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Carbohydrate-derived spiroketals: stereoselective synthesis of di-D-fructose dianhydrides

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Abstract—A one-pot synthesis of di-D-fructose dianhydrides (DFAs) having the 1,6,9,13-tetraoxadispiro[4.2.4.2]tetradecane and 1,7,10,15-tetraoxadispiro[5.2.5.2]hexadecane skeleton has been accomplished. The methodology relies on the ability of per-*O*-protected 1,2-*O*-isopropylidene β-D-fructofuranose and β-D-fructopyranose derivatives to undergo a tandem acetal cleavage-intermolecular glycosylation-intramolecular spiroketalization process by reaction with suitable acid promoters, such as boron trifluoride etherate or trifluoromethanesulfonic acid, in apolar organic solvents. Spirocyclization proceeds then under irreversible reaction conditions to give binary mixtures of di-D-fructofuranose (α,α and α,β diastereomers) or di-D-fructopyranose 1,2′:2,1′ dianhydrides (β,β and α,β), respectively, the stereochemical outcome being dependent on the non-participating or participating character of the protecting groups. Thus, benzylated and allylated derivatives afford, preferentially, the non-symmetric DFAs (α,β), with diastereomeric excess up to 92%. In contrast, the use of participating benzoyl groups favours the C_2-symmetric diastereomer in both series.

1. Introduction

The spiroketal unit represents a common feature in many biologically relevant natural products, including steroidal saponins, polyether ionophores, macrolide antibiotics, insect pheromones and toxic metabolites from algae and fungi,[1–4] being the target of much synthetic effort.[5–13] This structural element is also present in a unique class of cyclic disaccharides termed generically diketose dianhydrides, of which di-D-fructose dianhydrides (DAFs) are paradigmatic examples.[14] Some members of this class of compounds have been isolated from microorganisms[15] and higher plants.[16] Their potential use as sweeteners,[17,18] bifidogenic agents[19] or chiral templates[20,21] has triggered intense interest in the synthesis of these and related spiro-sugars.[22–27] The identification of DFAs as the major components of the thermolysis product of sucrose and D-fructose containing food materials, such as caramel and chicory,[28–30] and the need of pure standards for nutritional studies and analytical evaluation[31] has provided a further impetus.

Despite the variety of general methods existing for the construction of the spiroketal moiety, the control of the stereochemistry at the anomeric centres relies, almost exclusively, on the relative thermodynamic stability of the different isomers in the acid-catalyzed spiroketalization reaction. When all factors that control spiroketalization, that is, a maximum anomeric effect and minimum steric interactions, are reinforcing, a major isomer is produced. The stereoselectivity is lower when these factors are in conflict. In tricyclic systems,[32–35] however, such general statements must be applied carefully. A range of structures can usually accommodate the basic requirements, that is, oxygen substituents at anomeric centres in axial disposition and carbon substituents in equatorial disposition, with rather small differences in energy and low interconversion barriers.

In the case of DFAs, high yielding preparations have been previously achieved by protonic activation of D-fructose, sucrose or inulin with anhydrous hydrogen fluoride (HF) or its complex with pyridine.[36–38] Under such conditions, a fructosyl oxocarbenium cation is generated, which undergoes in situ glycosylation into the corresponding keto-disaccharide. Further spiroketalization is a reversible process that leads to a complex mixture of bis(spiro)disaccharides in which the two D-fructose constituents are joined through a central 1,4-dioxane ring. Up to five different

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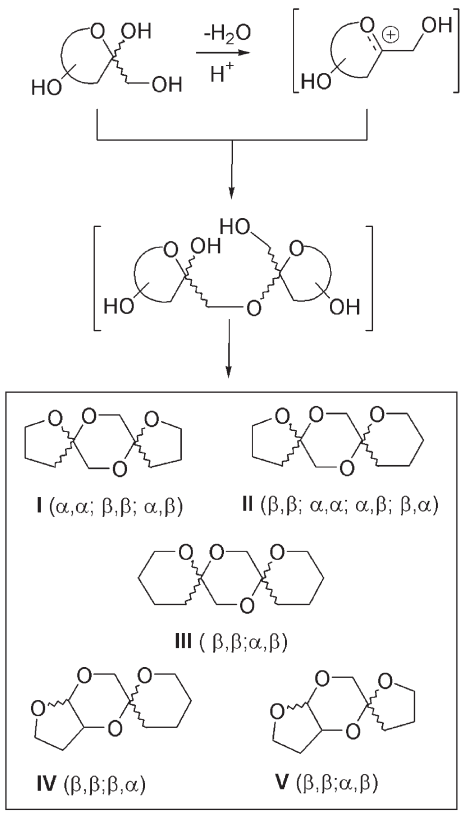
tricyclic cores (types I–V) and 13 DFA isomers that differ in the ring size, linking position and stereochemistry of the ketal stereocenters have been so far identified from reaction mixtures (Scheme 1).



Scheme 1. Acid-catalysed dimerization of ketoses.

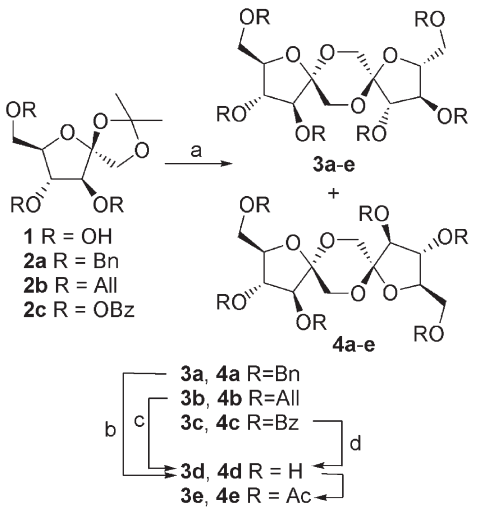
Difuranose DFA derivatives (types I and V) are formed at the early stages of the acid-promoted dimerization of D-fructose. However, they partially isomerize in the reaction medium to give mixed furanose–pyranose (types II and IV) and dipyranose species (type III). Although their relative proportions can be varied to some extent by modulation of the acid strength, isolation of pure samples from the isomeric mixtures remains a difficult task. We envisioned that isomerization reactions would be significantly slowed in anhydrous apolar solvents. Moreover, the use of protected D-fructose precursors should allow blocking the cyclic form of the monosaccharides and, eventually, controlling the stereochemical outcome of the dimerization process.[39] This concept has now been translated into stereoselective preparations of DFAs having the 1,6,9,13-tetraoxadispiro-[4.2.4.2]tetradecane and 1,7,10,15-tetraoxadispiro[5.2.5.2]-hexadecane core structure (types I and III, respectively). Our strategy relies on the ability of 1,2-*O*-isopropylidene D-fructose derivatives to undergo a tandem acetal cleavage—intermolecular glycosylation—intramolecular spiroketalization process by reaction with suitable acid promoters.[40,41] The scope and limitations of the methods as well as the factors influencing the relative proportions of the products are discussed.

2. Results and discussion

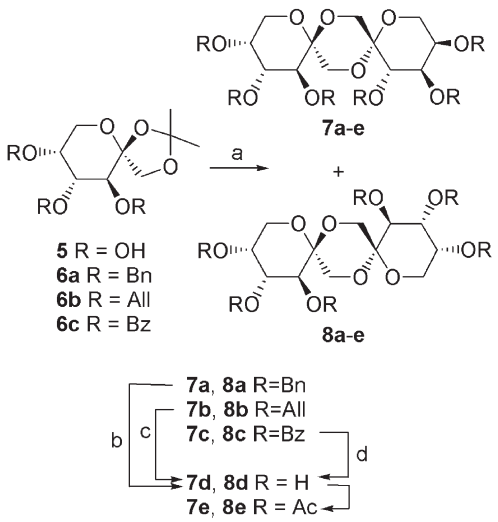
3,4,6-Tri-*O*-protected 1,2-*O*-isopropylidene-β-D-fructofuranoses **2a**-**c**, readily accessible from the known 1,2-*O*-isopropylidene-β-D-fructofuranose[42] **1**, were used as furanose-anchored precursors for the preparation of type I DFAs. First, a screening of their reactivity in the presence of a series of acid promoters was carried out (see Table 1 for selected results). Diethylaluminium chloride was found to be inefficient to provoke acetal cleavage in either toluene or dichloromethane, even using a large excess of reagent at 50 °C. Treatment with tin (IV) chloride or zinc chloride ($ZnCl_2{\cdot}Et_2O$) etherate resulted in removal of the isopropylidene group even at room temperature, but these reagents were unable to promote the subsequent glycosylation–spiroketalization reaction. A slight improvement was observed using $ZnCl_2{\cdot}Et_2O$ at 50 °C in toluene, although the final DFA products (**3a**–**c**, **4a**–**c**) were isolated in disappointingly low yields (4–15%) and poor stereoselectivities (Table 1, entries 1, 4 and 7). Interestingly, boron trifluoride diethyl etherate ($BF_3{\cdot}Et_2O$) and trifluoromethanesulfonic acid (triflic acid, TfOH) succeeded in promoting the desired tandem transformations in toluene (see Table 1, entries 2, 5, and 8 for results using $BF_3{\cdot}Et_2O$), which is in agreement with their broad use for the cleavage of acetal protecting groups, as glycosylation promoters and as spiroketalization catalysts.[40,41,43,44] The use of dichloromethane as solvent was detrimental in the case of $BF_3{\cdot}Et_2O$; in contrast, it resulted in improved yields in the case of the protic acid promoter TfOH (Table 1, entries 3, 6 and 9). Employing these optimal reaction conditions, conversion

Table 1. Acid-promoted dimerization of 1,2-*O*-isopropyliden-D-fructose derivatives (**2a**–**c** and **6a**–**c**) to give DFAs (**3a**–**c**, **4a**–**c** and **7a**–**c**, **8a**–**c**, respectively)

Entry	Starting material	Acid promoter (equiv.)	Solvent	Temp. (°C)	Reaction time (h)	Yield (%)	Products (ratio)
1	**2a**	$ZnCl_2{\cdot}Et_2O$ (4.0)	Toluene	50	16	4	**3a**:**4a** (1:1)
2	**2a**	$BF_3{\cdot}Et_2O$ (1.0)	Toluene	−20	4.5	64	**3a**:**4a** (2:5)
3	**2a**	TfOH (1.5)	CH_2Cl_2	−78→20	1	75	**3a**:**4a** (1:2)
4	**2b**	$ZnCl_2{\cdot}Et_2O$ (4.0)	Toluene	50	16	12	**3b**:**4b** (2:3)
5	**2b**	$BF_3{\cdot}Et_2O$ (1.0)	Toluene	−20	3	75	**3b**:**4b** (1:5)
6	**2b**	TfOH (1.5)	CH_2Cl_2	−78→20	1	92	**3b**:**4b** (1:7)
7	**2c**	$ZnCl_2{\cdot}Et_2O$ (4.0)	Toluene	50	16	15	**3c**:**4c** (2:3)
8	**2c**	$BF_3{\cdot}Et_2O$ (2.0)	Toluene	4	16	40	**3c**:**4c** (24:1)
9	**2c**	TfOH (1.5)	CH_2Cl_2	−78→20	2	91	**3c**:**4c** (25:1)
10	**6a**	$BF_3{\cdot}Et_2O$ (1.5)	Toluene	−20	5	65	**7a**:**8a** (1:25)
11	**6a**	TfOH (1.5)	CH_2Cl_2	−78→20	1.5	76	**7a**:**8a** (1:20)
12	**6b**	$BF_3{\cdot}Et_2O$ (1.5)	Toluene	−20	5	68	**7b**:**8b** (1:7)
13	**6b**	TfOH (1.5)	CH_2Cl_2	−78→20	1.5	87	**7b**:**8b** (1:6)
14	**6c**	$BF_3{\cdot}Et_2O$ (2.0)	Toluene	20	72	80	**7c**:**8c** (1:1)
15	**6c**	TfOH (2.0)	CH_2Cl_2	−78→20	3	87	**7c**:**8c** (1:1)



Scheme 2. Synthesis of type I DFAs. Reagents: (a) $BF_3{\cdot}Et_2O$ in toluene or TfOH in CH_2Cl_2 (see Table 1); (b) H_2/Pd–C, AcOH–MeOH–HCOOH (90–97%); (c) $PdCl_2$, MeOH (70–80%); (d) NaOMe/MeOH (>95%); (e) Ac_2O-pyridine (>95%).



Scheme 3. Synthesis of type III DFAs. Reagents: (a) $BF_3{\cdot}Et_2O$ in toluene or TfOH in CH_2Cl_2 (see Table 1); (b) H_2/Pd–C, AcOH–MeOH–HCOOH (>95%); (c) $PdCl_2$, MeOH (70–75%); (d) NaOMe/MeOH (>95%); (e) Ac_2O-pyridine (>95%).

yields into the corresponding dispiro-disaccharides **3a–c**, **4a–c** in the range 75–92% were obtained (Scheme 2).

It is noteworthy that only two of the three possible type I DAF structures (the α,α, β,β and α,β diastereomers) were formed in all cases, namely the hexa-*O*-protected di-α-D-fructofuranose 1,2′:2,1′-dianhydride (**3a–c**) and α-D-fructofuranose β-D-fructofuranose 1,2′:2,1′-dianhydride derivatives (**4a–c**). Their relative proportions were strongly dependent on the nature of the hydroxyl protecting groups. Thus, in the case of ether-type groups (**2a** and **2b**) the non-symmetric diastereomer (**4a** and **4b**) was favored, with 43 and 75% diastereomeric excess (de) values over the C_2-symmetric dianhydride (**3a** and **3b**). The stereochemical outcome of the spiroketalization reaction was reversed for the benzoyl counterpart (**2c**), leading to a 92% de in favour of the α,α (**3c**) over the α,β isomer (**4c**).

To implement this approach for the stereoselective preparation of dispiro-difructopyranose dianhydrides (type III DFAs), 3,4,5-tri-*O*-benzyl- (**6a**),[45] 3,4,5-tri-*O*-allyl- (**6b**) and 3,4,5-tri-*O*-benzoyl-β-D-fructopyranose (**6c**),[46] available in three steps from D-fructose via the corresponding monoacetonide **5**,[46] were used as pyranose-anchored D-fructose templates. As a general rule, the acid-promoted dimerization process proceeded more slowly in these cases, in agreement with the lower stability of the six-membered cyclic oxocarbenium cation. Nevertheless, satisfactory conversion rates were obtained using either $BF_3{\cdot}Et_2O$ or TfOH by increasing the proportion of the catalyst, the temperature or using longer reaction times, TfOH in dichloromethane providing the higher yields on the corresponding DFA products. Binary mixtures of the corresponding hexa-*O*-protected di-β-D-fructopyranose 1,2′:2,1′-dianhydride (**7a–c**) and α-D-fructopyranose β-D-fructopyranose 1,2′:2,1′-dianhydride (**8a–c**) were obtained in all cases (Scheme 3). As previously observed in the furanose series, a strong stereodirecting effect of the hydroxyl protecting groups in the generation of the spiroketal stereocentres was observed. Thus, while the benzoyl derivatives (**7c** and **8c**) were obtained in identical relative proportion (Table 1, entries 14 and 15), the non-symmetric α,β-diastereomer (**8a** and **8b**) was favoured in the case of the benzylated or allylated pairs (Table 1, entries 10–13).

Pure samples of the hexa-*O*-protected individual DFA isomers could be obtained in all cases after column chromatography. Nevertheless, in the case of the benzoylated derivatives (**3c**, **4c** and **7c**, **8c**), replacing the benzoyl groups into acetyl (to give **3e**, **4e** and **7e**, **8e**, respectively) prior to column chromatography was advantageous for preparative purposes. The structure of all DFAs prepared in this study was confirmed by microanalytical, NMR and MS data. The chemical shifts of the anomeric C-2 (C-2′) carbon atoms are particularly useful for diagnostic purposes, behaving as a fingerprint for a given DFA core structure.[14] The structural assignment was further confirmed by transformation into the known fully unprotected DFAs (**3d**, **4d**, **7d** and **8d**) by removal of the *O*-protecting groups through standard methodologies. The relative proportions of stereoisomers in the mixtures was established by GC chromatography after derivatization of the unprotected DFAs as the corresponding hexa-*O*-trimethylsilyl derivatives, following the procedure previously reported for determination of DFAs in food products.[31]

The possibility to control not only the ring size but also the stereochemistry at the spiroketal centres in the synthesis of DFAs is noteworthy. We hypothesized that, in contrast to the mineral acid-catalyzed reaction, spiroketalization occurs in apolar organic solvents under virtually irreversible conditions, thus limiting isomerization processes. To confirm this point, the hexabenzylated C_2-symmetric dianhydride **7a** was subjected to the reaction conditions previously used to promote dimerization of **6a**. No isomerization into the favored non-symmetric diastereomer **8a** was detected after 24 h, supporting the above assumption. The preference for non-symmetric over C_2-symmetric DFA structures in the case of non-participating protecting groups (i.e., benzyl and allyl) can be rationalized in terms of

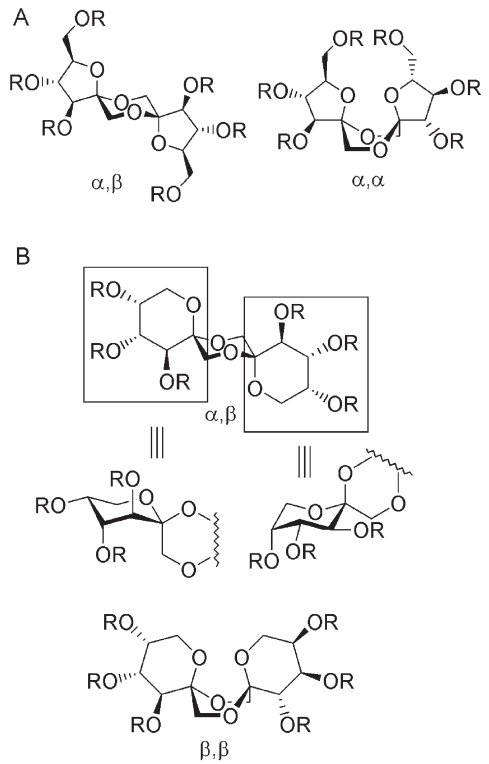


Figure 1. Conformations for non-symmetric and C_2-symemtric DFAs of types I (A) and III (B).

the relative stability of the incipient 1,4-dioxane ring leading to a given isomer. In the case of the α,β diastereomers, the central ring can accommodate the oxygen substituents in axial disposition and the carbon substituents in equatorial disposition in the chair conformation. Such situation does not prevail for the symmetric isomers, which must adopt a boat conformation at the central ring to accommodate the anomeric effect at both anomeric centres, a less favourable arrangement (Fig. 1(A) and (B)).[14]

The dimerization reaction of substrates bearing participating ester groups (**2c** and **6c**) probably proceeds through acyloxonium entities. The lower reactivity of these species as compared with the fructosyl cation is in agreement with the observed lower reactivity of benzoylated D-fructose derivatives towards dimerization (Table 1). In the furanose series, the formation of a *cis*-fused 2,3-acyloxonium cation intermediate (**9**) prevents O-1′ attack through the β-face in both the glycosylation and spirocyclization steps (Fig. 2(A)). Consequently, the thermodynamically less favoured di-α isomer **3c** is formed almost exclusively. In the pyranose series, however, glycosylation of the corresponding 2,3-acyloxonium cation (**10**) may compete with the attack by the benzoate group at C-5 to give a 2,5-acyloxonium intermediate (**11**), which blocks the nucleophilic attack by O-1′ through the α-face (Fig. 2(B)). At its turn, this cation will undergo selectively glycosylation-spiroketalization through the more accessible β-face to give **7c** (Fig. 2). It must be noticed that the α- and β-D-fructopyranose rings in α-fructopyranose β-fructopyranose 1,2′:2,1′-dianhydride derivatives adopts the $^4C_1$ and $^1C_4$ chair conformation, respectively, in order to fit the anomeric effect (Fig. 1(B)). The unfavourable steric interactions in the α-ring are

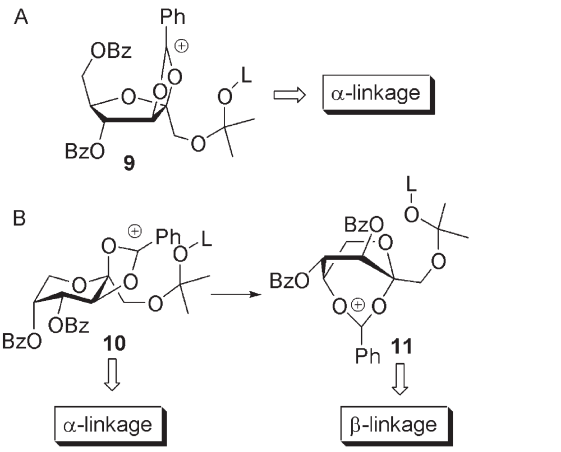


Figure 2. Probable structure of the acyloxonium cations involved in the dimerization reaction of benzoylated D-fructofuranose (A) and D-fructopyranose (B) precursors.

compensated by the gain in stability due to the chair arrangement of the central 1,4-dioxane ring in asymmetric dianhydrides, a situation that would not apply for a C_2-symmetric diastereomer. In fact, no dipyranose DFA derivatives having the α,α configuration have been reported up to date. Probably, the α-(2→1)-linked disaccharide derived from intermediate **10** would necessarily undergo spiroketalization through the β-face to give **8c**.

In conclusion, we have demonstrated that 1,2-*O*-isopropylidene-D-fructose derivatives are suitable precursors for the synthesis of difuranose and dipyranose DFAs. Boron trifluoride diethyl etherate complex and triflic acid are capable to promote acetal deprotection and dimerization to the corresponding spiro-cyclic disaccharides in organic solvents, under irreversible conditions. Both the ring size and the stereochemistry at the spiroketal centres can be controlled by judicious choice of the protecting groups in the monosaccharide template, non-participating groups favouring non-symmetric structures and participating groups the C_2-symmetric diastereomers.

3. Experimental

3.1. General methods

All solvents and reagents were purchased from commercial sources and used without further purification, except for toluene and dichloromethane, which were distilled under Ar stream over Na and CaH_2, respectively. 1,2-*O*-Isopropylidene-β-D-fructofuranose[42] (**1**), 1,2-*O*-isopropylidene-β-D-fructopyranose[46] (**5**) and 3,4,5-tri-*O*-benzoyl-1,2-*O*-isopropylidene-β-D-fructopyranose[46] (**6c**) were prepared according to described procedures. 3,4,5-Tri-*O*-benzyl-1,2-*O*-isopropylidene-β-D-fructopyranose (**6a**) has been previously obtained from **5** in 17% yield by treatment with benzyl bromide in tetrahydrofurane.[45] An improved preparation (70% yield), including full characterization data, is given hereinafter. Optical rotations were measured at room temperature in 1-cm or 1-dm tubes on a Perkin–Elmer 141 MC polarimeter. ^{1}H (and ^{13}C NMR) spectra were recorded at 300 (75.5) and 500 (125.7) MHz with Bruker 300 AMX and 500 DRX instruments, respectively. 2D

COSY, HMQC and HSQC experiments were used to assist on NMR assignments. Thin-layer chromatography (TLC) was carried out on aluminium sheets coated with Kieselgel 60 F254 (E. Merck), with visualisation by UV light and by charring with 10% H_2SO_4. Column chromatography was carried out on Silica Gel 60 (E. Merck, 230–400 mesh). FAB mass spectra were obtained with a Kratos MS-80 RFA instrument. The operating conditions were the following: the primary beam consisted of Xe atoms with a maximum energy of 8 keV; the samples were dissolved in thioglycerol, and the positive ions were separated and accelerated over a potential of 7 keV; NaI was added as cationizing agent. Elemental analyses were performed at the Instituto de Investigaciones Químicas (Sevilla, Spain).

Debenzylation of hexa-*O*-benzylated DAFs (**3a**, **4a**, **7a** and **8a**) or their mixtures was effected by catalytic hydrogenation with 10% Pd/C at 1 atm in 1:1 EtOAc–MeOH containing 10% formic acid. Deallylation reactions (**3b**, **4b**, **7b** and **8b**) were accomplished by treatment with $PdCl_2$ in MeOH.[47] Conventional debenzoylation (**3c**, **4c**, **7c** and **8c**) was carried out with methanolic NaOMe (1 M). Acetylation of fully unprotected DAF mixtures was performed with 1:1 Ac_2O–pyridine. In all cases, the physicochemical data for the individual fully unprotected DFAs (**3d**, **4d**, **7d** and **8d**) or the corresponding per-*O*-acetates (**3e**, **4e**, **7e** and **8e**) were identical to those previously reported.

3.1.1. 3,4,6-Tri-*O*-benzyl-1,2-*O*-isopropylidene-β-D-fructofuranose (2a). To a solution of **1** (1 g, 4.5 mmol) in DMF (15 mL), NaH (0.44 g, 18.2 mmol, 1.4 equiv.) and benzyl bromide (2.43 mL, 20 mmol, 1.5 equiv.) were added and the reaction mixture was stirred for 4 h at room temperature. Then, MeOH (5 mL) was added, the solvents were evaporated under reduced pressure and the residue was extracted with Et_2O (20 mL), washed with water (20 mL), dried ($MgSO_4$), concentrated and purified by column chromatography (1:8 EtOAc–petroleum ether) to furnish **2a** (1.78 g, 81%). R_f=0.33 (1:8 EtOAc–petroleum ether); $[\alpha]_D$=−27.3 (*c* 1.1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.49, 1.53 (2s, each 3H, CMe_2), 3.46 (dd, 1H, $J_{5,6a}$=6.2 Hz, $J_{6a,6b}$=9.8 Hz, H-6a), 3.70 (dd, 1H, $J_{5,6b}$=6.2 Hz, H-6b), 3.99 (d, 1H, $J_{1a,1b}$=9.4 Hz, H-1a), 4.06 (d, 1H, $J_{3,4}$=5.0 Hz, H-3), 4.09 (d, 1H, H-1b), 4.17 (td, 1H, $J_{4,5}$=5.0 Hz, H-5), 4.19 (t, 1H, H-4), 4.60–4.77 (m, 6H, C*H*$_2$Ph), 7.33–7.39 (m, 15H, Ph); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 26.4, 26.5 (C*Me*$_2$), 71.3 (C-1), 72.2 (C-6), 73.5 (3*C*H$_2$Ph), 80.1 (C-5), 83.2 (C-3), 84.5 (C-4), 109.2 (C-2), 111.5 (*C*Me$_2$), 127.5–138.1 (Ph); FABMS: *m*/*z* 513 (100%, $[M+Na]^+$). Anal. Calcd for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99; found: C, 73.52; H, 6.90.

3.1.2. 3,4,6-Tri-*O*-allyl-1,2-*O*-isopropylidene-β-D-fructofuranose (2b). To a solution of **1** (1.06 g, 4.8 mmol) in DMF (15 mL), NaH (0.87 g, 36 mmol) and allyl bromide (1.34 mL, 15.8 mmol) were added and the reaction mixture was stirred for 15 min at room temperature. Then water (5 mL) was added and the reaction mixture was extracted with Et_2O (5×40 mL). The organic layer was washed with H_2O (5×25 mL), dried ($MgSO_4$), and concentrated, and the residue purified by column chromatography (1:7 EtOAc–petroleum ether) to afford **2b** (1.31 g, 80%). R_f=0.50 (1:5 EtOAc–petroleum ether); $[\alpha]_D$=−32.1 (*c* 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.38, 1.43 (2s, each 3H, CMe_2), 3.52 (dd, 1H, $J_{6a,6b}$=10.0 Hz, $J_{5,6a}$=6.2 Hz, H-6a), 3.56 (dd, 1H, $J_{5,6b}$=6.4 Hz, H-6b), 3.87 (d, 1H, $J_{3,4}$=6.5 Hz, H-3), 3.94, (dd, 1H, $J_{4,5}$=5.1 Hz, H-4), 3.98 (ddd, 1H, H-5), 3.99 (d, 1H, $J_{1a,1b}$=9.5 Hz, H-1a), 4.05 (d, 1H, H-1b), 3.97–4.17 (m, 6H, CH_2O), 5.13–5.30 (m, 6H, C*H*$_2$=CH), 5.83–5.95 (m, 3H, CH$_2$=C*H*); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 26.5, 26.6 (C*Me*$_2$), 71.2, 71.3 (3CH_2), 72.2 (C-6), 72.4 (C-1), 80.1 (C-5), 83.2 (C-3), 84.5 (C-4), 109.0 (C-2), 111.5 (*C*Me$_2$), 117.0, 117.4 (3CH=*C*H$_2$), 134.2, 134.5 (3*C*H=CH$_2$); FABMS: *m*/*z* 341 (30%, $[M+H]^+$). Anal. Calcd for $C_{18}H_{28}O_6$: C, 63.51; H, 8.29; found: C, 63.46; H, 8.58.

3.1.3. 3,4,6-Tri-*O*-benzoyl-1,2-*O*-isopropylidene-β-D-fructofuranose (2c). A solution of **1** (1 g, 4.5 mmol) and benzoyl chloride (2.65 mL, 23.3 mmol) in pyridine (8 mL) was stirred for 16 h at room temperature. Iced water (40 mL) was added to the reaction mixture and the suspension was extracted with CH_2Cl_2 (2×20 mL), the organic layer was dried ($MgSO_4$) and concentrated. The resulting residue was purified by column chromatography (1:5 EtOAc–petroleum ether) to yield **2c** (1.77 g, 73%). R_f=0.43 (1:4 EtOAc–petroleum ether); $[\alpha]_D$=−52.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.26, 1.44 (2s, each 3H, CMe_2), 4.21 (d, 1H, $J_{1a,1b}$=9.4 Hz, H-1a), 4.36 (d, 1H, H-1b), 4.51 (ddd, 1H, $J_{4,5}$=5.1 Hz, $J_{5,6a}$=4.6 Hz, $J_{5,6b}$=6.4 Hz, H-5), 4.67 (dd, 1H, $J_{6a,6b}$=11.6 Hz, H-6a), 4.82 (dd, 1H, H-6b), 5.87 (d, 1H, $J_{3,4}$=5.1 Hz, H-3), 5.95 (t, 1H, H-4), 7.39–8.12 (m, 15H, Ph); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 26.0 (C*Me*$_2$), 65.1 (C-6), 71.3 (C-1), 75.9 (C-3), 77.0 (C-4), 79.2 (C-5), 108.9 (C-2), 112.0 (*C*Me$_2$), 128.2–134.5 (Ph), 165.6, 165.7, 166.1 (3CO); FABMS: *m*/*z* 555 (100%, $[M+Na]^+$). Anal. Calcd for $C_{30}H_{28}O_9$: C, 67.66; H, 5.30; found: C, 67.68; H, 5.29.

3.1.4. 2,3,4-Tri-*O*-benzyl-1,2-*O*-isopropylidene-β-D-fructopyranose (6a). Compound **6a** was prepared from **5** (0.6 g, 2.72 mmol) as above described for **2a**, followed by column chromatography purification (1:9→1:7 EtOAc–petroleum ether). Yield: 0.90 g (70%); $[\alpha]_D$=−98.5 (*c* 1.0, CH_2Cl_2); Lit. $[\alpha]_D$=−81.2 (*c* 0.92, $CHCl_3$); R_f=0.30 (1:5 EtOAc–petroleum ether); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.56, 1.66 (2s, each 3H, CMe_2), 3.84 (m, 1H, H-5), 3.88 (m, 2H, H-6), 4.04 (dd, 1H, $J_{3,4}$=2.5 Hz, $J_{4,5}$=9.9 Hz, H-4), 4.08 (d, 1H, H-3), 4.09 (d, 1H, $J_{1a,1b}$=8.7 Hz, H-1a), 4.11 (d, 1H, H-1b), 4.58–5.16 (m, 6H, C*H*$_2$Ph), 7.31–7.49 (m, 15H, Ph); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 26.3, 27.2 (C*Me*$_2$), 62.4 (C-6), 67.5 (C-3), 70.0 (C-4), 70.2 (C-5), 71.8 (C-1), 71.6, 72.0, 75.4 (*C*H$_2$Ph), 104.2 (C-2), 111.8 (*C*Me$_2$), 127.4–138.5 (Ph); FABMS: *m*/*z* 513 (100%, $[M+Na]^+$). Anal. Calcd for $C_{30}H_{34}O_6$: C, 73.45; H, 6.99; found: C, 73.49; H, 6.87.

3.1.5. 2,3,4-Tri-*O*-allyl-1,2-*O*-isopropylidene-β-D-fructopyranose (6b). Compound **6b** was prepared from **5** (1.19 g, 5.4 mmol) as above described for **2b**, followed by column chromatography purification (1:7 EtOAc–petroleum ether). Yield: 1.37 g (75%); (1:7 EtOAc–petroleum ether). R_f=0.53 (1:5 EtOAc–petroleum ether); $[\alpha]_D$=−113.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.38, 1.43 (2s, each 3H, CMe_2), 3.66 (d, 1H, $J_{3,4}$=2.9 Hz, H-3), 3.71 (dd, 1H, $J_{4,5}$=9.7 Hz, H-4), 3.75 (m, 1H, H-5), 3.79 (m, 2H, H-6), 3.96 (d, 1H, $J_{1a,1b}$=8.4 Hz, H-1a), 4.03 (d, 1H, H-1b), 4.04–4.17 (m, 6H, CH_2O), 5.08–5.30 (m, 6H, C*H*$_2$=CH),

5.83–5.95 (m, 3H, CH_2=C*H*); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 26.1, 27.2 (CMe_2), 70.9, 71.1, 74.4 (3CH_2O), 111.8 (*C*Me$_2$), 116.4, 116.6, 117.4 (3CH=*C*H$_2$), 134.9, 135.2 (3*C*H=CH$_2$); FABMS: *m*/*z* 341 (100%, [M+H]$^+$). Anal. Calcd for $C_{18}H_{28}O_6$: C, 63.51; H, 8.29; found: C, 63.63; H, 8.00.

3.2. General procedure for the preparation of difructose dianhydrides (3a–c, 4a–c, 7a–c, 8a–c)

(a) By treatment with $BF_3{\cdot}Et_2O$. To a stirred 0.15 M solution of the corresponding 1,2-*O*-isopropylidene-D-fructose derivative **2a**–**c** or **6a**–**c** in dry toluene under Ar, the acid promoter $BF_3{\cdot}Et_2O$ was added. Reaction conditions (equivalents of acid, reaction temperature and reaction time) are collected in Table 1. The reaction mixture was quenched by addition of MeOH, washed with 5% aq. $NaHCO_3$, the organic layer was dried ($MgSO_4$), the solvents were evaporated under reduced pressure, and the products were separated by column chromatography with the eluent indicated in each case.

(b) By treatment with TfOH. To a stirred 50 mM solution of the corresponding 1,2-*O*-isopropylidene-D-fructose derivative **2a**–**c** or **6a**–**c** in freshly distilled CH_2Cl_2 under Ar at −78 °C, TfOH was added. The reaction mixture was allowed to warm up to room temperature and stirred for the indicated time (Table 1). Et_3N (0.5 mL) was added, the reaction mixture was stirred for 10 min, the solvents were evaporated under reduced pressure and the products were separated by column chromatography with the eluent indicated in each case.

Conversion yields are collected in Table 1. For benzylated (**3a**, **4a** and **7a**, **8a**) and allylated derivatives (**3b**, **4b** and **7b**, **8b**), efficient separations of the individual diastereomers were achieved after column chromatography. In the case of perbenzoylated derivatives (**3c**, **4c** and **7c**, **8c**), however, only small amounts of the pure DFAs could be obtained after a second column chromatography. Transformation into the corresponding per-*O*-acetates (**3e**, **4e** and **7e**, **8e**) allowed the efficient separation of individual isomers (column chromatography, eluent 1:3 EtOAc–petroleum ether). The relative proportions of C_2-symmetric versus non-symmetric diastereomers in the reaction mixtures were determined by GC after transformation into the corresponding mixtures of fully unprotected DFAs (**3d**, **4d** or **7d**, **8d**) and further derivatization as the corresponding hexa-*O*-trimethylsilyl derivatives, following the protocol previously reported.[31] The identity of the peaks was confirmed by comparison with authentic standards.

3.2.1. 3,4,6,3′,4′,6′-Hexa-*O*-benzyl-di-α-D-fructofuranose 1,2′:2,1′-dianhydride (3a). R_f=0.33 (1:4 EtOAc–petroleum ether); $[\alpha]_D$=+71.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.58 (dd, 2H, $J_{6a,6b}$=10.9 Hz, $J_{5,6a}$=4.9 Hz, H-6a), 3.61 (dd, 2H, $J_{5,6b}$=4.9 Hz, H-6b), 3.84 (d, 2H, $J_{1a,1b}$=12.7 Hz, H-1a), 3.87 (dd, 2H, $J_{3,4}$=3.8 Hz, $J_{4,5}$=6.8 Hz, H-4), 4.06 (d, 2H, H-3), 4.12 (d, 2H, H-1b), 4.20 (dt, 2H, H-5), 4.43–4.73 (m, 12H, CH_2Ph), 7.26–7.33 (m, 30H, Ph); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 59.9 (C-1), 68.0 (C-6), 72.2, 72.7, 73.5 (*C*H$_2$Ph), 79.3 (C-5), 83.2 (C-4), 88.0 (C-3), 105.4 (C-2), 127.5–138.1 (Ph); FABMS: *m*/*z* 887 (100%, [M+Na]$^+$). Anal. Calcd for $C_{54}H_{56}O_{10}$: C, 74.98; H, 6.52; found: C, 74.77; H, 6.29.

3.2.2. 3,4,6,3′,4′,6′-Hexa-*O*-allyl-di-α-D-fructofuranose 1,2′:2,1′-dianhydride (3b). R_f=0.60 (1:3 EtOAc–petroleum ether); $[\alpha]_D$=+92.1 (*c* 0.55, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.52 (dd, 2H, $J_{5,6a}$=5.4 Hz, $J_{6a,6b}$=11.0 Hz, H-6a), 3.56 (dd, 2H, $J_{5,6b}$=4.9 Hz, H-6b), 3.70 (dd, 2H, $J_{3,4}$=3.9 Hz, $J_{4,5}$=6.7 Hz, H-4), 3.71 (d, 2H, $J_{1a,1b}$=12.8 Hz, H-1a), 3.86 (d, 2H, H-3), 3.97 (d, 2H, H-1b), 4.01 (m, 2H, H-5), 4.00–4.18 (m, 12H, CH_2O), 5.14–5.29 (m, 12H, CH_2=CH), 5.83–5.93 (m, 6H, CH_2=C*H*); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 59.7 (C-1), 69.8 (C-6), 71.2, 71.4, 72.4 (6CH_2O), 79.3 (C-5), 83.2 (C-4), 87.9 (C-3), 105.4 (C-2), 117.0, 117.3, 117.6 (6CH=*C*H$_2$), 134.2, 134.5, 134.7 (6*C*H=CH$_2$). Anal. Calcd for $C_{30}H_{44}O_{10}$: C, 63.81; H, 7.85; found: C, 63.46; H, 8.05.

3.2.3. 3,4,6,3′,4′,6′-Hexa-*O*-benzoyl-di-α-D-fructofuranose 1,2′:2,1′-dianhydride (3c). R_f=0.21 (1:20 EtOAc–toluene); $[\alpha]_D$=−1.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.17 (d, 2H, $J_{1a,1b}$=12.2 Hz, H-1a), 4.21 (d, 2H, H-1b), 4.58 (ddd, 2H, $J_{4,5}$=5.4 Hz, $J_{5,6a}$=4.9 Hz, $J_{5,6b}$=3.1 Hz, H-5), 4.66 (dd, 2H, $J_{6a,6b}$=11.9 Hz, H-6a), 4.79 (dd, 2H, H-6b), 5.55 (dd, 2H, $J_{3,4}$=1.8 Hz, H-4), 5.77 (d, 2H, H-3), 7.39–8.07 (m, 30H, Ph); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 60.8 (C-1), 63.0 (C-6), 80.0 (C-3), 80.4 (C-5), 78.4 (C-4), 103.8 (C-2), 128.2–133.5 (Ph), 164.7, 165.6, 166.0 (CO); FABMS: *m*/*z* 971 (100%, [M+Na]$^+$). Anal. Calcd for $C_{54}H_{44}O_{16}$: C, 68.35; H, 4.67; found: C, 68.20; H, 4.51.

3.2.4. 3,4,6-Tri-*O*-benzyl-α-D-fructofuranose 3,4,6-tri-*O*-benzyl-β-D-fructofuranose 1,2′:2,1′-dianhydride (4a). R_f=0.32 (1:4 EtOAc–petroleum ether); $[\alpha]_D$=−5.2 (*c* 3.4, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.46 (d, 1H, $J_{1'a,1'b}$=10.5 Hz, H-1′a), 3.60 (dd, 1H, $J_{5',6'a}$=5.8 Hz, $J_{6'a,6'b}$=9.6 Hz, H-6′a), 3.67 (dd, 1H, $J_{5',6'b}$=6.8 Hz, H-6′b), 3.68 (dd, 1H, $J_{5,6a}$=5.1 Hz, $J_{6a,6b}$=10.8 Hz, H-6a), 3.75 (dd, 1H, $J_{5,6b}$=4.6 Hz, H-6b), 3.84 (1H, d, $J_{1a,1b}$=13.1 Hz, H-1a), 3.95 (1H, dd, $J_{3,4}$=2.0 Hz, $J_{4,5}$=5.4 Hz, H-4), 4.04 (d, 1H, H-3), 4.14 (m, 1H, H-5), 4.15 (d, 1H, H-1′b), 4.18 (d, 1H, H-1b), 4.20 (m, 1H, H-3′), 4.21 (m, 1H, H-4′), 4.27 (bdd, 1H, H-5′), 4.39–4.74 (m, 12H, CH_2Ph), 7.21–7.31 (m, 30H, Ph); ^{13}C NMR (125.5 MHz, $CDCl_3$) δ 62.5 (C-1), 63.3 (C-1′), 70.1 (C-6), 71.6 (C-6′), 71.9, 72.0, 72.2, 72.4, 73.2, 73.4 (*C*H$_2$Ph), 80.2 (C-5), 81.8 (C-4′), 83.6 (C-4), 84.7 (C-5′), 88.2 (C-3, C-3′), 99.6 (C-2′), 102.5 (C-2), 127.4–138.1 (Ph); FABMS: *m*/*z* 887 (100%, [M+Na]$^+$). Anal. Calcd for $C_{54}H_{56}O_{10}$: C, 74.98; H, 6.52. Found: C, 75.05; H, 6.50.

3.2.5. 3,4,6-Tri-*O*-allyl-α-D-fructofuranose 3,4,6-tri-*O*-allyl-β-D-fructofuranose 1,2′:2,1′-dianhydride (4b). R_f=0.40 (1:3 EtOAc–petroleum ether); $[\alpha]_D$=+4.3 (*c* 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.46 (d, 1H, $J_{1'a,1'b}$=11.5 Hz, H-1′a), 3.51 (dd, 1H, $J_{5',6'a}$=6.4 Hz, $J_{6'a,6'b}$=9.8 Hz, H-6′a), 3.58 (dd, 1H, $J_{5',6'b}$=5.8 Hz, H-6′b), 3.59 (dd, 1H, $J_{5,6a}$=3.1 Hz, $J_{6a,6b}$=11.5 Hz, H-6a), 3.61 (dd, 1H, $J_{5,6b}$=3.8 Hz, H-6b), 3.65 (d, 1H, $J_{3',4'}$=6.2 Hz, H-3′), 3.69, (d, 1H, $J_{1a,1b}$=12.0 Hz, H-1a), 3.75 (dd, 1H, $J_{3,4}$=2.6 Hz, $J_{4,5}$=5.8 Hz, H-4), 3.84 (d, 1H, H-3), 4.01 (m, 1H, H-4′), 4.03 (m, 1H, H-5), 4.06 (m, 1H, H-5′), 4.06 (d, 1H, H-1b),

3.95–4.12 (m, 12H, CH_2O), 4.14 (d, 1H, H-1′b), 5.10–5.30 (m, 12H, CH_2=CH), 5.78–5.92 (m, 6H, CH_2=C*H*); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 62.7 (C-1), 63.5 (C-1′), 70.3 (C-6), 71.9 (C-6′), 70.9, 71.1, 71.2, 71.9, 72.3, 72.4 (CH_2O), 80.1 (C-5), 81.4 (C-5′), 83.8 (C-4), 84.6 (C-3′), 84.7 (C-4′), 88.3 (C-3), 99.6 (C-2′), 102.4 (C-2), 116.8, 117.1, 117.2, 117.3, 117.4, 117.9 (CH=*C*H_2), 134.0, 134.3, 134.4, 134.5, 134.6, 134.8 (*C*H=CH_2). Anal. Calcd for $C_{30}H_{44}O_{10}$: C, 63.81; H, 7.85; found: C, 63.74; H, 7.79.

3.2.6. 3,4,6-Tri-*O*-benzoyl-α-D-fructofuranose 3,4,6-tri-*O*-benzoyl-β-D-fructofuranose 1,2′:2,1′-dianhydride (4c). R_f=0.58 (1:2 EtOAc–petroleum ether); $[\alpha]_D$=−46.0 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.90 (d, 1H, $J_{1'a,1'b}$=11.8 Hz, H-1′a), 3.98 (d, 1H, $J_{1a,1b}$=11.9 Hz, H-1a), 4.38 (d, 1H, H-1b), 4.42 (d, 1H, H-1′b), 4.50 (ddd, 1H, $J_{4',5'}$=4.9 Hz, $J_{5',6'a}$=3.5 Hz, $J_{5,6b}$=4.3 Hz, H-5′), 4.63 (m, 1H, H-5), 4.67 (dd, 1H, $J_{5,6a}$=4.5 Hz, $J_{6a,6b}$=12.1 Hz, H-6a), 4.74 (dd, 1H, $J_{5,6b}$=3.4 Hz, H-6b), 4.82 (dd, 1H, $J_{6'a,6'b}$=10.5 Hz, H-6′a), 4.84 (dd, 1H, H-6′b), 5.52 (dd, 1H, $J_{3,4}$=1.1 Hz, $J_{4,5}$=4.9 Hz, H-4), 5.66 (d, 1H, H-3), 5.69 (1H, d, $J_{3',4'}$=6.8 Hz, H-3′), 6.03 (1H, dd, $J_{4',5'}$=4.9 Hz, H-4′), 7.10–8.10 (m, 30H, Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 61.7 (C-1), 63.1 (C-1′), 63.6 (C-6), 70.1 (C-6′), 77.3 (C-4), 78.9 (C-5), 80.2 (C-5′), 81.9 (C-3), 83.6 (C-4′), 88.2 (C-3′), 99.9 (C-2′), 102.1 (C-2), 128.0–133.5 (Ph), 164.5–166.0 (CO); FABMS: *m*/*z* 971 (100%, $[M+Na]^+$). Anal. Calcd for $C_{54}H_{44}O_{16}$: C, 68.35; H, 4.67; found: C, 68.52; H, 4.86.

3.2.7. 3,4,5,3′,4′,5′-Hexa-*O*-benzyl-di-β-D-fructopyranose 1,2′:2,1′-dianhydride (7a). R_f=0.47 (1:2 EtOAc–petroleum ether); $[\alpha]_D$=−88.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.59 (d, 2H, $J_{1a,1b}$=12.1 Hz, H-1a), 3.67 (dd, 2H, $J_{5,6a}$=0.5 Hz, $J_{6a,6b}$=11.6 Hz, H-6a), 3.75 (dd, 2H, $J_{5,6b}$=1.8 Hz, H-6b), 3.77 (m, 2H, H-5), 3.85 (d, 2H, H-1b), 3.91 (d, 2H, $J_{3,4}$=9.8 Hz, H-3), 4.02 (d, 2H, $J_{4,5}$=3.0 Hz, H-4), 4.63–4.95 (m, 12H, C*H*$_2$Ph), 7.20–7.35 (m, 30H, Ph); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 62.8 (C-6), 63.3 (C-1), 68.7 (C-4), 70.3 (C-5), 71.6 (C-3), 71.7, 72.5, 74.6 (CH_2O), 97.3 (C-2), 127.2–138.9 (Ph). Anal. Calcd for $C_{30}H_{44}O_{10}$: C, 74.98; H, 6.53; found: C, 74.84; H, 6.36.

3.2.8. 3,4,5,3′,4′,5′-Hexa-*O*-allyl-di-β-D-fructopyranose 1,2′:2,1′-dianhydride (7b). R_f=0.50 (1:2 EtOAc–petroleum ether); $[\alpha]_D$=−138.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.58 (d, 2H, $J_{3,4}$=9.8 Hz, H-3), 3.60 (d, 2H, $J_{1a,1b}$=11.8 Hz, H-1a), 3.68 (dd, 2H, $J_{6a,6b}$=13.2 Hz, $J_{5,6a}$=1.9 Hz, H-6a), 3.72 (m, 2H, H-5), 3.73 (dd, H, $J_{5,6b}$=1.9 Hz, H-6b), 3.81 (d, 2H, $J_{4,5}$=3.1 Hz, H-4), 4.00 (d, 2H, H-1b), 4.09–4.18 (m, 11H, CH_2O), 4.35 (ddt, 1H, $^2J_{H,H}$=12.4 Hz, $^3J_{H,H}$=2.5 Hz, $^4J_{H,H}$=1.3 Hz, CH_2O), 5.08–5.31 (m, 12H, C*H*$_2$=CH), 5.85–5.97 (m, 6H, CH_2=C*H*); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 61.6 (C-6), 64.5 (C-1), 71.0, 71.2, 74.0 (CH_2O), 73.8 (C-5), 77.8 (C-4), 78.7 (C-3), 97.0 (C-2), 116.7, 116.8, 117.3 (CH=*C*H_2), 135.1, 135.2, 135.3 (*C*H=CH_2). Anal. Calcd for $C_{30}H_{44}O_{10}$: C, 63.81; H, 7.85; found: C, 63.81; H, 7.88.

3.2.9. 3,4,5,3′,4′,5′-Hexa-*O*-benzoyl-di-β-D-fructopyranose 1,2′:2,1′-dianhydride (7c). R_f=0.31 (1:2 EtOAc–petroleum ether); $[\alpha]_D$=−226.5 (*c* 0.38, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.84 (d, 2H, $J_{1a,1b}$=12.6 Hz, H-1a), 4.05 (dd, 2H, $J_{5,6a}$=1.3 Hz, $J_{6a,6b}$=13.2 Hz, H-6a), 4.15 (d, 2H, H-1b), 4.23 (dd, 2H, $J_{5,6b}$=1.0 Hz, H-6b), 5.70 (m, 2H, H-5), 5.83 (dd, 2H, $J_{3,4}$=10.7 Hz, $J_{4,5}$=3.5 Hz, H-4), 5.97 (d, 2H, H-3), 7.09–8.10 (m, 30H, Ph); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 62.8 (C-6), 63.3 (C-1), 68.7 (C-4), 70.3 (C-5), 71.6 (C-3), 97.3 (C-2), 128.1–133.6 (Ph), 164.4–171.7 (CO); FABMS: *m*/*z* 971 (100%, $[M+Na]^+$). Anal. Calcd for $C_{54}H_{44}O_{16}$: C, 68.35; H, 4.67; found: C, 68.22; H, 4.54.

3.2.10. 3,4,5-Tri-*O*-benzyl-α-D-fructopyranose 3,4,5-tri-*O*-benzyl-β-D-fructopyranose 1,2′:2,1′-dianhydride (8a). R_f=0.44 (1:2 EtOAc–petroleum ether) $[\alpha]_D$=−36.9 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.33 (d, 1H, $J_{1'a,1'b}$=11.6 Hz, H-1′a), 3.54 (d, 1H, $J_{5,6a}$=0 Hz, $J_{6a,6b}$=12.6 Hz, H-6a), 3.66 (dd, 1H, $J_{5',6'a}$=3.7 Hz, $J_{6'a,6'b}$=11.0 Hz, H-6′a), 3.71 (d, 1H, $J_{1a,1b}$=11.6 Hz, H-1a), 3.73 (m, 1H, H-5), 3.77 (d, 1H, $J_{3',4'}$=9.8 Hz, H-3′), 3.77 (d, 1H, H-1′a), 3.79 (m, 2H, H-3, H-4), 3.82 (dd, 1H, $J_{5,6b}$=1.8 Hz, H-6b), 3.87 (m, 1H, H-5′), 3.97 (dd, 1H, $J_{5',6'b}$=2.3 Hz, H-6′b), 4.02 (dd, 1H, $J_{4',5'}$=3.1 Hz, H-4′), 4.18 (1H, d, H-1′b), 4.44–5.02 (m, 12H, C*H*$_2$Ph), 7.24–7.37 (m, 30H, Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 58.9 (C-6′), 60.6 (C-6), 61.2 (C-1), 61.3 (C-1′), 72.3 (C-5′), 71.3, 71.4, 72.1, 72.3, 73.5, 75.4 (*C*H_2Ph), 73.7 (C-4), 73.9 (C-3), 76.1 (C-3′), 77.6 (C-5), 78.3 (C-4′), 94.5 (C-2′), 95.8 (C-2), 127.5–138.5 (Ph); FABMS: *m*/*z* 887 (100%, $[M+Na]^+$). Anal. Calcd for $C_{54}H_{56}O_{10}$: C, 74.98; H, 6.52; found: C, 74.86; H, 6.54.

3.2.11. 3,4,5-Tri-*O*-allyl-α-D-fructopyranose 3,4,5-tri-*O*-allyl-β-D-fructopyranose 1,2′:2,1′-dianhydride (8b). R_f=0.40 (1:2 EtOAc–petroleum ether); $[\alpha]_D$=−34.6 (*c* 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.39 (d, 1H, $J_{1'a,1'b}$=11.4 Hz, H-1′a), 3.47 (d, 1H, $J_{3',4'}$=9.8 Hz, H-3′), 3.55 (d, 1H, $J_{3,4}$=3.0 Hz, H-3), 3.56 (d, 1H, $J_{1a,1b}$=12.1 Hz, H-1a), 3.59 (dd, 1H, $J_{5,6a}$=4.0 Hz, $J_{6a,6b}$=11.1 Hz, H-6a), 3.64 (dd, 1H, $J_{4,5}$=5.0 Hz, H-4), 3.73 (m, 4H, H-5, H-5′, H-6′a, H-6′b), 3.78 (d, 1H, H-1b), 3.79 (dd, 1H, $J_{4',5'}$=2.7 Hz, H-4′), 3.87 (dd, 1H, $J_{5,6b}$=4.0 Hz, H-6b), 3.99–4.15 (m, 11H, CH_2O), 4.21 (d, 1H, H-1′b), 4.35 (ddt, 1H, $^2J_{H,H}$=12.6 Hz, $^3J_{H,H}$=5.3 Hz, $^4J_{H,H}$=1.3 Hz, CH_2O), 5.09–5.17 (m, 12H, C*H*$_2$=CH), 5.80–5.95 (m, 6H, CH_2=C*H*); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 58.8 (C-6), 60.8 (C-1), 61.1 (C-6′), 61.4 (C-1′), 72.1 (C-5′), 73.7 (C-3′), 74.1 (C-5), 70.4, 70.9, 71.4, 71.6, 72.6, 74.6 (6CH_2O), 76.2 (C-4), 77.6 (C-3, C-4′), 94.3 (C-2′), 95.8 (C-2), 116.8, 116.9, 117.0, 117.2, 117.3, 117.4 (6CH=*C*H_2), 134.5, 134.9, 135.0, 135.1, 135.2, 135.3 (6*C*H=CH_2). Anal. Calcd for $C_{30}H_{44}O_{10}$: C, 63.81; H, 7.85; found: C, 63.98; H, 7.90.

3.2.12. 3,4,5-Tri-*O*-benzoyl-α-D-fructopyranose 3,4,5-tri-*O*-benzoyl-β-D-fructopyranose 1,2′:2,1′-dianhydride (8c). R_f=0.31 (1:2 EtOAc–petroleum ether); $[\alpha]_D$=−119.4 (*c* 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.83 (d, 1H, $J_{1'a,1'b}$=11.7 Hz, H-1′a), 3.89 (dd, 1H, $J_{5,6a}$=5.9 Hz, $J_{6a,6b}$=11.1 Hz, H-6a), 3.93 (d, 1H, $J_{1a,1b}$=11.5 Hz, H-1a), 3.95 (d, 1H, H-1b), 4.08 (d, 1H, H-1′b), 4.10 (m, 2H, H-6′a, H-6′b), 4.13 (dd, 1H, $J_{5,6b}$=10.6 Hz, H-6b), 5.56 (d, 1H, $J_{3,4}$=3.7 Hz, H-3), 5.61 (ddd, 1H, $J_{4,5}$=3.3 Hz, H-5), 5.73 (m, 1H, H-5′), 5.76 (d, 1H, $J_{3',4'}$=10.5 Hz, H-3′), 5.87 (dd, 1H, $J_{4,5}$=3.0 Hz, H-4), 7.22–8.15 (m, 30H, Ph); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 58.9 (C-6′), 60.6 (C-6), 61.2 (C-1), 61.3 (C-1′), 72.3 (C-5′), 73.7 (C-4), 73.9 (C-3), 76.1

(C-3′), 77.6 (C-5), 78.3 (C-4′), 94.5 (C-2′), 95.8 (C-2), 128.1–133.6 (Ph), 164.4–171.7 (CO); FABMS: *m/z* 971 (100%, $[M+Na]^+$).

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