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Synthesis of the Salmonella Type E_1 Core Trisaccharide as a Probe for the Generality of 1-(Benzenesulfinyl)piperidine/Triflic Anhydride Combination for Glycosidic Bond Formation from Thioglycosides

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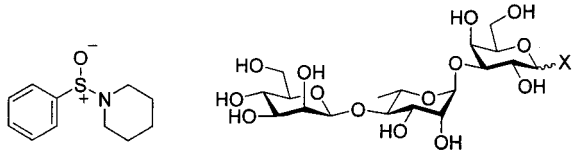
A synthesis of a chromogenic glycoside of the *Salmonella anatum* group E_1 core trisaccharide is presented in which all three glycosidic bonds, a 1,2-*cis*-equatorial, a 1,2-*trans*-axial, and a 1,2-*trans*-equatorial linkage representing three of the four main classes of glycosidic bond, are formed with thioglycoside donors activated under a single set of conditions by the combination of 1-(benzenesulfinyl)piperidine and trifluoromethanesulfonic anhydride. 2,3-*O*-Carbonyl- and 2,3-*O*-isopropylidene-α-L-rhamnopyranosyl thioglycosides are found to be highly α-selective rhamnosyl donors under these conditions.

Introduction

The efficient, stereocontrolled formation of glycosidic bonds is argueably the most fundamental reaction in glycoscience, the study of the chemistry and biology of carbohydrates, their oligomers, and conjugates.[1−5] Not surprisingly, therefore, there is an almost bewildering diversity of methods available for the synthesis of glycosidic bonds. Some of these can be said to be of purely historical value while others are in widespread use,[6] and yet more are introduced on an almost daily basis. Despite the large number of methods available, very few can be said to be applicable in all circumstances and to have the type of generality needed in a paradigm-simplifying, universal method such as will ultimately be required for a truly automated oligosaccharide synthesizer.[7] The thioglycosides, very widely employed stable glycosyl donors, provide a good illustration of the problem with a broad range of mostly unstable activators in common use depending on the precise linkage required and the array of protecting groups present.[8,9] Tables of reactivity have been compiled which categorize the effect of protecting groups on thioglycoside reactivity,[10,11] but among the thioglycosides only the highly performant sulfoxide method has been shown to enable the coupling of a broad range of donors to an equally broad cross section of acceptors under a small set of closely related reaction conditions.[12,13] The combination of 1-(benzenesulfinyl)piperidine (**1**, BSP) and triflic anhydride recently developed in



1 (BSP)

2: X = α,β-OH
3: X = β-O(CH$_2$)$_4$C$_6$H$_4$-4-NO$_2$

this laboratory for the activation of thioglycosides evolved,[14] via benzenesulfenyl triflate[15,16] and then *S*-aryl benzenethiosulfinates,[17] out of our studies on the application of the sulfoxide method to the synthesis of *β*-mannosides.[16,18,19] In view of the origins of this reagent combination and the constraints of broad generality and high reactivity imposed in the developmental stages, it is not surprising that the BSP/Tf_2O/thioglycoside method

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posseses many of the attributes of the sulfoxide method. Here, we illustrate this versatility through the synthesis of the trisaccharide core of the salmonella serotype E_1[20] with its 1,2-*cis*-equatorial, 1,2-*trans*-axial, and 1,2-*trans*-equatorial linkages, i.e., three of the four main classes, with only minor variations on a single set of reaction conditions.

Kochetkov and co-workers previously described two syntheses of the salmonella type E_1 core trisaccharide **2**. In the first of these the difficult β-mannoside linkage was introduced by anchimerically assisted β-glucoside formation followed by a three-step protocol for the gluco to manno inversion of stereochemistry. Both glycosidic bonds were established through the mercuric cyanide mediated coupling of glycosyl bromides to the appropriate alcohols.[21,22] The second synthesis was shorter insofar as the β-mannosidic linkage was introduced directly by means of Gorin's 4,6-di-*O*-acetyl-2,3-*O*-carbonate-protected α-mannosyl bromide[23] and an insoluble silver promoter. The α-rhamnosyl linkage was again formed by the mercuric cyanide mediated coupling of a rhamnosyl bromide and the galactose alcohol.[24] Thus, although shorter, the second route employed two different heavy or precious metal mediated coupling reactions. Several trisaccharide analogues were subsequently synthesized, in which the reducing end was capped as a phosphate ester[25] or conjugated to polyacrylamide,[26] by variations on the same themes. Trisaccharide **3** was later prepared by Thorson, who employed a different method for each of the three glycosidic bonds.[27] Thus, the α-rhamnoside was formed in a Koenigs−Knorr reaction using silver triflate as mediator, the β-galactoside was introduced by means of Danishefsky's glycal assembly method,[28] and finally the β-mannoside was obtained using a mannosyl transferase and GDP-mannose as the donor with the usual limitations on scale that this method entails. While the use of the enzymic coupling is relatively unusual, this last sequence is not atypical of present oligosaccharide synthesis with a different method often being required for each different linkage. In contrast to these previous syntheses of **2** and **3**, the one that we present below is direct, free of the use of precious or heavy metal promoters, and employs a single standardized glycosylation method for each of the three disparate linkages.

Results and Discussion

A series of thioglycoside donors were first prepared. Thus, D-galactose was converted to diol **4** by standard means followed by selective introduction of the 3-*O*-*p*-methoxybenzyl ether, as in **5**, by treatment first with dibutyltin oxide and then PMB chloride as described by Nicolaou and co-workers.[29] The pivalate ester was selected for protection of the remaining hydroxyl group, giving **6**, as it is reputed to minimize ortho ester formation in the course of neighboring group directed glycosylations.[30−32] *S*-Phenyl α-L-thiorhamnopyranoside[33] was converted to the 2,3-*O*-carbonate **7** and its 3-*O*-*tert*-butyldimethylsilyl ether **8** by standard means. Subsequent events led us to fall back on the 2,3-*O*-isopropylidene derivative **10,** which was also obtained routinely via **9**.[34] Finally, the two thioglycosides **12**[16] and **13** were obtained from diol **11**[35,36] by standard methods.

TABLE 1. Glycosidic Coupling Reactions

donor	acceptor	base	additive	product (% yield)	α/β selectivity
6	**14**	TTBP	$BF_3{\cdot}OEt_2$	**15** (75)	β only
6	**14**			**16** (80)	β only
8	**16**	TTBP		**17** (63)	α only
10	**16**	TTBP		**18** (64)	α only
12	**19**	TTBP		**21** (90)[a]	1/2
13	**20**	TTBP		**22** (92)[a,b]	1/9.6

[a] Yield for the anomeric mixture. [b] The yield of pure **22**β was 71%.

The formation of the β-galactosidic linkage to alcohol **14** was first attempted by activation of the thioglycoside **6** with BSP and triflic anhydride in the presence of BF_3 etherate and 2,4,6-tri-*tert*-butylpyrimidine (TTBP) as base when **15** was obtained in 75% yield as a pure β-anomer (Table 1). The pyrimidine TTBP is a convenient, crystalline alternative to 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP) that we recently introduced, whose nonhygroscopic, much less volatile nature operationally facilitates the sulfoxide and BSP methods alike.[37] The combination of DTBMP as base to buffer the sulfoxide glycosylation reaction and $BF_3{\cdot}$etherate, with which it does not form a complex,[38] was recommended by Kahne to minimize ortho ester formation in the course of neighboring group participation.[39] Subsequently, the PMB group was removed with DDQ to give **16** in 85% yield. A better overall method, however, simply involved omitting the base (and the BF_3) from the coupling of **6** and **14** when **16** was obtained directly in 80% yield (Table 1). Fortuitously, the acidic conditons of this coupling affected rearrangement of any kinetic ortho ester and the removal of the PMB protecting group, thereby revealing

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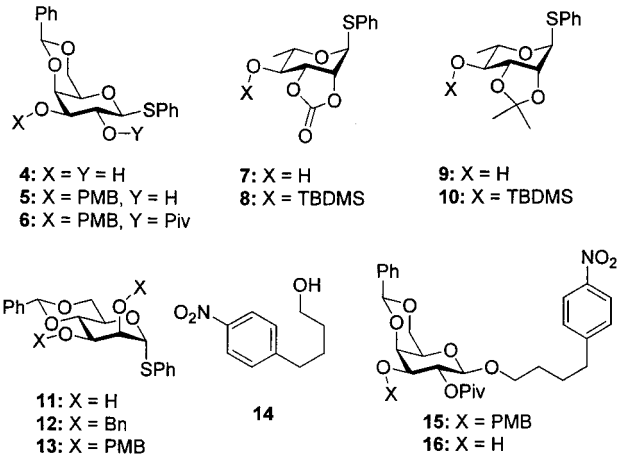
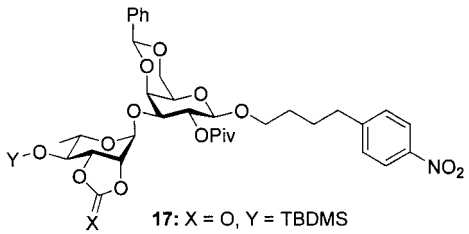
the galactose 3-OH for the next coupling and removing a step from the planned sequence.[40]

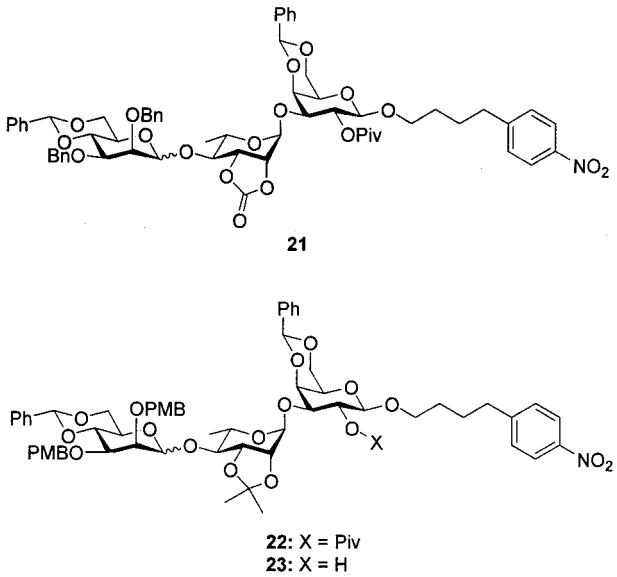


Previously we discovered that the important β-directing effect of the 4,6-*O*-benzylidene group in our thioglycoside approaches to β-mannosides is completely overridden by a 2,3-*O*-carbonate in the donor.[14,41] It seemed logical, therefore, that donors such as **8** would be highly α-selective in the rhamnosylation of alcohol **16**. The observation of the α-directing nature of the 2,3-*O*-carbonate in the benzenesulfenyl triflate and BSP/Tf_2O methods is in complete contrast to the β-directing effect of the same group in insoluble silver salt mediated mannosylation and rhamnosylations with glycosyl bromides.[23,42] When the BSP/Tf_2O conditions were applied to the coupling of the thioglycoside **8** with **16** in the presence of TTBP, the desired α-rhamnoside **17** was obtained in 63% yield as a single anomer (Table 1). We also investigated the formation of the α-rhamnosidic linkage by means of the 2,3-*O*-isopropylidene thioglycoside **10**. It proved to be very comparable to the carbonate **8** giving the disaccharide **18** in 64% yield as a single anomer (Table 1). This observation also contrasts with rhamnosylation using 4-*O*-benzoyl-2,3-*O*-cyclohexylidene-α-L-rhamnopyranosyl bromide and an insoluble silver salt promoter which is reported to be highly β-selective.[43,44]



The TBDMS group was removed from disaccharides **17** and **18** with TBAF in the standard manner to give the glycosyl acceptors **19** and **20**, respectively. Coupling of **19** with the mannosyl donor **12** under the standard BSP/Tf_2O conditions gave the trisaccharide **21** in 90% yield but as a disappointing 2:1 β:α mixture (Table 1). The poor anomeric selectivity in this coupling is obviously a function of the acceptor alcohol as we have previously conducted many couplings with **12** or the corresponding sulfoxide and found them to be highly β-selective. Much has rightly been made of the arming and disarming effects of protecting groups on glycosyl donor reactivity.[11,45,46] It is only recently, however, that their effects on glycosyl acceptors have begun to be studied in any systematic manner,[47,48] although it has long been recognized that benzylated acceptors are more reactive than the corresponding acetylated ones.[49,50] We presume that the poor selectivity with acceptor **19** is due to the strongly electron-withdrawing carbonate protecting group which reduces the nucleophilicity of the adjacent alcohol. In this manner the β-selective S_N2-like attack on the intermediate α-mannosyl triflate is retarded, thereby enabling competing glycosylation by the S_N1 pathway. Attention was therefore focused on the acetonide-protected acceptor **20**. In view of the fact that the acetonide group would eventually need to be removed under acidic conditions, the donor for this coupling was changed to the 2,3-di-*O*-(*p*-methoxybenzyl) thioglycoside **13** in order that all protecting groups other than the pivalate ester might be cleaved in a single step. Application of the BSP/Tf_2O method to the coupling of **13** with **20** in the presence of TTBP gave the trisaccharide **22** in excellent yield and selectivity (Table 1).

The pivalate ester was removed from **22** by saponification with sodium methoxide in hot methanolic THF to give **23** in 68% yield. Exposure of **23** to a 5% solution of trifluoroacetic acid in dichloromethane at room temperature, followed by neutralization with commercial tris-(2-aminoethyl)aminopolystyrene[51] and preparative TLC of the filtrate, afforded the target molecule (**3**) in 46% yield as a white crystalline solid whose physical and spectral parameters matched those reported in the literature.[27]



While the stereochemical assignment of the galactopyranosidic linkage in **15** and **16** is routine and that of

(40) In the developmental work on the BSP method numerous neighboring group-directed glycosylations were conducted in the absence of base without apparent detriment or ortho ester formation.[14]

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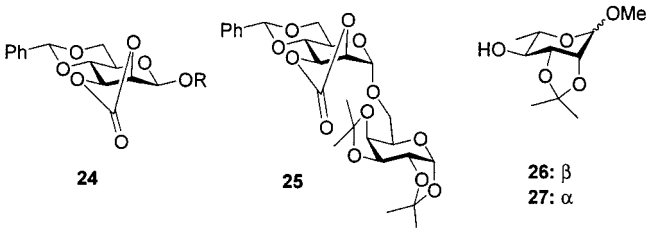
the mannopyranosidic ones in **21** and **22** almost so, on the basis of the well-established upfield chemical shift of the mannose H5 resonance in 4,6-*O*-benzylidene-protected β- but not α-mannosides[16] and on anomeric $^1J_{CH}$ coupling constants,[52] that of the rhamnosides **17** and **18** is far from obvious. The problem arises because, as is generally recognized, the 2,3-*O*-carbonate or the 2,3-*O*-isopropylidene group effectively flattens the pyranose ring into a half-chair conformation thereby excluding the application of the usual relationships between the anomeric $^1J_{CH}$ coupling constant and anomeric configuration in typical pyranosides with chair conformations.[52,53] For example, we noted earlier[41] that a series of 4,6-*O*-benzylidene-2,3-*O*-carbonyl-β-D-mannopyranosides (**24**)[54] and a similarly protected α-D-mannopyranoside (**25**)[41] had very similar anomeric $^1J_{CH}$ couplings of 170.9−172.0 and 171.2 Hz, respectively. Coincidentally, **24** and **25** also have similar chemical shifts for their mannose H1 and H5 resonances. The problem is all the more important because, as in the mannose series,[41] we report that both the 2,3-*O*-carbonate and 2,3-*O*-isopropylidene protected donors **8** and **10** are highly α-selective in our chemistry, with the probable intermediacy of glycosyl triflates,[14,19] whereas earlier workers using similarly protected rhamnosyl bromides in insoluble silver salt mediated couplings report high β-selectivity.[42−44] The assignment of stereochemistry in these established reports of β-selective rhamnosylations is based on correlations with known compounds after removal of the 2,3-*O*-carbonate or 2,3-*O*-alkylidene group, and no meaningful data are provided for the immediate coupling products with the cyclic protection in place.[42−44] Scrutiny of the physical data for **24** and **25** suggests that the most facile distinction between the two anomers is to be found in the $^3J_{H1,H2}$ coupling constant which is ~3 Hz in **24**[54] and <1 Hz in **25**.[41] If, as is very likely, the 2,3-*O*-carbonyl and 2,3-*O*-alkylidene α- and β-rhamnopyranosides adopt half-chair conformations similar to those of **24** and **25**, then a similar diagnostic should be available. A literature search revealed the $^3J_{H1,H2}$ coupling constants of methyl 2,3-*O*-isopropylidene-β- and α-L-rhamnopyranoside (**26** and **27**) to be 3 and 0 Hz, respectively, in strong support of this postulate.[55] On this basis we assign the newly formed linkages in **17** and **18**, both with their respective couplings of 0 Hz for the rhamnose moiety, as α-rhamnosides. In the case of **18** this assignment is ultimately borne out by conversion to the target molecule **3**, for which we measured anomeric $^1J_{CH}$ couplings of 155.0, 157.9, and 170.3 MHz consistent with the presence of two equatorial and one axial glycosidic bonds and whose physical characteritics were identical with those given by Thorson;[27] we see no reason to doubt the α-rhamnoside configuration of **17**.



In conclusion we have carried out a direct synthesis of the salmonella group E_1 core trisaccharide **3** in which all three glycosidic bonds, representing three of the four main classes, are formed with a single reagent combination under conditions that differ only by the presence or absence of a hindered base.

Experimental Section

General Procedures. Unless otherwise stated ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution at 300 and 75 MHz, respectively. Specific rotations were measured in $CHCl_3$ solution at ambient temperature (21 ± 1 °C) unless stated to the contrary. All solvents were dried and distilled by the standard protocols and all experiments conducted under an atmosphere of dry nitrogen or argon. Organic extracts were dried over anhydrous $MgSO_4$. HRMS were conducted by the Research Resources Laboratory of the University of Illinois at Chicago, IL, or the Mass Spectrometry Laboratory of the University of Minnesota. Microanalyses were carried out by Midwest Microlabs, Indianapolis, IN.

General Procedure for Glycosylation with BSP/Tf_2O. To a stirred solution containing thioglycoside (2.0 equiv), TTBP (4.0 equiv), BSP (2.0 equiv), and activated 4 Å powdered molecular sieves in CH_2Cl_2 (0.1 M) was added Tf_2O (2.0 equiv) at −60 °C under Ar. After 5 min, a solution of the glycosyl acceptor (1.0 equiv) in CH_2Cl_2 (1.0 M) was added. The reaction mixture was stirred at −60 °C for 1 hour and then warmed to 0 °C, quenched with saturated aqueous $NaHCO_3$, and diluted with EtOAc. The reaction mixture was washed with water, the water phase was extracted with EtOAc three times, and the combined organic phase was washed with water and brine, dried, filtered, and concentrated. The crude reaction mixture was isolated by column chromatography on silica gel.

***S*-Phenyl 4,6-*O*-Benzylidene-3-*O*-(*p*-methoxybenzyl)-2-*O*-pivaloyl-1-thio-β-D-galactopyranoside (6).** Phenyl 4,6-*O*-benzylidene-3-*O*-(*p*-methoxybenzyl)-1-thio-β-D-galactopyranoside (**5**)[29] (1.11 g, 2.32 mmol) and DMAP (0.14 g, 1.16 mmol) were dissolved in CH_2Cl_2 (30 mL), and Et_3N (0.9 mL, 0.706 g, 6.95 mmol) and pivaloyl chloride (0.58 mL, 4.63 mmol) were added at room temperature. The reaction mixture was stirred under reflux for 24 h, cooled to room temperature, and quenched with CH_3OH, diluted with CH_2Cl_2, and washed with saturated aqueous $NaHCO_3$ then brine. The organic phase was dried, filtered, concentrated, and purified by column chromatography on silica gel (eluent: EtOAc/hexane = 1/3 and then 1/1). The thioglycoside **6** (1.020 g, 1.80 mmol) was obtained in 78% yield as a white solid: mp 176 ± 1 °C; $[\alpha]_D$ +4.4° (*c*, 0.2); ^{1}H NMR δ 7.19−7.62 (m, 12 H), 6.83 (d, J = 8.7 Hz, 2H), 5.43 (s, 1H), 5.33 (t, J = 10.0 Hz, 1H), 4.69 (d, J = 9.6 Hz, 1H), 4.58 (d, J = 12.0 Hz, 1H), 4.57 (d, J = 12.0 Hz, 1H), 4.33 (dd, J = 1.6, 12.2 Hz, 1H), 4.12 (d, J = 3.3 Hz, 1H), 3.97 (dd, J = 1.4, 12.2 Hz, 1H), 3.78 (s, 3H), 3.66 (dd, J = 3.4, 10.0 Hz, 1H), 3.42 (broad s, 1H), 1.21 (s, 9H); ^{13}C NMR δ 176.6, 159.4, 137.9, 133.3, 132.5, 130.1, 129.3, 129.1, 128.9, 128.2, 127.9, 126.7, 113.9, 101.2, 86.0, 78.4, 73.5, 71.1, 70.1, 69.4, 68.1, 55.4, 38.9, 27.4. Anal. Calcd for $C_{32}H_{36}O_7S\cdot0.5H_2O$: C, 66.99; H, 6.50. Found: C, 66.72; H, 6.45.

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***S*-Phenyl 2,3-*O*-Carbonyl-1-thio-α-L-rhamnopyranoside (7).** To a stirred solution of phenyl 1-thio-α-L-rhamnopyranoside[33] (2.39 g, 9.3 mmol) in pyridine (12 mL) at 0 °C was added phosgene (7.4 mL of 20% in toluene, 14.0 mmol) dropwise by syringe pump, after which the reaction mixture was stirred for 1 h before it was poured slowly into a mixture of ice−water and saturated aqueous $NaHSO_3$. The water phase was extracted with EtOAc, and the combined organic phase was washed with water and brine, dried, filtered, and concentrated. The crude reaction mixture was triturated with Et_2O to afford **7** (1.818 g, 6.44 mmol) in 69% yield as white solid: mp 188 ± 1 °C; $[\alpha]_D$ −357.3° (*c*, 0.1); ^{1}H NMR δ 7.20−7.55 (m, 5H), 5.78 (s, 1H), 4.88 (d, J = 6.7 Hz, 1H), 4.71 (t, J = 7.0 Hz, 1H), 4.12−4.26 (m, 1H), 3.56−3.68 (m, 1H), 2.48 (d, J = 4.7 Hz, 1H), 1.23 (d, J = 6.1 Hz, 3H); ^{13}C NMR δ 153.5, 132.8, 129.5, 128.7, 82.2, 79.1, 77.8, 74.1, 66.5, 25.9. Anal. Calcd for $C_{13}H_{14}O_5S$: C, 55.31; H, 5.00. Found: C, 55.37; H, 4.94.

***S*-Phenyl 2,3-*O*-Isopropylidene-1-thio-α-L-rhamnopyranoside (9).**[34] To a stirred solution of phenyl 1-thio-α-L-rhamnopyranoside[33] (1.157 g, 4.51 mmol) and *p*-TsOH (0.082 g, 0.42 mmol, 10 mol %) in acetone (18 mL) was added 2,2-dimethoxypropane (5.2 mL, 4.442 g, 41.8 mmol, 10 equiv) at room temperature, and the reaction mixture was stirred overnight. After the starting material was consumed, the reaction mixture was diluted with CH_2Cl_2 (100 mL) and washed with saturated aqueous $NaHCO_3$ and water. The organic phase was dried, filtered, and concentrated. The crude reaction mixture was purified by column chromatography on silica gel (eluent: EtOAc/hexane = 1/5), and compound **9** (1.278 g, 4.31 mmol) was obtained in 95% yield as white solid: mp 78 ± 1 °C; $[\alpha]_D$ −220.0° (*c*, 0.6); ^{1}H NMR δ 7.20−7.54 (m, 5H), 5.75 (s, 1H), 4.35 (d, J = 5.5 Hz, 1H), 4.02−4.18 (m, 2H), 3.41−3.53 (m, 1H), 2.75−2.92 (broad s, 1H), 1.54 (s, 3H), 1.37 (s, 3H), 1.18 (d, J = 6.2 Hz, 3H); ^{13}C NMR δ 133.5, 132.0, 129.2, 129.1, 127.8, 109.9, 83.8, 78.5, 76.7, 75.3, 67.1, 28.3, 26.5, 17.2. Anal. Calcd for $C_{15}H_{20}O_4S\cdot 0.25H_2O$: C, 59.88; H, 6.87. Found: C, 59.52; H, 6.82.

***S*-Phenyl 2,3-*O*-Carbonate-4-*O*-(*tert*-butyldimethylsilyl)-1-thio-α-L-rhamnopyranoside (8).** The thiorhamnoside **7** was converted to the title compound **8**, analogously to the conversion of **9** to **10** described below, in 83% yield as a white solid: mp 81 ± 1 °C; $[\alpha]_D$ −208.8° (*c*, 0.3); ^{1}H NMR δ 7.32−7.52 (m, 5H), 5.76 (s, 1H), 4.85 (d, J = 7.2 Hz, 1H), 4.61 (t, J = 6.9 Hz, 1H), 4.08−4.20 (m, 1H), 3.50 (dd, J = 7.2, 9.6 Hz, 1H), 1.22 (d, J = 6.3 Hz, 3H), 0.92 (s, 9H), 0.20 (s, 3H), 0.12(s, 3H); ^{13}C NMR δ 188.3, 153.5, 132.8, 131.9, 129.5, 128.6, 82.5, 79.9, 78.0, 75.1, 67.2, 25.9, 18.2, 17.6, −4.3, −4.8. Anal. Calcd for $C_{19}H_{28}O_5SSi$: C, 57.54; H, 7.12. Found: C, 57.22; H, 6.98.

***S*-Phenyl 2,3-*O*-Isopropylidene-4-*O*-(*tert*-butyldimethylsilyl)-α-L-rhamnopyranoside (10).** To a stirred solution of **9** (0.846 g, 2.85 mmol) and imidazole (0.490 g, 7.13 mmol) in DMF (4 mL) was added TBDMSCl (0.526 g, 3.42 mmol) after which the reaction mixture was stirred at 40 °C overnight until the starting material was consumed. The reaction mixture was then diluted with EtOAc and washed with water, and the water phase was extracted with EtOAc three times. The combined organic phase was washed with brine, dried, filtered, and concentrated. The crude reaction mixture was purified by column chromatography on silica gel (eluent: EtOAc/hexane = 1/5) to give **10** (0.864 g, 2.10 mmol) in 74% yield as an oil: $[\alpha]_D$ −173.5° (*c*, 2.0); ^{1}H NMR δ 7.20−7.52 (m, 5H), 5.73 (s, 1H), 4.32 (d, J = 5.7 Hz, 1H), 3.96−4.04 (m, 2H), 3.41 (dd, J = 7.2, 9.6 Hz, 1H), 1.52 (s, 3H), 1.35 (s, 3H), 1.18 (d, J = 6.3 Hz, 3H), 0.90 (s, 9H), 0.16 (s, 3H), 0.09 (s, 3H); ^{13}C NMR δ 133.9, 131.9, 129.1, 127.6, 109.3, 84.1, 79.0, 76.9, 76.4, 67.8, 28.3, 26.7, 26.0, 18.3, 17.8, −3.8, −4.7. Anal. Calcd for $C_{21}H_{34}O_4SSi$: C, 61.42; H, 8.34. Found: C, 61.45; H, 8.43.

***S*-Phenyl 4,6-*O*-Benzylidene-2,3-di-*O*-(*p*-methoxybenzyl)-1-thio-α-D-mannopyranoside (13).** Phenyl 4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (**11**)[35,36] (0.461 g, 1.28 mmol), NaH (0.128 g, 3.19 mmol), and $Bu_4N^+I^-$ (1.204 g, 3.19 mmol) were mixed together and dried under vacuum for 30 min. DMF (10 mL) was then added, the reaction mixture was stirred for 30 min at room temperature before it was cooled to 0 °C, and *p*-methoxybenzyl chloride (0.502 g, 3.19 mmol) was added dropwise. The reaction mixture was first stirred for 15 min at 0 °C and then at room temperature for 5 h. It was quenched with saturated aqueous $NaHCO_3$, diluted with EtOAc, and washed with water. The water phase was extracted with EtOAc three times, and the combined organic phase was washed with water and brine, dried, filtered, and evaporated. The crude reaction mixture was purified by column chromatography on silica gel (eluent: EtOAc/hexane = 1/3), and **13** (0.491 g, 0.82 mmol) was obtained in 64% yield as oil: $[\alpha]_D$ +44.3° (*c*, 1.1); ^{1}H NMR δ 7.20−7.60 (m, 14H), 6.89 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 5.66 (s, 1H), 5.46 (s, 1H), 4.75 (d, J = 1.7 Hz, 1H), 4.66 (s, 2H), 4.59 (d, J = 11.7 Hz, 1H), 4.20−4.32 (m, 3H), 3.85−4.04 (m, 3H), 3.82 (s, 3H), 3.81 (s, 3H); ^{13}C NMR δ 159.5, 159.4, 137.8, 134.0, 131.8, 130.6, 130.0, 129.9, 129.5, 129.3, 129.0, 128.4, 127.8, 126.3, 114.0, 113.9, 101.6, 87.4, 79.2, 77.7, 75.9, 72.9, 72.8, 68.7, 65.7, 55.4. Anal. Calcd for $C_{35}H_{36}O_7S$: C, 69.98; H, 6.04. Found: C, 69.60; H, 5.98.

1-[4-(4-Nitrophenyl)]butyl 4,6-*O*-Benzylidene-3-*O*-(*p*-methoxybenzyl)-2-*O*-pivaloyl-β-D-galactopyranoside (15). To a stirred solution containing the thiogalactoside **6** (0.300 g, 0.53 mmol), BSP (0.111 g, 0.53 mmol), TTBP (0.264 g, 1.06 mmol), and powdered molecular sieves in CH_2Cl_2 (0.53 mL) at −60 °C was added freshly distilled Tf_2O (89.3 μL, 0.53 mmol). After 10 min, a mixture of 4-(4-nitrophenyl)-1-butanol (**14**) (0.14 mL, 0.80 mmol) and $BF_3\cdot Et_2O$ (0.39 mL, 4.25 mmol) in CH_2Cl_2 (1.4 mL) was added dropwise. The reaction mixture was stirred at −60 °C for 1 h and then warmed to 0 °C, quenched with aqueous $NaHCO_3$, diluted with EtOAc, and washed with water. The water phase was extracted with EtOAc, and the combined organic phase was washed with water and brine, dried, filtered, and concentrated. The crude reaction mixture was purified by column chromatography on silica gel (eluent: EtOAc/hexane = 1/3 then 1/1), and the saccharide **15** (0.260 g, 0.40 mmol) was obtained in 75% yield as a white solid: mp 153 ± 1 °C; $[\alpha]_D$ +4.7° (*c*, 0.3); ^{1}H NMR δ 8.09 (d, J = 6.8 Hz, 2H), 7.20−7.60 (m, 9H), 6.84 (d, J = 8.0 Hz, 2H), 5.47 (s, 1H), 5.36 (dd, J = 8.1, 10.2 Hz, 1H), 4.60 (d, J = 12.0 Hz, 1H), 4.57 (d, J = 12.0 Hz, 1H), 4.41 (d, J = 8.1 Hz, 1H), 4.26 (d, J = 12.3 Hz, 1H), 4.10 (d, J = 3.6 Hz, 1H), 4.02 (d, J = 12.6 Hz, 1H), 3.82−3.96 (m, 1H), 3.78 (s, 3H), 3.59 (dd, J = 3.4, 10.0 Hz, 1H), 3.40−3.52 (m, 1H), 3.33 (broad s, 1H), 2.60−2.74 (m, 2H), 1.50−1.80 (m, 4H), 1.17 (s, 9H); ^{13}C NMR δ 176.9, 159.4, 150.6, 146.3, 137.9, 130.2, 129.4, 129.3, 129.0, 128.2, 126.5, 123.7, 113.9, 101.3, 73.4, 71.0, 69.9, 69.3, 68.4, 66.7, 55.4, 38.9, 35.6, 29.2, 27.6, 27.3. Anal. Calcd for $C_{36}H_{43}O_{10}N$: C, 66.55; H, 6.67. Found: C, 66.32; H, 6.81.

Preparation of 1-[4-(4-Nitrophenyl)]butyl 4,6-*O*-Benzylidene-2-*O*-pivaloyl-1-thio-β-D-galactopyranoside (16) by Removal of the PMB Group from 15. PMB ether **15** (0.321 g, 0.49 mmol) was dissolved in a mixture of CH_2Cl_2 (9 mL) and H_2O (0.5 mL) at room temperature, and then DDQ (0.252 g, 1.08 mmol) was added at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and then at room temperature until the starting material was consumed. The reaction was quenched with saturated aqueous $NaHCO_3$, diluted with CH_2Cl_2, and washed with saturated aqueous $NaHCO_3$ and water until the organic phase was clear. The organic phase was washed with brine, dried, filtered, and concentrated. The crude reaction mixture was purified by column chromatography on silica gel (eluent: EtOAc/hexane = 1/3 and then 1/1), and the alcohol **16** (0.222 g, 0.42 mmol) was obtained in 85% yield as white foam: $[\alpha]_D$ −1.6° (*c*, 3.5); ^{1}H NMR δ 8.10 (d, J = 8.8 Hz, 2H), 7.20−7.58 (m, 7H), 5.55 (s, 1H), 5.09 (dd, J = 8.1, 9.9 Hz, 1H), 4.44 (d, J = 8.1 Hz, 1H), 4.30 (d, J = 12.9 Hz, 1H), 4.19 (d, J = 3.6 Hz, 1H), 4.07 (d, J = 12.9 Hz, 1H), 3.86−3.98 (m, 1H), 3.72 (ddd, J = 3.9, 10.5, 10.5 Hz, 1H), 3.40−3.54 (m, 2H), 2.62−2.78 (m, 2H), 2.47 (d, J = 10.8 Hz, 1H), 1.50−1.84 (m, 4H), 1.18 (s, 9H); ^{13}C NMR δ 178.2, 150.5, 146.4, 137.5, 129.4,

128.4, 126.5, 123.7, 101.4, 100.9, 75.7, 72.0, 71.9, 69.2, 68.8, 66.6, 35.6, 29.2, 27.6, 27.2, 27.1. Anal. Calcd for $C_{28}H_{35}O_9N\cdot 0.5H_2O$: C, 62.44, H, 6.74. Found: 62.47; H, 6.60.

Direct Formation of 1-[4-(4-Nitrophenyl)]butyl 4,6-*O*-Benzylidene-2-*O*-pivaloyl-1-thio-*β*-D-galactopyranoside (16) from Thioglycoside 6. Thioglycoside **6** (0.491 g, 0.87 mmol), BSP (0.182 g, 0.87 mmol), and powdered molecular sieves were dissolved in distilled CH_2Cl_2 (8.7 mL) at room temperature. This solution was cooled to −78 °C, stirred for 30 min, and then warmed to −60 °C, and Tf_2O (146 μL, 0.245 g, 0.87 mmol) was added. After 10 min, alcohol **14** (186 μL, 1.04 mmol) was added, and the reaction mixture was stirred at −60 °C for 1 h before warming to 0 °C. The reaction mixture was quenched with saturated aqueous $NaHCO_3$, diluted with EtOAc, and washed with water. The water phase was extracted with EtOAc, and the combined organic phase was washed with water and brine, dried, filtered, and concentrated. The crude reaction mixture was purified by column chromatography on silica gel (eluent: EtOAc/hexane = 1/3 and then 1/1), which afforded **16** (0.367 g, 0.69 mmol) in 80% yield as white foam with physical data identical to those of the above sample.

1-[4-(4-Nitrophenyl)]butyl 4,6-*O*-Benzylidene-2-pivaloyl-3-*O*-(2,3-*O*-carbonyl-4-*O*-(*tert*-butyldimethylsilyl)-α-L-rhamnopyranosyl)-*β*-D-galactopyranoside (17). Coupling of donor **8** (0.294 g, 0.74 mmol) with acceptor **16** (0.196 g, 0.37 mmol, 1.0 equiv) by the standard BSP protocol afforded **17** (0.190 g, 0.23 mmol) in 63% yield as a glass: $[\alpha]_D$ +6.7° (*c*, 0.2); ^{1}H NMR δ 8.11 (d, J = 8.7 Hz, 2H), 7.20−7.56 (m, 7H), 5.51 (s, 1H), 5.25 (dd, J = 7.4, 10.0 Hz, 1H), 5.10 (s, 1H), 4.61 (t, J = 7.0 Hz, 1H), 4.47 (d, J = 11.1 Hz, 1H), 4.45 (d, J = 12.0 Hz, 1H), 4.34 (d, J = 12.3 Hz, 1H), 4.30 (d, J = 3.3 Hz, 1H), 4.08 (d, J = 12.6 Hz, 1H), 3.84−4.00 (m, 2H), 3.78 (dd, J = 3.6, 9.9 Hz, 1H), 3.40−3.52 (m, 2H), 3.36 (dd, J =6.7, 10.0 Hz, 1H), 2.64−2.80 (m, 2H), 1.50−1.80 (m, 4H), 1.22 (d, J = 6.6 Hz, 1H), 1.15 (s, 9H), 0.85 (s, 9H), 0.13 (s, 3H), 0.07 (s, 3H); ^{13}C NMR δ 188.5, 176.8, 153.5, 150.4, 146.4, 137.4, 129.3, 128.4, 126.3, 123.8, 101.6, 101.1, 98.2 ($^1J_{CH}$ = 168.6 Hz), 80.3, 80.0, 76.9, 75.6, 74.5, 69.3, 69.2, 68.8, 66.4, 65.8, 38.9, 35.6, 29.2, 27.6, 27.3, 25.8, 21.2, 17.9, −4.3, −5.0. Anal. Calcd for $C_{41}H_{57}O_{14}NSi$: C, 60.35; H, 7.04. Found: C, 60.21; H, 7.06.

1-[4-(4-Nitrophenyl)]butyl 4,6-*O*-Benzylidene-2-pivaloyl-3-*O*-(2,3-*O*-isopropylidene-4-*O*-(*tert*-butyldimethylsilyl)-α-L-rhamnopyranosyl)-*β*-D-galactopyranoside (18). By the standard BSP protocol, coupling of thioglycoside **10** (0.258 g, 0.63 mmol) with acceptor **16** (0.197 g, 0.37 mmol) gave the disaccharide **18** (0.198 g, 0.24 mmol) in 64% yield as a white solid: mp 128 ± 1 °C; $[\alpha]_D$ −25.3° (*c*, 0.1); ^{1}H NMR (500 MHz) δ 8.10 (d, J = 8.4 Hz, 2H), 7.20−7.56 (m, 7H), 5.52 (s, 1H, $^1J_{CH}$ = 166.1 Hz), 5.27 (dd, J = 8.1, 10.4 Hz, 1H), 5.02 (s, 1H), 4.46 (d, J = 8.1 Hz, 1H), 4.32−4.38 (m, 2H), 4.07 (dd, J = 1.4, 12.3 Hz, 1H), 3.98−4.04 (m, 2H), 3.88−3.98 (m, 1H), 3.83 (dd, J = 6.4, 10.0 Hz, 1H), 3.73 (dd, J = 3.6, 10.5 Hz, 1H), 3.42−3.54 (m, 2H), 3.22−3.32 (m, 1H), 2.64−2.78 (m, 2H), 1.52−1.82 (m, 4H), 1.48 (s, 3H), 1.25 (s, 3H), 1.20 (d, J = 3.9 Hz, 3H), 1.18 (s, 9H), 0.8 (s, 9H), 0.11(s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz) δ 177.0, 150.8, 146.7, 137.9, 129.6, 129.4, 128.6, 126.6, 124.0, 109.2, 101.7, 101.5, 100.8, 80.2, 79.0, 77.7, 76.3, 76.2, 76.1, 69.8, 69.6, 68.8, 67.0, 66.9, 39.1, 35.9, 29.4, 28.4, 27.9, 27.5, 26.6, 26.2, 18.4, 18.3, −3.5, −4.6. Anal. Calcd for $C_{43}H_{63}O_{13}NSi$: C, 62.22; H, 7.65. Found: C, 62.05; H, 7.57.

1-[4-(4-Nitrophenyl)]butyl 4,6-*O*-Benzylidene-2-pivaloyl-3-*O*-(2,3-*O*-carbonyl-α-L-rhamnopyranosyl)-*β*-D-galactopyranoside (19). To a stirred solution of **17** (0.176 g, 0.22 mmol) in THF (20 mL) was added $Bu_4N^+F^-$ (0.43 mL of 1.0 N in THF, 0.43 mol) at 0 °C, followed by stirring for 1 h at 0 °C and then 4 h at room temperature until the starting material was consumed. The reaction mixture was diluted with EtOAc and washed with aqueous NH_4Cl and water. The water phase was extracted with EtOAc, and the combined organic phase was washed with water and brine, dried, filtered, and concentrated. The crude reaction mixture was purified by column chromatography on silica gel (eluent: EtOAc/hexane = 1/3 and then 1/1), and compound **19** (0.124 g, 0.18 mol) was obtained in 82% yield as a white solid: mp 168 ± 1 °C; $[\alpha]_D$ −13.9° (*c*, 0.2); ^{1}H NMR δ 8.11 (d, J = 7.0 Hz, 2H), 7.24−7.56 (m, 7H), 5.53 (s, 1H), 5.29 (dd, J = 8.1, 10.4 Hz, 1H), 5.07 (s, 1H), 4.71 (dd, J = 5.8, 7.6 Hz, 1H), 4.52 (d, J = 7.2 Hz, 1H), 4.45 (d, J = 8.4 Hz, 1H), 4.28−4.40 (m, 2H), 4.04−4.16 (m, 1H), 3.99 (t, J = 6.6 Hz, 1H), 3.87−3.96 (m, 1H), 3.85 (dd, J = 3.7, 10.0 Hz, 1H), 3.53 (t, J = 6.3 Hz, 1H), 3.48 (s, 1H), 3.40−3.58 (m, 1H), 2.66−2.78 (m, 2H), 1.46−1.80 (m, 4H), 1.29 (d, J = 6.9 Hz, 3H), 1.18 (s, 9H); ^{13}C NMR δ 176.9, 153.4, 150.4, 146.4, 137.2, 129.4, 129.3, 128.4, 126.4, 123.7, 101.4, 101.0, 98.0, 79.4, 77.6, 77.4, 75.2, 75.0, 70.8, 69.8, 69.1, 68.8, 68.5, 66.3, 39.0, 35.6, 29.2, 27.6, 18.8. Anal. Calcd for $C_{35}H_{43}O_{14}N\cdot 0.5H_2O$: C, 59.15; H, 6.24. Found: C, 59.25; H, 6.03.

1-[4-(4-Nitrophenyl)]butyl 4,6-*O*-Benzylidene-2-pivaloyl-3-*O*-(2,3-*O*-isopropylidene-α-L-rhamnopyranosyl)-*β*-D-galactopyranoside (20). Desilylation of **18**, by the same protocol used for the conversion of **17** to **19**, gave compound **20** (0.141 g, 0.20 mol) in 80% yield as a white solid: mp 85 ± 1 °C; $[\alpha]_D$ +28.3° (*c*, 0.2, $CHCl_3$); ^{1}H NMR (500 MHz) δ 8.10 (d, J = 8.4 Hz, 2H), 7.33−7.56 (m, 7H), 5.52 (s, 1H), 5.31 (dd, J = 8.1, 10.4 Hz, 1H), 5.02 (s, 1H), 4.46 (d, J = 8.1 Hz, 1H), 4.32 (d, J = 12.0 Hz, 1H), 4.28 (d, J = 4.2 Hz, 1H), 4.02−4.16 (m, 3H), 3.86−3.98 (m, 1H), 3.80−3.86 (m, 1H), 3.77 (dd, J = 3.4, 10.0 Hz, 1H), 3.40−3.52 (m, 2H), 3.30−3.40 (m, 1H), 2.64−2.78 (m, 2H), 2.20−2.30 (broad s, 1H), 1.50−1.80 (m, 4H), 1.48 (s, 3H), 1.20−1.30 (m, 6H), 1.17 (s, 9H); ^{13}C NMR (125 MHz) δ 177.0, 150.8, 146.7, 137.9, 129.6, 129.5, 128.6, 126.7, 124.0, 109.8, 101.6, 101.4, 100.7, 79.7, 78.0, 76.0, 75.7, 74.2, 70.0, 69.4, 68.9, 67.7, 66.8, 39.5, 35.8, 29.4, 28.1, 27.9, 27.5, 26.2, 18.3. Anal. Calcd for $C_{37}H_{49}O_{13}N$: C, 62.09; H, 6.90. Found: C, 61.60; H, 6.77.

1-[4-(4-Nitrophenyl)]butyl 4,6-*O*-Benzylidene-2-pivaloyl-3-*O*-[4-*O*-(2,3-*O*-dibenzyl-4,6-*O*-benzylidene-*β*-D-mannopyranosyl)-2,3-*O*-carbonyl-α-L-rhamnopyranosyl]-*β*-D-galactopyranoside (21*β*) and 1-[4-(4-Nitrophenyl)]butyl 4,6-*O*-Benzylidene-2-pivaloyl-3-*O*-[4-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranosyl)-2,3-*O*-carbonyl-α-L-rhamnopyranosyl]-*β*-D-galactopyranoside (21α). Coupling of **12** (0.067 g, 0.124 mmol) with **19** (0.043 g, 0.062 mmol) by the standard BSP protocol gave **21***β*α (0.064 g, 0.056 mmol) in 90% yield with a *β*:α ratio of 2:1 as determined from the ^{1}H NMR spectrum of the α:*β* mixture after column chromatography. Part of the *β*:α mixture was further purified by the preparative TLC on silica gel (eluent: EtOAc/hexane = 1/2) to give samples of the two pure isomers. The pure *β* isomer was a white solid: mp 108 ± 1 °C; $[\alpha]_D$ −16.3° (*c*, 1.7); ^{1}H NMR δ 8.10 (d, J = 8.7 Hz, 2H), 7.18−7.56 (m, 22H), 5.58 (s, 1H), 5.53 (s, 1H), 5.34 (dd, J = 7.6, 10.0 Hz, 1H), 5.10 (s, 1H), 4.64−4.76 (m, 4H), 4.58 (d, J = 12.6 Hz, 1H), 4.47 (d, J = 8.1 Hz, 1H), 4.42 (d, J = 7.5 Hz, 1H), 4.24−4.38 (m, 4H), 4.06−4.20 (m, 2H), 3.82−4.00 (m, 5H), 3.78 (dd, J = 3.4, 10.0 Hz, 1H), 3.48−3.62 (m, 3H), 3.48 (s, 1H), 3.26−3.36 (m, 1H), 2.68−2.78 (m, 2H), 1.56−1.80 (m, 4H), 1.30 (d, J = 6.3 Hz, 3H), 1.17 (s, 9H); ^{13}C NMR δ 176.9, 153.0, 150.4, 138.0, 137.6, 137.4, 129.5, 129.3, 129.0, 128.9, 128.5, 128.3, 128.2, 127.9, 127.8, 127.7, 126.4, 126.3, 126.2, 123.7, 101.7, 101.6, 101.1, 100.7, 98.2, 80.7, 78.8, 78.6, 78.2, 78.0, 77.6, 76.7, 75.8, 75.5, 74.9, 72.7, 69.4, 69.2, 68.8, 68.4, 67.7, 66.3, 64.2, 39.0, 35.6, 29.2, 27.6, 27.3, 17.7; ESIHRMS calcd for $C_{62}H_{69}O_{19}N_1Na$ $[M + Na]^+$ *m/e* 1154.4361, found *m/e* 1154.4292. The pure α isomer was a glass: $[\alpha]_D$ +8.3° (*c*, 0.1); ^{1}H NMR δ 8.10 (d, J = 8.8 Hz, 2H), 7.20−7.58 (m, 22H), 5.63 (s, 1H), 5.47 (s, 1H), 5.26 (dd, J = 8.0, 10.0 Hz, 1H), 4.90 (s, 1H), 4.80−4.92 (m, 2H), 4.56−4.72 (m, 4H), 4.38−4.48 (m, 3H), 4.33 (d, J = 11.7 Hz, 1H), 4.20−4.28 (m, 2H), 4.08 (d, J = 11.7 Hz, 1H), 3.64−3.98 (m, 8H), 3.40−3.52 (m, 2H), 3.28 (dd, J = 7.3, 10.4 Hz, 1H), 2.64−2.78 (m, 2H), 1.56−1.80 (m, 4H), 1.15 (s, 9H), 0.86 (d, J = 6.3 Hz, 3H); ^{13}C NMR δ 176.8, 152.9, 150.3, 137.9, 137.8, 137.4, 129.4, 129.3, 128.9, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 127.7, 127.6, 126.3, 126.2, 123.7, 101.5, 101.4, 101.1, 101.0, 97.9, 80.4,

78.9, 78.6, 77.4, 77.3, 76.6, 76.5, 75.5, 75.4, 74.1, 73.7, 69.3, 68.8, 68.4, 66.3, 64.9, 64.5, 38.9, 35.6, 29.2, 27.6, 27.3, 17.0; ESIHRMS calcd for $C_{62}H_{69}O_{19}N_1Na$ $[M + Na]^+$ *m/e* 1154.4361, found *m/e* 1154.4323.

1-[4-(4-Nitrophenyl)]butyl 4,6-*O*-Benzylidene-2-pivaloyl-3-*O*-[4-*O*-(4,6-*O*-benzylidene-2,3-di-*O*-(*p*-methoxybenzyl)-*β*-D-mannopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl]-*β*-D-galactopyranoside (22*β*) and 1-[4-(4-Nitrophenyl)]butyl 4,6-*O*-Benzylidene-2-pivaloyl-3-*O*-[4-*O*-(4,6-*O*-benzylidene-2,3-di-*O*-(*p*-methoxybenzyl)-α-D-mannopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl]-*β*-D-galactopyranoside (22α). By the standard BSP protocol, coupling of **13** (0.234 g, 0.39 mmol) with **20** (0.136 g, 0.19 mmol) gave the trisaccharide **22** (0.212 g, 0.18 mmol, α:*β* = 1:9.6) in 92% yield. The pure *β*-isomer (0.163 g, 0.14 mmol) was obtained by column chromatography on silica gel (eluent: EtOAc/hexane = 1/3) in 71% yield as white foam, and an α:*β* mixture (0.049 g, 0.04 mmol, α:*β* = 1:1.4) was obtained in 21% yield at the same time. Part of this mixture was purified by the preparative TLC on silica gel (eluent: EtOAc/hexane = 1/3) to give the pure α-anomer. *β* isomer: $[\alpha]_D$ −19.0° (*c*, 0.2); ^{1}H NMR (500 MHz) *δ* 8.10 (d, *J* = 8.7 Hz, 2H), 7.16−7.58 (m, 16H), 6.84 (d, *J* = 8.6 Hz, 2H), 6.78 (d, *J* = 8.6 Hz, 2H), 5.58 (s, 1H), 5.54 (s, 1H), 5.31 (dd, *J* = 8.2, 9.8 Hz, 1H), 5.04 (s, 1H), 4.90 (s, 1H, $^1J_{CH}$ 160.7 Hz), 4.70 (d, *J* = 11.7 Hz, 1H), 4.55(d, *J* = 11.7 Hz, 1H), 4.40−4.52 (m, 3H), 4.28−4.38 (m, 2H), 4.20 (dd, *J* = 5.7, 10.2 Hz, 1H), 4.02−4.18 (m, 3H), 3.84−4.02 (m, 5H), 3.79 (s, 3H), 3.77 (s, 3H), 3.72−3.80 (m, 1H), 3.44−3.62 (m, 4H), 3.20−3.30 (m, 1H), 2.68−2.80 (m, 2H), 1.56−1.80 (m, 4H), 1.47 (s, 3H), 1.30 (d, *J* = 6.2 Hz, 3H), 1.27 (s, 3H), 1.19 (s, 9H); ^{13}C NMR (125 MHz) *δ* 177.1, 159.6, 159.5, 150.7, 146.7, 138.0, 137.9, 130.8, 130.7, 130.6, 129.7, 129.6, 129.5, 129.4, 129.2, 128.6, 128.5, 126.7, 126.4, 124.0, 114.2, 114.0, 113.8, 109.6, 101.9, 101.7, 101.5, 100.7, 80.5, 78.9, 78.4, 77.9, 77.8, 77.6, 77.3, 76.5, 76.1, 75.6, 74.7, 72.0, 69.8, 69.5, 69.0, 68.0, 66.8, 65.4, 60.8, 55.7, 55.6, 39.2, 35.8, 29.4, 28.1, 27.9, 27.5, 26.6, 18.2, 14.6; ESIHRMS calcd for $C_{66}H_{79}O_{20}N_1Na$ $[M + Na]^+$ *m/e* 1228.5093, found *m/e* 1228.5032. The α-anomer was a glass: $[\alpha]_D$ +48.4° (*c*, 1.6); ^{1}H NMR (500 MHz) *δ* 8.13 (d, *J* = 8.7 Hz, 2H), 7.25−7.55 (m, 16H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.82 (d, *J* = 8.6 Hz, 2H), 5.65 (s, 1H), 5.53 (s, 1H), 5.32 (dd, *J* = 8.0, 10.0 Hz, 1H), 5.03 (s, 1H), 4.80 (d, *J* = 11.0 Hz, 1H), 4.77 (d, *J* = 12.5 Hz, 1H), 4.65 (d, *J* = 1.0 Hz, 1H), 4.60 (d, *J* = 11.5 Hz, 1H), 4.59 (d, *J* = 12.5 Hz, 1H), 4.48 (d, *J* = 8.0 Hz, 1H), 4.36 (dd, *J* = 1.2, 12.2 Hz, 1H), 4.18−4.26 (m, 2H), 4.00−4.14 (m, 3H), 3.92−3.98 (m, 1H), 3.90 (dd, *J* = 3.5, 10.5 Hz, 1H), 3.82 (s, 3H), 3.78 (s, 3H), 3.75 (dd, *J* = 3.5, 10.5 Hz, 1H), 3.71 (dd, *J* = 1.0, 3.0 Hz, 1H), 3.46−3.52 (m, 2H), 3.21 (dd, *J* = 7.5, 10.0 Hz, 1H), 2.70−2.80 (m, 2H), 1.50−1.75 (m, 4H), 1.48 (s, 3H), 1.27 (s, 3H), 1.17 (s, 9H), 0.88 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz) *δ* 177.1, 159.8, 150.7, 146.7, 137.9, 131.3, 130.4, 129.6, 129.5, 129.4, 129.2, 128.6, 128.5, 126.6, 124.0, 114.2, 114.1, 109.4, 101.8, 101.5, 100.9, 100.5, 80.5, 80.2, 79.6, 76.7, 76.6, 76.3, 76.1, 73.7, 73.6, 69.8, 69.0, 66.8, 65.9, 64.4, 55.7, 39.2, 35.9, 29.4, 28.4, 27.9, 27.5, 26.6, 17.4; ESIHRMS calcd for $C_{66}H_{79}O_{20}N_1Na$ $[M + Na]^+$ *m/e* 1228.5093, found *m/e* 1228.5031.

1-[4-(4-Nitrophenyl)]butyl 4,6-*O*-Benzylidene-3-*O*-[4-*O*-(4,6-*O*-benzylidene-2,3-di-*O*-(*p*-methoxybenzyl)-*β*-D-mannopyranosyl)-2,3-*O*-isopropylidene-α-L-rhamnopyranosyl]-*β*-D-galactopyranoside (23). To a stirred solution of **22***β* (0.073 g, 0.06 mmol) in a mixture of CH_3OH (10 mL) and THF (1 mL) was added Na (0.023 g, 10 mmol) at room temperature. After the dissolution of Na, the reaction mixture was warmed to 60 °C and stirred for 20 h. It was then cooled to room temperature and neutralized with Amberlyst-15 cation-exchange resin. Then the mixture was filtered, concentrated, and purified by column chromatography on silica gel (eluent: EtOAc/hexane = 1/1) to give **23** (0.046 g, 0.04 mmol) in 68% yield as glass together with recovered **22***β* (0.013 g, 0.01 mmol, 13%): $[\alpha]_D$ −35.2° (*c*, 0.2); ^{1}H NMR (500 MHz) *δ* 8.14 (d, *J* = 8.7 Hz, 2H), 7.18−7.58 (m, 16H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 5.62 (s, 1H), 5.58 (s, 1H), 5.27 (s, 1H), 4.97 (s, 1H), 4.72 (d, *J* = 11.7 Hz, 1H), 4.58 (d, *J* = 11.7 Hz, 2H), 4.55 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.32−4.40 (m, 3H), 4.26 (dd, *J* = 3.0, 6.3 Hz, 1H), 4.22 (d, *J* = 3.0 Hz, 1H), 4.09−4.17 (m, 3H), 3.98−4.06 (m, 1H), 3.90−3.96 (m, 3H), 3.88 (d, *J* = 3.0 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.54−3.70 (m, 4H), 3.50 (s, 1H), 3.28−3.38 (m, 1H), 2.66−2.80 (m, 2H), 2.48 (broad s, 1H), 1.61−1.88 (m, 4H), 1.51 (s, 3H), 1.32 (s, 3H), 1.31 (d, *J* = 6.3 Hz, 3H); ^{13}C NMR (125 MHz) *δ* 159.5, 150.7, 146.8, 138.0, 130.5, 129.6, 129.5, 129.4, 128.6, 128.5, 126.6, 126.4, 124.1, 114.1, 113.9, 109.7, 103.2, 101.7, 100.6, 100.3, 81.7, 79.0, 78.5, 77.9, 76.5, 76.0, 75.8, 74.7, 72.1, 70.1, 69.6, 69.5, 69.0, 68.1, 66.9, 65.4, 55.7, 35.8, 29.4, 28.2, 27.8, 26.9, 18.3; ESIHRMS calcd for $C_{61}H_{71}O_{19}N_1Na$ $[M + Na]^+$ *m/e* 1144.4518, found *m/e* 1144.4558.

1-[4-(4-Nitrophenyl)]butyl 3-*O*-(4-*O*-*β*-D-mannopyranosyl-α-L-rhamnopyranosyl)-*β*-D-galactopyranoside (3). To a stirred solution of trisaccharide **23** (15.8 mg, 0.014 mmol) in CH_2Cl_2 (2 mL) was added TFA (0.1 mL) dropwise at room temperature. After being stirred for 1.5 h, the reaction mixture was diluted with CH_2Cl_2 (5 mL), neutralized with 3.03 g of tris(2-aminoethyl)aminopolystyrene,[51] and filtered through a sintered funnel, washing first with CH_2Cl_2 to remove the nonpolar byproducts and then with CH_3OH to give a residue that was purified by the preparative TLC (eluent: $CHCl_3/CH_3OH$ = 3/1), producing the target molecule **3** (4.3 mg, 0.006 mmol) in 46% yield as a white solid: mp 240 ± 1 °C (lit.[27] mp 236−237.4 °C); $[\alpha]_D$ −52.9° (*c*, 0.2, H_2O); ^{1}H NMR (500 MHz, CH_3OH-d_4) *δ* 8.17 (d, *J* = 8.7 Hz, 2H), 7.48 (d, *J* = 8.7 Hz, 2H), 5.05 (s, 1H), 4.87 (s, 1H), 4.26 (d, *J* = 7.7 Hz, 1H), 3.92−4.00 (m, 6H), 3.85−3.92 (m, 2H), 3.72−3.80 (m, 3H), 3.45 (dd, *J* = 3.25, 9.4 HZ, 1H), 3.18−3.24 (m, 1H), 2.80 (t, *J* = 7.7 Hz, 2H), 1.75−1.80 (m, 2H), 1.60−1.75 (m, 2H), 1.34 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) *δ* 152.3, 146.6, 129.6, 123.4, 104.0 9 ($^1J_{CH}$ = 155.0 Hz), 102.8 ($^1J_{CH}$ = 170.3 Hz), 101.2 ($^1J_{CH}$ = 157.9 Hz), 80.7, 79.8, 77.1, 75.5, 74.4, 71.5, 71.4, 71.3, 71.0, 69.3, 69.0, 67.9, 67.5, 61.8, 61.3, 35.5, 29.2, 27.6, 17.3; ESIHRMS calcd for $C_{28}H_{43}O_{17}N_1Na$ $[M + Na]^+$ *m/e* 688.2429, found *m/e* 688.2452.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra for **3**, **21***β*,α, **22***β*,α, and **23** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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