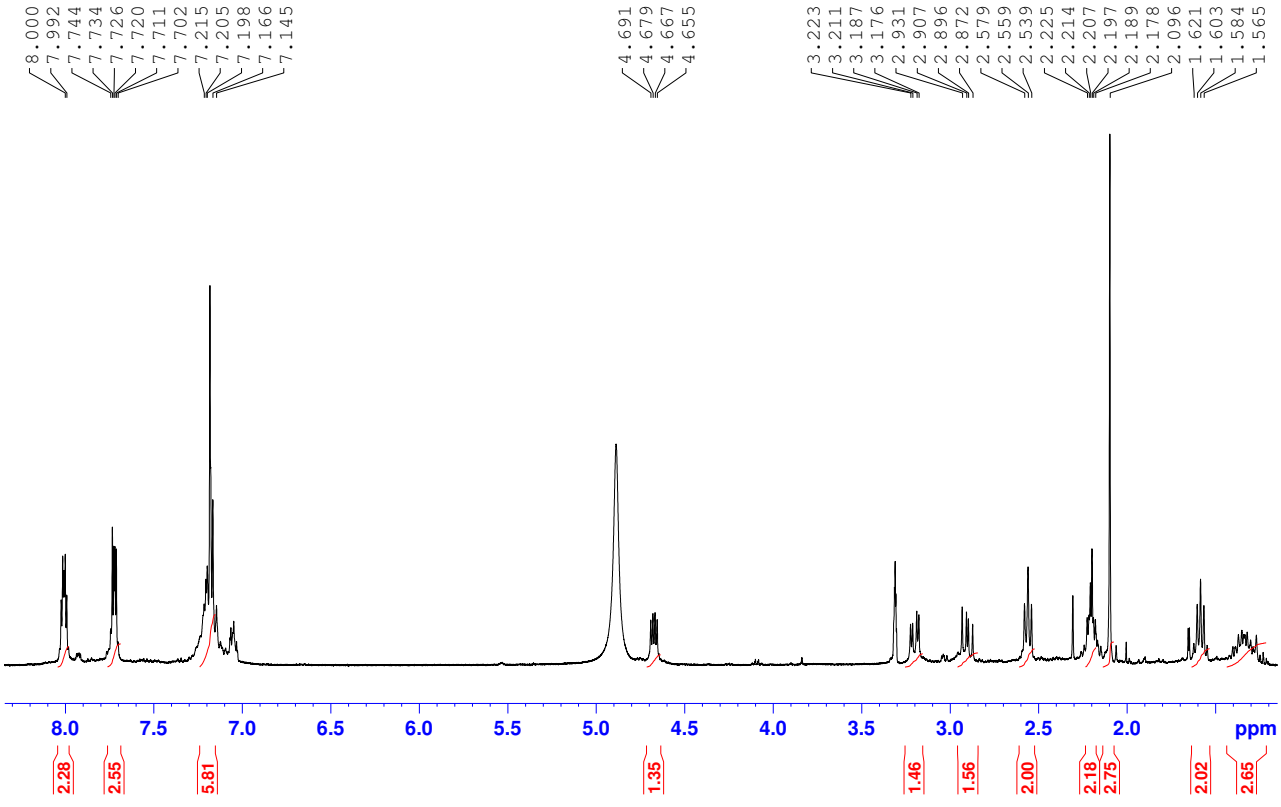
8.027
7.765
7.755
7.746
7.740
7.732
7.283
7.265
7.253
7.247
7.229
7.209
7.193
7.188
7.170
4.698
4.686
4.674
4.662
3.237
3.224
3.202
3.189
2.951
2.927
2.916
2.892
2.616
2.597
2.576
2.189
2.171
2.154
1.573
1.554
1.535
1.517
1.454
1.434
1.415
1.396
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
1.94
2.00
5.19
1.05
1.03
1.06
1.93
2.13
3.82
2.06
2.07
3.18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7.992
7.744
7.734
7.726
7.720
7.711
7.702
7.215
7.205
7.198
7.166
7.145
4.691
4.679
4.667
4.655
3.223
3.211
3.187
3.176
2.931
2.907
2.896
2.872
2.579
2.559
2.539
2.225
2.214
2.207
2.197
2.189
2.178
2.096
1.621
1.603
1.584
1.565
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm
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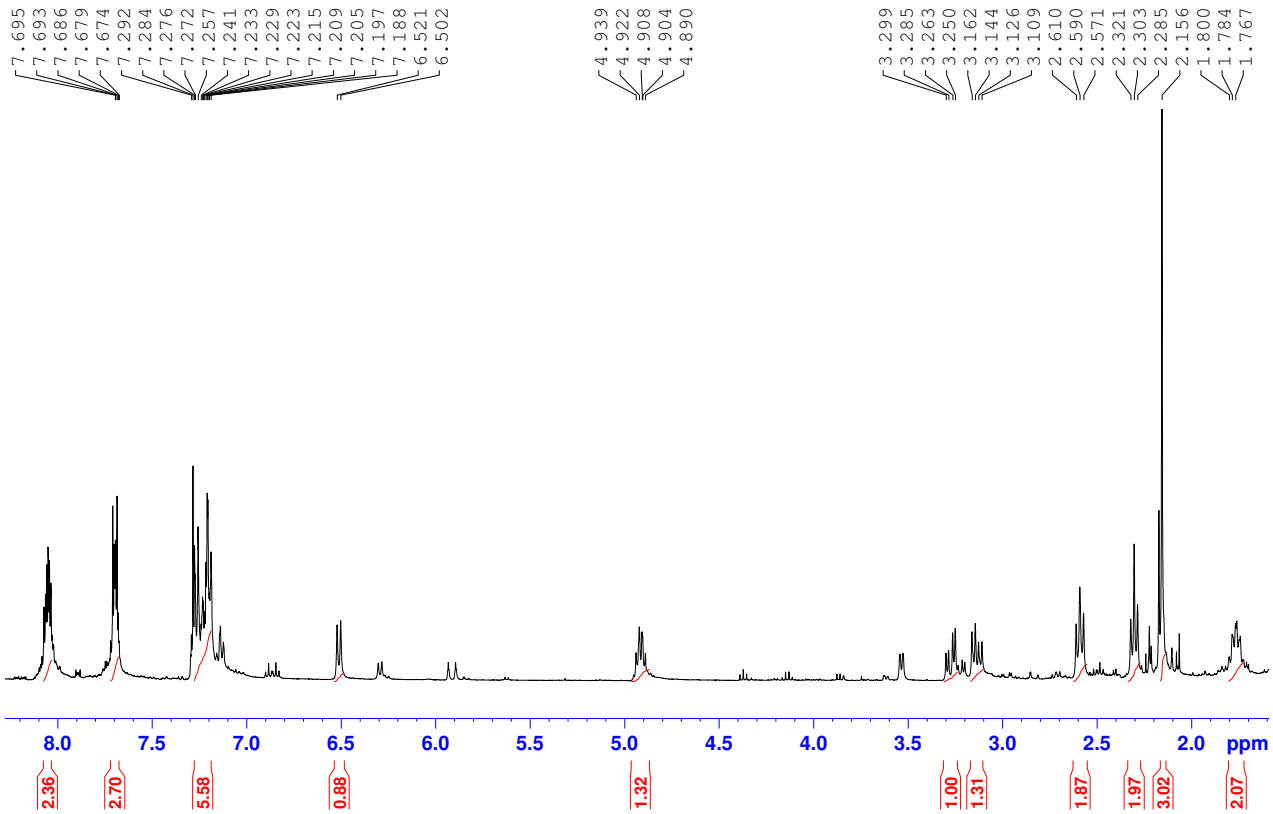
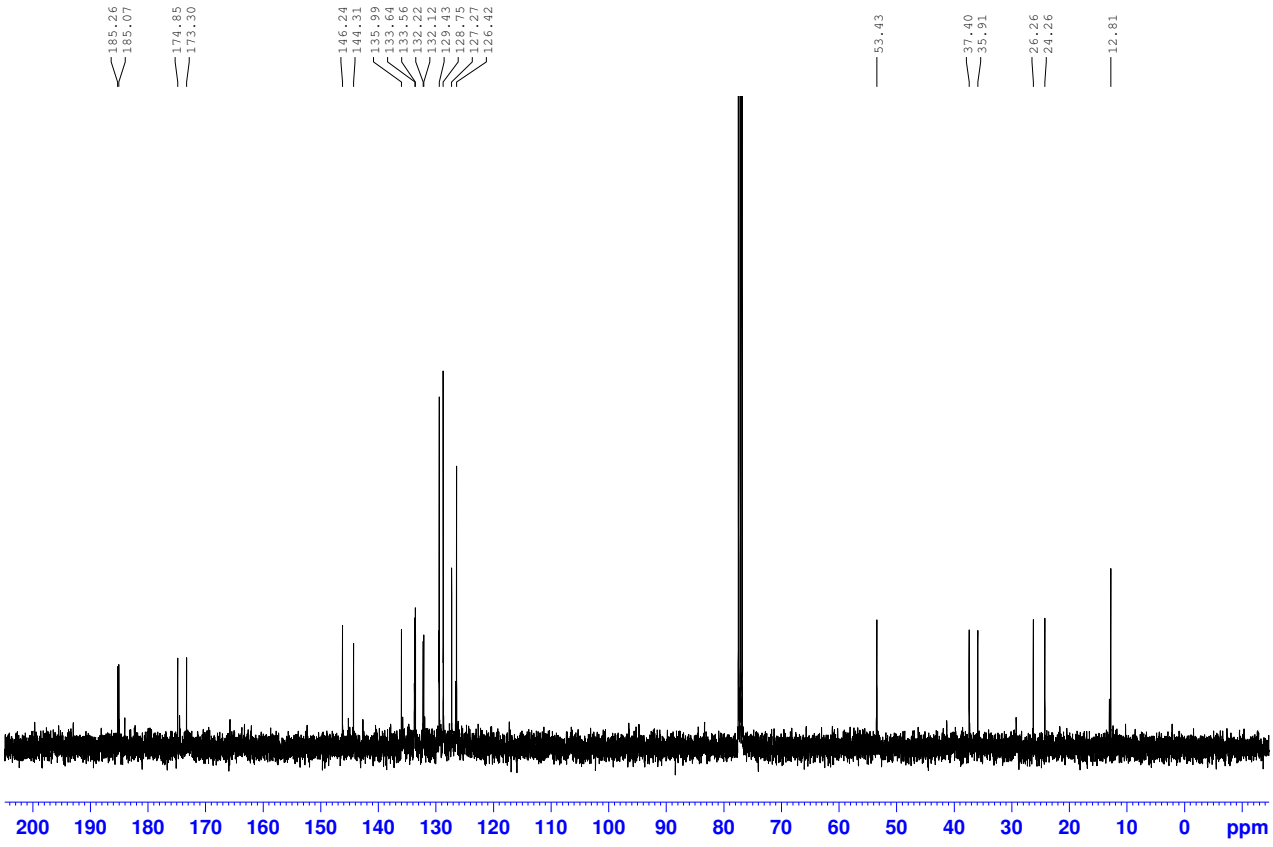
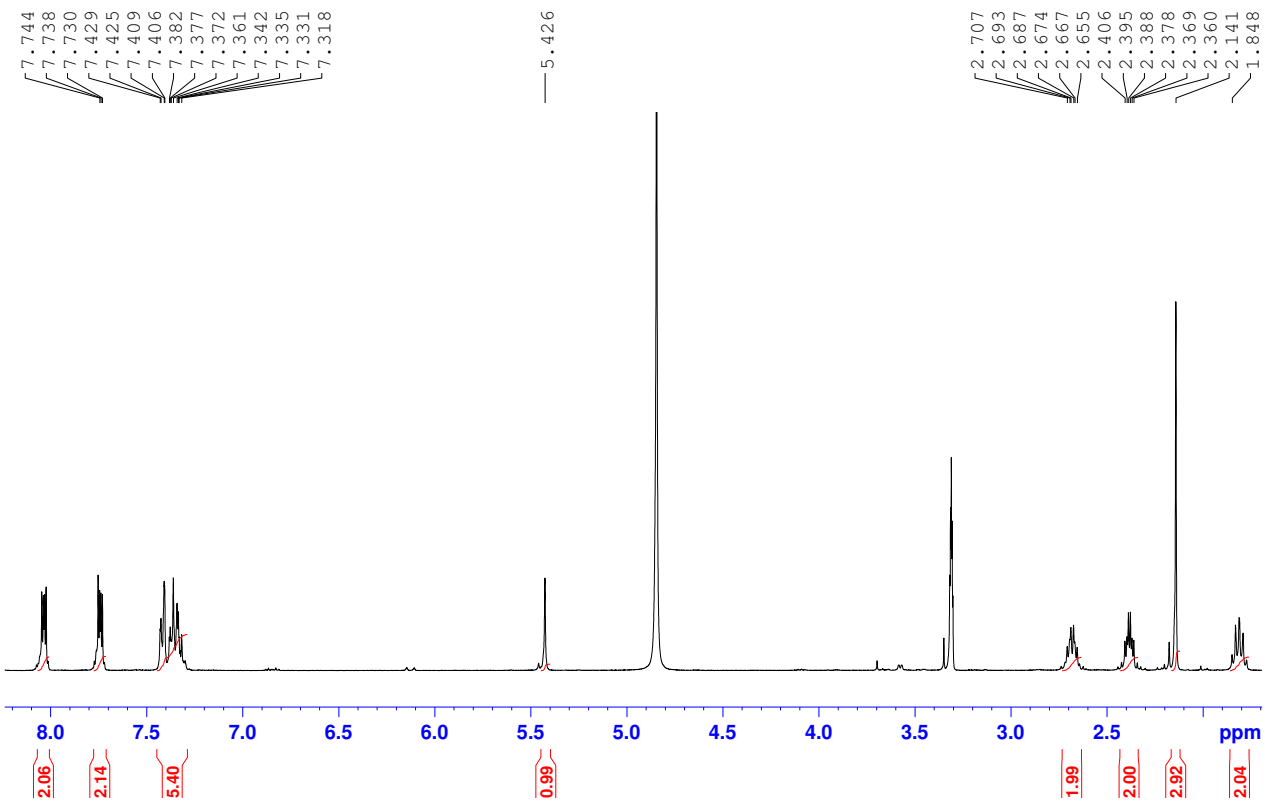
2.55
5.81
1.35
1.46
1.56
2.00
2.18
2.75
2.02
2.65

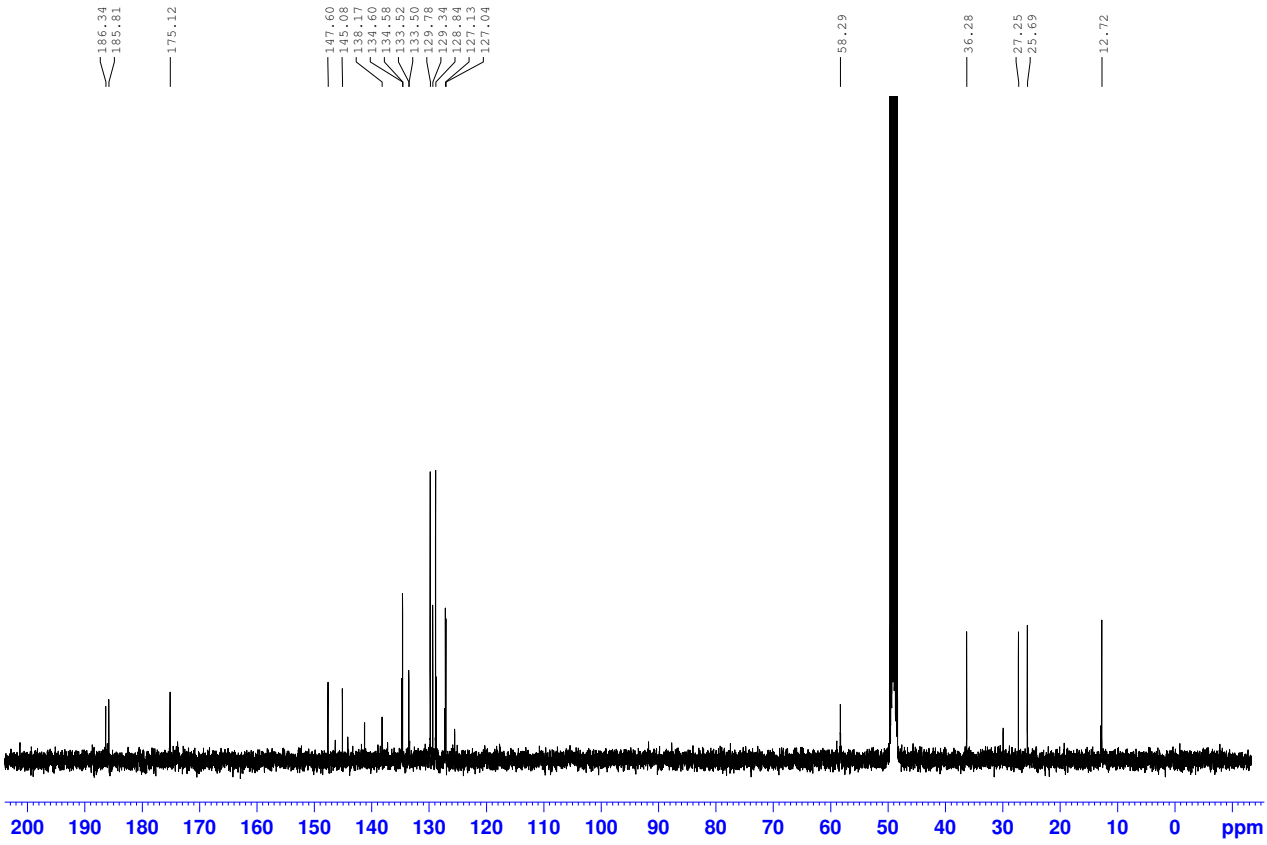


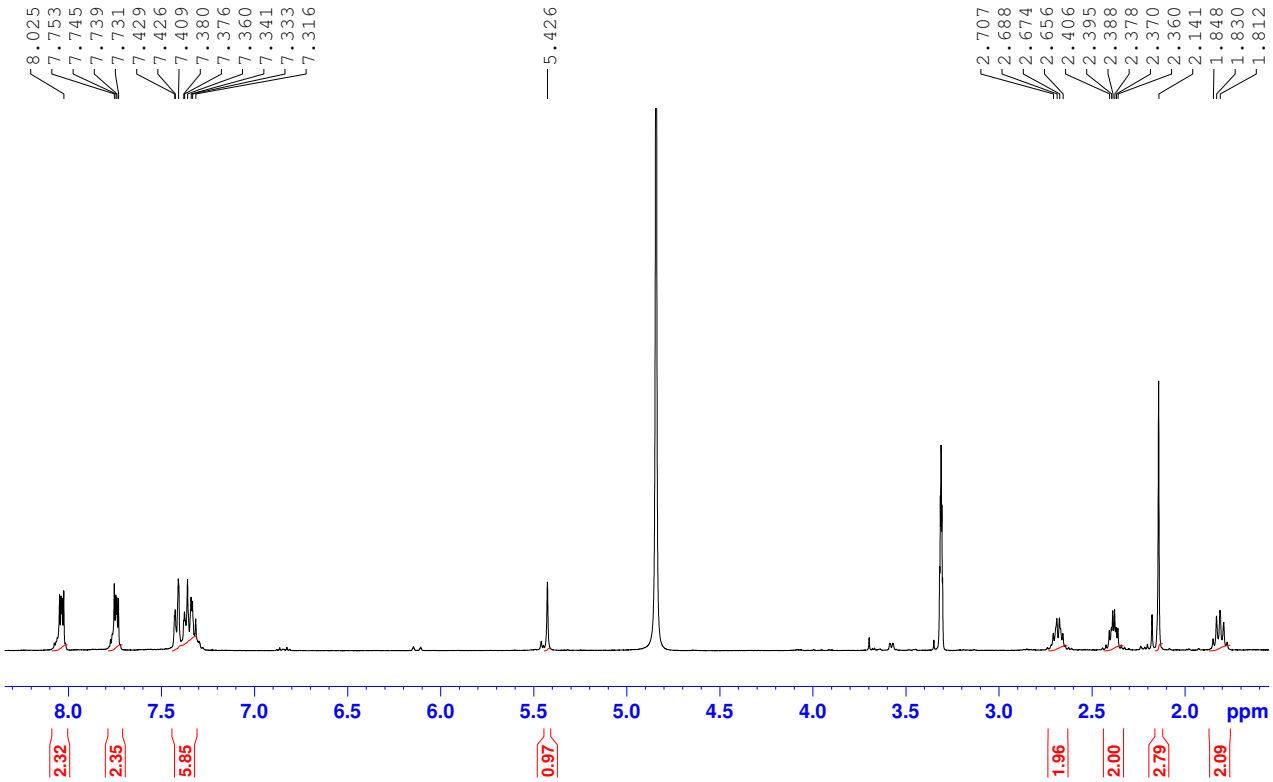
Avance III - 13C with 1H Power-gated Decoupling





Avance III - 13C with 1H Power-gated Decoupling

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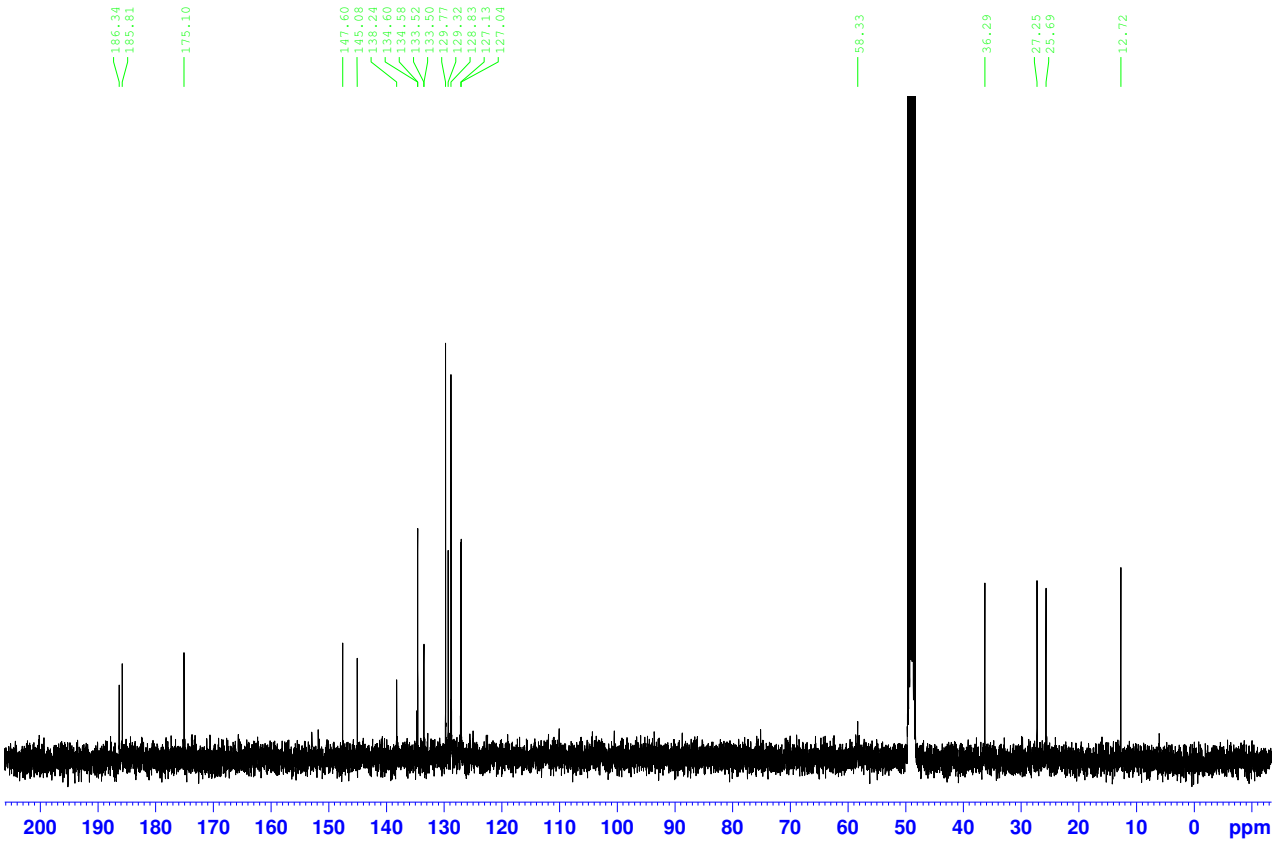
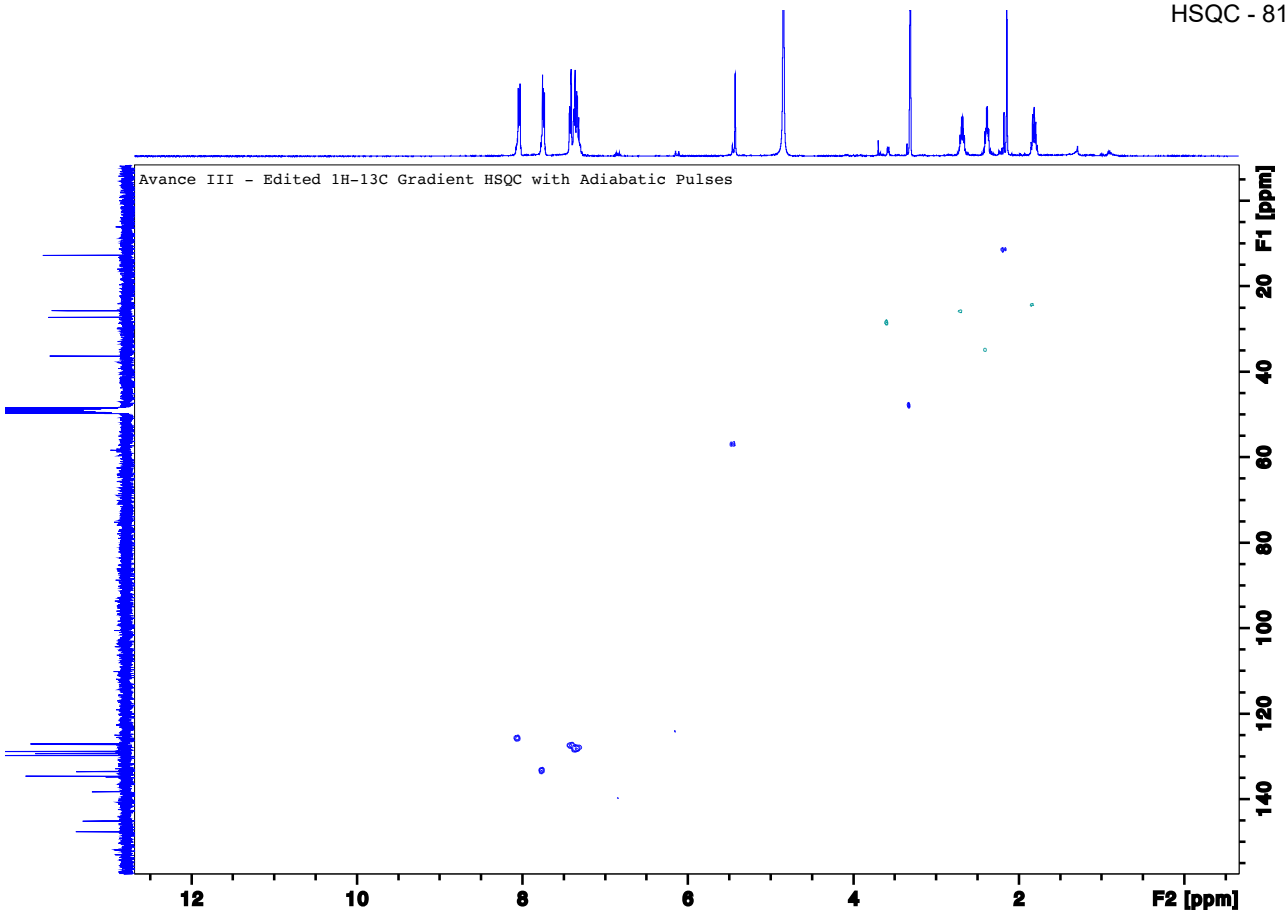
7.753
7.745
7.739
7.731
7.429
7.426
7.409
7.380
7.376
7.360
7.341
7.333
7.316
5.426
2.707
2.688
2.674
2.656
2.406
2.395
2.388
2.378
2.370
2.360
2.141
1.848
1.830
1.812
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm
2.32
2.35
5.85
0.97
1.96
2.00
2.79
2.09

81


186.34
185.81
175.10
147.60
145.08
138.24
134.60
134.58
133.52
133.50
129.77
129.32
128.83
127.13
127.04
58.33
36.29
27.25
25.69
12.72
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


Avance III - Edited 1H-13C Gradient HSQC with Adiabatic Pulses
F1 [ppm]
20
40
60
80
100
120
140
12
10
8
6
4
2
F2 [ppm]