SUPPLEMENTARY MATERIAL

for

Novel (−)-goniofufurone mimics: synthesis, antiproliferative activity and SAR analysis

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3,6-Anhydro-5-*O*-benzyl-7-*O*-hexyl-2-deoxy-L-*ido*-heptono-1,4-lactone (12). Colourless oil, $[\alpha]_D$ = –17.4 (*c* 0.5, $CHCl_3$); R_f = 0.14 (3:2 light petroleum/Et_2O). IR ($CHCl_3$): ν_{max} 1790 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (t, 3H, *J*=6.8 Hz, CH_3), 1.20–1.39 (m, 6H, 3×CH_2 from side chain), 1.51–1.65 (m, 2H, $OCH_2CH_2(CH_2)_3CH_3$), 2.69 (dd, 1H, $J_{2a,3}$=2.7, $J_{2a,2b}$=18.8 Hz, H-2a), 2.75 (dd, 1H, $J_{2b,3}$=4.7, $J_{2a,2b}$=18.8 Hz, H-2b), 3.46 (m, 2H, $OCH_2(CH_2)_4CH_3$), 3.75 (d, 2H, $J_{6,7}$=5.5 Hz, H-7), 4.21 (d, 1H, $J_{5,6}$=4.1 Hz, H-5), 4.26 (td, 1H, $J_{5,6}$=4.1, $J_{6,7}$=5.5 Hz H-6), 4.60 and 4.70 (2×d, 2H, J_{gem}=11.9 Hz, CH_2Ph), 4.92 (d, 1H, $J_{3,4}$=4.7 Hz, H-4), 4.98 (td, 1H, $J_{3,4}$=4.7, $J_{2a,3}$=2.9, $J_{2b,3}$=4.6 Hz, H-3), 7.30–7.45 (m, 5H, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.06 (CH_3), 22.61, 25.80, 29.62, 31.67 (4×CH_2 from side chain), 36.03 (C-2), 68.57 (C-7), 71.86 ($OCH_2(CH_2)_4CH_3$), 72.76 (CH_2Ph), 76.83 (C-3), 79.65 (C-6), 81.51 (C-5), 85.52 (C-4), 127.75, 128.17, 128.60, 137.17 (Ph), 175.35 (C=O). HRMS-Heated ESI-Orbitrap: *m/z* 371.18272 (M^++Na), calcd. for $C_{20}H_{28}NaO_5$: 371.18344.

3,6-Anhydro-5-*O*-benzyl-7-*O*-heptyl-2-deoxy-L-*ido*-heptono-1,4-lactone (13). Colourless oil; $[\alpha]_D$ = – 16.0 (*c* 0.5, $CHCl_3$); R_f = 0.28 (1:1 light petroleum/Et_2O). IR ($CHCl_3$): ν_{max} 1789 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (t, 3H, *J*=6.8 Hz, CH_3), 1.19–1.41 (m, 8H, 4×CH_2 from side chain), 1.58 (m, 2H, $OCH_2CH_2(CH_2)_4CH_3$), 2.69 (dd, 1H, $J_{2a,2b}$=18.9, $J_{2a,3}$=2.6 Hz, H-2a), 2.74 (dd, 1H, $J_{2a,2b}$=18.9, $J_{2b,3}$=4.7 Hz, H-2b), 3.38–3.54 (m, 2H, $OCH_2(CH_2)_5CH_3$), 3.65 (d, 2H, $J_{6,7}$=5.5 Hz, H-7), 4.21 (d, 1H, $J_{5,6}$=4.0 Hz, H-5), 4.27 (dd, 1H, $J_{5,6}$=4.1, $J_{6,7}$=5.5 Hz, H-6), 4.60 and 4.70 (2×d, 2H, J_{gem}=11.9 Hz, CH_2Ph), 4.92 (d, 1H, $J_{3,4}$=4.7 Hz, H-4), 4.98 (td, 1H, $J_{3,4}$=4.6, $J_{2a,3}$=2.9, $J_{2b,3}$=4.6 Hz, H-3), 7.29–7.40 (m, 5H, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.10 (CH_3), 22.62, 26.08, 29.14, 29.66, 31.81 (5×CH_2 from side chain), 36.03 (C-2), 68.57 (C-7), 71.86 ($OCH_2(CH_2)_5CH_3$), 72.76 (CH_2Ph), 76.83 (C-3), 79.65 (C-6), 81.51 (C-5), 85.53 (C-4), 127.75, 128.17, 128.60, 137.17 (Ph), 175.35 (C=O). HRMS-Heated ESI-Orbitrap: *m/z* 385.19874 (M^++Na), calcd. for $C_{21}H_{30}NaO_5$: 385.19909.

3,6-Anhydro-5-*O*-benzyl-7-*O*-octyl-2-deoxy-L-*ido*-heptono-1,4-lactone (14). Colourless oil, $[\alpha]_D$ = –14,8 (*c* 0.5, $CHCl_3$); R_f = 0.25 (1:1 light petroleum/Et_2O). IR ($CHCl_3$): ν_{max} 1790 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (t, 3H, *J*=6.9 Hz, CH_3), 1.22–1.38 (m, 10H, 5×CH_2 from side chain), 1.58 (m, 2H, $OCH_2CH_2(CH_2)_5CH_3$), 2.68 (dd, 1H, $J_{2a,2b}$=18.7, $J_{2a,3}$=2.5 Hz, H-2a), 2.71 (dd, 1H, $J_{2a,2b}$=18.7, $J_{2b,3}$=4.8 Hz, H-2b), 3.37–3.54 (m, 2H, $OCH_2(CH_2)_6CH_3$), 3.65 (d, 2H, $J_{6,7}$=5.5 Hz, H-7), 4.20 (d, 1H, $J_{5,6}$=4.0 Hz, H-5), 4.25 (td, 1H, $J_{5,6}$=4.1, $J_{6,7}$=5.5 Hz, H-6), 4.60 and 4.69 (2×d, 2H, J_{gem}=11.9 Hz, CH_2Ph), 4.92 (d, 1H, $J_{3,4}$=4.7 Hz, H-4), 4.97 (td, 1H, $J_{3,4}$=4.8, $J_{2a,3}$=2.5, $J_{2b,3}$=4.8 Hz, H-3), 7.29–7.43 (m, 5H, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.01 (CH_3), 22.56, 26.02, 29.16, 29.33, 29.56, 31.73 (6×CH_2 from side chain), 35.92 (C-2), 68.47 (C-7), 71.75 ($OCH_2(CH_2)_6CH_3$), 72.63 (CH_2Ph), 76.73 (C-3), 79.54 (C-6), 81.40 (C-5), 85.40 (C-4), 127.64, 128.05, 128.49. 137.10 (Ph), 175.26 (C=O). HRMS-Heated ESI-Orbitrap: *m/z* 399.21400 (M^++Na), calcd. for $C_{22}H_{32}NaO_5$: 399.21474; *m/z* 415.18765 (M^++K), calcd. for $C_{22}H_{32}KO_5$: 415.18868.

3,6-Anhydro-5-*O*-benzyl-7-*O*-nonyl-2-deoxy-L-*ido*-heptono-1,4-lactone (15). Colourless crystals, mp 34 °C (CH_2Cl_2/hexane), $[\alpha]_D$ = –10.8 (*c* 0.75, $CHCl_3$), R_f=0.33 (1:1 Et_2O/light petroleum). IR (film): ν_{max} 1773 (C=O). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.89 (t, 3H, *J*=6.9 Hz, CH_3), 1.18–1.39 (m, 12H, 6×CH_2 from side chain), 1.57 (m, 2H, $OCH_2CH_2(CH_2)_6CH_3$), 2.66–2.76 (*pseudo* d, 2H, 2×H-2), 3.45 (m, 2H, $OCH_2(CH_2)_7CH_3$), 3.65 (d, 2H, $J_{6,7}$=5.4 Hz,

H-7), 4.20 (d, 1H, $J_{5,6}$=4.3 Hz, H-5), 4.26 (m, 1H, $J_{5,6}$=4.3, $J_{6,7}$=5.4 Hz, H-6), 4.59 and 4.69 (2×d, 2H, J_{gem}=11.9 Hz, C*H*$_2$Ph), 4.92 (d, 1H, $J_{3,4}$=4.1 Hz, H-4), 4.98 (m, 1H, $J_{3,2a}$=2.8, $J_{3,2b}$=3.1, $J_{3,4}$=4.1 Hz, H-3), 7.29–7.43 (m, 5H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 14.05 (Me), 22.60, 26.04, 29.20, 29.40, 29.48, 29.58 and 31.81 (7×CH_2) 35.94 (C-2), 68.49 (C-7), 71.78 (O*C*H$_2$(CH$_2$)$_7$CH$_3$), 72.66 (*C*H$_2$Ph), 76.75 (C-3), 79.57 (C-6), 81.42 (C-5), 85.44 (C-4), 127.67, 128.08, 128.51 and 137.10 (Ph), 175.29 (C-1). LRMS (ESI$^+$): *m/z* 429 (M^++K), 413 (M^++Na), 391 (M^++H). HRMS (ESI$^+$): *m/z* 391.2482 (M^++H), calcd. for $C_{23}H_{35}O_5$: 391.2479; *m/z* 408.2745 (M^++NH_4), calcd. for $C_{23}H_{38}NO_5$: 408.2744; *m/z* 413.2290 (M^++Na), calcd. for $C_{23}H_{34}NaO_5$: 413.2298; *m/z* 429.2034 (M^++K), calcd. for $C_{23}H_{34}KO_5$ 429.2038.

3,6-Anhydro-5-*O*-benzyl-7-*O*-decyl-2-deoxy-L-*ido*-heptono-1,4-lactone (16). Colourless oil, [α]$_D$ = −11.1 (*c* 0.63, $CHCl_3$); R_f=0.44 (1:1 light petroleum/Et$_2$O). IR (film): ν_{max} 1788 (C=O). ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.89 (t, 3H, *J*=7.0 Hz, CH_3), 1.21–1.41 (m, 14H, 7×CH_2 from side chain), 1.49–1.64 (m, 2H, OCH$_2$C*H*$_2$(CH$_2$)$_7$CH$_3$), 2.72 (*pseudo* d, 2H, 2×H-2), 3.46 (m, 2H, OCH_2 from side chain), 3.65 (d, 2H, $J_{6,7}$=5.3 Hz, 2×H-7), 4.21 (d, 1H, $J_{5,6}$=4.1 Hz, H-5), 4.26 (m, 1H, $J_{5,6}$=4.1, $J_{6,7}$=5.3 Hz, H-6), 4.60 and 4.70 (2×d, 2H, J_{gem}=11.9 Hz, C*H*$_2$Ph), 4.92 (d, 1H, $J_{3,4}$=4.7 Hz, H-4), 4.99 (m, 1H, $J_{3,4}$=4.7 Hz, H-3), 7.30–7.42 (m, 5H, Ph). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 14.08 (Me), 22.66, 26.10, 29.30, 29.45, 29.55, 29.57, 29.63 and 31.87 (8×CH_2 from side chain), 36.00 (C-2), 68.53 (C-7), 71.84 (C-9), 72.74 (**C**H$_2$Ph), 76.79 (C-3), 79.62 (C-6), 81.50 (C-5), 85.51 (C-4), 127.71, 128.14, 128.56 and 137.15 (Ph), 175.29 (C-1). LRMS (CI): *m/z* 405 (M^++H). Anal. Found: C, 71.60; H, 9.29. Calculated for $C_{24}H_{36}O_5$: C, 71.26; H, 8.97.

3,6-Anhydro-5-*O*-benzyl-7-*O*-undecyl-2-deoxy-L-*ido*-heptono-1,4-lactone (17). White crystals, mp 30–32 °C (CH_2Cl_2/hexane); [α]$_D$ –12.8 (*c* 0.5, $CHCl_3$); R_f = 0.38 (3:2 light petroleum/Et$_2$O). IR ($CHCl_3$): ν_{max} 1788 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (t, 3H, *J*=7.0 Hz, CH_3), 1.22–1.38 (m, 16H, 8×CH_2 from side chain), 1.57 (m, 2H, OCH$_2$C*H*$_2$(CH$_2$)$_8$CH$_3$), 2.69 (dd, 1H, $J_{2a,2b}$=18.8, $J_{2a,3}$=2.7 Hz, H-2a), 2.75 (dd, 1H, $J_{2a,2b}$=18.8, $J_{2b,3}$=4.7 Hz, H-2b), 3.39–3.53 (m, 2H, OC*H*$_2$(CH$_2$)$_9$CH$_3$), 3.66 (d, 2H, $J_{6,7}$=5.5 Hz, H-7), 4.21 (br. d, 1H, $J_{5,6}$=4.0 Hz, H-5), 4.26 (td, 1H, $J_{5,6}$=4.0, $J_{6,7}$=5.5 Hz, H-6), 4.62 and 4.71 (2×d, 2H, J_{gem}=11.9 Hz, C*H*$_2$Ph), 4.93 (dd, 1H, $J_{3,4}$=4.7, $J_{4,5}$=0.9 Hz, H-4), 4.98 (td, 1H, $J_{3,4}$=4.7, $J_{2a,3}$=2.8, $J_{2b,3}$=4.7 Hz, H-3), 7.29–7.40 (m, 5H, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.08 (CH_3), 22.64, 26.07, 29.29, 29.43, 29.55, 29.57, 29.60, 29.65 and 31.86 (9×CH_2 from side chain), 35.97 (C-2), 68.51 (C-7), 71.81 (O*C*H$_2$(CH$_2$)$_9$CH$_3$), 72.70 (*C*H$_2$Ph), 76.77 (C-3), 79.59 (C-6), 81.45 (C-5), 85.47 (C-4), 127.69, 128.11, 128.54 and 137.12 (Ph), 175.29 (C=O). HRMS-Heated ESI-Orbitrap: *m/z* 441.26129 (M^++Na), calcd. for $C_{25}H_{38}NaO_5$: 441.26169; *m/z* 457.23465 (M^++K), calcd. for $C_{25}H_{38}KO$: 457.23563.

3,6-Anhydro-5-*O*-benzyl-7-*O*-dodecyl-2-deoxy-L-*ido*-heptono-1,4-lactone (18). White needles, mp 45–46 °C (CH_2Cl_2/hexane); [α]$_D$ = –13.0 (*c* 0.5, $CHCl_3$); R_f = 0.25 (3:2 light petroleum/Et$_2$O). IR ($CHCl_3$): ν_{max} 1788 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (t, 3H, *J*=6.7 Hz, CH_3), 1.19–1.37 (m, 18H, 9×CH_2 from side chain), 1.57 (m, 2H, OCH$_2$C*H*$_2$(CH$_2$)$_9$CH$_3$), 2.68 (dd, 1H, $J_{2a,2b}$=18.8, $J_{2a,3}$=2.7 Hz, H-2a), 2.74 (dd, 1H, $J_{2a,2b}$=18.8, $J_{2b,3}$=4.8 Hz, H-2b), 3.40–3.52 (m, 2H, OC*H*$_2$(CH$_2$)$_{10}$CH$_3$), 3.64 (d, 2H, $J_{6,7}$=5.5 Hz, H-7), 4.21 (d, 1H, $J_{5,6}$=4.1 Hz, H-5), 4.27 (td, 1H, $J_{5,6}$=4.1, $J_{6,7}$=5.5 Hz, H-6), 4.60 and 4.70 (2×d, 2H, J_{gem}=11.9 Hz, C*H*$_2$Ph), 4.92 (dd, 1H, $J_{3,4}$=4.7, $J_{4,5}$=0.8 Hz, H-4), 4.97 (td, 1H, $J_{3,4}$=4.7, $J_{2a,3}$=2.8, $J_{2b,3}$=4.7 Hz, H-3), 7.29–7.40 (m, 5H, Ph). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.07 (CH_3), 22.63, 26.06, 29.29, 29.42, 29.55, 29.56, 29.58, 29.60, 29.61, 31.86 (10×CH_2

from side chain), 35.96 (C-2), 68.50 (C-7), 71.79 (O*C*H$_2$(CH$_2$)$_{10}$CH$_3$), 72.68 (CH$_2$Ph), 76.76 (C-3), 79.58 (C-6), 81.44 (C-5), 85.45 (C-4), 127.68, 128.09, 128.53, 137.12 (Ph), 175.28 (C=O). HRMS-Heated ESI-Orbitrap: *m/z* 455.27712 (M^++Na), calcd. for $C_{26}H_{40}NaO_5$: 455.27734; *m/z* 471.25088 (M^++K), calcd. for $C_{26}H_{40}KO_5$: 471.25128.

3,6-Anhydro-5-*O*-benzyl-7-*O*-tridecyl-2-deoxy-L-*ido*-heptono-1,4-lactone (19). White needles, mp 44–46 °C (CH$_2$Cl$_2$/hexane), $[\alpha]_D$ = –13.0 (*c* 0.5, CHCl$_3$); R_f = 0.13 (7:3 light petroleum/Et$_2$O). IR (KBr): ν_{max} 1791 (C=O). ^{1}H NMR (400 MHz, CDCl$_3$): δ 0.89 (t, 3H, *J*=6.8 Hz, CH$_3$), 1.20–1.37 (m, 20H, 10×CH$_2$ from side chain), 1.58 (m, 2H, OCH$_2$C*H$_2$*(CH$_2$)$_{10}$CH$_3$), 2.69 (dd, 1H, $J_{2a,2b}$=18.9, $J_{2a,3}$=2.9 Hz, H-2a), 2.74 (dd, 1H, $J_{2a,2b}$=18.9, $J_{2b,3}$=4.7 Hz, H-2b), 3.37–3.53 (m, 2H, OC*H$_2$*(CH$_2$)$_{11}$CH$_3$), 3.65 (d, 2H, $J_{6,7}$=5.5 Hz, H-7), 4.21 (d, 1H, $J_{5,6}$=4.0 Hz, H-5), 4.26 (td, 1H, $J_{5,6}$=4.1, $J_{6,7}$=5.5 Hz, H-6), 4.61 and 4.70 (2×d, 2H, J_{gem}=11.9 Hz, C*H$_2$*Ph), 4.93 (d, 1H, $J_{3,4}$=4.7 Hz, H-4), 4.97 (ddd, 1H, $J_{3,4}$=4.7, $J_{2a,3}$=2.9, $J_{2b,3}$=4.6 Hz, H-3), 7.30–7.41 (m, 5H, Ph). ^{13}C NMR (100 MHz, CDCl$_3$): δ 14.13 (CH$_3$), 22.70, 26.13, 29.37, 29.41, 29.49, 29.56, 29.62, 29.63, 29.66, 29.68, 31.93 (11×CH$_2$ from side chain), 36.03 (C-2), 68.57 (C-7), 71.87 (O*C*H$_2$(CH$_2$)$_{11}$CH$_3$), 72.76 (*C*H$_2$Ph), 76.72 (C-3), 79.65 (C-6), 81.51 (C-5), 85.53 (C-4), 127.75, 128.17, 128.60, 137.17 (Ph), 175.34 (C=O). HRMS-Heated ESI-Orbitrap: *m/z* 469.29308 (M^++Na); calcd. for $C_{27}H_{42}NaO_5$: 469.29299; *m/z* 485.26669 (M^++K), calcd. for $C_{27}H_{42}KO_5$: 485.26693.

3,6-Anhydro-2-deoxy-L-*ido*-heptono-1,4-lactone (2). White crystals, mp 73–75 °C (EtOAc/pentane), lit.[1] mp 72–74 °C (EtOAc/pentane); $[\alpha]_D$ = –25.0 (*c* 0.44, H$_2$O), lit.[1] $[\alpha]_D^{20}$ = –32.0 (*c* 0.6, H$_2$O); R_f = 0.16 (3:2 EtOAc/CH$_2$Cl$_2$). IR (CHCl$_3$): ν_{max} 3378 (OH), 1780 (C=O). ^{1}H NMR (400 MHz, acetone-d_6): δ 2.46 (d, 1H, $J_{2a,2b}$=18.4 Hz, H-2a), 2.85 (dd, 1H, $J_{2a,2b}$=18.4, $J_{2b,3}$=6.2 Hz, H-2b), 2.89 (br. s, 2H, 2×OH), 3.77 (dd, 1H, $J_{6,7a}$=5.5, $J_{7a,7b}$=11.0 Hz, H-7a), 3.83 (dd, 1H, $J_{6,7b}$=5.3 Hz, $J_{7a,7b}$=11.0 Hz, H-7b), 4.00 (td, 1H, $J_{5,6}$=3.5, $J_{6,7}$=5.0 Hz, H-6), 4.41 (t, 1H, $J_{5,6}$=4.0 Hz, H-5), 4.88 (d, 1H, $J_{3,4}$=4.3 Hz, H-4), 4.95 (dd, 1H, $J_{3,4}$=4.4, $J_{2b,3}$=6.1 Hz, H-3); ^{13}C NMR (100 MHz, acetone-d_6): δ 36.55 (C-2), 60.96 (C-7), 75.24 (C-5), 77.57 (C-3), 82.21 (C-6), 89.14 (C-4), 176.13 (C=O). HRMS (ESI$^+$): *m/z* 175.06038 (M^++H), calculated for $C_7H_{11}O_5$: 175.06010.

3,6-Anhydro-7-*O*-hexyl-2-deoxy-L-*ido*-heptono-1,4-lactone (3). White crystals, mp 47–49 °C (CH$_2$Cl$_2$/hexane); $[\alpha]_D$ = –26.3 (*c* 0.3, CHCl$_3$); R_f = 0.15 (7:3 Et$_2$O/light petroleum). IR (KBr): ν_{max} 3290 (OH), 1775 (C=O). ^{1}H NMR (400 MHz, CDCl$_3$): δ 0.89 (t, 3H, *J*=6.8 Hz, CH$_3$), 1.22–1.38 (m, 6H, 3×C*H$_2$* from side chain), 1.59 (m, 2H, OCH$_2$C*H$_2$*(CH$_2$)$_3$CH$_3$), 2.67 (d, 1H, $J_{2a,2b}$=18.7 Hz, H-2a), 2.75 (dd, 1H, $J_{2a,2b}$=18.7, $J_{2b,3}$=5.7 Hz, H-2b), 3.52 (m, 2H, OC*H$_2$*(CH$_2$)$_4$CH$_3$), 3.88 (dd, 1H, $J_{6,7a}$=3.0, $J_{7a,7b}$=11.2 Hz, H-7a), 3.91 (dd, 1H, $J_{6,7b}$=3.4, $J_{7a,7b}$=11.2 Hz, H-7b), 4.12 (m, 1H, H-6), 4.23 (d, 1H, $J_{5,OH}$=3.6 Hz, OH), 4.54 (t, 1H, H-5), 4.87 (d, 1H, $J_{3,4}$=4.2 Hz, H-4), 5.01 (t, 1H, $J_{3,4}$=4.7 Hz, H-3). ^{13}C NMR (100 MHz, CDCl$_3$): δ 14.00 (CH$_3$), 22.53, 25.63, 29.37, 31.53 (4×CH$_2$ from side chain), 36.10 (C-2), 69.58 (C-7), 72.66 (O*C*H$_2$(CH$_2$)$_4$CH$_3$), 76.16 (C-5), 76.91 (C-3), 78.59 (C-6), 88.27 (C-4), 175.40 (C=O). HRMS-Heated ESI-Orbitrap: *m/z* 281.13567 (M^++Na), calcd. for $C_{13}H_{22}NaO_5$: 281.13649.

3,6-Anhydro-7-*O*-heptyl-2-deoxy-L-*ido*-heptono-1,4-lactone (4). White crystals, mp 41–42 °C (CH$_2$Cl$_2$/hexane); $[\alpha]_D$ = –33.2 (*c* 0.5, CHCl$_3$); R_f = 0.15 (7:3 Et$_2$O/light petroleum). IR (KBr): ν_{max} 3434 (OH), 1784 (C=O). ^{1}H NMR (400 MHz, CDCl$_3$): δ 0.88 (t, 3H, *J*=6.9 Hz, CH$_3$), 1.20–1.36 (m, 8H, 4×CH$_2$ from side chain), 1.59 (m, 2H, OCH$_2$C*H$_2$*(CH$_2$)$_4$CH$_3$), 2.67

[1] K. Bock, I. Lundt, C. Pedersen, *Carbohydr. Res.* **179** (1988) 87.

(d, 1H, $J_{2a,2b}$=18.7 Hz, H-2a), 2.75 (dd, 1H, $J_{2a,2b}$=18.7, $J_{2b,3}$=5.7 Hz, H-2b), 3.52 (m, 2H, OCH_2(CH_2)$_5$$CH_3$), 3.88 (dd, 1H, $J_{6,7a}$=3.1, $J_{7a,7b}$=11.1 Hz, H-7a), 3.91 (dd, 1H, $J_{6,7b}$=3.4, $J_{7a,7b}$=11.1 Hz, H-7b), 4.12 (m, 1H, H-6), 4.23 (d, 1H, $J_{5,OH}$=3.7 Hz, OH), 4.54 (t, 1H, $J_{5,6}$=3.1 Hz, H-5), 4.87 (d, 1H, $J_{3,4}$=4.2 Hz, H-4), 5.01 (m, 1H, H-3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.06 (CH_3), 22.58, 25.93, 29.02, 29.42, 31.71 (5×CH_2 from side chain), 36.10 (C-2), 69.59 (C-7), 72.66 (OCH_2(CH_2)$_5$$CH_3$), 76.17 (C-5), 76.91 (C-3), 78.59 (C-6), 88.27 (C-4), 175.39 (C=O). HRMS-Heated ESI-Orbitrap: *m/z* 295.15146 (M^++Na), calcd. for $C_{14}H_{24}NaO_5$: 295.15214.

3,6-Anhydro-7-*O*-octyl-2-deoxy-L-*ido*-heptono-1,4-lactone (5). White crystals, mp 51–53 °C (CH_2Cl_2/hexane); [α]$_D$ –26.2 (*c* 0.5, $CHCl_3$); R_f = 0.19 (4:1 Et_2O/light petroleum). IR (KBr): ν_{max} 3430 (OH), 1777 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, *J*=6.9 Hz, CH_3), 1.20–1.37 (m, 10H, 5×CH_2 from side chain), 1.60 (m, 2H, OCH_2CH_2(CH_2)$_5$$CH_3$), 2.68 (d, 1H, $J_{2a,2b}$=18.6 Hz, H-2a), 2.76 (dd, 1H, $J_{2a,2b}$=18.6, $J_{2b,3}$=5.7 Hz, H-2b), 3.52 (m, 2H, OCH_2(CH_2)$_6$$CH_3$), 3.88 (dd, 1H, $J_{6,7a}$=3.0, $J_{7a,7b}$=11.1 Hz, H-7a), 3.90 (dd, 1H, $J_{6,7b}$=3.4, $J_{7a,7b}$=11.1 Hz, H-7b), 4.12 (m, 1H, H-6), 4.25 (br. s, 1H, OH), 4.55 (d, 1H, $J_{5,6}$=3.2 Hz, H-5), 4.88 (d, 1H, $J_{3,4}$=4.2 Hz, H-4), 5.01 (m, 1H, H-3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.05 (CH_3), 22.60, 25.94, 29.14, 29.28, 29.38, 31.75 (6×CH_2 from side chain), 36.07 (C-2), 69.56 (C-7), 72.65 (OCH_2(CH_2)$_6$$CH_3$), 76.15 (C-5), 76.88 (C-3), 78.54 (C-6), 88.23 (C-4), 175.34 (C=O). HRMS-Heated ESI-Orbitrap: *m/z* 309.16760 (M^++Na), calcd. for $C_{15}H_{26}NaO_5$: 309.16779.

3,6-Anhydro-7-*O*-nonyl-2-deoxy-L-*ido*-heptono-1,4-lactone (6). Colourless crystals, mp 53 °C (CH_2Cl_2/hexane), [α]$_D$ = −35.0 (*c* 0.5, $CHCl_3$), R_f=0.32 (Et_2O). IR (film): ν_{max} 3277 (OH), 1774 (C=O). For ^{1}H and ^{13}C NMR spectra see, ref. 2. HRMS: *m/z* 301.2000 (M^++H), calcd. for $C_{16}H_{29}O_5$: 301.2010; *m/z* 318.2266 (M^++NH_4), calcd. for $C_{16}H_{32}NO_5$: 318.2275.

3,6-Anhydro-7-*O*-decyl-2-deoxy-L-*ido*-heptono-1,4-lactone (7). White crystals, mp 59–60 °C (CH_2Cl_2/hexane), [α]$_D$ = −29.1 (*c* 1.0, $CHCl_3$), R_f=0.25 (9:1 CH_2Cl_2/EtOAc). IR (film): ν_{max} 3481 (OH), 1773 (C=O). For NMR (^{1}H and ^{13}C) and LRMS spectra see, ref. 2. Anal. Found: C, 65.12; H, 9.56. Calculated for $C_{24}H_{36}O_5$: C, 64.94; H, 9.62.

3,6-Anhydro-7-*O*-undecyl-2-deoxy-L-*ido*-heptono-1,4-lactone (8). White crystals, mp 57 °C (CH_2Cl_2/hexane); [α]$_D$ –26.6 (*c* 0.5, $CHCl_3$); R_f = 0.15 (7:3 Et_2O/light petroleum). IR (KBr): ν_{max} 3444 (OH), 1775 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, *J*=7.1 Hz, CH_3), 1.21–1.34 (m, 16H, 8×CH_2 from side chain), 1.59 (m, 2H, OCH_2CH_2(CH_2)$_8$$CH_3$), 2.67 (d, 1H, $J_{2a,2b}$=18.7 Hz, H-2a), 2.75 (dd, 1H, $J_{2a,2b}$=18.7, $J_{2b,3}$=5.7 Hz, H-2b), 3.52 (m, 2H, OCH_2(CH_2)$_9$$CH_3$), 3.87 (dd, 1H, $J_{6,7a}$=3.1, $J_{7a,7b}$=11.1 Hz, H-7a), 3.90 (dd, 1H, $J_{6,7b}$=3.4, $J_{7a,7b}$=11.1 Hz, H-7b), 4.11 (m, 1H, H-6), 4.53 (d, 1H, $J_{5,6}$=3.3 Hz, H-5), 4.87 (d, 1H, $J_{3,4}$=4.3 Hz, H-4), 5.03 (m, 1H, H-3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.07 (CH_3), 22.63, 25.92, 29.27, 29.32, 29.37, 29.47, 29.53, 29.54, 31.85, (9×CH_2 from side chain), 36.05 (C-2), 69.52 (C-7), 72.61 (OCH_2(CH_2)$_9$$CH_3$), 76.09 (C-5), 76.86 (C-3), 78.56 (C-6), 88.23 (C-4), 175.37 (C=O). HRMS-Heated ESI-Orbitrap: *m/z* 351.21415 (M^++Na), calcd. for $C_{18}H_{32}NaO_5$: 351.21474.

[2] V. Popsavin, B. Srećo, G. Benedeković, M. Popsavin, J. Francuz, V. Kojić, G. Bogdanović, *Bioorg. Med. Chem. Lett.* **18** (2008) 5182.

3,6-Anhydro-7-*O*-dodecyl-2-deoxy-L-*ido*-heptono-1,4-lactone (9). White needles, mp 69–70 °C (CH_2Cl_2/hexane); $[\alpha]_D$ = –25.0 (*c* 0.5, $CHCl_3$); R_f = 0.15 (3:2 Et_2O/light petroleum). IR (KBr): ν_{max} 3447 (OH), 1775 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.88 (t, 3H, *J*=6.8 Hz, CH_3), 1.20–1.36 (m, 18H, 9×CH_2 from side chain), 1.59 (m, 2H, $OCH_2CH_2(CH_2)_9CH_3$), 2.66 (d, 1H, $J_{2a,2b}$=18.6 Hz, H-2a), 2.75 (dd, 1H, $J_{2a,2b}$=18.6, $J_{2b,3}$=5.7 Hz, H-2b), 3.52 (m, 2H, $OCH_2(CH_2)_{10}CH_3$), 3.86 (dd, 1H, $J_{6,7a}$=3.1, $J_{7a,7b}$=11.0 Hz, H-7a), 3.91 (dd, 1H, $J_{6,7b}$=3.4, $J_{7a,7b}$=11.1 Hz, H-7b), 4.11 (m, 1H, H-6), 4.22 (d, 1H, $J_{5,OH}$=3.7 Hz, OH), 4.53 (t, 1H, $J_{5,6}$=3.3 Hz, H-5), 4.86 (d, 1H, $J_{3,4}$=4.1 Hz, H-4), 5.01 (m, 1H, H-3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.08 (CH_3), 22.64, 25.93, 29.30, 29.33, 29.38, 29.48, 29.54, 29.58, 29.60, 31.87 (10×CH_2 from side chain), 36.06 (C-2), 69.54 (C-7), 72.62 ($OCH_2(CH_2)_{10}CH_3$), 76.11 (C-5), 76.86 (C-3), 78.56 (C-6), 88.23 (C-4), 175.35 (C=O). HRMS-Heated ESI-Orbitrap: *m/z* 365.23022 (M^++Na), calcd. for $C_{19}H_{34}NaO_5$: 365.23039.

3,6-Anhydro-7-*O*-tridecyl-2-deoxy-L-*ido*-heptono-1,4-lactone (10). White needles, mp 63–65 °C (CH_2Cl_2/hexane); $[\alpha]_D$ = –19.3 (*c* 0.5, $CHCl_3$); R_f = 0.17 (7:3 Et_2O/light petroleum). IR (KBr): ν_{max} 3450 (OH), 1785 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (t, 3H, *J*=6.8 Hz, CH_3), 1.21–1.34 (m, 20H, 10×CH_2 from side chain), 1.59 (m, 2H, $OCH_2CH_2(CH_2)_{10}CH_3$), 2.68 (d, 1H, $J_{2a,2b}$=18.6 Hz, H-2a), 2.76 (dd, 1H, $J_{2a,2b}$=18.6, $J_{2b,3}$=5.6 Hz, H-2b), 3.52 (m, 2H, $OCH_2(CH_2)_{11}CH_3$), 3.88 (dd, 1H, $J_{6,7a}$=3.0, $J_{7a,7b}$=11.1 Hz, H-7a), 3.92 (dd, 1H, $J_{6,7b}$=3.4, $J_{7a,7b}$=11.1 Hz, H-7b), 4.12 (m, 1H, H-6), 4.24 (d, 1H, $J_{5,OH}$=3.7 Hz, OH), 4.55 (t, 1H, $J_{5,6}$=3.0 Hz, H-5), 4.88 (d, 1H, $J_{3,4}$=4.1 Hz, H-4), 5.04 (m, 1H, H-3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.12 (CH_3), 22.70, 25.97, 29.36, 29.37, 29.42, 29.53, 29.59, 29.65, 29.67, 29.71, 31.92 (11×CH_2 from side chain), 36.11 (C-2), 69.61 (C-7), 72.69 ($OCH_2(CH_2)_{11}CH_3$), 76.21 (C-5), 76.92 (C-3), 78.57 (C-6), 88.27 (C-4), 175.37 (C=O). HRMS-Heated ESI-Orbitrap: *m/z* 379.24528 (M^++Na), calcd. for $C_{20}H_{36}NaO_5$: 379.24604.

NMR SPECTRA OF FINAL PRODUCTS

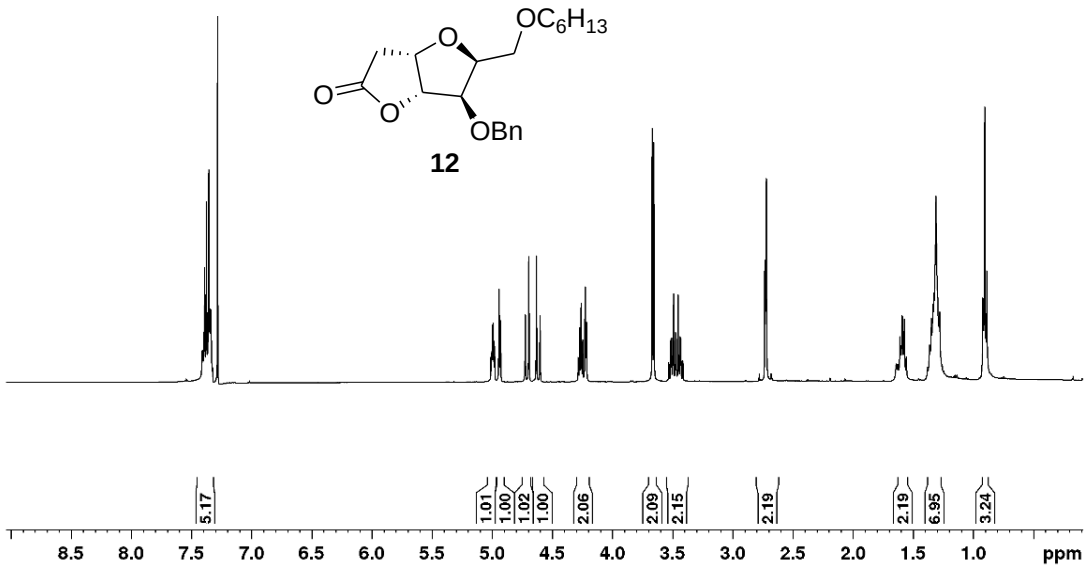


Fig. S-1. ^{1}H-NMR spectrum of **12** (400 MHz, $CDCl_3$).

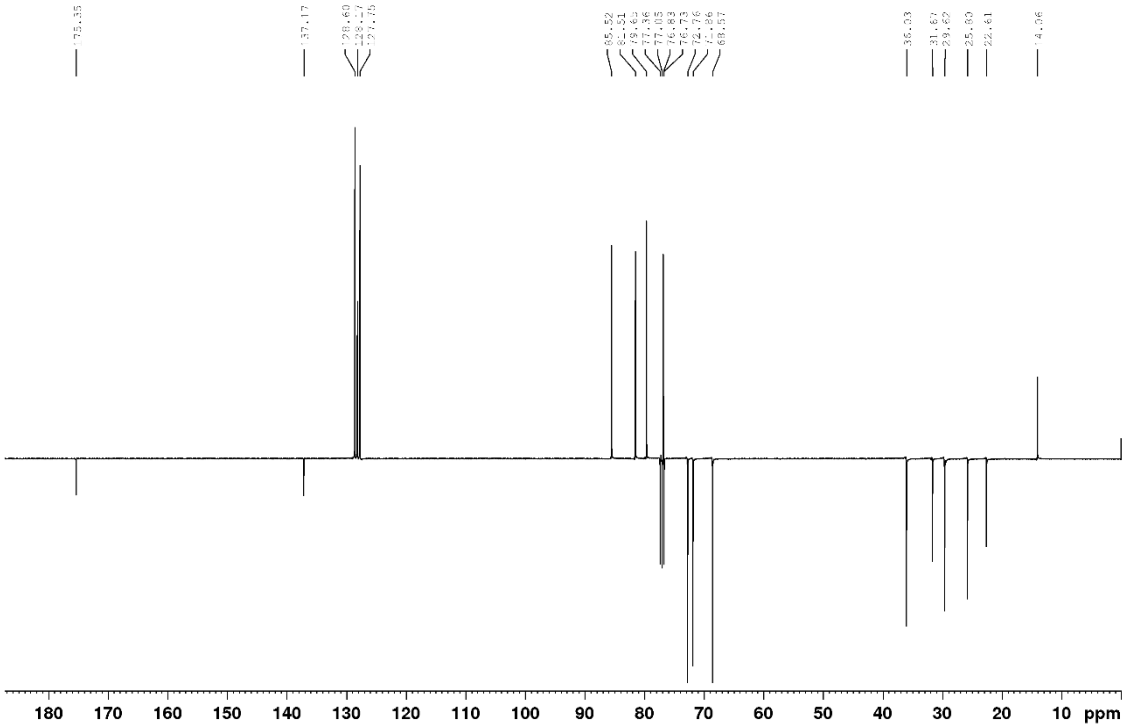


Fig. S-2. ^{13}C-NMR spectrum of **12** (100 MHz, $CDCl_3$).

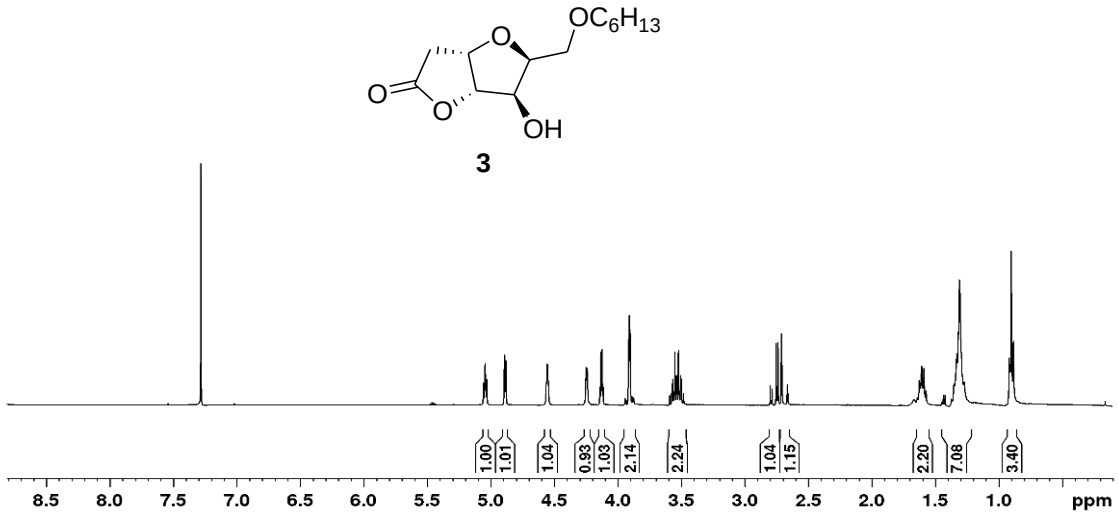


Fig. S-3. ^{1}H-NMR spectrum of **3** (400 MHz, $CDCl_3$).

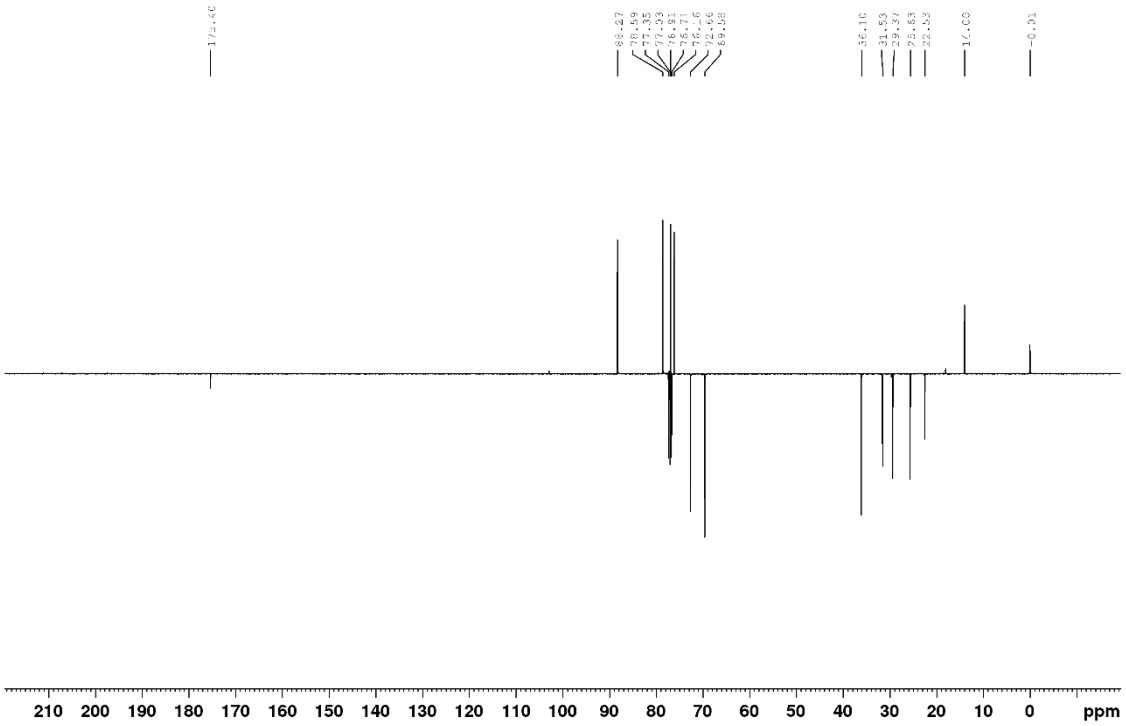


Fig. S-4. ^{13}C-NMR spectrum of **3** (100 MHz, $CDCl_3$).

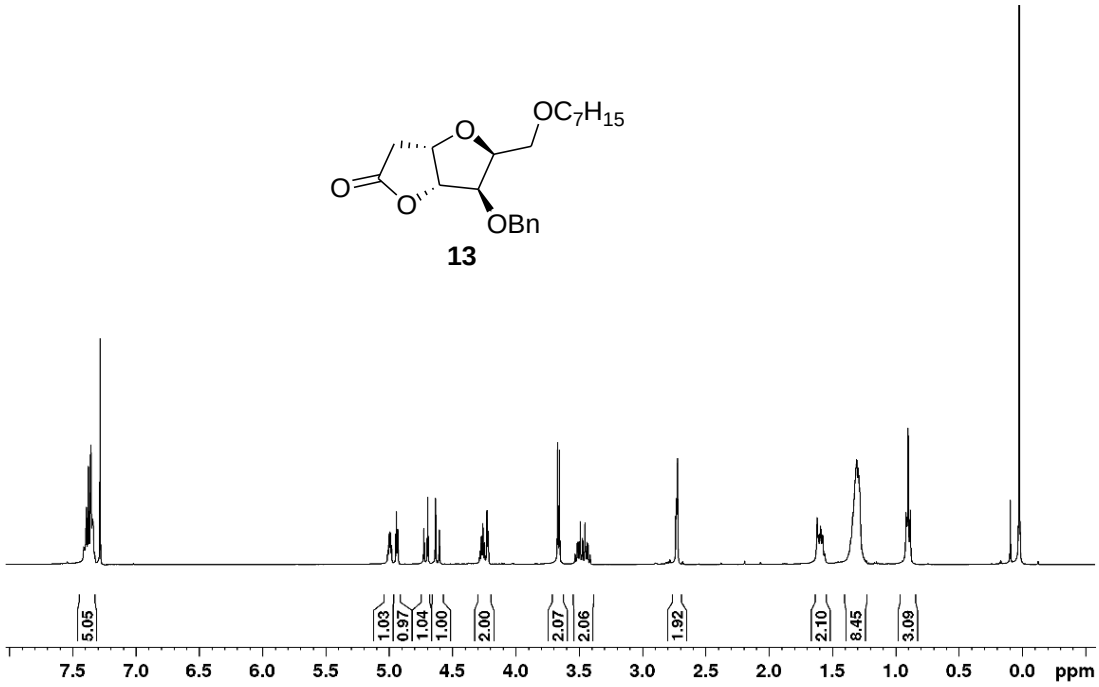


Fig. S-5. ^{1}H-NMR spectrum of **13** (400 MHz, $CDCl_3$).

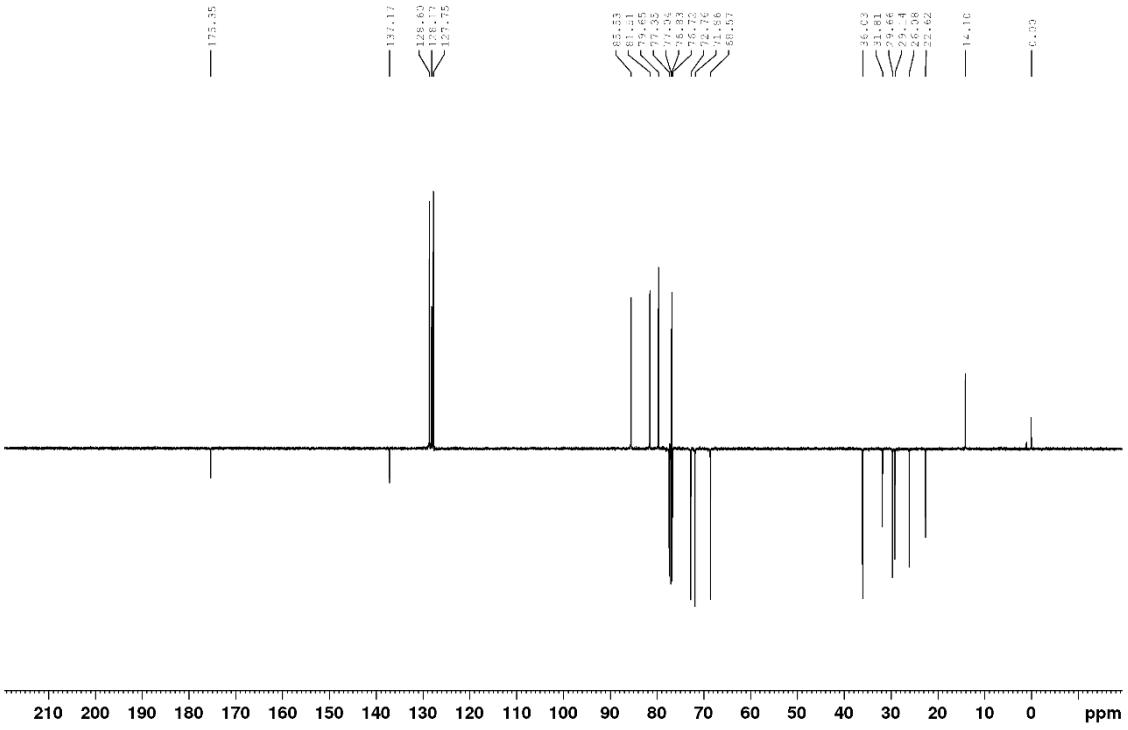


Fig. S-6. ^{13}C-NMR spectrum of **13** (100 MHz, $CDCl_3$).

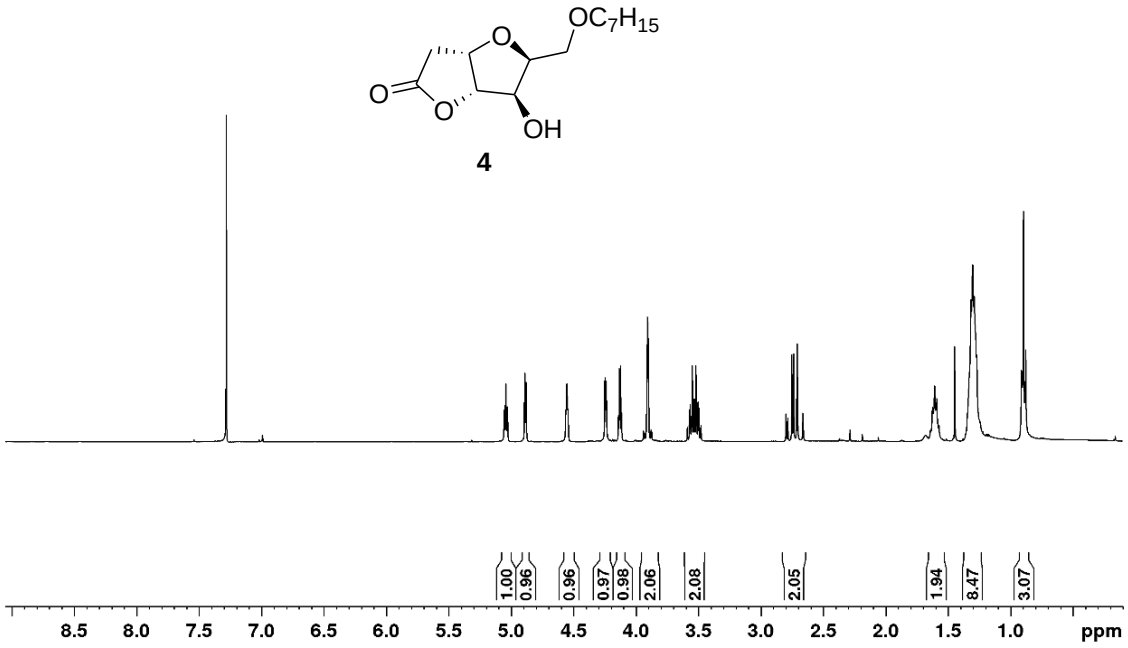


Fig. S-7. ^{1}H-NMR spectrum of **4** (400 MHz, $CDCl_3$).

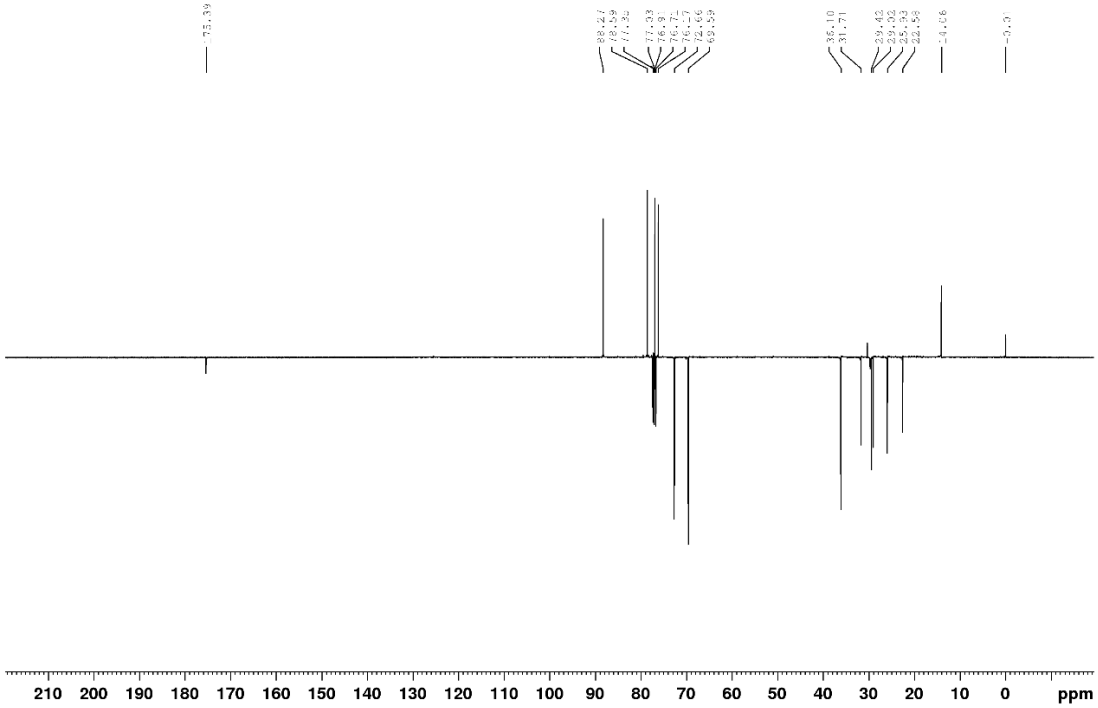


Fig. S-8. ^{13}C-NMR spectrum of **4** (100 MHz, $CDCl_3$).

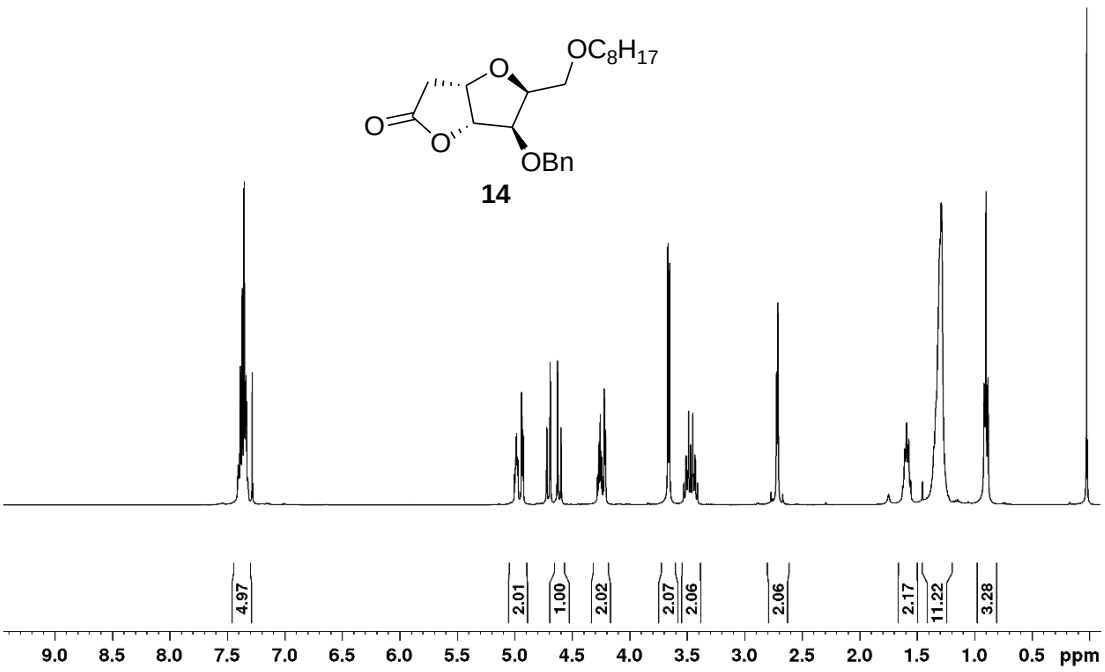


Fig. S-9. ^{1}H-NMR spectrum of **14** (400 MHz, $CDCl_3$).

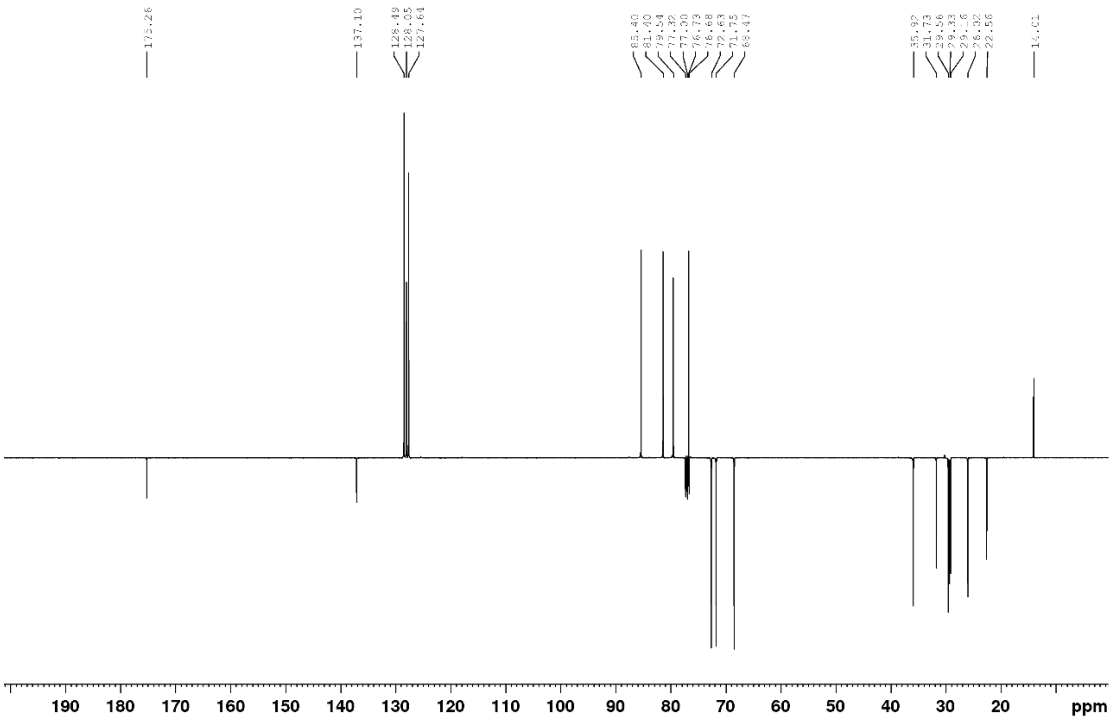


Fig. S-10. ^{13}C-NMR spectrum of **14** (100 MHz, $CDCl_3$).

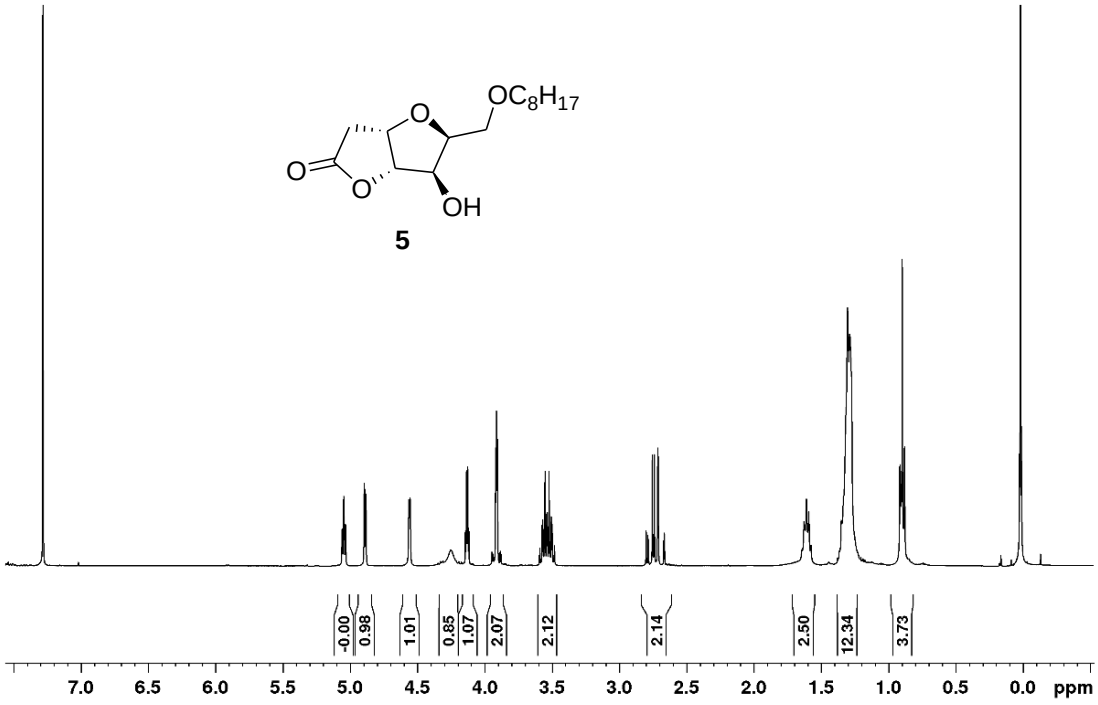


Fig. S-11. ^{1}H-NMR spectrum of **5** (400 MHz, $CDCl_3$).

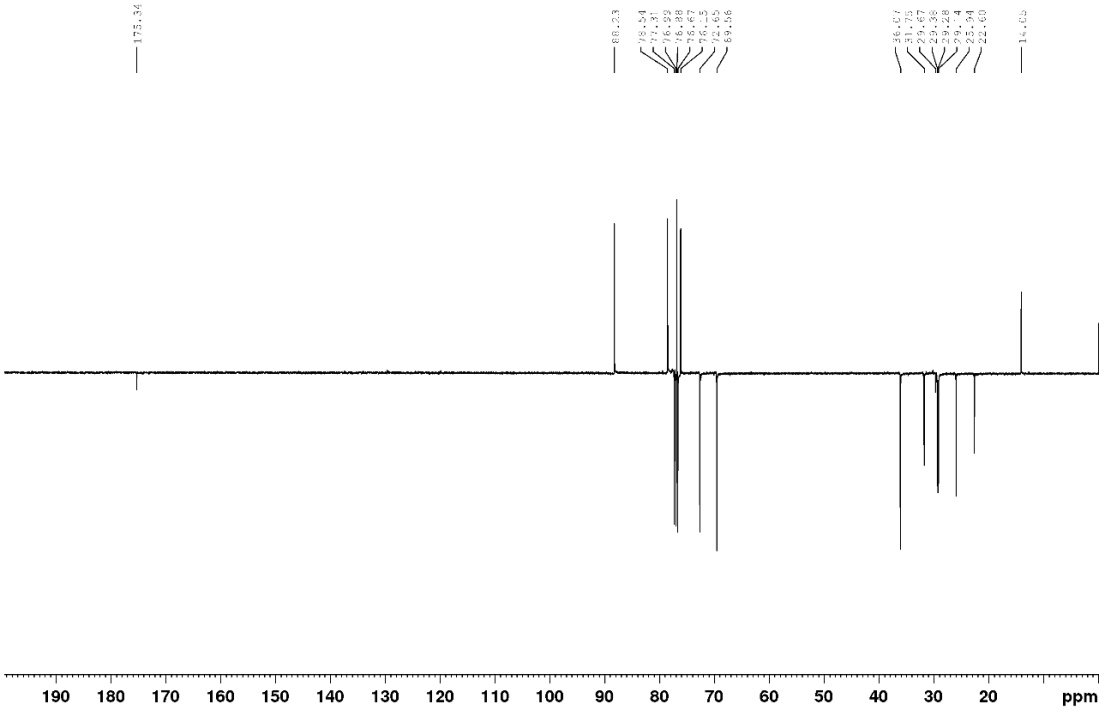


Fig. S-12. ^{13}C-NMR spectrum of **5** (100 MHz, $CDCl_3$).

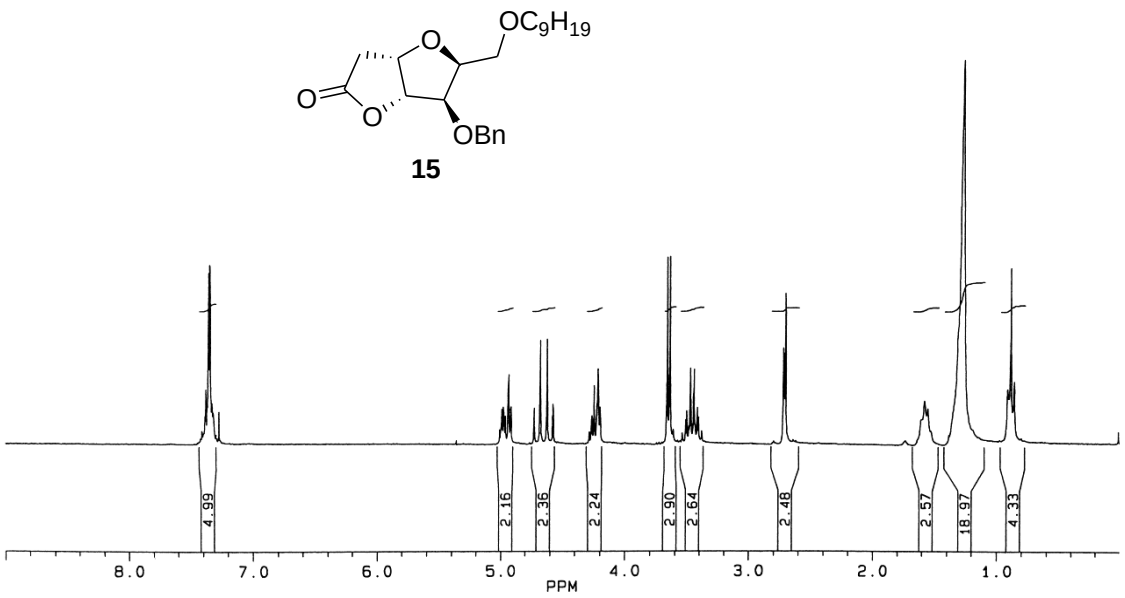


Fig. S-13. ^{1}H-NMR spectrum of **15** (250 MHz, $CDCl_3$)**.**

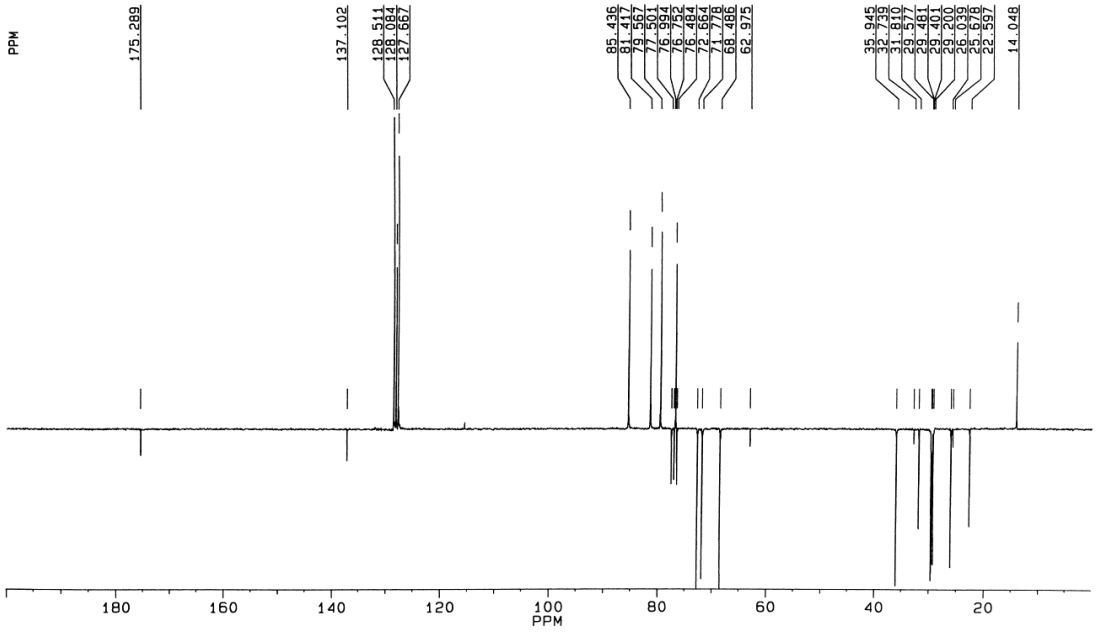


Fig. S-14. ^{13}C-NMR spectrum of **15** (63.9 MHz, $CDCl_3$).

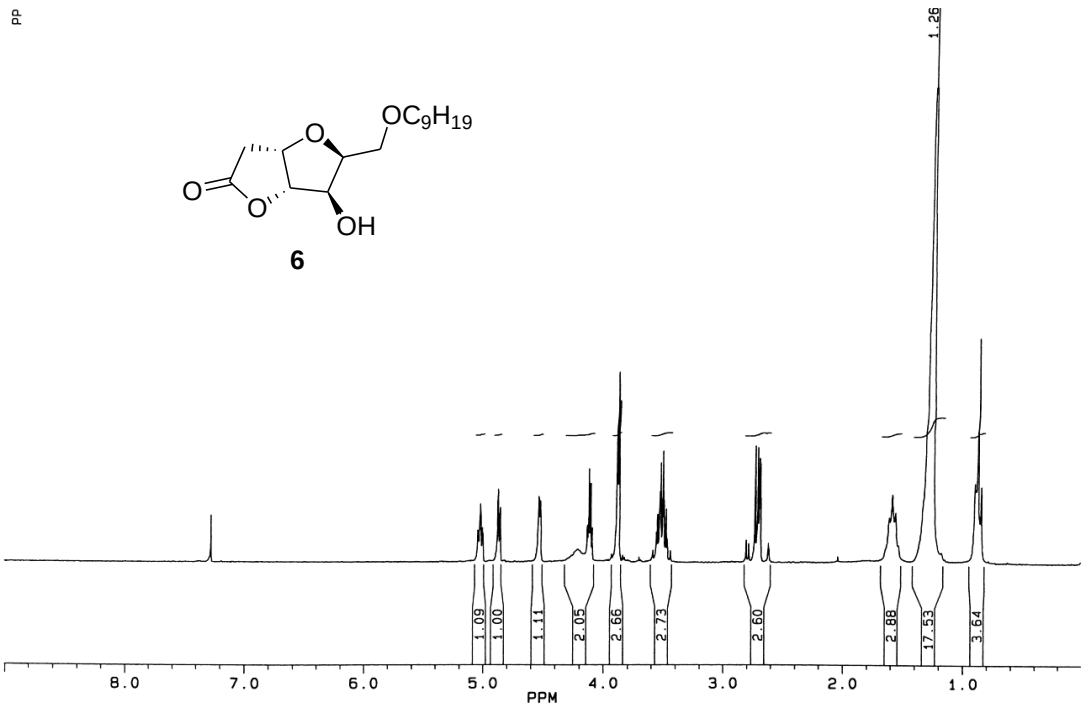


Fig. S-15. ^{1}H-NMR spectrum of **6** (250 MHz, $CDCl_3$).

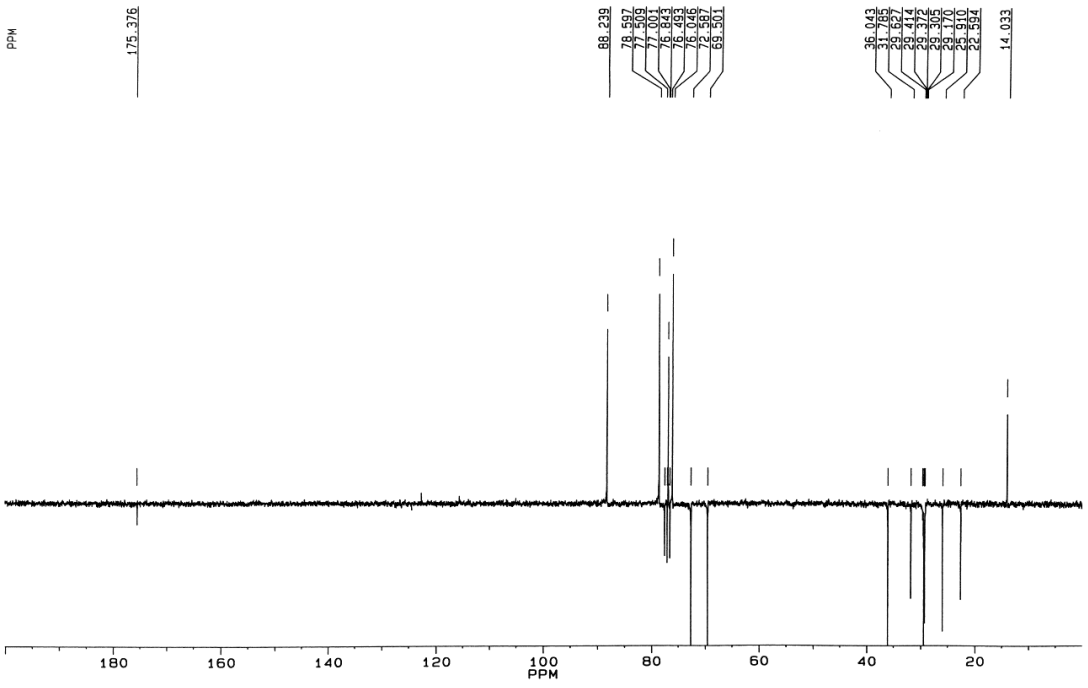


Fig. S-16. ^{13}C-NMR spectrum of **6** (63.9 MHz, $CDCl_3$).

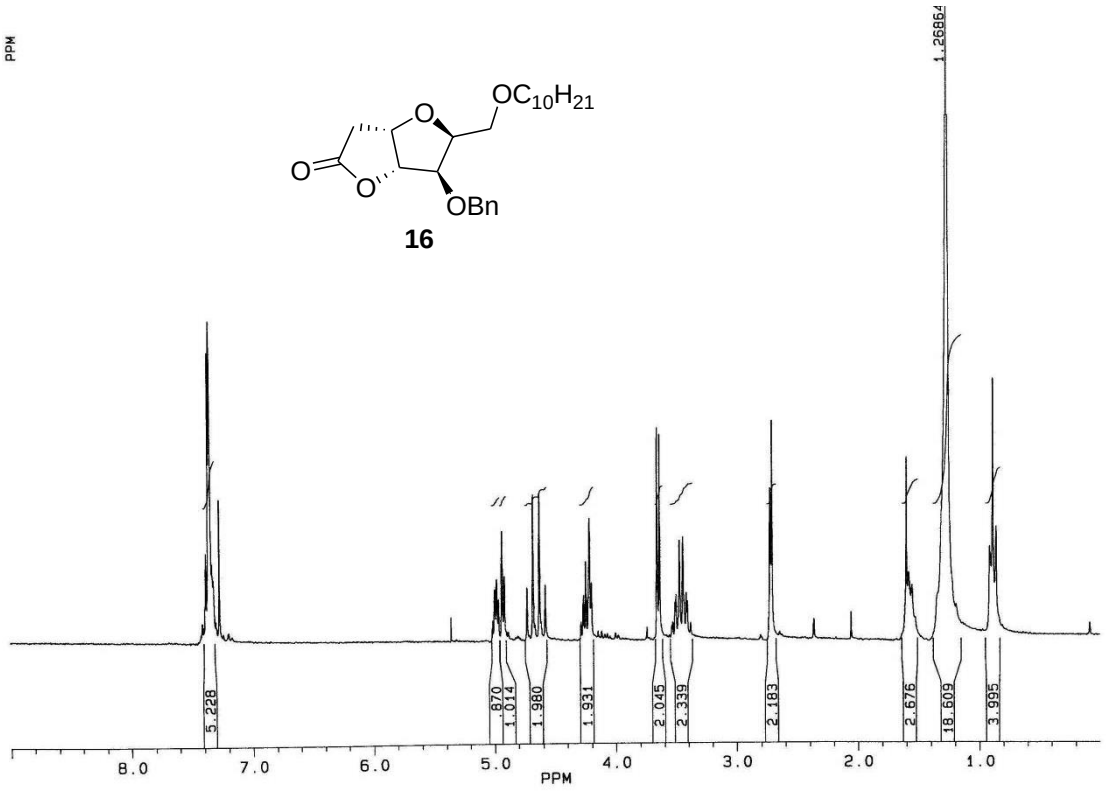


Fig. S-17. ^{1}H-NMR spectrum of **16** (250 MHz, $CDCl_3$)**.**

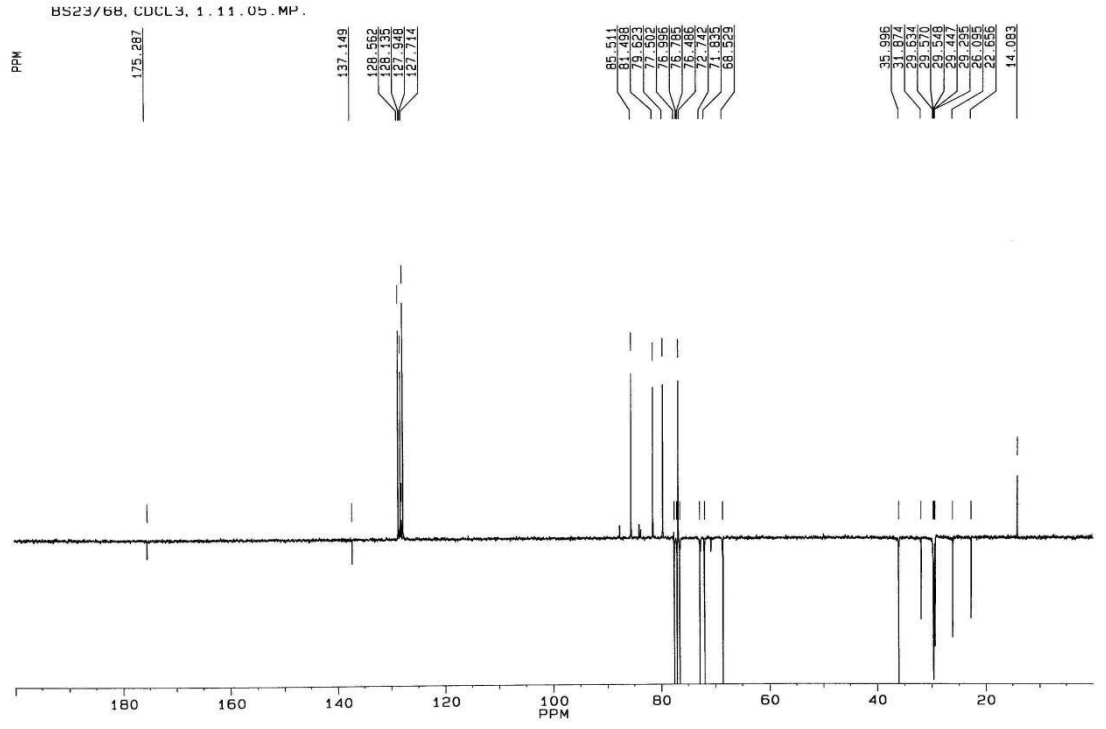


Fig. S-18. ^{13}C-NMR spectrum of **16** (63.9 MHz, $CDCl_3$).

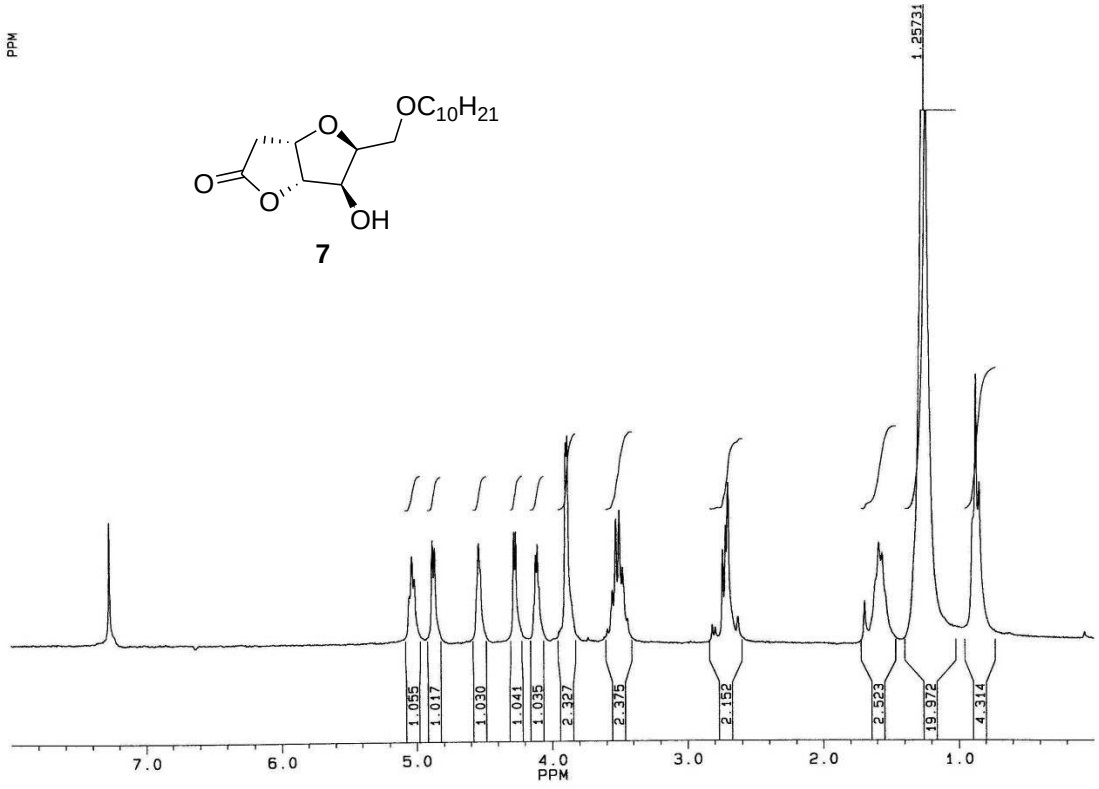


Fig. S-19. ^{1}H-NMR spectrum of **7** (250 MHz, $CDCl_3$).

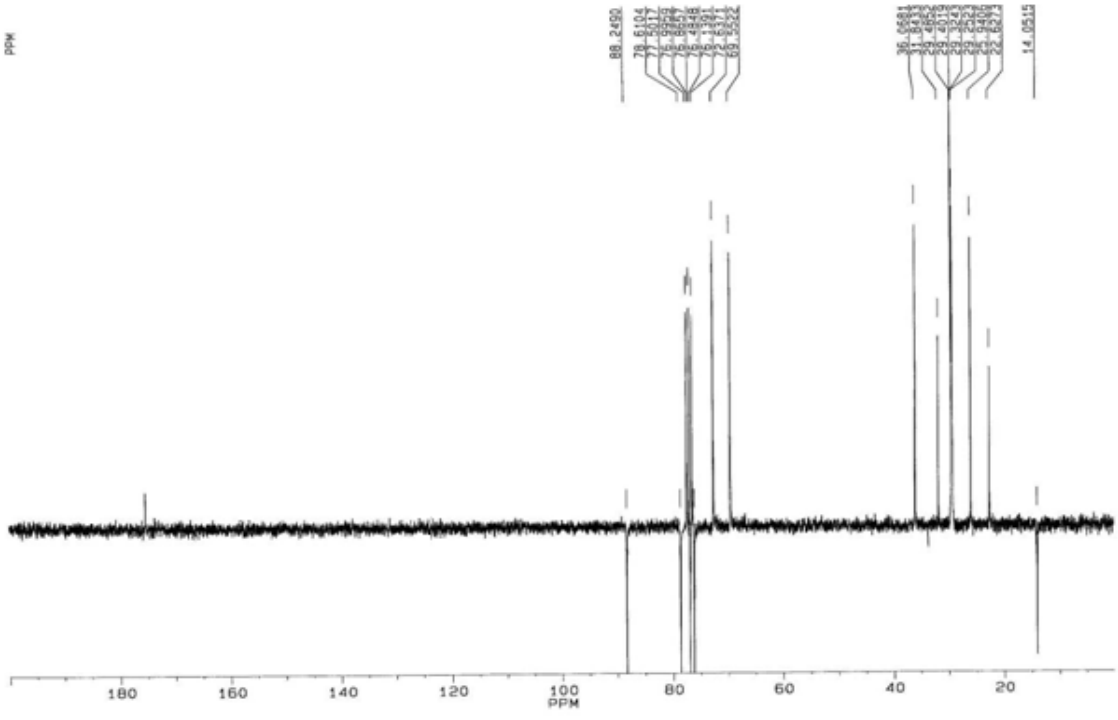
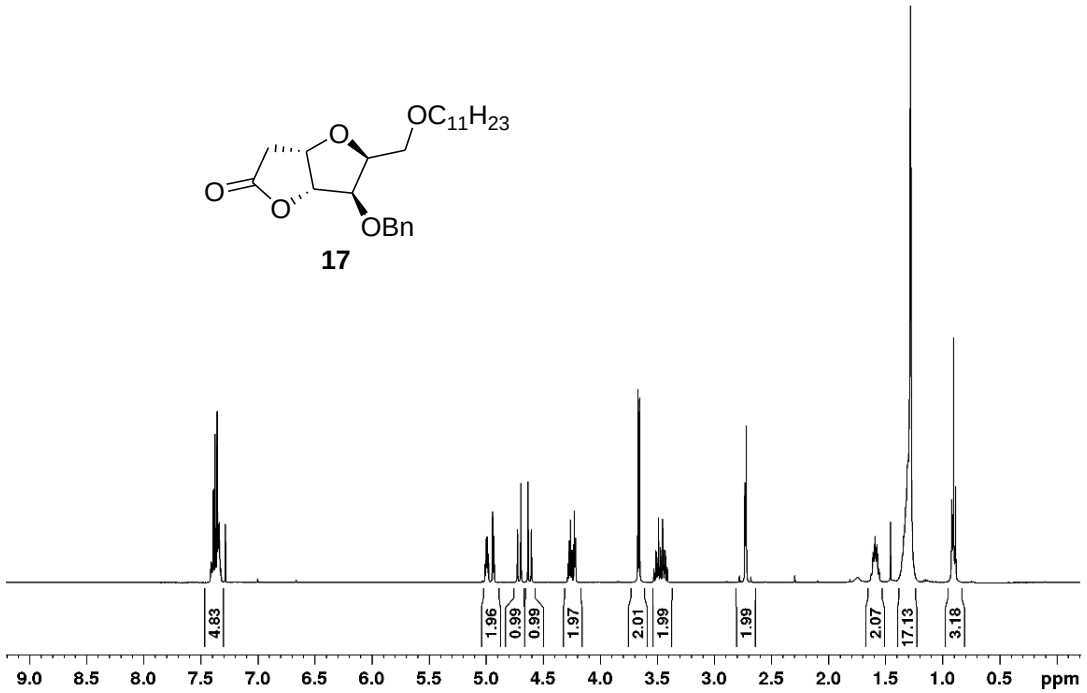


Fig. S-20. ^{13}C-NMR spectrum of **7** (63.9 MHz, $CDCl_3$).

299



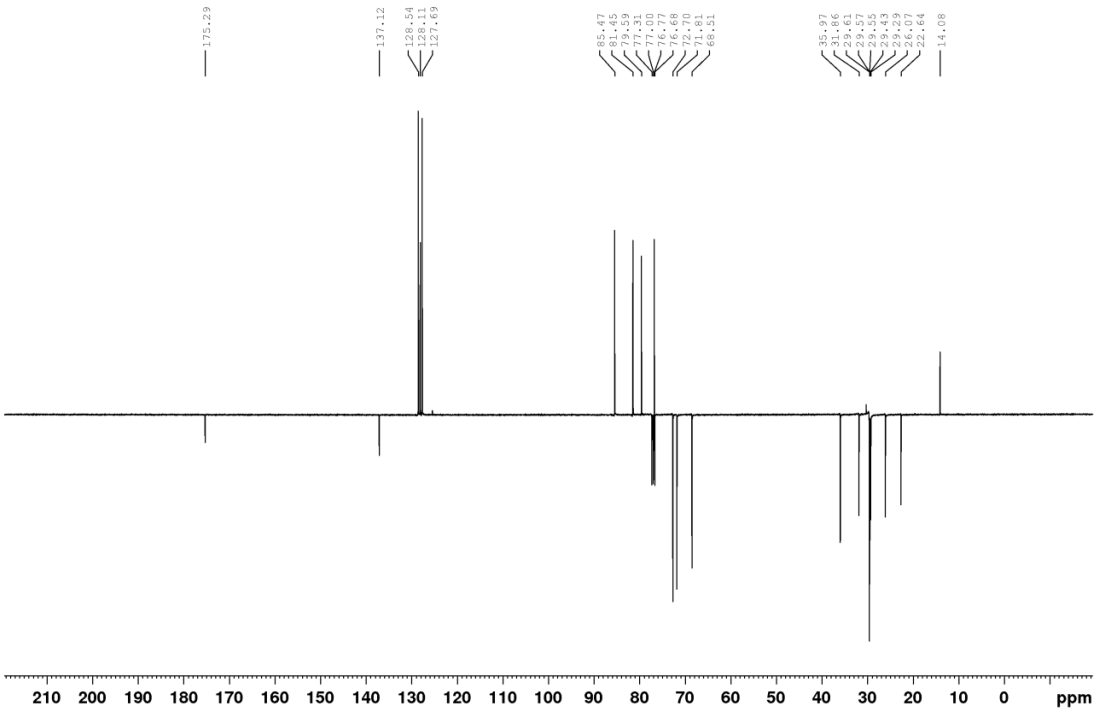
300

301 Fig. S-21. ^{1}H-NMR spectrum of **17** (400 MHz, $CDCl_3$).

302

303

304



305

306 Fig. S-22. ^{13}C-NMR spectrum of **17** (100 MHz, $CDCl_3$).

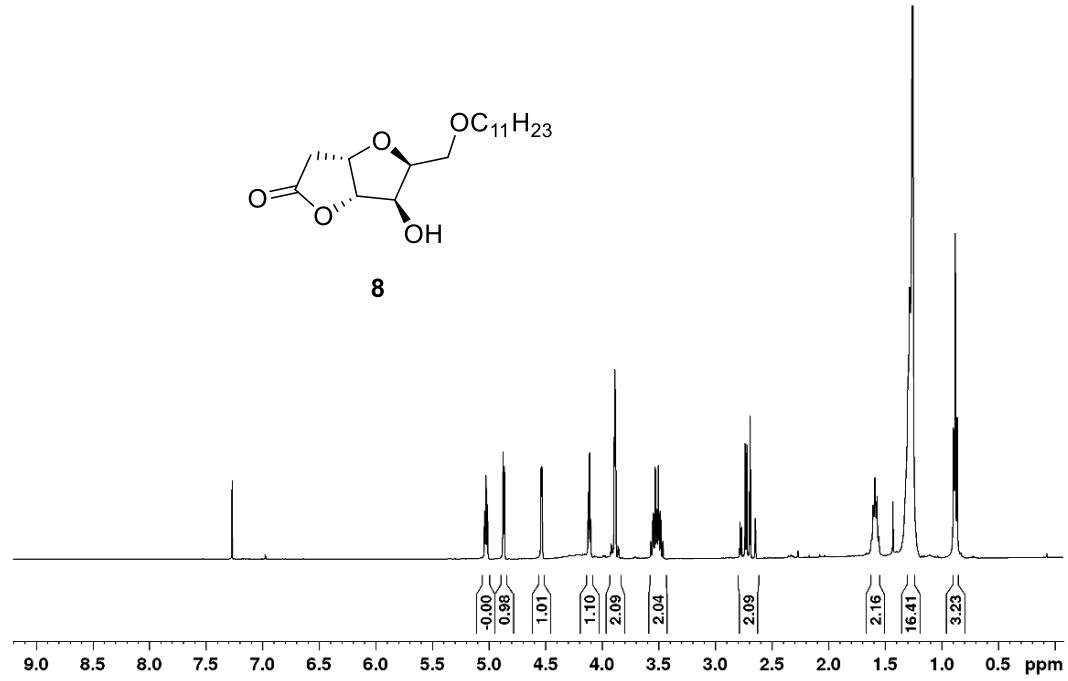


Fig. S-23. ^{1}H-NMR spectrum of **8** (400 MHz, $CDCl_3$).

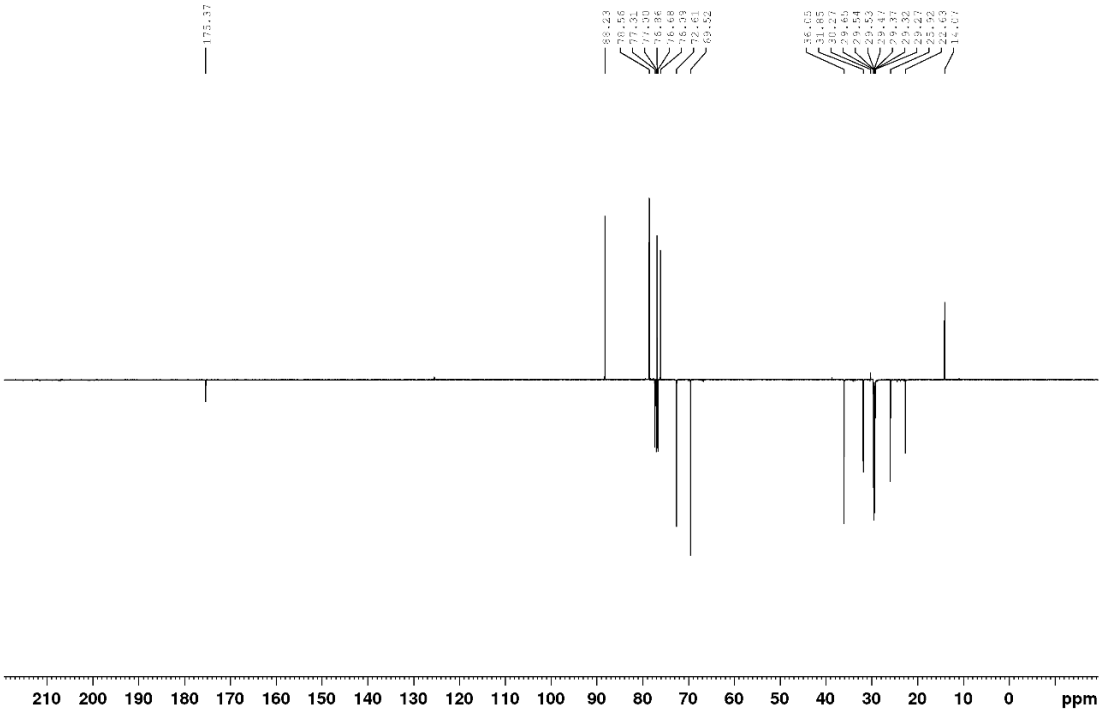


Fig. S-24. ^{13}C-NMR spectrum of **8** (100 MHz, $CDCl_3$).

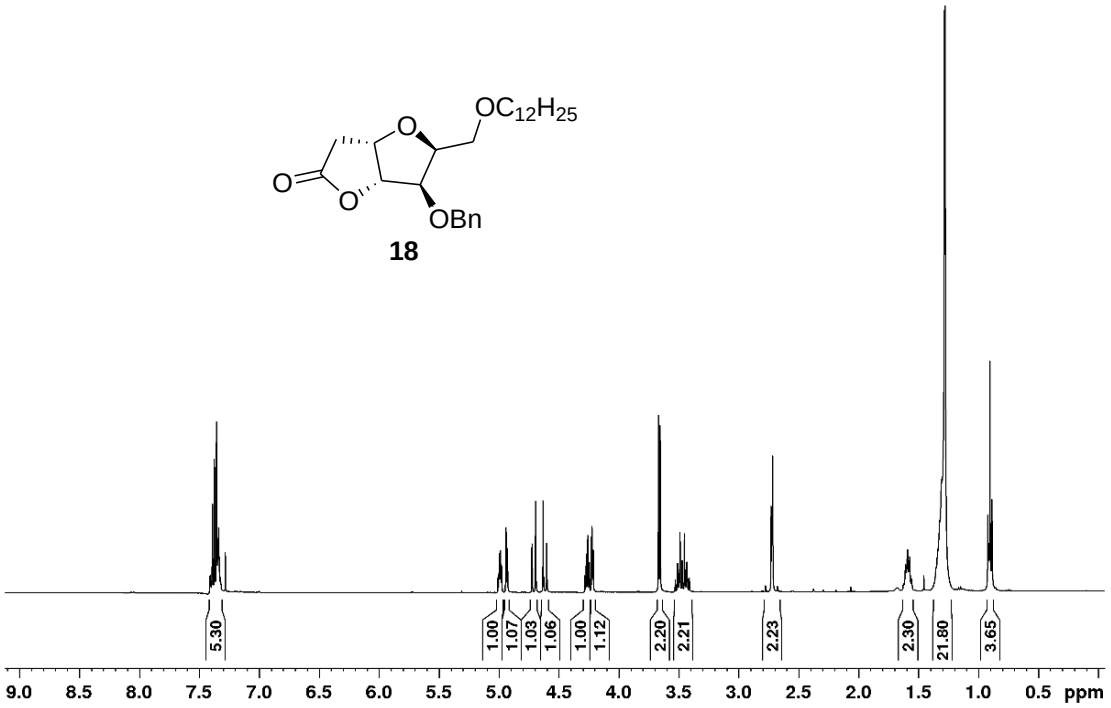


Fig. S-25. ^{1}H-NMR spectrum of **18** (400 MHz, $CDCl_3$).

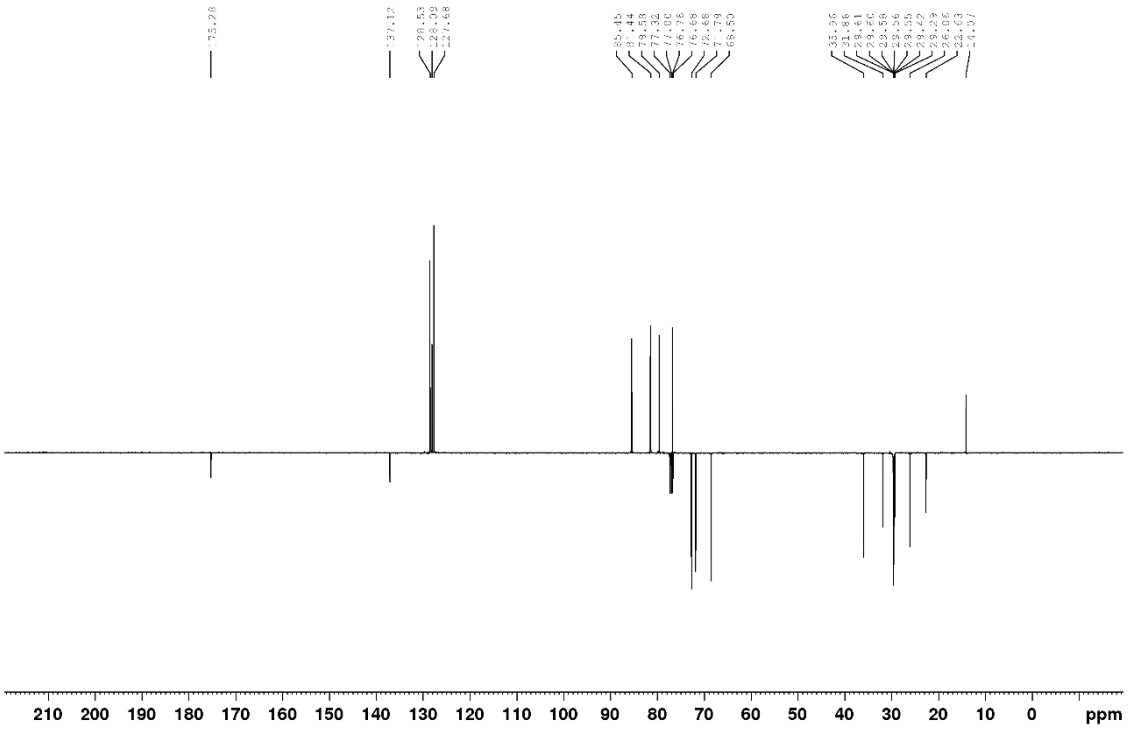
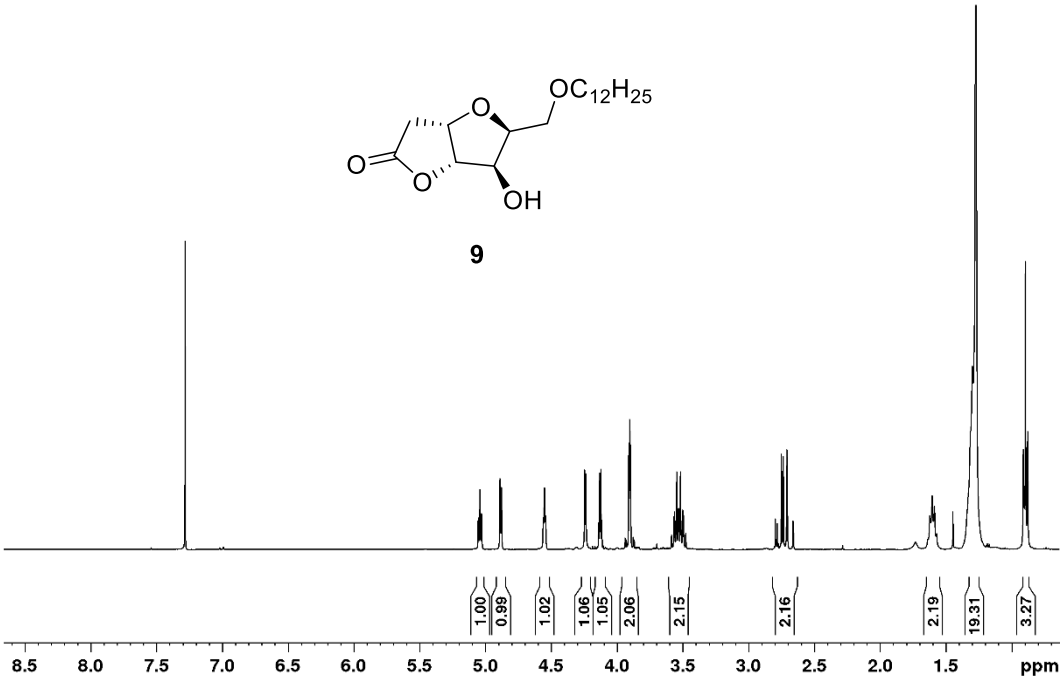


Fig. S-26. ^{13}C-NMR spectrum of **18** (100 MHz, $CDCl_3$).



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323 Fig. S-27. ^{1}H-NMR spectrum of **9** (400 MHz, $CDCl_3$).

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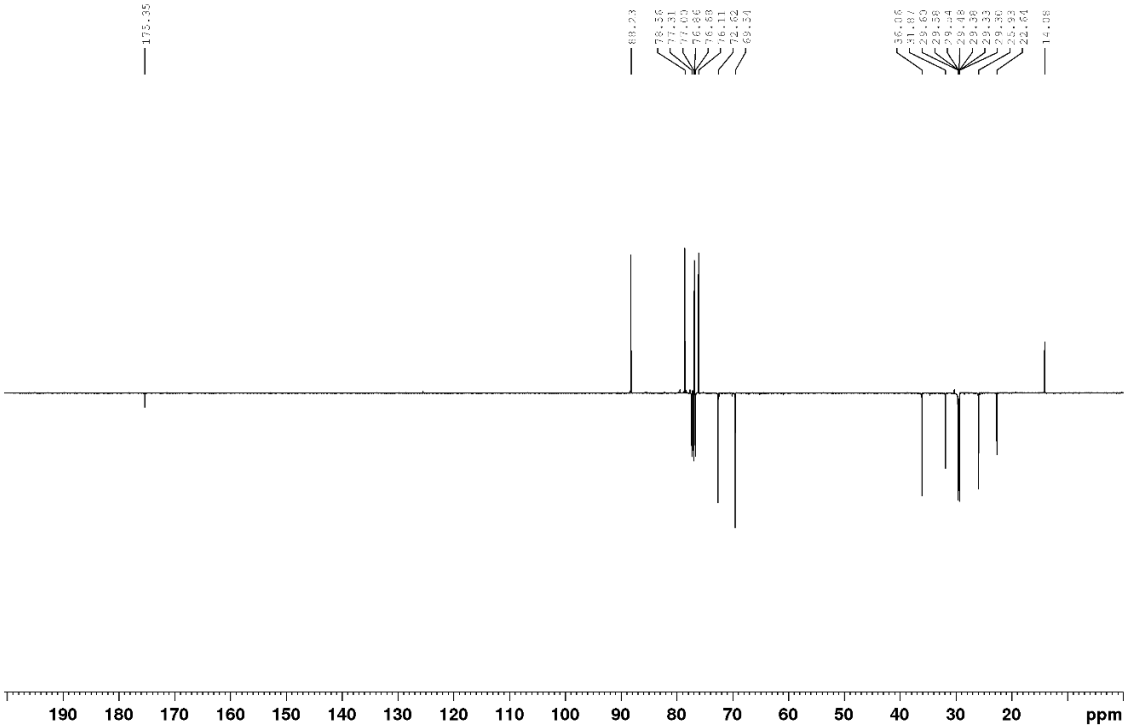

327

328 Fig. S-28. ^{13}C-NMR spectrum of **9** (100 MHz, $CDCl_3$).

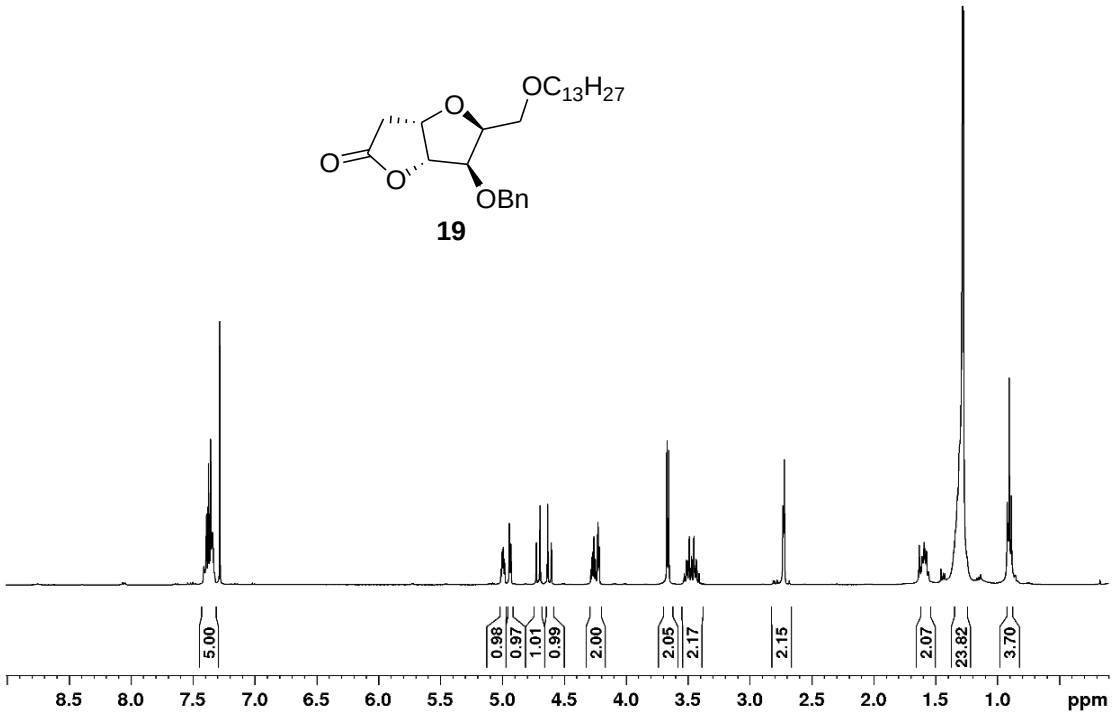

Fig. S-29. ^{1}H-NMR spectrum of **19** (400 MHz, $CDCl_3$).

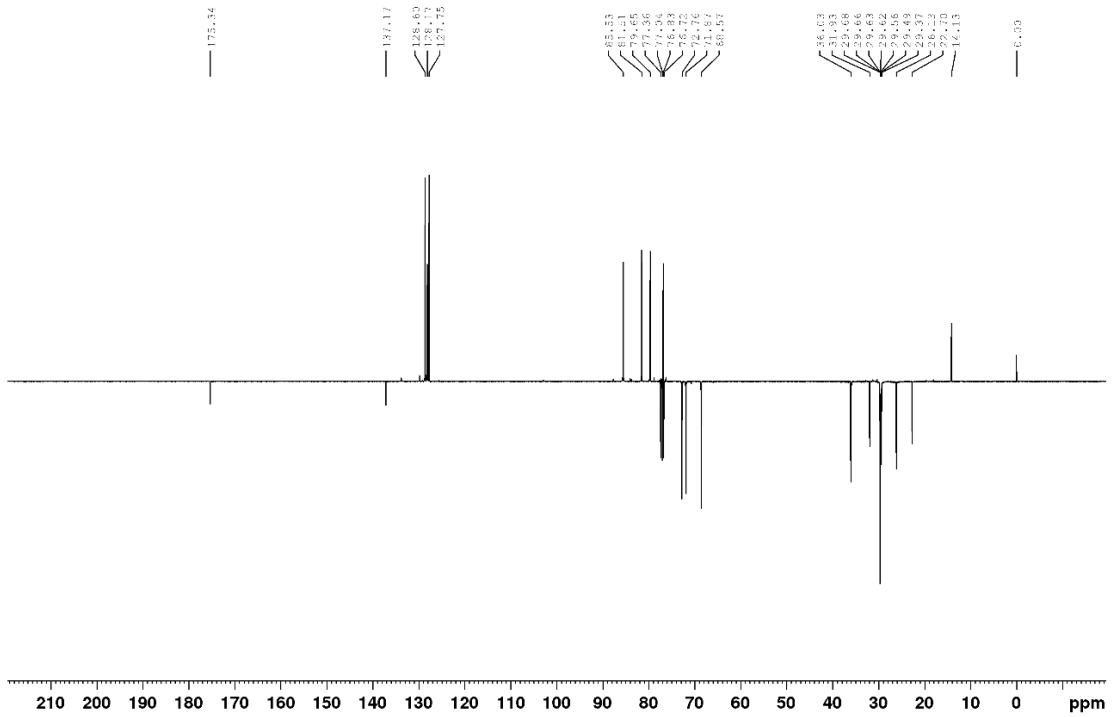

Fig. S-30. ^{13}C-NMR spectrum of **19** (100 MHz, $CDCl_3$).

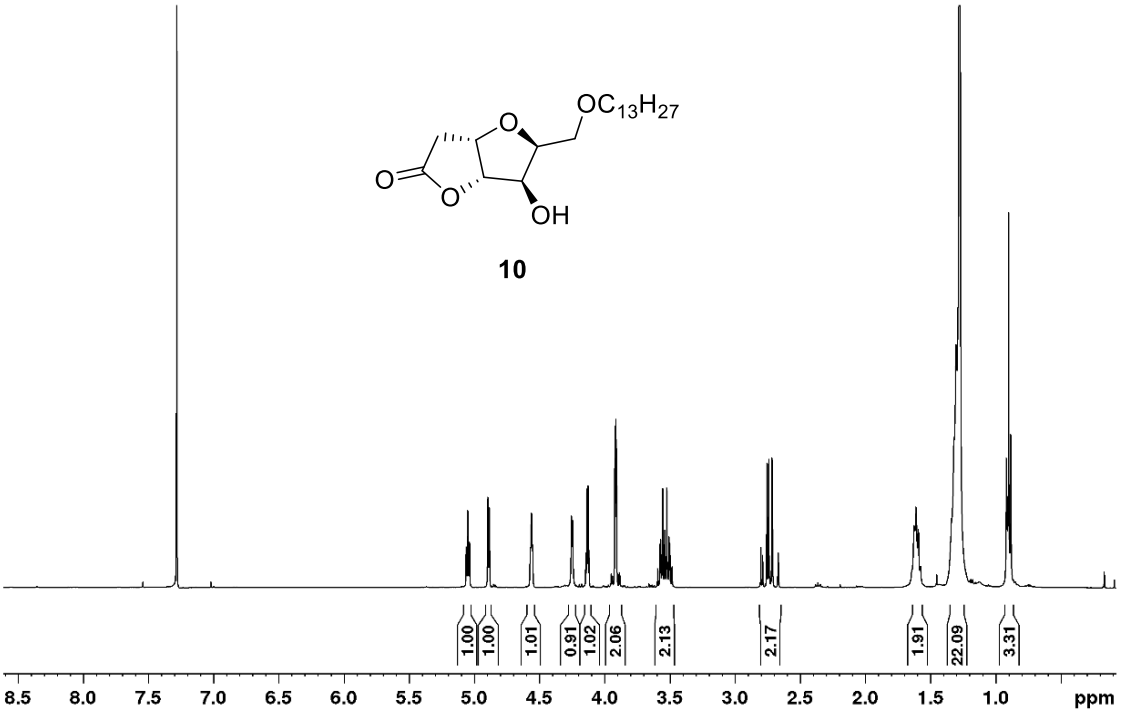

Fig. S-31. ^{1}H-NMR spectrum of **10** (400 MHz, $CDCl_3$).

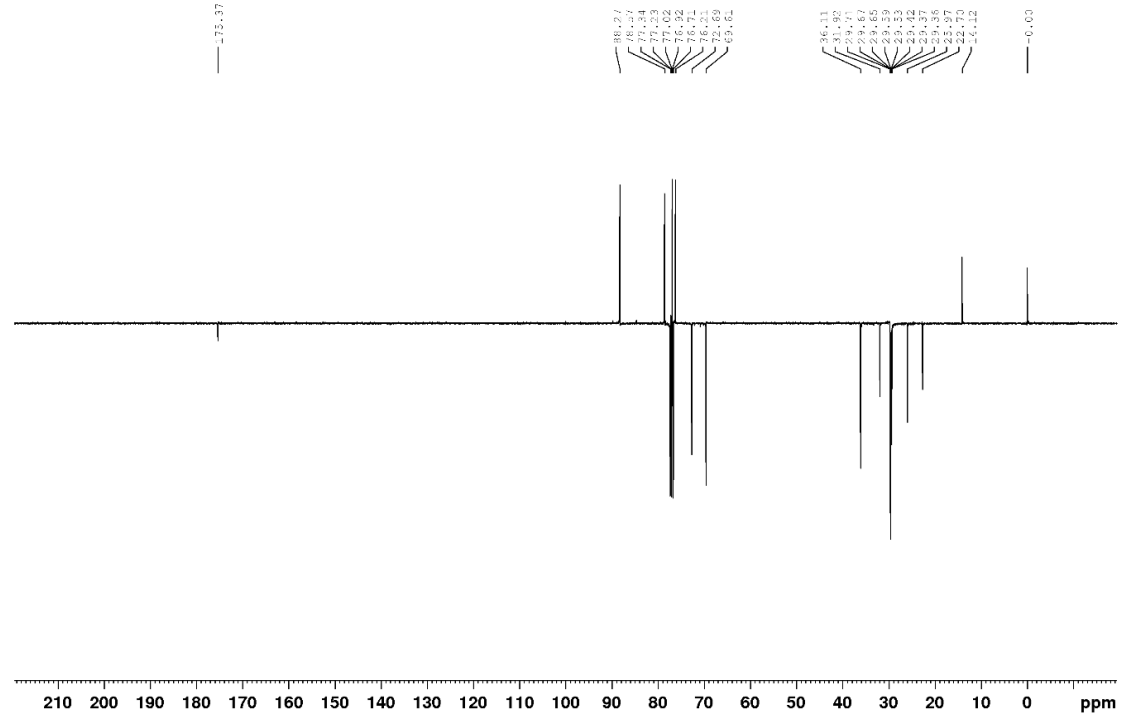

Fig. S-32. ^{13}C-NMR spectrum of **10** (100 MHz, $CDCl_3$).

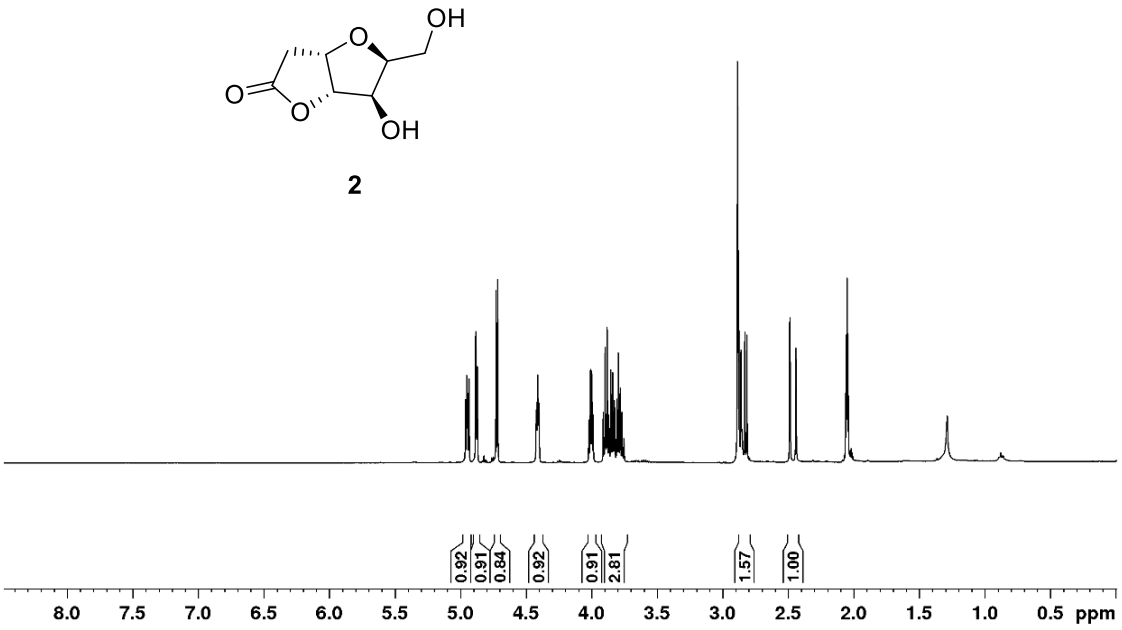

Fig. S-33. ^{1}H-NMR spectrum of **2** (400 MHz, acetone-d_6).

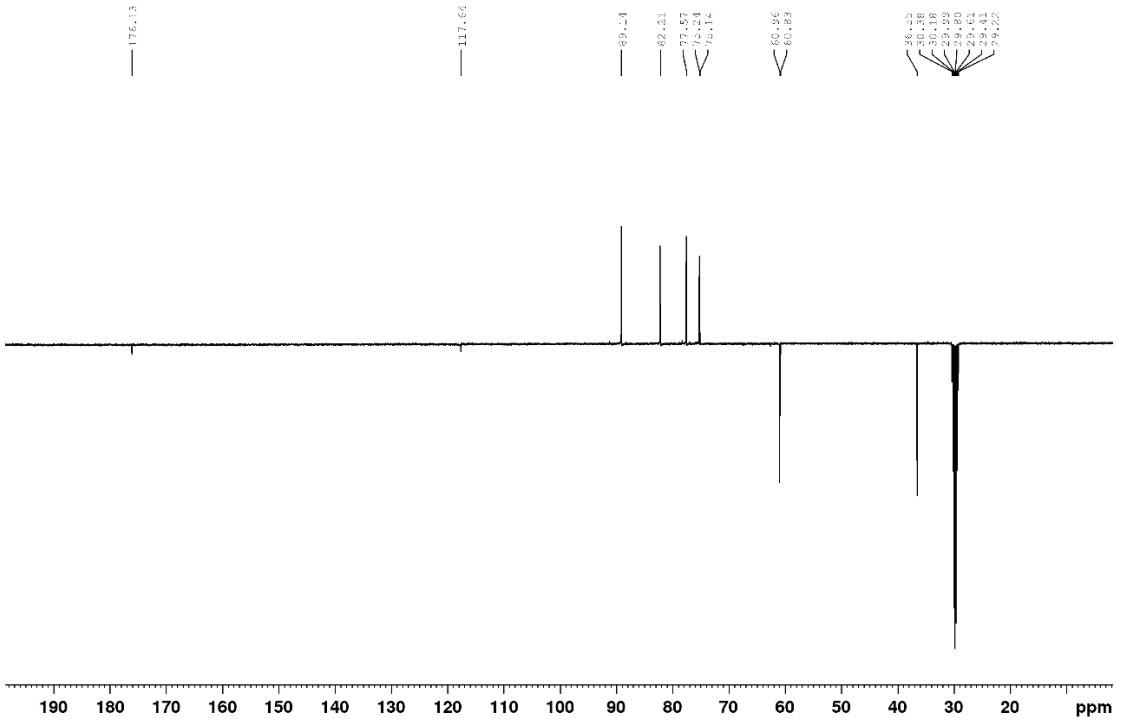

Fig. S-34. ^{13}C-NMR spectrum of **2** (100 MHz, acetone-d_6).

SAR ANALYSIS

TABLE S-1. Cytotoxicity data for SAR analysis.

Compounds	IC_{50} (μM) [a], 72 h							
	K562	HL-60	Jurkat	Raji	MCF-7	MDA-MB 231	HeLa	A549
1	2.96	224.61	2.49	23.42	51.27	598.66	785.31	2.36
2	2.69	9.97	9.51	7.40	9.64	0.24	5.22	31.45
3	0.70	4.91	8.87	1.11	12.34	15.62	3.54	2.43
4	1.02	1.10	11.53	5.98	2.38	9.76	0.56	4.43
5	0.74	0.68	19.78	4.25	0.34	28.70	3.41	4.19
6	8.61[b]	1.53[b]	6.64[b]	7.25	102.36	296.78	9.59[b]	0.92
7	1.25[b]	0.14[b]	103.27[b]	76.36	89.36	112.36	0.30[b]	29.05
8	0.18	1.83	16.26	2.79	2.28	26.57	4.11	7.72
9	3.46	8.25	8.02	3.52	5.31	7.63	2.25	3.96
10	4.87	3.96	4.29	4.88	15.36	36.47	10.32	0.025

[a] IC_{50} is the concentration of compound required to inhibit the cell growth by 50% compared to an untreated control. Values are means of three independent experiments. Coefficients of variation were less than 10%.

[b] Taken from reference 22.

The structure-activity relationships were accessed as follows: the IC_{50} values of two compounds were compared, and the Δ log IC_{50} was calculated (Δ log IC_{50} is a difference between the log IC_{50} values of an analogue and the corresponding control compound). Positive Δ log IC_{50} values show a decrease of antiproliferative activity, whereas negative values indicate an increase in the activity upon the structural modification being considered. The results are presented in Figure S-35.

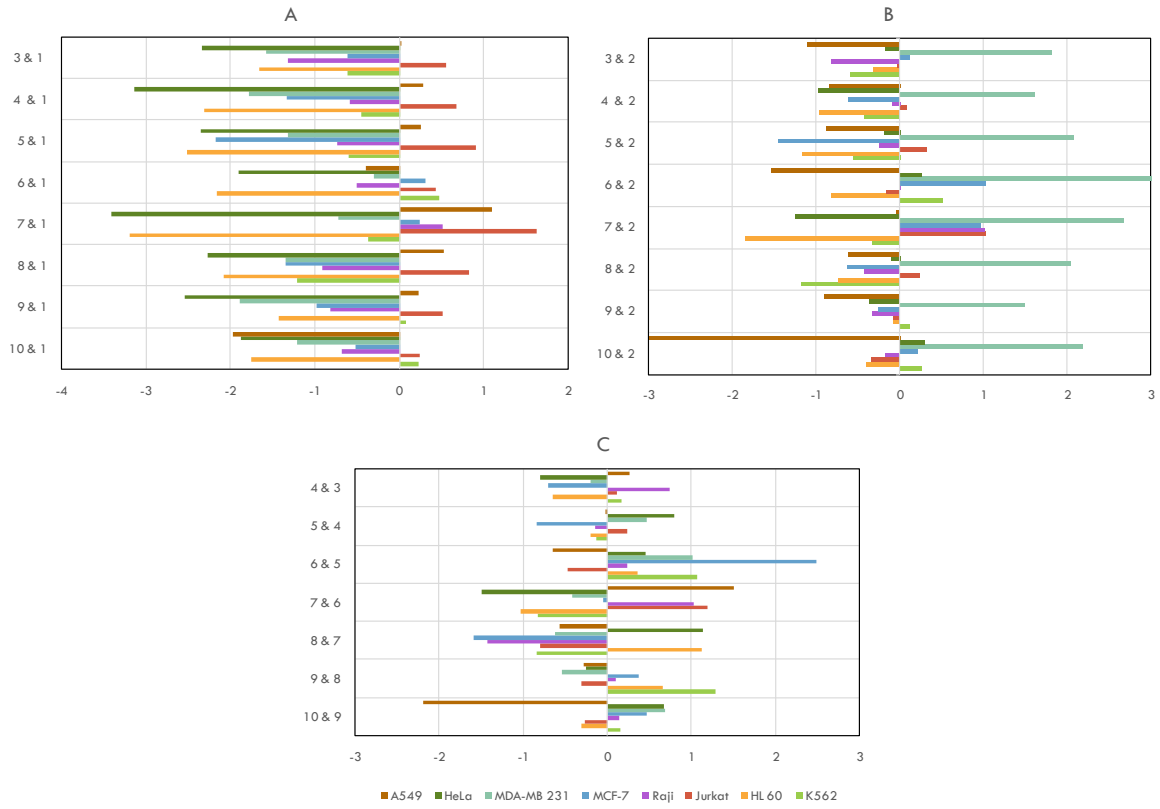

Fig. S-35. SAR Analysis. Influence of: (A) replacement of the hydroxybenzyl group in **1** with an alkoxymethyl chain; (B) introduction of an alkyl chain at the 7-OH position in molecule **2**; (C) increasing the number of carbon atoms in the side chain of analogues **3**–**10**.