Stereoselective 2-Deoxy-β-*O*-glycoside Synthesis Based on Remote Activation of Novel Oxathiine Donors

Alessandra Bartolozzi,[a] Giuseppe Capozzi,*[a] Stefano Menichetti,[b] and Cristina Nativi*[a]

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Stable glyco-fused 1,4-oxathiine derivatives, prepared by inverse electron-demand Diels–Alder reactions between suitable 1-glycals and 3-thioxopentane-2,4-dione, have been transformed into unusual glycosyl donors which, after "remote activation", react efficiently with glycosyl acceptors to afford 2-thio-β-*O*-glycosides with total stereoselectivity. Several *O*-nucleophiles were successfully glycosylated. Reductive removal of sulfur transformed the 2-thio-β-*O*-glycosides into the corresponding 2-deoxy-β-*O*-glycosides without affecting the stereochemistry of the anomeric carbon atom.

Introduction

The important role played by complex glycosyl derivatives such as oligosaccharides, glycolipids, and glycoproteins in cell surface recognition and cellular communication processes is well known and documented.[1−3] It is evident that a great effort has been devoted to optimization of *O*-glycosidation reactions as a key step towards obtaining these challenging molecules. Two determining features in glycosidation reactions are the availability of glycosyl donors that are stable during synthetic manipulations but efficiently triggered when needed and the achievement of a good level of stereocontrol in the formation of the anomeric linkage.

Elegant glycosidation reactions, affording enantiomerically enriched or enantiomerically pure glycosides, have been reported recently.[4−7] However, very few of them have been successfully employed in the preparation of 2-deoxyglycosides, a class of relevant compounds that includes aureolic acid, cardiac glycosides, and orthosomycines.[8−10] As a point of fact, the lack of assistance from proximal substituents and the low stability of donors make the stereoselective preparation of 2-deoxyglycosides, particularly the β-anomer, a real challenge. Although no general methodology suitable for the synthesis of 2-deoxysugars exists, one common strategy fruitfully employed for the stereoselective glycosidation of several glycon moieties consists of the introduction of a temporary participating group at the C-2 position of the donor. Easily removable species, such as halo, thiophenyl, or selenophenyl groups, have generally been chosen, resulting in the corresponding 2-deoxyglycosides as major or exclusive products. However, this strategy becomes unsatisfactory when C-2 substituted donors are too reactive, difficult to handle, or give limited anchimeric assistance.[11−13]

As we recently reported, a variety of glycals undergo cycloaddition under mild conditions with the electron-poor 3-thioxopentane-2,4-dione, to give the corresponding 1,2-glycofused 1,4-oxathiins **1**−**4** with total regioselectivity and remarkable stereoselectivity,[14,15] and in high yields (Figure 1).

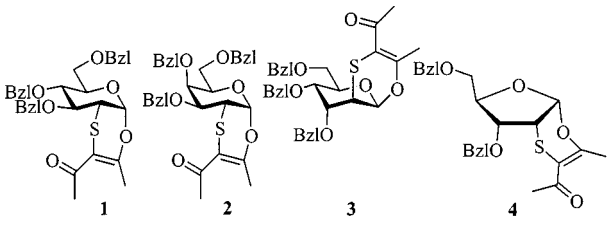

Figure 1. 1,2-Glycofused 1,4-oxathiins **1**−**4**

Cycloadducts **1**−**4** present some noteworthy features: (i) a reactive enole oxygen atom at C-1, (ii) an easily removable sulfur atom at C-2 of the sugar moiety, and also (iii) an oxathiine ring fused to the monosaccharide, which could provide anchimeric assistance favoring the attack of a glycosyl acceptor "*anti*" with respect to the oxathiine unit. These unique features prompted us to view these bicyclic 2-deoxy-2-thio-α-*O*-glycosides as potential donors for stereoselective glycosyl transfer. In this paper we report a new strategy for achieving 2-thio-2-deoxy-β-*O*-glycosides with total stereoselectivity, proceeding by "remote activation"[5,16] and glycosidation of glyco-fused 1,4-oxathiine derivatives quantitatively obtained from **1** and **2**. Subsequent desulfurization of the 2-thio-β-*O*-glucosides obtained resulted in the formation of the corresponding 2-deoxy-β-*O*-glucosides (Scheme 1).

Results and Discussion

We have already reported[14,15] that 3,4,6-tri-*O*-benzylglucal and 3,4,6-tri-*O*-benzylgalactal reacted with the phthali-

[a] Centro CNR "Chimica dei Composti Eterociclici", Dipartimento di Chimica Organica, Università di Firenze
Via Gino Capponi 9, 50121 Firenze, Italy
Fax: (internat.) + 39-055/247-6964
E-mail: capozzi@chimorg.unifi.it
nativi@chimorg.unifi.it
[b] Dipartimento di Chimica Organica e Biologica, Università di Messina,
Salita Sperone 31, 98166, Messina, Italy
Fax: (internat.) + 39-090/393895

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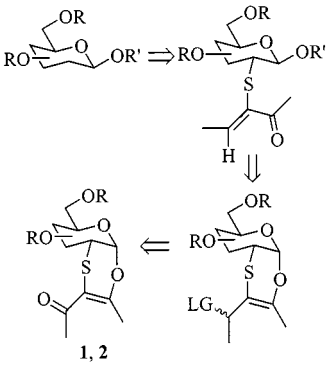
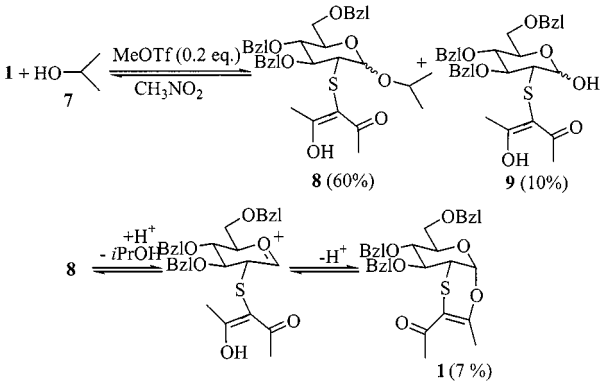
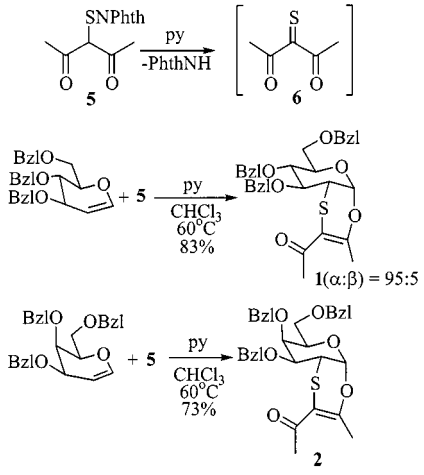


Scheme 1. Retrosynthetic scheme for 2-deoxy-β-*O*-glycosides synthesis



Scheme 3. Synthesis of **8**

mide derivative **5**[14,17,18] in the presence of pyridine or lutidine to form the corresponding cycloadducts **1** and **2**, with total regioselectivity and either high (**1**: α/β = 95:5)[15] or total stereoselectivity[14] (Scheme 2).



Scheme 2. Synthesis of cycloadducts **1** and **2**

In the presence of a weak base, the phthalimido derivative **5** generated the reactive electron-poor diene **6** (Scheme 2), which was trapped by electron-rich dienophiles such as tri-*O*-benzylglucal or tri-*O*-benzylgalactal. As expected,[19,20] preferential attack of the diene from the bottom face of the double bond of the dienophiles gave the α-cycloadducts **1** and **2**. These α-*O*-glycosides **1** and **2**, obtained as crystalline compounds by flash chromatography on silica gel, appeared suitable to be "activated" with protic or Lewis acids and then treated with acceptors for selective β-glycosyl transfer. In the first attempt, **1** was treated at room temperature in nitromethane with catalytic amounts of methyl triflate and an excess of 2-propanol (**7**) as acceptor.[21] The reaction was very slow, with starting material still present after 23 h. After this period, ^{1}H NMR analysis of the crude products revealed the presence of the expected *O*-glycoside **8** (60%), unchanged cycloadduct **1** (10%), and of hydrolyzed product **9** (10%) (Scheme 3).

The diagnostic signals of the enol protons at δ = 17.12 (α anomer) and δ = 16.97 (β anomer), together with those of the isopropyl moiety at δ = 1.19 (CH *i*Pr) and δ = 1.28 (2 CH_3 *i*Pr) enabled compound **8** to be structurally elucidated; it was formed as mixture of **8α/8β** isomers in a 10:1 ratio. To ascertain the cause of the observed lack of selectivity and the presence of residual reactant even after prolonged reaction times, we repeated the treatment of **1** with **7** in the presence of different promoters, and also under different reaction conditions. Mixtures of α and β anomers were generally formed; moreover, small quantities (7−13%) of starting material were, without exception, detected in the crude mixtures (Table 1).

As reported in Table 1, the best results were obtained with 0.2 equiv. of trimethylsilyl triflate as promoter (Entry 1). The use of 1.0 equiv. of the same promoter permitted exclusive formation of the α isomer, but **8** was isolated in poor yields since decomposition of starting material also occurred (Entry 2). Trifluoromethanesulfonic acid (triflic acid) (Entry 4) gave the same selectivity as obtained with trimethylsilyl triflate (see Entry 1), with comparable yields (68%). A remarkable degree of decomposition of starting material was also observed when the glycosidation was performed in the presence of *p*-toluenesulfonic acid (Entry 5). As mentioned for trimethylsilyl triflate (see Entry 2), methanesulfonic acid afforded **8** with good selectivity but in low yields (Entry 9). All the other promoters tested (trifluoroacetic anhydride, trifluoroacetic acid, aluminum trichloride, and titanium tetraisopropoxide) gave no interesting results, since the formation of side products was predominant or exclusive. In dichloromethane, as expected,[22] a slower reaction and a reversed α/β ratio were observed (Entry 3); indeed, after 23 h, the ^{1}H NMR spectrum of the crude mixture showed the formation of **8** in 1:8 α/β ratio and with 40% of starting material still unchanged.

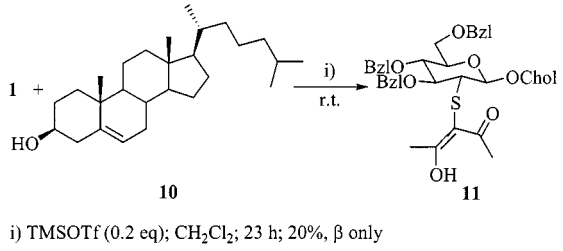
The presence of small quantities of starting material always detected with glycosyl derivative **8** suggested that the reaction depicted in Scheme 3 might be an equilibrium. This was tested by treating *O*-glycoside **8** in nitromethane with a catalytic amount of trimethylsilyl triflate (Scheme 3). After 23 h at room temperature, the ^{1}H NMR spectrum of the crude mixture clearly showed the formation of cycload-

Table 1. Treatment of cycloadduct **1** (1.0 equiv.) and 2-propanol (**7**) (2.0 equiv.) with different promoters in nitromethane

Entry	Promoter[a]	Equiv.	React. time (h)	Temp. (°C)	α/β ratio[b]	Yield of **7** (%)[c]
1	TMSOTf	0.2	23	25	9:1	75
2	TMSOTf	1.0	23	25	α	31[d]
3	TMSOTf	0.2	23	25	1:8	30[e]
4	TfOH	0.2	23	25	9:1	68
5	TsOH	0.2	23	−20 to 5	1:2	30[d]
6	$BF_3{\cdot}OEt_2$	0.2	23	25	3.5:1	49[d]
7	$TiCl_4$	0.2	23	25	1:2	trace[d]
8	$TiCl_4$	1.0	40	−20 to 5	–	< 15[d]
9	$MeSO_3H$	0.2	48	25	> 10:1	40[d]

[a] Other promoters, used unsuccessfully, are not reported. – [b] Estimated from the ^1H NMR signal ratio of the crude mixture. – [c] Isolated yields. – [d] Decomposition of starting material was observed. – [e] In CH_2Cl_2 as solvent.

duct **1** (7%), which had probably derived from the intramolecular attack of the enole oxygen atom of an intermediate oxonium ion onto the anomeric carbon atom. Glycosyl transfer on the basis of the cleavage of the anomeric carbon−oxygen bond of **1** was extended to more hindered glycosyl acceptors such as cholesterol (**10**) (Scheme 4).

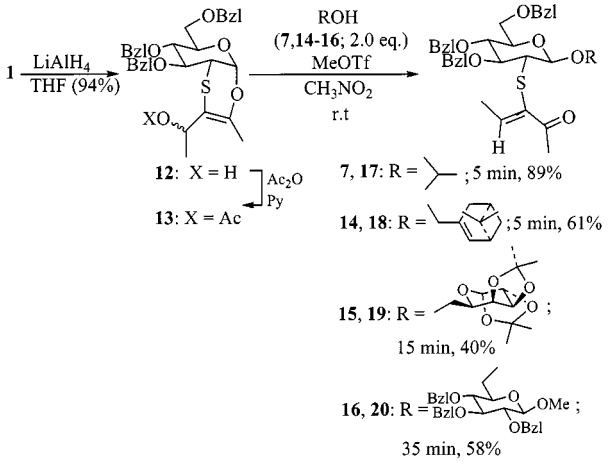


Scheme 4. Synthesis of **11**

As shown in Scheme 4, this reaction afforded the corresponding β-*O*-glycoside **11**[23] as a single product, but in disappointing low yields. Cycloadduct **1** (40%) was also recovered from the reaction mixture in this case.

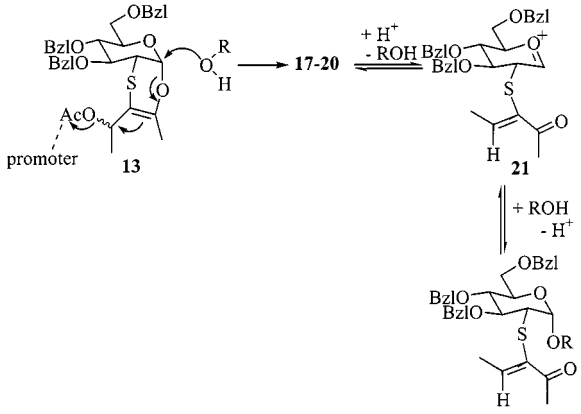
Since glycosyl transfer of cycloadduct **1** was not satisfactory, we tried to achieve "remote activation"[5,16] of the anomeric group.[21,24] Conversion of the α,β-unsaturated ketone into an allyl acetate would produce a system suitable to undergo remotely triggered substitution at the anomeric carbon atom.

Reduction of **1** with $LiAlH_4$ selectively afforded the allyl alcohol **12** (94%), which was then acetylated with acetic anhydride under standard conditions to give the allyl acetate **13** in quantitative yield. After removal of pyridine and excess of acetic anhydride under vacuum, the unusual donor **13** was treated, without further purification, with the appropriate acceptors **7** and **14**−**16** in the presence of a catalytic amount of methyl triflate. The reactions were performed in dry nitromethane at room temperature and quenched with pyridine on the turning of the color of the mixture from pale yellow to reddish, affording the β-glycosides **17**−**20**[25] (Scheme 5).



Scheme 5. Synthesis of 2-deoxy-2-thio-β-*O*-glycosides **17**−**20**

The timing of quenching is crucial for the success of β-glycosidation: the color change practically indicates the beginning of isomerization from β to α. The time at which this occurs depends on the individual glycoside (from 5 min for **17** to 35 min for **20**). Thus, a single glycosidation reaction can provide either anomer by careful tuning of the reaction time.[26] Attempts to use the alcohol **12** as the donor



Scheme 6. Oxonium ion **21** generation

for "remote activation"[5,16] did not afford the desired glycosides,[27] while use of a better leaving group than acetyl (mesyl) made the starting material highly unstable.

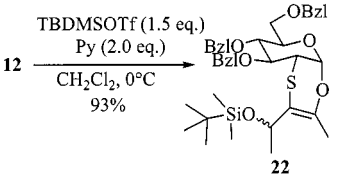
In contrast to **1**, the total β-stereoselectivity of glycosidation of **13** could be due to the higher reactivity of the acetate: the developing positive charge induced on **13** by the catalyst might be trapped by the acceptor before ring-opening of the oxathiine, as shown in Scheme 6, permitting a β-stereospecific glycosidation. Subsequent α,β-equilibration presumably proceeds through an oxonium intermediate **21** (Scheme 6), analogously to that giving rise to the product mixture in the glycosidation of the ketone **1**.

A further improvement on this glycosylation methodology was achieved by transforming the alcohol **12** into the corresponding *tert*-butyldimethylsilyl derivative **22**, which, unlike the acetate **13**, can be purified by column chromatography on silica gel and stored at −4 °C for several days without decomposition. Compound **22** was obtained by treating **12** with *tert*-butyldimethylsilyl triflate at 0 °C in dry dichloromethane in the presence of an excess of pyridine. The reaction was complete within 10 min and the crude diastereomeric mixture was purified by column chromatography on silica gel to give **22** (93%) (Scheme 7).

Although each diastereomer was perfectly separable by column chromatography, **22** was used as a diastereomeric mixture, since this did not influence the subsequent glycosidation. The silyl derivative **22** was treated with different O-nucleophiles (**14**, **16**, **23**, and **24**), in dry dichloromethane as solvent[28] and with trimethylsilyl triflate as promoter, to afford the corresponding β-*O*-glycosides (**18**, **20**, **25**, and **26**) in reasonable to good yields and with total stereoselectivity. Reaction conditions and yields are reported in Table 2.

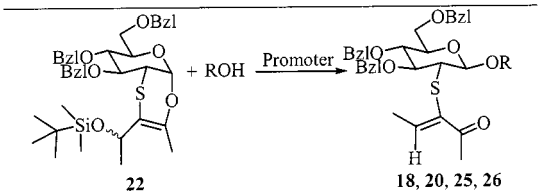
This methodology was successfully extended to the donor silyl derivative **27**, which in turn was obtained from the galacto derivative **2** as reported for **22** (see Scheme 7). Treatment of **27** with 2 equiv. of (1*R*,2*S*,5*R*)-(−)-menthol (**23**) afforded the 2-deoxy-2-thio-β-*O*-glycoside **28** in good yield (68%) and with total stereoselectivity (Scheme 8).

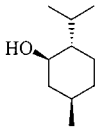
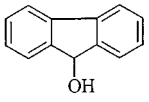
The thiosubstituted glycosides **17**−**20**, **25**, and **26** were readily transformed into the corresponding 2-deoxy-β-*O*-



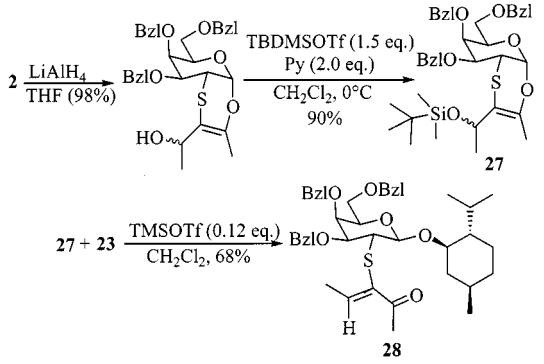
Scheme 7. Synthesis of silyl derivative **22**

Table 2. Glycosidation of **22** with acceptors **14**, **16**, **23**, and **24**



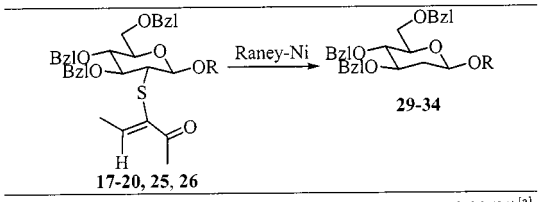
Entry	Acceptor	Solvent	Promoter (equiv.)	React. time (min)	Yield (%)[a]
1	**14**	CH_2Cl_2	0.02	5	39
2	**16**	CH_2Cl_2	0.13	15	38
3	 **23**	CH_2Cl_2	0.02	5	68
4	 **24**	CH_2Cl_2	0.12	25	52

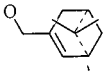
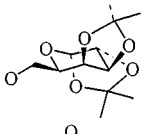
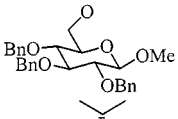
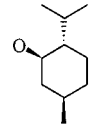
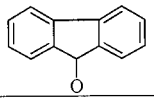
[a] Isolated yields.



Scheme 8. Syntheses of silyl derivative **27** and of 2-deoxy-2-thio-β-*O*-glycoside **28**

Table 3. Desulfurization of **17**−**20**, **25**, **26** with Raney nickel



Entry	Compound	OR	Product	Yield (%)[a]
1	**17**		**29**	67
2	**18**		**30**	69
3	**19**		**31**	51
4	**20**		**32**	56
5	**25**		**33**	65
6	**26**		**34**	67

[a] Isolated yields.

glycosides **29**−**34** by desulfurization with Raney nickel. Compounds obtained and reaction yields are reported in Table 3.

All reactions were performed in wet THF, using commercially available activated Raney nickel, with yields comparable to those reported in the literature.[24,29] The use of different solvents (benzene or ethanol) and of different desulfurizing agents ($NiCl_2/NaBH_4$[30] or NICRA[31]) for the synthesis of the 2-deoxydisaccharides **31**[20] (51%) and **32** (56%) produced no substantial improvements in yields.

Conclusions

These results clearly indicate that the acetate **13** and the silyl ether **22**, readily available with the aid of trivial and quantitative chemical transformations, are effective new donors for the stereospecific synthesis of 2-deoxy-2-thio-β-*O*-glycosides. The glycosidation, based on "remote activation" of **13** and **22**, was successfully accomplished with several acceptors and was fruitfully extended to the galacto derivative **27**. Desulfurization of 2-thio-β-*O*-glycosides **17**−**20**, **25**, and **26** readily afforded the corresponding 2-deoxy-β-*O*-glycosides **29**−**34**, useful precursors for a wide number of biologically important molecules. The extension of this method to the synthesis of 2-deoxyoligosaccharides is currently under investigation in our laboratories.

Experimental Section

General Remarks: Solvents were purified and dried according to standard procedures. All reactions were performed under nitrogen in dry solvents unless otherwise stated. − TLC was performed on glass-backed silica gel (Macherey−Nagel, Durasil-25-UV_{254}). Detection was effected by treatment with a solution of vanillin (3 g) and H_2SO_4 (4 mL) in EtOH (250 mL). − Flash chromatography was carried out on silica gel (Macherey−Nagel, 60M). Petroleum ether used was of the boiling range 35−70 °C; EtOAc was distilled before use. − $CHCl_3$ was washed with water and dried with $CaCl_2$ before use. − Optical rotations were determined at 25 °C with a Jasco DIP-370 polarimeter (1-dm cell). − NMR spectra were recorded with a Varian Gemini 200 instrument using $CDCl_3$ as solvent for ^1H NMR and ^{13}C NMR ($\delta_H = 7.26$ and $\delta_C = 77.0$, respectively) as reference. − Melting points are uncorrected and were recorded with a Büchi 510 apparatus. − Elemental analyses were performed with a Perkin−Elmer Elementary Analyzer 2400 Series II.

General Procedure for the Synthesis of *O*-Glycosides 8, 11: Compound **1** was dissolved in dry solvent (1 mL, 0.1 mmol) under N_2. Acceptor (2.0 equiv.) and TMSOTf (0.2 equiv.) were added at room temperature; the mixture was stirred for 20 h, then quenched with 2 drops of pyridine. The crude product was purified by flash chromatography on silica gel.

Isopropyl 2-*S*-(1′-Acetyl-2′-hydroxypropenyl)-3,4,6-tri-*O*-benzyl-2-thio-α/β-D-glucopyranoside (8): This compound was obtained according to the general procedure; compound **1** (53.7 mg, 0.10 mmol) and 2-propanol, after 23 h in dry CH_3NO_2, afforded **8** (39.7 mg, 75%) as a pale yellow oil (α/β = 9:1). Unreacted starting material (10 mg, 18%) and hydrolyzed product **9** (8%) were also isolated. − TLC (petroleum ether/EtOAc, 4:1): $R_f = 0.8$. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.19 (d, J = 8.0 Hz, 3 H), 1.28 (d, J = 8.0 Hz, 3 H), 2.40 (s, 3 H, CH_3CO_α), 2.42 (s, 3 H, CH_3CO_β), 2.81 (dd, $J_{2,3}$ = 12.0, $J_{1,2}$ = 4.0 Hz, 1 H, 2_α-H), 2.87 (dd, $J_{2,3}$ = 10.0, $J_{1,2}$ = 8.0 Hz, 1 H, 2_β-H), 3.41−3.96 (m, 6 H, 6_a-H, 6_b-H, 3-H, 4-H, 5-H, CH *i*Pr), 4.48−4.99 (m, 7 H, 1-H, 3 CH_2Ph), 7.08-7.42 (m, 15 H), 16.97 (s, 1 H, OH_β), 17.12 (s, 1 H, OH_α). − ^{13}C NMR ($CDCl_3$, 50 MHz) of α anomer: δ = 21.1, 23.2, 24.9, 57.1 (C-2), 68.3 (C-6), 69.7 (CH *i*Pr), 70.8 (C-3), 73.5, 75.1, 75.7, 79.8 (C-4), 80.4 (C-5), 96.8 (C-1), 104.5, 127.1, 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.3, 128.4, 137.8, 137.9, 138.4, 197.7. − $C_{35}H_{42}O_7S$ (606.8): calcd. C 69.28, H 6.98; found C 69.07, H 6.97.

Cholesteryl 2-*S*-(1′-Acetyl-2′-hydroxypropenyl)-3,4,6-tri-*O*-benzyl-2-thio-β-D-glucopyranoside (11): This compound was obtained according to the general procedure; compound **1** (51 mg, 0.09 mmol) and **10** (69.4 mg, 0.18 mmol), after 23 h in dry CH_2Cl_2, afforded **11** (16 mg, 20%) as a β anomer, together with unchanged starting material (20 mg, 40%). − TLC (petroleum ether/EtOAc, 8:1): R_f = 0.6. − Yellowish oil ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.85 (s, 6 H), 0.90−2.40 (m, 38 H), 2.43 (s, 6 H), 2.89 (dd, $J_{1,2}$ = 8.0, $J_{2,3}$ = 10.0 Hz, 1 H, 2-H), 3.41−3.69 (m, 6 H, 3-H, 4-H, 5-H, 6_a-H, 6_b-H, 1-H_{Chol}), 4.49−4.87 (m, 7 H, 1-H, 3 CH_2), 5.30−5.34 (m, 1 H), 7.15−7.37 (m, 15 H,), 16.97 (s, 1 H, OH). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 11.8, 18.7, 19.3, 21.0, 22.5, 22.8, 23.8, 24.3, 25.1, 28.0, 28.2, 29.4, 30.0, 31.8, 31.9, 35.7, 36.2, 36.8, 37.2, 37.7, 39.5, 39.7, 42.3, 50.2, 56.0, 56.1, 56.8 (C-2), 68.9 (C-6), 73.4 (C-3), 74.7, 74.8, 76.0, 77.3, 79.4 (C-4), 83.1 (C-5), 101.2 (C-1), 104.3, 122.1, 127.6, 127.7, 127.8, 127.9, 128.0, 128.4, 128.5, 137.9, 138.1, 138.2, 140.1, 196.7. − $C_{59}H_{80}O_7S$ (933.3): calcd. C 75.93, H 8.64; found C 76.01, H 9.00.

Glucopyranoside Derivative 12: $LiAlH_4$ (8.7 mg, 0.23 mmol) was added to an ice-cooled solution of **1** (250 mg, 0.46 mmol) in dry THF (2.5 mL). After 30 min, the reaction was complete; the mixture was diluted with CH_2Cl_2 and washed at 0 °C with a saturated solution of NH_4Cl (3 × 10 mL). The organic phase was dried with anhydrous Na_2SO_4, concentrated, and purified by column chromatography on silica gel (petroleum ether/AcOEt, 3:1), affording **12** (237 mg, 94%) as a mixture of two diastereoisomers. − TLC (petroleum ether/EtOAc, 3:1): R_f = 0.6, 0.5. − Pale yellow oil. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.36 (d, J = 6.6 Hz, 3 H), 1.55 (bd, 1 H, OH), 1.65 (bd, 1 H, OH), 1.99 (s, 3 H), 3.22 (dd, $J_{2,3}$ = 10.0, $J_{1,2}$ = 3.0 Hz, 1 H, 2-H), 3.67−3.84 (m, 4 H, 3-H, 4-H, 6_a-H, 6_b-H), 3.99 (m, 1 H, 5-H), 4.51−5.04 (m, 7 H), 5.53 (d, $J_{1,2}$ = 3.0 Hz,1 H, 1-H), 7.14−7.40 (m, 15 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 17.5, 22.0, 41.9 (C-2), 72.4 (C-6), 73.4, 75.1, 76.1, 66.1, 68.1, 78.1, 78.5, 94.81 ($C\text{-}1_A$), 94.82 ($C\text{-}1_B$), 102.4, 127.6, 127.7, 127.8, 127.9, 128.3, 137.7, 137.8, 138.2, 144.1. − $C_{32}H_{36}O_6S$ (548.7): calcd. C 70.05, H 6.61; found C 69.93, H 6.65.

Glucopyranoside Derivative 13: Ac_2O (51.5 μL, 0.55 mmol) and pyridine (43 μL, 0.55 mmol) were added to a solution of **12** (149.5 mg, 0.27 mmol) in dry CH_2Cl_2 (2.0 mL), followed by a catalytic amount of DMAP. After 15 h, the solution was filtered and the solvent evaporated to afford the acetyl derivative **13** (160 mg, 97%) as a mixture of diastereoisomers, which was used without any other purification. − Pale yellow oil. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.40 (d, J = 6.6 Hz, 3 H), 2.02 (s, 3 H), 2.07 (s, 3 H), 3.15−3.24 (m, 1 H, 2-H), 3.67−3.82 (m, 4 H, 3-H, 4-H, 6_a-H, 6_b-H), 3.95 (m, 1 H, 5-H), 4.48−5.05 (m, 6 H), 5.53 (d, $J_{1,2}$ = 3.0 Hz, 1 H, 1-H), 5.78 (bq, J = 6.6 Hz, 1 H, 1′′-H), 7.11−7.44 (m, 15 H).

General Procedure for the Synthesis of β-*O*-Glycosides 17−20 (Procedure A): Compound **13** was dissolved in dry solvent (1 mL,

0.1 mmol) under N_2; acceptor (2.0 equiv.) and MeOTf were added. After 5 min at room temperature, the reaction was quenched with a few drops of pyridine. The crude product was purified by flash chromatography on silica gel.

Isopropyl 2-*S*-(1′-Acetyl-2′-methylethenyl)-3,4,6-tri-*O*-benzyl-2-thio-β-D-glucopyranoside (17): This compound was obtained according to Procedure A; compounds **13** (48 mg, 0.08 mmol) and **7**, with MeOTf (0.4 equiv. in CH_2Cl_2; 0.2 equiv. in CH_3NO_2), afforded **17** (67% in CH_2Cl_2; 89% in CH_3NO_2) as a pale yellow oil. − TLC (petroleum ether/EtOAc, 4:1): R_f = 0.4. − $[\alpha]_D^{25}$ = −54.8 (*c* = 0.25, $CHCl_3$). − IR (neat): $\tilde{\nu}$ = 3030, 2972, 1677, 1570 cm^{-1}. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.13 (d, *J* = 6.0 Hz, 3 H), 1.22 (d, *J* = 6.0 Hz, 3 H), 2.09 (d, *J* = 7.0 Hz, 3 H), 2.38 (s, 3 H), 3.34 (dd, $J_{2,3}$ = 10.6, $J_{1,2}$ = 8.4 Hz, 1 H, 2-H), 3.42−3.77 (m, 5 H, 3-H, 4-H, 5-H+ 6_a-H, 6_b-H), 3.92−4.05 (m, 1 H), 4.41−4.92 (m, 7 H, 1-H + 3 CH_2Ph), 6.90 (q, *J* = 7.0 Hz, 1 H), 7.16−7.48 (m, 15 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 17.2, 21.7, 24.0, 27.6, 52.4 (C-2), 69.0, 70.9, 73.4, 74.7 (C-4), 74.8 (C-6), 79.3 (C-3), 83.5 (C-5), 102.8 (C-1), 128.1, 128.2, 128.3, 128.4, 128.8, 128.9, 138.5, 138.7, 139.6, 142.0, 196.9. −$C_{35}H_{42}O_6S$ (590.8): calcd. C 71.16, H 7.17; found C 70.91, H 7.20.

Mirtenyl 2-*S*-(1′-Acetyl-2′-methylethenyl)-3,4,6-tri-*O*-benzyl-2-thio-β-D-glucopyranoside (18): This compound was obtained according to Procedure A; compounds **13** (96.5 mg, 0.16 mmol) and **14**, with MeOTf (0.6 equiv.) in dry CH_3NO_2, afforded **18** (67 mg, 61%) as a pale yellow oil. − TLC (petroleum ether/EtOAc, 3:1): R_f = 0.6. − $[\alpha]_D^{25}$ = −44.4 (*c* = 0.38, $CHCl_3$). − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.82 (s, 3 H, CH_3 mirt.), 0.91 (d, *J* = 6.0 Hz, 1 H), 1.17 (d, *J* = 8.0 Hz, 1 H), 1.25 (s, 3 H, CH_3), 2.08 (d, *J* = 6.8 Hz, 3 H), 2.24−2.42 (m, 5 H), 3.28 (dd, $J_{1,2}$ = 10.0, $J_{2,3}$ = 8.0 Hz, 1 H, 2-H), 3.41−3.70 (m, 5 H, 3-H, 4-H, 5-H, 6_a-H, 6_b-H), 3.81−4.16 (AB part of an ABX system, J_{AB} = 12.0 Hz, J_{AX} = J_{BX} = 2.0 Hz, 2 H), 4.37 (d, $J_{1,2}$ = 10.0 Hz, 1 H, 1-H), 4.50−4.89 (m, 6 H, 3 CH_2Ph), 5.45 (m, 1 H), 6.94 (q, *J* = 6.0 Hz, 1 H), 7.13−7.44 (m, 15 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 16.8, 21.1, 26.1, 27.0 (4 CH_3), 31.2 [*C*-$(CH_3)_2$], 31.6, 37.9, 40.8, 43.3, 52.7 (C-2), 68.8 (CH_2), 71.9, 73.4, 74.8 (C-4), 75.0 (C-6), 78.8 (C-3), 83.1 (C-5), 103.4 (C-1), 112.3 (Cq), 119.7, 127.5, 127.7, 127.9, 128.2, 128.3, 128.4, 138.0, 138.3, 142.8, 144.2 (Cq). − $C_{42}H_{50}O_6S$ (682.9): calcd. C 73.87, H 7.38; found C 73.29, H 7.55.

6-[2-*S*-(1′-Acetyl-2′-methylethenyl)-3,4,6-tri-*O*-benzyl-2-thio-β-D-glucopyranosyl]-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (19): This compound was obtained according to Procedure A; compounds **13** (130 mg, 0.22 mmol) and **15**, with MeOTf (0.2 equiv.) in dry CH_3NO_2, afforded **19** as a pale yellow oil (β/α = 12:1). Column chromatography exclusively yielded **19** (70 mg, 40%) as the β anomer. − TLC (petroleum ether/EtOAc, 4:1): R_f = 0.4. − IR(-neat): $\tilde{\nu}$ = 3033, 2935, 1680, 1598, 1452 cm^{-1}. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.31 (s, 3 H, CH_3), 1.34 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3), 1.45 (s, 3 H, CH_3), 2.09 (d, *J* = 6.0 Hz, 3 H), 2.37 (s, 3 H, CH_3CO), 3.25−4.91 (m, 18 H), 4.41 (d, $J_{1,2}$ = 7.6 Hz, 1 H, 1-H), 5.51 (d, *J* = 4.8 Hz, 1 H), 7.02 (q, *J* = 5.8 Hz, 1 H, 2′-H), 7.14−7.46 (m, 15 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 16.9, 25.0, 26.0, 26.1, 27.1, 52.3 (C-2), 67.1, 68.7, 68.8, 70.4, 70.6, 71.4, 73.5, 74.80, 74.84, 78.5, 83.0, 96.2, 104.5 (C-1), 109.1 (2 C_q), 127.4, 127.5, 127.7, 127.8, 127.9, 128.3, 128.4, 137.7, 138.1, 138.4, 144.3, 196.9. $C_{44}H_{54}O_{11}S$ (791.0): calcd. C 66.81, H 6.88; found C 66.92, H 6.83.

Methyl 6-*O*-[2-*S*-(1′-Acetyl-2′-methylethenyl)-3,4,6-tri-*O*-benzyl-2-thio-β-D-glucopyranosyl]-2,3,4-tri-*O*-benzyl-β-D-glucopyranoside (20): This compound was obtained according to Procedure A; compounds **13** (102 mg, 0.17 mmol) and **16**, with MeOTf (0.4 equiv.) in dry CH_3NO_2, afforded **20** (99 mg, 58%) as a white solid. − TLC (petroleum ether/EtOAc, 4:1): R_f = 0.2. − M.p. 98−100 °C. − $[\alpha]_D^{25}$ = −7.1 (*c* = 0.3, $CHCl_3$). − ^1H−NMR ($CDCl_3$, 200 MHz): δ = 2.05 (d, *J* = 8.0 Hz, 3 H), 2.27 (s, 3 H), 3.30−3.75 (m, 14 H), 3.96 (m, 1 H), 4.33 (d, *J* = 8.0 Hz, 1 H), 4.44−4.97 (m, 13 H, 1-H, 6 CH_2), 6.80 (q, *J* = 6.0 Hz, 1 H), 7.11−7.37 (m, 30 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 16.7, 26.9, 52.1 (C-2), 57.2, 68.2, 68.7, 73.5, 74.6, 74.7, 74.9, 75.1, 74.8, 74.9, 78.2, 78.6, 82.1, 83.2, 84.6, 104.3, 104.4, 127.5, 127.6, 127.8, 127.9, 128.0, 128.1, 128.2, 128.4, 138.0, 138.1, 138.3, 138.5, 138.6, 138.9, 141.4, 196.7. − $C_{60}H_{66}O_{11}S$ (994.4): calcd. C 72.41, H 6.68; found C 72.42, H 6.90.

Glucopyranoside Derivative 22: Pyridine (46 μL, 0.60 mmol) was slowly added to an ice-cooled solution of **12** (160 mg, 0.30 mmol) in dry CH_2Cl_2 (2.0 mL), followed by dropwise addition of TBDMSOTf (103 μL, 0.45 mmol). The reaction was complete after 10 min. After dilution with CH_2Cl_2 (10 mL), the mixture was washed at 0 °C with a saturated solution of NH_4Cl (2 × 8 mL) and dried with anhydrous Na_2SO_4. Evaporation of the solvent and column chromatography on silica gel (petroleum ether/EtOAc, 3:1) afforded **22** (185 mg, 93%) as a mixture of two diastereoisomers (A/B = 1:3). − TLC (petroleum ether/EtOAc, 3:1): R_f = 0.7. − Pale yellow oil. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.06−0.10 (m, 6 H), 0.88−0.94 (m, 9 H), 1.39 (d, *J* = 6.6 Hz, 3 H), 1.91 (s, 3 H, CH_3CO_A), 1.99 (s, 3 H, CH_3CO_B), 3.16−3.30 (m, 1 H, 2-H), 3.69−3.87 (m, 4 H, 3-H, 4-H, 6_a-H, 6_b-H), 4.04−4.09 (m, 1 H, 5-H), 4.53−5.17 (m, 7 H), 5.45 (d, $J_{1,2}$ = 2.6 Hz, 1 H, 1_B-H), 5.52 (d, $J_{1,2}$ = 2.6 Hz, 1 H, 1_A-H), 7.15−7.48 (m, 15 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = −4.5 (CH_{3A}), −4.8 (CH_{3A}), −4.9 (CH_{3B}), −5.0 (CH_{3B}), 17.5, 18.0, 18.1 (tBu_A), 18.2 (tBu_B), 23.6, 24.0, 25.8, 41.7 ($C\text{-}2_B$), 43.0 ($C\text{-}2_A$), 67.5, 67.8, 68.2, 72.4 ($C\text{-}3_B$), 72.5 ($C\text{-}3_A$), 73.5, 75.2 (C-6), 78.4 ($C\text{-}4_A$), 78.6 ($C\text{-}4_B$), 78.9 ($C\text{-}5_B$), 79.3 ($C\text{-}5_A$), 94.6 (C-1), 104.6 ($C\text{-}2'_B$), 104.8 ($C\text{-}2'_A$), 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.3, 128.4, 137.8, 138.0, 138.3, 138.3, 140.0 ($C\text{-}1'_B$), 141.6 ($C\text{-}1'_A$). − $C_{38}H_{50}O_6SiS$ (662.9): calcd. C 68.84, H 7.60; found C 68.82, H 7.62.

General Procedure for the Synthesis of β-*O*-Glycosides 18, 20, 25, and 26 (Procedure B): Compound **22** was dissolved in dry CH_2Cl_2 (1 mL, 0.1 mmol) under N_2; acceptor (2.0 equiv.) and TMSOTf (CH_2Cl_2, 1 M) were added. After 5 min at room temperature, the reaction was quenched with a few drops of pyridine. The crude product was purified by flash chromatography on silica gel.

Compound 18: This compound was obtained according to Procedure B; compounds **22** (84 mg, 0.13 mmol) and **14**, in the presence of TMSOTf (0.02 equiv.), afforded **18** (34 mg, 39%) as a pale yellow oil.

Compound 20: This compound was obtained according to Procedure B; compounds **22** (34.5 mg, 0.05 mmol) and **16**, in the presence of TMSOTf (0.13 equiv.), afforded **20** (20 mg, 38%) as a yellow oil.

Menthyl 2-*S*-(1′-Acetyl-2′-methylethenyl)-3,4,6-tri-*O*-benzyl-2-thio-β-D-glucopyranoside (25): This compound was obtained according to Procedure B; compounds **22** (51.2 mg, 0.08 mmol) and **23**, in the presence of TMSOTf (0.017 equiv.), afforded **25** (36 mg, 68%) as a pale yellow oil. − TLC (petroleum ether/EtOAc, 4:1): R_f = 0.6. − $[\alpha]_D^{25}$ = +65 (*c* = 0.40, $CHCl_3$) . − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.72 (d, *J* = 10.0 Hz, 3 H), 0.78 (d, *J* = 6.0 Hz, 3 H), 0.85 (d, *J* = 8.0 Hz, 3 H), 0.90−1.19 (m, 1 H), 1.26−1.32 (m, 1 H), 1.40−1.62 (m, 2 H), 2.02 (d, *J* = 6.0 Hz, 3 H), 2.14−2.28 (m, 1 H), 2.31 (s, 3 H), 3.38−3.74 (m, 7 H, CH_2, 2-H, 3-H, 4-H, 5-H, $1\text{-}H_{Menth}$), 4.43 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1-H), 4.48−4.95 (m, 6 H, 3 CH_2), 6.78 (q, *J* = 8.0 Hz, 1 H), 7.15−7.45 (m, 15 H). − ^{13}C NMR

($CDCl_3$, 50 MHz): δ = 15.8, 16.5, 20.9, 22.34, 25.05, 27.1, 31.3, 34.5, 39.5, 48.0, 51.3, 69.3 (C-6), 73.7, 74.0, 74.7, 74.8, 75.9, 78.5, 83.0, 100.5 (C-1), 127.4, 127.6, 127.7, 127.8, 128.3, 128.4, 136.1, 138.3, 138.5, 139.7, 139.8, 196.3. − $C_{42}H_{54}O_6S$ (686.9): C 73.43, H 7.92; found C 73.70, H 8.09.

Fluorenyl 2-*S*-(1′-Acetyl-2′-methylethenyl)-3,4,6-tri-*O*-benzyl-2-thio-β-D-glucopyranoside (26): This compound was obtained according to Procedure B; compounds **22** (225 mg, 0.34 mmol) and **24**, in the presence of TMSOTf (0.12 equiv.) afforded **26** (125 mg, 52%) as a pale yellow oil. − $[\alpha]_D^{25}$ = +22 (*c* = 0.35, $CHCl_3$). − ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.71 (S, 3 H, CH_3CO), 1.72 (d, *J* = 8.0 Hz, 3 H), 3.51−3.82 (m, 6 H, 2-H, 3-H, 4-H, 5-H, 6_a-H, 6_b-H), 4.52−4.89 (m, 7 H, 1-H, 3 CH_2Ph), 5.73 (s, 1 H, 1-H_{Fluor}), 6.37 (q, *J* = 8.0 Hz, 2′-H), 7.17−7.71 (m, 23 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ =16.2 (CH_3), 26.0 (CH_3), 51.1 (C-2), 69.0, 73.6, 74.3, 74.8, 75.0, 78.4, 78.9, 82.8, 103.2 (C-1), 119.4, 119.8, 126.3, 126.9, 127.1, 127.5, 127.6, 127.7, 127.8, 127.9, 128.2, 128.4, 128.9, 129.0, 138.2, 138.3, 138.4, 140.3, 140.8, 141.0, 143.3, 196.4. − $C_{45}H_{44}O_6S$ (712.9): C 75.82, H 6.22; found C 75.70, H 6.29.

Galactopyranoside Derivative 27: $LiAlH_4$ (4.0 mg, 0.11 mmol) was added to an ice-cooled solution of **2** (120 mg, 0.22 mmol) in dry THF (2.0 mL). After 30 min, the reaction was complete; the mixture was diluted with CH_2Cl_2 and washed at 0 °C with a saturated solution of NH_4Cl (3 × 10 mL). The organic phase was dried with anhydrous Na_2SO_4, and removal of the solvent under reduced pressure afforded the corresponding allyl alcohol (98%) as a mixture of two diastereoisomers. The crude product was used without further purification. − TLC (petroleum ether/EtOAc, 3:1): R_f = 0.49, 0.45. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.34 (d, *J* = 6.6 Hz, 3 H, CH_3CH_A), 1.38 (d, *J* = 6.6 Hz, 3 H, CH_3CH_B), 1.85 (s, 3 H, CH_3CO_A), 1.95 (s, 3 H, CH_3CO_B), 3.53−3.79 (m, 6 H), 4.00 (m, 1 H), 4.153 (bq, *J* = 6.2 Hz, 1 H, CH_3CH), 4.40−4.96 (m, 6 H), 5.55 (d, *J* = 2.6 Hz, 1 H, 1-H), 7.26−7.41 (m, 15 H). − Pyridine (35 μL, 0.44 mmol) was slowly added to an ice-cooled solution of the crude alcohol (121 mg, 0.22 mmol) in dry CH_2Cl_2 (2.0 mL), followed by dropwise addition of TBDMSOTf (76 μL, 0.33 mmol). Reaction was complete after 10 min. After dilution with CH_2Cl_2 (10 mL), the mixture was washed at 0 °C with a saturated solution of NH_4Cl (2 × 8 mL), and dried with anhydrous Na_2SO_4. Evaporation of the solvent and column chromatography on silica gel (petroleum ether/EtOAc, 3:1) afforded **27** (131 mg, 90%) as a mixture of two diastereoisomers (A/B = 1:1.6) − TLC (petroleum ether/EtOAc, 3:1): R_f = 0.8. − Pale yellow oil. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.03 (s, 3 H, CH_{3A}), 0.06 (s, 3 H, CH_{3A}), 0.08 (s, 3 H, CH_{3B}), 0.10 (s, 3 H, CH_{3B}), 0.95 (s, 9 H, tBu_A), 0.98 (s,9 H, tBu_B), 1.26−1.36 (m, 3 H, CH_3CH), 1.86 (s, 3 H, CH_3CO_A), 1.94 (s, 3 H, CH_3CO_B), 3.56−3.71 (m, 3 H), 3.90−3.96 (m, 1 H), 4.16−4.24 (m, 1 H, 5-H), 4.38−4.95 (m, 8 H, 1-H, 1′-H, 3 CH_2Ph), 5.43 (d, $J_{1,2}$ = 1.8 Hz, 1 H, 1_B-H), 5.52 (d, $J_{1,2}$ = 2.5 Hz, 1 H, 1_B-H), 7.27−7.44 (m, 15 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = −5.1, −4.9, −4.7, 17.8, 18.0, 23.6, 23.9, 25.6, 25.7, 37.9 ($C\text{-}2_A$), 39.4 ($C\text{-}2_B$), 67.6, 67.7, 68.5, 71.0, 71.2, 73.3, 73.6, 73.7, 74.7, 75.6, 76.5, 95.0 ($C\text{-}1_B$), 95.1 ($C\text{-}1_A$), 105.0 ($C\text{-}2'_A$), 105.5 ($C\text{-}2'_B$), 127.5, 127.6, 127.7, 127.8, 128.1, 128.2, 128.3, 137.7, 138.0, 138.1, 138.3, 138.4, 139.4, 141.1. − $C_{38}H_{50}O_6SSi$ (662.9): C 68.84, H 7.60; found C 68.90, H 7.79.

Menthyl 2-*S*-(1′-Acetyl-2′-methylethenyl)-3,4,6-tri-*O*-benzyl-2-thio-β-D-galactopyranoside (28): This compound was obtained according to Procedure B; compounds **27** (75 mg, 0.11 mmol) and menthol **23**, in the presence of TMSOTf (0.12 equiv.), afforded **28** (30 mg, 40%) as a pale yellow oil. − TLC (petroleum ether/EtOAc, 7:1): R_f = 0.6. − $[\alpha]_D^{25}$ = −54.5 (*c* = 0.34, $CHCl_3$). − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.69 (d, *J* = 6.6 Hz, 3 H), 0.83 (d, *J* = 6.8 Hz, 3 H), 0.89 (d, *J* = 6.2 Hz, 3 H), 0.95−1.26 (m, 2 H), 1.56−1.65 (m, 2 H), 2.02 (d, *J* = 6.8 Hz, 3 H), 2.17−2.23 (m, 1 H), 2.30 (s, 3 H), 3.33−3.83 (m, 7 H, CH_2, 2-H, 3-H, 4-H, 5-H, 1′′-H), 4.35 (d, $J_{1,2}$ = 8.6 Hz, 1 H, 1-H), 4.35−4.90 (m, 6 H), 6.77 (q, *J* = 7.0 Hz, 1 H), 7.25−7.40 (m, 15 H, Ph) δ. − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 15.6, 16.5, 20.9, 22.3, 23.1, 24.7, 27.0, 31.4, 34.4, 39.6, 47.8, 49.1 (C-2), 69.2 (C-6), 72.3, 72.4, 73.3, 73.5, 74.3, 76.2, 81.7, 100.6 (C-1), 126.9, 127.1, 127.3, 127.4, 127.6, 127.8, 128.1, 128.3, 128.4, 137.9, 138.0, 138.8, 139.6, 139.9, 196.7 δ. − $C_{42}H_{54}O_6S$ (686.9): C 73.43, H 7.92; found C 73.30, H 7.99.

General Procedure for Raney Nickel Reductive Desulfurization: Commercially available Raney nickel[33] (0.6 mL) was added to an ice-cooled solution of 2-thioglycopyranoside (0.08 mmol) in THF (1.0 mL). The mixture was stirred at 0 °C for 10 min and the ice bath was then removed. After complete disappearance of starting material (TLC monitoring), the mixture was filtered through Celite. Evaporation of the solvent and column chromatography on silica gel afforded the desired compounds.

Isopropyl 3,4,6-Tri-*O*-benzyl-2-deoxy-β-D-glucopyranoside (29): This compound was obtained according to the general procedure; compound **17** (31 mg, 0.05 mmol) afforded compound **29** (17 mg, 67%) as a yellow oil. − TLC (petroleum ether/EtOAc, 3:1): R_f = 0.7. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.16 (d, *J* = 6.2 Hz, 3 H), 1.27 (d, *J* = 6.2 Hz, 3 H), 1.64−1.75 (m, 1 H, 2_{ax}-H), 2.18−2.36 (ddd, *J* = 1.8, *J* = 4.6, *J* = 12.4 Hz, 1 H, 2_{eq}-H), 3.42−3.53 (m, 2 H, 3-H, 4-H), 3.62−3.81 (m, 3 H, 5-H, 6_a-H, 6_b-H), 3.96−4.08 (m, 1 H, CH *i*Pr), 4.50−4.94 (m, 7 H, 1-H, 3 CH_2Ph), 7.21−7.36 (m, 15 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.8 (CH_3), 23.5(CH_3), 37.2 (C-2), 69.5 (C-6), 70.7 (C-1′), 71.3 (C-4), 73.4, 74.9, 75.1, 78.2 (C-3), 79.6 (C-5), 97.8 (C-1), 127.5, 127.7, 127.7, 128.0, 128.3, 128.4, 138.4. − $C_{30}H_{36}O_5$ (476.6): C 75.60, H 7.61; found C 75.53, H 7.77.

Mirtenyl 3,4,6-Tri-*O*-benzyl-2-deoxy-β-D-glucopyranoside (30): This compound was obtained according to the general procedure; compound **18** (28 mg, 0.04 mmol) afforded **30** (16 mg, 69%) as a colorless oil. − TLC (petroleum ether/EtOAc, 8:1): R_f = 0.6. − $[\alpha]_D^{25}$ = −38.8 (*c* = 0.38, $CHCl_3$). − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.80 (s, 3 H), 1.19 (d, *J* = 12.0 Hz, 1 H), 1.28 (s, 3 H), 1.63−1.75 (m, 1 H, 2_{ax}-H), 2.10−2.44 (m, 6 H, 2_{eq}-H, 5 H mirt), 3.36−3.81 (m, 5 H, 3-H, 4-H, 5-H, CH_2), 3.90−4.24 (AB part of an ABX system, J_{AB} = 12.8 Hz, J_{AX} = 1.8 Hz, J_{BX} = 1.4 Hz), 4.43−4.93 (m, 7 H, 1-H, 3 CH_2Ph), 5.50 (m, 1 H), 7.18−7.39 (m, 15 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.1 (CH_3), 26.2 (CH_3), 31.2 (CH_2), 31.5 (CH_2), 36.6 (C-2), 40.8 (CH), 43.4 (CH), 69.4, 71.3, 73.4, 75.2, 76.4 (CH), 78.2 (CH), 79.5 (CH), 98.6 (C-1), 120.0, 127.5, 127.7, 127.8, 128.0, 128.4, 138.5, 144.6 (Cq). − $C_{36}H_{42}O_5$ (554.7): C 77.95, H 7.63; found C 77.90, H 7.59.

6-(3,4,6-Tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-glucopyranoside (31): This compound was obtained according to the general procedure; compound **19** (48 mg, 0.06 mmol) afforded **31** (21 mg, 51%) as colorless oil. − TLC (petroleum ether/EtOAc, 4:1): R_f = 0.4. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.32 (s, 3 H, CH_3), 1.33 (s, 3 H, CH_3), 1.44 (s, 3 H, CH_3), 1.54 (s, 3 H, CH_3), 1.68 (m, 1 H, 2_{ax}-H), 2.46 (m, 1 H, 2_{eq}-H), 3.37−3.74 (m, 6 H, 4-H, 5′-H, 6_a-H, 6_b-H, 6_a′-H, 6_b′-H), 3.98−4.32 (m, 4 H, 3-H, 5-H, 2′-H, 4′-H), 4.48−4.92 (m, 8 H, 1-H, 3′-H, 3 CH_2Ph), 5.55 (d, $J_{1',2'}$ = 5.0 Hz, 1 H, 1′-H), 7.14−7.32 (m, 15 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 24.4, 25.0, 26.00, 26.04, 36.5 (C-2), 67.7, 68.8, 69.2, 70.4, 70.7, 71.2, 71.5, 73.5 (C-5), 74.9 (C-2′), 75.1 (C-5′), 78.0 (C-3′), 79.4 (C-4′), 96.4 (C-1′),

100.4 (C-1), 108.7 (C_q), 109.4, 127.6, 127.7, 127.8, 127.9, 128.1, 128.3, 128.4, 138.3, 138.5. − $C_{39}H_{48}O_{10}$ (676.8): C 69.21, H 7.15; found C 69.03, H 6.90.

Methyl 2,3,4-Tri-*O*-benzyl-6-*O*-(3,4,6-tri-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-β-D-glucopyranoside (32): This compound was obtained according to the general procedure; compound **20** (43 mg, 0.04 mmol) afforded **32** (21 mg, 56%) as a yellow oil. − TLC (petroleum ether/EtOAc, 3:1): R_f = 0.7. − M.p. 96−98 °C. − $[\alpha]_D^{25}$ = −60.2 (c = 0.83, $CHCl_3$). − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.64−1.75 (m, 1 H, H-2_{ax}), 2.22−2.30 (m, 1 H, 2_{eq}-H), 3.37−3.73 (m, 13 H, 3-H, 4-H, 5-H, 2′-H, 3′-H, 4-H′, 6_a-H, 6_b-H, 6_a′-H, 6_b′-H, OCH_3), 4.15−4.20 (m, 1 H, 5′-H), 4.30 (d, $J_{1',2'}$ = 7.8 Hz, 1′-H), 4.39 (bd, J = 8.0 Hz, 1 H, 1-H), 4.50−4.97 (m, 12 H, 6 CH_2Ph), 7.20−7.34 (m, 30 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 36.5 (C-2), 57.0 (OCH_3), 68.4, 69.2, 74.5, 74.7, 74.8, 74.9, 75.2, 75.7, 71.4, 73.4, 78.0, 78.1, 79.2, 82.2, 84.6, 100.4 (C-1), 104.6 (C-1′), 127.5, 127.7, 127.8, 127.9, 128.0, 128.1, 128.3, 128.4, 138.1, 138.3, 138.4, 138.5. − $C_{55}H_{60}O_{10}$ (881.1): C 74.98, H 6.86; found C 74.58, H 6.94.

Menthyl 3,4,6-Tri-*O*-benzyl-2-deoxy-β-D-glucopyranoside (33): This compound was obtained according to the general procedure; compound **25** (54 mg, 0.08 mmol), after 30 min, afforded **33** (29 mg, 65%) as a pale yellow oil. − TLC (petroleum ether/EtOAc, 6:1): R_f = 0.7. − $[\alpha]_D^{25}$ = −43.2 (c = 0.30, $CHCl_3$). − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.71−1.16 (m, 13 H), 1.20−1.32 (m, 1 H), 1.58−1.74 (m, 3 H, 2_{ax}-H, 2 $H_{ment.}$), 1.97−2.03 (m, 1 H), 2.24−2.35 (m, 2 H, 2_{eq}-H, 1 $H_{ment.}$), 3.34−3.73 (m, 6 H, 6_a-H, 6_b-H, 3-H + 4-H, 5-H,1′-H), 4.52−4.94 (m, 7 H, 1-H, 3 CH_2Ph), 7.26−7.33 (m, 15 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 21.0 (CH_3), 22.3 (CH_3), 25.1 (CH_3), 29.6(CH_2), 31.4 (CH), 34.3 (CH_2), 37.2 (CH_2), 40.6 (C-2), 47.8 (CH), 69.7 (C-6), 71.1, 73.6, 75.0, 75.1, 76.2, 78.2, 79.7, 96.3 (C-1), 127.5, 127.6, 127.7, 128.0, 128.1, 128.3, 128.4, 138.5. − $C_{37}H_{48}O_5$ (572.8): C 77.59, H 8.45; found C 77.30, H 8.56.

Fluorenyl 3,4,6-Tri-*O*-benzyl-2-deoxy-β-D-glucopyranoside (34): This compound was obtained according to the general procedure; compound **26** (125 mg, 0.18 mmol) afforded **34** (66 mg, 67%) as a yellow oil. − TLC (petroleum ether/EtOAc, 4:1): R_f = 0.6 − $[\alpha]_D^{25}$ = +8.6 (c = 0.18, $CHCl_3$). − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 1.76−1.89 (m, 1 H, 2_{ax}-H), 2.38−2.47 (ddd, J = 1.4, J = 4.4, J = 12.2 Hz, 1 H, 2_{eq}-H), 3.46−3.79 (m, 5 H, 3-H, 4-H, 5-H, 6-H), 4.56−4.96 (m, 7 H, 1-H + 3 CH_2Ph), 5.76 (s, 1 H, 1′-H), 7.18−7.85 (m, 23 H). − ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 37.2 (C-2), 69.6 (C-6), 71.4, 73.6, 75.0, 75.3 (C-1′), 78.1, 79.6, 80.6, 99.5 (C-1), 119.7, 120.0, 125.9, 126.7, 127.4, 127.7, 127.8, 127.9, 128.0, 128.5, 129.0, 129.1, 138.4, 138.5, 140.5, 140.8, 143.2, 143.6. − $C_{40}H_{38}O_5$ (598.7): C 80.24, H 6.40; found C 80.38, H 6.29.

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[1] P. Sears, C.-H. Wong, *Angew. Chem. Int. Ed.* **1999**, *38*, 2300−2324.
[2] R. A. Dwek, *Chem. Rev.* **1996**, *96*, 683−720.
[3] T. M. Hallis, H.-W. Liu, *Acc. Chem. Res.* **1999**, *32*, 579−588.
[4] B. G. Davis, *J. Chem. Soc., Perkin Trans. 1* **2000**, 2137−2160.
[5] S. Hanessian, B. Lou, *Chem. Rev.* **2000**, *100*, 4443−4463.
[6] Y. D. Vankar, R. R. Schmidt, *Chem. Soc. Rev.* **2000**, *29*, 201−216.
[7] S. J. Danishefsky, M. T. Bilodeau, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1380−1419.
[8] W. R. Roush, X.-F. Lin, *J. Am. Chem. Soc.* **1995**, *117*, 2236−2250.
[9] G. Grewal, N. Kaila, R. W. Franck, *J. Org. Chem.* **1992**, *57*, 2084−2092.
[10] K. C. Nicolaou, C. N. C. Boddy, S. Bräse, N. Winssinger, *Angew. Chem. Int. Ed.* **1999**, *38*, 2096−2152.
[11] C. H. Marzabadi, R. W. Franck, *Tetrahedron* **2000**, *56*, 8385−8417.
[12] J. Thiem, W. Klaffke, *Top. Curr. Chem.* **1990**, *154*, 285−334.
[13] R. W. Franck, S. M. Weinreb, *Studies in Natural Products Chemistry* (Ed.: Atta-Ur-Rahman), Elsevier, Amsterdam, **1989**, p. 173.
[14] G. Capozzi, A. Dios, R. W. Franck, A. Geer, C. Marzabadi, S. Menichetti, C. Nativi, M. Tamarez, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 777−779.
[15] G. Capozzi, R. W. Franck, M. Mattioli, S. Menichetti, C. Nativi, G. Valle, *J. Org. Chem.* **1995**, *60*, 6416−6426.
[16] S. Hanessian, in *Preparative Carbohydrate Chemistry* (Ed.: S. Hanessian), Marcel Dekker, New York, **1997**, p. 381−388.
[17] G. Capozzi, S. Menichetti, C. Nativi, A. Rosi, G. Valle, *Tetrahedron* **1992**, *48*, 9023−9032.
[18] G. Capozzi, S. Menichetti, C. Nativi, A. Rosi, R. W. Franck, *Tetrahedron Lett.* **1993**, *34*, 4253−4256.
[19] G. Capozzi, C. Falciani, S. Menichetti, C. Nativi, R. W. Franck, *Tetrahedron Lett.* **1995**, *36*, 6755−6758.
[20] G. Capozzi, C. Falciani, S. Menichetti, C. Nativi, B. Raffaelli, *Chem. Eur. J.* **1999**, *5*, 1748−1754.
[21] For a previous communication see: G. Capozzi, F. Mannocci, S. Menichetti, C. Nativi, S. Paoletti, *Chem. Commun.* **1997**, 2291−2292.
[22] P. Collins, R. Ferrier in *Monosaccharides*, John Wiley & Sons, New York, **1995**, p. 166.
[23] For cholesterol glycosilation see also: B. Lou, H. K. Huynh, S. Hanessian in *Preparative Carbohydrate Chemistry* (Ed.: S. Hanessian), Marcel Dekker, New York, **1997**, p. 431−448.
[24] For a possible method for activation of **1**, see: R. W. Franck, C. H. Marzabadi, *J. Org. Chem.* **1998**, *63*, 2197−2208.
[25] When dry dichloromethane was used as solvent, the reaction became more sluggish and the changing of the color of the mixture was less readily apparent, and therefore less synthetically helpful.
[26] This procedure, extended to α-glycosyl synthesis,[22] can give the desired compounds in low yields depending on the stability, under the reaction conditions, of reactants and products.
[27] A. Dios, C. Nativi, G. Capozzi, R. W. Franck, *Eur. J. Org. Chem.* **1999**, 1869−1874.
[28] Dry nitromethane was also used successfully. Comparable results in terms of yield and selectivity were obtained.
[29] K. Toshima, K. Tatsuta, *Chem. Rev.* **1993**, *93*, 1503−1531.
[30] T. G. Back, D. L. Baron, K. Yang, *J. Org. Chem.* **1993**, *58*, 2407−2410.
[31] S. Becker, Y. Fort, P. Caubère, *J. Org. Chem.* **1990**, *55*, 6194−6198.
[32] For an alternative synthesis of **31**, see ref.[24]
[33] A. I. Vogel in *Practical Organic Synthesis*, Longman, Birmingham, AL, **1962**, p 870.

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