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Variations on the $SnCl_4$ and CF_3CO_2Ag-promoted glycosidation of sugar acetates: a direct, versatile and apparently simple method with either α or β stereocontrol

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ABSTRACT

Glycosidation of sugar peracetates (D-*gluco*, D-*galacto*) with $SnCl_4$ and CF_3CO_2Ag led to either 1,2-*cis*-, or 1,2-*trans*-glycosides, depending primarily on the alcohols used. In particular, 1,2-*trans*-glycosides, expected from acyl-protected glycosyl donors, were formed in high yields with alcohols sharing specific features such as bulkiness, presence of electron-withdrawing groups or polyethoxy motifs. In contrast, simple alcohols afforded ~1:1 mixtures of 2,3,4,6-tetra-*O*-acetyl, and 3,4,6-tri-*O*-acetyl 1,2-*cis*-glycosides due to anomerization and/or acid-catalyzed fragmentation of 1,2-orthoester intermediates. After reacetylation or deacetylation, acetylated or fully deprotected 1,2-*cis*-glycosides (α-D-*gluco*, α-D-*galacto*) were obtained in ~90% yields by a simple and direct method.

1. Introduction

Most of the carbohydrates found in Nature display complex structures, which primarily involve monosaccharides linked to each other or to other types of aglycones by glycosidic bonds. Although *O*-, *S*-, *N*-, *C*-glycosidic linkages are known to be present in naturally occurring carbohydrates, O-glycosides play a prominent role, due to their abundance and importance.[1] In recent projects focusing on *C*-glycosyl aryls,[2] we obtained C-glycosylated hydro-, and benzo-quinones[3] as well as analogues bearing either one nitro group[4] or two methyl substituents in either *ortho* or *meta* disposition on the phenyl ring.[5] These last compounds afforded two series of *C*-glycosyl-chromane derivatives or *C*-glycosyl analogues of vitamin E whose antioxidant activities were investigated.[5] A stereocontrolled C-glycosidation promoted by $SnCl_4$ and CF_3CO_2Ag in anhydrous CH_2Cl_2 was the key step for preparing such *C*-aryl glycosides.[6] Use of CH_2Cl_2 containing EtOH as stabilizer led to byproducts identified as ethyl 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranoside and ethyl 3,4,6-tri-*O*-acetyl-α-D-glucopyranoside (~1:1 ratio) without any trace of the corresponding β-anomers.

Based on the generally accepted idea that acyl-protected glycosyl donors led to 1,2-*trans* glycosides due to neighbouring group participation,[1,7,8] the isolation of pure 1,2-*cis* anomers attracted our attention. Despite the formation of products regioselectively deacetylated at O-2, single α-anomers would be expected if the mixture was subsequently subjected to either acetylation or deacetylation. Moreover, due to the different polarities of the products obtained, the tri-*O*-acetyl glycosides could be easily separated by chromatography. Therefore, this method could provide a simple and rapid access to 1,2-*cis* sugar-derivatives with a free hydroxy group at C-2 and an α anomeric configuration opposite to that easily established by classical methods. Recent reports showed that such compounds[9] are of great interest in oligosaccharide synthesis as glycosyl acceptors[10] and for stereocontrolled glycosidations based on either intramolecular aglycon delivery[11] or participation of a recently introduced neighbouring group.[9b] All considered, our observation encouraged us to study glycosidations promoted by $SnCl_4$ and CF_3CO_2Ag for achieving direct syntheses of acyl-protected 1,2-*cis* glycosides.[12]

From the earlier reports describing O-glycosidations of glycosyl esters upon activation by Lewis acids,[8a] it appeared that $SnCl_4$ has found limited applications as a promoter, either alone[13–15] or in association with other salts, such as $AgClO_4$[16] and $Sn(OTf)_2$–$LiClO_4$.[17]

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Glycosylation reactions of benzyl-protected D-glucopyranose 1-*O*-acetate with silylated alcohols and the Mukaiyama catalyst ($SnCl_3ClO_4$) in Et_2O afforded α-glucosides with high stereoselectivity.[16] In contrast, glycosidations of sugar peracetates afforded either β-, or α-glycosides, due to anomerization,[14,15] depending on structural features and the reaction conditions. For example, it has been noted that increased amounts of MeOH decreased the catalytic efficiency of $SnCl_4$.[13] In the case of peracylated donors, it has been proposed that the order of addition is important for anomeric selectivity, and that combining acceptor and donor in solution followed by addition of $SnCl_4$ leads to mixtures of anomeric glycosides.[18a] These early reports were limited and did not bring a clear analysis of the stereoselectivity issue. Recently, glycosidations–anomerization of 1,6-anhydro-D-glucopyranuronic acid and anomerization of β-D-glucopyranuronic acids in the presence of $SnCl_4$ has been reported.[19] Similarly, β-to-α anomerization has been put forward to account for the exceptionally high α:β selectivity of glycosidation of a benzyl-protected D-mannopyranose ester[20] with $SnCl_3ClO_4$ as promoter.[18b] Other Lewis acids (e.g., $BF_3{\cdot}OEt_2$[21] or zeolite[22]) for the glycosidation of sugar acetates led to more complex mixtures, compared to our preliminary observations (high 1,2-*cis* stereoselectivity; deacetylation at O-2 mainly). We now report further data on the glycosidation of accessible sugar peracetates with various alcohols upon reaction with $SnCl_4$ and CF_3CO_2Ag or related Lewis acids, as promoters.

2. Results and discussion

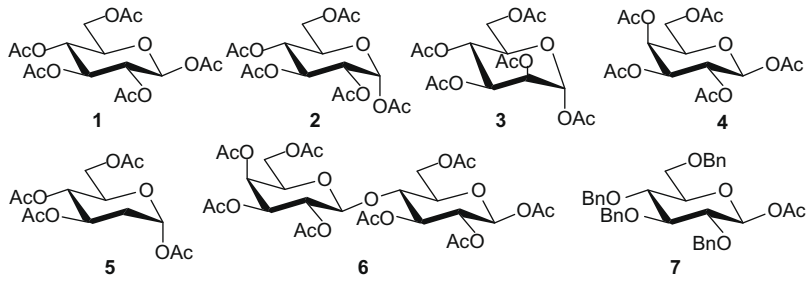
To establish the scope and limitations of the selected glycosidation conditions, we chose differently configured pyranose acetates (**1**–**7**) including activated donors of the 2-deoxy type (**5**) or a benzyl-protected analogue (**7**) (Scheme 1). Methyl β-D-glucopyranoside **8β** was used in one experiment.

The glycosyl donors were reacted with various alcohols in the presence of $SnCl_4$ and CF_3CO_2Ag using pure CH_2Cl_2 as solvent. The molar ratio of the reagents was generally 1:2.5:3:1.5 (sugar donor/ROH/$SnCl_4$/CF_3CO_2Ag), although $SnCl_4$ (from commercially available 1 M solution in CH_2Cl_2) used alone led sometimes to cleaner transformations (Table 1). In a few cases, the molar ratio sugar donor/ROH was 1:1.5 (entries 15, 16, 19 and 26). With diols (entries 17 and 20–22), the ratio was 1:0.33 and the yields were based on the alcohol used. Generally, the reactions were stopped after complete conversion of the substrate and possible intermediates (the α-anomerized substrate and especially the glycosyl chloride)[3,14,15,27] and the products were subjected to chromatography and checked by NMR (Scheme 2).

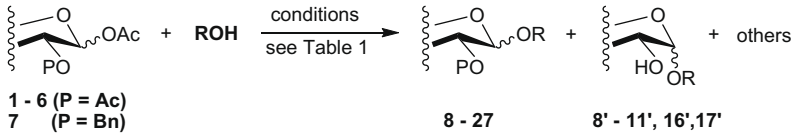
Experiments carried out with EtOH and disarmed donors such as D-glucopyranose acetates confirmed the lower reactivity of the α-anomer **2**, because **1** and **2** afforded essentially the same mixture of α-glucosides, but at significantly different rates with complete conversion achieved within 5 h versus 7 days, respectively (entries 4 and 5). When **1** (or its D-*galacto* analogue **4**) was reacted with MeOH or EtOH in the presence of $SnCl_4$ and CF_3CO_2Ag (entries 1, 4, 13 and 14), α-configured glycosides (~1:1 ratio) were obtained exclusively, with the more polar product being deacetylated at O-2. Compounds **8′α**,[23] **9′α** (for the β-anomer, see Ref. 24), **16′α**,[23a] and **17′α** were isolated in yields ranging from 26% to 42%. Such moderate yields were comparable to those reported for the regioselective deprotection of acetylated glycosides.[25] When the reaction mixtures were subsequently subjected to acetylation, the compounds **8α**, **9α**, **16α** and **17α** were obtained in ~90% yield. This yield is significantly higher than the 35% yield[26] reported for a recent synthesis of **8α.** Comparative experiments without adding CF_3CO_2Ag (entries 2 and 3) afforded the methyl tri-, and tetraacetylated glycosides, as anomeric mixtures.

In our conditions, the α:β ratio increased from 3:1 to 10:1 after 7 h of reaction in the presence of 5 equiv of $SnCl_4$ whereas use of $SnCl_4$ in lower amount (1 equiv) was reported to afford methyl tetra-*O*-acetyl-β-D-glucopyranoside **8β** in good yield, provided anomerization was avoided.[27] Glycosidation of **1** with *i*-PrOH (entry 6) occurred within 20 min, producing an anomeric mixture,[28] but when the reaction was allowed to proceed for 1 h, the α-anomer only was obtained in 60% yield. Use of allyl alcohol (entries 7 and 8) led mainly to α-glucosides[21,29] (with 3-,[21] or 4 OAc groups), with only trace amount of the β-anomer. Donor **4** and 1,12-dodecanediol (entry 17) led to a multicomponent mixture from which the bis-α-galactoside **20α**, a bolaform precursor[30] (Scheme 3) could be isolated in 21% yield, based on the diol used. For glycosidation of **3** and **5** with MeOH (entries 11, 12, 24 and 25), use of $SnCl_4$ and CF_3CO_2Ag led to multicomponent mixtures, but with 3 equiv of $SnCl_4$, the corresponding α-anomers (α-D-*manno* **15α**),[32] (2-deoxy-α-D-*arabino* **25α**),[33] were produced in moderate yields. This selectivity can be best explained by neighbouring group participation (for **3**) or anomerization. For 2-deoxy sugar **5**, the reaction was fast, as expected from the absence of electron-withdrawing group at C-2 resulting in a high reactivity.[34]

In the light of these glycosidations of sugar peracetates with simple alcohols, the $SnCl_4$–CF_3CO_2Ag couple appeared to produce more active species, as compared to $SnCl_4$ alone, thus permitting anomerization of β-anomers. Interestingly, when glycosidation of **1** with MeOH was attempted using a 3:1 mixture of CH_2Cl_2–THF as the solvent and $SnCl_4$, the starting material remained unchanged (entry 2, note c). The regioselectively O-2 deacetylated glycosides observed probably arose from 1,2-orthoesters produced from bicyclic dioxocarbenium ion intermediates and ROH. Acidic conditions are known to promote 1,2-orthoester transformation into ROAc and oxocarbenium intermediates, with a 2-OH group, which undergo preferential α-glycosidation.[15,22a,29d] Our attempts aiming at enhancing the yield of the O-2 deacetylated products were not successful. This fact further supports the formation of O-2 deacetylated products from 1,2-orthoesters, but, considering reports on $SnCl_4$-promoted regioselective debenzylation,[9h] regioselective deacetylation of the fully protected glycosides cannot be excluded.



Scheme 1. Aldopyranose acetates used as glycosyl donors.

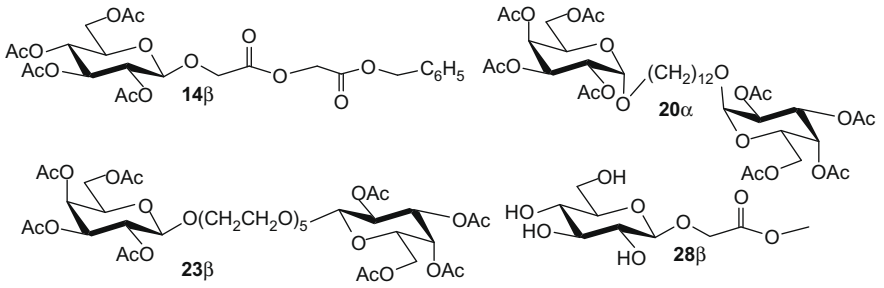


Scheme 2. General picture of the Lewis acid-promoted glycosidation of **1**–**7**.

Table 1
Glycosidation of sugar peracetates **1**–**7** and glycoside **8β** with various alcohols and $SnCl_4$, $SnCl_4$+CF_3CO_2Ag, or $BF_3{\cdot}Et_2O$ as promoter

Entry	Donor	ROH	Conditions,[a] time (h)[b]	Products (%)		
				8–**27**	**8′**–**11′ 16′**, **17′**	Others
1	**1**	MeOH	A, 4	**8α**, 36	**8′α**, 42	
2	**1**	MeOH	B, 3.3[c]	**8**, 36 α/β = 3:1	**8′**, 38 α/β = 3:1	
3	**1**	MeOH	C, 7	**8**, 45 α/β = 10:1	**8′**, 37 α/β = 10:1	
4	**1**	EtOH	A, 5	**9α**, 54	**9′α**, 26	
5	**2**	EtOH	A, 7 days	**9α**, 39	**9′α**, 30	
6	**1**	*i*PrOH	A, 20 min	**10α**, 50[d] **10β**, 14		
7	**1**	CH_2CHCH_2OH	A, 3	**11α**, 28[d] **11β**, 3	**11′α**, 24	
8	**1**	CH_2CHCH_2OH	B, 5	**11α**, 28[d] **11β**, 3	**11′α**, 17	
9	**1**	CF_3CH_2OH	A1, 75 min	**12β**, 47		
10	**1**	BnO_2CCH_2OH	A1, 2	**13β**, 45		**14β**, 2
11	**3**	MeOH	A, 5	Mixture	Other unidentified	
12			B, 3	**15α**, 52		
13	**4**	MeOH	A, 4	**16α**, 35	**16′α**, 40	
14	**4**	EtOH	A, 5	**17α**, 53	**17′α**, 36	
15	**4**	$HOCH_2CH_2Cl$[e]	A, 2	**18β**, 82		
16	**4**	$HOCH_2CCH$[e]	A, 1.5	**19β**, 84		
17	**4**	$HO(CH_2)_{12}OH$[f]	E, 5[g]	Multicomponent mixture		**20α**, 21[h]
18	**4**	$HO(CH_2CH_2O)_2CH_2CH_2Cl$	A, 2	**21β**, 81		
19	**4**	$HO(CH_2CH_2O)_2CH_2CH_2Cl$[e]	G, 100 min	**21**, 66 α/β = 1:5		
20	**4**	$HO(CH_2CH_2O)_5H$[f]	A2, 3	Multicomponent mixture		
21	**4**	$HO(CH_2CH_2O)_5H$[f]	D, 24	**22β**, 23[h]		**23β**, 15[h]
22	**4**	$HO(CH_2CH_2O)_5H$[f]	G1, 5	**22β**, 28[h]		**23β**, 45[h]
23	**4**	$HOCH_2CH(NHFmoc)CO_2Bn$[f]	A3, 3	**24β**, 43		
24	**5**	MeOH	A, 1	**25α**, 28		
25	**5**	MeOH	B, 45 min	**25α**, 55		
26	**6**	$HO(CH_2CH_2O)_2CH_2CH_2Cl$[e]	A, 2.5	**26β**, ~80		
27	**7**	CF_3CH_2OH	F, 2	**27**, 85 α/β = 6:4		
28	**7**	CF_3CH_2OH	F, 72	**27**, 76 α/β = 7:3		
29	**8β**	*i*PrOH	A, 19	**10α**, 28[i]	**10′α**, 11	**8**, 12.5 α/β = 5:1

Conditions: [a]Unless otherwise stated, the reactions were performed at rt in CH_2Cl_2 using a glycosyl donor (1 equiv) [typically 1 mmol (390 mg) in 5 mL CH_2Cl_2 for entries 1–5, 7, 8, 10–14, 17 ($CHCl_3$, 50 °C), 19 (**4**: 17 g), 21–22, or 0.256 mmol (100 mg) in 3 mL CH_2Cl_2 for entries 6, 9, 15 (**4**: 1 g), 16 (**4**: 2 g), 18 (**4**: 5 g), 23–25, 26 (**6**: 5 g), 27–29] and 2.5 equiv of the glycosyl acceptor ROH, with different promoters: $SnCl_4$–CF_3CO_2Ag (3 equiv:1.5 equiv-conditions A; 1.5 equiv:1.5 equiv-conditions A1; 2 equiv:1 equiv-conditions A2; 0.5 equiv:0.5 equiv-conditions A3); $SnCl_4$ (3 equiv-conditions B; 5 equiv-conditions C; 1.73 equiv-conditions D; 2 equiv-conditions E; 0.1 equiv-conditions F); $BF_3{\cdot}Et_2O$ (5 equiv-conditions G; 1.7 equiv-conditions G1). Commercially available 1 M solutions of $SnCl_4$ in CH_2Cl_2 were used. [b]Unless otherwise indicated. [c]Unreacted **1** was recovered when using a 3:1 mixture of CH_2Cl_2–THF as the solvent (time: 3 h), or when adding 0.4 equiv THF (time 5 h). [d]Products separated by chromatography. [e]The acceptor ROH was used in smaller excess (1.5 equiv). [f]Compared to the glycosyl donor (1 mol. equiv), the acceptor ROH was used in lower amount (0.33 mol. equiv). [g]Due to the poor solubility of diol (0.5 mmol), the reaction was performed at 50 °C in $CHCl_3$ (10 mL). [h]Yield calculated based on the alcohol. [i]Unoptimized yields.

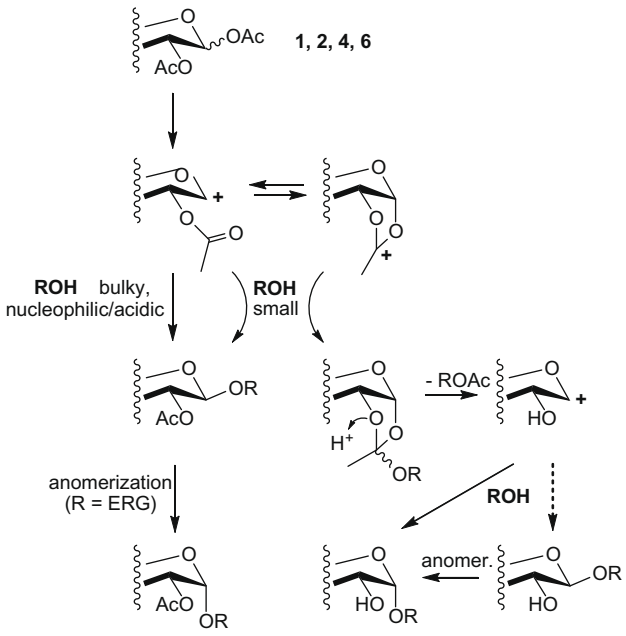


Scheme 3. Other glycosides obtained.

In sharp contrast with the previous results, the major products obtained with alcohols such as trifluoroethanol (entry 9), benzyl glycolate BnO_2CCH_2OH (entry 10), chloroethanol (entry 15), propargylic alcohol (entry 16), triethylene glycol monochlorohydrin $HO(CH_2CH_2O)_2CH_2CH_2Cl$ (entries 18, 19 and 26), pentaethylene glycol $HO(CH_2CH_2O)_5H$ (entries 20–22) and *N*-Fmoc-L-serine benzyl ester $HOCH_2CH(NHFmoc)CO_2Bn$ (entry 23), were β-glycosides, which were obtained in moderate (~45%) to excellent (~80%) yields (**12β**: 47%; **13β**:[35] 45%; **18β**:[36] 82%; **19β**:[37] 84%; **21β**:[38] 81%; **26β**:[39] ~80%; **22β** + **23β**: 38%; **24β**:[40] 43%). For comparison, **4** reacted with $HOCH_2CH(NHFmoc)CO_2Bn$ in the presence of $BF_3{\cdot}Et_2O$ with a poor selectivity, yielding a mixture from which **24β** was obtained in ~15% after column chromatography. Similarly, a lower selectivity was observed for the $BF_3{\cdot}Et_2O$-promoted synthesis of **21** (1:5 α:β mixture in 66% yield, entry 19), although a 72% yield was reported for a large-scale preparation of pure β-anomer.[38] Under conditions A, **21β** was prepared in an 81% yield on the 5-g scale (entry 18), while the lactose derivative **26β** (prepared on 0.4 and 5 g scale using 1.5 equiv of alcohol) was also produced in ~80% yield, which exceeded markedly the 43% yield previously published.[39] Benzyl glycolate (entry 10) led to β-D-glucosides **13β**[35] and a transesterified minor byproduct **14β**, with no isolable amounts of the corresponding α-anomers, known to result from oxidative degradation of isomaltulose.[41] As expected, the armed glycosyl donor **7** reacted under milder conditions[20] to afford anomers **27α** and **27β** in high yield, purified in 43% and 25% yield, respectively, after two successive chromatographic runs. Under Zemplén deacetylation, compound **13β** afforded the corresponding methyl ester **28β**[42] (Scheme 3).

The preferential formation of β-anomers with no significant amounts of partially deacetylated glycosides suggested that 1,2-orthoesters may not be primarily involved in these reactions. This should be related to the glycosyl acceptors employed, in terms of structure and electronic properties. In **24β,** the protected serine moiety appeared bulky while **12β** and **13β** displayed aglycons with electron-withdrawing groups. The polyethylene-derived alcohols do not share these features but the chain oxygen atoms are expected to interact with tin cations, thereby leading to complexes with milder Lewis acid properties. How this explains the observed β-selectivity remains questionable, although it is conceivable that, in the first mentioned cases, bulkiness and nucleophilicity (due to acidity) should favour the preferred stereocontrolled β-attack of the less-hindered oxocarbenium ion. In addition, due to either bulkiness or unfavourable electronic properties of the aglycon, the initially formed β-glycosides should not anomerize readily (Scheme 4).

Indeed, glycosides can anomerize by cleavage of either of the C–O bonds (*endo*-, or *exo*-cyclic). Under the conditions applied, cleavage of the endocyclic C–O bond is possible because this process accounts for the anomerization of α-*C*-glycopyranosyl aryls to the more stable β-anomers.[3] For 2,3,4,6-tetra-*O*-acetyl-*C*-D-glucopyranosyl 1,4-dimethoxybenzene (and its D-*galacto* analogue), such an α-to-β anomerization occurred over 4–5 h upon mild heating to 25–30 °C (CH_2Cl_2), while for 4-methoxy-3-(2,3,4-tri-*O*-acetyl-β-L-fucopyranosyl)toluene, the reaction proceeded at 0 °C.[6] In the first case, the somewhat stronger conditions can be readily rationalized by invoking the disarming effect of the acetoxy group at C6. It is also noteworthy that the β(1→4) interglycosidic linkage[43] in **6** was stable during the synthesis of **26β**. We believe that for the acetylated glycosides derived from simple alcohols (MeOH, EtOH and *i*-PrOH), β-to-α anomerization occurred mainly by cleavage of the *exo*-cyclic C–O bond, due to the electron-releasing properties of the aglycons (R = ERG, Scheme 4). Such a cleavage was evidenced by the fact that, when subjected to the glycosidation conditions in the presence of *i*-PrOH, methyl glucoside **8β** led to the corresponding isopropyl glucosides **10α** and **10′α** (entry 29).



Scheme 4. Possible reaction pathways for Lewis acid-promoted glycosidation of aldose acetates.[43]

Conversely, glycosides displaying electron-withdrawing aglycons should be reluctant to anomerization. In the presence of $SnCl_4$ (0.1 equiv), the armed benzyl-protected donor **7** and trifluoroethanol reacted to afford an anomeric mixture in high yield (entries 27 and 28), with the α:β ratio being 3:2 after 2 h, and 7:3 after 72 h. Thus, for trifluoroethyl glucosides **12β** and **27** (α:β mixture) and under the applied conditions, cleavage of both *endo*-, and *exo*-cyclic C–O bonds was limited.

In conclusion, glycosidation of sugar peracetates (D-*gluco*, D-*galacto*) with $SnCl_4$ and CF_3CO_2Ag led to either 1,2-*cis*-, or 1,2-*trans*-glycosides, depending primarily on the alcohols used. In particular, 1,2-*trans*-glycosides, expected from acyl-protected glycosyl donors, were formed in high yields with alcohols sharing specific features such as bulkiness, presence of electron-withdrawing groups or polyethoxy motifs. In contrast, simple alcohols afforded ~1:1 mixtures of 2,3,4,6-tetra-*O*-acetyl, and 3,4,6-tri-*O*-acetyl 1,2-*cis*-glycosides due to anomerization and/or acid-catalyzed fragmentation of 1,2-orthoester intermediates. After reacetylation or deacetylation, acetylated or fully deprotected 1,2-*cis*-glycosides (α-D-*gluco*, α-D-*galacto*) were obtained in ~90% yields by a simple and direct method.

3. Experimental

3.1. General methods

Methanol was distilled under nitrogen and over Mg turnings after adding few crystals of iodine. Dichloromethane was washed with H_2O, dried with K_2CO_3 and distilled over CaH_2. Chloroform was washed with H_2O, dried with K_2CO_3 (stirring for 1–2 h) and distilled over $CaSO_4$. 2,2,2-Trifluoroethanol was dried with $CaSO_4$, then stirred with $NaHCO_3$ to remove traces of acid and distilled. Thin-layer chromatography (TLC) was carried out on aluminium sheets coated with Silica Gel 60 F_{254} (Merck). TLC plates were inspected under UV light (λ = 254 nm) and developed after spraying a mixture of 10% H_2SO_4 in EtOH–H_2O (1:1 v/v) followed by heating. Silica gel column chromatography was performed with Geduran® silica gel Si 60 (40–63 μm) purchased from Merck (Darmstadt, Germany). NMR solvents were purchased from Euriso-Top

(Saint Aubin, France). ^{1}H and ^{13}C NMR spectra were recorded at 23 °C using Bruker Advance300, DRX300 or DRX500 spectrometers with TMS or the residual solvent as the internal standard. ^{19}F NMR spectra were recorded with a Bruker Advance400 spectrometer (376.24 MHz), with $CFCl_3$ as the external reference. The following abbreviations are used to explain the observed multiplicities: s, singlet; d, doublet; dd, doublet of doublet; ddd, doublet of doublet of doublet; t, triplet; td, triplet of doublet; q, quadruplet; m, multiplet; br, broad and p, pseudo. Structure elucidation was deduced from 1D and 2D NMR spectroscopy which allowed, in most cases, complete signal assignments based on COSY, HSQC and HMBC correlations. Melting points were measured in open capillary tubes with a Büchi apparatus. Optical rotations were determined with a Perkin–Elmer 241 polarimeter at room temperature. MS (ESI) mass spectra were recorded in the positive mode using a Thermo Finnigan LCQ spectrometer. HRMS (LSIMS) mass spectra were recorded in the positive mode using a Thermo Finnigan Mat 95 XL spectrometer. Elemental analyses were performed at the Service Central d'Analyses du CNRS (Vernaison, France).

3.2. Typical glycosidation procedure

A mixture of peracetylated glycopyranose (usually 0.256 mmol or 1 mmol, 1 equiv) and ROH (2.5 equiv) was dissolved in dry CH_2Cl_2. CF_3CO_2Ag (1.5 equiv) was added and the mixture was stirred at room temperature under argon for 5 min. A 1M solution of $SnCl_4$ in CH_2Cl_2 (3 equiv) was added dropwise (addition time 20–40 min) to the mixture upon stirring (see text and caption of Table 1 for details and similar conditions). After conversion of the substrate, as indicated by TLC monitoring, the reaction was quenched by adding saturated aqueous $NaHCO_3$. After stirring briefly, the mixture was filtered through a bed of Celite. The filtrate was repeatedly extracted with CH_2Cl_2, and the organic phase was washed with brine, before drying ($MgSO_4$) and concentration under reduced pressure. The residue was purified by silica gel column chromatography.

3.3. Methyl 3,4,6-tri-*O*-acetyl-α-D-glucopyranoside (8′α)

This compound was prepared from **1** (390 mg, 1 mmol), according to the general procedure and purified by silica gel chromatography to afford **8α** and **8′α** (Table 1). Compound **8′α**: colourless oil, R_f = 0.11, EtOAc–petroleum ether, 2:3, *v*/*v*; $[\alpha]_D^{22}$ +121.7 (*c* 1, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.16 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.6 Hz, H3), 4.93 (dd, 1H, $J_{3,4}$ = 9.6 Hz, $J_{4,5}$ = 9.9 Hz, H4), 4.76 (d, 1H, $J_{1,2}$ = 3.7 Hz, H1), 4.20 (dd, 1H, $J_{5,6a}$ = 4.7 Hz, $J_{6a,6b}$ = 12.2 Hz, H6a), 4.01 (dd, 1H, $J_{5,6b}$ = 2.3 Hz, $J_{6a,6b}$ = 12.2 Hz, H6b), 3.88 (dq, 1H, $J_{4,5}$ = 9.9 Hz, $J_{5,6a}$ = 4.7 Hz, $J_{5,6b}$ = 2.3 Hz, H5), 3.62 (ddd, 1H, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 9.6 Hz, $J_{2,OH}$ = 10.9 Hz, H2), 3.40 (s, 3H, OCH_3), 2.40 (d, 1H, $J_{2,OH}$ = 10.9 Hz, OH), 2.03, 2.00, 1.96 (3s, 9H, acetyl); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.4, 170.1, 170.0 (C=O, acetyl), 99.6 (C1), 73.7, 71.1, 68.4, 67.8 (C2, C3, C4, C5), 62.4 (C6), 60.0 (OCH_3), 21.2, 21.1, 21.0 ($COCH_3$); MS (CI, isobutane) $C_{13}H_{20}O_9$ (MW 320.29): *m*/*z* : 321 $[M+H]^+$ (10%), 289 $[M+H-MeOH]^+$ (100%), 229 (20%), 169 (55%); MS (ESI, positive mode) *m*/*z* : 343.1 $[M + Na]^+$ (100%).

3.4. Ethyl 3,4,6-tri-*O*-acetyl-α-D-glucopyranoside (9′α)

This compound was prepared from **1** (390 mg, 1 mmol), according to the general procedure and purified by silica gel chromatography to afford **9α** and **9′α** (Table 1). Compound **9′α** : colourless oil, R_f = 0.15, EtOAc–petroleum ether, 1:2, *v*/*v*; $[\alpha]_D^{22}$ +120.9 (*c* 1, CH_2Cl_2); lit.[24] for β-anomer : Mp 121 °C ; $[\alpha]_D^{22}$ +14.4 (EtOH); ^{1}H NMR ($CDCl_3$, 200 MHz): δ 5.20 (t, 1H, $J_{2,3} = J_{3,4}$ = 9.7 Hz, H3), 4.96 (t, 1H, $J_{3,4} = J_{4,5}$ = 9.7 Hz, H4), 4.89 (d, 1H, $J_{1,2}$ = 3.9 Hz, H1), 4.23 (dd, 1H, $J_{5,6a}$ = 4.5 Hz, $J_{6a,6b}$ = 12.2 Hz, H6a), 4.00 (dd, 1H, $J_{5,6b}$ = 2.3 Hz, $J_{6a,6b}$ = 12.2 Hz, H6b), 3.93 (m, 1H, H5), 3.76 (m, 1H, OCH_2CH_3), 3.58 (m, 1H, OCH_2CH_3), 3.58 (overlapped, H2), 2.26 (d, 1H, $J_{2,OH}$ = 11.2 Hz, OH), 2.05, 2.04, 1.99 (3s, 9 H, $COCH_3$), 1.24 (t, 3H, *J* = 7.1 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 171.1, 170.7, 169.7 (C=O, acetyl), 98.1 (C1), 73.5, 70.7, 68.1, 67.6 (C2, C3, C4, C5), 64.3, 62.1 (C_6, OCH_2CH_3), 20.9, 20.7, 20.6 ($COCH_3$), 15.0 (OCH_2CH_3) ; MS (CI, isobutane) $C_{14}H_{22}O_9$: MW 334.32, *m*/*z* : 335 $[M+H]^+$ (5%), 289 $[M+H-EtOH]^+$ (100%), 229 (25%), 169 (95%).

3.5. Trifluoroethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (12β)

This compound was prepared from **1** (100 mg) according to the typical procedure (Table 1, entry 9) and purified by column chromatography (EtOAc–petroleum ether, 2:3, *v*/*v*), as a white solid (52 mg, 0.12 mmol, 47%). Other less mobile products (R_f = 0.24 to R_f = 0.1) arising probably from partial deacetylation were not identified. Compound **12β**: Mp 127–130 °C; R_f = 0.53, EtOAc–petroleum ether, 2:3, *v*/*v*; $[\alpha]_D^{20}$ −16.3 (*c* 1, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.23 (t, 1H, *J* = 9.6 Hz, H3), 5.11 (t, 1H, *J* = 9.6 Hz, H4), 5.04 (dd, 1H, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 9.6 Hz, H2), 4.66 (d, 1H, $J_{1,2}$ = 7.8 Hz, H1), 4.27 (dd, 1H, $J_{5,6a}$ = 4.6 Hz, $J_{6a,6b}$ = 12.4 Hz, H6a), 4.19–4.06 (m, 2H, H6b, CH_2CF_3), 3.97 (qd, 1H, $^3J_{H,F}$ = 8.2 Hz, $^2J_{H,H}$ = 12.8 Hz, CH_2CF_3), 3.74 (ddd, 1H, $J_{4,5}$ = 9.9 Hz, $J_{5,6a}$ = 4.6 Hz, $J_{5,6b}$ = 2.4 Hz, H5), 2.10, 2.05, 2.03, 2.02 (4s, 12H, CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.0, 170.6, 169.8, 169.7 (4s, 4C, CH_3CO), 101.2 (C1), 72.7 (C3), 72.6 (C5), 71.1 (C2), 68.5 (C4), 66.3 (q, $^2J_{C,F}$ = 34.6 Hz, CH_2CF_3), 62.1 (C_6), 21.1, 21.0, 20.9 20.8 (4s, 4C, $COCH_3$); ^{19}F NMR (282.38 MHz, $CDCl_3$): δ = −74.85 (t, 3F, $^3J_{H,F}$ = 8.2 Hz, CH_2CF_3); MS (ESI, positive mode) *m*/*z* : 453.0 $[M+Na]^+$; Anal. Calcd for $C_{16}H_{21}F_3O_{10}$ (MW: 430.33): C, 44.66; H, 4.92; F, 13.24. Found: C, 44.97; H, 5.07; F, 13.02.

3.6. (Benzyloxycarbonyl)methylene 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (13β) and (benzyloxycarbonyl-methoxycarbonyl)methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (14β)

These compounds were prepared from **1** (390 mg, 1 mmol) (2 h) according to the typical procedure (Table 1, entry 10), whereby **1** (R_f = 0.45, EtOAc–petroleum ether, 2:3, *v*/*v*) was transformed into several compounds (R_f = 0.38, R_f = 0.23, EtOAc–petroleum ether, 2:3, *v*/*v*), purified by silica gel chromatography (EtOAc–petroleum ether, 1:3, *v*/*v*) to afford **13β** (223.5 mg, 45%) and **14β** (10 mg, 2%), both as colourless oil.

Compound **13β**: R_f = 0.38, EtOAc–petroleum ether, 2:3, *v*/*v*; $[\alpha]_D^{20}$ −26.8 (*c* 1, CH_2Cl_2); Lit.[35]: $[\alpha]_D^{20}$ −22.4 (*c* 1.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.3 (br s, 5H, H-Ar), 5.24 (t, 1H, *J* = 9.6 Hz, H3), 5.18 (s, 2H, OCH_2Ph), 5.09 (t, 1H, *J* = 9.6 Hz, H4), 5.05 (dd, 1H, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 9.6 Hz, H2), 4.67 (d, 1H, $J_{1,2}$ = 7.8 Hz, H1), 4.33 (s, 2H, OCH_2C=O), 4.25 (dd, 1H, $J_{5,6a}$ = 4.6 Hz, $J_{6a,6b}$ = 12.4 Hz, H6a), 4.12 (dd, 1H, $J_{5,6b}$ = 2.4 Hz, $J_{6a,6b}$ = 12.4 Hz, H6b), 3.68 (ddd, 1H, $J_{4,5}$ = 9.9 Hz, $J_{5,6a}$ = 4.6 Hz, $J_{5,6b}$ = 2.4 Hz, H5), 2.08, 2.03, 2.02, 2.01 (4s, 12H, CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.1, 170.6, 170.1, 169.8, 169.4 (5s, 5C, C=O), 135.6, 129.1, 129.0, 128.9 (4s, 6C, phenyl), 100.5 (C1), 72.9 (C3), 72.4 (C5), 71.3 (C2), 68.7 (C4), 67.2 (OCH_2Ph), 65.4 (OCH_2C=O), 62.2 (C6), 21.2, 21.1, 21.0, 21.0 (4s, 4C, $COCH_3$); MS (ESI, positive mode) *m*/*z* : 519.1 $[M+Na]^+$; Anal. Calcd for $C_{23}H_{28}O_{12}$ (MW: 496.46): C, 55.64; H, 5.68. Found: C, 55.78; H, 5.96.

Data for **14β**: R_f = 0.23, EtOAc–petroleum ether, 2:3, *v*/*v*; $[\alpha]_D^{20}$ −18.2 (*c* 1, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40–7.34 m, 5H, H-Ar), 5.23 (t, 1H, *J* = 9.6 Hz, H3), 5.23 (d, 1H, *J* = 12.3 Hz, OCH_2Ph), 5.18 (s, 1H, *J* = 12.0 Hz, OCH_2Ph), 5.09 (t, 1H, *J* = 9.6 Hz, H4), 5.05 (dd, 1H, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 9.6 Hz, H2), 4.73 (d, 2H, *J* = 4.2 Hz, OCH_2C=O), 4.65 (d, 1H, $J_{1,2}$ = 8.1 Hz, H1), 4.40 (d, 2H,

J = 1.2 Hz, OCH_2C=O), 4.25 (dd, 1H, $J_{5,6a}$ = 4.5 Hz, $J_{6a,6b}$ = 12.3 Hz, H6a), 4.13 (dd, 1H, $J_{5,6b}$ = 2.4 Hz, $J_{6a,6b}$ = 12.3 Hz, H6b), 3.66 (ddd, 1H, $J_{4,5}$ = 9.9 Hz, $J_{5,6a}$ = 4.5 Hz, $J_{5,6b}$ = 2.4 Hz, H5), 2.09, 2.07, 2.03, 2.01 (4s, 12H, CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.1, 170.6, 170.1, 169.9, 169.0, 167.5 (6s, 6C, C=O), 129.1, 128.9 (2s, 6C, phenyl), 100.5 (C1), 72.9 (C3), 72.3 (C5), 71.3 (C2), 68.6 (C4), 67.8 (OCH_2Ph), 65.0 (OCH_2C=O), 62.1 (C6), 61.3 (OCH_2C=O), 21.2, 21.1, 21.02, 21.01 (4s, 4C, COCH_3); MS (ESI, positive mode) m/z : 577.1 $[M+Na]^+$.

3.7. Methyl 3,4,6-tri-*O*-acetyl-α-D-galactopyranoside (16′α)

This compound was prepared from **4** (390 mg, 1 mmol), according to the general procedure and purified by silica gel chromatography to afford **16α** and **16'α** (Table 1). Compound **16′α:** colourless oil, R_f = 0.11, EtOAc–petroleum ether, 2:3, v/v; $[\alpha]_D^{22}$ +120.6 (c 0.6, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.35 (d, 1H, $J_{3,4}$ = 3.2 Hz, H4), 5.09 (dd, 1H, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.2 Hz, H3), 4.84 (d, 1H, $J_{1,2}$ = 4.0 Hz, H1), 4.13 (t, 1H, $J_{5,6}$ = 6.2 Hz, $J_{5,6'}$ = 6.4 Hz, H5), 4.06 (d, 2H, J = 7.0 Hz, H6a, H6b), 3.40 (s, 3H, OCH_3), 3.92 (br signal, H2), 2.23 (s, 1H, OH), 2.10, 2.02, 2.01 (3s, 9H, acetyl); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.1, 170.9, 170.6 (C=O, acetyl), 100.0 (C1), 71.0, 68.6, 67.4, 67.0 (C2, C3, C4, C5), 62.3 (C6), 56.0 (OCH_3), 21.2, 21.0, 21.0 (3s, 3C, COCH_3); Anal. Calcd for $C_{13}H_{20}O_9$ (MW 320.29): C, 48.75; H, 6.29; O, 44.96. Found: C, 48.86; H, 6.35; O, 44.61.

3.8. Ethyl 3,4,6-tri-*O*-acetyl-α-D-galactopyranoside (17′α)

This compound was prepared from **4** (390 mg, 1 mmol), according to the general procedure and purified by silica gel chromatography to afford **17α** and **17′α** (Table 1). Compound **17′α**: white crystals, Mp 95.5–96.5 °C (petroleum ether-EtOAc); R_f = 0.1, EtOAc–petroleum ether, 2:3, v/v; $[\alpha]_D^{22}$ +143.7 (c 0.65, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) : δ 5.39 (dd, 1H, $J_{3,4}$ = 3.4 Hz, $J_{4,5}$ = 0.9 Hz, H4), 5.13 (dd, 1H, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.4 Hz, H3), 4.99 (d, 1H, $J_{1,2}$ = 4.0 Hz, H1), 4.20 (t, 1H, J = 7.0 Hz, H5), 4.09 (m, 2H, H6a, H6b), 3.93 (ddd, 1H, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 10.4 Hz, H2), 3.80 (m, 1H, OC$H_2$$CH_3$), 3.60 (m, 1H, OC$H_2$$CH_3$), 2.14, 2.05, 2.05 (3s, 9 H, acetyl), 2.10 (s, 1H, OH), 1.28 (t, 3H, J = 7.1 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) : δ 171.1, 170.8, 170.6 (C=O, acetyl), 98.8 (C1), 71.2, 68.7, 67.4, 67.0 (C2, C3, C4, C5), 64.7, 62.2 (C6, OCH_2CH_3), 21.2, 21.0, 21.0 (3s, 3C, COCH_3), 15.4 (OCH_2CH_3) ; Anal. Calcd for $C_{14}H_{22}O_9$ (334.32): C, 50.30; H, 6.63; O, 43.07. Found: C, 50.60; H, 6.58; O, 43.37.

3.9. Chloroethyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (18β)

This compound was prepared from **4** (1.0 g) and freshly distilled 2-chloroethanol (260 μL, 3.84 mmol, 1.5 equiv) in anhydrous CH_2Cl_2 (30 mL) according to the typical procedure (Table 1, entry 15), whereby the crude product was purified by flash chromatography (EtOAc–petroleum ether 1:1). Crystallization from CH_2Cl_2–petroleum ether afforded **18β** (868 mg, 82%) as a white powder. Mp 102–105 °C (CH_2Cl_2–petroleum ether). Lit[36] : syrup ; R_f = 0.51, EtOAc–petroleum ether, 1:1, v/v; $[\alpha]_D^{20}$ +1.22 (c 1, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.35 (dd, 1H, $J_{4,5}$ = 0.9 Hz, $J_{3,4}$ = 3.4 Hz, H4), 5.18 (dd, 1H, $J_{1,2}$ = 7.9 Hz, $J_{2,3}$ = 10.5 Hz, H2), 4.98 (dd, 1H, $J_{3,4}$ = 3.4 Hz, $J_{2,3}$ = 10.5 Hz, H3), 4.50 (d, 1H, $J_{1,2}$ = 7.9 Hz, H1), 4.14–4.03 (m, 3H, H6a, H6b, 1H from OCH_2), 3.89 (td, 1H, $J_{4,5}$ = 0.9 Hz, $J_{5,6}$ = $J_{5,6'}$ = 6.6 Hz, H-5), 3.73 (ddd, 1H, J = 6 Hz, J = 7 Hz, J = 11 Hz, 1H from OCH_2), 3.63–3.57 (m, 2H, –CH_2Cl), 2.11, 2.03, 2.00, 1.94 (4s, 12H, CH_3CO); for ^{13}C NMR, see Ref. 36.

3.10. 1,12-Dodecyl bis-2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranoside (20α)

This compound was prepared from **4** (577.9 mg, 1.482 mmol) and 1,12-dodecanediol (100 mg, 0.494 mmol, 0.33 equiv) in dry $CHCl_3$ (10 mL) at 50 °C in the presence of $SnCl_4$ (1 M solution in CH_2Cl_2, 6 equiv) within 5 h (Table 1, entry 17) and purified by silica gel chromatography (EtOAc–petroleum ether, 1:4, v/v, then EtOAc) to afford **20α** (88 mg, 21%) as a colourless oil. R_f = 0.4, EtOAc–petroleum ether 1:1, v/v; $[\alpha]_D^{20}$ +121 (c 0.9, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.42 (dd, 2H, $J_{3,4}$ = 3.4 Hz, $J_{4,5}$ = 1.2 Hz, H4, H4′), 5.35 (m, 2H, $J_{2,3}$ = ~9 Hz, $J_{3,4}$ = 3.4 Hz, H3, H3′), 5.11 (m, 4H, H1, H1′, H2, H2′), 4.25 (t, 2H, J = 6.2 Hz, H5, H5′), 4.10 (m, 4H, H6a, H6b, H6a′, H6b′), 3.68 (m, 2H, OCH_2), 3.42 (m, 2H, OCH_2), 2.11, 2.04, 2.02, 1.96 (4s, 24H, CH_3CO), 1.57–1.49 (m, 4H, CH_2), 1.25 (s, 16H, CH_2). $^3J_{1,2}$ (3.8 Hz) and $^1J_{C1,H1}$ (170.5 Hz)[31] were measured by a 2D NMR experiment (SAPHIR-HSQC)[44]; ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.3, 170.3, 170.1, 169.9 (3s, 8C, CH_3CO), 95.9 (s, 2C, C1, C1′), 68.5 (s, 2C, OCH2), 68.1 (s, 2C, C2, C2′), 68.0 (s, 2C, C4, C4′), 67.5 (s, 2C, C3, C3′), 66.0 (s, 2C, C5, C5′), 61.7 (s, 2C, C6, C6′), 29.5, 29.3, 29.2, 29.2, 26.0 (5s, 10C, CH_2), 20.7, 20.6, 20.5 (3s, 8C, CH_3CO); MS (ESI, positive mode) m/z : 885.3 $[M+Na]^+$.

3.11. [2-[2-[2-[2-(2-Hydroxy)ethoxy]ethoxy]ethoxy]ethoxy]-ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (22β) and 3,6,9,12-Tetraoxatetradecan-1,14-di-yl bis-2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranoside (23β)

These compounds were prepared from **4** (491.4 mg, 1.26 mmol) and pentaethylene glycol (70 μL, 0.42 mmol, 0.33 equiv), in CH_2Cl_2 (8 mL) in the presence of $SnCl_4$ (1 M solution in CH_2Cl_2, 1.68 mL, 1.68 mmol, 1.33 equiv) (Table 1, entry 21). After 17 h, more $SnCl_4$ (0.5 mL, 0.5 mmol, 0.4 equiv) was added. After conversion of **4** (24 h), silica gel chromatography (EtOAc–petroleum ether, 1:3, 1:1, v/v; EtOAc) afforded **23β** (55 mg, 15%) followed by **22β** (55.4 mg, 23%), both as colourless oil. In another run (Table 1, entry 22), **4** (491.4 mg, 1.26 mmol) and pentaethylene glycol (70 μL, 0.42 mmol, 0.33 equiv) in CH_2Cl_2 (8 mL) were stirred at rt for 5 h after addition of $BF_3{\cdot}Et_2O$ (0.266 mL, 2.1 mmol, 1.67 equiv) to afford after purification **23β** (168.6 mg, 45%) and **22β** (67 mg, 28%) as colourless oils.

Compound **22β**: R_f = 0.23, EtOAc–MeOH, 10:1, v/v; $[\alpha]_D^{20}$ −6.4 (c 0.88, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.39 (bd, $J_{3,4}$ = 3.0 Hz, 1H, H4), 5.21 (dd, 1H, $J_{1,2}$ = 7.9 Hz, $J_{2,3}$ = 10.4 Hz, H2), 5.03 (dd, 1H, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.3 Hz, H3), 4.59 (d, 1H, $J_{1,2}$ = 7.9 Hz, H1), 4.2–3.6 (m, 23H, H5, H6a, H6b, OCH_2CH_2O), 2.16, 2.07, 2.06, 1.99 (4s, 12H, CH_3CO); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 170.3, 170.1, 169.5 (4s, 4C, CH_3CO), 101.3 (C1), 72.5, 70.65, 70.56, 70.53, 70.52, 70.49, 70.28, 70.24, 69.1, 61.7, 61.3 (11s, 11C, OCH_2CH_2O, C6), 70.9, 70.6, 68.8, 67.1 (4s, 4C, C2, C3, C4, C5), 20.76, 20.67, 20.65, 20.57 (CH_3CO); MS (ESI, positive mode) m/z : 591.2 $[M+Na]^+$.

Compound **23β**: R_f = 0.67, EtOAc–MeOH, 10:1, v/v; $[\alpha]_D^{20}$ −8.3 (c 1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): δ 5.38 (dd, 2H, $J_{3,4}$ = 3.3 Hz, $J_{4,5}$ = 0.5 Hz, H4), 5.18 (dd, 2H, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 10.4 Hz, H2), 4.99 (dd, 2H, $J_{2,3}$ = 10.4 Hz, $J_{3,4}$ = 3.3 Hz, H3), 4.54 (d, 2H, $J_{1,2}$ = 8.0 Hz, H1), 4.16 (dd, 2H, $J_{5,6}$ = 6.6 Hz, $J'_{6,6}$ = 11.3 Hz, H6), 4.12 (dd, 2H, $J'_{5,6}$ = 6.9 Hz, H6′), 3.95–3.88 (m, 3H, H_5, OCH_2), 3.74–3.70 (m, 3H), 3.75–3.61 (m, 16H, OCH_2CH_2O), 2.13, 2.04, 2.03, 1.96 (4s, 24H, CH_3CO); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3, 170.2, 170.1, 169.4 (4s, 8C, CH_3CO), 101.3 (s, 2C, C1, C1′), 70.8 (s, 2C, C3, C3′), 70.6 (s, 2C, CH_2CH_2O), 70.55 (s, 2C, C5, C5′), 70.5, 70.4, 70.2, 69.0 (4s, 8C, CH_2CH_2O), 68.7 (s, 2C, C2, C2′), 67.0 (s, 2C, C4, C4′), 61.2 (s, 2C, C6, C6′), 20.7, 20.6, 20.6, 20.5 (4s, 8C, CH_3CO); MS (ESI, positive mode) m/z : 921.3 $[M+Na]^+$.

3.12. Trifluoroethyl 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranoside (27α and trifluoroethyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside 27β

These compounds were prepared from **7**[45] (238 mg, 0.407 mmol) and 2,2,2-trifluoroethanol (74.5 μL, 1.02 mmol, 2.5 equiv) in the presence of $SnCl_4$ (Table 1, entries 27 and 28) and purified by silica gel chromatography (two successive runs with 35:65 then 3:7 petroleum ether–CH_2Cl_2 as the mobile phase) to afford **27α** (109 mg, 43%) then **27β** (62 mg, 25%).

Compound **27α:** colourless oil, R_f = 0.52, CH_2Cl_2; $[\alpha]_D^{20}$ +50.6 (*c* 0.92, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34–7.26 (m, 18H, Ph), 7.14–7.11 (m, 2H, Ph), 4.98 (d, 1H, *J* = 11 Hz, C*H*$_2$-Ar), 4.83 (d, 1H, *J* = 10.8 Hz, C*H*$_2$-Ar), 4.83 (d, 1H, *J* = 11 Hz, C*H*$_2$-Ar), 4.81 (d, 1H, $J_{1,2}$ = 3.7 Hz, H1), 4.78 (d, 1H, *J* = 12 Hz, C*H*$_2$-Ar), 4.62 (d, 1H, *J* = 11.8 Hz, C*H*$_2$-Ar), 4.59 (d, 1H, *J* = 12 Hz, C*H*$_2$-Ar), 4.47 (d, 1H, *J* = 10.8 Hz, C*H*$_2$-Ar), 4.46 (d, 1H, *J* = 12.1 Hz, C*H*$_2$-Ar), 3.98 (t, 1H, *J* = 9.2 Hz, H3), 3.88 (q, 2H, $^3J_{H,F}$ = 8.7 Hz, CH_2CF_3), 3.77–3.62 (m, 4H, H4, H5, H6a, H6b), 3.58 (dd, 1H, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 9.6 Hz, H2); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.1, 138.4, 138.1 (3s, 4C, C-ar), 128.8, 128.7, 128.4, 128.3, 128.2, 128.1, 128.0 (7s, 20C, CH-Ar), 123.8 (q, 1C, $^1J_{C,F}$ = 278.7 Hz, CF_3), 98.1 ($^1J_{C,H}$ = 169.4 Hz, C1), 81.9 (C3), 80.0 (C2), 77.6 (C4), 76.1, 75.5, 73.9, 73.7 (4s, 4C, CH_2-Ar), 71.3 (C5), 68.5 (C6), 65.0 (q, 1C, $^2J_{C,F}$ = 38 Hz, *C*H_2CF$_3$); ^{19}F NMR (376.24 MHz, $CDCl_3$): δ −74.0 (*C*F_3); MS (ESI, positive mode) *m/z* : 645.3 $[M+Na]^+$ (100%).

Compound **27β:** white needles, Mp 94–96 °C (petroleum ether); R_f = 0.41, CH_2Cl_2; $[\alpha]_D^{20}$ +8.4 (*c* 0.38, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34–7.26 (m, 18H, Ph), 7.16–7.12 (m, 2H, Ph), 4.93 (d, 1H, *J* = 10.9 Hz, C*H*$_2$-Ph), 4.92 (d, 1H, *J* = 10.7 Hz, C*H*$_2$-Ar), 4.81 (d, 1H, *J* = 10.7 Hz, C*H*$_2$-Ar), 4.78 (d, 1H, *J* = 10.9 Hz, C*H*$_2$-Ar), 4.68 (d, 1H, *J* = 10.7 Hz, C*H*$_2$-Ar), 4.60 (d, 1H, *J* = 12.3 Hz, C*H*$_2$-Ar), 4.53 (d, 1H, *J* = 12 Hz, C*H*$_2$-Ar), 4.52 (d, 1H, *J* = 10.7 Hz, C*H*$_2$-Ar), 4.50 (d, 1H, $J_{1,2}$ = 7.5 Hz, H1), 4.21 (dq, 1H, $^2J_{H,H}$ = 12.3 Hz, $^3J_{H,F}$ = 9 Hz, C*H*$_2$CF$_3$), 3.96 (dq, 1H, $^2J_{H,H}$ = 12.3 Hz, $^3J_{H,F}$ = 9 Hz, C*H*$_2$CF$_3$), 3.70 (m, 2H, H6a, H6b), 3.62 (m, 2H, H3, H4), 3.50 (br t, 1H, *J* = 7.8 Hz, H2), 3.45 (m, 1H, H5); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 138.8, 138.32, 138.28 (3s, 4C, C-Ar), 128.8, 128.7, 128.3, 128.2, 128.1, 128.1, 128.0 (7s, 20C, CH-Ar), 124.2 (q, 1C, $^1J_{C,F}$ = 278.3 Hz, CF_3), 104.1 ($^1J_{C,H}$ = 160.5 Hz, C_1), 84.8 (C3 or C4), 82.1 (C_2), 77.8 (C3 or C4), 76.2, 75.5 (2s, 2C, CH_2-Ar), 75.4 (C5), 75.3, 73.9 (2s, 2C, CH_2-Ar), 69.0 (C6), 66.4 (q, 1C, $^2J_{C,F}$ = 34.5 Hz, *C*H_2CF$_3$); ^{19}F NMR (376.24 MHz, $CDCl_3$): δ −74.55 (*C*F_3); MS (ESI, positive mode) *m/z* : 645.3 $[M+Na]^+$ (100%).

3.13. (Methoxycarbonyl)methylene β-D-glucopyranoside (28β)

Compound **13β** (130 mg) dissolved in 3 mL MeOH containing catalytic NaOMe was stirred for 1 h. After neutralization with a cation exchange resin (Amberlite IR-120, H^+ form), washing the resin with MeOH and evaporation of the volatiles, the residue was applied to silica gel chromatography (EtOAc–MeOH, 3:1, *v*/*v*) to afford **28β** (52 mg, 79%) as a colourless oil.[42] R_f = 0.53 (EtOAc–MeOH, 2:1, *v*/*v*); $[\alpha]_D^{20}$ −51.7 (*c* 1, CH_3OH); ^{1}H NMR (300 MHz, CD_3OD): δ 4.48 (d, 1H, *J* = 16.3 Hz, OC*H*$_2$C=O), 4.37 (d, 1H, $J_{1,2}$ = 7.6 Hz, H1), 4.34 (d, 1H, *J* = 16.3 Hz, OC*H*$_2$C=O), 3.87 (m, 1H, H6a), 3.77 (s, 3H, OC*H*$_3$), 3.66 (m, 1H, H6b), 3.42–3.23 (m, 4H, H2, H3, H4, H5); ^{13}C NMR (75 MHz, CD_3OD): δ 173.2 (CH_3CO), 104.4 (C1), 78.6, 78.1, 75.3, 71.9 (4s, 4C, C2, C3, C4, C5), 67.0 (OCH_2C=O), 63.1 (C6), 53.0 (OCH_3); MS (ESI, positive mode) *m/z* : 275.0 $[M+Na]^+$, 526.7 $[2M+Na]^+$; Anal. Calcd for $C_9H_{16}O_8$ (MW 252.22): C, 42.86; H, 6.39. Found C, 42.33; H, 6.69.

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