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Supporting Information

69451 Weinheim, Germany

Total Synthesis of Neurymenolide A Based on a Gold-Catalyzed Synthesis of 4-Hydroxy-2-pyrones**

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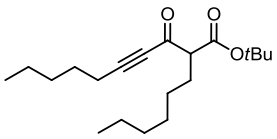
General. All reactions were carried out in flame-dried glassware under Argon. All solvents were purified by distillation over the drying agents indicated and were transferred under Argon: THF (Mg-anthracene), diethyl ether (Mg-anthracene), dichloromethane (CaH_2), acetonitrile (CaH_2), triethylamine (CaH_2), hexane (Na/K), toluene (Na/K). HOAc and MeOH were used as received. Flash chromatography: Merck silica gel 60 (230-400 mesh). IR: Nicolet FT-7199 spectrometer, wavenumbers in cm^{-1}. MS (EI): Finnigan MAT 8200, MS (CI): Finnigan MAT 95, MS (ESI) ESQ 3000; accurate mass determinations: Bruker APEX III FT-MS (7 T magnet). NMR: Spectra were recorded on a Bruker DPX 300, AV 400 or AV 500 spectrometer in the solvents indicated; ^{1}H and ^{13}C chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hz. The solvent signals were used as references ($CDCl_3$ δ_H = 7.24 ppm, δ_C = 77.0 ppm; C_6D_6 δ_H = 7.15 ppm, δ_C = 128.00 ppm; [D_6]-DMSO δ_H = 2.50 ppm, δ_C = 39.5 ppm; D_3COD δ_H = 3.31 ppm, δ_C = 49.00 ppm) and the chemical shifts converted to the TMS scale. Unless stated otherwise, all commercially available compounds (ABCR, Acros, Aldrich, Fluka, Lancaster, Strem) were used as received.

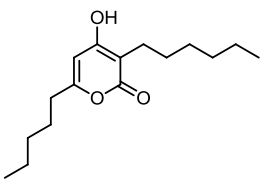
New Gold-Catalyzed Synthesis of 4-Hydroxy-2-pyrones. Pseudopyronine A

Compound 6g (R^1 = hexyl, R^2 = pentyl). *t*-Butyl octanoate (1.0 g, 0.5 mmol) was added dropwise to a



stirred solution of LDA (0.5 M in THF, 10 mL, 5 mmol) at –78 °C. The mixture was stirred at this temperature for 30 min before methyl 2-octynoate (771 mg, 0.5 mmol) was slowly introduced and stirring continued at –78 °C for 2 h. The mixture was poured into aq. sat. NH_4Cl (50 mL) and the organic phase extracted with Et_2O (3 x 50 mL), dried (Na_2SO_4) and concentrated. Flash chromatography of the residue (silica, hexanes/EtOAc, 99:1 → 95:5) gave keto ester **6g** as a colorless oil (1.34 g, 83 %). ^{1}H NMR (400 MHz, $CDCl_3$, mixture of keto/enol tautomers): δ = 0.85-0.93 (m, 6H), 1.23-1.43 (m, 12H), 1.46 & 1.50 (s each, Σ 9H), 1.53-1.62 (m, 2H), 1.80-1.93 (m, 1H), 2.22-2.29 (m, 1H), 2.36 (t, J = 7.1, 1H), 2.40 (t, J = 7.1, 1H), 3.33 (t, J = 7.4, 0.5H), 12.33 (s, 0.5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 13.9, 14.0, 14.0, 19.0, 19.4 22.0, 22.1, 22.5, 22.6, 27.0, 17.3, 27.8, 27.8, 27.9, 28.1, 28.2, 28.9, 29.0, 29.6, 30.9, 31.0, 31.5, 31.6, 61.9, 75.0, 79.6, 81.6, 81.7, 96.3, 99.2, 109.4, 152.3, 168.2, 172.8, 183.3. IR (film): $\tilde{\nu}$ = 2957, 2929, 2859, 2214, 1736, 1677, 1633, 1598, 1457, 1369, 1358, 1250, 1150, 1128, 845, 820; MS (EI): *m/z* (%) 322 (4), 266 (45), 249 (15), 238 (5), 223 (23), 210 (13), 195 (23), 177 (20), 139 (11), 123 (95), 98 (71), 82 (9), 67 (23), 57 (100), 41 (38); HRMS (EI): *m/z*: calcd for $C_{20}H_{34}O_3Na$ [$M+Na^+$]: 345.24001, found: 345.23988.

Representative Procedure for the Preparation of 4-Hydroxy-2-pyrones. Synthesis of



Pseudopyronine A (7g). A solution of substrate **6g** (325 mg, 1.0 mmol) and $SPhosAuNTf_2$ (**8**) (9 mg, 10 µmol, 1 mol%) in HOAc (5 mL) was stirred for 24 h before the acid was distilled off and the residue purified by flash chromatography (silica, hexane/HOAc, 4:1) to afford pseudopyronine A (**7g**) as a white solid (257 mg, 96 %). Mp = 111.5-112.5 °C (lit. 106-108 °C).[1] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.86-0.93 (m, 6H), 1.24-1.38 (m, 10H), 1.44-1.54 (m, 2H), 1.58-1.68 (m, 2H), 2.40-2.48 (m, 4H), 6.20 (s, 1H), 10.19 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 14.1, 22.3, 22.7, 23.1, 26.5, 28.0, 29.3, 31.1, 31.8, 33.5, 100.9, 103.4, 163.6, 167.2, 168.4; ^{1}H NMR (400 MHz,

[1] Giddens, A. C.; Nielsen, L.; Boshoff, H. I.; Tasdemir, D.; Perozzo, R.; Kaiser, M.; Wang, F.; Sacchettini, J. C.; Copp, B. R. *Tetrahedron* **2008**, *64,* 1242-1249.

CD_3OD): δ = 0.89 (t, J = 7.0, 3H), 0.92 (t, J = 7.0, 3H), 1.32-1.40 (m, 10H), 1.40-1.50 (m, 2H), 1.60-1.70 (m, 2H), 2.37 (t, J = 7.5, 2H), 2.46 (t, J = 7.6, 2H), 4.89 (br s, 1H), 5.98 (s, 1H); ^{13}C NMR (100 MHz, CD_3OD): δ = 14.2, 14.4, 23.4, 23.7, 23.9, 27.6, 29.0, 30.2, 32.2, 32.9, 34.2, 101.0, 103.9, 165.1, 167.7, 168.8; IR (film): $\tilde{\nu}$ = 2955, 2926, 2872. 2858, 2643, 1663, 1630, 1556, 1433, 1407, 1292, 1256, 1172, 1130, 992, 856, 758; MS (EI): m/z (%) 266 (17), 249 (3), 237 (3), 223 (11), 209 (14), 195 (100), 182 (9), 168 (19), 153 (10), 140 (15), 126 (11), 111 (7), 99 (11), 83 (4), 69 (10), 55 (21), 43 (21); HRMS (ESI–): m/z: calcd for $C_{16}H_{25}O_3$ [M-H]$^-$: 265.18092, found: 265.18085.

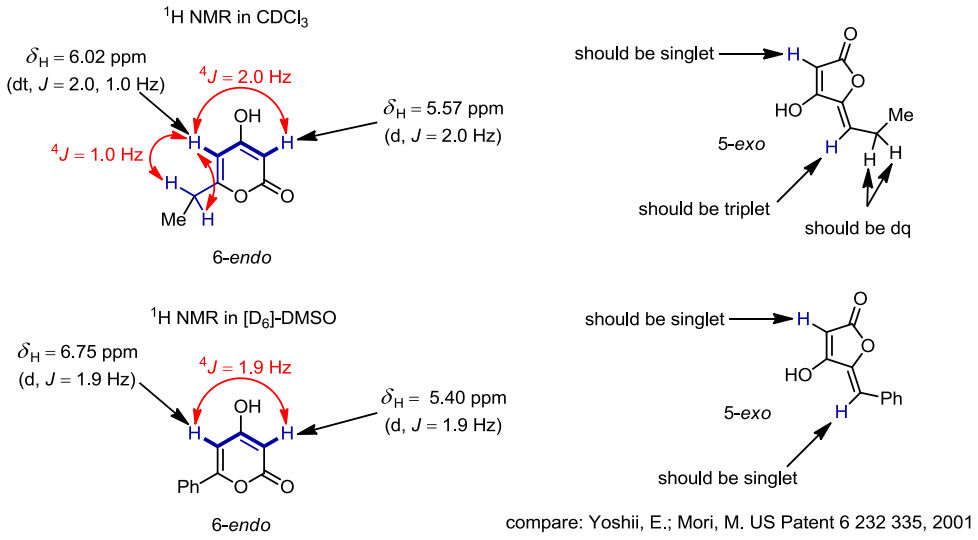
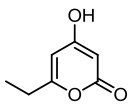
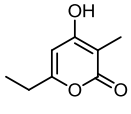


Figure S1. Analysis of the ^{1}H NMR data of compounds **7a** and **7c** (6-*endo* product) and comparison with known data for the tetronic acid (5-*exo* product) established their structures.

Compound 7a. Prepared analogously as colorless crystals (655 mg, 94%); after washing with Et_2O, the material was found analytically pure, thus requiring no flash chromatography. Mp = 106–107 °C (lit:[2a] 83 °C); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.33 (br s, 1 H), 6.02 (dt, J = 2.0, 1.0 Hz, 1 H), 5.59 (d, J = 2.0 Hz, 1 H), 2.52 (q, J = 7.5 Hz, 2 H), 1.20 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.9 (C), 168.5 (C), 168.3 (C), 100.6 (CH), 89.7 (CH), 26.8 (CH_2), 10.8 (CH_3); IR (film): $\tilde{\nu}$ = 2984, 2950, 2566, 1650, 1614, 1574, 1543, 1446, 1383, 1366, 1311, 1283, 1266, 1242, 1203, 1139, 937, 883, 835, 808, 782, 693, 661 cm^{-1}; MS (EI): m/z (%): 140 (37) [M^+], 111 (70), 99 (16), 69 (100), 57 (26), 29 (24); HRMS (EI): m/z: calcd for $C_7H_8O_3$ [M^+]: 140.0473, found: 140.0472. The spectroscopic data are in good agreement with the data reported in the literature.[2]



Compound 7b. Prepared analogously as a white solid (14.9 mg, 97%); after washing with Et_2O, the material was found analytically pure, thus requiring no flash chromatography. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 11.08 (br s, 1 H), 5.96 (br s, 1 H), 2.43 (q, J = 7.5 Hz, 2 H), 1.74 (s, 3 H), 1.09 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 165.0 (C), 164.9 (C), 163.8 (C), 98.2 (CH), 96.5 (C), 25.9 (CH_2), 10.9 (CH_3), 8.3 (CH_3); IR (film): $\tilde{\nu}$ = 2984, 2967, 2914, 2690, 1671, 1634, 1574, 1508, 1428, 1399, 1373, 1353, 1315, 1238, 1180, 1122, 1088, 1056, 1020, 947, 930, 845, 831, 752, 743, 667 cm^{-1}; MS (EI): m/z (%): 154 (88) [M^+], 126 (79), 111 (100), 99 (59), 83 (14), 69 (94); HRMS (EI): m/z: calcd for $C_8H_{10}O_3$ [M^+]: 154.0630, found: 154.0631.



[2] (a) Schmidt, D.; Conrad, J.; Klaiber, I.; Beifuss, U. *Chem. Commun.* **2006**, 4732–4734. (b) Zhang, X.; McLaughlin, M.; Muñoz, R. L. P.; Hsung, R. P.; Wang, J.; Swidorski, J. *Synlett* **2007**, 749–753.

Compound 7c. Prepared analogously as a white solid (18.7 mg, 99%); after washing with Et_2O, the material was found analytically pure, thus requiring no flash chromatography. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 11.85 (br s, 1 H), 7.84 (m, 2 H), 7.51 (m, 3 H), 6.75 (d, J = 1.9 Hz, 1 H), 5.40 (d, J = 1.9 Hz, 1 H); ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 170.5 (C), 163.0 (C), 160.1 (C), 131.1 (C), 130.9 (CH), 129.1 (2 × CH), 125.5 (2 × CH), 98.4 (CH), 89.6 (CH) ppm. The analytical data matched those reported in the literature.[2a,3]

Compound 7d. Prepared analogously as a white solid (18.6 mg, 82%); after washing with Et_2O, the material was found analytically pure, thus requiring no flash chromatography. Mp = 187-195 °C (decomp.); ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 1.11 (t, J = 7.5, 3H), 2.48 (dq, J = 7.5, 0.8, 2H), 6.08 (t, J = 0.8, 1H), 12.53 (br s, 1H); ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 10.7, 25.7, 84.9, 98.2, 160.4, 165.8, 166.7; IR (film): $\tilde{\nu}$ = 3082, 1656, 1565, 1428, 1411, 1380, 1326, 1222, 1157, 1048, 971, 943, 844, 791, 773, 741, 683; MS (EI): m/z (%) 220 (96), 218 (97), 192 (53), 190 (57), 177 (15), 175 (16), 163 (21), 161 (22), 135 (36), 133 (35), 122 (12), 120 (11), 111 (8), 99 (100), 83 (11), 69 (25), 57 (30), 53 (29), 39 (12), 29 (27); HRMS (EI): m/z: calcd for $C_7H_6O_3Br$ [M+Na^+]: 216.95059, found: 216.95071.

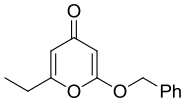
Compound 7e. Prepared analogously as a white solid (17.5 mg, 85%); after washing with Et_2O, the material was found analytically pure, thus requiring no flash chromatography. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 12.38 (br s, 1 H), 7.78 (m, 2 H), 7.51 (m, 3 H), 6.83 (d, J = 5.3 Hz, 1 H); ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 157.1 (d, J_{CF} = 23.7 Hz, C), 154.9 (d, J_{CF} = 6.0 Hz, C), 153.8 (d, J_{CF} = 9.2 Hz, C), 133.0 (C), 130.7 (CH), 130.4 (C), 129.1 (2 × CH), 125.3 (2 × CH), 98.9 (CH); IR (film): $\tilde{\nu}$ = 2885, 2641, 2587, 2551, 1625, 1577, 1549, 1495, 1453, 1399, 1356, 1174, 1071, 1048, 910, 859, 824, 770, 734, 685, 658 cm^{-1}; MS (EI): m/z (%): 206 (100) [M^+], 178 (27), 149 (21), 130 (18), 105 (42), 77 (53), 51 (27); HRMS (ESI+): m/z: calcd for $C_{11}H_7O_3FNa$ [M^+ + Na]: 229.0271, found: 229.0274.

Compound 7f. Prepared analogously as a white solid (8.3 mg, 45%). Mp = 116-118 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.27 (s, 9H), 5.66 (d, J = 2.3, 1H), 6.36 (d, J = 2.3, 1H), 11.00 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = –2.9, 92.5, 112.1, 169.7, 170.1, 175.1; IR (film): $\tilde{\nu}$ = 3133, 2961, 1681, 1650, 1631, 1571, 1421, 1283, 1243, 1222, 1188, 1088, 988, 921, 869, 839, 826, 702; MS (EI): m/z (%) 184 (22), 169 (81), 156 (2), 143 (10), 127 (6), 111 (6), 99 (20), 83 (8), 73 (100), 69 (21), 66 (3), 55 (4), 45 (16), 29 (3); HRMS (EI): m/z: calcd for $C_8H_{12}O_3Si$ [M+Na^+]: 184.05558, found: 184.05542.

Compound 7h. Prepared analogously as a yellow solid (26.2 mg, 98%); after washing with Et_2O, the material was found analytically pure. Because of the low solubility, flash chromatography results in loss of material. Mp = 239-242°C (decomp.); ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 5.30 (d, J = 2.0, 1H), 6.07 (s, 2H), 6.13 (d, J = 1.8, 1H), 6.88 (d, J = 16.0, 1H), 6.95 (d, J = 8.0, 1H), 7.14 (dd, J = 8.1, 1.4, 1H), 7.23 (d, J = 16.0, 1H), 7.33 (d, J = 1.4, 1H), 11.69 (br s, 1H); ^{13}C NMR (100 MHz, [D$_6$]-DMSO): δ = 89.6, 101.1, 101.4, 106.0, 108.5, 118.0, 123.6, 129.7, 133.9, 148.0, 148.4, 159.4, 162.9, 170.1; IR (film): $\tilde{\nu}$ = 1699, 1631, 1606, 1555, 1499, 1479, 1443, 1357, 1299, 1254, 1241, 1157, 1100, 1036, 1009, 959, 924, 840, 815, 796, 683; MS (EI): m/z (%) 258 (100), 241 (7), 230 (6), 214 (21), 199 (11), 188 (45), 175 (30), 160 (25), 145 (25), 130 (16), 117 (16), 102 (12), 89 (35), 77 (6), 69 (26), 51 (10), 39 (11), 29 (5); HRMS (EI): m/z: calcd for $C_{14}H_{10}O_5Na$ [M+Na^+]: 281.04204, found: 281.04205.

[3] Katritzky, A. R.; Wang, Z.; Wang, M.; Hall, C. D.; Suzuki, K. *J. Org. Chem.* **2005**, *70*, 4854–4856.

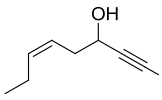
2-(Benzyloxy)-6-ethyl-2*H*-pyran-4-one (10). Prepared analogously as a white solid (21.6 mg, 94%).



Mp = 75-76 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.21, (t, *J* = 7.5, 3H), 2.51 (dt, *J* = 7.5, 0.5, 2H), 5.09 (s, 2H), 5.54 (d, *J* = 1.8, 1H), 5.99 (m, *J* = 1.8, 1H), 7.35-7.44 (m, 5H); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.7, 26.2, 71.2, 90.9, 111.1, 127.9, 128.9, 129.0, 133.7, 166.4, 167.1, 181.9; IR (film): $\tilde{\nu}$ = 3051, 2973, 2914, 1656, 1615, 1589, 1575, 1500, 1455, 1416, 1380, 1366, 1302, 1251, 1226, 103, 1157, 1091, 1059, 1029, 1005, 978, 924, 898, 800, 787, 740, 691, 681, 670; MS (EI): *m*/*z* (%) 230 (1) 174 (1), 132 (15), 91 (100), 77 (1), 65 (9), 51 (1), 40 (3), 29 (2) HRMS (EI): *m*/*z*: calcd for $C_{14}H_{14}O_3Na$ [*M+Na*$^+$]: 253.08351, found: 253.08334.

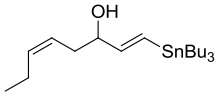
Total Synthesis of Neurymenolide A

(*Z*)-1-(Trimethylsilyl)oct-5-en-1-yn-3-ol (12). *n*-BuLi (1.6 M in hexane, 32 mL, 51 mmol) was added slowly to a stirred solution of ethynyltrimethylsilane (7.8 mL, 55 mmol) in THF (50 mL) at –78 °C. After stirring at this temperature for 30 min, freshly distilled (*Z*)-3-hexenal (3.6 g, 36.7 mmol, *Z:E* ≈ 85:15) was added dropwise and stirring continued for 30 min at –78°C before the cooling bath was removed and the mixture stirred at ambient temperature for 1 h. The solution was poured into aq. sat. NH_4Cl (100 mL), and the aqueous layer extracted with Et_2O (3 x 50mL), the combined organic layers dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography of the residue (silica gel, hexanes/EtOAc, 98:2 → 95:5) gave product **12** (6.1 g, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.17 (s, 9H), 0.98 (t, *J* = 7.5, 3H), 1.8 (br s, 1H), 2.03-2.14 (m, 2H), 2.44-2.50 (m, 2H), 4.38 (t, *J* = 6.2, 1H), 5.38-5.47 (m, 1H), 5.57-5.66 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = –0.2, 14.2, 20.8, 35.5, 62.4, 89.5, 106.2, 122.7, 135.9; IR (film): $\tilde{\nu}$ = 3341, 3013, 2962, 2176, 1456, 1407, 1334, 1305, 1249, 1125, 1041, 1002, 961, 886, 838, 759, 698; MS (EI): *m*/*z* (%) 196 (1), 181 (22), 167 (10), 151 (5), 127 (81), 122 (7), 99 (100), 91 (12), 83 (7), 75 (37), 55 (16), 41 (19), 29 (6); HRMS (EI): *m*/*z*: calcd for $C_{11}H_{20}OSi$ [*M*$^+$]: 196.12834, found: 196.12817. Characteristic signals of the *E*-isomer: ^{13}C NMR (100 MHz, $CDCl_3$): δ = –0.3, 13.7, 25.7, 40.9, 137.2.



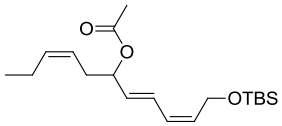
(*Z*)-1-Oct-5-en-1-yn-3-ol (13). K_2CO_3 (5 g, 36 mmol) was added to solution of compound **12** (3.40 g, 17.3 mmol) in methanol (50 mL) and the suspension stirred for 30 min. The mixture was poured into aq. sat. NH_4Cl (100 mL), the aqueous layer extracted with Et_2O (3 x 50mL), and the combined organic phases dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography of the residue (silica, pentane/Et_2O, 9:1 → 4:1) gave product **13** as a colorless oil (2.10 g, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (t, *J* = 7.5, 3H), 1.78 (br s, 1H), 2.05-2.14 (m, 2H), 2.46 (d, *J* = 2.1, 1H) 2.48-2.52 (m, 2H), 4.40 (dt, *J* = 6.2, 2.1, 1H), 5.40-5.49 (m, 1H), 5.60-5.68 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ =14.2, 20.8, 35.4, 61.8, 72.9, 84.4, 122.3, 136.2; IR (film): $\tilde{\nu}$ = 3325 (br), 3297, 3013, 2964, 2934, 2875, 1456, 1405, 1304, 1122, 1037, 969, 867, 795; MS (EI): *m*/*z* (%): 124 (0.2), 109 (12), 95 (23), 91 (26), 70 (38), 69 (35), 67 (35), 55 (62), 53 (15), 41 (100); Characteristic signals of the *E*-isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.00 (t, *J* = 7.3), 2.40-2.45 (m), 4.37 (dt, *J* = 6.0, 2.1).

(1*E*,5*Z*)-1-(Tributylstannyl)octa-1,5-dien-3-ol (14). Bu_3SnH (6.1 mL, 22.7 mmol) was added dropwise over 30 min via syringe pump to a stirred solution of alkyne **13** (1.89 g, 15.2 mmol) and $(PPh_3)_2PdCl_2$ (220 mg, 0.31 mmol, 2 mol%) in THF (50 mL) at 0 °C. The mixture was stirred at 0 °C for 30 min before the solvent was evaporated. Flash chromatography of the residue (silica, hexanes/EtOAc, 99:1 → 98:2) gave

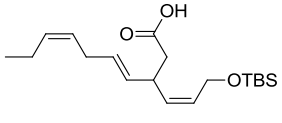


product **14** as a colorless oil (3.72 g, 59 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 7.3, 15H), 0.97 (t, *J* = 7.6, 3H), 1.25-1.36 (m, 6H), 1.45-1.55 (m, 6H), 1.56 (s, 1H), 2.01-2.11 (m, 2H), 2.28-2.34 (m, 2H), 4.07-4.16 (m, 1H), 5.31-5.40 (m, 1H), 5.51-5.61 (m, 1H), 6.03 (dd, *J* = 19.1, 5.1, 1H), 6.17 (dd, *J* = 19.1, 1.2, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 9.5, 13.7, 14.2, 20.7, 27.2, 29.1, 35.0, 74.7, 123.9, 127.8, 135.0, 150.1; IR (film): $\tilde{\nu}$ = 3329, 2957, 2924, 2872, 2852, 1601, 1463, 1418, 1363, 1418, 1376, 1338, 1292, 1249, 1179, 1070, 1039, 988, 961, 872, 768, 688, 661; MS (EI): *m*/*z* (%) 359 (100), 303 (23), 251 (6), 233 (4), 177 (27), 137 (35), 119 (7), 95 (2), 67 (7), 55 (4), 41 (5); HRMS (EI): *m*/*z*: calcd for $C_{20}H_{40}OSn$ [M^+]: 439.20067, found: 439.19998.

(2*Z*,4*E*,8*Z*)-1-((*tert*-Butyldimethylsilyl)oxy)undeca-2,4,8-trien-6-yl acetate (16). CuTC (2.2 g, 11.7 mmol) was added to a stirred solution of stannane **14** (3.23 g, 7.78 mmol) and alkenyl iodide **15** (2.73 g, 9.16 mmol) in degassed *N*-methyl-2-pyrrolidone (20 mL) at 0 °C and the resulting mixture stirred at 0 °C for 1 h, during which time the color of the originally tan suspension turned deep red and later back tan/grey. The mixture was diluted with *tert*-butyl methyl ether (20 mL). Celite® (ca. 5 g) was added and the suspension stirred for 5 min, before it was filtered. The residue was carefully rinsed with *tert*-butyl methyl ether (ca. 100mL) and the combined filtrates were washed with water (100 mL) and aq. sat. NH_4Cl (50 mL) before they were dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography of the residue (silica, hexanes/EtOAc, 98:2 → 95:5) furnished the desired alcohol (≈ 2.5 g) which contained tin impurities. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.08 (s, 6H), 0.90 (s, 9H), 0.97 (t, *J* = 7.5, 3H), 1.67 (d, *J* = 3.9, 1H), 2.02-2.11 (m, 2H), 2.26-2.39 (m, 2H), 4.16-4.25 (m, 1H), 4.36 (dd, *J* = 6.4, 1.6, 2H), 5.31-5.39 (m, 1H), 5.50-5.62 (m, 2H), 5.72 (dd, *J* = 15.2, 6.2, 1H), 5.96-6.03 (m, 1H), 6.49 (ddt, *J* = 15.2, 11.2, 1.2, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.1, 14.2, 18.3, 20.7, 25.9, 35.2, 59.7, 71.9, 123.5, 123.9, 125.3, 128.1, 131.3, 135.4, 136.7; IR (film): $\tilde{\nu}$ = 3329, 2957, 2924, 2872, 2852, 1601, 1463, 1418, 1376, 1338, 1292, 1249, 1179, 1070, 1039, 988, 961, 872, 768, 688, 661; MS (EI): *m*/*z* (%) 296 (1), 279 (1), 239 (5), 227 (100), 211 (21), 197 (3), 169 (12), 147 (12), 133 (8), 115 (13), 105 (17), 95 (75), 75 (65), 67 (32), 57 (5), 41 (29); HRMS (ESI): *m*/*z*: calcd for $C_{17}H_{32}O_2SiNa$ [$M+Na^+$]: 319.20638, found: 319.20664.



Ac_2O (1 mL, 10.6 mmol) was added dropwise to a stirred solution of this impure product (2.5 g), Et_3N (1.8 mL, 13 mmol) and DMAP (52 mg, 5 mol%) in CH_2Cl_2 (30 mL) at 0 °C. The mixture was stirred at 0 °C for 1 h, before the reaction was quenched with aq. sat. $NaHCO_3$ (50 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (3 x 50 mL), the combined extracts dried (Na_2SO_4) and concentrated *in vacuo*. Flash chromatography of the residue (silica, hexanes/EtOAc, 99:1 → 98:2) gave product **16** (2.45 g, 93 % over two steps). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.07 (s, 6H), 0.90 (s, 9H), 0.56 (t, *J* = 7.5, 3H), 1.99-2.09 (m, 2H), 2.04 (s, 3H), 2.29-2.48 (m, 2H), 4.28-4.32 (m, 2H), 5.23-5.35 (m, 2H), 5.45-5.66 (m, 3H), 5.93-6.00 (m, 1H), 6.48 (ddt, *J* = 15.2, 11.2, 1.1, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.1, 14.1, 20.7, 21.2, 18.3, 25.9, 32.3, 59.7 73.9, 122.8, 127.4, 127.9, 132.1, 132.2, 134.8, 170.2; IR (film): $\tilde{\nu}$ = 3016, 2957, 2930, 2857, 1739, 1370, 1231, 1079, 1018, 834, 774; MS (EI): *m*/*z* (%) 338 (0.2), 281 (1), 269 (3), 227 (4), 209 (4), 173 (1), 159 (4), 147 (26), 139 (2), 117 (100), 95 (14), 75 (31), 67 (9), 57 (2), 43 (13); HRMS (EI): *m*/*z*: calcd for $C_{19}H_{34}O_3SiNa$ [$M+Na^+$]: 361.21694, found: 361.21725.

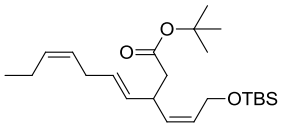


(4*E*,7*Z*)-3-((*Z*)-3-((*tert*-Butyldimethylsilyl)oxy)prop-1-en-1-yl)deca-4,7-dienoic acid (17). A solution of acetate **16** (1.37 g, 4.05 mmol) in THF (4 mL) was added dropwise to a solution of freshly prepared LDA (0.5 M in THF, 9.6

mL, 4.8 mmol) at –78 °C. After stirring for 5 min, a solution of TBSCl (1 M in THF/HMPA (3:2), 6 mL, 6 mmol) was introduced and the resulting mixture warmed to ambient temperature and stirred for 4 h. For work up, the mixture was poured into aq. sat. NH_4Cl (40 mL), the aqueous layer extracted with *tert*-butyl methyl ether (3 x 30 mL), and the combined extracts dried (Na_2SO_4) and concentrated *in vacuo*.

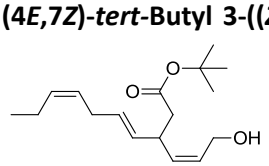
The crude silyl ester thus obtained was dissolved in MeOH (20 mL) and the solution cooled to 0 °C before K_2CO_3 (615 mg, 4.4 mmol) was added. The resulting suspension was stirred at 0 °C for 30 min before it was poured into aq. sat. NH_4Cl (50 mL + 50 mL water). The aqueous phase was extracted with *tert*-butyl methyl ether (3 x 50 mL), the combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*, and the residue purified by flash chromatography (silica, hexanes/EtOAc, 9:1 → 8:2) to give acid **17** (1.27 g, 93 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.06 (s, 6H), 0.90 (s, 9H), 0.95 (t, *J* = 7.5, 3H), 1.97-2.07 (m, 2H), 2.32-2.50 (m, 2H), 2.69-2.76 (m, 2H), 3.42-3.51 (m, 1H), 4.22-4.30 (m, 2H), 5.22-5.52 (m, 5H), 5.53-5.61(m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.2, 14.2, 18.3, 20.4, 25.9, 30.1, 37.2, 40.1, 59.6, 126.3, 129.4, 130.6, 130.6, 130.9, 132.6, 177.6; IR (film): $\tilde{\nu}$ = 3014, 2957, 2929, 2857, 1710, 1471, 1463, 1410, 1361, 1253, 1161, 1087, 1005, 965, 938, 834, 774, 716, 669; MS (EI): *m*/*z* (%) 305 (0.4), 281 (12), 263 (6), 237 (1), 206 (5), 161 (12), 147 (33), 137 (4), 105 (12), 91 (19), 75 (100), 69 (9), 55 (7), 41 (12); HRMS (EI): *m*/*z*: calcd for $C_{19}H_{34}O_3SiNa$ [*M*+*Na*$^+$]: 361.21694, found: 361.21731.

(4*E*,7*Z*)-*tert*-Butyl 3-((*Z*)-3-((*tert*-butyldimethylsilyl)oxy)prop-1-en-1-yl)deca-4,7-dienoate (18).



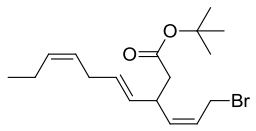
2,4,6-Trichlorobenzoyl chloride (1.2 mL, 7.6 mmol) was added to the solution of acid **17** (1.30 g, 3.83 mmol) and Et_3N (1.2 mL, 8.6 mmol) in toluene (40 mL). After stirring for 30 min, DMAP (500 mg, 4.1 mmol) and *t*-BuOH (3 mL) were introduced and stirring continued for 48 h. The mixture was then poured into aq. sat. $NaHCO_3$ (50 mL) and the aqueous layer extracted with pentane (3 x 20 mL). The combined organic phases were dried (Na_2SO_4) and concentrated *in vacuo*, and the residue purified by flash chromatography (silica, hexane/*tert*-butyl methyl ether, 200:1 → 100:1) to furnish ester **18** (1.11 g, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.06 (s, 6H), 0.89 (s, 9H), 0.95 (t, *J* = 7.6, 3H), 1.42 (s, 9H), 1.97-2.07 (m, 2H), 2.18-2.33 (m, 2H), 2.71-2.74 (m, 2H), 3.36-3.46 (m, 1H), 4.26 (dt, *J* = 6.0, 1.7, 2H), 5.21-5.47 (m, 5H), 5.50-5.57 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.1, –5.1, 14.2, 18.3, 26.0, 28.1, 30.1, 37.9, 41.7, 59.6, 80.3, 126.4, 128.8, 130.3, 131.1, 131.2, 132.5, 171.2; IR (film): $\tilde{\nu}$ = 3010, 2959, 2930, 2857, 1731, 1472, 1462, 1391, 1367, 1253, 1148, 1087, 1006, 965, 835, 775, 717, 669; MS (EI): *m*/*z* (%) 337 (2), 321 (15), 305 (2), 281 (85), 263 (24), 237 (4), 206 (31), 189 (12), 171 (18), 161 (44), 147 (100), 119 (19), 105 (19), 91 (27), 75 (90), 57 (26), 41 (8). HRMS (EI): *m*/*z*: calcd for $C_{23}H_{42}O_3SiNa$ [*M*+*Na*$^+$]: 417.27954, found: 417.27964.

(4*E*,7*Z*)-*tert*-Butyl 3-((*Z*)-3-hydroxyprop-1-en-1-yl)deca-4,7-dienoate. TBAF (1 M in THF, 1.2 mL, 1.2 mmol) was added to a stirred solution of ester **18** (313 mg, 0.79 mmol) in THF (8 mL). After stirring for 1 h, all volatile materials were evaporated and the residue purified by flash chromatography (silica, hexanes/EtOAc, 9:5 → 4:1) to give the title compound as a colorless syrup (210 mg, 95 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.5, 3H), 1.42 (s, 9H), 1.97-2.07 (m, 2H), 2.23 (br s, 1H), 2.24 (dd, *J* = 15.5, 9.6, 1H), 2.39 (dd, *J* = 15.5, 5.2, 1H), 2.69-2.75 (m, 2H), 3.53-3.64 (m, 1H), 4.04 (dd, *J* = 12.5, 6.4, 1H), 4.31 (ddd, *J* = 12.5, 7.9, 1.2, 1H), 5.25-5.49 (m, 5H), 5.67-5.75 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 20.4, 28.1, 30.1, 36.9, 41.2, 58.4, 80.9, 126.3, 128.9, 129.0, 131.2, 132.6, 134.0, 171.9; IR (film): $\tilde{\nu}$ = 3431, 3009, 2966, 2934, 2875, 1727, 1456, 1429, 1392, 1367, 1298, 1254, 1146, 1019,

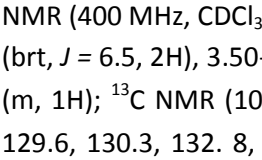


966, 843, 728 MS (EI): *m/z* (%) 263 (1), 224 (2), 206 (30), 191 (5), 177 (22), 161 (10), 147 (57), 117 (41), 95 (46), 91 (100), 79 (40), 67 (29), 57 (87), 41 (69), 29 (35); HRMS (ESI): *m/z*: calcd for $C_{17}H_{28}O_3Na$ [*M+Na*$^+$]: 303.19307, found: 303.19294.

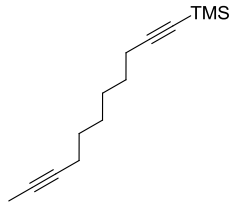
(4*E*,7*Z*)-*tert*-Butyl 3-((Z)-3-bromoprop-1-en-1-yl)deca-4,7-dienoate (19). A solution of PPh_3 (297 mg, 1.1 mmol) in CH_2Cl_2 (1 mL) was added to the solution of (4*E*,7*Z*)-*tert*-butyl 3-((*Z*)-3-hydroxyprop-1-en-1-yl)deca-4,7-dienoate (210 mg, 0.75 mmol) and CBr_4 (373 mg, 1.1 mmol) in CH_2Cl_2 (5 mL) at 0 °C. The mixture was stirred at 0 °C for 20 min before the reaction was quenched with aq. sat. NH_4Cl (5 mL). The organic phase was extracted with *tert*-butyl methyl ether (3 x 10 mL), the combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*, and the residue purified by flash chromatography (silica, hexane/*tert*-butyl methyl ether, 99:1) to give bomide **19** (237 mg, 92 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.5, 3H), 1.42 (s, 9H), 1.95-2.07 (m, 2H), 2.22-2.40 (m, 2H), 2.73 (brt, *J* = 6.5, 2H), 3.50-3.61 (m, 1H), 3.94-4.00 (m, 1H), 4.05-4.12 (m, 1H), 5.25-5.55 (m, 5H), 5.69-5.78 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2, 20.4, 27.1, 28.1, 30.2, 37.1, 41.2, 80.6, 125.7, 126.2, 129.6, 130.3, 132. 8, 135.9, 170.9; IR (film): $\tilde{\nu}$ = 3009, 2967, 2933, 2874, 1727, 1455, 1392, 1367, 1252, 1204, 1155, 1136, 1070, 1037, 966, 921, 869, 845, 766; MS (EI): *m/z* (%) 286 (1), 271 (2), 227 (7), 207 (77), 189 (6), 161 (20), 147 (100), 133 (10), 119 (26), 105 (32), 95 (56), 79 (28), 67 (17), 57 (61), 41 (45); HRMS (ESI): *m/z*: calcd for $C_{17}H_{27}O_2BrNa$ [*M+Na*$^+$]: 365.10867, found: 365.10856.



(4*E*,7*Z*)-*tert*-Butyl 3-((*Z*)-hex-1-en-4-yn-1-yl)deca-4,7-dienoate (20). A solution of 1-propynylmagnesium bromide (0.5 M in THF, 2.8 mL, 1.4 mmol) was added to solid CuI (26.6 mg, 0.14 mmol) at –15 °C and the resulting mixture stirred at this temperature for 30 min before a solution of bromide **19** (234 mg, 0.68 mmol) in THF (2 mL) was introduced. After stirring for 3 h at –10 °C, the reaction was quenched with aq. sat. NH_4Cl (25 mL). The aqueous layer was extracted with *tert*-butyl methyl ether (3 x 25 mL), the combined organic phases were dried (Na_2SO_4) and concentrated *in vacuo*, and the residue purified by flash chromatography (silica, hexane/*tert*-butyl methyl ether, 98:2) to give product **20** (202 mg, 98 %), which must be stored in the freezer. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 7.5, 3H), 1.42 (s, 9H), 1.76 (t, *J* = 2.6, 2H), 1.96-2.06 (m, 2H), 2.15-2.35 (m, 2H), 2.71 (br t, *J* = 6.6, 2H), 2.89-2.95 (m, 2H), 3.40-3.50 (m, 2H), 5.22-5.50 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 3.5, 14.2, 17.4, 20.4, 28.1, 30.2, 37.3, 41.6, 75.5, 77.2, 80.3, 125.6, 126.5, 128.8, 130.9, 132.0, 132.4, 171.2; IR (film): $\tilde{\nu}$ = 3010, 2966, 2920, 1729, 1456, 1431, 1367, 1293, 1256, 1176, 1145, 1087, 1019, 966, 911, 845, 797, 705; MS (EI): *m/z* (%) 287 (1), 246 (4), 231 (4), 217 (11), 187 (29), 177 (32), 171 (19), 157 (42), 143 (41), 131 (99), 117 (49), 105 (48), 91 (56), 79 (33), 67 (17), 57 (100), 41 (65); HRMS (ESI): *m/z*: calcd for $C_{20}H_{30}O_2Na$ [*M+Na*$^+$]: 325.21380, found: 325.21369.



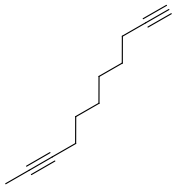
Undeca-1,9-diyn-1-yltrimethylsilane. Tf_2O was added dropwise to a solution of non-7-yn-1-ol (2.2 g, 15.7 mmol) and pyridine (1.35 mL, 16.7 mmol) in CH_2Cl_2 (60 ml) at –15 °C and the resulting mixture stirred at this temperature for 1h before it was diluted with hexane (60 mL) and filtered through Celite®, which was carefully rinsed with hexane. The combined filtrates were concentrated *in vacuo* (keeping the bath temperature < 20°C) to give the crude triflate as a colorless syrup (4.07 g, 95 %), which was used in the next step without delay.



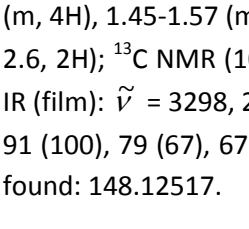
*n*BuLi (1.6 M in hexane, 12 mL, 19.2 mmol) was slowly added to a stirred solution of ethynyltrimethylsilane (3.8 mL, 21 mmol) in THF (60 mL) at –78 °C and the resulting solution stirred at 0 °C for 30 min. The mixture was then cooled to –78 °C before a solution of the crude triflate (4.05 g, 14.9

mmol) in THF (15 mL) was introduced. The mixture was warmed to 0 °C, stirred for 1 h, the reaction quenched with aq. sat. NH_4Cl (50 mL) and the aqueous phase extracted with hexane (3 x 50 mL). The combined extracts were dried (Na_2SO_4) and concentrated *in vacuo*, and the residue purified by flash chromatography (silica, hexane/*tert*-butyl methyl ether, 200:1) to give the title compound as a colorless syrup (2.90 g, 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.14 (s, 9H), 1.34-1.42 (m, 4H), 1.43-1.52 (m, 4H), 1.77 (t, *J* = 2.6, 3H), 2.08-2.15 (m, 2H), 2.21 (t, *J* = 7.1, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 0.2, 3.4, 18.6, 19.8, 28.3 (2C), 28.5, 28.9, 75.4, 79.2, 84.3, 107.6; IR (film): $\tilde{\nu}$ = 2935, 2859, 2174, 1248, 837, 758, 697 cm^{-1}; MS (EI): *m*/*z* (%) 220 (2), 205 (12), 192 (3), 177 (9), 163 (3), 145 (14), 131 (11), 117 (6), 109 (7), 97 (13), 83 (9), 73 (100), 67 (6), 59 (35), 53 (5), 43 (6); HRMS (EI): *m*/*z*: calcd for $C_{14}H_{24}Si$ [M^+]: 220.16473, found: 220.16494.

Undeca-1,9-diyne. K_2CO_3 (2.8 g, 20.3 mmol) was added to solution of undeca-1,9-diyn-1-yltrimethylsilane (913 mg, 4.14 mmol) in methanol (50 mL) and the suspension stirred for 4 h before it was poured into aq. sat. NH_4Cl (100 mL). The aqueous layer was extracted with pentane (3 x 50 mL) and the combined extracts dried (Na_2SO_4) and concentrated *in vacuo* to give the title compound as a colorless oil which was pure enough for further use (601 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35-1.44 (m, 4H), 1.45-1.57 (m, 4H), 1.77 (t, *J* = 2.6, 3H), 1.93 (t, *J* = 2.6, 1H), 2.09-2.15 (m, 2H), 2.18 (dt, *J* = 7.0, 2.6, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 3.4, 18.3, 18.7, 28.3, 28.3, 28.4, 28.9, 68.1, 75.4, 79.2, 84.6; IR (film): $\tilde{\nu}$ = 3298, 2934, 2859, 1459, 1434 cm^{-1}; MS (EI): *m*/*z* (%) 147 (1), 133 (6), 119 (22), 105 (92), 91 (100), 79 (67), 67 (57), 53 (49), 41 (58), 27 (31); HRMS (EI): *m*/*z*: calcd for $C_{11}H_{16}$ [M^+]: 148.12520, found: 148.12517.



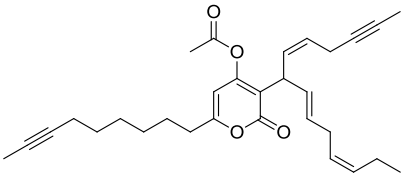
Methyl dodeca-2,10-diynoate. *n*BuLi (1.6 M in hexane, 4 mL, 6.4 mmol) was slowly added to a stirred solution of undeca-1,9-diyne (917 mg, 6.2 mmol) in THF (20 mL) at –78 °C and the resulting mixture stirred at this temperature for 30 min before methyl chloroformate (500 µL, 6.4 mmol) was introduced. The resulting mixture was stirred at –78 °C for 3h before the reaction was quenched with aq. sat. NH_4Cl (50 mL). The aqueous phase was extracted with *tert*-butyl methyl ether (3 x 30 mL), the combined extracts were dried (Na_2SO_4) and concentrated *in vacuo*, and the residue was purified by flash chromatography (silica, hexane/*tert*-butyl methyl ether, 99:1 → 95:5) to afford the title compound as a colorless syrup (1.06 g, 83%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36-1.43 (m, 4H), 1.44-1.52 (m, 2H), 1.54-1.63 (m, 2H), 1.77 (t, *J* = 2.5, 3H), 2.08-2.15 (m, 2H), 2.33 (t, *J* = 7.1, 2H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 3.4, 18.6, 18.6, 27.4, 28.2, 28.3, 28.8, 52.5, 72.9, 75.5, 79.1, 89.8, 154.2; IR (film): $\tilde{\nu}$ = 2936, 2859, 2234, 1712, 1434, 1248, 1075, 751; MS (EI): *m*/*z* (%) 205 (4), 191 (14), 175 (11), 163 (31), 147 (33), 131 (37), 124 (21), 119 (50), 111 (13), 105 (100), 98 (11), 91 (82), 79 (64), 67 (64), 59 (27), 53 (62), 41 (61), 27 (29); HRMS (ESI+): *m*/*z*: calcd for $C_{13}H_{18}O_2Na$ [M^+ + Na]: 229.11990, found: 229.12012.



***tert*-Butyl-3-oxo-2-((5*Z*,8*E*,11*Z*)-tetradeca-5,8,11-trien-2-yn-7-yl)tetradeca-4,12-diynoate (21).** A solution of ester **20** (260 mg, 0.86 mmol) in THF (0.5 mL) was slowly added to a stirred solution of freshly prepared LDA (0.5 M in THF, 1.67 mL, 0.84 mmol) at –78 °C. The mixture was stirred at this temperature for 25 min before a solution of methyl dodeca-2,10-diynoate (225 mg, 1.10 mmol) in THF (0.5 mL) was introduced. Stirring was continued at –78 °C for 3 h and for 1 h at 0 °C. The reaction was quenched with aq. sat. NH_4Cl (5 mL), the aqueous layer

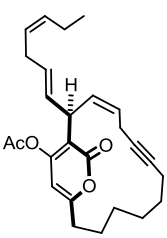
extracted with *tert*-butyl methyl ether (3 x 10 mL), the combined organic phases were dried (Na_2SO_4) and concentrated *in vacuo*, and the residue was purified by flash chromatography (silica, hexane/*tert*-butyl methyl ether, 100:1) to give product **21** (304 mg, 76 %). This product can be stored at –20°C for short periods of time. It exists as a mixture of (at least) three species (*keto*- and *enol* forms) in a ratio of ≈ 3:3:4 (NMR). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.5, 0.3 x 3H), 0.93 (t, *J* = 7.5, 0.3 x 3H), 0.94 (t, *J* = 7.5, 0.4x3H), 1.35-1.54 (m, 6H), 1.41 (s, 0.3 x 3H), 1.42 (s, 0.3 x 3H), 1.48 (s, 0.4 x 3H), 1.54-1.66 (m, 2H), 1.95-2.07 (m, 2H), 2.08-2.15 (m, 2H), 2.37 (dt, *J* = 7.0, 1.5, 1H), 2.44 (t, *J* = 7.1, 1H), 2.61-2.76 (m, 2H), 2.84-3.04 (m, 2H), 3.40 (dd, 9.6, 5.7, 0.6H), 3.75-3.88 (m, 0.6H), 3.28-3.35 (m, 0.4H), 5.18-5.61 (m, 5.6H), 5.69-5.77 (m, 0.4H), 12.51 (s, 0.3H); ^{13}C NMR (100 MHz, $CDCl_3$, resolved signals of the *ketone/enol* mixture): δ = 3.4, 3.4, 3.5, 14.2, 14.2, 17.5, 17.6, 18.6, 18.7, 19.0, 19.5, 20.4, 27.5, 27.8, 27.9, 28.0, 28.2, 28.3, 28.3, 28.4, 28.6, 28.8, 28.9, 30.1, 30.1, 30.2, 40.1, 40.1, 40.3, 66.5, 66.8, 75.2, 75.3, 75.4, 75.5, 75.5, 75.5,, 77.1, 79.0, 79.1, 80.1, 80.3, 82.0, 82.3, 96.6, 96.6, 100.0, 111.2, 125.1, 126.1, 126.2, 126.7, 127.1, 127.2, 128.1, 128.3, 129.0, 129.2, 130.7, 130.9, 131.6, 131.9, 132.2, 132.6, 132.6, 152.5, 166.2, 166.3, 172.1, 181.3, 181.4; IR (film): $\tilde{\nu}$ = 3008, 2934, 2859, 2212, 1733, 1676, 1631, 1587, 1456, 1392, 1368, 1250, 1148, 1098, 1035, 966, 910, 846, 732, 679; HRMS (EI): *m*/*z*: calcd for $C_{32}H_{44}O_3Na$ [*M*+*Na*$^+$]: 499.31827, found: 499.31808.

6-(Non-7-yn-1-yl)-2-oxo-3-((5*Z*,8*E*,11*Z*)-tetradeca-5,8,11-trien-2-yn-7-yl)-2*H*-pyran-4-yl acetate (23).



A solution of $XPhosAuNTf_2$ (**22**) (0.7 mg, 5 mol%) and compound **21** (6.5 mg, 13.6 µmol) in $MeNO_2$/HOAc (350 µL, 4:1) was stirred for 14 h at ambient temperature. For work up, the solvents were distilled off under vacuum while cooling the mixture to 0 °C. The residue was dissolved in CH_2Cl_2 (1 mL), and Et_3N (30 µL) and Ac_2O (15 µL) were added at 0 °C. After stirring for 30 min at 0 °C, the reaction was quenched with aq. sat. $NaHCO_3$ (3 mL), the aqueous layer extracted with *tert*-butyl methyl ether (3 x 5 mL), the combined organic phases were dried (Na_2SO_4) and concentrated *in vacuo*, and the residue quickly passed through a short pad of silica, eluting with a gradient of hexane/*tert*-butyl methyl ether (99:1 → 95:5) to give product **23** as a colorless syrup (4.6 mg, 73 %). This product can be stored at –20°C only for short periods of time. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 7.5, 3H), 1.29-1.51 (m, 6H), 1.59-1.68 (m, 2H), 1.76 (t, *J* = 2.6, 3H) 1.77 (t, *J* = 2.5, 3H), 1.97-2.06 (m, 2H), 2.08-2.15 (m, 2H), 2.29 (s, 3H), 2.44 (brt, *J* = 7.7, 2H), 2.73 (br t, *J* = 6.5, 2H), 2.83-3.00 (m, 2H), 4.44-4.51 (m, 2H), 5.25-5.34 (m, 1H), 5.36-5.63 (m, 3H), 5.59-5.67 (m, 1H), 5.73-5.81 (m, 1H), 5.89 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 3.4, 3.5, 14.2, 17.4, 18.6, 20.5, 21.0, 26.6, 28.1, 28.5, 28.8, 30.1, 33.5, 36.8, 75.6, 75.6, 76.9, 79.1, 101.6, 116.5, 126.3, 126.5, 128.9, 129.4, 129.6, 132.6, 158.1, 163.7, 163.7, 167.1; IR (film): $\tilde{\nu}$ = 3011, 2932, 2858, 1778, 1718, 1649, 1583, 1432, 1368, 1180, 1012, 1009, 972, 910, 876, 801, 728; MS (EI): *m*/*z* (%): 462 (19), 420 (63), 391 (16), 377 (27), 367 (48), 351 (70), 341 (32), 325 (100), 311 (9), 297 (11), 270 (13), 227 (16), 201 (20), 173 (35), 159 (66), 131 (26), 145 (20), 117 (28), 109 (33), 91 (49), 69 (53), 55 (56), 43 (84). HRMS (ESI): *m*/*z*: calcd for $C_{30}H_{38}O_4Na$ [*M*+*Na*$^+$]: 485.26623, found: 485.26654.

(*Z*)-2-((1*E*,4*Z*)-Hepta-1,4-dien-1-yl)-16-oxo-15-oxabicyclo[12.2.2]octadeca-1(17),3,14(18)-trien-6-yn-17-yl acetate (25).



Dried MS 5Å powder (100 mg) was added to a solution of compound **23** (7.8 mg, 17 µmol) in toluene (17 mL) and the resulting suspension stirred for 30 min before a solution of complex **24** (10 mM in toluene, 85 µL, 0.85 µmol, 5 mol%) was introduced. After stirring for 30 min at ambient temperature, the mixture was filtered through a pad of Celite®, which was thoroughly rinsed with *tert*-butyl methyl ether. The combined filtrates were concentrated *in vacuo* and the residue purified by flash chromatography (silica, hexane/*tert*-butyl methyl ether,

98:2 → 95:5) to give cycloalkyne **25** (6.1 mg, 88 %, ca. 1:1 mixture of atropisomers). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.94 (t, *J* = 7.5, ½·3H), 0.94 (t, *J* = 7.5, ½·3H), 1.06-1.38 (m, 5H), 143-1.55 (m, 1H), 1.66-1.87 (m, 2H), 1.97-2.05 (m, 2H), 2.05-2.18 (m, 2H), 2.20-2.27 (m, ½H), 2.26 (s, ½·3H), 2.28-2.36 (m, ½H), 2.36 (s, ½·3H), 2.61-2.76 (m, 4H), 2.85-2.93 (m, ½H), 3.06-3.15 (m, ½H), 4.26 (brt, *J* = 7.0, ½H), 4.60-4.65 (m, ½H), 5.24-5.32 (m, 1H), 5.37-3.49 (m, 2½H), 5.51-5.54 (m, 1H), 5.78 (brdd, *J* = 10.3, 7.2, ½H), 5.83 (ddt, *J* = 15.4, 7.6, 1.6, ½H), 5.91 (brdd, *J* = 10.3, 6.3, ½H), 6.02 (s, ½H), 6.03 (s, ½H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2, 14.2, 17.8, 18.2, 18.6, 18.7, 20.4, 20.5, 20.9, 21.3, 24.8, 25.0, 27.7, 27.9, 28.3, 28.7, 28.9, 29.0, 30.1, 30.1, 34.6, 35.1, 35.8, 36.3, 76.9, 77.3, 79.1, 79.6, 101.9, 103.3, 117.6, 118.0, 125.5, 126.1, 126.3, 126.4, 129.2, 129.2, 129.4, 130.3, 131.7, 131.7, 132.6, 132.6, 156.3, 158.8, 162.5, 163.3, 163.7, 164.7, 166.7, 167.0; IR (film): $\tilde{\nu}$ = 3011, 2929, 2857, 1779, 1711, 1647, 1582, 1460, 1432, 1368, 1331, 1257, 1176, 1111, 1070, 1037, 1010, 968, 896, 872, 788, 727; MS (ESI): *m*/*z* (%) 341.2 (M+Na), 839.4 (2M+Na); HRMS (EI): *m*/*z*: calcd for $C_{26}H_{32}O_4Na$ [$M+Na^+$]: 431.21928, found: 431.21960.

Neurymenolide A Acetate (2). H_2 was bubbled through a mixture containing cycloalkyne **25** (5.5 mg, 13.5 µmol), Lindlar catalyst (5.5 mg), quinoline (20 µL) in EtOAc/1-hexene (2 mL, 1:1) for 10 min. The suspension was then stirred under H_2 (1 atm) for 1 h before it was filtered through a pad of Celite®, which was thoroughly rinsed with *tert*-butyl methyl ether. The combined filtrates were concentrated *in vacuo* and the residue purified by flash chromatography (silica, hexane/*tert*-butyl methyl ether, 98:2 → 95:5) to provide neurymenolide A acetate (**2**) (4.7 mg, 84 %) as a ≈ 2:3 mixture of atropisomers. ^{1}H NMR (500 MHz, $CDCl_3$): δ =0.94 (t, *J* = 7.5, 2/5x3H), 0.95 (t, *J* = 7.5, 3/5x3H), 1.02-1.41 (m, 6H), 1.54-1.71 (m, 1H), 1.71-1.98 (3H), 2.02 (qi, *J* = 7.4, 2H), 2.20-2.25 (m, 2/5H), 2.22 (s, 3/5x3H), 2.25-36 (m, 3/5H), 2.34 (s, 2/5x3H), 2.37-4.48 (m, 1H), 2.63-2.75 (m, 1H), 2.71-2.77 (m, 2H), 2.77-2.88 (m, 1H), 4.12-4.18 (m, 2/5H), 4.48-4.53 (m, 3/5H), 5.19-5.61 (m, 7+1/5H), 5.64-5.70 (m, 2/5H), 5.76-5.82 (m, 2/5H), 5.98 (3/5H), 6.01 (2/5H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2, 14.3, 20.4, 20.5, 20.9, 21.2, 24.2, 25.5, 25.8, 26.2, 26.4, 26.9, 26.9, 27.1, 27.1, 27.2, 27.4, 27.6, 30.1 (x2), 33.7, 33.8, 37.1, 37.5, 102.5, 103.7, 116.9, 117.3, 126.3, 126.3, 127.2, 127.5, 129.2, 129.3, 129.4, 129.4, 129.8, 129.8, 129.8, 130.0, 130.1, 130.2, 132.6, 132.6, 157.2, 158.5, 162.1, 163.7, 164.2, 164.9, 166.7, 167.1; IR (film): $\tilde{\nu}$ = 3009, 2927, 2854, 1778, 1714, 1647, 1580, 1461, 1435, 1367, 1274, 1178, 1111, 1043, 1011, 967, 871, 788, 726, 698; MS (EI): *m*/*z* (%) 410 (69), 368 (100), 351 (11), 339 (24), 325 (14), 313 (10), 299 (96), 273 (33), 257 (11), 243 (7), 229 (7), 215 (8), 199 (13), 187 (10), 175 (13), 159 (15), 145 (15), 133 (16), 117 (22), 105 (23), 91 (42), 79 (33), 69 (48), 55 (42), 43 (71); HRMS (EI): *m*/*z*: calcd for $C_{26}H_{34}O_4Na$ [$M+Na^+$]: 433.23493, found: 433.23534.

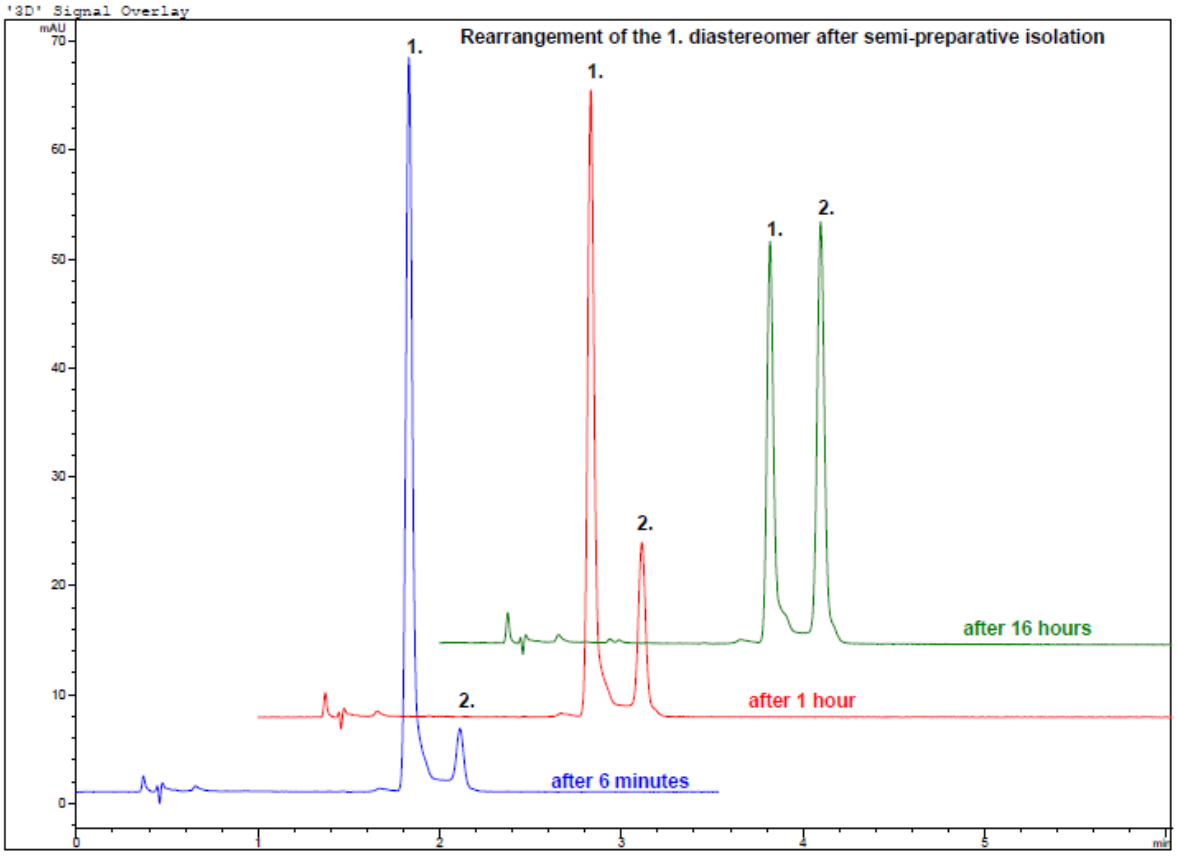


Figure S2. Preparative HPLC (Shimadzu LC-8A/10A, YMC (150 mm, ∅ 20 mm) ODS-A 5 µm, MeCN/H_2O (9:1), 15 mL/min) allowed the two atropisomers of **2** to be separated; however, they equilibrate quickly in solution as evident from the HPLC traced recorded 6 min, 1 h, and 16 h after collection of the pure atropisomer.

Table S1. Comparison of the ^{13}C NMR data ($CDCl_3$) of synthetic neurymenolide A acetate (**2**) with the reported data of the authentic sample.[4]

Synthetic sample	Literature Data			
	Major isomer		Minor isomer	
δ	δ	$\Delta\,\delta$	δ	$\Delta\,\delta$
14.2			14.2	0
14.3	14.2	0.1		
20.4	20.5	-0.1		
20.5			20.5	0
20.9			20.9	0
21.2	21.2	0		
24.2			25.5	-1.3
25.5	25.5	0		
25.8			25.8	0
26.2	26.2	0		
26.4	26.4	0		
26.9	26.9	0		
26.9			26.9	0
27.1			27.1	0
27.1	27.1	0		
27.2	27.2	0		
27.4			27.4	0
27.6			27.6	0
30.1			30.0	0.1
30.1	30.0	0.1		
33.7	33.7	0		
33.8			33.8	0
37.1	37.1	0		
37.5			37.5	0
102.5			102.5	0
103.7	103.7	0		
116.9			116.9	0
117.3	117.3	0		
126.3	126.3	0		
126.3			126.3	0
127.2	127.2	0		
127.5			127.5	0
129.2	129.3	-0.1		
129.3			129.4	-0.1
129.4			129.4	0
129.4	129.4	0		
129.8			129.7	0.1
129.8			129.8	0
129.8	129.8	0		
130.0	130.0	0		
130.1			130.1	0
130.2	130.2	0		
132.6	132.5	0.1		
132.6			132.6	0
157.2			157.2	0
158.5	158.5	0		
162.1			162.1	0
163.7	163.7	0		
164.2	164.2	0		
164.9			165.0	-0.1
166.7	166.6	0.1		
167.1			167.1	0

Neurymenolide A (1). K_2CO_3 (0.5 mg, 3.6 µmol) was added to solution of **2** (0.9 mg, 4.1 mmol) in methanol (0.5 mL) at 0 °C and the suspension stirred at this temperature for 30 min. The mixture was poured into aq. sat. NH_4Cl (5 mL), the aqueous layer quickly extracted with *tert*-butyl methyl ether (3 x 5 mL), and the combined organic phases were dried (Na_2SO_4) and concentrated *in vacuo* to give crude neurymenolide A (**1**) which was pure enough to ensure identity with the natural product.[4] Attempts to remove traces of impurities from the crude material lead to decomposition. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.5, 3H), 1.02-1.42 (m, 6H), 1.50-1.70 (m, 1H), 1.75-2.04 (m, 3H), 1.92-2.08 (m, 2H), 2.22-2.35 (m, 1H), 2.50-2.59 (m, 1H), 2.59-2.67 (m, 1H), 2.71-2.81 (m, 2H), 2.81-2.91 (m, 1H), 4.55-4.59 (m, 1H), 5.17-5-5.48 (m, 4H), 5.57-5.74 (m, 4H), 5.82 (s, 1H), 6.39 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 14.2, 20.5, 25.6, 26.6, 26.9, 27.0, 27.1, 27.7, 30.0, 33.5, 36.5, 101.3, 103.8, 125.9, 126.6, 126.9, 129.4, 129.9, 131.0, 133.0, 135.5, 164.6, 165.1, 165.1; MS (EI): *m*/*z* (%) 368 (80), 353 (5), 339 (16), 325 (8), 313 (8), 299 (100), 273 (19), 257 (8), 243 (6), 229 (6), 215 (8), 201 (9), 187 (10), 175 (14), 159 (16), 145 (19), 133 (24), 117 (25), 105 (34), 91 (61), 79 (54), 69 (71), 55 (73), 41 (89); MS (ESI): 391.2 (100%, M+Na), 759.5 (37%, 2M+Na); HRMS (ESI): *m*/*z*: calcd for $C_{24}H_{32}O_3Na$ [$M+Na^+$]: 391.22436, found: 391.22408.

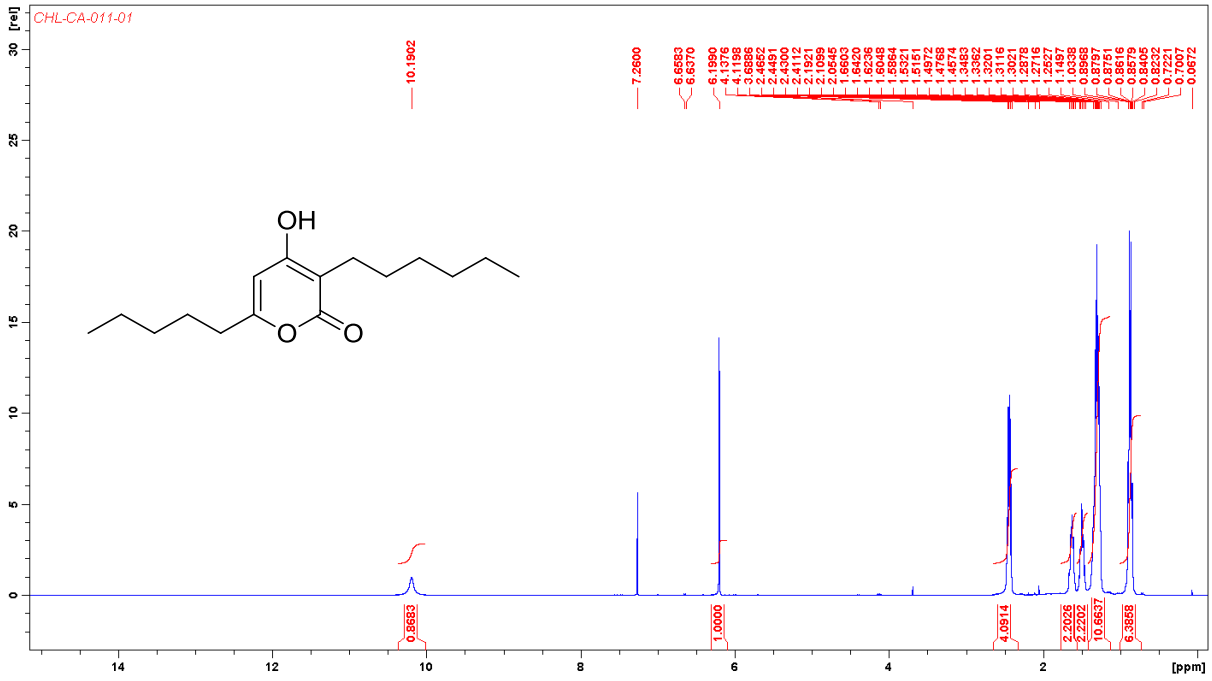
Table S2. Comparison of the ^{13}C NMR data ($CDCl_3$) of synthetic neurymenolide A with the published data.[4]

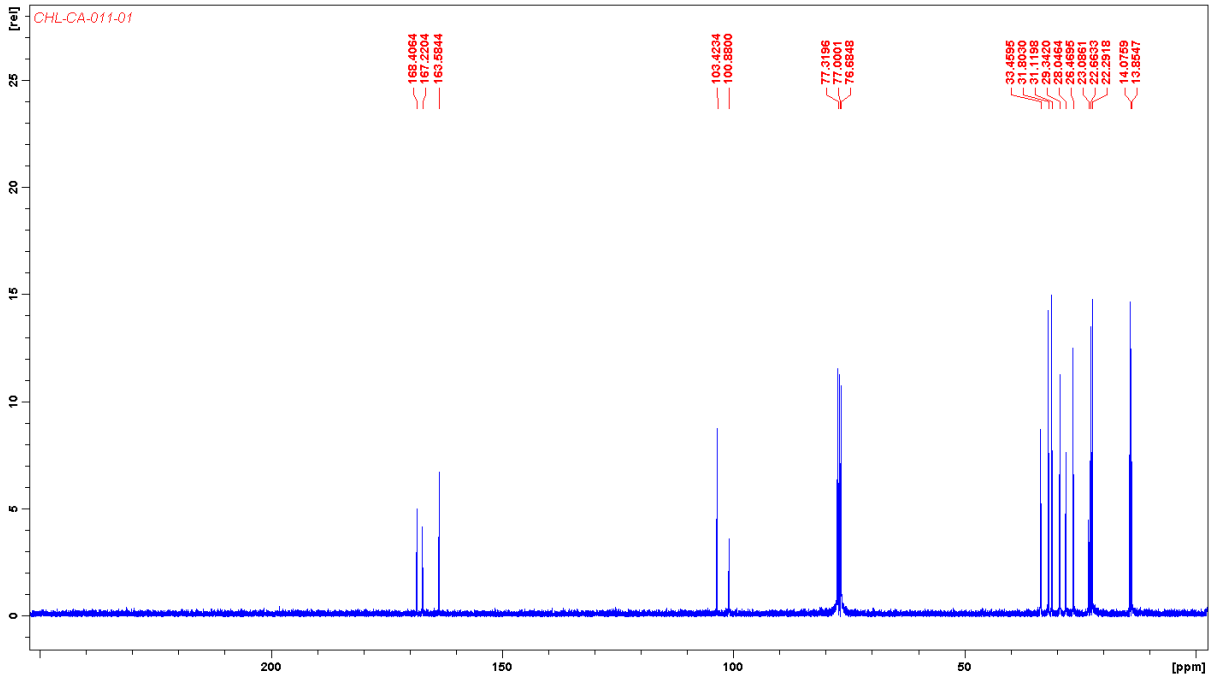
δ		$\Delta\delta$
Synthetic sample (125 MHz)	Authentic sample (150 MHz)	
14.2	14.2	0
20.5	20.5	0
25.6	25.6	0
26.6	26.6	0
26.9	26.9	0
27.0	27	0
27.1	27.1	0
27.7	27.7	0
30.0	30	0
33.5	33.5	0
36.5	36.5	0
101.3	101.4	-0.1
103.8	103.9	-0.1
125.9	125.9	0
126.6	126.6	0
126.9	127	-0.1
129.4	129.4	0
129.9	129.9	0
131.0	131	0
133.0	132.9	0.1
135.5	135.2	0.3
164.7	164.7	0
165.1	165.1	0
165.1	165.1	0

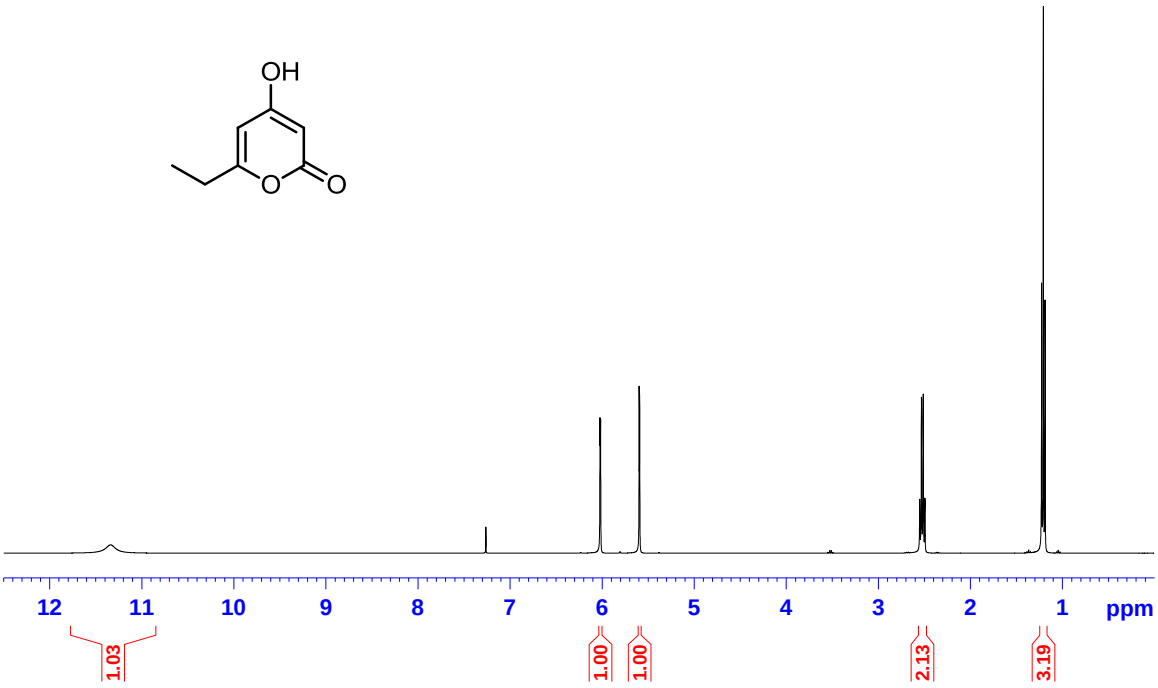
[4] E. P. Stout, A. P. Hasemeyer, A. L. Lane, T. M. Daenport, S. Engel, M. E. Hay, C. R. Fairchild, J. Prudhomme, K. L. Roch, W. Aalbersberg, J. Kubanek, *Org. Lett*. **2009**, *11*, 225-228.

NMR SPECTRA

Pseudopyronine



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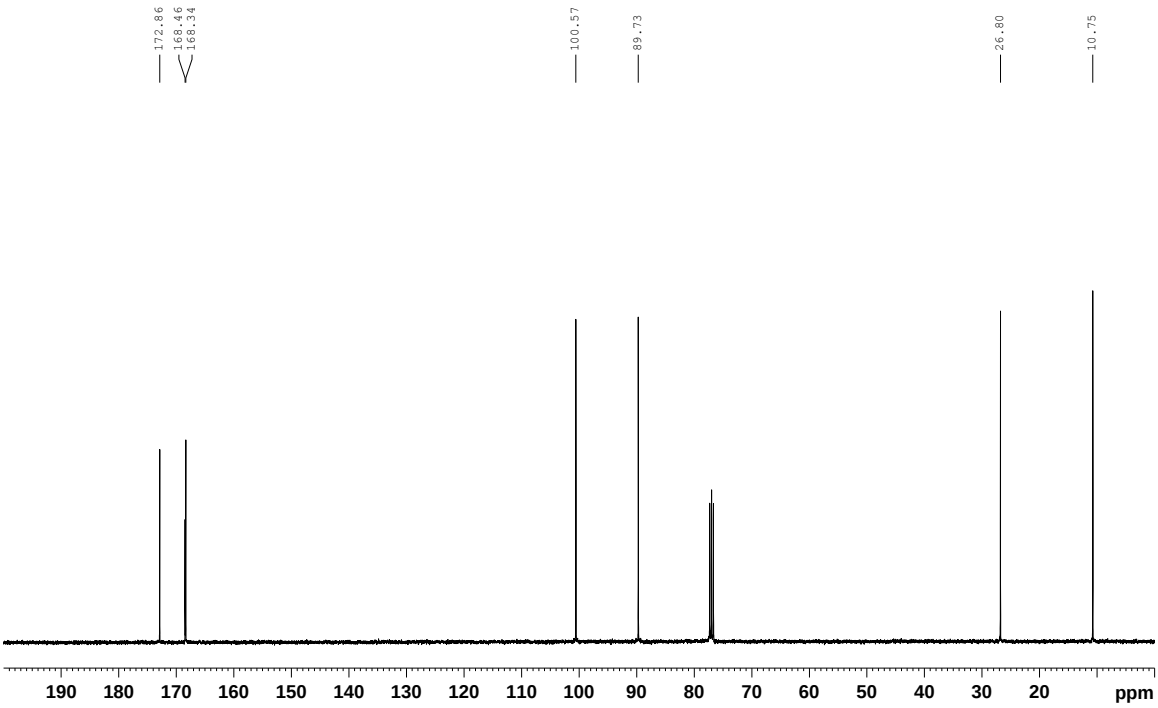
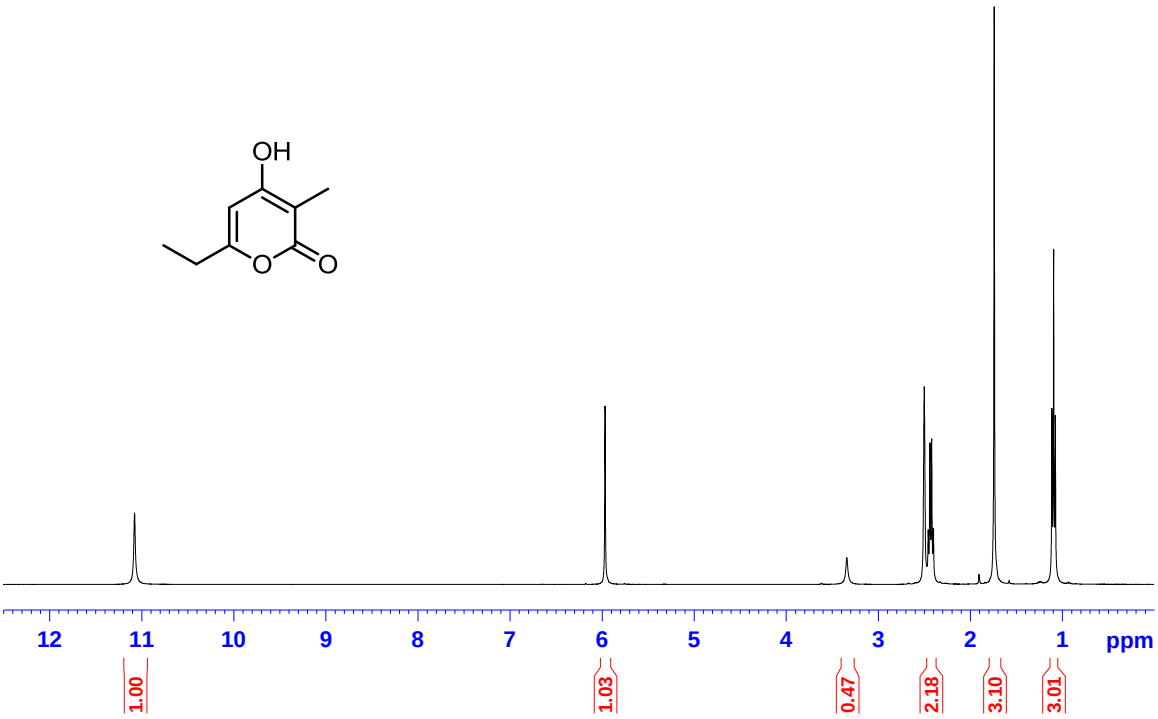
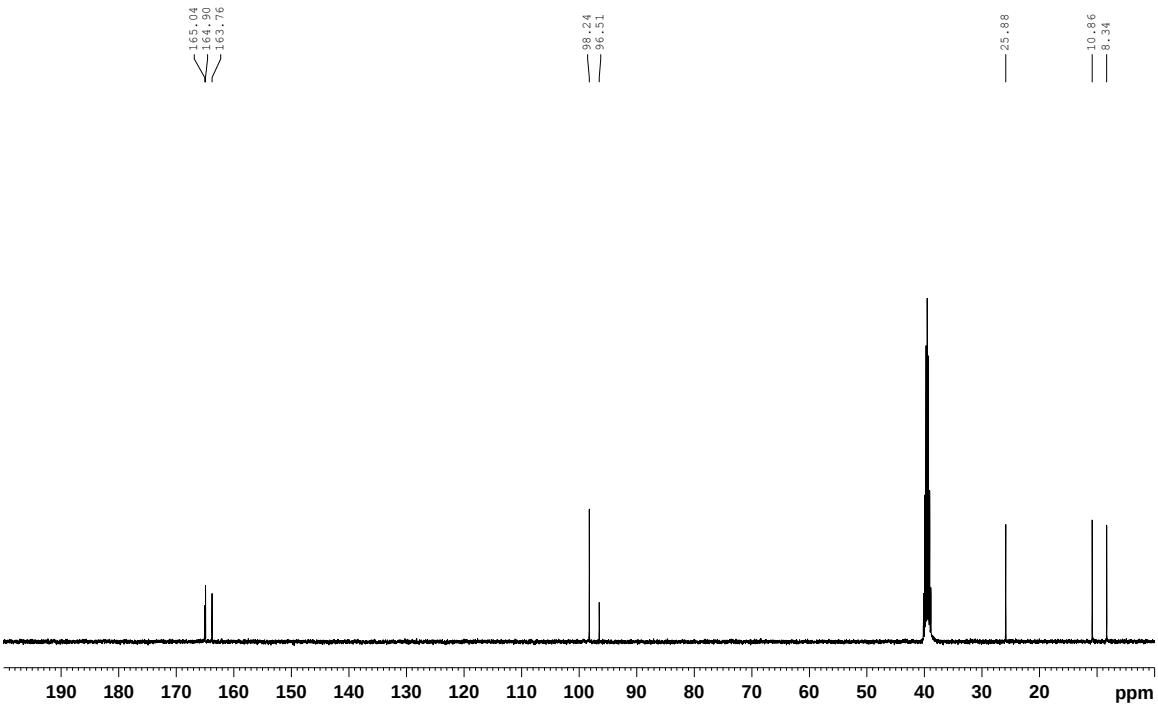
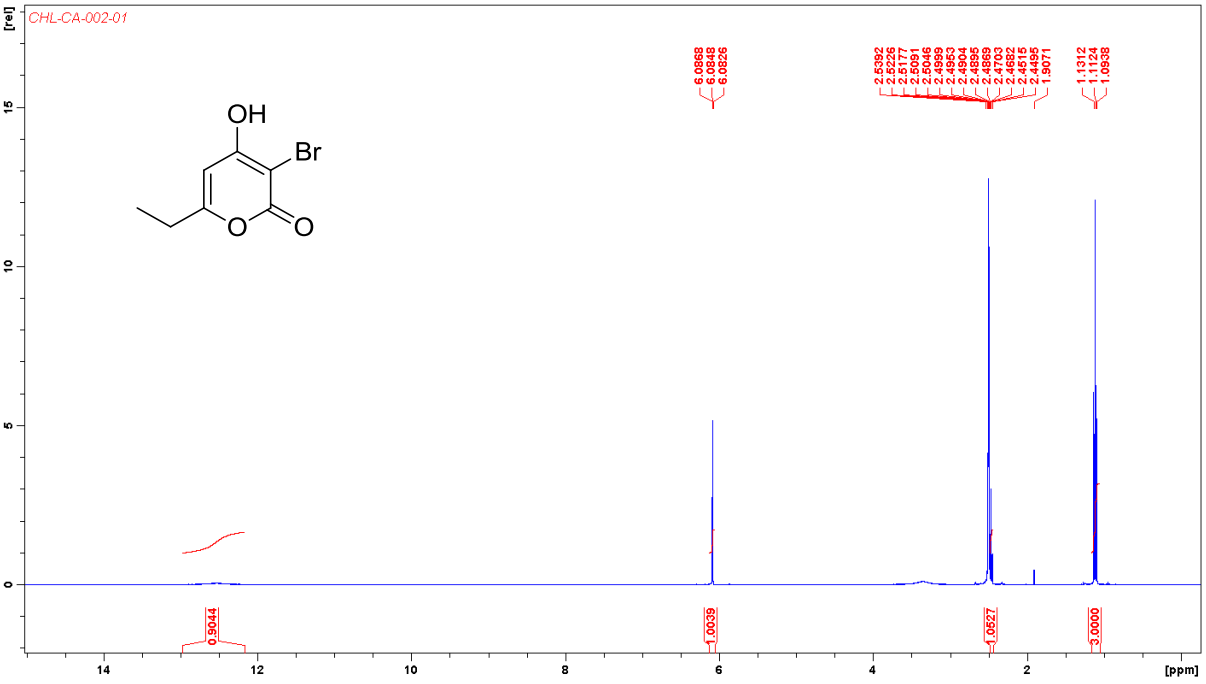
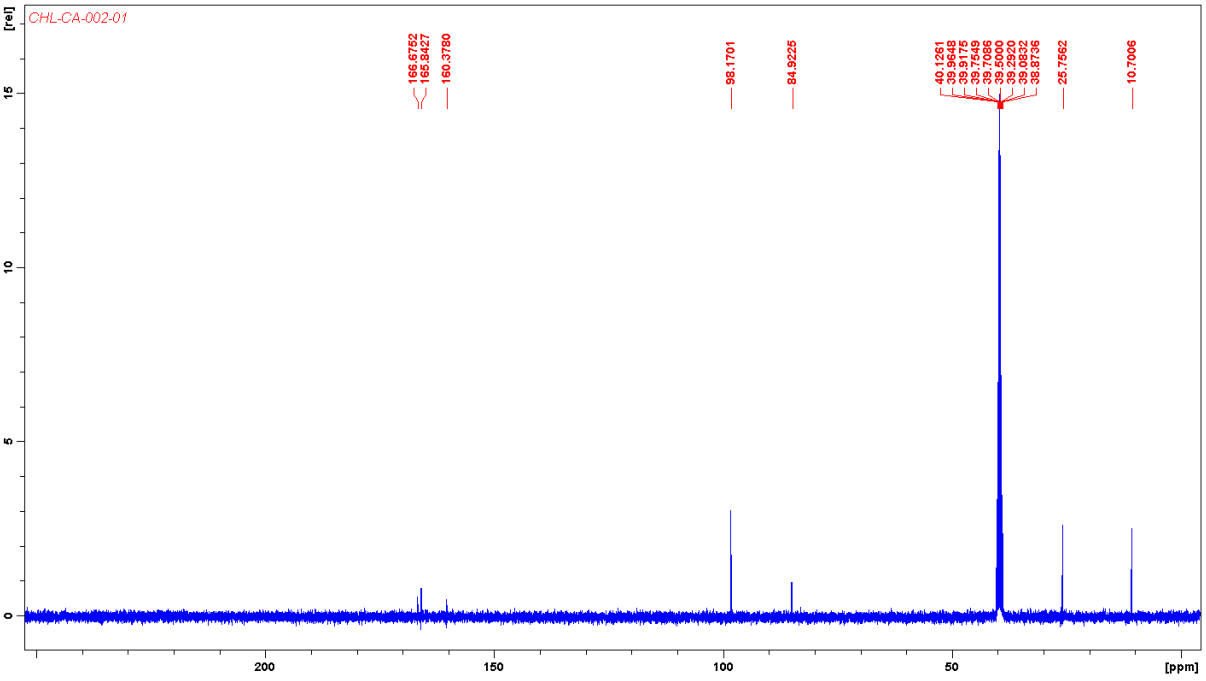
2.13
3.19

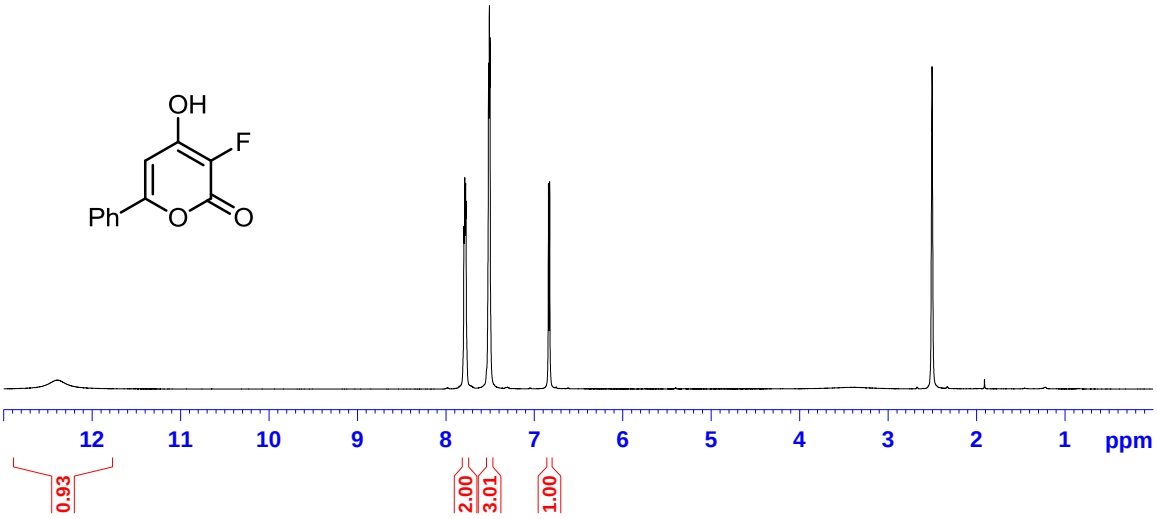

172.86
168.46
168.34
100.57
89.73
26.80
10.75
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

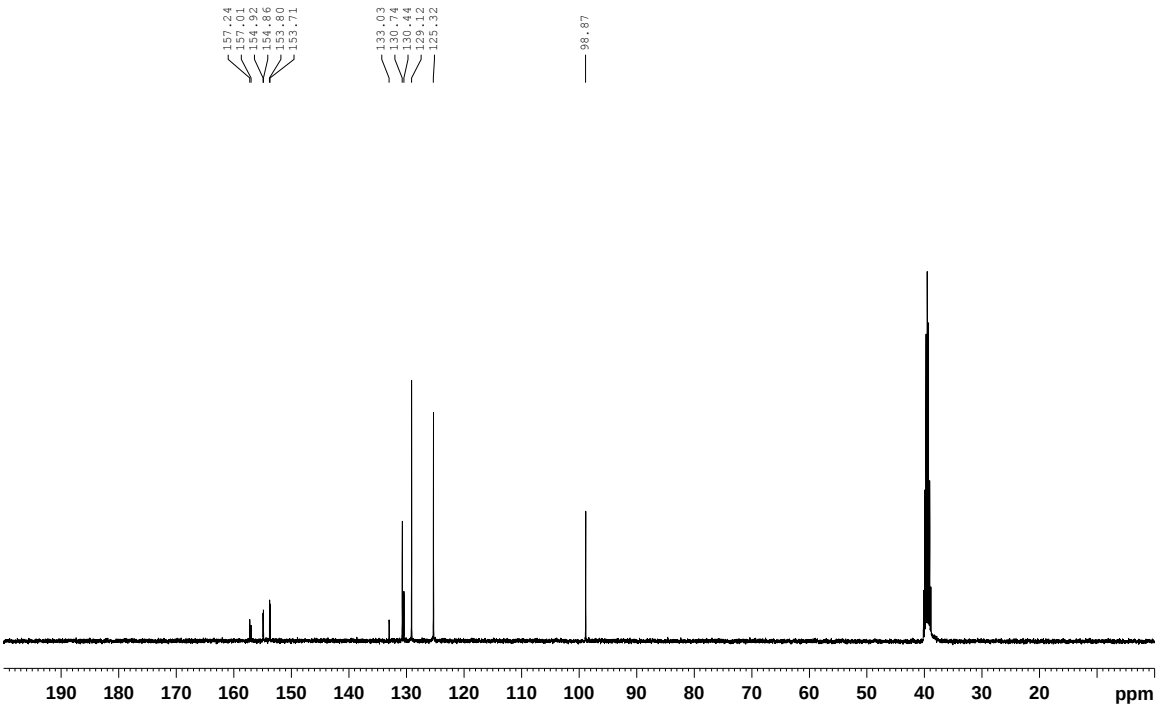

OH
O
O
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.03
0.47
2.18
3.10
3.01

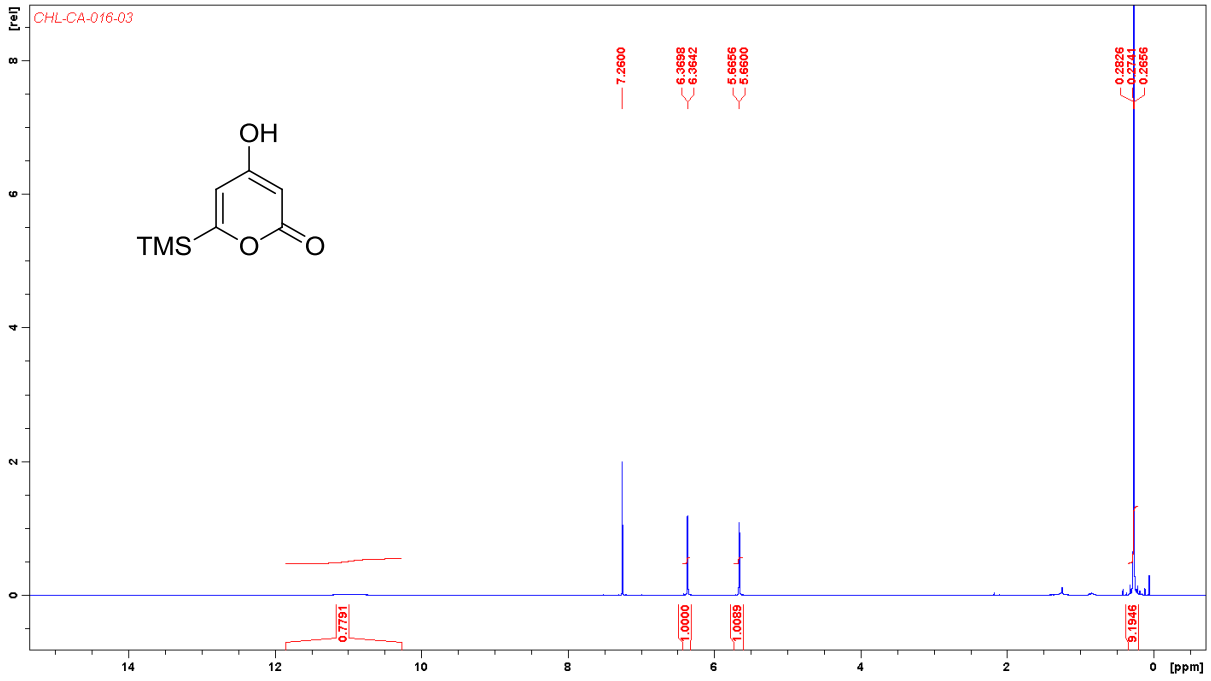

165.04
164.90
163.76
98.24
96.51
25.88
10.86
8.34
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

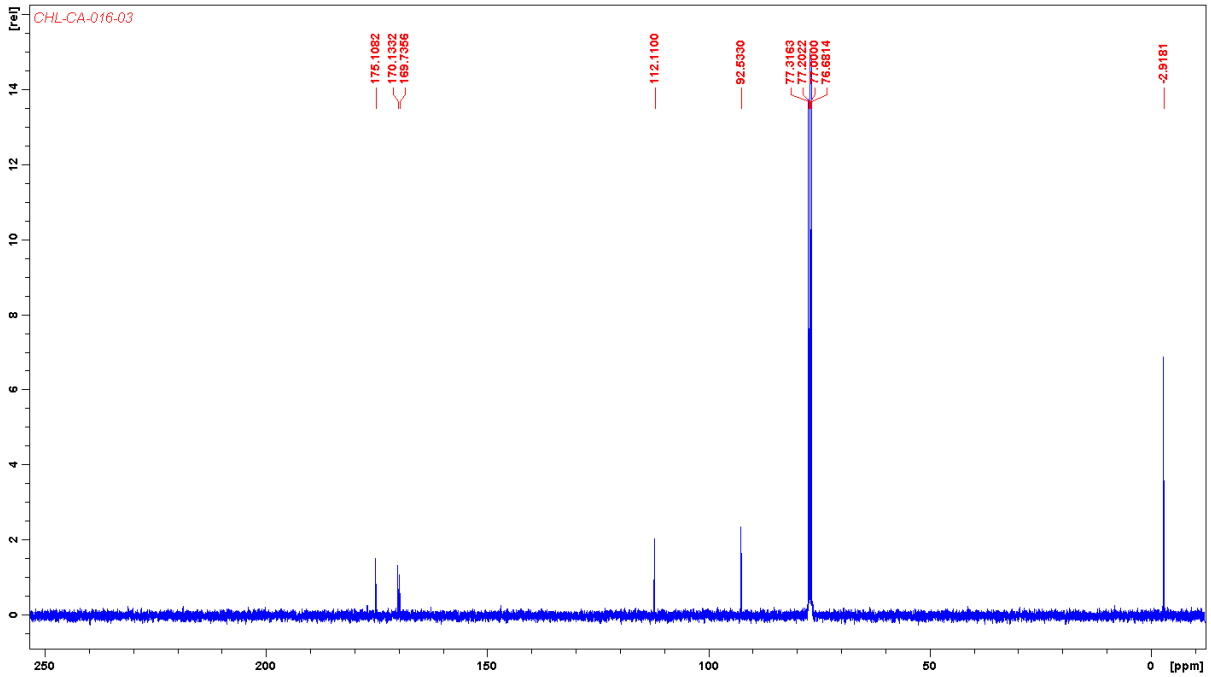

CHL-CA-002-01
[rel]
OH
Br
O
O
6.0868
6.0848
6.0826
2.5392
2.5226
2.5177
2.5091
2.5046
2.4963
2.4953
2.4904
2.4895
2.4869
2.4703
2.4682
2.4515
2.4495
1.9071
1.1312
1.1134
1.0938
0.9044
1.0039
1.0527
3.0000
[ppm]

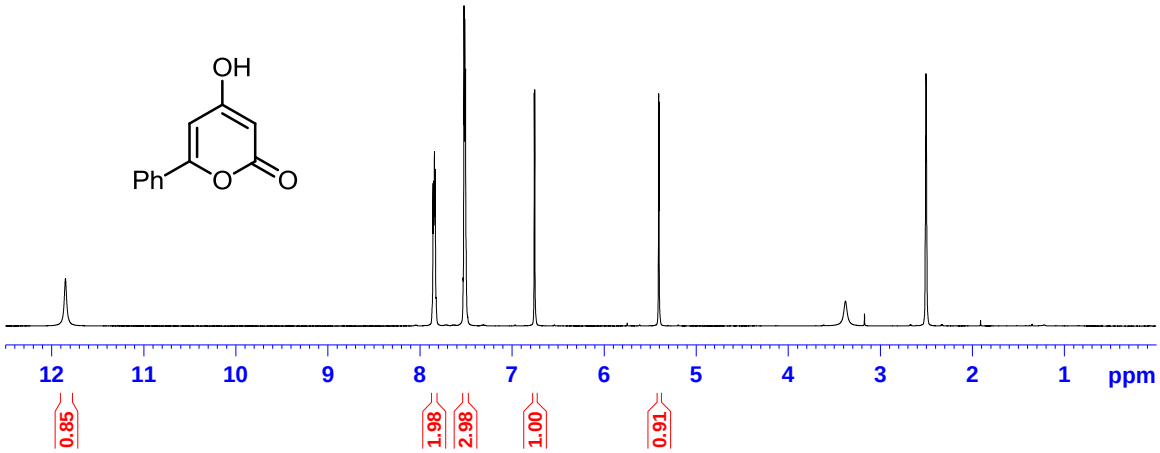

CHL-CA-002-01
[rel]
166.6752
165.8427
160.3780
98.1701
84.9225
40.1261
39.9648
39.9175
39.7549
39.7086
39.5000
39.2920
39.0832
38.8736
25.7562
10.7006
[ppm]

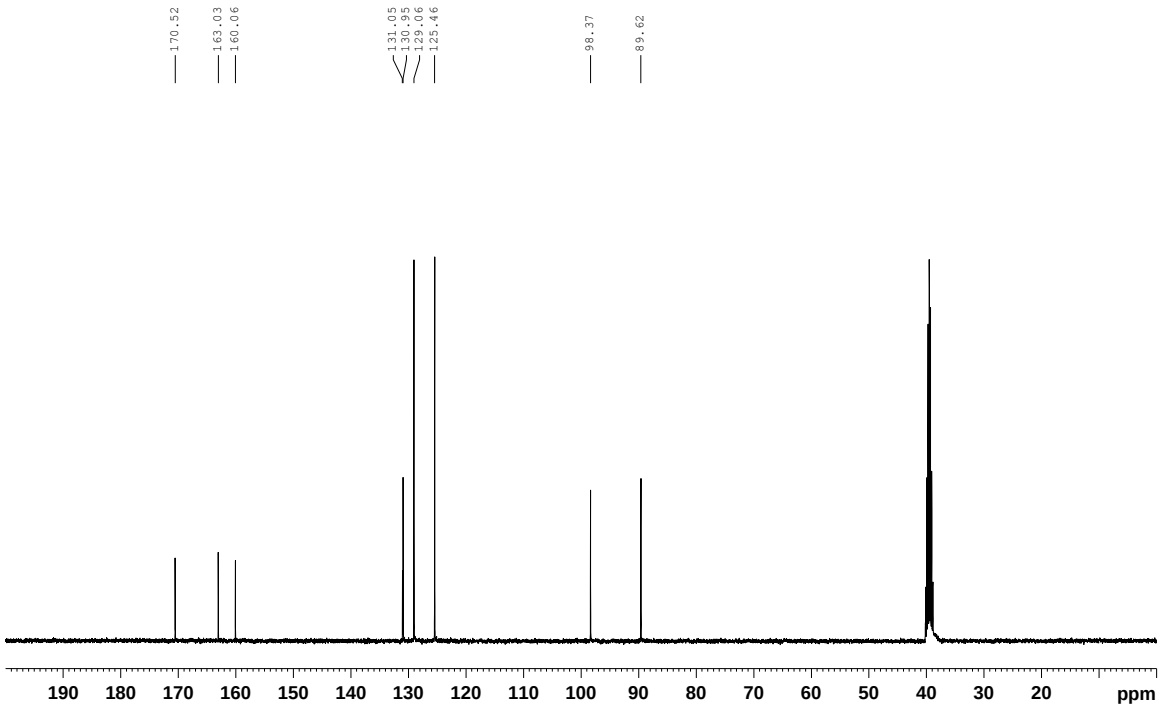

OH
F
Ph
O
O
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.93
2.00
3.01
1.00

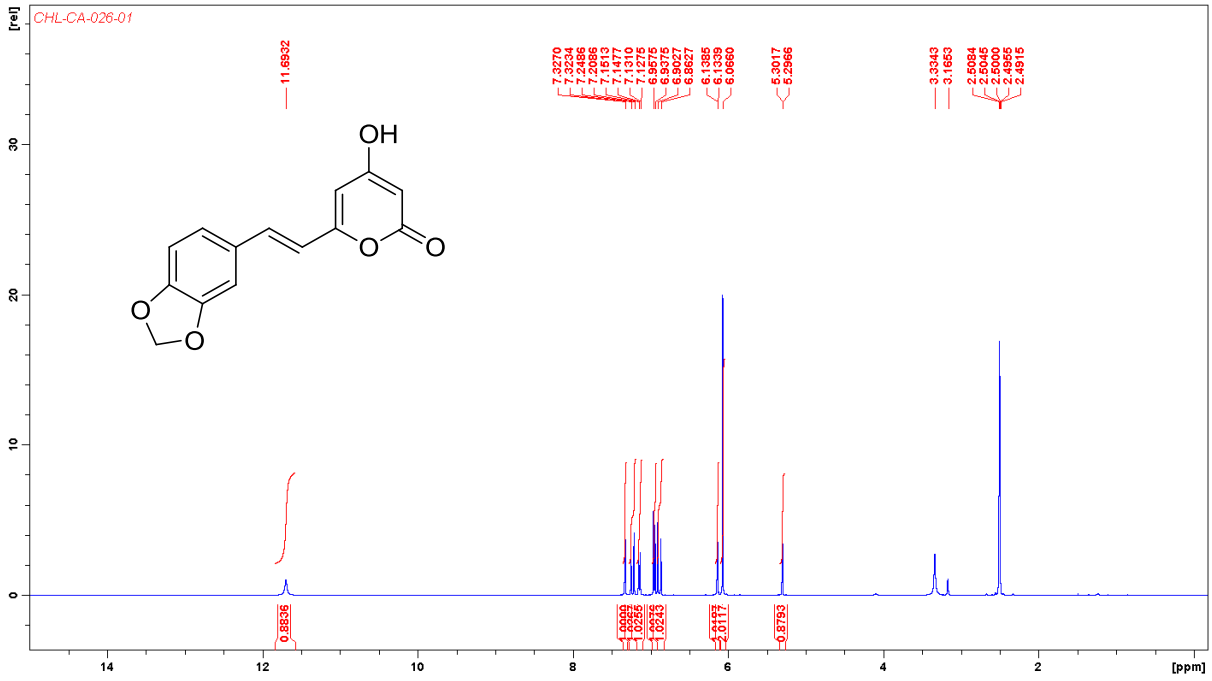

157.24
157.01
154.92
154.86
153.80
153.71
133.03
130.74
130.44
129.12
125.32
98.87
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

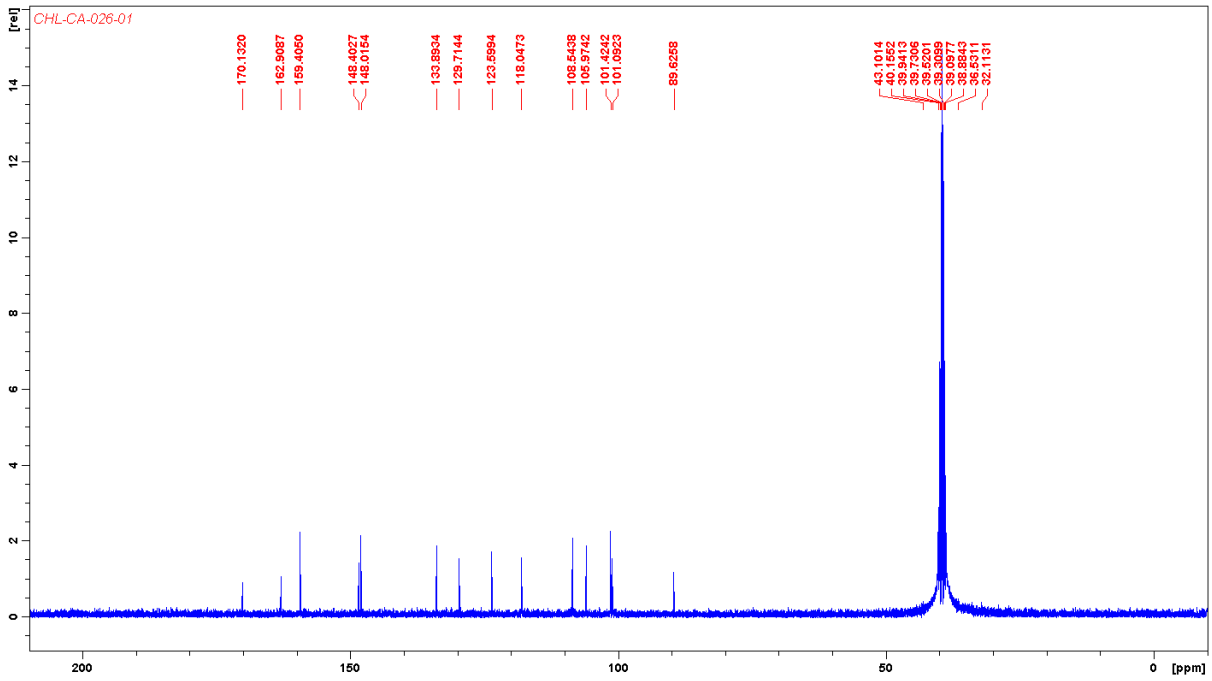

CHL-CA-016-03
[rel]
OH
TMS
O
O
7.2600
6.3698
6.3642
5.6656
5.6600
0.2826
0.2741
0.2656
0.7791
1.0000
1.0089
9.1946
[ppm]

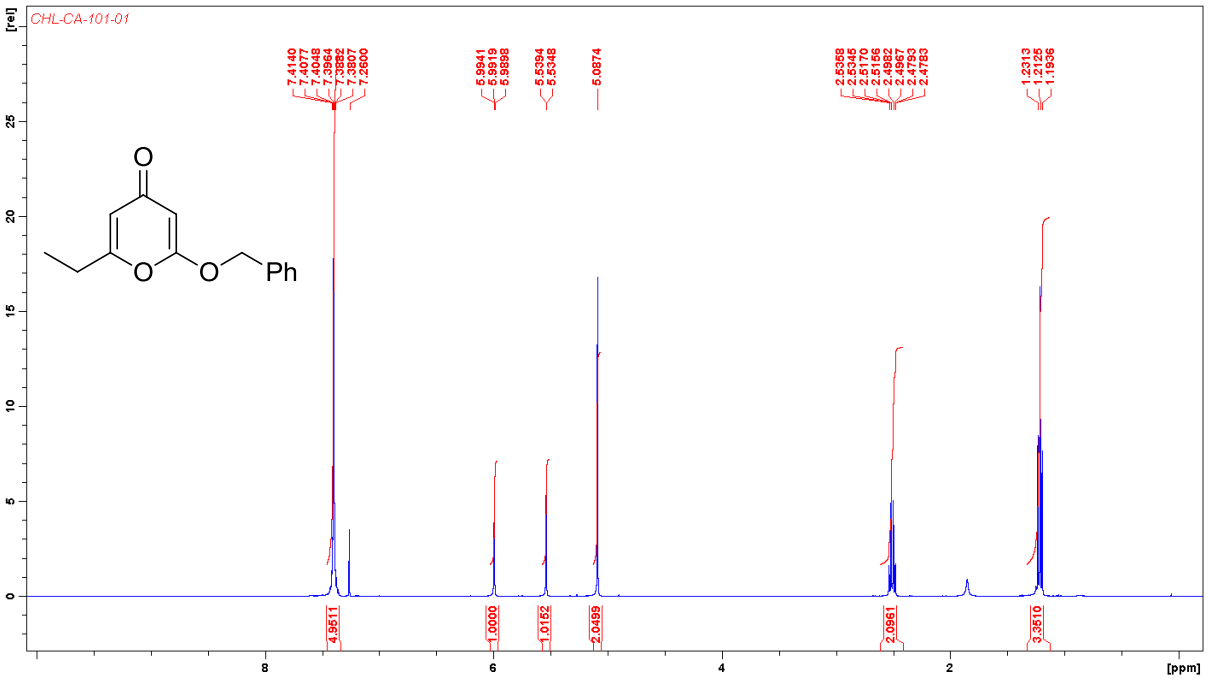

CHL-CA-016-03
[rel]
175.1082
170.1332
169.7356
112.1100
92.5330
77.3163
77.2022
77.0000
76.6814
-2.9181
[ppm]

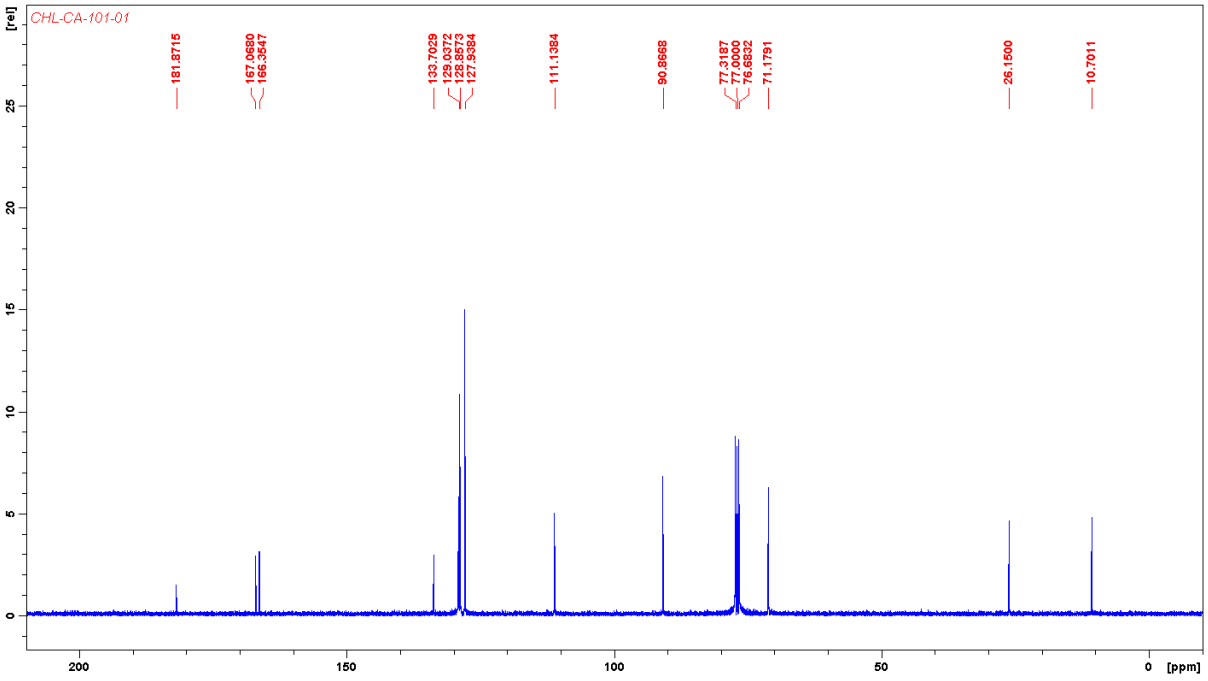

OH
Ph
O
O
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.85
1.98
2.98
1.00
0.91


170.52
163.03
160.06
131.05
130.95
129.06
125.46
98.37
89.62
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

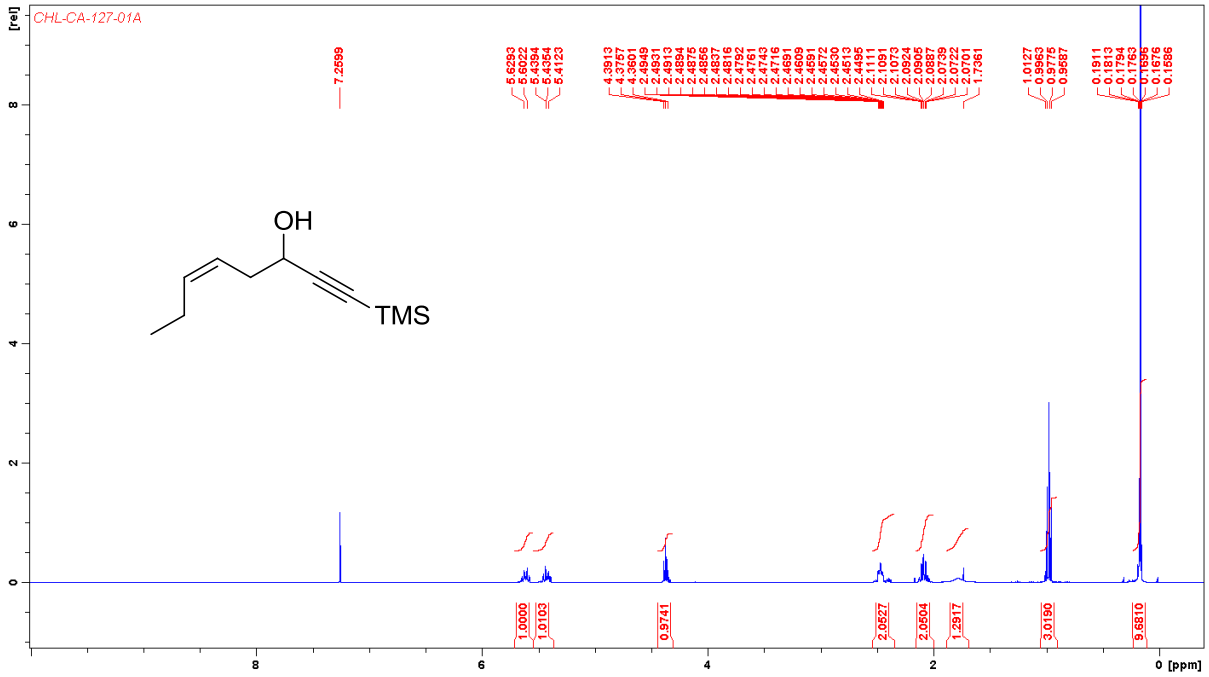

CHL-CA-026-01
[rel]
11.6832
7.3270
7.3234
7.2486
7.2066
7.1513
7.1477
7.1310
7.1276
6.9575
6.9375
6.9077
6.8627
6.1385
6.1339
6.0660
5.3017
5.2966
3.3343
3.1653
2.5094
2.5045
2.5000
2.4955
2.4915
OH
O
O
O
O
0.8836
1.0000
1.0265
1.0243
2.0117
0.8793
14
12
10
8
6
4
2
[ppm]

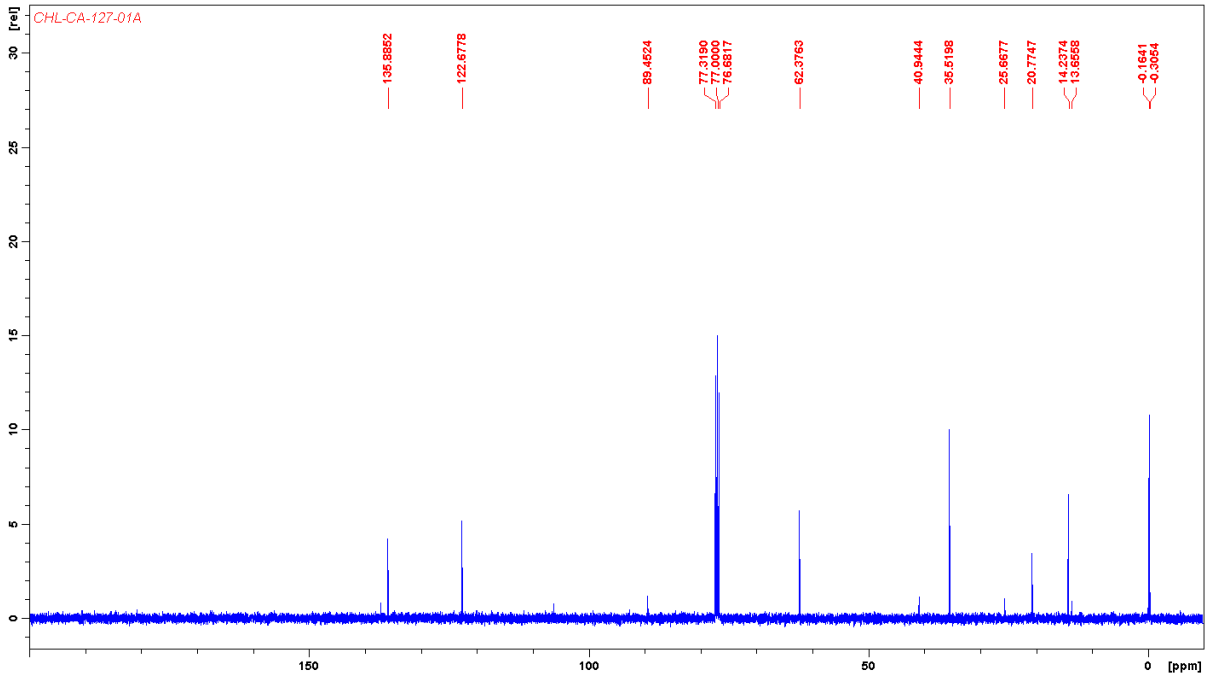

CHL-CA-026-01
[rel]
170.1320
162.9087
159.4050
148.4027
148.0154
133.8934
129.7144
123.5994
118.0473
108.5438
105.9742
101.4242
101.0923
89.6258
43.1014
40.1562
39.9413
39.7266
39.5201
39.3099
39.0977
38.8843
36.5311
32.1131
200
150
100
50
0
[ppm]


CHL-CA-101-01
[rel]
7.4140
7.4077
7.4048
7.3964
7.3892
7.3807
7.2600
5.9941
5.9913
5.9838
5.5394
5.5348
5.0874
2.5368
2.5345
2.5170
2.5156
2.4962
2.4957
2.4793
2.4783
1.2313
1.2125
1.1936
O
O
O
Ph
4.9511
1.0000
1.0162
2.0499
2.0961
3.3510
8
6
4
2
[ppm]

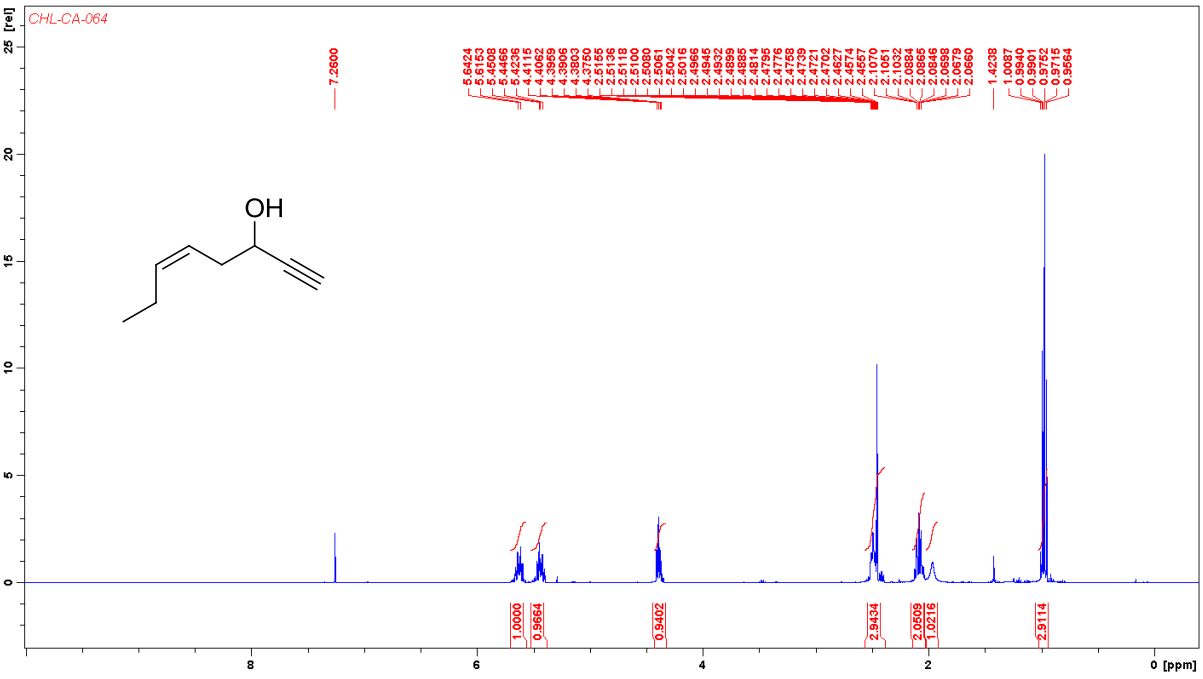

CHL-CA-101-01
[rel]
181.8715
167.0680
166.3547
133.7029
129.0372
128.8573
127.9384
111.1384
90.8668
77.3187
77.0000
76.6832
71.1791
26.1500
10.7011
200
150
100
50
0
[ppm]

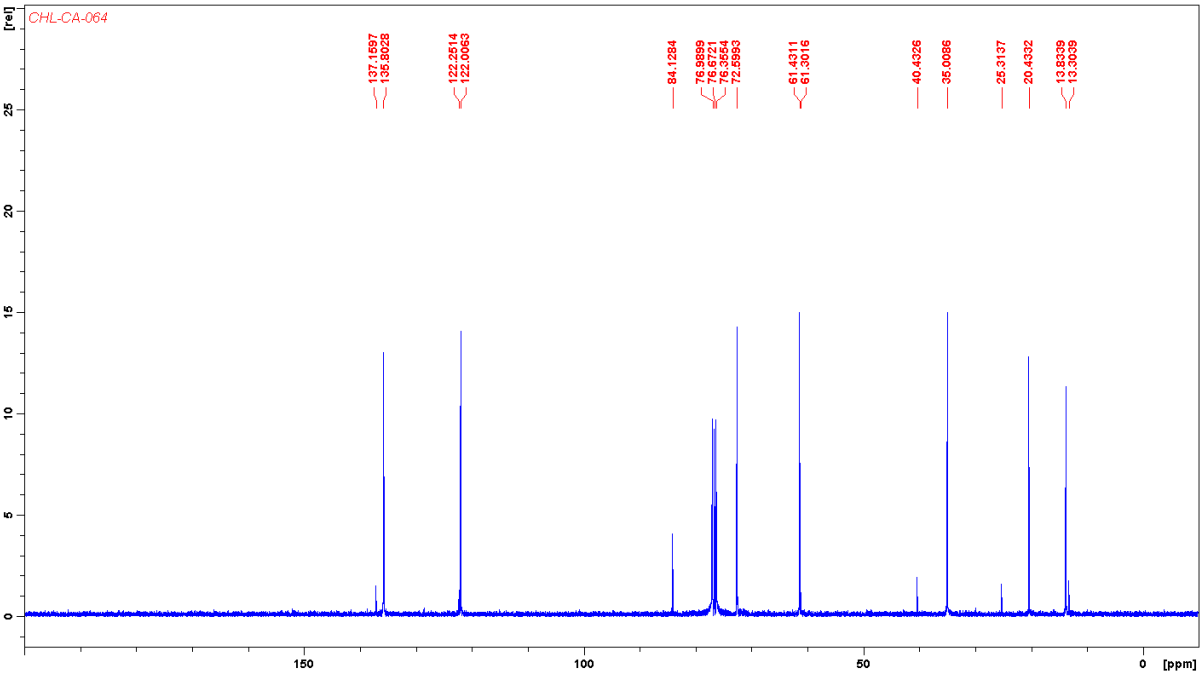
trace impurities derive from the E-isomer contained in the commercial sample of (Z)-3-hexenal



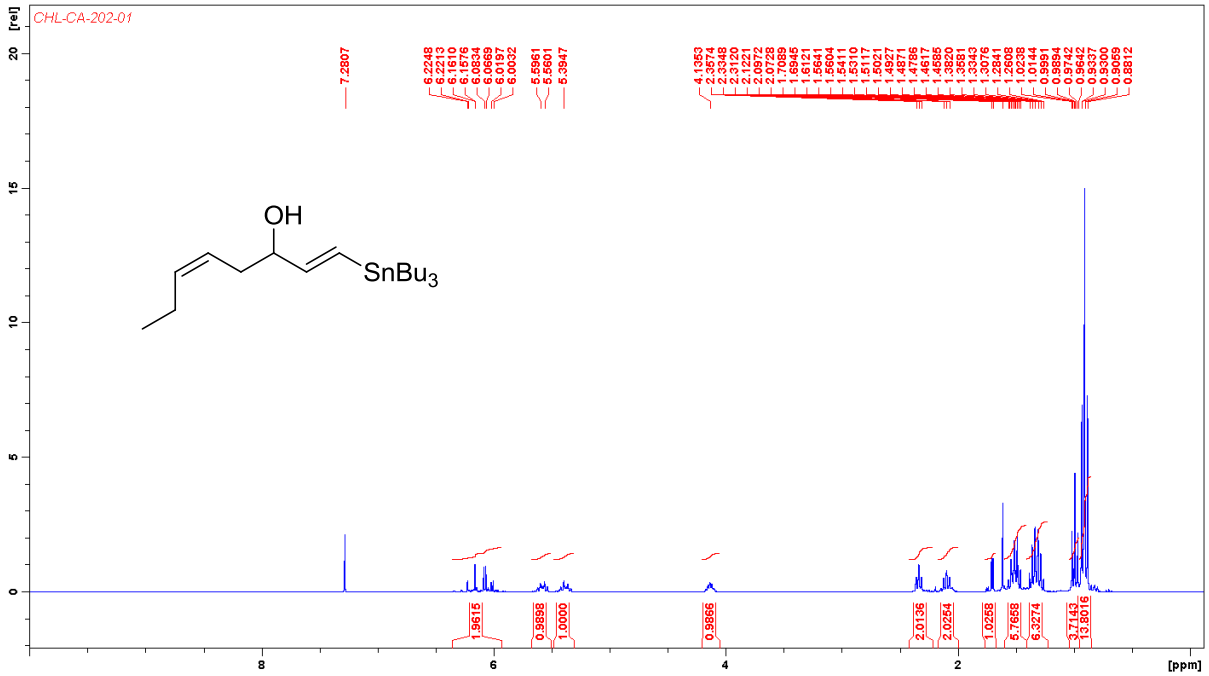


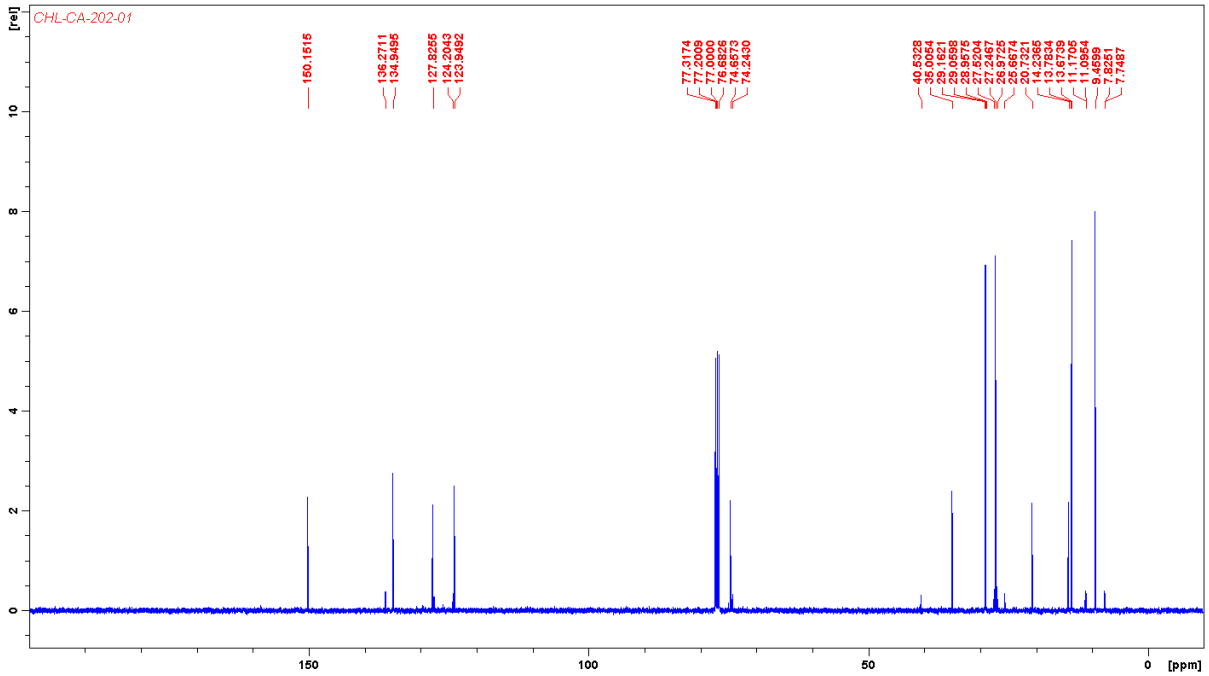
trace impurities derive from the E-isomer contained in the commercial sample of (Z)-3-hexenal

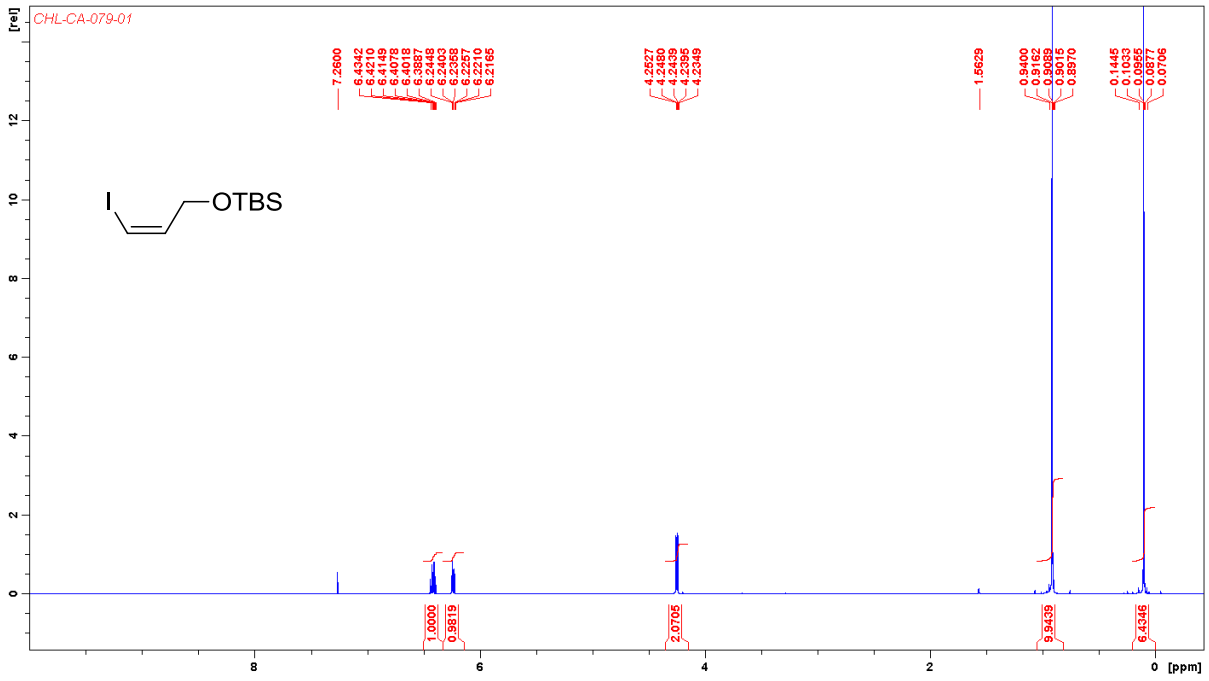


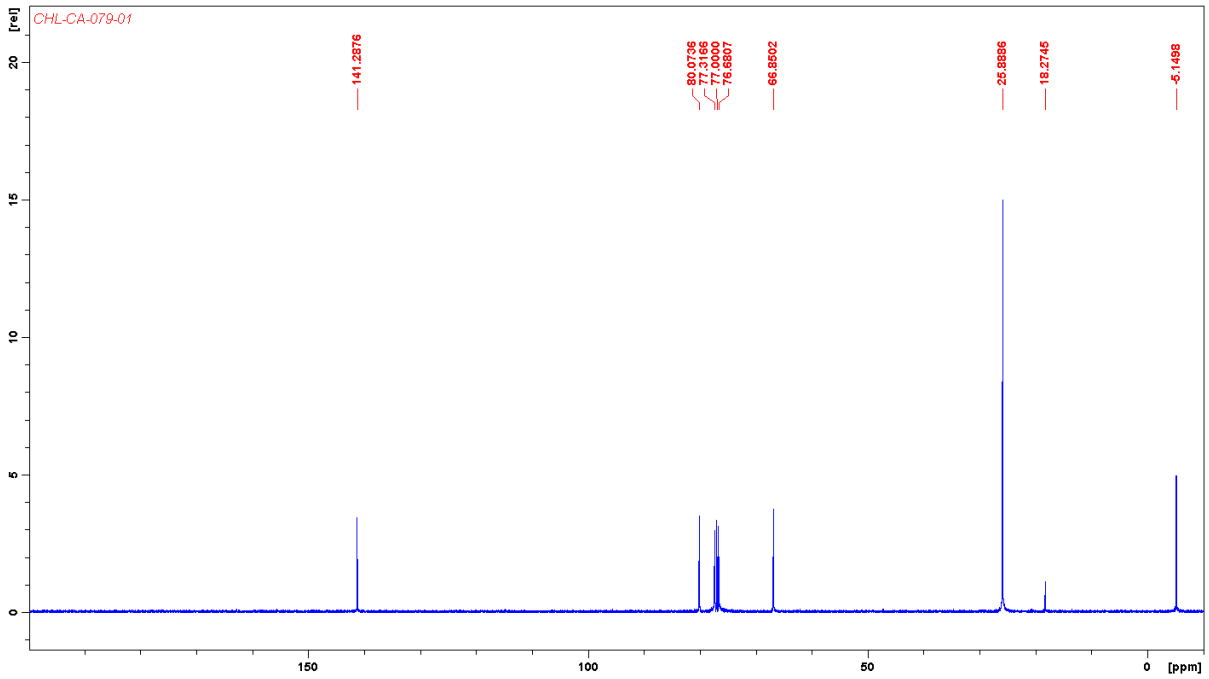


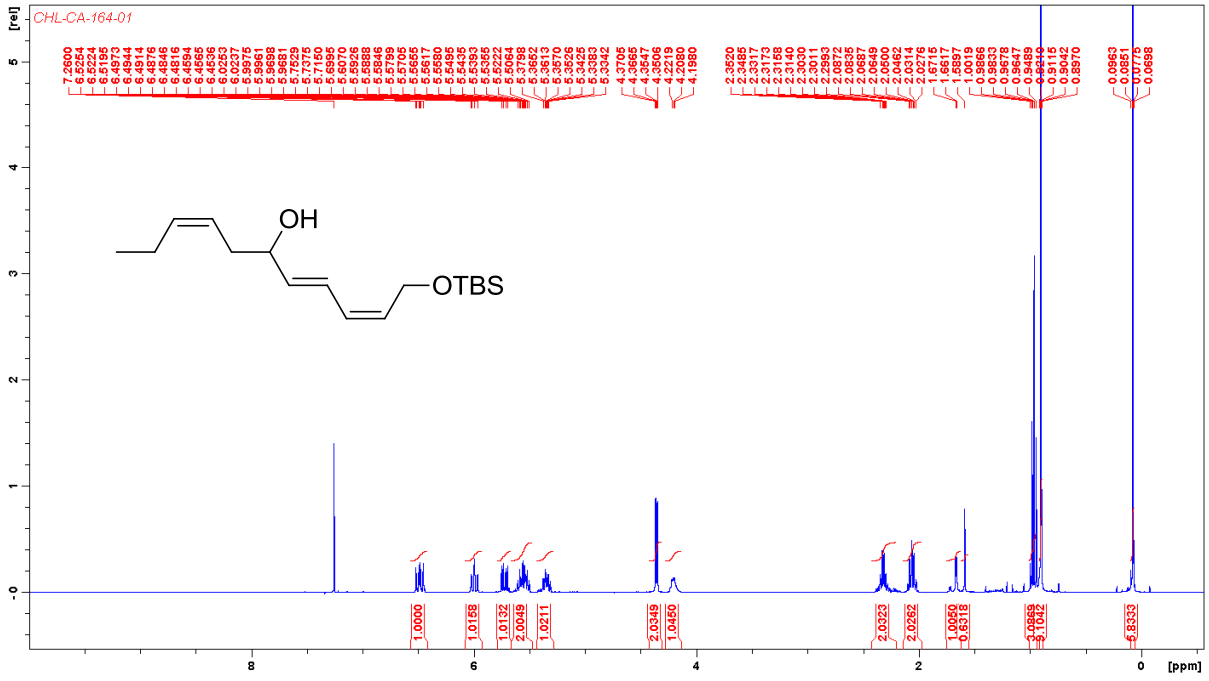
trace impurities derive from the E-isomer contained in the commercial sample of (Z)-3-hexenal

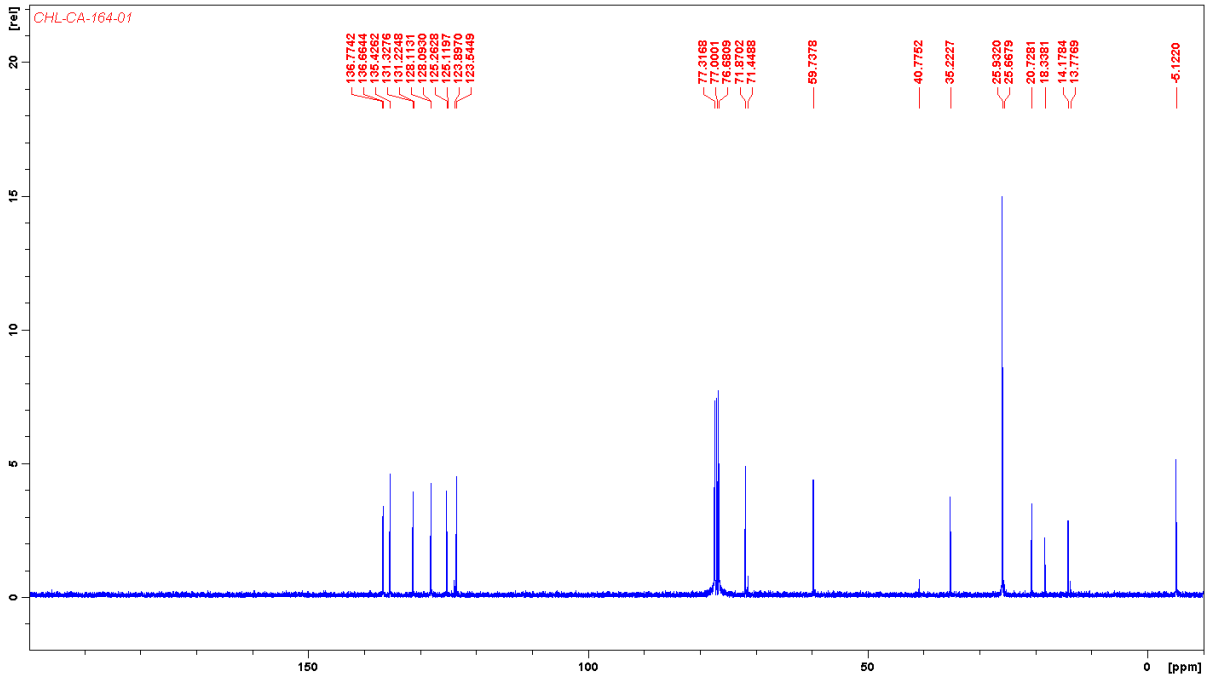


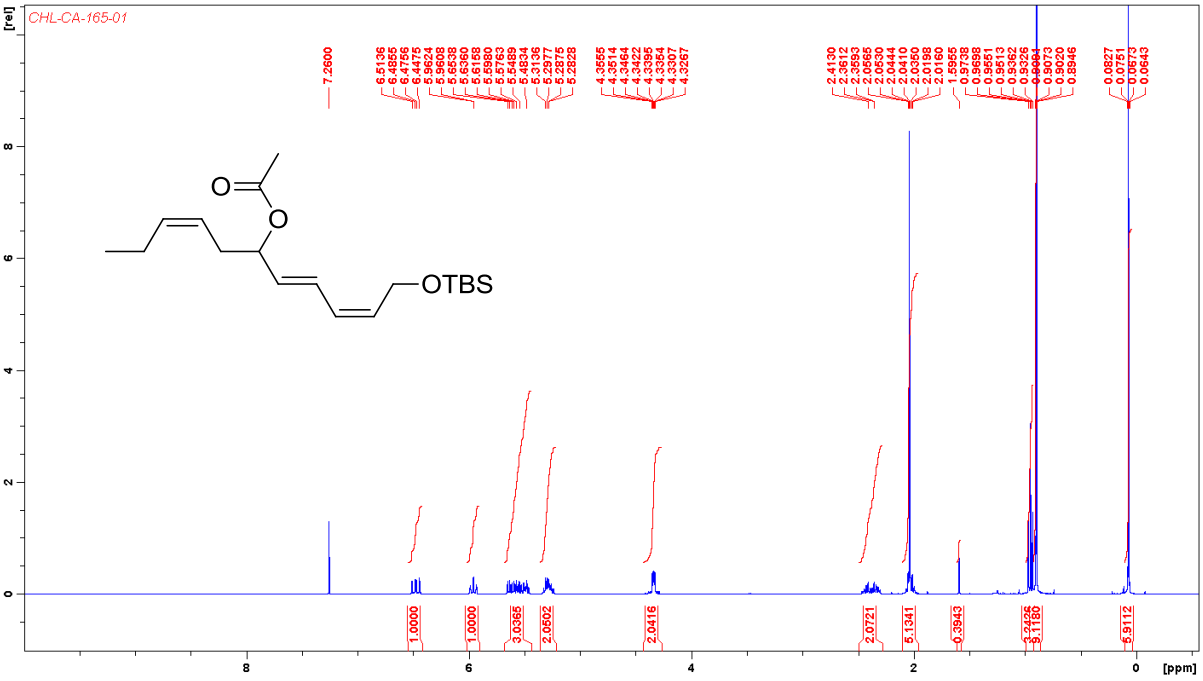


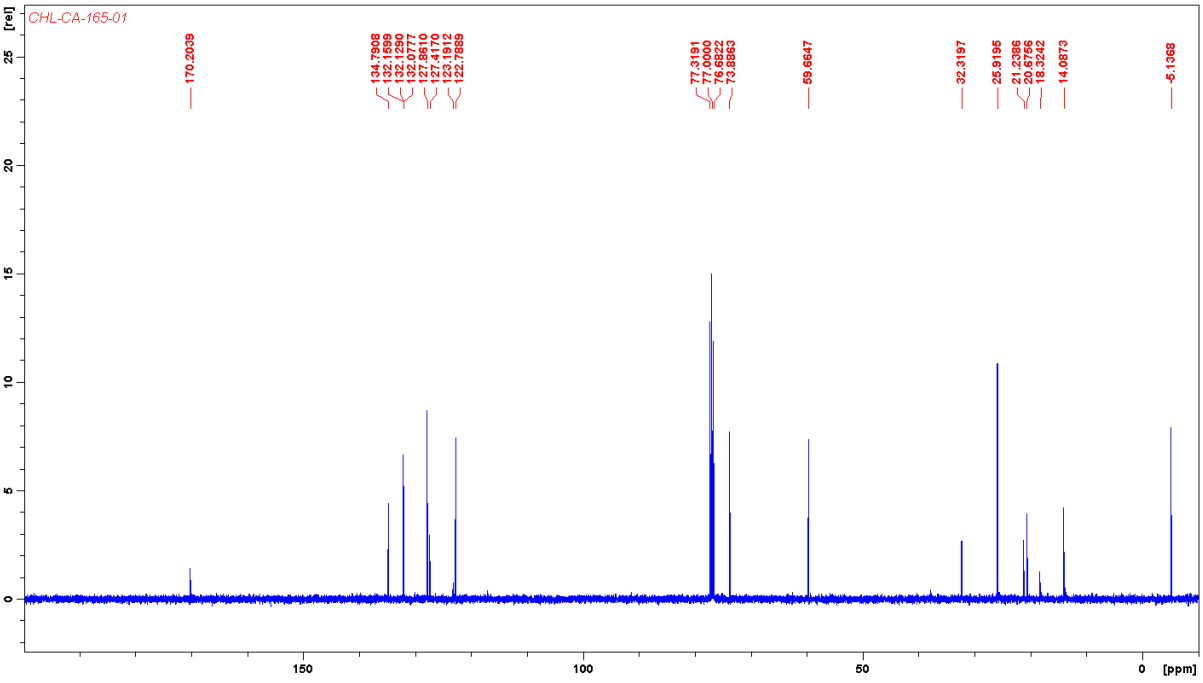

CHL-CA-079-01
[rel]
7.2600
6.4342
6.4210
6.4148
6.4078
6.4018
6.3887
6.2448
6.2403
6.2363
6.2257
6.2210
6.2165
4.2527
4.2480
4.2439
4.2395
4.2349
1.5629
0.9400
0.9162
0.9059
0.8915
0.8970
0.1445
0.1053
0.0956
0.0877
0.0706
OTBS
1.0000
0.9819
2.0705
9.9439
6.4346
[ppm]


CHL-CA-079-01
[rel]
141.2876
80.0736
77.3166
77.0000
76.6807
66.8502
25.8886
18.2745
-5.1498
[ppm]

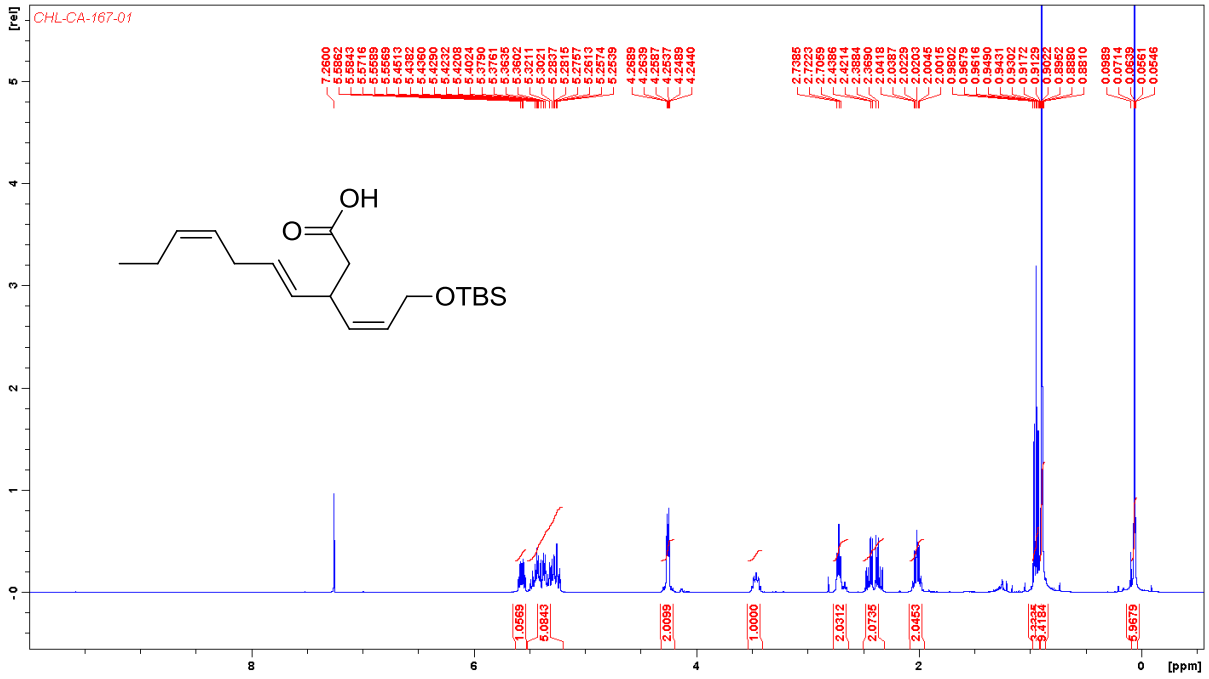

CHL-CA-164-01
[rel]
[ppm]
OH
OTBS

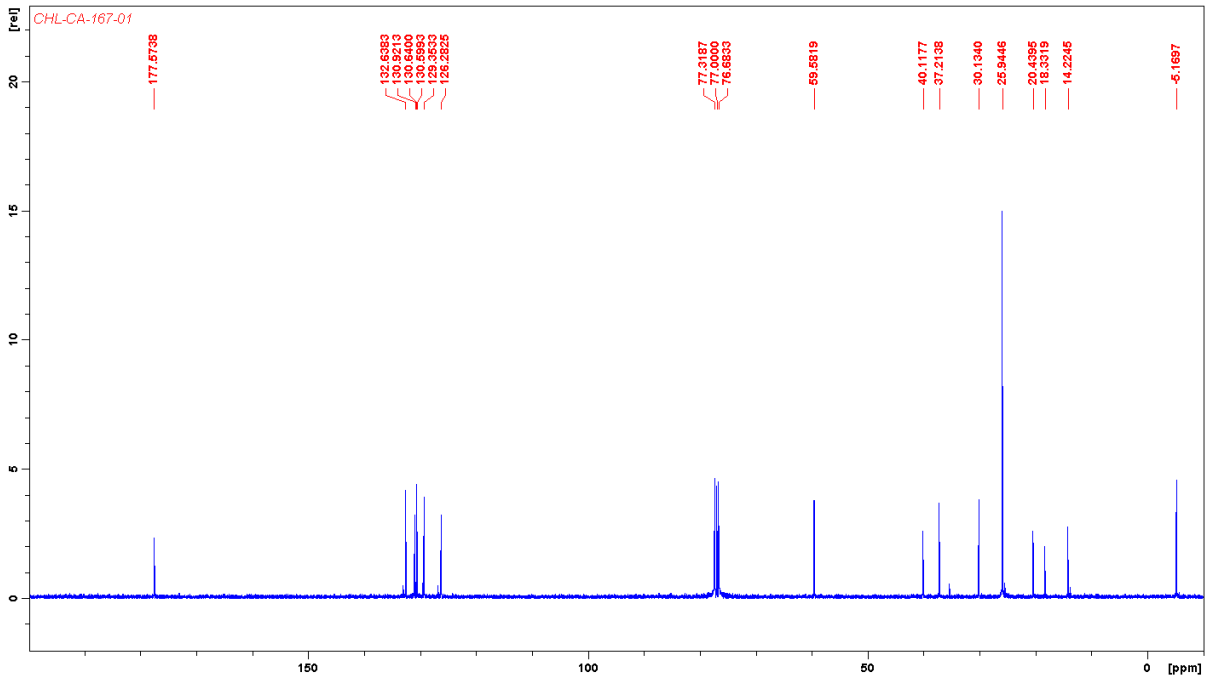

CHL-CA-164-01
[rel]
[ppm]


CHL-CA-165-01
[rel]
[ppm]
O
O
OTBS

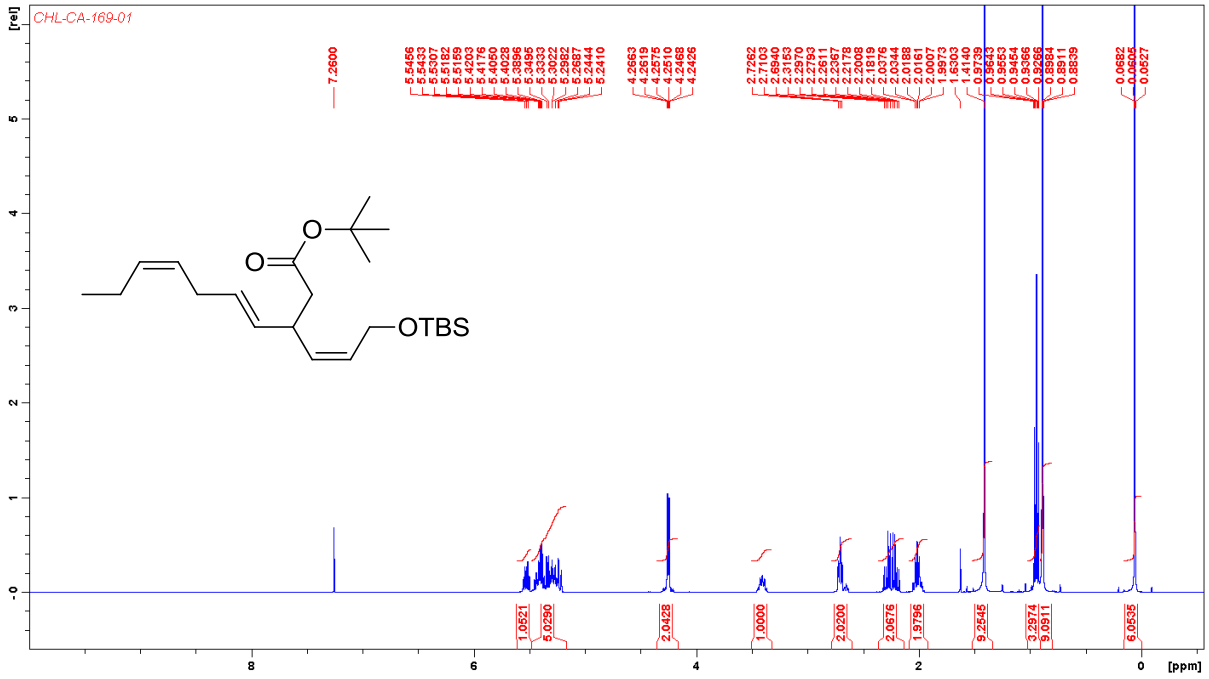

CHL-CA-165-01
[rel]
[ppm]

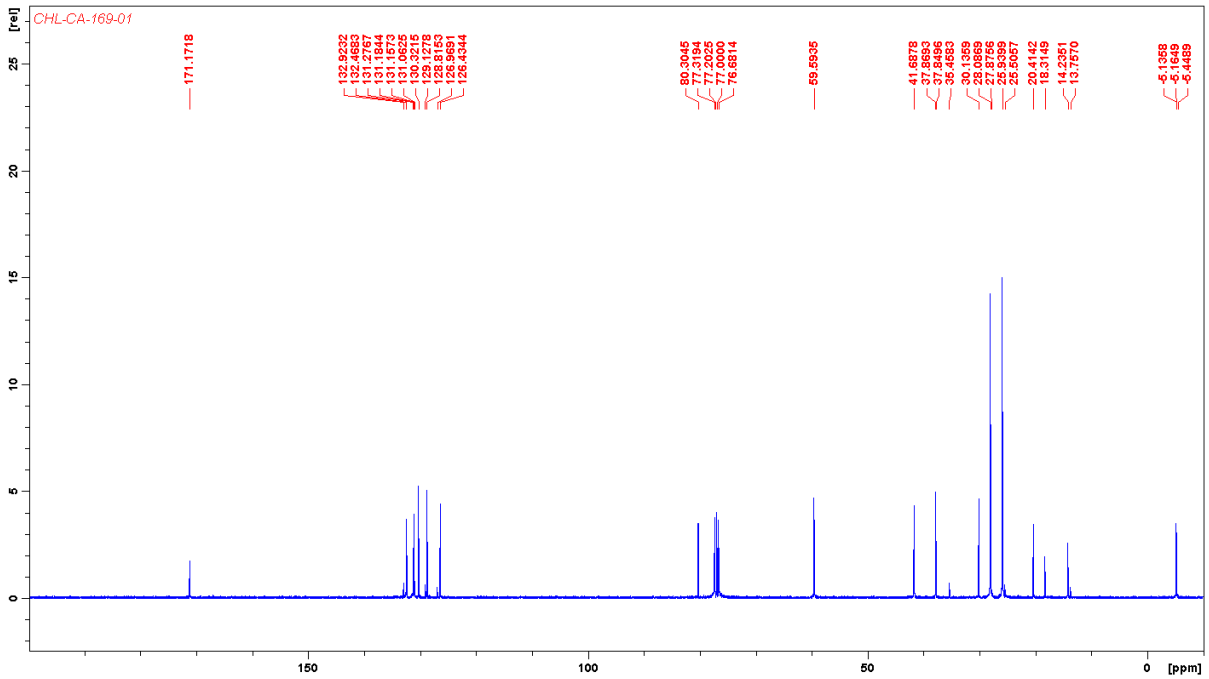
trace impurities derive from the E-isomer contained in the commercial sample of (Z)-3-hexenal

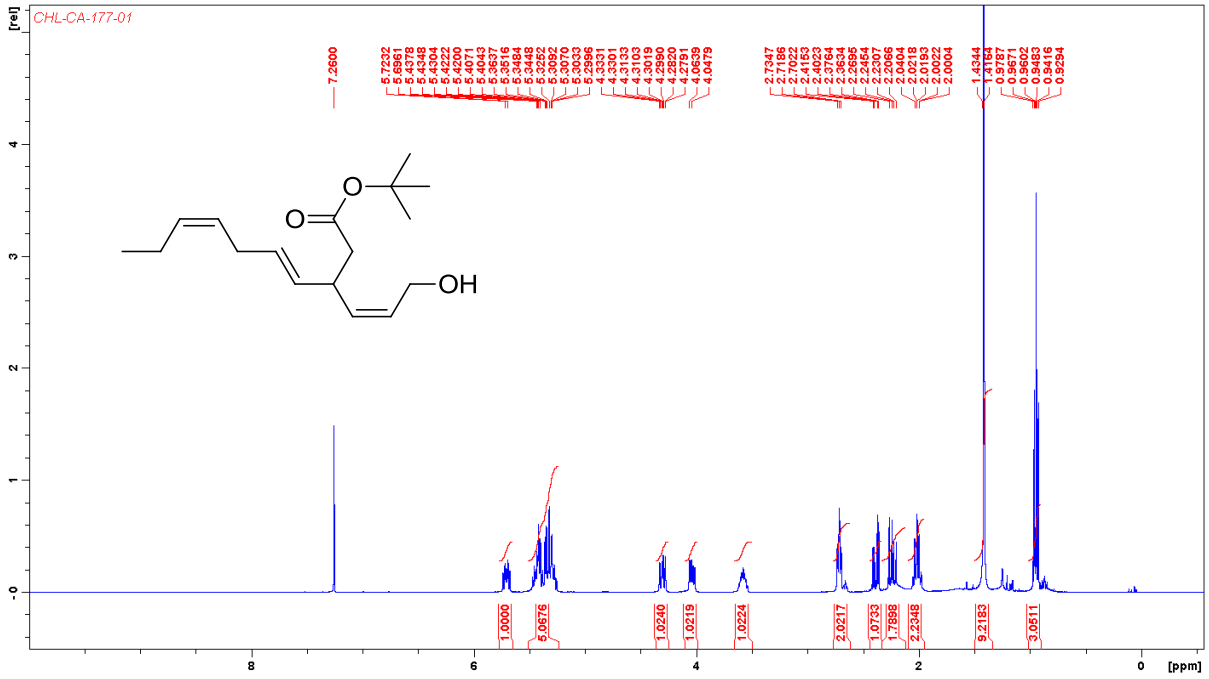


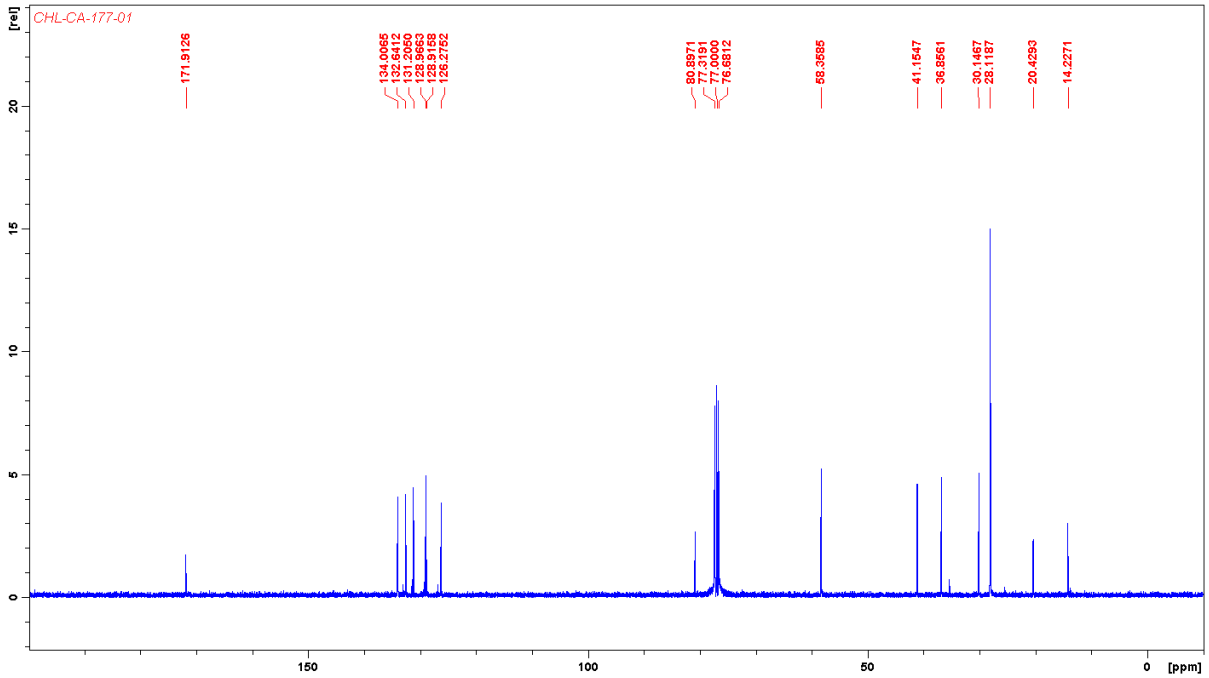


trace impurities derive from the E-isomer contained in the commercial sample of (Z)-3-hexenal

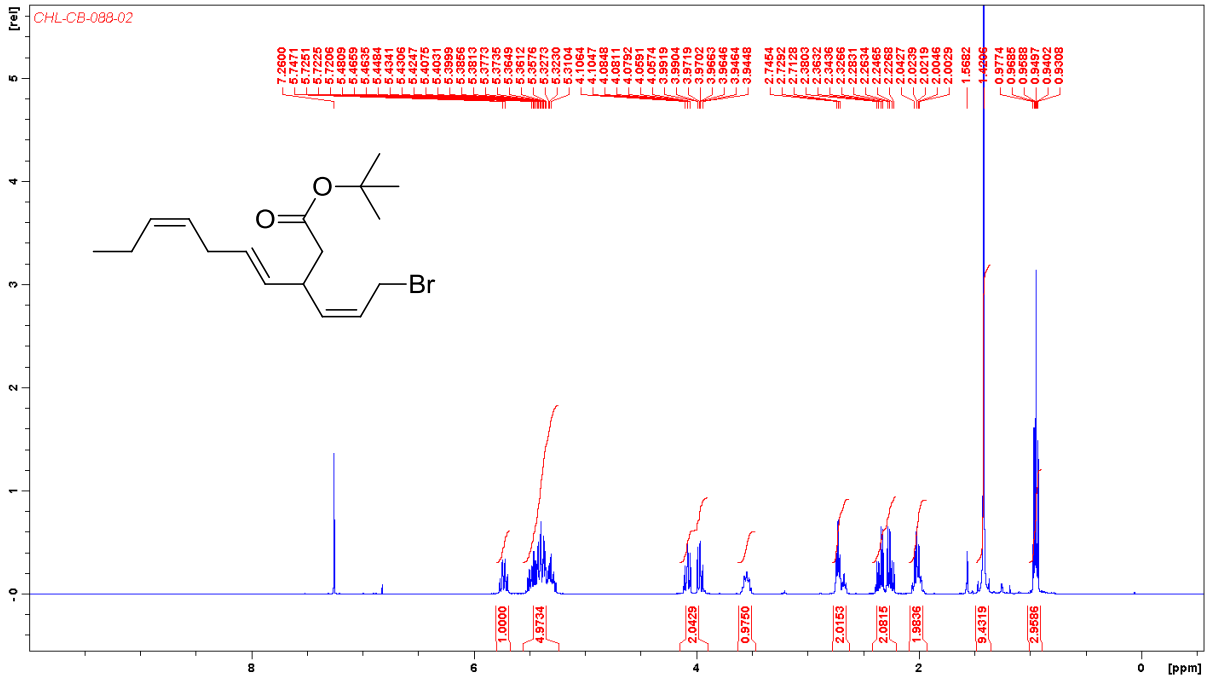


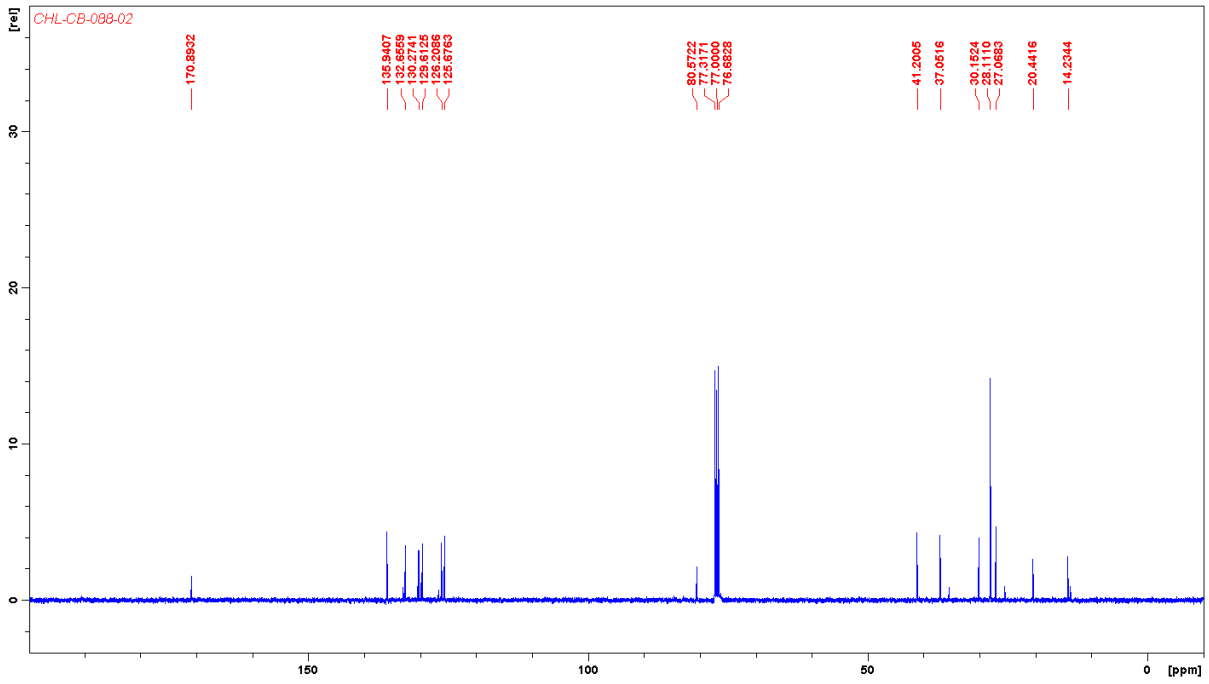



CHL-CA-177-01
[rel]
[ppm]
O
O
OH

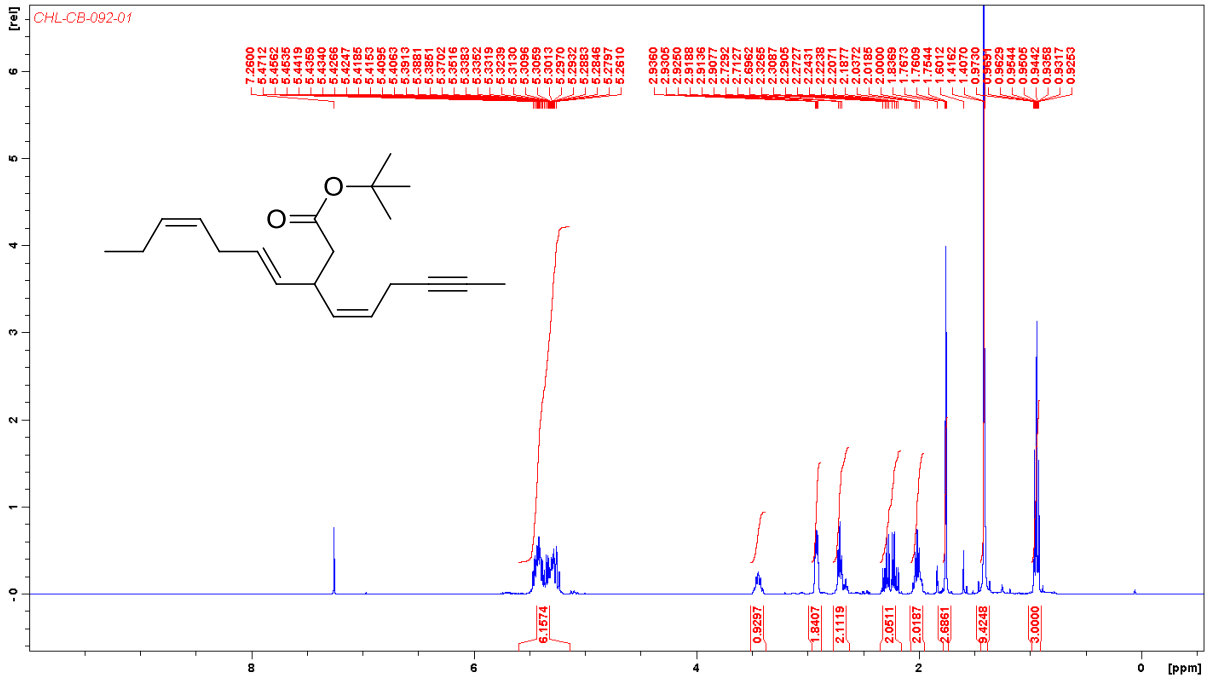

CHL-CA-177-01
[rel]
[ppm]

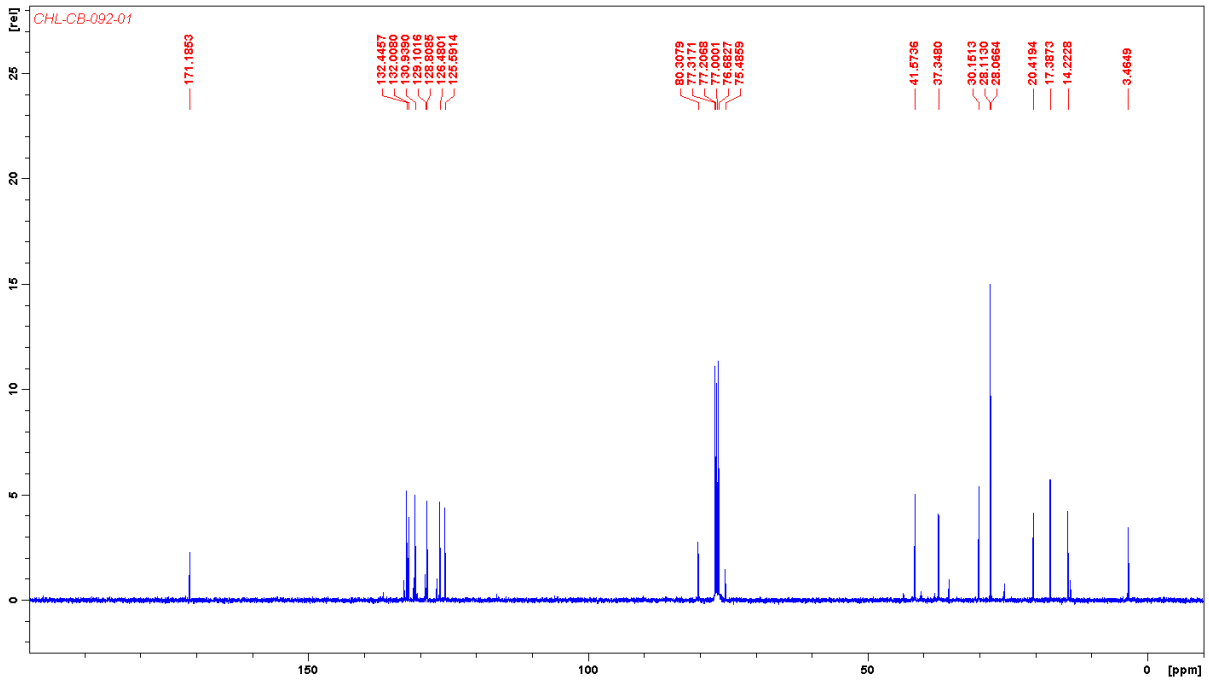
trace impurities derive from the E-isomer contained in the commercial sample of (Z)-3-hexenal

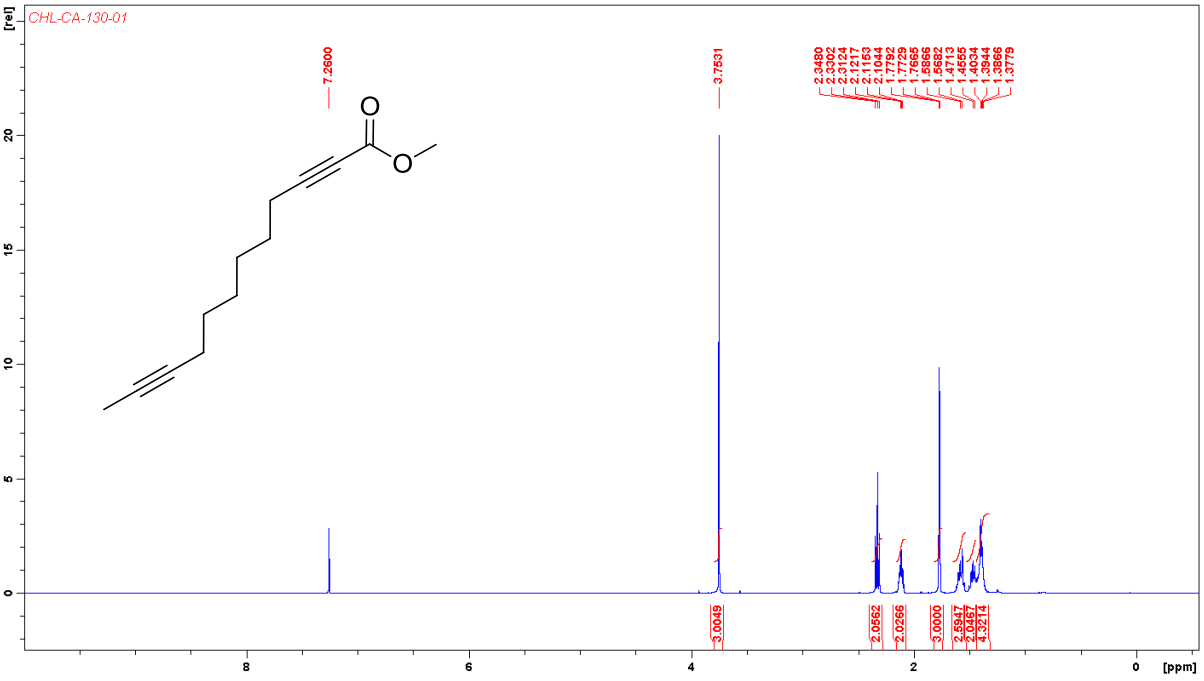


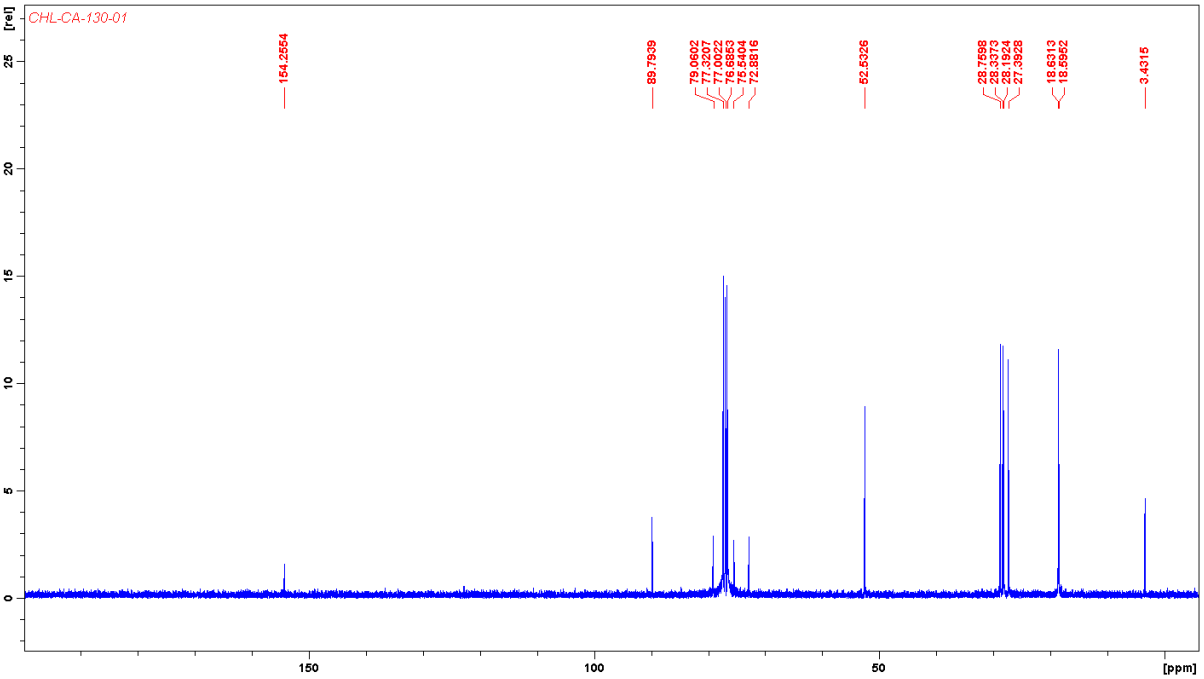


trace impurities derive from the E-isomer contained in the commercial sample of (Z)-3-hexenal

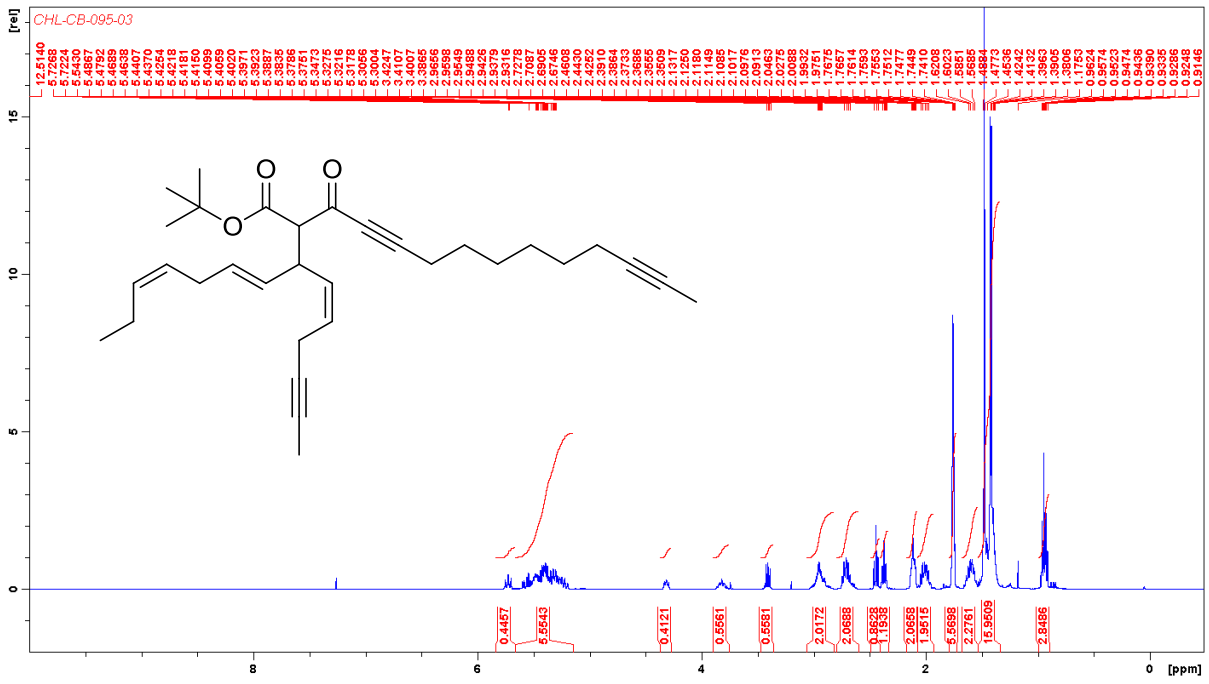


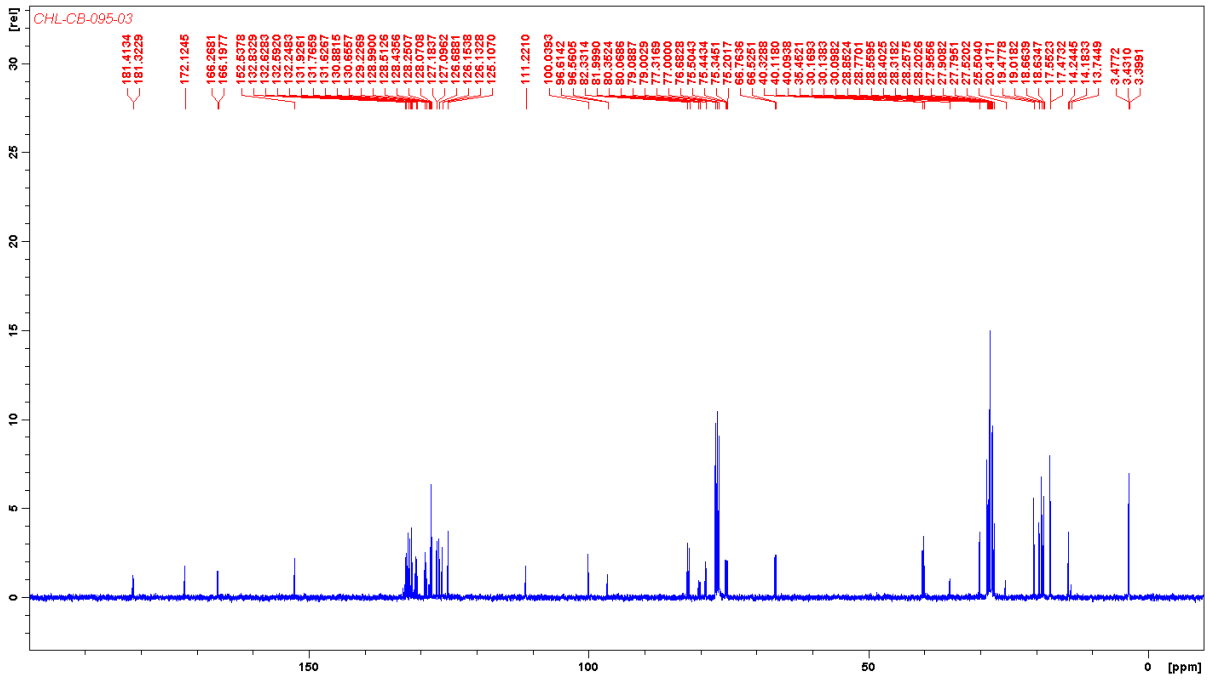


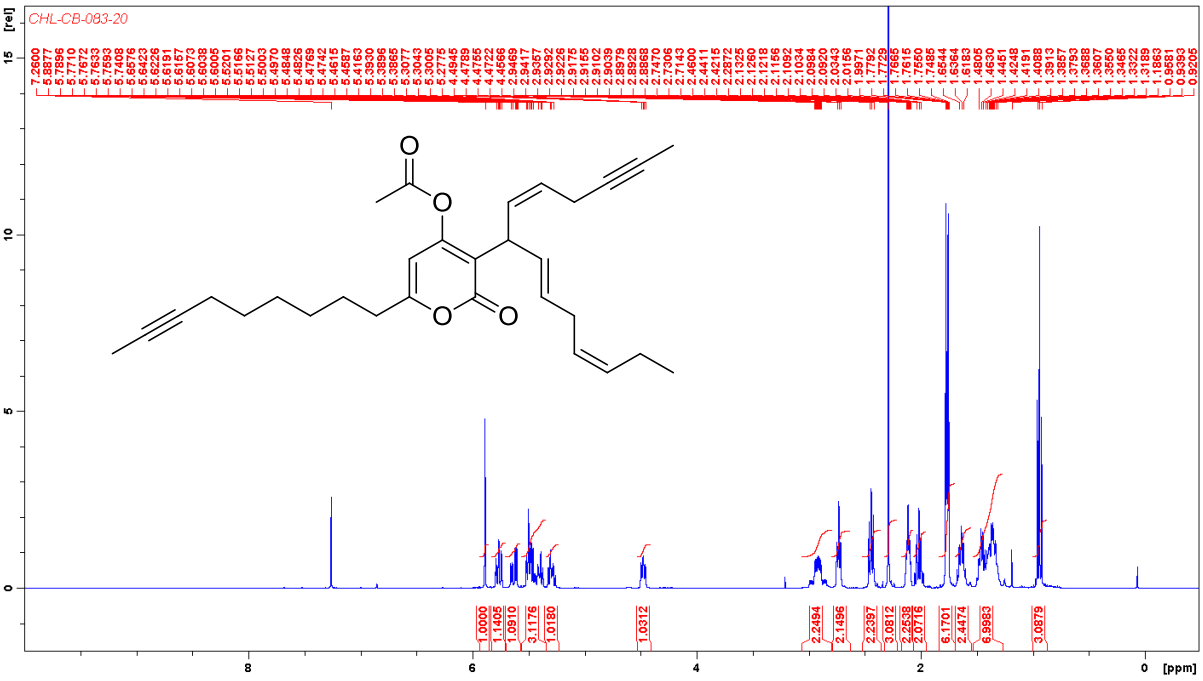

CHL-CA-130-01
[rel]
7.2600
3.7531
2.3480
2.3302
2.3124
2.2947
2.1153
2.1044
1.7792
1.7729
1.7685
1.5886
1.5692
1.4713
1.4555
1.4034
1.3944
1.3866
1.3779
3.0049
2.0562
2.0266
3.0000
2.5947
2.0467
4.3214
[ppm]


CHL-CA-130-01
[rel]
154.2554
89.7939
79.0602
77.3207
77.0022
76.6853
75.6404
72.8816
62.5326
28.7598
28.3773
28.1924
27.3928
18.6313
18.5962
3.4315
[ppm]

mixture of keto/enol tautomers



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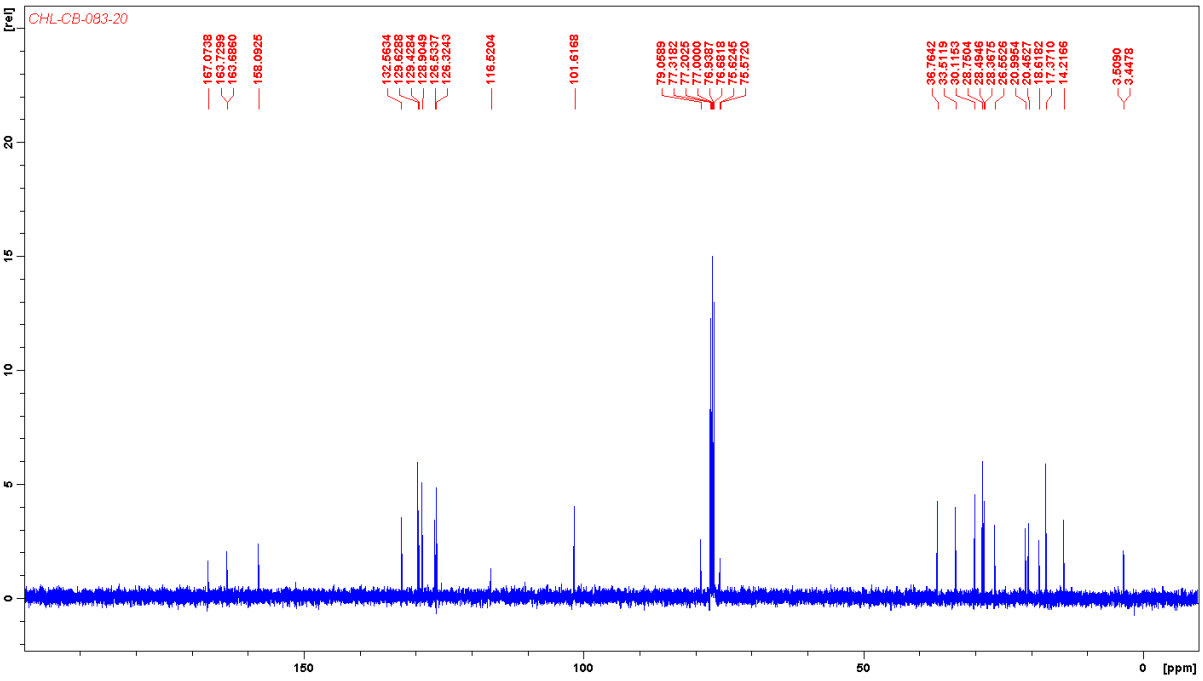
[ppm]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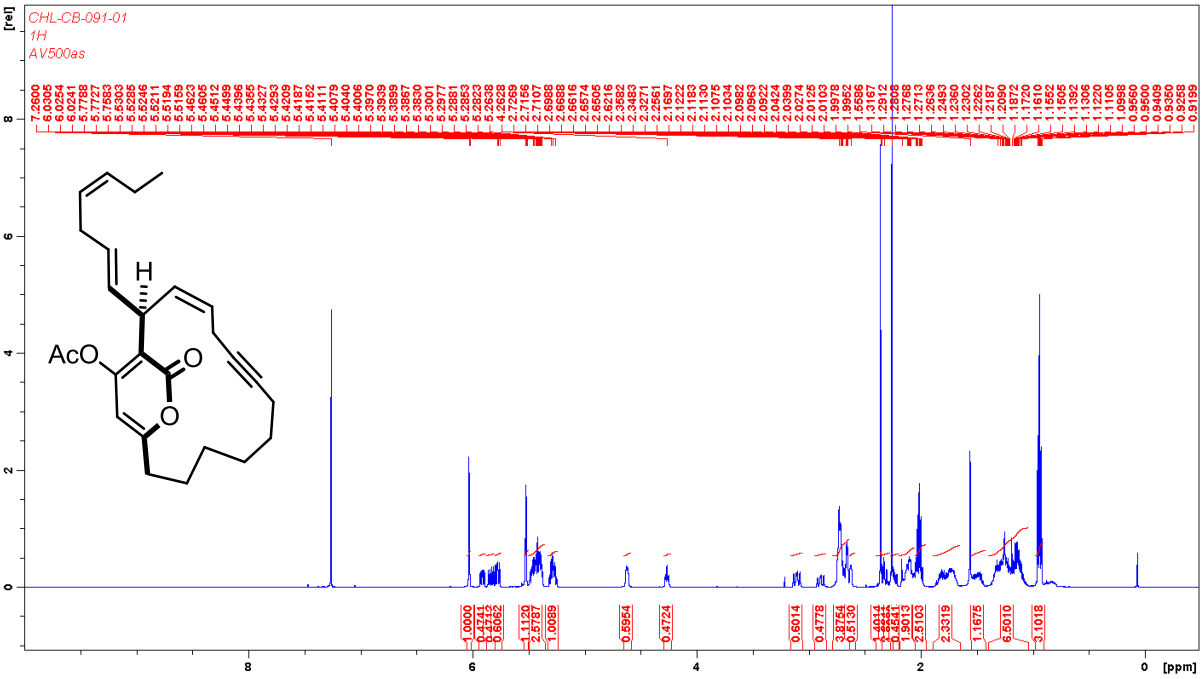
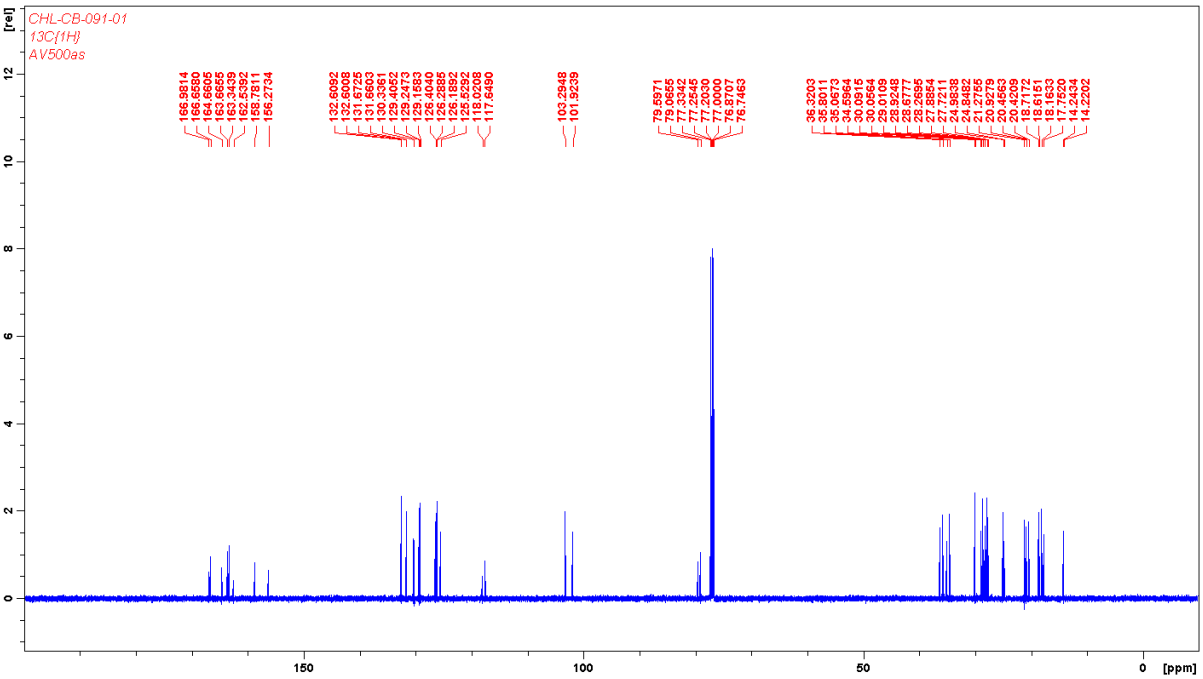
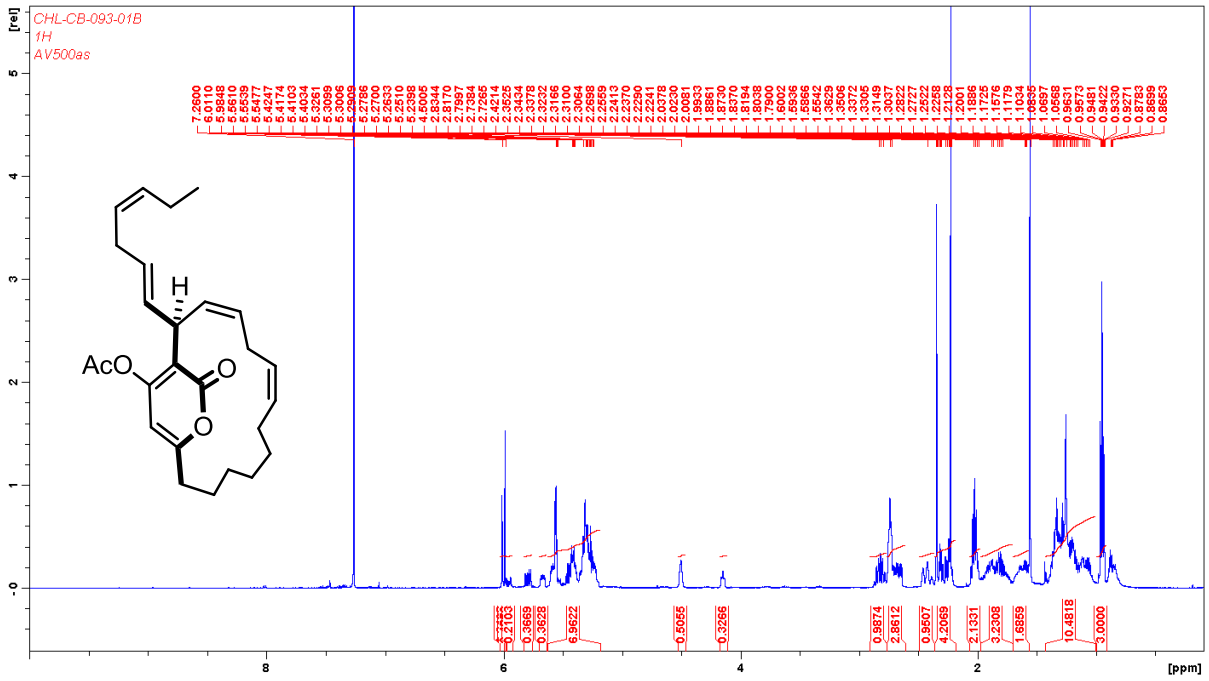
mixture of atropisomers

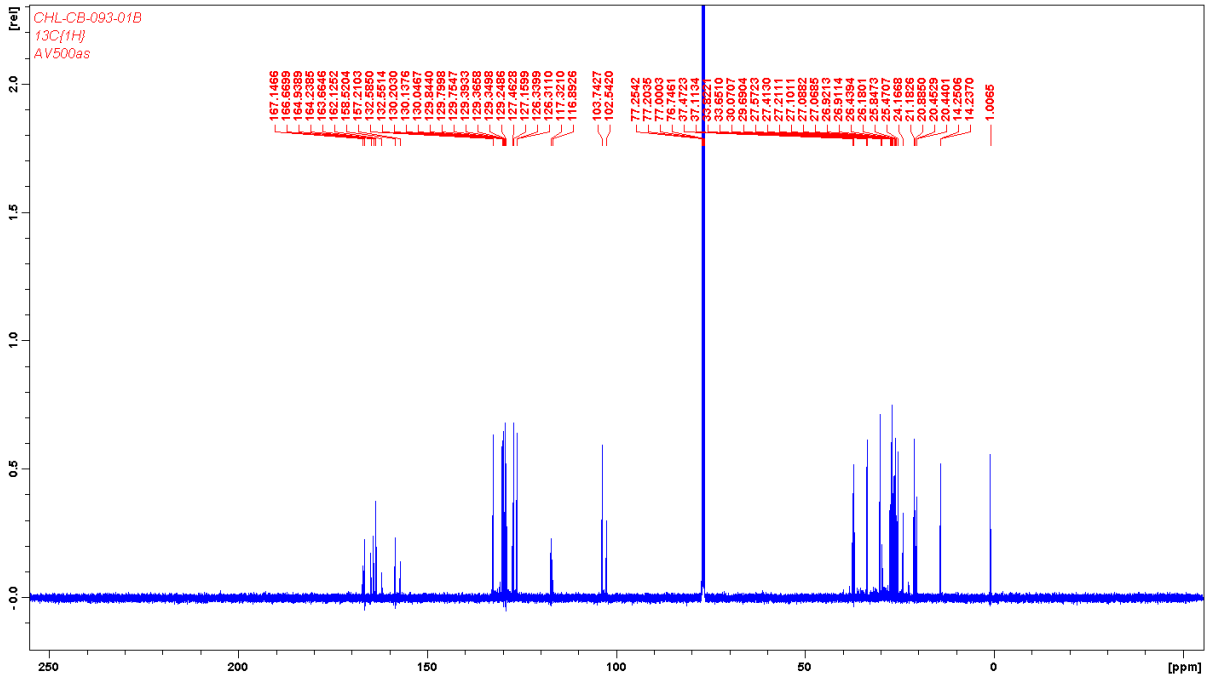




Neurymenolide A Acetate

mixture of atropisomers





Neurymenolide A

mixture of atropisomers