SUPPLEMENTARY MATERIAL

Synthetic Mimic of Carbohydrated-Based Anticancer Vaccines: Preparation of Carbohydrate Polymers Bearing Unimolecular Trivalent Carbohydrates Ligand by Controlled Living Radical Polymerization

Teng-Yuan Kuo, Li-An Chien, Ya-Chi Chang, Shuang-Yu Liou, Che-Chien Chang*

Department of Chemistry, Fu Jen Catholic University.; 510, Zhongzheng Rd., Xinzhuang Dist., New Taipei City, 24205 Taiwan, R.O.C.; E-mail:080686@mail.fju.edu.tw

This supplementary material includes:

1. Experimental procedures and characterization data of “acetylated” 10a and “acetylated” 10b…2.

2. NMR spectra (1H, 13C/DEPT, COSY) of compound 1, 3, 5, 7, 8, 10a, and 10b…………………5.

3. NMR spectra (1H, 13C/DEPT, COSY, HSQC, NOESY, ROESY) of “acetylated” 10a and “acetylated” 10b……………………………………………………………………………………………………23.
To a solution of 2-[2-(4-vinylbenzyloxy)ethoxy]ethyl O-(2,3,4,6-tetra-O-acetyl-α-D-galactopyranosyl)-(1→4)-3-O-acetamido-6-O-tert-butyldiphenylsilyl-2-deoxy-β-D-gluco-pyranoside (50mg, 0.05 mmol), and DMAP (10 mg, 0.082 mmol) in pyridine (2.5 mL) was added Ac$_2$O (2.5 mL) at room temperature. The reaction mixture was stirred at same temperature for 36 h, then diluted with DCM (100 mL). The resulting mixture was washed with 2 M HCl (20 mL) and 50% NaHCO$_3$ (20 mL). The organic layers were dried over MgSO$_4$ and concentrated in vacuum to give a crude product, which was purified by silica gel chromatography (EtOAc:hexane = 8:2) to afford the acetylated disaccharide as a white solid (0.05 g, 83%):  

α–isomer

mp 98.1–103.2 °C; [α]$^25_D$ +39.22 (c = 1.75, CHCl$_3$); IR (neat) 3276, 3072, 2933, 2859, 1748 (C=O), 1654 (NHCO), 1513, 1485, 1428, 1373, 1258, 1234, 1159, 1108, 1065, 1045, 960, 945, 905, 848, 825, 801, 780, 739, 703, 676 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.68–7.60 (m, 4H, Ph), 7.41–7.31 (m, 8H, Ph), 7.28 (d, $J$ = 8.1 Hz, 2H, para-), 6.68 (dd, $J$ = 17.6, 10.9 Hz, 1H, ArCH=CH$_2$), 6.24 (d, $J$ = 7.8 Hz, 1H, NHAc), 5.71 (d, $J$ = 17.6 Hz, 1H, ArCH=CH$_2$), 5.39 (d, $J$ = 2.2 Hz, 1H, H$_{4'}$), 5.24–5.20 (two overlapping d at 5.22, $J$ = 11.0 Hz, 1H, H$_3'$, and at 5.22, $J$ = 10.8 Hz, 1H, RCH=CH$_2$), 5.18 (d, $J$ = 3.8 Hz, 1H, H$_1'$, α–form), 5.06 (dd, $J$ = 11.0, 3.9 Hz, 1H, H$_2'$), 4.93 (d, $J$ = 8.2 Hz, 1H, H$_1$, β–form), 4.89 (dd, $J$ = 9.6, 9.1 Hz, 1H, H$_4$), 4.57 (d, $J$ = 12.3 Hz, 1H, H$_3$), 4.10 (d, $J$ = 7.8 Hz, 1H, H$_2$), 3.84 (m, 1H, H$_5$), 3.78 (m, 1H, H$_6$), 3.54 (m, 2H, H$_7$), 2.24 (s, 3H, CH$_3$), 1.70 (m, 2H, H$_8$).
ArCH₂O, AB), 4.54 (d, J = 12.3 Hz, 1H, ArCH₂O, AB), 4.33–4.24 (m, 2H, H₅', H₃), 4.13 (dd, J = 11.0, 8.4 Hz, 1H, H₆'a), 3.95 (dd, J = 11.0, 5.9 Hz, 1H, H₆'b), 3.90 (dt, J = 11.8, 3.8 Hz, 1H, H₁'₉b), 3.73–3.69 (m, 1H, H₁'₈b), 3.67–3.58 (m, 7H, CH₂×3, H₆a), 3.56 (dd, J = 11.5, 2.2 Hz, 1H, H₆b), 3.42 (ddd, J = 9.3, 6.7, 2.6 Hz, 1H, H₅), 3.41–3.35 (m, 1H, H₂), 2.09 (s, 3H, Ac), 2.003 (s, 3H, Ac), 1.998 (s, 3H, Ac), 1.94 (s, 3H, Ac), 1.93 (s, 3H, Ac), 1.01 (s, 9H, t–Bu); ¹³C NMR (125 MHz, CDCl₃) δ 171.0 (s), 170.9 (s), 170.3 (s), 170.1 (s), 169.7 (s), 169.5 (s), 137.5 (s), 137.1 (s), 136.4 (d), 135.6 (d×2), 135.6 (d×2), 133.3 (s), 133.2 (s), 129.6 (d), 129.6 (d), 127.9 (d×2), 127.6 (d×2), 127.6 (d×2), 126.3 (d×2), 113.9 (t), 99.6 (d), 96.0 (d), 75.8 (d), 74.7 (d), 72.9 (t), 72.3 (d), 70.7 (t), 70.4 (t), 69.4 (t), 68.3 (t), 67.5 (d), 67.4 (d), 67.1 (d), 66.2 (d), 63.2 (t), 60.9 (t), 56.9 (d), 26.7 (q×3), 23.4 (q), 20.8 (q), 20.7 (q), 20.6 (q), 20.6 (q×2), 19.2 (s); HRMS (ESI⁺): m/z calcd for C₅₃H₆₉NO₁₈Si [M+H]⁺: 1036.4362; found: 1036.4368.

2-[2-(4-Vinylbenzyloxy)ethoxy]ethyl O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→4)-3-O-acetyl-2-acetamido-6-O-tertbutyldiphenylsilyl-2-deoxy-β-D-glucopyranoside [acetylated 10b]

![Chemical structure](image)

To a solution of 2-[2-(4-vinylbenzyloxy)ethoxy]ethyl O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→4)-2-acetamido-6-O-tertbutyldiphenylsilyl-2-deoxy-β-D-glucopyranoside (30.1 mg, 0.0302 mmol), and DMAP (6.2 mg, 0.0513 mmol) in pyridine (1.5 mL) was added Ac₂O (1.5 mL) at room temperature. The reaction mixture was stirred at same temperature for 36 h, then diluted with DCM (100 mL). The resulting
mixture was washed with 2 M HCl (20 mL) and 50% NaHCO₃ (20 mL). The organic layers were dried over MgSO₄ and concentrated in vacuum to give a crude product, which was purified by silica gel chromatography (EtOAc:hexane = 9:1) to afford the acetylated disaccharide as a white solid (0.03 g, 85%):

β–isomer

[α]_{D}^{25} -123.33 (c = 0.21, CHCl₃); IR (neat) 3072, 2934, 2859, 1750 (C=O), 1672 (NHCO), 1589, 1472, 1462, 1429, 1369, 1222, 1165, 1135, 1112, 1046, 998, 960, 915, 824, 797, 740, 705, 675, 605 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.75 (d, J = 7.6 Hz, 2H, Ph), 7.71 (d, J = 7.6 Hz, 2H, Ph), 7.47–7.32 (m, 8H, overlapped with one d at 7.37, J = 7.9 Hz, Ph, para-), 7.29 (d, J = 7.9 Hz, para-), 6.69 (dd, J = 17.6, 10.9 Hz, 1H, ArCH=CH₂), 6.34 (d, J = 9.6 Hz, 1H, NHAc), 5.72 (d, J = 17.6 Hz, ArCH=CH₂), 5.29 (d, J = 3.4 Hz, 1H, H₄), 5.21 (d, J = 10.9 Hz, 1H, ArCH=CH₂), 5.05 (dd, J = 10.2, 8.2 Hz, 1H, H₂), 4.96 (t, J = 9.7 Hz, 1H, H₃), 4.91 (dd, J = 10.2, 3.4 Hz, 1H, H₃'), 4.77 (d, J = 8.2 Hz, 1H, H₁β, β–form), 4.68 (d, J = 12.4 Hz, 1H, ArCH₂O, AB), 4.59–4.53 (two overlapping d at 4.57, J = 8.0 Hz, 1H, H₁, β–form, and at 4.56, J = 12.4 Hz, 1H, ArCH₂O, AB), 4.15–4.03 (m, 4H, H₆, H₄, H₂), 3.96–3.81 (m, 3H, H₆, H₁α), 3.78–3.69 (m, 2H, H₁β, H₅), 3.65–3.49 (m, 6H, CH₂×3), 3.27 (d, J = 9.3 Hz, 1H, H₅), 2.11 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.04 (s, 3H, Ac), 1.96 (s, 3H, Ac), 1.92 (s, 3H, Ac), 1.78 (s, 3H, Ac), 1.06 (s, 9H, t-Bu); ¹³C NMR (125 MHz, CDCl₃) δ 170.9 (s), 170.4 (s), 170.3 (s), 170.2 (s), 168.9 (s), 168.9 (s), 137.3 (s), 137.2 (s), 136.4 (d), 136.0 (d×2), 135.4 (d×2), 133.4 (s), 132.2 (s), 129.9 (d), 129.8 (d), 128.4 (d×2), 127.9 (d×2), 127.6 (d×2), 126.3 (d×2), 114.0 (t), 101.9 (d), 100.3 (d), 75.2 (d), 74.3 (d), 73.4 (d), 73.0 (t), 71.6 (t), 71.1 (d), 70.7 (t), 70.6 (d), 69.4 (d), 69.1 (t), 67.9 (t), 67.0 (d), 61.3 (t), 61.1 (t), 53.6 (d), 26.8 (q×3), 23.1 (q), 20.9 (q), 20.6 (q), 20.6 (q), 20.5 (q), 20.5 (q), 19.3 (s); HRMS (ESI⁺): m/z calcd for C₅₃H₆₉NO₁₈Si [M+H]⁺: 1036.4362; found: 1036.4385.
$^1$H NMR (300 MHz, CDCl$_3$) of 1

HO\_\_\_O

1

\text{H NMR (300 MHz, CDCl}_3\text{)} of 1
$^{13}$C/DEPT NMR (75 MHz, CDCl$_3$) of 1
$^1$H NMR (300 MHz, CDCl$_3$) of 3
$^{13}\text{C}/\text{DEPT NMR (75 MHz, CDCl}_3\text{)}$ of 3
$^{1}{H}$ NMR (300 MHz, CDCl$_3$) of 5, α and β mixtures (α/β = 91/9)
\[^{13}\text{C/DEPT NMR (75 MHz, CDCl}_3\text{)}\text{ of 5 (only \text{\textalpha}-isomer)}\]
\(^1\)H NMR (300 MHz, CD\(_3\)OD) of 7
$^{13}$C/DEPT NMR (75 MHz, CD$_3$OD) of 7
$^1$H NMR (300 MHz, CDCl$_3$) of 8
$^{13}$C/DEPT NMR (75 MHz, CDCl$_3$) of 8
$^1$H NMR (500 MHz, CDCl$_3$) of 10a (α-isomer)
$^{13}$C/DEPT NMR (125 MHz, CDCl$_3$) of 10a (α-isomer)
1H NMR COSY (500 MHz, CDCl₃) of 10a (α-isomer)
$^{1}$H NMR COSY (500 MHz, CDCl$_3$) of 10a (α-isomer)
$^1$H NMR (500 MHz, CDCl$_3$) of 10b (β-isomer)
13C/DEPT NMR (125 MHz, CDCl3) of 10b (β-isomer)
$^1$H NMR COSY (500 MHz, CDCl$_3$) of 10b (β-isomer)
$^1$H NMR COSY (500 MHz, CDCl$_3$) of 10b (β-isomer)
acetylated 10a

$^1$H NMR (800 MHz, CDCl$_3$) of acetylated 10a (α-isomer)
$^1$H NMR COSY (800 MHz, CDCl$_3$) of acetylated 10a ($\alpha$-isomer)
$^1$H NMR COSY (800 MHz, CDCl$_3$) of acetylated 10a ($\alpha$-isomer)
$^1$H NMR COSY (800 MHz, CDCl$_3$) of acetylated 10a (α-isomer)
$^{1}H^{13}C$ NMR HSQC (800 MHz, CDCl$_3$) of acetylated 10a (α-isomer)
$^1$H-$^{13}$C NMR HSQC (800 MHz, CDCl$_3$) of acetylated 10a ($\alpha$-isomer)
$^1$H NMR NOESY (800 MHz, CDCl$_3$) of acetylated 10a (α-isomer)
$^1$H NMR NOESY (800 MHz, CDCl$_3$) of acetylated 10a ($\alpha$-isomer)
\[1^H\text{NMR (500 MHz, CDCl}_3\text{) of acetylated 10b (\(\beta\)-isomer)}\]
$^{13}$C/DEPT NMR (125 MHz, CDCl$_3$) of acetylated 10b (β-isomer)
${^1H}$ NMR COSY (500 MHz, CDCl$_3$) of acetylated $10b$ (β-isomer)
$^1$H NMR COSY (500 MHz, CDCl$_3$) of acetylated 10b (β-isomer)
acetylated 10b

\(^{1}H-^{13}C\) NMR HSQC(500 MHz, CDCl\textsubscript{3}) of acetylated 10b (\(\beta\)-isomer)
$^1$H-$^1$C NMR HSQC (500 MHz, CDCl$_3$) of acetylated 10b (β-isomer)
$^1$H NMR ROESY (500 MHz, CDCl$_3$) of acetylated 10b (β-isomer)
$^1$H NMR ROESY (500 MHz, CDCl$_3$) of acetylated 10b (β-isomer)