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The conversion of D-galactopyranosides into 2-amino-2-deoxy-D-talopyranosyl derivatives: Some new data [1,2]

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Abstract

The known oxidation–oximation–reduction sequence leading from D-galactopyranosides to 2-amino-2-deoxy-D-talopyranosides through replacement of the 2-hydroxy by a 2-amino group with inversion has been reinvestigated. The easily obtainable methyl 3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl)-β-D-galactopyranoside (**1**) was chosen as the suitably protected starting material. The single steps in the synthetic sequence were analyzed in some detail from the point of view of different reagents, stereoselectivities, side products, NMR spectra and conformations of intermediates. Owing to side reactions in the oxidative and reductive steps and to the incomplete diastereoselectivity in the latter, the overall yields in the conversion of **1** into methyl 2-acetamido-6-*O*-acetyl-2-deoxy-3,4-*O*-isopropylidene-β-D-talopyranoside did not exceed 50%. © 1996 Elsevier Science Ltd.

Keywords: Talosamine; Ulose oximes; Non-chair conformations; Dioxolane reductive opening

1. Introduction

As part of a program on the synthesis of analogues of immunogenic oligosaccharides selectively modified in specific positions of one of their monosaccharide units, we

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[1] Dedicated to the memory of Professor Giuseppe Bellucci.

[2] Part 6 of the series, Rare and Complex Saccharides from D-Galactose and other Milk-derived Carbohydrates. For Part 5, see ref. [1]. Presented in part at the 7th European Carbohydrate Symposium, Krakow, Poland, August 22–27, 1993, Abstr. A 122.

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needed a method for the preparation of a disaccharide intermediate in which a 2-acetamido-2-deoxy-D-talopyranosyl unit is β-linked to position 4 of a D-glucopyranose derivative. Owing to the difficulties still encountered in performing 1,2-cis stereocontrolled glycosylations [2], we focused our attention on an approach involving an amination with configurational inversion at position 2 of a β-D-galactopyranosyl unit (such as a protected lactose derivative), rather than using D-talosamine-derived donors. Although several methods for the conversion of galactose into talosamine derivatives have been reported [3–5], none seemed to be well suited for our project, apart from one [4] published after completion of this work.

The present paper reports on an explorative study carried out on methyl β-D-galactopyranoside derivatives as model compounds for the more complex disaccharides to be used as starting materials for the projected syntheses.

2. Results and discussion

Methyl 3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl)-β-D-galactopyranoside (**1**), directly obtained in high yields by acetonation of methyl β-D-galactopyranoside with excess of 2,2-dimethoxypropane as previously described [6], was envisaged as a good starting point for synthetic elaboration at position 2.

The most direct route to D-talosamine derivatives involves a nucleophilic displacement reaction by nitrogen nucleophiles on 2-sulfonates of **1**. Preliminary experiments on the reaction of sodium azide in DMF with the 2-triflate gave completely negative results, only the products arising from a ring-contraction reaction being obtained as an inseparable mixture of 1-diastereomers of (1-*R*,*S*)-2,5-anhydro-1-*C*-azido-3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl)-1-*O*-methyl-D-talitol. This result confirmed those previously reported on the reaction of α-D-galactopyranoside 2-imidazolylsulfonates [5] and α-L-fucopyranoside 2-triflates with several nucleophiles [7], in which ring contraction was the major or sole observed reaction pathway.

This approach was therefore abandoned, and the classical oxidation–oximation–reduction pathway [8,9] was applied to compound **1**. The oxidation of **1** without removal of the highly acid-labile mixed-acetal protecting group (MIP) requires a careful selection of reagents. Different types of Me_2SO-based oxidations [10], first tested for this purpose, led to different results. The treatment of **1** with Me_2SO–Ac_2O produced the corresponding 2-uloside **2** in a moderate isolated yield (44%), together with the 2-*O*-methylthiomethyl derivative **12** (35%, isolated), a product arising from a Pummerer rearrangement frequently encountered in this type of reaction [10]. The two reaction products were easily separated by silica gel chromatography and their structures firmly proved by NMR analysis (Tables 1 and 2). Compound **12** was further characterized through its 6-*O*-acetyl derivative **13**, obtained by selective deprotection at position 6, followed by routine acetylation.

The formation of **12** was completely prevented under the Swern oxidation conditions [Me_2SO–$(COCl)_2$] [10]. Also in this case, however, the yield of **2** did not exceed 40%, the major side-product being the symmetric acetal **14** (25%, isolated). The formation of **14** can be ascribed to a transacetalation reaction between **2** and its 6-*O*-deprotected

Table 1
Selected ^{1}H NMR parameters (δ, ppm; J, Hz; CD_3CN)

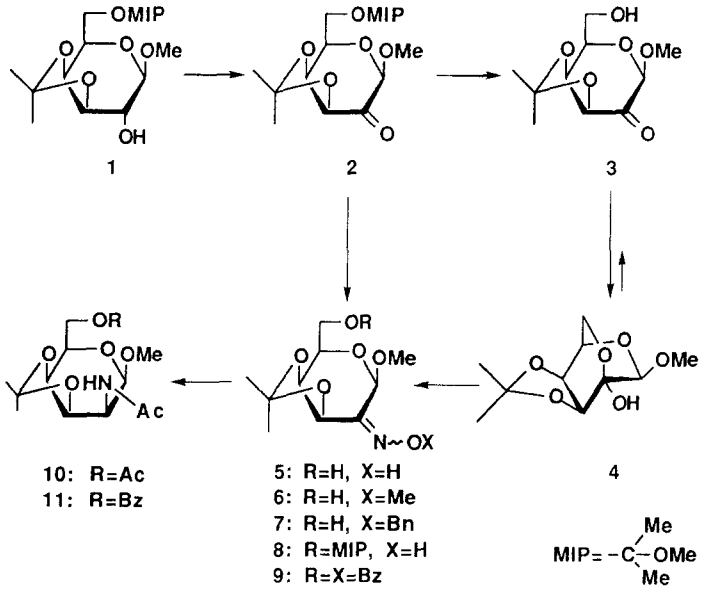
Compound	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$	$J_{1,3}$
12	4.19	3.66	4.03	4.15	3.84	3.58	3.57	8.23	7.14	5.37	2.02	5.40	6.84	n.d. [b]	—
13	4.20	3.67	4.06	4.15	3.98	4.28	4.19	8.21	7.04	5.41	2.07	7.81	4.22	11.54	—
2 [a]	4.20	—	3.80	4.03	3.60	3.89	3.77	—	—	5.69	1.76	6.85	5.44	9.71	0.97
14 [a]	4.48	—	4.13	4.29	3.86	4.00	3.82	—	—	5.83	1.51	n.d.	n.d.	n.d.	0.80
4	4.47	—	4.14	4.45	3.91	4.09	3.97	—	—	8.18	4.43	1.47	1.82	9.55	—
(*E*)-**5**	5.08	—	5.42	4.33	3.47	3.62	3.62	—	—	7.95	1.71	7.75	5.11	n.d.	0.63
(*Z*)-**5**	5.49	—	4.75	4.39	3.31	3.59	3.59	—	—	7.95	1.92	6.48	5.78	n.d.	0.49
(*E*)-**6**	5.07	—	5.32	4.34	3.47	3.63	3.59	—	—	7.92	1.72	7.11	5.15	11.19	0.75
(*Z*)-**6**	5.41	—	4.72	4.40	3.30	3.60	3.58	—	—	7.93	1.92	6.58	5.62	n.d.	0.6
(*E*)-**7**	5.06	—	5.39	4.35	3.47	3.63	3.63	—	—	7.88	1.69	6.95	5.18	n.d.	0.76
(*Z*)-**7**	5.49	—	4.70	4.39	3.29	3.60	3.60	—	—	7.92	1.93	6.61	5.61	n.d.	0.63
(*E*)-**8**	5.07	—	5.42	4.34	3.53	3.53	3.53	—	—	7.93	1.05	n.d.	n.d.	n.d.	0.76
(*Z*)-**8**	5.49	—	4.75	4.39	3.38	3.53	3.53	—	—	7.95	1.90	n.d.	n.d.	n.d.	0.61
(*E*)-**9**	5.36	—	5.59	4.56	4.08	4.56	4.53	—	—	7.41	1.90	6.92	5.24	11.56	0.51
(*Z*)-**9**	5.83	—	5.19	4.67	3.88	4.51	4.51	—	—	7.75	1.93	6.43	5.76	n.d.	0.49
10	4.52	4.26	4.38	4.25	4.02	4.27	4.20	2.88	5.03	6.84	2.44	7.38	4.70	11.48	0.45
11	4.52	4.32	4.42	4.29	4.22	4.55	4.48	2.40	6.54	5.33	2.51	7.48	4.60	11.48	0.4
16 [a]	4.86	3.22	4.65	3.79	3.87	4.57	4.43	8.43	8.08	5.49	2.18	7.62	4.41	11.60	—
21	4.51	4.50	4.88	3.89	3.91	4.54	4.41	1.33	4.07	3.00	1.40	7.00	5.63	10.06	—

[a] Spectra taken in C_6D_6.
[b] n.d., Not determined.

Table 2
Selected ^{13}C NMR signals (δ, ppm, CD_3CN)

Compound	Pyranose carbon atoms					
	1	2	3	4	5	6
12	104.11	76.33	79.37	75.02	72.77	61.08
13	104.00	76.17	79.34	74.69	71.36	63.94
2 [a]	100.34	198.12	78.27	78.01	72.40	60.44
14 [a]	100.66	198.26	78.24	78.06	72.37	60.62
4	101.71	93.03	76.74	74.16	67.61	64.41
(*E*)-**5**	100.24	151.13	65.68	73.31 [b]	73.51 [b]	61.79
(*Z*)-**5**	96.61	151.13	74.64	75.11	74.05	61.36
(*E*)-**6**	99.87	151.57	66.10	73.30 [b]	73.44 [b]	61.96
(*Z*)-**6**	96.55	150.62	74.48	75.18	74.11	61.52
(*E*)-**7**	99.84	152.15	66.37	73.35	73.35	62.00
(*Z*)-**7**	96.80	152.22	74.38	75.08	74.12	61.51
(*E*)-**8**	100.05	151.59	65.41	73.69	71.99	60.93
(*Z*)-**8**	96.45	150.96	74.65	75.42	72.55	60.56
(*E*)-**9**	99.63	160.02	68.75	73.43	71.14	64.42
(*Z*)-**9**	96.80	159.91	74.03	75.03	71.48	63.85
10	100.23	48.19	73.06	72.42	70.81	64.35
11	100.33	48.30	73.16	72.43	70.95	64.87
16 [a]	102.26	54.46	77.60	73.81	71.32	64.19
21	101.66	50.21	71.03	73.02	73.65	64.06

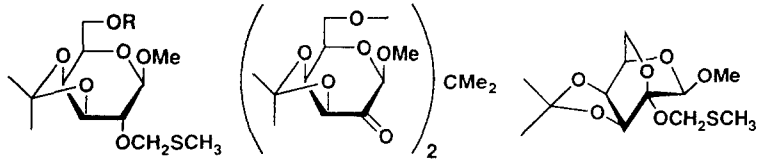
[a] Spectra taken in C_6D_6.
[b] Assignments may have to be interchanged.



Scheme 1.

counterpart formed in the reaction medium; an easy oxidation by the excess of reagent of the methanol formed in the transacetalation reaction may favour the formation of **14**.

As previously reported [1], when **1** was oxidized by the Pfitzner–Moffatt reagent [11] [Me_2SO–dicyclohexylcarbodiimide (DCC)–H_3PO_4–pyridine] the main product was the 2,5-dioxabicyclo[2.2.2]octane derivative **4** (Scheme 1), the hemiacetal form of the 6-deprotected ulose **3** [12], isolated in good yield (83%) as a crystalline product. The only isolated byproduct (7%) was the 2-*O*-methylthiomethyl derivative **15**, showing that, at least in part, deprotection at C-6 occurs in the reaction medium before workup. Its formation in appreciable amounts can be ascribed to higher reactivity of a hemiacetal hydroxyl group compared with an alcoholic one, methylthiomethyl derivatives being generally formed only in trace amounts under Pfitzner–Moffatt conditions [11].



An easy and satisfactory preparation of the ulose derivative **2** was subsequently found in the treatment of **1** with tetrapropylammonium perruthenate (TPAP) in the presence of a catalytic amount of 4-methylmorpholine *N*-oxide (NMO) [13] in dry dichloromethane.

By analogy with the results we recently obtained on the 1-deoxy analogue of **1** [1], **2** was obtained pure in good isolated yield (87%) after a rapid filtration through silica gel. Compound **2** was quantitatively transformed into the bicyclic derivative **4** by selective deprotection at position 6. We believe that the latter method of oxidation is the most reliable one for the preparation of ulosides containing an acid-labile group such as MIP present in **2**. It should, however, be pointed out that, for the purposes of the present work, preservation of the MIP protection at O-6 is not necessary, since the subsequent steps of the synthesis can be carried out on the deprotected derivative (**3**/**4**).

The oxime **5** was obtained as a mixture of *E* and *Z* diastereomers by standard treatment [8] with excess of hydroxylamine hydrochloride in pyridine, starting either from the uloside **2**, which loses its 6-*O*-MIP protecting group in the reaction medium, or from the bicyclo derivative **4**, reacting as its carbonyl tautomer **3.** Silica gel chromatography led to only a partial separation of the two diastereomers. The *O*-alkyloximes **6** and **7** were similarly prepared from **4** with *O*-methyl- and *O*-benzyl-hydroxylamine hydrochloride, and the *O*-benzoyloxime **9** by reaction of **5** with benzoyl chloride in pyridine. The *Z* and *E* forms of the oximes were differentiated by their NMR spectra (Tables 1 and 2) on the basis of the known effects caused by the oxime oxygen atom on the chemical shifts of *cis* vicinal carbons [14] and protons [15] (Tables 1 and 2).

By comparing the data reported in Tables 1 and 2, we can observe that *O*-substitution at the 2-hydroxyimino group produces very little, if any, change in the spectral parameters of the oximes both of the *E* and the *Z* series, pointing to similar conformational situations.

Although routine preparations of **5**, **6**, and **7** from crude **4** and the pertinent hydroxylamine hydrochloride derivative led in most cases to mixtures of *E*/*Z* isomers in ratios close to 1, in some runs we unexpectedly recovered a marked excess of the *Z* diastereoisomer, a fact that suggests equilibration between *E* and *Z* oximes in the reaction medium, or during workup. In order to confirm this hypothesis, the oximation of **4** was performed under the kinetically controlled conditions proposed by Tsuda et al. [16], that is, with hydroxylamine hydrochloride in methanol in the presence of an equimolar amount of Na_2CO_3. The oxime **5** was thus obtained (83% yield) with a strong prevalence of *E* diastereoisomer (*E*/*Z* ratio ca. 9:1). Conversely, a mild acid treatment of the above mixture with excess of pyridinium tosylate in ethyl acetate led to **5** in which the *Z* isomer prevailed (*E*/*Z* ratio ca. 1:4). The reported equilibration conditions [16] with a stronger acid catalyst, such as *p*-toluenesulfonic acid, led to more complex mixtures which were not analyzed further. The conclusion was that (*E*)- and (*Z*)-**5** are, respectively, the kinetically and the thermodynamically favoured oximes. PCMODEL molecular mechanics calculations [17] were in accordance with the latter conclusion, a difference of 0.4 kcal/mol in favour of (*Z*)-**5** being found.

Interestingly, when **2** was oximated under the kinetically controlled conditions, the 6-*O*-MIP group proved to be completely stable, good yields of the oxime **8** being obtained as a ca. 9:1 *E*/*Z* mixture.

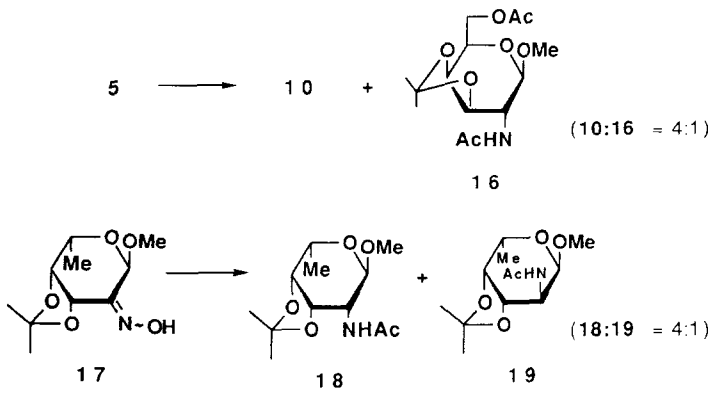
It may be mentioned that, although the absence of the two useful 1,2 and 2,3 proton coupling constants prevents accurate conformational deductions from ^1H NMR data, significant differences in the values of $J_{3,4}$ of the ketone **2** (5.69 Hz) and its oximes **5**–**9** (ca. 8 Hz) point to an unexpected difference in their conformations. On the other hand

the $J_{4,5}$ values are very similar (ca. 1.8 Hz) in **2** and **5–9**. Application of the Altona–Karplus equation [18] to these coupling constants gives H-3–C-3–C-4–H-4 and H-4–C-4–C-5–H-5 torsion angles of $-34°$ and 50° for **2**, and $\sim 0°$ for **5–9**, compatible with a somewhat flattened $^4C_1$ chair form for the former and a twist-boat form, possibly intermediate between $B_{2,5}$ and $^{3,O}B$, for the latter. Molecular mechanics computations (MMX) with PCMODEL [17] supported this hypothesis, which clearly requires confirmation by X-ray diffraction. Some recent diffractometric data on other 2-deoxy-2-hydroxyiminopyranose derivatives [19] provide proof for their conformational flexibility, but the reasons for the different conformations of the structurally very similar ketone **2** and its oximes remain unexplained.

One of the most commonly used methodologies for the stereoselective transformation of oximes and their *O*-alkyl and *O*-acyl derivatives into amino sugars uses lithium aluminium hydride (LAH) as the reducing agent [8,9,16,20]. Thus, when a 1:1 *E*/*Z* mixture of **5** was treated with LAH and the reaction product was acetylated, NMR analysis of the crude mixture revealed the main constituents to be the *talo* derivative (**10**) and its *galacto* diastereomer (**16**) in a ratio of 4:1, determined by the relative intensities of their anomeric carbon signals. Silica gel chromatography gave **10** and **16** in 64 and 17% yield, respectively.

The NMR spectra of **10** (Table 2) pointed to a non-chair conformation: $J_{2,3}$ and $J_{3,4}$ values (5.03 and 6.84 Hz) were in better agreement with a boat or twist-boat, rather then with a chair form. Anomalous *J* values were also reported [4] for the α anomer of a 6-*O*-trityl analogue of **10**. The NMR spectra of the previously unreported *galacto* isomer **16** (Table 2) are in agreement with a flattened $^4C_1$ conformation (Scheme 2).

The formation of a 4:1 ratio of the *talo* and the *galacto* amino isomers was unexpected since the conditions appeared to be favourable for a higher diastereoselectivity. Thus, hydride attack on 2-hydroxyimino derivatives of pyranosides is usually subject to anomeric stereocontrol [21], leading to the exclusive or highly preferred formation of 1,2-cis amines. Moreover, an *O*-isopropylidene group vicinal to a hydroxyimino function exerts a strong shielding effect to hydride attack, favouring practically exclusive



Scheme 2.

Table 3
Stereochemistry of some reductions of 2-hydroxyimino derivatives **5–9**

Compound	Reagent	*talo* / *galacto* [a] Ratio	Yield of isolated *talo* + *galacto* (%)
1:1 (*E*/*Z*)-**5**	$LiAlH_4$/THF	83:17	81
(*Z*)-**5**	$LiAlH_4$/THF	72:28	80
3:7 (*E*/*Z*)-**6**	$LiAlH_4$/THF	53:47	73
1:1 (*E*/*Z*)-**7**	$LiAlH_4$/THF	50:50	56
9:1 (*E*/*Z*)-**8**	$LiAlH_4$/THF	85:15	68
(*E*/*Z*)-**9**	BH_3/THF	100:0	65 [b]

[a] Determined by ^{13}C NMR on the basis of the anomeric C intensities.
[b] 20% of the 4-*O*-isopropyl derivative (**21**) was also isolated.

formation of the amino group cis to the ketal bridge, as shown, for instance, in LAH reductions of 2,3-*O*-isopropylidenepyranosid-4-ulose oximes in the *lyxo* and *ribo* series [8,9]. In the case of **5**, both its β-glycosidic methoxy group and the 3,4-*O*-isopropylidene group cis to it should therefore favour a stereospecific hydride attack on the α face to give the *talo* amine **10**. Surprisingly, the LAH reduction of an α analogue of **5**, methyl 6-deoxy-3,4-*O*-isopropylidene-α-L-*lyxo*-hexopyranosid-2-ulose oxime (**17**), in which the α-anomeric group would be expected to hinder hydride attack on the α-face, was reported [20] to give the *talo* and *galacto* amines in the same ratio (4:1) as obtained from **5**, whereas significantly lower diastereoselectivity would have been expected.

These data clearly show that the steric course of hydride reductions of pyranosidulose oximes cannot be explained exclusively in terms of steric hindrance to the approach of hydride. Other factors, such as binding of the reagent to oxygen or nitrogen atoms of the substrate by salt formation or coordination must play an important role.

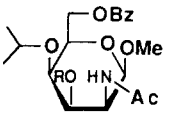
In some cases the stereochemistry of reductions of ulose oximes with LAH and other types of hydride donors have been shown to be highly dependent on such factors as the type of substitution on the oxime oxygen [21], *E* or *Z* configuration of the oxime, solvent [16], the presence of free OH groups, etc.

Some of these parameters have been checked by us and the results, summarized in Table 3, show that configuration on the C=N bond [(*E*)- or (*Z*)-**5**] and a free or substituted 6-OH (**5** or **8**) have little influence on the *talo*/*galacto* ratio in the amine products. On the other hand alkylation of the oxime oxygen (**6** and **7**) significantly reduces product stereoselectivity and yield.

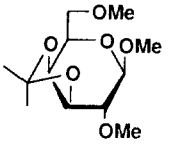
The use of diborane as a reducing agent has also been investigated. Diborane in THF has been reported to give very good results, both with respect to yields and stereoselectivity in the reductions of *O*-acylated oximes of aldopyranosid-2-uloses [22]. Treatment of a ca. 1:1 mixture of (*E*)- and (*Z*)-**9** with this reagent gave, after acetylative workup, a 65% yield of the pure *talo*-acetamido derivative **11**, but the main side-product (ca. 20%) was not the *galacto* epimer (which was totally absent), but rather a product of reductive opening of the dioxolane ring, namely, the 4-*O*-isopropyl derivative **20**, as proven by its NMR spectra.

The reductive ring opening of acetal rings by diborane in THF was reported by Fleming and Bolker [23] for several non-carbohydrate-derived acetals, under conditions,

however, which were much more drastic than those we used on **9**. This may imply some specific structural effect, possibly involving complexation of reagent to the hydroxyimino group or to an intermediate of its reduction, followed by intramolecular hydride transfer. The fact that the tri-*O*-methyl derivative **22** [24] is totally unreactive with diborane under the conditions used in the reduction of **9** supports this hypothesis.



20: R=H
21: R=Ac



22

The regiospecific ring opening observed in the **9** → **20** conversion, leading exclusively to the 4-*O*-isopropyl-3-OH product **20**, is in accordance with the results reported for the analogous reductions of diphenylmethylene acetals by chloroalane [25]. Also in the case of *O*-isopropylidene derivatives of some pyranosides of the β-L-*arabino* and α-L-*rhamno* series, chloroalane reductions have been found to produce dioxolane ring opening products with a high, if not complete, regioselectivity favouring the products with an axial isopropoxy group [26].

It can be concluded that the conversion of galactopyranosides into talosamine derivatives is not an ideal route. However, if one considers the easy availability of the starting material **1**, an overall yield of about 50% in a three-step sequence can still be considered as convenient.

3. Experimental

General methods are those reported in ref. [27].

*Oxidation of methyl 3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl)-β-*D*-galactopyranoside* (**1**).—*Method A (*Me_2SO/Ac_2O*).* A solution of **1** [6] (653 mg, 2.13 mmol) in Me_2SO (5 mL) and Ac_2O (1.5 mL) was stored at room temperature for 60 h. Saturated aq $NaHCO_3$ (5 mL) was added and the product was extracted with benzene (4 × 30 mL). Concentration and chromatography on silica gel (1:1 hexane–EtOAc + 0.1% Et_3N) gave **12** (268 mg, 35%) and then **2** (287 mg, 44%).

Methyl 3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl)-2-*O*-methylthiomethyl-β-D-galactopyranoside (**12**); R_f 0.73 (3:7 hexane–EtOAc); $[\alpha]_D$ +24.7° (*c* 1.3, $CHCl_3$); ^{1}H NMR (CD_3CN): see Table 1; further signals, δ 1.28 and 1.48 (2 s, 6 H, dioxolane CMe_2), 1.30 (s, 6 H, 2 MIP Me), 2.10 (s, 3 H, SMe), 3.16 (s, 3 H, MIP OMe), 3.43 (s, 3 H, OMe-1), 4.82 (s, 2 H, SCH_2O); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 13.26 (SMe), 24.72 (2 MIP Me), 26.60 and 28.07 (dioxolane CMe_2), 48.72 (MIP OMe), 56.66 (OMe-1), 75.08 (SCH_2), 100.75 (MIP CMe_2), 110.34 (dioxolane CMe_2). Anal. Calcd for $C_{16}H_{30}O_7S$: C, 52.4; H, 8.3. Found: C, 52.1; H, 8.0.

A solution of **12** (250 mg) in 10:1 MeOH–water (20 mL) containing AcOH (25 mg) was heated at 50 °C for 30 min. After neutralization with Et_3N (0.1 mL), the solvent was evaporated in vacuo and the residue coevaporated with toluene. The crude residue was dissolved in pyridine (6 mL), treated with Ac_2O (3 mL), and left 24 h at room temperature. The solution was evaporated and twice coevaporated with toluene to give pure methyl 6-*O*-acetyl-3,4-*O*-isopropylidene-2-*O*-methylthiomethyl-β-D-galactopyranoside (**13**) (206 mg, 90% yield), as an oil; R_f 0.83 (1:9 hexane–EtOAc); $[\alpha]_D$ +28.7° (*c* 1.0, $CHCl_3$); ^1H NMR (CD_3CN): see Table 1; further signals, δ 1.29 and 1.48 (2 s, 6 H, CMe_2), 2.03 (s, 3 H, MeCO), 2.10 (s, 3 H, SMe), 3.43 (s, 3 H, OMe-1), 4.81 (s, 2 H, SCH_2O); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 13.27 (SMe), 20.91 (*Me*CO), 26.60 and 27.98 (C*Me*$_2$), 56.73 (OMe), 75.11 (SCH_2O), 110.63 (*C*Me_2), 171.41 (Me*C*O). Anal. Calcd for $C_{14}H_{24}O_7S$: C, 50.0; H, 7.2. Found: C, 49.7; H, 6.9.

Methyl 3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl)-β-D-*lyxo*-hexopyranosid-2-ulose (**2**); R_f 0.50 (3:7 hexane–EtOAc); $[\alpha]_D$ −14.6° (*c* 0.9, $CHCl_3$); ^1H NMR (C_6D_6): see Table 1; further signals, δ 1.18 and 1.40 (2 s, 6 H, CMe_2), 1.28 (s, 6 H, 2 MIP Me), 3.14 (s, 3 H, MIP OMe), 3.34 (s, 3 H, OMe-1); ^{13}C NMR (C_6D_6): see Table 2; further signals, δ 24.52 (2 MIP Me), 26.20 and 27.40 (dioxolane C*Me*$_2$), 48.31 (MIP OMe), 56.54 (OMe-1), 100.18 (MIP *C*Me_2), 110.95 (dioxolane *C*Me_2). Anal. Calcd for $C_{14}H_{24}O_7$: C, 55.3; H, 8.0. Found: C, 54.9; H, 8.1.

Method B [$Me_2SO/(COCl)_2$]. To a solution of oxalyl chloride (0.20 mL, 2.28 mmol) in dry CH_2Cl_2 cooled at −60 °C was added a solution of dry Me_2SO (0.4 mL) in CH_2Cl_2 (1.3 mL) dropwise under stirring, followed, after 2 min, by a solution of **1** (698 mg, 2.28 mmol) in the same solvent (2.5 mL). Stirring was continued for 30 min at −60 °C, Et_3N (1.5 mL) was slowly added, and the reaction mixture was allowed to reach room temperature, then treated with water (10 mL). The organic phase was separated, the aqueous phase was extracted with CH_2Cl_2 (4 × 30 mL), the combined organic layers were washed with saturated aq NaCl, dried with $MgSO_4$, evaporated, and subjected to flash-chromatography over silica gel (3:7 hexane–EtOAc containing 0.1% Et_3N) to give **2** (340 mg, 49%) and then **14** (118 mg, 20%).

Methyl 3,4-*O*-isopropylidene-6-*O*-[1-methyl-1-(methyl 3,4-*O*-isopropylidene-β-D-*lyxo*-hexopyranosid-2-ulos-6-*O*-yl)ethyl]-β-D-*lyxo*-hexopyranosid-2-ulose (**14**); R_f 0.11 (9:1 CH_2Cl_2–acetone); $[\alpha]_D$ −45.5° (*c* 1.0, $CHCl_3$); ^1H NMR (C_6D_6): see Table 1; further signals, δ 1.27 and 1.44 (2 s, 12 H, 2 × dioxolane CMe_2), 1.35 (s, 6 H, acetal bridge CMe_2), 3.43 (s, 6 H, 2 OMe); ^{13}C NMR (C_6D_6): see Table 2; further signals, δ 24.94 (acetal bridge C*Me*$_2$), 26.21 and 27.41 (dioxolane C*Me*$_2$), 55.83 (OMe-1), 100.66 (acetal bridge *C*), 111.04 (dioxolane *C*Me_2). Anal. Calcd for $C_{23}H_{36}O_{12}$: C, 54.8; H, 7.2. Found: C, 54.8; H, 7.3.

Method C [$Me_2SO/DCC/H^+$]. As described in detail in ref. [1], the oxidation of **1** (5.9 g, 19.2 mmol) with Me_2SO/DCC gave, after chromatographic purification, the following products.

Methylthiomethyl (methyl 3,4-*O*-isopropylidene-β-D-*lyxo*-hexopyranosid)-2-ulo-2,6-pyranoside (**15**, 7% yield) and methyl 3,4-*O*-isopropylidene-β-D-*lyxo*-hexopyranosid-2-ulo-2,6-pyranose (**4**; a more careful chromatographic purification raised the yield from the reported [1] 73 to 83%).

Method D (TPAP / NMO). To a mixture of **1** (321 mg, 1.05 mmol) and powdered 4 Å molecular sieves (1 g) in CH_2Cl_2 (20 mL) was added pre-dried [13] 4-methylmorpholine *N*-oxide (211 mg, 1.59 mmol). After 30 min stirring, tetrapropylammonium perruthenate (16.8 mg, 5 mol%) was added and the resulting green mixture was stirred for 15 min at room temperature, when TLC (9:1 CH_2Cl_2–acetone) showed the oxidation to be complete. The mixture was filtered through Celite, diluted with CH_2Cl_2, washed with brine (2 × 10 mL), dried ($MgSO_4$), and concentrated. Column chromatography (EtOAc containing 0.1% Et_3N) of the residue afforded pure **2** (277 mg, 87%).

A solution of **2** (277 mg, 0.91 mmol) in MeOH (25 mL) and aq 60% AcOH (0.25 mL) was heated at 50 °C. After 1 h the reaction was complete (TLC, 3:7 hexane–EtOAc) and a single product (R_f 0.50) was formed. The solution was evaporated in vacuo to give pure **4** (202 mg, 96% yield), identical to the sample obtained by method C described above.

General procedures for the preparation of oximes and O-*alkyloximes of 3,4-O-isopropylidene-β-*D-lyxo-*hexopyranosid-2-ulose.*—The title compounds were obtained by the following methods.

Method A (kinetic conditions). To a solution of the pertinent ulose (1.00 mmol) in MeOH (20 mL) were added Na_2CO_3 (210 mg) and hydroxylamine hydrochloride (109 mg, 1.5 mmol) and the solution was heated at 80 °C under magnetic stirring until the starting material disappeared (TLC, 15–30 min). The solvent was evaporated in vacuo, the residue was extracted with hot EtOAc (3 × 30 mL), the organic extracts were combined and concentrated, and the crude reaction product was subjected to silica gel flash-chromatography (EtOAc).

Method B (mixed conditions). A solution of either **2** or **4** (1.00 mmol) in dry pyridine was treated with hydroxylamine hydrochloride or the pertinent *O*-alkylhydroxylamine hydrochloride (3.00 mmol) and stirred at room temperature until the starting material had completely disappeared (TLC, 24–36 h). The residue was coevaporated with toluene (4 × 40 mL) and the resulting syrup repeatedly extracted with hot EtOAc. The organic extracts were combined, dried, and evaporated, and the resulting residue was directly subjected to flash-chromatography on silica gel.

Method C (equilibrating conditions). A solution of oxime in which the *E*-form prevailed (1.00 mmol) in EtOAc (50 mL) was stirred at room temperature with pyridinium *p*-toluenesulfonate (800 mg) until an equilibrium was reached (2–3 days; TLC, EtOAc). After filtration and evaporation the residue was chromatographed (EtOAc) to give a *Z*-form enriched mixture of diastereoisomeric oximes.

The following products were obtained.

Methyl 3,4-*O*-isopropylidene-β-D-*lyxo*-hexopyranosid-2-ulose oxime (**5**). *E/Z* Diastereomeric mixtures of **5** in ratios ranging from 7:3 to 1:1 (NMR) and in yields of 75–92% were obtained by method B. An *E*-enriched mixture of **5** (*E/Z* 9:1, NMR) was obtained in 87% yield from **4** by method A.

A 2:8 *E/Z* mixture of **5** was obtained in 95% yield by method C starting from a 9:1 *E/Z* mixture of **5**. A partial separation of the two diastereomeric oximes was achieved by flash-chromatography on silica gel (3:7 hexane–EtOAc).

(*Z*)-**5**: R_f 0.37 (2:8 hexane–EtOAc); mp 198–200 °C (from EtOH); $[\alpha]_D$ −41.3° (*c* 0.8, MeOH); ^{1}H NMR (CD_3CN): see Table 1; further signals, δ 1.30 and 1.43 (2 s, 6 H,

CMe_2), 3.44 (s, 3 H, OMe); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 24.89 and 26.28 (CMe_2), 56.68 (OMe), 111.37 (CMe_2). Anal. Calcd for $C_{10}H_{17}NO_6$: C, 48.6; H, 6.9; N, 5.7. Found: C, 48.2; H, 6.7; N, 5.6.

(*E*)-**5**: R_f 0.28 (2:8 hexane–EtOAc); syrup; $[\alpha]_D$ −1.0° (*c* 2.0, MeOH); ^1H NMR (CD_3CN): see Table 1; further signals, δ 1.29 and 1.40 (2 s, 6 H, CMe_2), 3.39 (s, 3 H, OMe); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 24.76 and 26.28 (CMe_2), 55.62 (OMe), 111.37 (CMe_2). Anal. Calcd for $C_{10}H_{17}NO_6$: C, 48.6; H, 6.9; N, 5.7. Found: C, 48.4; H, 6.7; N, 5.4.

Methyl 3,4-*O*-isopropylidene-6-*O*-(1-methoxy-1-methylethyl)-β-D-*lyxo*-hexopyranosid-2-ulose oxime (**8**). A 9:1 *E*/*Z* mixture was obtained in 92% yield by method A.

(*Z*)-**8**: ^1H NMR (CD_3CN): see Table 1; further signals, δ 1.27 (s, 6 H, 2 MIP Me), 1.30 and 1.43 (2 s, 6 H, dioxolane CMe_2), 3.14 (s, 3 H, MIP OMe), 3.41 (s, 3 H, OMe-1); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 24.64 (MIP CMe_2), 24.96 and 26.22 (dioxolane CMe_2), 48.83 (MIP OMe), 56.50 (OMe-1), 101.15 (MIP CMe_2), 111.29 (dioxolane CMe_2).

(*E*)-**8**: ^1H NMR (CD_3CN): see Table 1; further signals, δ 1.29 (s, 6 H, MIP CMe_2), 1.32 and 1.42 (2 s, 6 H, dioxolane CMe_2), 3.16 (s, 3 H, MIP OMe), 3.37 (s, 3 H, OMe-1); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 24.71 (MIP CMe_2), 24.88 and 26.24 (dioxolane CMe_2), 48.73 (MIP OMe), 55.22 (OMe-1), 100.84 (MIP CMe_2), 111.24 (dioxolane CMe_2). Anal. Calcd for $C_{14}H_{25}NO_7$: C, 52.7; H, 7.9; N, 4.4. Found: C, 52.3; H, 7.7; N, 4.1.

Methyl 3,4-*O*-isopropylidene-β-D-*lyxo*-hexopyranosid-2-ulose *O*-methyloxime (**6**). Obtained by method B as a ca. 1:1 *E*/*Z* mixture in 80% yield. Flash-chromatography on silica gel (3:7 hexane–EtOAc) led to partial separation of the two oximes.

(*Z*)-**6**: syrup; R_f 0.35 (6:4 hexane–EtOAc); $[\alpha]_D$ −69.9° (*c* 1.2, MeOH); ^1H NMR (CD_3CN): see Table 1; further signals, δ 1.31 and 1.44 (2 s, 6 H, CMe_2), 3.43 (s, 3 H, OMe-1); 3.89 (s, 3 H, NOMe); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 24.96 and 26.23 (CMe_2); 56.38 (OMe-1), 63.26 (NOMe), 111.33 (CMe_2). Anal. Calcd for $C_{11}H_{19}NO_6$: C, 50.6; H, 7.3; N, 5.4. Found: C, 50.9; H, 7.6; N, 5.4.

(*E*)-**6**: syrup; R_f 0.27 (6:4 hexane–EtOAc); $[\alpha]_D$ +24.7° (*c* 0.9, $CHCl_3$); ^1H NMR (CD_3CN); see Table 1; further signals, δ 1.31 and 1.41 (2 s, 6 H, CMe_2), 3.40 (s, 3 H, OMe-1), 3.89 (s, 3 H, NOMe); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 24.84 and 26.23 (CMe_2), 55.35 (OMe-1), 62.96 (NOMe), 111.34 (CMe_2). Anal. Calcd for $C_{11}H_{19}NO_6$: C, 50.6; H, 7.3; N, 5.4. Found: C, 50.3; H, 7.0; N, 5.2.

Methyl 3,4-*O*-isopropylidene-β-D-*lyxo*-hexopyranosid-2-ulose *O*-benzyloxime (**7**). Obtained as an *E*/*Z* mixture (7:3) in 71% yield by method B. Careful chromatography on silica gel allowed a complete separation of the two oximes.

(*Z*)-**7**: R_f 0.74 (2:8 hexane–EtOAc); syrup; $[\alpha]_D$ −39.8° (*c* 1.0, $CHCl_3$); ^1H NMR (CD_3CN): see Table 1; further signals, δ 1.30 and 1.44 (2 s, 6 H, CMe_2), 3.44 (s, 3 H, OMe), 5.15 (s, 2 H, benzylic CH_2), 7.37 (m, 5 H, aromatic H); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 24.93 and 26.27 (CMe_2), 56.56 (OMe), 77.43 (benzylic CH_2), 111.39 (CMe_2), 128.85, 128.73, and 129.36 (aromatic CH), 138.62 (aromatic C). Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.5; H, 6.9; N, 4.2. Found: C, 60.2; H, 6.6; N, 4.0.

(*E*)-**7**: R_f 0.67 (2:8 hexane–EtOAc); syrup; $[\alpha]_D$ +9.3° (*c* 1.2, $CHCl_3$); ^1H NMR (CD_3CN): see Table 1; further signals, δ 1.31 and 1.42 (2 s, 6 H, CMe_2), 3.38 (s, 3 H,

OMe), 5.16 and 5.17 (AB system, 2 H, $J_{A,B}$ 12.50 Hz, benzylic CH_2), 7.37 (m, 5 H, aromatic H); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 24.95 and 26.25 (CMe_2), 57.27 (OMe), 77.28 (benzylic CH_2), 111.39 (CMe_2), 128.95, 129.01, and 129.37 (aromatic CH), 138.44 (aromatic C). Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.5; H, 6.9; N, 4.2. Found: C, 60.2; H, 6.8; N, 4.3.

*Methyl 6-O-benzoyl-3,4-O-isopropylidene-β-*D-lyxo*-hexopyranosid-2-ulose O-benzoyloxime* (**9**).—A solution of oxime **5** (290 mg, 1.17 mmol, ca. 6:4 *E/Z* mixture) and benzoyl chloride (1.5 mL, 16.6 mmol) in pyridine (7 mL) was stirred at room temperature for 4 h. The resulting mixture was diluted with CH_2Cl_2 (30 mL) and poured into ice–water. The organic phase was washed with water (4 × 10 mL), 1 M HCl, and saturated aq $NaHCO_3$, dried ($MgSO_4$), and evaporated to give a ca. 6:4 mixture of (*E/Z*)-**9** (456 mg, 90% yield). Careful chromatography of the residue on silica gel (7:3 hexane–EtOAc) separated the two *O*-benzoyloximes.

(*Z*)-**9**: R_f 0.50 (7:3 hexane–EtOAc); mp 76–79 °C (from EtOAc–hexane); $[\alpha]_D$ −12.1° (*c* 1.1, $CHCl_3$); ^1H NMR (CD_3CN): see Table 1; further signals, δ 1.42 and 1.56 (2 s, 6 H, CMe_2), 3.58 (s, 3 H, OMe), 7.43–7.70 (m, 6 H, aromatic H), 8.00–8.09 (m, 4 H, aromatic H); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 24.14 and 26.30 (CMe_2), 56.75 (OMe), 112.60 (CMe_2), 128.92 and 130.72 (aromatic C); 129.42, 129.74, 130.23, 130.44, 134.09, and 134.80 (aromatic CH), 163.47 and 166.78 (2 OCOPh). Anal. Calcd for $C_{24}H_{25}NO_8$: C, 61.2; H, 5.8; N, 3.2. Found: C, 61.5; H, 5.9; N, 2.9.

(*E*)-**9**: R_f 0.37 (7:3 hexane–EtOAc); mp 103–107 °C (from EtOAc–hexane); $[\alpha]_D$ +15.1° (*c* 0.7, $CHCl_3$); ^1H NMR (CD_3CN): see Table 1; further signals, δ 1.43 and 1.48 (2 s, 6 H, CMe_2), 3.53 (s, 3 H, OMe), 7.44–7.71 (m, 6 H, aromatic H), 7.99–8.12 (m, 4 H, aromatic H); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 25.16 and 26.49 (CMe_2), 56.11 (OMe), 112.03 (CMe_2), 129.45 and 130.83 (aromatic C), 129.53, 129.78, 130.29, 130.52, 134.18, and 134.79 (aromatic CH), 163.78 and 166.91 (2 OCOPh). Anal Calcd for $C_{24}H_{25}NO_8$: C, 61.2; H, 5.8; N, 3.2. Found: C, 61.4; H, 5.8; N, 3.0.

Lithium aluminium hydride reductions of the oximes **5**–**8**.—A solution of the pertinent oxime (2.0 mmol) in dry THF (10 mL) was slowly added under Ar, through a double-tipped needle, to a suspension of $LiAlH_4$ (450 mg) in THF (20 mL) cooled at 0 °C. The mixture was then slowly heated to 65 °C. After complete disappearance of the starting material (TLC, 2–4 h), unreacted hydride was decomposed by addition of H_2O (0.45 mL), then aq 15% NaOH (1.35 mL), and H_2O (0.45 mL), followed by 15 min stirring. The white slurry was filtered and repeatedly washed with EtOAc; the combined organic phases were dried ($MgSO_4$) and evaporated. The crude product was dissolved in dry pyridine (8 mL), treated with Ac_2O (4 mL), left overnight at room temperature, and, finally, repeatedly co-evaporated with toluene. The crude reaction mixtures were analyzed by NMR spectroscopy, and subjected to flash-chromatography over silica gel (97:3 CH_2Cl_2–MeOH). The composition of the crude mixtures and the isolated yields of acetamido derivatives **10** and **16** are collected in Table 3.

Methyl 2-acetamido-6-*O*-acetyl-2-deoxy-3,4-*O*-isopropylidene-β-D-talopyranoside (**10**); R_f 0.27 (97:3 CH_2Cl_2–MeOH); mp 112–114 °C (from EtOAc–hexane); $[\alpha]_D$ +7.7° (*c* 0.8, $CHCl_3$); ^1H NMR (CD_3CN): see Table 1; further signals, δ 1.27 and 1.42

(2 s, 6 H, CMe_2), 1.90 and 2.03 (2 s, 6 H, 2 MeCO), 3.36 (s, 3 H, OMe); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 20.95 and 23.24 (2 *Me*CO), 25.34 and 26.04 (CMe_2), 56.54 (OMe), 110.33 (CMe_2), 170.44 and 171.49 (2 Me*C*O). Anal. Calcd for $C_{14}H_{23}NO_7$: C, 53.0; H, 7.3; N, 4.4. Found: C, 52.8; H, 7.1; N, 4.3.

Methyl 2-acetamido-6-*O*-acetyl-2-deoxy-3,4-*O*-isopropylidene-β-D-galactopyranoside (**16**); R_f 0.16 (97:3 CH_2Cl_2–MeOH); mp 157–160 °C (from EtOAc–hexane); $[\alpha]_D$ +27.5° (*c* 1.0, $CHCl_3$); ^1H NMR (C_6D_6): see Table 1; further signals, δ 1.19 and 1.47 (2 s, 6 H, CMe_2), 1.56 and 1.70 (2 s, 6 H, 2 MeCO), 3.36 (s, 3 H, OMe); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 21.02 and 23.11 (2 *Me*CO), 26.47 and 28.13 (CMe_2), 57.05 (OMe), 111.03 (CMe_2), 172.80 and 173.24 (2 Me*C*O). Anal. Calcd for $C_{14}H_{23}NO_7$: C, 53.0; H, 7.3; N, 4.4. Found: C, 53.1; H, 7.2; N, 4.5.

The $LiAlH_4$ reduction of oximes **8** was performed by the previous procedure, modified in the acetylation step as follows: the crude reduction product was dissolved in MeOH (10 mL) and treated with Ac_2O (1.5 mL) until *N*-acetylation and 6-*O*-demethoxyisopropylation were complete (overnight). After evaporation of the solvent, the residue was conventionally acetylated (Ac_2O/pyr) to give a mixture of **10** and **16**, as reported in Table 3.

Diborane reduction of the O-*benzoyloxime* **9**.—A solution of **9** (ca. 6:4 *E*/*Z* mixture, 240 mg, 0.53 mmol) in dry THF (6 mL) was cooled under argon at −10 °C, treated with a commercial 1 M solution of diborane in THF (6 mL, 6 mmol), stirred 30 min at −10 °C, allowed to reach room temperature, and further stirred until TLC analysis (10:3 EtOAc–MeOH) showed the complete disappearance of the starting material (3 h). MeOH (5 mL) was added to the reaction mixture, followed, after 15 min, by Ac_2O (2.5 mL); after an additional stirring (1.5 h), the solution was treated with an excess of Amberlite IRA-743 resin (1.0 mL) and stirred for 30 min. The resin was filtered off and washed with MeOH, and the solution evaporated to dryness. TLC analysis of the crude reaction product (EtOAc) revealed the presence of a principal component (**11**, R_f 0.30) and a less mobile byproduct (**23**, R_f 0.14), which were completely separated through silica gel column chromatography (3:7 hexane–EtOAc).

Methyl 2-acetamido-6-*O*-benzoyl-2-deoxy-3,4-*O*-isopropylidene-β-D-talopyranoside (**11**) (131 mg, 65% yield); syrup; R_f 0.30 (EtOAc); $[\alpha]_D$ +3.8° (*c* 0.88, $CHCl_3$); ^1H NMR (CD_3CN): see Table 1; further signals, δ 1.28 and 1.43 (2 s, 6 H, CMe_2), 1.94 (s, 3 H, MeCO), 3.36 (s, 3 H, OMe), 6.35 (d, 1 H, $J_{2,NH}$ 9.35 Hz, NH), 7.44–7.66 (m, 3 H, aromatic H), 7.99–8.04 (m, 2 H, aromatic H); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 23.29 (*Me*CO), 25.41 and 26.08 (CMe_2), 56.57 (OMe), 110.37 (CMe_2), 129.56, 130.36, and 134.19 (aromatic CH), 130.96 (aromatic C), 166.96 (OCOPh), 170.55 (Me*C*O). Anal. Calcd for $C_{19}H_{25}NO_7$: C, 60.2; H, 6.6; N, 3.7. Found: C, 59.7; H, 6.1; N, 3.5.

Methyl 2-acetamido-6-*O*-benzoyl-2-deoxy-4-*O*-isopropyl-β-D-talopyranoside (**20**) (40 mg, 20% yield); crude syrup; R_f 0.14 (EtOAc); ^1H NMR (CD_3CN): δ 1.07 and 1.18 (2 d, 6 H, $CHMe_2$), 1.93 (s, 3 H, MeCO), 3.36 (s, 3 H, OMe), 3.76 (m, 1 H, H-4), 3.80 (m, 1 H, H-5), 3.82 (m, 1 H, H-3), 3.87 (m, 1 H, *J* 6.14 Hz, $CHMe_2$), 4.27 (m, 1 H, H-2), 4.40 (d, 1 H, $J_{1,2}$ 1.65 Hz, H-1), 4.40 (m, 1 H, $J_{6a,6b}$ 11.15, $J_{5,6b}$ 5.30 Hz, H-6b), 4.47 (m, 1 H, $J_{5,6a}$ 7.30 Hz, H-6a), 7.60–7.98 (m, 5 H, aromatic H); ^{13}C NMR (CD_3CN): δ 22.07 and 23.00 ($CHMe_2$), 23.63 (*Me*CO), 53.14 (C-2), 57.05 (OMe), 64.39 (C-6),

68.75 (C-4), 73.68 (C-5), 74.45 (C-3), 74.64 (*CH*Me_2), 101.96 (C-1), 129.65, 130.27, and 134.27 (aromatic CH), 130.50 (aromatic C), 167.53 (O*C*OPh), 173.63 (Me*CO*).

Compound **20** was conventionally acetylated to give quantitatively **21**, as a white solid; R_f 0.36 (EtOAc); mp 134–136 °C (from EtOAc–hexane); $[\alpha]_D$ −35.2° (*c* 0.5, $CHCl_3$); ^{1}H NMR (CD_3CN): see Table 1; further signals, δ 1.12 and 1.23 (2 d, 6 H, CH*Me*$_2$), 1.90 and 2.01 (2 s, 6 H, 2 MeCO), 3.40 (s, 3 H, OMe), 3.82 (m, 1 H, *J* 6.10 Hz, *CH*Me_2), 7.62–8.00 (m, 5 H, aromatic H); ^{13}C NMR (CD_3CN): see Table 2; further signals, δ 21.04 and 23.51 (2 *Me*CO), 22.28 and 23.17 (CH*Me*$_2$), 56.87 (OMe-1), 74.85 (*CH*Me_2), 129.62, 130.28, and 134.25 (aromatic CH), 130.92 (aromatic C), 166.82 (O*C*OPh), 170.63 (2 Me*CO*). Anal. Calcd for $C_{21}H_{29}NO_8$: C, 59.6; H, 6.9; N, 3.3. Found: C, 59.4; H, 6.7; N, 3.0.

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