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Synthesis of Anomerically Pure, Furanose-Free α-Benzyl-2-amino-2-deoxy-d-altro- and d-manno-pyranosides and Some of Their Derivatives

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Synthesis of Anomerically Pure, Furanose-Free α-Benzyl-2-amino-2-deoxy-D-altro- and D-manno-pyranosides and Some of Their Derivatives

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Abstract: The anomerically pure benzyl α-D-glycoside of 2-amino-2-deoxy-mannopyranoside was synthesized from D-glucopyranose *via* 2-amino-2-deoxy-D-altrose intermediates. Unlike the direct synthesis from mannosamine in the literature, our method provides furanose-free products. A new method for the preparation of *cis*-2,3-oxazolidinones of 2-amino-2-deoxy-sugars was developed. A selective removal of the glycosidic benzyl group in the presence of 4,6-*O*-benzylidene protection was developed, which may provide new routes for the synthesis of oligosaccharides. Furanose-free derivatives of α-benzyl-2-amino-2-deoxy-mannopyranuronic acids synthesized here offered possibilities for direct comparisons to prior literature preparations.

Keywords: altrosamine, mannosamine, mannosaminuronic acid, oxazolidinone

1 INTRODUCTION

Aminosugars constitute abundant building blocks of naturally occurring polysaccharides or antibiotics and are frequently found in the cell walls of bacteria.[1–12] The most frequently found aminosugars are members of the class of 2-amino-2-deoxy-D-hexoses. *N*-Acetyl-D-glucosamine, for example,

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is a major constituent of biologically important polysaccharides such as hyaluronic acid,[13] heparin/heparan,[14,15] and keratan sulfate[16,17] and is the anchor for *N*-linked glycans in many glycoproteins. *N*-Acetyl-D-galactosamine can be found in the chondroitin sulfate family,[17,18] in dermatan sulfate,[18,19] and as the *O*-glycosidically linked unit in many glycosylated proteins. It has been shown that metabolic pathways of *N*-acetyl-D-glucosamine and *N*-acetyl-D-mannosamine can be exploited for cell surface engineering.[20–23] Altered cell surface oligosaccharides thus offer a way for the study of cell–cell interactions. For such studies to be meaningful, it is important to have well-characterized simple carbohydrate building blocks and synthetic strategies in hand. The syntheses of 2-amino-2-deoxy-mannopyranosides can be accomplished from 2-acetamido-2-deoxy-mannopyranoside directly;[24,25] however, these syntheses suffer from the labor-intensive preparation of the starting material,[26] anomeric mixtures, and furanosidic by-products.[24] Syntheses of altropyranosides pose special problems because of the propensity of this configuration to form 1,6-anhydro sugars.[27]

In this article, we report the synthesis of *anomerically pure, furanose-free* 2-amino-2-deoxy-pyranose derivatives of D-altrose and D-mannose starting from inexpensive D-glucose. The protected mannosamines were subsequently converted into 2,3-oxazolidinones and 2-amino-2-deoxy-mannopyranuronic acids. All structures were confirmed by ^{1}H, ^{13}C, ^{1}H-^{1}H COSY, and ^{1}H-^{13}C correlation spectroscopy (COSY) (HETCOR) nuclear magnetic resonance (NMR) spectroscopy. Observed coupling constants were correlated with the molecule's average solution conformation by the Karplus equation.

2 RESULTS AND DISCUSSION

To synthesize benzyl-α-D-glycosides of 2-amino-2-deoxy-mannopyranose (mannosamine) and 2-amino-2-deoxy-mannopyranosido-6-uronic acid (mannosamine uronic acid), we prepared a series of precursors from D-glucose (**1**, Table 1, Scheme 1).

The benzyl glycoside of α-D-glucopyranose (**2**) was prepared by condensation of **1** with benzyl alcohol in the presence of toluenesulfonic acid and was converted in situ into the 4,6-*O*-benzylidene derivative **3** by a standard method.[28]

Because **3** was isolated as a hydrate, we found that the subsequent transformation of **3** into **4**, which was similar to the methyl glucoside analog,[29] significantly improved yields upon recrystallization and azeotropic drying of the starting material prior to treatment with methanesulfonyl chloride in pyridine. We subsequently converted the dimesylate into epoxide **5** with *allo*-configuration analogously to a published method for the methyl glucoside[28] with slight modifications. We found that CH_2Cl_2 and dioxane not only have equally good solvent properties compared to the reported 1,2-dichloroethane but also show no reactivity toward strong bases under the conditions employed.

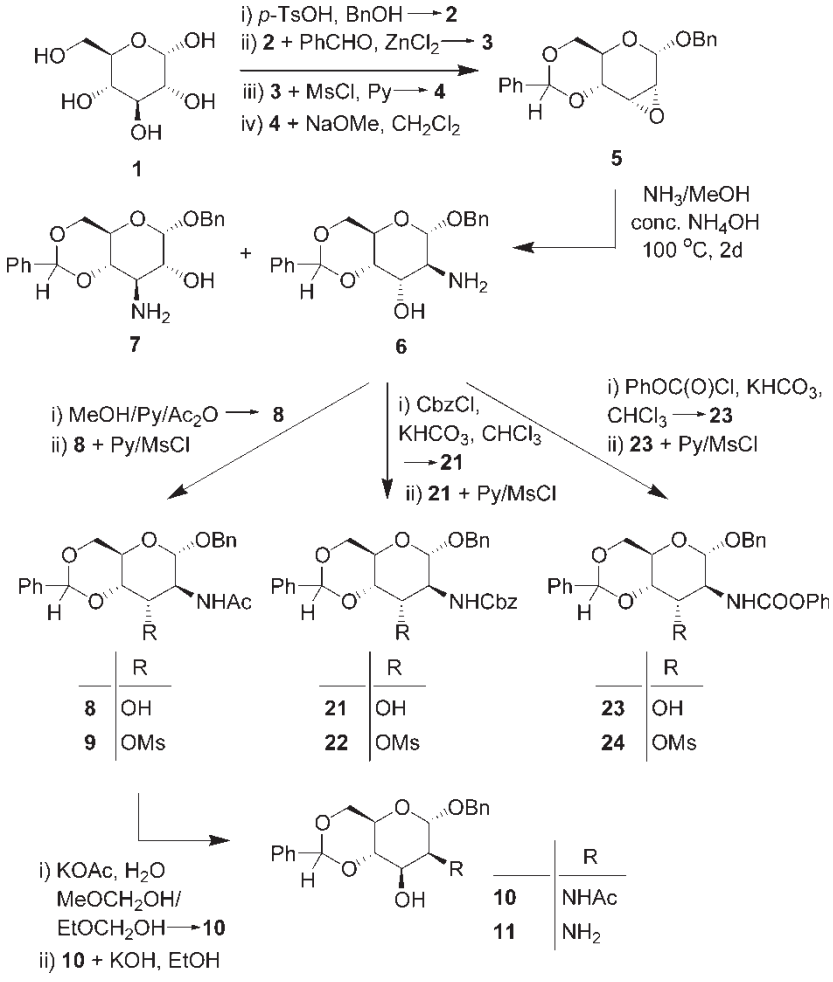
Table 1. ^{1}H NMR chemical shifts and coupling constants for compounds **4**–**6** and **8**

Ring proton	**4**	**5**	**6**	**8**
H-1	5.20	5.03	4.61	4.76
	$^{3}J_{1,2}$ 3.9	$^{3}J_{1,2}$ 2.7	$^{3}J_{1,2} < 1$	$^{3}J_{1,2} < 1$
H-2	4.62	3.46	3.35	4.47
	$^{3}J_{2,1}$ 3.9	$^{3}J_{2,1}$ 3.0	$^{3}J_{2,1} < 1$	$^{3}J_{2,1} < 1$
	$^{3}J_{2,3}$ 9.6	$^{3}J_{2,3}$ 4.2	$^{3}J_{2,3} < 1.8$	$^{3}J_{2,3}$ 3.3
				$^{3}J_{2,NH}$ 8.7
H-3	5.12	3.52	4.02	4.13
	$^{3}J_{3,2}$ 9.6	$^{3}J_{3,2}$ 4.5	$^{3}J_{3,2} < 1$	$^{3}J_{3,2}$ 3.0
	$^{3}J_{3,4}$ 9.6	$^{3}J_{3,4} < 1$	$^{3}J_{3,4} < 1$	$^{3}J_{3,4}$ 3.0
				$^{3}J_{3,OH}$ 7.2
H-4	3.72	~4.10 (subm)	3.95	3.71
	$^{3}J_{4,3}$ 9.3	$^{3}J_{4,3}$—	$^{3}J_{4,3}$ 3.0	$^{3}J_{4,3}$ 3.0
	$^{3}J_{4,5}$ 9.3	$^{3}J_{4,5}$—	$^{3}J_{4,5}$ 9.6	$^{3}J_{4,5}$ 9.6
H-5	3.97	3.94	4.23	4.34 (subm)
	$^{3}J_{5,4}$ 9.9	$^{3}J_{5,4}$ 8.7	$^{3}J_{5,4}$ 9.9	$^{3}J_{5,4}$—
	$^{3}J_{5,6a}$ 9.9	$^{3}J_{5,6a}$ 3.0	$^{3}J_{5,6a}$ 9.9	$^{3}J_{5,6a}$—
	$^{3}J_{5,6b}$ 5.1	$^{3}J_{5,6b}$ 1.8	$^{3}J_{5,6b}$ 5.1	$^{3}J_{5,6b}$—
H-6a	3.74	3.63	3.84	3.80
	$^{3}J_{6a,5}$ 10.2	$^{3}J_{6a,5}$ 3.3	$^{3}J_{6a,5}$ 10.2	$^{3}J_{6a,5}$ 3.3
	$^{2}J_{6a,6b}$ 10.2	$^{2}J_{6a,6b}$ 12.0	$^{2}J_{6a,6b}$ 10.2	$^{2}J_{6a,6b}$ 11.7
		$^{4}J_{6a,4?} < 1$		
H-6b	4.23	~4.10 (subm)	4.35	4.29
	$^{3}J_{6b,5}$ 5.1	$^{3}J_{6b,5}$—	$^{3}J_{6b,5}$ 5.4	$^{3}J_{6b,5}$ 4.8
	$^{2}J_{6b,6a}$ 10.5	$^{2}J_{6b,6a}$—	$^{2}J_{6b,6a}$ 10.2	$^{2}J_{6b,6a}$ 12.9
NH	—	—	—	5.68
				$^{3}J_{NH,2}$ 8.4

Note. δ in ppm, J in Hz; solvent was $CDCl_3$ unless stated otherwise.

The locked conformation of **5** resulted in good diastereoselectivity (**6**:**7** > 20:1) caused by *trans*-diaxial opening of the epoxide by NH_3.[30–32] Separation of **6** and **7**[33] was accomplished by repeated crystallizations from EtOH followed by a final recrystallization from THF-*i*-Pr_2O.

Compound **6** was selectively *N*-acetylated and 3-*O*-methanesulfonylated to yield compound **9** via **8**. The methyl glycoside analogs of **8** and **9** had been reported previously in the synthesis of mannomuramic acid.[34] In the synthesis of compound **10** from **9**, we considered that NaOAc in aq. methoxyethanol had been shown to cause displacement of one or two mesyl groups with configurational inversion.[35] The reaction is generally limited to a mesyl group with a neighboring amido group situated *trans*. Compound **8**, which tends to form a hydrate, was dried overnight in a vacuum pistol over P_2O_5 at 60°C prior to mesylation in pyridine. Compound **9** was found to be unstable when stored or heated. It had previously been noted that the analogous methyl-glycosides of **8** and **9** degraded upon recrystallization



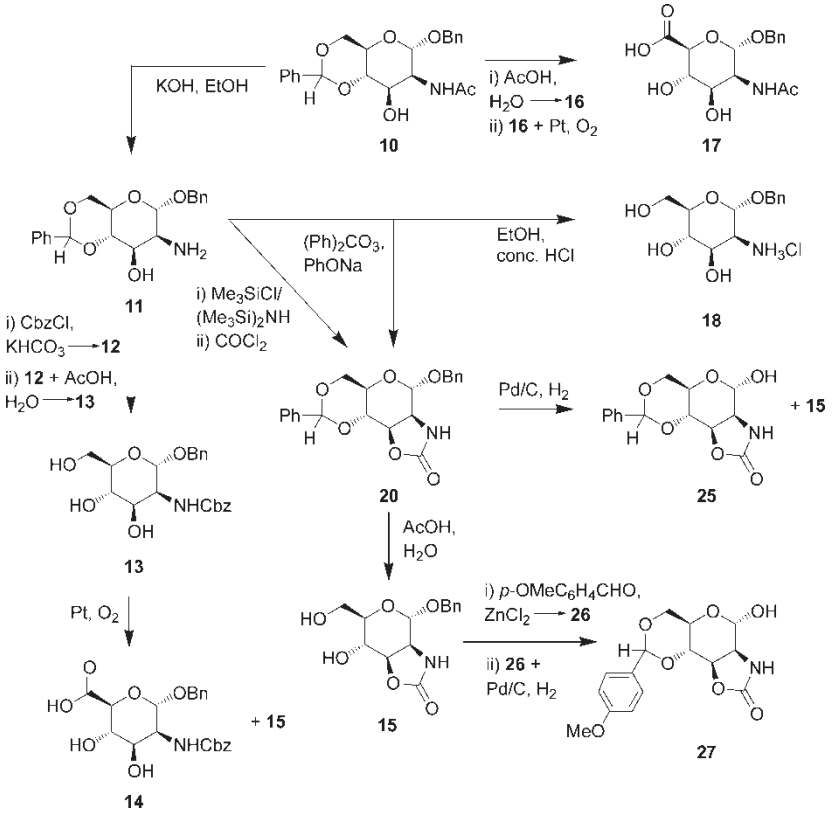
Scheme 1. Synthesis of compounds **10**, **11**, and **21**–**24**.

because of the eliminated methanesulfonic acid.[36] The diaxial arrangement of the mesyl and acetamido group favored substitution with inversion of configuration during subsequent treatment of **9** with KOAc in methoxyethanol and ethoxyethanol at elevated temperature for 2 days. Compound **10** with *manno*-configuration was isolated in good overall yield. The basicity of the medium is crucial in determining the extent and the mode of neighboring group participation of different acylamido groups.[37] Strongly basic media promote formation of aziridines.[37] Weak bases such as the acetate ion give rise to carbonyl oxygen participation and intermediate formation of oxazoline, which hydrolyzes spontaneously into the amido alcohol.

N-Deacetylation of **10** by KOH in boiling EtOH[38] yielded the free base **11** as a convenient starting material for subsequent synthetic steps (Scheme 2).

The ^{1}H NMR spectrum of **11** is shown in Fig. 1. The interpretation of NMR data in this article was based on the Karplus equation, which expresses the angular dependence between ^3J and the three-bond dihedral angle ϕ empirically.[39–41] In six-membered-ring systems, the approximate coupling constant is $^3J = 3–5$ Hz for *e-e* or *e-a* protons ($\phi \sim 60^\circ$, gauche) and 9–11 Hz for *a-a trans*-diaxial protons ($\phi \sim 180^\circ$). The structure of **11** was confirmed based upon ^{1}H NMR and ^{1}H-^{1}H COSY data (Fig. 1, Table 2). All observed coupling values were in agreement with the α-D-*manno*-pyrano-configuration ($^4C_1$-conformation).

The broad singlet at 4.85 ppm, which showed as an unresolved doublet pattern, was assigned to H-1. Proton 2 gave rise to a double doublet at 3.34 ppm with a constant of $^3J_{2,1} = 1.5$ Hz. The other splitting of $^3J_{2,3} = 4.8$ Hz was consistent with a 60° gauche angle and an equatorial-axial relationship between H-2 and H-3. Proton 3 caused a double doublet at 4.11 ppm with a small gauche coupling value of $^3J_{3,2} = 4.5$ Hz and a



Scheme 2. Synthesis of compounds **14**, **17**, **18**, and **25**–**27**.

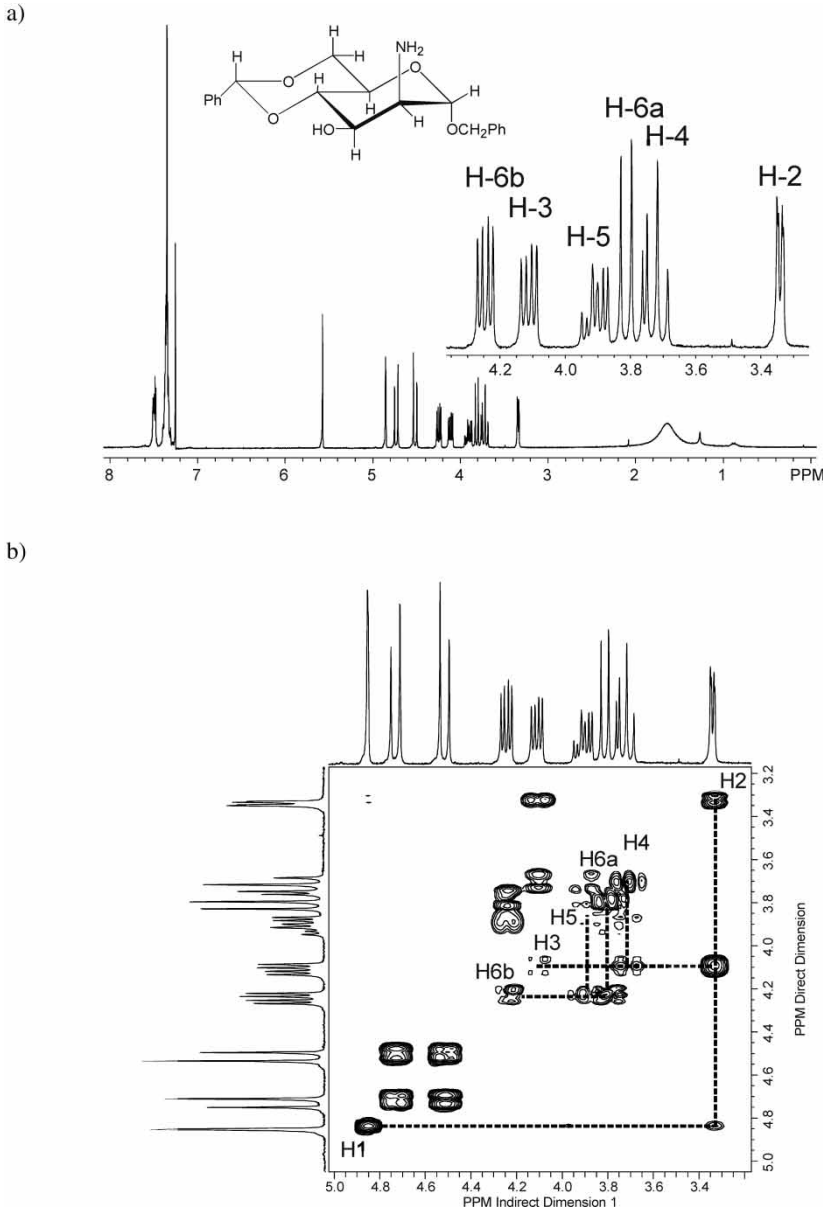


Figure 1. a) ^{1}H NMR spectrum of compound **11**; b) ^{1}H-^{1}H COSY spectrum of compound **11**.

large *trans*-diaxial coupling value of $^{3}J_{3,4} = 9.6$ Hz. Proton 4 produced a triplet at 3.72 ppm. The two coupling constants of $^{3}J_{4,3} = 9.3$ Hz and $^{3}J_{4,5} = 9.3$ Hz agreed with *trans*-diaxial 180° angles toward both H-3 and H-5. Proton 5 gave rise to a double triplet at 3.94 ppm. The two large

Table 2. ^{1}H NMR chemical shifts and coupling constants for compounds **10**–**14**

Ring proton	**10**	**11**	**12**	**13**	**13** (acetone)	**14** (pyridine)
H-1	4.96	4.85	5.00	4.76	4.90	5.70
	$^{3}J_{1,2}$ 1.2	$^{3}J_{1,2} < 1$	$^{3}J_{1,2} < 1$	$^{3}J_{1,2} < 1$	$^{3}J_{1,2}$ 1.2	$^{3}J_{1,2}$ 2.1
H-2	∼4.52 (subm)	3.34	∼4.27 (subm)	∼4.14 (subm)	4.09	∼5.05 (subm)
	$^{3}J_{2,1}$ 0.9	$^{3}J_{2,1}$ 1.5	$^{3}J_{2,1} < 1$	$^{3}J_{2,1}$—	$^{3}J_{2,1}$ 1.2	$^{3}J_{2,1}$—
	$^{3}J_{2,3}$—	$^{3}J_{2,3}$ 4.8	$^{3}J_{2,3}$ 4.8	$^{3}J_{2,3}$—	$^{3}J_{2,3}$ 4.5	$^{3}J_{2,3}$—
	$^{3}J_{2,NH}$—		$^{3}J_{2,NH}$ 4.8	$^{3}J_{2,NH}$—	$^{3}J_{2,NH}$ 8.4	$^{3}J_{2,NH}$—
H-3	4.37	4.11	4.33	3.49	4.01	4.89
	$^{3}J_{3,2}$ 4.8	$^{3}J_{3,2}$ 4.5	$^{3}J_{3,2}$ 5.4	$^{3}J_{3,2} <1$	$^{3}J_{3,2}$ 4.2	$^{3}J_{3,2}$ 6.9
	$^{3}J_{3,4}$ 9.9	$^{3}J_{3,4}$ 9.6	$^{3}J_{3,4}$ 9.9	$^{3}J_{3,4}$ 8.7	$^{3}J_{3,4}$ 9.0	$^{3}J_{3,4}$ 4.8
	$^{3}J_{3,OH}$ 2.1	$^{3}J_{3,OH}$—	$^{3}J_{3,OH}$ 2.7	$^{3}J_{3,OH}$—	$^{3}J_{3,OH}$ 4.2	
H-4	3.68	3.72	3.63	∼3.73 (subm)	∼3.70 (subm)	∼5.05 (subm)
	$^{3}J_{4,3}$ 9.6	$^{3}J_{4,3}$ 9.3	$^{3}J_{4,3}$ 9.6	$^{3}J_{4,3}$—	$^{3}J_{4,3}$—	$^{3}J_{4,3}$—
	$^{3}J_{4,5}$ 9.6	$^{3}J_{4,5}$ 9.3	$^{3}J_{4,5}$ 9.6	$^{3}J_{4,5}$—	$^{3}J_{4,5}$—	$^{3}J_{4,5}$—
H-5	3.94	3.91	3.90	∼4.05 (subm)	∼3.70 (subm)	∼5.05 (subm)
	$^{3}J_{5,4}$ 10.2	$^{3}J_{5,4}$ 9.9	$^{3}J_{5,4}$ 9.9	$^{3}J_{5,4}$—	$^{3}J_{5,4}$—	$^{3}J_{5,4}$—
	$^{3}J_{5,6a}$ 10.2	$^{3}J_{5,6a}$ 9.9	$^{3}J_{5,6a}$ 9.9	$^{3}J_{5,6a}$—	$^{3}J_{5,6a}$—	$^{3}J_{5,6a}$—
	$^{3}J_{5,6b}$ 4.8	$^{3}J_{5,6b}$ 4.5	$^{3}J_{5,6b}$ 4.8	$^{3}J_{5,6b}$—	$^{3}J_{5,6b}$—	$^{3}J_{5,6b}$ 5.1
H-6a	3.79	3.80	3.74	3.61	∼3.70 (subm)	—
	$^{3}J_{6a,5}$ 9.9	$^{3}J_{6a,5}$ 9.6	$^{3}J_{6a,5}$ 10.2	$^{3}J_{6a,5} < 1$	$^{3}J_{6a,5}$—	
	$^{2}J_{6a,6b}$ 9.9	$^{2}J_{6a,6b}$ 9.6	$^{2}J_{6a,6b}$ 10.2	$^{2}J_{6a,6b}$ 11.1	$^{2}J_{6a,6b}$—	
H-6b	4.24	4.24	4.21	∼3.84 (subm)	∼4.15 (subm)	—
	$^{3}J_{6b,5}$ 4.8	$^{3}J_{6b,5}$ 4.2	$^{3}J_{6b,5}$ 4.5	$^{3}J_{6b,5} < 1$	$^{3}J_{6b,5}$ 3.0	
	$^{2}J_{6b,6a}$ 9.9	$^{2}J_{6b,6a}$ 9.6	$^{2}J_{6b,6a}$ 9.9	$^{2}J_{6b,6a}$ 9.6	$^{2}J_{6b,6a}$—	
NH	5.82	—	5.00	6.34	6.17	8.56
	$^{3}J_{NH,2}$ 7.5		$^{3}J_{NH,2}$—	$^{3}J_{NH,2}$—	$^{3}J_{NH,2}$ 7.2	$^{3}J_{NH,2}$ 7.8

Note. δ in ppm, J in Hz; solvent was $CDCl_3$ unless stated otherwise.

constants of $^3J_{5,4} = 9.9$ Hz and $^3J_{5,6a} = 9.9$ Hz are due to a *trans*-diaxial 180° angle between H-5 and H-4 as well as H-5 and H-6a. The other constant of $^3J_{5,6b} = 4.5$ Hz was due to a 60° gauche angle and an axial-equatorial relationship between H-5 and H-6b. A 180° *trans*-diaxial angle to H-5 ($^3J_{6a,5} = 9.6$ Hz) and a geminal coupling with H-6b ($^2J_{6a,6b} = 9.6$ Hz) produced a triplet at 3.79 ppm for H-6a. Proton 6b caused a double doublet at 4.24 ppm. The smaller coupling of $^3J_{6b,5} = 4.2$ Hz was due to a gauche angle and an equatorial-axial relationship between H-6b and H-5, whereas the larger coupling of $^3J_{6a,6b} = 9.6$ Hz was due to a geminal coupling with H-6a. The benzylidene hydrogen without neighboring protons caused a singlet at 5.57 ppm. The two hydrogens of the benzyl group created two doublets at 4.52 ppm and 4.73 ppm, respectively.

Compound **11** was quantitatively converted to **12** (Scheme 2), which was de-*O*-benzylidenated by aq. acetic acid to give **13**, which was difficult to crystallize. The final compound was assumed to be a hydrate, consequently with a broad melting-point range. However, the observed optical rotation of +59.0° was significantly higher than the one previously reported.[25] NMR analysis clearly supported the α-pyranose configuration of **13** synthesized by us, which implies that the previously reported compound was possibly contaminated by the β-anomer or the furanoside form or both.

To accomplish oxidation to the carboxylic acid, compound **13** was dissolved in dioxane and was treated with oxygen in the presence of platinum catalyst for 10 h at 80°C. However, the desired product **14** was isolated in only low yield (21%) accompanied by the oxazolidinone **15**. Evidently, the *cis*-configuration of 2-benzyloxycarbonylamido and 3-OH-groups in **13** favored the cyclization with concurrent elimination of benzyl alcohol. An analogous reaction has been reported in the literature,[42,43] albeit with formation of a six-membered tetrahydro-1,3-oxazine-2-one ring. Apparently, the same kind of reaction can result in the formation of a *five*-membered oxazolidinone ring involving a single equatorial OH-group.

Compound **15** was unreactive toward Pt-catalyzed oxidation (*vide infra*). Better results were obtained after de-*O*-benzylidenation of **10** and oxidation of the intermediate **16** to give benzyl-2-acetamido-2-deoxy-mannopyranosiduronic acid **17** in 73% yield. Figure 2 shows the ^{1}H NMR spectrum of **17** with assignments based on ^{1}H-^{1}H COSY correlations. The ^3J values of the ring protons were all in agreement with the α-D-mannopyrano-configuration ($^4C_1$) (Table 3).

Trimethylsilylation of the amino alcohol **11** in the presence of hexamethyldisilazane followed by treatment with phosgene was used to prepare oxazolidinone-protected derivative **20** in excellent yield (90%) with virtually no side products. This new method for the preparation of *cis*-fused *gluco*-oxazolidinones appears to be particularly useful because it had previoulsy been shown that *trans*-fused *gluco*-oxazolidinone systems can be obtained in the same way.[44] Alternatively, compound **20** was obtained from **11** with diphenylcarbonate and NaOPh in DMF in only 72% yield. It

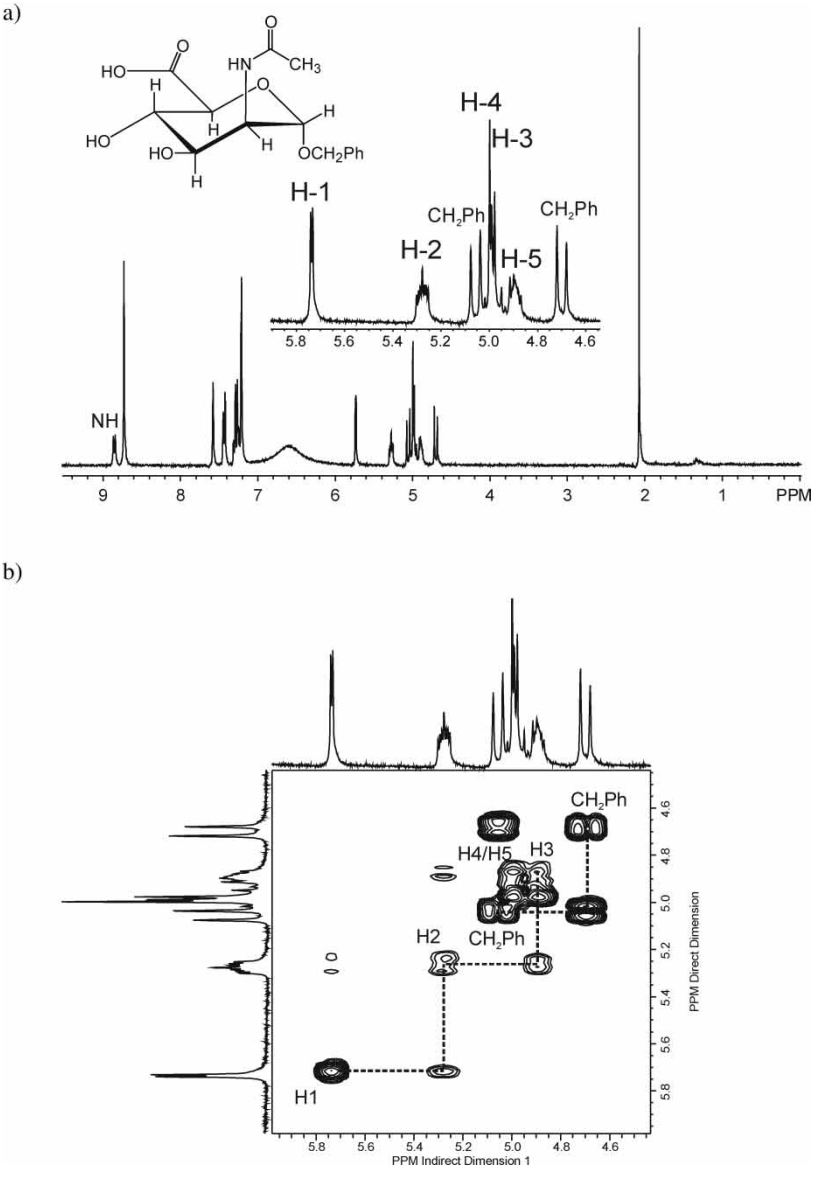


Figure 2. a) ^{1}H NMR spectrum of compound **17**; b) ^{1}H-^{1}H COSY spectrum of compound **17**.

could also be obtained from the mesylate derivative **22** (Scheme 1) in boiling ethoxyethanol; however, it was accompanied by several unidentified side products. Analogously, mesylate derivative **24** gave **20** with inversion of configuration as one of the components in a complicated product mixture.

Table 3. ^{1}H NMR chemical shifts and coupling constants for compounds **15**, **17**, **18**, **20**, and **21**

Ring proton	**15**	**15** (acetone)	**17** (pyridine)	**18** (pyridine)	**20**	**21**
H-1	5.01 $^{3}J_{1,2} < 1$	4.99 $^{3}J_{1,2} < 1$	5.74 $^{3}J_{1,2}$ 2.4	6.18 $^{3}J_{1,2} < 1$	4.95 $^{3}J_{1,2} < 1$	4.82 $^{3}J_{1,2} < 1$
H-2	4.01 $^{3}J_{2,1} < 1$ $^{3}J_{2,3}$ 7.5 $^{3}J_{2,NH} < 1$	4.09 $^{3}J_{2,1}$ 0.6 $^{3}J_{2,3}$ 7.5 $^{3}J_{2,NH} < 1$	5.28 $^{3}J_{2,1}$ 2.4 $^{3}J_{2,3}$ 7.2 $^{3}J_{2,NH}$ 4.2	~4.31 (subm) $^{3}J_{2,1} < 1$ $^{3}J_{2,3}$ 5.1	4.16 $^{3}J_{2,1} < 1$ $^{3}J_{2,3}$ 7.5	~4.23 (subm) $^{3}J_{2,1}$— $^{3}J_{2,3}$ 3.3 $^{3}J_{2,NH}$—
H-3	4.55 $^{3}J_{3,2}$ 7.5 $^{3}J_{3,4} < 1$	~4.50 (subm) $^{3}J_{2,1} < 1$ $^{3}J_{2,3} \sim 7$ $^{3}J_{2,NH} \sim 7$	~4.90 (subm) $^{3}J_{3,2}$— $^{3}J_{3,4}$—	4.81 $^{3}J_{3,2}$ 4.5 $^{3}J_{3,4}$ 9.6	4.77 $^{3}J_{3,2}$ 7.5 $^{3}J_{3,4}$ 7.5	4.16 $^{3}J_{3,2}$ 3.3 $^{3}J_{3,4} < 1$ $^{3}J_{3,OH}$ 6.9
H-4	~3.92 (subm) $^{3}J_{4,3}$— $^{3}J_{4,5}$—	~3.70 (subm) $^{3}J_{4,3}$— $^{3}J_{4,5}$—	4.98 $^{3}J_{4,3}$ 8.7 $^{3}J_{4,5}$ 8.7 $^{3}J_{4,OH}$ 3.9	4.69 $^{3}J_{4,3}$ 9.6 $^{3}J_{4,5}$ 9.6	3.92 $^{3}J_{4,3}$ 9.6 $^{3}J_{4,5}$ 9.6	3.74 (subm) $^{3}J_{4,3}$ 5.4 $^{3}J_{4,5}$—
H-5	~3.90 (subm) $^{3}J_{5,4}$— $^{3}J_{5,6a}$— $^{3}J_{5,6b}$—	~3.80 (subm) $^{3}J_{5,4} < 1$ $^{3}J_{5,6a}$ 10.5 $^{3}J_{5,6b}$ 5.1	~4.90 (subm) $^{3}J_{5,4}$— $^{3}J_{5,6a}$— $^{3}J_{5,6b}$—	~4.40 (subm) $^{3}J_{5,4}$— $^{3}J_{5,6a}$— $^{3}J_{5,6b}$ 5.1	3.86 $^{3}J_{5,4}$ 9.9 $^{3}J_{5,6a}$ 9.9 $^{3}J_{5,6b}$ 4.5	~4.25 (subm) $^{3}J_{5,4}$— $^{3}J_{5,6a}$— $^{3}J_{5,6b}$ 5.1
H-6a	3.62 $^{3}J_{6a,5} < 1$ $^{2}J_{6a,6b}$ 9.9 $^{3}J_{6a,OH} < 1$	~3.74 (subm) $^{3}J_{6a,5}$ 4.8 $^{2}J_{6a,6b}$—	—	~4.32 (subm) $^{3}J_{6a,5}$— $^{2}J_{6a,6b}$—	3.76 $^{3}J_{6a,5}$ 9.6 $^{2}J_{6a,6b}$ 9.6	3.76 $^{3}J_{6a,5}$ 11.4 $^{2}J_{6a,6b}$ 11.4
H-6b	3.71 $^{3}J_{6b,5} < 1$ $^{2}J_{6b,6a}$ 11.7 $^{3}J_{6b,OH} < 1$	3.89 $^{3}J_{6b,5}$ 4.8 $^{2}J_{6b,6a}$ 10.2	—	4.49 $^{3}J_{6b,5} < 1$ $^{2}J_{6b,6a}$ 11.4	4.26 $^{3}J_{6b,5}$ 4.5 $^{2}J_{6b,6a}$ 10.2	~4.30 (subm) $^{3}J_{6b,5}$ 5.4 $^{2}J_{6b,6a}$ 10.8
NH	6.8 $^{3}J_{NH,2}$—	6.67 $^{3}J_{NH,2}$—	8.85 $^{3}J_{NH,2}$ 7.5	—	5.68 $^{3}J_{NH,2}$—	5.01 $^{3}J_{NH,2}$ 8.7

Note. δ in ppm, J in Hz; solvent was $CDCl_3$ unless stated otherwise.

The stability of oxazolidinone protection groups toward acid is greater than toward base and allowed us to remove the benzylidene group in **20** to give **15** with retention of the 2,3-oxazolidinone group. We also observed that the oxazolidinone **15** was stable toward palladium-catalyzed hydrogenolysis and Pt-catalyzed oxidation. We attribute this to reduced adsorption of hydrophilic **15** on the catalyst surface. Although the benzylidene and the benzyl group in **20** were cleaved at comparable rates under hydrogenation conditions, compound (Scheme 2, Table 4) **25** was still isolated in satisfactory yield, because de-*O*-benzylidenated by-products were water soluble and easily removed during workup.

Peptide chemistry has seen the use of the *p*-nitrobenzyloxycarbonyl moiety as protective groups.[45] Such groups with electron-withdrawing nitro-substituents could be removed very quickly by hydrogenation. In analogy, an electron-donating substituent such as *p*-methoxy can be expected to slow down the hydrogenolytic rate of the benzylidene group.

Table 4. ^{1}H NMR chemical shifts and coupling constants for compounds **22**, **23**, and **25**–**27**

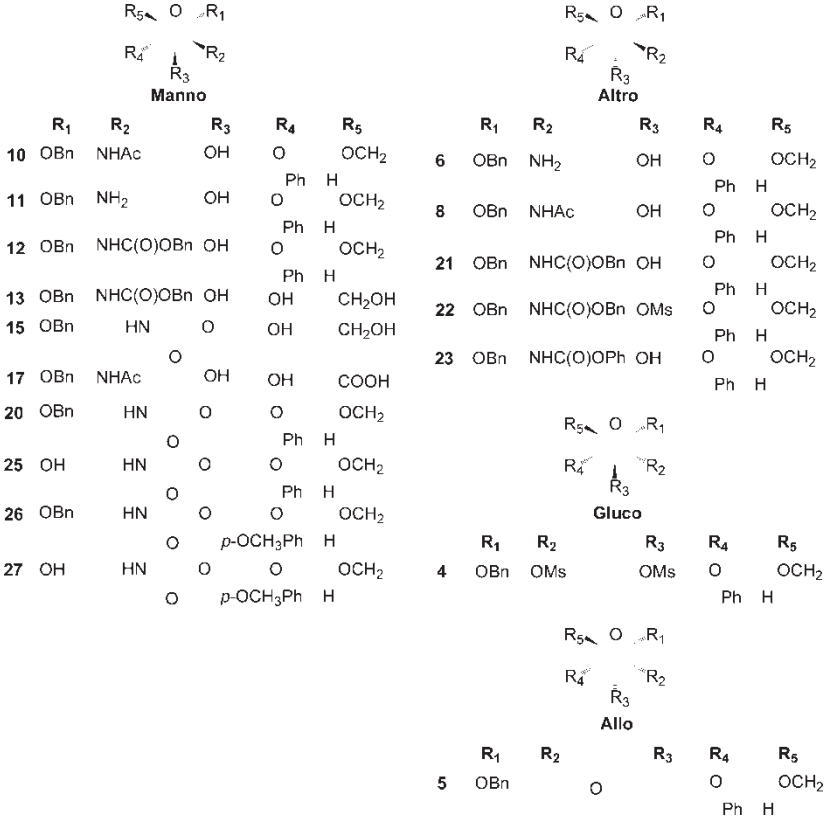
Ring proton	**22**	**23**	**25** (acetone)	**26**	**27**
H-1	4.78	4.92	∼4.0 (subm)	4.94	5.56
	$^{3}J_{1,2} < 1$	$^{3}J_{1,2} < 1$		$^{3}J_{1,2} < 1$	$^{3}J_{1,2} < 1$
H-2	∼5.13 (subm)	∼4.30 (subm)	4.73	4.15	4.6
	$^{3}J_{2,1} < 1$	$^{3}J_{2,1}$—	$^{3}J_{2,1}$ 7.2	$^{3}J_{2,1} < 1$	$^{3}J_{2,1} < 1$
	$^{3}J_{2,3} < 1$	$^{3}J_{2,3}$—	$^{3}J_{2,3}$ 7.2	$^{3}J_{2,3}$ 7.8	$^{3}J_{2,3}$ 8.1
				$^{3}J_{2,NH}$—	$^{3}J_{2,NH}$ 9.3
H-3	5.06	3.09	∼ 4.2 (subm)	4.76	5.09
	$^{3}J_{3,2} < 1$	$^{3}J_{3,2}$ 6.6	$^{3}J_{3,2}$—	$^{3}J_{3,2}$ 7.8	$^{3}J_{3,2}$ 7.5
	$^{3}J_{3,4} < 1$	$^{3}J_{3,4} < 1$	$^{3}J_{3,4}$—	$^{3}J_{3,4}$ 7.8	$^{3}J_{3,4}$ 7.5
H-4	∼3.73 (subm)	∼4.30 (subm)	∼3.80 (subm)	3.9	4.53
	$^{3}J_{4,3}$ 1.5	$^{3}J_{4,3}$—	$^{3}J_{4,3}$ 9.6	$^{3}J_{4,3}$ 9.6	$^{3}J_{4,3}$ 9.6
	$^{3}J_{4,5}$ 4.5	$^{3}J_{4,5}$—	$^{3}J_{4,5}$ 9.6	$^{3}J_{4,5}$ 9.6	$^{3}J_{4,5} < 1$
H-5	∼4.33 (subm)	∼3.80 (subm)	∼3.78 (subm)	∼3.85 (subm)	3.78
	$^{3}J_{5,4}$—	$^{3}J_{5,4}$—	$^{3}J_{5,4}$ 9.6	$^{3}J_{5,4}$ 9.9	$^{3}J_{5,4}$ 9.9
	$^{3}J_{5,6a}$—	$^{3}J_{5,6a}$—	$^{3}J_{5,6a}$ 9.6	$^{3}J_{5,6a}$ 9.9	$^{3}J_{5,6a}$ 9.9
	$^{3}J_{5,6b}$—	$^{3}J_{5,6b}$—	$^{3}J_{5,6b} < 1$	$^{3}J_{5,6b}$ 4.5	$^{3}J_{5,6b}$ 4.8
H-6a	∼3.69 (subm)	∼3.80 (subm)	∼4.2 (subm)	3.74	3.94
	$^{3}J_{6a,5}$ 3.3	$^{3}J_{6a,5}$—	$^{3}J_{6a,5}$—	$^{3}J_{6a,5}$ 9.6	$^{3}J_{6a,5}$ 9.9
	$^{2}J_{6a,6b}$—	$^{2}J_{6a,6b}$—	$^{2}J_{6a,6b}$—	$^{2}J_{6a,6b}$ 9.6	$^{2}J_{6a,6b}$ 9.9
	$^{4}J_{6a,4?}$—	$^{4}J_{6a,4?}$—			
H-6b	4.24	∼4.30 (subm)	∼4.0 (subm)	4.24	4.48
	$^{3}J_{6b,5}$ 5.1	$^{3}J_{6b,5}$—	$^{3}J_{6b,5}$—	$^{3}J_{6b,5}$ 4.5	$^{3}J_{6b,5}$ 4.5
	$^{2}J_{6b,6a}$ 10.2	$^{2}J_{6b,6a}$—	$^{2}J_{6b,6a}$—	$^{2}J_{6b,6a}$ 10.2	$^{2}J_{6b,6a}$ 10.2
NH	∼5.13 (subm)	5.26	∼7.4 (subm)	5.78	9.81
	$^{3}J_{NH,2}$—	$^{3}J_{NH,2}$ 9.0	$^{3}J_{NH,2}$—	$^{3}J_{NH,2}$—	$^{3}J_{NH,2}$—

Note. δ in ppm, J in Hz; solvent was $CDCl_3$ unless stated otherwise.

This approach proved fruitful with compound **26** (Scheme 2), in which the anisylidene group was somewhat more stable toward hydrogenation, resulting in **27** with improved yield. The anisylidene group could be removed with dilute acid in a subsequent step.

3 CONCLUSION

Benzyl-α-D-glycosides of 2-amino-2-deoxy-altropyranose, 2-amino-2-deoxy-mannopyranose, and 2-amino-2-deoxy-mannopyranosido-6-uronic acid were synthesized in good overall yields from α-D-glucose. Readily available starting material, high diastereoselectivities, good yields, and easy workup procedures allowed bulk production of pyranosidic furanose- and 1,6-anhydro-free derivatives of altrosamine and (Chart 1) mannosamine. Compounds were unequivocally identified by their NMR spectra and constitute well-characterized building blocks for further synthetic investigations of



	R_1	R_2	R_3	R_4	R_5
10	OBn	NHAc	OH	O	OCH_2
				Ph	H
11	OBn	NH_2	OH	O	OCH_2
				Ph	H
12	OBn	NHC(O)OBn	OH	O	OCH_2
				Ph	H
13	OBn	NHC(O)OBn	OH	OH	CH_2OH
15	OBn	HN	O	OH	CH_2OH
		O			
17	OBn	NHAc	OH	OH	COOH
20	OBn	HN	O	O	OCH_2
		O		Ph	H
25	OH	HN	O	O	OCH_2
		O		Ph	H
26	OBn	HN	O	O	OCH_2
		O	*p*-OCH_3Ph	H	
27	OH	HN	O	O	OCH_2
		O	*p*-OCH_3Ph	H	

	R_1	R_2	R_3	R_4	R_5
6	OBn	NH_2	OH	O	OCH_2
				Ph	H
8	OBn	NHAc	OH	O	OCH_2
				Ph	H
21	OBn	NHC(O)OBn	OH	O	OCH_2
				Ph	H
22	OBn	NHC(O)OBn	OMs	O	OCH_2
				Ph	H
23	OBn	NHC(O)OPh	OH	O	OCH_2
				Ph	H

	R_1	R_2	R_3	R_4	R_5
4	OBn	OMs	OMs	O	OCH_2
				Ph	H

	R_1	R_2	R_3	R_4	R_5
5	OBn	O		O	OCH_2
				Ph	H

Chart 1. Compounds analyzed by ^{1}H, ^{13}C, ^{1}H-^{1}H COSY and ^{1}H-^{13}C COSY-NMR spectroscopy.

amino sugars. In view of their central roles in the biosynthesis of sialic acids and considering recent advances in cell surface engineering, a variety of derivatives of these sugars may provide an experimental basis for modification and more detailed understanding of cell surface properties.

4 EXPERIMENTAL

Melting points were determined in a Thomas Hoover melting-point apparatus model No. 6404H and are uncorrected. Infrared spectra were taken with a Perkin-Elmer 337 spectrophotometer (KBr pellets). Optical rotations were measured with a O. C. Rudolph & Sons, Inc., model No. 956 polarimeter. The homogeneity of the compounds synthesized was determined by silica-gel thin-layer chromatography (TLC). The compounds were visualized by extinction of UV fluorescence and by spraying with 10–15% H_2SO_4–MeOH followed by heating for about 15 min at 120°C.

Deuterated solvents ($CDCl_3$, D_2O, pyridine-d_5, acetone-d_6, Me_2SO-d_6) were purchased from Aldrich (Milwaukee, WI) and dried over molecular sieves (5 Å). Traces of acid were removed by storing $CDCl_3$ over K_2CO_3. Standard 5 mm (OD) NMR tubes (Kimble & Kontes) were used. Approximately 10 mg of substance were added to the tube followed by 0.8 mL of deuterated solvent. NMR spectra were recorded at room temperature (rt) on a Varian Mercury 300-MHz instrument. The number of ^1H NMR transients was 128 and that of ^{13}C NMR was 2048. Two-dimensional ^1H-^1H COSY spectra were recorded with eight transients. All spectra were recorded spinning ($\upsilon = 20$ Hz). Chemical shift values are given in parts per million (ppm) relative to tetramethylsilane (Me_4Si) or one of the standard solvent peaks. Coupling constants J are given in Hertz.

All mass spectra were recorded on a Varian 1200 LC triple-quad mass spectrometer in electrospray ionization (ESI) mode (positive). Solutions of $c \sim 10^{-5}$ M were used in MeOH/H_2O (1:1). The analyte solution was sprayed by continuous infusion from the tip of a capillary with pneumatic assist (N_2 sheath gas) at a flow rate of 10 μL/min. Desolvation of the spray was accomplished at elevated temperature ($\vartheta = 50$°C API chamber, $\vartheta = 120$–150°C capillary). The instrument was operated at $\sim 5 \times 10^{-6}$ Torr with a mass window of m/z 0–1500. The detector was set to 1.2–1.5 kV. A full mass spectrum was acquired from which a single ion of interest was subsequently isolated in quadrupole 1 with a mass tolerance of ± 3 u. Collision-induced dissociation (CID) of the isolated ion was carried out at an argon background pressure of 1.0–1.4 mTorr with an excitation amplitude of 20–30 V (p-p).

Benzyl-4,6-*O*-benzylidene-α-D-glucopyranoside (3)

Anhydrous D-glucopyranose (270 g, 1.5 mol) was added to a solution of *p*-TsOH · H_2O (32 g) in BnOH (2.2 L) in a two-necked, round-bottomed

flask fitted with a reflux condenser and a capillary tube, which was fed with dry N_2. The condenser was connected to a vacuum pump by way of a trap cooled to -78°C. The mixture was magnetically stirred at 95°C/3 mm Hg for 3–4 h, after which time a total of 57 mL of water had been collected in the trap. The reaction mixture was neutralized with NaOMe, and the benzyl alcohol was distilled off in vacuo. The residual syrup was digested three times with *i*-Pr_2O (1 L total), which was decanted. The residue was shaken with a solution of freshly prepared anhydrous $ZnCl_2$ (150 g) and benzaldehyde (1.5 L) at rt for 30 h, and *i*-Pr_2O was added (1 L). The mixture was poured slowly with rapid stirring into ice water (3 L) and petroleum ether (2 L). The precipitate was filtered off and was washed three times, alternating cold water and petroleum ether. Compound **3** was recrystallized from EtOH and was azeotropically dried ($EtOH/PhCH_3$) to give 138 g (25% from D-glucose), mp 160–162°C, lit.[46] 161–162°C; $[\alpha]_D^{20}$ +108° (c, 1.0 in $CHCl_3$), lit.[46] $[\alpha]_D^{20}$ +107°.

Benzyl-4,6-*O*-benzylidene-2,3-di-*O*-methanesulfonyl-α-D-glucopyranoside (4)

A solution of compound **3** (11.0 g, 21.4 mmol) in absolute pyridine (30 mL) was cooled to -5°C, and methanesulfonyl chloride (6 mL) was added dropwise with magnetic stirring. The reaction mixture was stirred for 2 h and then kept at -5°C for 18 h and at rt for 5 h. The mixture was poured on ice with stirring. The solid was filtered off, air dried, and recrystallized from *i*-Pr-OH. Yield: 12.5 g (82.3%); mp 136–138°C; $[\alpha]_D^{25}$ +82.5° (c 1.00, pyridine); IR (ν in cm^{-1}): 1340 (sulfonate SO_2), 770, 705 (C_6H_5); ^{1}H NMR ($CDCl_3$, δ in ppm): δ 2.96 (s, 3H, SO_2CH_3), δ 3.11 (s, 3H, SO_2CH_3), δ 3.72 (t, 1H, $^3J_{4,3}$ 9.3, $^3J_{4,5}$ 9.3, H-4), δ 3.74 (t, 1H, $^3J_{6a,5}$ 10.2, $^2J_{6a,6b}$ 10.2, H-6a), δ 3.97 (dt, 1H, $^3J_{5,4}$ 9.9, $^3J_{5,6a}$ 9.9, $^3J_{5,6b}$ 5.1, H-5), δ 4.23 (dd, 1H, $^3J_{6b,5}$ 5.1, $^2J_{6b,6a}$ 10.5, H-6b), δ 4.62 (dd, 1H, $^3J_{2,1}$ 3.9, $^3J_{2,3}$ 9.6, H-2), δ 4.66 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Ph), δ 4.76 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Ph), δ 5.12 (t, 1H, $^3J_{3,2}$ 9.6, $^3J_{3,4}$ 9.6, H-3), δ 5.20 (d, 1H, $^3J_{1,2}$ 3.9, H-1), δ 5.52 (s, 1H, CHPh), δ 7.30–7.45 (m, 10H, H^{arom}); ^{13}C NMR ($CDCl_3$, δ in ppm): δ 36.17, 38.82, 38.94, 62.44, 68.54, 70.84, 75.75, 77.12, 79.04, 97.06, 101.89, 125.82, 127.97, 128.11, 128.25, 128.39, 129.32, 135.88, 136.03. Anal. calcd. for $C_{22}H_{26}O_{10}S_2$ (514.56): C, 51.35%; H, 5.10%; O, 31.10%; S, 12.47%. Found: C, 51.13%; H, 5.38%; O, 31.15%; S, 12.30%.

Benzyl-2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (5)

The compound was prepared in analogy to a previously published procedure for methyl-glucoside.[28] Compound **5**: mp 189°C; $[\alpha]_D^{25}$ +105° (c 1.00, pyridine);

IR (ν in cm^{-1}): 3475 (NH), 1675 (amide C═O), 770, 765 (C_6H_5); ^{1}H NMR ($CDCl_3$, δ in ppm): δ 3.46 (dd, 1H, $^3J_{2,1}$ 3.0, $^3J_{2,3}$ 4.2, H-2), δ 3.52 (dd ∼ d, 1H, $^3J_{3,4} < 1$, $^3J_{3,2}$ 4.5, H-3), δ 3.63 (ddd ∼ dt, 1H, $^4J_{6a,4}$ n. res., $^3J_{6a,5}$ 3.3, $^2J_{6a,6b}$ 12.0, H-6a), δ 3.94 (ddd, 1H, $^3J_{5,4}$ 8.7, $^3J_{5,6a}$ 3.0, $^3J_{5,6b}$ 1.8, H-5), δ 4.05–4.18 (m, 2H, H-4, H-6b), δ 4.65 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.3, CH_2Ph), δ 4.78 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.6, CH_2Ph), δ 5.03 (d, 1H, $^3J_{1,2}$ 2.7, H-1), δ 5.54 (s, 1H, CHPh), δ 7.27–7.50 (m, 10H, H^{arom}); ^{13}C NMR ($CDCl_3$, δ in ppm): δ 50.97, 53.68, 60.45, 69.12 70.03, 78.21, 93.28, 103.00, 126.49, 128.03, 128.19, 128.50, 128.64, 129.41. Anal. calcd. for $C_{20}H_{20}O_5$ (340.40): C, 70.58%; H, 5.92%; O, 23.51%. Found: C, 70.82%; H, 5.89%; O, 23.66%.

Benzyl-2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside (6)

Compound **5** (23.0 g, 67.6 mmol), satwated NH_3 in MeOH (920 mL), and concentrated NH_4OH (230 mL) were heated at 110°C in a 2-L stainless steel autoclave for 2 d. The solvent was removed in vacuo, and the crystalline residue was dissolved in THF and re-precipitated with *i*-Pr_2O. The product was recrystallized from absolute EtOH. Yield: 24.3 g (87%); mp 159–160°C; $[\alpha]_D^{25}$ +73.7° (c 0.68, pyridine); IR (ν in cm^{-1}): 3500, 3400 (NH_2), 750, 700 (C_6H_5); ^{1}H NMR ($CDCl_3$, δ in ppm): δ 3.35 (d, 1H, $^3J_{2,3}$ 1.8, H-2), δ 3.45 (s, 2H, CH_2Ph), δ 3.84 (t, 1H, $^2J_{6a,6b}$ 10.2, $^3J_{6a,5}$ 10.2, H-6a), δ 3.95 (dd, 1H, $^3J_{4,3}$ 3.0, $^3J_{4,5}$ 9.6, H-4), δ 4.02 (s, 1H, H-3), δ 4.23 (td, 1H, $^3J_{5,4}$ 9.9, $^3J_{5,6a}$ 9.9, $^3J_{5,6b}$ 5.1, H-5), δ 4.35 (dd, 1H, $^3J_{6b,5}$ 5.4, $^2J_{6b,6a}$ 10.2, H-6b), δ 4.61 (s, 1H, H-1), δ 5.64 (s, 1H, CHPh), δ 7.32–7.51 (m, 10H, H^{arom}); ^{13}C NMR ($CDCl_3$, δ in ppm): δ 54.73, 56.00, 58.90, 69.59, 71.15, 76.71, 102.62, 103.65, 126.45, 128.45, 129.30, 137.45; ESI-MS m/z 358.1 $[M+H]^+$. Anal. calcd. for $C_{20}H_{23}NO_5$ (357.40): C, 67.20%; H, 6.49%; N, 3.92%; O, 22.39%. Found: C, 67.48%; H, 6.76%; N, 3.47%; O, 22.62%.

A small amount of benzyl-3-amino-4,6-*O*-benzylidene-3-deoxy-α-D-glucopyranose (**7**) was isolated from the mother liquors[33] of the crystallizations.

Benzyl-2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-altropyranoside (8)

To a solution of **6** (15 g, 37.5 mmol) in dioxane (40 mL) and MeOH (300 mL), Ac_2O (5.4 mL) was added. The reaction mixture was stirred at rt for 1 h. Pyridine (5.4 mL) and another portion of Ac_2O (5.4 mL) were added, and stirring continued for 1 h at rt followed by a third portion of pyridine (10.8 mL) and Ac_2O (5.4 mL). The resulting mixture was evaporated in vacuo, and Et_2O (200 mL) was added. The product was filtered and washed with Et_2O. Recrystallization from dioxane-chloroform gave **8**. Yield: 15.0 g (89%); mp 205–207°C; $[\alpha]_D^{25}$ +51.2° (c 1.84, pyridine); IR (ν in cm^{-1}):

3475 (NH), 1675 (amide C═O), 765, 700 (C_6H_5); ^{1}H NMR ($CDCl_3$, δ in ppm): δ 2.03 (s, 1H, CH_3^{Ac}), δ 3.07 (d, 1H, $^3J_{OH,3}$ 7.5, OH), δ 3.71 (dd, 1H, $^3J_{4,3}$ 3.0, $^3J_{4,5}$ 9.6, H-4), δ 3.80 (ddd, 1H, $^2J_{6a,6b}$ 11.7, $J_{6a,5}$ 3.3, H-6a), δ 4.13 (dt, 1H, $^3J_{3,2}$ 3.0, $^3J_{3,OH}$ 7.2, $^3J_{3,4}$ 3.0, H-3), δ 4.29 (dd, 1H, $^3J_{6b,5}$ 4.8, $^2J_{6b,6a}$ 12.9, H-6b), δ 4.34 (subm., 1H, H-5), δ 4.47 (ddd, 1H, $^3J_{2,NH}$ 8.7, $^3J_{2,3}$ 3.3, $^3J_{2,1} < 1$, H-2), δ 4.59 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.0, CH_2Ph), δ 4.76 (s, 1H, H-1), δ 4.77 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.3, CH_2Ph), δ 5.63 (s, 1H, CHPh), δ 5.68 (d, 2H, $^3J_{NH,2}$ 8.4, NH), δ 7.33–7.50 (m, 10H, H^{arom}); ^{13}C NMR ($CDCl_3$, δ in ppm): δ 23.27, 52.01, 58.61, 67.55, 68.93, 69.95, 76.97, 77.09, 98.66, 102.22, 125.99, 127.95, 128.06, 128.09, 128.44, 128.97, 135.82, 136.75, 168.71. Anal. calcd. for $C_{22}H_{25}NO_6$ (399.4): C, 66.14%; H, 6.31%; N, 3.51. Found: C, 66.75%; H, 6.47%; N, 3.46%.

Benzyl-2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-methanesulfonyl-α-D-altropyranoside (9)

To a solution of **8** (5.5 g, 15.3 mmol) in absolute pyridine (20 mL), methanesulfonyl chloride (2 mL) was added dropwise with stirring at 0°C. After 24 h at 0°C, the reaction mixture was poured on ice with stirring. The precipitate was filtered off and recrystallized once from CH_2Cl_2-Et_2O and once from *i*-PrOH. It is important to preheat the solvents and cool them immediately for satisfactory crystallization. Yield: 5.8 g (92%); mp 96–100°C; $[\alpha]_D^{25}$ +31.0° (c 1.00, pyridine). Anal. calcd. for $C_{23}H_{27}NSO_8$ (447.52): C, 57.85%; H, 5.70%; N, 2.93%; S, 6.71%. Found: C, 57.09%; H, 5.87%; N, 2.41%; S, 6.04%. The compound was found to be unstable over time and was used immediately in the synthesis of **10**.

Benzyl-2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-mannopyranoside (10)

A mixture of compound **9** (5.5 g, 11 mmol), potassium acetate (8 g), water (20 mL), distilled methoxyethanol (80 mL), and ethoxyethanol (100 mL) was refluxed for 30 h, decolorized twice with charcoal, and then evaporated. The residue was shaken with water, filtered off, and recrystallized from *i*-PrOH. Yield: 3.70 g (79%); mp 220–222°C; $[\alpha]_D^{25}$ +29.0° (c 1.62, pyridine); IR (ν in cm^{-1}): 3350 (NH), 1625 (amide C═O), 750, 700 (C_6H_5); ^{1}H NMR ($CDCl_3$, δ in ppm): δ 2.08 (s, 3H, CH_3), δ 2.95 (d, 1H, $^3J_{OH,3}$ 2.1, OH), δ 3.68 (t, 1H, $^3J_{4,3}$ 9.6, $^3J_{4,5}$ 9.6, H-4), δ 3.79 (t, 1H, $^3J_{6a,5}$ 9.9, $^2J_{6a,6b}$ 9.9, H-6a), δ 3.94 (td, 1H, $^3J_{5,4}$ 10.2, $^3J_{5,6a}$ 10.2, $^3J_{5,6b}$ 4.8, H-5), δ 4.24 (dd, 1H, $^3J_{6b,5}$ 4.8, $^2J_{6b,6a}$ 9.9, H-6b), δ 4.37 (ddd, 1H, $^3J_{3,2}$ 4.8, $^3J_{3,OH}$ 2.1, $^3J_{3,4}$ 9.9, H-3), δ 4.52 (ddd, subm., 1H, $^3J_{2,1}$ 0.9, H-2), δ 4.54 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.0, CH_2Ph), δ 4.71 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Ph), δ 4.96 (d, 1H, $^3J_{1,2}$ 1.2, H-1), δ 5.58 (s, 1H, CHPh), δ 5.82 (d, 1H, $^3J_{NH,2}$ 7.5), δ 7.31–7.50 (m, 10H, H^{arom}); ^{13}C NMR ($CDCl_3$, δ in ppm): δ

23.73, 36.57, 53.98, 63.39, 67.54, 69.04, 70.06, 79.96, 99.14, 102.58, 126.43, 128.14, 128.30, 128.50, 128.74, 129.44, 136.78, 137.15, 171.70. Anal. calcd. for $C_{22}H_{25}NO_6 \cdot 0.5\ H_2O$ (418.4): C, 64.70%; H, 6.42%; N, 3.43%. Found: C, 65.08%; H, 6.42%; N, 3.57%.

Benzyl-2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-mannopyranoside (11)

A mixture of compound **10** (2.8 g, 6.7 mmol), KOH (12 g), and 95% EtOH (40 mL) was refluxed under N_2 for 10 h and then poured into hot water (150 mL). The resulting lumps of crude product were broken up. The suspension was stirred at −5°C overnight. The product was filtered and was recrystallized from EtOH–water with charcoal decolorization followed by recrystallization from THF-*i*-Pr_2O. Yield: 2.3 g (95%); mp 129–131°C; $[\alpha]_D^{25}$ +57.5° (c 2.2, DMF); IR (ν in cm^{-1}): 3450, 3400 (NH), 750, 700 (C_6H_5); ^{1}H NMR ($CDCl_3$, δ in ppm): δ 1.64 (s, broad, NH_2/OH), δ 3.34 (dd, 1H, $^3J_{2,1}$ 1.5, $^3J_{2,3}$ 4.8, H-2), δ 3.72 (t, 1H, $^3J_{4,3}$ 9.3, $^3J_{4,5}$ 9.3, H-4), δ 3.80 (t, 1H, $^3J_{6a,5}$ 9.6, $^2J_{6a,6b}$ 9.6, H-6a), δ 3.91 (td, 1H, $^3J_{5,4}$ 9.9, $^3J_{5,6a}$ 9.9, $^3J_{5,6b}$ 4.5, H-5), δ 4.11 (dd, 1H, $^3J_{3,2}$ 4.5, $^3J_{3,4}$ 9.6, H-3), δ 4.24 (dd, 1H, $^3J_{6b,5}$ 4.2, $^2J_{6b,6a}$ 9.6, H-6b), δ 4.52 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Ph), δ 4.73 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.0, CH_2Ph), δ 4.85 (s, 1H, H-1), δ 5.57 (s, 1H, CHPh), δ 7.30–7.51 (m, 10H, H^{arom}); ^{13}C-NMR ($CDCl_3$, δ in ppm): δ 36.56, 54.89, 63.63, 67.88, 69.18, 69.59, 79.95, 100.34, 101.69, 102.51, 126.47, 128.15, 128.18, 128.45, 128.70, 129.32, 137.14, 137.43. ESI-MS m/z 358.2 $[M+H]^+$, m/z 380.3 $[M+Na]^+$, m/z 396.2 $[M+K]^+$. Anal. calcd. for $C_{20}H_{23}NO_5$ (357.4): C, 67.20%; H, 6.49%; N, 3.92%. Found: C, 67.95%; H, 6.44%; N, 3.82%.

Benzyl-4,6-*O*-benzylidene-2-benzyloxycarbonylamido-2-deoxy-α-D-mannopyranoside (12)

Alcohol-free $CHCl_3$ (40 mL), $KHCO_3$ (4 g), and water (40 mL) were shaken for 1 h at rt. Compound **11** (0.8 g, 2.2 mmol) and benzylchloroformate (0.4 g) were added, and the mixture was shaken for 10 h at rt. The $CHCl_3$ layer was separated and was evaporated in vacuo at rt. Hexane (50 mL) and *i*-Pr_2O (10 mL) were added to the residue, and the precipitate was filtered. Recrystallization from *i*-Pr_2O afforded **12**. Yield: 1.05 g (95%); mp 117–118°C; $[\alpha]_D^{25}$ +8.5° (c 1.04, pyridine); IR (ν in cm^{-1}): 3355 (NH), 1710 (C═O), 745, 695 (C_6H_5); ^{1}H NMR ($CDCl_3$, δ in ppm): δ 2.54 (s, 1H, OH), δ 3.63 (t, 1H, $^3J_{4,3}$ 9.6, $^3J_{4,5}$ 9.6, H-4), δ 3.74 (t, 1H, $^3J_{6a,5}$ 10.2, $^2J_{6a,6b}$ 10.2, H-6a), δ 3.90 (dt, 1H, $^3J_{5,4}$ 9.9, $^3J_{5,6a}$ 9.9, $^3J_{5,6b}$ 4.8, H-5), δ 4.21 (dd, 1H, $^3J_{6b,5}$ 4.5, $^2J_{6b,6a}$ 9.9, H-6b), δ 4.27 (t, subm., 1H, $^3J_{2,NH}$ 4.8, $^3J_{2,3}$ 4.8, H-2), δ 4.33 (ddd, subm., 1H, $^3J_{3,2}$ 5.4, $^3J_{3,OH}$ 2.7, $^3J_{3,4}$ 9.9, H-3), δ 4.52 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Ph), δ 4.68 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.0, CH_2Ph), δ 5.00 (s, 1H, NH), δ 5.10 (s, 1H, H-1), δ 5.06–5.15 [m, mixing, 2H, $C(O)OCH_2Ph$], δ 6.53

(s, 1H, CHPh), δ 7.30–7.47 (m, 15H, H^{arom}); ^{13}C NMR ($CDCl_3$, δ in ppm): δ 36.18, 54.77, 63.02, 67.05, 67.26, 68.67, 69.69, 77.08, 79.44, 99.06, 102.20, 126.03, 127.72, 127.88, 128.11, 128.34, 128.38, 129.05, 136.44, 136.75. Anal. calcd. for $C_{28}H_{29}NO_7$ (491.51): C, 68.42%; H, 5.94%; N, 2.85%. Found: C, 68.07%; H, 6.12%; N, 2.35%.

Benzyl-2-benzyloxycarbonylamido-2-deoxy-α-D-mannopyranoside (13)

A solution of compound **12** (1.0 g, 2.0 mmol) in glacial acetic acid (9 mL) was heated to 80°C, and water (9 mL) was added dropwise over 0.5 h. The mixture was stirred and heated for 3 h. The solvents were evaporated in vacuo followed by repeated co-evaporation with water and finally with toluene for azeotropic drying. The remaining syrup was dissolved in a small volume of $CHCl_3$ followed by a small volume of *i*-Pr_2O saturated with water. The solvents were evaporated under a stream of nitrogen. The residue was washed with methyl cyclohexane and petroleum ether, and the crystalline precipitate was filtered and dried in a desiccator ($CaCl_2$) overnight. Yield: 0.7 g (85%); mp (decomp.) 51–60°C; $[\alpha]_D^{25}$ +59.0° (c 1.0, dioxane); previously reported as mixture with +38.7 (c 0.64, dioxane)[25]; ^1H NMR ($CDCl_3$, δ in ppm): δ 3.49 (d, 1H, $^3J_{3,4}$ 8.7, H-3), δ 3.61 (d, 1H, $^2J_{6a,6b}$ 11.1, H-6a), δ 3.73 (s, broad, 1H, H-4), δ 3.84 (d, broad, 1H, $^2J_{6b,6a}$ 9.6, H-6b), δ 4.05 (s, broad, 1H, H-5), δ 4.14 (s, broad, 1H, H-2), δ 4.35 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.4, CH_2Ph), δ 4.54 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.0, CH_2Ph), δ 4.76 (s, 1H, H-1), δ 4.92 (d, 1H, $^2J_{CH2Bz,CH2Bz}$ 12.0, CH_2Bz), δ 5.03 (d, 1H, $^2J_{CH2Bz,CH2Bz}$ 11.7, CH_2Bz), δ 6.34 (s, 1H, NH), δ 7.14–7.31 (m, 10H, H^{arom}); ^{13}C NMR ($CDCl_3$, δ in ppm): δ 54.52, 61.16, 67.07, 69.28, 69.85, 71.95, 77.08, 98.84, 127.66, 127.71, 127.93, 128.04, 128.24, 128.27, 135, 86, 136.64, 157.03; ^1H NMR (acetone-d_6, δ in ppm): δ 3.60–3.85 (m, 4H, H-4, H-5, H-6a, OH), δ 4.01 (dt, 1H, $^3J_{3,2}$ 4.2, $^3J_{3,OH}$ 4.2, $^3J_{3,4}$ 9.0, H-3), δ 4.09 (ddd, 1H, $^3J_{2,1}$ 1.2, $^3J_{2,NH}$ 8.4, $^3J_{2,3}$ 4.5, H-2), δ 4.15 (dd, 1H, subm., $^3J_{6b,5}$ 3.0, H-6b), δ 4.52 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.4, CH_2Ph), δ 4.75 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Ph), δ 4.90 (d, 1H, $^3J_{1,2}$ 1.2, H-1), δ 5.05 [m, mixing, 2H, $C(O)OCH_2Ph$], δ 6.17 (d, 1H, $^3J_{NH,2}$ 7.2, NH), δ 7.26–7.42 (m, 10H, H^{arom}); ^{13}C NMR (acetone, δ in ppm): δ 16.46, 31.38, 62.12, 66.18, 68.10, 68.80, 69.98, 73.66, 99.06, 127.72, 127.94, 128.01, 128.45, 128.48. Anal. calcd. for $C_{21}H_{25}NO_7$ (411.42): C, 59.85%; H, 6.46%; N, 3.33%. Found: C, 60.12%; H, 6.22%; N, 3.37%.

Benzyl-2-benzyloxycarbonylamido-2-deoxy-α-D-mannopyranuronic Acid (14)

To a solution of compound **13** (1.0 g, 2.43 mmol) in dioxane (10 mL) and water (100 mL), freshly reduced Pt (0.5 g from Adam's catalyst PtO_2) was added. The mixture was stirred vigorously at 70°C, and oxygen was introduced at a rate of

approximately 12 bubbles per second. The pH of the solution was kept between 7.0 and 7.5 with satwated $KHCO_3$. After 8 h, the suspension was filtered; the filtrate was concentrated, cooled, and acidified to pH 3 (3 M HCl). The yellow precipitate was filtered and recrystallized from aq. EtOH. Yield: 0.22 g (21%); mp 171–172°C; $[\alpha]_D^{25}$ +35.0° (c 1.0, dioxane) reported as mixture with +45.65 (c 0.34, dioxane)[25]; ^{1}H NMR (pyridine-d_5, δ in ppm): δ 4.71 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Bz), δ 4.89 (dd, 1H, $^3J_{3,2}$ 6.9, $^3J_{3,4}$ 4.8, H-3), δ 5.00–5.07 (m, 3H, H-2, H-4, H-5), δ 5.08 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.3, CH_2Bz), δ 5.24 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.6, CH_2Ph), δ 5.30 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.0, CH_2Ph), δ 5.70 (d, 1H, $^3J_{1,2}$ 2.1, H-1), δ 7.23–7.50 (m, 10H, H^{arom}), δ 8.56 (d, 1H, $^3J_{NH,2}$ 7.8, NH); ^{13}C NMR (pyridine-d_5, δ in ppm): δ 55.92, 66.78, 69.94, 70.81, 70.86, 74.84, 100.29, 128.06, 128.22, 128.33, 128.40, 128.86, 130.32, 132.95, 138.35, 158.01, 173.75.

Benzyl-α-D-mannopyranosido-[2,3:4′,5′]-2′-oxazolidinone (15)

Compound **20** (0.9 g, 3.2 mmol) was dissolved in glacial acetic acid (20 mL). The solution was heated to 90°C, water (10 mL) was added dropwise over 10 min, and stirring was continued for 1 h. The solution was cooled to rt, and the solvents were evaporated in vacuo. Repeated co-evaporation with water was followed by ethanol and finally toluene was performed. The residue was recrystallized from 1,2-dichloroethane. Yield: 0.6 g (85%); mp 125–126°C; $[\alpha]_D^{25}$ +33.6° (c 1.0, pyridine); IR (ν in cm^{-1}): 3350 (NH), 1775 (C═O), 740, 690 (C_6H_5); ^{1}H NMR (acetone, δ in ppm): δ 3.70 (s, subm., 1H, H-4), δ 3.74 (dd, subm., 1H, $^3J_{6a,5}$ 4.8, H-6a), δ 3.80 (dd, subm., 1H, $^3J_{5,6a}$ 10.5, $^3J_{5,6b}$ 5.1, H-5), δ 3.89 (d, 1H, $^3J_{6b,5}$ 4.8, $^2J_{6b,6a}$ 10.2, H-6b), δ 4.09 (dd, 1H, $^3J_{2,3}$ 7.5, $^3J_{2,1}$ 0.6, $^3J_{2,NH} < 1$, H-2), δ 4.50 (t, subm., 1H, $^3J_{3,2} \sim 7$, H-3), δ 4.53 (d, subm., 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Ph), δ 4.77 (d, subm., 1H, $^2J_{CH2Ph,CH2Ph}$ 12.0, CH_2Ph), δ 4.78 (subm., 1H, OH), δ 4.99 (s, 1H, H-1), δ 6.67 (s, broad, 1H, NH), δ 7.25–7.40 (m, 5H, $H^{arom.}$); ^{13}C NMR (acetone, δ in ppm): δ 31.40, 56.30, 61.76, 61.88, 68.61, 68.68, 70.42, 79.29, 95.84, 127.86, 128.33, 128.47, 137.70; ^{1}H NMR ($CDCl_3$, δ in ppm): δ 2.24 (s, broad, 2H, OH), δ 3.62 (dt∼d, 1H, $^3J_{6a,5} < 1$, $^3J_{6a,6b}$ 9.9, $^3J_{6a,OH} < 1$, H-6a), δ 3.71 (dd∼d, 1H, $^3J_{6b,5} < 1$, $^3J_{6b,6a}$ 11.7, $^3J_{6b,OH} < 1$, H-6b), δ 3.85–3.95 (m, 2H, H-4, H-5), δ 4.01 (d, 1H, $^3J_{2,1} < 1$, $^3J_{2,3}$ 7.5, H-2), δ 4.44 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Ph), δ 4.55 (d, 1H, $^3J_{3,2}$ 7.5, $^3J_{3,4} < 1$, H-3), δ 4.61 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.0, CH_2Ph), δ 5.01 (s, 1H, $^3J_{1,2} < 1$, H-1), δ 6.80 (s, broad, 1H, NH), δ 7.20–7.35 (m, 5H, $H^{arom.}$); ^{13}C NMR ($CDCl_3$, δ in ppm): δ 36.18, 56.23, 60.85, 66.75, 69.22, 69.36, 77.09, 79.52, 95.36, 127.93, 128.36, 136.41, 159.55. Anal. calcd. for $C_{14}H_{17}NO_6$ (295.28): C, 56.94%; H, 5.80%; N, 4.75%. Found: C, 57.12%; H, 5.89%; N, 4.88%.

An attempt to oxidize the product to the uronic acid derivative was unsuccessful.

Benzyl-2-acetamido-2-deoxy-α-D-mannopyranosiduronic Acid (17)

A solution of compound **10** (1.5 g, 3.6 mmol) in glacial acetic acid (9 mL) was heated to 80°C with stirring. Water (9 mL) was added dropwise over 20 min, and heating was continued for 20 min. After removal of the solvents in vacuo, water was added and evaporated in vacuo three times. We could not crystallize the de-*O*-benzylidenation product, benzyl-2-acetamido-2-deoxy-mannose (**16**), or its tri-*O*-acetyl derivative (**19**). The remainder, presumably **16**, was oxidized at 80°C in a suspension of freshly reduced Pt (0.5 g from Adam's catalyst PtO_2) in water (100 mL) with vigorous stirring and oxygenation. The pH was kept constant between 7.0 and 7.5 with $KHCO_3$. After 3 h, the mixture was filtered; the filtrate was concentrated in vacuo and acidified to pH 3 with 3 M HCl. The precipitation was complete after storage at 0°C overnight, and the product was filtered off. Recrystallization from EtOH-*i*-PrOH gave compound **17**. Yield: 0.85 g (73%); mp 208–209°C; $[\alpha]_D^{25}$ +59.0° (c 1.0, pyridine); IR (ν in cm^{-1}): 3340 (NH), 1700 (C═O), 760, 700 (C_6H_5); ^1H NMR (pyridine-d_5, δ in ppm): δ 2.07 (s, 3H, CH_3^{ac}), δ 4.70 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.4, CH_2Ph), δ 4.85–4.95 (m, 2H, H-5, H-3), δ 4.98 (dt, 1H, $^3J_{4,3}$ 8.7, $^3J_{4,5}$ 8.7, $^3J_{4,OH}$ 3.9, H-4), δ 5.06 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.0, CH_2Ph), δ 5.28 (ddd, 1H, $^3J_{2,1}$ 2.4, $^3J_{2,NH}$ 4.2, $^3J_{2,3}$ 7.2, H-2), δ 5.74 (d, 1H, $^3J_{1,2}$ 2.4, H-1), δ 6.60 (s, broad, 2H, OH), δ 7.22–7.45 (m, 5H, H^{arom}), δ 8.85 (d, 1H, $^3J_{NH,2}$ 7.5, NH); ^{13}C NMR (pyridine-d_5, δ in ppm): δ 23.36, 54.06, 69.90, 70.52, 70.67, 74.83, 100.13, 128.03, 128.30, 128.83, 138.27, 171.34, 173.55. Anal. calcd. for $C_{15}H_{19}NO_7$ (325.3): C, 55.38%; H, 5.89%; N, 4.31%. Found: C, 55.25%; H, 5.56%; N, 4.48%.

Benzyl-2-amino-2-deoxy-α-D-mannopyranoside * HCl (18)

A solution of compound **11** (0.2 g, 0.56 mmol) in EtOH (4 mL) was refluxed with conc. HCl (4 equiv.) for 2 min and was evaporated in vacuo. EtOAc was added to the residue, and the mixture was kept at −5°C overnight. The crude product was filtered off and recrystallized from EtOH-*i*-PrOH-Et_2O. Yield: 0.18 g (84%); mp 200–201°C; $[\alpha]_D^{25}$ +65.3° (c 1.0, water); ^1H NMR (pyridine-d_5, δ in ppm): δ 4.31 (dd∼d, subm., 1H, $^3J_{2,1} < 1$, $^3J_{2,3}$ 5.1, H-2), δ 4.32 (subm., 1H, H-6a), δ 4.40 (subm., 1H, $^3J_{5,6b}$ 5.4, H-5), δ 4.49 (dd∼d, 1H, $^3J_{6b,5} < 1$, $^2J_{6b,6a}$ 11.4, H-6b), δ 4.62 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Ph), δ 4.69 (t, 1H, $^3J_{4,3}$ 9.6, $^3J_{4,5}$ 9.6, H-4), δ 4.81 (dd, 1H, $^3J_{3,2}$ 4.5, $^3J_{3,4}$ 9.6, H-3), δ 4.97 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.4, CH_2Ph), δ 6.18 (s, 1H, H-1), δ 5.7–6.6 (s, broad, OH), δ 7.20–7.40 (m, 5H, H^{arom}); ^{13}C NMR (pyridine-d_5, δ in ppm): d 36.72, 55.87, 62.29, 68.48, 69.65, 70.31, 75.29, 98.65, 122.98, 124.36, 128.15, 128.53, 128.85, 136.10, 138.07, 149.14, 150.69. Anal. calcd. for $C_{13}H_{20}ClNO_5 \cdot 0.5\ H_2O$ (314.8): C, 49.44%; H, 6.90%; N, 4.51%. Found: C, 49.65%; H, 6.73%; N, 4.45%.

Benzyl-4,6-*O*-benzylidene-α-D-mannopyranosido-[2,3:4′,5′]-2′-oxazolidinone (20)

Method A

Compound **11** (1.43 g, 4.0 mmol) was heated in DMF (28 mL) with diphenylcarbonate (1.2 g, 5.6 mmol) and sodium phenoxide (0.12 g, 1.0 mmol) for 20 h at 110°C. Ice-cold water was added, and the precipitate was filtered and recrystallized from absolute EtOH. Yield: 1.2 g (72%); mp 136–138°C; $[\alpha]_D^{25}$ −30.0° (c 1.03, pyridine); IR (ν in cm^{-1}): 3325 (NH), 1760 (C═O), 735, 692 (C_6H_5); ^{1}H NMR ($CDCl_3$, δ in ppm): δ 3.76 (t, 1H, $^3J_{6a,5}$ 9.6, $^2J_{6a,6b}$ 9.6, H-6a), δ 3.86 (td, 1H, $^3J_{5,4}$ 9.9, $^3J_{5,6a}$ 9.9, $^3J_{5,6b}$ 4.5, H-5), δ 3.92 (dd∼t, 1H, $^3J_{4,3}$ 9.6, $^3J_{4,5}$ 9.6, H-4), δ 4.16 (d, 1H, $^3J_{2,3}$ 7.5, H-2), δ 4.26 (dd, 1H, $^3J_{6b,5}$ 4.5, $^2J_{6b,6a}$ 10.2, H-6b), δ 4.51 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Ph), δ 4.68 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Ph), δ 4.77 (t, 1H, $^3J_{3,2}$ 7.5, $^3J_{3,4}$ 7.5, H-3), δ 4.95 (s, 1H, H-1), δ 5.57 (s, 1H, CHPh), δ 5.68 (s, 1H, NH), δ 7.31–7.51 (m, 10H, H^{arom}); ^{13}C NMR ($CDCl_3$, δ in ppm): δ 36.17, 56.33, 59.78, 68.60, 69.64, 74.78, 77.08, 78.57, 95.99, 101.71, 125.92, 128.05, 128.07, 128.16, 128.46, 129.00, 136.04, 136.52, 158.29. Anal. calcd. for $C_{21}H_{21}NO_6$ (383.4): C, 65.78%; H, 5.52%; N, 3.66%. Found: C, 65.83%; H, 5.77%; N, 3.70%.

Method B

Compound **11** (0.3 g, 0.8 mmol), hexamethyldisilazane (1.5 mL), and dried xylene (20 mL) were refluxed for 12 h. The solution was concentrated in vacuo, and the residual solution was added dropwise to $CHCl_3$ (4 mL) containing phosgene (0.4 g, 4 mmol). The mixture was stirred at rt for 3 h and was evaporated in vacuo. The solid residue was dissolved in a minimal amount of dioxane, water (10 mL) was added, and the mixture was kept at 0°C for 2 h. The crude precipitate was filtered and recrystallized from absolute EtOH. Yield: 0.29 g (90%) with identical physical properties.

Benzyl-4,6-*O*-benzylidene-2-benzyloxycarbonylamido-2-deoxy-α-D-altropyranoside (21)

Alcohol-free $CHCl_3$ (40 mL), $KHCO_3$ (4 g), and water (40 mL) were shaken at rt for 1 h. Compound **6** (0.8 g, 2.2 mmol) and benzylchloroformate (0.4 g, 2.6 mmol) were added, and the mixture was shaken for 10 h at rt. The $CHCl_3$ layer was separated and evaporated under reduced pressure at rt. Hexane (50 mL) and *i*-Pr_2O (10 mL) were added to the residue; the precipitate was filtered off and recrystallized from *i*-PrOH. Yield: 1.0 g (92%); mp 161.5–162.5°C; $[\alpha]_D^{25}$ +24.8° (c 1.8, pyridine); IR (ν in cm^{-1}): 3350 (NH), 1700 (C═O), 745, 690 (C_6H_5); ^{1}H NMR ($CDCl_3$, δ in ppm): δ 3.09 (d, 1H,

$^3J_{OH,3}$ 7.2, OH), δ 3.74 (dd, subm., 1H, $^3J_{4,3}$ 5.4, H-4), δ 3.76 (t, 1H, $^3J_{6a,5}$ 11.4, $^2J_{6a,6b}$ 11.4, H-6a), δ 4.16 (dt, 1H, $^3J_{3,2}$ 3.3, $^3J_{3,OH}$ 6.9, H-3), δ 4.19–4.26 (m, subm., 1H, $^3J_{2,3}$ 3.3, H-2), δ 4.23–4.29 (m, subm., 1H, $^3J_{5,6b}$ 5.1, H-5), δ 4.30 (dd, subm., 1H, $^3J_{6b,5}$ 5.4, $^2J_{6b,6a}$ 10.8, H-6b), δ 4.58 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.0, CH_2Ph), δ 4.77 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.3, CH_2Ph), δ 4.82 (s, 1H, H-1), δ 5.01 (d, 1H, $^3J_{NH,2}$ 8.7, NH), δ 5.11 (s, 2H, CH_2Bz), δ 5.60 (s, 1H, CHPh), δ 7.32–7.50 (m, 10H, H^{arom}); ^{13}C NMR ($CDCl_3$, δ in ppm): δ 53.83, 59.04, 67.70, 68.36, 69.34, 70.37, 77.11, 99.17, 102.65, 126.40, 128.37, 128.46, 128.51, 128.63, 128.83, 128.85, 129.36, 135.99, 136.20, 137.17, 155.15. Anal. calcd. for $C_{28}H_{29}NO_7$ (491.51): C, 68.42%; H, 5.94%; N, 2.85%. Found: C, 68.39%; H, 5.83%; N, 2.80%.

Benzyl-4,6-*O*-benzylidene-2-benzyloxycarbonylamido-2-deoxy-3-*O*-methanesulfonyl-α-D-altropyranoside (22)

A solution of compound **21** (1.32 g, 3.2 mmol) in absolute pyridine (3 mL) was cooled to -5°C, and methanesulfonyl chloride (0.47 g, 4.1 mmol) was added dropwise with stirring. The reaction mixture was stirred for 2 h, kept in a freezer for 18 h, kept at rt for 3 h, and then poured on ice with stirring. The precipitate was filtered off, dried (desiccator, $CaCl_2$), and recrystallized from *i*-PrOH. Yield: 1.5 g (88%); mp 149–151°C; $[\alpha]_D^{25}$ +12.2° (c 1.0, pyridine); ^1H NMR ($CDCl_3$, δ in ppm): δ 1.56 (s, 3H, SO_2CH_3), δ 2.99 (s, broad, 4H, OCH_2Ph), δ 3.69 (dd, subm., 1H, $^3J_{6a,5}$ 3.3, H-6a), δ 3.73 (dd, subm., 1H, $^3J_{4,3}$ 1.5, $^3J_{4,5}$ 4.5, H-4), δ 4.24 (dd, 1H, $^3J_{6b,5}$ 5.1, $^2J_{6b,6a}$ 10.2, H-6b), δ 4.33 (subm., 1H, H-5), δ 4.55 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 12.6, CH_2Ph), δ 4.78 (d, subm., 1H, $^2J_{CH2Ph,CH2Ph}$ 12.0, CH_2Ph), δ 4.78 (d∼s, subm., 1H, $^3J_{1,2} < 1$, H-1), δ 5.06 (t∼s, 1H, $^3J_{3,2} < 1$, $^3J_{3,4} < 1$, H-3), δ 5.13 (t∼d, 1H, $^3J_{2,1} < 1$, $^3J_{2,3} < 1$, H-2), δ 5.58 (s, 1H, CHPh), δ 7.29–7.46 (m, 15H, H^{arom}); ^{13}C NMR ($CDCl_3$, δ in ppm): δ 36.57, 39.03, 59.20, 69.23, 69.82, 74.33, 98.44, 102.48, 126.22, 127.73, 128.09, 128.50, 128.70, 128.83, 129.43, 136.93. Anal. calcd. for $C_{29}H_{31}NO_9S$ (569.60): C, 61.60%; H, 5.49%; N, 2.46%; S, 5.63%. Found: C, 60.62%; H, 5.64%; N, 2.18%; S, 5.04%.

Benzyl-4,6-*O*-benzylidene-2-deoxy-2-phenoxycarbonylamido α-D-altropyranoside (23)

A solution of compound **6** (1.78 g, 5 mmol) in $CHCl_3$ was agitated for 15 min with a solution of 5% $KHCO_3$ in water (250 mL). Phenylchloroformate (0.8 g, 5.1 mmol) was added, and the mixture was stirred overnight. The $CHCl_3$ layer was separated and evaporated in vacuo. The residue was triturated with *i*-Pr_2O, filtered off, and recrystallized from EtOH–petroleum ether. Yield: 2.15 g (90%); mp 144–145°C; $[\alpha]_D^{25}$ +40.0° (c 1.0, pyridine); ^1H NMR ($CDCl_3$, δ in ppm): δ 3.09 (dd∼d, 1H, $^3J_{3,2}$ 6.6, $^3J_{3,4} < 1$, H-3), δ 3.78–

3.88 (m, 2H, H-5, H-6a), δ 4.22–4.38 (m, 3H, H-2, H-4, H-6b), δ 4.62 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Ph), δ 4.81 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.4, CH_2Ph), δ 4.92 (d∼s, 1H, $^3J_{1,2} < 1$, H-1), δ 5.26 (d, 1H, $^3J_{NH,2}$ 9.0, NH), δ 5.67 (s, 1H, CHPh), δ 7.1–7.5 (m, 15H, $H^{arom.}$); ^{13}C NMR ($CDCl_3$, δ in ppm): δ 53.56, 58.68, 67.88, 68.95, 70.03, 77.08, 98.66, 102.29, 121.21, 125.47, 126.02, 128.00, 128.09, 128.48, 129.00, 129.18. Anal. calcd. for $C_{27}H_{27}NO_7$ (477.49): C, 67.91%; H, 5.70%; N, 2.94%. Found: C, 68.41%; H, 6.01%; N, 3.04%.

4,6-*O*-Benzylidene-α-D-mannopyranosido-[2,3:4′,5′]-2′-oxazolidinone (25)

Compound **20** (0.2 g, 0.5 mmol) and 10% Pd/C (0.2 g) were stirred in dioxane (25 mL) in a hydrogenation apparatus ($p_{H2} = 1$ atm) for 24 h. The catalyst was filtered off, the solvent was evaporated in vacuo, and water was added to the residue. The crude precipitate was filtered off and recrystallized from dichloroethane and EtOAc-*i*-Pr_2O. Yield: 84.3 mg (60%); mp 155–160°C dec.; ^1H NMR (β-anomer, acetone, δ in ppm): δ 3.78 (t, subm., 1H, $^3J_{5,6b}$ 9.6, $^2J_{5,4}$ 9.6, H-5), δ 3.80 (t, subm., 1H, $^3J_{4,5}$ 9.6, $^3J_{4,3}$ 9.6, H-4), δ 3.9–4.1 (m, 2H, H-1, H-6b), δ 4.1–4.3 (m, 2H, H-6a, H-3), δ 4.73 (t, 1H, $^3J_{2,1}$ 7.2, $^3J_{2,3}$ 7.2, H-2), δ 5.34 (s, 1H, NH), δ 5.74 (s, 1H, CHPh), δ 7.3–7.6 (m, 6H, $H^{arom.}$, NH); ^{13}C NMR (β-anomer, acetone-d_6, δ in ppm): δ 57.43, 59.83, 68.70, 68.87, 69.40, 74.69, 79.02, 79.34, 92.08, 92.29, 101.52, 101.67, 126.50, 128.12, 128.94. Anal. calcd. for $C_{14}H_{15}NO_6$ (293.27): C, 57.34%; H, 5.16%; N, 4.78%. Found: C, 57.05%; H, 5.26%; N, 4.66%.

Benzyl-4,6-*O*-(*p*-methoxy)-benzylidene-α-D-mannopyranosido-[2,3:4′,5′]-2′-oxazolidinone (26)

Compound **15** (1.0 g, 3.4 mmol), anisaldehyde (10 mL), and fused $ZnCl_2$ (1.0 g) were shaken at rt for 2 d. Et_2O (20 mL) was added, and undissolved $ZnCl_2$ was filtered off. The solution was shaken with water (8 mL) and *i*-Pr_2O (12 mL) and stored at 0°C for 3 h. The crude precipitate was filtered and recrystallized from absolute EtOH. Yield: 0.9 g (75%); mp 187.5–188.5°C; $[\alpha]_D^{25}$ −47.0° (c 1.0, pyridine); IR (ν in cm^{-1}): 1750 (C═O, oxazolidinone), 745, 700 (C_6H_5); ^1H NMR ($CDCl_3$, δ in ppm): δ 3.74 (t, 1H, $^3J_{6a,5}$ 9.6, $^2J_{6a,6b}$ 9.6, H-6a), δ 3.79 (s, 3H, OCH_3), δ 3.85 (td, subm., 1H, $^3J_{5,4}$ 9.9, $^3J_{5,6a}$ 9.9, $^3J_{5,6b}$ 4.5, H-5), δ 3.90 (t, 1H, $^3J_{4,3}$ 9.6, $^3J_{4,5}$ 9.6, H-4), δ 4.15 (d, 1H, $^3J_{2,3}$ 7.8, H-2), δ 4.24 (dd, 1H, $^3J_{6b,5}$ 4.5, $^2J_{6b,6a}$ 10.2, H-6b), δ 4.51 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.4, CH_2Ph), δ 4.68 (d, 1H, $^2J_{CH2Ph,CH2Ph}$ 11.7, CH_2Ph), δ 4.76 (t, 1H, $^3J_{3,2}$ 7.8, $^3J_{3,4}$ 7.8, H-3), δ 4.94 (s, 1H, H-1), δ 5.52 (s, 1H, CHPh), δ 5.78 (s, 1H, NH), δ 6.85–7.40 (m, 9H, H^{arom}); ^{13}C NMR ($CDCl_3$, δ in

ppm): δ 36.17, 55.21, 56.33, 59.76, 68.56, 69.63, 74.81, 78.50, 96.00, 101.68, 113.48, 127.24, 128.04, 128.14, 128.45, 129.03, 136.05, 158.44, 159.96. Anal. calcd. for $C_{22}H_{23}NO_7$ (413.50): C, 63.90%; H, 5.61%; N, 3.39%. Found: C, 63.82%; H, 5.54%; N, 3.34%.

4,6-*O*-(*p*-Methoxy)-benzylidene-α-D-mannopyranosido-[2,3:4′,5′]-2′-oxazolidinone (27)

Compound **26** (0.21 g, 0.5 mmol) and 10% Pd/C (27 mg) were stirred in dioxane (25 mL) in a hydrogenation apparatus ($p_{H2} = 1$ atm) for 24 h. The catalyst was filtered off, the solvent was evaporated in vacuo, and water was added to the residue. The crude precipitate was filtered off and was recrystallized from absolute EtOH. Yield: 112 mg (70%); $[\alpha]_D^{25}$ −170° (c 1.0, pyridine); IR (ν in cm^{-1}): 1730 (C═O, oxazolidinone), 830 (*p*-MeO-C_6H_5); ^{1}H NMR ($CDCl_3$, δ in ppm): δ 3.67 (s, 3H, OCH_3), δ 3.78 (dt, 1H, $^3J_{5,4}$ 9.9, $^3J_{5,6a}$ 9.9, $^3J_{5,6b}$ 4.8, H-5), δ 3.94 (t, 1H, $^3J_{6a,5}$ 9.9, $^2J_{6a,6b}$ 9.9, H-6a), δ 4.48 (dd, 1H, $^3J_{6b,5}$ 4.5, $^2J_{6b,6a}$ 10.2, H-6b), δ 4.53 (dd∼d, subm., 1H, $^3J_{4,3}$ ∼9.6, $^3J_{4,5} < 1$, H-4), δ 4.60 (dd∼t, 1H, $^3J_{2,1} < 1$, $^3J_{2,3}$ 8.1, $^3J_{2,NH}$ 9.3, H-2), δ 5.02 (s, broad, 1H, OH-1), δ 5.09 (t, 1H, $^3J_{3,2}$ 7.5, $^3J_{3,4}$ 7.5, H-3), δ 5.56 (d∼s, broad, 1H, $^3J_{1,2} < 1$, H-1), δ 5.72 (s, 1H, CHPh), δ 7.04 (d, 1H, ^3J 8.1, H^{arom}, AB-splitting), δ 7.66 (d, 1H, ^3J 8.7, H^{arom}, AB-splitting), δ 9.81 (s, broad, 1H, NH); ^{13}C NMR ($CDCl_3$, δ in ppm, α/β-mixture): δ 36.59, 55.34, 57.06, 58.48, 60.45, 64.94, 69.60, 69.79, 75.55, 76.48, 79.88, 80.11, 92.84, 93.38, 102.05, 102.20, 113.95, 128.34, 128.39, 130.79, 159.65, 160.15, 160.58. Anal. calcd. for $C_{15}H_{17}NO_7$ (323.29): C, 55.73%; H, 5.31%; N, 4.33%. Found: C, 55.63%; H, 5.44%; N, 4.36%.

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