Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Total Synthesis of two Potent Anti-Inflammatory Macrolactones of the Oxacyclododecindione Type

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Supporting Information

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I. Experimental procedures for compounds of the b-series

Hex-5-en-2-ol (11b)[1]

Hex-5-en-2-one (33.6 g, 0.34 mol) was added to a suspension of lithium aluminium hydride (6.45 g, 0.17 mol, 0.5 equiv) in dry THF (500 mL) at 0 °C. The reaction mixture was stirred for 22 h and was allowed to warm up to room temperature. The reaction mixture was quenched with 3n hydrochloric acid (500 mL), extracted with diethyl ether (3 x 200 mL), dried over magnesium sulfate and filtered. Distillation in vacuo (250 mbar) yielded **29b** (32.29 g, 0.32 mol, 95%, Lit.[1]: 93%) as a colorless liquid.

R_f = 0.25 (cyclohexane/EtOAc 6:1), **b.p.:** 100–102 °C (250 mbar), **^{1}H-NMR, COSY** (400 MHz, $CDCl_3$): δ [ppm] = 5.81 (ddt, 1H, *J* = 17.0 Hz, *J* = 10.2 H, *J* = 6.7 Hz, C*H*=CH_2), 5.05–4.93 (m, 2H, CH=CH_2), 3.83–3.76 (m, 1H, C*H*-2), 2.21–2.05 (m, 2H, CH_2-4), 1.59–1.45 (m, 2H, CH_2-3), 1.17 (d, 3H, *J* = 6.2 Hz, CH_3-1). The data are in accordance with those reported in the literature.[1] **^{13}C-NMR** (100.6 MHz, $CDCl_3$): δ [ppm] = 138.6 (*C*H=CH_2), 114.8 (CH=*C*H_2), 67.7 (*C*-2), 38.4 (*C*-3), 30.2 (*C*-4), 23.5 (*C*-1). The data are in accordance with those reported in the literature.[1]

1-Methoxy-4-((hex-5-en-2-yloxy)methyl)benzene (12b)[2]

The title compound was prepared according to the procedure described for **12a** from hex-5-en-2-ol **11b** (10.00 g, 0.10 mol), sodium hydride (95%, 3.02 g, 0.12 mol, 1.2 equiv), *p*-methoxybenzyl chloride (13.5 mL, 0.10 mol, 1.0 equiv) in dry THF (400 mL). The product **12b** (22.01 g, 0.10 mol, quant.) was isolated as a colorless oil.

R_f = 0.56 (cyclohexane/EtOAc 10:1), **^{1}H-NMR** (300 MHz, $CDCl_3$): δ [ppm] = 7.30–7.25 (m, 2H, AA'-part of AA'XX'-spin system, *H*-2, *H*-6, PMB), 6.89–6.84 (m, 2H, XX'-part of AA'XX'-spin system, *H*-3, *H*-5, PMB), 5.82 (ddt, 1H, *J* = 16.9 Hz, *J* = 10.1 Hz, *J* = 6.6 Hz, C*H*=CH_2), 5.05–

4.92 (m, 2H, CH=CH_2), 4.51 (d, 1H, J = 11.2 Hz, CH_{2A}, OPMB), 4.38 (d, 1H, J = 11.2 Hz, CH_{2B}, OPMB), 3.80 (s, 3H, OCH_3), 3.47–3.47 (m, 1H, *H*-2), 2.25–2.04 (m, 2H, CH_2-4), 1.75–1.63 (m, 1H, CH_{2A}-3), 1.59–1.46 (m, 1H, CH_{2B}-3), 1.19 (d, 3H, J = 6.1 Hz, CH_3-1). The data are in accordance with those reported in the literature.[2] **^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ [ppm] = 159.2 (C_q-4, PMB), 138.9 (*C*H=CH_2), 131.0 (C_q-1, PMB), 129.3 (*C*H-2, *C*H-6, PMB), 114.6 (CH=*C*H_2), 113.9 (*C*H-3, *C*H-5, PMB), 74.1 (*C*H-2), 70.1 (O*C*H_2, PMB), 55.4 (O*C*H_3), 36.0 (*C*H_2-3), 30.0 (*C*H_2-4), 19.7 (*C*H_3-1). The data are in accordance with those reported in the literature.[2]

5-((4-Methoxybenzyl)oxy)-hexan-1-ol (13b)[3]

The title compound was prepared according to the procedure described for **13a** from alkene **12b** (10.00 g, 45.4 mmol) and 9-BBN (0.5M in THF, 109 mL, 54.5 mmol, 1.2 equiv). The product **13b** (8.85 g, 37.2 mmol, 82%, Lit.:[3] 78%) was isolated as a colorless oil.

R_f = 0.40 (cyclohexane/EtOAc 1:1), **^{1}H-NMR** (300 MHz, $CDCl_3$): δ [ppm] = 7.29–7.24 (m, 2H, AA'-part of AA'XX'-spin system, *H*-2, *H*-6, PMB), 6.89–6.84 (m, 2H, XX'-part of AA'XX'-spin system, *H*-3, *H*-5, PMB), 4.50 (d, 1H, J = 11.4 Hz, OCH_{2A}), 4.37 (d, 1H, J = 11.4 Hz, OCH_{2B}), 3.80 (s, 3H, CH_3, PMB), 3.63 (t, 2H, J = 6.3 Hz, CH_2-1), 3.55–3.45 (m, 1H, C*H*-5), 1.62–1.34 (m, 6H, CH_2-2, CH_2-3, CH_2-4), 1.18 (d, 3H, J = 6.1 Hz, CH_3-6). The data are in accordance with those reported in the literature.[3] **^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ [ppm] = 159.2 (*C*-4, PMB), 131.2 (*C*-1, PMB), 129.4 (*C*-2, *C*-6, PMB), 113.9 (*C*-3, *C*-5, PMB), 74.6 (*C*-5), 70.1 (O*C*H_2, PMB), 63.0 (*C*H_2OH), 55.4 (O*C*H_3), 36.5 (*C*-4), 32.9 (*C*-2), 21.9 (*C*H_3-6), 19.7 (*C*H_2-3). The data are in accordance with those reported in the literature.[3]

5-((4-Methoxybenzyl)oxy)-hexanal

The title compound was prepared according to the procedure described for 5-((4-methoxybenzyl)oxy)-4-methylhexanal from alcohol **13b** (700 mg, 2.94 mmol) and pyridinium chlorochromate (951 mg, 4.41 mmol, 1.5 equiv). The product (639 mg, 2.70 mmol, 92%) was isolated as a colorless oil.

R_f = 0.31 (cyclohexane/EtOAc 4:1), **^{1}H-NMR** (300 MHz, $CDCl_3$): δ [ppm] = 9.73 (t, 1H, *J* = 1.7 Hz, C*H*O), 7.28–7.23 (m, 2H, AA'-part of AA'XX'-spin system, *H*-2, *H*-6, PMB), 6.89–6.84 (m, 2H, XX'-part of AA'XX'-spin system, *H*-3, *H*-5, PMB), 4.50 (d, 1H, *J* = 11.3 Hz, OCH_{2A}, PMB), 4.35 (d, 1H, *J* = 11.3 Hz, OCH_{2B}, PMB), 3.79 (s, 3H, OCH_3, PMB), 3.55–3.45 (m, 1H, CH_2-5), 2.43–2.37 (m, 2H, CH_2-2), 1.77–1.35 (m, 4H, CH_2-3, CH_2-4), 1.18 (d, 3H, *J* = 6.1 Hz, CH_3-6). The data are in accordance with those reported in the literature.[4] **^{13}C-NMR** (100.6 MHz, $CDCl_3$): δ [ppm] = 202.7 (*C*HO), 159.1 (*C*-4, PMB), 131.0 (*C*-1, PMB), 129.3 (*C*-2, *C*-6, PMB), 113.8 (*C*-3, *C*-5, PMB), 74.0 (*C*-5), 70.1 (O*C*H_2, PMB), 55.3 (O*C*H_3), 43.9 (*C*H_2-2), 36.1 (*C*-4), 19.6 (*C*H_3-6), 18.3 (*C*H_2-3). The data are in accordance with those reported in the literature.[4]

(*E*)-Allyl 7-((4-methoxybenzyl)oxy)-2-methyloct-2-enoate (17b)

The title compound was prepared according to the procedure described for **17a** from 5-((4-methoxybenzyl)oxy)-hexanal (553 mg, 2.34 mmol) and phosphonium ylide **14** (1.14 g, 3.04 mmol, 1.3 equiv). The product **17b** (613 mg, 1.84 mmol, 79%) was isolated as a colorless oil.

R_f = 0.52 (cyclohexane/EtOAc 4:1), **^{1}H-NMR, COSY** (300 MHz, $CDCl_3$): δ [ppm] = 7.28–7.23 (m, 2H, AA'-part of AA'XX'-spin system, *H*-2, *H*-6, PMB), 6.89–6.84 (m, 2H, XX'-part of AA'XX'-spin system, *H*-3, *H*-5, PMB), 6.79 (tq, 1H, *J* = 7.3 Hz, *J* = 1.3 Hz, *H*-3), 5.96 (ddt, 1H, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 5.6 Hz, C*H*=CH_2), 5.33 (dq, 1H, *J* = 17.2 Hz, *J* = 1.5 Hz, CH=CH_{2A}), 5.23 (dq, 1H, *J* = 10.4 Hz, *J* = 1.5 Hz, CH=CH_{2B}), 4.64 (dt, 2H, *J* = 5.6 Hz, *J* = 1.5 Hz, CH_2CH=CH_2), 4.50

(d, 1H, J = 11.3 Hz, CH_{2A}, PMB), 4.36 (d, 1H, J = 11.3 Hz, CH_{2B}, PMB), 3.79 (s, 3H, OCH_3, PMB), 3.54–3.44 (m, 1H, *H*-7), 2.16 (q, 2H, J = 7.3 Hz, CH_2-4), 1.83 (q, J = 1.3 Hz, 3H, CH_3-2), 1.67–1.40 (m, 4H, CH_2-5, CH_2-6), 1.18 (d, 3H, J = 6.1 Hz, CH_3-8). **^{13}C-NMR, HSQC** (75.5 MHz, $CDCl_3$): δ [ppm] = 167.9 (*C*O), 159.2 (C_q-4, PMB), 142.8 (*C*H-3), 132.7 (*C*H=CH_2), 131.1 (C_q-1, PMB), 129.3 (*C*H-2, *C*H-6, PMB), 127.7 (C_q-2), 117.9 (CH=*C*H_2), 113.8 (*C*H-3, *C*H-5, PMB), 74.3 (*C*H-7), 70.1 (O*C*H_2, PMB), 65.2 (*C*H_2CH=CH_2), 55.4 (O*C*H_3), 36.5 (*C*H_2-6), 28.8 (*C*H_2-4), 24.7 (*C*H_2-5), 19.7 (*C*H_3-8), 12.5 (*C*H_3-2). **IR** (ATR): ũ [cm^{-1}] = 2966, 2935, 2863, 2838, 1710, 1513, 1248, 1181, 1173, 1142, 1092, 1036. **HRMS** (ESI): calcd for [$C_{20}H_{28}O_4$ + Na]$^+$: 355.1885, found: 355.1887.

(*E*)-Allyl 7-hydroxy-2-methyloct-2-enoate (18b)

The title compound was prepared according to the procedure described for **18a** from ester **17b** (1.56 g, 4.69 mmol) and DDQ (1.28 g, 5.63 mmol, 1.2 equiv). The product **18b** (920 mg, 4.34 mmol, 92%) was isolated as a colorless oil.

R_f = 0.16 (cyclohexane/EtOAc 4:1), **^{1}H-NMR** (400 MHz, $CDCl_3$): δ [ppm] = 6.79 (tq, 1H, J = 7.3 Hz, J = 1.7 Hz, *H*-3), 5.96 (ddt, 1H, J = 17.2 Hz, J = 10.4 Hz, J = 5.6 Hz, C*H*=CH_2), 5.33 (dq, 1H, J = 17.2 Hz, J = 1.5 Hz, CH=CH_{2A}), 5.23 (dq, 1H, J = 10.4 Hz, J = 1.5 Hz, CH=CH_{2B}), 4.64 (dt, 2H, J = 5.6 Hz, J = 1.5 Hz, CH_2CH=CH_2), 3.84–3.77 (m, 1H, *H*-7), 2.18 (q, 2H, J = 7.3 Hz, CH_2-4), 1.84 (q, 3H, J = 1.7 Hz, CH_3-2), 1.61–1.42 (m, 4H, CH_2-5, CH_2-6), 1.19 (d, 3H, J = 6.2 Hz, CH_3-8). **^{13}C-NMR** (100.6 MHz, $CDCl_3$): δ [ppm] = 167.9 (*C*O), 142.5 (*C*H-3), 132.7 (*C*H=CH_2), 127.9 (C_q-2), 117.9 (CH=*C*H_2), 68.0 (*C*H-7), 65.3 (*C*H_2CH=CH_2), 39.0 (*C*H_2-6), 28.7 (*C*H_2-4), 24.9 (*C*H_2-5), 23.8 (*C*H_3-8), 12.6 (*C*H_3-2). **IR** (ATR): ũ [cm^{-1}] = 3400, 2966, 2932, 2865, 1712, 1648, 1257, 1182, 1140, 1099, 992. **HRMS** (ESI): calcd for [$C_{12}H_{20}O_3$ + Na]$^+$: 235.1310, found: 235.1307.

(*E*)-Allyl 7-(2-(3,5-bis(benzyloxy)phenyl)acetoxy)-2,6-dimethyloct-2-enoate (20b)

The title compound was prepared according to the procedure described for **20a** from 3,5-bis(benzyloxy)phenylacetic acid (**19**) (499 mg, 1.43 mmol) and (*E*)-allyl 7-hydroxy-2-methyloct-2-enoate (**18b**) (304 mg, 1.43 mmol, 1.0 equiv). The product **20b** (535 mg, 0.99 mmol, 69%) was isolated as a colorless oil.

R_f = 0.48 (cyclohexane/EtOAc 4:1), **^{1}H-NMR, COSY** (400 MHz, $CDCl_3$): δ [ppm] = 7.44–7.31 (m, 10H, 2 x Ph), 6.75 (tq, 1H, *J* = 7.4 Hz, *J* = 1.3 Hz, *H*-3'), 6.56 (d, 2H, *J* = 2.2 Hz, *H*-2, *H*-6), 6.54 (t, 1H, *J* = 2.2 Hz, *H*-4), 5.96 (ddt, 1H, *J* = 17.2 Hz, *J* = 10.4 Hz, *J* = 5.6 Hz, C*H*=CH_2), 5.33 (dq, 1H, *J* = 17.2 Hz, *J* = 1.5 Hz, CH=CH_{2A}), 5.23 (dq, 1H, *J* = 10.4 Hz, *J* = 1.5 Hz, CH=CH_{2B}), 5.02 (s, 4H, 2 x OCH_2Ph), 4.97–4.89 (m, 1H, *H*-7'), 4.64 (dt, 2H, *J* = 5.6 Hz, *J* = 1.5 Hz, CH_2CH=CH_2), 3.53 (s, 2H, CH_2COO), 2.15 (q, 2H, *J* = 7.4 Hz, CH_2-4'), 1.84 (q, 3H, *J* = 1.3 Hz, CH_3-2'), 1.65–1.35 (m, 4H, CH_2-5', CH_2-6'), 1.21 (d, 3H, *J* = 6.3 Hz, CH_3-8'). **^{13}C-NMR, HSQC, HMBC** (100.6 MHz, $CDCl_3$): δ [ppm] = 171.1 (*C*OO), 167.8 (*C*OOAll), 160.1 (C_q-3, C_q-5), 142.5 (*C*H-3'), 136.9 (2 x C_q-1, Ph), 136.5 (C_q-1), 132.6 (*C*H=CH_2), 128.7 (2 x *C*H-3, 2 x *C*H-5, Ph), 128.1 (2 x *C*H-4, Ph), 128.1 (C_q-2'), 127.6 (2 x *C*H-2, 2 x *C*H-6, Ph), 117.9 (CH=*C*H_2), 108.5 (*C*H-2, *C*H-6), 100.9 (*C*H-4), 71.3 (*C*H-7'), 70.1 (2 x O*C*H_2Ph), 65.3 (*C*HCH=CH_2), 42.1 (*C*H_2COO), 35.6 (*C*H_2-6'), 28.5 (*C*H_2-4'), 24.5 (*C*H_2-5'), 20.1 (*C*H_3-8'), 12.5 (*C*H_3-2'). **IR** (ATR): ũ [cm^{-1}] = 3089, 3065, 3033, 2977, 2934, 2868, 1725, 1710, 1594, 1498, 1254, 1149, 1057, 737, 698. **HRMS** (ESI): calcd for $[C_{34}H_{38}O_6 + Na]^+$: 565.2566, found: 565.2562.

(*E*)-7-(2-(3,5-bis(benzyloxy)phenyl)acetoxy)-2-methyloct-2-enoic acid (21b)

The title compound was prepared according to the procedure described for **21a** from allyl ester **20b** (397 mg, 0.73 mol), $Pd(PPh_3)_4$ (43 mg, 37 µmol, 0.05 equiv) and sodium 4-toluenesulfinate

(196 mg, 1.10 mmol, 1.5 equiv). The product **21b** (337 mg, 0.67 mol, 92%) was isolated as a yellow oil.

R_f = 0.10 (cyclohexane/EtOAc 4:1), **^{1}H-NMR** (300 MHz, $CDCl_3$): δ [ppm] = 7.44–7.30 (m, 10H, 2 x Ph), 6.85 (tq, 1H, *J* = 7.4 Hz, *J* = 1.3 Hz, *H*-3'), 6.56 (d, 2H, *J* = 2.2 Hz, *H*-2, *H*-6), 6.54 (t, 1H, *J* = 2.2 Hz, *H*-4), 5.02 (s, 4H, 2 x O*C*H_2Ph), 4.97–4.88 (m, 1H, *H*-7'), 3.53 (s, 2H, *C*H_2COO), 2.17 (q, 2H, *J* = 7.4 Hz, *C*H_2-4'), 1.81 (s, 3H, *C*H_3-2'), 1.66–1.34 (m, 4H, *C*H_2-5', *C*H_2-6'), 1.21 (d, 3H, *J* = 6.3 Hz, *C*H_3-8'). **^{13}C-NMR** (100.6 MHz, $CDCl_3$): δ [ppm] = 173.4 (*C*OOH), 171.1 (*C*OO), 160.1 (*C*$_q$-3, *C*$_q$-5), 144.6 (*C*H-3'), 136.9 (2 x *C*$_q$-1, Ph), 136.4 (*C*$_q$-1), 128.7 (2 x *C*H-3, 2 x *C*H-5, Ph), 128.1 (2 x *C*H-4), 127.6 (2 x *C*H-2, 2 x *C*H-6, Ph), 127.5 (*C*$_q$-2'), 108.6 (*C*H-2, *C*H-6), 100.9 (*C*H-4), 71.3 (*C*H-7'), 70.1 (2 x O*C*H_2Ph), 42.1 (*C*H_2COO), 35.6 (*C*H_2-6'), 28.7 (*C*H_2-4'), 24.3 (*C*H_2-5'), 20.1 (*C*H_3-8'), 12.1 (*C*H_3-2'). **IR** (ATR): ũ [cm^{-1}] = 3089, 3064, 3033, 2976, 2933, 2868, 1725, 1683, 1593, 1498, 1290, 1148, 1057, 735, 698. **HRMS** (ESI): calcd for $[C_{31}H_{34}O_6 + Na]^+$: 525.2253, found: 525.2264.

5,7-Di-*O*-benzyl-10-methyl-10,11-dehydrocurvularin (22b)

The title compound was prepared according to the procedure described for **22a** from acid **21b** (20 mg, 40 µmol). The product **22b** (15 mg, 31 µmol, 78%) was isolated as a colorless oil.

R_f = 0.31 (cyclohexane/EtOAc 4:1), **^{1}H-NMR, COSY, NOESY** (400 MHz, $CDCl_3$): δ [ppm] = 7.43–7.26 (m, 10H, 2 x Ph), 6.60 (s_{br}, 1H, *H*-4), 6.52 (d, 1H, *J* = 2.2 Hz, *H*-6), 6.40 (s_{br}, 1H, *H*-11), 5.11–4.97 (m, 4H, 2 x O*C*H_2Ph), 4.93–4.85 (m, 1H, *H*-15), 3.35 (s, 2H, *C*H_2-2), 2.26 (s_{br}, 2H, *C*H_2-12), 1.95 (s, 3H, *C*H_3-10), 1.90–1.80 (m, 1H, *C*H_{2A}-13), 1.80–1.73 (m, 1H, *C*H_{2A}-14), 1.49–1.39 (m, 2H, *C*H_{2B}-13, *C*H_{2B}-14), 1.14 (d, 3H, *J* = 6.4 Hz, *C*H_3-15). **^{13}C-NMR, HSQC, HMBC** (100.6 MHz, $CDCl_3$): δ [ppm] = 199.3 (*C*O), 170.6 (br, *C*OO), 159.8 (*C*$_q$-5), 156.5 (*C*$_q$-7), 151.5 (*C*H-11), 138.2 (br, *C*$_q$-10), 136.8 (*C*$_q$-1, Ph), 136.6 (*C*$_q$-1, Ph), 133.0 (*C*$_q$-3), 128.7 (*C*H-3,

*C*H-5, Ph), 128.5 (*C*H-3, *C*H-5, Ph), 128.2 (*C*H-4, Ph), 127.8 (*C*H-4, Ph), 127.7 (*C*H-2, *C*H-6, Ph), 126.9 (*C*H-2, *C*H-6, Ph), 124.1 (C_q-8), 108.1 (*C*H-4), 100.3 (*C*H-6), 72.9 (*C*H-15), 70.3 (2 x O*C*H_2Ph), 39.7 (*C*H_2-2), 34.7 (br, *C*H_2-14), 30.7 (*C*H_2-12), 23.8 (*C*H_2-13), 20.2 (*C*H_3-15), 10.5 (*C*H_3-10). **IR** (ATR): ũ [cm^{-1}] = 3090, 3065, 3033, 2977, 2935, 2867, 1723, 1603, 1583, 1305, 1280, 1167, 1148, 735. **HRMS** (ESI): calcd for $[C_{31}H_{32}O_5 + H]^+$: 485.2328, found: 485.2336.

10-Methyl-10,11-dehydrocurvularin (23b)

The title compound was prepared according to the procedure described for **1** from lactone **22b** (28 mg, 58 µmol) and boron trichloride (1M in hexane, 0.58 mL, 0.58 mmol, 10.0 equiv). The product **23b** (16 mg, 52 µmol, 89%) was isolated as a yellow oil.

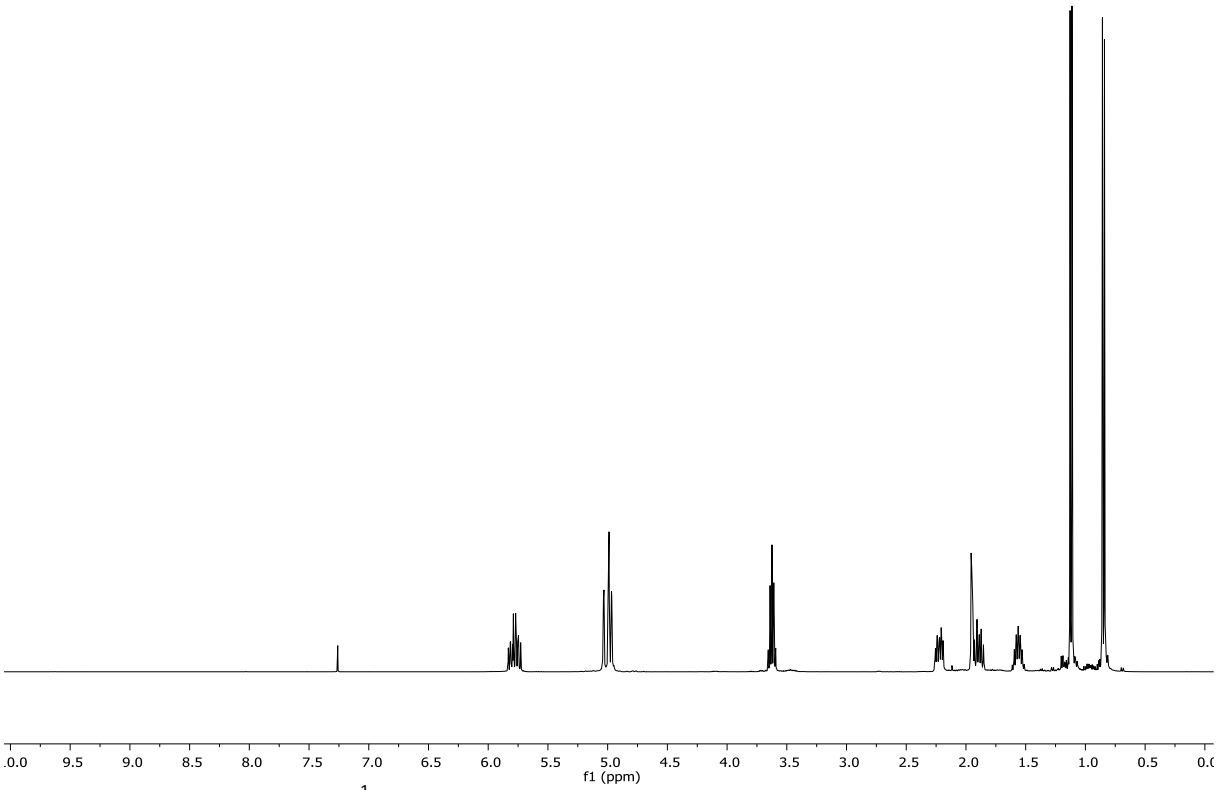
R_f = 0.20 (cyclohexane/EtOAc 2:1), **^{1}H-NMR** (400 MHz, Methanol-d_4): δ [ppm] = 6.46 (t, 1H, *J* = 6.5 Hz, *H*-11), 6.30 (d, 1H, *J* = 2.2 Hz, *H*-4), 6.25 (d, 1H, *J* = 2.2 Hz, *H*-6), 4.91–4.83 (m, 1H, *H*-15), 3.27 (d, 1H, *J* = 15.2 Hz, CH_{2A}-2), 3.24 (d, 1H, *J* = 15.2 Hz, CH_{2B}-2), 2.36–2.22 (m, 2H, CH_2-12), 1.87 (s, 3H, CH_3-10), 1.92–1.78 (m, 2H, CH_{2A}-13, CH_{2A}-14), 1.55–1.41 (m, 2H, CH_{2B}-13, CH_{2B}-14), 1.14 (d, 3H, *J* = 6.4 Hz, CH_3-15). **^{13}C-NMR, HSQC** (100.6 MHz, Methanol-d_4): δ [ppm] = 203.1 (*C*O), 172.3 (*C*OO), 160.0 (C_q-7), 157.0 (C_q-5), 153.3 (*C*H-11), 139.1 (C_q-10), 134.3 (C_q-3), 121.1 (C_q-8), 110.0 (*C*H-4), 102.4 (*C*H-6), 74.2 (*C*H-15), 40.5 (*C*H_2-2), 35.6 (*C*H_2-14), 31.4 (*C*H_2-12), 24.7 (*C*H_2-13), 20.2 (*C*H_3-15), 10.5 (*C*H_3-10). **IR** (ATR): ũ [cm^{-1}] = 3360, 2979, 2934, 2866, 1724, 1700, 1616, 1307, 1263, 1167, 1150, 732. **HRMS** (ESI): calcd for $[C_{17}H_{20}O_5 + Na]^+$: 327.1208, found: 327.1214.

4-Chloro-10-methyl-10,11-dehydrocurvularin (24b)

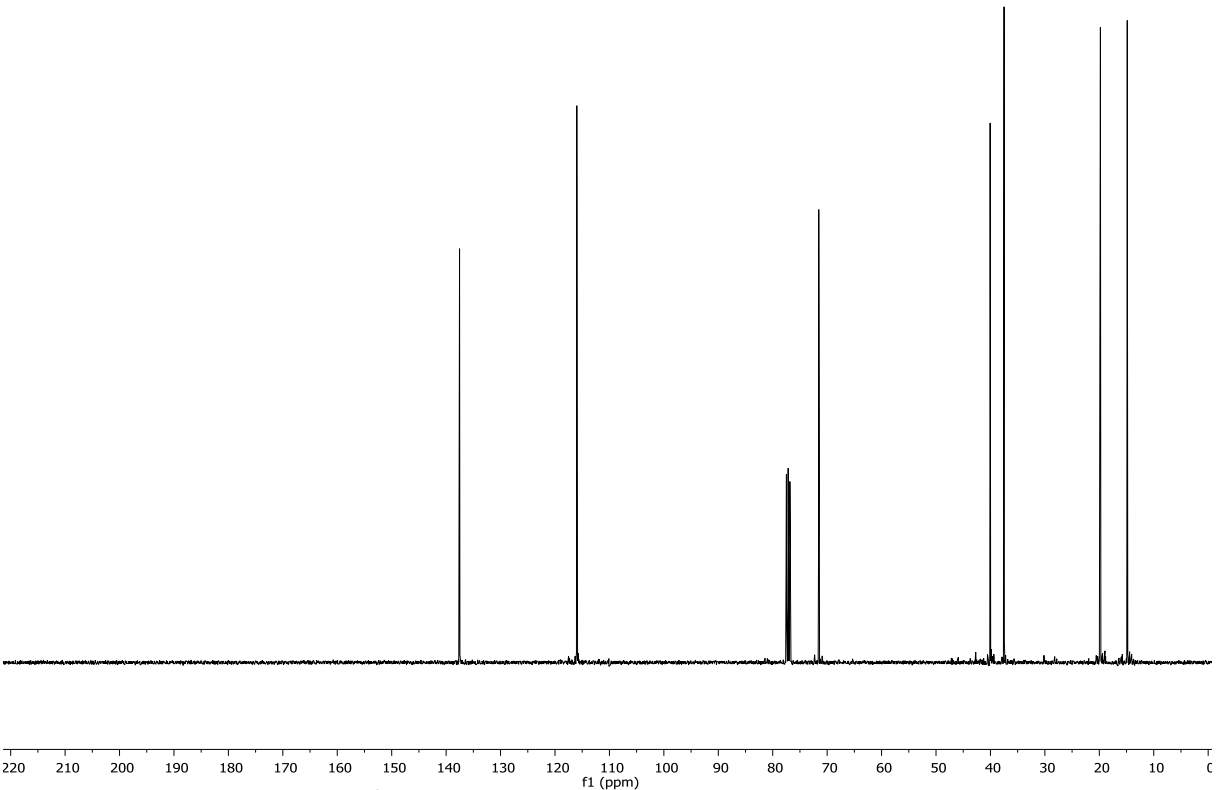
The title compound was prepared according to the procedure described for **2** from lactone **23b** (15 mg, 49 µmol), *N*-chlorosuccinimide (6.5 mg, 49 µmol, 1.0 equiv) and trifluoroacetic acid (6 µL, 74 µmol, 1.5 equiv). The product **24b** (9.2 mg, 27 µmol, 55%) was isolated as a yellow oil.

$\mathbf{R_f}$ = 0.16 (cyclohexane/EtOAc 2:1), **^{1}H-NMR, COSY, NOESY** (400 MHz, Methanol-d_4): δ [ppm] = 6.70 (ddd, 1H, *J* = 11.3 Hz, *J* = 5.4 Hz, *J* = 1.5 Hz, *H*-11), 6.45 (s, 1H, *H*-6), 4.94–4.87 (m, 1H, *H*-15), 3.64 (d, 1H, *J* = 17.2 Hz, CH_{2A}-2), 3.21 (d, 1H, *J* = 17.2 Hz, CH_{2B}-2), 2.54–2.45 (m, 1H, CH_{2A}-12), 2.11–2.01 (m, 1H, CH_{2B}-12), 2.00–1.90 (m, 1H, CH_{2A}-13), 1.87–1.86 (m, 3H, CH_3-10), 1.84–1.79 (m, 1H, CH_{2A}-14), 1.54–1.45 (m, 1H, CH_{2B}-14), 1.33–1.22 (m, 1H, CH_{2B}-13), 1.13 (d, 3H, *J* = 6.3 Hz, CH_3-15). **^{13}C-NMR, HSQC, HMBC** (100.6 MHz, Methanol-d_4): δ [ppm] = 201.6 (*C*O), 170.7 (*C*OO), 155.4 (C_q-5), 154.8 (C_q-7), 153.8 (*C*H-11), 138.3 (C_q-10), 132.0 (C_q-3), 122.8 (C_q-8), 113.7 (C_q-4), 103.5 (*C*H-6), 74.2 (*C*H-15), 38.6 (*C*H_2-2), 35.1 (*C*H_2-14), 31.2 (*C*H_2-12), 24.9 (*C*H_2-13), 20.2 (*C*H_3-15), 10.1 (*C*H_3-10). **IR** (ATR): ũ [cm^{-1}] = 3355, 2979, 2933, 2862, 1704, 1605, 1439, 1297, 1242, 1217, 1155, 732. **HRMS** (ESI): calcd for [$C_{17}H_{19}ClO_5$ + Na]$^+$: 361.0819, found: 361.0807.

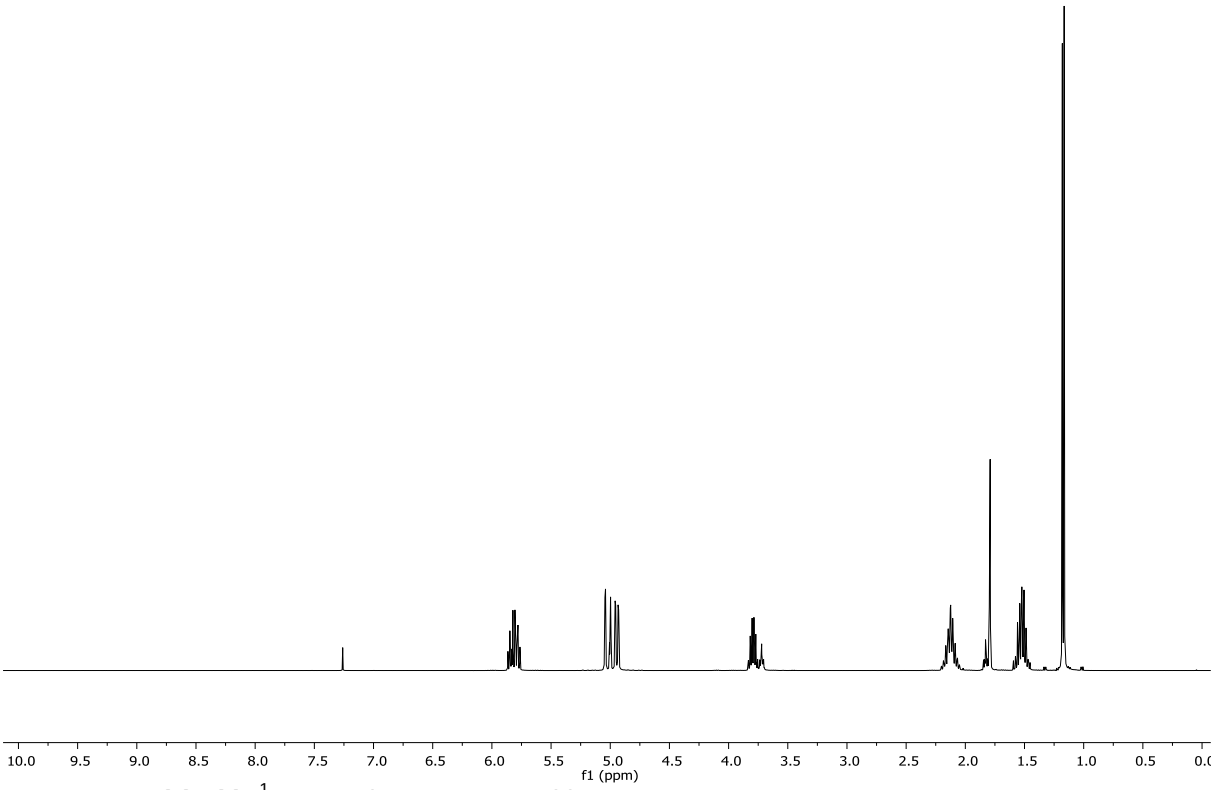
II. ^{1}H and ^{13}C spectra



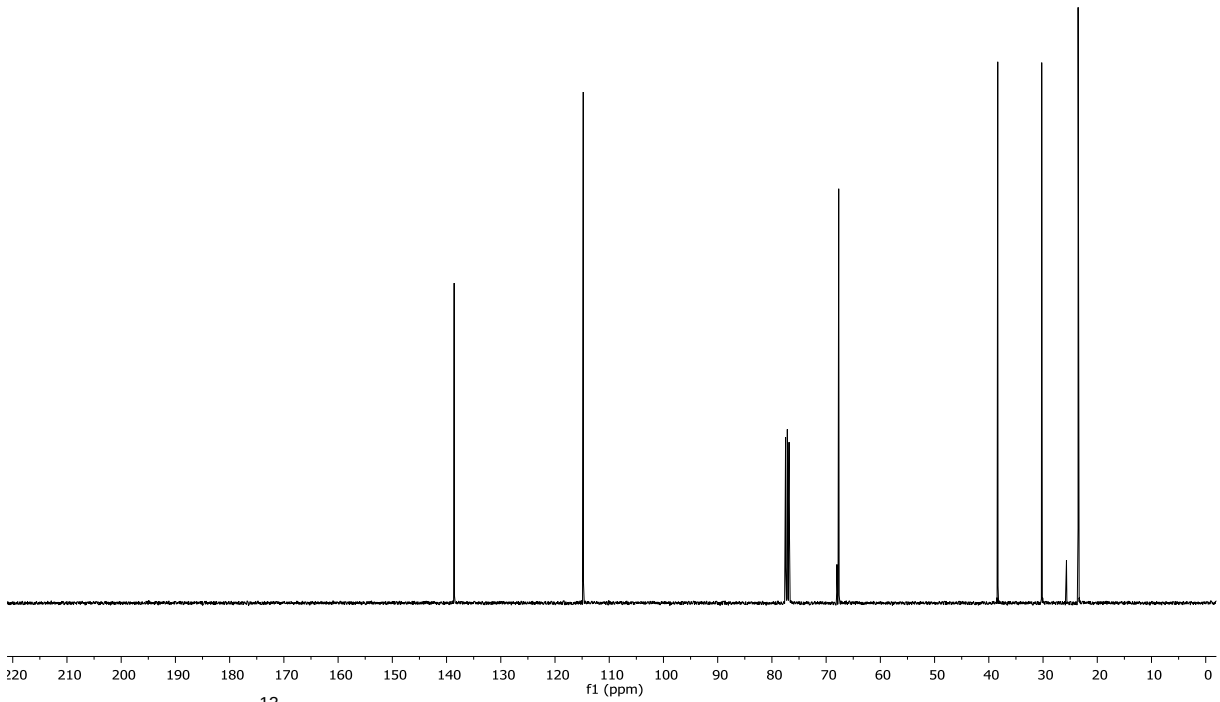
3-Methylhex-5-en-2-ol (11a): ^{1}H-NMR (400 MHz, $CDCl_3$)



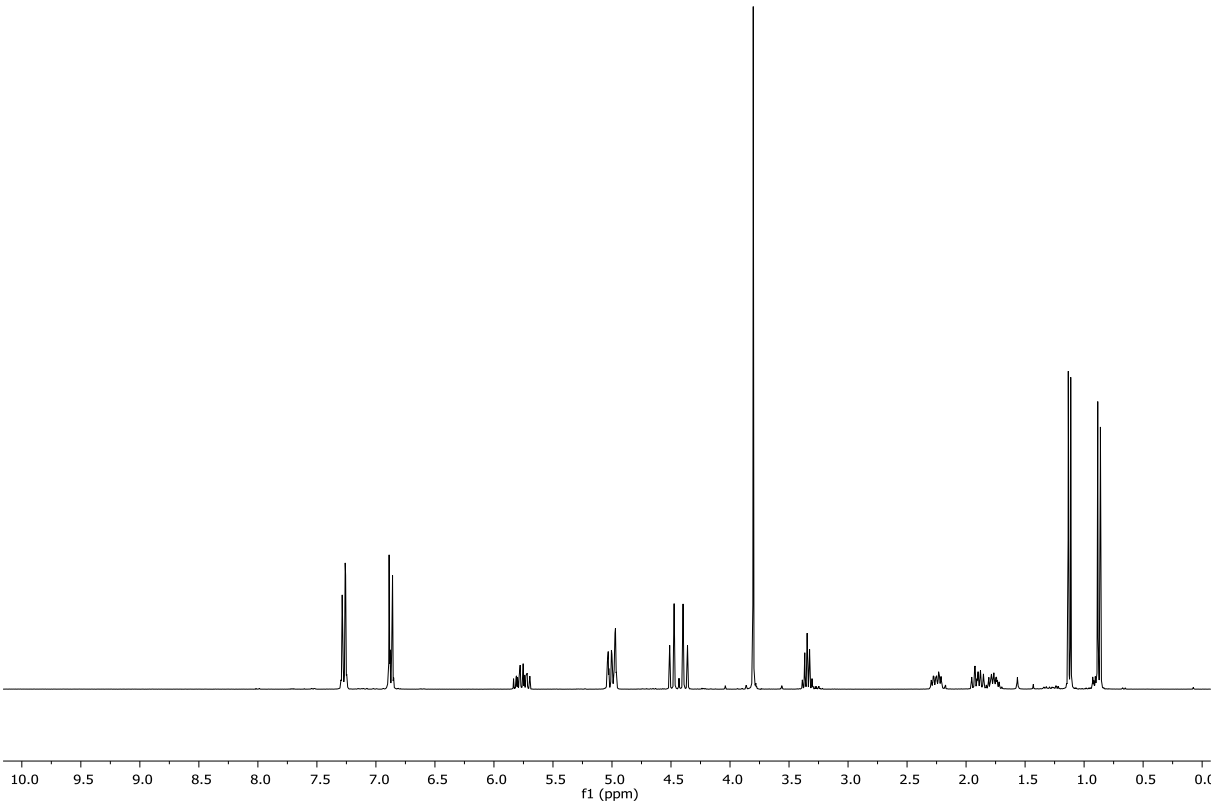
3-Methylhex-5-en-2-ol (11a): ^{13}C-NMR (100.6 MHz, $CDCl_3$)



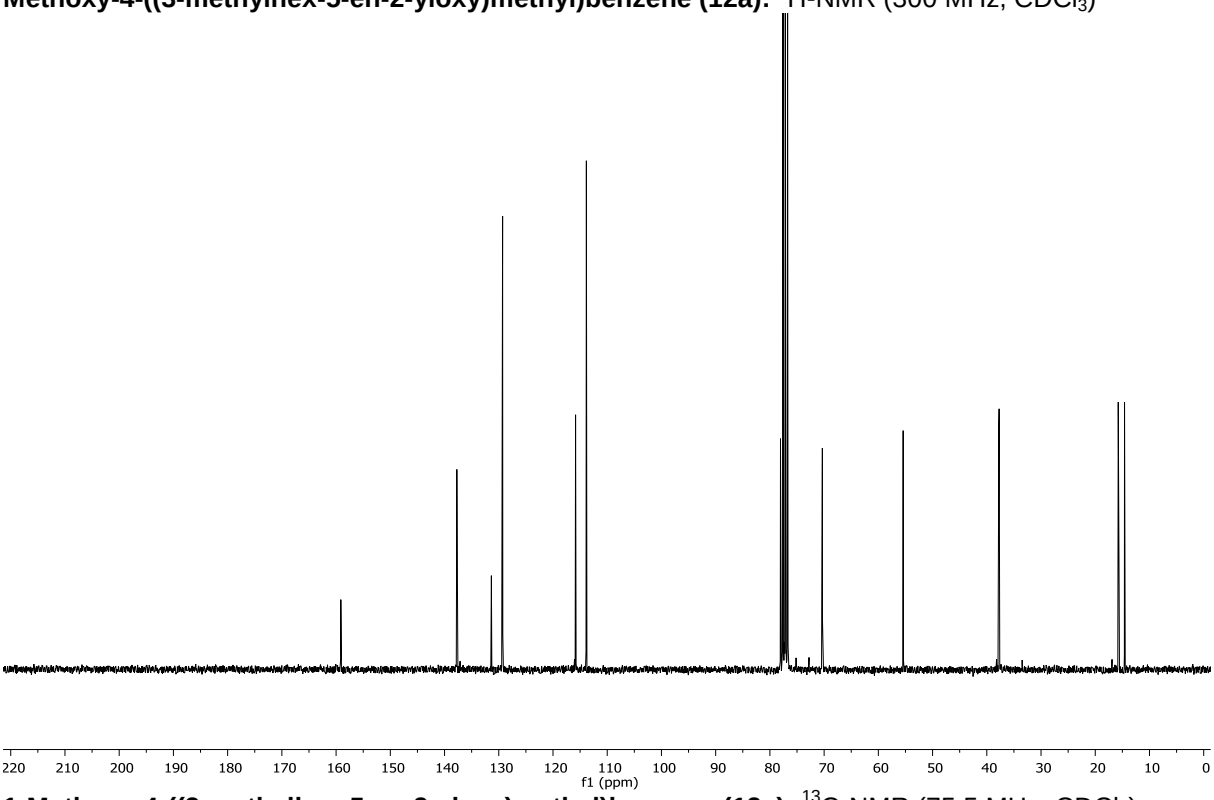
Hex-5-en-2-ol (11b): ^{1}H-NMR (400 MHz, $CDCl_3$)



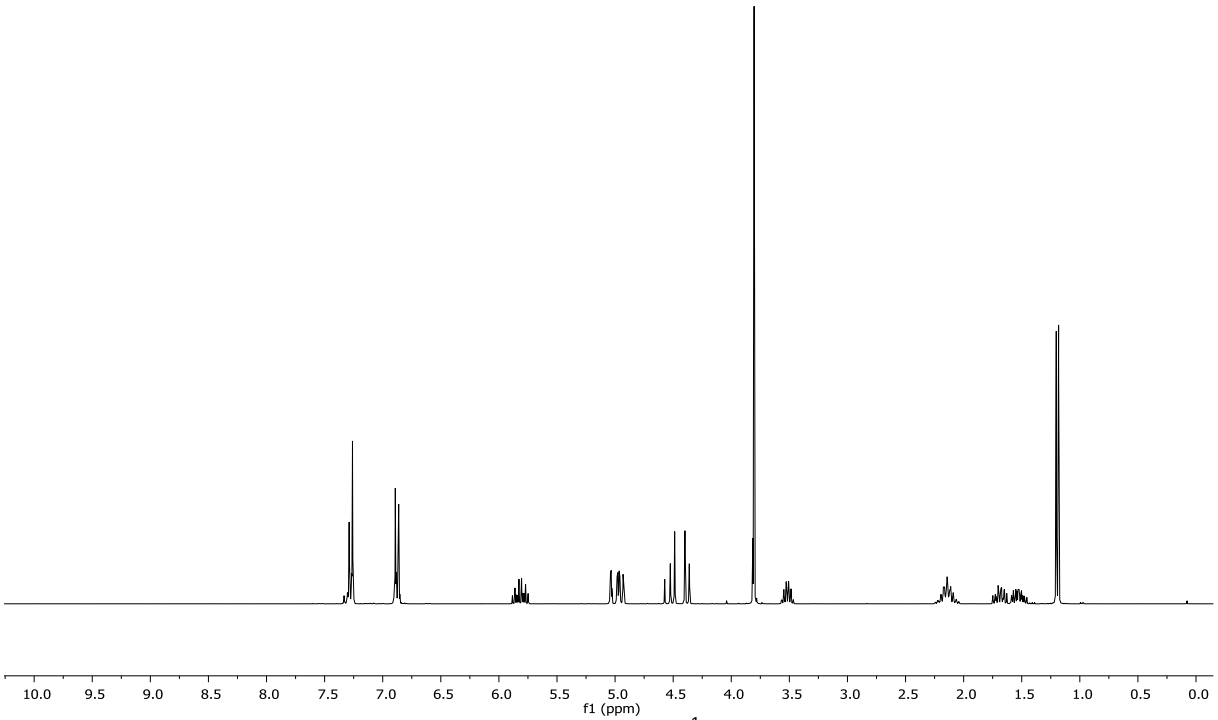
Hex-5-en-2-ol (11b): ^{13}C-NMR (100.6 MHz, $CDCl_3$)



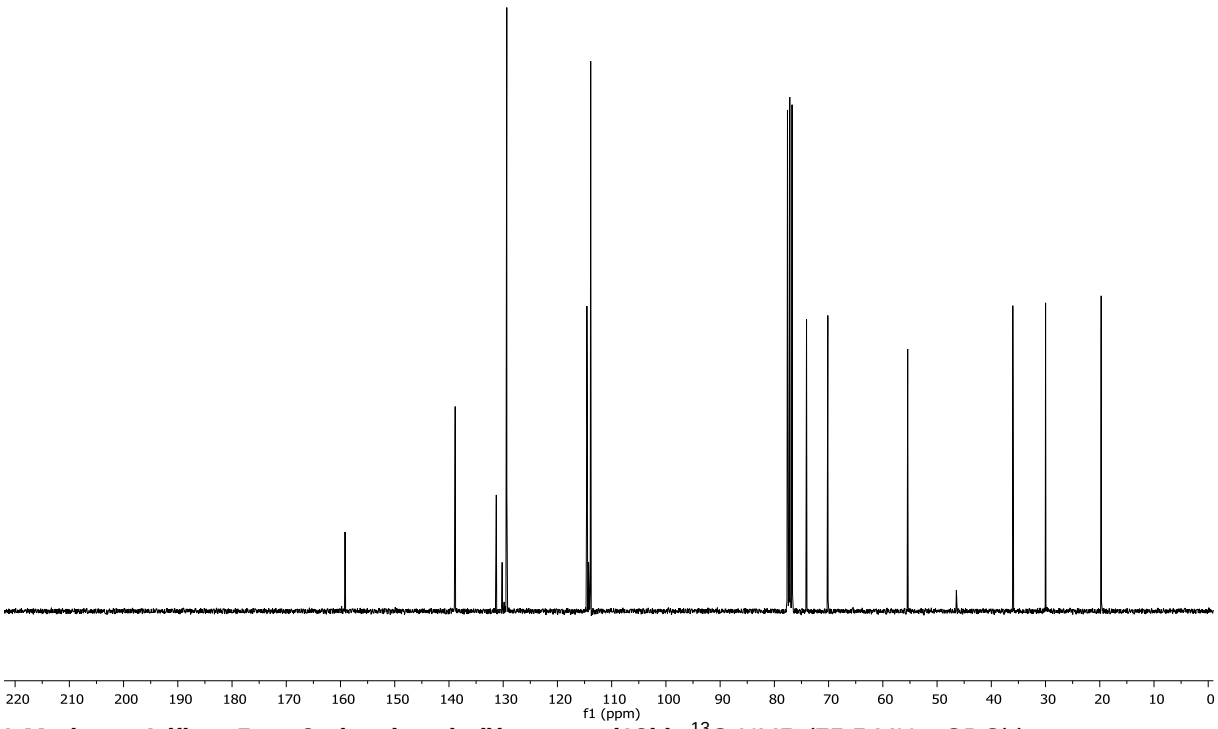
1-Methoxy-4-((3-methylhex-5-en-2-yloxy)methyl)benzene (12a): ^{1}H-NMR (300 MHz, $CDCl_3$)



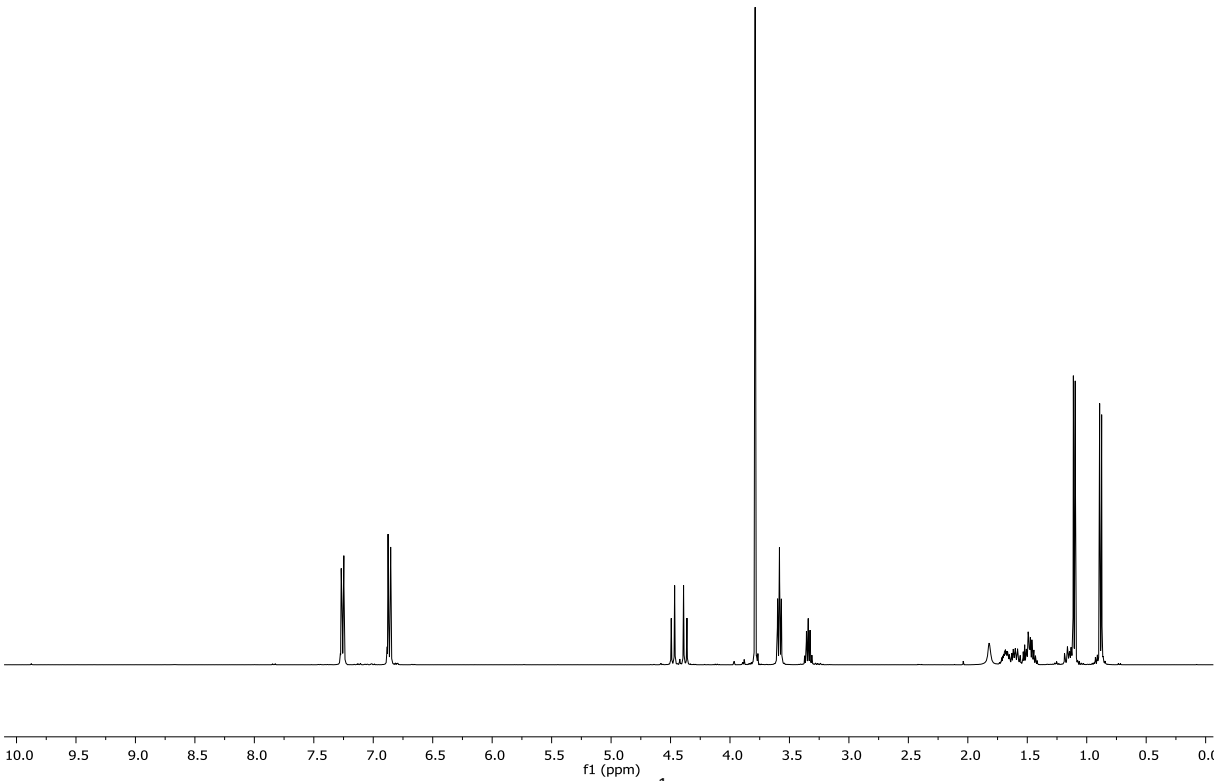
1-Methoxy-4-((3-methylhex-5-en-2-yloxy)methyl)benzene (12a): ^{13}C-NMR (75.5 MHz, $CDCl_3$)



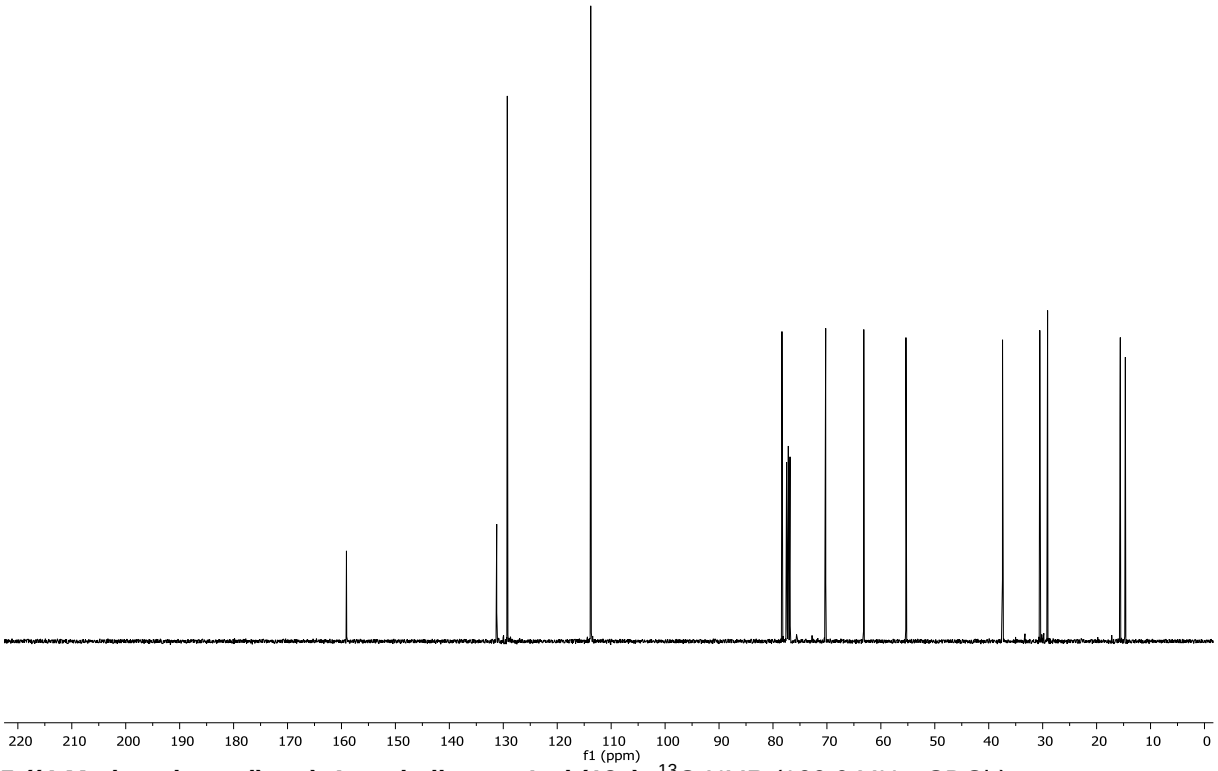
1-Methoxy-4-((hex-5-en-2-yloxy)methyl)benzene (12b): ^{1}H-NMR (300 MHz, $CDCl_3$)



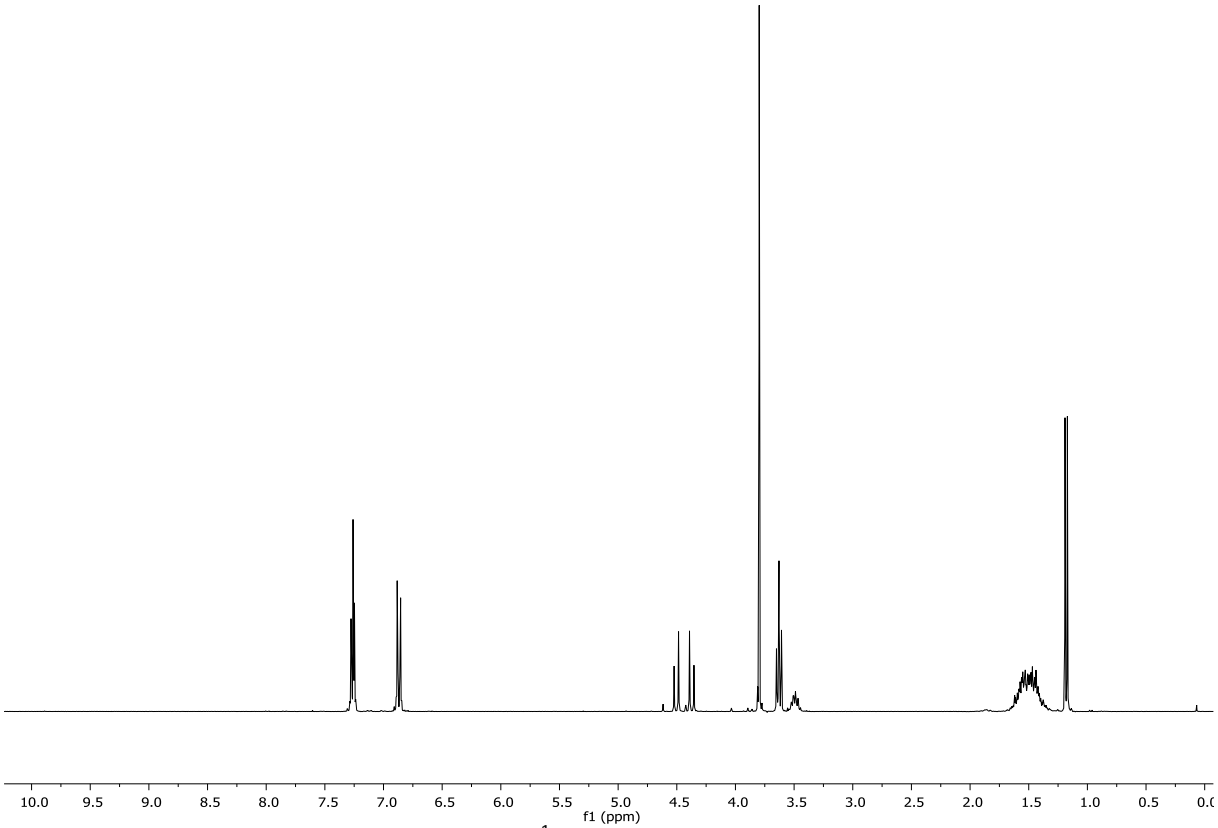
1-Methoxy-4-((hex-5-en-2-yloxy)methyl)benzene (12b): ^{13}C-NMR (75.5 MHz, $CDCl_3$)



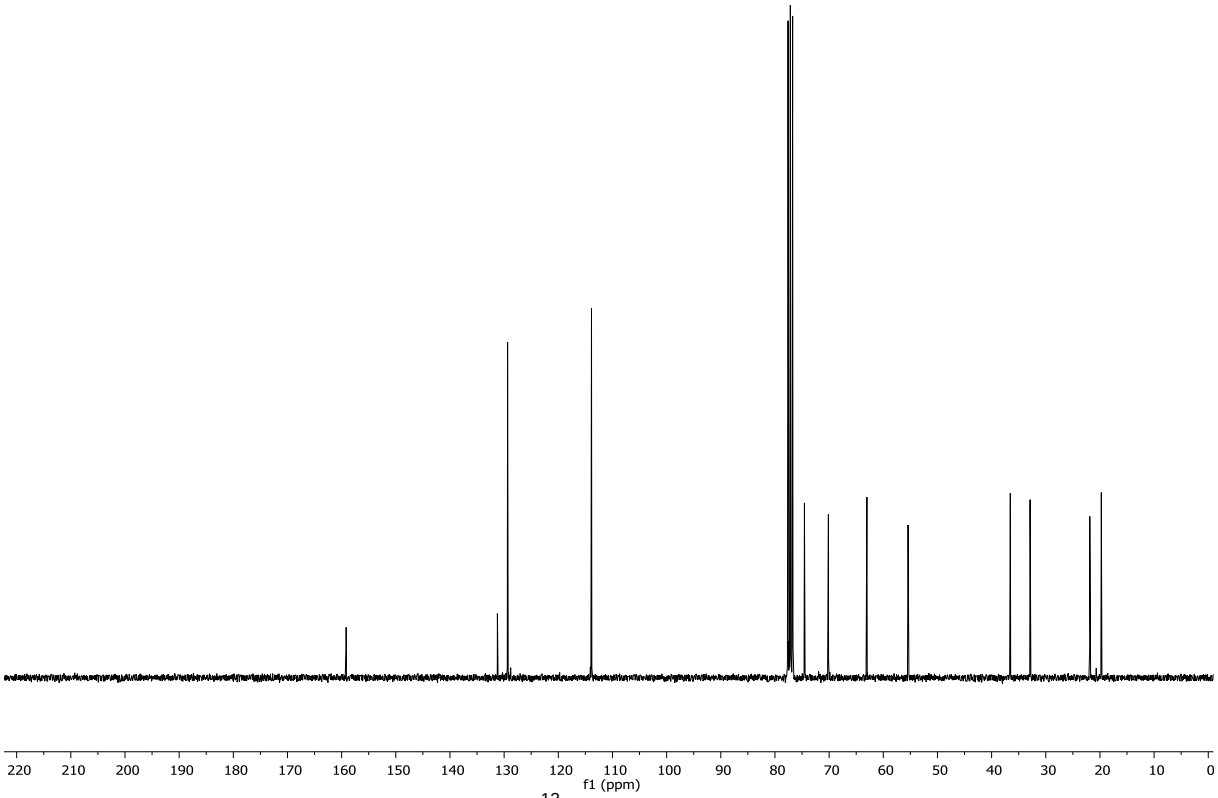
5-((4-Methoxybenzyl)oxy)-4-methylhexan-1-ol (13a): ^{1}H-NMR (400 MHz, $CDCl_3$)



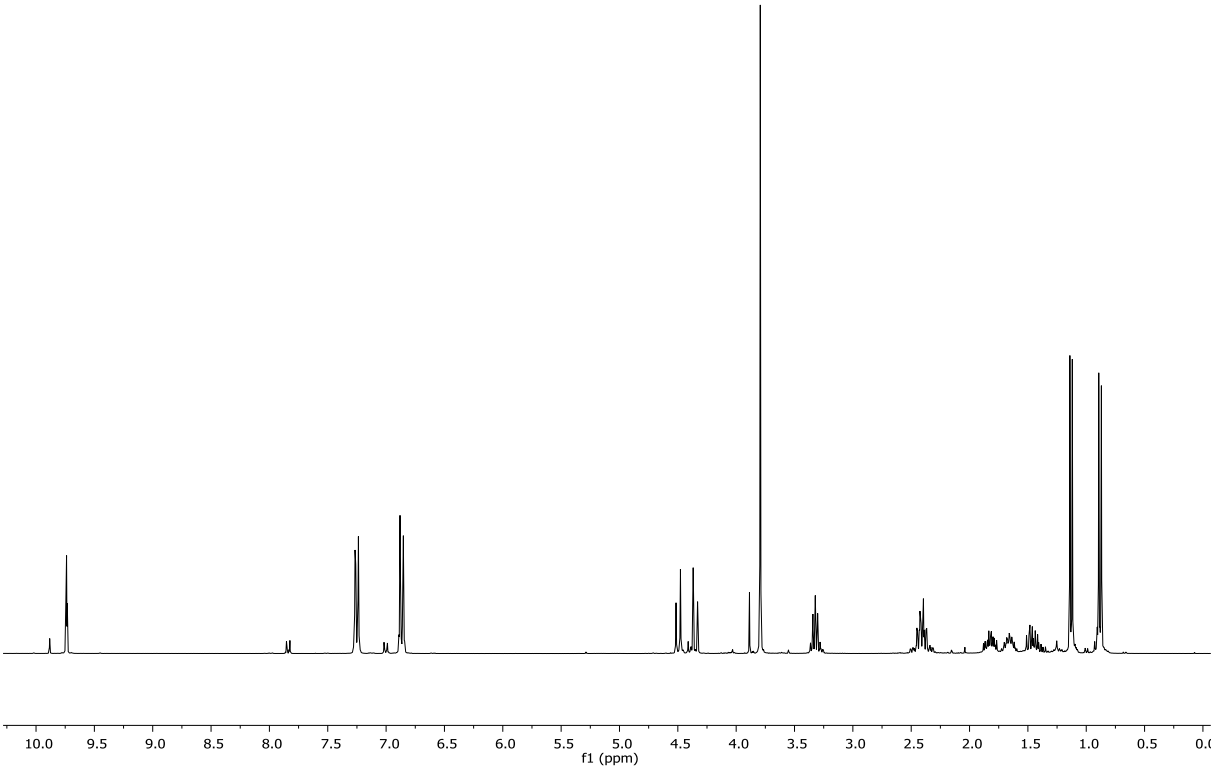
5-((4-Methoxybenzyl)oxy)-4-methylhexan-1-ol (13a): ^{13}C-NMR (100.6 MHz, $CDCl_3$)



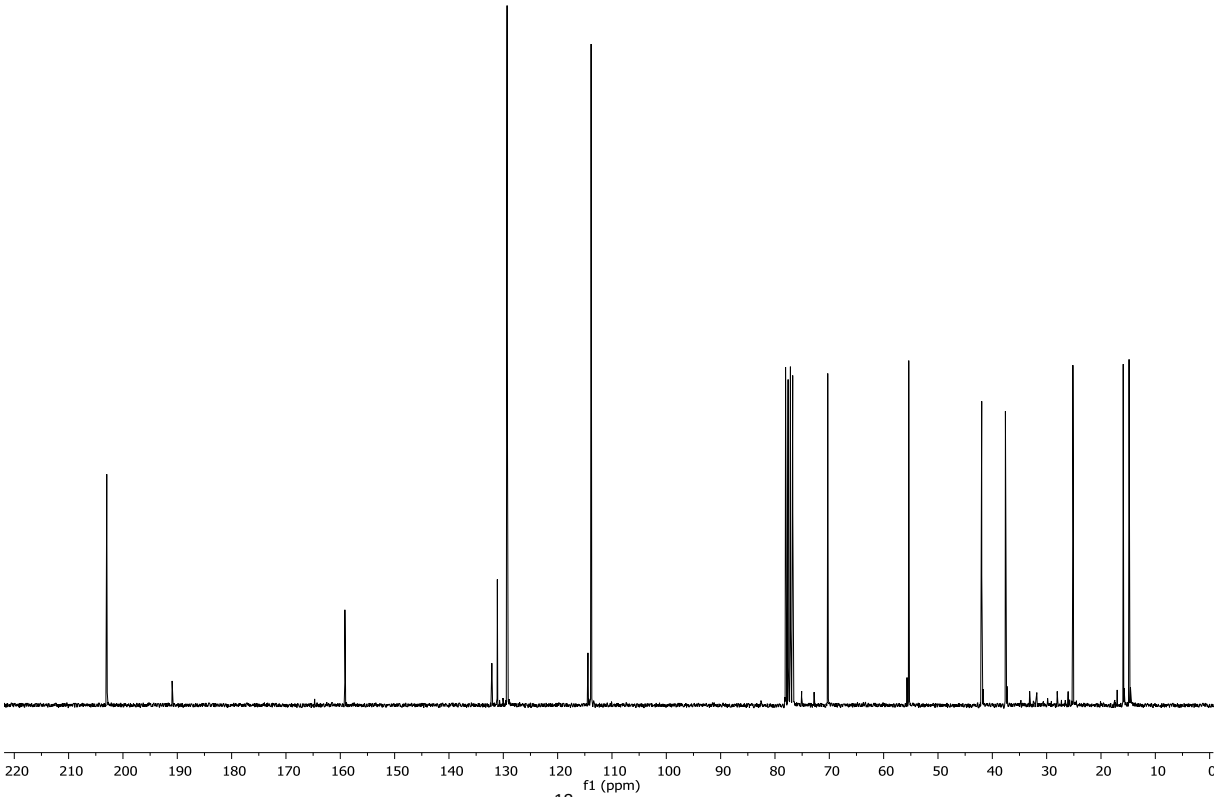
5-((4-Methoxybenzyl)oxy)hexan-1-ol (13b): ^{1}H-NMR (300 MHz, $CDCl_3$)



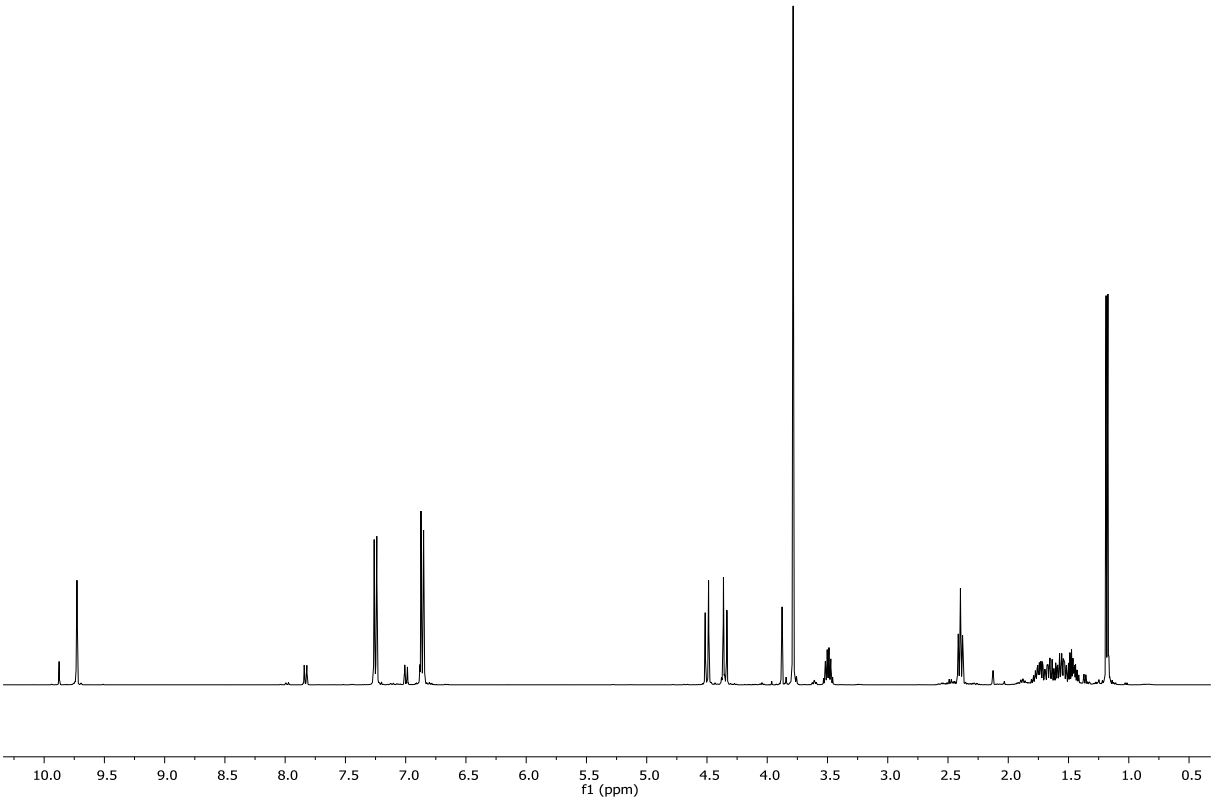
5-((4-Methoxybenzyl)oxy)hexan-1-ol (13b): ^{13}C-NMR (75.5 MHz, $CDCl_3$)



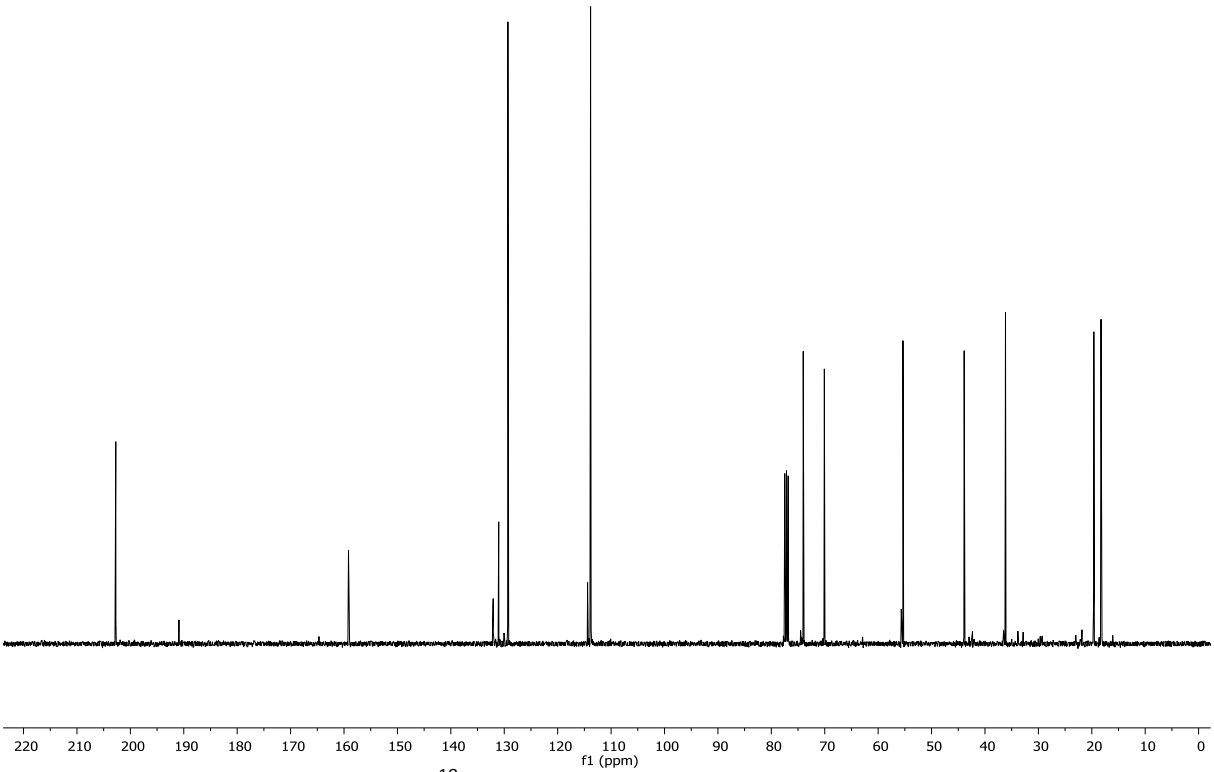
5-((4-Methoxybenzyl)oxy)-4-methylhexanal: ^{1}H-NMR (300 MHz, $CDCl_3$)



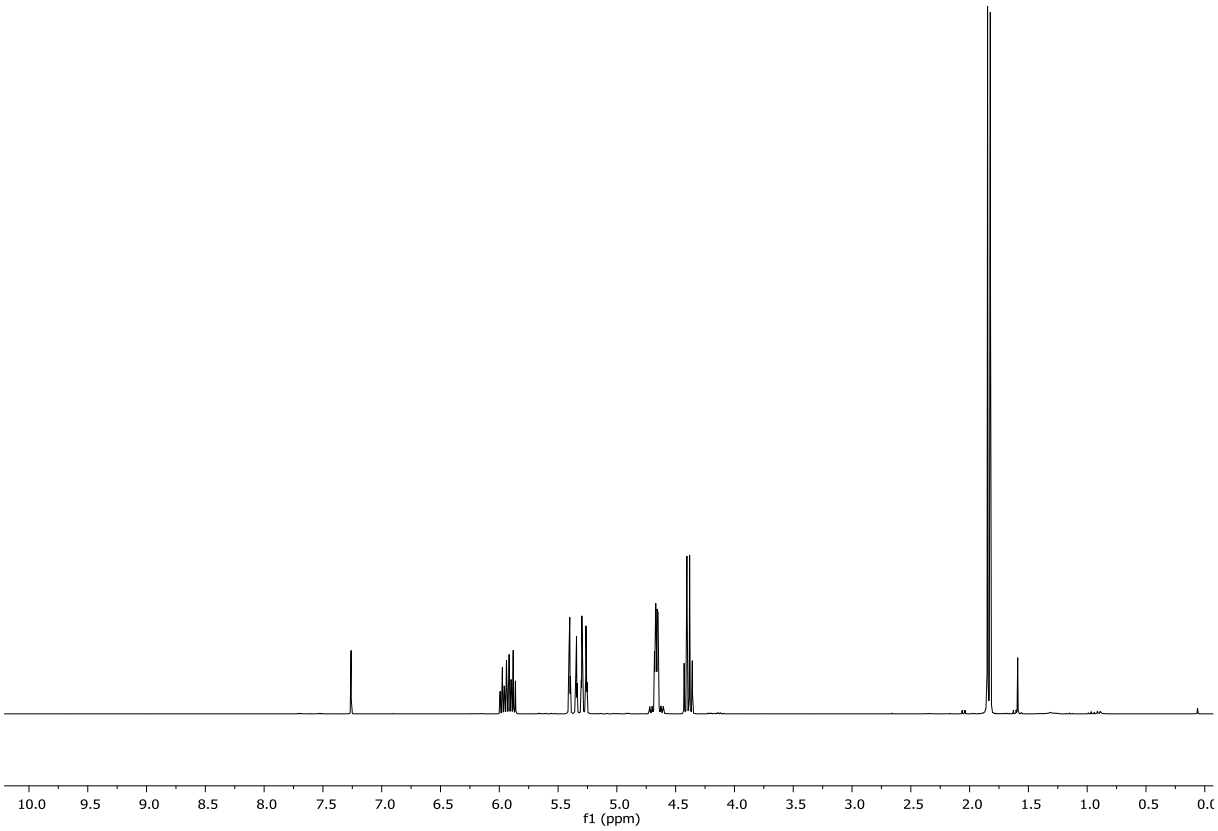
5-((4-Methoxybenzyl)oxy)-4-methylhexanal: ^{13}C-NMR (75.5 MHz, $CDCl_3$)



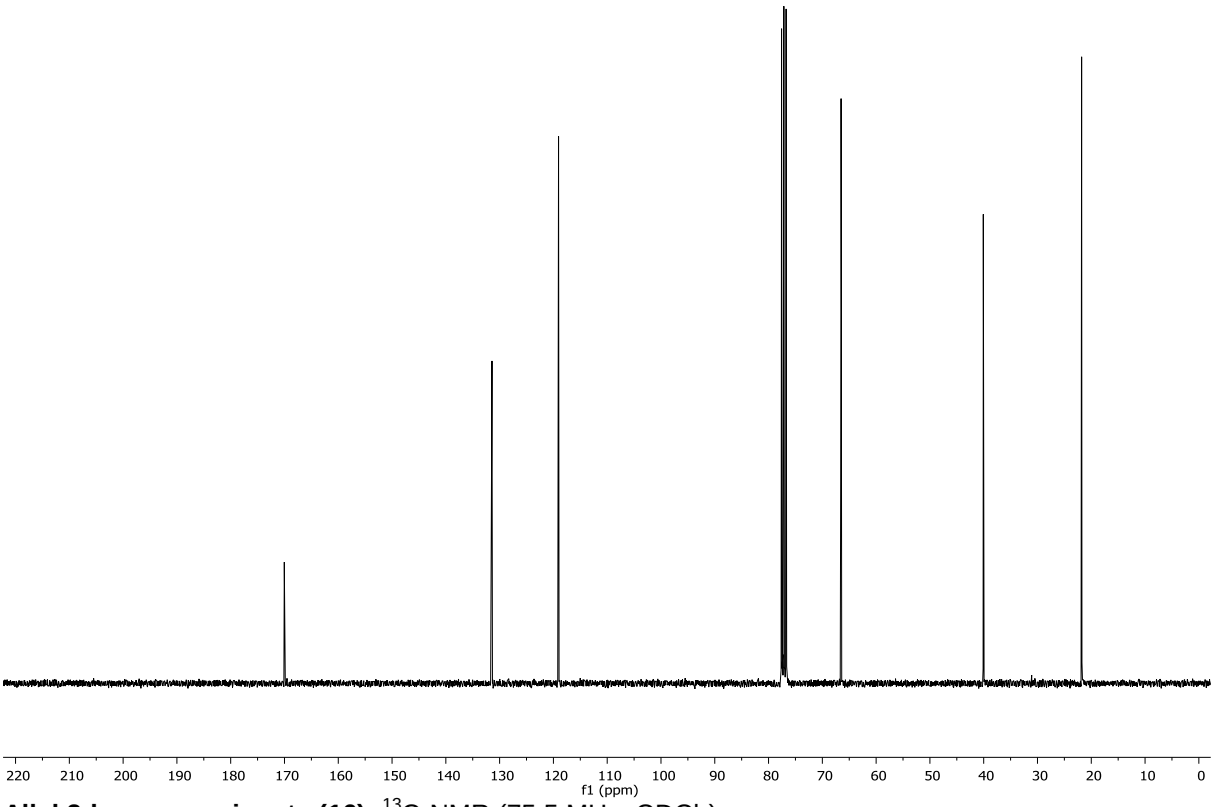
5-((4-Methoxybenzyl)oxy)hexanal: ^{1}H-NMR (400 MHz, $CDCl_3$)



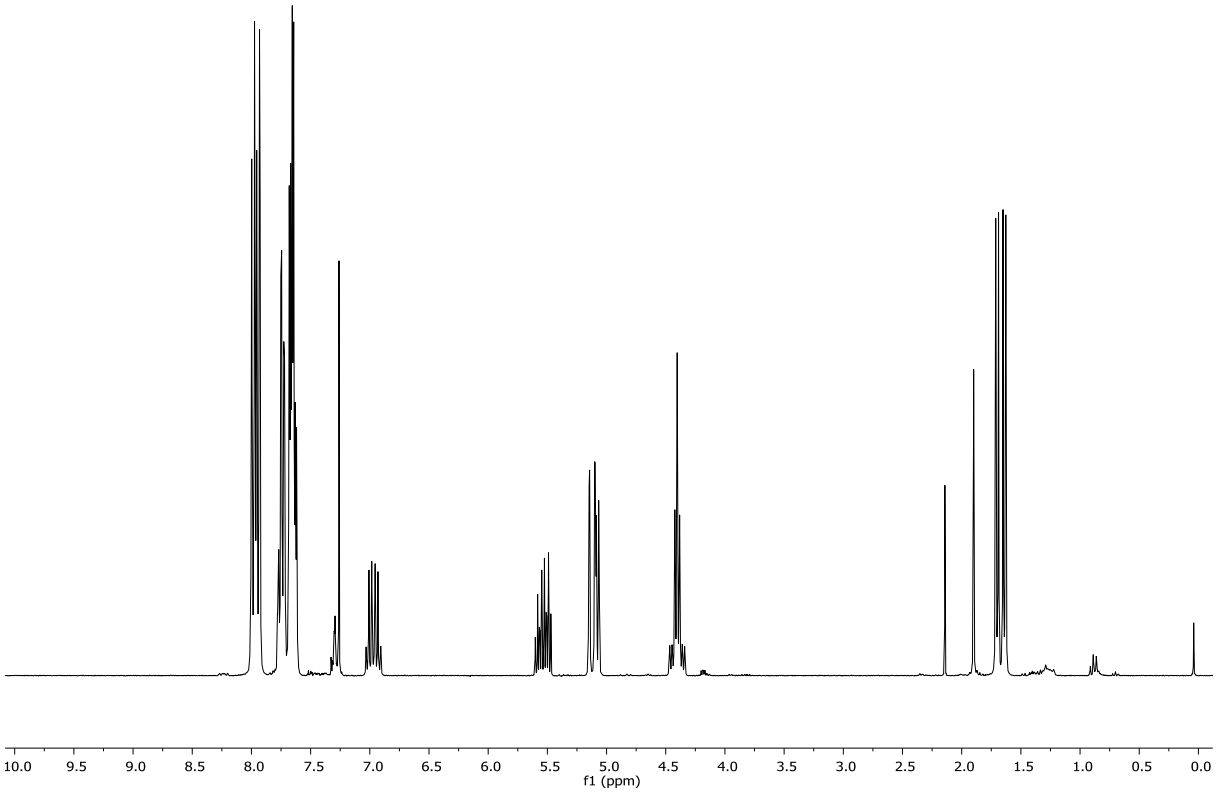
5-((4-Methoxybenzyl)oxy)hexanal: ^{13}C-NMR (100.6 MHz, $CDCl_3$)



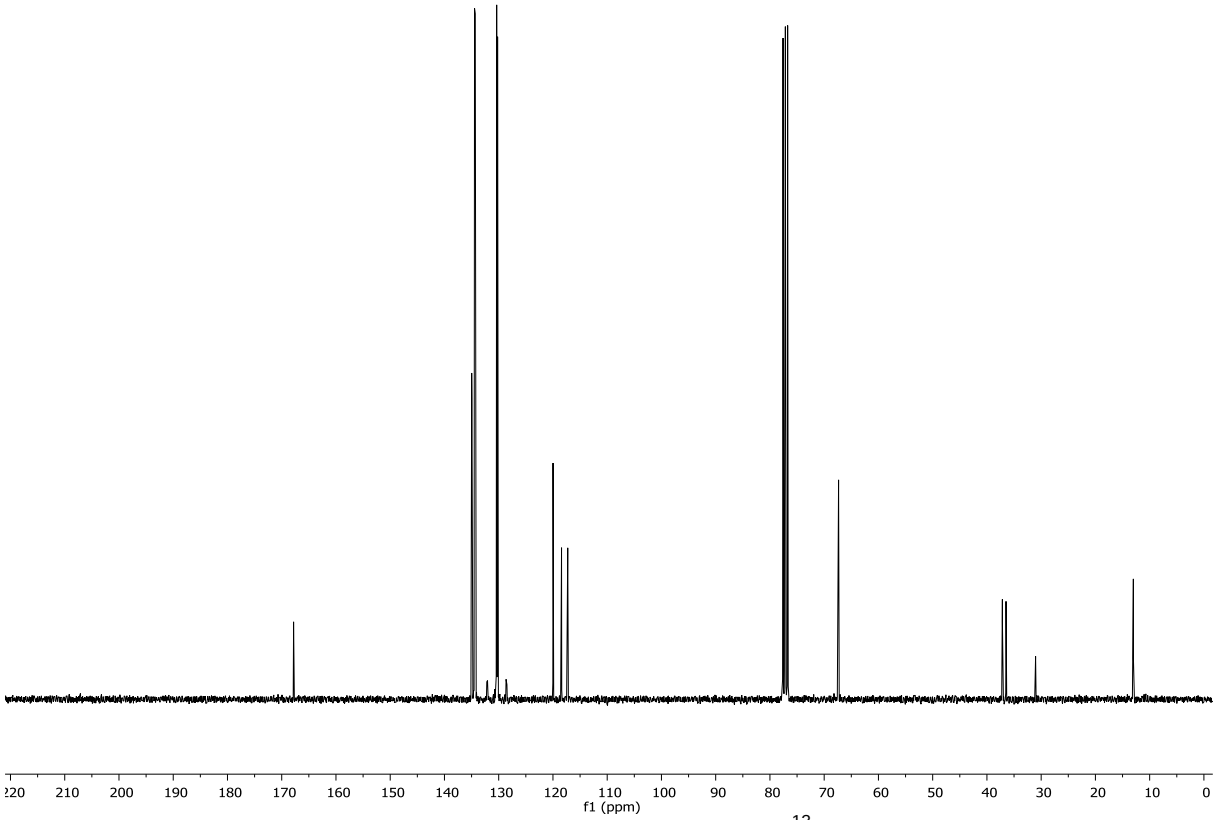
Allyl 2-bromopropionate (16): ^{1}H-NMR (300 MHz, $CDCl_3$)



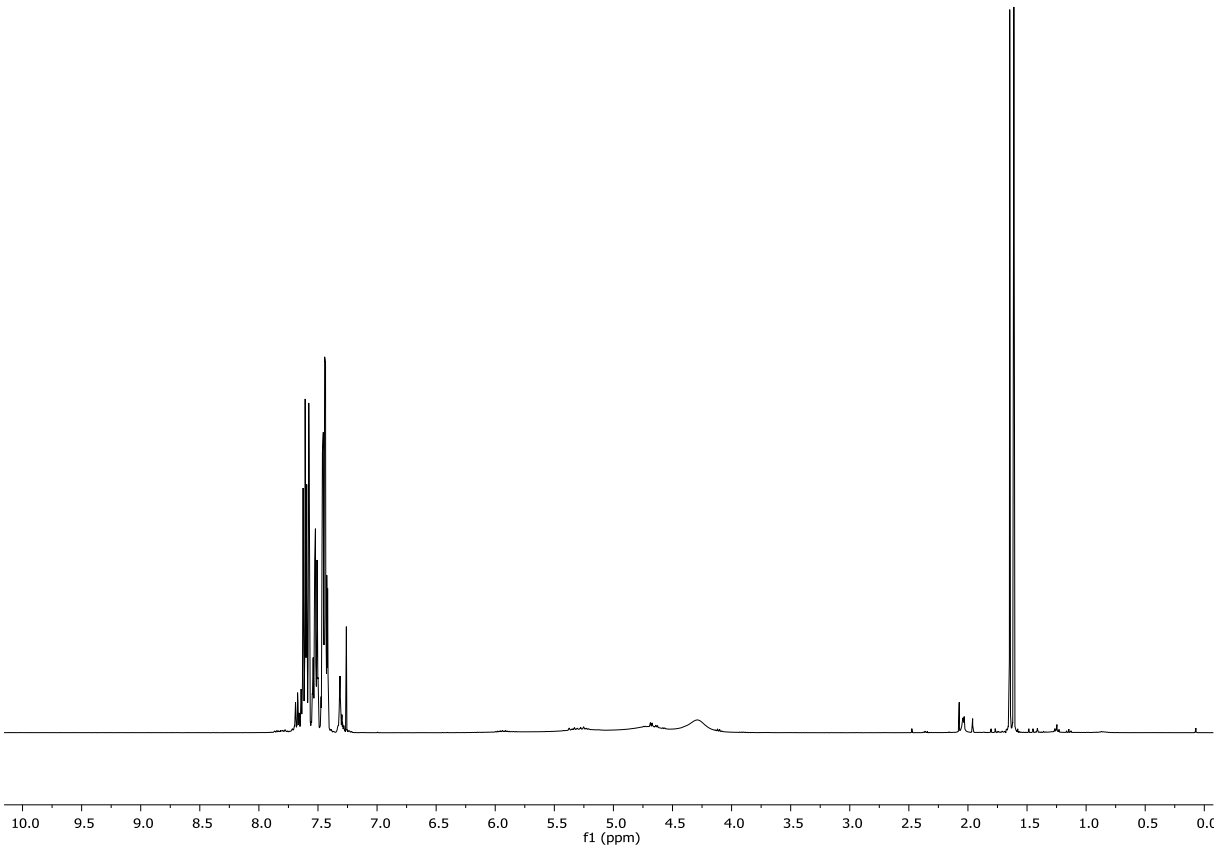
Allyl 2-bromopropionate (16): ^{13}C-NMR (75.5 MHz, $CDCl_3$)



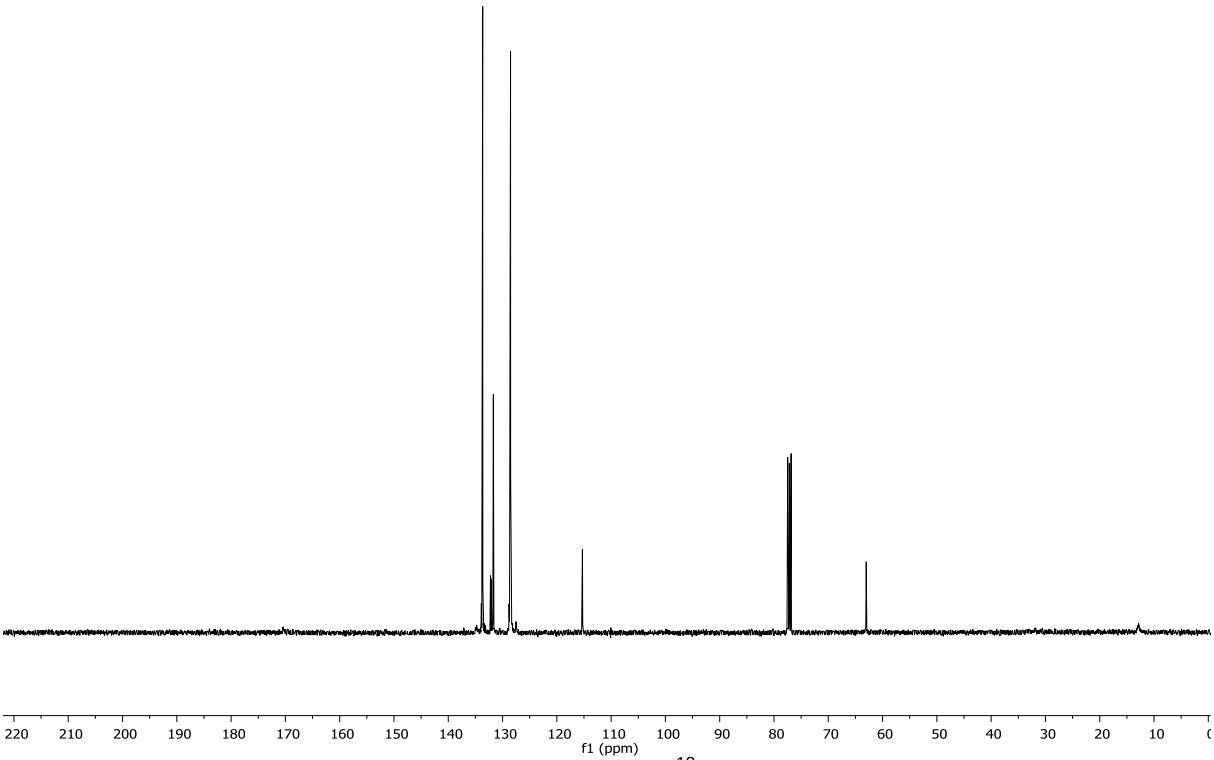
(1-Allyloxy-1-oxopropan-2-yl)triphenylphosphonium bromide: ^{1}H-NMR (300 MHz, $CDCl_3$)



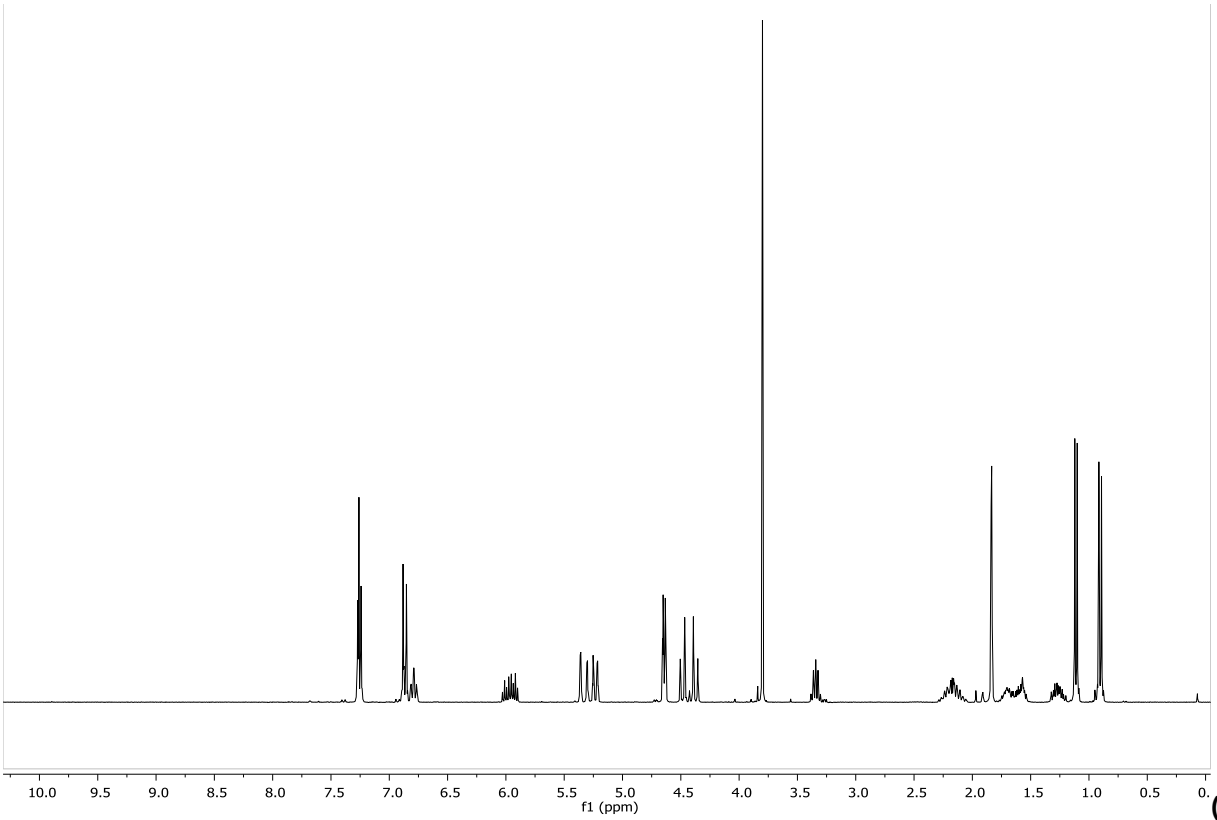
(1-Allyloxy-1-oxopropan-2-yl)triphenylphosphonium bromide: ^{13}C-NMR (75.5 MHz, $CDCl_3$)



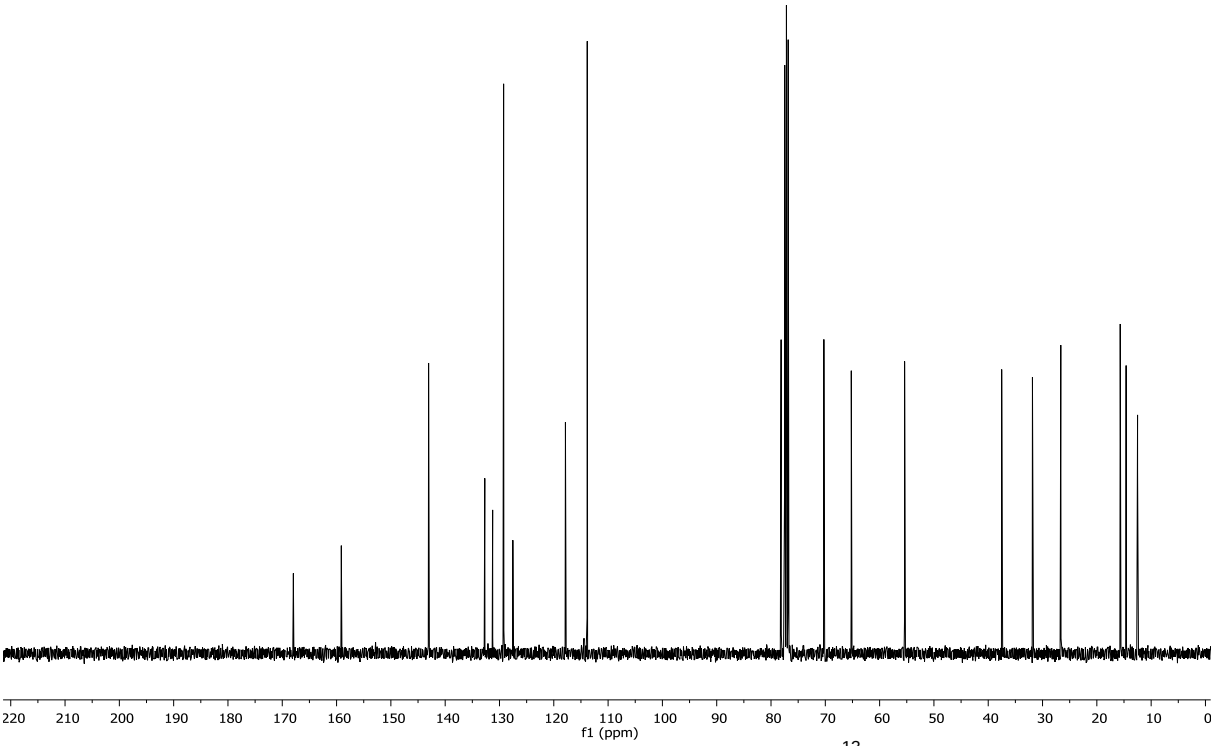
Allyl 2-(triphenylphosphoranylidene)propionate (14): ^{1}H-NMR (400 MHz, $CDCl_3$)



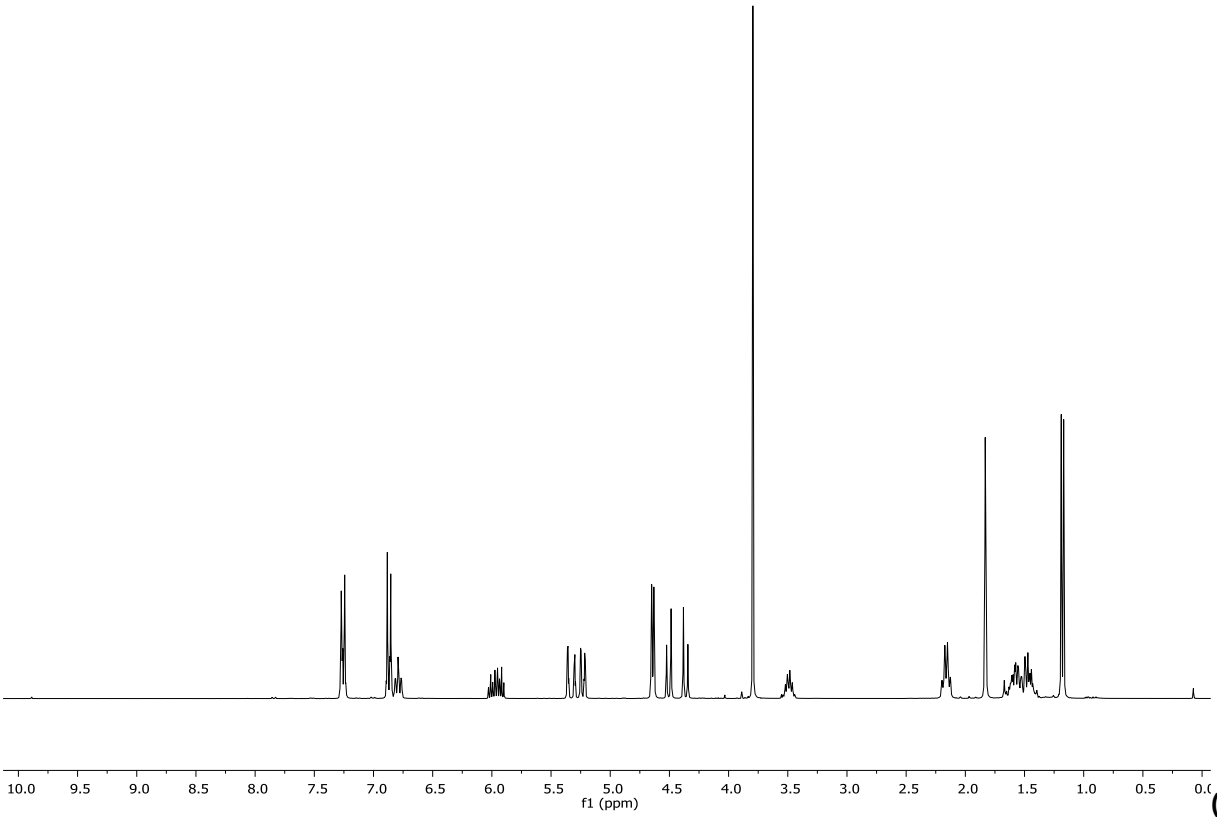
Allyl 2-(triphenylphosphoranylidene)propionate (14): ^{13}C-NMR (100.6 MHz, $CDCl_3$)



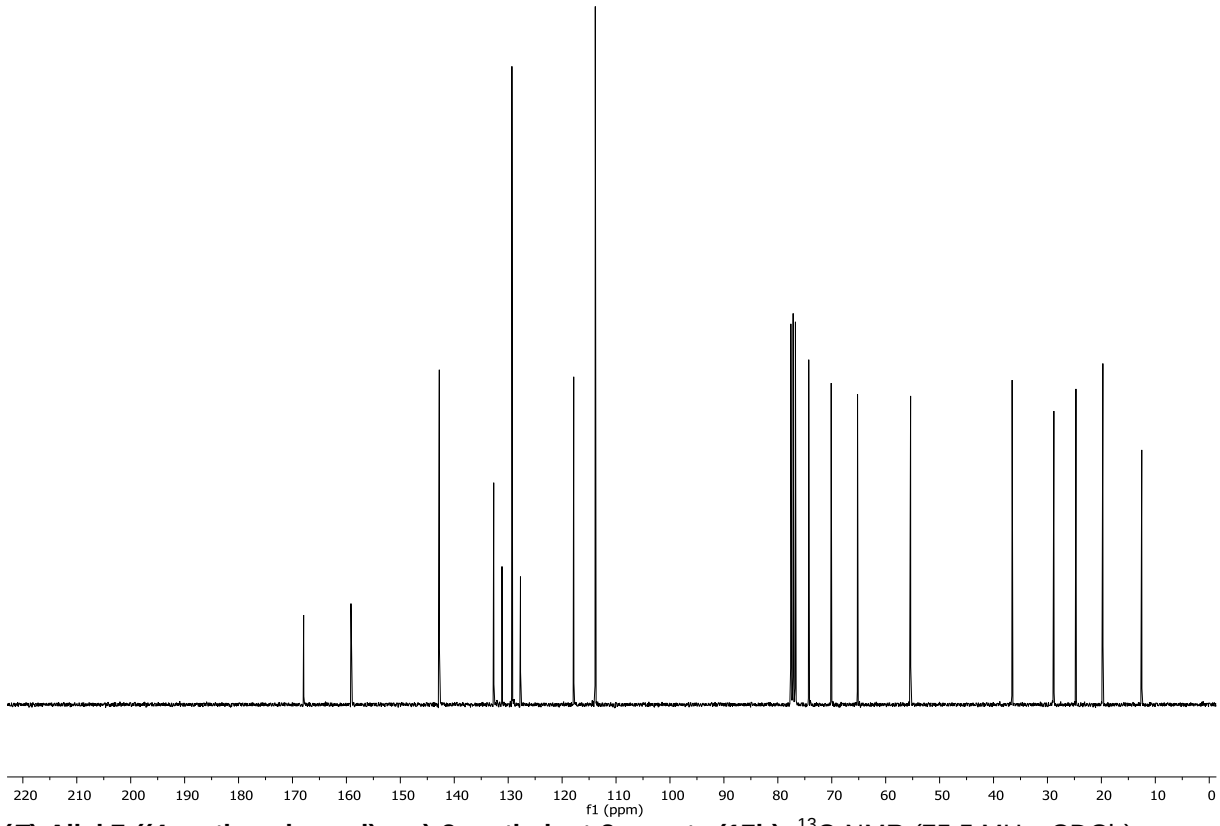
(*E*)-Allyl 7-((4-methoxybenzyl)oxy)-2,6-dimethyloct-2-enoate (17a): ^{1}H-NMR (300 MHz, $CDCl_3$)



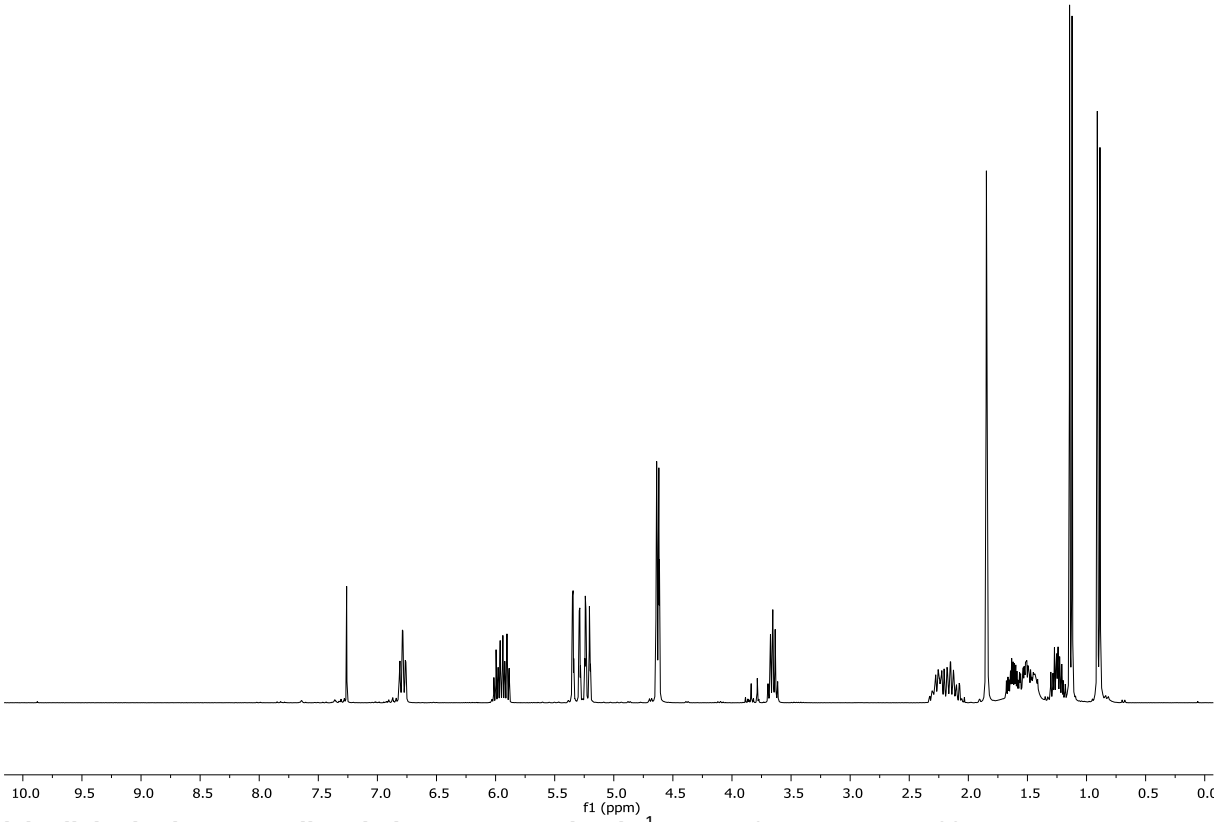
(*E*)-Allyl 7-((4-methoxybenzyl)oxy)-2,6-dimethyloct-2-enoate (17a): ^{13}C-NMR (100.6 MHz, $CDCl_3$)



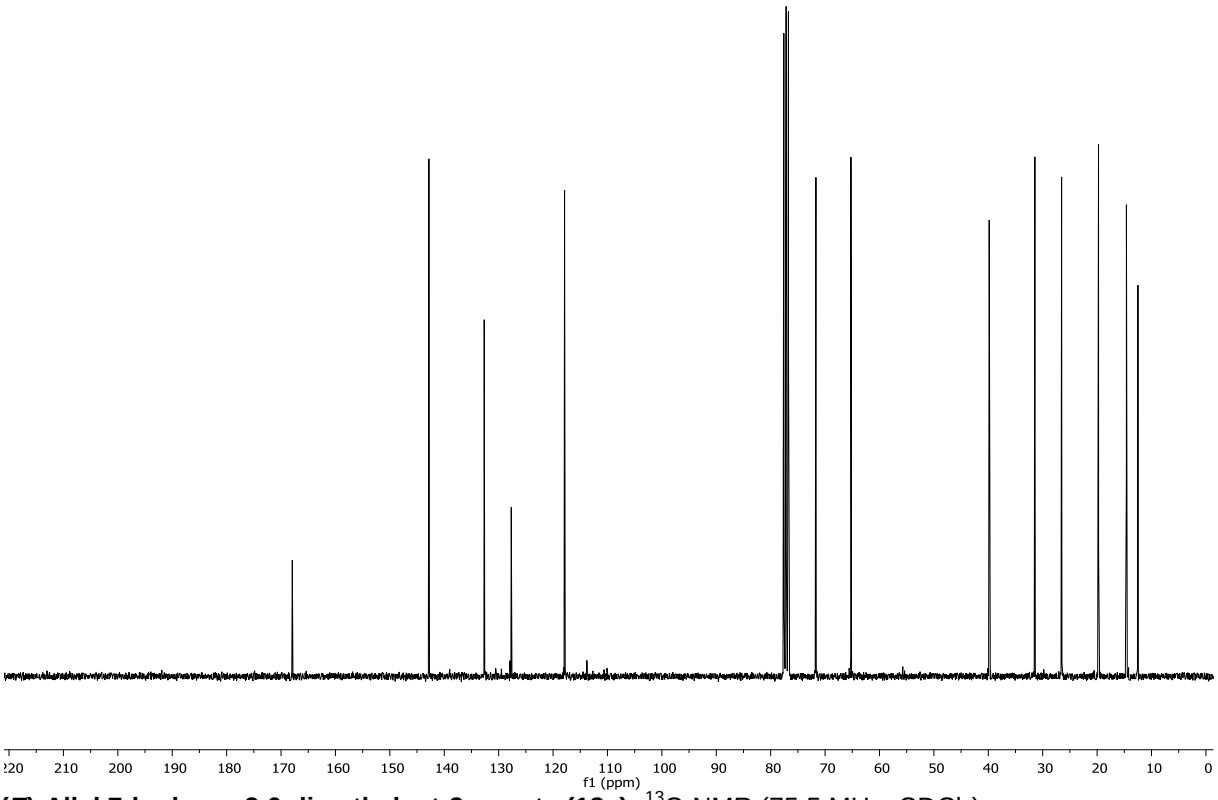
(*E*)-Allyl 7-((4-methoxybenzyl)oxy)-2-methyloct-2-enoate (17b): ^{1}H-NMR (300 MHz, $CDCl_3$)



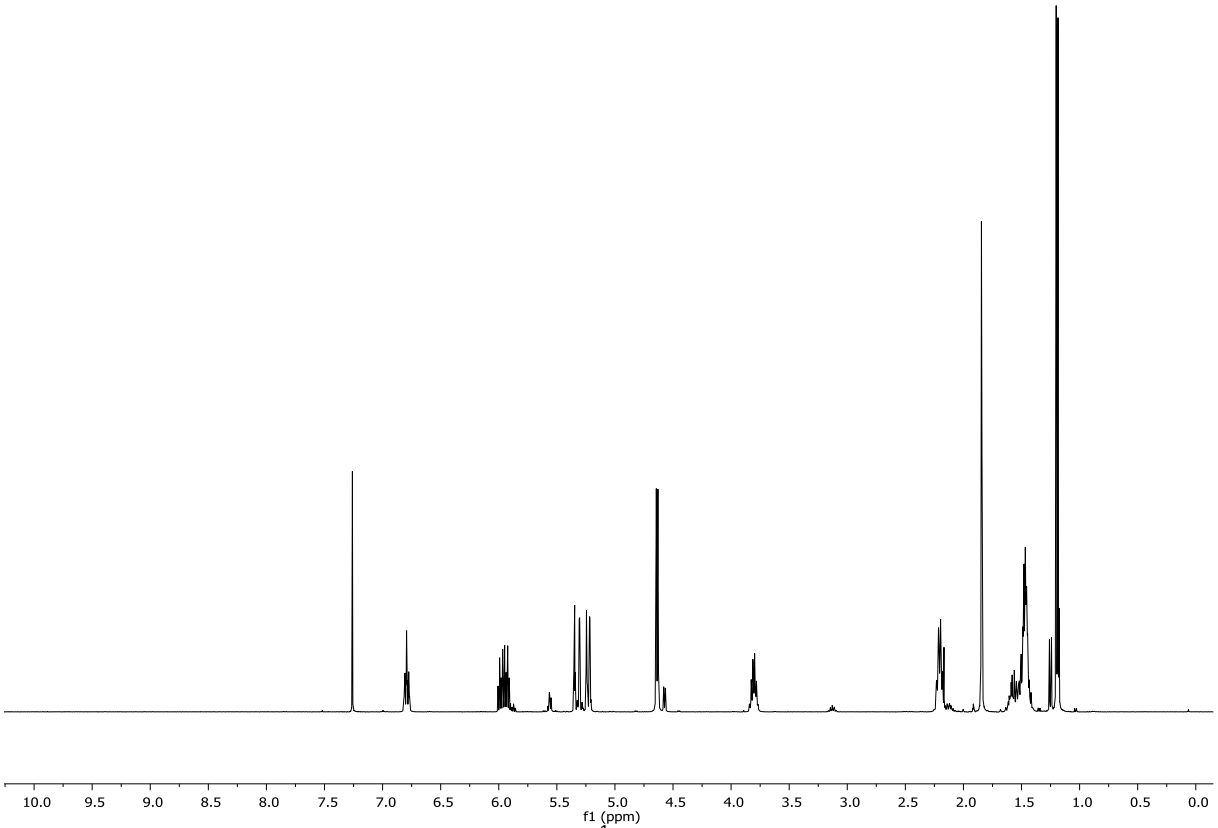
(*E*)-Allyl 7-((4-methoxybenzyl)oxy)-2-methyloct-2-enoate (17b): ^{13}C-NMR (75.5 MHz, $CDCl_3$)



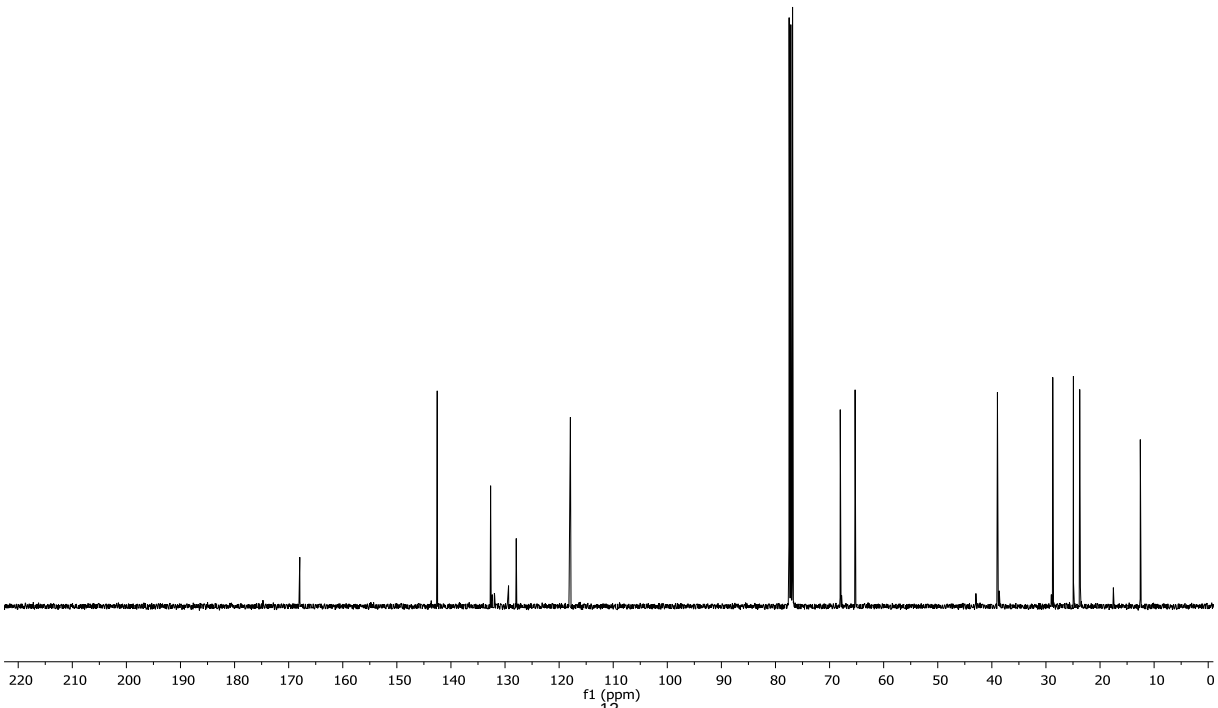
(*E*)-Allyl 7-hydroxy-2,6-dimethyloct-2-enoate (18a): ^{1}H-NMR (300 MHz, $CDCl_3$)



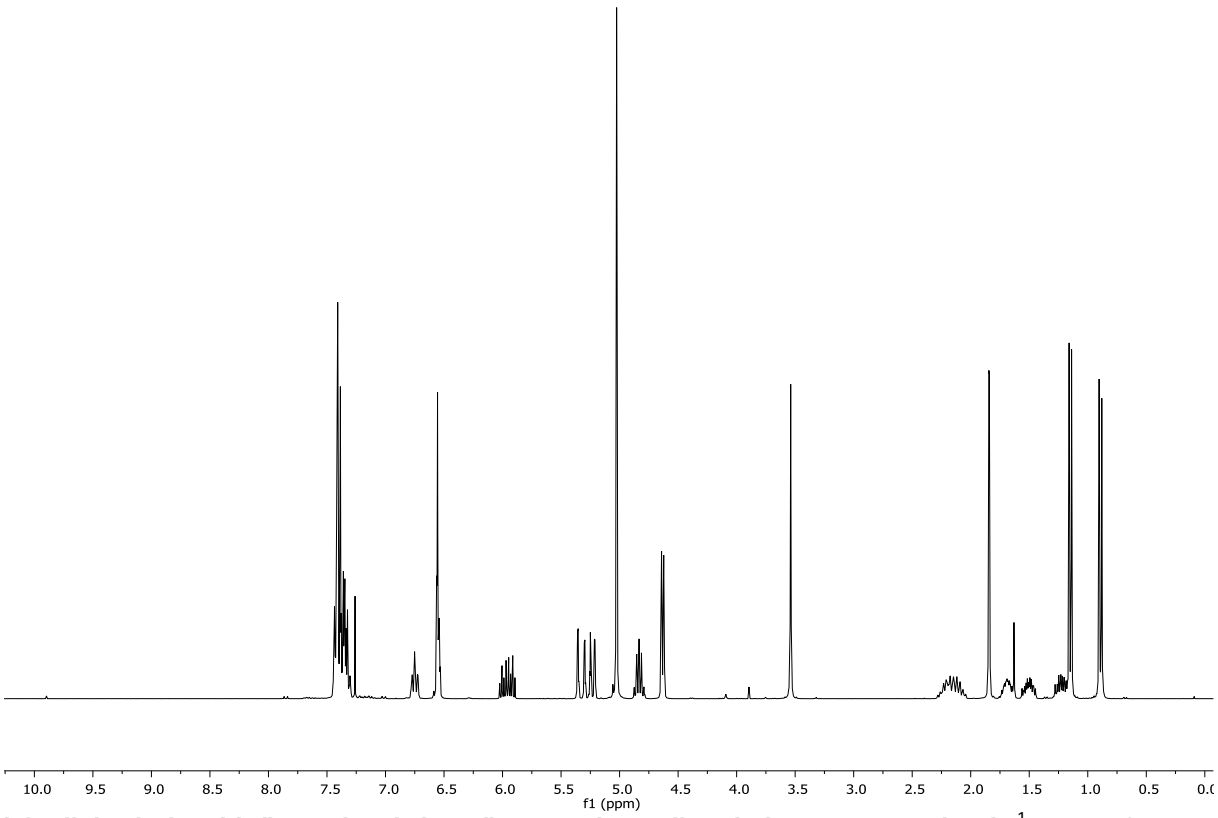
(*E*)-Allyl 7-hydroxy-2,6-dimethyloct-2-enoate (18a): ^{13}C-NMR (75.5 MHz, $CDCl_3$)



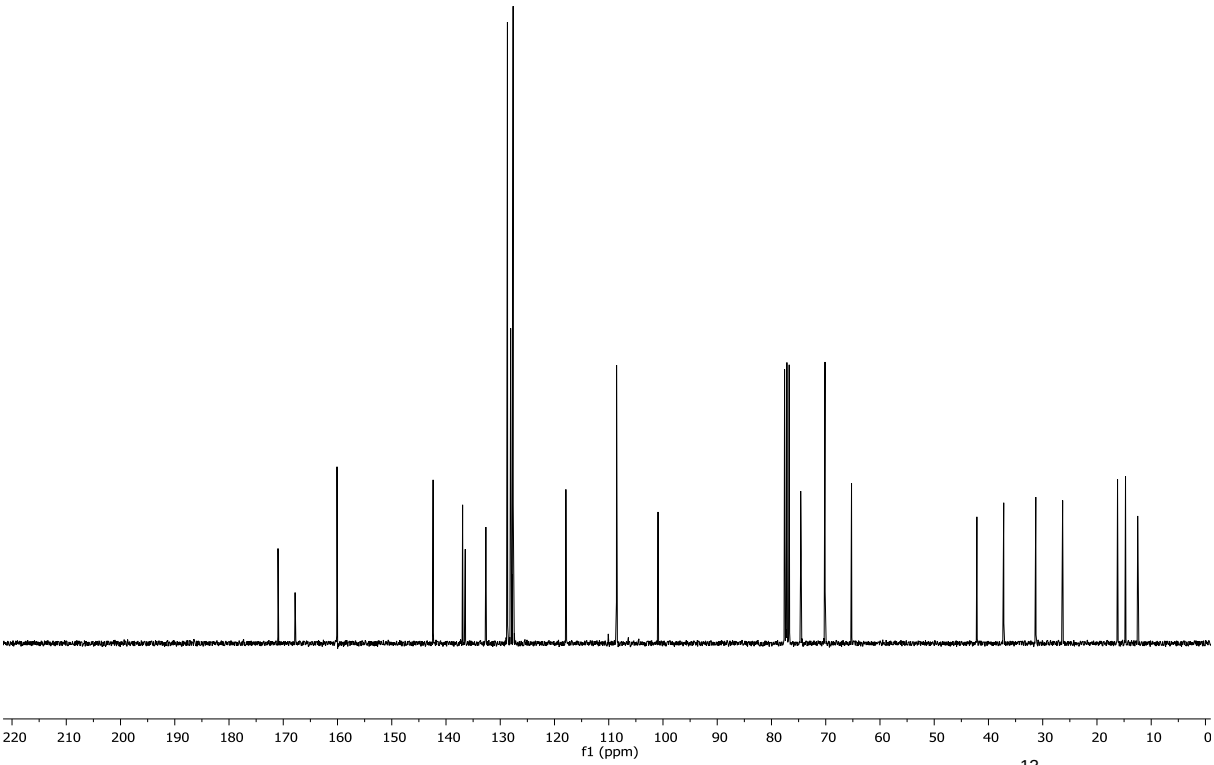
(*E*)-Allyl 7-hydroxy-2-methyloct-2-enoate (18b): ^{1}H-NMR (400 MHz, $CDCl_3$)



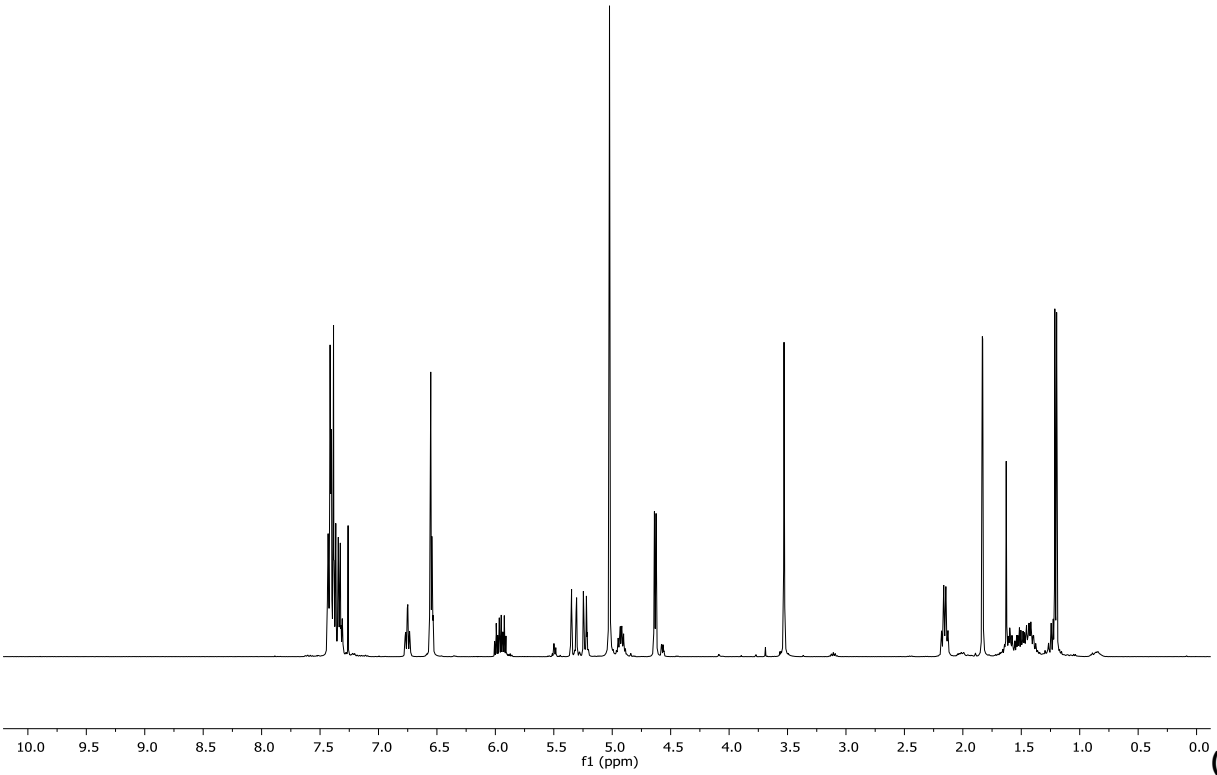
(*E*)-Allyl 7-hydroxy-2-methyloct-2-enoate (18b): ^{13}C-NMR (100.6 MHz, $CDCl_3$)



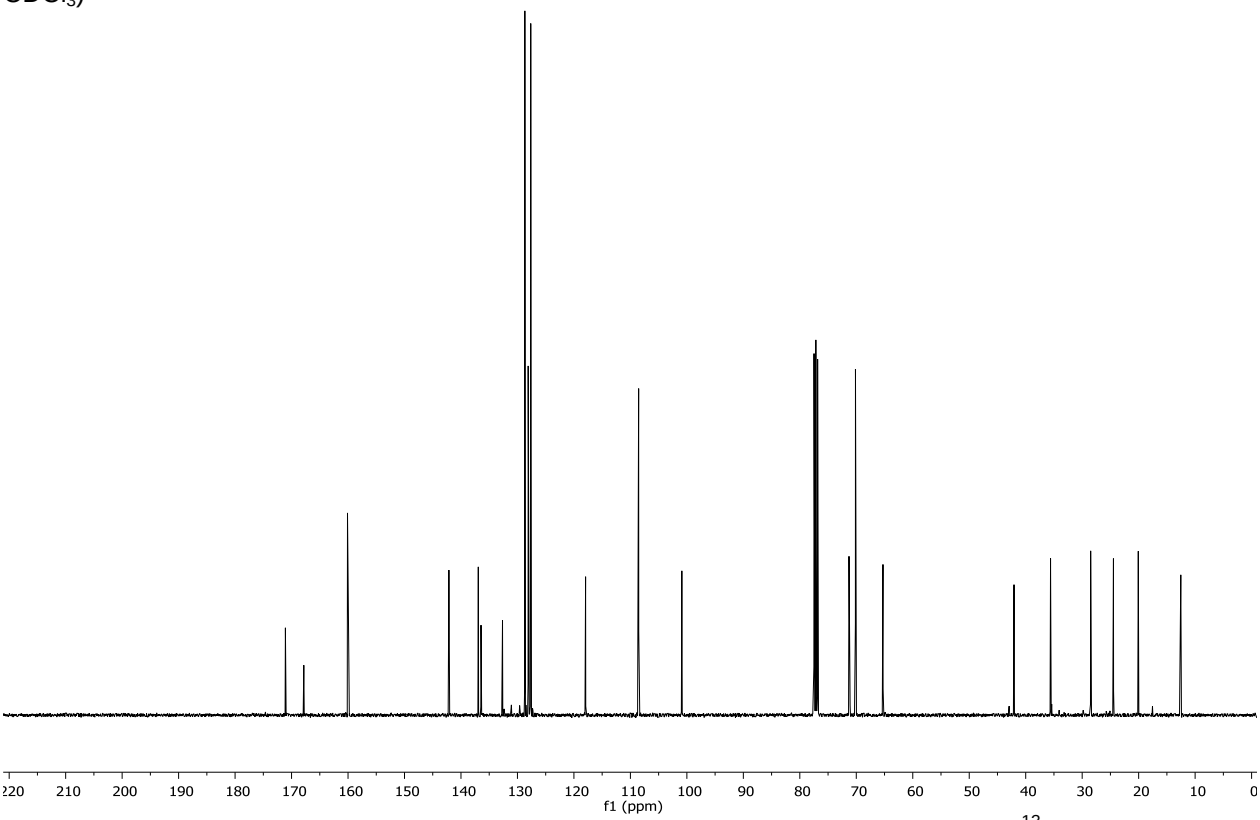
(*E*)-Allyl 7-(2-(3,5-bis(benzyloxy)phenyl)acetoxy)-2,6-dimethyloct-2-enoate (20a): ^{1}H-NMR (300 MHz, $CDCl_3$)



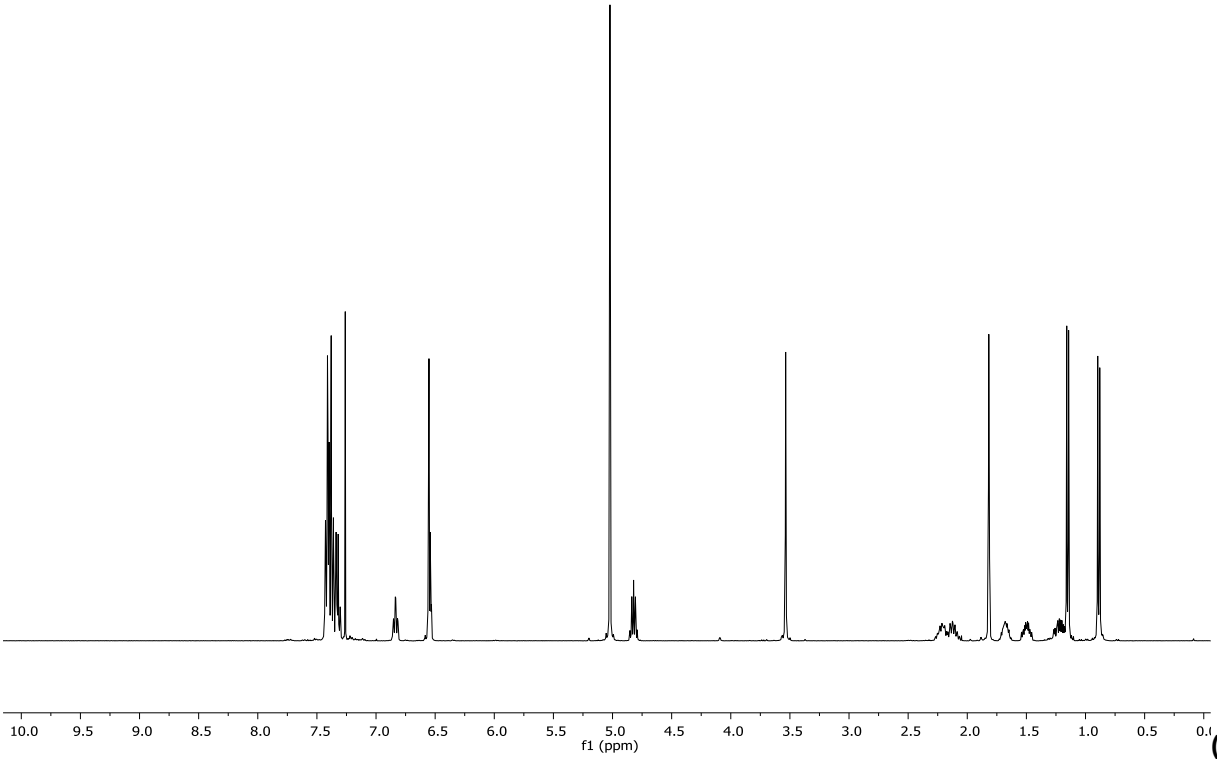
(*E*)-Allyl 7-(2-(3,5-bis(benzyloxy)phenyl)acetoxy)-2,6-dimethyloct-2-enoate (20a): ^{13}C-NMR (75.5 MHz, $CDCl_3$)



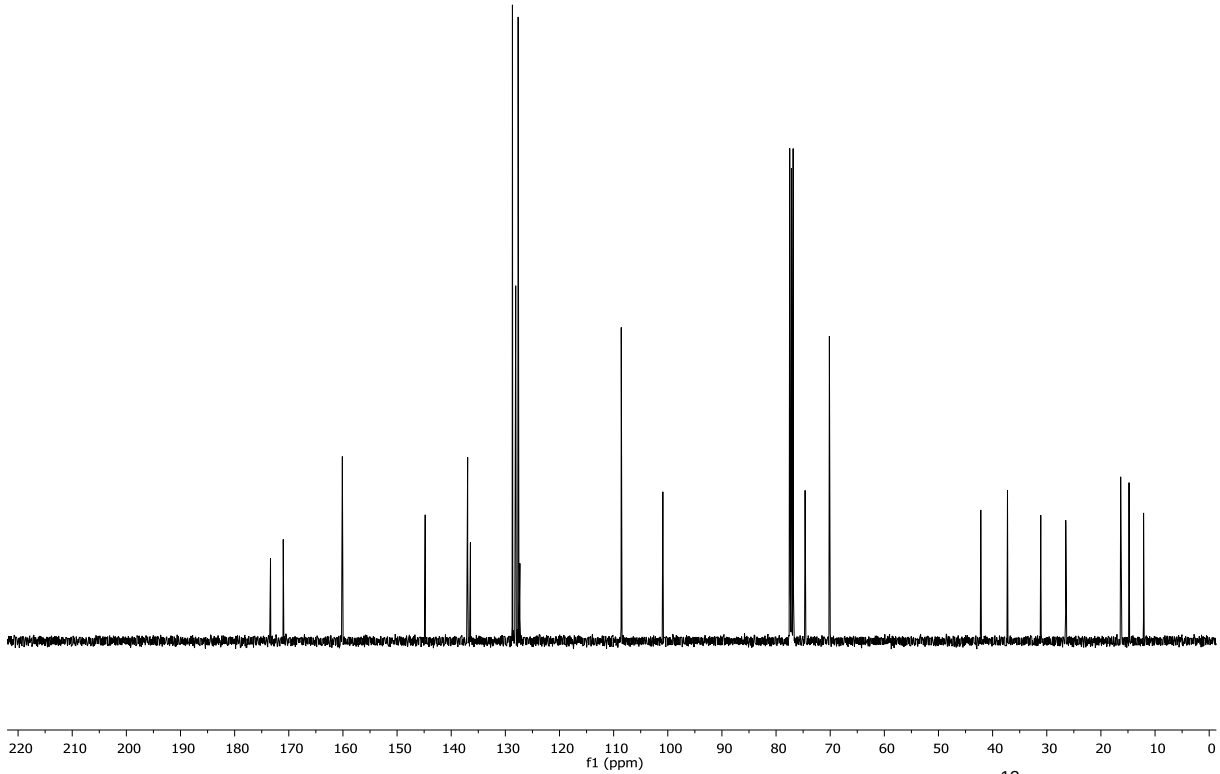
(*E*)-Allyl 7-(2-(3,5-bis(benzyloxy)phenyl)acetoxy)-2,6-dimethyloct-2-enoate (20b): ^{1}H-NMR (400 MHz, $CDCl_3$)



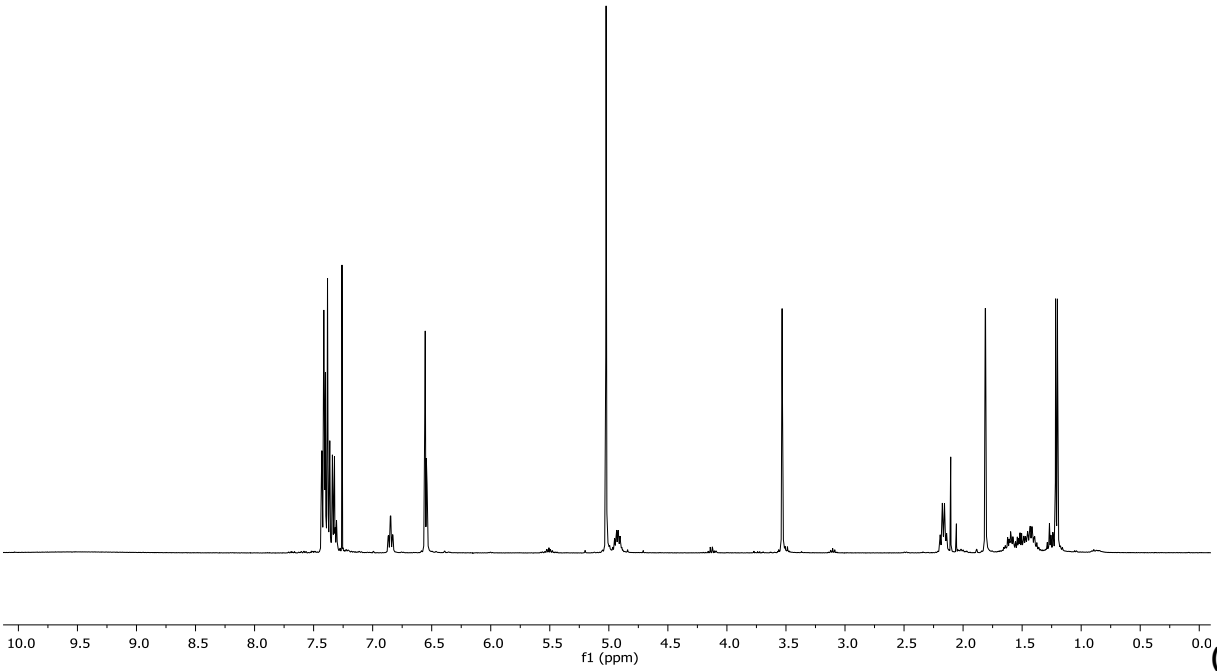
(*E*)-Allyl 7-(2-(3,5-bis(benzyloxy)phenyl)acetoxy)-2,6-dimethyloct-2-enoate (20b): ^{13}C-NMR (100.6 MHz, $CDCl_3$)



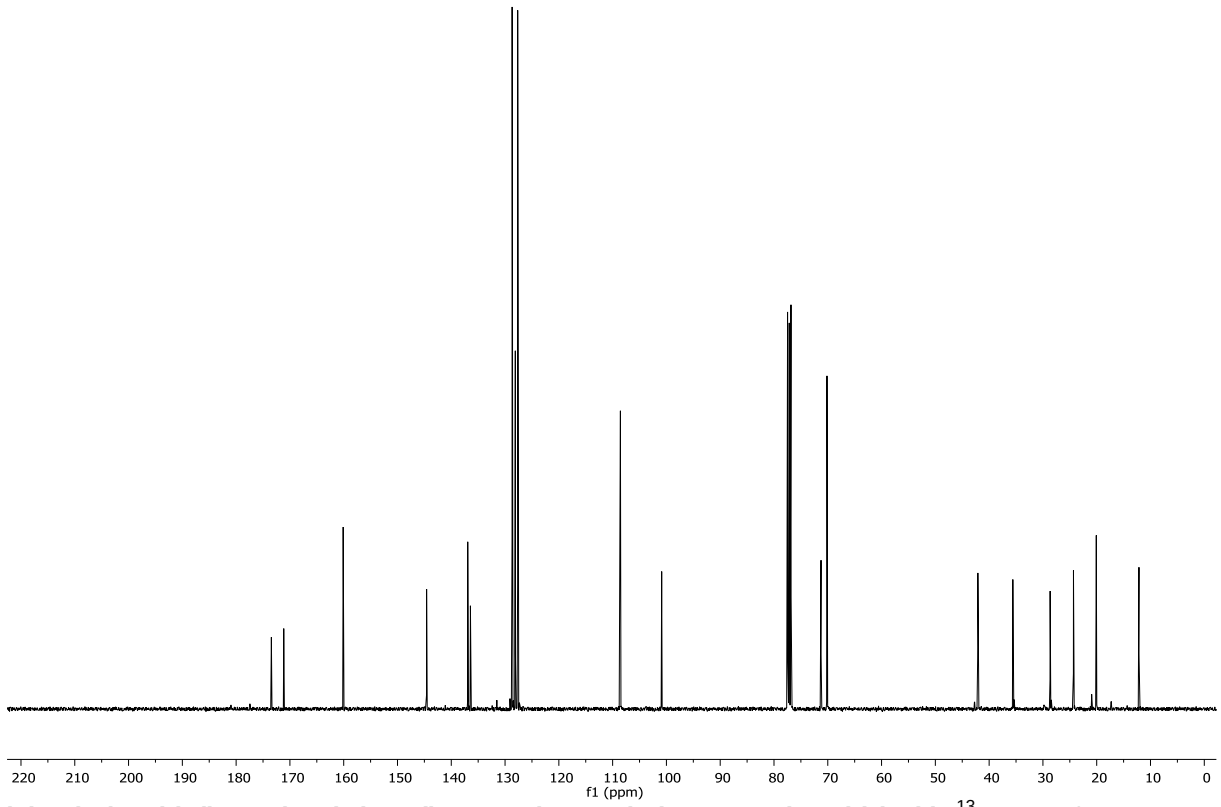
(*E*)-7-(2-(3,5-bis(benzyloxy)phenyl)acetoxy)-2,6-dimethyloct-2-enoic acid (21a): ^{1}H-NMR (300 MHz, $CDCl_3$)



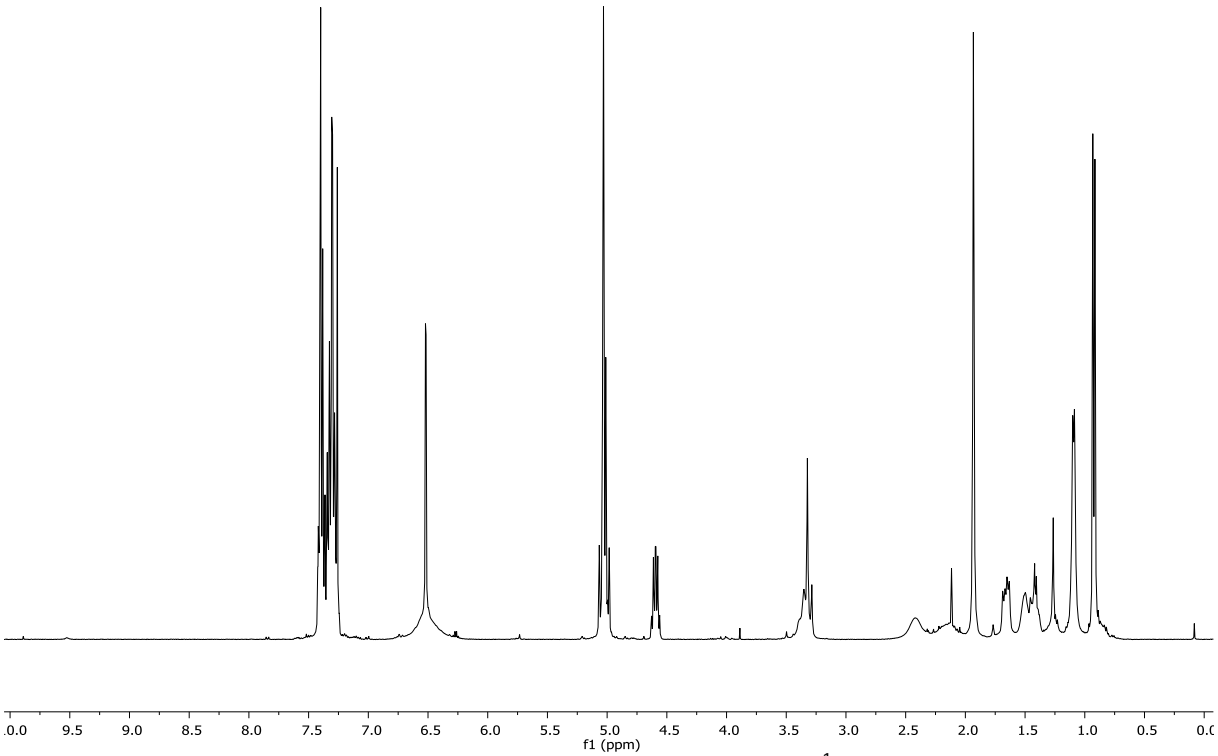
(*E*)-7-(2-(3,5-bis(benzyloxy)phenyl)acetoxy)-2,6-dimethyloct-2-enoic acid (21a): ^{13}C-NMR (75.5 MHz, $CDCl_3$)



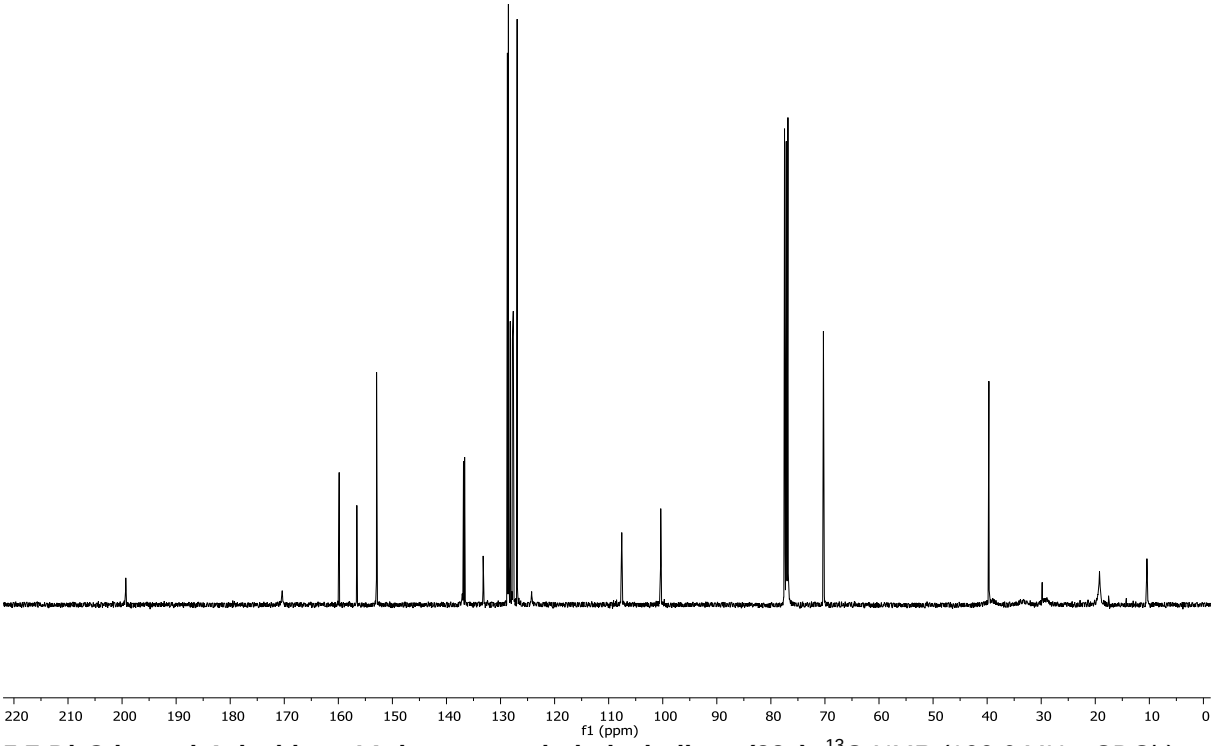
(*E*)-7-(2-(3,5-bis(benzyloxy)phenyl)acetoxy)-2-methyloct-2-enoic acid (21b): ^{1}H-NMR (400 MHz, $CDCl_3$)



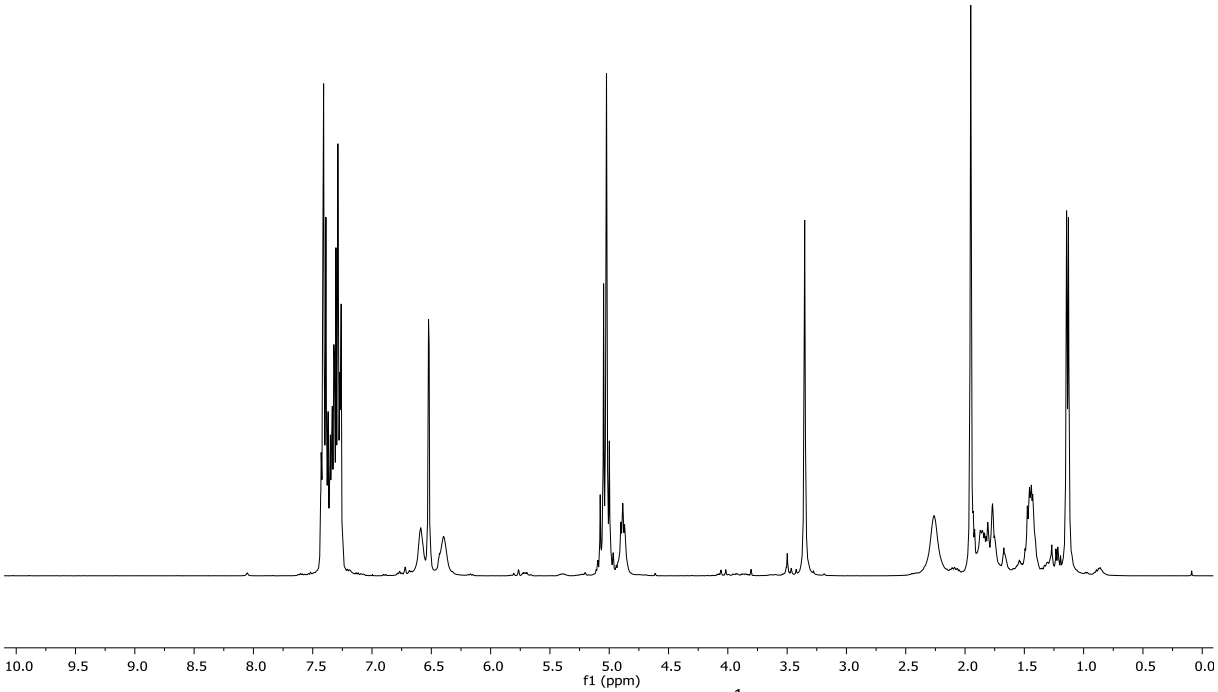
(*E*)-7-(2-(3,5-bis(benzyloxy)phenyl)acetoxy)-2-methyloct-2-enoic acid (21b): ^{13}C-NMR (100.6 MHz, $CDCl_3$)



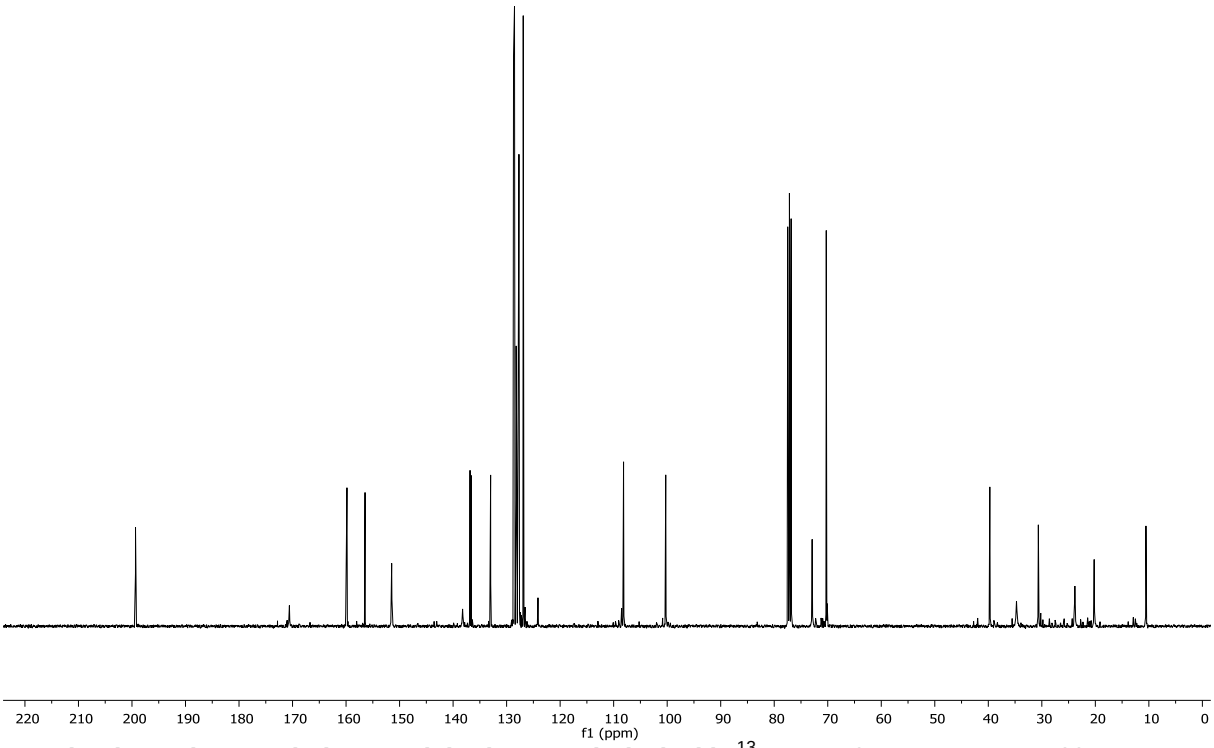
5,7-Di-*O*-benzyl-4-dechloro-14-deoxyoxacylododecindione (22a): ^{1}H-NMR (400 MHz, $CDCl_3$)



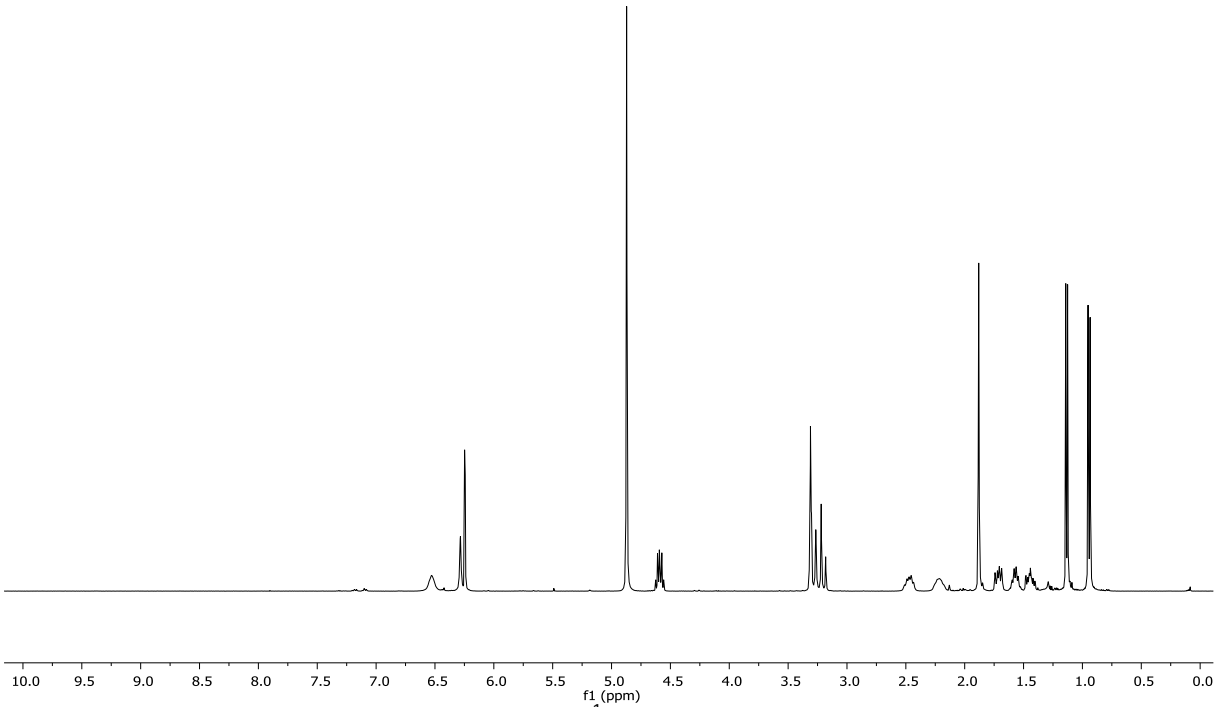
5,7-Di-*O*-benzyl-4-dechloro-14-deoxyoxacylododecindione (22a): ^{13}C-NMR (100.6 MHz, $CDCl_3$)



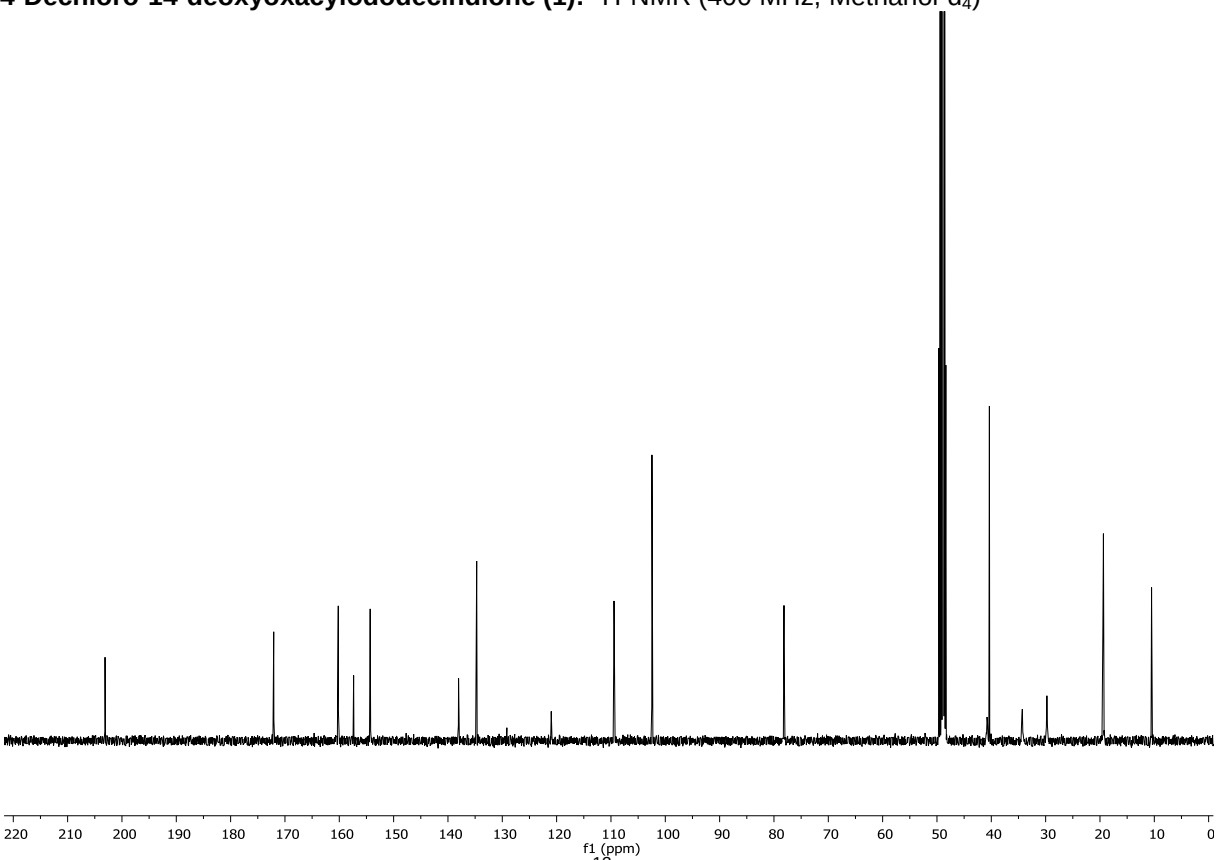
5,7-Di-*O*-benzyl-10-methyl-10,11-dehydrocurvularin (22b): ^{1}H-NMR (400 MHz, $CDCl_3$)



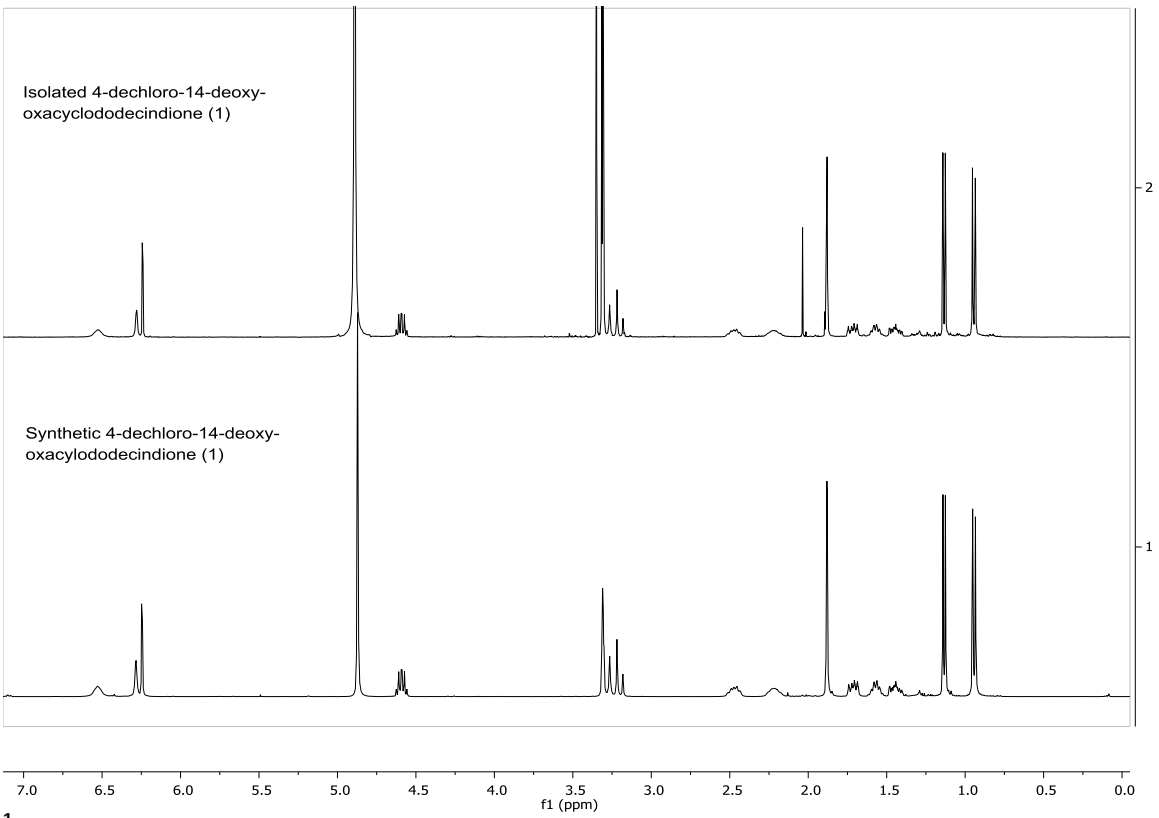
5,7-Di-*O*-benzyl-10-methyl-10,11-dehydrocurvularin (22b): ^{13}C-NMR (100.6 MHz, $CDCl_3$)



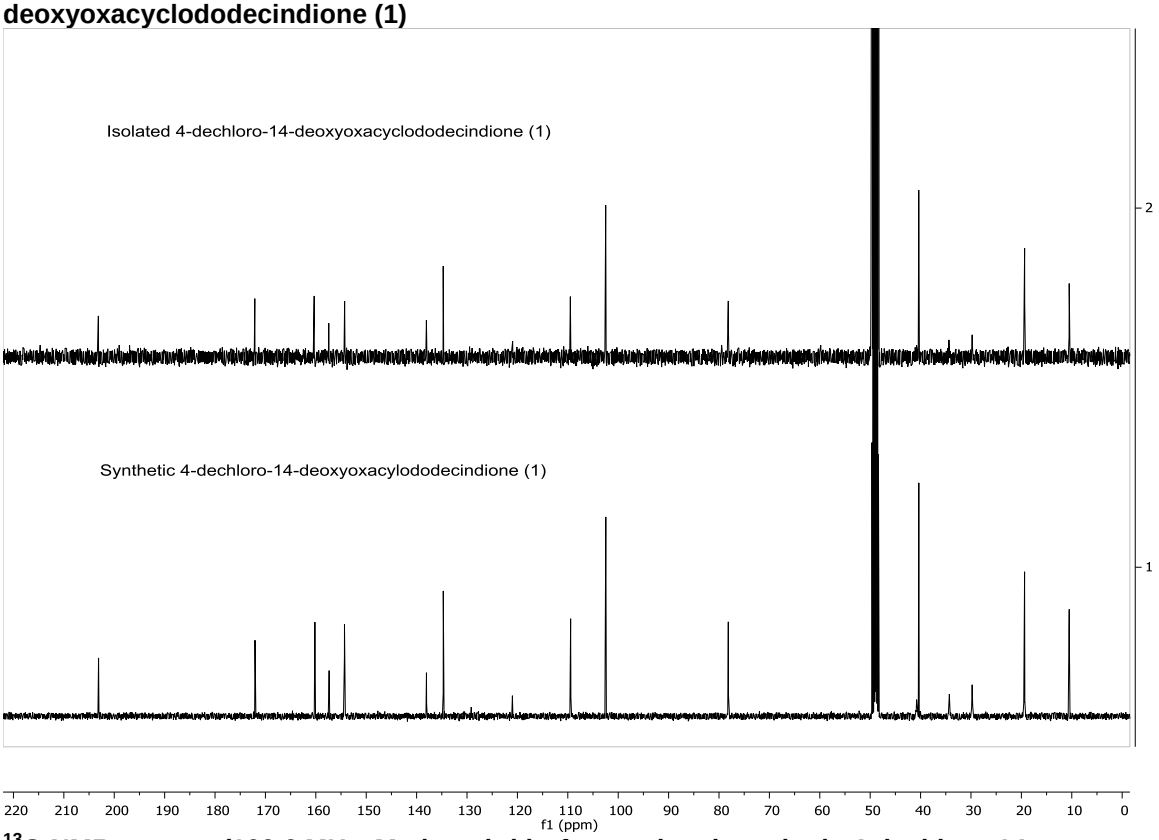
4-Dechloro-14-deoxyoxacylododecindione (1): ^{1}H-NMR (400 MHz, Methanol-d_4)



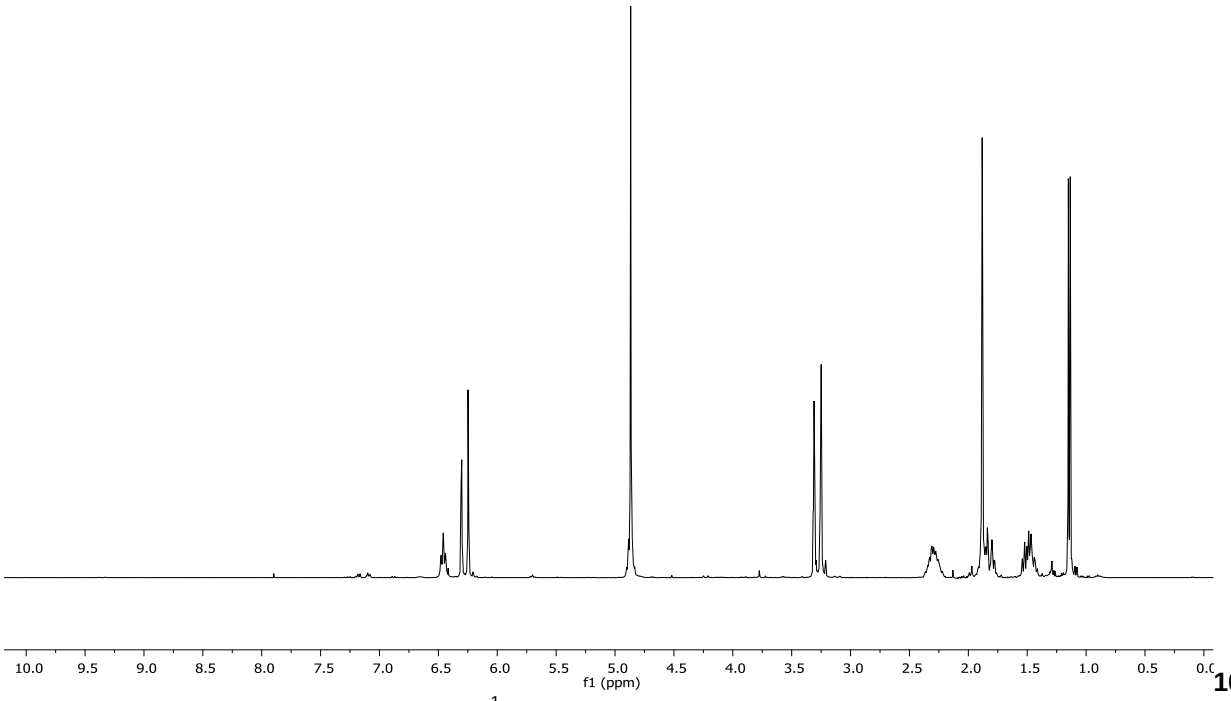
4-Dechloro-14-deoxyoxacylododecindione (1): ^{13}C-NMR (100.6 MHz, Methanol-d_4)



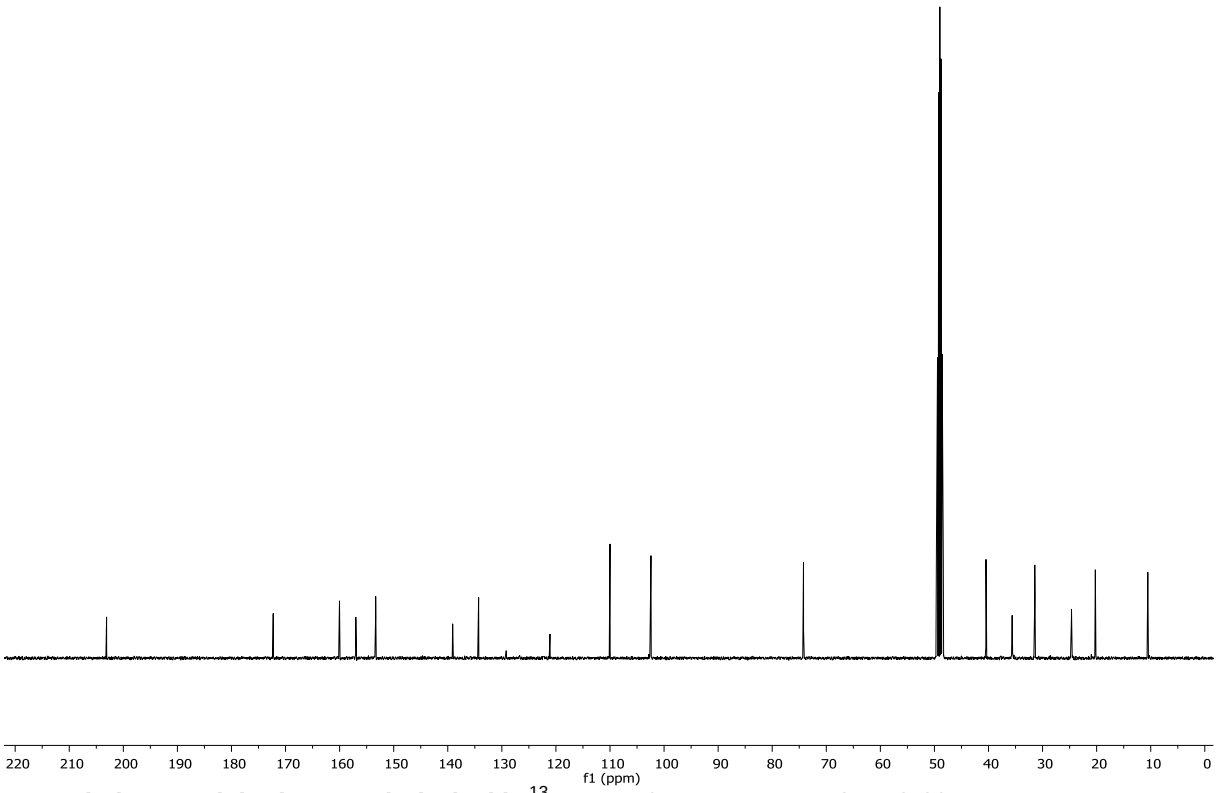
^{1}H-NMR-spectra (400 MHz, Methanol-d_4) of natural and synthetic 4-dechloro-14-deoxyoxacyclododecindione (1)



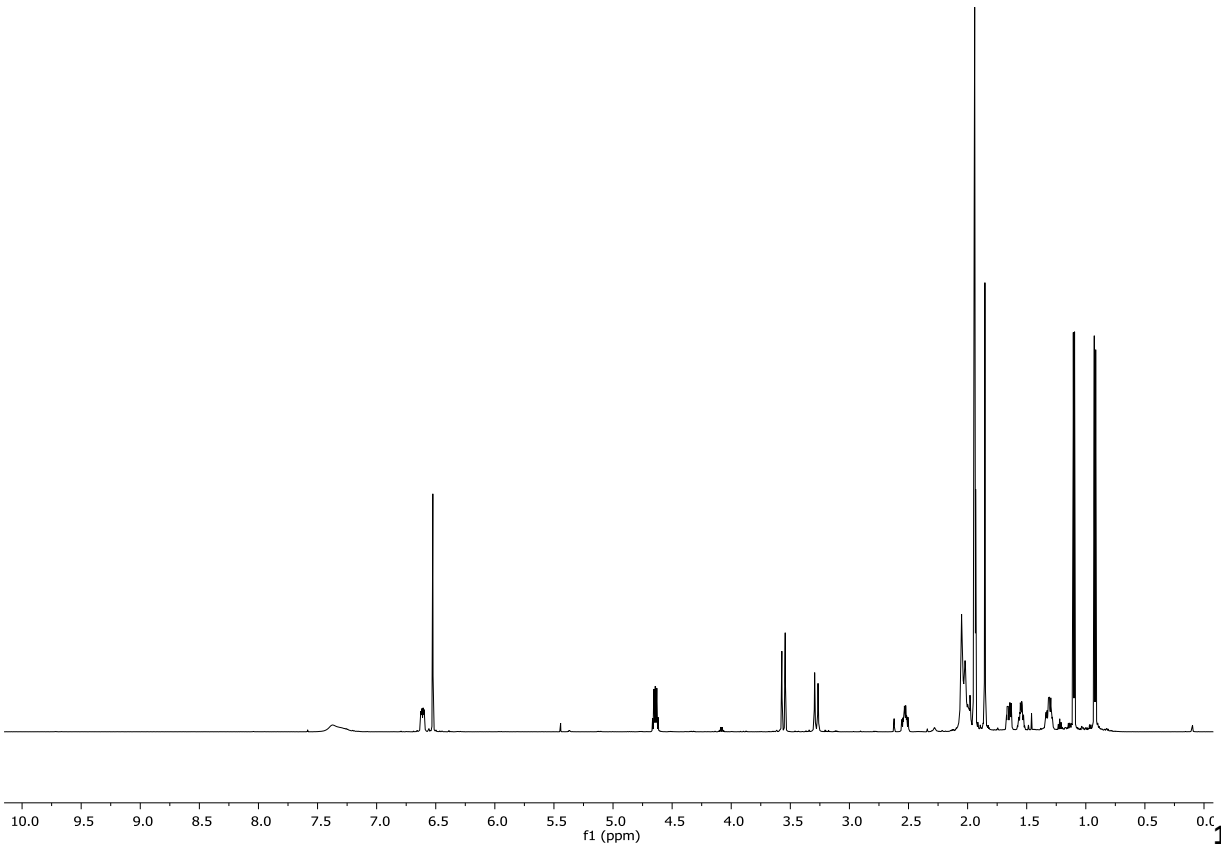
^{13}C-NMR-spectra (100.6 MHz, Methanol-d_4) of natural and synthetic 4-dechloro-14-deoxyoxacyclododecindione (1)



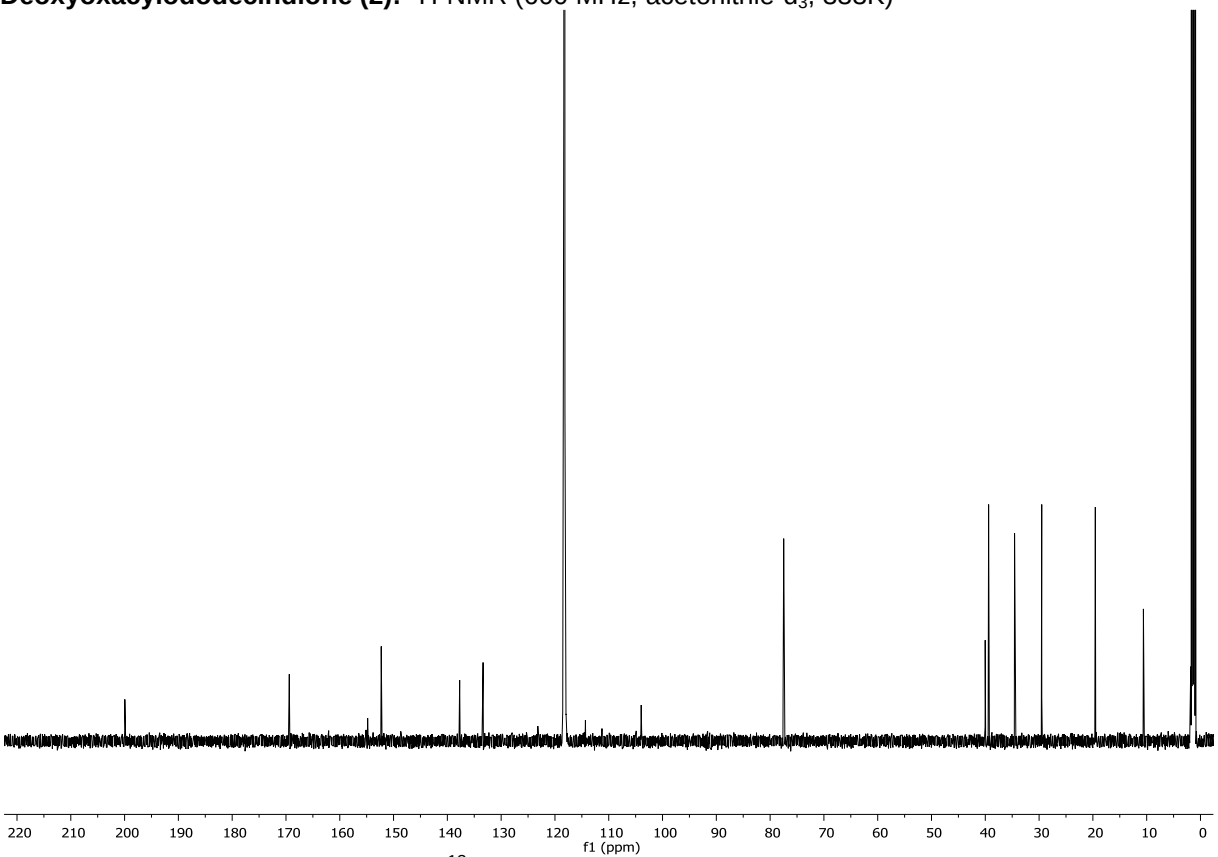
10-Methyl-10,11-dehydrocurvularin (23b): ^{1}H-NMR (400 MHz, Methanol-d_4)



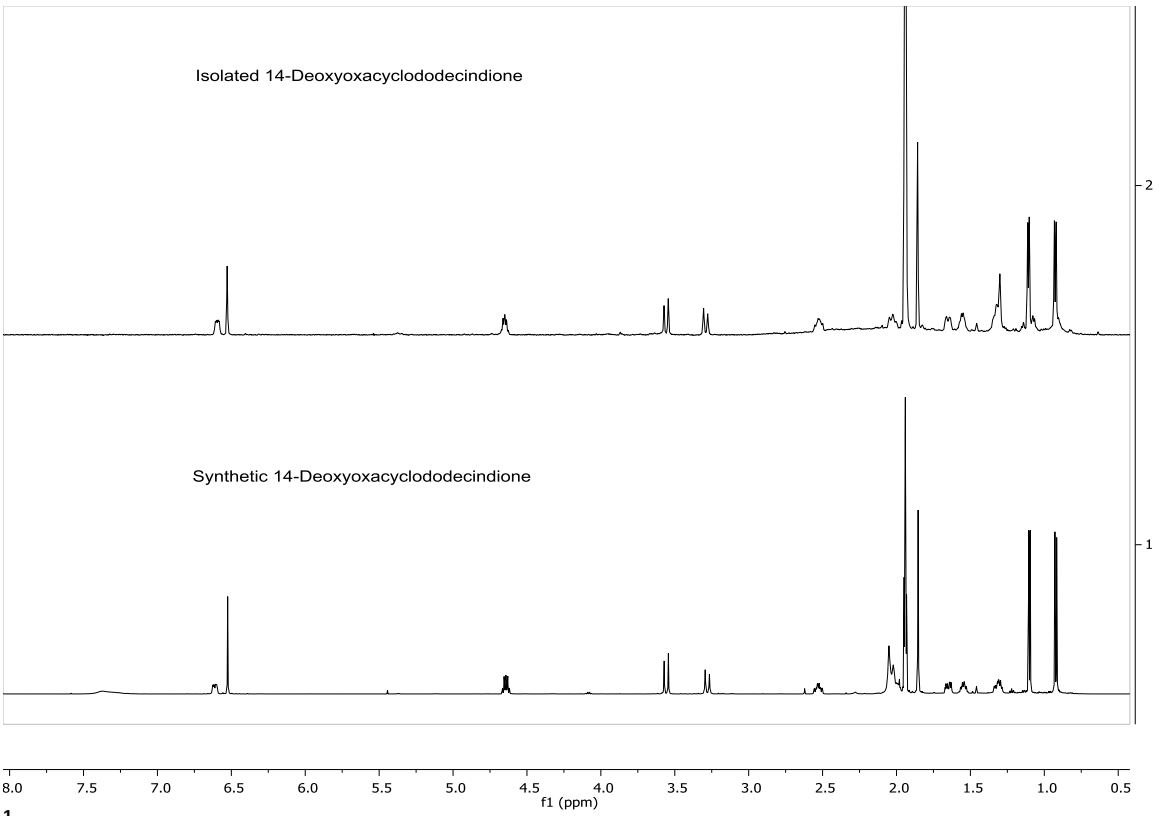
10-Methyl-10,11-dehydrocurvularin (23b): ^{13}C-NMR (100.6 MHz, Methanol-d_4)



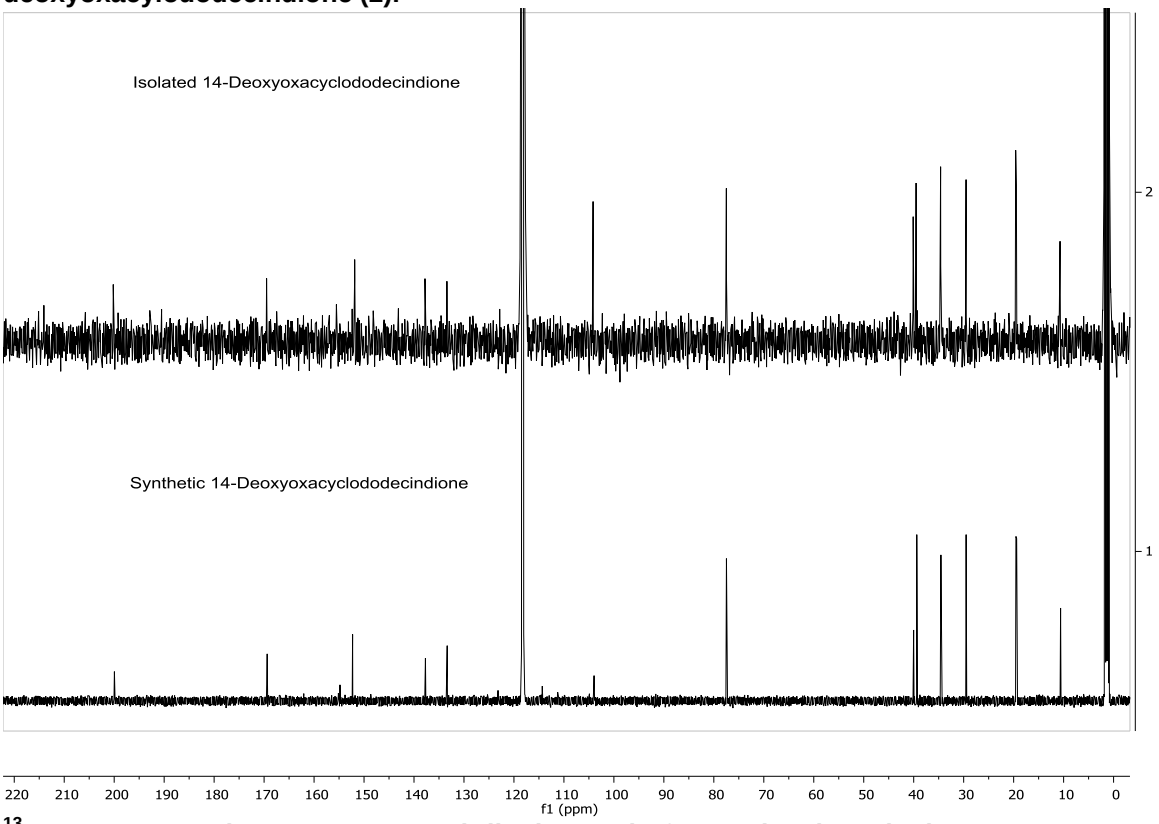
14-Deoxyoxacylododecindione (2): ^{1}H-NMR (600 MHz, acetonitrile-d_3, 333K)



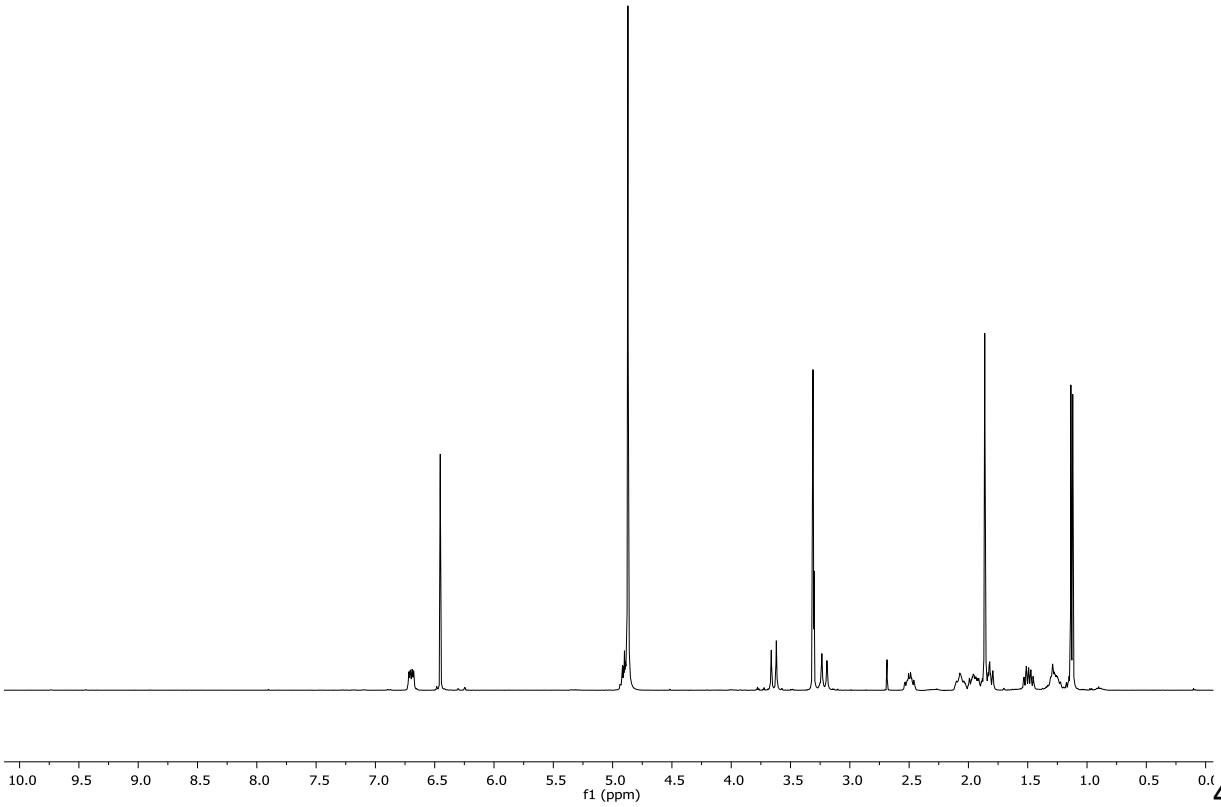
14-Deoxyoxacylododecindione (2): ^{13}C-NMR (150.9 MHz, acetonitrile-d_3, 333K)



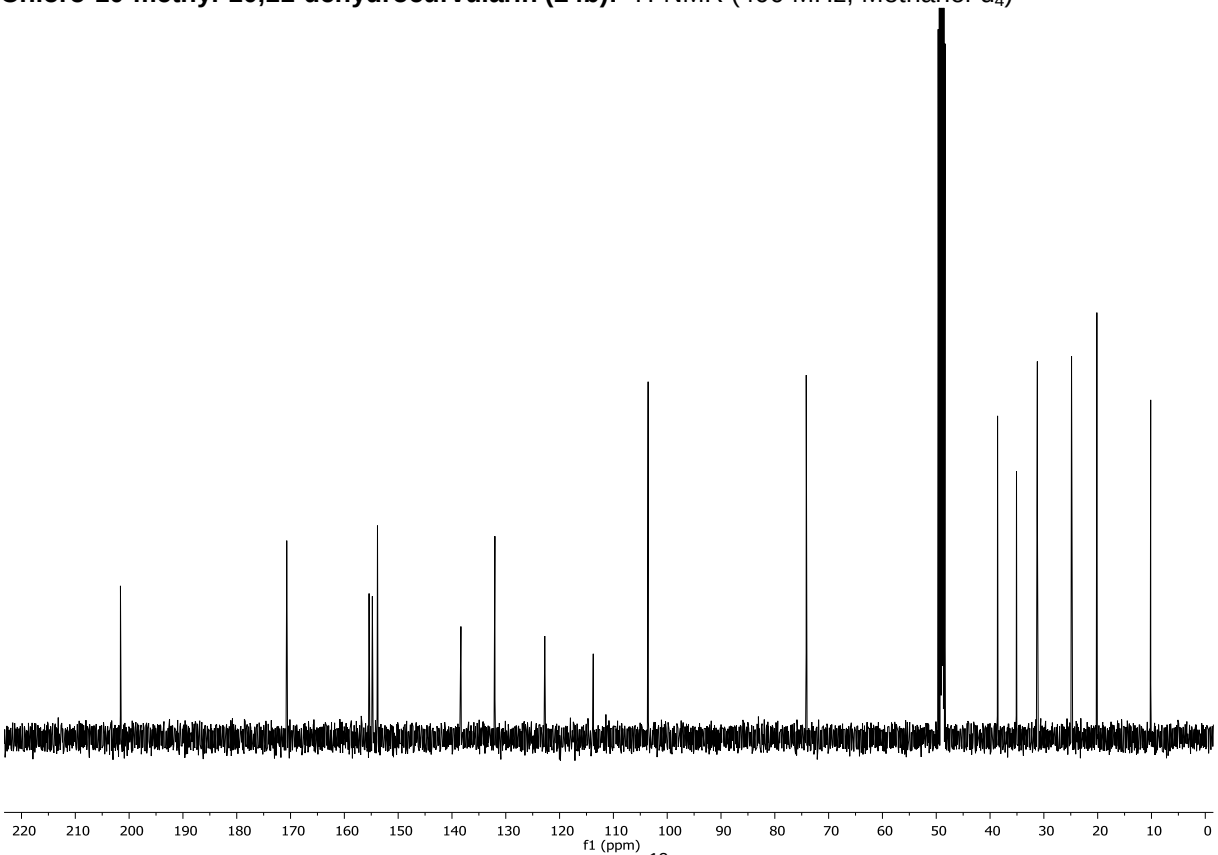
^{1}H-NMR-spectra (600 MHz, acetonitrile-d_3, 333K) of natural and synthetic 14-deoxyoxacylododecindione (2).



^{13}C-NMR-spectra (150.9 MHz, acetonitrile-d_3, 333K) of natural and synthetic 14-deoxyoxacylododecindione (2).



4-Chloro-10-methyl-10,11-dehydrocurvularin (24b): ^{1}H-NMR (400 MHz, Methanol-d_4)



4-Chloro-10-methyl-10,11-dehydrocurvularin (24b): ^{13}C-NMR (100.6 MHz, Methanol-d_4)

III. References

1. C. U. Grünanger and B. Breit, *Angew. Chem. Int. Ed.*, 2010, **49**, 967-970.
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