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SYNTHESIS OF DI- AND TRISACCHARIDES COMPRISING D-FRUCTOPYRANOSE WITH β2→1 GLYCOSIDIC LINKAGE USING β-D-FRUCTOPYRANOSYL FLUORIDE AS THE FRUCTOSYL DONOR

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Abstract – D-Fructose was converted into a stable, suitably protected fructosyl donor for iterative glycosylation, i.e., 1-*O*-acetyl-3,4,5-tri-*O*-benzyl-β-D-fructopyranosyl fluoride and a fructosyl acceptor, methoxymethyl 3,4,5-tri-*O*-benzyl-β-D-fructopyranoside in good yields. Glycosylation of the both substrates provided di- and trisaccharides comprising β-D-fructopyranose with β (2→1)-interglycosidic linkage.

Fructooligosaccharides are widely used for intestinal function controller, mineral absorption promoter, cholesterol suppressor, and lyposome stabilizer.[1] They might also be utilized as promising hosts for molecular recognition of some chiral molecules.[2] In order to solve the structure-activity relationships, fructooligosaccharides with structural diversity are required. As of now, however, they are mainly produced by enzymatic synthesis from sucrose,[3] and plant polysaccharide such as inulin affording linear and cyclic fructooligosaccharides, which comprise fructofuranosyl residue.[4] It is interesting that fructpyranosyl analogs of fructooligosaccharides would be expected to have unique properties different from that of the fructfuranosyl congeners.

Because of its feasibility being relatively low compared to aldohexosyl oligomers, chemical synthesis of ketohexosyl oligomers has been scarcely reported, where only the synthesis of aldohexosyl fructoses such as glucopyranosyl fructofuranosides are presented.[5] Aiming at a new function of fructopyranosyl oligomers, compared to that of the fructfuranosyl one, we here describe a chemical synthesis of fructpyranosyl oligomers being accessible by β-fructosylation using fructpyranosyl fluoride (**6** and **22**) as the glycosyl donors and 1-OH free fructpyranoses (**15** and **18**) as the acceptors. By chemical access

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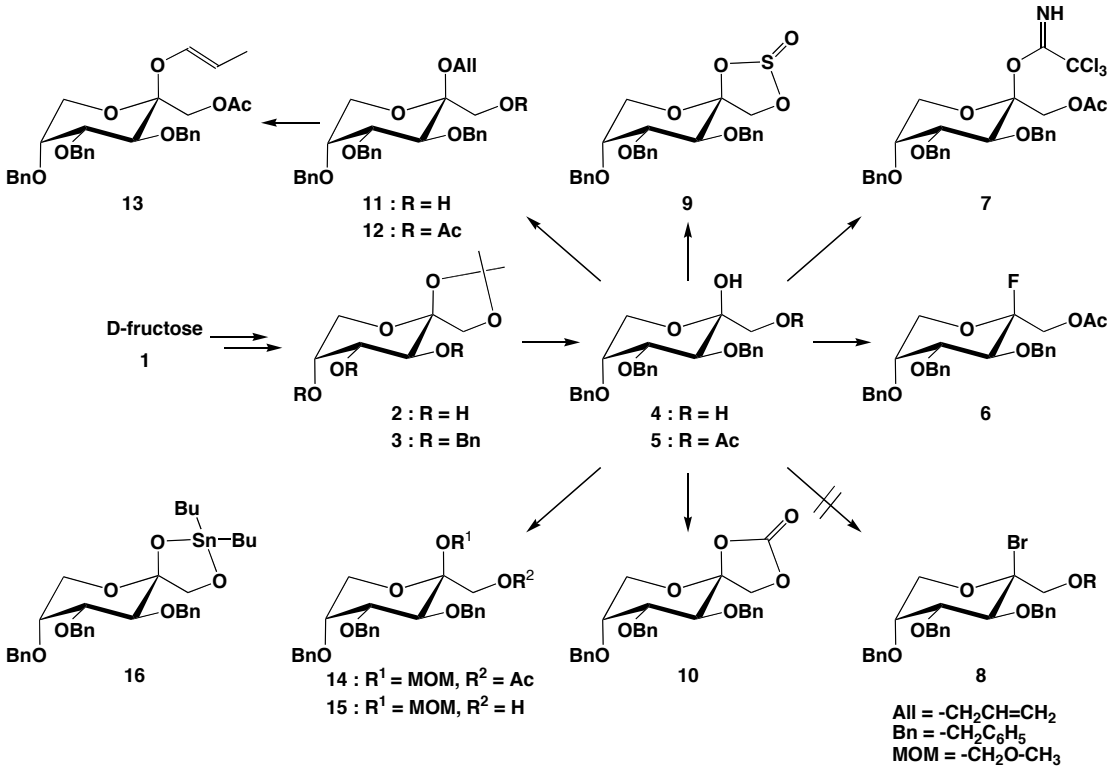
This paper is dedicated to the memory of the Emeritus Professor Kenji Koga of Tokyo University.

disaccharide (**17**-**19**) and trisaccharide (**23**), comprising D-fructopyranose with a β (2→1)-glycosidic linkage, were stereoselectively synthesized.



Scheme 1. Synthesis of Fructopyranosyl Donors and Acceptors

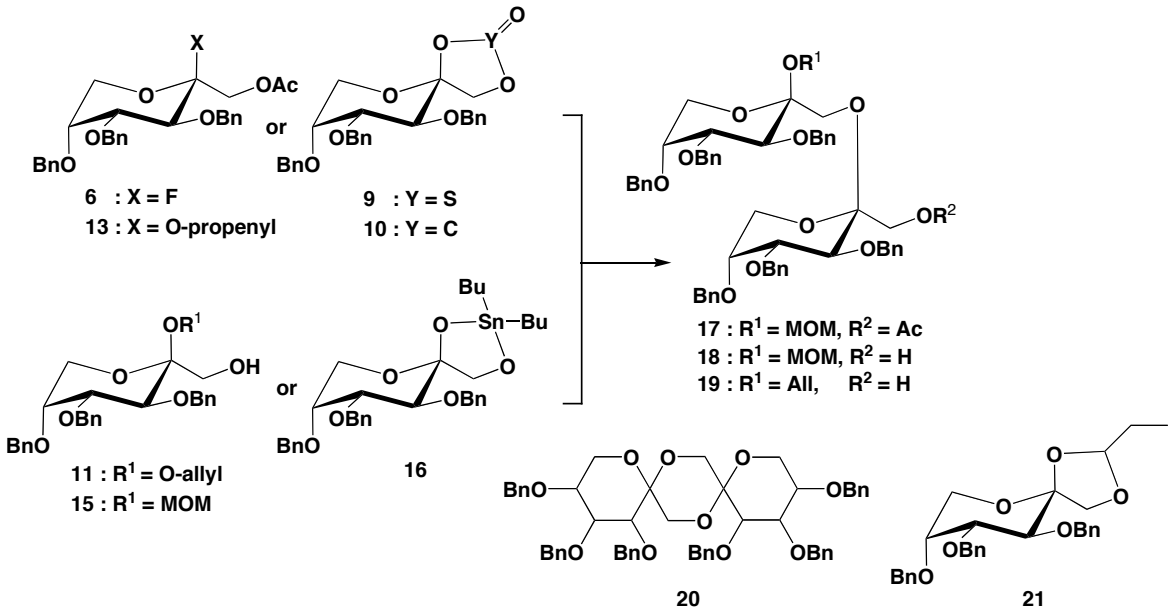
Synthesis of Fructosyl Donors and Acceptors : Glycosylation using glycosyl donors of aldohexoses has been extensively investigated, and numerous methods are utilized for the efficient chemical assembly of oligosaccharides.[6] However, glycosyl donors of ketohexoses have scarcely been demonstrated,[7] such that fructfuranosyl halides,[8] phosphite,[5] thio-,[9] and allyl β-D-fructopyranoside[10] were only used. We synthesized various fructopyranosyl donors possessing fluoride (**6**), imidate (**7**), 1-propenyl (**13**), as well as 1,2-sulfite (**9**) and 1,2-carbonate (**10**) as anomeric leaving groups (cf. Scheme 1). For fructosyl acceptors, 1-OH free compounds such as allyl and methoxymethyl (MOM) fructopyranosides (**11** and **15**) were prepared. Both donors and acceptors should have a permanent protecting group, e.g. benzyl group at 3,4,5-positions, and a temporary protecting group such as acetyl, allyl, or MOM group at 1- or 2-position, so that they might be readily removable and able to regenerate the free OH group without affecting the *O*-benzyl group. Accordingly, we selected 3,4,5-tri-*O*-benzyl-β-D-fructopyranose (**4**) as a key intermediate being convertible into the various fructosyl donors and acceptors we designed.

The compound (**4**)[11] was synthesized according to the reported method by a four-step sequence from D-fructose (**1**), of which the reaction conditions were appropriately revised such that the overall yield for all four steps was increased to 53% yield (cf. less than 30% by the reported method). Regioselective 1-*O*-acetylation of **4** with acetic anhydride in pyridine gave 1-*O*-acetate (**5**) in 84% yield along with 1,2-di-*O*-acetate as a minor product in less than 10% yield.

After which, various fructosyl donors were prepared from the above intermediates (**4**) and (**5**). The fructopyranosyl fluoride (**6**) was obtained by fluorination of **5** with DAST in a quantitative yield. The imidate (**7**) was obtained in low yield (23%) conceivably resulted from its instability. The bromide (**8**) was also less isolable in pure form. For spiro-cyclic analogs, 1,2-sulfite (**9**) was accessible through the reaction of **4** with $SOCl_2$ in pyridine in a quantitative yield. 1,2-Carbonate (**10**), an another cyclic donor, was obtained through the reaction of **4** with carbonyldiimidazole in 42% yield. Next, according to the reported method,[10] allyl β-D-fructopyranoside (**11**) was synthesized, which was readily converted into 1-propenyl β-D-fructopyranoside (**13**) *via* 1-*O*-acetate in 88% overall yield.

Conversely, some fructopyranosyl acceptors having a free 1-OH group were prepared as follows. Methoxymethyl β-D-fructopyranoside (**15**) was synthesized *via* 1-*O*-acetate (**14**) in 91% overall yield from **5**. Above-mentioned allyl β-D-fructopyranoside (**11**) seems to be a candidate for use as a fructosyl acceptor. Other than the 1-OH-free compounds (**11**) and (**15**), 1,2-stannyleneacetal (**16**) may be applicable for another type acceptor.

Synthesis of Fructopyranosyl Di- and Trisaccharides : Among various fructosyl donors described above, the imidate (**7**) was omitted for further glycosylation because of its low feasibility. Then the fluoride (**6**), 1,2-sulfite (**9**), 1,2-carbonate (**10**), and propenyl fructoside (**13**) were evaluated of their donor capacity (c.f. Table 1 and Scheme 2). As shown in Table 1, fructosyl fluoride (**6**) was found to be a most promising donor for the formation of β (2→1)-linked disaccharide (**17**). When Cp_2ZrCl_2-$AgClO_4$ (1 - 2 eq.)[12] was employed as the promoter, the expected disaccharide (**17**) was obtained in 57% yield (Run 4).



Scheme 2. Synthesis of Fructopyranosyl β(2→1)-Disaccharides

Other donors such as 1,2-sulfite (**9**), (Runs 5-8), 1,2-carbonate (**10**) (Run 9), and 1-propenyl

β-D-fructopyranoside (**13**) (Run 10) under various reaction conditions resulted in very poor yield for the expected disaccharides (**17**-**19**) formation. Propenyl fructoside (**13**) provided no disaccharide, but two unexpected products, spirocyclic ketals (**20**) and (**21**) in low yields (Run 10). The compound (**20**) was proposed to be di-D-fructopyranose 1,2' : 2,1'-dianhydride[13] on the basis of its spectral data. This compound's exact structure is still under investigation. Another compound (**21**) was determined by MS and NMR spectral data to be 1,2-*O*-propylidene-β-D-fructopyranose, which may be formed through TMSOTf-catalyzed intramolecular cyclization of the acceptor (**11**). Stannylene acetal-mediated fructosylation of **16** with fluoride (**6**) had only failed to recover the starting materials (Runs 11, 12).

Subsequently, the disaccharide derivative (**17**) was converted into the corresponding disaccharide donor (**22**) and acceptor (**18**). The de-*O*-MOM reaction of **17** was found to be very sensitive to various acidic conditions such as aq. HCl, aq. AcOH, TFA, $Ph_3C^+BF_4^-$ etc.[14] and decomposed the glycosidic bond as well. Only a short exposure time of **17** for 15 min to TMSBr[15] and subsequent fluorination in a one-pot process could afford the desired disaccharide fluoride (**22**) in 34% yield. Once the unreacted **17** was recycled again, overall conversion of **17** to **22** could be estimated at 51% yield. On the other hand, the disaccharide acceptor (**18**) was smoothly generated from **17** by de-*O*-acetylation with sodium methoxide in 91% yield.

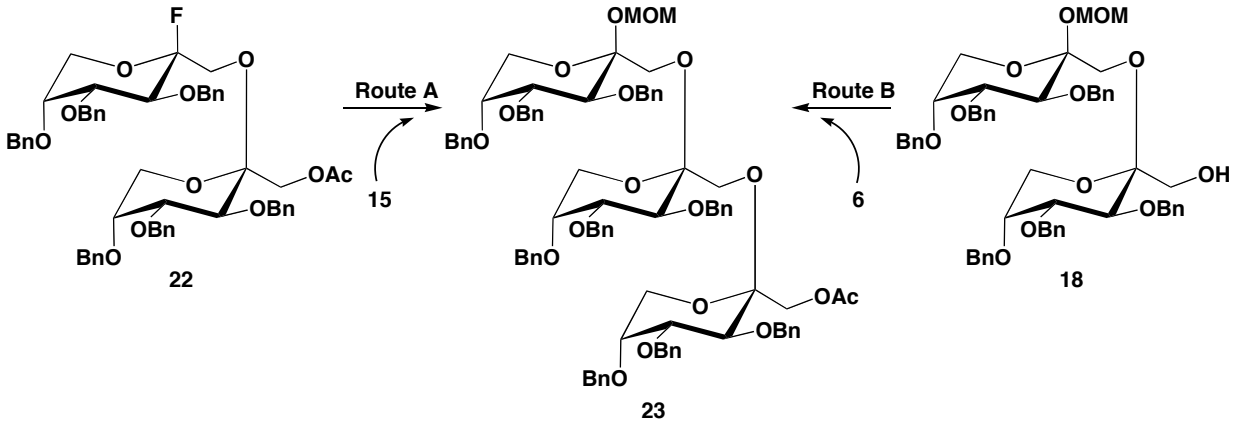
Table 1. Fructosylation Using Various Donors and Acceptors Generating Fructopyranosyl β (2→1)-Disaccharides

Run[a)]	Donor	Acceptor	A/D[b)]	Promotor	(eq.)[c)]	Time (h)	Product	Yields (%)
1	**6**	**15**	1	Cp_2HfCl_2-$AgClO_4$	(1 – 1)	6	**17**	11
2	**6**	**15**	1.2	Cp_2HfCl_2-$AgClO_4$	(1 – 2)	5	**17**	41
3	**6**	**15**	1	Cp_2ZrCl_2-$AgClO_4$	(1 – 2)	2	**17**	28
4	**6**	**15**	1.2	Cp_2ZrCl_2-$AgClO_4$	(1 – 2)	3	**17**	57
5	**9**	**11**	1	$Yb(OTf)_3$	(1)	20	**18**	17
6	**9**	**11**	1	$Yb(OTf)_3$	(1)	24	**18/20**	9/4
7	**9**	**11**	1	$Sc(OTf)_3$	(1)	24	**18/20**	5/3
8	**9**	**11**	1	$Cu(OTf)_2$	(1)	6	**18/20**	4/3
9	**10**	**15**	1	$Hf(OTf)_4$	(1)	24	**4/5**[d)]	85/98
10	**13**	**11**	1	TMSOTf	(1)	1	**20/21**	5/21
11	**6**	**16**	1.2	Cp_2HfCl_2-$AgClO_4$	(1 – 2)	16	**4/5**[e)]	84/92
12	**6**	**16**	1.2	Cp_2HfCl_2-$AgClO_4$	(1 – 2)	22	**4/5**[e)]	88/93

a) All the experiments were carried out in dichloroethane at room tenperature except for Run 5: in toluene, Run 8 : at 50℃, and Run 10 : at 0℃. b) A molar ratio of the Acceptor / Donor. c) Molar equivalent of the promoters to the donor. d) Along with the starting materials, a trace amount (0.4%) of **20** was isolated. e) No product was isolated, and only the starting materials were recovered.

Trisaccharide synthesis using the above disaccharides (**22**) and (**18**) was examined through two routes, where Route A means condensation of disaccharide donor (**22**) with monosaccharide acceptor (**15**), while Route B consists of monosaccharide donor (**6**) with disaccharide acceptor (**18**) (cf. Scheme 3). The reaction conditions employed were selected in reference to those of the disaccharide synthesis.

As shown in Table 2, both routes expressed similar results regarding the formation of the trisaccharide (**23**) in *ca*. 20% yield (c.f. Route A: Runs 1-2, and Route B: Runs 3-6). In these cases the difference of promoters is not significant.



Scheme 3. Synthesis of Fructopyranosyl-β(2→1)-trisaccharide (23)

Table 2. Synthesis of Fructopyranosyl β (2→1)-Trisaccharide (**23**) [a)]

Run	Donor	Acceptor	A / D [b)]	Promoter [c)]	Time (h)	Yield (%)
1	**22**	**15**	1.2	Cp_2HfCl_2-$AgClO_4$	7	19
2	**22**	**15**	1.2	Cp_2ZrCl_2-$AgClO_4$	1.5	20
3	**6**	**18**	1	Cp_2HfCl_2-$AgClO_4$	1	19
4	**6**	**18**	1	Cp_2ZrCl_2-$AgClO_4$	1.5	21
5	**6**	**18**	1.2	Cp_2ZrCl_2-$AgClO_4$	1.5	22
6	**6**	**18**	0.8	Cp_2ZrCl_2-$AgClO_4$	1.5	16

a) All the experiments were carried out at room temperature in dichloroethane.
b) A / D means molar ratio of the Acceptor / Donor. c) Molar equivalents of the promoters are 1 – 2, respectively based on the donor employed.

Structure Elucidation of the Fructopyranosyl Saccharides : Stereochemical elucidation of ketohexoses by NMR spectroscopy is rather complicated compared to that of aldohexoses, since an anomeric proton of the former is lacking. As such, $^3J_{1,2}$ coupling constants being commonly used for the latter are not applicable to determine the anomeric configuration. We utilized the HMBC and NOE

techniques of NMR spectra. For example, HMBC correlation was observed between C-2' and H-1, which assigned a C-2→C-1 interglycosidic bond, and NOE between H-6 and MOM protons supported the β-anomeric configuration. Similarly, β (2→1) configuration of trisaccharide (**23**) was also assigned as depicted in Figure 1.

Moreover, recently reported *J*-based configuration analysis, so called JBCA method,[16] using the degree of ^{3}J coupling constants between C-1 and H-3 is also applicable in our cases. As shown in Figure 1, the C-1 signal of the α-D-fructopyranoses appears as a double triplet with large $^{3}J_{C1,H3}$ coupling constants as H-3 and C-1 are arranged as *antiperiplanar* conformation for the Newman projection. On the other hand, C-1 of the β-anomer appears as a broad triplet with a relatively small $^{3}J_{C1,H3}$ coupling constant, reflecting the *synclinal* (*gauche*) arrangement of the Newman projection. It is likely that in D-fructopyranose series a β-configuration would be preferable, since they are thermodynamically more stable than the corresponding a-anomers through the anomeric effect.

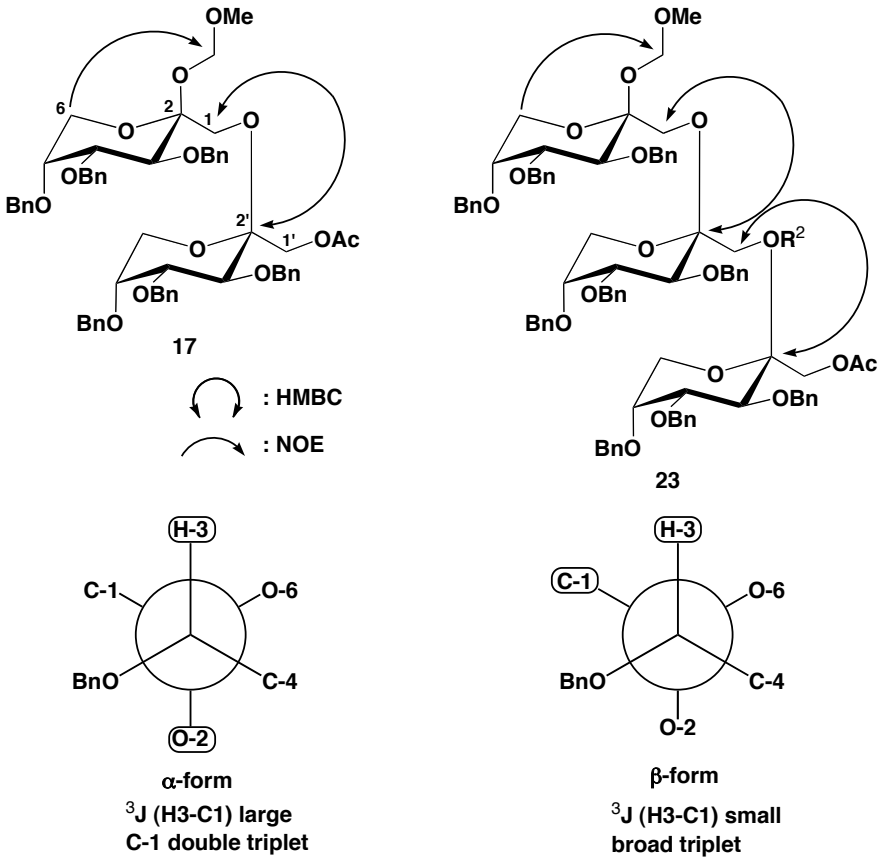


Figure 1. Structure Elucidation of Fructosyl oligosaccharides

Summary : A novel, preparatively useful access to homo-oligomers comprising fructopyranosyl moiety with the β (2→1) glycosidic linkage has been developed utilizing β-D-fructopyranosyl fluoride as the fructosyl donor and methoxymethyl β-D-fructopyranoside as the acceptor. This method would

contribute to chemical synthesis of various fructooligosaccharides as well as aiding their functional analyses of unique biological properties and molecular recognition. Further application of this method in the synthesis of linear and cyclic analogs of fructooligosaccharides is in progress.

EXPERIMENTAL

Melting points were determined on a Yamato MP-1 apparatus and are uncorrected. Spectral data were recorded on the following instruments; JASCO P-1080 ([α]D), JMS-AX 505 H (MS), and Varian XL-400 and VXR-300 (NMR in chloroform-*d* solution). TLC was achieved on silica gel 60 F254 (Merck Art. 5735). The spots were detected by UV light (254 nm) or charring with 10% aq. sulfuric acid. Column chromatography was carried out on silica gel (Kanto Kagaku Co.: up to 100 mesh) column. Compound (**2**),[17] (**3**),[11,18] and (**4**)[11] were prepared by our revised method based on the literatures.

1,2-*O*-Isopropylidene-β-D-fructopyranose (2) : A mixture of 1,2 : 4,5-di-*O*-isopropylidene-β-D-fructopyranose[19] (6.67 g, 27.6 mmol) and 0.1% aq. HCl (310 mL) was stirred at rt for 3 h. The resulting solution was neutralized with Na_2CO_3 and evaporated in vacuo to dryness. The residue was eluted from a silica gel column with $CHCl_3$-MeOH (2:1). The major fraction was concentrated and the residue crystallized from AcOEt to give 5.4 g (88.9%) of **2** as colorless crystals : mp 122-123°C [lit.,[17] 121°C]; $[\alpha]_D^{20}$ –148.6° (c = 1.0, H_2O) [lit.,[17] –158.9°, c = 1.0, H_2O]; MS (FAB) *m/z*: 221 $[M+H]^+$, 243 $[M+Na]^+$; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.76 (1H, dd, H-6a), 3.77 (1H, dd, H-4), 3.78 (1H, ddd, H-5), 3.92 (1H, dd, H-6b), 3.95 (1H, d, H-3), 3.99 (1H, d, H-1a), 4.17 (1H, d, H-1b), 1.43, 1.48 (each 3H, s, CH_3), 3.49 (1H, s, OH), 4.07 (1H, s, OH), 4.57 (1H, s, OH); $J_{1a,1b}$ = 9.0, $J_{3,4}$ = 10.0, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 2.0, $J_{5,6b}$ = 1.0, $J_{6a,6b}$ = 13.0 Hz; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 64.18 (C-6), 68.66 (C-5), 69.43 (C-3), 71.81 (C-4), 71.88 (C-1), 105.83 (C-2), 26.24, 26.41 (2 x CH_3), 111.92 ($\underline{C}(CH_3)_2$). Anal. Calcd for $C_9H_{16}O_6$: C, 49.09; H, 7.32. Found: C, 48.99; H, 7.30.

3,4,5-Tri-*O*-benzyl-1,2-*O*-isopropylidene-β-D-fructopyranose (3) : To a cooled (ice-bath) stirred suspension of 60% NaH (2.4 g, 60.0 mmol) in dry DMF (240 mL) was added dropwise a solution of compound (**2**) (2.2 g, 10 mmol) and benzyl bromide (7.5 mL, 60 mmol) in dry DMF (150 mL). The mixture was stirred at rt for further 2.5 h, diluted with MeOH (120 mL), poured into ice-water (500 mL), and extracted with Et_2O (3 x 150 mL). The combined organic phase was dried (Na_2SO_4), and evaporated to give the residue, which was purified through a silica gel column eluting with toluene-AcOEt (10:1). The major fraction was concentrated and recrystallized from hexane-AcOEt to give **3** (4.88 g, quantitative yield) as colorless needles : mp 81-82°C [lit.,[11] 76-77°C (Et_2O-petr. Ether)]; $[\alpha]_D^{20}$ –79.3° (c = 1.0, $CHCl_3$) [lit.,[11,18] –81.2°; –98.5°]; MS (FAB) *m/z*: 489 $[M-1]^+$, 513 $[M+Na]^+$; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.77 (1H, dd, H-6a), 3.81 (1H, ddd, H-5), 3.83 (1H, dd, H-6b), 3.92 (1H, dd, H-4), 3.95 (1H, d, H-3), 3.97 (1H, d, H-1a), 4.01 (1H, d, H-1b), 1.43, 1.49 (each 3H, s, CH_3); $J_{1a,1b}$ = 9.0, $J_{3,4}$ = 10.0, $J_{4,5}$ = 3.0, $J_{5,6a}$

= 1.5, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 13.0 Hz; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 61.35 (C-6), 71.89 (C-1), 73.40 (C-5), 75.21 (C-3), 80.15 (C-4), 105.83 (C-2), 26.20, 27.09 (2 x CH_3), 71.52, 72.01, 75.37 (3 x -$\underline{C}H_2$Ph). Anal. Calcd for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99. Found: C, 73.39; H, 7.08.

3,4,5-Tri-*O*-benzyl-β-D-fructopyranose (4) : A solution of **3** (0.49 g, 1.0 mmol) in 80% aq. AcOH (20 mL) was stirred at 110°C for 0.5 h. The resulting solution was concentrated in vacuo by co-evaporation with toluene. The residue was eluted from a silica gel column with toluene-AcOEt (1:1), affording 0.39 g (87.2%) of **4** as a colorless syrup (α:β = 1:4): $[\alpha]_D^{20}$ –40.2° (c = 1.0, $CHCl_3$) [lit.,[11] –42.6° (α:β = 1:25); MS (FAB) *m/z*: 473 $[M+Na]^+$; β-anomer: ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.52 (1H, d, H-1a), 3.57 (1H, dd, H-1b), 3.80 (1H, ddd, H-5), 3.80 (1H, dd, H-6a), 3.83 (1H, dd, H-6b), 3.94 (1H, dd, H-4), 4.02 (1H, d, H-3), 2.17 (1H, s, 1-OH), 3.29 (1H, s, 2-OH); $J_{1a,1b}$ = 11.0, $J_{3,4}$ = 9.5, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 2.0, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 40 Hz; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 61.13 (C-6), 66.02 (C-1), 73.25 (C-5), 75.66 (C-3), 79.06 (C-4), 97.87 (C-2) , 71.50, 72.01, 75.56 (3 x -$\underline{C}H_2$Ph); α-anomer: ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.45 (1H, d, H-1a), 3.65 (1H, d, H-3), 3.68 (1H, d, H-1b), 3.76 (1H, dd, H-6a), 3.90 (1H, dd, H-4), 3.94 (1H, dd, H-5), 4.01 (1H, d, H-6b), 2.06 (1H, s, 1-OH), 5.68 (1H, d, 2-OH); $J_{1a,1b}$ = 11.0, $J_{3,4}$ = 3.5, $J_{4,5}$ = 6.0, $J_{5,6a}$ = 1.0, $J_{6a,6b}$ = 10.5, $J_{1a,2\text{-OH}}$ = 1.5 Hz; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 57.64 (C-6), 64.81 (C-1), 71.70 (C-5), 74.18 (C-3), 74.47 (C-4), 97.14 (C-2) , 71.64, 73.37, 74.18 (3 x -$\underline{C}H_2$Ph)

1-*O*-Acetyl-3,4,5-tri-*O*-benzyl-β-D-fructopyranose (5) : To a stirred solution of **4** (1.25 g, 2.75 mmol) in dry pyridine (50 mL) was added Ac_2O (25 mL) at 0°C. The mixture was stirred at rt for 15 h, and concentrated in vacuo with toluene to give the residue, which was diluted with CH_2Cl_2 (50 mL), washed with water (3 x 50 mL), and dried (Na_2SO_4). The organic layer was evaporated to dryness, and purified through a silica gel column eluting with toluene-AcOEt (5:1). The major fraction was concentrated and crystallized from hexane-AcOEt to afford 0.85 g (63.1%) of **5** as colorless crystals. The two minor products were also isolated from the column, and identified as 1,6-di-*O*-acetyl-3,4,5-tri-*O*-benzyl-D-fructose (0.36 g, 24.4%) and the α-anomer of **5** (0.08 g, 6.0%). β-anomer: mp 79-80°C; $[\alpha]_D^{20}$ –51.8° (c = 1.0, $CHCl_3$); MS (FAB) *m/z*: 491 $[M+H]^+$, 515 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.80 (1H, ddd, H-5), 3.82 (1H, dd, H-6b), 3.90 (1H, dd, H-4), 3.91 (1H, dd, H-6b), 4.04 (1H, d, H-3), 4.10 (1H, d, H-1a), 4.16 (1H, d, H-1b), 2.06 (3H, s, -OCOCH$_3$), 3.16 (1H, s, 2-OH); $J_{1a,1b}$ = 11.5, $J_{3,4}$ = 9.5, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 1.0, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 12.5 Hz; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 60.73 (C-6), 66.24 (C-1), 72.59 (C-5), 75.39 (C-3), 78.94 (C-4), 97.03 (C-2), 20.82 (-OCO$\underline{C}$H$_3$), 70.93, 71.74, 75.54 (3 x -$\underline{C}H_2$Ph), 170.67 (-O$\underline{C}$OCH$_3$). α-anomer: MS (FAB) *m/z*: 515 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.58 (1H, d, H-3), 3.76 (1H, dd, H-6a), 3.94 (1H, dd, H-4), 3.95 (1H, ddd, H-5), 4.02 (1H, d, H-6b), 4.07 (1H, d, H-1a), 4.12 (1H, dd, H-1b), 2.03 (3H, s, -OCOCH$_3$), 5.63 (1H, d, 2-OH); $J_{1a,1b}$ = 11.0, $J_{3,4}$ = 3.0, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 2.0, $J_{6a,6b}$ = 11.0, $J_{1b,\,2\text{-OH}}$ = 1.5 Hz; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 57.50 (C-6), 65.66 (C-1), 71.66 (C-4), 73.93 (C-5), 74.58 (C-3), 96.19 (C-2), 20.89 (-OCO$\underline{C}$H$_3$), 73.07, 74.33, 75.56 (3 x $\underline{C}H_2$Ph), 170.69

(-OCOCH$_3$).

1,6-Di-*O*-acetyl-3,4,5-tri-*O*-benzyl-D-fructose: MS (FAB) *m/z*: 535 [M+H]$^+$, 557 [M+Na]$^+$; ^{1}H-NMR (400MHz, $CDCl_3$) δ: 3.81 (1H, ddd, H-5), 4.01 (1H, dd, H-4), 4.13 (1H, dd, H-6a), 4.26 (1H, d, H-3), 4.62 (2H, d, H-1), 4.73 (1H, dd, H-6b), 2.06, 2.13 (each 3H, s, -OCOCH$_3$); $J_{1a,1b}$ = 11.5, $J_{3,4}$ = 3.5, $J_{4,5}$ = 8.0, $J_{5,6a}$ = 3.5, $J_{5,6b}$ = 2.5, $J_{6a,6b}$ = 11.5 Hz; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 61.27 (C-6), 74.90 (C-1), 76.24 (C-5), 79.39 (C-4), 84.44 (C-3), 205.02 (C-2), 20.46, 20.90 (2 x -OCOCH$_3$), 67.98, 71.60, 74.11 (3 x -CH$_2$Ph), 170.25, 170.68 (2 x -OCOCH$_3$).

1-*O*-Acetyl-3,4,5-tri-*O*-benzyl-β-D-fructopyranosyl Fluoride (6) : Diethylaminosulfur trifluoride (DAST, 0.15 mL, 1.06 mmol) was added to a stirred solution of **5** (100 mg, 0.20 mmol) in dry CH_2Cl_2 (10 mL) at –30°C under N_2 atmosphere. The mixture was stirred at rt for 1 h, diluted with MeOH (0.5 mL), and evaporated in vacuo to dryness. The residue was partitioned between CH_2Cl_2 (10 mL) and 5% aq. $NaHCO_3$ (40 mL). The organic phase was washed with water (2 x 40 mL), dried (Na_2SO_4), and concentrated. Elution of the residue from a silica gel column with toluene-AcOEt (5:1→2:1 gradient) afforded an anomeric mixture of **6** (103 mg, quantitative) as a yellow syrup, which crystallized from hexane-AcOEt gave **6** (80.3 mg, 81.8%) as yellowish crystals: mp 73-74°C; $[\alpha]_D^{25}$ –20.9° (c = 1.0, $CHCl_3$); MS (FAB) *m/z*: 493 [M+H]$^+$, 517 [M+Na]$^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.80 (1H, dd, H-6a), 3.84 (1H, ddd, H-5), 3.97 (1H, dd, H-4), 3.99 (1H, dd, H-6b), 4.14 (1H, dd, H-3), 4.26 (2H, d, H-1), 2.03 (3H, s, -OCOCH$_3$); $J_{1a,1b}$ = 6.5, $J_{3,4}$ = 10.0, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 1.0, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 12.5, $J_{3,F}$ = 23.0 Hz; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 63.00 (d, C-6), 63.32 (d, C-1), 72.72 (C-5), 74.70 (d, C-3), 78.46 (C-4), 112.35 (d, C-2), 20.70 (-OCOCH$_3$), 71.32, 72.13, 75.55 (3 x -CH$_2$Ph), 170.05 (-OCOCH$_3$);, $^2J_{C1,F}$ = 31.0, $J_{C2,F}$ = 134.5, $^2J_{C3,F}$ = 20.0, $^3J_{C6,F}$ = 2.5 Hz.

1-*O*-Acetyl-3,4,5-tri-*O*-benzyl-β-D-fructopyranosyl Trichloroacetimidate (7) : To a stirred solution of **5** (49 mg, 0.1 mmol) in CH_2Cl_2 (1 mL) was added trichloroacetonitrile (0.092 mL, 0.92 mmol) and 60% NaH in oil (2.55 mg, 0.1 mmol). The mixture was stirred at rt for 1.5 h, and then concentrated in vacuo to dryness. The residue was eluted from a silica gel column with toluene-AcOEt (3:1) to give 14.6 mg (22.9%) of **7** as a yellowish syrup along with the starting material **5** (40.0 mg, 81.6% recovery). Compound (**7**): MS (FAB) *m/z*: 658 [M+Na]$^+$; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.82 (1H, dd, H-6a), 3.84 (1H, ddd, H-5), 3.90 (1H, dd, H-6b), 3.99 (1H, dd, H-4), 4.02 (1H, d, H-3), 4.19 (1H, d, H-1a), 4.26 (1H, d, H-1b), 1.57 (3H, s, -OCOCH$_3$); $J_{1a,1b}$ = 8.5, $J_{3,4}$ = 12.0, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 2.0, $J_{5,6b}$ = 1.0, $J_{6a,6b}$ = 12.5 Hz; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 62.92 (C-6), 72.89 (C-5), 74.56 (C-1), 76.21 (C-3), 80.16 (C-4), 86.79 (C-2), 20.00 (-OCOCH$_3$), 71.65, 72.05, 76.02 (3 x -CH$_2$Ph), 107.32, 107.89 (-OC(=NH)CCl$_3$ or -OC(=NH)CCl$_3$)), 124.12 (-OCOCH$_3$). Anal. Calcd for $C_{29}H_{32}O_7$: C, 70.56; H, 6.56. Found: C, 70.71; H, 6.55.

3,4,5-Tri-*O*-benzyl-β-D-fructopyranose 1,2-Cyclic Sulfite (9) : Thionyl chloride (7.1 μL, 0.10 mmol)

was added at 0°C to a solution of **4** (451 mg, 0.10 mmol) in Et_2O (10 mL) containing pyridine (32.4 μL, 0.4 mmol). The mixture was stirred at 0°C for 0.5 h, and then passed through a pad of Celite and silica gel. The eluent was concentrated in vacuo to afford 51 mg (quatitative) of **9** as a colorless syrup: $[\alpha]_D^{25}$ –78.0° (c = 1.0, $CHCl_3$); MS (FAB) *m/z*: 519 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.80 (1H, dd, H-6a), 3.85 (1H, ddd, H-5), 3.86 (1H, dd, H-6b), 3.98 (1H, dd, H-4), 4.14 (1H, d, H-3), 4.26 (1H, d, H-1a), 4.52 (1H, d, H-1b); $J_{1a,1b}$ = 9.0, $J_{3,4}$ = 10.0, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 2.0, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 13.5 Hz; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 62.91 (C-6), 72.00 (C-3), 72.14 (C-1), 72.91 (C-5), 79.90 (C-4), 111.91 (C-2), 71.90, 72.43, 75.36 (3 x -$\underline{C}H_2$Ph).

3,4,5-Tri-*O*-benzyl-β-D-fructopyranose 1,2-Cyclic Carbonate (10) : To a stirred solution of **4** (90.1 mg, 0.2 mmol) in dry THF (1.4 mL) was added *N,N'*-carbonyldiimidazol (48.6 mg, 0.3 mmol) in dry THF (0.6 mL). The mixture was stirred at rt for 24 h, and concentrated in vacuo to give the residue, which was purified through a silica gel column eluting with toluene-AcOEt (10:1). The major fraction was concentrated to afford 61.4 mg (64.4%) of **10** as a colorless syrup: $[\alpha]_D^{22}$ –62.4° (c = 1.0, $CHCl_3$); MS (FAB) *m/z*: 477 $[M+H]^+$, 499 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.83 (1H, dd, H-6a), 3.84 (1H, ddd, H-5), 3.93 (1H, dd, H-6b), 3.98 (1H, dd, H-4), 4.03 (1H, d, H-3), 4.06 (1H, d, H-1a), 4.10 (1H, d, H-1b); $J_{1a,1b}$ = 14.0, $J_{3,4}$ = 10.0, $J_{4,5}$ = 2.0, $J_{5,6a}$ = 1.0, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 13.0 Hz; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 64.21 (C-6), 71.57 (C-1), 72.85 (C-5), 74.73 (C-3), 79.11 (C-4), 105.97 (C-2), 72.03, 72.31, 75.22 (3 x -$\underline{C}H_2$Ph), 153.34 (C=O).

Allyl 3,4,5-Tri-*O*-benzyl-β-D-fructopyranoside (11) : Acetyl chloride (0.42 mL, 5.9 mmol) was added to a solution of **4** (1.0 g, 2.2 mmol) in allyl alcohol (22 mL), and the mixture was stirred at rt for 4 h. The resulting solution was evaporated with toluene in vacuo to give the residue, which was eluted from a silica gel column with toluene-AcOEt (10:1). The major fraction was concentrated to afford 0.77 g (70.6%) of **11** as a colorless syrup: $[\alpha]_D^{24}$ –60.0° (c = 1.0, $CHCl_3$); MS (FAB) *m/z*: 513 $[M+Na]^+$; ^{1}H-NMR (400MHz, $CDCl_3$) δ: 3.57 (1H, dd, H-6a), 3.67 (1H, d, H-1a), 3.70 (1H, d, H-1b), 3.78 (1H, dd, H-6b), 3.81 (1H, ddd, H-5), 4.07 (1H, dd, H-4), 4.24 (1H, d, H-3), 2.34 (1H, s, 1-OH), 4.08 (2H, m, -$\underline{C}H_2$-CH=CH_2), 5.19 (2H, m, -CH_2-CH=C$\underline{H}_2$), 5.93 (1H, m, -CH_2-C$\underline{H}$=CH_2); $J_{1a,1b}$ = 13.5, $J_{3,4}$ = 10.0, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 1.0, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 12.0 Hz; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 61.66 (C-6), 63.85 (C-1), 73.59 (C-5), 77.65 (C-3), 78.85 (C-4), 100.36 (C-2), 62.21 (-$\underline{C}H_2$-CH=CH_2), 71.69, 72.14, 75.43 (3 x -$\underline{C}H_2$Ph), 116.09 (-CH_2-CH=$\underline{C}H_2$), 134.79 (-CH_2-$\underline{C}$H=CH_2).

Allyl 1-O-Acetyl-3,4,5-tri-*O*-benzyl-β-D-fructopyranoside (12) : Acetic anhydride (1 mL, 10.5 mmol) was added to a solution of **11** (500 mg, 1.02 mmol) in pyridine (8.3 mL), and the mixture was stirred at rt for 1.5 h. The resulting solution was evaporated with toluene to give the residue, which was diluted with CH_2Cl_2 (40 mL), washed with water (2 x 80 mL), dried (Na_2SO_4), and concentrated in vacuo. The residue was purified through a silica gel column eluting with toluene-AcOEt (20:1) to give 488 mg

(89.4%) of **12** as a colorless syrup: $[\alpha]_D^{25}$ –46.6° (c = 1.0, $CHCl_3$); MS (FAB) *m/z*: 555 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.52 (1H, dd, H-6a), 3.80 (1H, ddd, H-5), 3.84 (1H, dd, H-6b), 4.04 (1H, dd, H-4), 4.13 (1H, d, H-1a), 4.23 (1H, d, H-3), 4.30 (1H, d, H-1b), 1.96 (3H, s, -OCOCH_3), 4.09 (2H,m, -CH_2-CH=CH_2), 5.18 (2H, m, -CH_2-CH=CH_2), 5.90 (1H, m, -CH_2-CH=CH_2); $J_{1a,1b}$ = 11.0, $J_{3,4}$ = 10.0, $J_{4,5}$ = 3.5, $J_{5,6a}$ = 1.0, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 12.5 Hz; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 61.23 (C-6), 63.08 (C-1), 73.44 (C-5), 77.25 (C-3), 78.82 (C-4), 100.54 (C-2), 20.82 (-OCOCH$_3$), 62.30 (-CH$_2$-CH=CH_2), 71.09, 72.14, 75.34 (3 x -CH$_2$Ph), 116.41 (-CH$_2$-CH=CH$_2$), 134.61 (-CH$_2$-CH=CH_2), 170.37 (-OCOCH$_3$).

2-Propenyl 1-O-Acetyl-3,4,5-tri-*O*-benzyl-β-D-fructopyranoside (13) : A mixture of **12** (429 mg, 0.81 mmol), 1,4-diazabicyclo[2.2.2]octane (78.0 mg, 0.70 mmol), and tris(triphenylphosphine)rhodium (I) chloride (11.1 mg, 0.01 mmol) in a mixed solvent of toluene (5.7 mL), water (1.9 mL), and EtOH (13.3 mL) was stirred at rt for 15 min, and then at 100°C for 6.5 h. The resulting mixture was diluted with $CHCl_3$ (40 mL), washed with brine (2 x 80 mL), dried (Na_2SO_4), and evaporated to dryness. The residue was chromatographed on silica gel eluting with toluene-AcOEt (20:1) to give 425 mg (99.1%) of **13** as a colorless syrup: $[\alpha]_D^{26}$ –81.6° (c = 1.0, $CHCl_3$); MS (FAB) *m/z*: 555 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.56 (1H, dd, H-6a), 3.81 (1H, ddd, H-5), 3.87 (1H, dd, H-6b), 4.02 (1H, dd, H-4), 4.11 (1H, d, H-1a), 4.22 (1H, d, H-3), 4.32 (1H, d, H-1b), 1.57 (3H, m -CH=CH-CH_3), 1.97 (3H, s, -OCOCH_3), 5.24 (1H, m, -CH=CH-CH$_3$), 6.32 (1H, m, -CH=CH-CH$_3$); $J_{1a,1b}$ = 11.5, $J_{3,4}$ = 10.0, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 1.0, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 12.5 Hz; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 61.53 (C-6), 63.36 (C-1), 73.39 (C-5), 74.61 (C-3), 78.81 (C-4), 100.88 (C-2), 12.50 (-CH=CH-CH$_3$), 20.79 (-OCOCH$_3$), 71.18, 72.19, 75.48 (3 x -CH$_2$Ph), 106.79 (-CH=CH-CH$_3$), 137.39 (-CH=CH-CH$_3$), 170.27 (-OCOCH$_3$).

Methoxymethyl 1-*O*-Acetyl-3,4,5-tri-*O*-benzyl-β-D-fructopyranoside (14) : To a stirred solution of **5** (1.23 g, 2.5 mmol) in THF (25 mL) was added MOM-Cl (0.2 mL, 1.2 mmol) and then 60% NaH in oil (120 mg, 3.0 mmol). The mixture was stirred at rt for 2 h, and the excess NaH was decomposed with AcOH monitoring with pH to neutral. The resulting mixture was poured into ice-water (20 mL), extracted with Et_2O (3 x 20 mL), dried (Na_2SO_4), and evaporated to dryness. The residue was eluted from a silica gel column with hexane-AcOEt (3:1→1:1 gradient) to give 1.42 g (quantitative) of **14** as a milky syrup: $[\alpha]_D^{24}$ –86.8° (c = 1.0, $CHCl_3$); MS (FAB) *m/z*: 559 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.54 (1H, dd, H-6a), 3.81 (1H, ddd, H-5), 3.88 (1H, dd, H-6b), 3.98 (1H, dd, H-4), 4.20 (1H, d, H-1a), 4.29 (1H, d, H-3), 4.44 (1H, d, H-1b), 2.00 (3H, s, -OCOCH_3), 3.42 (3H, s, -OCH$_2$OCH_3), 4.58, 4.99 (each 1H, d, -OCH_2OCH$_3$); $J_{1a,1b}$ = 12.0, $J_{3,4}$ = 10.0, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 1.0, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 12.5, J(OCH_2OCH$_3$) = 7.0 Hz; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 61.13 (C-6), 63.86 (C-1), 73.30 (C-5), 74.97 (C-3), 78.88 (C-4), 101.13 (C-2), 20.84 (-OCOCH$_3$), 55.97 (-OCH$_2$OCH$_3$), 71.03, 72.06, 75.46 (3 x -CH$_2$Ph), 89.12 (-OCH$_2$OCH$_3$), 170.17 (-OCOCH$_3$).

Methoxymethyl 3,4,5-Tri-*O*-benzyl-β-D-fructopyranoside (15) : Compound (**14**) (2.4 g, 4.46 mmol)

was dissolved in 0.5 M NaOMe in MeOH (220 mL). The solution was stirred at rt for 2 h, neutralized with acidic resin (Dowex 50W x 4), and filtered through a pad of Celite. The filtrate was concentrated in vacuo to dryness. The residue was diluted with CH_2Cl_2 (50 mL), washed with water (3 x 50 mL), dried (Na_2SO_4), and evaporated to give the crude product, which was purified through a silica gel column eluting with hexane-AcOEt (3:1) to affored 2.0 g (quantitative) of **15** as a milky syrup: $[\alpha]_D^{24}$ –95.7° (c = 1.0, $CHCl_3$); MS (FAB) *m/z*: 517 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.55 (1H, dd, H-6a), 3.66 (1H, d, H-1a), 3.70 (1H, s, OH), 3.80 (1H, ddd, H-5), 3.82 (1H, d, H-1b), 3.83 (1H, dd, H-6b), 3.95 (1H, dd, H-4), 4.23 (1H, d, H-3), 3.41 (3H, s, -$OCH_2OC\underline{H}_3$), 4.60, 4.94 (each 1H, d, -$OC\underline{H}_2OCH_3$); $J_{1a,1b}$ = 12.0, $J_{3,4}$ = 10.0, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 1.0, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 12.5, J($OC\underline{H}_2OCH_3$) = 7.0 Hz; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 61.53 (C-6), 64.50 (C-1), 73.48 (C-5), 76.58 (C-3), 78.90 (C-4), 101.68 (C-2), 56.01 (-$OCH_2O\underline{C}H_3$), 71.50, 72.19, 75.64 (3 x -$\underline{C}H_2Ph$), 89.20 (-$O\underline{C}H_2OCH_3$).

Methoxymethyl *O*-(1-*O*-Acetyl-3,4,5-tri-*O*-benzyl-β-D-fructopyranosyl)-(2→1)-3,4,5-tri-*O*-benzyl-β-D-fructopyranoside (17) (Experiment for Table 1, Run 4): To a stirred solution of **15** (58.8 mg, 0.12 mmol) in dry CH_2Cl_2 (4 mL) with MS-4A (powder, 200 mg) were added zirconocene dichloride (Cp_2ZrCl_2) (29.4 mg, 0.10 mmol), $AgClO_4$ (46.0 mg, 0.20 mmol), and fluoride (**6**) (49.0 mg, 0.10 mmol). The mixture was stirred at rt in the dark for 2.5 h, and then diluted with CH_2Cl_2 (2 mL), filtered through a pad of Celite. The filtrate was washed with aq. 5% $NaHCO_3$ (20 mL) and water (3 x 20 mL), dried (Na_2SO_4), and evaporated to give the residue, which was eluted from a silica gel column with toluene-AcOEt (3:1). The major fraction was concentrated to affored the disaccharide (**17**) (55.4 mg, 57.2%) as a colorless syrup: $[\alpha]_D^{22}$ –103.3° (c = 1.0, $CHCl_3$); MS (FAB) *m/z*: 967 $[M–H]^+$, 991 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.52 (1H, dd, H-6a), 3.71 (1H, ddd, H-5'), 3.74 (1H, d, H-1a), 3.76 (1H, ddd, H-5), 3.78 (1H, dd, H-6b), 3.81 (1H, dd, H-6'a), 3.89 (1H, d, H-1b), 3.92 (1H, dd, H-4), 3.97 (1H, dd, H-4'), 4.11 (1H, dd, H-6'b), 4.12 (1H, d, H-3'), 4.16 (1H, d, H-1'a), 4.36 (1H, d, H-1'b), 4.49 (1H, d, H-3), 1.95 (3H, s, -$OCOCH_3$), 3.36 (3H, s, -$OCH_2OC\underline{H}_3$), 4.51, 4.92 (each 1H, d, -$OC\underline{H}_2OCH_3$); $J_{1a,1b}$ = 11.0, $J_{3,4}$ = 10.5, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 1.5, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 13.0, J($OC\underline{H}_2OCH_3$) = 7.0, $J_{1'a,1'b}$ = 10.0, $J_{3',4'}$ = 10.0, $J_{4',5'}$ = 3.0, $J_{5',6'a}$ = 1.0, $J_{5',6'b}$ = 2.0, $J_{6'a,6'b}$ = 11.0 Hz; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 56.89 (C-6'), 61.80 (C-6), 62.41 (C-1), 63.80 (C-1'), 73.23 (C-5), 75.25 (C-3), 75.37(C-3'), 76.16 (C-5'), 78.74 (C-4), 78.99 (C-4'), 99.95 (C-2') 102.65 (C-2), 20.80 (-$OCO\underline{C}H_3$), 56.01 (-$OCH_2O\underline{C}H_3$), 70.88, 71.53, 72.21, 72.61, 75.19, 75.5 (6 x -$\underline{C}H_2Ph$), 89.07 (-$O\underline{C}H_2OCH_3$), 170.35 (-$O\underline{C}OCH_3$).

Methoxymethyl *O*-(3,4,5-Tri-*O*-benzyl-β-D-fructopyranosyl)-(2→1)-3,4,5-tri-*O*-benzyl-β-D-fructopyranoside (18): A solution of **17** (145.5 mg, 0.15 mmol) in 0.05 M NaOMe in MeOH (3 mL) was stirred at rt for 3 h. The resulting solution was neutralized with acidic resin (Dowex 50W x 4), and filtered through a pad of Celite. The filtrate was concentrated, diluted with CH_2Cl_2 (30 mL), washed with water (3 x 30 mL), dried (Na_2SO_4), and evaporated to dryness. The residue was eluted from a silica

gel column with toluene-AcOEt (2:1) to give 126.3 mg (90.8%) of **18** as a colorless syrup: $[\alpha]_D^{23}$ –110.9° (c = 1.0, $CHCl_3$); MS (FAB) *m/z*: 949 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.54 (1H, dd, H-6a), 3.70 (1H, ddd, H-5'), 3.72 (1H, d, H-1'a), 3.76 (1H, dd, H-6'a), 3.78 (1H, d, H-1'b), 3.79 (1H, ddd, H-5), 3.80 (1H, dd, H-6b), 3.86 (1H, d, H-1a), 3.91 (1H, d, H-1b), 3.94 (1H, dd, H-4), 4.01 (1H, dd, H-4'), 4.11 (1H, d, H-3'), 4.14 (1H, dd, H-6'b), 4.51 (1H, d, H-3), 2.00 (1H, s, 2'-OH), 3.37 (3H, s, -$OCH_2OC\underline{H}_3$), 4.53, 4.93 (each 1H, d, -$OC\underline{H}_2OCH_3$); $J_{1a,1b}$ = 11.0, $J_{3,4}$ = 10.5, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 1.5, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 13.0, J($OC\underline{H}_2OCH_3$) = 7.0, $J_{1'a,1'b}$ = 10.0, $J_{3',4'}$ = 10.0, $J_{4',5'}$ = 3.0, $J_{5',6'a}$ = 2.0, $J_{5',6'b}$ = 1.0, $J_{6'a,6'b}$ = 11.0 Hz; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 61.30 (C-6'), 61.73 (C-6), 62.37 (C-1), 64.58 (C-1'), 73.22 (C-5'), 75.34 (C-5), 75.41(C-3), 78.74 (C-4), 78.82 (C-3'), 79.01 (C-4'), 99.95 (C-2') 102.63 (C-2), 55.94 (-$OCH_2O\underline{C}H_3$), 71.33, 71.36, 72.20, 72.61, 75.34, 75.55 (6 x -$\underline{C}H_2Ph$), 89.03 (-$O\underline{C}H_2OCH_3$).

Allyl *O*-3,4,5-Tri-*O*-benzyl-β-D-fructopyranosyl-(2→1)-3,4,5-tri-*O*-benzyl-β-D-fructopyranoside (19) (Experiment for Table 1, Run 5): A suspension of 1,2-sulfite (**9**) (24.8 mg, 0.05 mmol), $Yb(OTf)_3$ (31.0 mg, 0.05 mmol), MS-3A (powder, 300 mg) in dry toluene (2 mL) was stirred at rt for 0.5 h. To this mixture was added **11** (24.5 ng, 0.05 mmol) in dry a solution of toluene (1 mL), and the resulting mixture was stirred at rt for 20 h. Subsequent dilution with $CHCl_3$ (20 mL), washing with aq. 5% $NaHCO_3$ (40 mL) and water (2 x 40 mL), drying (Na_2SO_4), filtration, and evaporation of the filtrate gave the residue. Purification through a silica gel column eluting with toluene-AcOEt (10:1) gave **19** (7.8 mg, 16.8%) as a colorless syrup, with which difructose-1,2' : 2,1'-dianhydride (**20**) (1.4 mg, 3.0%) was also isolated as a minor by-product. Compound (**19**): $[\alpha]_D^{26}$ –83.2° (c = 1.0, $CHCl_3$); MS (FAB) *m/z*: 945 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.58 (1H, dd, H-6a), 3.67 (1H, dd, H-1'a), 3.69 (1H, ddd, H-5'), 3.73 (1H, dd, H-1'b), 3.75 (1H, dd, H-6'a), 3.76 (1H, dd, H-6b), 3.77 (1H, ddd, H-5), 3.78 (1H, d, H-1a), 3.90 (1H, d, H-1b), 3.98(1H, dd, H-4), 4.00 (1H, dd, H-4'), 4.11 (1H, d, H-3'), 4.11 (1H, dd, H-6'b), 4.40 (1H, d, H-3), 2.56 (1H, dd, 1'-OH), 4.01 (2H, m, -$C\underline{H}_2$-$CH=CH_2$), 5.15 (2H, m, -CH_2-$CH=C\underline{H}_2$), 5.88 (1H, m, -CH_2-$C\underline{H}=CH_2$); $J_{1a,1b}$ = 9.5, $J_{3,4}$ = 10.5, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 1.5, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 12.5, $J_{1'a,\,1'\text{-OH}}$ = 8.0, $J_{1'b,\,1'\text{-OH}}$ = 2.0, $J_{1'a,1'b}$ = 9.5, $J_{3',4'}$ = 10.0, $J_{4',5'}$ = 3.0, $J_{5',6'a}$ = 2.0, $J_{5',6'b}$ = 1.5, $J_{6'a,6'b}$ = 11.5 Hz; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 61.48 (C-1), 61.67 (C-6', C-6), 64.79 (C-1'), 73.21 (C-5'), 75.51 (C-5), 75.90(C-3), 78.65 (C-4), 78.94 (C-4'), 78.96 (C-3'), 99.59 (C-2') 102.10 (C-2), 62.12 (-$\underline{C}H_2$-$CH=CH_2$), 71.40, 71.46, 72.17, 72.70, 75.43, 75.59 (6 x -$\underline{C}H_2Ph$), 89.97 (-$O\underline{C}H_2OCH_3$), 116.24 (-CH_2-$CH=\underline{C}H_2$), 135.06 (-CH_2-$\underline{C}H=CH_2$).

3,4,5-Tri-*O*-benzyl-1,2-*O*-propylidene-β-D-fructopyranose (21): Trimethylsilyl triflate (7.9 mL, 0.043 mmol) was added to a mixture of **11** (21.1 mg, 0.043 mmol) and **13** (23.0 mg, 0.043 mmol) in MeCN (3 mL) at 0°C. The resulting mixture was stirred at 0°C for further 1 h, diluted with CH_2Cl_2 (20 mL), washed with 5% aq. $NaHCO_3$ (40 mL), and water (2 x 20 mL), dried (Na_2SO_4), and evaporated to dryness. The residue was eluted from a silica gel column with toluene-AcOEt (10:1) to give **21** (4.5 mg, 21.4%)

along with the difructose-dianhydride (**20**) (1.9 mg, 5.1%) both as colorless syrups. Compound (**21**): $[\alpha]_D^{26}$ –82.4° (c = 1.0, $CHCl_3$); MS (FAB) *m/z*: 513 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.76 (1H, d, H-1a), 3.78 (1H, dd, H-6a), 3.80 (1H, dd, H-6b), 3.82 (1H, ddd, H-5), 3.95 (1H, d, H-1b), 3.95 (1H, dd, H-4), 4.01 (1H, d, H-3), 0.97 (3H, t, -CH_3), 1.74 (1H, m, -CH_{2a}-), 1.75 (1H, m, -CH_{2b}-), 5.08 (1H, t, -CH-); $J_{1a,1b}$ = 8.5, $J_{3,4}$ = 10.0, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 1.5, $J_{5,6b}$ = 1.5, $J_{6a,6b}$ = 11.5 Hz; ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 61.93 (C-6), 72.92 (C-1), 73.38 (C-5), 75.46(C-3), 80.02(C-4), 105.58 (C-2), 7.96 (-CH_3), 26.45 (-CH_2-), 71.68, 72.12, 75,34 (3 x $\underline{C}H_2$Ph), 105.21 (-CH-).

***O*-(1-*O*-Acetyl-3,4,5-tri-*O*-benzyl-β-D-fructopyranosyl)-(2→1)-3,4,5-tri-*O*-benzyl-β-D-fructopyranosyl Fluoride (22)**: Trimethylsilyl bromide (195 mL, 0.5 mmol) was added to a mixture of **17** (291 mg, 0.3 mmol) in CH_2Cl_2 (12 mL) containing MS-4A (powder, 300 mg). The mixture was stirred at rt for 15 min, neutralized with 5% aq. $NaHCO_3$, extracted with Et_2O (3 x 30 mL), dried (Na_2SO_4), and evaporated to dryness. The residue was used for subsequent fluorination without further purification.

Diethylaminosulfur trifluoride (DAST, 40 μL, 0.3 mmol) was added to the crude product described above in dry CH_2Cl_2 (8 mL) at –30°C under nitrogen atmosphere, and the resulting mixture was stirred at rt for 1 h. Subsequent addition of MeOH (0.1 mL), evaporation of the solvent gave the residue, which was dissolved in CH_2Cl_2 (10 mL), washed with 5% aq. $NaHCO_3$ (10 mL) followed by water (3 x 10 mL), dried (Na_2SO_4), and evaporated to dryness. The residue was purified through a silica gel column eluting with hexane-AcOEt (3:2) to afford 93.5 mg (33.6%) of **22** as a yellowish syrup along with the starting substrate (**17**) (79.7 mg, 27.4% recovery). Compound (**22**): MS (FAB) *m/z*: 949 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.73 (1H, ddd, H-5'), 3.76 (1H, d, H-1a), 3.80 (1H, dd, H-6'a), 3.81 (1H, dd, H-6a), ~3.82 (H-5), 3.84 (1H, d, H-1b), 3.92 (1H, dd, H-4), 3.93 (1H, dd, H-6b), 3.94 (1H, dd, H-4'), 3.96 (1H, dd, H-6'b), 4.16 (1H, d, H-1'a), 4.33 (1H, d, H-1'b), 4.61 (1H, d, H-3), 4.65 (1H, d, H-3'), 1.95 (3H, s, -OCOCH_3); $J_{1a,1b}$ = 10.0, $J_{3,4}$ = 10.0, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 1.0, $J_{5,6b}$ = 1.5, $J_{6a,6b}$ = 12.5, $J_{1'a,1'b}$ = 11.0, $J_{3',4'}$ = 10.0, $J_{4',5'}$ = 3.0, $J_{5',6'a}$ = 1.0, $J_{5',6'b}$ = 2.0, $J_{6'a,6'b}$ = 12.0 Hz; ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 60.93 (C-6'), 63.08 (d, C-6), 61.32 (d, C-1), 63.47 (C-1'), 73.07 (C-5), 74.34(C-3'), 74.78 (d, C-3), 78.19(C-4), 75.87 (C-5'), 78.87 (C-4'), 100.03 (C-2') 113.80 (d, C-2), 20.79 (-OCO$\underline{C}$H3), 70.91, 71.69, 72.14, 72.63, 75.25, 75.67 (6 x -$\underline{C}H_2$Ph), 170.24 (-O$\underline{C}$OCH_3); $^1J_{c2,F}$ = 87.0, $^2J_{C1,F}$ = 24.0, $^2J_{C3,F}$ = 10.0, $^3J_{C6,F}$ = 2.0 Hz.

Methoxymethyl *O*-(1-*O*-Acetyl-3,4,5-tri-*O*-benzyl-β-D-fructopyranosyl)-(2→1)-(3,4,5-tri-*O*-benzyl-β-D-fructopyranosyl)-(1→2)-3,4,5-tri-*O*-benzyl-β-D-fructopyranoside (23)—Route A: To a stirred solution of **15** (29.4 mg, 0.06 mmol) in dry CH_2Cl_2 (2.0 mL) were added orderly MS-4A (powder, 100 mg), Cp_2ZrCl_2 (14.7 mg, 0.05 mmol), $AgClO_4$ (23.0 mg, 0.1 mmol), and the disaccharide fluoride (**22**) (46.4 mg, 0.05 mmol). The mixture was stirred in the dark at rt for 1.5 h. The resulting mixture was diluted with CH_2Cl_2 (10 mL) and filtered through a pad of Celite. The filtrate was washed with 5% aq. $NaHCO_3$ (10 mL) and water (3 x 10 mL), dried (Na_2SO_4), and evaporated to dryness. The residue was

eluted from a silica gel column with toluene-AcOEt (2:1) to give **23** (13.9 mg, 19.8%) as a colorless syrup.

Route B: The disaccharide acceptor (**18**) (58.1 mg, 0.06 mmol) and the monosaccharide fluoride (**6**) (24.5 mg, 0.05 mmol) were treated as described for Route A, affording the trisaccharide (**23**) (15.6 mg, 22.2%): $[\alpha]_D^{23}$ –94.9° (c = 0.54, $CHCl_3$); MS (FAB) *m/z*: 1423 $[M+Na]^+$; ^{1}H-NMR (400 MHz, $CDCl_3$) δ: 3.51 (1H, dd, H-6a), 3.58 (1H, d, H-1a), 3.60 (1H, d, H-1'a), 3.61 (1H, ddd, H-5'), 3.69 (1H, dd, H-6'a), 3.71 (1H, ddd, H-5"), 3.74 (1H, d, H-1'b), 3.75 (1H, d, H-1b), 3.76 (1H, ddd, H-5), 3.77 (1H, dd, H-6b), 3.81 (1H, dd, H-6"a), 3,90 (1H, dd, H-4), 3.93 (1H, dd, H-4'), 3.98 (1H, dd, H-4"), 4.07 (1H, dd, H-6'b), 4.09 (1H, d, H-1"a), 4.10 (1H, d, H-3"), 4.12 (1H, dd, H-6"b), 4.24 (1H, d, H-1"b), 4.32 (1H, d, H-3'), 4.45 (1H, d, H-3), 1.90 (3H, s, $-OCOCH_3$), 3.37 (3H, s, $-OCH_2OC\underline{H}_3$), 4.52, 4.90 (each 1H, d, $-OC\underline{H}_2OCH_3$); $J_{1a,1b}$ = 9.5, $J_{3,4}$ = 10.0, $J_{4,5}$ = 3.0, $J_{5,6a}$ = 1.5, $J_{5,6b}$ = 2.0, $J_{6a,6b}$ = 13.0, $J_{1'a,1'b}$ = 9.0, $J_{3',4'}$ = 10.0, $J_{4',5'}$ = 3.0, $J_{5',6'a}$ = 2.0, $J_{5',6'b}$ = 1.0, $J_{6'a,6'b}$ = 13.0, $J_{1"a,1"b}$ = 11.0, $J_{3",4"}$ = 10.0, $J_{4",5"}$ = 3.0, $J_{5",6"a}$ = 1.5, $J_{5",6"b}$ = 3.0, $J_{6"a,6"b}$ = 13.0, $J(OC\underline{H}_2OCH_3)$ = 7.0 Hz; ^{13}C-NMR (75MHz, $CDCl_3$) δ: 60.97 (C-6"), 61.32 (C-1'), 61.43 (C-6'), 61.85 (C-6), 61.85 (C-1), 63.70 (C-1"), 73.31 (C-5"), 75.16 (C-5), 75.19 (C-5'), 75.43 (C-3'), 75.49 (C-3), 76.11 (C-3"), 78.70 (C-4), 78.83 (C-4'), 78.94 (C-4"), 99.95 (C-2"), 101.71 (C-2') 102.75 (C-2), 20.75 ($-OCO\underline{C}H3$), 56.10 ($-OCH_2O\underline{C}H_3$), 70.87, 71.56, 71.89, 71.96, 72.13, 72.58, 74.98, 75.27, 75.49 (9 x $-\underline{C}H_2Ph$).

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