Supporting Information

Synthesis of pandamarilactone-1

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7-Chloro-2-methylhept-3-yne-1,2-diol (SI-1)

A solution of isopropylmagnesium chloride (29.3 mL, 2.0 M in THF, 58.6 mmol) was added to a solution of 5-chloro-1-pentyne (6.20 mL, 58.5 mmol) in THF (100 mL) at 0 °C. The reaction mixture was stirred at RT for 1.5 h then cooled to 0 °C and *O*-trimethylsilylacetol[1] (8.56 g, 58.5 mmol) added. The reaction mixture was stirred at RT for 16 h then diluted with sat. aq. NH_4Cl solution (200 mL) and the THF removed *in vacuo*. The aqueous layer was diluted with water (800 mL), extracted with ether (3 × 900 mL), the combined organic layers washed with brine (900 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the crude silyl ether as a colourless oil (13.3 g, 91%). Citric acid (112 mg, 0.583 mmol) was then added to a solution of this silyl ether (13.3 g, 53.5 mmol) in methanol (75 mL) and the reaction mixture was stirred at RT for 4 h. The mixture was diluted with water (75 mL), the methanol removed *in vacuo* and the aqueous layer extracted with ethyl acetate (3 × 75 mL). The combined organic layers were washed with brine (75 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the *title compound* as a colourless oil (9.01 g, 87% overall from 5-chloro-1-pentyne) that was used in subsequent reactions without purification. R_f 0.25 (CH_2Cl_2/MeOH, 95:5); ν_{max} (thin film)/cm^{-1} 3375s, 2935m, 1442m, 1375m, 1291m, 1112m, 1057s, 1037s; δ_H (400 MHz, $CDCl_3$) 1.41 (3 H, s, CH_3), 1.94 (2 H, quin, *J* 7.0 Hz, C(6)H_2), 2.39 (2 H, t, *J* 7.0 Hz, C(5)H_2), 2.95 (2 H, bs, 2 × OH), 3.45 and 3.60 (2 × 1 H, 2 × d, *J* 11.0 Hz, C(1)H_2), 3.62 (2 H, t, *J* 7.0 Hz, C(7)H_2); δ_C (100 MHz, $CDCl_3$) 16.1 (C(5)), 25.6 (CH_3), 31.2 (C(6)), 43.7 (C(7)), 68.6 (C(2)), 70.7 (C(1)), 82.8 (C(4)), 83.0 (C(3)); HRMS (ESI$^+$) found 199.0489, $C_8H_{13}{}^{35}ClNaO_2$ (MNa^+) requires 199.0496.

2-(3-Chloropropyl)-4-methylfuran (5)

To a solution of diol **SI-1** (9.0 g, 51.0 mmol) in dichloromethane (340 mL) at RT was added $AgNO_3$-SiO_2 (17.3 g, 5% w/w, 5.10 mmol). The reaction mixture was stirred in the absence of light until TLC analysis showed complete consumption of starting material (~ 2 h); the mixture was then filtered and concentrated *in vacuo*. Purification by flash chromatography (SiO_2, petrol) afforded the *title compound* as a colourless oil (7.62 g, 94%). R_f 0.75 (petrol/ether, 95:5); ν_{max} (thin film)/cm^{-1} 2927w, 1619w, 1552w, 1443m, 1297w, 1112m, 928s, 805s, 744s, 648m; δ_H (400 MHz, C_6D_6) 1.70 (2 H, quin, *J* 7.0 Hz, C(2′)H_2), 1.78 (3 H, d, *J* 1.0 Hz, CH_3), 2.47 (2 H, t, *J* 7.0 Hz, C(1′)H_2), 3.05 (2 H, t, *J* 7.0 Hz, C(3′)H_2), 5.67 (1 H, s, C(3)H), 6.90 (1 H, q, *J* 1.0 Hz, C(5)H); δ_C (100 MHz, C_6D_6) 9.4 (CH_3), 25.0 (C(1′)), 30.8 (C(2′)), 43.6 (C(3′)), 108.4 (C(3)), 120.2 (C(4)), 137.8 (C(5)), 154.3 (C(2)); HRMS (EI^+) found 158.0502, $C_8H_{11}{}^{35}ClO$ (M^+) requires 158.0493.

4-(4-Methylfuran-2-yl)butyronitrile (6)

A solution of NaCN (0.792 g, 16.2 mmol) in DMSO (10 mL) was heated to 80 °C; the heating source was removed while a solution of furan **5** (2.33 g, 14.7 mmol) in DMSO (2 mL) was added dropwise with rapid stirring. The reaction mixture was then stirred at 80 °C for 8 h. The solution was cooled to RT, poured into water (60 mL) and extracted with ether (3 × 60 mL). The ether layers were combined, washed with water (100 mL), brine (100 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford the *title compound* as a colourless oil that was sufficiently pure to be used in subsequent reactions without further purification (2.17 g, 98%). R_f 0.20 (petrol/ether, 95:5); ν_{max} (thin film)/cm^{-1} 2945m, 2247m, 1793s, 1761s, 1618m, 1553m, 1456m, 1388m, 1114s, 937s; δ_H (400 MHz, $CDCl_3$) 1.98 (2 H, quin, *J* 7.0 Hz, C(3)H_2), 1.99 (3 H, s, CH_3), 2.35 (2 H, t, *J* 7.0 Hz, C(2)H_2), 2.74 (2 H, t, *J* 7.0 Hz, C(4)H_2), 5.93 (1 H, s, C(3′)H), 7.08 (1 H, s, C(5′)H); δ_C (100 MHz, $CDCl_3$) 9.7 (CH_3), 16.4 (C(2)), 24.0 (C(3)), 26.7 (C(4)), 109.1 (C(3′)), 119.3 (C(1)), 120.6 (C(4′)), 138.1 (C(5′)), 153.3 (C(2′)); HRMS (EI^+) found 149.0840, $C_9H_{11}NO$ (M^+) requires 149.0835.

4-(4-Methylfuran-2-yl)butylamine (7)

To a stirred suspension of $LiAlH_4$ (247 mg, 6.52 mmol) in ether (11.5 mL) at 0 °C was added nitrile **6** (648 mg, 4.34 mmol) as a solution in ether (3.5 mL). The reaction mixture was stirred at RT for 0.5 h then cooled to 0 °C and water (0.25 mL), 15% aq. NaOH solution (0.25 mL), and a further portion of water (0.80 mL) added sequentially. The mixture was stirred at RT for 10 min, filtered through a pad of Celite® then concentrated *in vacuo* to afford the *title compound* as a colourless oil (657 mg, 99%). R_f 0 (petrol/ether, 95:5); ν_{max} (thin film)/cm^{-1} 2928s, 2865m, 1553s, 1475s, 1387m, 1312m, 1120m, 942w; δ_H (400 MHz, $CDCl_3$) 1.30 (2 H, bs, NH_2), 1.49 (2 H, quin, *J* 7.5 Hz, C(2)H_2), 1.65 (2 H, quin, *J* 7.5 Hz, C(3)H_2), 1.98 (3 H, d, *J* 1.0 Hz, CH_3), 2.58 (2 H, t, *J* 7.5 Hz, C(4)H_2), 2.70 (2 H, t, *J* 7.5 Hz, C(1)H_2), 5.85 (1 H, s, C(3′)H), 7.05 (1 H, q, *J* 1.0 Hz, C(5′)H); δ_C (125 MHz, $CDCl_3$) 9.8 (CH_3), 25.3 (C(3)), 27.8 (C(4)), 33.0 (C(2)), 41.8 (C(1)), 107.7 (C(3′)), 120.4 (C(4′)), 137.3 (C(5′)), 156.1 (C(2′)); HRMS (ESI$^+$) found 154.1229, $C_9H_{16}NO$ (MH^+) requires 154.1226.

4-(4-Methylfuran-2-yl)butyraldehyde (8)

To a stirred solution of nitrile **6** (100 mg, 0.670 mmol) in dichloromethane (6 mL) at −78 °C was added DIBAL (0.804 mL, 1.0 M solution in hexanes, 0.804 mmol). After stirring at −78 °C for 1 h, the reaction mixture was poured into sat. aq. potassium sodium tartrate solution (6 mL) and stirred at RT for 1 h. The separated aqueous layer was extracted with dichloromethane (2 × 6 mL), then the combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (SiO_2, petrol/ether, 95:5) afforded the *title compound* as a colourless oil (53 mg, 52%). R_f 0.30 (petrol/ether, 95:5); ν_{max} (thin film)/cm^{-1} 2945m, 1754s, 1724s, 1453w, 1116m, 1055m, 956m; δ_H (400 MHz, $CDCl_3$) 1.96 (2 H, quin, *J* 7.0 Hz, C(3)H_2), 1.98 (3 H, s, CH_3), 2.48 (2 H, td, *J* 7.0 Hz, 1.5 Hz, C(2)H_2), 2.62 (2 H, t, *J* 7.0 Hz, C(4)H_2), 5.88 (1 H, s, C(3′)H), 7.06 (1 H, s, C(5′)H), 9.75 (1 H, t, *J* 1.5 Hz, C(1)H); δ_C (100 MHz, $CDCl_3$) 9.8 (CH_3), 20.6 (C(3)), 27.2 (C(4)), 43.0 (C(2)), 108.4

(C(3′)), 120.5 (C(4′)), 137.7 (C(5′)), 154.9 (C(2′)), 202.1 (C(1)); HRMS (EI$^+$) found 152.0840, $C_9H_{12}O_2$ (M^+) requires 152.0832.

Bis[4-(4-methylfuran-2-yl)butyl]amine (3)

A solution of amine **7** (650 mg, 4.24 mmol) and aldehyde **30** (538 mg, 3.54 mmol) in methanol (10 mL) was stirred at RT for 4 h. $NaBH_4$ (214 mg, 5.66 mmol) was added and the reaction mixture was stirred for a further 40 min before diluting with aq. NaOH solution (20 mL, 1.0 M). Methanol was removed *in vacuo*, the aqueous layer diluted with water (100 mL) and extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with brine (150 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (SiO, EtOAc/MeOH/aq. NH_3 (18 M), 95:5:1) afforded the *title compound* as a pale yellow oil (823 mg, 81%). R_f 0.41 (EtOAc/MeOH/aq. NH_3 (18 M), 100:10:1); ν_{max} (thin film)/cm^{-1} 2929s, 2862m, 1618w, 1552m, 1458m, 1387w, 1120m, 946m; δ_H (400 MHz, $CDCl_3$) 1.49−1.56 (4 H, m, 2 × C(2)H_2), 1.60−1.68 (4 H, m, 2 × C(3)H_2), 1.97 (6 H, d, *J* 1.0 Hz, 2 × CH_3), 2.58 (4 H, t, *J* 7.0 Hz, 2 × C(4)H_2), 2.60 (4 H, t, *J* 7.0 Hz, 2 × C(1)H_2), 5.85 (2 H, s, 2 × C(3′)H), 7.04 (2 H, q, *J* 1.0 Hz, 2 × C(5′)H); δ_C (100 MHz, $CDCl_3$) 9.8 (2 × CH_3), 25.9 (2 × C(3)), 28.0 (2 × C(4)), 29.6 (2 × C(2)), 49.7 (2 × C(1)), 107.7 (2 × C(3′)), 120.4 (2 × C(4′)), 137.3 (2 × C(5′)), 156.2 (2 × C(2′)); HRMS (ESI$^+$) found 290.2109, $C_{18}H_{28}NO_2$ (MH^+) requires 290.2115.

Bis[4-(4-methylfuran-2-yl)butyl]carbamic acid *tert*-butyl ester (9)

To a solution of amine **3** (810 mg, 2.80 mmol) in THF/H_2O (16 mL, 3:1) was added triethylamine (0.504 mL, 3.64 mmol) and di-*tert*-butyl dicarbonate (794 mg, 3.64 mmol). The reaction mixture was stirred at RT for 2 h then diluted with water (40 mL) and the THF removed *in vacuo*. The aqueous layer was extracted with dichloromethane (3 × 60 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (SiO_2, petrol/ether, 94:6) afforded the *title compound* as a colourless oil (954 mg, 88%). R_f 0.40 (petrol/ether, 9:1); ν_{max} (thin film)/cm^{-1} 2930m, 1693s, 1417m, 1366m, 1254w, 1164s, 799w; δ_H (400 MHz, $CDCl_3$) 1.43 (9 H, s, $C(CH_3)_3$), 1.53−1.61 (8 H, m, 2 × $C(2)H_2$ and 2 × $C(3)H_2$), 1.97 (6 H, d, *J* 1.0 Hz, 2 × CH_3), 2.58 (4 H, t, *J* 7.0 Hz, 2 × $C(4)H_2$), 3.15 (4 H, bs, 2 × $C(1)H_2$), 5.84 (2 H, s, 2 × C(3′)H), 7.04 (2 H, q, *J* 1.0 Hz, 2 × C(5′)H); δ_C (100 MHz, $CDCl_3$) 9.8 (2 × CH_3), 25.3 (2 × C(3)), 27.8 (2 × C(4)), 28.0 (2 × C(2)), 28.5 ($C(\mathit{C}H_3)_3$), 46.7 (2 × C(1)), 79.1 ($\mathit{C}(CH_3)_3$), 107.7 (2 × C(3′)), 120.4 (2 × C(4′)), 137.3 (2 × C(5′)), 155.6 (C=O), 156.0 (2 × C(2′)); HRMS (ESI$^+$) found 412.2445, $C_{23}H_{35}NNaO_4$ (MNa^+) requires 412.2458.

Bis[4-(2-methoxy-4-methyl-5-oxo-2,5-dihydrofuran-2-yl)butyl]carbamic acid *tert*-butyl ester (SI-2)

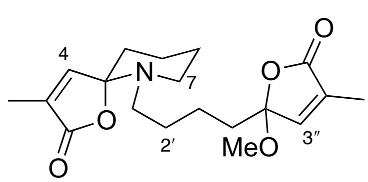
Oxygen was bubbled through a stirred solution of Rose Bengal (7.01 mg, 7.2 μmol, 10^{-4} M) and carbamate **9** (940 mg, 2.41 mmol) in methanol (72 mL) for 2 min. Maintaining the stream of oxygen, the solution was cooled to 0 °C and irradiated (Exo-Terra PT-2056 200 W lamp) for 1.5 h. The solvent was removed *in vacuo*, the resulting pink residue dissolved in pyridine (12 mL), acetic anhydride (0.228 mL, 2.41 mmol) added and the reaction mixture was stirred at RT for 3 h. The mixture was diluted with ethyl acetate (120 mL), the organic layer washed successively with water (120 mL), sat. aq. $CuSO_4$ solution (2 × 120 mL), brine (120 mL), then dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (SiO_2, petrol/ether, 1:3) afforded the *title compound* as a colourless viscous oil apparently as a single diastereomer (1.10 g, 94%). R_f 0.20 (petrol/ether, 1:1); ν_{max} (thin film)/cm^{-1} 2938w, 1768s, 1687m, 1418w, 1366w, 1317w, 1154m, 959m; δ_H (400 MHz, $CDCl_3$) 1.31−1.38 (4 H, m, 2 × $C(3)H_2$), 1.43 (9 H, s, $C(CH_3)_3$), 1.46−1.53 (4 H, m, 2 × $C(2)H_2$), 1.87 (4 H, t, *J* 8.5 Hz, 2 × $C(4)H_2$), 1.96 (6 H, d, *J* 1.5 Hz, 2 × CH_3), 3.12 (4 H, bs, 2 × $C(1)H_2$), 3.18 (6 H, s, 2 × OCH_3), 6.71 (2 H, q, *J* 1.5 Hz, 2 × C(3′)H); δ_C (125 MHz, $CDCl_3$) 10.5 (2 × CH_3), 20.7 (2 × C(3)), 28.0 (2 × C(2)), 28.4 ($C(\mathit{C}H_3)_3$), 36.9 (2 × C(4)), 46.4 (2 × C(1)), 50.9 (2 × OCH_3), 79.2 ($\mathit{C}(CH_3)_3$), 109.0 (2

× C(2′)), 133.9 (2 × C(4′)), 145.8 (2 × C(3′)), 155.5 (NC=O), 171.3 (2 × C(5′)); HRMS (ESI$^+$) found 504.2560, $C_{25}H_{39}NNaO_8$ (MNa^+) requires 504.2568.

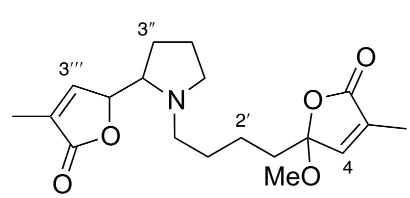
Bis[4-(2-methoxy-4-methyl-5-oxo-2,5-dihydrofuran-2-yl)butyl]amine (10)

To a solution of methoxybutenolide **SI-2** (100 mg, 0.208 mmol) in dichloromethane (1.4 mL) at 0 °C was added bromotrimethylsilane (0.260 mL, 1.97 mmol). The reaction mixture was stirred at RT for 5 h then diluted with sat. aq. $NaHCO_3$ solution (14 mL) and the aqueous layer extracted with ethyl acetate (3 × 14 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (SiO_2, $CHCl_3$/MeOH/aq. NH_3 (18 M), 95:5:1) afforded the *title compound* apparently as a single diastereomer as a yellow oil (63.0 mg, 80%). R_f 0.41 ($CHCl_3$/MeOH/aq. NH_3 (18 M), 100:10:1); ν_{max} (thin film)/cm^{-1} 2941m, 1764s, 1457w, 1319m, 1152m, 960m, 761w; δ_H (400 MHz, $CDCl_3$) 1.44−1.52 (4 H, m, 2 × C(3)H_2), 1.78−1.92 (8 H, m, 2 × C(2)H_2 and 2 × C(4)H_2), 1.96 (6 H, d, *J* 1.5 Hz, 2 × CH_3), 2.84 (4 H, t, *J* 8.5 Hz, 2 × C(1)H_2), 3.17 (6 H, s, 2 × OCH_3), 6.77 (2 H, q, *J* 1.5 Hz, 2 × C(3′)H); δ_C (100 MHz, $CDCl_3$) 10.6 (2 × CH_3), 20.9 (2 × C(3)), 26.6 (2 × C(2)), 36.9 (2 × C(4)), 47.9 (2 × C(1)), 51.0 (2 × OCH_3), 108.8 (2 × C(2′)), 134.1 (2 × C(4′)), 145.9 (2 × C(3′)), 171.3 (2 × C(5′)); HRMS (ESI$^+$) found 382.2214, $C_{20}H_{32}NO_6$ (MH^+) requires 382.2224.

6-[4-(2-Methoxy-4-methyl-5-oxo-2,5-dihydrofuran-2-yl)butyl]-3-methyl-1-oxa-6-azaspiro[4.5]dec-3-en-2-one (11) and **5-Methoxy-3-methyl-5-{4-[2-(4-methyl-5-oxo-2,5-dihydrofuran-2-yl)pyrrolidin-1-yl]butyl}-5*H*-furan-2-one (12)**



(11)



(12)

Concentrated H_2SO_4 (11.2 μL, 0.210 mmol) was added to a solution of methoxybutenolide **10** (100 mg, 0.262 mmol) in dichloromethane (2 mL) and the reaction mixture was stirred at RT for 5 d. The mixture was diluted with sat. aq. $NaHCO_3$ solution (20 mL) and the aqueous layer extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (SiO_2, petrol:ether, 1:3) afforded the *spirocycle* **11** as an inseparable mixture of diastereomers as a colourless oil (30.2 mg, 33%). R_f 0.40 (ether); ν_{max} (thin film)/cm^{-1} 2941m, 1763s, 1445w, 1311m, 1157m, 944m; δ_H (400 MHz, $CDCl_3$) 1.23−1.39 (4 H, m, C(2′)H_2 and C(3′)H_2), 1.60−1.75 (6 H, m, C(8)H_2, C(9)H_2 and C(10)H_2), 1.78−1.85 (2 H, m, C(4′)H_2), 1.91 (3 H, d, *J* 1.5 Hz, C(3)CH_3), 1.96 (3 H, d, *J* 1.5 Hz, C(4″)H_3), 2.30−2.47 (2 H, m, C(1′)H_2), 2.75 (2 H, bs, C(7)H_2), 3.17 (3 H, s, OCH_3), 6.70 (1 H, q, *J* 1.5 Hz, C(3″)H), 6.71 (1 H, q, *J* 1.5 Hz, C(4)H); δ_C (100 MHz, $CDCl_3$) 10.6 (C(4″)*C*H_3), 10.7 (C(3)*C*H_3), 20.8 (C(8)), 21.0 (C(3′)), 25.1 (C(9)), 27.6 (C(2′)), 36.1 (C(10)), 37.2 (C(4′)), 47.1 (C(7)), 49.8 (C(1′)), 51.0 (OCH_3), 101.8 (C(5)), 109.0 (C(2″)), 131.5 (C(3)), 133.9 (C(4″)), 145.9 (C(3″)), 149.8 (C(4)), 171.4 (C(5″)), 173.0 (C(2)); HRMS (ESI$^+$) found 372.1775, $C_{19}H_{27}NNaO_5$ (MNa^+) requires 372.1781. Further elution (EtOAc → EtOAc/MeOH, 98:2) afforded the *pyrrolidine derivative* **12** as an inseparable mixture of diastereomers as a colourless oil (22.0 mg, 24%). R_f 0.23 (EtOAc/MeOH, 98:2); ν_{max} (thin film)/cm^{-1} 2956w, 1761s, 1445w, 1048w, 620w; δ_H (500 MHz, $CDCl_3$) 1.32−1.41 (1 H, m, C(2′)*H*H′), 1.42−1.55 (3 H, m, C(2′)H*H′*, C(3′)*H*H′ and C(4″)*H*H′), 1.59−1.67 (2 H, m, C(3′)H*H′* and C(3″)*H*H′), 1.69−1.80 (2 H, m, C(4″)H*H′* and C(3″)H*H′*), 1.81−1.89 (2 H, m, C(1′)H_2), 1.93 (3 H, d, *J* 1.5 Hz, C(4‴)CH_3), 1.96 (3 H, d, *J* 1.5 Hz, C(3)CH_3), 2.18−2.28 (1 H, m, C(5″)*H*H′), 2.34−2.47 (1 H, m, C(4′)*H*H′), 2.77−2.92 (2 H, m, C(4′)H*H′*and C(2″)H), 3.05−3.15 (1 H, m, C(5″)H*H′*), 3.18 (3 H, s, OCH_3), 4.65−4.89 (1 H, m, C(2‴)H), 6.72 (1 H, q, *J* 1.5 Hz, C(4)H), 7.05 (1 H, quin, *J* 1.5 Hz, C(3‴)H); δ_C (125 MHz, $CDCl_3$) 10.5 (C(3)*C*H_3), 10.7 (C(4‴)*C*H_3), 21.1 (C(2′)), 23.8 (C(3″)), 25.8

(C(4″)), 28.7 (C(3′)), 37.2 (C(1′)), 50.9 (OCH_3), 54.1 (C(5″)), 55.0 (C(4′)), 65.2 (C(2″)), 83.3 (C(2‴)), 109.1 (C(5)), 131.1 (C(4‴)), 133.7 (C(3)), 145.9 (C(4)), 147.0 (C(3‴)), 171.4 (C(2)), 174.3 (C(5‴)); HRMS (ESI^+) found 372.1770, $C_{19}H_{27}NNaO_5$ (MNa^+) requires 372.1781.

Pandamarilactone-1 (SI-3)[2] and **pandamarilactonines A (SI-4)** and **B (SI-5)**[3]

[numbering as for (**11**) and (**12**), above]

Concentrated H_2SO_4 (27.9 µL, 0.524 mmol) was added to a solution of methoxybutenolide **10** (100 mg, 0.262 mmol) in dichloromethane (2 mL) and the reaction mixture was stirred at RT for 5 d. The mixture was diluted with sat. aq. $NaHCO_3$ solution (20 mL) and the aqueous layer extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography (SiO_2, petrol/ether, 1:3) afforded pandamarilactone-1 as a colourless oil (10.0 mg, 12%). R_f 0.40 (ether); ν_{max} (thin film)/cm^{-1} 2941m, 1749s, 1444w, 1308w, 1159w, 1055m, 990m, 897w; δ_H (500 MHz, $CDCl_3$) 1.48−1.57 (2 H, m, C(2′)H_2), 1.60−1.80 (6 H, m, C(8)H_2, C(9)H_2 and C(10)H_2), 1.90 (3 H, d, *J* 1.5 Hz, C(3)CH_3), 2.00 (3 H, s, C(4″)CH_3), 2.30 (2 H, app. q, *J* 7.0 Hz, C(3′)H_2), 2.37−2.53 (2 H, m, C(1′)H_2), 2.72−2.84 (2 H, m, C(7)H_2), 5.07 (1 H, t, *J* 8.0 Hz, C(4′)H), 6.71 (1 H, bs, C(4)H), 6.97 (1 H, d, *J* 1.5 Hz, C(3″)H); δ_C (125 MHz, $CDCl_3$) 10.5 (C(4″)*C*H_3), 10.7 (C(3)*C*H_3), 20.7 (C(8)), 23.9 (C(3′)), 25.0 (C(9)), 27.0 (C(2′)), 36.1 (C(10)), 47.1 (C(7)), 49.5 (C(1′)), 101.7 (C(5)), 113.9 (C(4′)), 129.2 (C(4″)), 131.5 (C(3)), 137.6 (C(3″)), 148.5 (C(2″)), 149.7 (C(4)), 171.0 (C(5″)), 172.9 (C(2)); HRMS (ESI^+) found 340.1530, $C_{18}H_{23}NNaO_4$ (MNa^+) requires 340.1519. Further elution (EtOAc → EtOAc/MeOH, 98:2) afforded pandamarilactonines A and B as an inseparable mixture (**SI-4**/**SI-5**, dr = 70:30) as a colourless oil (39.9 mg, 48%). In the NMR spectra of this product mixture, minor peaks were seen which were attributed to the alkene diastereomers pandamarilactonines C and D. R_f 0.25 (EtOAc/MeOH, 98:2); ν_{max} (thin film)/cm^{-1} 2950w, 1754s, 1051m, 991m, 758w; δ_H (500 MHz, $CDCl_3$) 1.37−1.84 (6 H, complex m, C(3′)H_2, C(3″)H2 and C(4″)H_2), 1.93 (3 H, d, *J* 1.5 Hz, C(4‴)CH_3), 1.99 (3 H, s, C(3)CH_3), 2.18−2.28 (1 H, m, C(5″)*H*H′), 2.33−2.51 (3 H, complex m, C(2′)H_2 and C(4′)*H*H′), 2.68−2.94 (2 H, complex m, C(4′)H*H′* and C(2″)H), 3.07−3.15 (1 H, m, C(5″)H*H′*), 4.70−4.73 and 4.77−4.83 (1 H, m, C(2‴)H in **SI-5** and **SI-4**, respectively), 5.16 and 5.18 (1 H, t, *J* 8.0 Hz, C(1′)H in **SI-5** and **SI-4**, respectively), 7.00 (1 H, d, *J* 1.5 Hz, C(4)H), 7.09 (1 H, quin, *J* 1.5 Hz, C(3‴)H); δ_C (125 MHz, $CDCl_3$) [peaks attributable to **SI-5** are starred] 10.5 (C(3)*C*H_3), 10.7/10.8* (C(4‴)*C*H_3), 23.8 (C(2′)), 24.0 (C(3″)), 25.7/27.1* (C(4″)), 28.3/28.4* (C(3′)), 54.2 (C(5″)), 55.0/55.8* (C(4′)), 65.2/66.3* (C(2″)), 83.4 (C(2‴)), 114.1 (C(1′)), 129.1 (C(3)), 130.8*/131.2 (C(4‴)), 137.7 (C(4)), 147.0/147.5* (C(3‴)), 148.6 (C(5)), 171.1 (C(2)), 174.3 (C(5‴)); HRMS (ESI$^+$) found 318.1692, $C_{18}H_{24}NO_4$ (MH^+) requires 318.1700.

10,10-Dideuteriopandamarilactone-1 (SI-6)

[numbering as for (**11**), above]

A sample of synthetic pandamarilactone-1 (10.0 mg, 0.0315 mmol) was dissolved in CD_3OD (0.5 mL) for characterisation. δ_H (500 MHz, CD_3OD) 1.59 (2 H, quin, *J* 7.0 Hz, C(2′)H_2), 1.71−1.75 (4 H, m, C(8)H_2 and C(9)H_2), 1.86 (3 H, d, *J* 1.5 Hz, C(3)CH_3), 1.95 (3 H, dd, *J* 1.5, 0.7 Hz, C(4″)CH_3), 2.32 (2 H, q, *J* 7.0 Hz, C(3′)H_2), 2.51 (2 H, t, *J* 7.0 Hz, C(1′)H_2), 2.83−2.86 (2 H, m, C(7)H_2), 5.27 (1 H, t, *J* 8.0 Hz, C(4′)H), 6.91 (1 H, q, *J* 1.5 Hz, C(4)H), 7.25 (1 H, q, *J* 1.5 Hz, C(3″)H); δ_C (125 MHz, CD_3OD) 10.3 (C(4″)*C*H_3), 10.9 (C(3)*C*H_3), 21.7 (C(8)), 24.7 (C(3′)), 25.9 (C(9)), 28.0 (C(2′)), 36.2 (1:2:3:2:1 quin, $^2J_{CD}$ 20.0 Hz, C(10)), 48.5 (C(7)), 50.8 (C(1′)), 107.7 (C(5)), 115.3 (C(4′)), 130.1 (C(4″)), 133.0 (C(3)), 139.7 (C(3″)), 150.3 (C(2″)), 151.0 (C(4)), 172.8 (C(5″)), 174.8 (C(2)); HRMS (ESI$^+$) found 342.1645, $C_{18}H_{21}D_2NNaO_4$ (MNa^+) requires 342.1645.

6-[4-(2-Hydroxy-4-methyl-5-oxo-2,5-dihydro-1*H*-pyrrol-2-yl)butyl]-3-methyl-1-oxa-6-azaspiro[4.5]dec-3-en-2-one (15)

[numbering as for (**11**), above]

A sample of synthetic pandamarilactone-1 (5.0 mg, 0.0158 mmol) was dissolved in ether (1.5 mL). 5% aq. H_2SO_4 (0.8 mL) was added and the mixture was stirred at RT for 10 min. TLC analysis showed the absence of pandamarilactone-1 in the ether layer. The ether layer was removed and the aqueous layer was rendered basic with conc. aq. NH_3 solution (0.7 mL). The aqueous layer was then extracted with chloroform (3 × 2.4 mL) and the combined organic layers were concentrated *in vacuo* to give a residue consisting of a mixture of pandamarilactone-1 and the hydroxylactam **15** (~1:1). Purification by flash chromatography [SiO_2, $CHCl_3$/MeOH/NH_3 (aq., 18 M), 95:5:1] afforded the *title compound* as a colourless oil (1.0 mg, 19%). R_f 0.50 [$CHCl_3$/MeOH/NH_3 (aq., 18 M), 100:10:1]; ν_{max} (thin film)/cm^{-1} 3328m, 2937m, 1745s, 1699s, 1659m, 1312m, 1156m; δ_H (700 MHz, CD_3OD) 1.21−1.33 (2 H, m, C(3′)H_2), 1.35−1.44 (2 H, m, C(2′)H_2), 1.68−1.78 (6 H, m, C(4′)H_2, C(8)H_2 and C(9)H_2), 1.81 (3 H, d, *J* 1.5 Hz, C(4″)CH_3), 1.88 (3 H, d, *J* 1.5 Hz, C(3)CH_3), 2.46 (2 H, t, *J* 7.0 Hz, C(1′)H_2), 2.79−2.86 (2 H, m, C(7)H_2), 6.57 (1 H, q, *J* 1.5 Hz, C(3″)H), 6.93 (1 H, q, *J* 1.5 Hz, C(4)H); δ_C (175 MHz, CD_3OD) 10.5 (C(4″)*C*H_3), 11.0 (C(3)*C*H_3), 21.8 (C(8)), 22.8 (C(3′)), 26.1 (C(9)), 29.0 (C(2′)), 38.9 (C(4′)), ~48 (obscured by CD_3OD, C(7)), 51.4 (C(1′)), 88.9 (C(2″)), 107.5 (C(5)), 133.2 (C(3)), 135.2 (C(4″)), 146.3 (C(3″)), 151.2 (C(4)), 175.0 (C(2)), 175.1 (C(5″)) [C(10) not seen]; HRMS (ESI$^+$) found 335.1957, $C_{18}H_{27}N_2O_4$ (MH^+) requires 335.1965.

^{13}C NMR data comparisons for pandamarilactone-1 ($CDCl_3$, ppm)

Green = identical
Amber = Δδ ±0.1 ppm
Red = Δδ –1.2 ppm

Lit. data[2] (1993)	Synthetic		Lit. data[4] (2005)
10.4	10.5	10.5	10.5
10.6	10.7	10.7	10.7
20.8	20.7	20.7	20.7
24.0	23.9	23.9	23.9
25.1	25.0	25.0	25.0
27.2	27.0	27.0	27.1
36.2	36.1	36.1	36.1
47.2	47.1	47.1	47.1
50.7	**49.5**	49.5	49.5
101.7	101.7	101.7	101.7
113.7	113.9	113.9	113.8
129.2	129.2	129.2	129.2
131.5	131.5	131.5	131.5
137.6	137.6	137.6	137.6
148.6	148.5	148.5	148.5
149.7	149.7	149.7	149.7
171.0	171.0	171.0	171.0
173.0	173.0	173.0	172.9

The data for synthetic pandamarilactone-1 show excellent correspondence with those reported in 2005[4] with no resonance differing by more than 0.1 ppm. The correspondence with the originally-reported data[2] is still very good, particularly in the low field region, apart from the resonance at 50.7/49.5 which most likely reflects an error in the original report.

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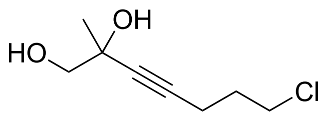
(4) Lopez, D. C.; Nonato, M. G. *Philippine J. Sci.* **2005**, *134*, 39.



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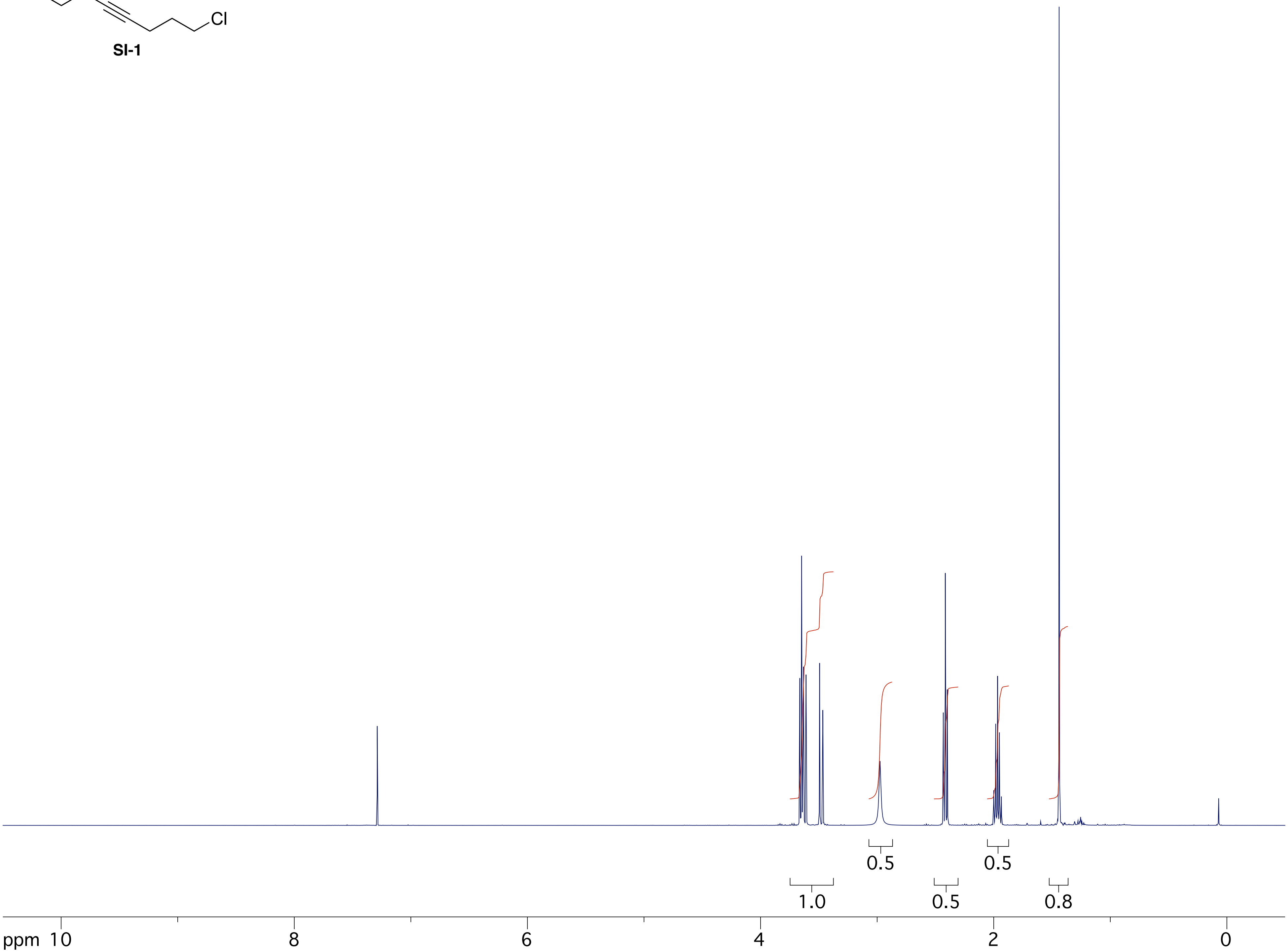

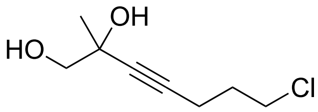

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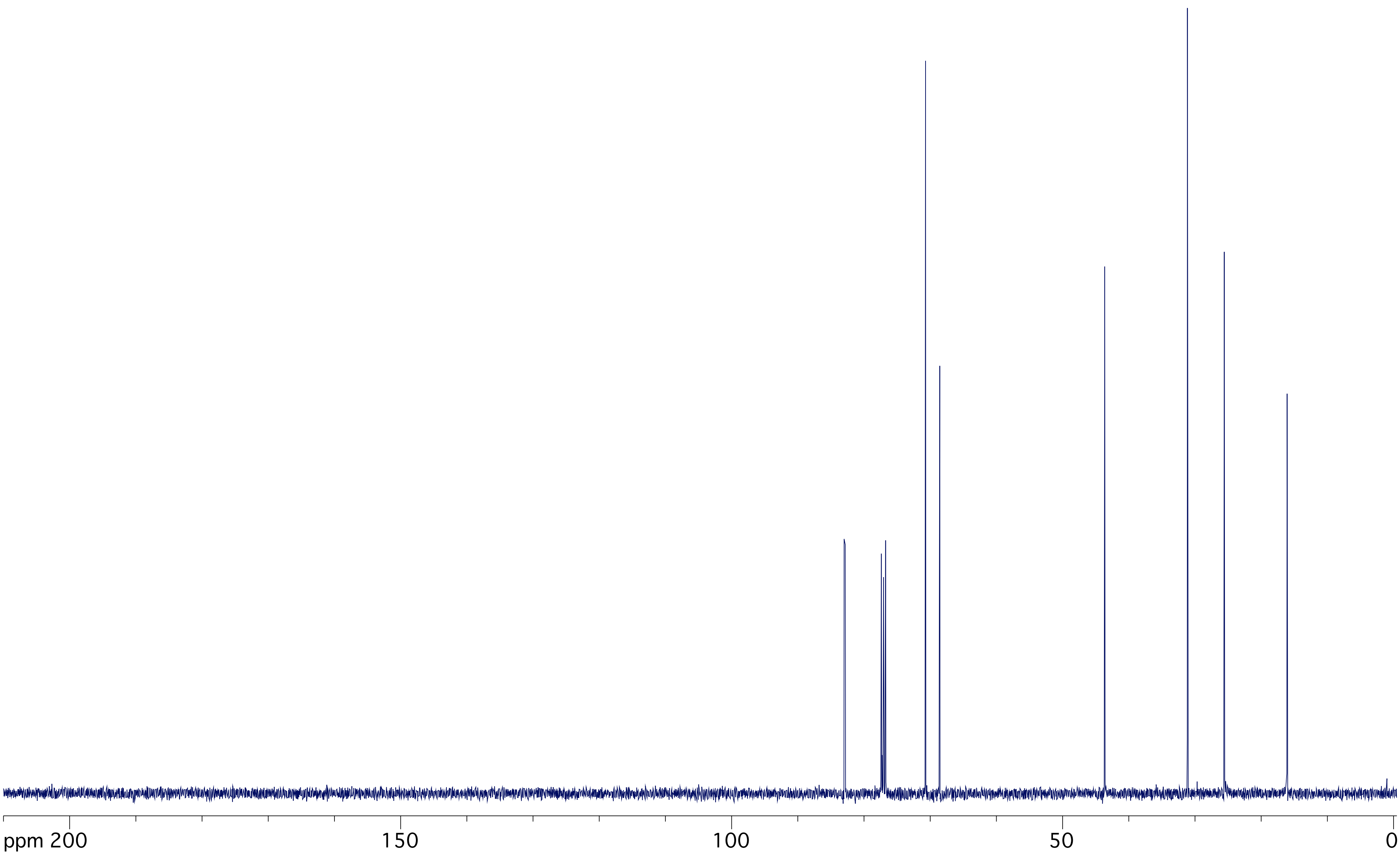

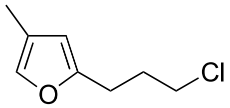

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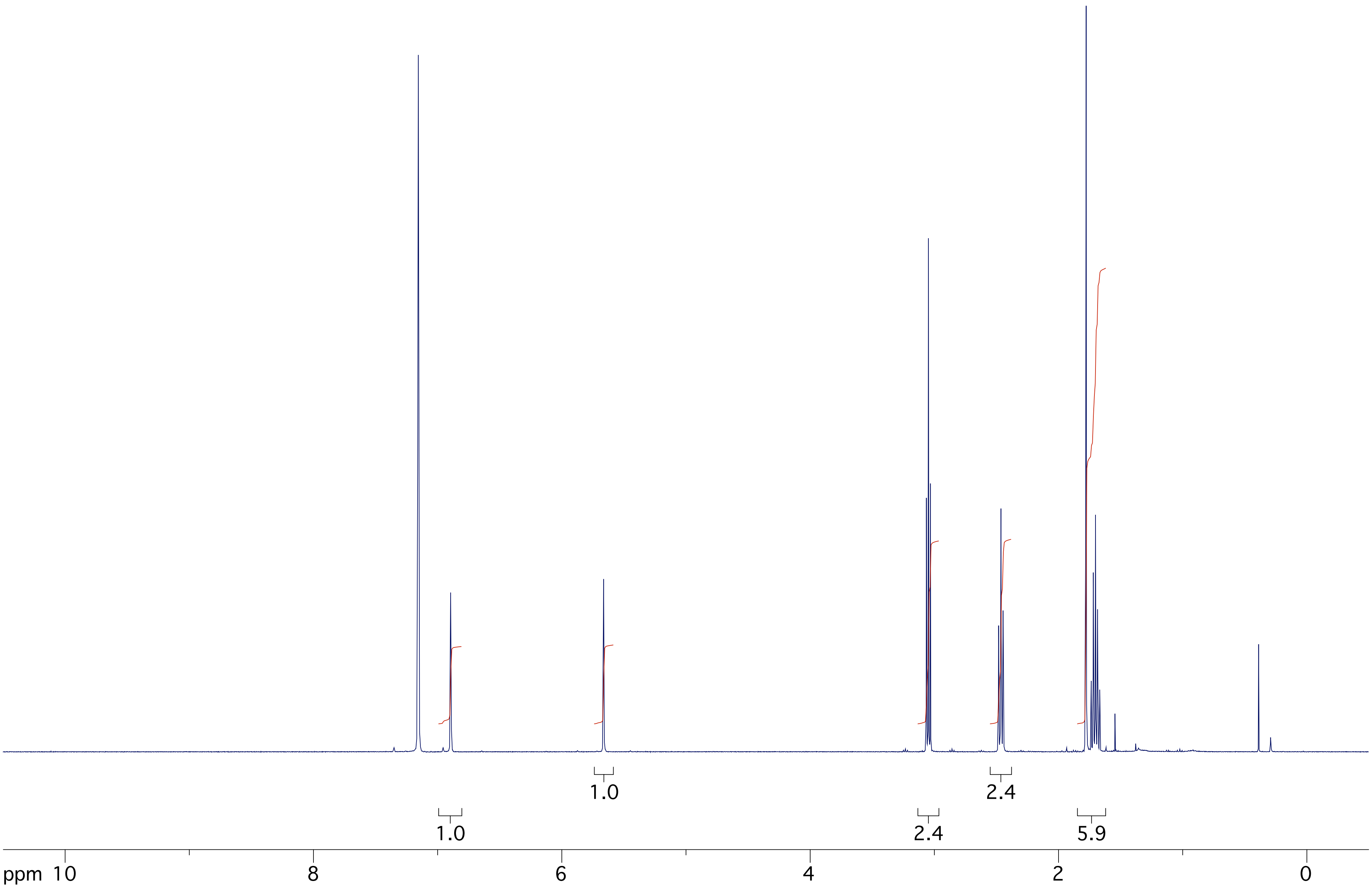

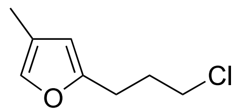

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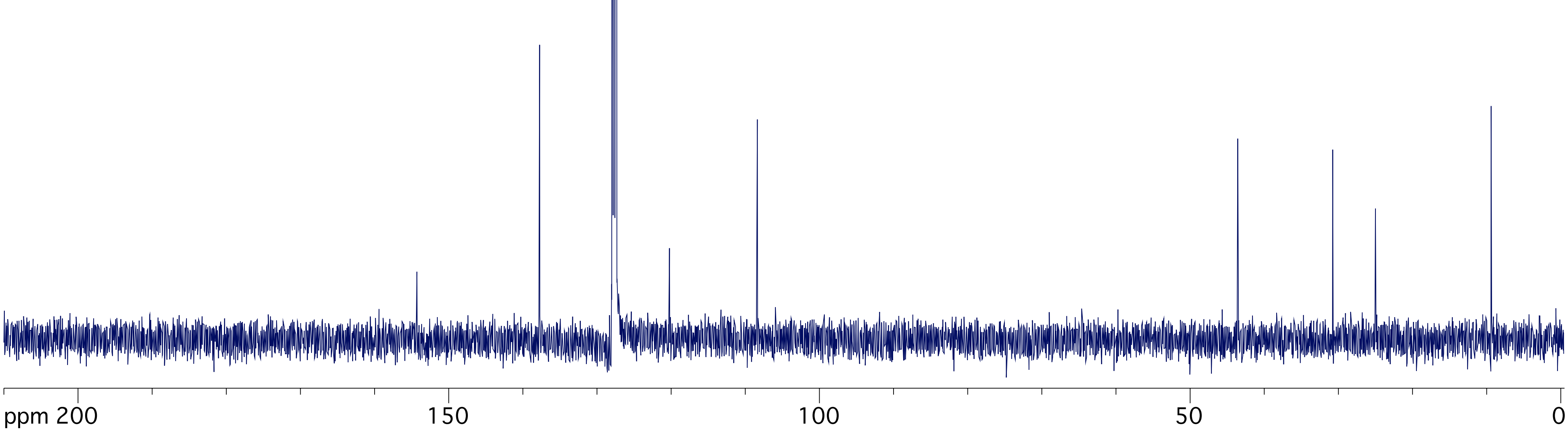

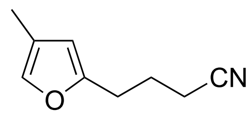

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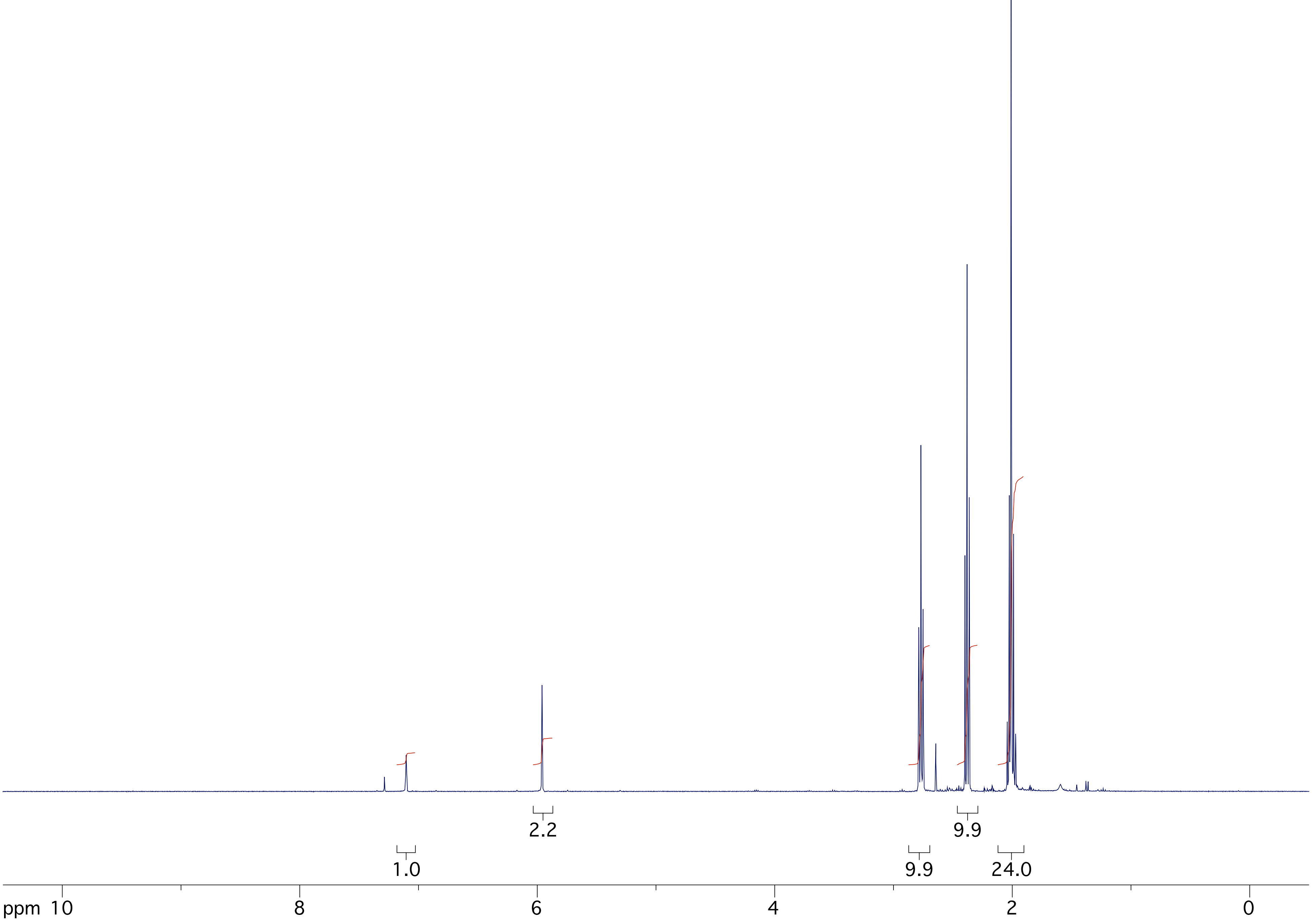

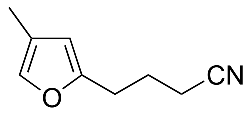

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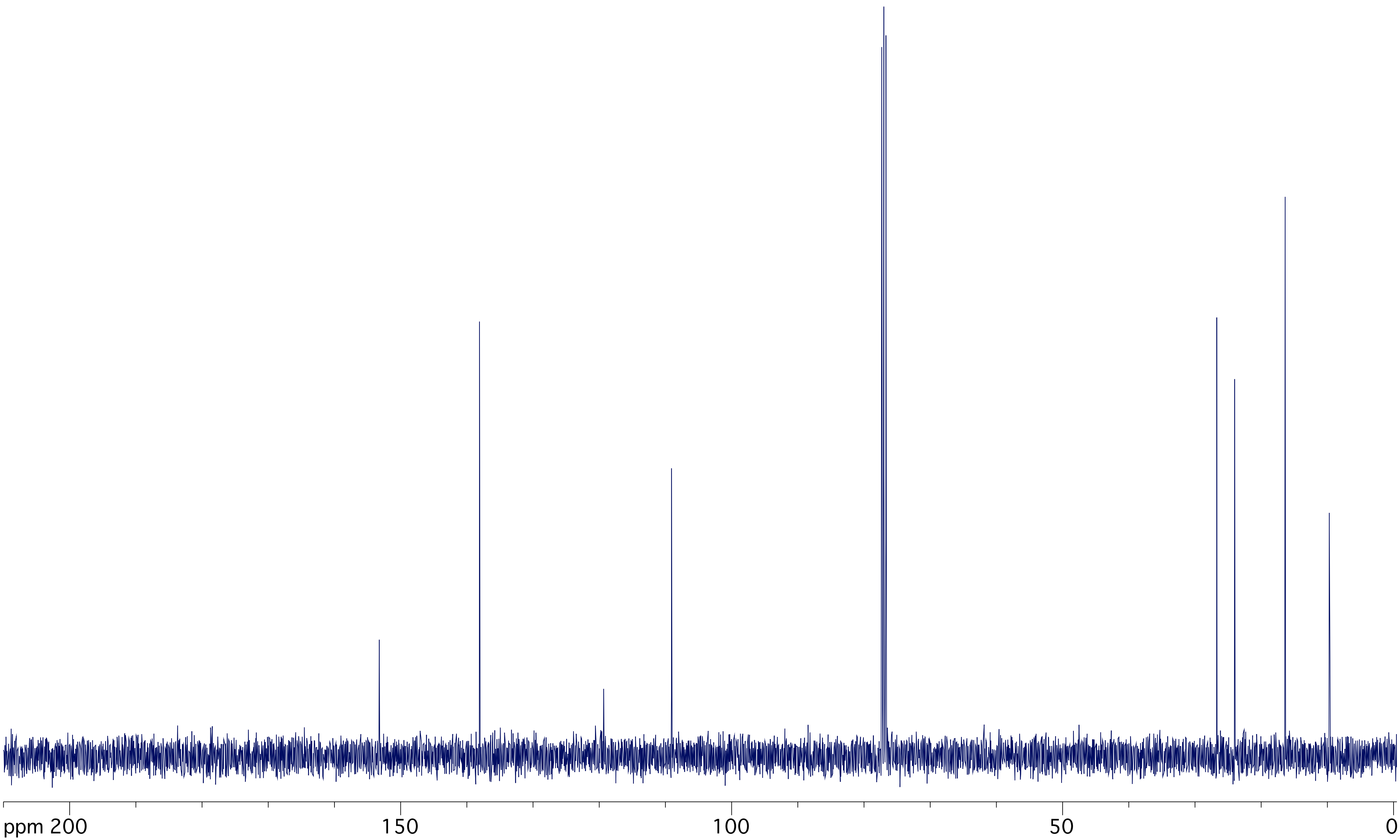

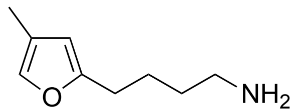

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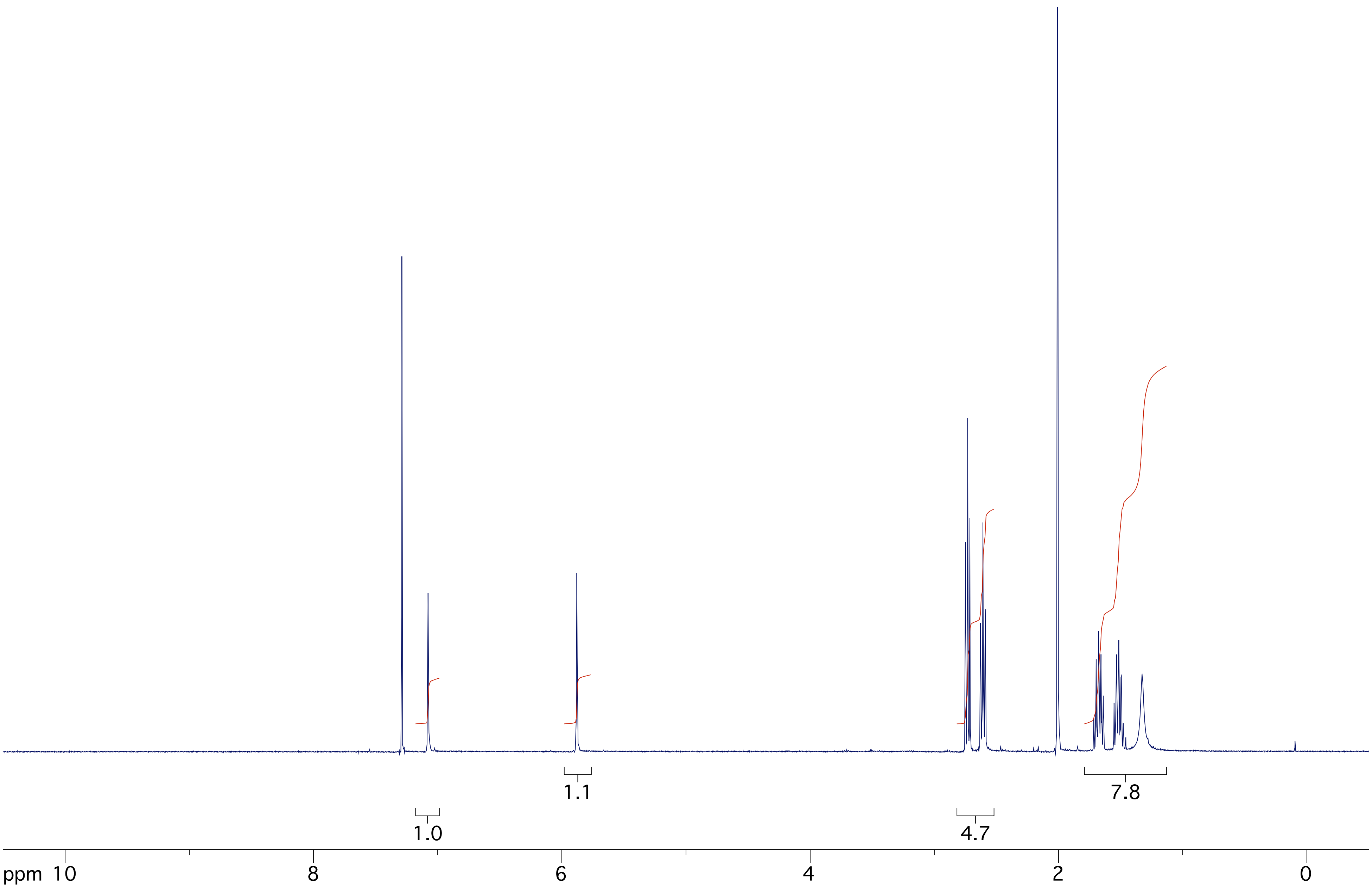

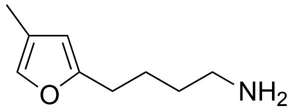

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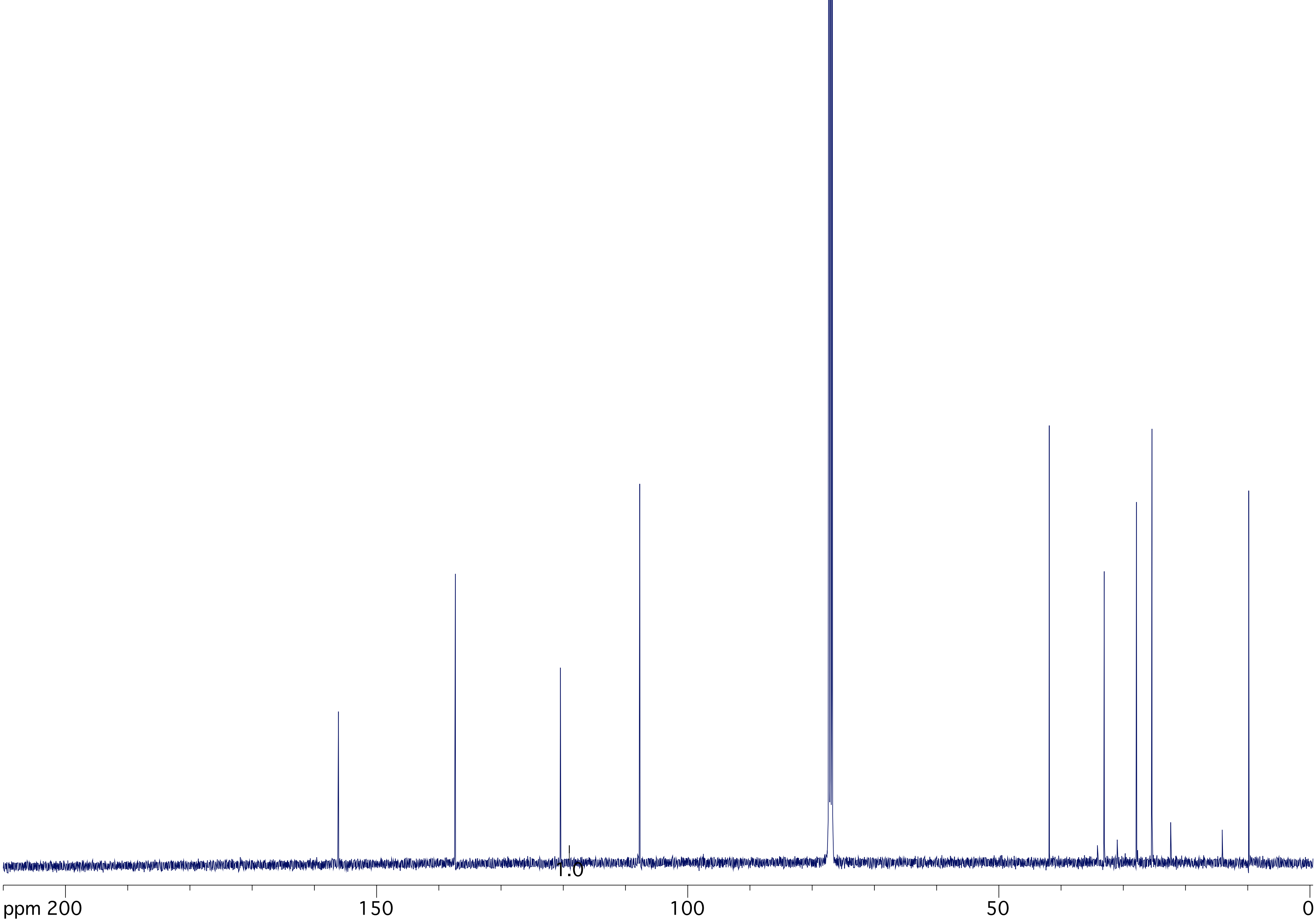

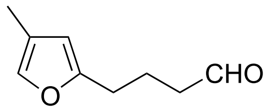

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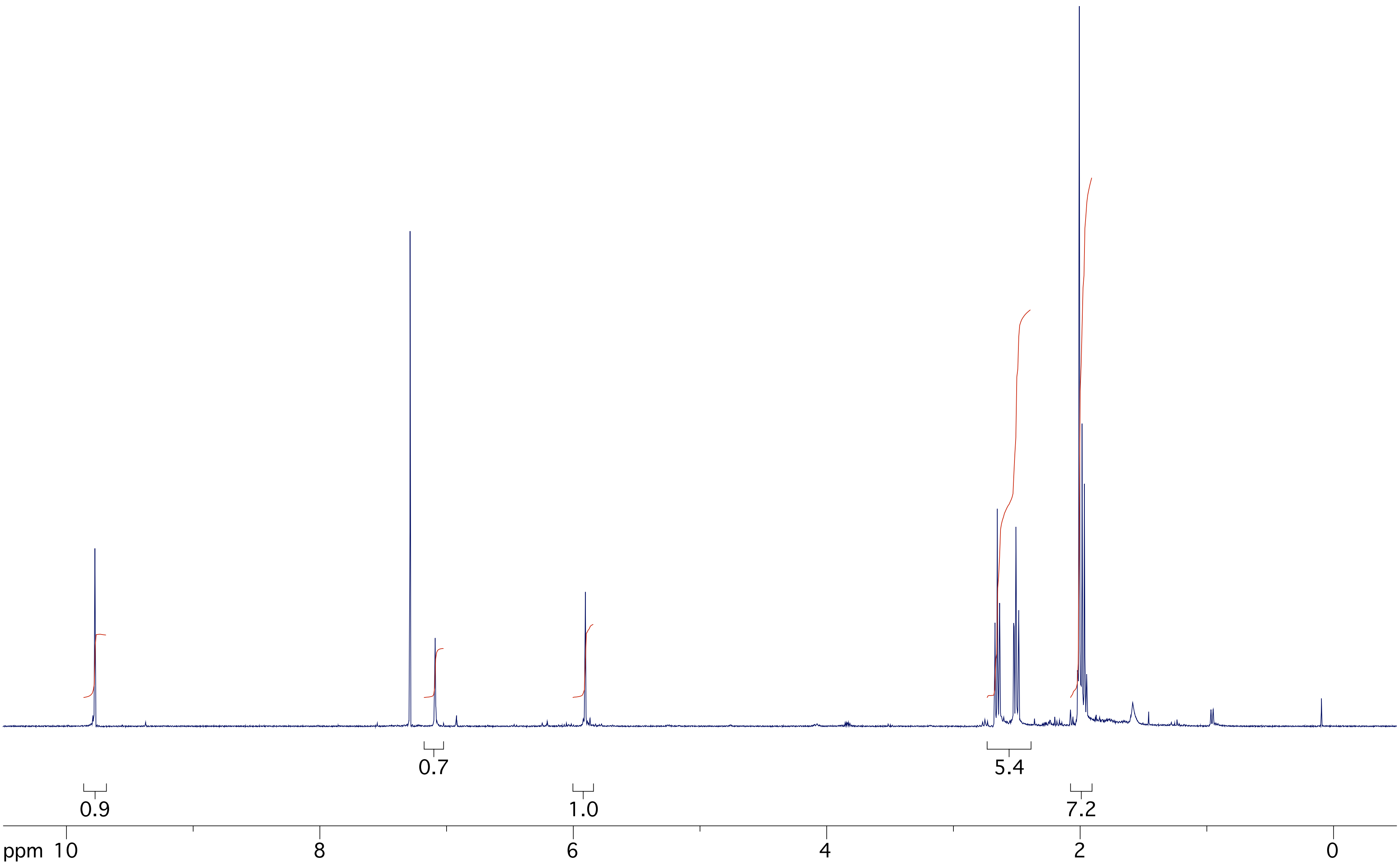

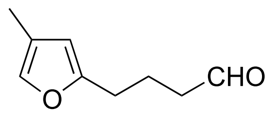

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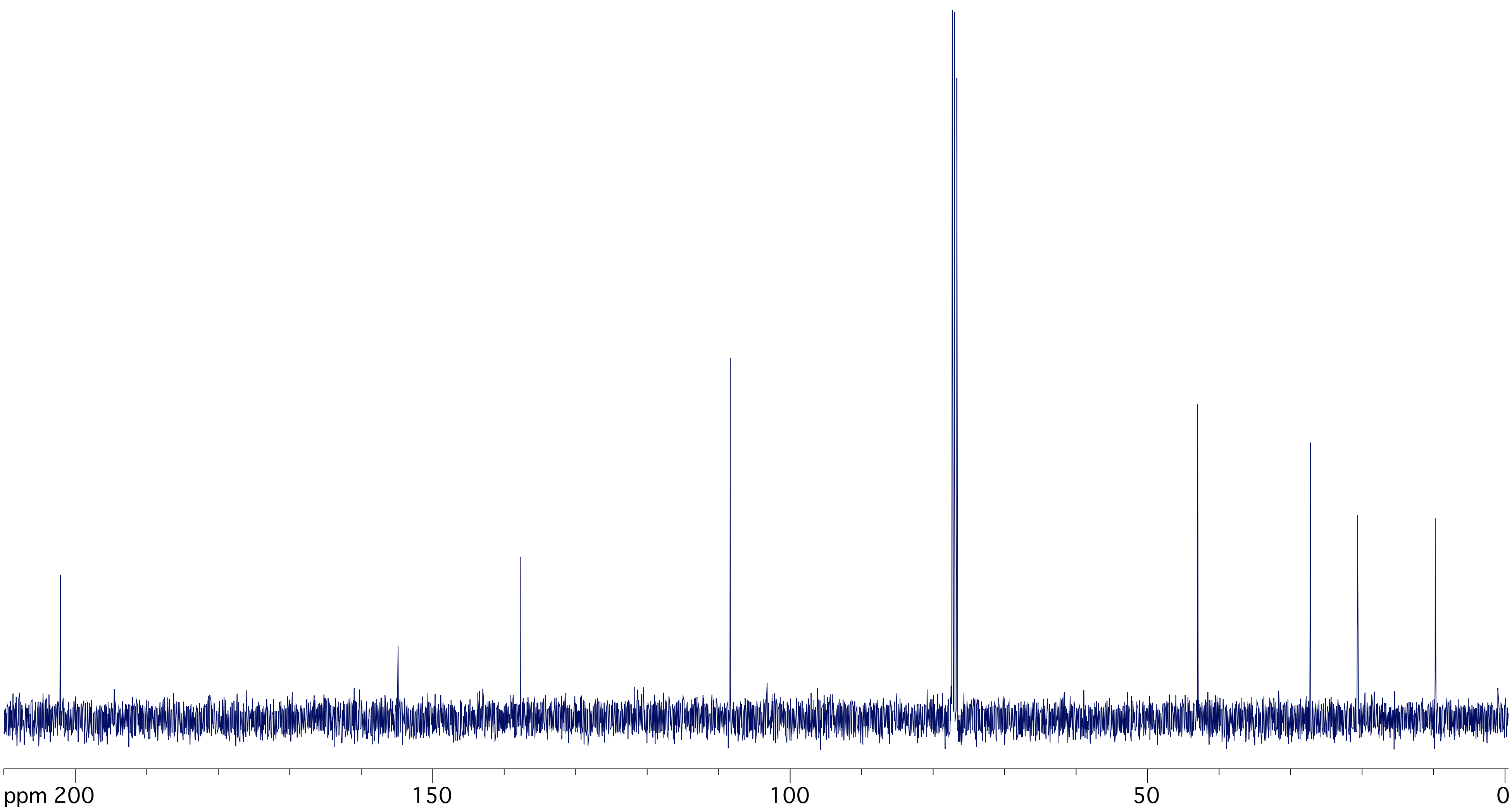

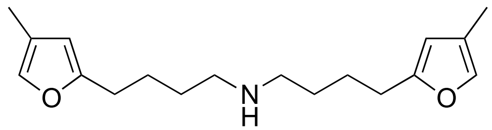

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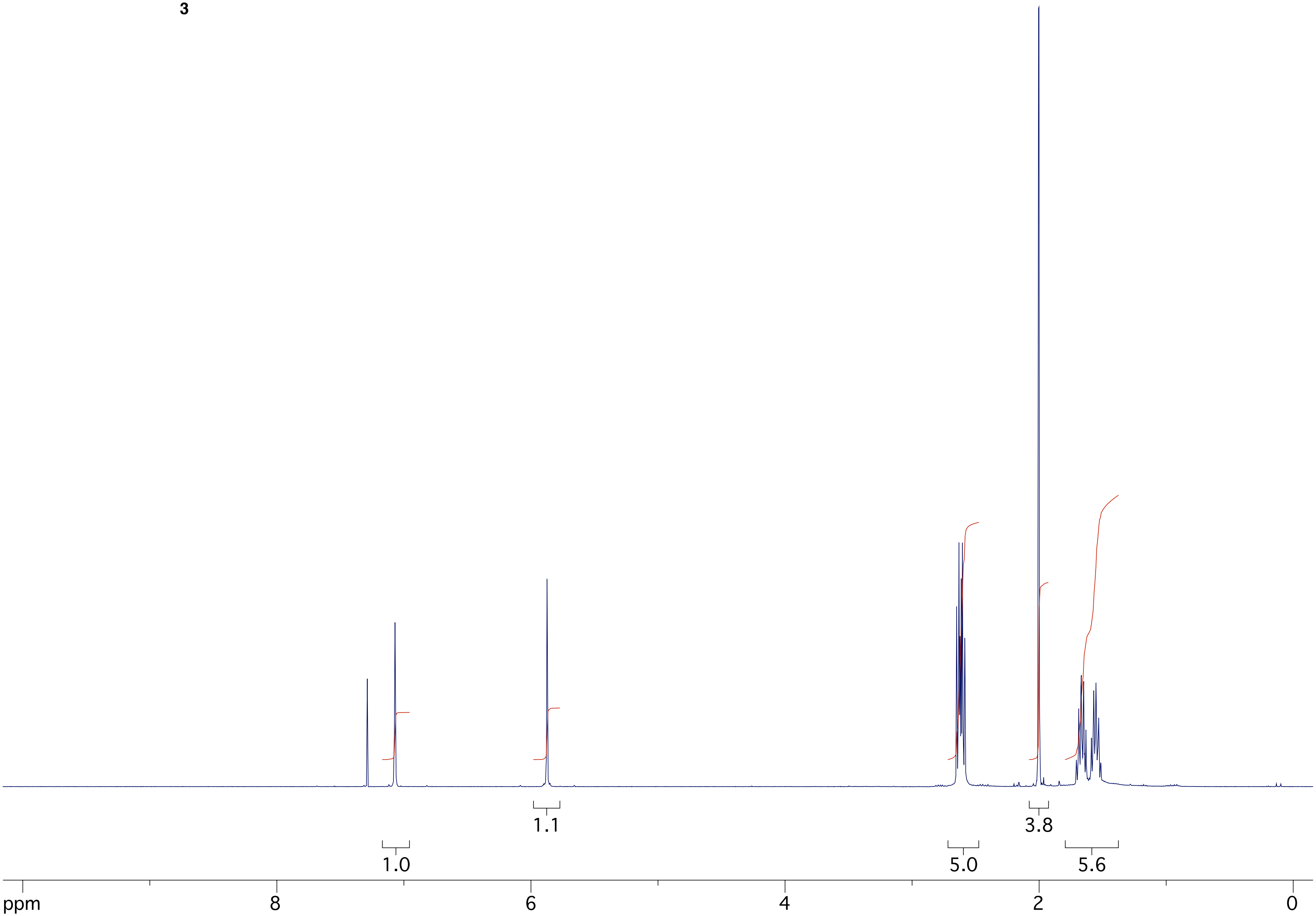

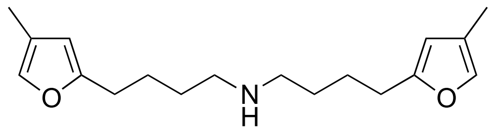

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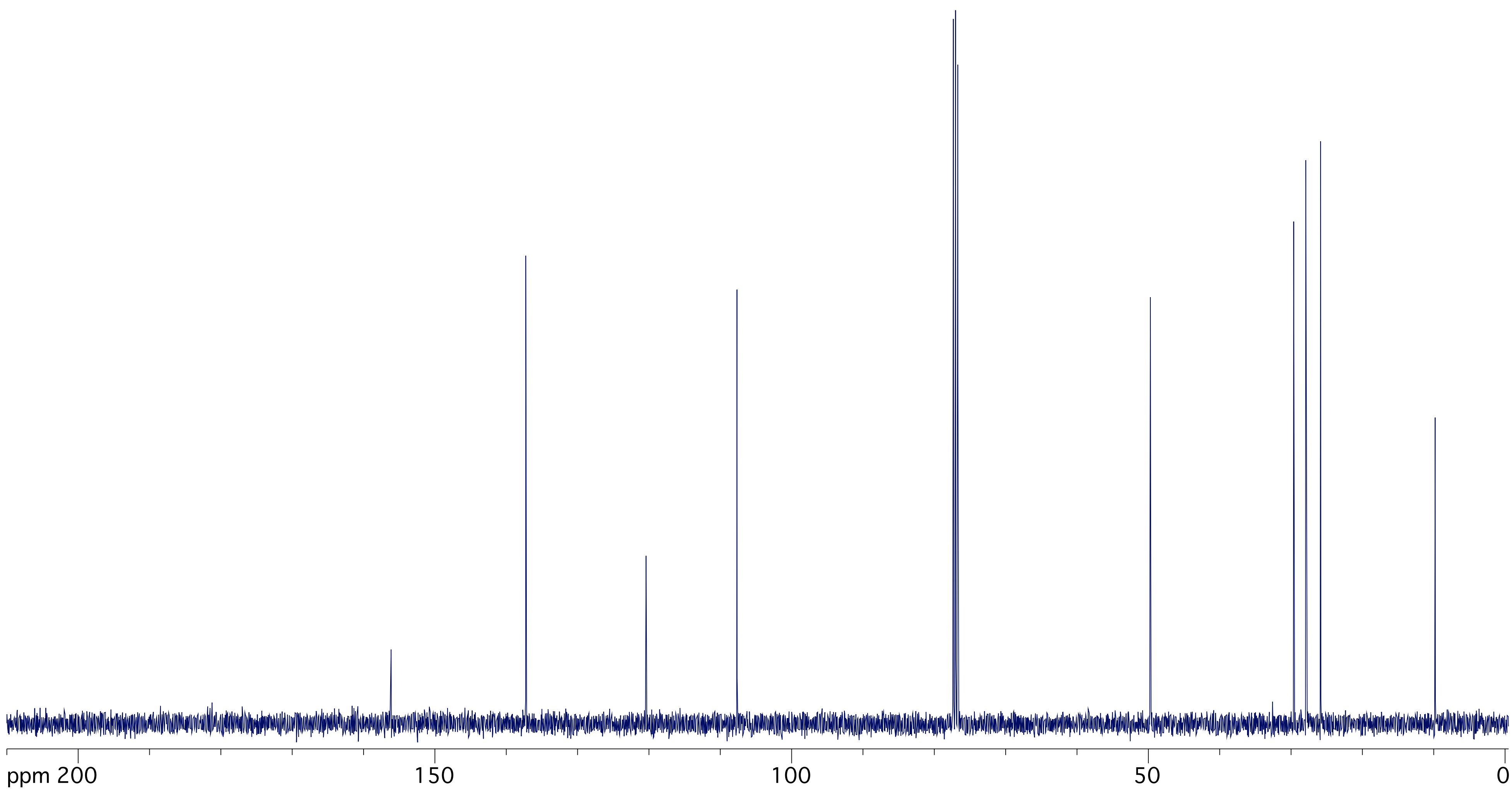

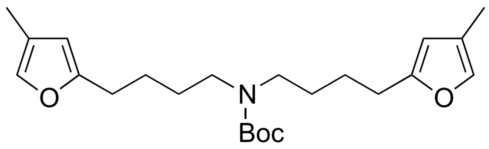

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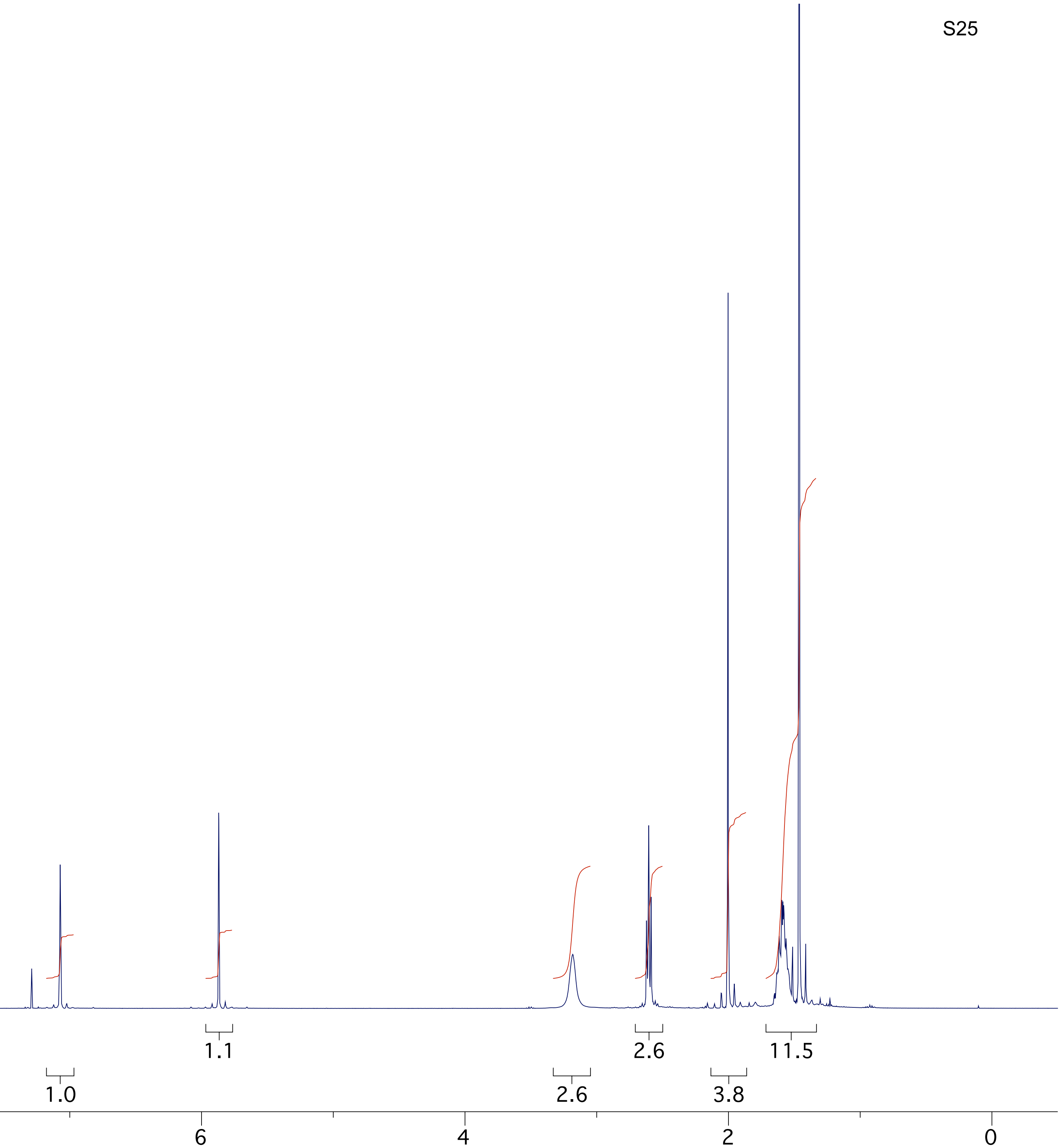

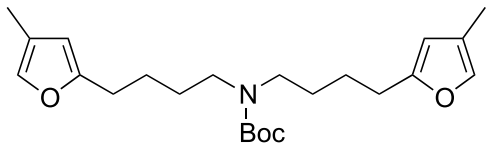

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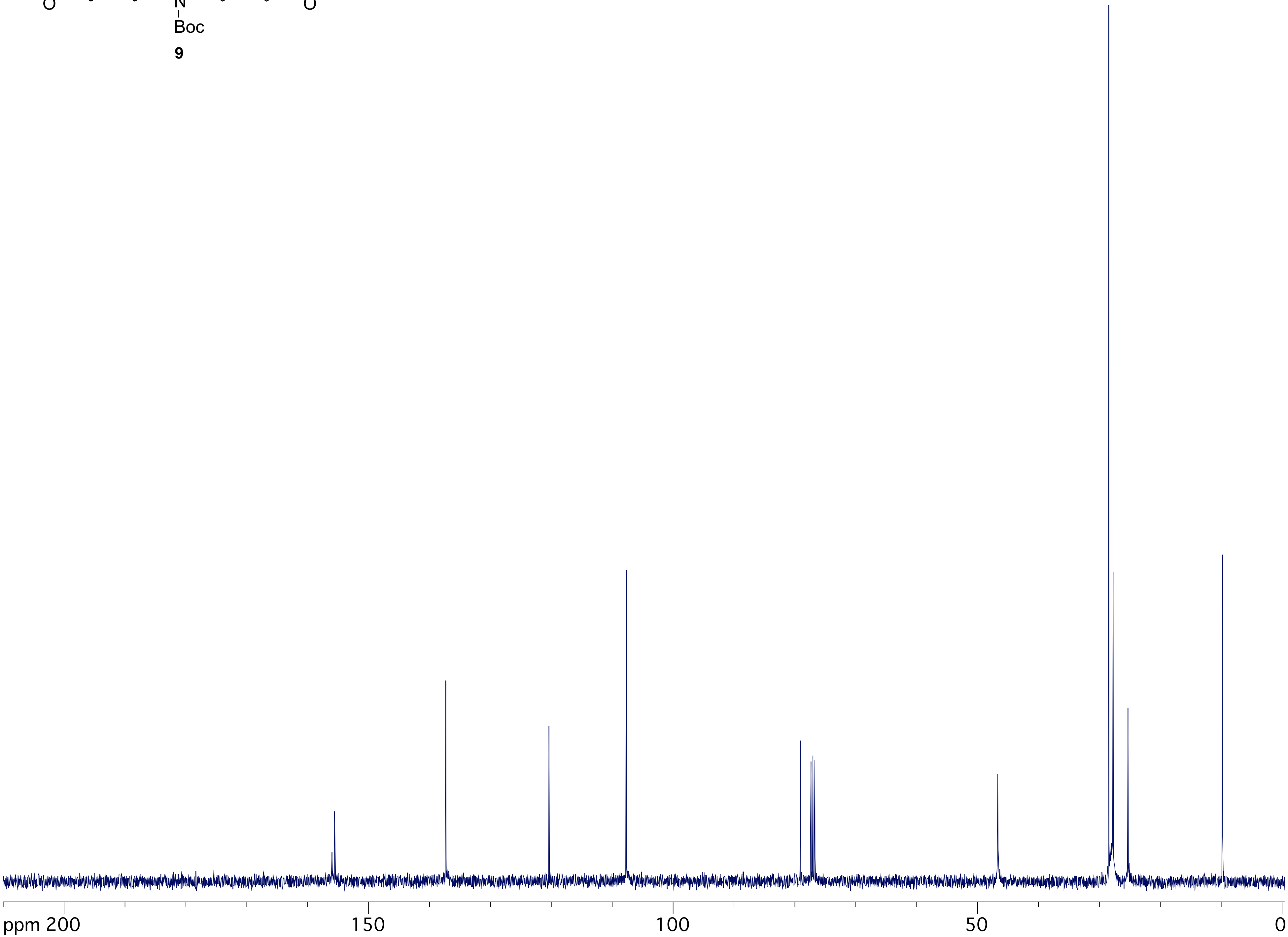

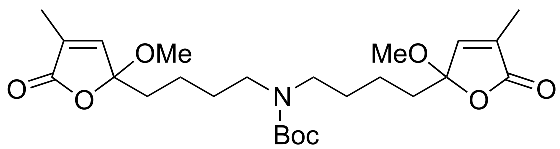

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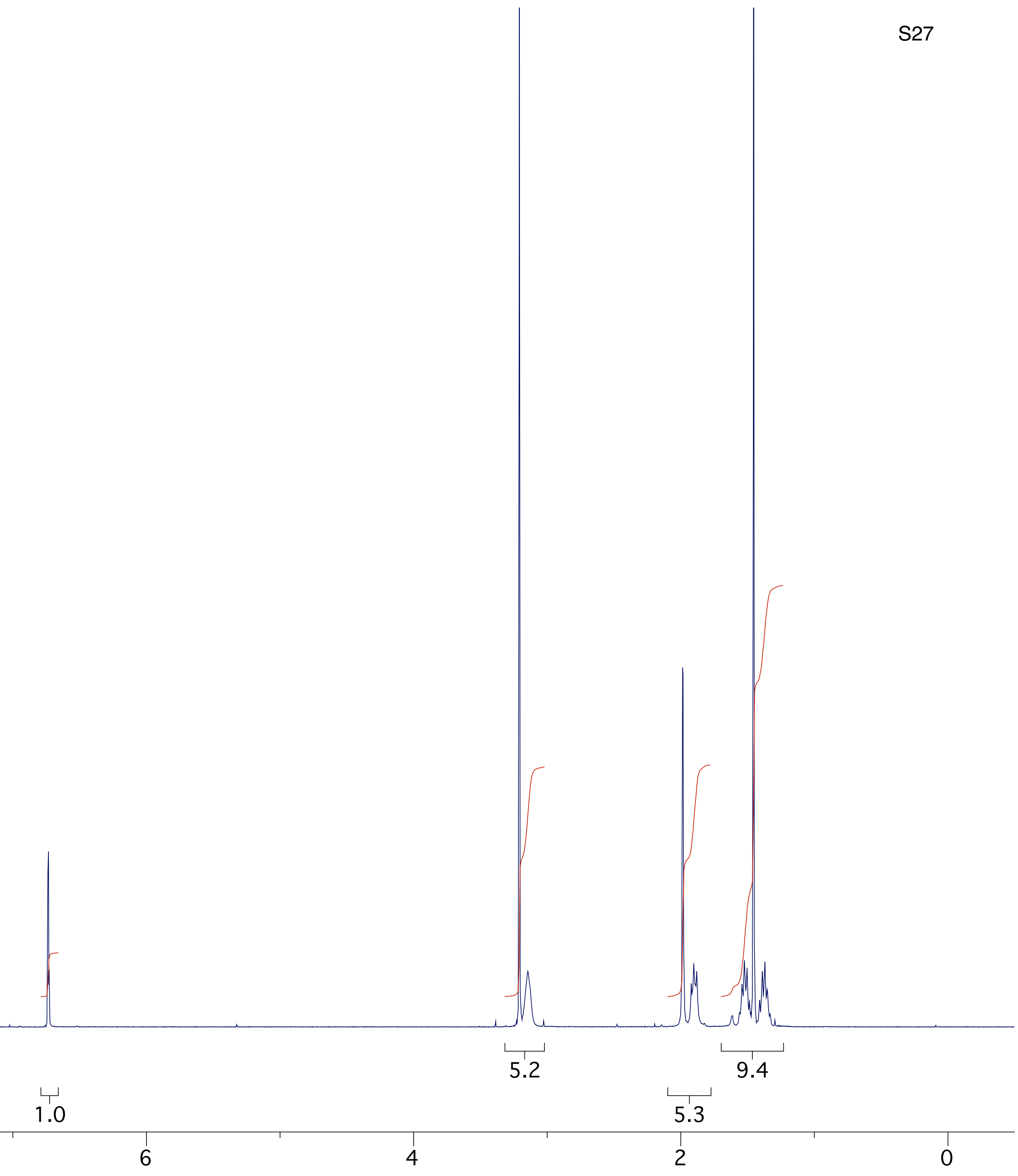

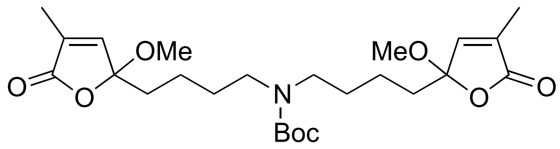

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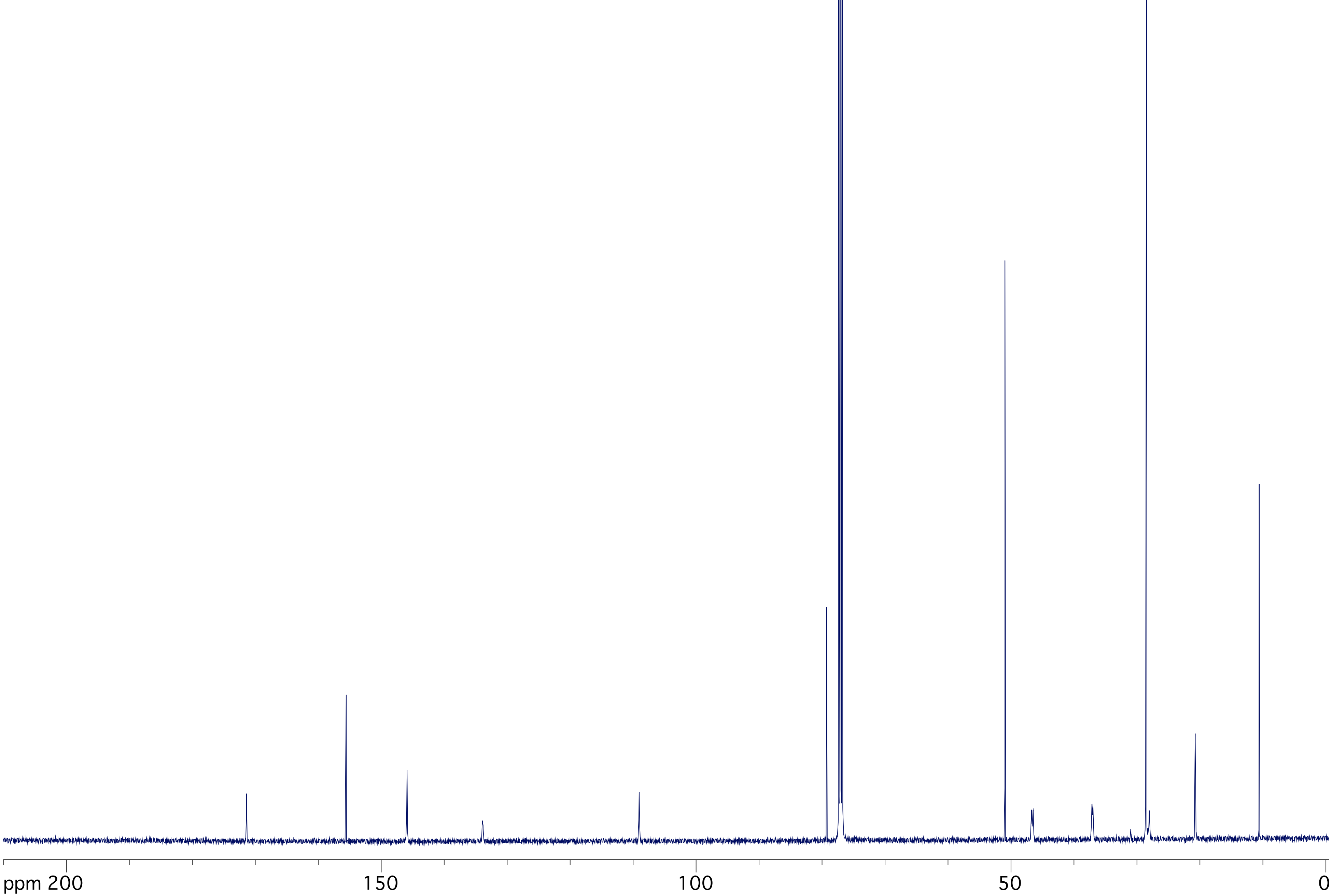

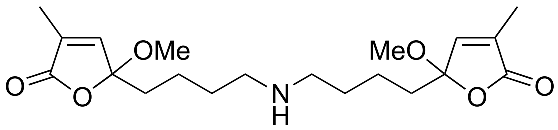

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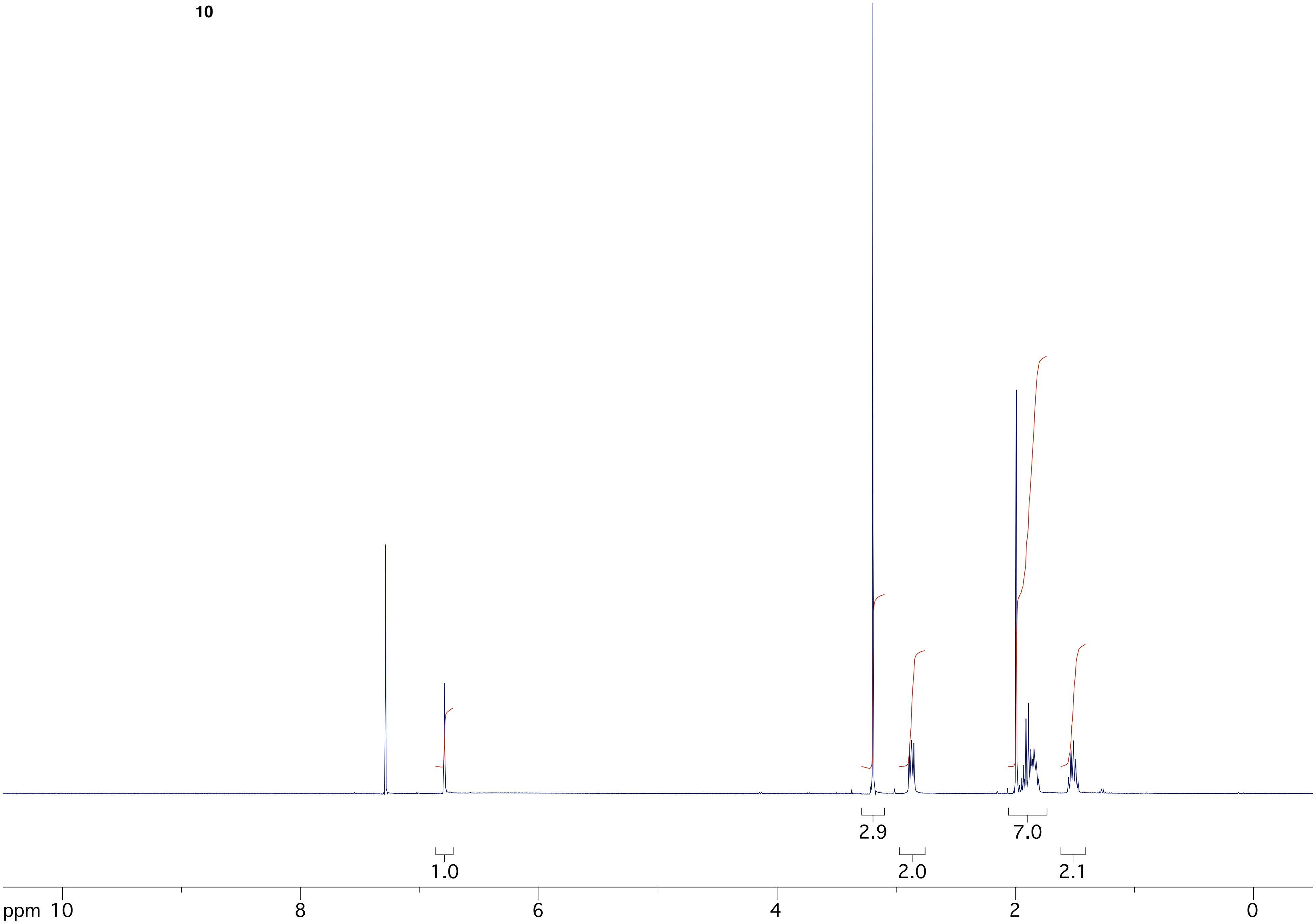

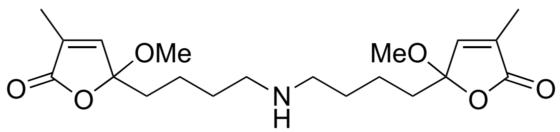

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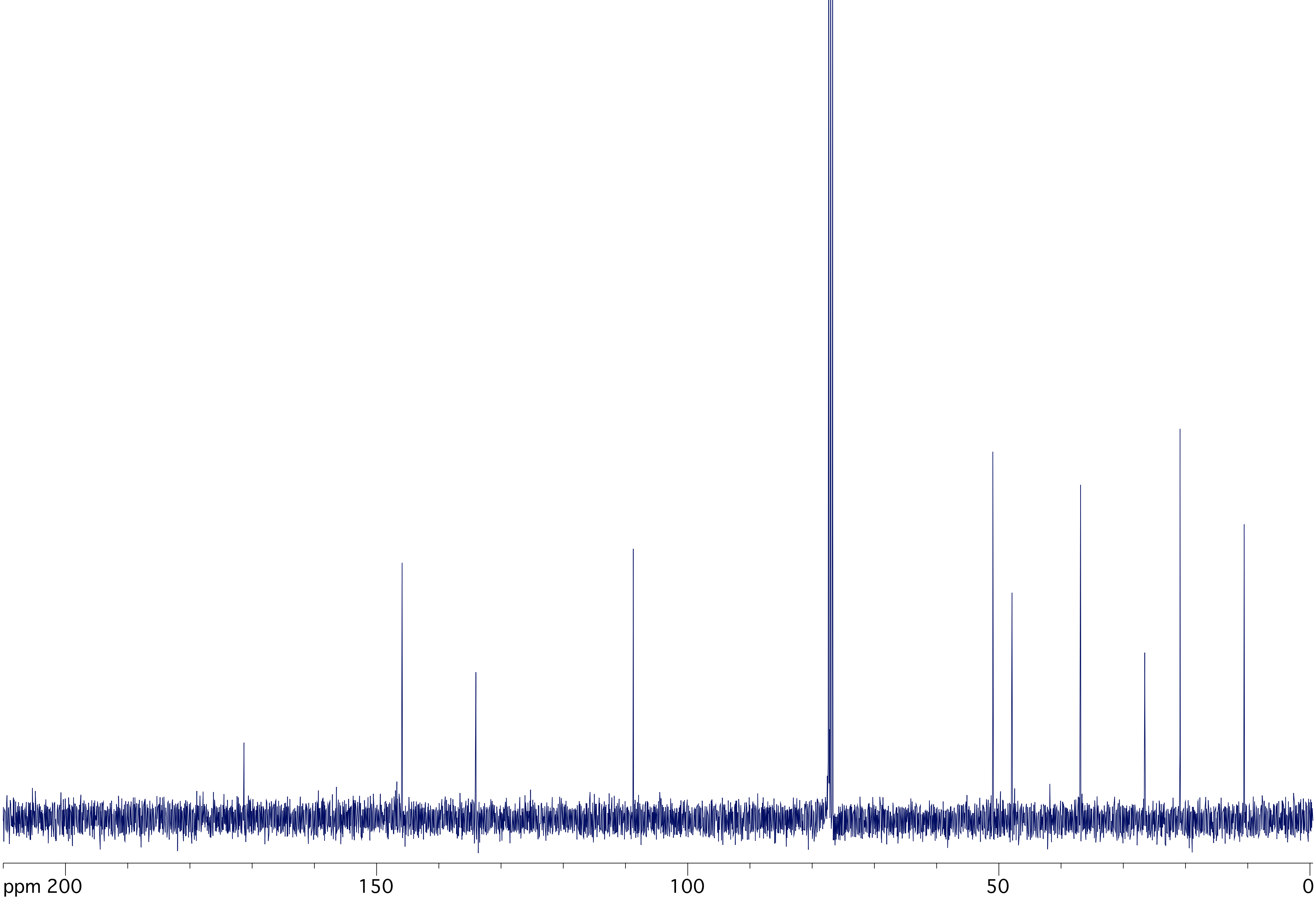

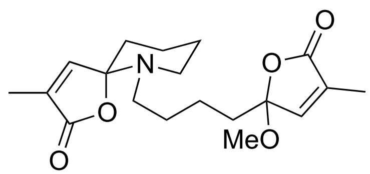

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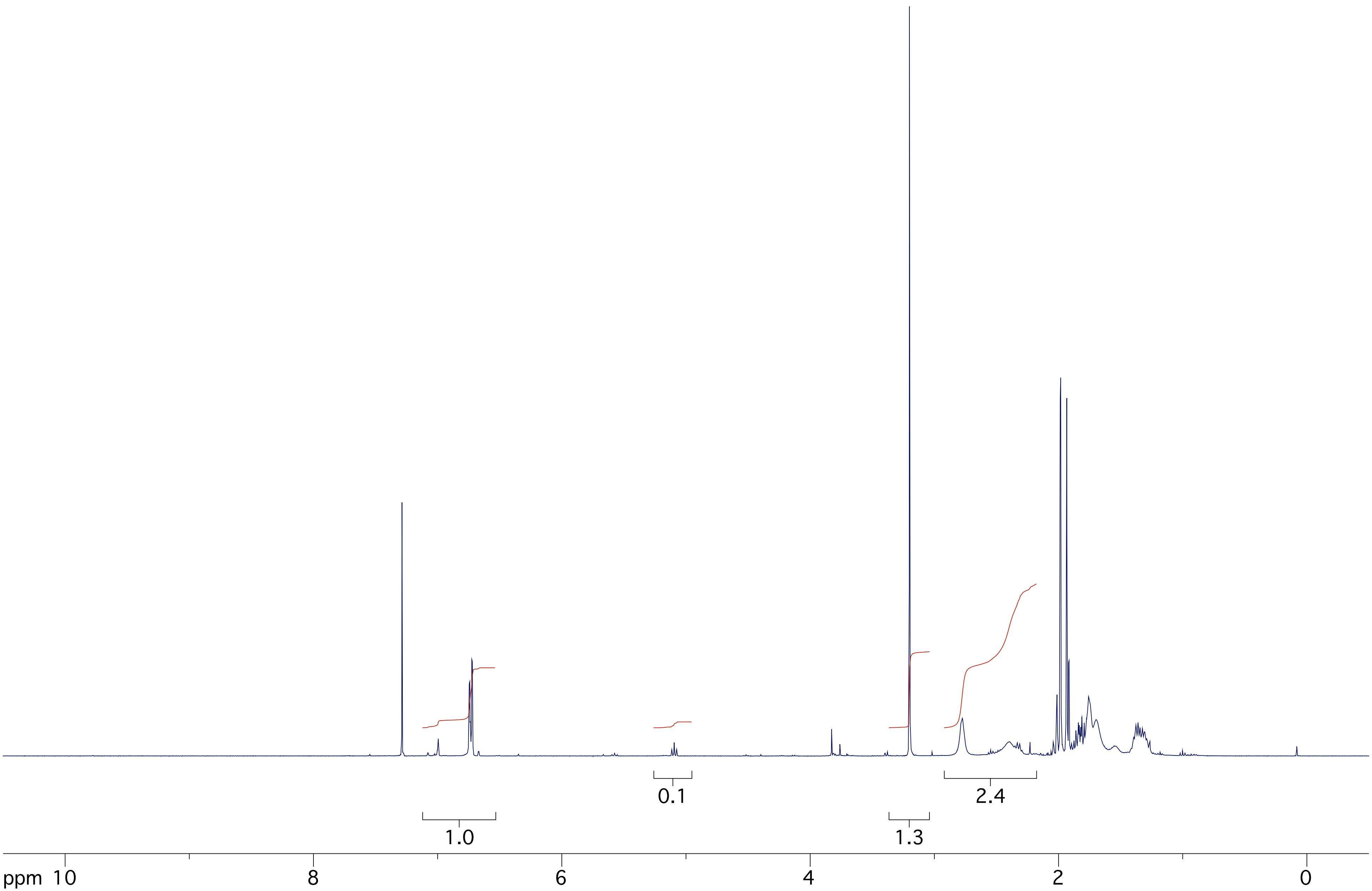

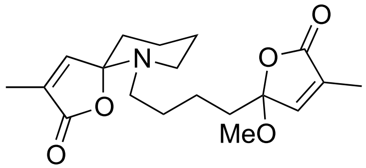

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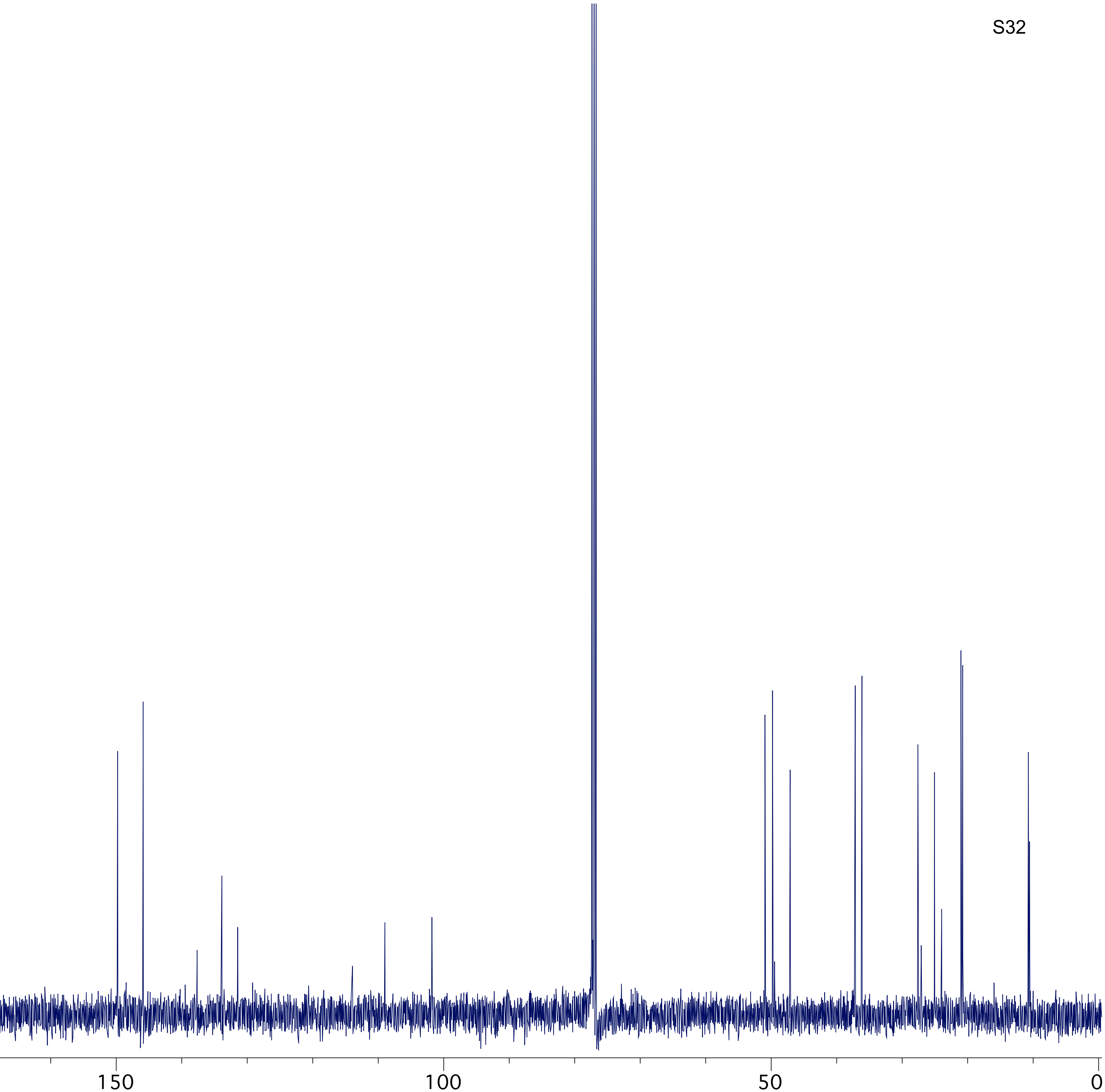
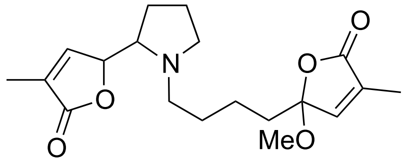
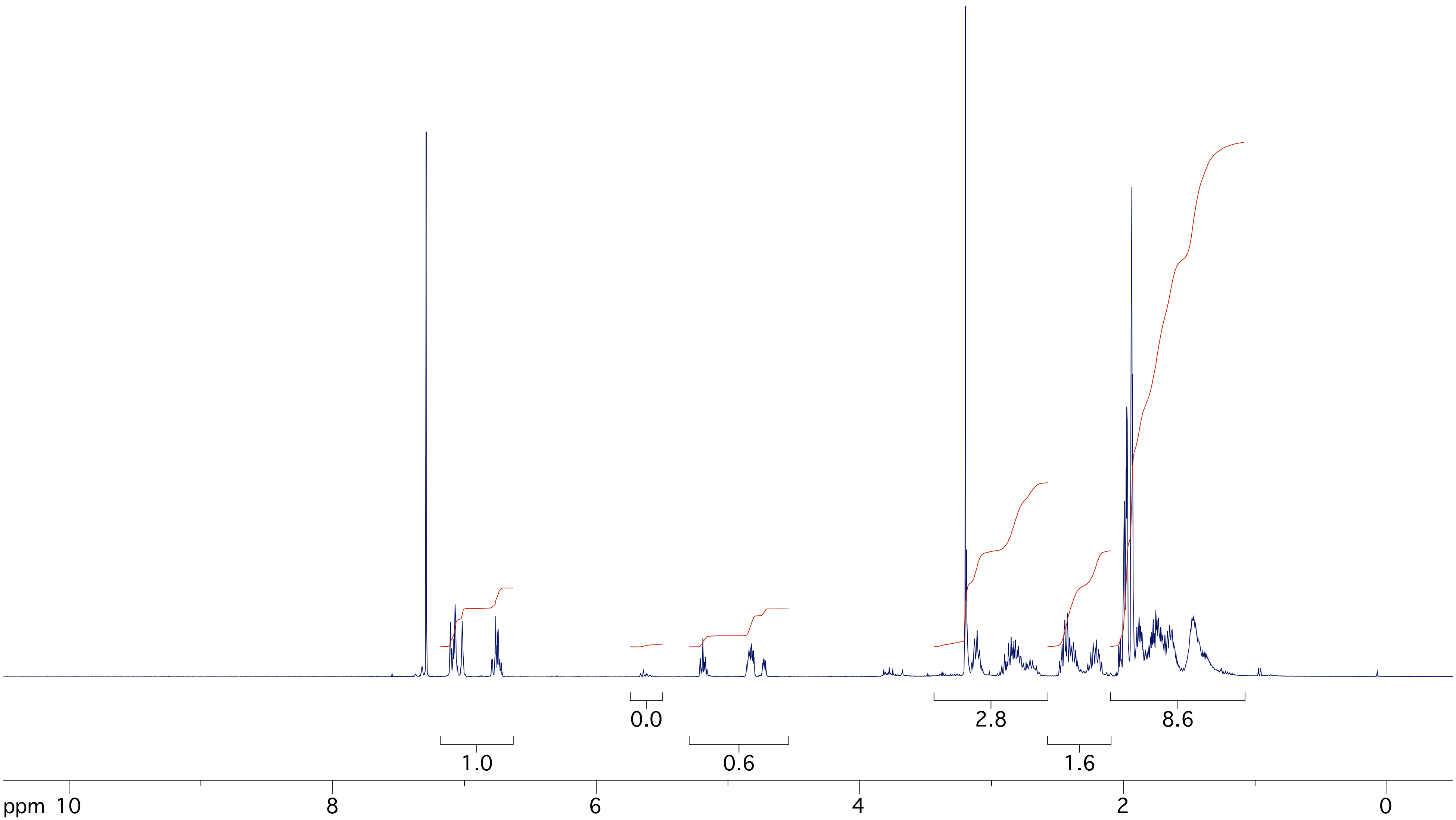
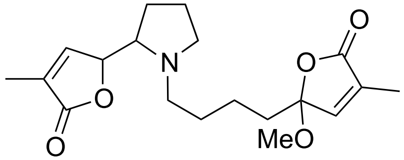


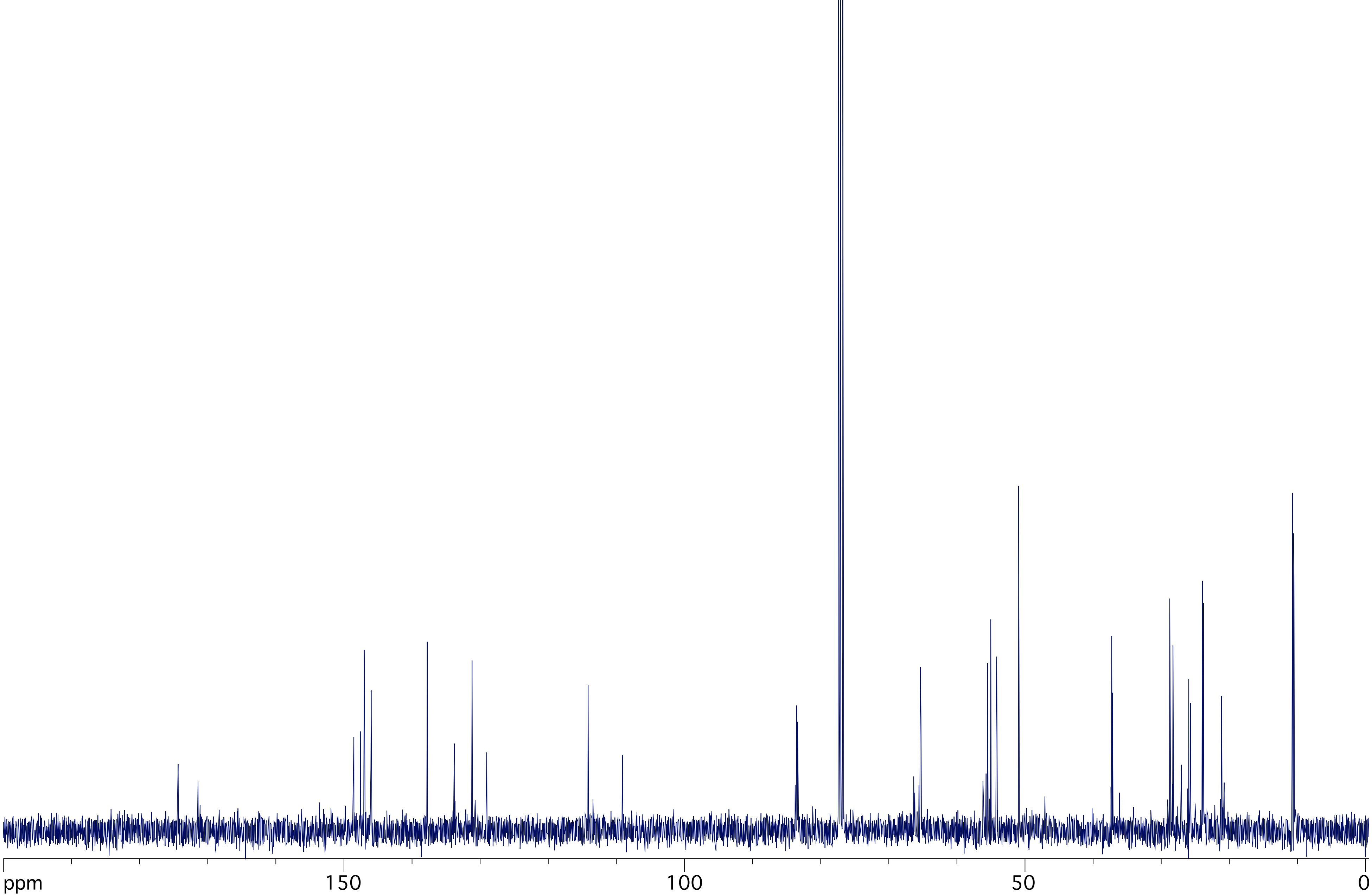


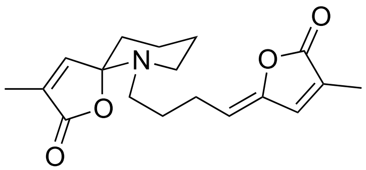
12
(mixture of diasteromers)



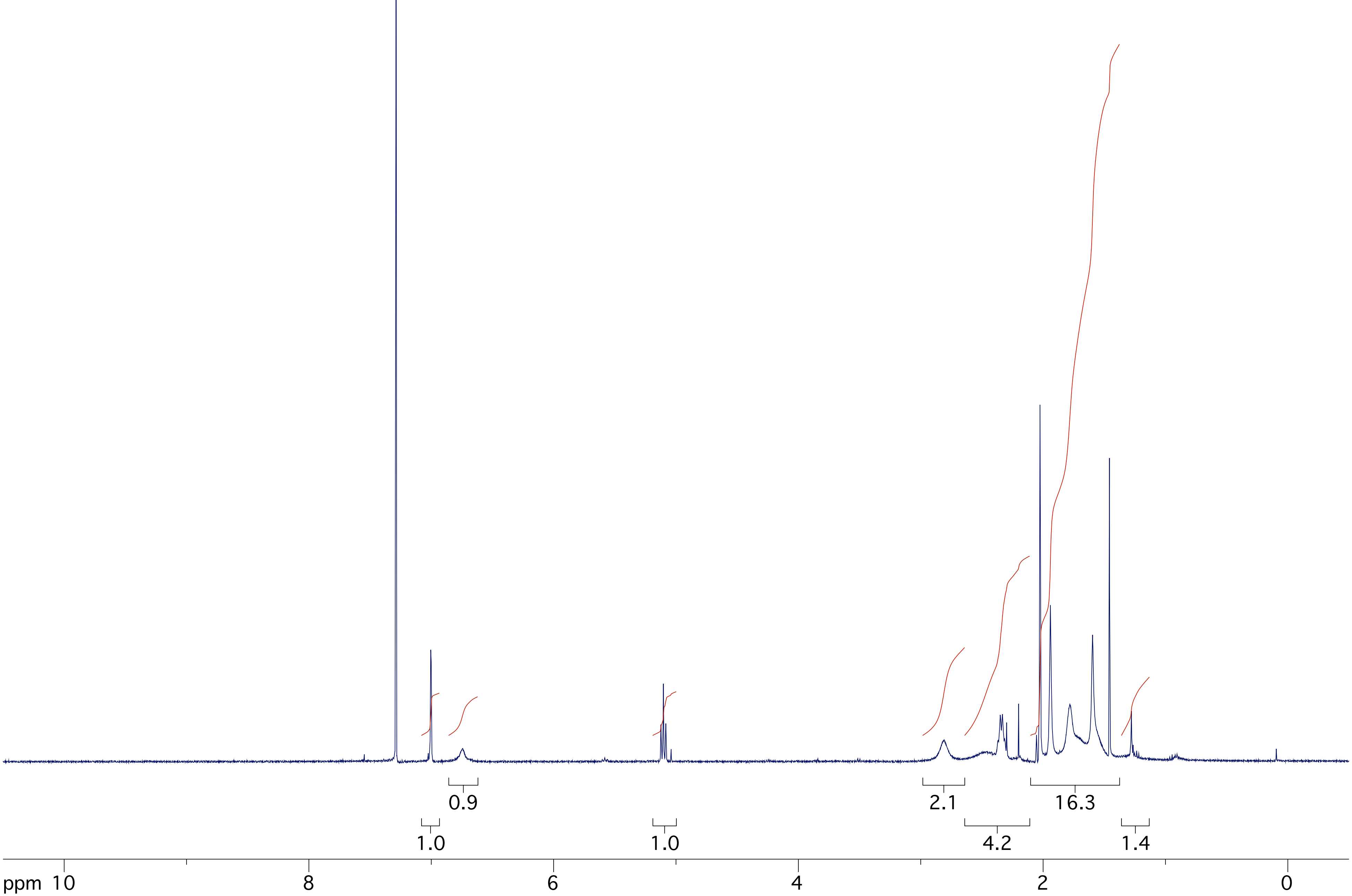


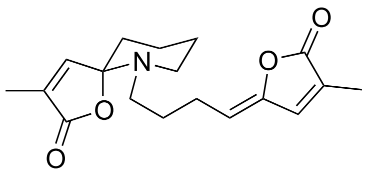
12
(mixture of diasteromers)



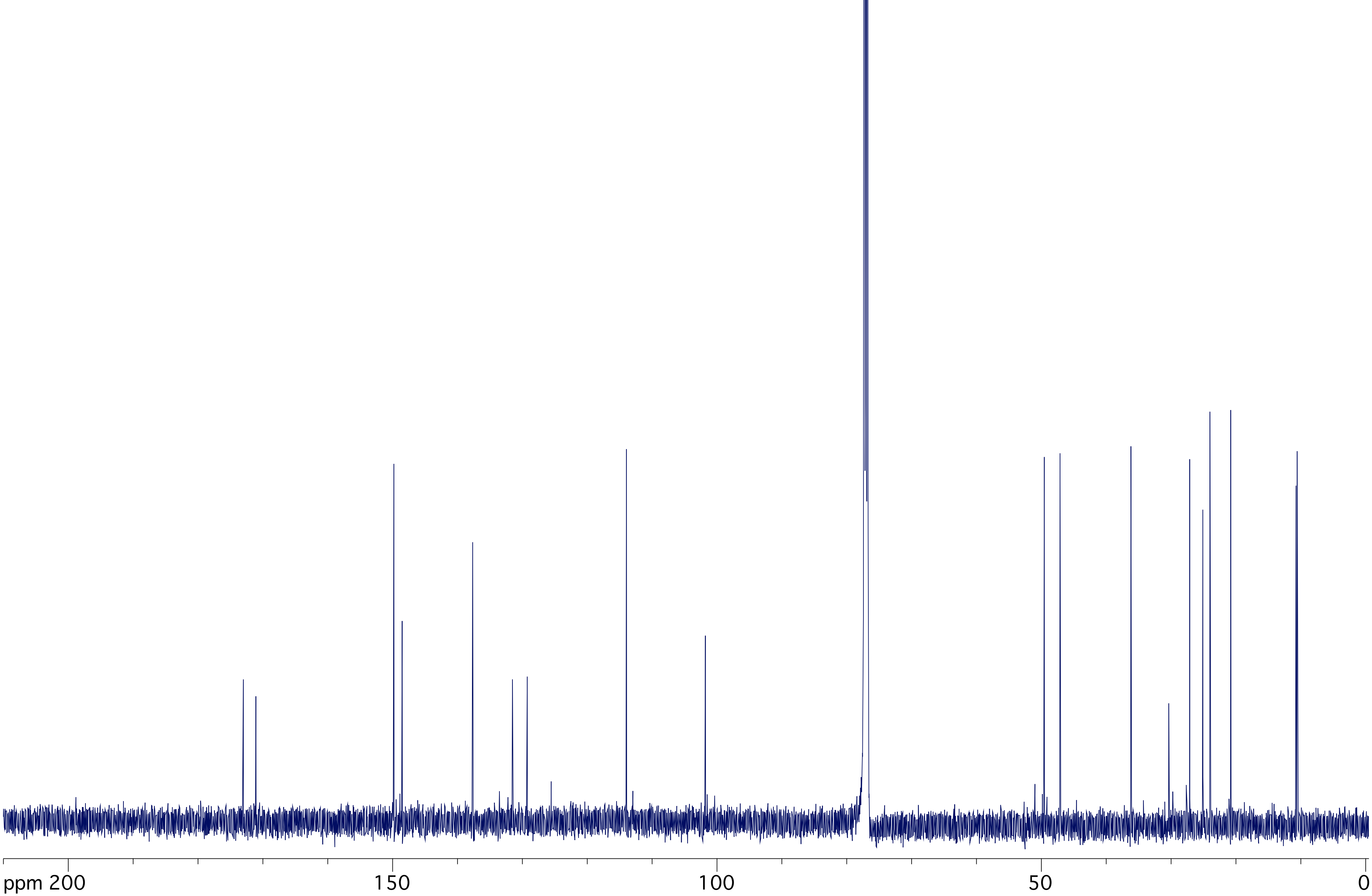


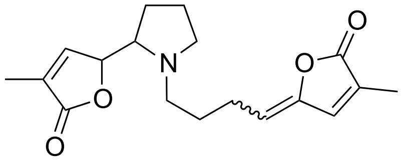
pandamarilactone-1 (**SI-3**)



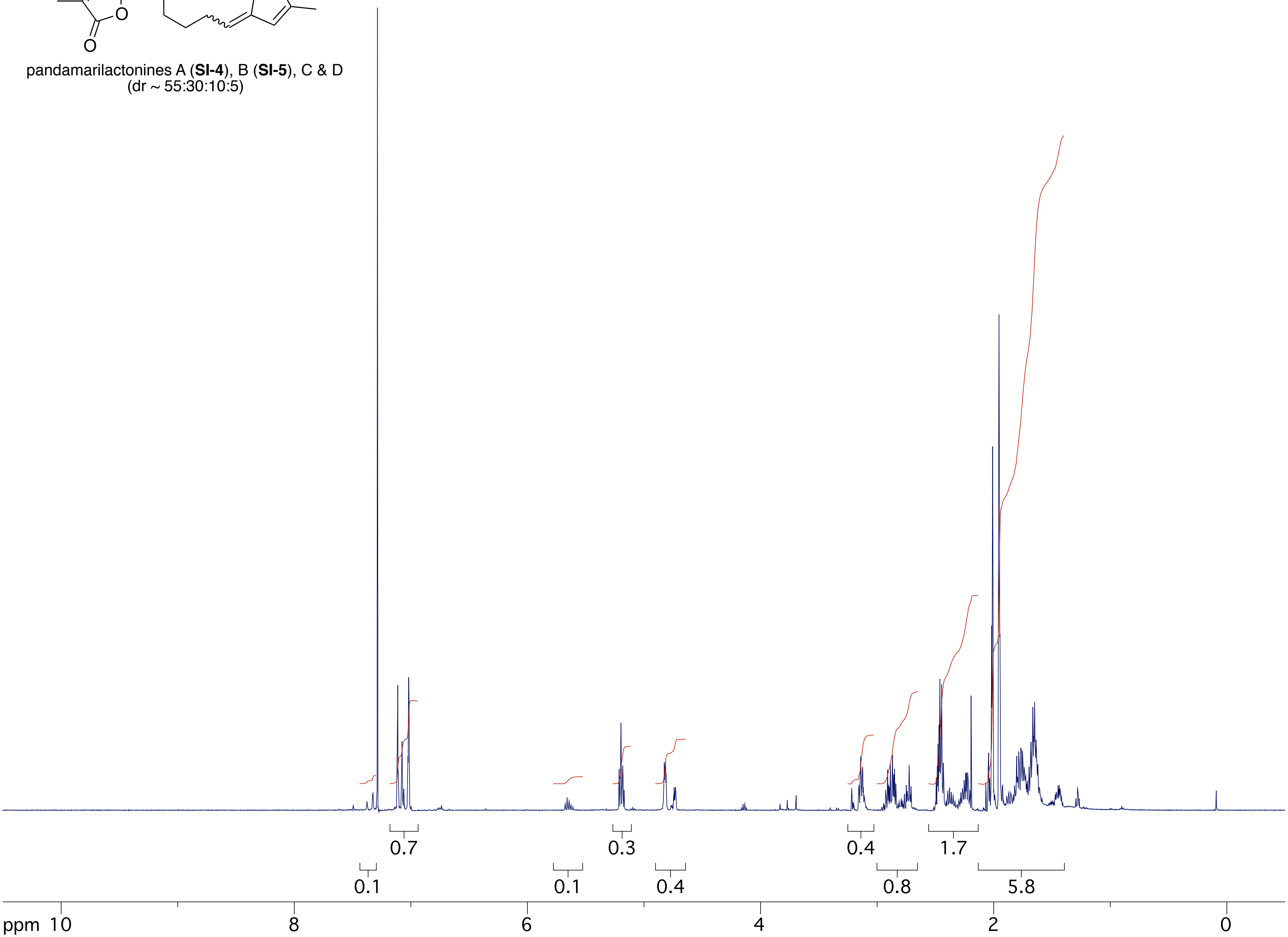


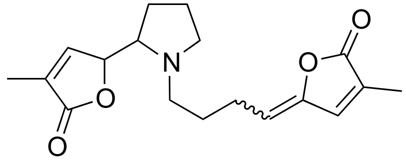
pandamarilactone-1 (**SI-3**)



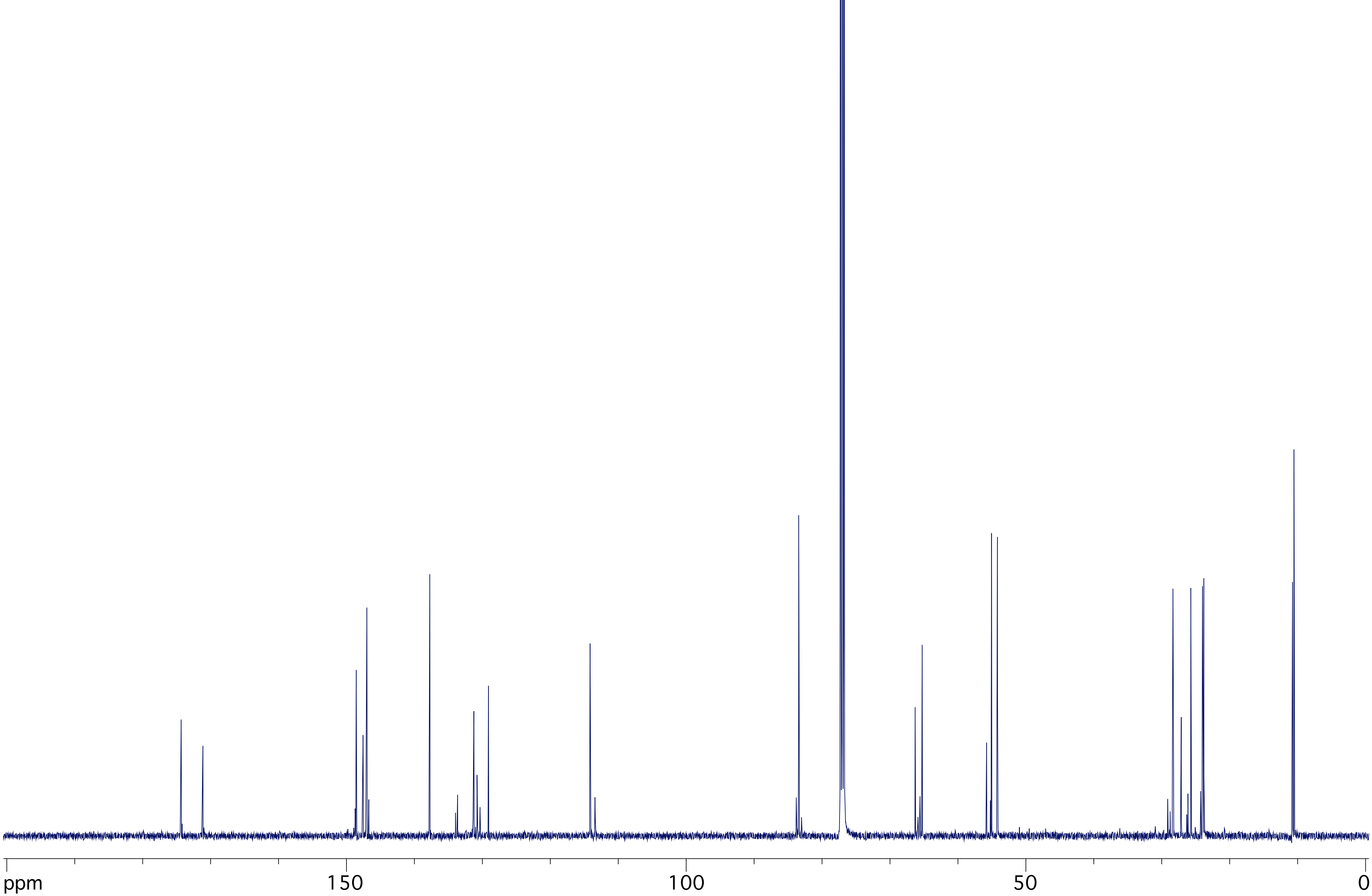


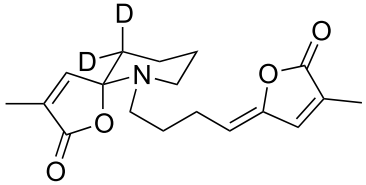
pandamarilactonines A (**SI-4**), B (**SI-5**), C & D
(dr ~ 55:30:10:5)



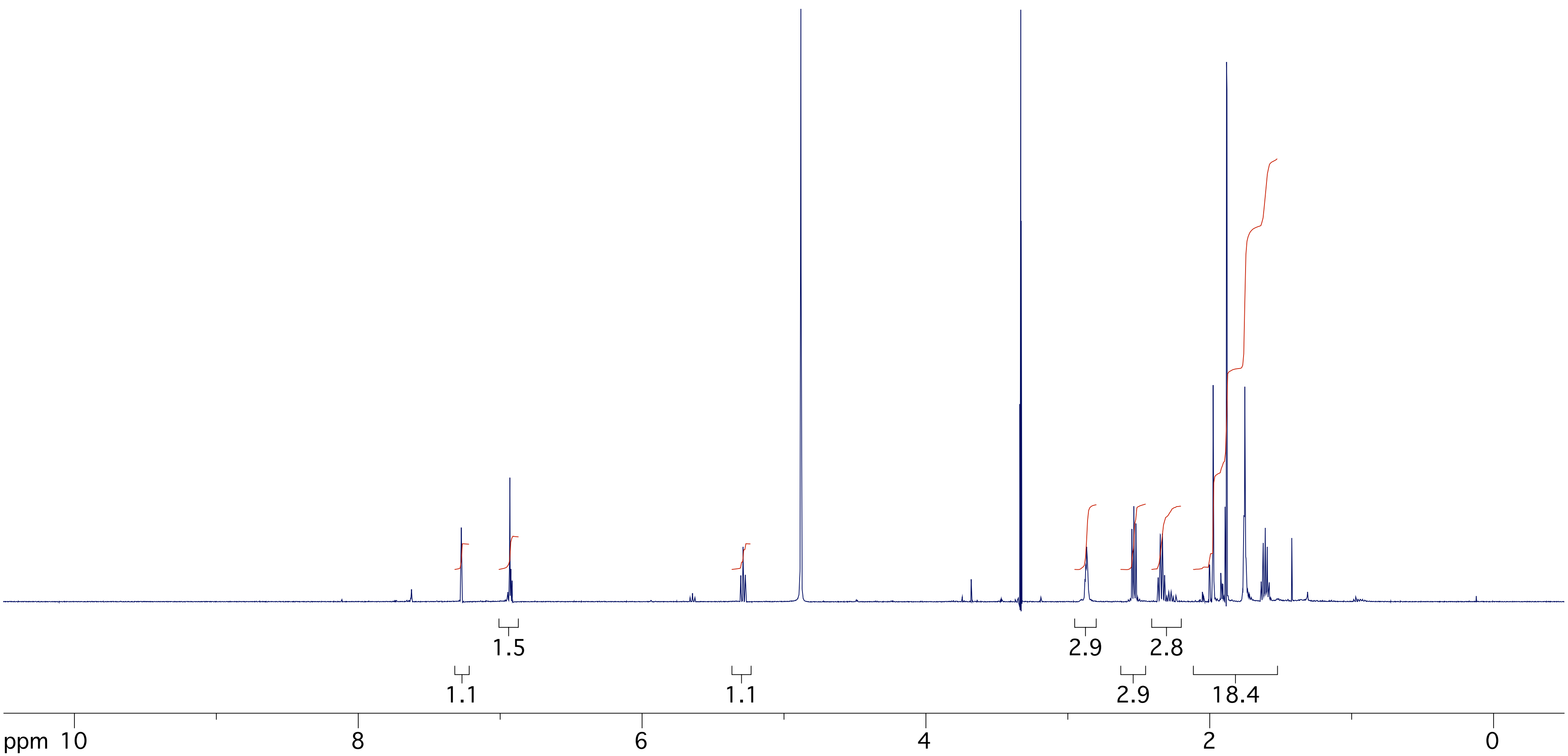


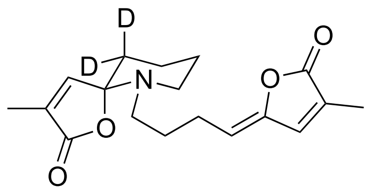
pandamarilactonines A (**SI-4**), B (**SI-5**), C & D
(dr ~ 55:30:10:5)



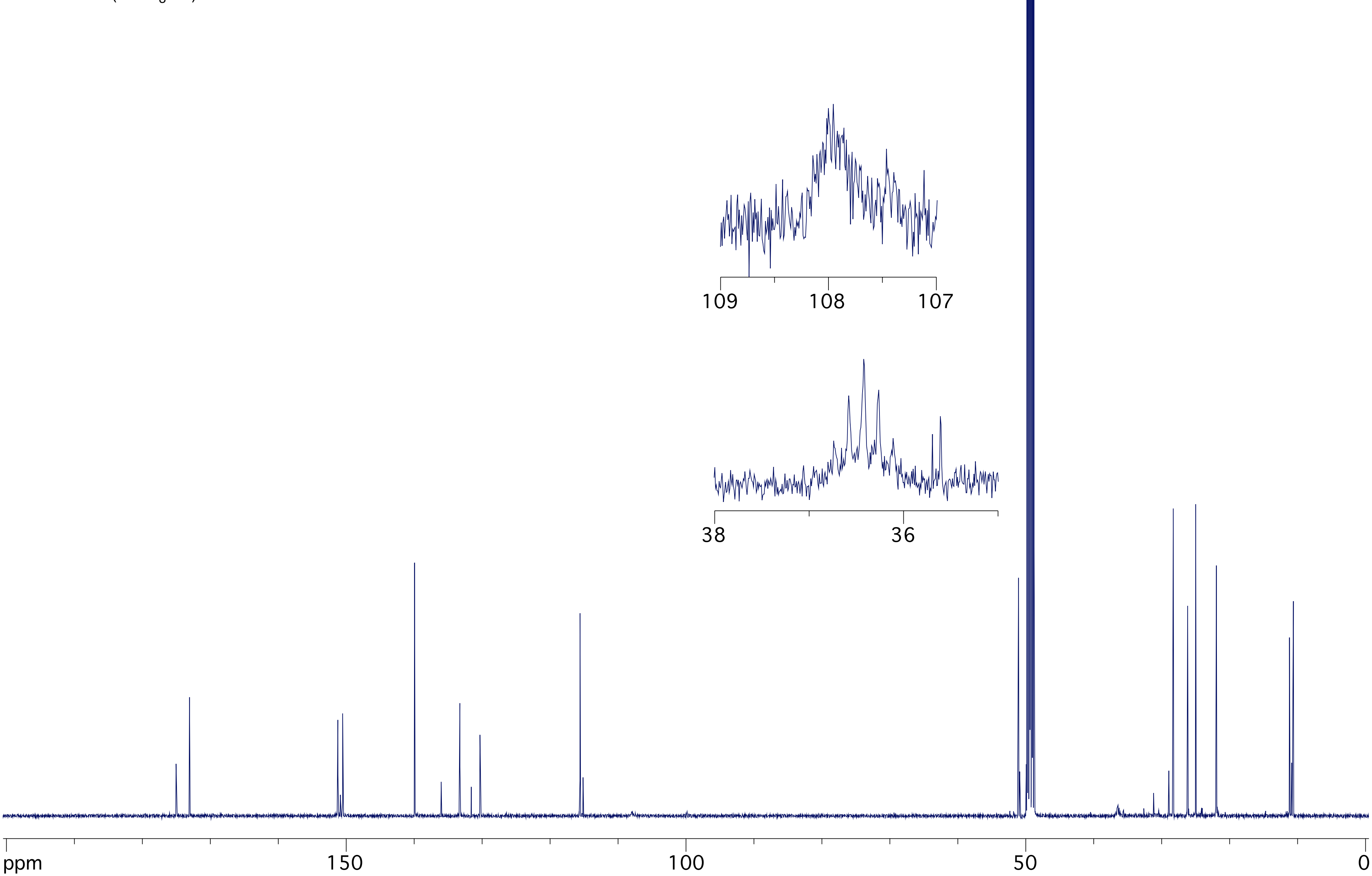


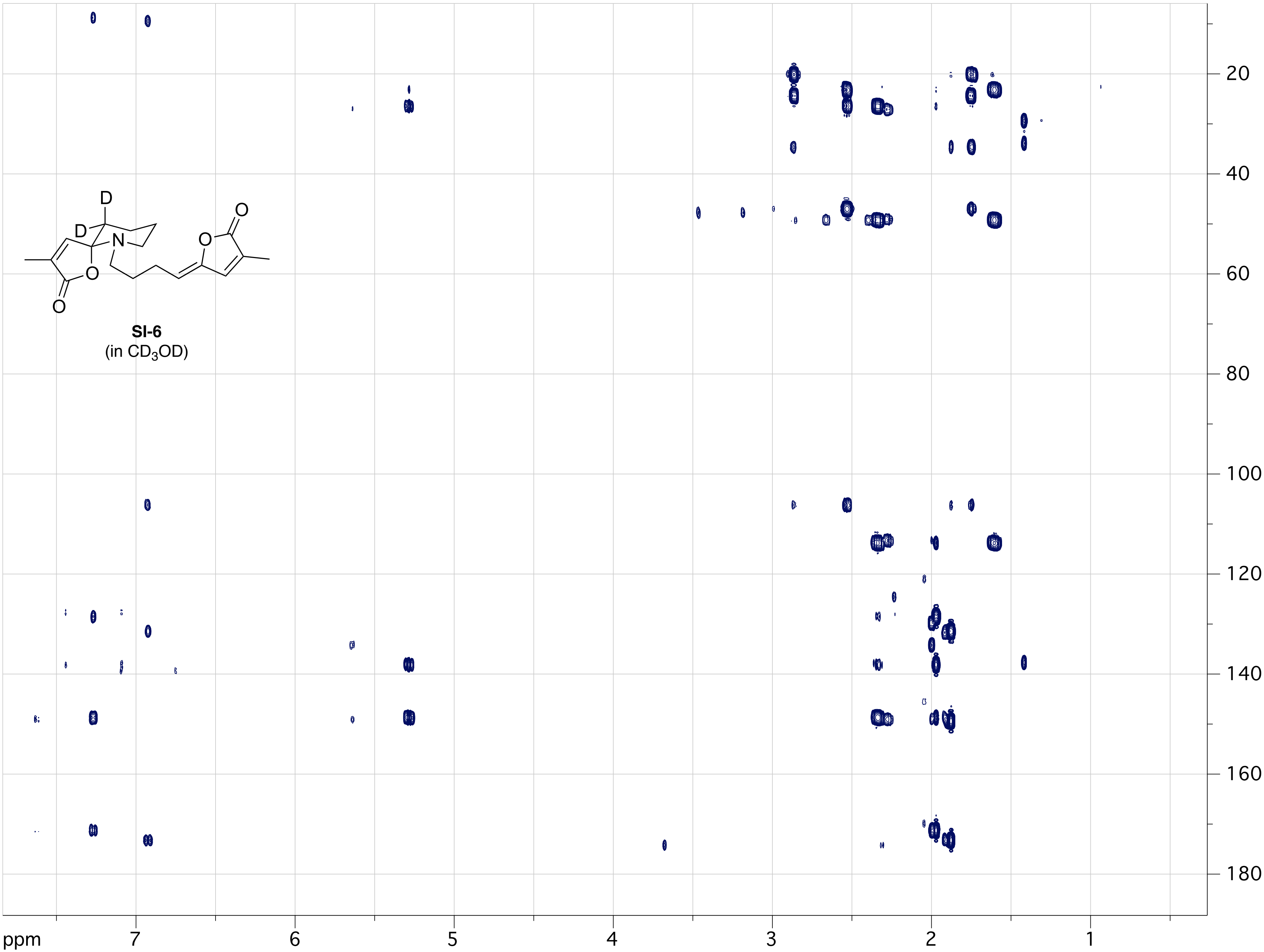
SI-6
(in CD_3OD)

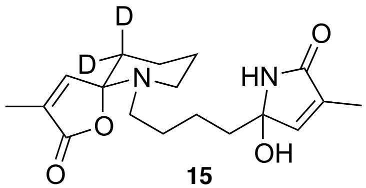




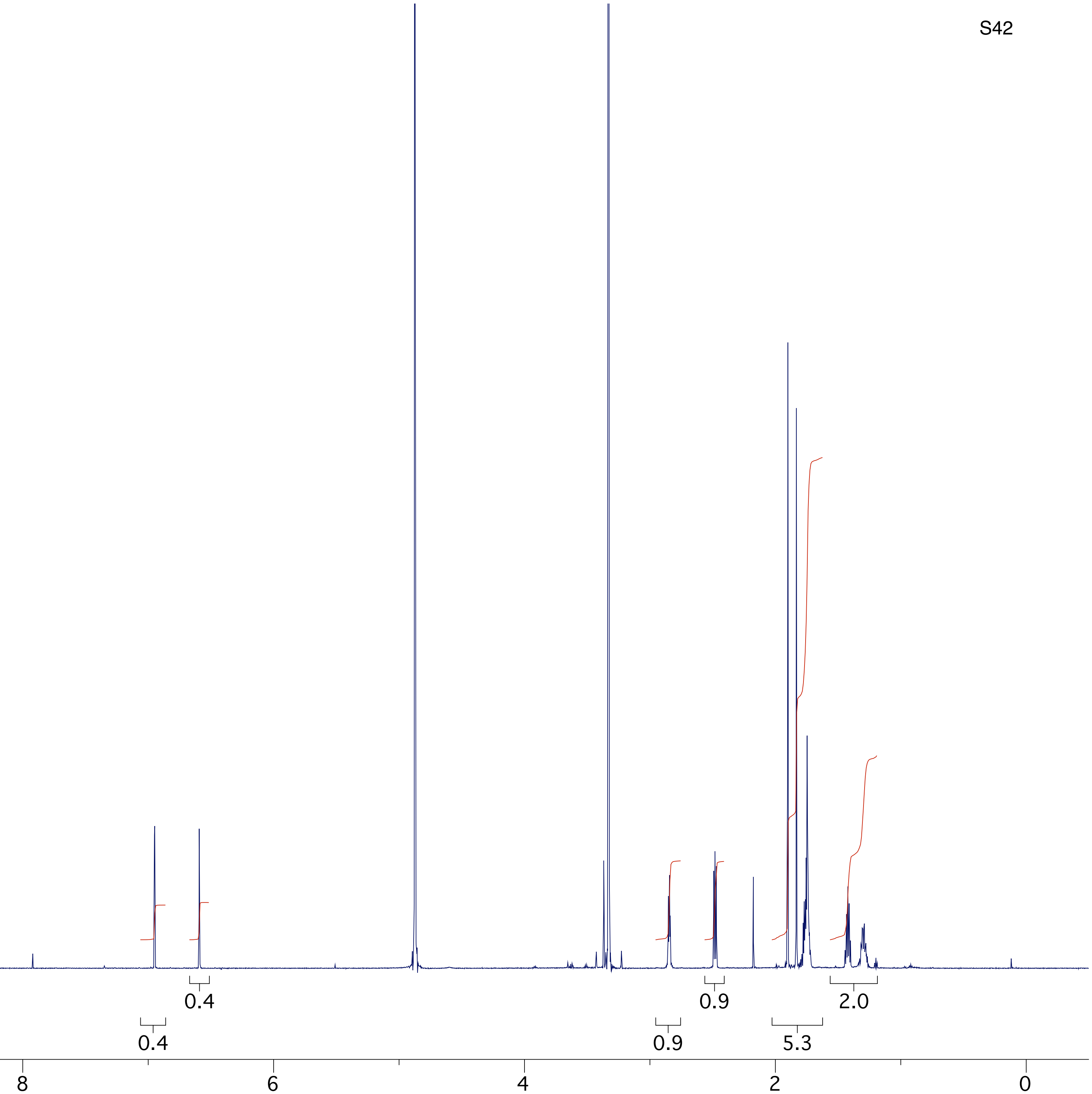
SI-6
(in CD_3OD)

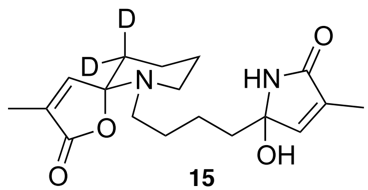



D
D
N
O
O
O
O
SI-6
(in CD_3OD)
ppm
7
6
5
4
3
2
1
20
40
60
80
100
120
140
160
180



15
(in CD_3OD)





15
(in CD_3OD)