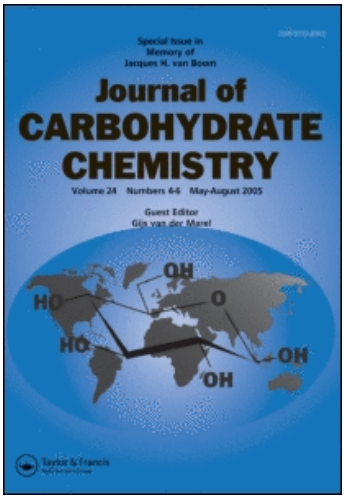

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SYNTHESIS OF RIBOFURANOSIDES BY CATALYSIS WITH LEWIS ACIDS. GLYCOSIDATION VERSUS TRANSACETYLATION

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ABSTRACT

Several ribofuranosyl derivatives bearing trichloroacetimidoyl or acetyl leaving groups in a Lewis acid promoted ribosylation reaction were prepared and used in an attempt to improve the yield and to avoid donor → acceptor transacetylation. Trichloroacetimidates were excellent donors affording disaccharides with very high yields under mild conditions. The corresponding 1-*O*-acetylated analogs could also be used with out transacetylation in the presence of boron trifluoride etherate.

INTRODUCTION

β-D-Ribofuranoside moieties have been identified as constituents of many bacterial polysaccharides[1-4] and natural products.[5,6] The formation of this β-D-ribofuranosidic bond was usually accomplished from 1-*O*-acetylated donors, mostly 1-*O*-acetyl-2,3,5-tri-*O*-

benzoyl-β-D-ribofuranose 1[7,8] and Lewis acids such as $SnCl_4$ or trimethylsilyl trifluoromethanesulfonate (TMSOTf) as catalysts. Furanosyl halides have also been used[9] but other potentially useful donors such as trichloroacetimidates,[10,11] cyanoethylidene,[12] thioglycosides[13] and fluorides[14] were only occasionally studied.

In this paper the use of several ribofuranosyl donors bearing trichloroacetimidoyl or acetyl leaving groups in the synthesis of disaccharides is reported.

RESULTS AND DISCUSSION

The crystalline 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl trichloroacetimidate 2 was prepared from 1 after *O*-deacetylation with hydrochloric acid in dioxane and treatment with trichloroacetonitrile and potassium carbonate in dichloromethane. The synthesis of the donors 3 and 4 have been reported earlier, whereas the synthesis of the donors 5 and 6 are described in the Experimental. Acceptors A-C were selected as representatives of the reactivity pattern found in the synthesis of oligosaccharides.

Acceptor A was previously condensed with 1 in the presence of TMSOTf[8] affording a very high yield of disaccharide 2A. When the same reaction was performed using the corresponding imidate 2, disaccharide 2A was obtained with a similar yield but in a faster reaction and milder conditions. The reaction of a slight excess of imidate 2 with the acceptors B and C in dichloromethane and TMSOTf as a catalyst, gave also the corresponding disaccharides in high yields (see Table 1). The structures of all disaccharides were confirmed by NMR spectroscopy. The ^1H NMR spectra showed typical singlets corresponding to H-1' at δ 5.19, 5.76 and 5.57 for the disaccharides 2A-2C, respectively. In the ^{13}C NMR spectra (Table 2) the signals for C-1' appeared at 105.4-107.4 ppm. The signal corresponding to the carbon bearing the free hydroxyl group in the acceptors was deshielded in accordance with the expected effect for ribosylation (61.2 → 67.6, 2A; 73.4 → 80.6, 2B; 68.3 → 74.9, 2C).

Donor 3 with an allyl group at position 3 was prepared previously[19] for the synthesis of *Haemophilus influenzae* type b oligosaccharides and could be successfully used

Table 1. Reaction conditions and results of ribosylation

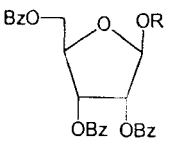
Exp	Donor [mmol]	Acceptor [mmol]	Promoter/$ClCH_2CH_2Cl$ [mmol] mL	Product	Yield %
1	2 [0.103]	A [0.086]	TMSOTf [0.0086]	2 A	81
2	2 [0.106]	B [0.084]	TMSOTf [0.0084]	2 B	90
3	2 [0.110]	C [0.092]	TMSOTf [0.0092]	2 C	75
4	3 [0.56]	A [0.37]	TMSOTf [0.094]	3 A	80[19]
5	5 [0.81]	A [0.63]	TMSOTf [0.063]	5 A	54
6	6 [0.274]	A [0.274]	TMSOTf [0.153]	6 A	81
7	6 [0.274]	A [0.274]	$BF_3.Et_2O$ [0.27]/0.07	6 A	79
8	6 [0.148]	B [0.086]	$BF_3.Et_2O$ [0.09]/0.04	6 B	45
9	6 [0.148]	C [0.158]	$BF_3.Et_2O$ [0.27]/0.07	6 C	40
10	4 [0.62]	A [0.31]	$BF_3.Et_2O$ [0.77]/0.40	4 A	72
11	4 [0.129]	B [0.086]	$BF_3.Et_2O$ [0.22]/0.05	4 B	74

Table 2. ^{13}C NMR Spectral data[a]

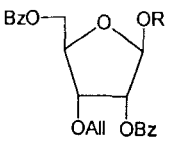
Acceptor							Donor					
compd	C-1	C-2	C-3	C-4	C-5	C-6	compd	C-1	C-2	C-3	C-4	C-5
A[b]	61.2	78.9	78.7	78.1	69.6		2	102.6	74.7	71.9	80.3	64.5
B	97.5	79.4	73.4	77.4	69.5	68.4	3	102.9	72.3	73.4	80.4	64.5
C	98.2	68.3	79.8	79.8	67.5	17.7	4	97.9	73.9	70.3	81.4	63.4
							5	102.4	70.6	73.9	81.9	63.7
							6	98.5	73.6	76.2	81.4	69.2
2A[b]	67.6	78.5	78.2	78.1	69.9			105.4	75.5	73.9	78.9	65.4
2B	97.6	79.3	80.6	76.6	69.8	68.3		107.4	75.5	72.4	78.3	64.9
2C	98.4	74.9	80.0	80.3	68.2	17.8		106.7	75.6	72.4	79.0	65.2
3A[b]	66.7	77.4	77.5	78.1	69.4			104.8	73.9	77.7	78.7	65.1
5A[b]	67.8	78.9	77.9	77.9	69.9			105.1	74.7	71.6	78.3	64.6
6A[b]	67.3	78.6	78.2	78.0	69.9			105.1	73.9	77.9	80.3	71.5
4B	97.6	79.5	80.8	76.5	69.8	68.5		107.2	74.6	71.1	77.6	64.6
6B	97.7	79.8	80.0	76.6	69.8	68.5		107.3	74.5	77.2	79.6	71.0
6C	98.7	72.9	80.3	80.4	68.1	18.0		106.0	74.2	77.5	80.4	70.9

a. Protective groups were as follows:
Allyl $-CH_2O-$ 71.2-71.9 ppm, $CH_2=$ 116.5-118.9 ppm, -CH= 133.5-134.2 ppm; Bz -CO- 165.3-166.3 ppm; Bn $-CH_2O-$ 71.3-73.5 ppm; Ac -CO- 169.2-170.5 ppm, $-CH_3$ 20.3-20.7 ppm.

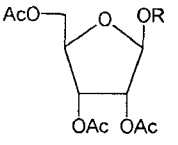
b. The C-2, C-3 and C-4 assignments may have to be interchanged.



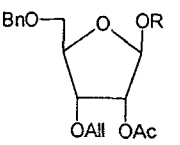
1 R=Ac
2 R=C(NH)CCl$_3$
2A - 2C ; R=A - C



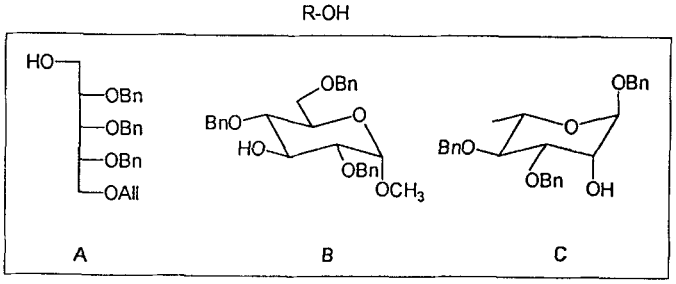
3 R=C(NH)CCl$_3$
3A R=A



4 R=Ac
5 R=C(NH)CCl$_3$
4A=5A; R=A
4B R=B



6 R=Ac
6A - 6C; R=A - C



for the ribosylation of acceptor A with high yield. One of the most important problems frequently found in Lewis acid catalysed ribosylation is the donor → acceptor acetyl group migration (transacetylation) which until now precluded the use of acetylated donors. Donor 5 was used for the ribosylation of acceptor A, and even though when the yield was moderate, the acetylated acceptor was only detected in < 5 %.

The results obtained with the ribofuranosyl trichloroacetimidates demonstrated their usefulness for the synthesis of oligosaccharides, especially for complex acceptors, or when high yield and/or fast and clean reactions were needed. However, the synthesis of these donors was generally more troublesome than the corresponding 1-*O*-acetylated analogs. In order to find an alternative method for inexpensive and simple acceptors, the reaction of the 1-*O*-acetylated donor 6 with A in the presence of several Lewis acids was

studied. TMSOTf and boron trifluoride etherate were both excellent catalysts for this reaction (Table 1, experiments 6 and 7). However, when the reactivity of the acceptor decreased, transacetylation became the main reaction with TMSOTf. At the same time no transacetylation was detected for reactions promoted by boron trifluoride etherate (Table 1, experiments 8 and 9). This fact could be explained probably by the bulky structure of the intermediate acyloxonium ion pair,[15] which hindered the attack on the orthoester carbon, resulting in the direct formation of disaccharide. The moderate to low yield obtained in this reaction was explained by the formation of the nonreducing disaccharide ribofuranosyl β,β-(1-1)-ribofuranose.[16]

Peracetylated ribofuranose 4 was also used as a donor in the presence of boron trifluoride etherate. The reaction of 4 with A gave the disaccharide in a yield exceeding that obtained with the corresponding imidate 5. Acceptor B in the same reaction affords the disaccharide in a good yield. The structure of 4B was confirmed by NMR spectroscopy. The ^{1}H NMR spectrum showed a singlet corresponding to H-1' at 5.51 ppm. In the ^{13}C NMR spectra a signal for C-1' was observed at 107.2 ppm and that for C-3 in the acceptor was deshielded (73.4 → 80.8).

In conclusion, for easily synthesized acceptors having reactive hydroxyl groups, the use of peracetylated ribofuranose and boron trifluoride etherate as promoter is recommended. For more complex acceptors the use of ribofuranosyl trichloroacetimidates is the method of choice.

EXPERIMENTAL

General procedures. Optical rotations were measured at 25 °C with a POLAMAT A automatic polarimeter, using a 5-cm 5-mL cell. NMR spectra were recorded at 25 °C with a BRUKER AC-250F spectrometer. Chemical shifts (δ) are given in ppm relative to the signal for internal tetramethylsilane; indirectly to $CDCl_3$, δ 77.03 for ^{13}C.

All compounds were purified by column chromatography on Kieselgel 60 (Fluka, < 230 mesh ASTM) and fractions were monitored by TLC on kieselgel 60 F_{254} (Merck). Detection was effected by charring with sulfuric acid after examination under UV light. Evaporations were conducted under reduced pressure at 50 °C (bath).

The characterization of the various compounds was performed by ^{1}H and ^{13}C NMR spectroscopy using homo- and heteronuclear correlation experiments and by elemental analysis, except for 6B which was contaminated by the free acceptor. In the latter case the structure was accessed only by NMR spectroscopy.

Synthesis of acceptors

5-*O*-Allyl-2,3,4-tri-*O*-benzyl-D-ribitol (A).[9] ^{1}H NMR ($CDCl_3$) δ 7.4-7.0 (m, 15H, 3 Ph), 5.88 (m, 1H, -CH_2-C*H*=CH_2), 5.18 (m, 2H, -CH_2-CH=C*H*$_2$), 4.9-4.4 (m, 6H, 3 PhCH_2), 4.0-3.3 (m, 9H, H-1a,1b,2,3,4,5a,5b and -C*H*$_2$-CH=CH_2).

Methyl 2,4,6-Tri-*O*-benzyl-α-D-glucopyranoside (B).[17] ^{1}H NMR ($CDCl_3$) δ 7.4-7.2 (m, 15H, Ph), 4.62 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 4.08 (t, 1H, $J_{3,4}$ = 9.1 Hz, H-3), 3.72 (m, 1H, H-5), 3.66 (m, 2H, H-6a,6b), 3.52 (t, 1H, $J_{4,5}$ = 9.1 Hz, H-4), 3.40 (dd, 1H, $J_{2,3}$ = 9.1 Hz, H-2), 3.30 (s, 3H, OCH_3).

Benzyl 3,4-Di-*O*-benzyl-α-L-rhamnopyranoside (C).[18] ^{1}H NMR ($CDCl_3$) δ 7.4-7.2 (m, 15H, Ph), 4.85 (d, 1H, $J_{1,2}$ = 1.3 Hz, H-1), 4.03 (dd, 1H, $J_{2,3}$ = 3.3 Hz, H-2), 3.86 (dd, 1H, $J_{3,4}$ = 9.1 Hz, H-3), 3.78 (m, 1H, $J_{5,6}$ = 6.2 Hz, H-5), 3.48 (t, 1H, $J_{4,5}$ = 9.1 Hz, H-4), 3.19 (s, 1H, OH), 1.80 (d, 3H, H-6).

Synthesis of donors

2,3,5-Tri-*O*-benzoyl-β-D-ribofuranosyl Trichloroacetimidate (2). α/β 1:8; ^{1}H NMR ($CDCl_3$) 2α-anomer δ 8.65 (s, 1H, C(NH)CCl_3), 8.2-7.8 (m, 6H, Ph), 7.65-7.2 (m, 9H, Ph), 6.89 (d, 1H, $J_{1,2}$ = 4.4 Hz, H-1), 5.93 (t, 1H, $J_{3,4}$ = 6.6 Hz, H-3), 5.66 (dd, 1H, $J_{2,3}$ = 6.6 Hz, H-2), 4.90 (m, 1H, H-4); 2β-anomer δ 8.70 (s, 1H, C(NH)CCl_3), 8.2-7.8 (m, 6H, PhCO), 7.65-7.2 (m, 9H, PhCO), 6.62 (s, 1H, H-1), 5.99 (d, 1H, $J_{2,3}$ = 4.9 Hz, H-2), 5.93 (dd, 1H, $J_{3,4}$ = 6.0 Hz, H-3), 4.90 (m, 1H, $J_{4,5a}$ = 4.5 Hz, $J_{4,5b}$ = 5.7 Hz, H-4), 4.70 (dd, 1H, $J_{5a,5b}$ = 11.9 Hz, H-5a), 4.61 (dd, 1H, H-5b).

Anal. Calcd for $C_{28}H_{22}O_8NCl_3$: C, 55.42; H, 3.66. Found: C, 55.13; H, 3.99.

3-*O*-Allyl-2,5-di-*O*-benzoyl-β-D-ribofuranosyl Trichloroacetimidate (3).[19] α/β 1:8; ^{1}H NMR ($CDCl_3$) 3α-anomer δ 8.51 (s, 1H, C(NH)CCl_3), 6.67 (d, 1H, $J_{1,2}$ = 4.3 Hz, H-1); 3β-anomer δ 8.63 (s, 1H, C(NH)CCl_3), 6.48 (s, 1H, H-1), 5.73 (d, 1H, $J_{2,3}$ = 4.3 Hz, H-2). For further NMR data, see Ref 19.

1,2,3,5-Tetra-*O*-acetyl-β-D-ribofuranose (4).[20] ^{1}H NMR δ 6.18 (s, 1H, H-1), 5.43-5.13 (m, 2H, H-2,3), 4.42-4.18 (m, 2H, H-5a,5b), 2.21-2.11 (4s, 12H, 4 CH_3CO).

2,3,5-Tri-*O*-acetyl-α,β-D-ribofuranosyl Trichloroacetimidate (5). A solution of methyl 2,3,5-tri-*O*-acetyl-β-D-ribofuranoside (2.0 g, 6.9 mmol) in 90 % trifluoroacetic acid (10 mL) was stirred for 5 h and the mixture was concentrated at room temperature and co-concentrated with toluene (2 x 10 mL). Then dichloromethane (50 mL) was added and the solution was washed with water, aq 5 % sodium hydrogencarbonate and water, dried, filtered and concentrated. A solution of the residue (589 mg, 2.13 mmol), potassium carbonate (186 mg, 1.34 mmol) and trichloroacetonitrile (0.2 mL) in dried dichloromethane (4 mL) was stirred for 12 h at room temperature. The mixture was filtered over celite, and the filtrate was concentrated to yield 5 (870 mg, 30 %) as an α,β mixture (1:10): R_F 0.8 (dichloromethane/acetone 2:1 v/v). ^{1}H NMR ($CDCl_3$) 5α-anomer δ 8.52 (s, 1H, C(NH)CCl_3), 6.52 (d, 1H, $J_{1,2}$ = 4.2 Hz, H-1); 5β-anomer δ 8.61 (s, 1H, C(NH)CCl_3), 6.28 (s, 1H, H-1), 5.48 (d, 1H, $J_{2,3}$ = 4.8 Hz, H-2), 5.36 (dd, 1H, $J_{3,4}$ = 7.2 Hz, H-3), 2.18-2.10 (3s, 9H, 3 CH_3CO).

1,2-Di-*O*-acetyl-3-*O*-allyl-5-*O*-benzyl-α,β-D-ribofuranose (6). To a cooled (0 °C) solution of 3-*O*-allyl-1,2-*O*-isopropylidene-α-D-ribofuranose (1.0 g, 4.3 mmol) in dimethylformamide (5 mL) was added powdered sodium hydroxide (0.7 g, 12.5 mmol) and stirred for 20 min. Then, to the mixture was added benzyl chloride (1.5 mL, 13.4 mmol). After 2 h, TLC (dichloromethane/acetone 20:1 v/v) indicated the disappearance of the starting material and a new spot at R_F 0.85. The mixture was then poured into water (20 mL) and extracted with dichloromethane (3 x 5 mL); the combined extracts were washed with water, dried, filtered and concentrated. A solution of the residue in dioxane/water (3:2 v/v, 20 mL) and Dowex-50 (H^+) resin (2 g) was stirred at 60 °C. After 16 h, TLC (dichloromethane/acetone 10:1 v/v) showed the reaction to be complete. The mixture was filtered over a glass filter and concentrated. To a solution of the residue in pyridine (5 mL) was added acetic anhydride (5 mL). After 4 h, TLC (hexane/ethyl acetate 4:1 v/v) showed the reaction to be complete. Column chromatography (hexane/ethyl acetate 5:1 v/v) of the residue afforded 6 (1.4 g, 89 %) as a syrup: R_F 0.61 (hexane/ethyl acetate 2:1 v/v). ^{1}H NMR ($CDCl_3$) 6β-anomer δ 6.15 (s, 1H, H-1), 5.23 (d, 1H, $J_{2,3}$ = 4.6 Hz, H-2), 4.15 (m, 1H, H-4), 4.25 (t, 1H, $J_{3,4}$ = 4.6 Hz, H-3), 3.65 (m, 2H, H-5a,5b).

Anal. Calcd for $C_{19}H_{24}O_7$: C, 62.63; H, 6.64. Found C, 62.71; H, 6.65.

TMSOTf promoted glycosylation. For details concerning amounts, see Table 1. Acceptor and donor were dried in a high vacuum system for 2 h. Dry dichloromethane (6 mL/mmol of donor) and molecular sieves 4Å were added and the mixture was stirred for 30 min. The reaction was cooled to 0 °C and TMSOTf was added under an argon atm. After 5 min, TLC (hexane/ethyl acetate) showed the reaction to be complete. Triethylamine was added and the mixture was filtered, washed with water, dried and concentrated. The resulting disaccharides were isolated via column chromatography.

5-*O*-Allyl-1-*O*-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2,3,4-tri-*O*-benzyl-D-ribitol (2A).[8] Column chromatography (toluene/acetone 90:1 v/v) of the residue afforded 2A as a syrup: $[\alpha]_D$ +51.2° (c 1, chloroform); ^{1}H NMR ($CDCl_3$) δ 8.2-7.8 (m, 6H, Ph), 7.6-7.1 (m, 24H, Ph), 5.87 (m, 1H, $-CH_2-CH=CH_2$), 5.80 (dd, 1H, $J_{3',4'}$ = 6.6 Hz, H-3'), 5.65 (d, 1H, $J_{2',3'}$ = 5.0 Hz, H-2'), 5.24 (m, 2H, $-CH_2-CH=CH_2$), 5.19 (s, 1H, H-1').

Methyl 2,4,6-Tri-*O*-benzyl-1-*O*-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-α-D-glucopyranoside (2B). Column chromatography (toluene/acetone 90:1 v/v) of the residue afforded 2B as a syrup: $[\alpha]_D$ +38.2° (c 1, chloroform); R_F 0.56 (toluene/acetone 20:1 v/v); ^{1}H NMR ($CDCl_3$) δ 8.2-7.8 (m, 6H, Ph), 7.60-7.15 (m, 15H, Ph), 5.85 (m, 2H, H-2',3'), 5.76 (s, 1H, H-1'), 4.7-4.4 (m, 6H, $PhCH_2$), 4.59 (m, 1H, H-4'), 4.54 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 4.53 (m, 1H, H-5a'), 4.17 (t, 1H, $J_{3,4}$ = 9.2 Hz, H-3), 3.64 (m, 1H, H-5b'), 3.60 (m, 2H, H-6a,6b), 3.54 (m, 2H, H-2,4), 3.29 (s, 3H, OCH_3).

Anal. Calcd for $C_{55}H_{52}O_{13}$: C, 71.72; H, 5.69. Found: C, 72.08; H, 6.09.

Benzyl 3,4-Di-*O*-benzyl-1-*O*-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-α-L-rhamnopyranoside (2C). Column chromatography (toluene/acetone 90:1 v/v) of the residue afforded 2C as a syrup: $[\alpha]_D$ +20.6° (c 1, chloroform); R_F 0.56 (hexane/ethyl acetate 3:1 v/v), 0.70 (toluene/acetone 20:1 v/v); ^{1}H NMR ($CDCl_3$) δ 8.2-7.8 (m, 6H, Ph), 7.65-7.20 (m, 15H, Ph), 5.86 (dd, 1H, H-3'), 5.84 (d, 1H, H-2'), 5.57 (s, 1H, H-1'), 4.96 (d, 1H, $J_{1,2}$ = 1.6 Hz, H-1), 4.65 (m, 1H, H-4'), 4.58 (m, 2H, H-5'a,5'b), 4.15 (bt, 1H, $J_{2,3}$ = 2.5 Hz, H-2), 3.92 (dd, 1H, t, 1H, $J_{4,5}$ = 9.3 Hz, H-4), 1.20 (d, 3H, H-6).

Anal. Calcd for $C_{53}H_{50}O_{12}$: C, 72.42; H, 5.73. Found C, 73.11; H, 6.19.

1-*O*-(3-*O*-Allyl-2,5-di-*O*-benzoyl-β-D-ribofuranosyl)-5-*O*-allyl-2,3,4-tri-*O*-benzyl-D-ribitol (3A).[19] Column chromatography (toluene/acetone 90:1 v/v) of the residue afforded 3A as a syrup: ^{1}H NMR ($CDCl_3$) δ 5.43 (d, 1H, $J_{2',3'}$ = 4.3 Hz, H-2'), 5.04 (s, 1H, H-1'). For further NMR data, see Ref 19.

1-*O*-(2,3,5-Tri-*O*-acetyl-β-D-ribofuranosyl)-5-*O*-allyl-2,3,4-tri-*O*-benzyl-D-ribitol (4A=5A).[21] Column chromatography (toluene/acetone 50:1 v/v) of the residue afforded 4A as a syrup: $[\alpha]_D$ -10° (c 1, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.4-7.2 (m, 15H, Ph), 6.0-5.8 (m, 1H, $-CH_2-CH=CH_2$), 5.4-5.2 (m, 2H, $-CH_2-CH=CH_2$), 5.31 (m, 1H, H-3'), 5.23 (m, 1H, H-2'), 4.92 (s, 1H, H-1'), 4.28 (m, 1H, H-4'), 4.27 (m, 1H, H-5b'), 4.08 (m, 1H, H-5a'), 2.10, 2.00 and 1.96 (3s, 9H, 3 CH_3CO).

1-*O*-(2-*O*-Acetyl-3-*O*-allyl-5-*O*-benzyl-β-D-ribofuranosyl)-5-*O*-allyl-2,3,4-tri-*O*-benzyl-D-ribitol (6A).[9] Column chromatography (toluene/ethyl acetate 10:1 v/v) of the residue afforded 6A as a syrup: $[\alpha]_D$ -15.2° (c 1, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.4-7.2 (m, 20H, Ph), 6.0-5.8 (m, 2H,$-CH_2-CH=CH_2$), 5.4-5.2 (m, 4H, $-CH_2-CH=CH_2$), 5.15 (m, 1H, H-2'), 4.96 (s, 1H, H-1'), 4.12 (m, 1H, H-4'), 4.03 (m, 1H, H-3'), 3.55 (dd, 2H, H-5a',5b'), 2.15 (s, 3H, CH_3CO).

Boron trifluoride etherate promoted glycosylation. For details concerning amounts, see Table 1. To a cooled (0°C) and stirred solution of acceptor and donor in dry dichloroethane (23 mL/mmol of donor) was added a solution of boron trifluoride etherate in dichloroethane. After 15 min, TLC (hexane/ethyl acetate) indicated a faster moving spot. The mixture was treated with an excess of solid sodium hydrogencarbonate and, after the addition of diethyl ether and aq 5 % sodium hydrogencarbonate, the organic layer was washed with water, dried and concentrated. The resulting disaccharides were isolated via column chromatography.

Methyl 3-*O*-(2,3,5-Tri-*O*-acetyl-β-D-ribofuranosyl)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (4B). Column chromatography (toluene/acetone 100:1 v/v) of the residue afforded 4B as a syrup: $[\alpha]_D$ +11.0° (c 1, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.4-7.2 (m, 15H, Ph), 5.51 (s, 1H, H-1'), 5.36 (m, 2H, H-2',3'), 4.54 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 4.21 (m, 1H, H-4'), 4.18 (m, 1H, H-5a'), 4.11 (m, 1H, H-3), 4.10 (m, 1H, H-5b'), 3.70 (m, 1H, H-5), 3.68 (m, 1H, H-6a), 3.60 (m, 1H, H-6b), 3.55 (m, 1H, H-4), 3.45 (dd, 1H, $J_{2,3}$ = 10.7 Hz, H-2), 3.26 (s, 3H, OCH_3), 2.10, 2.00 and 1.87 (3s, 9H, 3 CH_3CO).

Anal. Calcd for $C_{39}H_{56}O_{13}$: C, 63.92; H, 7.70. Found C, 64.01; H, 7.78.

Methyl 3-*O*-(2-*O*-Acetyl-3-*O*-allyl-5-*O*-benzyl-β-D-ribofuranosyl)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (6B). Column chromatography (toluene/acetone 100:1 v/v) of the residue afforded 6B contaminated with some B: ^{1}H NMR ($CDCl_3$) δ 7.45-7.15 (m,

20H, Ph), 5.79 (m, 1H, $-CH_2-CH=CH_2$), 5.48 (s, 1H, H-1'), 5.32 (d, 1H, $J_{2',3'}$ = 4.4 Hz, H-2'), 4.54 (d, 1H, $J_{1,2}$ = 3 Hz, H-1), 4.09 (m, 1H, H-3), 4.05 (m, 1H, H-3'), 3.96 (m, 2H, H-5a',5b'), 3.85 (m, 1H, H-4'), 3.72 (m, 1H, H-5), 3.63 (m, 2H, H-6a,6b), 3.56 (m, 1H, H-4), 3.42 (m, 1H, H-2), 3.26 (s, 3H, OCH_3), 2.04 (s, 3H, CH_3CO).

Benzyl 2-*O*-(2-*O*-Acetyl-3-*O*-allyl-5-*O*-benzyl-β-D-ribofuranosyl)-3,4-di-*O*-benzyl-α-L-rhamnopyranoside (6C). Column chromatography (toluene/ethyl acetate 10:1 v/v) of the residue afforded 6C as a syrup: $[\alpha]_D$ -40.3° (c 1, chloroform); ^1H NMR ($CDCl_3$) δ 7.4-7.2 (m, 20H, Ph), 6.0-5.8 (m, 1H, $-CH_2-CH=CH_2$), 5.4-5.2 (m, 2H, $-CH_2-CH=CH_2$), 5.35 (m, 1H, H-2'), 5.32 (s, 1H, H-1'), 4.86 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1), 4.18 (m, 1H, H-2), 4.13 (m, 2H, H-3',4'), 3.87 (m, 1H, H-3), 3.70 (m, 1H, H-5), 3.50 (m, 2H, H-5',4), 2.10 (s, 3H, CH_3CO), 1.35 (d, 3H, H-6).

Anal. Calcd for $C_{44}H_{50}O_{10}$: C, 71.53; H, 6.82. Found C, 72.05; H, 7.22.

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