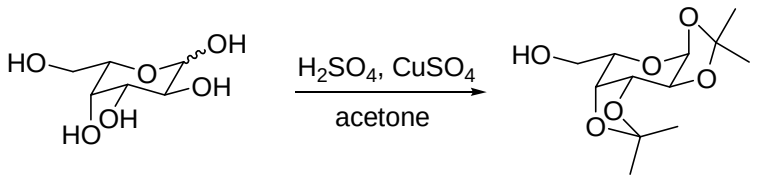
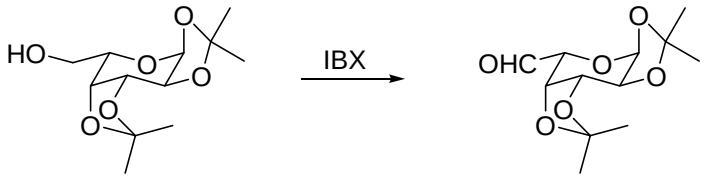
SI Appendix

Chemical Synthesis of Fucose Analogs



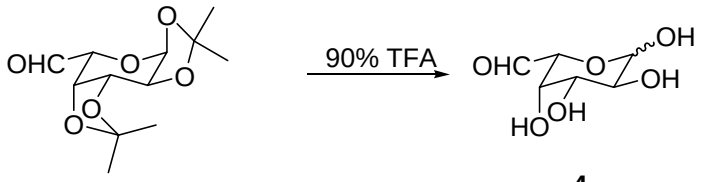
1 **2**

1,2,3,4-Di-O-Isopropylidene-L-Galactopyranoside (2). Anhydrous $CuSO_4$ (1.11 g, 6.93 mmol) and anhydrous L-galactose (500 mg, 2.77 mmol) were suspended in dry acetone (6 mL) and treated with concentrated H_2SO_4 (50 μL). The resulting mixture was shaken at room temperature for 24 h. The cupric sulfate was removed by filtration and washed with acetone. The combined organic phases were neutralized by addition of $Ca(OH)_2$, filtered and concentrated. Purification by silica gel column chromatography (EtOAc:hexane, 1:3) gave 400mg the desired product as a colorless oil in 56% yield. ^{1}HNMR (500 MHz, $CDCl_3$): δ 5.59 (d, *J* = 5.1 Hz, 1H, H-1), 4.64 (dd, *J* = 7.9, 2.4 Hz, 1H, H-3), 4.36 (dd, *J* = 5.1, 2.4 Hz, 1H, H-2), 4.29 (dd, *J* = 7.9, 1.6 Hz, 1H, H-4), 3.89 (m, 2H, H-6), 3.77 (m, 1H, H-5), 1.62 (s, 3H, CH_3), 1.56 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.36 (s, 3H, CH_3). MS (ESI): 206.3.



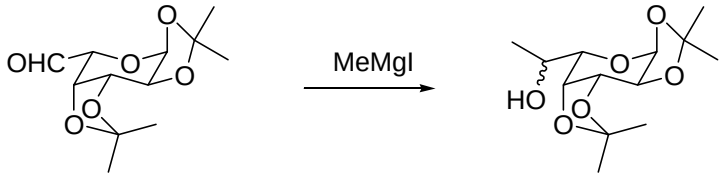
2 **3**

1,2,3,4-Di-O-Isopropylidene-6-Aldehydo-L-galactopyranoside (3). A suspension of compound **2** (0.40 g, 1.54 mmol) and 45% 2-iodoxybenzoic acid (IBX) (2.87 g, 4.61 mmol) in EtOAc (17 mL) was heated to reflux for 4h. When TLC showed no starting material remaining, the reaction was quenched by addition of saturated aqueous Na_2CO_3. The organic layer was separated and the aqueous was extracted with additional EtOAc (20 mL x 2). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. Purification by silica gel column chromatography (EtOAc:hexane, 1:4) gave 0.32 g product as colorless oil in 80% yield. ^{1}HNMR (500 MHz, $CDCl_3$): δ 9.63 (s, 1H, CHO), 5.68 (d, *J* = 4.9 Hz, 1H, H-1), 4.66 (dd, *J* = 7.8, 2.5 Hz, 1H, H-3), 4.61 (dd, *J* = 7.8, 2.3 Hz, 1H, H-4), 4.39 (dd, *J* = 4.9, 2.5 Hz, 1H, H-2), 4.2 (d, *J* = 2.2 Hz, 1H, H-5), 1.52 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.36 (s, 3H, CH_3), 1.33 (s, 3H, CH_3). ^{13}CNMR (125 MHz, $CDCl_3$): δ 200.2, 110.0, 109.0, 96.2, 73.2, 71.7, 70.5, 70.4, 26.0, 25.8, 24.8, 24.2. MS (ESI): 258.5.



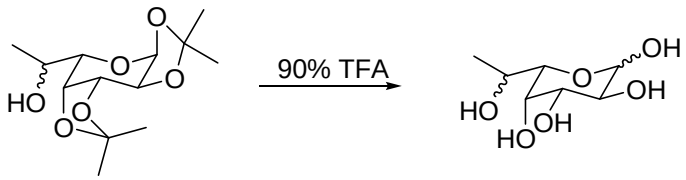
3 **4**

6-Aldehydo-L-Galactopyranoside (4). A solution of aldehyde **3** (60 mg, 0.22 mmol) in a mixture of TFA and water (3 mL, 9:1) was stirred at room temperature for 2h. 10 mL toluene was added to dilute the reaction mixture and evaporated under reduced pressure to give 41 mg of product as oil in quantitive yield. MS (ESI): 178.2.



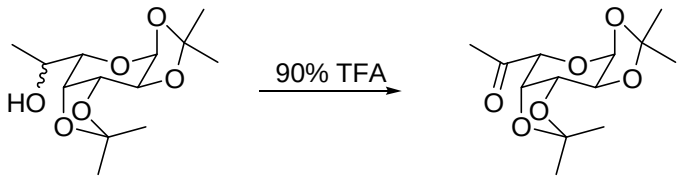
3 **5**

1,2,3,4-Di-O-Isopropylidene-6-Methyl-L-Galactopyranoside (5). A solution of the aldehyde **3** (180 mg, 0.7 mmol) in ether (4 mL) was added dropwise to a 0.5 N methylmagnsesium iodide solution in ether (3.5 mL, 1.75 mmol) and the reaction mixture was stirred at room temperature for 2 h. The reaction was quenched by the addition of aqueous saturated ammonium chloride. The mixture was diluted with water, extracted with ether and the organic solution was dried over anhydrous Na_2SO_4, filtered and concentrated, and evaporated. Purification by silica gel column chromatography (EtOAc:hexane, 1:4) gave 150 mg product as colorless oil in 78% yield. (a mixture of two isomers in ratio 5.3:1, the NMR only identify the major isomer) ^{1}HNMR (500 MHz, $CDCl_3$): δ 5.59 (d, *J* = 5.0 Hz, 1H, H-1), 4.61 (dd, *J* = 8.0, 2.5 Hz, 1H, H-3), 4.34 (dd, *J* = 5.0, 2.4 Hz, 1H, H-2), 4.29 (dd, *J* = 8.0, 1.9 Hz, 1H, H-4), 4.02 (td, *J* = 6.8, 6.4 Hz, 1H, H-6), 3.50 (dd, *J* = 6.8, 1.8 Hz, 1H, H-5), 1.54 (s, 3H, CH_3), 1.47 (s, 3H, CH_3), 1.35 (s, 6H, 2 x CH_3), 1.26 (d, *J* = 6.4 Hz, 3H, H-7). ^{13}CNMR (125 MHz, $CDCl_3$): δ 109.4, 108.7, 96.4, 72.2, 71.6, 70.9, 70.7, 66.9, 26.0, 25.9, 24.9, 24.3, 17.9. MS (ESI): 274.5.



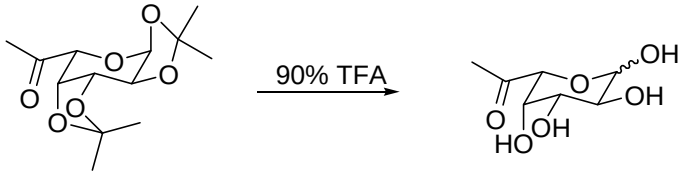
5 **6**

6-Methyl-L-Galactopyranoside (6). A solution of compound **5** (50 mg, 0.18 mmol) in a mixture of TFA and water (3 mL, 9:1) was stirred at room temperature for 2h. 10 mL toluene was added to dilute the reaction mixture and evaporated under reduced pressure to give 32 mg of product as oil in 90% yield. MS (ESI): 194.2.



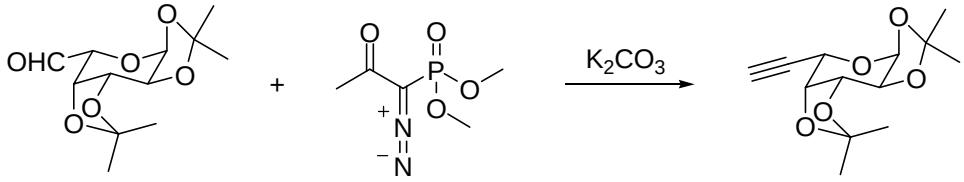
5 **7**

1,2,3,4-Di-O-Isopropylidene-6-Dehydro-6-Methyl-L-Galactopyranoside (7). A suspension of compound **5** (100 mg, 0.37 mmol) and 45% 2-iodoxybenzoic acid (IBX) (0.69 g, 1.1 mmol) in EtOAc (6 mL) was heated to reflux for 4h. When TLC showed no starting material remaining, the reaction was quenched by addition of saturated aqueous Na_2CO_3. The organic layer was separated and the aqueous was extracted with additional EtOAc (10 mL x 2). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. Purification by silica gel column chromatography (EtOAc:hexane, 1:4) gave 87 mg product as colorless oil in 87% yield. ^{1}HNMR (500 MHz, $CDCl_3$): δ 5.65 (d, *J* = 5.0 Hz, 1H, H-1), 4.65 (dd, *J* = 7.9, 2.5 Hz, 1H, H-3), 4.57 (dd, *J* = 7.8, 2.2 Hz, 1H, H-4), 4.36 (dd, *J* = 5.0, 2.5 Hz, 1H, H-2), 4.18 (d, *J* = 2.2 Hz, 1H, H-5), 2.27 (s, 3H, CH_3CO), 1.51 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.35 (s, 3H, CH_3), 1.32 (s, 3H, CH_3). ^{13}CNMR (125 MHz, $CDCl_3$): δ 207.6, 109.6, 108.9, 96.4, 73.8, 72.4, 70.6, 70.3, 27.9, 25.9, 25.8, 24.8, 24.2. MS (ESI): 272.2.



7 **8**

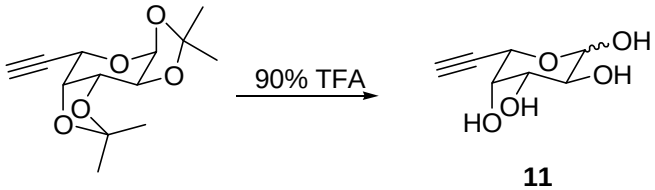
6-Dehydro-6-Methyl-L-Galactopyranoside (8). A solution of ketone **7** (60 mg, 0.22 mmol) in a mixture of TFA and water (3 mL, 9:1) was stirred at room temperature for 2h. 10 mL toluene was added to dilute the reaction mixture and evaporated under reduced pressure to give 41 mg of product in quantitive yield. MS (ESI): 192.3.



3 **9** **10**

1,2,3,4-Di-O-Isopropylidene-6-Ethylyl-L-Galactopyranoside (10). To a solution of aldehyde **3** (80 mg, 0.31 mmol) and K_2CO_3 (86 mg, 0.62 mmol) in 2 mL of dry methanol was added dimethyl 1-diazo-2-oxopropylphosphate **9** (72 mg, 0.37 mmol). The reaction mixture was stirred for 5h and concentrated. The residue was partitioned between EtOAc and water. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. Purification by silica gel column chromatography (EtOAc:hexane, 1:7) gave 72 mg product as colorless oil in 91% yield. ^{1}HNMR (500 MHz, $CDCl_3$): δ 5.54 (d, *J* = 5.1 Hz, 1H, H-1), 4.62 (dd, *J* = 7.8, 2.5 Hz, 1H, H-3), 4.60 (t, *J* = 2.1 Hz, 1H, H-5), 4.31 (dd, *J* = 5.1, 2.5 Hz, 1H, H-2), 4.28 (dd, *J* = 7.8, 2.1 Hz, 1H, H-4), 2.53 (d, *J* = 2.3

Hz, H-7), 1.53 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.38 (s, 3H, CH_3), 1.33 (s, 3H, CH_3). ^{13}CNMR (125 MHz, $CDCl_3$): δ 109.9, 108.8, 96.4, 78.8, 74.5, 72.6, 70.6, 70.1, 60.0, 26.1, 25.9, 24.8, 24.4. MS (ESI): 254.2.



10 **11**

6-Methyl-L-Galactopyranoside (11). A solution of compound **10** (72 mg, 0.28 mmol) in a mixture of TFA and water (3 mL, 9:1) was stirred at room temperature for 2h. 10 mL toluene was added to dilute the reaction mixture and evaporated under reduced pressure to give 43 mg of product as oil in 93% yield. MS (ESI): 174.1.

1. Link AJ, Tirrell DA (2003) Cell surface labeling of Escherichia coli via copper(I)-catalyzed [3+2] cycloaddition. *J Am Chem Soc* 125:11164-11165.