Supporting Information

Expedient synthesis of triazole-linked glycosyl amino acids and peptides

Brian H. M. Kuijpers,[†] Stan Groothuys,[†] A. (Bram) R. Keereweer,[†] Peter J. L. M. Quaedflieg,[‡] Richard H. Blaauw,[§] Floris L. van Delft,[†] and Floris P. J. T. Rutjes^{*,†}

Department of Organic Chemistry, NSRIM, University of Nijmegen, Toernooiveld 1, 6525 ED Nijmegen, The Netherlands, DSM Research, Life Sciences – Advanced Synthesis, Catalysis and Development, P.O. Box 18, 6160 MD Geleen, The Netherlands, Chiralix B.V., Toernooiveld 100, 6525 EC-Nijmegen, The Netherlands

[†] University of Nijmegen.

[‡] DSM Research.

[§] Chiralix B.V.

General information:

^1H and ^{13}C nuclear magnetic resonance (NMR) were recorded on a Varian Inova 400 (400 MHz) or a Bruker DMX300 (300 MHz) spectrometer. The chemical shifts (δ) are given in ppm downfield from tetramethylsilane. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. IR spectra were recorded on an ATI Mattson, Genesis series FTIR spectrometer. Commercially available reagents were used as received.

General procedure for the cycloaddition:

To a solution of the glycoside (1 equiv) and the amino acid derivative (1 equiv) in *tert*-butanol (0.5 M) was added a mixture of $\text{Cu}(\text{OAc})_2$ (20 mol%) and sodium ascorbate (40 mol%) in H_2O (0.04 M and 0.08 M respectively). The reaction was stirred overnight, water was added and the product was extracted with DCM (2 $\times$). The combined organic layers were washed with aqueous NaHCO_3 (except for the free acids), aqueous NaCl , dried over NaSO_4 and evaporated *in vacuo*. The product was purified by flash chromatography using EtOAc/heptane mixtures.

Methyl (R)-2-[(*tert*-Butoxycarbonyl)amino]-3-[1-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)[1,2,3]triazol-4-yl]propionate (15)

White solid. 76 mg (0.13 mmol, 91%). R_f = 0.37 (EtOAc/heptane 2/1). $[\alpha]_D^{25}$ = -32.8 (c = 0.69, CH_2Cl_2). IR (film): ν 3391, 2980, 2362, 2340, 1738, 1709, 1498. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.60 (s, 1H), 5.83-5.80 (m, 1H), 5.47-5.38 (m, 3H), 5.26-5.21 (m, 1H), 4.64-4.62 (m, 1H), 4.31 (dd, J = 12.6, 5.0 Hz, 1H), 4.15 (dd, J = 12.6, 2.0 Hz, 1H), 3.99 (ddd J = 10.1, 5.0, 2.1, 1H), 3.73 (s, 3H), 3.28 (dd, J = 15.0, 5.3, 1H), 3.20 (dd, J = 15.0, 4.6 Hz 1H), 2.09 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H), 1.89 (s, 3H), 1.45 (s, 9H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ = 171.4, 170.2, 169.6, 169.1, 168.8, 155.2, 143.4, 120.6, 85.8, 80.0, 75.3, 72.6, 70.4, 67.9, 61.7, 53.1, 52.6, 28.8, 28.6, 21.0, 20.9, 20.8, 20.4. 1455. HRMS (ESI) calculated for $\text{C}_{25}\text{H}_{37}\text{O}_{13}\text{N}_4$ ($\text{M}+\text{H}^+$) 601.2357, found 601.2383.

Methyl (R)-2-[(*tert*-Butoxycarbonyl)amino]-3-[1-(2,3,4,6-tetra-*O*-acetyl- β -D-galactopyranosyl)[1,2,3]triazol-4-yl]propionate (16)

White solid. 44 mg (0.07 mmol, 89%). $R_f = 0.32$ (EtOAc/heptane 2/1). $[\alpha]_D = -14.1$ ($c = 1.41$, CH_2Cl_2). IR (film): ν 3373, 2976, 2358, 2332, 1753, 1709. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.93 (s, 1H), 5.78 (d, $J = 9.3$ Hz, 1H), 5.59-5.42 (m, 3H), 5.24 (dd, $J = 10.4$, 3.3 Hz, 1H), 4.67-4.59 (m, 1H), 4.24-4.10 (m, 3H), 3.73 (s, 3H), 3.29 (dd, $J = 15.1$, 5.2 Hz, 1H), 3.21 (dd, $J = 15.1$, 4.6 Hz, 1H), 2.23 (s, 3H), 2.05 (s, 3H), 2.01 (s, 3H), 1.90 (s, 3H), 1.45 (s, 9H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ = 171.5, 170.1, 169.7, 169.6, 169.0, 155.2, 143.4, 120.8, 86.4, 80.0, 74.3, 70.8, 68.0, 67.1, 61.3, 53.2, 52.7, 30.0, 28.6, 21.0, 20.8, 20.5. HRMS (ESI) calculated for $\text{C}_{25}\text{H}_{37}\text{O}_{13}\text{N}_4$ ($\text{M}+\text{H}^+$) 601.2357, found 601.2347.

Methyl (*R*)-2-[(*tert*-Butoxycarbonyl)amino]-3-{1-(2,3,4,6-tetra-*O*-benzyl- β -D-glucopyranosyl)[1,2,3]triazol-4-yl}propionate (17)

White solid. 64 mg (0.08 mmol, 87%). R_f = 0.47 (EtOAc). Major isomer: IR (film): ν 3391, 3028, 2915, 2362, 2323, 1744, 1714, 1498. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.46 (s, 1H), 7.36-7.27 (m, 13H), 7.24-7.20 (m, 3H), 7.19-7.13 (m, 3H), 6.99-6.94 (m, 2H), 4.93 (d, J = 11.1 Hz, 1H), 4.89 (d, J = 10.9 Hz, 1H), 4.85 (d, J = 10.7 Hz, 1H), 4.60 (d, J = 10.8 Hz, 1H), 4.54 (d, J = 12.1 Hz, 1H), 4.48 (d, J = 12.1 Hz, 1H), 4.47 (d, J = 10.6 Hz, 1H), 4.07-3.96 (m, 1H), 4.02 (d, J = 10.5 Hz, 1H), 3.90-3.76 (m, 2H), 3.74-3.65 (m, 3H), 3.64 (s, 3H), 3.24 (d, J = 4.5 Hz, 2H), 1.41 (s, 9H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ = 171.6, 155.2, 143.0, 138.0, 137.7, 136.9, 128.4, 128.4, 128.3, 128.2, 127.9, 127.8, 127.7, 127.7, 121.4, 87.6, 85.5, 81.0, 80.2, 78.2, 77.4, 75.9, 75.4, 75.1, 73.7, 68.6, 53.2, 52.7, 28.6. HRMS (ESI) calculated for $\text{C}_{45}\text{H}_{53}\text{O}_{19}\text{N}_4$ ($\text{M}+\text{H}^+$) 793.3812, found 793.3837

Methyl 3-{1-[2-(acetylamino)-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-glucopyranosyl][1,2,3]triazol-4-yl}-(*R*)-2-[(*tert*-butoxycarbonyl)amino]propionate (18)

White solid. 70 mg (0.12 mmol, 91%). $R_f = 0.44$ (EtOAc). $[\alpha]_D = -44.5$ ($c = 0.91$, CH_2Cl_2). IR (film): ν 3304, 2976, 2250, 1753. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.69 (s, 1H), 6.2 (br d, $J = 9.0$ Hz, 1H), 5.93 (d, $J = 10.0$ Hz, 1H), 5.65 (d, $J = 8.6$ Hz, 1H), 5.45 (dd, $J = 10.0, 9.8$ Hz, 1H), 5.21 (dd, $J = 9.8, 9.6$ Hz, 1H), 4.65-4.52 (m, 2H), 4.27 (dd, $J = 12.6, 4.7$ Hz, 1H), 4.13 (dd, $J = 12.6, 2.1$ Hz, 1H), 4.03 (ddd, $J = 10.1, 4.7, 2.1$ Hz, 1H), 3.71 (s, 3H), 3.28 (dd, $J = 14.8, 5.7$, 1H), 3.16 (dd, $J = 14.8, 4.9$, 1H), 2.07 (s, 3H), 2.06 (s, 6H), 1.77 (s, 3H), 1.43 (s, 9H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ = 171.6, 170.7, 170.4, 170.3, 169.1, 155.4, 142.9, 121.7, 86.2, 80.0, 75.1, 72.3, 68.2, 61.9, 53.7, 53.3, 52.6, 28.8, 28.6, 23.0, 21.0, 21.0, 20.9.

Methyl 3-{1-[2-(acetylamino)-3,4,6-tri-*O*-acetyl-2-deoxy- β -D-galactopyranosyl][1,2,3]triazol-4-yl}-(*R*)-2-[(*tert*-butoxycarbonyl)amino]propionate (19)

White solid. 17 mg (0.03 mmol, 72%). $R_f = 0.41$ (EtOAc). $[\alpha]_D = -22.0$ ($c = 0.58$, CH_2Cl_2). IR (film): ν 3321, 2980, 2353, 2340, 1748. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.72 (s, 1H), 5.90-5.87 (m, 2H), 5.68 (br d, $J = 8.6$ Hz, 1H), 5.50 (d, $J = 2.7$ Hz, 1H), 5.45-5.34 (m, 1H), 4.75-4.59 (m, 2H), 4.27-4.04 (m, 3H), 3.73 (s, 3H), 3.30 (dd, $J = 14.5, 4.9$ Hz, 2H), 3.17 (dd, $J = 14.5, 4.4$ Hz, 1H), 2.22 (s, 3H), 2.03 (s, 3H), 2.03 (s, 3H), 1.79 (s, 3H), 1.44 (s, 9H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ = 171.6, 170.6, 170.2, 169.9, 155.5, 142.8, 121.9, 86.7, 79.9, 74.1, 72.0, 66.8, 61.6, 53.3, 52.6, 50.4, 28.7, 23.2, 21.0.

Methyl 3-{1-[2-(acetylamino)-3,4,6-tri-*O*-benzoyl-2-deoxy- β -D-glucopyranosyl][1,2,3]triazol-4-yl}-(*R*)-2-[(*tert*-butoxycarbonyl)amino]propionate (20)

White solid. 23 mg (0.03 mmol, 30%). $R_f = 0.33$ (EtOAc/heptane 1/1). $[\alpha]_D^{25} = +5.0$ ($c = 1.38$, CH_2Cl_2). IR (film): ν 3321, 2980, 2353, 2340, 1748. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 8.01 (d, $J = 6.8$ Hz, 2H), 7.94-7.78 (m, 4H), 7.73 (s, 1H), 7.53-7.32 (m, 9H), 6.05 (d, $J = 9.6$ Hz, 1H), 5.89-5.80 (m, 3H), 5.70-5.69 (m, 1H), 4.84-4.79 (m, 1H), 4.67-4.62 (m, 1H), 4.64 (dd, $J = 12.4, 2.8$ Hz, 1H), 4.47 (dd, $J = 12.4, 4.8$ Hz, 1H), 4.36 (ddd, $J = 9.2, 4.8, 2.4$, 1H), 3.70 (s, 3H), 3.32 (dd, $J = 14.4, 5.4$, 1H), 1.72 (s, 3H), 1.42 (s, 9H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ = 170.9, 167.0, 166.3, 165.2, 143.4, 134.2, 134.0, 133.7, 130.3, 130.2, 130.1, 129.7, 129.0, 128.9, 128.8, 128.6, 122.2, 87.2, 77.8, 76.0, 73.3, 69.3, 63.3, 54.8, 53.7, 53.0, 29.1, 23.5. HRMS (ESI) calculated for $\text{C}_{40}\text{H}_{44}\text{N}_5\text{O}_{12}$ ($\text{M}+\text{H}^+$) 786.2987, found 786.3059.

Methyl (*R*)-2-[(*tert*-Butoxycarbonyl)amino]-3-{1-(1,3,4,6-tetra-*O*-acetyl-D-glucopyranos-2-yl)[1,2,3]triazol-4-yl}propionate (21)

White solid. 43 mg (0.07 mmol, 71%). $R_f = 0.30$ (EtOAc/heptane 2/1). Major isomer: IR (film): ν 3382, 2980, 2358, 2336, 2250, 1744. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.39 (s, 3H), 6.13 (d, $J = 8.6$ Hz, 1H), 5.75-5.70 (m, 1H), 5.46 (br d, $J = 7.6$ Hz, 1H), 5.26-5.09 (m, 1H), 4.63 (dd, $J = 10.6, 8.9$ Hz, 1H), 4.59-4.51 (m, 1H), 4.34 (dd, $J = 12.4, 4.4$ Hz, 1H), 4.13 (dd, $J = 12.4, 1.6$ Hz, 1H), 4.05-4.01 (m, 1H), 3.66 (s, 3H), 3.18 (br d, $J = 4.1$ Hz, 2H), 2.06 (s, 3H), 2.00 (s, 3H), 1.96 (s, 3H), 1.84 (s, 3H), 1.39 (s, 9H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ = 171.4, 170.3, 169.3, 169.0, 168.0, 155.1, 142.9, 122.1, 91.6, 80.1, 73.2, 72.0, 68.1, 62.8, 61.5, 53.1, 52.6, 28.6, 21.0, 20.8, 20.7, 20.5. HRMS (ESI) calculated for $\text{C}_{25}\text{H}_{36}\text{N}_4\text{O}_{13}\text{Na}$ ($\text{M}+\text{Na}^+$) 623.2177, found 623.2180.

¹H NMR spectrum of compound 10a in CDCl₃. The spectrum shows peaks from 0 to 8 ppm. Key peaks are labeled with their chemical shifts: 2.1837, 2.0791, 8.6875, 2.3475, 0.9173, 1.1129, 1.2301, 4.1634, 0.9691, 6.0748, 1.1282, 2.0000, 3.4598, 3.0266, 3.1818, and 3.1451. The x-axis is labeled (ppm) and ranges from 0.0 to 7.0.

Methyl (2*S*)-3-{1-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)[1,2,3]triazol-4-yl}-2-[(4-Tolylsulfonyl)amino]propionate (29)

White solid. 60 mg (0.09 mmol, 64%). R_f = 0.28 (EtOAc/heptane 2/1). $[\alpha]_D^{25} = -8.6$ ($c = 0.40$, CH_2Cl_2). IR (film): ν 3481, 3278, 3140, 2950, 2362, 2254, 1744, 1601. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.73 (d, $J = 8.2$ Hz, 2H), 7.60 (s, 1H), 7.29 (d, $J = 8.0$ Hz, 2H), 5.83 (d, $J = 9.0$ Hz, 1H), 5.57 (d, $J = 8.8$ Hz, 1H), 5.42 (t, $J = 9.3$ Hz, 1H), 5.38 (t, $J = 9.2$ Hz, 1H), 5.24 (dd, $J = 10.0, 9.2$ Hz, 1H), 4.32 (dd, $J = 12.7, 4.9$ Hz, 1H), 4.284.26 (m, 1H), 4.16 (dd, $J = 12.7, 2.0$ Hz, 1H), 4.00 (ddd, $J = 10.0, 6.8, 2.0$ Hz, 1H), 3.57 (s, 3H), 3.19 (d, $J = 5.2$ Hz, 2H), 2.42 (s, 3H), 2.10 (s, 3H), 2.07 (s, 3H), 2.07 (s, 3H), 1.89 (s, 3H), 1.58 (s, 3H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ = 170.5, 170.3, 169.7, 169.1, 169.1, 143.5, 142.5, 136.8, 129.6, 127.2, 120.9, 85.9, 75.3, 72.7, 70.5, 67.9, 61.7, 54.9, 53.0, 29.7, 21.9, 21.1, 20.9, 20.9, 20.5. HRMS (ESI) calculated for $\text{C}_{27}\text{H}_{34}\text{O}_{13}\text{N}_4\text{NaS}$ ($\text{M}+\text{Na}^+$) 677.1741, found 677.1767.

Methyl (S)-2-[(*tert*-Butoxycarbonyl)amino]-4-[1-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)[1,2,3]triazol-4-yl]butanoate (30).

White solid. 50 mg (0.08 mmol, 80%). R_f = 0.29 (EtOAc/heptane 2/1). $[\alpha]_D = -28.4$ (c = 0.89, CH_2Cl_2). IR (film): ν 3382, 2980, 1753, 1710. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.57 (s, 1H), 5.86-5.80 (m, 1H), 5.44-5.36 (m, 2H), 5.26-5.19 (m, 1H), 5.17, (br d, J = 8.6 Hz, 1H), 4.31 (d, J = 5.1 Hz, 1H), 4.28 (dd, J = 12.7, 4.9 Hz, 1H), 4.13 (dd, J = 12.7, 2.0 Hz, 1H), 3.98 (ddd, J = 10.1, 4.9, 2.0 Hz, 1H), 3.71 (s, 3H), 2.78 (t, J = 8.0 Hz, 2H), 2.24-2.16 (m, 1H), 2.06 (s, 3H), 2.05 (s, 3H), 2.03-1.95 (m, 1H), 2.00 (s, 3H), 1.85, (s, 3H), 1.42 (s, 9H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ = 172.6, 170.2, 169.7, 169.1, 168.7, 155.2, 147.2, 119.4, 85.7, 80.1, 75.2, 72.8, 70.3, 67.9, 61.7, 53.1, 52.6, 32.5, 28.6, 22.1, 21.0, 20.9, 20.8, 20.5. HRMS (ESI) calculated for $\text{C}_{26}\text{H}_{38}\text{N}_4\text{O}_{13}\text{Na}$ ($\text{M}+\text{Na}^+$) 637.2333, found 637.2374.

Methyl (S)-2-[(*tert*-Butoxycarbonyl)amino]-5-[1-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)[1,2,3]triazol-4-yl]pentanoate (31).

White solid. 45 mg (0.07 mmol, 76%). $R_f = 0.29$ (EtOAc/heptane 2/1). Major isomer: $[\alpha]_D = -11.1$ ($c = 0.76$, CH_2Cl_2). IR (film): ν 3378, 2958, 1744, 1714. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.54 (s, 1H), 5.85 (d, $J = 8.8$ Hz, 1H), 5.45-5.36 (m, 2H), 5.24 (dd, $J = 9.8$, 9.4 Hz, 1H), 5.15 (br d, $J = 8.2$ Hz, 1H), 4.35-4.26 (m, 1H), 4.32 (dd, $J = 12.7$, 5.0 Hz, 1H), 4.15 (dd, $J = 12.7$, 2.0 Hz, 1H), 4.01 (ddd, $J = 10.2$, 4.9, 2.0 Hz, 1H), 3.74 (s, 3H), 2.84-2.65 (m, 2H), 2.09 (s, 3H), 2.07 (s, 3H), 2.04 (s, 3H), 1.80 (s, 3H), 1.88-1.57 (m, 4H), 1.43 (m, 9H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ = 173.1, 170.4, 169.8, 169.3, 169.0, 155.5, 148.2, 119.3, 86.0, 80.1, 75.4, 72.8, 70.8, 68.1, 61.9, 53.6, 52.7, 32.3, 28.8, 25.7, 25.5, 21.2, 21.0, 21.0, 20.6. HRMS (ESI) calculated for $\text{C}_{27}\text{H}_{40}\text{N}_4\text{O}_{13}\text{Na}$ ($\text{M}+\text{Na}^+$) 651.2490, found 651.2521.

Methyl 2-[(*tert*-Butoxycarbonyl)amino]-2-methyl-3-{1-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)[1,2,3]triazol-4-yl}propionate (32)

White solid. 55 mg (0.09 mmol, 85%). $R_f = 0.15$ (EtOAc/heptane 2/1). Mixture of diastereoisomers: IR (film): ν 3382, 2958, 2362, 1748, 1709. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.52 (s, 1H), 7.51 (s, 1H), 5.82 (d, J = 9.2 Hz, 1H), 5.81 (d, J = 9.4 Hz, 1H), 5.43-5.27 (m, 6H), 5.21 (t, J = 10.3 Hz, 2H), 4.28 (dd, J = 12.5, 5.0 Hz, 2H), 4.12 (dd, J = 12.5, 2.0 Hz, 2H), 4.01-3.97 (m, 4H), 2.05 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 1.99 (s, 3H), 1.84 (s, 3H), 1.84 (s, 3H), 1.42 (s, 9H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3)

δ = 173.8, 173.8, 170.2, 170.2, 169.6, 169.6, 169.1, 169.1, 168.7, 168.6, 154.2, 154.2, 143.6, 143.6, 121.0, 121.0, 85.8, 85.8, 79.9, 75.3, 75.2, 72.6, 72.5, 70.7, 70.5, 67.9, 67.9, 61.7, 61.7, 59.3, 59.2, 52.9, 52.8, 28.6, 28.6, 23.8, 23.7, 21.0, 20.8, 20.8, 20.4, 20.3. HRMS (ESI) calculated for $\text{C}_{26}\text{H}_{38}\text{N}_4\text{O}_{13}\text{Na}$ ($\text{M}+\text{Na}^+$) 637.2333, found 637.2352.

(S)-2-[(*tert*-Butoxycarbonyl)amino]-3-[1-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)[1,2,3]triazol-4-yl]propanenitrile(33).

White solid. 34 mg (0.06 mmol, 60%). $R_f = 0.14$ (EtOAc/heptane 1/1). $[\alpha]_D = -8.8$ ($c = 1.01$, CH_2Cl_2). IR (film): ν 3356, 2980, 2254, 1753, 1714. ^1H -NMR (400 MHz, CDCl_3) δ = 7.79 (s, 1H), 5.87 (d, $J = 8.8$ Hz, 1H), 5.75 (bd, $J = 5.7$ Hz, 1H), 5.45 (t, $J = 9.3$ Hz, 1H), 5.40 (t, $J = 9.3$ Hz, 1H), 5.25 (dd, $J = 10.0, 9.4$ Hz, 1H), 4.96 (bs, 1H), 4.26 (dd, $J = 12.7, 5.1$, 1H), 4.19 (dd, $J = 12.7, 2.2$ Hz, 1H), 4.05-4.01 (ddd, $J = 10.2, 5.1, 2.1$ Hz, 1H), 3.28 (dd, $J = 15.0, 5.3$ Hz, 1H), 3.20 (dd, $J = 15.0, 5.5$ Hz, 1H), 2.09 (s, 3H), 2.08 (s, 3H), 2.04 (s, 3H), 1.9 (s, 3H). ^{13}C -NMR (75 MHz, CDCl_3) δ = 170.5, 169.8, 169.3, 169.2, 154.3, 142.1, 121.6, 118.0, 86.2, 81.2, 75.6, 72.7, 70.8, 68.1, 61.9, 42.5, 29.7, 28.7, 21.2, 21.1, 21.0, 20.7. HRMS (ESI) calculated for $\text{C}_{24}\text{H}_{33}\text{N}_5\text{O}_{11}\text{Na}$ ($\text{M}+\text{Na}^+$) 590.2075, found 590.2080.

Methyl (S)-2-{{(S)-2-[(*tert*-Butoxycarbonyl)amino]propanoyl}amino}-3-{1-(2,3,4,6-tetra-*O*-acetyl- β -D-glucopyranosyl)[1,2,3]triazol-4-yl}propionate (36)

White solid. 45 mg (0.07 mmol, 51%). R_f = 0.18 (EtOAc/heptane 2/1). $[\alpha]_D^{25}$ = -1.3 (c = 0.80, CH_2Cl_2). IR (film): ν 3365, 2971, 2358, 2250, 1748, 1511. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.63 (s, 1H), 6.88 (d, J = 7.8 Hz, 1H), 5.82 (d, J = 9.2 Hz, 1H), 5.42 (t, J = 9.5 Hz, 1H), 5.34 (t, J = 9.4 Hz, 1H), 5.27-5.17 (m, 1H), 5.23 (dd, J = 10.2, 9.2 Hz, 1H), 4.90 (dt, J = 8.0, 5.1 Hz, 1H), 4.33 (dd, J = 12.7, 5.3 Hz, 1H), 4.25-4.12 (m, 1H), 4.15 (dd, J = 12.7, 2.2 Hz, 1H), 4.00 (ddd, J = 10.2, 5.1, 2.1 Hz, 1H), 3.76 (s, 3H), 3.34 (dd, J = 15.0, 5.1 Hz, 1H), 3.26 (dd, J = 15.0, 5.1 Hz, 1H), 2.09 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H), 1.90 (s, 3H), 1.45 (s, 9H), 1.35 (d, J = 7.0 Hz, 3H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ = 172.4, 170.9, 170.3, 169.6, 169.1, 169.0, 155.1, 143.3, 120.5, 85.9, 80.0, 75.4, 72.6, 70.6, 67.9, 61.7, 52.9, 51.6, 50.3, 28.6, 28.0, 21.0, 20.9, 20.8, 20.4, 18.9. HRMS (ESI) calculated for $\text{C}_{28}\text{H}_{41}\text{O}_{14}\text{N}_5\text{Na}$ ($\text{M}+\text{Na}^+$) 694.2548, found 694.2544.

Methyl (S)-2-[[[(2S)-1-(tert-Butoxycarbonyl)pyrrolidin-2-ylcarbonyl]amino]-3-{1-(2,3,4,6-tetra-O-acetyl- β -D-glucopyranosyl)[1,2,3]triazol-4-yl}]propionate (37)

White solid. 48 mg (0.07 mmol, 49%). R_f = 0.14 (EtOAc/heptane 2/1). $[\alpha]_D^{25}$ = -33.7379 (c = 1.03, CH_2Cl_2). IR (film): ν 3360, 3140, 2980, 2358, 2336, 2254, 1752, 1679, 1524. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.62 (br s, 1H), 7.15-6.91 (m, 1H), 5.89-5.74 (m, 1H), 5.44-5.32 (m, 2H), 5.26-5.12 (m, 1H), 4.95-4.76 (m, 1H), 4.34-4.09 (m, 3H), 3.99 (ddd, J = 10.0, 4.9, 2.2 Hz, 1H), 3.71 (s, 3H), 3.52-3.34 (m, 2H), 3.30-3.20 (m, 2H), 2.20-1.96 (m, 2H), 2.05 (s, 3H), 2.04 (s, 3H), 2.00 (s, 3H), 1.92-1.75 (m, 2H), 1.85 (s, 3H), 1.44 (s, 9H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ = 172.3, 170.9, 170.2, 169.7, 169.2, 168.8, 145.7, 143.5, 120.7, 86.0, 80.5, 75.5, 73.1, 70.7, 68.3, 62.0, 61.2, 52.8, 51.9, 47.3, 28.9, 28.8, 24.4, 21.0, 20.9, 20.8, 20.4. HRMS (ESI) calculated for $\text{C}_{30}\text{H}_{43}\text{O}_{14}\text{N}_5\text{Na}$ ($\text{M}+\text{Na}^+$) 720.2704, found 720.2732.

Methyl (R)-2-[(*tert*-Butoxycarbonyl)amino]-3-[1-(2,2',3,3',4',6,6'-hepta-*O*-acetyl- β -D-lactosyl)[1,2,3]triazol-4-yl]propionate (39)

White solid. 74 mg (0.08 mmol, 83%). $R_f = 0.17$ (EtOAc/heptane 2/1). $[\alpha]_D = -17.8$ ($c = 1.08$, CH_2Cl_2). IR (film): ν 3378, 2980, 2366, 2250, 1744. $^1\text{H-NMR}$ (400 MHz, CDCl_3) $\delta = 7.50$ (s, 1H), 5.75 (d, $J = 9.0$ Hz, 1H), 5.44-5.29 (m, 4H), 5.08 (dd, $J = 10.4, 7.9$ Hz, 1H), 4.94 (dd, $J = 10.4, 3.3$ Hz, 1H), 4.60-4.53 (m, 1H), 4.50 (d, $J = 7.8$ Hz), 4.43 (d, $J = 11.9$ Hz), 4.13-4.03 (m, 4H), 3.94-3.86 (m, 3H), 3.67 (s, 3H), 3.21 (dd, $J = 14.7, 5.4$ Hz, 1H), 3.14 (dd, $J = 14.7, 4.6$ Hz, 1H), 2.11 (s, 3H), 2.06 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H), 2.01 (s, 3H), 1.92 (s, 3H), 1.83 (s, 3H), 1.39 (s, 9H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) $\delta = 171.6, 170.3, 170.1, 170.0, 170.0, 169.3, 169.2, 169.0, 155.3, 143.4, 120.7, 101.3, 85.8, 80.2, 76.3, 76.0, 72.7, 71.2, 71.2, 70.8, 69.4, 67.0, 62.0, 61.2, 53.3, 52.8, 28.9, 28.8, 21.3, 21.2, 21.2, 21.1, 21.1, 21.0, 20.6$. HRMS (ESI) calculated for $\text{C}_{37}\text{H}_{53}\text{N}_4\text{O}_{21}$ (MH^+) 889.3202, found 889.3248.

Methyl (S)-2-(((S)-2-[(*tert*-Butoxycarbonyl)amino]propanoyl)amino)-3-[1-(2,2',3,3',4',6,6'-hepta-*O*-acetyl- β -D-lactosyl)[1,2,3]triazol-4-yl]propionate (40)

White solid. 117 mg (0.12 mmol, 81%). R_f = 0.13 (EtOAc/heptane 2/1). $[\alpha]_D^{25}$ = -0.5 (c = 1.13, CH_2Cl_2). IR (film): ν 3382, 3144, 2980, 2362, 2254, 1752, 1502. $^1\text{H-NMR}$ (400 MHz, CDCl_3) δ = 7.58 (s, 1H), 6.94 (d, J = 7.8 Hz, 1H), 5.78 (d, J = 9.3 Hz, 1H), 5.41-5.25 (m, 4H), 5.14 (dd, J = 10.5, 7.8 Hz, 1H), 4.99 (dd, J = 10.2, 3.4 Hz, 1H)

4.89 (dt, J = 8.0, 5.2 Hz, 1H), 4.55-4.48 (m, 2H), 4.21-4.10 (m, 4H), 3.95-3.40 (m, 3H), 3.75 (s, 3H), 3.32 (dd, J = 15.1, 4.9 Hz, 1H), 3.25 (dd, J = 15.1, 5.4 Hz, 1H), 2.17 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 1.98 (s, 3H), 1.89 (s, 3H), 1.44 (s, 9H), 1.33 (d, J = 7.1 Hz, 3H). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ = 172.4, 170.9, 170.1, 170.0, 169.8, 169.2, 169.2, 168.8, 155.1, 143.1, 120.4, 101.1, 85.7, 80.0, 76.2, 75.8, 72.4, 71.0, 71.0, 70.8, 69.2, 66.7, 61.8, 61.0, 52.8, 51.5, 50.3, 28.6, 28.1, 21.1, 21.0, 21.0, 20.9, 20.9, 20.8, 20.5, 18.8. HRMS (ESI) calculated for $\text{C}_{40}\text{H}_{57}\text{O}_{22}\text{N}_5\text{Na}$ ($\text{M}+\text{Na}^+$) 982.3393, found 982.3440.

(S)-2-[(*tert*-Butoxycarbonyl)amino]-3-[4-(2,3,4,6-tetra-*O*-benzyl- β -D-glucopyranosyl)[1,2,3]triazol-1-yl]propionic acid (44a)

White solid. 54 mg (0.07 mmol, 70%). R_f = 0.46 (EtOAc + 1% HOAc). $[\alpha]_D^{25}$ = +35.5 (c = 0.68, CHCl_3). IR (film) ν : 3399, 3058, 2885, 2362, 2327, 1735. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 7.52 (s, 1 H), 7.30-6.97 (m, 20 H), 5.41 (br d, J = 5.3 Hz, 1H), 4.92-4.73 (m, 5H), 4.57-4.46 (m, 6H), 4.17 (d, J = 10.8 Hz, 1H), 3.90 (t, J = 9.1 Hz, 1H), 3.79 (t, J = 8.8 Hz, 1H), 3.72-3.57 (m, 4H), 1.41 (s, 9H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz) δ : 170.3, 155.2, 145.0, 138.3, 137.9, 137.7, 137.6, 129.0, 128.3, 128.3, 128.2, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 125.2, 124.6, 86.8, 81.8, 80.8, 79.4, 78.1, 75.8, 75.2, 75.0, 73.8, 73.6, 69.1, 54.0, 51.4, 28.6. HRMS (ESI) calculated for $\text{C}_{44}\text{H}_{51}\text{N}_4\text{O}_9$ ($\text{M}+\text{H}^+$) 779.3656, found 779.3648.

(S)-2-[(*tert*-Butoxycarbonyl)amino]-3-[4-(2,3,4,6-tetra-*O*-benzyl- β -D-glucopyranosyl)[1,2,3]triazol-1-yl]butyric acid (44b)

White solid. 58 mg (0.07 mmol, 73%). R_f = 0.53 (EtOAc + 1% HOAc). $[\alpha]_D^{25}$ = +21.0 (c = 1.06, CHCl_3). IR (film) ν : 3391, 3019, 2902, 2859, 2353, 2327, 1714. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 8.93 (br s, 1H), 7.60 (s, 1H), 7.31-6.96 (m, 20H), 5.55 (br s, 1H), 4.92 (d, J = 11.3 Hz, 1H), 4.88 (d, J = 11.5 Hz, 1H), 4.84 (d, J = 10.7 Hz, 1H), 4.62 (d, J = 10.7 Hz, 1H), 4.55-4.24 (m, 8H), 3.90 (dd, J = 9.0, 8.6 Hz, 1H), 3.79 (t, J = 8.6 Hz, 1H), 3.71-3.60 (m, 4H), 2.47 (br s, 1H), 2.19 (br s, 1H), 1.45 (s, 9H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz) δ : 173.2, 155.7, 145.1, 138.4, 137.9, 137.8, 137.7, 128.3, 128.1, 127.9, 127.7, 127.6, 124.0, 87.0, 81.8, 80.5, 79.4, 78.2, 75.7, 75.2, 74.9, 73.8, 73.4, 69.1, 51.4, 47.1, 33.8, 28.6. HRMS (ESI) calculated for $\text{C}_{45}\text{H}_{53}\text{N}_4\text{O}_9$ ($\text{M}+\text{H}^+$) 793.3812, found 793.3854.

(S)-2-[(*tert*-Butoxycarbonyl)amino]-3-[4-(2,3,4,6-tetra-*O*-benzyl- β -D-glucopyranosyl)[1,2,3]triazol-1-yl]pentanoic acid (44c)

White solid. 59 mg (0.07 mmol, 71%). R_f = 0.59 (EtOAc + 1% HOAc). $[\alpha]_D^{25}$ = +11.2 (c = 0.92, CHCl_3). IR (film) ν : 3417, 3334, 3062, 3028, 2920, 2863, 2362, 2332, 2237, 1701. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 9.87 (br s, 1H), 7.42 (s, 1H), 7.29-6.98 (m, 20H), 5.26 (d, J = 7.6 Hz, 1H), 4.93 (d, J = 11.1 Hz, 1H), 4.89 (d, J = 11.1 Hz, 1H), 4.84 (d, J = 10.9 Hz, 1H), 4.62 (d, J = 10.9 Hz, 1H), 4.57-4.52 (m, 3H), 4.48 (d, J = 12.3 Hz, 1H), 4.28 (d, J = 10.9 Hz, 1H), 4.30-4.10 (m, 3H), 3.89 (t, J = 9.2 Hz, 1H), 3.81 (dd, J = 9.0, 8.8 Hz, 1H), 3.74-3.67 (m, 3H), 3.63-3.59 (m, 1H), 1.92-1.62 (m, 4H), 1.42 (s, 9H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz) δ : 173.7, 155.0, 145.0, 138.0, 137.4, 137.3, 137.3, 128.5, 127.9, 127.9, 127.8, 127.7, 127.7, 127.5, 127.4, 127.4, 127.2, 127.2, 127.1, 127.1, 124.8, 122.5, 86.5, 81.3, 79.8, 78.9, 77.8, 75.3, 74.7, 74.4, 73.5, 73.0, 68.7, 52.3, 49.4, 29.3, 28.2, 25.9. HRMS (ESI) calculated for $\text{C}_{46}\text{H}_{54}\text{N}_4\text{NaO}_9$ ($\text{M}+\text{Na}^+$) 829.3788, found 829.3787.

Methyl (*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-{4-(2,3,4,6-tetra-*O*-benzyl- β -D-glucopyranosyl)[1,2,3]triazol-1-yl}propionate (45)

White solid. 175 mg (0.22 mmol, 69%). $R_f = 0.40$ (EtOAc/heptane 1/1). $[\alpha]_D^{25} = +21.9$ ($c = 0.96$, CHCl_3). IR (film) ν : 3028, 2924, 2850, 2353, 2332, 1748, 1714. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 7.43 (s, 1H), 7.33-7.00(m, 20H), 5.31 (br d, $J = 6.2$ Hz, 1H), 4.94 (d, $J = 11.1$ Hz, 1H), 4.90 (d, $J = 11.1$ Hz, 1H), 4.85 (d, $J = 10.8$ Hz, 1H), 4.86-4.80 (m, 1H), 4.75-4.65 (m, 2H), 4.61 (d, $J = 11.7$ Hz, 1H), 4.58 (d, $J = 10.9$ Hz, 1H), 4.56 (d, $J = 12.1$ Hz, 1H), 4.51 (d, $J = 9.7$ Hz, 1H), 4.51 (d, $J = 12.1$ Hz, 1H), 4.28 (d, $J = 10.7$ Hz, 1H), 3.92 (dd, $J = 9.4, 9.2$ Hz, 1H), 3.81 (dd, $J = 9.0, 8.8$ Hz, 1H), 3.75-3.67 (m, 6H), 3.63-3.60 (m, 1H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz) δ : 181.1, 168.7, 154.4, 145.2, 138.0, 137.4, 137.4, 127.9, 127.8, 127.7, 127.4, 127.3, 127.2, 127.2, 127.1, 123.6, 86.5, 81.4, 80.4, 79.1, 77.8, 75.3, 74.7, 74.5, 73.6, 73.1, 68.8, 53.5, 52.8, 50.6, 28.1. HRMS (ESI) calculated for $\text{C}_{45}\text{H}_{52}\text{N}_4\text{NaO}_9$ ($\text{M}+\text{Na}^+$) 815.3632, found 815.3615.

(S)-2-[(*tert*-Butoxycarbonyl)amino]-3-[4-(2,3,4,6-tetra-*O*-benzyl- α -D-glucopyranosyl)[1,2,3]triazol-1-yl]propionic acid (47a)

White solid. 10 mg (0.01 mmol, 60%). $R_f = 0.52$ (EtOAc + 1% HOAc). $[\alpha]_D = +55.2$ ($c = 0.48$, CHCl_3). IR (film) ν : 3404, 3032, 2915, 2859, 2358, 2336, 1709. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 7.67 (s, 1H), 7.31-7.09 (m, 20H), 5.48 (br d, $J = 4.7$ Hz, 1H), 5.29 (br d, $J = 4.9$ Hz, 1H), 4.95-4.90 (m, 2H), 4.80-4.74 (m, 3H), 4.68-4.58 (m, 4H), 4.49 (d, $J = 10.8$ Hz, 1H), 4.45 (d, $J = 12.1$ Hz, 1H), 4.04-3.94 (m, 2H), 3.75 (t, $J = 8.9$ Hz, 1H), 3.67-3.55 (m, 3H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz) δ : 170.3, 155.2, 142.9, 138.5, 137.9, 137.8, 137.7, 129.0, 128.5, 128.3, 128.0, 127.9, 127.7, 127.6, 125.6, 125.3, 82.4, 80.7, 79.4, 78.0, 75.5, 75.1, 73.6, 73.4, 73.0, 69.2, 68.6, 54.1, 51.3, 28.6. HRMS (ESI) calculated for $\text{C}_{44}\text{H}_{50}\text{N}_4\text{NaO}_9$ ($\text{M} + \text{Na}^+$) 801.3475, found 801.3445.

(S)-2-[(*tert*-Butoxycarbonyl)amino]-3-[4-(2,3,4,6-tetra-*O*-benzyl- α -D-glucopyranosyl)[1,2,3]triazol-1-yl]butyric acid (47b)

White solid. 49 mg (0.06 mmol, 60%). R_f = 0.53 (EtOAc + 1% HOAc). $[\alpha]_D^{25} = +60.0$ ($c = 0.31$, CHCl_3). IR (film) ν : 3408, 3023, 2976, 2872, 2353, 2332, 1705. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz) δ : 7.64 (s, 1H), 7.34-7.09 (m, 20H), 5.45 (br s, 1H), 5.28 (d, $J = 5.5$ Hz, 1H), 4.98 (d, $J = 11.1$ Hz, 1H), 4.85 (d, $J = 10.9$ Hz, 1H), 4.80 (d, $J = 10.7$ Hz, 1H), 4.69 (d, $J = 11.7$ Hz, 1H), 4.61 (d, $J = 11.7$ Hz, 1H), 4.56 (d, $J = 12.3$ Hz, 1H), 4.49 (d, $J = 10.7$ Hz, 1H), 4.46 (d, $J = 12.1$ Hz, 1H), 4.45-4.20 (m, 3H), 3.98 (dd, $J = 9.4, 9.2$ Hz, 1H), 3.75-3.56 (m, 5H), 2.47 (br s, 2H), 1.44 (s, 9H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz, ppm) δ : 155.4, 143.3, 138.6, 137.6, 137.4, 128.3, 128.1, 127.9, 127.7, 127.6, 124.8, 82.4, 80.4, 79.7, 78.4, 75.5, 75.1, 73.6, 73.4, 72.5, 69.2, 69.0, 46.3, 32.8, 30.0, 28.7. HRMS (ESI) calculated for $\text{C}_{45}\text{H}_{53}\text{N}_4\text{O}_9$ ($\text{M}+\text{H}^+$) 793.3812, found 793.3836.