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SYNTHESIS OF GALACTO- AND MANNOSUCROSES

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Abstract – A concise synthesis of β-D-fructofuranosyl α-D-galactopyranoside (**2**), and β-D-fructofuranosyl α-D-mannopyranoside (**3**) is described. Inversion of the C-3 α-hydroxy group of α-D-galactopyranosyl and α-D-mannopyranosyl β-D-psicofuranosides **10** and **11** *via* oxidation and stereoselective reduction furnished the corresponding β-D-fructofuranosides in excellent yields.

(+)-Sucrose (**1**) is the most popular disaccharide and an important nutriment for human life. Its structure is categorized as a non-reducing disaccharide, of which β-D-fructofuranosyl bond is connected with α-D-glucose at each anomeric position. β-D-Fructofuranosyl disaccharides[1] containing D-galactose and D-mannose instead of D-glucose are called galactosucrose (**2**)[2,3] and mannosucorse (**3**).[3a,3b,4] However, they have received less attention. Since we have found an excellent β-D-psicofuranosyl donor for the glycosylation reaction with D-glucose accepter, the stereoselective synthesis of **1** was performed by the stereo-inversion of α-D-glucopyranosyl β-D-psicofuranoside to β-D-fructofuranosyl α-D-glucopyranoside.[5] More recently, we have reported the synthesis of α-D-glucopyranosyl β-D-psicofuranoside (**4**), α-D-galactopyranosyl β-D-psicofuranoside (**5**), and α-D-mannopyranosyl β-D-psicofuranoside (**6**).[6]

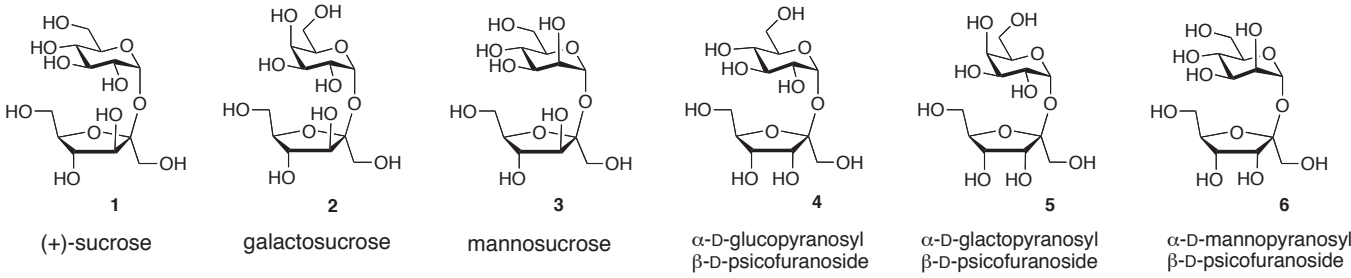
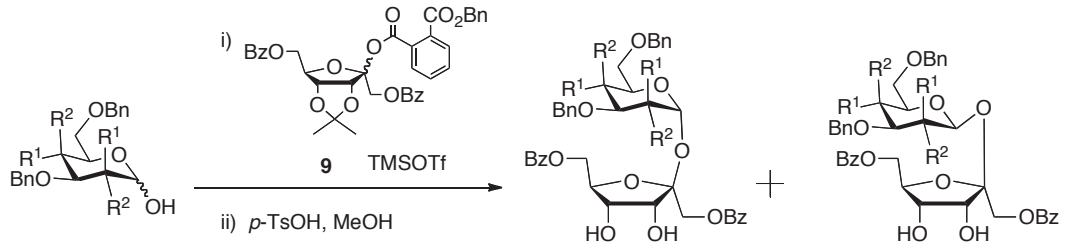


Figure 1. Structures of non-reducing disaccharides **1**–**6**

Because α-D-galactopyranosyl β-D-psicofuranoside and α-D-mannopyranosyl β-D-psicofuranoside are in hand, the same stereo-inversion as reported for the synthesis of **1** would provide the corresponding galacto- and mannosucorose (**2**) and (**3**). In this note, we describe the synthesis of **2** and **3** *via* stereoselective β-D-psicosylation and stereo-conversion of the C-3 α-hydroxy group to β-hydroxy group on the furanose ring.

In our recent report for the synthesis of α-D-hexopyranosyl β-D-psicofuranosides **4**–**6**,[6] glycosylation of D-hexopyranose with psicofuranosyl donor **9** gave the corresponding disaccharides. Galactopyranosyl psicosides **10** and **10'** and mannopyranosyl psicosides **11** and **11'** were prepared respectively, as shown in Scheme 1.

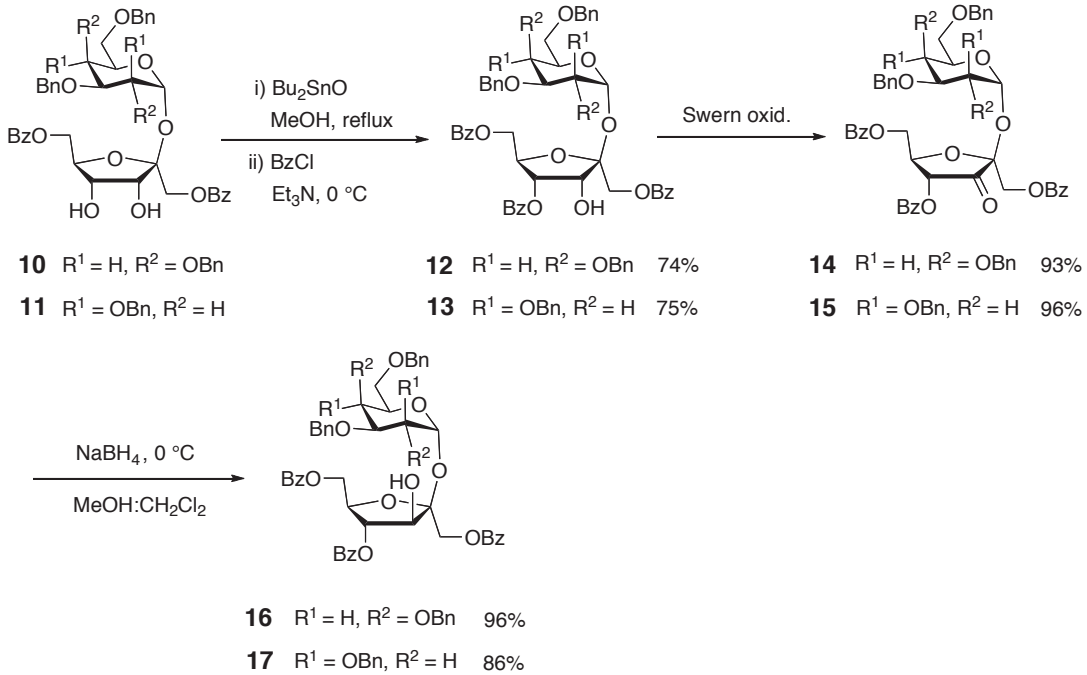


7 R^1 = H, R^2 = OBn
8 R^1 = OBn, R^2 = H

10 R^1 = H, R^2 = OBn
11 R^1 = OBn, R^2 = H

10' R^1 = H, R^2 = OBn
11' R^1 = OBn, R^2 = H

Scheme 1. β-D-Psicofuranosylation of **7** and **8** [ref. 6]



10 R^1 = H, R^2 = OBn
11 R^1 = OBn, R^2 = H

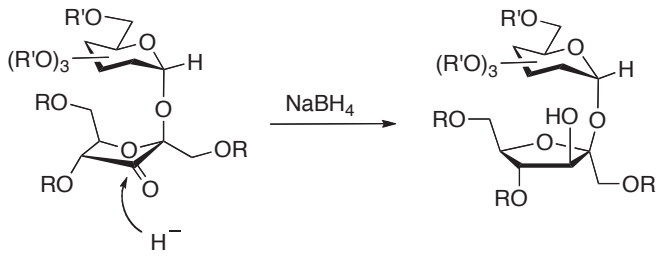
12 R^1 = H, R^2 = OBn 74%
13 R^1 = OBn, R^2 = H 75%

14 R^1 = H, R^2 = OBn 93%
15 R^1 = OBn, R^2 = H 96%

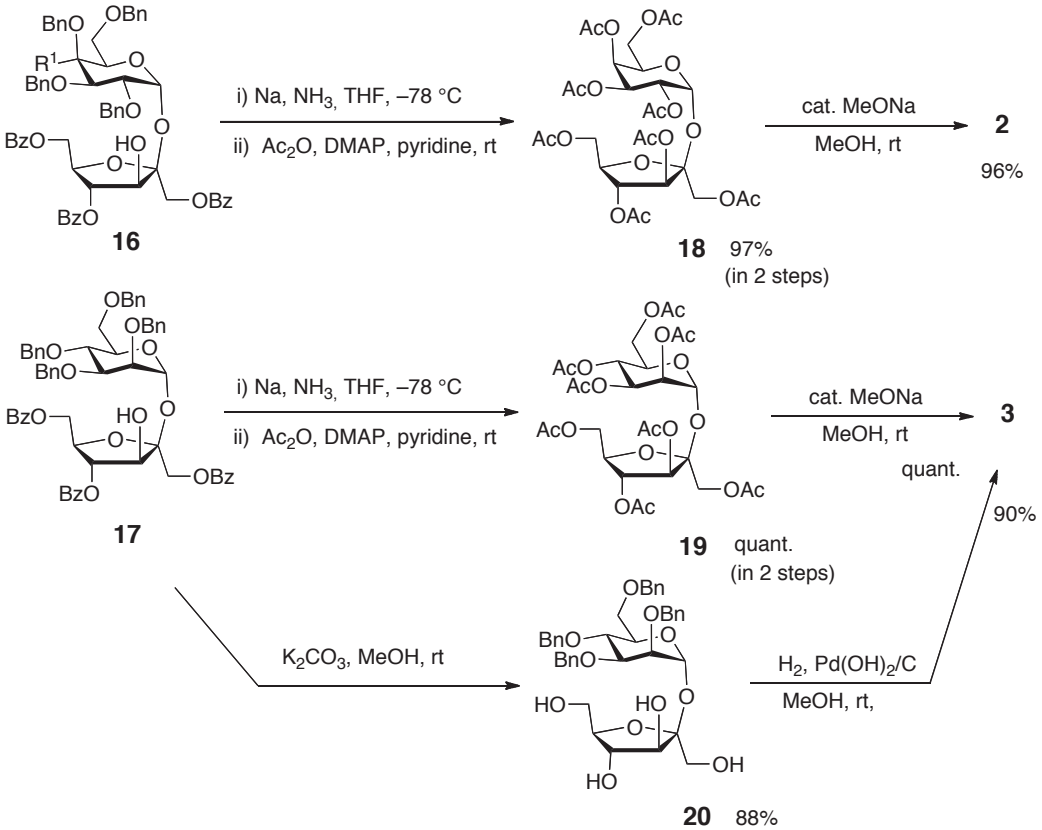
16 R^1 = H, R^2 = OBn 96%
17 R^1 = OBn, R^2 = H 86%

Scheme 2. Synthesis of **16** and **17**

In order to synthesize **2** and **3**, the C-3 α-hydroxy group on the β-D-psicofuranosyl ring in **10** and **11**, must be inverted to β-orientation (Scheme 2). For this purpose, differentiation of the C-3 or C-4 α-hydroxy group was necessary. Treatment of the vicinal 3,4-diol of **10** with dibutyltin oxide gave a stannylene intermediate, which underwent monobenzoylation with benzoyl chloride in the presence of Et_3N to give **12** in 74% yield.[7] Similarly, compound **11** was converted to **13** in 75% yield. Swern oxidation of the C-3 hydroxy group for **12** and **13** afforded carbonyl compounds **14** and **15** in 93 and 96% yields, respectively. Reduction of the carbonyl group by $NaBH_4$ was carried out in a 1:1 mixture of CH_2Cl_2 and MeOH at 0 ºC. Because of presence of the axial β-glycosyl bond, a hydride attacks to carbonyl face from the bottom side of the ring selectively to give C-3 β-hydroxy group (Scheme 3).[8] In fact, compounds **16** and **17** were obtained from **14** and **15** in 96 and 86% yields, respectively.



Scheme 3



Scheme 4. Synthesis of **2** and **3**

These oxidation and reduction steps furnished the conversion of β-D-psicofuranose ring to β-D-fructofuranose ring in excellent yields. Steps remaining to **2** or **3** require deprotections of three *O*-benzoyl and four *O*-benzyl groups. First, we examined deprotection of all the protecting groups at once. Compound **16** was subjected to Birch reduction conditions in liq. ammonia and resulted crude product was acetylated with acetic anhydride in pyridine to give octaacetate **18** in 97% yield. Removal of all acetyl groups of **18** under Zempén's condition gave galactosucrose (**2**) in 96% yield. Physical and spectroscopic data of both **18** and **2** were accorded with those reported in literature.[2a] By the same two steps, compound **17** afforded mannosucrose (**3**) *via* octaacetate **19** in quantitaive yield. Alternatively, stepwise deprotections of compound **17** also gave **3** in excellent yield. Methanolysis of three benzoates of **17** gave tetraol **20** in 88% yield. Hydrogenolysis of the remaining *O*-benzyl groups afforded the desired compound **3** in 90% yield. These spectroscopic and physical data of **3** are in accordance of those reported previously.[4]

In conclusion, conversion of α-D-hexopyranosyl β-D-psicofuranoside to α-D-hexopyranosyl β-D-fructofuranoside has been performed and chemically pure galacto- and mannosucroses were obtained in high yields. Although the chemical conversion to these two disacharides from (+)-sucrose were reported, they have been synthesized for the first time via glycosidation pathway. This synthetic route will be useful for a general synthesis of α-D-hexopyranosyl β-D-fructofuranoside.

EXPERIMENTAL

General. Specific rotations were measured on a JASCO P-2200 polarimeter using $CHCl_3$, MeOH, or H_2O as a solvent. ^{1}H NMR and ^{13}C NMR spectra were measured on JEOL JNM-AL-300 (300 MHz and 75 MHz), JEOL JNM-ECA 600 (600 MHz and 150 MHz), or Varian UNITY INOVA 400 NB (400 MHz and 100 MHz) spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) relative to the resonance of the solvent or to tetramethylsilane (0.00 ppm) for ^{1}H NMR spectra and ppm relative to the resonance of the solvent or to MeCN (1.47 ppm) when D_2O was used, for ^{13}C NMR spectra. IR spectra were recorded on a JASCO FT/IR-410 spectrophotometer. Low and high-resolution mass spectra (LRMS and HRMS) were obtained on a JEOL JMS 303HF spectrometer using fast atom bombardment (FAB) ionization. Silica gel (230–400 mesh) was used for flash chromatography. Analytical thin-layer chromatography (TLC) was performed on glass pre-coated with silica gel (0.25 mm thickness). All moisture sensitive reactions were carried out under an argon atmosphere. THF was dried over sodium/benzophenone ketyl, and CH_2Cl_2 was dried over P_2O_5, and they were distilled prior to use.

2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranosyl 1,4,6-tri-*O*-benzoyl-β-D-psicofuranoside (12): A

mixture of diol **10** (53.6 mg, 58.8 μmol) and Bu_2SnO (14.6 mg, 58.8 μmol) in MeOH (3.9 mL) was heated at reflux for 45 min. To the reaction mixture were added Et_3N (82 μL, 588 μmol) and benzoyl chloride (68 μL, 588 μmol) 0 °C and then the mixture was stirred for 10 min at the same temperature. After evaporation of solvent, the crude product was purified by silica gel flash chromatography eluted with 15% EtOAc in hexane to give **12** (44.3 mg, 74%) as a colorless syrup. R_f = 0.43 (30% EtOAc in hexane). $[\alpha]^{22}_D$ +41.3 (*c* 0.90, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.08–8.00 (6H, m), 7.60–7.15 (29H, m), 5.64 (1H, d, $J_{1',2'}$ = 3.7 Hz, H-1'), 5.48 (1H, t, $J_{3,4} = J_{4,5}$ = 4.9 Hz, H-4), 4.94–4.88 (3H, m), 4.73–4.62 (5H, m), 4.57–4.46 (5H, m), 4.38 (1H, d, *J* = 11.9 Hz), 4.21 (1H, ddd, $J_{5',6'a}$ = 8.5, $J_{5',6'b}$ = 3.0, $J_{4',5'}$ = 0.7 Hz, H-5'), 4.05 (1H, d, *J* = 5.1 Hz, O*H*), 4.00 (1H, dd, $J_{2',3'}$ = 10.1, $J_{1',2'}$ = 3.7 Hz, H-2'), 3.86 (1H, dd, $J_{2',3'}$ = 10.1, $J_{3',4'}$ = 2.6 Hz, H-3'), 3.78 (1H, dd, $J_{3',4'}$ = 2.6, $J_{4',5'}$ = 0.7 Hz, H-4'), 3.59 (1H, dd, $J_{6'a,6'b}$ = 9.6, $J_{5',6'a}$ = 8.5 Hz, H-6'a), 3.26 (1H, dd, $J_{6'a,6'b}$ = 9.6, $J_{5',6'b}$ = 3.0 Hz, H-6'b). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 167.0, 166.1, 165.7, 138.8, 138.4, 138.2, 137.1, 133.3, 133.0, 132.8, 130.0, 129.9, 129.8, 129.7, 129.5, 129.3, 128.4, 128.3, 128.3, 128.3, 128.1, 128.1, 128.0, 128.0, 127.9, 127.7, 127.6, 127.3, 127.3, 107.5, 90.3, 79.1, 78.8, 75.6, 75.4, 74.3, 73.6, 73.5, 73.3, 72.3, 72.2, 70.5, 70.3, 65.2, 63.4. IR (film): 3424, 3019, 1721, 1453, 1272, 1095, 1026, 712 cm^{-1}. MS (FAB) *m*/*z*: 1037 $[M+Na]^+$. HRMS (FAB) *m*/*z*: Calcd for $C_{61}H_{58}O_{14}Na$, 1037.3724; found, 1037.3716.

2,3,4,6-Tetra-*O*-benzyl-α-D-mannopyranosyl 1,4,6-tri-*O*-benzoyl-β-D-psicofuranoside (13): Compound **13** was obtained from **11** by the same manner described for the synthesis of **12** in 75% yield as a colorless syrup. R_f = 0.70 (40% EtOAc in hexane). $[\alpha]^{20}_D$ +4.8 (*c* 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07–8.03 (4H, m), 7.94–7.91 (2H, m), 7.59–7.13 (29H, m), 5.53 (1H, d, $J_{1',2'}$ = 1.6 Hz, H-1'), 5.43 (1H, dd, $J_{4,5}$ = 5.5, $J_{3,4}$ = 5.4 Hz, H-4), 4.85 (1H, d, *J* = 10.8 Hz), 4.82 (1H, dd, $J_{3,4}$ = 5.4, $J_{3,OH}$ = 5.2 Hz, H-3), 4.75 (1H, d, *J* = 12.5 Hz), 4.73 (1H, dd, $J_{6a,6b}$ = 11.5, $J_{5,6a}$ = 5.7 Hz, H-6a), 4.66 (1H, ddd, $J_{5,6a}$ = 5.7, $J_{4,5}$ = 5.5, $J_{5,6b}$ = 3.8 Hz H-5), 4.64 (1H, d, *J* = 12.4 Hz), 4.59 (1H, d, *J* = 12.3 Hz), 4.58 (1H, d, *J* = 12.4 Hz), 4.55 (1H, dd, $J_{6a,6b}$ = 11.5, $J_{5,6b}$ = 3.8 Hz, H-6b), 4.51 (1H, d, *J* = 12.3 Hz), 4.47 (1H, d, *J* = 10.8 Hz), 4.45 (1H, d, *J* = 12.5 Hz), 4.34 (2H, s), 4.13–4.08 (1H, m, H-5'), 3.97 (1H, d, $J_{3,OH}$ = 5.2 Hz, O*H*), 3.87–3.77 (4H, m, H-2', 3', 4', 6'a), 3.63 (1H, dd, *J* = 9.9, 7.0 Hz, H-6'b). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.6, 166.2, 165.7, 138.2, 138.1, 138.0, 137.6, 133.4, 133.3, 133.1, 129.9, 129.7, 129.6, 129.5, 129.2, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.7, 127.62, 127.57, 127.5, 127.4, 107.6, 91.1, 80.1, 79.0, 75.0, 74.8, 74.3, 74.0, 73.4, 72.4, 72.3 (2C), 71.8, 69.4, 65.5, 62.6. IR (film): 3456, 3031, 2918, 1724, 1601, 1496, 1453, 1273, 1110, 741, 711 cm^{-1}. MS (FAB) *m*/*z*: 1037 $[M+Na]^+$. HRMS (FAB) *m*/*z*: Calcd for $C_{61}H_{58}O_{14}Na$, 1037.3724; found, 1037.3717.

1,4,6-Tri-*O*-benzoyl-β-D-*erythro*-2,3-hexodiulofuranosyl 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranoside (14): A solution of DMSO (16.0 μL, 226 μmol) in CH_2Cl_2 (0.2 mL) was added to a solution of oxalyl chloride (9.9 μL, 113 μmol) in CH_2Cl_2 (1.5 mL) at −78 °C and the reaction was stirred for 15 min at the same temperature. To this mixture was added disaccharide **12** (38.3 mg, 37.7 μmol) in CH_2Cl_2 (1.2 mL) at −78 °C and the whole was stirred for 1 h at same temperature prior to the addition of Et_3N (63 μL, 0.45 mmol). The reaction was allowed to warm up to rt and sat. aqueous NH_4Cl solution was added to the mixture. The aqueous layer was extracted with EtOAc and combined organic layer was washed with water and brine, dried over $MgSO_4$, and evaporated under vacuum. The residue was purified by flash chromatography on silica gel eluted with 20% EtOAc in hexane to give **14** (35.5 mg, 93%) as a colorless syrup. R_f = 0.50 (30% EtOAc in hexane). $[\alpha]^{22}_D$ +52.1 (*c* 1.04, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.07–7.94 (6H, m), 7.65–7.56 (2H, m), 7.45–7.03 (27H, m), 6.27 (1H, d, $J_{4',5'}$ = 8.3 Hz, H-4'), 5.77 (1H, d, $J_{1,2}$ = 3.7 Hz, H-1), 4.97 (1H, d, *J* = 10.5 Hz), 4.86 (1H, d, *J* = 11.7 Hz), 4.78–4.72 (4H, m), 4.67–4.44 (5H, m), 4.65 (1H, ddd, $J_{4',5'}$ = 8.3, $J_{5',6'b}$ = 2.8, $J_{5',6'a}$ = 2.6 Hz, H-5'), 4.58 (1H, dd, $J_{6'a,6'b}$ = 11.9, $J_{5',6'a}$ = 2.6 Hz, H-6'a), 4.12 (1H, dd, $J_{3,4}$ = 2.1, $J_{4,5}$ = 0.7 Hz, H-4), 3.97 (1H, dd, $J_{2,3}$ = 10.3, $J_{1,2}$ = 3.7 Hz, H-2), 3.90 (1H, dd, $J_{2,3}$ = 10.3, $J_{3,4}$ = 2.1 Hz, H-3), 3.82 (1H, ddd, $J_{5,6a}$ = 8.9, $J_{5,6b}$ = 4.8, $J_{4,5}$ = 0.7 Hz, H-5), 3.70 (1H, dd, $J_{5,6a}$ = 8.9, $J_{6a,6b}$ = 8.8 Hz, H-6a), 3.41 (1H, dd, $J_{6a,6b}$ = 8.8, $J_{5,6b}$ = 4.8 Hz, H-6b). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 205.7, 166.1, 165.0, 164.8, 138.7 (2C), 138.1, 137.9, 133.8, 133.3, 133.2, 129.9, 129.7, 129.6, 129.3, 128.9, 128.5, 128.4, 128.3, 128.2, 128.2, 128.1, 127.8, 127.7, 127.5, 127.5, 127.4, 127.4, 127.3, 97.7, 90.7, 78.1, 75.8, 75.2, 74.7, 74.7, 73.3, 73.0, 72.9, 69.8, 68.9, 66.9, 66.9, 63.1. IR (film): 2923, 1783, 1729, 1601, 1452, 1268, 1094, 752, 709 cm^{-1}. MS (FAB) *m*/*z*: 1035 $[M+Na]^+$. HRMS (FAB) *m*/*z*: Calcd for $C_{61}H_{56}O_{14}Na$, 1035.3568; found 1035.3575.

1,4,6-Tri-*O*-benzoyl-β-D-*erythro*-2,3-hexodiulofuranosyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranoside (15): Compound **15** was obtained from **13** by the same manner described for the synthesis of **14** in 96% yield as a colorless syrup. R_f = 0.60 (30% EtOAc in hexane). $[\alpha]^{20}_D$ +67.0 (*c* 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.19–8.17 (2H, m), 8.04–7.98 (4H, m), 7.63–7.55 (2H, m), 7.46–7.11 (27H, m), 6.41 (1H, d, $J_{4',5'}$ = 8.4 Hz, H-4'), 5.78 (1H, d, $J_{1,2}$ = 1.6 Hz, H-1), 4.91 (1H, d, *J* = 10.8 Hz), 4.79 (1H, dd, *J* = 12.4, 2.4 Hz), 4.70–4.52 (8H, m), 4.46 (1H, d, *J* = 11.6 Hz), 4.44 (1H, d, *J* = 12.4 Hz), 4.38 (1H, d, *J* = 12.4 Hz), 4.26 (1H, t, $J_{3,4}$ = $J_{4,5}$ = 9.6 Hz, H-4), 3.84 (1H, dd, $J_{3,4}$ = 9.6, $J_{2,3}$ = 3.1 Hz, H-3), 3.82–3.77 (1H, m, H-5), 3.75 (1H, dd, $J_{2,3}$ = 3.1, $J_{1,2}$ = 1.6 Hz), 3.57 (2H, d, $J_{5,6}$ = 10.8 Hz, H-6). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 205.0, 166.4, 165.1, 164.8, 138.6, 138.5, 138.4, 137.7, 133.8, 133.4, 133.2, 130.0, 129.7, 129.2, 129.0, 128.6, 128.5, 128.3, 128.2, 127.9, 127.6, 127.5, 127.3, 97.4, 91.7, 79.4, 76.0, 75.1, 74.2, 74.1, 73.5, 73.1, 72.6, 72.4, 69.3, 68.3, 66.7, 63.2. IR (film): 3065, 3031, 2916, 2865, 1785, 1731, 1602, 1496, 1452, 1365, 1268, 1110, 739, 709 cm^{-1}. MS (FAB) *m*/*z*: 1035 $[M+Na]^+$. HRMS (FAB) *m*/*z*: Calcd

for $C_{61}H_{56}O_{14}Na$, 1035.3568; found, 1035.3573.

1,4,6-Tri-*O*-benzoyl-β-D-fructofuranosyl 2,3,4,6-tetra-*O*-benzyl-α-D-galactopyranoside (16): To a solution of **14** (32.0 mg, 31.5 μmol) in MeOH–CH_2Cl_2 (1:1, 2.0 mL), was added sodium borohydride (2.4 mg, 63 μmol) at 0 °C, and the reaction mixture was stirred for 30 min at the same temperature. The reaction was quenched with sat. aqueous NH_4Cl solution and extracted with EtOAc. The organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by flash column chromatography on silica gel eluted with 20% EtOAc in hexane to give disaccharide **16** (30.6 mg, 96%) as a colorless syrup. R_f = 0.43 (30% EtOAc in hexane). $[\alpha]^{23}_D$ +29.0 (*c* 1.06, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.06–8.02 (6H, m), 7.61–7.17 (29H, m), 5.80 (1H, d, $J_{1,2}$ = 3.7 Hz, H-1), 5.70 (1H, t, $J_{3',4'} = J_{4',5'}$ = 7.4 Hz, H-4'), 4.94 (1H, d, J = 11.4 Hz), 4.79 (1H, d, J = 11.9 Hz), 4.73–4.29 (13H, m), 4.12 (1H, ddd, $J_{5,6a}$ = 7.2, $J_{5,6b}$ = 5.5, $J_{4,5}$ = 0.9 Hz, H-5'), 4.07 (1H, dd, $J_{2,3}$ = 10.1, $J_{1,2}$ = 3.7 Hz, H-2), 3.98 (1H, dd, $J_{2,3}$ = 10.1, $J_{3,4}$ = 2.4 Hz, H-3), 3.93 (1H, dd, $J_{3,4}$ = 2.4, $J_{4,5}$ = 0.9 Hz, H-4), 3.59 (1H, dd, $J_{6a,6b}$ = 9.2, $J_{5,6a}$ = 7.2 Hz, H-6a), 3.45 (1H, dd, $J_{6a,6b}$ = 9.2, $J_{5,6b}$ = 5.5 Hz, H-6b). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.1, 165.8, 165.7, 138.4 (2C), 137.7, 137.6, 133.4, 133.1, 132.9, 129.8, 129.7, 129.7, 129.6, 129.1, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.0, 127.8, 127.6, 127.5, 127.5, 127.5, 104.2, 91.5, 78.7, 77.7, 77.5, 77.2, 75.1, 74.9, 74.7, 73.4, 73.2, 72.8, 70.6, 69.2, 64.5, 64.3. IR (film): 3449, 3018, 1724, 1453, 1269, 1096, 711 cm^{-1}. MS (FAB) *m/z*: 1037 $[M+Na]^+$. HRMS (FAB) *m/z*: Calcd for $C_{61}H_{58}O_{14}Na$, 1037.3724; found 1037.3717.

1,4,6-Tri-*O*-benzoyl-β-D-fructofuranosyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranoside (17): Compound **17** was obtained from **15** by the same reaction manner described for the synthesis of **16** in 86% yield as a colorless syrup. R_f = 0.52 (30% EtOAc in hexane). $[\alpha]^{20}_D$ +23.3 (*c* 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05–7.97 (6H, m), 7.58–7.55 (2H, m), 7.46–7.41 (5H, m), 7.32–7.22 (17H, m), 7.21–7.11 (5H, m), 5.70 (1H, d, J = 2.2 Hz, H-1), 5.65 (1H, dd, $J_{3',4'}$ = 7.7, $J_{4',5'}$ = 7.5 Hz, H-4'), 4.85 (1H, d, J = 11.0 Hz), 4.68–4.47 (7H, m), 4.65 (1H, dd, $J_{6'a,6'b}$ = 12.1, $J_{5',6'a}$ = 6.2 Hz, H-6'a), 4.54 (1H, dd, $J_{6'a,6'b}$ = 12.1, $J_{5',6'b}$ = 4.4 Hz, H-6'b), 4.53 (1H, dd, $J_{3',OH}$ = 8.8, $J_{3',4'}$ = 7.7 Hz, H-3'), 4.39 (1H, d, J = 11.7 Hz), 4.38 (1H, ddd, $J_{4',5'}$ = 7.5, $J_{5',6'a}$ = 6.2, $J_{5',6'b}$ = 4.4 Hz, H-5'), 4.34 (1H, d, J = 11.7 Hz), 4.15 (1H, ddd, $J_{4,5}$ = 9.2, $J_{5,6b}$ = 6.4, $J_{5,6a}$ = 1.8 Hz, H-5), 3.92 (1H, dd, $J_{4,5}$ = 9.2, $J_{3,4}$ = 8.8 Hz, H-4), 3.89 (1H, dd, $J_{3,4}$ = 8.8, $J_{2,3}$ = 2.7 Hz, H-3), 3.77 (1H, dd, $J_{6a,6b}$ = 10.3, $J_{5,6a}$ = 1.8 Hz, H-6a), 3.72 (1H, dd, $J_{2,3}$ = 2.7, $J_{1,2}$ = 2.2 Hz, H-2), 3.67 (1H, dd, $J_{6a,6b}$ = 10.3, $J_{5,6b}$ = 6.4 Hz, H-6b), 3.63 (1H, d, $J_{3,OH}$ = 8.8 Hz, OH). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 166.1, 165.9, 165.7, 138.2, 138.1, 137.9, 137.8, 133.5, 133.3, 133.0, 129.9, 129.8, 129.7, 129.5, 129.4, 128.9, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6,127.5, 127.4, 127.3, 127.2, 103.9, 91.3, 79.2, 77.6, 77.5, 77.0, 75.0, 74.8, 74.7, 73.3, 72.9, 72.5, 72.1, 69.2, 64.6 (2C). IR

(film): 3479, 3032, 2916, 1729, 1602, 1496, 1453, 1268, 1096, 709 cm^{-1}. MS (FAB) *m/z*: 1037 $[M+Na]^+$. HRMS (FAB) *m/z*: Calcd for $C_{61}H_{58}O_{14}Na$, 1037.3724; found, 1037.3721.

1,3,4,6-Tetra-*O*-acetyl-β-D-fructofuranosyl 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (18): Liq. NH_3 (4 mL) was condensed into a 2-necked flask at −78 °C and to which was added ca. 30 mg of sodium metal. To the resultant dark blue solution was added a solution of **16** (28.9 mg, 28.4 μmol) in THF (2 mL) and the mixture was vigorously stirred for 30 min at the same temperature. The reaction was quenched with acetic acid (0.1 mL) and MeOH (3 mL). Solvent was removed and the residue was acetylated in pyridine (5 mL) with acetic anhydride (1 mL) in presence of 4-(dimethylamino)pyridine (10 mg) overnight at rt. The reaction mixture was condensed and the residue was purified by flash chromatography on silica gel eluted with 50% EtOAc in hexane to give **18** (18.9 mg, 97%) as a colorless syrup. R_f = 0.45 (60% EtOAc in hexane). $[\alpha]^{23}_D$ +56.1 (*c* 0.83, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.72 (1H, d, $J_{1,2}$ = 3.7 Hz, H-1), 5.49 (1H, d, $J_{4',5'}$ = 6.6 Hz, H-4'), 5.49–5.45 (1H, m), 5.38 (1H, dd, *J* = 6.6, 6.4 Hz), 5.34 (1H, dd, $J_{2,3}$ = 11.0, $J_{3,4}$ = 3.3 Hz, H-3), 5.15 (1H, dd, $J_{2,3}$ = 11.0, $J_{1,2}$ = 3.7 Hz, H-2), 4.49 (1H, t, *J* = 6.1 Hz), 4.34–4.31 (2H, m), 4.23–4.04 (5H, m), 2.14 (3H, s), 2.13 (3H, s), 2.11 (3H, s), 2.11 (3H, s), 2.10 (3H, s), 2.09 (3H, s), 2.06 (3H, s), 1.99 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.4 (2C), 170.3, 170.1, 170.0, 169.9, 169.9, 169.7, 103.5, 90.3, 78.6, 75.3, 74.5, 67.9, 67.4, 67.3, 67.0, 63.9, 63.0, 61.6, 20.7 (2C), 20.6 (2C), 20.59 (2C), 20.56, 20.53. IR (film): 2965, 1748, 1372, 1228, 1053, 756 cm^{-1}. MS (FAB) *m/z*: 701 $[M+Na]^+$. HRMS (FAB) *m/z*: Calcd for $C_{28}H_{38}O_{19}Na$, 701.1905; found, 701.1911.

1,3,4,6-Tetra-*O*-acetyl-β-D-fructofuranosyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (19): Compound **19** was obtained from **17** by the same reaction manner described for the synthesis of **18** in quantitative yield as a colorless syrup. R_f = 0.19 (50% EtOAc in hexane). $[\alpha]^{20}_D$ –8.4 (*c* 0.30, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.44 (1H, d, $J_{3',4'}$ = 6.6 Hz, H-3'), 5.43 (1H, d, $J_{1,2}$ = 2.1 Hz, H-1), 5.40 (1H, dd, $J_{3',4'}$ = 6.6, $J_{4',5'}$ = 6.4 Hz, H-4'), 5.34 (1H, dd, $J_{3,4}$ = 10.1, $J_{2,3}$ = 2.9 Hz, H-3), 5.31 (1H, dd, $J_{3,4}$ = 10.1, $J_{4,5}$ = 9.9 Hz, H-4), 5.12 (1H, dd, $J_{2,3}$ = 2.9, $J_{1,2}$ = 2.1 Hz, H-2), 4.36 (1H, dd, *J* = 11.9, 4.6 Hz), 4.32–4.23 (3H, m), 4.27 (1H, d, $J_{1'a,1'b}$ = 12.3 Hz, H-1'a), 4.22–4.17 (2H, m), 4.18 (1H, d, $J_{1'a,1'b}$ = 12.3 Hz, H-1'b), 2.17 (3H, s), 2.16 (3H, s), 2.11 (3H, s), 2.10 (3H, s), 2.10 (3H, s), 2.09 (3H, s), 2.06 (3H, s), 1.99 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.7, 170.5, 170.0, 170.0, 169.9, 169.8, 169.7, 169.6, 103.5, 91.3, 78.7, 76.0, 74.8, 70.1, 69.9, 68.7, 65.6, 63.7, 63.5, 62.3, 20.9, 20.8 (2C), 20.7 (3C), 20.6, 20.5. IR (film): 2960, 1747, 1437, 1371, 1223 cm^{-1}. MS (FAB) *m/z*: 701 $[M+Na]^+$. HRMS (FAB) *m/z*: Calcd for $C_{28}H_{38}O_{19}Na$, 701.1905; found, 701.1911.

β-D-Fructofuranosyl α-D-galactopyranoside (2): A 5 μL of 1 M NaOMe in MeOH solution was added to **18** (17.4 mg, 25.6 μmol) in MeOH (0.5 mL), and the reaction was stirred for 3 h at rt. The reaction mixture was neutralized with Dowex 50W × 2. After filtration through a pad of Celite, the filtrate was concentrated under vacuum, dissolved in water, and lyophilized to afford galactosucrose (**2**, 8.5 mg, 96%) as a white solid. R_f = 0.32 (25% H_2O in MeCN). $[\alpha]^{22}_D$ +72.4 (*c* 1.00, H_2O). ^{1}H NMR (400 MHz, D_2O) δ: 5.43 (1H, d, $J_{1,2}$ = 3.8 Hz, H-1), 4.20 (1H, d, $J_{3',4'}$ = 8.8 Hz, H-3'), 4.13 (1H, dd, $J_{5,6b}$ = 7.3, $J_{5,6a}$ = 5.6 Hz, H-5), 4.05 (1H, dd, $J_{3',4'}$ = 8.8, $J_{4',5'}$ = 7.9 Hz, H-4'), 4.01 (1H, d, $J_{3,4}$ = 3.1 Hz, H-4), 3.91 (1H, dd, $J_{2,3}$ = 10.3, $J_{3,4}$ = 3.1 Hz, H-3), 3.88–3.79 (4H, m, H-5', 6'a, 6'b, 2), 3.75 (1H, dd, $J_{6a,6b}$ = 11.8, $J_{5,6a}$ = 5.6 Hz, H-6a), 3.70 (1H, dd, $J_{6a,6b}$ = 11.8, $J_{5,6b}$ = 7.3 Hz, H-6b), 3.67 (2H, s, H-1'). ^{13}C NMR (100 MHz, D_2O) δ: 103.7, 92.4, 81.4, 76.6, 74.1, 71.5, 69.2, 69.2, 68.0, 62.4, 61.5, 60.9. IR (KBr): 3386, 1654, 1421, 1073 cm^{-1}. MS (FAB) *m/z*: 365 $[M+Na]^+$. HRMS (FAB) *m/z*: Calcd for $C_{12}H_{22}O_{11}Na$, 365.1060; found, 365.1053.

β-D-Fructofuranosyl 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranoside (20): A mixed suspension of **17** (16.6 mg, 16.4 μmol) and K_2CO_3 (22.9 mg, 166 μmol) in MeOH (2.2 mL) was stirred for 1 h at rt. After filtration of the reaction mixture through a Celite pad, the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography eluted with EtOAc to give tetraol **20** (10.1 mg, 88%) as a white semisolid. R_f = 0.20 (EtOAc). $[\alpha]^{20}_D$ +8.6 (*c* 0.81, MeOH). ^{1}H NMR (400 MHz, CD_3OD) δ: 7.36–7.25 (18H, m), 7.24–7.13 (2H, m), 5.52 (1H, $J_{1,2}$ = 2.2 Hz, H-1), 4.80 (1H, d, *J* = 11.0 Hz, C*H*HPh), 4.68 (2H, s, CH_2Ph), 4.61 (1H, d, *J* = 12.1 Hz, C*H*HPh), 4.60–4.56 (2H, m, CH_2Ph), 4.50 (1H, d, *J* = 11.0 Hz, CH*H*Ph), 4.48 (1H, d, *J* = 12.1 Hz, CH*H*Ph), 4.07 (1H, d, $J_{3',4'}$ = 8.8 Hz, H-3'), 4.01–3.86 (4H, m, H-4', 5', 6'a, 6'b), 3.78 (1H, dd, $J_{6a,6b}$ = 10.6, $J_{5,6a}$ = 5.5 Hz, H-6a), 3.78–3.63 (4H, m, 3, 4, 5, 6b), 3.72 (1H, dd, $J_{2,3}$ = 2.6, $J_{1,2}$ = 2.2 Hz, H-2), 3.42 (1H, d, $J_{1'a,1'b}$ = 11.9 Hz, H-1'a), 3.32 (1H, d, $J_{1'a,1'b}$ = 11.9 Hz, H-1'b). ^{13}C NMR (150 MHz, CD_3OD) δ: 139.8 (2C), 139.7, 139.6, 129.4, 129.3, 129.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 105.7, 92.5, 83.8, 80.4, 77.9, 77.0, 75.9, 75.8, 75.3, 74.4, 73.6, 73.4, 73.1, 70.1, 63.6, 63.3. IR (film): 3417, 2922, 1454, 1071 cm^{-1}. MS (FAB) *m/z*: 725 $[M+Na]^+$. HRMS (FAB) *m/z*: Calcd for $C_{40}H_{46}O_{11}Na$, 725.2938; found, 725.2934.

β-D-Fructofuranosyl α-D-mannopyranoside (3): Synthesis from **19**. Compound **3** was obtained from **19** by the same reaction manner described for the synthesis of **2** in a quantitative yield as a white solid. R_f = 0.61 (25% H_2O in MeCN). $[\alpha]^{20}_D$ +11.8 (*c* 0.44, H_2O). ^{1}H NMR (400 MHz, D_2O) δ: 5.35 (1H, d, $J_{1,2}$ = 2.0 Hz, H-1), 4.18 (1H, d, $J_{3',4'}$ = 8.8 Hz, H-3'), 4.06 (1H, dd, $J_{3',4'}$ = 8.8, $J_{4',5'}$ = 8.1 Hz, H-5'), 3.90 (1H, dd, $J_{3,4}$ = 9.5, $J_{2,3}$ = 3.3 Hz, H-3), 3.90–3.75 (6H, m, H-5, 6, 5', 6'), 3.86 (1H, dd, $J_{2,3}$ = 3.3, $J_{1,2}$ = 2.0 Hz, H-2), 3.70 (1H, dd, $J_{4,5}$ = 9.7, $J_{3,4}$ = 9.5 Hz, H-4), 3.66 (2H, s, H-1'). ^{13}C NMR (75 MHz, D_2O) δ: 104.6, 94.3,

82.0, 76.6, 74.5, 74.0, 71.8, 70.8, 67.1, 63.0, 61.6, 61.3. IR (KBr): 3376, 2927, 1272, 1069 cm^{-1}. Synthesis from **20**. A suspension of **20** (10.1 mg, 14.4 μmol) and 20% $Pd(OH)_2$ on carbon (10 mg) in MeOH (1 mL) was stirred overnight under H_2 atmosphere. The reaction was filtered through a Celite pad and concentrated under vacuum to give (**3**, 4.4 mg, 90%) as a white solid.

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