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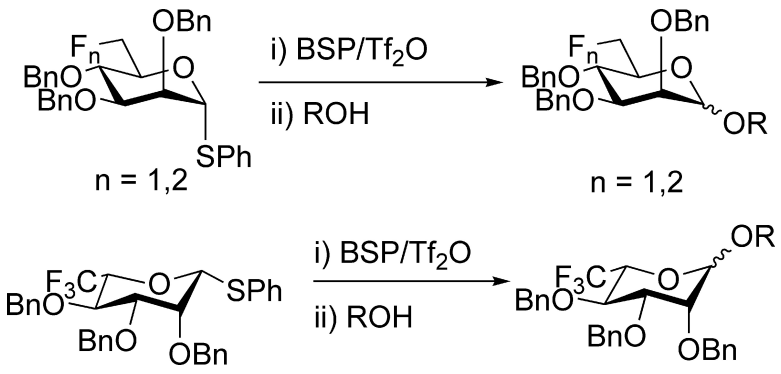

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Synthesis and Glycosylation of a Series of 6-Mono-, Di-, and Trifluoro *S*-Phenyl 2,3,4-Tri-*O*-benzyl-thiorhamnopyranosides. Effect of the Fluorine Substituents on Glycosylation Stereoselectivity

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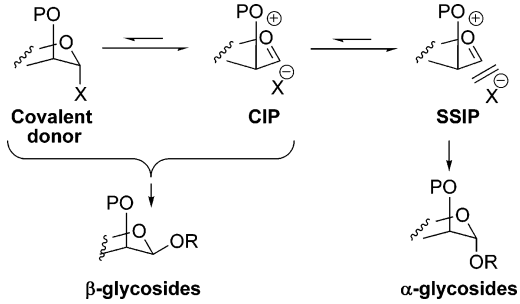
Abstract: A series of 6-mono-, di-, and trifluoro analogs of *S*-phenyl 2,3,4-tri-*O*-benzyl-D- or L-thiorhamnopyranoside has been synthesized and used as donors in glycosylation reactions, with activation by the 1-benzenesulfinyl piperidine/triflic anhydride system. The stereochemical outcome of the glycosylation reactions was found to depend on the electron-withdrawing capability of the disarming substituent at the 6-position, i.e., on the number of fluorine atoms present. The results are explained with regard to the increased stability of the glycosyl triflates, shown to be intermediates in the reaction by low-temperature ^{1}H NMR experiments, with increased fluorine content.

Introduction

β-Linked rhamnopyranosides, important structural units of many naturally occurring oligosaccharides, especially bacterial capsular polysaccharides,[1] constitute important synthetic targets. Consequently, methods of stereoselective β-rhamnopyranosylation are greatly desired. Similar to β-mannopyranosylation,[2−4] stereocontrolled β-rhamnopyranosylation is challenging due to the simultaneous occurrence of the anomeric effect and steric repulsion between the axial C-2 substituent on the rhamnosyl donor and the approaching nucleophile, both favoring the formation of the α-isomer. In a broader sense, the stereoselective construction of such 1,2-cis glycosylic linkages depends on a number of factors which influence the equilibrium between the proposed intermediates of the reaction: covalent donors and ion pairs, contact (CIP) or solvent separated (SSIP) (Scheme 1).[5,6]

β-Selectivity results from the attack on the covalent triflate or the associated CIP, whereas α-selectivity arises from attack on the SSIP. Destabilization of the oxacarbenium ion results in a diminished concentration of the SSIP and, therefore, in increased β-selectivity. For instance, the striking difference in selectivity observed in 4,6-*O*-benzylidene-directed glycosylations on going from highly β-selective mannopyranoside[7−12] donors to the α-selective glucopyranoside donors[10,12−16] is attributed to a shift in the equilibria toward the covalent donor in the manno series, largely due to the compression of the O2−C2−C3−O3 torsion angle on going from the covalent glycosyl triflate to the oxacarbenium ion, as compared to the relaxation of this torsion angle in the gluco series.[17,18] The problem of the chemical synthesis of β-rhamnosides parallels that of the β-mannosides but is indisputably more difficult, owing to the

Scheme 1. Mechanism of Glycosylation



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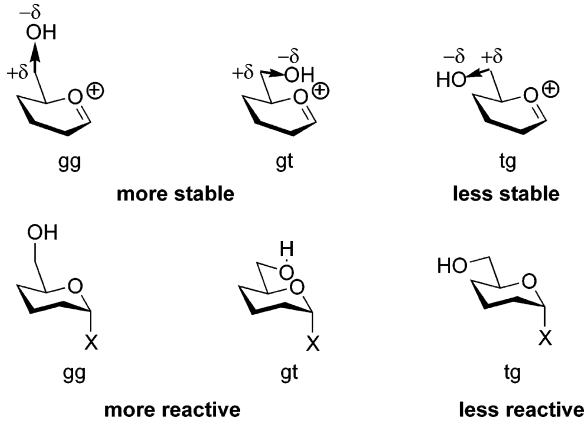
Scheme 2. Effect of the C5−C6 Conformation



6-deoxy functionality. In effect, the absence of the electron-withdrawing C−O bond at C6 influences the equilibrium between the intermediates of the reaction and, therefore, impinges directly on the reaction mechanism. Furthermore, the use of disarming 4,6-*O*-benzylidene-protected donors,[9,11,19−22] as in our recent solution to the β-mannosylation problem, is not possible because of the deoxy nature of the system.

Cognizant of the β-directing effect of disarming, nonparticipating substituents at the 2-position,[23−25] as well as of the 3,4-*O*-carbonate group[26] in homogeneous rhamnosylation reactions, we were drawn to the potential influence of the substituents at the 6-position on the selectivity of the rhamnosylation reaction. Indeed, several examples of the directing effect of electron-withdrawing groups at the 6-position on glycosylation reactions have been reported in the literature.[27−31] First, in their studies of the influence of the reactant structure on galactopyranosylation with galactosyl sulfonates, Schuerch and co-workers reported a remarkably high β-selectivity in the methanolysis of 6-*O*-(*N*-phenylcarbamoyl)-2,3,4-tri-*O*-benzyl-D-galactopyranosyl triflate[28,29] and, more generally, a noticeable enhancement in β-selectivity on going from less to more electron-withdrawing protective groups at the 6-position of 2,3,4-tri-*O*-benzyl-D-galactopyranose derivatives.[28] Second, the well-known deactivating effect of 4,6-*O*-acetal protecting groups on glycosyl transfers and hydrolyses, utilized, for example, in 4,6-*O*-benzylidene-directed β-mannopyranosylation reactions,[7−12] was demonstrated not to be wholly "torsional disarmament",[32,33] but in part to be an electronic effect, associated with locking C5−C6 in the *tg* conformation (Scheme 2).[30] In the *tg* conformer, the C6−O6 bond acts as a dipole with the negative terminus directed away from the electron-deficient center of the oxacarbenium ion, thereby destabilizing this key glycosyl transfer intermediate, whereas in the *gg* and *gt* conformers, this dipole is gauche to the developing positive charge, making the oxacarbenium ion more stable.[30] Third, the β-directing effect of electron-withdrawing groups at the 5-position is displayed in the synthesis of D-mannuronic acid oligomers, where thiomannuronic acid ester donors were shown to give excellent β-selectivities.[31]

Accordingly, we set out to probe 6-mono-, di-, and trifluoro-substituted rhamnopyranosides as donors in glycosylation reactions, foreseeing an improvement in the β-selectivity caused by the destabilization of the intermediate oxacarbenium ion by the presence of the strongly electron-withdrawing substituent(s) at the 6-position and the consequent shift of the key equilibria (Scheme 1) toward the covalent donor. Furthermore, fluorine-substituted carbohydrates have been a topic of interest for many years,[34−40] owing to the fact that fluorine, strategically positioned in target molecules, may greatly modify their chemical and biological properties and biological activity. Moreover, the excellent NMR properties of ^{19}F labels allow the detection of the position, conversion, or other interactions of the labeled compounds by in vivo or in vitro ^{19}F NMR measurements.[41−45] The fluorine atom can mimic either a hydrogen atom or a hydroxyl group and thus can turn a substrate into an inhibitor of a critical enzyme, improve stability of a drug, and/or protect crucial bonds from hydrolytic cleavage.[40] Thus, fluorinated carbohydrates can be used as cores in the development of drugs against viral infections and cancer,[39,40,46−48] as well as to probe biochemical processes.[49] For example, the ability of the electron-withdrawing fluorine substituents to decelerate a particular reaction is used in the elucidation of enzyme mechanisms or in the inhibition of a process of interest. Thus, a fluorine substituent in the carbohydrate moiety of the *clofarabine*, a medicine marketed for the treatment of leukemia,[50] increases the hydrolytic stability of the drug by disfavoring positive charge development on the anomeric carbon, required for the hydrolytic cleavage of nucleosides.[40] Similarly, the mechanism-based fluorinated glycoside inhibitors designed by Withers and co-workers[51−53] for identification of the active site residues of

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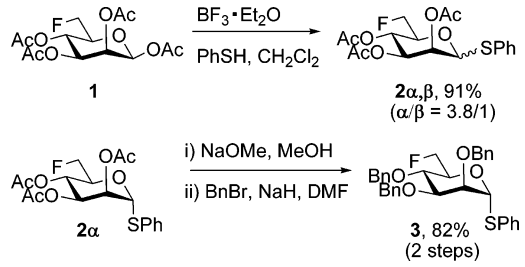
"retaining" glysosidases, function through destabilization of the putative oxacarbenium intermediate of the studied enzymatic reaction by the electron-withdrawing fluorine substituent.[51−53] Similar characteristics are to be expected from the 6-mono-, di-, and trifluoro-substituted rhamnopyranosides, thereby making them candidates for inhibitors of glycoside processing enzymes, in addition to potential β-selective rhamnosyl donors.

Results

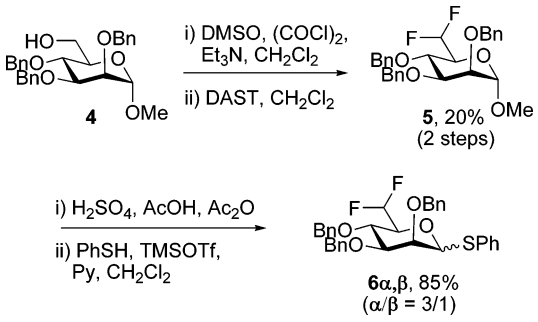
Preparation of Donors. Preparation of the D-monofluoro donor **3** was straightforward and followed the protocol outlined in Scheme 3, starting from the known 1,2,3,4-tetra-*O*-acetyl-6-deoxy-6-fluoro-β-D-mannopyranose **1**,[54] easily available through the reaction of 1,2,3,4-tetra-*O*-acetyl-β-D-mannopyranose[55] with *N*,*N*-diethylaminosulfur trifluoride (DAST),[54] and proceeding via the intermediacy of the corresponding tri-*O*-acetyl thioglycoside **2**.

Scheme 3. Synthesis of a Monofluoro Donor



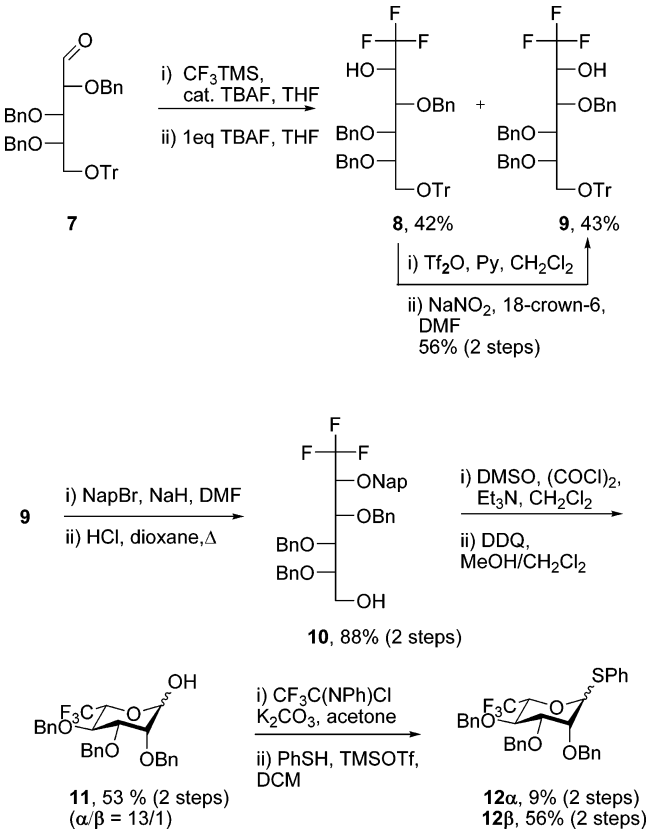
The difluoro derivative **5** was synthesized in a similar manner by deoxofluorination with DAST, following conversion of the 6-OH group of the mannopyranoside derivative **4**[56] to the corresponding aldehyde[57] (Scheme 4). One-pot hydrolysis of the anomeric OMe group and acetylation of the pyranose in acidic media,[58] followed by Lewis acid-promoted substitution with thiophenol, gave **6** as a mixture of α and β isomers, easily separable by means of chromatography.

Scheme 4. Synthesis of a Difluoro Donor



In this proof of principle study, D-mannose was selected as a precursor for the synthesis of the mono- and difluoromethyl analogs **3** and **6** in view of its low cost and availability and the rapid access to the target donors. The trifluorinated donor **12** required the development of an entirely different strategy, in which the Ruppert−Prakash reagent[59] was utilized as a suitable fluorine-containing building block for the introduction of the trifluoromethyl moiety into the arabinose precursor (Scheme 5). The trifluoromethyl analog of an L-rhamnopyranoside donor was selected as target on account of the low cost and availability of L-arabinose. Thus, derivative **7**[60] was converted to **8** and **9** by a two-step, one-pot protocol, starting with TBAF-catalyzed nucleophilic addition of CF_3TMS to the aldehyde,[61,62] followed by the cleavage of the intermediate TMS ether. The undesired diastereomer **8** failed to undergo Mitsunobu inversion[63,64] but was successfully transformed to **9** by a method involving displacement of the derived triflate with nitrite anion.[65−70] 2-Naphthyl-methylation of **9**, followed by the removal of the trityl group in acidic media, gave **10**.

Scheme 5. Synthesis of a Trifluoro Donor



Differential protection of **10** in this manner allows potential difficulties related to the increase of the furanose content as the methyl group is replaced with the trifluoromethyl group,

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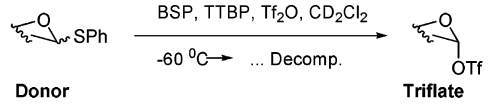
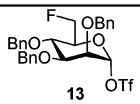
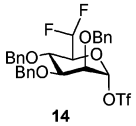
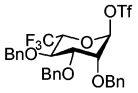
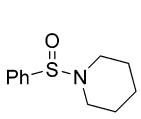
Table 1. Variable-Temperature ^{1}H NMR Experiments



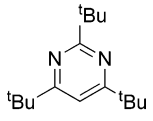
donor	triflate	δ_{H1}, ppm	decomp. T, ^{0}C
3	 **13**	6.05 (s)	-10 to 0
6α	 **14**	6.06 (s)	0 to +10
12β	 **15**	6.03 (s)	+10 to r.t.

known to occur in the L-fucose series,[62] to be avoided. Swern oxidation, followed by oxidative cleavage of the 2-methylnaphthyl ether gave **11** predominantly as the α-isomer. Obvious routes for the conversion of the pyranose derivative **11** to the donor **12** via reaction of the anomeric hydroxyl group with tributylphosphine and sulfur nucleophiles (e.g., diphenyl disulfide), or via acetylation of **11** followed by the Lewis acid-promoted reaction with thiophenol, failed. This is presumably due to the strong electron-withdrawing nature of the CF_3 substituent at the 5-position, diminishing the nucleophilicity of the hydroxyl group or, in the case of the acetate, prohibiting its effective activation with the Lewis acid. Therefore, pyranose derivative **11** was treated with *N*-phenyltrifluoroacetimidoyl chloride[71] to give the more reactive *N*-phenyltrifluoroacetimidate derivative,[72−77] which was instantly converted to donor **12** with thiophenol under Lewis acid-catalyzed conditions.

Investigation of the Key Intermediates. Variable-temperature ^{1}H NMR experiments were conducted for donors **3**, **6α**, and **12*β***, in which activation was performed by the BSP/Tf_2O couple in CD_2Cl_2 (Table 1).



BSP



TTBP

In all three cases, the thioglycosides followed the typical pattern previously observed in our laboratory:[10,13,25,78,79] clean activation at −60 °C directly gave putative glycosyl triflate intermediates, which underwent decomposition on warming. Interestingly, the stability of the observed intermediates **13**, **14**, and **15** exhibited a direct correlation with the number of fluorine substituents at the 6-position. Thus, the decomposition of **13** was completed by 0 °C, whereas the decomposition of **14** and **15** required higher temperatures (+10 °C and room temperature, respectively).

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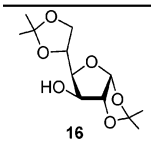
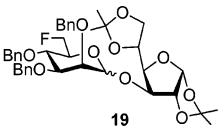
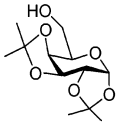
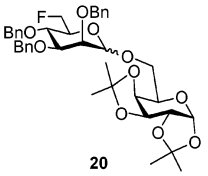
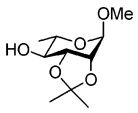
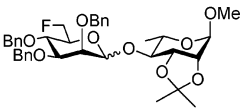
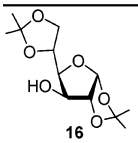
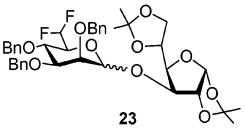
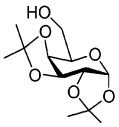
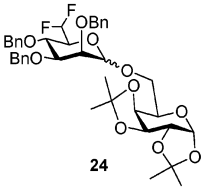
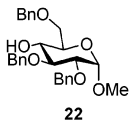
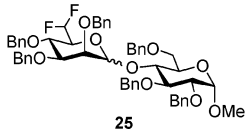
Table 2. Glycosylation of the Donor **3**

acceptor	product	α/β ratio[a] (yield, %)[b]
 **16**	 **19**	2.3/1 (88)
 **17**	 **20**	1.2/1 (84)
 **18**	 **21**	1/1.6 (84)

[a] Determined from ^{1}H NMR spectrum of the crude reaction mixture. [b] Total isolated yield.

Table 3. Glycosylation of the Donor **6α**

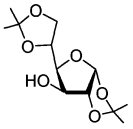
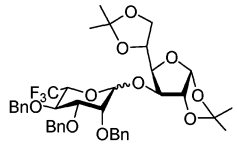
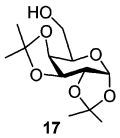
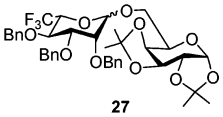
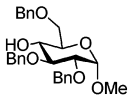
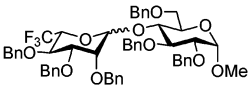
acceptor	product	α/β ratio[a] (yield, %)[b]
 **16**	 **23**	1/2.3 (80)
 **17**	 **24**	1/3.0 (76)
 **22**	 **25**	1/1.8 (68)

[a] Determined from ^{1}H NMR spectrum of the crude reaction mixture. [b] Total isolated yield.

Glycosylation Reactions. In light of the results obtained from the low-temperature NMR experiments, the glycosylation reactions (Tables 2−4) were performed by the following modus operandi: donors were first activated at −60 °C by the BSP/Tf_2O couple in the presence of TTBP, the solution of the acceptor was then added, and the reaction mixture was allowed to warm slowly to room temperature. The assignment of the

(72) Yu, B.; Tao, H. *Tetrahedron Lett.* **2001**, *42*, 2405−2407.
(73) Yu, B.; Tao, H. *J. Org. Chem.* **2002**, *67*, 9099−9102.
(74) Sun, J.; Han, X.; Yu, B. *Carbohydr. Res.* **2003**, *338*, 827−833.
(75) Zhang, Z.; Yu, B. *J. Org. Chem.* **2003**, *68*, 6309−6313.
(76) Li, M.; Han, X.; Yu, B. *J. Org. Chem.* **2003**, *68*, 6842−6845.
(77) Peng, W.; Sun, J.; Lin, F.; Han, X.; Yu, B. *Synlett* **2004**, 259−262.
(78) Crich, D.; Sun, S. *J. Am. Chem. Soc.* **1997**, *119*, 11217−11223.
(79) Crich, D.; Jayalath, P. *J. Org. Chem.* **2005**, *70*, 7252−7259.

Table 4. Glycosylation of the Donor **12*β***

acceptor	product	α/β ratio (yield, %)[a]
 **16**	 **26**	1/5.3[b] (50)
 **17**	 **27**	1/6.3 (83)
 **22**	 **28**	1/1.2 (69)

[a] Total isolated yield. [b] Determined from ^{1}H NMR spectrum of the crude reaction mixture.

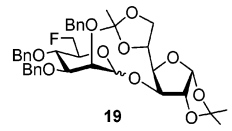
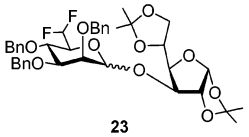
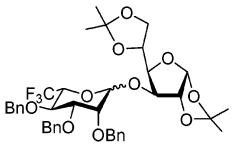
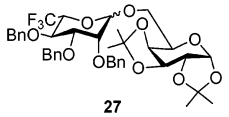
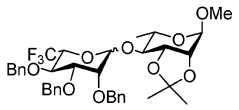
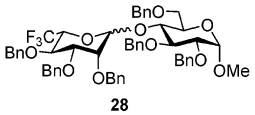
stereochemistry of the so-formed glycosidic products was made on the basis of the magnitude of the $^1J_{C1,H1}$ coupling constants.[80,81]

Glycosylation of the monofluoro donor **3** proceeded in good yield, but poor selectivity. In all but one case, a preference for the α- over *β*-isomer was observed (Table 2). A significant change in selectivity was detected going to the difluoro thioglycoside donor **6α**, with which the desired *β*-isomer was the major product of the glycosylation reactions, reaching a maximum of 3/1 *β*/α with a primary alcohol as acceptor (Table 3). A further improvement in *β*-selectivity was observed going from the difluoro donor **6α** to the trifluoro analog **12*β***, with the exception of glycosylation of acceptor **22** for which the α/*β* ratio was only 1/1.2 (Table 4).

The formation of significant amounts of the pyranose byproduct **11** was observed in coupling reactions with trifluoro donor **12*β***, which led us to examine further glycosylation reactions under the modified conditions. Thus, **12*β*** was activated at −60 °C by the BSP/Tf_2O couple in the presence of TTBP, followed by addition of the acceptor, and the reaction mixture was maintained at −60 °C for an extended period of time (18 h or, for the acceptor **22**, 24 h) before it was quenched. Application of this modified procedure gave a significant improvement in the yield and selectivity for the reaction of donor **12*β*** with acceptor **16** (Table 5) and decreased the amount of the byproduct **11** in the majority of cases.

To further probe the effect of the fluorine substituent(s) at the 6-position, glycosylation reactions with the analogous nonfluorinated substrates, the rhamno- (**30**)[82] and mannopyranoside derivatives (**31**),[83] were examined for comparison. The results of these coupling reactions under the original conditions with the acceptor **16** are presented in Table 6 (entries 1 and 2) along with pertinent literature examples (entries 3 and 4), in

Table 5. Glycosylations under the Modified Conditions

donor/ acceptor	product	α/β ratio (yield, %)[a]
3/16	 **19**	2.3/1[b] (78)
6α/16	 **23**	1/2.2[b] (78)
12β/16	 **26**	1/8.6[b] (87)
12β/17	 **27**	1/6.3 (83)
12β/18	 **29**	1/3.7[b] (67)
12β/22	 **28**	1/1.3 (70)

[a] Total isolated yield. [b] Determined from ^{1}H NMR spectrum of the crude reaction mixture.

which preactivation of donors **32**[84] or **33**[15] was performed at −78 °C. In accordance with the general pattern, each of these donors showed a high preference for the formation of α-linked products.

Deprotection of Disaccharides. In order to ascertain whether or not introduction of the fluorine atoms into rhamnopyranosides in this manner complicates deprotection, disaccharides **26*β***, **27*β***, **28*β***, and **29*β*** were submitted to the transformations described in Scheme 6. Hydrogenolysis of **28*β*** proceeded efficiently and resulted in a quantitative yield of **36**.

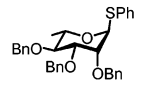
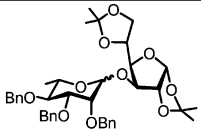
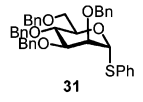
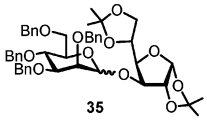
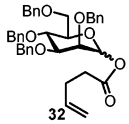
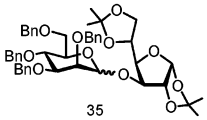
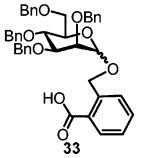
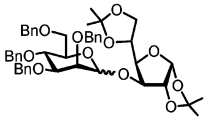
Cleavage of the acetonide protecting groups,[85] followed by the hydrogenolysis over $Pd(OH)_2$, enabled **37** and **38** to be obtained from **26*β*** and **29*β***, respectively. Hydrogenolysis of the benzyl ethers in **27*β*** was uneventful and gave **39** in quantitative yield.

Discussion

It is evident that introduction of fluorine atoms at the 6-position of the rhamnopyranoside donor enhances the *β*-se-

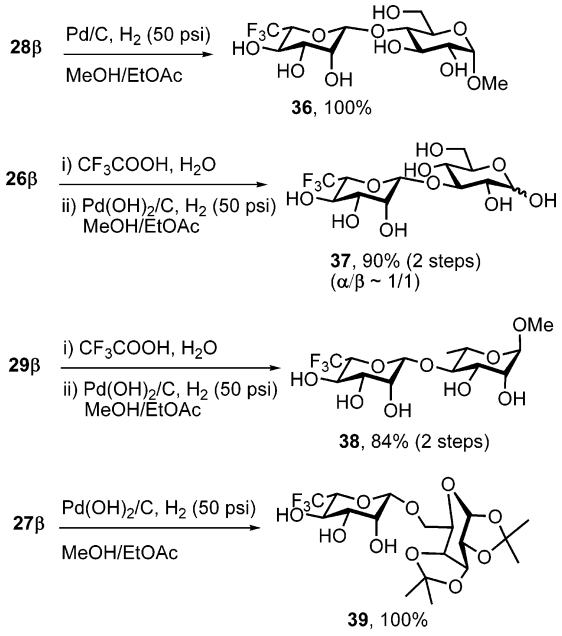
(80) Bock, K.; Pedersen, C. *J. Chem. Soc., Perkin Trans.* **1974**, *2*, 293−297.
(81) Duus, J. O.; Gotfredsen, C. H.; Bock, K. *Chem. Rev.* **2000**, *100*, 4589−4614.
(82) Furukawa, J.-I.; Kobayashi, S.; Nomizu, M.; Nishi, N.; Sakairi, N. *Tetrahedron Lett.* **2000**, *41*, 3453−3457.
(83) Charbonnier, F.; Penades, S. *Eur. J. Org. Chem.* **2004**, 3650−3656.
(84) Choi, T. J.; Baek, J. Y.; Jeon, H. B.; Kim, K. S. *Tetrahedron Lett.* **2006**, *47*, 9191−9194.
(85) Lemieux, R. U.; Hendriks, K. B.; Stick, R. V.; James, K. *J. Am. Chem. Soc.* **1975**, *97*, 4056−4062.

Table 6. Glycosylation Reactions with Rhamno- and Mannopyranoside Donors

donor	activation conditions	product	α/β ratio (yield, %)[a]
 **30**	BSP/Tf_2O, -60 °C	 **34**	7.6/1[b] (74)
 **31**	BSP/Tf_2O, -60 °C	 **35**	10.1/1[b] (79)
 **32**	PhSeOTf, -78 °C	 35	α only (83)[84]
 **33**	Tf_2O, -78 °C	 **35**	α only (77)[15]

[a] Total isolated yield. [b] Determined from ^{1}H NMR spectrum of the crude reaction mixture.

Scheme 6. Deprotection of Trifluororhamnopyranosides



lectivity of the rhamnosylation reaction. This is in agreement with the hypothesis of the dependence of the stereochemical outcome of the glycosylation reaction on the nature of the substituents at the 6-position, their influence on the stability of the intermediate oxacarbenuim ion and, consequently, on the key equilibria (Scheme 1). The β/α ratio of the disaccharide products increases going from nonfluorinated substrates to monofluoro donor **3** to difluoro donor **6α**, and further to trifluoro donor **12*β***. The increase in formation of the β-linked products with the monofluro donor as compared to the mannopyranoside donor can be attributed to the higher electronegativity of fluorine as compared to oxygen and obvious steric factors. Poor selectivity in the glycosylation of acceptor **19** with difluoro and trifluoro donors **6α** and **12*β***, as compared with the good β-selectivity in reactions with acceptors **16**, **17**, and **18**, is attributable to the sterically hindered nature of this acceptor and the stereochemical matching/mismatching phenomenon.[86,87]

The effect of the electron-withdrawing group at the 6-position on the stability of the covalent triflate was further demonstrated by low-temperature ^{1}H NMR experiments, in which decomposition temperatures increase with the number of fluorine atoms at C6. Surprisingly, introduction of the disarming substiuents to the rhamnosyl donors did not significantly influence the activation step (Table 1): in all cases putative glycosyl triflate intermediates were obtained from all thioglycosyl donors within minutes upon treatment with the BSP/Tf_2O pair at −60 °C.

Experimental Section

General. Unless otherwise noted, reactions were conducted under an inert atmosphere of argon or nitrogen. All ^{1}H, ^{13}C, and ^{19}F spectra were recorded in $CDCl_3$, except for the spectra of the compounds **36**, **37**, and **38** where CD_3OD was used as a solvent. All ^{19}F spectra were referenced to $CFCl_3$.

General Procedure for Variable-Temperature ^{1}H NMR Experiments. A solution of **3**, **6α**, or **12*β*** (0.02 to 0.05 mmol, 1 equiv) in CD_2Cl_2 (1 g) containing BSP (1 equiv) and TTBP (2 equiv) was placed into an NMR tube and cooled to −60 °C in the NMR probe. The first ^{1}H spectrum was obtained, then the sample was quickly removed from the probe and kept cool in a −60 °C acetone/dry ice bath during the addition of Tf_2O (1.1 equiv). The sample was returned to the NMR probe, and the ^{1}H spectrum was recorded again. The temperature was increased by 10 °C increments every 10 min, and ^{1}H NMR spectra were acquired at each temperature.

General Coupling Protocol (Method A). To a stirred solution of donor **3**, **6α**, or **12*β*** (1 equiv) in CH_2Cl_2 (~0.03 M), containing BSP (1 equiv), TTBP (2 equiv), and activated 3 Å powdered molecular sieves, Tf_2O (1.1 equiv) was added at −60 °C. The reaction mixture was stirred for 5 min at this temperature, and solution of acceptor **16**, **17**, **18**, or **22** (1.2 equiv) in CH_2Cl_2 (~0.09 M) was added dropwise. The reaction mixture was stirred for an additional 2 min at this temperature, then slowly warmed to room temperature, filtered, washed (saturated aq $NaHCO_3$), dried (Na_2SO_4), and concentrated. The crude was filtered through a pad of silica gel (with ethyl acetate as an eluent) and chromatographed using SiO_2.

General Coupling Protocol (Method B). To a stirred solution of donor **3**, **6α**, or **12*β*** (1 equiv) in CH_2Cl_2 (~0.03 M), containing BSP (1 equiv), TTBP (2 equiv), and activated 3 Å powdered molecular sieves, Tf_2O (1.1 equiv) were added at −60 °C. The reaction mixture was stirred for 5 min at this temperature, and solution of acceptor (1.2 equiv) in CH_2Cl_2 (~0.09 M) was added dropwise. The reaction mixture was stirred for an additional 18 h (for acceptors **16**, **17**, and **18**) or 24 h (for **22**) at −60 to −65 °C, then filtered, washed (saturated aq $NaHCO_3$), dried (Na_2SO_4), and concentrated. The crude reaction mixture was filtered through a pad of silica gel (with ethyl acetate as an eluent) and chromatographed using SiO_2.

2,3,4-Tri-*O*-benzyl-6-fluoro-α-D-rhamnopyranosyl-(1→3)-1,2:5,6-di-*O*-iso-propylidene-α-D-glucofuranose (19α) and 2,3,4-Tri-*O*-benzyl-6-fluoro-*β*-D-rhamnopyranosyl-(1→3)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (19*β*). Prepared by method A or method B (18 h at −60 to −65 °C) from **3** (50 mg, 0.092 mmol) and **16** (29 mg, 0.113 mmol). Purification by radial chromatography (SiO_2, hexanes to 1/4 ethyl acetate/hexanes) gave **19α** (41 mg, 64%, method A or 36 mg,

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57%, method B) and **19*β*** (15 mg, 24%, method A or 13 mg, 21%, method B). **19α**: $[\alpha]^{24}_D$ +11.6 (*c* 0.55, $CHCl_3$); ^1H NMR (501 MHz) δ 7.28−7.41 (m, 15H), 5.80 (d, J = 3.5 Hz, 1H), 5.26 (d, J = 1.3 Hz, 1H), 4.97 (d, J = 10.6 Hz, 1H), 4.76 (d, J = 12.5 Hz, 1H), 4.52−4.76 (m, 7H), 4.27 (s, 1H), 4.08−4.13 (m, 1H), 3.98−4.07 (m, 4H), 3.85 (dd, J = 9.4, 2.9 Hz, 1H), 3.72−3.82 (m, 2H), 1.49 (s, 3H), 1.41 (s, 3H), 1.34 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (126 MHz) δ 138.2, 138.04, 138.00, 128.6, 128.4, 128.2, 128.0, 127.9, 127.8, 127.73, 127.70, 112.1, 109.5, 105.2 ($^1J_{CH}$ = 182.6 Hz), 98.8 ($^1J_{CH}$ = 172.5 Hz), 83.8, 82.3 (d, J = 172.9 Hz), 81.4, 80.3, 79.5, 75.5, 73.9, 73.7 (d, J = 6.5 Hz), 72.5, 72.4, 72.11, 72.09 (d, J = 18.5 Hz), 67.8, 27.0, 26.9, 26.2, 25.6; ^{19}F (282 MHz) δ −233.8 (td, J = 47.7, 26.7 Hz, 1F); FABHRMS calcd for $C_{39}H_{47}FNaO_{10}$ $[M + Na]^+$, 717.3051; found, 717.3041. **19*β***: $[\alpha]^{23}_D$ −41.9 (*c* 0.32, $CHCl_3$); ^1H NMR (501 MHz) δ 7.39−7.42 (m, 2H), 7.27−7.36 (m, 13H), 5.91 (d, J = 3.3 Hz, 1H), 4.93 (d, J = 10.6 Hz, 1H), 4.88 (d, J = 12.1 Hz, 1H), 4.77 (d, J = 12.1 Hz, 1H), 4.42−4.67 (m, 8H), 4.31−4.33 (m, 1H), 4.28−4.29 (m, 1H), 4.13 (t, J = 7.5 Hz, 1H), 4.03−4.07 (m, 1H), 3.89 (t, J = 9.5 Hz, 1H), 3.84−3.87 (m, 1H), 3.52−3.55 (m, 1H), 3.40−3.49 (m, 1H), 1.50 (s, 3H), 1.43 (s, 3H), 1.32 (s, 3H), 1.31 (s, 3H); ^{13}C NMR (126 MHz) δ 138.3, 138.0, 128.53, 128.48, 128.3, 128.22, 128.17, 128.0, 127.8, 127.7, 127.6, 112.0, 108.6, 105.0 ($^1J_{CH}$ = 182.6 Hz), 99.9 ($^1J_{CH}$ = 155.3 Hz), 83.1, 82.23 (d, J = 172.9 Hz), 82.17, 81.2, 80.6, 75.3, 75.1 (d, J = 18.5 Hz), 74.2, 74.1, 73.6 (d, J = 6.5 Hz), 73.2, 71.8, 66.1, 26.8, 26.6, 26.4, 25.2; ^{19}F (282 MHz) δ −232.3 (td, J = 47.3, 23.7 Hz, 1F); FABHRMS calcd for $C_{39}H_{47}FNaO_{10}$ $[M + Na]^+$, 717.3051; found, 717.3033.

2,3,4-Tri-*O*-benzyl-6-fluoro-α-D-rhamnopyranosyl-(1→6)-1,2:3,4-di-*O*-iso-propylidene-α-D-galactopyranose (20α) and 2,3,4-Tri-*O*-benzyl-6-fluoro-*β*-D-rhamnopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (20*β*). Prepared by method A from **3** (50 mg, 0.092 mmol) and **17** (29 mg, 0.113 mmol). Purification by radial chromatography (SiO_2, hexanes to 1/4 ethyl acetate/hexanes) gave **20α** (28 mg, 43%) and **20*β*** (28 mg, 43%). **20α**: $[\alpha]^{24}_D$ −10.2 (*c* 0.58, $CHCl_3$); ^1H NMR (400 MHz) δ 7.27−7.40 (m, 15H), 5.52 (d, J = 5.0 Hz, 1H), 4.99 (d, J = 1.6 Hz, 1H), 4.95 (d, J = 10.8 Hz, 1H), 4.51−4.78 (m, 8H), 4.32 (dd, J = 5.0, 2.4 Hz, 1H), 4.16 (dd, J = 8.0, 1.8 Hz, 1H), 3.90−4.03 (m, 3H), 3.83 (dd, J = 2.9, 1.9 Hz, 1H), 3.73−3.81 (m, 2H), 3.66−3.72 (m, 1H), 1.51 (s, 3H), 1.44 (s, 3H), 1.34 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (101 MHz) δ 138.4, 138.3, 138.2, 128.44, 128.35, 128.1, 127.9, 127.8, 127.64, 127.62, 127.56, 109.4, 108.6, 97.6 ($^1J_{CH}$ = 169.4 Hz), 96.3 ($^1J_{CH}$ = 178.3 Hz), 82.3 (d, J = 173.2 Hz), 80.0, 75.3, 74.4, 73.8 (d, J = 6.6 Hz), 72.5, 72.1, 71.4 (d, J = 17.7 Hz), 71.0, 70.7, 70.6, 65.7, 65.4, 26.1, 26.0, 24.9, 24.6; ^{19}F (282 MHz) δ −234.2 (td, J = 47.5, 27.9 Hz, 1F); FABHRMS calcd for $C_{39}H_{47}FNaO_{10}$ $[M + Na]^+$, 717.3051; found, 717.3045. **20*β***: $[\alpha]^{24}_D$ −78.4 (*c* 0.62, $CHCl_3$); ^1H NMR (400 MHz) δ 7.48−7.53 (m, 2H), 7.22−7.36 (m, 13H), 5.60 (d, J = 5.0 Hz, 1H), 5.02 (d, J = 12.4 Hz, 1H), 4.98 (d, J = 10.8 Hz, 1H), 4.92 (d, J = 12.4 Hz, 1H), 4.70 (d, J = 3.2 Hz, 1H), 4.56−4.65 (m, 3H), 4.49 (s, 1H), 4.45 (d, J = 12.0 Hz, 1H), 4.31−4.36 (m, 2H), 4.19−4.25 (m, 2H), 4.10−4.14 (m, 1H), 4.02 (d, J = 2.9 Hz, 1H), 3.92 (t, J = 9.6 Hz, 1H), 3.62 (dd, J = 10.7, 8.5 Hz, 1H), 3.49 (dd, J = 9.4, 3.0 Hz, 1H), 3.36−3.48 (m, 1H), 1.49 (s, 3H), 1.45 (s, 3H), 1.34 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (101 MHz) δ 138.4, 138.2, 137.9, 128.8, 128.44, 128.35, 128.2, 128.1, 127.8, 127.6, 127.5, 109.6, 108.8, 102.4 ($^1J_{CH}$ = 155.1 Hz), 96.4 ($^1J_{CH}$ = 179.9 Hz), 82.2 (d, J = 173.9 Hz), 81.6, 75.3, 74.8 (d, J = 18.4 Hz), 73.7, 73.5 (d, J = 7.4 Hz), 72.4, 71.6, 71.0, 70.8, 70.5, 70.0, 68.0, 26.04, 25.99, 25.1, 24.4; ^{19}F (282 MHz) δ −232.7 (td, J = 47.5, 24.8 Hz, 1F); FABHRMS calcd for $C_{39}H_{47}FNaO_{10}$ $[M + Na]^+$, 717.3051; found, 717.3064.

Methyl 2,3,4-Tri-*O*-benzyl-6-fluoro-α-D-rhamnopyranosyl-(1→4)-2,3-*O*-iso-propylidene-α-L-rhamnopyranoside (21α) and Methyl 2,3,4-Tri-*O*-benzyl-6-fluoro-*β*-D-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (21*β*). Prepared from **3** (50 mg, 0.092 mmol) and **18** (25 mg, 0.113 mmol) by method A. Purification by radial chromatography (SiO_2, hexanes to 1/4 ethyl acetate/hexanes), followed by HPLC (SiO_2, hexanes to 1/4 ethyl acetate/hexanes) gave **21α** and **21*β*** (51 mg, 84%, α/β = 1/1.6). **21α**: $[\alpha]^{23}_D$ +42.9 (*c* 0.21, $CHCl_3$); ^1H NMR (501 MHz) δ 7.26−7.40 (m, 15H), 4.97 (d, J = 10.6 Hz, 1H), 4.86 (d, J = 1.3 Hz, 1H), 4.49−4.82 (m, 8H), 4.11 (t, J = 9.8 Hz, 1H), 4.04 (d, J = 5.7 Hz, 1H), 3.95−4.06 (m, 1H), 3.93 (dd, J = 7.2, 5.8 Hz, 1H), 3.86 (dd, J = 9.4, 3.0 Hz, 1H), 3.73 (dd, J = 2.8, 1.8 Hz, 1H), 3.46−3.55 (m, 1H), 3.33 (s, 3H), 3.29 (dd, J = 10.1, 7.5 Hz, 1H), 1.50 (s, 3H), 1.27 (s, 3H), 1.00 (d, J = 6.2 Hz, 3H); ^{13}C NMR (126 MHz) δ 138.5, 138.4, 138.1, 128.5, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 109.1, 99.3 ($^1J_{CH}$ = 171.4 Hz), 98.0 ($^1J_{CH}$ = 166.2 Hz), 82.2 (d, J = 172.0 Hz), 80.3, 80.1, 75.9, 75.5, 73.9 (d, J = 5.6 Hz), 73.8, 72.9, 72.4, 71.1 (d, J = 18.5 Hz), 64.7, 54.9, 28.1, 26.4, 17.2; ^{19}F (282 MHz) δ −236.6 (td, J = 48.3, 30.9 Hz, 1F); FABHRMS calcd for $C_{37}H_{45}FNaO_9$ $[M + Na]^+$, 675.2945; found, 675.2932. **21*β***: $[\alpha]^{23}_D$ −71.2 (*c* 0.16, $CHCl_3$); ^1H NMR (501 MHz) δ 7.41−7.45 (m, 2H), 7.25−7.36 (m, 13H), 4.91−4.98 (m, 3H), 4.87 (s, 1H), 4.78 (d, J = 12.5 Hz, 1H), 4.66 (d, J = 3.7 Hz, 1H), 4.58 (d, J = 10.8 Hz, 1H), 4.56 (d, J = 3.7 Hz, 1H), 4.53 (d, J = 11.9 Hz, 1H), 4.44 (d, J = 11.7 Hz, 1H), 4.14 (dd, J = 7.2, 5.7 Hz, 1H), 4.09 (d, J = 5.5 Hz, 1H), 3.95 (d, J = 3.1 Hz, 1H), 3.85 (t, J = 9.5 Hz, 1H), 3.68−3.73 (m, 1H), 3.61−3.68 (m, 1H), 3.57 (dd, J = 9.3, 3.0 Hz, 1H), 3.40−3.48 (m, 1H), 3.39 (s, 3H), 1.48 (s, 3H), 1.35 (d, J = 6.2 Hz, 3H), 1.32 (s, 3H); ^{13}C NMR (126 MHz) δ 138.8, 138.2, 138.1, 128.5, 128.4, 128.2, 128.1, 127.9, 127.7, 127.6, 127.5, 109.4, 99.8 ($^1J_{CH}$ = 157.2 Hz), 97.9 ($^1J_{CH}$ = 168.3 Hz), 82.44 (d, J = 173.9 Hz), 82.38, 78.5, 77.8, 76.1, 75.2, 75.0 (d, J = 18.5 Hz), 74.00, 73.97, 73.9 (d, J = 7.4 Hz), 71.3, 64.3, 54.9, 27.8, 26.5, 17.7; ^{19}F (282 MHz) δ −231.9 (td, J = 47.7, 23.7 Hz, 1F); FABHRMS calcd for $C_{37}H_{45}FNaO_9$ $[M + Na]^+$, 675.2945; found, 675.2921.

2,3,4-Tri-*O*-benzyl-6,6-difluoro-α-D-rhamnopyranosyl-(1→3)-1,2:5,6-di-*O*-iso-propylidene-α-D-glucofuranose (23α) and 2,3,4-Tri-*O*-benzyl-6,6-difluoro-*β*-D-rhamnopyranosyl-(1→3)-1,2:5,6-di-*O*-iso-propylidene-α-D-glucofuranose (23*β*). Prepared by method A from **6α** (50 mg, 0.089 mmol) and **16** (28 mg, 0.107 mmol) or by method B (18 h at −60 to −65 °C) from **23α** (25 mg, 0.044 mmol) and **16** (14 mg, 0.054 mmol). Purification by radial chromatography (SiO_2, hexanes to 1/4 ethyl acetate/hexanes) gave **23α** (17 mg, 26%, method A or 8 mg, 25%, method B) and **23*β*** (34 mg, 54%, method A or 17 mg, 53%, method B). **23α**: $[\alpha]^{24}_D$ +2.7 (*c* 0.26, $CHCl_3$); ^1H NMR (500 MHz) δ 7.28−7.39 (m, 15H), 6.01 (t, J = 54.4 Hz, 1H), 5.80 (d, J = 3.7 Hz, 1H), 5.29 (d, J = 1.7 Hz, 1H), 4.94 (d, J = 10.5 Hz, 1H), 4.74 (d, J = 12.3 Hz, 1H), 4.64 (d, J = 12.5 Hz, 1H), 4.63 (d, J = 10.6 Hz, 1H), 4.53−4.59 (m, 3H), 4.26 (d, J = 1.8 Hz, 1H), 3.99−4.12 (m, 5H), 3.78−3.87 (m, 2H), 3.76 (t, J = 2.4 Hz, 1H), 1.49 (s, 3H), 1.41 (s, 3H), 1.33 (s, 3H), 1.29 (s, 3H); ^{13}C NMR δ 138.0, 137.8, 137.7, 128.6, 128.44, 128.42, 128.2, 128.1, 127.8, 127.7, 113.9 (t, J = 244.1 Hz), 112.1, 109.4, 105.2 ($^1J_{CH}$ = 182.6 Hz), 99.0 ($^1J_{CH}$ = 172.5 Hz), 83.6, 81.3, 81.0, 79.0, 75.4, 73.7, 73.6, 72.5, 72.4, 72.1, 71.2 (t, J = 20.4 Hz), 67.8, 26.9, 26.8, 26.1, 25.6; ^{19}F (471 MHz) δ −132.9 (ddd, J = 285.0, 54.0, 9.4 Hz, 1F), −133.8 (ddd, J = 285.0, 54.3, 15.0 Hz, 1F); ESIHRMS calcd for $C_{39}H_{46}F_2NaO_{10}$ $[M + Na]^+$, 735.2957, found, 735.2947. **23*β***: $[\alpha]^{24}_D$ −52.8 (*c* 0.07, $CHCl_3$); ^1H NMR (501 MHz) δ 7.25−7.40 (m, 15H), 6.09 (td, J = 54.7, 3.1 Hz, 1H), 5.85 (d, J = 3.7 Hz, 1H), 4.82 (d, J = 10.8 Hz, 1H), 4.80 (d, J = 12.1 Hz, 1H), 4.72 (d, J = 12.1 Hz, 1H), 4.62−4.68 (m, 2H), 4.58 (d, J = 11.9 Hz, 1H), 4.52 (d, J = 11.9 Hz, 1H), 4.45 (d, J = 3.9 Hz, 1H), 4.39 (q, J = 6.0 Hz, 1H), 4.29 (d, J = 2.9 Hz, 1H), 4.24−4.27 (m, 1H), 3.98−4.07 (m, 3H), 3.88 (dd, J = 2.6, 1.7 Hz, 1H), 3.57−3.64 (m, 2H), 1.49 (s, 3H), 1.42 (s, 3H), 1.29 (s, 3H), 1.28 (s, 3H); ^{13}C NMR δ 138.1, 137.9, 137.6, 128.6, 128.5, 128.4, 128.2, 128.13, 128.09, 128.06, 127.82, 127.79, 127.5, 113.8 (t, J = 244.1 Hz), 112.0, 108.7, 105.0 ($^1J_{CH}$ = 182.6 Hz), 99.3 ($^1J_{CH}$ = 157.4 Hz), 82.9, 81.3, 80.8, 79.6, 74.5, 74.2 (t, J = 22.7 Hz), 73.7, 73.6, 72.8, 72.2, 66.4, 26.8, 26.7, 26.3, 25.0; ^{19}F (471 MHz) δ −129.5 (dd, J = 287.9, 51.8 Hz, 1F), −131.2 (dd, J = 287.9, 54.8 Hz, 1F); ESIHRMS calcd for $C_{39}H_{46}F_2NaO_{10}$ $[M + Na]^+$, 735.2957; found, 735.2952.

2,3,4-Tri-*O*-benzyl-6,6-difluoro-α-D-rhamnopyranosyl-(1→6)-1,2:3,4-di-*O*-iso-propylidene-α-D-galactopyranose (24α) and 2,3,4-Tri-*O*-benzyl-6,6-difluoro-*β*-D-rhamnopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (24*β*). Prepared by method A from **6α** (50 mg, 0.089 mmol) and **17** (28 mg, 0.107 mmol). Purification by radial chromatography (SiO_2, hexanes to 1/4 ethyl acetate/hexanes) gave **24α** (12 mg, 19%) and **24*β*** (36 mg, 57%). **24α**: $[\alpha]^{23}_D$ −9.3 (*c* 0.20, $CHCl_3$); ^{1}H NMR (501 MHz) *δ* 7.25−7.39 (m, 15H), 5.97 (t, *J* = 54.5 Hz, 1H), 5.53 (d, *J* = 5.0 Hz, 1H), 5.04 (d, *J* = 1.7 Hz, 1H), 4.92 (d, *J* = 10.6 Hz, 1H), 4.74 (d, *J* = 12.5 Hz, 1H), 4.70 (d, *J* = 12.5 Hz, 1H), 4.59−4.64 (m, 2H), 4.58 (s, 2H), 4.32 (dd, *J* = 5.0, 2.5 Hz, 1H), 4.15 (dd, *J* = 7.9, 1.8 Hz, 1H), 4.05 (t, *J* = 9.6 Hz, 1H), 3.94−3.98 (m, 1H), 3.92 (dd, *J* = 9.3, 3.0 Hz, 1H), 3.84−3.91 (m, 1H), 3.76−3.82 (m, 2H), 3.69 (dd, *J* = 10.8, 6.1 Hz, 1H), 1.51 (s, 3H), 1.43 (s, 3H), 1.33 (s, 6H); ^{13}C NMR (126 MHz) *δ* 138.2, 138.1, 138.0, 128.5, 128.4, 128.1, 127.90, 127.87, 127,73, 127.68, 127.5, 114.0 (t, *J* = 243.6 Hz), 109.5, 108.7, 97.5 ($^1J_{CH}$ = 170.0 Hz), 96.4 ($^1J_{CH}$ = 180.0 Hz), 79.6, 75.2, 74.1, 73.8, 72.5, 72.2, 71.0, 70.7, 70.58 (t, *J* = 19.9 Hz), 70.55, 65.9, 65.3, 26.1, 26.0, 25.0, 24.6; ^{19}F (471 MHz) *δ* −133.2 (ddd, *J* = 285.0, 54.0, 9.4 Hz, 1F), −134.5 (ddd, *J* = 285.0, 54.0, 16.6 Hz, 1F); ESIHRMS calcd for $C_{39}H_{46}F_2NaO_{10}$ $[M + Na]^+$, 735.2957; found, 735.2947. **24*β***: $[\alpha]^{23}_D$ −95.2 (*c* 0.65, $CHCl_3$); ^{1}H NMR (501 MHz) *δ* 7.48−7.51 (m, 2H), 7.23−7.35 (m, 13H), 6.02 (td, *J* = 54.4, 1.9 Hz, 1H), 5.59 (d, *J* = 5.0 Hz, 1H), 4.99 (d, *J* = 12.3 Hz, 1H), 4.92 (d, *J* = 10.6 Hz, 1H), 4.88 (d, *J* = 12.3 Hz, 1H), 4.60−4.63 (m, 1H), 4.63 (d, *J* = 10.8 Hz, 1H), 4.56 (s, 1H), 4.48 (d, *J* = 11.9 Hz, 1H), 4.36 (d, *J* = 11.9 Hz, 1H), 4.33−4.35 (m, 1H), 4.23 (dd, *J* = 8.0, 1.7 Hz, 1H), 4.19 (dd, *J* = 10.8, 2.4 Hz, 1H), 4.10−4.13 (m, 1H), 4.04 (t, *J* = 9.0 Hz, 1H), 4.01 (d, *J* = 2.6 Hz, 1H), 3.64 (dd, *J* = 10.8, 8.3 Hz, 1H), 3.50−3.58 (m, 2H), 1.48 (s, 3H), 1.45 (s, 3H), 1.34 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (126 MHz) *δ* 138.4, 137.9, 137.8, 128.7, 128.5, 128.4, 128.3, 128.1, 127.9, 127.71, 127.66, 127.6, 113.9 (t, *J* = 244.2 Hz), 109.6, 108.8, 102.3 ($^1J_{CH}$ = 157.4 Hz), 96.4 ($^1J_{CH}$ = 180.0 Hz), 80.7, 75.0, 74.0 (t, *J* = 21.8 Hz), 73.63, 76.57, 72.3, 71.5, 71.3, 70.8, 70.5, 70.1, 68.0, 26.1, 26.0, 25.1, 24.4; ^{19}F (471 MHz) *δ* −131.1 (ddd, *J* = 286.5, 54.6, 15.7 Hz, 1F), −132.2 (ddd, *J* = 286.5, 54.3, 15.2 Hz, 1F); ESIHRMS calcd for $C_{39}H_{46}F_2NaO_{10}$ $[M + Na]^+$, 735.2957; found, 735.2953.

Methyl 2,3,4-Tri-*O*-benzyl-6,6-difluoro-α-D-rhamnopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (25α) and Methyl 2,3,4-Tri-*O*-benzyl-6,6-difluoro-*β*-D-rhamnopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (25*β*). Prepared by method A from **6α** (50 mg, 0.089 mmol) and **22** (50 mg, 0.107 mmol). Purification by radial chromatography (SiO_2, elution consecutive plates with hexanes to 1/4 ethyl acetate/hexanes and then with 1/9 to 1/3 diethyl ether/hexanes) gave **25α** (22 mg, 27%) and **25*β*** (33 mg, 41%). **25α**: $[\alpha]^{24}_D$ +4.9 (*c* 0.39, $CHCl_3$); ^{1}H NMR (500 MHz) *δ* 7.19−7.38 (m, 28H), 7.11−7.15 (m, 2H), 5.84 (t, *J* = 54.6 Hz, 1H), 5.32 (d, *J* = 2.0 Hz, 1H), 5.10 (d, *J* = 11.7 Hz, 1H), 4.88 (d, *J* = 10.8 Hz, 1H), 4.67 (d, *J* = 12.1 Hz, 1H), 4.53−4.64 (m, 6H), 4.46−4.51 (m, 2H), 4.26 (d, *J* = 12.1 Hz, 1H), 4.21 (d, *J* = 12.1 Hz, 1H), 4.00 (t, *J* = 9.4 Hz, 1H), 3.80−3.89 (m, 3H), 3.66−3.75 (m, 5H), 3.54 (dd, *J* = 9.5, 3.5 Hz, 1H), 3.39 (s, 3H); ^{13}C NMR *δ* 138.8, 138.4, 138.2, 138.0, 137.8, 128.5, 128.4, 128.3, 128.2, 128.12, 128.06, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 127.3, 127.1, 126.6, 114.1 (t, *J* = 244.1 Hz), 100.5 ($^1J_{CH}$ = 172.7 Hz), 97.7 ($^1J_{CH}$ = 171.3 Hz), 81.4, 79.9, 79.2, 78.2, 75.7, 75.02, 74.97, 73.6, 73.3, 73.2, 72.3, 72.0, 71.4 (t, *J* = 20.4 Hz), 69.7, 69.0, 55.3; ^{19}F (471 MHz) *δ* −132.2 (ddd, *J* = 285.0, 53.6, 6.8 Hz, 1F), −133.2 (ddd, *J* = 285.0, 53.3, 11.5 Hz, 1F); ESIHRMS calcd for $C_{55}H_{58}F_2NaO_{10}$ $[M + Na]^+$, 939.3896; found, 939.3887. **25*β***: $[\alpha]^{24}_D$ −26.0 (*c* 0.57, $CHCl_3$); ^{1}H NMR (500 MHz) *δ* 7.20−7.43 (m, 30H), 5.81 (t, *J* = 54.5 Hz, 1H), 5.06 (d, *J* = 11.0 Hz, 1H), 4.85 (d, *J* = 10.6 Hz, 1H), 4.76−4.82 (m, 4H), 4.59−4.67 (m, 3H), 4.58 (d, *J* = 12.1 Hz, 1H), 4.44−4.51 (m, 3H), 4.33 (d, *J* = 12.1 Hz, 1H), 4.02 (t, *J* = 9.0 Hz, 1H), 3.88−3.97 (m, 2H), 3.70−3.74 (m, 1H), 3.68 (d, *J* = 2.8 Hz, 1H), 3.62 (dd, *J* = 11.0, 1.8 Hz, 1H), 3.52−3.57 (m, 2H), 3.40 (s, 3H), 3.32−3.39 (m, 1H), 3.29 (dd, *J* = 9.0, 2.9 Hz, 1H); ^{13}C NMR *δ* 139.3, 138.6, 138.3, 138.1, 137.8, 128.5, 128.44, 128.41, 128.14, 128.07, 127.97, 127.95, 127.9, 127.84, 127.81, 127.75, 127.5, 127.4, 127.3, 114.3 (t, *J* = 244.6 Hz), 100.7 ($^1J_{CH}$ = 157.6 Hz); 98.3 ($^1J_{CH}$ = 165.6 Hz), 81.3, 80.0, 79.5, 77.6, 75.4, 74.9, 74.4, 73.92, 73.85 (t, *J* = 22.7 Hz), 73.6, 72.5, 73.4 (d, *J* = 2.8 Hz), 71.8, 69.6, 68.8, 55.3; ^{19}F (471 MHz) *δ* −128.8 (ddd, *J* = 286.5, 54.0, 13.7 Hz, 1F), −131.6 (ddd, *J* = 286.5, 54.9, 8.8 Hz, 1F); ESIHRMS calcd for $C_{55}H_{58}F_2NaO_{10}$ $[M + Na]^+$, 939.3896; found, 939.3923.

2,3,4-Tri-*O*-benzyl-6,6,6-trifluoro-α-L-rhamnopyranosyl-(1→3)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (26α) and 2,3,4-Tri-*O*-benzyl-6,6,6-trifluoro-*β*-L-rhamnopyranosyl-(1→3)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (26*β*). Prepared by method A or method B (18 h at −60 to −65 °C) from **12*β*** (25 mg, 0.043 mmol) and **16** (14 mg, 0.052 mmol). Purification by radial chromatography (SiO_2, hexanes to 3/17 ethyl acetate/hexanes) gave **26α** (3 mg, 10%, method A), **26*β***, and **11α,*β*** (combined yield 16 mg, **26*β*/11α,*β*** = 1/0.42, **26*β*** 40%, **11α,*β*** 17%, method A) or only **26α** (3 mg, 10%, method B) and **26*β*** (24 mg, 77%, method B). **26α**: white solid; mp 100−102 °C; $[\alpha]^{18}_D$ −42.0 (*c* 0.20, $CHCl_3$); ^{1}H NMR (400 MHz) *δ* 7.24−7.40 (m, 15H), 5.77 (d, *J* = 3.7 Hz, 1H), 4.87 (s, 1H), 4.85 (d, *J* = 2.9 Hz, 1H), 4.82 (s, 1H), 4.62−4.69 (m, 4H), 4.52−4.62 (m, 1H), 4.31 (d, *J* = 2.9 Hz, 1H), 4.15 (d, *J* = 3.7 Hz, 1H), 4.02−4.12 (m, 4H), 3.89−3.95 (m, 1H), 3.78 (dd, *J* = 9.2, 3.1 Hz, 1H), 3.67−3.69 (m, 1H), 1.49 (s, 3H), 1.36 (s, 3H), 1.30 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (101 MHz) *δ* 138.1, 138.0, 137.9, 128.5, 128.4, 128.2, 128.1, 127.9, 127.78, 127.76, 124.3 (q, *J* = 280.9 Hz), 112.1, 109.6, 105.3 ($^1J_{CH}$ = 182.6 Hz), 95.7 ($^1J_{CH}$ = 170.0 Hz), 81.7, 80.8, 79.0, 77.0, 74.9, 74.5, 73.8, 73.3 72.9, 71.9, 69.8 (q, *J* = 30.2 Hz), 67.9, 26.8, 26.6, 26.2, 24.9; ^{19}F (376 MHz) *δ* −74.6 (d, *J* = 6.3 Hz, 3F); ESIHRMS calcd for $C_{39}H_{45}F_3NaO_{10}$ $[M + Na]^+$, 735.2863; found, 735.2855. **26*β***: white solid; mp 87−89 °C; $[\alpha]^{18}_D$ +30.5 (*c* 0.80, $CHCl_3$); ^{1}H NMR (500 MHz) *δ* 7.40−7.45 (m, 2H), 7.27−7.37 (m, 13H), 5.84 (d, *J* = 3.5 Hz, 1H), 4.88−4.93 (m, 2H), 4.84 (d, *J* = 12.5 Hz, 1H), 4.76 (d, *J* = 3.5 Hz, 1H), 4.68 (d, *J* = 10.1 Hz, 1H), 4.60 (s, 1H), 4.57 (d, *J* = 11.7 Hz, 1H), 4.54 (d, *J* = 11.9 Hz, 1H), 4.18 (d, *J* = 2.8 Hz, 1H), 4.15 (t, *J* = 9.4 Hz, 1H), 4.02−4.10 (m, 2H), 3.93−4.00 (m, 2H), 3.87 (d, *J* = 2.8 Hz, 1H), 3.71−3.78 (m, 1H), 3.52 (dd, *J* = 9.4, 2.8 Hz, 1H), 1.49 (s, 3H), 1.37 (s, 3H), 1.31 (s, 3H), 1.21 (s, 3H); ^{13}C NMR (126 MHz) *δ* 138.2, 137.62, 137.59, 128.5, 128.4, 127.3, 128.24, 128.20, 128.0, 127.9, 127.6, 123.5 (q, *J* = 280.2 Hz), 112.0, 109.2, 105.4 ($^1J_{CH}$ = 183.5 Hz), 102.6 ($^1J_{CH}$ = 157.8 Hz), 83.9, 83.3, 81.5, 81.0, 75.5, 74.1, 73.6, 73.23, 73.21 (q, *J* = 30.5 Hz), 72.5, 72.2, 67.9, 26.84, 26.82, 26.1, 25.4; ^{19}F (471 MHz) *δ* −75.4 (d, *J* = 6.5 Hz, 3F); ESIHRMS calcd for $C_{39}H_{45}F_3NaO_{10}$ $[M + Na]^+$, 735.2863; found, 735.2863.

2,3,4-Tri-*O*-benzyl-6,6,6-trifluoro-α-L-rhamnopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (27α) and 2,3,4-Tri-*O*-benzyl-6,6,6-trifluoro-*β*-L-rhamnopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (27*β*). Prepared by method A or method B (18 h at −60 to −65 °C) from **12*β*** (25 mg, 0.043 mmol) and **17** (14 mg, 0.052 mmol). Purification by radial chromatography (SiO_2, hexanes to 1/4 ethyl acetate/hexanes) gave **27α** (4 mg, 11%, method A), **27*β***, and **11α,*β*** (combined yield 24 mg, **27*β*/11α,*β*** = 1/0.08, **27*β*** 72%, **11α,*β*** 6%, method A) or only **27α** (4 mg, 11%, method B) and **27*β*** (23 mg, 72%, method B). **27α**: $[\alpha]^{15}_D$ −35.6 (*c* 0.18, $CHCl_3$); ^{1}H NMR (501 MHz) *δ* 7.24−7.40 (m, 15H), 5.50 (d, *J* = 5.1 Hz, 1H), 4.99 (d, *J* = 1.1 Hz, 1H), 4.85 (d, *J* = 10.3 Hz, 1H), 4.72 (s, 2H), 4.66 (d, *J* = 10.3 Hz, 1H), 4.57−4.61 (m, 3H), 4.32 (dd, *J* = 5.0, 2.6 Hz, 1H), 4.19−4.26 (m, 1H), 4.09−4.15 (m, 2H), 3.83−3.93 (m, 3H), 3.80 (dd, *J* = 2.9, 2.0 Hz, 1H), 3.55 (dd, *J* = 8.8, 5.9 Hz, 1H), 1.51 (s, 3H), 1.42 (s, 3H), 1.33 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (126 MHz) *δ* 138.2, 138.1, 128.4, 128.3, 128.0, 127.9, 127.74, 127.70, 124.4 (q, *J* = 280.2 Hz), 109.5, 108.6, 97.9 ($^1J_{CH}$ = 173.7 Hz), 96.2 ($^1J_{CH}$ = 180.0 Hz), 79.1, 75.1, 73.94, 73.87, 72.6, 72.4, 70.7, 70.5, 69.8 (q, *J* = 29.6 Hz), 66.5, 65.8, 26.2, 25.8, 25.0, 24.4; ^{19}F (471

MHz) δ −75.8 (d, J = 6.5 Hz, 3F); ESIHRMS calcd for $C_{39}H_{45}F_3NaO_{10}$ [M + Na]$^+$, 753.2863; found, 753.2851. **27*β***: $[\alpha]^{15}_D$ +29.1 (*c* 0.43, $CHCl_3$); ^{1}H NMR (500 MHz) δ 7.44−7.49 (m, 2H), 7.24−7.35 (m, 13H), 5.52 (d, J = 5.0 Hz, 1H), 4.96 (d, J = 12.5 Hz, 1H), 4.89 (d, J = 10.1 Hz, 1H), 4.88 (d, J = 12.3 Hz, 1H), 4.66 (d, J = 9.9 Hz, 1H), 4.59 (dd, J = 8.0, 2.3 Hz, 1H), 4.52 (d, J = 11.7 Hz, 1H), 4.484 (s, 1H), 4.479 (d, J = 11.7 Hz, 1H), 4.32 (dd, J = 5.0, 2.4 Hz, 1H), 4.19 (dd, J = 8.1, 1.8 Hz, 1H), 4.13 (t, J = 9.4 Hz, 1H), 4.04 (ddd, J = 8.0, 6.2, 1.6 Hz, 1H), 3.98 (dd, J = 9.4, 6.0 Hz, 1H), 3.92 (d, J = 2.9 Hz, 1H), 3.74 (dd, J = 9.4, 8.4 Hz, 1H), 3.66−3.73 (m, 1H), 3.52 (dd, J = 9.5, 2.9 Hz, 1H), 1.55 (s, 3H), 1.45 (s, 3H), 1.34 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (126 MHz) δ 138.4, 137.74, 137.67, 128.43, 128.39, 128.3, 128.2, 127.9, 127.8, 127.62, 127.55, 123.6 (q, J = 281.1 Hz), 109.1, 108.6, 102.0 ($^1J_{CH}$ = 156.5 Hz), 96.2 ($^1J_{CH}$ = 179.6 Hz), 81.4, 75.5, 73.8, 73.7, 73.2 (q, J = 30.5 Hz), 72.9, 71.9, 70.7, 70.5, 68.1, 65.6, 26.0, 24.9, 24.4; ^{19}F (471 MHz) δ −75.3 (d, J = 5.8 Hz, 3F); ESIHRMS calcd for $C_{39}H_{45}F_3NaO_{10}$ [M + Na]$^+$, 753.2863; found, 753.2835.

Methyl 2,3,4-Tri-*O*-benzyl-6,6,6-trifluoro-α-L-rhamnopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (28α) and Methyl 2,3,4-Tri-*O*-benzyl-6,6,6-trifluoro-*β*-L-rhamnopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (28*β*). Prepared by method A from **12*β*** (50 mg, 0.086 mmol) and **22** (48 mg, 0.103 mmol) or by method B (24 h at −60 to −65 °C) from **12*β*** (25 mg, 0.043 mmol) and **22** (24 mg, 0.052 mmol). Purification by radial chromatography (SiO_2, hexanes to 3/17 ethyl acetate/hexanes) gave **28α**, **28*β***, and **11α,*β*** (combined yield 56 mg, **28α**/**28*β***/**11α,*β*** = 1/1.2/0.02, **28α** 31%, **28*β*** 38%, **11α,*β*** <1%, method A or 31 mg, **28α**/**28*β***/**11α,*β*** = 1/1.29/0.41, **28α** 31%, **28*β*** 39%, **11α,*β*** 12%, method B). Analytical samples were obtained by further purification by radial chromatography (SiO_2, 1/7 to 3/17 ethyl acetate/hexanes). **28α**: $[\alpha]^{18}_D$ −2.7 (*c* 1.12, $CHCl_3$); ^{1}H NMR (500 MHz) δ 7.18−7.37 (m, 30H), 5.23 (d, J = 1.5 Hz, 1H), 4.92 (d, J = 10.5 Hz, 1H), 4.84 (d, J = 10.3 Hz, 1H), 4.70−4.77 (m, 2H), 4.62 (d, J = 10.3 Hz, 1H), 4.54−4.58 (m, 6H), 4.52 (d, J = 9.4 Hz, 1H), 4.41 (d, J = 12.1 Hz, 1H), 4.33−4.40 (m, 1H), 4.10 (t, J = 9.4 Hz, 1H), 3.79−3.88 (m, 3H), 3.61−3.65 (m, 2H), 3.52−3.57 (m, 2H), 3.43 (dd, J = 11.1, 3.4 Hz, 1H), 3.35 (s, 3H); ^{13}C NMR (126 MHz) δ 138.3, 138.11, 138.07, 138.03, 137.97, 137.8, 128.5, 128.4, 128.24, 128.22, 128.1, 128.0, 127.73, 127.67, 127.5, 127.4, 124.3 (q, J = 281.1 Hz), 97.9 ($^1J_{CH}$ = 168.7 Hz), 97.2 ($^1J_{CH}$ = 170.0 Hz), 80.6, 79.8, 78.5, 75.4, 75.2, 74.3, 74.1, 73.8, 73.6, 73.4, 72.33, 72.31, 70.4 (q, J = 29.6 Hz), 69.7, 68.8, 55.3; ^{19}F (471 MHz) δ −75.8 (d, J = 6.5 Hz, 3F); ESIHRMS calcd for $C_{55}H_{57}F_3NaO_{10}$ [M + Na]$^+$, 957.3802; found, 957.3778. **28*β***: $[\alpha]^{17}_D$ +35.3 (*c* 0.85, $CHCl_3$); ^{1}H NMR (500 MHz) δ 7.18−7.42 (m, 28H), 7.11−7.15 (m, 2H), 4.99 (d, J = 11.6 Hz, 1), 4.82 (d, J = 9.9 Hz, 1H), 4.72−4.80 (m, 3H), 4.58−4.68 (m, 5H), 4.48 (d, J = 12.3 Hz, 1H), 4.35 (d, J = 11.6 Hz, 1H), 4.25 (d, J = 11.6 Hz, 1H), 4.22 (d, J = 11.7 Hz, 1H), 4.02 (t, J = 9.5 Hz, 1H), 3.90 (dd, J = 11.0, 2.0 Hz, 1H), 3.87 (t, J = 9.4 Hz, 1H), 3.76−3.82 (m, 1H), 3.51−3.61 (m, 5H), 3.45 (s, 3H), 3.14 (dd, J = 9.4, 2.8 Hz, 1H); ^{13}C NMR (126 MHz) δ 138.7, 138.5, 138.4, 137.88, 137.85, 137.6, 128.5, 128.42, 128.39, 128.3, 128.20, 128.15, 128.1, 127.9, 127.73, 127.67, 127.4, 127.34, 127.29, 123.6 (q, J = 281.1 Hz), 102.2 ($^1J_{CH}$ = 158.3 Hz), 97.7 ($^1J_{CH}$ = 165.6 Hz), 82.01, 81.97, 79.8, 76.9, 75.5, 75.4, 73.7, 73.4, 73.1, 72.9 (q, J = 29.6 Hz), 72.8, 71.9, 69.6, 69.3, 55.4; ^{19}F (471 MHz) δ −75.4 (d, J = 5.8 Hz, 3F); ESIHRMS calcd for $C_{55}H_{57}F_3NaO_{10}$ [M + Na]$^+$, 957.3802; found, 957.3787.

Methyl 2,3,4-Tri-*O*-benzyl-6,6,6-trifluoro-α-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (29α) and Methyl 2,3,4-Tri-*O*-benzyl-6,6,6-trifluoro-*β*-L-rhamnopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (29*β*). Prepared from **12*β*** (25 mg, 0.043 mmol) and **18** (11 mg, 0.052 mmol) by method B. Purification by radial chromatography (SiO_2, hexanes to 3/17 ethyl acetate/hexanes) gave **29α** (5 mg, 15%), **29*β*** (15 mg, 52%), and **11α,*β*** (1 mg, 4%). **29α**: $[\alpha]^{15}_D$ −11.3 (*c* 0.08, $CHCl_3$); ^{1}H NMR (400 MHz) δ 7.40−7.45 (m, 2H), 7.29−7.38 (m, 13H), 5.57 (d, J = 1.2 Hz, 1H), 4.84−4.89 (m, 2H), 4.79 (d, J = 12.4 Hz, 1H), 4.74 (d, J = 12.4 Hz, 1H), 4.66 (d, J = 10.2 Hz, 1H), 4.61 (d, J = 11.7 Hz, 1H), 4.57 (d, J = 11.7 Hz, 1H), 4.15 (t, J = 9.2 Hz, 1H), 3.98−4.11 (m, 3H), 3.79−3.85 (m, 2H), 3.54−3.62 (m, 1H), 3.48−3.53 (m, 1H), 3.38 (s, 3H), 1.54 (s, 3H), 1.36 (s, 3H), 1.26 (d, J = 6.1 Hz, 3H);^{13}C NMR (126 MHz) δ 138.1, 138.0, 137.8, 128.4, 128.3, 128.0, 127.8, 127.73, 127.68, 127.6, 124.1 (q, J = 280.2 Hz), 109.7, 98.0 ($^1J_{CH}$ = 167.4 Hz), 97.2 ($^1J_{CH}$ = 175.9 Hz), 79.1, 78.7, 78.3, 76.1, 75.3, 74.3, 73.8, 72.42, 72.36, 70.6 (q, J = 29.6 Hz), 63.6, 54.9, 27.9, 26.4, 18.0; ^{19}F (471 MHz) δ −75.8 (d, J = 5.8 Hz, 3F); ESIHRMS calcd for $C_{37}H_{43}F_3NaO_9$ [M + Na]$^+$, 711.2757; found, 711.2765. **29*β***: $[\alpha]^{15}_D$ +40.6 (*c* 0.29, $CHCl_3$); ^{1}H NMR (400 MHz) δ 7.40−7.45 (m, 2H), 7.26−7.35 (m, 13H), 4.98 (d, J = 12.6 Hz, 1H), 4.89 (d, J = 9.9 Hz, 1H), 4.83 (s, 1H), 4.81 (d, J = 12.7 Hz, 1H), 4.64−4.69 (m, 2H), 4.46−4.56 (m, 3H), 4.10−4.16 (m, 2H), 3.92 (d, J = 2.9 Hz, 1H), 3.70−3.79 (m, 2H), 3.54 (dd, J = 9.2, 2.9 Hz, 1H), 3.40 (dd, J = 9.7, 7.1 Hz, 1H), 3.37 (s, 3H), 1.47 (s, 3H), 1.30 (s, 3H), 1.28 (d, J = 6.3 Hz, 3H); ^{13}C NMR (101 MHz) δ 138.3, 137.8, 137.7, 128.4, 128.3, 128.2, 127.9, 127.8, 127.6, 127.5, 123.6 (q, J = 280.9 Hz), 109.0, 101.2 ($^1J_{CH}$ = 155.2 Hz), 98.4 ($^1J_{CH}$ = 167.2 Hz), 83.9, 82.0, 76.2, 75.7, 75.5, 73.9, 73.7, 73.5, 73.1 (q, J = 30.2 Hz), 71.9, 63.7, 54.9, 28.0, 25.9, 17.9; ^{19}F (376 MHz) δ −74.4 (d, J = 6.3 Hz, 3F); ESIHRMS calcd for $C_{37}H_{43}F_3NaO_9$ [M + Na]$^+$, 711.2757; found, 711.2769.

2,3,4-Tri-*O*-benzyl-α-L-rhamnopyranosyl-(1→3)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (34α) and 2,3,4-Tri-*O*-benzyl-*β*-L-rhamnopyranosyl-(1→3)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (34*β*). Prepared by method A from **30**[82] (50 mg, 0.095 mmol) and **16** (30 mg, 0.115 mmol). Purification by radial chromatography (SiO_2, hexanes to 3/17 ethyl acetate/hexanes) gave **34α** (42 mg, 65%) and **34*β*** (6 mg, 10%). **34α**: $[\alpha]^{23}_D$ −68.1 (*c* 0.80, $CHCl_3$); ^{1}H NMR (501 MHz) δ 7.25−7.41 (m, 15H), 5.77 (d, J = 3.9 Hz, 1H), 4.93 (d, J = 11.4 Hz, 1H), 4.86 (d, J = 12.3 Hz, 1H), 4.75 (d, J = 1.5 Hz, 1H), 4.63−4.69 (m, 4H), 4.28 (d, J = 3.1 Hz, 1H), 4.14−4.19 (m, 2H), 4.05−4.09 (m, 2H), 3.94−4.01 (m, 1H), 3.90 (dd, J = 8.4, 5.9 Hz, 1H), 3.75 (dd, J = 9.2, 3.1 Hz, 1H), 3.69 (dd, J = 3.0, 1.9 Hz, 1H), 3.60 (t, J = 9.4 Hz, 1H), 1.49 (s, 3H), 1.38 (s, 3H), 1.31 (s, 3H), 1.28 (s, 3H), 1.28 (d, J = 6.2 Hz, 3H); ^{13}C NMR (126 MHz) δ 139.1, 138.6, 138.5, 128.64, 128.59, 128.4, 128.04, 127.98, 127.9, 127.8, 127.6, 112.2, 109.4, 105.4 ($^1J_{CH}$ = 182.7 Hz), 96.1 ($^1J_{CH}$ = 168.2 Hz), 82.0, 81.2, 80.5, 80.1, 76.9, 75.5, 75.1, 73.6, 72.8, 72.2, 68.8, 68.0, 27.0, 26.4, 25.5, 17.9; ESIHRMS calcd for $C_{39}H_{48}NaO_{10}$ [M + Na]$^+$, 699.3145; found, 699.3107. **34*β***: $[\alpha]^{22}_D$ +13.3 (*c* 0.06, $CHCl_3$); ^{1}H NMR (501 MHz) δ 7.22−7.45 (m, 15H), 5.87 (d, J = 3.5 Hz, 1H), 4.96 (d, J = 10.6 Hz, 1H), 4.91 (d, J = 12.6 Hz, 1H), 4.84 (d, J = 12.6 Hz, 1H), 4.80 (d, J = 3.7 Hz, 1H), 4.66 (d, J = 10.8 Hz, 1H), 4.56 (d, J = 12.0 Hz, 1H), 4.49−4.53 (m, 2H), 4.16 (d, J = 2.6 Hz, 1H), 4.01−4.08 (m, 2H), 3.92−3.99 (m, 2H), 3.86 (d, J = 2.8 Hz, 1H), 3.62 (t, J = 9.4 Hz, 1H), 3.46 (dd, J = 9.0, 2.6 Hz, 1H), 3.30−3.37 (m, 1H), 1.50 (s, 3H), 1.39 (d, J = 6.1 Hz, 3H), 1.37 (s, 3H), 1.31 (s, 3H), 1.21 (s, 3H); ^{13}C NMR (126 MHz) δ 138.8, 138.7, 138.4, 128.7, 128.6, 128.41, 128.37, 128.0, 127.94, 127.86, 127.8, 112.1, 109.3, 105.7 ($^1J_{CH}$ = 183.5 Hz), 102.8 ($^1J_{CH}$ = 155.8 Hz), 84.5, 83.0, 82.6, 81.4, 80.3, 75.7, 74.3, 74.2, 72.8, 72.4, 72.1, 68.2, 27.12, 27.09, 26.5, 25.7, 18.3; ESIHRMS calcd for $C_{39}H_{48}NaO_{10}$ [M + Na]$^+$, 699.3145; found, 699.3122.

2,3,4,6-Tri-*O*-benzyl-α-D-mannopyranosyl-(1→3)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (35α) and 2,3,4,6-Tri-*O*-benzyl-*β*-D-mannopyranosyl-(1→3)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (35*β*). Prepared by method A from **31**[83] (50 mg, 0.079 mmol) and **16** (25 mg, 0.095 mmol). Purification by radial chromatography (SiO_2, hexanes to 1/4 ethyl acetate/hexanes) gave **35α** (44 mg, 71%) and **35*β*** (5 mg, 8%). **35α**: $[\alpha]^{24}_D$ +16.3 (*c* 0.10, $CHCl_3$); lit. $[\alpha]_D$ +15.9 (*c* 0.08, $CHCl_3$);[88] ^{1}H NMR (501 MHz) δ 7.21−7.40 (m, 18H), 7.15−7.20 (m, 2H), 5.81 (d, J = 3.5 Hz, 1H), 5.25 (s, 1H), 4.90 (d, J

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= 10.5 Hz, 1H), 4.76 (d, J = 12.3 Hz, 1H), 4.65−4.70 (m, 3H), 4.49−4.61 (m, 4H), 4.28 (s, 1H), 3.97−4.11 (m, 5H), 3.75−3.86 (m, 5H), 1.49 (s, 3H), 1.41 (s, 3H), 1.34 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (126 MHz) δ 138.6, 138.50, 138.47, 138.4, 128.63, 128.58, 128.55, 128.4, 128.1, 128.0, 127.92, 127.86, 127.8, 112.2, 109.5, 105.5 ($^1J_{CH}$ = 182.9 Hz), 99.1 ($^1J_{CH}$ = 170.4 Hz), 83.9, 81.6, 80.8, 79.8, 75.5, 75.0, 74.5, 73.7, 72.9, 72.8, 72.5, 72.3, 69.5, 67.9, 27.14, 27.05, 26.3, 25.8. Spectral data recorded in C_6D_6 matched that reported in literature.[88] **35*β***: $[\alpha]^{23}_D$ −41.9 (*c* 0.32, $CHCl_3$); ^{1}H NMR (501 MHz) δ 7.20−7.43 (m, 20H), 5.92 (d, J = 3.7 Hz, 1H), 4.90 (d, J = 12.1 Hz, 1H), 4.89 (d, J = 10.6 Hz, 1H), 4.79 (d, J = 11.9 Hz, 1H), 4.72 (d, J = 11.9 Hz, 1H), 4.55−4.60 (m, 3H), 4.53 (d, J = 11.9 Hz, 1H), 4.49 (s, 1H), 4.45−4.48 (m, 2H), 4.35 (d, J = 2.9 Hz, 1H), 4.31 (dd, J = 5.1, 3.1 Hz, 1H), 4.10−4.13 (m, 1H), 4.03−4.07 (m, 1H), 3.96 (t, J = 9.5 Hz, 1H), 3.85 (d, J = 2.8 Hz, 1H), 3.77−3.83 (m, 2H), 3.52 (dd, J = 9.4, 2.9 Hz, 1H), 3.43 (ddd, J = 9.6, 4.7, 2.4 Hz, 1H), 1.50 (s, 3H), 1.39 (s, 3H), 1.31 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (126 MHz) δ 138.80, 138.75, 138.5, 138.4, 128.64, 128.61, 128.56, 128.4, 128.3, 128.1, 128.0, 127.9, 127.8, 112.2, 108.8, 105.3 ($^1J_{CH}$ = 182.9 Hz), 99.9 ($^1J_{CH}$ = 154.1 Hz), 83.2, 82.6, 80.89. 80.85, 76.8, 75.5, 74.9, 74.7, 74.3, 74.0, 73.5, 72.1, 69.6, 66.4, 27.1, 26.9, 26.6, 25.5; ESIHRMS calcd for $C_{46}H_{54}NaO_{11}$ [M + Na]$^+$, 805.3564; found, 805.3522.

Methyl 6,6,6-Trifluoro-*β*-L-rhamnnopyranosyl-(1→4)-α-D-glucopyranoside (36). A mixture of **28*β*** (16 mg, 0.017 mmol) and Pd/C (15 wt %, 14 mg, 0.02 mmol) in MeOH/ethyl acetate (1 mL/2 mL) was shaken overnight in a pressure vessel under an atmosphere of hydrogen (50 psi). The reaction mixture was filtered twice through a pad of Celite (with MeOH as an eluent) and concentrated to give **36** (7 mg, quantitative). $[\alpha]^{16}_D$ +107.0 (*c* 0.29, MeOH); ^{1}H NMR (400 MHz) δ 4.92 (s, 1H), 4.67 (d, J = 3.8 Hz, 1H), 4.01 (d, J = 2.9 Hz, 1H), 3.90−3.97 (m, 1H), 3.84 (t, J = 9.5 Hz, 1H), 3.76 (t, J = 9.4 Hz, 1H), 3.66−3.73 (m, 1H), 3.59−3.66 (m, 2H), 3.43−3.50 (m, 2H), 3.37−3.43 (m, 4H); ^{13}C NMR (101 MHz) δ, 125.4 (q, J = 280.1 Hz), 102.8 ($^1J_{CH}$ = 162.1 Hz), 101.0 ($^1J_{CH}$ = 172.4 Hz), 79.2, 75.0, 74.9 (q, J = 29.3 Hz), 74.5, 73.6, 72.1, 71.5, 67.3, 63.2, 55.6; ^{19}F (377 MHz) δ −75.9 (d, J = 6.3 Hz, 3F); ESIHRMS calcd for $C_{13}H_{21}F_3NaO_{10}$ [M + Na]$^+$, 417.0985; found, 417.0983.

6,6,6-Trifluoro-*β*-L-rhamnopyranosyl-(1→3)-α,*β*-D-glucopyranose (37). A mixture of **26*β*** and **11α,*β*** (40 mg, **26*β*/11α,*β*** = 6/1, **26*β*** 0.049 mmol), trifluoroacetic acid (1.8 mL), and water (0.2 mL) was stirred for 15 min at room temperature and then rapidly concentrated under reduced pressure. Purification by radial chromatography (SiO_2, $CHCl_3$ to 1/9 MeOH/$CHCl_3$), collecting only the more polar fractions, gave the product as a clear oil (29 mg, 90%). A mixture of the product and $Pd(OH)_2$/C (50% H_2O, 15 wt %, 38 mg, 0.027 mmol) in MeOH/ethyl acetate (2 mL/1 mL) was shaken for 24 h in a pressure vessel under an atmosphere of hydrogen (50 psi). The reaction mixture was filtered twice through a pad of Celite (with MeOH as an eluent), concentrated, and washed with CH_2Cl_2 to give **37** (17 mg, 90%, two steps, α/*β* ∼ 1/1). White solid; mp 141 °C (decomp); $[\alpha]^{19}_D$ +55.7 (*c* 0.30, MeOH); ^{1}H NMR (500 MHz) δ 5.16 (d, J = 3.7 Hz, 1H, $H_1\alpha$), 5.04 (dd, J = 4.5, 0.6 Hz, 2H), 4.55 (d, J = 7.7 Hz, 1H, $H_1\beta$), 4.04 (d, J = 3.1 Hz, 2H), 3.92 (t, J = 9.2 Hz, 1H), 3.87 (t, J = 9.5 Hz, 2H), 3.84 (dd, J = 11.9, 2.4 Hz, 1H), 3.58−3.82 (m, 8H), 3.45−3.53 (m, 5H), 3.26 (dd, J = 9.2, 7.9 Hz, 1H); ^{13}C NMR (101 MHz) δ 125.3 (q, J = 280.4 Hz), 102.2 ($^1J_{CH}$ = 162.2 Hz), 102.0 ($^1J_{CH}$ = 161.8 Hz), 97.7 ($^1J_{CH}$ = 159.6 Hz, $C_1\beta$), 93.5 ($^1J_{CH}$ = 168.1 Hz. $C_1\alpha$), 86.0, 83.3, 77.8, 75.0 (q, J = 29.5 Hz), 74.6, 74.4, 73.0, 72.2, 71.8, 71.7, 71.4, 71.3, 67.3, 62.5, 62.4; ^{19}F (377 MHz) δ −75.6 (d, J = 6.3 Hz, 3F), −75.7 (d, J = 6.3 Hz, 3F); ESIHRMS calcd for $C_{12}H_{19}F_3NaO_{10}$ [M + Na]$^+$, 403.0828; found, 403.0817.

Methyl 6,6,6-Trifluoro-*β*-L-rhamnnopyranosyl-(1→4)-α-L-rhamnopyranoside (38). A mixture of **29*β*** (10 mg, 0.015 mmol), trifluoroacetic acid (1.8 mL), and water (0.2 mL) was stirred for 15 min at room temperature, and then rapidly concentrated under reduced pressure. The reaction mixture was filtered through a pad of silica gel (with 3/7 mixture of hexanes/ethyl acetate as an eluent) and concentrated. The residue was dissolved in MeOH/ethyl acetate (2 mL/1 mL), and $Pd(OH)_2$/C (50% H_2O, 15 wt %, 6 mg, 0.004 mmol) was added. The reaction mixture was shaken overnight in the pressure vessel under an atmosphere of hydrogen (50 psi) and then concentrated. Purification by column chromatography (SiO_2, 3/17 to 1/4 MeOH/$CHCl_3$) gave **38** (5 mg, 84%, two steps). Mp 86 °C (decomp); $[\alpha]^{16}_D$ −20.9 (*c* 0.23, MeOH); ^{1}H NMR (400 MHz) δ 4.78 (s, 1H), 4.57 (d, J = 1.6 Hz, 1H), 3.96 (d, J = 3.1 Hz, 1H), 3.80−3.90 (m, 3H), 3.77 (dd, J = 9.1, 3.3 Hz, 1H), 3.63−3.72 (m, 1H), 3.59 (t, J = 9.3 Hz, 1H), 3.53 (dd, J = 8.8, 3.1 Hz, 1H), 3.34 (s, 3H), 1.29 (d, J = 6.1 Hz, 3H); ^{13}C NMR (126 MHz) δ 125.3 (q, J = 280.2 Hz), 102.5 ($^1J_{CH}$ = 158.6 Hz), 102.4 ($^1J_{CH}$ = 168.7 Hz), 84.8, 74.9 (q, J = 29.6 Hz), 74.4, 71.8, 71.5, 70.7, 67.9, 67.1, 55.2, 17.9; ^{19}F (377 MHz) δ −75.7 (d, J = 6.3 Hz, 3F); ESIHRMS calcd for $C_{13}H_{21}F_3NaO_9$ [M + Na]$^+$, 401.1035; found, 401.1030.

6,6,6-Trifluoro-*β*-L-rhamnopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (39). A mixture of **27*β*** (13 mg, 0.017 mmol) and $Pd(OH)_2$/C (50% H_2O, 15 wt %, 15 mg, 0.01 mmol) in MeOH/ethyl acetate (1 mL/2 mL) was shaken for 24 h in the pressure vessel under an atmosphere of hydrogen (50 psi). The reaction mixture was filtered twice through a pad of Celite (with MeOH and then with ethyl acetate as an eluent) and concentrated to give **39** (8 mg, quantitative). $[\alpha]^{16}_D$ −17.0 (*c* 0.37, $CHCl_3$); ^{1}H NMR (500 MHz) δ 5.52 (d, J = 5.1 Hz, 1H), 4.59−4.65 (m, 2H), 4.33 (dd, J = 5.0, 2.4 Hz, 1H), 4.29 (dd, J = 7.9, 1.5 Hz, 1H), 4.09 (br s, 1H), 3.96−4.06 (m, 3H), 3.82 (dd, J = 9.5, 6.8 Hz, 1H), 3.54−3.68 (m, 2H), 3.24 (br s, 3H), 1.52 (s, 3H), 1.45 (s, 3H), 1.35 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (126 MHz) δ 123.3 (q, J = 280.6 Hz), 109.5, 108.8, 100.0 ($^1J_{CH}$ = 159.2 Hz), 96.2 ($^1J_{CH}$ = 180.6 Hz), 73.5, 73.4 (q, J = 30.7 Hz), 70.7, 70.6, 70.5, 69.5, 67.8, 66.9, 65.6, 26.0, 24.8, 24.5; ^{19}F (471 MHz) δ −75.8 (d, J = 5.8 Hz, 3F); ESIHRMS calcd for $C_{18}H_{27}F_3NaO_{10}$ [M + Na]$^+$, 483.1454; found, 483.1437.

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Supporting Information Available: Details of the preparation of all donors and copies of NMR spectra for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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