New Factors Governing Stereoselectivity in Borohydride Reductions of β-D-Glycoside-2-uloses − The Peculiar Effect of "Activated" DMSO

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Dedicated to Professor András Lipták on the occasion of his 65th birthday

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Comparative evaluation of the *manno*/*gluco* ratios obtained in the conventional reductions of β-D-glucoside-2-uloses (**1**–**4**, **13** and **14**) reveals the influence of the substitution pattern: the presence of a 4,6-*O*-acetal function results in lower stereoselectivity in the monosaccharide-uloside cases and low stereoselectivity in the disaccharide-uloside cases, while the absence of a 4,6-*O*-acetal group provides distinctly higher stereoselectivity. The 3-*O*-benzyl and 3-*O*-allyl ethers *vicinal* to the carbonyl to be reduced have a similar influence on the steric outcome of the carbonyl reduction. A peculiar effect of acetoxydimethylsulfonium acetate ("activated" DMSO) was observed. In all cases, its presence strongly increased the *manno*-selectivity of the reduction. A simple, preparatively expedient, commonly suitable protocol has been elaborated for achieving high *manno*-selectivities and, hence, satisfactory yields.

Introduction

Most *N*-linked glycoprotein glycans share a common pentasaccharide core structure in which β-D-mannose is the branching point. The β-D-mannopyranosidic linkage is also found in the cell walls of certain bacteria and in bivalve molluscs. The construction of the β-D-mannosidic bond is one of the most difficult issues in oligosaccharide chemistry.[1] The recent development of numerous diverse and innovative strategies for the synthesis of β-D-mannopyranosides is well reviewed.[2] The oxidation-reduction[3] method is one of the most commonly used strategies for the synthesis of β-D-mannosides and involves β-D-glycosid-2-uloses (2-oxoglycosides) as key intermediates. These are generated from suitably protected β-D-glucosides in which the 2-OH can selectively be liberated and oxidized. The alternate protocol to β-D-glycosiduloses is the direct glycosidation of 2-oxoglycosyl (ulosyl) bromides in the presence of an insoluble promoter. The common key parameter of both the oxidation-reduction[3] and ulosyl bromide[2a,4] approaches concerns the degree of *manno*-selectivity achievable upon hydride reduction of the 2-keto group in β-D-glucosiduloses. However, borohydride reduction of β-D-glycosid-2-uloses using known procedures does not always give high selectivity.[3e,4b] The steric outcome of the carbonyl reduction is not only dependent on the anomeric configuration but also on the nature of the 3-*O*-blocking group *vicinal* to the C-2 carbonyl.[4b] The presence of a 3-*O*-sulfonyl or 3-*O*-acyl function results in low stereoselectivity (2:1 and 5:1 in favour of the *manno*-epimer, respectively). The same seems to be the case for a 3-*O*-allyl group, because the reduction of β-D-glycosid-2-ulose **1** proceeds with low stereoselectivity (7:3 in favour of the *manno*-epimer[3e]) in the presence of a 3′-*O*-allyl function, while the reduction of glycosidulose **2**, with a similar blocking group pattern but with benzyl protection at *O*-3, gives the respective β-D-mannoside stereoselectively (*manno*/*gluco* ratio >10:1[3d]). Here, we report a simple, generally applicable protocol to achieve high *manno*-selectivity.

Results and Discussion

In the framework of our studies on the carbonyl reduction, β-D-glucosiduloses **3** (analogous to compound **2**) and **4** (analogous to disaccharide **1**) were prepared and their carbonyl functions were reduced, as described for **2**[3d] and **1**,[3e] in order to make a direct comparison of the effect of 3-*O*-allyl and 3-*O*-benzyl groups (Figure 1).

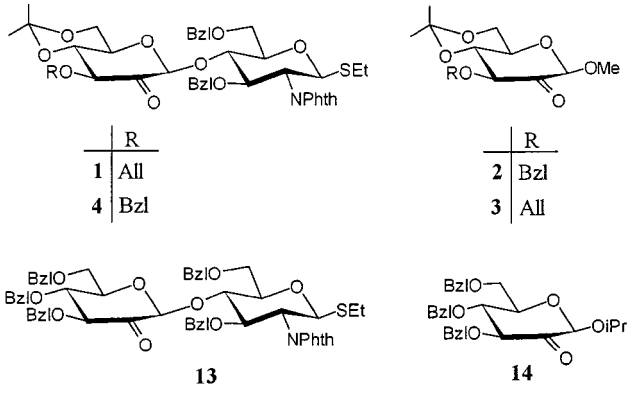

Figure 1. β-D-Glucoside-2-uloses

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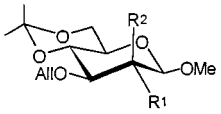
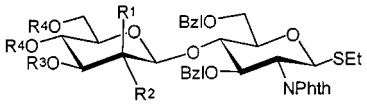
Methyl 3-*O*-allyl-β-D-glucopyranoside[5] was treated with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid to afford methyl 3-*O*-allyl-4,6-*O*-isopropylidene-β-D-glucopyranoside (**5**) (Figure 2).





	R1	R2
5	OH	H
6	H	OH

	R1	R2	R3	R4
7	H	OAc	Bzl	Ac
8	H	OH	Bzl	H
9	H	OH	Bzl	Me_2C
10	H	OH	All	Me_2C
11	OH	H	Bzl	Me_2C
12	OH	H	All	Me_2C

Figure 2. Selectively protected β-D-glucosides and β-D-mannosides

Oxidation of **5** with methyl sulfoxide/acetic anhydride resulted in ulose **3**, which was reduced with $NaBH_4$ in 1:1 dichloromethane/methanol to stereoselectively yield the corresponding *manno*-derivative **6**. Only traces of **5** could be detected by TLC.

Condensation of ethyl 3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside[3e] and 2,4,6-tri-*O*-acetyl-3-*O*-benzyl-α-D-glucopyranosyl bromide[6] in dichloromethane/toluene, in the presence of silver triflate as a promoter, afforded disaccharide **7** (Figure 2). Zemplén *O*-deacetylation of **7** (→ **8**), isopropylidenation with 2,2-dimethoxypropane (→ **9**), and oxidation of OH-2′ using methyl sulfoxide/acetic anhydride after conventional workup (procedure A) afforded β-D-glucosidulose **4**. The crude 2′-ulose **4** was reduced with $NaBH_4$ in 1:2 dichloromethane/2-propanol to give a mixture of the *gluco*- (**9**) and *manno*- (**11**) epimers in an approximately 3:7 ratio (TLC). The isomers (**9** and **11**) were separated by column chromatography resulting in the *manno*- (**11**, 52%) and the *gluco*- (**9**, 36%) epimers, so that **9** could be recycled.

As evidenced by compounds **1**, **3** and their analogues **4** and **2**, the allyl and benzyl groups had a similar influence on the steric outcome of the carbonyl reduction (Table, entries A−D). Reduction of β-D-glycosidulose **13**[3f] under the conditions described for **1** and **4** afforded the corresponding *manno*-derivative stereoselectively (*manno*/*gluco* ratio >10:1, Entry E). Considering the results of conventional carbonyl reductions of β-D-glycosiduloses **2**, **3** and **14** (entries A, B and F) as well as ulosides **1**, **4** and **13** (entries C, D and E), the following picture emerges concerning stereoselectivities influenced by the substitution pattern: the presence of a 4,6-*O*-acetal function (fixing a certain conformation of the ulose part of these molecules) results in lower stereoselectivity in the monosaccharide-uloside cases and low stereoselectivity in the disaccharide-uloside cases.

Due to the very poor solubility of $NaBH_4$ in aprotic solvents, either a protic or the combination of an aprotic and protic solvent (most frequently MeOH/CH_2Cl_2,1:1) has been used for reductions with this reagent.[4b] Recently, the tetrabutylammonium borohydride reagent in tetrahydrofuran has been applied to the reduction of β-D-glycosidulose **13**.[3f] To our great surprise, and much to our delight, when workup protocol B was chosen for the preparation of **4**, and the residue was treated with tetrabutylammonium borohydride in tetrahydrofuran at 0 °C, the corresponding *manno*-epimer (**11**) was obtained in a stereoselective manner (*manno*/*gluco* ratio 91:9, entry G). The high *manno*-selectivity observed under these conditions served as the starting point for a systematic evaluation of relevant reaction parameters. Interestingly, when workup protocol A was used for the preparation of β-D-glycosidulose **4**, and the residue was treated with tetrabutylammonium borohydride in tetrahydrofuran at 0 °C, the *manno* (**11**) and *gluco* (**9**) epimers were obtained in approximately a 1:1 ratio (entry H). Considering the difference between workup protocols A and B, it was initially suspected that the remaining DMSO enhanced the stereoselectivity of the carbonyl reduction of β-D-glycosidulose **4**. Therefore, β-D-glycosidulose **4** was prepared by workup protocol A and the reduction was carried out in 1:1 THF/DMSO solution with tetrabutylammonium borohydride to give the *manno* (**11**) and *gluco* (**9**) isomers in a ratio of 65:35 (entry I). Consequently, the presence of DMSO modestly increased the *manno*-selectivity. It is noteworthy that a similar effect of DMSO on the borohydride reduction of a cyclohexanone was observed, although the nature of the selectivity enhancement by DMSO was not understood.[7] In order to gain an insight into the factors governing the stereoselectivities of reductions in examples shown in entries G and H, the reaction parameters were reconsidered. Acetic anhydride reacts slowly with dimethyl sulfoxide at room temperature to give acetoxydimethylsulfonium acetate ("activated" DMSO).[8] We assumed that acetoxydimethylsulfonium acetate was present in the residue obtained by workup protocol B of the oxidation reaction. This ionic species obviously could not be present in the residue obtained by workup protocol A. In an experiment designed to provide evidence for the effect of "activated" DMSO the mixture of acetic anhydride/methyl sulfoxide (1:2) was kept overnight at room temperature and then co-concentrated with toluene to give presumably a mixture of DMSO and "activated" DMSO. When the reduction of β-D-glycosidulose **4**, prepared by workup protocol A, was carried out in THF solution with tetrabutylammonium borohydride in the presence of DMSO containing "activated" DMSO (procedure 2 for the preparation of **11**), the corresponding *manno*-epimer (**11**) was obtained in a stereoselective manner (entry J). The examples shown in entries G, H, and J clearly reveal that the presence of "activated" DMSO greatly enhanced the *manno*-selectivity of the carbonyl reductions. Procedure 2 is a generally applicable protocol for the stereoselective reduction of β-D-glycosid-2-uloses obtained either by oxidation of the corresponding β-D-glucosides with DMSO/acetic anhydride according to workup protocol B ("activated" DMSO is generated during the oxidation reaction) or by any other route, such as the ulosyl bromide approach.

The preparation and the reduction of β-D-glycosidulose **1**[3e] was undertaken under the conditions used for β-D-gly-

cosidulose **4** shown in entries G, H, and J. These experiments afforded stereochemical results identical with those obtained for ulose **4** (entry K, L, and M). Thus, the yield obtained in the preparation of ethyl (3-*O*-allyl-4,6-*O*-isopropylidene-β-D-mannopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**12**) could be increased from 53% up to 81% (entry C and L). The suitably protected disaccharide-thioglycoside building block **12**, which contains a β-mannosidic linkage, has been successfully applied in the synthesis of complex fucosylated and nonfucosylated core structures of xylose containing carbohydrate chains from *N*-glycoproteins.[3e,9]

In order to establish the stereochemical outcome of the carbonyl reduction in the absence of the 4,6-*O*-acetal function both in the presence and absence of "activated" DMSO, the preparation of β-D-glycosidulose **13** was carried out according to the procedure described for compound **4**. Borohydride reduction of **13**, obtained by workup protocol A, and reduction of **13**, obtained by workup protocol B, provided a stereoselective and a highly *manno*-selective (an essentially stereospecific) course of reduction (entries N and O), respectively. In monosaccharide-uloside cases **2** and **3**, obtained by workup protocol B, carbonyl reductions proceeded in a stereospecific manner (entries P and Q).

Conclusion

New factors governing stereoselectivity in borohydride reductions of β-D-glucoside-2-uloses were observed. The substitution pattern influenced the stereoselectivity of the reduction as follows: the 3-*O*-benzyl and 3-*O*-allyl ethers *vicinal* to the carbonyl to be reduced had a similar influence on the steric outcome of the carbonyl reduction. The presence of a 4,6-*O*-acetal function resulted in lower stereoselectivity in the monosaccharide-uloside cases and low stereoselectivity in the disaccharide-uloside cases, while the absence of a 4,6-*O*-acetal group provided distinctly higher stereoselectivity. A peculiar effect of acetoxydimethylsulfonium acetate ("activated" DMSO) was observed. In all cases, the presence of this species strongly increased the *manno*-selectivity of the reduction even in the presence of a 4,6-*O*-acetal function. A simple, preparatively expedient, generally applicable protocol has been elaborated for achieving high *manno*-selectivities and, hence, satisfactory yields. A systematic study of the nature of the selectivity enhancement by "activated" DMSO is in progress.

Experimental Section

General: Optical rotations were measured with a Perkin−Elmer 241 polarimeter. NMR spectra were recorded with a Bruker WP-200 SY spectrometer for solutions in $CDCl_3$ (internal Me_4Si). The reactions were monitored by TLC on Kieselgel 60 F_{254} (Merck, Darmstadt) with detection by UV light and/or by charring with 50% sulfuric acid. Column chromatography was performed on silica gel 60 (63−200 μm). For HPLC a Hewlett Packard 1090 series II Liquid Chromatograph equipped with a diode array and refractive index detector was used. Mixtures of *gluco*/*manno*-epimers were separated on LiChrosorb Si 0.5 μm column (0.4 × 20 cm) with different (appropriate) ratios of hexane/EtOAc as the mobile phase flowing at a rate of 1 mL min^{-1} at 40 °C. Effluent was monitored at 254 nm for compounds bearing benzyl ethers and by refractive index detector for compounds containing non-UV absorbing protecting groups. Products were identified by using relevant standards. Solvents were HPLC grade.

Methyl 3-*O*-Allyl-4,6-*O*-isopropylidene-β-D-glucopyranoside (5): *p*-Toluenesulfonic acid (100 mg, 0.53 mmol) was added to a stirred suspension of methyl 3-*O*-allyl-β-D-glucopyranoside[5] (1 g, 4.27 mmol) in 2,2-dimethoxypropane (5 mL, 40.66 mmol) at room temperature. The reaction was stopped after 20 min by adding sodium hydrogen carbonate. The mixture was diluted with dichloromethane and the organic layer was washed with water, dried, and concentrated. Column chromatography (6:4 hexane/EtOAc, R_f 0.51) of the syrupy residue afforded **5** (1.08 g, 92%). $[\alpha]_D$ −28.5 (c = 0.34, $CHCl_3$). − ^{1}H NMR ($CDCl_3$): δ = 1.42 and 1.50 (2 × s, each 3 H, CMe_2), 2.73 (br. s, 1 H, OH), 3.26 (m, 1 H, H-5), 3.43 (m, 2 H, H-6_a and H-6_b), 3.56 (s, 3 H, OMe), 3.65 (m, $J_{2,3}$ = 10.0 Hz, 1 H, H-2), 3.78 (dd, $J_{3,4}$ = 10.0 Hz, 1 H, H-3), 3.93 (dd, $J_{4,5}$ = 5.5 Hz, 1 H, H-4), 4.28 (d, $J_{1,2}$ = 7.5 Hz, 1 H, H-1), 4.31 (m, 2 H, CH_2=CH−CH_2O), 5.25 (m, 2 H, CH_2=CH−CH_2O), 5.95 (m, 1 H, CH_2=CH−CH_2O). − ^{13}C NMR ($CDCl_3$): δ = 19.1 and 29.1 (CMe_2), 57.3 (OMe), 62.1 (C-6), 73.3 (CH_2=CH−CH$_2$O), 99.3 (CMe$_2$), 104.2 (C-1), 117.0 (CH$_2$=CH−CH_2O), 135.1 (CH_2=CH−CH_2O). − $C_{13}H_{22}O_6$ (274.14): calcd. C 56.90, H 8.09; found C 56.83, H 8.14.

Methyl 3-*O*-Allyl-4,6-*O*-isopropylidene-β-D-mannopyranoside (6) (Table, entry B): A solution of **5** (750 mg, 2.73 mmol) in 1:2 acetic anhydride/methyl sulfoxide (6 mL) was kept at room temperature for 16 h and then concentrated. The residue was dissolved in dichloromethane and washed with water, dried, and concentrated. The crude 2-ulose and its hydrate **3** were dissolved in 1:1 dichloromethane/methanol (6 mL) and cooled to 0 °C. Sodium borohydride (517 mg, 13.67 mmol) was added to the reaction mixture in one portion. After stirring for 1 h at room temperature, the mixture was diluted with dichloromethane, washed with water, dried, and concentrated. TLC (6:4 hexane/EtOAc) of the residue showed complete disappearance of **3**, traces of **5** (R_f 0.51), and a major product **6** (R_f 0.30). Column chromatography of the residue gave **6** (638 mg, 85%). $[\alpha]_D$ −61.9 (c = 0.27, $CHCl_3$). − ^{1}H NMR ($CDCl_3$): δ = 1.42 and 1.52 (2 × s, each 3 H, CMe_2), 2.52 (br. s, 1 H, OH), 3.18 (m, 1 H, H-5), 3.47 (dd, $J_{3,4}$ = 9.3 Hz, 1 H, H-3), 3.56 (s, 3 H, OMe), 3.90 (m, 2 H, H-6_a and H-6_b), 4.08 (dd, $J_{4,5}$ = 9.6 Hz, 1 H, H-4), 4.12 (m, $J_{2,3}$ = 3.3 Hz, 1 H, H-2), 4.22 (m, 2 H, CH_2=CH−CH_2O), 4.41 (d, $J_{1,2}$ < 1 Hz, 1 H, H-1), 5.25 (m, 2 H, CH_2=CH−CH_2O), 5.92 (m, 1 H, CH_2=CH−CH_2O). − ^{13}C NMR ($CDCl_3$): δ = 19.2 and 29.2 (CMe_2), 57.2 (OMe), 62.1 (C-6), 71.3 (CH_2=CH−CH$_2$O), 99.7 (CMe$_2$), 101.4 (C-1), 117.4 (CH$_2$=CH−CH_2O), 134.7 (CH_2=CH−CH_2O). − $C_{13}H_{22}O_6$ (274.14): calcd. C 56.90, H 8.09; found C 56.94, H 8.11.

Ethyl (2,4,6-Tri-*O*-acetyl-3-*O*-benzyl-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (7): A solution of ethyl 3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside[3f] (720 mg, 1.35 mmol) and 2,4,6-tri-*O*-acetyl-3-*O*-benzyl-α-D-glucopyranosyl bromide[6] (1.86 g, 4.05 mmol) in dichloromethane (13 mL) containing powdered 4A molecular sieves (3 g) was stirred for 30 min under argon. A solution of silver triflate (1.40 g, 5.44 mmol) in toluene (33 mL) was added dropwise in the dark during 1.5 h at −45 °C and stirring was continued for 1 h at −40 °C. Pyridine (2 mL) was added and

the mixture was diluted with dichloromethane, filtered through Celite, washed with aq 10% sodium thiosulfate and water, dried, filtered, and concentrated. Column chromatography (95:5 dichloromethane/acetone, R_f 0.69) of the residue afforded **7**, isolated as a syrup (1.02 g, 83%). $[\alpha]_D$ +16.2 (c = 0.32, $CHCl_3$). – ^{1}H NMR ($CDCl_3$): δ = 1.16 (t, 3 H, CH_3CH$_2$S), 1.97 (s, 6 H, 2 × OAc), 1.98 (s, 3 H, OAc), 2.62 (m, 2 H, CH$_3$CH_2S), 4.59 (d, $J_{1',2'}$ = 8.8 Hz, 1 H, H-1′), 5.20 (d, $J_{1,2}$ = 10.2 Hz, 1 H, H-1), 6.79–7.80 (m, 19 H, 3 Ph and Phth). – ^{13}C NMR ($CDCl_3$): δ = 14.8 (CH_3CH$_2$S), 20.5, 20.6 and 20.8 (3 × COCH_3), 23.8 (CH$_3$CH_2S), 54.7 (C-2), 81.04 (C-1), 100.3 (C-1′), 167.4–170.6 (COCH$_3$ and COPhth). – $C_{49}H_{53}O_{14}NS$ (911.32): calcd. C 64.52, H 5.86; found C 64.60, H 5.81.

Ethyl (3-*O*-Benzyl-4,6-*O*-isopropylidene-β-D-glucopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (9): A solution of **7** (790 mg, 0.87 mmol) and sodium methoxide (94 mg, 1.74 mmol) in methanol (5 mL) was stirred overnight. The solution was neutralised with Amberlite IR-120 (H^+) resin, filtered, concentrated, and dichloromethane (2 × 10 mL) was evaporated from the residue to afford amorphous **8**. To a solution of **8** (595 mg, 0.76 mmol) in 2,2-dimethoxypropane (8 mL, 65.1 mmol) was added *p*-toluenesulfonic acid monohydrate (50 mg, 0.26 mmol). After 30 min, solid sodium bicarbonate was added. The mixture was diluted with dichloromethane, washed with water, dried, filtered, and concentrated. Column chromatography (6:4 hexane/EtOAc) of the residue gave **9** (580 mg, 81% for two steps). $[\alpha]_D$ +44.3 (c = 0.29, $CHCl_3$). – ^{1}H NMR ($CDCl_3$): δ = 1.16 (t, 3 H, CH_3CH$_2$S), 1.39 and 1.40 (2 × s, each 3 H, CMe$_2$), 2.63 (m, 2 H, CH$_3$CH_2S), 4.59 (d, $J_{1',2'}$ = 7.5 Hz, 1 H, H-1′), 5.20 (d, $J_{1,2}$ = 10.0 Hz, 1 H, H-1), 6.85–7.79 (m, 19 H, 3 Ph and Phth). – ^{13}C NMR ($CDCl_3$): δ = 14.8 (CH_3CH$_2$S), 23.6 (CH$_3$CH_2S), 19.0 and 29.0 [(CH_3)$_2$C], 54.7 (C-2), 81.0 (C-1), 99.1 (Me$_2$C), 103.3 (C-1′). – $C_{46}H_{51}O_{11}NS$ (825.32): C 66.88, H 6.23; found C 66.81, H 6.19.

Ethyl (3-*O*-Benzyl-4,6-*O*-isopropylidene-β-D-*arabino*-hexopyranosyl-2-ulose)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (4): A solution of **9** (100 mg, 0.12 mmol) in 1:2 acetic anhydride/methyl sulfoxide (3 mL) was kept at room temperature for 16 h.

Workup Protocol A: The reaction mixture was concentrated to dryness under high vacuum (oil pump) and the residue was dissolved in dichloromethane and washed with water, dried, and concentrated to give crude 2′-ulose **4**.

Workup Protocol B: The reaction mixture from the oxidation was co-concentrated with toluene (3 × 5 mL) to give a residue containing crude 2′-ulose **4**.

Ethyl (3-*O*-Benzyl-4,6-*O*-isopropylidene-β-D-mannopyranosyl)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (11):

Procedure 1: To a solution of **4**, obtained by workup protocol A, in dichloromethane (1 mL) was added a solution of sodium borohydride (23 mg, 0.61 mmol) in 2-propanol (1 mL) at 0 °C. After 20 min, TLC (6:4 hexane/EtOAc) showed the absence of **4** and the presence of the *gluco*- (**9**, R_f 0.65) and *manno*- (**11**, R_f 0.35) epimers in the ratio 3:7. The mixture was diluted with dichloromethane, washed with water, dried, filtered, and concentrated. Column chromatography of the residue gave **11** (52 mg, 52%) {$[\alpha]_D$ +34.5 (c = 0.17, $CHCl_3$)} and **9** (36 mg, 36%), partially contaminated with **11**, which was recycled.

Procedure 2: Methyl sulfoxide (2 mL) and acetic anhydride (1 mL) was kept at room temperature for 16 h and then co-concentrated with toluene (3 × 5 mL) to give DMSO containing acetoxydimethylsulfonium acetate ("activated" DMSO). To a solution of **4** (prepared by workup protocol A) in DMSO containing "activated" DMSO (1 mL) and tetrahydrofuran (1 mL) was added tetrabutylammonium borohydride (62 mg, 0.24 mmol) at 0 °C. After 20 min, TLC (6:4 hexane/EtOAc) showed the absence of **4**, and the presence of the *gluco*- (**9**, R_f 0.65) and *manno*- (**11**, R_f 0.35) epimers in a ratio of about 1:9. The mixture was diluted with dichloromethane, washed with water, dried, filtered, and concentrated. HPLC investigation of the residue revealed the *gluco*- (**9**) and *manno*- (**11**) epimers in a ratio of 12:88. Column chromatography of the mixture yielded **11** (80 mg, 80%). – ^{1}H NMR ($CDCl_3$): δ = 1.17 (t, 3 H, CH_3CH$_2$S), 1.40 and 1.43 (2 × s, each 3 H, CMe$_2$), 2.60 (m, 2 H, CH$_3$CH_2S), 4.60 (d, $J_{1',2'}$ < 1 Hz, 1 H, H-1′), 5.22 (d, $J_{1,2}$ = 10.3 Hz, 1 H, H-1), 6.86–7.79 (m, 19 H, 2 Ph and Phth). – ^{13}C NMR ($CDCl_3$): δ = 14.9 (CH_3CH$_2$S), 23.7 (CH$_3$CH_2S), 19.2 and 29.2 [(CH_3)$_2$C], 54.7 (C-2), 62.0 (C-6′), 68.6 (C-6), 81.1 (C-1), 99.5 (Me$_2$C), 100.7 (C-1′). – $C_{46}H_{51}O_{11}NS$ (825.32): C 66.88, H 6.23; found C 66.92, H 6.26.

Table 1. Stereoselectivities in borohydride reductions of β-D-glucoside-2-uloses shown in Figure 1

Entry	β-D-glycoside-2-uloses	Hydride	Solvent	*manno*/*gluco* ratio	β-D-mannoside yield	ref.
A	**2**[a]	$NaBH_4$	MeOH/CH_2Cl_2 (1:1)	>10:1[b]	83%	3d
B	**3**[a]	$NaBH_4$	MeOH/CH_2Cl_2 (1:1)	>10:1[b]	85%	[e]
C	**1**[a]	$NaBH_4$	*i*PrOH/CH_2Cl_2 (2:1)	7:3[b]	53%	3e
D	**4**[a]	$NaBH_4$	*i*PrOH/CH_2Cl_2 (2:1)	7:3[b]	52%	[e]
E	**13**[a]	$NaBH_4$	*i*PrOH/CH_2Cl_2 (2:1)	>10:1[b]	77%	[e]
F	**14**[a]	$NaBH_4$	MeOH/CH_2Cl_2 (2:1)	>50:1	91%	4b
G	**4**[c]	Bu_4NBH_4	THF	91:9[d]	82%[g]	[e]
H	**4**[a]	Bu_4NBH_4	THF	54:46[d]	[f]	[e]
I	**4**[a]	Bu_4NBH_4	THF/DMSO (1:1)	65:35[d]	[f]	[e]
J	**4**[a]	Bu_4NBH_4	THF/′act′ DMSO (1:1)	88:12[d]	80%[g]	[e]
K	**1**[a]	Bu_4NBH_4	THF	55:45[d]	[f]	[e]
L	**1**[c]	Bu_4NBH_4	THF	91:9[d]	81%[g]	[e]
M	**1**[a]	Bu_4NBH_4	THF/′act′ DMSO (1:1)	90:10[d]	79%[g]	[e]
N	**13**[a]	Bu_4NBH_4	THF	81:19[d]	68%[g]	[e]
O	**13**[c]	Bu_4NBH_4	THF	98:2[d]	81%[g]	3f
P	**2**[c]	Bu_4NBH_4	THF	>99:1[d]	91%[g]	[e]
Q	**3**[c]	Bu_4NBH_4	THF	>99:1[d]	93%[g]	[e]

[a] Workup protocol A. – [b] Determined by TLC. – [c] Workup protocol B. – [d] Determined by HPLC. – [e] This paper. – [f] Mixture of *manno*/*gluco* epimers not separated. [g] Calculated from the corresponding *gluco* derivative.

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