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FULL PAPER

DOI: 10.1002/ejoc.201500732

Simultaneous Application of Arylmethylene Acetal and Butane Diacetal Groups for Protection of Hexopyranosides: Synthesis and Chemoselective Ring-Opening Reactions

Mihály Herczeg,[a] Fruzsina Demeter,[a,b] Erika Mező,[a,b] Máté Pap,[a] and Anikó Borbás*[a]

Keywords: Carbohydrates / Acetals / Ring opening / Reduction / Protecting groups / Chemoselectivity

The reductive cleavage of 4,6-*O*-arylmethylene acetals of hexopyranosides is an effective method for the regioselective formation of a benzyl-type ether at either the C-4 or the C-6 hydroxyl group. The compatibility of this method with Ley's butane diacetal (BDA) protection was studied. 4,6-*O*-(2-Naphthyl)methylene, benzylidene, and *p*-methoxybenzylidene acetals were introduced to 2,3-*O*-BDA-protected gluco- and galactosides, and the bis-acetalated products were subjected to reductive acetal openings with different reagents. $LiAlH_4$–$AlCl_3$ reduced the 4,6-acetals with complete chemo- and regioselectivity to give the corresponding 4-*O*-ethers. The use of Et_3SiH–BF_3·Et_2O led to a mixture of differently reduced products, because transformation of the 4,6-acetal into the related 6-*O*-ether and reduction of the BDA system into a butane-2,3-diyl group took place competitively. BH_3·NMe_3–$AlCl_3$ selectively cleaved the 4,6-acetal ring to give the 6-*O*-ethers as the major or exclusive products.

Introduction

Carbohydrates play essential roles in a wide range of biological processes, whose survey, on a molecular level, demands the synthesis of various structurally defined oligosaccharides and glycoconjugates. The chemical synthesis of complex carbohydrates and glycoconjugates requires a careful protecting group strategy that can be used to differentiate a collection of hydroxyl groups during the synthetic process.[1–5] Besides their masking function, protecting groups also play a fundamental role in tuning the reactivity of the carbohydrate building blocks, and can control the stereochemical outcome of glycosylation reactions. Despite remarkable progress in the development of straightforward procedures for the rapid differentiation of the hydroxyl groups of ■■ ((<=Author: do you agree with the change?)) ■■ sugars,[3–9] there is an ongoing need for the invention of new and reliable protecting groups, and there is also a need to study the scope and limitations of different combinations of the protecting groups currently used in oligosaccharide synthesis.

The use of cyclic acetals is one of the most efficient ways to discriminate between the different functionalities on a carbohydrate ring.[4,9] Benzylidene-type acetals are especially useful for the 4,6-*O*-protection of hexopyranosides because the regioselective reductive ring opening of these acetals to the corresponding benzyl-type ethers allows the release of either one of the two masked hydroxyl groups. Thus, the introduction and reductive opening of the 4,6-*O*-benzylidene, 4,6-*O*-*p*-methoxybenzylidene, or the 4,6-*O*-(2-naphthyl)methylene acetals represents a very effective two-step method for the regioselective formation of benzyl or related ethers. The reductive transformation requires a hydride donor reagent in combination with a protic or a Lewis acid, and it can produce, depending on the reagents and conditions, either the 4-OH/6-*O*-arylmethyl or the 6-OH/4-*O*-arylmethyl product.[4,10]

Due to the pioneering work of Ley and coworkers, vicinal *trans*-diequatorial diols can be selectively protected using cyclic diacetal groups, such as dispiroketal,[11] cyclohexane diacetal,[12] or butane diacetal (BDA)[13] groups, of which the BDA group is the most widely used. The high regioselectivity in the protection of *trans*-1,2-diols in the presence of other polyols is due to the formation of the sterically less demanding *trans* ring junction. Moreover, the control of configuration at the two acetal centres by the operation of anomeric effects ensures complete stereoselectivity in the acetalation. The additional tuning effect on the glycosylation reactivity of the diacetal-protected building blocks in oligosaccharide assembly further enhances the synthetic utility of the 1,2-diacetals.[14–16]

Although both 4,6-*O*-benzylidene-type and diacetal-type protecting groups are widely used in oligosaccharide synthesis, there are only two precedents for the full protection of a carbohydrate ring by their joint application. A pentenyl glucoside was equipped with a 4,6-*O*-benzylidene group

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201500732.

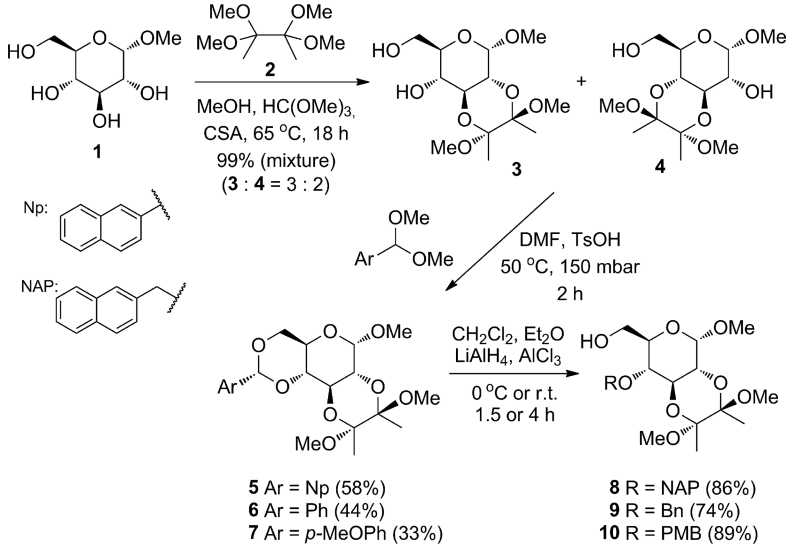
and a 2,3-*O*-dispiroketal group in the Fraser–Reid laboratory,[16] and allyl 2,3-BDA-4,6-*O*-benzylidene-D-glucopyranoside was prepared by Pinto and coworkers.[17] However, reductive cleavage of a 4,6-acetal in the presence of a diacetal group has not been investigated until now. The reduction of the diacetal system of a BDA group to give a butane-2,3-diyl group has been achieved by using either Et_3SiH and $BF_3{\cdot}Et_2O$[18] or sodium cyanoborohydride and HCl;[19] both of these reagent systems are commonly used for the regioselective ring cleavage of 4,6-*O*-benzylidene acetals to give 6-*O*-benzyl ethers.[20,21]

As the reductive opening of 4,6-*O*-benzylidene-type acetals can discriminate highly effectively between the C-4 and C-6 alcohol products, we decided to study the compatibility of this method with diacetal protection. Thus, fully protected gluco- and galactopyranosides were prepared through the simultaneous use of a butane diacetal and different benzylidene-type acetals, and reductive openings of the 4,6-arylmethylene rings were investigated using various reagents.

Results and Discussion

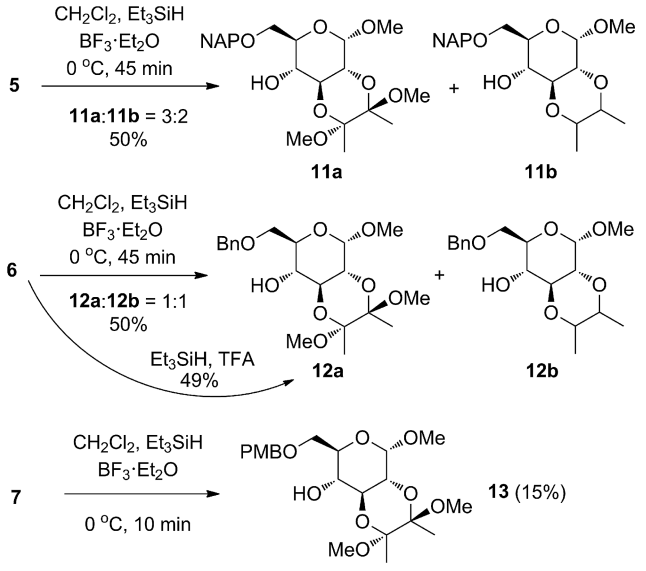
We started our investigations with the introduction of the acetal groups to methyl α-D-glucopyranoside. Compound **1** was treated with 2,2,3,3-tetramethoxybutane (**2**)[13a] in boiling methanol with catalytic camphorsulfonic acid (CSA) and trimethyl orthoformate (4 equiv.) for 18 h to give an inseparable, ca. 3:2 mixture of the 2,3-diacetal and 3,4-diacetal regioisomers (i.e., **3** and **4**), in accordance with literature results[13a,22] (Scheme 1). This mixture was then treated with acetalating reagents, including 2-naphthaldehyde dimethyl acetal, benzaldehyde dimethyl acetal, and *p*-methoxybenzaldehyde dimethyl acetal, in DMF under *p*-toluenesulfonic acid (TsOH) catalysis to give the corresponding 4,6-*O*-arylmethylene derivatives **5**–**7**. The fully protected products could easily be separated from 2,6-diol **4**, which remained unchanged in the reactions, by column chromatography, and compounds **5**, **6**, and **7** were isolated in 58, 44, and 33% yields, respectively, over two steps.

Among the various reagent systems that have been introduced for the reductive ring cleavage of benzylidene-type acetals, we planned to use the $LiAlH_4$–$AlCl_3$ reagent combination[23,24] to release the 4-OH group, and the Et_3SiH–$BF_3{\cdot}Et_2O$ combination[19] to liberate the 6-OH group, because these reagents are often reliable in providing the corresponding alkyl derivatives in high yield and with high regioselectivity. Thus, 4,6-*O*-(2-naphthyl)methylene derivative **5** was treated with a mixture of $LiAlH_4$ and $AlCl_3$ in a 3:1 ratio (forming AlH_3),[24,25] to give 4-*O*-(2-naphthyl)methyl ether **8** exclusively in 86% yield. Reductive cleavage of the 4,6-*O*-(*p*-methoxy)benzylidene acetal of **7** using the same AlH_3 reagent also proceeded with complete selectivity to give **10** in 89% yield. For the opening of the benzylidene ring of **6**, an equimolar mixture of $LiAlH_4$ and $AlCl_3$ (forming AlH_2Cl)[24] was used, and the required 4-*O*-benzyl ether (i.e, **9**) was obtained in 74% yield. The above reductive transformations of the different 4,6-acetals turned out to be completely chemoselective; the $LiAlH_4$–$AlCl_3$ system did not affect the 2,3-*O*-butane diacetal protecting group. To achieve the opposite regioselectivity during the 4,6-acetal cleavage, compounds **5**–**7** were treated with Et_3SiH and $BF_3{\cdot}Et_2O$ (Scheme 2). It should be noted that this reagent combination, using acetonitrile as the solvent, has been used by Shing et al. on a BDA-protected arabinoside derivative for the reduction of the diacetal system into a butane-2,3-diyl group in an 8 h reaction.[18] Bearing in mind the considerably higher rate of the reductive cleavage of the benzylidene ring with this reagent system,[19,26] we expected that the BDA moiety could survive the arylmethylene-opening reactions. Compound **5** was treated with Et_3SiH



Scheme 1. Double acetalation of methyl α-D-glucopyranoside (**1**), and reductive cleavage of the 4,6-*O*-arylmethylene rings of **5**–**7** with $LiAlH_4$–$AlCl_3$.

(12 equiv.) and $BF_3{\cdot}Et_2O$ (2 equiv.) in anhydrous dichloromethane at 0 °C, and after 45 min TLC showed the almost complete consumption of the starting material and the formation of one major product, together with some polar degradation compounds. Unfortunately, the seemingly single product turned out to be an inseparable 3:2 mixture of the desired **11a** and its BDA-reduced counterpart **11b**. Similarly, reductive cleavage of the 4,6-*O*-benzylidene acetal of **6** in the presence of a 2,3-BDA moiety with Et_3SiH and $BF_3{\cdot}Et_2O$ showed only moderate chemoselectivity. Although the opening reaction of the 4,6-acetal ring dominated again, reduction of the butane diacetal system into a butane-2,3-diyl group took also place to some extent, to result in a 1:1 mixture of **12a** and **12b**, which could not be separated.

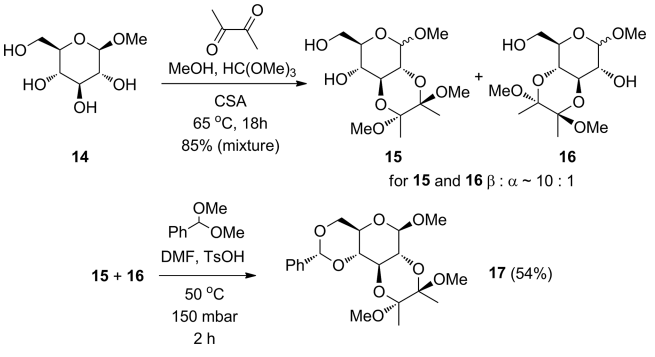


Scheme 2. Reductive opening of the 4,6-*O*-acetal rings of **5**–**7** using Et_3SiH in combination with $BF_3{\cdot}Et_2O$ or TFA.

Treatment of 4,6-*O*-(*p*-methoxy)benzylidene derivative **7** with the same reagent combination led to complete loss of the 4,6-acetal ring. When the reaction was repeated using a lesser amount (1 equiv.) of $BF_3{\cdot}Et_2O$, chemoselective reductive opening of the 4,6-acetal took place to give the desired 6-*O*-(*p*-methoxy)benzyl (PMB) derivative (i.e., **13**) in 15% yield. Reduction of the BDA group was not observed; the yield of **13** was low due to the formation of substantial amounts of polar degradation products. We also tested the ring opening of the 4,6-benzylidene ring of compound **6** using a combination of Et_3SiH (5 equiv.) and trifluoroacetic acid (TFA; 5 equiv.).[27] Although this reduction gave the desired 6-ether derivative (i.e., **12a**) chemoselectively, the 49% yield was unsatisfactory.

$BH_3{\cdot}NMe_3$–$AlCl_3$, used in tetrahydrofuran as solvent, is an effective reagent for the regioselective opening of 4,6-*O*-benzylidene[28] or 4,6-*O*-(2-naphthyl)methylene[29] acetals of hexopyranosides to give the corresponding 6-*O*-ethers. (Note that the use of toluene with this reagent results in a reversal of the regioselectivity.) Therefore, compounds **5**–**7** were treated with $BH_3{\cdot}NMe_3$ (6 equiv.) and $AlCl_3$ (6 equiv.) in THF at room temperature. We were pleased to find that this reagent system cleaved the 4,6-acetals with complete chemoselectivity, without affecting the diacetal system of the BDA group (Scheme 3). However, the regioselectivity of the reaction was strongly influenced by the type of the acetal. Starting from (2-naphthyl)methylene acetal **5**, 6-*O*-ether **11a** was formed exclusively in a yield of 75%. The ring opening of the benzylidene acetal also proceeded with good selectivity to give the regioisomeric 6- and 4-*O*-ethers in a ratio of 7:2, while the reductive cleavage of the (*p*-methoxy)benzylidene acetal took place without notable regioselectivity to give a ca. 1:1 mixture of the 6- and 4-*O*-PMB derivatives.

Next, the double acetalation and 4,6-acetal opening procedure was studied on methyl β-D-glucopyranoside. This time, following the procedure described by Hense et al.,[13b] commercially available butane-2,3-dione was used to introduce the BDA protecting groups. Thus, compound **14** was treated with butane-2,3-dione and trimethyl orthoformate in the presence of CSA in boiling methanol for 18 h to give an inseparable mixture of the 2,3- and 3,4-BDA-protected β-methyl derivatives, along with a small amount of their anomers (**15** and **16**; Scheme 4). Similar anomerisation during the BDA-protection of methyl α-D-galactopyranoside was also observed by Frost and coworkers.[13a] The resulting mixture was treated directly with benzaldehyde dimethyl acetal in the presence of a catalytic amount of TsOH to give fully protected derivative **17** as a 10:1 anomeric mixture in 54% yield.



Scheme 4. Double acetalation of methyl β-D-glucopyranoside (**14**).

The pure β-anomer of **17** could be obtained in crystalline form, and its structure was confirmed by X-ray crystallography (Figure 1).

Reductive cleavage of the 4,6-*O*-benzylidene ring of **17** with a mixture of $LiAlH_4$ and $AlCl_3$ proceeded again with complete selectivity to give 4-*O*-benzyl ether **18** in 83% yield. Attempted transformation of **17** into the corresponding 6-*O*-ether derivative using Et_3SiH (12 equiv.) and $BF_3{\cdot}Et_2O$ (2 equiv.) gave an inseparable 1:1 mixture of the desired **19a** and its reduced butane-2,3-diyl counterpart **19b** in 48% overall yield. When the reaction was repeated using 1 equiv. of $BF_3{\cdot}Et_2O$, a higher yield was achieved, but the ratio of products **19a** and **19b** hardly changed.

$BH_3{\cdot}NMe_3$–$AlCl_3$ proved to be a very efficient reagent combination for the cleavage of the 4,6-benzylidene ring.

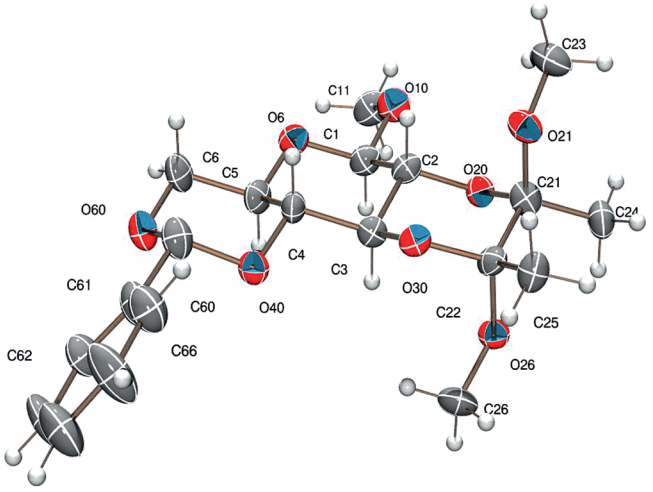
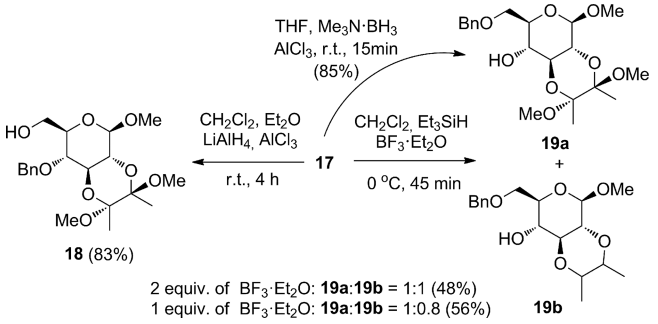


Figure 1. ORTEP view of **17**.

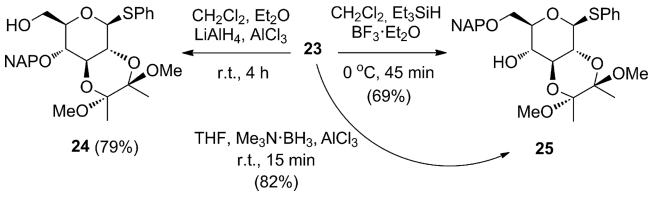
The reduction proceeded with complete chemo- and regioselectivity to give 6-*O*-ether **19a** in 85% yield (Scheme 5).



Scheme 5. Reductive openings of the 4,6-acetal of **17**.

Phenyl 1-thio-β-D-glucopyranoside (**20**) was also included in our studies. Compound **20** was treated with 2,2,3,3-tetramethoxybutane (**2**), trimethyl orthoformate, and methanol, in the presence of CSA, and the resulting regioisomeric diacetals (i.e., **21**[30] and **22**[30]) were separated to give the required 2,3-BDA derivative (i.e., **21**) in 39% yield (Scheme 6). In this case, the (2-naphthyl)methylene acetal was introduced to the 4,6-position by using the corresponding dimethyl acetal reagent in DMF, with TsOH catalysis, to give the expected double acetalated product (i.e., **23**) in 68% yield; unreacted **21** was also recovered in 21% yield (Scheme 6).

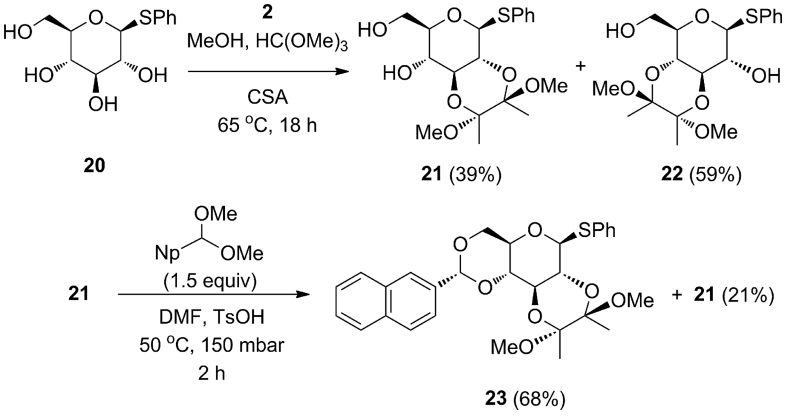
Reductive cleavage of the 4,6-*O*-(2-naphthyl)methylene acetal of **23** with a mixture of $LiAlH_4$ and $AlCl_3$ proceeded with complete selectivity to give the expected 4-*O*-ether (i.e., **24**[31]) in 79% yield. Transformation of **23** into 6-*O*-NAP derivative **25** was successfully carried out, without affecting the diacetal group, by using Et_3SiH (12 equiv.) and $BF_3{\cdot}Et_2O$ (1 equiv.) as the reducing agents. The $BH_3{\cdot}NMe_3$–$AlCl_3$ reagent also opened the 4,6-acetal with complete chemo- and regioselectivity to give the 6-*O*-ether in an excellent 82% yield (Scheme 7).



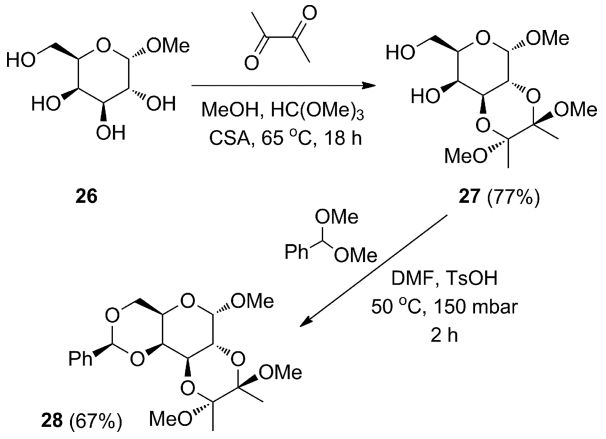
Scheme 7. Reductive 4,6-acetal-cleavage reactions of **23**.

In order to explore the reductive cleavage of a *cis*-annelated acetal ring in the presence of the BDA protecting group, double acetalation of methyl α-D-galactopyranoside **26** was also executed. The synthesis of the bis-acetalated **28** started from methyl α-D-galactopyranoside (**26**) (Scheme 8). Treatment of **26** with butane-2,3-dione and trimethyl orthoformate in boiling methanol in the presence of catalytic $BF_3{\cdot}Et_2O$ led to the regioselective formation of 2,3-*O*-BDA-protected galactopyranoside **27**,[13a] which was then treated with benzaldehyde dimethyl acetal in DMF using TsOH as a catalyst to give fully protected derivative **28** in 67% yield.

Reductive cleavage of the 4,6-*O*-benzylidene ring of **28** using the $LiAlH_4$–$AlCl_3$ reagent combination gave 4-*O*-benzyl ether **29** with complete chemo- and regioselectivity in 84% yield. Our attempt to synthesize the BDA-protected 6-*O*-ether derivative using Et_3SiH and $BF_3{\cdot}Et_2O$ was unsuc-

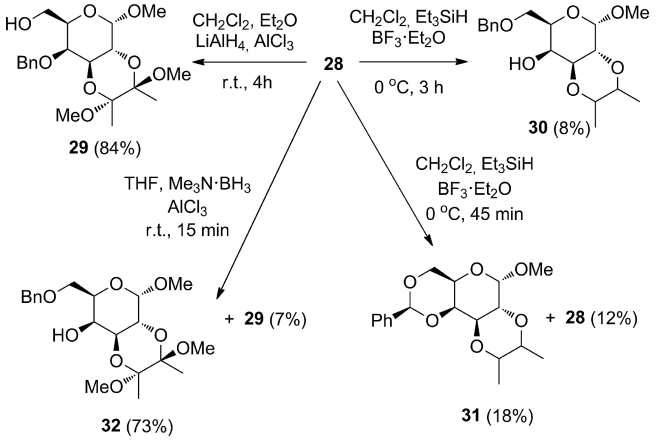


Scheme 6. Full protection of phenyl 1-thio-β-D-glucopyranoside (**20**) by two consecutive acetal-exchange reactions.



Scheme 8. Double acetalation of **26**.

cessful. The reaction of **28** with Et_3SiH in the presence of $BF_3{\cdot}Et_2O$ (2 equiv.) showed a very low conversion after 3 h; the only product was **30**, in which both the benzylidene acetal and the butane diacetal were reduced. Interestingly, when half of the amount of the Lewis acid was used, the reaction took place with opposite chemoselectivity to that expected. Only the butane diacetal system was reduced to give **31**, bearing an unchanged 4,6-acetal ring, in 18% yield (Scheme 9). The combination of $BH_3{\cdot}NMe_3$ with $AlCl_3$ proved to be an efficient reagent system to reduce the *cis*-annelated 4,6-benzylidene ring of **28** without affecting the butane diacetal system. The reductive cleavage also showed good regioselectivity to give 6-*O*-ether **32** in 73% yield, together with the regioisomeric 4-*O*-ether in 7% yield.



Scheme 9. Reductive cleavage of the benzylidene ring of **28** with different reagents.

Conclusions

In summary, three reagent systems, $LiAlH_4$–$AlCl_3$, $BH_3{\cdot}NMe_3$–$AlCl_3$, and Et_3SiH–$BF_3{\cdot}Et_2O$, have been used for the reductive cleavage of 4,6-*O*-benzylidene-type acetals of glucoside and galactoside derivatives bearing a 2,3-*O*-BDA protecting group. Using the $LiAlH_4$–$AlCl_3$ reagent combination, chemo- and regioselective reduction of the 4,6-acetal and highly efficient formation of the corresponding 4-*O*-ether were observed in all cases.

The reactions with $BH_3{\cdot}NMe_3$–$AlCl_3$ in THF also showed complete chemoselectivity; the butane diacetal moieties remained intact, and exclusive cleavage of the 4,6-acetals took place to give the expected 6-*O*-ethers with varying regioselectivity. The reduction of the 4,6-*O*-(2-naphthyl)-methylene acetals gave the 6-*O*-NAP ethers exclusively, while reduction of the *p*-methoxybenzylidene derivative yielded the 4-*O*- and 6-*O*-PMB ethers in almost equal amounts. The benzylidene acetals could be transformed into the 6-*O*-benzyl ethers with high or complete regioselectivity, depending on the anomeric configuration.

Et_3SiH–$BF_3{\cdot}Et_2O$ proved to be an inappropriate reagent system for the chemoselective transformation of 4,6-acetals into the corresponding 4-*O*-ethers in the presence of a 2,3-*O*-BDA moiety. As well as the expected ring-opening reaction, hydrolysis of the 4,6-acetal ring and reduction of the butane diacetal system to give a butane-2,3-diyl group took place competitively to give a complex mixture, from which the desired 4-*O*-ether-2,3-*O*-BDA derivative could not be isolated in pure form.

Taking advantage of the chemoselective acetal openings, dually acetalated glycosyl donors such as thioglucoside **23** can be regarded as useful building blocks for the preparation of 1,2-*cis*-α-linked oligoglycosyl fragments elongated at the C-4 or C-6 positions. It is worth noting that 2,3-*O*-BDA-protected donors represent a different level of reactivity in glycosylation reactions and allow an orthogonal deprotection method compared to their widely used ether-protected counterparts. Therefore, the simultaneous use of arylmethylene acetal and butane diacetal groups for the protection of hexopyranosides would offer an attractive alternative to the protecting group systems used currently in oligosaccharide synthesis.

The synthesis of orthogonally protected maltooligosaccharide derivatives by using this simultaneous acetal–diacetal protecting group approach is in progress, and the results will be reported in due course.

Experimental Section

General Methods: Optical rotations were measured at room temperature with a Perkin–Elmer 241 automatic polarimeter. TLC analysis was carried out on Kieselgel 60 F_{254} (Merck) silica gel plates, which were visualized by immersing in a sulfuric acid solution (5% in EtOH) followed by heating. Column chromatography was carried out on silica gel 60 (Merck 0.063–0.200 mm), flash column chromatography was carried out on silica gel 60 (Merck 0.04–0 063 mm). Organic solutions were dried with $MgSO_4$ and concentrated under vacuum. ^1H NMR (360 and 400 MHz) and ^{13}C NMR (90.54 and 100.28 MHz) spectra were recorded with Bruker DRX-360 and Bruker DRX-400 spectrometers. Chemical shifts are referenced to $SiMe_4$ (δ = 0.00 ppm for ^1H) and to the solvent signal ($CDCl_3$: δ = 77.00 ppm for ^{13}C). MS (MALDI-TOF) analysis was carried out in positive reflectron mode with a BIFLEX III mass spectrometer (Bruker, Germany) with delayed-ion extraction. The matrix solution was a saturated solution of 2,4,6-trihydroxy-acetophenone (THAP) in MeCN. Elemental analysis (C, H, S) was car-

ried out with an Elementar Vario MicroCube instrument. X-ray diffraction data for compound **17** were collected with a Bruker-Nonius MACH3 diffractometer at 293 K, using Mo K_α radiation λ = 0.71073 Å. All non-hydrogen atoms were refined anisotropically.

CCDC-1056686 contains the supplementary crystallographic data for compound **17**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

General Method A: Formation of butanedione dimethyl acetal using 2,2,3,3-tetramethoxybutane; **3**, **4**, **21**, and **22**. A suspension of tetraol **1** or **20** (2–5 mmol, 1.0 equiv.) in a solution of 2,2,3,3-tetramethoxybutane (1.2 equiv.) and trimethyl orthoformate (4.0 equiv.) in methanol (2–5 mL/mmol of tetraol) was treated with (+)-camphor-10-sulfonic acid (0.05 equiv.). The mixture was stirred under argon at 65 °C for 18 h. The cooled reaction mixture was then treated with powdered $NaHCO_3$ (ca. 0.5 g), and concentrated under reduced pressure. Purification by column chromatography on silica gel gave the protected carbohydrates.

General Method B: Formation of butanedione dimethyl acetal using butane-2,3-dione; **15**, **16**, and **27**. (+)-Camphor-10-sulfonic acid (0.1 equiv.) was added to a solution of tetraol **14** or **26** (5.00 mmol), butane-2,3-dione (1.1 equiv.), and trimethyl orthoformate (4.0 equiv.) in anhydrous methanol (15.0 mL). The mixture was stirred at 65 °C for 18 h, and then it was neutralized by the addition of triethylamine (100 μL). The mixture was concentrated under reduced pressure, and purified by column chromatography on silica gel.

General Method C: Formation of the 4,6-*O*-acetal ring; **5**, **6**, **7**, **17**, **23**, and **28**. A regioisomeric mixture of diols (**3** + **4** or **15** + **16**) or diol **21** or **27** (3.00 mmol) was dissolved in anhydrous DMF (5.0 mL), and naphthaldehyde dimethyl acetal, benzaldehyde dimethyl acetal, or *p*-methoxybenzaldehyde dimethyl acetal (1.1–1.5 equiv.) and TsOH (0.25 or 0.10 equiv.) were added. The mixture was stirred at 50 °C under reduced pressure (150 mbar). After 2 h, the reaction mixture was neutralized by the addition of triethylamine, and then concentrated in vacuo. Purification by column chromatography on silica gel gave the diacetal derivatives.

General Method D: Reductive ring-opening reaction of the 4,6-*O*-acetal with $LiAlH_4$–$AlCl_3$; **8**, **9**, **10**, **18**, **24**, and **29**. A diacetal derivative **5**, **6**, **7**, **17**, **23**, or **28** (1.00 mmol) was dissolved in anhydrous CH_2Cl_2 and anhydrous Et_2O. $LiAlH_4$ was added, and then a solution of $AlCl_3$ in anhydrous Et_2O was added ■■ ((<=Author: please check the first two sentences of this paragraph read correctly)) ■■ . The reaction mixture was stirred at 0 °C (**10**: 1.5 h) or room temperature (**8**, **9**, **18**, **24**, and **29**: 4 h). The reaction mixture was diluted with EtOAc (20.0 mL) and H_2O (5.0 mL), filtered, washed with EtOAc, and concentrated ■■ ((<=Author: Please clarify this sentence: what was filtered, what was washed, and what was concentrated?)) ■■ . Purification by column chromatography on silica gel gave the corresponding 4-*O*-ether derivative.

General Method E: (Reductive ring-opening reaction of the 4,6-*O*-acetal with Et_3SiH–$BF_3{\cdot}Et_2O$; **11a**,**b**, **12a**,**b**, **13**, **19a**,**b**, **25**, **30**, and **31**). A 4,6-*O*-acetal derivative **5**, **6**, **7**, **17**, **23**, or **28** (0.60 mmol) was dissolved in anhydrous CH_2Cl_2 (4.0 mL), and the solution was cooled to 0 °C. Et_3SiH (12.0 equiv.) and $BF_3{\cdot}Et_2O$ (2.0 or 1.0 equiv.) were added. The reaction mixture was stirred for 10 min (**13**), or 45 min (**11a**,**b**, **12a**,**b**, **19a**,**b**, **25**, and **31**), or 3 h (**30**). The mixture was diluted with CH_2Cl_2 (100 mL), washed with saturated aqueous $NaHCO_3$ (2× 10.0 mL), dried with $MgSO_4$, and concentrated. The crude product was purified by column chromatography on silica gel.

General Method F: (Reductive ring-opening reaction of the 4,6-*O*-acetal with $BH_3{\cdot}NMe_3$–$AlCl_3$; **11a**, **12a**, **13**, **19a**, **25**, and **32**). A 4,6-*O*-acetal derivative **5**, **6**, **7**, **17**, **23**, or **28** (1.00 mmol) was dissolved in anhydrous THF (3.0 mL), and molecular sieves (4 Å; 0.5 g) and $(CH_3)_3N{\cdot}BH_3$ (6.0 equiv.) were added. The mixture was stirred for 30 min at room temperature. After 30 min, $AlCl_3$ (6.0 equiv.) was added, and the reaction mixture was stirred at room temperature for 15 min. The mixture was diluted with CH_2Cl_2 (100 mL), washed with water (2× 15.0 mL), dried with $MgSO_4$, and concentrated. The crude product was purified by column chromatography on silica gel.

Methyl 2,3-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-α-D-glucopyranoside (3) and Methyl 3,4-*O*-(Dimethoxybutane-2′,3′-diyl)-α-D-glucopyranoside (4): Compound **1** (20.0 g, 100.0 mmol) was converted into **3** and **4** by method A. Purification by column chromatography on silica gel (*n*-hexane/acetone, 1:1) gave compounds **3** and **4** (31.8 g, 99%, inseparable mixture) as a white foam.

Data for **3** (from the reaction mixture to prepare **13** from **7** by general method E): White foam. $[\alpha]_D^{24}$ = –54.3 (*c* = 0.09, $CHCl_3$); ref.[22] $[\alpha]_D^{24}$ = –58 (*c* = 1.1). R_f = 0.33 (*n*-hexane/acetone, 1:1). ^{1}H NMR (400 MHz, [D$_4$]methanol): δ = 4.68 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 3.91 (dd, $J_{3,4}$ = 8.9, $J_{2,3}$ = 10.2 Hz, 1 H, 3-H), 3.80 (dd, $J_{5,6}$ = 2.1, J_{gem} = 11.9 Hz, 1 H, 6-Ha), 3.70 (dd, $J_{5,6}$ = 5.1, J_{gem} = 11.9 Hz, 1 H, 6-Hb), 3.64 (dd, $J_{1,2}$ = 3.6, $J_{2,3}$ = 10.3 Hz, 1 H, 2-H), 3.54–3.52 (m, 1 H, 5-H), 3.51–3.46 (m, 1 H, 4-H), 3.41 (s, 3 H, C-1-OCH_3), 3.28, 3.23 (2 s, 6 H, 2 OCH_3 BDA), 1.28, 1.27 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, [D$_4$]methanol): δ = 101.1, 100.7 (2 C, 2 C$_q$ BDA), 99.3 (1 C, C-1), 74.4, 70.7, 69.8, 68.8 (4 C, skeleton carbons), 62.3 (1 C, C-6), 55.4 (1 C, C-1-OCH$_3$), 48.2, 48.1 (2 C, 2 OCH$_3$ BDA), 18.1, 17.8 (2 C, 2 CH$_3$ BDA) ppm. MS (MALDI-TOF): *m*/*z* = 331.17 [M + Na]$^+$. $C_{13}H_{24}O_8$ (308.15): calcd. C 50.64, H 7.85; found C 50.69, H 7.89.

Data for **4** (from the reaction to prepare **5**): White foam. $[\alpha]_D^{24}$ = +188.8 (*c* = 0.37, $CHCl_3$); ref.[32] $[\alpha]_D^{24}$ = +258 (*c* = 1.2). R_f = 0.33 (*n*-hexane/acetone, 1:1). ^{1}H NMR (360 MHz, $CDCl_3$): δ = 4.78 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 3.92 (t, *J* = 9.8 Hz, 1 H), 3.84–3.61 (m, 5 H), 3.42 (s, 3 H, C-1-OCH_3), 3.34 (d, *J* = 6.9 Hz, 1 H, O*H*), 3.29, 3.25 (2 s, 6 H, 2 OCH_3 BDA), 3.13 (s, 1 H, O*H*), 1.31, 1.28 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 99.3 (1 C, C-1), 99.0, 98.9 (2 C, 2 C$_q$ BDA), 69.4, 69.3, 69.1, 65.4 (4 C, skeleton carbons), 60.2 (1 C, C-6), 54.6 (1 C, C-1-OCH$_3$), 47.3 (2 C, 2 OCH$_3$ BDA), 17.1, 17.0 (2 C, 2 CH$_3$ BDA) ppm. MS (MALDI-TOF): *m*/*z* = 331.29 [M + Na]$^+$. $C_{13}H_{24}O_8$ (308.15): calcd. C 50.64, H 7.85; found C 50.68, H 7.90.

Methyl 2,3-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-4,6-*O*-(2-naphthyl)methylene-α-D-glucopyranoside (5): A mixture of compounds **3** and **4** (1.00 g, 3.24 mmol) was converted into **5** by method C using naphthaldehyde dimethyl acetal (0.98 g, 4.86 mmol, 1.5 equiv.) and TsOH (0.25 equiv.). The crude product was purified by silica gel chromatography (*n*-hexane/acetone, 7:3) to give **5** (884 mg, 58%) as a colourless syrup, and unreacted **4** (570 mg, 39%) as a colourless syrup. $[\alpha]_D^{24}$ = –29.1 (*c* = 0.03, $CHCl_3$). R_f = 0.36 (*n*-hexane/acetone, 7:3). ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.94–7.43 (m, 7 H, arom), 5.67 (s, 1 H, H$_{ac}$), 4.77 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.33–4.26 (m, 2 H, 6-Ha, 4-H), 3.90 (dd, $J_{1,2}$ = 3.6, $J_{2,3}$ = $J_{5,6}$ = 9.7 Hz, 2 H, 2-H, 6-Hb), 3.83 (t, $J_{2,3}$ = $J_{3,4}$ = 9.8 Hz, 1 H, 3-H), 3.77 (t, $J_{4,5}$ = $J_{5,6}$ = 9.3 Hz, 1 H, 5-H), 3.43 (s, 3 H, C-1-OCH_3), 3.28, 3.26 (2 s, 6 H, 2 OCH_3 BDA), 1.35, 1.32 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 134.7, 133.6, 132.9 (3 C, 3 C$_q$ arom), 128.4, 128.0, 127.7, 126.4, 126.0, 125.7, 123.9 (7 C, arom), 101.6 (1 C, C$_{ac}$), 100.1, 99.4 (2 C, 2 C$_q$ BDA), 98.7 (1 C, C-1), 79.0, 69.0, 66.5, 63.0 (4 C, skeleton carbons), 69.2 (1 C, C-6), 55.2 (1 C, C-1-OCH$_3$),

48.0 (2 C, 2 OCH_3 BDA), 17.8, 17.7 (2 C, 2 CH_3 BDA) ppm. MS (MALDI-TOF): m/z = 469.33 [M + Na]$^+$. $C_{24}H_{30}O_8$ (446.19): calcd. C 64.56, H 6.77; found C 64.61, H 6.83.

Methyl 4,6-*O*-Benzylidene-2,3-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-glucopyranoside (6): A mixture of compounds **3** and **4** (5.00 g, 16.20 mmol), benzaldehyde dimethyl acetal (2.67 mL, 17.80 mmol), and TsOH (0.25 equiv.) were treated according to general method C. The crude product was purified by silica gel chromatography (*n*-hexane/acetone, 7:3) to give **6** (2.80 g, 44%) as a colourless syrup. $[\alpha]_D^{24}$ = –58.9 (c = 0.09, $CHCl_3$). R_f = 0.49 (*n*-hexane/acetone, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.32 (m, 5 H, arom), 5.52 (s, 1 H, H_{ac}), 4.75 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.27–4.22 (m, 2 H, 4-H, 6-Ha), 3.86 (dd, $J_{1,2}$ = 3.5, $J_{2,3}$ = 10.1 Hz, 2 H, 2-H, 6-Hb), 3.76 (t, $J_{2,3}$ = $J_{3,4}$ = 10.1 Hz, 1 H, 3-H), 3.69 (t, $J_{4,5}$ = $J_{5,6}$ = 9.3 Hz, 1 H, 5-H), 3.42 (s, 3 H, C-1-OCH_3), 3.27, 3.26 (2 s, 6 H, 2 OCH_3 BDA), 1.35, 1.31 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.2 (1 C, C_q arom), 128.7, 127.9, 126.0 (5 C, arom), 101.2 (1 C, C_{ac}), 99.9, 99.2 (2 C, 2 C_q BDA), 98.5 (1 C, C-1), 78.7, 68.8, 66.3, 63.2 (4 C, skeleton carbons), 68.9 (1 C, C-6), 54.9 (1 C, C-1-OCH_3), 47.8, 47.7 (2 C, 2 OCH_3 BDA), 17.6, 17.5 (2 C, 2 CH_3 BDA) ppm. MS (MALDI-TOF): m/z = 419.26 [M + Na]$^+$. $C_{20}H_{28}O_8$ (396.18): calcd. C 60.59, H 7.12; found C 60.62, H 7.17.

Methyl 2,3-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-4,6-*O*-(4-methoxy)benzylidene-α-D-glucopyranoside (7): A mixture of compound **3** and **4** (5.00 g, 16.20 mmol) was treated according to general method C using *p*-methoxybenzaldehyde dimethyl acetal (3.0 mL, 17.80 mmol, 1.1 equiv.) and TsOH (0.25 equiv.). The crude product was purified by silica gel chromatography (*n*-hexane/acetone, 7:3) to give **7** (2.29 g, 33%) as a colourless syrup. $[\alpha]_D^{24}$ = –60.5 (c = 0.10, $CHCl_3$). R_f = 0.38 (*n*-hexane/acetone, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.85 (m, 4 H, arom), 5.48 (s, 1 H, H_{ac}), 4.75 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.26–4.21 (m, 2 H), 3.87–3.80 (m, 2 H), 3.77 (s, 3 H, PMB-OCH_3), 3.75–3.65 (m, 2 H), 3.42 (s, 3 H, C-1-OCH_3), 3.27, 3.26 (2 s, 6 H, 2 OCH_3 BDA), 1.35, 1.31 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.8, 129.7 (2 C, 2 C_q arom), 127.4, 113.3 (4 C, arom), 101.2 (1 C, C_{ac}), 99.8, 99.2 (2 C, 2 C_q BDA), 98.5 (1 C, C-1), 78.6, 68.8, 66.2, 63.2 (4 C, skeleton carbons), 68.8 (1 C, C-6), 55.0 (1 C, C-1-OCH_3), 54.9 (1 C, PMB-OCH_3), 47.8, 47.7 (2 C, 2 OCH_3 BDA), 17.5, 17.4 (2 C, 2 CH_3 BDA) ppm. MS (MALDI-TOF): m/z = 449.24 [M + Na]$^+$. $C_{21}H_{30}O_9$ (426.19): calcd. C 59.14, H 7.09; found C 59.20, H 7.13.

Methyl 2,3-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-4-*O*-(2-naphthyl)-methyl-α-D-glucopyranoside (8): Compound **5** (3.00 g, 6.72 mmol) was converted into **8** by method D using anhydrous CH_2Cl_2 (10.0 mL), anhydrous Et_2O (2× 5.0 mL), $LiAlH_4$ (1.14 g, 30.24 mmol), and $AlCl_3$ (1.34 g, 10.08 mmol) at room temperature. Purification by column chromatography on silica gel (*n*-hexane/acetone, 7:3) gave compound **8** (2.59 g, 86%) as a white foam. $[\alpha]_D^{24}$ = +5.1 (c = 0.04, $CHCl_3$). R_f = 0.31 (*n*-hexane/acetone, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81–7.43 (m, 7 H, arom), 5.12 (d, J_{gem} = 11.4 Hz, 1 H, NAP-CH_{2a}), 4.84 (d, J_{gem} = 11.4 Hz, 1 H, NAP-CH_{2b}), 4.73 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.27 (dd, J = 8.6, J = 10.0 Hz, 1 H), 3.84–3.71 (m, 5 H), 3.39 (s, 3 H, C-1-OCH_3), 3.32, 3.28 (2 s, 6 H, 2 OCH_3 BDA), 2.13 (s, 1 H, OH), 1.36, 1.35 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.8, 133.2, 132.9 (3 C, 3 C_q arom), 128.1, 127.9, 127.6, 126.6, 126.1, 126.0, 125.9 (7 C, arom), 99.9, 99.4 (2 C, 2 C_q BDA), 97.9 (1 C, C-1), 75.0, 71.3, 70.4, 68.5 (4 C, skeleton carbons), 74.9 (1 C, NAP-CH_2), 61.9 (1 C, C-6), 55.0 (1 C, C-1-OCH_3), 48.0, 47.9 (2 C, 2 OCH_3 BDA), 18.0, 17.7 (2 C, 2 CH_3 BDA) ppm. MS (MALDI-TOF): m/z = 471.09 [M + Na]$^+$. $C_{24}H_{32}O_8$ (448.21): calcd. C 64.27, H 7.19; found C 64.32, H 7.24.

Methyl 4-*O*-Benzyl-2,3-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-glucopyranoside (9): Compound **6** (396 mg, 1.00 mmol) was converted to **9** by method D using anhydrous CH_2Cl_2 (3.0 mL), anhydrous Et_2O (2× 1.0 mL), $LiAlH_4$ (171 mg, 4.50 mmol), and $AlCl_3$ (200 mg, 1.50 mmol) at room temperature. Purification by column chromatography on silica gel (*n*-hexane/acetone, 7:3) gave compound **9** (294 mg, 74%) as a colourless syrup. $[\alpha]_D^{24}$ = –7.6 (c = 0.45, $CHCl_3$). R_f = 0.32 (*n*-hexane/acetone, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.25 (m, 5 H, arom), 4.97 (d, J_{gem} = 11.0 Hz, 1 H, Ph-CH_{2a}), 4.73 (d, $J_{1,2}$ = 3.3 Hz, 1 H, 1-H), 4.67 (d, J_{gem} = 11.0 Hz, 1 H, Ph-CH_{2b}), 4.24 (t, $J_{2,3}$ = $J_{3,4}$ = 9.4 Hz, 1 H, 3-H), 3.82–3.77 (m, 3 H, 2-H, 6-Ha,b), 3.75–3.65 (m, 2 H, 4-H, 5-H), 3.41 (s, 3 H, C-1-OCH_3), 3.30, 3.28 (2 s, 6 H, 2 OCH_3 BDA), 2.65 (s, 1 H, OH), 1.36, 1.35 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.1 (1 C, C_q arom), 128.1, 127.7, 127.5 (5 C, arom), 99.6, 99.0 (2 C, 2 C_q BDA), 97.6 (1 C, C-1), 74.6 (1 C, Ph-CH_2), 74.5, 71.2, 70.2, 68.1 (4 C, skeleton carbons), 61.4 (1 C, C-6), 54.7 (1 C, C-1-OCH_3), 47.8, 47.6 (2 C, 2 OCH_3 BDA), 17.7, 17.4 (2 C, 2 CH_3 BDA) ppm. MS (MALDI-TOF): m/z = 421.27 [M + Na]$^+$. $C_{20}H_{30}O_8$ (398.19): calcd. C 60.29, H 7.59; found C 60.34, H 7.63.

Methyl 2,3-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-4-*O*-(4-methoxy)-benzyl-α-D-glucopyranoside (10): Compound **7** (426 mg, 1.00 mmol) was converted into **10** by method D using anhydrous CH_2Cl_2 (3.0 mL), anhydrous Et_2O (2× 1.0 mL), $LiAlH_4$ (170 mg, 4.50 mmol), and $AlCl_3$ (200 mg, 1.50 mmol) at 0 °C. Purification by column chromatography on silica gel (*n*-hexane/EtOAc, 65:35) gave compound **10** (379 mg, 89%) as a colourless syrup. $[\alpha]_D^{24}$ = –7.9 (c = 0.45, $CHCl_3$). R_f = 0.10 (*n*-hexane/acetone, 65:35). ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.28–6.84 (m, 4 H, arom), 4.89–4.86 (m, 1 H, PMB-CH_{2a}), 4.70 (s, 1 H, 1-H), 4.62–4.59 (m, 1 H, PMB-CH_{2b}), 4.22–4.18 (m, 1 H), 3.80–3.64 (m, 8 H, 5 skeleton H, PMB-OCH_3), 3.37 (s, 3 H, C-1-OCH_3), 3.31, 3.26 (2 s, 6 H, 2 OCH_3 BDA), 2.69 (s, 1 H, OH), 1.34 (s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 158.9, 130.2 (2 C, 2 C_q arom), 129.2, 113.4 (4 C, arom), 99.5, 98.9 (2 C, 2 C_q BDA), 97.5 (1 C, C-1), 74.0 (1 C, PMB-CH_2), 74.2, 71.2, 70.1, 68.0 (skeleton carbons, 4 C), 61.2 (1 C, C-6), 54.7, 54.5 (2 C, PMB-OCH_3, C-1-OCH_3), 47.5, 47.3 (2 C, 2 OCH_3 BDA), 17.5, 17.3 (2 C, 2 CH_3 BDA) ppm. MS (MALDI-TOF): m/z = 451.10 [M + Na]$^+$. $C_{21}H_{32}O_9$ (428.20): calcd. C 58.87, H 7.53; found C 58.90, H 7.57.

Methyl 2,3-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-6-*O*-(2-naphthyl)-methyl-α-D-glucopyranoside (11a) and Methyl 2,3-*O*-(Butane-2′,3′-diyl)-6-*O*-(2-naphthyl)methyl-α-D-glucopyranoside (11b)

Reaction 1: Compound **5** (300 mg, 0.67 mmol) was converted into **11a** and **11b** by method E using $BF_3{\cdot}Et_2O$ (2.0 equiv.). The crude product was purified by silica gel chromatography (*n*-hexane/acetone, 85:15) to give **11a** and **11b** (150 mg, 50%) as an inseparable mixture (**11a**/**11b** = 3:2 based on the NMR spectra) as a colourless syrup.

Reaction 2: Compound **5** (446 mg, 1.00 mmol) was converted into **11a** by method F. Purification by column chromatography on silica gel (*n*-hexane/acetone, 7:3) gave compound **11a** (336 mg, 75%) as a white foam.

Data for the Mixture of **11a** and **11b**: R_f = 0.17 (*n*-hexane/acetone, 85:15). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81–7.72 (m, 10.5 H, arom), 4.81–4.68 (m, 4.5 H, 2 NAP-CH_2, 2 1-H), 4.06–4.01 (m, 1 H), 3.83–3.73 (m, 8 H), 3.41 (s, 4.5 H, 2 C-1-OCH_3), 3.27, 3.23 (2 s, 6 H, 2 OCH_3 BDA), 2.95 (s, 0.5 H, OH **11b**), 2.85 (s, 1 H, OH

11a), 1.34, 1.31 (2 s, 6 H, 2 CH_3 BDA), 1.15–1.11 (m, 4 H, 2 CH_3 butane-2′,3′-diyl) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.5, 133.2, 133.0 (6 C, 6 C_q arom), 128.2, 127.8, 127.6, 126.4, 126.0, 125.8, 125.6 (14 C, arom), 99.8, 99.5 (2 C, 2 C_q BDA), 98.1 (1 C, C-1 **11a**), 97.9 (1 C, C-1 **11b**), 77.9, 77.0, 76.9, 76.3, 70.8, 70.6, 69.4, 69.1, 68.7, 68.1 (10 C, 8 skeleton carbons, 2 C*H* butane-2′,3′-diyl), 73.7 (2 C, 2 NAP-*C*H_2), 69.5, 69.4 (2 C, 2 C-6), 55.1, 55.0 (2 C, 2 C-1-O*C*H_3), 47.9, 47.8 (2 C, 2 O*C*H_3 BDA), 17.8, 17.6, 17.2 (4 C, 2 *C*H_3 BDA, 2 *C*H_3 butane-2′,3′-diyl) ppm. MS (MALDI-TOF): *m*/*z* = 471.22 [M (**11a**) + Na]$^+$, 411.20 [M (**11b**) + Na]$^+$.

Data for **11a**: $[\alpha]_D^{24}$ = –43.5 (*c* = 0.06, $CHCl_3$). R_f = 0.45 (*n*-hexane/acetone, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83–7.45 (m, 7 H, arom), 4.80–4.7 (m, 3 H, NAP-CH_2, 1-H), 4.03 (dd, *J* = 10.2, *J* = 8.9 Hz, 1 H), 3.83–3.73 (m, 5 H), 3.42 (s, 3 H, C-1-OCH_3), 3.28, 3.24 (2 s, 6 H, 2 OCH_3 BDA), 2.66 (s, 1 H, O*H*), 1.34, 1.32 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.5, 133.3, 133.1 (3 C, C_q arom), 128.3, 127.9, 127.7, 126.5, 126.2, 125.9, 125.7 (7 C, arom), 99.9, 99.6 (2 C, 2 C_q BDA), 98.1 (1 C, C-1), 73.8 (1 C, NAP-*C*H_2), 70.8, 69.4, 68.9, 68.2 (4 C, skeleton carbons), 69.5 (1 C, C-6), 55.2 (1 C, C-1-O*C*H_3), 48.0, 47.9 (2 C, 2 O*C*H_3 BDA), 17.8, 17.7 (2 C, 2 *C*H_3 BDA) ppm. MS (MALDI-TOF): *m*/*z* = 471.42 [M + Na]$^+$. $C_{24}H_{32}O_8$ (448.21): calcd. C 64.27, H 7.19; found C 64.35, H 7.25.

Methyl 6-*O*-Benzyl-2,3-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-glucopyranoside (12a) and methyl 6-*O*-benzyl-2,3-*O*-(butane-2′,3′-diyl)-α-D-glucopyranoside (12b)

Reaction 1: Compound **6** (396 mg, 1.00 mmol) was converted into **12a** and **12b** by method E using BF_3·Et_2O (1.0 equiv.). The crude product was purified by silica gel chromatography (*n*-hexane/acetone, 7:3) to give **12a** and **12b** (199 mg, 50%) as an inseparable mixture (**12a**/**12b** = 1:1 based on the NMR spectra) as a colourless syrup.

Reaction 2: Et_3SiH (798 μL, 5.00 mmol) and trifluoroacetic acid (382 μL, 5.00 mmol) were added to a solution of **6** (396 mg, 1.00 mmol) in anhydrous CH_2Cl_2 (4.0 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 10 min. The mixture was diluted with EtOAc (100 mL), washed with saturated aqueous $NaHCO_3$ (2× 10.0 mL) and H_2O (2× 10.0 mL), dried with $MgSO_4$, and concentrated. The crude product was purified by column chromatography on silica gel (*n*-hexane/acetone, 7:3) to give **12a** (194 mg, 49%) as a colourless syrup.

Reaction 3: Compound **6** (260 mg, 0.656 mmol) was converted into **12a** by method F. Purification by column chromatography on silica gel (*n*-hexane/acetone, 7:3) gave compound **12a** (180 mg, 69%) as a white foam, and compound **9** (54 mg, 20%) as a white foam.

Data for the Mixture of **12a** and **12b**: R_f = 0.49 (*n*-hexane/acetone, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.26 (m, 10 H, arom), 4.80 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.78 (d, $J_{1,2}$ = 3.4 Hz, 1 H, 1-H), 4.63–4.54 (m, 4 H, 2 Ph-CH_2), 4.05–4.00 (m, 1 H), 3.82–3.69 (m, 10 H), 3.44–3.37 (m, 3 H), 3.41 (s, 6 H, 2 C-1-OCH_3), 3.30, 3.23 (2 s, 6 H, 2 OCH_3 BDA), 3.15 (s, 2 H, O*H*), 1.34, 1.31 (2 s, 6 H, 2 CH_3 BDA), 1.16–1.12 (m, 6 H, 2 CH_3 butane-2′,3′-diyl) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.8 (2 C, 2 C_q arom), 128.2, 127.5, 127.4 (10 C, arom), 99.6, 99.3 (2 C, 2 C_q BDA), 97.8, 97.7 (2 C, 2 C-1), 77.4, 76.9, 76.8, 76.1, 70.7, 70.5, 69.3, 68.6, 68.3, 67.9 (10 C, 8 skeleton carbons, 2 C*H* butane-2′,3′-diyl), 73.4 (2 C, 2 Ph-*C*H_2), 69.2, 69.0 (2 C, 2 C-6), 55.0, 54.9 (2 C, 2 C-1-O*C*H_3), 47.8, 47.7 (2 C, 2 O*C*H_3 BDA), 17.6, 17.5, 17.1 (4 C, 2 *C*H_3 BDA, 2 *C*H_3 butane-2′,3′-diyl) ppm. MS (MALDI-TOF): *m*/*z* = 421.26 [M (**12a**) + Na]$^+$, 361.26 [M (**12b**) + Na]$^+$.

Data for **12a**: $[\alpha]_D^{24}$ = –42.7 (*c* = 0.84, $CHCl_3$). R_f = 0.42 (*n*-hexane/acetone, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.26 (m, 5 H, arom), 4.76 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.58 (q, J_{gem} = 12.0 Hz, 2 H, Ph-CH_2), 4.02 (dd, *J* = 8.6, *J* = 10.1 Hz, 1 H), 3.81–3.69 (m, 5 H), 3.41 (s, 3 H, C-1-OCH_3), 3.27, 3.23 (2 s, 6 H, 2 OCH_3 BDA), 2.98 (s, 1 H, O*H*), 1.34, 1.31 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.9 (1 C, C_q arom), 128.2, 127.5, 127.4 (5 C, arom), 99.7, 99.3 (2 C, 2 C_q BDA), 97.9 (1 C, C-1), 73.4 (1 C, Ph-*C*H_2), 70.7, 69.3, 68.5, 68.0 (4 C, skeleton carbons), 69.2 (1 C, C-6), 54.9 (1 C, C-1-O*C*H_3), 47.8, 47.7 (2 C, 2 O*C*H_3 BDA), 17.6, 17.5 (2 C, 2 *C*H_3 BDA) ppm. MS (MALDI-TOF): *m*/*z* = 421.22 [M + Na]$^+$. $C_{20}H_{30}O_8$ (398.19): calcd. C 60.29, H 7.59; found C 60.33, H 7.64.

Methyl 2,3-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-6-*O*-(4-methoxy)-benzyl-α-D-glucopyranoside (13)

Reaction 1: Compound **7** (200 mg, 0.47 mmol) was converted into **13** by method E using BF_3·Et_2O (1.0 equiv.). The crude product was purified by silica gel chromatography (*n*-hexane/acetone, 7:3) to give **13** (30 mg, 15%) as a colourless syrup. Compound **3** (34 mg, 17%) was also isolated from the reaction mixture as a white foam.

Reaction 2: Compound **7** (425 mg, 1.00 mmol) was converted into **13** by method F. Purification by column chromatography on silica gel (*n*-hexane/acetone, 7:3) gave compound **13** (101 mg, 24%) as a white foam, and compound **10** (81 mg, 20%) as a white foam. $[\alpha]_D^{24}$ = –43.3 (*c* = 0.33, $CHCl_3$). R_f = 0.26 (*n*-hexane/acetone, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27–6.86 (m, 4 H, arom), 4.77 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.53 (q, J_{gem} = 11.7 Hz, 2 H, PMB-CH_2), 4.02 (dd, *J* = 8.8, *J* = 10.2 Hz, 1 H), 3.80 (s, 3 H, PMB-OCH_3), 3.79–3.66 (m, 5 H), 3.43 (s, 3 H, C-1-OCH_3), 3.29, 3.25 (2 s, 6 H, 2 OCH_3 BDA), 2.56 (s, 1 H, O*H*), 1.34, 1.32 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 130.1 (2 C, 2 C_q arom), 129.4, 113.9 (4 C, arom), 99.9, 99.5 (2 C, 2 C_q BDA), 98.1 (1 C, C-1), 73.4 (1 C, PMB-*C*H_2), 70.6, 69.4, 69.2, 68.2 (4 C, skeleton carbons), 69.3 (1 C, C-6), 55.4, 55.2 (2 C, PMB-O*C*H_3, C-1-O*C*H_3), 48.1, 47.9 (2 C, 2 O*C*H_3 BDA), 17.9, 17.8 (2 C, 2 *C*H_3 BDA) ppm. MS (MALDI-TOF): *m*/*z* = 451.20 [M + Na]$^+$. $C_{21}H_{32}O_9$ (428.20): calcd. C 58.87, H 7.53; found C 58.90, H 7.55.

Methyl 2,3-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-β-D-glucopyranoside (15) and Methyl 3,4-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-β-D-glucopyranoside (16): Compound **14** (2.00 g, 10.3 mmol) was converted into a mixture of **15** and **16** by method B. Purification by column chromatography on silica gel (*n*-hexane/acetone, 6:4) gave compounds **15** and **16** (2.70 g, 85%, inseparable mixture) as a white foam. R_f = 0.28 (*n*-hexane/acetone, 6:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.47 (d, $J_{1,2}$ = 7.9 Hz, 1 H, 1-H), 4.29 (d, $J_{1,2}$ = 7.5 Hz, 0.7 H, 1-H), 3.91–3.68 (m, 7.3 H), 3.57, 3.54 (2 s, 5.1 H, 2 C-1-OCH_3), 3.52–3.37 (m, 4.6 H), 3.31, 3.30, 3.28, 3.26 (4 s, 10.2 H, 4 OCH_3 BDA), 2.73 (s, 0.7 H, O*H*), 2.37 (s, 1 H, O*H*), 1.34, 1.33, 1.30 (3 s, 10.2 H, 4 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 104.6, 101.7 (2 C, 2 C-1), 99.8, 99.7, 99.6, 99.5 (4 C, 4 C_q BDA), 76.3, 74.1, 72.6, 71.8, 71.2, 69.3, 67.5, 65.7 (8 C, skeleton carbons), 62.1, 61.2 (2 C, 2 C-6), 57.6, 57.1 (2 C, 2 O*C*H_3), 48.2, 48.1, 48.0, 47.9 (4 C, 4 O*C*H_3 BDA), 17.7, 17.6 (4 C, 4 *C*H_3 BDA) ppm. MS (MALDI-TOF): *m*/*z* = 331.22 [M + Na]$^+$. $C_{13}H_{24}O_8$ (308.15): calcd. C 50.64, H 7.85; found C 50.71, H 7.93.

Methyl 4,6-*O*-Benzylidene-2,3-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-β-D-glucopyranoside (17): A mixture of compounds **15** and **16** (600 mg, 1.95 mmol), benzaldehyde dimethyl acetal (444 mg, 2.92 mmol, 1.5 equiv.), and TsOH (45 mg, 0.237 mmol, 0.12 equiv.) were treated according to general method C. The crude product was purified by silica gel chromatography (*n*-hexane/acetone, 8:2) to give **17** (417 mg, 54%) as white crystals, m.p. 269–273 °C. $[\alpha]_D^{24}$ = –190.1 (*c* = 0.08, $CHCl_3$). R_f = 0.41 (*n*-hexane/acetone, 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.34 (m, 5 H, arom), 5.53 (s, 1 H, H_{ac}), 4.52 (d, $J_{1,2}$ = 8.0 Hz, 1 H, 1-H), 4.32 (dd, $J_{5,6}$ = 4.8, J_{gem} = 10.4 Hz, 1 H, 6-Ha), 4.00 (t, $J_{2,3}$ = $J_{3,4}$ = 9.8 Hz, 1 H, 3-H), 3.81 (t, $J_{5,6}$ = J_{gem} = 10.3 Hz, 1 H, 6-Hb), 3.70 (t, $J_{4,5}$ = $J_{3,4}$ = 9.4 Hz, 1 H, 4-H), 3.62 (dd, 1 H, $J_{2,3}$ = 9.7, $J_{1,2}$ = 8.1 Hz, 2-H), 3.56 (s, 3 H, C-1-OCH_3), 3.50–3.44 (m, 1 H, 5-H), 3.30, 3.29 (2 s, 6 H, 2 OCH_3 BDA), 1.34, 1.33 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.3 (1 C, C_q arom), 129.0, 128.3, 126.3 (5 C, arom.), 102.2 (1 C, C_{ac}), 101.3 (1 C, C-1), 99.8, 99.5 (2 C, 2 C_q BDA), 77.9, 70.4, 69.5, 67.6 (4 C, skeleton carbons), 68.9 (1 C, C-6), 57.4 (1 C, C-1-OCH_3), 48.2, 48.1 (2 C, 2 OCH_3 BDA), 17.7, 17.6 (2 C, 2 CH_3 BDA) ppm. MS (MALDI-TOF): m/z = 419.19 [M + Na]$^+$. $C_{20}H_{28}O_8$ (396.18): calcd. C 60.59, H 7.12; found C 60.69, H 7.20.

Methyl 4-*O*-Benzyl-2,3-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-β-D-glucopyranoside (18): Compound **17** (396 mg, 1.00 mmol) was converted into **18** by method D using anhydrous CH_2Cl_2 (9.0 mL), anhydrous Et_2O (2× 3.0 mL), $LiAlH_4$ (171 mg, 4.50 mmol), and $AlCl_3$ (600 mg, 4.50 mmol). Purification by column chromatography on silica gel (*n*-hexane/acetone, 7:3) gave compound **18** (330 g, 83%) as a white foam. $[\alpha]_D^{24}$ = –105.4 (c = 1.08, $CHCl_3$). R_f = 0.42 (*n*-hexane/acetone, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.28 (m, 5 H, arom), 4.96 (d, J_{gem} = 11.0 Hz, 1 H, Ph-CH_{2a}), 4.65 (d, J_{gem} = 11.0 Hz, 1 H, Ph-CH_{2b}), 4.44 (d, $J_{1,2}$ = 7.9 Hz, 1 H, 1-H), 3.91 (t, $J_{2,3}$ = $J_{3,4}$ = 9.8 Hz, 1 H, 3-H), 3.85 (d, J_{gem} = 11.9 Hz, 1 H, 6-Ha), 3.72 (dd, $J_{5,6}$ = 4.2, J_{gem} = 11.9 Hz, 1 H, 6-Hb), 3.66 (t, $J_{4,5}$ = $J_{3,4}$ = 9.3 Hz, 1 H, 4-H), 3.55–3.52 (m, 1 H, 2-H), 3.51 (s, 3 H, C-1-OCH_3), 3.41–3.39 (m, 1 H, 5-H), 3.31, 3.30 (2 s, 6 H, 2 OCH_3 BDA), 2.26 (s, 1 H, OH), 1.36, 1.34 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.2 (1 C, C_q arom), 128.4, 128.1, 127.8 (5 C, arom), 101.4 (1 C, C-1), 99.4, 99.3 (2 C, 2 C_q BDA), 77.8 (1 C, C-5), 74.9 (1 C, Ph-CH_2), 74.5 (1 C, C-4), 73.5 (1 C, C-3), 69.5 (1 C, C-2), 61.8 (1 C, C-6), 56.9 (1 C, C-1-OCH_3), 47.9, 47.8 (2 C, 2 OCH_3 BDA), 17.8, 17.5 (2 C, 2 CH_3 BDA) ppm. MS (MALDI-TOF): m/z = 421.22 [M + Na]$^+$. $C_{20}H_{30}O_8$ (398.19): calcd. C 60.29, H 7.59; found C 60.36, H 7.71.

Methyl 6-*O*-Benzyl-2,3-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-β-D-glucopyranoside (19a) and Methyl 6-*O*-Benzyl-2,3-*O*-(butane-2′,3′-diyl)-β-D-glucopyranoside (19b)

Reaction 1: Compound **17** (150 mg, 0.378 mmol) was converted into **19a** and **19b** by method E using $BF_3{\cdot}Et_2O$ (2.0 equiv.) and molecular sieves (4 Å; 0.5 g). The crude product was purified by silica gel chromatography (*n*-hexane/acetone, 7:3) to give **19a** and **19b** (71 mg, 47%) as an inseparable mixture (**19a**/**19b** = 1:1 based on the NMR spectra) as a colourless syrup.

Reaction 2: Compound **17** (160 mg, 0.403 mmol) was converted into **19a** and **19b** by method E using $BF_3{\cdot}Et_2O$ (1.0 equiv.) and molecular sieves (4 Å; 0.5 g). The crude product was purified by silica gel chromatography (*n*-hexane/acetone, 7:3) to give **19a** and **19b** (90 mg, 56%) as an inseparable mixture (**19a**/**19b** = 1:0.8 based on the NMR spectra) as a colourless syrup.

Reaction 3: Compound **17** (160 mg, 0.403 mmol) was converted into **19a** by method F. Purification by column chromatography on silica gel (*n*-hexane/acetone, 7:3) gave compound **19a** (136 mg, 85%) as a white foam.

Data for the mixture of **19a** and **19b**: R_f = 0.50 (*n*-hexane/acetone, 6:4). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.27 (m, 10 H, arom), 4.63–4.56 (m, 4 H, 2 Ph-CH_2), 4.43 (d, $J_{1,2}$ = 7.9 Hz, 1 H, 1-H), 4.36 (d, $J_{1,2}$ = 7.7 Hz, 1 H, 1-H), 3.80–3.63 (m, 9 H), 3.55, 3.53 (2 s, 6 H, 2 C-1-OCH_3), 3.42–3.31 (m, 7 H), 3.28, 3.27 (2 s, 6 H, 2 OCH_3 BDA), 1.33 (s, 6 H, 2 CH_3 BDA), 1.18–1.15 (m, 6 H, 2 CH_3 butane-2′,3′-diyl) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.9 (2 C, 2 C_q arom), 128.5, 127.8, 127.7 (10 C, arom), 101.5, 101.4 (2 C, 2 C-1), 99.6, 99.5 (2 C, 2 C_q BDA), 80.6, 77.6, 77.3, 76.8, 75.1, 74.9, 72.5, 69.4, 69.2, 69.1 (10 C, 8 skeleton carbons, 2 CH butane-2′,3′-diyl), 73.7 (2 C, 2 Ph-CH_2), 70.2 (2 C, 2 C-6), 56.9 (2 C, 2 C-1-OCH_3), 48.1, 47.9 (2 C, 2 OCH_3 BDA), 17.7, 17.6, 17.3 (4 C, 2 CH_3 BDA, 2 CH_3 butane-2′,3′-diyl) ppm. MS (MALDI-TOF): m/z = 421.21 [M (**19a**) + Na]$^+$, 361.18 [M (**19b**) + Na]$^+$.

Data for **19a**: $[\alpha]_D^{24}$ = –126.9 (c = 0.45, $CHCl_3$). R_f = 0.40 (*n*-hexane/acetone, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.27 (m, 5 H, arom), 4.60 (d, J_{gem} = 3.5 Hz, 2 H, Ph-CH_2), 4.43 (d, $J_{1,2}$ = 7.9 Hz, 1 H, 1-H), 3.77–3.69 (m, 5 H), 3.51 (s, 4 H, 1 skeleton H, C-1-OCH_3), 3.29, 3.27 (2 s, 6 H, 2 OCH_3 BDA), 2.97 (s, 1 H, OH), 1.33 (s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.9 (1 C, C_q arom), 128.4, 127.7, 127.6 (5 C, arom), 101.4 (1 C, C-1), 99.5, 99.4 (2 C, 2 C_q BDA), 75.1, 72.5, 69.2, 69.0 (4 C, skeleton carbons), 73.7 (1 C, Ph-CH_2), 70.1 (1 C, C-6), 56.8 (1 C, C-1-OCH_3), 48.0, 47.9 (2 C, 2 OCH_3 BDA), 17.7, 17.2 (2 C, 2 CH_3 BDA) ppm. MS (MALDI-TOF): m/z = 421.27 [M + Na]$^+$. $C_{20}H_{30}O_8$ (398.19): calcd. C 60.29, H 7.59; found C 60.33, H 7.68.

Phenyl 2,3-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-1-thio-β-D-glucopyranoside (21) and Phenyl 3,4-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-1-thio-β-D-glucopyranoside (22):[3,30] Compound **20** (2.72 g, 10.00 mmol) was converted into **21** and **22** by method A. Purification by column chromatography on silica gel (CH_2Cl_2/CH_3OH, 95:5) gave compound **21** (1.50 g, 39%) as a white foam, and compound **22** (2.26 g, 59%) as a white foam.

Data for **21**: $[\alpha]_D^{24}$ = –142.5 (c = 0.33, $CHCl_3$); ref.[30] $[\alpha]_D^{25}$ = –156.9 (c = 1.0). R_f = 0.40 (CH_2Cl_2/CH_3OH, 95:5). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50–7.23 (m, 5 H, arom), 4.83 (d, $J_{1,2}$ = 9.7 Hz, 1 H, 1-H), 3.90–3.87 (m, 1 H, 6-Ha), 3.82–3.75 (m, 2 H, 6-Hb, 4-H), 3.74 (t, $J_{2,3}$ = $J_{3,4}$ = 9.5 Hz, 1 H, 3-H), 3.60 (t, $J_{1,2}$ = $J_{2,3}$ = 9.7 Hz, 1 H, 2-H), 3.44–3.39 (m, 1 H, 5-H), 3.28, 3.22 (2 s, 7 H, 2 OCH_3 BDA, C-4-OH), 2.55 (t, $J_{6a,b,OH}$ = 6.5 Hz, 1 H, C-6-OH), 1.33, 1.32 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 133.4 (1 C, C_q arom), 131.5, 129.0, 127.5 (5 C, arom), 100.2, 99.8 (2 C, 2 C_q BDA), 85.3 (1 C, C-1), 80.1 (1 C, C-5), 74.4 (1 C, C-3), 68.2 (1 C, C-2), 67.6 (1 C, C-4), 62.4 (1 C, C-6), 48.3, 48.0 (2 C, 2 OCH_3 BDA), 17.7, 17.6 (2 C, 2 CH_3 BDA) ppm. MS (MALDI-TOF) m/z = 409.17 [M + Na]$^+$. $C_{18}H_{26}O_7S$ (386.46): calcd. C 55.94, H 6.78, S 8.30; found C 56.42, H 6.81, S 9.01.

Data for **22**: $[\alpha]_D^{24}$ = +118.8 (c = 0.04, $CHCl_3$); ref.[30] $[\alpha]_D^{25}$ = +100.4 (c = 1.0). R_f = 0.47 (CH_2Cl_2/CH_3OH, 95:5). ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.53–7.28 (m, 5 H, arom), 4.59 (d, $J_{1,2}$ = 9.4 Hz, 1 H, 1-H), 3.90–3.48 (m, 6 H), 3.30, 3.22 (2 s, 6 H, 2 OCH_3 BDA), 3.10 (s, 1 H, OH), 2.45 (s, 1 H, OH), 1.33, 1.28 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 131.4 (1 C, C_q arom), 132.7–128.0 (5 C, arom), 99.6, 99.3 (2 C, 2 C_q BDA), 88.1 (1 C, C-1), 77.8, 73.2, 69.1, 65.2 (4 C, skeleton carbons), 61.1 (1 C, C-6), 47.7 (2 C, 2 OCH_3 BDA), 17.5, 17.4 (2 C, 2 CH_3 BDA) ppm. MS (MALDI-TOF) m/z = 409.11 [M + Na]$^+$. $C_{18}H_{26}O_7S$ (386.46): calcd. C 55.94, H 6.78, S 8.30; found C 56.21, H 6.84, S 8.51.

Phenyl 2,3-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-4,6-*O*-(2-naphthyl)methylene-1-thio-β-D-glucopyranoside (23): Compound **21** (500 mg, 1.29 mmol) was treated according to method C using naphthaldehyde dimethyl acetal (393 mg, 1.94 mmol, 1.5 equiv.) and TsOH (50 mg, 0.258 mmol, 0.2 equiv.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc, 95:5) gave compound **23** (465 mg, 68%) as a colourless syrup. Unreacted **21** was recovered (145 mg, 21%). Data for **23**: $[\alpha]_D^{24}$ = –123.2 (c = 0.50, $CHCl_3$). R_f = 0.55 (*n*-hexane/acetone, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93–7.25 (m, 12 H, arom), 5.68 (s, 1 H, H_{ac}), 4.91 (d,

$J_{1,2}$ = 10.1 Hz, 1 H, 1-H), 4.36 (dd, J_{gem} = 10.4, $J_{5,6}$ = 4.9 Hz, 1 H, 6-Ha), 4.07 (t, $J_{4,5}$ = $J_{3,4}$ = 9.5 Hz, 1 H, 4-H), 3.85 (t, J_{gem} = $J_{5,6b}$ = 10.3 Hz, 1 H, 6-Hb), 3.82–3.77 (m, 2 H, 2-H, 3-H), 3.59–3.53 (m, 1 H, 5-H), 3.29, 3.25 (2 s, 6 H, 2 OCH_3 BDA), 1.35, 1.34 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.6, 133.6, 133.2, 132.9 (4 C, C_q arom), 131.9–123.9 (12 C, arom), 101.5 (1 C, C_{ac}), 100.5, 99.7 (2 C, 2 C_q BDA), 86.2 (1C, C-1), 77.8 (1C, C-2), 71.6 (1C, C-5), 71.2 (1C, C-4), 69.0 (1C, C-3), 68.8 (1C, C-6), 48.3, 48.1 (2C, 2 OCH_3 BDA), 17.7 (2C, 2 CH_3 BDA) ppm. MS (MALDI-TOF) m/z = 547.16 [M + Na]$^+$. $C_{29}H_{32}O_7S$ (524.19): calcd. C 66.39, H 6.15, S 6.11; found C 66.43, H 6.20, S 6.17.

Phenyl 2,3-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-4-*O*-(2-naphthyl)-methyl-1-thio-β-D-glucopyranoside (24): Compound **23** (125 mg, 0.238 mmol) was converted into **24** by method D using anhydrous CH_2Cl_2 (350 μL), anhydrous Et_2O (2× 170 μL), $LiAlH_4$ (40 mg, 1.071 mmol), and $AlCl_3$ (47 mg, 0.357 mmol) at room temperature. Purification by column chromatography on silica gel (*n*-hexane/EtOAc, 75:25) gave compound **24** (99 mg, 79%) as a white foam. $[\alpha]_D^{24}$ = –102.6 (*c* = 0.04, $CHCl_3$). R_f = 0.42 (*n*-hexane/EtOAc, 75:25). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81–7.20 (m, 12 H, arom), 5.09 (d, J_{gem} = 11.3 Hz, 1 H, NAP-CH_{2a}), 4.81 (m, 2 H, NAP-CH_{2b}, 1-H), 3.98 (t, $J_{4,5}$ = $J_{3,4}$ = 9.5 Hz, 1 H, 4-H), 3.86 (dd, $J_{3,4}$ = 12.0, $J_{2,3}$ = 2.4 Hz, 1 H, 3-H), 3.74–3.66 (m, 3 H, 2-H, 6-Ha,b), 3.47–3.42 (m, 1 H, 5-H), 3.31, 3.25 (2 s, 6 H, 2 OCH_3 BDA), 2.14 (s, 1 H, C-6-O*H*), 1.37, 1.35 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.7, 133.3, 133.0 (4 C, C_q arom), 131.6–126.0 (12 C, arom), 100.2, 99.7 (2 C, 2 C_q BDA), 85.0 (1 C, C-1), 79.8, 75.4, 74.6, 68.4 (4 C, skeleton carbons), 75.0 (1 C, NAP-*C*H_2), 62.3 (1 C, C-6), 48.2, 48.0 (2 C, 2 OCH_3 BDA), 17.9, 17.7 (2 C, 2 CH_3 BDA) ppm. MS (MALDI-TOF) m/z = 549.21 [M + Na]$^+$. $C_{29}H_{34}O_7S$ (526.64): calcd. C 66.14, H 6.51, S 6.09; found C 66.23, H 6.61, S 6.16.

Phenyl 2,3-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-6-*O*-(2-naphthyl)-methyl-1-thio-β-D-glucopyranoside (25)

Reaction 1: Compound **23** (100 mg, 0.191 mmol) was converted into **25** by method E using BF_3·Et_2O (1.0 equiv.). The crude product was purified by silica gel chromatography (*n*-hexane/EtOAc, 65:35) to give **25** (69 mg, 69%) as a colourless syrup.

Reaction 2: Compound **23** (165 mg, 0.315 mmol) was converted into **25** by method F. Purification by column chromatography on silica gel (*n*-hexane/acetone, 7:3) gave compound **25** (136 mg, 82%) as a white foam. $[\alpha]_D^{24}$ = –107.5 (*c* = 0.37, $CHCl_3$). R_f = 0.19 (*n*-hexane/EtOAc, 65:35). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83–7.19 (m, 12 H, arom), 4.81 (d, $J_{1,2}$ = 9.8 Hz, 1 H, 1-H), 4.73 (d, J_{gem} = 1.0 Hz, 2 H, NAP-CH_2), 3.86–3.73 (m, 4 H), 3.67–3.56 (m, 2 H), 3.28, 3.19 (2 s, 6 H, 2 OCH_3 BDA), 2.86 (s, 1 H, C-4-O*H*), 1.34, 1.33 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.5, 133.5, 133.3, 133.1 (4 C, 4 C_q arom), 131.7–125.7 (12 C, arom), 100.2, 99.7 (2 C, 2 C_q BDA), 85.2 (1 C, C-1), 79.1, 74.4, 68.8, 67.9 (4 C, skeleton carbons), 73.8 (1 C, NAP-*C*H_2), 70.2 (1 C, C-6), 48.2, 48.0 (2 C, 2 OCH_3 BDA), 17.7, 17.7 (2 C, 2 CH_3 BDA) ppm. MS (MALDI-TOF) m/z = 549.21 [M + Na]$^+$. $C_{29}H_{34}O_7S$ (526.64): calcd. C 66.14, H 6.51, S 6.09; found C 66.21, H 6.59, S 6.17.

Methyl 2,3-*O*-(2′,3′-Dimethoxybutane-2′,3′-diyl)-α-D-galactopyranoside (27): Compound **26** (1.00 g, 5.15 mmol) was converted into **27** by method B. Purification by column chromatography on silica gel (*n*-hexane/acetone, 7:3) gave compound **27** (1.225 g, 77%) as white crystals, m.p. 81–84 °C; ref.[13a] m.p. 88–91 °C. $[\alpha]_D^{24}$ = –32.9 (*c* = 0.24, $CHCl_3$). R_f = 0.43 (*n*-hexane/acetone, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.84 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.19 (dd, *J* = 10.1, *J* = 3.5 Hz, 1 H), 4.09–4.035 (m, 2 H), 3.95–3.81 (m, 3 H), 3.43 (s, 3 H, C-1-OCH_3), 3.27, 3.26 (2 s, 6 H, 2 OCH_3 BDA), 2.97 (s, 1 H, O*H*), 2.46 (s, 1 H, O*H*), 1.34, 1.31 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 100.2, 100.1 (2 C, 2 C_q BDA), 98.4 (1 C, C-1), 70.3, 69.0, 66.3, 65.1 (4 C, skeleton carbons), 62.6 (1 C, C-6), 55.2 (1 C, C-1-O*C*H_3), 48.0 (2 C, 2 O*C*H_3 BDA), 17.8, 17.7 (2 C, 2 *C*H_3 BDA) ppm. MS (MALDI-TOF): m/z = 331.16 [M + Na]$^+$. $C_{13}H_{24}O_8$ (308.15): calcd. C 50.64, H 7.85; found C 50.71, H 7.90.

Methyl 4,6-*O*-Benzylidene-2,3-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-galactopyranoside (28): Compound **27** (600 mg, 1.946 mmol) was converted into **28** by method C using benzaldehyde dimethyl acetal (444 mg, 2.92 mmol, 1.5 equiv.) and TsOH (0.25 equiv.). The crude product was purified by silica gel chromatography (*n*-hexane/acetone, 8:2) to give **28** (513 mg, 67%) as white crystals, m.p. 270–273 °C. $[\alpha]_D^{24}$ = –3.67 (*c* = 0.27, $CHCl_3$). R_f = 0.33 (*n*-hexane/acetone, 8:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.30 (m, 5 H, arom), 5.57 (s, 1 H, H_{ac}), 4.90 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.35 (dd, *J* = 3.6, *J* = 10.3 Hz, 1 H), 4.26–4.17 (m, 4 H), 4.09 (dd, *J* = 1.4, *J* = 12.4 Hz, 1 H), 3.44 (s, 3 H, C-1-OCH_3), 3.29, 3.25 (2 s, 6 H, 2 OCH_3 BDA), 1.34, 1.32 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.8 (1 C, C_q arom), 128.7, 128.0, 126.5 (5 C, arom), 100.7 (1 C, C_{ac}), 100.1, 99.9 (2 C, 2 C_q BDA), 98.9 (1 C, C-1), 74.5, 65.1, 64.9, 63.1 (4 C, skeleton carbons), 69.6 (1 C, C-6), 55.3 (1 C, C-1-O*C*H_3), 47.9, 47.9 (2 C, 2 O*C*H_3 BDA), 17.8, 17.7 (2 C, 2 *C*H_3 BDA) ppm. MS (MALDI-TOF): m/z = 419.17 [M + Na]$^+$. $C_{20}H_{28}O_8$ (396.18): calcd. C 60.59, H 7.12; found C 60.67, H 7.19.

Methyl 4-*O*-Benzyl-2,3-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-galactopyranoside (29): Compound **28** (100 mg, 0.252 mmol) was converted into **29** by method D using anhydrous CH_2Cl_2 (375 μL), anhydrous Et_2O (2 187 μL), $LiAlH_4$ (43 mg, 1.135 mmol), and $AlCl_3$ (50 mg, 0.378 mmol) at room temperature. Purification by column chromatography on silica gel (*n*-hexane/acetone, 8:2) gave compound **29** (84 mg, 84%) as a colourless syrup. $[\alpha]_D^{24}$ = –65.6 (*c* = 0.13, $CHCl_3$). R_f = 0.25 (*n*-hexane/acetone, 7:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.27 (m, 5 H, arom), 5.00 (d, J_{gem} = 11.2 Hz, 1 H, Ph-CH_{2a}), 4.83 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.63 (d, J_{gem} = 11.3 Hz, 1 H, Ph-CH_{2b}), 4.34 (dd, $J_{2,3}$ = 10.6, $J_{1,2}$ = 3.6 Hz, 1 H, 2-H), 4.13 (dd, $J_{2,3}$ = 10.6, $J_{3,4}$ = 2.5 Hz, 1 H, 3-H), 3.81–3.77 (m, 3 H, 4-H, 6-Ha,b), 3.61–3.60 (m, 1 H, 5-H), 3.39 (s, 3 H, C-1-OCH_3), 3.29, 3.28 (2 s, 6 H, 2 OCH_3 BDA), 2.19 (s, 1 H, O*H*), 1.35, 1.33 (2 s, 6 H, 2 CH_3 BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.5 (1 C, C_q arom), 128.8, 128.4, 127.9 (5 C, arom), 99.9, 99.6 (2 C, 2 C_q BDA), 98.5 (1 C, C-1), 74.8, 70.9, 67.9, 65.8 (4 C, skeleton carbons), 74.2 (1 C, Ph-*C*H_2), 62.6 (1 C, C-6), 55.2 (1 C, C-1-O*C*H_3), 47.9, 47.9 (2 C, 2 O*C*H_3 BDA), 17.9, 17.8 (2 C, 2 *C*H_3 BDA) ppm. MS (MALDI-TOF): m/z = 421.20 [M + Na]$^+$. $C_{20}H_{30}O_8$ (398.19): calcd. C 60.29, H 7.59; found C 60.34, H 7.63.

Methyl 6-*O*-Benzyl-2,3-*O*-(butane-2′,3′-diyl)-α-D-galactopyranoside (30): Compound **28** (100 mg, 0.252 mmol) was converted into **30** by method E using BF_3·Et_2O (2.0 equiv.) and molecular sieves (4 Å; 0.5 g). The crude product was purified by silica gel chromatography (*n*-hexane/acetone, 8:2) to give **30** (8 mg, 8%) as a colourless syrup. $[\alpha]_D^{24}$ = +112.5 (*c* = 0.02, MeOH). R_f = 0.27 (*n*-hexane/acetone, 8:2). ^{1}H NMR (360 MHz, $CDCl_3$): δ = 7.37–7.26 (m, 5 H, arom), 4.95 (d, J_{gem} = 11.7 Hz, 1 H, Ph-CH_{2a}), 4.87 (d, $J_{1,2}$ = 3.6 Hz, 1 H, 1-H), 4.64 (d, J_{gem} = 11.7 Hz, 1 H, Ph-CH_{2b}), 4.00 (dd, $J_{2,3}$ = 10.0, $J_{1,2}$ = 3.7 Hz, 1 H, 2-H), 3.88 (dd, $J_{2,3}$ = 10.0, $J_{3,4}$ = 2.6 Hz, 1 H, 3-H), 3.81–3.77 (m, 4 H, 4-H, 6-Ha,b, C*H*a butane-2′,3′-diyl), 3.64–3.55 (m, 2 H, 5-H, C*H*b butane-2′,3′-diyl), 3.41 (s, 3 H, C-1-OCH_3), 1.88 (s, 1 H, O*H*), 1.19–1.15 (m, 6 H, 2 CH_3 butane-2′,3′-diyl) ppm. ^{13}C NMR (90 MHz, $CDCl_3$): δ = 128.7, 128.6, 128.1 (5

C, arom), 98.5 (1 C, C-1), 78.2, 77.3, 75.2, 74.9, 73.8, 70.7 (6 C, 4 skeleton carbons, 2 *C*H butane-2′,3′-diyl), 74.3 (1 C, Ph-*C*H$_2$), 62.8 (1 C, C-6), 55.4 (1 C, C-1-O*C*H$_3$), 17.7, 17.4 (2 C, 2 *C*H$_3$ butane-2′,3′-diyl) ppm. MS (MALDI-TOF): *m*/*z* = 361.19 [M + Na]$^+$. $C_{18}H_{26}O_6$ (338.17): calcd. C 63.89, H 7.74; found C 63.93, H 7.78.

Methyl 4,6-*O*-Benzylidene-2,3-*O*-(butane-2′,3′-diyl)-α-D-galactopyranoside (31): Compound **28** (230 mg, 0.580 mmol) was treated according to method E using $BF_3{\cdot}Et_2O$ (1.0 equiv.) and molecular sieves (4 Å; 0.5 g). The crude product was purified by silica gel chromatography (CH_2Cl_2/EtOAc, 8:2) to give **31** (42 mg, 18%) as a colourless syrup. Unreacted **28** was recovered (28 mg, 12%). Data for **31**: $[\alpha]_D^{24}$ = +60.1 (*c* = 0.08, $CHCl_3$). R_f = 0.59 (CH_2Cl_2/EtOAc, 85:15). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54–7.33 (m, 5 H, arom), 5.56 (s, 1 H, H_{ac}), 4.96 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.27–4.24 (m, 2 H), 4.11–4.06 (m, 3 H), 3.91 (dd, $J_{2,3}$ = 10.1, $J_{3,4}$ = 3.3 Hz, 1 H), 3.69 (s, 1 H), 3.46 (s, 4 H, 1 *C*H butane-2′,3′-diyl, C-1-O*CH*$_3$), 1.17–1.14 (m, 6 H, 2 *CH*$_3$ butane-2′,3′-diyl) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.0 (1 C, C_q arom), 128.9, 128.1, 126.6 (5 C, arom), 101.0 (1 C, C_{ac}), 99.0 (1 C, C-1), 77.7, 77.6, 74.7, 72.7, 72.5, 63.1 (6 C, 4 skeleton carbons, 2 *C*H butane-2′,3′-diyl), 69.7 (1 C, C-6), 55.5 (1 C, C-1-O*C*H$_3$), 17.4 (2 C, 2 *C*H$_3$ butane-2′,3′-diyl) ppm. MS (MALDI-TOF): *m*/*z* = 359.27 [M + Na]$^+$. $C_{18}H_{24}O_6$ (336.38): calcd. C 64.27, H 7.19; found C 64.34, H 7.23.

Methyl 6-*O*-Benzyl-2,3-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-α-D-galactopyranoside (32): Compound **28** (230 mg, 0.580 mmol) was treated according to method F. Purification by column chromatography on silica gel (CH_2Cl_2/EtOAc, 8:2) gave compound **32** (169 mg, 73%) as a white foam, and compound **29** (17 mg, 7%) as a white foam. Data for **32**: $[\alpha]_D^{24}$ = –11.5 (*c* = 0.15, $CHCl_3$). R_f = 0.53 (CH_2Cl_2/EtOAc, 8:2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.27 (m, 5 H, arom), 4.83 (d, $J_{1,2}$ = 3.5 Hz, 1 H, 1-H), 4.59 (d, J_{gem} = 3.4 Hz, 2 H, Ph-C*H*$_2$), 4.21 (dd, $J_{2,3}$ = 10.4, $J_{1,2}$ = 3.6 Hz, 1 H, 2-H), 4.06 (dd, $J_{2,3}$ = 10.4, $J_{3,4}$ = 3.1 Hz, 1 H, 3-H), 4.02–4.0 (m, 1 H, 4-H), 3.97 (t, $J_{4,5}$ = $J_{5,6a}$ = 5.8 Hz, 1 H, 5-H), 3.78 (dd, J_{gem} = 9.9, $J_{5,6a}$ = 5.6 Hz, 1 H, 6-Ha), 3.73–3.68 (m, 1 H, 6-Hb), 3.43 (s, 3 H, C-1-OC*H*$_3$), 3.25, 3.24 (2 s, 6 H, 2 OC*H*$_3$ BDA), 2.67 (s, 1 H, O*H*), 1.33, 1.31 (2 s, 6 H, 2 C*H*$_3$ BDA) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.1 (1 C, C_q arom), 128.5, 127.8 (5 C, arom), 100.2 (2 C, 2 C_q BDA), 98.4 (1 C, C-1), 73.7 (1 C, Ph-*C*H$_2$), 69.6 (1 C, C-6), 69.5 (1 C, C-5), 68.4 (1 C, C-4), 66.5 (1 C, C-3), 65.2 (1 C, C-2), 55.3 (1 C, C-1-O*C*H$_3$), 48.0 (2 C, 2 O*C*H$_3$ BDA), 17.9, 17.8 (2 C, 2 *C*H$_3$ BDA) ppm. MS (MALDI-TOF): *m*/*z* = 421.30 [M + Na]$^+$. $C_{20}H_{30}O_8$ (398.19): calcd. C 60.29, H 7.59; found C 60.36, H 7.64.

Supporting Information (see footnote on the first page of this article): Crystallographic data for compound **17**; copies of ^{1}H and ^{13}C NMR spectra for all described compounds.

Acknowledgments

The authors gratefully acknowledge financial support for this research from the Hungarian Research Fund (OTKA K 109208) and the Mizutani Foundation for Glycoscience (150091). This research was also supported by the European Union (EU) and the State of Hungary, cofinanced by the European Social Fund in the framework of TÁMOP 4.2.4. A/2-11-1-2012-0001, National Excellence Program. The authors wish to thank Dr. Attila Bényei for the X-ray measurement.

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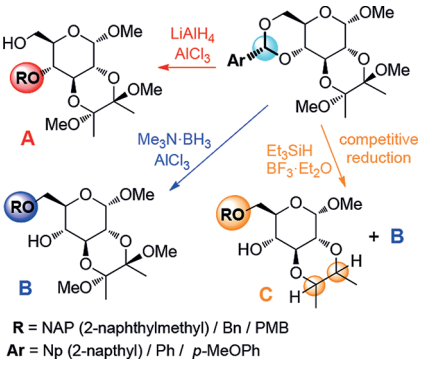
Received: June 4, 2015

The reductive cleavage of various arylmethylene acetals in the presence of butane diacetals was studied for the first time. Three reagent systems were used to gain access to either 4-hydroxy or 6-hydroxy glycoside derivatives. With the proper choice of reagents, benzylidene-type acetals can be opened regio- and chemoselectively in high yields.



Keywords: Carbohydrates / Acetals / Ring opening / Reduction / Protecting groups / Chemoselectivity

