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# Preparation of diamino pseudodisaccharide derivatives from 1,6-anhydro-β-D-hexopyranoses via aziridine-ring cleavage

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**Abstract**—Twelve positional isomers of diamino pseudodisaccharide derivatives with gluco–gluco configuration have been prepared using aziridine-ring cleavage of epimino derivatives of 1,6-anhydro-β-D-hexopyranoses of the D-*allo*, D-*manno*, and D-*galacto* configuration by 2-, 3-, and 4-amino derivatives of 1,6-anhydro-β-D-glucopyranose. The N-substitution of the aziridine ring by a 2-nitrobenzenesulfonyl group and ionic-liquid solvent (*N*-methylpyridinium tosylate) was used to obtain cleavage products in high yield (64–93%). The cleavage reactions proceeded according to the Fürst–Plattner rule and only trans-diaxial stereoisomers were formed.


*Keywords:* Ring-opening reactions; Stereospecific synthesis; Aziridines; Nitrobenzenesulfonamides; Ionic-liquid solvent

## 1. Introduction

The term *pseudodisaccharide* covers a wide range of compounds, which structurally resemble common disaccharides. One of the structural type of pseudodisaccharides has two coupled monosaccharide units in which the linkage (usually etheric, thio, or imino linkage) does not interconnect anomeric carbon atoms. These compounds cannot be hydrolyzed to monosaccharides by enzymatic action and thus can act as enzyme inhibitors (glycosidases and glycosyltransferases). There are some examples in the literature of the preparation of isomeric pseudodisaccharides for studies of their use as glycosidase inhibitors, such as those based on D-glucose[1] that inhibit threhalase and others, which inhibit glucosidase,[2] mannosidase,[3] and galactosidase.[4,5] Whereas the diversity of pseudodisaccharide molecules is great due to positional and configurational isomerism, synthetic methods for their preparation are rather limited because glycosidation procedures cannot be applied. General methods for the formation of etheric, thio, or imino linkages, such as nucleophilic substitution, small-ring opening, or addition to an activated double bond, applied to pseudodisaccharide synthesis mostly result in mixtures of products and tedious separation has to be performed.

Recently, we published a series of papers[6,12,21,22] dealing with reactivity and stereoselectivity in nucleophilic cleavage reactions of sugar aziridines based on 1,6-anhydrohexoses. We elaborated reaction conditions for aziridine-ring cleavage to obtain only one isomer of the cleavage product with well-defined and predictable stereochemistry. By the aziridine-ring-opening protocol applied to sugar aziridines and sugar nucleophiles, a structural series of pseudodisaccharides could be produced. In this paper, we use cleavage reactions of four 1,6-anhydro-epimino-hexoses with three amino-1,6-anhydro-glucoses for the preparation of 12 isomeric pseudodisaccharide derivatives.

## 2. Results and discussion

The starting nosylepimines **1**–**4** (Fig. 1), were prepared from suitably substituted 1,6-anhydrohexoses (possessing OTs, $N_3$, and OBn groups on the tetrahydropyran

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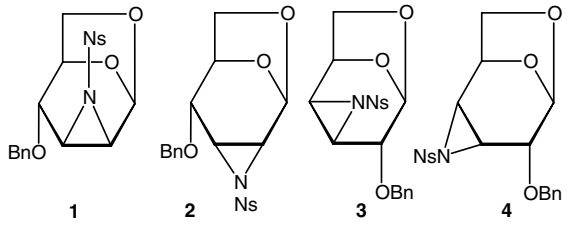



**Figure 1.** Epimino derivatives of 1,6-anhydro-β-D-hexopyranoses **1**–**4** used for aziridine-ring cleavage (Ns = 2-nitrobenzenesulfonyl).

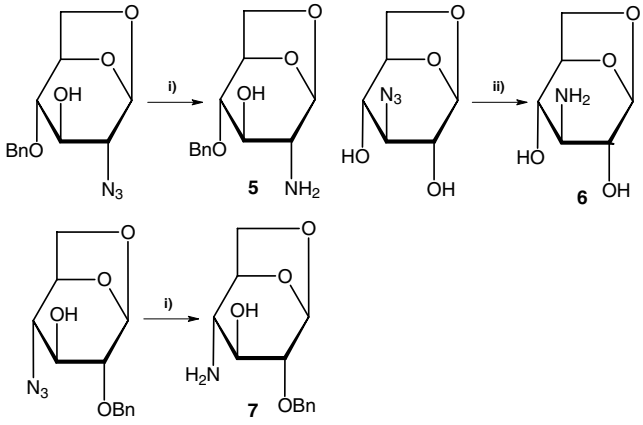
ring) by sodium borohydride (compounds **2**, **3**, and **4**—Refs. 6 and 7) or lithium aluminum hydride (compound **1**—Refs. 6 and 8) reduction. Subsequent N-nosylation using 2-nitrobenzenesulfonyl chloride in a triethylamine–tetrahydrofuran mixture at −40 °C afforded[6,7] the mentioned *N*-nosylepimino derivatives **1**–**4**.

The sugar nucleophiles, 2-amino-1,6-anhydro-4-*O*-benzyl-2-deoxy- and 4-amino-1,6-anhydro-2-*O*-benzyl-4-deoxy-β-D-glucopyranose (**5** and **7**), were prepared by reduction of the corresponding azido derivatives by $NaBH_4$ in THF/MeOH. 3-Amino-1,6-anhydro-3-deoxy-β-D-glucopyranose (**6**) was prepared by hydrogenation of the corresponding azido derivative over 10% palladium-on-charcoal catalyst (Scheme 1). In comparison with previous preparation of derivatives **5**–**7** (compound **5**—Ref. 9, compound **6**—Ref. 10, compound **7**—Ref. 11), our preparative approach gave better yields.

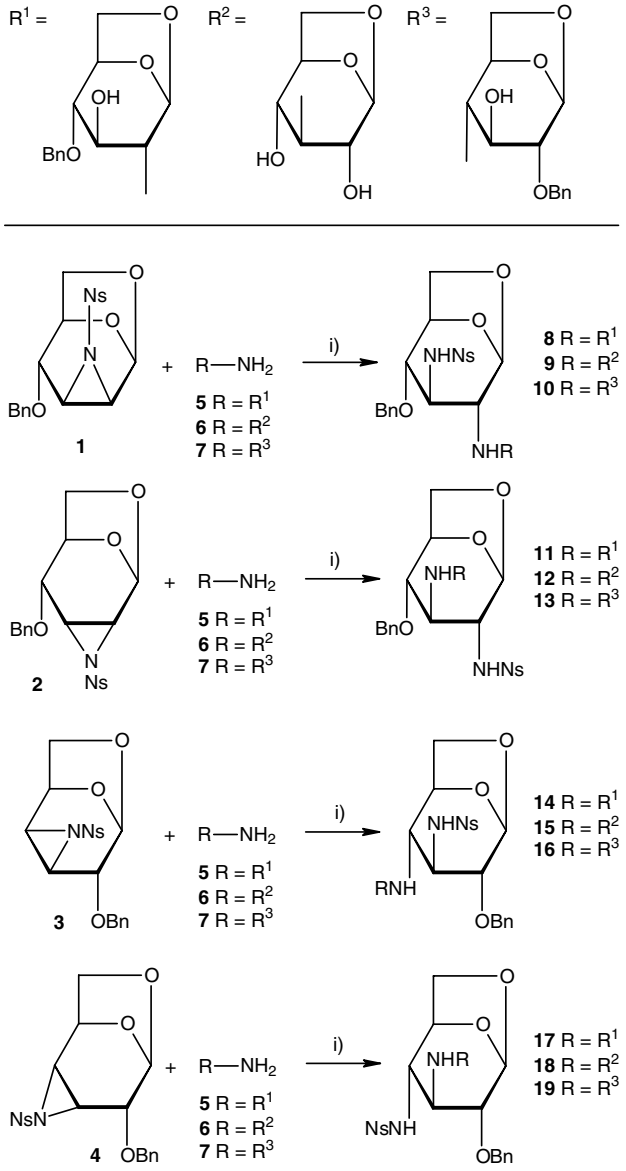
The aziridine-ring cleavage of molten reactants at 160 °C under argon atmosphere gave only 25–39% yields. Cleavage reactions performed in common solvents such as ethanol or dimethylformamide led to the decomposition of nosyl epimines (loss of nosyl group or rearrangement of the epimine to a hexenopyranose[12]). However, we found that the reaction could be performed at lower temperature 100–120 °C if *N*-methylpyridinium tosylate in 50% (w/w) was used as an ionic-liquid environment. Under these reaction conditions, pseudodisaccharides **8**–**19** were obtained in the yields 93%, 76%, 86%, 75%, 66%, 80%, 64%, 82%, 67%, 82%, 68%, and 89% (see Scheme 2).

The cleavage reactions produced the isomers with trans-diaxial disposition of the introduced amino group and the sulfonamido group only; no diequatorial isomers were detected in the reaction mixtures. Therefore we can conclude that in all cases, the cleavage of the aziridine ring proceeded stereochemically in accordance with the Fürst–Plattner rule[13] prediction (trans-diaxial aziridine-ring cleavage).

The structure of derivatives **8**–**19** was determined by $^1H$ and $^{13}C$ NMR spectroscopies (for NMR data—see Tables 1–3). Structure assignment of protons and carbons inside each 1,6-anhydrohexose unit was achieved




**Scheme 1.** Preparation of sugar nucleophiles **5**–**7**. Reagents and conditions: (i) 1. $NaBH_4$/THF, rt, 2. MeOH, reflux, **5**—79%, **7**—68%; (ii) $H_2$, 10% Pd/C, MeOH, rt, 91%.




**Scheme 2.** Reactions of 2,3-*manno*-, 2,3-*allo*-, 3,4-*galacto*, and 3,4-*allo*-epimine **1**–**4** with 2-, 3-, and 4-amino derivatives **5**, **6**, and **7**. Reagent and condition: (i) *N*-methylpyridinium tosylate, 115–120 °C.

**Table 1.** $^1$H NMR chemical shifts of compounds **8**–**19** in $CDCl_3$

| Compound | H-1 | H-2 | H-3 | H-4 | H-5 | H-6$_{endo}$ | H-6$_{exo}$ | Other protons |
|---|---|---|---|---|---|---|---|---|
| **8** | 5.42 t<br>5.02 m | 2.53 m<br>2.21 br | 3.74 m<br>3.55 m | 3.50 m<br>3.25 dd | 4.50 m<br>4.50 m | 4.08 dd<br>3.86 dd | 3.70 dd<br>3.62 dd | 2 × OBn: 4.71 d + 4.61 d, 4.60 d + 4.56 d, 7.27–7.38 m (10H); NH–Ns: 6.17 d, 8.08 m, 7.83 m, 7.68 m (2H); OH: 2.35 d |
| **9** | 5.45 t<br>5.22 t | 2.57 q<br>3.20 m | 3.77 br d<br>2.41 m | 3.56 br s<br>3.10 m | 4.55 dt<br>4.33 m | 4.14 dd<br>3.97 dd | 3.74 dd<br>3.56 dd | OBn: 4.66 s (2H), 7.32–7.41 (5H); NH–Ns: 6.20 br d, 8.12 m, 7.85 m, 7.73 m (2H); OH + NH: 2.70 br + 2.30 br |
| **10** | 5.49 t<br>5.32 br s | 2.53 br s<br>3.08 dd | 3.82 m<br>3.39 m | 3.53 q<br>2.11 dd | 4.53 dt<br>4.15 br d | 4.10 dd<br>3.38 dd | 3.72 dd<br>3.46 dd | 2 × OBn: 4.68 d + 4.62 d, 4.55 s (2H), 7.29–7.37 m (10H); NH–Ns: 6.11 br d, 8.06 dd, 7.82 dd, 7.69 dt, 7.61 dt; OH + NH: 2.33 br d, 2.19 br s |
| **11**[a] | 5.28 t<br>5.24 t | 3.58 m<br>2.52 m | 2.91 p<br>3.68 m | 3.17 m<br>3.36 m | 4.50 m<br>4.59 m | 4.16 dd<br>4.06 dd | 3.57 dd<br>3.72 dd | 2 × OBn: 4.63 d + 4.55 d, 4.48 d + 4.42 d, 7.25–7.36 m (10H); NH–Ns: 8.17 dd, 7.79 dt, 7.75 dd, 7.72 dt |
| **12** | 5.34 br s<br>5.34 br s | 3.58 m<br>3.16 q | 2.85 p<br>2.68 p | 3.24 q<br>3.46 q | 4.57 m<br>4.49 m | 4.07 dd<br>4.03 dd | 3.69 dd<br>3.68 dd | OBn: 4.55 d + 4.46 d, 7.26–7.36 (5H); NH–Ns: 6.53 br, 8.16 m, 7.75 m (2H), 7.69 m |
| **13** | 5.11 t<br>5.45 t | 3.61 m<br>3.32 t | 2.88 p<br>3.79 m | 3.25 m<br>2.40 m | 4.55 m<br>4.30 br d | 4.34 dd<br>4.03 dd | 3.62 dd<br>3.64 dd | 2 × OBn: 4.79 d + 4.67 d, 4.60 d + 4.54 d, 7.29–7.41 m (10H); NH–Ns: 6.36 br s, 7.86 dd, 7.75 dd, 7.65 dt, 7.60 dt; NH + OH: 2.34 br s |
| **14** | 5.39 t<br>5.35 t | 3.16 q<br>2.73 m | 3.78 m<br>3.71 m | 2.81 m<br>3.38 dd | 4.54 m<br>4.54 m | 4.12 dd<br>3.92 dd | 3.73 dd<br>3.69 dd | 2 × OBn: 4.66 d + 4.57 d, 4.37 d + 4.15 d, 7.22–7.36 m (8H), 7.05 m (2H); NH–Ns: 6.03 d, 8.16 m, 7.82 m (2H), 7.70 dt; OH: 2.64 d |
| **15** | 5.39 t<br>5.34 t | 3.17 q<br>3.35 q | 3.69 m<br>3.01 p | 2.84 q<br>3.56 m | 4.49 dt<br>4.54 dt | 4.16 br d<br>4.32 dd | 3.73 dd<br>3.68 dd | OBn: 4.26 d + 4.21 d, 7.26 m (3H), 7.04 m (2H); NH–Ns: 6.05 br, 8.26 dd, 7.84 dd, 7.79 dt, 7.73 dt |
| **16** | 5.39 t<br>5.47 t | 3.11 q<br>3.30 m | 3.76 m<br>3.79 m | 2.85 m<br>2.74 m | 4.45 m<br>4.52 m | 4.13 dd<br>4.06 dd | 3.71 dd<br>3.72 dd | 2 × OBn: 4.61s (2H), 4.32 d + 4.14 d, 7.20–7.36 m (8H), 7.01 m (2H); NH–Ns: 6.06 br d, 8.16 m, 7.83 m, 7.73 m (2H); OH: 2.53 br d |
| **17** | 5.40 t<br>5.12 t | 3.22 q<br>2.49 b | 2.82 m<br>3.72 m | 3.63 m<br>3.38 m | 4.35 dt<br>4.55 dt | 4.32 dd<br>4.03 dd | 3.51 dd<br>3.68 dd | 2 × OBn: 4.66 s (2H), 4.48 d + 4.45 d, 7.24–7.38 m (10H); NH–Ns: 6.52 d, 8.14 dd, 7.76 dd, 7.72 dt, 7.68 dt; OH: 2.56 d; NH: 2.03 br |
| **18**[a] | 5.43 m<br>5.33 t | 3.16 q<br>3.23 q | 2.68 p<br>2.87 p | 3.62 m<br>3.16 q | 4.40 dt<br>4.41 dt | 3.79 dd<br>4.22 dd | 3.60 dd<br>3.64 dd | OBn: 4.54 d + 4.51 d, 7.26–7.36 (5H); NH–Ns: 8.19 dd, 7.82 dd, 7.80 dt, 7.74 dt |
| **19** | 5.33 m<br>5.46 t | 3.04 m<br>3.28 q | 2.87 m<br>3.50 dp | 3.62 m<br>2.57 m | 4.42 dt<br>4.40 dt | 4.54 dd<br>4.11 dd | 3.63 dd<br>3.69 dd | 2 × OBn: 4.53 d + 4.43 d, 4.26 d + 4.22 d, 7.25–7.34 m (8H), 7.11 m (2H); NH–Ns: 6.48 br s, 8.16 dd, 7.74 dd, 7.71 dt, 7.67 dt; NH: 2.14 br d; OH: 2.38 d |

First line for each compound represents parameters of diamino substituted tetrahydropyran ring.
[a] The mixture of $CDCl_3 + CD_3OD$ (9:1) was used due to very low solubility of the sample in $CDCl_3$.

using correlated homonuclear 2D-COSY and heteronuclear $^1$H, $^{13}$C-2D-HMQC spectra. The diamino substituted unit is difficult to recognize from $^1$H NMR spectra, since only the >C*H*–NH– protons are significantly upfield shifted ($\delta$ 2.1–3.0 ppm) while >C*H*–Ns protons appear at $\delta$ 3.5–3.8 ppm together with >C*H*–OR protons, but it can be clearly recognized by two upfield signals in $^{13}$C NMR spectra (>*C*H–NH– at $\delta$ 56.7–60.9 ppm and >*C*H–Ns at $\delta$ 50.8–55.2 ppm).

The gluco configuration of all 1,6-anhydrohexose units in prepared pseudodisaccharides **8**–**19** is confirmed by the observed values of proton–proton coupling constants (vicinal $J_{1,2}$, $J_{2,3}$, $J_{3,4}$, $J_{4,5} \approx 1.3$–2.8 Hz and long-range $J_{1,3}$, $J_{2,4}$, $J_{3,5} \approx 0.5$–1.8 Hz are typical for 1,6-anhydrohexose derivatives with gluco configuration[14–16]). The tetrahydropyran ring in some derivatives adopts the preferred chair form $^1C_4$ common for 1,6-anhydrohexopyranoses[15,17] as it is indicated by small values of $J_{2,3}$ and $J_{3,4}$ constants ($\leqslant$2.4 Hz). For the other derivatives (cf. compounds **8**–**10**, **14**–**15**, **18**), somewhat higher values of $J_{2,3}$, $J_{3,4}$ couplings in the range 2.5–5.1 Hz indicate the presence of certain population of less preferred tetrahydropyran ring conformation (boat form $B_{O,3}$) in a conformational equilibrium. Compounds **16** and **17** have boundary values (2.5–2.95 Hz) for $J_{2,3}$ and $J_{3,4}$ couplings (Fig. 2).

When using the reference values $J_{2,3} \approx J_{3,4} = 1.7$ Hz for $^1C_4$-form and $J_{2,3} \approx J_{3,4} = 8.8$ Hz for $B_{O,3}$-form (calculated from a series of 1,6-anhydro-β-D-glucopyranose derivatives by Grindley et al.[17]) we can estimate the range of the $B_{O,3}$-form population fractions for compounds **8**–**10**, **14**–**15**, **18** as 11–48%.

**Table 2.** $^1$H NMR coupling constants of compounds **8**–**19** in $CDCl_3$

| Compound | $J$(1,2) | $J$(2,3) | $J$(3,4) | $J$(4,5) | $J$(5,6$_{endo}$) | $J$(5,6$_{exo}$) | $J$(6$_{endo}$,6$_{exo}$) | $J$(*gem*) (OBn) | $J$(1,3) | $J$(2,4) | $J$(3,5) | $J$(1,4) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **8** | 1.8 | 1.8 | 2.0 | 1.8 | 0.6 | 5.2 | 8.0 | 12.3 | 1.3 | 1.3 | 1.7 | 0.6 |
| | [a] | 3.1 | 3.4 | 1.7 | 0.8 | 5.2 | 7.5 | 12.2 | 1.2 | 0.9 | [a] | <0.5 |
| **9** | 1.8 | 2.0 | 2.0 | 2.0 | 0.6 | 5.2 | 8.0 | [a] | 0.8 | 1.2 | 1.4 | 0.6 |
| | 1.7 | 2.7 | 3.0 | 1.8 | 1.0 | 5.4 | 7.3 | [a] | 1.1 | 1.0 | 1.4 | ~0.5 |
| **10** | 1.6 | 2.0 | 1.9 | 2.0 | 0.4 | 5.2 | 8.0 | 12.1 | 1.2 | 1.3 | 1.4 | 0.6 |
| | 1.2 | 4.4 | 5.1 | 1.6 | 0.8 | 5.0 | 7.2 | [a] | 0.9 | ~0 | 0.8 | <0.3 |
| **11**[b] | ~1.8 | ~1.0 | ~1.1 | [a] | 0.8 | 5.5 | 7.5 | 11.6 | ~1.8 | ~0.5 | [a] | [a] |
| | ~1.6 | ~1.2 | ~1.2 | [a] | 0.8 | 5.5 | 7.4 | 12.0 | ~1.6 | [a] | ~1.2 | [a] |
| **12** | 1.4 | 1.6 | 1.8 | 1.8 | 0.7 | 5.6 | 7.5 | 12.1 | 1.4 | 1.2 | 1.5 | 0.6 |
| | 1.4 | 2.1 | 2.1 | 1.8 | 0.8 | 5.6 | 7.5 | [a] | 1.2 | 1.0 | 1.8 | <0.3 |
| **13** | 1.7 | ~1.5 | 2.1 | 1.4 | 0.7 | 5.4 | 7.3 | 12.1 | 1.7 | 1.4 | 1.5 | 0.7 |
| | 1.5 | 2.5 | 2.1 | 1.8 | 0.8 | 5.3 | 7.3 | 12.2 | 1.5 | 1.1 | 1.5 | ~0.5 |
| **14** | 1.5 | 2.7 | 2.3 | 1.9 | 0.5 | 5.1 | 8.0 | 12.3 | 1.35 | 1.0 | 1.0 | 0.6 |
| | 1.1 | 4.2 | 4.2 | 1.5 | 0.8 | 5.2 | 7.4 | 12.0 | 1.0 | 0.6 | 1.0 | <0.3 |
| **15** | 2.0 | 2.7 | 3.1 | 1.3 | 0.5 | 4.9 | 7.9 | 12.1 | 1.2 | 1.0 | 1.3 | 0.7 |
| | 1.3 | 3.2 | 3.2 | 1.7 | 0.8 | 5.2 | 7.3 | [a] | 1.2 | 0.9 | 1.3 | 0.4 |
| **16** | 1.6 | 2.95 | 2.5 | 1.6 | <0.5 | 5.1 | 7.9 | 11.8 | 1.2 | 1.0 | 1.3 | 0.5 |
| | 1.7 | 1.8 | 2.0 | 2.1 | 0.9 | 5.6 | 7.2 | [a] | 1.35 | 1.6 | 1.2 | 0.5 |
| **17** | 1.7 | 1.7 | 1.5 | 1.3 | 0.65 | 5.4 | 7.6 | 12.0 | 1.4 | 1.2 | 1.5 | 0.7 |
| | 1.7 | 2.5 | 2.6 | 1.8 | 0.65 | 5.25 | 7.6 | [a] | 1.4 | 1.0 | 1.5 | 0.6 |
| **18**[b] | 2.0 | 2.0 | 2.0 | 2.1 | 0.9 | 5.4 | 7.5 | 12.1 | 1.3 | 1.2 | 1.5 | <0.3 |
| | 1.3 | 3.6 | 3.6 | 1.7 | 0.8 | 5.3 | 7.6 | [a] | 1.0 | 0.8 | 1.1 | <0.5 |
| **19** | 2.2 | 1.8 | 1.8 | 1.8 | 0.8 | 5.3 | 7.4 | 11.7 | 1.7 | 1.6 | 1.8 | 0.7 |
| | 2.1 | 1.7 | 1.7 | 1.7 | 0.9 | 5.5 | 7.2 | 12.0 | 1.3 | 1.0 | 1.6 | 0.8 |

First line for each compound represents parameters of diamino substituted tetrahydropyran ring.
[a] Value of parameter could not be estimated.
[b] The mixture of $CDCl_3$ + $CD_3OD$ (9:1) was used due to very low solubility of the sample in $CDCl_3$.

## 3. Experimental

### 3.1. General remarks

Melting points were determined on a Boëtius melting-point microapparatus and are uncorrected. The optical rotations were measured on an Autopol III (Rudolph Research, Flanders, NJ) polarimeter at 25 °C. The $^1$H and $^{13}$C NMR spectra were measured on a Varian UNITY-500 instrument ($^1$H at 500 MHz and $^{13}$C at 125.7 MHz) in $CDCl_3$ (ref.: TMS for $^1$H and the chloroform signal at $\delta$ 77.0 ppm for $^{13}$C) at 25 °C. The $^1$H, $^1$H-COSY and $^1$H, $^{13}$C-HMQC techniques were used for the structural assignments. TLC was carried out on MERCK DC Alufolien with Kiesegel $F_{254}$ with the following solvent systems: $S_1$ hexane–ethyl acetate—3:2 and $S_2$ ethyl acetate. TLC plates were visualized by UV detection at 254 nm and by an anisaldehyde solution in sulfuric acid. Column chromatography was performed on silica gel 60 MERCK (70–230 mesh ASTM) with hexane–ethyl acetate gradient elution. The solvents were evaporated on a vacuum rotary evaporator at 40 °C. Light petroleum (PE) refers to the 40–60 °C distillation fraction. 2-Nitrobenzenesulfonyl chloride (purity 97%) was purchased from Fluka. *N*-Methylpyridinium tosylate was prepared by mixing of commercially available methyl tosylate with 1.1 equiv of dry pyridine at room temperature and drying of the resulting solid in a vacuum desiccator over $P_2O_5$. All reactions (except hydrogenation) were carried out under argon atmosphere. Solutions and extracts were dried over anhydrous sodium sulfate. Residues from evaporated chromatographic fractions were dried in a desiccator over $P_2O_5$ and then crystallized from the given solvent mixtures. The $^1$H NMR spectral parameters are given in Tables 1 and 2, and those of $^{13}$C NMR spectra are given in Table 3.

### 3.2. 2-Amino-1,6-anhydro-4-*O*-benzyl-2-deoxy-β-D-glucopyranose (5)

1,6-Anhydro-2-azido-4-*O*-benzyl-2-deoxy-β-D-glucopyranose[8] (5.17 g, 18.7 mmol), $NaBH_4$ (1.4 g, 37 mmol), and tetrahydrofuran (50 mL) were mixed and stirred at rt for 44 h. Methanol (20 mL) was added and the mixture was being refluxed for 2 h. After cooling to rt, the solvents were evaporated off and a white solid was partitioned between dichloromethane (50 + 2 × 15 mL) and 10% aqueous NaOH (20 mL). The combined dichloromethane extracts were dried and evaporated. The resi-

**Table 3.** $^{13}C$ NMR chemical shifts of compounds **8**–**19** in $CDCl_3$

| Compound | C-1 | C-2 | C-3 | C-4 | C-5 | C-6 | Other carbons |
|---|---|---|---|---|---|---|---|
| **8** | 102.05<br>102.80 | 58.46<br>60.27 | 52.77<br>70.25 | 76.64<br>78.88 | 74.96<br>74.79 | 65.48<br>66.06 | 2 × OBn: 71.42, 71.10, 137.65, 137.51, 128.47(4), 127.92(2), 127.88(2), 127.77(2);<br>NH–Ns: 147.81, 133.71, 133.66, 132.88, 130.91, 125.54 |
| **9** | 101.86<br>102.31 | 58.37<br>71.04 | 51.96<br>60.65 | 76.78<br>71.80 | 74.58<br>76.70 | 65.53<br>65.66 | OBn: 71.51, 137.14, 127.98(2), 128.64(2), 128.20; NH–Ns: 147.81, 133.88, 133.47,<br>133.10, 130.94, 125.58 |
| **10** | 102.54<br>101.21 | 58.51<br>80.44 | 51.31<br>71.46 | 76.87<br>60.40 | 74.40<br>76.90 | 65.47<br>67.50 | 2 × OBn: 71.86, 71.27, 137.63, 137.29, 128.56(2), 128.48(2), 128.06, 127.94,<br>127.91(4); NH–Ns: 147.85, 133.76, 133.68, 132.86, 131.08, 125.56 |
| **11**[a] | 100.76<br>101.90 | 54.40<br>59.02 | 56.81<br>68.60 | 76.48<br>78.46 | 73.85<br>73.99 | 65.18<br>65.43 | 2 × OBn: 71.29, 70.94, 137.40, 137.10, 128.38(2), 128.36(2), 127.83(2), 127.65(2),<br>127.58(2), NH–Ns: 147.37, 134.74, 133.49, 132.99, 130.11, 125.29 |
| **12** | 101.05<br>102.08 | 54.99<br>70.38 | 57.81<br>61.50 | 76.20<br>70.47 | 73.93<br>76.81 | 65.55<br>65.58 | OBn: 71.16, 137.18, 128.58(2), 128.08, 128.02(2); NH–Ns: 147.49, 135.01, 133.62,<br>133.21, 130.16, 125.41 |
| **13** | 100.67<br>100.37 | 54.91<br>77.54 | 57.65<br>68.34 | 77.31<br>60.01 | 74.11<br>76.50 | 65.53<br>66.44 | 2 × OBn: 71.92, 71.10, 137.69, 137.36, 128.57(2), 128.49(2), 127.98, 127.92(2),<br>127.81, 127.58(2); NH–Ns: 147.52, 135.38, 133.29, 132.91, 129.93, 125.37 |
| **14** | 100.11<br>103.41 | 76.10<br>60.43 | 51.89<br>71.11 | 58.00<br>80.21 | 76.60[a]<br>74.97[a] | 66.33<br>66.61 | 2 × OBn: 71.64, 71.55, 137.86, 136.72, 128.48(2), 128.45(2), 128.05, 127.83,<br>127.78(2), 127.60(2); NH–Ns: 147.82, 133.93, 133.67, 133.03, 131.11, 125.35 |
| **15** | 99.84<br>101.88 | 76.15<br>70.93 | 50.84<br>60.50 | 58.20<br>70.68 | 77.16<br>76.76 | 66.49<br>65.42 | OBn: 71.76, 136.52, 128.50(2), 128.16, 127.53(2); NH–Ns: 147.78, 137.70, 133.95,<br>133.25, 131.29, 125.37 |
| **16** | 100.27<br>101.05 | 75.92<br>78.62 | 52.28<br>69.58 | 57.65<br>59.40 | 76.46<br>76.08 | 66.40<br>67.00 | 2 × OBn: 72.00, 71.55, 137.68, 136.85, 128.47(2), 128.40(2), 127.99, 127.91,<br>127.86(2), 127.49(2); NH–Ns: 147.84, 133.79, 133.73, 132.96, 130.95, 125.43 |
| **17** | 100.17<br>101.68 | 76.22<br>59.81 | 57.19<br>70.26 | 54.93<br>78.31 | 75.76<br>74.69 | 65.59<br>65.82 | 2 × OBn: 71.90, 71.62, 137.46, 137.13, 128.56(2), 128.54(2), 128.07, 128.01,<br>127.95(2), 127.86(2); NH–Ns: 135.52, 147.56, 125.44, 133.00, 133.39, 130.02 |
| **18**[a] | 100.25<br>102.09 | 75.94<br>70.38 | 60.85<br>56.97 | 54.09<br>69.58 | 76.78<br>75.75 | 65.28<br>65.84 | OBn: 71.73, 136.94, 128.46(2), 128.05, 128.00(2); NH–Ns: 134.82, 147.48, 125.32,<br>133.14, 133.57, 130.12 |
| **19** | 99.93<br>99.87 | 76.59<br>77.12 | 56.73<br>67.86 | 55.18<br>58.70 | 75.73<br>77.01 | 65.76<br>66.43 | 2 × OBn: 71.79, 71.72, 137.35, 137.28, 128.52(2), 128.42(2), 128.04, 127.90,<br>127.64(2), 127.59(2); NH–Ns: 135.61, 147.51, 125.41, 133.06, 133.25, 129.99 |

First line for each compound represents parameters of diamino substituted tetrahydropyran ring.
[a] The mixture of $CDCl_3 + CD_3OD$ (9:1) was used due to very low solubility of the sample in $CDCl_3$.

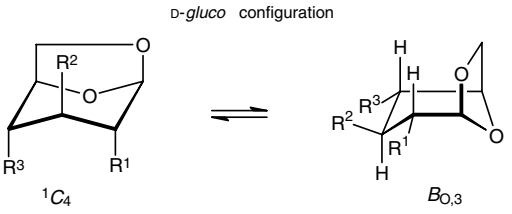



**Figure 2.** Conformational equilibrium of tetrahydropyran ring.

due was crystallized from EtOH–$Et_2O$–PE mixture to afford 3.7 g of **5**. Yield 79%, mp 148–152 °C (lit.[18] mp 151–152 °C). $^1H$ and $^{13}C$ NMR data were the same as described in Ref. 18.

### 3.3. 3-Amino-1,6-anhydro-3-deoxy-β-D-glucopyranose (6)

A mixture of 1,6-anhydro-3-azido-3-deoxy-β-D-glucopyranose[19] (1.8 g, 9.6 mmol), methanol (50 mL), and 10% palladium on charcoal (50 mg) was hydrogenated under atmospheric pressure at rt for 2 h. The catalyst was filtered off with suction and washed with 5% (w/v) $NH_3$ solution in methanol (50 mL). The combined filtrates were evaporated and dried in a vacuum desiccator over $P_2O_5$ for 2 h. The residue was crystallized from EtOH–$Et_2O$ mixture to afford 1.4 g (91%). Physical constants and $^1H$ and $^{13}C$ NMR data matched that reported.[10]

### 3.4. 4-Amino-1,6-anhydro-2-*O*-benzyl-4-deoxy-β-D-glucopyranose (7)

1,6-Anhydro-4-azido-2-*O*-benzyl-4-deoxy-β-D-glucopyranose[20] (3.5 g, 12.6 mmol), $NaBH_4$ (1.0 g, 26 mmol), and tetrahydrofuran (40 mL) were mixed and stirred at rt for 21 h. Methanol (10 mL) was added and the mixture was being refluxed for 2 h. After cooling to rt, the solvents were evaporated off and a white solid was partitioned between dichloromethane ($50 + 2 \times 15$ mL) and 10% aqueous NaOH (20 mL). The combined dichloromethane extracts were dried and evaporated. The residue was crystallized from EtOH–$Et_2O$–PE mixture to afford 2.2 g (68%). Physical constants and $^1H$ and $^{13}C$ NMR data matched that reported.[11]

### 3.5. General procedure for aziridine-ring cleavage

A mixture of nosylepimine, aminoglucose, and equal weight amount (50% w/w) of *N*-methylpyridinium tosylate was placed into a silicone oil bath preheated to 130 °C. After melting (ca. 10 min), the temperature

of the bath was lowered and maintained between 115 and 120 °C and the mixture was stirred for the given time. The reaction course was monitored by TLC in $S_1$ (for compounds: **8**, **10**, **11**, **13**, **14**, **16**, **17**, and **19**) or $S_2$ (for compounds: **9**, **12**, **15**, and **18**) solvent system. The mixture was cooled to rt and partitioned between water (5 mL) and EtOAc (5 mL). An additional amount of water (10 mL) was added and the mixture was extracted by dichloromethane (3 × 20 mL). The combined dichloromethane extracts were dried and evaporated. The residue was chromatographed on silica gel (20–30 g, gradient elution from hexane–ethyl acetate 3:2 mixture to pure ethyl acetate) to remove traces of unreacted nosylepimine and to obtain pure pseudodisaccharide derivative. Yields and characterization data are given below for individual compounds.

**3.5.1. 1,6-Anhydro-2-(1,6-anhydro-4-*O*-benzyl-2-deoxy-β-D-glucopyranos-2-ylamino)-4-*O*-benzyl-2,3-dideoxy-3-(2-nitrobenzene-1-sulfonamido)-β-D-glucopyranose (8).** Prepared from nosylepimine **1** (418 mg, 1 mmol), 2-aminoglucose **5** (377 mg, 1.5 mmol), and *N*-methylpyridinium tosylate (800 mg). Reaction time 2 h. Yield 621 mg (93%); mp 70–75 °C (EtOH–$Et_2O$–PE); $[\alpha]_D$ −55 (*c* 0.28 $CHCl_3$). Anal. Calcd for $C_{32}H_{35}N_3O_{11}S$: C, 57.39; H, 5.27; N, 6.27; S, 4.79. Found: C, 56.99; H, 5.26; N, 5.98; S, 5.13.

**3.5.2. 1,6-Anhydro-2-(1,6-anhydro-3-deoxy-β-D-glucopyranos-3-ylamino)-4-*O*-benzyl-2,3-dideoxy-3-(2-nitrobenzene-1-sulfonamido)-β-D-glucopyranose (9).** Prepared from nosylepimine **1** (418 mg, 1 mmol), 3-aminoglucose **6** (200 mg, 1.2 mmol), and *N*-methylpyridinium tosylate (600 mg). Reaction time 90 min. Yield 440 mg (76%); mp 156–157 °C (EtOAc–$Et_2O$–PE); $[\alpha]_D$ −89 (*c* 0.29 $CHCl_3$). Anal. Calcd for $C_{25}H_{29}N_3O_{11}S$: C, 51.81; H, 5.04; N, 7.25; S, 5.53. Found: C, 51.72; H, 4.98; N, 6.99; S, 5.54.

**3.5.3. 1,6-Anhydro-2-(1,6-anhydro-2-*O*-benzyl-4-deoxy-β-D-glucopyranos-4-ylamino)-4-*O*-benzyl-2,3-dideoxy-3-(2-nitrobenzene-1-sulfonamido)-β-D-glucopyranose (10).** Prepared from nosylepimine **1** (418 mg, 1 mmol), 4-aminoglucose **7** (377 mg, 1.5 mmol), and *N*-methylpyridinium tosylate (800 mg). Reaction time 2 h. Yield 574 mg (86%); mp 72–75 °C (EtOH–$Et_2O$–PE); $[\alpha]_D$ −65 (*c* 0.3 $CHCl_3$). Anal. Calcd for $C_{32}H_{35}N_3O_{11}S$: C, 57.39; H, 5.27; N, 6.27; S, 4.79. Found: C, 57.37; H, 5.20; N, 6.04; S, 4.93.

**3.5.4. 1,6-Anhydro-3-(1,6-anhydro-4-*O*-benzyl-2-deoxy-β-D-glucopyranos-2-ylamino)-4-*O*-benzyl-2,3-dideoxy-2-(2-nitrobenzene-1-sulfonamido)-β-D-glucopyranose (11).** Prepared from nosylepimine **2** (418 mg, 1 mmol), 2-aminoglucose **5** (377 mg, 1.5 mmol), and *N*-methylpyridinium tosylate (800 mg). Reaction time 2 h. Yield 499 mg (75%); mp 191–192 °C (EtOH–$Et_2O$–PE); $[\alpha]_D$ −38 (*c* 0.33 $CHCl_3$). Anal. Calcd for $C_{32}H_{35}N_3O_{11}S$: C, 57.39; H, 5.27; N, 6.27; S, 4.79. Found C, 57.29; H, 5.15; N, 6.06; S, 5.06.

**3.5.5. 1,6-Anhydro-3-(1,6-anhydro-3-deoxy-β-D-glucopyranos-3-ylamino)-4-*O*-benzyl-2,3-dideoxy-2-(2-nitrobenzene-1-sulfonamido)-β-D-glucopyranose (12).** Prepared from nosylepimine **2** (418 mg, 1 mmol), 3-aminoglucose **6** (200 mg, 1.2 mmol), and *N*-methylpyridinium tosylate (600 mg). Reaction time 105 min. Yield 381 mg (66%); mp 75–79 °C (EtOAc–$Et_2O$–PE); $[\alpha]_D$ −56 (*c* 0.25 $CHCl_3$). Anal. Calcd for $C_{25}H_{29}N_3O_{11}S$: C, 51.81; H, 5.04; N, 7.25; S, 5.53. Found C, 51.45; H, 5.03; N, 6.93; S, 5.36.

**3.5.6. 1,6-Anhydro-3-(1,6-anhydro-2-*O*-benzyl-4-deoxy-β-D-glucopyranos-4-ylamino)-4-*O*-benzyl-2,3-dideoxy-2-(2-nitrobenzene-1-sulfonamido)-β-D-glucopyranose (13).** Prepared from nosylepimine **2** (418 mg, 1 mmol), 4-aminoglucose **7** (377 mg, 1.5 mmol), and *N*-methylpyridinium tosylate (800 mg). Reaction time 2 h. Yield 538 mg (80%); mp 65–68 °C (EtOH–$Et_2O$–PE); $[\alpha]_D$ 16 (*c* 0.23 $CHCl_3$). Anal. Calcd for $C_{32}H_{35}N_3O_{11}S$: C, 57.39; H, 5.27; N, 6.27; S, 4.79. Found C, 57.29; H, 5.33; N, 5.88; S, 4.78.

**3.5.7. 1,6-Anhydro-4-(1,6-anhydro-4-*O*-benzyl-2-deoxy-β-D-glucopyranos-2-ylamino)-2-*O*-benzyl-3,4-dideoxy-3-(2-nitrobenzene-1-sulfonamido)-β-D-glucopyranose (14).** Prepared from nosylepimine **3** (418 mg, 1 mmol), 2-aminoglucose **5** (377 mg, 1.5 mmol), and *N*-methylpyridinium tosylate (800 mg). Reaction time 2 h. Yield 428 mg (64%); mp 169–170 °C (EtOAc–$Et_2O$–PE); $[\alpha]_D$ −87 (*c* 0.26 $CHCl_3$). Anal. Calcd for $C_{32}H_{35}N_3O_{11}S$: C, 57.39; H, 5.27; N, 6.27; S, 4.79. Found C, 57.04; H, 5.33; N, 5.95; S, 4.74.

**3.5.8. 1,6-Anhydro-4-(1,6-anhydro-3-deoxy-β-D-glucopyranos-3-ylamino)-2-*O*-benzyl-3,4-dideoxy-3-(2-nitrobenzene-1-sulfonamido)-β-D-glucopyranose (15).** Prepared from nosylepimine **3** (418 mg, 1 mmol), 3-aminoglucose **6** (200 mg, 1.2 mmol), and *N*-methylpyridinium tosylate (600 mg). Reaction time 2 h. Yield 476 mg (82%, after crystallization 315 mg, 54%); mp 80–85 °C (EtOAc–$Et_2O$–PE); $[\alpha]_D$ −93 (*c* 0.26 $CHCl_3$). Anal. Calcd for $C_{25}H_{29}N_3O_{11}S$: C, 51.81; H, 5.04; N, 7.25; S, 5.53. Found C, 51.73; H, 5.13; N, 6.95; S, 5.76.

**3.5.9. 1,6-Anhydro-4-(1,6-anhydro-2-*O*-benzyl-4-deoxy-β-D-glucopyranos-4-ylamino)-2-*O*-benzyl-3,4-dideoxy-3-(2-nitrobenzene-1-sulfonamido)-β-D-glucopyranose (16).** Prepared from nosylepimine **3** (418 mg, 1 mmol), 4-aminoglucose **7** (377 mg, 1.5 mmol), and *N*-methylpyridinium tosylate (800 mg). Reaction time 2 h. Yield 450 mg (67%); mp 72–76 °C (EtOH–$Et_2O$–PE); $[\alpha]_D$

−106 (*c* 0.29 $CHCl_3$). Anal. Calcd for $C_{32}H_{35}N_3O_{11}S$: C, 57.39; H, 5.27; N, 6.27; S, 4.79. Found C, 57.27; H, 5.13; N, 6.03; S, 4.83.

**3.5.10. 1,6-Anhydro-3-(1,6-anhydro-4-*O*-benzyl-2-deoxy-β-D-glucopyranos-2-ylamino)-2-*O*-benzyl-3,4-dideoxy-4-(2-nitrobenzene-1-sulfonamido)-β-D-glucopyranose (17).** Prepared from nosylepimine **4** (418 mg, 1 mmol), 2-aminoglucose **5** (377 mg, 1.5 mmol), and *N*-methylpyridinium tosylate (800 mg). Reaction time 1 h 45 min. Yield 549 mg (82%); mp 69–72 °C (EtOH–$Et_2O$–PE); $[\alpha]_D$ −19 (*c* 0.29 $CHCl_3$). Anal. Calcd for $C_{32}H_{35}N_3O_{11}S$: C, 57.39; H, 5.27; N, 6.27; S, 4.79. Found C, 57.03; H, 5.26; N, 6.00; S, 4.91.

**3.5.11. 1,6-Anhydro-3-(1,6-anhydro-3-deoxy-β-D-glucopyranos-3-ylamino)-2-*O*-benzyl-3,4-dideoxy-4-(2-nitrobenzene-1-sulfonamido)-β-D-glucopyranose (18).** Prepared from nosylepimine **4** (418 mg, 1 mmol), 3-aminoglucose **6** (180 mg, 1.12 mmol), and *N*-methylpyridinium tosylate (600 mg). Reaction time 90 min. Yield 391 mg (68%); mp 156–159 °C (EtOAc–$Et_2O$–PE); $[\alpha]_D$ −36 (*c* 0.35 $CHCl_3$). Anal. Calcd for $C_{25}H_{29}N_3O_{11}S$: C, 51.81; H, 5.04; N, 7.25; S, 5.53. Found C, 51.81; H, 5.00; N, 7.10; S, 5.58.

**3.5.12. 1,6-Anhydro-3-(1,6-anhydro-2-*O*-benzyl-4-deoxy-β-D-glucopyranos-4-ylamino)-2-*O*-benzyl-3,4-dideoxy-4-(2-nitrobenzene-1-sulfonamido)-β-D-glucopyranose (19).** Prepared from nosylepimine **4** (418 mg, 1 mmol), 4-aminoglucose **7** (377 mg, 1.5 mmol), and *N*-methylpyridinium tosylate (800 mg). Reaction time 2 h. Yield 598 mg (89%); mp 70–72 °C (EtOH–$Et_2O$–PE); $[\alpha]_D$ 3 (*c* 0.44 $CHCl_3$). Anal. Calcd for $C_{32}H_{35}N_3O_{11}S$: C, 57.39; H, 5.27; N, 6.27; S, 4.79. Found C, 57.11; H, 5.36; N, 6.02; S, 4.74.

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## References

1. Ogawa, S.; Yokoi, S.; Kimura, N.; Shibata, Y.; Chida, N. *Carbohydr. Res.* **1988**, *181*, 57–66.
2. Carvalho, I.; Haines, A. H. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1795–1800.
3. Blériot, Y.; Dintinger, T.; Guillo, N.; Tellier, C. *Tetrahedron Lett.* **1995**, *36*, 5175–5178.
4. Saotome, C.; Kanie, Y.; Kanie, O.; Wong, C. H. *Bioorg. Med. Chem.* **2000**, *8*, 2249–2261.
5. Vonhoff, S.; Heightman, T. D.; Vasella, A. *Helv. Chim. Acta* **1998**, *81*, 1710–1725.
6. Kroutil, J.; Karban, J.; Buděšínský, M. *Carbohydr. Res.* **2003**, *338*, 2825–2833.
7. Kroutil, J.; Karban, J. *Carbohydr. Res.* **2005**, *340*, 503–506.
8. Karban, J.; Buděšínský, M.; Černý, M.; Trnka, T. *Collect. Czech. Chem. Commun.* **2001**, *66*, 799–819.
9. Nagy, L.; Yamaguchi, T.; Mitsunaga, T.; Wakita, H.; Jezowska-Bojczuk, M.; Nomura, M.; Kozlowski, H. *Ach-Models Chem.* **1998**, *135*, 941–951.
10. Trnka, T.; Černý, M.; Buděšínský, M.; Pacák, J. *Collect. Czech. Chem. Commun.* **1975**, *40*, 3038–3045.
11. Černý, M.; Černý, I.; Pacák, J. *Collect. Czech. Chem. Commun.* **1976**, *41*, 2942–2951.
12. Kroutil, J.; Karban, J.; Trnka, T.; Buděšínský, M.; Černý, M. *Collect. Czech. Chem. Commun.* **2002**, *67*, 1805–1819.
13. Fürst, A.; Plattner, P. A. *Abstracts of Papers*, 12th International Congress on Pure Applied Chemistry, New York, 1951; p 409.
14. Buděšínský, M.; Trnka, T.; Černý, M. *Collect. Czech. Chem. Commun.* **1979**, *44*, 1949–1964.
15. Černý, M.; Staněk, J. *Adv. Carbohydr. Chem. Biochem.* **1977**, *34*, 23–177.
16. Heyns, K.; Weyer, J. *Liebigs Ann. Chem.* **1968**, *718*, 224–234.
17. Grindley, T. B.; Cude, A.; Kralovic, J.; Thangarasa, R. In *Frontiers in Biomedicine and Biotechnology. Levoglucosenone and Levoglucosans, Chemistry and Applications*; ATL Press: New York, 1994; pp 147–164.
18. Černý, M.; Juláková, O.; Pacák, J.; Buděšínský, M. *Collect. Czech. Chem. Commun.* **1975**, *40*, 2116–2119.
19. Paulsen, H.; Koebernick, H.; Stenzel, W.; Köll, P. *Tetrahedron Lett.* **1975**, *16*, 1493–1494.
20. van der Klein, P. A. M.; Filemon, W.; Veeneman, G. H.; van der Marel, G. A.; van Boom, J. H. *J. Carbohydr. Chem.* **1992**, *11*, 837–848.
21. Kroutil, J.; Trnka, T.; Buděšínský, M.; Černý, M. *Eur. J. Org. Chem.* **2002**, *2002*, 2449–2459.
22. Kroutil, J.; Jeništová, J. *Collect. Czech. Chem. Commun.* **2005**, *70*, 2075–2085.