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SUPPLEMENTARY MATERIAL TO

Novel (–)-goniofufurone mimics: Synthesis, antiproliferative activity and SAR analysis

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PHYSICAL AND SPECTRAL DATA OF THE SYNTHESIZED COMPOUNDS

*3,6-Anhydro-5-*O*-benzyl-7-*O*-hexyl-2-deoxy-*L*-ido-heptono-1,4-lactone* ***(12)***. Colourless oil; IR ($CHCl_3$, cm^{-1}): 1790 (C=O); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 0.89 (3H, *t*, J = 6.8 Hz, CH_3), 1.20–1.39 (6H, *m*, 3×CH_2 from side chain), 1.51–1.65 (2H, *m*, $OCH_2C\mathbf{H}_2(CH_2)_3CH_3$), 2.69 (1H, *dd*, $J_{2a,3}$ = 2.7, $J_{2a,2b}$ = 18.8 Hz, H-2a), 2.75 (1H, *dd*, $J_{2b,3}$ = 4.7, $J_{2a,2b}$ = 18.8 Hz, H-2b), 3.46 (2H, *m*, $OC\mathbf{H}_2(CH_2)_4CH_3$), 3.75 (2H, *d*, $J_{6,7}$ = 5.5 Hz, H-7), 4.21 (1H, *d*, $J_{5,6}$ = 4.1 Hz, H-5), 4.26 (1H, *td*, $J_{5,6}$ = 4.1, $J_{6,7}$ = 5.5 Hz H-6), 4.60 & 4.70 (2H, 2×*d*, J_{gem} = 11.9 Hz, $C\mathbf{H}_2Ph$), 4.92 (1H, *d*, $J_{3,4}$ = 4.7 Hz, H-4), 4.98 (1H, *td*, $J_{3,4}$ = 4.7, $J_{2a,3}$ = 2.9, $J_{2b,3}$ = 4.6 Hz, H-3), 7.30–7.45 (5H, *m*, Ph); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 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 ($O\mathbf{C}H_2(CH_2)_4CH_3$), 72.76 ($\mathbf{C}H_2Ph$), 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*): Calcd. for $C_{20}H_{28}NaO_5$: 371.18272. Found: 371.18344 (M^++Na); $[\alpha]_D$ = –17.4 (*c* 0.5, $CHCl_3$); R_F = 0.14 (3:2 light petroleum/Et_2O).

*3,6-Anhydro-5-*O*-benzyl-7-*O*-heptyl-2-deoxy-*L*-ido-heptono-1,4-lactone* ***(13)***. Colourless oil; IR ($CHCl_3$, cm^{-1}): 1789 (C=O); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 0.89 (3H, *t*, J = 6.8 Hz, CH_3), 1.19–1.41 (8H, *m*, 4×CH_2 from side chain), 1.58 (2H, *m*, $OCH_2C\mathbf{H}_2(CH_2)_4CH_3$), 2.69 (1H, *dd*, $J_{2a,2b}$ = 18.9, $J_{2a,3}$ = 2.6 Hz, H-2a), 2.74 (1H, *dd*, $J_{2a,2b}$ = 18.9, $J_{2b,3}$ = 4.7 Hz, H-2b), 3.38–3.54 (2H, *m*, $OC\mathbf{H}_2(CH_2)_5CH_3$), 3.65 (2H, *d*, $J_{6,7}$ = 5.5 Hz, H-7), 4.21 (1H, *d*, $J_{5,6}$ = 4.0 Hz, H-5), 4.27 (1H, *dd*, $J_{5,6}$ = 4.1, $J_{6,7}$ = 5.5 Hz, H-6), 4.60 & 4.70 (2H, 2×*d*,

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J_{gem} = 11.9 Hz, C**H**$_2$Ph), 4.92 (1H, *d*, $J_{3,4}$ = 4.7 Hz, H-4), 4.98 (1H, *td*, $J_{3,4}$ = 4.6, $J_{2a,3}$ = 2.9, $J_{2b,3}$ = 4.6 Hz, H-3), 7.29–7.40 (5H, *m*, Ph); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 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 (O**C**H$_2$(CH$_2$)$_5$CH$_3$), 72.76 (CH$_2$Ph), 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*): Calcd. for $C_{21}H_{30}NaO_5$: 385.19909. Found: 385.19874 (M^++Na); $[\alpha]_D$ = – 16.0 (*c* 0.5, $CHCl_3$); R_F = 0.28 (1:1 light petroleum/Et_2O).

3,6-Anhydro-5-O-*benzyl-7*-O-*octyl-2-deoxy*-L-ido-*heptono-1,4-lactone* ***(14)***. Colourless oil; IR ($CHCl_3$, cm^{-1}): 1790 (C=O); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 0.89 (3H, *t*, *J* = 6.9 Hz, CH_3), 1.22–1.38 (10H, *m*, 5×CH_2 from side chain), 1.58 (2H, *m*, OCH$_2$C**H**$_2$(CH$_2$)$_5$CH$_3$), 2.68 (1H, *dd*, $J_{2a,2b}$ = 18.7, $J_{2a,3}$ = 2.5 Hz, H-2a), 2.71 (1H, *dd*, $J_{2a,2b}$ = 18.7, $J_{2b,3}$ = 4.8 Hz, H-2b), 3.37–3.54 (2H, *m*, OC**H**$_2$(CH$_2$)$_6$CH$_3$), 3.65 (2H, *d*, $J_{6,7}$ = 5.5 Hz, H-7), 4.20 (1H, *d*, $J_{5,6}$ = 4.0 Hz, H-5), 4.25 (1H, *td*, $J_{5,6}$ = 4.1, $J_{6,7}$ = 5.5 Hz, H-6), 4.60 & 4.69 (2H, 2×*d*, J_{gem} = 11.9 Hz, C**H**$_2$Ph), 4.92 (1H, *d*, $J_{3,4}$ = 4.7 Hz, H-4), 4.97 (1H, *td*, $J_{3,4}$ = 4.8, $J_{2a,3}$ = 2.5, $J_{2b,3}$ = 4.8 Hz, H-3), 7.29–7.43 (5H, *m*, Ph); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 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 (O**C**H$_2$(CH$_2$)$_6$CH$_3$), 72.63 (**C**H$_2$Ph), 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*): Calcd. for $C_{22}H_{32}NaO_5$: 399.21474. Found: 399.21400 (M^++Na), Calcd. for $C_{22}H_{32}KO_5$: 415.18868. Found (*m/z*) 415.18765 (M^++K); $[\alpha]_D$ = –14.8 (*c* 0.5, $CHCl_3$); R_F = 0.25 (1:1 light petroleum/Et_2O).

3,6-Anhydro-5-O-*benzyl-7*-O-*nonyl-2-deoxy*-L-ido-*heptono-1,4-lactone* ***(15)***. Colourless crystals; m.p.: 34 °C (CH_2Cl_2/hexane), IR (film, cm^{-1}): 1773 (C=O). ^{1}H-NMR (250 MHz, $CDCl_3$, δ / ppm): 0.89 (3H, *t*, *J* = 6.9 Hz, CH_3), 1.18–1.39 (12H, *m*, 6×CH_2 from side chain), 1.57 (2H, *m*, OCH$_2$C**H**$_2$(CH$_2$)$_6$CH$_3$), 2.66–2.76 (2H, *pseudo d*, 2×H-2), 3.45 (2H, *m*, OC**H$_2$**(CH$_2$)$_7$CH$_3$), 3.65 (2H, *d*, $J_{6,7}$ = 5.4 Hz, H-7), 4.20 (1H, *d*, $J_{5,6}$ = 4.3 Hz, H-5), 4.26 (1H, *m*, $J_{5,6}$ = 4.3, $J_{6,7}$ = 5.4 Hz, H-6), 4.59 & 4.69 (2H, 2×*d*, J_{gem} = 11.9 Hz, C**H**$_2$Ph), 4.92 (1H, *d*, $J_{3,4}$ = 4.1 Hz, H-4), 4.98 (1H, *m*, $J_{3,2a}$ = 2.8, $J_{3,2b}$ = 3.1, $J_{3,4}$ = 4.1 Hz, H-3), 7.29–7.43 (5H, *m*, Ph); ^{13}C-NMR (62.9 MHz, $CDCl_3$, δ / ppm): 14.05 (Me), 22.60, 26.04, 29.20, 29.40, 29.48, 29.58 & 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 & 137.10 (Ph), 175.29 (C-1); LRMS (ESI^+) (*m/z*): 429 (M^++K), 413 (M^++Na), 391 (M^++H); HRMS (ESI^+) (*m/z*): Calcd. for $C_{23}H_{35}O_5$: 391.2479. Found: 391.2482 (M^++H), Calcd. for $C_{23}H_{38}NO_5$: 408.2744. Found: 408.2745 (M^++NH_4), Calcd. for $C_{23}H_{34}NaO_5$: 413.2298. Found: 413.2290 (M^++Na), Calcd. for $C_{23}H_{34}KO_5$: 429.2038. Found: 429.2034 (M^++K); $[\alpha]_D$ = –10.8 (*c* 0.75, $CHCl_3$); R_F = 0.33 (1:1 Et_2O/light petroleum).

3,6-Anhydro-5-O-*benzyl-7*-O-*decyl-2-deoxy*-L-ido-*heptono-1,4-lactone* ***(16)***. Colourless oil; Anal. Calcd. for $C_{24}H_{36}O_5$: C, 71.26; H, 8.97 %. Found: C, 71.60; H, 9.29 %; IR (film, cm^{-1}): 1788 (C=O). ^{1}H-NMR (250 MHz, $CDCl_3$, δ / ppm): 0.89 (3H, *t*, J = 7.0 Hz, CH_3), 1.21–1.41 (14H, *m*, 7×CH_2 from side chain), 1.49–1.64 (2H, *m*, $OCH_2C\mathbf{H}_2(CH_2)_7CH_3$), 2.72 (2H, *pseudo d*, 2×H-2), 3.46 (2H, *m*, OCH_2 from side chain), 3.65 (2H, *d*, $J_{6,7}$ = 5.3 Hz, 2×H-7), 4.21 (1H, *d*, $J_{5,6}$ = 4.1 Hz, H-5), 4.26 (1H, *m*, $J_{5,6}$ = 4.1, $J_{6,7}$ = 5.3 Hz, H-6), 4.60 & 4.70 (2H, 2×*d*, J_{gem} = 11.9 Hz, C$\mathbf{H}_2$Ph), 4.92 (1H, d, $J_{3,4}$ = 4.7 Hz, H-4), 4.99 (1H, *m*, $J_{3,4}$ = 4.7 Hz, H-3), 7.30–7.42 (5H, *m*, Ph); ^{13}C-NMR (62.9 MHz, $CDCl_3$, δ / ppm): 14.08 (Me), 22.66, 26.10, 29.30, 29.45, 29.55, 29.57, 29.63 & 31.87 (8×CH_2 from side chain), 36.00 (C-2), 68.53 (C-7), 71.84 (C-9), 72.74 (**C**H_2Ph), 76.79 (C-3), 79.62 (C-6), 81.50 (C-5), 85.51 (C-4), 127.71, 128.14, 128.56 & 137.15 (Ph), 175.29 (C-1); LRMS (CI) (*m/z*): 405 (M^++H); $[\alpha]_D$ = −11.1 (*c* 0.63, $CHCl_3$); R_F = 0.44 (1:1 light petroleum/Et_2O).

3,6-Anhydro-5-O-*benzyl-7*-O-*undecyl-2-deoxy*-L-ido-*heptono-1,4-lactone* ***(17)***. White crystals, m.p: 30–32 °C (CH_2Cl_2/hexane); IR ($CHCl_3$, cm^{-1}): 1788 (C=O); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 0.90 (3H, *t*, J = 7.0 Hz, CH_3), 1.22–1.38 (16H, *m*, 8×CH_2 from side chain), 1.57 (2H, *m*, $OCH_2C\mathbf{H}_2(CH_2)_8CH_3$), 2.69 (1H, *dd*, $J_{2a,2b}$ = 18.8, $J_{2a,3}$ = 2.7 Hz, H-2a), 2.75 (1H, *dd*, $J_{2a,2b}$ = 18.8, $J_{2b,3}$ = 4.7 Hz, H-2b), 3.39–3.53 (2H, *m*, $OC\mathbf{H}_2(CH_2)_9CH_3$), 3.66 (2H, *d,* $J_{6,7}$ = 5.5 Hz, H-7), 4.21 (1H, *brd*, $J_{5,6}$ = 4.0 Hz, H-5), 4.26 (1H, *td*, $J_{5,6}$ = 4.0, $J_{6,7}$ = 5.5 Hz, H-6), 4.62 & 4.71 (2H, 2×*d*, J_{gem} = 11.9 Hz, C$\mathbf{H}_2$Ph), 4.93 (1H, *dd*, $J_{3,4}$ = 4.7, $J_{4,5}$ = 0.9 Hz, H-4), 4.98 (1H, *td*, $J_{3,4}$ = 4.7, $J_{2a,3}$ = 2.8, $J_{2b,3}$ = 4.7 Hz, H-3), 7.29–7.40 (5H, *m*, Ph); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 14.08 (CH_3), 22.64, 26.07, 29.29, 29.43, 29.55, 29.57, 29.60, 29.65 & 31.86 (9×CH_2 from side chain), 35.97 (C-2), 68.51 (C-7), 71.81 (O**C**$H_2(CH_2)_9CH_3$), 72.70 (**C**H_2Ph), 76.77 (C-3), 79.59 (C-6), 81.45 (C-5), 85.47 (C-4), 127.69, 128.11, 128.54 & 137.12 (Ph), 175.29 (C=O); HRMS – Heated ESI-Orbitrap (*m/z*): Calcd. for $C_{25}H_{38}NaO_5$: 441.26169. Found: 441.26129 (M^++Na), Calcd. for $C_{25}H_{38}KO$: 457.23563. Found: 457.23465 (M^++K); $[\alpha]_D$ –12.8 (*c* 0.5, $CHCl_3$); R_F = 0.38 (3:2 light petroleum/Et_2O).

3,6-Anhydro-5-O-*benzyl-7*-O-*dodecyl-2-deoxy*-L-ido-*heptono-1,4-lactone* ***(18)***. White needles, m.p.: 45–46 °C (CH_2Cl_2/hexane); IR ($CHCl_3$, cm^{-1}): 1788 (C=O); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 0.89 (3H, *t*, J = 6.7 Hz, CH_3), 1.19–1.37 (18H, *m*, 9×CH_2 from side chain), 1.57 (2H, *m*, $OCH_2C\mathbf{H}_2(CH_2)_9CH_3$), 2.68 (1H, *dd*, $J_{2a,2b}$ = 18.8, $J_{2a,3}$ = 2.7 Hz, H-2a), 2.74 (1H, *dd*, $J_{2a,2b}$ = 18.8, $J_{2b,3}$ = 4.8 Hz, H-2b), 3.40–3.52 (2H, *m*, $OC\mathbf{H}_2(CH_2)_{10}CH_3$), 3.64 (2H, *d*, $J_{6,7}$ = 5.5 Hz, H-7), 4.21 (1H, *d*, $J_{5,6}$ = 4.1 Hz, H-5), 4.27 (1H, *td*, $J_{5,6}$ = 4.1, $J_{6,7}$ = 5.5 Hz, H-6), 4.60 & 4.70 (2H, 2×d, J_{gem} = 11.9 Hz, C$\mathbf{H}_2$Ph), 4.92 (1H, *dd*, $J_{3,4}$ = 4.7, $J_{4,5}$ = 0.8 Hz, H-4), 4.97 (1H, *td*, $J_{3,4}$

= 4.7, $J_{2a,3}$ = 2.8, $J_{2b,3}$ = 4.7 Hz, H-3), 7.29–7.40 (5H, *m*, Ph); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 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 (**C**H_2Ph), 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*): Calcd. for $C_{26}H_{40}NaO_5$: 455.27734. Found: 455.27712 (M^++Na), Calcd. for $C_{26}H_{40}KO_5$: 471.25128. Found: 471.25088 (M^++K); $[\alpha]_D$ = –13.0 (*c* 0.5, $CHCl_3$); R_F = 0.25 (3:2 light petroleum/Et_2O).

*3,6-Anhydro-5-*O*-benzyl-7-*O*-tridecyl-2-deoxy-L-*ido*-heptono-1,4-lactone* ***(19)***. White needles; m.p.: 44–46 °C (CH_2Cl_2/hexane), IR (KBr, cm^{-1}): 1791 (C=O); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 0.89 (3H, *t*, *J* = 6.8 Hz, CH_3), 1.20–1.37 (20H, *m*, 10×CH_2 from side chain), 1.58 (2H, *m*, $OCH_2C\mathbf{H}_2(CH_2)_{10}CH_3$), 2.69 (1H, *dd*, $J_{2a,2b}$ = 18.9, $J_{2a,3}$ = 2.9 Hz, H-2a), 2.74 (1H, *dd*, $J_{2a,2b}$ = 18.9, $J_{2b,3}$ = 4.7 Hz, H-2b), 3.37–3.53 (2H, *m*, $OC\mathbf{H}_2(CH_2)_{11}CH_3$), 3.65 (2H, *d*, $J_{6,7}$ = 5.5 Hz, H-7), 4.21 (1H, *d*, $J_{5,6}$ = 4.0 Hz, H-5), 4.26 (1H, *td*, $J_{5,6}$ = 4.1, $J_{6,7}$ = 5.5 Hz, H-6), 4.61 & 4.70 (2H, 2×*d*, J_{gem} = 11.9 Hz, C**H**$_2$Ph), 4.93 (1H, *d*, $J_{3,4}$ = 4.7 Hz, H-4), 4.97 (1H, *ddd*, $J_{3,4}$ = 4.7, $J_{2a,3}$ = 2.9, $J_{2b,3}$ = 4.6 Hz, H-3), 7.30–7.41 (5H, *m*, Ph); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 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_2Ph), 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*): Calcd. for $C_{27}H_{42}NaO_5$: 469.29299. Found: 469.29308 (M^++Na), Calcd. for $C_{27}H_{42}KO_5$: 485.26693. Found: 485.26669 (M^++K); $[\alpha]_D$ = –13.0 (*c* 0.5, $CHCl_3$); R_F = 0.13 (7:3 light petroleum/Et_2O).

*3,6-Anhydro-2-deoxy-*L*-*ido*-heptono-1,4-lactone* ***(2)***. White crystals; m.p.: 73–75 °C (EtOAc/ pentane), lit.[1] m.p.: 72–74 °C (EtOAc/pentane); IR ($CHCl_3$, cm^{-1}): 3378 (OH), 1780 (C=O); ^{1}H-NMR (400 MHz, acetone-d_6, δ / ppm): 2.46 (1H, *d*, $J_{2a,2b}$ = 18.4 Hz, H-2a), 2.85 (1H, *dd*, $J_{2a,2b}$ = 18.4, $J_{2b,3}$ = 6.2 Hz, H-2b), 2.89 (2H, *brs*, 2×OH), 3.77 (1H, *dd*, $J_{6,7a}$ = 5.5, $J_{7a,7b}$ = 11.0 Hz, H-7a), 3.83 (1H, *dd*, $J_{6,7b}$ = 5.3 Hz, $J_{7a,7b}$ = 11.0 Hz, H-7b), 4.00 (1H, *td*, $J_{5,6}$ = 3.5, $J_{6,7}$ = 5.0 Hz, H-6), 4.41 (1H, *t*, $J_{5,6}$ = 4.0 Hz, H-5), 4.88 (1H, *d*, $J_{3,4}$ = 4.3 Hz, H-4), 4.95 (1H, *dd*, $J_{3,4}$ = 4.4, $J_{2b,3}$ = 6.1 Hz, H-3); ^{13}C-NMR (100 MHz, acetone-d_6, δ / ppm): 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*): Calcd for $C_7H_{11}O_5$: 175.06010. Found: 175.06038 (M^++H), $[\alpha]_D$ = –25.0 (*c* 0.44, H_2O), lit.[1] $[\alpha]_D^{20}$ = –32.0 (*c* 0.6, H_2O); R_F = 0.16 (3:2 EtOAc/CH_2Cl_2).

*3,6-Anhydro-7-*O*-hexyl-2-deoxy-*L*-*ido*-heptono-1,4-lactone* ***(3)***. White crystals; m.p.: 47–49 °C (CH_2Cl_2/hexane); IR (KBr, cm^{-1}): 3290 (OH), 1775 (C=O); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 0.89 (3H, *t*, *J* = 6.8 Hz, CH_3), 1.22–1.38 (6H, *m*, 3×C**H**$_2$ from side chain), 1.59 (2H, *m*, $OCH_2C\mathbf{H}_2(CH_2)_3CH_3$), 2.67 (1H,

d, $J_{2a,2b}$ = 18.7 Hz, H-2a), 2.75 (1H, *dd*, $J_{2a,2b}$ = 18.7, $J_{2b,3}$ = 5.7 Hz, H-2b), 3.52. (2H, *m*, OC**H**$_2$(CH$_2$)$_4$CH$_3$), 3.88 (1H, *dd*, $J_{6,7a}$ = 3.0, $J_{7a,7b}$ = 11.2 Hz, H-7a), 3.91 (1H, *dd*, $J_{6,7b}$ = 3.4, $J_{7a,7b}$ = 11.2 Hz, H-7b), 4.12 (1H, *m*, H-6), 4.23 (1H, *d*, $J_{5,OH}$ = 3.6 Hz, OH), 4.54 (1H, *t*, H-5), 4.87 (1H, *d*, $J_{3,4}$ = 4.2 Hz, H-4), 5.01 (1H, *t*, $J_{3,4}$ = 4.7 Hz, H-3); ^{13}C-NMR (100 MHz, CDCl$_3$, δ / ppm): 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*): Calcd. for C$_{13}$H$_{22}$NaO$_5$: 281.13649. Found: 281.13567 (M$^+$+Na); $[\alpha]_D$ = –26.3 (*c* 0.3, CHCl$_3$); R_F = 0.15 (7:3 Et$_2$O/light petroleum).

3,6-Anhydro-7-O-*heptyl-2-deoxy*-L-ido-*heptono-1,4-lactone* ***(4)***. White crystals, m.p.: 41–42 °C (CH$_2$Cl$_2$/hexane); IR (KBr, cm^{-1}): 3434 (OH), 1784 (C=O); ^{1}H-NMR (400 MHz, CDCl$_3$, δ / ppm): 0.88 (3H, *t*, *J* = 6.9 Hz, CH$_3$), 1.20–1.36 (8H, *m*, 4×CH$_2$ from side chain), 1.59 (2H, *m*, OCH$_2$C**H**$_2$(CH$_2$)$_4$CH$_3$), 2.67 (1H, *d*, $J_{2a,2b}$ = 18.7 Hz, H-2a), 2.75 (1H, *dd*, $J_{2a,2b}$ = 18.7, $J_{2b,3}$ = 5.7 Hz, H-2b), 3.52 (2H, *m*, OC**H**$_2$(CH$_2$)$_5$CH$_3$), 3.88 (1H, *dd*, $J_{6,7a}$ = 3.1, $J_{7a,7b}$ = 11.1 Hz, H-7a), 3.91 (1H, *dd*, $J_{6,7b}$ = 3.4, $J_{7a,7b}$ = 11.1 Hz, H-7b), 4.12 (1H, *m*, H-6), 4.23 (1H, *d*, $J_{5,OH}$ = 3.7 Hz, OH), 4.54 (1H, *t*, $J_{5,6}$ = 3.1 Hz, H-5), 4.87 (1H, *d*, $J_{3,4}$ = 4.2 Hz, H-4), 5.01 (1H, *m*, H-3); ^{13}C-NMR (100 MHz, CDCl$_3$, δ / ppm): 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 (O**C**H$_2$(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*): Calcd. for C$_{14}$H$_{24}$NaO$_5$: 295.15214. Found: 295.15146 (M$^+$+Na), $[\alpha]_D$ = –33.2 (*c* 0.5, CHCl$_3$); R_F = 0.15 (7:3 Et$_2$O/light petroleum).

3,6-Anhydro-7-O-*octyl-2-deoxy*-L-ido-*heptono-1,4-lactone* ***(5)***. White crystals; m.p.: 51–53 °C (CH$_2$Cl$_2$/hexane); IR (KBr, cm^{-1}): 3430 (OH), 1777 (C=O); ^{1}H-NMR (400 MHz, CDCl$_3$, δ / ppm): 0.88 (3H, *t*, *J* = 6.9 Hz, CH$_3$), 1.20–1.37 (10H, *m*, 5×CH$_2$ from side chain), 1.60 (2H, *m*, OCH$_2$C**H**$_2$(CH$_2$)$_5$CH$_3$), 2.68 (1H, *d*, $J_{2a,2b}$ = 18.6 Hz, H-2a), 2.76 (1H, *dd*, $J_{2a,2b}$ = 18.6, $J_{2b,3}$ = 5.7 Hz, H-2b), 3.52 (2H, *m*, OC**H**$_2$(CH$_2$)$_6$CH$_3$), 3.88 (1H, *dd*, $J_{6,7a}$ = 3.0, $J_{7a,7b}$ = 11.1 Hz, H-7a), 3.90 (1H, *dd*, $J_{6,7b}$ = 3.4, $J_{7a,7b}$ = 11.1 Hz, H-7b), 4.12 (1H, *m*, H-6), 4.25 (1H, *brs*, OH), 4.55 (1H, *d*, $J_{5,6}$ = 3.2 Hz, H-5), 4.88 (1H, *d*, $J_{3,4}$ = 4.2 Hz, H-4), 5.01 (1H, *m*, H-3); ^{13}C-NMR (100 MHz, CDCl$_3$, δ / ppm): 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 (O**C**H$_2$(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*): Calcd. for C$_{15}$H$_{26}$NaO$_5$: 309.16779. Found: 309.16760 (M$^+$+Na), $[\alpha]_D$ –26.2 (*c* 0.5, CHCl$_3$); R_F = 0.19 (4:1 Et$_2$O/light petroleum).

3,6-Anhydro-7-O-*nonyl-2-deoxy*-L-ido-*heptono-1,4-lactone* ***(6)***. Colourless crystals; m.p.: 53 °C (CH$_2$Cl$_2$/hexane), IR (film, cm^{-1}): 3277 (OH), 1774 (C=O); For ^{1}H- and ^{13}C-NMR spectra see, ref. 2; HRMS (*m/z*): Calcd. for C$_{16}$H$_{29}$O$_5$:

301.2010. Found: 301.2000 (M^++H), Calcd. for $C_{16}H_{32}NO_5$: 318.2275. Found: 318.2266 (M^++NH_4); $[\alpha]_D$ = −35.0 (*c* 0.5, $CHCl_3$); R_F = 0.32 (Et_2O).

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

3,6-Anhydro-7-O-*undecyl-2-deoxy*-L-ido-*heptono-1,4-lactone (**8**)*. White crystals, m.p.: 57 °C (CH_2Cl_2/hexane); IR (KBr, cm^{-1}): 3444 (OH), 1775 (C=O); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 0.88 (3H, *t*, *J* = 7.1 Hz, CH_3), 1.21–1.34 (16H, *m*, 8×CH_2 from side chain), 1.59 (2H, *m*, $OCH_2C\mathbf{H}_2(CH_2)_8CH_3$), 2.67 (1H, *d*, $J_{2a,2b}$ = 18.7 Hz, H-2a), 2.75 (1H, *dd*, $J_{2a,2b}$ = 18.7, $J_{2b,3}$ = 5.7 Hz, H-2b), 3.52 (2H, *m*, $OC\mathbf{H}_2(CH_2)_9CH_3$), 3.87 (1H, *dd*, $J_{6,7a}$ = 3.1, $J_{7a,7b}$ = 11.1 Hz, H-7a), 3.90 (1H, *dd*, $J_{6,7b}$ = 3.4, $J_{7a,7b}$ = 11.1 Hz, H-7b), 4.11 (1H, *m*, H-6), 4.53 (1H, *d*, $J_{5,6}$ = 3.3 Hz, H-5), 4.87 (1H, *d*, $J_{3,4}$ = 4.3 Hz, H-4), 5.03 (1H, *m*, H-3); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 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 ($O\mathbf{C}H_2(CH_2)_9CH_3$), 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*): Calcd. for $C_{18}H_{32}NaO_5$: 351.21474. Found: 351.21415 (M^++Na); $[\alpha]_D$ –26.6 (*c* 0.5, $CHCl_3$); R_F = 0.15 (7:3 Et_2O/light petroleum).

3,6-Anhydro-7-O-*dodecyl-2-deoxy*-L-ido-*heptono-1,4-lactone (**9**)*. White needles, m.p.: 69–70 °C (CH_2Cl_2/hexane); IR (KBr, cm^{-1}): 3447 (OH), 1775 (C=O); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 0.88 (3H, *t*, *J* = 6.8 Hz, CH_3), 1.20–1.36 (18H, *m*, 9×CH_2 from side chain), 1.59 (2H, *m*, $OCH_2C\mathbf{H}_2(CH_2)_9CH_3$), 2.66 (1H, *d*, $J_{2a,2b}$ = 18.6 Hz, H-2a), 2.75 (1H, *dd*, $J_{2a,2b}$ = 18.6, $J_{2b,3}$ = 5.7 Hz, H-2b), 3.52 (2H, *m*, $OC\mathbf{H}_2(CH_2)_{10}CH_3$), 3.86 (1H, *dd*, $J_{6,7a}$ = 3.1, $J_{7a,7b}$ = 11.0 Hz, H-7a), 3.91 (1H, *dd*, $J_{6,7b}$ = 3.4, $J_{7a,7b}$ = 11.1 Hz, H-7b), 4.11 (1H, *m*, H-6), 4.22 (1H, *d*, $J_{5,OH}$ = 3.7 Hz, OH), 4.53 (1H, *t*, $J_{5,6}$ = 3.3 Hz, H-5), 4.86 (1H, *d,* $J_{3,4}$ = 4.1 Hz, H-4), 5.01 (1H, *m*, H-3); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 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 ($O\mathbf{C}H_2(CH_2)_{10}CH_3$), 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*): Calcd. for $C_{19}H_{34}NaO_5$: 365.23039. Found: 365.23022 (M^++Na); $[\alpha]_D$ = –25.0 (*c* 0.5, $CHCl_3$); R_F = 0.15 (3:2 Et_2O/light petroleum).

3,6-Anhydro-7-O-*tridecyl-2-deoxy*-L-ido-*heptono-1,4-lactone (**10**)*. White needles, m.p.: 63–65 °C (CH_2Cl_2/hexane); IR (KBr, cm^{-1}): 3450 (OH), 1785 (C=O); ^{1}H-NMR (400 MHz, $CDCl_3$, δ / ppm): 0.89 (3H, *t*, *J* = 6.8 Hz, CH_3), 1.21–1.34 (20H, *m*, 10×CH_2 from side chain), 1.59 (2H, *m*, $OCH_2C\mathbf{H}_2(CH_2)_{10}CH_3$), 2.68 (1H, *d*, $J_{2a,2b}$ = 18.6 Hz, H-2a), 2.76 (1H, *dd*,

$J_{2a,2b}$ = 18.6, $J_{2b,3}$ = 5.6 Hz, H-2b), 3.52 (2H, *m*, OC**H**$_2$(CH$_2$)$_{11}$CH$_3$), 3.88 (1H, *dd*, $J_{6,7a}$ = 3.0, $J_{7a,7b}$ = 11.1 Hz, H-7a), 3.92 (1H, *dd*, $J_{6,7b}$ = 3.4, $J_{7a,7b}$ = 11.1 Hz, H-7b), 4.12 (1H, *m*, H-6), 4.24 (1H, *d*, $J_{5,OH}$ = 3.7 Hz, OH), 4.55 (1H, *t*, $J_{5,6}$ = 3.0 Hz, H-5), 4.88 (1H, *d*, $J_{3,4}$ = 4.1 Hz, H-4), 5.04 (1H, *m*, H-3); ^{13}C-NMR (100 MHz, $CDCl_3$, δ / ppm): 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 (O**C**H$_2$(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*): Calcd. for $C_{20}H_{36}NaO_5$: 379.24604. Found: 379.24528 (M^++Na); $[\alpha]_D$ = –19.3 (*c* 0.5, $CHCl_3$); R_F = 0.17 (7:3 Et_2O/light petroleum).

NMR SPECTRA OF FINAL PRODUCTS

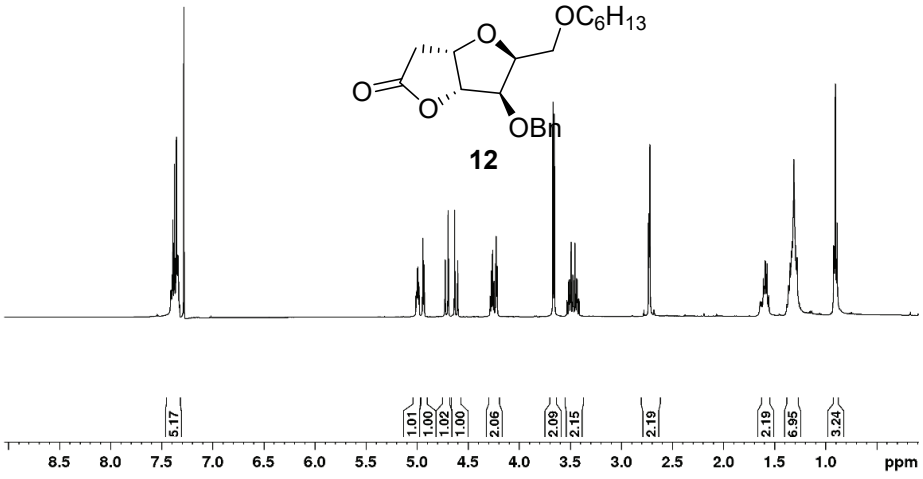

Fig. S-1. ^{1}H-NMR spectrum of **12** (400 MHz, $CDCl_3$).

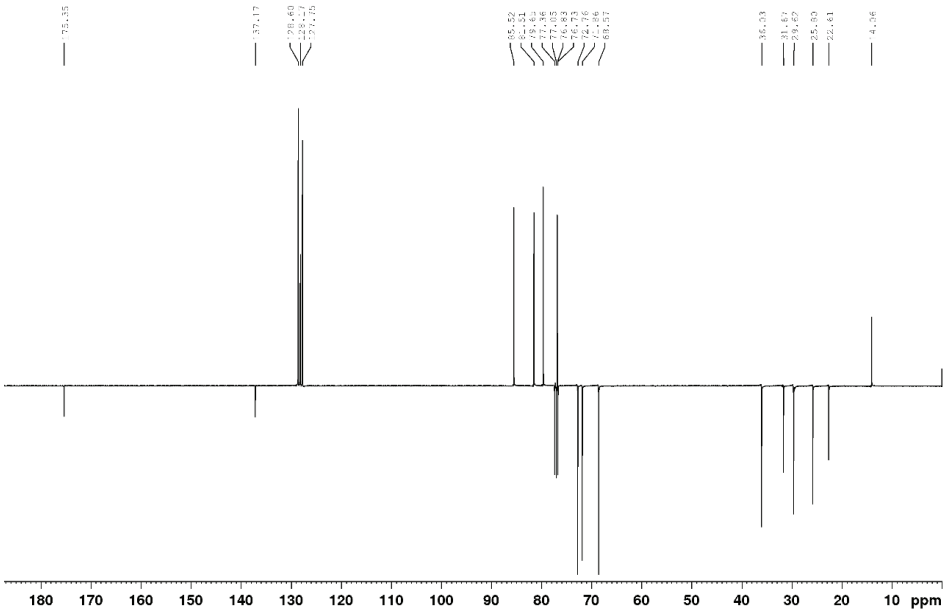

Fig. S-2. ^{13}C-NMR spectrum of **12** (100 MHz, $CDCl_3$).

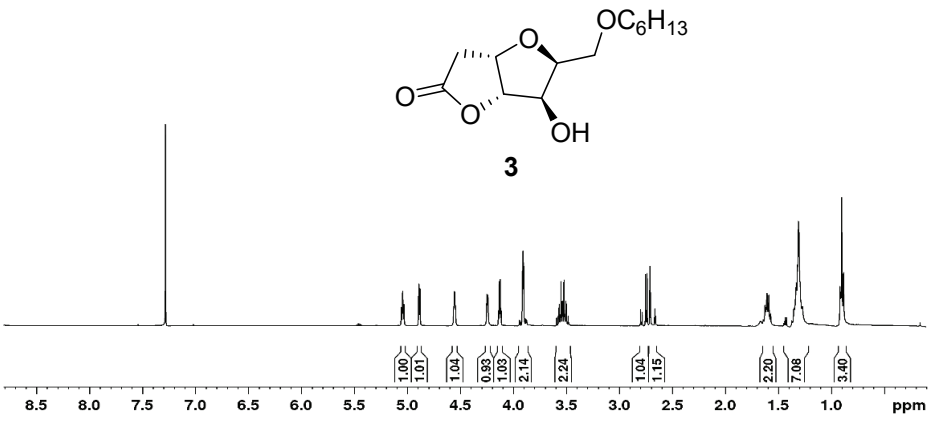

Fig. S-3. ^{1}H-NMR spectrum of **3** (400 MHz, $CDCl_3$).

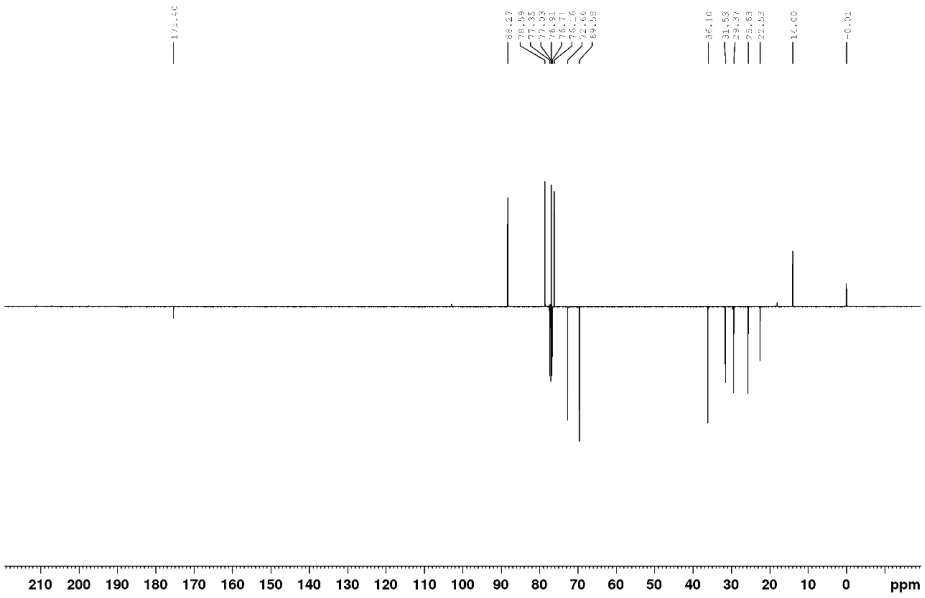

Fig. S-4. ^{13}C-NMR spectrum of **3** (100 MHz, $CDCl_3$).

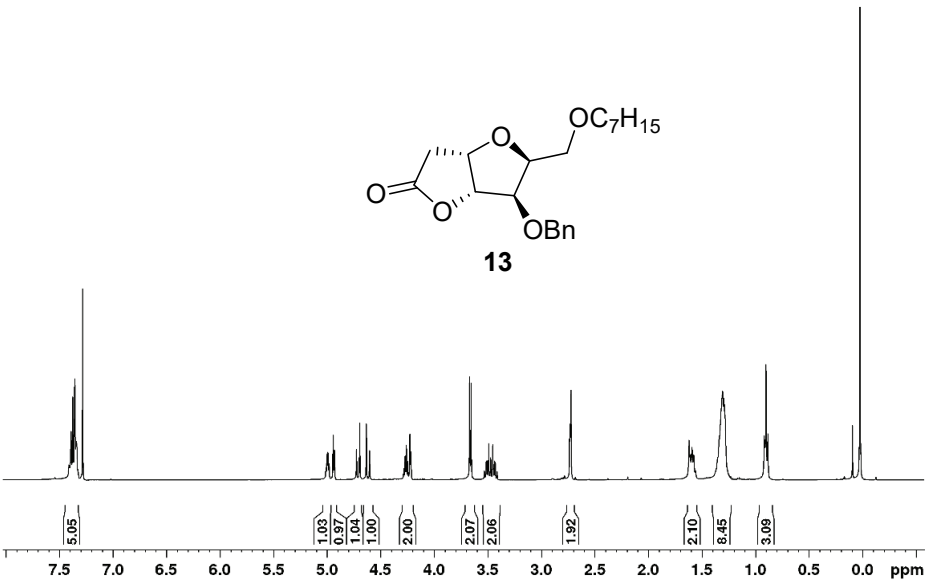

Fig. S-5. ^{1}H-NMR spectrum of **13** (400 MHz, $CDCl_3$).

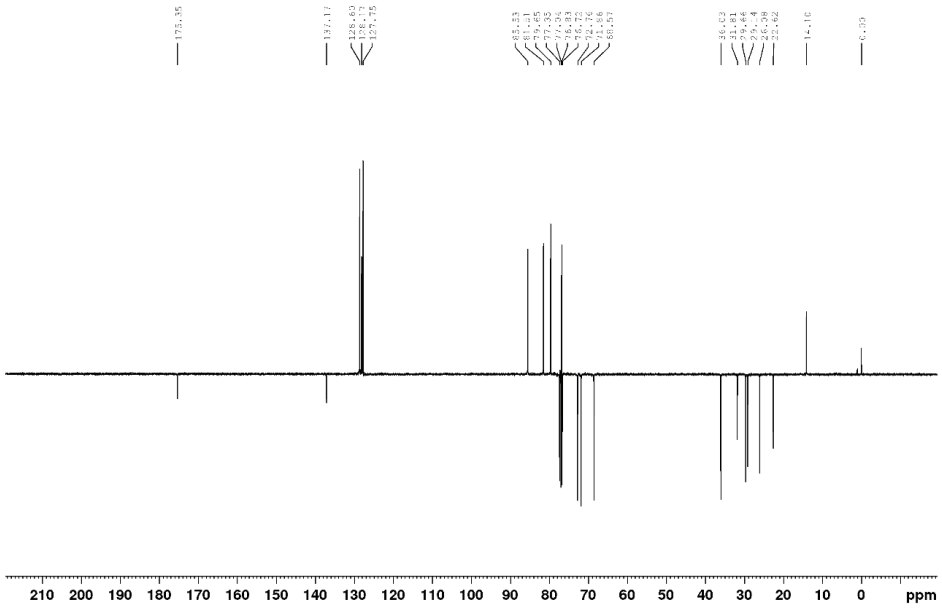

Fig. S-6. ^{13}C-NMR spectrum of **13** (100 MHz, $CDCl_3$).

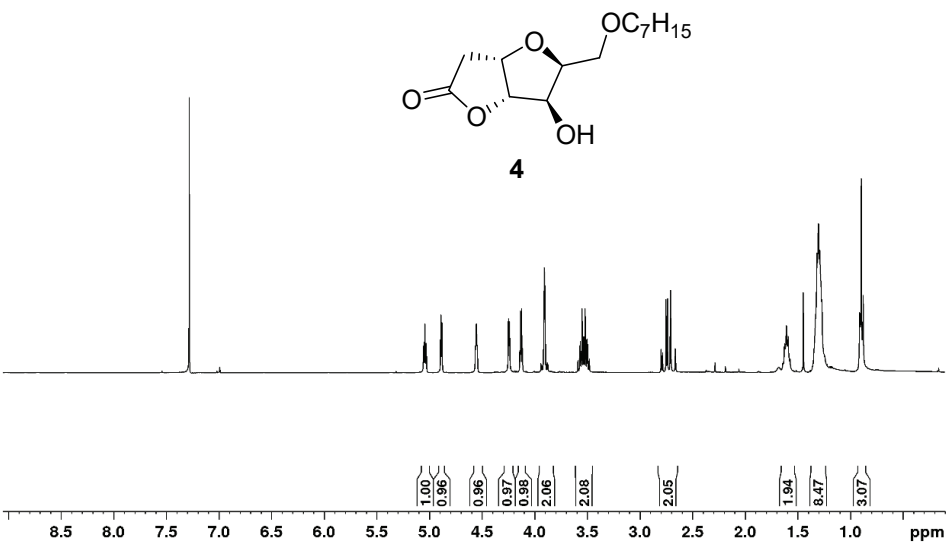

Fig. S-7. ^{1}H-NMR spectrum of **4** (400 MHz, $CDCl_3$).

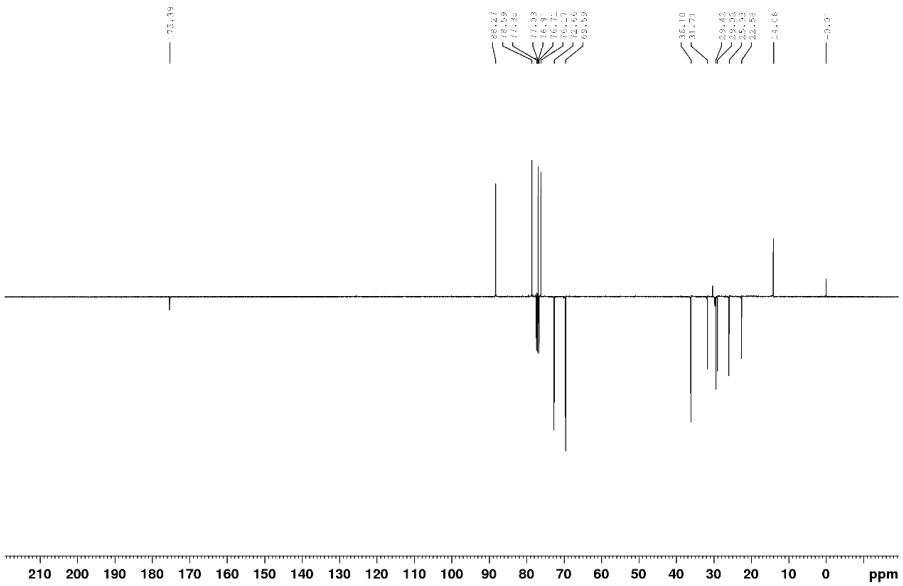

Fig. S-8. ^{13}C-NMR spectrum of **4** (100 MHz, $CDCl_3$).

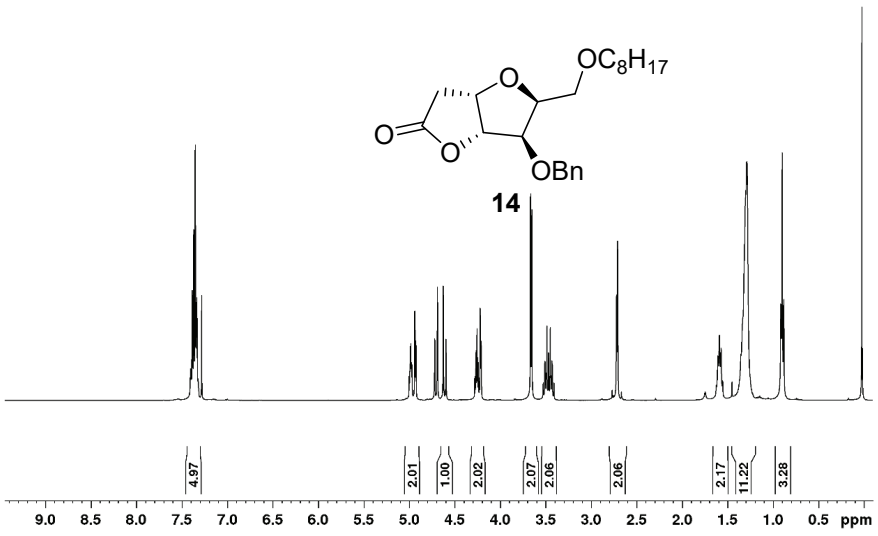

Fig. S-9. ^{1}H-NMR spectrum of **14** (400 MHz, $CDCl_3$).

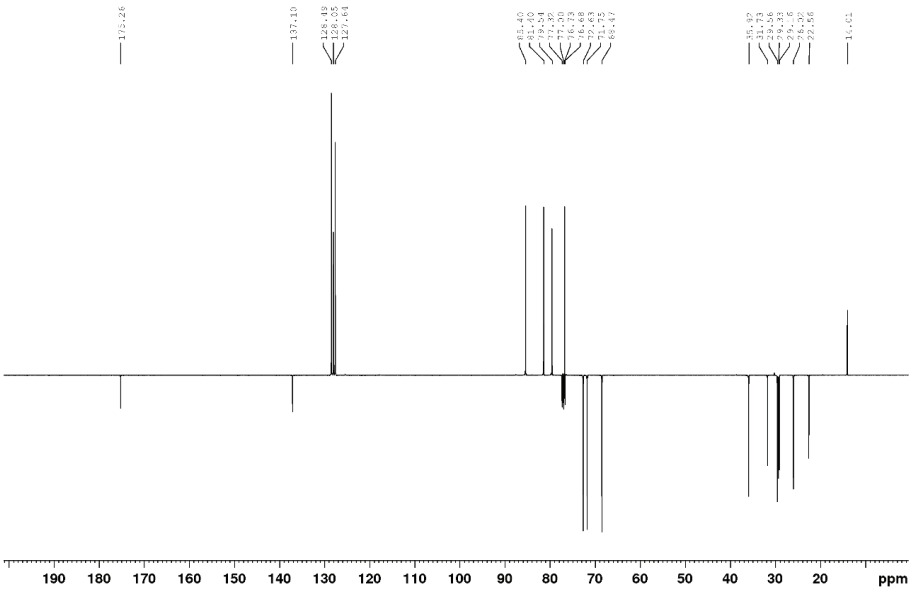

Fig. S-10. ^{13}C-NMR spectrum of **14** (100 MHz, $CDCl_3$).

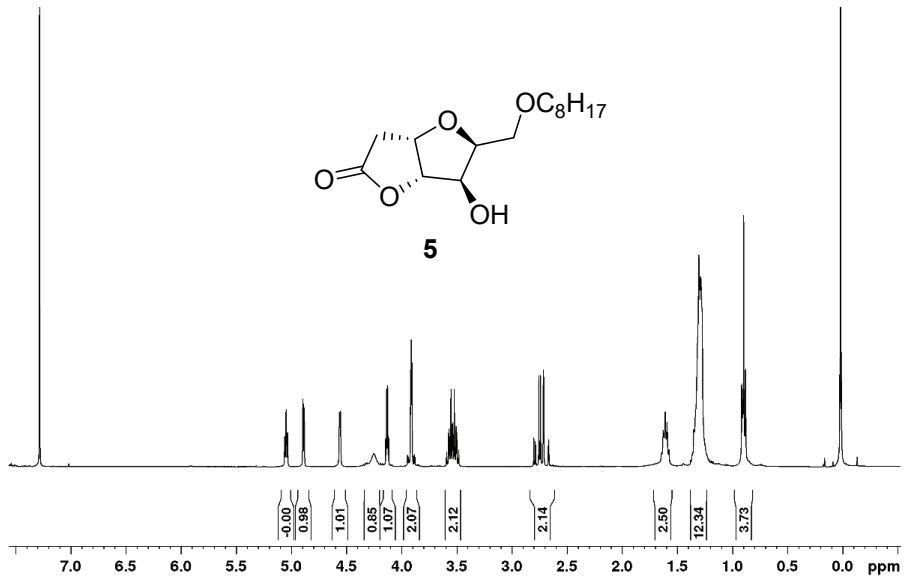

Fig. S-11. ^{1}H-NMR spectrum of **5** (400 MHz, $CDCl_3$).

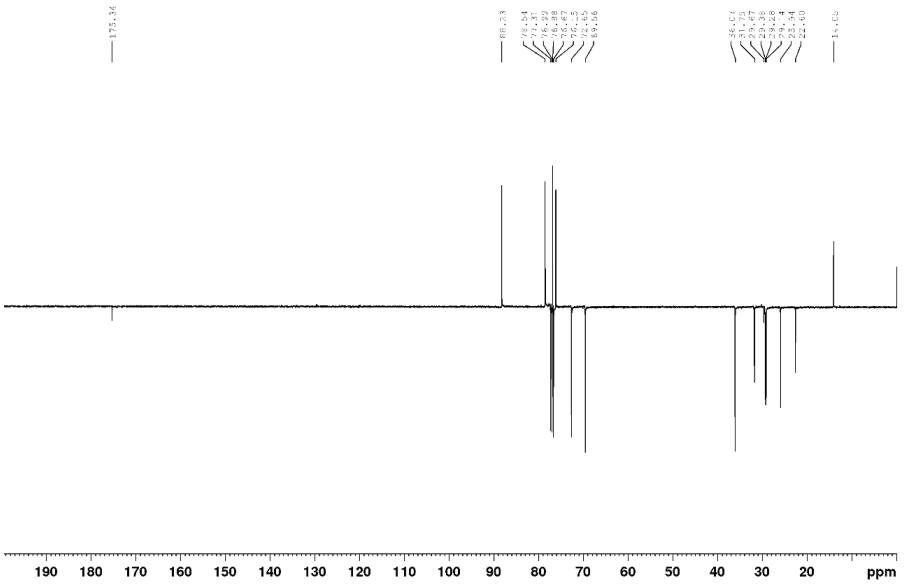

Fig. S-12. ^{13}C-NMR spectrum of **5** (100 MHz, $CDCl_3$).

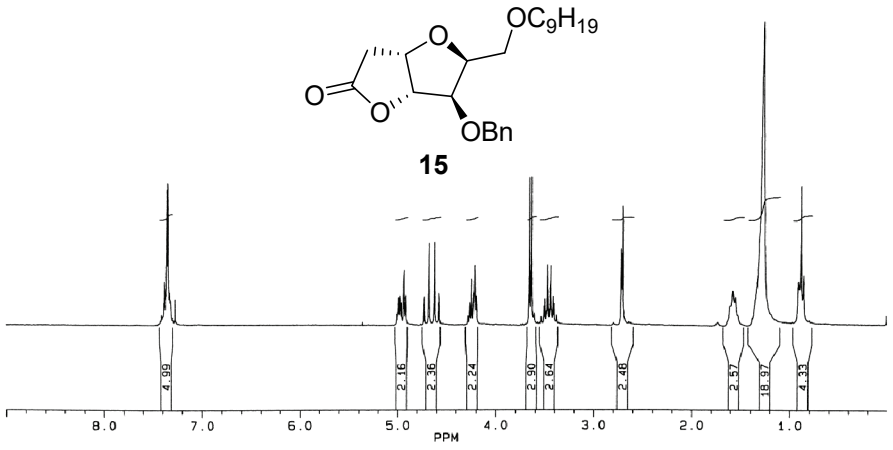

Fig. S-13. ^{1}H-NMR spectrum of **15** (250 MHz, $CDCl_3$).

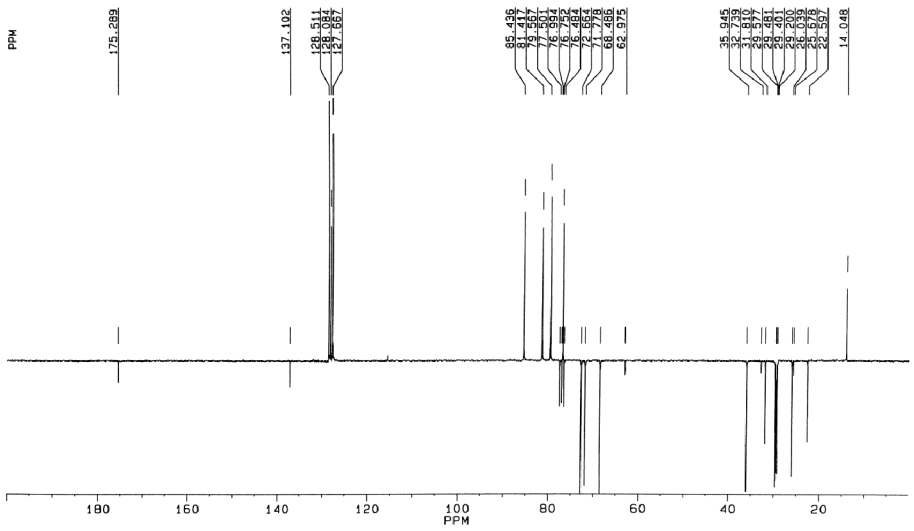

Fig. S-14. ^{13}C-NMR spectrum of **15** (63.9 MHz, $CDCl_3$).

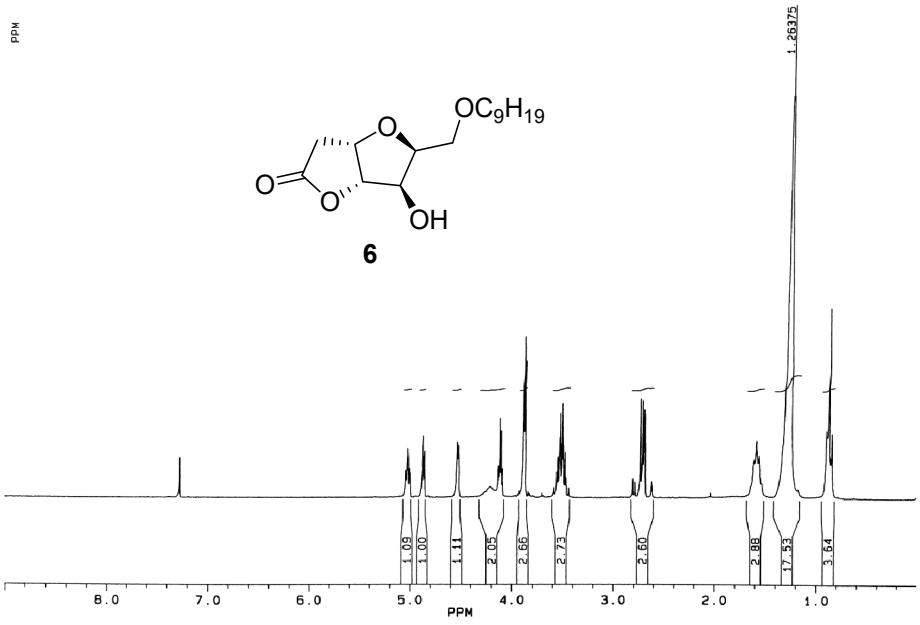

Fig. S-15. ^{1}H-NMR spectrum of **6** (250 MHz, $CDCl_3$).

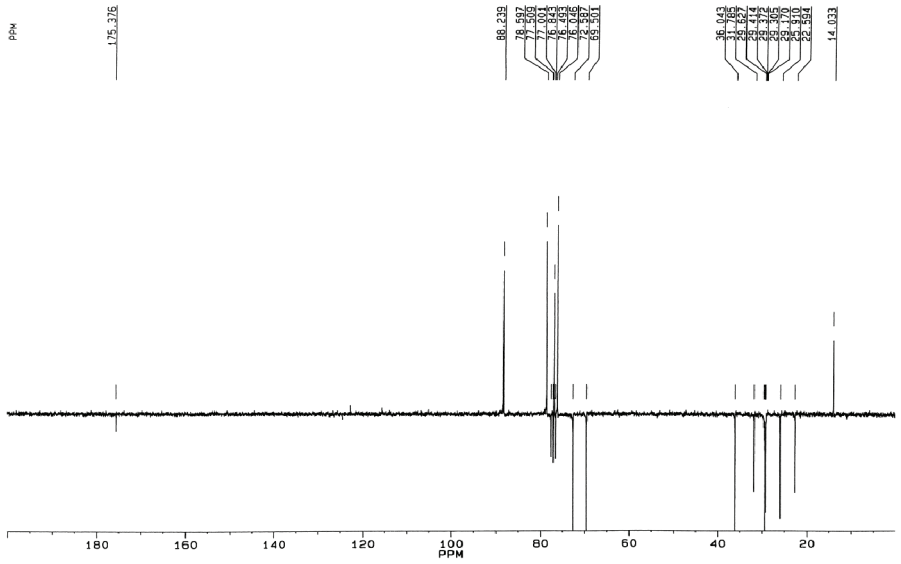

Fig. S-16. ^{13}C-NMR spectrum of **6** (63.9 MHz, $CDCl_3$).

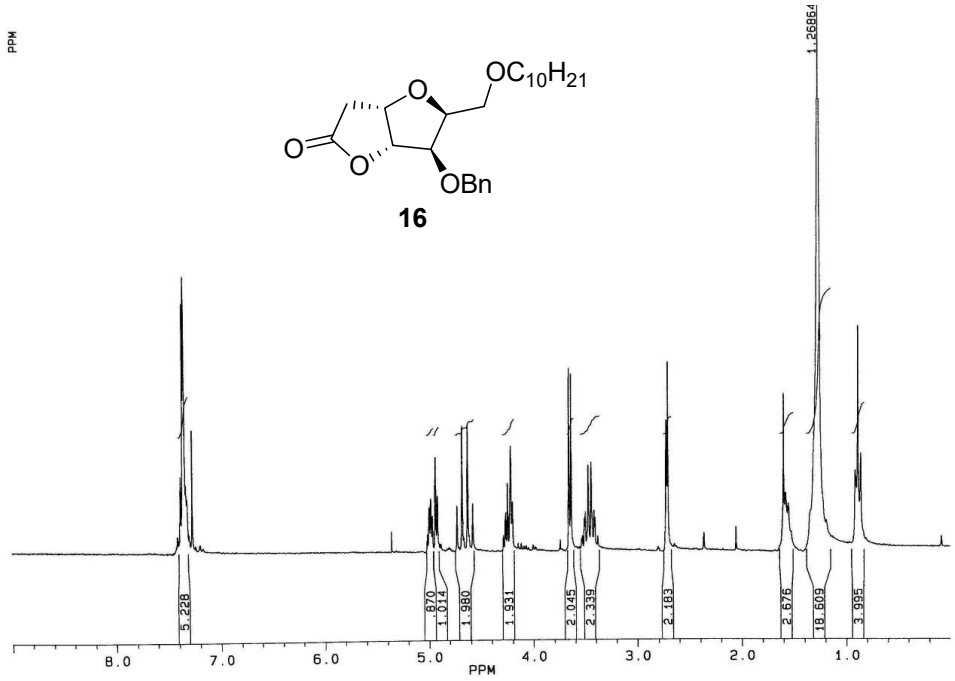

Fig. S-17. ^{1}H-NMR spectrum of **16** (250 MHz, $CDCl_3$).

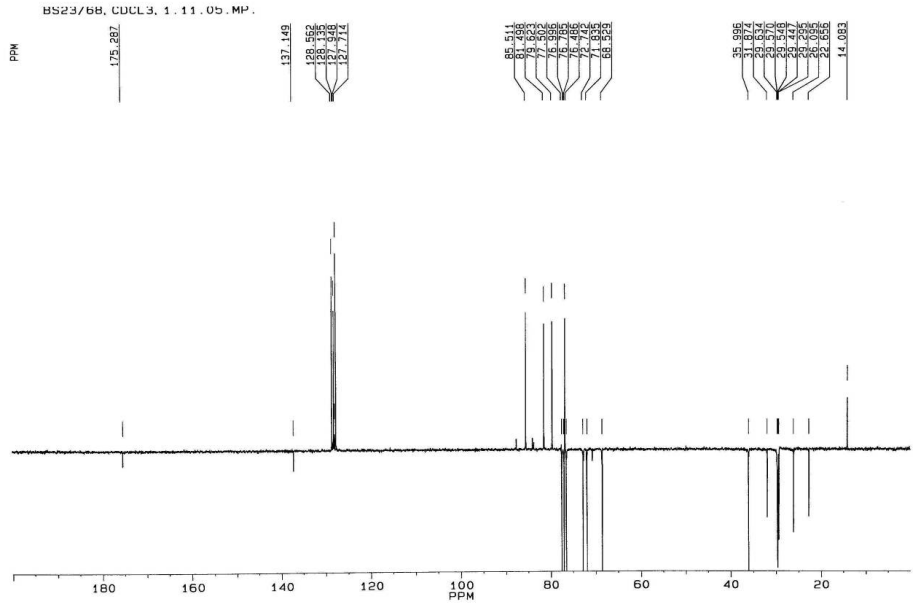

Fig. S-18. ^{13}C-NMR spectrum of **16** (63.9 MHz, $CDCl_3$).

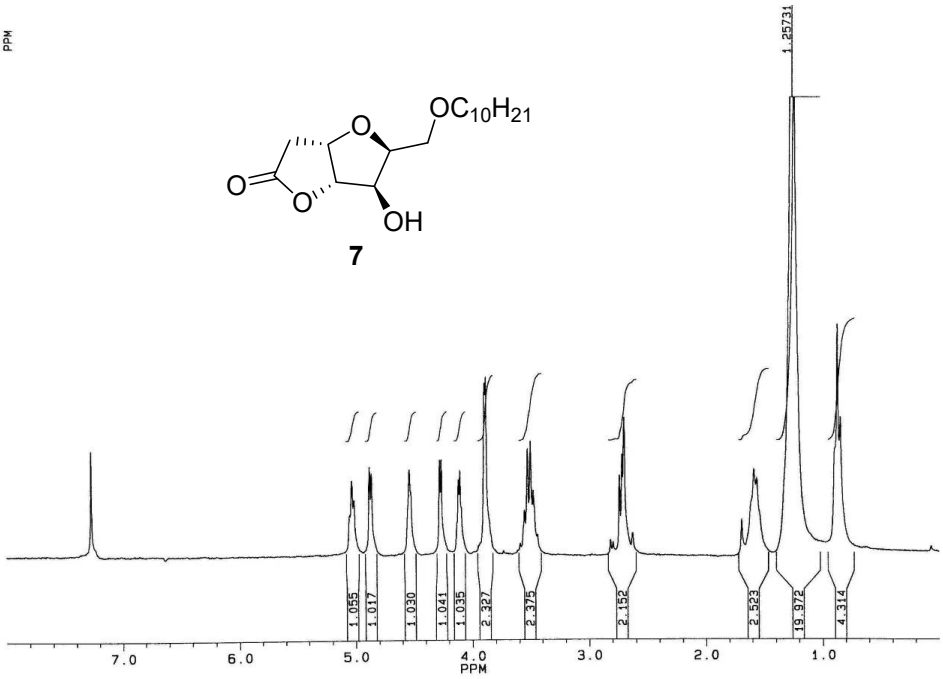

Fig. S-19. ^{1}H-NMR spectrum of **7** (250 MHz, $CDCl_3$).

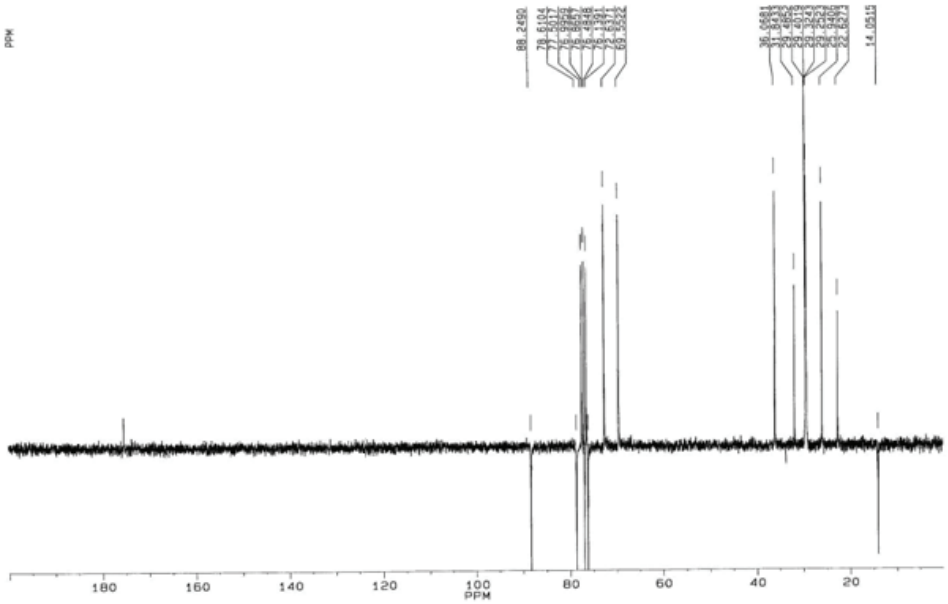

Fig. S-20. ^{13}C-NMR spectrum of **7** (63.9 MHz, $CDCl_3$).

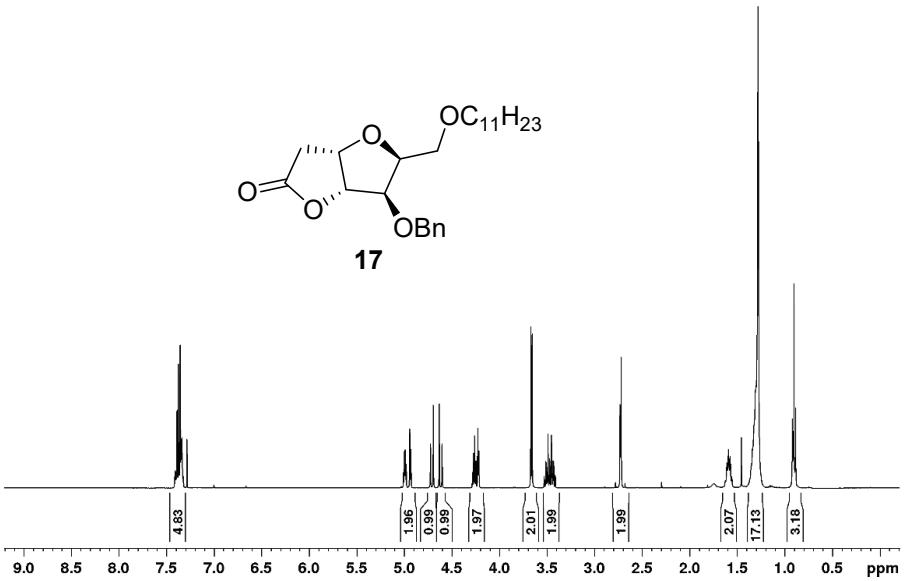

Fig. S-21. ^{1}H-NMR spectrum of **17** (400 MHz, $CDCl_3$).

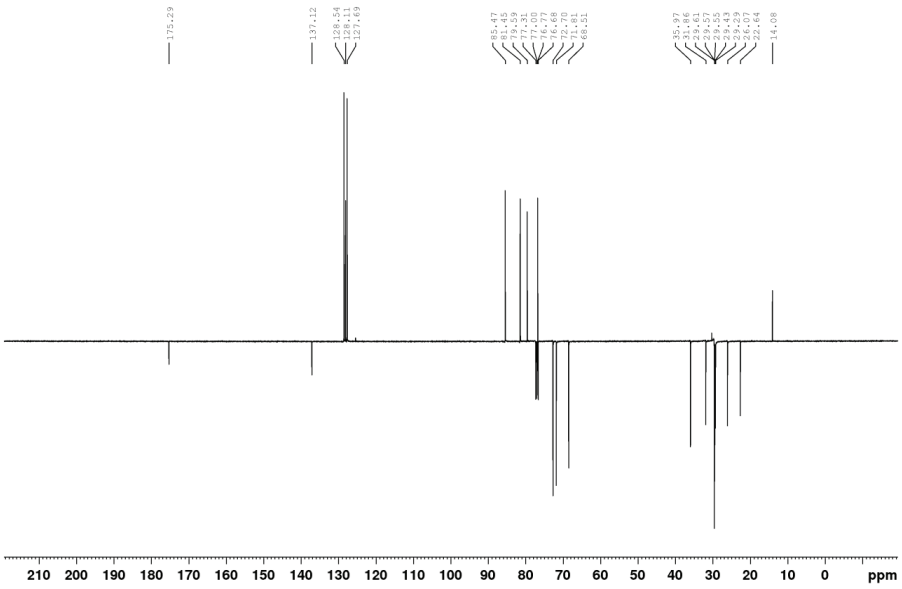

Fig. S-22. ^{13}C-NMR spectrum of **17** (100 MHz, $CDCl_3$).

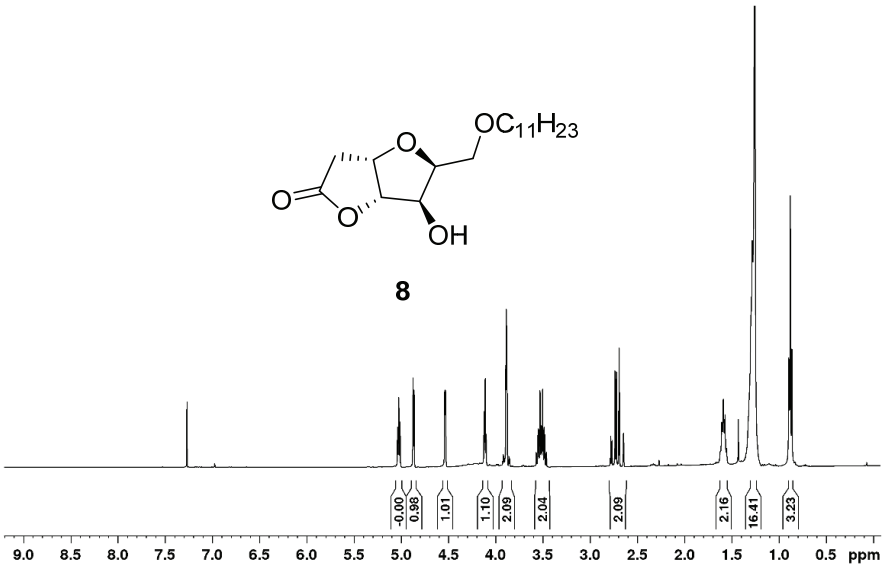

Fig. S-23. ^{1}H-NMR spectrum of **8** (400 MHz, $CDCl_3$).

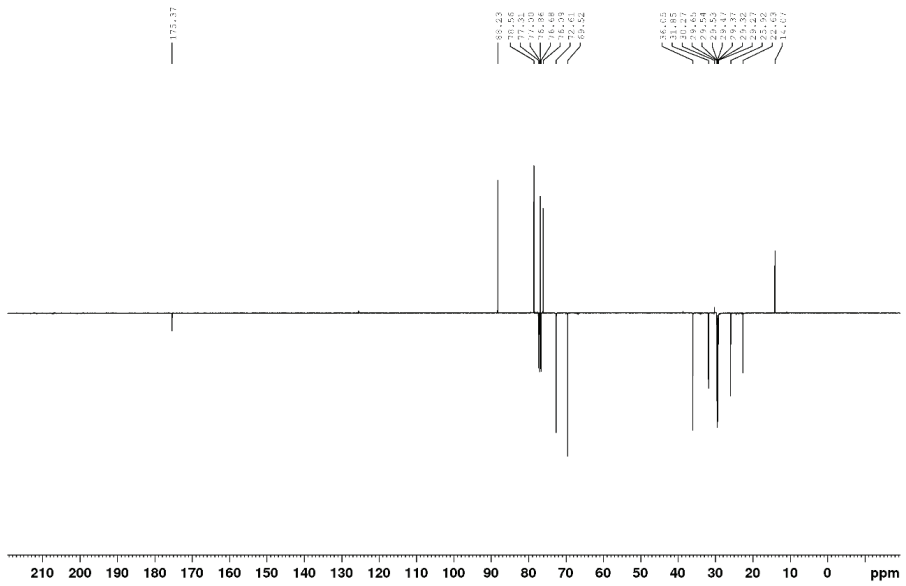

Fig. S-24. ^{13}C-NMR spectrum of **8** (100 MHz, $CDCl_3$).

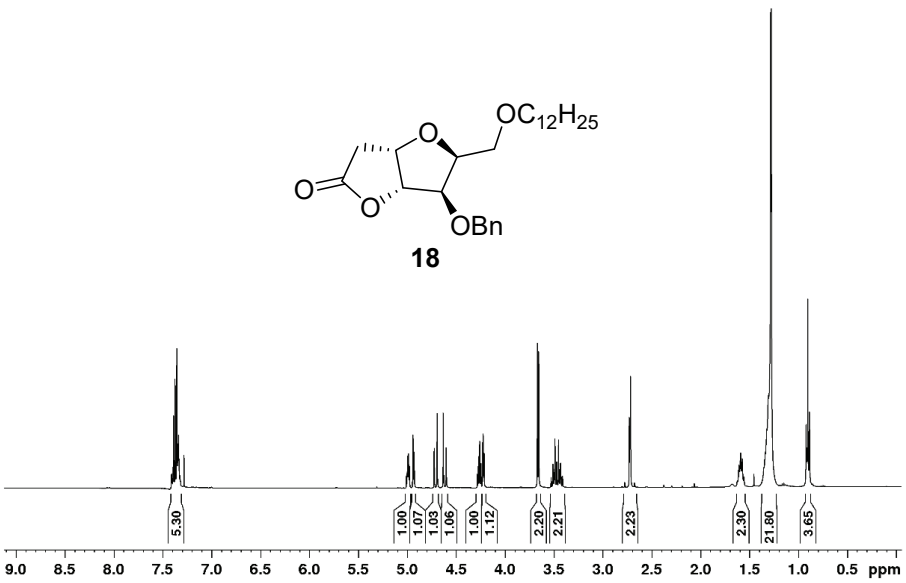

Fig. S-25. ^{1}H-NMR spectrum of **18** (400 MHz, $CDCl_3$).

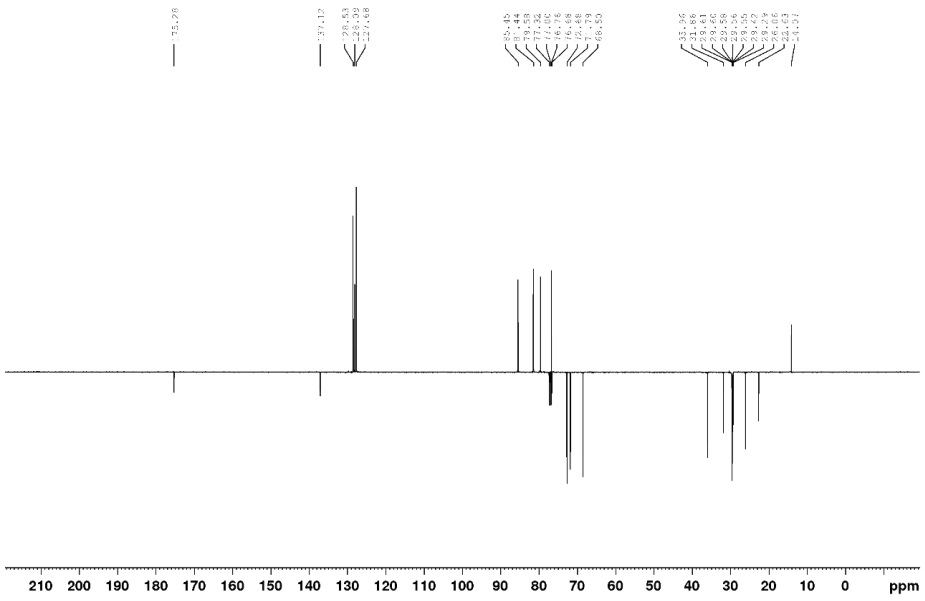

Fig. S-26. ^{13}C-NMR spectrum of **18** (100 MHz, $CDCl_3$).

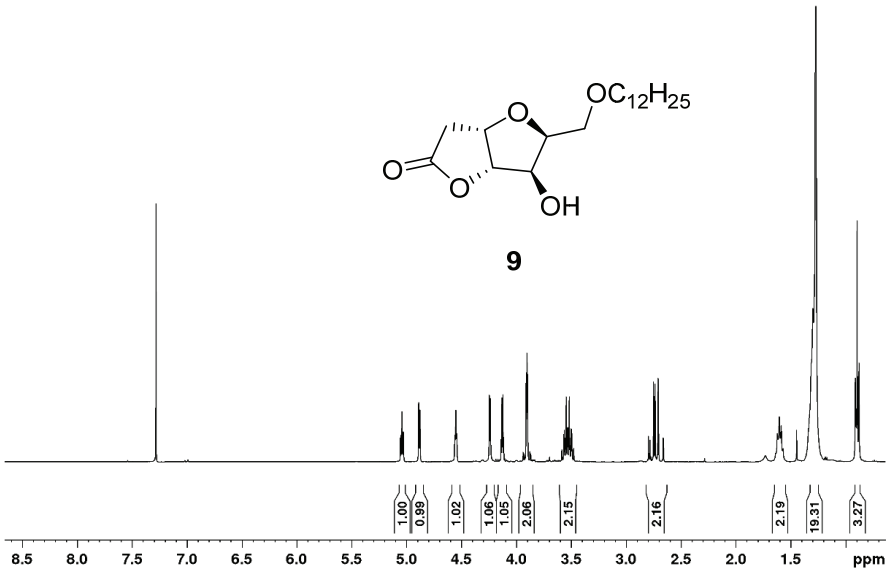

Fig. S-27. ^{1}H-NMR spectrum of **9** (400 MHz, $CDCl_3$).

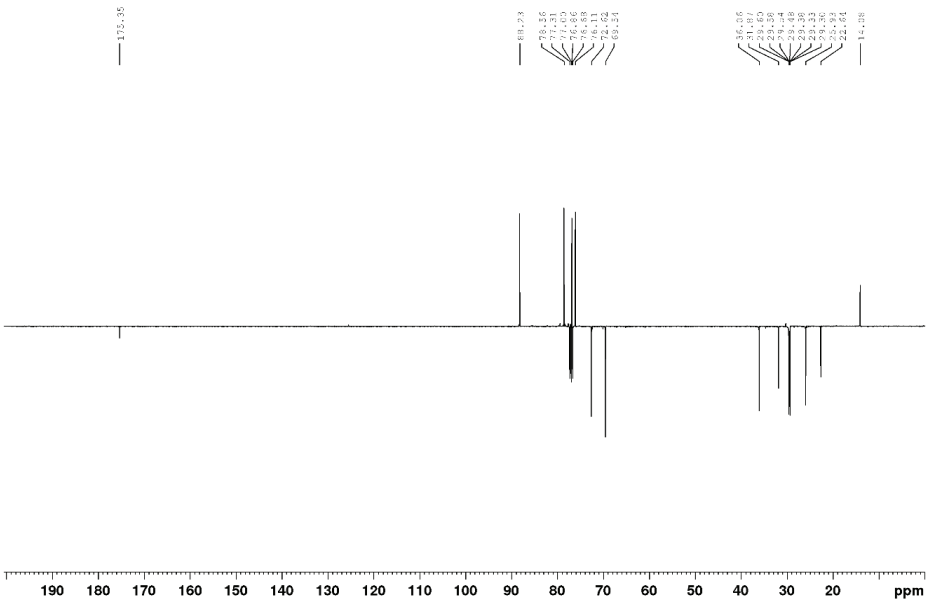

Fig. S-28. ^{13}C-NMR spectrum of **9** (100 MHz, $CDCl_3$).

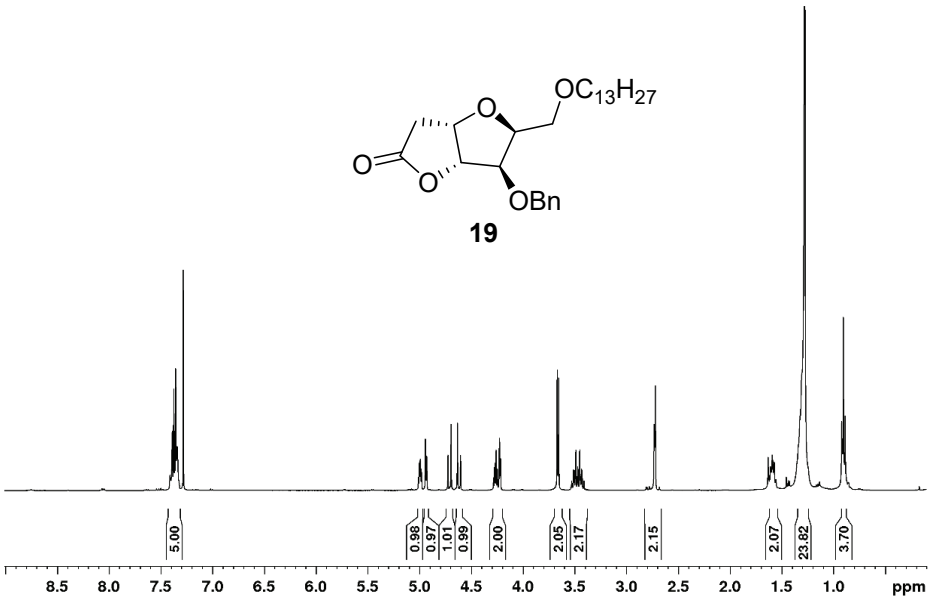

Fig. S-29. ^{1}H-NMR spectrum of **19** (400 MHz, $CDCl_3$).

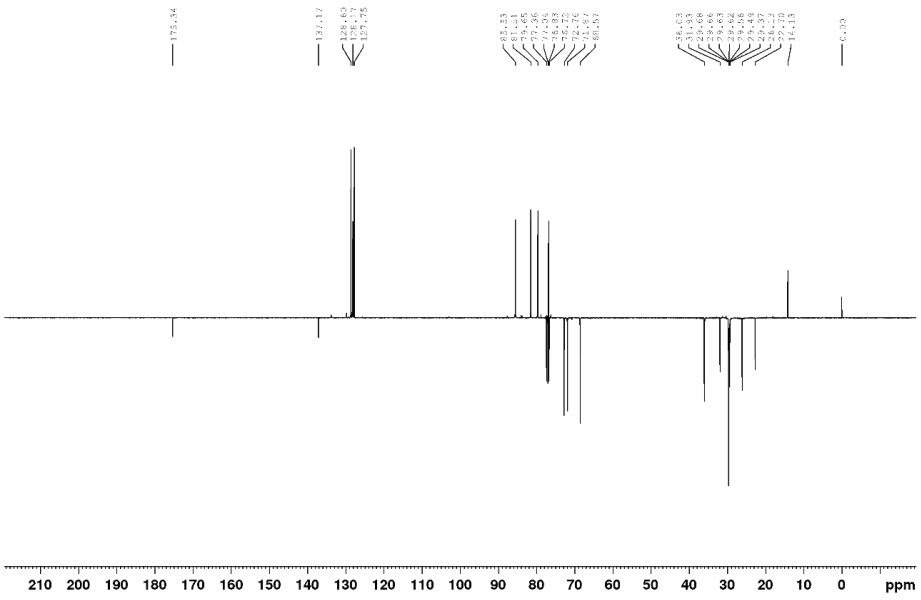

Fig. S-30. ^{13}C-NMR spectrum of **19** (100 MHz, $CDCl_3$).

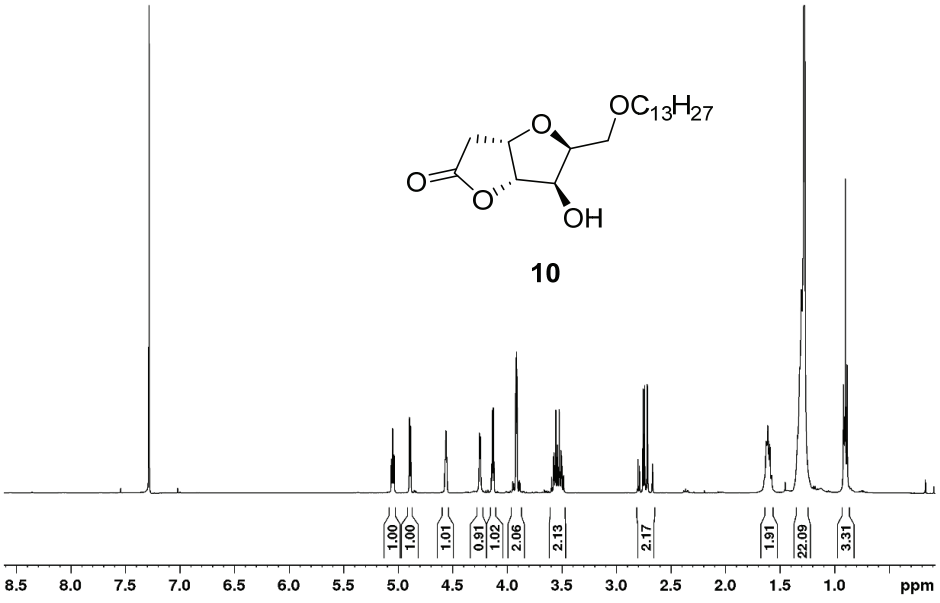

Fig. S-31. ^{1}H-NMR spectrum of **10** (400 MHz, $CDCl_3$).

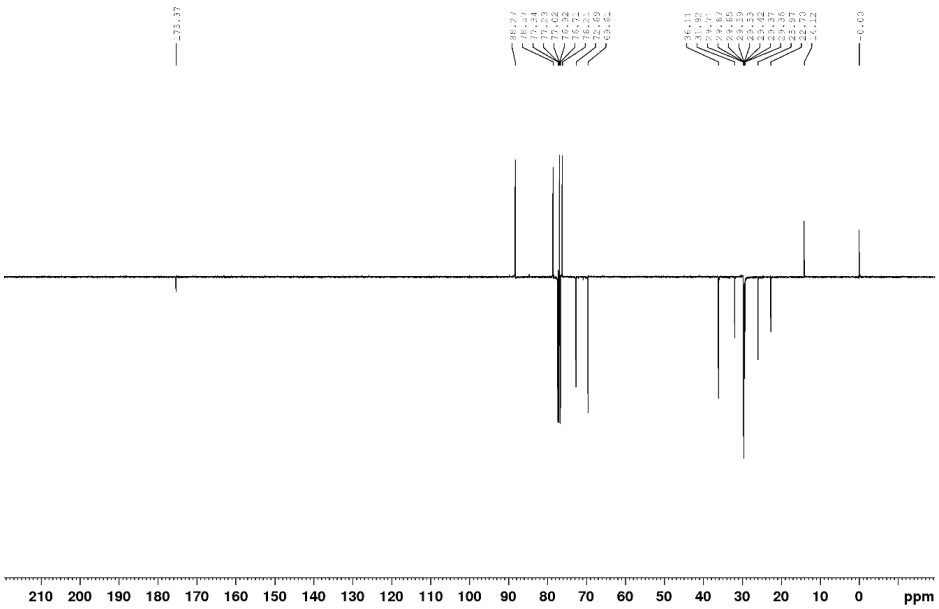

Fig. S-32. ^{13}C-NMR spectrum of **10** (100 MHz, $CDCl_3$).

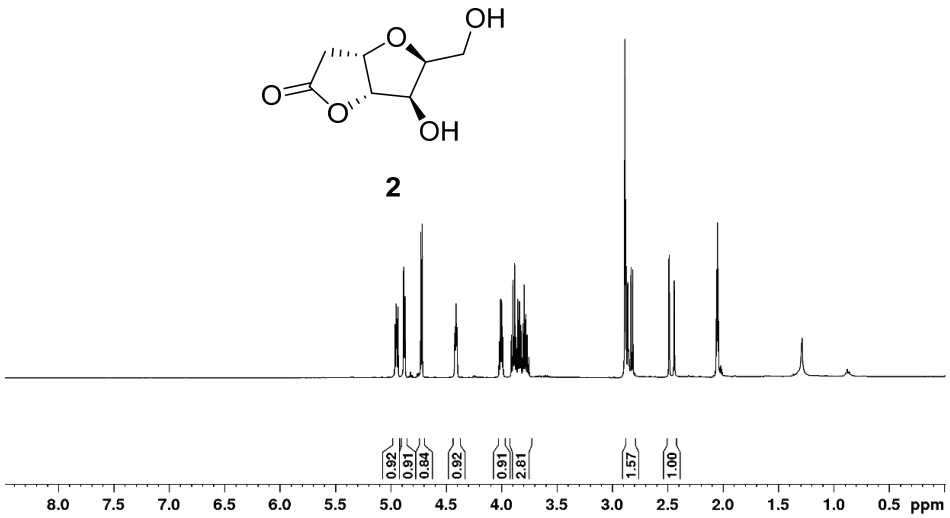

Fig. S-33. ^{1}H-NMR spectrum of **2** (400 MHz, acetone-d_6).

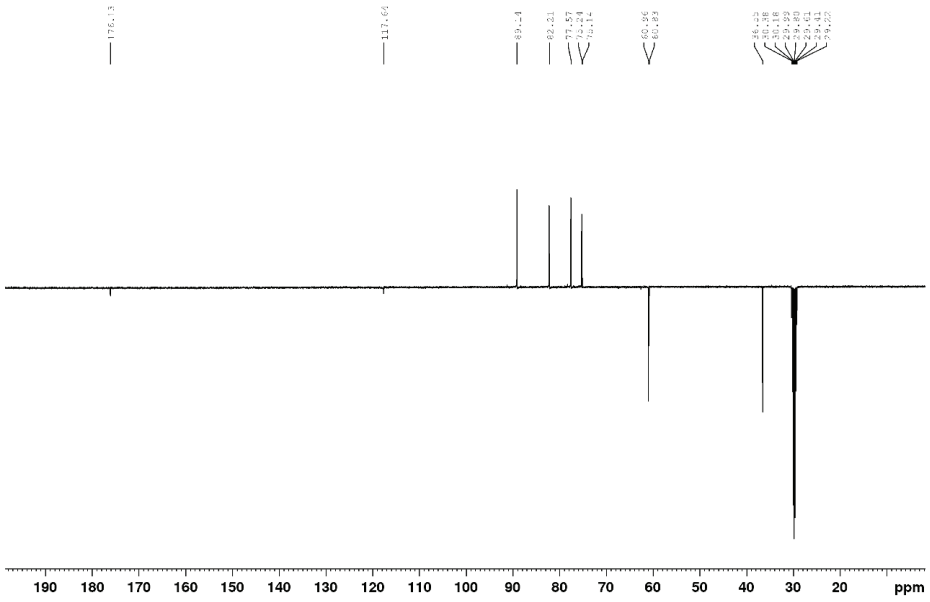

Fig. S-34. ^{13}C-NMR spectrum of **2** (100 MHz, acetone-d_6).

SAR ANALYSIS

TABLE S-I. Cytotoxicity data for SAR analysis

Compound	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 Δlog IC_{50} was calculated (Δlog IC_{50} is a difference between the log IC_{50} values of an analogue and the corresponding control compound). Positive Δlog IC_{50} values show a decrease in the 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.

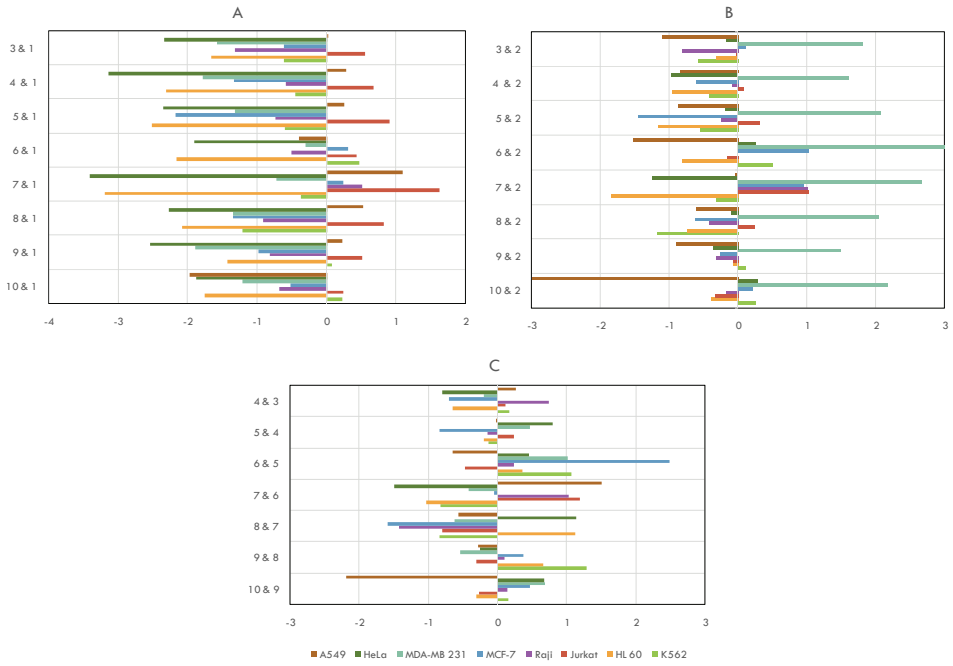

Fig. S-35. SAR Analysis. Influence of: (A) replacement of the hydroxybenzyl group in **1** with an alkoxymethyl chain; (B) introduction of an alkyl chain at the 7-OH position in molecule **2**; (C) increasing the number of carbon atoms in the side chain of analogues **3**–**10**

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1. K. Bock, I. Lundt, C. Pedersen, *Carbohydr. Res.* **179** (1988) 87
2. V. Popsavin, B. Srećo, G. Benedeković, M. Popsavin, J. Francuz, V. Kojić, G. Bogdanović, *Bioorg. Med. Chem. Lett.* **18** (2008) 5182.