Electronic Supplementary Information

Phenylenediamine catalysis of click glycosylations in water: Practical and direct access to unprotected neoglycoconjugates

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General Methods

Thin layer chromatography was performed on Merck 60F 254 sheets with detection by UV and by charring with 5% ethanolic H$_2$SO$_4$. Unless otherwise stated, TLC was eluted with ethyl acetate / isopropanol / water 3:2:1. Hygroscopic reagents were dried in vacuo immediately prior to weighing. NMR spectra were taken on Bruker DPX 250, AM 300, AV 360 or DRX 400 spectrometers, using the residual protonated solvent as internal standard. Chemical shifts δ are given in parts per million (ppm). Mass spectra were taken on a ThermoFinnigan Mat 95, with Electrospray ionization in the positive (ESI$^+$) or negative (ESI) mode of detection, or on a Jeol JMS-700, with Fast Atom Bombardment ionization in the positive mode of detection (FAB$^+$). Residual free copper was first estimated with Quantofic® Copper test sticks (Macherey-Nagel) and then quantified by CHEMets® Kit Copper K-3510 (CHEMetrics) colorimetric assay.

Methyl 3-O-propargyl-α-D-glucopyranoside:

To a solution of methyl 4,6-O-benzylidene-3-O-propargyl-α-D-glucopyranoside$^1$ (500 mg, 1.56 mmol) in MeOH (20.0 ml) was added 2.1 g of Dowex 50WX8-H$^+$ resin. The suspension was stirred at 50°C overnight. The reaction mixture was filtered off, and neutralized with solid NaHCO$_3$, filtered and the solvent was evaporated. The residue was purified by column
chromatography over silica gel (Petroleum Ether/EtOAc 1/4) to yield 356 mg (98%) of methyl 3-O-propargyl-α-D-glucopyranoside as a colourless oil. 1H NMR (360 MHz, MeOD-d4) δ: 4.65 (d, 1H, J1,2 4.0 Hz, H-1); 4.49 (d, 2H, 2J 2.0 Hz, OCH2CCH); 3.80 (dd, 1H, J6a,6b 12.0, J6a,5 2.0 Hz, H-6a); 3.67 (dd, 1H, J6b,6a 12.0, J6b,5 5.5 Hz, H-6b); 3.57 (dd, 1H, J2,3 9.5, J3,4 8.5 Hz, H-3); 3.54 (ddd, 1H, J4,5 10.0, J5,6b 5.5, J5,6a 2.0 Hz, H-5); 3.47 (dd, 1H, J2,3 9.5, J2,1 4.0 Hz, H-2); 3.41 (s, 3H, OCH3); 3.36 (dd, 1H, J4,5 10.0, J4,3 8.5 Hz, H-4); 2.81 (t, 1H, 4J 2.5 Hz, CH2CCH). 13C NMR (90 MHz, DMSO-d6) δ: 99.7 (C-1); 81.4 (C-3); 81.3 (OCH2CCH); 76.3 (OCH2CCH); 72.6 (C-5); 71.6 (C-2); 69.4 (C-4); 60.7 (C-6); 59.2 (OCH2CCH); 54.3 (OCH3). MS (ESI+): m/z 255.2 [M+Na]+. HRMS (ESI+): Calcd. for C10H16O6Na 255.0839, found 255.0834.

N-acetyl-L-phenylalanine propargylamide :

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\text{N-Acetyl-L-phenylalanine (324 mg, 1.56 mmol) was dissolved in dry CH}_2\text{Cl}_2 (6.0 ml) with DMAP (19.0 mg, 0.16 mmol, 0.1 eq.) and EDC•HCl (449 mg, 2.34 mmol, 1.5 eq.). Propargylamine (100 μl, 86.0 mg, 1.56 mmol, 1.0 eq.) was added and the reaction mixture was stirred at room temperature overnight under an argon atmosphere until TLC (CH2Cl2/MeOH 9:1) showed complete conversion. The reaction mixture was washed three times with water, and the organic layer was dried over sodium sulfate, filtered and concentrated. The residue was purified by flash chromatography over silica gel (CH2Cl2 / MeOH 9/1) to give 99.0 mg (26 %) of N-acetyl-L-phenylalanine propargylamide as a white solid. 1H NMR (300 MHz, CDCl3) δ: 7.35-7.25 (m, 3H, H-3', H-4', H-5'); 7.20 (m, 2H, H-2', H-6'); 6.47 (t, 1H, 3J 5.3 Hz, CONHCH2); 6.41 (d, 1H, JNH,2 7.5 Hz, CH3CONH); 4.69 (td, 1H, J2,3 7.5, J2,NH 7.5 Hz, H-2); 3.95 (dd, 2H, J 5.3, 4J 2.5 Hz, CH2CCH); 3.05 (d, 2H, J3,2 7.5 Hz, H-3); 2.19 (t, 1H, 4J 2.5 Hz, CH2CCH); 1.97 (s, 3H, CH3). 13C NMR (75 MHz, CDCl3) δ: 170.9 ( C-1); 170.4 ( CH3CONH); 136.6 ( C-1'); 129.5 ( C-2', C-6'); 128.9 ( C-3', C-5'); 127.3 ( C-4'); 79.1 (CH2CCH); 71.8 (CH2CCH); 54.6 (C-2); 38.7 (C-3); 29.3 (CH2CCH); 23.3 (CH3). MS (ESI+): m/z 267.1 [M+Na]+. HRMS (ESI+): Calcd. for C14H16N2O2Na 267.11040, found 267.10907.
4-Hydroxymethyl-1-(β-D-glucopyranosyl)-1H-[1,2,3]-triazole (2):

**Procedure A:**

To a solution of β-D-glucopyranosyl azide (53.0 mg, 260 µmol, 1 eq.) in H₂O (730 µl) were added propargyl alcohol (15 µl, 14.5 mg, 260 µmol, 1 eq.), o-phenylenediamine (104 µl, 40.5 mg per ml of H₂O, 4.2 mg, 39 µmol, 15 mol%), sodium ascorbate (104 µl, 49.5 mg per ml of H₂O, 5.1 mg, 26 µmol, 10 mol%) and copper sulfate pentahydrate (104 µl, 31.2 mg per ml of H₂O, 3.2 mg, 13 µmol, 5 mol%). The reaction mixture was stirred at room temperature under an argon atmosphere for 45 min. After this time, TLC showed complete conversion and activated charcoal (100 mg) was added to the reaction mixture, which was stirred overnight under an air atmosphere. The reaction mixture was then filtered through a celite plug and eluted with water. The solvent was evaporated to dryness to give 66.4 mg (98%) of 4-hydroxymethyl-1-(β-D-glucopyranosyl)-1H-[1,2,3]-triazole(2) as a colourless oil. 

1H NMR (300 MHz, methanol-d₄) δ: 8.13 (s, 1H, H-5); 5.61 (d, 1H, J₁',₂' 9.5 Hz, H-1'); 4.71 (s, 2H, CH₂OH); 3.95-3.85 (m, 2H, H-2', H-6a'); 3.72 (dd, 1H, J₆a',₆b' 12.0, J₅',₆b' 5.0 Hz, H-6b'); 3.62-3.45 (m, 3H, H-3', H-4', H-5'). 

13C NMR (75 MHz, methanol-d₄) δ: 149.1 (C-4); 123.4 (C-5); 89.5 (C-1'); 81.1 (C-5'); 78.5 (C-3'); 74.0 (C-2'); 70.9 (C-4'); 62.4 (C-6'); 59.4 (CCH₂OH). Residual copper ~ 0.10 mol%. MS (ESI⁺): m/z 284.1 [M+Na]⁺. HRMS (ESI⁺): Calcd. for C₉H₁₅N₅O₆Na 284.08531, found 284.08604.

4-((Dimethylamino)methyl)-1-(β-D-glucopyranosyl)-1H-[1,2,3]-triazole (3):

Following Procedure A, 4-((dimethylamino)methyl)-1-(β-D-glucopyranosyl)-1H-[1,2,3]-triazole (3) was obtained from β-D-glucopyranosyl azide (51.3 mg, 250 µmol, 1 eq.) in H₂O (600 µl), dimethylaminopropyne (27 µl, 20.8 mg, 250 µmol, 1 eq.), o-phenylenediamine (200 µl, 20.3 mg per ml of H₂O, 4.0 mg, 37.5 µmol, 15 mol%), sodium ascorbate (100 µl, 49.5 mg per ml of H₂O, 4.9 mg, 25.0 µmol, 10 mol%) and copper sulfate pentahydrate (100 µl, 31.2
mg per ml of H₂O, 3.1 mg, 12.5 µmol, 5 mol%). The reaction mixture was stirred at room temperature for 45 min, and activated charcoal was added followed by 45 min of stirring under an air atmosphere. Purification by filtration and evaporation gave 53.7 mg (75%) of 4-((dimethylamino)methyl)-1-(β-D-glucopyranosyl)-1H-[1,2,3]-triazole (3) as a white solid. ¹H NMR (300 MHz, methanol-d4) δ: 8.12 (s, 1H, H-5'); 5.60 (d, 1H, J₁',2' 9.0 Hz, H-1'); 3.89 (dd, 1H, J_2',1' 9.0, J₂',3' 9.0 Hz, H-2'); 3.88 (dd, 1H, J_6a',6b' 12.0, J₆a',₅' 2.0 Hz, H-6a'); 3.71 (dd, 1H, J_6a',6b' 12.0, J₃',₆b' 5.0 Hz, H-6b'); 3.66 (s, 2H, CH₂N(CH₃)₂); 3.58 (dd, 1H, J₅',₄' 9.0, J₅',₆b' 5.0, J₅',₆a' 2.0 Hz, H-5'); 3.56 (dd, 1H, J₃',₄' 9.0, J₃',₂' 8.5 Hz, H-3'); 3.49 (dd, 1H, J₄',₃' 9.0, J₄',₅' 9.0 Hz, H-4'); 2.29 (s, 6H, 2 CH₃). ¹³C NMR (62.5 MHz, methanol-d₄) δ: 144.7 (C-4); 124.8 (C-5); 89.7 (C-1'); 81.3 (C-5'); 78.7 (C-3'); 74.2 (C-2'); 71.0 (C-4'); 62.6 (C-6'); 54.4 (CH₂N(CH₃)₂); 45.0 (2 CH₃). Residual copper ~ 0.16 mol%. MS (ESI⁺): m/z 311.1 [M+Na]⁺. HRMS (ESI⁺): Calcd. for C₁₁H₂₀N₄O₃Na 311.13259, found 311.13230.

Ammonium 3-[1'-(β-D-glucopyranosyl)-1'H-[1',2',3']-triazol-4'-yl]propanoate (4):

Following Procedure A, ammonium 3-[1'-(β-D-glucopyranosyl)-1'H-[1',2',3']-triazol-4'-yl]propanoate (4) was obtained from β-D-glucopyranosyl azide (51.3 mg, 250 µmol, 1 eq.) in H₂O (600 µl), ammonium 4-pentynoate (28.8 mg, 250 µmol, 1 eq.), o-phenylenediamine (200 µl, 20.3 mg per ml of H₂O, 4.0 mg, 37.5 µmol, 15 mol%), ammonium ascorbate (100 µl, 48.3 mg per ml of H₂O, 4.8 mg, 25.0 µmol, 10 mol%) and copper sulfate pentahydrate (100 µl, 31.2 mg per ml of H₂O, 3.1 mg, 12.5 µmol, 5 mol%). The reaction mixture was stirred at room temperature for 2 hours, and activated charcoal was added followed by 45 min of stirring under an air atmosphere. Purification by filtration and evaporation gave 62.5 mg (78%) of ammonium 3-[1'-(β-D-glucopyranosyl)-1'H-[1',2',3']-triazol-4'-yl]propanoate (4) as a white solid. ¹H NMR (250 MHz, methanol-d₄) δ: 8.09 (s, 1H, H-5'); 5.55 (d, 1H, J₁',₂' 9.0 Hz, H-1'); 3.87 (dd, 1H, J₆a',₆b' 12.0, J₅',₆a' 1.5 Hz, H-6a'); 3.86 (dd, 1H, J₁',₂' 9.0, J₂',₃' 9.5 Hz, H-2'); 3.70 (dd, 1H, J₆a',₆b' 12.0, J₅',₆b' 5.0 Hz, H-6b'); 3.60-3.40 (m, 3H, H-3’, H-4’, H-5’); 3.00 (t, 2H, J₃,₂' 7.0 Hz, H-3); 2.59 (t, 2H, J₂,₃ 7.0 Hz, H-2). ¹³C NMR (62.5 MHz, methanol-d₄) δ: 148.8 (C-4'); 122.6 (C-5'); 89.7 (C-1'); 81.2 (C-5’'); 78.6 (C-3’'); 74.2 (C-2’'); 71.0 (C-4’'); 62.6 (C-6’'); 36.9 (C-2); 23.0 (C-3). Residual copper ~ 0.04 mol%. MS
[1’-(β-D-Glucopyranosyl)-1’H-[1’,2’,3’]-triazol-4’-yl]-methyl 2-acetamido-2-deoxy-β-D-glucopyranoside (5):

Following Procedure A, [1’-(β-D-glucopyranosyl)-1’H-[1’,2’,3’]-triazol-4’-yl]-methyl 2-acetamido-2-deoxy-β-D-glucopyranoside (5) was obtained from β-D-glucopyranosyl azide (115 mg, 560 µmol, 1 eq.) in H2O (1570 µl), propargyl 2-acetamido-2-deoxy-β-D-glucopyranoside3 (145 mg, 560 µmol, 1 eq.), o-phenylenediamine (224 µl, 40.5 mg per ml of H2O, 9.1 mg, 84.0 µmol, 15 mol%), sodium ascorbate (224 µl, 49.5 mg per ml of H2O, 11.1 mg, 56.0 µmol, 10 mol%) and copper sulfate pentahydrate (224 µl, 31.2 mg per ml of H2O, 7.0 mg, 28.0 µmol, 5 mol%). The reaction mixture was stirred at room temperature for 2 hours, and activated charcoal was added followed by overnight stirring under an air atmosphere. Purification by filtration and evaporation gave 247.4 mg (95%) of [1’-(β-D-glucopyranosyl)-1’H-[1’,2’,3’]-triazol-4’-yl]-methyl 2-acetamido-2-deoxy-β-D-glucopyranoside (5) as a white solid. 1H NMR (360 MHz, methanol-d4) δ: 8.18 (s, 1H, H-5’); 5.61 (d, 1H, J1:2 9.0 Hz, H-1’); 4.91 (d, 1H, J 12.5 Hz, CCH3O); 4.78 (d, 1H, J 12.5 Hz, CCH3H); 4.57 (d, 1H, J1,1:2 8.5 Hz, H-1); 3.91 (dd, 1H, J 12.0, 3J 1.5 Hz, H-6a or H-6a’); 3.88 (dd, 1H, J 12.0, 3J 2.0 Hz, H-6a or H-6a’); 3.88 (dd, 1H, J2:1:1 9.0, 3J 3.0 Hz, H-2’); 3.71 (dd, 1H, J 12.0, 3J 5.5 Hz, H-6b or H-6b’); 3.70 (dd, 1H, J 12.0, 3J 5.0 Hz, H-6b or H-6b’); 3.60 (dd, 1H, J3:4 10.0, 3J 8.5 Hz, H-3’); 3.59 (dd, 1H, J2,1 8.5, 3J 8.5 Hz, H-2); 3.58 (dd, 1H, J3:4 9.0, 3J 8.5 Hz, H-3’); 3.50 (dd, 1H, J4:5 9.0, 3J 9.5 Hz, H-4’); 3.49 (dd, 1H, J4,5 8.0 Hz, H-4); 3.42-3.26 (m, 2H, H-5, H-5’); 1.92 (s, 3H, CH3). 13C NMR (90 MHz, methanol-d4) δ: 174.1 (C=O); 145.9 (C-4’); 124.8 (C-5’); 101.6 (C-1’); 81.3 (C-3); 78.5 (C-3’); 78.2 (C-5); 75.9 (C-4); 74.3 (C-2’); 72.3 (C-5’); 71.1 (C-4’); 63.0 (C-6 or C-6’); 62.8 (CCH3O); 62.5 (C-6 or C-6’); 57.6 (C-2); 23.1 (CH3). Residual copper ~ 0.31 mol%. MS (ESI⁺) : m/z 487.0 [M+Na⁺]. HRMS (ESI⁺) : Calcd. for C17H28N4O11Na 487.16468, found 487.16533.
Methyl 3-O-[1’-(β-D-glucopyranosyl)-1’H-[1’,2’,3’]-triazol-4’y]-methyl-α-D-glucopyranoside (6):

Following Procedure A, methyl 3-O-[1’-(β-D-glucopyranosyl)-1’H-[1’,2’,3’]-triazol-4’y]-methyl-α-D-glucopyranoside (6) was obtained from β-D-glucopyranosyl azide (114 mg, 555 µmol, 1 eq.) in H2O (1560 µl), methyl 3-O-propargyl-α-D-glucopyranoside (129 mg, 555 µmol, 1 eq.), O-phenylenediamine (220 µl, 40.5 mg per ml of H2O, 8.9 mg, 82.5 µmol, 15 mol%), sodium ascorbate (220 µl, 49.5 mg per ml of H2O, 10.9 mg, 55.5 µmol, 10 mol%) and copper sulfate pentahydrate (220 µl, 31.2 mg per ml of H2O, 6.9 mg, 27.5 µmol, 5 mol%). The reaction mixture was stirred at room temperature for 45 min, and activated charcoal was added followed by overnight stirring under an air atmosphere. Purification by filtration and evaporation gave 239.1 mg (98%) of methyl 3-O-[1’-(β-D-glucopyranosyl)-1’H-[1’,2’,3’]-triazol-4’y]-methyl-α-D-glucopyranoside (6) as a white solid. 1H NMR (360 MHz, methanol-d4) δ: 8.18 (s, 1H, H-5’); 5.60 (d, 1H, J1”,2” 9.0 Hz, H-1”); 5.00 (d, 1H, J12.0 Hz, CCHaHbOC); 4.95 (d, 1H, J12.0 Hz, CCHaHbOC); 4.67 (d, 1H, J1,2 3.5 Hz, H-1); 3.92-3.84 (m, 2H, H-2”, H-6a’); 3.81 (dd, 1H, J6a,6b 12.0, J6a,5 2.5 Hz, H-6a); 3.71 (dd, 1H, J1,2 3.5 Hz, H-1); 3.92-3.84 (m, 2H, H-2”, H-6a’); 3.81 (dd, 1H, J6a,6b 12.0, J6a,5 2.5 Hz, H-6a); 3.71 (dd, 1H, J1,2 3.5 Hz, H-1); 3.92-3.84 (m, 2H, H-2”, H-6a’); 3.81 (dd, 1H, J6a,6b 12.0, J6a,5 2.5 Hz, H-6a); 3.71 (dd, 1H, J1,2 3.5 Hz, H-1); 3.92-3.84 (m, 2H, H-2”, H-6a’); 3.81 (dd, 1H, J6a,6b 12.0, J6a,5 2.5 Hz, H-6a); 3.71 (dd, 1H, J1,2 3.5 Hz, H-1); 3.92-3.84 (m, 2H, H-2”, H-6a’); 3.81 (dd, 1H, J6a,6b 12.0, J6a,5 2.5 Hz, H-6a); 3.71 (dd, 1H, J1,2 3.5 Hz, H-1); 3.92-3.84 (m, 2H, H-2”, H-6a’). 13C NMR (90 MHz, methanol-d4) δ: 147.1 (C-4’); 124.2 (C-5’); 101.5 (C-1’); 89.8 (C-1’); 84.3 (CH); 81.3 (CH); 78.6 (CH); 74.3 (C-2’); 73.7 (2 CH); 71.5 (CH); 71.1 (CH); 67.0 (CCH2OC); 62.7, 62.6 (C-6, C-6’); 55.8 (CH3). Residual copper ~ 0.40 mol%. MS (ESI+): m/z 460.1 [M+Na]+. HRMS (ESI+) : Calcd. for C16H27N3O11Na 460.15378, found 460.15485.
Tris((1-β-D-glucopyranosyl)-1H-[1,2,3]-triazol-4-yl)methyl)amine (7):

Following procedure A, tris((1-β-D-glucopyranosyl)-1H-[1,2,3]-triazol-4-yl)methyl)amine (7) was obtained from triprop-2-ynylamine (22 µl, 20.3 mg, 154.5 µmol), β-D-glucopyranosyl azide (95 mg, 463.5 µmol, 3 eq.), sodium ascorbate (185 µl, 49.5 mg per ml of H₂O, 9.2 mg, 46.4 µmol, 0.30 eq.), copper sulfate pentahydrate (185 µl, 31.2 mg per ml of H₂O, 5.8 mg, 23.2 µmol, 0.15 eq.) and o-phenylenediamine (370 µl, 20.3 mg per ml of H₂O, 7.5 mg, 69.5 µmol, 0.45 eq.) in H₂O (1110 µl). The reaction mixture was stirred at room temperature for 45 min, then activated charcoal was added followed by overnight stirring under an air atmosphere. Purification by filtration through an alumina plug and evaporation gave 106.2 mg (92%) of tris((1-β-D-glucopyranosyl)-1H-[1,2,3]-triazol-4-yl)methyl)amine as white powder.

$^1$H NMR (300 MHz, D₂O/methanol-d₄ 1:1) δ: 8.22 (s, 3H, 3 H-5); 5.68 (d, 3H, J₁',₂' 9.0 Hz, 3 H-1'); 3.97 (dd, 3H, J₂',₁' 9.0, J₂',₃' 9.0 Hz, 3 H-2'); 3.90 (dd, 3H, J₆ₐ',₆₉' 12.5, J₆ₐ',₅' 2.0 Hz, 3 H-6ₐ'); 3.83 (s, 6H, 3 NCH₂C); 3.76 (dd, 3H, J₆ₐ',₆₉' 12.5, J₅',₆₉' 5.0 Hz, 3 H-6₉'); 3.67 (ddd, 3H, J₅',₄₉' 9.5, J₅',₆₉' 5.0, J₅',₆₆' 2.0 Hz, 3 H-5'); 3.66 (dd, 3H, J₃',₂₉' 9.0, J₃',₄₉' 9.0 Hz, 3 H-3'); 3.58 (dd, 3H, J₄',₃₉' 9.0, J₄',₅₉' 9.5 Hz, 3 H-4'); $^{13}$C NMR (75 MHz, D₂O/ methanol-d₄ 1:1) δ: 145.1 (3 C-4); 125.3 (3 C-5); 89.1 (3 C-1'); 80.5 (3 C-5'); 77.8 (3 C-3'); 73.8 (3 C-2'); 70.5 (3 C-4'); 62.0 (3 C-6'); 48.4 (3 NCH₂C). Residual copper below detection limit. MS (ESI⁺): m/z 769.3 [M+Na]⁺. HRMS (ESI⁺): Calcd. for C$_{27}$H$_{42}$N$_{10}$O$_{15}$Na 1273.39911, found 1273.40023.
4-(1'-Methyl-1H-imidazol-5'-yl)-1-(β-D-glucopyranosyl)-1H-[1,2,3]-triazole (8):

Procedure B:

To a solution of β-D-glucopyranosyl azide (64.5 mg, 314 µmol, 1 eq.) in H₂O (253 µl) and tBuOH (628 µl), were added 5-ethynyl-1-methyl-1H-imidazole (32.9 µl, 33.4 mg, 314 µmol, 1 eq.), o-phenylenediamine (125 µl, 40.5 mg per ml of H₂O, 5.1 mg, 47.1 µmol, 15 mol%), sodium ascorbate (125 µl, 49.5 mg per ml of H₂O, 6.2 mg, 31.4 µmol, 10 mol%) and copper sulfate pentahydrate (125 µl, 31.2 mg per ml of H₂O, 3.9 mg, 15.7 µmol, 5 mol%). The reaction mixture was stirred at room temperature under an argon atmosphere for one hour. After this time, TLC showed complete conversion. The solvents were evaporated and the residue was dissolved in MeOH/H₂O, (1/1), (5 ml), activated charcoal (~150 mg) was added and the suspension was stirred under an air atmosphere overnight. The reaction mixture was then filtered through a celite plug and eluted with MeOH/H₂O (1/1). The solvents were evaporated to dryness to give 86.6 mg (89%) of 4-(1'-methyl-1H-imidazol-5'-yl)-1-(β-D-glucopyranosyl)-1H-[1,2,3]-triazole (8) as a white solid.

1H NMR (360 MHz, methanol-d4): δ: 8.48 (s, 1H, H-5); 7.75 (s, 1H, H-2’); 7.31 (s, 1H, H-4’); 5.73 (d, 1H, J1”-2” 9.0 Hz, H-1”); 4.00 (dd, 1H, J2”,1” 9.0, J2”,3” 9.0 Hz, H-2”); 3.91 (dd, 1H, J6a”,6b” 12.0, J6a”,5” 2.0 Hz, H-6a”); 3.84 (s, 3H, NCH3); 3.7 (dd, 1H, J6a”,6b” 12.0, J6b”,5” 5.0 Hz, H-6b’); 3.68 (dd, 1H, J5”,4” 9.5, J5”,6b” 5.0, J5”,6a” 2.0 Hz, H-5”); 3.67 (dd, 1H, J3”,4” 9.0, J3”,2” 9.0 Hz, H-3”); 3.59 (dd, 1H, J4”,3” 9.0, J4”,5” 9.5 Hz, H-4”). 13C NMR (75 MHz, methanol-d4) δ: 141.3 (C-2’); 138.6 (C-4’); 129.0 (C-4’); 124.3 (C-5’); 123.3 (C-5); 89.0 (C-1’); 80.4 (C-5’); 77.5 (C-3’); 73.6 (C-2’); 70.3 (C-4’); 61.7 (C-6’); 33.7 (CH3). Residual copper ~ 0.05 mol%. MS (ESI⁺): m/z 334.1 [M+Na]⁺. HRMS (ESI⁺): Calcd. for C₁₂H₁₇N₅O₅Na 334.11219, found 334.11288.

4-(1'-Hydroxycyclohexyl)-1-(β-D-glucopyranosyl)-1H-[1,2,3]-triazole (9):
Following Procedure B, 4-(1'-hydroxycyclohexyl)-1-(β-D-glucopyranosyl)-1H-[1,2,3]-triazole (9) was obtained from β-D-glucopyranosyl azide (55.3 mg, 270 µmol, 1 eq.) in H₂O (107 µl) and tBuOH (539 µl), 1-ethynlycyclohexanol (34.6 µl, 33.5 mg, 270 µmol, 1 eq.), o-phenylenediamine (216 µl, 20.3 mg per ml of H₂O, 4.4 mg, 40.5 µmol, 15 mol%), sodium ascorbate (108 µl, 49.5 mg per ml of H₂O, 5.3 mg, 27.0 µmol, 10 mol%) and copper sulfate pentahydrate (108 µl, 31.2 mg per ml of H₂O, 3.4 mg, 13.5 µmol, 5 mol%). The reaction mixture was stirred at room temperature for 45 min, and solvents were evaporated. The residue was dissolved in MeOH/H₂O (1/1), and activated charcoal was added followed by overnight stirring under an air atmosphere. Purification by filtration and evaporation gave 87.4 mg (98%) of 4-(1'-hydroxycyclohexyl)-1-(β-D-glucopyranosyl)-1H-[1,2,3]-triazole (9) as a white solid. 1H NMR (300 MHz, methanol-d4) δ: 8.04 (s, 1H, H-5); 5.58 (d, 1H, J₁₋₂= 9.0 Hz, H-1’); 3.91 (dd, 1H, J₃',4' = 9.0 Hz, H-2’); 3.88 (dd, 1H, J₆a₋₆b = 12.0, J₆a₋₅ = 1.5 Hz, H-6a’); 3.71 (dd, 1H, J₆b₋₆a = 12.0, J₆b₋₅ = 5.5 Hz, H-6b’); 3.61-3.50 (m, 1H, H-5’); 3.56 (dd, 1H, J₃₋₄ = 9.0, J₅₋₂ = 9.0 Hz, H-3’); 3.49 (dd, 1H, J₄₋₃ = 9.0, J₄₋₅ = 8.5 Hz, H-4’); 2.10-1.20 (m, 10H, H-2’,3’,4’,5’,6’). 13C NMR (75 MHz, methanol-d4) δ: 157.1 (C-4); 121.8 (C-5); 89.7 (C-1’); 81.2 (C-5’); 78.7 (C-3’); 74.1 (C-2’); 71.0 (C-4’); 70.4 (C-1’); 62.5 (C-6’); 70.4 (2 CH₂); 26.7 (C-4’); 23.2 (2 CH₂). Residual copper ~ 0.07 mol%. MS (ESI⁺) : m/z 352.2 [M+Na]⁺. HRMS (ESI⁺) : Calcd. for C₁₄H₂₅N₄O₆Na 352.14791, found 352.14832.

4-Phenyl-1-(β-D-glucopyranosyl)-1H-[1,2,3]-triazole (10):

Following Procedure B, 4-phenyl-1-(β-D-glucopyranosyl)-1H-[1,2,3]-triazole (10) was obtained from β-D-glucopyranosyl azide (64.1 mg, 312 µmol, 1 eq.) in H₂O (125 µl) and tBuOH (625 µl), ethynylbenzene (35.0 µl, 31.9 mg, 312 µmol, 1 eq.), o-phenylenediamine (250 µl, 20.3 mg per ml of H₂O, 5.1 mg, 46.8 µmol, 15 mol%), sodium ascorbate (125 µl, 49.5 mg per ml of H₂O, 6.2 mg, 31.2 µmol, 10 mol%) and copper sulfate pentahydrate (125 µl, 31.2 mg per ml of H₂O, 3.9 mg, 15.6 µmol, 5 mol%). The reaction mixture was stirred at room temperature for 45 min, and solvents were evaporated. The residue was dissolved in MeOH/H₂O (1/1), and activated charcoal was added followed by overnight stirring under an
air atmosphere. Purification by filtration and evaporation gave 93.0 mg (97%) of 4-phenyl-1-((\(\beta\)-d-glucopyranosyl)-1'H-[1,2,3]-triazole\(^{1}\) (10) as a white solid. \(^{1}\)H NMR (250 MHz, methanol-d\(\text{4}\)) \(\delta\) : 8.57 (s, 1H, H-5); 7.84 (dd, 2H, \(\text{J}\) 7.0, \(\text{J}\) 1.5 Hz, H-2', H-6'); 7.44 (tt, 2H, \(\text{J}\) 7.0, \(\text{J}\) 1.5 Hz, H-3', H-5') 7.35 (tt, 1H, \(\text{J}\) 7.0, \(\text{J}\) 1.5 Hz, H-4'); 5.66 (d, 1H, J\(_{1',2''}\) 9.0 Hz, H-1’'); 3.96 (dd, 1H, J\(_{2'',1''}\) 9.0, J\(_{2'',3''}\) 9.0 Hz, H-2’’); 3.91 (dd, 1H, J\(_{6''a',6''b'}\) 12.0, J\(_{6''a',5''}\) 1.5 Hz, H-6’’); 3.74 (dd, 1H, J\(_{6b',6a'}\) 12.0, J\(_{6b',5''}\) 5.0 Hz, H-6b’’); 3.61 (ddd, 1H, J\(_{5'',4''}\) 9.0, J\(_{5'',6b''}\) 5.0, J\(_{5'',6a''}\) 1.5 Hz, H-5’’); 3.61 (dd, 1H, J\(_{3'',4''}\) 8.5, J\(_{3'',2''}\) 9.0 Hz, H-3’’); 3.53 (dd, 1H, J\(_{4'',3''}\) 8.5, J\(_{4'',5''}\) 9.0 Hz, H-4’’). \(^{13}\)C NMR (62.5 MHz, methanol-d\(\text{4}\)) \(\delta\) : 149.0 (C-4); 131.7 (C-1’'); 130.1 (C-3’,5’); 129.6 (C-4’); 126.9 (C-2’,6’); 121.5 (C-5); 89.9 (C-1’'); 81.3 (C-3’’); 78.6 (C-3’’); 74.2 (C-2’’); 71.0 (C-4’’); 62.5 (C-6’’). Residual copper \(\sim\) 0.07 mol%. MS (ESI\(^{+}\) : m/z 330.0 [M+Na]\(^{+}\). HRMS (ESI\(^{+}\) : Calcd. for C\(_{14}\)H\(_{17}\)N\(_{3}\)O\(_{5}\)Na 330.10604, found 330.10775.

**N-acetyl-L-phenylalanine (1’-(\(\beta\)-d-glucopyranosyl)-1’H-[1’,2’,3’]-triazol-4-yl)methylamide (11)**:

Following Procedure B, N-acetyl-L-phenylalanine (1’-(\(\beta\)-d-glucopyranosyl)-1’H-[1’,2’,3’]-triazol-4-yl)methylamide was obtained from \(\beta\)-d-glucopyranosyl azide (53.2 mg, 259 \(\mu\)mol, 1 eq.) in H\(_{2}\)O (103 \(\mu\)l) and tBuOH (518 \(\mu\)l), N-acetyl-L-phenylalanine propargylamide (63.6 mg, 259 \(\mu\)mol, 1 eq.), o-phenylenediamine (207 \(\mu\)l, 20.3 mg per ml of H\(_{2}\)O, 4.2 mg, 38.9 \(\mu\)mol, 15 mol%), sodium ascorbate (104 \(\mu\)l, 49.5 mg per ml of H\(_{2}\)O, 5.1 mg, 26.0 \(\mu\)mol, 10 mol%) and copper sulfate pentahydrate (104 \(\mu\)l, 31.2 mg per ml of H\(_{2}\)O, 3.2 mg, 13.0 \(\mu\)mol, 5 mol%). The reaction mixture was stirred at room temperature for 45 min, and solvents were evaporated. The residue was dissolved in MeOH/H\(_{2}\)O, and activated charcoal was added followed by overnight stirring under an air atmosphere. Purification by filtration and evaporation gave 98.2 mg (84%) of N-acetyl-L-phenylalanine (1’-(\(\beta\)-d-glucopyranosyl)-1’H-[1’,2’,3’]-triazol-4-yl)methylamide (11) as a slightly beige solid. \(^{1}\)H NMR (360 MHz, dimethylsulfoxide-d\(\text{6}\)) \(\delta\) : 7.85 (s, 1H, H-5'); 7.30-7.15 (m, 5H, H-Ar); 5.48 (d, 1H, J\(_{1',2''}\) 9.5 Hz, H-1’’); 4.48 (dd, 1H, J\(_{2,3b}\) 9.5, J\(_{2,3a}\) 5.0 Hz, H-2'); 4.31 (s, 2H, CH\(_{2}\)NH); 3.73-3.63 (m, 1H,
H-6a’’); 3.70 (dd, 1H, J2''-1''= 9.5, J2''-3''= 9.0 Hz, H-2’’); 3.50-3.40 (m, 2H, H-6b’’, H-5’’); 3.38 (dd, 1H, J3''-2''= 9.0, J3''-4''= 9.0 Hz, H-3’’); 3.23 (dd, 1H, J4''-3''= 9.0, J4''-5''= 9.0 Hz, H-4’’); 2.99 (dd, 1H, J5''a,5''b= 13.5, J3a,2 5.0 Hz, H-3a); 2.75 (dd, 1H, J5''b,5''a= 13.5, J3b,2 9.5 Hz, H-3b); 1.76 (s, 3H, CH3). $^{13}$C NMR (75 MHz, methanol-d4) δ: 173.9 (C-I); 173.4 (CH3C=O); 146.4 (C-4’’); 138.5 (C-1’’’); 130.4 (C-2’’’); 129.6 (C-3’’’); 128.0 (C-4’’’); 123.5 (C-5’’); 89.7 (C-1’’); 81.3 (C-5’’); 78.6 (C-3’’); 74.2 (C-2’’); 71.1 (C-4’’); 62.6 (C-6’’); 56.6 (C-2); 39.0 (C-3); 35.9 (CH2NH); 22.6 (CH3). Residual copper ~ 0.08 mol%. HRMS (FAB$^+$) : Calcd. for C20H27N3O7Na 472.1803, found 472.1816.

4-Undecyl-1-(β-d-glucopyranosyl)-1H-[1,2,3]-triazole (12):

**Procedure C**

To a solution of β-d-glucopyranosyl azide (140.3 mg, 684 μmol, 1 eq.) in H2O (546 μl) and tBuOH (1370 μl), were added tridec-1-yne (163 μl, 123.3 mg, 684 μmol, 1 eq.), o-phenylenediamine (274 μl, 40.5 mg per ml of H2O, 11.1 mg, 102.6 μmol, 15 mol%), sodium ascorbate (274 μl, 49.5 mg per ml of H2O, 13.6 mg, 68.4 μmol, 10 mol%) and copper sulfate pentahydrate (274 μl, 31.2 mg per ml of H2O, 8.5 mg, 34.2 μmol, 5 mol%). The reaction mixture was stirred at room temperature under an argon atmosphere for 2 hours. After this time, TLC showed complete conversion. The reaction mixture was stirred one hour under an air atmosphere, and activated charcoal (~150 mg) was added and the suspension was stirred under an air atmosphere overnight. The reaction mixture was then filtered through a celite plug and washed with H2O/tBuOH (1/1). Elution with ACN/H2O gave after concentration to dryness, 224.1 mg (85%) of 4-undecyl-1-(β-d-glucopyranosyl)-1H-[1,2,3]-triazole (12) as a white solid. $^1$H NMR (250 MHz, methanol-d4) δ: 7.94 (s, 1H, H-5); 5.56 (d, 1H, J1’’-2’’= 9.0 Hz, H-1’’); 3.88 (dd, 1H, J2’’-1’’= 9.0, J2’’-3’’= 8.5 Hz, H-2’’); 3.88 (dd, 1H, J6a’’-6b’’= 12.0, J6a,5’’= 1.5 Hz, H-6a’’); 3.71 (dd, 1H, J6b’’-6a’’= 12.0, J6b,5’’= 5.0 Hz, H-6b’’); 3.56 (ddd, 1H, J5’’-4’’= 9.0, J5’’-6b’’= 5.0, J5’’-6a’’= 1.5 Hz, H-5’’); 3.56 (dd, 1H, J5’’-4’’= 9.0, J5’’-2’’= 8.5 Hz, H-3’’); 3.48 (dd, 1H, J4’’-3’’= 9.0, J4’’-5’’= 9.0 Hz, H-4’’); 2.71 (t, 2H, J1’’-2’’= 7.5 Hz, H-1’’); 1.67 (tt, 2H, J2’’-1’’= J2’’-3’’= 7.2 Hz, H-2’’); 1.37-1.25 (m, 16H, H-3’’); 0.90 (t, 3H, J1’’-1’’= 6.7 Hz, H-1’’). $^{13}$C NMR (62.5 MHz, methanol-d4) δ: 149.4 (C-4’’); 122.5 (C-5’’); 89.7 (C-1’’); 81.3 (C-5’’); 78.7 (C-3’’); 74.1
(C-2’); 71.0 (C-4’); 62.5 (C-6’); 33.2 (CH₂); 30.9 (2 CH₂); 30.8 (CH₂); 30.7 (CH₂); 30.6 (2 CH₂); 30.4 (CH₂); 26.4 (CH₂); 23.9 (CH₂); 14.6 (C-11’). Residual copper ~ 0.06 mol%. MS (ESI⁺): m/z 408.2 [M+Na]⁺. HRMS (ESI⁺): Calcd. for C_{19}H_{35}N_{3}O_{5}Na 408.24689, found 408.24681.

Kinetic effect of added o-phenylenediamine

Reaction of β-glucosyl azide (0.25 M) with propargyl alcohol (0.25 M) in the presence of copper sulfate (5.0 mol%, 12.5 mM) and sodium ascorbate (10.0 mol%, 25.0 mM) was performed with or without added o-phenylenediamine (15.0 mol%, 37.5 mM). The conversion was followed by ¹H-NMR spectroscopy (400 MHz) in D₂O under Ar, and estimated by integration of the H-2 signal of the starting material (δ 3.25 ppm) and anomeric signal of the product (δ 5.75 ppm). The reactions were initiated by copper sulfate addition.

References
