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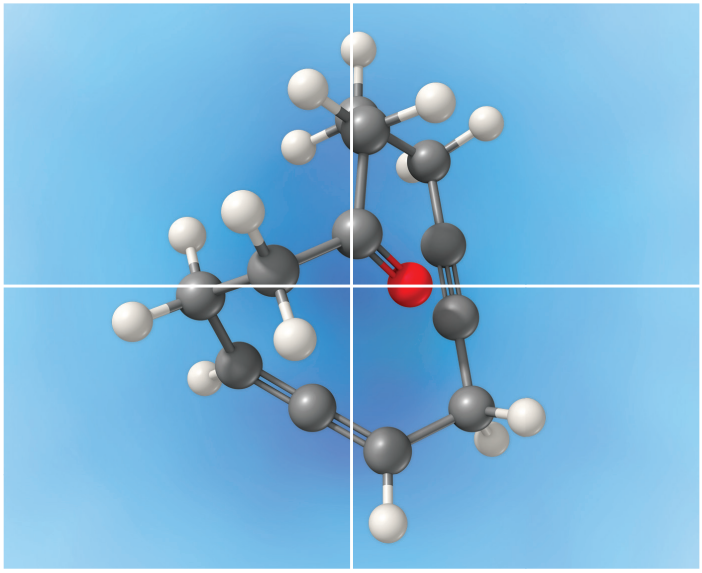

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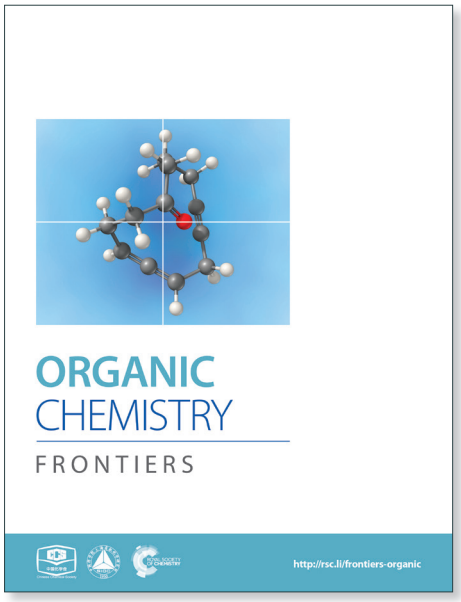

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ARTICLE TYPE

Synthesis of 2-Deoxy-*C*-glycosides via Lewis Acid-Mediated Rearrangement of 2,3-Anhydro-1-thiopyranosides

De-Cai Xiong, Chao Gao, Wenming Li, Yuan Wang, Qin Li, and Xin-Shan Ye*

Abstract: An approach to the regio- and stereo-selective construction of 2-deoxy-*C*-glycosides via Lewis acid-mediated rearrangement of 2,3-anhydro-1-thiopyranosides was disclosed. Treatment of 2,3-anhydro-1-thiopyranosides with phenols in the presence of TMSOTf, the migration-*O*-glycosylation and Fries-like *O* to *C* rearrangement took place in succession, providing aryl 2-thio-2-deoxy-*C*-glycosides with the single thermodynamically favourable configuration ($^1C_4$ or $^4C_1$) in good to excellent yields. The coupling reaction of 2,3-anhydro-1-thiopyranosides with trimethylsilylated or tributylstanylated nucleophiles in the presence of TMSOTf or $Sc(OTf)_3$, via the migration-*C*-glycosylation process, afforded 2-thio-2-deoxy-*C*-glycosides in a stereospecific manner in moderate to good yields and with the C-1 and C-2 substituents opposite. The 2-thio-functionality was further removed to produce the corresponding 2-deoxy-*C*-glycosides. This method may provide a convenient route to the preparation of 2-deoxy-*C*-glycosides.

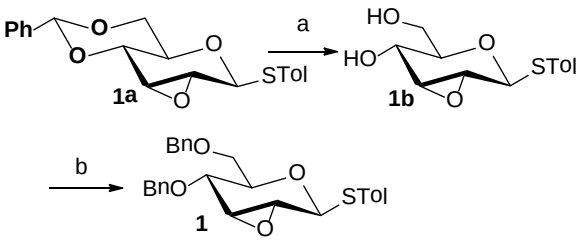
Keywords: 2,3-anhydro-1-thiopyranoside, 2-deoxy-*C*-glycoside, phenol, trimethylsilylated nucleophile, Lewis acid, rearrangement

Introduction

C-Glycosides are a class of carbohydrate analogues in which the glycosidic oxygen is replaced by a carbon atom. This novel *C*-*C* glycosidic bond is unique and it confers remarkable stability to both enzymatic and/or chemical hydrolysis. In addition, *C*-glycosides exist in natural products and exhibit a diverse range of biological activities.[1] In particular, the 2-deoxy-*C*-glycoside structure is embodied in a variety of therapeutically important natural products such as pluramycins, galtamycin, and aquayamycin.[2] Therefore, the synthesis of *C*-glycosides has been one of the main topics in carbohydrate chemistry. The stereoselective assembly of 2-deoxy-*C*-glycosyl linkages is more challenging than that of other *C*-glycosyl linkages due to the inexistence of participating groups at the 2-position. So far, a series of chemical transformations have been reported for the synthesis of 2-deoxy-*C*-glycosides,[3] these transformations mainly include the electrophilic reaction,[4] cross-coupling reaction,[5] free radical reaction,[6] cyclization,[7] intramolecular *O*-*C* rearrangement,[8] umpolung,[9] and other miscellaneous reactions. These reactions involve various glycosyl donors such as glycosyl halides,[10] glycosyl actates,[11] and glycals.[12] Although advances have been achieved, stereospecific *C*-glycosylation remains a difficult task. Therefore, it would be highly desirable to develop new approaches to synthesize diverse 2-deoxy-*C*-glycosides.

2,3-Anhydro-1-thioglycosides[13] are a type of intriguing donors. They can undergo stereoselectivity-controllable glycosylation reactions generating 2-thio-2-deoxyglycosides. These coupling reactions occurred both regio- and stereo-selectively: the arylthio groups migrated to the position 2 and the nucleophile attacked at the anomeric position; the groups at C-1 and C-2 adopt *trans*-configuration and the substituents at C-1 and C-3 adopt *cis*-configuration. Inspired by these results, we reasoned that *C*-glycosylation might highly benefit from 2,3-anhydro-1-thioglycosides. Herein we report *C*-glycosylations of 2,3-anhydro-1-thioglycosides with phenols via *O*-*C* rearrangement or with trimethylsilylated (tributylstanylated) nucleophiles.

Results and Discussion

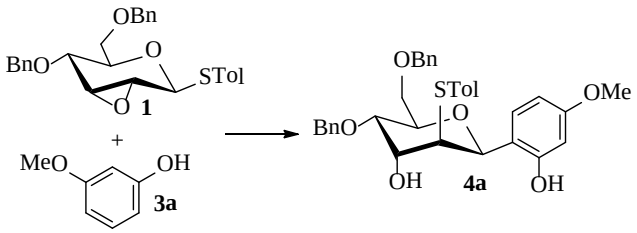


Scheme 1. Synthesis of 2,3-anhydro-1-thioglycoside **1**. (a) CSA, MeOH, 54%; (b) **1b** (1.0 equiv.), BnBr (7.5 equiv.), Ag_2O (8.0 equiv.), KI (8.0 equiv.), 91%.

Firstly, *p*-tolyl 2,3-anhydro-4,6-di-*O*-benzyl-1-thio-*β*-D-allopyranoside (**1**) was prepared (Scheme 1). Treatment of thioglycoside **1a**[13a,j] with CSA in MeOH provided the de-benzylidene product **1b** in 54% yield. By using Ag_2O, *O*-benzylation of **1b** proceeded very smoothly and compound **1** was obtained in 91% yield. Next, the reaction of 2,3-anhydro-1-thio-*β*-glycoside **1** with *m*-methoxyphenol (**3a**) was carried out to explore the feasibility of *C*-glycosylation of **1** (Table 1). As expected, the reaction of **1** and **3a** in the presence of $BF_3{\cdot}Et_2O$ afforded the desired 2-tolylthio-*C*-glycoside **4a** in 9% yield with

high β-selectivity (entry 1). Encouraged by this result, a series of other Lewis acids including $SnCl_4$, TMSOTf, $Sc(OTf)_3$, and $Cu(OTf)_2$ were screened in order to find out the optimal conditions (entries 2–5). The results indicated that the reaction displayed the highest efficiency when TMSOTf was used (entry 3, 65% yield), whereas $Sc(OTf)_3$ and $SnCl_4$ took the second place in around 50% yield (entries 2 and 4). Notably, the use of $Cu(OTf)_2$ resulted in no detectable product **4a** (entry 5). Therefore, TMSOTf was chosen as the preferred Lewis acid in the following experiments.

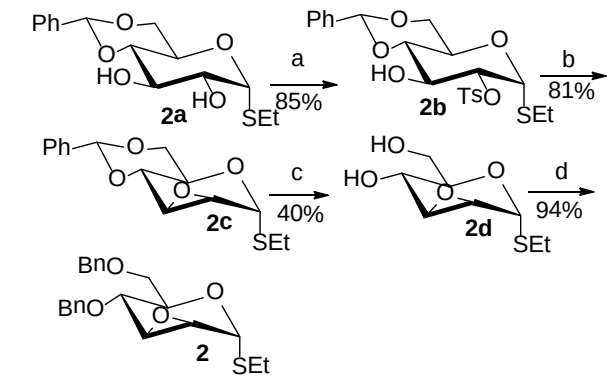
Table 1. Screening of Optimal Reaction Conditions[a]



Entry	Lewis acid	Yield[b] (%)	β / α ratio[c]
1	$BF_3{\cdot}Et_2O$	9	1:0
2	$SnCl_4$	46	1:0
3	TMSOTf	65	1:0
4	$Sc(OTf)_3$	55	1:0
5	$Cu(OTf)_2$	0	-

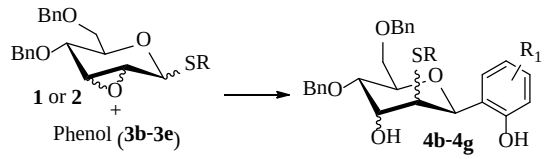
[a]Conditions: **1** (0.122 mmol), **3a** (0.146 mmol) and Lewis acid (0.122 mmol) in CH_2Cl_2 (3 mL) from -78 °C to rt; [b]Isolated yield after chromatography; [c]Ratio determined by ^1H NMR spectra after chromatography.

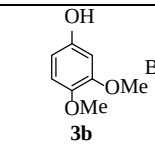
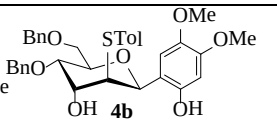
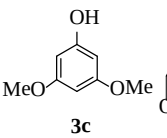
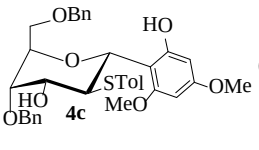
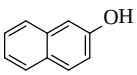
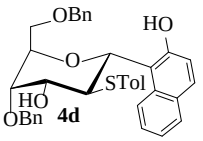
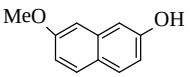
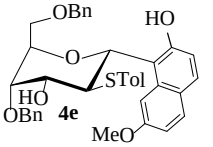
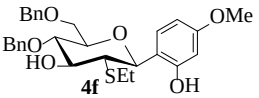
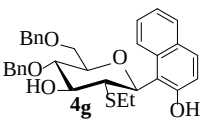
With the above optimized conditions in hand, we next turned our attention to exploration of the scope of phenols for *C*-glycosylation with **1** in the presence of TMSOTf (Table 2, entries 1-4). The results showed that electron-rich phenols **3b**-**3e** were suitable substrates for this reaction. Reaction of 3,4-dimethoxyphenol (**3b**) with **1** afforded product **4b** with β-configuration in 90% yield (entry 1), and reaction of 3,5-dimethoxyphenol (**3c**) with **1** furnished product **4c** with α-configuration in 65% yield (entry 2). Gratifyingly, reactions of 2-naphthol (**3d**) and 7-methoxy-2-naphthol (**3e**) provided products **4d** and **4e** with α-configuration in 71% and 73% yield, respectively (entries 3 and 4).



Scheme 2. Synthesis of anhydro-thio-α-glycoside **2**. (a) **2a** (1.0 equiv), TsCl (2.0 equiv), Ag_2O (2.0 equiv), KI (0.4 equiv), CH_2Cl_2, 12 h; (b) **2b** (1.0 equiv), NaOMe (3.0 equiv), MeOH; (c) **2c** (1.0 equiv), CSA (0.3 equiv), MeOH; (d) **2d** (1.0 equiv), BnBr (7.5 equiv), Ag_2O (8.0 equiv), KI (1.0 equiv), DMF.

Table 2. The *O*-*C* Rearrangement Reactions of **1** or **2** with Phenols[a]



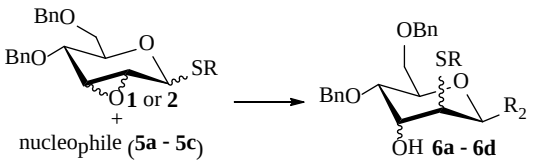
Entry	Donor	Acceptor	Product	Yield[b] [%]	α / β Ratio[c]
1	**1**	 **3b**	 **4b**	90	0:1
2	**1**	 **3c**	 **4c**	65	1:0
3	**1**	 **3d**	 **4d**	71	1:0
4	**1**	 **3e**	 **4e**	73	1:0
5	**2**	**3a**	 **4f**	81	0:1
6	**2**	**3d**	 **4g**	79	0:1

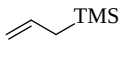
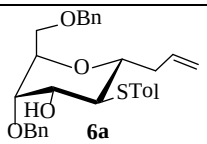
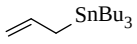
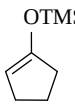
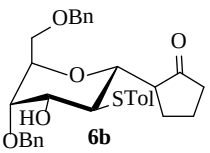
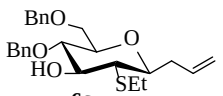
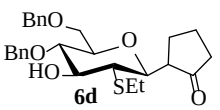
[a]Conditions: **1** or **2** (0.122 mmol), acceptor (0.146 mmol), TMSOTf (0.122 mmol) and 4 Å MS in CH_2Cl_2 (3 mL) from -78 °C to rt. [b]Isolated yield after chromatography. [c]Ratio determined by ^1H NMR spectra after chromatography.

To investigate the influence of the anomeric configuration of thioglycosides, ethyl 2,3-anhydro-1-thio-α-glycoside **2** was prepared (Scheme 2). Initially, ethyl 4,6-*O*-benzylidene-1-thio-α-D-glucopyranoside (**2a**)[15] was selectively sulfonated at the 2-position to obtain the mono-sulfonate **2b** in 85% yield. Then, **2b** was treated with sodium methoxide in methanol providing anhydro-glycoside **2c** in 81% yield. Next, debenzylidenation of **2c**, which was followed by benzylation, gave the desired ethyl

2,3-anhydro-1-thio-α-glycoside **2** smoothly. Subsequently, compound **2** was employed to check the *C*-glycosylation reaction (Table 2, entries 5 and 6). As shown, the *C*-glycosylations of **2** with phenols **3a** and **3d** proceeded with high β-anomeric selectivity in 81% and 79% yield, respectively. It seems that the substituent at C-1 is not always opposite to the thio-group at C-2 when phenols are used as substrates. The aryl group at C-1always occupies the equatorial position.

Table 3. Reactions of **1** or **2** with Trimethylsilylated (Tributylstanylated) Nucleophiles[a]



Entry	Donor	Acceptor	Product	Yield[b] [%]	α / β Ratio[c]
1	**1**	 **5a**	 **6a**	50	1:0
2	**1**	 **5b**	**6a**	64	1:0
3	**1**	 **5c**	 **6b**	10 (51[d])	1:0
4	**2**	**5a**	 **6c**	trace (46[d])	0:1
5	**2**	**5b**	**6c**	41	0:1
6	**2**	**5c**	 **6d**	trace (70[d])	0:1

[a]Conditions: donor (0.122 mmol), acceptor (0.146 mmol), TMSOTf (0.122 mmol) and 4 Å MS in CH_2Cl_2 (3 mL) from -78 °C to rt. [b]Isolated yield after chromatography. [c]Ratio determined by ^{1}H NMR spectra after chromatography. [d]$Sc(OTf)_3$ as Lewis acid.

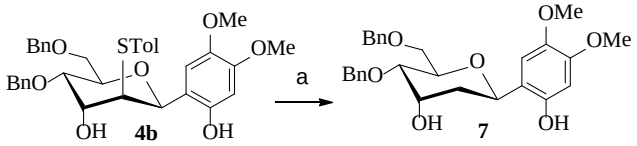
Given the successful results from phenols as substrates, we next want to test the reaction of 2,3-anhydro-1-thioglycosides with trimethylsilylated (tributylstanylated) nucleophiles, which failed in the previous report.[15a] Thus, upon treatment with TMSOTf at -78 °C, the reaction of anhydro-donor **1** with allyltrimethylsilane (**5a**) proceeded smoothly, providing *C*-glycoside **6a** with α-anomeric selectivity in 50% isolated yield (Table 3, entry 1). When tributylallylstanane (**5b**) was used as the substrate, coupling product **6a** was also obtained with α-stereoselectivity in 64% yield (Table 3, entry 2). However, under the same conditions, when 1-(trimethylsiloxy)cyclopentene (**5c**) was used for the reaction, only a small amount of *C*-glycoside **6b** was isolated (10% yield) with α-stereochemistry. Fortunately, compound **6b** was prepared from **5c** and **1** in an improved yield (51% yield) when $Sc(OTf)_3$ was used as the promoter (Table 3, entry 3). Similarly, when donor **2** was reacted with **5b** in the presence of TMSOTf at -78 °C, coupling product **6c** was gained in 41% yield and with β-stereoselectivity (Table 3, entry 5). Again, by using $Sc(OTf)_3$ as Lewis acid, the *C*-glycosylations of **2** with **5a** and **5c** were greatly improved, producing *C*-glycosides **6c** and **6d** with β-stereochemistry in 46% and 70% yield, respectively (Table 3, entries 4 and 6). It is apparent that the group at C-1 is opposite to the thio-group at C-2 when using trimethylsilylated or tributylstanylated nucleophiles as substrates.

Table 4. Characteristic NMR Data of *C*-Glycosyl Compounds

Compound	NOE	$^3J_{H,H}$ [Hz]	Comformation	Configuration
4a	$H_1 \leftrightarrow H_5$	$^3J_{H1,H2}$ = 2.8 $^3J_{H2,H3}$ = 2.8 $^3J_{H3,H4}$ = 2.8 $^3J_{H4,H5}$ = 10.0	$^4C_1$	β
4b	$H_1 \leftrightarrow H_5$	$^3J_{H1,H2}$ = 2.5 $^3J_{H2,H3}$ = 3.5 $^3J_{H3,H4}$ = 2.5 $^3J_{H4,H5}$ = 10.0	$^4C_1$	β
4c	$H_1 \leftrightarrow H_3$ $H_1 \leftrightarrow H_{6a}$ $H_1 \leftrightarrow H_{6b}$	$^3J_{H1,H2}$ = 11.0 $^3J_{H3,H4}$ = 2.0 $^3J_{H4,H5}$ = 3.0	$^1C_4$	α
4d		$^3J_{H1,H2}$ = 10.8	$^1C_4$	α
4e	$H_1 \leftrightarrow H_3$ $H_1 \leftrightarrow H_{6a}$ $H_1 \leftrightarrow H_{6b}$	$^3J_{H1,H2}$ = 10.5 $^3J_{H3,H4}$ = 2.5 $^3J_{H4,H5}$ = 2.5	$^1C_4$	α
4f		$^3J_{H1,H2}$ = 11.0	$^4C_1$	β
4g		$^3J_{H1,H2}$ = 10.5	$^4C_1$	β
6a	$H_1 \leftrightarrow H_3$ $H_1 \leftrightarrow H_{6a}$ $H_1 \leftrightarrow H_{6b}$	$^3J_{H1,H2}$ = 6.5 $^3J_{H2,H3}$ = 6.5	$^1C_4$	α
6b	$H_1 \leftrightarrow H_3$ $H_1 \leftrightarrow H_{6a}$ $H_1 \leftrightarrow H_{6b}$	$^3J_{H1,H2}$ = 9.0 $^3J_{H2,H3}$ = 9.0	$^1C_4$	α
6c		$^3J_{H1,H2}$ = 10.5	$^4C_1$	β
6d		$^3J_{H1,H2}$ = 11.0	$^4C_1$	β

The anomeric configurations of the coupling products were unambiguously identified by their NMR analyses (Table 4).[16] In the NMR spectra of **4a**, the coupling constants of hydrogen signals $^3J_{H1,H2}$ = 2.8 Hz (axial-equatorial relationship), $^3J_{H2,H3}$ =

2.8 Hz, $^3J_{H3,H4}$ = 2.8 Hz, and $^3J_{H4,H5}$ = 10.0 Hz (axial-axial relationship), suggest that the sugar ring exists in a $^4C_1$ conformation; the nuclear Overhauser effect (NOE) between H-1 and H-5 indicates the H-1 is in the axial position; Therefore, the anomeric configuration of **4a** is *β*. By the similar analyses, the NMR data of **4b** are consistent with a *β*-anomeric configuration and a $^4C_1$ conformation. For compound **4c**, the values of $^3J_{H1,H2}$ = 11.0 Hz (axial-axial relationship), $^3J_{H3,H4}$ = 2.0 Hz and $^3J_{H4,H5}$ = 3.0 Hz (axial-equatorial relationship) suggest the $^1C_4$ conformation and α-anomeric configuration. The structure of **4c** was further confirmed by the observations of NOEs between H-1 and H-3, H-1 and H-6. Using the same way, the structures of compounds **4d**, **4e**, **6a**, and **6b** were identified with α-anomeric configuration and in the $^1C_4$ conformation. Compounds **4f**, **4g**, **6c**, and **6d** with *β*-anomeric configuration and in $^4C_1$ conformation were analyzed from their ^{1}H NMR by a large $^3J_{H1,H2}$ coupling constant (>10 Hz, axial-axial relationship).[17]



Scheme 3. Desulfurization of compound **4b**. (a) AIBN, *n*-Bu_3SnH, 105 °C, 72%.

After having checked the feasibility of *C*-glycosylations of 2,3-anhydro-1-thiopyranosides with phenols and trimethylsilylated (tributylstanylated) nucleophiles, the desulfurization of 2-tolylthio-*C*-glycoside **4b** was carried out (Scheme 3). After treatment of **4b** with tri-*n*-butyltin hydride and AIBN in toluene at 105 °C, the 2-deoxy-*C*-glycoside **7** was obtained in 72% isolated yield. The anomeric configuration of **7** is completely consistent with that identified in **4b**.

Although the details are not yet known, a proposed mechanism for *C*-glycosylation is shown in Figure 1. The reaction may proceed through an oxocarbenium ion **A** or intermediate **B**.[13a] When phenol as nucleophile attacks the anomeric carbon at low temperature, a phenolic glycoside **C** would be generated. During raising the reaction temperature to room temperature, **C** would rearrange to the thermodynamically favourable *C*-glycoside **G** or **H** via the Fries-like *O* to *C* rearrangement.[18] The exclusive anomeric configuration may be attributed to the only stable conformation ($^1C_4$ or $^4C_1$), arising from the severe repulsion between the tolylthio group at C-2 and the aryl group at C-1 with other atoms or groups. Different substituents on phenol may result in different conformations. The aryl group at C-1 is always in equatorial position, but not always opposite to the thio-group at C-2, as in the case of coupling products **4a** and **4b**. When the nucleophilic attack is performed by a trimethylsilylated (tributylstanylated) nucleophile, it would form a *C*-glycoside **I** with the C-1 and C-2 substituents opposite.

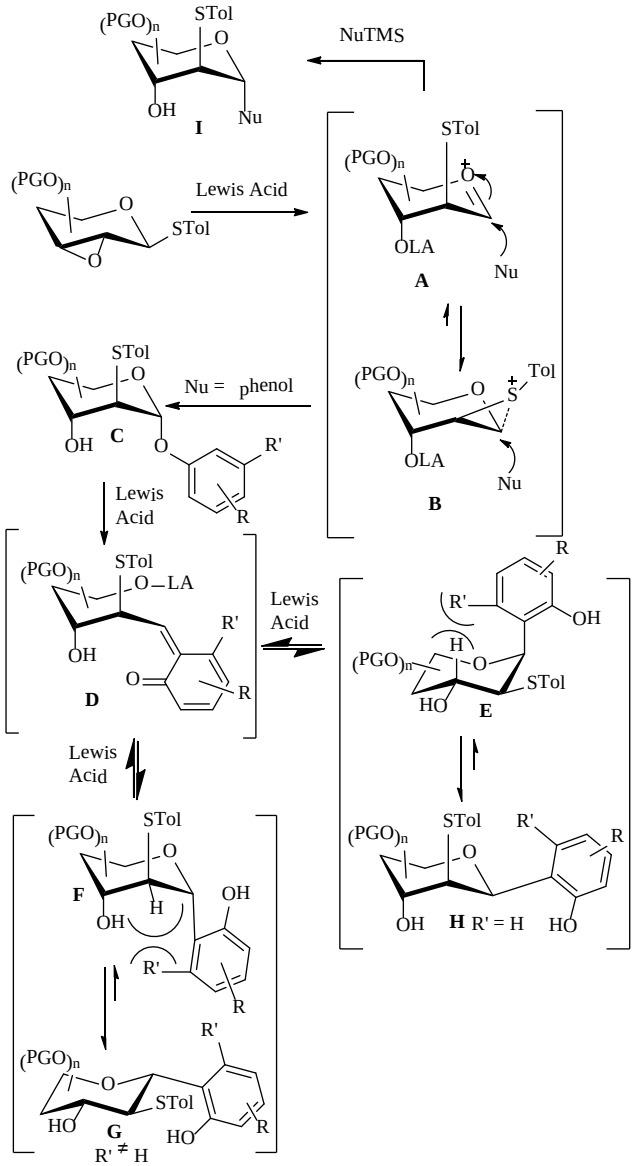


Figure 1. A proposed pathway leading to *C*-glycosides.

Conclusions

We have described a new method for the synthesis of 2-deoxy-*C*-glycosides which is both facile and highly stereoselective. By utilizing 2,3-anhydro-1-thiopyranosides and a variety of nucleophiles, this method affords *C*-glycosides via the Lewis acid-mediated rearrangement. Promoted by TMSOTf, a reaction of 2,3-anhydro-1-thiopyranosides with phenols gives aryl 2-thio-2-deoxy-*C*-glycosides, resulting from the successive migration-*O*-glycosylation and Fries-like *O* to *C* rearrangement. These reactions provide *C*-glycosides with a single anomeric configuration in good to excellent yields. The formed configuration depends on the thermodynamically favourable chair conformation ($^1C_4$ or $^4C_1$) of the *C*-glycoside, and the aryl group at C-1 always takes the equatorial position. By treatment of 2,3-anhydro-1-thiopyranosides with trimethylsilylated (tributylstanylated) nucleophiles in the presence of TMSOTf or $Sc(OTf)_3$, the migration–*C*-glycosylation reaction proceeds, producing 2-thio-2-deoxy-*C*-glycosides in moderate to good

yields and with the C-1 and C-2 substituents opposite. Finally, treatment of the resulting 2-thio-2-deoxy-*C*-glycosides with tri-*n*-butyltin hydride and AIBN can afford the corresponding 2-deoxy-*C*-glycosides. This method may find applications in the preparation of 2-deoxy-*C*-glycosides with biological importance.

Experimental Section

General Methods

All chemicals were purchased as reagent grade and used without further purification, unless noted otherwise. Dichloromethane (CH_2Cl_2) was distilled over calcium hydride (CaH_2). Methanol was distilled from magnesium. DMF was stirred with CaH_2 and distilled under reduced pressure. Toluene was distilled over sodium. All reactions were carried out under anhydrous conditions with freshly distilled solvents, unless stated otherwise. Reactions were monitored by analytical thin-layer chromatography on silica gel 60 F_{254} precoated on aluminium plates. Spots were detected under UV light and/or by staining with acidic ceric ammonium molybdate. Column chromatography was performed on silica gel (200—300 mesh). ^{1}H-NMR spectra were recorded on a JEOL AL-300, Varian INOVA-500 or Advance DRX Bruker-500 spectrometers at 25 ^{o}C. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ = 0 ppm) in deuterated chloroform. ^{13}C-NMR spectra were obtained by using the same NMR spectrometers and were calibrated with $CDCl_3$ (δ = 77.00 ppm). Mass spectra were recorded using a PE SCLEX QSTAR spectrometer.

General Procedures for *C*-Glycosylations

To a mixture of acceptors (0.146 mmol), donor **1** or **2** (0.122 mmol) and 4 Å molecular sieves was added CH_2Cl_2 (3 mL). The mixture was stirred for 10 min at room temperature and then cooled down to -72 ^{o}C. Lewis acid (0.122 mmol) was added and the temperature was raised until TLC showed that the donor was consumed. After neutralization by triethylamine, the reaction mixture was concentrated, and the residue was purified by column chromatography on silica gel to afford product.

***p*-Tolyl 2,3-anhydro-1-thio-*β*-D-allopyranoside (1b)**

To an ice-cooled solution of *p*-tolyl-2,3-anhydro-4,6-*O*-benzylidene-1-thio-*β*-D-allopyranoside (**1a**)[13a,13j] (500 mg, 1.40 mmol) in methanol (30 mL) was added *D*-camphorsulfonic acid (102.6 mg, 0.44 mmol). The mixture was stirred at room temperature for 30 min, followed by addition of triethylamine (0.1 mL). The solution was concentrated, and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 1:1) to provide **1b** (269 mg, 54% yield) as a colorless oil, and unreacted **1a** was recovered (90.0 mg, 18%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 (brs, 1H), 2.35 (s, 3H), 2.52 (brs, 1H), 3.37 (d, 1H, *J* = 4.0 Hz), 3.44-3.48 (m, 1H), 3.66 (d, 1H, *J* = 4.0 Hz), 3.74 (dd, 1H, *J* = 5.0 Hz, 12.0 Hz), 3.82-3.85 (m, 2H), 5.16 (d, 1H, *J* = 8.5 Hz), 7.14 (d, 2H, *J* = 7.5 Hz), 7.43 (d, 1H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.16, 54.82, 59.16, 62.54, 65.64, 74.58, 79.95, 127.66, 129.84, 133.55, 138.82; HRMS (ESI) Anal. Calcd for $C_{13}H_{16}O_4S$ $[M+NH_4]^+$: 286.1108, found: 286.1108.

***p*-Tolyl 2,3-anhydro-4,6-di-*O*-benzyl-1-thio-*β*-D-allopyranoside (1)**

To a solution of **1b** (203 mg, 0.76 mmol) in DMF (10 mL) was added Ag_2O (1.4 g, 6.05 mmol), KI (1.0 g, 6.05 mmol) and BnBr (0.67 mL, 5.66 mmol). After stirring for 8 h at room temperature, the reaction mixture was concentrated. The mixture was filtered and the filtrate was concentrated to give a residue that was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 12:1) to yield **1** (308 mg, 91% yield) as a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.30 (s, 3H), 3.28 (d, 1H, *J* = 4.5 Hz), 3.56 (d, 1H, *J* = 4.0 Hz), 3.64 (dd, 1H, *J* = 4.5 Hz, 11.0 Hz), 3.68-3.72 (m, 2H), 3.77 (dd, 1H, *J* = 1.5 Hz, 9.5 Hz), 4.54-4.63 (m, 3H), 5.13 (s, 1H), 7.03 (d, 2H, *J* = 8.0 Hz), 7.24-7.35 (m, 10H), 7.44-7.47 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.07, 52.39, 58.46, 69.10, 71.55, 71.67, 72.82, 73.22, 80.09, 127.42, 127.57, 127.81, 127.84, 128.21, 128.32, 129.52, 133.37, 137.67, 138.17, 138.32; HRMS (ESI) Anal. Calcd for $C_{27}H_{28}O_4S$ $[M+NH_4]^+$: 466.2047, found: 466.2049.

Ethyl 2,3-anhydro-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (2c)

To a solution of ethyl 4,6-*O*-benzylidene-1-thio-α-D-glucopyranoside (**2a**)[15a] (2.00 g, 4.29 mmol) in CH_2Cl_2 (50 mL) was added Ag_2O (1.94 g, 8.39 mmol), KI (0.33 g, 1.99 mmol) and toluenesulfonyl chloride (1.60 g, 8.39 mmol). The reaction mixture was stirred for 12 h. Then the mixture was filtered and the filtrate was concentrated to yield the crude product which was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 5:1, containing 1% triethylamine), providing compound **2b** (2.55 g, 85% yield) as a white solid.

To a solution of **2b** (1.95 g, 4.18 mmol) in MeOH (25 mL) was added NaOMe (30% in MeOH, 3mL, 15.99 mmol). After stirring for 1 d at room temperature, the reaction mixture was concentrated and the residue was dissolved in ethyl acetate. Then the solution was washed with brine and water. The organic layer was dried, filtered, and concentrated. The crude product was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 15:1, containing 1% triethylamine) to yield **2c** (0.99 g, 81% yield) as a white solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33 (t, 3H, *J* = 7.5 Hz), 2.67 (qd, 1H, *J* = 7.5 Hz, 13.0 Hz), 2.77 (qd, 1H, *J* = 7.5 Hz, 13.0 Hz), 3.28 (d, 1H, *J* = 4.0 Hz), 3.50 (d, 1H, *J* = 3.5 Hz), 3.72 (d, 1H, *J* = 10.5 Hz), 3.76 (d, 1H, *J* = 10.0 Hz), 3.93 (td, 1H, *J* = 4.5 Hz, 10.0 Hz), 4.22 (dd, 1H, *J* = 4.5 Hz, 10.5 Hz), 5.51 (s, 1H), 5.57 (s, 1H), 7.35-7.41 (m, 3H), 7.49-7.52 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.09, 25.20, 51.90, 53.96, 62.05, 69.33, 75.28, 80.15, 102.44, 126.17, 128.36, 129.27, 137.02; HRMS (ESI) Anal. Calcd for $C_{15}H_{18}O_4S$ $[M+Na]^+$: 317.0818, found: 317.0821.

Ethyl 2,3-anhydro-1-thio-α-D-mannopyranoside (2d)

To an ice-cooled solution of **2c** (250 mg, 0.85 mmol) in MeOH (20 mL) was added *D*-camphorsulfonic acid (63.5 mg, 0.27 mmol). The mixture was stirred at room temperature for 30 min, followed by addition of triethylamine (0.1 mL). The solution was concentrated and the residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 1:1) to yield **2d** (70.1 mg, 40% yield) as a colorless oil and the recovered unreacted **2c** (70.0 mg, 28%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.33 (t, 3H, *J* = 7.5 Hz), 1.62 (s, 1H), 1.92 (t, 1H, *J* = 6.0 Hz), 2.55 (d, 1H), 2.63-2.78 (m, 2H), 3.27 (d, 1H, *J* = 3.5 Hz), 3.33 (d, 1H, *J* = 3.5 Hz), 3.77-3.84 (m, 3H), 3.97 (dd, 1H, *J* = 5.0 Hz, 9.0 Hz), 5.47 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.07, 25.21, 51.52, 55.46, 63.20, 63.28, 69.17, 79.40; HRMS (ESI) Anal. Calcd for $C_8H_{14}O_4S$ $[M+Na]^+$: 229.0505, found: 229.0498.

Ethyl 2,3-anhydro-4,6-di-*O*-benzyl-1-thio-α-D-mannopyranoside (2)

To a solution of **2d** (210 mg, 1.02 mmol) in DMF (10 mL) was

added Ag_2O (1.89 g, 8.17 mmol), KI (1.35 g, 8.17 mmol) and BnBr (0.91 mL, 7.69 mmol). After stirring for 8 h at room temperature, the reaction mixture was concentrated. The mixture was filtered and the filtrate was concentrated to give a residue that was purified by column chromatography on silica gel (petroleum ether/ethyl acetate, 12:1) to yield **2** (370 mg, 94%) as a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (t, 3H, J = 7.5 Hz), 2.64 (qd, 1H, J = 7.5 Hz, 13.0 Hz), 2.76 (qd, 1H, J = 7.5 Hz, 13.0 Hz), 3.21 (d, 1H, J = 3.5 Hz), 3.36 (d, 1H, J = 4.0 Hz), 3.58 (d, 1H, J = 3.0 Hz), 3.71 (d, 1H, J = 9.5 Hz), 4.00 (dt, 1H, J = 3.5 Hz, 9.5 Hz), 4.44 (d, 1H, J = 12.5 Hz), 4.46 (d, 1H, J = 12.0 Hz), 4.58 (d, 1H, J = 12.5 Hz), 4.70 (d, 1H, J = 11.5 Hz), 5.51 (s, 1H), 7.25-7.34 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.96, 24.84, 51.30, 53.45, 67.48, 68.94, 69.27, 72.19, 73.14, 79.25, 127.54, 127.72, 127.99, 128.26, 128.46, 137.29, 138.12; HRMS (ESI) Anal. Calcd for $C_{22}H_{26}O_4S$ $[M+NH_4]^+$: 404.1890, found: 404.1892.

2-(4,6-Di-*O*-benzyl-2-deoxy-2-*p*-tolylthio-β-D-altropyranosyl)-5-methoxyphenol (4a)

Compound **4a** was isolated after column chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) as a colorless oil (65% yield): R*f* 0.30 (petroleum ether/ethyl acetate, 2:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (s, 3H, tolyl CH_3), 2.63 (s, 1H, OH), 3.53 (t, 1H, J = 2.8 Hz, H-2), 3.69 (dd, 1H, J = 4.4 Hz, 10.4 Hz, H-6a), 3.75 (dd, 1H, J = 1.6 Hz, 10.4 Hz, H-6b), 3.77 (s, 3H, OCH_3), 3.98 (ddd, 1H, J = 2.0 Hz, 4.4 Hz, 10.0 Hz, H-5), 4.18 (dd, 1H, J = 2.8 Hz, 10.0 Hz, H-4), 4.33 (t, 1H, J = 2.8 Hz, H-3), 4.50 (d, 1H, J = 11.6 Hz, $PhCH_2$), 4.56 (d, 1H, J = 12.0 Hz, $PhCH_2$), 4.57 (d, 1H, J = 11.6 Hz, $PhCH_2$), 4.65 (d, 1H, J = 12.0 Hz, $PhCH_2$), 5.47 (d, 1H, J = 2.0 Hz, H-1), 6.38 (dd, 1H, J = 2.4 Hz, 8.4 Hz), 6.46 (d, 1H, J = 2.4 Hz), 6.83 (d, 1H, J = 8.8 Hz), 6.98 (d, 2H, J = 8.4 Hz), 7.01 (d, 2H, J = 8.4 Hz), 7.23-7.38 (m, 10H), 8.36 (s, 1H, ArOH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.03, 55.22, 57.22 (C-2), 68.07 (C-3), 68.93 (C-6), 71.31 (C-4), 72.02, 73.48, 75.23 (C-5), 77.25 (C-1), 102.35, 105.97, 114.56, 127.31, 127.66, 127.75, 128.15, 128.24, 128.45, 128.60, 129.70, 131.30, 132.27, 137.21, 137.38, 138.02, 157.80, 160.29; HRMS (ESI) Anal. Calcd for $C_{34}H_{36}O_6S$ $[M+NH_4]^+$: 466.2047, found: 466.2049.

2-(4,6-Di-*O*-benzyl-2-deoxy-2-*p*-tolylthio-β-D-altropyranosyl)-4,5-dimethoxyphenol (4b)

Compound **4b** was isolated after column chromatography on silica gel (petroleum ether/ethyl acetate, 2:1) as a colorless oil (90% yield): R*f* 0.30 (petroleum ether/ethyl acetate, 1:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.28 (s, 3H, tolyl CH_3), 2.67 (d, 1H, J = 1.0 Hz, OH), 3.55 (dd, 1H, J = 2.5 Hz, 3.5 Hz, H-2), 3.69 (s, 3H, OCH_3), 3.70 (dd, 1H, J = 4.5 Hz, 11.0 Hz, H-6a), 3.75 (dd, 2H, J = 2.5 Hz, 11.0 Hz, H-6b), 3.84 (s, 3H, OCH_3), 3.98 (ddd, 1H, J = 2.0 Hz, 4.5 Hz, 10.0 Hz, H-5), 4.16 (dd, 1H, J = 2.5 Hz, 10.0 Hz, H-4), 4.38 (t, 1H, J = 3.0 Hz, H-3), 4.51 (d, 1H, J = 11.5 Hz, $PhCH_2$), 4.55 (d, 1H, J = 12.0 Hz, $PhCH_2$), 4.58 (d, 1H, J = 11.5 Hz, $PhCH_2$), 4.65 (d, 1H, J = 12.5 Hz, $PhCH_2$), 5.43 (d, 1H, J = 2.0 Hz, H-1), 6.37 (s, 1H), 6.47 (s, 1H), 6.97-7.02 (m, 4H), 7.24-7.38 (m, 10H), 8.07 (s, 1H, ArOH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.99, 55.77, 56.58, 57.37 (C-2), 68.22 (C-3), 68.90 (C-6), 71.31 (C-4), 72.03, 73.48, 75.20 (C-5), 77.39 (C-1), 101.78, 109.97, 112.36, 127.66, 127.72, 128.14, 128.25, 128.44, 128.60, 129.66, 131.38, 132.26, 137.17, 137.44, 138.00, 142.06, 149.43, 150.91; HRMS (ESI) Anal. Calcd for $C_{35}H_{38}O_7S$ $[M+Na]^+$: 625.2231, found: 625.2238.

2-(4,6-Di-*O*-benzyl-2-deoxy-2-*p*-tolylthio-α-D-altropyranosyl)-3,5-dimethoxyphenol (4c)

Compound **4c** was isolated after column chromatography on silica gel (petroleum ether/ethyl acetate, 6:1) as a colorless oil (65% yield): R*f* 0.35 (petroleum ether/ethyl acetate, 2:1); $[\alpha]_D^{20}$ -84.4 (c 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.26 (s, 3H, tolyl CH_3), 2.63 (d, 1H, J = 6.5 Hz, OH), 3.52 (dd, 1H, J = 5.5 Hz, 10.5 Hz, H-6a), 3.62 (dd, 1H, J = 5.5 Hz, 10.5 Hz, H-6b), 3.67 (t, 1H, J = 10.5 Hz, H-2), 3.74 (s, 3H, OCH_3), 3.75-3.79 (m, 1H, H-3), 3.81 (s, 3H, OCH_3), 3.87 (t, 1H, J = 2.0 Hz, 3.0 Hz, H-4), 4.26-4.32 (m, 1H, H-5), 4.47 (s, 2H, $PhCH_2$), 4.73 (d, 1H, J = 12.0 Hz, $PhCH_2$), 4.76 (d, 1H, J = 12.0 Hz, $PhCH_2$), 5.33 (d, 1H, J = 11.0 Hz, H-1), 6.00 (d, 1H, J = 2.0 Hz), 6.02 (d, 1H, J = 2.5 Hz), 6.94 (d, 1H, J = 8.0 Hz), 7.14 (dd, 2H, J = 2.5 Hz, 6.0 Hz), 7.25-7.37 (m, 10H), 7.73 (s, 1H, ArOH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.05, 53.48 (C-2), 55.26, 55.55, 67.46 (C-6), 68.71 (C-3), 70.43 (C-1), 72.92, 73.39, 74.96 (C-5), 76.09 (C-4), 91.11, 94.72, 105.95, 127.54, 127.80, 127.91, 128.48, 128.58, 129.22, 129.43, 133.76, 137.60, 158.04, 158.25, 161.35; HRMS (ESI) Anal. Calcd for $C_{35}H_{38}O_7S$ $[M+Na]^+$: 625.2231, found: 625.2238.

1-(4,6-Di-*O*-benzyl-2-deoxy-2-*p*-tolylthio-α-D-altropyranosyl)-2-naphthol (4d)

Compound **4d** was isolated after column chromatography on silica gel (petroleum ether/ethyl acetate, 5:1) as a colorless oil (71% yield): R*f* 0.20 (petroleum ether/ethyl acetate, 3:1); $[\alpha]_D^{20}$ -40.0 (c 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.13 (s, 3H), 2.81 (d, 1H, J = 6.0 Hz), 3.76 (dd, 1H, J = 5.2 Hz, 10.4 Hz), 3.80 (dd, 1H, J = 5.2 Hz, 10.4 Hz), 3.96 (t, 1H, J = 10.8 Hz), 4.04 (t, 1H, J = 2.8 Hz), 4.07-4.12 (m, 1H), 4.34-4.37 (m, 1H), 4.55 (d, 1H, J = 12.0 Hz), 4.59 (d, 1H, J = 12.0 Hz), 4.83 (s, 2H), 5.79 (d, 1H, J = 10.8 Hz), 6.45 (d, 2H, J = 8.0 Hz), 6.63 (d, 2H, J = 8.0 Hz), 6.93 (d, 1H, J = 8.8 Hz), 7.26-7.45 (m, 12H), 7.56 (d, 1H, J = 8.8 Hz), 7.66 (d, 1H, J = 7.6 Hz), 7.96 (d, 1H, J = 8.8 Hz), 8.05 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.87, 54.57, 68.43, 69.61, 73.07, 73.14, 73.62, 75.43, 76.13, 119.29, 122.73, 122.90, 126.00, 127.67, 127.90, 127.99, 128.00, 128.23, 128.64, 128.80, 129.00, 129.70, 130.19, 131.96, 132.74, 136.87, 137.46, 137.69; HRMS (ESI) Anal. Calcd for $C_{35}H_{38}O_7S$ $[M+NH_4]^+$: 610.2622, found: 610.2645.

1-(4,6-Di-*O*-benzyl-2-deoxy-2-*p*-tolylthio-α-D-altropyranosyl)-7-methoxy-2-naphthol (4e)

Compound **4e** was isolated after column chromatography on silica gel (petroleum ether/ethyl acetate, 6:1) as a colorless oil (73% yield): R*f* 0.35 (petroleum ether/ethyl acetate, 2:1); $[\alpha]_D^{20}$ -133.2 (c 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.12 (s, 3H, tolyl CH_3), 2.81 (d, 1H, J = 6.5 Hz, OH), 3.73 (s, 1H, OCH_3), 3.80 (dd, 1H, J = 4.5 Hz, 10.5 Hz, H-6a), 3.85 (dd, 1H, J = 4.5 Hz, 10.5 Hz, H-6b), 3.98 (t, 1H, J = 10.5 Hz, H-2), 4.07 (t, 1H, J = 2.5 Hz, H-4), 4.20 (ddd, 1H, J = 3.0 Hz, 6.0 Hz, 13.5 Hz, H-3), 4.32-4.34 (m, 1H, H-5), 4.56 (d, 1H, J = 12.0 Hz, $PhCH_2$), 4.60 (d, 1H, J = 12.0 Hz, $PhCH_2$), 4.82 (s, 2H, $PhCH_2$), 5.79 (d, 1H, J = 11.0 Hz), 6.52 (d, 2H, J = 8.0 Hz), 6.64 (d, 2H, J = 8.0 Hz), 6.80 (d, 1H, J = 8.5 Hz), 6.95 (dd, 1H, J = 2.0 Hz, 8.0 Hz), 7.26-7.43 (m, 11H), 7.48 (d, 1H, J = 8.5 Hz), 7.55 (d, 1H, J = 8.5 Hz), 8.08 (brs, 1H, ArOH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.87, 54.60 (C-2), 55.11, 69.37 (C-6), 69.74 (C-3), 73.14, 73.61 (C-1), 75.33 (C-5), 76.27 (C-4), 102.88, 114.60, 116.81, 127.27, 127.93, 128.04, 128.62, 128.65, 128.99, 129.68, 129.94, 131.81, 133.96, 136.82, 137.46, 137.64, 157.89; HRMS (ESI) Anal. Calcd for $C_{38}H_{38}O_6S$ $[M+NH_4]^+$: 640.2727, found: 640.2714.

2-(4,6-Di-*O*-benzyl-2-deoxy-2-*p*-ethylthio-β-D-glucopyranosyl)-5-methoxyphenol (4f)

Compound **4f** was isolated after column chromatography on silica gel (petroleum ether/acetone, 5:1) as a colorless oil (81% yield): *Rf* 0.40 (petroleum ether/acetone, 2:1); $[\alpha]_D^{20}$ +78.4 (c 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.98 (t, 3H, *J* = 7.5 Hz, ethyl CH_3), 1.80-1.85 (m, 2H, ethyl CH_2), 2.87 (t, 1H, *J* = 10.5 Hz, H-2), 3.13 (d, 1H, *J* = 1.0 Hz, OH), 3.51-3.59 (m, 2H, H-3 and H-5), 3.68 (dd, 1H, *J* = 2.0 Hz, 10.0 Hz, H-6a), 3.76-3.84 (m, 5H, H-6b, OCH_3 and H-4), 4.36 (d, 1H, *J* = 11.0 Hz, H-1), 4.46 (d, 1H, *J* = 12.5 Hz, $PhCH_2$), 4.58 (d, 1H, *J* = 12.0 Hz, $PhCH_2$), 4.59 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.97 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 6.42 (dd, 1H, *J* = 2.5 Hz, 8.5 Hz), 6.47 (d, 1H, *J* = 2.5 Hz), 7.08 (d, 1H, *J* = 8.5 Hz), 7.25-7.34 (m, 10H), 7.86 (s, 1H, ArOH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.71, 26.28, 53.77 (C-2), 55.29, 68.04 (C-6), 73.46, 74.85, 75.57 (C-3), 77.39 (C-4), 78.01 (C-5), 83.48 (C-1), 102.82, 105.71, 115.56, 127.72, 127.76, 127.79, 128.10, 128.40, 128.43, 130.38, 137.92, 138.37, 156.97, 160.96; HRMS (ESI) Anal. Calcd for $C_{29}H_{34}O_6S$ $[M+NH_4]^+$: 528.2414, found: 528.2430.

1-(4,6-Di-*O*-benzyl-2-deoxy-2-*p*-ethylthio-β-D-glucopyranosyl)-2-naphthol (4g)

Compound **4g** was isolated after column chromatography on silica gel (petroleum ether/acetone, 8:1) as a colorless oil (79% yield): R*f* 0.35 (petroleum ether/acetone, 3:1); $[\alpha]_D^{20}$ +90.4 (c 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.67 (t, 3H, *J* = 7.5 Hz, ethyl CH_3), 1.41-1.59 (m, 2H, ethyl CH_2), 3.19 (d, 1H, *J* = 1.5 Hz, OH), 3.25 (t, 1H, *J* = 11.5 Hz, H-2), 3.66-3.73 (m, 3H, H-6a, H-3 and H-5), 3.82 (dd, 1H, *J* = 2.5 Hz, 10.0 Hz, H-6b), 3.94 (t, 1H, *J* = 9.0 Hz, H-4), 4.47 (d, 1H, *J* = 12.0 Hz, $PhCH_2$), 4.60 (d, 1H, *J* = 12.5 Hz, $PhCH_2$), 4.63 (d, 1H, *J* = 11.5 Hz, $PhCH_2$), 5.01 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 5.44 (d, 1H, *J* = 10.5 Hz, H-1), 7.16 (d, 1H, *J* = 9.0 Hz), 7.26-7.35 (m, 11H), 7.44-7.47 (m, 1H), 7.72-7.75 (m, 2H), 8.07 (d, 1H, *J* = 8.5 Hz), 8.50 (s, 1H, ArOH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.34, 26.23, 52.80 (C-2), 67.89 (C-6), 73.41, 74.91, 75.81 (C-3), 77.36 (C-4), 77.60 (C-1), 78.37 (C-5), 115.27, 119.66, 123.12, 123.16, 125.98, 127.73, 127.80, 128.13, 128.22, 128.42, 128.73, 130.49, 132.38, 137.86, 138.33, 154.69; HRMS (ESI) Anal. Calcd for $C_{32}H_{34}O_5S$ $[M+NH_4]^+$: 548.2465, found: 548.2454.

3-(4,6-Di-*O*-benzyl-2-deoxy-2-*p*-tolylthio-α-D-altropyranosyl)-1-propene (6a)

Compound **6a** was isolated after column chromatography on silica gel (petroleum ether/acetone, 18:1) as a colorless oil (50% or 64% yield): R*f* 0.35 (petroleum ether/ethyl acetate, 6:1); $[\alpha]_D^{20}$ -17.2 (c 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.32 (s, 3H, tolyl CH_3), 2.57-2.63 (m, 1H, C*H*$_2$CHCH$_2$), 2.65 (d, 1H, *J* = 4.5 Hz, OH), 2.75-2.80 (m, 1H, C*H*$_2$CHCH$_2$), 3.19 (t, 1H, *J* = 6.5 Hz, H-2), 3.50 (dd, 1H, *J* = 4.5 Hz, 10.5 Hz, H-6a), 3.55 (dd, 1H, *J* = 5.5 Hz, 10.5 Hz, H-6b), 3.76 (ddd, 1H, *J* = 4.5 Hz, 6.5 Hz, 8.0 Hz, H-1), 3.86-3.91 (m, 2H, H-3 and H-4), 4.09 (dd, 1H, *J* = 5.0 Hz, 9.5 Hz, H-5), 4.45 (d, 1H, *J* = 12.0 Hz, $PhCH_2$), 4.51 (d, 1H, *J* = 12.0 Hz, $PhCH_2$), 4.56 (d, 1H, *J* = 11.5 Hz, $PhCH_2$), 4.62 (d, 1H, *J* = 11.5 Hz, $PhCH_2$), 5.05-5.11 (m, 2H, =CH_2), 5.80-5.89 (m, 1H, -CH=), 7.09 (d, 2H, *J* = 8.0 Hz), 7.27-7.35 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.11, 37.14, 51.97 (C-2), 68.19 (C-3), 69.02 (C-6), 71.18 (C-5), 72.03, 73.32, 74.36 (C-4), 74.73 (C-1), 117.05, 127.65, 127.90, 127.95, 128.35, 128.47, 129.16, 129.81, 133.53, 134.92, 137.80, 137.93, 138.04; HRMS (ESI) Anal. Calcd for $C_{30}H_{34}O_4S$ $[M+NH_4]^+$: 508.2516, found: 508.2518.

2-(4,6-Di-*O*-benzyl-2-deoxy-2-*p*-tolylthio-α-D-altropyranosyl)-cyclopentone (6b)

Compound **6b** was isolated after column chromatography on silica gel (petroleum ether/acetone, 10:1) as a colorless oil (51% yield): R*f* 0.30 (petroleum ether/acetone, 5:1); $[\alpha]_D^{20}$ -42.0 (c 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.67-1.71 (m, 1H), 1.83-1.88 (m, 1H), 1.96-2.05 (m, 2H), 2.08-2.15 (m, 1H), 2.28 (t, 1H, *J* = 8.5 Hz), 2.32 (s, 3H), 2.72 (d, 1H, *J* = 6.0 Hz), 3.11 (td, 1H, *J* = 3.5 Hz, 9.0 Hz), 3.26 (t, 1H, *J* = 9.0 Hz), 3.47 (d, 2H, *J* = 6.0 Hz), 3.79 (qd, 1H, *J* = 3.5 Hz, 6.0 Hz, 9.5 Hz), 3.86 (t, 1H, *J* = 3.5 Hz), 4.01 (dd, 1H, *J* = 4.0 Hz, 9.0 Hz), 4.05 (td, 1H, *J* = 3.5 Hz, 5.5 Hz), 4.41 (d, 1H, *J* = 12.0 Hz, $PhCH_2$), 4.45 (d, 1H, *J* = 12.0 Hz, $PhCH_2$), 4.57 (d, 1H, *J* = 12.0 Hz, $PhCH_2$), 4.65 (d, 1H, *J* = 12.0 Hz, $PhCH_2$), 7.10 (d, 2H, *J* = 8.0 Hz), 7.26-7.36 (m, 10H), 7.38 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.59, 21.15, 23.35, 39.19, 50.52, 51.33, 68.01, 68.78, 71.90, 72.47, 73.40, 73.63, 75.40, 127.58, 127.62, 127.77, 127.83, 128.07, 128.38, 128.46, 129.86, 134.36, 137.93, 138.33, 219.69; HRMS (ESI) Anal. Calcd for $C_{32}H_{36}O_5S$ $[M+NH_4]^+$: 550.2622, found: 550.2627.

3-(4,6-Di-*O*-benzyl-2-deoxy-2-*p*-ethylthio-β-D-glucopyranosyl)-1-propene (6c)

Compound **6c** was isolated after column chromatography on silica gel (petroleum ether/acetone, 15:1) as a colorless oil (46% or 41% yield): R*f* 0.35 (petroleum ether/acetone, 5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.28 (t, 3H, *J* = 7.5 Hz, ethyl CH_3), 2.37-2.42 (m, 2H, H-2 and C*H*$_2$CHCH$_2$), 2.55-2.67 (m, 2H, ethyl CH_2), 2.78-2.83 (m, 1H, C*H*$_2$CHCH$_2$), 3.02 (d, 1H, *J* = 1.5 Hz, OH), 3.33 (ddd, 1H, *J* = 3.0 Hz, 8.0 Hz, 10.5 Hz, H-1), 3.39 (ddd, 1H, *J* = 2.0 Hz, 4.5 Hz, 9.5 Hz, H-5), 3.49 (t, 1H, *J* = 8.5 Hz, 9.5 Hz, H-4), 3.54-3.58 (m, 1H, H-3), 3.69 (dd, 1H, *J* = 4.5 Hz, 11 Hz, H-6b), 3.74 (dd, 1H, *J* = 2.0 Hz, 10.5 Hz, H-6a), 4.57 (d, 1H, *J* = 12.5 Hz, $PhCH_2$), 4.61 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.63 (d, 1H, *J* = 12.5 Hz, $PhCH_2$), 4.91 (d, 1H, *J* = 11.5 Hz, $PhCH_2$), 5.09-5.15 (m, 2H, =CH_2), 5.91-5.99 (m, 1H, -CH=), 7.26-7.35 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.29, 25.03, 36.91, 53.75 (C-2), 69.17 (C-6), 73.40, 74.60, 76.15 (C-3), 78.55 (C-4, C-5), 78.96 (C-1), 117.10, 127.51, 127.71, 127.99, 128.31, 128.38, 134.78, 138.47; HRMS (ESI) Anal. Calcd for $C_{25}H_{32}O_4S$ $[M+NH_4]^+$: 446.2359, found: 446.2357.

2-(4,6-Di-*O*-benzyl-2-deoxy-2-*p*-ethylthio-β-D-glucopyranosyl)-cyclopentone (6d)

Compound **6d** was isolated after column chromatography on silica gel (petroleum ether/acetone, 10:1) as a colorless oil (70% yield): R*f* 0.30 (petroleum ether/acetone, 5:1); $[\alpha]_D^{20}$ -23.2 (c 1.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.26 (t, 3H, *J* = 7.5 Hz, ethyl CH_3), 1.73-1.84 (m, 1H), 2.00-2.15 (m, 4H), 2.28-2.34 (m, 1H), 2.42 (t, 1H, *J* = 10.5 Hz, H-2), 2.55-2.66 (m, 2H, ethyl CH_2), 2.86 (dd, *J* = 9.0 Hz, 1H), 2.97 (d, 1H, *J* = 1.5 Hz, OH), 3.39 (ddd, 1H, *J* = 2.0 Hz, 4.0 Hz, 9.5 Hz, H-5), 3.54 (dd, 1H, *J* = 9.0 Hz, 10.0 Hz, H-4), 3.61-3.67 (m, 2H, H-3, H-6a), 3.72 (dd, 1H, *J* = 4.0 Hz, 11.5 Hz, H-6b), 3.87 (dd, 1H, *J* = 2.0 Hz, 11.0 Hz, H-1), 4.50 (d, 1H, *J* = 12.5 Hz, $PhCH_2$), 4.54 (d, 1H, *J* = 12.0 Hz, $PhCH_2$), 4.66 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 4.89 (d, 1H, *J* = 11.0 Hz, $PhCH_2$), 7.27-7.33 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.09, 20.84, 22.76, 23.46, 39.07, 50.19, 51.42 (C-2), 68.94 (C-6), 73.16, 74.61, 75.56 (C-3), 77.19 (C-1), 78.35 (C-5), 78.47 (C-4), 127.47, 127.70, 127.98, 128.26, 128.39, 138.47, 219.58; HRMS (ESI) Anal. Calcd for $C_{27}H_{34}O_5S$ $[M+NH_4]^+$: 488.2465, found: 488.2474.

2-(4,6-Di-*O*-benzyl-2-deoxy-β-D-altropyranosyl)-4,5-di-methoxy-phenol (7)

Compound **7** was isolated after column chromatography on silica gel (toluene–CH_3CN, 6:1) as a colorless oil (72% yield): R*f* 0.40 (toluene–CH_3CN, 4:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99-2.06 (m, 1H), 2.18 (dd, 1H, J = 3.2 Hz, 12.0 Hz), 2.49 (s, 1H), 3.71 (d, 2H, OCH_3, J = 2.4 Hz), 3.75 (d, 1H, J = 2.4 Hz), 3.78 (s, 1H), 3.83 (s, 1H), 3.98 (d, 1H, J = 10.0 Hz), 4.31 (d, 1H, J = 2.0 Hz), 4.47-4.51 (m, 2H), 4.59-4.62 (m, 2H), 5.00 (dd, 1H, J = 2.0 Hz, 11.6 Hz, H-1), 6.49 (s, 1H), 6.50 (s, 1H), 7.24-7.31 (m, 10H), 7.93 (s, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 36.97, 55.85, 56.61, 64.30, 68.70, 71.79, 73.44, 73.69, 74.01, 74.49, 102.13, 110.36, 115.70, 127.70, 127.78, 127.99, 128.21, 128.42, 128.60, 137.35, 137.98, 142.14, 149.40, 149.97; HRMS (ESI) Anal. Calcd for $C_{28}H_{32}O_7$ $[M+H]^+$: 481.2221, found: 481.2232.

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Notes and references

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†Electronic Supplementary Information (ESI) available: Copies of NMR spectra of **1, 1b**, **2c**, **2d**, **2**, **4a-4g**, **6a-6d, 7**. See DOI:10.1039/b000000x/

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