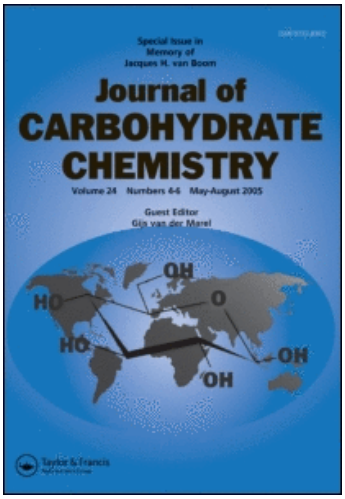

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Synthesis and Taste Properties of 4,1',4',6'-Tetrahalodeoxysucrose Analogues

A. S. Sofian[a]; C. Kuan Lee[a]
[a] Department of Chemistry, National University of Singapore, Kent Ridge, Singapore

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Synthesis and Taste Properties of 4,1′,4′,6′-Tetrahalodeoxysucrose Analogues

A. S. Md Sofian* and C. Kuan Lee

Department of Chemistry, National University of Singapore,
Kent Ridge, Singapore

ABSTRACT

The synthesis of a series of 1,4,6-trideoxy-1,4,6-trihalo-β-D-hexulofuranosyl 4-deoxy-4-halo-α-D-hexopyranosides is described. The 4-chloro-, 4-bromo- and 4-iodo-4-deoxy-β-D-fructofuranosyl analogues were synthesized from a 3′,4′-*lyxo*-epoxide using the respective alkali metal halides. The corresponding 4-halodeoxytagatofuranosyl analogues, on the other hand, were obtained by direct halide displacement of the 4′-*O*-trifluoromethanesulfonyl derivative, which was derived by regioselective sulfonylation of 1,6-di-*O*-trityl-β-D-fructofuranosyl 6-*O*-trityl-α-D-glucopyranoside *via* its stannylene acetal. The sweetness intensities of these tetrahalodeoxy compounds strongly suggest that both size and configuration of the halogen substituents at C-4 and C-4′ are critical for sweetness enhancement.

Key Words: Sweetness; Tetrahalodeoxysucrose analogues; Halogenation; Sucrose.

*Correspondence: A. S. Md Sofian, Department of Chemistry, National University of Singapore, Kent Ridge, Singapore 119260; E-mail: scip8192@nus.edu.sg.

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INTRODUCTION

The Shallenberger-Acree-Kier AH,B,γ-hypothesis[1,2] is the most widely accepted model used to explain sweet taste chemoreception. For sucrose and its derivatives, the AH,B,γ-glucophore appears to span the two sugar rings and both are involved in recognition, since glucopyranosyl and fructofuranosyl derivatives are generally less sweet than sucrose and definitely very much less sweet than halodeoxy sucrose analogues.

The location of the γ-site(s) in sucrose is still not very clear, but since halogenation of some or all the C-4, 1′, 4′ and 6′ positions of sucrose produced derivatives with enhanced sweetness, the halogen(s) at one or more of these positions could, therefore, be acting as the γ-site(s).

If indeed the halogen(s) function as the γ-site(s), the stereochemistry at C-4 and/or C-4′ is critical for sweet taste induction. For example, 1,6-dichloro-1,6-dideoxy-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside[3,4] (sucralose) is 650 times sweeter than sucrose, but its *gluco*-isomer is only 100 times sweeter.[5] Recently, 1,4,6-trichloro-1,4,6-trideoxy-β-D-tagatofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside[6] was reported to be only about 205 times sweeter than sucrose, whereas its C-4′ epimer, 1,4,6-trichloro-1,4,6-trideoxy-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside[7] is 2200 times sweeter.

Continuing our research programme on the structure-sweetness relationship of halodeoxy sucroses, we now report the synthesis and taste characteristics of a series of 1,4,6-trideoxy-1,4,6-trihalo-β-D-fructofuranosyl 4-deoxy-4-halo-α-D-glucopyranosides, 1,4,6-trideoxy-1,4,6-trihalo-β-D-fructofuranosyl 4-deoxy-4-halo-α-D-galactopyranosides, and 1,4,6-trideoxy-1,4,6-trihalo-β-D-tagatofuranosyl 4-deoxy-4-halo-α-D-galactopyranosides.

RESULTS AND DISCUSSION

A convenient starting material for the synthesis of the target compounds **29–31** is 3,4-anhydro-1,6-di-*O*-trityl-β-D-*lyxo*-hexulofuranosyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside[8] **(1)** (Scheme 1). This was converted to the corresponding 4-halodeoxy fructofuranosyl derivatives by regioselective epoxide ring-opening reaction[8] with lithium chloride (→ **2**), lithium bromide (→ **3**), and sodium iodide (→ **4**) in dimethylformamide, in the presence of acetic acid. The 4′-halo-3′-hydrin structures for **2–4** were determined from ^{1}H NMR spectra of **2–4** and their acetylated derivatives **5–7**. The signals due to H-4′ appeared as triplets at δ ∼ 4.2 in the spectra of **2–4**. These signals resonate at lower field (δ ∼ 4.5) after acetylation (**5–7**), suggesting the presence of a halogen substituent at C-4′. The characteristic downfield shift of a doublet at δ ∼ 5.9 (**5–7**) from δ ∼ 4.5 (**2–4**) revealed the position of acetylation to be at C-3′. The ^{13}C NMR spectra of **2**, **3** and **4** also showed that the resonance due to C-4′ has shifted upfield by ∼1.5 to 35.5 ppm.

Detritylation of compounds **5–7** in acetic acid-dichloromethane (1:1) in the presence of conc HCl at 0°C gave **8–10** in good yields (∼70%). Heating of **8–10** in *iso*-butyl methyl ketone (MIBK) in the presence of acetic acid resulted in a migration of the acetyl group from C-4 to C-6.[9] After tritylation of the reaction mixtures, the migrated products were isolated as 1′,6′-di-*O*-trityl ethers **14–16**,

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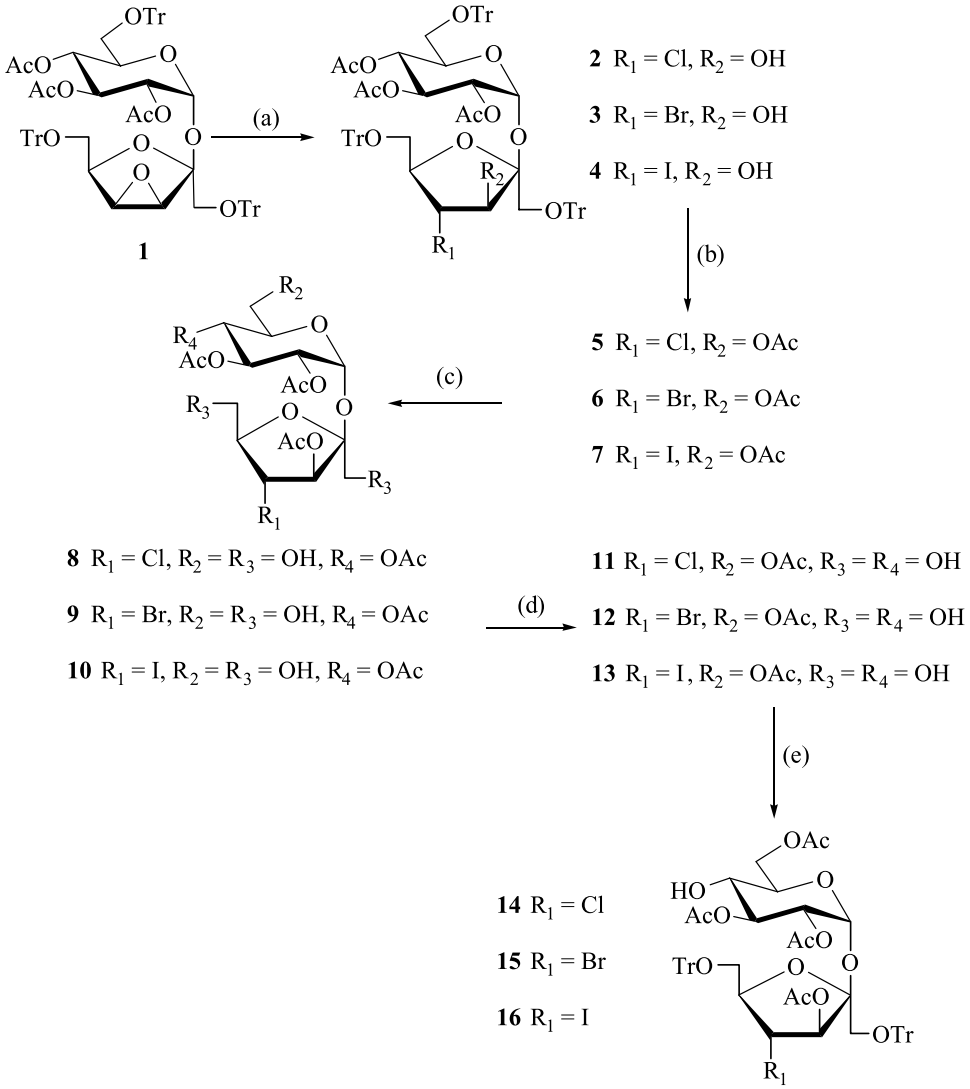
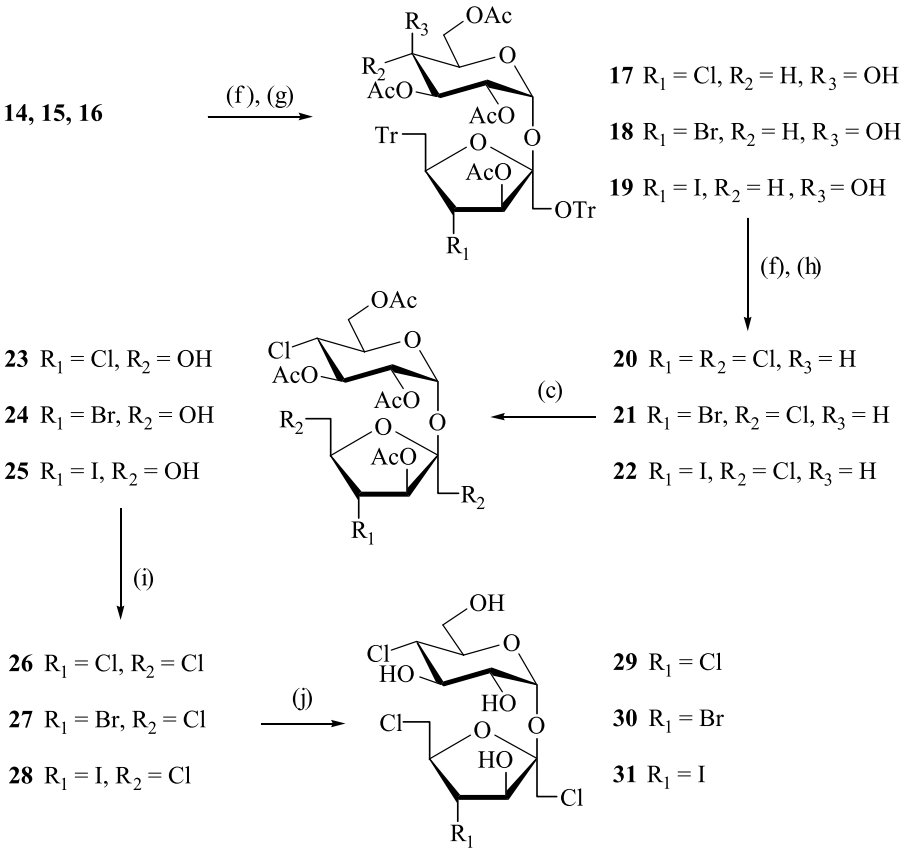


Scheme 1. (a) for **2**: LiCl/AcOH, DMF, 120°C; for **3**: LiBr/AcOH, DMF, 120°C; for **4**: NaI/AcOH, DMF, 120°C; (b) Ac_2O, pyr; (c) AcOH-CH_2Cl_2 (1:1), conc HCl, 0°C; (d) MIBK, AcOH, 110°C; (e) TrCl, pyr.

whereas unchanged starting materials (**8–10**) were recovered as 6,1′,6′-tri-*O*-trityl derivatives **5–7**.

The conversion of **14–16** into 4-chloro-4-deoxy sucrose analogues **20–22**, as shown in Scheme 2, involved the epimerization of the hydroxyl group at C-4 using trifluoromethanesulfonyl anhydride-sodium nitrite[10–12] (**17–19**), followed by triflation, and then nucleophilic displacement with lithium chloride (**20–22**, respectively). The *gluco*-configuration of the resultant products was confirmed from the signal due to

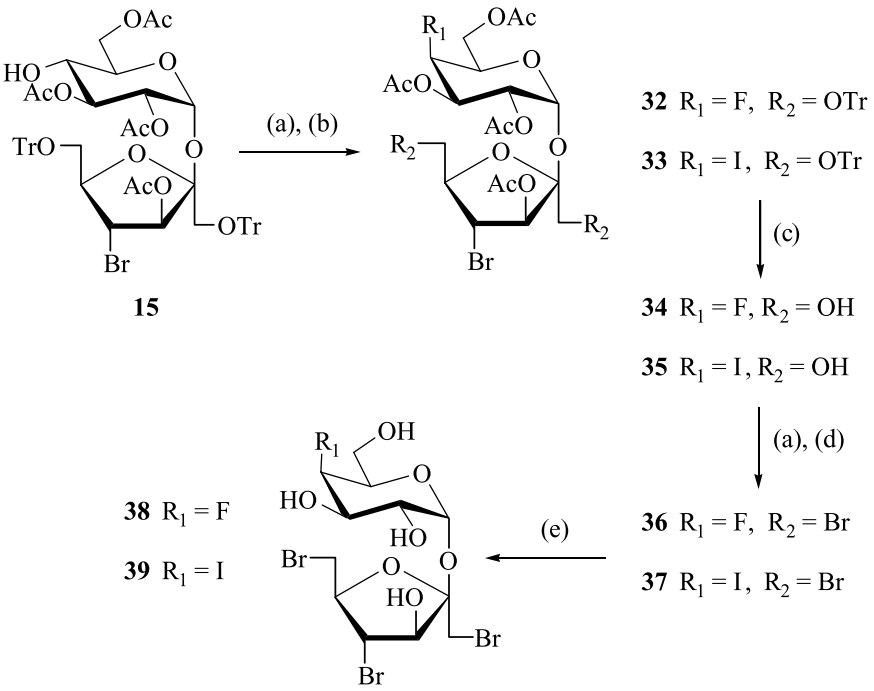


Scheme 2. (f) Tf_2O, pyr/CH_2Cl_2; (g) $NaNO_2$, DMF, rt; (h) LiCl, acetone, rt; (i) TPP/CCl_4, pyr; (j) NaOMe, MeOH, 0°C.

H-4 in their ^{1}H NMR data ($\delta \sim 3.7$, $J_{3,4} = J_{4,5} = \sim 10.0$ Hz). The presence of a chlorine substituent on C-4 was deduced from their ^{13}C NMR and MS spectra. Detritylation (→ **23–25**), chlorination (→ **26–28**) and finally deacetylation gave the target molecules, **29–31**.

The synthesis of 1,4,6-tribromo-1,4,6-trideoxy-β-D-fructofuranosyl 4-deoxy-4-fluoro-, **(38)** and 4-iodo-α-D-galactopyranoside **(39)** is shown in Scheme 3. The C-4 fluorodeoxy *galacto*sucrose derivative **(32)** was obtained by reaction of the corresponding 4-*O*-triflate of **15** with tris(dimethylamino)sulfur (trimethylsilyl)difluoride (TASF) while reaction with potassium iodide in dichloromethane gave the corresponding iodo derivative, **(33)**. Detritylation (→ **34**, **35**), and subsequent bromination (→ **36**, **37**) and deacetylation then afforded the free sugars, **38** and **39**.

Regioselective sulfonylation of 1,6-di-*O*-trityl-β-D-fructofuranosyl 6-*O*-trityl-α-D-glucopyranoside,[9] to give 4′-*O*-triflate,[13] **40** *via* its stannylene acetal[14] offers an efficient route towards 4′-deoxy-4′-halo-*tagato*sucrose analogues (Scheme 4). Nucleophilic displacement of the C-4′ triflate group in **40** with lithium bromide and potassium

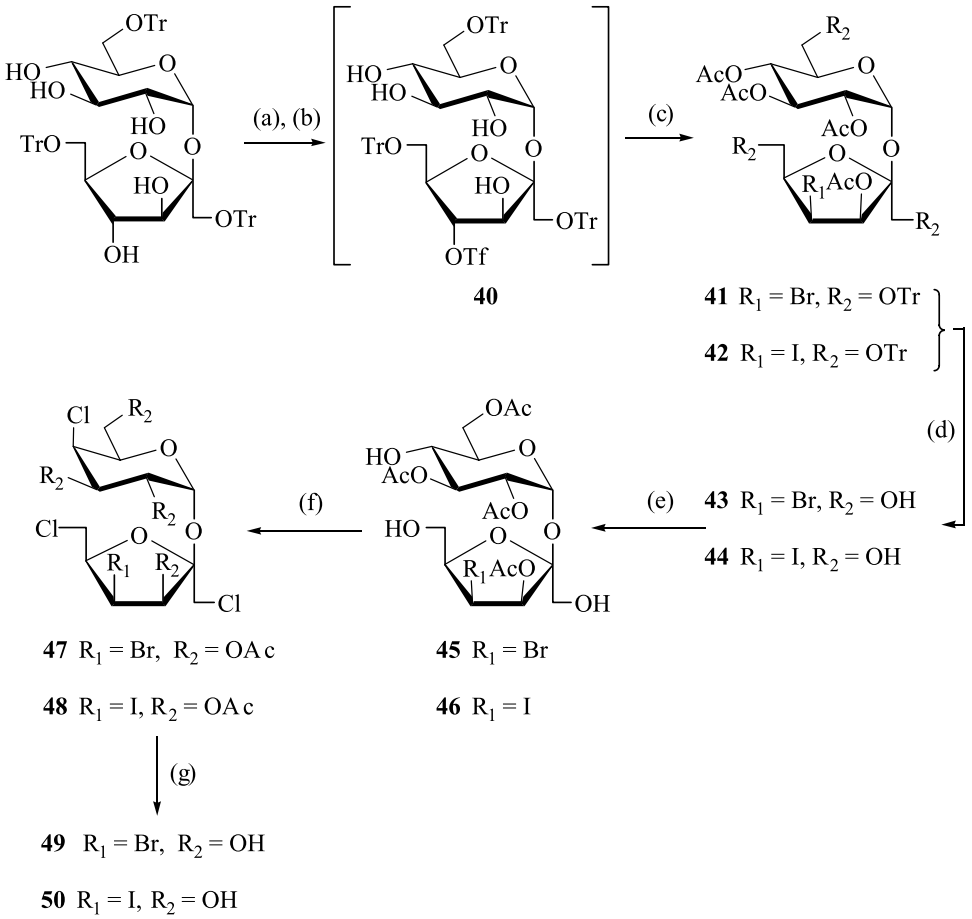


Scheme 3. (a) Tf_2O, pyr /CH_2Cl_2; (b) for **32**: TASF, CH_2Cl_2, 40°C; for **33**: KI, acetone, rt; (c) AcOH-CH_2Cl_2 (1:1), conc HCl, 0°C; (d) LiBr, acetone, 40°C; (e) NaOMe, MeOH, 0°C.

iodide, followed by acetylation gave **41**[13] and **42**, respectively. Detritylation (→ **43**, **44**), and then migration of the acetyl group from C-4 to C-6 afforded **45** and **46**, respectively. Chlorination at C-4, 1′ and 6′ (→ **47**, **48**) proceeded *via* nucleophilic displacement of the corresponding 4,1′,6′-tri-*O*-triflate derivatives with lithium chloride. The *galacto* configuration of **47** and **48** was confirmed from their ^{1}H NMR spectra. H-4 appears as a doublet of a doublet ($J_{3,4} = \sim 3.5$ Hz $J_{4,5} = \sim 1.0$ Hz) at δ 4.54. Conventional Zemplén deacetylation furnished **49** and **50**.

Treatment of **40** with TASF did not give the desired C-4′-fluoro derivative; instead, after acetylation, the 3′,4′-*lyxo*-epoxide,[8] **1** was isolated. It appears that the basicity of the fluoride anion facilitates formation of an alkoxide at C-3′, which then displaces the C-4′ triflate group to form the *lyxo* epoxide.

Taste panel evaluation showed that 4-fluoro- and 4-iodo-1′,4′,6′-tribromo-4,1′,4′,6′-tetradeoxy*galacto*sucrose, **38** and **39**, are about 200 and 520 times sweeter than sucrose, respectively. It is interesting that the corresponding 4-bromo- and 4-chloro isomers are very much sweeter (7500 and 7000 × sucrose, respectively).[15–17] The size of a halogen substituent at C-4 of 4,1′,4′,6′-tetrahalodeoxy*galacto*sucrose derivatives thus appears to be important. The significant difference in sweetness between 4-chloro-[7] and 4-fluoro-1′,4′,6′-trichloro-4,1′,4′,6′-tetrahalodeoxy*galacto*sucrose[16,17] (2200 and 200 times sweeter than sucrose, respectively) further illustrates the importance of size of the halogen substituent at C-4 in *galacto*sucroses on sweetness.



Scheme 4. (a) *n*-Bu_2SnO, toluene, azeotropic distillation; (b) Tf_2O, pyr/CH_2Cl_2; (c) for **41**: LiBr, acetone, rt; Ac_2O, pyr; for **42**: KI, acetone, rt; Ac_2O, pyr; (d) AcOH-CH_2Cl_2 (1:1), conc HCl, 0°C; (e) MIBK, AcOH, 110°C; (f) Tf_2O, pyr/CH_2Cl_2; LiCl, acetone; (g) NaOMe, MeOH, rt.

In contrast to *galacto*sucrose derivatives, all the corresponding 4,1′,4′,6′-tetrahalodeoxysucrose derivatives showed much lower sweetness intensities (190 to 370 times). These results indicate the importance of configuration of the halogen substituents at C-4. Furthermore, the results also suggested that there is a correlation between sweetness of these compounds and hydrophobicities of their halogen substituents at C-4′.

Surprisingly, both 4-bromo-1,6-dichloro-1,4,6-trideoxy-β-D-tagatofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside **(49)** and 1,6-dichloro-1,4,6-trideoxy-4-iodo-β-D-tagatofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside **(50)** are bitter, unlike 1,4,6-trichloro-1,4,6-trideoxy-β-D-tagatofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside,[6] which was reported to have a sweetness of 205 times relative to sucrose.

A discussion of the taste panel assessment and structure-sweetness relationship will be reported in a forthcoming paper elsewhere.

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EXPERIMENTAL

General methods. Melting points were determined with a Thermo Galen Hot Stage Microscope. Optical rotations were measured with a Perkin Elmer 241 polarimeter at 26°C. NMR spectra were recorded at 298K in $CDCl_3$ (unless otherwise specified) on a Bruker DPX 300 spectrometer (300.13 MHz for ^1H and 75.47 MHz for ^{13}C). Mass spectra were recorded on a Finnigan TSQ 7000 (ion trap) spectrometer using electron spray ionization (ESI) with a spray voltage of 4.5 KV. The elemental composition of ions was determined with a resolution of 7000 (10% valley definition). Flash chromatography was performed on Silica Gel 60 (0.63–0.200 nm, Merck). Thin-layer chromatography was run on glass plates precoated with silica gel $60F_{254}$ (Merck, Darmstadt, Germany); detection was effected by observation under short wavelength UV light (254 nm), then spraying with 10% sulphuric acid in ethanol and charring them on a hot plate.

4-Chloro-4-deoxy-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (2). A solution of **1** (10.5 g, 8.91 mmol) in DMF (60 mL) was heated overnight at 110°C with AcOH (1 mL) and LiCl (8.90 g, 0.21 mol). After all starting material had reacted as indicated by TLC (ethyl acetate-hexane, 1:2), DMF was removed under reduced pressure at 50°C. The residue was taken up in dichloromethane, filtered and the organic layer washed successively with satd aq $NaHCO_3$ and brine. It was dried (Na_2SO_4), filtered and concentrated to a syrup. Flash column chromatography (ethyl acetate-hexane, 1:3) gave **2** (7.10 g, 66%): mp 128–130°C (methanol); $[\alpha]_D$ + 53° (*c* 2.45, $CHCl_3$); ^1H NMR δ 1.57, 1.76, 1.86 (s, 9H, 3 × CH_3), 2.73–3.39 (m, 7H, H-1′a,b, H-5′, H-6a,b, and H-6′a,b), 3.93–3.99 (m, 1H, H-5), 4.20 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 9.7 Hz, H-4′), 4.47 (t, 1H, H-3′), 4.71 (dd, 1H, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ 10.0 Hz, H-2), 4.97 (t, 1H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4), 5.17 (t, 1H, H-3), 5.69 (d, 1H, H-1) and 7.11–7.39 (m, 45H, Ar-H). ^{13}C NMR δ 170.2, 169.2, 169.0 (3 × *C*OCH_3), 143.6, 143.4, 128.6–126.9 (Ar-C), 104.8 (C-2′), 88.7 (C-1), 87.1 (*C*Ph_3) 80.9 (C-5′), 79.1 (C-3′), 70.2, 69.8, 69.2, 68.4 (C-2, 3, 4, 5), 64.5, 61.8, 61.6 (C-1′, 6, 6′), 58.5 (C-4′) and 20.5, 20.3, 20.1 (3 × CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1235.4324:1237.4295. Found: 1235.4277: 1237.4323.

4-Bromo-4-deoxy-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (3). Compound **1** (10.2 g, 8.66 mmol) in DMF (60 mL) was treated with AcOH (1 mL) and LiBr (12.9 g, 0.15 mol) as described above. Flash column chromatography (ethyl acetate-hexane, 1:3) gave **3** (7.65 g, 71%): mp 135–137°C (methanol); $[\alpha]_D$ + 53° (*c* 1.58, $CHCl_3$); ^1H NMR δ 1.57, 1.77, 1.86 (s, 9H, 3 × CH_3), 2.73–3.42 (m, 7H, H-1′a,b, H-6a,b, H-6′a,b and OH), 4.02–4.08 (m, 2H, H-5, 5′), 4.20 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 10.0 Hz, H-4′), 4.54 (t, 1H, H-3′), 4.71 (dd, 1H, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 4.98 (t, 1H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4), 5.17 (t,1 H, H-3), 5.72 (d, 1H, H-1) and 7.11–7.39 (m, 45H, Ar-H). ^{13}C NMR δ 170.2, 169.2, 169.0 (3 × *C*OCH_3), 143.6, 143.4, 128.6–126.9 (Ar-C), 105.0 (C-2′), 88.9 (C-1), 87.2, 87.1 (*C*Ph_3), 81.5 (C-5′), 79.9 (C-3′), 70.4, 70.0, 69.4, 68.6 (C-2, 3, 4, 5), 64.7, 62.0, 61.7 (C-1′, 6, 6′), 48.3 (C-4′) and 20.7, 20.5, 20.3 (3 × CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1279.3819:1281.3799. Found: 1279.3782:1281.3795.

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4-Deoxy-4-iodo-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (4). Treatment of **1** (10.5 g, 8.94 mmol) with NaI (30 g, 0.2 mol) as described for **2** gave, after column chromatography (ethyl acetate-hexane, 1:3), **4** (8.5 g, 73%): 123–125°C (methanol); $[\alpha]_D$ + 51° (*c* 1.62, $CHCl_3$); ^{1}H NMR δ 1.67, 1.87, 1.95 (s, 9H, 3 × CH_3), 2.84–3.54 (m, 7H, H-1′a,b, H-5, H-6a,b and H-6′a,b), 4.22–4.31 (m, 2H, H-4′, 5), 4.64–4.71 (m, 1H, H-3′), 4.81 (dd, 1H, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 10.1 Hz, H-2), 5.09 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 10.1 Hz, H-4), 5.27 (t, 1H, H-3), 5.85 (d, 1H, H-1) and 7.21–7.50 (m, 45H, Ar-H). ^{13}C NMR δ 170.2, 169.2, 169.0 (3 × *C*OCH_3), 143.6, 143.4, 128.8–127.0 (Ar-C), 105.2 (C-2′), 88.9 (C-1), 87.2, 87.1, 87.0 (*C*Ph_3), 82.9 (C-5′), 81.6 (C-3′), 70.4, 70.0, 69.4, 68.5 (C-2, 3, 4, 5), 64.7, 62.0, 61.5 (C-1′, 6, 6′), 23.7 (C-4′) and 20.6, 20.5, 20.3 (3 × CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1327.3680. Found: 1327.3656.

3-*O*-Acetyl-4-chloro-4-deoxy-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (5). Acetylation of **2** (8.4 g, 6.93 mmol) in pyridine with acetic anhydride gave **5** (7.4 g, 85%): mp 108–110°C (methanol); $[\alpha]_D$ + 41° (*c* 0.90, $CHCl_3$); ^{1}H NMR δ 1.63, 1.67, 1.86, 1.87 (s, 12H, 4 × CH_3), 2.95–3.42 (m, 6H, H-1′a,b, H-6a,b and H-6′a,b), 4.02–4.08 (m, 2H, H-5, 5′), 4.53 (t, 1H, $J_{3',4'}$ = $J_{4',5'}$ = 9.4 Hz, H-4′), 4.67 (dd, 1H, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 5.12–5.16 (m, 2H, H-3, 4), 5.76 (d, 1H, H-1), 5.86 (d, 1H, H-3′) and 7.12–7.40 (m, 45H, Ar-H). ^{13}C NMR δ 170.4, 169.2, 169.1, 169.0 (4 × *C*OCH_3), 143.6, 143.5, 143.4, 128.7–127.1 (Ar-C), 103.4 (C-2′), 88.6 (C-1), 87.2, 86.7 (*C*Ph_3), 81.7 (C-5′), 77.8 (C-3′), 70.7, 69.7, 69.6, 68.9 (C-2, 3, 4, 5), 65.1, 61.8, 61.5 (C-1′, 6, 6′), 55.5 (C-4′) and 20.8, 20.7, 20.4, (4 × CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1277.4430:1279.4400. Found: 1277.4493:1279.4433.

3-*O*-Acetyl-4-bromo-4-deoxy-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (6). Acetylation of **3** (7.5 g, 5.97 mmol) in the usual manner gave **6** (6.7 g, 86%): mp 133–135°C (methanol); $[\alpha]_D$ + 40° (*c* 1.27, $CHCl_3$); ^{1}H NMR δ 1.63, 1.67, 1.85, 1.87 (s, 12H, 4 × CH_3), 2.96–3.44 (m, 6H, H-1′a,b, H-6a,b and H-6′a,b), 4.06–4.15 (m, 2H, H-5, 5′), 4.52 (t, 1H, $J_{3',4'}$ = $J_{4',5'}$ = 10.0 Hz, H-4′), 4.67 (dd, 1H, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 5.11–5.20 (m, 2H, H-3, 4), 5.80 (d, 1H, H-1), 5.92 (d, 1H, H-3′) and 7.13–7.41 (m, 45H, Ar-H). ^{13}C NMR δ 170.4, 169.2, 169.1, 169.0 (4 × *C*OCH_3), 143.6, 143.5, 128.5–126.9 (Ar-C), 103.5 (C-2′), 88.5 (C-1), 87.2, 86.7 (*C*Ph_3), 82.0 (C-5′), 78.1 (C-3′), 70.7, 69.6, 69.5, 68.8 (C-2, 3, 4, 5), 65.1, 61.7, 61.3 (C-1′, 6, 6′), 44.3 (C-4′) and 20.7, 20.5, 20.4, (4 × CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1321.3925:1323.3905. Found: 1321.3940:1323.3920.

3-*O*-Acetyl-4-deoxy-4-iodo-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (7). Acetylation of **4** (8.3 g, 6.36 mmol) in the usual manner gave **7** (7.45 g, 87%): 205–207°C (methanol); $[\alpha]_D$ + 47° (*c* 1.09, $CHCl_3$); ^{1}H NMR δ 1.64, 1.67, 1.85, 1.87 (s, 12H, 4 × CH_3), 2.95–3.48 (m, 6H, H-1′a,b, H-6a,b and H-6′a,b), 4.04–4.08 (m, 1H, H-5′), 4.17–4.22 (m, 1H, H-5), 4.47 (t, 1H, $J_{3',4'}$ = $J_{4',5'}$ = 10.4 Hz, H-4′), 4.68 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 5.11–5.24 (m, 2H, H-3, 4), 5.83 (d, 1H, H-1) 5.93 (d, 1H, H-3′) and 7.12–7.41 (m, 45H, Ar-H). ^{13}C NMR δ 170.4, 169.2, 169.1, 169.0 (4 × *C*OCH_3), 143.6, 143.4,

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128.7–127.0 (Ar-C), 103.7 (C-2′), 88.5 (C-1), 87.2, 87.1, 86.6 (CPh_3), 83.4 (C-5′), 79.8 (C-3′), 70.8, 69.6, 69.4, 68.8 (C-2, 3, 4, 5), 65.2, 61.5, 61.1 (C-1′, 6, 6′), 20.7, 20.6, 20.4 (4 × $COCH_3$) and 18.5 (C-4′). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1369.3786. Found: 1369.3809.

3-*O*-Acetyl-4-chloro-4-deoxy-β-D-fructofuranosyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (8). To a solution of **5** (4.30 g, 3.43 mmol) in ice-cold dichloromethane-acetic acid (1:1, 100 mL), was added drop-wise conc HCl (1.0 mL). After all starting material had reacted (1.5 h), the solution was neutralized (Na_2CO_3), filtered, concentrated and chromatographed (ethyl acetate-hexane, 2:1) to give **8** (1.32 g, 73%) as a colourless syrup; $[\alpha]_D$ + 10° (*c* 0.59, $CHCl_3$); ^{1}H NMR δ 1.95, 1.97, 2.00, 2.22 (s, 12H, 4 × CH_3), 3.45–3.92 (m, 7H, H-1′a,b, H-5′, H-6a,b and H-6′a,b), 4.09–4.13 (m, 1H, H-5), 4.52 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 9.4 Hz, H-4′), 4.77 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.4 Hz, H-2), 4.84 (t, 1H, $J_{3,4} = J_{4,5}$ = 10.4 Hz, H-4), 5.22 (d, 1H, H-3′), 5.39 (t, 1H, H-3) and 5.57 (d, 1H, H-1). ^{13}C NMR δ 171.4, 170.1, 170.0, 169.9 (4 × *C*OCH$_3$), 104.1 (C-2′), 89.8 (C-1), 82.8 (C-5′), 80.0 (C-3′), 71.3, 70.4, 69.2, 68.7 (C-2, 3, 4, 5), 63.9, 61.6, 58.3 (C-1′, 6, 6′), 53.9 (C-4′) and 20.6, 20.5, 20.5 (4 × CO*C*H$_3$). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 551.1143:553.1114. Found: 551.1136:553.1098.

3-*O*-Acetyl-4-bromo-4-deoxy-β-D-fructofuranosyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (9). Treatment of **6** (6.96 g, 5.36 mmol) as for **8** gave, after column chromatography (ethyl acetate-hexane, 2:1), **9** (2.17 g, 71%) as a yellowish syrup; $[\alpha]_D$ + 11° (*c* 0.53, $CHCl_3$); ^{1}H NMR δ 1.95, 1.97, 2.00, 2.22 (s, 12H, 4 × CH_3), 3.51–3.87 (m, 6H, H-1′a,b, H-6a,b and H-6′a,b), 3.99–4.13 (m, 2H, H-5, 5′), 4.49 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 10.0 Hz, H-4′), 4.77 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 4.84 (t, 1H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4), 5.29 (d, 1H, H-3′), 5.40 (t, 1H, H-3) and 5.57 (d, 1H, H-1). ^{13}C NMR δ 171.4, 170.1, 170.0, 169.5 (4 × *C*OCH$_3$), 104.4 (C-2′), 89.8 (C-1), 83.2 (C-5′), 80.3 (C-3′), 71.3, 70.4, 69.2, 68.7 (C-2, 3, 4, 5), 63.9, 61.6, 58.3 (C-1′, 6, 6′), 42.6 (C-4′) and 20.6, 20.5 (4 × CO*C*H$_3$). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 595.0638:597.0618. Found: 595.0624:597.0611.

3-*O*-Acetyl-4-deoxy-4-iodo-β-D-fructofuranosyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (10). Treatment of **7** (5.43 g, 4.03 mmol) as for **8** gave, after flash chromatography (ethyl acetate-hexane, 2:1), **10** (1.57 g, 63%) as a colourless syrup; $[\alpha]_D$ + 14° (*c* 1.54, $CHCl_3$); ^{1}H NMR δ 1.95, 1.97, 1.98, 2.00 (s, 12H, 4 × CH_3), 3.48–3.76 (m, 6H, H-1′a,b, H-6a,b and H-6′a,b), 3.84–3.88 (m, 1H, H-5′), 4.09–4.13 (m, 1H, H-5), 4.45 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 10.4 Hz, H-4′), 4.78 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 4.85 (t, 1H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4), 5.31 (d, 1H, H-3′), 5.39 (t, 1H, H-3) and 5.58 (d, 1H, H-1). ^{13}C NMR δ 171.3, 170.1, 170.0, 169.9 (4 × *C*OCH$_3$), 104.6 (C-2′), 89.8 (C-1), 84.8 (C-5′), 81.7 (C-3′), 71.3, 70.4, 69.2, 68.7 (C-2, 3, 4, 5), 63.9, 61.5, 58.2 (C-1′, 6, 6′), 20.6, 20.5 (4 × CO*C*H$_3$) and 16.8 (C-4′). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 643.0500. Found: 643.0494.

3-*O*-Acetyl-4-chloro-4-deoxy-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-α-D-glucopyranoside (14). A solution of **8** (1.02 g, 1.93 mmol) in MIBK (20 mL) and AcOH (1.0 mL) was heated under reflux, and the progress of the reaction

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was monitored by ^{1}H NMR. After most starting material had reacted for ~8 h, the mixture was concentrated by co-distilling several times with MeOH. The yellow syrupy residue was dissolved in pyridine (20 mL) and stirred with trityl chloride (2.7 g, 9.69 mmol) at 80°C for about 48 h and worked-up by pouring into ice-water and extracting it with dichloromethane. The organic layer was washed with dil HCl (10%), satd aq $NaHCO_3$, brine, dried (Na_2SO_4), filtered and concentrated. Column chromatography (ethyl acetate-hexane, 2:3, then 1:1) gave pure **14** (0.95 g, 49%) as a colourless syrup; $[\alpha]_D$ + 29° (*c* 2.35, $CHCl_3$); ^{1}H NMR δ 1.62, 1.88, 1.93, 1.94 (s, 12H, 4 × CH_3), 3.07–3.40 (m, 6H, H-1′a,b, H-6a,b and H-6′a,b), 3.90–4.19 (m, 3H, H-4, 5, 5′), 4.34 (t, 1H, $J_{3',4'}$ = $J_{4',5'}$ = 9.4 Hz, H-4′), 4.55 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 5.01 (t, 1H, $J_{3,4}$ = 10.0 Hz, H-3), 5.48 (d, 1H, H-1), 5.82 (d, 1H, H-3′) and 7.12–7.40 (m, 30H, Ar-H). ^{13}C NMR δ 171.6, 171.3, 169.5, 169.2 (4 × *C*OCH_3), 143.7, 143.6, 128.7, 127.8, 127.1 (Ar-C), 103.3 (C-2′), 88.6 (C-1), 87.2, 87.1 (*C*Ph_3), 81.8 (C-5′), 77.9 (C-3′), 73.0, 70.5, 69.6, 69.2 (C-2, 3, 4, 5), 64.9, 63.3, 62.7 (C-1′, 6, 6′), 55.9 (C-4′) and 20.7, 20.6, 20.4, 20.2 (4 × CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1035.3334:1037.3305. Found: 1035.3338:1037.3348.

3-*O*-Acetyl-4-bromo-4-deoxy-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-α-D-glucopyranoside (15). Treatment of **9** (1.65 g, 2.88 mmol) in MIBK (35 mL) with AcOH (1.5 mL) as for **14** gave, after flash chromatography (ethyl acetate-hexane, 2:3, then 1:1), pure **15** (1.78 g, 58%) as a colourless syrup; $[\alpha]_D$ + 32° (*c* 2.80, $CHCl_3$); ^{1}H NMR δ 1.90, 1.93, 1.94, 2.04 (s, 12H, 4 × CH_3), 2.98–3.41 (m, 6H, H-1′a,b, H-6a, b and H-6′a,b), 3.91–4.35 (m, 4H, H-4, 4′,5, 5′), 4.56 (dd, 1H, $J_{1,2}$ = 4.2 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 5.01 (t, 1H, $J_{3,4}$ = 10.0 Hz, H-3), 5.50 (d, 1H, H-1), 5.89 (d, 1H, $J_{3',4'}$ = 9.1 Hz, H-3′) and 7.12–7.41 (m, 30H, Ar-H). ^{13}C NMR δ 171.6, 171.3, 169.5, 169.2 (4 × *C*OCH_3), 143.7, 143.6, 128.7–127.1 (Ar-C), 103.5 (C-2′), 88.6 (C-1), 87.2, 87.0 (*C*Ph_3), 82.2 (C-5′), 78.3 (C-3′), 73.0, 70.5, 69.5, 69.2 (C-2, 3, 4, 5), 64.9, 63.4, 62.5 (C-1′, 6, 6′), 44.6 (C-4′) and 21.0, 20.8, 20.6, 20.4 (4 × CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M+Na]^+$ 1079.2829:1081.2809. Found: 1079.2835:1081.2835.

3-*O*-Acetyl-4-deoxy-4-iodo-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-α-D-glucopyranoside (16). A solution of **10** (1.57 g, 2.53 mmol) in MIBK (35 mL) was treated with AcOH (1.5 mL) as for **14** gave, after flash chromatography (ethyl acetate-hexane, 2:3, then 1:1), pure **16** (1.56 g, 56%) as a colourless syrup; $[\alpha]_D$ + 38° (*c* 2.40, $CHCl_3$); ^{1}H NMR δ 2.02, 2.03, 2.04, 2.14 (s, 12H, 4 × CH_3), 3.11–3.52 (m, 6H, H-1′a,b, H-6a,b and H-6′a,b), 4.01–4.45 (m, 4H, H-4, 4′, 5, 5′), 4.66 (dd, 1H, $J_{1,2}$= 3.8 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 5.11 (t, 1H, $J_{3,4}$ = 10.0 Hz, H-3), 5.62 (d, 1H, H-1), 6.01 (d, 1H, $J_{3',4'}$ = 9.7 Hz, H-3′) and 7.22–7.51 (m, 30H, Ar-H). ^{13}C NMR δ 171.6, 171.3, 169.5, 169.2 (4 × *C*OCH_3), 143.7, 143.6, 128.8–127.1 (Ar-C), 103.8 (C-2′), 88.6 (C-1), 87.1, 87.0 (*C*Ph_3), 83.7 (C-5′), 80.0 (C-3′), 73.0, 70.5, 69.6, 69.2 (C-2, 3, 4, 5), 64.9, 63.4, 62.3 (C-1′, 6, 6′), 21.0, 20.8, 20.5, 20.4 (4 × CO*C*H_3) and 18.6 (C-4′). HRMS-ESI (positive mode): calcd for $[M+Na]^+$ 1127.2691. Found: 1127.2694.

3-*O*-Acetyl-4-chloro-4-deoxy-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-α-D-galactopyranoside (17). A solution of **14** (0.85 g, 0.84 mmol) in dry CH_2Cl_2-pyridine (15:1, 32.0 mL) at -78°C was treated with trifluoromethanesulfonic

anhydride (0.30 mL, 1.83 mmol). The mixture was stirred for 15 min at − 78°C, then for about 2 h at 0°C. It was then diluted with dichloromethane and the organic solution was washed successively with aq $KHSO_4$ (10%), satd $NaHCO_3$ and water, dried (Na_2SO_4), filtered and concentrated. The residue was dissolved in DMF (50 mL) and sodium nitrite (0.90 g, 13.0 mol) was added. The solution was then stirred at room temperature overnight, concentrated, and the residue diluted with dichloromethane. The filtered solution was again concentrated. Flash chromatography (ethyl acetate-hexane, 1:1) gave **17** (0.70 g, 82%): mp 108–110°C (ether-hexane); $[\alpha]_D$ + 38° (*c* 2.02, $CHCl_3$); ^{1}H NMR δ 1.72, 1.95, 2.05, 2.14 (s, 12H, 4 × CH_3), 3.15–3.21 (2 × d, 2H, $J_{1'a,1'b}$ = 9.9 Hz, H-1′a,b), 3.36–3.53 (m, 2H, H-6′a,b), 4.01–4.33 (m, 5H, H-4, 5, 5′ and H-6a,b), 4.44 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 9.7 Hz, H-4′), 5.06 (dd, 1H, $J_{2,3}$ = 10.9 Hz, $J_{3,4}$ = 2.6 Hz, H-3), 5.10 (dd, 1H, $J_{1,2}$ = 3.4 Hz, H-2), 5.67 (d, 1H, H-1), 5.94 (d, 1H, H-3′) and 7.22–7.52 (m, 30H, Ar-H). ^{13}C NMR δ 170.6, 169.9, 169.4, 169.0 (4 × *C*OCH_3), 143.5, 143.4, 128.5–126.9 (Ar-C), 102.9 (C-2′), 88.6 (C-1), 87.0, 86.9 (*C*Ph_3), 81.6 (C-5′), 77.4 (C-3′), 69.9, 68.0, 67.5, 66.6 (C-2, 3, 4, 5), 64.6, 63.0, 62.6 (C-1′, 6, 6′), 55.6 (C-4′) and 20.7, 20.5, 20.3, 20.2 (4 × CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1035.3334:1037.3305. Found: 1035.3354:1037.3347.

3-*O*-Acetyl-4-bromo-4-deoxy-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-α-D-galactopyranoside (18). Treatment of **15** (1.65 g, 1.56 mmol) with trifluoromethanesulfonic anhydride (0.52 mL, 3.17 mmol) as above gave, after flash chromatography (ethyl acetate-hexane, 1:1), **18** (1.31 g, 79%): mp 190–192°C (ether-hexane); $[\alpha]_D$ + 50° (*c* 0.98, $CHCl_3$); ^{1}H NMR δ 1.71, 1.96, 2.05, 2.13 (s, 12H, 4 × CH_3), 3.14–3.20 (2 × d, 2H, $J_{1'a,1'b}$ = 9.8 Hz, H-1′a,b), 3.38–3.51 (m, 2H, H-6′a,b), 4.00–4.35 (m, 5H, H-4, 5, 5′ and H-6a,b), 4.41 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 9.8 Hz, H-4′), 5.05–5.09 (m, 2H, H-2, 3), 5.69 (d, 1H, $J_{1,2}$ = 2.7 Hz, H-1), 6.00 (d, 1H, H-3′) and 7.21–7.51 (m, 30H, Ar-H). ^{13}C NMR δ 170.8, 170.0, 169.6, 169.2 (4 × *C*OCH_3), 143.7, 143.6, 128.8–127.1 (Ar-C), 103.3 (C-2′), 88.8 (C-1), 87.2, 87.1 (*C*Ph_3), 82.2 (C-5′), 78.1 (C-3′), 70.1, 68.2, 67.7, 66.8 (C-2, 3, 4, 5), 64.8, 63.3, 62.7 (C-1′, 6, 6′), 44.6 (C-4′) and 20.9, 20.5, 20.4 (4 × CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1079.2829:1081.2809. Found: 1079.2847:1081.2843.

3-*O*-Acetyl-4-deoxy-4-iodo-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-α-D-galactopyranoside (19). Trifluoromethanesulfonic anhydride treatment of **16** (1.46 g, 1.32 mmol) as above gave, after flash chromatography (ethyl acetate-hexane, 1:1), **19** (1.01 g, 69%): mp 200–202°C (ether-hexane); $[\alpha]_D$ + 53° (*c* 1.15, $CHCl_3$); ^{1}H NMR δ 1.70, 1.97, 2.05, 2.13 (s, 12H, 4 × CH_3), 3.12–3.19 (2 × d, 2H, $J_{1'a,1'b}$ = 9.6 Hz, H-1′a,b), 3.41–3.51 (m, 2H, H-6′a,b), 3.98–4.38 (m, 6H, H-4, 4′, 5, 5′ and H-6a,b), 5.04–5.10 (m, 2H, H-2, 3), 5.70 (d, 1H, $J_{1,2}$ = 2.7 Hz, H-1), 6.00 (d, 1H, $J_{3',4'}$ = 9.8 Hz, H-3′) and 7.20–7.50 (m, 30H, Ar-H). ^{13}C NMR δ 170.8, 170.0, 169.5, 169.2 (4 × *C*OCH_3), 143.7, 143.6, 128.8–127.1 (Ar-C), 103.5 (C-2′), 88.8 (C-1), 87.1 (*C*Ph_3), 83.7 (C-5′), 79.7 (C-3′), 70.1, 68.1, 67.6, 66.8 (C-2, 3, 4, 5), 64.8, 63.1, 62.4 (C-1′, 6, 6′), 21.1, 20.9, 20.5, 20.3 (4 × CO*C*H_3) and 18.6 (C-4′). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1127.2691. Found: 1127.2690.

3-*O*-Acetyl-4-chloro-4-deoxy-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-glucopyranoside (20). Compound **17** (1.13 g, 1.12

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mmol) was treated with trifluoromethanesulfonic anhydride (0.4 mL, 2.44 mmol) as above. The crude syrup obtained after work-up in the usual manner was dissolved in acetone (20 mL) and stirred with LiCl (0.30 g, 7.06 mmol) at room temperature for ~ 12 h. When all starting material had reacted, the solvent was removed and the residue taken up in dichloromethane and filtered. The filtrate was then washed with satd aq $NaHCO_3$ and brine; dried (Na_2SO_4), filtered and concentrated. Flash column chromatography (ether-hexane, 1:1) gave **20** (0.85 g, 74%): mp 98–100°C (ether-hexane); $[\alpha]_D$ + 27° (*c* 1.77, $CHCl_3$); ^{1}H NMR δ 1.63, 1.90, 1.96, 2.06 (s, 12H, 4 × CH_3), 3.08–3.38 (m, 4H, H-1′a,b and H-6′a,b), 3.67 (t, 1H, $J_{3,4} = J_{4,5}$ = 10.4 Hz, H-4), 4.05–4.23 (m, 4H, H-5, 5′ and H-6a,b), 4.34 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 9.1 Hz, H-4′), 4.54 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.4 Hz, H-2), 5.26 (t, 1H, H-3), 5.55 (d, 1H, H-1), 5.83 (d, 1H, H-3′) and 7.14–7.40 (m, 30H, Ar-H). ^{13}C NMR δ 170.3, 169.5, 169.4, 169.1 (4 × *C*OCH_3), 143.6, 143.5, 128.7, 127.8, 127.1 (Ar-C), 103.5 (C-2′), 88.6 (C-1), 87.2, 87.1 (*C*Ph_3), 81.9 (C-5′), 78.0 (C-3′), 71.3, 70.3 (C-2, 3, 5), 64.8, 63.1, 62.5 (C-1′, 6, 6′), 55.8, 55.3 (C-4, 4′) and 20.7, 20.5, 20.3 (4 × CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1053.2996:1055.2966:1057.2936. Found: 1053.2994:1055.2987:1057.3031.

3-*O*-Acetyl-4-bromo-4-deoxy-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-glucopyranoside (21). Compound **18** (0.47 g, 0.44 mmol) was treated as described for **20**, gave after flash column chromatography (ether-hexane, 1:1), **21** (0.39 g, 81%) as a colourless syrup; $[\alpha]_D$ + 28° (*c* 1.28, $CHCl_3$); ^{1}H NMR δ 1.63, 1.92, 1.96, 2.07 (s, 12H, 4 × CH_3), 3.08–3.20 (2 × d, 2H, $J_{1'a,1'b}$ = 9.6 Hz, H-1′a,b), 3.27 (dd, 1H, $J_{5',6'a}$ = 2.1 Hz, $J_{6'a,6'b}$ = 10.8 Hz, H-6′a), 3.37 (dd, 1H, $J_{5',6'b}$ = 4.7 Hz, H-6′b), 3.68 (t, 1H, $J_{3,4} = J_{4,5}$ = 10.1 Hz, H-4), 4.07–4.35 (m, 5H, H-4′, 5, 5′ and H-6a,b), 4.54 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.1 Hz, H-2), 5.26 (t, 1H, H-3), 5.57 (d, 1H, H-1), 5.90 (d, 1H, $J_{3',4'}$ = 9.1 Hz, H-3′) and 7.14–7.40 (m, 30H, Ar-H). ^{13}C NMR δ 170.3, 169.5, 169.4, 169.1 (4 × *C*OCH_3), 143.6, 143.5, 128.7–127.2 (Ar-C), 103.7 (C-2′), 88.6 (C-1), 87.3, 87.1 (*C*Ph_3), 82.4 (C-5′), 78.5 (C-3′), 71.3, 70.4 (C-2, 3, 5), 65.0, 63.2, 62.4 (C-1′, 6, 6′), 55.4 (C-4), 44.5 (C-4′) and 20.8, 20.6, 20.5, 20.3 (CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1097.2491:1099.2461:101.2441. Found: 1097.2481:1099.2462: 1101.2482.

3-*O*-Acetyl-4-deoxy-4-iodo-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-glucopyranoside (22). Treatment of **19** (0.70 g, 0.63 mmol) as above gave, after flash column chromatography (ether-hexane, 1:1), **22** (0.50 g, 70%): mp 93–95°C (ether-hexane); $[\alpha]_D$ + 35° (*c* 0.57, $CHCl_3$); ^{1}H NMR δ 1.62, 1.94, 1.96, 2.07 (s, 12H, 4 × CH_3), 3.06–3.19 (2 × d, 2H, $J_{1'a,1'b}$ = 9.7 Hz, H-1′a,b), 3.29–3.41 (m, 2H, H-6′a,b), 3.69 (t, 1H, $J_{3,4} = J_{4,5}$ = 10.1 Hz, H-4), 4.09–4.33 (m, 5H, H-4′, 5, 5′ and H-6a,b), 4.54 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.1 Hz, H-2), 5.27 (t, 1H, H-3), 5.60 (d, 1H, H-1), 5.92 (d, 1H, $J_{3',4'}$ = 9.7 Hz, H-3′) and 7.14–7.41 (m, 30H, Ar-H). ^{13}C NMR δ 170.3, 169.5, 169.4, 169.1 (4 × *C*OCH_3), 143.6, 143.5, 128.8, 128.7, 127.8, 127.1 (Ar-C), 103.9 (C-2′), 88.6 (C-1), 87.2, 87.1 (*C*Ph_3), 83.8 (C-5′), 80.1 (C-3′), 71.3, 70.4, 70.3 (C-2, 3, 5), 65.0, 63.2, 62.2 (C-1′, 6, 6′), 55.4 (C-4), 21.0, 20.6, 20.5, 20.3 (4 × CO*C*H_3) and 18.4 (C-4′). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1145.2352:1147.2322. Found: 1145.2370:1147.2375.

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3-*O*-Acetyl-4-chloro-4-deoxy-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-glucopyranoside (23). Treatment of **20** (0.82 g, 0.80 mmol) with ice-cold CH_2Cl_2-AcOH (1:1, 20 mL) and conc HCl (0.15 mL) as above gave, after flash chromatography (ethyl acetate-hexane, 2:1), **23** (0.32 g, 73%): mp 131–133°C (ether-hexane); $[\alpha]_D$ + 3.3° (*c* 2.02, $CHCl_3$); ^{1}H NMR δ 2.06, 2.10, 2.12, 2.26 (s, 12H, 4 × CH_3), 3.54–3.95 (m, 5H, H-4, H-1′a,b and H-6′a,b), 4.06–4.11 (m, 1H, H-5), 4.28–4.55 (m, 4H, H-4′, 5′ and H-6a,b), 4.80 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.1 Hz, H-2), 5.43 (d, 1H, $J_{3',4'}$ = 9.4 Hz, H-3′), 5.50 (t, 1H, $J_{3,4}$ = 10.1 Hz, H-3) and 5.66 (d, 1H, H-1). ^{13}C NMR δ 170.7, 170.5, 170.2, 169.5 (4 × *C*OCH$_3$), 103.9 (C-2′), 89.7 (C-1), 83.3 (C-5′), 78.5 (C-3′), 71.0, 70.8, 70.5 (C-2, 3, 5), 64.2, 62.3, 59.2 (C-1′, 6, 6′), 54.9, 54.0 (C-4, 4′) and 20.6, 20.5, 20.4, 20.3 (4 × CO*C*H$_3$). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 569.0805:571.0775:573.0745. Found: 569.0811:571.0789: 573.0771.

3-*O*-Acetyl-4-bromo-4-deoxy-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-glucopyranoside (24). Treatment of **21** (0.36 g, 0.33 mmol) as described above gave, after flash chromatography (ethyl acetate-hexane, 2:1), **24** (0.15 g, 76%): mp 114–115°C (ether-hexane); $[\alpha]_D$ + 6.7° (*c* 1.12, $CHCl_3$); ^{1}H NMR δ 1.98, 2.03, 2.06, 2.20 (s, 12H, 4 × CH_3), 3.46–3.73 (m, 4H, H-1′a,b and H-6′a,b), 3.83 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 10.2 Hz, H-4), 4.08–4.46 (m, 5H, H-4′, 5, 5′ and H-6a,b), 4.74 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.2 Hz, H-2), 5.41 (d, 1H, $J_{3',4'}$ = 9.8 Hz, H-3′), 5.42 (t, 1H, H-3) and 5.59 (d, 1H, H-1). ^{13}C NMR δ 170.6, 170.5, 170.2, 169.5 (4 × *C*OCH$_3$), 104.1 (C-2′), 89.7 (C-1), 83.7 (C-5′), 78.9 (C-3′), 71.0, 70.8, 70.5 (C-2, 3, 5), 64.2, 62.3, 59.1 (C-1′, 6, 6′), 54.9 (C-4), 42.6 (C-4′) and 20.7, 20.6, 20.5, 20.4 (4 × CO*C*H$_3$). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 613.0300:615.0270:617.0250. Found: 613.0281:615.0268:617.0260.

3-*O*-Acetyl-4-deoxy-4-iodo-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-glucopyranoside (25). Treatment of **22** (0.42 g, 0.37 mmol) as above gave, after flash chromatography (ethyl acetate-hexane, 1:1), **25** (0.18 g, 75%) as a colourless syrup; $[\alpha]_D$ + 5.9° (*c* 0.76, $CHCl_3$); ^{1}H NMR δ 1.99, 2.03, 2.06, 2.20 (s, 12H, 4 × CH_3), 3.45–3.90 (m, 5H, H-4, H-1′a,b and H-6′a,b), 4.17–4.44 (m, 5H, H-4′, 5, 5′ and H-6a,b), 4.75 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.2 Hz, H-2), 5.40 (d, 1H, $J_{3',4'}$ = 10.4 Hz, H-3′), 5.41 (t, 1H, $J_{3,4}$ = 10.2 Hz, H-3) and 5.58 (d, 1H, H-1). ^{13}C NMR δ 170.7, 170.4, 170.1, 169.5 (4 × *C*OCH$_3$), 104.3 (C-2′), 89.5 (C-1), 85.4 (C-5′), 80.5 (C-3′), 71.1, 70.8, 70.5 (C-2, 3, 5), 64.3, 62.2, 58.7 (C-1′, 6, 6′), 54.9 (C-4), 20.7, 20.6, 20.5, 20.4 (4 × CO*C*H$_3$) and 16.2 (C-4′). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 661.0161:663.0131. Found: 661.0164:663.0105.

3-*O*-Acetyl-1,4,6-trichloro-1,4,6-trideoxy-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-glucopyranoside (26). To a stirred solution of **23** (0.13 g, 0.25 mmol) and triphenylphosphine (0.57 g, 2.17 mmol) in pyridine (10 mL) at 0°C was added CCl_4 (0.35 mL, 2.27 mmol) drop-wise under an argon atmosphere. The reaction mixture was stirred at 0°C for 0.5 h, then at room temperature for a further 0.5 h, before being heated at about 85°C for 2 h. When TLC (ethyl acetate-hexane, 1:2) showed that all the starting material had reacted, the reaction mixture was diluted with dichloromethane and then washed with dil HCl (10%), satd aq $NaHCO_3$ and brine;

dried (Na_2SO_4), filtered and concentrated. Flash column chromatography (ethyl acetate-hexane, 1:3) gave **26** (0.13 g, 92%) as a colourless syrup; $[\alpha]_D$ + 18° (*c* 2.67, $CHCl_3$); ^{1}H NMR δ 2.05, 2.10, 2.13, 2.24 (s, 12H, 4 × CH_3), 3.61–3.89 (m, 5H, H-4, H-1′a,b and H-6′a,b), 4.23–4.54 (m, 5H, H-4′, 5, 5′ and H-6a,b), 4.85 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.1 Hz, H-2), 5.45 (t, 1H, $J_{3,4}$ = 10.1 Hz, H-3), 5.64 (d, 1H, $J_{3',4'}$ = 8.4 Hz, H-3′) and 5.66 (d, 1H, H-1). ^{13}C NMR δ 170.1, 169.6, 169.4, 169.3 (4 × *C*OCH$_3$), 102.7 (C-2′), 89.4 (C-1), 82.4 (C-5′), 78.1 (C-3′), 70.7, 70.6, 70.2 (C-2, 3, 5), 62.8 (C-6), 56.1, 54.9 (C-4, 4′), 46.1, 42.3 (C-1′, 6′) and 20.5, 20.3, 20.2, 20.1 (CO*C*H$_3$). HRMS-ESI (positive mode): calcd for [M + Na]$^+$ 605.0127:607.0097:609.0068. Found: 605.0129:607.0110:609.0082.

3-*O*-Acetyl-4-bromo-1,6-dichloro-1,4,6-trideoxy-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-glucopyranoside (27). Treatment of **24** (0.15 g, 0.26 mmol) as for **26**, gave after column chromatography (ethyl acetate-hexane, 1:3) **27** (0.14 g, 88%) as a colourless syrup; $[\alpha]_D$ + 22° (*c* 1.62, $CHCl_3$); ^{1}H NMR δ 1.99, 2.03, 2.07, 2.17 (s, 12H, 4 × CH_3), 3.53–3.84 (m, 5H, H-4, H-1′a,b and H-6′a,b), 4.16–4.45 (m, 5H, H-4′, 5, 5′ and H-6a,b), 4.78 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.1 Hz, H-2), 5.39 (t, 1H, $J_{3,4}$ = 10.1 Hz, H-3), 5.60 (d, 1H, H-1) and 5.64 (d, 1H, $J_{3',4'}$ = 9.1 Hz, H-3′). ^{13}C NMR δ 170.3, 169.8, 169.6, 169.5 (4 × *C*OCH$_3$), 103.1 (C-2′), 89.7 (C-1), 82.8 (C-5′), 78.7 (C-3′), 70.9, 70.8, 70.5 (C-2, 3, 5), 63.0 (C-6), 55.1 (C-4), 44.2 (C-4′), 46.3, 42.4 (C-1′, 6′) and 20.8, 20.6, 20.5, 20.3 (4 x CO*C*H$_3$). HRMS-ESI (positive mode): calcd for [M + Na]$^+$ 648.9622:650.9602:652.9572:654.9543. Found: 648.9632:650.9601:652.9581:654.9558.

3-*O*-Acetyl-1,6-dichloro-1,4,6-trideoxy-4-iodo-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-glucopyranoside (28). Compound **25** (0.16 g, 0.24 mmol) was treated with triphenylphosphine (0.55 g, 2.10 mmol) and CCl_4 (0.32 mL, 2.08 mmol) as described for **26** gave, after column chromatography (ethyl acetate-hexane, 1:3), **28** (0.15 g, 89%): mp 62–64°C (ether-hexane); $[\alpha]_D$ + 31° (*c* 0.23, $CHCl_3$); ^{1}H NMR δ 1.98, 2.03, 2.08, 2.17 (s, 12H, 4 × CH_3), 3.51–3.86 (m, 5H, H-4, H-1′a,b and H-6′a,b), 4.16–4.45 (m, 5H, H-4′, 5, 5′ and H-6a,b), 4.78 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.1 Hz, H-2), 5.38 (t, 1H, $J_{3,4}$ = 10.1 Hz, H-3) and 5.59–5.64 (m, 2H, H-1, 3′). ^{13}C NMR δ 170.3, 169.7, 169.6, 169.5 (4 × *C*OCH$_3$), 103.3 (C-2′), 89.7 (C-1), 84.2 (C-5′), 80.3 (C-3′), 70.8, 70.5 (C-2, 3, 5), 63.0 (C-6), 55.1 (C-4), 46.2, 42.3 (C-1′, 6′), 20.9, 20.6, 20.5, 20.3 (4 × CO*C*H$_3$) and 17.3 (C-4′). HRMS-ESI (positive mode): calcd for [M + Na]$^+$ 696.9483: 698.9453. Found: 696.9475: 698.9453.

1,4,6-Trichloro-1,4,6-trideoxy-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-glucopyranoside (29). A solution of **26** (0.13 g, 0.22 mmol) in methanol was treated with methanolic NaOMe at pH ∼9 for 1 h. The reaction was monitored by TLC (MeOH-$CHCl_3$, 3:17). The mixture was neutralized using Amberlite IR120 (H^+) ion exchange resin, filtered and concentrated to afford 29 (0.089 g, 94%) as a colourless syrup; $[\alpha]_D$ + 41° (*c* 0.25, H_2O); ^{1}H NMR (D_2O) δ 4.14 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 9.7 Hz, H-2), 4.29–4.51 (m, 8H, H-1′a,b, H-3, 4, H-6a,b and H-6′a,b), 4.64–4.72 (m, 2H, H-4′,5), 4.83–4.90 (m, 1H, H-5′), 5.09 (d, 1H, $J_{3',4'}$ = 9.7 Hz, H-3′) and 6.03 (d, 1H, H-1). ^{13}C NMR (D_2O) δ 104.1 (C-2′), 93.6 (C-1), 82.5 (C-5′), 78.3 (C-3′),

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73.6, 73.1, 72.1 (C-2, 3, 5), 61.1 (C-6), 59.5, 58.5 (C-4, 4′) and 44.5, 43.9 (C-1′, 6′). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 436.9704:438.9675: 440.9645:442.9616:444.9586. Found: 436.9709:438.9687:440.9648:442.9594: 444.9583.

4-Bromo-1,6-dichloro-1,4,6-trideoxy-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-glucopyranoside (30). Treatment of **27** (0.11 g, 0.17mmol) as for 29 gave 30 as a colourless syrup (0.072 g, 91%); $[\alpha]_D$ + 40° (*c* 0.27, H_2O); ^1H NMR (D_2O) δ 4.12 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 9.8 Hz, H-2), 4.27–4.52 (m, 8H, H-1′a,b, H-3, 4, H-6a,b and H-6′a,b), 4.61–4.68 (m, 2H, H-4′, 5), 4.92–4.99 (m, 1H, H-5′), 5.13 (d, 1H, $J_{3',4'}$ = 10.1 Hz, H-3′) and 6.02 (d, 1H, H-1). ^{13}C NMR (D_2O) δ 104.1 (C-2′), 93.6 (C-1), 82.9 (C-5′), 78.7 (C-3′), 73.6, 73.1, 72.1 (C-2, 3, 5), 61.1 (C-6), 58.5 (C-4), 48.3 (C-4′) and 44.4, 43.9 (C-1′, 6′). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 480.9199:482.9179:484.9140:486.9120: 488.9090. Found: 480.9191:482.9180: 484.9138:486.9143: 488.9118.

1,6-Dichloro-1,4,6-trideoxy-4-iodo-β-D-fructofuranosyl 4-chloro-4-deoxy-α-D-glucopyranoside (31). Deacetylation of **28** (0.14 g, 0.21mmol) as for 29, gave 31 as a colourless syrup (0.092, 88%); $[\alpha]_D$ + 32° (*c* 0.32, H_2O); ^1H NMR (D_2O) δ 4.13 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 9.8 Hz, H-2), 4.28–4.68 (m, 10H, H-1′a,b, H-3, 4, 4′, 5, H-6a,b and H-6′a,b), 5.00–5.06 (m, 1H, H-5′), 5.12 (d, 1H, $J_{3',4'}$ = 10.4 Hz, H-3′) and 6.03 (d, 1H, H-1). ^{13}C NMR (D_2O) δ 104.0 (C-2′), 93.5 (C-1), 84.4 (C-5′), 80.3 (C-3′), 73.6, 73.1, 72.1 (C-2, 3, 5), 61.1 (C-6), 58.5 (C-4), 44.3, 43.9 (C-1′, 6′) and 22.2 (C-4′). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 528.9060:530.9031:532.9001. Found: 528.9088:530.9046:532.8986.

3-*O*-Acetyl-4-bromo-4-deoxy-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-O-acetyl-4-deoxy-4-fluoro-α-D-galactopyranoside (32). A solution of **15** (0.68 g, 0.64 mmol) in CH_2Cl_2-pyridine (15:1, 32 mL) at − 78°C was treated with trifluoromethanesulfonic anhydride (0.20 mL, 1.22 mmol) as described above, and worked-up in the usual manner. To a thoroughly dried crude product in CH_2Cl_2 (20 mL) was added TASF (0.72 g, 2.61 mmol). The mixture was heated to about 45 °C for 0.5 h when TLC (ether-hexane, 1:1) indicated that all starting material had been consumed. The reaction mixture was washed successively with satd $NaHCO_3$ and brine; dried (Na_2SO_4), filtered and concentrated, and chromatographed (ether-hexane, 1:1) to give **32** (0.49 g, 72%): mp 94–96°C (ether-hexane); $[\alpha]_D$ + 36° (*c* 0.82, $CHCl_3$); ^1H NMR δ 2.21, 2.45, 2.56, 2.61 (s, 12H, 4 × CH_3), 3.60–4.00 (m, 4H, H-1′a,b and H-6′a,b), 4.54–4.83 (m, 4H, H-5, 5′ and H-6a,b), 4.90 (t, 1H, $J_{3',4'}$ = $J_{4',5'}$ = 10.0 Hz, H-4′), 5.35 (dd, 1H, $J_{3,4}$ = 1.7 Hz, $J_{4,F}$ 50.9 Hz, H-4), 5.46–5.61 (m, 2H, H-2, 3), 6.24 (d, 1H, $J_{1,2}$ = 3.1 Hz, H-1), 6.49 (d, 1H, H-3′) and 7.71–8.00 (m, 30H, Ar-H). ^{13}C NMR δ 170.3, 170.2, 169.2, 169.0 (4 × *C*OCH_3), 143.7, 143.6, 128.7–127.1 (Ar-C), 103.4 (C-2′), 88.6 (C-1), 87.2 (*C*Ph_3), 86.9 ($J_{4,F}$ = 185.2 Hz, C-4), 82.2 (C-5′), 78.1 (C-3′), 68.2 ($J_{3,F}$ = 17.1 Hz, C-3), 67.4 ($J_{5,F}$ = 18.2 Hz, C-5), 66.5 (C-2), 64.8, 62.3, 62.2 (C-1′, 6, 6′), 44.4 (C-4′) and 20.7, 20.5, 20.4 (CO*C*H_3). ^{19}F NMR δ -143.9 (dt, $J_{F,H-3}$ = 30.5 Hz, $J_{F,H-4}$ = 50.9 Hz, $J_{F,H-5}$ = 15.3 Hz). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1081.2786:1083.2766. Found: 1081.2770:1083.2788.

3-*O*-Acetyl-4-bromo-4-deoxy-1,6-di-*O*-trityl-β-D-fructofuranosyl 2,3,6-tri-O-acetyl-4-deoxy-4-iodo-α-D-galactopyranoside (33). Compound **15** (0.89 g, 0.84 mmol) was triflated as above and treated with KI (0.45 g, 2.71 mmol) in acetone (25 mL) at room temperature for ~ 12 h, to give, after flash column chromatography (ether-hexane, 1:1), **33** (0.70 g, 71%): mp 99–101°C (ether-hexane); $[\alpha]_D$ + 50° (*c* 1.34, $CHCl_3$); ^{1}H NMR δ 1.59, 1.85, 1.98, 2.03 (s, 12H, 4 × CH_3), 3.01–3.09 (2 × d, 2H, $J_{1'a,1'b}$ = 9.75 Hz, H-1′a,b), 3.30–3.41 (m, 2H, H-6′a,b), 3.53–3.97 (m, 3H, H-5 and H-6a,b), 4.15–4.32 (m, 3H, H-3, 4′, 5), 4.56 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 2.8 Hz, H-4), 4.97 (dd, 1H, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 10.4 Hz, H-2), 5.48 (d, 1H, H-1), 5.91 (d, 1H, $J_{3',4'}$ = 9.7 Hz, H-3′) and 7.14–7.41 (m, 30H, Ar-H). ^{13}C NMR δ 170.1, 169.9, 169.2, 169.0 (4°*C*OCH_3), 143.6, 143.5, 128.6–127.0 (Ar-C), 103.4 (C-2′), 88.7 (C-1), 87.1 87.0 (*C*Ph_3), 82.3 (C-5′), 77.8 (C-3′), 69.1, 68.2, 66.6 (C-2, 3, 5), 68.5, 64.5, 62.8 (C-1′, 6, 6′), 44.4 (C-4′), 35.1 (C-4) and 20.8, 20.7, 20.4, 20.3 (4 × CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1189.1847:1191.1827. Found: 1189. 1883:1191.1872.

3-*O*-Acetyl-4-bromo-4-deoxy-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-deoxy-4-fluoro-α-D-galactopyranoside (34). Treatment of **32** (0.38 g, 0.36 mmol) with ice-cold CH_2Cl_2-AcOH (1:1, 20 mL) and conc HCl (0.07 mL) as described above, gave after flash chromatography (ethyl acetate-hexane, 1:1), **34** (0.17 g, 82%) as a colourless syrup; $[\alpha]_D$ + 27° (*c* 1.01, $CHCl_3$); ^{1}H NMR δ 2.08, 2.11, 2.13, 2.23 (s, 12H, 4 × CH_3), 3.54–3.97 (m, 4H, H-1′a,b and H-6′a,b), 4.11–4.41 (m, 4H, H-5, 5′ and H-6a,b), 4.49 (t, 1H, $J_{3',4'}$ = $J_{4',5'}$ = 10.0 Hz, H-4′), 4.93 (dd, 1H, $J_{3,4}$ = 2.1 Hz, $J_{4,F}$ 50.9 Hz, H-4), 5.17–5.34 (m, 2H, H-2, 3), 5.47 (d, 1H, H-3′) and 5.73 (d, 1H, $J_{1,2}$ = 2.8 Hz, H-1). ^{13}C NMR δ 170.5, 170.4, 170.2, 170.1 (4 × *C*OCH_3), 103.8 (C-2′), 89.8 (C-1), 86.8 ($J_{4,F}$ = 185.2 Hz, C-4), 83.4 (C-5′), 78.6 (C-3′), 67.7 ($J_{3,F}$ = 18.2 Hz, C-3), 67.3 ($J_{5,F}$ = 17.6 Hz, C-5), 67.1 (C-2), 63.8, 59.3 (C-1′, 6′), 61.5 ($J_{6,F}$ = 6.5 Hz, C-6), 42.6 (C-4′) and 20.6, 20.6, 20.6, 20.3 (4 × CO*C*H_3). ^{19}F NMR δ -143.27 (dt, $J_{F,H-3}$ = 30.5 Hz, $J_{F,H-4}$ = 53.4 Hz, $J_{F,H-5}$ = 22.9 Hz). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 597.0595:599.0575. Found: 597.0622:599.0578.

3-*O*-Acetyl-4-bromo-4-deoxy-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-deoxy-4-iodo-α-D-galactopyranoside (35). Treatment of **33** (0.65 g, 0.56 mmol) as described above, gave after flash chromatography (ethyl acetate-hexane, 1:1), **35** (0.32 g, 85%) as a colourless syrup; $[\alpha]_D$ + 37° (*c* 1.05, $CHCl_3$); ^{1}H NMR δ 2.09, 2.11, 2.13, 2.23 (s, 12H, 4 × CH_3), 3.53–3.81 (m, 4H, H-1′a,b and H-6′a,b), 3.92–4.32 (m, 4H, H-5, 5′and H-6a,b), 4.46–4.53 (m, 2H, H-3, 4′), 4.70 (dd, 1H, $J_{3,4}$ = 4.0 Hz, $J_{4,5}$ = 1.5 Hz, H-4), 5.22 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.6 Hz, H-2), 5.47 (d, 1H, $J_{3',4'}$ = 9.7 Hz, H-3′) and 5.67 (d, 1H,, H-1). ^{13}C NMR δ 170.4, 170.3, 170.2, 169.9 (4 × *C*OCH_3), 103.8 (C-2′), 89.8 (C-1), 83.5 (C-5′), 78.4 (C-3′), 69.8, 67.5, 67.0 (C-2, 3, 5), 67.9, 64.0, 59.6 (C-1′, 6, 6′), 42.6 (C-4′), 34.9 (C-4) and 20.8, 20.7, 20.6, 20.4 (4 × CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 704.9656:706.9636. Found: 704.9667:706.9656.

3-*O*-Acetyl-1,4,6-tribromo-1,4,6-trideoxy-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-deoxy-4-fluoro-α-D-galactopyranoside (36). Compound **34** (0.18 g, 0.31 mmol) was triflated as described above and treated with LiBr (0.60 g) in acetone (20 mL) at

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45°C overnight. Column chromatography (ether-hexane, 1:1) gave **36** (0.13 g, 59%) as a colourless syrup; $[\alpha]_D$ + 46° (*c* 0.94, $CHCl_3$); ^1H NMR δ 2.02, 2.05, 2.05, 2.13 (s, 12H, 4 × CH_3), 3.46 (d, 1H, $J_{1'a,1'b}$ = 11.0 Hz, H-1′a), 3.54 (d, 1H, H-1′b), 3.56 (dd, 1H, $J_{5'6'a}$ = 6.3 Hz, $J_{6'a,6'b}$ = 11.5 Hz, H-6′a), 3.64 (dd, 1H, $J_{5',6'b}$ = 3.8 Hz, H-6′b), 4.13–4.38 (m, 5H, H-4′, 5, 5′, 6a,b), 4.85 (dd, 1H, $J_{3,4}$ = 2.1 Hz, $J_{4,F}$ = 49.5 Hz, H-4), 5.10-5.23 (m, 2H, H-2, 3), 5.63 (d, 1H, $J_{1,2}$ = 3.1 Hz, H-1) and 5.69 (d, 1H, $J_{3',4'}$ = 9.4 Hz, H-3′). ^{13}C NMR δ 170.3, 170.2, 169.7, 169.5 (4 × *C*OCH_3), 102.4 (C-2′), 90.2 (C-1), 86.9 ($J_{4,F}$ = 185.2 Hz, C-4), 82.5 (C-5′), 79.1 (C-3′), 68.0 ($J_{3,F}$ = 18.2 Hz, C-3), 67.6 ($J_{5,F}$ = 17.6 Hz, C-5), 66.7 (C-2), 62.3 ($J_{6,F}$ = 6.5 Hz, C-6), 45.7 (C-4′), 34.0, 30.0 (C-1′,6′) and 20.8, 20.7, 20.6, 20.3 (4 × CO*C*H_3). ^{19}F NMR δ -142.9 (dt, $J_{F,H-3}$ = 30.5 Hz, $J_{F,H-4}$ = 53.4 Hz, $J_{F,H-5}$ = 30.5 Hz). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 720.8907:722.8887:724.8867:726.8847. Found: 720.8888:722.8891:724.8855:726.8861.

3-*O*-Acetyl-1,4,6-tribromo-1,4,6-trideoxy-β-D-fructofuranosyl 2,3,6-tri-*O*-acetyl-4-deoxy-4-iodo-α-D-galactopyranoside (37). Treatment of **35** (0.34 g, 0.50 mmol) as for **36** gave, after column chromatography (ether-hexane, 1:1), **37** (0.21 g, 52%) as a colourless syrup; $[\alpha]_D$ + 54° (*c* 1.76, $CHCl_3$); ^1H NMR δ 2.02, 2.06, 2.06, 2.13 (s, 12H, 4 × CH_3), 3.43 (d, 1H, $J_{1'a,1'b}$ = 11.0 Hz, H-1′a), 3.52 (d, 1H, H-1′b), 3.54 (dd, 1H, $J_{5',6'a}$ = 6.3 Hz, $J_{6'a,6'b}$ = 11.1 Hz, H-6′a), 3.63 (dd, 1H, $J_{5',6'b}$ = 3.8 Hz, H-6′b), 3.74–3.78 (m, 1H, H-5), 4.06–4.08 (m, 2H, H-6a,b), 4.21 (t, 1H, $J_{3',4'}$ = $J_{4',5'}$ = 9.4 Hz, H-4′), 4.32–4.43 (m, 2H, H-3, 5′), 4.63 (dd, 1H, $J_{3,4}$ = 3.8 $J_{4,5}$ = 1.4 Hz, H-4), 5.19 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.4 Hz, H-2), 5.55 (d, 1H, H-1), 5.68 (d, 1H, H-3′). ^{13}C NMR δ 170.1, 169.8, 169.6, 169.4 (4 × *C*OCH_3), 102.4 (C-2′), 90.2 (C-1), 82.6 (C-5′), 78.9 (C-3′), 68.7 (C-6), 69.3, 67.7, 67.3 (C-2, 3, 5), 45.7 (C-4′), 34.2 (C-4), 33.8, 29.9 (C-1′, 6′) and 20.9, 20.8, 20.7, 20.3 (4 × CO*C*H_3). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 828.7968:830.7948:832.7928:834.7908. Found: 828.7962:830.7951:832.7937:834.7944.

1,4,6-Tribromo-1,4,6-trideoxy-β-D-fructofuranosyl 4-deoxy-4-fluoro-α-D-galactopyranoside (38). Deacetylation of **36** (0.10 g, 0.14 mmol) in methanolic-NaOMe (∼ pH 9) at 0°C gave **38** (0.065 g, 86%) as a colourless syrup; $[\alpha]_D$ + 45° (*c* 2.01, MeOH); ^1H NMR (D_2O) δ 4.17–4.56 (m, 8H, H-2, 3, 1′a,b, 6′a,b and 6a,b), 4.60 (t, 1H, $J_{3',4'}$ = $J_{4',5'}$ = 10.0 Hz, H-4′), 4.75 (m, 1H, $J_{F,5}$ = 31.0 Hz, H-5), 4.94–5.01 (m, 1H, H-5′), 5.19 (d, 1H, 10.0 Hz, H-3′), 5.42 (d, 1H, $J_{3,4}$ = 2.1 Hz, $J_{F,4}$ = 50.9 Hz, H-4), 6.05 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1). ^{13}C NMR (D_2O) δ 103.5 (C-2′), 93.5 (C-1), 90.9 ($J_{F,4}$ = 177.6 Hz, C-4), 82.8 (C-5′), 79.4 (C-3′), 71.3 ($J_{F,3}$ = 17.6 Hz, C-3), 68.4 ($J_{F,5}$ = 14.7 Hz, C-5), 68.3 ($J_{F,2}$ = 2.9 Hz, C-2), 60.6 ($J_{F,6}$ = 5.9 Hz, C-6), 49.6 (C-4′), 32.1, 32.0 (C-1′, 6′). ^{19}F NMR (D_2O) δ -144.3 (dt, $J_{F,H-4}$ = 45.8 Hz, $J_{F,H-3}$ = 30.5 Hz, $J_{F,H-5}$ = 30.5 Hz). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 552.8485:554.8465:556.8445:558.8424. Found: 552.8476:554.8474:556.8457:558.8439.

1,4,6-Tribromo-1,4,6-trideoxy-β-D-fructofuranosyl 4-deoxy-4-iodo-α-D-galactopyranoside (39). Compound **37** (0.18 g, 0.22 mmol) was treated with methanolic-NaOMe (∼pH 9) at 0°C to give **39** (0.11 g, 77%) as a colourless syrup; $[\alpha]_D$ + 49° (*c* 0.96, MeOH); ^1H NMR (D_2O) δ 3.79 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 4.09–4.34 (m, 7H, H-1′a,b, 5, 6a,b, 6′a,b), 4.40 (dd, 1H, $J_{3,4}$ = 4.0 Hz, H-3), 4.67 (t,

1H, $J_{3',4'} = J_{4',5'} = 9.7$ Hz, H-4′), 4.94–5.01 (m, 1H, H-5′), 5.13 (d, 1H, H-4), 5.18 (d, 1H, H-3′) and 5.97 (d, 1H, H-1). ^{13}C NMR (D_2O) δ 103.5 (C-2′), 93.4 (C-1), 83.0 (C-5′), 79.2 (C-3′), 71.3, 71.1 (C-2, 3), 68.0 (C-5), 66.8 (C-6), 49.5 (C-4′), 42.6 (C-4) and 32.3, 32.2 (C-1′, 6′). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 660.7545:662.7525:664.7505:666.7485. Found: 660.7563:662.7525:664.7496:666.7510.

3-*O*-Acetyl-4-bromo-4-deoxy-1,6-di-*O*-trityl-β-D-tagatofuranosyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (41). To a solution of 1,6-di-*O*-trityl-β-D-fructofuranosyl 6-*O*-trityl-α-D-glucopyranoside (7.35 g, 6.88 mmol) in toluene (150 mL) was added *n*-dibutyltin oxide (1.71 g, 6.87 mmol). The reaction mixture was heated under azeotropic distillation overnight. The reaction mixture was concentrated and dried under vacuum for 2 h. The crude product was dissolved in CH_2Cl_2 (100 mL) and pyridine (7 mL) and cooled to $\sim -$ 60°C. Trifluoromethanesulfonic anhydride (2.2 mL, 13.4 mmol) was added drop-wise to the stirred mixture under argon atmosphere. The temperature was then allowed to rise to 0°C, stirred for ~10 min, worked-up in the usual manner, and chromatographed (ethyl acetate-hexane, 1:1).

A solution of the triflate in acetone (50 mL) was stirred with LiBr (0.44 g) at room temperature overnight, and worked-up in the usual manner. The crude syrupy product was then acetylated (acetic anhydride/pyridine). Column chromatography (ethyl acetate-hexane, 1:2) gave **41** as a yellowish syrup (2.2 g, 25%); $[\alpha]_D$ + 72° (*c* 1.20, $CHCl_3$); ^{1}H NMR δ 1.54, 1.71, 1.89, (s, 12H, 4 × CH_3), 2.69 (dd, 1H, $J_{5,6a} = 2.0$ Hz, $J_{6a,6b} = 10.0$ Hz, H-6a), 3.18 (dd, 1H, $J_{5,6b} = 2.0$ Hz, H-6b), 3.25 (s, 2H, H-1′a,b), 3.32 (dd, 1H, $J_{5'6'a} = 4.9$ Hz, $J_{6'a,6'b} = 10.1$ Hz, H-6′a), 3.40 (dd, 1H, $J_{5'6'b} = 6.6$ Hz, H-6′b), 4.01–4.04 (m, 1H, H-5), 4.19–4.25 (m, 1H, H-5′), 4.52 (t, 1H, $J_{3',4'} = J_{4',5'} = 5.0$ Hz, H-4′), 4.80 (dd, 1H, $J_{1,2} = 3.5$ Hz, $J_{2,3} = 9.7$ Hz, H-2), 5.19–5.30 (m, 3H, H-3, 3′, 4), 5.44 (d, 1H, H-1) and 7.08–7.33 (m, 45H, Ar-H). ^{13}C NMR δ170.3, 169.9, 169.8, 169.0 (4 × *C*OCH$_3$), 143.7, 143.2, 128.7, 128.0, 127.8, 127.3, 126.8 (Ar-C), 104.7 (C-2′), 90.4 (C-1), 87.4, 87.1, 86.1 (*C*Ph$_3$), 78.7 (C-5′), 73.0 (C-3′), 70.8 (C-3), 70.6 (C-2), 69.4 (C-5), 68.6 (C-4), 65.4 (C-6′), 64.7 (C-1′), 60.7 (C-6), 50.0 (C-4′) and 20.8, 20.6, 20.5, 20.4 (4 x CO*C*H$_3$). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1321.3925:1323.3905. Found: 1321.3900: 1323.3927.

3-*O*-Acetyl-4-deoxy-4-iodo-1,6-di-*O*-trityl-β-D-tagatofuranosyl 2,3,4-tri-*O*-acetyl-6-*O*-trityl-α-D-glucopyranoside (42). The 4′-*O*-triflate of **40** as prepared for **41** was treated with KI (1.0 g) in acetone (50 mL) at room temperature for ~12 h, and then acetylated to give **42** (2.4 g, 26%): mp 120–122 °C (methanol); $[\alpha]_D$ + 57° (*c* 0.78, $CHCl_3$); ^{1}H NMR δ 1.47, 1.83, 1.90, 1.94 (s, 12H, 4 × CH_3), 2.69 (dd, 1H, $J_{5,6a} = 2.1$ Hz, $J_{6a,6b} = 10.1$ Hz, H-6a), 3.17–3.46 (m, 5H, H-1′a,b, H-6′a,b and H-6a,b), 3.80–3.86 (m, 1H, H-5′), 4.06–4.09 (m, 1H, H-5), 4.34 (t, 1H, $J_{3',4'} = J_{4',5'} = 5.6$ Hz, H-4′), 4.81 (dd, 1H, $J_{1,2} = 3.8$ Hz, $J_{2,3} = 9.8$ Hz, H-2), 4.95 (d, 1H, H-3′), 5,20–5.34 (m, 2H, H-3, 4), 5.39 (d, 1H, H-1) and 7.05–7.37 (m, 45H, Ar-H). ^{13}C NMR δ170.3, 170.0, 169.5, 168.9 (4 × *C*OCH$_3$), 143.8, 143.7, 128.8, 128.6, 127.7, 127.0, 126.8 (Ar-C), 105.1 (C-2′), 91.0 (C-1), 87.5, 87.0, 86.0 (*C*Ph$_3$), 78.4 (C-5′), 73.5 (C-3′), 70.7, 70.6 (C-2, 3), 69.6 (C-5), 68.8 (C-6′), 68.4 (C-4), 63.8 (C-1′), 60.5 (C-6), 26.4 (C-4′) and 20.8, 20.7, 20.5, 20.4 (4 × CO*C*H$_3$). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 1369.3786. Found: 1369.3812.

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3-*O*-Acetyl-4-bromo-4-deoxy-β-D-tagatofuranosyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (43). Detritylation of **41** (2.62 g, 2.02 mmol) as described above afforded, after chromatography (ethyl acetate-hexane, 5:1), **43** as a colourless syrup (0.71 g, 61%); $[\alpha]_D$ + 72° (*c* 0.66, $CHCl_3$); ^{1}H NMR δ 2.01, 2.06, 2.07, 2.27 (s, 12H, 4 × CH_3), 3.56–3.93 (m, 6H, H-1′a,b, H-6a,b and H-6′a,b), 4.18–4.23 (m, 1H, H-5), 4.36–4.42 (m, 1H, H-5′), 4.67 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 6.0 Hz, H-4′), 4.86 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 5.00 (t, 1H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4), 5.39 (d, 1H, H-3′), 5.46 (t, 1H, H-3), 5.64 (d, 1H, H-1). ^{13}C NMR δ 170.4, 170.2, 170.0, 169.9 (4 × *C*OCH$_3$), 105.7 (C-2′), 90.5 (C-1), 78.7 (C-5′), 72.9 (C-3′), 71.5, 70.6, 69.4, 68.7 (C-2, 3, 4, 5), 64.1, 63.7, 61.2 (C-6, 1′, 6′), 45.8 (C-4′) and 20.6, 20.5 (4 × CO*C*H$_3$). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 595.0638:597.0618. Found: 595.0645:597.0624.

3-*O*-Acetyl-4-deoxy-4-iodo-β-D-tagatofuranosyl 2,3,4-tri-*O*-acetyl-α-D-glucopyranoside (44). Detritylation of **42** (2.27 g, 1.69 mmol) as described above, gave after flash column chromatography (ethyl acetate-hexane, 5:1), **44** as a yellowish syrup (0.73 g, 70%); $[\alpha]_D$ + 71° (*c* 1.53, $CHCl_3$); ^{1}H NMR δ 1.95, 1.98, 2.01, 2.21 (s, 12H, 4 × CH_3), 3.40–3.59 (m, 2H, H-6a,b), 3.64–3.79 (m, 4H, H-1′a,b and H-6′a,b), 4.07–4.10 (m, 1H, H-5), 4.16–4.22 (m, 1H, H-5′), 4.55 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 6.6 Hz, H-4′), 4.78 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 4.96 (t, 1H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4), 5.17 (d, 1H, H-3′), 5.36 (t, 1H, H-3), 5.58 (d, 1H, H-1). ^{13}C NMR δ170.6, 170.0, 169.9, 169.6 (4 × *C*OCH$_3$), 105.7 (C-2′), 90.7 (C-1), 81.7 (C-5′), 73.8 (C-3′), 71.6, 70.4, 69.3, 68.6 (C-2, 3, 4, 5), 66.6, 63.8, 61.0 (C-1′, 6, 6′), 20.6, 20.5 (4 × CO*C*H$_3$) and 20.3 (C-4′). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 643.0500. Found: 643.0499.

3-*O*-Acetyl-4-bromo-4-deoxy-β-D-tagatofuranosyl 2,3,6-tri-*O*-acetyl-α-D-glucopyranoside (45). Compound **43** (0.46 g, 0.80 mmol) in MIBK (20 mL) was treated with AcOH (0.45 mL) as for **14**, to give, after flash column chromatography (ethyl acetate-hexane, 5:1), **45** as a colourless syrup (0.30 g, 65%); $[\alpha]_D$ + 60° (*c* 0.72, $CHCl_3$); ^{1}H NMR δ 2.02, 2.03, 2.07, 2.17 (s, 12H, 4 × CH_3), 3.42–3.56 (m, 3H, H-1′a,b and H-4), 3.73–3.86 (m, 2H, H-6′a,b), 4.13–4.18 (m, 1H, H-5), 4.26 (dd, 1H, $J_{5,6a}$ = 2.1 Hz, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.31–4.36 (m, 1H, H-5′), 4.39 (dd, 1H, $J_{5,6b}$ = 3.8 Hz, H-6b), 4.63 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 6.0 Hz, H-4′), 4.76 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 5.20 (t, 1H, $J_{3,4}$ = 10.0 Hz, H-3), 5.32 (d, 1H, H-3′), 5.48 (d, 1H, H-1). ^{13}C NMR δ 171.8, 171.5, 170.6, 169.9 (4 × *C*OCH$_3$), 105.6 (C-2′), 90.6 (C-1), 81.2 (C-5′), 72.7 (C-3′), 72.2, 71.4, 70.4, 68.8 (C-2, 3, 4, 5), 64.2, 64.1, 62.7 (C-6, 1′, 6′), 46.1 (C-4′), 20.8, 20.7, 20.7 (4 × CO*C*H$_3$). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 595.0638:597.0618. Found 595.0639:597.0629.

3-*O*-Acetyl-4-deoxy-4-iodo-β-D-tagatofuranosyl 2,3,6-tri-*O*-acetyl-α-D-glucopyranoside (46). Compound **44** (0.48 g, 0.774 mmol) was treated as for **14** to give, after chromatography (ethyl acetate-hexane, 5:1), **45** (0.38 g, 79%) as colourless syrup; $[\alpha]_D$ + 54° (*c* 1.05, $CHCl_3$); ^{1}H NMR δ 2.02, 2.03, 2.07, 2.18 (s, 12H, 4 × CH_3), 3.43 (d, 1H, $J_{1'a,1'b}$ = 12.2 Hz, H-1′a), 3.49 (t, 1H, $J_{3,4} = J_{4,5}$ = 10.0 Hz, H-4), 3.56 (d, 1H, H-1′b), 3.67 (dd, 1H, $J_{5',6'a}$ = 10.0 Hz, $J_{6'a,6'b}$ = 12.0 Hz, H-6′a), 3.79 (dd, 1H, $J_{5',6'b}$ = 3.0 Hz, H-6′b), 4.05–4.23 (m, 2H, H-5, 5′), 4.29 (dd, 1H, $J_{5,6a}$ = 2.1 Hz, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.40 (dd, 1H, $J_{5,6b}$ = 3.8 Hz, H-6b), 4.51 (t, 1H,

$J_{3',4'}$ = $J_{4',5'}$ = 6.0 Hz, H-4′), 4.75 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 5.15 (t, 1H, H-3), 5.20 (d, 1H, H-3′), 5.51 (d, 1H, H-1). ^{13}C NMR δ 171.7, 171.5, 170.7, 169.6 (4 × *C*OCH$_3$), 105.8 (C-2′), 90.8 (C-1), 81.8 (C-5′), 73.7 (C-3′), 72.2 (C-3), 71.7 (C-5), 70.3 (C-2), 68.7 (C-4), 66.4 (C-6′), 64.6 (C-1′), 62.5 (C-6), 20.9, 20.8, 20.7 (4 × CO*C*H$_3$) and 19.7 (C-4′). HRMS-ESI (positive mode): calcd for [M + Na]$^+$ 643.0500. Found 643.0493.

3-*O*-Acetyl-4-bromo-1,6-dichloro-1,4,6-trideoxy-β-D-tagatofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranoside (47). Compound **45** (0.16 g, 0.28 mmol) was triflated and reacted with LiCl (0.21 g) in acetone (15 mL), as described above, to give, after flash chromatography (ethyl acetate-hexane, 1:2), **47** (0.11 g, 63%) as a colourless syrup; [α]$_D$ + 82° (*c* 1.41, CHCl$_3$); ^{1}H NMR δ 2.02, 2.06, 2.16 (s, 12H, 4 × CH$_3$), 3.50–3.73 (m, 4H, H-1′a,b and H-6′a,b), 4.08–4.22 (m, 2H, H-6a,b), 4.29–4.35 (m, 1H, H-5′), 4.54 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ = 1.0 Hz, H-4), 4.60–4.64 (m, 1H, H-5), 4.81 (dd, 1H, $J_{3',4'}$ = 5.9 Hz, $J_{4',5'}$ 4.5 Hz, H-4′), 5.21 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.8 Hz, H-2), 5.28 (dd, 1H, H-3), 5.41 (d, 1H, H-3′) and 5.53 (d, 1H, H-1). ^{13}C NMR δ 170.2, 170.2, 169.9, 169.6 (4 × *C*OCH$_3$), 104.5 (C-2′), 91.3 (C-1), 80.3 (C-5′), 72.5 (C-3′), 68.1 (C-3), 67.8 (C-5), 67.4 (C-2), 62.9 (C-6), 59.2 (C-4), 50.0 (C-4′), 45.0 (C-1′), 44.2 (C-6′) and 20.8, 20.6 (4 × CO*C*H$_3$). HRMS-ESI (positive mode): calcd for [M + Na]$^+$ 648.9622:650.9592:652.9563:654.9543. Found: 648.9611:650.9595:652.9559:654.9548.

3-*O*-Acetyl-1,6-dichloro-1,4,6-trideoxy-4-iodo-β-D-tagatofuranosyl 2,3,6-tri-*O*-acetyl-4-chloro-4-deoxy-α-D-galactopyranoside (48). Compound **46** (0.26 g, 0.419 mmol) was treated with trifluoromethanesulfonic anhydride (0.40 mL, 2.44 mmol) and LiCl (0.25 g) in acetone (15 mL), to give, after column chromatography (ethyl acetate-hexane, 1:2), **48** (0.19 g, 67%); [α]$_D$ + 77° (*c* 0.82, CHCl$_3$); ^{1}H NMR δ 2.02, 2.02, 2.06, 2.15 (s, 12H, 4 × CH$_3$), 3.54–3.76 (m, 4H, H-6′a,b and H-1′a,b), 3.87–3.93 (m, 1H, H-5′), 4.10 (dd, 1H, $J_{5,6a}$ = 7.3 Hz, $J_{6a,6b}$ = 11.0 Hz, H-6a), 4.21 (dd, 1H, $J_{5,6b}$ = 6.0 Hz, H-6b), 4.54 (dd, 1H, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ = 1.4 Hz, H-4), 4.62–4.67 (m, 1H, H-5), 4.80 (t, 1H, $J_{3',4'}$ = $J_{4',5'}$ = 6.0 Hz, H-4′), 5.10 (d, 1H, H-3′), 5.19 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.8 Hz, H-2), 5.35 (dd, 1H, H-3) and 5.55 (d, 1H, H-1). ^{13}C NMR δ 170.2, 170.1, 169.9, 169.3 (4 × *C*OCH$_3$), 104.7 (C-2′), 91.5 (C-1), 80.1 (C-5′), 73.2 (C-3′), 68.1, 68.0, 67.4 (C-2, 3, 5), 62.6 (C-6), 59.1 (C-4), 48.5, 44.7 (C-1′, 6′), 27.6 (C-4′) and 20.8, 20.7 (4 × CO*C*H$_3$). HRMS-ESI (positive mode): calcd for [M + Na]$^+$ 696.9483:698.9453:700.9424:702.9394. Found: 696.9460:698.9424:700.9442: 702.9406.

4-Bromo-1,6-dichloro-1,4,6-trideoxy-β-D-tagatofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside (49). Deacetylation (MeOH-NaOMe, pH ~10) of **47** (0.091 g, 0.145 mmol), as described for **29** afforded **49** as a colourless syrup (0.0612 g, 92%); [α]$_D$ + 40° (*c* 2.87, MeOH); ^{1}H NMR (D$_2$O) δ 4.26–4.29 (m, 2H, H-6a,b), 4.38–4.46 (m, 4H, H-1′a,b and H-6′a,b), 4.49 (dd, 1H, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 4.47 (dd, 1H, $J_{3,4}$ = 3.5 Hz, H-3), 4.96–5.02 (m, 1H, H-5′), 5.07–5.13 (m, 2H, H-4, 5), 5.34 (d, 1H, $J_{3',4'}$ = 5.2 Hz, H-3′), 5.45 (dd, 1H, $J_{4',5'}$ = 3.8 Hz, H-4′) and 6.00 (d, 1H, H-1). ^{13}C NMR (D$_2$O) δ 104.8 (C-2′), 94.6 (C-1), 79.8 (C-5′), 73.9 (C-3′), 71.1, 68.7, 68.6 (C-2, 3, 5), 63.6 (C-4), 60.6 (C-6), 55.8 (C-4′), 45.9, 43.9 (C-1′, 6′). HRMS-ESI

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(positive mode): calcd for $[M + Na]^+$ 480.9200:482.9179:484.9150:486.9120. Found: 480.9204:482.9183:484.9148:486.9128.

1,6-Dichloro-1,4,6-trideoxy-4-iodo-β-D-tagatofuranosyl 4-chloro-4-deoxy-α-D-galactopyranoside (50). Deacetylation of **48** (0.18 g, 0.266 mmol) as described for **29** gave **50** as a yellowish syrup (0.12 g, 89%); $[\alpha]_D$ + 51° (*c* 4.26, MeOH); ^{1}H NMR (D_2O) δ 4.26–4.48 (m, 7H, H-1′a,b, 6′a,b, H-6a,b and H-5′), 4.50 (dd, 1H, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 4.85 (dd, 1H, $J_{3,4}$ = 3.5 Hz, H-3), 4.88 (d, 1H, $J_{3',4'}$ = 5.9 Hz, H-3′), 5.13–5.18 (m, 2H, H-4, 5), 5.48 (dd, 1H, $J_{4',5'}$ = 4.0 Hz, H-4′) and 6.01 (d, 1H, H-1). ^{13}C NMR (D_2O) δ 104.9 (C-2′), 94.9 (C-1), 78.9 (C-5′), 74.2 (C-3′), 71.4 (C-5), 68.8, 68.7 (C-2, 3), 63.7 (C-4), 60.6 (C-6), 50.2, 44.1 (C-1′, 6′) and 36.6 (C-4′). HRMS-ESI (positive mode): calcd for $[M + Na]^+$ 528.9060:530.9031:532.9001. Found: 528.9057:530.9045:532.9012.

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REFERENCES

1. Shallenberger, R.S.; Acree, T.E. Molecular theory of sweet taste. Nature **1967**, *216*, 480–482.
2. Kier, L.B. A molecular theory of sweet taste. J. Pharm. Sci. **1972**, *61*, 1394–1397.
3. Hough, L.; Phadnis, S.P.; Khan, R.; Jenner, M.R. Sweeteners. Br. Pat. 1 543 167, 1979.
4. Hough, L.; Phadnis, S.P.; Khan, R.; Jenner, M.R. Chloroderivatives of Sucrose. Br. Pat. 1 543 168, 1979.
5. Hough, L.; Khan, R. Intense sweeteners derived from sucrose. In *Sweet-Taste Chemoreception*; Mathlouthi, M., Kanters, J.A., Birch, G.G., Eds.; Elsevier Applied Science: London, 1993; 269–282.
6. Lee, C.K.; Kang, H.C.; Linden, A. Synthesis, structure and sweetness of 1,4,6-Trichloro-1,4,6-trideoxy-β-D-tagatofuranosyl 4-Chloro-4-deoxy-α-D-galactopyranoside. J. Carbohydr. Chem. **1999**, *18* (2), 241–253.
7. Lee, C.K. Synthesis of an intensely sweet chlorodeoxysucrose: mechanism of 4′-chlorination of sucrose by sulphuryl chloride. Carbohydr. Res. **1987**, *162*, 53–63.
8. Khan, R.; Jenner, M.R.; Lindseth, H.; Mufti, K.S.; Patel, G. Ring-opening reactions of sucrose epoxides: synthesis of 4′-derivatives of sucrose. Carbohydr. Res. **1987**, *162*, 199–207.
9. McKeown, G.G.; Serenius, R.S.; Hayward, L.D. Selective substitution in sucrose. I. The synthesis of 1′,4,6′-Tri-*O*-methyl sucrose and C_4 to C_6 acetyl migration in sucrose. Can. J. Chem. **1957**, *35*, 28–36.
10. Simiand, C.; Driguez, H. Synthesis of sucrose analogs modified at position 4. J. Carbohydr. Chem. **1995**, *14* (7), 977–983.

11. Blanc-Muesser, M.; Driguez, H. A convenient method for the *S*-Glycosidic bond formation. Synthesis of *p*-Iodophenyl 4′-Thiomaltotrioside and its 2″,3″-unsaturated analog. J. Chem. Soc., Perkin Trans. 1 **1998**, *1* (12), 3345–3351.
12. Albert, R.; Dax, K.; Link, R.W.; Stütz, A.E. Carbohydrate triflates: reaction with nitrite, leading directly to *epi*-Hydroxy compounds. Carbohydr. Res. **1983**, *118*, C5–C6.
13. A.S.Md., Sofian; Lee, C.K.; Linden, A. Regioselective sulfonylation of 6,1′,6′-Tri-*O*-tritylsucrose through Dibutylstannylation: synthesis of 4′-*O*-sulfonyl derivatives of sucrose. Carbohydr. Res. **2002**, *337* (24), 2377–2381.
14. Holzapfel, C.W.; Koekemoer, J.M.; Marais, M.F. Sucrose derivatives and the selective benzoylation of the secondary hydroxyl groups of 6,1′,6′-Tri-*O*-tritylsucrose. S. Afr. J. Chem. **1984**, *37*, 57–61.
15. Jenner, M.R. Sucralose: How to make sugar sweeter. In *Sweeteners: Discovery, Molecular Design, and Chemoreception*; Walter, D.E., Orthoefer, F.T., Dubois, G.E., Eds.; ACS Symposium Series 450, 1991; 68–87. Washington, DC.
16. Jackson, G.; Jenner, M.R.; Khan, R.A.; Lee, C.K.; Mufti, K.S.; Patel, G.D.; Rathbone, E.B. Brit. Pat. 2 104 063, 1982.
17. Jackson, G.; Jenner, M.R.; Khan, R.A.; Lee, C.K.; Mufti, K.S.; Patel, G.D.; Rathbone, E.B. Eur. Pat. Appl. EP 73 093, 1983.

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MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016