On the origin of the regioselectivity in glycosylation reactions of 1,2-diols†

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The assistance of neighboring protecting groups with different orientations in 1,2-diol acceptors and the reactivity of both reaction partners, the donor and the acceptor, have been evaluated as factors that determine the regioselectivity of glycosylation reactions. It has been established, by experimental and theoretical studies, that the regioselectivity for the glycosylation of a given OH group can be considerably increased by the presence of groups able to form a hydrogen bond with that OH group. Moreover higher regioselectivities are observed when armed donor/activated acceptor combinations are avoided.

Introduction

Despite the important role of carbohydrates in many biological processes,[1] considerable effort is still required for the preparation of highly complex oligosaccharides. An important advance in this context is the development of strategies that avoid protecting-group manipulations.[2,3] A good understanding of the factors that affect the stereo-[4] and regioselectivity[5,6] of glycosylation reactions would be highly desirable.[7]

Regarding the regiochemical outcome of glycosylation reactions in diol systems very interesting studies addressed at understanding the factors that determine the regiochemistry have been described.[5,6,8] Nevertheless, there are many basic aspects that remain unsolved and prediction of the regiochemistry of the processes is still not possible. The majority of the studies described are due to the group of Fraser-Reid, who invoked the MATCH concept for regioselectivity based on Reciprocal Donor Acceptor Selectivity (RDAS), paying special attention to the role of glycosyl donors and particularly the C2 substituent of mainly pentenyl derivatives, with different kind of acceptors.[5] It is noteworthy, that from these studies no apparent relationship between reactivity and selectivity of the donor has been found.[9] On the other hand, the group of Vasella pointed out the importance of all the possible H bonds in the acceptor, diagnosed by its IR and ^{1}H NMR spectra, when studying the glycosylation reactions of diol acceptors, principally with diazirine glycosyl donors.[6]

During the past decade, we have been working on the synthesis of inositolphosphoglycans as potential mediators in the insulin signaling process.[10,11] In this context, we have studied several factors, such as the influence of the nature of the glycosyl acceptor on reactivity,[12] stereoselectivity,[13] and regioselectivity[8a] in glycosylation reactions. Throughout our studies we have observed an unprecedented dependence of the regiochemistry in glycosylation reactions on the absolute configuration of the acceptor.[8a] Most of the results could be rationalized by DFT calculations, which indicated that stereoelectronic factors, H bonds between the donor and the acceptor and the assistance of the protecting groups adjacent to the OH group to be glycosylated played an important role in the complex prior to the transition state.[8a] Fig. 1 shows in a simple model system how, according to DFT calculations, the OH group to be glycosylated (on C2 in this case) is activated by the adjacent acetyl group increasing its nucleophilicity (compare atomic distances for both OH groups with their corresponding neighboring group).

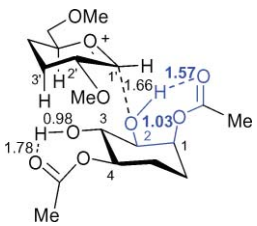

Fig. 1 Model system proposed to explain the regioselectivity observed in the reaction of 2-benzyloxy glycosyl donors with the 1,2-*trans*-diequatorial diol system obtained from a D-*chiro*-inositol partially benzoylated.[8a]

Herein, considering both donor and acceptor partners we describe a deeper assessment of some of the basic factors that can affect the regiochemical outcome of glycosylation reactions. In particular, the assistance of benzyl or benzoyl substituents, showing different orientations within the *trans* (**1**) and *cis* (**2**) 1,2-diol acceptors in their reactions with armed and disarmed trichloroacetimidate donors **3**, has been evaluated along with the effect of the reactivity of both the donor and the acceptor on the regioselectivity of the glycosylation (Fig. 2).[9] For the sake of clarity, acceptors with benzyl and benzoyl substituents will be denoted as **a** and **d** indicating activated or deactivated acceptors respectively. The same reasoning has been followed with armed (**a**) and disarmed (**d**) glycosyl donors.

From the analysis of the obtained results it can be deduced that, if the stereoelectronic effects do not determine the opposite (which it is difficult to predict),[8a] the sense of the regioselectivity

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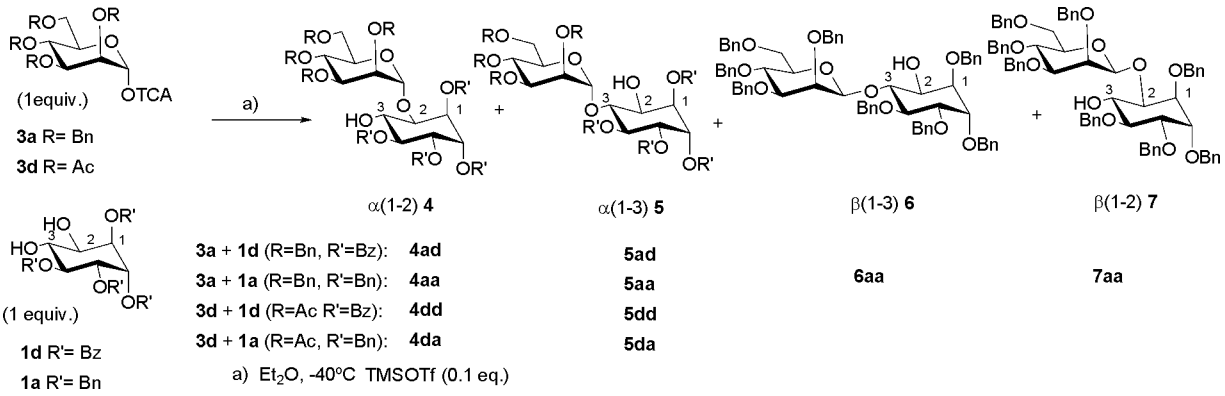
Table 1 Glycosylation reactions of trichloroacetimidates **3** and D-*chiro*-inositol acceptors **1**



		Yield of glycosylation (%)						
Entry	Donor/acceptor	α(1–2) **4**	α(1–3) **5**	β(1–3) **6**	β(1–2) **7**	trisac.	Overall yield	Ratio C_2/C_3[a]
1	**3a** + **1d**	43	17	–	–	–	60	2.5/1
2	**3a** + **1a**	35	14	7	4	16[b]	76	1.5/1
3	**3d** + **1d**	32	9	–	–	–	41	3.8/1
4	**3d** + **1a**	40	6	–	–	–	46	8/1

[a] Selectivities have been calculated on isolated yields after flash chromatography. [b] As a mixture of isomers.

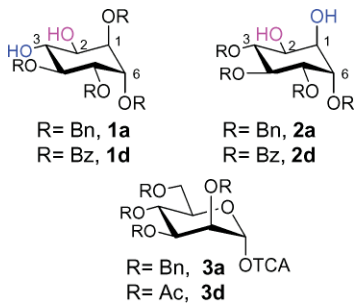


Fig. 2 Diol acceptors *trans* **1** and *cis* **2** and donors **3** used in this study. Activated and armed groups are denoted as **a**, deactivated and disarmed groups as **d**.

seems to be mainly determined by the strength of the hydrogen bonds formed between each OH group with the neighboring protecting group in the acceptor, which can be predicted by a simple theoretical calculation. Additionally, the reactivity of both donor and acceptor determines the degree of the regioselectivity. In order to establish a general rule that allows some prediction of the regiochemical outcome of a given glycosylation reaction, we have corroborated the theory of neighboring group assistance in the transition state by analyzing, not only the results obtained in the cases mentioned above (Fig. 2), but also the regiochemistry obtained in other representative cases described in the literature.

Results and discussion

Regioselectivity of the reactions of D-*chiro*-inositol 1,2-*trans* diol acceptors (1) with donors (3)

In order to assess the significance of the reactivity/selectivity balance in the regiochemical outcome of the reaction,[9] the behavior of acceptors **1a** and **1d**[14] when treated with donors of different reactivities was evaluated. The mannosyl trichloroacetimidates **3a** and **3d**[15]were chosen as armed and disarmed donors to minimize the formation of the β isomers and steric interactions with the equatorial substituent at C2 that may play a decisive role in the regioselectivity of the process.[8a] The results of these reactions under the same experimental conditions are summarized in Table 1.

Both glycosyl acceptors **1a** and **1d** are glycosylated at C2 by both armed and disarmed mannosyl donors **3a** and **3d**. Good overall yields were observed with the armed donor **3a** (entries 1 and 2); however, better regioselectivities were found with the disarmed donor **3d** (entries 3 and 4). The best regioselectivity (C2/C3 = 8:1) was observed when the less reactive donor **3d** was treated with the more reactive acceptor **1a** affording the pseudodisaccharides in a modest combined yield of 46% yield (entry 4). When the reaction was carried out with the most reactive partners **1a** and **3a**, no control of stereoselectivity or regioselectivity was observed, and a mixture of all possible pseudodisaccharides **4**–**7** and pseudotrisaccharides was obtained (entry 2).

The regioselectivity of these acceptors had been previously studied with other glycosyl donors (Fig. 3). Donor **I** reacted with moderate regioselectivity with both acceptors **1a** and **1d** to form preferentially the (1–2) pseudodisaccharides.[11c] The regioselectivity towards this position dramatically increased when the

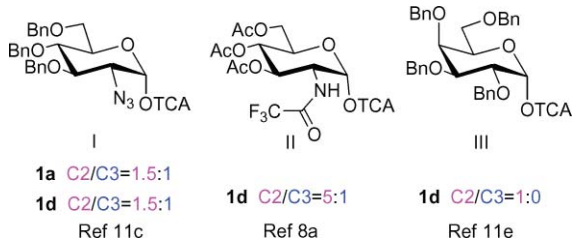


Fig. 3 Regioselectivity observed in the reactions of glycosyl donors **I–III** with diol acceptors *trans* (**1**).

benzoylated acceptor **1d** reacted with donor **II**,[8a] which shows a participating group at C2. Reaction with donor **III**,[11e] used by us in the preparation of fagopyritol (**B1**),[16] afforded the corresponding pseudodisaccharide with complete regioselectivity.

Therefore donors **3**, as well as donors **I–III** of a different nature, react with acceptor **1d** preferentially or exclusively at the C2 position. According to our previous investigations, we postulated that, in the absence of other stereoelectronic effects which are difficult to predict, the O(2)-H bond should be weaker than the O(3)-H one as a consequence of a stronger hydrogen bond between the O(2)-H and the axial C_1-substituent than between the O(3)-H and the equatorial C_4-substituent. These interactions favor glycosylation towards position 2 (Fig. 4).

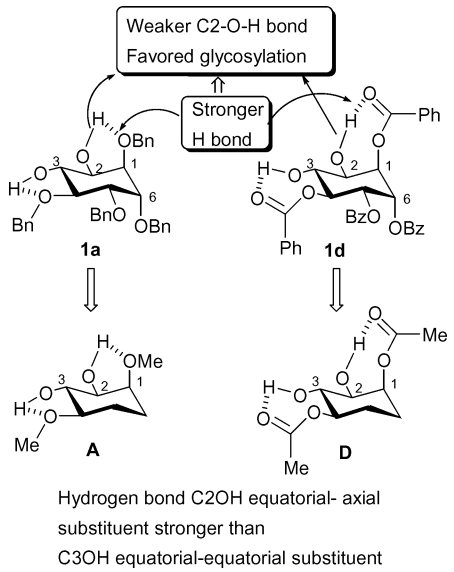


Fig. 4 Structures **A** and **D** will be used as model systems for diol acceptors *trans* **1a** and **1d**.

In order to corroborate this hypothesis, we decided to carry out a theoretical study of these interactions at the DFT (B3LYP)[17] level by using the Gaussian 03 program.[18,19] As model structures for this study the glycosyl acceptors **1a** and **1d** were simplified by locating methyl instead of benzyl (**A**) and acetyl instead of benzoyl (**D**) groups in only positions 1 and 4, adjacent to both hydroxy groups, of the cyclitol ring with axial and equatorial orientation respectively (Fig. 4).

Structures **A** and **D**[20] show both hydroxy groups involved in hydrogen bonds with the adjacent protecting groups (Fig. 5). The effects produced by these bonds are similar in both structures although a bit smaller in the case of the methoxylated model **A**. The small differences in distances and angles reveal that the hydrogen bond between OH(2) and the axial group at position 1 is slightly stronger than the bond between OH(3) and the equatorial group at position 4. NBO analyses[21] show small charge donations from the lone pairs of the carbonylic oxygen along with the π-C=O bond to the O–H antibonding orbital that weakens this bond (slight variations in the Wiberg bond indexes of the O–H bonds are also observed). These data show the same trend: a slightly stronger hydrogen bond between OH(2) and the adjacent axial group and, as a consequence, a weaker O(2)–H bond that favors glycosylation at this position.

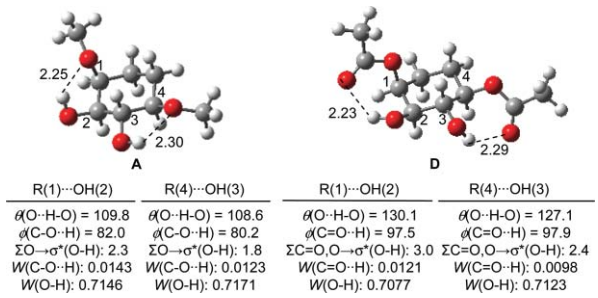
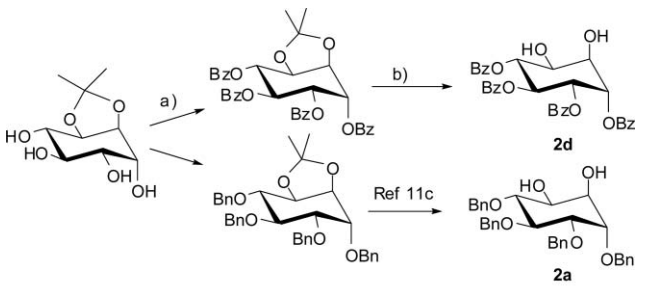


Fig. 5 Representative distances (Å) and angles (°) of the hydrogen bonds found between OH groups and the adjacent protecting groups in the model acceptors. The total amounts (kcal mol^{-1}) of small orbital interactions evaluated by means of a second-order perturbational analysis of the Fock matrix on the NBO basis are also indicated. *W* represents the Wiberg bond indexes between selected atoms.

According to our previous studies[8a] in which complexes prior to TSs were modeled (see Fig. 1), the small differences observed between both hydrogen bonds of the acceptor in the ground state are expected to become greater in the corresponding transition states, when the bond between donor and acceptor is being formed (compare distances C2OH. . ..O=C-C1: 2.23 Å of **D** in Fig. 5 with the corresponding complex shown in Fig. 1 :1.57 Å). Thus, we can conclude that a prediction of the regiochemical outcome of the reaction can be made by a careful analysis of the strength of the hydrogen bonds in which the OHs that can be glycosylated are involved.

Regioselectivity of the reactions of mannosyl donors with D-*chiro*-inositol 1,2-*cis* diol acceptors (2)

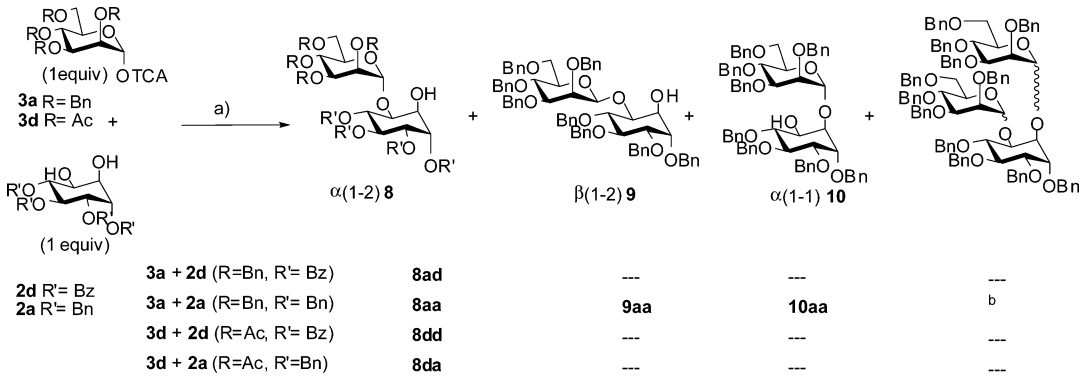
With the aim of analyzing the effect of the same factors on the regioselectivity of the glycosylation of 1,2-*cis* diols, the acceptors **2a** and **2d** were also subjected to treatment with donors **3**. Acceptor **2a** had been previously used by us in the synthesis of the glycosaminyl α(1→2) L-*chiro*-inositol structural motif by regioselective glycosylation with 2-deoxy-2-azidohexosaminyl trichloroacetimidates.[11c] Acceptor **2d** was prepared as shown in Scheme 1 following a synthetic strategy similar to that used in the preparation of **2a** from a monoisopropylidene derivative of D-*chiro*-inositol.



Scheme 1 Synthesis of acceptors **2**.

The reactions of the armed and disarmed mannosyl donors **3** with the 1,2-*cis* diol acceptors **2** were carried out under the experimental conditions used in previous experiments (Table 2).

Table 2 Glycosylation reactions of trichloroacetimidates **3** with D-*chiro*-inositol acceptors **2**



a) Et_2O, -40ºC, TMSOTf (0.1 equiv) 1h. b) Mixture of pseudotrisaccharides (1-1:1-2)

Entry	Donor/acceptor	Yield of glycosylation (%) α(1–2) **8**	β(1–2) **9**	α(1–1) **10**	trisac.	Overall yield.	Ratio C2/C1[a]
1	**3a** + **2d**	61	–	–	–	61	1/0
2	**3a** + **2a**	21	6	10	16[b]	53	2.7/1
3	**3d** + **2d**	28	–	–	–	28	1/0
4	**3d** + **2a**	45	–	–	–	45	1/0

[a] Selectivities have been calculated on isolated yields after flash chromatography. [b] Mixture of pseudotrisaccharides (1–1:1–2).

The disarmed donor **3d** reacted with complete regioselectivity with both **2d** and **2a** to afford the α(1→2) pseudodisaccharides **8dd** and **8da** in 28 and 45% yield, respectively. Complete regioselectivity for the α(1→2) product was also observed in the reaction of the armed glycosyl donor **3a** with the less reactive acceptor **2d**: the pseudodisaccharide **8ad** was obtained in 61% yield. However, the reaction of the armed donor **3a** with the activated acceptor **2a** afforded a 21:6:10:16 mixture of the α(1→2), β(1→2), and α(1→1) pseudodisaccharides **8–10** along with a mixture of pseudotrisaccharides in 53% combined yield. This considerable decrease in the regio- and stereoselectivity clearly evidenced that with donor/acceptor pairs in which both reaction partners are reactive, low regioselectivities and the formation of pseudotrisaccharides can be expected.

Apart from the reasonable influence of reactivity on regioselectivity,[9] a number of interesting features were observed in the examples analyzed, such as the high regioselectivity for glycosylation at the equatorial hydroxy group in the two 1,2-*cis* diols **2a** and **2d**. The reactions of these acceptors had also been carried out with other 2-azido-2-deoxy-D-glucopyranosyl trichloroacetimidates to mainly afford the (1–2) disaccharides.[11c]

The low tendency shown by these acceptors to undergo glycosylation at the axial hydroxy group, that contrasts with other examples described in the literature (see below), can also be explained on the basis of the results of the DFT calculations (Fig. 5) carried out to gain an understanding of the regiochemical outcome of the reactions of 1,2-*trans* diol acceptors **1** collected in Table 1. According to these calculations, a hydrogen bond from a vicinal substituent can assist glycosylation at a given position. Both acyloxy and alkoxy substituents can have such an effect, although the latter to a lesser extent. Thus, because of the presence of the acyloxy substituent at the 3-position, the hydroxy group at C2 in compound **2d** will be more activated toward glycosylation than the hydroxy group at C1, which cannot be assisted by the axial substituent at C6 (Fig. 2). As a consequence, even the reaction with the armed donor **3a** proceeds with complete regioselectivity (entry 1, Table 2). Nevertheless, the regioselectivity dramatically decreases in the reaction of the armed donor **3a** with the more reactive acceptor **2a** (entry 2, Table 2) due probably to the higher reactivity of both donor and acceptor and the less efficient assistance of the alkoxy group at C3 compared with the acyloxy group present in **2d**.

Regioselectivity with other *cis* and *trans* diols

Our hypothesis of neighboring group assistance is supported by most of the examples described in the literature, which show the same tendency even with several glycosyl donors (for more details of each case see the ESI†). Such is the case of mannose acceptors **IV**α and **IV**β[6] (Fig. 6). It can be seen that in **IV**β the axial and equatorial hydroxyl groups are glycosylated with benzylated α-glucopyranosyl trichloroacetimidate in similar ratios (a/e = 46:54), whereas the axial hydroxy group in **IV**α, unable to form hydrogen bonds with neighbouring protecting groups, remains almost unreactive (a/e = 12:88). It is remarkable that although Vasella pointed out the importance of hydrogen bonds in the regioselectivity of glycosylation reactions, the different regioselectivity obtained for **IV**α and **IV**β is attributed to possible

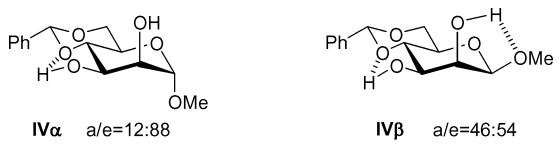


Fig. 6 Regioselectivity observed for diol acceptors **IV**α and **IV**β.

stereoelectronic factors and not to neighboring group activation through hydrogen bonds. It is also important to note that in acceptors **IV** an additional hydrogen bond with the oxygen in the ring is possible producing an activation of the hydroxyl group in the axial position, decreasing the regioselectivity that could be expected.

The glycosylations of other 1,2-*cis* diol acceptors described in the literature are represented in Fig. 7 and Fig. 8. Although the axial hydroxy group in the allose acceptor **V** would be expected to be less reactive than the equatorial one due to steric factors, it undergoes glycosylation preferentially.[6] However it must be taken into account that this axial hydroxy group could also form hydrogen bonds with the neighboring groups located at position 4 as well as with the methoxy group at position 1. This latter bond is the strongest one in **V**α, as revealed a simple theoretical calculation.[22]

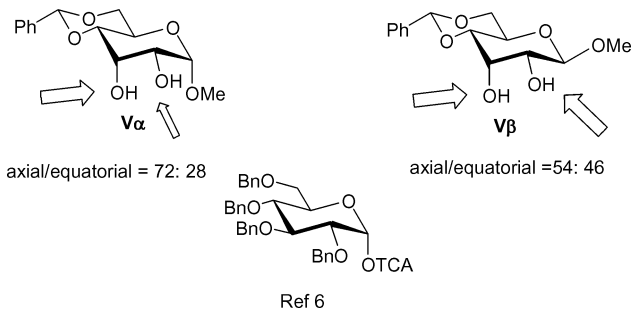


Fig. 7 Regioselectivity observed for diol acceptors **V**α and **V**β. The arrows indicate the hydroxy groups that undergo glycosylation preferentially, probably due to hydrogen bond activation.

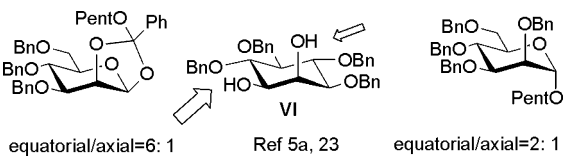


Fig. 8 Regioselectivity observed for 1,2-cis diol acceptor **VI**.

The ratio of glycosylation at the equatorial or axial position in inositol **VI** depends on the glycosyl donor (RDAS),[5a,23] the regioselectivity being higher with a disarmed donor.[9] The equatorial OH group is preferred for the glycosylation, probably due to steric hindrance, as was pointed out by the authors, as well as to a stronger hydrogen bond with the adjacent benzyl group, again in agreement with our theoretical calculations.[23]

In the case of 1,2-*trans*-diequatorial diols most of the examples described in the literature afforded low regioselectivities.[6,24] However, the reasoning of neighboring group assistance could also explain some results observed with diaxial diols, such as altrose[25] and iduronic and glucuronic derivatives[26] that glycosylate preferentially at the OH indicated in each case (Fig. 9).[27]

Conclusions

The experiments described herein show clearly the importance of an adequate reactivity balance between the donor and the acceptor for glycosylation reactions to proceed in good yield with good regio- and stereoselectivity. Although it is difficult to predict

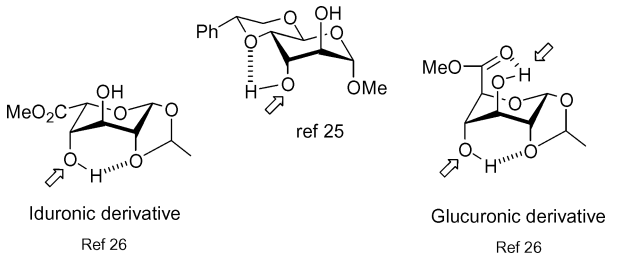


Fig. 9 Regioselectivity observed for some diol acceptors. The arrows indicate the hydroxy groups that undergo glycosylation preferentially, probably due to hydrogen bond activation.

the best donor/acceptor pair for a given glycosylation reaction, our results indicate that it is reasonable to avoid reactions with activated acceptors and armed donors, as such combinations tend to lead to lower regioselectivities and the formation of undesirable pseudotrisaccharides. We also confirmed that glycosylation at a particular position can be favored by the presence of substituents able to form a hydrogen bond with the hydroxy group at that position. A careful analysis of the strength of the hydrogen bonds of the OHs that can be glycosylated with the neighboring groups through a simple computationally inexpensive calculation could be used to predict the regiochemical outcome of glycosylation reactions of a given 1,2-diol system.

Experimental

General

Diethyl ether and dichloromethane were distilled from sodium benzophenone and calcium hydride, respectively. Molecular sieves (4Å, powdered) were dried in an oven at 100 °C and activated for 5 min under vacuum at 500 °C. All reactions were carried out under an atmosphere of dry argon with oven-dried glassware and freshly distilled and dried solvents, unless otherwise stated. TLC was performed on silica gel GF_{254}. Silica gel (230–400 mesh) was used for flash chromatography, and eluents are given as volume to volume ratios (v/v). All aqueous solutions were saturated unless otherwise stated. ^{1}H (300, 400 and 500 MHz) and ^{13}C NMR (125 and 75 MHz) spectra were recorded at 25 °C in $CDCl_3$ unless otherwise noted; chemical shifts are given in ppm relative to $CDCl_3$ (7.27 ppm), and coupling constants are reported in Hz. Resonances were assigned by means of 2D spectra (COSY, HMQC).

General method of glycosylation

A mixture of the donor and the acceptor was co-evaporated 3 times with toluene, 4-Å molecular sieves were added, and the residue was dried under vacuum overnight. The mixture was dissolved in ether under an argon atmosphere and stirred at room temperature for 30 min, then TMSOTf (0.1 M solution; 0.08 equiv.) was added at –40 °C, and the reaction mixture was stirred for 1 h at –40 °C. The reaction was then quenched with Et_3N, and the mixture was concentrated and purified by flash chromatography.

Competitive experiment of acceptors (1d) and (1a) with 3,4,6-tri-*O*-benzyl-2-azido-2-deoxy-α-D-glucopyranosyl-trichloroacetimidate. A mixture of 3,4,6-tri-*O*-benzyl-2-azido-2-deoxy-α-D-glucopyranosyl-trichloroacetimidate (87 mg, 0.14 mmol),

1,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol **1d** (83 mg, 0.14 mmol) and 1,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol **1a** (76 mg, 0.14 mmol) was co-evaporated 3 times with toluene, 4-Å molecular sieves were added and the residue was dried under vacuum. The mixture was disolved in ether (3 mL) in an argon atmosphere and stirred at room temperature for 30 min, then 0.08 equiv. (112 µl of a solution 0.1 M) of TMSOTf was added at –40 °C and the reaction mixture stirring for 1 h at –40 °C. Then it was quenched with Et_3N, concentrated and purified by flash chromatography (Hexane/EtOAc 4:1 to 1:1), to give 37 mg (26%) of a mixture (2:1) of 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranosyl-α(1→2)-1,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol and 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranosyl-α(1→3)-1,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol, 17 mg (12%) of 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranosyl-β(1→2)-1,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol, 16 mg (11%) of 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranosyl-β(1→3)-1,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol, 14 mg (9%) of a mixture (5:1) of 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranosyl-α(1→2)-1,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol and 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranosyl-α(1→3)-1,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol, 3 mg (2%) 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranosyl-β(1→2)-1,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol, 68 mg (81%) of the unreactive acceptor **1d** and 37.8 mg (50%) of the unreactive acceptor **1a**. Data of 2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-D-glucopyranosyl-β(1→2)-1,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol: $[\alpha]_D^{20}$ +20.6 (c = 0.15, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.17–7.76 (4 Hortho, 8H); 7.60–7.10 (m, 15H, 3Bn and 12H, 4Bz); 6.00–5.95 (m, 2H, H_4 and H_6); 5.85 (bt, 1H, *J* = 3.7 Hz, H_1); 5.77 (dd, 1H, *J* = 10.4 and 3.3 Hz, H_5); 4.80–4.32 (3 AB syst, 6H); 5.22 (d, 1H, *J* = 8.1 Hz, $H_{1'}$); 4.54 (ddd, 1H, *J* = 12.8, 9.7 and 3.1 Hz, H_3); 4.36 (dd, 1H, *J* = 9.7 and 3.7 Hz, H_2); 3.64 (dd, 1H, *J* = 11.0 and 4.0 Hz, $H_{6'a}$); 3.60 (m, 1H, $H_{5'}$); 3.55 (dd, 1H, *J* = 11.0 and 1.8 Hz, $H_{6'b}$); 3.41–3.37 (m, 3H, $H_{3'}$, $H_{4'}$ and $H_{2'}$) and 3.20 (d, 1H, *J* = 3.3 Hz, C_3OH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.6, 165.7, 165.2 and 164.9 (4CO), 138.4, 138.1 and 138.1 (3C, Bn), 134.0, 133.8, 133.7 and 133.5 (4CH para), 130.4–127.8 (15CH, Bn and 16CH, Bz), 129.7, 129.6, 129.4 and 129.2 (4C, Bz), 103.3 ($C_{1'}$), 83.3 (CH), 79.0 (CH), 77.8 (CH), 77.7 (CH_2), 75.7 (CH), 75.3 (CH_2), 73.7 (CH_2), 72.3 (CH), 72.2 (CH), 70.8 (CH), 70.1 (CH), 68.9 (CH), 68.5 (CH_2) and 66.5 (CH). FAB HRMS calcd. for $C_{61}H_{55}O_{14}N_3$+Na^+: 1076.3581, found: 1076.3613. Data of the other pseudodisaccharides have been previously described in ref 11c.

2,3,4,6-Tetra-*O*-benzyl-D-manopyranosyl-α(1→2)-1,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol (4ad) and 2,3,4,6-tetra-*O*-benzyl-D-manopyranosyl-α(1→3)-1,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol (5ad). These pseudodisaccharides were prepared from 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-trichloroacetimidate **3a** (62 mg, 0.09 mmol) and 1,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol (**1d**) (53 mg, 0.09 mmol) as described in the general method, adding 0.08 equiv. (72 µl of a solution 0.1 M) of TMSOTf at –40 °C, in dry ether (2 ml) and stirring the reaction mixture for 1 h at –40 °C, yielding after flash chromatography (Hexane/EtOAc 6:1 to 4:1), 32 mg of the pseudodisaccharide **4ad** (32%) and 30 mg of a mixture (1:1.5) of the pseudodisaccharides **4ad** and **5ad** (28%). Data of the α(1→2) pseudodisaccharide **4ad**: $[\alpha]_D^{20}$ +71.1 (c = 1.3, $CHCl_3$). ^{1}H NMR (500 MHz, C_6D_6): δ = 8.27–7.40 (4 H ortho, 8H); 7.30–6.77 (m, 20H, 4Bn and 12H, 4Bz); 6.64 (t, 1H, *J* = 10.4 Hz, H_4); 6.46 (dd, 1H, *J* = 10.5 and 3.7 Hz, H_5); 6.42 (bt, 1H, *J* = 3.7 Hz, H_6); 6.21 (bt, 1H, *J* = 3.7 Hz, H_1); 5.50 (s, 1H, $H_{1'}$); 4.97–4.30 (4 AB syst, 8H); 4.73 (dd, 1H, *J* = 9.4 and 3.6 Hz, H_2); 4.56 (m, 1H, H_3); 4.48 (m, 1H, $H_{5'}$); 4.23 (t, 1H, *J* = 9.4 Hz, $H_{4'}$); 4.04 (bs, 1H, $H_{2'}$); 4.02 (dd, 1H, *J* = 9.4 and 3.0 Hz, $H_{3'}$); 3.82 (m, 2H, $2H_{6'}$) and 3.40 (s, 1H, C_3OH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.5, 165.9, 165.3 and 165.1 (4CO), 138.7, 138.6, 138.6 and 138.2 (4C, Bn), 134.1, 134.0, 133.6 and 133.5 (4CH para), 130.3–127.7 (16CH, Bz and 20CH, Bn), 129.8, 129.4, 129.2 and 129.1 (4C, Bz), 97.8 ($C_{1'\alpha}$, $J_{C1'\text{-}H1'}$ = 171.7 Hz), 79.7 (CH), 77.6 (CH), 75.0 (CH_2), 74.9 (CH), 74.8 (CH), 73.7 (CH_2), 72.9 (CH_2), 72.7 (CH), 72.5 (CH), 72.0 (CH_2), 71.6 (CH), 70.3 (CH), 69.6 (CH_2), 69.2 (CH) and 68.2 (CH). HSQC (500 MHz, $CDCl_3$): $J_{C1'\text{-}H1'}$: 171.7 Hz. Elemental analysis calcd. for $C_{68}H_{62}O_{15}$: 72.97% C and 5.58% H; found: 72.79% C and 5.89% H. Data of the acetylated α(1→2) pseudodisaccharide **4ad**: ^{1}H NMR (500 MHz, C_6D_6): δ = 6.53 (t, 1H, *J* = 10.0 Hz, H_3). Data of the α(1→3) pseudodisaccharide **5ad**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.15–8.00 (4 Hortho, 8H); 7.75–7.00 (m, 20H, 4Bn and 12H, 4Bz); 5.99 (m, 1H, H_4); 5.94 (t, 1H, *J* = 3.7 Hz, H_6); 5.80 (dd, 1H, *J* = 10.6 and 3.6 Hz, H_5); 5.77 (t, 1H, *J* = 3.7 Hz, H_1); 5.04 (d, 1H, *J* = 2.3 Hz, $H_{1'}$); 4.75–4.00 (4 AB syst, 8H); 4.29 (m, 1H, H_2); 4.20 (m, 1H, $H_{5'}$); 4.17 (t, 1H, *J* = 9.9 Hz, H_3); 3.88 (dd, 1H, *J* = 8.9 and 2.5 Hz, $H_{3'}$); 3.74 (t, 1H, *J* = 9.0 Hz, $H_{4'}$); 3.57 (m, 2H, $2H_{6'}$); 3.54 (t, 1H, *J* = 2.3 Hz, $H_{2'}$) and 3.44 (s, 1H, C_2OH). ^{13}C NMR (125 MHz, C_6D_6): δ = 166.4, 166.3, 165.7 and 165.3 (4CO), 139.7, 139.5, 139.3 and 138.8 (4C, Bn), 134.2, 133.9, 133.8 and 133.6 (4CH para), 130.7–128.0 (16CH, Bz and 20CH, Bn), 129.7, 129.5, 129.5 and 129.2 (4C, Bz), 101.5 ($C_{1'\alpha}$, $J_{C1'\text{-}H1'}$ = 170.3 Hz.), 82.2 (CH), 80.4 (CH), 76.8 (CH), 76.6 (CH), 74.6 (CH_2), 73.3 (CH_2), 73.2 (CH), 72.7 (CH_2), 72.2 (CH), 71.5 (CH_2), 71.1 (CH), 70.6 (CH), 70.4 (CH), 69.7 (CH_2) and 69.0 (CH). Elemental analysis calcd. for $C_{68}H_{62}O_{15}$: 72.97% C and 5.58% H; found: 73.03% C and 5.69% H.

2,3,4,6-Tetra-*O*-benzyl-D-manopyranosyl-α(1→2)-1,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol (4aa), 2,3,4,6-tetra-*O*-benzyl-D-manopyranosyl-α(1→3)-1,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol (5aa) 2,3,4,6-tetra-*O*-benzyl-D-manopyranosyl-β(1→2)-1,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol (6aa) and 2,3,4,6-tetra-*O*-benzyl-D-manopyranosyl-β(1→3)-1,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol (7aa). These pseudodisaccharides were prepared from 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl-trichloroacetimidate **3a** (42 mg, 0.061 mmol) and 1,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol **1a** (33 mg, 0.061 mmol) as described in the general method, adding 0.08 equiv. (49 µl of a solution 0.1 M) of TMSOTf at –40 °C to rt, in dry ether (1.7 ml) and stirring the reaction mixture for 1 h at –40 °C, yielding after flash chromatography (Hexane/EtOAc 6:1 to 4:1), 23 mg of the pseudodisaccharide **4aa** (35%), 9 mg of the pseudodisaccharide **5aa** (14%), 5 mg of the pseudodisaccharide **6aa** (8%) and 3 mg of the pseudodisaccharide **7aa** (4%). Data of the α(1→2) pseudodisaccharide **4aa**: $[\alpha]_D^{20}$ +15.0 (c = 0.9, $CHCl_3$). ^{1}H NMR (500 MHz, C_6D_6): δ = 7.50–7.15 (m, 40H, 8Bn); 5.24 (s, 1H, $H_{1'}$); 5.11–4.42 (8 AB syst, 16H); 4.60 (m, 1H, $H_{5'}$); 4.40 (m, 1H, $H_{4'}$); 4.39 (m, 1H, H_3); 4.29–420 (m, 3H, $H_{3'}$, H_2 and H_4); 4.10 (dd, 1H, *J* = 9.6 and 2.6 Hz, H_5); 3.94–3.81 (m, 6H, $H_{2'}$, H_1, H_6 and $2H_{6'}$) and 3.38 (bs, 1H, C_3OH).

^{13}C NMR (125 MHz, C_6D_6): δ = 140.7, 140.1, 140.1, 139.9, 139.8, 139.8, 139.7 and 138.5 (8C, Bn), 129.3–128.0 (40CH, Bn), 98.3 ($C_{1'\alpha}$, $J_{C1'\text{-}H1'}$ = 170.3 Hz), 83.1 (CH), 81.2 (CH), 80.5 (CH), 79.7 (CH), 77.0 (CH), 77.0 (CH), 76.6 (CH), 76.5 (CH), 76.4 (CH_2), 75.6 (CH_2), 74.6 (CH_2), 74.5 (CH_2), 74.4 (CH), 74.2 (CH_2), 74.1 (CH_2), 73.7 (CH_2), 73.6 (CH), 73.1 (CH_2) and 70.5 (CH_2). Elemental analysis calcd. for $C_{68}H_{70}O_{11}$: 76.81% C and 6.63% H; found: 77.25% C and 6.82% H. Data of the acetylated α(1→2) pseudodisaccharide **4aa**: ^{1}H NMR (500 MHz, C_6D_6): δ = 6.13 (t, 1H, *J* = 9.5 Hz, H_3). Data of the α(1→3) pseudodisaccharide **5aa**: $[\alpha]_D^{20}$ −4.0 (c = 0.45, $CHCl_3$). ^{1}H NMR (500 MHz, C_6D_6): δ = 7.40–7.10 (m, 40H, 8Bn); 5.54 (s, 1H, $H_{1'}$); 5.14–4.43 (8 AB syst, 16H); 4.75 (m, 1H, $H_{5'}$); 4.46 (m, 1H, H_2); 4.32 (t, 1H, *J*= 9.1 Hz, H_3); 4.22 (t, 1H, *J*= 9.2 Hz, H_4); 4.21 (s, 1H, $H_{3'}$); 4.16 (t, 1H, *J*= 9.5 Hz, $H_{4'}$); 4.12 (dd, 1H, *J*= 9.3 and 2.9 Hz, H_5); 4.06 (t, 1H, *J*= 3.4 Hz, H_1); 4.00 (s, 1H, $H_{2'}$); 3.90 (d, 1H, *J*= 9.3 Hz, $H_{6'a}$); 3.86 (t, 1H, *J* = 3.4 Hz, H_6) and 3.77 (dd, 1H, *J* = 10.1 and 7.5 Hz, $H_{6'b}$). ^{13}C NMR (125 MHz, C_6D_6): δ = 140.6, 140.0, 139.9, 139.9, 139.8, 139.8, 139.7 and 138.5 (8C, Bn), 129.2–127.6 (40CH, Bn), 101.5 ($C_{1'\alpha}$, $J_{C1'\text{-}H1'}$= 170.0 Hz), 86.1 (CH), 82.3 (CH), 81.4 (CH), 80.8 (CH), 78.8 (CH), 77.4 (CH), 76.4 (CH), 76.1 (CH), 75.6 (CH_2), 75.0 (CH_2), 74.1 (CH_2), 74.0 (CH_2), 73.8 (CH), 73.8 (CH_2), 73.8 (CH_2), 73.5 (CH_2), 72.7 (CH_2), 72.4 (CH) and 70.9 (CH_2). Elemental analysis calcd. for $C_{68}H_{70}O_{11}$: 76.81% C and 6.63% H; found: 76.55% C and 6.87% H. Data of the β(1→3) pseudodisaccharide **6aa**: $[\alpha]_D^{20}$ −30.0 (c = 0.2, $CHCl_3$). ^{1}H NMR (500 MHz, C_6D_6): δ = 7.65–7.10 (m, 40H, 8Bn); 5.44–4.32 (8 AB syst, 16H); 5.11 (s, 1H, $H_{1'}$); 4.55–4.45 (m, 2H, H_3 and H_2); 4.33 (t, 1H, *J*= 9.5 Hz, H_4); 4.20 (t, 1H, *J*= 9.1 Hz, $H_{4'}$); 4.14 (dd, 1H, *J*= 2.9 Hz, $H_{2'}$); 4.04 (dd, 1H, *J*= 9.6 and 2.7 Hz, H_5); 3.91–3.85 (m, 3H, H_1, H_6 and $H_{6'a}$); 3.79 (dd, 1H, *J*= 11.0 and 5.7 Hz, $H_{6'b}$); 3.60 (m, 1H, $H_{5'}$); 3.51 (dd, 1H, *J*= 9.0 and 2.9 Hz, $H_{3'}$) and 2.98 (bs, 1H, O*H*). ^{13}C NMR (125 MHz, C_6D_6): δ = 141.0, 140.3, 140.2, 140.1, 140.1, 139.7, 139.6 and 139.2 (8C, Bn), 129.4–128.3 (40CH, Bn), 101.8 ($C_{1'\beta}$, $J_{C1'\text{-}H1'}$= 153.6 Hz), 83.6 (CH), 82.8 (CH), 81.0 (CH), 80.5 (CH), 79.2 (CH), 77.2 (CH), 76.5 (CH), 76.3 (CH_2), 75.8 (CH), 75.7 (CH), 75.4 (CH_2), 75.2 (CH_2), 74.3 (CH_2), 74.3 (CH_2), 74.2 (CH_2), 74.2 (CH_2), 72.9 (CH), 72.2 (CH_2) and 70.8 (CH_2). Elemental analysis calcd. for $C_{68}H_{70}O_{11}$: 76.81% C and 6.63% H; found: 76.90% C and 6.77% H. Data of the acetylated β(1→3) pseudodisaccharide **6aa** ^{1}H NMR (500 MHz, C_6D_6): δ = 5.79 (dd, 1H, *J*= 10.1 and 3.4 Hz, H_2). Data of the β(1→2) pseudodisaccharide **7aa**: $[\alpha]_D^{20}$ −38.0 (c = 0.15, $CHCl_3$).^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38–7.12 (m, 40H, 8Bn); 4.98–4.39 (8 AB syst, 16H); 4.65 (s, 1H, $H_{1'}$); 4.11 (t, 1H, *J*= 3.6 Hz, H_1); 3.98 (d, 1H, *J*= 2.9 Hz, $H_{2'}$); 3.95 (t, 1H, *J*= 9.5 Hz, H_3); 3.91 (t, 1H, *J*= 9.6 Hz, $H_{4'}$); 3.89 (dd, 1H, *J*= 9.6 and 3.3 Hz, H_2); 3.81 (dd, 1H, *J*= 9.7 and 3.5 Hz, H_5); 3.76 (m, 2H, $H_{6'a}$ and H_4); 3.68 (dd, 1H, *J*= 10.7 and 1.5 Hz, $H_{6'b}$); 3.62 (t, 1H, *J*= 3.6 Hz, H_6); 3.49 (dd, 1H, *J*= 9.5 and 2.9 Hz, $H_{3'}$); 3.43 (m, 1H, $H_{5'}$) and 2.40 (bs, 1H, C_3OH). ^{13}C NMR (125 MHz, C_6D_6): δ = 140.4, 140.3, 140.2, 140.1, 139.8, 139.8, 139.7 and 138.6 (8C, Bn), 129.3–128.2 (40CH, Bn), 104.4 ($C_{1'\beta}$, $J_{C1'\text{-}H1'}$= 161.6 Hz), 83.6 (CH), 82.8 (CH), 82.1 (CH), 80.7 (CH), 78.2 (CH), 78.1 (CH), 76.7 (CH), 76.5 (CH), 76.1 (CH_2), 75.9 (CH), 75.7 (CH_2), 75.3 (CH_2), 74.7 (CH_2), 74.3 (CH_2), 74.1 (CH), 73.6 (CH_2), 73.5 (CH_2), 72.2 (CH_2) and 70.8 (CH_2).Elemental analysis calcd. for $C_{68}H_{70}O_{11}$: 76.81% C and 6.63% H; found: 77.02% C and 6.86% H.

2,3,4,6-Tetra-*O*-acetyl-D-manopyranosyl-α(1→2)-1,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol (4dd), 2,3,4,6-tetra-*O*-acetyl-D-manopyranosyl-α(1→3)-1,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol (5dd). These pseudodisaccharides were prepared from 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-trichloroacetimidate **3d** (61 mg, 0.124 mmol) and 1,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol **1d** (74 mg, 0.124 mmol) as described in the general method, adding 0.08 equiv. (99 μl of a solution 0.1 M) of TMSOTf at −40 °C, in dry ether (2 ml) and stirring the reaction mixture for 1 h at −40 °C, yielding after flash chromatography (Hexane/EtOAc 1:1), 37 mg of the pseudodisaccharide **4dd** (32%) and 10 mg of the pseudodisaccharide **5dd** (9%). Data of the α(1→2) pseudodisaccharide **4dd**: $[\alpha]_D^{20}$ +81.7 (c = 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, C_6D_6): δ = 8.37–8.05 (4 H ortho, 8H); 7.20–6.80 (m, 12H, 4Bz); 6.43 (t, 1H, *J*= 9.9 Hz, H_4); 6.35–6.31 (m, 2H, H_6 and H_5); 5.99 (bt, 1H, *J*= 3.3 Hz, H_1); 5.80–5.69 (m, 1H, $H_{2'}$, $H_{3'}$ and $H_{4'}$); 5.45 (s, 1H, $H_{1'}$); 4.74 (m, 1H, $H_{5'}$); 4.66 (dd, 1H, *J*= 9.7 and 3.3 Hz, H_2); 4.55 (dd, 1H, *J* = 12.1 and 2.0 Hz, $H_{6'a}$); 4.37 (dd, 1H, *J* = 12.1 and 6.4 Hz, $H_{6'b}$); 4.14 (m, 1H, H_3); 2.60 (s, 1H, C_3OH); 2.00, 1.77, 1.75 and 1.73 (4 s, 12H, 4CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.8, 169.9, 169.8 and 169.7 (4O*C*OCH_3), 166.4, 166.1, 165.6 and 165.1 (4CO), 133.9, 133.8, 133.6 and 133.5 (4CH para), 130.6–128.1 (16CH, Bz), 130.4, 130.1, 129.9 and 129.8 (4C, Bz), 96.6 ($C_{1'}$), 75.6, 73.4, 71.5, 71.1, 70.7, 70.1, 69.8, 69.6, 67.4, 67.2 and 63.1 (10CH and 1CH_2), 20.9, 20.6, 20.6 and 20.5 (4CH_3). FAB HRMS calcd. for $C_{48}H_{46}O_{19}$+Na: 949.2531, found: 949.2517. Data of the α(1→3) pseudodisaccharide **5dd**: $[\alpha]_D^{20}$ +68.2 (c = 0.5, $CHCl_3$).^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.17–7.75 (4 H ortho, 8H); 7.65–7.20 (m, 12H, 4Bz); 6.09 (t, 1H, *J*= 10.1 Hz, H_4); 5.92 (t, 1H, *J*= 3.8 Hz, H_6); 5.81–5.77 (m, 1H, H_1 and H_5); 5.34 (dd, 1H, *J*= 9.6 and 3.3 Hz, $H_{3'}$); 5.10 (t, 1H, *J*= 9.6 Hz, $H_{4'}$); 5.05 (d, 1H, *J*= 1.8 Hz, $H_{1'}$); 5.00 (m, 1H, $H_{2'}$); 4.46 (m, 1H, $H_{5'}$); 4.41 (m, 1H, H_2); 4.30 (t, 1H, *J*= 9.7 Hz, H_3); 4.15 (dd, 1H, *J*= 12.1 and 6.4 Hz, $H_{6'a}$); 4.04 (dd, 1H, *J*= 12.3 and 2.4 Hz, $H_{6'b}$), 2.90 (s, 1H, C_2OH); 2.00, 1.90, 1.80 and 1.75 (4 s, 12H, 4OCH_3).^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.9, 170.1, 169.9 and 169.3 (4O*C*OCH_3), 165.9, 165.8, 165.5 and 165.1 (4CO), 134.3, 134.2, 133.7 and 133.6 (4CH para), 130.4–128.7 (16CH, Bz), 130.4, 130.2, 130.0 and 129.1 (4C, Bz), 99.5 ($C_{1'}$), 80.3, 71.9, 71.2, 70.3, 69.9, 69.6, 69.5, 68.8, 68.8, 66.7 and 63.0 (10CH and 1CH_2), 21.0, 20.8, 20.8 and 20.7 (4CH_3). FAB HRMS calcd. for $C_{48}H_{46}O_{19}$+Na: 949.2531, found: 949.2526.

2,3,4,6-Tetra-*O*-acetyl-D-manopyranosyl-α(1→2)-1,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol (4da), 2,3,4,6-tetra-*O*-acetyl-D-manopyranosyl-α(1→3)-1,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol (5da). These pseudodisaccharides were prepared from 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl-trichloroacetimidate **3d** (28 mg, 0.057 mmol) and 1,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol **1a** (31 mg, 0.057 mmol) as described in the general method, adding 0.08 equiv. (45 μl of a solution 0.1 M) of TMSOTf at −40 °C in dry ether (2 ml) and stirring the reaction mixture for 1 h at −40 °C, yielding after flash chromatography (Hexane/EtOAc 2:1), 20 mg of the pseudodisaccharide **4da** (40%) and 3 mg of the pseudodisaccharide **5da** (6%). Data of the α(1→2) pseudodisaccharide **4da**: $[\alpha]_D^{20}$ +11.3 (c = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.13 (m, 20H, 4Bn); 5.37 (dd, 1H, *J* = 10.2 and 3.5 Hz, $H_{3'}$); 5.24 (t, 1H, *J* = 10.3 Hz, $H_{4'}$); 5.18 (m, 1H, $H_{2'}$); 4.97–4.35 (4 AB syst, 8H); 4.74 (s, 1H, $H_{1'}$); 4.40

(m, 1H, $H_{5'}$); 4.20 (dd, 1H, J= 12.3 and 5.8 Hz, $H_{6'a}$); 4.10 (dd, 1H, J= 12.1 and 2.2 Hz, $H_{6'b}$); 3.92 (t, 1H, J= 9.5 Hz, H_3); 3.86 (dd, 1H, J= 9.6 and 2.7 Hz, H_2); 3.82 (dd, 1H, J= 9.6 and 2.4 Hz, H_5); 3.73 (t, 1H, J= 9.5 Hz, H_4); 3.67 (m, 2H, H_6 and H_1); 2.75 (s, 1H, C_3OH); 2.15, 2.02, 2.00 and 1.97 (4 s, 12H, $4CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.0, 170.4, 170.2 and 170.2 ($4OCOCH_3$), 139.3, 138.8, 138.5 and 138.3 (4C, Bn), 128.7–127.9 (20CH, Bn), 96.2 ($C_{1'}$), 82.1 (CH), 79.6 (CH), 78.6 (CH), 75.9 (CH_2), 75.2 (CH), 74.4 (CH), 73.9 (CH_2), 73.7 (CH_2), 73.5 (CH_2), 72.6 (CH), 70.3 (CH), 69.4 (CH), 69.0 (CH), 66.4 (CH) and 62.8 (CH_2), 21.3, 21.1, 21.0 and 21.0 ($4CH_3$).Elemental analysis calcd. for $C_{48}H_{54}O_{15}$: 66.19% C and 6.24% H; found: 66.23% C and 6.39% H. Data of the α(1→3) pseudodisaccharide **5da**: $[\alpha]_D^{20}$ + 10.0 (c = 0.3, $CHCl_3$).^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40–7.20 (m, 20H, 4Bn); 5.36–5.32 (m, 2H, $H_{3'}$ and $H_{2'}$); 5.20–5.15 (m, 1H, $H_{1'}$ and $H_{4'}$); 4.96–4.25 (4 AB syst, 8H); 4.57 (m, 1H, $H_{5'}$); 4.20 (dd, 1H, J= 12.1 and 6.0 Hz, $H_{6'a}$); 4.00 (dd, 1H, J= 12.1 and 2.4 Hz, $H_{6'b}$); 3.90 (t, 1H, J= 9.2 Hz, H_4); 3.85 (dd, 1H, J= 9.7 and 3.5 Hz, H_2); 3.75–3.64 (m, 4H, H_5, H_1, H_3 and H_6); 2.33 (d, 1H, $J_{H2\text{-}OH}$= 10.1 Hz, C_2OH); 2.15, 2.00, 1.95 and 1.92 (4 s, 12H, $4CH_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.0, 170.3, 170.2 and 169.9 ($4OCOCH_3$), 139.2, 138.7, 138.6 and 138.4 (4C, Bn), 128.9–127.7 (20CH, Bn), 99.3 ($C_{1'\alpha}$, $J_{C1'\text{-}H1'}$= 178.1 Hz), 82.0 (CH), 81.4 (CH), 79.8 (CH), 78.5 (CH), 76.0 (CH_2), 73.8 (CH_2), 73.7 (CH_2), 73.7 (CH), 73.6 (CH_2), 70.4 (CH), 69.8 (CH), 69.7 (CH), 68.6 (CH), 66.4 (CH) and 63.3 (CH_2), 21.1, 21.0, 21.0 and 20.9 ($4CH_3$). Elemental analysis calcd. for $C_{48}H_{54}O_{15}$: 66.19% C and 6.24% H; found: 66.37% C and 6.51% H. Data of the acetylated α(1→3) pseudodisaccharide **5da**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.08 (dd, 1H, J= 10.7 and 2.7 Hz, H_2).

1,2-*O*-Isopropyliden-3,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol

Benzoyl chloride (0.32 ml, 2.80 mmol) was added to a solution of 1,2-*O*-isopropyliden-D-*chiro*-inositol (77 mg, 0.35 mmol) and DMAP (4 mg, 0.035 mmol) in dry pyridine (2 ml) at room temperature. The reaction mixture was stirred for 24 h. The solvent was evaporated, the residue redissolved in CH_2Cl_2, washed with cold water and brine, dried over Na_2SO_4 and the solvent evaporated. The crude was purified by flash chromatography (Hexane/EtOAc= 8:1) to give the title compound quantitatively as a white solid (0.22 g). $[\alpha]_D^{20}$ +78.8 (c = 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.08 (d, 2H, J= 8.0 Hz, H ortho); 7.96 (d, 2H, J= 8.0 Hz, H ortho); 7.87 (d, 2H, J= 8.0 Hz, H ortho); 7.83 (d, 2H, J= 8.0 Hz, H ortho); 7.60–7.22 (m, 12H, 4Bz); 6.07 (t, 1H, J= 3.2 Hz, H_6); 6.02 (t, 1H, J= 8.9 Hz, H_4); 5.91 (dd, 1H, J= 9.1 and 3.2 Hz, H_5); 5.86 (dd, 1H, J= 6.4 and 8.8 Hz, H_3); 4.62 (dd, 1H, J= 6.3 and 5.4 Hz, H_2); 4.55 (dd, 1H, J= 6.3 and 3.3 Hz, H_1); 1.73 (s, 3H, CH_3) and 1.40 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.0, 165.8, 165.5 and 165.4 (4CO); 133.9, 133.6, 133.5 and 133.5 (4CHpara); 130.4–128.5 (16CH, Bz); 129.5, 129.3, 129.2 and 129.1 (4C); 76.8 (C_2); 75.2 (C_1); 73.7 (C_3); 70.4 (C_5); 70.0 (C_4); 69.6 (C_6); 27.9 (CH_3) and 26.2 (CH_3). FAB HRMS calcd. for $C_{37}H_{32}O_{10}$+Na^+: 659.1893, found: 659.1880. Elemental analysis calcd. for $C_{37}H_{32}O_{10}$: C, 69.80%; H, 5.07%; found: C, 69.90% and H, 5.17%.

3,4,5,6-Tetra-*O*-benzoyl-D-*chiro*-inositol (2d). A TFA:H_2O = 9:1 (4 ml) solution was added at room temperature to a round-bottomed flask charged with 1,2-*O*-isopropyliden-3,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol (0.18 g, 0.301 mmol). The reaction mixture was stirred for 3 h, whereupon the solvent was evaporated, the residue co-evaporated 4 times with toluene and purified by flash chromatography (Hexane/EtOAc 4:1→1:1) to give **2d** as a white solid (0.164 g, 91%). $[\alpha]_D^{20}$ +99.8 (c = 0.6, $CHCl_3$);^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.06 (d, 2H, J= 8.0 Hz, H ortho); 7.98 (d, 2H, J= 8.0 Hz, H ortho); 7.86 (d, 2H, J= 8.0 Hz, H ortho); 7.81 (d, 2H, J= 8.0 Hz, H ortho); 7.63–7.22 (m, 12H, 4Bz); 6.18 (t, 1H, J= 10.1 Hz, H_4); 5.99 (dd, 1H, J= 10.1 and 3.4 Hz, H_5); 5.95 (t, 1H, J= 3.4 Hz, H_6); 5.83 (t, 1H, J= 10.1 Hz, H_3); 4.41 (bs, 1H, H_1); 4.30 (m, 1H, H_2); 3.37 (bs, 1H, C_1OH) and 3.33 (bs, 1H, C_2OH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.8, 166.2, 165.8 and 165.6 (4CO); 134.0, 133.8, 133.5 and 133.5 (4CH para); 129.4, 129.3, 129.3 and 129.1 (4C, Bz); 130.3–128.6 (16CH, Bz); 74.8 (CH); 71.5 (CH); 71.0 (CH); 70.4 (CH); 70.3 (CH) and 70.3 (CH). FAB HRMS calcd. for $C_{34}H_{28}O_{10}$+Na: 619.1580, found: 619.1574. Elemental analysis calcd. for $C_{34}H_{28}O_{10}$: C, 68.45%; H, 4.73%; found: C, 68.47% and H, 4.77%.

2,3,4,6-Tetra-*O*-benzyl-D-manopyranosyl-α(1→2)-3,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol (8ad). This pseudodisaccharide was prepared from **2d** (30 mg, 0.050 mmol) and **3a** (34 mg, 0.050 mmol) as described in the general method, adding 0.1 equiv. (50 µl of a solution 0.1 M) of TMSOTf at –40 °C in dry ether (1.7 ml) and stirring the reaction mixture for 1 h at –40 °C. After flash chromatography (Hexane/EtOAc 3:1→1:1) 34 mg of pseudodisaccharide **8ad** (61%) and 11 mg of acceptor **2d** (55%) were obtained. Data of **8ad**: $[\alpha]_D^{20}$ +79.0 (c = 0.5, $CHCl_3$), ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07–7.80 (4 H ortho, 8H); 7.63–7.18 (m, 20H, 4Bn and 12H, 4Bz); 6.15 (t, 1H, J= 10.1 Hz, H_4); 6.07 (t, 1H, J= 10.1 Hz, H_3); 5.96 (dd, 1H, J= 10.1 and 3.3 Hz, H_5); 5.89 (bt, 1H, J= 3.4 Hz, H_6); 5.01 (d, 1H, J= 1.6 Hz, $H_{1'}$); 4.74–4.34 (8H, 4 AB systems); 4.35 (m, 1H, H_2); 4.29 (m, 1H, H_1); 3.79 (t, 1H, J= 9.5 Hz, $H_{4'}$); 3.68 (m, 1H, $H_{5'}$); 3.65 (dd, 1H, J= 9.3 and 2.5 Hz, $H_{3'}$); 3.55 (bt, 1H, J= 2.2 Hz, $H_{2'}$); 3.41 (dd, 1H, J= 10.6 and 2.2 Hz, $H_{6'a}$); 3.38 (dd, 1H, J= 10.6 and 5.5 Hz, $H_{6'b}$) and 3.32 (bs, 1H, C_1OH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.1, 166.1, 165.6 and 165.4 (4CO); 138.8, 138.6, 138.5 and 138.4 (4C, Bn); 133.9, 133.5, 133.5 and 133.4 (4CH para); 130.2–127.6 (20CH, Bn and 16CH, Bz); 129.5, 129.4, 129.4 and 129.3 (4C, Bz); 95.0 ($C_{1'\alpha}$, $J_{C1'\text{-}H1'}$: 168.6 Hz); 79.5 (CH); 77.5 (CH); 75.7 (CH); 74.8 (CH_2); 74.7 (CH); 73.6 (CH_2); 73.2 (CH_2); 72.8 (CH); 72.8 (CH_2); 70.9 (CH); 70.7 (CH); 70.3 (CH); 70.2 (CH); 69.0 (CH_2) and 67.4 (CH). Elemental analysis calcd. for $C_{68}H_{62}O_{15}$+$2H_2O$: C, 70.74% and H, 5.64%; found: C, 70.83% and H, 5.47%.

2,3,4,6-Tetra-*O*-benzyl-D-manopyranosyl-α(1→2)-3,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol (8aa) and 2,3,4,6-tetra-*O*-benzyl-D-manopyranosyl-β(1→2)-3,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol (9aa), 2,3,4,6-tetra-*O*-benzyl-D-manopyranosyl-α(1→1)-3,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol (10aa). These pseudodisaccharides **8aa** (23 mg, 21%), **9aa** (7 mg, 6%) and **10aa** (11 mg, 10%) were prepared from donor **3a** (66 mg, 0.096 mmol) and acceptor **2a** (52 mg, 0.096 mmol) as described in the general method, adding 0.08 equiv. (77 µl of a solution 0.1 M) of TMSOTf at –40 °C in dry ether (2 ml) and stirring the reaction mixture for 1 h at –40 °C. The crude was purified by flash chromatography (Hexane/EtOAc 6:1→4:1). Data of **8aa**: $[\alpha]_D^{20}$ +35.2 (c = 0.9, $CHCl_3$), ^{1}H NMR (500 MHz, C_6D_6): δ = 7.50–7.15 (m, 40H, 8Bn); 5.28 (s, 1H, $H_{1'}$); 5.11–4.34 (16H, 8 AB systems); 4.57

(m, 1H, H_4); 4.47–4.43 (m, 2H, $H_{4'}$ and $H_{5'}$); 4.33 (m, 1H, H_2); 4.24 (dd, 1H, J= 8.9 and 2.5 Hz, $H_{3'}$); 4.21–4.18 (m, 2H, $H_{1\text{ and }5}$); 4.06 (m, 1H, H_6); 4.05 (t, 1H, J= 9.8 Hz, H_3); 3.90 (t, 1H, J= 2.4 Hz, $H_{2'}$); 3.76 (dd, 1H, J= 11.1 and 4.1 Hz, $H_{6'a}$) and 3.65 (bd, 1H, J= 11.1 Hz, $H_{6'b}$). ^{13}C NMR (125 MHz, C_6D_6): δ = 140.5, 140.2, 140.0, 139.9, 139.8, 139.7, 139.7 and 138.4 (8C, Bn); 129.3–128.0 (40CH, Bn); 95.4 ($C_{1'\alpha}$, $J_{C1'\text{-}H1'}$: 171.5 Hz); 83.1 (CH); 81.2 (CH); 80.9 (CH); 80.9 (CH); 77.1 (CH); 77.1 (CH); 76.6 (CH_2); 76.4 (CH_2); 76.2 (CH); 76.1 (CH); 75.7 (CH_2); 74.4 (CH_2); 73.9 (CH_2); 73.9 (CH_2); 73.8 (CH_2); 73.4 (CH); 73.2 (CH_2); 70.1 (CH_2) and 67.7 (CH). Elemental analysis calcd. for $C_{68}H_{70}O_{11}$: C, 76.81% and H, 6.63%; found: C, 76.64% and H, 6.32%. Data of acetylated **8aa** : ^{1}H NMR (500 MHz, C_6D_6): δ = 5.82 (bt, 1H, J= 3.8 Hz, H_1). Data of **9aa**: $[\alpha]_D^{20}$ –3.7 (c = 0.3, $CHCl_3$), ^{1}H NMR (500 MHz, C_6D_6): δ = 7.55–7.10 (m, 40H, 8Bn); 5.19–4.36 (16H, 8 AB systems); 4.64 (m, 1H, H_1); 4.41 (t, 1H, J= 9.6 Hz, H_4); 4.35 (m, 1H, $H_{1'}$); 4.29 (dd, 1H, J= 9.7 and 3.2 Hz, H_5); 4.23 (dd, 1H, J= 9.7 and 3.0 Hz, H_2); 4.19 (bt, 1H, J= 3.3 Hz, H_6); 4.13 (t, 1H, J= 9.7 Hz, H_3); 4.11 (t, 1H, J= 9.7 Hz, $H_{4'}$); 3.77 (d, 1H, J= 4.1 Hz, $H_{2'}$); 3.71 (m, 2H, $H_{6'a\text{ and }6'b}$); 3.29–3.26 (m, 2H, $H_{3'}$ and $H_{5'}$). ^{13}C NMR (125 MHz, C_6D_6): δ = 140.8, 140.6, 140.2, 140.1, 139.9, 139.8, 139.7 and 138.3 (8C, Bn); 129.4–127.8 (40CH, Bn); 103.5 ($C_{1'}$); 83.4 (CH); 83.3, 83.2, 82.7, 81.3, 77.8, 76.3, 76.3, 76.2, 76.1, 75.6, 75.6, 75.4, 74.3, 74.0, 73.7, 72.3, 70.5 and 70.4 (10CH and 9CH_2). Elemental analysis calcd. for $C_{68}H_{70}O_{11}$: C, 76.81% and H, 6.63%; found: C, 76.70% and H, 6.44%. Data of **10aa**: $[\alpha]_D^{20}$ +44.9 (c = 0.5, $CHCl_3$), ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.20 (m, 40H, 8Bn); 4.90–4.43 (16H, 8 AB systems); 4.64 (s, 1H, $H_{1'}$); 4.00 (m, 1H, $H_{5'}$); 3.98 (t, 1H, J= 3.6 Hz, H_1); 3.92–3.88 (m, 2H, H_2 and $H_{4'}$); 3.87 (t, 1H, J= 9.3 Hz, H_4); 3.71 (dd, 1H, J= 8.8 and 2.6 Hz, $H_{3'}$); 3.66 (dd, 1H, J= 10.6 and 5.1 Hz, $H_{6'a}$); 3.62 (dd, 1H, J= 10.6 and 2.1 Hz, $H_{6'b}$); 3.56 (t, 1H, J= 3.1 Hz, H_6); 3.54 (dd, 1H, J= 9.4 and 3.0 Hz, H_5); 3.48 (t, 1H, J= 9.3 Hz, H_3); 3.43 (t, 1H, J= 2.6 Hz, $H_{2'}$) and 2.50 (s, 1H, C_2OH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 139.2, 139.1, 138.8, 138.6, 138.5, 138.5, 138.3 and 137.9 (8C, Bn); 128.8–127.7 (40CH, Bn); 98.5 ($C_{1'}$); 82.6 (CH); 82.0 (CH); 80.4 (CH); 79.6 (CH); 76.5 (CH); 76.1 (CH_2); 75.8 (CH); 75.7 (CH_2); 75.3 (CH_2); 75.2 (CH); 74.4 (CH); 73.6 (CH_2); 73.5 (CH_2); 73.4 (CH_2); 73.3 (CH_2); 73.0 (CH_2); 72.5 (CH); 70.8 (CH) and 69.4 (CH_2). HSQC (500 MHz, C_6D_6): $C_{1'\alpha}$, $J_{C1'\text{-}H1'}$: 170.2 Hz. Elemental analysis calcd. for $C_{68}H_{70}O_{11}$: C, 76.81% and H, 6.63%; found: C, 76.98% and H, 6.78%.

2,3,4,6-Tetra-*O*-acetyl-D-manopyranosyl-α(1→2)-3,4,5,6-tetra-*O*-benzoyl-D-*chiro*-inositol (8dd). This pseudodisaccharide **8dd** (13 mg, 28%) was prepared from donor **3d** (33 mg, 0.067 mmol) and acceptor **2d** (40 mg, 0.067 mmol) as described in the general method, adding 0.1 equiv. (67 µl of a solution 0.1 M) of TMSOTf at –40 °C in dry ether (1.7 ml) and stirring the reaction mixture for 1 h at –40 °C. The crude was purified by flash chromatography (Hexane/EtOAc 3:1→1:1) recovering 18 mg of acceptor **2d**. (45%). $[\alpha]_D^{20}$ +56.4 (c = 0.6, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05–7.80 (4 H ortho, 8H); 7.63-7.23 (m, 12H, 4Bz); 6.12 (t, 1H, J= 10.1 Hz, H_3); 5.93 (t, 1H, J= 3.5 Hz, H_5); 5.76 (m, 2H, H_4 and H_2); 5.68 (d, 1H, J= 2.2 Hz, $H_{1'}$); 5.39 (dd, 1H, J= 9.9 and 4.2 Hz, $H_{3'}$); 5.28 (t, 1H, J= 9.9 Hz, $H_{4'}$); 4.96 (dd, 1H, J= 4.0 and 2.4 Hz, $H_{2'}$); 4.38 (t, 1H, J= 3.7 Hz, H_6); 4.25 (dd, 1H, J= 12.1 and 4.9 Hz, $H_{6'a}$); 4.21 (ddd, 1H, J= 13.5, 10.3 and 2.9 Hz, H_1); 4.15 (dd, 1H, J= 12.1 and 2.6 Hz, $H_{6'b}$); 3.73 (m, 1H, $H_{5'}$); 2.68 (d, 1H, $J_{H1\text{-}OH}$= 11.0 Hz, C_1OH); 2.07–1.95 (4 s, 12H, 4CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.1, 170.7, 170.2 and 169.8 (4O*C*OCH$_3$); 134.1, 133.6, 133.5 and 133.4 (4CH para); 130.2–125.2 (16CH, Bz); 129.9, 129.3, 129.3 and 129.1 (4C, Bz); 97.9 ($C_{1'\alpha}$, $J_{C1'\text{-}H1'}$: 176.2 Hz); 73.7, 72.1 (CH); 71.7, 70.6, 70.3, 70.1, 69.9, 69.8, 66.1, 62.5 and 62.2 (10CH and 1CH_2); 21.1, 21.0, 21.0 and 20.9 (4CH_3). FAB HRMS calcd. for $C_{48}H_{46}O_{19}$+Na^+: 949.2531, found: 949.2524.

2,3,4,6-Tetra-*O*-acetyl-D-manopyranosyl-α(1→2)-3,4,5,6-tetra-*O*-benzyl-D-*chiro*-inositol (8da). This pseudodisaccharide **8da** (48 mg, 45%) was prepared from donor **3d** (60 mg, 0.121 mmol) and acceptor **2a** (66 mg, 0.121 mmol) as described in the general method, adding 0.08 equiv. (96 µl of a solution 0.1 M) of TMSOTf at –40 °C in dry ether (1.7 ml) and stirring the reaction mixture for 1 h at –40 °C. The crude was purified by flash chromatography (Hexane/EtOAc 2:1) recovering 35 mg of acceptor **2a** (52%). $[\alpha]_D^{20}$ +32.2 (c = 2.1, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.20 (m, 20H, 4Bn); 5.26 (dd, 1H, J= 9.7 and 3.1 Hz, $H_{2'}$); 5.25–5.20 (m, 1H, $H_{3'}$); 5.22 (t, 1H, J= 9.7 Hz, $H_{4'}$); 5.03–4.58 (8H, 4 AB systems); 4.89 (s, 1H, $H_{1'}$); 4.22 (m, 1H, $H_{5'}$); 4.09–4.05 (m, 1H, $H_{2\text{ and }1}$); 3.97 (t, 1H, J= 9.7 Hz, H_4); 3.95 (m, 1H, H_6); 3.93 (dd, 1H, J= 9.7 and 2.6 Hz, H_5); 3.87 (dd, 1H, J= 12.6 and 4.2 Hz, $H_{6'a}$); 3.82 (dd, 1H, J= 12.5 and 2.2 Hz, $H_{6'b}$); 3.79 (t, 1H, J= 9.6 Hz, H_3); 2.50 (s, 1H, C_1OH); 2.15, 2.00, 1.98 and 1.85 (4 s, 12H, 4CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.9, 170.6, 170.4 and 169.8 (4O*C*OCH$_3$); 138.9, 138.8, 138.8 and 138.5 (4C, Bn); 128.9–127.5 (20CH, Bn); 94.2 ($C_{1'}$); 82.2, 80.4, 80.0, 76.1, 75.8, 75.8, 75.7, 74.0, 73.6, 69.9, 69.6, 68.7, 66.4, 65.6 and 61.9 (11 CH and 5CH_2); 21.2, 21.0, 20.9 and 20.9 (4CH_3). Elemental analysis calcd. for $C_{48}H_{54}O_{15}$+H_2O: C, 64.85% and H, 6.34%; found: C, 65.10% and H, 6.58%. Data of acetylated **8da**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.29 (bt, 1H, J= 2.8 Hz, H_1).

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20 Structure **D** is the most stable conformation found for the acetylated model. In the case of the methoxylated model, another structure (**A′** see ESI†) in which one of the $H_3CO\cdots H$–O has been replaced by a hydrogen bond O–H$\cdots$O between both OH groups along with a OCH_2–H$\cdots$O bond resulted in being about 2 kcal mol^{-1} more stable than **A**. However, structure **A** has been chosen in this study in order to simultaneously assess the activating ability of each adjacent group and for comparative purposes with **D**. Besides, according to our previous work (ref. 8a), with structures such as **A** during the glycosidic bond formation, the other OH group could participate in the formation of additional hydrogen bonds between the donor and the acceptor in the transition state.

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22 Differences in the strength of hydrogen bonds of **Vα** and **Vβ** can be observed by means of a theoretical calculation like those indicated in Fig. 5, using the corresponding model only with methoxy groups in adjacent positions to OH groups (see ESI†): **Vα** *d*(OHax$\cdots$OMe1) = 2.03; *d*(OHeq$\cdots$OHax) = 2.34; *d*(OHeq$\cdots$OMe1) = 2.67; Wiberg bond indexes: 0.0264, 0.0133 and 0.0021 respectively; **Vβ** *d*(OHeq$\cdots$OMe1) = 2.39; *d*(OHax$\cdots$OMe4) = 2.28; Wiberg bond indexes: 0.0089 and 0.0092 respectively.

23 Small differences in the strength of the hydrogen bonds of **VI** can be observed in the corresponding model (see ESI†): *d*(OHax$\cdots$OMe) = 2.32; *d*(OHeq$\cdots$OMe) = 2.27; Wiberg bond indexes: 0.0087 and 0.0139 respectively.

24 For some examples of regioselective glycosylation of 1,2-*trans*-diequatorial diols in which the steric factors seems to be determinant see: (*a*) U. Ellervik and U. G. Magnusson, *J. Org. Chem.*, 1998, **63**, 9314; (*b*) H. Dietrich, J. F. Espinosa, J. L. Chiara, J. Jimenez-Barbero, Y. Leon, I. Varela-Nieto, J.-M. Mato, F. H. Cano, C. Foces-Foces and M. Martín-Lomas, *Chem.–Eur. J.*, 1999, **5**, 320; (*c*) M. L. Bohn, M. I. Colombo, P. L. Pisano, C. A. Storz and E. A. Rúveda, *Carbohydr. Res.*, 2007, **342**, 2522; (*d*) B. Mukhopadhyay, S. V. Maurer, R. M. Rudolph, Nadine, van Well, D. A. Russell and R. A. Field, *J. Org. Chem.*, 2005, **70**, 9059.

25 B. Fraser-Reid, G. N. Anikumar, L. G. Nair, K. V. Radhakrishnan, J. C. López, A. M. Gómez and C. Uriel, *Aus. J. Chem.*, 2002, **55**, 123.
26 (*a*) R. Ojeda, J. L. de Paz, M. Martín-Lomas and J. M. Lassaletta, *Synlett*, 1999, 1316; (*b*) H. N. Yu, J. Furukawa, T. Ikeda and C. Wong, *Org. Lett.*, 2004, **6**, 723.
27 (*a*) An interesting special regioselective glycosylation in lactose derivatives has been described: H. Paulsen and M. Paal, *Carbohydrate Res.*, 1985, **137**, 39–62; (*b*) H. Paulsen and K. M. Steiger, *Carbohydrate Res.*, 1987, **169**, 105–25; (*c*) H. Paulsen, D. Hadamczyk, W. Kutschker and A. Buensch, *Liebigs Ann. Chem.*, 1985, **1**, 129–41. In this case the regioselectivity (*3-OH versus 4-OH*) can be inverted depending on the reaction conditions (homogeneous or heterogeneous) and as a consequence it is difficult to rationalize and compare. Paulsen pointed out that the reactivity of the glycosyl donor, acceptor, and catalyst had to be properly matched for successful regioselective coupling.