Pergamon

Tetrahedron 57 (2001) 2973–2980

TETRAHEDRON

Stereoselective synthesis of β-*C*-D-glucopyranosides using the reaction of TMSCN and Grignard reagents with cyclic five-membered sulfonium salt intermediates

Hui Liu and Irina P. Smoliakova*

Chemistry Department, University of North Dakota, Grand Forks, ND 58202-9024, USA

Received 20 December 2000; accepted 6 February 2001

Abstract—In the presence of a Lewis acid, ArSCl adducts of tri-*O*-benzyl-D-glucal react with vinyl ethers to form cyclic five-membered sulfonium salt intermediates. The latter are capable of reacting with TMSCN and Grignard reagents furnishing exclusively 2-*S*-(aryl)-2-thio-β-*C*-D-glucopyranosides. The one-pot reaction also proceeds with high stereoselectivity of C–C bond formation in the lateral chain providing exclusively or predominantly *C*-glycosides with (*S*)-configuration of the chiral center in the lateral chain. © 2001 Elsevier Science Ltd. All rights reserved.

1. Introduction

Synthesis of *C*-glycosides and related compounds has been an important direction in modern synthetic organic chemistry.[1] These non-hydrolyzable analogs of *O*-glycosides have a number of valuable properties and applications,[2] including their use as chiral precursors in syntheses of other compounds.[3] The major challenge in the preparation of *C*-glycosides is to obtain α- or β-isomers with high stereoselectivity.[1] One possible approach to solve this problem is the use of cyclic intermediates.[4] Recently, we have shown that episulfonium-like intermediates (**3a**,**b**), generated in the presence of a Lewis acid from ArSCl adducts (**2a**,**b**) of glycals (e.g. **1a**,**b**), react with a number of *C*-nucleophiles, including silyl enol ethers,[5–7] allyltrimethylsilane,[5–7] Grignard reagents,[8] and vinyl ethers[9] to form *C*-glycosides (Scheme 1).

In all the reactions, major isomers were β-gluco (starting from D-glucals) or β-galacto (from D-galactal) derivatives. In addition, small amounts of the corresponding α-manno isomers were isolated as well. For the *C*-nucleophiles studied, the best ratio of the isomers, β-gluco/α-manno ≥ 97:3, was achieved using the 2,4,6-mesitylthio derivatives and $SnCl_4$ in CH_2Cl_2. In the case of vinyl ethers,[9] the reaction had a second intermediate, the five-membered sulfonium salt.[10,11] It was demonstrated that this intermediate can be quenched with H_2O, MeOH, or a donor of hydride ion to furnish aldehydes or ketones, acetals, and ethers, respectively (Scheme 2).[9]

In this paper, we disclose our results on the synthesis of *C*-glycosides with a functionalized lateral chain using the reaction of the five-membered sulfonium intermediates with TMSCN and Grignard reagents.

2. Results and discussion

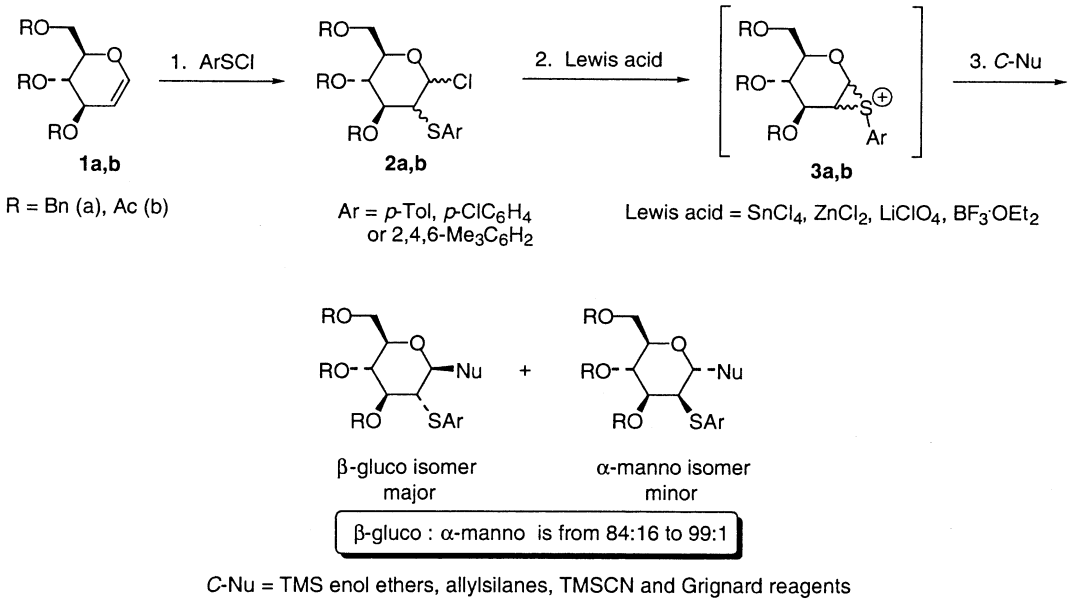
Intermediate **5**, forming in the reaction of *p*-TolSCl adduct (**2**) of tri-*O*-benzyl-D-glucal (**1**) with 1-methoxy-2-methylpropene (**4**) in the presence of $SnCl_4$, was selected as the model sulfonium salt and was prepared as previously described.[9] It was found that TMSCN reacted with sulfonium salt **5** at temperatures above −40°C to give *C*-glycoside **6** in 86% yield (Scheme 3). The ^1H NMR spectrum analysis revealed that the isolated product has β-gluco structure ($J_{1,2}=J_{2,3}=10.3$ Hz). The ^{13}C NMR spectrum of the isolated product contained only one set of the signals, confirming that the reaction also proceeded with complete stereocontrol of the C–C bond formation in the lateral chain. It is significant that no diastereomers of **6** were detected in the reaction mixture.

To extend this work, we studied the reaction of sulfonium salt **5** with Grignard reagents. The latter were chosen because of their availability, easy handling, and the possibility of introducing different groups in the lateral chain of *C*-glycosides. Also, organomagnesium compounds have been reported to be excellent nucleophiles in a similar reaction, the ArS-mediated coupling of two vinyl ethers.[10] We found that sulfonium salt **5** readily reacted with MeMgBr in

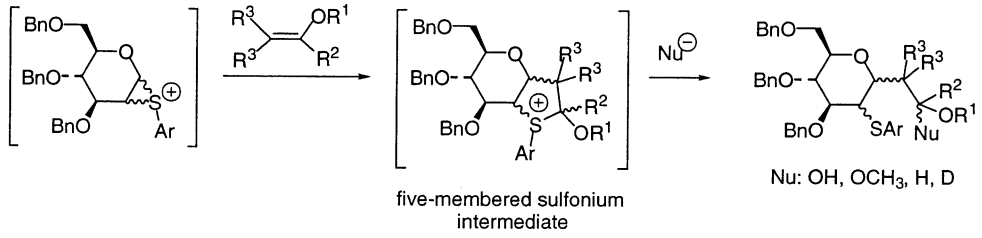
Keywords: *C*-glycosides; episulfonium ions; sulfonium salts; Grignard reagents; trimethylsilylcyanide.

* Corresponding author. Fax: +1-701-777-2331;
e-mail: ismoliakova@mail.chem.und.nodak.edu

PII: S0040-4020(01)00160-0



Scheme 1.



Scheme 2.

the range of −20–+20°C to give *C*-glycoside **7** in a high yield (Scheme 3). Again, the isolated product was a single isomer having the β-gluco configuration. Similarly, PhMgBr and methallylmagnesium chloride reacted with sulfonium salt **5** to provide responding *C*-glycosides **8** and **10** in a high yield (Scheme 3). In both the cases, the compounds were only isomers of β-gluco configuration (^{1}H NMR data) and no traces of other isomers were detected.

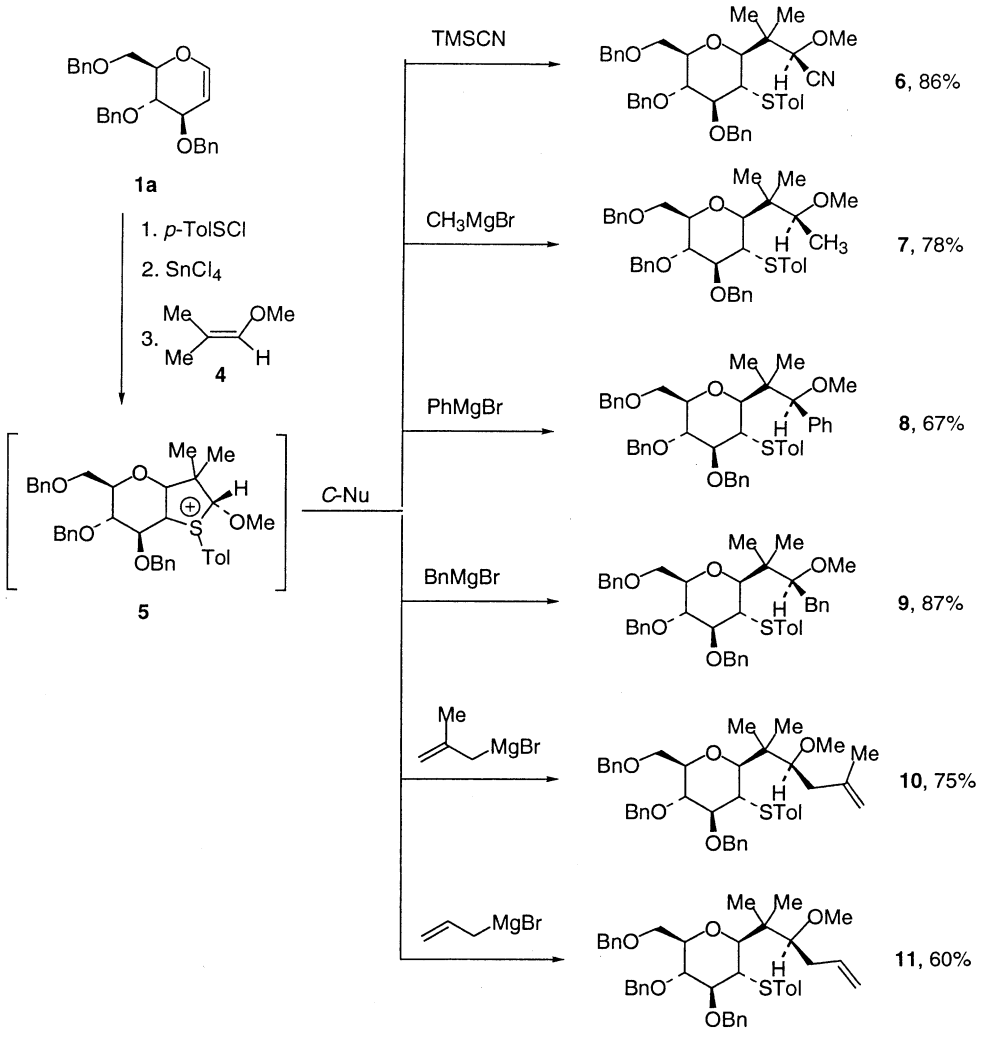
When BnMgBr was employed in the reaction with the sulfonium salt, the isolated product **9** was a mixture of two diastereomers in a ratio of 8:1 (Scheme 3). The compounds were separated using TLC chromatography and analyzed by ^{1}H NMR spectroscopy. The two isomers both had the β-gluco configuration and differed only in the absolute configuration of the chiral center in the lateral chain.

The reaction of allylmagnesium bromide with intermediate **5** proceeded with poor stereoselectivity, providing two β-gluco isomers **11** in a ratio of 3:1. In order to improve the stereoselectivity, we varied a number of parameters/conditions of the reaction. First, different Lewis acids were used in the reaction of sulfonium intermediate **5** with allylmagnesium bromide. It is well known that the change of a Lewis acid in various reactions may lead to different stereochemical results;[12] however, in the reaction studied here, the substitution of $SnCl_4$ for $ZnCl_2$ or $LiClO_4$ did not improve the ratio of the isomers (3:2 and 5:2, respectively).

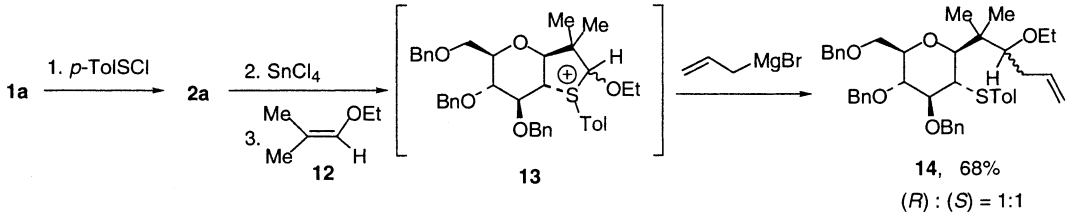
Since the size of the substituents in the reaction complex might be important for the stereochemical outcome, we replaced the MeO group with an EtO substituent in the sulfonium intermediate by reacting pyranosyl chloride **2a** with 1-ethoxy-2-methylpropene (**12**, Scheme 4). The reaction of intermediate **13** with allylmagnesium bromide gave a high yield of *C*-glycoside **14**, however without any significant improvement of the stereoselectivity.

We also synthesized sulfonium salt **15** with the bulky 2,4,6-trimethylphenyl (mesityl, Mes) substituent at the sulfur atom (Scheme 5). The introduction of the bulky aryl group affected the stereoselectivity of the reaction; however, still two diastereomers of **16** ((*S*)/(*R*)=4:1) were formed.

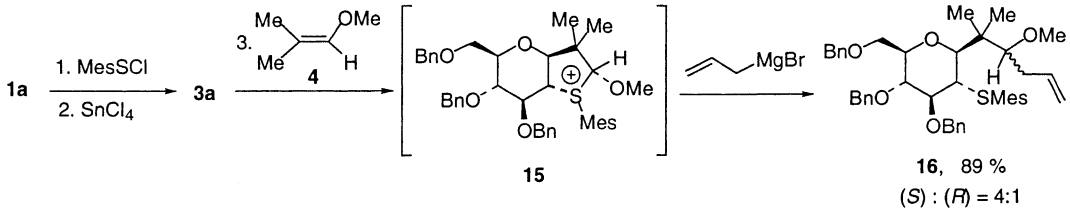
We then extended our investigation to see if the sulfonium intermediates obtained from other vinyl ethers react with TMSCN and Grignard reagents in a highly stereoselective fashion as well. It was found that sulfonium intermediate **18** prepared from pyranosyl chloride **2a** and methyl vinyl ether (**17**) reacted with TMSCN and PhMgBr to furnish β-*C*-D-glucopyranosides **19** and **20**, respectively, with high stereoselectivity ((*R*)/(*S*) ≥ 95:5) though in a low yield



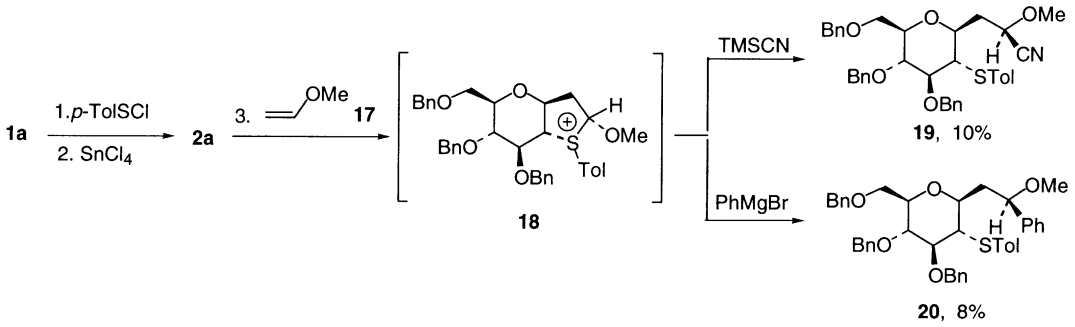
Scheme 3.



Scheme 4.



Scheme 5.

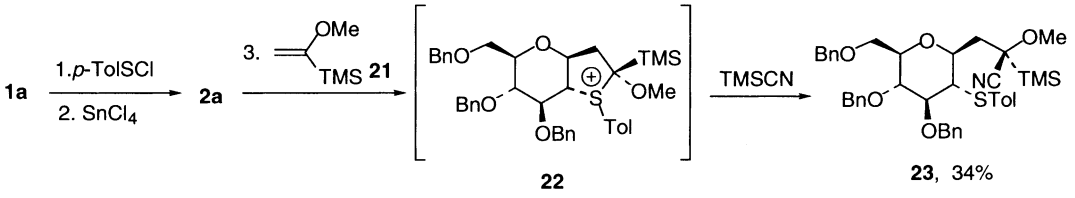


Scheme 6.

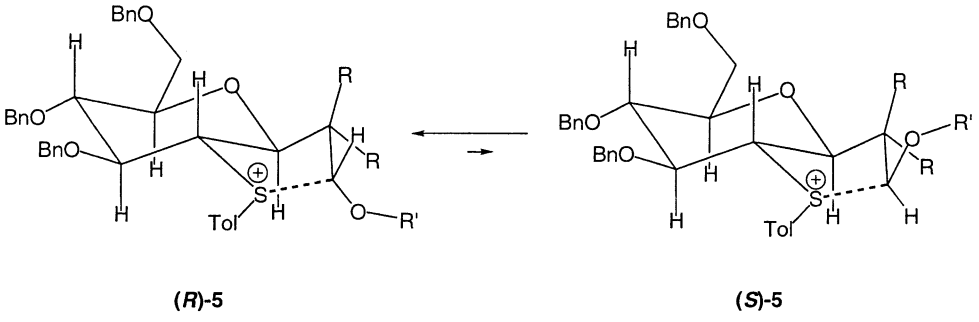
(Scheme 6). Similar results were obtained with sulfonium salt **22** prepared from α-substituted vinyl ether **21** (Scheme 7).

In all the reactions studied, we observed either the exclusive or predominant formation of one diastereomer. Using X-ray crystal analysis of the sulfoxide prepared from *C*-glycoside **6**, the (*R*) absolute configuration of the chiral center in the lateral chain has been established. Presumably, *C*-glycosides **7**–**8**, **10**, **16**, **19**, **20**, **23** and major isomers of **9**, **11**, and **14** have the same configuration as glycoside **6**.

In order to explain the observed stereoselectivity, we considered possible structures of the sulfonium intermediate in detail. For the similar sulfonium salts prepared by the ArS-mediated dimerization of two vinyl ethers, the S–C(OR) bond length was determined to be somewhat longer than it was expected for the ordinary C–S bond.[11]



Scheme 7.



Scheme 8.

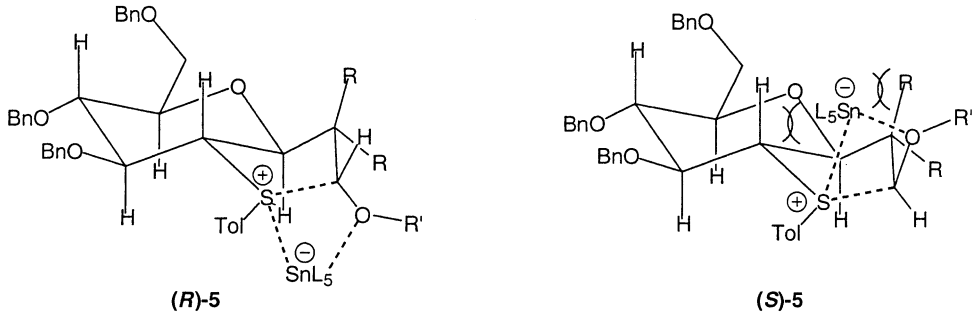
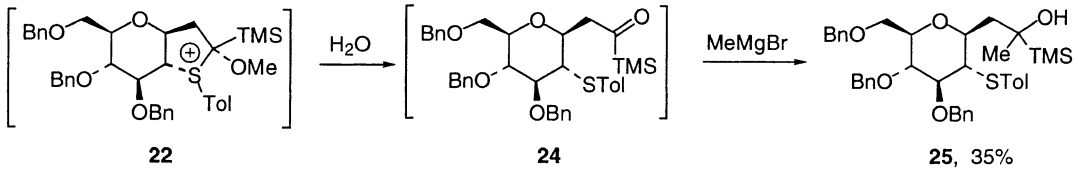


Figure 1. Coordination of SnL_5^- with the sulfonium intermediates.



Scheme 9.

Based on these data, we suggest that intermediate **5** is likely to exist as an equilibrating mixture of two isomeric forms, (*R*)-**5** and (*S*)-**5** (Scheme 8). Isomer (*R*)-**5**, having the alkoxy group *trans* relative to the hydrogen at C(2) of the pyranose ring, must be the predominant one. The S_N2-like attack of a nucleophile would give the product with the inverse configuration of the chiral center.

Another contributing, if not determining, factor to the stereoselectivity of the reaction is the possible chelate effect. We suggest that the tin atom is coordinated with the sulfur and oxygen atoms of the sulfonium salt (Fig. 1). Because of the steric hindrance, formation of the chelate complex with intermediate (*S*)-**5** would be unlikely. The coordination of the metal with isomer (*R*)-**5** appears to be more probable and leads to an increase in the stability of the (*R*)-intermediate. Thus, the possible chelate effect also predicts the preferable formation of the (*R*)-product.[†]

It is noteworthy that in the reactions studied, RMgBr also reacted with $SnCl_4$ and, as a result, organotin by-products, e.g. Bn_4Sn and Ph_3SnOH, were isolated as well.[13] In the case of PhMgBr, BnMgBr and methallylmagnesium chloride, the use of 4 equiv. of the Grignard reagents was sufficient and increasing these quantities up to 8 equiv. did not result in a noticeable change in the yield or stereoselectivity. However, for MeMgBr and allylmagnesium bromide, the reaction of the sulfonium intermediates with 4 equiv. of the Grignard reagents did not take place. Apparently, under these reaction conditions, the Grignard reagents were converted to Me_4Sn and similar organotin species, which were nonreactive toward the sulfonium intermediates. The use of 8 equiv. of MeMgBr and allylmagnesium bromide, however, provided high yields of the desired *C*-glycosides.

It is interesting that the reaction of intermediate **22** with MeMgBr provided β-*C*-D-glucoside **25** bearing a hydroxyl group in the lateral chain (Scheme 9). The compound was isolated in a single isomeric form, but we could not determine the absolute configuration of the chiral center in the lateral chain. We suggest that, under the conditions used, the Grignard reagent did not react with the sulfonium salt **22**. After quenching the reaction mixture with ice–water, intermediate **22** was instantly converted to the corresponding aldehyde **24**[9] that further reacted with MeMgBr. Similar results were observed in previous studies of the reaction of triallylborane with cyclic sulfonium salts that had been generated from simple vinyl ethers.[14] No reaction was observed between the sulfonium salt and triallylborane. However, when water was introduced, the corresponding carbonyl compound was formed that further reacted with triallylborane. It is noteworthy that triallylborane is known to react with both ketones/aldehydes and water.

In summary, we describe a highly stereoselective method for synthesis of 2-(*S*-aryl)-2-thio-β-*C*-D-glucopyranosides having different functional groups in the lateral chain. The proposed protocol involves an efficient one-pot coupling of four components: glucal, ArSCl, vinyl ether, and external *C*-nucleophile.

3. Experimental

3.1. Instrumentation and materials

^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 500 spectrometer. Chemical shifts are given in ppm relative to TMS; coupling constants, *J*, are provided in Hz. Mass spectrometric data were obtained on a Finnigan MAT 95 mass spectrometer. IR spectra were recorded on an ATI Mattson Genesis Series FTIR spectrometer. Optical rotation data were measured on an Autopol III automatic polarimeter. Preparative TLC was carried out by using glass plates, 200×250 mm, with an unfixed layer of Aldrich silica gel 60, 230–400 mesh. Analytical TLC was performed on E. Merck precoated plates of silica gel 60 F_{254}. All reactions were carried out under an atmosphere of dry nitrogen using oven-dried or flame-dried glassware and freshly distilled and dried solvents.

Arylsulfenyl chlorides were obtained from 4-methylbenzenethiol and 2,4,6-trimethylaryl (mesityl) disulfide using SO_2Cl_2.[15] Methyl vinyl ether was synthesized from *n*-butyl vinyl ether and MeOH in the presence of $Hg(OAc)_2$.[16] 1-Methoxy-2-methylpropene and 1-ethoxy-2-methylpropene were prepared by pyrolysis of the corresponding acetals using *p*-toluenesulfonic acid as a catalyst. Other chemicals were purchased from Aldrich Chemical.

3.2. General procedure for synthesis of *C*-glycosides 6–11, 14, 16, 19, 22, and 24

To a solution of 0.208 g tri-*O*-benzyl-D-glucal (0.5 mmol) in CH_2Cl_2 (20 mL), 0.28 mL 1.8 M solution of *p*-TolSCl (0.5 mmol) in CH_2Cl_2 was added dropwise at room temperature. The color changed from yellow to colorless within 20 min. The mixture then was cooled to −78°C, and 0.6 mL of 1.0 M solution of vinyl ether (0.6 mmol) in CH_2Cl_2 was added, followed by 0.6 mL of 1.0 M solution of $SnCl_4$ (0.6 mmol) in CH_2Cl_2. The mixture was stirred at −78°C for 30 min, then 2 mmol (TMSCN or 3.0 M solution of PhMgBr in ether) or 4 mmol (1.0 M solution of allylmagnesium bromide in ether, 0.5 M solution of

[†] Reactions of intermediate (>*R*)-**5** give cyano derivatives **6** and **19** with the (*R*) absolute configuration; however, other products have the (*S*) configuration due to different priorities of the CN and alkyl groups.

2-methylallylmagnesium bromide in THF, 3.0 M solution of MeMgBr in ether or 2.0 M solution of BnMgBr in ether) of a C–Nu was added. The temperature was slowly raised to −30°C within 2 h. Then the mixture was stirred at rt for 12 h, quenched with saturated solution of $NaHCO_3$, extracted with ether, and dried over Na_2SO_4. Preparative TLC of the crude material after solvent removal in vacuum afforded a *C*-glycoside. Yields and isomer ratios of the *C*-glycosides are given in Schemes 3–6.

3.2.1. (2*R*)-2-Methoxy-3-methyl-3-*C*-[3,4,6-tri-*O*-benzyl-2-*S*-(*p*-tolyl)-2-thio-β-D-glucopyranosyl]butanenitrile (6). R_f 0.43 (1:2 ether–hexane); $[\alpha]^{28}_D$=−38.1° (*c* 0.0359, $CHCl_3$); IR (neat, ν, cm^{-1}): 2233 w (CN); ^1H NMR: 1.06 and 1.25 (two s, 6H, $C(CH_3)_2$), 2.31 (s, 3H, CH_3), 3.26 (br. t, $J_{1,2}$=$J_{2,3}$=10.3 Hz, 1H, H-2), 3.46 (m, 1H, H-5), 3.48 (s, 3H, OCH_3), 3.58 (d, 1H, H-1), 3.65 (m, 3H, H-3, H-4 and H-6a), 3.70 (dd, $J_{5,6b}$=11.0 Hz, 1H, H-6b), 4.48 (s, 1H, CHCN), 4.52 and 4.58 (two d, J_{AB}=12.2 Hz, 2H, CH_2Ph), 4.60 and 4.77 (two d, J_{AB}=11.0 Hz, 2H, CH_2Ph), 4.77 and 4.88 (two d, J_{AB}=10.4 Hz, 2H, CH_2Ph), 7.28 (m, 19H, H-Arom); ^{13}C NMR: 19.9, 21.1, and 21.4 ($3CH_3$ groups), 42.9 ($C(CH_3)_2$), 52.8 (CHS), 58.6 (OCH_3), 69.5, 73.6, 74.8, and 76.4 ($4OCH_2$ groups), 79.1, 79.7, 82.2, and 85.4 (4CHOR groups), 117.6 (CN), 127.9, 127.9, 128.0, 128.1, 128.2, 128.5, 128.6, 128.8, 128.9, 130.3 and 130.9 (C-Arom); HRMS (EI): Calcd for $C_{40}H_{45}SO_5N$ 651.3016; Found: M^+ *m/e* 651.3034.

3.2.2. (2*S*)-3-Methoxy-2-methyl-2-*C*-[3,4,6-tri-*O*-benzyl-2-*S*-(*p*-tolyl)-2-thio-β-D-glucopyranosyl]butane (7). R_f 0.47 (1:2 ether–hexane); $[\alpha]^{20}_D$=−39.3° (*c* 0.0207, $CHCl_3$); IR (neat, ν, cm^{-1}): 1497 s (arom. ring); ^1H NMR: 0.99 and 1.01 (two s, 6H, $C(CH_3)_2$), 1.05 (d, J_{AB}=6.2 Hz, 3H, CH_3), 2.34 (s, 3H, CH_3), 3.31 (s, 3H, OCH_3), 3.38 (t, $J_{1,2}$=8.9 Hz, $J_{2,3}$=9.0 Hz, 1H, H-2), 3.40 (m, 1H, H-5), 3.45 (d, 1H, H-1), 3.53 (dd, $J_{3,4}$=6.4 Hz, 1H, H-3), 3.57 (quart., J_{AB}=6.2 Hz, 1H, C*H*CH_3), 3.64 (m, 2H, H-6), 3.66 (br. t, $J_{4,5} \approx$ 7.5 Hz, 1H, H-4), 4.45 and 4.65 (two d, J_{AB}=11.2 Hz, 2H, CH_2Ph), 4.54 and 4.60 (two d, J_{AB}=12.1 Hz, 2H, CH_2Ph), 4.57 and 4.80 (two d, J_{AB}=9.8 Hz, 2H, CH_2Ph), 7.26 (m, 19H, H-Arom); ^{13}C NMR: 12.7, 19.5, 19.6, and 21.1 ($4CH_3$ groups), 42.9 ($C(CH_3)_2$), 50.9 (CHS), 57.0 (OCH_3), 70.0, 73.2, 73.6, and 74.6 ($4OCH_2$ groups), 78.7, 79.2, 80.1, 83.2 and 83.4 (5CHO groups), 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.2, 128.3, 129.7, 132.8, 136.4, 138.3, and 138.6 (C-Arom); HRMS: Calcd for $C_{40}H_{48}SO_5Na$ 663.3120; Found: $(MNa)^+$ *m/e* 663.3098.

3.2.3. (3*S*)-3-Methoxy-2-methyl-3-phenyl-2-*C*-[3,4,6-tri-*O*-benzyl-2-*S*-(*p*-tolyl)-2-thio-β-D-glucopyranosyl]propane (8). R_f 0.36 (1:4 ether–hexane); $[\alpha]^{20}_D$=−22.4° (*c* 0.0264, $CHCl_3$); IR (neat, ν, cm^{-1}): 1493 s (arom. ring); ^1H NMR: 0.92 and 1.09 (two s, 6H, $C(CH_3)_2$), 2.34 (s, 3H, CH_3), 3.19 (s, 3H, OCH_3), 3.28 (d, $J_{1,2}$=8.5 Hz, 1H, H-1), 3.40 (dd, $J_{2,3}$=8.8 Hz, 1H, H-2), 3.42 (ddd, $J_{4,5}$=7.0 Hz, $J_{5,6a}$=3.4 Hz, $J_{5,6b}$=7.9 Hz, 1H, H-5), 3.51 (dd, $J_{2,3}$= 8.8 Hz, $J_{3,4}$=6.0 Hz, 1H, H-3), 3.63 (dd, $J_{3,4}$=6.0 Hz, 1H, H-4), 3.64 (m, 1H, H-6b), 3.70 (m, 2H, H-6), 4.42 and 4.62 (two d, J_{AB}=11.2 Hz, 2H, CH_2Ph), 4.54 and 4.79 (two d, J_{AB}=11.0 Hz, 2H, CH_2Ph), 4.60 and 4.65 (two d, J_{AB}=12.3 Hz, 2H, CH_2Ph), 4.65 (s, 1H, H-3′), 7.25 (m, 24H, H-Arom); ^{13}C NMR: 19.5, 19.6, and 21.1 ($3CH_3$ groups), 43.9 ($C(CH_3)_2$), 50.2 (CHS), 56.9 (OCH_3), 70.3, 73.2, 73.4, and 74.3 ($4OCH_2$ groups), 77.9, 78.0, 82.1, 82.6, and 86.8 (5CHO groups), 127.1, 127.4, 127.5, 127.7, 127.8, 128.1, 128.2, 128.3, 128.4, 128.9, 129.6, 129.7, 129.8, 131.4, 132.5, 136.7, 138.2, 138.3, 138.6, and 139.0 (C-Arom); HRMS: Calcd for $C_{45}H_{50}SO_5Na$ 725.3277; Found: $(MNa)^+$ *m/e* 725.3255.

3.2.4. (3*S*)-3-Methoxy-2-methyl-4-phenyl-2-*C*-[3,4,6-tri-*O*-benzyl-2-*S*-(*p*-tolyl)-2-thio-β-D-glucopyranosyl]butane [(3*S*)-9, major isomer]. R_f 0.36 (1:9 ether–hexane); $[\alpha]^{20}_D$=−30.9° (*c* 0.0042, $CHCl_3$); ^1H NMR: 1.00 and 1.18 (two s, 6H, $C(CH_3)_2$), 2.34 (s, 3H, CH_3), 2.57 (dd, $J_{4a',4b'}$=13.4 Hz, $J_{4a',3'}$=9.9 Hz, 1H, H-4a′), 2.85 (dd, $J_{4b',3'}$=2.3 Hz, 1H, H-4b′), 2.91 (s, 3H, OCH_3), 3.40 (dd, $J_{1,2}$=9.0 Hz, $J_{2,3}$=7.3 Hz, 1H, H-2), 3.42 (ddd, $J_{4,5}$=9.2 Hz, $J_{5,6a}$=2.3 Hz, $J_{5,6b}$=4.9 Hz, 1H, H-5), 3.48 (d, 1H, H-1), 3.56 (dd, 1H, H-3′), 3.58 (dd, $J_{4,5}$=9.2 Hz, $J_{3,4}$=7.0 Hz, 1H, H-4), 3.63 (dd, $J_{5,6a}$=2.3 Hz, $J_{6a,6b}$=10.9 Hz, 1H, H-6a), 3.65 (dd $J_{5,6b}$=4.9 Hz, 1H, H-6b), 3.69 (dd, 1H, H-3), 4.48 and 4.68 (two d, J_{AB}=11.2 Hz, 2H, CH_2Ph), 4.61 (m, 2H, CH_2Ph), 4.62 and 4.85 (two d, J_{AB}=10.8 Hz, 2H, CH_2Ph), 7.23 (m, 19H, H-Arom); ^{13}C NMR: 19.5, 19.6, and 21.1 ($3CH_3$ groups), 37.0 (CH_2Ph), 43.9 ($C(CH_3)_2$), 51.3 (CHS), 61.2 (OCH_3), 69.6, 73.2, 73.7, and 74.8 ($4OCH_2$ groups), 78.6, 79.0, 83.5, 83.6, and 87.8 (5CHO groups), 127.5, 127.6, 127.8, 127.7, 127.9, 128.1, 128.2, 128.3, 128.4, 129.6, 129.8, 131.7, 132.7; 136.5, 138.2, 138.4, 138.5, and 140.8 (C-Arom); HRMS: Calcd for $C_{46}H_{52}O_5S$ 716.3522; Found: M^+ *m/e* 716.3557.

3.2.5. (3*R*)-3-Methoxy-2-methyl-4-phenyl-2-*C*-[3,4,6-tri-*O*-benzyl-2-*S*-(*p*-tolyl)-2-thio-β-D-glucopyranosyl]butane [(3*R*)-9, minor isomer]. R_f 0.34 (1:9 ether–hexane); $[\alpha]^{20}_D$=−41.4° (*c* 0.0007, $CHCl_3$); IR (neat, ν, cm^{-1}): 1496 s (arom. ring); ^1H NMR: 0.97 and 1.14 (two s, 6H, $C(CH_3)_2$), 2.34 (s, 3H, CH_3), 2.62 (dd, $J_{4a',4b'}$=13.5 Hz, $J_{4a',3'}$=10.0 Hz, 1H, H-4a′), 2.89 (dd, $J_{4b',3'}$=2.3 Hz, 1H, H-4b′), 2.91 (s, 3H, OCH_3), 3.38 (dd, $J_{1,2}$=8.4 Hz, $J_{2,3}$= 6.5 Hz, 1H, H-2), 3.48 (ddd, $J_{4,5}$=8.8 Hz, $J_{5,6a}$=2.6 Hz, $J_{5,6b}$=5.3 Hz, 1H, H-5), 3.54 (dd, $J_{3,4}$=5.4 Hz, 1H, H-4), 3.58 (dd, $J_{6a,6b}$=10.9 Hz, 1H, H-6a), 3.62 (dd, 1H, H-6b), 3.66 (d, 1H, H-1), 3.73 (dd, 1H, H-3), 3.78 (dd, 1H, H-3′), 4.38 and 4.59 (two d, J_{AB}=11.4 Hz, 2H, CH_2Ph), 4.51 and 4.55 (two d, J_{AB}=12.2 Hz, 2H, CH_2Ph), 4.50 and 4.77 (two d, J_{AB}=11.1 Hz, 2H, CH_2Ph), 7.24 (m, 19H, H-Arom); ^{13}C NMR: 19.2, 19.6 and 21.1 ($3CH_3$ groups), 37.4 (CH_2Ph), 43.9 ($C(CH_3)_2$), 49.9 (CHS), 60.7 (OCH_3), 70.2, 73.0, 73.2, and 73.8 ($4OCH_2$ groups), 78.3, 78.7, 81.8, 82.3, and 87.0 (5CHO groups), 127.4, 127.5, 127.8, 128.1, 128.2, 128.3, 128.4, 129.6, 129.7, 129.8, 131.7, and 132.5 (C-Arom); HRMS: Calcd for $C_{46}H_{52}SO_5Na$ 739.3433; Found: $(MNa)^+$ *m/e* 739.3409.

3.2.6. (4*S*)-4-Methoxy-2,5-dimethyl-5-*C*-[3,4,6-tri-*O*-benzyl-2-*S*-(*p*-tolyl)-2-thio-β-D-glucopyranosyl]-1-hexene (10). R_f 0.42 (1:8 ether–hexane); $[\alpha]^{28}_D$=−43.7° (*c* 0.0036, $CHCl_3$); IR (neat, ν, cm^{-1}): 1647 (C=C); ^1H NMR: 0.96 and 1.12 (two s, 6H, $C(CH_3)_2$), 1.72 (s, 3H, CH_3C=), 2.15 (m, 2H, CH_2C=), 2.31 (s, 3H, CH_3), 3.36 (s, 3H, OCH_3), 3.39 (m, 3H, H-2, H-4, and H-5), 3.55 (dd, $J_{3',4a'}$=9.2 Hz, $J_{3',4b'}$=3.8 Hz, 1H, H-3′), 3.61 (dd, $J_{6a,6b}$=11.0 Hz,

$J_{5,6a}$=2.2 Hz, 1H, H-6a), 3.62 (m, 1H, H-4), 3.67 (d, $J_{1,2}$=6.8 Hz, 1H, H-1), 3.69 (dd, $J_{6a,6b}$=11.0 Hz, $J_{5,6b}$= 4.6 Hz, 1H, H-6a), 4.49 and 4.67 (two d, J_{AB}=11.1 Hz, 2H, CH_2Ph), 4.55 and 4.57 (two d, J_{AB}=12.4 Hz, 2H, CH_2Ph), 4.60 and 4.82 (two d, J_{AB}=10.8 Hz, 2H, CH_2Ph), 4.80 and 4.85 (two br. s, 2H, H-1′), 7.25 (m, 19H, H-Arom); ^{13}C NMR: 20.0, 20.1, 21.0, and 22.9 (4CH_3 groups), 39.1 (CH_2C═), 43.8 ($C(CH_3)_2$), 51.1 (CHS), 60.8 (OCH_3), 69.5, 73.2, 73.7, and 74.7 (4OCH_2 groups), 78.6, 78.9, 83.3, 83.6, and 84.2 (5CHO groups), 112.5 (C═CH_2), 127.4, 127.5, 127.6, 127.8, 128.1, 128.3, 128.4, 129.8, 131.0, 132.7 and 136.3 (C-Arom), 144.3 (═CH_2). HRMS: Calcd for $C_{43}H_{52}O_5S$ 680.3522; Found: M^+ *m/e* 680.3535.

3.2.7. (4*S*)-4-Methoxy-5-methyl-5-*C*-[3,4,6-tri-*O*-benzyl-2-*S*-(*p*-tolyl)-2-thio-β-D-glucopyranosyl]-1-hexene [(4*S*)-11, major isomer]. R_f 0.34 (1:9 ethyl acetate–hexane); $[\alpha]^{20}_D$=−52.1° (*c* 0.0022, $CHCl_3$); IR (neat, ν, cm^{-1}): 1639 (C═C); ^{1}H NMR: 0.96 and 1.15 (two s, 6H, $C(CH_3)_2$), 2.18 (m, 1H, H-3a′), 2.31 (m, 1H, H-3b′), 2.33 (s, 3H, CH_3), 3.38 (s, 3H, OCH_3), 3.37 (m, 4H, H-1, H-2, H-5, and H-3′), 3.56 (dd, $J_{2,3}$=9.2 Hz, $J_{3,4}$=6.8 Hz, 1H, H-3), 3.62 (dd, $J_{6a,6b}$=11.0 Hz, $J_{5,6a}$=2.3 Hz, 1H, H-6a), 3.65 (dd, $J_{5,6a}$=5.0 Hz, 1H, H-6b), 3.68 (br. t, $J_{3,4}$=$J_{4,5}$= 6.8 Hz, 1H, H-4), 4.48 and 4.67 (two d, J_{AB}=11.2 Hz, 2H, CH_2Ph), 4.54 and 4.58 (two d, J_{AB}=12.3 Hz, 2H, CH_2Ph), 4.62 and 4.85 (two d, J_{AB}=10.8 Hz, 2H, CH_2Ph), 4.99 (m, 2H, H-1′), 5.86 (m, 1H, H-2′), 7.25 (m, 19H, H-Arom); ^{13}C NMR: 20.1, 20.1, and 21.4 (3CH_3 groups), 35.5 (CH_2C═), 43.6 ($C(CH_3)_2$), 51.5 (CHS), 60.6 (OCH_3), 69.7, 73.2, 74.8, and 75.9 (4OCH_2 groups), 78.5, 79.2, 83.4, 83.8, and 85.9 (5CHO groups), 115.7 (═CH_2), 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.3, 128.4, 129.6, 129.8, 131.0, 133.3, and 136.5 (C-Arom), 137.5 (═CH); HRMS: Calcd for $C_{42}H_{50}O_5S$ 666.3392; Found: M^+ *m/e* 666.3366.

3.2.8. (4*R*)-4-Methoxy-5-methyl-5-*C*-[3,4,6-tri-*O*-benzyl-2-*S*-(*p*-tolyl)-2-thio-β-D-glucopyranosyl]-1-hexene [(4*R*)-11, minor isomer]. R_f 0.33 (1:9 ethyl acetate–hexane, 1:9); $[\alpha]^{20}_D$=−41.1° (*c* 0.0009, $CHCl_3$); IR (neat, ν, cm^{-1}): 1640 (C═C); ^{1}H NMR: 0.87 and 1.05 (two s, 6H, $C(CH_3)_2$), 2.20 (m, 1H, H-3a′), 2.33 (m, 1H, H-3b′), 2.34 (s, 3H, CH_3), 3.32 (s, 3H, OCH_3), 3.34 (m, 1H, H-2), 3.47 (ddd, $J_{4,5}$=8.9 Hz, $J_{5,6a}$=2.6 Hz, $J_{5,6b}$=4.9 Hz, 1H, H-5), 3.53 (dd, $J_{3,4}$=5.4 Hz, 1H, H-4), 3.57 (dd, $J_{6a,6b}$=9.0 Hz, 1H, H-6a), 3.63 (m, 3H, H-6b, H-1, H-4′), 3.72 (dd, $J_{2,3}$=6.5 Hz, 1H, H-3), 4.40 and 4.60 (two d, J_{AB}=11.3 Hz, 2H, CH_2Ph), 4.51 and 4.77 (two d, J_{AB}=10.9 Hz, 2H, CH_2Ph), 4.53 and 4.57 (two d, J_{AB}=11.3 Hz, 2H, CH_2Ph), 5.03 and 5.13 (two m, 2H, H-1′), 5.96 (m, 1H, H-2′), 7.25 (m, 19H, H-Arom); ^{13}C NMR: 19.9, 19.3, and 21.1 (3CH_3 groups), 35.7 (CH_2C═), 43.7 ($C(CH_3)_2$), 49.9 (CHS), 60.5 (OCH_3), 70.2, 73.1, 73.2, and 73.9 (4OCH_2 groups), 78.2, 78.8, 82.1, 82.2, and 84.5 (5CHO groups), 115.9 (═CH_2), 127.4, 127.5, 127.6, 127.7, 127.8, 127.9, 128.0, 128.3, 128.4, 129.6, 129.8, 131.0, 133.3, and 136.5 (C-Arom), and 137.5 (═CH); HRMS: Calcd for $C_{42}H_{50}SO_5Na$ 689.3277; Found: $(MNa)^+$ *m/e* 689.3303.

3.2.9. (4*S*)-4-Methoxy-5-methyl-5-*C*-[3,4,6-tri-*O*-benzyl-2-*S*-(mesityl)-2-thio-β-D-glucopyranosyl]-1-hexene [(4*R*)-16). R_f 0.47 (6:1 hexane–ethyl acetate); $[\alpha]^{21}_D$=−33.0° (*c* 0.0021, $CHCl_3$); ^{1}H NMR: 0.97 and 1.07 (two s, 6H, $C(CH_3)_2$), 2.20 (m, 1H, H-3a′), 2.30 (s, 3H, *para*-CH_3), 2.44 (m, 1H, H-3b′), 2.47 (s, 6H, *ortho*-CH_3 of Mes), 3.34 (dd, J_1=8.6 Hz, J_2=3.4 Hz, 1H, H-4′), 3.41 (m, 2H, H-3 and H-4), 3.46 (s, 3H, OCH_3), 3.52 (m, 2H, H-2 and H-6b), 3.57 (d, $J_{1,2}$=4.7 Hz, 1H, H-1), 3.60 (dd, *J*=11.0, 2.3 Hz, 1H, H-6b), 3.76 (m, 1H, H-5), 3.80 and 4.27 (two d, J_{AB}=12.0 Hz, 2H, CH_2Ph), 3.91 and 3.99 (two d, J_{AB}= 11.8 Hz, 2H, CH_2Ph), 4.53 and 4.56 (two d, J_{AB}=12.2 Hz, 2H, CH_2Ph), 5.05 (m, 2H, H-1′), 5.93 (m, 1H, H-2′), 7.20 (m, 19H, H-Arom); ^{13}C NMR: 18.5 and 20.1 ($C(CH_3)_2$), 21.0 (*para*-CH_3), 22.3 (*ortho*-CH_3), 35.3 (CH_2C═), 42.7 ($C(CH_3)_2$), 43.1 (CHS), 60.7 (OCH_3), 69.9, 70.9, 71.0, and 73.1 (4OCH_2 groups), 76.7, 78.1, 78.2, 84.7, and 86.1 (5CHO groups), 115.9 (═CH_2), 127.3, 127.4, 127.5, 127.6, 127.8, 128.06, 128.11, 128.15, 128.2, 128.5, 128.6, 129.2, 137.7, 137.9, and 138.6 (C-Arom), 143.3 (═CH); HRMS: Calcd for $C_{44}H_{54}SO_5Na$ 717.3590; Found: $(MNa)^+$ *m/e* 717.3590.

3.2.10. (2*S*)-2-Methoxy-3-*C*-[3,4,6-tri-*O*-benzyl-2-*S*-(*p*-tolyl)-2-thio-β-D-glucopyranosyl]propanenitrile (19). R_f 0.29 (1:2 ether–hexane); $[\alpha]^{28}_D$=−30.0° (*c* 0.0012, $CHCl_3$); IR (neat, ν, cm^{-1}): 2243 w (CN); ^{1}H NMR: 2.32 (s, 3H, CH_3), 1.96 and 2.71 (two ddd, $J_{1a',1b'}$=13.8 Hz, $J_{1a',1}$=10.0 Hz, $J_{1b',1}$=2.6 Hz, $J_{1a',2'}$=5.2 Hz, $J_{1b',2'}$=9.7 Hz, 2H, H-1a′ and H-1b′), 2.91 (t, $J_{1,2}$=$J_{2,3}$=10.6 Hz, 1H, H-2), 3.36 (ddd, $J_{4,5}$=8.4 Hz, $J_{5,6a}$=2.0 Hz, $J_{5,6b}$=3.6 Hz, 1H, H-5), 3.43 (s, 3H, OCH_3), 3.55 (m, 2H, H-1 and H-3), 3.68 (m, 1H, H-3), 3.70 and 3.75 (two dd, $J_{6a,6b}$=11.0 Hz, 2H, H-6a and H-6b), 4.30 (dd, 1H, H-2′), 4.50 and 4.59 (two d, J_{AB}=12.2 Hz, 2H, CH_2Ph), 4.58 and 4.83 (two d, J_{AB}=10.8 Hz, 2H, CH_2Ph), 4.88 and 5.06 (two d, J_{AB}= 10.3 Hz, 2H, CH_2Ph), 7.28 (m, 19H, H-Arom); ^{13}C NMR: 21.1 (CH_3), 36.1 (CH_2), 56.8 (CHS), 58.0 (OCH_3), 68.7, 73.4, 75.0, and 76.2 (4OCH_2), 68.4, 76.4, 78.6, 79.4, and 84.2 (5OCH groups), 117.8 (CN), 127.6, 127.7, 127.8, 127.9, 128.0, 128.1, 128.3, 128.4, 128.5, 130.0, 130.1, 130.7, 132.5, 132.7, 134.5, 137.6, and 138.1 (C-Arom); HRMS: Calcd for $C_{38}H_{41}SO_5N$ 623.2705; Found: M^+ *m/e* 623.2727.

3.2.11. (1*S*)-1-Methoxy-1-phenyl-2-*C*-[3,4,6-tri-*O*-benzyl-2-*S*-(*p*-tolyl)-2-thio-β-glucopyranosyl]ethane (20). R_f 0.43 ($CHCl_3$); $[\alpha]_D^{21.0}$ =−21.5° (*c* 0.0015, $CHCl_3$); ^{1}H NMR (500 MHz): 1.56 and 2.73 (two ddd, $J_{1,2a'}$=11.3 Hz, $J_{1,2b'}$=1.7 Hz, $J_{2a'2b'}$=12.4 Hz, $J_{1',2a'}$=2.5 Hz, $J_{1',2b'}$= 10.7 Hz, 2H, H-2b′), 2.28 (s, 3H, CH_3), 2.83 (t, $J_{2,3}$= 10.5 Hz, $J_{1,2}$=10.6 Hz, 1H, H-2), 3.19 (s, 3H, OCH_3), 3.42 (ddd, $J_{4,5}$=9.5 Hz, $J_{5,6a}$=6.3 Hz, $J_{5,6b}$=3.2 Hz, 1H, H-5), 3.60 (dd, $J_{3,4}$=8.8 Hz, $J_{2,3}$=10.5 Hz, 1H, H-3), 3.63 (dd, 1H, H-4), 3.69 (ddd, 1H, H-1), 3.73 (m, 2H, H-6a and H-6b), 4.42 (dd, 1H, H-1′), 4.60 (two d, J_{AB}=12.2 Hz, 2H, CH_2Ph), 4.75 (two d, J_{AB}=10.9 Hz, 2H, CH_2Ph), 4.95 (two d, J_{AB}=10.4 Hz, 2H, CH_2Ph), 7.28 (m, 24H, H-Arom); ^{13}C NMR (125 MHz): 21.0 (CH_3), 41.7 (CH_2), 56.8 (CHS), 57.1 (OCH_3), 69.6, 73.8, 75.2, and 76.4 (4OCH_2 groups), 77.2, 79.1, 80.3, and 85.4 (4CHOR groups), 126.7, 127.4, 127.6, 127.7, 127.8, 128.0, 128.3, 128.4, 128.6, 128.7, 128.8, 130.0, 122.5, 132.8, and 142.6 (C-Arom); HRMS: Calcd for $C_{43}H_{46}SO_5Na$ 697.2928; Found: $(MNa)^+$ *m/e* 697.2964.

3.2.12. (3*S*)-2-Methoxy-2-trimethylsilyl-3-*C*-[3,4,6-tri-*O*-benzyl-2-*S*-(*p*-tolyl)-2-thio-β-glucopyranosyl]propanenitrile (23). R_f 0.53 (1:6 ether–hexane); $[\alpha]^{22}_D$=−54.3° (*c*

0.0015, $CHCl_3$); IR (neat, ν, cm^{-1}): 2212 (CN); ^1H NMR: 0.13 (s, 9H, $Si(CH_3)_3$), 1.62 (dd, $J_{3a',1}$=9.8 Hz, $J_{3a',3b'}$= 14.8 Hz, 1H, H-3a′), 2.18 (s, 3H, CH_3), 2.59 (dd, $J_{3b',1}$= 1.2 Hz, $J_{3a',3b'}$=14.8 Hz, 1H, H-3b′), 2.85 (t, $J_{1,2}$=10.6 Hz, $J_{2,3}$=10.6 Hz, 1H, H-2), 3.25 (m, $J_{5,6a}$=1.9 Hz, $J_{6a,6b}$= 9.8 Hz, 1H, H-6a), 3.42 (s, 3H, OCH_3), 3.46 (dd, $J_{2,3}$= 10.6 Hz, $J_{3,4}$=8.7 Hz, 1H, H-3), 3.53 (m, $J_{1,3a'}$=9.8 Hz, $J_{1,3b'}$=1.2 Hz, $J_{1,2}$=10.6 Hz, 1H, H-1), 3.68 (m, $J_{5,6b}$= 10.2 Hz, $J_{6a,6b}$=9.8 Hz, 1H, H-6b), 3.70 (m, $J_{3,4}$=8.7 Hz, $J_{4,5}$=6.3 Hz, 1H, H-4), 3.60 (m, $J_{4,5}$=6.3 Hz, $J_{5,6a}$=1.9 Hz, $J_{5,6b}$=10.2 Hz, 1H, H-5), 4.45 and 4.57 (two d, J_{AB}= 11.8 Hz, 2H, CH_2Ph), 4.59 and 4.77 (two d, J_{AB}=10.8 Hz, 2H, CH_2Ph), 4.82 and 4.96 (two d, J_{AB}=10.3 Hz, 2H, CH_2Ph), 7.23 (m, 19H, H-Arom); ^{13}C NMR: −3.9 [$Si(CH_3)_3$], 21.1 (CH_3), 36.5 (CH_2), 55.9 (OCH_3), 57.6 (CHS), 69.2 (*C*TMS), 68.8, 74.1, 75.3, and 76.6 (4OCH_2 groups), 76.9, 79.1, 79.8, and 84.8 (4CHO groups), 119.6 (CN), 127.5, 127.6, 127.7, 127.8, 127.9, 128.1, 128.3, 128.4, 129.8, 132.1, 137.3, 138.4. and 138.5 (C-Arom); HRMS: Calcd for $C_{41}H_{49}SO_5Si$ 695.3101; Found: M^+ *m/e* 695.3112.

3.2.13. 2-Trimethylsilyl-3-*C*-[3,4,6-tri-*O*-benzyl-2-*S*-(*p*-tolyl)-2-thio-β-glucopyranosyl]-2-propanol (25). R_f 0.25 (3:1 ether–hexane); $[\alpha]^{22}_D$=+15.8° (*c* 0.0033, $CHCl_3$); IR (neat, ν, cm^{-1}): 3507 (OH); ^1H NMR: −0.04 (s, 9H, $Si(CH_3)_3$), 1.26 (s, 3H, CH_3), 1.27 (s, 1H, OH), 1.62 (dd, $J_{3a',3b'}$=14.8 Hz, $J_{3a',1}$=10.6 Hz, 1H, H-3a′), 2.24 (dd, $J_{3a',3b'}$=14.8 Hz, $J_{3b',1}$=2.0 Hz, 1H, H-3b′), 2.35 (s, 3H, CH_3), 2.98 (t, $J_{2,3}$=$J_{1,2}$=10.3 Hz, 1H, H-2), 3.51 (m, 1H, H-5), 3.60 (m, 1H, H-3), 3.63 (m, 2H, H-4, H-6a), 3.68 (dd, $J_{6a,6b}$=10.7 Hz, $J_{5,6b}$=2.28 Hz, 1H, H-6b), 3.83 (ddd, $J_{1,2}$=10.3 Hz, $J_{3a',1}$=10.6 Hz, $J_{3b',1}$=2.0 Hz, 1H, H-1), 4.48 and 4.55 (two d, J_{AB}=12.1 Hz, 2H, CH_2Ph), 4.58 and 4.85 (two d, J_{AB}=10.8 Hz, 2H, CH_2Ph), 4.92 and 5.11 (two d, J_{AB}=10.3 Hz, 2H, CH_2Ph), 7.32 (m, 19H, H-Arom); ^{13}C NMR: −4.6 [$Si(CH_3)_3$], 21.0 and 22.5 (two CH_3), 38.9 (CH_2), 57.7 (CHS), 65.1 (*C*TMS) 69.2, 73.4, 74.9, and 76.2 (4OCH_2 groups), 78.4, 79.4, 79.6, and 84.2 (4CHO groups), 127.6, 127.7, 127.8, 127.9, 128.1, 128.3, 128.4, 128.5, 131.4, 132.6, 137.5, 137.9, 138.0, and 138.4 (C-Arom); HRMS: Calcd for $C_{40}H_{50}SO_5SiNa$ 693.3046; Found: $(MNa)^+$ *m/e* 693.3046.

Acknowledgements

Authors acknowledge the National Institute of General Medical Sciences (grant No. 1 R15 GM/OD55965-01) and the University of North Dakota for financial support. The UND NMR facility was funded by the National Science Foundation (grant No. CHE-9871134). We also would like to thank Ms. Jianchun Gong for performing some of the experiments.

References

1. (a) Levy, D. E.; Tang, C. *The Chemistry of C-Glycosides*, *Tetrahedron Organic Chemistry Series*, Vol. 13; Elsevier: Tarrytown, NY, 1995. (b) Postema, M. H. D. *C-Glycoside Synthesis*, CRC: Boca Raton, FL, 1995. (c) Nicotra, F. *Top. Curr. Chem.* **1997**, *187*, 55. (d) Du, Y.; Linhardt, R. J.; Vlahov, I. R. *Tetrahedron* **1998**, *54*, 9913–9959. (e) Beau, J.-M.; Gallagher, T. *Top. Curr. Chem.* **1998**, *187*, 1. (f) Jaramillo, C.; Knapp, S. *Synthesis* **1994**, 1.
2. (a) Rohr, J.; Thiericke, R. *Nat. Prod. Rep.* **1992**, 103. (b) Murenetz, N. V. *Antibiot. Khimioter.* **1990**, *35*, 47. (c) Hacksell, U.; Daves, Jr., G. D. *Prog. Med. Chem.* **1985**, *22*, 1.
3. (a) Hanessian, S. *Total Synthesis of Natural Products: The Chiron Approach*, Pergamon: Oxford, 1983. (b) Wolbers, P.; Hoffmann, H. M. R. *Tetrahedron* **1999**, *55*, 1905. (c) Paterson, L.; Keown, L. E. *Tetrahedron Lett.* **1997**, *38*, 5727–5730. (d) Smith III, A. B.; Zhuang, L.; Brook, C. S.; Boldi, A. M.; McBriar, M. D.; Moser, W. H.; Murase, N.; Nakayama, K.; Verhoest, P. R.; Lin, Q. *Tetrahedron Lett.* **1997**, *38*, 8667–8610.
4. Smoliakova, I. P. *Curr. Org. Chem.* **2000**, *4*, 589–608.
5. Smoliakova, I. P.; Caple, R.; Gregory, D.; Smit, W. A.; Shashkov, A. S.; Chizhov, O. S. *J. Org. Chem.* **1995**, *60*, 1221–1227.
6. Smoliakova, I. P.; Kim, Y. H.; Barnes, M. J.; Caple, R.; Smit, W. A.; Shashkov, A. S. *Mendeleev Commun.* **1995**, 15–16.
7. Han, M.; Koikov, L. K.; Smoliakova, I. P. *Carbohydr. Res.* **2000**, *323*, 202–207.
8. Smoliakova, I. P.; Caple, R.; Brenny, J. W.; Smit, W. A.; Kryschenko, Y. K.; Shashkov, A. S.; Chizov, O. S.; Krimer, M. Z.; Morar, G. V.; Kalyan, Y. B. *Synlett* **1995**, 275–276.
9. Smoliakova, I. P.; Han, M.; Gong, J.; Caple, R.; Smit, W. A. *Tetrahedron* **1999**, *55*, 4559–4572.
10. (a) Koikov, L. N.; Han, M.; Wellman, D. M.; Kelly, J. A.; Smoliakova, I. P. *Synth. Commun.* **2000**, *30*, 3451. (b) Smoliakova, I. P.; Smit, W. A.; Osinov, B. D. *Tetrahedron Lett.* **1991**, *32*, 2601–2604. (c) Smoliakova, I. P.; Caple, R.; Magnuson, V. R.; Polyakov, V. R.; Smit, W. A.; Shashkov, A. S.; Ohinov, B. D. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1065–1069.
11. In a similar reaction with more simple substrates, such intermediates were isolated and their structures were proven by X-ray crystallographic analysis: Lazareva, M. I.; Kryschenko, Y. K.; Caple, R.; Wakefield, D.; Hayford, A.; Smit, W. A.; Shashkov, A. S. *Tetrahedron Lett.* **1998**, *39*, 8787–3790.
12. Santelli, M.; Pons, J.-M. *Lewis Acids and Selectivity in Organic Synthesis*, CRC: Boca Raton, FL, 1996.
13. Spessard, G. O.; Miessler, G. L. *Organometallic Chemistry*, Prentice-Hall: Upper Saddle River, NJ, 1996; p. 118.
14. Smoliakova, I. P.; Smit, W. A.; Bubnov, Y. N.; Shashkov, A. S. *Bull. Acad. Sci. USSR, Div. Chem.* **1990**, 1100–1107.
15. Fiser, M.; Fiser, L. F. P. *Reagents for Organic Synthesis*, Vol. 5; Wiley: New York, 1975; p. 523.
16. Burgstahler, A. W.; Nordin, I. C. *J. Am. Chem. Soc.* **1961**, *38*, 198–206.