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Spacer-Mediated Synthesis of Contra-Thermodynamic Spiroacetals: Stereoselective Synthesis of C_2-Symmetric Difructose Dianhydrides

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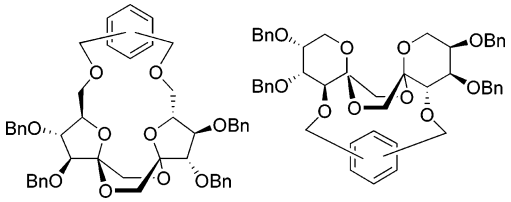

The xylylene moiety (ortho, meta, and para) was employed as a rigid tether in the spacer-mediated synthesis of difructose dianhydrides (DFAs), a unique class of bis-spiroacetal derivatives present in food products. The synthetic methodology exploits the suitability of triflic acid to promote spirocyclization in organic solvents under irreversible reaction conditions, using anomeric isopropylidene fructose derivatives as precursors. Advantage was taken of the strong dependence of the conformational properties of DFAs on the relative configuration of the spiroketal centers. Highly stereoselective syntheses of the contra-thermodynamic difructofuranose and difructopyranose diastereomers, namely the C_2-symmetric derivatives having the β-configuration at both anomeric centers, have been accomplished by judicious choice of the xylylene positional isomer and of the linking position to the fructose building blocks. Interestingly, the rigid spacer concept has also been implemented to favor intermolecular processes leading to higher macrocyclic architectures that incorporate the bis-spiro fructodisaccharide subunit.

1. Introduction

Spiroacetal substructures are widely distributed in natural compounds with diverse origins, including plants, fungi, marine organisms, and insects.[1] Many of these compounds exhibit important biological activities, and consequently, there is a sustained interest in the stereocontrolled construction of these moieties.[2] Most methods rely on the acid-catalyzed cyclization of a ketodiol intermediate and thus lead to a thermodynamic mixture of spiroacetals. When all factors that control spiroketalization, i.e., a maximum anomeric effect and minimum steric interactions, are reinforcing, a major isomer is produced. In a number of natural products, however, these factors are in conflict, and these contra-thermodynamic acetals have been more difficult to access.[3] The difficulty is exacerbated for polyfunctional tricyclic bis-spiroacetal systems, since then a range of structures can usually accommodate the basic requirements, that is, oxygen substituents at spiroacetal centers in axial orientation and carbon substituents in equatorial disposition, with small differences in energy and low interconversion barriers. This basic framework is the prevalent underlying structural element of a unique class of spirodisaccharides isolated from microorganisms and higher plants, namely di-D-fructose dianhydrides (DFAs).[4] The identification of DFAs as the major oligosaccharide components in some food products, such as caramel or chicory,[5] and their promising prebiotic properties[4,6] have provided a further impetus to the synthesis of these and related spirosugars.[7]

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(1) For reviews, see: (a) Mead, K. T.; Brewer, B. N.*Curr. Org. Chem.* **2003**, *7*, 227−256. (b) M. A. Brimble, D. P. Furkert, *Curr. Org. Chem.* **2003**, *7*, 1−24. (c) Brimble, M. A.; Farès, F. A. *Tetrahedron* **1999**, *55*, 7661−7706. (d) Pietruszka, J. *Angew. Chem., Int. Ed.* **1998**, *37*, 2629−2636. (e) Perron, F.; Albizati, K. F. *Chem. Rev.* **1989**, *89*, 1617−1661.

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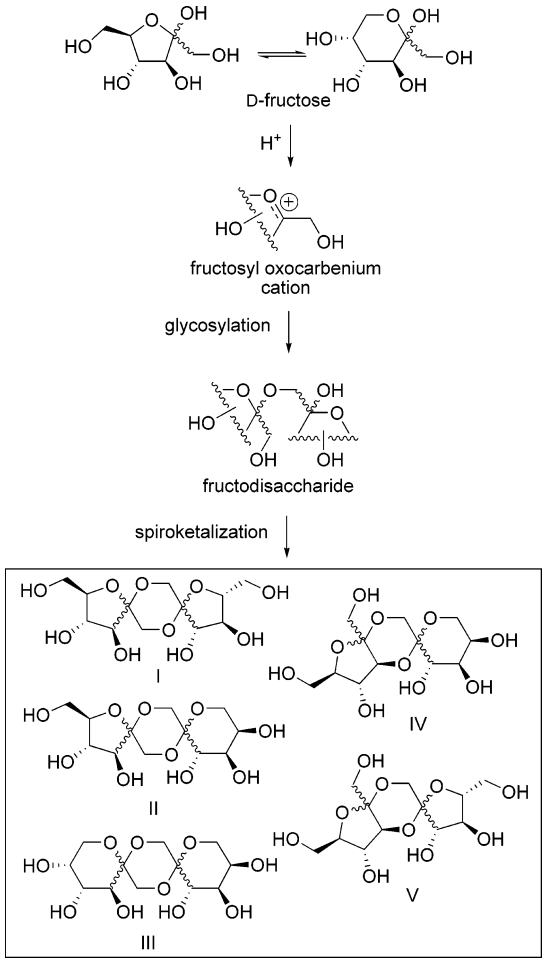
DFAs are formed during protonic activation of fructose-containing materials. Under such conditions, a fructosyl oxocarbenium cation is generated, which undergoes in situ glycosylation to the corresponding ketodisaccharide. Further spiroacetalization is a reversible process that leads to a complex mixture of spirodisaccharides in which the two D-fructose constituents are joined through a central 1,4-dioxane ring. Up to five different tricyclic cores and 13 DFA isomers that differ in the ring size, linking position, and stereochemistry of the acetal stereocenters have been identified from reaction mixtures (Scheme 1).[8] This structural and stereochemical diversity makes DFAs ideal targets for evaluating new synthetic methodologies.

Thermodynamic DFAs have different configurations (α,*β*) at the acetal centers and can position all oxygens to favor double anomeric stabilization at each of them with the central 1,4-dioxane ring in a chair conformation (Figure 1a). These DFAs have been previously prepared by setting up an equilibrium and then separating the major isomers.[4,8] Such a scenario does not prevail in the case of DFAs having identical configurations at both acetal centers (α,α or *β*,*β*), for which full anomeric and steric stabilization is not possible because one of the ring oxygens would be necessarily equatorial in the chair arrangement (Figure 1b). These contra-thermodynamic DFAs tend to adopt instead a boat or skew-boat conformation at the central ring, the gain on steric energy being compensated by a more efficient anomeric effect stabilization (Figure 1c).[9]

SCHEME 1. Spiroacetal Disaccharide Cores (Types I−V) Formed by Acid Treatment of D-Fructose



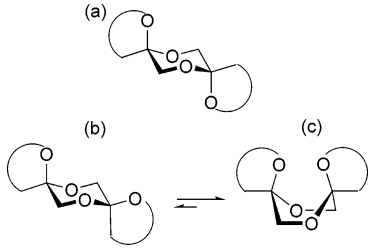


FIGURE 1. Chair (a and b) and boat (c) conformational arrangements at the central 1,4-dioxane ring in thermodynamic (α,*β*; up) and contra-thermodynamic DFAs (α,α or *β*,*β*; down).

We have previously reported the stereoselective preparation of some α,*β*-thermodynamic and α,α-contra-thermodynamic DFAs by using participating or nonparticipating protecting group

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(3) The term "contra-thermodynamic" designates diastereomers that are energetically strongly disfavored and, consequently, cannot be access under reversible kinetics or thermodynamic conditions. For remarkable recent examples of stereoselective syntheses of contra-thermodynamic spiroacetal frameworks, see: (a) Takaoka, L. R.; Buckmelter, A. J.; LaCruz, T. E.; Rychnovsky, S. D. *J. Am. Chem. Soc*. **2005**, *127*, 528−529. (b) LaCruz, T. E.; Rychnovsky, S. D. *Org. Lett*. **2005**, *7*, 1873−1875.

(4) For a review, see: Manley-Harris, M.; Richards, G. N. *Adv. Carbohydr. Chem. Biochem.* **1997**, *52*, 207−266.

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(8) (a) Defaye, J.; García Fernández, J. M. *Carbohydr. Res.* **1994**, *251*, 1−15. (b) Defaye, J.; García Fernández, J. M. *Carbohydr. Res.* **1994**, *251*, 17−31. (c) Defaye, J.; García Fernández, J. M. *Carbohydr. Res.* **1992**, *237*, 223−247.

(9) Bock, K.; Pedersen, C.; Defaye, J.; Gadelle, A. *Carbohydr. Res.* **1991**, *216*, 141−148.

motifs that shift the reaction outcome in the desired direction under irreversible reaction conditions.[10] A main limitation of this approach was, however, its unsuitability to access the *β*,*β*-contra-thermodynamic bis-spiroacetals. We speculated that the above-mentioned conformational differences could be exploited in the design of stereoselective syntheses of the elusive thermodynamically unfavored DFA diastereomers. In this paper, we utilize an approach that employs a rigid spacer judiciously installed between the ketose moieties under reaction for the remote control of the stereochemistry at the newly formed spirocenters.[11] Two conceptually different strategies have been explored and compared, namely the use of xylylene positional isomer spacers to promote intramolecular or, conversely, intermolecular glycosylation−bis-spiroketalization. The synthesis of the precursors, the influence of the tether structure on the reaction outcome, and the scope and limitations of the methods to access C_2-symmetric bis-spiroacetals with the 1,6,9,13-tetraoxadispiro[4.2.4.2]tetradecane and 1,7,10,15-tetraoxadispiro[5.2.5.2]hexadecane cores (type I and type III DFAs) are discussed.

2. Results and Discussion

2.1. Retrosynthetic Analysis. Our strategy for the stereoselective synthesis of D-fructose-derived bis-spiroacetal derivatives stems from the analysis of the particular conformational properties of these compounds as dictated by stereoelectronic factors. Three difuranoid type I DFAs, namely the nonsymmetric α,*β* and the C_2-symmetric α,α and *β*,*β* isomers (**1**−**3**), and two dipyranoid type III DFAs, the α,*β* and *β*,*β* isomers (**4** and **5**, respectively), are known. Examination of the respective molecular models revealed remarkable differences in the atomic distances between homologous hydroxyl groups at the two D-fructose subunits as a function of the relative stereochemistry of the spiroacetal centers, assuming the limit chair and boat arrangements at the central 1,4-dioxane ring. Thus, the primary hydroxyl groups must be significantly closer in **2** and **3** as compared with the thermodynamic DFA **1**, while the distance between the hydroxyl groups at positions C-3 and C-3′ should be above 2 Å shorter in the contra-thermodynamic dipyranose isomer **5** as compared with **4** (Figure 2). Consequently, the introduction of a distance restriction between these nonreacting hydroxyls was contemplated as a means for configurational control.

To check this concept, some prior considerations are important. First, the ring size of the fructose precursors must be preserved during the glycosylation−spiroketalization process. Second, both the protecting groups and the tether group must be stable under the acidic conditions needed for spiroacetal formation and easily removable in a later step. Third, since contra-thermodynamic spiroacetals have a strong tendency to isomerize to give the thermodynamic derivatives, the spiroketalization reaction must be carried out under irreversible reaction conditions. Following our previous work on the activation of anomeric isopropylydene groups in benzyl-protected fructose derivatives with trifluoromethanesulfonic acid,[10b] we conceived the use of xylylene positional isomer spacers to comply with those requirements.[11]

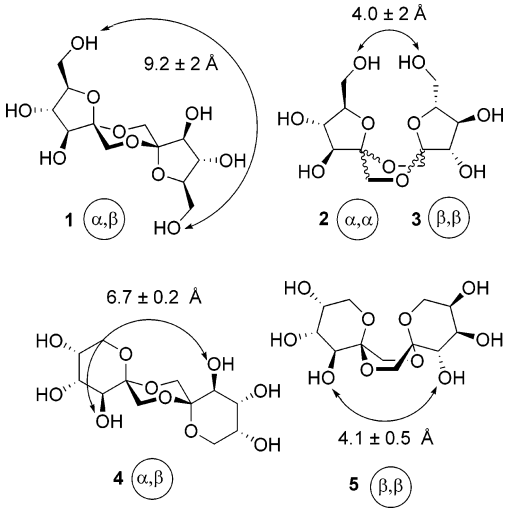


FIGURE 2. Conformations of the known type I (**1**−**3**) and type III (**4** and **5**) DFAs with indication of the O-6−O-6′ and O-3−O-3′ interatomic distances, respectively.

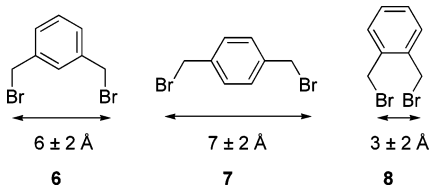


FIGURE 3. Interatomic distances between the benzylic methylene carbon atoms in the α,α′-dibromoxylene positional isomers **6**−**8**.

Preliminary calculations indicated that *m*- and *o*-xylylene bridges might provide the appropriate distance to favor the boat arrangement upon intramolecular bis-spirocyclization (Figure 3). The *p*-xylylene positional isomer would give rise to rather constrained intramolecular bis-spiroacetals, both in the case of chair or boat arrangements. Consequently, the intermolecular reaction, leading initially to a linear dimer, was expected to occur to a much greater extent. Interestingly, the molecular models suggested that further macrocyclization would be strongly favored in the case of the C_2-symmetric contra-thermodynamic derivatives, featuring a concave shape, while the nonsymmetric thermodynamic derivatives would rather tent to oligomerize. A comparative study of the reactivity of the *m*-, *o*-, and *p*-xylylene-bridged precursors seemed, therefore, intriguing.

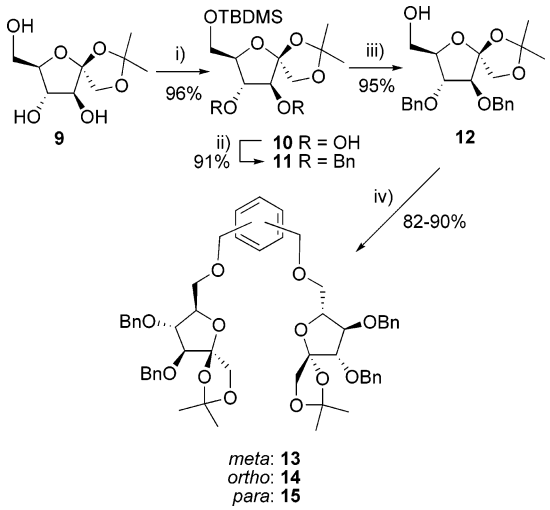
2.2. Synthesis of Xylylene-Tethered D-Fructose Precursors. To install the xylylene tether onto the D-fructofuranose scaffold, the reaction sequence depicted in Scheme 2 was implemented. Regioselective *tert*-butyldimethylsilylation of the primary hydroxyl in the 1,2-*O*-isopropylidene derivative **9** (→ **10**), available in one step from the commercial monosaccharide,[12] followed by protection of the secondary hydroxyls as benzyl ethers (→ **11**), fluorolysis of the silyl group (→ **12**), and nucleophilic substitution reaction of the resulting alcohol with the corre-

(10) (a) Benito, J. M.; Gómez-García, M.; Ortiz Mellet, C.; García Fernández, J. M.; Defaye, J. *Org. Lett.* **2001**, *3*, 549−552. (b) Benito, J. M.; Rubio, E. M.; Gómez-García, M.; Ortiz Mellet, C.; García Fernández, J. M. *Tetrahedron* **2004**, 60, 5899−5906.

(11) The rigid spacer concept has been previously exploited in anomeric configuration control during glycosidic bond-forming reactions. See: (a) Müller, M.; Huchel, U.; Geyer, A.; Schmidt, R.-R. *J. Org. Chem.* **1999**, *64*, 6190−6201. (b) Jung, K.-H.; Müller, M.; Schmidt, R.-R. *Chem. Rev.* **2000**, *100*, 4423−4442. (c) Müller, M.; Schmidt, R.-R. *Eur. J. Org. Chem.* **2001**, 2055−2066. For a preliminary communication on the extension of this concept to the synthesis of C_2-symmtric carbohydrate-derived spiroacetals, see: (d) Rubio, E. M.; Ortiz Mellet, C.; García Fernández, J. M. *Org. Lett.* **2003**, *5*, 873−876.

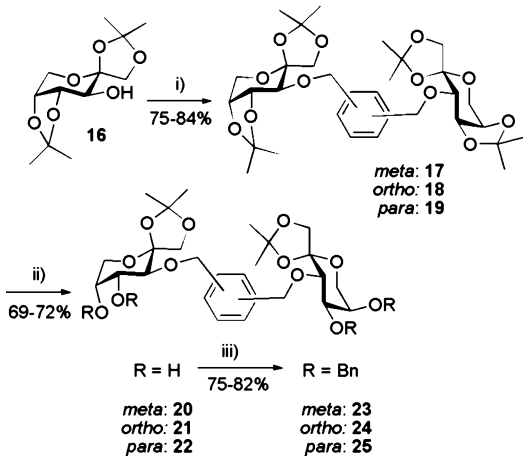
(12) Chittenden, G. J. F. *J. Chem. Soc., Chem. Commun.* **1980**, 882−883.

SCHEME 2. Tethering Reaction Sequence for Difructofuranose Derivatives[a]



[a] Reagents and conditions: (i) TBDMSCl, imidazole, DMF, rt, 16 h; (ii) BnBr, NaH, DMF, rt, 5 h; (iii) TBAF, THF, 0 °C, 3 h; (iv) NaH, DMF, **6**−**8**, rt, 1 h.

SCHEME 3. Tethering Reaction Sequence for Difructopyranose Derivatives[a]



[a] Reagents and conditions: (i) NaH, DMF, **6**−**8**, rt, 1 h; (ii) 60% aq AcOH, 45 °C, 2 h; (iii) BnBr, NaH, DMF, rt, 4 h.

sponding α,α′-dibromoxylene **6**−**8** afforded the target dimers **13**−**15**. The preparation of the D-fructopyranose analogues **23**−**25** started by the tethering reaction of the readily available 1,2:4,5-diacetonide **16**[13] (→ **17**−**19**). Regioselective hydrolysis of the nonanomeric acetal group (→ **21**−**23**) and subsequent benzylation provided the desired C_2-symmetric precursors (Scheme 3).

2.3. Synthesis of Fructofuranosyl Bis-spiroacetals (Type I DFAs). Activation of the xylylene-tethered difuranose derivatives **13**−**15** with trifluoromethanesulfonic acid (TfOH) in dichloromethane promoted the tandem isopropylidene cleavage−glycosylation−spiroketalization transformation. In the three cases, two groups of products, accounting for 82−94% of the total reaction mixture, were formed, corresponding to the intramolecular reaction compounds (**26** and **27**; **29** and **30**; and **32** and **33**) and the macrocyclic derivatives resulting from double bis-spirocylization (**28**, **31**, and **34**, respectively), as seen from mass spectrometry data. In the case of the *m*-xylylene derivative, the intramolecular fraction (78%) consisted of an inseparable 1:2 mixture of the tetracyclic spiro-disaccharides having the α,*β* (**26**) and α,α (**27**) configuration at the new stereogenic centers. The thermodynamic α,*β* isomer was not detected in the corresponding fraction obtained from the *o*- and *p*-xylylene-tethered derivatives, which contained exclusively the contrathermodynamic C_2-symmetric bis-spirocetals with α,α (**29** and **32**) and *β*,*β* (**30** and **33**) anomeric configurations. Compounds **29** and **30** (88% yield, 1:9 relative proportion) could be separated and characterized in pure form. In the case of the *p*-xylylene derivative, the intramolecular reaction was actually disfavored (19% yield), affording a 4:1 mixture of **32** and **33** (Scheme 4).

Simultaneous removal of the xylylene spacer and the benzyl protecting groups was accomplished in quantitative yield by catalytic hydrogenolysis. The identity and the relative proportions of isomeric DFAs were established by gas chromatography after trimethylsilylation of the mixtures of the unprotected compounds **1**−**3** and comparison with authentic standards.[14] The pure spirodisaccharides could be obtained by column chromatography of the corresponding peracetylated products and further deacetylation as previously reported.[15−17] Hydrogenation of **29** and **30** separately afforded exclusively the pure bis-spirodisaccharides **2** and **3**, respectively, discarding any possible isomerization reaction during the deprotection step. Upon treatment with mineral acid in water solution, both **2** and **3** rapidly isomerized to give mixtures where the thermodynamic bis-spiroacetals, having α,*β* configuration at anomeric centers, were the predominating structures, thus confirming their contrathemodynamic character.

No pure compounds could be isolated from the respective macrocyclic fractions **28** (16%), **31** (6%), and **34** (68%). Catalytic hydrogenation of the crude mixtures provided the α,*β* (**1**) and α,α (**2**) diastereomers in 1:2 relative proportion in the three cases (Scheme 4).

It is worth mentioning that, using the above reaction conditions, the intermolecular dimerization of the unbridged tri-*O*-benzylated derivative of **1** afforded the corresponding α,*β* and α,α diastereomers in 3:1 relative proportion.[10b] In the intramolecular transformation, the xylylene spacer favors first the construction of a large ring upon the glycosylation step and then a boat conformation in the dioxane central ring during spiroacetalization, resulting in a reverse diastereoselection. In the intermolecular process, the second bis-spirocyclization reaction leading to macrocyclic derivatives is favored in the case of symmetric arrangements, which also result in the contrathermodynamic α,α framework being the major substructure.

The differences in the stereoselectivity of the above spirocyclization reactions as a function of the substitution pattern of the xylylene spacer are remarkable and must be ascribed to the interplay of stereoelectronic effects at the 1,4-dioxane ring and the geometrical constraints imposed by the rigid tether. It is known that stereoelectronic effects do also influence the conformations of the five-membered rings in DFAs. Thus, α-D-

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(14) Ratsimba, V.; García Fernández, J. M.; Defaye, J.; Nigay, H., Voilley, A. *J. Chromatogr. A* **1999**, *844*, 283−293.

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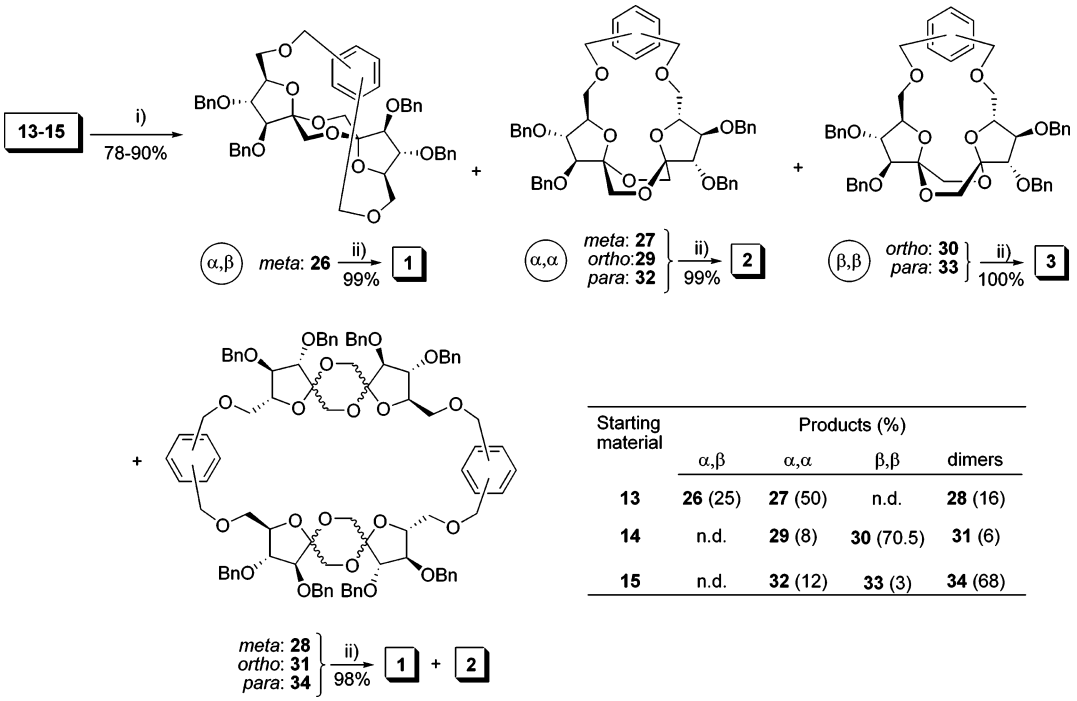
SCHEME 4. Synthesis of Type I DFAs[a]



Starting material	Products (%)			
	α,β	α,α	β,β	dimers
13	**26** (25)	**27** (50)	n.d.	**28** (16)
14	n.d.	**29** (8)	**30** (70.5)	**31** (6)
15	n.d.	**32** (12)	**33** (3)	**34** (68)

[a] Reagents and conditions: (i) TfOH, CH_2Cl_2, rt, 1 h (see table inset for yields; n.d.: not detected); (ii) 10% Pd/C, H_2, 1:1 EtOAc−MeOH, 10% HCOOH.

fructofuranose rings in DFA derivatives have been shown to adopt a rather rigid ^3E conformation by X-ray, ^{1}H NMR and molecular modeling data.[4] In *β*-linked D-fructofuranosyl moieties, however, skewed conformations around E_O are privileged.[4] As a consequence, the hydroxymethyl groups in C_2-symmetric difuranose DFA derivatives are further apart in the case of the di-α isomer **2** and drawn nearer in the case of the di-*β* counterpart **3**, which is in agreement with the later isomer being strongly favored for the shorter *o*-xylylene spacer. This represents the first stereoselective synthesis of this particular DFA, a minor constituent of fructose and sucrose caramel.[14]

2.4. Synthesis of Fructopyranosyl Bis-spiroacetals (Type III DFAs). Treatment of the *m*-xylylene-bridged difructopyranose derivative **23** with trifluoromethanesulfonic acid in dichloromethane led to a mixture of the corresponding bis-spirodisaccharides **35** (α,*β*) and **36** (*β*,*β*) in 1:4 relative proportion (59% yield), together with an inseparable mixture of macrocyclic products **37** (24% yield), resulting from double bis-spirocyclization reaction. Considering that the dimerization reaction of 3,4,5-tri-*O*-benzyl-1,2-*O*-isopropylydene-*β*-D-fructopyranose, an untethered analogue of **23**, led to a 25:1 ratio in favor of the α,*β*-diastereomer,[10b] the selectivity toward the C_2-symmetric *β*,*β* counterpart in the intramolecular reaction is increased by a factor of 100. Further shortening the intermonosaccharide distance by using the *o*-xylylene tether (**24**) afforded the di-*β* DFA derivative **38** as the sole intramolecular reaction product (42% yield) together with the corresponding macrocyclic compounds **39** (35%). Conversely, the larger *p*-xylylene bridge (**25**) totally prevented intramolecular spirocyclization, leading exclusively to the formation of the macrocyclic compounds **40** in 72% yield. Catalytic hydrogenolysis of **35** quantitatively yielded the fully deprotected thermodynamic type III DFA **4**, while **36** and **38** provided exclusively the contra-thermodynamic diastereomer **5** (Scheme 5).[18]

The lower yield, but higher stereoselectivity, of the intramolecular reactions in dipyranose derivatives, in comparison with the difuranose series, is probably due to the higher rigidity of the resulting tetracyclic systems as a consequence of the attachment of the xylylene segment to secondary hydroxyl groups. Noteworthy, a strong preference was also observed for the contra-thermodynamic *β*,*β*-structure in the macrocyclic fractions (**37**, **39**, and **40**). Thus, after catalytic hydrogenation the unprotected spiro-disaccharides **4** and **5** were obtained in 1:6 relative proportion. That strongly suggests that the first bis-spiroacetal formed in the intermolecular reaction acted as a tether-like template to control the stereochemical issues of the next intramolecular bis-spirocyclyzation process during macrocyclic ring formation.[19] Although no pure compounds could be isolated from the *m*- and *o*-xylylene-bridged macrocyclic fractions, in the case of the *p*-xylylene positional isomer the main reaction product could be separated by crystallization (35% yield). Single crystal X-ray diffraction let ascribe unequivocally the all-*β*,*β* **40** structure. Consequently, after catalytic hydrogenation the di-*β*-fructopyranose DFA **5** was the only reaction product (Scheme 5).

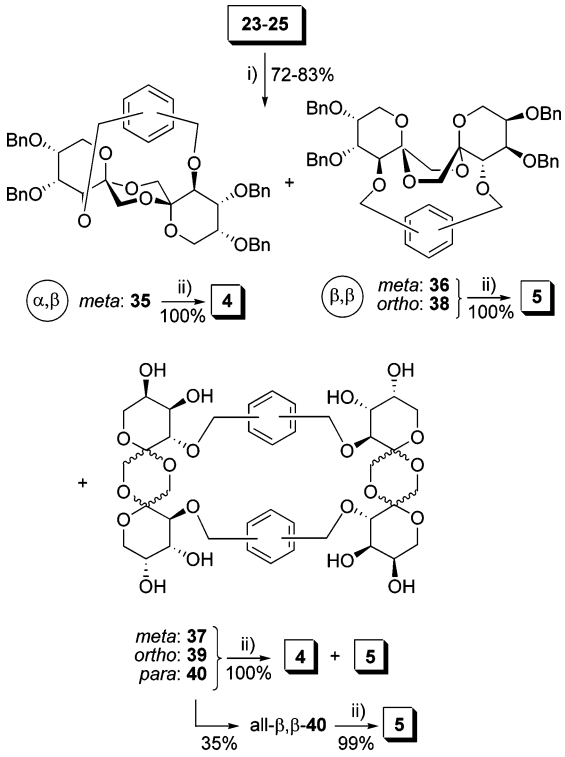
Interestingly, the crystal structure of the all-*β*,*β* **40** derivative (Figure 3) evidenced a significantly distorted chair conformation at the 1,4-dioxane rings (Figure 4), instead of the skew-boat conformation previously observed in the crystal structure of the complex of the parent DFA **5** with Sr^{2+}.[20] Most probably,

(18) A stereospecific synthesis of **5**, via a transient fructosyl fluoride intermediate, has previously been reported. See: García Fernández, J. M.; Schnelle, R.-R.; Defaye, J. *Tetrahedron: Asymmetry* **1995**, *6*, 307−312.

(19) An example of remote stereochemical control in the stereoselective synthesis of spiroketals by a preexisting cyclic acetal functionality has recently been reported. See: Ghosh, S.; Hsung, R. P.; Liu, J. *J. Am. Chem. Soc.* **2005**, *127*, 8260−8261.

(20) (a) Angyal, S. J.; Craig, D. C.; Defaye, J.; Gadelle, A. *Can. J. Chem.* **1990**, *68*, 1140−1144. (b) Gattuso, G.; Nepogodiev, S. A.; Stoddart, J. F. *Chem. Rev.* **1998**, *98*, 1919−1958.

SCHEME 5. Synthesis of Type III DFAs[a]



Starting material	Products (%)		
	α,β	β,β	dimers
23	**35** (11.5)	**36** (47.5)	**37** (24)
24	n.d.	**38** (42)	**39** (35)
25	n.d.	n.d.	**40** (72)

[a] Reagents and conditions: (i) TfOH, CH_2Cl_2, rt, 1 h (see table inset for yields; n.d.: not detected); (ii) 10% Pd/C, H_2, 1:1 EtOAc−MeOH, 10% HCOOH.

contra-thermodynamic DFAs exibit a conformational equilibrium in solution rather than a defined conformation at the central ring. It any case, the barrier on going from the chair to the boat conformation must be much lower in the contra-thermodynamic DFAs as compared with the thermodynamic counterparts. Our results show that these differences in conformational barriers can be put forward in the design of stereoselective syntheses of tricyclic bis-spiroacetal systems.

2.5. Summary and Conclusions. The results here reported demonstrate that the rigid spacer concept can be successfully applied to the control of the stereochemistry in the preparation of bis-spiroacetals. This is particularly noteworthy for fructose derivatives because two (intramolecular reaction) or four (intermolecular macrocyclization) quaternary stereogenic centers are formed with high anomeric control, which is generally not observed for fructosyl donors. Limiting the conformational space during the intramolecular reaction leading to the bis-spiroketal framework, by judicious choice of the spacer and of the linking positions on the reactive subunits, allows access to the thermodynamically less stable C_2-symmetric diastereomers with high stereoselectivity. On the other hand, the spacer can be tuned to prevent the intramolecular process, then favoring the formation of higher macrocycles while still controlling the stereochemical outcome, which may represent an original strategy

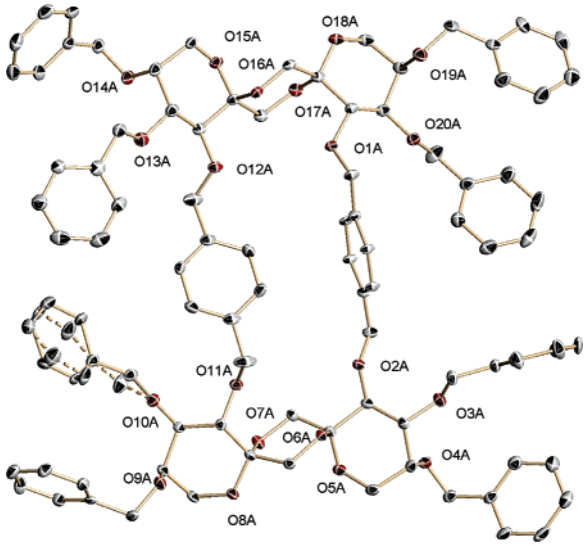


FIGURE 4. Structure of all-β,β **40** in the crystal. Hydrogens are omitted for clarity. One of the benzyl groups, showing disorder, is depicted in the two different positions apparently observed.

for the preparation of a new type of spiroacetal-arene hybrid polycyclic receptors. On the whole, a powerful methodology for spiroacetal synthesis in general can be based on this new conceptual approach.

3. Experimental Section

6-*O*-*tert*-Butyldimethylsilyl-1,2-*O*-isopropylidene-β-D-fructofuranose (10). To a solution of 1,2-*O*-isopropylidene-β-D-fructofuranose[12] **9** (1.288 g, 5.8 mmol) and imidazole (596 mg, 8.8 mmol) in DMF (25 mL) was added *tert*-butylchlorodimethylsilane (970 mg, 6.44 mmol), and the reaction mixture was stirred overnight. The solvent was removed under reduced pressure, the residue was partitioned between CH_2Cl_2 and water, and the organic layer was washed with water, dried ($MgSO_4$), filtered, and concentrated. Yield: 1.878 g (96%). R_f = 0.70 (3:1 EtOAc−petroleum ether). $[\alpha]_D$ = −27.0 (*c* 1.2, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 4.07 (d, 1 H, $J_{1a,1b}$ = 9.2 Hz, H-1a), 4.03 (dd, 1 H, $J_{3,4}$ = 7.8 Hz, $J_{4,5}$ = 6.3 Hz, H-4), 4.01 (d, 1 H, H-1b), 3.92 (d, 1 H, H-3), 3.76 (dd, 1 H, H-5), 3.76 (d, 1 H, $J_{6a,6b}$ = 12.1 Hz, $J_{5,6a}$ = 5.3 Hz, H-6a), 3.65 (dd, 1 H, $J_{5,6b}$ = 7.8 Hz, H-6b), 2.77 (bs, 2 H, 2 OH), 1.38, 1.47 (2 s, each 3 H, CMe_2), 0.88 (s, 9 H, $SiCMe_3$), 0.06 (s, 6 H, $SiMe_2$). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 111.3 (CMe_2), 108.6 (C-2), 80.6 (C-5), 77.4 (C-3, C-4), 70.9 (C-1), 64.6 (C-6), 26.2, 26.5 (CMe_2), 25.8 ($SiCMe_3$), 18.3 ($SiCMe_3$), −5.5 ($SiMe_2$). FABMS: *m*/*z* 357 (100, $[M + Na]^+$). Anal. Calcd for $C_{15}H_{30}O_6Si$: C, 55.14; H, 9.25. Found: C, 55.24; H, 9.40.

3,4-Di-*O*-benzyl-6-*O*-*tert*-butyldimethylsilyl-1,2-*O*-isopropylidene-β-D-fructofuranose (11). To a solution of **10** (760 mg, 2.2 mmol) in dry DMF (30 mL) were added NaH (360 mg, 9 mmol) and benzyl bromide (1.40 mL, 11 mmol). The reaction mixture was stirred for 5 h at room temperature, MeOH (10 mL) was added, and the solvent was evaporated. The resulting residue was extracted with Et_2O (30 mL), washed with water (10 mL), dried ($MgSO_4$), concentrated, and purified by column chromatography (1:8 EtOAc−petroleum ether) to yield **11** (1.07 g, 95%). R_f = 0.58 (1:5 EtOAc−petroleum ether). $[\alpha]_D$ = −37.2 (*c* 1.0, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.39−7.43 (m, 10 H, 2 Ph), 4.62−4.80 (m, 4 H, 2 CH_2), 4.25 (dd, 1 H, $J_{3,4}$ = 6.3 Hz, $J_{4,5}$ = 4.4 Hz, H-4), 4.11 (d, 1 H, $J_{1a,1b}$ = 9.2 Hz, H-1a), 4.07 (d, 1 H, H-3), 4.02 (m, 1 H, H-5), 3.98 (d, 1 H, H-1b), 3.81 (m, 2 H, H-6a, H-6b), 0.17 (s, 6 H, $SiMe_2$), 1.53, 1.56 (2 s, each 3 H, CMe_2), 0.98 (s, 9 H, $SiCMe_3$). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ (ppm) 127.6−139.5

(Ph), 111.3 (*C*Me$_2$), 108.8 (C-2), 84.9 (C-5), 83.0 (C-4), 81.9 (C-3), 72.1, 72.2 (CH$_2$), 71.2 (C-1), 64.8 (C-6), 26.3, 26.4 (C*Me*$_2$), 25.9 (SiC*Me*$_3$), 18.3 (Si*C*Me$_3$), −5.5 (SiMe$_2$). FABMS: *m*/*z* 537 (10, [M + Na]$^+$), 457 (20, [M − ^{t}Bu]$^+$). Anal. Calcd for $C_{29}H_{42}O_6Si$: C, 67.66; H, 8.22. Found: C, 67.69; H. 8.03.

3,4-Di-*O*-benzyl-1,2-*O*-isopropylidene-β-D-fructofuranose (12). To a stirred solution of **11** (590 mg, 1.14 mmol) in THF (25 mL) under Ar was added TBAF (1 m in THF, 114 μL, 1.0 equiv) at 0 °C. The reaction mixture was stirred for 3 h until dissappearance of the starting material, diluted with Et$_2$O (25 mL), washed with water (2 × 10 mL), dried (MgSO$_4$), filtered, and concentrated. Purification of the residue by column chromatography (1:2 EtOAc−petroleum ether) gave **12** (521 mg, 92%). R_f = 0.10 (1:5 EtOAc−petroleum ether). $[\alpha]_D$ = −77.0 (*c* 1.0, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.30−7.38 (m, 10 H, 2 Ph), 4.74−4.57 (m, 4 H, 2 CH$_2$), 4.41 (dd, 1 H, $J_{3,4}$ = 7.1 Hz, $J_{4,5}$ = 9.3 Hz, H-4), 4.06 (dd, 1 H, $J_{1a,1b}$ = 11.2 Hz, H-1a), 4.05 (d, 1 H, H-3), 4.04 (ddd, 1 H, $J_{5,6a}$ = 3.0 Hz, $J_{5,6b}$ = 3.8 Hz, H-5), 3.97 (d, 1 H, H-1b), 3.75 (dd, 1 H, $J_{6a,6b}$ = 12.1 Hz, H-6a), 3.59 (dd, 1 H, H-6b), 2.53 (bs, 1 H, OH), 1.53, 1.47 (2 s, each 3 H, CMe$_2$). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 111.7 (*C*Me$_2$), 127.6−139.6 (Ph), 108.5 (C-2), 83.2 (C-5), 81.8 (C-4), 81.7 (C-3), 72.2, 72.8 (CH$_2$), 71.1 (C-1), 63.4 (C-6), 26.1, 26.4 (C*Me*$_2$). FABMS: *m*/*z* 423 (100, [M + Na]$^+$). Anal. Calcd for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found: C, 68.94; H, 6.99.

General Procedure for the Preparation of (*O*-6→*O*-6′)-Xylylene-Tethered Fructofuranose Derivatives 13−15. To a solution of **12** (450 mg, 1.123 mmol) in dry DMF (10 mL) was added NaH (60 mg, 2.81 mmol). The suspension was stirred for 5 min, and then the corresponding bis(bromomethyl)benzene **6**−**8** (148.5 mg, 0.56 mmol) was added. The reaction mixture was stirred for 1 h at room temperature, and the reaction was quenched by addition of saturated aqueous NH$_4$Cl. The solvents were evaporated, and the residue was partitioned between Et$_2$O (20 mL) and water (20 mL). The organic phase was separated, washed with water (2 × 10 mL), dried (Na$_2$SO$_4$), filtered, and concentrated. The resulting residue was purified by column chromatography (1:3 EtOAc−petroleum ether).

1,3-Bis[(3,4-di-*O*-benzyl-1,2-*O*-isopropylidene-β-D-fructofuranos-6-*O*-yl)methyl]benzene (13). Yield: 441 mg (87%). R_f = 0.47 (2:5 EtOAc−petroleum ether). $[\alpha]_D$ = −30.3 (*c* 0.6, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.31−7.22 (m, 24 H, 5 Ph), 4.70−4.56 (m, 12 H, 6 C*H*$_2$Ph), 4.13 (m, 4 H, H-4, H-5), 4.04 (d, 2 H, $J_{1a,1b}$ = 9.5 Hz, H-1a), 4.01 (d, 2 H, $J_{3,4}$ = 6.0 Hz, H-3), 3.94 (d, 2 H, H-1b), 3.64 (dd, 2 H, $J_{6a,6b}$ = 10.0 Hz, $J_{5,6a}$ = 6.0 Hz, H-6a), 3.58 (dd, 2 H, $J_{5,6b}$ = 6.0 Hz, H-6b), 1.48, 1.44 (2 s, each 6 H, 2 CMe$_2$). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 138.5−127.0 (Ph), 111.8 (*C*Me$_2$), 109.1 (C-2), 84.5 (C-4), 83.0 (C-3), 80.2 (C-5), 73.5, 72.2, 72.0 (*C*H$_2$Ph), 72.1 (C-6), 71.2 (C-1), 27.4 (C*Me*$_2$). FABMS: *m*/*z* 925 (70, [M + Na]$^+$). Anal. Calcd for $C_{54}H_{62}O_{12}$: C, 71.82; H, 6.92. Found: C, 71.83; H, 6.63.

1,2-Bis[(3,4-di-*O*-benzyl-1,2-*O*-isopropylidene-β-D-fructofuranos-6-*O*-yl)methyl]benzene (14). Yield: 416 mg (82%). R_f = 0.50 (2:5 EtOAc−petroleum ether). $[\alpha]_D$ = −26.7 (*c* = 0.7 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31−7.22 (m, 24 H, 5 Ph), 4.70−4.54 (m, 12 H, 6 C*H*$_2$Ph), 4.09 (m, 4 H, H-4, H-5), 4.02 (d, 2 H, $J_{1a,1b}$ = 9.5 Hz, H-1a), 3.98 (d, 2 H, $J_{3,4}$ = 6.5 Hz, H-3), 3.92 (d, 2 H, H-1b), 3.61 (dd, 2 H, $J_{6a,6b}$ = 9.5 Hz, $J_{5,6a}$ = 6.0 Hz, H-6a), 3.58 (dd, 2 H, $J_{5,6b}$ = 6.0 Hz, H-6b), 1.45, 1.41 (2 s, each 6 H, 2 CMe$_2$). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 137.9−127.7 (Ph), 111.5 (*C*Me$_2$), 109.0 (C-2), 84.4 (C-4), 83.1 (C-3), 80.1 (C-5), 72.4, 72.3, 72.0 (*C*H$_2$Ph), 72.1 (C-6), 71.3 (C-1), 26.4 (C*Me*$_2$). FABMS: *m*/*z* 925 (20%, [M + Na]$^+$). Anal. Calcd for $C_{54}H_{62}O_{12}$: C, 71.82; H, 6.92. Found: C, 71.74; H, 7.00.

1,4-Bis[(3,4-di-*O*-benzyl-1,2-*O*-isopropylidene-β-D-fructofuranos-6-*O*-yl)methyl]benzene (15). Yield: 452 mg (90%). R_f = 0.52 (2:5 EtOAc−petroleum ether). $[\alpha]_D$ = −25.4 (*c* 0.6, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31−7.24 (m, 24 H, 5 Ph), 4.68−4.55 (m, 12 H, 6 C*H*$_2$Ph), 4.11 (m, 4 H, H-4, H-5), 4.02 (d, 2 H, $J_{1a,1b}$ = 9.0 Hz, H-1a), 3.99 (d, 2 H, $J_{3,4}$ = 6.0 Hz, H-3), 3.92 (d, 2 H, H-1b), 3.62 (dd, 2 H, $J_{6a,6b}$ = 10.0 Hz, $J_{5,6a}$ = 6.5 Hz, H-6a), 3.56 (dd, 2 H, $J_{5,6b}$ = 6.0 Hz, H-6b), 1.46, 1.43 (2 s, each 6 H, 2 CMe$_2$). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 138.0−127.7 (Ph), 111.5 (*C*Me$_2$), 109.0 (C-2), 84.4 (C-4), 83.1 (C-3), 80.2 (C-5), 73.3, 72.2, 72.0 (*C*H$_2$Ph), 72.3 (C-6), 71.3 (C-1), 26.5 (C*Me*$_2$). FABMS: *m*/*z* 925 (10, [M + Na]$^+$). Anal. Calcd for $C_{54}H_{62}O_{12}$: C, 71.82; H, 6.92. Found: C, 71.84; H, 6.67.

General Procedure for the Preparation of (*O*-3→*O*-3′)-Xylylene-Tethered Fructopyranose Derivatives 17−19. To a solution of 1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranose[13] **16** (490 mg, 1.88 mmol) in dry DMF (20 mL) was added NaH (188 mg, 4.71 mmol), and the suspension was stirred at room temperature for 15 min. A solution of the corresponding bis(bromomethyl)-benzene **6**−**8** (249 mg, 0.94 mmol) was then added, and the reaction mixture was further stirred for 1 h at room temperature. The reaction was quenched by addition of Et$_2$O (8 mL) and water (4 mL), and the organic layer was separated and washed with water (5 × 5 mL), dried (MgSO$_4$), concentrated, and purified by column chromatography (1:3 EtOAc−petroleum ether).

1,3-Bis[(1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranos-3-*O*-yl)methyl]benzene (17). Yield: 489 mg (84%). R_f = 0.41 (2:5 EtOAc−petroleum ether). $[\alpha]_D$ = −110.7 (*c* 1.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.29−7.24 (m, 4 H, Ph), 4.93, 4.61 (2 d, 2 H, $^2J_{H,H}$ = 12.0 Hz, C*H*Ph), 4.35 (dd, 2 H, $J_{3,4}$ = 7.2 Hz, $J_{4,5}$ = 5.6 Hz, H-4), 4.20 (dd, 2 H, $J_{5,6a}$ = 2.4 Hz, H-5), 4.12 (dd, 2 H, $J_{6a,6b}$ = 13.6 Hz, H-6a), 4.05 (d, 2 H, $J_{1a,1b}$ = 8.4 Hz, H-1a), 3.93 (d, 2 H, H-6b), 3.86 (d, 2 H, H-1b), 3.47 (d, 2 H, H-3), 1.51, 1.47, 1.36, 1.25 (4 s, 24 H, CMe$_2$). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 138.3−126.9 (Ph), 112.1, 109.0 (*C*Me$_2$), 104.4 (C-2), 77.7 (C-4), 76.2 (C-3), 73.8 (C-5), 73.0 (C-1), 71.9 (*C*H$_2$-Ph), 60.2 (C-6), 28.2, 26.9, 26.2, 26.1 (C*Me*$_2$); FABMS: *m*/*z* 645 (30, [M + Na]$^+$). Anal. Calcd for $C_{32}H_{46}O_{12}$: C, 61.72; H, 7.45. Found: C, 61.46; H, 7.27.

1,2-Bis[(1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranos-3-*O*-yl)methyl]benzene (18). Yield: 437 mg (75%). R_f = 0.41 (2:5 EtOAc−petroleum ether). $[\alpha]_D$ = −73.9 (*c* 1.05, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.31−7.22 (m, 4 H, Ph), 5.30 (s, 2 H, C*H*$_2$Ph), 5.09, 4.64 (2 d, 2 H, $^2J_{H,H}$ = 12.0 Hz, C*H*Ph), 4.33 (dd, 2 H, $J_{3,4}$ = 7.2 Hz, $J_{4,5}$ = 6.4 Hz, H-4), 4.18 (ddd, 2 H, $J_{5,6b}$ = 5.6 Hz, $J_{5,6a}$ = 1.2 Hz, H-5), 4.11 (dd, 2 H, $J_{6a,6b}$ = 13.2 Hz, H-6a), 3.98 (dd, 2 H, H-6b), 3.93 (d, 2 H, $J_{1a,1b}$ = 8.4 Hz, H-1a), 3.82 (d, 2 H, H-1b), 3.48 (d, 2 H, H-3), 1.64, 1.54, 1.36, 1.35 (4 s, 24 H, CMe$_2$). ^{13}C NMR (100.6 MHz, $CDCl_3$): δ (ppm) 136.2−127.6 (Ph), 112.1, 109.0 (*C*Me$_2$), 104.4 (C-2), 77.7 (C-4), 76.4 (C-3), 73.8 (C-5), 72.0 (C-1), 70.5 (*C*H$_2$Ph), 60.2 (C-6), 28.2, 26.8, 26.2 (C*Me*$_2$). FABMS: *m*/*z* 645 (30, [M + Na]$^+$). Anal. Calcd for $C_{32}H_{46}O_{12}$: C, 61.72; H, 7.45. Found: C, 61.88; H, 7.59.

1,4-Bis[(1,2:4,5-di-*O*-isopropylidene-β-D-fructopyranos-3-*O*-yl)methyl]benzene (19). Yield: 527 mg, 83%. R_f = 0.41 (2:5 EtOAc−petroleum ether). $[\alpha]_D$ = −108.3 (*c* 0.62, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.30−7.21 (m, 4 H, Ph), 4.93, 4.62 (2 d, 4 H, $^2J_{H,H}$ = 11.9 Hz, C*H*Ph), 4.36 (dd, 2 H, $J_{3,4}$ = 7.2 Hz, $J_{4,5}$ = 5.8 Hz, H-4), 4.20 (dd, 2 H, $J_{5,6a}$ = 2.1 Hz, H-5), 4.12 (dd, 2 H, $J_{6a,6b}$ = 13.4 Hz, H-6a), 4.05 (d, 2 H, $J_{1a,1b}$ = 8.5 Hz, H-1a), 3.97 (d, 2 H, H-6b), 3.86 (d, 2 H, H-1b), 3.47 (d, 2 H, H-3), 1.56, 1.52, 1.38, 1.36, (4 s, 24 H, CMe$_2$). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 137.6−127.7 (Ph), 112.2, 109.0 (*C*Me$_2$), 104.4 (C-2), 77.8 (C-4), 76.1 (C-3), 73.8 (C-5), 72.8 (C-1), 71.9 (*C*H$_2$-Ph), 60.2 (C-6), 28.2, 26.9, 26.2, 26.0 (C*Me*$_2$). FABMS: *m*/*z* 645 (100, [M + Na]$^+$). Anal. Calcd for $C_{32}H_{46}O_{12}$: C, 61.72; H, 7.45. Found: C, 61.50; H, 7.20.

General Procedure for the Preparation of Selectively Protected Bis(fructopyranose) Derivatives 20−22. A solution of the fully protected derivative **17**, **18**, or **19** (380 mg, 0.61 mmol) was dissolved in 60% aq AcOH (2 mL) and stirred at 45 °C for 2 h. The reaction mixture was then diluted with water (5 mL) and extracted with EtOAc (4 × 4 mL). The organic phase was washed with saturated aqueous NaHCO$_3$ (6 mL), dried (MgSO$_4$), filtered,

and concentrated. The resulting residue was purified by column chromatography (45:5:3 EtOAc−EtOH−H_2O).

1,3-Bis[(1,2-*O*-isopropylidene-β-D-fructopyranos-3-*O*-yl)methyl]benzene (20). Yield: 260 mg (69%). R_f 0.50 (45:5:3 EtOAc−EtOH−H_2O). $[\alpha]_D = -111.7$ (*c* 1.25, $CHCl_3$). ^{1}H NMR (500 MHz, CD_3OD): δ (ppm) 7.31−7.29 (m, 4 H, Ph), 4.96, 4.63 (2 d, 2 H, $^2J_{H,H}$ = 11.4 Hz, C*H*Ph), 4.82 (s, 2 H, C*H*Ph), 3.94 (d, 2 H, $J_{1a,1b}$ = 8.0 Hz, H-1a), 3.91 (dd, 2 H, $J_{3,4}$ = 9.6 Hz, $J_{4,5}$ = 3.5 Hz, H-4), 3.89 (dd, 2 H, $J_{6a,6b}$ = 12.4 Hz, $J_{5,6a}$ = 1.2 Hz, H-6a), 3.84 (m, 2 H, H-5), 3.81 (d, 2 H, H-1b), 3.66 (d, 2 H, H-3), 3.61 (dd, 2 H, $J_{5,6b}$ = 1.9 Hz, H-6b), 1.40, 1.32 (2 s, 12 H, CMe_2). ^{13}C NMR (125.7 MHz, CD_3OD): δ (ppm) 138.7−126.9 (Ph), 111.5 (*C*Me_2), 105.9 (C-2), 75.7 (C-3), 74.7 (*C*H_2Ph), 71.6 (C-1), 71.5 (C-4), 70.1 (C-5), 64.2 (C-6), 25.9, 25.2 (C*Me*$_2$); FABMS: *m*/*z* 565 (100, $[M + Na]^+$). Anal. Calcd for $C_{26}H_{38}O_{12}$: C, 57.56; H, 7.06. Found: C, 57.51; H, 6.85.

1,2-Bis[(1,2-*O*-isopropylidene-β-D-fructopyranos-3-*O*-yl)methyl]benzene (21). Yield: 230 mg (70%). R_f = 0.50 (45:5:3 EtOAc−EtOH−H_2O). $[\alpha]_D = -171.1$ (*c* 0.61, $CHCl_3$). ^{1}H NMR (300 MHz, CD_3OD): δ (ppm) 7.51−7.30 (m, 4 H, Ph), 5.19, 4.75 (2 d, 2 H, $^2J_{H,H}$ = 11.7 Hz, C*H*Ph), 4.90 (s, 2 H, CH_2Ph), 3.95 (dd, 2 H, $J_{3,4}$ = 9.8 Hz, $J_{4,5}$ = 3.4 Hz, H-4), 3.91 (m, 2 H, H-6a), 3.88 (dd, 2 H, H-5), 3.85 (d, 2 H, $J_{1a,1b}$ = 8.7 Hz, H-1a), 3.81 (d, 2 H, H-1b), 3.73 (d, 2 H, H-3), 3.64 (dd, 2 H, $J_{6a,6b}$ = 12.3 Hz, $J_{5,6b}$ = 1.7 Hz, H-6b), 1.43, 1.35 (2 s, 12 H, CMe_2). ^{13}C NMR (75.5 MHz, CD_3OD): δ (ppm) 138.1−129.0 (Ph), 112.8 (*C*Me_2), 107.2 (C-2), 77.0 (C-3), 73.6 (*C*H_2Ph), 73.0 (C-1), 72.7 (C-4), 71.5 (C-5), 65.6 (C-6), 27.2, 26.6 (C*Me*$_2$); FABMS: *m*/*z* 565 (100, $[M + Na]^+$). Anal. Calcd for $C_{26}H_{38}O_{12}$: C, 57.56; H, 7.06. Found: C, 57.64; H, 7.09.

1,4-Bis[(1,2-*O*-isopropylidene-β-D-fructopyranos-3-*O*-yl)methyl]benzene (22). Yield: 237 mg (72%). R_f = 0.50 (45:5:3 EtOAc−EtOH−H_2O). $[\alpha]_D = -159.5$ (*c* 1.01, $CHCl_3$). ^{1}H NMR (500 MHz, CD_3OD): δ (ppm) 7.38 (m, 4 H, Ph), 4.97, 4.63 (2 d, 2 H, $^2J_{H,H}$ = 11.4 Hz, C*H*Ph), 4.85 (s, 2 H, CH_2Ph), 3.94 (d, 2 H, $J_{1a,1b}$ = 8.5 Hz, H-1a), 3.92 (dd, 2 H, $J_{3,4}$ = 9.8 Hz, $J_{4,5}$ = 3.0 Hz, H-4), 3.90 (dd, 2 H, $J_{6a,6b}$ = 12.4 Hz, $J_{5,6a}$ = 1.2 Hz, H-6a), 3.85 (m, 2 H, H-5), 3.81 (d, 2 H, H-1b), 3.67 (d, 2 H, H-3), 3.62 (dd, 2 H, $J_{5,6b}$ = 1.8 Hz, H-6b), 1.42, 1.32 (2 s, 12 H, CMe_2). ^{13}C NMR (125.7 MHz, CD_3OD): δ (ppm) 139.4−129.1 (Ph), 112.9 (*C*Me_2), 107.2 (C-2), 77.0 (C-3), 76.0 (*C*H_2Ph), 72.9 (C-1), 72.8 (C-4), 71.5 (C-5), 65.6 (C-6), 25.9, 25.2 (C*Me*$_2$). FABMS: *m*/*z* 565 (100, $[M + Na]^+$). Anal. Calcd for $C_{26}H_{38}O_{12}$: C, 57.56; H, 7.06. Found: C, 57.53; H, 6.73.

General Procedure for the Preparation of Benzylated Bis-(fructopyranose) derivatives 23−25. To a solution of **20**, **21**, or **22** (88 mg, 0.16 mmol) in dry DMF (3 mL) was added NaH (65 mg, 1.62 mmol), and the suspension was stirred at room temperature for 15 min. Benzyl bromide (81 μL, 0.65 mmol, 4 equiv) was then added, and the mixture was further stirred for 15 min. The reaction was quenched by addition of Et_2O (10 mL) and water (5 mL), and the organic phase was separated, washed with water (5 × 5 mL), dried ($MgSO_4$), and concentrated.

1,3-Bis[(4,5-di-*O*-benzyl-1,2-*O*-isopropylidene-β-D-fructopyranos-3-*O*-yl)methyl]benzene (23). Yield: 110 mg (75%). R_f = 0.46 (1:2 EtOAc−petroleum ether). $[\alpha]_D = -66.8$ (*c* 1.6, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.38−7.23 (m, 24 H, Ph), 5.01, 4.56 (d, 4 H, $^2J_{H,H}$ = 11.6 Hz, C*H*Ph), 4.73, 4.67 (d, 4 H, $^2J_{H,H}$ = 12.6 Hz, C*H*Ph), 4.61, 4.57 (d, 4 H, $^2J_{H,H}$ = 12.5 Hz, C*H*Ph), 3.98 (d, 2 H, $J_{1a,1b}$ = 8.5 Hz, H-1a), 3.93 (d, 2 H, H-1b), 3.91 (d, 2 H, $J_{3,4}$ = 9.8 Hz, H-3), 3.88 (dd, 2 H, $J_{4,5}$ = 2.5 Hz, H-4), 3.75 (m, 6 H, H-5, H-6a, H-6b), 1.44, 1.37 (2 s, 12 H, CMe_2). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 138.5−126.6 (Ph), 111.8 (*C*Me_2), 105.9 (C-2), 80.2 (C-4), 75.4 (C-3), 75.3 (*C*H_2Ph), 73.4 (C-5), 72.0, 71.5 (*C*H_2Ph), 71.9 (C-1), 61.3 (C-6), 27.1, 26.2 (C*Me*$_2$). FABMS: *m*/*z* 925 (80, $[M + Na]^+$). Anal. Calcd for $C_{54}H_{62}O_{12}$: C, 71.82; H, 6.92. Found: C, 71.72; H, 6.84.

1,2-Bis[(4,5-di-*O*-benzyl-1,2-*O*-isopropylidene-β-D-fructopyranos-3-*O*-yl)methyl]benzene (24). Yield: 110 mg (75%). R_f = 0.46 (1:2 EtOAc−petroleum ether). $[\alpha]_D = -48.5$ (*c* = 0.72, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.49−7.21 (m, 24 H, Ph), 5.04, 4.72 (2 d, 4 H, $^2J_{H,H}$ = 12.5 Hz, C*H*Ph), 4.67, 4.61 (2 d, 4 H, $^2J_{H,H}$ = 13.0 Hz, C*H*Ph), 4.55 (s, 4 H, C*H*Ph), 3.88 (m, 4 H, H-3, H-4), 3.81 (d, 2 H, $J_{1a,1b}$ = 8.5 Hz, H-1a), 3.73 (m, 8 H, H-1b, H-5, H-6a, H-6b), 1.43, 1.41 (2 s, 12 H, CMe_2). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 138.5−127.4 (Ph), 111.6 (*C*Me_2), 105.9 (C-2), 80.3 (C-4), 75.1 (C-3), 73.4 (C-5), 72.0, 71.9, 71.6 (*C*H_2Ph), 71.9 (C-1), 61.6 (C-6), 26.9, 26.4 (C*Me*$_2$). FABMS: *m*/*z* 925 (100, $[M + Na]^+$). Anal. Calcd for $C_{54}H_{62}O_{12}$: C, 71.82; H, 6.92. Found: C, 71.60; H, 6.80.

1,4-Bis[(4,5-di-*O*-benzyl-1,2-*O*-isopropylidene-β-D-fructopyranos-3-*O*-yl)methyl]benzene (25). Yield: 184 mg (82%). R_f = 0.46 (1:2 EtOAc−petroleum ether). $[\alpha]_D = -97.3$ (*c* 0.84, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.31−7.24 (m, 24 H, Ph), 5.02, 4.62 (2 d, 4 H, $^2J_{H,H}$ = 11.4 Hz, C*H*Ph), 4.74, 4.68 (2 d, 4 H, $^2J_{H,H}$ = 12.6 Hz, C*H*Ph), 4.61, 4.59 (2 d, 4 H, $^2J_{H,H}$ = 11.7 Hz, C*H*Ph), 3.99 (d, 2 H, $J_{1a,1b}$ = 8.5 Hz, H-1a), 3.95 (d, 2 H, H-1b), 3.91 (m, 4 H, H-3, H-4), 3.77 (m, 6 H, H-5, H-6a, H-6b), 1.45, 1.39 (2 s, 12 H, CMe_2). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 138.5−127.6 (Ph), 111.8 (*C*Me_2), 105.9 (C-2), 80.1 (C-4), 75.2 (C-3, *C*H_2Ph), 73.4 (C-5), 72.0 (*C*H_2Ph), 71.5 (C-1), 61.3 (C-6), 27.1, 26.2 (C*Me*$_2$). FABMS: *m*/*z* 925 (50, $[M + Na]^+$). Anal. Calcd for $C_{54}H_{62}O_{12}$: C, 71.82; H, 6.92. Found: C, 71.74; H, 6.71.

***m*-Xylylene-Mediated Synthesis of Type I DFA Derivatives 26−28.** To a solution of the *m*-xylylene-tethered bis(D-fructofuranose) **13** (400 mg, 0.44 mmol) in dry CH_2Cl_2 (60 mL) at −78 °C under Ar was added trifluoromethanesulfonic acid (60 μL). The reaction mixture was stirred for 1 h, allowed to reach room temperature, and then stirred for an additional 1 h. Et_3N (10 drops) was added, and the resulting solution was stirred for 10 min and then concentrated. Column chromatography (1:3 EtOAc−petroleum ether) of the residue afforded first the two-component inseparable mixture of intramolecular reaction products **26** and **27** (1:2, 270 mg, 78%). A second fraction contained the corresponding macrocyclization compounds **28** (55 mg, 16%), as seen from FABMS data. Removal of the xylylene and benzyl groups in the mixture of **26** and **27** by catalytic hydrogenation afforded the corresponding DFAs **1** and **2** in quantitative yield, whose relative proportions and identities were confirmed by GC, using authentic standards. The macrocyclic fraction **28** quantitatively yielded the spirodisaccharides **1** and **2** in 1:2 ratio after catalytic hydrogenation. The binary mixtures of **1** and **2** could be separated by conventional acetylation, column chromatography and Zemplén deacetylation as previously reported. The individual DFAs exhibited spectroscopic properties identical to those in the literature.[4]

***o*-Xylylene-Mediated Synthesis of Type I DFA Derivatives 29−31.** To a solution of the *o*-xylylene-tethered bis(D-fructofuranose) **14** (400 mg, 0.44 mmol) in dry CH_2Cl_2 (60 mL) at −78 °C under Ar was added trifluoromethanesulfonic acid (60 μL). The reaction mixture was stirred for 1 h, allowed to reach room temperature, and then stirred for an additional 1 h. Et_3N (10 drops) was added, and the resulting solution was stirred for 10 min and then concentrated. Column chromatography (1:3 EtOAc−petroleum ether) of the residue afforded the pure tetracyclic spirodisaccharides **29** (30 mg, 9%) and **30** (275 mg, 79%) and the macrocyclic fraction **31** (20 mg, 6%). Removal of the xylylene and benzyl groups in **29** and **30** by catalytic hydrogenation afforded the corresponding pure DFAs **2** and **3** in quantitative yield. The macrocyclic fraction **28** quantitatively yielded the spirodisaccharides **1** and **2** in 1:2 ratio after catalytic hydrogenation.

3,4,3′,4′-Tetra-*O*-benzyl-6,6′-*O*-(*o*-xylylene)-di-α-D-fructofuranose 1,2′:2,1′-Dianhydride (29). R_f = 0.48 (1:3 EtOAc−petroleum ether). $[\alpha]_D = +96.7$ (*c* 0.83, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.28−7.24 (m, 24 H, 5 Ph), 4.70−4.54 (m, 12 H, 6 CH_2), 4.14 (d, 2 H, $J_{1a,1b}$ = 11.8 Hz, H-1a), 4.13 (m, 2 H, H-5), 4.00 (d, 2 H, $J_{3,4}$ = 3.3 Hz, H-3), 3.88 (d, 2 H, H-1b), 3.77 (dd, 2 H, $J_{6a,6b}$ = 12.2 Hz, $J_{5,6a}$ = 2.0 Hz, H-6a), 3.61 (dd, 2 H, H-4), 3.47 (dd, 2 H, $J_{5,6a}$ = 8.4 Hz, H-6b). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 137.7−127.6 (Ph), 102.9 (C-2), 88.7 (C-3), 83.1

(C-4), 81.5 (C-5), 72.3, 71.9, 71.4 (CH_2), 70.8 (C-6), 63.9 (C-1). Anal. Calcd for $C_{48}H_{50}O_{10}$: C, 73.26; H, 6.40. Found: C, 73.29; H, 6.12.

3,4,3′,4′-Tetra-*O*-benzyl-6,6′-*O*-(*o*-xylylene)-di-β-D-fructofuranose 1,2′:2,1′-Dianhydride (30). R_f 0.40 (1:3 EtOAc−petroleum ether). $[\alpha]_D$ = +91.5 (*c* 0.83, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.40−7.17 (m, 24 H, 5 Ph), 4.99 (d, 2 H, $^3J_{H,H}$ = 11.2 Hz, CH_2), 4.78 (d, 2 H, $^3J_{H,H}$ = 11.2 Hz, CH_2), 4.61−4.52 (dd, 2 H, CH_2), 4.12 (ddd, 2 H, $J_{5,6a}$ = 1.8 Hz, $J_{5,6b}$ = 1.3 Hz, $J_{4,5}$ = 6.3 Hz, H-5), 4.02 (dd, 2 H, $J_{3,4}$ = 7.2 Hz, H-4), 3.83 (dd, 2 H, $J_{6a,6b}$ = 11.3 Hz, H-6a), 3.76 (d, 2 H, $J_{1a,1b}$ = 11.2 Hz, H-1a), 3.74 (dd, 2 H, H-6b), 3.70 (d, 2 H, H-3), 3.68 (d, 2 H, H-1b); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 137.6−127.5 (Ph), 103.1 (C-2), 84.3 (C-3), 82.9 (C-4), 81.8 (C-5), 74.7 (C-6), 73.0, 72.8, 72.2 (CH_2), 64.8 (C-1). Anal. Calcd for $C_{48}H_{50}O_{10}$: C, 73.26, H, 6.40. Found: C, 73.21; H, 6.40.

***p*-Xylylene-Mediated Synthesis of Type I DFA Derivatives 32−34.** To a solution of the *p*-xylylene-tethered bis(D-fructofuranose) **13** (400 mg, 0.44 mmol) in dry CH_2Cl_2 (60 mL) at −78 °C under Ar was added trifluoromethanesulfonic acid (60 μL). The reaction mixture was stirred for 1 h, allowed to reach room temperature, and then stirred for an additional 1 h. Et_3N (10 drops) was added, and the resulting solution was stirred for 10 min and then concentrated. Column chromatography (1:3 EtOAc−petroleum ether) of the residue afforded first the two-component inseparable mixture of intramolecular reaction products **32** and **33** (4:1, 66.5 mg, 19%). A second fraction contained the corresponding macrocyclization compounds **34** (217.5 mg, 63%), as seen from FABMS data. Removal of the xylylene and benzyl groups in the mixture of **32** and **33** by catalytic hydrogenation afforded the corresponding DFAs **2** and **3** in quantitative yield, whose relative proportions and identities were confirmed by GC, using authentic standards. The macrocyclic fraction **34** quantitatively yielded the spirodisaccharides **1** and **2** in 1:2 ratio after catalytic hydrogenation.

***m*-Xylylene-Mediated Synthesis of Type III DFA Derivatives 35−37.** To a solution of the *m*-xylylene-tethered D-fructopyranose derivative **23** (340 mg, 0.37 mmol) in dry CH_2Cl_2 (60 mL) at −78 °C was added trifluoromethanesulfonic acid (50 μL, 1.5 equiv) under Ar. The reaction mixture was stirred for 1 h, allowed to reach room temperature, and then stirred for an additional 4 h. Et_3N (3 drops) was added, and the resulting solution was stirred for 10 min and then concentrated. Column chromatography of the residue (1:3 EtOAc−petroleum ether) afforded the corresponding bis-spiroacetals **35** (34 mg, 11.5%) and **36** (137 mg, 47.5%) and a fraction consisting of macrocyclization products **37** (69.8 mg, 24%) arising from double bis(spiroacetalation). Catalytic hydrogenolysis of **35** and **36** proceeded in quantitative yield to give the corresponding difructopyranose DFAs **4** and **5**, respectively. Under the same conditions, the macrocyclic fraction **37** afforded a mixture of **4** and **5** in 1:6 relative proportion. The identity of the unprotected DFAs **4** and **5** and their relative proportions in mixtures were established by GC and comparison with authentic samples. The individual compounds, coming either from catalytic hydrogenolysis of **35** and **36** or from the separation of the mixtures of **4** and **5** by peracetylation, column chromatography, and deacetylation, exhibited spectroscopic properties identical to those previously reported.[4]

4,5-Di-*O*-benzyl-α-D-fructopyranose 4′,5′-Di-*O*-benzyl-β-D-fructopyranose 3,3′-*O*-(*m*-Xylylene) 1,2′:2,1′-Dianhydride (35). R_f = 0.40 (1:2 EtOAc−petroleum ether). $[\alpha]_D$ = −40.2 (*c* 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.39−7.12 (m, 24 H, Ph), 4.99, 4.61 (2 d, 2 H, $^2J_{H,H}$ = 12.0 Hz, C*H*Ph), 4.72, 4.67 (2 d, 2 H, $^2J_{H,H}$ = 12.5 Hz, C*H*Ph), 4.70, 4.59 (2 d, 2 H, $^2J_{H,H}$ = 12.5 Hz, C*H*Ph), 4.42, 4.35 (2 d, 2 H, $^2J_{H,H}$ = 12.0 Hz, C*H*Ph), 4.37 (s, 2 H, CH_2Ph), 4.31, 4.24 (2 d, 2 H, $^2J_{H,H}$ = 11.6 Hz, C*H*Ph), 4.21 (d, 1 H, $J_{1a,1b}$ = 11.3 Hz, H-1a*β*), 4.15 (d, 1 H, $J_{1a,1b}$ = 11.8 Hz, H-1aα), 3.89 (m, 3 H, H-4α, H-5α, H-6aα), 3.86 (dd, 1 H, $J_{3,4}$ = 9.5 Hz, $J_{4,5}$ = 3.4 Hz, H-4*β*), 3.73 (d, 1 H, H-1bα), 3.72 (dd, 1 H, $J_{6a,6b}$ = 11.9 Hz, $J_{5,6a}$ = 3.3 Hz, H-6a*β*), 3.71 (d, 1 H, $J_{3,4}$ = 3.2 Hz, H-3α), 3.69 (d, 1 H, H-3*β*), 3.69 (dd, 1 H, $J_{6a,6b}$ = 10.2 Hz, $J_{5,6b}$ = 4.1 Hz, H-6bα), 3.62 (m, 1 H, H-5*β*), 3.54 (d, 1 H, H-1b*β*), 3.44 (d, 1 H, H-6b*β*). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 139.9−124.6 (Ph), 96.2 (C-2*β*), 94.5 (C-2α), 78.8 (C-3α), 77.2 (C-4*β*), 76.7 (C-3*β*), 73.3 (C-5*β*), 72.4 (C-4α), 71.3 (C-5α), 73.7, 72.0, 71.8, 70.5 (*C*H_2Ph), 63.5 (C-1α), 61.2 (C-1*β*), 60.1 (C-6*β*), 57.2 (C-6α). FABMS: *m*/*z* 809 (20, $[M + Na]^+$). Anal. Calcd for $C_{48}H_{50}O_{10}$: C, 73.26; H, 6.40; found: C, 73.28; H, 6.32.

4,5,4′,5′-Tetra-*O*-benzyl-3,3′-*O*-(*m*-xylylene)-di-β-D-fructopyranose 1,2′:2,1′-Dianhydride (36). R_f = 0.35 (1:2 EtOAc−petroleum ether). $[\alpha]_D$ = −110.5 (*c* 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.39−7.12 (m, 24 H, Ph), 4.80−4.44 (m, 12 H, C*H*Ph), 3.97 (d, 1 H, $J_{1a,1b}$ = 12.1 Hz, H-1a), 3.96 (dd, 1 H, $J_{3,4}$ = 9.9 Hz, $J_{4,5}$ = 3.1 Hz, H-4), 3.88 (d, 1 H, H-3), 3.73 (dd, 1 H, $J_{6a,6b}$ = 12.5 Hz, $J_{5,6a}$ = 2.0 Hz, H-6a), 3.71 (m, 1 H, H-5), 3.62 (d, 1 H, H-6b), 3.59 (d, 1 H, H-1b). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 139.9−124.6 (Ph), 97.6 (C-2), 79.2 (C-3), 77.8 (C-4), 73.9 (C-5), 73.8, 72.2, 71.6 (*C*H_2Ph), 66.4 (C-1), 61.5 (C-6). Anal. Calcd for $C_{48}H_{50}O_{10}$: C, 73.26; H, 6.40. Found: C, 73.49; H, 6.19.

***o*-Xylylene-Mediated Synthesis of Type III DFA Derivatives 35−37.** To a solution of the *o*-xylylene-tethered D-fructopyranose derivative **24** (340 mg, 0.37 mmol) in dry CH_2Cl_2 (60 mL) at −78 °C was added trifluoromethanesulfonic acid (50 μL, 1.5 equiv) under Ar. The reaction mixture was stirred for 1 h, allowed to reach room temperature, and then stirred for an additional 4 h. Et_3N (3 drops) was added, and the resulting solution was stirred for 10 min and then concentrated. Column chromatography of the residue (1:3 EtOAc−petroleum ether) afforded the corresponding bis-spiroacetal **38** (124 mg, 42%) and the corresponding macrocyclic derivatives **39** (101.8 mg, 35%). Catalytic hydrogenolysis of **38** proceeded in quantitative yield to give the corresponding di-β-D-fructopyranose DFA **5**, respectively. Under the same conditions, the macrocyclic fraction **39** afforded a mixture of **4** and **5** in 1:6 relative proportion.

4,5,4′,5′-Tetra-*O*-benzyl-3,3′-*O*-(*o*-xylylene)-di-β-D-fructopyranose 1,2′:2,1′-Dianhydride (38). R_f = 0.36 (1:2 EtOAc−petroleum ether). $[\alpha]_D$ = −139.7 (*c* 0.71, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.31−7.21 (m, 24 H, Ph), 4.96, 4.78 (2 d, 4 H, $^2J_{H,H}$ = 8.3 Hz, C*H*Ph), 4.75, 4.66 (2 d, 4 H, $^2J_{H,H}$ = 12.9 Hz, C*H*Ph), 4.64 (s, 4 H, CH_2Ph), 4.51 (d, 2 H, $J_{1a,1b}$ = 11.6 Hz, H-1a), 4.07 (d, 2 H, $J_{3,4}$ = 10.2 Hz, H-3), 4.05 (dd, 2 H, $J_{4,5}$ = 2.6 Hz, H-4), 3.85 (m, 2 H, H-5), 3.80 (bd, 2 H, $J_{6a,6b}$ = 12.6 Hz, H-6a), 3.76 (d, 2 H, H-6b), 3.72 (d, 2 H, H-1b). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 138.5−127.6 (Ph), 95.0 (C-2), 77.9 (C-3), 76.2 (C-4), 73.5 (C-5), 71.7, 71.4, 69.2 (*C*H_2Ph), 66.2 (C-1), 60.8 (C-6). FABMS: *m*/*z* 809 (100, $[M + Na]^+$). Anal. Calcd for $C_{48}H_{50}O_{10}$: C, 73.26; H, 6.40. Found: C, 73.15; H, 6.12.

***p*-Xylylene-Mediated Synthesis of Type III DFA Derivatives 40.** To a solution of the *p*-xylylene-tethered D-fructopyranose derivative **25** (340 mg, 0.37 mmol) in dry CH_2Cl_2 (60 mL) at −78 °C was added trifluoromethanesulfonic acid (50 μL, 1.5 equiv) under Ar. The reaction mixture was stirred for 1 h, allowed to reach room temperature, and then stirred for an additional 4 h. Et_3N (3 drops) was added, and the resulting solution was stirred for 10 min and then concentrated. No intramolecular reaction compounds were detected in this case. Column chromatography of the residue (1:3 EtOAc−petroleum ether) provided only the macrocyclization derivatives **40** (209 mg, 72%). Crystallization from EtOAc yielded the all-*β*,*β* **40** macrocyclic dimer in pure form (101.8 mg, 35%). Catalytic hydrogenolysis of **40** afforded mixtures of **4** and **5** in 1:6 relative proportions, while the all-*β*,*β* **40** isomer yielded exclusively the contra-thermodynamic diastereomer **5**.

Cyclobis[4,5,4′,5′-tetra-*O*-benzyl-di-β-D-fructopyranose 1,2′:2,1′-dianhydride] 3^I,3^{II}:$3'^I$,$3'^{II}$-Di-*O*-(*p*-xylylene) (all-*β*,*β* 40). R_f = 0.54 (1:2 EtOAc−petroleum ether). $[\alpha]_D$ = −138.3 (*c* 0.82, $CHCl_3$). Mp: 213.5−214.8 °C (EtOAc). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 7.25−7.13 (m, 48 H, Ph), 4.86, 4.68 (2 d, 8 H, $^2J_{H,H}$ = 10.9 Hz, C*H*Ph), 4.71, 4.66 (2 d, 8 H, $^2J_{H,H}$ = 12.6 Hz, C*H*Ph), 4.53, 4.46 (2 d, 8 H, $^2J_{H,H}$ = 11.6 Hz, C*H*Ph), 4.01 (d, 4 H, $J_{1a,1b}$ = 12.1 Hz, H-1a), 3.95 (dd, 4 H, $J_{3,4}$ = 9.9 Hz, $J_{4,5}$ = 3.0

Hz, H-4), 3.87 (d, 4 H, H-3), 3.76 (bd, 4 H, $J_{6a,6b}$ = 12.8 Hz, H-6a), 3.72 (m, 4 H, H-5), 3.71 (d, 4 H, H-6b), 3.66 (d, 24 H, H-1b). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (ppm) 138.5−127.4 (Ph), 97.8 (C-2), 79.6 (C-3), 78.1 (C-4), 73.8 (C-5), 74.6, 72.5, 71.5 (CH_2Ph), 64.4 (C-1), 61.5 (C-6). FABMS: *m/z* 1595 (20, $[M + Na]^+$). Anal. Calcd for $C_{96}H_{100}O_{20}$: C, 73.26; H, 6.40. Found: C, 73.15; H, 6.49.

X-ray Crystal Struture Analysis for all-β,β 40. C_{96} H_{100} O_{20}, M_r = 1573.76, colorless block (0.07 × 0.05 × 0.04 mm^3) from AcOEt, monoclinic, space group C_2 (no. 5), a = 59.445(3) Å, b = 10.5079(5) Å, c = 25.8107(11) Å, β = 95.554(2)°, V = 16046.8(13) Å^3, Z = 8, ρ_{calcd} = 1.303 g cm^{-3}, λ(Synchrotron) = 0.6934 Å, F(000) = 6688, μ = 0.091 mm^{-1}, T = 150 (2) K. A total of 78891 reflections collected, 20722 of which are independent for 1.92° < θ < 27.50°; 13790 [$I > 2\sigma(I)$] reflections were used for refinement. A very weakly diffracting crystal was used for data collection. Three runs of 600 frames each were measured with φ values of 0, 120, and 240 degrees and scan ranges of 0.3 degrees in ω at the Daresbury Synchrotron Radiation Source, SRS Station 9.8 (provided of a Bruker-Nonius APEXII CCD area detector). Reflections were corrected for Lorentz polarization effects and absorption applied by SADABS: Area-Detector Absorption Correction, Bruker-AXS within SAINT+ package, v. 7.06, 1996. The structure was solved by direct methods (SIR-97, Giacovazzo, C. SIR-97 Program for Crystal Structure Solution, Inst. di Ric. per lo Sviluppo di Metodologie Cristallograpfiche, CNR, University of Bari, Italy, 1997) and refined on F^2 by full-matrix least-squares techniques (SHELXTL-6.12 "Program for Structure Solution, Refinement and Presentation" BRUKER AXS Inc., 5465 East Cheryl Parkway, Madison, WI).The asymmetric unit showed the presence of one complete molecule and two independent half molecules. The refinement was performed stepwise, first with isotropic thermal parameters for all atoms, and then with anisotropic displacement parameters for all non-hydrogen atoms. Disorder fundamentally affected some of the terminal phenyl or benzyl rings. Geometrically constrained refinements were carried out for the cyclic rings were high residuals evidenced some kind of disorder. In the whole independent molecule only the terminal benzyl group (C42A to C48A, and C42Z to C48Z) was observed disordered, apparently in two different positions. From an initially fully constrained refinement the different positional, thermal and occupancy parameters were successively liberated. Eventually the two disordered moieties were refined first as free isotropic atoms, with only the occupancy factor constrained to be equal for both moieties, and then anisotropically refined. An identical model of disorder was carefully detected for both half independent molecules. It affected, in both cases, three of the terminal benzyl groups (C14/C20; C36/C41 and C43/C48) and one of the bridging phenyl rings (C3, C4, C6 and C7). In all cases, two complementary—with equal occupancy—moieties were enough to reasonably model the detected disorder. All disordered atoms of the terminal benzyl groups were refined first as free isotropic atoms and then introducing anisotropy displacement parameters despite this was strongly discouraged considering the relative proximity of some of the disordered atoms in the mean asymmetric unit. In the case of the central phenyl ring, the disorder only affected four of the ring atoms (C3, C4, C6, and C7). Anistropic thermal parameters were included for these atoms, as their separation allows physical meaning of these values. When observing the packing of molecules, the intermolecular contacts clearly make evident the necessary "synchronized" presence of disorder moieties to avoid short interatomic contacts. Hydrogen atoms were included in calculated positions refined with positional and thermal riding parameters. Final R factors are slightly over usual standards, most probably as a consequence of the very weak scattering power of the sample used and the heavy disorder present in the crystal. Data were collected to 2θ = 55° (completeness to 99.2%), 2515 parameters gave, R1 = 0.0874, w$R2$ = 0.2239 [for 13790 reflections with $I > 2\sigma(I)$], R1 = 0.1122, wR2 = 0.2532 (all data) (S = 1.063). The final difference map displayed no electron density higher than 0.395 e Å^{-3}. CCDC-258519 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK; fax: (+44)-1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk).

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Supporting Information Available: General experimental procedures, ORTEP plot for all-β,β **40** with full numbering system, and Tables 1S−6S containing relevant crystallographic parameters, as well as the complete X-ray crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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