

## Towards the Synthesis of 1-Deoxy-1-nitropiperidinoses

by Marie-Pierre Collin and Andrea Vasella\*

Laboratorium für Organische Chemie, ETH Zürich, HCI, Wolfgang Pauli-Strasse 10, CH-8093 Zürich  
(e-mail: vasella@org.chem.ethz.ch)

In the course of the first of several attempts to elaborate methods for the synthesis of 1-nitropiperidinoses, lincosamine was transformed into lactam **6** via hemiacetal **1**, lactone **2**, amide **3**, oxo amide **4**, and its cyclic tautomer **5**. Treatment of the *N*-Boc-protected lactam oxime **9**, obtained from lactam **6**, with brominating agents failed to provide the bromonitroso carbamate **10**. The *N*-Boc-protected lactam **13** derived from **6** was reduced to hemiacetal **14**, but the corresponding *N*-Boc-aminooxime did not tautomerise to the *C(I)*-hydroxylamine, and nitron **17**, a potential precursor of the nitropiperidine **12**, was not formed. Oxidation of the anomeric azide **20** with  $\text{HOF} \cdot \text{MeCN}$  failed to provide the expected nitropiperidine **21**. The phosphinimines **22** derived from **20** did not react with  $\text{O}_3$ . In the next approach to 1-nitropiperidinoses, we treated the *N*-Boc-protected hemiacetal **25**, obtained from the known gluconolactam **23** with *N*-benzylhydroxylamine. The resulting nitron **26** exists in equilibrium with the anomeric *N*-benzyl-glycosylhydroxylamine that was oxidized to the anomeric nitron **28**. Ozonolysis of **28** led to the hemiacetal **25**, resulting from the desired, highly reactive protected nitropiperidine **29**, that was evidenced by an IR band at  $1561\text{ cm}^{-1}$ . Similarly to the synthesis of nitron **26**, reaction of the *N*-tosyl-protected hemiacetal **31** with *N*-benzylhydroxylamine and oxidation provided the anomeric *N*-benzylhydroxylamines **33** via the *p*-toluenesulfonamido nitron **32**. Their oxidation with  $\text{MnO}_2$  led to the anomeric nitron **34**. Ozonolysis of **34** as evidenced by  $^1\text{H-NMR}$  and ReactIR spectroscopy led to the highly reactive nitropiperidine **35**. Like **29**, **35** was transformed during workup, and only the hemiacetal **31** was isolated. The similarly prepared lincosamine-derived nitron **17** was subjected to ReactIR-monitored ozonolysis that evidenced the formation of the protected nitropiperidine **12**, but only led to the isolation of **14**. The facile transformation of the nitropiperidinoses to hemiacetals is rationalised by heterolysis of the anomeric C,N bond, recombination of the ion pair, and denitrosation of the resulting anomeric nitrite by a nucleophile. Attempts to convert the 1-deoxy-1-nitropiperidine **35** to uloses **43** by base-catalysed *Michael* additions or *Henry* reactions were unsuccessful.

**Introduction.** – 1-Deoxy-1-nitropiperidinoses, carbohydrates where the ring O-atom of a nitropyranose is replaced by an NH or NR group, are not known. These nitropiperidinoses should be deprotonated under mild conditions, without  $\beta$ -elimination, resulting in an inversion of polarity. This should allow elongating the C-chain at the anomeric centre by a *Michael* addition, or reaction with an aldehyde, similarly as it is known for 1-deoxy-1-nitropyranoses [1–4]. It appeared necessary to protect the ring N-atom of nitropiperidinoses by a strong  $\pi$ - and  $\sigma$ -acceptor substituent to prevent the intrinsically facile heterolysis of the anomeric C,N bond, generating a nitrite anion and an immonium cation. An even more readily occurring solvolysis of a chain-elongated, *N*-protected nitropiperidine should allow introduction of a second substituent at the anomeric centre, *viz.*, a hetero-nucleophile, or a C-nucleophile derived from a weakly basic carbanion, as in a *Kornblum* reaction [5]. Thus, 1-deoxy-1-*C*-nitropiperidinoses

possess a high potential for the synthesis of a variety of piperidinoses modified at C(1) and C(2), the introduction of substituents at the ring N-atom adding a further dimension of diversity.

Naturally occurring [6] and synthetic piperidine derivatives, and other saccharide mimics possessing a ring N-atom, such as pyrrolidines, indolizidines, pyrrolizidines, and nortropanes, with nojirimycin and deoxynojirimycin as prototypes, were thoroughly studied as glycosidase inhibitors [7], and their chemistry has been reviewed periodically [6][8]. A range of biological properties of piperidinoses and other N-containing sugars are known, beyond their activity as glycosidase inhibitors [9].

For these reasons, we considered it worthwhile to explore the synthesis and transformations of 1-deoxy-1-nitropiperidinoses, in spite of the obvious obstacle of the facile solvolysis of the anomeric C,N bond. We had a particular interest in exploring their application to the synthesis of novel lincomycin analogues [10][11]. In spite of the need for new antibiotics, pyranosyl moieties of carbohydrate-derived antibiotics have not, to the best of our knowledge, been replaced by piperidiniosyl analogues. Chain-elongated, piperidine-derived analogues of lincomycin appeared attractive. Molecular modelling<sup>1)</sup> of the crystal structure of the 50S ribosomal subunit of the eubacterium *Deinococcus radiodurans* [12] in complex with clindamycin revealed a cavity around C(1) that allows introducing two substituents at the anomeric centre besides replacing C(5)–O by a C(5)–NH or NR group (R = alkyl, acyl, sulfonyl).

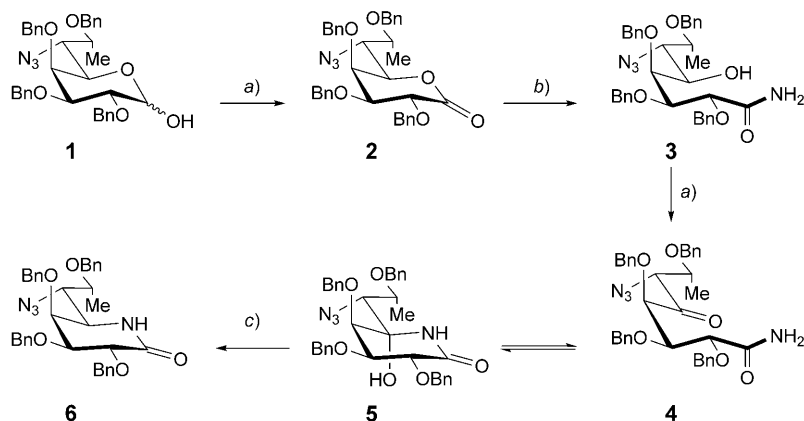
We planned to prepare such lincomycin analogues *via* an intermediate nitropiperidine, to be synthesized by analogy to the known methods for the preparation of nitropyranoses [1][2]. The first route should proceed *via* an *N*-Boc-protected lincosamine-derived 1,5-lactam. We considered that the transformation of such a lactam into the corresponding hydroximolactam [13], followed by treatment with Br<sub>2</sub>, oxidation of the intermediate bromo-nitroso carbamate to the bromo-nitro carbamate, and debromination should lead to the desired *N*-Boc-protected nitropiperidines. According to the alternative route [3], we planned to reduce the *N*-Boc-protected lactam to an *N*-protected piperidine and transform it into an *N*-(acylamino)-alkylnitrone. Ozonolysis of this nitrone should lead to an *N*-Boc-protected nitropiperidine.

**Synthesis.** – Following the first of the above mentioned methods for the synthesis of nitropyranoses, we prepared the required lincosamine-derived lactam **6** (*Scheme 1*) from the known protected *galacto*-octopyranose **1** [11] according to a method developed by our group [13][14] and by others [15][16]. Oxidation of **1** with Dess – Martin's periodinane led to the lactone **2**. Ammonolysis of crude **2** gave amide **3** that was oxidized with Dess – Martin's periodinane to the oxo amide **4**. *In situ* acid-catalysed tautomerisation to **5** and reduction with NaCNBH<sub>3</sub> led to the desired lactam **6**. It was purified by column chromatography, and obtained as a colourless oil in 60% overall yield on a 30-g scale.

To prepare the required lactam-oxime intermediate **9** (*Scheme 2*; cf. [13][17]), we treated lactam **6** with Lawesson's reagent. The expected thiolactam **7** was isolated in a yield of 75%. *N*-Boc Protection of **7**, followed by treatment of the resulting

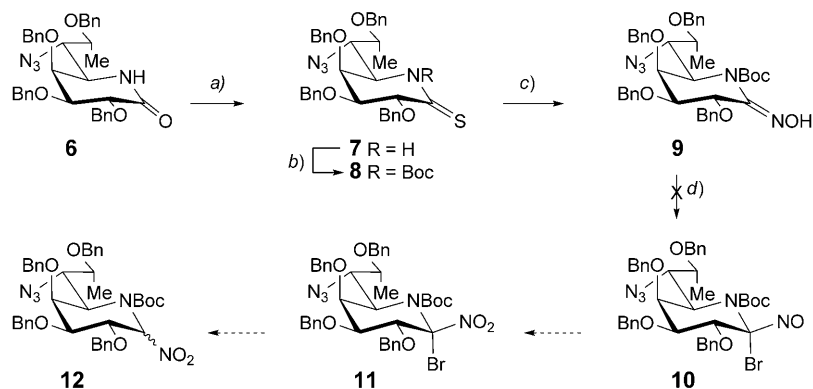
<sup>1)</sup> Molecular modelling was performed using the Moloc program. We thank Paul Gerber, Gerber Molecular Design, for access to the programme.

Scheme 1



a) Dess–Martin's periodinane,  $\text{CH}_2\text{Cl}_2$ . b)  $\text{NH}_3$ ,  $\text{CH}_2\text{Cl}_2$ ,  $-40^\circ$  to  $25^\circ$ . c)  $\text{HCO}_2\text{H}$ ,  $\text{NaBH}_3\text{CN}$ ,  $\text{MeCN}$ ,  $70^\circ$ ; 58% from **1**.

Scheme 2



a) Lawesson's reagent, toluene,  $60^\circ$ ; 75%. b)  $\text{Boc}_2\text{O}$ , 4-(Dimethylamino)pyridine (DMAP),  $\text{CH}_2\text{Cl}_2$ . c)  $\text{NH}_2\text{OH} \cdot \text{HCl}$ ,  $\text{NaHCO}_3$ ,  $\text{MeOH}$ ; 90% from **7**. d) Conditions tried: 1.  $\text{Br}_2$ ,  $\text{NaOH}$ ,  $0^\circ$ ; 2.  $\text{Br}_2$ ,  $\text{Py}$ ,  $-78^\circ$  to  $25^\circ$ ; 3. *N*-bromoacetamide,  $\text{ZnO}$ ,  $\text{H}_2\text{O}$ ,  $\text{CH}_2\text{Cl}_2$ ,  $25^\circ$ ; 4. *N*-bromosuccinimide,  $\text{NaHCO}_3$ ,  $\text{CH}_2\text{Cl}_2$ ,  $\text{H}_2\text{O}$ ,  $25^\circ$ ; 5. oxone,  $\text{KBr}$ , *Alox*,  $\text{CHCl}_3$ ,  $45^\circ$  to reflux.

*N*-Boc-thiolactam **8**<sup>2)</sup> with  $\text{NH}_2\text{OH} \cdot \text{HCl}$  yielded 90% of the lactam oxime **9** (Scheme 2).

The coupling constants for the pyranose ring of lactone **2**, lactam **6**, thiolactam **7**, and lactam oxime **9** in  $\text{CDCl}_3$  solution, compiled in Table 1 (*Exper. Part*), evidence for all these compounds a preferred  $^4\text{C}_1$  conformation. The equatorial orientation of the

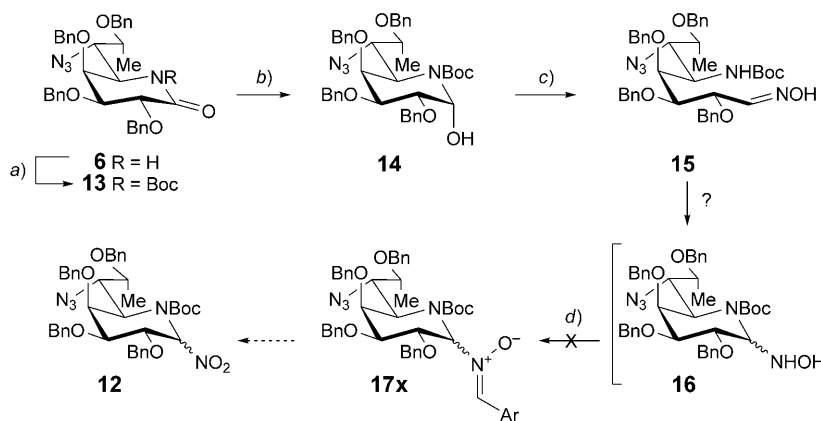
<sup>2)</sup> Attempts to isolate thiolactam **8** resulted in decomposition; it was used directly for the synthesis of **9**.

side chain of the *N*-Boc-protected lactam oxime **9** is surprising in view of the allylic strain [18]. It is tempting to rationalise the ring conformation of **9** by postulating a (*Z*)-configuration and an intramolecular H-bond to the *N*-alkoxy carbonyl group. There is, however, no evidence for this H-bond, and the related *N*-Boc-protected piperidines **18** and **19** (see below *Scheme 4*) that cannot form such a H-bond (and possess an axial C(1)OAc group) also adopt a  $^4C_1$  conformation.

We had expected bromination of **9** to yield the bromo-nitroso intermediate **10** that we intended to oxidize to the bromo-nitro carbamate **11** and then debrominate to the desired nitropiperidine **12**. Unfortunately, all attempts to transform **9** into the bromo-nitroso carbamate **10** (*Scheme 2*) failed to provide the desired product. Although **9** was consumed, TLC revealed a complex mixture of products that could not be separated. No blue or blue-green colour characteristic of nitroso compounds was ever observed, and the IR spectrum of the reaction mixture did not show any nitroso band at  $1560\text{ cm}^{-1}$ .

In a second approach, we first aimed at transforming the *N*-Boc-protected lactam **13** to one of the nitrones **17x** (*Scheme 3*). *N*-Boc protection of lactam **6** yielded 80% of the desired **13** that was reduced with *Super-Hydride*<sup>®</sup> to the *N,O*-hemiacetal **14**. Treating **14** with  $\text{NH}_2\text{OH} \cdot \text{HCl}$  led to a 7:3 (*E/Z*)-mixture of the *N*-Boc-protected amino oximes **15**<sup>3)</sup> (85% from **13**).

Scheme 3



a)  $\text{Boc}_2\text{O}$  ( $\text{Boc} = (\text{tert-butoxy})\text{carbonyl}$ ), DMAP,  $\text{ClCH}_2\text{CH}_2\text{Cl}$ ,  $70^\circ$ ; 80%. b) *Super-Hydride*<sup>®</sup> (1.0M  $\text{LiEt}_3\text{BH}$  in THF), THF. c)  $\text{NH}_2\text{OH} \cdot \text{HCl}$ ,  $\text{NaHCO}_3$ , EtOH; 85% from **13**.

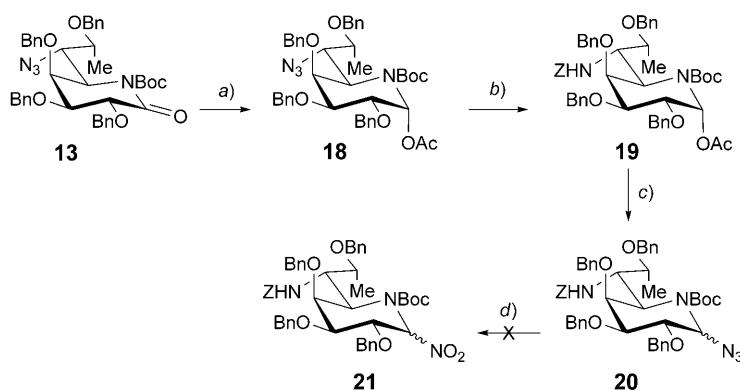
The  $^1\text{H}$ -NMR spectrum of the *N*-Boc-protected lactam **13** in  $\text{CDCl}_3$  shows a *W* coupling of 1.5 Hz between  $\text{H}-\text{C}(3)$  and  $\text{H}-\text{C}(5)$ . Together with the other relevant coupling constants (*Table 1* in *Exper. Part*), this suggests a conformational equilibrium with contributions of  $E_4$ ,  $^3H_4$ , and  $^2S_4$ . The configuration of **14** is evidenced by the  $J(1,2)$  value of 3.6 Hz and the downfield shift of  $\text{H}-\text{C}(5)$ ; the ring conformation is close to  $^4C_1$ .

<sup>3)</sup> The  $^1\text{H}$ -NMR spectrum of **15** in  $(\text{D}_6)\text{DMSO}$  at  $100^\circ$  shows the  $\text{H}-\text{C}(1)$  signal of the (*E*)-oxime at  $\delta$  7.44 ppm (*d*,  $J = 7.5\text{ Hz}$ , 0.7 H), while  $\text{H}-\text{C}(1)$  of the (*Z*)-oxime resonates at 6.95 ppm (*d*,  $J = 6.5\text{ Hz}$ , 0.3 H). The  $^1\text{H}$ -NMR spectrum did not show any signal of the cyclic tautomer **16**.

The oximes **15** did not react with benzaldehyde, 4-chlorobenzaldehyde, or the more highly electrophilic 4-nitrobenzaldehyde under neutral, acidic, or basic conditions to form a desired nitrone **17x**. It appeared that the *N*-Boc protecting group significantly reduced the nucleophilicity of the N-atom, preventing tautomerisation to the cyclic hydroxylamine **16** and condensation with the aldehydes.

In view of this result, we modified our approach. Recently, Carmeli and Rozen have described the oxidation of alkyl azides to NO<sub>2</sub> derivatives by a HOF·MeCN complex [19]. To apply this method to lincosamine, we had to replace the N<sub>3</sub> group at C(6) by a NHCbz group, and to synthesise glycosyl azide **20** as precursor of the desired nitro derivative (*Scheme 4*). Azide **20** was prepared from lactam **13** that was reduced to the *N,O*-hemiacetal, and acetylated to yield 90% of **18** (*Scheme 4*). This azido acetate was reduced with propane-1,3-dithiol in a pyridine/Et<sub>3</sub>N/H<sub>2</sub>O mixture [20], and the resulting amine was *N*-(benzyloxy)carbonylated to **19** (75%). Treatment of **19** with TMS-N<sub>3</sub> and BF<sub>3</sub>·OEt<sub>2</sub> [21] yielded 83% of the glycosyl azides **20**. The <sup>1</sup>H-NMR spectra of **18** and **19** in (D<sub>6</sub>)DMSO evidence a very similar <sup>4</sup>C<sub>1</sub> conformation. The α-D-configuration of **18** and **19** was deduced from *J*(1,2) = 4.2 Hz, while the spectrum of **20** in (D<sub>6</sub>)DMSO, recorded at 100°, evidenced a mixture of rotamers that precluded the determination of the anomeric configuration.

Scheme 4

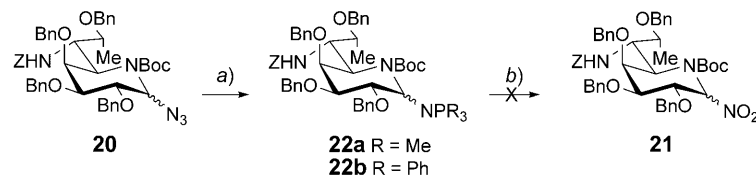


a) 1. Super-Hydride®, THF, 0°; 2. Ac<sub>2</sub>O, DMAP, Et<sub>3</sub>N, CH<sub>2</sub>Cl<sub>2</sub>; 90%. b) 1. Propane-1,3-dithiol, Et<sub>3</sub>N, Py, H<sub>2</sub>O; 2. CbzCl (Cbz = (benzyloxy)carbonyl), Et<sub>3</sub>N, CH<sub>2</sub>Cl<sub>2</sub>; 75%. c) Me<sub>3</sub>SiN<sub>3</sub> (TMS-N<sub>3</sub>), BF<sub>3</sub>·OEt<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>; 83%. d) HOF·MeCN, CHCl<sub>3</sub>.

Numerous attempts to oxidise azide **20** with HOF·MeCN failed to provide the desired nitro derivative **21**. Analysis of the reaction mixture by IR spectroscopy did not show the characteristic bands of a NO<sub>2</sub> group at 1560 and at 1360 cm<sup>-1</sup>.

Our next approach to the desired 1-nitropiperidine was based upon the ozonolysis of phosphimines, according to a method reported by Corey *et al.* [22]. Me<sub>3</sub>P or Ph<sub>3</sub>P transformed the azide **20** to the methyl and phenyl phosphimines **22a** and **22b**, respectively. Solutions of the phosphimines in MeOH or CH<sub>2</sub>Cl<sub>2</sub> were treated with O<sub>3</sub>, and the reaction was followed by IR spectroscopy, monitoring the disappearance of the N<sub>3</sub> band at 2102 cm<sup>-1</sup>. However, under these reaction conditions the phosphimines **22** did not react with O<sub>3</sub> (*Scheme 5*).

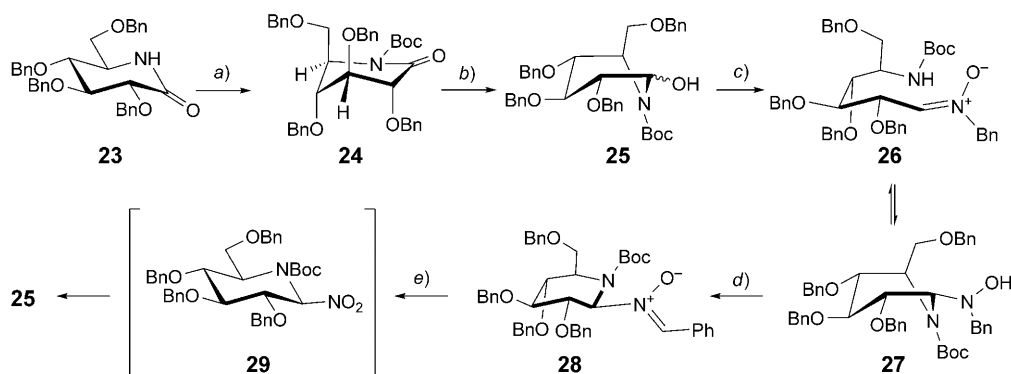
Scheme 5



a)  $\text{R}_3\text{P}$  (R = Me, Ph), THF. b)  $\text{O}_3$ ,  $\text{CH}_2\text{Cl}_2$  or MeOH,  $-78^\circ$ .

To avoid a conceivable influence of the *galacto*-configuration upon our attempts of obtaining 1-nitropiperidinoses (*cf.* [23]), it appeared commendable to explore further methods using the known 2,3,4,6-tetra-*O*-benzyl-gluconolactam **23** [14] (Scheme 6). We aimed at treating the known *N,O*-hemiacetal **25** [24], obtained by reduction of the *N*-protected gluconolactam **24**, with  $\text{BnNHOH} \cdot \text{HCl}$  to obtain an open-chain nitrone **26**. This nitrone is significantly more highly electrophilic than oxime **15**, and should thus equilibrate with its cyclic tautomer, the *N*-Bn-hydroxylamine **27** (Scheme 6) that we hoped to oxidise to the cyclic nitrone **28** and further to the desired nitropiperidine **29**.

Scheme 6



a)  $\text{Boc}_2\text{O}$ , DMAP, MeCN; 88% [24]. b)  $\text{NaBH}_4$ , 1N HCl to pH 6, EtOH; 75% [24]. c)  $\text{BnNHOH}$ , Py,  $60^\circ$ ; 80%. d)  $\text{MnO}_2$ ,  $\text{ClCH}_2\text{CH}_2\text{Cl}$ , reflux; 90%. e)  $\text{O}_3$ ,  $\text{CH}_2\text{Cl}_2$ ,  $-78^\circ$ .

The protected *N,O*-hemiacetal **25** was prepared from the *O*-benzylated gluconolactam **23** by *N*-Boc protection (88%), followed by reduction with  $\text{NaBH}_4$  at pH 6 in 75% yield [24] (Scheme 6). Reaction of **25** with  $\text{BnNHOH}$  in dry pyridine yielded 75% of a 1 : 1 mixture of the open-chain nitrone **26** and its cyclic tautomer, hydroxylamine **27** [25–27]<sup>4</sup>). Treatment of the mixture **26/27** with  $\text{MnO}_2$  oxidised **27** to the cyclic nitrone **28** that was isolated in a yield of 90%, evidencing the shift of the equilibrium  $\text{26} \rightleftharpoons \text{27}$  towards the *N*-benzyl hydroxylamine **27**. Not surprisingly, oxidation of **27** involves the benzylic  $\text{CH}_2$  group, as reported for similar compounds [28]. The  $\beta$ -D-configuration of

<sup>4</sup>) Sharp  $^1\text{H}$ -NMR signals were observed in  $(\text{D}_6)\text{DMSO}$  at  $100^\circ$ . Under these conditions, only signals for **27** were observed.

the anomeric centre and the (*Z*)-configuration of the nitrone were established by X-ray crystal structure analysis; the conformation will be discussed below. As expected, the broad peaks in the  $^1\text{H-NMR}$  spectra of the carbamate **28** (in  $\text{CDCl}_3$ ) at ambient temperature reveal the presence of rotamers. Sharp  $^1\text{H-NMR}$  signals of **28** were observed only at  $100^\circ$  in ( $\text{D}_6$ )DMSO. Although the  $^1\text{H-NMR}$  spectra of the reaction mixture resulting from ozonolysis at  $-78^\circ$  did not show sharp peaks, we refrained from recording the spectra at a higher temperature, considering the presumed facile solvolysis of the expected 1-nitropiperidinoses. The only isolated products obtained by ozonolysis of **28** at  $-78^\circ$  are indeed the known *N,O*-hemiacetals **25** [24] suggesting that the 1-nitropiperidinose **29** was formed, but rapidly solvolysed upon warming to ambient temperature and/or during workup.

The conformation of the anomers of **25** – the  $B_{3,N}$  conformation of the  $\alpha$ -D anomer is shown in *Scheme 6* – was determined before [24].

Crystals of the *N*-Boc-protected nitrone **28** were obtained by slow evaporation of a solution in  $\text{MeOH}/\text{H}_2\text{O}$ , and their structure was established by X-ray analysis<sup>5)</sup> (*Fig.*), revealing the  $\beta$ -D- and (*Z*)-configuration, and the  $^2S_N$  conformation that lifts the oxyimino and the substituent at C(5) out of the plane of the *N*-Boc group and is also preferred in  $\text{CDCl}_3$  solution.

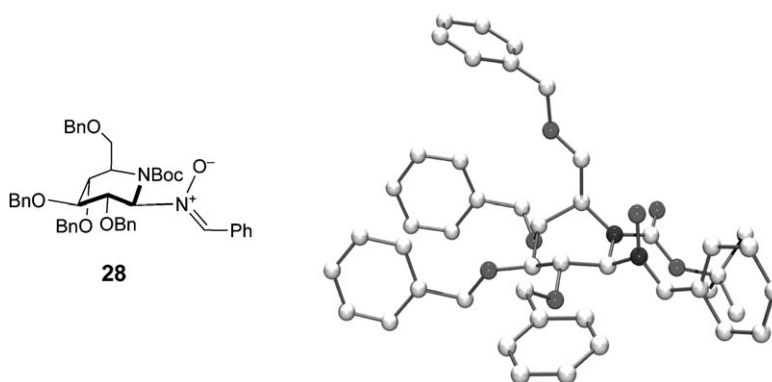


Figure. Ball-and-stick representation of the crystal structure of the nitrone **28**

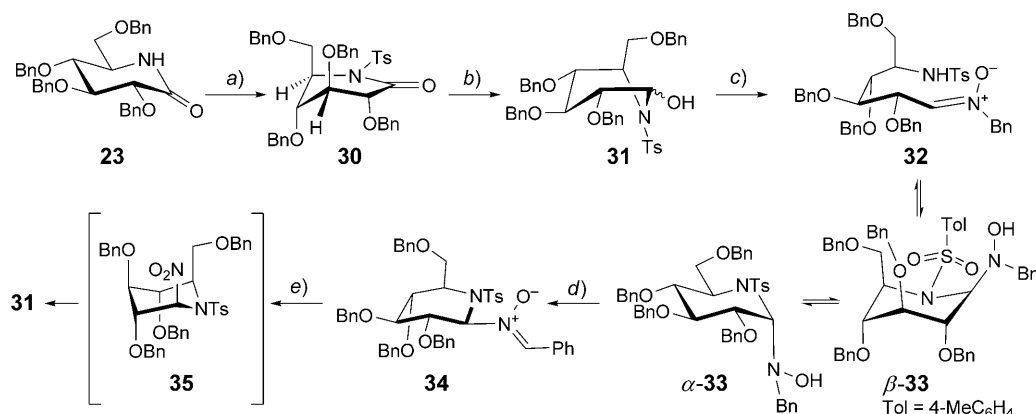
As it proved difficult to *in situ* analyse the product of ozonolysis by  $^1\text{H-NMR}$  spectroscopy, we monitored the ozonolysis of nitrone **28** by ReactIR at  $-78^\circ$ . The IR spectrum of the *N*-Boc-protected nitrone **28** is characterised by a band at  $1717\text{ cm}^{-1}$ , typical of a carbamoyl group, while the  $\text{N}=\text{CH}$  nitrone band (at *ca.*  $1600\text{ cm}^{-1}$ ) was weak, so that the reaction could not be monitored by following the disappearance of this band. Formation of the *N*-Boc-protected (presumably  $\beta$ -D-configured) 1-nitropiperidinose **29** is, however, supported by the appearance of a band at  $1568\text{ cm}^{-1}$ , characteristic of a  $\text{NO}_2$  group, and of a  $\text{C}=\text{O}$  band at  $1701\text{ cm}^{-1}$  assigned to  $\text{PhCHO}$ .

<sup>5)</sup> The crystallographic data have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-699259. Copies of the data can be obtained free of charge via [http://www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif) (or from the CCDC, 12 Union Road, Cambridge CB21EZ (fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk).

The difficulty of analysing the product of ozonolysis by  $^1\text{H}$ -NMR spectroscopy (on account of the rotamers) and the facile solvolysis of the *bona fide* **29** showed that the Boc group is not an appropriate *N*-protecting group. It was, therefore, substituted by the Ts group, although it has been evidenced that a *N*-sulfonyl group is rather a weaker electron acceptor than a *N*-carbonyl group [29]. The Ts group has, however, the advantage of not giving rise to discernible rotamers.

The *O*-benzylated gluconolactam **23** was *N*-tosylated by treatment with BuLi and TsCl [21] to yield 77% of the *N*-Ts lactam **30** (Scheme 7). Similarly as described for the Boc-protected gluconolactam **24** (Scheme 6), **30** was reduced with DIBAL-H to the *N,O*-hemiacetals **31** (85%). The reaction of **31** with BnNHOH in dry pyridine (*cf.* [25][26][28]) provided, after filtration through silica gel, mostly a *ca.* 3:1  $\beta$ -D/ $\alpha$ -D-mixture of the anomeric hydroxylamines  $\alpha$ -**33**/ $\beta$ -**33** and small amounts of the open-chain nitrone **32** that correlated with a very polar spot on the TLC. The interpretation of the  $^1\text{H}$ -NMR spectrum of the mixture **32/33** is based on  $J(1,2)$  of 2.0 Hz for the major ( $\beta$ -D), and of 7.2 Hz for the minor ( $\alpha$ -D) isomer, evidencing a flattening of the chair for  $\beta$ -**33**. One large (8.0 Hz) and one small (2.0 Hz)  $J(5,6)$  value of  $\beta$ -**33** is in agreement with a pseudoaxial  $\text{CH}_2\text{OBn}$  group, shifted to higher fields by the tolyl group. The minor  $\alpha$ -**33** is characterized by two similar  $J(5,6)$  values, denoting an equatorial  $\text{CH}_2\text{OBn}$  group. Both H–C(1) are equatorial, and thus shifted to lower field.

Scheme 7



a) BuLi, TsCl, DMAP, THF,  $-78^\circ$  to  $0^\circ$ ; 77%. b) Diisobutylaluminum hydride (DIBAL-H), toluene,  $0^\circ$ ; 85%. c) BnNHOH, Py,  $100^\circ$ . d)  $\text{MnO}_2$ ,  $\text{ClCH}_2\text{CH}_2\text{Cl}$ , reflux; 78% from **30**. e)  $\text{O}_3$ ,  $\text{CH}_2\text{Cl}_2$ ,  $-78^\circ$ .

By comparison to the *N*-Boc-protected analogues **26/27**, the nitronine  $\rightleftharpoons$  hydroxylamine equilibrium, **32**  $\rightleftharpoons$  **33**, is displaced in favour of **33**, in agreement with the weaker electron-acceptor properties of the Ts group (*cf.* [29]) and, conceivably, less-distabilizing steric interactions. Oxidation of the mixture **32/33** with  $\text{MnO}_2$  [28] led to the cyclic nitronine **34** in a yield of 78%.

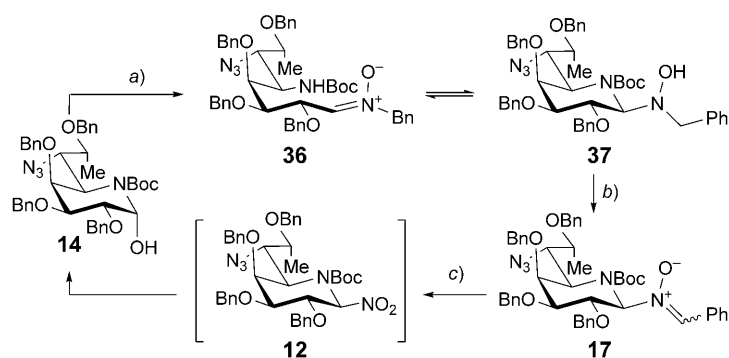
Similarly as in the *N*-Boc-protected series, the pyranose ring of the *N*-Ts lactam **30** exists as mixture of equilibrating  $^3H_4$  and  $^2S_N$  conformers, as evidenced by the coupling constants (Table 2 in *Exper. Part*) and particularly by the *W* coupling ( $J =$

1.5 Hz) between H–C(3) and H–C(5). The preferred conformation of the *N*-Ts nitrone **34** is  $^2S_N$ , avoiding the allylic strain resulting from destabilizing interactions of the *N*-Ts group with an equatorial side chain at C(5) and the equatorial nitronyl substituent. The pyranose ring of  $\alpha$ -D-**31** in  $CDCl_3$  adopts a  $B_{3,N}$  conformation, as depicted in *Scheme 7*, while  $\beta$ -D-**31** most likely adopts a conformational equilibrium between  $^1C_4$  and  $B_{3,N}$ . The large  $J(1,OH)$  value of 11.8 Hz suggests an intramolecular H-bond with the pseudoaxial C(3)OBn group of the  $^1C_4$  and the C(6)OBn group of the  $B_{3,N}$  conformer.

Ozonolysis of the *N*-Ts nitrone **34** at  $-78^\circ$  in  $CH_2Cl_2$  led to the *N,O*-hemiacetals **31**, similarly as observed for the *N*-Boc-protected analogue **28**, again suggesting that a 1-nitropiperidinose (**35**) was formed *in situ*, but solvolysed upon increasing the temperature. Ozonolysis of **34** in  $CD_2Cl_2$  at  $-78^\circ$  was thus monitored by  $^1H$ -NMR spectroscopy, starting at  $-78^\circ$  and slowly raising the temperature to  $-10^\circ$ . The  $\beta$ -D-nitron **34** was characterized by a chemical shift for H–C(1) of 5.45 ppm ( $J(1,2) = 7.9$  Hz), while the H–C(1) signal of the ozonolysis product at  $-10^\circ$  was shifted downfield by 0.6 ppm ( $\delta$  6.05 ppm,  $J(1,2) = 3.6$  Hz), and evidenced that a single product was formed. This chemical shift is in agreement with those observed for nitropyranses [1][3].  $J(1,2)$  of 3.6 Hz for the 1-nitropiperidinose **35** evidences either that the conformation of the piperidinose ring changed from  $^2S_N$  towards  $^1C_4$ , or that the expected 1-nitropiperidinose isomerised to the  $\alpha$ -D-anomer. No signal of the hydrolysis product **31** of **35** was observed up to  $-10^\circ$ , indicating that the 1-nitropiperidinose **35** is stable up to that temperature. Solvolysis appears to occur upon warming to ambient temperature. The ozonolysis of the *N*-tosyl nitrone **34** was also followed by ReactIR. A comparison of the IR spectra of the nitron and of the ozonolysis mixture revealed new bands of both the  $NO_2$  group ( $1569\text{ cm}^{-1}$ ) and the  $C=O$  group of PhCHO ( $1701\text{ cm}^{-1}$ ).

The method developed for the synthesis of 1-nitropiperidinose from gluconolactam **23** was then tested on the *N*-Boc-protected *N,O*-hemiacetal **14** derived from lincomycin (*Scheme 8*). The hemiacetal **14** reacted with BnNHOH in BuOH to give exclusively nitron **36** as a single isomer in 90% yield. Attempted oxidation of **36** with

Scheme 8



a) BnNHOH, BuOH,  $80^\circ$ ; 90%. b) LiI,  $PbO_2$ , Py, toluene,  $60^\circ$ ; 63%. c)  $O_3$ ,  $CH_2Cl_2$ ,  $-78^\circ$ .

MnO<sub>2</sub> in refluxing ClCH<sub>2</sub>CH<sub>2</sub>Cl did not lead to the desired cyclic nitrone **17**, and starting material was recovered. We had to conclude that, under these reaction conditions, nitrone **36** did not cyclise to the cyclic hydroxylamine **37**. To favour the cyclisation, we explored activating **36** with a *Lewis* acid [30]. Treatment of **36** with MnO<sub>2</sub> and LiI in toluene and pyridine led indeed to the cyclic nitrone **17** in a yield of 30–35%. We assume that the Li<sup>+</sup> cation coordinates with the O<sup>–</sup> of nitrone **36**, enhancing its electrophilic properties, and favouring cyclisation to the hydroxylamine **37** that is oxidised to nitrone **17**. As it is conceivable that LiI is oxidized to I<sub>2</sub> that might act as the oxidant, we treated nitrone **36** with I<sub>2</sub> in toluene and pyridine at 60°, but did not observe the desired nitrone **17**.

We screened *Lewis* acids, oxidising agents, and bases to optimise the oxidation of **36** to the nitrone **17**. The best result was obtained with 5 equiv. of PbO<sub>2</sub> and 2 equiv. of LiI in toluene/pyridine 2:1 at 60°, yielding 63% of a 1:2 mixture of two diastereoisomeric nitrones **17**.

The mixture of rotamers due to the *N*-Boc group and the overlapping <sup>1</sup>H-NMR signals allowed only a tentative determination of the configuration and conformation of the two diastereoisomers of **17**. The <sup>1</sup>H-NMR spectrum of the mixture in (D<sub>6</sub>)DMSO solution at 100° is characterised by two *singlets* at 7.81 and at 7.73 ppm and two H–C(1) *doublets* at 6.01 and 5.81 ppm (*J*(1,2) = 5.1 and 5.7 Hz), respectively. The coupling constants of the piperidine ring of **17** are best interpreted in terms of a *B*<sub>3,N</sub> conformation, avoiding the allylic strain resulting from the interaction of the *N*-Boc group with an equatorial side chain at C(5) and the equatorial nitronyl substituents. The similarity of the coupling constants and the chemical shift for H–C(1) evidence the formation of (*E/Z*)-isomers rather than of two anomers.

Ozonolysis of nitrone **17** gave the *N,O*-hemiacetal **14** at ambient temperature, the only product to be isolated. It is assumed that the desired 1-deoxy-1-nitropiperidine **12** was generated *in situ* and transformed to the *N,O*-hemiacetal **14** upon workup. As observed for the ozonolysis product of the *N*-Boc-protected gluconolactam derivative **28**, it was not possible to analyze the ozonolysis product of **17** by <sup>1</sup>H-NMR spectroscopy, and the ozonolysis of **17** was monitored by ReactIR. Two prominent new bands appeared, one characteristic of the NO<sub>2</sub> group (1561 cm<sup>–1</sup>) and one of the C=O group of PhCHO (1701 cm<sup>–1</sup>).

The mechanism for the solvolysis of the 1-nitropiperidine has to account for the formation of the hemiacetals in the absence of H<sub>2</sub>O. Heterolysis of the 1-nitropiperidine **35** is assumed to generate the ion pair **38** that may evolve, by internal return, to the nitrite **40** that would be hydrolysed, during workup or chromatography, and lead to the *N,O*-hemiacetal **31** (*Scheme 9*). The nitrite **40** is expected to show a strong IR band at 1650 cm<sup>–1</sup>. In agreement with ReactIR and <sup>1</sup>H-NMR spectroscopy following the progress of ozonolysis, no such band appeared during ozonolysis of the nitrones **17**, **28**, or **34** at –78°, meaning that the heterolysis/recombination occurs only at a higher temperature.

As the 1-nitropiperidines could not be isolated, we screened *Michael* additions and *Henry* reactions of the crude mixture of the *bona fide* *N*-tosylated 1-nitropiperidine **35** obtained by ozonolysis of nitrone **34** at –78°. The mixture was treated with acrylonitrile, methyl acrylate, or 4-nitrobenzaldehyde, and a base (Et<sub>4</sub>NOH, DBU, NaH, *t*-BuSNa, NaOMe, *t*-BuOK, Bu<sub>4</sub>NF, or KF), slowly raising the temperature from

The reaction scheme illustrates the conversion of compound **35** to compound **31**. Compound **35** is a 1,2,3,6-tetra-*O*-benzyl-4-nitro-4-(*p*-toluenesulfonyl)pyrrolidine. It is in equilibrium with its zwitterionic form **38**, which features a positively charged nitrogen atom double-bonded to the adjacent carbon, and a nitrite group ( $\text{O}^- \text{N}=\text{O}$ ) at the 4-position. Compound **38** is in equilibrium with intermediate **40**, where the nitrogen is neutral and the 4-position has a nitro group ( $\text{O}=\text{N}-\text{O}$ ) with a lone pair on the oxygen. Intermediate **40** then reacts with water ( $\text{H}_2\text{O}$ ) to yield compound **31**, which is 1,2,3,6-tetra-*O*-benzyl-4-(*p*-toluenesulfonyl)pyrrolidine, where the nitro group has been replaced by a hydroxyl group.

We thank Dr. *B. Bernet* for carefully checking and commenting the analytical data, Dr. *P. Seiler* for determining the crystal structure, and the *Swiss National Science Foundation* and *Syngenta AG*, Basel, for their generous support.

*General.* See [10].

6-Azido-2,3,4,7-tetra-O-benzyl-6,8-dideoxy-D-erythro-D-galacto-octono-1,5-lactone (**2**). A soln. of the crude hemiacetal **1** (28 g, 46 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1 l) was treated at 25° with a soln. of Dess–Martin periodinane (30 g, 70 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (100 ml), stirred for 6 h, and diluted with a 1 : 1 mixture of a sat. NaHCO<sub>3</sub> soln. and a sat. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> soln. (500 ml). The layers were separated, and the aq. layer was extracted twice with CH<sub>2</sub>Cl<sub>2</sub>. The combined org. layers were dried (MgSO<sub>4</sub>) and evaporated to afford **2** (27 g, quant.), which was used for the next step without further purification. Colourless oil. *R*<sub>f</sub> (hexane/AcOEt 4 : 1) 0.48. [ $\alpha$ ]<sub>D</sub><sup>25</sup> = +88.1 (*c* = 1.51, CHCl<sub>3</sub>). IR (ATR): 3062w, 3031w, 2924w, 2888w, 2104s, 1740m, 1497w, 1464w, 1453w, 1407w, 1380w, 1360m, 1350m, 1291w, 1277w, 1234w, 1207w, 1184s, 1137s, 1092s, 1076s, 1054s, 1043s, 1025s, 999m, 984m, 955m, 940m, 899w, 874m, 827w, 809w, 789w, 743s, 732s, 694s, 662m, 611w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>); assignments based on selective homodecoupling experiments): see Table I; additionally, 7.45–7.25 (*m*, 20 arom. H); 5.18 (*d*, *J* = 11.1), 5.05 (*d*, *J* = 10.8), 4.81 (*d*, *J* = 10.8),

4.80 (*d*, *J* = 12.0), 4.74 (*d*, *J* = 12.0), 4.69 (*d*, *J* = 12.0), 4.60 (*d*, *J* = 12.0), 4.53 (*d*, *J* = 12.0) (4 PhCH<sub>2</sub>). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>; assignments based on a HSQC spectrum): see Table 1; additionally, 138.04, 137.46, 137.23, 137.20 (4s); 128.46–127.25 (several *d*); 75.22, 74.91, 73.00, 71.02 (4t, 4 PhCH<sub>2</sub>). HR-ESI-MS: 646.2337 (65, [M + K]<sup>+</sup>, C<sub>36</sub>H<sub>37</sub>KN<sub>3</sub>O<sub>6</sub><sup>+</sup>; calc. 646.7932), 630.2577 (100, [M + Na]<sup>+</sup>, C<sub>36</sub>H<sub>37</sub>N<sub>3</sub>NaO<sub>6</sub><sup>+</sup>; calc. 630.2575). Anal. calc. for C<sub>36</sub>H<sub>37</sub>N<sub>3</sub>O<sub>6</sub> (607.70): C 71.15, H 6.14, N 6.91; found: C 70.88, H 6.18, N 7.01.

Table 1. Selected <sup>1</sup>H-NMR Chemical Shifts [ppm] and Coupling Constants [Hz], and <sup>13</sup>C-NMR Chemical Shifts [ppm] of the Lactones and Lactams **2**, **6**, **7**, **9**, and **13**, of the *N,O*-Hemiacetal **14** in CDCl<sub>3</sub>, and of the Glycosyl Acetates **18** and **19** in (D<sub>6</sub>)DMSO

|                     | <b>2</b> | <b>6</b>  | <b>7</b>       | <b>9</b> | <b>13<sup>a</sup></b> | <b>14</b> | <b>18</b> | <b>19<sup>b</sup></b> |
|---------------------|----------|-----------|----------------|----------|-----------------------|-----------|-----------|-----------------------|
| H–C(1)              | –        | –         | –              | –        | –                     | 4.80      | 6.75      | 6.81                  |
| H–C(2)              | 4.49     | 4.38      | 4.49           | 4.55     | 4.30                  | 3.94      | 3.92      | 3.89                  |
| H–C(3)              | 3.87     | 3.82      | 3.78           | 3.83     | 3.96                  | 3.70      | 3.97      | 3.73                  |
| H–C(4)              | 4.23     | 4.27      | 4.27           | 4.24     | 3.95                  | 4.26      | 4.32      | 4.19                  |
| H–C(5)              | 3.79     | 3.16      | 3.21           | 3.12     | 4.30                  | 3.25      | 3.1       | 3.43                  |
| H–C(6)              | 4.17     | 3.73–3.71 | 3.66–3.58      | 3.89     | 4.38                  | 4.77      | 4.93      | 5.25                  |
| H–C(7)              | 4.10     | 3.73      | 3.66–3.58      | 3.77     | 3.61                  | 4.08      | 3.98      | 3.82                  |
| H <sub>3</sub> C(8) | 1.22     | 1.32      | 1.39           | 1.32     | 1.32                  | 11.23     | 1.10      | 1.01                  |
| <i>J</i> (1,2)      | –        | –         | –              | –        | –                     | 3.6       | 4.2       | 4.2                   |
| <i>J</i> (2,3)      | 9.3      | 9.9       | 9.3            | 8.4      | 5.1                   | 9.3       | 9.9       | 9.3                   |
| <i>J</i> (3,4)      | 2.4      | 1.5       | 1.2            | 2.1      | 4.5                   | 3.3       | 3.0       | 3.3                   |
| <i>J</i> (4,5)      | 1.5      | 2.4       | 2.1            | 3.0      | 3.6                   | 2.1       | 0         | 0                     |
| <i>J</i> (5,6)      | 10.2     | 9.3       | 8.7            | 9.6      | 7.8                   | 10.8      | 10.8      | 10.5                  |
| <i>J</i> (6,7)      | 2.7      | 5.7       | <sup>a</sup> ) | 4.8      | 6.9                   | 2.1       | 2.1       | 3.3                   |
| <i>J</i> (7,Me)     | 6.3      | 5.7       | 5.4            | 6.0      | 5.7                   | 6.3       | 6.3       | 6.3                   |
| C(1)                | 169.24   | 171.50    | 203.17         | 151.43   | 169.39                | 80.83     | 79.97     |                       |
| C(2)                | 76.93    | 76.98     | 80.89          | 76.16    | 79.51                 | 77.19     | 75.18     |                       |
| C(3)                | 80.21    | 81.04     | 81.48          | 81.61    | 80.26                 | 78.03     | 76.61     |                       |
| C(4)                | 72.26    | 73.81     | 73.94          | 73.59    | 70.51                 | 74.76     | 74.95     |                       |
| C(5)                | 76.87    | 55.84     | 60.82          | 55.59    | 56.37                 | 53.97     | 54.73     |                       |
| C(6)                | 61.75    | 64.47     | 64.50          | 64.41    | 64.85                 | 63.61     | 63.26     |                       |
| C(7)                | 74.91    | 76.48     | 76.57          | 74.42    | 71.95                 | 75.18     | 75.07     |                       |
| C(8)                | 13.57    | 15.96     | 15.13          | 15.53    | 16.18                 | 13.54     | 13.54     |                       |

<sup>a</sup>) *J*(3,5) = 1.5 Hz. <sup>b</sup>) The majority of the <sup>13</sup>C-signals were broad and not assigned.

6-Azido-2,3,4,7-tetra-*O*-benzyl-6,8-dideoxy-D-erythro-D-galacto-octonamide (**3**). NH<sub>3</sub> was condensed at –40° into a soln. of **2** (27 g, 41 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (200 ml), and the mixture was stirred for 4 h. Evaporation gave **3** (25 g, quant.), which was used for the next step without further purification. Pale yellow powder. *R*<sub>f</sub> (hexane/AcOEt 3:2) 0.43. [α]<sub>D</sub><sup>25</sup> = –11.7 (*c* = 1.03, CHCl<sub>3</sub>). IR (ATR): 3445w, 3356w, 3188w, 3065w, 3031w, 2984w, 2942w, 2890w, 2101m, 1680s, 1587w, 1497w, 1454w, 1395w, 1380m, 1348w, 1327w, 1305w, 1274m, 1261m, 1217w, 1085s, 1072s, 1025m, 936w, 906w, 880w, 748s, 694s. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>; assignments based on selective homodecoupling experiments): 7.41–7.26 (*m*, 20 arom. H); 6.67 (br. *s*, NH); 5.84 (br. *s*, NH); 4.66 (*d*, *J* = 11.4), 4.63 (*s*), 4.53 (*d*, *J* = 12.0), 4.53 (*d*, *J* = 11.7), 4.47 (*d*, *J* = 11.4), 4.44 (*d*, *J* = 11.7), 4.43 (*d*, *J* = 12.0) (4 PhCH<sub>2</sub>); 4.16–4.11 (*m*, H–C(2), H–C(3)); 4.02 (*qd*, *J* = 6.3, 2.4, H–C(7)); 3.96 (br. *d*, *J* = 6.0, H–C(4)); 3.69 (*dd*, *J* = 10.2, 3.0, H–C(6)); 3.61 (br. *dd*, *J* = 10.2, 7.8, H–C(5)); 2.75 (*d*, *J* = 7.8, OH); 1.18 (*d*, *J* = 6.3, Me). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>; assignments based on a HSQC spectrum): 174.49 (*s*, C=O); 138.33, 137.58, 137.32, 136.42 (4s); 128.66–127.29 (several *d*); 79.84 (*d*, C(3)); 79.60 (*d*, C(2)); 77.08 (*d*, C(4)); 75.76 (*d*, C(7)); 75.42, 73.75, 73.29, 70.57 (4t, 4 PhCH<sub>2</sub>); 69.67 (*d*, C(5)); 64.45 (*d*, C(6)); 13.49 (*q*, Me). HR-ESI-MS: 663.2562 (38,

$[M + K]^+$ ,  $C_{36}H_{40}KN_3O_6^+$ ; calc. 663.2579), 647.2835 (100,  $[M + Na]^+$ ,  $C_{36}H_{40}N_3NaO_6^+$ ; calc. 647.2840), 625.3008 (20,  $[M + H]^+$ ,  $C_{36}H_{41}N_4O_6^+$ ; calc. 625.3021).

**6-Azido-2,3,4,7-tetra-O-benzyl-6,8-dideoxy-D-glycero-D-galacto-oct-5-ulosonamide (4).** A soln. of **3** (25 g, 40 mmol) in  $CH_2Cl_2$  (600 ml) was treated at 25° with a soln. of *Dess–Martin* periodinane (30 g, 70 mmol) in  $CH_2Cl_2$  (200 ml), stirred for 6 h, and treated with a 1 : 1 mixture of a sat.  $NaHCO_3$  soln. and a sat.  $Na_2S_2O_3$  soln. (200 ml). The layers were separated, and the aq. layer was extracted twice with  $CH_2Cl_2$ . The combined org. layers were dried ( $MgSO_4$ ) and evaporated to afford **4** (23 g, quant.), which was used for the next step without further purification. Colourless oil.  $R_f$  (hexane/AcOEt 1 : 1) 0.47.  $[\alpha]_D^{25} = +54.3$  ( $c = 0.99$ ,  $CHCl_3$ ). IR (ATR): 3473w, 3327w, 3063w, 3031w, 2975w, 2927w, 2872w, 2103m, 1726m, 1684m, 1584w, 1496w, 1454w, 1395w, 1379w, 1337w, 1268w, 1211w, 1107m, 1086m, 1068s, 1026m, 911w, 822w, 735s, 695s.  $^1H$ -NMR (300 MHz,  $CDCl_3$ ; assignments based on selective homodecoupling experiments): 7.41–7.10 (*m*, 20 arom. H); 6.61 (*br. d*,  $J = 3.3$ , NH); 5.75 (*br. d*,  $J = 3.3$ , NH); 4.53 (*d*,  $J = 11.4$ ), 4.51 (*d*,  $J = 11.7$ , 2 H) (3 PhCH); 4.50 (*d*,  $J = 7.2$ , H–C(2)); 4.48 (*d*,  $J = 10.2$ ), 4.40 (*d*,  $J = 11.1$ ), 4.37 (*d*,  $J = 11.4$ ), 4.34 (*d*,  $J = 11.4$ ) (4 PhCH); 4.24 (*d*,  $J = 6.6$ , H–C(6)); 4.17 (*dd*,  $J = 7.2$ , 2.7, H–C(3)); 4.13 (*d*,  $J = 3.0$ , H–C(4)); 3.98 (*quint.*,  $J = 6.3$ , H–C(7)); 3.93 (*d*,  $J = 11.4$ , PhCH); 1.25 (*d*,  $J = 6.0$ , Me).  $^{13}C$ -NMR (75 MHz,  $CDCl_3$ ): 206.78 (*s*, C(5)); 173.22 (*s*, C(1)); 137.37, 137.03, 136.83, 136.37 (4s); 128.55–127.64 (several *d*); 81.65 (*d*, C(3)); 81.12 (*d*, C(2)); 79.57 (*d*, C(4)); 75.77 (*d*, C(7)); 75.23, 74.10, 72.07, 70.83 (4t, 4 PhCH<sub>2</sub>); 67.82 (*d*, C(6)); 16.57 (*q*, Me). HR-MALDI-MS: 661.2391 (38,  $[M + K]^+$ ,  $C_{36}H_{38}KN_4O_6^+$ ; calc. 661.2423), 645.2679 (100,  $[M + Na]^+$ ,  $C_{36}H_{38}N_4NaO_6^+$ ; calc. 645.2684), 623.2854 (20,  $[M + H]^+$ ,  $C_{36}H_{39}N_4O_6^+$ ; calc. 623.2876).

**5-Amino-6-azido-2,3,4,7-tetra-O-benzyl-5,6,8-trideoxy-D-erythro-D-galacto-octono-1,5-lactam (6).** A soln. of **4** (23 g, 36 mmol) in MeCN (670 ml) and 98%  $HCOOH$  (250 ml) was treated with  $NaCNBH_3$  (14 g, 22.3 mmol), heated to 70° for 4 h, cooled to 25°, and poured into AcOEt/sat. aq.  $NaHCO_3$  soln. The layers were separated, and the aq. layer was extracted twice with AcOEt. The combined org. layers were washed with brine, dried ( $MgSO_4$ ), and evaporated. FC (hexane/AcOEt 95 : 5 → 1 : 1) gave **6** (13 g, 58% from **1**). Yellow oil.  $R_f$  (hexane/AcOEt 3 : 1) 0.19.  $[\alpha]_D^{25} = +106.2$  ( $c = 1.27$ ,  $CHCl_3$ ). IR (ATR): 3212w, 3064w, 3030w, 2936w, 2869w, 2107s, 1672s, 1496w, 1453m, 1381w, 1345w, 1289m, 1208w, 1100s, 1046m, 1026m, 908w, 819w, 732s, 695s.  $^1H$ -NMR (300 MHz,  $CDCl_3$ ; assignments based on selective homodecoupling experiments): see Table I; additionally, 7.47–7.26 (*m*, 20 arom. H); 6.80 (*br. s*, NH); 5.24 (*d*,  $J = 11.4$ ), 5.19 (*d*,  $J = 10.8$ ), 4.86 (*d*,  $J = 11.1$ ), 4.84 (*d*,  $J = 12.0$ ), 4.77 (*d*,  $J = 12.0$ ), 4.65 (*d*,  $J = 11.7$ ), 4.63 (*d*,  $J = 10.8$ ), 4.48 (*d*,  $J = 11.7$ ) (4 PhCH<sub>2</sub>).  $^{13}C$ -NMR (75 MHz,  $CDCl_3$ ; assignments based on a HSQC spectrum): see Table I; additionally, 138.02, 137.92, 137.77, 136.93 (4s); 128.55–127.40 (several *d*); 75.42, 74.27, 73.14, 70.80 (4t, 4 PhCH<sub>2</sub>). HR-MALDI-MS: 645.2478 (38,  $[M + K]^+$ ,  $C_{36}H_{38}KN_4O_5^+$ ; calc. 645.2474), 629.2740 (60,  $[M + Na]^+$ ,  $C_{36}H_{38}N_4NaO_5^+$ ; calc. 629.2734), 607.2920 (100,  $[M + H]^+$ ,  $C_{36}H_{39}N_4O_5^+$ ; calc. 607.2915). Anal. calc. for  $C_{36}H_{38}N_4O_5$  (606.72): C 71.27, H 6.31, N 9.23; found: C 71.02, H 6.43, N 9.04.

**5-Amino-6-azido-2,3,4,7-tetra-O-benzyl-5,6,8-trideoxy-D-erythro-D-galacto-octono-1,5-thiolactam (7).** A soln. of **6** (660 mg, 1.09 mmol) in toluene (20 ml) was treated with *Lawesson's* reagent (400 mg, 0.98 mmol), heated to 60° for 2 h, and evaporated. FC (hexane/AcOEt 98 : 2 → 4 : 1) gave **7** (520 mg, 75%). Yellow oil.  $R_f$  (hexane/AcOEt 4 : 1) 0.46.  $[\alpha]_D^{25} = +122.4$  ( $c = 0.46$ ,  $CHCl_3$ ). IR (ATR): 3297w, 3063w, 3030w, 2870w, 2108s, 1595w, 1496m, 1453m, 1380w, 1356w, 1288m, 1263w, 1209w, 1177w, 1091m, 1059m, 1025m, 907m, 730s, 694s.  $^1H$ -NMR (300 MHz,  $CDCl_3$ ; assignments based on selective homodecoupling experiments): see Table I; additionally, 9.04 (*br. s*, NH); 7.53–7.49 (*m*, 2 arom. H); 7.40–7.21 (*m*, 18 arom. H); 5.45 (*d*,  $J = 10.8$ ), 5.20 (*d*,  $J = 10.8$ ), 4.89 (*d*,  $J = 10.8$ ), 4.81 (*d*,  $J = 12.3$ ), 4.74 (*d*,  $J = 11.7$ ), 4.71 (*d*,  $J = 11.7$ ), 4.63 (*d*,  $J = 10.8$ ), 4.47 (*d*,  $J = 11.7$ ) (4 PhCH<sub>2</sub>).  $^{13}C$ -NMR (75 MHz,  $CDCl_3$ ): see Table I; additionally, 138.23, 138.10, 137.96, 136.51 (4s); 129.10–127.78 (several *d*); 76.57, 74.07, 73.41, 71.08 (4t, 4 PhCH<sub>2</sub>). HR-MALDI-MS: 645.2506 (10,  $[M + Na]^+$ ,  $C_{36}H_{38}N_4NaO_4^+$ ; calc. 645.2506), 623.2687 (100,  $[M + H]^+$ ,  $C_{36}H_{39}N_4O_4^+$ ; calc. 623.2687). Anal. calc. for  $C_{36}H_{38}N_4O_4S$  (622.79): C 69.43, H 6.25, N 8.69; found: C 69.26, H 6.25, N 8.69.

**(Z)-6-Azido-2,3,4,7-tetra-O-benzyl-5-C-[(tert-butoxy)carbonyl]amino-5,6,8-trideoxy-D-erythro-D-galacto-octonhydroximo-1,5-lactam (9).** A soln. of **7** (100 mg, 0.16 mmol) in  $CH_2Cl_2$  (5 ml) was treated with DMAP (2 mg, 0.16 mmol) and  $Boc_2O$  (70 mg, 0.32 mmol), stirred for 1 h, diluted with MeOH (5 ml), treated with  $NH_2OH \cdot HCl$  (56 mg, 0.80 mmol) and  $NaHCO_3$  (68 mg, 0.80 mmol), heated to 60°,

stirred for 1 h, and evaporated. A soln. of the residue in AcOEt was washed with H<sub>2</sub>O and brine, dried (MgSO<sub>4</sub>), and evaporated. FC (hexane/AcOEt 95:5 → 1:1) gave **9** (103 mg, 90%). Colourless oil. *R*<sub>f</sub> (hexane/AcOEt 1:1) 0.59.  $[\alpha]_D^{25} = +38.2$  (*c* = 0.84, CHCl<sub>3</sub>). IR (ATR): 3365w, 3063w, 3030w, 2869w, 2106s, 1710m, 1644m, 1496w, 1453m, 1381w, 1358w, 1288m, 1207w, 1069m, 1026m, 953w, 911w, 732s, 694s. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>; assignments based on selective homodecoupling experiments): see Table I; additionally, 7.42–7.25 (*m*, 20 arom. H); 7.07 (*br. s*, OH); 5.09 (*d*, *J* = 11.1), 4.94 (*d*, *J* = 11.4), 4.79 (*d*, *J* = 11.7), 4.73 (*d*, *J* = 11.4), 4.71 (*d*, *J* = 11.4), 4.66 (*d*, *J* = 11.4), 4.62 (*d*, *J* = 12.0), 4.50 (*d*, *J* = 12.0) (4 PhCH<sub>2</sub>); 1.49 (*s*, *t*-Bu). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): see Table I; additionally, 158.90 (*s*, C=O); 138.06, 137.92, 137.85, 137.40 (4s); 128.37–127.54 (several *d*); 81.84 (*s*, Me<sub>3</sub>C); 73.98 (2 C), 72.79, 70.77 (3t, 4 PhCH<sub>2</sub>); 28.18 (*q*, Me<sub>3</sub>C). HR-MALDI-MS: 644.2860 (5, [M – Boc + H + Na]<sup>+</sup>, C<sub>36</sub>H<sub>39</sub>N<sub>5</sub>NaO<sub>5</sub><sup>+</sup>; calc. 644.2843), 622.3035 (100, [M – Boc + 2 H]<sup>+</sup>, C<sub>36</sub>H<sub>40</sub>N<sub>5</sub>O<sub>5</sub><sup>+</sup>; calc. 622.3024).

6-Azido-2,3,4,7-tetra-O-benzyl-5-C-[[*tert*-butoxy]carbonyl]amino]-5,6,8-trideoxy-D-erythro-D-galacto-octono-1,5-lactam (**13**). A soln. of **6** (100 mg, 0.16 mmol) and DMAP (20 mg, 0.16 mmol) in ClCH<sub>2</sub>CH<sub>2</sub>Cl was heated to 70°, treated with Boc<sub>2</sub>O (70 mg, 0.32 mmol), stirred for 6 h, and evaporated. FC (hexane/AcOEt 98:2 → 4:1) gave **13** (90 mg, 80%). Colourless oil. *R*<sub>f</sub> (hexane/AcOEt 4:1) 0.53.  $[\alpha]_D^{25} = +59.1$  (*c* = 1.08, CHCl<sub>3</sub>). IR (ATR): 3030w, 2977w, 2930w, 2870w, 2114m, 1709s, 1693m, 1654w, 1496w, 1453w, 1367m, 1308w, 1278w, 1251m, 1207w, 1150m, 1122m, 1074s, 1027m, 965w, 934w, 909w, 857w, 790w, 773w, 732s, 695s. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>; assignments based on selective homodecoupling experiments): see Table I; additionally, 7.41–7.25 (*m*, 20 arom. H); 4.80 (*d*, *J* = 11.7), 4.77 (*d*, *J* = 11.4), 4.74 (*d*, *J* = 11.1), 4.71 (*d*, *J* = 11.4), 4.70 (*d*, *J* = 11.7), 4.52 (*d*, *J* = 10.8), 4.25 (*d*, *J* = 10.8), 4.22 (*d*, *J* = 11.4) (4 PhCH<sub>2</sub>); 1.50 (*s*, *t*-Bu). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): see Table I; additionally, 152.44 (*s*, C=O of Boc); 137.90, 137.66, 137.51, 137.27 (4s); 128.35–127.61 (several *d*); 81.14 (*s*, Me<sub>3</sub>C); 75.33, 74.78, 74.10, 73.42 (4t, 4 PhCH<sub>2</sub>); 28.11 (*q*, Me<sub>3</sub>C). HR-MALDI-MS: 729.3246 (30, [M + Na]<sup>+</sup>, C<sub>41</sub>H<sub>46</sub>N<sub>4</sub>NaO<sub>7</sub><sup>+</sup>; calc. 729.3259), 629.2734 (41, [M – Boc + H + Na]<sup>+</sup>, C<sub>36</sub>H<sub>38</sub>N<sub>4</sub>NaO<sub>5</sub><sup>+</sup>; calc. 629.2734), 607.2913 (100, [M – Boc + 2 H]<sup>+</sup>, C<sub>36</sub>H<sub>39</sub>N<sub>4</sub>O<sub>5</sub><sup>+</sup>; calc. 607.2915). Anal. calc. for C<sub>41</sub>H<sub>46</sub>N<sub>4</sub>O<sub>7</sub> (706.84): C 69.67, H 6.56, N 7.93; found: C 69.51, H 6.65, N 7.86.

6-Azido-2,3,4,7-tetra-O-benzyl-5-C-[[*tert*-butoxy]carbonyl]amino]-5,6,8-trideoxy-D-erythro-α-D-galacto-octopyranose (**14**). At 0°, a soln. of **13** (870 mg, 1.23 mmol) in THF (10 ml) was treated dropwise with a 1M Super-Hydride® soln. (6.2 ml, 6.2 mmol), stirred for 1 h, and treated with a sat. aq. NaHCO<sub>3</sub> soln. THF was evaporated, and the aq. layer was extracted twice with CH<sub>2</sub>Cl<sub>2</sub>. The combined org. layers were dried (MgSO<sub>4</sub>) and evaporated to afford **14** (880 mg, quant.), which was used for the next step without further purification. Colourless oil. *R*<sub>f</sub> (hexane/AcOEt 4:1) 0.35.  $[\alpha]_D^{25} = +48.2$  (*c* = 1.05, CHCl<sub>3</sub>). IR (ATR): 3212w, 3064w, 3031w, 2980w, 2931w, 2871w, 2110m, 1734m, 1714m, 1496w, 1454w, 1393w, 1368w, 1285m, 1256m, 1208w, 1147s, 1094s, 1051m, 1026m, 911w, 848w, 733s, 695s. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>, 60°; assignments based on selective homodecoupling experiments): 7.46–7.25 (*m*, 20 arom. H); 4.80 (*br. s*, H–C(1), after addition of D<sub>2</sub>O: *d*, *J* = 3.3); 4.77 (*br. d*, *J* = 10.8, H–C(6)); 4.91 (*d*, *J* = 11.7), 4.81 (*d*, *J* = 11.7), 4.79 (*d*, *J* = 11.4), 4.78 (*d*, *J* = 11.4) (2 PhCH<sub>2</sub>); 4.74, 4.66 (2s, 2 PhCH<sub>2</sub>); 4.26 (*br. d*, *J* = 2.1, H–C(4)); 4.08 (*qd*, *J* = 6.3, 2.1, H–C(7)); 3.94 (*dd*, *J* = 9.3, 3.6, H–C(2)); 3.70 (*dd*, *J* = 9.0, 3.3, H–C(3)); 3.25 (*br. d*, *J* = 10.8, H–C(5)); 3.02 (*br. s*, exchange with D<sub>2</sub>O, OH); 1.36 (*s*, *t*-Bu); 1.23 (*d*, *J* = 6.3, Me). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>, 60°): 154.24 (*s*, C=O); 138.85, 138.62, 138.38, 138.08 (4s); 128.30–127.15 (several *d*); 80.95 (*s*, Me<sub>3</sub>C); 80.83 (*d*, C(1)); 78.03 (*d*, C(3)); 77.19 (*d*, C(2)); 75.80 (*d*, C(7)); 74.76 (*d*, C(4)); 74.22, 73.45, 72.89, 70.52 (4t, 4 PhCH<sub>2</sub>); 63.31 (*d*, C(6)); 53.97 (*d*, C(5)); 28.21 (*q*, Me<sub>3</sub>C); 13.54 (*q*, Me). HR-MALDI-MS: 747.3167 (30, [M + K]<sup>+</sup>, C<sub>41</sub>H<sub>48</sub>KN<sub>4</sub>O<sub>7</sub><sup>+</sup>; calc. 747.3155), 731.3421 (100, [M + Na]<sup>+</sup>, C<sub>41</sub>H<sub>48</sub>N<sub>4</sub>NaO<sub>7</sub><sup>+</sup>; calc. 731.3415), 607.2877 (80, [M – Boc + H]<sup>+</sup>, C<sub>36</sub>H<sub>39</sub>N<sub>4</sub>O<sub>5</sub><sup>+</sup>; calc. 607.2920), 591.2970 (55, [M – Boc – OH + 2 H]<sup>+</sup>, C<sub>36</sub>H<sub>39</sub>N<sub>4</sub>O<sub>4</sub><sup>+</sup>; calc. 591.2966). Anal. calc. for C<sub>41</sub>H<sub>48</sub>N<sub>4</sub>O<sub>7</sub> (708.85): C 69.47, H 6.83, N 7.90; found: C 69.51, H 6.85, N 7.83.

(*E/Z*)-6-Azido-2,3,4,7-tetra-O-benzyl-5-C-[[*tert*-butoxy]carbonyl]amino]-5,6,8-trideoxy-D-erythro-D-galacto-octose Oxime (**15**). A soln. of crude **14** (880 mg, 1.23 mmol) in abs. EtOH (50 ml) was added to a soln. of NH<sub>2</sub>OH · HCl (2.78 g, 0.041 mmol) and NaHCO<sub>3</sub> (1.39 g, 0.02 mmol) in abs. EtOH (150 ml). The mixture was heated to 80° for 24 h, cooled to 25°, and evaporated. A soln. of the residue in AcOEt was washed with H<sub>2</sub>O and brine, dried (Na<sub>2</sub>SO<sub>4</sub>), and evaporated. FC (hexane/AcOEt 95:5 → 4:1) gave **15** (760 mg, 85% from **13**). Colourless oil. *R*<sub>f</sub> (hexane/AcOEt 2:1) 0.53.  $[\alpha]_D^{25} = +7.2$  (*c* = 1.1, CHCl<sub>3</sub>). IR (ATR): 3428w (*br.*), 3064w, 3031w, 2978w, 2872w, 2104m, 1712m, 1688w, 1495m, 1454m, 1391w, 1366w,

1307w, 1254w, 1162m, 1069s, 1027m, 939w, 912w, 733s, 695s.  $^1\text{H-NMR}$  (300 MHz,  $(\text{D}_6)$ DMSO,  $100^\circ$ , (*E/Z*) 7:3; assignments based on selective homodecoupling experiments): 11.09 (s, OH (*Z*)); 10.81 (s, OH (*E*)); 7.44 (*d*,  $J = 7.5$ , H–C(1) (*E*)); 7.37–7.25 (*m*, 20 arom. H); 6.95 (*d*,  $J = 6.0$ , H–C(1) (*Z*)); 5.97 (br. s, NHBOc); 5.05 (*dd*,  $J = 6.0$ , 2.7, H–C(2) (*Z*)); 4.73–4.39 (*m*, 4 PhCH<sub>2</sub>); 4.32 (*dd*,  $J = 7.5$ , 4.2, H–C(2) (*E*)); 4.02 (*t*,  $J = 7.2$ , 1 H); 3.87–3.68 (*m*, 4 H); 1.35 (s, *t*-Bu (*Z*)); 1.33 (s, *t*-Bu (*E*)); 1.20 (*d*,  $J = 6.0$ , Me).  $^{13}\text{C-NMR}$  (75 MHz,  $(\text{D}_6)$ DMSO,  $100^\circ$ ; (*E/Z*) 7:3): 154.92 (s, C=O); 149.74 (*d*, C(1) (*E*)); 147.72 (*d*, C(1) (*Z*)); 138.35–137.87 (several *s*); 127.95–127.02 (several *d*); 80.39 (*d*, 1 C (*E*)); 78.55 (*d*, 1 C (*Z*)); 77.10 (*d*, 1 C (*E*)); 76.71 (*d*, 1 C (*Z*)); 75.22 (*d*, 1 C (*E*)); 73.84 (*t*, PhCH<sub>2</sub> (*E*)); 73.62 (*t*, PhCH<sub>2</sub> (*Z*)); 73.53 (*t*, PhCH<sub>2</sub> (*Z*)); 73.19 (*t*, PhCH<sub>2</sub> (*E*)); 71.84 (*d*, 1 C (*E*)); 70.85 (*t*, PhCH<sub>2</sub> (*Z*)); 70.22 (*t*, PhCH<sub>2</sub> (*E*)); 69.83 (*t*, PhCH<sub>2</sub>); 64.99 (*d*, C(6)); 50.44 (*d*, C(5)); 28.07 (*q*, Me<sub>3</sub>C); 13.92 (*q*, Me); *s* of Me<sub>3</sub>C hidden by the noise. HR-MALDI-MS: 762.3274 (6,  $[M + K]^+$ , C<sub>41</sub>H<sub>49</sub>KN<sub>5</sub>O<sub>7</sub><sup>+</sup>; calc. 762.3264), 746.3533 (17,  $[M + Na]^+$ , C<sub>41</sub>H<sub>49</sub>N<sub>5</sub>NaO<sub>7</sub><sup>+</sup>; calc. 746.3524), 724.3709 (100,  $[M + H]^+$ , C<sub>41</sub>H<sub>50</sub>N<sub>5</sub>O<sub>7</sub><sup>+</sup>; calc. 724.3405). Anal. calc. for C<sub>41</sub>H<sub>49</sub>N<sub>5</sub>O<sub>7</sub> (723.87): C 68.03, H 6.82, N 9.67; found: C 67.79, H 6.85, N 9.42.

*1-O-Acetyl-6-azido-2,3,4,7-tetra-O-benzyl-5-[(tert-butoxy)carbonylamino]-5,6,8-trideoxy-D-erythro-α-D-galacto-octopyranose (18)*. At  $0^\circ$ , a soln. of **13** (460 mg, 0.66 mmol) in THF (50 ml) was treated dropwise with a 1M *Super-Hydride*<sup>®</sup> soln. (2.6 ml, 2.6 mmol), stirred for 1 h, and treated with a sat. aq. NaHCO<sub>3</sub> soln. After evaporation of THF, the aq. layer was extracted twice with CH<sub>2</sub>Cl<sub>2</sub>. The combined org. layers were dried (MgSO<sub>4</sub>) and evaporated to afford crude **14**. A soln. of crude **14** in CH<sub>2</sub>Cl<sub>2</sub> (20 ml) was treated with Et<sub>3</sub>N (2 ml), DMAP (40 mg, 0.30 mmol), and Ac<sub>2</sub>O (1 ml), stirred for 12 h, and evaporated. A soln. of the residue in AcOEt was washed with sat. aq. NaHCO<sub>3</sub> soln. and brine, dried (MgSO<sub>4</sub>), and evaporated. FC (hexane/AcOEt 95:5 → 4:1) gave **18** (470 mg, 90% from **13**). *R*<sub>f</sub> (hexane/AcOEt 4:1) 0.40.  $[\alpha]_D^{25} = +30.0$  (*c* = 1.17, CHCl<sub>3</sub>). IR (ATR): 3031w, 2978w, 2932w, 2870w, 2107m, 1754m, 1734m, 1715m, 1496w, 1454w, 1368w, 1340w, 1286m, 1254m, 1225w, 1154s, 1118m, 1093m, 1053s, 1026s, 938w, 862w, 817w, 735s, 696s.  $^1\text{H-NMR}$  (300 MHz,  $(\text{D}_6)$ DMSO,  $100^\circ$ ; assignments based on selective homodecoupling experiments): see Table I, additionally: 7.40–7.23 (*m*, 20 arom. H); 4.86 (*d*,  $J = 11.7$ ), 4.80 (*d*,  $J = 12.0$ ), 4.72 (*d*,  $J = 11.7$ , 2 H), 4.64 (*d*,  $J = 11.7$ ), 4.58 (*d*,  $J = 11.7$ ), 4.56 (*d*,  $J = 10.5$ ), 4.53 (*d*,  $J = 11.7$ ) (4 PhCH<sub>2</sub>); 2.06 (s, AcO); 1.31 (s, *t*-Bu).  $^{13}\text{C-NMR}$  (75 MHz, CDCl<sub>3</sub>,  $60^\circ$ ): see Table I, additionally, 168.23 (s, OC=O); 152.98 (s, NC=O); 138.52, 138.42, 137.92, 138.08 (4s); 127.88–127.03 (several *d*); 81.10 (s, Me<sub>3</sub>C); 73.64, 72.33, 71.95, 69.87 (4t, 4 PhCH<sub>2</sub>); 27.71 (*q*, Me<sub>3</sub>C); 20.32 (*q*, MeC=O). HR-MALDI-MS: 789.3310 (27, C<sub>43</sub>H<sub>50</sub>KN<sub>4</sub>O<sub>8</sub><sup>+</sup>,  $[M + K]^+$ ; calc. 789.3260), 773.3527 (71,  $[M + Na]^+$ , C<sub>43</sub>H<sub>50</sub>N<sub>4</sub>NaO<sub>8</sub><sup>+</sup>; calc. 773.3521), 591.2960 (100,  $[M - \text{Boc} - \text{OAc} + 2\text{H}]^+$ , C<sub>36</sub>H<sub>39</sub>N<sub>4</sub>O<sub>8</sub><sup>+</sup>; calc. 591.2966). Anal. calc. for C<sub>43</sub>H<sub>50</sub>N<sub>4</sub>O<sub>8</sub> (750.89): C 68.78, H 6.71, N 7.46; found: C 69.84, H 6.68, N 7.31.

*1-O-Acetyl-2,3,4,7-tetra-O-benzyl-6-[(benzyloxy)carbonylamino]-5-[(tert-butoxy)carbonylamino]-5,6,8-trideoxy-D-erythro-α-D-galacto-octopyranose (19)*. A 1M soln. of **18** (770 mg, 1.03 mmol) in pyridine/H<sub>2</sub>O 5:1 (12 ml) was treated with propane-1,3-dithiol (2.1 ml, 20.7 mmol) and Et<sub>3</sub>N (2 ml), stirred for 6 h, and evaporated. At  $0^\circ$ , a soln. of the residue in CH<sub>2</sub>Cl<sub>2</sub> (20 ml) was treated with Et<sub>3</sub>N (1 ml, 7.21 mmol) and CbzCl (740 μl, 5.15 mmol), warmed to  $25^\circ$ , stirred for 4 h, and diluted with sat. aq. NaHCO<sub>3</sub> soln. The layers were separated, and the aq. layer was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined org. layers were dried (MgSO<sub>4</sub>) and evaporated. FC (hexane/AcOEt 85:5 → 4:1) gave **19** (677 mg, 75%). *R*<sub>f</sub> (hexane/AcOEt 4:1) 0.20.  $[\alpha]_D^{25} = +44.7$  (*c* = 1, CHCl<sub>3</sub>). IR (ATR): 3335w, 3032w, 2977w, 1720s, 1498m, 1454m, 1369m, 1307m, 1228s, 1159m, 1092s, 1032m, 953w, 902w, 856w, 738s, 698s.  $^1\text{H-NMR}$  (300 MHz,  $(\text{D}_6)$ DMSO,  $100^\circ$ ): see Table I, additionally: 7.40–7.16 (*m*, 25 arom. H); 6.8 (br. s, NH); 5.15 (br. *d*,  $J = 12.6$ ), 5.03 (*d*,  $J = 12.6$ ) (PhCH<sub>2</sub>); 4.64 (s, PhCH<sub>2</sub>); 4.61–4.52 (*m*, 5 PhCH); 4.45 (*d*,  $J = 12.0$ , PhCH); 3.89 (*dd*,  $J = 9.3$ , 4.2, H–C(2)); 3.82 (*qd*,  $J = 6.3$ , 3.6, H–C(7)); 3.73 (*dd*,  $J = 9.3$ , 3.3, H–C(3)); 2.03 (s, AcO); 1.27 (s, *t*-Bu).  $^{13}\text{C-NMR}$  (300 MHz,  $(\text{D}_6)$ DMSO,  $100^\circ$ ): 168.21 (s, OC=O); 155.93, 153.11 (2s, 2 NC=O); 139.22, 138.71, 138.49, 137.95, 137.25 (5s); 129.00–126.00 (several *d*); 80.57 (s, Me<sub>3</sub>C); 80.00–51.00 (broad signals); 27.83, 27.70 (2q, 2 Me<sub>3</sub>C); 21.00–20.00 (broad signals, Me). HR-MALDI-MS: 897.3760 (14,  $[M + K]^+$ , C<sub>51</sub>H<sub>58</sub>KN<sub>2</sub>O<sub>10</sub><sup>+</sup>; calc. 897.3723), 881.3983 (22,  $[M + Na]^+$ , C<sub>51</sub>H<sub>58</sub>N<sub>2</sub>NaO<sub>10</sub><sup>+</sup>; calc. 881.3984), 699.3413 (100,  $[M - \text{Boc} - \text{OAc} + 2\text{H}]^+$ , C<sub>44</sub>H<sub>47</sub>N<sub>2</sub>O<sub>6</sub><sup>+</sup>; calc. 699.3434).

*2,3,4,7-Tetra-O-benzyl-6-[(benzyloxy)carbonylamino]-5-[(tert-butoxy)carbonylamino]-5,6,8-trideoxy-D-erythro-α-D-galacto-octopyranosyl Azide (20)*. A soln. of **19** (670 mg, 0.78 mmol) and TMS-N<sub>3</sub> (1.04 ml, 7.8 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (20 ml) was treated with 4-Å mol. sieves, stirred for 30 min at  $25^\circ$ , cooled to  $-50^\circ$ , treated with BF<sub>3</sub>·OEt<sub>2</sub> (106 μl, 0.86 mmol), stirred for 15 min, diluted with sat. aq. NaHCO<sub>3</sub> soln.,

and filtered over *Celite*. The layers were separated, and the aq. layer was extracted with  $\text{CH}_2\text{Cl}_2$ . The combined org. layers were dried ( $\text{MgSO}_4$ ) and evaporated. FC (hexane/AcOEt 95:5  $\rightarrow$  4:1) gave **20** (550 mg, 83%).  $R_f$  (hexane/AcOEt 4:1) 0.30.  $[\alpha]_D^{25} = +16.8$  ( $c = 1$ ;  $\text{CHCl}_3$ ). IR (ATR): 3064w, 3031w, 2976w, 2931w, 2865w, 2101m, 1719m, 1700m, 1586w, 1497w, 1453w, 1367m, 1326m, 1304m, 1223m, 1159m, 1092s, 1065s, 1053s, 1026m, 908m, 856w, 729s, 695s.  $^1\text{H-NMR}$  (300 MHz,  $(\text{D}_6)\text{DMSO}$ ,  $100^\circ$ ): broad signals. HR-MALDI-MS: 880.3664 (14,  $[M + K]^+$ ,  $\text{C}_{49}\text{H}_{55}\text{KN}_5\text{O}_8^+$ ; calc. 880.3682), 864.3959 (34,  $[M + \text{Na}]^+$ ,  $\text{C}_{49}\text{H}_{55}\text{N}_5\text{NaO}_8^+$ ; calc. 864.3943), 699.3404 (100,  $[M - \text{Boc} - \text{N}_3 + 2\text{H}]^+$ ,  $\text{C}_{44}\text{H}_{47}\text{N}_2\text{O}_6^+$ ; calc. 699.3434).

**2,3,4,6-Tetra-O-benzyl-5-[[tert-butoxycarbonyl]amino]-1,5-deoxy-d-glucopyranose N-Benzylimine N-Oxide (26)** and **2,3,4,6-Tetra-O-benzyl-1-N-benzyl-5-[[tert-butoxycarbonyl]amino]-5-deoxy-1-N-hydroxy- $\beta$ -D-glucopyranosylamine (27)**. A soln. of  $\text{BnNHOH} \cdot \text{HCl}$  (490 mg, 3.06 mmol) in MeOH was treated with  $\text{NaHCO}_3$  (120 mg, 1.41 mmol), stirred for 15 min, and evaporated. A soln. of the residue in  $\text{CH}_2\text{Cl}_2$  was washed with  $\text{H}_2\text{O}$  and brine. The org. layer was dried ( $\text{MgSO}_4$ ) and evaporated to afford  $\text{BnNHOH}$ . A soln. of **25** [14] (390 mg, 0.61 mmol) in dry pyridine (5 ml) was treated with  $\text{BnNHOH}$  and 4-Å mol. sieves, heated for 12 h at  $80^\circ$ , filtered, and evaporated. TLC showed two spots in a ratio of ca. 1:1. FC (hexane/AcOEt 98:2  $\rightarrow$  0:100) provided two fractions that revealed the same two spots on TLC (ca. 1:1) corresponding to **26/27** (340 mg, 75%). Colourless oil. **26**:  $R_f$  (hexane/AcOEt 4:1) 0.59. **27**:  $R_f$  (AcOEt) 0.50. **26/27**:  $[\alpha]_D^{25} = +13.25$  ( $c = 1.18$ ,  $\text{CHCl}_3$ ). IR (ATR): 3251w, 3030w, 2869w, 1692m, 1604w, 1496w, 1453w, 1391w, 1365w, 1340w, 1257w, 1208m, 1164m, 1090m, 1056s, 1025s, 1006s, 862w, 818w, 735s, 696s.  $^1\text{H-NMR}$  (300 MHz,  $(\text{D}_6)\text{DMSO}$ ,  $100^\circ$ ; assignments based on selective homodecoupling experiments): see Table 2; additionally, 7.77 (br. s, 1 arom. H); 7.38–7.21 (m, 24 arom. H); 4.76 (d,  $J = 12.9$ ), 4.76 (d,  $J = 10.8$ ), 4.64 (d,  $J = 11.7$ ), 4.61 (d,  $J = 11.1$ ), 4.46 (d,  $J = 12.3$ ), 4.40 (d,  $J = 12.0$ ), 4.08 (d,  $J = 13.8$ ), 3.70 (d,  $J = 14.1$ ) (4  $\text{PhCH}_2$ ); 3.02 (s, OH, HDO); 1.41 (s, *t*-Bu).  $^{13}\text{C-NMR}$  (75 MHz,  $(\text{D}_6)\text{DMSO}$ ,  $100^\circ$ ): see Table 2; additionally, 154.76 (s, C=O); 138.70, 138.59, 138.44 (2 C), 138.06 (4s); 128.52–126.21 (several d); 79.95 (s,  $\text{Me}_3\text{C}$ ); 73.27, 73.01, 72.17, 71.15, 59.25 (5t, 5  $\text{PhCH}_2$ ); 27.96 (q,  $\text{Me}_3\text{C}$ ). HR-MALDI-MS: 783.3411 (38,  $[M + K]^+$ ,  $\text{C}_{46}\text{H}_{52}\text{KN}_2\text{O}_7^+$ ; calc. 783.3412), 767.3652 (77,  $[M + \text{Na}]^+$ ,  $\text{C}_{46}\text{H}_{52}\text{N}_2\text{NaO}_7^+$ ; calc. 767.3667), 544.2460 (13,  $[M - \text{Boc} - \text{BnNHOH} + \text{H} + \text{Na}]^+$ ,  $\text{C}_{34}\text{H}_{35}\text{NNaO}_4^+$ ; calc. 544.2458), 522.2629 (55,  $[M - \text{Boc} - \text{BnNHOH} + 2\text{H}]^+$ ,  $\text{C}_{34}\text{H}_{36}\text{NO}_4^+$ ; calc. 522.2639). Anal. calc. for  $\text{C}_{46}\text{H}_{52}\text{N}_2\text{O}_7$  (744.93): C 74.17, H 7.04, N 3.76; found: C 73.90, H 7.17, N 3.83.

**2,3,4,6-Tetra-O-benzyl-5-[[tert-butoxycarbonyl]amino]-5-deoxy-1-N-(phenylmethylidene)- $\beta$ -D-glucopyranosylamine N-Oxide (28)**. A soln. of **26/27** (130 mg, 0.17 mmol) and  $\text{MnO}_2$  (73 mg, 0.85 mmol) in  $\text{ClCH}_2\text{CH}_2\text{Cl}$  (5 ml) was kept at reflux for 48 h, cooled to r.t., filtered over *Celite*, and evaporated. FC (hexane/AcOEt 95:5  $\rightarrow$  4:1) gave **28** (120 mg, 90%). Colourless crystals. M.p.  $68-70^\circ$ .  $R_f$  (hexane/AcOEt 4:1) 0.44.  $[\alpha]_D^{25} = -60.6$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ). IR (ATR): 3062w, 3030w, 2975w, 2931w, 2868w, 1705m, 1578w, 1564w, 1496w, 1454m, 1391w, 1366m, 1331m, 1255w, 1213w, 1156m, 1133m, 1067s, 1027s, 924w, 881w, 852w, 806w, 773w, 733s, 693s.  $^1\text{H-NMR}$  (300 MHz,  $(\text{D}_6)\text{DMSO}$ ,  $100^\circ$ ; assignments based on selective homodecoupling experiments): see Table 2; additionally, 8.29–8.22 (m, 2 arom. H); 7.91 (br. s,  $\text{CH}=\text{N}$ ); 7.44–7.08 (m, 23 arom. H); 4.75 (s,  $\text{PhCH}_2$ ); 4.73 (d,  $J = 11.8$ ), 4.67 (d,  $J = 11.7$ ) (2  $\text{PhCH}$ ); 4.62 (s,  $\text{PhCH}_2$ ); 4.56 (d,  $J = 11.7$ ), 4.41 (d,  $J = 11.1$ ) (2  $\text{PhCH}$ ); 1.36 (s, *t*-Bu).  $^{13}\text{C-NMR}$  (75 MHz,  $(\text{D}_6)\text{DMSO}$ ,  $100^\circ$ ): see Table 2; additionally, 153.66 (s, C=O); 138.30, 138.15, 137.93, 137.53 (4s); 134.45 (d,  $\text{CH}=\text{N}$ ); 130.44 (s); 129.77–127.17 (several d); 81.20 (s,  $\text{Me}_3\text{C}$ ); 74.46, 72.87, 72.32, 71.34 (4t, 4  $\text{PhCH}_2$ ); 27.84 (q,  $\text{Me}_3\text{C}$ ). HR-MALDI-MS: 781.3248 (38,  $[M + K]^+$ ,  $\text{C}_{46}\text{H}_{50}\text{KN}_2\text{O}_7^+$ ; calc. 781.3250), 765.3506 (77,  $[M + \text{H} + \text{Na}]^+$ ,  $\text{C}_{46}\text{H}_{50}\text{N}_2\text{NaO}_7^+$ ; calc. 765.3510), 544.2460 (13,  $[M - \text{Boc} - \text{PhCHNO} + \text{H} + \text{Na}]^+$ ,  $\text{C}_{34}\text{H}_{35}\text{NNaO}_4^+$ ; calc. 544.2458), 522.2629 (55,  $[M - \text{Boc} - \text{PhCHNO} + \text{H}]^+$ ,  $\text{C}_{34}\text{H}_{36}\text{NO}_4^+$ ; calc. 522.2639). Anal. calc. for  $\text{C}_{46}\text{H}_{50}\text{N}_2\text{O}_7$  (742.91): C 74.37, H 6.78, N 3.77; found: C 74.18, H 6.87, N 3.66.

**Crystal-Structure Analysis of 28**. Crystals of **28** were obtained by slow evaporation of a soln. of **28** in MeOH/ $\text{H}_2\text{O}$  (dimensions of the analyzed crystal: cube  $0.15 \times 0.13 \times 0.10$  mm).  $\text{C}_{46}\text{H}_{50}\text{N}_2\text{O}_7$ ,  $M_r$  742.88, orthorhombic  $\text{P}2_12_12_1$ ;  $a = 9.1192(11)$ ,  $b = 12.2196(12)$ ,  $c = 36.9155(16)$ ,  $V = 4113.6(7) \text{ \AA}^3$ ,  $D_x = 1.200 \text{ Mg/m}^3$ ,  $Z = 4$ . The reflections were measured on a *Bruker Nonius-Kappa* CCD diffractometer (graphite monochromator,  $\text{MoK}_\alpha$  radiation,  $\lambda = 0.71070$ ) at 220 K. All the calculations were performed using *maXus* (*Bruker Nonius*, Delft, *MacScience*, Japan). The structure was solved by direct methods and refined by full-matrix least-squares analysis (SHELXL-97) including an isotropic extinction correction. All non-H-atoms were refined anisotropically (H-atoms isotropic, whereby H-positions are based on

Table 2. Selected  $^1\text{H}$ -NMR Chemical Shifts [ppm] and Coupling Constants [Hz], and  $^{13}\text{C}$ -NMR Chemical Shifts [ppm] of the N-Bocylated and N-Tosylated 5-Amino-5-deoxyglucopyranose Derivatives **27** and **28** in ( $D_6$ )DMSO at  $100^\circ$ , of **30** and **31** in  $\text{CDCl}_3$ , and of **34** and **35** in  $\text{CD}_2\text{Cl}_2$

|                                | <b>27</b>     | <b>28</b>     | <b>30</b> | $\alpha\text{-D-31}^{\text{a}}$ | $\beta\text{-D-31}^{\text{a}}$ | <b>34</b> | <b>35<sup>c</sup></b> |
|--------------------------------|---------------|---------------|-----------|---------------------------------|--------------------------------|-----------|-----------------------|
| H–C(1)                         | 5.08          | 5.53          | –         | 5.37                            | 5.70                           | 5.43      | 6.04                  |
| H–C(2)                         | 4.25–4.18     | 4.31          | 4.31      | 3.62                            | 3.74                           | 4.30      | 4.51                  |
| H–C(3)                         | 3.58          | 3.77          | 3.72      | 3.19                            | 3.81                           | 3.40      | 3.54                  |
| H–C(4)                         | 3.96          | 3.95          | 4.01      | 3.86                            | 4.07                           | 3.82      | 3.88                  |
| H–C(5)                         | 4.25–4.18     | 3.91–3.82     | 4.82      | 4.03–3.99                       | 3.97–3.91                      | 4.36–4.29 | 4.07                  |
| H <sub>a</sub> –C(6)           | 3.78          | 3.91–3.82     | 3.83      | 3.69                            | 3.97–3.91                      | 3.86      | 3.82                  |
| H <sub>b</sub> –C(6)           | 3.78          | 3.91–3.82     | 3.78      | 3.53                            | 3.69–3.65                      | 3.66      | 3.70                  |
| $J(1,\text{OH})$               | –             | –             | –         | 6.2                             | 11.8                           | –         | –                     |
| $J(1,2)$                       | <sup>b)</sup> | 8.4           | –         | 3.5                             | 3.0                            | 7.9       | 3.6                   |
| $J(2,3)$                       | 6.6           | 9.9           | 7.5       | 8.1                             | 6.8                            | 10.8      | 6.3                   |
| $J(3,4)$                       | 9.3           | 5.1           | 2.7       | 8.2                             | 5.6                            | 6.0       | 5.3                   |
| $J(3,5)$                       | –             | –             | 1.5       | –                               | –                              | –         | –                     |
| $J(4,5)$                       | 7.2           | <sup>b)</sup> | 2.7       | 4.8                             | 2.3                            | 1.1       | 1.2                   |
| $J(5,6_{\text{a}})$            | 5.7           | <sup>b)</sup> | 10.8      | 5.9                             | <sup>b)</sup>                  | 10.1      | 4.0                   |
| $J(5,6_{\text{b}})$            | 5.7           | <sup>b)</sup> | 6.6       | 3.1                             | <sup>b)</sup>                  | 4.8       | 8.8                   |
| $J(6_{\text{a}},6_{\text{b}})$ | 5.7           | <sup>b)</sup> | 10.8      | 9.7                             | <sup>b)</sup>                  | 10.1      | 9.3                   |
| C(1)                           | 83.17         | 84.71         | 168.83    |                                 |                                | 85.95     |                       |
| C(2)                           | 78.42         | 80.42         | 79.69     |                                 |                                | 75.71     |                       |
| C(3)                           | 80.57         | 81.82         | 81.73     |                                 |                                | 82.04     |                       |
| C(4)                           | 77.44         | 76.05         | 75.90     |                                 |                                | 81.64     |                       |
| C(5)                           | 59.25         | 55.76         | 60.14     |                                 |                                | 57.99     |                       |
| C(6)                           | 71.00         | 70.29         | 70.06     |                                 |                                | 71.91     |                       |

<sup>a)</sup> The majority of the  $^{13}\text{C}$ -signals were not assigned. <sup>b)</sup> Not determined.

stereochemical considerations).  $R = 0.0398$ ,  $R_w = 0.0872$  for 500 parameters and 3189 reflections,  $\theta < 24.10^\circ$ .

2,3,4,6-Tetra-O-benzyl-5-deoxy-5-[(4-methylphenylsulfonyl)amino]-D-glucono-1,5-lactam (**30**). A soln. of **23** [14] (1 g, 1.86 mmol) in THF (20 ml) was cooled to  $-78^\circ$ , treated with a 1.6M BuLi in hexane (1.5 ml, 1.86 mmol), stirred for 15 min, treated with DMAP (227 mg, 1.86 mmol) and TsCl (710 mg, 3.72 mmol), allowed to warm to  $25^\circ$ , stirred for 1 h, diluted with sat.  $\text{NH}_4\text{Cl}$  soln., and extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times$ ). The combined org. layers were washed with  $\text{H}_2\text{O}$  and brine, dried ( $\text{MgSO}_4$ ), and evaporated. FC (hexane/AcOEt 95 : 5  $\rightarrow$  4 : 1) gave **30** (1.0 g, 77%). Colourless oil.  $R_f$  (hexane/AcOEt 3 : 1) 0.63.  $[\alpha]_D^{25} = +1.3$  ( $c = 1.58$ ,  $\text{CHCl}_3$ ). IR (ATR): 3063w, 3031w, 2923w, 2866w, 1721m, 1596w, 1495w, 1453m, 1397w, 1352m, 1307w, 1292w, 1264w, 1187m, 1168s, 1072s, 1026m, 909w, 888w, 811w, 732s, 695s, 674m, 655m.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ; assignments based on selective homodecoupling experiments): see Table 2; additionally, 7.86 (br. d,  $J = 8.1$ , 2 arom. H); 7.32–7.25 (m, 16 arom. H); 7.21 (br. dd,  $J = 5.7$ , 2.4, 2 arom. H); 7.12 (br. dd,  $J = 7.2$ , 3.9, 2 arom. H); 7.06 (br. d,  $J = 8.1$ , 2 arom. H); 4.98 (d,  $J = 11.4$ , PhCH); 4.61 (d,  $J = 11.7$ ), 4.53 (d,  $J = 11.4$ ) (2 PhCH); 4.51 (s, PhCH<sub>2</sub>); 4.47 (d,  $J = 11.4$ , PhCH); 4.39 (s, PhCH<sub>2</sub>); 2.36 (s, Me).  $^{13}\text{C}$ -NMR (75 MHz,  $\text{CDCl}_3$ ; assignments based on a HSQC spectrum): see Table 2; additionally, 144.50, 137.45, 137.37, 137.26, 136.86, 135.41 (6s); 129.03–127.68 (several d); 74.06, 73.50, 72.95, 71.29 (4t, 4 PhCH<sub>2</sub>); 21.74 (q, Me). HR-MALDI-MS: 730.2221 (38,  $[M + K]^+$ ,  $\text{C}_{41}\text{H}_{41}\text{KNO}_7\text{S}^+$ ; calc. 730.2235), 714.2486 (100,  $[M + Na]^+$ ,  $\text{C}_{41}\text{H}_{41}\text{NNaO}_7\text{S}^+$ ; calc. 714.2496). Anal. calc. for  $\text{C}_{41}\text{H}_{41}\text{NO}_7\text{S}$  (691.84): C 71.18, H 5.97, N 2.02; found: C 70.90, H 6.16, N 1.99.

2,3,4,6-Tetra-O-benzyl-5-deoxy-5-[(4-methylphenylsulfonyl)amino]- $\alpha/\beta$ -D-glucopyranose (**31**). A soln. of DIBAL-H (4.2 ml, 4.16 mmol) in toluene (20 ml) was cooled to  $0^\circ$ , treated dropwise with a

soln. of **30** (720 mg, 1.04 mmol) in toluene (5 ml), stirred for 30 min, treated with ice cubes, and stirred for 30 min at 25°. After filtration over *Celite*, evaporation and FC (hexane/AcOEt 95:5 → 3:1) gave **31** (616 mg, 85%). Colourless oil.  $R_f$  (hexane/AcOEt 3:1) 0.54.  $[\alpha]_D^{25} = +27.6$  ( $c = 1.05$ , CHCl<sub>3</sub>). IR (ATR): 3422w, 3063w, 3030w, 2923w, 2869w, 1598w, 1496w, 1453m, 1397w, 1347m, 1307w, 1208w, 1161s, 1088s, 1070s, 1027s, 983m, 965m, 915w, 814w, 734s, 696s, 665s. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>; assignments based on a DQF-COSY spectrum;  $\alpha/\beta$  7:3): 7.92 (*d*,  $J = 8.3$ , 2 arom. H ( $\beta$ )); 7.74 (*d*,  $J = 8.3$ , 2 arom. H ( $\alpha$ )); 7.38–7.13 (*m*, 20 arom. H); 7.10 (*d*,  $J = 8.6$ , 2 arom. H ( $\alpha$ )); 6.78 (*d*,  $J = 8.1$ , 2 arom. H ( $\beta$ )); 5.70 (*dd*,  $J = 11.8$ , 2.9, H–C(1) ( $\beta$ )); 5.37 (*dd*,  $J = 6.2$ , 3.5, H–C(1) ( $\alpha$ )); 4.80 (*d*,  $J = 11.5$ , PhCH ( $\beta$ )); 4.68 (*d*,  $J = 11.4$ , PhCH ( $\alpha$ )); 4.61 (*2d*,  $J = 10.9$  and 11.6, 2 PhCH ( $\alpha$ )); 4.55 (*d*,  $J = 11.4$ , 2 PhCH ( $\alpha$ )); 4.49 (*s*, PhCH<sub>2</sub> ( $\beta$ )); 4.46–4.40 (*m*, PhCH ( $\alpha$ ), 3 PhCH ( $\beta$ )); 4.41 (*d*,  $J = 11.5$ , PhCH ( $\alpha$ )); 4.35 (*d*,  $J = 11.6$ , PhCH ( $\alpha$ )); 4.09 (*d*,  $J = 5.7$ , HO ( $\alpha$ )); 4.07 (*dd*,  $J = 5.6$ , 2.3, H–C(4) ( $\beta$ )); 4.03–3.99 (*m*, PhCH ( $\beta$ ), H–C(5) ( $\alpha$ ), HO ( $\beta$ )); 3.97–3.91 (*m*, PhCH ( $\beta$ ), H–C(5) ( $\beta$ ), H<sub>a</sub>–C(6) ( $\beta$ )); 3.86 (*dd*,  $J = 8.4$ , 4.8, H–C(4) ( $\alpha$ )); 3.81 (*br. d*,  $J \approx 5.9$ , H–C(3) ( $\beta$ )); 3.74 (*dd*,  $J = 6.8$ , 3.0, H–C(2) ( $\beta$ )); 3.69 (*dd*,  $J = 9.7$ , 5.9, H<sub>a</sub>–C(6) ( $\alpha$ )); 3.69–3.65 (*m*, H<sub>b</sub>–C(6) ( $\beta$ )); 3.62 (*dd*,  $J = 8.1$ , 3.1, H–C(2) ( $\alpha$ )); 3.53 (*dd*,  $J = 9.7$ , 3.1, H<sub>b</sub>–C(6) ( $\alpha$ )); 3.19 (*t*,  $J = 8.2$ , H–C(3) ( $\alpha$ )); 2.35 (*s*, Me ( $\beta$ )); 2.33 (*s*, Me ( $\alpha$ )). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>; assignments based on a HSQC spectrum;  $\alpha/\beta$  7:3): 143.55–135.92 (several *s*); 129.48–127.49 (several *d*); 83.26 (*d*, C(2) ( $\alpha$ )); 81.61 (*d*, C(1) ( $\alpha$ )); 81.23 (*d*, C(2) ( $\beta$ )); 80.99 (*d*, C(3) ( $\alpha$ )); 79.70 (*d*, C(3) ( $\beta$ )); 76.59 (*d*, C(1) ( $\beta$ )); 76.49 (*d*, C(4) ( $\alpha$ )); 74.64 (*d*, C(4) ( $\beta$ )); 74.41 (*t*, PhCH<sub>2</sub> ( $\alpha$ )); 73.54 (*t*, PhCH<sub>2</sub> ( $\alpha$ )); 73.29 (*t*, PhCH<sub>2</sub> ( $\beta$ )); 73.14 (*t*, PhCH<sub>2</sub> ( $\alpha$ )); 72.88 (*t*, PhCH<sub>2</sub> ( $\alpha$ )); 72.20 (*t*, PhCH<sub>2</sub> ( $\beta$ )); 71.82 (*t*, PhCH<sub>2</sub> ( $\beta$ )); 71.35 (*t*, PhCH<sub>2</sub> ( $\beta$ )); 70.42 (*t*, C(6) ( $\beta$ )); 69.71 (*t*, C(6) ( $\alpha$ )); 58.64 (*d*, C(5) ( $\alpha$ )); 55.08 (*d*, C(5) ( $\beta$ )); 21.58 (*q*, Me ( $\beta$ )); 21.52 (*q*, Me ( $\alpha$ )). HR-MALDI-MS: 732.2383 (38,  $[M + K]^+$ , C<sub>41</sub>H<sub>43</sub>N<sub>7</sub>O<sub>7</sub>S<sup>+</sup>; calc. 732.2392), 716.2664 (100,  $[M + Na]^+$ , C<sub>41</sub>H<sub>43</sub>NNaO<sub>7</sub>S<sup>+</sup>; calc. 716.2652). Anal. calc. for C<sub>41</sub>H<sub>43</sub>N<sub>7</sub>O<sub>7</sub>S (693.86): C 70.97, H 6.25, N 2.02; found: C 70.88, H 6.45, N 1.96.

**2,3,4,6-Tetra-O-benzyl-1,5-dideoxy-5-[(4-methylphenylsulfonyl)amino]-D-glucopyranose N-Benzylimine N-Oxide (32)** and **2,3,4,6-Tetra-O-benzyl-1-N-benzyl-5-deoxy-1-N-hydroxy-5-[(4-methylphenylsulfonyl)amino]- $\alpha$ -D- and - $\beta$ -D-glucopyranosylamine (33)**. A soln. of BnNH<sub>2</sub>·HCl (230 mg, 1.44 mmol) in MeOH (5 ml) was treated with NaHCO<sub>3</sub> (120 mg, 1.44 mmol), stirred for 15 min, and evaporated. A soln. of the residue in CH<sub>2</sub>Cl<sub>2</sub> was washed with H<sub>2</sub>O and brine. The org. layer was dried (MgSO<sub>4</sub>) and evaporated to afford BnNH<sub>2</sub>. A mixture of the crude BnNH<sub>2</sub>, **31** (200 mg, 0.28 mmol), and 4-Å mol. sieves in dry pyridine (5 ml) was heated for 12 h at 100° and evaporated. FC (hexane/AcOEt 98:2 → 1:1) afforded **32/33**. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>;  $\alpha$ -**33**/ $\beta$ -**33** ca. 3:1, traces of **32**): 7.76 (*d*,  $J = 8.2$ , 2 arom. H); 7.62 (*d*,  $J = 8.2$ , 2 arom. H); 7.40–7.05 (*m*, 26 arom. H, 1 H of  $\alpha$ -**33**); 6.92 (*d*,  $J = 7.4$ , 1 arom. H of  $\beta$ -**33**); 5.60 (*d*,  $J = 7.1$ , H–C(1) of  $\alpha$ -**33**); 5.26 (*d*,  $J = 2.2$ , H–C(1) of  $\beta$ -**33**); 5.19 (*dd*,  $J = 6.1$ , 7.4, H–C(2) of  $\beta$ -**33**); 4.82 (*d*,  $J = 11.8$ , PhCH of  $\alpha$ -**33**); 4.70 (*d*,  $J = 12.1$  and 11.6, 2 PhCH of  $\alpha$ -**33**); 4.32 (*d*,  $J = 11.3$ , PhCH of  $\alpha$ -**33**); 4.30 (*d*,  $J = 11.6$ , PhCH of  $\alpha$ -**33**); 4.23 (*dt*,  $J = 4.7$ , 2.9, 1 H of  $\alpha$ -**33**); 4.14 (*dd*,  $J = 9.9$ , 3.6, 1 H of  $\alpha$ -**33**); 4.65–3.94 (*m*, 10 H and 4 H of  $\alpha$ -**33**); 3.60 (*dd*,  $J = 4.7$ , 9.6, H<sub>a</sub>–C(6) of  $\beta$ -**33**); 3.46 (*dq*,  $J = 8.8$ , 2.2, H<sub>a</sub>–C(6) of  $\alpha$ -**33**); 3.16 (*dd*,  $J = 6.9$ , 9.6, H<sub>b</sub>–C(6) of  $\beta$ -**33**); 2.77 (*dd*,  $J = 7.9$ , 10.2, H<sub>b</sub>–C(6) of  $\alpha$ -**33**); 2.37 (*s*, Me of  $\alpha$ -**33**); 2.31 (*s*, Me of  $\beta$ -**33**).

**2,3,4,6-Tetra-O-benzyl-5-deoxy-5-[(4-methylphenylsulfonyl)amino]-1-N-(phenylmethylidene)- $\beta$ -D-glucopyranosylamine N-Oxide (34)**. A soln. of **32/33** in ClCH<sub>2</sub>CH<sub>2</sub>Cl (5 ml) was treated with MnO<sub>2</sub> (625 mg, 7.20 mmol), kept at reflux for 48 h, and filtered over *Celite*. Evaporation and FC (hexane/AcOEt 95:5 → 4:1) gave **34** (120 mg, 78% from **30**). Colourless oil.  $R_f$  (hexane/AcOEt 4:1) 0.38.  $[\alpha]_D^{25} = -45.4$  ( $c = 1.0$ , CHCl<sub>3</sub>). IR (ATR): 3062w, 3030w, 2869w, 1735m, 1597w, 1578w, 1563w, 1495w, 1453m, 1350m, 1305w, 1241w, 1207w, 1187m, 1165s, 1142w, 1086s, 1069s, 1027m, 982w, 904w, 836w, 811w, 734s, 693s, 665m. <sup>1</sup>H-NMR (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>; assignments based on selective homodecoupling experiments): see Table 2; additionally, 8.19–8.14 (*m*, 2 arom. H); 7.64 (*s*, HC=N); 7.65–7.41 (*m*, 2 arom. H); 7.47–7.41 (*m*, 3 arom. H); 7.35–6.97 (*m*, 22 arom. H); 4.70 (*d*,  $J = 10.6$ ), 4.67 (*d*,  $J = 11.3$ ), 4.62 (*d*,  $J = 11.8$ ), 4.61 (*d*,  $J = 11.3$ ) (4 PhCH); 4.53 (*s*, PhCH<sub>2</sub>); 4.42 (*d*,  $J = 11.7$ ), 4.37 (*d*,  $J = 10.8$ ) (2 PhCH); 2.28 (*s*, Me). <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>; assignments based on a HSQC spectrum): see Table 2; additionally, 143.98 (*d*, CH=N); 138.06, 137.98, 137.87, 137.23, 136.13, 135.83 (6s); 130.75–127.39 (several *d*); 75.99, 74.38, 73.14, 70.72 (4t, 4 PhCH<sub>2</sub>); 21.74 (*q*, Me). HR-MALDI-MS: 835.2850 (38,  $[M + K]^+$ , C<sub>48</sub>H<sub>48</sub>KN<sub>2</sub>O<sub>7</sub>S<sup>+</sup>; calc. 835.2814); 819.3059 (100,  $[M + Na]^+$ , C<sub>48</sub>H<sub>48</sub>N<sub>2</sub>NaO<sub>7</sub>S<sup>+</sup>; calc. 819.3074). Anal. calc. for C<sub>48</sub>H<sub>48</sub>N<sub>2</sub>O<sub>7</sub>S (796.98): C 72.34, H 6.07, N 3.51; found: C 72.05, H 6.14, N 3.42.

2,3,4,6-Tetra-O-benzyl-1,5-dideoxy-5-[(4-methylphenylsulfonyl)amino]-1-nitro- $\alpha$ -D-glucopyranose (**35**). A soln. of **34** (100 mg, 0.14 mmol) in  $\text{CD}_2\text{Cl}_2$  (5 ml) was cooled to  $-78^\circ$ .  $\text{O}_3$  was bubbled through the soln. until disappearance of **34**. The soln. was purged with  $\text{N}_2$ , and a  $^1\text{H-NMR}$  spectrum of the reaction mixture was recorded.  $^1\text{H-NMR}$  (300 MHz,  $\text{CD}_2\text{Cl}_2$ ,  $-10^\circ$  assignments based on selective homodecoupling experiments): see Table 2; additionally, 7.72 (d,  $J=8.3$ , 1 arom. H); 7.36–6.99 (m, 23 arom. H); 4.67 (s,  $\text{PhCH}_2$ ); 4.49 (d,  $J=11.8$ ), 4.41 (d,  $J=12.1$ ) (2  $\text{PhCH}$ ); 4.39 (s,  $\text{PhCH}_2$ ); 4.28 (d,  $J=11.6$ ), 4.21 (d,  $J=11.6$ ) (2  $\text{PhCH}$ ); 2.27 (s, Me). TLC showed two spots, one of  $\text{PhCHO}$ , and one of **31**, identified by  $^1\text{H-NMR}$  after evaporation of the solvent.

6-Azido-2,3,4,7-tetra-O-benzyl-5-[(tert-butoxy)carbonyl]amino-1-5,6,8-trideoxy-D-erythro-D-galacto-octose N-Benzylimine N-Oxide (**36**). A soln. of  $\text{BnNHOH} \cdot \text{HCl}$  (225 mg, 1.41 mmol) in MeOH (5 ml) was treated with  $\text{NaHCO}_3$  (120 mg, 1.41 mmol), stirred for 15 min, and evaporated. A soln. of the residue in  $\text{CH}_2\text{Cl}_2$  was washed with  $\text{H}_2\text{O}$  and brine. The org. layer was dried ( $\text{MgSO}_4$ ) and evaporated. A mixture of the residue ( $\text{BnNHOH}$ ), **14** (200 mg, 0.282 mmol), and 4-Å mol. sieves in BuOH (10 ml) was heated to  $80^\circ$  for 12 h, cooled to  $25^\circ$ , filtered over Celite, and evaporated. A soln. of the residue in AcOEt was washed with 0.1N HCl and brine, dried ( $\text{MgSO}_4$ ), and evaporated. FC (hexane/AcOEt 95:5  $\rightarrow$  1:1) gave **36** (208 mg, 90%). Colourless oil.  $R_f$  (hexane/AcOEt 4:1) 0.19.  $[\alpha]_D^{25} = +6.7$  ( $c=1.02$ ,  $\text{CHCl}_3$ ). IR (ATR): 3434w, 3064w, 3031w, 2978w, 2927w, 2869w, 2103m, 1711m, 1584w, 1495m, 1454m, 1391w, 1381w, 1366w, 1306w, 1247w, 1220w, 1162m, 1070s, 1048m, 1027m, 940w, 909w, 859w, 733s, 695s.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ; assignments based on selective homodecoupling experiments): 7.39–7.20 (m, 20 arom. H, NH); 6.60 (d,  $J=6.6$ , H–C(1)); 5.09 (dd,  $J=6.9$ , 2.4, H–C(2)); 4.98 (d,  $J=10.2$ ), 4.59 (d,  $J=11.4$ ), 4.57 (d,  $J=11.1$ ), 4.52 (d,  $J=11.1$ ), 4.51 (d,  $J=12.0$ ), 4.43 (d,  $J=12.0$ , 2 H), 4.41 (d,  $J=10.2$ ), 4.37 (d,  $J=12.0$ ) (9  $\text{PhCH}$ ); 4.23 (br. d,  $J \approx 9.0$ , H–C(4)); 4.09 (d,  $J=11.1$ ,  $\text{PhCH}$ ); 3.77 (br. t,  $J=10.2$ , H–C(5)); 3.73 (dd,  $J=8.4$ , 2.4, H–C(3)); 3.71 (qd,  $J=6.3$ , 2.4, H–C(7)); 3.55 (dd,  $J=10.5$ , 2.1, H–C(6)); 1.37 (s, *t*-Bu); 1.31 (d,  $J=6.0$ , Me).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ; assignments based on a HSQC spectrum): 155.00 (s, C=O); 138.16 (2d, HC=N, 1 arom. C); 137.88 (2 C), 137.59, 132.13 (3s, 4 arom. C); 129.35–127.25 (several d); 79.68 (s,  $\text{Me}_3\text{C}$ ); 78.13 (d, C(3)); 76.45 (d, C(4)); 75.77 (d, C(7)); 74.87, 74.40 (2t, 2  $\text{PhCH}_2$ ); 73.69 (d, C(2)); 72.14, 70.35, 69.85 (3t, 3  $\text{PhCH}_2$ ); 65.44 (d, C(6)); 50.26 (d, C(5)); 28.30 (q,  $\text{Me}_3\text{C}$ ); 14.10 (q, Me). HR-MALDI-MS: 852.3735 (69,  $[M+K]^+$ ,  $\text{C}_{48}\text{H}_{53}\text{KN}_5\text{O}_7^+$ ; calc. 852.3733), 836.3989 (100,  $[M+Na]^+$ ,  $\text{C}_{48}\text{H}_{53}\text{N}_5\text{NaO}_7^+$ ; calc. 836.3994), 814.4170 (41,  $[M+H]^+$ ,  $\text{C}_{48}\text{H}_{56}\text{N}_5\text{O}_7^+$ ; calc. 814.4174), 606.3075 (51,  $[M-\text{Boc}-\text{BnNOH}+H+OH]^+$ ,  $\text{C}_{36}\text{H}_{38}\text{N}_4\text{O}_4^+$ ; calc. 606.2842), 591.2963 (21,  $[M-\text{Boc}-\text{BnNOH}+H]^+$ ,  $\text{C}_{36}\text{H}_{38}\text{N}_4\text{O}_4^+$ ; calc. 591.2971). Anal. calc. for  $\text{C}_{48}\text{H}_{53}\text{N}_5\text{O}_7$  (813.99): C 70.83, H 6.81, N 8.60; found: C 70.56, H 6.90, N 8.35.

(*E/Z*)-6-Azido-2,3,4,7-tetra-O-benzyl-5-[(tert-butoxy)carbonyl]amino-1-5,6,8-trideoxy-1-N-(phenylmethylidene)-D-erythro- $\beta$ -D-galacto-octopyranosylamine N-Oxide (**17**). A soln. of **36** (110 mg, 0.13 mmol), LiI (36 mg, 0.27 mmol), and  $\text{PbO}_2$  (325 mg, 1.35 mmol) in toluene/pyridine 2:1 (6 ml) was heated to  $60^\circ$  for 4 h, cooled to r.t., filtered over Celite, and evaporated. FC ( $\text{Al}_2\text{O}_3$  Akt. 1, hexane/AcOEt 98:2  $\rightarrow$  4:1) gave **17** (79 mg, 63%). Slightly pink oil.  $R_f$  (hexane/AcOEt 3:1) 0.17.  $[\alpha]_D^{25} = -2.5$  ( $c=1.2$ ,  $\text{CHCl}_3$ ). IR (ATR): 3031w, 2978w, 2932w, 2865w, 2107m, 1710m, 1578w, 1563w, 1496w, 1454m, 1368m, 1326m, 1244m, 1150w, 1091s, 1047m, 1026m, 922w, 875w, 849w, 805w, 776w, 732s, 693s.  $^1\text{H-NMR}$  (300 MHz, ( $\text{D}_6$ )DMSO,  $100^\circ$ ; (*E*)/(*Z*) 3:2; assignments based on selective homodecoupling experiments): 7.39–7.20 (m, 2 arom. H); 7.84 (s, HC=N (*E*)); 7.73 (s, HC=N (*Z*)); 7.45–7.18 (m, 23 arom. H); 6.01 (d,  $J=5.7$ , H–C(1) (*Z*)); 5.81 (d,  $J=5.1$ , H–C(1) (*E*)); 4.92–4.26 (m, 11.4 H); 4.10 (br. t,  $J=7.5$ , 1 H (*E*)); 3.96–3.86 (m, 1.4 H); 3.83 (dd,  $J=8.1$ , 1.8, 1 H (*E*)); 1.38 (s, *t*-Bu (*E*)); 1.34 (s, *t*-Bu (*Z*)); 1.23 (d,  $J=6.0$ , Me (*E*)); 1.15 (d,  $J=6.3$ , Me (*Z*)).  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CDCl}_3$ ,  $60^\circ$ ; (*E*)/(*Z*) 3:2): 154.94 (s, C=O); 138.87–137.87 (several s); 131.91 (s); 130.32 (s); 130.23 (d, HC=N (*Z*)); 129.93 (d, HC=N (*E*)); 128.63–127.04 (several d); 86.46 (d, 1 C); 83.00 (s,  $\text{Me}_3\text{C}$ ); 81.46 (d, C (*E*)); 80.37 (d, C (*Z*)); 77.87 (d, C (*E*)); 76.44 (d, C (*Z*)); 76.20 (d, C (*Z*)); 75.59 (d, C (*E*)); 75.08 (d, C (*Z*)); 74.32 (t,  $\text{PhCH}_2$  (*E*)); 73.99 (d, C (*E*)); 73.84 (t,  $\text{PhCH}_2$  (*Z*)); 73.68 (t,  $\text{PhCH}_2$  (*Z*)); 73.43 (t,  $\text{PhCH}_2$  (*E*),  $\text{PhCH}_2$ ); 70.51 (t,  $\text{PhCH}_2$  (*Z*)); 70.35 (t,  $\text{PhCH}_2$  (*E*)); 65.25 (d, C(6)); 55.72 (d, C(5) (*Z*)); 55.59 (d, C(5) (*E*)); 28.21 (q,  $\text{Me}_3\text{C}$  (*E*)); 28.12 (q,  $\text{Me}_3\text{C}$  (*Z*)); 15.57 (q, Me). HR-ESI-MS: 850.3611 (2,  $[M+K]^+$ ,  $\text{C}_{48}\text{H}_{53}\text{KN}_5\text{O}_7^+$ ; calc. 850.3577); 834.3838 (100,  $[M+Na]^+$ ,  $\text{C}_{48}\text{H}_{53}\text{N}_5\text{NaO}_7^+$ ; calc. 834.3837). Anal. calc. for  $\text{C}_{48}\text{H}_{53}\text{N}_5\text{O}_7$  (811.98): C 71.00, H 6.58, N 8.63; found: C 71.00, H 6.64, N 8.46.

## REFERENCES

- [1] B. Aebischer, A. Vasella, H.-P. Weber, *Helv. Chim. Acta* **1982**, *65*, 621.
- [2] B. Aebischer, J. H. Bieri, R. Prewo, A. Vasella, *Helv. Chim. Acta* **1982**, *65*, 2251.
- [3] B. Aebischer, A. Vasella, *Helv. Chim. Acta* **1983**, *66*, 789.
- [4] R. Meuwly, A. Vasella, *Helv. Chim. Acta* **1984**, *67*, 1568; D. Beer, J. H. Bieri, I. Macher, R. Prewo, A. Vasella, *Helv. Chim. Acta* **1986**, *69*, 1172; A. Vasella, *Pure Appl. Chem.* **1991**, *63*, 507.
- [5] N. Kornblum, *Angew. Chem.* **1975**, *87*, 797; N. Kornblum, A. S. Erickson, *J. Org. Chem.* **1981**, *46*, 1037; R. Meuwly, A. Vasella, *Helv. Chim. Acta* **1985**, *68*, 997; A. Vasella, R. Wyler, *Helv. Chim. Acta* **1990**, *73*, 1742.
- [6] N. Asano, R. J. Nash, R. J. Molyneux, G. W. J. Fleet, *Tetrahedron: Asymmetry* **2000**, *11*, 1645.
- [7] 'Iminosugars as Glycosidase Inhibitors, Nojirimycin and Beyond', Ed. A. E. Stütz, VCH, Weinheim, 1999.
- [8] T. Heightman, A. T. Vasella, *Angew. Chem., Int. Ed.* **1999**, *38*, 750; V. H. Lillielund, H. H. Jensen, X. Liang, M. Bols, *Chem. Rev.* **2002**, *102*, 515; H. Takahata, Y. Banba, H. Ouchi, H. Nemoto, A. Kato, I. Adachi, *J. Org. Chem.* **2003**, *68*, 3603.
- [9] A. Mitrakou, N. Tountas, A. E. Raptis, R. J. Bauer, H. Schulz, S. A. Raptis, *Diabetic Med.* **1998**, *15*, 657; T. M. Block, X. Lu, F. M. Platt, G. R. Foster, W. H. Gerlich, B. S. Blumberg, R. A. Dwek, *Proc. Natl. Acad. Sci. U.S.A.* **1994**, *91*, 2235; D. Durantel, N. Branza-Nichita, S. Carrouée-Durantel, T. D. Butters, R. A. Dwek, N. Zitzmann, *J. Virol.* **2001**, *75*, 8987; T. Cox, R. Lachmann, C. Hollak, J. Aerts, S. van Weely, M. Hřebíček, F. Platt, T. Butters, R. Dwek, C. Moyses, I. Gow, D. Elstein, A. Zimran, *Lancet* **2000**, *355*, 1481; 'Iminosugars: From Synthesis to Therapeutic Applications', Eds. P. Compain, O. R. Martin, Wiley, Chichester, 2007; A. H. Futerman, J. L. Sussman, M. Horowitz, I. Silman, A. Zimran, *Trends Pharmacol. Sci.* **2004**, *25*, 147; P. Compain, O. R. Martin, C. Boucheron, G. Godin, L. Yu, K. Ikeda, N. Asano, *ChemBioChem* **2006**, *7*, 1356; F. Marcelo, Y. He, S. A. Yuzwa, L. Nieto, J. Jiménez-Barbero, M. Sollogoub, D. J. Vocadlo, G. D. Davies, Y. Blériot, *J. Am. Chem. Soc.* **2009**, *131*, 5390; H. Li, Y. Blériot, C. Chantreau, J.-M. Mallet, M. Sollogoub, Y. Zhang, E. Rodríguez-García, P. Vogel, J. Jiménez-Barbero, P. Sinaÿ, *Org. Biomol. Chem.* **2004**, *2*, 1492; H. Li, T. Liu, Y. Zhang, S. Favre, C. Bello, P. Vogel, T. D. Butters, N. G. Oikonomakos, J. Marrot, Y. Blériot, *ChemBioChem* **2008**, *9*, 253; C. Norez, S. Noel, M. Wilke, M. Bijvelds, H. Jorna, P. Melin, H. DeJonge, F. Becq, *FEBS Lett.* **2006**, *580*, 2081; D. D. Dhavale, M. M. Matin, *ARKIVOC* **2005**, 110.
- [10] M.-P. Collin, S. N. Hobbie, E. C. Böttger, A. Vasella, *Helv. Chim. Acta* **2008**, *91*, 1838.
- [11] M.-P. Collin, S. N. Hobbie, E. C. Böttger, A. Vasella, *Helv. Chim. Acta* **2009**, *92*, 230.
- [12] F. Schlünzen, R. Zarivach, J. Harms, A. Bashan, A. Tocilj, R. Albrecht, A. Yonath, F. Franceschi, *Nature* **2001**, *413*, 814.
- [13] R. Hoos, A. B. Naughton, W. Thiel, A. Vasella, W. Weber, K. Rupitz, S. G. Withers, *Helv. Chim. Acta* **1993**, *76*, 2666.
- [14] R. Hoos, A. B. Naughton, A. Vasella, *Helv. Chim. Acta* **1993**, *76*, 1802.
- [15] H. S. Overkleeft, J. van Wiltenburg, U. K. Pandit, *Tetrahedron Lett.* **1993**, *34*, 2527.
- [16] H. S. Overkleeft, J. van Wiltenburg, U. K. Pandit, *Tetrahedron* **1994**, *50*, 4215.
- [17] G. Papandreou, M. K. Tong, B. Ganem, *J. Am. Chem. Soc.* **1993**, *115*, 11682.
- [18] R. W. Hoffmann, *Chem. Rev.* **1989**, *89*, 1841; R. W. Armstrong, B. R. Teegarden, *J. Org. Chem.* **1992**, *57*, 915; P. Magnus, J. Lacour, W. Bauta, B. Mugrage, V. Lynch, *J. Chem. Soc., Chem. Commun.* **1991**, 1362; B. I. Glänzer, Z. Györgydeák, B. Bernet, A. Vasella, *Helv. Chim. Acta* **1991**, *74*, 343; J. Podlech, D. Seebach, *Liebigs Ann. Chem.* **1995**, 1217; D. Seebach, B. Lamatsch, R. Amstutz, A. K. Beck, M. Dobler, M. Egli, R. Fitzi, M. Gautschi, B. Herradón, P. C. Hidber, J. J. Irwin, R. Locher, M. Maestro, T. Maetzke, A. Mouño, E. Pfammatter, D. A. Plattner, C. Schickli, W. B. Schweizer, P. Seiler, G. Stucky, W. Petter, J. Escalante, E. Juaristi, D. Quintana, C. Miravittles, E. Molins, *Helv. Chim. Acta* **1992**, *75*, 913.
- [19] M. Carmeli, S. Rozen, *J. Org. Chem.* **2006**, *71*, 4585.
- [20] H. Bayley, D. N. Standring, J. R. Knowles, *Tetrahedron Lett.* **1978**, 3633; N. Panday, T. Granier, A. Vasella, *Helv. Chim. Acta* **1998**, *81*, 475; Y. Zhang, M. A. Wolfert, G.-J. Boons, *Bioorg. Med. Chem.* **2007**, *15*, 4800.

- [21] A. Gagnon, S. J. Danishefsky, *Angew. Chem., Int. Ed.* **2002**, *41*, 1581.
- [22] E. J. Corey, B. Samuelsson, F. A. Luzzio, *J. Am. Chem. Soc.* **1984**, *106*, 3682.
- [23] J. Pabba, B. P. Rempel, S. G. Withers, A. Vasella, *Helv. Chim. Acta* **2006**, *89*, 635.
- [24] T. Granier, A. Vasella, *Helv. Chim. Acta* **1998**, *81*, 865.
- [25] H. Ulrich, A. A. Sayigh, *Angew. Chem.* **1962**, *74*, 468.
- [26] P. Merino, S. Franco, F. L. Merchan, T. Tejero, *Synth. Commun.* **1997**, *27*, 3529.
- [27] S. Cicchi, M. Corsi, M. Marradi, A. Goti, *Tetrahedron Lett.* **2002**, *43*, 2741.
- [28] S. Cicchi, M. Marradi, A. Goti, A. Brandi, *Tetrahedron Lett.* **2001**, *42*, 6503.
- [29] I. Chataigner, C. Panel, H. Gérard, S. R. Piettre, *Chem. Commun.* **2007**, 3288.
- [30] M. A. Voinov, I. A. Grigor'ev, *Russ. Chem. Bull.* **2002**, *51*, 297.
- [31] K. Mahmood, A. Vasella, B. Bernet, *Helv. Chim. Acta* **1991**, *74*, 1555.

Received August 29, 2010