β-Lactams from D-Erythrose-Derived Imines: A Convenient Synthesis of 2,3-Diamino-2,3-dideoxy-D-mannonic-Acid Derivatives

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The D-*manno*-configured *N*-anisylated β-lactam **40**, the β-lactam carboxylic acids **4** and **43**, and the corresponding phosphonic-acid isosters **49** and **50** have been synthesized from D-glucose in 8–10 steps, respectively. None of these compounds exhibited a significant inhibitory activity *in vitro* against the sialidases of *Vibrio cholerae*, *Salmonella typhimurium*, *Influenza A* (N9), and *Influenza B* virus. Cycloaddition of the *in situ* generated imines derived from the D-erythroses **6**, **16**, and **17** with the ketene from mesyloxyacetyl chloride (**20**) gave the 2-mesyloxy-D-hexono-1,3-lactams **25**, **27a/b**, **28a/b/c**, and **29** in 23, 69, 57, and 90% yield, respectively (*Scheme 3*). Transformation of **27a/b** and **29** (> 85%) to the corresponding azides, followed by oxidative *N*-deprotection, gave **30a/b** (45%) and **34** (80%). Subsequent alkylation of the ring N-atom in **31a** with benzyl bromoacetate and dibenzyl (triflyloxymethyl)phosphonate **46** gave the carboxylate **41** (77%) and the phosphonate **47** (55%; *Schemes 4* and *5*). Hydrogenolysis of **41** gave the β-lactam amino acid **43**, besides its hydrolysis product **44**. Reductive *N*-acylation of the azido group in **41** (93%), followed by hydrogenolytic debenzylation, yielded the 2-trifluoroacetamido *N*-(carboxymethyl)-β-lactam **4** (56%). Similarly, **47** gave the 2-trifluoroacetamide **48** (89%), and hence, the 2-amino-*N*-(phosphonoylmethyl)-β-lactams **49** (40%) and **50**, resulting from deacylation of **49** (14%). Aminolysis and carbamoylation of the protected β-lactams **31a** and **35** led to the 2,3-diamino-2,3-dideoxy-D-mannonamides **51** and **53**, respectively (*Scheme 6*).

Introduction. – Nonproteinogenic, enantiomerically pure 2,3-diamino acids are frequent components of antibiotics [1][2], antifungal dipeptides [3], and other biologically active compounds [4][5]. Enantiomerically pure 2,3-diamino and 2,3,4-triamino acids have been obtained by hydrolysis of appropriately substituted β-lactams [6] accessible by [2 + 2]-cycloaddition of either enantiomerically pure, glycine-derived ketenes to imines, or phthalimido ketenes to enantiomerically pure α-amino-imines ([7] and refs. cit. therein). 2,3-Diamino acids have also been prepared by substitutive opening of enantiomerically pure aziridines by azide. The aziridines have been obtained *via* amino alcohols resulting from an enantioselective aminohydroxylation of crotonates [8], by the addition of enantiomerically pure lithium amides to α,β-unsaturated esters and subsequent introduction of a second amino group [9], and by a few other established methods from α-amino acids [10]. A new approach describes the 1,3-dipolar cycloaddition of morpholin-2-one-derived azomethine ylides to aromatic imines. Hydrogenolysis of the resulting perhydroimidazo-morpholinones yields 2,3-diamino-3-arylpropanoic acids [11].

Amino sugars [12–14] are ubiquitous structural motives of primary and secondary metabolites and essential components of a variety of pharmacologically active

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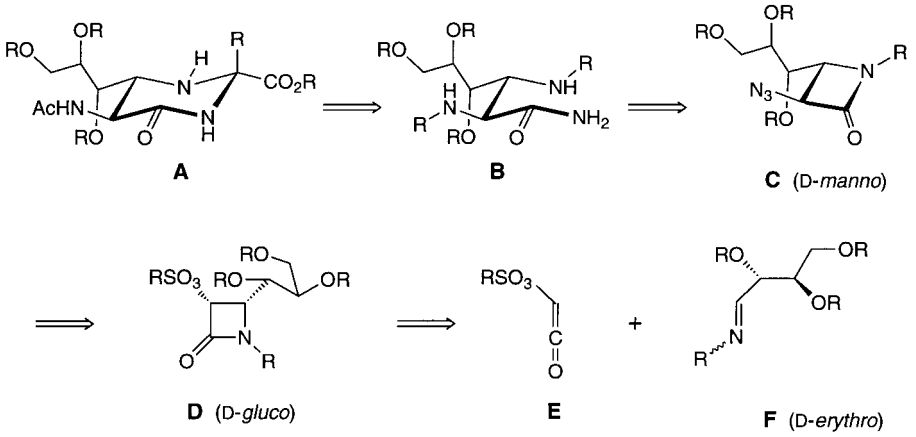
substances[2]). Several 2,3-diamino-2,3-dideoxy sugars play a pivotal role as cell-wall constituents (lipopolysaccharides, LPS [24]) of *Gram*-positive [25] and *Gram*-negative bacterial strains, such as the hospital pathogen *Pseudomonas aeruginosa* [26]. Since the discovery of 2,3-diacetamido-2,3-dideoxy-D-glucose as a constituent of lipid A of some Rhodospirillaceae [27], 2,3-diaminohexoses have received considerable attention [28]. The arsenal of methods available for the synthesis of 2,3-diaminohexoses and their derivatives is rather limited, and the methods are not very practical (for the synthesis of vicinal diamines in general, see [29]). 2,3-Diaminohexoses have been obtained *via* nucleophilic substitution by azide of 2,3-epimino sugars [30] and 2,3-anhydro sugars, followed by activation and nucleophilic displacement of the resulting secondary alcohol by nitrogen nucleophiles [18][27][31][32], by nucleophilic azide displacement of 1,2-disulfonates [33], by addition of nitrogen nucleophiles to nitro alkenes [34], and by addition of nitrosyl chloride to 3-azido-D-glycals [35].

Among the 2,3-diamino sugars, 2,3-diamino-2,3-dideoxy-D-mannose is of particular interest as precursor of 6-amino-6-deoxy-Neu5Ac [36] and related potential sialidase inhibitors [37] such as **A** (*Scheme 1*). A convenient access to mannose derivatives of type **B** appeared desirable, and β-lactams of type **C** appeared suitable precursors. For their synthesis, we decided to evaluate [2 + 2] ketene-imine cycloadditions (for reviews, see [38]) of erythrose-derived imines **F** with a substituted ketene **E**. The imines **F** have not yet been described, but they appear to be readily accessible from *aldehydo*-D-erythroses. Substitution of the β-lactams **D** will afford the D-*manno* azides **C**; these lactams are of additional interest in view of the synthesis of azetidine analogues of Neu5Ac.

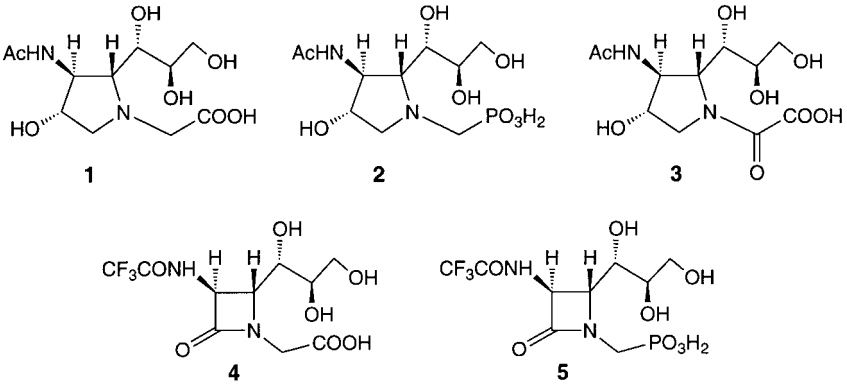
Scheme 1



While pyrrolidine-1-acetic acid **1** and the related methylphosphonic acid **2** (but not the corresponding oxalamide **3**) inhibit *V. cholerae* neuraminidase [39], four-membered ring analogues of Neu5Ac are unknown. We wondered about the

[2]) Examples include the aminoglycoside antibiotics (*cf.* [15–17]), various cytostatica [18–20], the muramyl peptides ([21] and refs. cit. therein), glycosidase inhibitors [22], and various peptidomimetics [23].

potential sialidase inhibition of the related azetidinones and azetidines, and included the synthesis of the azetidinones **4** and **5** in our plans, opting – on the basis of previous results [40][41] – for the trifluoroacetamido rather than for the acetamido group.

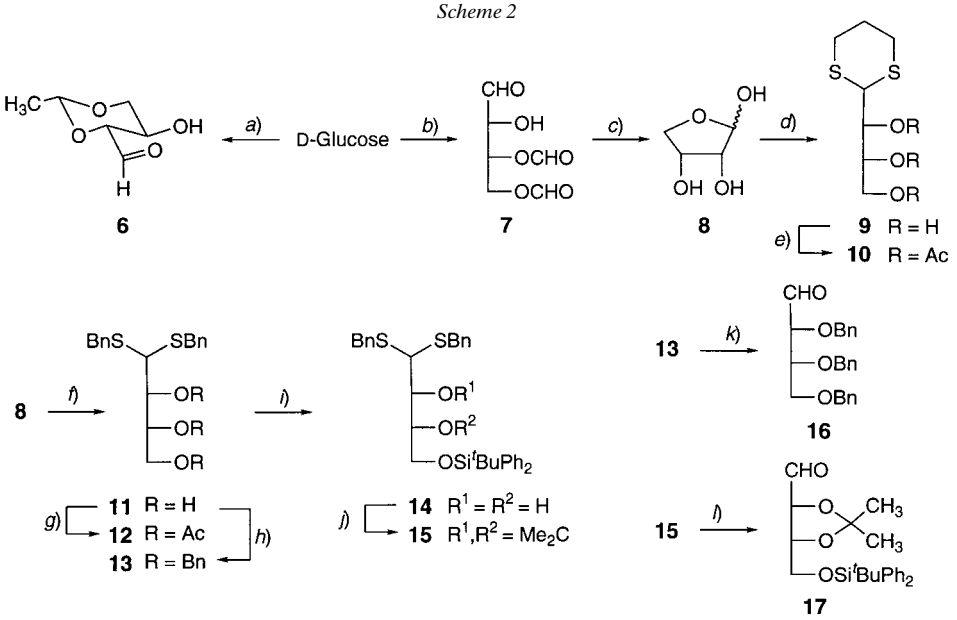


The first [2+2] cycloaddition of sugar-derived imines (generated from L-glyceraldehyde and 3-deoxy-L-glyceraldehyde) to ketenes is due to *Hubschwerlen* and *Schmid* [42]. Since then, only a few similar cycloadditions have been reported; *i.e.*, the synthesis of a 2,3-diamino-D-pentose from D-glyceraldehyde [43], of a 2,3-diamino-4-deoxyhexose from 4-deoxythreose [44][45], of a 2,3,4-triamino-5-phenylpentose from β-phenylserine aldehyde [5][46], and of 2,3-diaminohexoses from D- [47] and L-threose [48]. All of these cycloadditions to *N*- or *O*-substituted ketenes resulted in 3,4-*cis*-configured β-lactams [49], suggesting that the *trans*-configured 2,3-diamino-D-mannono-1,3-lactam **C** (carbohydrate nomenclature) has to be prepared by cycloaddition of a ketene precursor possessing a leaving group, followed by invertive replacement of the leaving group by a nitrogen substituent. As 3-(sulfonyloxy)-β-lactams lead to higher yields of substitution products [45][50] than their 3-halogenated analogues [51], a (sulfonyloxy)acetyl chloride appeared to be a favourable ketene precursor [52][53].

(Phenylsulfonyl)oxy- and (tosyloxy)acetic acid, and their acid chlorides have first been synthesised by *Lichtenberger* and *Faure* in 1948 [54]. The synthesis is based on sulfonylation and subsequent acidic hydrolysis of hydroxyacetonitrile, and the authors pointed out that this method cannot be used for the preparation of (mesyloxy)acetic acid. However, *Warner-Lambert* have been granted a patent in 1965 [55] for the synthesis of (mesyloxy)acetyl chloride by the procedure of *Lichtenberger* and *Faure*. A few years later, *Lattrell* and *Lohaus* reported the synthesis of a variety of (sulfonyloxy)acetic acids by a similar procedure [52], whereas *Havbrandt* and *Wachtmeister*, and *Plapp et al.* reported the synthesis of (mesyloxy)acetic acid from bromo- and iodoacetic acid and silver mesylate [56][57]. We aimed at a reproducible synthesis of (mesyloxy)acetyl chloride.

Results. – 1. *Preparation of the β-Lactams.* The protected D-erythroses **6** [58][59], **16**, and **17**[3]) were prepared as starting materials for the envisaged imines (*Scheme 2*). As the synthesis of the dithioacetal **9** [63] could not be conveniently scaled up due to its solubility in H_2O, we prepared the more lipophilic dibenzyl dithioacetal **11**. D-Erythrose (**8**) was produced by $Pb(OAc)_4$ cleavage of glucose according to *Perlin* and *Brice* [64][65]. The procedure was improved by replacing the very slow filtration of the Pb salts by centrifugation, and the acidic hydrolysis of the formate ester **7** by simple evaporation of its aqueous solution. Acid-catalyzed dithioacetalisation of the resulting **8** with BnSH, followed by chromatography on a short silica-gel column, gave **11** that was additionally characterized as the triacetate **12**. The synthesis of **11** was conveniently performed on a 250-g scale, resulting in an overall yield of 50–60% from D-glucose. On the one hand, benzylation of **11** to **13**, followed by thioacetal cleavage, yielded 77% of **16**; on the other hand, silylation of **11** to **14**, followed by isopropylidenation to **15** and thioacetal cleavage, led in 88% yield to **17**.

Scheme 2



a) Paraldehyde, cat. H_2SO_4; $NaIO_4$, H_2O; 55%. *b*) $Pb(OAc)_4$, $AcOH/H_2O$ 100 : 2. *c*) H_2O, 40°, co-evaporation; 80–90% from D-glucose. *d*) $HS(CH_2)_3SH$, $Zn(OTf)_2$, HCl, −15 to −25°; 28%. *e*) Ac_2O, pyridine; 89%. *f*) BnSH, HCl, −60 to −25°; 60%). *g*) Ac_2O, pyridine; 95%. *h*) NaH, BnBr, DMF; 90%. *i*) ^{t}BuPh$_2$SiCl, 1*H*-imidazole, DMF; quant. *j*) $CuSO_4$, acetone; 90% from **11**. *k*) $CuCl_2$, CuO, acetone/H_2O 99 : 1; 86%. *l*) $HgCl_2$, $CaCO_3$, MeCN/H_2O 9 : 1; 98%.

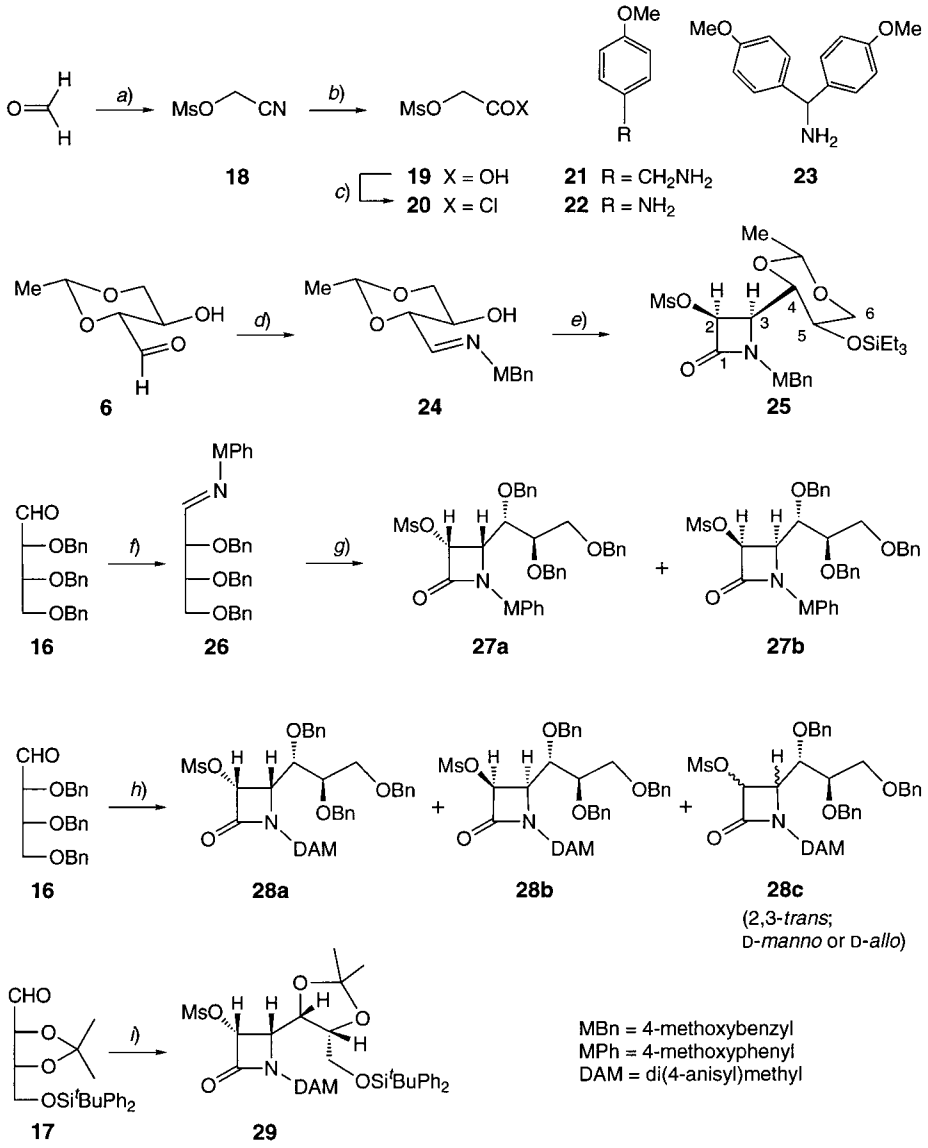
[3]) 2,3,4-Tri-*O*-benzyl-D-erythrose (**16**) has not been described, whereas 2,3,4-tri-*O*-benzyl-D-threose has recently been reported [60]. Racemic **17** [61] and its L-enantiomer [62] are known. We investigated the synthesis of a few other D-erythrose derivatives. The preparation of 2,3,4-tris-*O*-(2-nitrobenzyl)- and 2,3,4-tris-*O*-[(3,4-dimethoxyphenyl)methyl]-D-erythrose dibenzyl dithioacetals failed due to decomposition during base-catalyzed *O*-alkylation, whereas cleavage of the 2,3,4-tris-*O*-[(trimethylsilylethoxy)methyl]-D-erythrose dibenzyl dithioacetal led to decomposition during workup. The reaction of D-erythrose dibenzyl dithioacetal with (2-methoxyethoxy)methyl chloride (MEMCl) under standard conditions did not go to completion.

We were not able to reproduce the rudimentary protocols for the preparation of (mesyloxy)acetic acid (**19**) [52][55]. The nucleophilic displacement of bromoacetic acid with silver methanesulfonate [56] was hampered by the instability of the Ag salt, and proved unreliable. Several other methods, such as mesylation of glycolic acid with MsCl/pyridine, hydrolysis of methyl mesyloxyacetate [56] with $HCOOH/H_2SO_4$ [52], and oxidative cleavage of 1,4-bis(mesyloxy)but-2-ene [65] with $KMnO_4$ were either unsuccessful, or gave mixtures. Extensive experimentation led to a protocol that ensured satisfactory yields of crystalline, pure **19** on a scale of over 200 g starting from formaldehyde (*Scheme 3*). It proved to be critical to carefully control the temperature during mesylation of the intermediate hydroxyacetonitrile, to not exceed the duration of the strongly exothermic hydrolysis of **18**, and to crystallize **19** at 4°. For the conversion of **19** to the acid chloride **20**, oxalyl chloride proved superior to $SOCl_2$ (80 *vs.* 36–57%). Distillation of the product in high vacuum gave pure, slightly yellow **20**, which solidified below 4° to a colourless solid that was stable for months when kept under Ar in the refrigerator.

For the preparation of imines (*Scheme 3*), we used amines that have already been successfully applied in the synthesis of β-lactams [38][66], namely 4-methoxybenzylamine (**21**), *p*-anisidine (**22**), and bis(4-methoxyphenyl)methylamine (**23**). The ethylidene-D-erythrose **6** reacted only with **21** (to **24**), but not with the less nucleophilic aniline **22**, evidencing the dimerisation of **6** to a less reactive hemiacetal in solution [59]. To avoid side reactions with the acid chloride **20**, HO–C(3) of the imine **24** was protected *in situ* with Et_3SiCl prior to addition of the ketene precursor. Attempts to protect HO–C(3) with MEMCl or $MEMNEt_3^+Cl^-$ failed, and the corresponding Me_3Si ether proved unstable under the conditions of the cycloaddition. Triethylsilylation of **24**, followed by addition of the acetyl chloride **20** in the presence of Et_3N, yielded the *cis*-disubstituted β-lactam **25**, besides several side products (mostly *N*-acylation products and probably 2:1 addition products [38], as indicated by IR bands at 1660–1680 cm^{-1}). The yield of **25** was only 23% from **6**, and the reaction was not optimized. The tribenzyl ether **16** reacted readily with the aniline **22**. Under optimized conditions, cycloaddition of the phenylimine **26** gave 69% of a 3:1 mixture of the *cis*-β-lactams **27a/b**, with the desired D-*gluco*-isomer **27a** as the major product. Crucial improvements resulted from substituting Et_3N by $^iPr_2EtN$ (superior to 1,2,2,6,6-pentamethylpiperidine), avoiding excess of **20** (*i.e.*, adding it at the rate of its consumption), using CH_2Cl_2/DMF 9:1 as the solvent rather than pure CH_2Cl_2, DMF, or toluene, and performing the cycloaddition at ambient temperature rather than at 0° or below. The product mixture could, however, not be separated. Cycloaddition to the analogous [bis(4-methoxyphenyl)methyl]imine yielded an inseparable mixture **28a/b/c** of three of the four possible diastereoisomers in a ratio of 25:35:40. The main isomer is a 2,3-*trans*- and the minor isomers are 2,3-*cis*-substituted β-lactams. The best result was obtained by transforming the conformationally restricted isopropylidene acetal **17** into the [bis(4-methoxyphenyl)methyl]imine and further, under the same conditions as above, to the D-*gluco*-configured **29** in 90% yield. Both β-lactams **27a/b** and **29** were prepared in batches of up to 30 g without decrease in yield.

The condensation of **6** with the methoxybenzylamine **21** and of **16** with the aniline **22** led initially to two products with a higher R_f value of which the slower-migrating product was progressively and more or less completely transformed into the faster-

Scheme 3



a) NaCN, H_2O; MsCl; 68%. *b*) H_2SO_4, H_2O, 120°; 75%. *c*) $(COCl)_2$, CH_2Cl_2/DMF 99:1; 80%. *d*) **21**, $MgSO_4$, CH_2Cl_2. *e*) Et_3SiCl, Et_3N, CH_2Cl_2; **20**, Et_3N, CH_2Cl_2; 23% from **6**. *f*) **22**, CH_2Cl_2, molecular sieves (3 Å). *g*) **20**, $^iPr_2EtN$, CH_2Cl_2/DMF; 69% (**27a**/**b** 3:1) from **16**. *h*) **23**, CH_2Cl_2, molecular sieves (3 Å); **20**, $^iPr_2EtN$, CH_2Cl_2/DMF; 57% (**28a**/**b**/**c** 25:35:40). *i*) **23**, CH_2Cl_2, molecular sieves (3 Å); **20**, $^iPr_2EtN$, CH_2Cl_2/DMF; 90% from **15**.

migrating one. This agrees well with literature data showing that (*E*)- and (*Z*)-aldimines equilibrate, resulting, as a rule, in (*E*)/(*Z*)-mixtures >99:1 [67][68] (for mixtures of (*E*)- and (*Z*)-aldimines, see, *e.g.*, [69][70]). The imines were usually

treated directly with the ketene precursor. The imines **24** and **26** derived from benzylamine **21** and the aniline **22** were isolated, whereas the less stable imine derived from **17** and the benzhydrylamine **23** decomposed during workup.

The ^{1}H- and ^{13}C-NMR spectra of **24** and **26** show only signals of the (*E*)-diastereoisomer (**24**: H–C(1) at 7.84 and C(1) at 165.87 ppm; **26**: H–C(1) at 7.84 and C(1) at 162.28 ppm). J(1,2) Value of **24** is distinctly smaller (1.1 Hz) than J(1,2) value of **26** (5.8 Hz), indicating different conformations, presumably due to an intramolecular H-bond in **24**.

The D-*gluco*-configuration of **25** was established by X-ray crystallography (*Fig. 1*). The structure is poorly resolved and has, therefore, not been deposited with the *Cambridge Crystallographic Data Centre*. Nevertheless, it clearly indicates the *cis*-configuration at C(2) and C(3), the D-*altro*-configuration, and a *gauche*-arrangement of the C(3)–N and C(4)–O bonds.

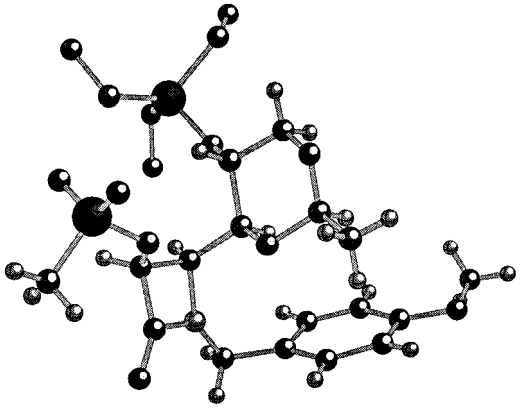


Fig. 1. *Solid-state structure of* **25**

The configuration of the hexonic-acid-derived β-lactams **27a/b**, **28a/b**, and **29** was assigned as follows. The 2,3-*cis* (= 2,3-D- or -L-*threo*) configuration is evidenced by the characteristic J(2,3) value of 5.2–5.5 Hz (*Table 3* in the *Exper. Part*; *cf.* [71]), and by comparison with **25**. The 4,5-D-*erthyro*-configuration follows from the configuration of the imines (there is no evidence for epimerisation). Hence, the lactams must possess the D-*altro* (3,4-D-*erythro*)- or D-*allo* (3,4-D-*threo*)-configuration. As a rule, the *threo*-isomers are characterised by a larger coupling constant. To check the validity of this rule for **27a/b**, **28a/b**, and **29**, one has to analyse the staggered conformers **A1**–**A3** (3,4-D-*erthyro*) and **G1**–**G3** (3,4-D-*threo*) obtained by rotation around the C(4)–C(3) bond (*Fig. 2*). Conformer **A2** is disfavoured by the synclinal arrangement of the C(4)–C(5) bond to both the C(3)–C(2) and C(3)–N bonds locating the side chain directly above the lactam ring. Conformer **A1** (and **A2**) is favoured over **A3** by a *gauche*-orientation [72] of the N–C(3) and O–C(4) bonds. Thus, conformer **A1** should be preferred by D-*altro*- and D-*allo*-configured β-lactams. The substituents at O–C(2), N–C(3), and O–C(4) may (weakly) contribute to the conformational equilibrium. A similar consideration applies to the 3,4-D-*threo* (D-*gluco* and D-*manno*)-configured β-lactams. **G1** and **G3** are favoured over **G2** by a *gauche*-orientation of the

N–C(3) and O–C(4) bonds and by a single *gauche*-orientation of the C(4)–C(5) bond either to the C(3)–N or the C(3)–C(2) bond. Conformer **G3** (H above the lactam ring, but synclinal position of *C*-substituents) should be slightly favoured over **G1** (RO group above the lactam ring, no synclinal interaction of *C*-substituents). Thus, a small $J(3,4)$ value is expected for the D-*altro*-configured β-lactams and a rather large $J(3,4)$ value for the D-*gluco*-configured β-lactams. $J(3,4) = 2.5$ Hz of **25** is in keeping with conformation **A1** that is also observed in the solid state. On the one hand, $J(3,4)$ values of 2.4 and 4.5 Hz indicate the D-*altro*-configuration for **27b** and **28b**, respectively. The weak influence of the MsO group on the size of this coupling is apparent from $J(3,4)$ values of 1.4–1.7 Hz [73] for the structurally related 2-deoxy-D-*ribo*-hexono-1,3-lactams. On the other hand, $J(3,4)$ values of 7.3, 6.0, and 9.5 Hz evidence the D-*gluco*-configuration for **27a**, **28a**, and **29**, respectively (*Table 3*). The *singlet* for H–C(2) of **28c** indicates a 2,3-*trans*-substitution (= 2,3-D- or -L-*erythro*) and, thus a D-*allo*- or D-*manno*-configuration. Due to overlapping signals, the $J(3,4)$ value of **28c** could not be determined. Even the ^{13}C-NMR data (*Table 4* in the *Exper. Part*) do not allow to unambiguously assign the absolute configuration of **28c**.

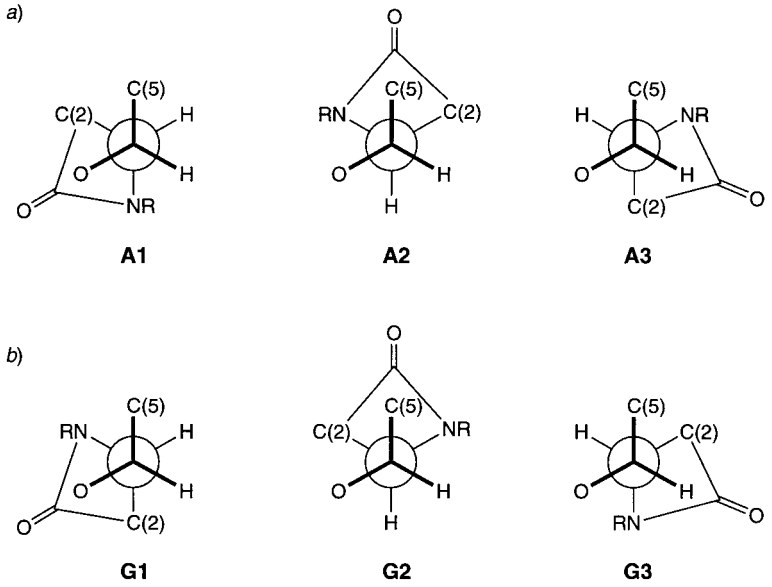


Fig. 2. Newman *projections looking along the C(4)–C(3) bond* a) *for staggered conformers of the* D-altro- or D-allo-*configured* β*-lactams, and* b) *for staggered conformers of the* D-gluco- *or* D-manno-*configured* β*-lactams*

Formation of the 2,3-*cis*-β-lactams **25**, **27a/b**, **28a/b**, and **29** is rationalised by assuming an attack of the ketene **20** on the (*E*)-configured imine **A**, leading to the s-*cis*-azonia diene **B** followed by conrotatory ring closure to either the D-altrono-1,3-lactam **C** (solid arrows in *Fig. 3,a*) or the D-glucono-1,3-lactam **D** (dashed arrows). Similarly, the D-*manno*- or D-*allo*-configured **28c** results from a (*Z*)-imine [74], indicating that the (*Z*)-imine derived from **16** and **23** is more reactive than its (*E*)-isomer (*cf.* [67][70]), or that it equilibrates more slowly than the imine **26**.

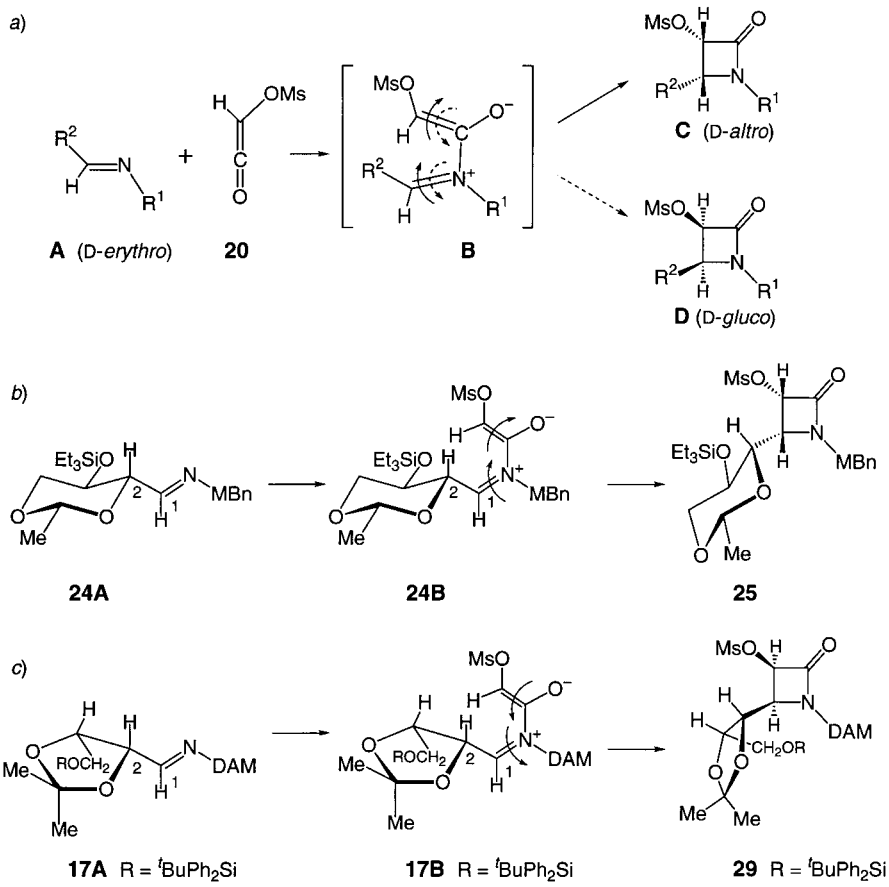


Fig. 3. a) *Formation of the intermediate* **B** *in the reaction of the* (E)*-imine* **A** *with the ketene* **20** *and its conrotatory ring closure leading to* D*-altrono- and* D*-gluconolactam* **C** *and* **D.** b) c) *Ring closure of the intermediate* **24B** *to the* D*-altronolactam* **25** *and of* **17B** *to the* D*-gluconolactam* **29**, *respectively.*

The imines derived from the cyclic aldehydes **6** and **17** led to single lactams possessing an opposite configuration at C(2) and C(3), indicating opposite directions of the conrotatory ring closure of the zwitterionic intermediates **24B** and **17B** (*Fig. 3,b* and *c*). The imines derived from the acyclic aldehyde **16**, however, gave mixtures of *cis*-substituted β-lactams resulting from both directions of conrotatory ring closure. The following factors may *a priori* influence the reaction path: the conformation of the (*E*)-imine, the conformation of the intermediate oxy-azoniadiene, and steric interactions during the conrotatory ring closure. Ampac 6.0 calculations [75] indicate that the imines **24A** and **17A**, and the corresponding oxy-azoniadienes **24B** and **17B** prefer a conformation characterized by an antiperiplanar arrangement of H–C(1) and H–C(2) (as depicted in *Fig. 3,b* and *c*). The conrotatory ring closure requires a s-*cis*-azoniadiene. The conformer of **24B** and **17B**, which possesses a completely planar diene system ($\sphericalangle C{=}N^+{-}C{=}C = 0°$) is destabilized by steric interactions between H–C(2) and the olefinic H-atom. These are alleviated by twisting around the N^+–C

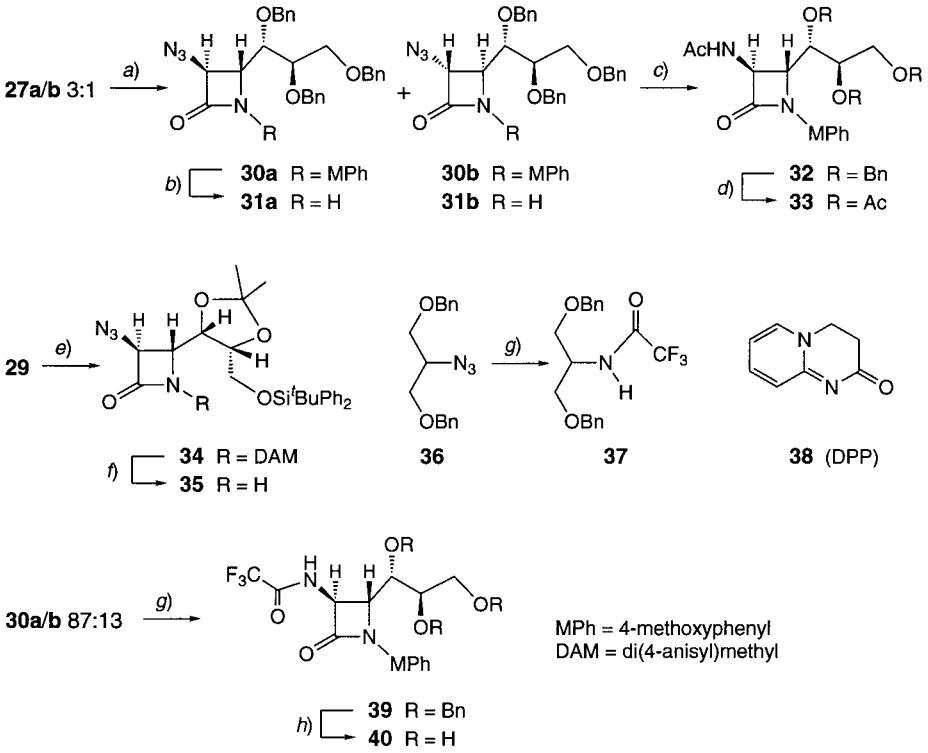
bond, leading to two helical conformers. Ampac 6.0 calculations show that these conformers ($\measuredangle C{=}N^+{-}C{=}C$ *ca.* $\pm 50°$) possess the same energy ($\Delta E < 0.5$ kcal/mol). Moreover, they equilibrate easily ($\Delta E^{\neq}$ *ca.* 4–6 kcal/mol). As a single β-lactam was obtained, the helicity of the oxy-azoniadienes cannot be a product-determining factor. However, while conrotatory ring closure of **24B** and **17B** to the gluconolactam involves a weak steric interaction between the (mesyloxy)methylene group and H–C(2), ring closure to the altronolactam is disfavoured by a stronger interaction between the (mesyloxy)methylene group and O–C(2). Thus, **17B** should be easily converted to the gluconolactam. Later stages of the ring closure of **24B** to the gluconolactam have to overcome severe steric interactions between the (mesyloxy)methylene and the bulky Et_3SiO group (compare with H in **17B**, the (silyloxy)alkyl group is far away); thus one expects that **24B** will cyclise to the altronolactam (arrows in *Fig. 3*,*b*), but more slowly than **17B**. Indeed, high yields of the gluconolactam **29** and a sluggish reaction to the altronolactam **25** were observed.

2. *Transformations of the β-Lactams.* Only the cycloaddition products containing D-*gluco*-β-lactams as the main isomer (*i.e.*, **27a/b** and **29**) were transformed into azido derivatives. Treatment of the methanesulfonates **27a/b** 3:1 with LiN_3 and of **29** with Bu_4NN_3 gave the azido compounds **30a/b** 87:13 and **34**, respectively, in high yields (*Scheme 4*). The diastereoisomers **30a/b** were separated on a small scale by flash chromatography, but their *N*-dearylation products **31a/b**, formed upon treatment with ceric ammonium nitrate (CAN) in $MeCN/H_2O$, were much more easily separated. *N*-Dearylation and chromatography yielded up to 45% of the 2-azido-D-mannonolactam **31a**, but only on a scale of less than 200 mg, while *N*-debenzylation of **34** with CAN [45][76], yielding 80% of **35**, was readily scaled up. Selective catalytic hydrogenation of the azido groups of **30a/b** 87:13 by 10% Pd/C in EtOH (6 bar of H_2), followed by *N*-acetylation and chromatography, yielded 70% of the acetamide **32**, which was debenzylated with 20% $Pd(OH)_2/C$ in aqueous MeOH (8 bar of H_2), followed by acetylation, to afford 83% of the tetraacetate **33**.

The inversion of configuration at C(2) of the azido compounds **30**, **31**, **34**, and **35** (IR band at 2110–2215 cm^{-1}) and of the acetamides **32** and **33** (IR band at 1682 and 1690 cm^{-1}) was revealed by small $J(2,3)$ values of 0.8–2.4 Hz (*Table 3*). The D-*allo*-configuration of **30b** and **31b** is evidenced by small $J(3,4)$ (**30b**: 1.0, **31b**: 3.2 Hz) and the D-*manno*-configuration of the *N*-protected lactams **30a**, **32**, and **33** by large $J(3,4)$ values (8.1–8.8 Hz; $J(3,4)$ value of **34** could not be determined). These values are larger than those of the corresponding D-*gluco*-methanesulfonates, indicating that conformer **G3** (*Fig. 2*) is less populated in the methanesulfonates due to the destabilizing interaction between the MsO group and the side chain. The *N*-deprotected lactams **31a** and **35**, however, show only medium $J(3,4)$ values (5.6 and 5.4 Hz). Here, conformer **G1**, which possesses antiperiplanar C–C bonds is more strongly favoured on account of the absence of the unfavourable interaction between *N*-protecting group and side chain.

The lactam moiety of the *N*-protected lactams **25**, **27**–**30**, and **32**–**34** is characterized by an IR band at 1750–1763 cm^{-1}. *N*-Deprotection leads to a shift of this band to higher wave numbers (**31a** and **31b**: 1775, **35**: 1780 cm^{-1}). Substitution of the MsO by the N_3 group leads to a shielding of H–C(2) and H–C(3) (*Table 3*). The chemical shifts of C(1) and C(3) are only weakly influenced by the configuration at C(2) and C(3), the substituent at C(2), and the *N*-protecting group; C(1) of **25** and **27**–**35** resonating at 161.3–166.9 and C(3) at 55.2–60.9 ppm (*Table 4*). C(2) of the acetamides **32** and **33** (59.0–61.0 ppm) resonates at higher field than C(2) of the azido derivatives **30**, **31**, **34**, and **35** (64.6–68.1 ppm) and C(2) of the methanesulfonates **25** and **27**–**29** (77.3–80 ppm).

Scheme 4



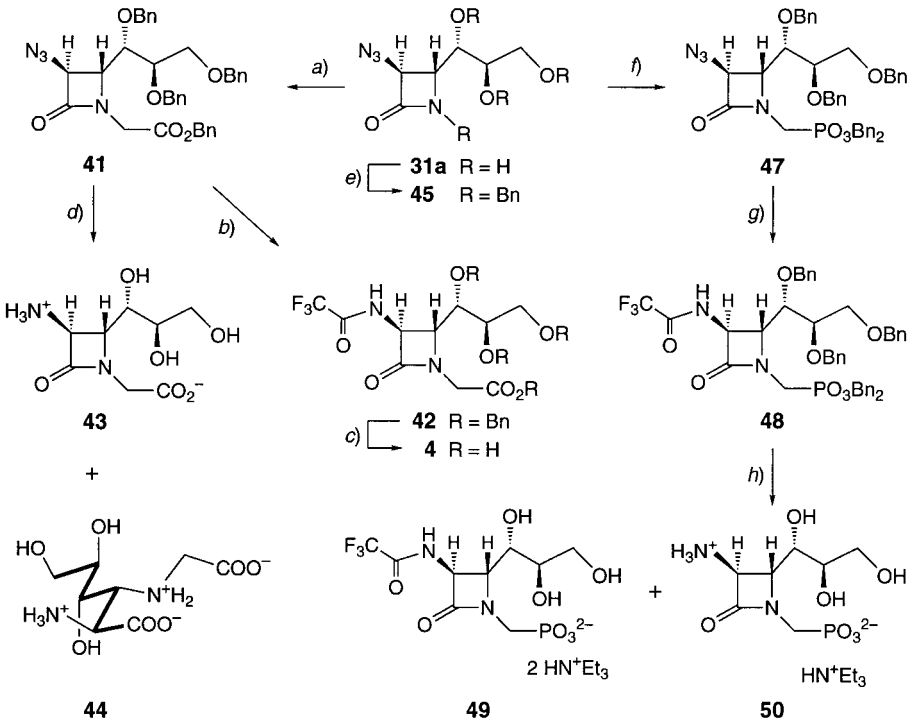
a) LiN_3, molecular sieves (3 Å), 1,3-dimethylimidazolidin-2-one; 86% (**30a/b** 87:13). *b*) CAN, $MeCN/H_2O$; **31a** (45%), **31b** (< 20%). *c*) 10% Pd/C, 6 bar of H_2, EtOH; Ac_2O, pyridine; 70%. *d*) 20% $Pd(OH)_2/C$, 8 bar of H_2, $MeOH/H_2O$ 5:1; Ac_2O, pyridine; 83%. *e*) Bu_4NN_3, molecular sieves (3 Å), 1,3-dimethylimidazolidin-2-one; 89%). *f*) CAN, $MeCN/H_2O$; 80%. *g*) $(CF_3CO)_2O$, PPh_3, THF; **38**, H_2O; 78%. *h*) 20% $Pd(OH)_2/C$, 7.5 bar of H_2, dioxane/$MeOH/H_2O$; 91%.

The transformation of the N_3 into the trifluoroacetamido group was first investigated with the azido compound **36** [77] (*Scheme 4*). Treating **36** with trifluorothioacetic acid, in analogy with the reductive acetylation of azides with AcSH [78], led in 60–70% yield to the trifluoroacetamide **37**, but the rather strongly acidic conditions and the price of CF_3COSH prompted us to search for a better solution. *Horner* and *Gross* [79] reported in 1955 that heating organic azides with Ph_3P in the presence of a carboxylic acid leads to carboxamides. This method was used for the synthesis of formamides [80] and palmitamides [81]. In 1984/85, *Vilarrasa et al.* [82], and *Roberts et al.* [83] reinvestigated the *Horner-Gross* reaction, and concluded that trifluoroacetamides are not accessible by this method. Still, a non-acidic variant of the *Horner-Gross* reaction might allow a mild one-pot reductive trifluoroacetylation of alkyl azides. $CF_3CO_2CH_2CF_3$, *N*-(trifluoroacetyloxy)succinimide, and CF_3COSEt in the presence of Ph_3P gave only traces of **37**. However, trifluoroacetic anhydride in the presence of Ph_3P and 3,4-dihydropyrido[2,1-*b*]pyrimidin-2(2*H*)-one (DPP; **38**) [84] transformed **36** smoothly into **37**. Similarly, reductive trifluoroacetylation of **30a/b**

87:13 to **39** proceeded smoothly[4]) and led, after debenzylation by CAN, in two steps and in 70% yield to the triol **40**.

N-Alkylation of the β-lactam **31a** with benzyl bromoacetate was investigated under several conditions (*Scheme 5* and *Table 1*). The highest yields resulted from adding Ag_2O and $BrCH_2CO_2Bn$ in portions to **31a** in 1,3-dimethylimidazolidin-2-one (*N*,*N*-dimethylethyleneurea; DMEU) over several days. The reductive trifluoroacetylation of **41** led in high yields to the trifluoroacetamido derivative **42**. Catalytic hydrogenation of **42** afforded the carboxylic acid **4**, which was purified by reversed-phase HPLC and isolated in 56% yield. Hydrogenation of the azido lactam **41** and preparative reversed-phase HPLC (0.1M $Et_3NH^+HCO_3^-$) gave a 2:3:3 mixture (54%) of the β-lactam **43** and the diamino dicarboxylic acid **44**, which resulted from hydrolysis of **43**, and Et_3N.

Scheme 5



a) Ag_2O, $BrCH_2CO_2Bn$, 1,3-dimethylimidazolidin-2-one; 77%. *b*) $(CF_3CO)_2O$, PPh_3, THF; **38**, H_2O; 93%. *c*) 20% $Pd(OH)_2/C$, 7 bar of H_2, MeOH/H_2O 5:1; 56%. *d*) 20% $Pd(OH)_2/C$, 7 bar of H_2, ^{t}BuOH/H_2O 4:1; 54% of **43**/**44**/Et_3N 2:3:3. *e*) $ClCH_2PO_3Bn_2$, KF/Al_2O_3, K_2CO_3, Bu_4NI, MeCN; 88%. *f*) NaH, 12-crown-4, 1,3-dimethylimidazolidin-2-one/THF, then **46**; 55%. *g*) As *b*); 89%. *h*) 20% $Pd(OH)_2/C$, 6.5 bar of H_2, ^{t}BuOH/0.1M $Et_3NH^+HCO_3^-$ 3:1; 40% of **49**, 14% of **50**.

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[4]) Presumably, the azide is first reduced to a phosphanimine. Addition of DPP to the mixture of azide, PPh_3, and $(CF_3CO)_2O$ is accompanied by the appearance of an intense yellow colour that is immediately discharged upon addition of H_2O, suggesting that DPP assists in the hydrolytic breakdown of an *N*-acylphosphaniminium intermediate.

Table 1. N-*Benzyloxycarbonylmethylation of* **31a**

Equiv. of $BrCH_2CO_2Bn$	Reagent	Solvent	Temp. [°]	Time [h]	Yield of **41** [%]
2.0	Ag_2O	DMF	60	68	47
3.0	Ag_2O	MeCN	80–90	27	42
2.1	Ag_2O	DMEU	70	65	53
3.1	Ag_2O	DMEU	25–80	124	69
2.5	Ag_2O	DMEU	25–75	216	77
4.0	KF on Al_2O_3	MeCN	25	192	40
3.0	KF on Al_2O_3, K_2CO_3, Bu_4NI	MeCN	25	168	62

Initial attempts to alkylate **31a** with dibenzyl (chloromethyl)phosphonate [85] gave the *N*-benzylated lactam **45** (88%; *Scheme 5*). This result is not surprising considering the ready benzylation of amines by benzyl phosphates and phosphonates (see, *e.g.*, [86]). For an effective *N*-(dibenzyl)phosphonomethylation, the Cl substituent of the reagent must be replaced by a better leaving group. Indeed, *N*-alkylation with dibenzyl (triflyloxymethyl)phosphonate (**46**) [39] gave the desired dibenzyl phosphonate **47** in 55% yield. The preparation of dibenzyl (triflyloxymethyl)phosphonate was optimized, affording 72% of pure **46**; a similar protocol, yielding 65% of crude **46**, has recently been published [87]. The reductive trifluoroacetylation of **47** yielded 89% of the trifluoroacetamide **48**. Hydrogenolytic debenzylation of **48**, followed by preparative reversed phase HPLC (0.1M $Et_3NH^+HCO_3^-$) and lyophilisation, led to the salt **50**·2 Et_3N (14%) and to a mixture of the trifluoroacetamide **49** and incompletely debenzylated products. Drying of **50**·2 Et_3N at 0.01 Torr for 3 d resulted in complete loss of Et_3N and afforded the mono-triethylammonium salt **50**. The mixture containing **49** was converted to the free phosphonic acid and again hydrogenated. Preparative reversed-phase HPLC gave the pure bis[triethylammonium] salt **49** (40%).

The trifluoroacetamido compounds **37**, **39**, **40**, **42**, **4**, **48**, and **49** show IR bands at 1712–1730 cm^{-1} and the characteristic *q*'s in the ^{13}C-NMR spectra at 157.4–159.1 ppm (C=O, ^2J(C,F) = 37.3–38.3 Hz) and at 110–117 ppm (CF_3, ^1J(C,F) = 286–290 Hz; *Table 4* in *Exper. Part*). For **37**, **42**, and **48**, the corresponding ^{13}C-NMR signals were too weak to be assigned. The CH_2COO group of **41**–**44** gives rise to an *AB* system at 3.84–4.23 ppm characterised by a large vicinal coupling (17.5–18.0 Hz), and to a ^{13}C *t* at 43.7–46.6 ppm and a *s* at 168.3–168.8 (ester) or at 175.0–176.0 ppm (acid or carboxylate). The CH_2PO_3 group of **47**–**50** resonates in the ^{1}H-NMR spectrum as two *dd* at 3.29–3.95 ppm showing ^2J(H,P) of 8.1–9.5 and 11.2–14.3 ppm. In the broad-band P-decoupled spectra, the *dd*'s collapse to an *AB* system (J_{AB} = 15.4–15.9 Hz). In the ^{13}C-NMR spectra, the CH_2PO_3 group of the benzyl esters **47** and **48** appears as a *dt* at 38.3 and 38.7 ppm showing ^1J(C,P) of 151.8 and 154.3 Hz, respectively. The corresponding *dt* of the ammonium phosphonates **49** and **50** is shifted downfield by *ca.* 3 ppm and shows smaller ^1J(C,P) values of 138.5 and 141.7 Hz, respectively. As expected, the ^{31}P signal of **49** and **50** (12.2 and 11.4 ppm, resp.) is shifted upfield by *ca.* 10 ppm relative to the ^{31}P signal of the benzyl phosphonates **47** and **48** (22.5–22.6 ppm).

The β-lactam moiety of **39**–**43**, **45**, and **47**–**50** is evidenced by IR bands at 1748–1774 cm^{-1}, the C(1) *s* at 163.3–171.8, and the C(3) *d* at 58.6–62.5 ppm (*Table 4*). The small J(2,3) value of 1.4–2.6 Hz reveal the 2,3-*trans*-configuration (*Table 3*). J(3,4) = 7.2–8.1 Hz of the protected β-lactams **39**, **42**, **45**, **47**, and **48**, and J(3,4) = 3.3–5.2 Hz of the triols **40**, **4**, **43**, **49**, and **50** indicate the D-*manno*-configuration. Similarly to the *N*-deprotected β-lactams (see above), the *N*-protected triols show a higher population of the **G1** conformation (*Fig. 2*). Compound **44** is hardly a β-lactam as its J(2,3) = 3.9 Hz is too large for a *trans*- and too small for a *cis*-substituted β-lactam (compare with J(2,3) = 5.2–5.4 Hz for **25**, **27a**/**b**, **28a**/**b**, and **29**). The upfield shift of C(3) of **44** (6 ppm relative to **43**) clearly indicates that the β-lactam ring has been opened. Indeed, C(3) of **44** resonates at a similar position as C(3) of the mannonamides **51** and **53** (*Fig. 6*; 54.6 *vs.* 53.4 and 51.9 ppm). C(1) of **44** appears at 168.25 ppm, which hints either to an acid (compare with δ(^{13}C(1)) of 2,3-diaminocarbonic acids (180–182 ppm

[88]) of a 2-amino-3-benzamidocarbonic acid (168 ppm [89]), and of 2-aminocarbonic acids (172–179 ppm [90])), or to an amide (compare with $\delta(^{13}C(1))$ of **51** and **53** (171.3 and 169.5 ppm). β-Lactams are usually hydrolysed under basic condition (alkali hydroxide), but hydrolysis also occurs under acidic conditions (*e.g.*, with $HBF_4 \cdot 2\ Et_2O$ in CH_2Cl_2 [91]). Formation of an amide can be excluded, as it requires contact with NH_3. Presumably, neighbouring-group participation is responsible for the facile hydrolysis of **43**.

Table 2. *Comparison of the ^1H- and ^{13}C-NMR Chemical Shifts* [ppm] *in D_2O of* **43**/**44**/*Et_3N 2 : 3 : 3*, **49**, *and* **50**/*Et_3N 1 : 2 with Those of Et_3N in the Presence of AcOH or Glycine*

	43/**44**/Et_3N 2 : 3 : 3	**49**	**50**/ET_3N 1 : 2		
$(CH_3CH_2)_3N$	1.28	1.28	1.32		
$(CH_3CH_2)_3N$	3.20	3.20	3.24		
HDO	4.76	4.78	4.78		
$(CH_3CH_2)_3N$	8.41	8.39	8.43		
$(CH_3CH_2)_3N$	46.83	46.70	46.85		
	Et_3N	Et_3N/AcOH 2 : 1	Et_3N/AcOH 1 : 1	Et_3N/glycine 2 : 1	Et_3Nglycine 1 : 1
$(CH_3CH_2)_3N$	1.03	1.20	1.30	1.15	1.23
$(CH_3CH_2)_3N$	2.55	2.93	3.22	2.89	3.06
HDO	4.79	4.79	4.79	4.80	4.80
$(CH_3CH_2)_3N$	13.08	9.10	8.25	9.23	8.70
$(CH_3CH_2)_3N$	48.48	46.18	46.76	46.09	46.47

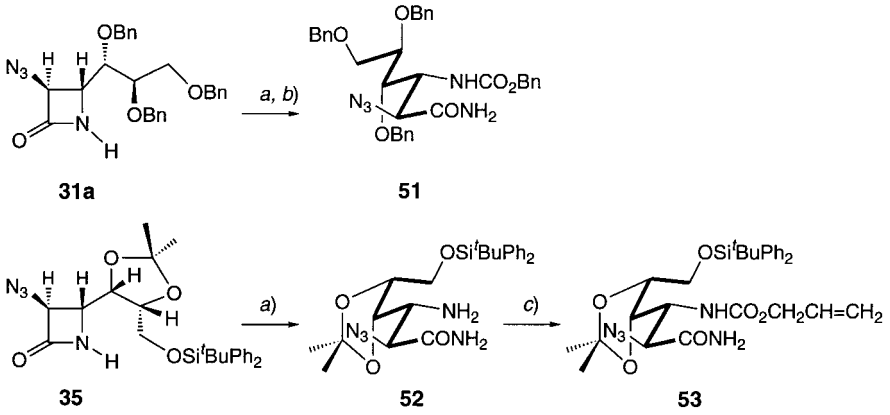
The lyophilised mixture **43**/**44**/Et_3N 2 : 3 : 3 contained equimolar amounts of **44** and Et_3N. This raised the question of whether **44** was a triethylammonium salt or merely complexed to NEt_3. The ^1H- and ^{13}C-NMR chemical shifts for the Et_3N moiety in this mixture are similar to the corresponding shifts of the diammonium salt **49** and the 1 : 2 mixture of the monoammonium salt **50** and Et_3N (*Table 2*). A comparison with the shifts of Et_3N, Et_3N/AcOH 2 : 1, Et_3N/AcOH 1 : 1, Et_3N/glycine 2 : 1, and Et_3N/glycine 1 : 1 shows that Et_3N of **43**/**44**, **49**, and **50** is nearly completely protonated. Not surprisingly, Et_3N is a stronger base than the amino groups of **43**, **44**, and **50**.

The vicinal couplings $J(3,4)$, $J(4,5)$, $J(5,6)$, and $J(5,6')$ of the triols **40**, **4**, **43**, **49**, and **50** (3.3–5.2, 8.1–9.9, 5.0–5.8, and 2.2–5.1 Hz, respectively; *Table 3* in *Exper. Part*) are roughly similar to the corresponding values for DANA (1.2, 9.3, 6.0, and 2.7 Hz, respectively [37]) and indicate a similar conformation of the glycerol side chain of these triols and of DANA (Neu5Ac2en).

3. *Aminolysis of the β-Lactams.* Aminolysis [92][93] of monocyclic, *N*-acylated or *N*-alkylated β-lactams by hydrazine [94], or *O*-benzylhydroxylamine [95] and ring opening by sulfur ylides [96] are well documented. Nocardicins, however, do not undergo ring opening with aqueous hydroxylamine [97], and monocyclic, *N*-unprotected β-lactams were stable in boiling liquid NH_3 [98]. Aminolysis of monocyclic *N*-alkyl β-lactams requires a large excess of NH_3 and long reaction times at elevated temperature and pressure [93][99], while the analogous ring opening of *N*-unprotected monocyclic β-lactams has not been reported to date ([98], for a nucleophilic opening of a *N*-Boc β-lactam by aqueous NH_3, see [100]).

Keeping a solution of **31a** or **35** in NH_3-saturated MeOH in a sealed flask for a few days resulted in a clean and nearly quantitative formation of 2-azido-3-amino amides, which were transformed into the carbamates **51** and **53**, respectively (*Scheme 6*). The carbamates **51**–**53** are the first derivatives of 3-amino-2-azido-2,3-dideoxy-D-mannonic acid; they are related to known derivatives of diaminononulosonates, intermediates for the synthesis of *N*-acetyl-6-amino-6-deoxyneuraminic acid [36].

Scheme 6



a) NH_3/MeOH. *b*) 1-(Benzyloxycarbonyl)benzotriazole in EtOH or *N*-[(benzyloxycarbonyl)oxy]succinimide in DMF; 92%. *c*) 1-(Allyloxycarbonyl)benzotriazole, 1,3-dimethylimidazolidin-2-one; 87%.

The mannonamides **51**–**53** are characterised by medium $J(2,3)$ (4.9–6.9 Hz) and small $J(3,4)$ values (1.5–3.9 Hz; *Table 3* in *Exper. Part*), indicating a preferred *zig-zag* conformation, as depicted in *Scheme 6*. By comparison to the β-lactam precursor, C(1) of **51** and **53** is shifted downfield (*ca.* 7 ppm) and C(3) is slightly shifted upfield (*ca.* 3.6 ppm; *Table 4* in *Exper. Part*).

4. *Inhibition of Sialidases.* Compounds **40**, **4**, **43**/**44**/Et_3N 2:3:3, **49**, and **50**·2 Et_3N were tested against the sialidases of *Vibrio cholerae*, *Salmonella typhimurium* (LT2 strain), *Influenza A* (N2) and *Influenza B* (B/Lee/70) virus with DANA [101] as a reference inhibitor, by *Warren*'s thiobarbituric-acid assay [102][5]). None of them showed any significant inhibition.

We thank the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, for financial support.

Experimental Part

General. See [103].

Standard Peracetylation. A *ca.* 0.05M soln. of the polyol in pyridine was treated with 20 equiv. of Ac_2O and 0.2 equiv. of DMAP and stirred at 22°. After aqueous workup, the peracetate was purified by FC.

*(*R*)-2,4-*O*-Ethylidene-*D*-erythrose* (**6**). By a variation of the procedure in [58]: at 0°, a soln. of (*R*)-4,6-*O*-ethylidene-D-glucopyranose[6]) (5.00 g, 24.20 mmol) in H_2O (15 ml) was added dropwise in 45 min to a strongly stirred soln. of $NaIO_4$ (10.50 g, 48.88 mmol) in H_2O (100 ml). The pH was monitored (pH electrode) and constantly adjusted to 4.0 by addition of sat. aq. $NaHCO_3$ soln. After 1 h at 0°, the ice bath was removed and the pH adjusted to 6.5–7. The suspension was stirred for an additional 2 h at 22°. Excess $NaIO_4$ (checked with KI starch paper) was destroyed by the dropwise addition of ethylene glycol. After lyophilisation, the resulting white powder was extracted with hot AcOEt (8 × 30 ml), until TLC failed to show product in the extracts. Evaporation and FC (toluene/acetone 3:1) of the resulting yellowish foam gave **6** (3.2 g, 91%). Colourless solid. R_f (CH_2Cl_2/MeOH 10:1) 0.57. M.p. 149° (toluene/acetone; [58]: 150–151°). $[\alpha]_D^{25} = -34.2$ ($c = 8.06$, H_2O; 48 h) ([58]: $[\alpha]_D^{25} = -36.2$ at equilibrium ($c = 8.2$, H_2O)).

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5) We thank Prof. *Laver* (Influenza Research Unit, Australian National University, Canberra, Australia) for his help in establishing the assays and for generous gifts of *Influenza A* and *B*, and *S. typhimurium* sialidases.

6) Obtained from D-glucose according to [58]: 60% yield, colourless microcrystalline solid. R_f (CH_2Cl_2/MeOH 7:1) 0.45. M.p. 175° (EtOH). $[\alpha]_D^{25} = -1.1$ ($c = 19.6$, H_2O; after 48 h).

3,4-Di-O-*formyl*-D-*erythrose* (**7**) *and* D-*Erythrose* (**8**). By an improved variant of the procedure in [64] adapted for large scale: anh. D-glucose (200 g, 1.11 mol) was dissolved under stirring in lukewarm H_2O (150 ml). The resulting syrup was cooled to 18° and slowly added under vigorous stirring to precooled (18°) anh. AcOH (7.5 l) in a 10-l beaker. A constant stream of N_2 was directed over the surface of the mechanically stirred suspension. Within a period of 45 min, $Pb(OAc)_4$ (1093.8 g, 2.467 mol; *Fluka purum* containing 15% of AcOH) was added portionwise so as to keep the temp. below 30°. After complete addition, the suspension was stirred under ice cooling for 45 min, until a clear, yellowish soln. was formed, and the temp. dropped from 28 to 16°. After addition of oxalic acid (222.13 g, 2.467 mol), stirring was continued at 22° for 60 min to complete the lead-oxalate precipitation. The viscous white suspension was centrifuged (1300–1500 rpm, 15 min) in 4 portions of 1 l at 17–18°. The clear supernatant was decanted, and the white sediment was thoroughly mixed with excess anh. AcOH and centrifuged again. This procedure was repeated, and the collected supernatants were evaporated at $T < 35°$. The resulting, turbid oil was taken up in AcOEt (2.8 l), and the white suspension formed was quickly washed with ice water (4 × 120 ml). The combined aq. phases were extracted with AcOEt (4 × 220 ml). The combined org. phases were dried (Na_2SO_4) and evaporated to yield crude **7** (199 g, quant.; R_f (toluene/acetone 2 : 1) 0.75) as a slightly yellow syrup. Crude **7** was treated with H_2O (300 ml) and evaporated at $T < 40°$. This procedure was repeated (7 cycles) until the distilled liquids no longer showed the typical HCOOH smell, and the weight remained constant, affording **8** (122.89 g, 92%). Pure, almost colourless honey. R_f (i-PrOH/H_2O 10 : 1) 0.66. $[\alpha]_D^{25} = -30$ ($c = 1$, H_2O, after 48 h) ([64]: $[\alpha]_D^{25} = -30$ to -32.5 (after 72 h)).

D-*Erythrose Propane-1,3-diyl Dithioacetal* (**9**) *and 2,3,4-Tri*-O-*acetyl*-D-*erythrose Propane-1,3-diyl Dithioacetal* (**10**). A suspension of **8** (39.25 g, 0.294 mol; 10% H_2O content assumed) in dry dioxane (600 ml) was treated with 4-Å molecular sieves (10 g) and $Zn(OTf)_2$ (11.24 g, 30.92 mmol), stirred at 22° for 5 min, treated slowly with propane-1,3-dithiol (108.9 g, 1.006 mol), and stirred for 16 h. After the addition of $MgSO_4$ (20.0 g, 0.166 mol), fuming HCl (100 ml), and more propane-1,3-dithiol (35.36 g, 0.327 mol), stirring was continued for 4 h at 22°. The suspension was poured onto ice (*ca.* 400 ml) and quickly neutralized by addition of solid Na_2CO_3 and $NaHCO_3$. The viscous white mixture was suction-filtered over a sand/*Celite*/sand bed, and the remaining solid was washed with acetone (1000 ml), EtOH (1000 ml), and MeOH (1000 ml). The combined filtrates were evaporated to a thin paste, which was co-evaporated with toluene (2 × 300 ml) and *o*-xylene (200 ml). Further evaporation with mesitylene (200 ml) and FC of the green amorphous residue (CH_2Cl_2/MeOH 15 : 1) afforded **9** (20.25 g, 28%) as a slightly yellowish solid. A small sample of **9** (100 mg) was peracetylated under standard conditions. FC (hexane/AcOEt 4 : 1) gave **10** (142 mg, 89%).

Data of **9**: R_f (CH_2Cl_2/MeOH 15 : 1) 0.32. M.p. 141° (CH_2Cl_2/MeOH).

Data of **10**: Colourless solid. R_f (hexane/AcOEt 2 : 1) 0.42. M.p. 65° (hexane/AcOEt). $[\alpha]_D^{25} = +7.2$ ($c = 0.96$, $CHCl_3$). IR (KBr): 2960*w*, 2940*w*, 2920*w*, 1745*s*, 1430*m*, 1370*s*, 1240*s* (br.), 1045*s*. ^{1}H-NMR (400 MHz, (D_6)acetone): 1.98, 1.99, 2.07 (3*s*, 3 AcO); 2.01–2.04 (*m*, CH_2CH_2S); 2.62–2.69 (*m*, 1 H), 2.72–2.80 (*m*, 1 H), 2.89–2.98 (*m*, 1 H), 3.01–3.09 (*m*, 1 H) (2 CH_2S); 4.08 (*d*, $J = 8.7$, H–C(1)); 4.23 (*dd*, $J = 6.8$, 12.2, H–C(4)); 4.30 (*dd*, $J = 3.6$, 12.2, H′–C(4)); 5.58 (*td*, $J \approx 3.9$, 6.8, H–C(3)); 5.65 (*dd*, $J = 4.2$, 8.7, H–C(2)). ^{13}C-NMR (50 MHz, (D_6)acetone): 20.58 (*q*, 2 Me); 20.76 (*q*, Me); 26.12 (*t*, CH_2CH_2S); 27.28, 27.32 (2*t*, 2 CH_2S); 44.67 (*d*, C(1)); 61.54 (*t*, C(4)); 71.36, 71.43 (2*d*, C(2), C(3)); 170.24, 170.39, 170.63 (3*s*, 3 C=O). CI-MS (NH_3): 279 (6), 278 (9), 277 (64), 219 (10), 218 (11), 217 (100, $[M - AcOH - AcO]^+$), 159 (7). Anal. calc. for $C_{13}H_{20}O_6S_2$ (336.43): C 46.41, H 5.99, S 18.30; found: C 46.70, H 6.13, S 18.80.

D-*Erythrose Dibenzyl Dithioacetal* (**11**) *and 2,3,4-Tri*-O-*acetyl*-D-*erythrose Dibenzyl Dithioacetal* (**12**). Fuming HCl (400 ml) was added at −25° to **8** (159.0 g, 1.324 mol; 10% H_2O content assumed). The mixture was shaken vigorously until a clear soln. had formed (*ca.* 45 min) and treated with a precooled (−20°) portion of BnSH (100 ml, 0.848 mol). The suspension was shaken vigorously for 10 min, cooled again to −25° (EtOH-dry ice cooling bath). This procedure was repeated with three more portions of BnSH (1 × 0.848 mol, 2 × 0.543 mol; total: 327.92 ml, 2.78 mol). After complete addition, the mixture was cooled to −60° and allowed to slowly warm to 15°. The resulting caramel suspension was shaken vigorously for 10 min and subsequently poured onto ice/NaCl 2 : 1 (400 g). The org. layer was separated, and the yellow aq. phase was extracted with Et_2O (3 × 600 ml). The combined org. phases were washed to neutrality with portions of sat. aq. $NaHCO_3$ soln. (*ca.* 150 ml). The combined aq. phases (pH adjusted to 7.5 with solid $NaHCO_3$) were extracted with Et_2O (3 × 300 ml). The combined org. phases were dried (Na_2SO_4) and evaporated. FC (2.5 kg of silica gel *60*; toluene/acetone 2 : 1) of the amber, oily residue (470.95 g, 101%) gave crude **11** (372.46 g, 80%), which was further purified by FC (2.5 kg of silica gel *60*; toluene/acetone 5 : 1 (6 l) → 4 : 1 (2 l) → 3 : 1 (2 l) → 2 : 1 (2 l) → 1 : 1): 280.0 g (60%) of **11**. A small sample (150 mg) was peracetylated under standard conditions. FC (hexane/AcOEt 7 : 1) gave **12** (194 mg, 95%).

Data of **11**: Colourless oil. R_f (toluene/acetone 2 : 1) 0.29. $[\alpha]_D^{25} = -160.9$ ($c = 0.42$, $CHCl_3$). IR (film): 3400*s* (br.), 3060*w*, 3030*w*, 2920*w*, 1600*m*, 1495*m*, 1455*m*, 1070*s*, 1030*s*, 765*m*, 700*m*. ^{1}H-NMR (400 MHz, (D_6)acetone/

D_2O): 3.58 (*dd*, *J* = 5.4, 11.3, H–C(4)); 3.70 (*dd*, *J* = 3.4, 11.3, H′–C(4)); 3.735, 3.77 (2*d*, *J* ≈ 12.5, PhCH_2); 3.755 (*ddd*, *J* = 3.4, 5.4, 8.5, H–C(3)); 3.77, 3.82 (2*d*, *J* = 12.7, PhCH_2); 3.88 (*dd*, *J* = 2.2, 8.5, H–C(2)); 4.11 (*d*, *J* = 2.2, H–C(1)); 7.16–7.25 (*m*, 10 arom. H). ^{13}C-NMR (50 MHz, (D_6)acetone): 36.22, 36.28 (2*t*, 2 PhCH_2); 55.64 (*d*, C(1)); 64.68 (*t*, C(4)); 72.81 (*d*, C(3)); 76.56 (*d*, C(2)); 127.59 (2*d*); 129.20 (4*d*); 129.90 (2*d*); 129.93 (2*d*); 139.48, 139.69 (2*s*). CI-MS (NH_3): 370 (13), 369 (24), 368 (100, $[M+NH_4]^+$), 350 (9, M^+). Anal. calc. for $C_{18}H_{22}O_3S_2$ (350.50): C 61.68, H 6.33, S 18.30; found: C 61.81, H 6.33, S 18.13.

Data of **12**: Colourless solid. R_f (hexane/AcOEt 3:1) 0.58. M.p. 80° (hexane/AcOEt). ^{1}H-NMR (400 MHz, (D_6)acetone): 1.69, 1.95, 2.08 (3*s*, 3 AcO); 3.72 (*d*, *J* = 3.9, H–C(1)); 3.75 (*s*, PhCH_2); 3.79, 3.86 (2*d*, *J* = 13.2, PhCH_2); 4.07 (*dd*, *J* = 5.0, 12.4, H–C(4)); 4.19 (*dd*, *J* = 2.9, 12.4, H′–C(4)); 5.22 (*ddd*, *J* = 2.9, 5.0, 7.8, H–C(3)); 5.53 (*dd*, *J* = 3.9, 7.8, H–C(2)); 7.05–7.37 (*m*, 10 arom. H).

2,3,4-Tri-O-*benzyl*-D-*erythrose Dibenzyl Dithioacetal* (**13**). A soln. of **11** (41.20 g, 0.118 mol) in dry DMF (420 ml) was cooled to 0°, treated portionwise with 95% NaH (11.28 g, 0.470 mol) over a 30-min period, and stirred at 0° until gas evolution subsided. The caramel mixture was treated with Bu_4NI (2.18 g, 5.90 mmol) in one portion and then, at 0°, dropwise with a soln. of BnBr (45.95 ml, 0.388 mol) in dry DMF (260 ml). After complete addition (90 min), stirring was continued at 0° for 3 h and at 22° for 2 h. MeOH (100 ml) was cautiously added in portions, and the mixture was stirred vigorously at 22° for 30 min. The clear, brown soln. was poured onto ice and thoroughly mixed with ice/NH_4Cl 2:1 (300 g). Extraction with Et_2O (4 × 500 ml) was followed by washing the org. phases with brine (2 × 100 ml) and H_2O (2 × 100 ml). Drying ($MgSO_4$), evaporation, and drying in high vacuum (24 h) gave a crude yellow solid (80.17 g, 109%). FC (hexane/AcOEt 18:1) gave **13** (65.68 g, 90%). Colourless solid. R_f (hexane/AcOEt 10:1) 0.42. M.p. 76° (hexane/AcOEt). $[\alpha]_D^{25} = -49.3$ (*c* = 0.39, $CHCl_3$). IR (KBr): 3058*w*, 3030*w*, 2950*w*, 2910*w*, 2850*w*, 1490*m*, 1450*m*, 1120*s*, 1095*s*, 750*m*, 695*m*. ^{1}H-NMR (400 MHz, C_6D_6): 3.56, 3.60 (2*d*, *J* = 13.7, PhCH_2); 360–3.68 (*m*, 2 H–C(4)); 3.67, 3.81 (2*d*, *J* = 13.3, PhCH_2); 3.92 (*td*, *J* ≈ 3.2, 7.2, H–C(3)); 4.04, 4.39 (2*d*, *J* = 11.6, PhCH_2); 4.20 (*d*, *J* = 2.3, H–C(1)); 4.215 (*dd*, *J* = 2.3, 7.4, H–C(2)); 4.29 (*s*, PhCH_2); 4.74, 5.14 (2*d*, *J* = 11.1, PhCH_2); 6.95–7.24 (*m*, 23 arom. H); 7.41 (*d*, *J* = 7.1, 2 arom. H). ^{13}C-NMR (50 MHz, (D_6)acetone): 35.59, 36.77 (2*t*, 2 PhCH_2); 53.19 (*d*, C(1)); 69.73 (*t*, C(4)); 72.40, 73.72, 75.74 (3*t*, 3 PhCH_2); 79.76 (*d*, C(3)); 82.16 (*d*, C(2)); 127.54–129.98 (several *d*); 139.37, 139.45 (2*s*); 139.53 (2*s*); 139.73 (*s*). CI-MS (NH_3): 638 (3, $[M+NH_4]^+$), 499 (11), 498 (34), 497 (100, $[M-BnS]^+$), 407 (7), 391 (18), 389 (11), 347 (11), 301 (9), 299 (21), 191 (11), 108 (32), 106 (11). Anal. calc. for $C_{39}H_{40}O_3S_2$ (620.88): C 75.44, H 6.49, S 10.33; found: C 75.40, H 6.70, S 10.38.

4-O-*[(*tert-*Butyl)diphenylsilyl]*-D-*erythrose Dibenzyl Dithioacetal* (**14**) *and 4*-O-*[(*tert-*Butyl)diphenylsilyl]-2,3*-O-*isopropylidene*-D-*erythrose Dibenzyl Dithioacetal* (**15**). A soln. of **11** (30.0 g, 85.59 mmol) in dry DMF (300 ml) under Ar was treated with 4-Å molecular sieves (5 g) and sublimed 1*H*-imidazole (12.0 g, 176.26 mmol), and dropwise with a soln. of (*t*-Bu)Ph_2SiCl (24.70 g, 89.87 mmol) in dry DMF (200 ml). After complete addition (2 h), the mixture was stirred for 3 h at 22°, poured onto ice/NaCl 2:1 (*ca.* 300 g), and extracted with Et_2O (3 × 300 ml). The combined Et_2O phases were washed with brine (100 ml) and sat. aq. $NaHCO_3$ soln. (100 ml), dried (Na_2SO_4), and evaporated. Drying at high vacuum for 20 h gave crude **14** (50.5 g, quant.). A pure sample of **14** was obtained by FC (hexane/AcOEt 7.5:1). A soln. of crude **14** (50.0 g, 84.90 mmol) in dry acetone (1300 ml) was treated with anh. $CuSO_4$ (34.0 g, 0.213 mol) and vigorously stirred under Ar at 50–55° for 7 d. The mixture was cooled to 22°, treated with solid $NaHCO_3$ (15 g), stirred at 22° for 3 h, and suction-filtered over a sand/*Celite*/sand bed. The residue was washed with acetone (500 ml). The filtrate was treated with sat. aq. $NaHCO_3$ soln. (10 ml) and evaporated. Drying at high vacuum for 12 h and MPLC (2 kg of silica gel *60*, hexane/AcOEt/Et_3N 40:1:0.01) gave **15** (48.45 g, 90% from **11**).

Data of **14**: Colourless oil. R_f (hexane/AcOEt 6:1) 0.44. $[\alpha]_D^{25} = -41.9$ (*c* = 0.50, $CHCl_3$). IR ($CHCl_3$): 3500*m* (br.), 3065*w*, 3005*w*, 2960*w*, 2930*w*, 2860*w*, 1495*m*, 1470*m*, 1455*m*, 1430*m*, 1390*w*, 1360*w*, 1115*m*, 1040*s*, 705*m*. ^{1}H-NMR (400 MHz, (D_6)acetone): 1.04 (*s*, *t*-Bu); 3.73 (*d*, *J* = 5.6, exchange with D_2O, HO–C(3)); 3.77, 3.815 (2*d*, *J* = 13.1, PhCH_2); 3.81–3.87 (*m*, H–C(4)); 3.82, 3.88 (2*d*, *J* = 12.8, PhCH_2); 3.90–3.97 (*m*, addn. of $D_2O \rightarrow$ change, H–C(3), H′–C(4)); 4.02 (*ddd*, *J* = 2.3, 5.7, 8.0, addn. of $D_2O \rightarrow$ *dd*, *J* = 2.4, 8.0, H–C(2)); 4.09 (*d*, *J* = 5.7, exchange with D_2O, HO–C(2)); 4.21 (*d*, *J* = 2.2, H–C(1)); 7.17–7.28 (*m*, 10 arom. H); 7.38–7.44 (*m*, 6 arom. H); 7.72–7.75 (*m*, 4 arom. H). ^{13}C-NMR (50 MHz, (D_6)acetone): 19.80 (*s*, Me_3C); 27.22 (*q*, Me_3C); 36.28 (*t*, 2 PhCH_2); 55.64 (*d*, C(1)); 66.91 (*t*, C(4)); 73.06 (*d*, C(3)); 75.74 (*d*, C(2)); 127.58, 127.61 (2*d*); 128.53 (4*d*); 129.16 (2*d*); 129.20 (2*d*); 129.87 (2*d*); 129.92 (2*d*); 130.53 (2*d*); 134.29 (2*s*); 136.35 (4*d*); 139.39, 139.63 (2*s*). Anal. calc. for $C_{34}H_{40}O_3S_2Si$ (588.91): C 69.34, H 6.85, S 10.89; found: C 69.49, H 6.65, S 10.61.

Data of **15**: Colourless oil. R_f (hexane/AcOEt/Et_3N 25:1:0.01) 0.35. $[\alpha]_D^{25} = -11.8$ (*c* = 0.58, $CHCl_3$). IR ($CHCl_3$): 3060*w*, 3000*w*, 2960*w*, 2930*w*, 2890*w*, 2860*w*, 1495*m*, 1455*m*, 1425*m*, 1380*w*, 1370*w*, 1165*m*, 1110*s*, 1070*s*, 705*s*. ^{1}H-NMR (400 MHz, C_6D_6): 1.16 (*s*, *t*-Bu); 1.19, 1.45 (2*s*, Me_2C); 3.72 (*d*, *J* = 12.9, 2 PhC*H*); 3.79 (*d*, *J* =

12.9, PhC*H*); 3.79 (*d*, *J* = 7.6, H–C(1)); 3.84 (*d*, *J* = 13.0, PhC*H*); 3.85 (*dd*, *J* = 4.3, 10.8, H–C(4)); 3.90 (*dd*, *J* = 7.0, 10.8, H′–C(4)); 4.26 (*dt*, *J* ≈ 4.2, 6.6, H–C(3)); 4.38 (*dd*, *J* = 6.4, 7.6, H–C(2)); 6.94–7.26 (*m*, 16 arom. H); 7.75–7.82 (*m*, 4 arom. H). ^{13}C-NMR (50 MHz, (D_6)acetone): 19.74 (*s*, Me_3C); 25.44, 27.59 (2*q*, *Me*$_2$C); 27.27 (*q*, *Me*$_3$C); 35.11, 36.47 (2*t*, 2 PhCH_2); 50.31 (*d*, C(1)); 63.61 (*t*, C(4)); 79.47 (*d*, C(3)); 81.23 (*d*, C(2)); 109.25 (*s*, Me_2C); 127.72, 127.79 (2*d*); 128.52 (4*d*); 129.28 (4*d*); 129.84 (2*d*); 129.94 (2*d*); 130.59 (2*d*); 134.24, 134.48 (2*s*); 136.39 (2*d*); 136.52 (2*d*); 138.73, 139.02 (2*s*). Anal. calc. for $C_{37}H_{44}O_3S_2Si$ (628.97): C 70.66, H 7.05, S 10.20; found: C 70.78, H 7.28, S 9.99.

2,3,4-Tri-O-*benzyl*-D-*erythrose* (**16**). At 22° under Ar, a vigorously stirred soln. of **13** (65.65 g, 105.5 mmol) in acetone/H_2O 99:1 (1500 ml) was treated with $CuCl_2$ (35.50 g, 264.0 mmol) and CuO (42.0 g, 528.1 mmol) and stirred for 3 h at reflux. The mixture was cooled to 18° and suction-filtered over a sand/*Celite*/sand bed. The residue was washed with Et_2O (3 × 150 ml). The clear, light-yellow filtrate was dried ($MgSO_4$) and evaporated. FC (hexane/AcOEt 7:1) gave **16** (35.45 g, 86%). Slightly yellowish oil. R_f (hexane/AcOEt 6:1) 0.31. $[\alpha]_D^{25} = +6.1$ (*c* = 1.19, $CHCl_3$). IR ($CHCl_3$): 3060*w*, 3030*w*, 3010*w*, 2900*w*, 2870*w*, 1730*s*, 1495*m*, 1465*m*, 1365*m*, 1100*s*, 700*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.64 (*dd*, *J* = 5.2, 9.9, H–C(4)); 3.75 (*dd*, *J* = 6.6, 9.9, H′–C(4)); 3.99 (*ddd*, *J* = 3.7, 5.2, 6.6, H–C(3)); 4.08 (*dd*, *J* = 1.5, 3.7, H–C(2)); 4.51 (*s*, PhCH_2); 4.63 (br. *s*, PhCH_2); 4.65, 4.72 (2*d*, *J* = 11.9, PhCH_2); 7.28–7.37 (*m*, 15 arom. H); 9.67 (*d*, *J* = 1.5, H–C(1)). ^{13}C-NMR (50 MHz, (D_6)acetone): 67.91 (*t*, C(4)); 72.21, 72.85, 73.17 (3*t*, 3 PhCH_2); 78.77 (*d*, C(3)); 82.60 (*d*, C(2)); 127.46–128.29 (several *d*); 137.20, 137.63, 137.69 (3*s*); 201.60 (*s*, C(1)). CI-MS (NH_3): 391 (1, $[M+1]^+$), 283 (3, $[M-BnO]^+$), 265 (6, $[M-BnO-H_2O]^+$), 223 (11), 193 (11), 181 (29), 175 (23, $[M-BnO-BnOH]^+$), 133 (27), 107 (17), 91 (100). Anal. calc. for $C_{25}H_{26}O_4$ (390.48): C 76.90, H 6.71; found: C 76.64, H 6.56.

4-O-*[(*tert*-Butyl)diphenylsilyl]-2,3*-O-*isopropylidene*-D-*erythrose* (**17**). At 22°, a soln. of **15** (369 mg, 0.63 mmol) in MeCN/H_2O 9:1 (5 ml) was treated with $CaCO_3$ (313 mg, 3.13 mmol) and $HgCl_2$ (748 mg, 2.75 mmol), stirred for 22 h under Ar, and suction-filtered (sand/*Celite* bed). The clear filtrate was concentrated to *ca*. 1 ml, and the solid residue was washed with AcOEt (2 × 10 ml). The combined concentrate and washings were washed with 1M aq. KI soln. (5 × 5 ml) and 30% aq. $Na_2S_2O_3$ soln. (2 × 10 ml). The combined aq. phases were extracted with AcOEt (7 ml). The combined org. phases were dried (Na_2SO_4) and evaporated to give a lemon-yellow oil. FC (hexane/AcOEt 12:1) gave a red oil (due to HgI_2), which was taken up in dry benzene (5 ml), filtered over a cotton plug, evaporated to dryness, then taken up in cyclohexane/benzene 1:1 (5 ml), filtered again, and finally evaporated to give pure **17** (245 mg, 98%). Colourless oil. R_f (hexane/AcOEt 5:1) 0.51. $[\alpha]_D^{25} = +43.3$ (*c* = 1.01, $CHCl_3$). IR ($CHCl_3$): 3045*w*, 2990*m*, 2930*w*, 2855*m*, 1730*s*, 1490*w*, 1470*m*, 1430*w*, 1385*m*, 1375*w*, 1164*m*, 1142*m*, 1113*s*, 1090*s*, 1065*s*, 1010*s*, 705*s*. ^{1}H-NMR (400 MHz, C_6D_6): 1.12 (*s*, *t*-Bu); 1.39, 1.53 (2*s*, Me_2C); 3.62 (*dd*, *J* = 2.6, 11.6, H–C(4)); 3.75 (*dd*, *J* = 3.4, 11.6, H′–C(4)); 3.92 (*ddd*, *J* = 2.6, 3.4, 8.1, H–C(3)); 4.05 (*dd*, *J* = 2.4, 8.1, H–C(2)); 7.20–7.27 (*m*, 6 arom. H); 7.76 (*dd*, *J* = 1.7, 7.7, 2 arom. H); 7.85 (*dd*, *J* = 1.8, 7.7, 2 arom. H); 9.93 (*d*, *J* = 2.4, H–C(1)). ^{13}C-NMR (50 MHz, (D_6)acetone): 19.63 (*s*, Me_3C); 25.01, 27.49 (2*q*, *Me*$_2$C); 27.00 (*q*, *Me*$_3$C); 61.95 (*t*, C(4)); 80.21 (*d*, C(3)); 81.47 (*d*, C(2)); 110.97 (*s*, Me_2C); 128.57 (2*d*); 128.64 (2*d*); 130.68, 130.72 (2*d*); 133.52, 133.72 (2*s*); 136.30 (2*d*); 136.47 (2*d*); 201.11 (*s*, C(1)). CI-MS (NH_3): 418 (7), 417 (28), 416 (100, $[M+NH_4]^+$), 400 (10), 399 (31, $[M+1]^+$), 398 (20), 381 (7). Anal. calc. for $C_{23}H_{30}O_4Si$ (398.57): C 69.31, H 7.59; found: C 69.15, H 7.56.

(Mesyloxy)acetonitrile (**18**) *and (Mesyloxy)acetic Acid* (**19**). A vigorously stirred soln. of NaCN (200.0 g, 4.08 mol) in dist. H_2O (530 ml) was treated dropwise at −15° under N_2 with 37% aq. HCHO (311.4 ml, 4.088 mol). After completion of the addition (45 min), stirring was continued at −5 to 0° for additional 15 min. The vigorously stirred soln. of hydroxyacetonitrile was cooled to −25 to −30° (dry ice/EtOH cooling bath) and treated with MsCl (317.1 ml, 4.081 mol) at such a rate (*ca*. 2 h) that the temp. of the mixture remained below −5°. The mixture was allowed to warm to +15° within 4 h. Upon addition of H_2O (500 ml) to the white suspension, about half of the solids went into soln. Filtration over a glass frit *G3* left a colourless amorphous solid, which was dried under high vacuum over P_2O_5 at 25° for 12 h, yielding a first fraction of **18** (171 g, 31% based on NaCN). The clear filtrate was divided in half. Each half was extracted with toluene (3 × 400 ml) and CH_2Cl_2 (3 × 200 ml). The combined org. phases were dried (Na_2SO_4) and evaporated at $T < 33°$ to give a second fraction of **18** (orange oil, 205 g, 37%). The first, solid fraction of **18** was suspended in H_2O (380 ml) in a 1-l three-neck round-bottom flask and carefully treated with precooled (0°) conc. H_2SO_4 (280 ml). The three necks of the flask were fitted with air-plus double-wall reflux condensers. The flask was immersed in an oil bath preheated to 120°. After vigorous stirring for *ca*. 10 min, the strongly exothermic reaction started (*caution: strong gas evolution*!). The oil bath was immediately removed until the peak of the reaction had passed, then stirring was continued at 120° for *ca*. 20 min, until gas evolution subsided. After addition of H_2O (120 ml) and cooling to r.t., the mixture was kept at 4–5° for 3–5 d. The crystalline mass of **19** was filtered off and washed

with cold Et_2O (50 ml). The clear, yellow-orange filtrate was kept at $-5°$ for further 2–3 d. A second crystalline crop of **19**, comparable in quality to the first, was filtered off and washed with cold Et_2O (50 ml). The mother liquor was extracted with Et_2O (6 × 500 ml) to yield a third fraction, which was recrystallized in hot AcOEt. The first, solid fraction of **18** gave 183.66 g (94%) of **19**, the second, oily fraction of **18** additional 131.43 g (56%) of **19** (total average yield: 315.1 g, 75%).

Data of **18**: R_f (toluene/AcOEt/Et_3N 3:1:0.02) 0.42. M.p. 42.5–43.5° ([54]: 31–32°; [55]: 41°). IR ($CHCl_3$): 3020*w*, 2960*m*, 2940*m*, 1375*s*, 1360*s*, 1180*s*, 1022*s*, 970*s*, 760*s*. ^{1}H-NMR (400 MHz, (D_6)acetone): 3.18 (*s*, MsO); 4.81 (*s*, CH_2). ^{13}C-NMR (50 MHz, (D_6)acetone): 38.10 (*q*, MsO); 54.10 (*t*, CH_2); 115.19 (*s*, C≡N). EI-MS: 310 (12), 265 (9), 150 (24, $[M+15]^+$), 135 (54), 120 (11, $[M-15]^+$), 79 (100, Ms^+).

Data of **19**. Colourless, crystalline plates. R_f (i-Pr_2O/HCOOH/H_2O 90:7:3) 0.35 (best detected with the bromocresol green/bromophenol blue/$KMnO_4$ reagent [104]). M.p. 110–111° ([55]: 113–114°). IR (KBr): 3130*s* (br.), 1745*s*, 1725*s* (br.), 1360*s*, 1260*s*, 1170*s*, 1060*s*, 820*s*. ^{1}H-NMR (400 MHz, (D_6)acetone): 3.19 (*s*, MsO); 4.82 (*s*, CH_2). ^{13}C-NMR (50 MHz, (D_6)acetone): 38.47 (*q*, MsO); 65.62 (*t*, CH_2); COOH hidden by noise. CI-MS (C_4H_{10}): 169 (8), 155 (100, $[M+1]^+$), 137 (54, $[M-OH]^+$), 97 (8).

(Mesyloxy)acetyl Chloride (**20**). Under N_2 and at 25°, a suspension of **19** (60.0 g, 0.389 mol) in dry CH_2Cl_2/DMF 99:1 (300 ml) was slowly treated with a soln. of freshly distilled oxalyl chloride (50.0 ml, 0.582 mol) in dry CH_2Cl_2 (100 ml). After completion of the addition (90 min), the suspension was stirred at 50° for 1 h. Excess oxalyl chloride and most of the solvent were distilled off. Fractional high-vacuum distillation (oil bath preheated to 90–100°, final oil-bath temp. < 130°) of the viscous, oily residue afforded **20** (53.70 g, 80%). Slightly yellow, clear lequid (crystalline at $T<-10°$). n_D^{22} 1.457 ([56]: 1.460). B.p. 72–75° at 0.25 Torr ([56]: 99–100° at 2 Torr). IR (film): 1810*s*, 1362*s*, 1180*s*, 1060*s*, 955*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.13 (*s*, MsO); 4.99 (*s*, CH_2). ^{13}C-NMR (50 MHz, $CDCl_3$): 39.11 (*q*, MsO); 69.91 (*t*, CH_2); 168.52 (*s*, C=O). EI-MS: 250 (14), 137 (73, $[M-Cl]^+$), 65 (51), 64 (28), 63 (100, $COCl^+$).

*(*R*)-1-Deoxy-2,4-O-ethylidene-1-[(*E*)-(4-methoxybenzyl)imino]-*D*-erythritol* (**24**). At 25°, a soln. of **6** (1.00 g, 6.84 mmol) in dry CH_2Cl_2 (50 ml) was treated with anh. $MgSO_4$ (1.23 g, 10.26 mmol) and dropwise with **21** (0.89 ml, 6.84 mmol), and vigorously stirred for 3 h. A small aliquot (*ca.* 5 ml) was filtered over *Celite*, and the filtrate was evaporated. Drying at high vacuum (30 min) yielded **24** as a colourless, viscous honey, which was immediately characterized. The rest of the material was discarded. R_t (toluene/AcOEt/Et_3N 3:1:0.02) 0.31. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.37 (*d*, $J=5.1$, Me); 3.48 (*dd*, $J=10.3$, 10.7, H_{ax}–C(4)); 3.80 (*s*, MeO, HO–C(3)); 3.84 (*ddd*, $J=5.1$, 8.9, 10.2, H–C(3)); 3.95 (*qd*, $J\approx1.5$, 8.9, H–C(2)); 4.17 (*dd*, $J=5.1$, 10.8, H_{eq}–C(4)); 4.56 (br. *s*, ArCH_2); 4.75 (*q*, $J=5.1$, Me*CH*); 6.86–6.89, 7.13–7.16 (*AA′BB′*, 4 arom. H); 7.84 (*d*, $J=1.1$, H–C(1)). ^{13}C-NMR (50 MHz, (D_6)acetone): 20.41 (*q*, Me); 55.26 (*q*, MeO); 63.56 (*t*, Ar*C*H_2); 64.96 (*d*, C(3)); 69.76 (*t*, C(4)); 79.60 (*d*, C(2)); 99.34 (*d*, Me*C*H); 114.02 (2*d*); 129.12 (2*d*); 129.91, 158.89 (2*s*); 165.87 (*d*, C(1)).

*(*R*)-3-Deoxy-4,6-*O*-ethylidene-2-*O*-mesyl-3-[(4-methoxybenzyl)amino]-5-*O*-(triethylsilyl)-*D*-altrono-1,3-lactam* (**25**). A soln. of **6** (0.50 g, 3.42 mmol) in dry CH_2Cl_2 (15 ml) was treated with anh. $MgSO_4$ (0.618 g, 5.13 mmol) and **21** (0.44 ml, 3.42 mmol), and stirred under Ar for 3 h at 25°. After filtration of the crude soln. of **24** over a glass frit, dilution with dry CH_2Cl_2 (20 ml) and addition of freshly activated 3-Å molecular sieves (300 mg), Et_3N (0.48 ml, 3.42 mmol), and Et_3SiCl (0.57 ml, 3.42 mmol), the suspension was stirred at 25° for 20 h, and suction-filtered over a *Celite* pad. After evaporation and drying (1 h at high vacuum), the semi-solid (silyl ether of **24**) was dissolved in dry CH_2Cl_2 (25 ml), cooled to 0°, treated with freshly activated 3-Å molecular sieves (250 mg) and a soln. of Et_3N (0.95 ml, 6.84 mmol) in dry CH_2Cl_2 (25 ml), and the mixture was stirred under Ar for 10 min. The mixture was treated with a soln. of **20** (725 mg, 4.2 mmol) in dry CH_2Cl_2 (12.5 ml), stirred for 1 h at 0° and for 14 h at 25°, treated with additional Et_3N (0.48 ml, 3.456 mmol) and **20** (557 mg, 3.215 mmol), stirred for 4 h, treated with additional Et_3N (0.48 ml, 3.456 mmol) and **20** (557 mg, 3.215 mmol), and stirred for 1 h. The dark brown mixture was poured into ice/sat. aq. $NaHCO_3$ soln. (20 ml). The org. phase was separated and washed with sat. aq. $NaHCO_3$ soln. (2 × 50 ml), sat. aq. NH_4Cl soln. (50 ml), and H_2O (50 ml). The combined aq. phases were extracted with CH_2Cl_2 (100 ml). The combined org. phases were dried (Na_2SO_4), evaporated, and dried (12 h at high vacuum) to give a crude evil-smelling black oil (2.19 g). FC (hexane/AcOEt 2:1) yielded **25** (412 mg, 23%). Slightly yellow solid. R_f (toluene/AcOEt 3:1) 0.50 (blue-violet colour on TLC with mostain reagent). M.p. 123°. $[\alpha]_D^{25}=-101.1$ ($c=0.92$, $CHCl_3$). IR (KBr): 3030*w*, 3000*m*, 2960*m*, 2940*m*, 2910*w*, 2880*w*, 1760*s*, 1610*m*, 1515*m*, 1415*m*, 1360*s*, 1185*s*, 1245*s*, 1110*s*, 1095*s*, 830*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): see *Table 3*; additionally, 0.556, 0.560 (2*q*, $J=7.9$, ($Me$$CH_2$)$_3$Si); 0.90 (*t*, $J=7.9$, (MeCH_2)$_3$Si)); 1.23 (*d*, $J=5.1$, *Me*CH); 3.26 (*s*, MsO); 3.80 (*s*, MeO); 4.26 (*q*, $J=5.1$, Me*CH*); 4.29, 4.39 (2*d*, $J=15.0$, ArCH_2); 6.86–6.88, 7.13–7.16 (*AA′BB′*, 4 arom. H). ^{13}C-NMR (50 MHz, $CDCl_3$; assignment based on a ^{1}H/^{13}C-COSY spectrum): see *Table 4*; additionally, 4.66 (*t*, Me*C*H_2)$_3$Si); 6.52 (*q*, ($Me$$CH_2$)$_3$Si); 20.34

Table 3. *Selected ^{1}H-NMR* (400–600 MHz) *Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the β-Lactams* **25**, **27**–**35**, **39**–**42**, **4**, **43**, **45**, *and* **47**–**50**, *the Mannonic Acid* **44**, *and the Mannonamides* **51**–**53**

	Solvent	H–C(2)	H–C(3)	H–C(4)	H–C(5)	H–C(6)	H′–C(6)	*J*(2,3)	*J*(3,4)	*J*(4,5)	*J*(5,6)	*J*(5,6′)	*J*(6,6′)
25	$CDCl_3$	5.54	4.06	3.48	3.83	3.17	3.99	5.2	2.5	9.4	9.9	5.2	10.6
27a[a])	$CDCl_3$	5.61	4.81	4.15	3.78	3.635	3.865	5.5	7.3	4.4	4.0	5.2	10.1
27b[a])	$CDCl_3$	5.47	4.705	4.34	3.90	3.630	3.74	5.5	2.4	8.7	2.2	2.7	10.5
28a	(D_6)Acetone	5.71	4.52	[b])	[b])	[b])	[b])	5.5	6.0	[b])	[b])	[b])	[b])
28b	(D_6)Acetone	5.61	4.45	[b])	[b])	[b])	[b])	5.4	4.5	[b])	[b])	[b])	[b])
28c	(D_6)Acetone	5.10	[b])	[b])	[b])	[b])	[b])	0	[b])	[b])	[b])	[b])	[b])
29	(D_6)Benzene	5.10	4.36	4.49	4.39	3.80	3.89	5.3	9.5	6.7	3.8	3.0	11.8
30a	$CDCl_3$	4.44	4.16	3.91	3.67	3.63	3.71	1.9	8.2	5.6	3.3	3.8	9.5
30b	$CDCl_3$	5.03	4.29	4.19	3.81	3.67	3.67	1.8	1.0	4.5	4.9	4.9	[b])
31a	(D_6)Acetone	4.48[c])	3.75[d])	3.91	3.86	3.71	3.80	2.1	5.6	4.8	4.7	4.5	10.4
31b	(D_6)Acetone	4.75[c])	3.84	3.94	3.87	3.71	3.87	2.0	3.2	4.6	4.9	4.5	10.5
32	(D_6)Acetone	4.94[e])	4.46	4.12	4.00	3.71	3.86	2.5	8.1	3.5	5.3	5.0	10.4
33	(D_6)Acetone	4.89[e])	4.56	5.50	5.33	4.18	4.37	2.4	8.8	4.7	6.4	3.8	12.1
34	(D_6)Benzene	3.50	3.82	3.82	3.91	3.61	3.74	0.8	[b])	[b])	4.8	3.8	11.6
35	(D_6)Acetone	3.90[c])	3.25	3.525	3.95	3.527	3.60	2.2	5.4	6.4	5.8	5.3	11.2
39	(D_6)Acetone	5.24[e])	4.635	4.22	3.92	3.68	3.82	2.4	7.8	4.1	4.8	5.3	10.2
40	(D_6)Acetone	5.15	4.60	3.93	3.53	3.62	3.68	2.5	3.3	9.0	5.0	5.1	11.4
41	(D_6)Acetone	4.50	4.05	4.05	3.96	3.69	3.73	1.4	[b])	2.5	5.3	5.5	10.5
42	(D_6)Acetone	5.06	4.27	4.15	4.02	3.65	3.70	2.6	7.2	2.4	5.6	5.9	10.3
4	D_2O	5.00	4.20	3.87	3.68	3.58–3.68	3.81	2.2	4.9	8.1	[b])	2.5	12.2
43[a])	D_2O	4.43	4.23	3.87	3.61	3.66	3.78–3.95	2.1	4.4	8.7	5.8	3.1	11.8
44[a])	D_2O	4.15	3.78–3.95	3.92	3.78–3.95	3.66	3.78–3.95	3.9	4.9	6.1	5.8	[b])	11.8
45	(D_6)Benzene	3.96	3.65	3.55	3.38–3.42	3.38–3.42	3.42	2.1	8.1	3.9	[b])	[b])	[b])
47	(D_6)Benzene	3.98[f])	4.225[g])	3.69	3.62	3.49	3.53	2.1	7.2	4.4	5.0	4.7	10.2
48	(D_6)Acetone	5.02[e])[f])	4.31[g])	4.18	4.05	3.685	3.742	2.1	7.0	3.3	5.4	5.3	10.3
49[a])	D_2O	5.01	4.22	3.81	3.68	3.635	3.83	<2	5.2	8.6	5.7	2.2	11.2
50[a])	D_2O	4.30	4.28	3.80	3.67–3.74	3.66	3.86	[b])	3.8	9.9	5.5	2.6	12.3
51	(D_6)Benzene	4.045	4.87[d])	4.035	3.63	3.51	3.58	6.8	1.5	6.4	4.0	3.6	10.5
52	$CDCl_3$	4.05	3.40	4.38	4.30	3.76	3.93	6.9	3.9	6.2	4.3	7.3	10.8
53	(D_6)Benzene	4.25	4.91[d])	4.49	4.34	3.99	4.06	4.9	<3	6.7	5.9	7.0	10.7

[a]) Assignment based on ^{1}H/^{1}H-COSY spectrum. [b]) Not determined due to overlapping signals. [c]) ^4J(2,NH): <1 (**31a** and **31b**) and 2.1 Hz (**35**). [d]) ^3J(3,NH): 0.9 (**31a**), 9.1 (**51**), and 8.5 Hz (**53**). [e]) ^3J(2,NH): 8.6 (**32** and **42**), 8.1 (**33**), 8.9 (**39**), and 8.3 Hz (**48**). [f]) ^5J(2,P): 1.5 (**47**), and *ca.* 1 Hz (**48**). [g]) ^4J(3,P): 2.7 Hz (**47** and **48**).

(*q*, *Me*CH); 55.18 (*q*, MeO); 98.78 (*d*, MeCH); 113.97 (2*d*); 126.55 (*s*); 129.67 (2*d*); 159.37 (*s*). CI-MS (C_4H_{10}): 518 (11), 517 (29), 516 (87, $[M+1]^+$), 396 (11), 122 (10), 121 (100, $MeOC_6H_4CH_2^+$). Anal. calc. for $C_{23}H_{37}NO_8SSi$ (515.70): C 53.57, H 7.23, N 2.72, S 6.22; found: C 53.83, H 7.20, N 2.69, S 6.50.

2,3,4-Tri-O-*benzyl-1-deoxy-1-[(*E*)-(4-methoxyphenyl)imino]*-D-*erythritol* (**26**). At 0°, a soln. of **16** (120 mg, 0.31 mmol) and **22** (38 mg, 0.31 mmol) in dry CH_2Cl_2 (10 ml) was treated with 3-Å molecular sieves (200 mg) and stirred for 4 h. After filtering an aliquot (*ca.* 4 ml) over a cotton plug, evaporation and drying (1 h under high vacuum) gave **26**. Colourless oil. R_f (toluene/AcOEt/Et_3N 3:1:0.02) 0.60. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.71 (*dd*, *J* = 5.7, 10.3, H–C(4)); 3.81 (*dd*, *J* = 4.7, 10.3, H′–C(4)); 3.82 (*s*, MeO); 4.02 (*q*, *J* ≈ 5.0, H–C(3)); 4.34 (*dd*, *J* = 4.8, 5.7, H–C(2)); 4.55 (*s*, PhCH_2); 4.62 (*d*, *J* = 11.9), 4.71 (*d*, *J* = 12.0) (PhCH_2); 4.72 (*d*, *J* = 12.1), 4.76 (*d*, *J* = 11.9) (PhCH_2); 6.84–6.87, 6.99–7.03 (*AA′BB′*, 4 arom. H); 7.26–7.35 (*m*, 15 arom. H); 7.84 (*d*, *J* = 5.8, H–C(1)). ^{13}C-NMR (50 MHz, $CDCl_3$): 55.45 (*q*, MeO); 69.58 (*t*, C(4)); 71.92, 72.65, 73.40 (3*t*, 3 PhCH_2); 79.75 (*d*, C(3)); 80.72 (*d*, C(2)); 114.16 (2*d*); 122.13 (2*d*); 127.51–128.33 (several *d*); 137.99, 138.17, 138.37 (3*s*); 144.08, 158.27 (2*s*); 162.28 (*d*, C(1)).

4,5,6-Tri-O-*benzyl-3-deoxy-2*-O-*mesyl-3-[(4-methoxyphenyl)amino]*-D-*glucono-1,3-lactam* (**27a**) *and 4,5,6-Tri*-O-*benzyl-3-deoxy-2*-O-*mesyl-3-[(4-methoxyphenyl)amino]*-D-*altrono-1,3-lactam* (**27b**). At 25° and under Ar, a soln. of sublimed **22** (6.38 g, 51.8 mmol) in dry CH_2Cl_2 (300 ml) was treated with 3-Å molecular sieves

Table 4. *Selected ^{13}C-NMR* (50–125 MHz) *Chemical Shifts* [ppm] *of the β-Lactams* **25**, **27**–**35**, **39**–**42**, **4**, **43**, **45**, *and* **47**–**50**, *the Mannonic Acid* **44**, *and the Mannonamides* **51** *and* **53**. *J*(C,F) and *J*(C,P) [Hz] in Parentheses

	Solvent	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	R–C(2)	NCH or NCH_2
25[a])	$CDCl_3$	163.37	77.75	55.89	76.50	61.90	71.19	Ms: 39.16	44.21
27a	$CDCl_3$	161.29	77.85[b])	57.77	78.19[b])	78.39[b])	67.93	Ms: 39.35	–
27b	$CDCl_3$	161.5	77.34[b])	57.98	77.45[b])	80.66[b])	67.56	Ms: 39.35	–
28a	(D_6)Acetone	165.00	78.31[b])	58.48	78.45[b])	79.29	69.64	Ms: 39.24	61.74
28b	(D_6)Acetone	166.90	78.31[b])	58.48	78.45[b])	79.29	68.60	Ms: 39.01	62.93
28c	(D_6)Acetone	163.93	78.01[b])	60.90	79.90[b])	79.29	69.42	Ms: 39.27	63.42
29	(D_6)Benzene	162.77	78.30	58.27	79.04	77.74	63.36	Ms: 39.08	62.76
30a	$CDCl_3$	161.99	66.90	61.58	78.15[b])	79.77[b])	66.90	–	–
30b	$CDCl_3$	161.57	64.58	60.25	72.54	77.05	68.34	–	–
31a	(D_6)Acetone	164.51	68.10	57.26	78.99[b])	79.16[b])	69.41	–	–
31b	(D_6)Acetone	164.86	67.08	57.04	77.99[b])	79.19[b])	69.73	–	–
32	$CDCl_3$	165.20	61.47	58.58	80.93	78.83	67.83	Ac: 22.26, 170.25	–
33	$CDCl_3$	164.85	59.73[b])	59.08[b])	73.25	71.10	61.90	Ac: 22.47, 170.03	–
34[a])	(D_6)Benzene	162.71	64.70	58.82	79.97	77.93	62.99	–	62.97
35	(D_6)Benzene	162.58	66.95	55.21	76.70[b])	76.97[b])	62.30	–	–
39	(D_6)Acetone	163.28	60.99[b])	59.39[b])	81.48	79.78	69.06	CF_3CO: 116.78 (287.5), 157.40 (37.3)	–
40	CD_3OD	165.43	62.26	58.59	73.47	71.80	64.70	CF_3CO: 117.15 (290), 159.1 (38.0)	–
41	(D_6)Acetone	164.77	67.45	60.58	80.19	78.06	69.31	–	43.70
42[a])	(D_6)Acetone	165.17	59.48	60.77	81.56	78.53	69.58	CF_3CO: hidden	43.71
4[a])	D_2O	167.93	57.64	62.18	70.71	72.81	62.89	CF_3CO: 110.08 (286.8), 158.90 (38.2)	46.64
43[a])	D_2O	165.48	57.13	60.66	69.77	72.67	62.78	–	45.96
44[a])	D_2O	168.25	56.15	54.58	69.03	72.31	62.14	–	45.10
45	(D_6)Acetone	164.83	67.23	59.58	78.76[b])	81.10[b])	69.08	–	46.07
47	(D_6)Acetone	164.41 (1.8)	67.75	61.17	78.62[b])	80.86[b])	69.41	–	38.31 (151.8)
48	(D_6)Acetone	165.01	59.90	61.07	81.40	78.98	69.59	CF_3CO: hidden	38.68 (154.3)
49	D_2O	167.44	57.18	62.50	70.58	72.47	62.86	CF_3CO: 115.71 (286.1), 158.63 (38.3)	41.96 (138.5)
50	D_2O	171.8	56.68	60.41	69.84	72.38	62.75	–	41.31 (141.7)
51[a])	(D_6)Benzene	171.31	64.23	53.40	76.69	78.27	68.43	–	–
53[a])	(D_6)Benzene	169.48	65.26	51.92	74.29	78.04	63.23	–	–

[a]) Assignment based on ^{1}H/^{13}C-COSY spectrum. [b]) Assignments may be interchanged.

(20 g), vigorously stirred, and treated dropwise with a soln. of **16** (20.255 g, 51.8 mmol) in dry CH_2Cl_2 (50 ml) over a 2-h period. After stirring for 3 h and the addition of anh. $MgSO_4$ (10 g), the suspension was stirred for 18 h at 0°. After dilution with dry CH_2Cl_2 to a total volume of 800 ml, more anh. $MgSO_4$ (5 g) was added, and stirring was continued at 0°. After 50 h total reaction time, the suspension was suction-filtered over a *Celite* pad under Ar. The solid residue was washed with dry CH_2Cl_2 (*ca.* 100 ml). The filtrate was diluted with dry DMF (80 ml), vigorously stirred, treated with ^{i}Pr$_2$EtN (13.30 ml, 77.7 mmol) and then dropwise with a soln. of **20** (6.36 ml, 54.39 mmol) in dry CH_2Cl_2 (60 ml) over a 3-h period, and stirred at 24° for 19 h. After the addition of a soln. of **20** (1.21 ml, 10.36 mmol) in dry CH_2Cl_2 (20 ml), the mixture was stirred for 26 h and poured on excess 5% aq. tartaric acid (*ca.* 200 ml). The brown org. phase was washed with brine (150 ml) and ice-water (200 ml).

The combined H_2O phases were extracted with CH_2Cl_2 (100 ml), and the combined org. phases were dried ($MgSO_4$) and evaporated. The brown oil (41.48 g, 127%) was dried in high vacuum for 20 h. FC (toluene/AcOEt 20:1) gave inseparable **27a/b** 3:1 (22.56 g, 69%). Slightly yellowish oil. R_f (hexane/AcOEt 3:1) 0.31 (blue-violet colour on TLC with mostain reagent). $[\alpha]_D^{25} = +15.6$ ($c = 0.43$, $CHCl_3$). IR (KBr): 3020*w*, 2960*w*, 2940*w*, 2910*w*, 2870*w*, 1758*s*, 1515*m*, 1370*s*, 1180*s*, 1250*s*, 1100*s*, 830*s*, 700*s*. ^{1}H-NMR (400 MHz, $CDCl_3$, **27a/b** 3:1; assignment based on selective homonuclear decoupling experiments): see *Table 3*; additionally, 3.14 (*s*, 0.25 H), 3.21 (*s*, 0.75 H) (MsO); 3.77 (*s*, 0.75 H), 3.80 (*s*, 0.25 H) (MeO); 4.43 (*d*, $J = 11.1$, 0.75 H), 4.48–4.60 (*m*, 4.25 H) (5 PhC*H*); 4.69 (*d*, $J = 11.6$, 0.75 H), 4.70 (*d*, $J = 11.4$, 0.25 H) (PhC*H*); 6.73–6.78 (*m*, 1.5 H), 6.86–6.89 (*m*, 0.5 H), 6.90–6.95 (*m*, 1.5 H), 7.09–7.13 (*m*, 0.5 H) (*AA′BB′*); 7.16–7.40 (*m*, 15 arom. H). ^{13}C-NMR (50 MHz, $CDCl_3$, **27a/b** 3:1): see *Table 4*, additional signals of **27a**: 55.39 (*q*, MeO); 72.11, 73.39, 74.24 (3*t*, 3 Ph*C*H$_2$); 113.88 (2*d*); 120.49 (2*d*); 130.38 (*s*); 127.42–128.37 (several *d*); 137.64–138.08 (several *s*); 156.95 (*s*); additional signals of **27b**: 55.39 (*q*, MeO); 72.11, 73.52, 74.72 (3*t*, 3 Ph*C*H$_2$); 114.65 (2*d*); 118.66 (2*d*); 128.98 (*s*); *ca.* 156.5 (*s*). CI-MS (NH_3): 634 (11), 633 (42), 632 (100, $[M+1]^+$), 631 (6), 280 (7), 183 (20), 181 (25), 155 (11), 91 (33, Bn^+). Anal. calc. for $C_{35}H_{37}NO_8S$ (631.75): C 66.54, H 5.90, N 2.22, S 5.07; found: C 66.63, H 6.01, N 2.28, S 4.98.

4,5,6-Tri-O-*benzyl-3-deoxy-2*-O-*mesyl-3-{[bis(4-methoxyphenyl)methyl]amino}*-D-*glucono-1,3-lactam* (**28a**), *4,5,6-Tri*-O-*benzyl-3-deoxy-2*-O-*mesyl-3-{[bis(4-methoxyphenyl)methyl]amino}*-D-*altrono-1,3-lactam* (**28b**), *and 4,5,6-Tri*-O-*benzyl-3-deoxy-2*-O-*mesyl-3-{[bis(4-methoxyphenyl)methyl]amino}*-D-*allono- or* -D-*mannono-1,3-lactam* (**28c**). A precooled (0°) soln. of **16** (605 mg, 1.54 mmol) in dry CH_2Cl_2 (10 ml) was treated with 3-Å molecular sieves (400 mg) and **23** (377 mg, 1.54 mmol). After stirring at 0° for 17 h, more **16** (95 mg, 0.24 mmol) was added, and the suspension was further stirred at 0° for 5 h. The resulting soln. of the imine was warmed to 25°, treated with *Hünig*'s base (0.4 ml, 2.31 mmol) and dropwise with a soln. of **20** (0.216 ml, 1.848 mmol) in dry CH_2Cl_2 (8.5 ml) over a 2-h period, and stirred for 26 h. The amber mixture was diluted with CH_2Cl_2 (*ca.* 30 ml) and poured into a cold (4°) soln. of tartaric acid (500 mg) in H_2O (10 ml). The org. phase was separated and washed with sat. aq. NaCl (2×10 ml) and H_2O (10 ml). Collected H_2O phases were extracted with CH_2Cl_2 (5 ml) and combined org. phases were dried (Na_2SO_4) and evaporated to give, after further drying at high vacuum, a brown oil (1.62 g, 140%). FC (hexane/AcOEt 2:1) gave an inseparable mixture of **28a/b/c** 25:35:40. Slightly yellowish oil (660 mg, 57%). R_f (hexane/AcOEt 2:1) 0.29 (pink colour on TLC with mostain reagent). $[\alpha]_D^{25} = -32.1$ ($c = 0.80$, $CHCl_3$). IR ($CHCl_3$): 3020*w*, 3000*w*, 2960*w*, 2940*w*, 2910*w*, 2870*w*, 2840*w*, 1762*s*, 1669*m*, 1621*m*, 1512*m*, 1465*w*, 1455*m*, 1370*m*, 1179*s*, 1250*s*, 1061*s*, 1036*s*, 820*m*, 700*m*. ^{1}H-NMR (600 MHz, (D_6)acetone, **28a/b/c** 25:35:40): see *Table 3*; additionally, 3.09 (*s*, 1.05 H), 3.23 (*s*, 0.75 H), 3.26 (*s*, 1.2 H) (MsO); 3.71 (*s*, 0.75 H), 3.75 (*s*, 1.2 H), 3.769 (*s*, 1.2 H), 3.771 (*s*, 1.05 H), 3.78 (*s*, 0.75 H), 3.79 (*s*, 1.05 H) (2 MeO); 3.64–3.94 (*m*, H–C(5), 2 H–C(6)); 4.00 (*dd*, $J = 4.2, 6.0$, 0.35 H), 4.13–4.16 (*m*, 0.5 H), 4.22 (*t*, $J = 6.0$, 0.25 H), 4.30 (*d*, $J = 11.7$, 0.25 H), 4.37 (*d*, $J = 11.7$, 0.25 H), 4.40–4.60 (*m*, 5.4 H) (H–C(3), H–C(4), 5 PhC*H*); 4.68 (*d*, $J =$ 10.8, 0.25 H), 4.71 (*d*, $J = 10.8$, 0.4 H), 4.79 (*d*, $J = 10.8$, 0.35 H) (PhC*H*); 5.10 (*s*, 0.4 H), 5.61 (*d*, $J = 5.4$, 0.35 H), 5.71 (*d*, $J = 5.5$, 0.25 H) (H–C(2)); 5.69 (br. *s*, 0.4 H), 5.72 (br. *s*, 0.25 H), 5.79 (br. *s*, 0.35 H) (Ar_2CH); 6.70 (*d*, $J = 8.8$, 0.7 H), 6.80 (*d*, $J = 8.8$, 0.5 H), 6.84 (*d*, $J = 8.8$, 0.8 H) (2 arom. H); 6.87–6.93 (*m*, 2 arom. H); 7.08–7.37 (*m*, 19 arom. H); irrad. at 5.61: 4.45 (*dd*, $J = 5.5, 4.5$, $\rightarrow d$, $J = 4.5$, H–C(3) of **28b**); irrad. at 5.71: 4.52 (*t*, $J = 5.8$, $\rightarrow d$, $J = 6.0$, H–C(3) of **28a**). ^{13}C-NMR (50 MHz, (D_6)acetone, **28a/b/c** 25:35:40): see *Table 4*; additionally, 55.38 (*q*, 0.65 C), 55.48 (*q*, 1.35 C) (2 MeO); 71.34–74.39 (several *t*, 3 Ph*C*H$_2$); 110.22 (*d*, 0.35 C), 113.94 (*d*, 0.85 C), 114.54 (*d*, 2 C), 114.67 (*d*, 0.8 C) (4 arom. C); 128.23–129.32 (several *d*); 130.08 (*d*, 0.5 C), 130.16 (*d*, 0.7 C), 130.42 (*d*, 0.7 C), 130.49 (*d*, 1.3 C), 131.58 (*d*, 0.8 C) (4 arom. C); 130.31 (*s*, 0.25 C), 131.44 (*s*, 0.25 C), 132.24 (*s*, 0.4 C), 132.41 (*s*, 0.35 C), 132.70 (*s*, 0.35 C), 133.02 (*s*, 0.4 C) (2 arom. C); 138.97–139.68, (several *s*); 159.63 (*s*, 0.5 C), 159.94 (*s*, 0.8 C), 160.02 (*s*, 0.7 C) (2 arom. C). CI-MS (NH_3): 770 (8), 769 (17, $[M+NH_4]^+$), 753 (11), 752 (26, $[M+1]^+$), 661 (16), 660 (44, $[M-Bn]^+$), 646 (10), 644 (100, $[M-BnO]^+$), 543 (13), 536 (15), 527 (12), 526 (40), 442 (7), 347 (16), 318 (9), 317 (41). Anal. calc. for $C_{43}H_{45}NO_9S$ (751.90): C 68.69, H 6.03, N 1.86, S 4.26; found: C 68.52, H 6.15, N 1.88, S 4.50.

6-O-*[(*tert*-Butyl)diphenylsilyl]-3-deoxy-4,5*-O-*isopropylidene-2*-O-*mesyl-3-{[bis(4-methoxyphenyl)methyl]-amino}*-D-*glucono-1,3-lactam* (**29**). A precooled (0°) soln. of fresh, crude **17** (obtained from dithioacetal cleavage of 635 mg (1.078 mmol) of **15**) in dry CH_2Cl_2 (12 ml) was treated with 3-Å molecular sieves (500 mg) and **23** (262 mg, 1.08 mmol), and stirred in an ice bath for 21 h. Under Ar, the resulting soln. of the imine was suction-filtered over a *Celite*/sand pad. The residue was washed with dry CH_2Cl_2 (3×6 ml). The filtrate was treated with 3-Å molecular sieves, dry DMF (5 ml), and dropwise with a soln. of **20** (0.151 ml, 1.293 mmol) in dry CH_2Cl_2 (5 ml) over a 90-min period, and stirred at 25° for 13 h. The mixture was poured into 5% aq. tartaric acid (30 ml). The org. phase was separated and washed with brine (15 ml) and H_2O (15 ml), dried ($MgSO_4$),

and evaporated. FC (toluene/AcOEt 15:1) gave **29** (740 mg, 90% from **15**). Yellowish oil[7]). R_f (toluene/AcOEt 7:1) 0.44 (pink colour on TLC with mostain reagent). $[\alpha]_D^{25} = +20.0$ ($c = 0.97$, $CHCl_3$). IR ($CHCl_3$): 3040*w*, 3020*w*, 3000*w*, 2960*w*, 2935*w*, 2900*w*, 2860*w*, 1763*s*, 1612*m*, 1514*m*, 1465*m*, 1435*m*, 1374*m*, 1335*w*, 1305*w*, 1250*s*, 1112*s*, 820*m*, 705*m*. ^{1}H-NMR (500 MHz, C_6D_6): see *Table 3*; additionally, 1.06, 1.48 (2*s*, Me_2C); 1.13 (*s*, *t*-Bu); 2.62 (*s*, MsO); 3.29, 3.30 (2*s*, 2 MeO); 5.95 (*s*, Ar_2CH); 6.78 (*d*, $J = 8.8$), 6.82 (*d*, $J = 8.8$) (4 arom. H); 7.23–7.35 (*m*, 8 arom. H); 7.48 (*dd*, $J = 0.5$, 8.8, 2 arom. H); 7.83–7.87 (*m*, 4 arom. H). ^{13}C-NMR (125 MHz, C_6D_6): see *Table 4*; additionally, 19.41 (*s*, Me_3C); 24.76, 27.33 (2*q*, Me_2C); 27.10 (*q*, Me_3C); 54.78, 54.83 (2*q*, 2 MeO); 109.03 (*s*, Me_2C); 114.18 (2*d*); 114.27 (2*d*); 127.95–130.53 (several *d*); 131.49, 132.16, 133.28, 133.54 (4*s*); 136.20 (2*d*); 136.26 (2*d*); 159.72, 159.74 (2*s*). CI-MS (NH_3): 761 (5, $[M+1]^+$), 760 (10, M^+), 228 (17), 227 (100, $(MeOC_6H_4)_2CH^+$). Anal. calc. for $C_{41}H_{49}NO_9SSi$ (759.99): C 64.80, H 6.50, N 1.84, S 4.22; found: C 65.06, H 6.55, N 2.11, S 4.46.

2-Azido-4,5,6-tri-O-*benzyl-2,3-dideoxy-3-[(4-methoxyphenyl)amino]*-D-*mannono-1,3-lactam* (**30a**) *and 2-Azido-4,5,6-tri*-O-*benzyl-2,3-dideoxy-3-[(4-methoxyphenyl)amino]*-D-*allono-1,3-lactam* (**30b**). A soln. of **27a/b** 3:1 (598 mg, 0.946 mmol) in dry 1,3-dimethylimidazolidin-2-one (12 ml) was treated with 3-Å molecular sieves (300 mg) and LiN_3 (185 mg, 3.786 mmol) and stirred at 50° for 19 h and at 70° for 50 h. The mixture was poured into ice-water (30 ml) and the resulting milky-yellow suspension extracted with Et_2O (9 × 50 ml). The combined Et_2O extracts were washed with brine (2 × 50 ml) and H_2O (50 ml). The aq. phases were extracted with Et_2O (80 ml). The combined org. phases were dried (Na_2SO_4), evaporated, and further dried in high vacuum. FC (toluene/AcOEt 25:1) of the yellow oil (718 mg) gave **30a/b** 87:13 (470 mg, 86%). Weakly yellowish oil. A small sample of **30a/b** 87:13 was separated by prep. HPLC (toluene/AcOEt 50:1).

Data of **30a/b** 87:13: Anal. calc. for $C_{34}H_{34}N_4O_5$ (578.67): C 70.57, H 5.92, N 9.68; found: C 70.55, H 5.99, N 9.75.

Data of **30a**: Oil. R_f (toluene/AcOEt 25:1) 0.27 (violet colour on TLC with mostain reagent). $[\alpha]_D^{25} = -60.7$ ($c = 0.39$, $CHCl_3$). IR ($CHCl_3$): 3060*w*, 3025*w*, 3010*w*, 2940*w*, 2910*w*, 2870*w*, 2115*s*, 1758*s*, 1515*s*, 1455*m*, 1385*w*, 1250*s*, 1140*s*, 1115*m*, 1090*m*, 830*m*, 700*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): see *Table 3*; additionally, 3.76 (*s*, MeO); 4.22, 4.44 (2*d*, $J = 10.7$, PhCH_2) 4.49, 4.53 (2*d*, $J = 10.7$, PhCH_2); 4.55, 4.72 (2*d*, $J = 11.9$, PhCH_2); 6.74–6.77 (*m*), 6.85–6.87 (*m*, *AA′BB′*); 7.18–7.37 (*m*, 15 arom. H). ^{13}C-NMR (50 MHz, $CDCl_3$): see *Table 4*; additionally, 55.36 (*q*, MeO); 71.71, 73.38, 74.15 (3*t*, 3 PhCH_2); 113.93 (2*d*); 120.89 (2*d*); 127.83–128.45 (several *d*); 130.19 (*s*); 136.92, 137.44, 137.56 (3*s*); 156.80 (*s*). CI-MS (NH_3): 580 (14), 579 (38, $[M+1]^+$), 554 (16), 553 (49), 552 (40), 551 (100, $[M+1-N_2]^+$), 445 (22), 443 (26, $[M-N_2-BnO]^+$), 435 (11), 434 (33), 344 (12), 339 (12), 337 (20), 282 (13), 231 (11), 191 (12), 181 (11), 152 (20), 147 (25), 124 (20), 108 (12), 107 (94, $C_7H_7O^+$).

Data of **30b**: R_f (toluene/AcOEt 25:1) 0.34 (violet colour on TLC with mostain reagent). $[\alpha]_D^{25} = -2.3$ ($c = 0.52$, $CHCl_3$). IR ($CHCl_3$): 3060*w*, 3025*w*, 3010*w*, 2935*w*, 2910*w*, 2870*w*, 2115*s*, 1755*s*, 1515*s*, 1455*m*, 1395*w*, 1250*s*, 1150*m*, 1115*m*, 1090*m*, 830*w*, 700*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): see *Table 3*; additionally, 3.78 (*s*, MeO); 4.20, 4.29 (2*d*, $J = 11.2$, PhCH_2); 4.54 (*s*, PhCH_2); 4.62, 4.73 (2*d*, $J = 11.9$, PhCH_2); 6.76–6.80 (*m*), 7.00–7.03 (*m*) (*AA′BB′*); 7.19–7.40 (*m*, 15 arom. H). ^{13}C-NMR (50 MHz, $CDCl_3$): see *Table 4*; additionally, 55.41 (*q*, MeO); 72.77, 73.40, 73.61 (3*t*, 3 PhCH_2); 114.54 (2*d*); 118.98 (2*d*); 127.85–128.48 (several *d*); 129.69 (*s*); 137.10 (*s*); 137.58 (2*s*); 156.49 (*s*). CI-MS (C_4H_{10}): 580 (14), 579 (49, $[M+1]^+$), 554 (15), 553 (45), 552 (38), 551 (100, $[M+1-N_2]^+$), 496 (17), 443 (25, $[M-N_2-BnO]^+$), 435 (15), 434 (48), 353 (9), 344 (19), 337 (16), 282 (17), 281 (26), 229 (11), 228 (32), 191 (17), 181 (34), 179 (19), 152 (19), 147 (20), 124 (15), 108 (12), 107 (98, $C_7H_7O^+$).

3-Amino-2-azido-4,5,6-tri-O-*benzyl-2,3-dideoxy*-D-*mannono-1,3-lactam* (**31a**) *and 3-Amino-2-azido-4,5,6-tri*-O-*benzyl-2,3-dideoxy*-D-*allono-1,3-lactam* (**31b**). Under Ar, a vigorously stirred soln. of **30a/b** 87:13 (2.11 g, 3.64 mmol) in MeCN (60 ml) at −30° was treated dropwise with a soln. of ceric ammonium nitrate (CAN; 4.00 g, 7.29 mmol) in H_2O (28 ml) over a period of 40 min. The temp. was allowed to rise to −15° during the first 60 min of the reaction, and then kept between −20 and −15°. After 70 min, a second portion of CAN (0.5 g, 0.911 mmol) was added, and, after 100 min, a third portion (1.5 g, 2.73 mmol). After a total reaction time of 140 min, the orange suspension was diluted with AcOEt (150 ml) and 10% aq. Na_2SO_3 soln. (100 ml), and suction-filtered over a *Celite*/sand bed. The solid residue was washed with AcOEt (100 ml), and the aq. phase of the clear biphasic filtrate was discarded. The org. phase was washed with 10% aq. Na_2SO_3 soln. (120 ml), 5% aq.

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[7]) To completely remove HgI_2 and mercury mercaptides, the chromatographed material required being taken up in dry benzene, filtered over a cotton plug, evaporated, taken up in benzene/cyclohexane 1:1, and again filtered and evaporated.

$NaHCO_3$ soln. (2×100 ml), and brine (2×80 ml). The combined H_2O phases were extracted with AcOEt (3×70 ml), and the combined org. phases were dried ($MgSO_4$). Evaporation and FC (toluene/AcOEt 9:1) gave **31a** (770 mg, 45%) and **31b** (not isolated)[8]). A 2:1 mixture of **31a**/**b** obtained from a smaller batch was separated by FC (hexane/AcOEt 3:1).

Data of **31a**: light-yellow oil that solidified to a microcrystalline solid in the freezer. R_f (toluene/AcOEt 7:1) 0.28; R_f (hexane/AcOEt 3:1) 0.30. M.p. 63° (AcOEt). $[\alpha]_D^{25} = -124.0$ ($c = 0.58$, $CHCl_3$). IR ($CHCl_3$): 3420*m*, 3080*w*, 3060*w*, 3020*w*, 3000*w*, 2940*m*, 2900*w*, 2870*w*, 2110*s*, 1775*s*, 1495*m*, 1455*m*, 1360*w*, 1300*w*, 1250*m*, 1110*m*, 1090*s*, 1075*s*, 1030*s*, 750*m* (br.), 700*s*. ^{1}H-NMR (400 MHz, (D_6)acetone): see *Table 3*; additionally, 4.57 (*s*, PhCH_2); 4.63, 4.71 (2*d*, $J = 11.4$, PhCH_2); 4.675, 4.755 (2*d*, $J = 11.9$, PhCH_2); 7.24–7.39 (*m*, 15 arom. H); 7.52 (br. *s*, exchange with D_2O, NH). ^{13}C-NMR (50 MHz, (D_6)acetone): see *Table 4*; additionally, 72.79, 73.77, 73.91 (3*t*, 3 PhCH_2); 128.32–129.06 (several *d*); 139.20, 139.35, 139.56 (3*s*). CI-MS (NH_3): 474 (32), 473 (100, $[M+1]^+$), 446 (21), 445 (72, $[M+1-N_2]^+$), 418 (109), 339 (8), 337 (17, $[M-N_2-BnO]^+$), 328 (7), 282 (8), 231 (14), 229 (8), 147 (21), 107 (41, BnO^+), 91 (20, Bn^+). Anal. calc. for $C_{27}H_{28}N_4O_4$ (472.54): C 68.63, H 5.97, N 11.86; found: C 68.57, H 5.91, N 11.63.

Data of **31b**: Yellow oil. R_f (hexane/AcOEt 3:1) 0.20. $[\alpha]_D^{22} = +16.1$ ($c = 0.39$, $CHCl_3$). IR ($CHCl_3$): 3410*w*, 3080*m*, 3060*m*, 3020*m*, 3005*m*, 2940*m*, 2900*w*, 2870*w*, 2110*s*, 1775*s*, 1495*m*, 1455*w*, 1365*w*, 1310*w*, 1255*w*, 1195*m*, 1095*w*, 1075*w*, 750*m* (br.), 700*m*. ^{1}H-NMR (400 MHz, (D_6)acetone): see *Table 3*; additionally, 4.55 (*s*, PhCH_2); 4.61, 4.67 (2*d*, $J = 11.4$, PhCH_2); 4.65, 4.76 (2*d*, $J = 11.8$, PhCH_2); 7.22–7.40 (*m*, 1 H exchanged with D_2O, 15 arom. H, NH). ^{13}C-NMR (50 MHz, (D_6)acetone): see *Table 4*; additionally, 73.12, 73.77, 74.48 (3*t*, 3 PhCH_2); 128.30–129.07 (several *d*); 139.26, 139.42, 139.48 (3*s*). CI-MS (NH_3): 475 (7), 474 (36), 473 (100, $[M+1]^+$), 447 (11), 446 (32), 445 (89, $[M+1-N_2]^+$), 418 (11), 355 (6), 354 (6), 337 (15, $[M-N_2-BnO]^+$), 107 (10, BnO^+), 91 (9, Bn^+). Anal. calc. for $C_{27}H_{28}N_4O_4$ (472.54): C 68.63, H 5.97, N 11.86; found: C 68.55, H 6.15, N 11.87.

2-Acetamido-4,5,6-tri-O-*benzyl-2,3-dideoxy-3-[(4-methoxyphenyl)amino]*-D-*mannono-1,3-lactam* (**32**). A soln. of **30a/b** 87:13 (185 mg, 0.32 mmol) in dry EtOH (5 ml) was treated with 10% Pd/C (36 mg) and stirred vigorously at 25° for 7 h under 6 bar of H_2. After suction-filtration over a *Celite*/sand bed, the residual catalyst was washed with MeOH (*ca.* 100 ml). Evaporation of the filtrates left a brown oil (142 mg), which was acetylated under standard conditions. FC (toluene/AcOEt 1.3:1) gave **32** (134 mg, 70%). Colourless oil. R_f (toluene/AcOEt 1:1) 0.30. $[\alpha]_D^{25} = -5.6$ ($c = 0.53$, $CHCl_3$). IR ($CHCl_3$): 3430*w* (br.), 3010*w*, 3005*w*, 2940*w*, 2920*w*, 2860*w*, 1750*s*, 1682*s*, 1511*s*, 1455*m*, 1385*w*, 1370*w*, 1245*s*, 1195*m*, 1180*m*, 1140*m*, 1115*m*, 1090*m*, 1070*m*, 830*w*, 700*m*. ^{1}H-NMR (400 MHz, (D_6)acetone): see *Table 3*; additionally, 1.86 (*s*, AcN); 3.73 (*s*, MeO); 4.39, 4.67 (2*d*, $J = 11.1$, PhCH_2); 4.54 (*s*, PhCH_2); 4.69, 4.74 (2*d*, $J = 11.7$, PhCH_2); 6.76–6.80 (*m*), 6.99–7.02 (*m*) (*AA′BB′*); 7.18–7.42 (*m*, 15 arom. H); 7.71 (*d*, $J = 8.6$, exchanged with D_2O, NH). ^{13}C-NMR (50 MHz, $CDCl_3$): see *Table 4*; additionally, 55.03 (*q*, MeO); 71.90, 72.96, 73.87 (3*t*, 3 PhCH_2); 113.57 (2*d*); 121.31 (2*d*); 127.30–128.14 (several *d*); 130.19 (*s*); 137.30, 137.81, 138.10 (3*s*); 156.45 (*s*). CI-MS (C_4H_{10}): 597 (10), 596 (45), 595 (100, $[M+1]^+$), 594 (5), 497 (16), 496 (44, $[M+1-AcNH-CH=C=O]^+$). Anal. calc. for $C_{36}H_{38}N_2O_6$ (594.71): C 72.71, H 6.44, N 4.71; found: C 72.71, H 6.48, N 4.59.

2-Acetamido-4,5,6-tri-O-*acetyl-2,3-dideoxy-3-[(4-methoxyphenyl)amino]*-D-*mannono-1,3-lactam* (**33**). A suspension of 20% $Pd(OH)_2$/C (*Pearlman*'s catalyst, 110 mg) in MeOH/H_2O 4:1 (15 ml) was prehydrogenated under 8 bar of H_2 for 45 min, treated with a soln. of **32** (265 mg, 0.445 mmol) in MeOH (3 ml), vigorously stirred under 8 bar of H_2 for 112 h, and suction-filtered over a *Celite*/sand bed. The residual catalyst was thoroughly washed with MeOH (*ca.* 120 ml). The combined filtrates were evaporated to dryness, and the residual oil was co-evaporated with toluene (3×10 ml) and dried at high vacuum. The crude product (131 mg) was acetylated under standard conditions. FC (toluene/acetone 2:1) of the crude (177 mg) gave **33** (166 mg, 83%). Colourless foam. R_f (toluene/acetone 2:1) 0.25. M.p. 48° (acetone). $[\alpha]_D^{25} = +56.6$ ($c = 0.83$, $CHCl_3$). IR ($CHCl_3$): 3435*w* (br.), 3040*w*, 3030*w*, 2960*m*, 2940*m*, 2910*w*, 2840*w*, 1750*s*, 1690*m*, 1515*s*, 1465*m*, 1440*m*, 1370*w*, 1250*s*, 1140*m*, 1050*m*, 830*m* (br.). ^{1}H-NMR (400 MHz, (D_6)acetone): see *Table 3*; additionally, 1.76 (*s*, AcN); 1.95 (*s*, 2 AcO); 1.99 (*s*, AcO); 3.76 (*s*, MeO); 6.91–6.93 (*m*), 7.30–7.32 (*m*) (*AA′BB′*); 7.86 (br. *d*, $J = 8.1$, exchange with D_2O, NH). ^{13}C-NMR (50 MHz, $CDCl_3$): see *Table 4*; additionally, 20.29, 20.54, 20.59 (3*q*, 3 Me); 55.69 (*q*, MeO); 59.08, 59.73 (2*d*, C(2), C(3)); 61.90 (*t*, C(6)); 71.10 (*d*, C(5)); 73.25 (*d*, C(4)); 114.73 (2*d*); 122.05 (2*d*); 130.92, 157.65 (2*s*); 164.85 (*s*, C(1)); 170.57, 170.92, 171.31 (3*s*, 3 C=O). CI-MS (NH_3): 468 (3, $[M+NH_4]^+$), 453 (4), 452 (21), 451 (100, $[M+1]^+$), 353 (11), 352 (60, $[M+1-AcNH-CH=C=O]^+$), 234 (6), 134 (3). Anal. calc. for $C_{21}H_{26}N_2O_9$ (450.45): C 56.00, H 5.82, N 6.22; found: C 56.11, H 5.84, N 6.03.

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[8]) Under identical conditions, a 15-g batch of **30a/b** 87:13 yielded *ca.* 35% of **31a**.

*2-Azido-6-*O*-[(*tert*-butyl)diphenylsilyl]-2,3-dideoxy-4,5-*O*-isopropylidene-3-{[bis(4-methoxyphenyl)methyl]amino}-*D*-mannono-1,3-lactam* (**34**). Under Ar, a soln. of **29** (345 mg, 0.454 mmol) in dry 1,3-dimethylimidazolidin-2-one (15 ml) was treated with 3-Å molecular sieves (300 mg) and Bu_4NN_3[9]) (575 mg, 2.01 mmol), stirred at 25° for 24 h, at 50° for 24 h, and at 60° for 48 h. The cold mixture was poured on ice-water (50 ml), the pH was adjusted to 7 with 20% aq. NH_4Cl soln., and extracted with Et_2O (4 × 30 ml). The combined org. phases were dried (Na_2SO_4) and evaporated. The crude product was dried at high vacuum and 50°. FC (hexane/AcOEt 4:1) of the yellow oil gave **34** (286 mg, 89%). Colourless foam. R_f (hexane/AcOEt 2:1) 0.55 (pink colour on TLC with mostain reagent). $[\alpha]_D^{25} = -103.4$ ($c = 0.47$, $CHCl_3$). IR ($CHCl_3$): 3000*w*, 2960*m*, 2940*m*, 2860*w*, 2115*s*, 1760*s*, 1615*m*, 1515*s*, 1385*m*, 1375*w*, 1250*s*, 1180*s*, 1115*s*, 1075*s*, 1040*s*, 825*m*, 705*s*. ^{1}H-NMR (500 MHz, C_6D_6): see *Table 3*; additionally, 1.14 (*s*, *t*-Bu); 1.16, 1.40 (2*s*, Me_2C); 3.28, 3.29 (2*s*, 2 MeO); 5.97 (*s*, Ar_2CH); 6.76–6.79 (*m*), 6.82–6.85 (*m*), 7.38–7.41 (*m*), 7.49–7.52 (*m*) (2 *AA′BB′*); 7.19–7.29 (*m*, 6 arom. H); 7.80–7.86 (*m*, 4 arom. H). ^{13}C-NMR (125 MHz, C_6D_6; assignment based on a ^{1}H/^{13}C-COSY spectrum): see *Table 4*; additionally, 19.19 (*s*, Me_3C); 25.17, 27.46 (2*q*, Me_2C); 27.08 (*q*, Me_3C); 54.73, 54.75 (2*q*, 2 MeO); 109.63 (*s*, Me_2C); 114.07 (2*d*); 114.32 (2*d*); 128.07 (2*d*); 128.10 (2*d*); 129.44 (2*d*); 130.12, 130.22 (2*d*); 130.61 (2*d*); 132.17 (2*s*); 133.35, 133.40 (2*s*); 136.11 (2*d*); 136.15 (2*d*); 159.58, 159.64 (2*s*). CI-MS (NH_3): 681 (15), 680 (47), 679 (100, $[M+1-N_2]^+$), 678 (18), 622 (22), 621 (50), 468 (24), 270 (22), 242 (31), 229 (85), 228 (823), 227 (6027, $(MeOC_6H_4)_2CH^+$). Anal. calc. for $C_{40}H_{46}N_4O_6Si$ (706.91): C 67.96, H 6.56, N 7.93; found: C 68.00, H 6.74, N 7.76.

*3-Amino-2-azido-6-*O*-[(*tert*-butyl)diphenylsilyl]-2,3-dideoxy-4,5-*O*-isopropylidene-*D*-mannono-1,3-lactam* (**35**). A vigorously stirred soln. of **34** (74 mg, 0.104 mmol) in MeCN (10 ml) at −15° was slowly treated dropwise with a soln. of CAN (172 mg, 0.314 mmol) in H_2O (1 ml), stirred for 2 h, treated with more CAN (57 mg, 0.104 mmol), warmed within 3 h to 0°, and stirred for 3.5 h at 0°. The yellow-orange soln. was poured on a 1:1 mixture of 10% aq. Na_2SO_3 soln. and sat. aq. $NaHCO_3$ soln. (12 ml), and extracted with Et_2O (3 × 25 ml). The combined Et_2O phases were washed with sat. aq. $NaHCO_3$ soln. (2 × 5 ml) and H_2O (2 × 5 ml), and the aq. phases were extracted back with Et_2O (10 ml). The combined org. phases were dried (Na_2SO_4) and evaporated. FC (toluene/AcOEt 7:1) gave **35** (40 mg, 80%). Colourless oil. R_f (hexane/AcOEt 2:1) 0.47; (toluene/AcOEt 7:1) 0.25. $[\alpha]_D^{25} = +84.2$ ($c = 0.30$, $CHCl_3$). IR ($CHCl_3$): 3420*s*, 3250*w*, 3115*w*, 3070*w*, 3050*m*, 2995*s*, 2960*w*, 2930*m*, 2895*s*, 2860*s*, 2112*s*, 1780*s*, 1605*m*, 1592*m*, 1472*m*, 1465*s*, 1430*m*, 1385*s*, 1375*m*, 1260*s*, 1168*m*, 1115*s*, 1075*s*, 704*s*. ^{1}H-NMR (400 MHz, C_6D_6): see *Table 3*; additionally, 1.13 (*s*, 12 H), 1.30 (*s*, 3 H) (Me_3C, Me_2C); 3.95 (*q*, $J \approx 5.8$, H–C(5)); 5.26 (br. *s*, exchange with D_2O, NH); 7.19–7.27 (*m*, 6 arom. H); 7.71–7.77 (*m*, 4 arom. H). ^{13}C-NMR (100 MHz, C_6D_6): see *Table 4*; additionally, 19.31 (*s*, Me_3C); 25.23, 27.08 (2*q*, Me_2C); 27.03 (*q*, Me_3C); 109.15 (*s*, Me_2C); 127.93, 128.17 (2*d*); 128.21 (2*d*); 128.57 (2*d*); 130.38, 130.40 (2*s*); 136.01 (2*d*); 136.06 (2*d*). CI-MS (NH_3): 498 (12, $[M+NH_4]^+$), 483 (10), 482 (37), 481 (100, $[M+1]^+$), 453 (14, $[M+1-N_2]^+$), 320 (9), 192 (8). Anal. calc. for $C_{25}H_{32}N_4O_4Si$ (480.64): C 62.47, H 6.71, N 11.66; found: C 62.67, H 6.73, N 11.57.

N-{2-(Benzyloxy)-1-[(benzyloxy)methyl]ethyl} Trifluoroacetamide (**37**). Under Ar, a soln. of **36** [77] (310 mg, 1.042 mmol) in dry THF (10 ml) was treated with Ph_3P (382 mg, 1.46 mmol) and $(CF_3CO)_2O$ (0.233 ml, 1.67 mmol), stirred for 48 h, treated with **38** (278 mg, 1.88 mmol → lemon yellow colour), stirred for 3 min, treated with H_2O (0.19 ml, 10.42 mmol), stirred for 19 h, treated with more H_2O (0.3 ml, 16.45 mmol), and stirred for 51 h. The weakly yellowish suspension ws diluted with AcOEt (20 ml) and suction-filtered over a *Celite*/sand bed (residue washed with 60 ml of AcOEt). The clear, light-yellow filtrate was evaporated and dried at high vacuum for 4 h. FC (hexane/AcOEt 6:1) gave **37** (300 mg, 78%). Colourless oil. R_f (hexane/AcOEt 6:1) 0.27. IR ($CHCl_3$): 3420*m*, 3050*w*, 3005*m*, 2900*m*, 2860*m*, 1725*s*, 1530*m*, 1450*m*, 1355*m*, 1168*s*, 1100*s*, 695*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.58 (*dd*, $J = 5.7$, 9.5, H–C(2), H′–C(1′)); 3.68 (*dd*, $J = 4.3$, 9.5, H′–C(2), H′–C(1′)); 4.31 (*m*, H–C(2)); 4.53 (*s*, 2 $PhCH_2$); 6.66 (br. *s*, NH); 7.26–7.38 (*m*, 10 arom. H). ^{13}C-NMR (50 MHz, (D_6)acetone): 51.00 (*d*, C(1)); 69.25 (*t*, C(2), C(1′)); 73.51 (*t*, 2 $PhCH_2$); 128.30 (2*d*); 128.35 (4*d*); 129.06 (4*d*); 139.31 (2*s*); signals for F_3C–C=O hidden by noise. CI-MS (NH_3): 458 (18), 386 (22), 385 (100, $[M+NH_4]^+$), 263 (12), 182 (9). Anal. calc. for $C_{19}H_{20}F_3NO_3$ (367.37): C 62.12, H 5.49, F 15.51, N 3.81; found: C 62.06, H 5.70, F 15.43, N 3.62.

*4,5,6-Tri-*O*-benzyl-2,3-dideoxy-3-[(4-methoxyphenyl)amino]-2-(trifluoroacetamido)-*D*-mannono-1,3-lactam* (**39**). Under Ar, a cooled (0°) soln. of **30a**/**b** 87:13 (1.055 g, 1.82 mmol) in dry THF (10 ml) was treated with Ph_3P (669 mg, 2.55 mmol) and $(CF_3CO)_2O$ (0.407 ml, 2.92 mmol), stirred at 0° for 1 h, and at 23° for 49 h, treated with **38** (486 mg, 3.28 mmol, → canary-yellow soln.), stirred for 5 min, treated with H_2O (0.148 ml,

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[9]) Conveniently and safely synthesized on large scale according to [105].

8.20 mmol), stirred for 44 h, diluted with AcOEt (50 ml), and suction-filtered over a *Celite*/sand bed. Evaporation and FC (toluene/AcOEt 10:1) of the amber-coloured oil (1.43 g) gave **39** (920 mg, 78%). Weakly yellowish oil. An anal. sample was obtained by HPLC (toluene/Et_2O 10:1). R_f (toluene/AcOEt 10:1) 0.23. $[\alpha]_D^{25} = -3.0$ ($c = 0.94$, $CHCl_3$). IR ($CHCl_3$): 3420*w*, 3230*w*, 3060*w*, 3020*w*, 2920*w*, 2860*w*, 1760*s*, 1730*s*, 1515*s*, 1455*m*, 1385*w*, 1370*w*, 1249*s*, 1180*s*, 1170*s*, 1115*m*, 1095*s*, 830*m*, 700*m*. ^{1}H-NMR (400 MHz, (D_6)acetone): see *Table 3*; additionally, 3.74 (*s*, MeO); 4.39, 4.660 (2*d*, $J = 11.1$, PhCH_2); 4.51 (*s*, PhCH_2); 4.665, 4.715 (2*d*, $J = 11.9$, PhCH_2); 6.79–6.82 (*m*), 6.99–7.02 (*m*) (*AA′BB′*); 7.11–7.39 (*m*, 15 arom. H); 9.21 (*d*, $J = 8.9$, exchange with D_2O, NH). ^{13}C-NMR (50 MHz, (D_6)acetone): see *Table 4*; additionally, 55.70 (*q*, MeO); 72.68, 73.69, 74.58 (3*t*, 3 PhCH_2); 114.57 (2*d*); 121.74 (2*d*); 128.24–129.09 (several *d*); 131.95 (*s*); 138.90, 139.29, 139.53 (3*s*); 157.77 (*s*). CI-MS (NH_3): 666 (8, $[M + NH_4]^+$), 651 (8), 650 (40), 649 (100, $[M + 1]^+$), 496 (12), 419 (9). Anal. calc. for $C_{36}H_{35}F_3N_2O_6$ (648.68): C 66.66, F 8.79, N 4.32; found: C 66.50, F 8.61, N 4.29.

*2,3-Dideoxy-3-[(4-methoxyphenyl)amino]-2-(trifluoroacetamido)-*D*-mannono-1,3-lactam* (**40**). A suspension of 10% Pd/C (60 mg) in dioxane/H_2O 1:1 (5 ml) was hydrogenated, treated with soln. of **39** (171 mg, 0.263 mmol) in dioxane/H_2O 1:1 (6.5 ml), vigorously stirred under 7.5 bar of H_2 for 7 h, treated with MeOH (3 ml) and 20% *Pearlman*'s catalyst (80 mg), and stirred under 7.5 bar of H_2 for 135 h. The mixture was diluted with EtOH, and repeatedly treated with *Celite* and centrifuged (EtOH was used to suspend the residue after each centrifugation cycle). Evaporation of the combined supernatants and FC (CH_2Cl_2/MeOH 12:1) gave **40** (91 mg, 91%). Colourless oil. R_f (CH_2Cl_2/MeOH 10:1) 0.32. $[\alpha]_D^{25} = -20.0$ ($c = 0.80$, $CHCl_3$). IR ($CHCl_3$): 3605*w*, 3350*m* (br.), 2980*w*, 2940*w*, 2820*w*, 1750*m*, 1712*s*, 1515*s*, 1360*m*, 1250*m*, 1175*m*, 1015*s*, 832*w*. ^{1}H-NMR (400 MHz, (D_6)acetone): see *Table 3*; 3.53 (*qd*, $J \approx 5.0$, 9.0, addition of $D_2O \rightarrow$ 3.46, *ddd*, $J = 3.7$, 5.0, 9.0, H–C(5)); 3.62 (br. *dd*, $J \approx 5.0$, 11.0, addition of $D_2O \rightarrow$ 3.57, *dd*, $J = 5.1$, 11.4, H–C(6)); 3.70–3.78 (*m*, addition of $D_2O \rightarrow$ 3.68, *dd*, $J = 5.1$, 11.4, H′–C(6)); 3.76 (*s*, MeO); 3.80–3.87 (br. *s*, exchange with D_2O, HO–C(6)); 3.93 (*ddd*, $J = 3.3$, 6.7, 8.8, addition of $D_2O \rightarrow$ 3.87, *dd*, $J = 3.4$, 9.0, H–C(4)); 4.03 (*d*, $J = 5.7$, exchange with D_2O, HO–C(5)); 4.56 (*d*, $J = 6.8$, exchange with D_2O, HO–C(4)); 4.66 (*dd*, $J = 2.6$, 3.2, H–C(3)); 5.15 (br. *s*, addition of $D_2O \rightarrow$ 4.98, *d*, $J = 2.3$, H–C(2)); 6.86–6.90 (*m*), 7.49–7.53 (*m*) (*AA′BB′*); 9.16 (br. *s*, exchange with D_2O, NH). ^{1}H-NMR (400 MHz, CD_3OD): 3.42 (*ddd*, $J = 3.3$, 5.4, 9.1, H–C(5)); 3.55 (*dd*, $J = 5.3$, 11.4, H–C(6)); 3.69 (*dd*, $J = 3.3$, 11.3, H′–C(6)); 3.77 (*s*, MeO); 3.81 (*dd*, $J = 3.3$, 9.1, H–C(4)); 4.62 (*dd*, $J = 2.3$, 3.3, H–C(3)); 5.01 (*d*, $J = 2.3$, H–C(2)); 6.89–6.93 (*m*), 7.46–7.50 (*m*) (*AA′BB′*). ^{13}C-NMR (CD_3OD, 50 MHz): see *Table 4*, additionally, 55.88 (*q*, MeO); 115.01 (2*d*); 123.06 (2*d*); 131.61, 158.71 (2*s*). CI-MS (NH_3): 397 (15), 396 (100, $[M + NH_4]^+$), 380 (13), 379 (90, $[M + 1]^+$), 378 (10). Anal. calc. for $C_{15}H_{17}F_3N_2O_6$ (378.31): C 47.62, H 4.53, F 15.07, N 7.40; found: C 47.67, H 4.69, F 14.84, N 7.20.

*2-Azido-4,5,6-tri-*O*-benzyl-3-{[(benzyloxycarbonyl)methyl]amino}-2,3-dideoxy-*D*-mannono-1,3-lactam* (**41**). Under Ar, a soln. of **31a** (202 mg, 0.43 mmol) in dry 1,3-dimethylimidazolidin-2-one (10 ml) was treated with 3-Å molecular sieves (300 mg), freshly prepared Ag_2O [106] (99 mg, 0.43 mmol), and benzyl bromoacetate (98 mg, 0.43 mmol), and stirred in the dark at 24° for 24 h and then at 40° for 64 h. After the addition of more Ag_2O (50 mg, 0.21 mmol) and benzyl bromoacetate (49 mg, 0.21 mmol), stirring was continued at 50° for 32 h. The same amounts of both reagents and 3-Å molecular sieves (250 mg) were added, and the suspension was stirred at 60° for 24 h. The same amounts of reagents were added a third time, and the suspension was stirred at 75° for 50 h. The suspension was cooled to 18° and suction-filtered over a *Celite*/sand bed (washing with 100 ml of AcOEt). Evaporation of the clear, weakly yellowish filtrate and FC (toluene/AcOEt 25:1) gave **41** (205 mg, 77%). Colourless oil. R_f (toluene/AcOEt 15:1) 0.28. $[\alpha]_D^{25} = -74.7$ ($c = 0.61$, $CHCl_3$). IR ($CHCl_3$): 3060*w*, 3030*w*, 3005*w*, 2960*w*, 2950*w*, 2930*w*, 2870*w*, 2115*s*, 1770*s*, 1748*s* (sh), 1495*m*, 1455*m*, 1410*m*, 1385*m*, 1355*w*, 1260*m*, 1189*s*, 1095*s* (br.), 1030*s*, 700*s*. ^{1}H-NMR (400 MHz, (D_6)acetone): see *Table 3*; additionally, 3.97 (*d*, $J = 18.1$), 4.23 (*d*, $J = 18.0$) (CH_2N); 4.51, 4.74 (2*d*, $J = 11.5$, PhCH_2); 4.54, 4.57 (2*d*, $J = 12.1$, PhCH_2); 4.67, 4.72 (2*d*, $J = 12.0$, PhCH_2); 5.00, 5.05 (2*d*, $J = 12.3$, PhCH_2); 7.24–7.38 (*m*, 20 arom. H). ^{1}H-NMR (400 MHz, CD_3OD): 3.58 (*dd*, $J = 5.1$, 10.4, H–C(6)); 3.61 (*dd*, $J = 5.5$, 10.4, H′–C(6)); 3.82 (*dt*, $J \approx 3.2$, 5.1, H–C(5)); 3.91 (*dd*, $J = 3.2$, 6.7, H–C(4)); 3.95, 4.21 (2*d*, $J = 18.0$, CH_2N); 4.00 (*dd*, $J = 2.1$, 6.8, H–C(3)); 4.32 (*d*, $J = 2.1$, H–C(2)); 4.37, 4.60 (2*d*, $J = 11.5$, PhCH_2); 4.47, 4.52 (2*d*, $J = 11.9$, PhCH_2); 4.55, 4.61 (2*d*, $J = 12.0$, PhCH_2); 4.97, 5.03 (2*d*, $J = 12.2$, PhCH_2); 7.18–7.37 (*m*, 20 arom. H). ^{13}C-NMR (50 MHz, (D_6)acetone): see *Table 4;* additionally, 67.28 (*t*, PhCH_2); 72.88 (*t*, 2 PhCH_2); 73.75 (*t*, PhCH_2); 128.33–129.17 (several *d*); 136.50, 138.90, 139.12, 139.25 (4*s*); 168.63 (*s*, C=O). CI-MS (NH_3): 623 (7), 622 (32), 621 (78, $[M + 1]^+$), 610 (12), 595 (12), 594 (41), 593 (100, $[M + 1 - N_2]^+$), 575 (6), 533 (12), 507 (24), 506 (70), 488 (7), 487 (7), 486 (13), 485 (36), 430 (8), 418 (8), 399 (22), 398 (86), 377 (8), 340 (14), 323 (23), 108 (30), 91 (12, Bn^+). Anal. calc. for $C_{36}H_{36}N_4O_6$ (620.71): C 69.66, H 5.85, N 9.03; found: C 69.68, H 5.78, N 9.20.

*4,5,6-Tri-*O*-benzyl-3-{[(benzyloxycarbonyl)methyl]amino}-2,3-dideoxy-2-(trifluoroacetamido)-*D*-mannono-1,3-lactam* (**42**). At 25° and under Ar, a soln. of **41** (538 mg, 0.866 mmol) in dry THF (7.5 ml) was treated with

PPh_3 (318 mg, 1.213 mmol) and $(CF_3CO)_2O$ (0.193 ml, 1.39 mmol), stirred for 48 h, treated with **38** (231 mg, 1.556 mmol), stirred for 5 min, treated with H_2O (0.15 ml, 8.33 mmol), stirred for 20 h, and diluted with AcOEt (*ca.* 40 ml). Suction-filtration over a *Celite*/sand bed, evaporation, and FC (toluene/AcOEt 6:1) gave **42** (554 mg, 93%). Colourless oil. R_f (toluene/AcOEt 5:1) 0.33. $[\alpha]_D^{25} = -22.9$ ($c = 1.72$, $CHCl_3$). IR ($CHCl_3$): 3500*w*, 3415*w*, 3230*w*, 3060*w*, 3020*w*, 2930*w*, 2870*w*, 1774*s*, 1730*s*, 1565*m*, 1545*m*, 1495*w*, 1455*m*, 1240*m*, 1175*s*, 1095*s*, 695*s*. ^{1}H-NMR (400 MHz, (D_6)acetone): see *Table 3*; additionally, 4.025, 4.15 (2*d*, $J = 18.0$, CH_2N); 4.48, 4.78 (2*d*, $J = 11.5$, PhCH_2); 4.485, 4.53 (2*d*, $J = 12.0$, PhCH_2); 4.67, 4.71 (2*d*, $J = 12.1$, PhCH_2); 4.95, 5.01 (2*d*, $J = 12.3$, PhCH_2); 7.23–7.37 (*m*, 20 arom. H); 9.40 (br. *d*, $J = 8.6$, exchange with D_2O, NH). ^{13}C-NMR (50 MHz, (D_6)acetone; assignment based on a ^{1}H/^{13}C-COSY spectrum): see *Table 4*; additionally, 67.27 (*t*, Ph*C*H_2); 73.03, 73.19, 73.72 (3*t*, 3 Ph*C*H_2); 128.28–129.24 (several *d*); 136.69, 139.21, 139.31, 139.51 (4*s*); 165.17 (*s*, C(1)); 168.91 (*s*, C=O). CI-MS (NH_3): 709 (9), 708 (22, $[M + NH_4]^+$), 693 (10), 692 (43), 691 (100, $[M + 1]^+$). Anal. calc. for $C_{38}H_{37}F_3N_2O_7$ (690.72): C 66.08, H 5.40, F 8.25, N 4.05; found: C 65.96, H 5.65, F 8.41, N 3.96.

3-[(Carboxymethyl)amino]-2,3-dideoxy-2-(trifluoroacetamido)-D-*mannono-1,3-lactam* (**4**). A suspension of 20% *Pearlman*'s catalyst (121 mg) in MeOH/H_2O 5:1 (5 ml) was hydrogenated, treated dropwise with a soln. of **42** (394 mg, 0.57 mmol) in MeOH/H_2O 5:1 (7 ml), vigorously stirred under 7 bar of H_2 for 97 h, treated with *Celite*, and centrifuged several times. The combined supernatants were suction-filtered over a *Celite*/*RP-18* silica/sand bed. The clear filtrate was concentrated to a small volume, diluted with dioxane/H_2O 1:2 (5 ml) and lyophilized. The residue was taken up in H_2O (5 ml), pressure-filtered over a 0.2-μm membrane filter (*Merck Anotop*), and lyophilized. Prep. *RP18*-HPLC (H_2O/MeCN 40:1) of the colourless foam (213 mg) afforded **4** (169 mg, 56%, purification not optimized). Colourless snowy solid. R_f (^{i}PrOH/H_2O/HCOOH 20:1:0.03) 0.68; R_f (AcOEt/HCOOH/H_2O 85:10:5) 0.28. Anal. HPLC (*RP-18*): t_R (H_2O/MeCN 5:1, flow: 0.5 ml/min, refractometric detection) 4.45 min. M.p. 172°. $[\alpha]_D^{25} = -58.4$ ($c = 0.60$, H_2O). IR (KBr): 3390*s* (br.), 2915*m* (br.), 1760*s*, 1730*s*, 1715*s*, 1650–1550*s* (br.), 1430*m*, 1390*m*, 1315*s*, 1235*s*, 1185*s*, 1110*m*, 1080*m*, 1040*m*, 966*w*, 895*w*, 835*w*. ^{1}H-NMR (400 MHz, D_2O): see *Table 3*; additionally, 3.94, 4.11 (2*d*, $J = 17.7$, CH_2N). ^{13}C-NMR (50 MHz, D_2O; assignment based on a ^{1}H/^{13}C-COSY spectrum): see *Table 4*; additionally, 176.14 (br. *s*, CO_2H). ESI-MS (H_2O/MeOH): 369 (14, $[M + K]^+$), 353 (100, $[M + Na]^+$), 331 (35, $[M + 1]^+$). Anal. calc. for $C_{10}H_{13}F_3N_2O_7 \cdot 2.5\ H_2O$ (375.26): C 32.01, H 4.83, N 7.47; found: C 32.21, H 4.64, N 7.60.

2-Amino-3-[(carboxymethyl)amino]-2,3-dideoxy-D-*mannono-1,3-lactam* (**43**) *and 2-Amino-3-[(carboxymethyl)amino]-2,3-dideoxy*-D-*mannonic Acid* (**44**). A suspension of 20% *Pearlman*'s catalyst (121 mg) in *t*-BuOH/H_2O 4:1 (5 ml) was hydrogenated, treated dropwise with a soln. of **41** (553 mg, 0.89 mmol) in *t*-BuOH/H_2O 4:1 (20 ml), vigorously stirred under 7 bar of H_2 for 4 d, treated with *Celite* (*ca.* 100 mg), and centrifuged. The supernatant was decanted, and the residue was resuspended in H_2O (*ca.* 25 ml), and centrifuged again (this procedure was repeated twice). The combined supernatants were suction-filtered over a sand/*RP18*-silica/*Celite*/sand bed. Lyophilization, prep. *RP18*-HPLC (0.1M $Et_3NH^+HCO_3^-$ adjusted to pH 7.3 with AcOH, 2% MeCN, flow: 8 ml/min, refract. detection), and lyophilization gave **43**/**44**/Et_3N 2:3:3 (149 mg, 54%). Slightly yellow, snowy solid. Anal. HPLC (*RP-18*): t_R (H_2O/MeCN 35:1; flow: 0.5 ml/min, refractometric detection) 3.57 min. $[\alpha]_D^{25} = +10.8$ ($c = 0.66$, H_2O). ^{1}H-NMR (D_2O, 600 MHz, **43**/**44**/Et_3N 2:3:3; assignment based on a ^{1}H/^{1}H-COSY spectrum): see *Table 3*; additionally, 1.28 (*t*, $J = 7.3$, 5.4, H, ($MeCH_2)_3N$); 3.20 (*q*, $J = 7.3$, 3.6 H, ($MeCH_2)_3N$); 3.84 (*d*, $J = 17.6$, 0.6 H), 3.91 (*d*, $J = 17.6$, 0.6 H), 3.99 (*d*, $J = 17.5$, 0.4 H), 4.025 (*d*, $J = 17.5$, 0.4 H) (CH_2N). ^{13}C-NMR (150 MHz, D_2O, **43**/**44**/Et_3N 2:3:3; assignment based on a ^{1}H/^{13}C-COSY spectrum): see *Table 4*; additional signals of **43** and **44**: 175.07, 175.19 (2*s* of similar intensity, 2 C=O); signals of Et_3N: 8.41 (*t*, ($MeCH_2)_3N$); 46.83 (*t*, ($MeCH_2)_3N$).

2-Azido-4,5,6-tri-O-*benzyl-3-(benzylamino)-2,3-dideoxy*-D-*mannono-1,3-lactam* (**45**). A soln. of **31a** (138 mg, 0.29 mmol) in dry MeCN (3 ml) was treated with dibenzyl (chloromethyl)phosphonate [85] (238 mg, 0.76 mmol) in dry MeCN (0.6 ml), KF on Al_2O_3 (584 mg, *ca.* 1.17 mmol), K_2CO_3 (40 mg, 0.29 mmol), and Bu_4NI (23 mg, 0.062 mmol), stirred for 64 h, and suction-filtered over a *Celite*/sand bed (washing with AcOEt). Evaporation and FC (hexane/AcOEt 4:1) gave **45** (144 mg, 88%). Colourless oil. R_f (toluene/AcOEt 5:1) 0.60; (hexane/AcOEt 4:1) 0.27. $[\alpha]_D^{25} = -119.8$ ($c = 0.62$, $CHCl_3$). IR ($CHCl_3$): 3060*w*, 3000*w*, 3005*w*, 2975*w*, 2880*w*, 2115*s*, 1761*s*, 1495*m*, 1455*m*, 1400*m*, 1365*m*, 1090*s*, 1078*s*, 1048*s*, 1030*s*, 700*s*. ^{1}H-NMR (400 MHz, C_6D_6): see *Table 3*; additionally, 3.92 (*d*, $J = 15.0$), 4.68 (*d*, $J = 14.9$, PhCH_2N); 4.08, 4.48 (2*d*, $J = 11.4$, PhCH_2); 4.15, 4.20 (2*d*, $J = 12.0$, PhCH_2); 4.22, 4.36 (2*d*, $J = 11.8$, PhCH_2); 6.93–7.20 (*m*, 20 arom. H). ^{13}C-NMR (50 MHz, (D_6)acetone): see *Table 4*; additionally, 72.82, 73.59, 73.69 (3*t*, 3 Ph*C*H_2); 128.09–129.25 (several *d*); 137.08, 138.94, 139.07, 139.25 (4*s*). CI-MS (NH_3): 591 (7), 590 (17), 535 (9, $[M + 1 - N_2]^+$), 482 (13), 481 (36), 480 (100, $[M + 1 - N_3{-}CH{=}C{=}O]^+$), 427 (7), 373 (7), 372 (29, $[M - N_3{-}CH{=}C{=}O - BnO]^+$), 108 (18). Anal. calc. for $C_{34}H_{34}N_4O_4$ (562.67): C 72.58, H 6.09, N 9.96; found: C 72.37, H 5.94, N 9.88.

Dibenzyl (Trifluoromethanesulfonyloxy)methylphosphonate [39] (**46**). Under Ar, a soln. of dibenzyl (hydroxymethyl)phosphonate [39][107] (6.47 g, 22.13 mmol) in dry CH_2Cl_2 (60 ml) was cooled to $-78°$, treated with dry $^iPr_3N$ [108] (3.80 g, 26.55 mmol) and Tf_2O (4.17 ml, 25.45 mmol), stirred at $-70°$ for 30 min, and allowed to warm to $-25°$ over 120 min. The yellow soln. was poured into cold 5% aq. tartaric acid (50 ml). The org. phase was washed with 10% $NaHCO_3$ soln. (50 ml) and H_2O (50 ml). The aq. phases were extracted with CH_2Cl_2 (50 ml). The combined org. layers were dried ($MgSO_4$). Evaporation at $T \leq 20°$ gave an amber oil that was immediately purified by FC at $-20°$ (AcOEt/hexane 3:2) to yield **46** (6.76 g, 72%). Weakly yellowish oil, stable under Ar at $-25°$ for more than 8 weeks. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.47 (*d*, ^2J(H,P) = 8.9, irrad. at P → *s*, TfOCH_2); 5.09, 5.14 (2*dd*, *J* = 11.6, ^3J(H,P) = 9.6, irrad. at P → 2*d*, *J* = 11.6, 2 PhCH_2); 7.34–7.41 (*m*, 10 arom. H). ^{13}C-NMR (50 MHz, $CDCl_3$): 66.58 (*dt*, ^1J(C,P) = 168.7, TfO*C*H_2); 69.30 (*dt*, ^2J(C,P) = 6.4, 2 Ph*C*H_2); 128.30 (2*d*); 128.78 (4*d*); 129.04 (4*d*); 134.93 (*d*, ^3J(C,P) = 5.3, 2 arom. C).

*2-Azido-4,5,6-tri-*O*-benzyl-2,3-dideoxy-3-[[(dibenzyloxyphosphoryl)methyl]amino]-*D*-mannono-1,3-lactam* (**47**). Under Ar, a vigorously stirred soln. of **31a** (386 mg, 0.816 mmol) in dry 1,3-dimethylimidazolidin-2-one/THF 4:3 (14 ml) was treated with 3-Å molecular sieves, cooled to $-10°$, and treated with 97% NaH (40 mg, 1.63 mmol). The pink suspension, formed within 20 min, was treated with a soln. of 12-crown-4 (29 mg, 0.163 mmol) in dry THF (1 ml) and then dropwise with a soln. of dibenzyl (trifluoromethanesulfonyloxy)methylphosphonate (520 mg, 1.164 mmol) in dry THF (1.5 ml) within 30 min, upon which the colour of the suspension changed to orange. After complete addition, the mixture was cooled to $-30°$, and then allowed to warm to 0° within 120 min. The mixture was poured on sat. aq. NH_4Cl soln. (*ca.* 10 ml), diluted with brine (10 ml), and extracted with Et_2O (5 × 25 ml). The combined extracts were dried ($MgSO_4$) and evaporated. FC (hexane/AcOEt 1.75:1) of the yellow oil (900 mg) gave **47** (336 mg, 55%). Slightly yellowish oil. R_f (hexane/AcOEt 2:1) 0.20; (toluene/acetone 3:1) 0.56. $[\alpha]_D^{25} = -82.2$ (*c* = 1.01, $CHCl_3$). IR ($CHCl_3$): 3000*w*, 2930*w*, 2870*w*, 2115*s*, 1770*s*, 1500*m*, 1455*m*, 1400*w*, 1250*m*, 1100*s*, 1030*s*, 1010*s*, 1000*s*, 700*s*. ^{1}H-NMR (400 MHz, C_6D_6): see *Table 3*; additionally, 33.54 (*dd*, *J* = 16.0, ^2J(H,P) = 8.1, irrad. at P → *d*, *J* = 15.9, NCH); 3.95 (*dd*, *J* = 15.8, ^2J(H,P) = 14.3, irrad. at P → *d*, *J* = 15.9, NCH); 4.235 (*s*, PhCH_2); 4.25, 4.50 (2*d*, *J* = 11.4, PhCH_2); 4.41, 4.47 (2*d*, *J* = 11.8, PhCH_2); 4.90 (*d*, ^3J(H,P) = 8.1, irrad. at P → *s*, PhCH_2); 4.92 (*d*, ^3J(H,P) = 7.9, irrad. at P → *s*, PhCH_2); 6.99–7.28 (*m*, 25 arom. H). ^{13}C-NMR (50 MHz, (D_6)acetone): see *Table 4*; additionally, 68.03 (*dt*, ^2J(C,P) = 5.7, 2 Ph*C*H_2); 72.98, 73.42, 73.75 (3*t*, 3 Ph*C*H_2); 128.30–129.19 (several *d*); 137.34 (*d*, ^3J(C,P) = 4.9, 2 arom. C); 138.93, 139.24, 139.34 (3*s*). ^{31}P-NMR (81 MHz, $CDCl_3$): 22.60 (*s*). CI-MS (NH_3): 748 (11), 747 (21, $[M+1]^+$), 719 (9, $[M+1-N_2]^+$), 338 (11), 321 (11), 292 (18), 198 (9), 126 (16), 109 (8), 108 (100), 106 (45), 91 (14, Bn^+). Anal. calc. for $C_{42}H_{43}N_4O_7P \cdot 0.5\,H_2O$ (755.81): C 66.74, H 5.87, N 7.41, P 4.10; found: C 66.87, H 6.03, N 7.32, P 4.28.

*4,5,6-Tri-*O*-benzyl-2,3-dideoxy-3-[[(dibenzyloxyphosphoryl)methyl]amino]-2-(trifluoroacetamido)-*D*-mannono-1,3-lactam* (**48**). Under Ar, a soln. of **47** (508 mg, 0.68 mmol) in dry THF (8 ml) was treated with Ph_3P (250 mg, 0.95 mmol) and $(CF_3CO)_2O$ (0.152 ml, 1.09 mmol), stirred for 50 h, treated with **38** (181 mg, 1.22 mmol), stirred for 5 min, treated with H_2O (0.20 ml, 11.1 mmol), and stirred for 27 h. The suspension was diluted with AcOEt (20 ml) and filtered over a *Celite*/sand bed (washing with 3 × 20 ml of AcOEt). Evaporation of the yellowish filtrate and FC (hexane/AcOEt 7:4) gave **48** (495 mg, 89%). Colourless oil. R_f (hexane/AcOEt 7:4) 0.28. $[\alpha]_D^{25} = -21.2$ (*c* = 0.10, $CHCl_3$). IR ($CHCl_3$): 3410*w*, 3250*w* (br.), 3060*w*, 3040*w*, 3000*w*, 2960*w*, 2940*w*, 2870*w*, 1770*s*, 1728*s*, 1545*m*, 1500*m*, 1455*m*, 1390*m*, 1240*s*, 1170*m*, 1100*s*, 1027*s*, 1010*s*, 998*s*, 700*m*. ^{1}H-NMR (400 MHz, (D_6)acetone): see *Table 3*; additionally, 3.745 (*dd*, *J* = 15.9, ^2J(H,P) = 9.1), 3.91 (*dd*, *J* = 16.0, ^2J(H,P) = 13.6) (NCH_2); 4.47, 4.51 (2*d*, *J* = 12.1, PhCH_2); 4.66, 4.82 (2*d*, *J* = 11.1, PhCH_2); 4.71, 4.73 (2*d*, *J* = 12.5, PhCH_2); 4.92 (*dd*, *J* = 11.9, ^3J(H,P) = 8.3), 4.99 (*dd*, *J* = 11.9, ^3J(H,P) = 7.5) (PhCH_2); 4.96 (*d*, ^3J(H,P) = 7.8, PhCH_2); 7.24–7.38 (*m*, 25 arom. H); 9.45 (br. *d*, *J* = 8.3, NH). ^{1}H-NMR (400 MHz, (D_6)acetone/D_2O): 3.61 (*dd*, *J* = 5.5, 10.3, H–C(6)); 3.66 (*dd*, *J* = 5.5, 10.3, H′–C(6)); 3.75 (*dd*, *J* = 16.2, ^2J(H,P) = 9.0, irrad. at P → *d*, *J* = 16.2), 3.97 (*dd*, *J* = 16.2, ^2J(H,P) = 13.2, irrad. at P → *d*, *J* = 16.2) (CH_2N); 3.96 (*dt*, *J* = 3.0, 5.5, H–C(5)); 4.13 (*dd*, *J* = 3.0, 7.4, H–C(4)); 4.23 (*td*, *J* ≈ 2.5, 7.4, ^4J(H,P) ≈ 2.5, irrad. at P → *dd*, *J* = 2.5, 7.4, H–C(3)); 4.41, 4.45 (2*d*, *J* = 12.1, PhCH_2); 4.58, 4.75 (2*d*, *J* = 11.2, PhCH_2); 4.65, 4.68 (2*d*, *J* = 11.9, PhCH_2); 4.87 (*dd*, *J* = 11.8, ^3J(H,P) = 8.5, irrad. at P → *d*, *J* = 11.8), 4.935 (*dd*, *J* = 11.9, ^3J(H,P) = 7.5, irrad. at P → *d*, *J* ≈ 11.2, 2 H); 4.98 (*dd*, *J* = 11.9, ^3J(H,P) = 8.3, irrad. at P → *d*, *J* = 11.8) (2 PhCH_2); 5.02 (br. *s*, *J* ≈ 2.0, ^5J(H,P) ≈ 1, irrad. at P → *d*, *J* = 2.3, H–C(2)); 7.20–7.30 (*m*, 25 arom. H). ^{13}C-NMR (50 MHz, (D_6)acetone): see *Table 4*; additionally, 68.13, 68.20 (2*dt*, ^2J(C,P) = 5.9, 2 Ph*C*H_2); 73.13, 73.53, 73.69 (3*t*, 3 Ph*C*H_2); 128.24–129.21 (several *d*); 137.47 (*d*, ^3J(C,P) = 6.5, 2 arom. C); 139.14, 139.33, 139.52 (3*s*). ^{31}P-NMR (81 MHz, (D_6)acetone): 22.46 (*s*). CI-MS (NH_3): 834 (11, $[M+NH_4]^+$), 819 (14), 818 (50), 817 (100, $[M+1]^+$), 727 (9, $[M+2-Bn]^+$), 538 (9), 383 (8), 283 (8), 282 (37), 265 (25), 221 (7), 108 (24, $BnOH^+$), 106 (13). Anal. calc. for $C_{44}H_{44}F_3N_2O_8P \cdot H_2O$ (834.83): C 63.30, H 5.55, N 3.35; found: C 62.86, H 6.02, N 2.89 (partial decomposition during drying at high vacuum).

*Bis[triethylammonium] 2,3-Dideoxy-3-[(phosphonatomethyl)amino]-2-(trifluoroacetamido)-*D*-mannono-1,3-lactam* (**49**) *and Triethylammonium 2-Amino-2,3-dideoxy-3-[(phosphonatomethyl)amino]-*D*-mannono-1,3-lactam* (**50**). A suspension of 20% *Pearlman*'s catalyst (140 mg) in *t*-BuOH/0.1M $Et_3NH^+HCO_3^-$ 3:1 (10 ml) was hydrogenated, treated dropwise with a soln. of **48** (380 mg, 0.465 mmol) in *t*-BuOH/0.1M $Et_3NH^+HCO_3^-$ 3:1 (12 ml), vigorously stirred under 6.5 bar of H_2 for 90 h, treated with more catalyst (102 mg suspended in 3 ml of H_2O), stirred for 30 h, and diluted with H_2O (5 ml). After addition of *Celite* (*ca.* 200 mg), the suspension was centrifuged, the supernatant decanted, and the semi-solid residue was resuspended in H_2O (3×15 ml) and centrifuged again. The combined supernatants were lyophilized. The viscous residue was taken up in H_2O (*ca.* 10 ml), filtered over a pad of *RP18* silica gel, pressure-filtered over a 0.2-μm membrane filter (*Merck Anotop*), and lyophilized again. Prep. *RP18*-HPLC (0.1M $Et_3NH^+HCO_3^-$ adjusted to pH 7.3 with AcOH, 2% MeCN, flow: 8 ml/min, refract. detection) of the yellowish honey (382 mg) and lyophilization gave **50** · Et_3N (37 mg, 14%) and a mixture of **49** and incompletely debenzylated products (327 mg), which was converted to the phosphonic acid by elution over a cation exchange column (*Amberlite IR 120*, H^+ form). Repeated hydrogenation (262 mg of 20% *Pearlman*'s catalyst in 10 ml of *t*-BuOH/H_2O 1:1) and prep. *RP-18*-HPLC gave **49** (106 mg, 40%).

Data of **49**: Colourless, snowy solid. M.p. 135° (dec.; sinter point at 110°). Anal. *RP18*-HPLC: t_R (0.1M $Et_3NH^+HCO_3^-$ adjusted to pH 7.3 with AcOH, 2% MeCN, flow: 0.5 ml/min) 11.10 min. $[\alpha]_D^{25} = -38.2$ ($c = 0.98$, H_2O). IR (KBr): 3400*s* (br.), 3260*s* (br.), 3120*s* (sh), 2970*m*, 2930*s*, 2740*m*, 2670*s*, 2485*m*, 1748*s*, 1720*s*, 1565*m*, 1555*m*, 1470*m*, 1430*m*, 1395*m*, 1225*m*, 1185*m* (sh), 1165*s*, 1110*s* (br.), 1070*s* (br.), 1035*s*. ^{1}H-NMR (600 MHz, D_2O; assignment based on a ^{1}H/^{1}H-COSY spectrum): see *Table 3*; additionally, 1.28 (t, $J = 7.3$, 18 H, 2 ($MeCH_2$)$_3$N$^+$D); 3.20 (q, $J = 7.3$, 12 H, 2 (MeCH_2)$_3$N$^+$D); 3.38 (dd, $J = 15.1$, ^2J(H,P) = 9.5, irrad. at P → d, J = 15.4, NCH); 3.625 (dd, $J = 15.1$, ^2J(H,P) ≈ 11.5, irrad. at P → d, $J = 15.4$, NCH). ^{13}C-NMR (50 MHz, D_2O): see *Table 4*; additionally, 8.39 (q, 2 ($MeCH_2$)$_3$N$^+$D); 46.70 (t, 2 (MeCH_2)$_3$N$^+$D). ^{31}P-NMR (162 MHz, D_2O): 12.16 (s). Anal. calc. for $C_{21}H_{44}F_3N_4O_8P$ (568.57): C 44.36, H 7.80, N 9.85; found: C 44.11, H 8.09, N 9.68.

Data of **50** · 2 Et_3N: Anal. *RP18*-HPLC: t_R (0.1M $Et_3NH^+HCO_3^-$ adusted to pH 7.3 with AcOH, 2% MeCN, flow: 0.5 ml/min): 5.21 min. IR (KBr): 3380*s* (br.), 2970*s*, 2930*m*, 2750*m*, 2730*m*, 2680*s*, 2600*w*, 2490*w*, 1750*m*, 1630*m*, 1580*m*, 1470*m*, 1430*m*, 1395*m*, 1345*m*, 1220*m*, 1205*m* (sh), 1165*s*, 1070*s* (br.), 1035*s*, 970*m*. ^{1}H-NMR (600 MHz, D_2O; assignment based on a ^{1}H/^{1}H-COSY spectrum): see *Table 3*, additionally, 1.32 (t, $J = 7.3$, 27 H, 3 ($MeCH_2$)$_3$N$^+$D); 3.24 (q, $J = 7.3$, 18 H, 3 (MeCH_2)$_3$N$^+$D); 3.29 (dd, $J = 15.4$, ^2J(H,P) = 8.8, irrad. at P → d, J ≈ 15.0, NCH); 3.67–3.74 (m, irrad. at P → strong change, H–C(5), NCH). ^{13}C-NMR (D_2O, 50 MHz): see *Table 4*; additionally, 8.43 (q, 3 ($MeCH_2$)$_3$N$^+$D); 46.85 (t, 3 (MeCH_2)$_3$N$^+$D). ^{31}P-NMR (D_2O, 162 MHz): 11.44 (s). ESI-MS (H_2O/MeOH): 102 (100, Et_3NH^+).

Data of **50**: Et_3N was removed by drying a sample of **50** · 2 Et_3N for 3 d at 0.02 Torr. M.p. 145° (dec.). $[\alpha]_D^{25} = -40.2$ ($c = 0.30$, H_2O). Anal. calc. for $C_{13}H_{30}N_3O_7P \cdot 0.25\ H_2O$ (375.87): C 41.54, H 8.18, N 11.18; found: C 41.71, H 8.38, N 10.99.

*2-Azido-3-[(benzyloxycarbonyl)amino]-4,5,6-tri-*O*-benzyl-2,3-dideoxy-*D*-mannonamide* (**51**). A soln. of **31a** (320 mg, 0.68 mmol) in sat. NH_3 in dry MeOH (saturated at −5°, 20 ml, violet-coloured) was kept under Ar in a tightly sealed flask at 4° for 7 d. The slightly yellowish soln. was warmed to 20° and evaporated. The dried (20 h under high vacuum), crude 3-aminoacetamide (330 mg) was dissolved in dry EtOH (15 ml) under Ar, treated with 1-(benzyloxycarbonyl)benzotriazole (1-Z-Bt, 182 mg, 0.72 mmol)[10]), stirred at 23° for 24 h, treated with a second portion of 1-Z-Bt (178 mg, 0.70 mmol), stirred at 45° for 24 h, treated with a third portion of 1-Z-Bt (156 mg, 0.62 mmol), stirred at 55° for 3 h, treated with a fourth portion of 1-Z-Bt (168 mg, 0.663 mmol), and stirred at 55° for 44 h. The mixture was cooled to 20°, suction-filtered over a *Celite*/sand bed and the filtrate evaporated to dryness. The residue was taken up in Et_2O (75 ml) and washed with sat. aq. $NaHCO_3$ soln. (2×15 ml), brine (15 ml), and H_2O (15 ml). The combined aq. phases were washed back with Et_2O (10 ml). The combined org. phases were dried ($MgSO_4$) and evaporated. FC (hexane/AcOEt 1.5:1) of the resulting yellow oil gave **51** (390 mg, 92%). Colourless oil, solidifying to a microcrystalline solid upon drying in high vacuum. An anal. sample was obtained by HPLC (hexane/AcOEt 2:1). R_f (hexane/AcOEt 1:1) 0.48. M.p. 77–78° (AcOEt). $[\alpha]_D^{25} = +3.3$ ($c = 0.90$, $CHCl_3$). IR ($CHCl_3$): 3505*m*, 3420*m*, 3395*m*, 3350*w*, 3180*w*, 3060*w*, 3000*w*, 2876*w*, 2110*s*, 1720*s*, 1698*s*, 1500*s*, 1450*m*, 1310*m*, 1250*s*, 1085*s*, 695*s*. ^{1}H-NMR (400 MHz, C_6D_6): see *Table 3*; additionally, 4.04 (br. d, $J = 6.4$, irrad. at 3.63 → 4.035, br. s of H–C(4), → 4.04, d (J ≈ 6.4) of H–C(2), irrad. at 4.87 → 4.04, d (J ≈ 6.4), of H–C(4), → 4.045, s of H–C(2), H–C(2), H–C(4)); 4.28, 4.33 (2d, $J = 12.0$, PhCH_2); 4.43–4.58 (m, 2 PhCH_2); 5.02, 5.06 (2d, $J = 12.4$, PhCH_2); 5.88 (d, $J = 9.1$, NH–C(3)); 5.92, 6.13 (2 br.

[10]) In larger batches, *N*-[(benzyloxycarbonyl)oxy]succinimide in dry DMF gave faster reactions and higher yields.

s, NH_2); 7.02–7.22 (*m*, 18 arom. H); 7.26 (*d*, *J* = 7.3, 1 arom. H); 7.40 (*d*, *J* = 7.3, 1 arom. H). ^{13}C-NMR (125 MHz, C_6D_6; assignment based on a ^{1}H/^{13}C-COSY spectrum): see *Table 4*; additionally, 67.13 (*t*, Ph*C*H_2); 72.67, 73.41, 74.12 (3*t*, 3 Ph*C*H_2); 127.46–128.51 (several *d*); 136.87, 138.23, 138.46, 138.66 (4*s*); 156.78 (*s*, C=O). CI-MS (NH_3): 642 (18), 641 (46, $[M+NH_4]^+$), 624 (14, $[M+1]^+$), 598 (13), 597 (39), 596 (100, $[M+1-N_2]^+$), 517 (26), 516 (78, $[M-BnO]^+$), 490 (10), 489 (14), 488 (47, $[M-N_2-BnO]^+$). Anal. calc. for $C_{35}H_{37}N_5O_6$ (623.71): C 67.40, H 5.98, N 11.23; found: C 67.50, H 6.22, N 11.09.

*3-Amino-2-azido-6-*O*-[(*tert*-butyl)diphenylsilyl]-2,3-dideoxy-4,5-*O*-isopropylidene-*D*-mannonamide* (**52**) *and 3-[(Allyloxycarbonyl)amino]-2-azido-6-*O*-[(*tert*-butyl)diphenylsilyl]-2,3-dideoxy-4,5-*O*-isopropylidene-*D*-mannonamide* (**53**). A soln. of **42** (368 mg, 0.77 mmol) in sat. NH_3 in dry MeOH (saturated at −5°, 12 ml, violet coloured) was kept under Ar in a tightly sealed flask at 4° for 10 d. Evaporation and drying at high vacuum gave **52** (380 mg, yellowish oil). It was immediately dissolved in dry 3-dimethylimidazolidin-2-one (10 ml), cooled to −10°, treated with 1-(allyloxycarbonyl)benzotriazole (173 mg, 0.79 mmol), kept at 4° for 46 h, and poured into a 1:1 mixture of ice and solid $NaHCO_3$ (*ca.* 5 g). After extraction with Et_2O (5 × 30 ml), the combined org. phases were washed with brine (2 × 8 ml) and H_2O (5 ml), and dried (Na_2SO_4). Evaporation and FC (toluene/AcOEt 2:1) gave **53** as colourless oil (387 mg, 87%). An anal. sample was obtained by anal. HPLC (hexane/AcOEt 2:1).

Data of **52**: R_f (toluene/AcOEt 1:1) 0.18. IR ($CHCl_3$): 3515*w*, 3463*w*, 3400*w*, 3007*m*, 2933*m*, 2860*w*, 2116*s*, 1693*s*, 1572*m*, 1428*m*, 1383*m*, 1374*w*, 1258*m* (br.), 1113*s*, 1084*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): see *Table 3*; additionally, 1.07 (*s*, *t*-Bu); 1.35, 1.42 (2*s*, Me_2C); 2.2–2.4 (br. *s*, exchange with D_2O, NH_2); 5.57 (br. *s*, exchange with D_2O, NH_2); 7.27–7.46 (*m*, 6 arom. H); 7.64–7.70 (*m*, 4 arom. H).

Data of **53**: R_f (toluene/AcOEt 1:1) 0.51. M.p. 36°. $[\alpha]_D^{25} = -18.3$ (*c* = 1.02, $CHCl_3$). IR ($CHCl_3$): 3508*m*, 3440*m*, 3400*w*, 2990*m*, 2930*m*, 2890*m*, 2860*w*, 2115*s*, 1720*s*, 1700*s*, 1570*m*, 1500*s*, 1470*w*, 1430*m*, 1385*m*, 1375*m*, 1330*m*, 1250*s*, 1160*m*, 1112*s*, 1100*m*, 1050*s* (br.), 705*s*. ^{1}H-NMR (500 MHz, C_6D_6): see *Table 3*; additionally, 1.09 (*s*, 3 H), 1.25 (br. *s*, 12 H) (Me_3C, Me_2C); 4.38 (br. *dd*, *J* = 5.4, 13.7, 1 allyl. H); 4.53 (br. *dd*, *J* = 4.1, 13.5, 1 allyl. H); 4.96 (*dd*, *J* = 1.2, 10.5, 1 olef. H); 5.13 (br. *d*, *J* = 17.4, 1 olef. H); 5.55 (*d*, *J* = 8.5, NH–C(3)); 5.67–5.76 (*m*, 1 olef. H, NH); 5.90 (br. *s*, NH); 7.21–7.31 (*m*, 6 arom. H); 7.78–7.90 (*m*, 4 arom. H). ^{13}C-NMR (125 MHz, C_6D_6; assignment based on a ^{1}H/^{13}C-COSY spectrum): see *Table 4*; additionally, 20.54 (*s*, Me_3C); 24.29, 26.71 (2*q*, Me_2C); 27.17 (*q*, Me_3C); 65.97 (*t*, CH_2=CHCH_2); 108.80 (*s*, Me_2C); 117.46 (*t*, CH_2=CHCH_2); 128.13 (2*d*); 128.18 (2*d*); 130.08 (2*d*); 133.19 (*d*, CH_2=CHCH_2); 133.69, 133.75 (2*s*); 136.12 (2*d*); 136.18 (2*d*); 155.37 (*s*, C=O). CI-MS (NH_3): 601 (11), 600 (39), 599 (100, $[M+NH_4]^+$), 583 (11), 582 (29, $[M+1]^+$), 539 (15), 525 (19), 524 (59), 505 (11), 504 (39), 499 (11), 498 (34), 447 (10), 446 (38), 394 (12), 379 (40), 361 (15). Anal. calc. for $C_{29}H_{39}N_5O_6Si$ (581.74): C 59.87, H 6.76, N 12.04; found: C 60.09, H 6.82, N 11.82.

Thiobarbituric-Acid Assay [101]: See [103].

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