Published in final edited form as:
Carbohydr Res. 2006 July 24; 341(10): 1467–1475.

On the nitrile effect in L-rhamnopyranosylation

David Crich* and **Mitesh Patel**
Department of Chemistry, University of Illinois at Chicago, 845 West Taylor Street, Chicago, IL 60607-7061, USA

Abstract

It is shown that the use of 5% acetonitrile or propionitrile in dichloromethane functions to increase the β-selectivity of a number of L-rhamnopyranosylation reactions conducted by the thioglycoside method with activation by the 1-benzenesulfinyl piperidine/trifluoromethanesulfonic anhydride couple. The use of more significant quantities of acetonitrile or propionitrile results in the formation of complex reaction mixtures containing little coupled product, but from which Ritter-type products can be isolated.

Keywords

Deoxy sugars; Acetonitrile; Nitrilium ion

1. Introduction

While significant advances have been made in the stereo-controlled formation of β-mannopyranosides in recent years, through both direct† and indirect methods,[1–19] their 6-deoxy congenors, the β-rhamnopyranosides, continue to pose significant challenges. In the D-series, characterized by the scarcity of D-rhamnose itself,[20] we have successfully devised methods based on stereochemically controlled β-mannosylation, followed by effcient deoxygenation at the 6-position by radical fragmentation of modified 4,6-*O*-acetals,[21–23] but the L-series, while accessible by indirect methods,[24–26] continues to pose significant challenges to direct stereocontrolled synthesis. We report here on our attempts to use the 'nitrile effect' to enhance the β-selectivity of solution-phase rhamnosylation reactions.

2. Results and discussion

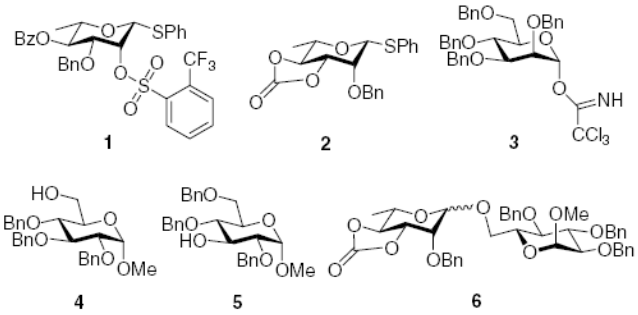
As we have discussed,[6] based on our determination that a transient contact oxacarbenium ion/triflate anion pair (CIP) is the reactive species in our benzylidene acetal mediated β-mannosylation systems,[27] we considered the key to successful β-L-rhamnosylation to lie in the use of disarming non-participating protecting groups. The function of these groups is to destabilize the oxacarbenium ion, so as to shift the CIP/glycosyl triflate equilibrium toward the glycosyl triflate, which is the established resting state.[6,28] In this manner, the concentration of the α-selective solvent-separated ion pair (SSIP), and of any free oxacarbenium ions is minimized resulting in enhanced β-selectivity (Scheme 1).

* Corresponding author. Tel.: +1 312 996 5189; fax: +1 312 996 0431; e-mail: dcrich@uic.edu.

Supplementary data
Copies of the ^{1}H and ^{13}C NMR spectra for disaccharides. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2006.03.036.

†We distinguish between direct methods, which afford the desired glycosidic bond in a single step, and indirect methods, requiring either prior attachment of the acceptor to the donor, or correction of stereochemistry after formation of the glycosidic bond.

On this basis, following the early work of Schuerch,[7] we surveyed of 2-*O*-sulfonyl protected rhamnosyl donors, ultimately arriving at the 4-*O*-benzoyl-2-*O*-sulfonyl system **1**.[6,29] A number of other non-participating electron-withdrawing protecting groups for O2, including phosphates, nitrate, cyanate, and a vinylous ester, were also surveyed but found to be less successful than the optimum sulfonate **1**.[6] Interestingly, 2,3-*O*-carbonyl and 2,3-*O*-alkylidene protected mannosyl and rhamnosyl thioglycosides were found to be highly α-selective in a number of homogeneous solution phase glycosylations.[3,30–32] This contrasts with their use in heterogenous glycosylations in the form of glycosyl bromides with activation by insoluble silver salts when they are β-selective.[33–37] We ascribe the α-selectivity of these 2,3-*O*-carbonates in homogeneous glycosylations to the half-chair conformation imposed on the pyranose ring, for which we have provided crystallographic evidence,[38] which reduces the energy barrier to oxacarbenium ion formation: the β-directing effect observed with the bromides and insoluble silver salts is simply a function of the mode of adsorption onto the promoter surface.[31] This understanding of the reactivity of the 2,3-*O*-carbonates led us to the 3,4-*O*-carbonyl protected thioglycoside **2**, which exhibits comparable β-selectivity in our systems to sulfonate **1**.[31]

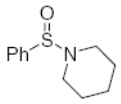


Although donors **1** and **2** gave moderate to excellent β-selectivity with simple secondary and tertiary alcohols, and with more reactive carbohydrate acceptors, they only afford modest selectivity with more typical secondary carbohydrate acceptors.[6,29,31,39] As a consequence, we turned our attention to the well-known β-directing effect of acetonitrile in glycosylation reactions.[40–44] We were encouraged in this endeavor by preliminary results from the Schmidt group in which it was found that 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl trichloroacetimidate **3** gave approximately a 1:1 β:α mixture of anomers in good yield on coupling to methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **4**, and to methyl 2,4,6-tri-*O*-benzyl-α-D-glucopyranoside **5**, in propionitrile at −80 °C on activation with trimethylsilyl triflate,[44] when high α-selectivity would have been expected in non-participating solvents.[45,46]

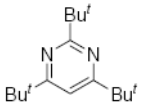
Working with donor **2** and coupling to acceptor **4**, we surveyed the effect of propionitrile‡ under our BSP/Tf_2O/TTBP conditions,[3,4,47] with the formation of rhamnoside **6** (Table 1). In neat dichloromethane (Table 1, entry 1), **6** was formed in good yield with a 6:1 β:α ratio. By contrast, in neat propionitrile extensive decomposition of the donor was observed, most of the acceptor was recovered unchanged, and <10% of the coupled product **6** was discernible in the crude reaction mixture, albeit with a β:α ratio of at least 5:1 (Table 1, entry 2). This result was somewhat surprising as propionitrile had previously been demonstrated to be a satisfactory solvent for BSP type coupling reactions with other simple thioglycosides,[3] and in the closely

‡Propionitrile has a lower freezing point (−93 °C) than acetonitrile (−48 °C), making it the nitrile of choice when used in significant proportion in low temperature glycosylations. It was demonstrated by Schmidt that propionitrile and acetonitrile have similar directing effects in other glycosylation reactions.[44]

related sulfoxide couplings,[48] but was nevertheless reproducible. Reducing the amount of propionitrile until it was simply an additive in the main solvent resulted in the restoration of efficient coupling, and with some increase in β-selectivity, with a maximum approaching 8:1 for the solvent ratio of 5/95 (v/v) propionitrile/dichloromethane (Table 1, entry 4). It was subsequently shown that comparable results could be obtained with low proportions of acetonitrile in dichloromethane (Table 1, entries 6–8), and because of the greater ease of removal, the mixed acetonitrile/dichloromethane system was selected for use in further coupling reactions.



BSP

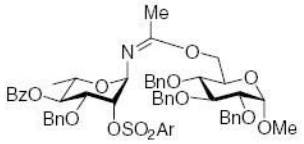


TTBP

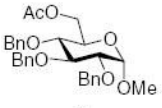
A further series of coupling reactions were then conducted with donor **2** in the 95/5 dichloromethane/acetonitrile solvent mixture with the results indicated in Table 2. In each a shift in the ratio of products, favoring the β-anomer, is observed on inclusion of acetonitrile, sometimes improving an already β-selective reaction, sometimes changing a previously α-selective reaction into a β-selective one, and other times reducing α-selectivity.

A similar series of experiments were conducted with donor **1** with similar consequences (Table 3). A comparison between the results presented in Tables 2 and 3 reveals donor **1** to be generally more β-selective than donor **2**, whether the couplings are conducted in pure dichloromethane or with the inclusion of acetonitrile.

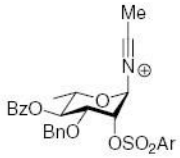
As is clear from the ensemble of results presented in Tables 1–3, the isolated yields of coupled products are generally lower when a nitrile is included in the solvent mixture, falling to a minimum with the use of pure propionitrile. In an attempt to shed further light on this problem, the coupling of donor **1** with the primary acceptor **4** was conducted in a 70/30 mixture of dichloromethane and acetonitrile. Examination of the crude reaction mixture by ^{1}H NMR spectroscopy revealed the almost complete absence of the anticipated coupled product **13** and the formation of one major product, which was isolated by chromatography on silica gel in 30% yield, and tentatively assigned structure **18**. This assignment is based on the rhamnose anomeric hydrogen signal at δ 5.13 whose broad singlet nature is typical for an α-rhamnoside in this series, and on the 3H singlet at δ 1.99, attributed to the imidate methyl group. On standing in deuteriochloroform, this unstable compound underwent decomposition to acetate **19**, thereby providing further support for product **18**, which is obviously formed by attack of the acceptor on the intermediate nitrilium ion **20**. Unfortunately, attempts to detect the formation of nitrilium ion **20**, or its congenor arising from donor **2**, by low temperature NMR spectroscopy have so far been unsuccessful. Presumably, the increased concentration of acetonitrile leads to a stabilization of nitrilium ion **20** and diverts nucleophilic attack away from the anomeric center toward the sp-hydrolized carbon. In support of this mechanism, we note that a variety of glycosyl nitrilium ions have been captured intramolecularly by this ‘Ritter-like’ capture mode by various nucleophiles and that this chemistry has been applied in the synthesis of sugar β-peptide libraries.[49,50]



18



19



20

Finally, we note the unexpectedly high amounts of α-anomeric products **10**α and **14**α observed on coupling of acceptor **9** to donors **1** and, especially, **2**. In our very extensive studies on the formation of the β-D-mannopyranosides,[4] acceptor **9** typically delivers β-selectivities in excess of 10:1; certainly, it is usually a more β-selective acceptor than the glucose 4-OH derivative **7**. However, comparison of Table 2, entries 2 and 3, reveals that the roles are reversed in coupling to L-rhamnopyranosyl donor **2**. We believe this to be a manifestation of stereochemical matching/mismatching,[51] a phenomenon that is gaining increasingly wide recognition in glycosidic bond forming reactions.[52–54]

3. Experimental

3.1. General methods

All solvents were dried and distilled by standard procedures. Trifluoromethanesulfonic anhydride was distilled over P_2O_5. Acceptors and donors were dried at 40 °C under vacuum for 2 h before use. BSP and TTBP were dried at room temperature under vacuum for 2 h before use. Optical rotations were determined with an Autopol III polarimeter for solutions in $CHCl_3$. NMR spectra were recorded for $CDCl_3$ solutions with a Bruker Avance spectrometer at 500 MHz (^{1}H) or 125 MHz (^{13}C). Chemical shifts are in parts per million downfield from tetramethylsilane. High resolution mass spectra were recorded with a Waters Q-TOF2 instrument. Microanalyses were conducted by Midwest Microlabs, Indianapolis, IN. The anomeric stereochemistry of all coupled products was assigned on the basis of the anomeric $^1J_{CH}$ coupling constants.[55]

3.2. General procedure for coupling reactions

Tf_2O (0.40 mmol) was added dropwise to a stirred solution of donor (0.27 mmol), BSP (0.35 mmol), and TTBP (0.80 mmol) in CH_3CN (0.5 mL) and CH_2Cl_2 (7.0 mL) under argon at −60 °C. After stirring for 1 h at −60 °C, the acceptor (0.80 mmol) in CH_2Cl_2 (2.5 mL) was added slowly over a period of 1 min. The reaction mixture was stirred for 3 h at −60 °C, then quenched at −60 °C with saturated $NaHCO_3$, and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layer was dried (Na_2SO_4), and the solvent was removed under reduced pressure. Purification by silica gel column chromatography (EtOAc/hexane) afforded the corresponding α/β rhamnosides.

3.2.1. Methyl 6-*O*-(2-*O*-benzyl-3,4-*O*-carbonyl-α-L-rhamnopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (6α)—$[\alpha]_D^{21}$ −3.6 (*c* 1.1, $CHCl_3$), lit.[31] −32.7; IR: 1813 $cm^{-1;}$ ^{1}H NMR ($CDCl_3$): δ 7.38–7.21 (m, 20H, arom H), 5.01 (d, 1H, ^2J = 11.0 Hz, –CH_2Ph), 4.86 (d, 1H, ^2J = 11.0 Hz, –CH_2Ph), 4.81–4.77 (m, 2H, –CH_2Ph), 4.77 (s, 1H, H-1^{II}), 4.74 (d, 1H, ^2J = 12.0 Hz, –CH_2Ph), 4.68 (d, 1H, ^2J = 12.0 Hz, –CH_2Ph), 4.60 (d, 1H, ^2J = 12.5 Hz, –

CH_2Ph), 4.54 (d, 1H, J = 4.0 Hz, H-1^I), 4.50–4.48 (dd, 1H, $J_{2,3}$ = 11.5 Hz, $J_{3,4}$ 3.0 Hz, H-3^{II}), 4.46 (d, 1H, ^2J = 11.0 Hz, –CH_2Ph), 4.41–4.36 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 9.5 Hz, H-4^{II}) 4.05 (m, 1H, H-5^{II}), 4.02 (m, 1H, H-2^{II}), 3.98 (t, 1H, $J_{2,3}$, $J_{3,4}$ = 10.0 Hz, H-3^I), 3.83–3.81 (dd, 1H, $J_{6a,6b}$ = 10.5 Hz, $J_{5,6a}$ = 1.5 Hz, H-6^I), 3.71–3.68 (m, 1H, H-5^I), 3.54–3.50 (dd, 1H, $J_{6a,6b}$ = 11.5 Hz, $J_{5,6b}$ = 5.5 Hz, H-6^I), 3.50–3.47 (dd, 1H, $J_{2,3}$ = 9.5 Hz, $J_{1,2}$ = 3.5 Hz, H-2^I), 3.37 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 10.0 Hz, H-4^I), 3.32 (s, 3H, –OCH_3), 1.34 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6^{II}); ^{13}C NMR: δ 153.7, 138.6, 138.0, 136.8, 128.6, 128.52, 128.45, 128.18, 128.11, 128.00,127.98, 127.92, 127.80, 127.74, 127.71, 99.4 ($^1J_{CH}$ = 172.3 Hz), 98.0 ($^1J_{CH}$ = 167.1 Hz), 82.0, 80.5, 80.0, 77.9, 77.4, 75.8, 75.0, 74.1, 73.4, 72.9, 69.7, 68.6, 66.7, 55.2, 17.7; ESIMS *m*/*z* calcd for $C_{42}H_{46}O_{11}Na$ $[M+Na]^+$: 749.2938. Found: 749.2938.

3.2.2. Methyl 6-*O*-(2-*O*-benzyl-3,4-*O*-carbonyl-β-L-rhamnopyranosyl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (6β)—$[\alpha]_D^{21}$ +46.6 (*c* 1.0, $CHCl_3$), lit.[31] +52.3; IR: 1810 $cm^{-1;}$ ^1H NMR ($CDCl_3$): δ 7.37–7.26 (m, 20H, arom H), 5.0 (d,1H, ^2J = 11.0 Hz, –CH_2Ph), 4.89–4.80 (m, 5H, –CH_2Ph), 4.73 (d, 1H, ^2J = 10.5 Hz, –CH_2Ph), 4.68 (d, 1H, ^2J = 10.5 Hz, –CH_2Ph), 4.66 (s, 1H, H-1^{II}), 4.58 (d, 1H, J = 3.5 Hz, H-1^I), 4.48–4.44 (dd, 1H, $J_{3,4}$ = 11.5 Hz, $J_{4,5}$ = 9.0 Hz, H-4^{II}), 4.29–4.27 (dd, 1H, $J_{6a,6b}$ = 11.5 Hz, $J_{5,6a}$ = 3.0 Hz, H-6^I), 4.25 (d, 1H, $J_{2,3}$ = 2.0 Hz, H-2^{II}), 4.13–4.10 (dd, 1H, $J_{3,4}$ = 12.0 Hz, $J_{2,3}$ = 2.5 Hz, H-3^{II}), 3.99 (t, 1H, $J_{2,3}$, $J_{3,4}$ = 9.0 Hz, H-3^I), 3.76–3.69 (m, H-5^I, H-6^I, H-5^{II}), 3.61 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 8.5 Hz, H-4^I), 3.46–3.43 (dd, 1H, $J_{2,3}$ = 10.0 Hz, $J_{1,2}$ = 4.0 Hz, H-2^I), 3.36 (s, 3H, –OCH_3), 1.39 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6^{II}); ^{13}C NMR: δ 153.9, 138.8, 138.3, 138.1 137.2, 128.5, 128.41, 128.39, 128.1, 128.0, 127.9, 127.8, 127.6, 101.2 ($^1J_{CH}$ = 157.5 Hz), 98.3 ($^1J_{CH}$ = 166.9 Hz), 81.8, 81.6, 80.0, 77.9, 77.6, 75.6, 75.2, 73.8, 73.5, 73.4, 71.0, 70.0, 68.0, 55.3, 17.8; ESIMS *m*/*z* calcd for $C_{42}H_{46}O_{11}Na$ $[M+Na]^+$: 749.2938. Found: 749.2969.

3.2.3. Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2-*O*-benzyl-3,4-*O*-carbonyl-α-L-rhamnopyranosyl)-α-D-glucopyranoside (8α)—$[\alpha]_D^{21}$−11.7 (*c* 1.0, $CHCl_3$), lit.[31] −19.6; IR: 1811 $cm^{-1;}$ ^1H NMR ($CDCl_3$): δ 7.33–7.21 (m, 20H, arom H), 5.09 (d, 1H, ^2J = 11.0 Hz, –CH_2Ph), 5.0 (s, 1H, H-1^{II}), 4.76 (d, 1H, ^2J = 12.0 Hz, –CH_2Ph), 4.63–4.56 (m, 4H, H-1^I –CH_2Ph), 4.52 (d, 1H, ^2J = 12.0 Hz, –CH_2Ph), 4.45–4.41 (m, 2H, –CH_2Ph), 4.25–4.23 (m, 2H, H-3^{II}, H-4^{II}), 4.11–4.08 (m, 1H, H-5^{II}), 3.93 (s, 1H, H-2^{II}), 3.82–3.80 (m, 2H, H-3^I, H-4^I), 3.62 (m, 1H, H-5^I), 3.58–3.53 (m, 2H, H-2^I, H-6^I), 3.41–3.38 (dd, 1H, $J_{6a,6b}$ = 11.0 Hz, $J_{5,6a}$ = 3.0 Hz, H-6^I), 3.35 (s, 3H, –OCH_3), 0.97 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6^{II}); ^{13}C NMR: δ 153.9, 138.2, 137.8, 137.5, 136.9, 128.7, 128.5, 128.4, 128.2, 128.08, 128.01, 127.90, 127.85, 127.75, 127.70, 98.6 ($^1J_{CH}$ = 172.8 Hz), 97.9 ($^1J_{CH}$ 166.1 Hz), 80.6, 80.2, 79.6, 78.2, 77.9, 77.5, 75.8, 74.1, 73.8, 73.6, 73.3, 72.6, 69.8, 69.0, 68.7, 55.3, 17.3; ESIMS *m*/*z* calcd for $C_{42}H_{46}O_{11}Na$ $[M+Na]^+$: 749.2938. Found: 749.2941.

3.2.4. Methyl 2,3,6-tri-*O*-benzyl-4-*O*-(2-*O*-benzyl-3,4-*O*-carbonyl-β-L-rhamnopyranosyl)-α-D-glucopyranoside (8β)—$[\alpha]_D^{21}$ +18.8 (*c* 1.0, $CHCl_3$), lit[31]. +56.1; IR: 1811 $cm^{-1;}$ ^1H NMR ($CDCl_3$): δ 7.38–7.25 (m, 18H, arom H), 7.11 (m, 2H, arom H), 4.99 (d, 1H, ^2J = 11.5 Hz, –CH_2Ph), 4.76–4.65 (m, 6H, H-1^I, H-1^{II}, –CH_2Ph), 4.61 (d, 1H, ^2J = 12.0 Hz, –CH_2Ph), 4.52 (d,1H, ^2J = 12.0 Hz, –CH_2Ph), 4.31–4.25 (m, 2H, H-4^{II}, –CH_2Ph), 3.86 (t, 1H, $J_{2,3}$, $J_{3,4}$ = 9.0 Hz, H-3^I), 3.82 (dd, 1H, $J_{6a,6b}$ = 10.5 Hz, $J_{5,6a}$ = 1.5 Hz, H-6^I), 3.73 (m, 1H, H-6^I), 3.69–3.62 (m, 2H, H-4^I, H-5^I), 3.53–3.48 (m, 4H, H-2^I, H-2^{II}, H-3^{II}, H-5^{II}), 3.44 (s, 3H, –OCH_3), 1.24 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6^{II}); ^{13}C NMR: δ 154.0, 138.6, 138.4, 137.8, 137.5, 128.6, 128.5, 128.4, 128.2, 128.15, 128.09, 128.05, 128.00, 127.87, 127.85, 127.42, 127.37, 101.5 ($^1J_{CH}$ = 165.0 Hz), 97.7 ($^1J_{CH}$ = 163.1 Hz), 82.2, 81.5, 80.0, 77.9, 76.2, 75.7, 73.44, 73.37, 73.10, 72.98, 70.6, 69.5, 68.8, 55.5, 17.7; ESIMS *m*/*z* calcd for $C_{42}H_{46}O_{11}Na$ $[M+Na]^+$: 749.2938. Found: 749.2923.

3.2.5. Methyl 4-*O*-(2-*O*-benzyl-3,4-*O*-carbonyl-α-L-rhamnopyranosyl)-2,3-*O*-isopropylidiene-α-L-rhamnopyranoside (10α)—$[\alpha]_D^{21}$ −68.5 (*c* 1.0, $CHCl_3$); IR: 1819 $cm^{31;}$ ^1H NMR ($CDCl_3$): δ 7.36–7.31 (m, 5H, arom H), 5.48 (d, 1H, $J_{1,2}$ = 1.0 Hz, H-1^{II}), 4.85 (s, 1H, H-1^I), 4.76 (d, 1H, ^2J = 12.0 Hz, –CH_2Ph), 4.70 (d, 1H, ^2J = 12.0 Hz, –CH_2Ph), 4.45 (m, 2H, H-3^{II}, H-4^{II}), 4.13 (m, 1H, H-2^{II}), 4.06 (m, 3H, H-2^I, H-3^I, H-5^{II}), 3.58 (m, 1H, H-5^I), 3.50 (m, 1H, H-4^I), 3.36 (s, 3H, –OCH_3), 1.51 (s, 3H, –$C(CH_3)_2$), 1.38 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6^{II}), 1.34 (s, 3H, –$C(CH_3)_2$), 1.26 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6^I); ^{13}C NMR: δ 153.7, 136.9, 128.5, 128.1, 127.7, 109.6, 98.1 ($^1J_{CH}$ = 174.9 Hz), 97.9 ($^1J_{CH}$ = 167.4 Hz), 80.3, 78.4, 78.2, 77.9, 76.1, 74.6, 72.8, 69.2, 63.5, 54.9, 27.9, 26.3, 17.9, 17.8; ESIMS *m*/*z* calcd for $C_{24}H_{32}O_{10}Na$ $[M+Na]^+$: 503.1893. Found: 503.1892.

3.2.6. Methyl 4-*O*-(2-*O*-benzyl-3,4-*O*-carbonyl-β-L-rhamno-pyranosyl)-2,3-*O*-isopropylidiene-α-L-rhamnopyranoside (10β)—$[\alpha]_D^{21}$ +5.6 (*c* 0.7, $CHCl_3$); IR: 1810 $cm^{31;}$ ^1H NMR ($CDCl_3$): δ 7.37–7.30 (m, 5H, arom H), 4.86–4.79 (q, 2H, ^2J = 12.5 Hz, –CH_2Ph), 4.83 (s, 1H, H-1^I), 4.75 (d, 1H, $J_{1,2}$ = 1.0 Hz, H-1^{II}), 4.52–4.48 (dd, 1H, $J_{4,5}$ = 11.5 Hz, $J_{3,4}$ = 9.5 Hz, H-4^{II}), 4.37 (t, 1H, $J_{2,3}$, $J_{3,4}$ = 6.0 Hz, H-3^I), 4.21 (d, 1H, $J_{2,3}$ = 1.5 Hz, H-2^{II}), 4.13–4.11 (m, 2H, H-3^{II}, H-2^I), 3.76 (m, 1H, H-5^{II}), 3.70 (m, 1H, H-5^I), 3.39–3.36 (dd, 1H, $J_{4,5}$ = 10.0 Hz, $J_{3,4}$ = 7.0 Hz, H-4^I), 3.37 (s, 3H, –OCH_3), 1.48 (s, 3H, –$C(CH_3)_2$), 1.44 (d, 3H, $J_{5,6}$ = 6.0 Hz H-6^{II}), 1.33 (s, 3H, –$C(CH_3)_2$), 1.25 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6^I); ^{13}C NMR: δ 153.9, 137.1, 128.4, 128.1, 128.0, 109.0, 100.9 ($^1J_{CH}$ = 157.1 Hz), 98.2 ($^1J_{CH}$ = 166.5 Hz), 83.4, 81.8, 77.9, 76.40, 75.8, 73.6, 73.2, 71.1, 63.9, 54.9, 28.0, 26.1, 17.8, 17.7; ESIMS *m*/*z* calcd for $C_{24}H_{32}O_{10}Na$ $[M+Na]^+$: 503.1888. Found: 503.1885.

3.2.7. Methyl 3-*O*-benzyl-4,6-*O*-benzylidiene-2-*O*-(2-*O*-benzyl-3,4-*O*-carbonyl-α-L-rhamnopyranosyl)-α-D-manno-pyranoside (12α)—$[\alpha]_D^{21}$ 369.9 (*c* 0.9, $CHCl_3$); IR: 1810 $cm^{-1;}$ ^1H NMR ($CDCl_3$): δ 7.52 (dd, 2H, *J* = 8.5 Hz, *J* = 2.5 Hz, arom H), 7.40–7.30 (m, 13H, arom H), 5.65 (s, 1H, H-7^I), 4.87 (d, 1H, ^2J = 11.5 Hz, –CH_2Ph), 4.83 (s, 1H, H-1^{II}), 4.82 (d, 1H, ^2J = 12.5 Hz, –CH_2Ph), 4.67 (dd, 1H, $J_{3,4}$ = 11.0 Hz, $J_{2,3}$ = 2.5 Hz, H-3^{II}), 4.66 (d, 1H, ^2J = 12.0 Hz, –CH_2Ph), 4.63 (d, 1H, ^2J = 12.0 Hz, –CH_2Ph), 4.49 (d, 1H, $J_{1,2}$ = 2.0 Hz, H-1^I), 4.45 (m, 1H, H-5^{II}), 4.35 (dd, 1H, $J_{4,5}$ = 11.5 Hz, $J_{3,4}$ = 10.0 Hz, H-4^{II}), 4.25 (dd, 1H, $J_{6a,6b}$ = 10.0 Hz, $J_{5,6a}$ = 4.5 Hz, H-6^I), 4.21 (m, 1H, H-2^{II}), 4.1 (dd, 1H, $J_{2,3}$ = 3.5 Hz, $J_{1,2}$ = 1.5 Hz, H-2^I), 4.03 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 10.0 Hz, H-4^I), 3.94 (dd, 1H, $J_{3,4}$ = 9.5 Hz, $J_{2,3}$ = 3.0 Hz, H-3^I), 3.84 (t, 1H, $J_{5,6a}$, $J_{6a,6b}$ = 10.5 Hz, H-6^I), 3.76 (m, 1H, H-5^I), 3.35 (s, 3H, –OCH_3), 1.11 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6^{II}); ^{13}C NMR: δ 153.8, 138.0, 137.4, 137.0, 129.0, 128.6, 128.4, 128.2, 127.9, 127.8, 126.0, 101.6 ($^1J_{CH}$ = 162.4 Hz), 98.8 ($^1J_{CH}$ = 165.9 Hz), 97.6 ($^1J_{CH}$ 169.3 Hz), 80.2, 79.1, 77.9, 75.0, 74.4, 74.0, 73.8, 73.3, 68.9, 68.7, 63.9, 55.0, 17.5; ESIMS *m*/*z* calcd for $C_{35}H_{38}O_{11}Na$ $[M+Na]^+$: 657.2307. Found: 657.2306.

3.2.8. Methyl 3-*O*-benzyl-4,6-*O*-benzylidiene-2-*O*-(2-*O*-benzyl-3,4-*O*-carbonyl-β-L-rhamnopyranosyl)-α-D-manno-pyranoside (12β)—$[\alpha]_D^{21}$ +29.3 (*c* 0.6, $CHCl_3$); IR: 1811 $cm^{-1;}$ ^1H NMR ($CDCl_3$): δ 7.49 (dd, 2H, *J* = 8.5 Hz, *J* = 3.0 Hz, arom H), 7.45 (d, 2H, *J* = 7.5 Hz, arom H), 7.40–7.37 (m, 4H, arom H), 7.34–7.31 (m, 4H, arom H), 7.27 (m, 3H, arom H), 5.56 (s, 1H, H-7^I), 4.94 (m, 4H, H-1^I, –CH_2Ph), 4.79 (s, 1H, H-1^{II}), 4.60 (d, 1H, ^2J = 11.5 Hz, –CH_2Ph), 4.44 (dd, 1H, $J_{4,5}$ = 11.5 Hz, $J_{3,4}$ = 9.5 Hz, H-4^{II}), 4.32 (m, 1H, H-6^I), 4.28 (d, 1H, $J_{2,3}$ = 2.0 Hz, H-2^{II}), 4.11 (t, 1H, $J_{1,2}$, $J_{2,3}$ = 2.5 Hz, H-2^I), 4.0 (m, 2H, H-3^I, H-4^I), 3.92 (dd, 1H, $J_{3,4}$ = 11.5 Hz, $J_{2,3}$ = 2.5 Hz, , H-3^{II}), 3.81 (m, 2H, H-5^I, H-6^I), 3.60 (m, 1H, H-5^{II}), 3.38 (s, 3H, –OCH_3), 1.42 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6^{II}); ^{13}C NMR: δ 153.9, 138.5, 137.5, 137.4, 129.0, 128.5, 128.2, 128.0, 127.92, 127.86, 127.5, 126.0, 101.9 ($^1J_{CH}$ = 164.8 Hz), 101.6 ($^1J_{CH}$ = 160.5 Hz), 101.2 ($^1J_{CH}$ = 174.8 Hz), 81.5, 79.4, 77.8, 76.4, 73.8, 73.7, 73.2, 71.0, 69.1, 63.7, 54.9, 17.8; ESIMS *m*/*z* calcd for $C_{35}H_{38}O_{11}Na$ $[M+Na]^+$: 657.2307. Found: 657.2307.

3.2.9. Methyl 6-*O*-[(4-*O*-benzoyl-3-*O*-benzyl-2-*O*-(2-trifluoromethylbenzenesulfonyl)-α-L-rhamnopyranosyl)]-2,3, 4-tri-*O*-benzyl-α-D-glucopyranoside (13α)—$[\alpha]_D^{21}$ +31.9 (*c* 1.0, $CHCl_3$), lit.[29] −30.2; ^{1}H NMR ($CDCl_3$): δ 8.22 (d, 1H, *J* = 7.5 Hz, arom H), 7.95 (d, 2H, *J* = 8.5 Hz, arom H), 7.73 (d, 1H, *J* = 8.0 Hz, arom H), 7.59–7.26 (m, 17H, arom H), 7.14 (m, 1H, arom H), 7.06 (t, 2H, *J* = 8.0 Hz, arom H), 6.94 (d, 2H, *J* = 7.5 Hz, arom H), 5.28 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 9.5 Hz, H-4^{II}), 5.12 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1^{II}), 5.03–5.01 (m, 2H, H-2^{II}, $-CH_2Ph$), 4.94 (d, 1H, ^2J = 11.0 Hz, $-CH_2Ph$), 4.85 (d, 1H, ^2J = 11.0 Hz, $-CH_2Ph$), 4.83 (d, 1H, ^2J = 12.0 Hz, $-CH_2Ph$), 4.72 (d, 1H, ^2J = 12.5 Hz, $-CH_2Ph$), 4.62 (d, 1H, $J_{1,2}$ = 3.0 Hz, H-1^{I}), 4.55 (d, 1H, ^2J = 11.0 Hz, $-CH_2Ph$), 4.30–4.23 (q, 2H, *J* = 12.5 Hz, $-CH_2Ph$), 4.02 (t, 1H, $J_{2,3}$, $J_{3,4}$ = 9.5 Hz, H-3^{I}), 3.90–3.83 (m, 3H, H-6^{I}, H-3^{II}, H-5^{II}), 3.79–3.76 (m, 1H, H-5^{I}), 3.60–3.57 (dd, 1H, $J_{6a,6b}$ = 11.0 Hz, $J_{5,6a}$ = 6.5 Hz, H-6^{I}), 3.54 (dd, 1H, $J_{2,3}$ = 9.5 Hz, $J_{1,2}$ = 3.0 Hz, H-2^{I}), 3.40–3.36 (m, 4H, H-4^{I}, $-OCH_3$), 1.19 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6^{II}); ^{13}C NMR: δ 165.3, 138.6, 138.0, 137.9, 137.0, 135.2, 133.5, 133.2, 132.0, 131.6, 129.8, 129.7, 128.52, 128.48, 128.37, 128.31, 128.26, 128.20, 128.16, 128.08, 128.07, 128.00, 127.96, 127.92, 127.8, 127.6, 97.9 ($^1J_{CH}$ 172.9 Hz), 97.8 ($^1J_{CH}$ 157.3 Hz), 82.0, 79.9, 77.8, 76.8, 75.9, 75.2, 73.6, 73.3, 72.5, 71.5, 70.2, 67.0, 66.8, 55.2, 17.3; ESIMS *m*/*z* calcd for $C_{55}H_{55}O_{13}F_3NaS$ $[M+Na]^+$: 1035.3213. Found: 1035.3218.

3.2.10. Methyl 6-*O*-[(4-*O*-benzoyl-3-*O*-benzyl-2-*O*-(2-trifluoromethylbenzenesulfonyl)-β-L-rhamnopyranosyl)]-2,3, 4-tri-*O*-benzyl-α-D-glucopyranoside (13β)—$[\alpha]_D^{21}$ +59.0 (*c* 1.0, $CHCl_3$), lit.[29] +22.9; ^{1}H NMR ($CDCl_3$): δ 8.22 (d, 1H, *J* = 7.5 Hz, arom H), 7.96–7.94 (dd, 2H, *J* = 7.5 Hz, *J* 0.5 Hz, arom H), 7.66 (d, 1H, *J* = 8.0 Hz, arom H), 7.59 (t, 1H, *J* = 7.0 Hz, arom H), 7.46–7.18 (m, 15H, arom H), 7.11 (t, 2H, *J* = 7.5 Hz, arom H), 7.04 (d, 2H, *J* = 7.0 Hz, arom H), 5.41 (d, 1H, $J_{2,3}$ = 3.0 Hz, H-2^{II}), 5.29 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 9.5 Hz, H-4^{II}), 4.98 (d, 1H, ^2J = 11.0 Hz, $-CH_2Ph$), 4.86–4.82 (m, 2H, $-CH_2Ph$), 4.75 (d, 1H, ^2J = 12.0 Hz, $-CH_2Ph$), 4.66 (s, 1H, H-1^{II}), 4.64 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1^{I}), 4.56–4.49 (m, 3H, $-CH_2Ph$), 4.37 (d, 1H, ^2J = 12.5 Hz, $-CH_2Ph$), 4.27–4.24 (dd, 1H, $J_{6a,6b}$ = 11.5 Hz, $J_{5,6a}$ = 3.5 Hz, H-6^{I}), 3.91 (t, 1H, $J_{2,3}$, $J_{3,4}$ = 9.0 Hz, H-3^{I}), 3.69–3.63 (m, 3H, H-5^{I}, H-6^{I}, H-3^{II}), 3.56–3.52 (m, 2H, H-2^{I}, H-5^{II}), 3.43 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 9.5 Hz, H-4^{I}), 3.36 (s, 3H, $-OCH_3$), 1.26 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6^{II}); ^{13}C NMR: δ 165.2, 139.1, 138.6, 138.4, 136.8, 136.5, 133.24, 133.22, 131.9, 130.9, 129.8, 129.6, 128.5, 128.4, 128.34, 128.26, 128.25, 128.17, 128.0, 127.92, 127.86, 127.74, 127.55, 127.52, 98.3 ($^1J_{CH}$ 165.9 Hz), 97.8 ($^1J_{CH}$ 156.8 Hz), 81.7, 79.6, 77.4, 77.2, 75.6, 74.9, 73.4, 72.5, 71.0, 70.9, 69.9, 67.1, 55.2, 17.6; ESIMS *m*/*z* calcd for $C_{55}H_{55}O_{13}F_3NaS$ $[M+Na]^+$: 1035.3213. Found: 1035.3209.

3.2.11. Methyl 4-*O*-[(4-*O*-benzoyl-3-*O*-benzyl-2-*O*-(2-trifluoromethylbenzenesulfonyl)-α-L-rhamnopyranosyl)]-2,3-*O*-isopropylidiene-α-L-rhamnopyranoside (14α)—$[\alpha]_D^{21}$ +21.5 (*c* 0.5, $CHCl_3$), lit.[29] −55.2; ^{1}H NMR ($CDCl_3$): δ 8.26 (d, 1H, *J* = 7.5 Hz, arom H), 7.94 (d, 2H, *J* = 7.5 Hz, arom H), 7.76 (d, 1H, *J* = 7.5 Hz, arom H), 7.58–7.50 (m, 3H, arom H), 7.42 (t, 2H, *J* = 8.0 Hz, arom H), 7.17 (t, 1H, *J* = 7.5 Hz, arom H), 7.1 (t, 2H, arom H), 6.99 (d, 2H, *J* = 7.5 Hz, arom H), 5.48 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1^{II}), 5.28 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 9.5 Hz, H-4^{II}), 5.19 (t, 1H, $J_{1,2}$, $J_{2,3}$ = 2.5 Hz, H-2^{II}), 4.86 (s, 1H, H-1^{I}), 4.39 (d, 1H, ^2J = 12.0 Hz, $-CH_2Ph$), 4.30 (d, 1H, ^2J = 12.0 Hz, $-CH_2Ph$), 4.12–4.11 (m, 2H, H-2^{I}, H-3^{I}), 3.91–3.86 (m, 2H, H-3^{II}, H-5^{II}), 3.66–3.63 (m, 1H, H-5^{I}), 3.48–3.45 (m, 1H, H-4^{I}), 3.39 (s, 3H, $-OCH_3$), 1.55 (s, 3H, $-C(CH_3)_2$), 1.37 (s, 3H, $-C(CH_3)_2$), 1.27 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6^{I}), 1.22 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6^{II}); ^{13}C NMR: δ 165.2, 137.1, 135.5, 133.3, 133.1, 131.9, 131.7, 129.8, 129.7, 128.3, 128.24, 128.20, 128.1, 127.7, 127.5, 109.7, 98.0 ($^1J_{CH}$ = 165.4 Hz), 97.2 ($^1J_{CH}$ = 171.6 Hz), 79.3, 77.8, 77.1, 76.0, 73.7, 72.4, 71.4, 67.7, 63.9, 55.0, 28.0, 26.4, 17.7, 17.5. Anal calcd for $C_{37}H_{41}F_3O_{12}S$: C, 57.96; H, 5.39. Found: C, 57.66; H, 5.23.

3.2.12. Methyl 4-*O*-[(4-*O*-benzoyl-3-*O*-benzyl-2-*O*-(2-trifluoromethylbenzenesulfonyl)-β-L-rhamnopyranosyl)]-2,3-*O*-isopropylidiene-α-L-rhamnopyranoside (14β)—$[agr;]_D^{21}$ +43.6 (c 0.7, $CHCl_3$), lit.[29] +30.7; ^{1}H NMR ($CDCl_3$): δ 8.28 (m, 1H, arom H), 7.96 (d, 2H, *J* = 8.0 Hz, arom H), 7.74 (m, 1H, arom H), 7.59–7.52 (m, 3H, arom H), 7.43 (t, 2H, *J* = 7.5 Hz, arom H), 7.16 (t, 1H, *J* = 7.0 Hz, arom H), 7.08 (t, 2H, *J* = 7.5 Hz, arom H), 7.0 (d, 2H, *J* = 7.5 Hz, arom H), 5.34 (d, 1H, $J_{2,3}$ = 3.0 Hz, H-2^{II}), 5.30 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 9.5 Hz, H-4^{II}), 4.80 (s, 2H, H-1^{I}, H-1^{II}), 4.82 (d, 1H, ^2J = 12.5 Hz, –CH_2Ph), 4.34 (d, 1H, ^2J = 12.0 Hz, –CH_2Ph), 4.16 (t, 1H, $J_{2,3}$, $J_{3,4}$ = 6.5 Hz, H-3^{I}), 4.05 (d, 1H, $J_{2,3}$ = 6.0 Hz, H-2^{I}), 3.70–3.68 (dd, 1H, $J_{3,4}$ = 10.0 Hz, $J_{2,3}$ = 3.0 Hz, H-3^{II}), 3.56 (m, 1H, H-5^{II}), 3.49 (m, 1H, H-5^{I}), 3.42–3.39 (m, 1H, H-4^{I}), 3.34 (s, 3H, –OCH_3), 1.50 (s, 3H, –$C(CH_3)_2$), 1.31 (s, 3H, –$C(CH_3)_2$), 1.30 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6^{II}), 1.26 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6^{I}); ^{13}C NMR: δ 165.2, 136.83, 136.80, 133.3, 132.7, 131.8, 131.2, 129.8, 129.7, 128.4, 128.2, 128.0, 127.85, 127.80, 127.75, 127.70, 127.65, 127.61, 108.9, 98.0 ($^1J_{CH}$ = 166.6 Hz), 97.6 ($^1J_{CH}$ = 155.1 Hz), 82.8, 78.0, 76.3, 76.1, 75.7, 72.6, 71.06, 71.05, 63.8, 54.7, 28.1, 26.1, 17.7, 17.5. Anal calcd for $C_{37}H_{41}F_3O_{12}S$: C, 57.96; H, 5.39. Found: C, 58.03; H, 5.39.

3.2.13. Methyl 3-*O*-benzyl-4,6-*O*-benzylidiene-2-*O*-[(4-*O*-benzoyl-3-*O*-benzyl-2-*O*-(2-trifluoromethylbenzenesulfonyl)-α-L-rhamnopyranosyl)]-α-D-mannopyranoside (15α)—$[α]_D^{21}$ −24.3 (*c* 1.1, $CHCl_3$), lit.[29] −35.6; ^{1}H NMR ($CDCl_3$): δ 8.27 (d, 1H, *J* = 7.5 Hz, arom H), 7.92 (d, 2H, *J* = 7.5 Hz, arom H), 7.75 (d, 1H, *J* = 7.5 Hz, arom H), 7.57–7.39 (m, 10H, arom H), 7.34 (d, 2H, *J* = 7.0 Hz, arom H), 7.26–7.19 (m, 4H, arom H), 7.14 (t, 2H, *J* = 7.5 Hz, arom H), 6.99 (d, 2H, *J* = 7.0 Hz, arom H), 5.66 (s, 1H, H-7^{I}), 5.30 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 10.0 Hz, H-4^{II}), 5.18 (d, 1H, $J_{1,2}$ = 1.0 Hz, H-1^{II}), 5.11 (t, 1H, $J_{1,2}$, $J_{2,3}$ = 3.0 Hz, H-2^{II}), 4.82 (d, 1H, ^2J = 11.5 Hz, –CH_2Ph), 4.72 (s, 1H, H-1^{I}), 4.70 (d, 1H, ^2J = 11.5 Hz, –CH_2Ph), 4.39–4.30 (m, 4H, H-6^{I}, H-5^{II}, –CH_2Ph), 4.19 (s, 1H, H-2^{I}), 4.02–3.98 (m, 3H, H-3^{I}, H-4^{I}, H-3^{II}), 3.88 (t, 1H, $J_{5,6a}$, $J_{6a,6b}$ = 10.0 Hz, H-6^{I}), 3.81 (m, 1H, H-5^{I}), 3.41 (s, 3H, –OCH_3), 1.07 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6^{II}); ^{13}C NMR: δ 165.4, 138.0, 137.5, 137.1, 135.0, 133.5, 133.1, 132.0, 131.7, 129.9, 129.7, 129.0, 128.4, 128.32, 128.26, 128.23, 128.18, 127.7, 127.6, 126.1, 101.6 ($^1J_{CH}$ = 162.3 Hz), 99.0 ($^1J_{CH}$ = 170.5 Hz), 96.5 ($^1J_{CH}$ = 170.6 Hz), 78.7, 74.5, 74.1, 73.8, 73.1, 72.4, 71.7, 68.8, 67.2, 63.9, 55.1, 17.2; ESIMS *m*/*z* calcd for $C_{48}H_{47}F_3O_{13}NaS$ $[M+Na]^+$: 943.2587. Found: 943.2598.

3.2.14. Methyl 3-*O*-benzyl-4,6-*O*-benzylidiene-2-*O*-[(4-*O*-benzoyl-3-*O*-benzyl-2-*O*-(2-trifluoromethylbenzenesulfonyl)-β-L-rhamnopyranosyl)]-α-D-mannopyranoside (15β)—$[α]_D^{21}$ +51.1 (*c* 1.0, $CHCl_3$), lit.[29] +25.6; ^{1}H NMR ($CDCl_3$): δ 8.35 (m, 1H, arom H), 7.94–7.92 (dd, 2H, *J* = 8.0 Hz, 1.0 Hz, arom H), 7.77 (m, 1H, arom H), 7.59–7.26 (m, 15H, arom H), 7.16 (t, 1H, *J* = 7.5 Hz, arom H), 7.07 (t, 2H, *J* = 7.5 Hz, arom H), 6.96 (d, 2H, *J* = 7.0 Hz, arom H), 5.69 (s, 1H, H-7^{I}), 5.47 (d, 1H, $J_{2,3}$ = 2.5 Hz, H-2^{II}), 5.26 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 10.0 Hz, H-4^{II}), 4.98 (d, 1H, ^2J = 12.0 Hz, –CH_2Ph), 4.89 (s, 1H, H-1^{II}), 4.67 (d, 1H, ^2J = 12.0 Hz, –CH_2Ph), 4.63 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1^{I}), 4.44 (d, 1H, ^2J = 12.5 Hz, –CH_2Ph), 4.31 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 9.5 Hz, H-4^{I}), 4.25–4.19 (m, 2H, H-6^{I}, –CH_2Ph), 4.15 (m, 1H, H-2^{I}), 4.00–3.98 (dd, 1H, $J_{3,4}$ = 9.5 Hz, $J_{2,3}$ 2.5 Hz, H-3^{I}), 3.81 (t, 1H, $J_{5,6a}$, $J_{6a,6b}$ = 10.0 Hz, H-6^{I}), 3.75 (m, 1H, H-5^{I}), 3.49–3.46 (dd, 1H, $J_{3,4}$ = 9.5 Hz, $J_{2,3}$ = 2.5 Hz, H-3^{II}), 3.42 (m, 1H, H-5^{II}), 3.33 (s, 3H, –OCH_3), 1.29 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6^{II}); ^{13}C NMR: δ 165.2, 138.9, 137.8, 137.0, 136.9, 133.2, 132.6, 132.0, 131.1, 129.8, 129.7, 128.8, 128.5, 128.4, 128.20, 128.17, 127.95, 127.91, 127.86, 127.81, 127.72, 127.65, 127.60, 127.57, 126.1, 101.5 ($^1J_{CH}$ = 164.5 Hz), 100.9 ($^1J_{CH}$ = 171.8 Hz), 98.6 ($^1J_{CH}$ = 161.0 Hz), 79.0, 77.6, 76.6, 76.5, 75.9, 73.6, 72.3, 71.0, 70.8, 68.9, 64.0, 54.7, 17.6; ESIMS *m*/*z* calcd for $C_{48}H_{47}F_3O_{13}NaS$ $[M+Na]^+$: 943.2587. Found: 943.2542.

3.2.15. Methyl 3-*O*-[(4-*O*-benzoyl-3-*O*-benzyl-2-*O*-(2-trifluoromethylbenzenesulfonyl)-α-L-rhamnopyranosyl)]-2,4, 6-tri-*O*-benzyl-α-D-

mannopyranoside (17α)—$[\alpha]_D^{21}$ +6.9 (*c* 0.7, $CHCl_3$), lit.[29] −23.1; ^{1}H NMR ($CDCl_3$): δ 8.16 (d, 1H, *J* = 8.5 Hz, arom H), 7.72 (m, 3H, arom H), 7.56–7.07 (m, 21H, arom H), 7.01 (t, 2H, *J* = 7.5 Hz, arom H), 6.88 (d, 2H, *J* = 7.5 Hz, arom H), 5.36 (s, 1H, H-1^{II}), 5.30 (t, 1H, $J_{3,4}$, $J_{4,5}$ 10.0 Hz, H-4^{II}), 5.03 (s, 1H, H-2^{II}), 4.85 (s, 1H, H-1^{I}), 4.81–4.71 (m, 3H, –CH_2Ph), 4.62–4.55 (m, 2H, –CH_2Ph), 4.45 (d, 1H, ^2J = 11.0 Hz, –CH_2Ph), 4.21–4.10 (m, 3H, H-3^{I}, –CH_2Ph), 4.03 (m, 1H, H-5^{II}), 4.00–3.93 (m, 3H, H-2^{I}, H-4^{I}, H-3^{II}), 3.82 (m, 1H, H-6^{I}), 3.78–3.72 (m, 2H, H-5^{I}, H-6^{I}), 3.34 (s, 3H, –OCH_3), 1.13 (d, 3H, $J_{5,6}$ = 6.0 Hz, H-6^{II}); ^{13}C NMR: δ 165.2, 138.4, 138.3, 138.0, 136.7, 134.9, 133.5, 133.1, 131.9, 131.7, 129.7, 129.6, 128.5, 128.3, 128.1, 127.74, 127.71, 127.69, 127.64, 127.59, 127.54, 127.50, 127.3, 98.7 ($^1J_{CH}$ 169.8 Hz), 93.5 ($^1J_{CH}$ 171.6 Hz), 76.9, 75.0, 74.8, 73.9, 73.8, 73.6, 73.4, 73.2, 72.2, 71.5, 71.3, 69.0, 67.1, 54.9, 17.3; ESIMS *m*/*z* calcd for $C_{55}H_{55}O_{13}F_3KS$ $[M+K]^+$: 1051.2953. Found: 1051.2914.

3.2.16. Methyl 3-*O*-[(4-*O*-benzoyl-3-*O*-benzyl-2-*O*-(2-trifluoromethylbenzenesulfonyl)-β-L-rhamnopyranosyl)]-2,4, 6-tri-*O*-benzyl-α-D-mannopyranoside (17β)—

$[\alpha]_D^{21}$ +68.9 (*c* 1.1, $CHCl_3$), lit.[29] +35.2; ^{1}H NMR ($CDCl_3$): δ 8.23 (d, 1H, *J* = 7.0 Hz, arom H), 7.90 (dd, 2H, *J* = 8.0 Hz, *J* = 0.5 Hz, arom H), 7.67 (d, 1H, *J* = 9.0 Hz, arom H), 7.56 (t, 1H, *J* = 7.0 Hz arom H), 7.45–7.24 (m, 19H, arom H), 7.15 (t, 1H, *J* = 7.5 Hz, arom H), 7.06 (t, 2H, *J* = 7.5 Hz, arom H), 6.90 (d, 2H, *J* = 7.5 Hz, arom H), 5.27 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 9.0 Hz, H-4^{II}), 5.13 (d, 1H, $J_{2,3}$ = 2.5 Hz, H-2^{II}), 4.88 (d, 1H, ^2J = 13.0 Hz, –CH_2Ph), 4.77 (t, 2H, ^2J = 10.5 Hz, –CH_2Ph), 4.72 (s, 1H, H-1^{II}), 4.71 (d, 1H, ^2J = 12.0 Hz, –CH_2Ph), 4.65 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1^{I}), 4.60–4.57 (m, 2H, –CH_2Ph), 4.30 (d, 1H, ^2J = 12.5 Hz, –CH_2Ph), 4.13 (d, 1H, ^2J = 12.5 Hz, –CH_2Ph), 4.02 (dd, 1H, $J_{3,4}$ = 9.5 Hz, $J_{2,3}$ = 2.5 Hz, H-3^{I}), 3.94 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 9.5 Hz, H-4^{I}), 3.89 (m, 1H, H-2^{I}), 3.79–3.75 (m, 3H, H-5^{I}, H-6^{I}), 3.48 (m, 1H, H-5^{II}), 3.41–3.39 (dd, 1H, $J_{3,4}$ = 9.5 Hz, $J_{2,3}$ = 3.0 Hz, H-3^{II}), 3.32 (s, 3H, –OCH_3), 1.26 (d, 3H, $J_{5,6}$ = 6.5 Hz, H-6^{II}); ^{13}C NMR: δ 165.2, 139.1, 139.0, 138.4, 136.7, 136.5, 133.2, 132.7, 131.8, 131.0, 129.7, 129.6, 128.40, 128.37, 128.32, 128.25, 128.17, 128.10, 127.9, 127.8, 127.6, 127.55, 127.47, 127.2, 100.2 ($^1J_{CH}$ = 155.4 Hz) ($^1J_{CH}$ = 164.5 Hz), 83.4, 78.2, 76.7, 76.2, 75.0, 74.8, 73.5, 73.1, 72.3, 71.9, 71.2, 70.8, 69.4, 54.7, 17.7; ESIMS *m*/*z* calcd for $C_{55}H_{55}O_{13}F_3KS$ $[M+Na]^+$: 1035.3213. Found: 1035.3236.

3.3. Methyl 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-gluco-pyranoside

Tf_2O (0.027 mL, 0.16 mmol) was added dropwise to a stirred solution of donor **1** (70 mg, 0.11 mmol) and BSP (29 mg, 0.14 mmol), in CH_3CN (1.2 mL) and CH_2Cl_2 (1.8 mL) under argon at −60 °C. After stirring for 1 h at −60 °C, acceptor **4** (150 mg, 0.32 mmol) in CH_2Cl_2 (1.0 mL) was added over a period of 1 min. The reaction mixture was stirred for 3 h at −60 °C, then quenched at −60 °C with saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. (3 × 15 mL). The combined organic layer was dried (Na_2SO_4), and the solvent was removed under reduced pressure. Examination of the crude reaction mixture by ^{1}H NMR spectroscopy revealed the formation of one very major product, tentatively assigned as the imidate (**18**). Purification by silica gel column chromatography (EtOAc/hexane) afforded the unstable 18 (30 mg, 27%) and acetate **19** (10 mg, 6%). Compound **18** rapidly decomposed on standing in $CDCl_3$ to a mixture of **19** and several other compounds. It was characterized by the following signals: ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.13 (s, 1H, H-1^{II}), 4.62 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1^{I}), 3.42 (s, 3H, –OCH_3), 1.99 (s, 3H, CH_3C(OR)=N), 1.17 (d, 3H $J_{5,6}$ = 6.3 Hz, H-6^{II}).

3.3.1. Methyl 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-gluco-pyranoside (19)—

$[\alpha]_D^{21}$ +18.0 (*c* 0.8, $CHCl_3$), lit.[56] +28.6; ^{1}H NMR ($CDCl_3$): δ 7.37–7.26 (m, arom H), 5.09 (d, 1H, ^2J = 10.5 Hz, –CH_2Ph), 4.89–4.79 (m, 3H, –CH_2Ph), 4.68 (d, 1H, ^2J = 12.5 Hz, –CH_2Ph), 4.59–4.55 (m, 2H, –CH_2Ph), 4.26–4.24 (m, 2H, H-6), 4.01 (t, 1H, $J_{3,4}$, $J_{4,5}$ = 9.5 Hz, H-3), 3.81 (m, 1H, H-5), 3.55–3.52 (dd, 1H, $J_{2,3}$ = 9.5 Hz, $J_{1,2}$ = 3.5 Hz, H-2), 3.48 (t, 1H, $J_{4,5}$, $J_{3,4}$ = 9.0 Hz, H-4), 3.37 (s, 3H, –OCH_3), 2.02 (s, 3H, CH_3CO); ^{13}C NMR: δ 170.7, 138.6,

138.0, 137.8, 128.50, 128.48, 128.45, 128.13, 128.09, 128.01, 127.99, 127.92, 127.7, 98.1, 82.0, 79.8, 75.8, 75.0, 73.4, 68.5, 63.0, 55.2, 20.9.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

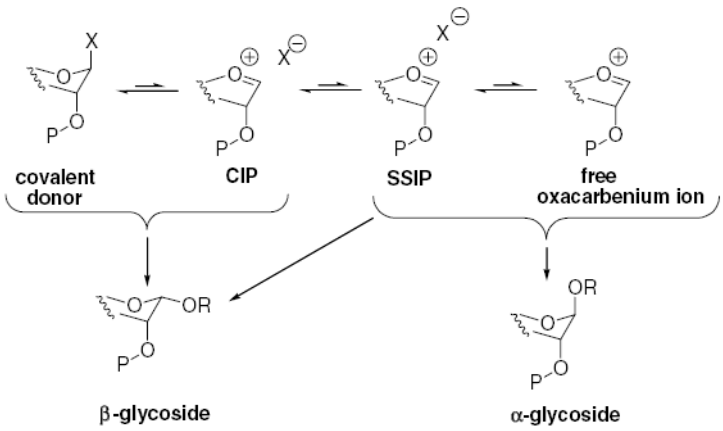
Acknowledgements

We thank the NIH (GM59335) for support of this work, and John Picione for first recognizing the α-selective coupling of donor **2** with acceptor **9**.

References

1. Crich D, Sun S. J Org Chem 1997;62:1198–1199.
2. Crich D, Sun S. Tetrahedron 1998;54:8321–8348.
3. Crich D, Smith M. J Am Chem Soc 2001;123:9015–9020. [PubMed: 11552809]
4. Crich D, Lim LBL. Org React 2004;64:115–251.
5. Crich D. J Carbohydr Chem 2002;21:663–686.
6. Crich D, Hutton TK, Banerjee A, Jayalath P, Picione J. Tetrahedron: Asymmetry 2005;16:105–119.
7. Srivastava VK, Schuerch C. J Org Chem 1981;46:1121–1126.
8. Ito Y, Kanie O, Ogawa T. Angew Chem, Int Ed 1996;35:2510–2512.
9. Ito Y, Ogawa T. Angew Chem, Int Ed Engl 1994;33:1765–1767.
10. Barresi F, Hindsgaul O. Can J Chem 1994;72:1447–1465.
11. Cumpstey I, Chayajarus K, Fairbanks AJ, Redgrave AJ, Seward CMP. Tetrahedron: Asymmetry 2004;15:3207–3221.
12. Ziegler T, Lemanski G. Angew Chem, Int Ed 1998;37:3129–3132.
13. Stork G, La Clair JJ. J Am Chem Soc 1996;118:247–248.
14. Abdel-Rahman AA-H, El Ashry ESH, Schmidt RR. Carbohydr Res 2002;337:195–206. [PubMed: 11844489]
15. Kaji E, Lichtenthaler FW. Trends Glycosi Glycotechnol 1993;5:121–142.
16. Hodosi G, Kovác P. J Am Chem Soc 1997;119:2335–2336.
17. El Ashry ESH, Rashed N, Ibrahim ESI. Curr Org Synth 2005;2:175–213.
18. Pozsgay, V. In Carbohydrate in Chemistry and Biology; Ernst, B., Hart, G. W., Sinaÿ, P., Eds.; Wiley-VCH: Weinheim, 2000; Vol. 1, pp 319–343.
19. Ito, Y.; Ohnishi, Y. In Glycoscience: Chemistry and Chemical Biology; Fraser-Reid, B., Kuniaki, T., Thiem, J., Eds.; Springer: Berlin, 2001; Vol. 2, pp 1589–1619.
20. Ramm M, Lobe M, Hamburger M. Carbohydr Res 2003;338:109–112. [PubMed: 12504387]
21. Crich D, Yao Q. J Am Chem Soc 2004;126:8232–8236. [PubMed: 15225064]
22. Crich, D.; Bowers, A. A. J. Org. Chem., in press.
23. Kwon YT, Lee YJ, Lee K, Kim KS. Org Lett 2004;6:3901–3904. [PubMed: 15496059]
24. Schüle G, Ziegler T. Liebigs 1996:1599–1607.
25. Lau R, Schüle G, Schwaneberg U, Ziegler T. Liebigs 1995:1745–1754.
26. Lichtenthaler FW, Metz TW. Tetrahedron Lett 1997;38:5477–5480.
27. Crich D, Chandrasekera NS. Angew Chem, Int Ed 2004;43:5386–5389.
28. Crich D, Sun S. J Am Chem Soc 1997;119:11217–11223.
29. Crich D, Picione J. Org Lett 2003;5:781–784. [PubMed: 12605514]
30. Crich D, Cai W, Dai Z. J Org Chem 2000;65:1291–1297. [PubMed: 10814088]
31. Crich D, Vinod AU, Picione J. J Org Chem 2003;68:8453–8458. [PubMed: 14575470]
32. Codée JDC, Litjens REJN, den Heeten R, Overkleeft HS, van Boom JH, van der Marel GA. Org Lett 2003;5:1519–1522. [PubMed: 12713313]
33. Gorin PAJ, Perlin AS. Can J Chem 1961;39:2474–2485.

34. Iversen T, Bundle DR. Carbohydr Res 1980;84:C13–C15.
35. Paulsen H, Kutschker W, Lockho3 O. Chem Ber 1981;114:3233–3241.
36. Backinowsky LV, Balan NF, Shashkov AS, Kochetkov NK. Carbohydr Res 1980;84:225–235.
37. Barresi, F.; Hindsgaul, O. In Modern Methods in Carbohydrate Synthesis; Khan, S. H., O'Neill, R. A., Eds.; Harwood Academic Publishers: Amsterdam, 1996; pp 251–276.
38. Crich D, Vinod AU, Picione J, Wink DJ. ARKIVOC 2005;6:339–344.
39. Bedini E, Carabellese A, Barone G, Parrilli M. J Org Chem 2005;70:8064–8070. [PubMed: 16277328]
40. Majumdar, D.; Boons, G.-J. In Handbook of Reagents for Organic Synthesis: Reagents for Glycoside, Nucleotide, and Peptide Synthesis; Crich, D., Ed.; Wiley: Chichester, 2005; pp 11–15.
41. Pougny JR, Sinaÿ P. Tetrahedron Lett 1976;17:4073–4076.
42. Ratcliffe AJ, Fraser-Reid B. J Chem Soc, Perkin Trans 1 1990:747–750.
43. Braccini J, Derouet C, Esnault J, de Penhoat CH, Mallet JM, Michon V, Sinaÿ P. Carbohydr Res 1993;246:23–41.
44. Schmidt RR, Behrendt M, Toepfer A. Synlett 1990:694–696.
45. Fügedi P, Liptak A, Nanasi P, Neszmelyi A. Carbohydr Res 1982;107:C5–C8.
46. Uriel C, Gomez AM, Lopez JC, Fraser-Reid B. J Carbohydr Chem 2005;24:665–675.
47. Crich D, Smith M, Yao Q, Picione J. Synthesis 2001:323–326.
48. Kahne D, Walker S, Cheng Y, Engen DV. J Am Chem Soc 1989;111:6881–6882.
49. Schweizer F, Lohse A, Otter A, Hindsgaul O. Synlett 2001:1434–1436.
50. Lohse A, Schweizer F, Hindsgaul O. Comb Chem High Throughput Screening 2002;5:389–394.
51. Masamune S, Choy W, Peterson JS, Sita LR. Angew Chem, Int Ed Engl 1985;24:1–76.
52. Paulsen, H. In Selectivity a Goal for Synthetic Efficiency; Bartmann, W., Trost, B. M., Eds.; Verlag Chemie: Weinheim, 1984; pp 169–190.
53. Spijker NM, van Boeckel CAA. Angew Chem, Int Ed Engl 1991;30:180–183.
54. Fraser-Reid B, López JC, Gómez AM, Uriel C. Eur J Org Chem 2004:1387–1395.
55. Bock K, Pedersen C. J Chem Soc, Perkin Trans 2 1974:293–297.
56. Prosperi D, Ronchi S, Lay L, Rencurosi A, Russo G. Eur J Org Chem 2004:395–405.



Scheme 1.
Abbreviated glycosylation mechanism.

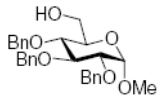
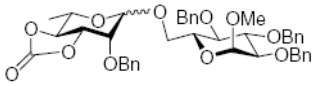
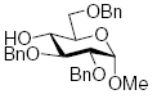
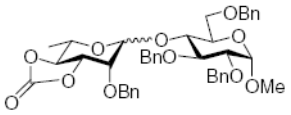
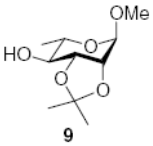
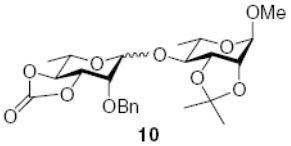
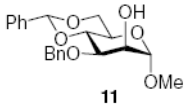
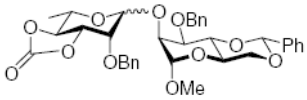
Table 1

The effect of varying quantities of propionitrile and acetonitrile on the formation of **6** from **2** and **4** at −60 °C

Entry	Solvent (v/v)	Yield (%) 6	β:α ratio
1	$EtCN/CH_2Cl_2$ 0:100	81	6:1
2	$EtCN/CH_2Cl_2$ 100:0	<10	>5:1
3	$EtCN/CH_2Cl_2$ 10:90	69	6.8:1
4	$EtCN/CH_2Cl_2$ 5:95	80	7.9:1
5	$EtCN/CH_2Cl_2$ 2.5:97.5	78	6.6:1
6	CH_3CN/CH_2Cl_2 5:95	76	7.2:1
7	CH_3CN/CH_2Cl_2 2.5:97.5	80	8:1
8	CH_3CN/CH_2Cl_2 1.25:98.75	98	4.5:1

Table 2

Coupling reactions with donor **2** in CH_2Cl_2/CH_3CN 95/5 (v/v) and in pure CH_2Cl_2

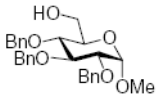
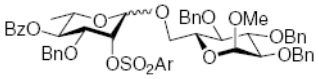
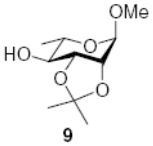
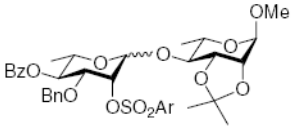
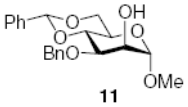
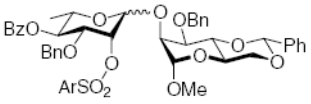
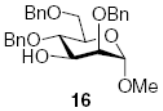
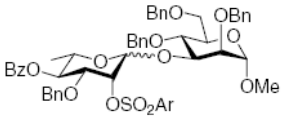
Entry	Acceptor	Product	Yield[a] (%) CH_2Cl_2	(β:α ratio)[b] CH_2Cl_2/ CH_3CN (95/5)
1	 **4**	 **6**	87 (5.8:1)	76% (7.2:1)
2	 **7**	 **8**	70 (1:1.1)	55% (2.1:1)
3	 **9**	 **10**	85 (1:8.1)	72% (1:4.2)
4	 **11**	 **12**	87 (1:2.1)	77% (1:1.2)

[a] Yields refer to isolated products.

[b] Ratios were determined on the crude reaction mixtures by integration of the ^{1}H NMR spectra.

Table 3

Further coupling reactions with donor **1** in CH_2Cl_2/CH_3CN 95/5 (v/v) and in pure CH_2Cl_2

Entry	Acceptor	Product[a]	Yield[a] (%) CH_2Cl_2	(β:α ratio)[b] CH_2Cl_2/ CH_3CN (95/5)
1	 **4**	 **13**	87 (12.7:1)	88% (16:1)
2	 **9**	 **14**	85 (1:1.4)	78% (1.2:1)
3	 **11**	 **15**	92 (2.6:1)	88% (3.9:1)
4	 **16**	 **17**	74 (2.4:1)	42% (3.5:1)

[a] Ar = *p*-$CF_3C_6H_4$

[b] Yields refer to isolated products.

[c] Ratios were determined on the crude reaction mixtures by integration of the ^1H NMR spectra.